Extractives from the Meliaceae and Simaroubaceae of Madagascar

Extractives from the Meliaceae and Simaroubaceae of Madagascar

by

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In memoriam

Alan Hugh Coombes

19 October 1921 – 9 November 2001

PREFACE

The experimental work carried out in this thesis was carried out in the School of Pure and Applied Chemistry, University of Natal, South Africa, under the supervision of Professor D.A. Mulholland.

This study represents original work by the author and has not been submitted in any other form to another university. Where use has been made of the work of others, it has been duly acknowledged in the text.

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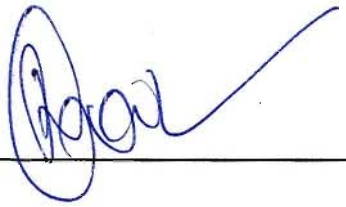

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The debt of gratitude that I owe Professor Dulcie Mulholland is as impossible to express as it is to repay (at a rough guess, about the same size as Argentina's). If I can pass on to students but a fraction of the interest, knowledge, enthusiasm, ability to inspire, and friendship that she has shown me in the past five years they will be well served.

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To Dr Philip Boshoff, for HRMS determinations.

And, as always, to the greatest of unsung heroes, Gill

Elen silá luménn omentielvo

LIST OF ABBREVIATIONS

Ac	acetate
Ang	angelate
brs	broad singlet
brm	broad multiplet
Bz	benzoate
c	concentration
d	doublet
dd	doublet of doublets
DMSO	dimethyl sulphoxide
dt	doublet of triplets
Glc	glucose
Hz	hertz
Me	methyl
m	multiplet
M.p.	melting point
ppm	parts per million
q	quartet
s	singlet
t	triplet
Tig	tiglate
tlc	thin layer chromatography
TMS	tetramethylsilane

^{1}H NMR spectroscopy	proton nuclear magnetic resonance spectroscopy
^{13}C NMR spectroscopy	carbon 13 nuclear magnetic resonance spectroscopy
COSY	correlated nuclear magnetic resonance spectroscopy
DEPT	distortionless enhancement by polarisation transfer
EIMS	electron impact mass spectroscopy
FABMS	fast atom bombardment mass spectroscopy
FTIR	Fourier transformed infrared spectroscopy
GC/MS	gas chromatography/mass spectroscopy
HETCOR	heteronuclear chemical shift correlation.
HMBC	heteronuclear multiple bond coherence.
HRMS	high resolution mass spectroscopy
HSQC	heteronuclear multiple quantum coherence
NOESY	nuclear Overhauser effect spectroscopy

LIST OF SCHEMES

Chapter 1		Page
Scheme 1:	Formation of the terpenoid precursors *iso*pentenyl pyrophosphate (IPP) **1-2** and dimethylallyl pyrophosphate (DMAPP) **1-3** from mevalonate **1-1**	1
Scheme 2:	Formation of the terpenoid precursors geranyl pyrophosphate (GPP) **1-4**, farnesyl pyrophosphate (FPP) **1-5** and geranylgeranyl pyrophosphate (GGPP) **1-6** from IPP **1-2** and DMAPP **1-3**	2
Scheme 3:	Formation of (*S*)-squalene-2,3-epoxide **1-10** from farnesylfarnesyl pyrophosphate (FFPP) **1-7**, *via* presqualene pyrophosphate **1-8**	3
Scheme 4:	Chair-boat-chair-boat cyclisation of (*S*)-squalene-2,3-epoxide **1-10** to form lanosterol **1-11** and cycloartenol **1-13** *via* the protosteryl carbocation **1-12**	4
Scheme 5:	Chair-chair-chair-boat cyclisation of (*S*)-squalene-2,3-epoxide **1-10** to form the C-20 epimeric dammarenediols **1-14**, or limonoid precursors euphol **1-16** and tirucalloll **1-17**	5
Scheme 6:	Formation of apo-euphol/tirucallol **1-43** from euphol **1-16** or tirucallol **1-17**, or Δ^7 isomers **1-44** or **1-45**	13
Scheme 7:	Oxidative rearrangement of butyrospermyl acetatel **1-46** to 7-ketoapo-euphol derivative **1-47**	13
Scheme 8:	Formation of apo-euphol/tirucallol **1-43** from the dammarenyl carbocation **1-15**	14
Scheme 9:	The apo rearrangement *via* the 7α,8α-epoxy intermediate **1-48**	14
Scheme 10:	The apo rearrangement of 7α,8α-epoxy methyl elemolate ester **1-49**	14
Scheme 11:	The apo rearrangement of the 7α,8α-epoxy melianotetraol triacetate **1-51**	15
Scheme 12:	Formation of the 13,18,14-cyclopropane ring in glabretal **1-53**	15
Scheme 13:	Sidechain oxidation and furan ring formation as proposed by Halsall *et al.*	17
Scheme 14:	*In vitro* conversion of turraeanthin **1-57** into **1-58** *via* intermediate **1-59**	18
Scheme 15:	Apo change conversion of limonoid **1-58** into **1-61** *via* 7α,8α-epoxy intermediate **1-60**	18
Scheme 16:	D ring lactone formation	20
Scheme 17:	Synthesis of andirobin **1-76** from 7-deacetoxy-7-oxokhivorin **1-77**	22
Scheme 18:	Synthesis of methyl angolensate **1-28** from 7-deacetoxy-7-oxokhivorin **1-77**	23
Scheme 19:	Synthesis of trijugin B ring by pinacol-pinacolone rearrangement	24
Scheme 20:	Biosynthesis of mexicanolide **1-79** *via* C-9,C-10 ring A rotation and C-2,C-30 Michael recyclisation	25
Scheme 21:	Laboratory synthesis of mexicanolide **1-79**	25
Scheme 22:	Biosynthesis of 3,30-diacetylphragmalin **1-84** from xyloccensin F **1-83**	27
Scheme 23:	Proposed biosynthesis of entilin A **1-33**	29
Scheme 24:	Biosynthesis of methyl ivorensate **1-90**	30
Scheme 25:	Laboratory synthesis of methyl ivorensate **1-90** from methyl angolensate **1-28**	30
Scheme 26:	Biosynthesis of limonin **1-25**	31

Scheme 27: Proposed biosynthesis of nimbin **1-94** 33
Scheme 28: Proposed biosynthesis of nimbin **1-94** 33
Scheme 29: Proposed biosynthesis of nimbin class limonoids heudebolin **1-97**, ohchinolide **1-98**, ohchinal **1-99** and salannin **1-100** 34
Scheme 30: Synthesis of toonacilin analogue **1-104** from toonafolin **1-102** 35
Scheme 31: Biosynthesis of evodulone **1-105** from azadiradione **1-64** 36
Scheme 32a: Proposed biosynthesis of carapolide precursor obacunyl acetate **1-126** from proceranone **1-125** *via* evodulone **1-105** 40
Scheme 32b: Proposed biosynthesis of carapolides from precursor obacunyl acetate **1-126** 41
Scheme 33: Relationships among limonoid classes 42
Scheme 34: Formation of the simarolide**1-131** C-ring lactone and C-17 ketone 49
Scheme 35: Loss of C-4 axial methyl group by *trans* elimination-decarboxylation 51
Scheme 36: Loss of C-4 equatorial methyl group by decarboxylation *via* a six membered transition state 52
Scheme 37: Cleavage of C-13, C-17 bond by retroaldol rearrangement 53
Scheme 38: Proposed biosynthesis of shinjulactone B **1-160** from ailanthone **1-161** 58
Scheme 39: Attempted *in vivo* conversion of ailanthone **1-161** into shinjulactone B **1-160** 59
Scheme 40: Proposed mechanism for formation of spirolactone sideproducts **1-164** and **1-165** during attempted *in vivo* conversion of ailanthone **1-161** into shinjulactone B **1-160** 59
Scheme 41: Formation of both *R* and *S* configurations by nucleophilic attack on cation at C-5 60
Scheme 42: Formation of sergeolide **1-179** by "Claisen-like" rearrangement of isobrucein B **1-178** 62
Scheme 43: Proposed biosynthesis of shinjudilactone **1-184** from ailanthone **1-161** *via* diketone **1-182** 62
Scheme 44: Laboratory synthesis of shinjulactone C **1-151** from ailanthone **1-161** *via* intermediate diketone **1-183** 63

LIST OF FIGURES

Chapter 1 **Page**

Figure 1: Subclassification of the C_{20} quassinoids by variations in the structure of the A ring 54
Figure 2: The five basic quassinoid skeletal 65
Figure 3: Subclassification of the C_{20} quassinoids by variations in the structure of the A ring 65

LIST OF TABLES

Chapter 1

Table 1:	The Meliaceae family	**7**
Table 2:	Limonoid and protolimonoid classification	**11**
Table 3:	The Simaroubaceae family	**45**

Chapter 2

Table 2.1:	^{1}H and ^{13}C NMR assignments for compounds **TS 1**, sericeanin A, and **TS 1a**	**93**

Chapter 3

Table 3.1:	Variation in $J_{9,11}$ and $J_{11,12}$ in relation to the nature of ring B, and of C-8 and C-14	**102**

Chapter 4

Table 4.1:	^{1}H and ^{13}C NMR assignments for compound **MA 1**, 1,3-diacetylvilasinin	**109**
Table 4.2:	^{1}H and ^{13}C NMR assignments for compound **MA 2**, 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin	**112**

Chapter 5

Table 5.1:	^{13}C NMR assignments for compound **SM 1**, 5α-stigmastan-3-one	**128**
Table 5.2:	^{1}H and ^{13}C NMR assignments for compound **SM 2**, samaderine B	**130**
Table 5.3:	^{1}H and ^{13}C NMR assignments for compound **SM 3**, samaderine E	**132**
Table 5.4:	^{1}H and ^{13}C NMR assignments for compound **SM 4**, brucein D	**134**
Table 5.5:	^{1}H and ^{13}C NMR assignments for compound **SM 5**, indaquassin X	**136**
Table 5.6:	^{1}H and ^{13}C NMR assignments for compound **SM 6**, 15-acetylbrucein D	**138**

Chapter 6

Table 6.1:	^{1}H and ^{13}C NMR assignments for compound **NL 1**, leandreanin A	**149**
Table 6.2:	^{1}H and ^{13}C NMR assignments for compound **NL 2**, leandreanin B	**156**
Table 6.3:	^{1}H and ^{13}C NMR assignments for compound **NL 3**, leandreanin C	**160**

Chapter 7

Table 7.1:	^{1}H and ^{13}C NMR assignments for compound **QP 1**, azadiradione	**169**
Table 7.2:	^{1}H and ^{13}C NMR assignments for compound **QP 2**, 6α-hydroxyazadiradione	**171**
Table 7.3:	^{1}H and ^{13}C NMR assignments for compound **QP 3**,7-deacetyl-7-angeloyl-6α-hydroxyazadiradione	**173**
Table 7.4:	^{1}H and ^{13}C NMR assignments for compound **QP 4**, quivisianthone	**180**
Table 7.5:	^{1}H and ^{13}C NMR assignments for compound **QP 5**, swietenolide	**184**
Table 7.6:	^{1}H and ^{13}C NMR assignments for compound **QP 6**, 2α-hydroxyswietenolide	**186**

Table 7.7:	^{1}H and ^{13}C NMR assignments for compound **QP 7**, proceranolide	**189**
Table 7.8:	^{1}H and ^{13}C NMR assignments for compound **QP 8,** 7-detigloyl-7-angeloyl-ruageanin B	**192**
Table 7.9:	^{1}H and ^{13}C NMR assignments for compound **QP 9**, quivisianolide A	**198**
Table 7.10:	^{1}H and ^{13}C NMR assignments for compound **QP 10**, quivisianolide B	**201**
Table 7.11:	^{1}H and ^{13}C NMR assignments for compound **QP 11**, quivisianone	**205**
Table 7.12:	^{1}H and ^{13}C NMR assignments for compound **QP 12**, melianone	**207**
Table 7.13:	^{1}H and ^{13}C NMR assignments for compound **QP 13**, melianol	**211**

ABSTRACT

This work describes the isolation and structural elucidation of extractives from four species of the Meliaceae and one of the Simaroubaceae families. All five species examined are endemic to the island of Madagascar.

One novel *seco*-ring A protolimonoid with a bourjotinolone A-type side-chain was isolated from *Turraea sericea*, while *Malleastrum antsingyense* yielded one known and one novel limonoid of the vilasinin group. *Neobeguea leandreana* was found to contain three novel limonoids of the phragmalin class, including a relatively rare 17-keto *seco*-ring D compound and one containing a oxidized C-19 methyl group. *Quivisia papinae* has afforded eight novel and five known protolimonoids and limonoids of the azadiradione, evodulone, and mexicanolide classes. Included among these are a mexicanolide group limonoid with a 17-keto *seco*-ring D, and two further mexicanolide limonoids containing a hitherto unreported 9α,11α-epoxide ring and a $\Delta^{9(11)}$-double bond.

One C_{19} and four C_{20} quassinoids, of which one is novel, together with a known but rare triterpenoid, were isolated from the Madagascan Simaroubaceae *Samadera madagascariensis*. These findings support the suggestion that this species is closely related to, if not synonymous with, the companion species *Samadera indica* and *Quassia indica*.

A literature survey on the effect of structural variations in ring B on coupling constants in 11,12-disubstituted havanensin-group limonoids was also undertaken, resulting in the observation of a remarkable correlation between ring structure and coupling constant values for a wide range of compounds isolated from different sources. An explanation for these observations is advanced.

TABLE OF CONTENTS

		Page
Preface		*iv*
Acknowledgements		*v*
List of Abbreviations		*vi*
List of Schemes		*vii*
List of Figures		*viii*
List of Tables		*ix*
Abstract		*xi*
Chapter 1		
1.1	Introduction	
1.1.1	Triterpenoids of plant origin	1
1.2	Limonoids and the Meliaceae Family	
1.2.1	The Meliaceae Family	6
1.2.2	Limonoids	7
1.2.3	The Biosynthesis and Classification of Limonoids	8
1.2.3.1	Class I: Protolimonoids	11
1.2.3.2	Class II: The Havanensin group	16
1.2.3.3	Class III: The Gedunin group	19
1.2.3.4	Class IV	21
1.2.3.4.1	Class IVa: The Andirobin group	22
1.2.3.4.2	Class IVb: The Trijugin group	23
1.2.3.4.3	Class IVc: The Mexicanolide group	24
1.2.3.4.4	Class IVd: The Phragmalin group	26
1.2.3.4.5	Class IVe: The Entilin group	28
1.2.3.5	Class V: The Methyl ivorensate group	29
1.2.3.6	Class VI: The Obacunol group	31
1.2.3.7	Class VII: The Nimbin group	32
1.2.3.8	Class VIII: The Toonafolin group	35
1.2.3.9	Class IX: The Evodulone group	35
1.2.3.10	Class X: The Prieurianin group	36
1.2.3.11	Class XI	38
1.2.3.11.1	Class XIa: The carapa spirolactone group	39
1.2.3.11.2	Class XIb: The carapolide group	39
1.2.4	The Biological Activity of Limonoids	43
1.3	Quassinoids and the Simaroubaceae Family	
1.3.1	The Simaroubaceae Family	45
1.3.2	Quassinoids	46

1.3.3 A Brief Historical Review of the Biosynthesis, Structural Elucidation, and Biological Activity of Quassinoids 47

1.4 References 73

Chapter 2 Extractives from *Turraea sericea*

2.1 Introduction 82

2.2 Extractives from *Turraea sericea*

2.2.1 Structural elucidation of compound **TS 1**, sericeanin A 89

2.3 Foreword to Experimental 94

2.4 Experimental 95

2.5 References 96

Chapter 3 The effect of the structure of ring B on variations in the coupling constants $J_{9,11}$ and $J_{11,12}$ in 11,12-disubstituted havanensin group limonoids: A literature survey and A revision of the stereochemistry at C-11 in turraflorins A-C from *Turraea floribunda*

3.1 Introduction 99

3.2 Results and Discussion 100

3.3 References 104

Chapter 4 Extractives from *Malleastrum antsingyense*

4.1 Introduction 105

4.2 Extractives from *Malleastrum antsingyense*

4.2.2 Structural elucidation of compound **MA 1**, 1,3-diacetylvilasinin 106

4.2.2 Structural elucidation of compound **MA 2**, 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin 110

4.3 Experimental 113

4.4 References 114

Chapter 5 Extractives from *Samadera madagascariensis*

5.1 Introduction

5.1.1 Preface 116

5.1.2 Literature Survey 117

5.2 Extractives from *Samadera madagascariensis*

5.2.1 Structural elucidation of compound **SM 1**, 5α-stigmastan-3-one 127

5.2.2 Structural elucidation of compound **SM 2**, samaderine B 128

5.2.3 Structural elucidation of compound **SM 3**, samaderine E 131

5.2.4 Structural elucidation of compound **SM 4**, brucein D 133
5.2.5 Structural elucidation of compound **SM 5**, indaquassin X 135
5.2.6 Structural elucidation of compound **SM 6**, 15-acetylbrucein D 137
5.3 Chemotaxonomic observations 138
5.4 Experimental 139
5.5 References 142

Chapter 6 Extractives from *Neobeguea leandreana*
6.1 Introduction 145
6.2 Extractives from *Neobeguea leandreana*
6.2.1 Structural elucidation of compound **NL 1**, leandreanin A 147
6.2.2 Structural elucidation of compound **NL 2**, leandreanin B 154
6.2.3 Structural elucidation of compound **NL 3**, leandreanin C 157
6.3 Experimental 161
6.4 References 163

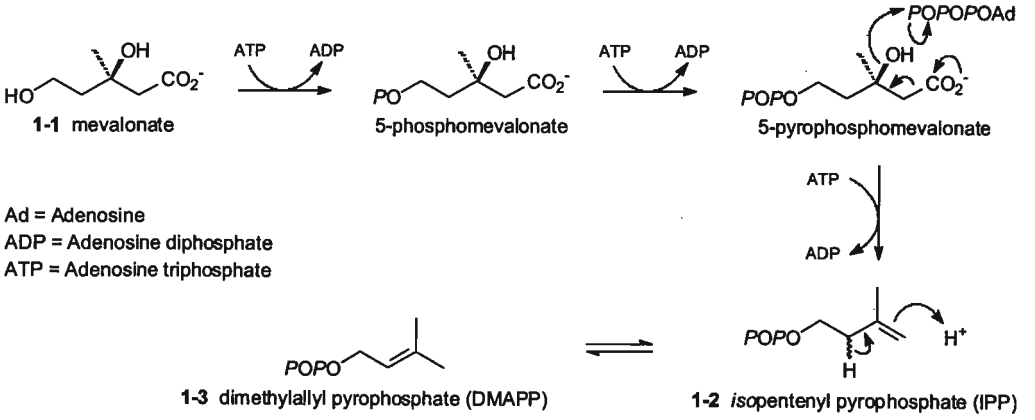
Chapter 7 Extractives from *Quivisia papinae*
7.1 Introduction 164
7.2 Extractives from *Quivisia papinae*
7.2.1 Structural elucidation of compound **QP 1**, azadiradione 165
7.2.2 Structural elucidation of compound **QP 2**, 6α-hydroxyazadiradione 169
7.2.3 Structural elucidation of compound **QP 3**, 7-deacetyl-7-angeloyl-6α-hydroxy-azadiradione 171
7.2.4 Structural elucidation of compound **QP 4**, quivisianthone 174
7.2.5 Structural elucidation of compound **QP 5**, swietenolide 181
7.2.6 Structural elucidation of compound **QP 6**, 2α-hydroxyswietenolide 185
7.2.7 Structural elucidation of compound **QP 7**, proceranolide 186
7.2.8 Structural elucidation of compound **QP 8**, 3-detigloyl-3-angeloyl-ruageanin B 190
7.2.9 Structural elucidation of compound **QP 9**, quivisianolide A 195
7.2.10 Structural elucidation of compound **QP 10**, quivisianolide B 199
7.2.11 Structural elucidation of compound **QP 11**, quivisianone 202
7.2.12 Structural elucidation of compound **QP 12**, melianone 205
7.2.13 Structural elucidation of compound **QP 13**, melianol 210
7.3 The chemotaxonomic significance of mexicanolide limonoids in the Quivisianthioideae 211
7.4 Experimental 212
7.5 References 218

Chapter 1

1.1 Introduction

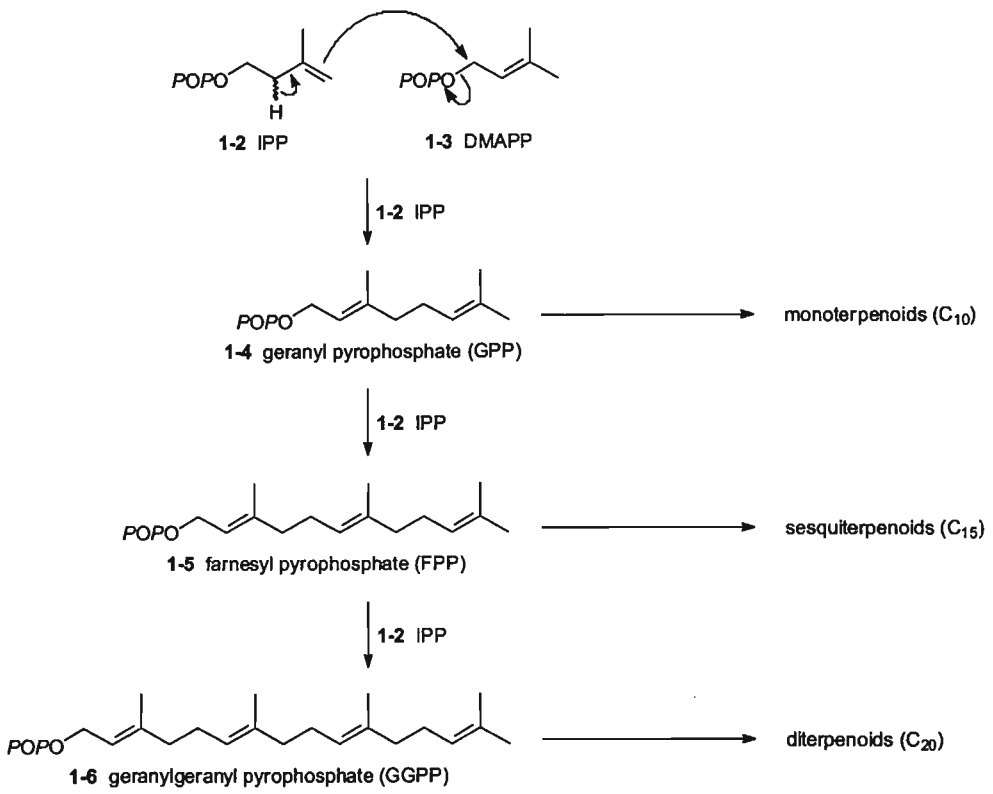
1.1.1 Triterpenoids of plant origin

The term terpenoid, or isoprenoid, is a generic one encompassing compounds derived from a common biosynthetic pathway initially involving mevalonate **1-1** as precursor [1], which undergoes a series of enzyme-catalysed phosphorylation reactions to yield *iso*pentenyl pyrophosphate (IPP) **1-2** and the isomeric dimethylallyl pyrophosphate (DMAPP) **1-3** (scheme 1) [2].



Scheme 1: Formation of the terpenoid precursors *iso*pentenyl pyrophosphate (IPP) **1-2** and dimethylallyl pyrophosphate (DMAPP) **1-3** from mevalonate **1-1** [2].

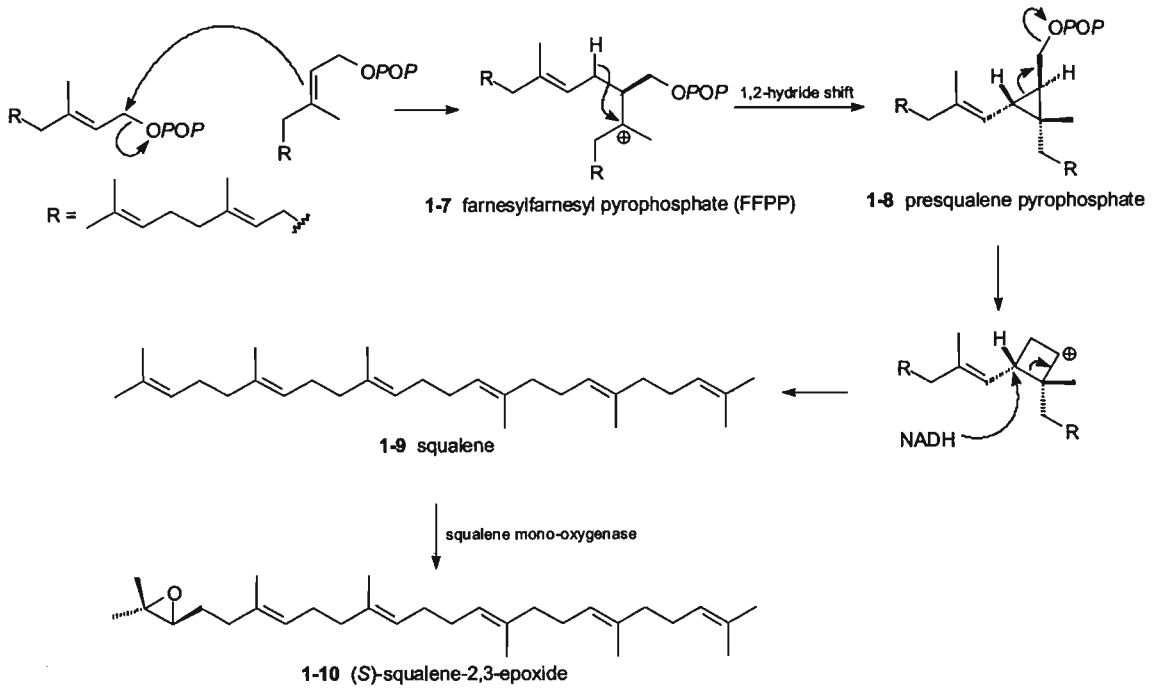
Enzyme-catalysed condensation of IPP **1-2** with DMAPP **1-3** leads successively to the polyprenyl pyrophosphates geranyl pyrophosphate (GPP) **1-4**, farnesyl pyrophosphate (FPP) **1-5**, and geranylgeranyl pyrophosphate (GGPP) **1-6**. GPP **1-4**, FPP **1-5** and GGPP **1-6** are the precursors for terpenoids with C_{10}, C_{15} and C_{20} skeleta, which are known as monoterpenoids, sesquiterpenoids and diterpenoids, respectively (scheme 2).



Scheme 2: Formation of the terpenoid precursors geranyl pyrophosphate (GPP) **1-4**, farnesyl pyrophosphate (FPP) **1-5** and geranylgeranyl pyrophosphate (GGPP) **1-6** from IPP **1-2** and DMAPP **1-3** [2].

Dimerisation of two FPP **1-6** molecules produces farnesylfarnesyl pyrophosphate (FFPP) **1-7**, which subsequently undergoes a 1,2-hydride shift to give presqualene pyrophosphate **1-8**. Further reaction of **1-8** with nicotinamide adenine dinucleotide (NADH) produces squalene **1-9**, which then undergoes enzymatic oxidation to give (*S*)-squalene-2,3-epoxide **1-10** (scheme 3). Cyclisation of (*S*)-squalene-2,3-epoxide **1-10** leads to compounds with C_{30} skeleta, which are known as triterpenoids.

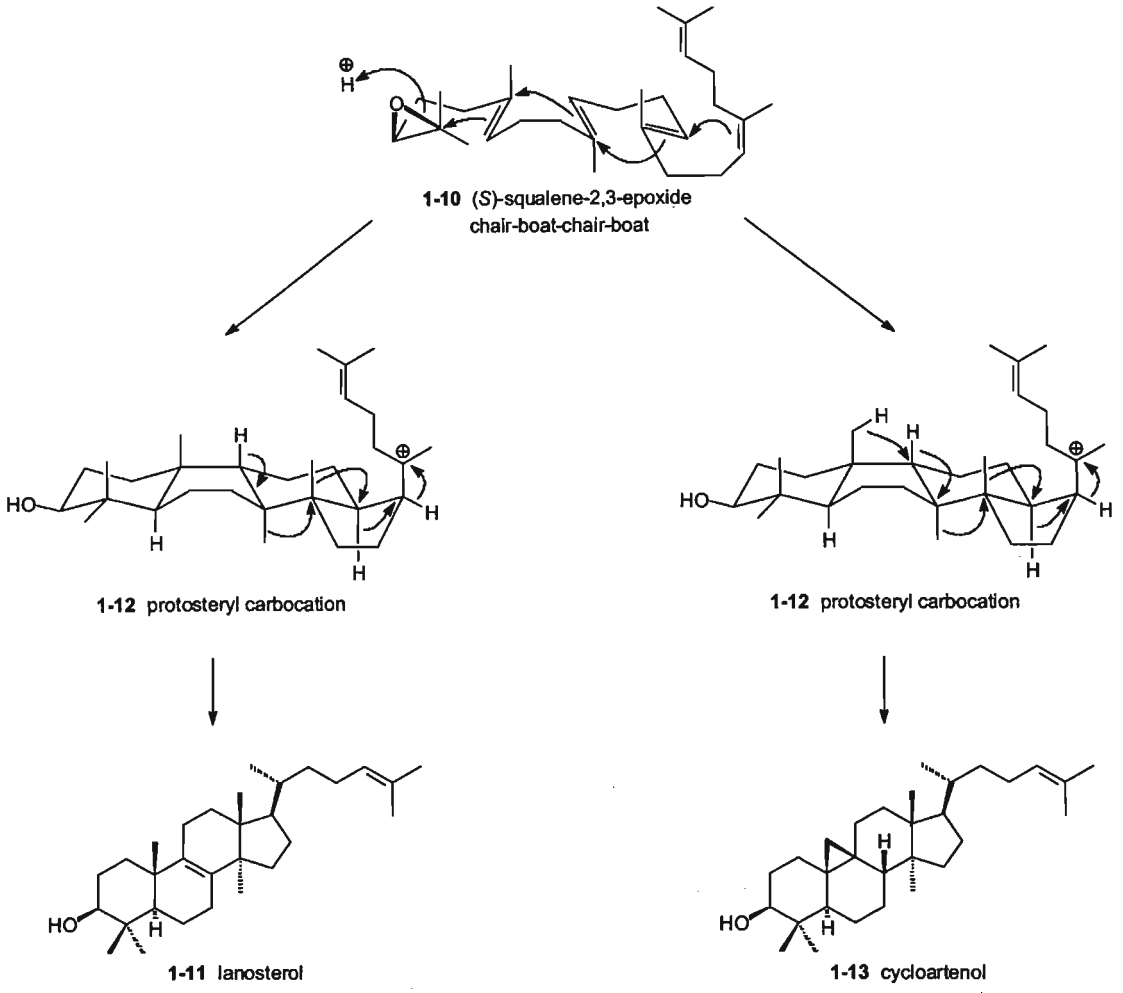
The triterpenoids form a large group of naturally-occurring compounds which are widely distributed as secondary metabolites throughout the plant kingdom. A smaller group, which includes lanosterol **1-11** from wool fat [3,4,5], is of animal origin.



Scheme 3: Formation of (*S*)-squalene-2,3-epoxide **1-10** from farnesylfarnesyl pyrophosphate (FFPP) **1-7**, *via* presqualene pyrophosphate **1-8** [2].

The vast array of different structural skeleta encountered within the triterpenoids arise as a consequence of the fact that (*S*)-squalene-2,3-epoxide **1-10** can adopt a multitude of different conformations on an enzyme surface prior to cyclisation [6,7], with Wagner-Meerwein 1,2-hydride shifts and/or the formation of different cationic intermediates at various stages in the process also playing a role [8].

Cyclisation of (*S*)-squalene-2,3-epoxide **1-10** in the chair-boat-chair-boat conformation leads to the formation of the protosteryl carbocation **1-12**, from which H-9 is either lost, forming lanosterol **1-11**, or in which H-9 migrates to C-8, initiating formation of the 9,10 cyclopropane ring which characterises cycloartenol **1-13** (scheme 4) [9].

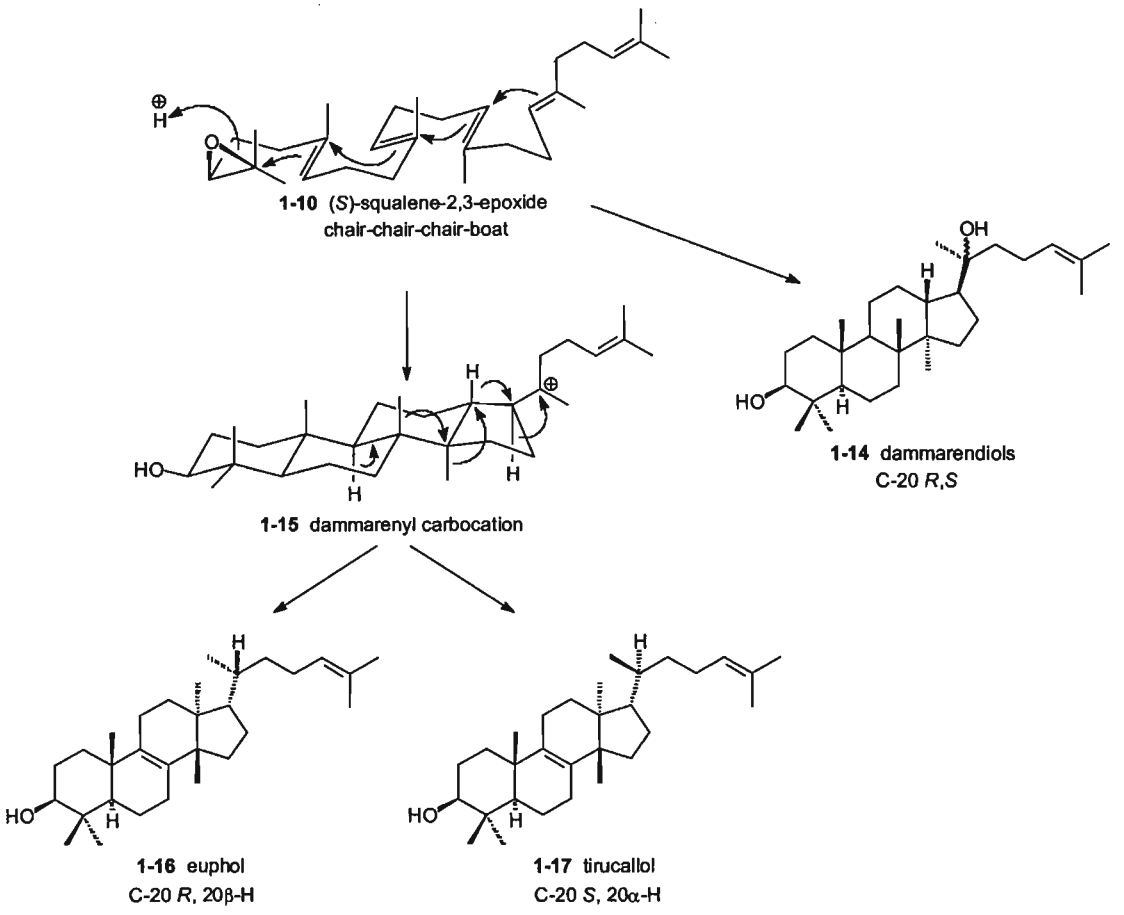


Scheme 4: Chair-boat-chair-boat cyclisation of (*S*)-squalene-2,3-epoxide **1-10** to form lanosterol **1-11** and cycloartenol **1-13** *via* the protosteryl carbocation **1-12** [9].

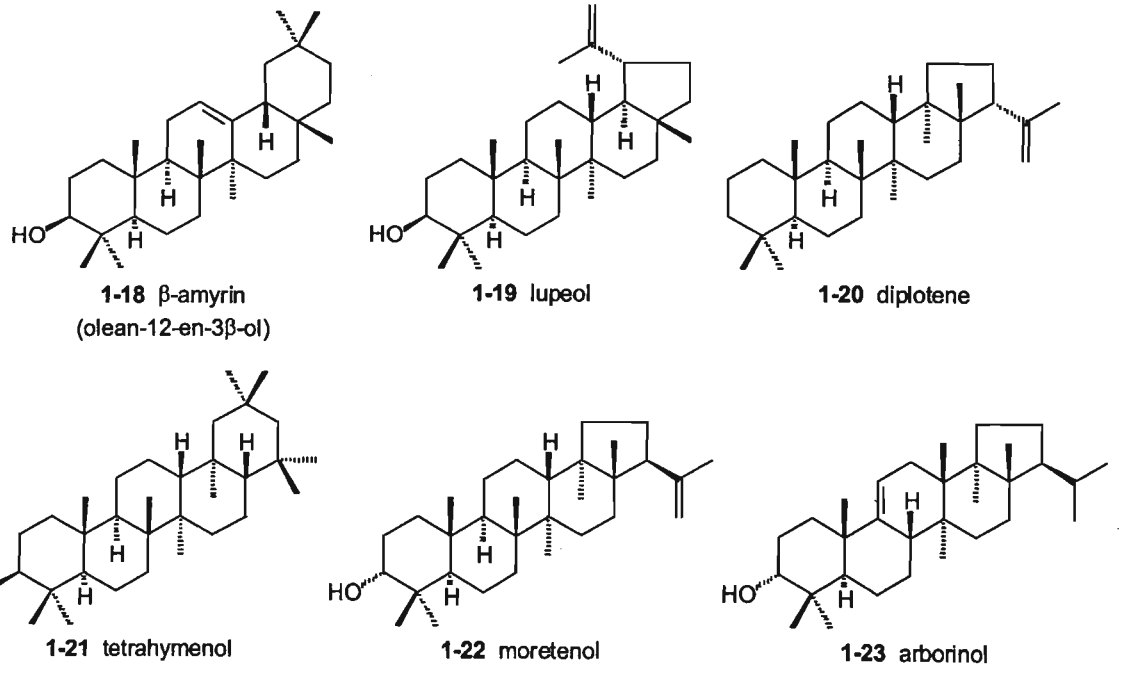
Cyclisation of (*S*)-squalene-2,3-epoxide **1-10** in the chair-chair-chair-boat conformation leads to the formation of the epimeric C-20 dammarendiols **1-14** *via* the dammarenyl carbocation **1-15**, which can alternatively undergo a series of methyl migrations and 1,2-hydride shifts to form the C-20 epimers euphol **1-16** and tirucallol **1-17** (scheme 5). These latter compounds, which differ only in their stereochemistry at C-20, play an important role in limonoid biosynthesis and will be discussed more fully later in this chapter[†].

---

† Cyclisation of (*S*)-squalene-2,3-epoxide **1-10** *via* other conformations is also possible, and a number of skeletal types arising from those conformations already discussed have been omitted for clarity. Thus chair-chair-chair-boat cyclisation leads also to pentacyclic triterpenoids such as β-amyrin **1-18** and lupeol **1-19**, while the all-chair conformation produces compounds such as diplotene **1-20** and tetrahymanol **1-21** [10], the chair-chair-chair-chair-boat conformation affords moretenol **1-22** [11], and the chair-boat-chair-chair-boat conformation gives arborinol **1-23** [12].



Scheme 5: Chair-chair-chair-boat cyclisation of (*S*)-squalene-2,3-epoxide **1-10** to form the C-20 epimeric dammarenediols **1-14**, or limonoid precursors euphol **1-16** and tirucalloll **1-17** [9].



1.2 Limonoids and the Meliaceae Family

1.2.1 The Meliaceae Family

The Meliaceae, or Mahogany Family, is a medium-sized pantropic family of some five hundred and fifty species in fifty-one genera. It is well known for its timber trees such as the West Indian Mahogany *Swietenia mahogani*, and the tropical African species *Khaya senegalensis* (African Mahogany) and *Khaya nyasica* (Red Mahogany). In Southern Africa, the Mountain Mahogany, *Entandrophragma caudatum,* is known for its timber, while the ubiquitous Syringa (Chinaberry), *Melia azedarach,* introduced from India, is an invasive alien characterised by its particularly poisonous fruit.

The name Meliaceae was first used by Ventenat in 1799 [13] to describe a family comprising only eight genera, although a decade earlier de Jussieu had placed sixteen genera into a family he called the Melieae [14]. Only ten of these now remain within the Meliaceae, while six of Ventenat's are still included. A number of subsequent studies have appeared, with A. de Jussieu (~1830) [15], Hooker (1862) [16], de Candolle (1878) [17] and Harms [18,19] all making considerable contributions.

The current circumscription is that of Pennington and Styles, who have divided the Meliaceae into four subfamilies, as shown in Table 1, on the basis of pollen morphology and other botanical characteristics [20]. Some forty species in seven genera are endemic to Madagascar and the adjacent islands of the Indian Ocean, while two subfamilies, the Capuronianthoideae and the Quivisianthoideae, each contain only one species confined to Madagascar alone; the sole member of the latter subfamily is one of the species investigated in this study.

Species of the Meliaceae produce a wide range of compounds, including flavonoids, chromones, coumarins, benzofurans, and mono-, sesqui- and diterpenoids. Sterols of the pregnane and stigmastane classes and dammarane, lupane, oleanane and squalane triterpenoids are common, but alkaloids are rare. Species of the Meliaceae are characterised, however, by the production of a group of tetranortriterpenoid compounds known as limonoids, which are discussed further in the following section.

TABLE 1: The Meliaceae family

(Numbers in brackets indicate number of species in genus [20]; genera given in bold type occur in Southern and Eastern Africa and Madagascar)

SUBFAMILY 1	Meliodeae
Tribe	**Genus**
1. Turraeeae	*Munronia(10), Naregamia(2),* ***Turraea(65), Humbertioturraea(3-4), Calodecaryia(1-2), Nymania(1)***
2. Melieae	***Melia(~5)****, Azadirachta(2)*
3. Vavaeeae	*Vavaeeae(4)*
4. Trichilieae	***Trichilia(~66), Pseudobersama(1),*** *Pterorhachis(1-2), Walsura(7),* ***Lepidotrichilia(4), Malleastrum(12), Ekebergia(4), Astrotrichilia(14),*** *Owenia(6), Cipadessa(1-2)*
5. Aglaieae	*Aglaia(~100), Lansium(1-5), Aphanamixis(4), Reinwardtiodendron(4-5), Sphaerosacme(1)*
6. Guareeae	*Heckeldora(1), Cabralea(6), Ruagea(6),* ***Turraeanthus(3), Guarea(35),*** *Chisocheton(30), Megaphyllaea(1-2), Synoum(1-2), Anthocarapa(2-3), Pseudocarapa(3), Dysoxylum(60)*
7. Sandoriceae	*Sandoricum(3-5)*
SUBFAMILY 2	Quivisianthoideae
	Quivisianthe(1)
SUBFAMILY 3	Capuronianthoideae
	Capuronianthus(1)
SUBFAMILY 4	Swietenioideae
1. Cedreleae	*Cedrela(5), Toona(6)*
2. Swietenieae	***Khaya(7), Neobeguea(3),*** *Soymida(1),* ***Entandrophragma(11),*** *Chukrasia(1-2)* ***Pseudocedrela(1),*** *Schmardaea(1), Swietenia(3),* ***Lovoa(2)***
3. Xylocarpeae	***Carapa(3-4), Xylocarpus(2-3)***

1.2.2 Limonoids

Studies on species of the Meliaceae, Rutaceae and Cneoraceae families in the past four decades have yielded a unique group of tetranortriterpenoid substances characteristic of these families. They have also been reported from the genus *Harrisonia*, from another family within the order Rutales, the Simaroubaceae. *Harrisonia* is the only genus within the Simaroubaceae to produce limonoids and its position within that family, no doubt prompted in part by this observation, is currently the subject of some debate†.

Although the quantities of some limonoids present are quite often absurdly large – the timber of some species may contain up to 1% of a single component, so that a single large tree can yield more than 100kg of a particular limonoid [22], the co-occurrence of mixtures of different esters of the same

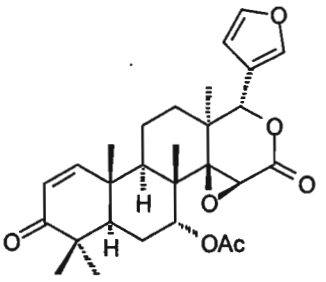
† "Quassinoids have only been found in the Simaroubaceae, which as a family is free of limonoids except for the seemingly aberrant genus *Harrisonia*, which alone among genera traditionally assigned to the Simaroubaceae produces limonoids, but not quassinoids. Recent studies of DNA profiles support the contention that *Harrisonia* is not a typical Simaroubaceae (Morton, C., unpublished)." [21].

limonoid very often renders their separation difficult, with isomerisation and interconversion of esters during isolation further complicating matters.

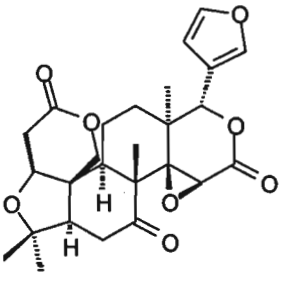
These problems notwithstanding, a very large number of limonoids have been isolated and characterised. A recent review on the Meliaceae of Southern and Eastern Africa and Madagascar listed over two hundred compounds isolated from species of this region alone [23], while the Dictionary of Natural Products has over seven hundred entries.

1.2.3 The Biosynthesis and Classification of Limonoids

The limonoid chemistry of the Meliaceae began with the isolation of gedunin **1-24** from the West African timber tree *Entandrophragma angolense* (Welw.) C.DC. [24], although a complete structural elucidation did not appear [25] until after that of limonin **1-25** from the genus *Citrus*, the first limonoid to be characterised [26,27,28] and from which the name of this group of compounds is derived†.



1-24 gedunin



1-25 limonin

A limonoid may be defined as a tetranortriterpenoid with a β-substituted furanyl ring attached to a twenty-two carbon nucleus at C-17α. The nature of the nucleus may vary considerably, ranging from simple tetracyclic structures with all four rings intact, as in azadirone **1-26**, through successively more complex structures in which one or more of the rings has been opened and/or oxidised, such as obacunol **1-27**, methyl angolensate **1-28** and prieurianin **1-29**, to those such as phragmalin **1-30**, voamatin C **1-31**, carapolide B **1-32**, entilin A **1-33** and khayalactone **1-34**, in which rearrangement of the triterpenoid nucleus has rendered the original tetracyclic skeleton almost unrecognisable.

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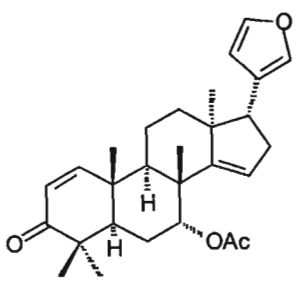
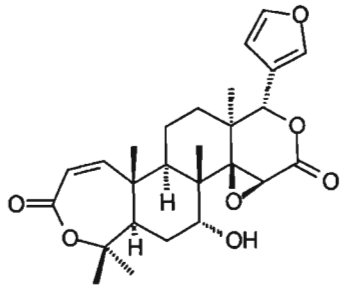
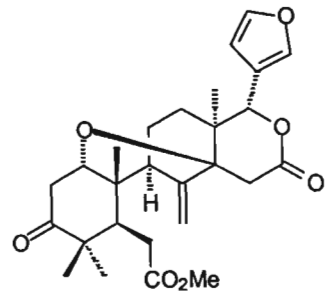
† This structural elucidation occupied the minds of three research groups, including two future Nobel Laureates (D.H.R.Barton and E.J.Corey) for over four years; the three publications quoted run to some 60 pages. In contrast, in a recent isolation in this laboratory [29] the structure is dismissed (with foreknowledge, admittedly, but also with the aid of the battery of modern ^{1}H and ^{13}C NMR techniques currently available) within one single page.



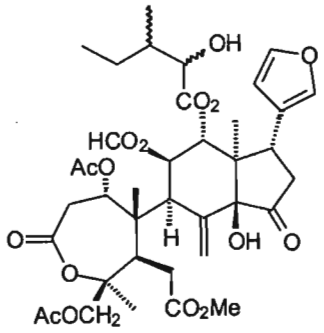
1-26 azadirone



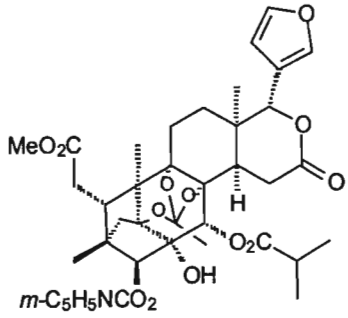
1-27 obacunol



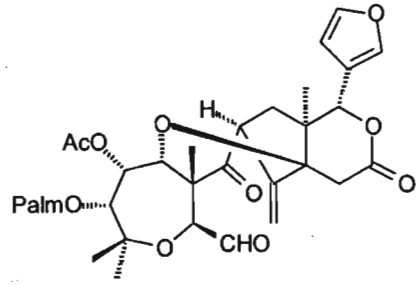
1-28 methyl angolensate



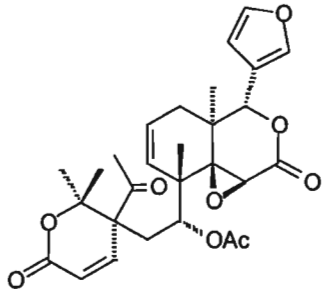
1-29 prieurianin



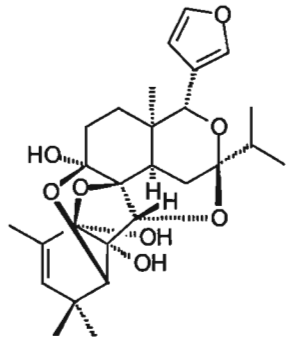
1-30 phragmalin



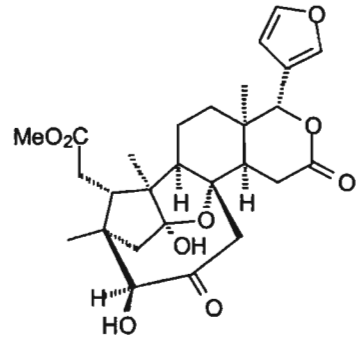
1-31 voamatin C



1-32 carapolide B



1-33 entilin A



1-34 khayalactone

Although it is apparent that the more complex limonoids must be obtained from simpler ones *via* a series of (ep)oxidations, ring opening/lactonisation reactions, and rearrangements, the use of radioactively labelled precursors normally employed in the study of biosynthetic pathways in living systems is precluded, simply, by the size of the tree species involved[†]. Elucidation of these pathways has developed primarily by the isolation and characterisation of as many limonoids as possible, and the verification of such biosynthetic relationships as are suggested by their structures by synthesis *in vitro*. These efforts have met with varying degrees of success, but sufficient laboratory evidence has been accumulated to produce a generally accepted overall description of the processes involved.

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† Radioactive tracer studies have, however, been successfully carried out in research into the biosynthesis of *Citrus* limonoids [30], and in studies on the quassinoids, which are discussed more fully in the following section.

Classification of the known limonoids was originally based on the extent of modification of the four carbocyclic rings [22], with ten of the sixteen possible groups known at that time[†]. The term modification[‡] was used here in a specific sense, in that "ring opening", both by bond cleavage to form *seco*-compounds and by Baeyer-Villiger peroxidation of ketones to lactones, were considered as modifications, while double bond epoxidations, epoxide reductions, and any other reaction not resulting in a change in the triterpenoid skeleton were excluded[§].

This original classification has recently been revised to include groups arising from molecular rearrangements in addition to the previously considered ring opening reactions. Including the protolimonoids, and although four have been added, the classes now number eleven, as two additional subgroups have been added to group IV, and the remaining two together form class XI (Table 2).

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† Taylor included the protolimonoids, which are limonoid precursors in which the furan ring has not yet fully formed, in his discussion, giving a total of sixteen groups in all.

‡ The expression "oxidation" used by Taylor is even more confusing.

§ He remarks:

> "It has been suggested that 12-ketones in which ring D is a lactone...are unstable and give rise to the quassinoids. If this is correct, this would cut the number of possible groups down to thirteen..."

If the requirements for this exclusion are that ring C be left unchanged to carry the 12-ketone and that ring D has undergone expansion to the lactone, this would surely imply that *four* groups should be excluded (D only , A and D, B and D, and A, B and D). In addition, examples of compounds from all four of these groups had been characterised at this time, with those with ring D lactonised only and those in which rings B and D had been oxidised among the most plentiful, while Taylor himself notes that:

> "Those which are missing are the ones in which rings A,C; B,C; and A,B,C, are oxidised."

This argument is apparently based (the reference quoted [31] is not explicit) on a laboratory synthesis [32], again quoted without reference, in which gedunin, rather than the 12-oxo derivative, is reported to undergo an apparent retro-aldol reaction on treatment with base.

TABLE 2: Limonoid and protolimonoid classification [22,23]

(new groups added in bold)

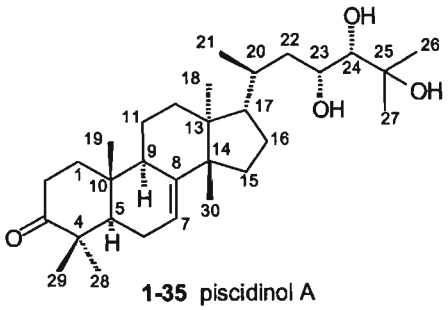
Class	Group	Ex*	Sidechain	Ring A	Ring B	Ring C	Ring D
I	Protolimonoids		Intact	Usually intact	Intact	Intact	Intact
	Ia Δ^7	37					
	Ib Δ^{14}	40					
II	Havanensin	56	Furan	Intact	Intact	Intact	Intact
III	Gedunin	24	Furan	Intact	Intact	Intact	Lactone
IVa	Andirobin	76	Furan	Intact	Open	Intact	Lactone
IVb	**Trijugin**	**78**	**Furan**	**Intact**	**Open**	**Contracted**	**Lactone**
IVc	Mexicanolide	79	Furan	Intact	Opened and recyclised	Intact	Lactone
IVd	Phragmalin	30	Furan	Intact	Opened and recyclised with 4,29,1 bridge	Intact	Lactone
IVe	**Entilin**	**33**	**Furan**	**Modified**	**Cleavage of C-9,C-10 bond**	**Intact**	**Lactone**
V	Methyl ivorensate	90	Furan	Open or Lactone	Open	Intact	Lactone
VI	Obacunol	27	Furan	Open or Lactone	Intact	Intact	Lactone
VII	Nimbin	94	Furan	Intact	Intact	Open	Intact
VIII	Toonafolin	102	Furan	Intact	Open or Lactone	Intact	Intact
IX	Evodulone	105	Furan	Open or Lactone	Intact	Intact	Intact
X	Prieurianin	29	Furan	Open or Lactone	Open	Intact	Intact
XIa	**Carapa spirolactone**	**118**	**Furan**	**Contracted**	**Intact**	**Intact**	**Intact**
XIb	**Carapolide**	**32**	**Furan**	**Contracted**	**Cleavage of C-9,C-10 bond**	**Intact**	**Lactone**

*: numbers refer to example structures in the text and in scheme 33, p.42.

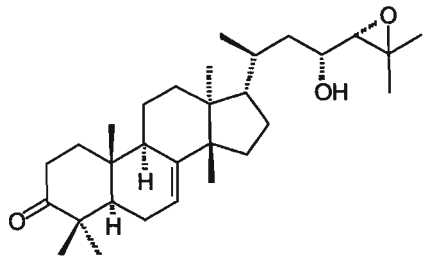
1.2.3.1 Class I: Protolimonoids

Protolimonoids, as their name suggests, are formally considered to be the biosynthetic precursors of the limonoids [22]. In these compounds the eight membered sidechain remains intact, although it is often highly oxygenated, and is often cyclised to form a five, six, or seven-membered ether ring.

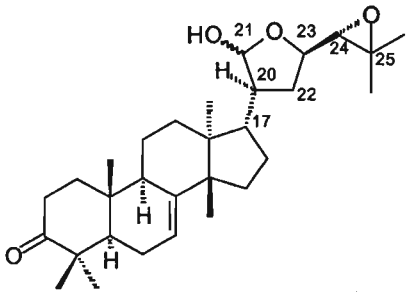
The protolimonoids can be divided into two classes. The first, of which piscidinol A **1-35** [33,34], niloticin **1-36** [33,35], melianone **1-37** [36], sapelin A **1-38** [37,38] and sapelin B **1-39** [38] are examples, has a Δ^7-double bond and a methyl group at C-14β, while the second group, represented by the corresponding chisocheton A **1-40** [39], sapelin C **1-41** [40] and sapelin E **1-42** has a Δ^{14}-double bond, a methyl group at C-8β, and are oxygenated at C-7α.



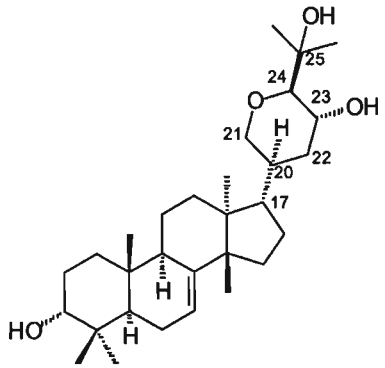
1-35 piscidinol A



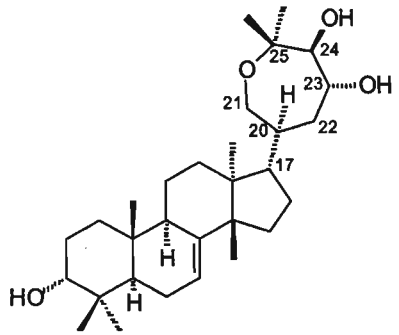
1-36 niloticin



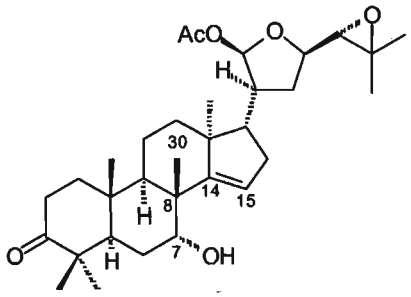
1-37 melianone



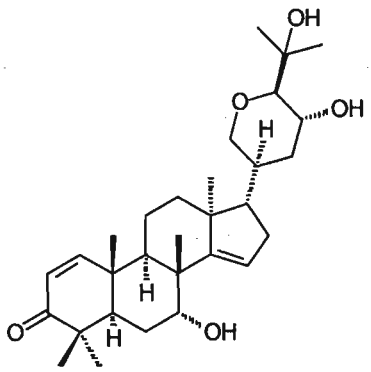
1-38 sapelin A



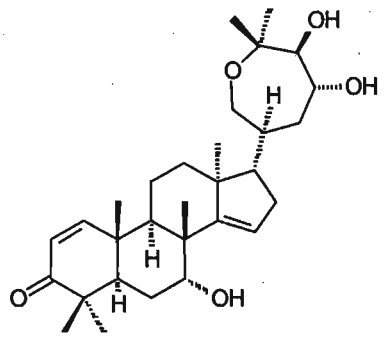
1-39 sapelin B



1-40 chisocheton A



1-41 sapelin C

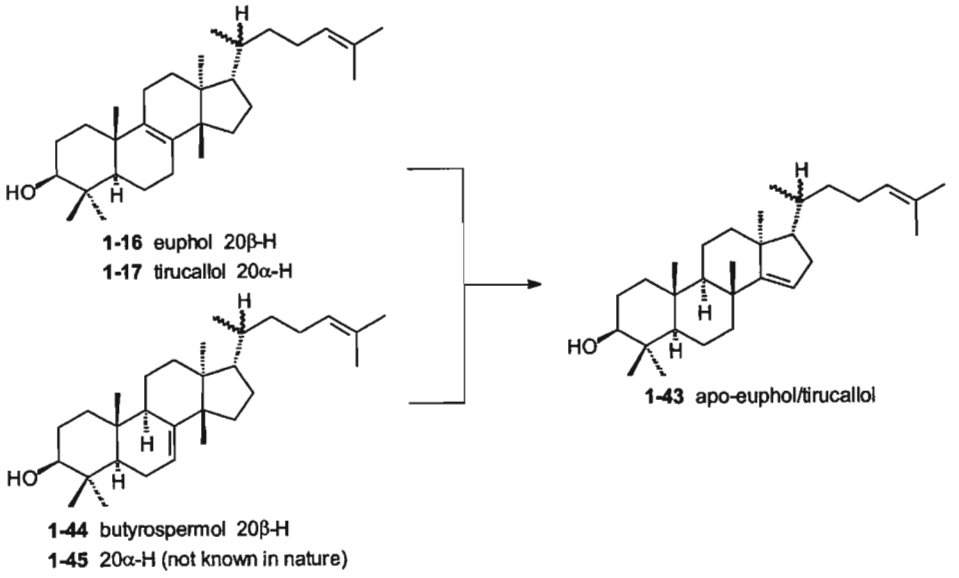


1-42 sapelin E

The isolation of limonin led Barton *et al.* [26] to suggest that limonoids were derived from a compound having the so-called apo-structure **1-43**, which was in turn derived either:

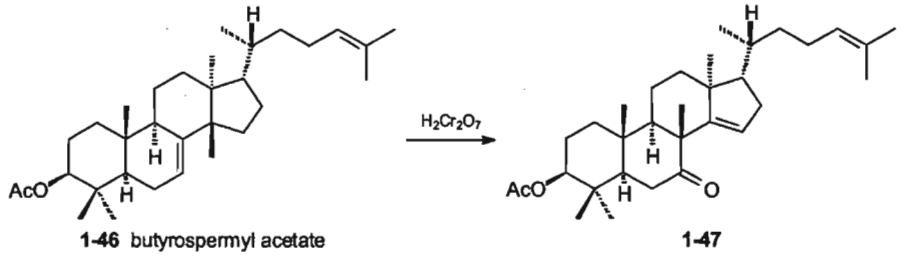
a) from either euphol **1-16** or tirucallol **1-17** *via* the apo rearrangement, initiated by nucleophilic attack on the Δ^8-double bond, and involving migration of the C-14β methyl group to C-8β and subsequent formation of the $\Delta^{14\text{-double}}$ bond, or

b) from butyrospermol **1-44**, the Δ^7 isomer of euphol, or the hypothetical tirucallol equivalent [41,42] **1-45** (scheme 6)



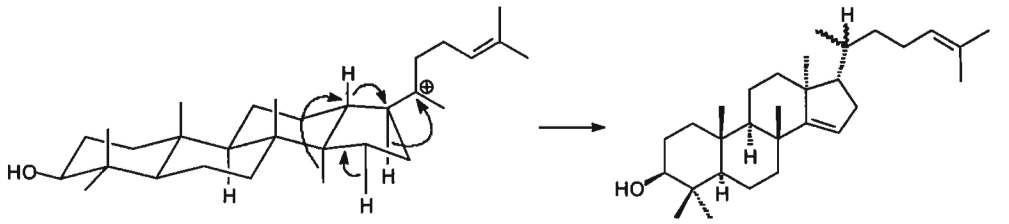
Scheme 6: Formation of apo-euphol/tirucallol **1-43** from euphol **1-16** or tirucallol **1-17**, or Δ^7 isomers **1-44** or **1-45** [26].

Spring *et al.* have shown that such an oxidative rearrangement is possible by oxidising dihydrobutyrospermyl acetate (euph-7-en-3β-yl acetate) **1-46** to the corresponding 7-keto-apo-euphol derivative **1-47** with chromic acid [43] (scheme 7).



Scheme 7: Oxidative rearrangement of butyrospermyl acetatel **1-46** to 7-ketoapo-euphol derivative **1-47** [43].

The proposal that the apo-euphol/tirucallol epimer might arise directly from squalene **1-10** *via* the dammarenyl carbocation **1-15** has also been advanced, in a mechanism in which loss of H-15 accompanies migration of the methyl group from C-14α to C-13β rather than the customary loss of H-9 and methyl migration from C-8β to C-13β [41,44] (scheme 8).

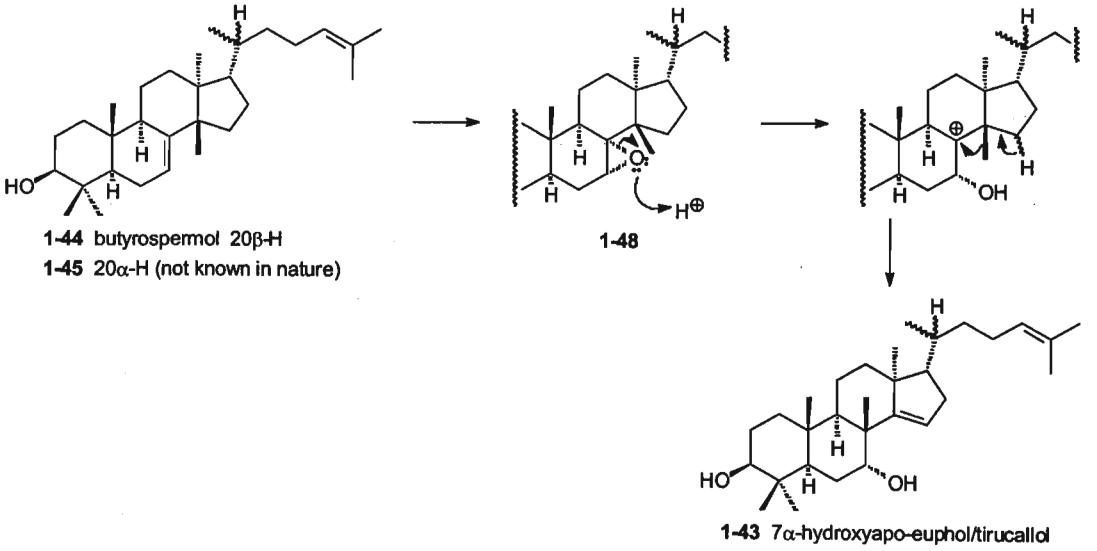


1-15 dammarenyl carbocation

1-43 apo-euphol/tirucallol

Scheme 8: Formation of apo-euphol/tirucallol **1-43** from the dammarenyl carbocation **1-15** [41,44].

The same authors, noting that all naturally occurring compounds having the apo-structure hitherto isolated were oxygenated at C-7α, proposed that this rearrangement occurred *via* a 7α,8α-epoxy intermediate **1-48** [41,45] (scheme 9). They supported this proposal with a laboratory conversion of the 7α,8α-epoxy methyl elemolate ester **1-49** to the corresponding 7α-hydroxyapo-derivative **1-50** by treatment with boron trifluoride etherate [45] (scheme 10).

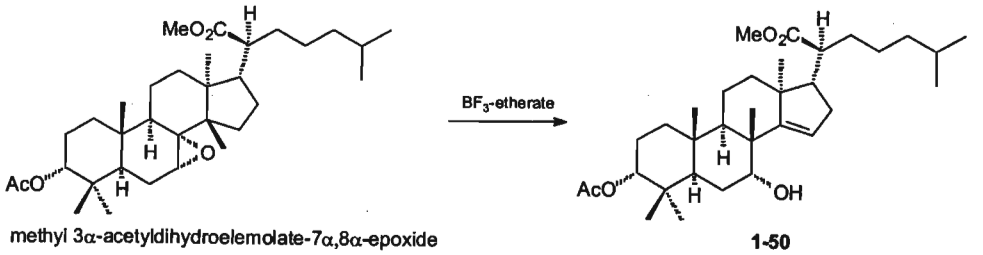


1-44 butyrospermol 20β-H
1-45 20α-H (not known in nature)

1-48

1-43 7α-hydroxyapo-euphol/tirucallol

Scheme 9: The apo rearrangement *via* the 7α,8α-epoxy intermediate **1-48** [41,45].

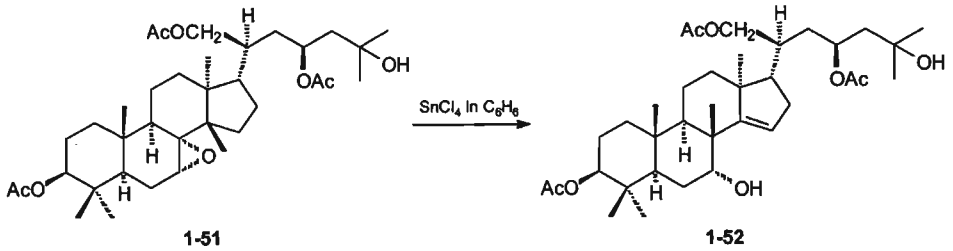


1-49 methyl 3α-acetyldihydroelemolate-7α,8α-epoxide

1-50

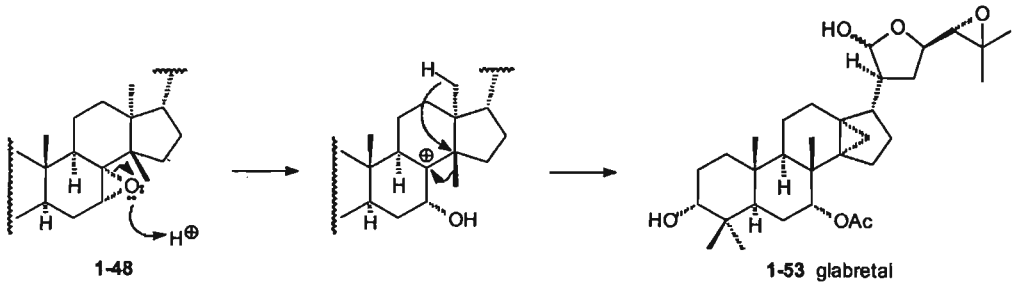
Scheme 10: The apo rearrangement of 7α,8α-epoxy methyl elemolate ester **1-49** [45].

A similar result was reported by Lavie *et al.* who converted 7α,8α-epoxy melianotetraol triacetate **1-51**, obtained by $LiAlH_4$ reduction of naturally occurring melianone **1-37** from *Melia azedarach* L., into the corresponding 7α-hydroxyapo-derivative **1-52** by treatment with $SnCl_4$ [46,47] (scheme 11).



Scheme 11: The apo rearrangement of the 7α,8α-epoxy melianotetraol triacetate **1-51** [46,47].

A comparison of the structures presented on page 12 shows that the same sidechains occur in both pre-apo change compounds and those in which the change has taken place, and therefore that there is no specific stage at which it occurs. The isolation of glabretal **1-53** [48], in which the Δ^{14}-double bond has been replaced by a 13,18,14-cyclopropane ring, has been rationalised by a variation [22] on the apo change mechanism in which methyl migration from C-14β to C-8β is accompanied by capture of the C-18 methyl group rather than loss of H-15 (scheme 12).

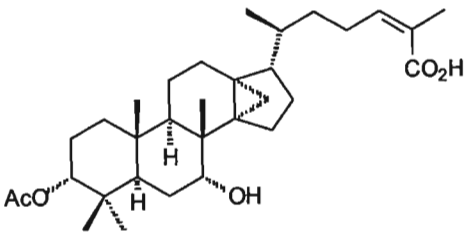


Scheme 12: Formation of the 13,18,14-cyclopropane ring in glabretal **1-53** [46,47].

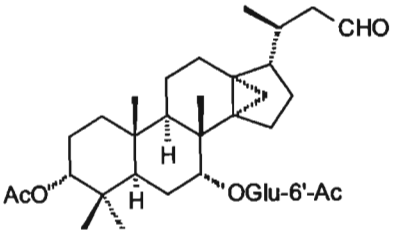
It has also been proposed that the cyclopropyl ring is an intermediate in the apo change, but that its lability precludes its isolation *in vitro* [22]. The later isolation of such compounds as dysoxylic acid A **1-54** from *Dysoxylum pettigrewianum* [49] and cumindyoside B **1-55** from *Dysoxylum cumingianum*† [50] suggest otherwise, however, as such instability is unlikely to survive the enzymatic conditions

† Neither of these species is quoted in the Missouri Botanic Gardens database [51].

necessary for oxidation of the side chain in **1-54** and even less so when the side chain has been cleaved, as in **1-55**.

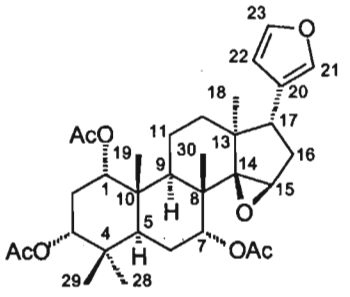


1-54 dysoxylic acid A



1-55 cumindyoside B

1.2.3.2 Class II: The Havanensin group

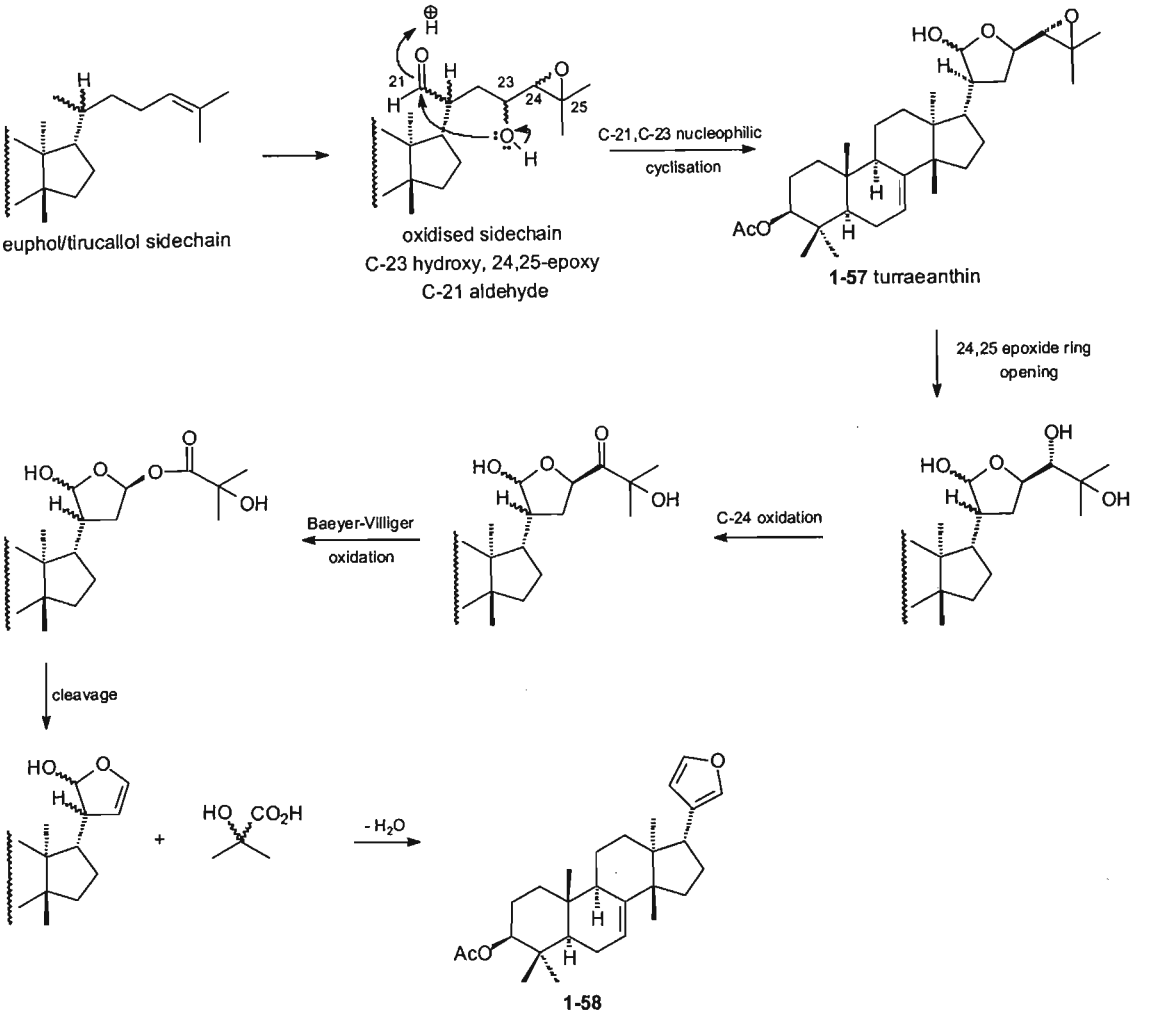


1-56 havanensin-1α,3α,7α-triacetate

This group, in addition to the intact tetracyclic skeleton present in the protolimonoids, possesses an intact β-substituted furan ring at C-17α. The group takes its name from the first compound of the class to be characterised, that of havanensin triacetate **1-56** from *Trichilia havanensis* Jacq. [52], and members of the group are the simplest of the limonoids.

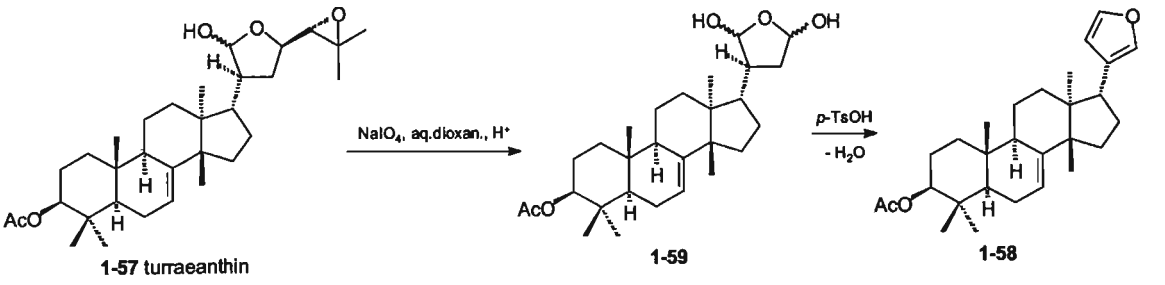
A mechanism involving stepwise oxidation of the sidechain was proposed by Halsall *et al.* to account for the *in vitro* conversion of the melianone **1-37** analogue turraeanthin **1-57**, isolated earlier from *Turraeanthus africanus* (Welw. ex C.DC.) Pellegr. [42,52,53], to the limonoid **1-58**. Successive oxidation steps produce a hydroxy group at C-23, a 24,25-epoxy group, and an aldehyde at C-21, followed by nucleophilic C-21,C-23 cyclisation to form the observed hemiacetal ring. Opening of the 24,25-epoxide ring and subsequent oxidation produces a ketone at C-24, which then undergoes Baeyer-Villiger oxidative cleavage of the C-23,C-24 bond to give a dihydrofuran ring, which finally affords the furan ring, with the loss of four carbon atoms, by dehydration (scheme 13). Treatment of

turraeanthin with acidic $NaIO_4$ afforded the labile cyclic hemiacetal **1-59**, which was dehydrated *in situ* to give limonoid **1-58** in high yield (scheme 14)[†].

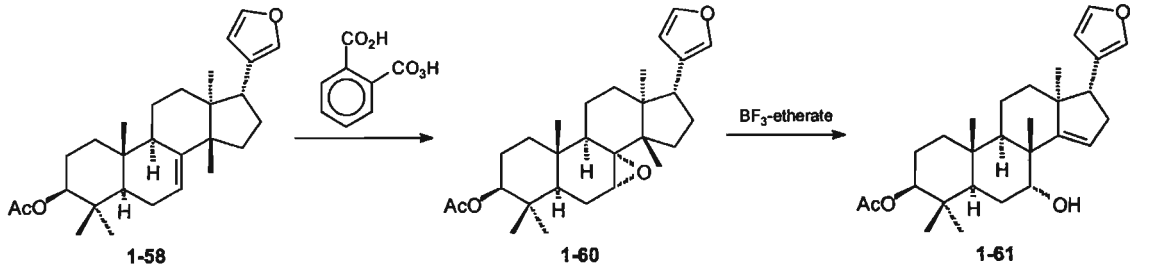


Scheme 13: Sidechain oxidation and furan ring formation as proposed by Halsall *et al.* [42,52].

[†] The earlier comment (p.15) that there does not appear to be a specific point in cyclisation of the sidechain at which the apo change occurs notwithstanding, limonoid **1-58** remains to this day the only compound recorded with an intact furan ring and in which the apo change has not occurred. The preceding statement could thus perhaps be modified to the effect that the apo change, while not occurring at a specific point, precedes final formation of the furan ring. Halsall *et al.* subsequently reported the conversion of **1-58** into the corresponding 7α,8α-epoxy compound **1-60** with monoperphthalic acid, and the apo change transformation of **1-60** into **1-61** with boron trifluoride etherate [54] (scheme 15).

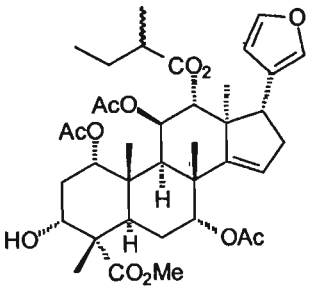


Scheme 14: *In vitro* conversion of turraeanthin **1-57** into **1-58** *via* intermediate **1-59** [42,52].

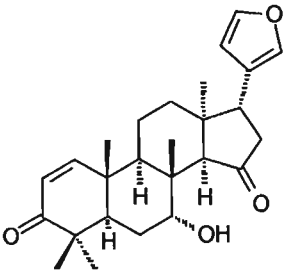


Scheme 15: Apo change conversion of limonoid **1-58** into **1-61** *via* 7α,8α-epoxy intermediate **1-60** [54].

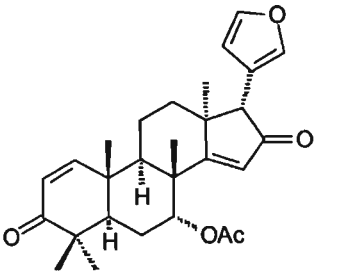
A large number of limonoids of this group, displaying a wide variety of substitution and oxidation patterns, have been isolated and characterised. The D ring is present most often as a 14β,15β-epoxide, as in havanensin triacetate **1-56**, or as a Δ^{14}-double bond, as in the highly esterified deoxyhavanensin derivative **1-62** [55], but it can also have a ketone at C-15, as in neotrichilenone **1-63** [56], an α,β-unsaturated ketone, as in azadiradione **1-64** [57], or corresponding 14β,15β-epoxide, as in khayanthone **1-65** [58]. A ketone at C-16 can lead to epimerisation and/or oxygenation at C-17; so 17-*epi*azadiradione **1-66** [59] , and both epimeric C-17 alcohols **1-67** and **1-68** have been reported [60,61]. Vilasinin **1-69** [62] and sendanin **1-70** [63] are examples of havanensin group compounds in which oxygenation of the C-28 or C-29 methyl group has resulted in the formation of 6α,28 and 19,29 ether linkages.



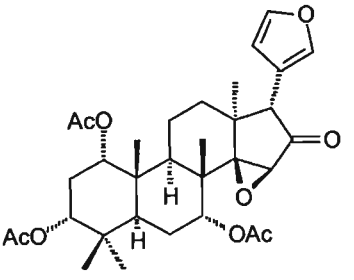
1-62



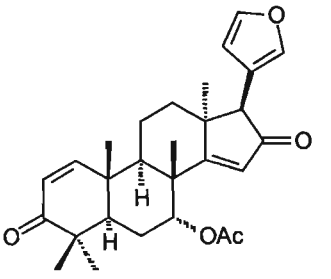
1-63 neotrichilenone



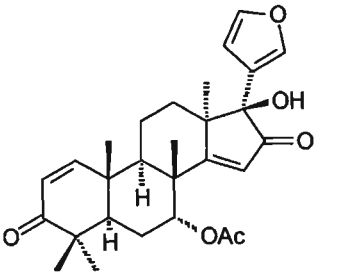
1-64 azadiradione



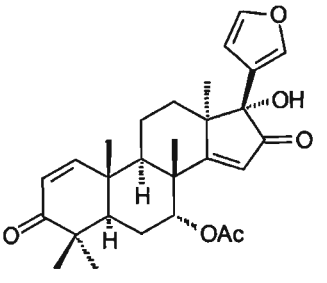
1-65 khayanthone



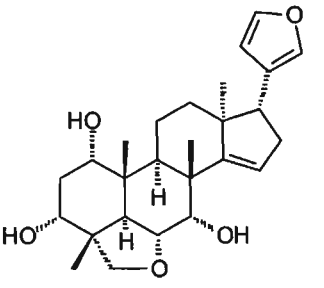
1-66 17-*epi*-azadiradione



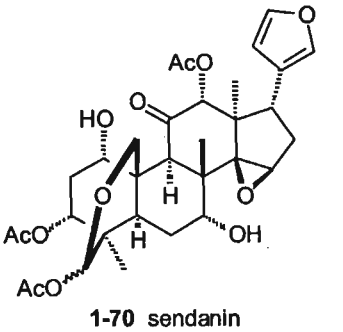
1-67 17β-hydroxyazadiradione



1-68 17α-hydroxy-17-*epi*-azadiradione

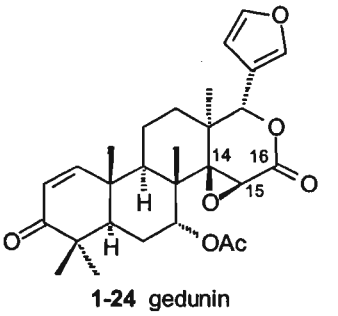


1-69 vilasinin



1-70 sendanin

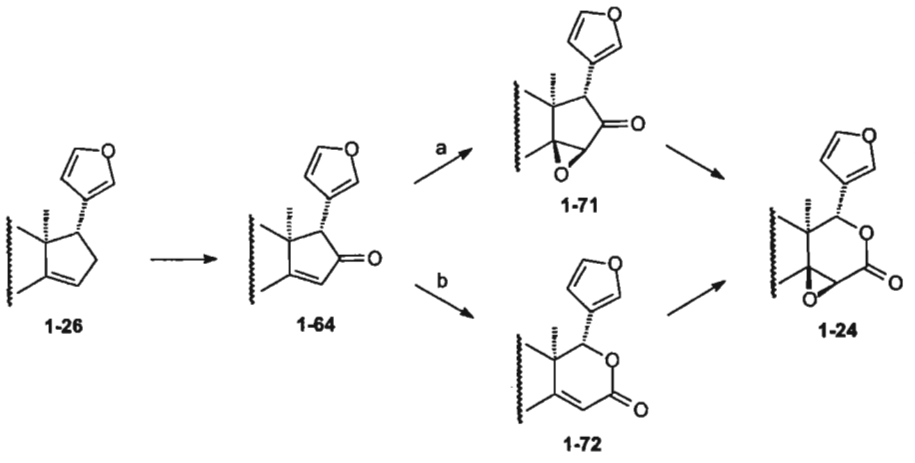
1.2.3.3 Class III: The Gedunin group



1-24 gedunin

This group is named after gedunin **1-24**, the first limonoid from the Meliaceae to be fully described. Members of the class possess a skeleton in which rings A, B and C are intact and ring D is a six-membered lactone.

As was the case with the havanensin group, a great deal of early study concentrated on the elaboration of the mechanism by which the ring D lactone arises. This has resulted in a pathway which is among the best understood in limonoid biosynthesis, and which is solidly underpinned by a variety of isolated intermediates and experimental results. The key step is the allylic oxidation at C-16 of a deoxyhavanensin-type D ring, containing a Δ^{14}-double bond, to give an azadiradione-type α,β-unsaturated ketone, followed by Baeyer-Villiger ring expansion to the lactone [22] (scheme 16).



Scheme 16: D ring lactone formation [22]

The *in vitro* allylic oxidation of azadirone **1-26** to azadiradione **1-64** by treatment with SeO_2 has been reported [57], as has the conversion of epoxyazadiradione **1-71** into gedunin **1-24** [64] with perbenzoic acid (scheme 16)[†].

Given the successes accomplished by such early workers in this field as Halsall *et al.* in the conversion of protolimonoid sidechains into the defining limonoid furan ring, it must have seemed logical to assume that any sidechain, whether cyclic and/or oxygenated, should be considered a possible furan ring precursor. However, the isolation of photogedunin **1-73** together with gedunin **1-24** from *Cedrela odorata* L. [65], and, more importantly, its laboratory synthesis by photolysis of

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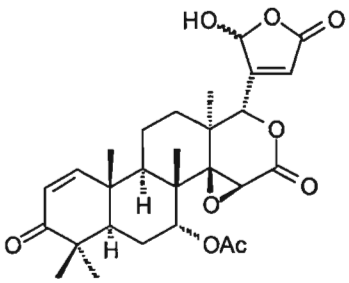
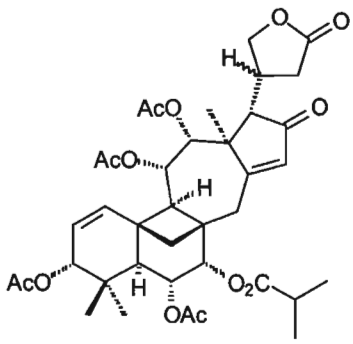
† This of course does not specify whether epoxidation occurs before (pathway a) or after (pathway b) the Baeyer-Villiger oxidation. The overwhelming majority enjoyed in the literature by 14β,15β-epoxy compounds over their Δ^{14}-double bond counterparts, of which there are a scant four reports at present, suggests that the former pathway predominates, with the double bond in these four compounds then reappearing after the event. What has *not* been reported, to our knowledge, is the direct laboratory conversion of an α,β-unsaturated 16-keto D ring system, such as azadiradione **1-64**, into either gedunin **1-24** or its deoxy unsaturated analogue **1-72**, but this would be inconclusive in any case as an initial step involving epoxidation of the double bond by the peroxy acids used to effect the ring opening reaction could not be ruled out.

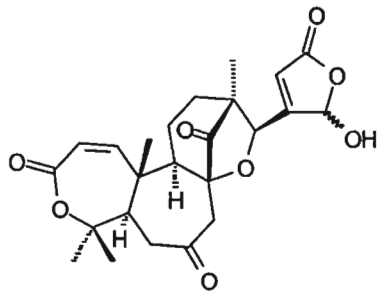
gedunin **1-24**, suggests that in many cases these compounds are limonoid oxidation products rather than the protolimonoids they were originally assumed to be†.



1-73 photogedunin



1-74 delevoyin C



1-75 cedashnine

1.2.3.4 Class IV

The original subdivision of this class into three subgroups [22] has been revised into one of five [23], which at first impression are so different that it is difficult to see that they have a common origin. Class IV compounds may all formally be characterised as having rings A and D intact, a ring D lactone, and a ring B which has undergone C-7,C-8 bond cleavage; it is the rearrangements that occur subsequent to this cleavage that give rise to the bewildering complexity of compounds that have been reported.

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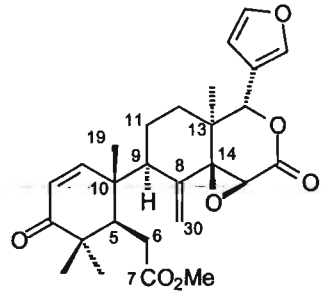
† It seems inconceivable that the conditions necessary to produce the extensive modifications of the triterpenoid skeleton exhibited by delevoyin C **1-74** from *Entandrophragma delevoyi* De Wild [66] and cedashnine **1-75** from *Cedrelopsis grevei* [67], to mention but two of a large number of this type of compound which have subsequently been isolated, would not also have resulted in a complete synthesis of the furan ring.

As to whether these are true natural products or artefacts arising from the extraction and isolation processes (what Connolly *et al.* [39], in reporting a series of such compounds from *Chisocheton paniculatus* (Roxb.) Hiern, described as

"...the influence of Glasgow sunshine...")

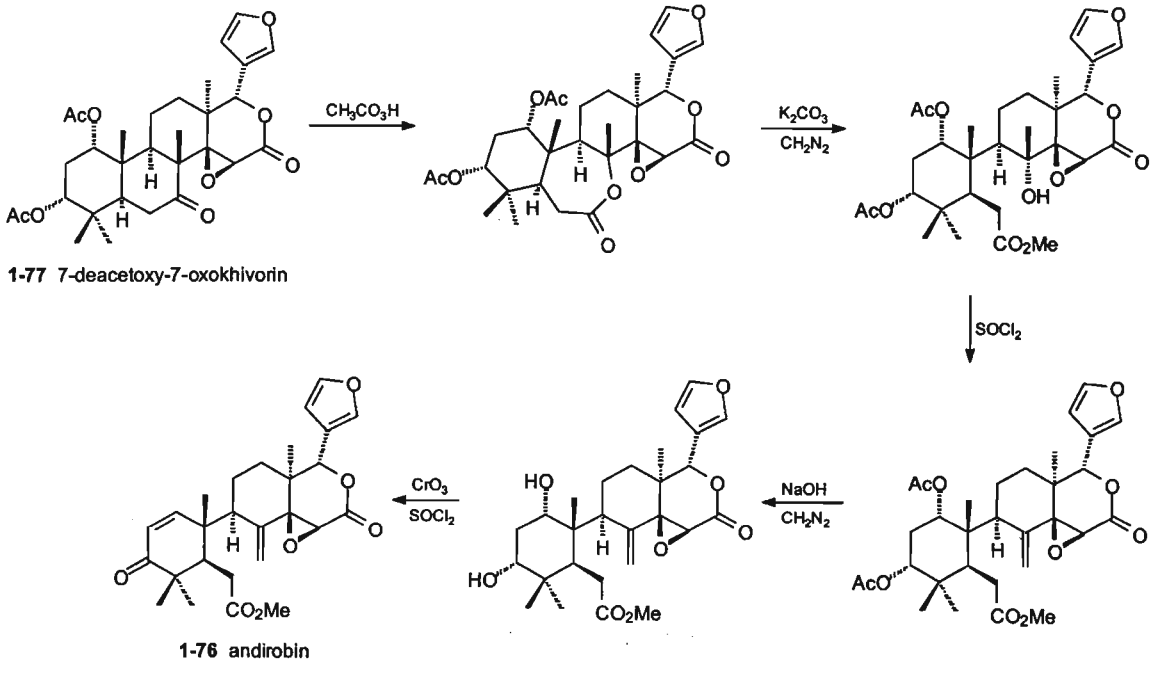
there is no definitive answer.

1.2.3.4.1 Class IVa: The Andirobin Group



1-76 andirobin

The simplest of the class IV limonoids, C-7,C-8 bond cleavage in this group results in the formation of an exocyclic $\Delta^{8(30)}$-double bond and a carbomethoxy group at C-7. Given the overall similarity of andirobin **1-76** to gedunin **1-24**, the biosynthetic link is self-evident, and this has been experimentally verified, by Baeyer-Villiger oxidation, from the gedunin analogue 7-deacetoxy-7-oxokhivorin **1-77** [68] (scheme 17).



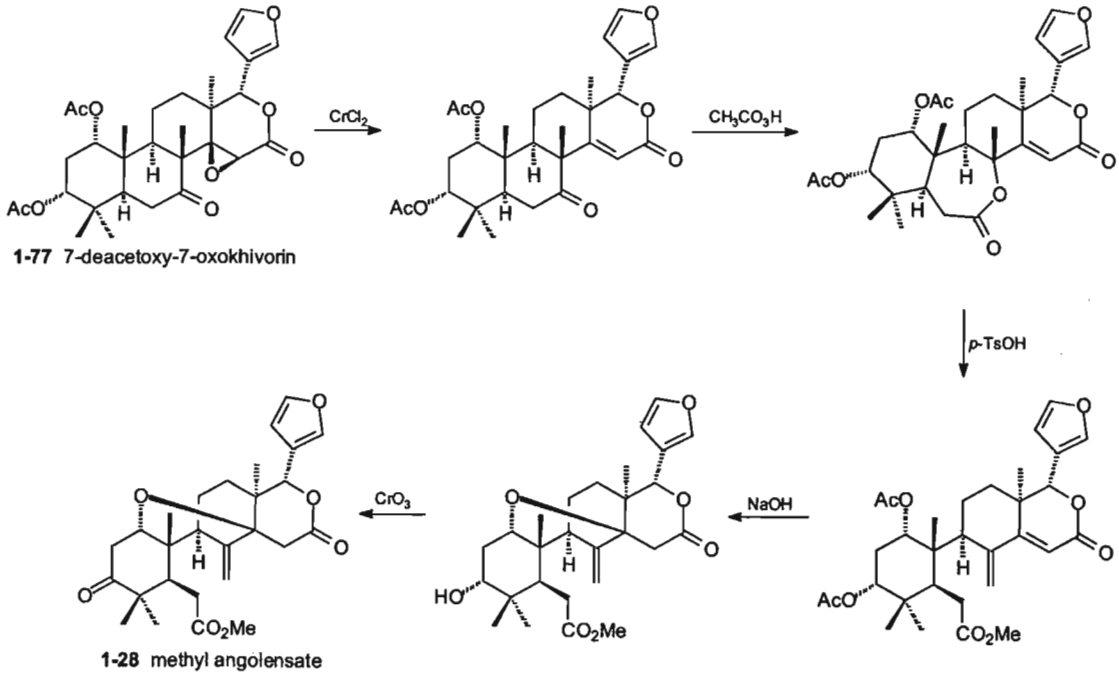
1-77 7-deacetoxy-7-oxokhivorin

1-76 andirobin

Scheme 17: Synthesis of andirobin **1-76** from 7-deacetoxy-7-oxokhivorin **1-77** [68].

The andirobin group compound methyl angolensate **1-28**, which together with gedunin **1-24** was one of the very first limonoids to be isolated from *Entandrophragma angolense* [24], was synthesised in

similar fashion involving the fortuitous discovery that reduction of the 14β,15β-epoxide linkage to the corresponding Δ^{14}-double bond induced spontaneous nucleophilic attack by the C-1α hydroxy group to form the 1α,14β-oxide bridge [68,69] (scheme 18).

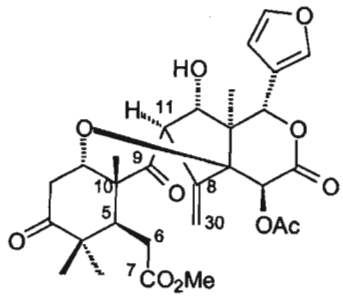


1-77 7-deacetoxy-7-oxokhivorin

1-28 methyl angolensate

Scheme 18: Synthesis of methyl angolensate **1-28** from 7-deacetoxy-7-oxokhivorin **1-77** [68,69].

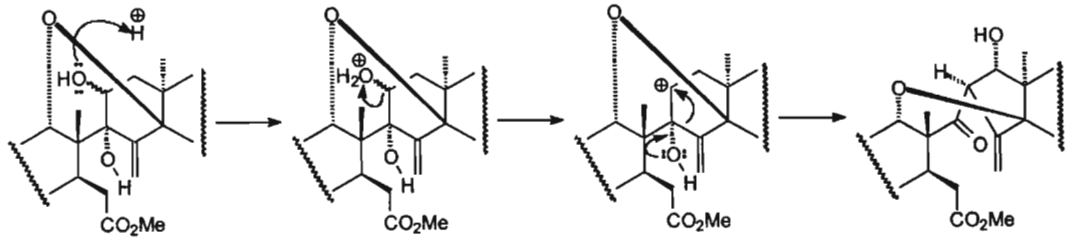
1.2.3.4.2 Class IVb: The Trijugin Group



1-78 trijugin B

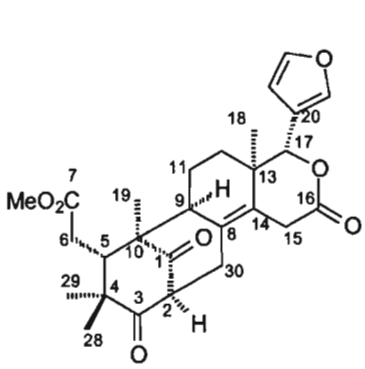
Named after the trijugins from *Heynea trijuga* Roxb. [70] (syn. *Trichilia connaroides* var. *connaroides* (Wight et Arn.) Bentv. [51]), members of this group have ring A intact, ring B opened, ring C

contracted, and a D ring lactone. They are proposed to arise, *via* a pinacol-pinacolone rearrangment, from a hypothetical C-9,C-11-dihydroxymethyl angolensate-type precursor (scheme 19).

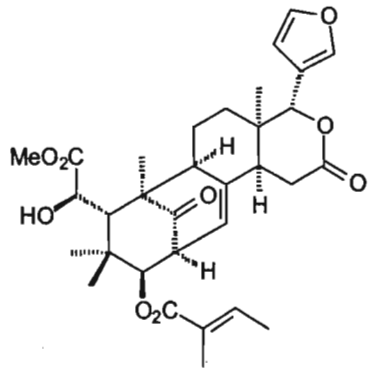


Scheme 19: Synthesis of trijugin B ring by pinacol-pinacolone rearrangement.

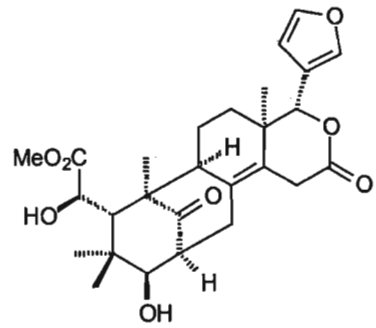
1.2.3.4.3 Class IVc: The Mexicanolide Group



1-79 mexicanolide



1-80 swietenine

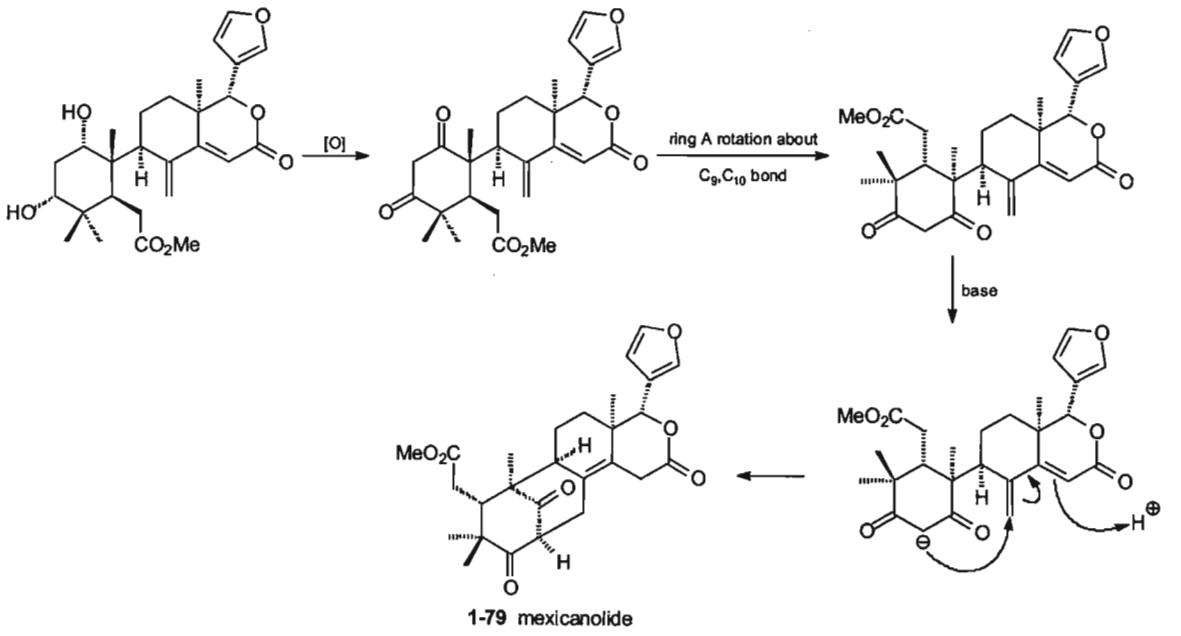


1-81 swietenolide

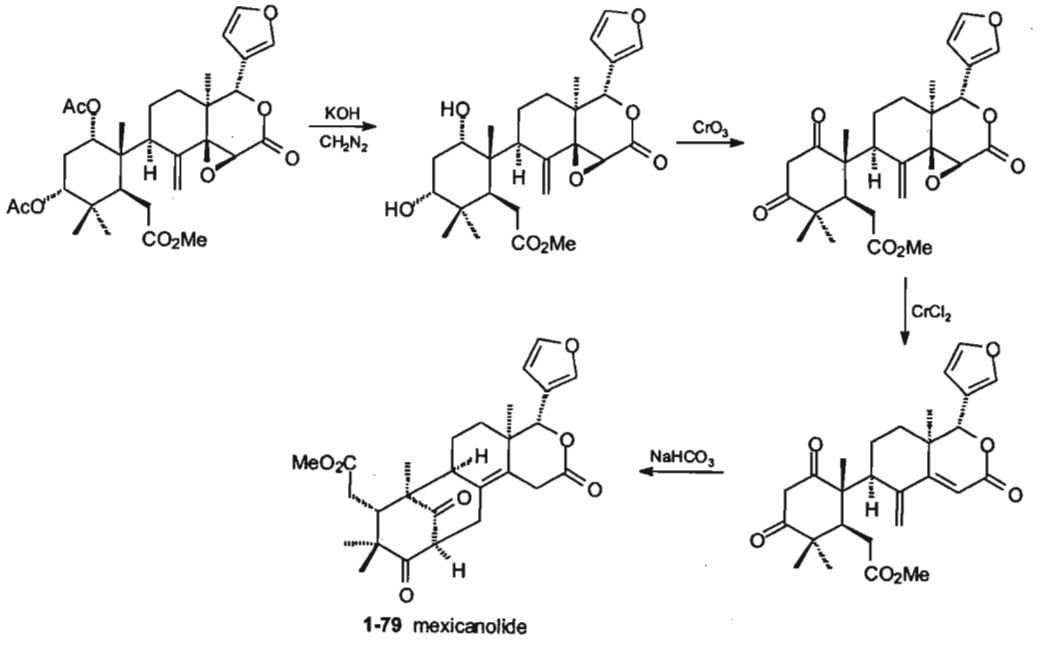
Members of this group have rings A and C intact, a ring D lactone, and a B ring which has undergone rotation about the C-9,C-10 bond before recyclisation occurs by bond formation between C-2 and C-30. The proposed biosynthetic pathway (scheme 20), involving spontaneous Michael addition of a ring A 1,3-diketone, has been experimentally substantiated in the laboratory, but does not explain how the naturally occurring isomeric swietenine **1-80** type compounds are formed, as synthetic attempts produce only the Δ^{8}-double bond mexicanolide isomers, with no trace of the $\Delta^{8(30)}$- or Δ^{14}-double bond analogues [69,71,72] (scheme 21).

Many of the large number of these compounds that have been reported, despite being derivatives of earlier isolates (in particular, those with hydroxy substituents at C-2 and C-6), have been given trivial names of their own which have subsequently entered common usage. An example of this is

compound **1-81**, which formally should be 3-deoxy-3β,6β-dihydroxymexicanolide, but which is found universally in the literature as swietenolide.

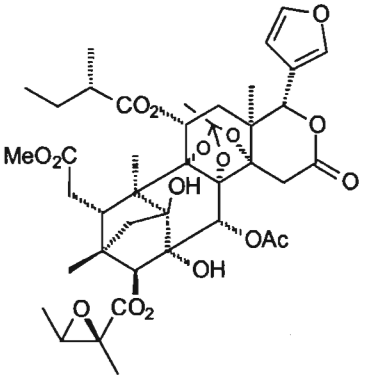


Scheme 20: Biosynthesis of mexicanolide **1-79** *via* C-9,C-10 ring A rotation and C-2,C-30 Michael recyclisation [69,71,72].

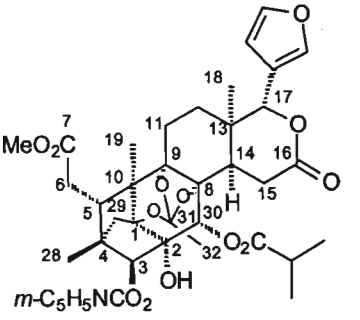


Scheme 21: Laboratory synthesis of mexicanolide **1-79** [69,71,72].

1.2.3.4.4 Class IVd: The Phragmalin Group



1-82 utilin



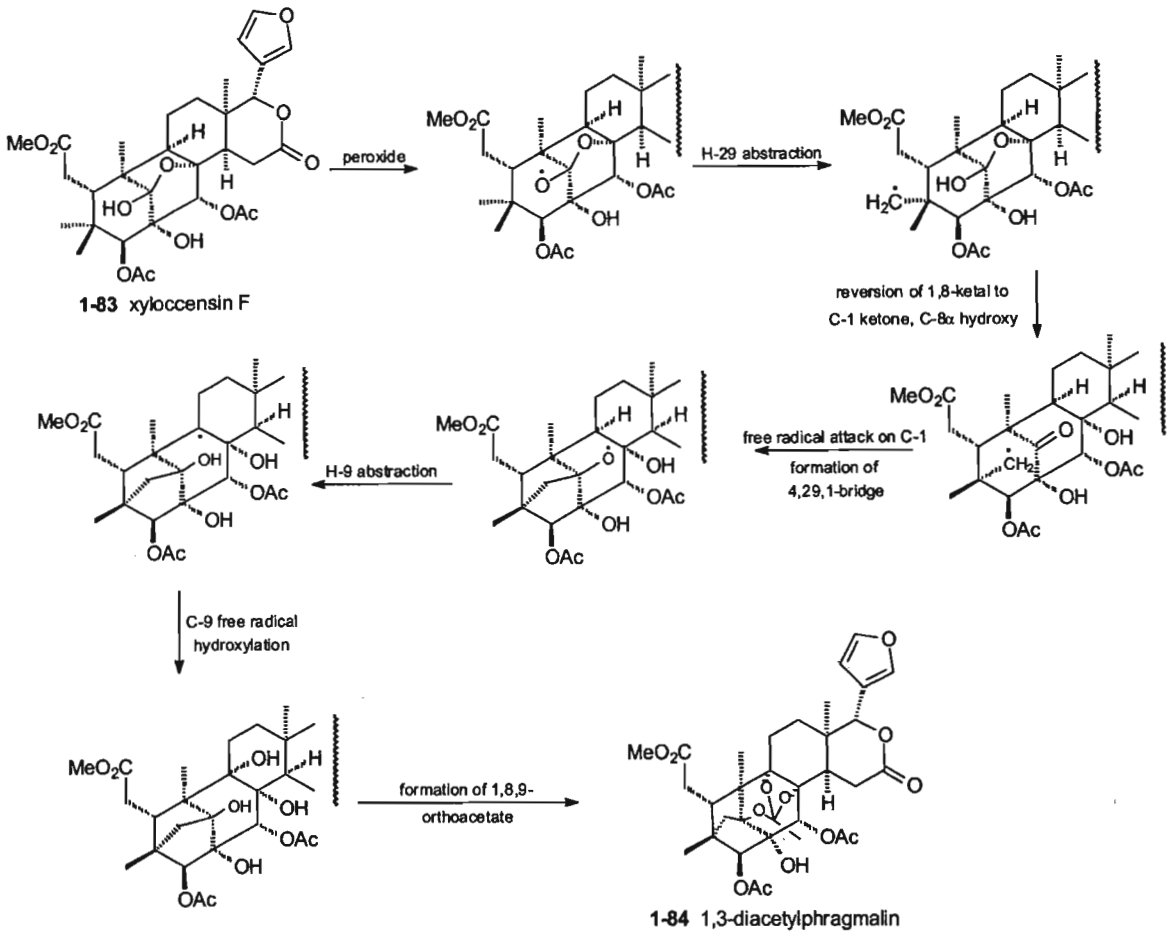
1-30 phragmalin

Members of this group as it was originally defined [22] were analogues of either utilin **1-82**, which was one of the very early limonoids isolated [24], or phragmalin **1-30** [73]. The structures of both were finally established only by X-ray crystallography [73,74].

The class IVd limonoids, as usual, have rings A and C intact and a ring D lactone. However, they possess also a 4,29,1-methylene bridge and an orthoacetate linkage, which occurs at 8,9,14 in utilin **1-82** and at 1,8,9 in phragmalin **1-30**.

The biosynthesis of the phragmalin **1-30** 1,8,9 B ring orthoacetate, as proposed by Taylor [75], was presumed to begin with a mexicanolide-like compound such as xyloccensin F **1-83**, in which the $\Delta^{8(14)}$-double bond, having first been oxidised to give the 8α,14α-epoxide, had subsequently undergone acid-catalysed epoxide ring opening to give a Δ^{14}-double bond and hydroxy group at C-8α, followed by reduction to the 14,15-dihydro derivative and nucleophilic attack on the ketone at C-1 to give the 1,8-ketal.

Abstraction of a hydrogen from the C-1 hydroxy group affords an oxygen radical, which initiates construction of the 4,29,1-bridge by a sequence of free radical H atom abstraction/oxidation reactions, and culminates in the formation of the 1,8,9-orthoacetate to give 3,30-diacetylphragmalin **1-84** (scheme 22).



1-83 xyloccensin F

1-84 1,3-diacetylphragmalin

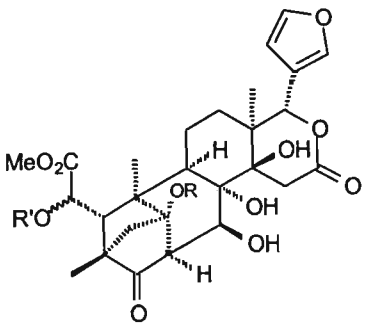
Scheme 22: Biosynthesis of 3,30-diacetylphragmalin **1-84** from xyloccensin F **1-83** [75].

However, three compounds **1-85,1-86,1-87** that have recently been isolated from a Brazilian specimen of *Khaya senegalensis* (Desr.) A.Juss. [76,77] do not fit into Taylor's original classification [22] for the class IVc phragmalin group, nor do they fall into the mexicanolide class which lack the 4,29,1-bridge. Taylor's definition has thus been modified [23] to include compounds with the 4,29,1-bridge but not necessarily the 1,8,9- or 8,9,14-orthoacetate†.

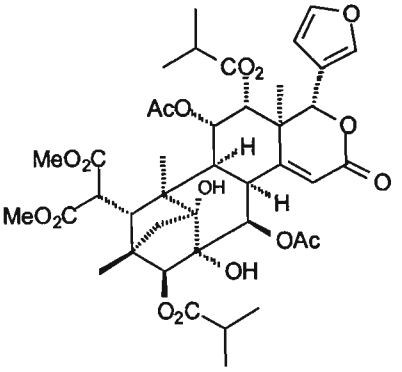
† This has alarming implications for the biosynthesis given in scheme 22. In his review [22], Taylor quotes the example of tabularin from *Chukrasia tabularis* A.Juss [78] (*not* the flavone isolated from the same source by Purushothaman *et al.* [79]), which had been tentatively identified as having structure **1-88** on the basis of ^{1}H and ^{13}C NMR spectral analysis. He remarks:

> "...tabularin, to which a ring A bridged structure unsubstituted at C8 or C9 has been ascribed. If this is correct, then the biosynthetic hypothesis is not correct in this case, and probably not in other cases."

He then weakens his own counterargument on the grounds that the missing C-1 ketone resonance upon which the structure of tabularin rests may be due to the weakness of the sample rather than the proposed structure. Taylor gave no structure for tabularin **1-88** in his discussion [22], and the entry in his accompanying checklist is buried in a section labelled "Unknown or doubtful structures", which no doubt accounts for its absence both from the Dictionary of Natural Products (the entry given is to the flavone mentioned above) and from citation in the later publications [76,77].

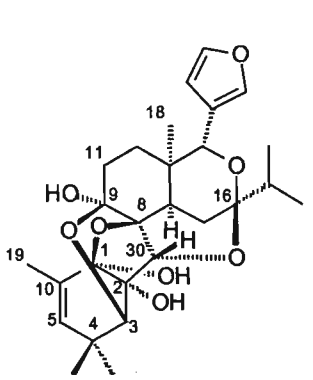


1-85 R = R' = H
1-86 R = H, R' = Ac
1-87 R = Ac, R' = H

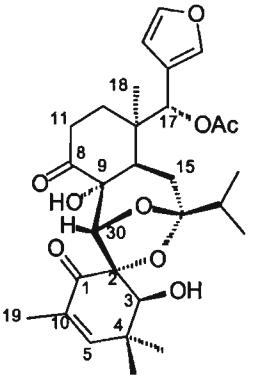


1-88 tabularin

1.2.3.4.5 Class IVe: The Entilin Group



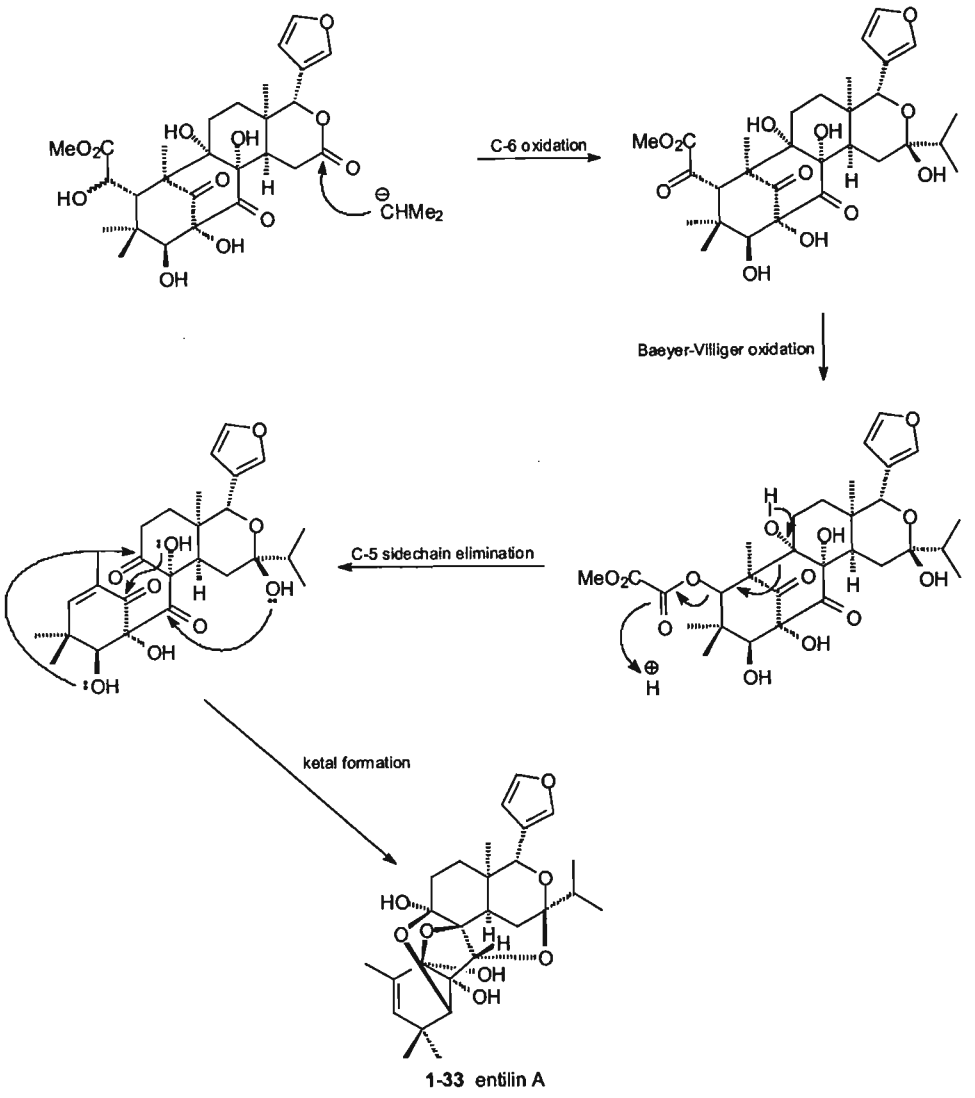
1-33 entilin A



1-89 entilin D

Together with the group IVb trijugin group, this is the second subclass to be added [23] to the original Taylor classification [22]. Members of the class have been isolated from only one species to date, *Entandrophragma utile* (Dawe et Sprague), and currently number only four examples based on two structural templates, of which entilin A **1-33** and entilin D **1-89** are examples [80,81].

These compounds have only an intact ring C remaining of the original group IV criteria. Cleavage of the ring B C-9,C-10 bond, loss of the C-5 sidechain and ketal formation with the ring D lactone C-16 all combine to produce compounds which are amongst the most rearranged of all limonoids [23] (scheme 23).



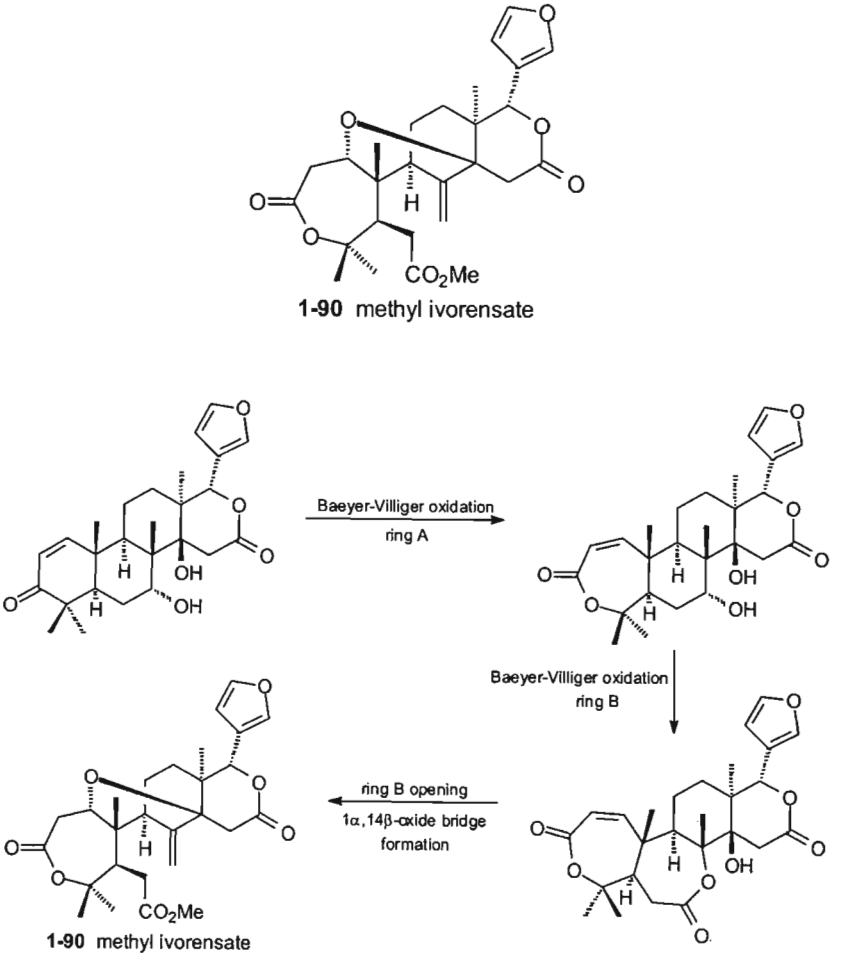
Scheme 23: Proposed biosynthesis of entilin A **1-33** [23].

1.2.3.5 Class V: The Methyl ivorensate Group

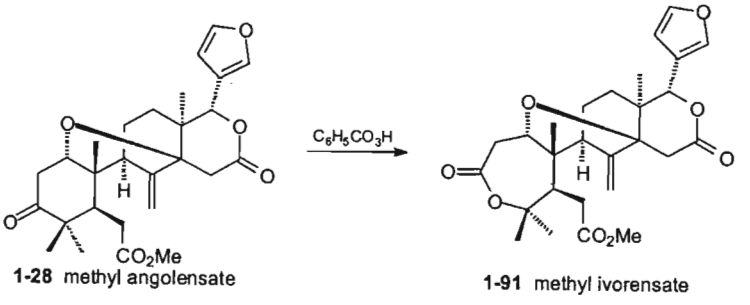
Members of this small group have an intact ring C, an andirobin-type open ring B with an exocyclic 8,30-double bond, and rings A and D both lactonised. The title compound **1-90** was originally isolated from *Khaya ivorensis* A.Chev. [82].

The biosynthetic pathway presumably involves the same Baeyer-Villiger ring B sequence proposed for methyl angolensate **1-28**, with a second such oxidation providing the ring A lactone (scheme 24). The biosynthesis is presented here with oxidation of ring A preceding that of B, and with lactonisation of both rings taking place before cleavage of the Δ^7-double bond; the 1α,14β-oxide bridge is then simultaneously established by nucleophilic attack on a Δ^1-double bond by a hydroxy group at C-14β

instead of the other way round. There is, however, no reason to suppose that these oxidations must follow a particular order. A laboratory synthesis of methyl ivorensate **1-90** has been achieved by perbenzoic acid oxidation of methyl angolensate **1-28**, with A ring oxidation occurring as the final stage [83] (scheme 25).



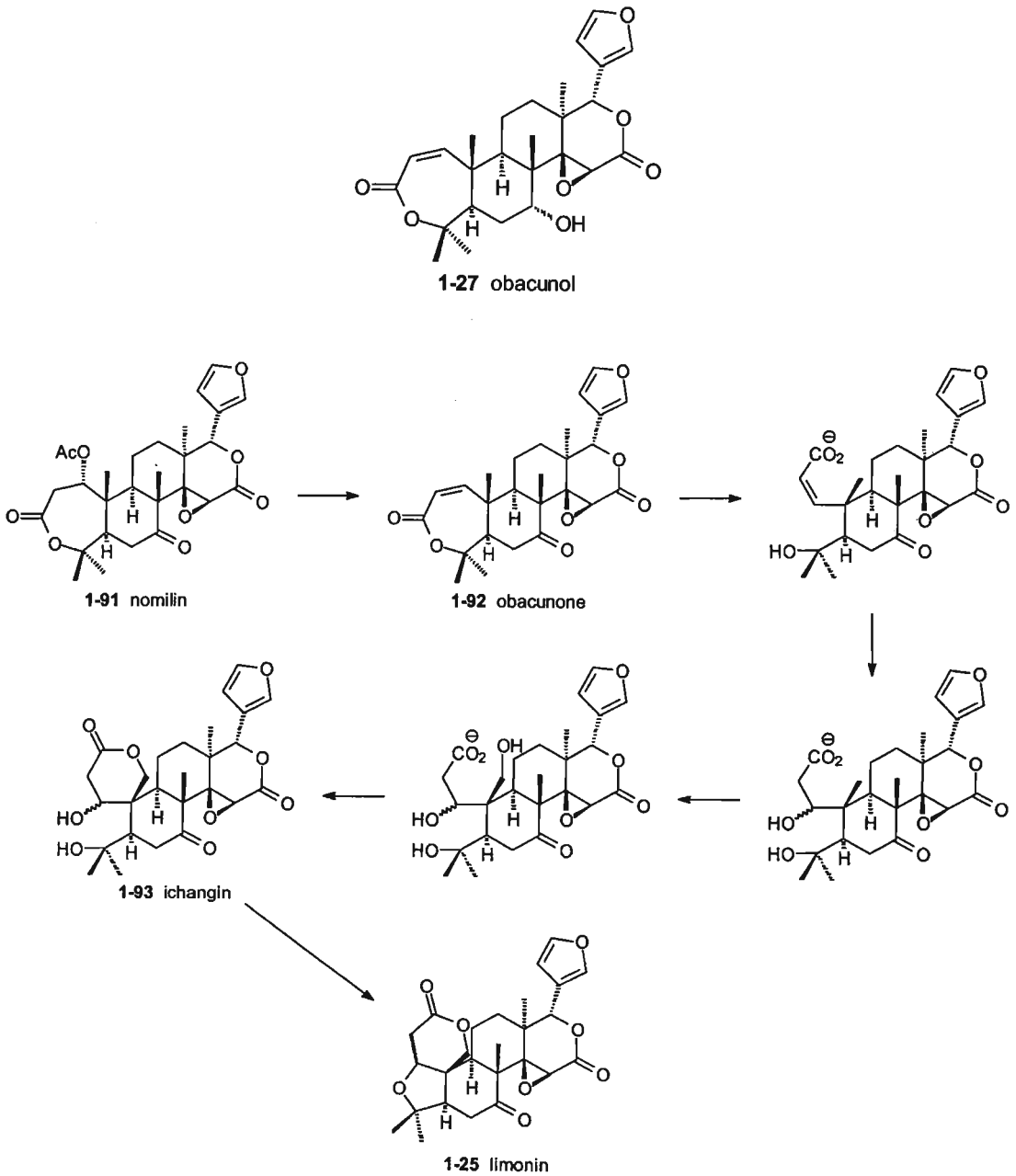
Scheme 24: Biosynthesis of methyl ivorensate **1-90** [83].



Scheme 25: Laboratory synthesis of methyl ivorensate **1-90** from methyl angolensate **1-28** [83].

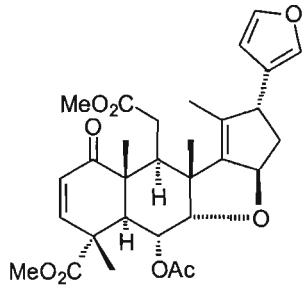
1.2.3.6 Class VI: The Obacunol Group

Limonoids of this group have rings A and D oxidised to lactones while rings B and C remain intact, and are noted in the Meliaceae chiefly by their scarcity [22]. They are, however, well represented in the Rutaceae, where radioactive tracer experiments have shown the related compounds nomilin **1-91** and obacunone **1-92**, *via* the intermediate ichangin **1-93**, are precursors of limonin **1-25** in *Citrus* species [84,85,86] (scheme 26). Obacunol **1-27** was originally reported from *Lovoa trichiliodes* Harms [87].

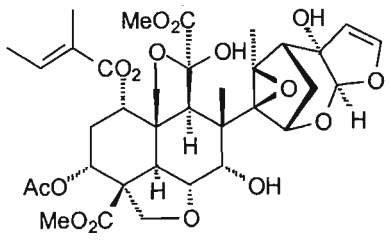


Scheme 26: Biosynthesis of limonin **1-25** [82].

1.2.3.7 Class VII: The Nimbin Group



1-94 nimbin



1-95 azadirachtin

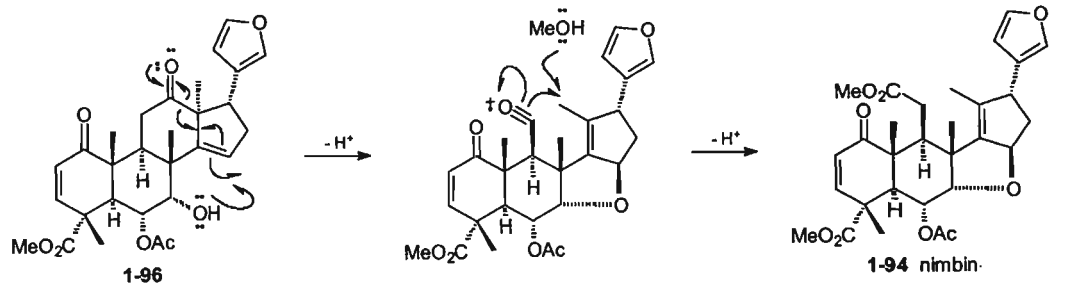
At first impression the definition of this group – rings A, B, and D intact, and ring C only "oxidised" – would appear to lead to easily recognisable ring C analogues of evodulone **1-105** (p.36) or toonafolin **1-102** (p.35) where ring C has been lactonised or opened. However, elaboration of ring C occurs only in conjunction with a number of other reactions which produce a wide variety of complex structures of such diversity that it was not until Taylor's review [22] that these were recognised as having a common origin. Nimbin **1-94** itself was first isolated in 1964 [88], with the structure following some five years later [89]. Like many compounds of this group, it is found in *Azadirachta indica* A.Juss, the source of azadirachtin **1-95**, which is perhaps the single most investigated limonoid known to man. The size of this group and the complexity of the structures established bear testimony to the interest displayed in the biological and pharmacological properties of compounds of this type.

Much debate has arisen in the literature as to the exact mechanism involved in the opening of ring C [22,90,91,92]. Nimbin **1-94** can arise from a 12-oxodeoxyhavanensin-like precursor such as **1-96** by a free radical mechanism [92] (scheme 27), or by nucleophilic attack of the hydroxy group at C-7α on C-15 [22] (scheme 28)†.

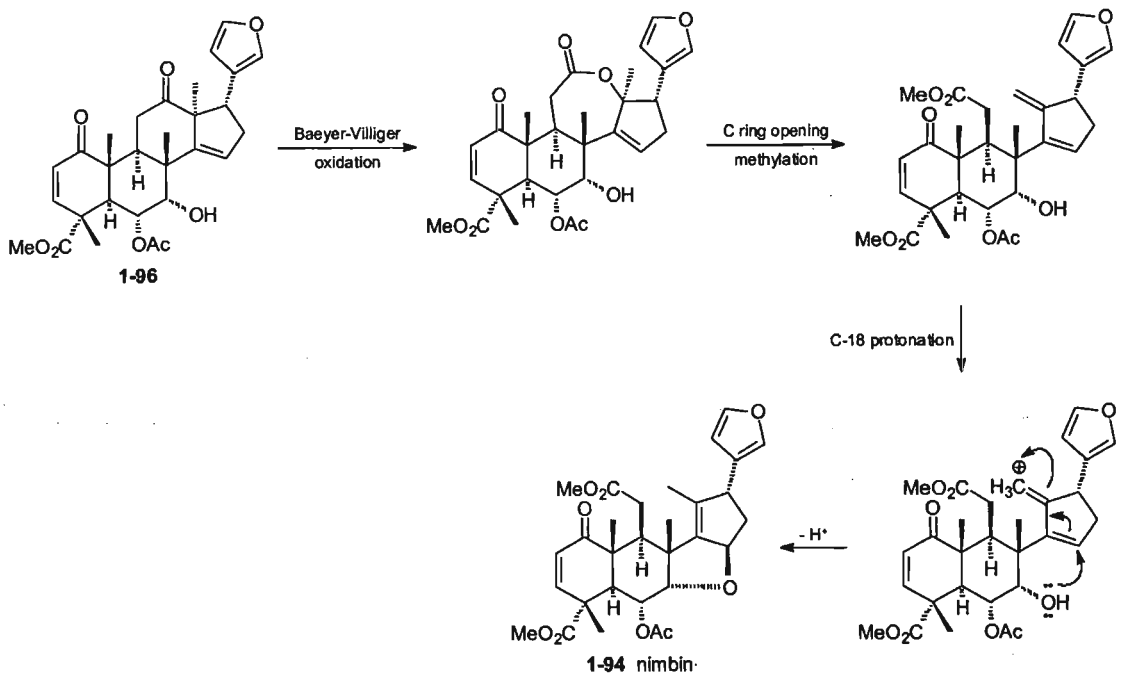
† Taylor [22] has noted:

> "This cyclisation probably depends on the extra flexibility bestowed upon the molecule by the opening of ring C, as 7,15-oxides do not occur in other groups."

If this is indeed the case then the latter rather than the former biosynthesis is favoured.



Scheme 27: Proposed biosynthesis of nimbin **1-94** [92].

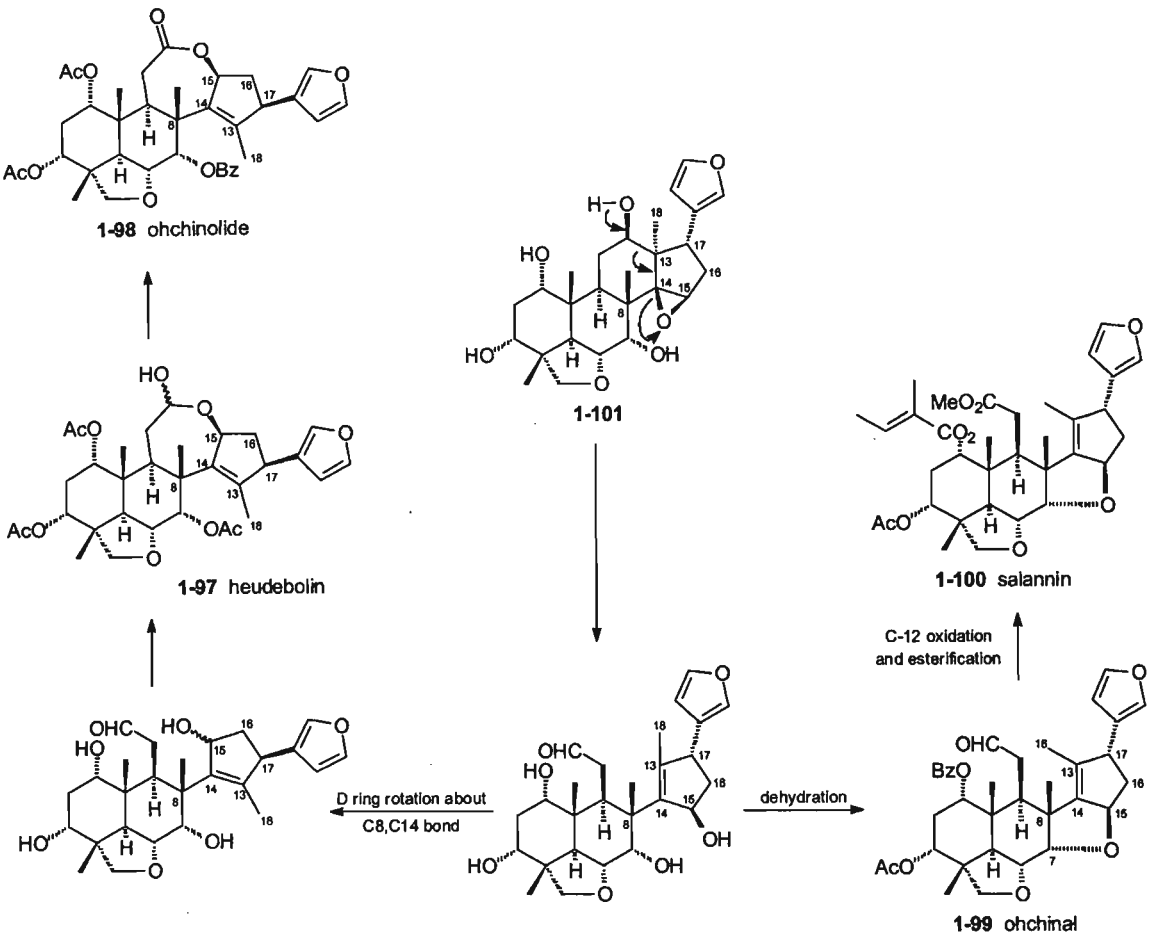


Scheme 28: Proposed biosynthesis of nimbin **1-94** [22].

The related compounds heudebolin **1-97** from *Trichilia heudelotti* Planch. ex Oliv. [91] and ohchinolide A **1-98** from *Melia azedarach* [93] both display a lactonised but nevertheless unopened ring C, in what appears to be a direct verification of scheme 28, although the 7α,15-oxide link is absent.

A possible unifying biosynthesis is given in scheme 29 [22], in which a 14,15-epoxy, C-12β-hydroxy precursor **1-101** undergoes hydrolytic rather than oxidative ring C opening to yield a compound with a Δ^{13}-double bond, hydroxy group at C-15β, and aldehyde at C-12. This intermediate then either undergoes dehydration, to form the 7α,15β-oxide linkage, producing ohchinal **1-99** [93], dehydration and oxidation/esterification at C-12, yielding salannin **1-100** [94], or D ring rotation about the C-8,C-14

bond and nucleophilic attack of the C-15-hydroxy group on the aldehyde carbonyl to give a hemiacetal C ring†, yielding heudebolin **1-97**, with further oxidation to the lactone giving ohchinolide **1-98**.

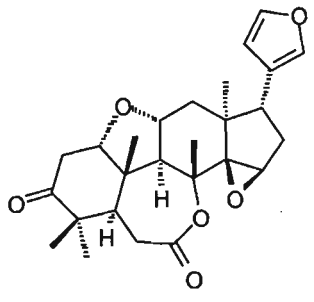


Scheme 29: Proposed biosynthesis of nimbin class limonoids heudebolin **1-97**, ohchinolide **1-98**, ohchinal **1-99** and salannin **1-100** [22].

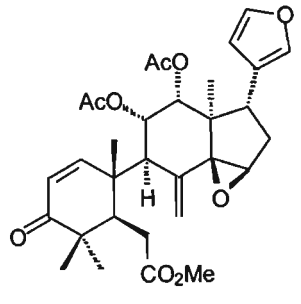
† The C-15 oxygen has been shown to be β in both ohchinolide **1-98** by X-ray crystallographic studies [93], and in heudebolin **1-97** and related hemiacetals by ^{1}H NMR spectroscopy [95], which corresponds to a C-15α-hydroxy group before rotation of the D ring. This can be rationalised in terms of the proposed biosynthesis only by noting that the hydroxy group at C-15 is an allylic one and therefore subject to epimerisation, which is preferable, however, to Taylor's proposal which invokes the same allylic alcohol in a mechanism in which the

> "...hydrate of the aldehyde attacks the allylic C-15 with inversion to give compounds similar to heudebolin...".

1.2.3.8 Class VIII: The Toonafolin group



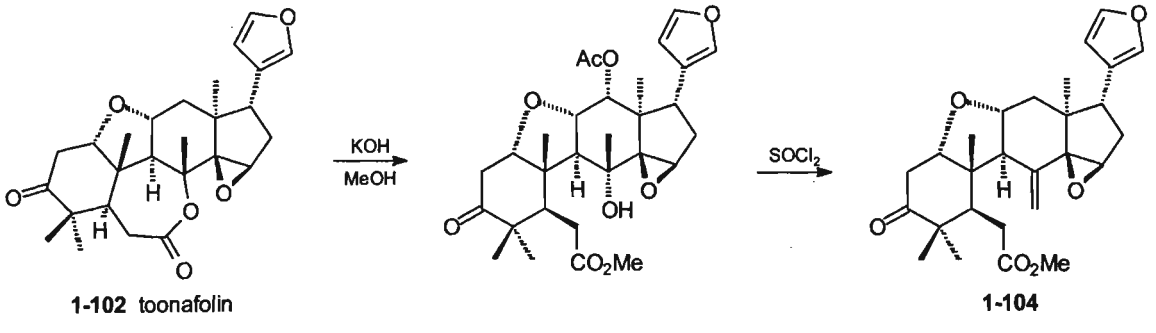
1-102 toonafolin



1-103 toonacilin

Limonoids of this group have rings A, C and D intact and ring B either lactonised, as in toonafolin **1-102**, or opened, as in toonacilin **1-103**; both compounds were isolated from *Toona ciliata* var. *australis* M.J.Roem [96,97].

Toonafolin **1-102** is readily converted into the 1α,11α-oxide toonacilin analogue **1-104** on hydrolysis and treatment with thionyl chloride [97] (scheme 30).

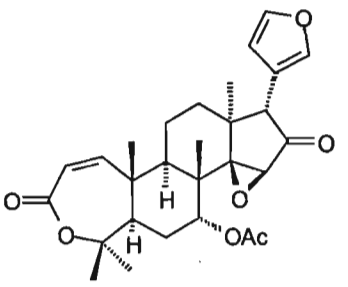


1-102 toonafolin **1-104**

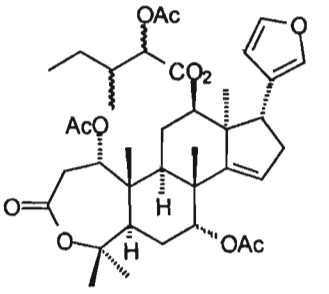
Scheme 30: Synthesis of toonacilin analogue **1-104** from toonafolin **1-102** [97].

1.2.3.9 Class IX: The Evodulone group

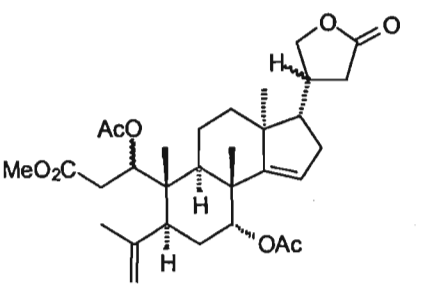
Suspicions of this group's existence preceded the discovery of its first members, evodulone **1-105** from *Carapa procera* DC. [98] and corresponding de-epoxy analogue dregeana 3 **1-106** from *Trichilia dregeana* Sond. [99], as limonoids of this type are generally considered to be precursors for the group X or prieurianin class [22].



1-105 evodulone

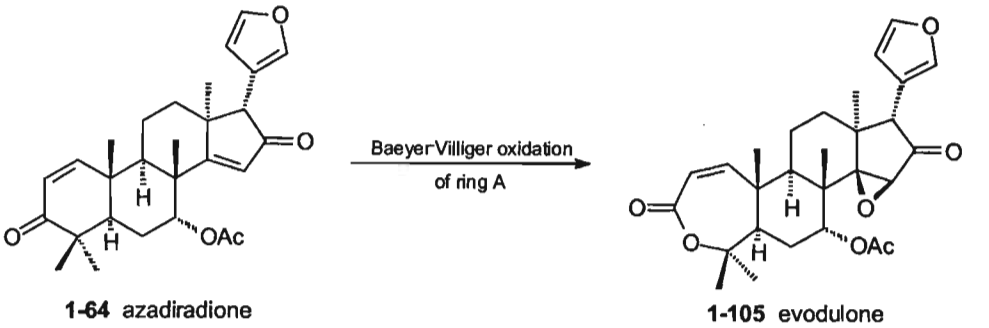


1-106 dregeana 3



1-107 nymania 2

This is a small group with rings B,C and D intact and ring A lactonised; only the furan ring modified nymania 2 **1-107** [100] from *Nymania capensis* (Thunb.) Lindb. has hitherto been reported in which ring A has undergone ring opening. Their biosynthetic origin, by Baeyer-Villiger ring A oxidation of havanensin class precursors, is self-evident; evodulone **1-105** itself is the ring A lactone equivalent of azadiradione **1-64** (scheme 31).

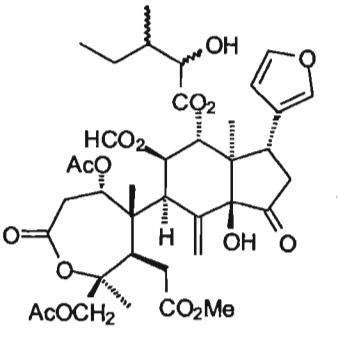


1-64 azadiradione

1-105 evodulone

Scheme 31: Biosynthesis of evodulone **1-105** from azadiradione **1-64.**

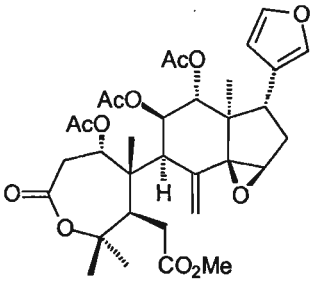
1.2.3.10 Class X: The Prieurianin group



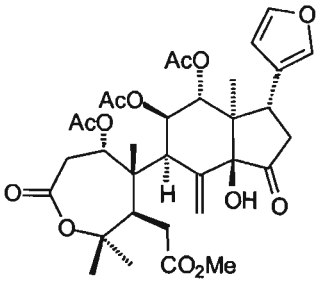
1-29 prieurianin

Prieurianin **1-29** joins phragmalin **1-30** and utilin **1-82** (and limonin **1-25** itself, for that matter) in the company of those limonoids who structural complexities delayed their structural elucidation until well after they were first found. In this case, fully a decade elapsed between the first report [101] and the determination of the complete structure [102]. In prieurianin **1-29** and related compounds, rotation about the C-9,C-10 bond that joins the two parts of the molecule together is restricted, resulting in poorly resolved ^{1}H NMR spectra from which little could be garnered; once this was realised, and the problem circumvented by spectra acquired at 60°C, the structure was readily established, and finally confirmed by an X-ray crystal analysis [102].

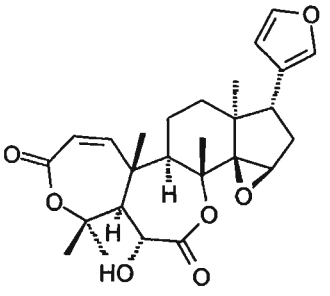
Limonoids of this group have rings C and D intact, and rings A and B oxidised. Theoretically, then, they could arise either by Baeyer-Villiger oxidation of the B ring of an evodulone-type precursor, or from A ring oxidation of a toonafolin-type compound. As mentioned in section 1.2.9, however, the former pathway is supported by the isolation of such ring B-open compounds as nymania 4 **1-108** from *Nymania capensis* [100] and dregeana 2 **1-109** from *Trichilia dregeana* [99], as well as the significant ring intact dilactone surenone **1-110** from *Toona ciliata* [103]†.



1-108 nymania 4



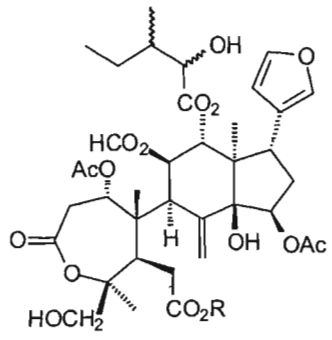
1-109 dregeana 2



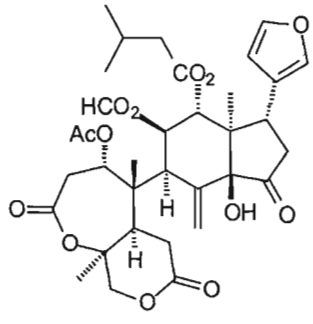
1-110 surenone

The lability of the C-29 hydroxy group in this class is indicated by the fact that Trichilia substance Tr C **1-111** and the related ethyl ester trichilia substance Tr A **1-112** from *Trichilia roka* (Forssk.) Chiov. are the only two compounds to have been reported in which it has not reacted further [104]. Such diverse structures as rohitukin **1-113** from *Aphanamixis polystacha* (Wall.) R.Parker [105] and hispidin A **1-114** from *Trichilia hispida* T.D.Penn. [106] are then easily seen as the 7,29-lactone and 3,29-acetal respectively.

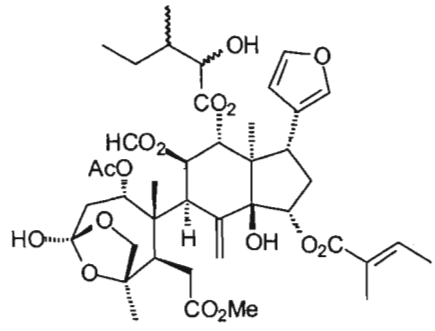
† Although it should be pointed out that this is the only compound of this type reported to date.



1-111 R = Me trichilia substance Tr-C
1-112 R = Et trichilia substance Tr-A

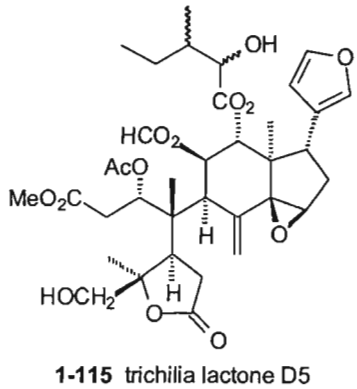


1-113 rohitukin

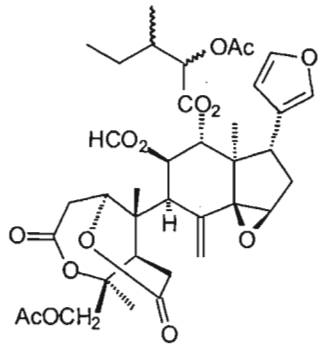


1-114 hispidin A

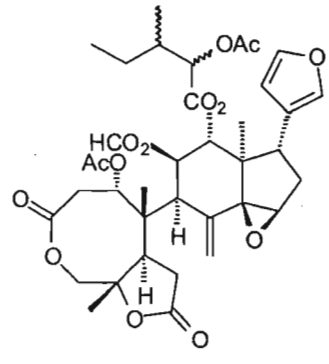
The structure of trichilia lactone D5 **1-115** from *Trichilia prieuriana* [107,108] is less easily accounted for, as it is based very largely on that for dregeanin from *Trichilia dregeana* [109] being the revised structure dregeanin Y **1-117** [110] rather than the originally proposed dregeanin X **1-116** [105]. However the evidence for structure **1-117** rather than **1-116** rests rather gingerly on hydrolysis experiments and unusual IR and ^{13}C NMR spectral data [110]; although trichilia lactone D5 **1-115** follows readily enough from dregeanin Y **1-117**, the structure will be secure only once that of dregeanin has been definitely established by more modern NMR techniques.



1-115 trichilia lactone D5



1-116 dregeanin X



1-117 dregeanin Y

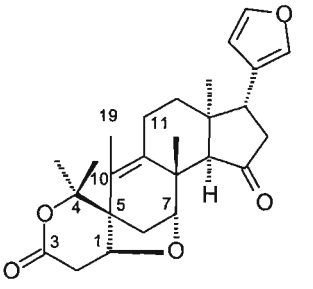
1.2.3.11 Class XI

The carapolide group comprises two subgroups. Class XIa, the carapa spirolactone group, contains only the single compound carapa spirolactone **1-118** from *Carapa procera* [111], while class XIb has as members the seven carapolides A-G **1-119,1-32,1-20,1-121,1-122,1-123,1-124** from *Carapa procera* [112] and *Carapa grandifolia* [113]. Carapa spirolactone **1-118** and carapolide A **1-119** were both originally placed by Taylor in the obacunol group [22], but both of these and the related compounds carapolides B-G **1-32,1-120,1-121,1-122,1-123,1-124** found later are all sufficiently

different, albeit arising from a common biosynthetic origin (scheme 32b), to warrant their removal to form the final new additions to the revised system of limonoid classification [23].

Biosynthesis of these limonoids may occur from either evodulone **1-105** or obacunone **1-92** type precursors. D ring oxidation apparently occurs independently of the modifications of the A and B rings; thus carapa spirolactone **1-118**, in which the D ring is intact, is segregated from the other class XI compounds, which possess a D ring lactone [23] (scheme 32a).

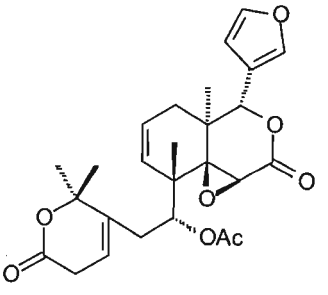
1.2.3.11.1 Class XIa: The Carapa spirolactone group



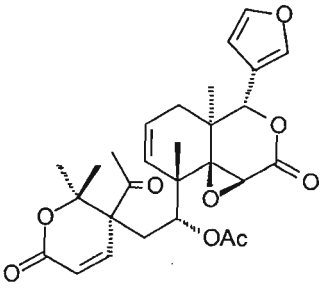
1-118 carapa spirolactone

As mentioned above, together with intact B and C rings, carapa spirolactone **1-118** has an intact D ring, while the 7-membered A ring has contracted to a 1,5-spirolactone *via* cleavage of the C-1,C-10 bond [23] (scheme 32b).

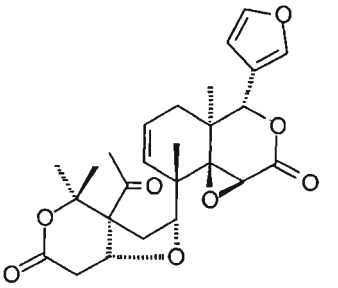
1.2.3.11.2 Class XIb: The Carapolide group



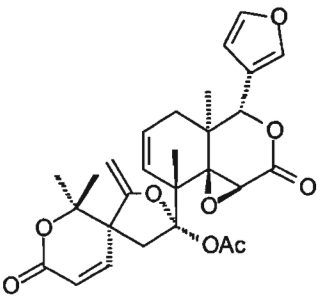
1-119 carapolide A



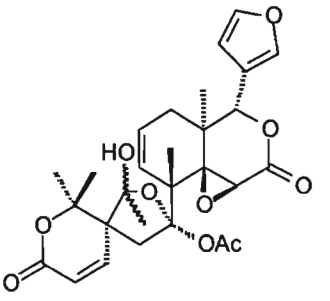
1-32 carapolide B



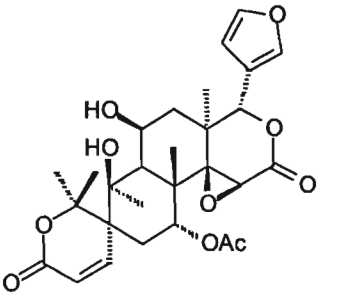
1-120 carapolide C



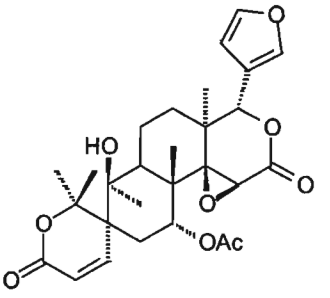
1-121 carapolide D



1-122 carapolide E



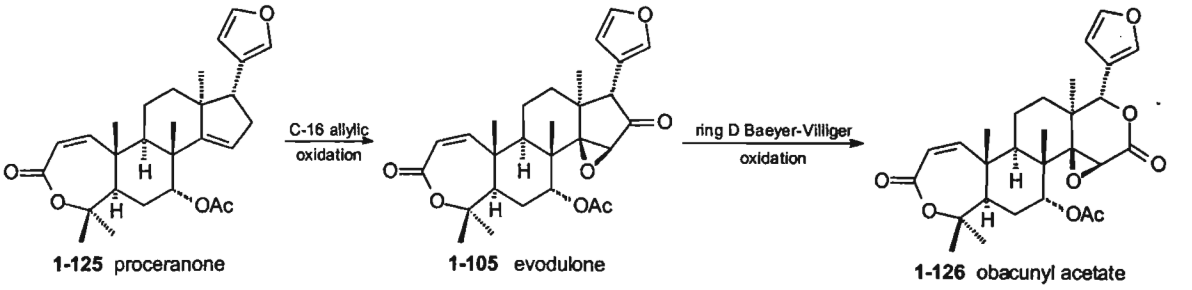
1-123 carapolide F



1-124 carapolide G

In common with carapa spirolactone **1-118**, the carapolides have a contracted ring A and an intact ring C. However, ring D in these compounds has been lactonised, while ring B has undergone C-9,C-10 bond cleavage.

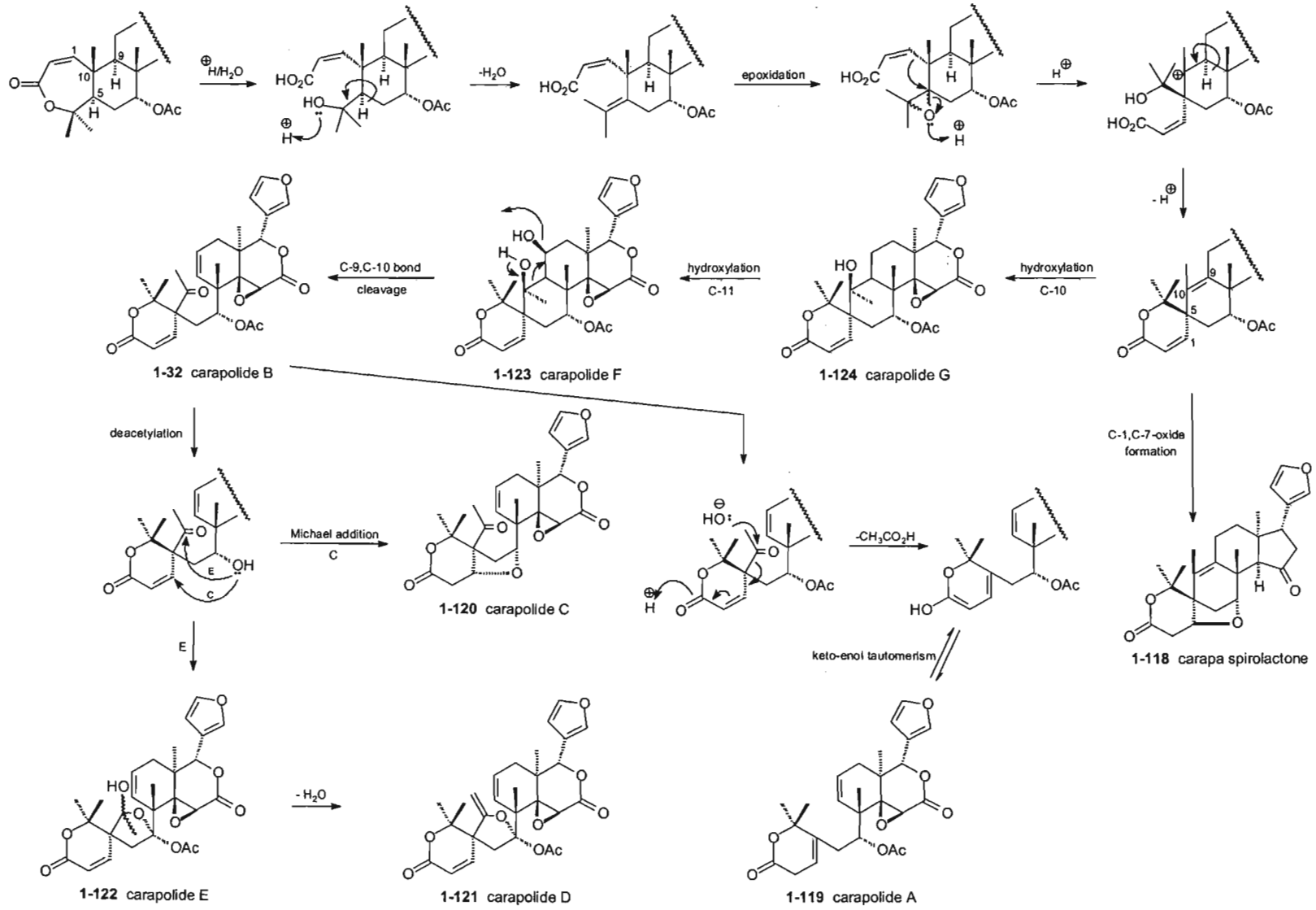
Independent Baeyer-Villiger ring D oxidation



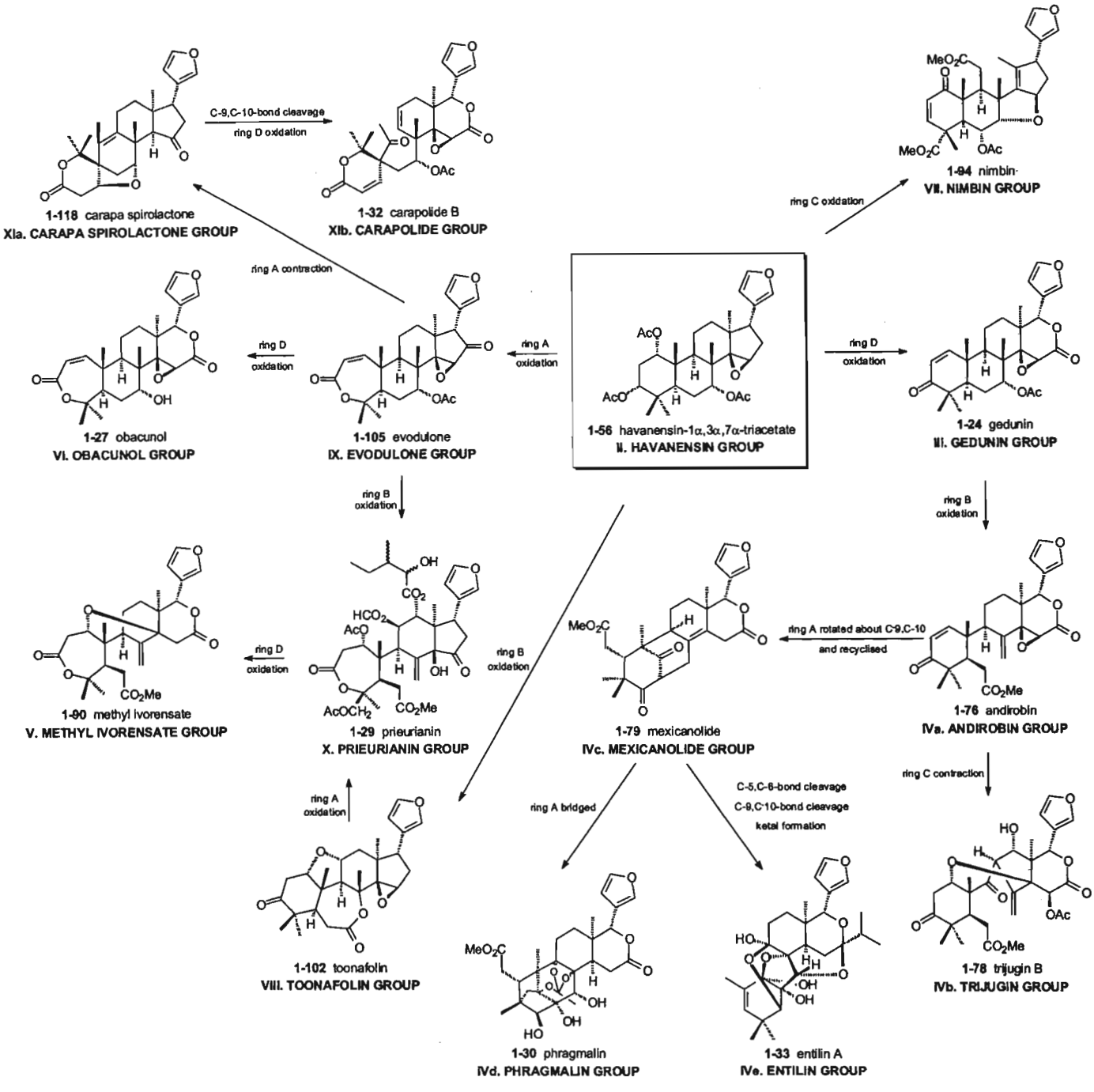
1-125 proceranone **1-105** evodulone **1-126** obacunyl acetate

Scheme 32a: Proposed biosynthesis of carapolide precursor obacunyl acetate **1-126** from proceranone **1-125** *via* evodulone **1-105**.

Ring A/B modification:



Scheme 32b: Proposed biosynthesis of carapolides from precursor obacunyl acetate **1-126** [23].



Scheme 33: Relationships among limonoid classes [23].

The revised overall relationship between the limonoid classes, incorporating the newly added group IVc. (trijugin B **1-78**), group IVe. (entilin A **1-33**), and groups XIa. (carapa spirolactone **1-118**) and XIb. (carapolide B **1-32**) is shown in scheme 33.

1.2.4 The Biological Activity of Limonoids

In the last major review of the biological activity of limonoids, Champagne *et al.* [114] detailed the biological and pharmacological activity of over seventy compounds, which included insect antifeedant and growth regulatory properties, antifungal, bacteriocidal, and antiviral activity, and as diuretics, spermicides, hypoglycaemates, and muscle relaxants. This review specifically excludes the insecticidal and antifeedant activity of azadirachtin **1-95**, which is known to affect over two hundred species of insects and mites [115], but remark in passing that

> "Neem preparations have been used to treat blood disorders, hepatitis, eye diseases, cancer, ulcers, constipation, diabetes, indigestion, sleeplessness, stomachache, boils, burns, cholera, gingivitis, malaria, measles, nausea, snakebite, rheumatism, and syphilis." [114],

while

> "Neem formulations are used as antiseptics, astringents, emollients, febrifuges, anodynes, diuretics, parasticides, pediculicides, purgatives, sedatives, stomachics and tonics." [114].

On a somewhat more modest note, the *Citrus* limonoids limonin **1-25** and nomilin **1-91** have been found to be potent inducers of glutathione *S*-transferase activity in mice [116,117], which reduce the carcinogenic activity of xenocarcinogens by facilitating their excretion, and nomilin **1-91** displays marked tumour development inhibition activity [118].

Limonoids related to swietenine **1-80** and swietenolide **1-81** from *Swietenia mahogani* have been found to have platelet aggregation inhibition properties [119], while the rubrins, a series of prieurianin-class limonoids with an A-ring 3,29 acetal structure like that of hispidin A **1-114**, from *Trichilia rubra* C.DC. are potent cell adhesion inhibitors [120].

Extracts from *Ekebergia capensis* Sparrm. are important in Zulu traditional medicine in South Africa, being used to induce or facilitate labour in pregnant women [121], while the bark of both *Trichilia dregeana* and *Trichilia emetica* is used as an abortifacient [122], and that of *Entandrophragma angolense* as a treatment for peptic ulcers in Nigeria [123].

1.3 Quassinoids and the Simaroubaceae Family

1.3.1 The Simaroubaceae Family

The pantropical Simaroubaceae DC., or Quassia family, was first described by De Candolle in 1811 [124]. In 1964 it was defined in Engler's Syllabus [125] as comprising some thirty-two genera and one hundred and seventy species in six subfamilies.

In contrast to the Meliaceae family, for which the Pennington and Styles monograph [20] is practically the last word on the subject, the Simaroubaceae family is only loosely knit, albeit that its member genera are reasonably well defined, and the question of affinity has given rise to much debate. Five of the subfamilies have subsequently been raised to familial rank [126,127], and the current circumscription [128] of forty-four species in sixteen genera contains only members of the original subfamily Simarouboideae, as is shown in Table 3.

Species of the Simaroubaceae produce tryptophan alkaloids such as β-carbolines and canthinones, anthraquinones, and flavonoids. However, just as the defining characteristic for species of the Meliaceae is their production of limonoids, so the Simaroubaceae are characterised by a group of related structures known as quassinoids, which are discussed further in the following section.

TABLE 3: The Simaroubaceae family

(Numbers in brackets indicate number of species in genus [128])†

SUBFAMILY 1	Simarouboideae
Tribe	**Genus**
1. Simaroubeae	*Pierreodendron(1), Samadera(1), Simarouba(3), Simaba(4), Hannoa(2), Odyendea (1) Quassia(3), Eurycoma(1)*
2. Picrasmae	*Castela(4), Holacantha(1), Brucea(5), Perreira(2), Picrasma(4), Picrolemma(1), Ailanthus(6)*
3. Soulameae	*Soulamea(6)*

† These authors exclude the genus *Harrisonia* from the family, citing an earlier finding [129] that :

> "...the genus *Harrisonia* is exceptional: alkaloids and quassinoids seem to be absent while chromones and limonoids suggest affinity with Rutaceous genera."

See further discussion on following page.

1.3.2 Quassinoids

The quassinoids or simaroulides comprise a unique group of extremely bitter-tasting terpenoid compounds found almost exclusively in the Simaroubaceae family. They are of particular interest as they share a common biosynthetic pathway with the limonoids, yet the latter are confined to the Meliaceae and Rutaceae, other families within the Rutales. Over three hundred quassinoids have been isolated and characterised to date; only one report of the isolation of both limonoids and quassinoids from within a single species has appeared [21]. This is from the genus *Harrisonia*; as previously mentioned, the position of this genus within the family is currently being reconsidered (see footnote, p.7).

Many species of this family, and two in particular, *Quassia amara* L. (Surinam quassia) and *Picrasma excelsa* (Sw.) Planch. (Jamaica quassia), have long been known to contain bitter substances known collectively as "quassin". The Aztecs reportedly used a tea prepared from the wood as an aperitif, digestive tonic, diuretic and laxative, while West Indian natives apparently

> "...carved "quassia cups" out of the wood, added hot water, and let these stand long enough that the extremely bitter resin in the wood would be drawn into the water. They then sipped the mixture when indigestion or other stomach upsets developed or the appetite needed a boost." [130].

Quassin is currently used in a variety of herbal and homeopathic remedies for stomach-soothing and bile-stimulating† purposes [130], the treatment of such diverse disorders as thrush, mouth fungal and sinus infections, eczema [132], anorexia nervosa, fever, blennorrhagia, liver disorders and malaria [133], and as a flavourant in foods, liqueurs and tonic wines [130]. It is also an effective pesticide and insect repellent [130,134], particularly against lice [130,133], and, in Australia, in preventing possums nesting inside the roofs of houses [135].

Usage within the ethnobotanical and traditional medical fields notwithstanding, the enormous increase in interest that has arisen in compounds of this nature is the result of the discovery that they display marked antileukemic activity and a wide range of other biological properties.

1.3.3 A Brief Historical Review of the Biosynthesis, Structural Elucidation, and Biological Activity of Quassinoids

Chemical studies on the structures of these compounds were initiated in 1950 with the first separation of quassin **1-127** and neoquassin **1-128** from the wood of *Quassia amara* [136]. Despite the subsequent accumulation, by early researchers, of a considerable body of structural information [137-

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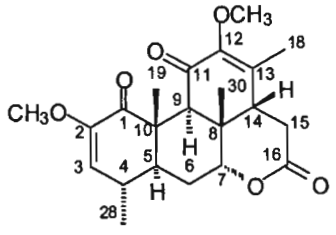
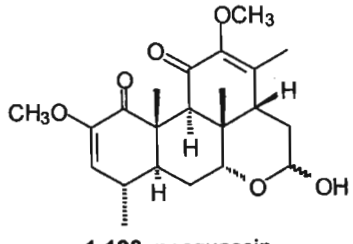
† Not only bile stimulating, it appears. From a recent report [131] on *Eurycoma longifolia* Jack, also known as "tongkat ali":

> **"Jungle boogie"**
>
> Kuala Lumpur - Malaysia has patented a jungle plant reputed to boost male sex drive and says developing 'tongkat ali' will give the country a big push into the herbal medicine industry. Villagers have long used tongkat ali, which means 'Ali's walking stick' and describes the shape of the plant's root, to improve blood circulation and cure skin diseases.
>
> "An aphrodisiac is not its only benefit ... your energy level increases, you are more fit, more alert. When your energy increases you can do many things," said the director of medicinal plants at the Forest Research Institute Malaysia (FRIM), Azizol Abdul Kadir. FRIM has taken out two local patents on tongkat ali and applied for three others in a bid to protect Malaysian interests as multinational drug companies scour the world's rainforests in search of new products.
>
> Tongkat ali could be marketed next year as a "health enhancer" that in time could outsell ginseng, Azizol said. The plant's legendary aphrodisiac effect has made it a popular additive at even the smallest roadside tea stalls and spawned 140 brands of tongkat ali pills.
>
> For four years FRIM has led the country's research into tongkat ali, one of 1 300 Malaysian jungle plants said to have medicinal properties. The plant also grows in neighbouring Thailand and Indonesia. In May, Malaysia unveiled plans for its $13.2 billion biotechnology industry. With 85 researchers from various government agencies, the tongkat ali project is a test case for that future 'BioValley', said Azizol.
>
> The local market for herbal remedies is worth $526,000 annually, Azizol said. Sales of herbal remedies in the United States totalled $15 billion in 1999.
>
> FRIM is now testing tongkat ali pills on volunteers. Early results were "very positive", said Azizol."

139], the complete structures were finally established only in 1962 [140,141] by a combination of classical chemistry and the (then) novel technique of ^{1}H NMR spectroscopy.

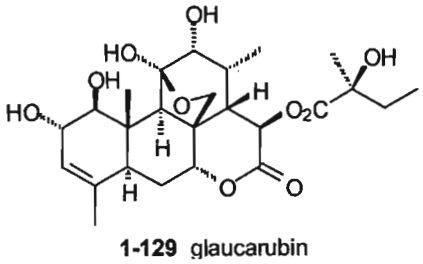


1-127 quassin

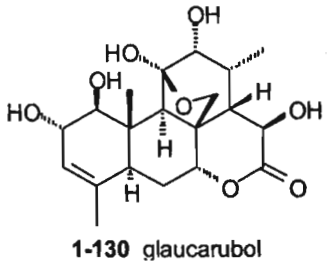


1-128 neoquassin

Among the earliest C_{20} quassinoid structures to be established after quassin **1-127** and neoquassin **1-28** were those, in 1964, of glaucarubin **1-129** and its related C-15 parent alcohol glaucarubol **1-130** [142,143] from the seeds of *Simarouba glauca* C.DC. The stereochemistry was unambiguously confirmed by an X-ray crystal structure determination for glaucarubin **1-129** shortly thereafter [144]. In this compound C-30 has been oxidised to a hydroxymethyl group, which has then formed a hemiketal linkage to a carbonyl group at C-11.



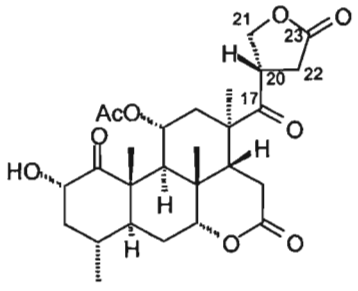
1-129 glaucarubin



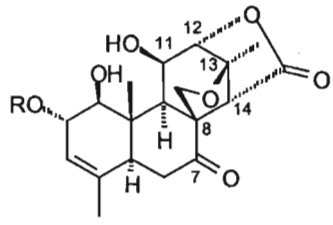
1-130 glaucarubol

In the same year the X-ray crystal structure [145] of simarolide **1-131** from the bark of *Simarouba amara* Aubl. was published [146]. The first account of a quassinoid with a tetracyclic C_{20} nucleus similar to that of quassin **1-127**, but with an additional five carbon atom sidechain containing a ketone at C-17 and a γ-lactone ring, the absolute stereochemistry of simarolide **1-131** was shown to be identical to that found in triterpenoids.

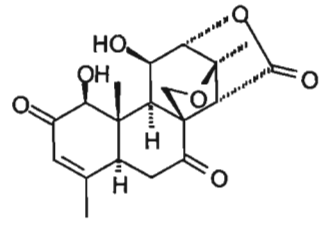
Also described in 1964 [147] were samaderine C (**1-132**, R = H) and its 2-keto analogue samaderine B **1-133** from *Samadera indica* Gaert., the first examples of a quassinoid with a C_{19} skeleton, an ether linkage between the C-30 hydroxymethyl group and C-13 rather than C-11, and in which the 7,14-δ-lactone has been replaced by a γ-lactone between C-14 and C-12.



1-131 simarolide



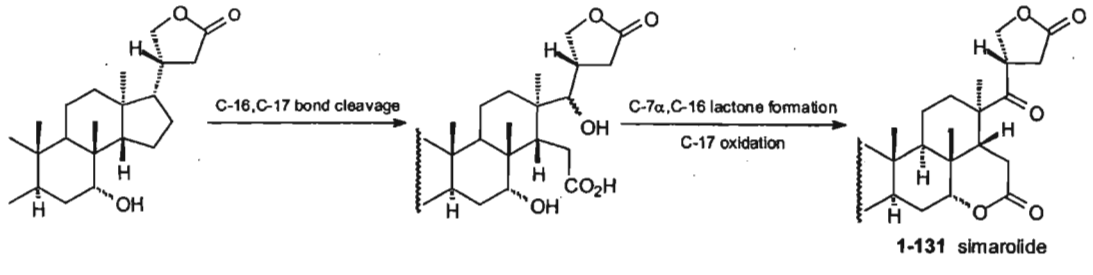
1-132 samaderine C



1-133 samaderine B

The immediately noticeable resemblance between the simarolide **1-131** sidechain γ-lactone and the characteristic limonoid furan ring, in addition to the highly important stereochemical synonomy, supported a series of earlier results [143,148-151] suggesting that these compounds represented a later stage in the same biosynthetic pathway.

This proposed biosynthesis [143,152†,153] has in common with that of the limonoids [26] both the loss of the four terminal sidechain carbon atoms and consequent formation of the preliminary sidechain lactone, and the apo change necessary to establish the methyl group at C-8β and hydroxy group at C-7α. However, conversion of the sidechain lactone to the fully-fledged limonoid furan ring does not occur, and in addition one of the methyl groups at C-4 (shown later to be that in the α/equatorial position, and discussed more fully later on) is also lost. Cleavage of the C-16,C-17 bond and subsequent lactonisation of the carboxyl group at C-16 with the hydroxy group at C-7α, followed by oxidation of the hydroxy group at C-17, yields the basic skeleton of simarolide **1-131** (scheme 34).



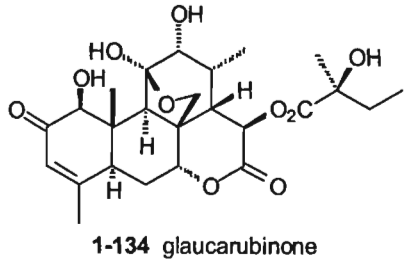
1-131 simarolide

Scheme 34: Formation of the simarolide**1-131** C-ring lactone and C-17 ketone.

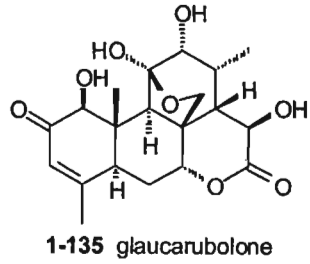
† Where the term "quassinoid" is first used to describe collectively the "bitter principles of the quassin group".

A great deal of effort in the late 1960's and early 1970's focussed on the further elucidation of the biosynthetic pathways leading to the then recently discovered C_{19}, C_{20}, and C_{25} quassinoid skeleta, and the elaboration of the relationship between these compounds and the closely related limonoids. However, the triterpenoidal origin of the quassinoids in general – the X-ray crystal structures of glaucarubin **1-129** and simarolide **1-131** notwithstanding – can be considered to have been unequivocally established only by the results of a series of tracer experiments, in which the proposed quassinoid biosynthetic pathway was experimentally verified using labelled mevalonate precursors [154-157].

Further investigation of the seeds of *Simarouba glauca* [158] had revealed, among others, the presence of two further "...minor principles...", which were reported to be the 2-keto analogues (*via* correlation by manganese dioxide oxidation) of glaucarubin **1-129** and glaucarubol **1-130**. These were named glaucarubinone **1-134** and glaucarubolone **1-135** respectively.



1-134 glaucarubinone



1-135 glaucarubolone

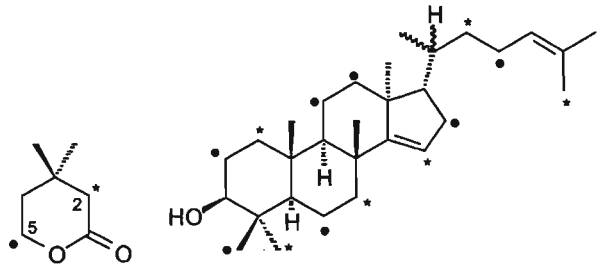
Both 2-^{14}C-(2*) and 5-^{14}C-(5°)-mevalonic acid lactone (MVA) **1-136** were incorporated into glaucarubinone **1-134** and glaucarubulone **1-135** *via* viable seeds of *Simarouba glauca.* The expected labelling patterns in the proposed apo-euphol/tirucallol triterpenoid precursor **1-137** and in glaucarubolone† **1-135** are indicated respectively by the symbols* and °.

---

† It is not immediately clear why these "minor principles" rather than, say glaucarubin **1-129**, which is reported as "...the major bitter constituent..." of *Simarouba glauca* seeds, were used, given the low levels of radioactive incorporation that bedevil tracer research in general and the reported failure of similar attempts to introduce 2-^{14}C mevalonic acid into limonoin in the seeds of *Citrus* species [159]. Polonsky [153] remarks only that

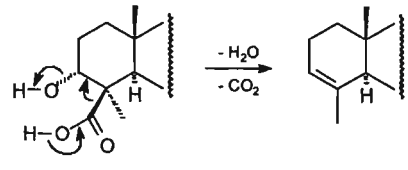
> "Glaucarubinone or glaucarubolone react readily with diazomethane to give...1-O-methyl derivative[s]...[which]...was shown to be a suitable starting material for the degradations required in the biosynthetic studies.".

Hydrolysis of the radioactive C-15 ester glaucarubinone also isolated from both 2-^{14}C and 5-^{14}C MVA incorporation immediately established that the acid residue, derived from isoleucine, was inactive and thus that labelling had occurred only in the C_{20} skeleton [156].



1-136 **1-137** apo-euphol/tirucallol **1-135** glaucarubolone

Kuhn-Roth oxidation of 2-^{14}C glaucarubolone produced only inactive acetic acid, establishing that the three methyl groups at C-4,C-10 and C-13 were unlabelled and, specifically, that the methyl group at C-4 was derived from the methyl group of MVA and thus from the β axial methyl group in the triterpenoid precursor†. A previous suggestion [44] that the loss of a methyl group at C-4 arose as a result of a *trans* elimination-decarboxylation involving a C-3α hydroxy and a C-4β carboxy group (scheme 35) was thus superseded‡ by a mechanism involving formation of a 3-keto triterpenoid precursor common to all quassinoids and subsequent decarboxylation of the resulting β-keto-acid (scheme 36). The suggested six membered transition state required for this transformation is much more easily achieved *via* a C-4 equatorial carboxyl residue than would be the case if it were placed axially§.

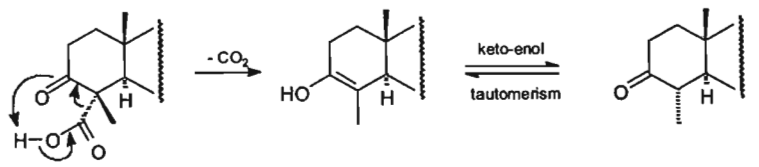


Scheme 35: Loss of C-4 axial methyl group by *trans* elimination-decarboxylation [44].

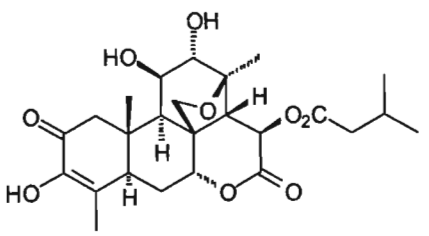
† The results of these experiments, conducted over a five-year period, were described in detail in two early reviews [152,153]. The triterpenoid precursor C-4 methyl groups in the latter publication are unfortunately mislabelled, which threatens to derail the entire thrust of the argument.

‡ This suggestion, proposed before the results of the labelling experiments became available, was also made at a time when no naturally occurring quassinoid with oxygenation at C-3 had been isolated, and was thus further discounted by the later discovery of bruceins A,B and C **1-138,1-139,1-140** from the seed of *Brucea amarrissima* Merr [160].

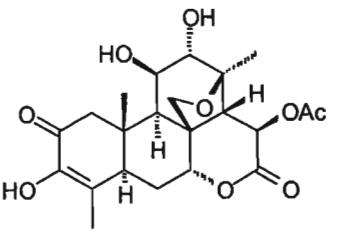
§ And, incidentally, could explain how loss of the α/equatorial methyl group from the triterpenoid precursor could yet afford the equatorial C-28 methyl group at C-4 observed in simarolide **1-131**, as the keto-enol tautomerism invoked to re-establish the C-3 ketone would presumable favour formation of the more stable equatorial methyl substituent.



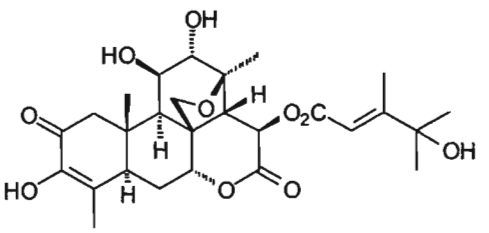
Scheme 36: Loss of C-4 equatorial methyl group by decarboxylation *via* a six membered transition state [153].



1-138 brucein A



1-139 brucein B

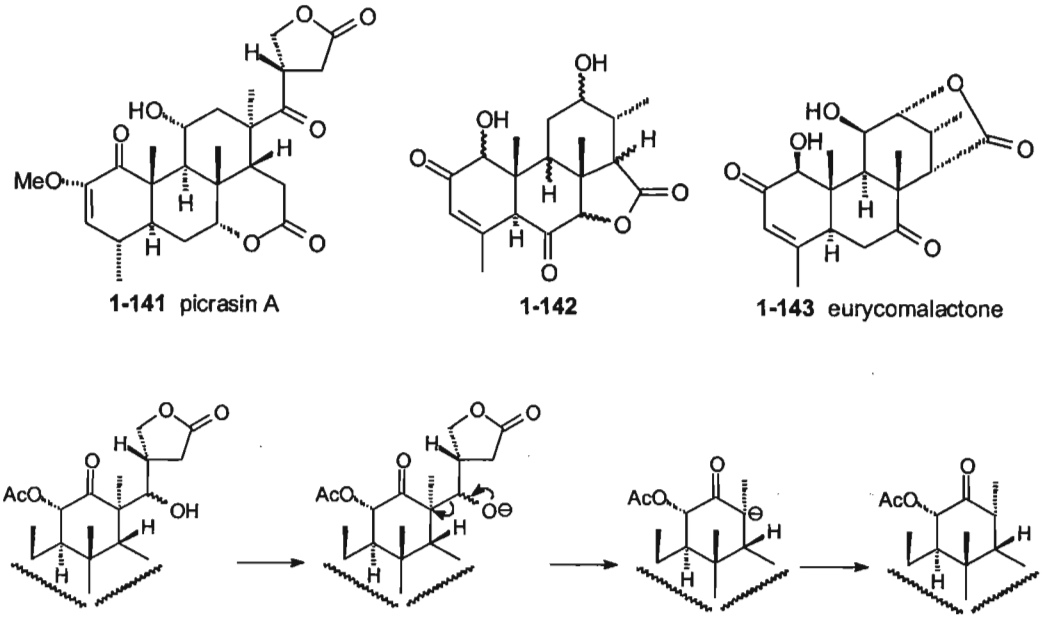


1-140 brucein C

Further degradative studies showed that C-1 and C-15 were labelled by (2*), and C-12 and C-16 by (5*) MVA respectively, in accordance with the proposed quassinoid biogenesis from triterpenoid precursors; in particular, the presence of five labelled carbon atoms in 5-^{14}C glaucarubolone established unambiguously the triterpenoidal origin of these compounds, and thus that they should indeed be regarded as degraded triterpenoids.

The argument, as it is for the limonoids, as to whether they form directly from a cationic dammarane intermediate resulting from the cyclisation of squalene, or indirectly *via* the apo change from a euphol/tirucallol precursor has been previously discussed in Section 1.2.3 and will not be repeated here. It should be noted, however, that - as discussed in more detail later - the group D C_{25} quassinoids such as simarolide **1-131** isolated thus far are uniformly *S* at C-20, which would appear to favour a tirucallol rather than euphol origin.

The structure of the second C_{25} quassinoid to be characterised was reported independently in 1970 as picrasin A **1-141** from the wood of *Picrasma quassiodes* Bennet [161] and nigakilactone G from *Picrasma ailanthoides* Planchon [162]. By this time the structures of some further twenty novel C_{20} quassinoids had been established, together with those of five C_{19} structures, which, without exception, were oxygenated at C-12. The absence of an oxygen atom at C-12 in either simarolide **1-131** or picrasin A **1-141**, and the already noticeable predominance of C_{20} quassinoids over their much scarcer C_{25} and C_{19} counterparts was rationalised [153,163] on the basis that the C_{25} quassinoids were intermediates in the biosynthesis of the other groups, in which the required cleavage of the C13,C-17 bond is facilitated either by the presence of a 12,17-dione† or by retroaldol reaction of the corresponding 17-ol-12-one (scheme 37). Formation of the C_{19} quassinoids then requires the additional loss of C-16, by a process for which a satisfactory explanation has yet to be advanced.



Scheme 37: Cleavage of C-13,C-17 bond by retroaldol rearrangement

† C-13,C-17 bond cleavage *via* a β-diketone intermediate was first suggested by Hikino [163]. Although the hypothesis has been much quoted by subsequent authors, no mechanism, to our knowledge, has yet appeared. In addition, both processes result in a ketone at C-12, of which fewer than ten such examples have been reported to date. The argument that such cleavage does occur, but that the resultant C-12 ketone almost invariably then undergoes reduction and/or subsequent methylation/dehydration is surely refuted by the wide variety of quassinoids reported with keto groups at C-1, C-2, C-3 and elsewhere. Even less unlikely, as in the case of simarolide **1-131** itself, is the Wolf-Kishner/Clemmenson type cleavage needed to produced an unsubstituted C-12.

By 1973 the number of quassinoids characterised totalled some fifty-five examples, of which the majority (forty-six, or ~84%) were members of the C_{20} decanortriterpenoid, or picrasane class, while the C_{25} group was unchanged at the two mentioned earlier and the C_{19} group had increased by two [153]. One of these was eurycomalactone, which was originally assigned [164] structure **1-142** containing a hitherto unreported 7,14-γ-lactone, but which was subsequently revised to that of **1-143** by X-ray crystallographic analysis [165].

In her review [153] Polonsky subclassified the C_{20} quassinoids further on the basis of variations in the structure of ring A (figure 1).

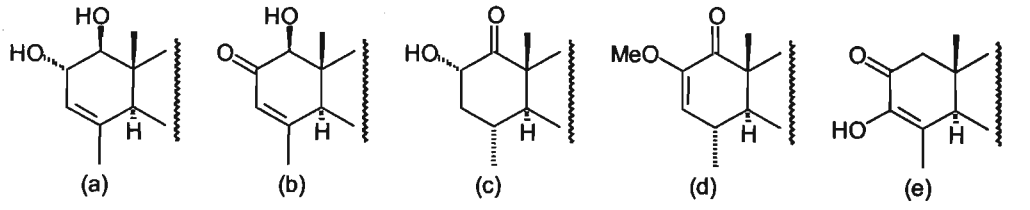
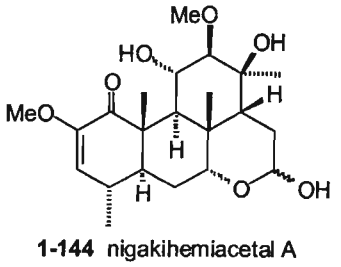
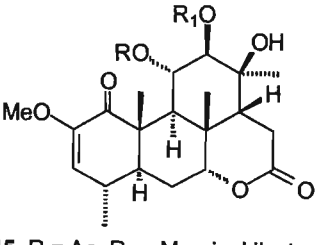


Figure 1: Subclassification of the the C_{20} quassinoids by variations in the structure of the A ring [153].

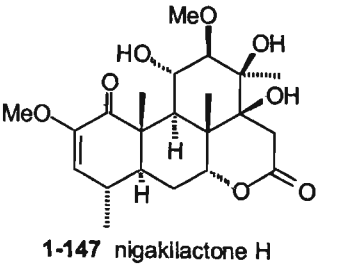
She also noted that C-30 in these compounds, without exception, occurred either as an unoxidised methyl group (as in quassin **1-127**) or as a hydroxymethyl moiety which had undergone further reaction to form either a hemiketal linkage to C-11 (as in glaucarubin **1-129**) or an ether bridge to C-13 (as in brucein A **1-138**).



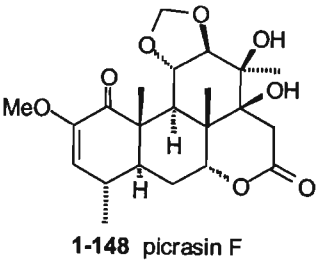
1-144 nigakihemiacetal A



1-145 R = Ac R_1 = Me nigakilactone E
1-146 R = H R_1 = Me nigakilactone F



1-147 nigakilactone H



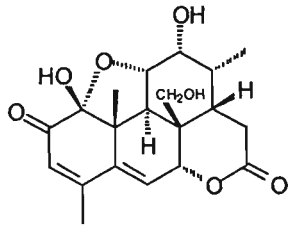
1-148 picrasin F

At that time no C_{20} quassinoid had been found with a C-30 hydroxymethyl group *not* involved in bonding to C-11 or C-13, while nigakihemiacetal A **1-144** and the closely related nigakilactones E,F and H **1-145,1-146,1-147** from *Picrasma ailanthoides* [162,166,167], and picrasin F **1-148** from *Picrasma quassioides* [168] had been shown to possess an unoxidised C-30 methyl group and a hydroxy substituent at C-13β.

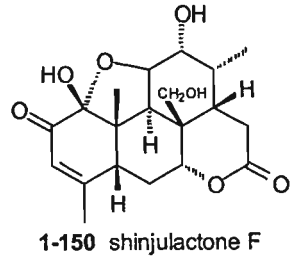
This would appear to suggest that whereas the 11,30-hemiacetal linkage arises as a result of initial oxidation of the C-30 methyl group to a primary alcohol, and which reaction is presumably sufficiently facile to occur without exception once the initial oxidation has taken place, the 13,30-ether bridge arises from attack of the C-13β-hydroxy group and occurs less readily.

Subsequent results have not supported the latter suggestion. Of the sixty-six C_{20} quassinoids with a 13,30-ether bridge isolated to date, all but nine have been reported from the genus *Brucea*, and none at all from *Picrasma*; on the other hand, twenty-eight of thirty-three compounds with the hydroxy group at C-13β originate from *Picrasma*, with none reported from *Brucea*. Although these two genera are included in the same subtribe, the Picrasmeae, they have previously been characterised as chemically very different [128]. If the hydroxy group at C-13β was indeed an intermediate in the formation of the 13,30-ether bridge, it seems logical to assume that at least one report of both types of compound occurring as co-isolates would have appeared.

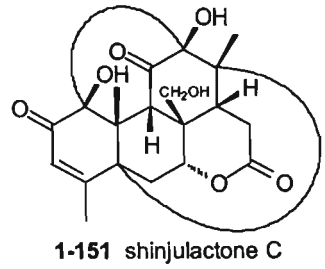
The former proposal, however, appears to have been verified. Only four compounds have subsequently been characterised possessing a hydroxymethyl group at C-30; in two of these, karinolide **1-149** from *Simaba multiflora* A.Juss [169] and shinjulactone F **1-150** from *Ailanthus altissima* Swingle [170], formation of the 11,30-hemiacetal has presumably been pre-empted by that between C-1 and C-11, while the steric constraints introduced by formation of the C-1,C-12 and C-5,C-13 bonds in shinjulactone C **1-151**, also from *Ailanthus altissima* [171] prevent it occurring here. Only shinjulactone G **1-152**, again from *Ailanthus altissima* [172], admits no explanation.



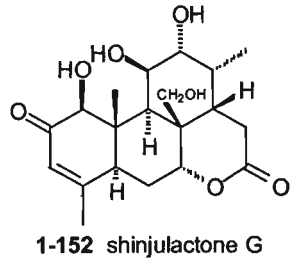
1-149 karinolide



1-150 shinjulactone F



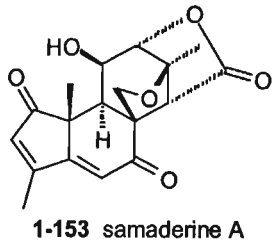
1-151 shinjulactone C



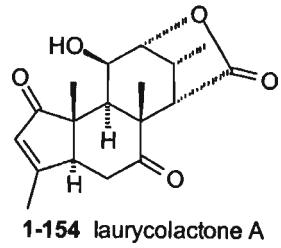
1-152 shinjulactone G

Interest in quassinoids increased dramatically in the years following the first Polonsky review [153] and was fuelled mainly by the discovery that these compounds displayed marked antileukemic activity. As a result, the period between 1973 and the second Polonsky review in 1985 [173] saw an enormous increase in the number and complexity of quassinoids characterised, coupled to an even larger surge in research into their biological activity. Thus, in contrast to a mere two references to the amoebicidal activity of glaucarubin **1-131** [174], and the use of quassinoidal principles in antiamoebic herbal medicines [175] in the initial review in 1973, the second contains references to bioassay studies on over forty compounds.

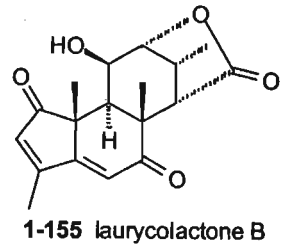
A number of extractives isolated in this period displayed new structural features. These included the discovery of new groups of quassinoids with C_{19} and C_{25} skeleta, those with a hitherto unreported C_{18} skeleton, and a wide variety of variations on the picrasane skeleton, which has continued to provide the vast majority of compounds reported.



1-153 samaderine A

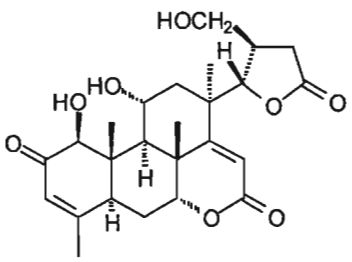


1-154 laurycolactone A

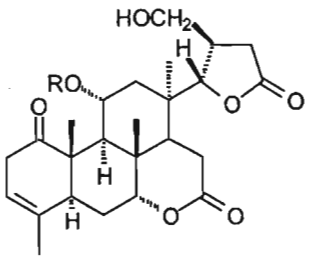


1-155 laurycolactone B

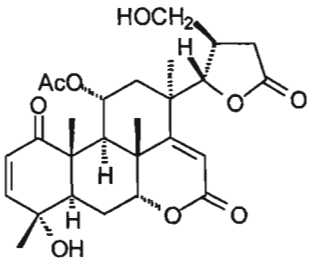
The C_{18} quassinoid group, in which ring A has undergone further contraction, currently comprises only three compounds. Samaderine A **1-153**, first isolated from *Samadera indica* in 1962 [176], was fully characterised, by X-ray crystallography, only in 1978 [177]. Laurycolactones A **1-154** and B **1-155** were subsequently isolated from the Vietnamese *Eurycoma longifolia*; their structures, likewise, were established by X-ray analysis [165].



1-156 soulameolide



1-157 R = Ac simarinolide
1-158 R = H



1-159 guanepolide

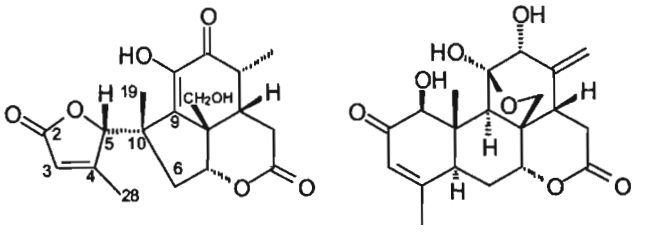
The new C_{25} quassinoid skeleton is very closely related to that existing in compounds already isolated, differing only in that construction of the sidechain lactone occurs *via* a hydroxy group at C-17 rather than at C-21. As for simarolide **1-131**, the structure of soulameolide **1-156** from the trunk bark of the New Caledonian species *Soulamea tomentosa* Brogn. et Gris and the first representative of this class, was based on a X-ray analysis [178]. Shortly thereafter three further compounds, simarinolide **1-157**, its deacetyl analogue **1-158** [180] and guanepolide **1-159** were reported from the fruits of *Simaba multiflora*† [179]. Guanepolide **1-159** was the first quassinoid reported to have an equatorially oriented hydroxy group at C-4 in addition to the axially oriented methyl group; the pathway quoted does not specify exactly how this occurs, but presumably nucleophilic attack on the C-4 carbocation resulting from migration of the Δ^3-double bond to the Δ^2 position is less sterically hindered by H-5α than by 3H-19.

The lack of oxygenation at C-12 in all four of these compounds supports further the hypothesis advanced earlier that the cleavage of the C-13,C-17 bond necessary for the formation of the far more commonly occurring C_{20} skeleton is facilitated by the presence of an oxygen atom at this position.

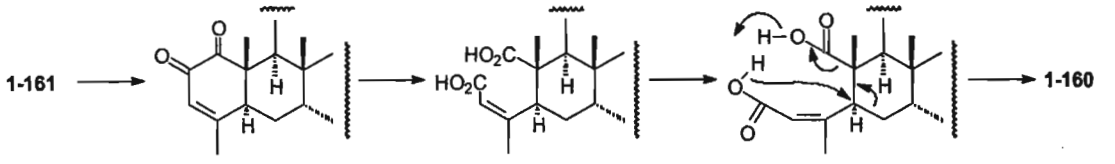
---

† Quoted in [173] as "...*Simaba* cf *orinocensis*, which has recently been revised to *Simaba moretii* Feuillet." *S Simaba orinocensis* Kunth is currently considered [51,181] synonymous with *Simaba multiflora*; no mention is made of *Simaba moretii*.

The new C_{19} skeletal class is represented in the period 1973-1985 by only one compound. The structure of shinjulactone B, from *Ailanthus altissima* [182], was unequivocally characterised as **1-160** by X-ray crystallography. The stereospecific *R* configuration at C-5 was considered to arise from a mechanism involving cleavage of the C1,C-2 bond of a 1,2-diketo precursor, followed by concerted nucleophilic attack on C-5, decarboxylation, and simultaneous contraction of ring B (scheme 38).

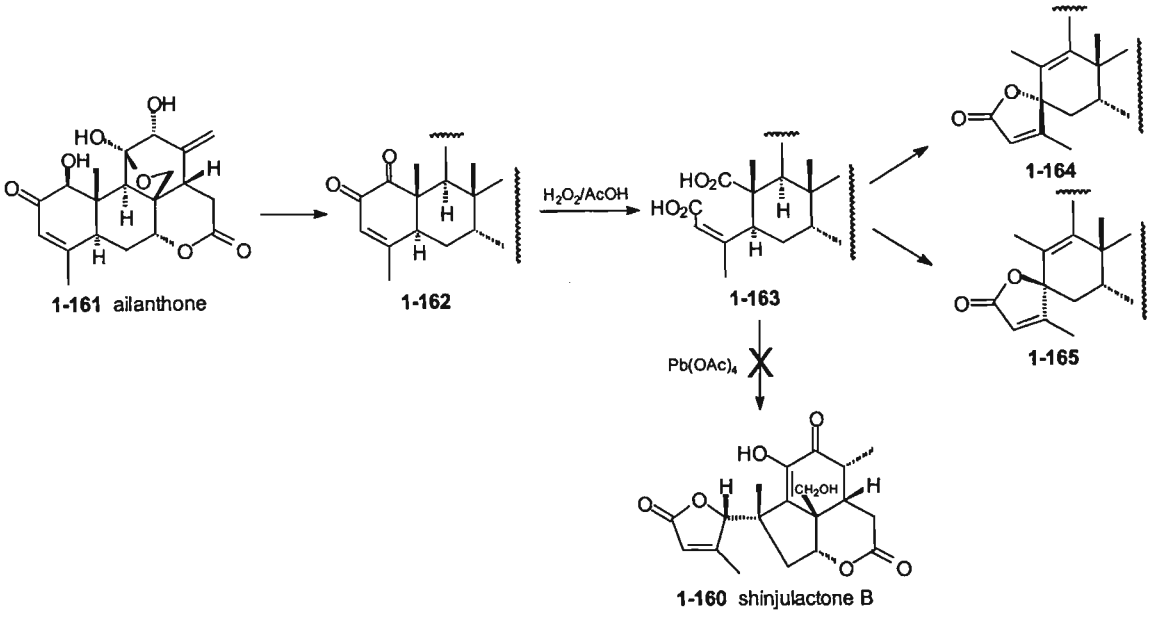


1-160 shinjulactone B **1-161** ailanthone

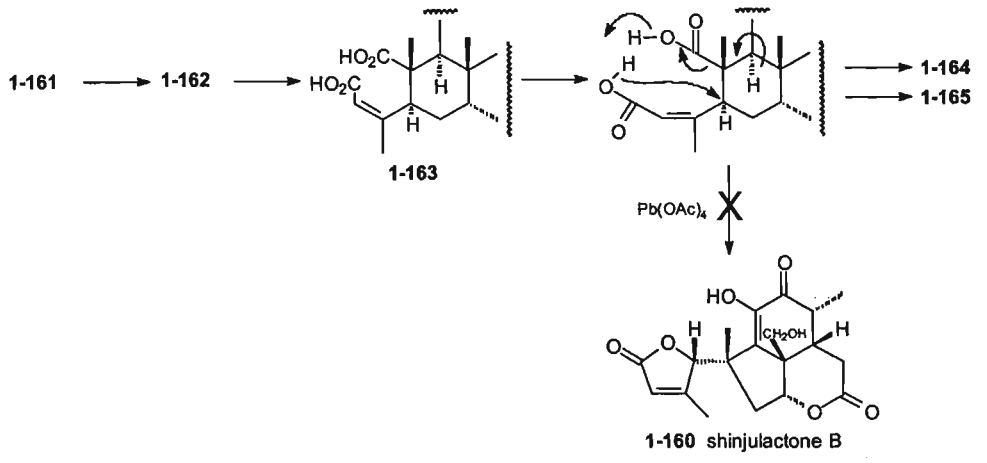


Scheme 38: Proposed biosynthesis of shinjulactone B **1-160** from ailanthone **1-161** [182].

Subsequent attempts by the same authors to convert the dicarboxylic acid **1-163**, prepared from ailanthone **1-161** *via* the dione **1-162** [183,184], into shinjulactone B **1-160** were unsuccessful, resulting instead in the formation of the spiro derivatives **1-164** and **1-165** (scheme 39). This was rationalised on the basis that decarboxylation at C-10 was followed, not by the desired C-5,C-10 bond migration, but by deprotonation at C-9, whose acidity is unusually enhanced by the ketone at C-11 [183] (scheme 40).



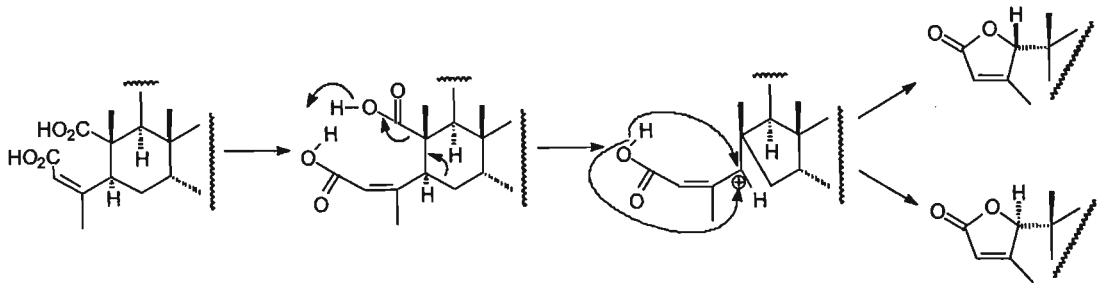
Scheme 39: Attempted *in vitro* conversion of ailanthone **1-161** into shinjulactone B **1-160** [183,184].



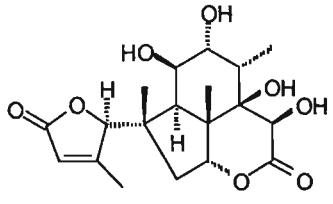
Scheme 40: Proposed mechanism for formation of spirolactone sideproducts **1-164** and **1-165** during attempted *in vitro* conversion of ailanthone **1-161** into shinjulactone B **1-160** [183].

The simultaneous isolation, from the same plant, of C_{25} quassinoids of this type with both *R* and *S* configurations at C-5 has subsequently been reported, suggesting that a somewhat different mechanism may be in operation. Thus eurylactones A **1-166** and B **1-167**, from *Eurycoma longifolia* [185], and more recently, polyandrol **1-168** and its C-5 epimers **1-169** and **1-170**, from *Castela polyandra* [186,187], can arise only if the C-10 decarboxylation and C-5,C-10 bond migration steps

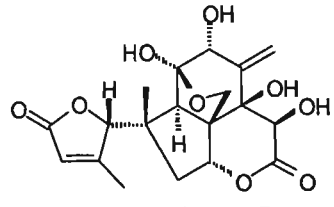
occur first, producing a carbocation intermediate which can then undergo nucleophilic attack from either side (scheme 41)†.



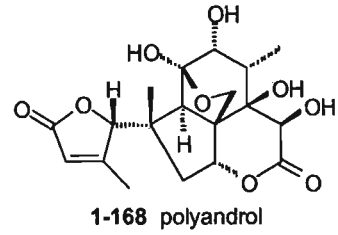
Scheme 41: Formation of both *R* and *S* configurations by nucleophilic attack on cation at C-5.



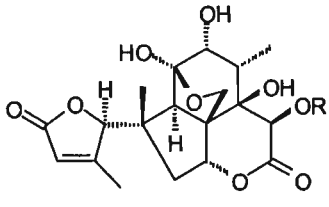
1-166 eurylactone A



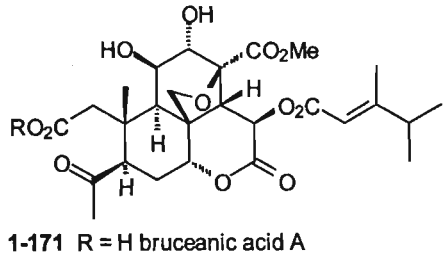
1-167 eurylactone B



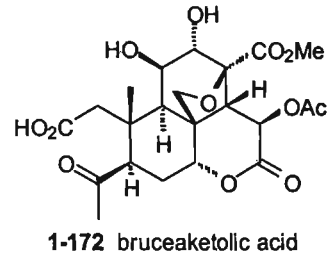
1-168 polyandrol



1-169 R = H
1-170 R = Ac



1-171 R = H bruceanic acid A
1-176 R = Me bruceanic acid A methyl ester

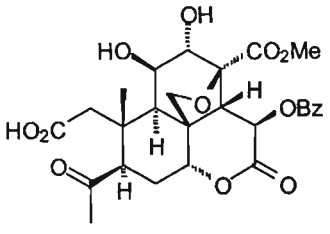


1-172 bruceaketolic acid

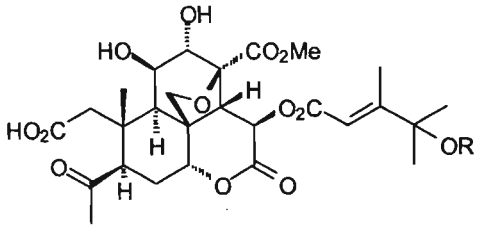
Bruceanic acid A **1-171**, the first of a series of *seco*-ring A C_{20} quassinoids, was isolated in 1975 from an Ethiopian sample of *Brucea antidysenterica* Mill [188]. Bruceaketolic acid **1-172** was subsequently reported from *Brucea javanica* (L.) Merr. [189] and more recently a reinvestigation of *Brucea*

† Itokawa *et al.* [185], in their discussion on eurylactones A **1-168** and **1-169**, note specifically that "...one of the most interesting features in **1** [eurylactone A] is that the configuration at C-5 is opposite to that in **2** [eurylactone B]." They mention the previously proposed biosynthesis [182], but then conclude, without further discussion, that "Compounds **1** and **2** were also considered to be derived by a similar pathway...and each configuration at C-5 was identical with the proposed biogenetic pathway." The logic behind this line of reasoning is not clear.

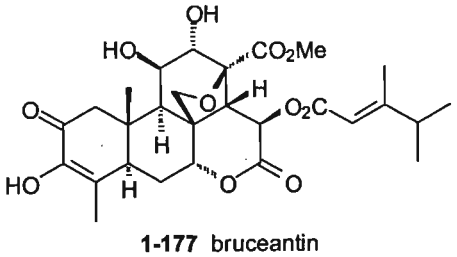
antidysenterica yielded bruceanic acids B **1-173**, C **1-174** and D **1-175**, and the methyl ester of bruceanic acid A **1-176** [190][†].



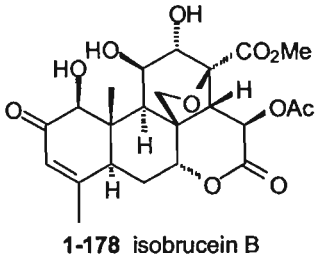
1-173 bruceanic acid B



1-174 R = H bruceanic acid C
1-175 R = Ac bruceanic acid D



1-177 bruceantin



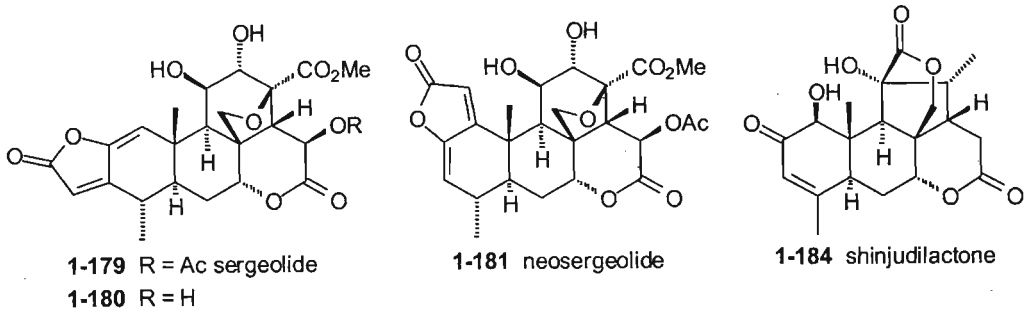
1-178 isobrucein B

In 1982 a novel quassinoid with a butenolide ring attached to the A ring of a normal C_{20} skeleton was reported from the French Guyanan species *Picrolemma pseudocoffea* Ducke, where it was accompanied by the known quassinoid isobrucein B **1-178**. Named sergeolide **1-179**, this compound was proposed to arise from the 1-acetyl derivative of isobrucein B *via* a Claisen-type rearrangement followed by double bond migration and lactonisation [191][‡] (scheme 42).

---

† Whether these are true extractives or artefacts of the separation procedure remains unresolved. Kupchan *et al.* [188] noted that bruceantin **1-177** was readily converted to bruceanic acid A **1-171** within 24 hours on exposure to air if left on a tlc plate. Bruceanic A methyl ester **1-176** can easily be accounted for in terms of the reported methanol-chloroform mixtures [190] used for elution.

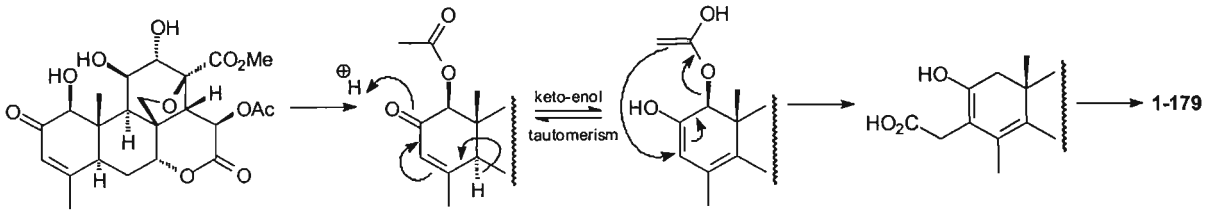
‡ It must be pointed out that the formal Claisen rearrangement differs from the mechanism proposed here to such a degree that it can hardly be called "Claisen-like". In particular, the migration occurs to the *o*- and *p*-positions with such specificity that no reaction occurs if these positions are filled, and no migration to the *m*-position has ever been observed [192]. In any event such a rearrangement from the equatorial substituent at C-1 in isobrucein B would surely encounter such steric interference from the hydroxy group at C-2 as to render it virtually impossible. In addition the concerted pericyclic rearrangement governing this mechanism requires that the oxygen functionality is excluded from the migration and remains at the reaction terminus, whereas this mechanism is equally insistent that cleavage of the C-1 oxygen bond plays an integral role without which the rearrangement will not occur. Finally the "double bond migration" involves migration of the Δ^4-double bond through the relatively stable conjugated Δ^3 position into a far more sterically strained α,β-unsaturated γ lactone. Altogether an unsatisfactory state of affairs.



1-179 R = Ac sergeolide
1-180 R = H

1-181 neosergeolide

1-184 shinjudilactone

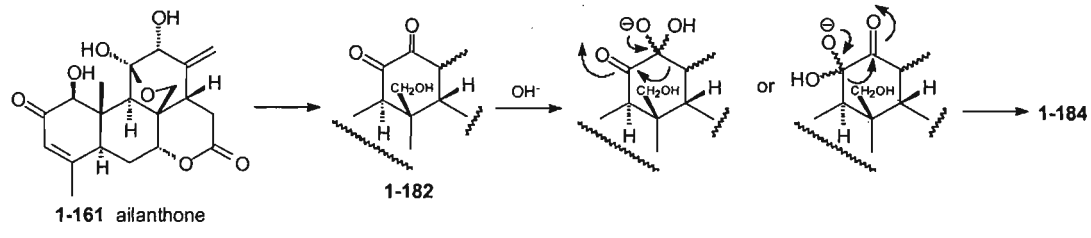


1-178 isobrucein B

Scheme 42: Formation of sergeolide **1-179** by "Claisen-like" rearrangement of isobrucein B **1-178** [191].

Only two further examples of this type have been reported, both from *Picrolemma pseudocoffea*; the 15-deacetyl analogue **1-180** [193] and, more recently, neosergeolide **1-181**, in which the butenolide ring is now attached to the A ring at C-1,C-2 [194]. The structure of **1-181** has been confirmed by X-ray crystallography, in contrast to the preceding two which were based on spectroscopic analysis only.

Shinjudilactone **1-184**, isolated simultaneously with shinjulactone C **1-151** from *Ailanthus altissima*, is one of a number of picrasane-type quassinoids with rearrangements of the C ring and 11,30-ether bridge [171,195]. A proposed biosynthetic mechanism (scheme 43) accounting for the rearrangement was supported by the ready conversion of ailanthone **1-161** into shijudilactone **1-184** by treatment of the intermediate diketone **1-182** with $NaHCO_3$, which initiates ring contraction and subsequent lactonisation.

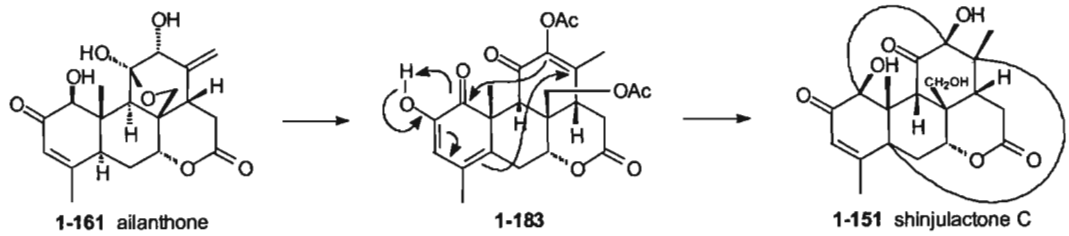


1-161 ailanthone

1-182

Scheme 43: Proposed biosynthesis of shinjudilactone **1-184** from ailanthone **1-161** *via* diketone **1-182** [195].

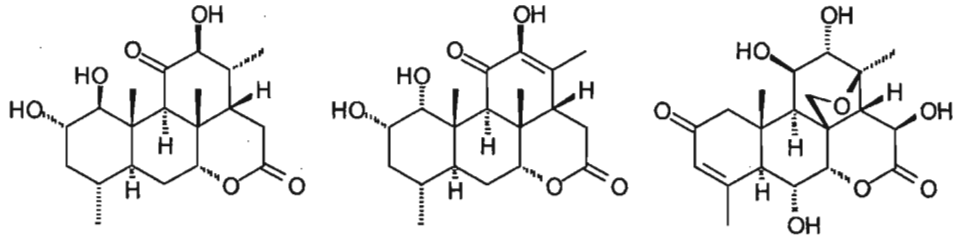
The same group also subsequently succeeded in converting ailanthone **1-161** into shinjulactone C **1-151**. The key step in this synthesis involved a thermally induced [4+2] intramolecular cycloaddition of the intermediate diketone **1-183** [184] (scheme 44).



1-161 ailanthone **1-183** **1-151** shinjulactone C

Scheme 44: Laboratory synthesis of shinjulactone C **1-151** from ailanthone **1-161** *via* intermediate diketone **1-183** [184].

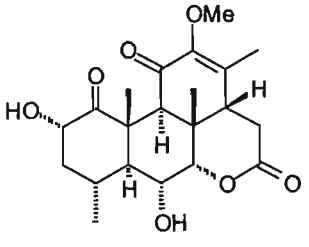
Only three compounds characterised prior to 1973 could not be placed within Polonsky's original subclassification [153] of the C_{20} quassinoids, as given on page 54, on the basis of variations in the structure of ring A. These were chapparolide **1-185** and castelanolide **1-186** from *Castela nicholsoni* Torr et A.Gray [196], and brucein G† **1-187** from *Brucea sumatrana* Roxb. [197]. As such they were presumably considered sufficiently similar to those mentioned not to warrant a separate classification of their own.



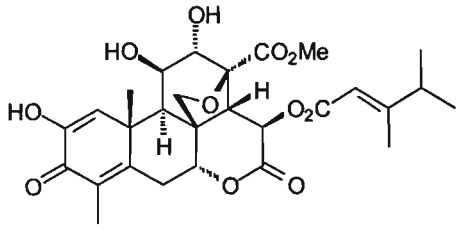
1-185 chapparolide **1-186** castelanolide **1-187** brucein G

† This compound is not mentioned in either review. Polonsky's second review [173] reports the isolation of 6α-hydroxypicrasin B **1-188** as the only 6α-hydroxy quassinoid isolated up to that date (1970); however the reference cited [198] mentions a second unpublished structure [199].

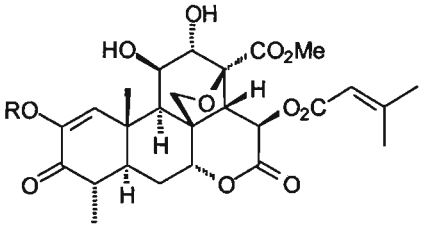
In 1975 a series of compounds such as dehydrobruceantin **1-189** with the 2-hydroxy-3-keto-substitution pattern classified by Polonsky as type (e), but with double bonds at Δ^1 and Δ^4 rather than just at Δ^3 was reported from *Brucea antidysenterica* [188]. 1979 saw the appearance of the first of the bruceosin **1-190** type compounds with a hitherto unreported 2-hydroxy-3-keto-2-ene substitution pattern [200-206]. Bruceosin **1-190** is doubly distinguished in that it is also the aglycone of bruceoside A **1-191**, the first quassinoid glycoside to be fully described [200,207].



1-188 6α-hydroxypicrasin B



1-189 dehydrobruceantin



1-190 R = H bruceosin
1-191 R = Glu bruceantinoside A

Polonsky's second review [173] was published in 1985, and includes some sixty new C_{20} quassinoids, together with the novel C_{18}, C_{19} and C_{25} quassinoid classes described above (apart from the new C_{19} quassinoid shinjulactone B **1-160**, no other C_{19} compounds were reported between 1973 and 1985) (figure 2). Despite enlarging the C_{20} quassinoid subclassification to include, as subgroup (f) (figure 3), sergeolide **1-179**, no mention of either the dehydrobruceantin- **1-189** or bruceosin-type **1-190** quassinoids described above is made. The reason for this omission is not clear; although these compounds are isomeric to those of the (e) group, so are those of the (b) group, which nevertheless are classified separately.

As mentioned previously, a significant section of the review is devoted to biological studies, with various quassinoids reported to have anti-leukemic, antiviral, anti-malarial, and anti-inflammatory properties, as well as acting as insecticides, antifeedants and amoebicides.

The first reported total syntheses of two C_{20} quassinoids are also discussed. The first, fittingly, was that of *dl*-quassin **1-127** itself [208,209], with the same group subsequently succeeding [210,211] with that of *dl*-castelanolide **1-186**.

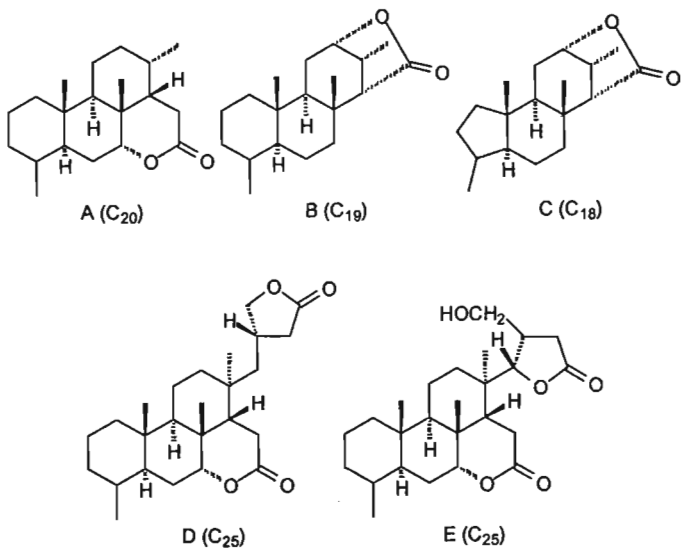


Figure 2: The five basic quassinoid skeleta [173].

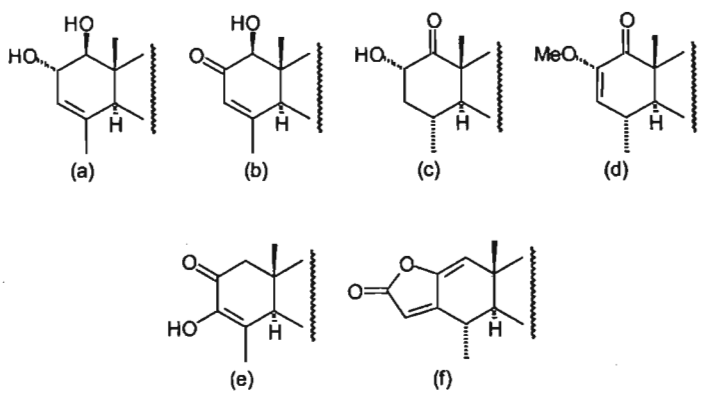
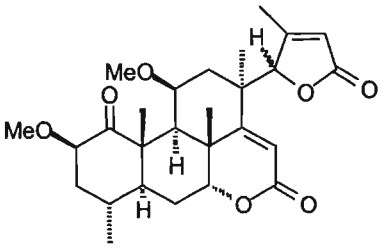


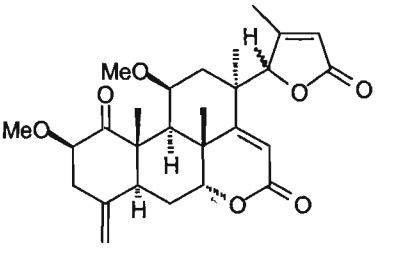
Figure 3: Subclassification of the the C_{20} quassinoids by variations in the structure of the A ring [173].

The related C_{25} quassinoids odyendane **1-192** and odyendene **1-193**, isolated from the stem bark of the Central African species *Odyendea gabonensis* (Pierre) Engler, were reported in 1985 shortly after

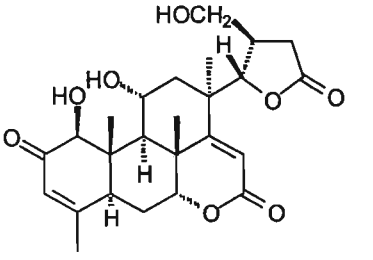
the appearance of the review [212]. These are apparently the first (and, to date, the only) type E C_{25} quassinoids with the *S* configuration at C-17†.



1-192 odyendane



1-193 odyendene



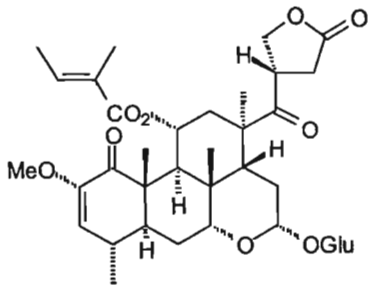
1-194 indaquassin F

The fifteen years that have elapsed since the last review have seen a tremendous increase in the overall number of quassionoids isolated and characterised. As mentioned earlier, no further C_{18} quassinoids have been reported. Among the three further C_{25} quassinoids of the D group to come to light is the only reported C_{25} quassinoid glycoside javacinoside E **1-195** from the Indonesian species *Picrasma javanica* Blume [214], and klaineanolide A **1-196** from the root bark of the Central African species *Hannoa klaineana* Pierre et Engler [215], unique in Group D quassinoids in having an equatorially oriented hydroxy substituent at C-4. This brings the totals in the D and E groups to six and five compounds respectively.

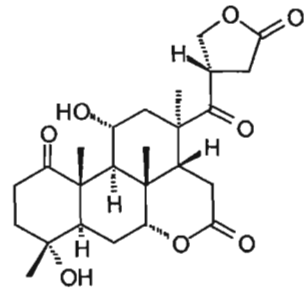
The three new additions to the C_{19} shinjulactone B group, ailanquassin A **1-197** from *Ailanthus malabarica* DC. [216] and cedronolactones B **1-198** and C **1-199** from *Simaba cedron* Planchon [217] are respectively *R* and *S* at C-5. The eight members of this group are now split evenly on the basis of their C-5 configuration.

† There exists some confusion in the literature as to the configuration at C-17 in these compounds. They are reported in the Dictionary of Natural Products as *S*, which at once places them at variance with all of those previously discussed, in which the stereochemistry at C-17 and C-20 is given uniformly as *R*. However the structures drawn in the original paper do not give the configuration explicitly and the perspective diagram is ambiguous. The Chemical Abstracts entry (1985, **103**, 175417p) is equally noncommittal. Such proof as does exist that the configuration at C-17 is indeed *R* comes from the observation that treatment of odyendene **1-193** with base resulted in the formation of a hydroxylactone in which the 22,23-double bond has been reduced and a hydroxy substituent is placed at C-17, apparently – from the structure given – in the β orientation, and thus presumably resulting from oxidation(?) of the H-17 originally present.

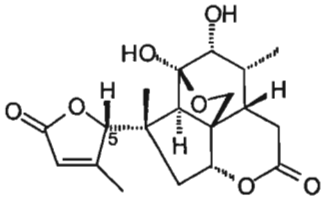
In the only other type E C_{25} quassinoid subsequently reported [213], indaquassin F **1-196** from 1994, the configuration at C-17 is given explicitly as *R*.



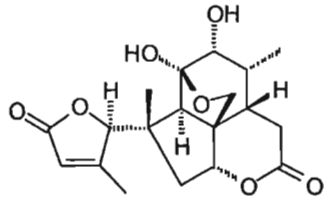
1-195 javanicinoside E



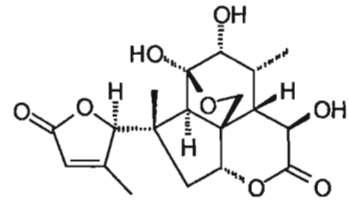
1-196 klaineanolide A



1-197 ailanquassin A



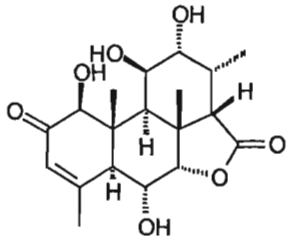
1-198 cedronolactone B



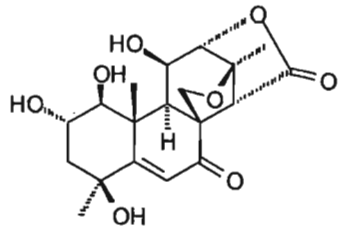
1-199 cedronolactone C

Eurycoma longifolia has recently yielded longlilactone **1-200** [218] and two related compounds [219,220] containing the 7,14-γ-lactone ring originally proposed for eurycomalactone **1-143** (p.53).

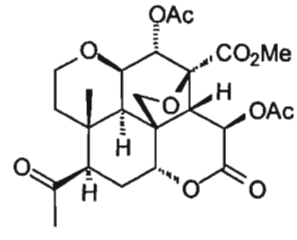
"Old" or "original" C_{19} quassinoids of the group B or samaderine C **1-132** type now number some fifteen compounds. Included in these are indaquassin A **1-201** [221], which is the only C_{19} compound reported thus far with an axial 4β-hydroxy substituent, and samaderine C 2-glucoside (**1-132**, R = Glu), the only known C_{19} glycoside [222]. Both compounds were isolated from *Quassia indica*.



1-200 longilactone



1-201 indaquassin A

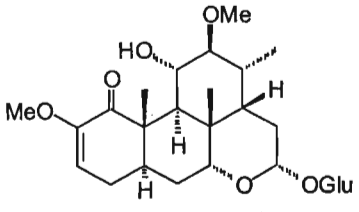


1-202 javanicin

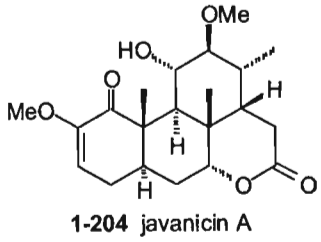
The C_{20} quassinoid A group now comprises over two hundred and seventy-five structures, or some 95% of those isolated to date. While the majority of these either fit into the original Polonsky (a) – (f) subgroup classification, possess the unclassified dehydrobruceantin- **1-189** or bruceosin-type **1-190** structures, or are minor variations of these groups of the order of chapparolide **1-185**, castelanolide **1-**

186, or brucein G **1-187**, a number of compounds have been reported with significant modifications of the picrasane skeleton.

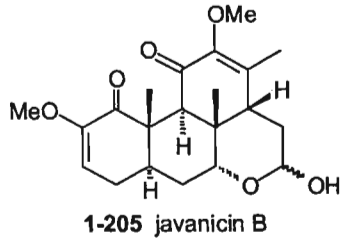
Among these are the javanicins†, a group of twenty-three compounds and a further nine associated glycosides isolated exclusively, as their name suggests, from *Picrasma javanica*. The first such compound reported [224] was that of the glycoside javanicinoside A **1-203**, with javanicins A **1-204**, B **1-205**, C **1-206** and D **1-207** following shortly thereafter [225,226].



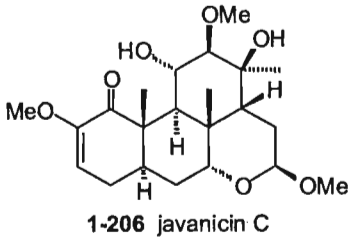
1-203 javanicinoside A



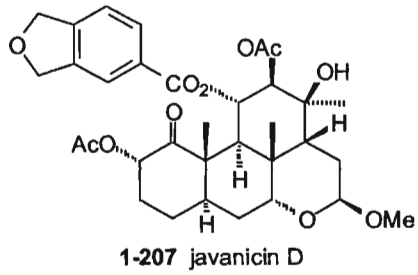
1-204 javanicin A



1-205 javanicin B



1-206 javanicin C



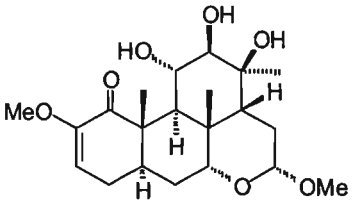
1-207 javanicin D

This group is characterised as a whole by the disappearance of the equatorial C-4 methyl substituent to give a series of 4-desmethylpicrasane compounds (javanicin F [227], in fact, is just 4-desmethylquassin), while each of the javanicins B **1-205**, C **1-206** and D **1-207** isolated above introduces a motif which has re-occurred in subsequent structures. Thus javanicin B **1-205** is the first to have the C-16-hemiacetal hydroxy group and javanicin D **1-207** the 11α-piperonyloate ester. Methylation of C-16 in both javanicins C **1-206** and D **1-207** gives the 16β-methoxy substituent, in contrast to which javanicinoside A **1-203** possesses the 16α-configuration. This appears to be a virtually consistent feature; all subsequent C-16 glycosides found are α at C-16, while only one C-16α methoxy substituted quassinoid, javanicin Q **1-208**, has been reported [228].

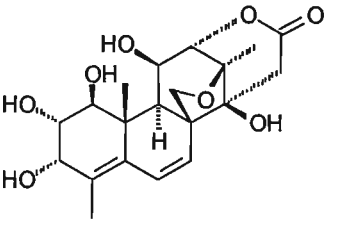
† Not to be confused with javanicin **1-202**, isolated at the same time from *Brucea javanica* L. [223]. This compound is interesting in its own right, as it is the only example to date of a C_{20} quassinoid with an additional δ-lactone instead of the A ring. Its formation is easily rationalised in the light of the fact that it was isolated from the same species that provided the *seco*-ring A C_{20} quassinoid bruceaketolic acid **1-172** [189].

Longilactone **1-200** and javanicin **1-202** are both examples of quassinoids which have cyclised "the wrong way" - to C-7 rather than C-11 in longilactone **1-200** and to C-11 rather than C-4 in javanicin **1-202**. In similar fashion indaquassin B **1-209** from *Quassia indica* [221] and cedronolactone D **1-210** from *Simaba cedron* [217] are C_{20} quassinoids in which lactonisation has occurred between C-14 and C-11 rather than between C-14 and C-7.

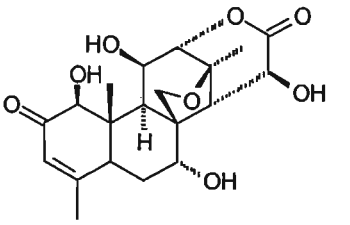
Ailantinol D **1-211** from *Ailanthus altissima* is the only further example of the shijudilactone **1-184** type to have been reported [229]. The related compound ailantinol A [230] from the same species is even further degraded, with cleavage of the C-11,C-12 bond producing the *seco*-ring D structure **1-212**.



1-208 javanicin Q

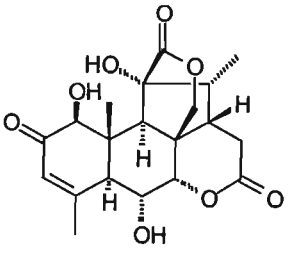


1-209 indaquassin B

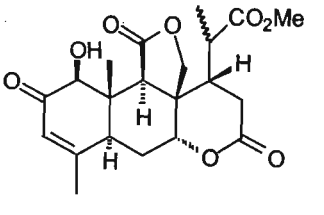


1-210 cedronolactone D

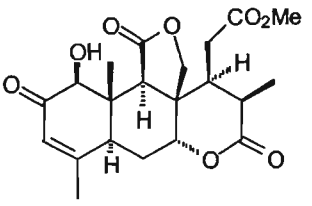
Similar in structure to ailantinol A **1-212** is vilmorinine B **1-213** from the related species *Ailanthus vilmoriana* Dode. However this compound, in addition, not only has the highly unusual H-14α configuration, but has also lost C-20 altogether. So have the parent acid compound vilmorinine C **1-214**, 1-epimer vilmorinine D **1-215**, unique 5-epimer vilmorinine E **1-216**, and equally unusual 5,15-diepimeric vilmorinine F **1-217** [230]. Vilmorinine A, in contrast, has retained C-20 and the usual H-14β, but has undergone further fission of the C-ring and subsequent formation of a 1,7-ether bridge to yield structure **1-218** [231].



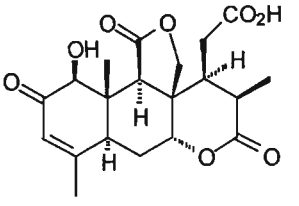
1-211 ailantinol D



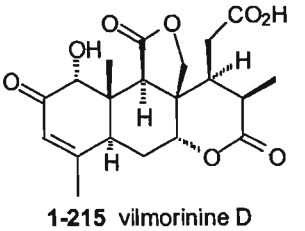
1-212 ailantinol A



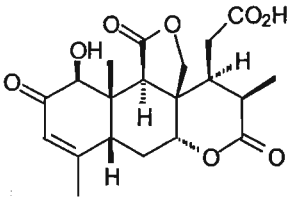
1-213 vilmorinine B



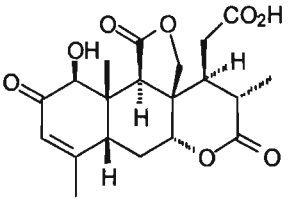
1-214 vilmorinine C



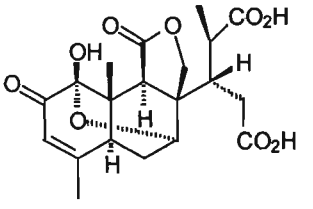
1-215 vilmorinine D



1-216 vilmorinine E



1-217 vilmorinine F



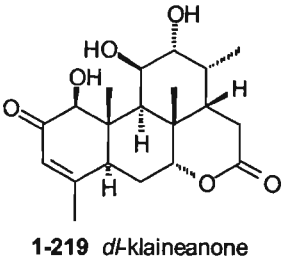
1-218 vilmorinine A

In their full paper report of the total synthesis [232] of *dl*-klaineanone **1-219**, Grieco *et al.* [233] remark that

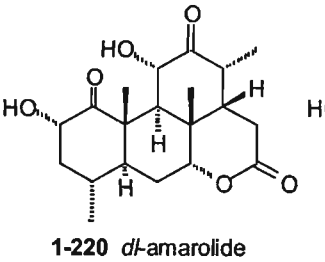
> "Since the report in the literature dealing with the total synthesis of quassin (**3**) in 1980, there have been a plethora of publications[3] dealing with studies directed towards the synthesis of quassinoids."

This comment was made in 1989, yet the accompanying reference listed some forty-seven publications. Interest in the following decade has waxed rather than waned; however, twelve years on, only thirteen total syntheses of these compounds have been published. Proof indeed of the exceptional difficulties associated with syntheses of this nature.

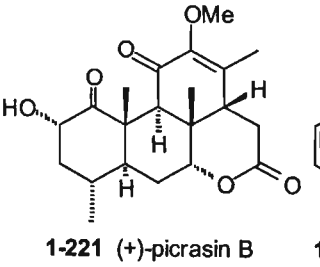
Hirota *et al.* have published total syntheses of *dl*-klaineanone **1-219** and *dl*-amarolide **1-220** (in 35 steps!) [234,235], and enantioselective total syntheses of (+)-picrasin B **1-221**, its 2,3-dehydro analogue **1-222**, and (+)-quassin **1-127** have also appeared [236,237].



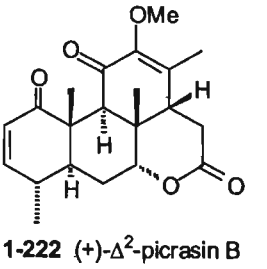
1-219 *dl*-klaineanone



1-220 *dl*-amarolide



1-221 (+)-picrasin B

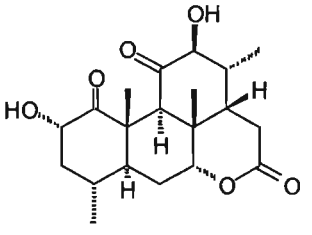


1-222 (+)-Δ^2-picrasin B

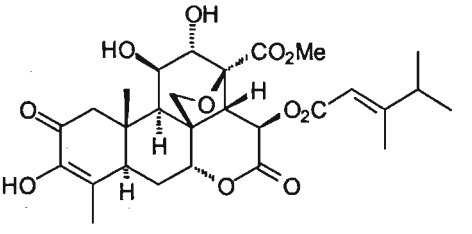
The latter researchers were subsequently able to achieve a partial synthesis of (-)-shinjulactone H **1-223** from (+)-quassin **1-127** [238].

Two syntheses of bruceantin **1-224** have been published. An enantiospecific synthesis of the (-) isomer was achieved in 1990 only by using (-)-15-deoxybruceolides **1-225** and **1-226** as relay compounds [239]. The formal total synthesis reported later [240] was not enantioselective.

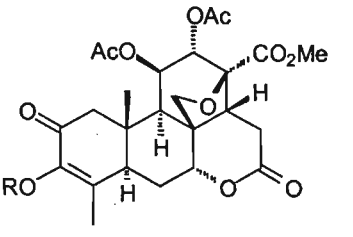
Total syntheses of racemic chaparrinone **1-227** [244], racemic glaucarubolone **1-135** [242] and racemic holocanthone **1-230** [242] were succeeded later by accounts of enantiospecific syntheses of (-)-chaparrinone **1-227**, (-)-glaucarubolone **1-135**, and (+)-glaucarubinone **1-134** [243]. The same group has also achieved racemic syntheses of shinjulactone C **1-151** [244], 14β,15β-dihydroxyklaineanone **1-229** [245], simalikalactone D **1-230** [246], and, very recently, shinjudilactone **1-184** and its C-13 epimer **1-231** [247]. The absolute configuration of the sidechain of the naturally occurring (+)-isomer from *Simaba guianensis* [248] was also established as *S*.



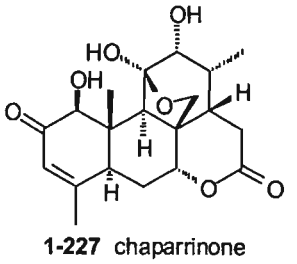
1-223 (-)-shinjulactone H



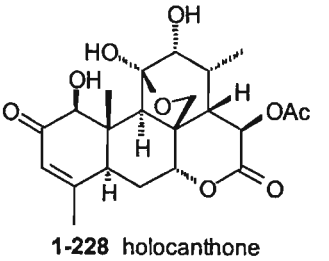
1-224 bruceantin



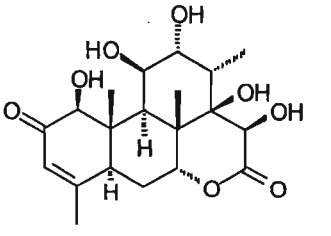
1-225 R = TBS
1-226 R = Ac



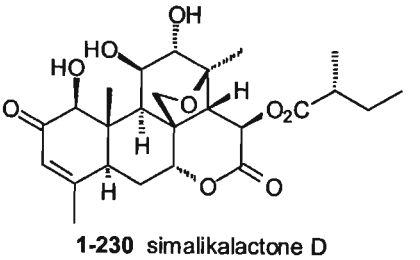
1-227 chaparrinone



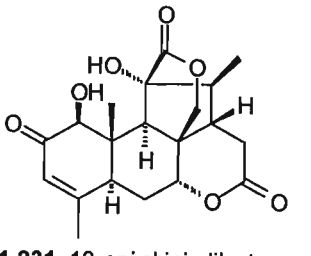
1-228 holocanthone



1-229 14β,15β-dihydroxyklaineanone

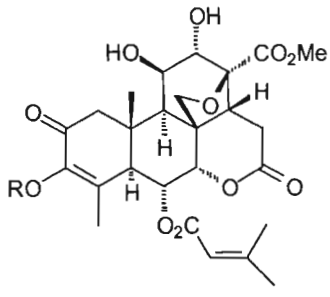


1-230 simalikalactone D

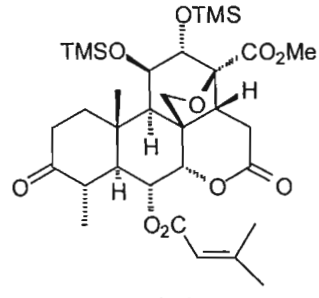


1-231 13-*epi*-shinjudilactone

The only non-picrasane quassinoid synthesis reported to date is that of the C_{19} quassinoid *dl*-samaderine B **1-133** [249].



1-232 R = Glc bruceoside C
1-233 R = H



1-234

In only one case has a total synthesis of a quassinoid *not* resulted in confirmation of the structure originally assigned to the isolated natural product. Bruceoside C **1-232** was originally isolated from *Brucea javanica* and the structure of both it and its derived aglycone **1-233** were determined exclusively by spectroscopic studies [250]. A later total synthesis showed this structure to be incorrect† [251].

It seems apposite to conclude this survey with the same compound with which it began, namely quassin **1-127**. A very recent report [252] on a total synthesis of the (+) isomer details a twenty-eight step procedure from (*S*)-carvone in ~2.6% yield, a marked improvement on the only previous enantiospecific process (p.70) [237], which required thirty-five steps for an overall yield of only 0.02%.

† The authors [251] were not able to assign a structure to bruceoside C, other than to note that the NMR data of their synthetic material, whose structure was considered unambiguously based both on spectral data and on a single crystal X-ray analysis of the intermediate **1-234**, did not agree with that reported originally [250]. However, in the light of their report that "...an authentic sample of bruceoside C...hydrolysed under the conditions reported in the literature." gave an aglycon "...different from the synthetically derived material, since they exhibited very different R_f values in several solvent systems.", and that "Needless to say, the ^1H NMR spectrum of the isolated aglycon differs...from our synthetic material.", that it is a pity that they did not record the spectra necessary to assign a structure before conducting the hydrolysis.

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Chapter 2

Extractives from *Turraea sericea*

2.1 Introduction

The pantropic genus *Turraea* L. was first described in 1771 by Linnaeus [1] and included by Ventenat in the family Meliaceae[†] in 1799 [2]. In 1896 it was placed by Harms in both the subfamily Melioideae[‡] and tribe Turraeeae [4], where it is now accompanied [5] by the four smaller genera *Munronia*, *Humbertioturraea*, *Naregamia* and *Calodecaryia*, and the monotypic genus *Nymania*. Inclusion of the latter in this genus has been the subject of much botanical debate and is discussed further later in this chapter.

The genus comprises sixty to seventy species of shrubs and small trees widely distributed in Africa and the Indian Ocean islands and to a lesser extent in Asia and Australia. Some thirty-five of these are endemic to the Madagascan archipelago [5].

South African varieties are known commonly as honeysuckles.

Although certain African species of the genus are reputed to be lethally poisonous [6-8], they have nevertheless been found medicinally useful by indigenous tribes in the treatment of rheumatism, heart disease and dropsy [7], the preparation of purgatives [8,9] and emetics [8], as an anthelmintic [9], and as remedies for diarrhoea and ulcers [6], fevers [8] and headaches [10]. In addition they are used magically by witchdoctors to induce trances prior to divining ceremonies [7].

To date only eight species of this genus have been investigated.

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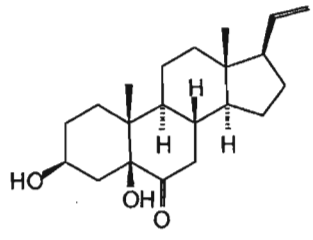
† Although Ventenat was the first to use the name Meliaceae, his definition of the family comprised only eight genera, of which six are now regarded as true Meliaceae; of the sixteen genera incorporated a decade earlier by de Jussieu [3] into his rather larger family Melieae, only ten now remain.

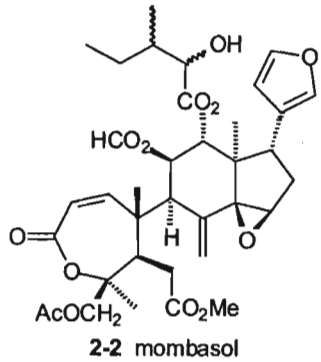
‡ It is interesting that all but two of the true Meliaceae mentioned above belong to the subfamily in question.

Turraea villosa Benn.: is an Indian species whose aerial parts yielded the novel unusual *cis*-A, B ring fused pregnane phytosteroid villosterol **2-1** [11].

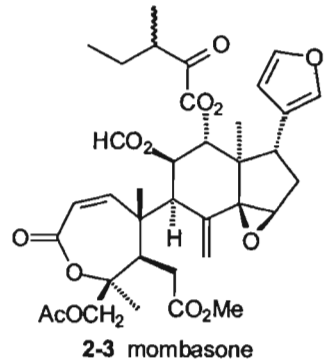


2-1 villosterol

Turraea mombasana C.DC.: Investigation of the root bark of a specimen of this East African shrub afforded the closely related prieurianin-class limonoids mombasol **2-2** and mombasone **2-3** [12].

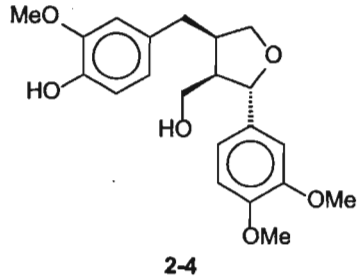


2-2 mombasol



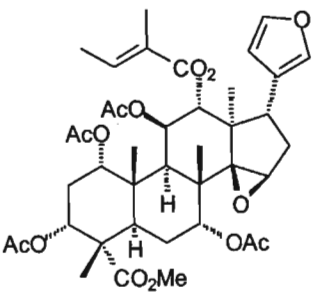
2-3 mombasone

Turraea nilotica Kotschy et Peyr.: The lignan lariciresinol 4'-methyl ether **2-4**, isolated from the cytotoxic extract of the leaves of a Sudanese sample [13], was found to be inactive [14].



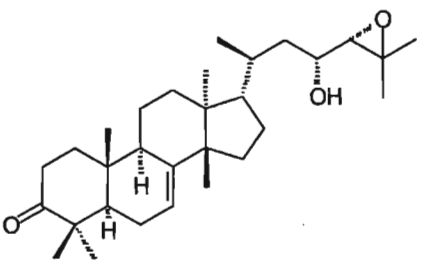
2-4

A more recent investigation of the rootbark of a Kenyan specimen afforded the havanensin-class insect antifeedant limonoid nilotin **2-5** [15].

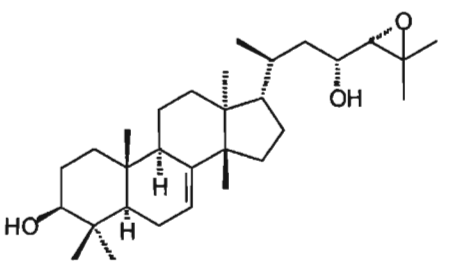


2-5 nilotin

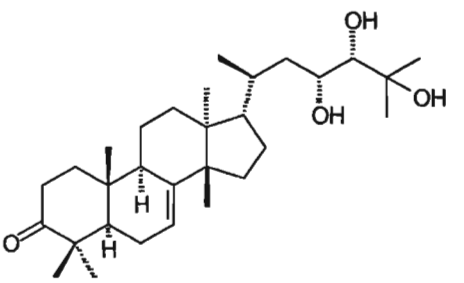
In contrast, a previous study in this laboratory of the stem bark and wood of a South African sample found only the protolimonoid niloticin **2-6** and two related compounds, **2-7** and **2-8** [16].



2-6 niloticin

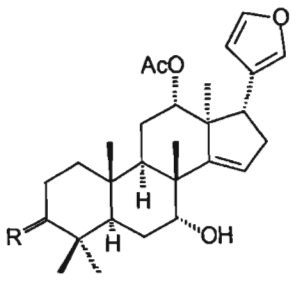


2-7

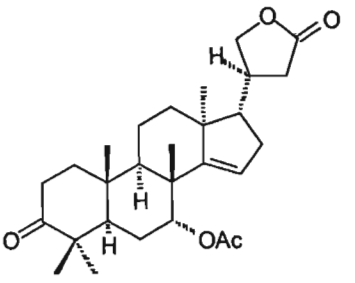


2-8

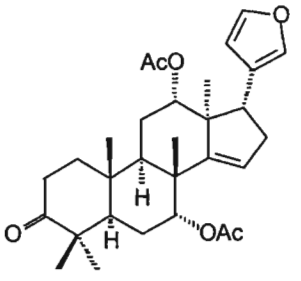
Turraea robusta Gürke: The havanensin-class limonoid mzikonone **2-9** has been reported as the major limonoid from the root bark of this East African species [17]. Further investigation furnished the closely related mzikonol **2-10**, together with the protolimonoid lactone turranolide **2-11**, the known limonoids azadirone **2-12**, 1,2-dihydroazadirone **2-13** and nimbolinin B **2-14**, and butyrospermol [18].



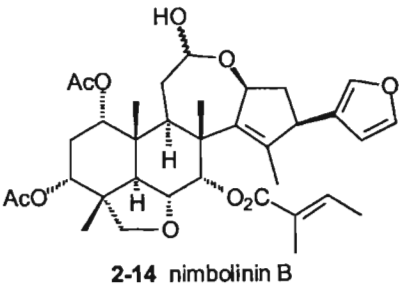
2-9 R = O mzikonone
2-10 R = H, β OH mzikonol



2-11 turranolide

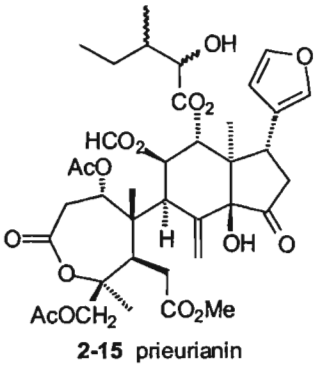


2-12 $\Delta^{1,2}$ azadirone
2-13 1,2-dihydroazadirone

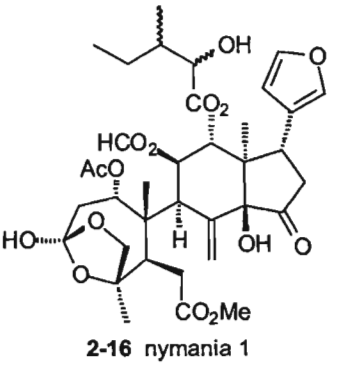


2-14 nimbolinin B

Turraea obtusifolia Hochstetter: Previous investigations of this South African tree in this laboratory have yielded the complex limonoids prieurianin **2-15** [19] and nymania 1 **2-16** [20] from the whole plant and seeds respectively.



2-15 prieurianin

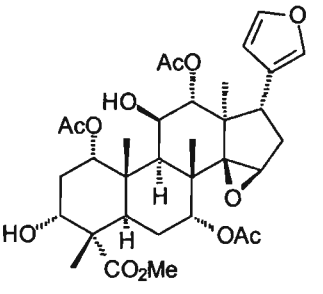


2-16 nymania 1

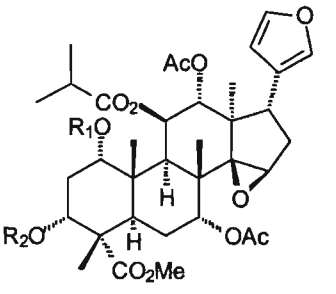
The monotypic South African genus *Nymania* Lindb. [22], previously known as *Aitonia* Thunb. [21], was considered by both de Jussieu [3] and Ventenat [4] to belong to the Meliaceae. Subsequent authors have placed it at various times in six different families. Its incorporation into the tribe Turraeeae, subfamily Melioideae by Pennington and Styles [5] was supported by the later isolation of prieurianin **2-15** from the bark and timber [21], together with four previously unreported limonoids of similar complexity called nymania substances 1-4 [23]. As prieurianin-type limonoids are considered

to be characteristic taxonomic markers, the presence of nymania 1 **2-16** in *T. obtusifolia* justifies further this inclusion, and in particular their observation on the close relationship between *Nymania* and *Turraea*.

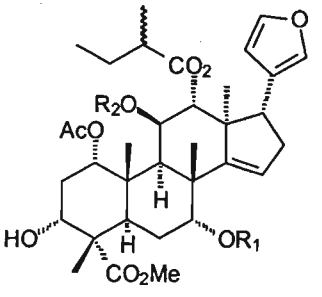
Turraea floribunda Hochstetter: is noted for its sweetly scented flowers. A variety of novel havanensin-class limonoids have been reported from the stembark **2-17,18,19** [19] and rootbark **2-20,21,22,23,24** [24,25].



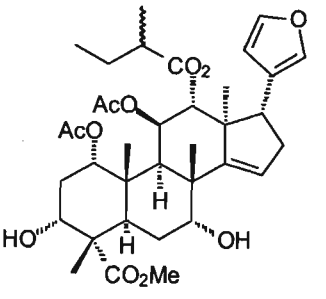
2-17 turraea A



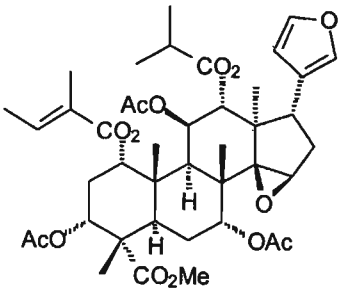
2-18 R_1 = Ac, R_2 = H turraea B
2-19 R_1 = H, R_2 = Ac turraea C



2-20 R_1 = H, R_2 = H
2-21 R_1 = Ac, R_2 = H
2-22 R_1 = Ac, R_2 = Ac

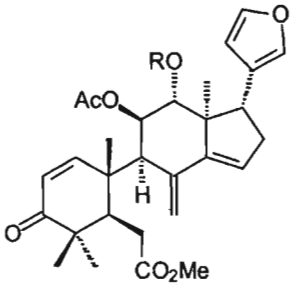


2-23

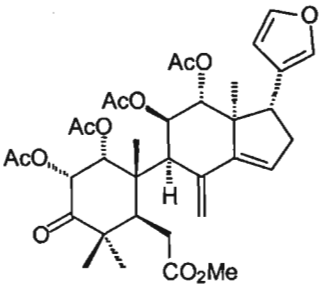


2-24

The seed yielded the 11,12-disubstituted toonafolin-group limonoids turraflorins A-C **2-25,26,27** [26]. For reasons more fully discussed in Chapter 3, the 11α,12α-disubstitution pattern originally proposed was later revised [27] to that of 11β,12α.

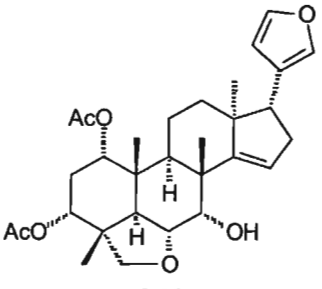


2-25 R = Ac turraflorin A
2-26 R = H turraflorin B

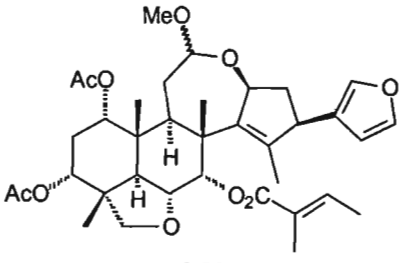


2-27 turraflorin C

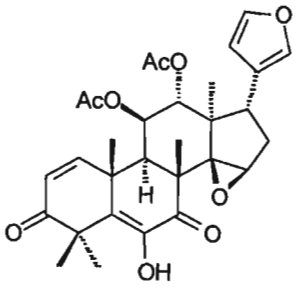
Turraea holstii Gürke: A recent investigation [27] in this laboratory of the stem and root bark of this East African species yielded, together with the known havanensin-class vilasinin derivative **2-28**, the novel limonoids 12-*O*-methylnimbolin B[†] **2-29**, havanensin-class cedrelone **2-30** and neotrichilenone **2-31,32,33,34** analogues, and the toonafolin-group compound 11-*epi*-toonacilin **2-35**.



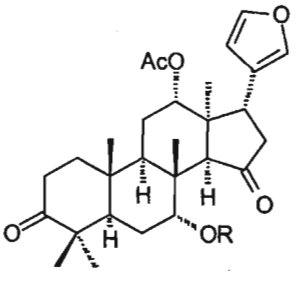
2-28



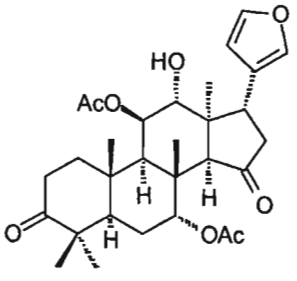
2-29



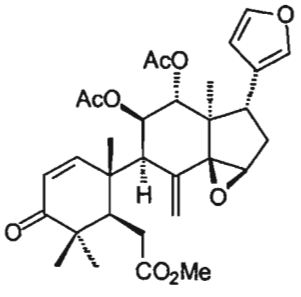
2-30



2-31 Δ^{14} R = H
2-32 R = H
2-33 R = Ac



2-34



2-35 11-*epi*toonacilin

Three novel protolimonoids, holstinones A-C **2-36,37,38** were also isolated [28].

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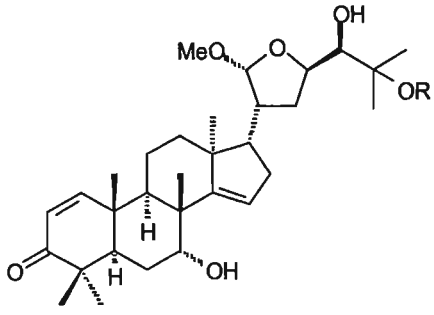
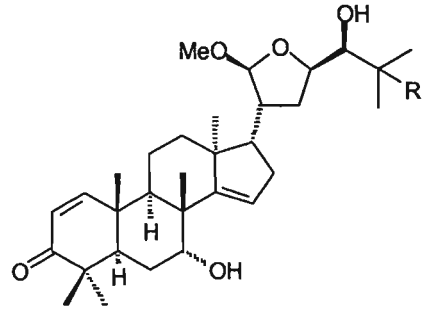
† Methylation was suspected to be an artefact of the extraction process.



2-36 R = Me holstinone A
2-38 R = H holstinone C



2-37 R = OH holstinone B
2-39 R = Cl holstinone B*

The structure of holstinone B **2-37** was subsequently revised to that of holstinone B* **2-39** [29][†].

2.2 Extractives from *Turraea sericea*

Turraea sericea Smith. (*Oncoba capreaefolia* J.G. Baker [31]) is locally named "lafara" in the southwestern part of Madagascar, where a decoction of the stem bark or the leaves is used for the treatment of diptheria, sore throat and angina [32]. Other than the Mauritian species *Turraea casimiriana*, an infusion of whose leaves and stems are reported to affect capillary permeability [33], it is the first *Turraea* species of Indian Ocean island origin to undergo investigation.

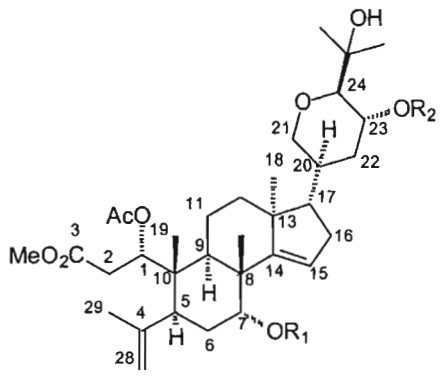
The methanol extracts of both the leaves and the stem bark were shown by ^{1}H NMR spectroscopy to contain only sugars and were not investigated further, while the hexane and dichloromethane extracts of each were sufficiently similar, by ^{1}H NMR spectroscopy and tlc analysis, to be combined. No compounds of interest were isolated from the leaves, while the stembark yielded the novel protolimonoid sericeanin A **TS 1**.

---

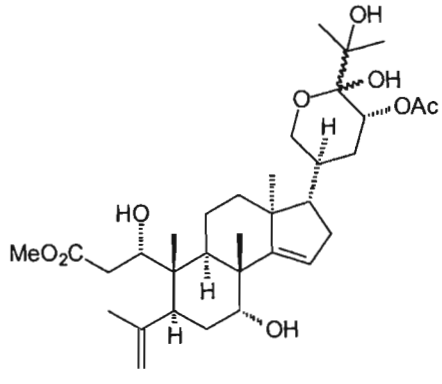
† Breen *et al.* reported a similar 25-chloro substituted compound, bourjotinolone C, from the Australian Rutaceae *Flindersia bourjotiana* [30]. They considered this to be an artefact of their extraction process, in which the sample was washed with dilute HCl to extract alkaloids. The sample investigated in our laboratories was extracted elsewhere with methanol, so the possibility of contamination, and thus that holstinone B* has an origin similar to that of bourjotinolone C, cannot be excluded.

2.2.1 Structural elucidation of compound TS 1, sericeanin A

(spectra vol II, p.s1-9)



2-46 R_1 = Ac R_2 = H, C-1ξ
2-47 R_1 = R_2 = H sericeanin A **TS 1**
2-49 R_1 = R_2 = Ac **TS 1a**

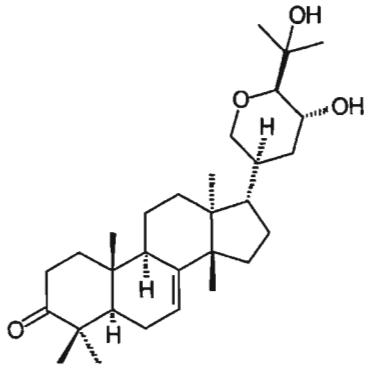


2-48

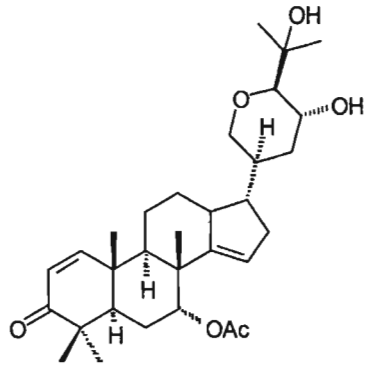
The ^{13}C NMR spectrum of compound **TS 1** showed signals for thirty-three carbon atoms, while the ^{1}H NMR spectrum displayed resonances ascribable to acetate and carbomethoxy methyl group protons. This suggested that **TS 1** was triterpenoidal in nature.

The pair of singlets at δ4.83 and δ4.98 in the ^{1}H NMR spectrum, coupled in the COSY spectrum to a downfield methyl resonance at δ1.78, and to signals at δ115.85(CH_2, C-28) and δ23.09(CH_3, C-29) in the HETCOR spectrum, were ascribed to 2H-28 and 3H-29, respectively, of a *seco*-ring A structure. These assignments were supported by a fully substituted signal at δ171.89, ascribed to C-3, in the ^{13}C NMR spectrum, and a carbomethoxy resonance at δ3.61 and 51.92(CH_3), characteristic of carboxylic acid methyl esters.

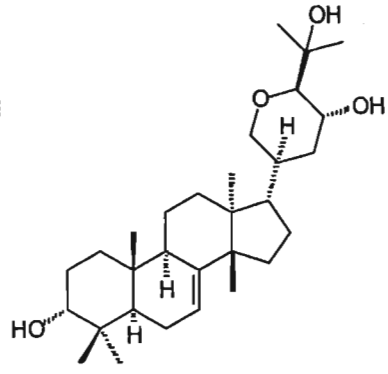
A coupled pair of doublets at δ3.42 (dd, J = 11.63, 2.32Hz) and δ3.97(br d, J = 11.53Hz), correlated to a methylene carbon resonance at δ69.98, and a series of coupled multiplets at δ2.88, δ3.85, and δ1.49 and δ1.93, correlating, respectively, to ^{13}C NMR signals at δ86.56(CH), 64.37(CH), and 36.29(CH_2), are characteristic of 2H-21, H-24, H-23, and 2H-22 in a bourjotinolone A-type sidechain.



2-40 bourjotinolone A

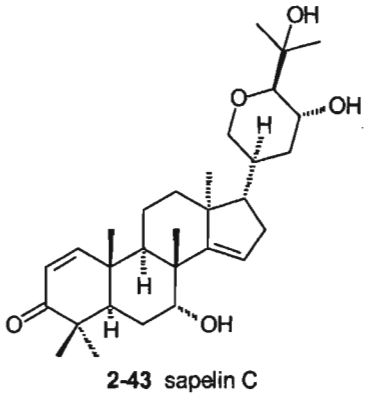


2-41 grandifoliolenone

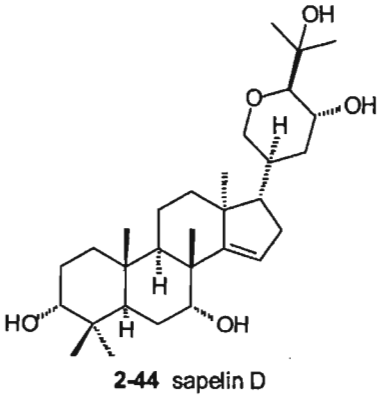


2-42 sapelin A

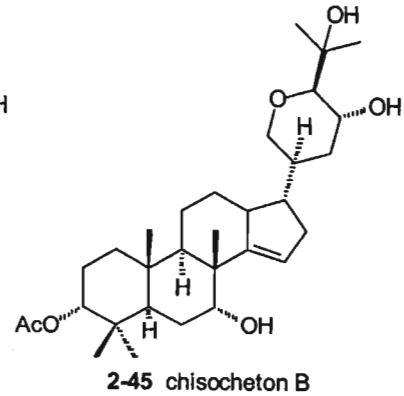
Side chain cyclisation by formation of a six-membered ether ring was first reported in bourjotinolone A **2-40** from the Australian Rutaceae *Flindersia bourjotiana* [30], and was subsequently found in grandifoliolenone **2-41** from *Khaya grandifoliola* C.DC. [34], sapelins A, C and D **2-42,43,44** from *Entandrophragma cylindricum* Sprague [35,36], and chisocheton B **2-45** from *Chisocheton paniculatus* Hiern [37], by which time the 23*R*,24*R* stereochemistry was firmly established on the basis of a characteristic coupling constant of ~9Hz for $J_{23,24}$. These results and identical values for H-23 and H-24 notwithstanding, the first fully assigned spectral data for bourjotinolone A **2-40** from *Trichilia hispida* Pennington appeared [38] with the stereochemistry incorrectly depicted as 23*R*,24*S*. Subsequent authors [39-42], without exception, have given it as 23*R*,24*R*.



2-43 sapelin C



2-44 sapelin D



2-45 chisocheton B

A literature survey based on this information revealed that sericeanin A **TS 1** is the 7-deacetyl analogue of the compound **2-46** recently isolated from *T. elegans* ssp. *elegans* [42], and thus has the structure **2-47**. Comparison showed our ^{1}H NMR data to be very similar to the literature values,

except that H-7β occurs at δ3.85 rather than δ5.12, and H-15 at δ5.48 as opposed to δ5.30†, which places the acetyl ester at C-1 (δ5.43m, H-1, δ77.01(CH), C-1; lit. [42] δ5.47br d, *J* = 9.8Hz, H-1, δ76.6(CH), C-1). The differences in assigned values for C-5, C-6, C-9, C-12, C-18 and C-19 were resolved by recourse to the corresponding values obtained for the related 24ξ-hydroxy analogue **2-48** very recently obtained from *T. emetica* Vahl [45].

Comparison of the ^{1}H NMR spectra of the diacetate **TS 1a** with that of **TS 1** showed the expected downfield shift of H-7β from δ3.85 to δ5.12, while H-23β, likewise, has moved from δ3.85 to δ4.92, where it appears as a triplet of doublets (*J* = 9.55, 4.66Hz), coupled to a doublet at δ3.13 (*J* = 9.16Hz), ascribed to H-24α. Thus **TS 1a** has the structure **2-49**, and the stereochemistry of **TS 1** is confirmed as 23*R*, 24*R*. Also observed was the equally expected upfield shift of H-15 from δ5.48 to δ5.28.

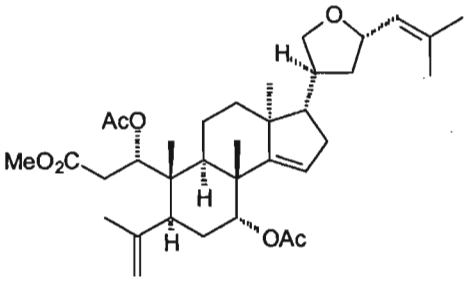
An HRMS of the diacetate **TS 1a 2-49** of this compound gave a molar mass of 642.3810 g.mol^{-1}, corresponding to the molecular formula $C_{37}H_{54}O_9$ (calc. for $[C_{37}H_{56}O_{10} - H_2O]^+$ 642.3768 g.mol^{-1}) and thus $C_{33}H_{52}O_8$ for **TS 1**. A series of peaks at *m/z* 600 ($[M\text{-}HOAc]^+$), 582 ($[M\text{-}HOAc\text{-}H_2O]^+$), 540 ($[M\text{-}2HOAc]^+$), and 522 ($[M\text{-}2HOAc\text{-}H_2O]^+$) in the EIMS are due to the loss of two molecules of acetic acid and one of H_2O, while that at 458 $[M\text{-}C_{10}H_{18}O_6]^+$ can be ascribed to the loss of the bourjotinolone A sidechain [45].

The stereochemistry at C-1 in sericeanin A **2-47** could not be determined from our NMR spectra. Garcez *et al.* [42] do not specify the stereochemistry at C-1 in their compound **2-46**, while Gunatilaka *et al.* [45] specify their structure **2-48** to be *S* at C-1 without explanation‡. No X-ray crystal structure of a *seco*-ring A limonoid has yet been reported, but a study of the ring-intact analogue meliavolin **2-51** from *Melia volkensii* Gürke shows the configuration of the C-1 acetate ester in this compound is indeed *S* [47]. On the assumption, then, that cleavage of the C-2,C-3 bond leaves the stereochemistry at C-1 unchanged, it is assigned as *S* in sericeanin A **TS 1**.

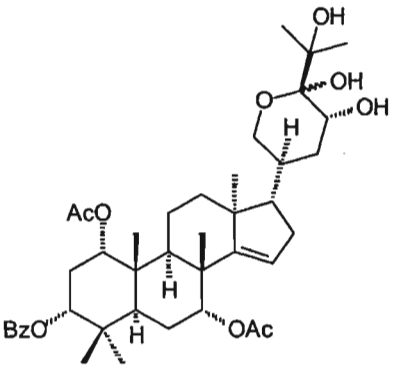
---

† This upfield shift of H-15 on acetylation of the 7α-hydroxy group is well known [43,44].

‡ Mohammad *et al.* [46] assign the stereochemistry at C-1 in their compound methyl argentinate **2-50** from *Aglaia argentea* Blume to be *S* on the basis of a NOESY correlation between H-1 and 3H-19, which is optimistic as rotation about the C10,C-1 bond would give rise to such a correlation irrespective of the stereochemistry at C-1.



2-50 methyl argentinate



2-51 meliavolin

The fully assigned ^{1}H and ^{13}C NMR spectral data, together with reference ^{13}C NMR data for comparison, are given in Table 2.1 below.

Table 2.1: ^{1}H and ^{13}C NMR assignments for compounds **TS 1**, sericeanin A, and **TS 1a**

[^{1}H NMR 300MHz, ^{13}C 75MHz, $CDCl_3$, *J* in Hz]

[Lit. [42] ^{1}H NMR 200MHz, ^{13}C 50MHz, $CDCl_3$, *J* in Hz]

[Lit. [45] ^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	2-47 TS 1		2-49 TS 1a	2-46	2-48
	δC	δH	δH	Ref. [42]	Ref. [45]
1	77.01 (CH)	5.43m	5.47d 9.59	76.6	
2	35.27 (CH_2)	a 2.36m b 2.83m	a 2.40m b 2.78d 13.18	35.3	
3	171.89 (C)	-		171.8	
4	145.47 (C)	-		144.8	
5	42.80 (CH)	2.62dd 12.76,2.93		34.6	42.8
6	29.88 (CH_2)	a 1.71m b 2.07m		35.0	29.9
7	71.68 (CH)	3.85m	5.12br s	74.8	
8	44.48 (C)*	-		42.3	
9	32.96 (CH)	2.14m		44.1	35.6
10	44.32 (C)*	-		44.0	
11	18.35 (CH_2)	1.85m		18.5	
12	34.27 (CH_2)	a 1.55m b 2.03m		29.2	
13	46.25 (C)	-		46.0	
14	161.72 (C)	-		159.1	
15	120.05 (CH)	5.48m	5.28m	119.4	
16	34.74 (CH_2)	a 2.01m b 2.10m		34.8	
17	52.39 (CH)	2.00m		52.4	
18	14.84 (CH_3)	0.92s		20.2	14.6
19	19.59 (CH_3)	0.96s		15.0	19.6
20	35.85 (CH)	1.88m		35.9	
21	69.98 (CH_2)	a 3.42dd 11.63,2.32 b 3.97d 11.53	a 3.52dd 11.54,2.56 b 3.99 d 11.41	70.0	
22	36.29 (CH_2)	a 1.49m b 1.93m		36.3	
23	64.37 (CH)	3.85m	4.92 td 9.55,4.66	64.4	
24	86.56 (CH)	2.88m	3.13d 9.16	86.5	
25	74.24 (C)	-		74.2	
26	24.03 (CH_3)	1.25s		24.0	
27	28.61 (CH_3)	1.29s		28.5	
28	115.85 (CH_2)	a 4.83s b 4.98s	a 4.82s b 4.99s	116.3	
29	23.09 (CH_3)	1.78s		22.7	
30	27.01 (CH_3)	1.10s		26.7	
$CH_3\underline{C}O$	170.24 (C)	-		170.2	
$\underline{C}H_3CO$	20.99 (CH_3)	1.98s		20.9	
$\underline{C}H_3O$	51.92 (CH_3)	3.61s		52.0	

*: values within column interchangeable

2.3 Foreword to Experimental

This section describes the general analytical and instrumental techniques employed throughout this study.

General Chromatography

All compounds were isolated using gravity column and preparative thin layer chromatography.

Initial column chromatography of crude extracts was carried out using Merck 7734 coarse silica gel (particle size 0.2-0.5mm, 35-70 mesh ASTM), while purification of individual compounds was achieved using the finer grade Merck 9385 (particle size 0.040-0.063mm, 230-400mesh ASTM). The mobile phases used were varying ratios of hexane, dichoromethane, ethyl acetate and methanol, and in rare instances benzene and diethyl ether. Separations were monitored by tlc on Merck 1.05553 aluminium foil-backed plates by inspection under ultraviolet light (254and 366nm) and/or by spraying the plate with an anisaldehyde:H_2SO_4:methanol (1:2:97) mixture and heating.

In cases when compounds of very similar R_f values resisted separation, or were overly resistant to purification, preparative thin layer chromatography was carried out using analytical Merck 1.05553 thin layer chromatography plates. Although the quantities that can be separated are limited (a 20cmx20cm plate is cut into two 20cm by 10cm sections, each of which can be loaded with only ~20-25mg of sample mixture), separations are rapid, allowing multiple elution of the plates which increases their efficiency enormously. In many cases compounds which had resisted exhaustive attempts using column chromatography were finally purified only by employing this technique.

Nuclear Magnetic Resonance Spectroscopy (NMR Spectroscopy)

NMR spectra were recorded at room temperature on either a 300MHz Varian Gemini instrument or a 400MHz Varian UNITY-INOVA spectrophotometer. Chemical shifts (δ) are expressed in ppm relative to tetramethylsilane (TMS) as internal standard and coupling constants are given in Hz. ^{1}H NMR spectra were referenced against the C<u>H</u>Cl_3 and C<u>H</u>D_2OD signals at δ7.24 and δ3.34, respectively, and ^{13}C NMR spectra to the corresponding signals at δ77.0 and δ49.0.

Infrared Spectroscopy (IR Spectroscopy)

IR spectra were recorded on a Nicolet Impact 400D Fourier-Transform Infrared (FT-IR) spectrometer, using NaCl windows with $CHCl_3/CH_3OH$ as solvents against an air background.

Melting points (M.p.)

Melting points were determined on a Kofler micro-hot stage melting point apparatus and are uncorrected.

Mass Spectrometry

GC/MS spectra were recorded on a Finnigan 1020 GC mass spectrometer, and HRMS on a Kratos 9/50 HRMS instrument at the Cape Technikon.

Optical Rotations

Optical rotations were measured at room temperature in $CHCl_3$ on an Optical Activity AA-5 Polarimeter, using a series A2 (4x200mm) stainless steel unjacketed flow tube.

2.4 Experimental

Turraea sericea was collected in April 1997 in Morondava in southwestern Madagascar. A voucher specimen (006-Mj/Mdul) is deposited at the Laboratory of Pharmacodynamy of the University of Antananarivo. Plant identification was confirmed by the Department of Botany at the Parc Zoologique et Botanique de Tsimbazaza.

The air-dried, milled leaves (219g) and stembark (326g) were each extracted successively for 24 hours in a Soxhlet apparatus with hexane, dichloromethane and methanol, yielding 6.80g, 4.12g and 28.47g, and 3.92g, 3.13g and 20.69g of extract respectively. No compounds of interest were isolated from the leaves, while the stembark yielded sericeanin A **TS 1**. Acetylation of **TS-1** by a standard procedure [48] gave compound **TS 1a**.

Compound **TS 1**
(spectra vol II, p.s1-8)

methyl-1α-acetoxy-7α,23R,25-trihydroxy-20S,24R-21,24-epoxy-3,4-seco-apotirucall-4(28),14(15)-dien-3-oate, sericeanin A

pale yellow gum, 9mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 2.1, p.93.

Compound **TS 1a**
(spectra vol II, p.s9)

methyl-1α,7α,23R-triacetoxy-25-hydroxy-20S,24R-21,24-epoxy-3,4-seco-apotirucall-4(28),14(15)-dien-3-oate

pale yellow gum, 8mg
^{1}H NMR spectra: data and peak assignments Table 2.1, p.93.

Optical Rotation:

$[\alpha]_D = 0.0^{o}$ (too small to be measured)

IR spectrum:

υ_{max}(NaCl) 3490, 1449, 1380, 1245, 1042 cm^{-1}.

Mass spectrum:

HRMS found 642.3810, calc. for $[C_{37}H_{56}O_{10}-H_2O]^+$ 642.3768 $g.mol^{-1}$.
EIMS *m/z* 642 $[M-H_2O^+]$, 600 $[M-AcOH]^+$, 582 $[M-AcOH-H_2O]^+$, 540 $[M-2AcOH]^+$, 522 $[M-2AcOH-H_2O]^+$, 458 $[M-C_{10}H_{18}O_4]^+$, 339, 253, 145, 107.

2.5 References

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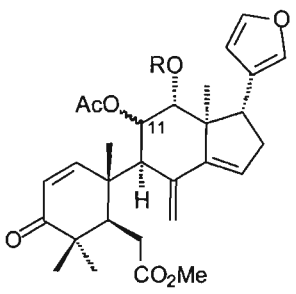
Chapter 3

The effect of the structure of ring B on variations in the coupling constants $J_{9,11}$ and $J_{11,12}$ in 11,12-disubstituted havanensin group limonoids: A literature survey and A revision of the stereochemistry at C-11 in turraflorins A-C from *Turraea floribunda*

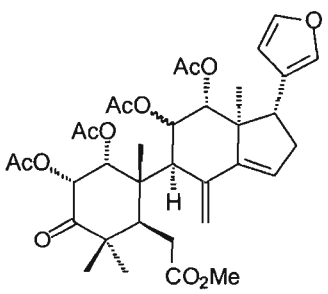
3.1 Introduction

In a previous study carried out in this laboratory, J.J.Nair isolated three limonoids from the seed of *Turraea floribunda* Hochstetter [1]. Named turraflorins A **3-1**, B **3-2**, and C **3-3** [2], they were characterised as Δ^1, Δ^{14}-double bond analogues of the *seco*-ring B toonafolin group limonoid toonacilin **3-4** isolated by Kraus *et al.* from *Toona ciliata* var. *australis* M.J.Roem [3][†].

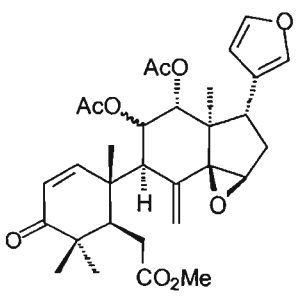


R = Ac turraflorin A **3-1** ~~~ = ····· **3-1a** ~~~ = —

R = H turraflorin B **3-2** ~~~ = ····· **3-2a** ~~~ = —



turraflorin C **3-3** ~~~ = ····· **3-3a** ~~~ = —



toonacilin **3-4** ~~~ = ····· 11-*epi*-toonacilin **3-26** ~~~ = —

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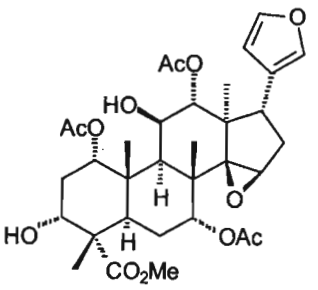
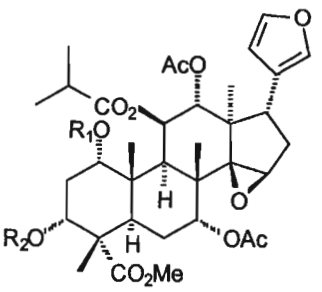
† The Missouri Botanical Garden database [4] gives *Toona ciliata* M.Roem. (syn. *Cedrela toona* Roxb. ex Rottler & Willd.), *T.australis* (F. Muell.) Harms, and *T.ciliata* var. *australis* F. Muell. It is unclear as to which of these three species Kraus *et al.* are referring.

The stereochemistry at C-11 and C-12 in toonacilin **3-4** was unequivocally established from a X-ray crystal structure determination rather than by analysis of ^{1}H NMR coupling constants and these values were not given in the publication [3]. The stereochemistry at C-11 and C-12 in turraflorins A-C **3-1,2,3** was assigned as 11α,12α on the basis of $J_{9,11}$ and $J_{11,12}$ coupling constants of 6Hz and 11Hz, as they differed widely from the corresponding values of ~3-5Hz and ~3-5Hz, respectively, for the 11β,12α-disubstituted ring B intact limonoids, turraea A **3-5**, B **3-6**, and C **3-7** obtained earlier from *T.floribunda* bark [5].



3-5 turraea A



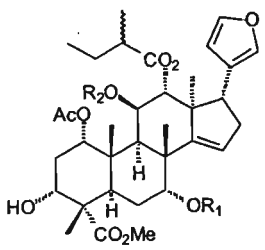
3-6 R_1 = Ac, R_2 = H turraea B
3-7 R_1 = H, R_2 = Ac turraea C

Values for $J_{9,11}$ and $J_{11,12}$ in toonacilin **3-4** were discovered in a subsequent publication [6], and proved (H-9 br s, $J_{11,12}$ = 4.3Hz) to be significantly different from those obtained for the turraflorins A-C **3-1,2,3**. That the substitution pattern in the latter should therefore be revised to 11β,12α is easily inferred; an explanation, then, as to why the $J_{9,11}$ and $J_{11,12}$ coupling constants in the ring B-open turraflorins **3-1,2,3** differs so sharply from those of the ring B-intact compounds turraea A-C **3-5,6,7** is less easily arrived at.

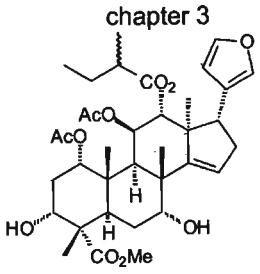
This discrepancy prompted a literature investigation into the effects of the structural features at C-8 and C-14, and, in particular, the differences arising from an open or intact ring B, on the coupling constants $J_{9,11}$ and $J_{11,12}$.

3.2 Results and Discussion

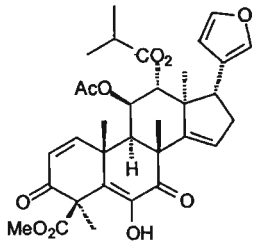
The results of the survey are given in Table 3.1.



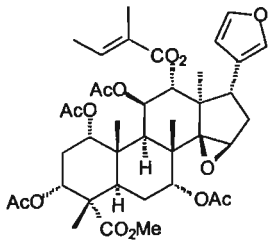
3-8 R_1 = H, R_2 = H
3-9 R_1 = Ac, R_2 = H
3-10 R_1 = Ac, R_2 = Ac



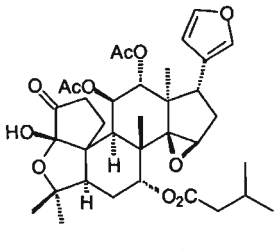
3-11



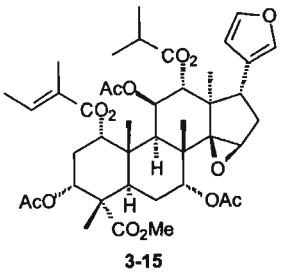
3-12



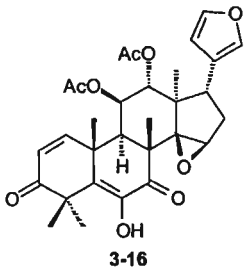
3-13 nilotin



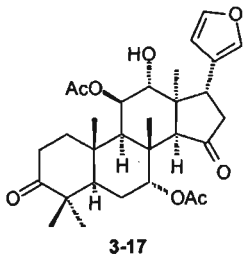
3-14 dumsin



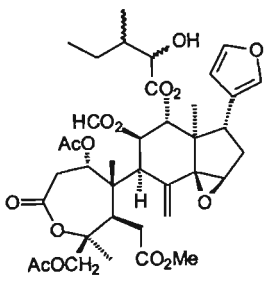
3-15



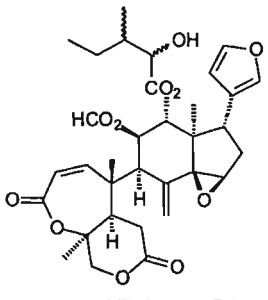
3-16



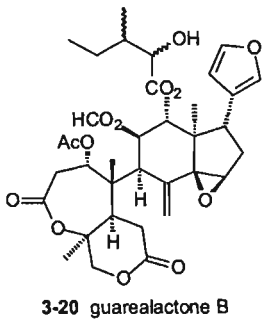
3-17



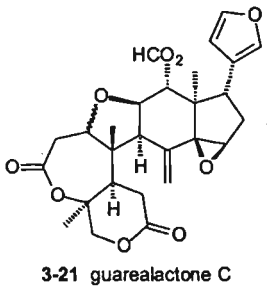
3-18 14,15-epoxyprieurianin



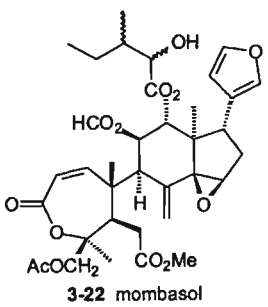
3-19 trichilia lactone D4



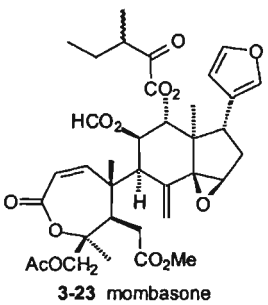
3-20 guarealactone B



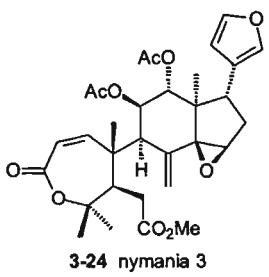
3-21 guarealactone C



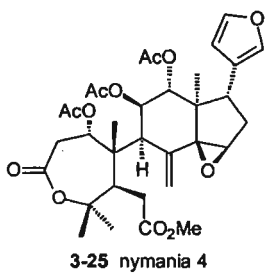
3-22 mombasol



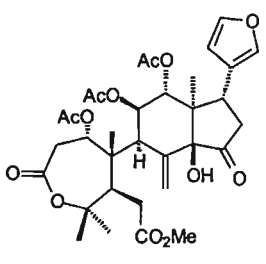
3-23 mombasone



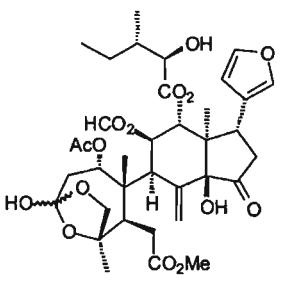
3-24 nymania 3



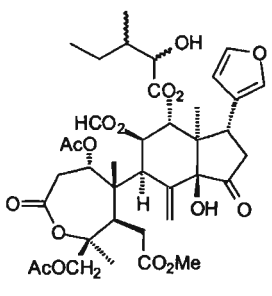
3-25 nymania 4



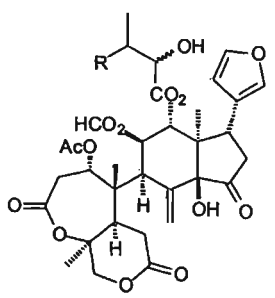
3-27 dregeana-2



3-28 nymania 1/rubrin E



3-29 prieurianin



3-30 R = Me 2'-hydroxyrohitukin
3-31 R = Et Trichila substance Tr B

Table 3.1: Variation in $J_{9,11}$ and $J_{11,12}$ in relation to the nature of ring B, and of C-8 and C-14

(Chemical shifts and coupling constants quoted are for each of H-9α, H-11, and H-12β for each of compounds **3-1** to **3-31**)

Compound type			H-9α	H-11	H-12β	Reference
Ring B intact						
A: Δ^{14}						
H-11α						
	3-8		2.89d 4.4	5.04m	5.13d 3.3	[7]
	3-9		2.65d 4.4	3.60m	4.70d 3.3	[7]
	3-10		2.97d 4.7	5.04m	5.14d 3.6	[7]
	3-11		2.90d 3.8	5.08m	5.15d	[7]
	3-12		2.97d 5.1	5.73dd 5.1, 4.7	5.36d 4.7	[8]
H-11β						
	-		-	-	-	-
B: 14,15-epoxide						
H-11α						
	3-5	turraea A	3.00d 3	obscured	4.36d 3	[5]
	3-6	turraea B	3.63d 3	5.15m	6.68d $W_{1/2}$ 5	[5]
	3-7	turraea C	3.45d 4.5	5.77m	4.95d 3	[5]
	3-13	nilotin	3.38d 3.5	5.16t 3.5	4.85d 3.5	[9]
	3-14	dumsin	3.38d 4.5	5.17dd 4.0,4.5	5.41d 4	[10]
	3-15		3.41d 3.9	5.17t 3.6	4.89d 3.5	[11]
	3-16		2.92s	5.36br s	5.19br s	[12]
H-11β			-	-	-	-
	-		-	-	-	-
C: 14α-H, 15-keto						
H-11α						
	3-17		obscured	5.45br m	3.83br s	[12]
H-11β						
	-		-	-	-	-
Ring B open						
D: Δ^{14}						
H-11α						
	3-1a	turraflorin A	2.84d 6	5.45dd 11, 6	5.82d 11	[2]
	3-2a	turraflorin B	2.84d 6	5.31dd 11, 6	4.30d 11	[2]
	3-3a	turraflorin C	2.84d 6	5.25dd 11, 6	5.80d 11	[2]
H-11β						
	-		-	-	-	-
E: 14,15-epoxide						
H-11α						
	3-18	14,15-epoxyprieurianin	obscured	5.56m	5.81d 10.6	[13]
	3-19	trichilia lactone D4	3.66d 8	5.50dd 11, 8	6.04d 11	[14]
	3-20	guarealactone B	3.65d 7	5.59dd 11, 7	5.89d 11	[14]
	3-21	guarealactone C	3.26d 9	4.27t 9	5.56d 9	[14]
	3-22	mombasol	3.15d 7.3	5.75dd 7.2, 7.2	5.95d 7.2	[15]
	3-23	mombasone	3.11d 7.3	5.75dd 7.2, 7.2	6.01d 7.3	[15]
	3-24	nymania 3	3.12d 6.7	5.60m	5.91d 11.1	[16]
	3-25	nymania 4	3.53d 6.9	5.45m	5.71d 10.1	[16]
	3-26	11-*epi*-toonacilin	2.97d 7.2	dd 10.8, 7.2	5.68d 10.8	[12]
H-11β						
	3-4	toonacilin	2.58br s 2.57br s	5.34d 4.3 5.35d 4.4	5.36d 4.3 5.33d 4.4	[4] [17]
F: 14β-hydroxy, 15-keto						
H-11α						
	3-27	dregeana 2	3.72d 7	5.22m	5.93d 11	[18]
	3-28	nymania 1/rubrin E	4.19d 8.2	5.37dd 8.5, 10.7	6.08d 10.7	[16,19]
	3-29	prieurianin	3.85d 8	5.46dd 11, 8	6.16d 11	[14]
	3-30	2'-hydroxyrohitukin	3.76d 7	5.45dd 12, 7	6.13d 12	[20]
	3-31	trichilia substance Tr B	3.78d 7	5.47dd 11, 7	6.16d 11	[21]†
H-11β						
	-		-	-	-	-

† Unfortunately incorrectly recorded in the Dictionary of Natural Products as 11α,12α-disubstituted; as such it would have been the only representative of its class.

It became apparent, while conducting this survey, that 11α,12α-substitution occurs much more rarely than does 11β,12α, and that any conclusions about $J_{9,11}$ and $J_{11,12}$ for this substitution pattern are based essentially on only one reported example, the values obtained for toonacilin **3-4** itself. Any misgivings about general conclusions being drawn from a single set of reported values should, however, be allayed by the recent acquisition [17] of $J_{9,11}$ and $J_{11,12}$ coupling constants for toonacilin **3-4** virtually identical to those obtained originally [6].

It can readily be seen from Table 3.1 that when ring B is open, the 11β,12α-substitution pattern is characterised by large coupling constants (of the order of ~6-8Hz and 7-11Hz for $J_{9,11}$ and $J_{11,12}$, respectively; *eg.* turraflorin A **3-1a**, $J_{9,11}$ = 6Hz, $J_{11,12}$ = 11Hz), while 11α,12α-substitution affords much smaller values (*eg.* toonacilin **3-4**, $J_{11,12}$ = 4.4Hz, $J_{9,11}$ unresolvable broad singlet at 400MHz [17]).

Conversely, when ring B is intact, small coupling constants ($J_{9,11}$ ~3-5Hz, $J_{11,12}$ ~3-5Hz, respectively; *eg.* dumsin **3-14**, $J_{9,11}$ = 4.5Hz, $J_{11,12}$ = 4Hz) indicate the 11β,12α-substitution pattern; while ring B intact 11α,12α-disubstituted examples have yet to be reported, they presumably would exhibit larger values.

Examination of molecular models reveals that while ring C can be chair-like in ring B-cleaved compounds, giving rise to dihedral angles of ~45° and ~180° for H-9/H-11α and H-11α/H-12β, respectively, it can only be boat-shaped if ring B is intact, with the corresponding angles both very close to 90°.

Remarkably, within the broad open/closed ring B subdivision, the conformations adopted appear to be independent of the C-14,C-15 substitution pattern and/or the hybridisation state of C-14 in particular. Thus similar $J_{9,11}$ and $J_{11,12}$ values are observed for compounds in group A, with a Δ^{14}-double bond and sp^2 hybridised C-14 (*eg.* **3-10**, $J_{9,11}$ = 4.7Hz, $J_{11,12}$ = 3.6Hz), group B analogues, with a 14β,15β-epoxide ring and C-14 sp^3 hybridised (*eg.* turraea C **3-7**, $J_{9,11}$ = 4.5Hz, $J_{11,12}$ = 3Hz), and the single group C representative **3-17**, with C-14 also sp^3 hybridised but with H-14α ($J_{9,11}$ obscured, $J_{11,12}$ br s), as these compounds all have an intact ring B. The compounds of the corresponding groups D, E and F, which are all characterised by an open ring B, display equally comparable $J_{9,11}$ and $J_{11,12}$ values; *cf.* turraflorin A **3-1a** ($J_{9,11}$ = 6Hz, $J_{11,12}$ = 11Hz), nymania 3 **3-24** ($J_{9,11}$ = 6.7Hz, $J_{11,12}$ = 11.1Hz), and

trichilia substance Tr B ($J_{9,11}$ = 7Hz, $J_{11,12}$ = 11Hz), irrespective of whether ring D has a Δ^{14}-double bond, 14β,15β-epoxide ring, or hydroxy group at C-14β and ketone at C-15.

The stereochemistry at C-11 in the turraflorins is thus reassigned as β, giving revised structures **3-1a**, **3-2a** and **3-3a**, respectively, for turraflorins A, B and C [12].

3.3 References

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Chapter 4

Extractives from *Malleastrum antsingyense*

4.1 Introduction

The genus *Malleastrum* (Baill.) J.F.Leroy is a relatively recent addition to the Meliaceae family. Even *Malleastrum boivinianum* (Baill.) J.F.Leroy and *Malleastrum depauperatum* (Baill.) J.F.Leroy, the two members of this genus first described by Baillon and included by him in the section *Malleastrum* of *Cipadessa*, date back only to 1874 [1]. De Candolle (1878) [2] initially followed Baillon, as did Harms (1896) [3]; both authors subsequently [4,5] placed later species in *Trichilia*, with Harms [5] creating the new section *Pterotorhachis* for *Trichilia ramiflora* C.DC.

In 1964 Leroy raised *Malleastrum* to generic rank and included within it *Pterotorhachis*[†] and eleven other species [6], where it has subsequently remained[‡]. The genus, within the tribe Trichilieae, subfamily Meliodeae [7], currently comprises twenty-four species [8], with the five most recent additions being included as recently as 1996 [9], and is confined to Madagascar and the Comores.

The chemistry of this genus has not been investigated previously.

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† Including *Trichilia ramiflora* C.DC., renamed as *Malleastrum ramiflorum* (C.DC.) J.-F. Leroy [6].

‡ Pennington and Styles [7] considered Leroy to be "fully justified". They give in their circumscription "about twelve species"; these are presumably the original twelve species identified by Leroy.

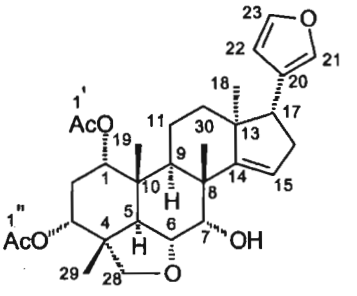
4.2 Extractives from *Malleastrum antsingyense*

Malleastrum antsingyense J.F.Leroy is locally named "andremanamora" in northern Madagascar [10].

The methanol extract of the stem bark was shown by ^{1}H NMR to contain only sugars and was not investigated further, while the hexane and dichloromethane extracts were sufficiently similar, by ^{1}H NMR and tlc analysis, to be combined. The extract proved to be composed of a major component, **MA 1**, comprising ~20% of the total extract mass, and a plethora of minor components which proved very difficult to separate and from which only one further compound, **MA 2**, could be isolated.

4.2.1 Structural elucidation of compound MA 1, 1,3-diacetylvilasinin

(spectra vol II, p.s10-19)



4-1 1,3-diacetylvilasinin **MA 1**

An HRMS of this compound gave a molar mass of 512.2784 g.mol^{-1}, corresponding to the molecular formula $C_{30}H_{40}O_7$ (calc. 512.2774 g.mol^{-1}) and eleven double bond equivalents. The ^{1}H and ^{13}C NMR spectra showed the presence of two acetate esters (δ1.98s, 3H; δ170.38(C) and 21.08(CH_3); δ2.01s, 3H, δ170.10(C) and 21.18(CH_3)), a furan ring (δ7.35s, δ142.59(CH), H-23; δ7.23s, δ139.70(CH), H-21; δ6.26s, δ111.03(CH), H-22; and δ124.46(C), C-20) and a Δ^{14} double bond (δ5.59d J = 1.83Hz, δ120.74(CH), H-15; δ159.80(C), C-14), leaving five remaining double bond equivalents to be accounted for – in the absence of other signals – within the triterpenoid skeleton.

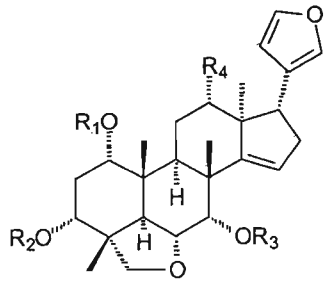
A correlation in the NOESY spectrum between H-15 and a doublet (J = 3.11Hz) at δ4.17, coupled to a resonance at δ72.81(CH), established this as H-7β, and thus the presence of a hydroxy group at C-7α. Couplings in the COSY spectrum between H-7 and a double doublet (J = 12.46, 3.11Hz) at δ4.13, which in turn is coupled to a doublet (J = 12.46Hz) at δ2.65, allow these to be assigned to H-6

and H-5, respectively, and the corresponding signals at δ73.99(CH) and δ39.61(CH) to C-6 and C-5. The large $J_{5,6}$ coupling constant indicates that H-6, as is almost invariable for substituents in this position, is β [11,12]. The proton resonances at δ4.66(1H, t, J = 4.66Hz) and δ4.90 (1H, m), correlating in the HSQC spectrum to methine C-O signals at δ72.23 and δ71.72, respectively, are both seen to be coupled in the COSY spectrum to a pair of coupled multiplets at δ2.06 and δ2.15, which are characteristic of 2H-2 in an A ring with acetate groups at C-1α and C-3α. C-2 occurs at δ27.63.

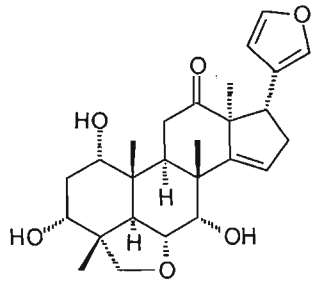
The presence of only four quaternary methyl resonances rather than the expected five and the appearance of a 2H multiplet signal at δ3.57, correlated in the HMBC spectrum to C-5 and seen to be coupled in the HSQC spectrum to a methylene C-O resonance at δ77.81, intimated that the methyl group at either C-28 or C-29 had been oxidised to form an oxygenated methylene carbon.

A literature survey based on this information revealed **MA 1** to be the known limonoid 1,3-diacetyl vilasinin **4-1**, in which the fifth double bond equivalent is satisfied by the formation of a tetrahydrofuran ring *via* a 6α,28 ether linkage. Vilasinin **4-2** was initially isolated from an Indian specimen of *Azadirachta indica* L [13], although the 1,3-diacetyl-7-cinnamoyl derivative nimbolin A **4-3** had previously been found in Nigerian samples of both *Azadirachta indica* and *Melia azedarach* L. [14], as was the 12-keto analogue nimbidinin **4-4**, also from an Indian source [15]. A wide variety of derivatives have subsequently been characterised, almost exclusively from *Melia* and *Azadirachta* spp. [16-24], with 1,3-diacetylvilasinin **4-1**, in particular, being found in *Melia volkensii* Gürke [20], *Chisocheton paniculatus* Hiern [21], *Azadirachta indica* [22] and two African *Turraea* species recently investigated in this laboratory, *Turraea holstii* Gürke [25] and *Turraea parvifolia* Deflers [26]†. The fully assigned ^{1}H and ^{13}C NMR spectral data, together with reference ^{13}C NMR data for comparison, are given in Table 4.1 below.

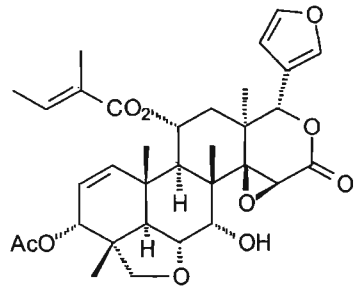
† Together with the *Turraea* and *Chisocheton* extractives, 12α-acetoxy-3-acetylvilasinin – trichilinin **4-5**, from *Trichilia roka* (Forssk.) Chiov. [27] – are the only examples from non *Melia/Azadirachta* sources.



4-2 R_1, R_2, R_3, R_4 = H vilasinin
4-3 R_1, R_2 = Ac R_3 = Cinn R_4 = H nimbolin A
4-5 R_1, R_3 = H R_2 = Ac R_4 = OAc trichilinin

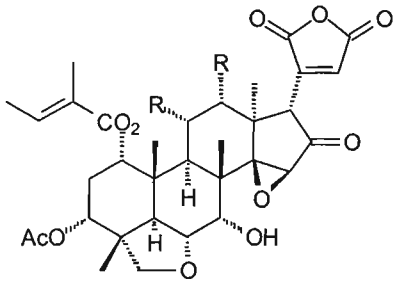


4-4 nimbidinin

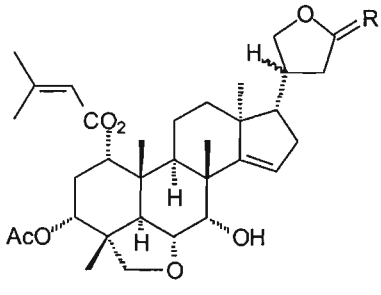


4-6 piscidofuran

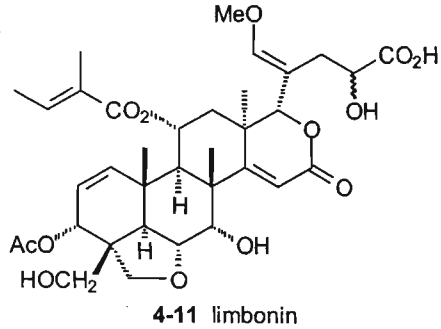
Formation of the 6α,28 ether linkage does not appear to occur at a specific point in limonoid biosynthesis. The ring is found in the havanensin-type limonoids, has been recorded once in the gedunin group - piscidofuran **4-6** from *Walsura piscidia* Roxb. [28] - and is practically ubiquitous in the highly oxidised ring C opened nimbin group, suggesting that ether formation certainly takes place after that of the furan ring, and later rather than sooner. However, in limbocidin **4-7** and its 11,12-bis(deoxy) derivative **4-8** [29], and, more recently, azadirachtolide **4-9** and its 23-deoxy analogue **4-10** [30], all from *Azadirachta indica*, ether formation has preceded that of the furan ring, although side chain cyclisation and the associated loss of four carbon atoms has taken place†.



4-7 R = OH limbocidin
4-8 R = H



4-9 R = O azadirachtolide
4-10 R = H_2



4-11 limbonin

† In limbonin **4-11** [31] formation of the ether linkage and oxidative opening of ring D to form the gedunin skeleton have both occurred without cyclisation of the sidechain. This is unusual in its own right, an exception to the normally accepted limonoid biosynthesis pathway, and apparently confined to *Azadirachta*. The same argument might then be applied to compounds **4-7** to **4-10** also. Of course the alternative explanation, that oxidation of the furan ring subsequent to its formation is responsible for compounds **4-7** to **4-10** cannot be discounted, but this then does not explain how limbonin **4-11** arises.

Table 4.1: ^{1}H and ^{13}C NMR assignments for compound **MA 1**, 1,3-diacetylvilasinin

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

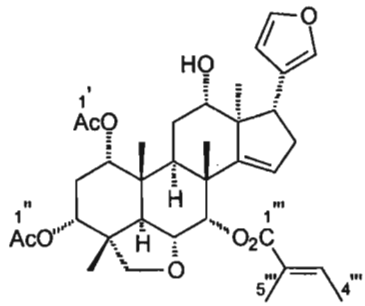
[Lit. [25] ^{1}H NMR 300MHz, ^{13}C 75MHz, $CDCl_3$, *J* in Hz]

Position	δC	4-1 Ref. [25]	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	72.23 (CH)	72.2	4.66t 2.65	3,5,19	2α,2β	2α,2β,11α,19
2	27.63 (CH_2)	27.2	α 2.06m β 2.15m	-	1,2β,3 1,2α,3	1,2β,3 1,2α,3
3	71.72 (CH)	71.7	4.90m	1,2α,3,29	2α,2β	2α,2β,28,29
4	42.27 (C)	42.3	-	2β,5,29	-	-
5	39.61 (CH)	39.6	2.65d 12.46	1,3,7,19,28,29	6	9,28
6	73.99 (CH)	72.8	4.13dd 12.46,3.11	5,7,28	5,7	19,29,30
7	72.81 (CH)	74.0	4.17d 3.11	5,30	6	15
8	45.80 (C)	45.8	-	9,30	-	-
9	33.60 (CH)	33.6	2.51m	5,7,12α,12β,19,30	11α,11β	5,11α18
10	39.17 (C)	39.2	-	2α,5,9,19	-	-
11	15.16 (CH_2)	15.2	α 1.23m β 1.60m	-	9,11β,12α,12β 9,11α,12α,12β	1,9,11β,12α 11α,12β,19,30
12	32.88 (CH_2)	32.9	α 1.72m β 1.58m	17,18	11α,11β,12β 11α,11β,12α	11α,12β,18,22 12α,17,30
13	47.35 (C)	47.4	-	12α,12β,17,18	-	-
14	159.80 (C)	159.9	-	9,12α,16α,16β,18,30	-	-
15	120.74 (CH)	120.7	5.59d 1.83	16α,16β	-	7,16α,16β,30
16	34.31 (CH_2)	34.3	α 2.55m β 2.40m	15,17	15,16β,17 15,16α,17	15,16β,21 15,16α,17
17	51.50 (CH)	51.5	2.80dd 10.81,7.33	15,18	16α,16β	12β,16β
18	21.13 (CH_3)*	21.2	0.82s	12α,12β,17	-	9,12α,16α,22,2'
19	15.35 (CH_3)	26.2	0.96s	5,9	-	1,2β,6,11β,29,30
20	124.46 (C)	124.5	-	17,21,22,23	-	-
21	139.70 (CH)	139.7	7.23s	17,22,23	-	16α,17,18
22	111.03 (CH)	111.1	6.26s	17,21	23	12α,16α,17,18,23
23	142.59 (CH)	142.6	7.35s	21,22	22	22
28	77.81 (CH_2)	77.9	3.57m	5,29	-	3,5,29
29	19.43 (CH_3)	15.4	1.18s	5,28	-	2β,3,6,19,28
30	26.22 (CH_3)	19.5	1.09s	9	-	6,7,11β,15,19
1'	170.38 (C)#	170.3	-	2',2''	-	-
2'	21.08 (CH_3)*	21.1	1.98s	-	-	18
1''	170.10 (C)#	170.0	-	2',2''	-	-
2''	21.18 (CH_3)*	21.2	2.01s	-	-	28

*,#: interchangeable within column

4.2.2 Structural elucidation of compound MA 2, 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin

(spectra vol II, p.s20-29)



4-12 MA 2

An HRMS of this compound gave a molar mass of 610.3149 g.mol^{-1}, corresponding to the molecular formula $C_{35}H_{46}O_9$ (calc. 610.3142 g.mol^{-1}) and thirteen double bond equivalents. Comparison of the ^{1}H and ^{13}C NMR spectra of **MA 2** with that of **MA 1** showed them to be very similar, with **MA 2** also having two acetate esters, a furan ring, and a C-14,C-15 double bond. The presence of an additional tiglate ester[†] was inferred from resonances at δ166.80(C) (C-1'''); δ128.79(C) (C-2'''); δ6.92qq *J* = 5.86, 1.24Hz, δ137.21(CH) (H-3'''); δ1.74d *J* = 5.86Hz, δ14.92(CH_3) (3H-4'''); and δ1.88s, δ12.20(CH_3) (3H-5'''), and that of a further secondary hydroxyl group from signals at δ3.99 (dd *J* = 8.60, 6.95Hz) and δ76.07(CH). A doublet at δ2.63 (*J* = 12.45Hz) and double doublet (*J* = 12.63, 2.74Hz) at δ4.16 were assigned by direct comparison to H-5 and H-6, with esterification at C-7 shifting H-7 downfield to δ5.63d (*J* = 2.56Hz); the corresponding carbon resonances occur at δ41.49(CH), δ72.91(CH) and δ73.79(CH), respectively.

That **MA 2** is also a vilasinin derivative is readily evident from the characteristic missing quaternary methyl signal and additional methylene C-O resonance at δ78.08, which is assigned as before to C-28. The 2H-28 resonances now appear as a pair of coupled doublets (*J* = 7.60Hz) at δ3.40 and δ3.48, replacing the 2H multiplet signal at δ3.57 observed in **MA 1**. The remaining five double bond equivalents are then also accounted for.

---

† In a tiglate ester the 3H-4''' and 3H-5''' methyl groups are *cis* with respect to the $\Delta^{2'''}$ double bond, giving rise to the characteristic H-3''' shift of ~δ6.9. When 3H-4''' and 3H-5''' are *trans*, as occurs in the angelate ester, H-3''' occurs at ~δ6.0 [32].

A correlation in the HMBC spectrum between the resonance at δ3.99 and that at 50.82(CH), ascribable to C-17 by comparison with compound **MA 1**, places the remaining hydroxy group at C-12; NOESY correlations between H-12 and signals at δ2.98 (t, *J* = 9.34Hz, H-17) and δ1.13 (s, 3H-30) assign H-12 as β, and hence the C-12 hydroxy group as α.

The downfield acetate ester methyl group proton signal showed NOESY correlations to both 2H-2 and 3H-18. Examination of a molecular model showed that while correlations to 2H-2 are possible from an acetate at either C-1 or C-3, only an acetate at C-1 can correlate to 3H-18. If the second acetate ester occurred at C-7, its methyl signal would be expected to correlate to H-5. As no such correlations were observed, the tiglate ester was assigned to C-7 and the second acetate to C-3 (although a NOESY correlation between the tiglate 3H-5''' and H-5 is observed, this in itself is not sufficient evidence as such NOESY correlations would arise irrespective of whether the tiglate ester is placed at C-1,C-3 or C-7. In conjunction, however, with the absence of the second acetate methyl ester signal correlation mentioned above we believe it to do so). **MA 2** is thus 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin **4-12**. The fully assigned ^{1}H and ^{13}C NMR spectral data are given in Table 4.2 below.

1,3-Diacetyl-12β-hydroxy-7-tigloylvilasinin **4-12** has reportedly been isolated from *Azadirachta indica* [24]†. However, while the literature ^{13}C NMR data agree well with our assignments, the chemical shifts for H-1 (δ5.08, br s) and H-3 (δ5.61, br s) differ sharply. A perusal of these values for various other 1,3-di-estervilasinin derivatives, both with [17,23] and without [13,17,18,20,22] a hydroxy/ester group at C-12α, reveal that with a single exception†, neither value is downfield of δ5.00. We can only conclude that the values for H-1 and H-3 in this reference have been misquoted.

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† Where it is reported in the publication abstract as "...1,2-diacetyl...". The stereochemistry at C-12 is assigned on the basis that "...H-12 coupled with one of the protons on C-11 to a very large extent." (H-12 is given as δ3.50d *J* = 7.51Hz). However, no limonoid with a hydroxy/ester substituent at C-12β has ever been reported, the authors themselves did not remark further on what would have been a unique discovery, and the Dictionary of Natural Products gives the stereochemistry at C-12 as α.

† 3-Acetyl-1,7-ditigloylvilasinin [17], where H-1 is given as δ5.30. H-3, in common with our, and literature values, occurs at δ4.95.

From a chemotaxonomic standpoint, the isolation of the vilasinin limonoids **MA 1** and **MA 2** confirms the botanically based placing of *Malleastrum*. All other species that have yielded vilasinin limonoids are members of the subfamily Melioideae, with *Trichilia* in particular a fellow member of the same tribe.

Table 4.2: ^{1}H and ^{13}C NMR assignments for compound **MA 2**, 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin [^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	72.68 (CH)	4.66dd 2.38,2.56	5,19	2	2,11α
2	27.57 (CH_2)*	2.17m	-	1,3	1,3,19,29,2',2''
3	71.96 (CH)	4.91dd 2.56,2.57	1,5,29	2	2,29
4	42.24 (C)	-	5,29	-	-
5	41.49 (CH)	2.63d 12.45	28β	6	9,28α,5'''
6	72.91 (CH)	4.16dd 12.63,2.74	5, 28β	5,7	7,19,29,30
7	73.79 (CH)	5.63d 2.56	5,6,30	6	6,30
8	44.49 (C)	-	9,30	-	-
9	36.05 (CH)	2.79dd 12.45,7.33	5,7,19,30	11α,11β	5,18
10	39.21 (C)	-	5,9	-	-
11	27.39 (CH_2)*	α 1.10m β 2.05m	9	9,12 9,12	1,9,11β 11α,12
12	76.07 (CH)	3.99dd 8.60,6.95	11α,17,18	11α,11β	11β,17,30
13	53.17 (C)	-	11β, 15,17,18	-	-
14	156.11 (C)	-	16,18,30	-	-
15	122.94 (CH)	5.61m	16	16	16
16	36.08 (CH_2)	2.36dd 9.34,2.20	17	15,17	15,17
17	50.82 (CH)	2.98t 9.34	12,15,18	16	12,16
18	14.73 (CH_3)	0.86s	12,17	-	9,22,2',5'''
19	15.36 (CH_3)	1.02s	5,8	-	1,2,6,11β,29,30
20	125.61 (C)	-	17,22,23	-	-
21	140.31 (CH)	7.30s	17,22,23	-	16,17,18
22	111.96 (CH)	6.41s	17,21	23	16,17,18,23
23	142.94 (CH)	7.33s	21,22	22	22
28	78.08 (CH_2)	α 3.40d 7.60 β 3.48d 7.60	5,29	- -	5,28β 28α,29
29	19.47 (CH_3)	1.16s	5,28α,28β	28α	2,3,6,19,28β
30	26.97 (CH_3)	1.13s	9	28α	6,7,12,19
1'	169.94 (C)	-	2'	-	-
2'	21.31 (CH_3)	1.94s	-	-	2,18
1''	169.90 (C)	-	2''	-	-
2''	21.06 (CH_3)	1.90s	-	-	2
1'''	166.80 (C)	-	3''',5'''	-	-
2'''	128.79 (C)	-	4''',5'''	-	-
3'''	137.21 (CH)	6.92qq 5.86,1.24	-	4''',5'''	4'''
4'''	14.62 (CH_3)	1.74d 5.86	3'''	3'''	3''',5'''
5'''	12.20 (CH_3)	1.88s	3'''	3'''	5,18,4'''

*: interchangeable within column

4.3 Experimental

Malleastrum antsingyense was collected in April 1997 in the Bemaraha Tsingy area in southwestern Madagascar. A voucher specimen (009-Mj/Mdul) is deposited at the Department of Botany of the University of Antananarivo. Plant identification was confirmed by the Department of Botany at the Parc Zoologique et Botanique de Tsimbazaza.

The air-dried, milled stembark (232g) was extracted successively for 24 hours in a Soxhlet apparatus with hexane, dichloromethane and methanol, yielding 7.80g, 1.05g and 13.22g of extract respectively. The combined hexane-dichloromethane extract yielded compounds **MA 1** and **MA 2**.

Compound **MA 1**
(spectra vol II, p.s10-19)

1,3-diacetylvilasinin

pale yellow gum, 1.827g
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 4.1, p.109.

M.p. 125-127°C (lit. value [21] 128-131°C).

Optical Rotation:
$[\alpha]_D$ = -5.3° (c, 0.91 in $CHCl_3$)(lit. value [41] -1°).

IR spectrum:
υ_{max}(NaCl) 3453, 2932, 1732, 1376, 1252, 1052 cm^{-1}.

Mass spectrum:
HRMS found 512.2784, calc. for $[C_{30}H_{40}O_7]^+$ 512.2744g.mol^{-1}.
EIMS *m/z* 512.2784, 497.2543 $[M-CH_3]^+$, 494.2684 $[M-H_2O]^+$, 479.2395 $[M-CH_3-H_2O]^+$, 434.2417 $[M-AcOH-H_2O]^+$, 430.2325 $[M-C_5H_6O]^+$, 417.2270 $[M-C_6H_7O]^+$, 359.2001 $[M-CH_3-H_2O-2HOAc]^+$, 81 $[C_5H_5O]^+$.

Compound **MA 2**
(spectra vol II, p.s20-29)

1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin

pale yellow gum, 10mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 4.2, p.112.

Optical Rotation:

$[\alpha]_D = 0.0^{\circ}$ (too small to be measured).

IR spectrum:

υ_{max}(NaCl) 3415, 2976, 2935, 1747, 1385, 1256, 1057 cm^{-1}.

Mass spectrum:

HRMS found 610.3149, calc. for $[C_{35}H_{46}O_9]^+$ 610.3142g.mol^{-1}.

EIMS *m/z* 610.3149, 592.3047 $[M\text{-}H_2O]^+$, 550.2920 $[M\text{-}HOAc]^+$, 510.2637 $[M\text{-}TigOH]^+$, 495.2395 $[M\text{-}TigOH\text{-}CH_3]^+$, 492.2517 $[M\text{-}TigOH\text{-}H_2O]^+$, 450.2397 $[M\text{-}TigOH\text{-}HOAc]^+$ 435.2184 $[M\text{-}TigOH\text{-}HOAc\text{-}CH_3]^+$, 417.2067 $[M\text{-}TigOH\text{-}HOAc\text{-}CH_3\text{-}H_2O]^+$, 375.1977 $[M\text{-}TigOH\text{-}2HOAc\text{-}CH_3]^+$, 357.1843 $[M\text{-}TigOH\text{-}2HOAc\text{-}CH_3\text{-}H_2O]^+$, 83.0496 $[C_5H_7O]^+$.

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Chapter 5

Extractives from *Samadera madagascariensis*

5.1 Introduction

5.1.1 Preface

This species was collected as part of a collaboration agreement with Dr Milijaona Randrianarivelojosia of the University of Antananarivo in Madagascar, and identified as *Samadera madagascariensis* Jussieu (Simaroubaceae). A preliminary literature survey conducted before commencing investigation revealed only one previous report on *Samadera madagascariensis* [1], which noted in passing that this species was regarded, by Capuron, as synonymous with *Samadera indica* Gaertn. on botanical grounds [2].

However, although *Samadera indica* has been extensively investigated [3-9], none of the subsequent publications that we were able to obtain [5,8,9] make mention of this synonymy, and a much later botanical monograph [10,56] distinguishes between them. It therefore seemed a worthwhile exercise, on chemotaxonomic grounds, to continue the study.

While research was in progress, a reference [11] on the genus *Quassia* L. uncovered another botanical publication [12] in which the entire genus *Samadera* Gaertn. was considered to be only a section, within the family Simaroubaceae, of *Quassia*, and therefore that *Samadera madagascariensis*, *via Samadera indica*, can be considered as synonymous with *Quassia indica* (Gaertn.) Nooteboom. On the other hand, a recent chemogeographical study distinguishes between *Quassia indica* and *Samadera indica*, yet identifies *Samadera madagascariensis* explicitly with the latter [13].

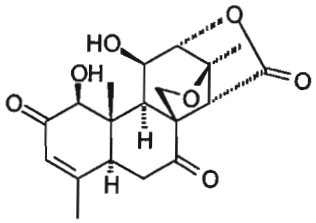
As no publication on *Quassia indica* refers to synonymy with either *Samadera madagascariensis* or *Samadera indica* [14,15,16], the questions of affinity and synonymity appear by no means to be resolved, further underpinning the chemotaxomic grounds for this investigation.

5.1.2 Literature Survey

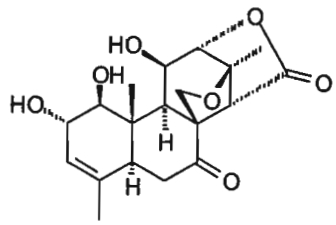
In view of the uncertainty surrounding the genera *Samadera* and *Quassia* (and, as described on p.45, the whole Simaroubaceae family), this survey covers the literature for both.

The genus *Samadera* currently comprises [13] only *Samadera indica*, which occurs in Sri Lanka, Java and India, and the recently - tentatively - identified *Samadera bidwillii* [17][†]. *Quassia* has five members; together with the Indonesian *Quassia indica* are included the Congolese *Quassia africana* (Baill.) Baill.; Guyanan *Quassia multiflora* (A.Juss.) Nooteboom, Australian *Quassia bidwillii*[‡], and *Quassia amara* L. from Central America.

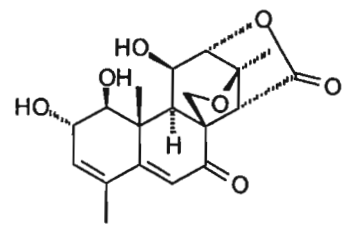
Samadera indica (Gaertn.): Early studies yielded the C_{19} quassinoids samaderines B **5-1**, C **5-2**, D **5-3**, cedronin **5-4**, cedronolin **5-5**, and dihydrosamaderine B **5-6** [4,6].



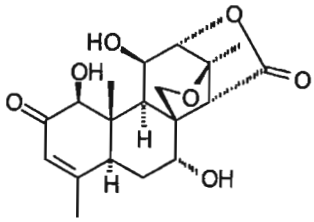
5-1 samaderine B



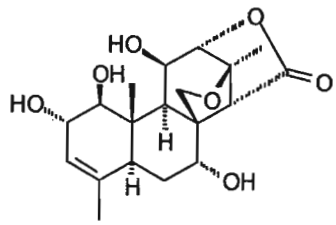
5-2 samaderine C



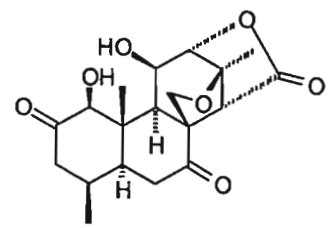
5-3 samaderine D



5-4 cedronin



5-5 cedronolin



5-6 3,4-dihydrosamaderine B

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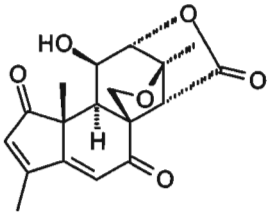
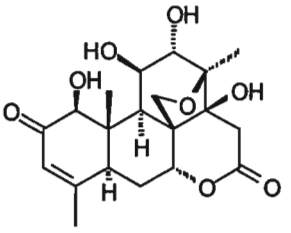
† Indicative of the confusion that frequently surrounds the classification of Simaroubaceous species is the comment that this species was "...originally described as *Hyptandria bidwillii* J.D.Hooker and ...subsequently... as *Samadera bidwillii* J.D.Hooker (Oliver), then as *Quassia bidwillii* (J.D.Hooker) Nooteboom, and finally as *Simaba bidwillii* (J.D.Hooker) Feuillet." [17]. Cedronin **5-4** and cedronolin **5-5** are ascribed in the Dictionary of Natural Products to a later isolation from *Samadera cedron*, yet the original reference gives the source as a Guyanese specimen of *Simaba cedron* Planch [18].

‡ *Quassia kerstingii* Little [19] is considered synonymous with *Pierrodendron kerstingii* (Engl.) Little and *Quassia gabonensis* Pierre [20] with *Odyendea gabonensis* Pierre ex Engl., and both species are excluded from this survey. On the other hand, a very recent publication [21] on "...a newly discovered taxon known only from north-eastern New South Wales, Australia." names the species *Quassia bidwillii*. As both reports emanate from the Australian National Herbarium, it is assumed that this species is distinct from the *S. bidwillii* discussed earlier, and is treated as such.

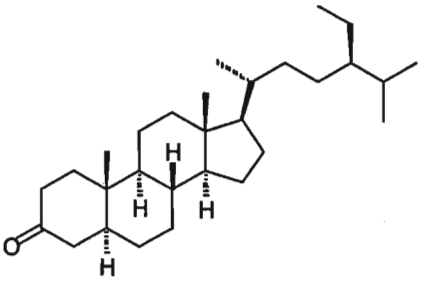
A preliminary investigation by the same authors had also afforded the novel C_{18} quassinoid samaderine A **5-7** [3], whose structure was established, much later, by crystallographic analysis in a study in which the antileukemic C_{20} quassinoid samaderine E **5-8** was also isolated [8,9].



5-7 samaderine A

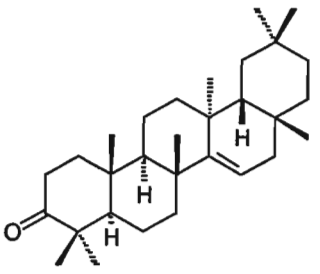


5-8 samaderine E

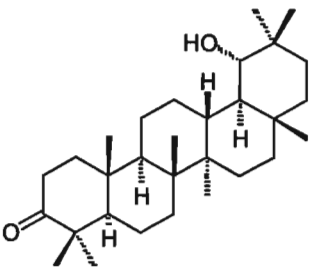


5-9 5α-stigmastan-3-one

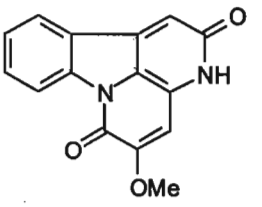
Non-quassinoidal compounds reported from this species are the ketosteroid 5α-stigmastan-3-one **5-9** from the peel [3], the taraxane triterpenoid taraxerone **5-10** [3] and oleanane derivative **5-11** [5] from the bark, and the canthinone alkaloid indacanthinone **5-12** from the wood [7].



5-10 taraxerone

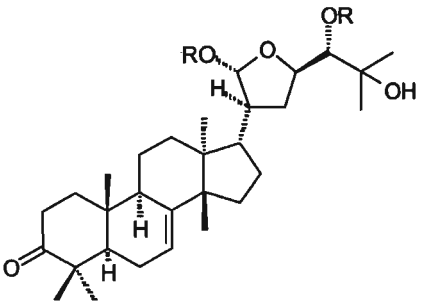


5-11

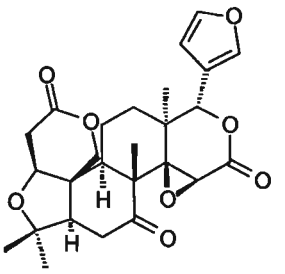


5-12 indacanthinone

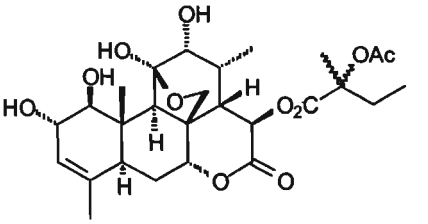
Samadera madagascariensis Jussieu: has also yielded, from the twigs and leaves [1], samaderines B and C **5-1,2**, together with the limonoid precursors melianodiol **5-13** and corresponding diacetate **5-14**.



5-13 R = H melianodiol
5-14 R = Ac melianodiol diacetate



5-15 limonin

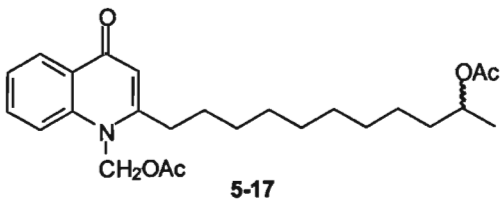


5-16 2'-acetylglaucarubin

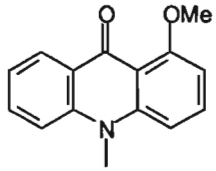
Samadera bidwillii: is an Australian species endemic to the Northern Territory, whose recent investigation has afforded a wide range of metabolites [17]. The known limonoid limonin **5-15** and quassinoid 2'-acetylglaucarubin **5-16** were isolated, together with three alkaloids **5-17,18,19** and seven lignans **5-20,21,22,23,24,25,26**.

The biosynthetic and chemotaxonomic importance of the compounds isolated in this study of *Samadera bidwillii* lies in the fact that this is the first report in which a quassinoid, a limonoid, and bicyclo-octane lignans have been found to co-occur in a single species. Quassinoids have previously been found only in the Simaroubaceae, which (other than the genus *Harrisonia*[†]) as a family is devoid of limonoids, albeit that A-ring modified limonoids of the type exemplified by limonin are typical of the Rutaceae rather than the Meliaceae. Bicyclo-octane lignans and acridone alkaloids, on the other hand, are widespread in the Rutaceae, but only rarely reported from either the Simaroubaceae or Meliaceae.

† "...except for the seemingly aberrant genus *Harrisonia*, which alone among genera traditionally assigned to the Simaroubaceae produces limonoids, but not quassinoids. Recent studies of DNA profiles support the contention that *Harrisonia* is not a typical Simaroubaceae (Morton, C., unpublished)" [17].



5-17



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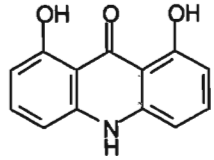
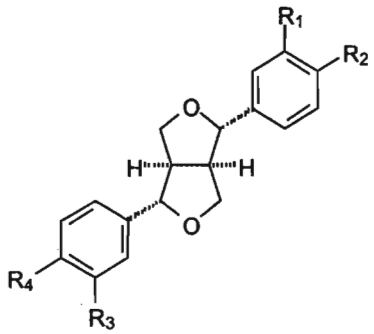
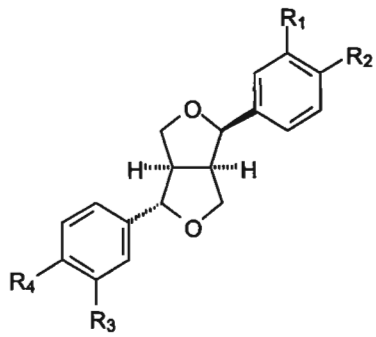


5-19

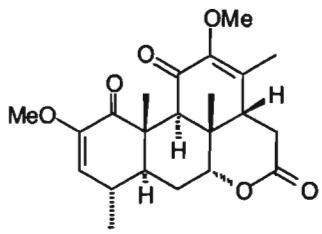


5-20 $R_1R_2 = OCH_2O$ $R_3R_4 = OCH_2O$ sesamin
5-22 $R_1 = R_2 = R_3 = R_4 = OMe$ eudesmin
5-24 $R_1 = R_2 = OMe$ $R_3R_4 = OCH_2O$ spinescin

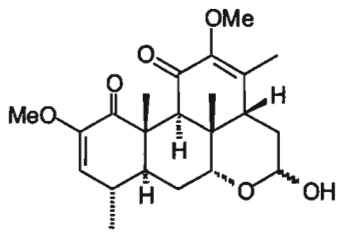


5-21 $R_1R_2 = OCH_2O$ $R_3R_4 = OCH_2O$ episesamin
5-23 $R_1 = R_2 = R_3 = R_4 = OMe$ epieudesmin
5-25 $R_1 = R_2 = OMe$ $R_3R_4 = OCH_2O$ fargesin
5-26 $R_1R_2 = OCH_2O$ $R_3 = R_4 = OMe$ neofargesin

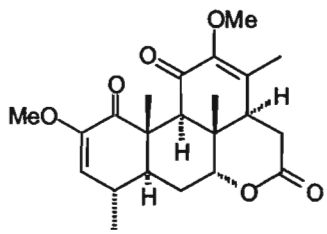
Quassia amara L.: or Surinam quassia, is the source of the bitter crystalline principle quassin, which was first reported in 1835 [22]. Subsequent investigations commencing a century later [23-26] established this to be a mixture of the two major components quassin **5-27** and neoquassin **5-28**, whose structures were finally elucidated in 1962 [27,28], and minor elements isoquassin **5-29** and the 18-hydroxy derivative **5-30** [29], reported in 1966.



5-27 quassin

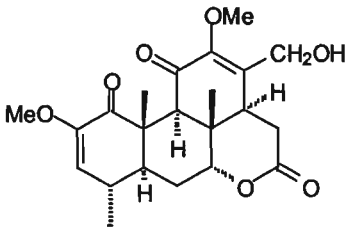


5-28 neoquassin

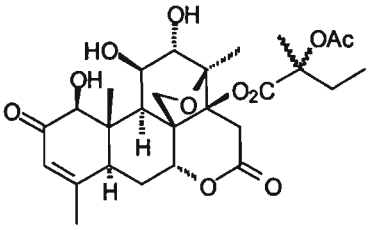


5-29 isoquassin

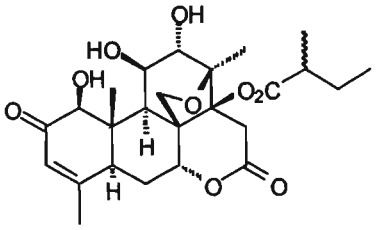
Bioassay-guided fractionation of the sap of a Costa Rican specimen yielded the antileukemic quassinoids quassimarin **5-31** and simalikalactone D **5-32** [30]. The latter compound had originally been found in the related species *Quassia africana* [31].



5-30

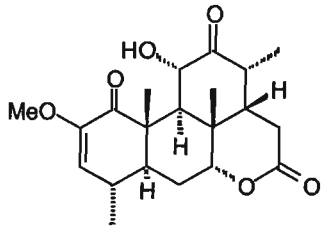


5-31 quassimarin

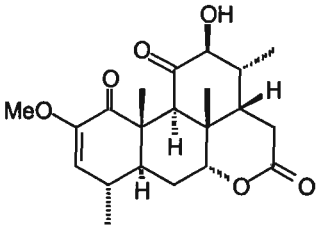


5-32 simalikalactone D

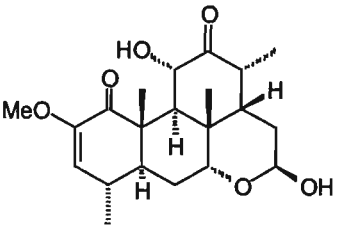
Simalikalactone C **5-33** and its 11-keto isomer **5-34** were isolated from the wood together with the novel dihydronorneoquassin **5-35** [32]. Compounds **5-33** and **5-34** had also previously been reported from *Quassia africana* [31], and simultaneously from *Aeschrion crenata* (= *Picrasma crenata*) [33] where they had been named as paraine and isoparaine respectively.



5-33 simalikalactone C/paraine

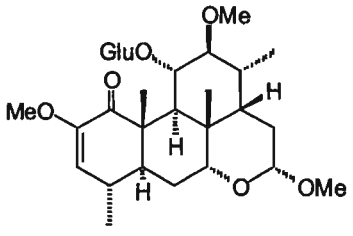


5-34 isoparaine

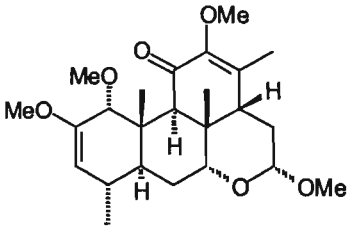


5-35

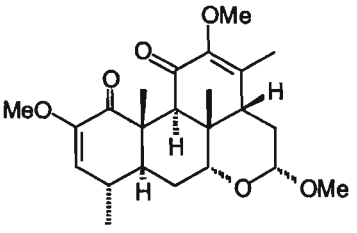
Further investigation by the same researchers [34] resulted in the isolation of the novel quassinoid derivatives **5-36,37,38** and parain analogues **5-39,40.** Compounds **5-38** [32] and **5-39** [33] had previously been synthesized, but had not been reported from natural sources.



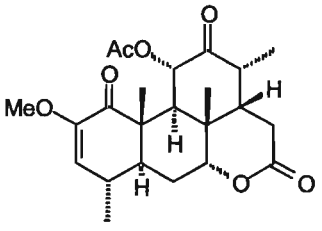
5-36



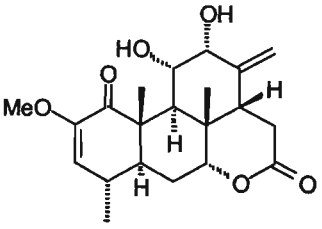
5-37



5-38

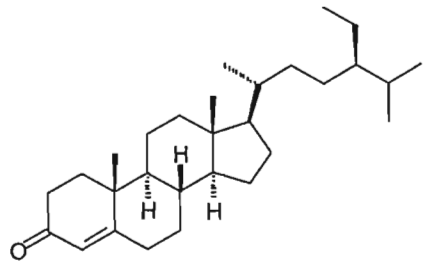


5-39

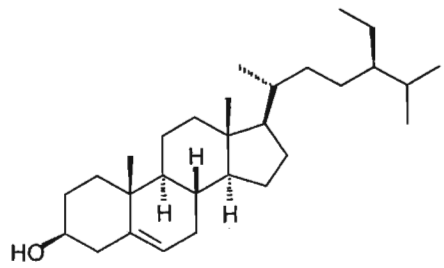


5-40

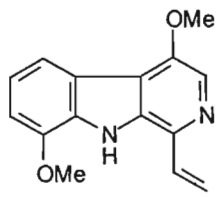
Non-quassinoidal compounds isolated from this species include an early report of the triterpenoid stigmast-4-en-3-one **5-41** and β-sitosterol **5-42** from the wood of a Brazilian sample [35], and a series of carboline **5-43,44** [36] and canthinone **5-45,46,47,48,49** alkaloids [36-38], also from the wood.



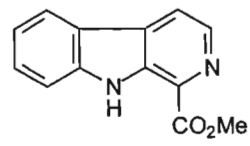
5-41 stigmast-4-en-3-one



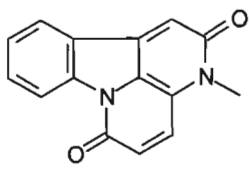
5-42 β-sitosterol



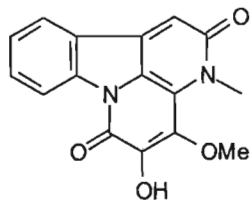
5-43



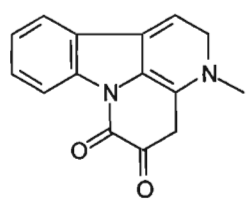
5-44



5-45



5-46



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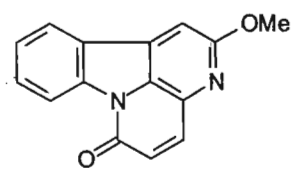

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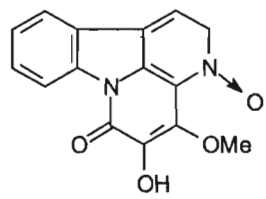

5-49

Quassia multiflora (A.Juss) Nooteboom: is not mentioned in a recent chemogeographical study [13], and is considered to be synonymous with *Simaba multiflora* (which is, and is of similar geographical origin) in all four publications on this species to date [39-42][†]. Chemical Abstracts, however, lists it as a separate species. This survey is thus confined to those reports listed by Chemical Abstracts under the entry *Quassia multiflora* and excludes those abstracted under *Simaba multiflora*.

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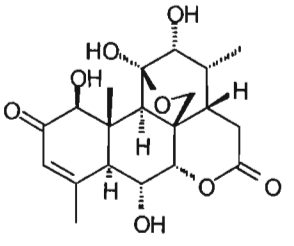
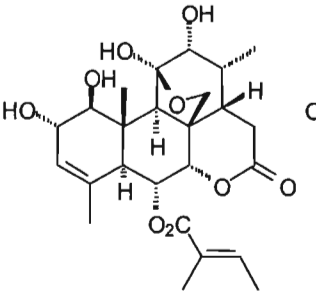
† Albeit by the same research group.

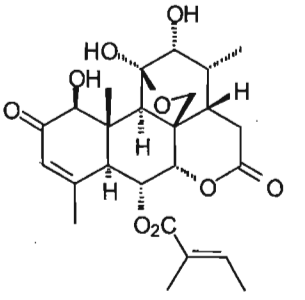
A series of publications have detailed the isolation and characterisation, from the roots of this species, of the novel quassinoid 6α-hydroxychaparrinone **5-50**, and related tigloyl esters of chaparrin **5-51** and chaparrinone **5-52** [39], the novel glabretal-type triterpenoid **5-53** [40], and, also novel, the squalene triterpenoids quassiols A-D **5-54,55,56,57** [41,42]. The absolute stereochemistry of quassiol A **5-54** was subsequently established by a total synthesis [43].



5-50 6α-hydroxychaparrinone



5-51



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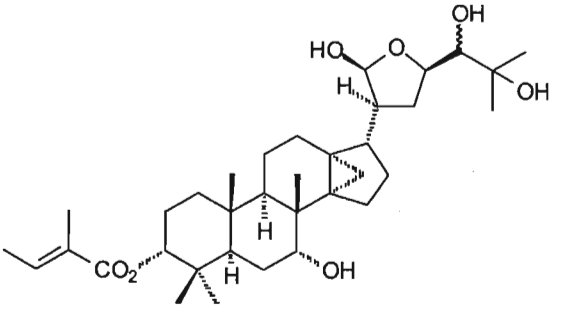
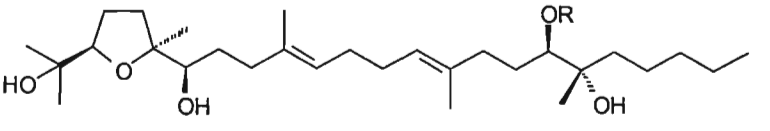
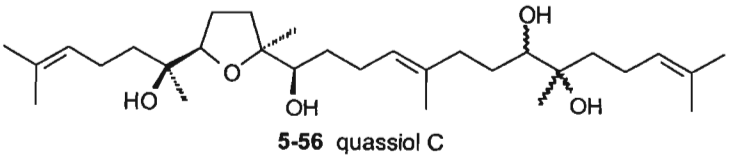


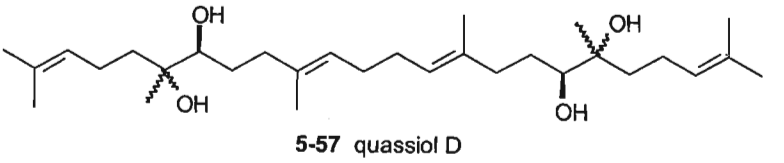
5-53



5-54 R = H quassiol A
5-55 R = H quassiol B



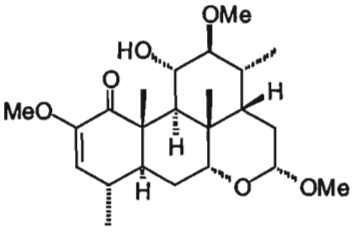
5-56 quassiol C



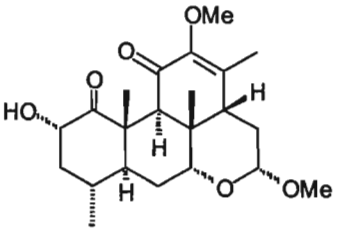
5-57 quassiol D

Quassia africana Baill.: is endemic to Central Africa. An early study [31] resulted in the isolation of the two novel quassinoids simalikalactones C **5-33** and D **5-32** and known compounds simalikalactones A and B, both previously isolated, as nigakilactone B **5-58** [44] and picrasin B **5-59** [45] respectively, from *Picrasma qussioides* Bennett. Also reported was simalikahemiacetal A, identified as neoquassin **5-28**.

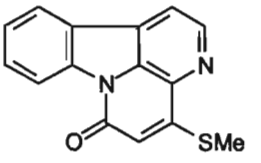
Investigation of the root bark of a Zaïrean sample yielded quassin **5-27** itself, and the canthinone and carboline alkaloids **5-60,61** and **5-62** [46]. A further canthinone analogue **5-63** and the rare thiocanthinone derivative **5-64** have also recently been reported [47].



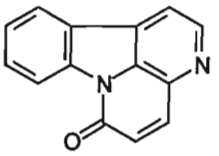
5-58 similakalactone A/nigakilactone B



5-59 simalikalactone B/picrasin B



5-64



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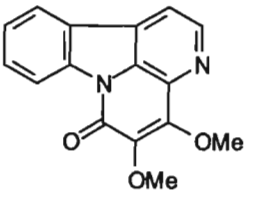
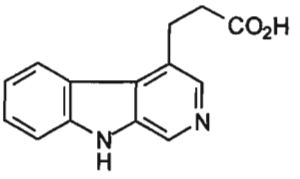
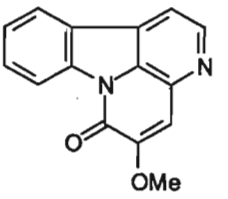


5-61

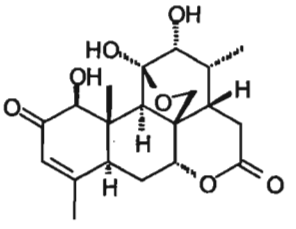


5-62



5-63

Quassia bidwillii: occurs exclusively in north-eastern New South Wales, is considered distinct from *Samadera bidwillii* [17,21], and is reported to contain the insecticidal quassinoid chapparinone **5-65**.

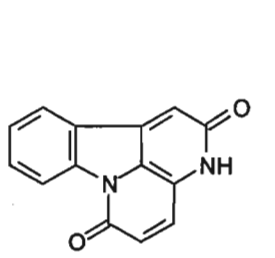


5-65 chaparrinone

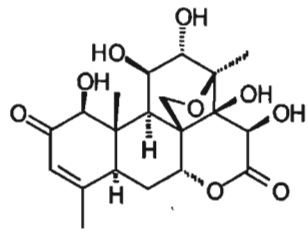
Quassia indica (Gaertn.) Nooteboom: is an Indonesian species which has surprisingly been investigated only in the last 10-15 years, given both its tortuous taxonomic history and its

pharmacological reputation. It is used in the treatment of malaria [16] and rheumatism [48], as an insecticide [48], and as an anti-inflammatory and antipyretic [14].

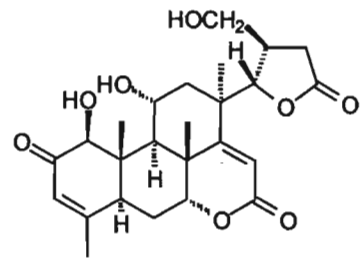
An investigation of the bark of *Quassia indica* [14,15] yielded, together with the known canthinone alkaloid **5-66** from *Simaba multiflora* [49], the known quassinoids samaderines B-E **5-1,5-2,5-3,5-8**, dihydrosamaderine B **5-6**, and cedronin **5-4**, all previously found in *Samadera indica* [3,4,6], brucein D **5-67**, from *Brucea amarissima* (Lour.) Desv. ex Gomez [50] and *Brucea javanica* (L.) Merr [51], and soulameolide **5-68**, a relatively rare C_{25} quassinoid originally found in *Soulamea tomentosa* Brogn. et Gris [52]. The structure of the first example of a new class of rearranged C_{20} quassinoids, indaquassin B **5-69** was also elucidated, along with the C_{19} quassinoid indaquassin A **5-70**, C_{25} quassinoid indaquassin F **5-71**, and the three further novel C_{20} quassinoids indaquassins C-E **5-72,73,74**.



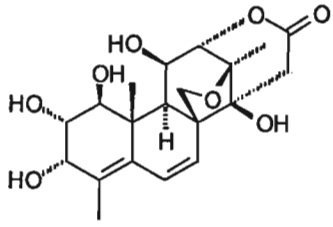
5-66



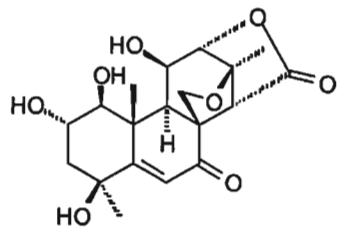
5-67 brucein D



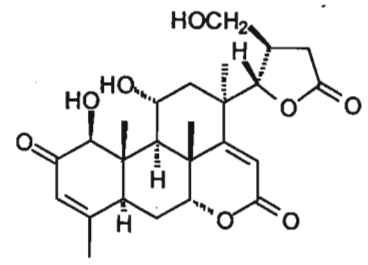
5-68 soulameolide



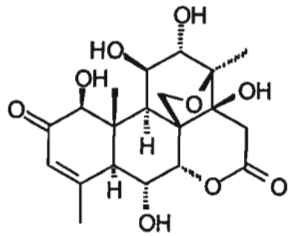
5-69 indaquassin B



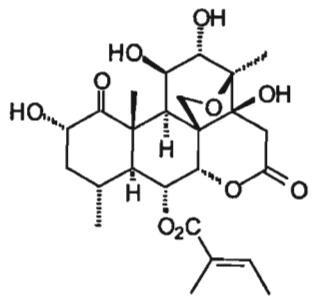
5-70 indaquassin A



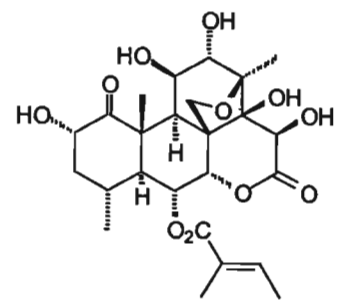
5-71 indaquassin F



5-72 indaquassin C

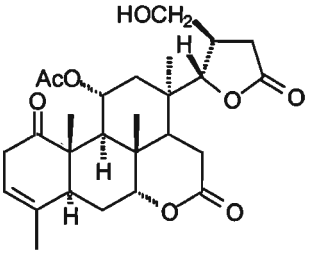


5-73 indaquassin D

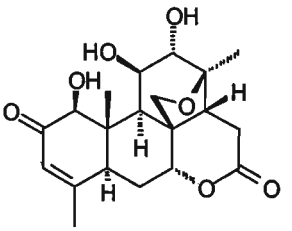


5-74 indaquassin E

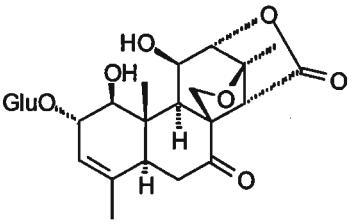
A study on the stem of this species has also proved fruitful, with six known and four novel quassinoids reported [16]. The former are samaderines B **5-1**,C **5-2** [4,6] and E **5-8** [8], from *Samadera indica*, indaquassin C **5-72**, the C_{25} quassinoid simarinolide **5-75**, originally from *Simaba orinocensis* H.B.K. [53], and **5-76**, described as novel, but subsequently found to be identical to ailanquassin B from the Indian species *Ailanthus malabarica* DC. [54]. Among the novel isolates is the first (and to date, the only) C_{19} quassinoid glycoside, samaderine C 2-glucoside **5-77**, together with samaderines X **5-78** and Z **5-79**, and indaquassin X **5-80**. Virtually all of these compounds displayed cytotoxic, antimalarial, cell adhesion inhibitory or anti-inflammatory properties, with samaderine X **5-78** and samaderine B **5-1**, in particular, both displaying significant activity in all four areas.



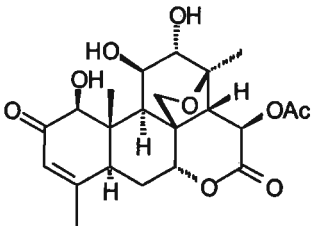
5-75 simarinolide



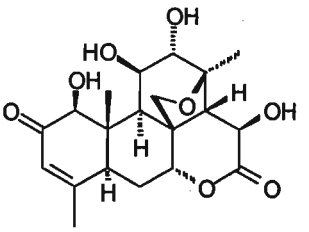
5-76 ailanquassin B



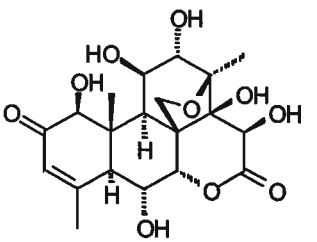
5-77 samaderine C 2-glucoside



5-78 samaderine X



5-79 samaderine Z



5-80 indaquassin X

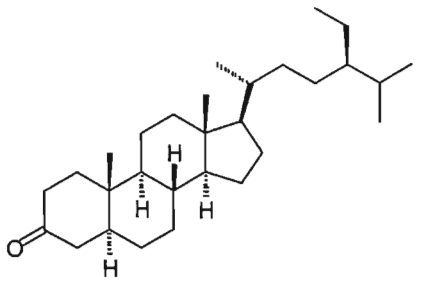
5.2 Extractives from *Samadera madagascariensis*

Samadera madagascariensis Jussieu is locally named "fatriana" in Madagascar [10]. A decoction of the rootbark is used as a febrifuge [55] and of the leaves as a treatment for dysentery and stomach ache [56], while the juice of the fresh leaves is used to treat wounds and burns [56].

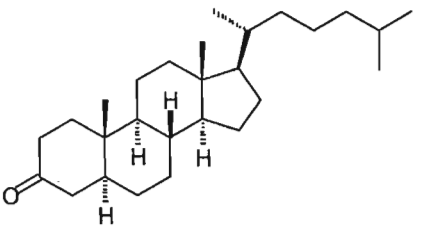
One novel and four known quassinoids, together with a known steroid, were isolated during the course of this study.

5.2.1 Structural elucidation of compound SM 1, 5α-stigmastan-3-one

(spectra vol II, p.s30-34)



5-9 5α-stigmastan-3-one **SM 1**



5-81 cholestan-3-one

An EIMS† of compound **SM 1** gave an $[M]^+$ peak at 414 $g.mol^{-1}$, corresponding to the molecular formula $C_{29}H_{50}O$ and five double bond equivalents. A signal at δ212.3 and the presence of twenty nine rather than thirty carbon resonances in the ^{13}C NMR spectrum, and of six rather than seven quaternary methyl group resonances in the ADEPT spectrum, collectively suggested that **SM 1** was a ketosteroid.

A literature survey revealed compound **SM 1** to be 5α-stigmastan-3-one **5-9**, previously reported from the peel of *Samadera indica* [3]. ^{13}C NMR assignments were made by comparison with literature data for 3-cholestanone **5-81** [57] for the tetracyclic skeleton and β-sitosterol **5-42** for the side-chain [58]‡; these are presented together in Table 5.1.

† HRMS analyses are not carried out on common compounds.

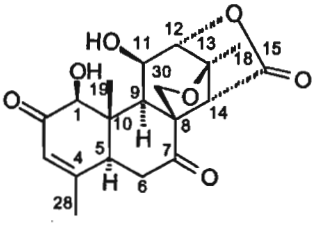
‡ This compound illustrates the problems encountered when identifying a common extractive first isolated before the advent of routine ^{13}C NMR spectroscopy; as the compound has been found previously, subsequent isolations are usually not reported, so the ^{13}C NMR spectral data does not enter the public domain.

Table 5.1: ^{13}C NMR assignments for compound **SM 1**, 5α-stigmastan-3-one
[^1H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]
[Lit. [57] ^1H NMR 100MHz, ^{13}C 25MHz, $CDCl_3$, *J* in Hz]
[Lit. [58] ^1H NMR 300MHz, ^{13}C 75MHz, $CDCl_3$, *J* in Hz]

Position	δC	5-81 Ref. [57]	5-42 Ref. [58]
1	38.56 (CH_2)	38.5	-
2	38.20 (CH_2)	38.1	-
3	212.30 (C)	211.2	-
4	44.73 (CH_2)	44.6	-
5	46.70 (CH)	46.7	-
6	28.96 (CH_2)	29.0	-
7	31.72 (CH_2)	31.7	-
8	35.39 (CH)	35.6	-
9	53.78 (CH)	53.8	-
10	35.63 (C)	35.4	-
11	21.43 (CH_2)	21.4	-
12	39.88 (CH_2)	39.9	-
13	42.58(C)	42.5	-
14	56.14(CH_2)	56.2	-
15	24.23 (CH_2)	24.2	-
16	28.25 (CH_2)	28.2	-
17	56.26 (CH)	56.2	-
18	12.05 (CH_3)	12.1	-
19	11.45 (CH_3)	11.4	-
20	36.15 (CH)	-	36.14
21	18.71 (CH_3)	-	18.78
22	33.89 (CH_2)	-	33.95
23	26.04 (CH_2)	-	26.08
24	45.81 (CH)	-	45.84
25	29.12 (CH)	-	29.15
26	19.81 (CH_3)	-	19.81
27	19.01 (CH_3)	-	19.03
28	23.04 (CH_2)	-	23.07
29	11.96 (CH_3)	-	11.97

5.2.2 Structural elucidation of compound SM 2, samaderine B

(spectra vol II, p.s35-44)



5-1 samaderine B **SM 2**

An HRMS for this compound gave a molar mass of 362.1369 $g.mol^{-1}$, suggesting a molecular formula of $C_{19}H_{22}O_7$ (calc. 362.1366 $g.mol^{-1}$) and nine double bond equivalents. In the absence of any signals attributable to ester substituents in the ^1H NMR spectrum, the appearance of nineteen resonances in

the ^{13}C NMR spectrum immediately suggested that compound **SM 2** was a C_{19} quassinoid, with further inspection of the ^{13}C NMR and ADEPT spectra furnishing two carbonyl groups, a lactone, and a trisubstituted double bond. Five C-O resonances were also noted, comprising one fully substituted, one oxymethylene, and three oxymethine carbon atoms.

A literature survey conducted on this basis revealed that compound **SM 2** might be samaderine B, which has been previously isolated from *Samadera indica* [4,6] and more recently from both the bark [15] and stems [16] of *Quassia indica*. However, while our spectra were recorded in $CD_3OD/CDCl_3$†, the literature data was obtained either in C_5D_5N [16] or DMSO-d_6 [59]; although sufficiently similar for a gross comparison, significant differences were observed - in particular, the values for C-1 and C-12 appeared interchanged. However, a match of $\Delta\delta \leq 0.05$ ppm for all signals in the ^{13}C NMR spectrum was attained in comparison with the non-assigned values recorded from a total synthesis [60].

Confirmation that compound **SM 2** was indeed samaderine B **5-1** was established by analysis of the 2D spectra. An HMBC correlation between the C-2 α,β-unsaturated carbonyl carbon resonance at δ196.48(C) and the 1H singlet signal at δ4.13 established this as H-1, with C-1 occurring at δ80.70. The C-1 resonance showed HMBC correlations to a 3H methyl group singlet resonance at δ1.28, assigned to 3H-19; C-19 at δ10.58(CH_3) in turn displays an HMBC correlation to a 1H doublet signal at δ2.17(d J = 3.66Hz), ascribed to H-9, with C-9 occurring at δ49.40(CH). Of the remaining two quaternary methyl group signals, that at δ1.92 was assigned to 3H-28 (downfield, as expected, due to deshielding by the Δ^3-double bond) and therefore that at δ1.55 must be 3H-18; C-28 and C-18 occur at δ21.89(CH_3) and δ20.61(CH_3).

Further HMBC correlation of the 3H-18 resonance to a fully substituted carbon signal at δ87.66 designates this as the C-13 end of the 13,30-ether bridge, which is confirmed by HMBC correlation to one of a pair of coupled doublets at δ4.82 (J = 8.33Hz), ascribed to one of the C-30 bridgehead protons by COSY coupling to the other at δ3.81 (J = 8.33Hz), with 2H-30 both showing an HMBC correlation to C-9 and an HSQC correlation to the C-30 oxymethylene signal at δ75.45. The fully substituted resonance at δ60.52 must then be C-8.

† Not sufficiently soluble in either individual solvent alone.

NOESY correlations between H-9 and H-1 confirm the α-stereochemistry at C-1, and between H-9 and a 1H multiplet at 2.95m establish this as H-5, with C-5 occurring at δ47.51(CH). A COSY correlation between the H-5 resonance and a pair of coupled multiplets at δ2.43 and δ2.98 enable these to be assigned as 2H-6, which, in turn, display an HMBC correlation to a fully substituted carbon resonance at δ203.38, which can only be C-7.

The fully assigned spectral data, together with ^{13}C NMR literature data for comparison, are presented in Table 5.2.

Table 5.2: ^{1}H and ^{13}C NMR assignments for compound **SM 2**, samaderine B

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3/CD_3OD$, *J* in Hz]

[Lit. [16] ^{1}H NMR 270MHz, ^{13}C 67.8MHz, C_5D_5N, *J* in Hz]

[Lit. [59] ^{1}H NMR 100MHz, ^{13}C 25MHz, DMSO-d_6, *J* in Hz]

[Lit. [60] ^{1}H NMR 400MHz, ^{13}C 100MHz, DMSO-d_6/$CDCl_3$, *J* in Hz]

Position	δC	5-1 Ref. [16]	5-1 Ref. [59]	5-1 Ref. [60][a]	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	80.70 (CH)	82.1	83.2	80.71	4.13s	19	-	5,9,11
2	196.48 (C)	197.8	196.9	196.43	-	1	-	-
3	124.39 (CH)	125.3	123.8	124.40	6.12s	28	-	28
4	160.85 (C)	160.6	16.05	16.079	-	28	-	-
5	47.51 (CH)	47.7	46.6*	47.55	2.95m	19,28	6α,6β	1,6α,9,28
6	38.93 (CH_2)	39.1	38.6	38.94	β 2.43m α 2.98m	-	5,6α 5,6β	6α,28 5,6β,28
7	203.38 (C)	204.9	204.9	203.33	-	5,6α,6β	-	-
8	60.52 (C)	61.5	60.2	60.53	-	9,14	-	-
9	49.40 (CH)	50.2	48.5*	49.44	2.17d 3.66	1,14,19,30a,30b	11	1,5,11
10	46.89 (C)	47.6	46.6	46.91	-	1,5,6α,9,19	-	-
11	70.09 (CH)	70.8	69.4	70.10	4.75m	9	9,12	1,9,12
12	83.74 (CH)	84.9	80.6	83.74	4.31d 3.30	14,18	11	11,18
13	87.66 (C)	87.9	86.5	87.67	-	14,18,30b	-	-
14	56.25 (CH)	56.7	55.3	56.28	3.60s	9,18,30b	-	18,30a
15	171.94 (C)	172.8	171.2	171.91	-	-	-	-
18	20.61 (CH_3)	20.7	20.4	20.65	1.55s	14	-	12,14
19	10.58 (CH_3)	10.4	9.9	10.60	1.28s	1,9	-	6β,30b
28	21.89 (CH_3)	21.5	21.3	21.91	1.92s	-	-	3,5,6α,6β
30	75.45 (CH_2)	75.6	74.3	75.48	a 3.81d 8.33 b 4.82d 8.33	9	30b 30a	14,30b 13,19,30a

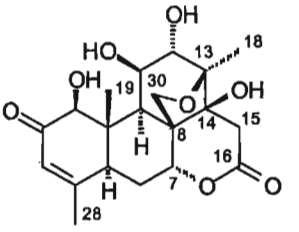
*: interchangeable

[a]: values not assigned in reference

Samaderine B has been shown to exhibit a wide range of antimalarial, cytotoxic, anti-inflammatory and cell adhesion inhibitory properties [16].

5.2.3 Structural elucidation of compound SM 3, samaderine E

(spectra vol II, p.s45-54)



5-8 samaderine E **SM 3**

The molar mass of compound **SM 3** was determined by HRMS analysis to be 394.1615 g.mol^{-1}, corresponding to the molecular formula $C_{20}H_{26}O_8$ (calc 394.1628 g.mol^{-1}) and eight double bond equivalents. The extra carbon resonance, in conjunction with the absence of substituent esters in the ^{1}H NMR spectrum, immediately suggested that **SM 3** was a C_{20} quassinoid. The appearance of a downfield quaternary methyl signal (δ1.98s, δ22.70(CH_3)), attributable to C-28, and two further quaternary methyl resonances (δ1.17s, δ11.43(CH_3), to C-19; and δ1.32s, δ16.48(CH_3), to C-18), supported this assumption. Also apparent was the pair of coupled doublets at δ3.80 and δ4.58 (J = 7.50Hz), correlating to a resonance at δ69.97, and characteristic of C-30 in a 13,30-ether bridge.

The oxymethine resonance at δ80.27 was assigned to C-7 by correlation in the HMBC spectrum with 2H-30; the corresponding H-7 signal at δ5.17 was seen to be coupled in the COSY spectrum to a pair of coupled multiplets at δ1.80 (H-6β, by NOESY coupling to 3H-19) and δ2.39 (H-6α), which were coupled in turn to a doublet (J = 12.64Hz) at δ2.84, assigned to H-5. Resonances for C-5 and C-6 were at δ43.88 and δ28.39, respectively.

An isolated pair of coupled doublets (J = 18.86Hz) at δ3.66 and δ2.58, correlated to the remaining methylene signal at δ36.31, were assigned to H-15α (NOESY coupling to H-9) and H-15β, respectively, and supported by HMBC correlations to fully substituted signals at δ172.17, ascribed to the D ring lactone carbonyl carbon at C-16, and at δ80.42, assigned to C-14.

A literature survey revealed that **SM 3** was the known quassinoid samaderine E **5-8**, which has also been previously isolated both from *Samadera indica* [8,9] and *Quassia indica* [15,16]. Differences in

the solvents in which NMR spectra were recorded [11,12] again required a detailed analysis of the 2D NMR spectra for confirmation of the structure; these values are presented in Table 5.3.

C_{20} quassinoids with the 13,30-ether bridge and a hydroxy group at C-14 but not at C-15 are rare, with only two other examples, indaquassins C **5-72** [15,16] and D **5-73** [15] from *Quassia indica* reported thus far.

Table 5.3: ^{1}H and ^{13}C NMR assignments for compound **SM 3**, samaderine E
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3/CD_3OD$, *J* in Hz]
[Lit. [15] ^{1}H NMR 400MHz, ^{13}C 100MHz, C_5D_5N, *J* in Hz]
[Lit. [16] ^{1}H NMR 270MHz, ^{13}C 67.8MHz, CD_3OD, *J* in Hz]

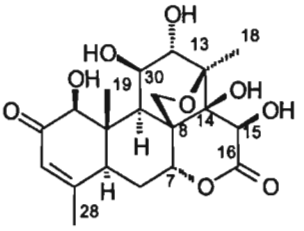
Position	δC	5-8 Ref. [15]	5-8 Ref. [16]ª	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	82.03 (CH)	83.0	83.7	4.14s	19	-	5,9
2	198.52 (C)	198.5	200.6	-	1	-	-
3	124.50 (CH)	125.0	125.9	6.07s	28	5	28
4	164.83 (C)	163.4	166.3	-	28	-	-
5	43.88 (CH)	43.8	45.4	2.84d 12.64	1,3,7,9,19,28	3,6α,6β	1,6α,9,28
6	28.39 (CH_2)	28.4	29.8	β 1.80m α 2.39m	-	5,6α,7 5,6β,7	6α,7,19 5,6β,7,28
7	80.27 (CH)	80.2	82.4	5.17br s	30a,30b	6α,6β	6α,6β,30a
8	47.02 (C)	46.4	45.9*	-	9,11,15β,30a,30b	-	-
9	46.03 (CH)	47.6	47.5	2.11m	1,7,12,19,30a,30b	11	1,5,11,15α
10	48.12 (C)	48.5	47.5*	-	1,9,19	-	-
11	74.42 (CH)	75.5	76.3*	4.47m	9,12	9,12	9,12
12	80.25 (CH)	81.5	82.2	3.74br s	9,11,16	11	11,16
13	83.36 (C)	83.6	84.9	-	11,12,18,30b	-	-
14	80.42 (C)	81.4	83.7	-	9,12,15α,15β,18,30a,30b	-	-
15	36.31 (CH_2)	37.8	38.0	β 2.58d 18.86 α 3.66d 18.86	-	15α 15β	15α,18 9,15β
16	172.17 (C)	171.0	174.0	-	15α,15β	-	-
18	16.48 (CH_3)	17.8	17.9	1.32s	12	-	12,15β
19	11.43 (CH_3)	11.5	12.3	1.17s	1,9	-	6β,30b
28	22.70 (CH_3)	22.2	23.3	1.98s	3	-	3,5,6α
30	69.97 (CH_2)	70.3	71.7	a 3.80d 7.51 b 4.58d 7.50	9	30b 30a	7,30b 19,30a

ª: * values measured in C_5D_5N

Samaderine E **5-8** has antimalarial and cytotoxic properties [8,16].

5.2.4 Structural elucidation of compound SM 4, brucein D

(spectra vol II, p.s55-63)



5-67 brucein D **SM 4**

Comparison of the NMR spectra of **SM 4** and samaderine E **SM 3** reveal them to be virtually identical, other than the replacement, in the ^{1}H NMR spectrum, of the isolated pair of coupled doublets at δ3.66 and δ2.58 with a singlet at δ5.22, and, in the ^{13}C NMR spectrum, of the corresponding methylene carbon resonance at δ36.31 with an oxymethine carbon doublet signal at δ69.76. This suggests that the only difference between these compounds is that **SM 4** has a hydroxy group at C-15. A correlation in the HMBC spectrum between the singlet signal at δ5.22 and C-16 at δ174.86 confirms this as H-15, while a NOESY correlation to H-9 at δ2.25, as occurs in samaderine E **SM 3**, confirms that H-15 is α, and thus that the hydroxy group at C-15 is β.

Compound **SM 4** is thus 15β-hydroxysamaderine E, which has previously been isolated, as the known compound brucein D **5-67**, from *Brucea amarissima* [50], *Brucea javanica* [51], and *Quassia indica* [15]. The fully assigned spectral data are presented in Table 5.4. No ^{13}C NMR data were reported in either of the previous references [15,51]†.

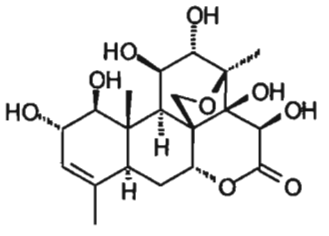
† We were unfortunately not able to obtain an HRMS determination of the molar mass and molecular formula for **SM 4**, and the lack of literature values for direct comparison of the ^{13}C NMR spectral data might suggest that our structure could at best be described as tentative. However, in the light of the similarities in the ^{13}C NMR spectral data for this compound and that of samaderine E **SM 3** and the acetyl ester **SM 6**, for which HRMS values and molecular formulae were obtained, we consider the structure to be beyond doubt.

Table 5.4: ^{1}H and ^{13}C NMR assignments for compound **SM 4**, brucein D

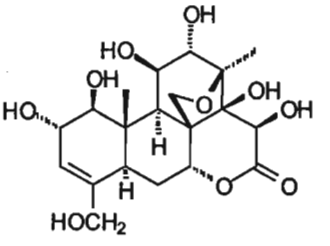
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3/CD_3OD$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	82.04 (CH)	4.13s	9,19	-	5,9,11
2	198.36 (C)	-	1	-	-
3	124.45 (CH)	6.07s	28	5	28
4	164.58 (C)	-	28	-	-
5	43.60 (CH)	2.87d 12.46	19,28	3,6α,6β	1,6α,9,28
6	27.91 (CH_2)	β 1.78m α 2.37m	-	5,6α,7 5,6β,7	6α,7,19 5,6β,7,28
7	79.91 (CH)	5.16br s	-	6α,6β	6α,6β,30a
8	49* (C)	-	9,11,30a	-	-
9	45.50 (CH)	2.25m	1,12,19,30a,30b	11	1,5,11,15
10	48.25 (C)	-	1,9,19	-	-
11	74.18 (CH)	4.55m	12	9,12	1,9
12	80.09 (CH)	3.80br s	11,18,30a,30b	11	18
13	84.02 (C)	-	12,13,18,30b	-	-
14	81.27 (C)	-	9,12,18,30b	-	-
15	69.76 (CH)	5.22s	-	-	9
16	174.86 (C)	-	15	-	-
18	17.73 (CH_3)	1.41s	12	-	12
19	11.41 (CH_3)	1.17s	1,9	-	6β,30b
28	22.68 (CH_3)	1.97s	-	-	3,6α
30	69.45 (CH_2)	a 3.86d 7.14 b 4.52m	9	30b 30a	7,30b 19,30a

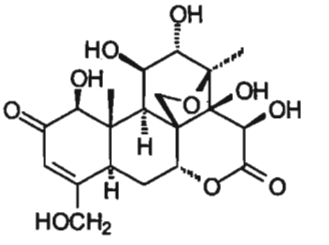
*: obscured by solvent



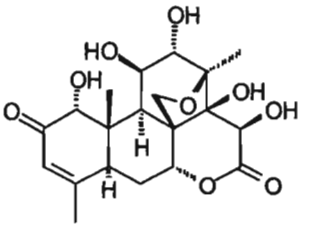
5-82 brucein E



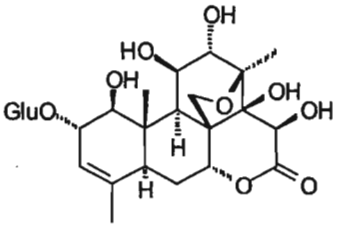
5-83 brucein F



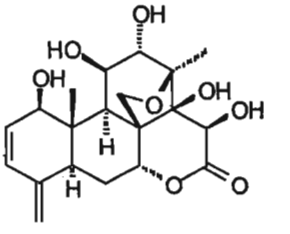
5-84 yadanziolide A/brucein H



5-85 yadanziolide C



5-86 yadanzigan



5-87 bruceene

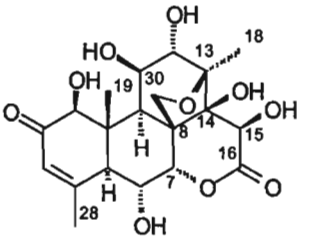
C_{20} Quassinoids with the 13,30-ether bridge and oxygenation at both C-14 and C-15 occur more frequently than their 15-desoxy counterparts, but are still uncommon, with eight examples reported to date. The 2α-hydroxy and 2α,18-dihydroxy brucein D analogues bruceins E **5-82** and F **5-83** have also been found in *Brucea amarissima* [50,61], while the closely related *Brucea javanica* has yielded

the 18-hydroxy derivative yadanziolide A (bruceine H) **5-84** [62,63] and unusual 1-epimer yadanziolide C **5-85** [62]. Yadanzigan (brucein E 2-glucoside) **5-86** and bruceene **5-87** have also been reported from this species [64,65]. The remaining isolate **5-88** from *Soulamea amara* [66] is the benzoate analogue of **SM 6**, to be discussed further in section 5.2.6.

Brucein D **5-67** is reported to demonstrate significant antisarcomic activity [67].

5.2.5 Structural elucidation of compound SM 5, indaquassin X

(spectra vol II, p.s64-73)



5-80 indaquassin X **SM 5**

The molecular formula of compound **SM 5** was determined by FABMS (found 449.2, 427.3 g.mol^{-1}; calc. for $[M+Na]^+$ 449.4, for $[M+H]^+$ 427.4 g.mol^{-1}) as $C_{20}H_{26}O_{10}$[†]; a difference, relative to samaderine E **SM 3**, of an additional two oxygen atoms. Inspection of the ^{13}C NMR spectrum showed it to be very similar to that of samaderine E **SM 3**, except that the methylene carbon signals at δ28.39 and δ36.31, assigned to C-6 and C-15, respectively, had been replaced by two oxymethine carbon resonances at δ67.68 and δ69.69. The latter signal was assigned to C-15 by comparison with the corresponding resonance in brucein D **SM 4**, and by virtue of a HMBC correlation between the associated H-15 singlet proton resonance at δ5.29 and that of the C-16 ester carbonyl at δ173.92, while a NOESY coupling between H-15 and H-9 (δ2.22d J = 4.76Hz) again infers that the hydroxy group is β. That the second hydroxy group is located at C-6 is confirmed by a series of COSY-coupled resonances at δ2.85 (d, J = 10.99Hz, H-5), δ3.86 (dd, J = 10.99, 2.75Hz, H-6) and δ5.05 (d, J = 2.75Hz, H-7), and the stereochemistry of the hydroxy group as α by NOESY correlations between H-6β and the 3H-19 quaternary methyl singlet resonance at δ1.20. **SM 5** is thus the 6α,15β-dihydroxy analogue of

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† The $[M]^+$ peak at *m/z* 426.1526 could not be observed in the EIMS, which did, however, show the $[M-H_2O]^+$ peak at *m/z* 408.1420 (calc. for $[C_{20}H_{24}O_9]^+$ 408.1420).

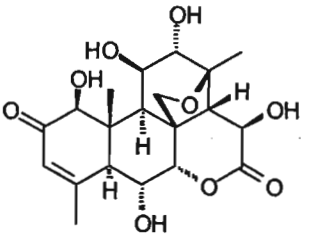
samaderine E **SM 3**, and as such is the previously reported indaquassin X **5-80** from *Quassia indica* [16]. The fully assigned spectral data, together with literature values for comparison, are presented in Table 5.5.

Table 5.5: ^{1}H and ^{13}C NMR assignments for compound **SM 5**, indaquassin X

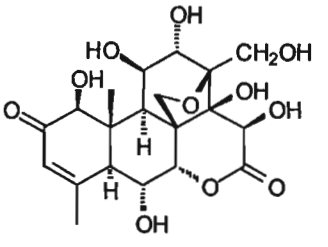
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3/CD_3OD$, *J* in Hz]

[Lit. [16] ^{1}H NMR 270MHz, ^{13}C 67.8MHz, CD_3OD, *J* in Hz]

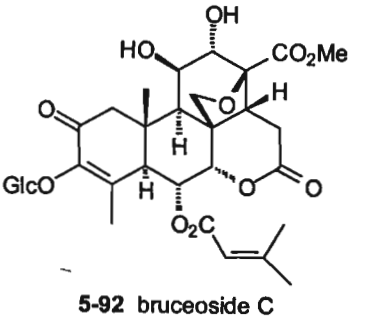
Position	δC	5-80 Ref. [16]*	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	81.69 (CH)	83.9	4.09s	3,19	-	5,9,11
2	197.73 (C)	200.3	-	1	-	-
3	126.05 (CH)	127.9	6.08d 1.10	28	5	19,28
4	166.84 (C)	168.8	-	28	-	-
5	48.90 (CH)*	50.6	2.85d 10.99	1,7,9,19	3,6	1,9
6	67.68 (CH)	69.4	3.86dd 10.99,2.75	7	5,7	7,19
7	83.84 (CH)	85.8	5.05d 2.75	30a	6	6,30a
8	49.73 (C)*	51.8	-	9,11,30a,30b	-	-
9	44.01 (CH)	45.7	2.22d 4.76	1,6,7,19,30a,30b	11	1,5,11,15
10	50.36 (C)	52.3	-	1,6,9,19	-	-
11	73.81 (CH)	76.1	4.56d 4.94	9,12	9,12	1,9,12
12	80.16 (CH)	82.5	3.80br s	9,18	11	11,18
13	83.89 (C)	85.4	-	11,12,18,30b	-	-
14	81 (C)*	83.1	-	9,12,15,18,30b	-	-
15	69.69 (CH)	71.6	5.26s	-	-	9,18
16	173.92 (C)	176.1	-	15	-	-
18	17.44 (CH_3)	19.1	1.39s	12	-	12,15
19	12.15 (CH_3)	13.3	1.20s	1,9	-	3,6,30b
28	26.93 (CH_3)	27.9	2.27s	3	-	3,5
30	68.64 (CH_2)	70.5	a 3.90m b 4.47d 7.51	9	30b 30a	7,30b 19,30a



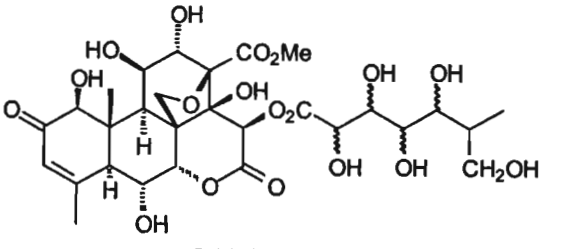
5-89 brucein G



5-91 yadanziolide B



5-92 bruceoside C

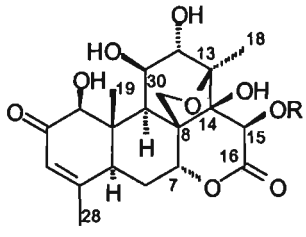


5-90 brucein Q

Quassinoids of this type with a hydroxy or ester group at C-6α are also uncommon, with only seven others having been reported to date. Together with the previously mentioned indaquassins C **5-72** [15,16], D **5-73** [15] and E **5-74** [15] from *Quassia indica* should be included bruceins G **5-89** [68] and Q† **5-90** [69] from *Brucea sumatrana*, and yadanziolide B **5-91**, from *Brucea javanica* [70]. *Brucea javanica* is also reported [71] to have yielded the unusual glucoside bruceoside C **5-92**, the structure of whose aglycone was later shown by total synthesis [72] to be incorrect; see discussion p.72.

5.2.6 Structural elucidation of compound SM 6, 15-acetylbrucein D

(spectra vol II, p.s74-83)



5-88 R = Bz
5-93 R = Ac 15-acetylbrucein D **SM 6**

An HRMS of compound **SM 6** gave a molar mass of 452.1681 g.mol^{-1}, suggesting a molecular formula of $C_{22}H_{28}O_{10}$ (calc. 452.1683 g.mol^{-1}) and a difference, relative to samaderine E **SM 3**, of $C_2H_2O_2$. This is attributed to an acetate ester (δ2.18, s, 3H; δ169.94(C) and 20.50(CH_3)), which is placed at C-15 by virtue of the downfield shift of H-15 from δ5.26 in indaquassin X **SM 5** to δ6.30 in **SM 6**, and a NOESY correlation between the acetate methyl proton resonance at δ2.18 and a quaternary methyl group proton signal at δ1.37, assigned to 3H-18. A further NOESY correlation between H-15 and H-9 at δ2.40 indicates that H-15, as expected, is α, and thus the C-15 acetate is β. The remainder of the ^{1}H and ^{13}C signals are readily assigned by comparison with those of samaderine E **SM 3** and indaquassin X **SM 5**, and are presented in Table 5.6. **SM 6** is thus the novel compound 15-acetylbrucein D **5-93**, although, as mentioned in section 5.2.4, the benzoyl ester analogue **5-88** has previously been isolated from *Soulamea amara* [66].

† The stereochemistry at C-1, C-6 and in the C-15 ester substituent was not originally established. As all quassinoids identified thus far have β and α stereochemistry at C-1 and C-6, respectively, it is assumed that these were also, and are presented as such; the same however cannot be said for the ester.

Table 5.6: ^{1}H and ^{13}C NMR assignments for compound **SM 6**, 15-acetylbrucein D
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3/CD_3OD$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	81.82 (CH)	4.20s	19	-	5,9,11
2	198.39 (C)	-	1	-	-
3	124.52 (CH)	6.08d 0.91	28	5,28	28
4	164.35 (C)	-	28	-	-
5	43.67 (CH)	2.91d 12.51	19,28	3,6α,6β	19
6	27.93 (CH_2)	β 1.88dd 12.77,2.38 α 2.40m	-	5,6α,7 5,6β,7	6α,7 5,6β,7,28
7	80.43 (CH)	5.15br s	-	6α,6β	6α,6β,30a
8	50.44 (C)	-	6α,11,30a,30b	-	-
9	48.21 (CH)	2.240m	12,19,30a,30b	11	1,5,11,15
10	49 (C)*	-	1,6α,19	-	-
11	74.13 (CH)	4.55m	12	9,12	1,9,12
12	79.65 (CH)	3.75br s	11,18	11	11,18
13	81.08 (C)	-	11,12,18	-	-
14	83.73 (C)	-	12,18,30b	-	-
15	71.96 (CH)	6.30s	-	-	9
16	170.11 (C)#	-	15	-	-
18	17.55 (CH_3)	1.37s	12	-	12,CH_3CO
19	11.38 (CH_3)	1.17s	1,9	-	6β,30b
28	22.65 (CH_3)	1.97s	-	3	3,5,6α
30	69.30 (CH_2)	a 3.85d 7.29 b 4.55m	9	30b 30a	7,30b 19,30a
CH_3CO	169.94 (C)#	-	CH_3CO	-	-
CH_3CO	20.50 (CH_3)	2.18s	-	-	18

#: interchangeable

*: obscured by solvent

5.3 Chemotaxonomic observations

Of the five known compounds isolated in this study, 5α-stigmastan-3-one **SM 1** has previously been reported from *Samadera indica* [3], which has also yielded samaderine B **SM 2** [4,6] and samaderine E **SM 3** [8,9]. Samaderine B **SM 2** has also previously been reported from *Samadera madagascariensis* [1], and both compounds have been found in *Quassia indica* [15,16]. *Quassia indica* has also yielded both the relatively uncommon 6-hydroxy quassinoid indaquassin X **SM 5** [16], of which only eight examples have been isolated to date, and the similarly infrequently encountered 14,15-dioxygenated quassinoid brucein D **SM 4**, of which an equal number of reports are known.

From a chemotaxonomic point of view, the evidence gathered in this investigation supports the suggested synonymy, on botanical grounds [2,12], of these three species.

5.4 Experimental

Samadera madagascariensis was collected in April 1997 in the Foulpouinte area in eastern Madagascar. A voucher specimen (007-Mj/Mdul) is deposited at the Department of Botany of the University of Antananarivo. Plant identification was confirmed by the Department of Botany at the Parc Zoologique et Botanique de Tsimbazaza.

The air-dried, milled stembark (471g) was extracted successively for 24 hours in a Soxhlet apparatus with hexane, dichloromethane and methanol, yielding extracts of masses 9.46g, 4.24g and 29.29g, respectively. An ^{1}H NMR spectrum of the hexane extract showed it to be virtually pure 5α-stigmastan-3-one **SM 1** and it was not investigated further. The known compounds samaderine B **SM 2** and brucein D **SM 4** were isolated from the dichloromethane extract, and samaderine E **SM 3** and indaquassin X **SM 5** from the methanol extract, in which the only novel compound, 15-acetylbrucein D **SM 6**, was also found.

Compound **SM 1**
(spectra vol II, p.s30-34)

5α-stigmastan-3-one

white solid, 41mg
^{13}C NMR spectra: data and peak assignments Table 5.1, p.128.

M.p. 151-153°C (lit. value [3] 157-159°C).

Optical Rotation:

$[\alpha]_D = +40^{\circ}$ (c, 0.396 in $CHCl_3$) (lit. value [3] +41.4°).

IR spectrum:

υ_{max}(NaCl) 2935, 2865, 1724, 1478, 1437, 1379, 1262 cm^{-1}.

Mass spectrum:

EIMS *m/z* 414 $[M]^+$, 317, 231, 163, 123, 95, 69, 43.

Compound **SM 2**
(spectra vol II, p.s35-44)

samaderine B

off-white semi-crystalline solid, 39.5mg

^{1}H and ^{13}C NMR spectra: data and peak assignments Table 5.2, p.130.

M.p. 219-221°C (lit. value [4] 235-240°C).

Optical Rotation:

$[\alpha]_D$ = + 59 (c, 0.518 in $CHCl_3$) (lit. value [4] +67.5° (in C_5H_5N)).

IR spectrum:

υ_{max}(NaCl) 3462, 2982, 2929, 2883. 1800, 1771, 1719, 1676, 1385, 1256, 1127, 1011 cm^{-1}.

Mass spectrum:

HRMS found 362.1369, calc. for $[C_{19}H_{22}O_7]^+$ 362.1366 $g.mol^{-1}$.

EIMS *m/z* 362.1369, 344.1268 $[M-H_2O]^+$, 263.0922, 247.0970, 237.1120, 235.0974.

Compound **SM 3**[†]

(spectra vol II, p.s45-54)

samaderine E

colourless gum, 9.5mg

^{1}H and ^{13}C NMR spectra: data and peak assignments Table 5.3, p.132.

IR spectrum:

υ_{max}(NaCl) 3409, 2929, 1742, 1707, 1666, 1391, 1262, 1227, 1087, 1028 cm^{-1}.

Mass spectrum:

HRMS found 394.1615, calc. for $[C_{20}H_{26}O_8]^+$ 394.1628 $g.mol^{-1}$.

EIMS *m/z* 394.1615, 376.1520 $[M-H_2O]^+$, 362.1364, 348.1571, 232.1091, 167.0708, 165.0553, 151.0750, 135.0807.

† The samples of samaderine E **SM 3**, brucein D **SM 4**, indaquassin X **SM 5** and the novel 15-acetylbrucein D **SM 6** were accidentally knocked over, by an unauthorised window cleaner, while drying after acquisition of the NMR spectra. Enough material was recovered for IR (except indaquassin X **SM 5**) and HRMS data to be obtained, but optical rotation measurements were not attempted.

Compound **SM 4**
(spectra vol II, p.s55-63)

brucein D

pale yellow gum, 6.8mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 5.4, p.134.

IR spectrum:
υ_{max}(NaCl) 3415, 2929, 1736, 1666, 1455, 1385, 1268, 1163, 1081 cm^{-1}.

Compound **SM 5**
(spectra vol II, p.s64-73)

indaquassin X

colourless gum, 15.0mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 5.5, p.136.

Mass spectrum:
FABMS found 449.2, 427.3; calc. for $C_{20}H_{26}O_{10}$: $[M+Na]^+$ 449.4, for $[M+H]^+$ 427.4 $g.mol^{-1}$.
EIMS *m/z* 408.1420 $[M-H_2O]^+$, 390.1300 $[M-2H_2O]^+$, 197.0468, 184.0732, 169.0502, 154.0264, 151.0305, 137.0239.

Compound **SM 6**
(spectra vol II, p.s74-83)

15-acetylbrucein D

pale yellow solid, 8.6mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 5.6, p.138.

IR spectrum:
υ_{max}(NaCl) 3424, 2929, 2854, 1746, 1671, 1473, 1386, 1238, 1157, 1077, 835, 761 cm^{-1}.

Mass spectrum:
HRMS found 452.1681, calc. for $[C_{22}H_{28}O_{10}]^+$ 452.1683 $g.mol^{-1}$.
EIMS *m/z* 452.1681, 434.1587 $[M-H_2O]^+$, 416.1471 $[M-2H_2O]^+$, 392.1469 $[M-HOAc]^+$, 249.1122, 232.1088, 151.0754.

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Chapter 6

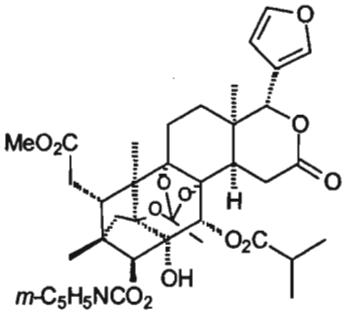
Extractives from *Neobeguea leandreana*

6.1 Introduction

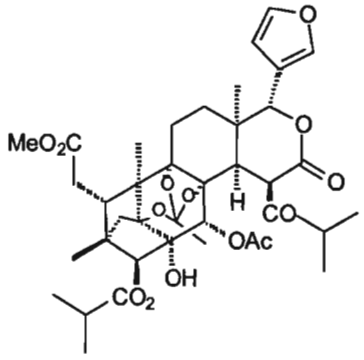
First described in 1958 by Leroy, *Neobeguea* is a relatively recent addition to the Meliaceae family, where it is placed in the tribe Swietenieae, subfamily Swietenioideae [1]. It is considered to be botanically closely related to the genus *Khaya* [2].

The genus comprises only three species, all of which are endemic to the dry thorny forests of the deep south of Madagascar, where the arid climate has resulted in the reduced leaves, shortened branches, and underground water storage organs which characterise its species [3].

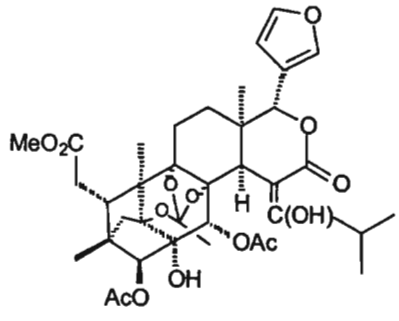
Neobeguea leandreana Leroy and *Neobeguea mahafalensis* Leroy are both known to the local populace by the name of "Handy" and are reported to have medicinal properties; literature reports, however, on their medicinal usage are non-specific and anecdotal only [3,4,5].



6-1 phragmalin



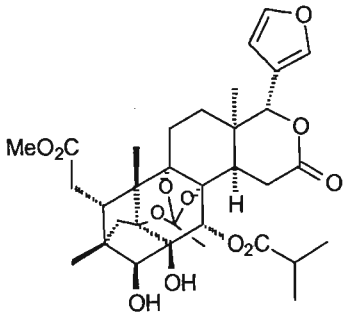
6-2 pseudrelone A_2



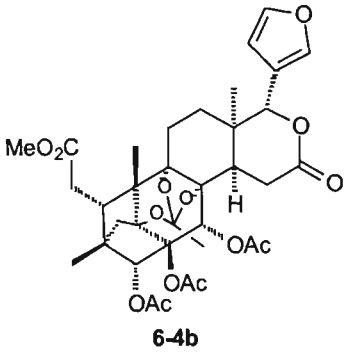
6-3 neobeguin

<u>*Neobeguea mahafalensis* Leroy</u>: is the only species to have previously been investigated. Two studies in our laboratories have yielded the known phragmalin **6-1** class limonoid pseudrelone A_2 **6-2**

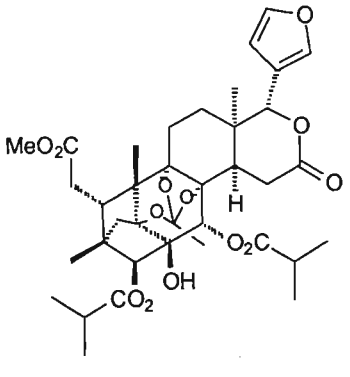
[5], previously found in *Pseudocedrela kotschyii* (Schweinf.) Harms [6], and, more recently, the novel phragmalin **6-1** group limonoid neobeguin **6-3** [7]†. Stigmasterol and β-amyrin were also found [7].



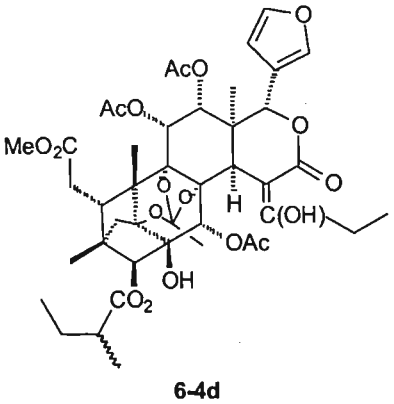
6-4a



6-4b



6-4c



6-4d

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† In their report on the isolation and characterisation by X-ray crystallography of phragmalin **6-1**, Arndt *et al.* [8] published a 3-D perspective drawing in which the configuration of both that of the C-2, C-1 bond *and* that of the C-2 hydroxy substituent are depicted as α. This structure also gives the methyl groups at C-19 and C-28 as α and β respectively, and that of H-3 as α. However, the accompanying structure **6-4a** is drawn with both the C-19 methyl group and the hydroxy group at C-2 as β.

This apparent contradiction has given rise to much confusion in the literature. The structure of xyloccensin E from *Xylocarpus moluccensis* (Lam.) M.Roem [9], identified as phragmalin **6-1** triacetate, was given as **6-4b** (the comment that " 2-H,3-H coupling requires that the oxygen at C-3 be β oriented." notwithstanding), and that of the related ester from *Chukrasia tabularis* A.Juss [10] as **6-4c**, while the the configuration at C-2 in the 3-D perspective drawing and structure **6-4d** is again at variance in a publication on busseins C-M from *Entandrophragma bussei* Harms. [11]. The Dictionary of Natural Products gives these compounds with all three bonds exclusively α.

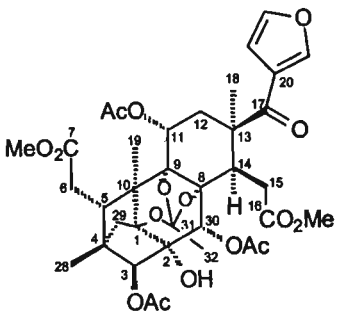
Attempts to construct models with conformations other than those given in the perspective drawings confirm that this is the only possible conformation that these molecules can assume. We suggest therefore that the β-configurations assigned to the C-19 methyl group and C-2 hydroxy substituent in structures **6-4a** to **6-4d** are "artificial" in the sense that the C-2,C-1 and C-10,C-1 bonds must be shown as α to emphasise the position of the 4,29,1 bridge and the 1,8,9 orthoacetate linkage that characterise these compounds, and therefore these groups are given as β only to adhere to the convention that a tetrahedral carbon atom must be shown to have two bonds in the plane of the page, and one bond each with the α and β configurations respectively.

6.2 Extractives from *Neobeguea leandreana*

The methanol extract of the stembark was shown by ^{1}H NMR spectroscopy to contain only sugars and was not investigated further, while the hexane and dichloromethane extracts were sufficiently similar, by ^{1}H NMR and tlc analysis, to be combined. Three novel phragmalin **6-1** group limonoids, *viz.* leandreanin A **NL 1**, leandreanin B **NL 2**, and leandreanin C **NL 3** were isolated.

6.2.1 Structural elucidation of compound NL 1, leandreanin A

(spectra vol II, p.s84-93)



6-5 leandreanin A **NL 1**

An HRMS of this compound gave a molar mass of 732.2612 g.mol^{-1}, corresponding to the molecular formula $C_{36}H_{44}O_{16}$ (calc. 732.2625 g.mol^{-1}) and fifteen double bond equivalents.

The ^{1}H and ^{13}C NMR spectra of this compound showed a carbonyl carbon signal at δ198.60 and unusual downfield furanyl ring resonances (δ7.98s, δ146.56(CH), H-21; δ7.40s, δ142.97(CH), H-23; δ6.73s, δ110.65(CH), H-22; and δ125.51(C), C-20). This immediately inferred the presence of a *seco*-ring D 17-keto limonoid, which is supported by correlation of the C-17 resonance in the HMBC spectrum to multiplets at δ3.32, ascribed to H-14 (δ44.16(CH), C-14), and δ2.35, assigned to 2H-12 (δ35.99(CH_2), C-12), and to a quaternary methyl signal (δ1.52s, δ27.99(CH_3)) assigned to C-18[†].

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† Repeated attempts to obtain an HMBC correlation between H-21 and/or H-22 and the ^{13}C NMR ketonic carbon resonance, which would irrefutably confirm its placement at C-17, proved fruitless for reasons which are not clear. 3-Acetylfuran, which could have been used as a test sample to "calibrate" the NMR spectrometer, could not be obtained, but acetophenone readily showed the desired correlations. Given that the evidence for our structure is overwhelming (see p.6-7), the lack of such a correlation is not crucial; nevertheless we are at a loss as to why it is not observed.

Couplings in the COSY spectrum between the H-14 resonance and a pair of double doublets at δ2.95 (dd, *J* = 17.21, 3.48Hz) and δ3.43 (dd, *J* = 17.21, 7.32Hz) designate these as H-15a and H-15b, respectively, with the corresponding C-15 resonance occurring at δ30.69(CH_2). A COSY correlation between the 2H-12 multiplet and a broad singlet at δ5.40, coupled in the HMBC spectrum to a oxymethine resonance at δ67.16 and ascribed to H-11, establishes an acetate ester at C-11, while an HMBC correlation to the 2H-15 resonances establishes the C-16 carbomethoxy carbonyl carbon at δ175.68(C), and attached methyl ester at δ3.66(s, 3H) and 51.61(CH_3)). NOESY correlations between H-14 and 3H-18, and between H-11 and a quaternary methyl signal at δ1.18, assigned to 3H-19 (δ15.93(CH_3), C-19), designate the stereochemistry of the proton at these positions as H-14α and H-11β, respectively.

That **NL 1** possesses a phragmalin-type 4,29,1-bridge and 1,8,9-orthoacetate linkage can immediately be deduced from the characteristic pair of coupled doublets (δ1.65d, δ1.81d, *J* = 10.80Hz), assigned to 2H-29, and the quaternary carbon signal at δ118.87, which is ascribed to the orthoacetate carbon C-31. The C-29 resonance appears characteristically at δ39.17 [10].

The fully substituted C-O resonance at δ85.75 is assigned to C-1 by virtue of HMBC correlations to both 2H-29 and 3H-19, while that at δ78.07s, which lacks the 3H-19 correlation, is ascribed to C-2. The remaining fully substituted C-O signals at δ86.38s/δ86.55s are thus those of C-8/C-9, which could not be distinguished. An HMBC correlation to H-14α of the oxymethine signal at δ70.50 establishes this as C-30, and therefore that the final oxymethine resonance at δ82.60 is C-3.

The quaternary methyl group proton resonance at δ0.79 is assigned to 3H-28 by NOESY correlation to the H-3 singlet at δ4.63, with 3H-28 in turn displaying a NOESY correlation to H-5 at δ2.55m (δ36.31(CH), C-5) and 2H-6 at δ2.25m (δ34.03(CH_2), C-6). An HMBC correlation between 2H-6 and a second carbomethoxy signal at δ172.45 confirms this as C-7, with the accompanying methyl ester resonances at δ3.52(3H,s) and δ51.74(CH_3).

The three acetate esters (δ1.96s, 3H; δ170.43(C) and 21.33(CH_3); δ2.17s, 3H, δ167.68(C) and 21.05(CH_3); δ2.17s, 3H, 169.67(C) and 20.95(CH_3)) are placed at C-3, C-30 and C-11α respectively,

with NOESY correlations to the H-29a and H-5 resonances establishing that H-3 is α and H-30 is β, respectively, as expected.

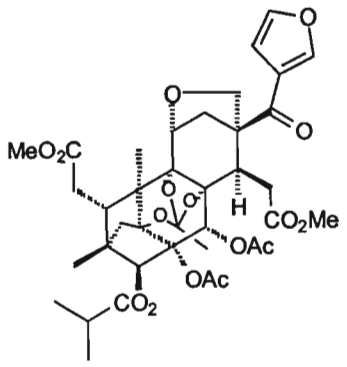
Leandreanin A **NL 1** thus has structure **6-5**. The fully assigned ^{1}H and ^{13}C NMR spectral data are given in Table 6.1 below.

Table 6.1: ^{1}H and ^{13}C NMR assignments for compound **NL 1**, leandreanin A

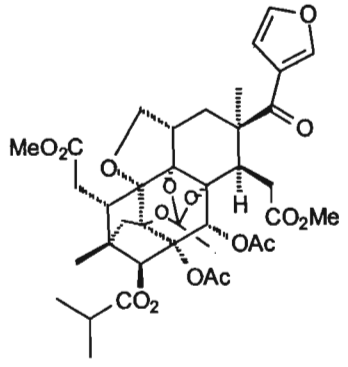
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δ_C	δ_H	HMBC correlation C→H	COSY correlation	NOESY correlation
1	85.75 (C)	-	19,29a,29b,30	-	-
2	78.07 (C)	-	3,29a,29b	-	-
3	82.60 (CH)	4.63s	5,28,29a,29b,30	-	28,29a
4	45.33 (C)*	-	3,5,6,28,29a,29b	-	-
5	36.31 (CH)	2.55m	3,6,19,28,29a	6	28
6	34.07 (CH_2)	2.25m	3	5	19,28
7	172.45 (C)	-	5,6,7-MeO	-	-
8	86.38 (C)#	-	14,15a,15b	-	-
9	86.55 (C)#	-	12,14,19,30	-	-
10	45.15 (C)*	-	5,6,19,29a,29b	-	-
11	67.16 (CH)	5.40br s	12	12	12,19
12	35.99 (CH_2)	2.35m	11β	11β	11β,18,21,22
13	47.86 (C)	-	11β,12,14,15a,15b,18	-	-
14	44.16 (CH)	3.32m	15a,15b,18	15a,15b	18,11-OAc
15	30.69 (CH_2)	a 2.95dd 17.21,3.48 b 3.43dd 17.21,7.32	14	14,15b 14,15a	14,15b,18 14,15a
16	175.68 (C)	-	14,15a,15b,16-MeO	-	-
17	198.60 (C)	-	12,14,18	-	-
18	27.99 (CH_3)	1.52s	12,14	-	11β,14,15a,21,22,11-OAc
19	15.93 (CH_3)	1.18s	-	-	11β
20	125.51 (C)	-	21,22,23	-	-
21	146.56 (CH)	7.98s	22,23	22,23	12,18,30-OAc
22	110.65 (CH)	6.73s	21	21,23	12,18,23,30-OAc
23	142.97 (CH)	7.40s	21,22	21,22	22
28	14.35 (CH_3)	0.79s	3	-	3,6
29	39.17 (CH_2)	a 1.65d 10.80 b 1.81d 10.80	3,28	29b 29a	3,29b 19,29a
30	70.50 (CH)	5.02s	14	-	5,12,30-OAc
31	118.87 (C)	-	-	-	-
32	20.29 (CH_3)	1.55s	-	-	11-OAc
				-	
7 MeO	51.74 (CH_3)	3.52s	-	-	-
16-MeO	51.61 (CH_3)	3.66s	-	-	-
				-	
3-OAc	170.43 (C)	-	3,3-OAc	-	-
	21.33 (CH_3)*	1.96s	-	-	-
11-OAc	169.67 (C)	-	11-OAc	-	-
	20.95 (CH_3)*	2.17s	-	-	14,32
30-OAc	167.68 (C)	-	30,30-OAc	-	-
	21.05 (CH_3)*	2.17s	-	-	21,22,30

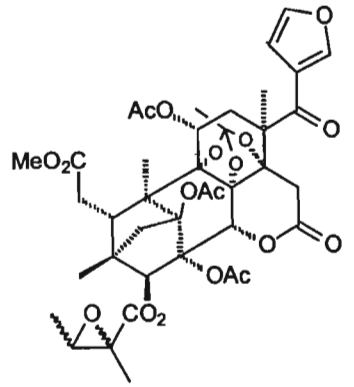
*, #, +: interchangeable within column



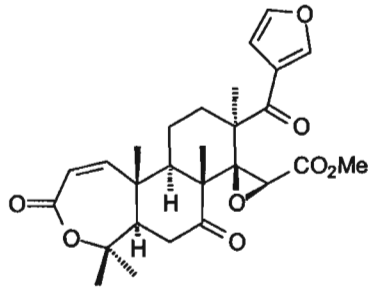
6-6a



6-6b



6-7 febrinolide



6-8 oriciopsin

Only one 17-keto *seco*-ring D limonoid with the 1,8,9-orthoacetate linkage has previously been characterised†. The structure of pseudrelone B from *Pseudocedrela kotschyii*, previously isolated in our laboratories [12], was originally given as that of **6-6a**, but subsequently revised [13] to that of **6-6b** after X-ray crystallographic analysis.

The 17-keto *seco*-ring D limonoid febrinolide **6-7** with a 8,9,14-orthoacetate has been reported from *Soymida febrifuga* A.Juss. [14], while a much simpler obacunone-type compound, oriciopsin **6-8** [15] has been isolated from *Oriciopsis glaberrima* Engl. (Rutaceae).

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† Two other tantalising references have been encountered without structures being given. In [5]

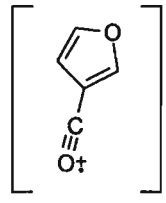
> " the mother liquor gave a strange compound which may, or may not, be a 17-keto limonoid, which we have previously isolated before from *Entandrophragma caudatum* [ref]."

The accompanying ^{1}H NMR data ("δ H 7.98s, 7.38s, 6.72s, 4.65s, 3.64s, 3.64s, 3.52s...") is very similar to the values we have obtained for **NL 1**, but no further information (the reference quoted is to an M.Sc. thesis in which we can find no mention of the compound under discussion) is forthcoming.

In [12]

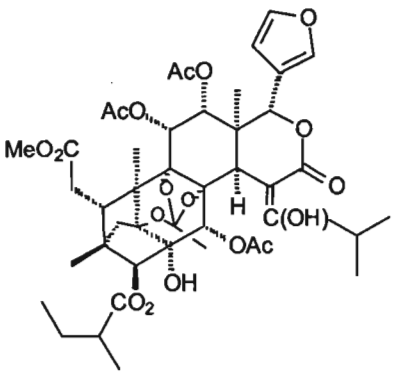
> "...while pseudrelone C is a ring D-opened derivative of phragmalin (Nakanishi, K., pers.comm.)..."

In this publication [15] the appearance of a peak at *m/z* 95 in the mass spectrum, corresponding to the fragment **6-9**, is considered "...convincing support...". for the proposed *seco*-ring D 17-keto structure. We have observed an identical fragment in our mass spectrum, and consider that the evidence for our structure for **NL 1**, the lack of the previously mentioned direct HMBC correlation notwithstanding, is conclusive.

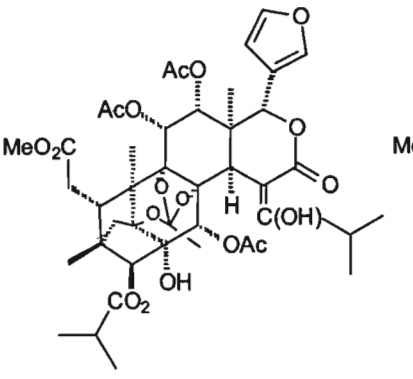


6-9

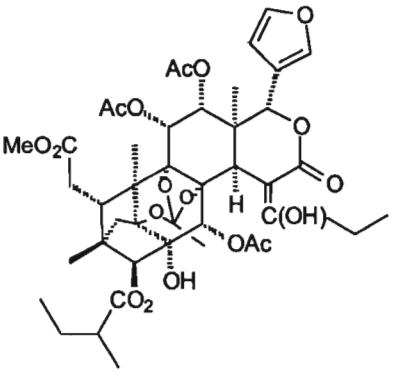
Although they are not as rare as the *seco*-ring D compounds, phragmalin-class **6-1** limonoids are not widespread in the Meliaceae. They currently number some thirty examples drawn from only six species, all of which are members of the tribe Swietenieae, subfamily Swietenioideae. The twelve busseins A-M **6-10,11,12,13,14,15,16,17,18,19,20,21** were reported from *Entandrophragma bussei* Engl. in a single investigation [11]. The five chukrasins A-E **6-22,23,24,25,26** [16] and other phragmalin derivatives **6-27,28,29,30,31** [10,17] have all come from *Chukrasia tabularis* A.Juss. Besides febrinolide **6-7**, *Soymida febrifuga* A.Juss. has yielded febrinins A **6-32** and B **6-33** [18] and epoxy febrinin B derivatives **6-34,35** [14].



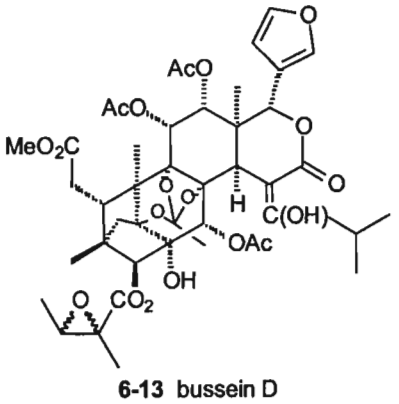
6-10 bussein A



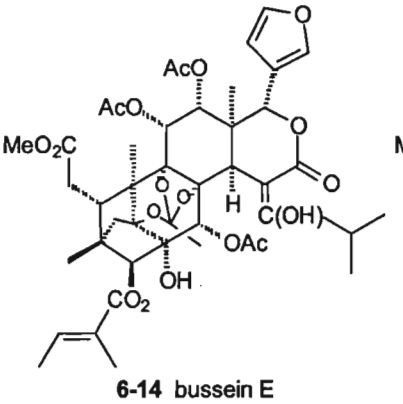
6-11 bussein B



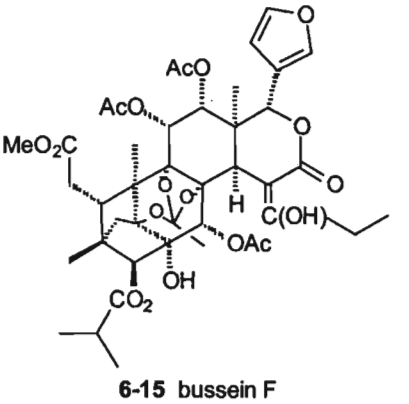
6-12 bussein C



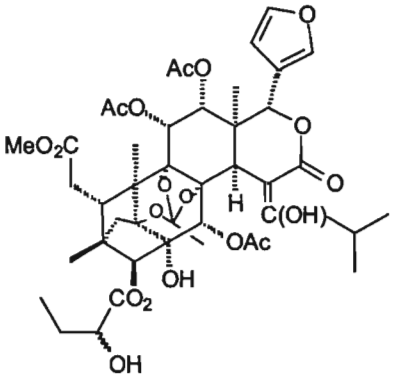
6-13 bussein D



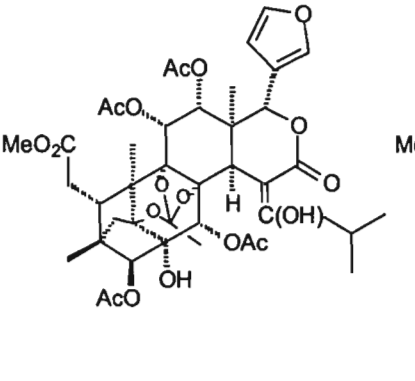
6-14 bussein E



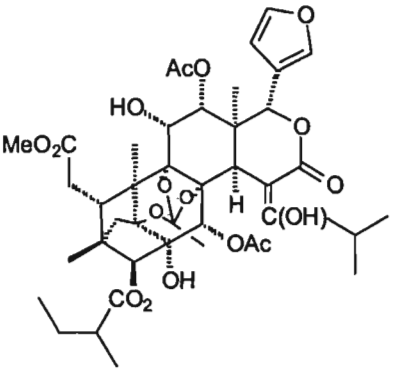
6-15 bussein F



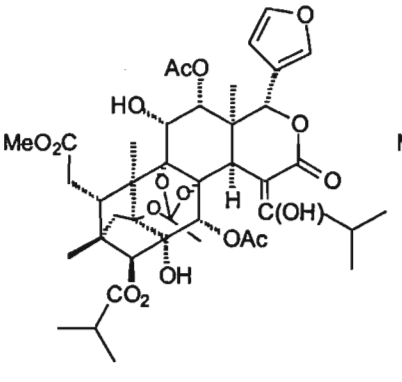
6-16 bussein G



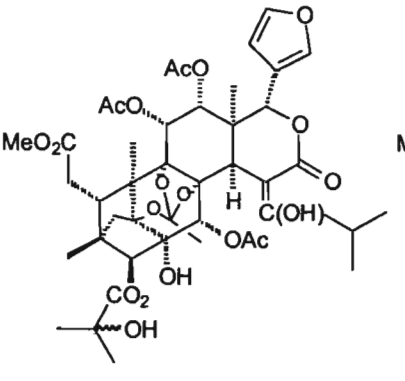
6-17 bussein H



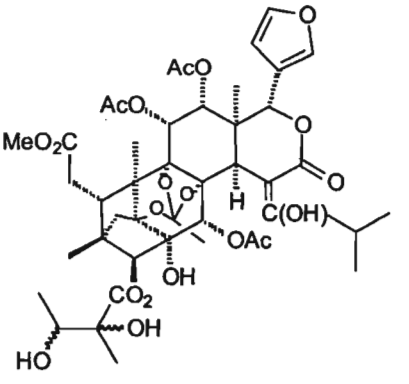
6-18 bussein J



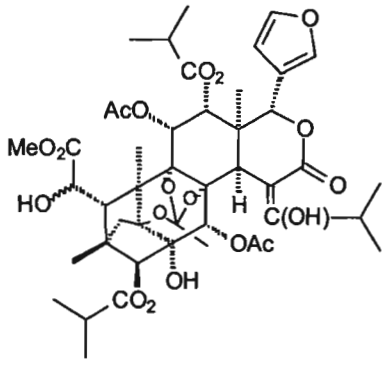
6-19 bussein K



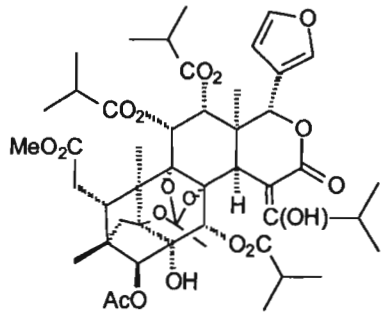
6-20 bussein L



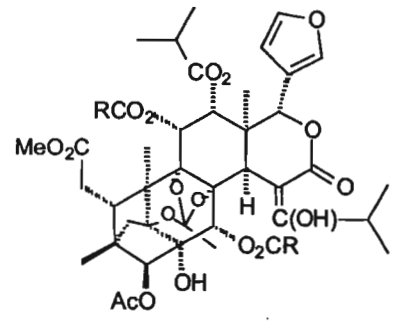
6-21 bussein M



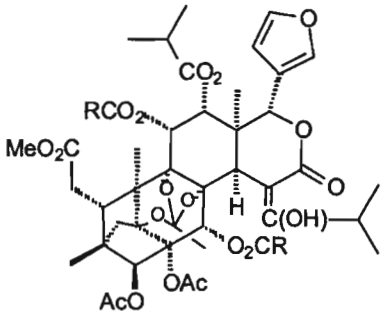
6-22 chukrasin A



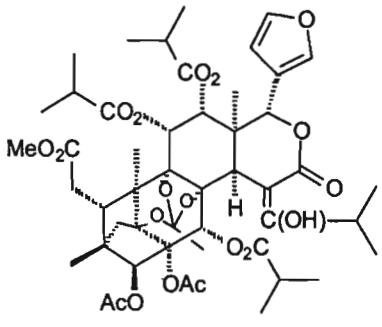
6-23 chukrasin B



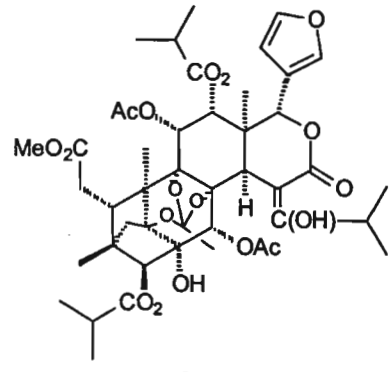
6-24 R = CH_3/Pr^i chukrasin C



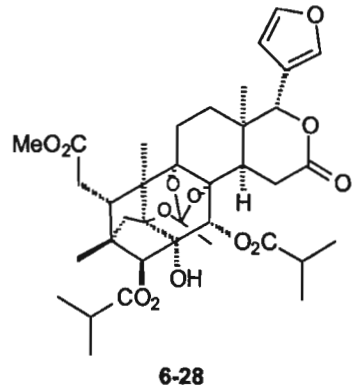
6-25 R = CH_3/Pr^i chukrasin D



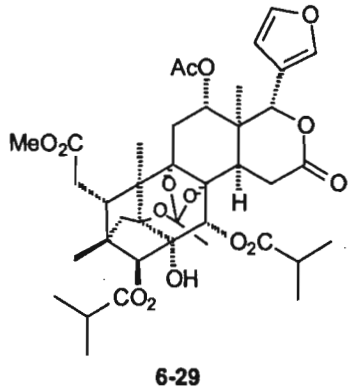
6-26 chukrasin E



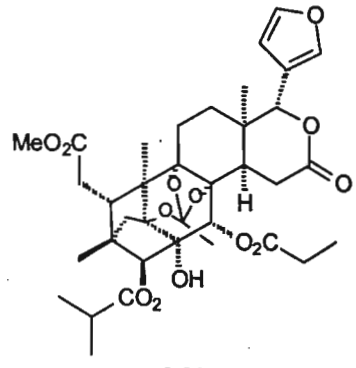
6-27



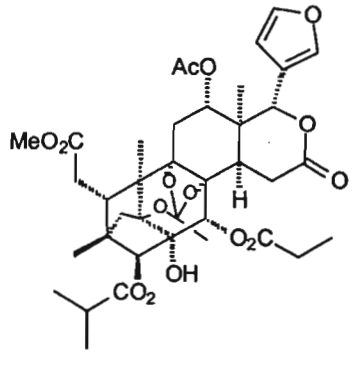
6-28



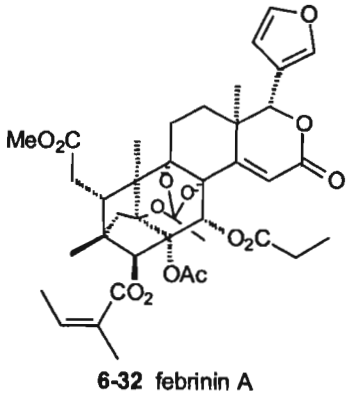
6-29



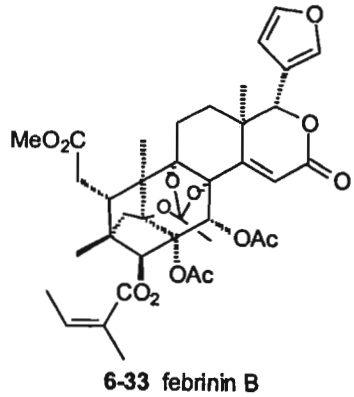
6-30



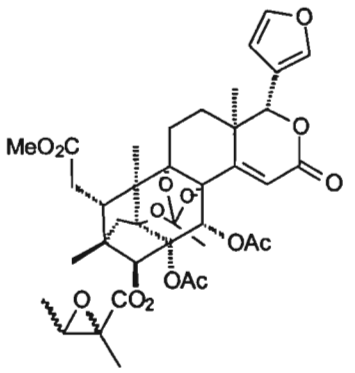
6-31



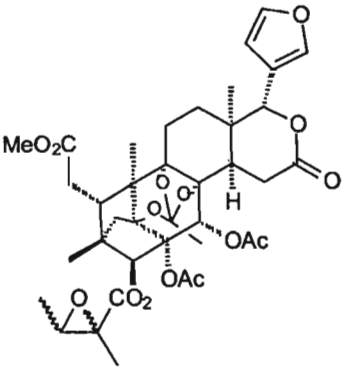
6-32 febrinin A



6-33 febrinin B



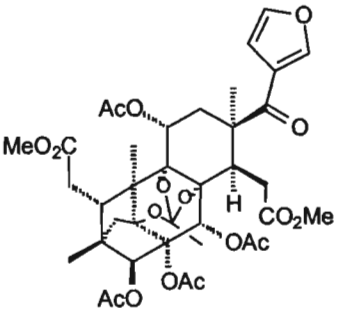
6-34 epoxyfebrinin B



6-35 dihydroepoxyfebrinin B

6.2.2 Structural elucidation of compound NL 2, leandreanin B

(spectra vol II, p.s94-103)



6-36 leandreanin B **NL 2**

An HRMS of this compound gave a molar mass of 774.2750 g.mol^{-1}, corresponding to the molecular formula $C_{38}H_{46}O_{17}$ (calc. 774.2730 g.mol^{-1}) and a difference, relative to leandreanin A **NL 1**, of C_2H_2O. Comparison of the ^1H and ^{13}C NMR spectra of these two compounds revealed them to be very similar, with the major differences being the appearance, in the ^{13}C NMR spectrum, of a fourth ester carbonyl carbon signal and quaternary methyl carbon resonance, and in the ^1H NMR spectrum, of a fourth acetyl methyl proton singlet signal. In addition, the proton singlet resonances at δ4.63 and δ5.02, ascribed to H-3 and H-30 in **NL 1**, have shifted downfield to δ5.03 and δ5.59, in **NL 2**, while the corresponding C-3 and C-30 ^{13}C NMR resonances have shifted upfield to δ80.71 and δ67.87.

The fully substituted C-O signal at δ86.38 displays HMBC correlations to multiplets at δ2.62 and δ2.35, ascribed to H-5 and 2H-12, respectively (δ35.70(CH), C-5; δ35.79(CH_2), C-12, by comparison with **NL 1**), and is assigned to C-9. Both this C-9 resonance and that at δ85.34 correlate to 3H-19

(1.20s, 3H; δ16.11(CH_3), C-19, by comparison with **NL 1**), establishing this as C-1. The remaining signal at δ85.69 displays an HMBC correlation to a multiplet at δ3.26, ascribed to 2H-15 (δ30.22(CH_2), C-15, by comparison with **NL 1**), and must thus be the unaccounted for C-8; however, it also displays correlations to both H-3 and H-29b at δ1.80m (δ1.55m, H-29a, δ39.97(CH_2), C-29, by comparison with **NL 1**), suggesting that the resonances for C-8 and C-2 are superimposed. The intensity of this signal is approximately double that of those for C-1 and C-9, which are of the same multiplicity.

Comparison of the ^{13}C NMR spectra for chukrasins B **6-23** and E **6-26** reveals that acetylation at C-2 shifts the C-3 resonance upfield from δ83.2 to δ80.2, while leaving that for C-30 unchanged at δ68.5, and, significantly, causing a sharp downfield shift in the C-2 signal from δ77.1 to δ83.0. Thus, if it is accepted that the signals for C-2 and C-8 are superimposed at δ85.69, then leandreanin B **NL 2** is the novel 2-acetylleandreanin A **6-36**. The fully assigned ^{1}H and ^{13}C NMR spectral data are given in Table 6.2 below.

Table 6.2: ^{1}H and ^{13}C NMR assignments for compound **NL 2**, leandreanin B

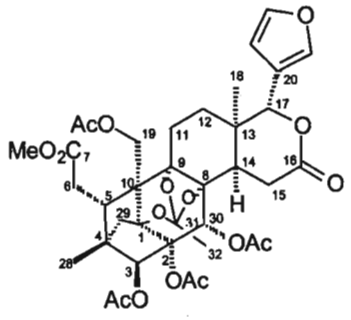
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δ_C	δ_H	HMBC correlation C→H	COSY correlation	NOESY correlation
1	85.34 (C)	-	19,29a,29b,30	-	-
2	85.69 (C)*	-	3,29b	-	-
3	80.71 (CH)	5.03s	5,28,29a,29b,30	-	28,29a
4	46.07 (C)*	-	3,5,6,28,29a,29b	-	-
5	35.70 (CH)	2.62m	3,6,19,28,29a,29b	6	28
6	33.95 (CH_2)	2.32m	3,19	5	19,28
7	172.32 (C)	-	6,7-MeO	-	-
8	85.69 (C)*	-	3,14,15,30	-	-
9	86.38 (C)	-	11,12,14,19	-	-
10	45.67 (C)	-	5,6,11,19,29a,29b	-	-
11	67.02 (CH)	5.43brs	12	12	12,19
12	35.79 (CH_2)	2.35m	18	11	11β,18,21,22
13	47.22 (C)	-	11,12,14,15,18	-	-
14	44.49 (CH)	3.21m	12,15,18	15	18,11-OAc
15	30.22 (CH_2)	3.26m	14	14	14,15b,18
16	175.77 (C)	-	14,15	-	-
17	199.52 (C)	-	12,14,18	-	-
18	28.81 (CH_3)	1.47s	12,14	-	11β,14,15a,21,22,11-OAc
19	16.11 (CH_3)	1.20s	5	-	11β
20	126.03 (C)	-	21,22,23	-	-
21	146.26 (CH)	8.02s	22,23	22,23	12,18,30-OAc
22	110.99 (CH)	6.77s	21	21,23	12,18,23,30-OAc
23	142.54 (CH)	7.39s	21,22	21,22	22
28	14.57 (CH_3)	0.79s	3,29b	-	3,6
29	39.97 (CH_2)	a 1.55m b 1.80m	3,28	29b 29a	3,29b 19,29a
30	67.87 (CH)	5.59s	3,14,15,29b	-	5,12,30-OAc
31	118.93 (C)	-	32	-	-
32	20.27 (CH_3)	1.56s	-	-	11-OAc
				-	
7 MeO	51.82 (CH_3)	3.54s	-	-	-
16-MeO	51.54 (CH_3)	3.67s	-	-	-
				-	
2-OAc	170.03 (CH_3)	-	-	-	-
	21.55 (C)*	2.07s	-		
3-OAc	170.05 (C)#	-	3,3-OAc	-	-
	20.96 (CH_3)$	2.04s	-	-	-
11-OAc	169.70 (C)#	-	11,11-OAc	-	-
	20.84 (CH_3)$	2.16s	-	-	14,32
30-OAc	166.78 (C)#	-	30,30-OAc	-	-
	21.42 (CH_3)+	1.98s	-	-	21,22,30

*, #, +, $: interchangeable within column

6.2.3 Structural elucidation of compound NL 3, leandreanin C

(spectra vol II, p.s104-113)



6-37 leandreanin C **NL 3**

An HRMS of this compound gave a molar mass of 744.2631 g.mol^{-1}, corresponding to the molecular formula $C_{37}H_{44}O_{16}$ (calc. 744.2629 g.mol^{-1}) and sixteen double bond equivalents.

Inspection of the ^{1}H and ^{13}C NMR spectra of this compound revealed the characteristic signals of the 4,29,1-bridge and 1,8,9-orthoacetate (δ119.35(C), C-31; δ1.66m/δ2.24m, 2H, 2H-29, δ38.84(CH_2), C-29; δ1.62s, 3H, 3H-32, by HMBC correlation to C-31). In contrast to compounds **NL 1** and **NL 2**, however, the furan ring protons are no longer shifted downfield (δ7.65s, δ141.91(CH), H-21; δ7.36s, δ143.30(CH), H-23; δ6.38s, δ109.10(CH), H-22; and δ122.27(C), C-20), while C-21 and C-22 both correlate in the HMBC spectrum to a 1H proton resonance at δ5.71, which is coupled to a oxymethine signal at δ69.63, and is assigned therefore to H-17. **NL 3** thus has a "normal" ring D lactone, within which are C-14 (δ47.54(CH), HMBC correlation to H-17), H-14 (δ2.24m, HSQC correlation to C-14), and C-15 (δ30.22(CH_2), HMBC correlation to H-14), with H-15β (by NOESY correlation to H-17) at δ2.28m and H-15α at δ2.81 (dd, J = 15.39, 3.66Hz). C-16 occurs at δ174.13(C), by HMBC correlation to both H-14 and 2H-15, 3H-18 at δ1.20, by NOESY correlation to H-17, and C-13 at δ38.93(C), by HMBC correlations to H-17, 2H-15 and 3H-18.

Further perusal of these spectra, however, uncovered that **NL 3** has only three quaternary methyl resonances rather than the expected four; furthermore, it possesses a oxymethylene signal at δ68.82 correlating in the HSQC spectrum to a remarkable pair of coupled doublets (J = 13.82Hz) at δ4.29 and δ4.73.

An HMBC correlation between 2H-15 and a fully substituted C-O resonance at δ86.17 establishes this as C-8. The C-8 signal is correlated to a singlet resonance at δ5.95, ascribed to H-30, and from which a further HMBC correlation to a oxymethine signal at δ81.28 designates this as C-3; HSQC correlations place C-30 at δ68.63(CH) and H-3 as a singlet at δ5.16. The C-3 resonance displays HMBC correlations to H-30, 2H-29, a multiplet at δ2.50, assigned to H-5, and to a 3H methyl singlet signal at δ0.92, which correlates also to C-29, and can therefore only be 3H-28; HSQC correlations place the C-5 resonance at δ32.90(CH) and that of C-28 at δ13.67(CH_3). This suggests that it is the C-19 methyl group that is missing, and consequently that the signals at δ4.29 and δ4.73 can be ascribed to 2H-19.

HMBC correlations between both the H-3 and 3H-28 resonances and a fully substituted signal at δ46.09 establishes this as C-4, and therefore that the fully substituted signal at δ45.14 can be ascribed to C-10. This latter assignment is further supported by HMBC correlations between the C-10 resonance and 2H-29, and also to a pair of coupled multiplets at δ2.34 and δ2.50, which are ascribed to 2H-6 by HMBC correlation to C-5.

Final confirmation that it is indeed C-19 that has been oxidised can be seen from HMBC correlations between 2H-19 and C-10, and between one of them and C-5. It then remains only to assign the remaining fully substituted C-O resonances at δ85.95 and δ85.19 to C-9 and C-2, respectively, on the basis of an HMBC correlation between the H-5 and C-9 resonances on one hand, and between the 2H-29 and C-2 signals on the other.

The quaternary methyl signals and corresponding ester carbonyl resonances in the ^{13}C NMR spectrum are superimposed to the extent that they cannot be distinguished. Despite the fact that the acetate ester methyl signals are well separated in the ^{1}H NMR spectrum, they are also superimposed on underlying signals, which makes it very difficult to determine with certainty which signal is responsible for a given HMBC correlation, while the fact that three of these acetate esters occur at the adjacent C-2, C-3 and C-30 make it virtually impossible to assign them on the basis of NOESY correlations. Thus the only acetate ester methyl signal that can be unequivocally assigned is that at δ2.11, which is placed at C-19 on the basis of NOESY correlations to the 2H-19 resonance at δ4.29 and to the H-11α resonance at δ1.88m.

To our knowledge, this is the first report of a phragmalin limonoid with an oxygenated C-19 methyl group, and leandreanin C **NL 3** thus has the novel structure **6-37**. The fully assigned ^{1}H and ^{13}C NMR spectral data are given in Table 6.3 below.

Table 6.3: ^{1}H and ^{13}C NMR assignments for compound **NL 3**, leandreanin C

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δ_C	δ_H	HMBC correlation C→H	COSY correlation	NOESY correlation
1	85.73 (C)	-	3,19a,19b,28,30	-	-
2	85.19 (C)	-	19a,19b,29a,29b,30	-	-
3	81.28 (CH)	5.16s	5,28,29a,29b,30	-	28,29a
4	46.09 (C)	-	3,6,28,29a,29b	-	-
5	32.90 (CH)	2.50m	3,6,19,28,29a,29b	6a,6b	6,28,30
6	30.89 (CH_2)	a 2.34m b 2.50m	3	5,6b 5,6a	5,28
7	171.33 (C)	-	6	-	-
8	86.17 (C)	-	15α,15β,18,30	-	-
9	85.95 (C)	-	5,11α,11β,19a,19b,30	-	-
10	45.14 (C)	-	6,19a,19b,29a,29b	-	-
11	25.83 (CH_2)	α 1.88m β 2.12m	-	11β,12a,12b 11α,12a,12b	11β,12a,12b,19-OAc 11α,12a,12b
12	31.59 (CH_2)	a 1.08m b 1.14m	18	11α,11β,12b 11α,11β,12a	11α,11β,12b 11α,11β,12a
13	38.93 (C)	-	15α,15β,17,18	-	-
14	47.54 (CH)	2.24m	15α,15β,17,18	15α,15β	18
15	30.22 (CH_2)	α 2.28m β 2.81dd 15.39, 3.66	14	14,15β 14,15α	14,15β,18 15α,30
16	174.13 (C)	-	14,15α,15β	-	-
17	69.63 (CH)	5.71s	14,18	-	15β,16,21,22,30
18	21.06 (CH_3)*	1.20s	17	-	11α,11β,14,15α,17,21,22
19	68.82 (CH_2)	a 4.29d 13.82 b 4.73d 13.82	5	19b 19a	19b,19-OAc 19a
20	122.27 (C)	-	17,21,22,23	-	-
21	141.91 (CH)	7.65s	17,22,23	22,23	17,18,30
22	109.10 (CH)	6.38s	17,21,23	21,23	17,18,23,30
23	143.30 (CH)	7.36s	17,21,22	21,22	22
28	13.67 (CH_3)	0.92s	29b	-	3,5,6b
29	38.84 (CH_2)	a 1.66m b 2.24	3,5,28	29b 29a	3,29b 19b,29a
30	68.63 (CH)	5.95s	3	-	5,12b,17,15β
31	119.35 (C)	-	32	-	-
32	20.63 (CH_3)*	1.62s	-	-	-
				-	
7 MeO	51.55 (CH_3)	3.66s	-	-	-
				-	
2-OAc	169.03 (CH_3)*	-	-	-	
	21.31 (C)#	1.94s$	-	-	
3-OAc	169.44 (C)*	-	-	-	-
	21.44 (CH_3)#	2.06s$	-	-	-
19-OAc	169.69 (C)*	-	-	-	-
	21.55 (CH_3)#	2.11s	11α,19a	-	11α,19a
30-OAc	170.28 (C)*	-	-	-	-
	21.55 (CH_3)#	2.28s$	-	-	-

*,#,+,$: interchangeable within column

6.3 Experimental

Neobeguea leandreana was collected in August 1997 in the Bekopaka area in southwestern Madagascar. A voucher specimen (010-Mj/Mdul) is deposited at the Department of Botany of the University of Antananarivo. Plant identification was confirmed by the Department of Botany at the Parc Zoologique et Botanique de Tsimbazaza.

The air-dried, milled stembark (304g) was extracted successively for 24 hours in a Soxhlet apparatus with hexane, dichloromethane and methanol, yielding 7.94g, 3.85g and 18.64g of extract respectively. The combined hexane-dichloromethane extract yielded leandreanin A **NL 1**, leandreanin B **NL 2** and leandreanin C **NL 3**.

Compound **NL 1**
(spectra vol II, p.s84-93)

leandreanin A

pale yellow gum, 19.2mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 6.1, p.149.

Optical Rotation:
$[\alpha]_D = +7^{O}$ (c, 0.354 in $CHCl_3$).

IR spectrum:
υ_{max}(NaCl) 2965, 2924, 1748, 1672, 1379, 1239, 1081 cm^{-1}.

Mass spectrum:
HRMS found 732.2612, calc. for $[C_{36}H_{44}O_{16}]^{+}$ 732.2625 $g.mol^{-1}$
FABMS *m/z* 755 $[M+Na]^{+}$, 733 $[M+H]^{+}$, 715, 673 $[M-AcOH]^{+}$, 630, 581, 539, 511, 479, 437, 415, 389, 355, 329, 279, 257, 237, 217, 201, 182, 154, 136, 107, 95.

Compound **NL 2**
(spectra vol II, p.s94-103)

2-acetylleandreanin A, leandreanin B

pale yellow gum, 13.0mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 6.2, p.156.

Optical Rotation:

$[\alpha]_D = -22^o$ (c, 0.224 in $CHCl_3$)

IR spectrum:

υ_{max}(NaCl) 2953, 1748, 1678, 1444, 1315, 1239 cm^{-1}

Mass spectrum:

HRMS found 774.2750, calc. for $[C_{38}H_{46}O_{17}]^+$ 774.2730 $g.mol^{-1}$.

FABMS *m/z* 797 $[M+Na]^+$, 775 $[M+H]^+$, 731, 715, 613, 581, 539, 511, 479, 451, 399, 357, 339, 307, 279, 213, 107, 95, 69, 55.

Compound **NL 3**

(spectra vol II, p.s104-113)

leandreanin C

pale yellow gum, 10.0mg

^1H and ^{13}C NMR spectra: data and peak assignments Table 6.3, p.160.

Optical Rotation:

$[\alpha]_D = -30^o$ (c, 0.164 in $CHCl_3$).

IR spectrum:

υ_{max}(NaCl) 2953, 1754, 1379, 1251, 1063 cm^{-1}.

Mass spectrum:

HRMS found 744.2631, calc. for $[C_{37}H_{44}O_{16}]^+$ 744.2629 $g.mol^{-1}$ (by "peak matching" only)†.

† Only the fax shown on p.s113 was supplied for leandreanin C **NL 3.** A full spectrum will be included in the final copy of the thesis.

6.4 References

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Chapter 7

Extractives from *Quivisia papinae*

7.1 Introduction

Quivisia papinae Baillon ex Grandidier is an endemic Madagascan species originally placed, on botanical grounds, in the genus *Trichilia*, tribe Trichilieae, subfamily Melioideae by Harms, who thought it to be very similar to the genus *Ekebergia* [1]. However, according to Pennington and Styles [2]...

> "The fruit structure is, however, quite unique in the family, a dry loculicidal capsule, containing dry winged seeds. These distinctive fruit and seed characters, which have already been shown to be important at the subfamily level, indicate the great isolation and antiquity of *Quivisianthe* and we have no hesitation at this stage in placing it in its own subfamily, the *Quivisianthoideae*."

...of which it is currently the only member[†].

No information at present, anecdotal or otherwise, is available about this species' medicinal properties.

The relationship to *Ekebergia* was supported by a previous investigation, in this laboratory, of the wood and stembark of this species [3]. The bark yielded a limonoid tentatively identified as **7-1a** by comparison of its ^{1}H NMR spectrum with that of 3α-hydroxy analogue **7-1b** previously reported as *Ekebergia pterophylla* compound 1 [5], while the wood yielded the coumarin **7-2**, which as a class of compound had not previously been found in any genus of the Meliaceae other than *Ekebergia*[‡].

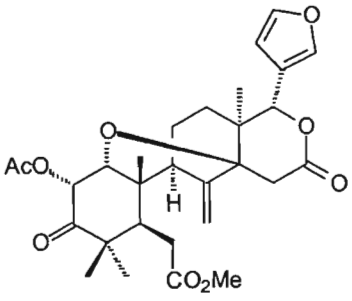
---

† Pennington and Styles [2] mention "One or two species in Madagascar." However, in the only previous publication on this species, Mulholland and Taylor [3] note that

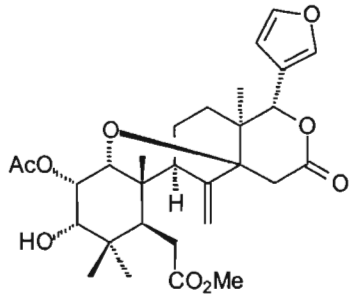
> "...Pennington and Styles...created a new subfamily, Quivisianthoideae in which it is the sole species."

It is also currently listed as such in the Missouri Botanic Gardens database [4].

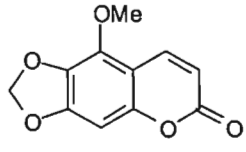
‡ Nor since, it appears, other than the ubiquitous aesculetin **7-3**, scopoletin **7-4** and scoparone **7-5** reported from *Khaya senegalensis* [6].



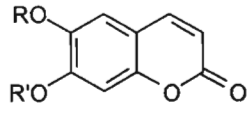
7-1a



7-1b *Ekebergia pterophylla* compound 1



7-2



7-3a R = R' = H aesculetin
7-3b R = Me, R' =H scopoletin
7-3c R = R' = Me scoparone

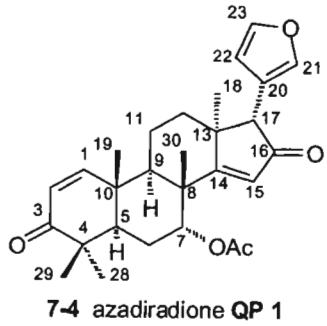
7.2 Extractives from *Quivisia papinae*

Quivisia papinae Baill. is locally named "hompy" in southern Madagascar [7].

Altogether thirteen compounds – two protolimonoid and three havanensin-, one evodulone- and seven mexicanolide-class limonoids were isolated from the seeds of *Quivisia papinae* during the course of this study. Eight of the limonoids were found to be new, with two of the mexicanolide group limonoids in particular, **QP 9**, with a $\Delta^{9(11)}$ double bond, and **QP 10**, with the corresponding 9α,11α-epoxide ring, displaying features hitherto unreported in limonoid chemistry, while a third, **QP 11**, is a 17-keto *seco*-ring D compound as unique to this class as leandreanin A **NL 1** (Chapter 6) is within the limonoids of the phragmalin group.

7.2.1 Structural elucidation of compound QP 1, azadiradione

(spectra vol II, p.s114-123)

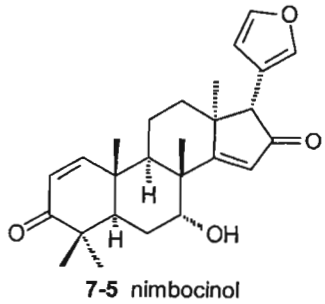


7-4 azadiradione **QP 1**

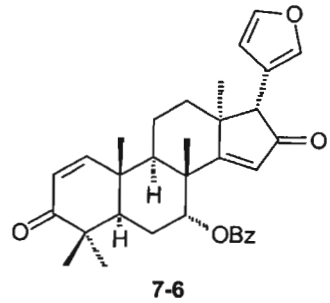
An HRMS of this compound gave a molar mass of 450.2414 g.mol^{-1}, corresponding to the molecular formula $C_{28}H_{34}O_5$ (calc. 450.2406 g.mol^{-1}) and twelve double bond equivalents. The ^{1}H and ^{13}C NMR spectra showed the presence of five quaternary methyl resonances, an acetate ester (δ1.93s, 3H; δ20.97(CH_3) and 169.61(C)), a furan ring (δ7.46s, δ141.64(CH), H-21; δ7.41s, δ142.80(CH), H-23; δ6.25s, δ111.12(CH), H-22; and δ118.39(C), C-20) and a Δ^1 double bond (δ7.13d J =10.16, δ156.74(CH), H-1; δ5.87d J = 10.16, δ125.91(CH), H-2), correlated in the HMBC spectrum to a quaternary carbonyl resonance at δ204.0, ascribed to C-3. Also immediately evident was the unusual fully substituted carbon signal at δ192.36.

The five quaternary methyl signals suggested this compound to be an unrearranged limonoid, and a singlet at δ3.41, ascribed to H-17, that it possessed a havanensin rather than gedunin skeleton; C-17 occurs at δ60.71(CH), by HMBC correlation to H-21 and H-22. Correlation in the HMBC spectrum between H-17 and a second carbonyl signal at δ205.08 established this as C-16, with further correlations placing the second, trisubstituted, double bond at Δ^{14} (δ5.86s, 1H, H-15, δ123.27(CH), C-15; δ192.36(C), C-14). Compound **QP 1** thus contains α,β-unsaturated ketones in rings A and D.

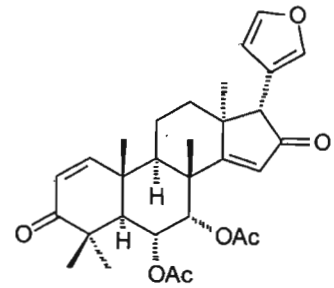
A literature survey conducted on this basis revealed **QP 1** to be the known havanensin group limonoid azadiradione **7-4**, which was first isolated from *Melia azadirachta* L. [8]†. The 7-benzoyl analogue **7-6** has been reported from *Azadirachta indica* [12], while *Swietenia mahogani* C.DC has recently afforded the 6α-acetoxy derivative mahonin **7-7** [13].



7-5 nimbocinol



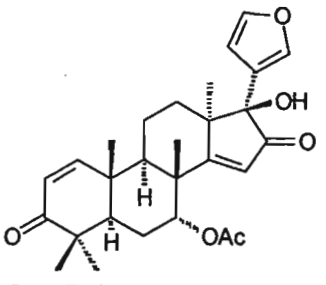
7-6



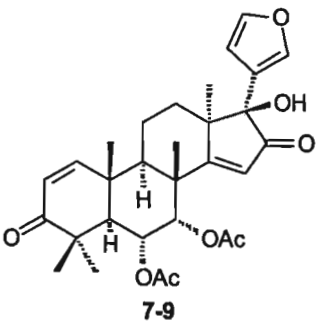
7-7 mahonin

† The Dictionary of Natural Compounds has recently changed the entry under which azadiradione **7-4** is listed, and it is now given as the acetate ester of the parent alcohol nimbocinol **7-5** from *Azadirachta indica* A.Juss [9]. The reasons for this are unfathomable, as nimbocinol was isolated some 15 years after azadiradione **7-4**, and its structural elucidation rests heavily on a comparison of its ^{1}H [10] and ^{13}C NMR [11] spectra with that of the former compound, and in particular on the predicted upfield shift of H-15 that occurs on acetylation of the C-7 hydroxy group [10] (see p.91).

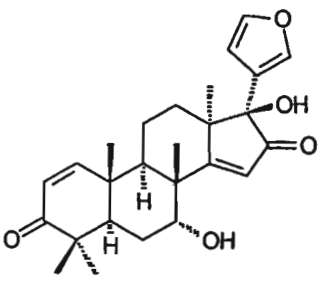
Azadirachta indica [13] and *Melia azadirachta* [10] are also the sources of 17β-hydroxyazadiradione **7-8**, the first limonoid to be characterised with a hydroxy group at this position. Such compounds are rare, with only the 6α-acetoxy analogue **7-9** from *Chisocheton paniculatus* (Roxb.) Hiern [15] and 17β-hydroxynimbocinol **7-10** [16] from *Azadirachta indica* being reported. The 17β-(2-hydroxyethyl) ether derivative marnoodin **7-11**, again from *Azadirachta indica*, is the only gedunin-class limonoid of this type to have been found [17].



7-8 17β-hydroxyazadiradione



7-9



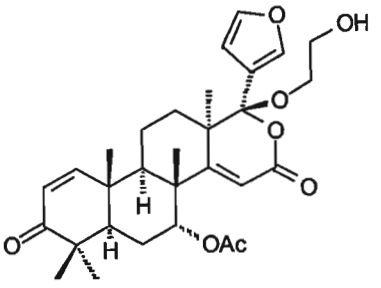
7-10 17β-hydroxynimbocinol

Also isolated only from *Azadirachta indica* are limonoids with a C-17β furan ring. 17-*Epi*-azadiradione **7-12** [11] and 17-*epi*-nimbocinol **7-13** [18], whose structure has been confirmed by X-ray analysis [19], have recently been joined by 17-*epi*-17α-hydroxyazadiradione **7-14** [20][†], while 17-*epi*-17α-hydroxygedunin-type limonoids are represented by nimolicinol **7-15** [21][‡]. The fully assigned ^{1}H and ^{13}C NMR spectra, together with reference ^{13}C NMR data for comparison, are given in Table 7.1 below.

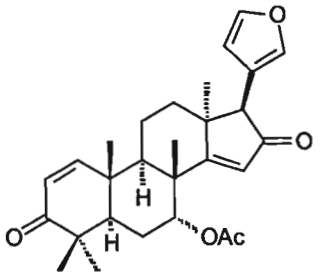
---

† That inversion at/hydroxylation of C-17 occurs only in this very small group of compounds surely points to their having a common origin, for which the most likely suggestion would be loss of H-17 to form a planar carbocation intermediate which could then readily undergo inversion and/or nucleophilic attack by a hydroxy group or water. However, the keto group at C-16 (and, by conjugation, even the Δ^{14} double bond), while readily enhancing the acidity of H-17 and hence increasing the ease of its removal, would give rise to a *carbanion* intermediate...

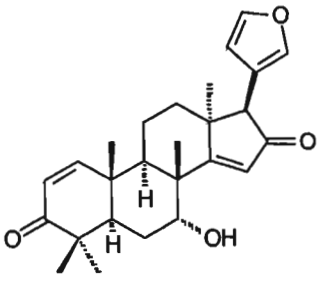
‡ Although not mentioned in the publication, ring D in nimolicinol **7-15** is a hemiacetal and as such should display the characteristic doubling of the ^{13}C NMR signals. In marnoodin **7-11**, however, etherification presumably has the same effect as that of esterification *i.e.* to "lock" the ring into whichever of the two possible conformations is the most stable.



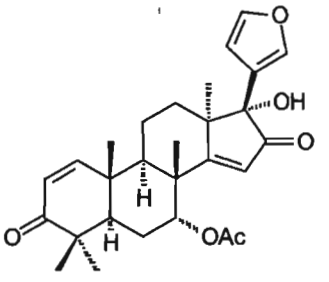
7-11 mamoodin



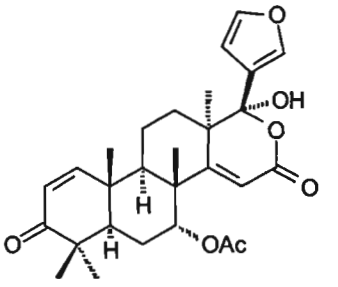
7-12 17-*epi*-azadiradione



7-13 17-*epi*-nimbocinol



7-14 17-*epi*-17α-hydroxyazadiradione



7-15 nimolicinol

Table 7.1: ^{1}H and ^{13}C NMR assignments for compound **QP 1**, azadiradione

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

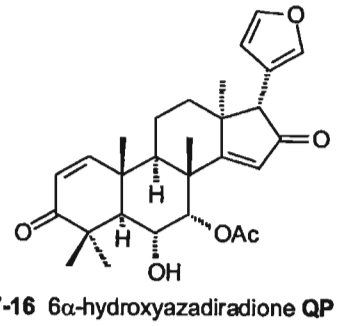
[Lit. [11] ^{1}H NMR 90MHz, ^{13}C 22.6MHz, $CDCl_3$, *J* in Hz]

Position	δC	7-4 Ref. [11]	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	156.74 (CH)	156.76	7.13d 10.16	19	2	2,9,11α,19
2	125.91 (CH)	125.84	5.87 d 10.16	-	1	1
3	204.02 (C)	203.88	-	1,28,29	-	-
4	44.06 (C)	44.01	-	2,5,28,29	-	-
5	46.06 (CH)	38.16	2.17dd 12.63,2.57	1,19,28,29	6α,6β	9,28,2'
6	23.40 (CH_2)	23.40	1.90m	5	5,7	-
7	73.86 (CH)	73.84	5.31brs	30	6α,6β	6,15,30
8	44.53 (C)	44.50	-	15,30	-	-
9	38.15 (CH)	46.06	2.47bmm	1,19,30	11α,11β	1,5,11α,18
10	39.97 (C)	39.95	-	1,2,5,19	-	-
11	15.79 (CH_2)	15.73	α 2.08m β 1.85m	9	9,12α,12β 9,12α,12β	1,9,11β 11α,19,30
12	30.26 (CH_2)	30.26	α 2.08m β 1.85m	17,18	11α,11β 11α,11β	12β,18,22 12α,17
13	47.98 (C)	47.91	-	15,17,18	-	-
14	192.36 (C)	192.35	-	15,18,30	-	-
15	123.27 (CH)	123.25	5.86s	-	-	7,30
16	205.08 (C)	204.92	-	15,17	-	-
17	60.71 (CH)	60.68	3.41s	15,18	-	12β,21,22'
18	26.43 (CH_3)	26.39	1.01s	17	-	9,12α,21,22,2'
19	19.02 (CH_3)	18.94	1.23s	5	-	1,6β,11β
20	118.39 (C)	118.44	-	-	-	-
21	141.64 (CH)	142.71	7.46s	17,22	-	17,18
22	111.12 (CH)	111.13	6.25s	17,21	23	12α,17,18,23
23	142.80 (CH)	141.61	7.41s	21,22	22	22
28	26.97 (CH_3)*	26.91	1.07s*	29	-	5,6α
29	21.27 (CH_3)*	21.22	1.08s*	28	-	6β,19
30	26.30 (CH_3)	26.20	1.32s	-	-	6β,7,11β,15
1'	169.61 (C)	169.53	-	2'	-	-
2'	20.97 (CH_3)	20.86	1.93s	1'	-	5

*: values interchangeable

7.2.2 Structural elucidation of compound QP 2, 6α-hydroxyazadiradione

(spectra vol II, p.s124-133)



7-16 6α-hydroxyazadiradione **QP 2**

The molar mass of compound **QP 2** was determined by HRMS analysis to be 466.2355 $g.mol^{-1}$, corresponding to the molecular formula $C_{28}H_{34}O_6$ (calc. 466.2355 $g.mol^{-1}$) and a difference, relative to **QP 1**, of a single oxygen atom. Comparison of the ^1H and ^{13}C NMR spectra of **QP 2** with those of **QP 1** revealed them to be very similar, with the only difference being the appearance of a double doublet at δ4.41 (J = 11.54, 2.75Hz) in the ^1H NMR spectrum, coupled in the HSQC spectrum to a newly appeared oxymethine resonance at δ68.15, while the C-6 methylene signal at δ23.40 had disappeared. Couplings in the COSY spectrum to a doublet at δ5.45 (J = 2.75), ascribed to H-7, and to a doublet at δ2.28 (J = 11.54), ascribed to H-5, established this as H-6. HMBC correlations to C-7 at δ77.98 and C-5 at δ50.08 confirmed this placing, and NOESY correlations to 3H-19 and 3H-30 that H-6 is β.

QP 2 is thus the novel compound 6α-hydroxyazadiradione **7-16**, or 6-deacetylmahonin. The fully assigned ^1H and ^{13}C NMR spectral data are given in Table 7.2 below.

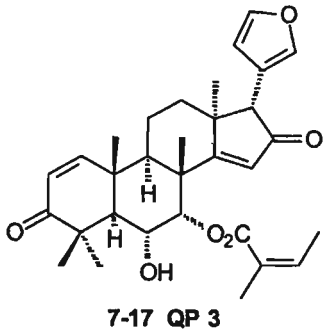
Table 7.2: ^{1}H and ^{13}C NMR assignments for compound **QP 2**, 6α-hydroxyazadiradione

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	156.13 (CH)	7.07d 10.07	5,19	2	2,9,11α,19
2	126.85 (CH)	5.91d 10.07	-	1	1
3	205.48 (C)	-	1,28,29	-	-
4	45.74 (C)	-	2,5,28,29	-	-
5	50.08 (CH)	2.28d 11.54	1,7,19,28,29	6	9,28
6	68.15 (CH)	4.41dd 11.54,2.75	1,5,7	5,7	7,19,30
7	77.98 (CH)	5.45d 2.75	5,30	6	6,15,30
8	45.14 (C)	-	15,30	-	-
9	37.04 (CH)	2.44brm	1,5,7,19,30	11α,11β	1,5,11α,18
10	40.81 (C)	-	1,2,5,19	-	-
11	16.07 (CH_2)	α 2.10m β 1.82m	9	9,12α,12β 9,12α,12β	1,9,11β 11α,19,30
12	30.46 (CH_2)	α 2.10m β 1.87m	17,18	11α,11β 11α,11β	12β,18,22 12α,17
13	48.21 (C)	-	15,17,18	-	-
14	191.61 (C)	-	15,18,30	-	-
15	123.61 (CH)	5.86s	-	-	7,30
16	204.96 (C)	-	15,17	-	-
17	61.13 (CH)	3.41s	15,18	-	12β,21,22
18	27.10 (CH_3)	1.02s	17	-	9,12α,21,22,2'
19	21.32 (CH_3)*	1.17s	5	-	1,6,11β,29,30
20	118.45 (C)	-	-	-	-
21	141.81 (CH)	7.46s	17,22	-	17,18
22	111.27 (CH)	6.25s	17,21	23	12α,17,18,23
23	143.00 (CH)	7.41s	21,22	22	22
28	32.19 (CH_3)	1.30s	5,29	-	5,29
29	21.22 (CH_3)*	1.40s	28	-	6,19
30	26.37 (CH_3)	1.36s	-	-	6,7,11β,15,19
1'	171.71 (C)	-	2'	-	-
2'	20.56 (CH_3)	2.01s	1'	-	7

7.2.3 Structural elucidation of compound QP 3, 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione

(spectra vol II, p.s134-143)



7-17 QP 3

The molecular formula of compound **QP 3** was determined by HRMS (found 506.2672; calc. 506.2668 g.mol^{-1}) to be $C_{31}H_{38}O_6$ with a difference, relative to compound **QP 2**, of C_3H_4. Inspection of the ^{1}H NMR spectrum revealed the characteristic signal at δ6.02 attributable to H-3' of an angelate ester (for a discussion on the differences in the chemical shift of the H-3' signal in tiglate and angelate esters, see p.110), which was then assigned by analysis of the COSY, HSQC and HMBC spectra (δ168.31(C), C-1'; δ127.28(C), C-2'; δ6.02qq J = 6.13, 1.10Hz, δ139.15(CH), H-3'; δ1.92m, δ16.22(CH_3), 3H-4'; δ1.80s, δ20.83(CH_3), 3H-5'). Further correlation in the HMBC spectrum between C-1' and H-7β, and between C-1' and both 3H-4' and 3H-5' confirmed the ester location at C-7α.

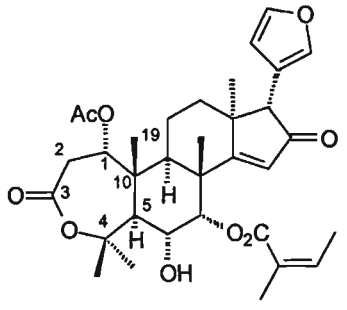
The remaining ^{1}H and ^{13}C NMR signals were virtually identical to those of **QP 2**. As the 7-deacetyl-7-angeloyl analogue of **QP 2**, compound **QP 3** thus has the novel structure **7-17**. The fully assigned ^{1}H and ^{13}C NMR spectral data are given in Table 7.3 below.

Table 7.3: ^{1}H and ^{13}C NMR assignments for compound **QP 3**, 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione [^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	156.18 (CH)	7.06d 10.07	5,9,19	2	2,9,11α,19
2	126.80 (CH)	5.90d 10.07	-	1	1
3	205.49 (C)	-	1,28,29	-	-
4	45.74 (C)	-	2,5,28,29	-	-
5	50.39 (CH)	2.26d 11.54	1,6,7,19,28,29	6β	9,28,5'
6	68.19 (CH)	4.46dd 11.54,2.19	1,5,7β	5,7	-
7	77.05 (CH)	5.61d 2.19	5,6,30	6	6,15,30
8	45.23 (C)	-	7,9,15,30	-	-
9	37.41 (CH)	2.46brm	1,5,7,19,30	11α,11β	1,5,11α,18
10	40.89 (C)	-	1,2,5,19	-	-
11	16.15 (CH_2)	α 2.10m β 1.88m	9	9,12α,12β 9,12α,12β	1,9,11β 11α,19,30
12	30.36 (CH_2)	α 2.10m β 1.87m	17,18	11α,11β 11α,11β	12β,18,22 12α,17
13	48.31 (C)	-	15,17,18	-	-
14	191.25 (C)	-	7,9,15,17,18,30	-	-
15	123.83 (CH)	5.93s	-	-	7,30'
16	204.93 (C)	-	15,17	-	-
17	61.06 (CH)	3.39s	15,18	-	12β,21,22
18	26.91 (CH_3)	0.97s	15,17	-	9,12α,21,22,5'
19	21.10 (CH_3)	1.18s	1,2,5	-	1,6,11β
20	118.51 (C)	-	17,21,22,23	-	-
21	141.79 (CH)	7.43s	17,22	-	17,18
22	111.31 (CH)	6.22s	17,21,23	23	12α,17,18,23
23	142.94 (CH)	7.39s	21,22	22	22
28	32.26 (CH_3)	1.28s	5,29	-	5,29
29	20.54 (CH_3)	1.40s	28	-	6,19,28
30	26.57 (CH_3)	1.38s	-	-	6,7,11β,15
1'	168.38 (C)	-	7,4',5'	-	-
2'	127.28 (C)	-	4',5'	-	-
3'	139.15 (CH)	6.02qq 6.13,1.10	4',5'	4'	4',5'
4'	16.22 (CH_3)	1.92m	3',4',5'	3'	3'
5'	20.83 (CH_3)	1.80s	3'	-	3'

7.2.4 Structural elucidation of compound QP 4, quivisianthone

(spectra vol II, p.s144-153)



7-18 quivisianthone **QP 4**

The molar mass of this compound was determined by HRMS to be 582.2816 g.mol^{-1}, which corresponds to the molecular formula $C_{33}H_{42}O_9$ (calc.582.2829 g.mol^{-1}) and thirteen double bond equivalents.

Inspection of the ^{1}H and ^{13}C NMR spectra revealed, in addition to the usual furan ring resonances (δ7.42s, δ141.82(CH), H-21; δ7.39s, δ143.06(CH), H-23; δ6.19s, δ111.24(CH), H-22; and δ118.43(C), C-20), the presence of resonances ascribable to an angelate ester (δ169.22(C), C-1'; δ126.99(C), C-2'; δ6.07qq *J* = 7.33, 1.47Hz, δ140.15(CH), H-3'; δ1.97m, δ16.17(CH_3), 3H-4'; δ1.88s, δ20.62(CH_3), 3H-5'), an acetate ester (δ2.00s, δ21.39(CH_3), 168.21(C)), an additional ester carbonyl signal at δ169.63, and a fully substituted C-O resonance at δ86.65.

That **QP 4** has the same D ring as that present in the previous three compounds can be inferred from signals at δ205.00(C), δ190.46(C) and δ124.65(CH), and δ60.76(CH) in the ^{13}C NMR spectrum, which are ascribed to C-16, C-14 and C-15, and C-17, respectively. The singlet resonances at δ5.99 and δ3.39 are ascribed to H-15 and H-17.

In similar fashion the same B ring 6α-hydroxy, 7α-angeloyloxy substitution pattern can be deduced from a series of COSY-coupled signals at δ2.41(d, *J* = 10.81Hz, H-5), 4.42(dd, *J* = 10.81, 2.93Hz, H-6β) and 5.55 (d, *J* = 2.93Hz, H-7β) and HMBC correlations between C-1' and H-7β, and between C-1' and both 3H-4' and 3H-5'.

HMBC correlations between C-17 and a quaternary methyl proton singlet signal at δ0.93, and between C-14 and another at δ1.38, established these as 3H-18 and 3H-30 resonances, respectively. Further correlation from 3H-30 to a methine resonance at δ32.77 designated this as C-9, which, in turn, is correlated to a third quaternary methyl singlet signal at δ1.25, ascribed to 3H-19. The 3H-19 resonance correlates to a methine signal at δ48.58, assigned to C-5, and to an oxymethine resonance at δ74.31, ascribed to C-1.

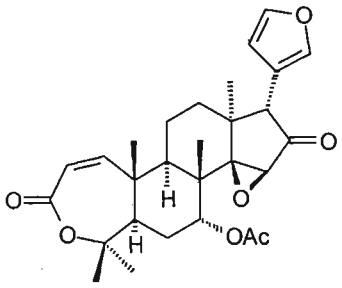
A doublet of doublets (J = 9.34, 6.41Hz) at δ4.84, attributed to H-1, are seen to coupled in the COSY spectrum to two pairs of double doublets at δ2.62 (J = 12.82, 9.34Hz; H-2α, by NOESY coupling to H-5) and δ3.00 (J = 12.82, 6.41Hz; H-2β). The H-2α and H-2β resonances both display correlations in the HMBC spectrum to the remaining carbonyl signal at δ169.63, ascribed to C-3 in a seven-membered lactone ring. The fully substituted C-O resonance at δ86.65, correlating to both H-5 and two superimposed quaternary methyl singlet signals at δ1.70 in the HMBC spectrum, which must be 3H-28 and 3H-29, can then be assigned to C-4. Final confirmation is provided by a faint but distinct HMBC correlation between the 3H-28/29 resonances and that of C-3 .

The acetate ester is placed at C-1 due to an HMBC correlation between C-1" and H-1. NOESY correlations to both 3H-19 and 3H-30 establish H-1 as β and hence the acetate as α.

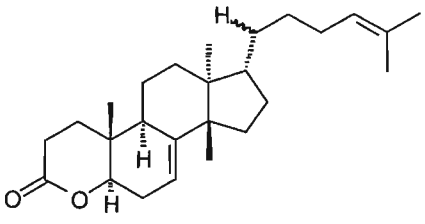
Quivisianthone **QP 4** is thus assigned structure **7-18**, and as such is a novel evodulone-class limonoid. The fully assigned ^{1}H and ^{13}C NMR spectra are given in Table 7.4 below.

The 7-membered ring A lactone which characterises the evodulone group is infrequently encountered in the Meliaceae, and no examples to date have been reported possessing both the ring A lactone and the azadiradione-type ring D. Although the first limonoid, evodulone **7-19** itself (with an 14β,15β-epoxide ring), from *Carapa procera* DC. [22], was only the third such compound to be isolated having what was to become the evodulone skeleton. The first was that of the euphol/tirucallol protolimonoid entandrolide **7-20b** [23] from *Entandrophragma angolense* (Welw. ex C.DC.) C.DC., whose impact was substantially lessened by presenting the structure as that of **7-20a** in which both C-4 and C-21 had unaccountably been completely omitted; publication of the second, the butanolide tricoccin S_{13} **7-21** from *Cneorum tricoccon* L. (Cneoraceae) [24]; however, prompted the rapid announcement of both

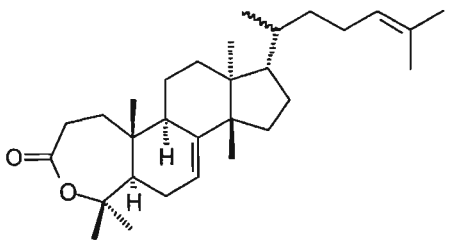
evodulone **7-19** and the two related compounds surenin **7-22** and surenone **7-23** from *Toona sureni* (Blume) Merrill [25].



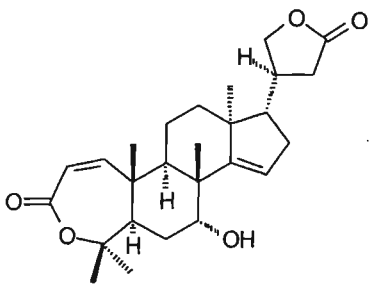
7-19 evodulone



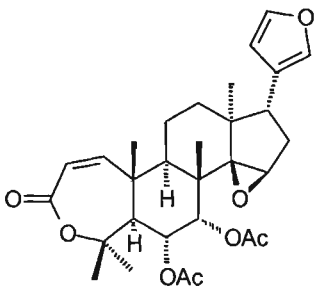
7-20a entandrolide [21]



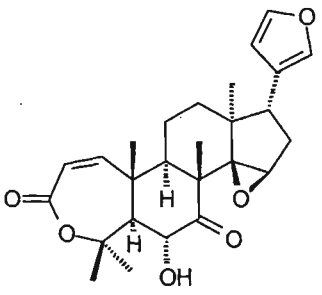
7-20b entandrolide



7-21 tricoccin S_{13}



7-22 surenin



7-23 surenone

Evodulone-group limonoids isolated subsequently can be divided into two groups depending on whether they have an A ring with a Δ^1 double bond or a 1,2-dihydro-ring A with an oxygenated substituent - almost invariably an acetate ester - at C-1α[†].

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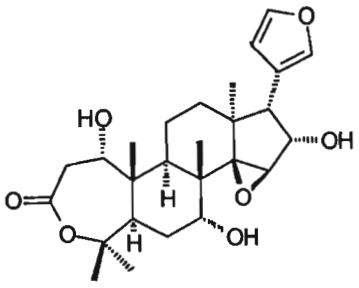
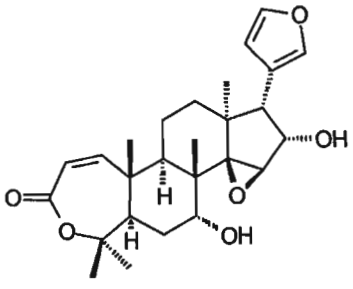
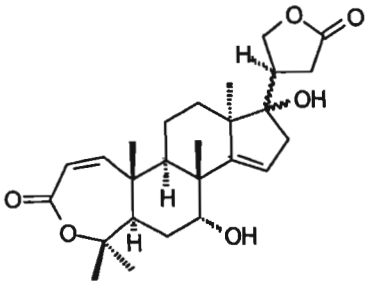
† Tricoccin S_{32} **7-24**, from *Cneorum tricoccon* is the only reported exception to date, with a hydroxy group at C-1 [26].



7-24 tricoccin S_{32}

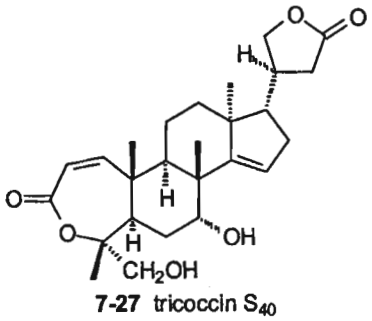


7-25 tricoccin S_{22}

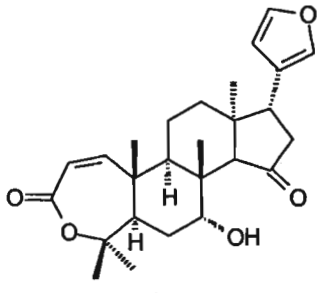


7-26 tricoccin S_{38}

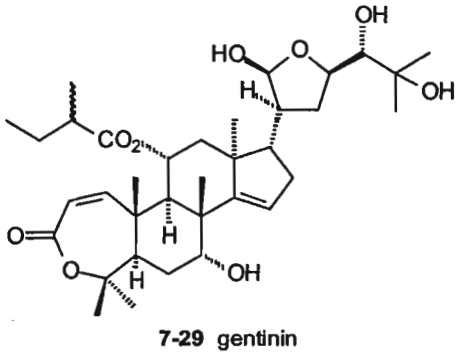
Unsaturated ring A compounds include the limonoid tricoccin S_{22} **7-25** and butanolide tricoccin S_{13} **7-21** analogues S_{38} **7-26** and S_{40} **7-27**, all from *Cneorum tricoccon* [26,27], ouabanginone **7-28** from *Teclea ouabangiensis* Aubrév. & Pellegr. (Rutaceae) [28], and the protolimonoid gentinin **7-29** from *Aglaia argentea* Blume [29].



7-27 tricoccin S_{40}



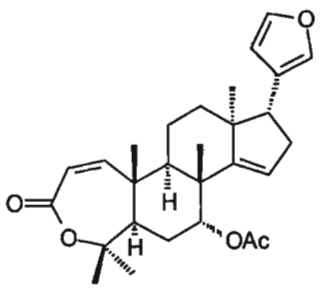
7-28 ouabanginone



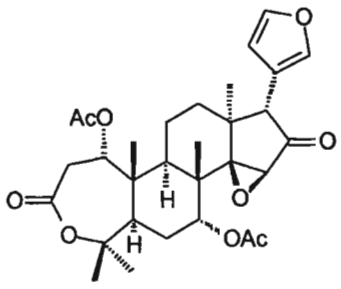
7-29 gentinin

1α-Acetoxy compounds are now in the majority, the earlier predominance of unsaturated ring A isolates notwithstanding. Proceranone **7-30** has been reported from *Carapa procera* [30], while *Carapa grandiflora* Sprague has afforded evodulone **7-19** and carapolides H **7-31** and I **7-32** [31].

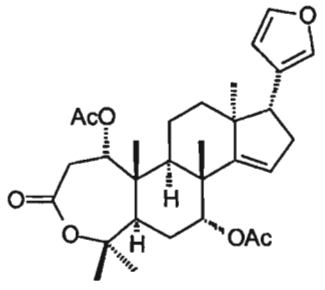
This latter compound, as kihadalactone A, has also been reported, together with the butanolide kihadalactone B **7-33**, from *Phellodendron amurense* Rupr. (Rutaceae) [32]†.



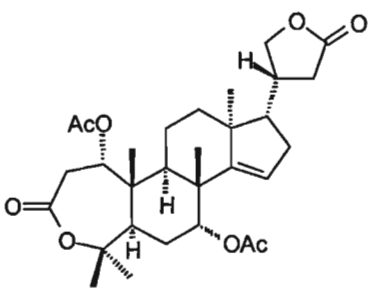
7-30 proceranone



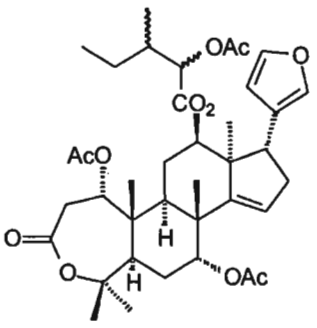
7-31 carapolide H



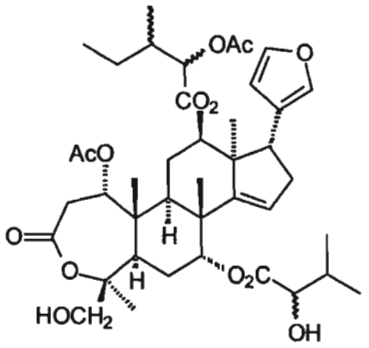
7-32 carapolide I/kihadalactone A



7-33 kihadalactone B



7-34 dregeana 3



7-35 dregeana 4

A number of these compounds have been isolated from *Trichilia* species. The acetoxyvalerate ester derivatives dregeana 3 **7-34** and dregeana 4 **7-35** were reported from *Trichilia dregeana* Sonder [33]. Isomeric to dregeana 4 **7-35**, and also possessing the uncommon oxygenated C-29, is rubralin B **7-37**, which together with related compounds rubralins A **7-36** and C **7-38** were obtained from *Trichilia rubra* C.DC. [34]. Dregeana 4 **7-33** has recently also been found in *Trichilia emetica* Vahl. [35].

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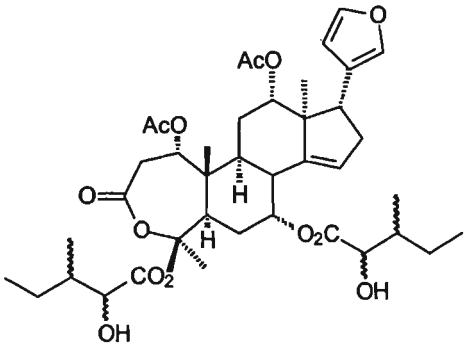
† Kishi *et al.* [32] do not show H-20 explicitly in their publication, but report that

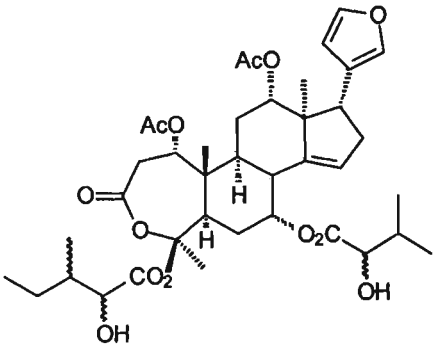
> "The absolute configuration at C-20 was determined to be *S* on the basis of the observation of a negative Cotton effect..." and
>
> "On thermolysis, **2** [kihadalactone B] afforded compound **10**,...which was identified as tricoccin S_{13} acetate."

An *S* configuration at C-20 corresponds to H-20 being β, which is how the structure is given in the Dictionary of Natural Products. Epe *et al.*'s original publication [24] contains an ORTEP stereoscopic diagram which quite clearly shows that H-20 is α, yet ascribes the "determined *S* configuration" to a proposed tirucallol precursor.

It is not clear where the confusion arises.

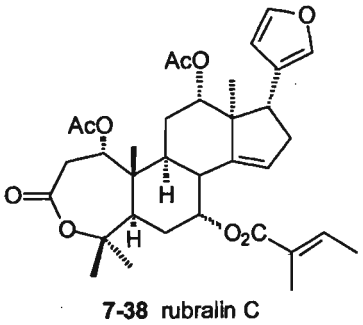


7-36 rubralin A

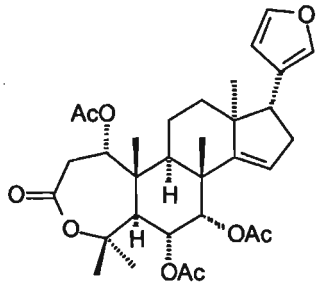


7-37 rubralin B

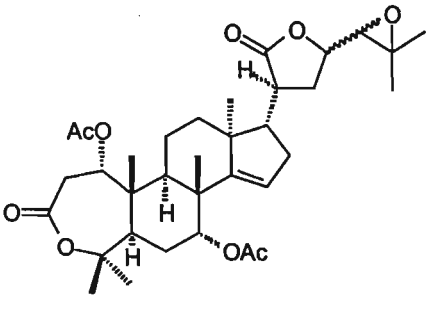
A study in our laboratories of *Entandrophragma delevoyi* de Wild has yielded the 6α-acetoxy derivative delevoyin B **7-39** [36], and the protolimonoid phebaloparvilactone **7-40** has been reported from the Australian species *Phebalum squamulosum* ssp *parvifolium* P.G.Wilson (Rutaceae) [37].



7-38 rubralin C



7-39 delevoyin B



7-40 phebaloparvilactone

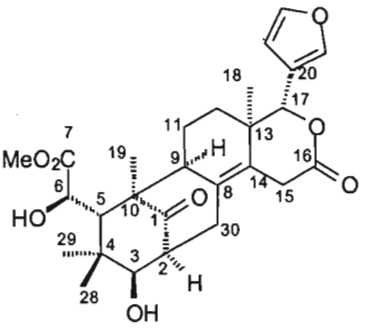
Table 7.4: ^{1}H and ^{13}C NMR assignments for compound **QP 4**, quivisianthone

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	74.31 (CH)	4.84dd 9.34,6.41	2α,2β,5,9,19,2'	2α,2β	2β,11α,19
2	37.76 (CH_2)	α 2.62dd 12.82,9.34 β 3.00dd 12.82,6.41	-	1,2β 1,2α	2β,5,28 1,2α
3	169.63 (C)	-	1,2α,2β,28,29	-	-
4	86.65 (C)	-	5,28,29	-	-
5	48.57 (CH)	2.41d 10.81	1,7,19,28,29	6	2α,9,28,5'
6	67.91 (CH)	4.42dd 10.81,2.93	5,7,28,29	5,7	7,19,29,30
7	76.62 (CH)	5.55d 2.93	5,30	6	6,15,30
8	43.73 (C)*	-	7,9,15,30	-	-
9	32.77 (CH)	3.11m	5,7,19,30	11α,11β	5,11α,18,5'
10	43.97 (C)*	-	2β,5,19	-	-
11	16.67 (CH_2)	α 1.39m β 1.80m	9	9,12α,12β 9,12α,12β	1,9,11β,12α,18 11α,19,30
12	30.77 (CH_2)	α 1.80m β 1.97m	17,18	11α,11β 11α,11β	11α,12β,17 11β,12α,17
13	47.82 (C)	-	12α,12β,15,17,18	-	-
14	190.46 (C)	-	9,12β,15,17,18,30	-	-
15	124.65 (CH)	5.99s	-	-	7,30
16	205.00 (C)	-	15,17	-	-
17	60.76 (CH)	3.38s	15,18	-	12α,12β,21,22
18	26.89 (CH_3)	0.93s	12α,12β,15,17	-	9,11α,21,22,4',5'
19	17.40 (CH_3)	1.25s	1,5,9	-	1,6,11β,29,30
20	118.43 (C)	-	17,21,22,23	-	-
21	141.82 (CH)	7.42s	17,22,23	-	17,18
22	111.24 (CH)	6.19s	17,21,23	23	12α,17,18,23
23	143.06 (CH)	7.39s	21,22	22	22
28	28.05 (CH_3)#	1.70s	5,29	-	2α,5,29
29	32.68 (CH_3)#	1.70s	5,28	-	6,19,28
30	25.48 (CH_3)	1.38s	-	-	6,7,11β,15,19
1'	168.21 (C)	-	7,4',5'	-	-
2'	126.99 (C)	-	4',5'	-	-
3'	140.15 (CH)	6.07qq 7.33,1.47	4',5'	4'	4',5'
4'	16.17 (CH_3)	1.97m	3',4',5'	3'	18,3'
5'	20.62 (CH_3)	1.88s	3'	-	5,18,3'
1''	169.22 (C)	-	1,2''	-	-
2''	21.39 (CH_3)	2.00s	-	-	-

7.2.4 Structural elucidation of compound QP 5, swietenolide

(spectra vol II, p.s154-163)



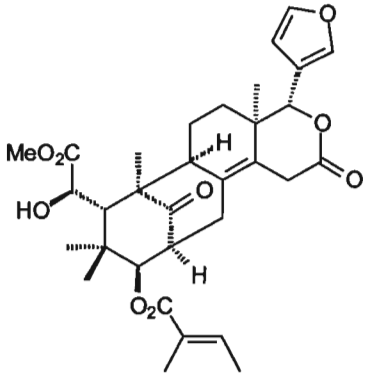
7-41 swietenolide **QP 5**

The molar mass of compound **QP 5** was determined to be 486.2272 g.mol^{-1}, corresponding to the molecular formula $C_{27}H_{34}O_8$ (calc. 486.2253 g.mol^{-1}) and eleven double bond equivalents.

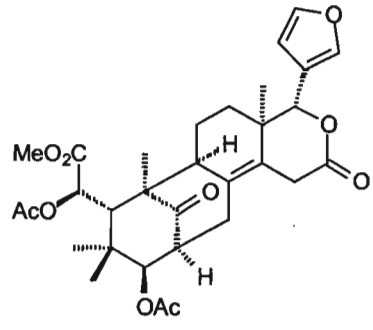
Immediately noticeable in the ^{1}H and ^{13}C NMR spectra of **QP 5** are the presence of only four rather than five quaternary methyl signals, a much further downfield carbonyl resonance (219.92(C)), a completely substituted double bond (δ129.26(C) and 131.02(C)), and a furan ring (δ7.45s, δ141.27(CH), H-21; δ7.38s, δ143.11(CH), H-23; δ6.37s, δ110.03(CH), H-22; and δ121.04(C), C-20). The C-21 and C-22 resonances both correlate in the HMBC spectrum to a singlet at δ5.44, ascribed to H-17. The H-17 signal, in turn, correlates both to the resonance at δ131.02, assigned to C-14, and to a quaternary methyl signal at δ18.12, which must be C-18. The resonance at δ129.26 can then only be C-8.

The C-14 resonance correlates, in the HMBC spectrum, to a pair of coupled doublets at δ3.43 and δ4.00 (J = 21.06Hz), assigned to H-15α (by NOESY coupling to 3H-18) and H-15β, respectively. The 2H-15 resonances, in turn, are seen to correlate in the HMBC spectrum to an ester signal at δ171.55(C), ascribed to C-16, while the second ester carbonyl resonance at δ176.05 correlates to the resonances ascribed to the protons and carbons of a methoxy group at δ3.80s and 53.49(CH_3). **QP 5** thus contains a gedunin type D-ring lactone, a $\Delta^{8(14)}$ double bond, and a carbomethoxy group.

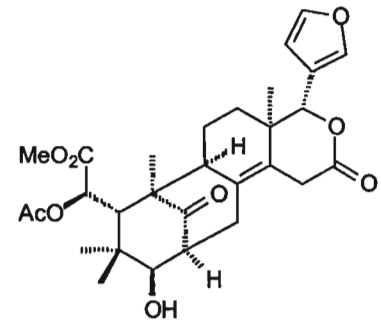
A literature survey conducted on this basis revealed this compound to be the known mexicanolide group limonoid swietenolide **7-41**, which was first isolated from *Swietenia macrophylla* King in 1951 [38], although the structure was finally elucidated only much later [39-41]. In addition to the D-ring lactone and $\Delta^{8(14)}$ double bond, they are further distinguished by the presence of a keto group at C-1 and hydroxy/acyloxy groups at C-3β and C-6. They have subsequently been found primarily in *Swietenia* spp., with the 3-tigloyl **7-42** [42], 3,6-diacetyl **7-43** [42,43,44], 6-acetyl **7-44** and 2α-hydroxy-3-tigloyl-15α-acetyloxy-30α-*iso*propanoyloxy **7-45** [44] derivatives reported from *Swietenia macrophylla*, and 3-acetyl **7-46** [45,46], 3-tigloyl **7-42**, 3,6-diacetyl **7-43**, 6-acetyl **7-44** and 3-tigloyl-6-acetyl **7-47** [46] analogues from *Swietenia mahogani* Jacq. Surprisingly, this latter publication [46] is the only other reference to that of swietenolide **7-41** itself.



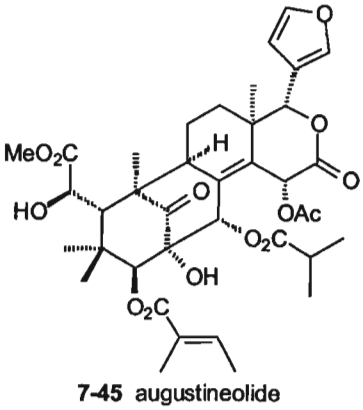
7-42



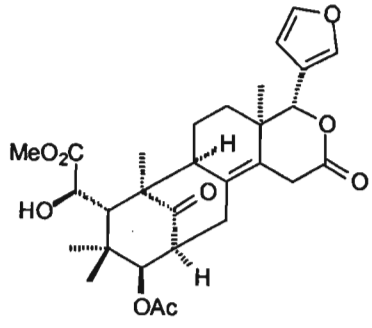
7-43



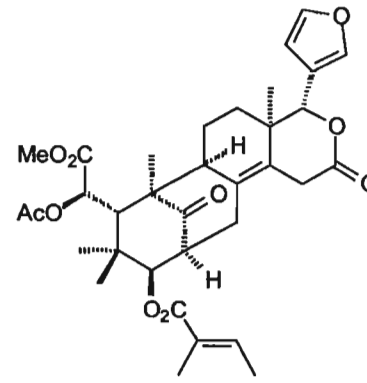
7-44



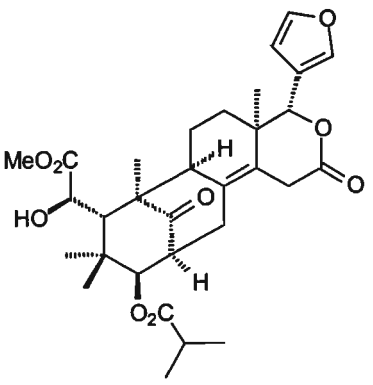
7-45 augustineolide



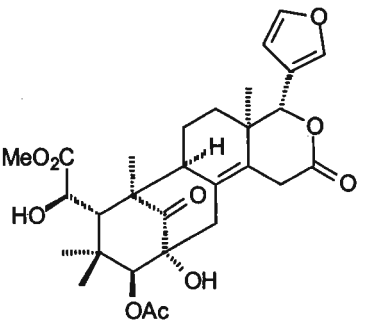
7-46



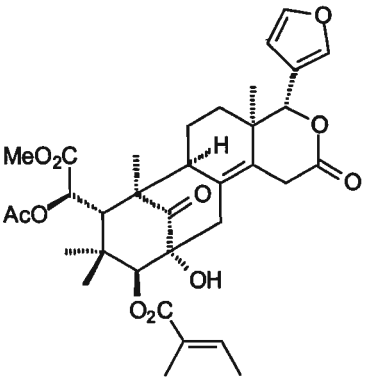
7-47



7-48



7-49



7-50

In addition to the 3-tigloyl **7-42** and 3,6-diacetyl **7-43** analogues, *Khaya ivorensis* A.Chev. has also afforded the 3-*iso*butanoyl derivative **7-48** [47], and, more recently, the 2α-hydroxy-3-acetyl and 2α-hydroxy-3-tigloyl-6-acetyl compounds **7-49** and **7-50** have been reported from *Khaya senegalensis* (Desr.) A.Juss. [48] and *Trichilia connaroides* (Wight et Arn.) Bentv., respectively [49].

The fully assigned ^{1}H and ^{13}C NMR spectral data, together with reference values for comparison, are given in Table 7.5 below.

Table 7.5: ^{1}H and ^{13}C NMR assignments for compound **QP 5**, swietenolide

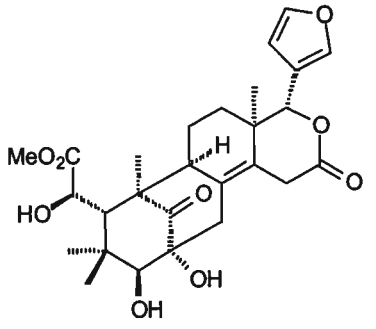
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

[Lit. [45] ^{1}H NMR 300MHz, ^{13}C 75MHz, $CDCl_3$, *J* in Hz]

Position	δC	7-41 Ref. [45]	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	219.92 (C)	219.80	-	2,19,30β	-	-
2	50.17 (CH)	49.99	3.01ddd 9.71,5.68,2.38	30β	3,30α,30β	3,29,30α,30β
3	78.77 (CH)	78.50	3.55d 9.71	5,28,29,30α,30β	2	2,28,29
4	39.88 (C)	39.66	-	5,6,28,29	-	-
5	44.20 (CH)	44.00	3.22brs	3,6,19,28,29	6	6,11a,11b,28,29
6	73.79 (CH)	73.57	4.51brs	5	5,CH_3O	5,11a,11b,19,CH_3O
7	176.05 (C)	175.83	-	5,6,CH_3O	-	-
8	129.26 (C)	129.05	-	2,9,11a(b),15α,15β,30α,30β	-	-
9	53.20 (CH)	52.96	2.05m	5,11a(b),12α,12β,19,30β	11a,11b	11a(b),19
10	54.19 (C)	53.99	-	6,11a,11b,19	-	-
11	18.97 (CH_2)	29.08	a 1.75m b 1.83m	12α	9,11b,12α,12β 9,11a,12α,12β	9,12α 9,12β
12	29.33 (CH_2)	18.74	α 1.10m β 1.70m	11a,11b,17,18	11a,11b,12β 11a,11b,12α	18,22 17
13	38.05 (C)	37.81	-	11a,11b,12α,15β,17,18	-	-
14	131.02 (C)	130.75	-	12α,15α,15β,17,18,30α,30β	-	-
15	33.39 (CH_2)	33.15	α 3.43d 21.06 β 4.00d 21.06	-	15β 15α	15β,18 15α,17,30β
16	171.55 (C)	171.43	-	15α,15β	-	-
17	80.71 (CH)	80.51	5.44s	12α,12β,18	21	12β,15β,21,22
18	18.12 (CH_3)	17.91	0.96s	12α,12β,17	-	9,12α,15α,21,22
19	18.12 (CH_3)	17.91	1.38s	5	-	6,9,11a(b),29
20	121.04 (C)	120.81	-	17,21,22	-	-
21	141.27 (CH)	141.06	7.45s	17,22,23	22	12α,18
22	110.03 (C)	109.80	-	17,21,23	21,23	12α,17,18,23
23	143.11 (CH)	142.88	7.38m	21,22	21,23	22
28	23.84 (CH_3)	23.22	0.97s	29	-	3,5,29,CH_3O
29	23.43 (CH_3)	23.63	0.85s	3,5,28	-	3,28
30	34.01 (CH_2)	33.80	α 1.98m β 3.15dd 14.46, 2.38	2,3	2,30β 2,30α	2,30β 2,15α,15β,30α
CH_3O	53.49 (CH_3)	53.23	3.80s	5	-	6,28

7.2.6 Structural elucidation of compound QP 6, 2α-hydroxyswietenolide

(spectra vol II, p.s164-173)



7-51 2α-hydroxyswietenolide **QP 6**

An HRMS of this compound gave a molar mass of 502.2195 g.mol^{-1}, which corresponds to the molecular formula $C_{27}H_{34}O_9$ (calc. 502.2203 g.mol^{-1}) and a difference, relative to swietenolide **QP 5**, of an additional single oxygen atom. Comparison of the ^{1}H and ^{13}C NMR spectra of these two compounds revealed them to be very similar, with the major difference being the disappearance of the ^{1}H resonance at δ3.01, assigned to H-2 in swietenolide **QP 5**, and downfield shift of the corresponding C-2 signal from δ50.17 (CH) in **QP 5** to δ79.57 (C) in **QP 6**. This immediately infers that the additional oxygen atom can be placed at C-2, and therefore that **QP 6** is the novel compound 2α-hydroxyswietenolide **7-51**.

Comparison of the ^{13}C NMR spectra for the 3-acetyl analogues 3-acetyl swietenolide **7-46** and 2α-hydroxy-3-acetylswietenolide **7-49** reveals that hydroxylation at C-2 shifts C-3 and C-30 downfield from δ79.94 and δ33.89 in **7-46** to δ86.9 and δ44.6 in **7-49** [45,46,48]. C-3 and C-30 occur in **7-51** at δ87.08 and δ44.68, respectively. Finally, a similar comparison of C-2 in 3-acetylswietenolide **7-46** and swienolide **7-41** reveal a downfield shift of ~2 ppm from δ47.86 to δ49.99 on deacetylation at C-3 [45,46]; our value, at δ79.57, bears the same relationship to the δ77.8 recorded for C-2 in 2α-hydroxy-3-acetylswietenolide **7-49** [49]. The fully assigned ^{1}H and ^{13}C NMR spectral data are given in Table 7.6 below.

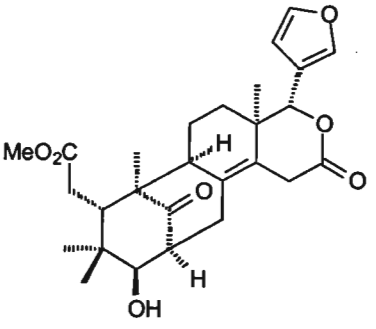
Table 7.6: ^{1}H and ^{13}C NMR assignments for compound **QP 6**, 2α-hydroxyswietenolide

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	218.99 (C)	-	3,19,30α	-	-
2	79.57 (C)	-	3,30α,30β	-	-
3	87.08 (CH)	3.44s	5,28,29,30α,30β	-	28,29
4	40.16 (C)	-	3,5,6,28,29	-	-
5	44.29 (CH)	3.13brs	3,6,19,28,29	6	6,9,11a(b),12β,17,28,29,CH_3O
6	73.54 (CH)	4.49brs	5	5	5,11a(b),12β,19,CH_3O
7	175.79 (C)	-	5,6,CH_3O	-	-
8	126.76 (C)	-	15α,15β,30α,30β	-	-
9	52.78 (CH)	2.03m	5,19,30α	11a,11b	11a,11b,19
10	53.13 (C)	-	5,6,19	-	-
11	18.91 (CH_2)	a 1.81m b 1.84m	-	9,11b,12α,12β 9,11a,12α,12β	5,6,9,11b,12α,12β 5,6,9,11a,12α,12β
12	29.19 (CH_2)	α 1.14m β 1.70m	17,18	11a,11b,12β 11a,11b,12α	11a,11b,12β,18,22 5,6,12α,17,21,22
13	38.23 (C)	-	11a,11b,17,18	-	-
14	132.54 (C)	-	15α,15β,17,18,30β	-	-
15	33.54 (CH_2)	α 3.43m β 4.02d 21.06	-	15β 15α	15β 15α,17,30β
16	171.14 (C)	-	15α,15β	-	-
17	80.57 (CH)	5.43s	18	21	12β,15β,18,21,22,CH_3O
18	18.10 (CH_3)	0.97s	17	-	11a(b),15α,21,22, 30α
19	18.10 (CH_3)	1.48s	5	-	6,9,11a(b),12α,29
20	120.94 (C)	-	17,21,22,23	-	-
21	141.29 (CH)	7.46s	17,22,23	17,18,21,22,23	17,18
22	110.01 (CH)	6.37s	17,21,23	21,23	12α,12α,17,18,23
23	143.16 (CH)	7.39s	21,22	21,22	22
28	23.69 (CH_3)	0.86s	29	-	3,5,29,30β,CH_3O
29	22.77 (CH_3)	0.92s	5,28	-	3,5,19,28
30	44.68 (CH_2)	α 3.43m β 1.62m	-	30β 30α	30β 28,29,30α
CH_3O	53.62 (CH_3)	3.81s	5,6	-	5,6,28

7.2.7 Structural elucidation of compound QP 7, proceranolide

(spectra vol II, p.s174-183)



7-52 proceranolide **QP 7**

An HRMS of compound **QP 7** gave a molar mass of 470.2293 g.mol^{-1}, which corresponds to the molecular formula $C_{27}H_{34}O_7$ (calc. 470.2305 g.mol^{-1}), and a difference, again relative to swietenolide **QP 5**, of one less oxygen atom. Comparison of the ^1H and ^{13}C NMR spectra with those of swietenolide **QP 5** revealed the only significant difference to be the replacement of the 1H broad singlet resonance at δ4.51, assigned to H-6 in **QP 5**, with a 2H multiplet at δ2.36, and upfield shift of the corresponding C-6 from δ73.79(CH) in **QP 5** to δ33.76(CH_2) in **QP 7**.

QP 7 is therefore 6-deoxyswietenolide, which has previously been isolated, as proceranolide **7-52**, from *Carapa procera* DC. [50], *Khaya ivorensis* A.Chev [47] and *Cabralea eichleriana* C.DC. [51,52]. The proceranolides differ from their swietenolide counterparts within the mexicanolide class only in the absence of the hydroxy group at C-6, and as with the latter compounds, have been isolated with a variety of different esters at C-3. One such is the acetyl derivative **7-53**, reported variously as fissinolide from *Cedrela fissilis* Vell [53], grandifoliolin from *Khaya grandifoliola* C.DC. [54] and angustinolide from *Cedrela angustifolia* Moc. et Sessé ex DC. [55], *Cabralea eichleriana* [51] and *Guarea trichiliodes* L. [56]†. Others include the *iso*butanoyl analogue khayasin **7-54** from *Khaya senegalensis* [58,59]‡, *Khaya grandifoliola* [60] and *Khaya madagascariensis* Jumelle et Perrier [60], and the related compounds khayasin T **7-55** and khayasin B **7-56** from *Khaya senegalensis* [59].

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† Lavie *et al.* [55] considered that the $\Delta^{8(14)}$ double bond in both fissinolide and proceranolide lay instead between C-8 and C-9. In this and two subsequent papers [51,56] the fissinolide isolated was referred to angustinolide. In a rebuttal of his argument, Taylor *et al.* [57] showed conclusively that the double bond does indeed lie between C-8 and C-14 as originally proposed; to date, the only $\Delta^{8,9}$ mexicanolide group limonoid listed in the Dictionary of Natural Products is (erroneously) that of the original angustinolide from *Cedrela angustifolia* [55]. The physical data of the two compounds are very similar: fissinolide m.p. 169-170°C, $[\alpha]_D$ –165 [53], angustinolide m.p. 168-171°C, $[\alpha]_D$ –185 [55].

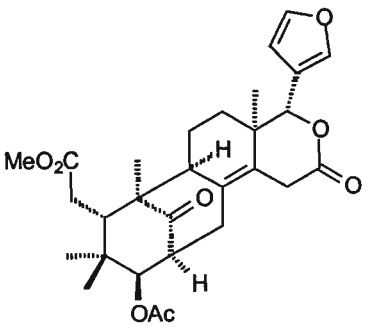
‡ In their preliminary announcement [58] on the characterisation of khayasin **7-54**, Adesogan *et al.* note that

> "...the main constituent (*ca.*. 85%) is the isobutyryl ester of the 3β-alcohol (**I**)...", but also that
>
> "The remainder is probably largely the acetate of the same alcohol."

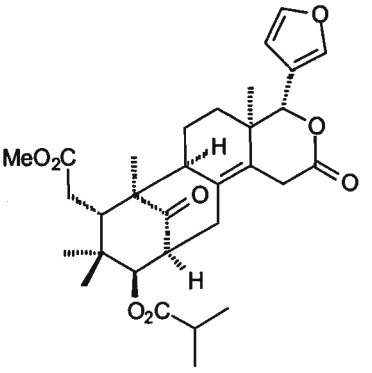
However, in their report of grandifoliolin [54], the same authors remark that

> "This acetate...has not been described before as a natural product, although we have isolated the corresponding isobutyrate, khayasin, from the timber of *Khaya senegalensis*[3]."

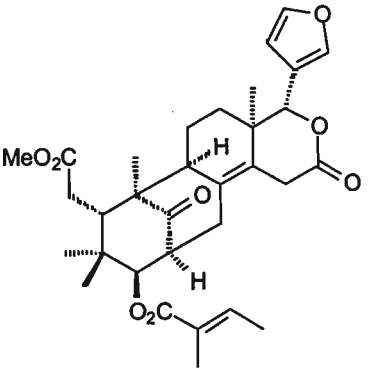
The reference 3 given is to [58] above.



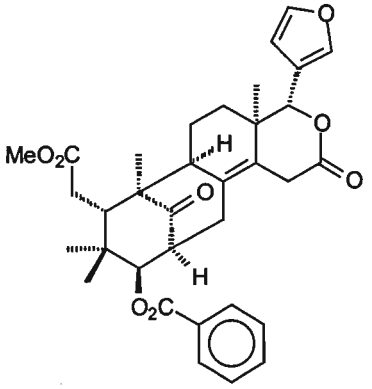
7-53 fissinolide/grandifoliolin



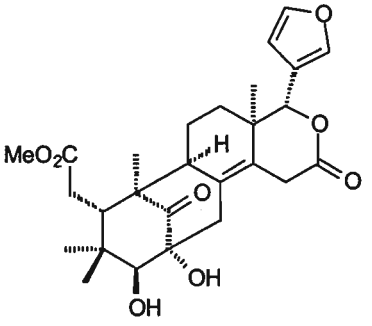
7-54 khayasin



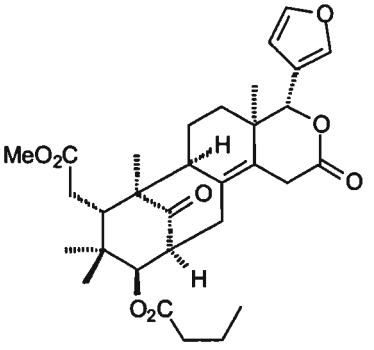
7-55 khayasin T



7-56 khayasin B



7-57 2-hydroxyproceranolide



7-58 proceranolide butanoate

Recent investigations have yielded 2α-hydroxyproceranolide **7-57** from *Khaya senegalensis* [61], the insect antifeedant proceranolide butanoate **7-58** from *Khaya ivorensis* [62][§], and proceranolide **7-52** and khayasin T **7-55** from *Swietenia mahogani* [46].

The fully assigned ^{1}H and ^{13}C NMR spectral data, together with reference data for comparison, are given in Table 7.7 below.

§ With a structure unusually confirmed by the esterification of proceranolide **7-52** with butanoyl anhydride.

Table 7.7: ^{1}H and ^{13}C NMR assignments for compound **QP 7**, proceranolide

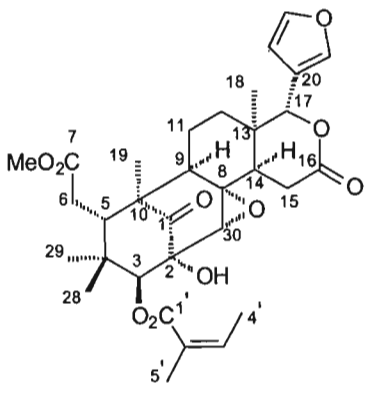
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

[Lit. [46] ^{1}H NMR 300MHz, ^{13}C 75MHz, $CDCl_3$, *J* in Hz]

Position	δ_C	7-52 Ref. [46]	δ_H	HMBC correlation C→H	COSY correlation	NOESY correlation
1	220.14 (C)	220.08	-	19,30β	-	-
2	50.23 (CH)	50.15	3.03ddd 9.71,5.68,2.38	30β	3,30α	3,29,30α,30β
3	77.31 (CH)	77.23	3.72d 9.71	5,28,29,30α,30β	2	2,28,29
4	39.52 (C)	39.30	-	3,5,6,28,29	-	-
5	39.48 (CH)	39.30	3.22dd10.07,3.29	3,5,6,19,28,29	6	6,11a(b),28
6	33.76 (CH)	33.54	2.36m	5	5	5,19,28,29
7	174.58 (C)	174.39	-	5,6,CH_3O	-	-
8	128.42 (C)	128.57	-	15β,30α,30β	-	-
9	52.03 (CH)	51.76	1.95m	19,30β	-	11a(b),19
10	53.83 (C)	53.61	-	5,6,19	-	-
11	18.96 (CH_2)	18.74	a 1.70m b 1.75m	-	9,11b,12α,12β 9,11a,12α,12β	9,12α 9,12β
12	28.83 (CH_2)	28.56	α 1.01m β 1.76m	18	11a,11b,12β 11a,11b,12α	18 17
13	38.15 (C)	37.88	-	17,18	-	-
14	131.62 (C)	131.20	-	15α,15β,17,18,30β	-	-
15	33.31 (CH_2)	33.06	α 3.45dt 21.24,2.38 β 4.04d 21.24	-	15β 15α	15β,18,30β 15α,17,30β
16	171.67 (C)	171.73	-	15α,15β	-	-
17	80.44 (CH)	80.25	5.56s	12β,18	-	12β,15β,21,22
18	17.79 (CH_3)	17.54	1.01s	12β,17	-	15α,21,22
19	17.14 (CH_3)	16.92	1.11s	5	-	6,11a(b),29
20	121.02 (C)	120.78	-	17,21,22,23	-	-
21	141.94 (CH)	141.71	7.55s	17,22,23	22,23	12α,17,18
22	110.32 (C)	110.09	6.47s	17,21	21,23	12α,17,18,23
23	142.85 (CH)	142.62	7.37s	21,22	21,22	22
28	24.04 (CH_3)	20.17	0.79s	29	-	3,5,11a(b),29
29	20.39 (CH_3)	23.90	0.71s	3,5,28	-	2,3,6,19,28
30	33.51 (CH_2)	33.33	α 1.95m β 3.17dd 14.29,2.38	-	2,30β 2,30α	2,30β 2,15α,15β,30α
$\underline{C}H_3O$	52.23 (CH_3)	51.97	3.69s	5	-	-

7.2.8 Structural elucidation of compound QP 8, 3-detigloyl-3-angeloylruageanin B

(spectra vol II, p.s184-193)



7-59 QP 8

The molar mass of this compound was determined by HRMS to be 584.2634 g.mol^{-1}, corresponding to the molecular formula $C_{32}H_{40}O_{10}$ (calc. 584.2621 g.mol^{-1}) and thirteen double bond equivalents. Inspection of the ^{1}H and ^{13}C NMR spectra revealed the usual furan ring (δ7.44s, δ141.11(CH), H-21; δ7.40s, δ143.37(CH), H-23; δ6.40s, δ110.38(CH), H-22; and δ120.39(C), C-20), carbomethoxy ester (δ3.70s, 3H, δ52.73(CH_3); δ173.98(C), C-7) and four quaternary methyl resonances characteristic of the mexicanolide-type rearranged limonoids. **QP 8** differs significantly, however, from the preceding three compounds discussed in that it does not possess a $\Delta^{8(14)}$ double bond.

An angeloyl ester (δ166.73(C), C-1'; 126.68(C), C-2'; δ6.21 qq *J* = 7.33, 1.46Hz, H-3', δ141.40(CH), C-3'; δ2.03 d, 3H, *J* = 7.33Hz, 3H-4', δ16.37(CH_3), C-4'; δ2.07 d, 3H, *J* = 1.46Hz, 3H-5', δ21.19(CH_3), C-5') was placed at C-3 by virtue of an HMBC correlation between C-1' and C-3 at δ84.70, with the corresponding resonance at δ5.13 ascribed to H-3. That H-3 is a singlet is easily accounted for by an HMBC correlation to a fully substituted C-O resonance at δ78.53, assigned to C-2.

The remaining ester carbonyl resonance at δ171.56 must then be C-16, which is correlated in the HMBC spectrum to the H-17 singlet signal at δ5.12 and a pair of COSY-coupled signals at δ2.82 (dd *J* = 16.11, 5.31Hz) and δ3.51m, ascribed to 2H-15, and which in turn are coupled in both the COSY and HMBC spectra to a signal at δ1.56 (dd *J* = 13.92, 5.31Hz, 1H, H-14) and δ45.47(CH), ascribed to C-14. A NOESY correlation between the H-17 resonance and the double doublet at δ2.82 establishes

this as H-15β. The resonance ascribed to H-14 is then further correlated to a fully substituted signal at δ63.64, which itself is further correlated to a resonance at δ3.52 (s, 1H), ascribed to H-30. From the corresponding resonance ascribed to C-30 at δ67.54 it can be inferred that **QP 8** possesses an 8,30-epoxide ring, which then accounts for the tenth and final oxygen atom, and thirteenth and final double bond equivalent. Final proof for these assignments is provided by an HMBC correlation between the H-30 resonance and that of C-2; NOESY correlations between H-14 and 3H-18, and between H-30 and 3H-5' establish their stereochemistry as α and β respectively.

Compound **QP 8**, as structure **7-59**, is novel, albeit very closely related to the known ruageanin B **7-60** isolated by Mootoo *et al.* from *Ruagea glabra* Triana et Planchon, which has a tigloyl rather than angeloyl ester at C-3 [63]. The fully assigned ^{1}H and ^{13}C NMR spectral data, together with reference data for comparison, are given in Table 7.8 below.

Compounds in which the $\Delta^{8(14)}$ double bond which characterise the swietenolides has been replaced by a 8α,30α-epoxide ring are considered to be derivatives of swietenine **7-61**†. They occur both with and without oxygenation at both C-2 and C-6.

The first compound of this type to be reported was that of xylocarpin **7-62** from the seed of *Xylocarpus granatum* Koenig [65], with *Swietenia humilis* Zuccarini reportedly affording two 2α-hydroxy-3-acyloxy esters shortly thereafter [66]‡.

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† Although the $\Delta^{8(30)}$ double bond is reported to be resistant to epoxidation [64], early workers did accomplish the corresponding reduction reaction with chromous chloride [65,66].

‡ The "pure" compounds discussed in this publication were mixtures of the *iso*butanoyl and tigloyl esters of 2α-hydroxyswietenine and its 8α,30α-epoxy analogue. The epoxide *iso*butanoyl ester **7-63** has subsequently entered the lexicon as humilin B [42,67,68], although not named as such in the original paper [66]. Even more confusingly, it was misidentified as the acetyl ester by Taylor in his review [64] (in which he also misidentified xylocarpin **7-62** as its 3-deacetyl analogue); the epoxide tigloyl ester he omitted from his review altogether. Not to be outdone, the Dictionary of Natural Products has appended a hydroxy group at C-6, although it does remark that the entry is "under review".

Mootoo *et al.* [63] presumably decided that the confusion was impenetrable, and therefore considered ruageanin B **7-60** to be novel.

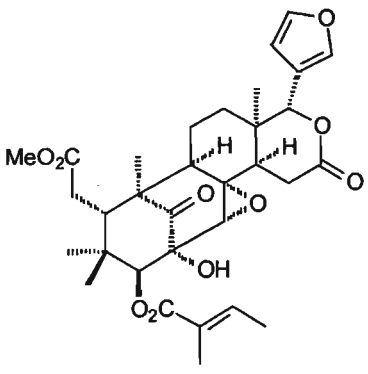
Table 7.8: ^{1}H and ^{13}C NMR assignments for compound **QP 8,** 3-detigloyl-3-angeloylruageanin B

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

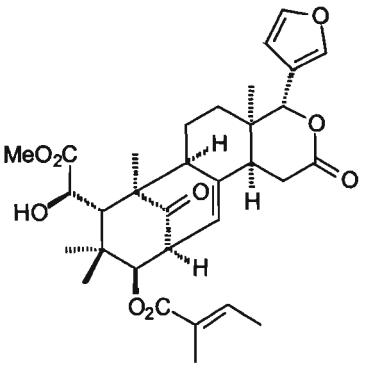
[Lit. [63] ^{1}H NMR 500MHz, ^{13}C 125MHz, $CDCl_3$, *J* in Hz]

[Lit. [68] ^{1}H NMR 500MHz, ^{13}C 125MHz, $CDCl_3$, *J* in Hz]

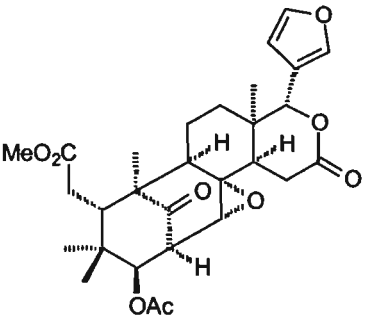
Position	δC	7-60 Ref. [63]	7-60 Ref. [68]	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	213.24 (C)	213.00	213.1	-	19,30	-	-
2	78.53 (C)	78.37	78.4	-	3,30	-	-
3	84.70 (CH)	84.79	84.8	5.13s	5,28,29	-	28,29,30,5'
4	40.18 (C)	40.12	40.1	-	3,5,6,28,29	-	-
5	42.83 (CH)	42.32	42.4	3.15dd 8.51,2.64	3,6,9,19,28,29	6	6,11a(b),28,5'
6	33.37 $(CH_2)^*$	32.94	33.2	2.32m	5	5	5,11a(b),19,28,29, CH_3O
7	173.98 (C)	173.86	174.2	-	5,6,CH_3O	-	-
8	63.64 (C)	63.14	63.2	-	9,11(a(b),14,15α,15β,19,30	-	-
9	55.48 (CH)	55.14	55.2	1.89m	5,11a(b),12β,14,19	11a(b)	-
10	49.49 (C)	49.11	49.1	-	5,6,9,11a(b),19	-	-
11	19.79 (CH_2)	19.44	19.5	a 1.81m b 1.85m	-	9,11b,12α,12β 9,11a,12α,12β	9,11b,12α,12β 9,11a,12α,12β
12	33.46 $(CH_2)^*$	33.20	33.0	α 1.20m β 1.98m	9,14,17,18	11a,11b,12β 11a,11b,12α	11a(b) 11a(b),15β,17
13	36.57 (C)	36.23	36.2	-	14,15α,15β,17,18	-	-
14	45.47 (CH)	45.24	45.3	1.56dd 13.92,5.31	12β,15α,15β,17,18,30	15α,15β	15α,17,18,22
15	33.77 (CH_2)	33.49	33.5	α 2.82dd 16.11,5.31 β 3.51m	14,18	14,15β 14,15α	14,15β,30,5' 12β,15α,17,30,5'
16	171.56 (C)	171.21	171.3	-	14,15α,15β,17	-	-
17	79.33 (CH)	78.89	79.0	5.12s	12α,12β,15α,18	-	15β,21,22,4',5'
18	26.81 (CH_3)	26.26	26.3	0.98s	12α,14,17	-	14,21,22
19	16.37 (CH_3)	16.12	16.1	1.14s	5	-	6,9,11a(b),29
20	120.39 (C)	120.17	120.3	-	17,21,22,23	-	-
21	141.11 (CH)	140.89	141.0	7.44s	17,22,23	-	12β,17,18
22	110.38 (CH)	110.10	110.2	6.40s	17,21,23	23	12β,17,18,23
23	143.37 (CH)	143.11	143.2	7.40s	21,22	22	22
28	22.34 (CH_3)	22.00#	22.0#	0.78s	29	-	3,5,6,29,CH_3O,4',5'
29	21.14 (CH_3)	20.53#	20.5#	0.97s	5,28	-	3,6,CH_3O
30	67.54 (CH)	67.38	67.4	3.52s	3	-	15α,15β,5'
1'	166.73 (C)	166.92	167.0	-	3,5'	-	-
2'	126.68 (C)	127.77	127.8	-	4',5'	-	-
3'	141.40 (CH)	139.75	139.8	6.21qq 7.33,1.46	4',5'	4',5'	4',5'
4'	16.37 (CH_3)	14.63	14.7	2.03d 7.33	3'	3'	28,3'
5'	21.19 (CH_3)	12.60	12.6	2.07d 1.46	3'	3'	15α,15β,28,30,3'
CH_3O	52.73 (CH_3)	52.39	52.4	3.70s	-	-	28,5'



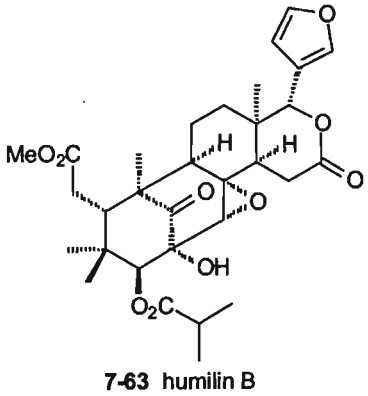
7-60 ruageanin B



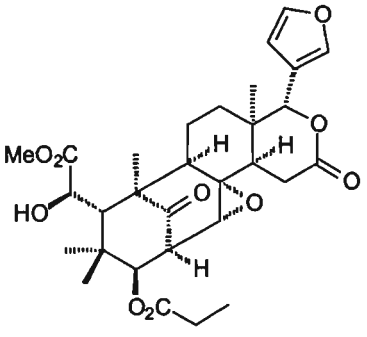
7-61 swietenine



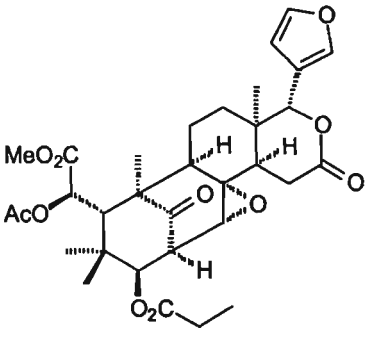
7-62 xylocarpin



7-63 humilin B

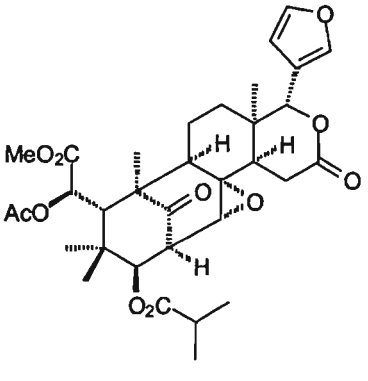


7-64 swietemahonin A

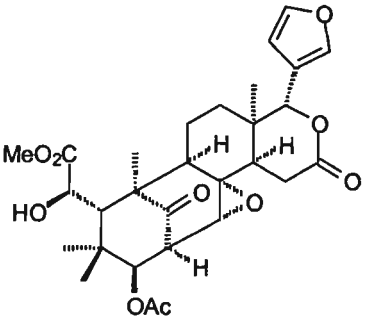


7-65 swietemahonin B

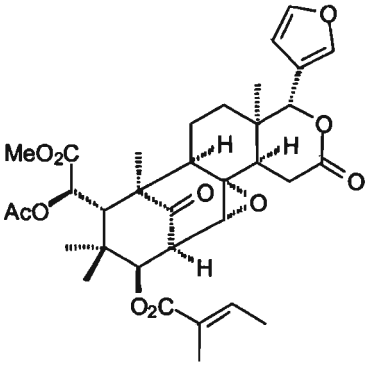
A hiatus of almost twenty years elapsed before the next report, that of swietemahonolide **7-65** and the swietemahonins A-G **7-65,66,67,68,69,70,71** from the seed of *Swietenia mahogani* [45,46,67]‡. The latter were the first compounds of this subgroup to be found with an oxygen substituent at C-6.



7-66 swietemahonin C

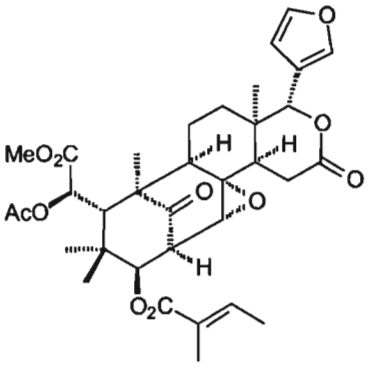


7-67 swietemahonin D

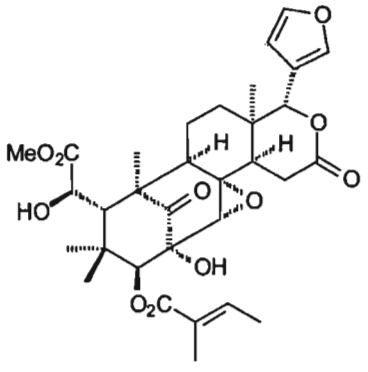


7-68 swietemahonin E

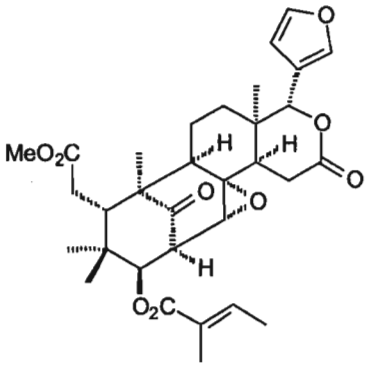
‡ Swietemahonin F **7-70** had reportedly been previously isolated from *Swietenia macrophylla* [42], but Kadota *et al.* [67] noted sufficient discrepancies in the spectral data of the two compounds to distinguish between them.



7-69 swietemahonin F

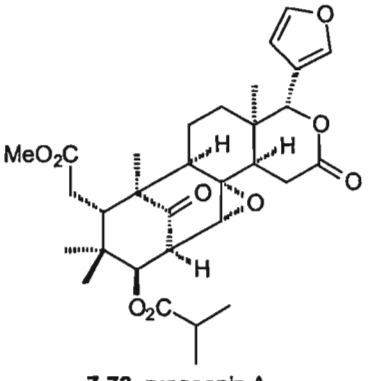


7-70 swietemahonin G

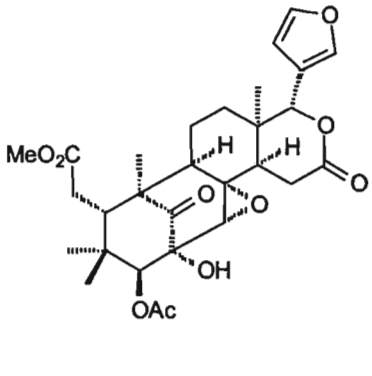


7-71 swietemahonolide

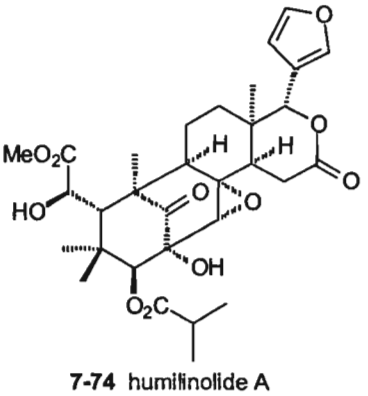
The fruit of *Ruagea glabra* has given, together with ruageanin B **7-60** previously mentioned, xylocarpin **7-62** and the novel ruageanins A **7-72** and C **7-73** [63], while the seed of *Swietenia humilis* has afforded the humilinolides A **7-74** and B **7-75** [69,70] and, more recently, humilinolide F **7-76** [70]†.



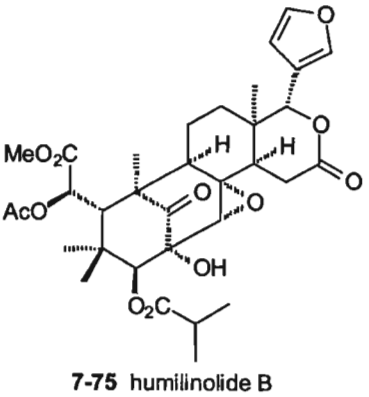
7-72 ruageanin A



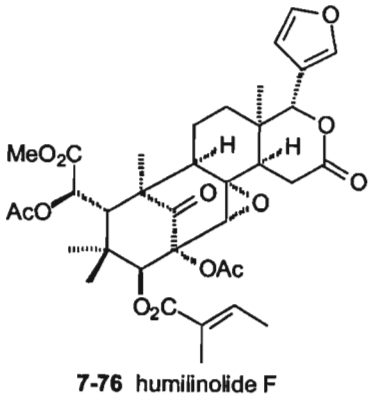
7-73 ruageanin C



7-74 humilinolide A



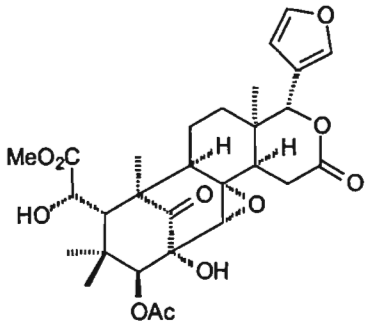
7-75 humilinolide B



7-76 humilinolide F

† Still further confusion. Humilin B **7-63** and swietemahonin C **7-66** were also reported to have been isolated, but the structures presented have an acetyl group at C-2. Humilin B **7-63** has a hydroxy group at C-2; swietemahonin C **7-66** is unsubstituted.

The seeds of a Mexican specimen of *Swietenia macrophylla* has recently reportedly yielded three new epoxy limonoids together with humilin B **7-63** [68]. Comparison of the ^{1}H and ^{13}C NMR spectral data for two of them with literature values reveal them to be the known compounds ruageanin B **7-60** and humilinolide A **7-72**; the remaining, novel, compound has structure **7-77**.



7-77

7.2.9 Structural elucidation of compound QP 9, quivisianolide A

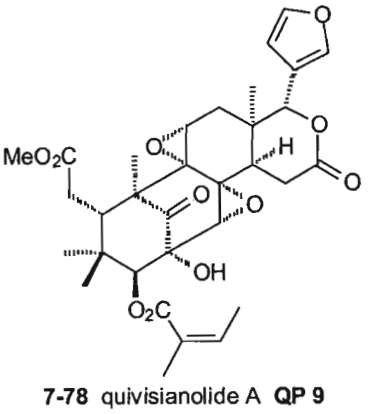
(spectra vol II, p.s194-203)

An HRMS analysis of this compound gave a molar mass of 598.2424 g.mol^{-1}, which suggests a molecular formula of $C_{32}H_{38}O_{11}$ (calc. 598.2414 g.mol^{-1}) and a difference, relative to compound **QP 8**, of one additional double bond equivalent and an additional oxygen atom. A comparison of the ^{1}H and ^{13}C NMR spectra of this compound with those of **QP 8** reveal it to be very similar in structure, with **QP 9** again displaying the four quaternary methyl singlet resonances, C-7 carbomethoxy ester (δ3.72s, 3H, δ52.87(CH_3); δ175.58(C)), and D ring lactone (δ4.97, 1H, H-17; δ82.81(CH), C-17; δ169.02(C), C-16; δ2.76 dd J = 18.50, 6.96Hz, H-15α; δ3.62 dd J = 18.50, 12.45Hz, H-15β; δ28.97(CH_2), C-15; δ1.64 dd J = 12.45, 6.96Hz; H-14; δ38.66(CH), C-14) signals characteristic of a mexicanolide-type structure.

In common with **QP 8**, then, **QP 9** has a ketone at C-1 (δ208.87(C), albeit slightly upfield), 8α,30α-epoxide ring (δ62.10(C), C-8; δ3.39s, 1H, H-30; δ62.10(CH), C-30), a hydroxy group at C-2α (δ78.49(C)), and an angeloyl ester at C-3β ((δ166.38(C), C-1'; 126.42(C), C-2'; δ6.24m, H-3', δ141.85(CH), C-3'; δ2.05 m, 3H-4', δ16.28(CH_3), C-4'; δ2.07 m, 3H-5', δ21.19(CH_3), C-5').

HMBC spectrum, to an unusual pair of coupled doublets at δ1.98 and δ2.39 (J = 15.20 Hz) which must be 2H-12, with the corresponding C-12 resonance occurring at δ27.72. Coupling between the 2H-12 signals, and the C-12 resonance in the COSY and HMBC spectra to a 1H broad singlet at δ3.25 in the ^{1}H NMR and methine resonance at δ56.65 in the ^{13}C NMR spectrum establishes these as H-11 and C-11, especially as the characteristic upfield methylene ^{13}C NMR resonance at ~20 ppm normally attributable to this carbon is missing.

An HMBC correlation occurs between H-14 and a fully substituted C-O resonance at δ62.35, which in turn displays HMBC correlations to H-12α, H-30, a quaternary methyl singlet at δ0.90, attributable (by HMBC correlation to C-1) to 3H-19, and a double doublet at δ3.21 (J = 7.69, 5.68Hz) assigned (by HMBC correlation to C-7) to H-5. This resonance must then be C-9, and **QP 9**, with a second epoxide ring at C-9,C-11, has the novel structure **7-78**.



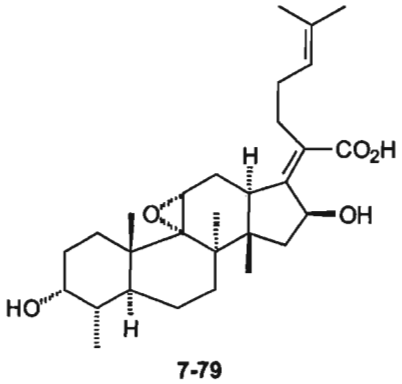
7-78 quivisianolide A **QP 9**

The stereochemistry of the 9,11-epoxide ring is assigned as α on the basis of the $J_{11,12}$ coupling constants. In the β conformation, H-11 and H-12α are virtually co-planar, with an H-11,H-12α dihedral angle of 0°, which would give rise to a $J_{11,12}$ value of ~10-15Hz. On the other hand, an α-oriented epoxide ring results in H-11 virtually bisecting the geminal H-12α,H-12β bond angle, giving rise to $J_{11,12}$ values of 3-4Hz, which present themselves in this compound as the observed broad singlet. It should be noted, however, that the observed doublets for both H-12α and H-12β would then be expected to be double doublets; it is difficult to explain why this is not observed. The use of NOESY correlations in this compound is not as conclusive as one could wish for, as most of the correlations observed can arise in either conformation. However, the β-epoxide conformation should lead to

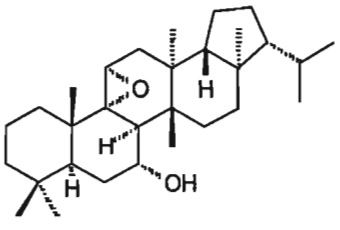
NOESY correlations in this compound is not as conclusive as one could wish for, as most of the correlations observed can arise in either conformation. However, the β-epoxide conformation should lead to NOESY correlations of different intensities; although both distances are sufficiently small for NOESY correlations to occur, the H-11,H-12β distance is much larger than that between H-11 and H-12α. On the other hand, the α-epoxide conformation leads to virtually identical H-11,H-12 distances and therefore equal NOESY correlations, as observed in our spectrum.

Construction of a model with a $\Delta^{9(11)}$ double bond, in an attempt to predict a favoured side from which epoxidation might occur, is equally unhelpful. From a steric point of view 3H-18, 3H-19, H-14 and the ketone at C-1 all favour formation of the β-oriented epoxide ring, but this argument could then be applied equally to epoxidation of the $\Delta^{8(30)}$ double bond, which gives rise exclusively to 8α,30α-epoxide rings (see discussion, p.7-31).

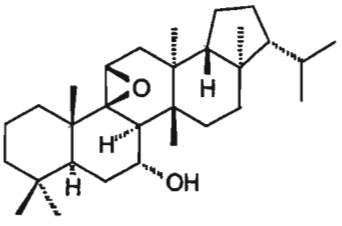
This is the first report, to our knowledge, of a limonoid with either a 9,11-epoxide ring or two epoxide rings. Even within the terpenoids as a whole there are only three examples of such compounds; the fusidane derivative **7-79** from the fungi *Fusidium coccineum* Fuckel [71] and the epimeric fernene epoxides **7-80,81** from *Cyathea lepifera* (J.Sm. ex Hooker) Copel. [72]. The fully assigned ^{1}H and ^{13}C NMR spectral data are given in Table 7.9 below.



7-79



7-80



7-81

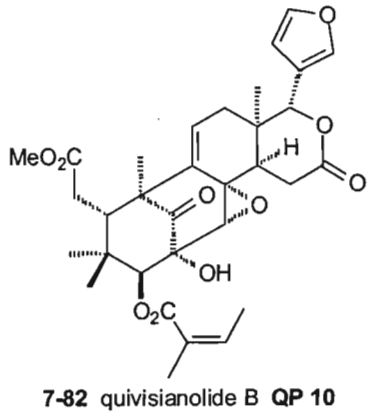
Table 7.9: ^{1}H and ^{13}C NMR assignments for compound **QP 9**, quivisianolide A

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	208.87 (C)	-	19,30	-	-
2	78.49 (C)	-	3,30	-	-
3	84.59 (CH)	5.28s	5,28,29	-	28,29,30
4	39.23 (C)	-	3,5,6,28,29	-	-
5	43.30 (CH)	3.21dd 7.69,5.68	3,6,19,28,29	6a,6b	6a,6b,12β,15β,28,30
6	32.14 (CH_2)	a 2.35dd 16.48,7.69 b 2.47dd 16.48,5.68	5,19(28)	5	5,12β,28,29
7	173.58 (C)	-	5,6a,6b,CH_3O	-	-
8	62.10 (C)	-	14,15α,17	-	-
9	62.35 (C)	-	5,12α,14,19,30	-	-
10	50.75 (C)	-	5,6a,6b,19	-	-
11	56.65 (CH)	3.25brs	12α,12β	12α,12β	6a,6b,12α,12β,19, CH_3O
12	27.72 (CH_2)	α 1.98d 15.20 β 2.39d 15.20	11,14,17,18	11,12β 11,12α	11,12β,17,18 11,12α,15β
13	34.35 (C)	-	11,12α,12β,14,15α,17,18	-	-
14	38.66 (CH)	1.64dd 12.45,6.96	12α,15α,15β,17,18,30	15α,15β	15α,18,21,22,30
15	28.97 (CH_2)	α 2.76dd 18.50,6.96 β 3.62dd 18.50,12.45	14	14,15β 14,15α	14,15β,30,4',5' 5,12β,15α
16	169.02 (C)	-	15α,15β,17	-	-
17	82.81 (CH)	4.97s	12β,18	-	12α,12β,21,22
18	23.58 (CH_3)	1.07s	12α,12β,14	-	12α,21,22
19	23.97 (CH_3)	0.90s	-	-	-
20	121.98 (C)	-	17,21,22,23	-	-
21	140.83 (CH)	7.29s	17,22,23	22,23	14,17,18
22	109.45 (CH)	6.16s	17,21	21,23	14,17,18,23
23	143.94 (CH)	7.38s	21,22	17,21,22	22
26	10.86 (CH_3)*	0.90s	5,29	-	3,5,6a,6b,29,5'
29	21.50 (CH_3)	0.81s	3,5,28	-	3,6a,6b,28
30	64.80 (CH)	3.49s	3	-	3,14,15α,5'
1'	166.38 (C)	-	3,3',5'	-	-
2'	126.42 (C)	-	4',5'	-	-
3'	141.85 (CH)	6.24m	4',5'	4',5'	4',5'
4'	16.28 (CH_3)	2.05m	3'	3',5'	15α,28,30,3'
5'	21.19 (CH_3)	2.07m	3'	3',4'	28,3'
CH_3O	52.87 (CH_3)	3.72s	-	-	-

7.2.10 Structural elucidation of compound QP 10, quivisianolide B

(spectra vol II, p.s204-213)



7-82 quivisianolide B **QP 10**

An HRMS analysis of this compound revealed a molar mass of 582.2474 g.mol^{-1}, corresponding to the molecular formula $C_{32}H_{38}O_{10}$ (calc. 582.2465 g.mol^{-1}). Relative to compound **QP 9**, **QP 10** has one oxygen atom less, but the same number of double bond equivalents.

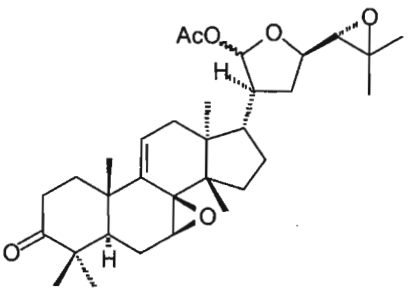
A comparison of the ^{1}H and ^{13}C NMR spectra of this compound with those of **QP 9** again reveals much similarity. As before, **QP 10** displays the four quaternary methyl singlet resonances, C-7 carbomethoxy ester (δ3.67s, 3H, δ52.50(CH_3); δ173.12(C)), and D ring lactone (δ5.06, 1H, H-17; δ82.19(CH), C-17; δ169.50(C), C-16; δ2.74 dd *J* = 18.50, 6.96Hz, H-15α; δ3.02 dd *J* = 18.50, 12.09Hz, H-15β; δ29.23(CH_2), C-15; δ1.81 dd *J* = 12.09, 6.96Hz; H-14; δ39.18(CH), C-14) signals characteristic of a mexicanolide-type structure.

QP 10 therefore has a ketone at C-1 (δ210.16(C), again slightly upfield of that in **QP 8**, but downfield of that in **QP 9**), 8α,30α-epoxide ring (δ61.42(C), C-8; δ3.47s, 1H, H-30; δ64.40(CH), C-30), a hydroxy group at C-2α (δ79.20(C)), and an angeloyl ester at C-3β ((δ166.39(C), C-1'; 126.50(C), C-2'; δ6.24m, H-3', δ141.88(CH), C-3'; δ2.08 m, 3H-4', δ16.28(CH_3), C-4'; δ2.05 m, 3H-5', δ21.15(CH_3), C-5').

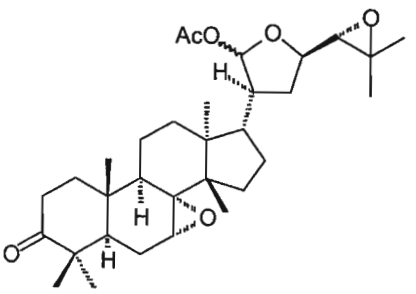
The ADEPT spectrum of compound **QP 10** shows the additional double bond, whose carbon resonances are visible at δ127.12 and δ136.89, to be trisubstituted. This can be placed at $\Delta^{9(11)}$ by the same chain of reasoning used to assign the 9,11-epoxide ring in compound **QP 9**, with HSQC and

HMBC correlations visible from C-17 at δ82.19 to 3H-18 at δ1.02, from C-18 at δ23.50 to 2H-12 at δ2.14m and 2.56 dd (J = 18.86, 2.74Hz, H-12β, by NOESY coupling at H-15β and H-17), and finally from 2H-12 and C-12 at δ31.95 to a 1H multiplet at δ5.84 and corresponding methine resonance at δ127.12, assigned to C-11. As before, the characteristic upfield methylene ^{13}C NMR resonance at ~20ppm normally attributable to this carbon is missing.

An HMBC correlation between H-14 at δ1.81 and the remaining fully substituted olefinic carbon resonance at δ136.89, which, in turn, displays HMBC correlations to 2H-12, H-30, 3H-19 (δ1.26s, 3H, assigned by HMBC correlation to C-1), and a multiplet at δ2.95, assigned (by HMBC correlation to C-7) to H-5, establishes this beyond doubt as C-9. **QP 10** is thus the novel compound **7-82**, and as such is the first reported example of a mexicanolide limonoid (or any other type, for that matter) possessing both a $\Delta^{9(11)}$ double bond and an epoxide ring at 8α,30α[†].



7-83



7-84 cneorin NP_{38}

[†] Compound **7-83** from *Chisocheton paniculatus* Hiern has recently appeared in the literature, where it is claimed to be the first reported example possessing both a $\Delta^{9(11)}$ double bond *and* a 7β,8β-epoxide ring [73]. However the proof supplied by the authors is hardly convincing; they cite cneorin NP_{38} **7-84** from *Cneorum tricoccon* [74], which also possesses an (α-) epoxide ring, as a basis for comparison, but do not explain why they assign their ring as β (H-7 occurs at δ2.95 (brs, $W_{1/2}$ 6Hz) in **7-84** and at δ2.78 (no multiplicity given) in **7-83**), nor did they use NOESY or any other 2D NMR techniques, which must surely have been available on the Bruker WM-400 spectrometer quoted in their experimental, to support their argument. Although there is unquestionably a double bond in their molecule, the same cannot be said for their argument as to its position, or indeed their entire structure.

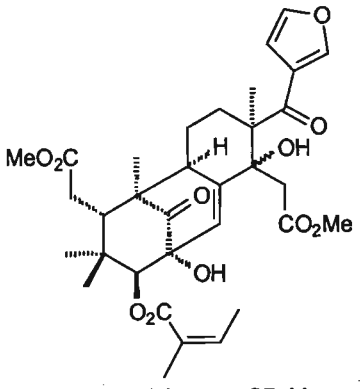
Table 7.10: ^{1}H and ^{13}C NMR assignments for compound **QP 10**, quivisianolide B

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	210.16 (C)	-	19,30	-	-
2	79.20 (C)	-	3,30	-	-
3	84.76 (CH)	5.05s	5,28,29	-	28,29,30,OH
4	39.46 (C)	-	3,5,6,28,29	-	-
5	47.61 (CH)	2.95m	3,6,19,28,29	6	6,11,28
6	31.38 (CH_2)	2.30m	5,19	5	5,11,19,28,29
7	173.12 (C)	-	5,6,CH_3O	-	-
8	61.42 (C)	-	11,14,15β,17	-	-
9	136.89 (C)	-	5,12α,12β,14,19,30	-	-
10	51.73 (C)	-	5,6,11,19	-	-
11	127.12 (CH)	5.84m	12α,12β	12α,12β	6,12α,12β,19,CH_3O
12	31.95 (CH_2)	α 2.14m β 2.56dd 18.86,2.74	11,14,18	11,12β 11,12α	11,12β,17,18 11,12α,15α,17
13	35.41 (C)	-	12α,12β,14,15α,18	-	-
14	39.18 (CH)	1.81dd 12.09,6.96	12α,15α,15β,18	15α,15β	15β,18,21,22,30
15	29.23 (CH_2)	α 3.02dd 18.50,12.09	14,18	14,15β	12β,15β
		β 2.74dd 18.50,6.96		14,15α	14,15α,30
16	169.50 (C)	-	15α,15β,17	-	-
17	82.19 (CH)	5.06s	12α,12β,14,18	-	12α,12β,18,21,22
18	23.50 (CH_3)	1.02s	12α,12β,14	-	12α,14,17,21,22
19	14.45 (CH_3)	1.26s	3,5	-	-
20	120.06 (C)	-	17,21,22,23	-	-
21	140.77 (CH)	7.33s	17,22,23	-	14,17,18
22	109.56 (CH)	6.24s	17,21,23	23	14,17,18,23
23	143.88 (CH)	7.40s	21,22	22	22
28	20.70 (CH_3)	0.80s	5	-	3,5,5'
29	23.71 (CH_3)	0.83s	-	-	3,6,4'
30	64.40 (CH)	3.47s	3,14	-	3,14,15β
1'	166.39 (C)	-	3,4',5'	-	-
2'	126.50 (C)	-	4',5'	-	-
3'	141.88 (CH)	6.24m	4',5'	4',5'	15β,4',5'
4'	16.28 (CH_3)	2.05m	3'	3',5'	5,15β,28,3'
5'	21.15 (CH_3)	2.07m	3'	3',4'	3,30,3'
CH_3O	52.50 (CH_3)	3.72s	-	-	5,6,11
OH	-	4.05 brs	1,2,3	-	3

7.2.11 Structural elucidation of compound QP 11, quivisianone

(spectra vol II, p.s214-223)



7-85 quivisianone **QP 11**

An HRMS of this compound gave a molar mass of 614.2735 g.mol^{-1}, corresponding to the molecular formula $C_{33}H_{42}O_{11}$ (calc 614.2727 g.mol^{-1}) and thirteen double bond equivalents. Visible in the the ADEPT spectrum are the four quaternary methyl group singlet resonances characteristic of a mexicanolide-type skeleton.

Inspection of the ^{1}H and ^{13}C NMR spectra of this compound showed a carbonyl signal at δ210.88 and unusual downfield furanyl ring resonances (δ8.13s, δ148.51(CH), H-21; δ7.38s, δ142.93(CH), H-23; δ6.82s, δ110.80(CH), H-22; and δ124.50(C), C-20) of a *seco*-ring D 17-keto limonoid similar to compound **NL 1** from *Neobeguea leandreana* (Chapter 6). As reported for that compound, support for this assumption could not be obtained by direct HMBC correlation between H-21 and/or H-22 and C-17, but indirectly by the appearance of a peak at *m/z* 95.0141 in the HRMS, corresponding, as before, to fragment **6-9** (calc. for $C_5H_3O_2$ 95.0133). In addition, an HMBC correlation can be seen between C-17 and a quaternary methyl singlet at δ1.46, established as 3H-18 by NOESY correlations to both H-21 and H-22.

The 3H-18 resonance is also correlated in the HMBC spectrum to a methylene resonance at δ33.73, ascribed to C-12, a fully substituted signal at δ55.24, assigned to C-13, and a second fully substituted C-O resonance at δ~77†, which can then only be C-14. The C-14 resonance correlates to a 1H doublet signal at δ2.62 (J = 12.09Hz), assigned to H-15b (δ2.52, H-15a, by COSY coupling; δ42.37(CH_2), C-15, by HSQC correlation), from which further HMBC correlation establish the C-16 carbomethoxy carbonyl at δ170.22(C) and attached methyl ester at δ3.56(s, 3H) and δ51.79(CH_3). The 2H-15 resonance also correlates in the HMBC spectrum to a fully substituted olefinic resonance at δ140.07, which can only be C-8.

HSQC correlations between C-12 and a pair of COSY-coupled multiplets at δ1.74 and δ2.40 specify these as 2H-12, which are also COSY-coupled to another pair of coupled multiplets at δ1.60 and δ1.45, assigned to 2H-11. The 2H-11 resonances display further coupling to a 1H multiplet at δ2.32, assigned to H-9, with the corresponding C-9 resonance occurs at δ55.01(CH). The C-9 resonance correlates in the HMBC spectrum to a quaternary methyl signal at δ1.15, assigned to 3H-19, a doublet at δ3.16 (J = 9.16Hz) whose assignment as H-5 is confirmed by COSY couplings to 2H-6 at δ2.35m, with both H-5 and 2H-6 correlating in the HMBC spectrum to C-7 at δ172.85(C), and to a 1H singlet signal at δ5.82, assigned to H-30. With C-30 at δ127.68(CH), compound **QP 11** thus possesses the $\Delta^{8(30)}$ double bond which characterise the swietenine **7-61** type mexicanolide limonoids. The remaining ketone carbonyl signal at δ214.33 can then be assigned to C-1; the C-5 and C-6 resonances are at δ40.52(CH) and δ33.05(CH_2) respectively.

The singlet resonance at δ4.82, ascribed to H-3 on the basis of HMBC correlations to both C-5 and C-30, also displays a correlation to what must be the second fully substituted C-O resonance obscured by the solvent peak, and which is assigned to C-2.

The stereochemistry at C-14 is not easily determined, as the direct NOESY correlation between H-14 and 3H-18 that permitted the corresponding assignment in compound **NL 1** is not available, and that

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† The molecular formula prescribes 33 carbon atoms, of which 21 are designated in the ADEPT spectrum as of methyl, methylene and methine multiplicities, leaving 12 fully substituted carbons to be accounted. Only 10 such signals were observed in the ^{13}C NMR spectrum, suggesting that the remaining two were obscured by the solvent peak and thus could be attributed to fully substituted, oxygenated, carbons, whose presence would be revealed only by correlations in the HMBC spectrum, as they would of course not appear in the ADEPT spectrum.

the correlation that is observed between 2H-15 and 3H-18 is inconclusive as it can arise from both possible conformations. With the stereochemistry at C-14 undefined, then, compound **QP 11** has the novel structure **7-85**[†].

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† A literature survey conducted to ascertain the extent of oxygenation at C-14 and its accompanying stereochemistry revealed interesting results. Some ninety-five compounds to date have been reported which possess both the D ring lactone and 14β,15β-epoxide ring, compared to about fifteen which possess the lactone and Δ^{14} double bond. This suggests that the oxidative biosynthetic milieu in which the five-membered D ring undergoes Baeyer-Villiger oxidation is responsible also for epoxidation of the Δ^{14} double bond, and therefore that these compounds are the most likely precursors for oxygenation at C-14. The isolation of the 14β,15β-epoxy *seco*-ring D compound, oriciopsin **6-8** from *Oriciopsis galberrima*, as detailed in Chapter 6, would appear to support this hypothesis, with the 14β-hydroxy group resulting from subsequent opening of the epoxide ring; if this is indeed the case then the hydroxy group at C-14 can only be β.

The question then arises, however, as to the effect of such an epoxide ring opening on C-15, which would surely be the oxygenation of this position also. The isolation of a 14,15-dihydroxy compound has yet to be announced, while only eleven compounds have been isolated with oxygenation at both C-14 and C-15; these without exception have a 1α,14β-oxide ring, and presumably arise by nucleophilic attack of the hydroxy group at C-1 on the epoxide C-14 position. This hypothesis is supported by the fact that no compound has yet been isolated that is oxygenated at C-15 but not at C-14. As **QP 11** is not oxygenated at C-15, its C-14 hydroxy group cannot have arisen in this fashion.

What remains, then, is oxygenation of C-14 either by direct oxidation or nucleophilic attack on a Δ^{14} double bond. Again a literature survey is revealing. Intramolecular nucleophilic substitution yields almost exclusively oxide rings that are C-14β, but of the twelve compounds possessing a oxygen functionality at C-14 that is *not* part of a ring - and hence could not have formed by an intramolecular route - C-14 has the β configuration in five compounds and α in seven. This suggests that intramolecular substitution occurs more easily than oxidation, with the enantiomeric predominance arising from the different steric environments of the two faces of the molecule, and that only when this does not occur can oxidation at C-14 give rise to the carbocation necessary for inversion to occur.

Table 7.11: ^{1}H and ^{13}C NMR assignments for compound **QP 11**, quivisianone

[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	δH	HMBC correlation C→H	COSY correlation	NOESY correlation
1	214.33 (C)	-	19,30	-	-
2	77 (C)*	-	3,30	-	-
3	85.62 (CH)	4.82s	5,28,29	-	28,29,5'
4	39.62 (C)	-	6,28,29	-	-
5	40.52 (CH)	3.16d 9.16	3,6,9,19	6	6,11β,28,30
6	33.05 (CH_2)	2.35m	5	5	5,19
7	172.85 (C)	-	5,6,7-CH_3O	-	-
8	140.07 (C)	-	15a,15b	-	-
9	55.01 (CH)	2.42m	5,19,30	11α,11β	18
10	50.26 (C)	-	19	-	-
11	22.43 (CH_2)	α 1.60m β 1.45m	12α	9,11β,12α,12β 9,11α,12α,12β	11β,12α,21,22 5,11α,12β,15a,15b
12	33.73 (CH_2)	α 1.74m β 2.40m	18	11α,11β,12β 11α,11β,12α	12β,18 11α,11β,12α,21,22
13	55.24 (C)	-	18	-	-
14	77 (C)*	1.81dd 12.09,6.96	15b,18	-	-
15	42.37 (CH_2)	a 2.52m b 2.62d 12.09	-	15b 15a	15b 15a,18
16	170.22 (C)	-	15a,15b,16-CH_3O	-	-
17	201.88 (C)	-	18	-	-
18	19.20 (CH_3)	1.46s	-	-	15a,15b,21,22
19	15.82 (CH_3)	1.15s	5	-	6,9
20	124.50 (C)	-	21,22,23	-	-
21	148.51 (CH)	8.13s	22,23	22,23	12β,18
22	110.80 (CH)	6.82s	21	21,23	12β,18,23
23	142.93 (CH)	7.36s	21,22	21,22	12β,18,22
28	22.55 (CH_3)	0.74s	29	-	3,3',5'
29	20.59 (CH_3)	0.77s	5,28	-	3,19,5'
30	127.68 (CH)	5.80s	3	-	3,16-CH_3O,4',5'
1'	167.64 (C)	-	3,4',5'	-	-
2'	127.66 (C)	-	4',5'	-	-
3'	141.10 (CH)	6.20dd 7.33,1.47m	4',5'	4',5'	4',5'
4'	16.27 (CH_3)	2.05m	3'	3',5'	5,3'
5'	20.81 (CH_3)	2.09m	3'	3',4'	3,30,3'
7-CH_3O	52.20 (CH_3)	3.49s	-	-	26,5'
16-CH_3O	51.79 (CH_3)	3.56s			-
2-OH	-	4.10brs	1,2,3,30	-	3,16-CH_3O,30
14-OH	-	4.81brs	15	-	18,30

7.2.12 Structural elucidation of compound QP 12, melianone

(spectra vol II, p.s224-228)

An HRMS of this compound gave a molar mass of (470.3407 g.mol^{-1}), corresponding to the molecular formula $C_{30}H_{46}O_4$ (calc. 470.3396 g.mol^{-1}) and eight double bond equivalents.

Initial inspection of the ^{13}C NMR spectrum - the molecular formula notwithstanding - showed the presence of forty six resonances. However, the spectrum displays two oxymethine signals at δ102.00 and δ97.98, which are characteristic of a five-membered hemiacetal ring, in which rapid equilibration in solution gives rise to two C-21 epimers [75]. Closer analysis of the remaining signals then revealed 30 of these to be made up of 15 pairs of very narrowly separated signals of identical multiplicity, and 14 others. Under the assumption, then, that each these pairs of signals arises from a single carbon position in each of the two C-21 epimeric forms, compound **QP 12** further possesses a ketone (δ217.48/δ217.12 (C)), a trisubstituted double bond (δ145.93/145.76 (C), δ118.39/118.29 (CH)), another oxymethine carbon (δ78.66, (CH)), and a trisubstituted epoxide ring (δ67.95/65.52 (CH), δ58.31/57.52 (C)).

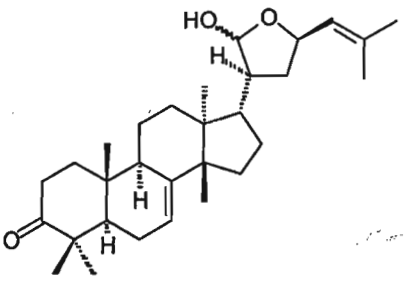
A literature survey conducted on this basis revealed compound **QP 12** to be the known pre-apo change protolimonoid melianone **7-86**, with a C-3 ketone, Δ^7 double bond, and 24,25-epoxide ring [76]. Fully assigned ^1H and ^{13}C spectral data, together with reference values for comparison, are presented in Table 7.12 below.

Table 7.12: ^{1}H and ^{13}C NMR assignments for compound **QP 12**, melianone

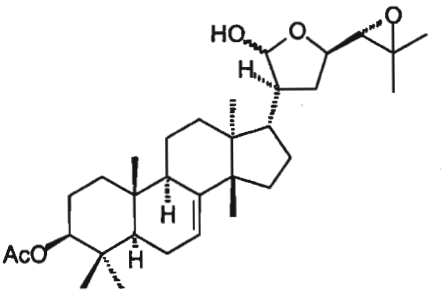
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

[Lit. [76] ^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC	7-86 Ref. [76]	δH
1	38.70 (CH_2)	38.52	
2	35.31 (CH_2)	35.12	
3	217.18/217.12 (C)	216.79/216.73	4.55m
4	48.09 (C)	47.88	
5	52.62/52.54 (CH)	52.46/52.40	
6	23.47 (CH_2)	23.25	
7	118.39/118.29 (CH)	118.18/118.09	5.30m
8	145.93/145.76 (C)	145.78/145.63	
9	49.80/48.56 (CH)	49.64/48.42	
10	35.12 (C)	34.91	
11	17.91 (CH_2)	17.76	
12	35.41 (CH_2)	35.19	
13	43.96/43.77 (C)	43.81/43.59	
14	50.99/50.63(C)	50.82/50.46	
15	34.45 (CH_2)	34.31	
16	27.67/27.51 (C)	27.47/27.32	
17	47.25/45.44 (CH)	47.09/45.23	
18	12.95 (CH_3)	12.75	
19	24.72 (CH_3)	24.56	
20	34.03/31.87 (CH)	33.80/31.69	
21	102.00/97.98 (CH)	101.82/97.78	5.35m
22	31.70/31.50 (CH_2)	31.54/31.33	
23	78.66 (CH)	78.45/77.05	3.90m
24	67.95/65.52 (CH)	67.76/65.39	2.70m
25	58.31/57.52 (C)	57.98/57.23	
26	25.21/25.13 (CH_3)	25.02/24.92	
27	19.63/19.41(CH_3)	19.46/19.22	
28	24.58 (CH_3)	24.41	
29	21.78 (CH_3)	21.59	
30	22.83 (CH_3)	22.62	



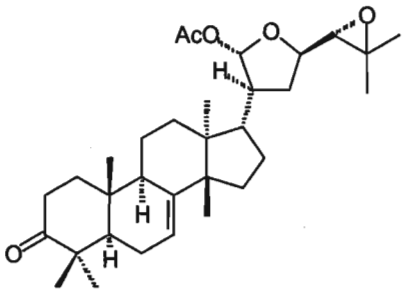
7-87 flindissol



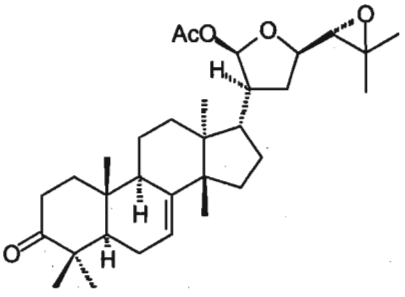
7-88 turraeanthin

Melianone **7-86** itself was first isolated from the fruit of *Melia azedarach* L. [77] in 1966, but the distinguishing five-membered hemiacetal ring had previously been found in flindissol **7-87** from the Australian Rutaceae *Flindersia dissosperma* Domin [78], and turreanthin **7-88** from the West African *Turreanthus africanus* (Welw. ex C.DC.) Pellegr. had been shown to possess both the hemiacetal ring and the 24,25-epoxide ring which have subsequently come to characterise these compounds [79,80].

The complete structure presented a year later [81] assigned the configurations at both C-23 and C-24 as *R*.



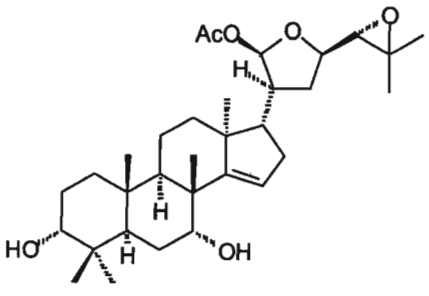
7-89a



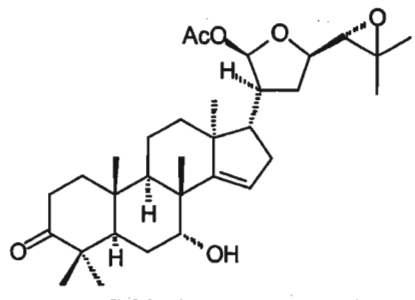
7-89b

The characteristic "doubling" of the resonances in a ^{13}C NMR spectrum that arises from the presence in solution of a rapidly equilibrating mixture of the C-21 epimers was first reported in 1977 [75], while analysis a decade later of the spectra of the separated C-21α and C-21β acetate esters **7-89a**, **7-89b** demonstrated that the equilibrium favoured the β epimer [82]. This same publication reported an X-ray crystal structure of the related compound **7-90** from *Melia toosendan* Sieb. et Zucc., which confirmed the earlier suggestion, on chemical grounds [83], that the configuration at C-24 be revised to *S*.

Melianone has subsequently been reported from *Entandrophragma caudatum* (Sprague) Sprague [84], *Trichilia hirta* L. [85], *Trichilia connaroides* [49], *Guarea guidonia* Sleumer [86] and *Guarea grandiflora* A.D.C.[70] from the Meliaceae, *Eurycoma longifolia* [87] from the Simaroubaceae, and, as cneorin-NP_{37}, from *Neochamaela pulverata* (Vent.) Erdtman† (Cneoraceae) [88].



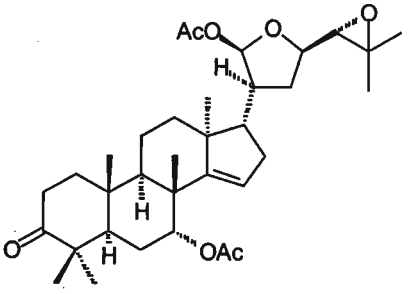
7-90



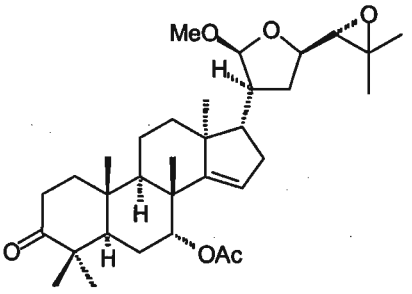
7-91 chisocheton A

† Given as *N. pulverulentum* at The Missouri Botanic Gardens database [4].

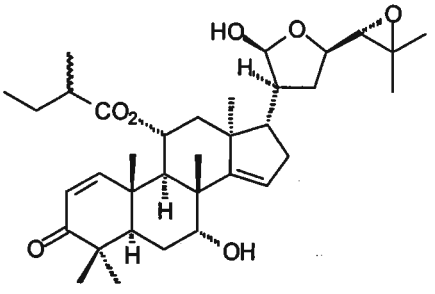
As is evident from **7-90**, the sidechain that characterises melianone **7-86** is not confined to pre-apo change protolimonoids. Further examples of this are the C-21β-acetate chisocheton A **7-91** from *Chisocheton paniculatus* [15][†], 7-acetyl-21β-acetate dihydrobruceajavanicin A **7-92** and its methoxy analogue **7-93**, from *Brucea javanica* [89], gentinones A **7-94** and B **7-95** from *Aglaia argentea* Bl [29] [‡], and glabretal derivative 3-oxoskimmiarepin **7-96** from the Brazilian Rutaceae *Zanthoxylum petiolare* St.Hil. [90]. The 7α,8α-epoxy compound cneorin NP_{38} **7-85** from *Neochamaela pulverulenta* [74] [§], could be considered as an intermediate in the apo-change mechanism[#].



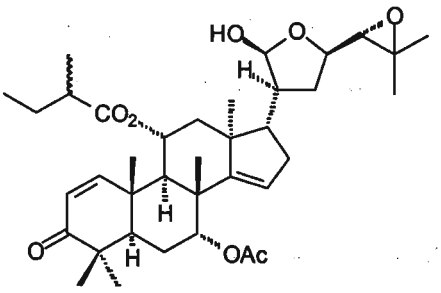
7-92



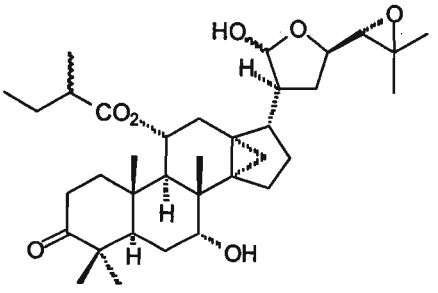
7-93



7-94 gentinone A



7-95 gentinone B



7-96 3-oxoskimmiarepin

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† Reported independently as cneorin NP_{35} from *Neochamaela pulverulenta* [27].

‡ A report in which the unesterified C-21β epimers were apparently isolated; Omobuwajo *et al.* note [29]:

"Gentinone A... was, like other known compounds possessing the same sidechain, an epimeric mixture with respect to the hemiacetal carbon, containing the C-21α epimer as a minor component."

§ The only compound in which the C-24 configuration is given explicitly as *R*, this publication predates the X-ray structure of **7-90** and is based on an analysis of the chemical shift of 3H-18.

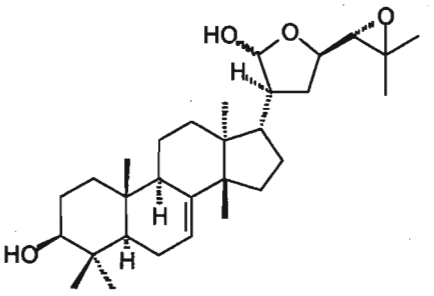
The purported 7β,8β-epoxy ring compound **7-83** exclude for the reasons given in the footnote on on p.37.

7.2.13 Structural elucidation of compound QP 13, melianol

(spectra vol II, p.s229-233)

An HRMS of this compound gave a molar mass of 472.3550 g.mol^{-1}, corresponding to the molecular formula $C_{30}H_{48}O_4$ (calc. 472.3553 g.mol^{-1}) and a difference, relative to **QP 12**, of an additional 2 hydrogen atoms and one less double bond.

In common with that for compound **QP 12**, the ^{13}C NMR spectrum for **QP 13** displayed two characteristic five-membered hemiacetal ring oxymethine signals at δ102.03 and δ98.03 amid a total of 48, which could be further resolved into a further 17 paired and 12 unpaired resonances. Among these was an additional oxymethine resonance at δ79.44/79.40 which is easily assigned, given the absence of a ketone signal corresponding to that observed in **QP 12**, to C-3. The remainder of the spectrum is very similar to that of **QP 12**; comparison with literature values revealed compound **QP 13** to be the related protolimonoid melianol **7-97** [76].



7-97 melianol **QP 13**

Melianol **7-97** was first reported, together with melianone **7-86**, from *Melia azedarach*. [81], and at the same time as the acetyl analogues turraeanthin **7-88** [79,80] and aphanamixin from *Aphanamixis polystacha* Wall et Parker [91,92]†. In contrast to melianone **7-86**, however, it is much less common,

† Aphanamixin is distinguished from turraeanthin **7-88** in the Dictionary of Natural Products only by having, like cneorin NP_{38} **7-84**, an *R* configuration at C-24, that the original publications [91,92] do not specify. The authors also claim that the differences in observed physical properties between turraeanthin **7-88** and aphanamixin are because: [91]

> "...it is...firmly established that aphanamixin and turraeanthin are C-21 epimers."

In his review, Taylor [64] omits aphanamixin, but includes the aphanamixin reference in his entry for turraeanthin **7-88**. He distinguishes between melianol **7-97**, which he gives as having a hydroxy at C3α, and turreanthin/aphanamixin **7-88**, whose acetate ester he places at C-3β. The references cited [79,80,81, 91], however, give the stereochemistry consistently as β.

having been subsequently reported only once since from *Melia toosendan*, where it occurs as a mixture of the methyl stearate, palmitate, myristate and laurate esters [76].

Table 7.13: ^{1}H and ^{13}C NMR assignments for compound **QP 13**, melianol
[^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]
[Lit. [76] ^{1}H NMR 400MHz, ^{13}C 100MHz, $CDCl_3$, *J* in Hz]

Position	δC*	Reference [76]	δH
1	37.35 (CH_2)	37.28	
2	27.86/27.80 (CH_2)	27.70	
3	79.44/79.40 (CH)	79.24	3.22dd 11.56,3.78
4	39.17 (C)	39.03	
5	50.96/50.91 (CH)	50.85/50.82	
6	23.42 (CH_2)	23.27	
7	118.45/118.36 (CH)	118.28/118.17	5.25m
8	145.77/145.60 (C)	145.71/145.53	
9	49.87/48.94 (CH)	49.67/48.88	
10	35.23 (C)	35.11	
11	17.73 (CH_2)	17.64	
12	35.43 (CH_2)	35.23	
13	43.99/43.80 (C)	43.87/43.69	
14	50.85/50.63(C)	50.79/50.52	
15	34.43 (CH_2)	34.32	
16	27.50/27.30 (C)	27.40/27.17	
17	47.32/45.43 (CH)	47.17/45.24	
18	13.26 (CH_3)	13.15	
19	24.17 (CH_3)	24.06	
20	34.01/32.03 (CH)	33.90/31.90	
21	102.03/98.02 (CH)	101.83/97.80	
22	31.70/31.64 (CH_2)	31.61/31.49	
23	78.71 (CH)	78.50/77.02	5.23m
24	67.96/65.52 (CH)	67.85/65.49	2.82d 7.54 2.69d 7.53
25	58.27/57.50 (C)	57.97/57.24	3.90m
26	25.23/25.14 (CH_3)	25.05/24.99	
27	19.65/19.42(CH_3)	19.51/19.30	
28	27.66/27.55 (CH_3)	27.55	
29	14.92 (CH_3)	14.80	
30	22.79 (CH_3)	22.64	

7.3 The chemotaxonomic significance of mexicanolide limonoids in the Quivisianthioideae

Both of the Melioideae and Swietenioideae subfamilies of the Meliaceae contain limonoids of the havanensin, gedunin, andirobin, methyl ivorensate, obacunol and evodulone groups. However, toonafolin, capensolactone and prieurianin limonoids have been isolated only from the Melioideae, while those of the phragmalin and mexicanolide classes are found only in the Swietenioideae [6].

Thus, the isolation of the series of mexicanolide limonoids **QP 5-QP 11** suggests, the earlier affinity to *Ekebergia* notwithstanding, that the subfamily Quivisianthioideae is more closely related to genera of the subfamily Swietenioideae.

In particular, the $\Delta^{9(11)}$ double bond in quivisianolide B **QP 10** and corresponding 9α,11α-epoxide ring in quivisianolide **QP 9** are novel features never before reported in over seven hundred limonoids, while 17-keto *seco*-ring D compounds are rare at best, and unknown within the mexicanolide class.

In the words of J.P.Commerson (1771):

"May I announce to you that Madagascar is the naturalists' promised land?
Nature seems to have retreated there into a private sanctuary, where she could work on different models from any she has used elsewhere.
There, you meet bizarre and marvellous forms at every step….
What an admirable country, this Madagascar."

7.4 Experimental

Quivisia papinae was collected in April 1999 in the Bezaha Mahafaly area in southern Madagascar. A voucher specimen (02/99-Mj/Mdul) is deposited at the Department of Botany of the University of Antananarivo. Plant identification was confirmed by the Department of Botany at the Parc Zoologique et Botanique de Tsimbazaza.

The air-dried, milled stembark (701g) was extracted successively for 24 hours in a Soxhlet apparatus with hexane, dichloromethane, ethyl acetate and methanol, yielding extracts of masses 19.47g, 27.99g, 20.28 and 189.15g, respectively. Only the hexane and dichloromethane extracts were examined during the course of this investigation, while the ethyl acetate and methanol extracts have been stored for future study.. Compound **QP 10** was isolated from the hexane extract, **QP 2** and **QP 3** from both, and the remaining ten from the dichoromethane extract only.

Compound **QP 1**
(spectra vol II, p.s114-123)

azadiradione

pale yellow gum, 7.1mg
^{13}C NMR spectra: data and peak assignments Table 7.1, p.169.

Optical Rotation:

$[\alpha]_D$ = +31° (c, 0.112 in $CHCl_3$)(lit. value [10] +35.5°).

IR spectrum:

υ_{max}(NaCl) 2927, 2360, 2342, 1736, 1707, 1672, 1244, 1033 cm^{-1}.

Mass spectrum:

HRMS found 450.2414, calc. for $[C_{28}H_{34}O_5]^+$ 450.2406 $g.mol^{-1}$.

EIMS *m/z* 450.2414, 435.2187 $[M-CH_3]^+$, 407.2225, 391.2244, 390.2205 [M-HOAc]$^+$, 375.1941 $[M-HOAc-CH_3]^+$, 241.1228, 175.0750, 174.0682, 137.0971, 121.0652, 93.0704.

Compound **QP2**

(spectra vol II, p.s124-133)

6α-hydroxyazadiradione

pale yellow gum, 18.1mg

^1H and ^{13}C NMR spectra: data and peak assignments Table 7.2, p.171.

Optical Rotation:

$[\alpha]_D$ = +23° (c, 0.312 in $CHCl_3$).

IR spectrum:

υ_{max}(NaCl) 3462, 2924, 1730, 1700, 1666, 1602, 1379, 1233, 1151 cm^{-1}.

Mass spectrum:

HRMS found 466.2355, calc. for $[C_{28}H_{34}O_6]^+$ 466.2355 $g.mol^{-1}$.

EIMS *m/z* 466.2355, 451.2110 $[M-CH_3]^+$, 406.2116 [M-HOAc]$^+$, 381.1690 $[M-HOAc-CH_3]^+$, 299.1273, 227.1079, 174.0685, 121.0652, 83.0493.

Compound **QP3**

(spectra vol II, p.s134-143)

6α-hydroxy-7-deacetyl-7-angeloylazadiradione

pale yellow solid, 35.0mg

^1H and ^{13}C NMR spectra: data and peak assignments Table 7.3, p.173.

M.p. 91-94°C.

Optical Rotation:

$[\alpha]_D$ = +69° (c, 0.658 in $CHCl_3$).

IR spectrum:

υ_{max}(NaCl) 3485, 2959, 1707, 1678, 1602, 1461, 1391, 1233, 1151 cm^{-1}.

Mass spectrum:

HRMS found 506.2672, calc. for $[C_{31}H_{38}O_6]^+$ 506.2668 $g.mol^{-1}$.

EIMS *m/z* 506.2672, 423.2176, 407.2232 [M-HOTig]$^+$, 174.0672, 121.0653, 83.0484.

Compound **QP4**

1α-acetoxy-1,2-dihydro-7-deacetyl-7-angeloylproceranone, quivisianthone

pale yellow gum, 14.5mg

^1H and ^{13}C NMR spectra: data and peak assignments Table 7.4, p.180.

Optical Rotation:

$[\alpha]_D$ = +0.0 (too small to be measured).

IR spectrum:

υ_{max}(NaCl) 3468, 2947, 1730, 1707, 1607, 1461, 1391, 1321, 1233, 1157 cm^{-1}.

Mass spectrum:

HRMS found 582.2816 (by FABMS), calc. for $[C_{33}H_{42}O_9]^+$ 582.2829 $g.mol^{-1}$.

EIMS *m/z* 567.2549, 524.2430, 509.2169, 466.2362, 451.2123, 441.1910, 381.1711, 339.1612, 229.1217, 174.0685, 121.0655, 83.0498.

Compound **QP 5**

(spectra vol II, p.s154-163)

swietenolide

pale yellow gum, 12.8mg

^1H and ^{13}C NMR spectra: data and peak assignments Table 7.5, p.184.

Optical Rotation:

$[\alpha]_D$ = -145^o (c, 0.224 in $CHCl_3$)(lit. value [21] -136^o).

IR spectrum:

υ_{max}(NaCl) 3474, 2929, 1719, 1461, 1385, 1256 cm^{-1}.

Mass spectrum:

HRMS found 486.2272, calc. for $[C_{27}H_{34}O_8]^+$ 486.2253 $g.mol^{-1}$.

EIMS *m/z* 466.2358, 451.2105, 397.2012, 301.1817, 283.1693, 273.1839, 255.1758, 137.0969, 119.0856, 69.0699.

Compound **QP 6**
(spectra vol II, p.164-173)

2α-hydroxyswietenolide

pale yellow gum, 9.3mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 7.6, p.186.

Optical Rotation:
$[\alpha]_D = -108^{o}$ (c, 0.162 in $CHCl_3$).

IR spectrum:
υ_{max}(NaCl) 3462, 2941, 1724, 1461, 1385, 1256 cm^{-1}.

Mass spectrum:
HRMS found 502.2195, calc. for $[C_{27}H_{34}O_9]^+$ 502.2203 $g.mol^{-1}$.
EIMS *m/z* 502.2195, 484.2099 $[M-H_2O]^+$, 413.1852, 406.1976, 378.2017, 360.1930, 342.1806, 317.1741, 299.1649, 271.1686, 223.0977, 195.1018, 166.0992, 153.0911, 119.0858, 95.0501.

Compound **QP 7**
(spectra vol II, p.s174-183)

proceranolide

pale yellow gum, 9.2mg
^{13}C NMR spectra: data and peak assignments Table 7.7, p.189.

Optical Rotation:
$[\alpha]_D = -130^{o}$ (c, 0.11 in $CHCl_3$)(lit. value [50] -141^{o}).

IR spectrum:
υ_{max}(NaCl) 3474, 2924, 2853, 2388, 1730, 1473, 1438, 1385, 1303, 1251 cm^{-1}.

Mass spectrum:
HRMS found 470.2293, calc. for $[C_{27}H_{34}O_7]^+$ 470.2305 $g.mol^{-1}$.
EIMS *m/z* 470.2293, 450.2392, 417.1913, 374.2081, 346.2153, 328.2029, 273.1844, 211.1331, 210.1258, 209.1183, 187.1489, 149.0967, 137.0972, 119.0856, 82.9854, 69.0694, 55.0997.

Compound **QP 8**

(spectra vol II, p.s184-193)

3-detigloyl-3-angeloylruageanin B

pale yellow gum, 17.3mg

^{1}H and ^{13}C NMR spectra: data and peak assignments Table 7.8, p.192.

Optical Rotation:

$[\alpha]_D = -67^{o}$ (c, 0.298 in $CHCl_3$).

IR spectrum:

υ_{max}(NaCl) 3468, 2965, 2929, 1724, 1467, 1391, 1262, 1233, 1134, 1034 cm^{-1}.

Mass spectrum:

HRMS found 584.2634, calc. for $[C_{32}H_{40}O_{10}]^{+}$ 584.2621 $g.mol^{-1}$.

EIMS *m/z* 584.2634, 566.2557 $[M-H_2O]^{+}$, 485.2148 [M-HOAng]$^{+}$, 467.2078 $[M-HOAng-H_2O]^{+}$, 449.1974, 425.1952, 407.1871, 224.1053, 197.1164, 196.1098, 164.0837, 137.0972, 122.0733, 95.0502, 83.0494, 55.0551.

Compound **QP 9**

(spectra vol II, p.s194-203)

quivisianolide A

pale yellow gum, 9.4mg

^{1}H and ^{13}C NMR spectra: data and peak assignments Table 7.9, p.198.

Optical Rotation:

$[\alpha]_D = -99^{o}$ (c, 0.152 in $CHCl_3$).

IR spectrum:

υ_{max}(NaCl) 2918, 1742, 1233, 1145, 1046 cm^{-1}.

Mass spectrum:

HRMS found 598.2424, calc. for $[C_{32}H_{38}O_{11}]^{+}$ 598.2414 $g.mol^{-1}$.

EIMS *m/z* 598.2424, 497.1816 [M-HOAng]$^{+}$, 421.1655, 403.1581, 175.0755, 83.0497, 55.0548.

Compound **QP 10**
(spectra vol II, p.s204-213)

quivisianolide B

pale yellow gum, 7.8mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 7.10, p.201.

Optical Rotation:
$[\alpha]_D = -123^{o}$ (c, 0.122 in $CHCl_3$).

IR spectrum:
υ_{max}(NaCl) 3462, 2929, 1736, 1461, 1443, 1390, 1227, 1145, 1046 cm^{-1}.

Mass spectrum:
HRMS found 582.2474, calc. for $[C_{32}H_{38}O_{10}]^{+}$ 582.2465 $g.mol^{-1}$.
EIMS *m/z* 582.2474, 564.2338 $[M-H_2O]^{+}$, 483.1987, 482.1926 $[M-HOAng]^{+}$, 472.2435, 444.2460, 423.1804, 344.1675, 311.1268, 251.1089, 197.1143, 175.0759, 95.0502, 83.0496.

Compound **QP 11**
(spectra vol II, p.s214-223)

quivisianone

pale yellow gum, 6.8mg
^{1}H and ^{13}C NMR spectra: data and peak assignments Table 7.11, p.205.

Optical Rotation:
$[\alpha]_D = -240^{o}$ (c, 0.104 in $CHCl_3$).

IR spectrum:
υ_{max}(NaCl) 3468, 2959, 1742, 1654, 1461, 1443, 1237, 1163, 1046 cm^{-1}.

Mass spectrum:
HRMS found 614.2735, calc. for $[C_{33}H_{42}O_{11}]^{+}$ 614.2727 $g.mol^{-1}$.
EIMS *m/z* 614.2735, 572.2169, 542.2340, 514.2208.

Compound **QP 12**
(spectra vol II, p.s224-228)

melianone

pale yellow gum, 16.1mg

^{1}H and ^{13}C NMR spectra: data and peak assignments Table 7.12, p.207.

Optical Rotation:

$[\alpha]_D$ = -54° (c, 0.278 in $CHCl_3$)(lit. value [81] -62°).

IR spectrum:

υ_{max}(NaCl) 3433, 2947, 1713, 1701, 1461, 1391 cm^{-1}.

Mass spectrum:

HRMS found 470.3407, calc. for $[C_{30}H_{46}O_4]^+$ 470.3396 $g.mol^{-1}$

EIMS *m/z* 470.3407, 452.3300 $[M-H_2O]^+$, 437.3063, 383.2609, 381.2804, 365.2472, 297.2226, 271.2063, 245.1900, 202.0780, 166.0999, 133.1018, 109.0652, 95.0502, 55.0546.

Compound **QP 13**

(spectra vol II, p.s229-233)

melianol

pale yellow gum, 12.2mg

^{1}H and ^{13}C NMR spectra: data and peak assignments Table 7.13, p.211.

Optical Rotation:

$[\alpha]_D$ = -34° (c, 0.192 in $CHCl_3$)(lit. value [81] -38°).

IR spectrum:

υ_{max}(NaCl) 3409, 2929, 2877, 1713, 1461, 1385, 1040, 981 cm^{-1}.

Mass spectrum:

HRMS found 472.3550, calc. for $[C_{30}H_{48}O_4]^+$ 472.3553 $g.mol^{-1}$.

EIMS *m/z* 457.3328, 439.3202, 421.3114, 411.3258, 401.3058, 385.2757, 367.2619, 349.2512, 299.2370, 281.2258, 213.1633, 187.1489, 159.1176, 133.1020, 95.0882, 69.0696.

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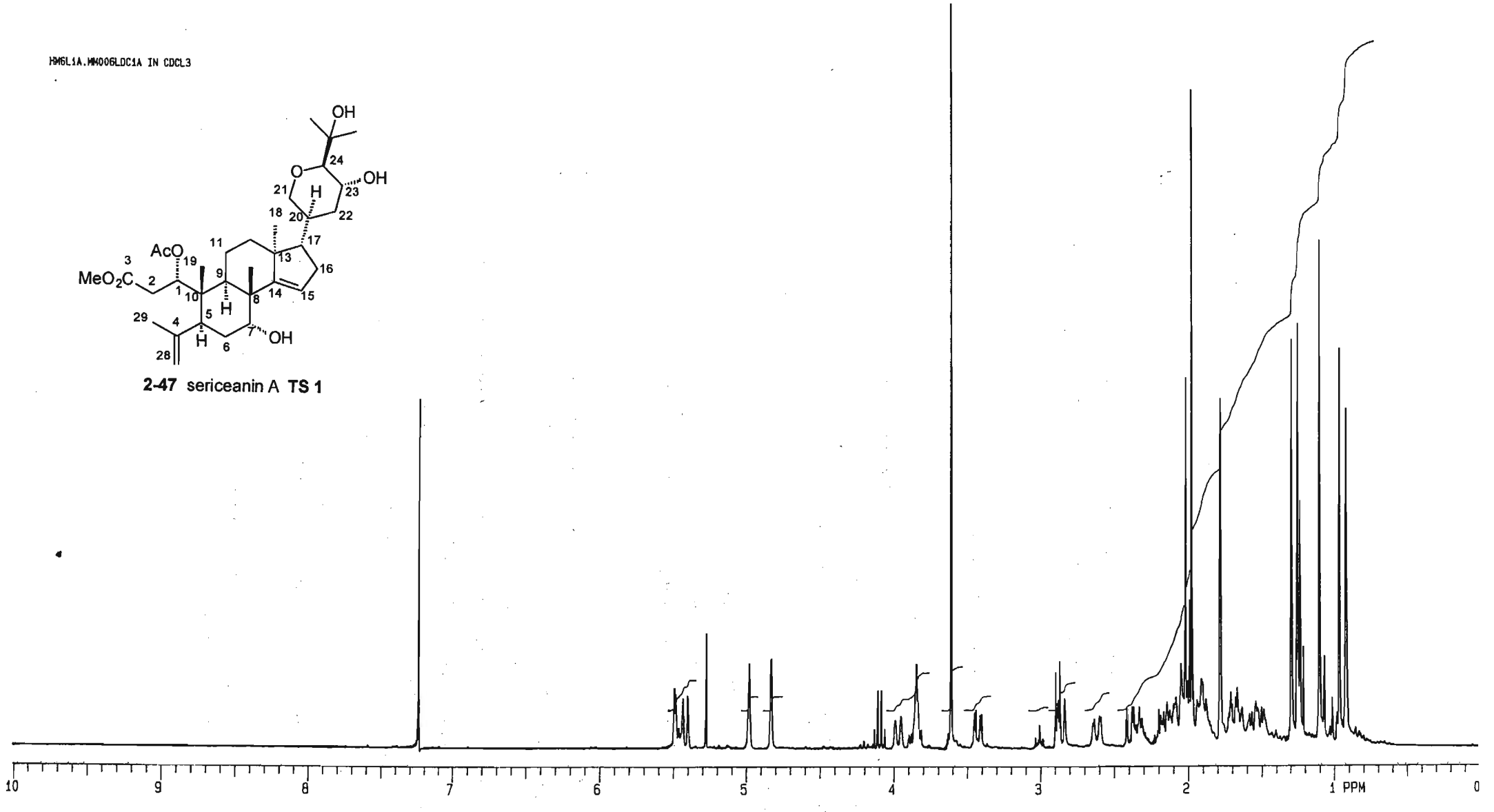
Extractives from the Meliaceae and Simaroubaceae of Madagascar

Volume II

Spectra

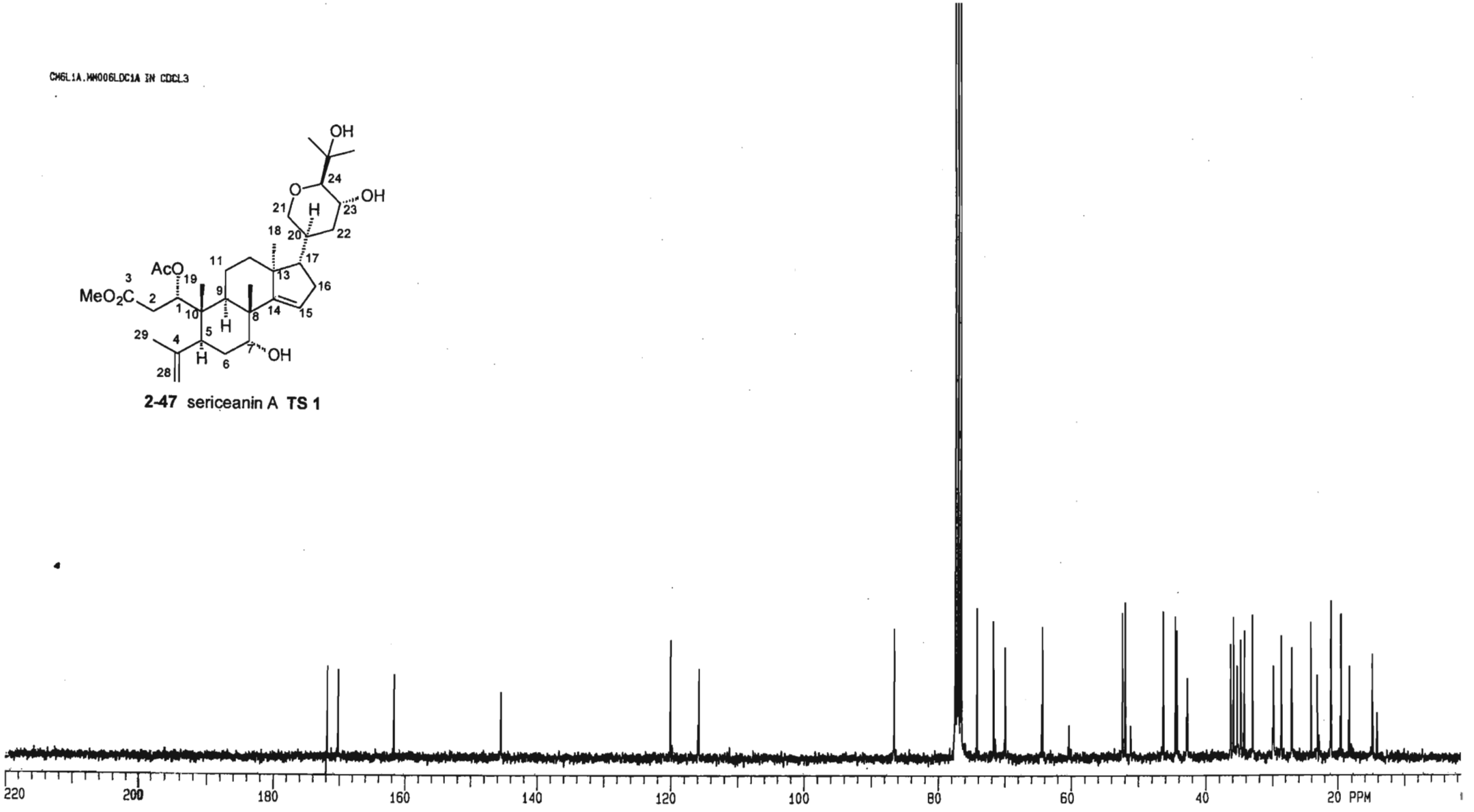
INDEX

		Pages
Chapter 2		
1.	Spectra for compound **TS 1**, sericeanin A	s1 - s7
	Spectra for compound **TS 1a**, sericeanin A diacetate	s8 - s9
Chapter 4		
2.	Spectra for compound **MA 1**, 1,3-diacetylvilasinin	s10 - s19
3.	Spectra for compound **MA 2**, 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin	s20 - s29
Chapter 5		
4.	Spectra for compound **SM 1**, 5α-stigmastan-3-one	s30 - s34
5.	Spectra for compound **SM 2**, samaderine B	s35 - s44
6.	Spectra for compound **SM 3**, samaderine E	s45 - s54
7.	Spectra for compound **SM 4**, brucein D	s55 - s63
8.	Spectra for compound **SM 5**, indaquassin X	s64 - s73
9.	Spectra for compound **SM 6**, 15-acetylbrucein D	s74 - s83
Chapter 6		
10.	Spectra for compound **NL 1**, leandreanin A	s84 - s93
11.	Spectra for compound **NL 2**, leandreanin B	s94 - s103
12.	Spectra for compound **NL 3**, leandreanin C	s104 - s113
Chapter 7		
13.	Spectra for compound **QP 1**, azadiradione	s114 - s123
14.	Spectra for compound **QP 2**, 6α-hydroxyazadiradione	s124 - s133
15.	Spectra for compound **QP 3**, 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione	s134 - s143
16.	Spectra for compound **QP 4**, quivisianthone	s144 - s153
17.	Spectra for compound **QP 5**, swietenolide	s154 - s163
18.	Spectra for compound **QP 6**, 2α-hydroxyswietenolide	s164 - s173
19.	Spectra for compound **QP 7**, proceranolide	s174 - s183
20.	Spectra for compound **QP 8**, 3-detigloyl-3-angeloylruageanin B	s184 - s193
21.	Spectra for compound **QP 9**, quivisianolide A	s194 - s203
22.	Spectra for compound **QP 10**, quivisianolide B	s204 - s213
23.	Spectra for compound **QP 11**, quivisianone	s214 - s223
24.	Spectra for compound **QP 12**, melianone	s224 - s228
25.	Spectra for compound **QP 13**, melianol	s229 - s233



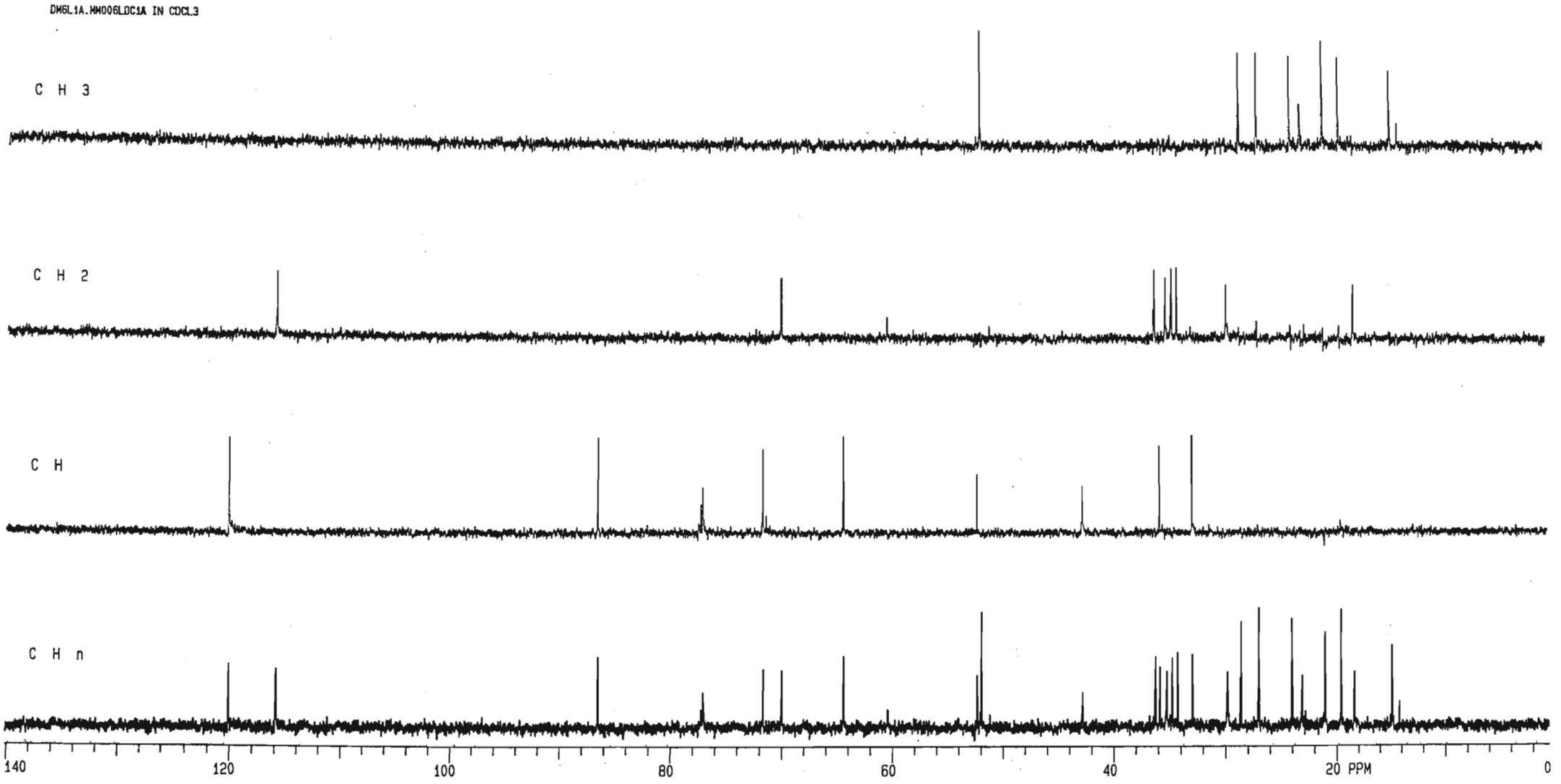
2-47 sericeanin A **TS 1**

Spectrum TS 1.1: ^{1}H NMR Spectrum of sericeanin A TS 1

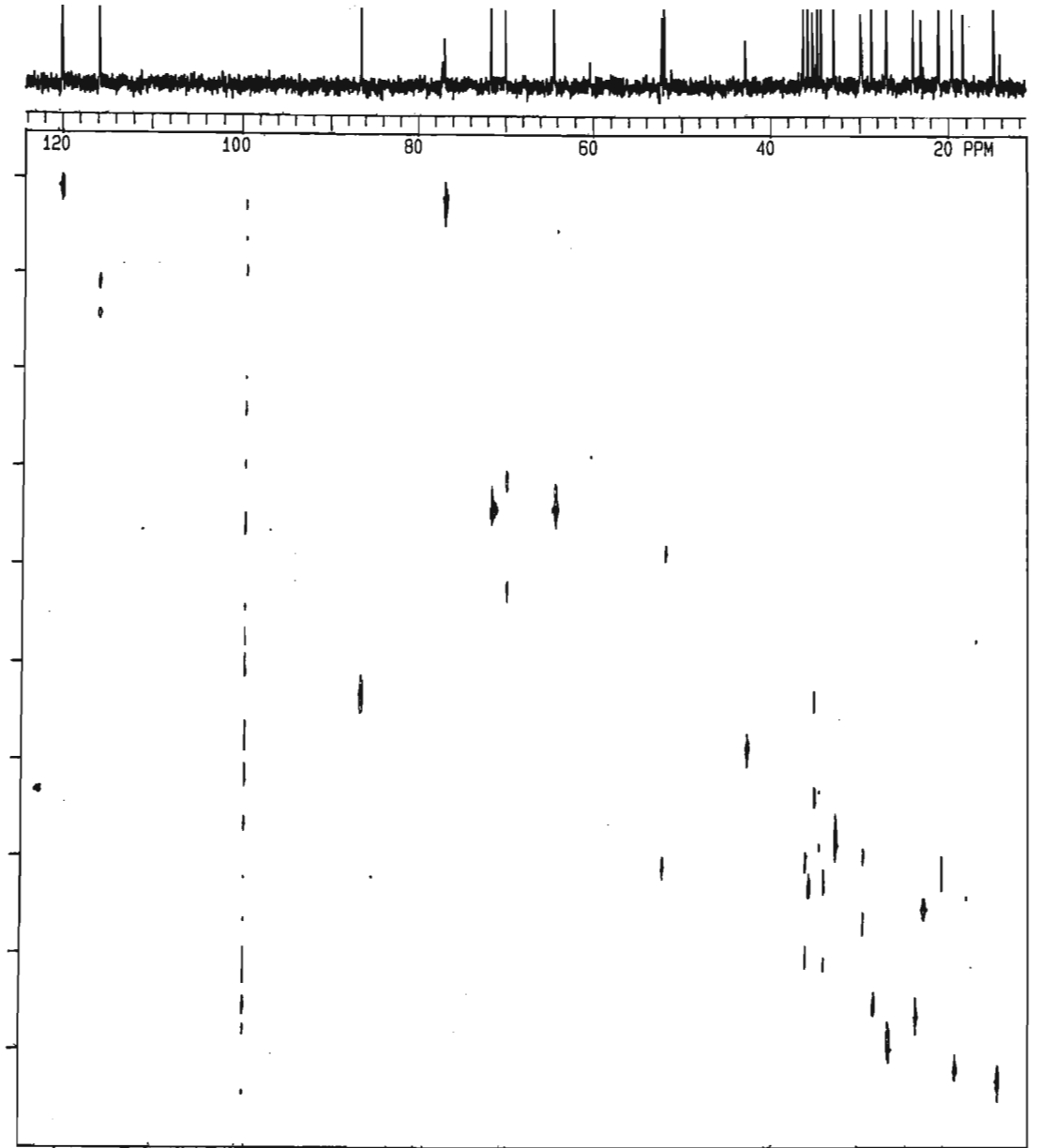


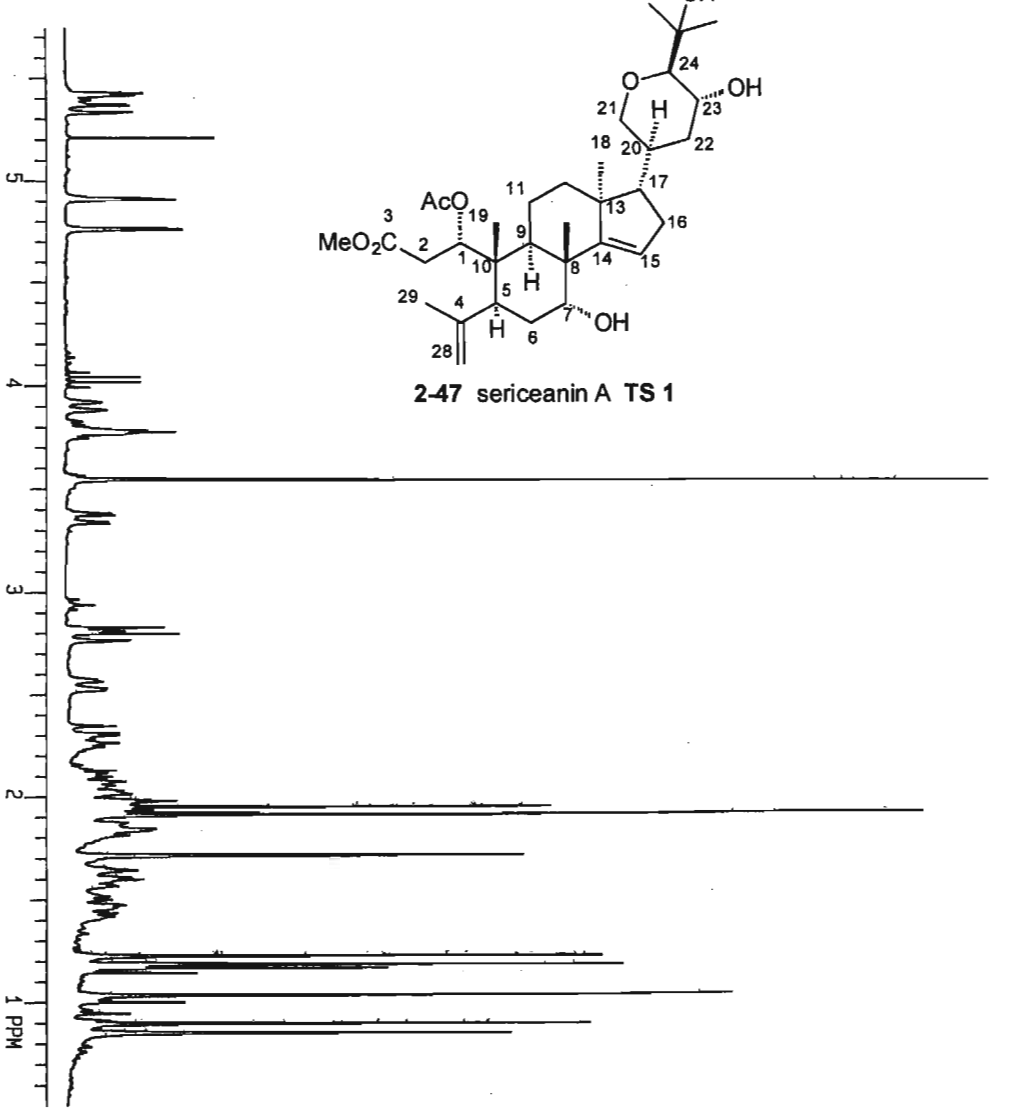
2-47 sericeanin A **TS 1**

Spectrum TS 1.2: ^{13}C NMR Spectrum of sericeanin A TS 1



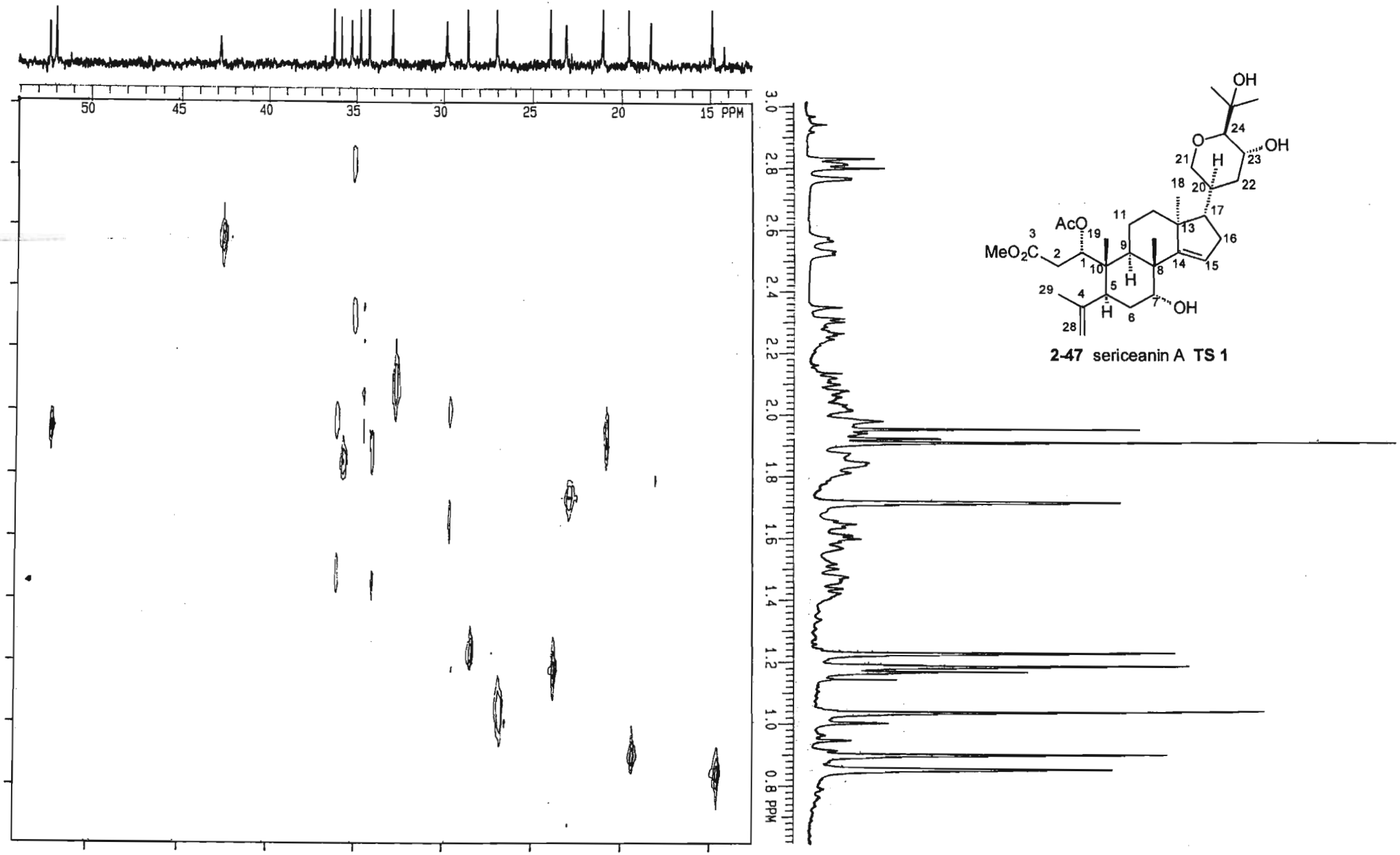
Spectrum TS 1.3: ADEPT Spectrum of sericeanin A TS 1





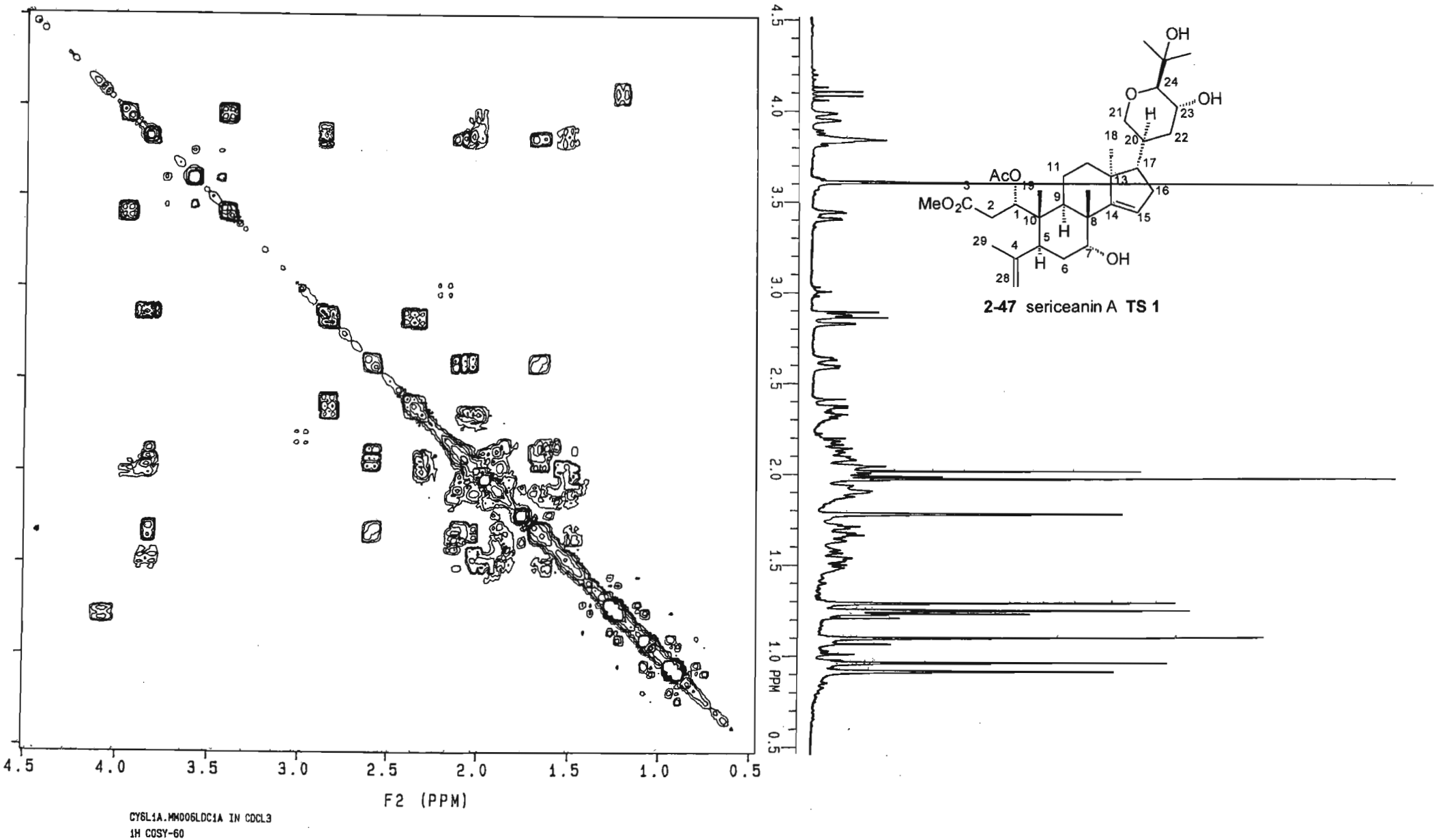
2-47 sericeanin A **TS 1**

Spectrum TS 1.4: HETCOR Spectrum of sericeanin A TS 1

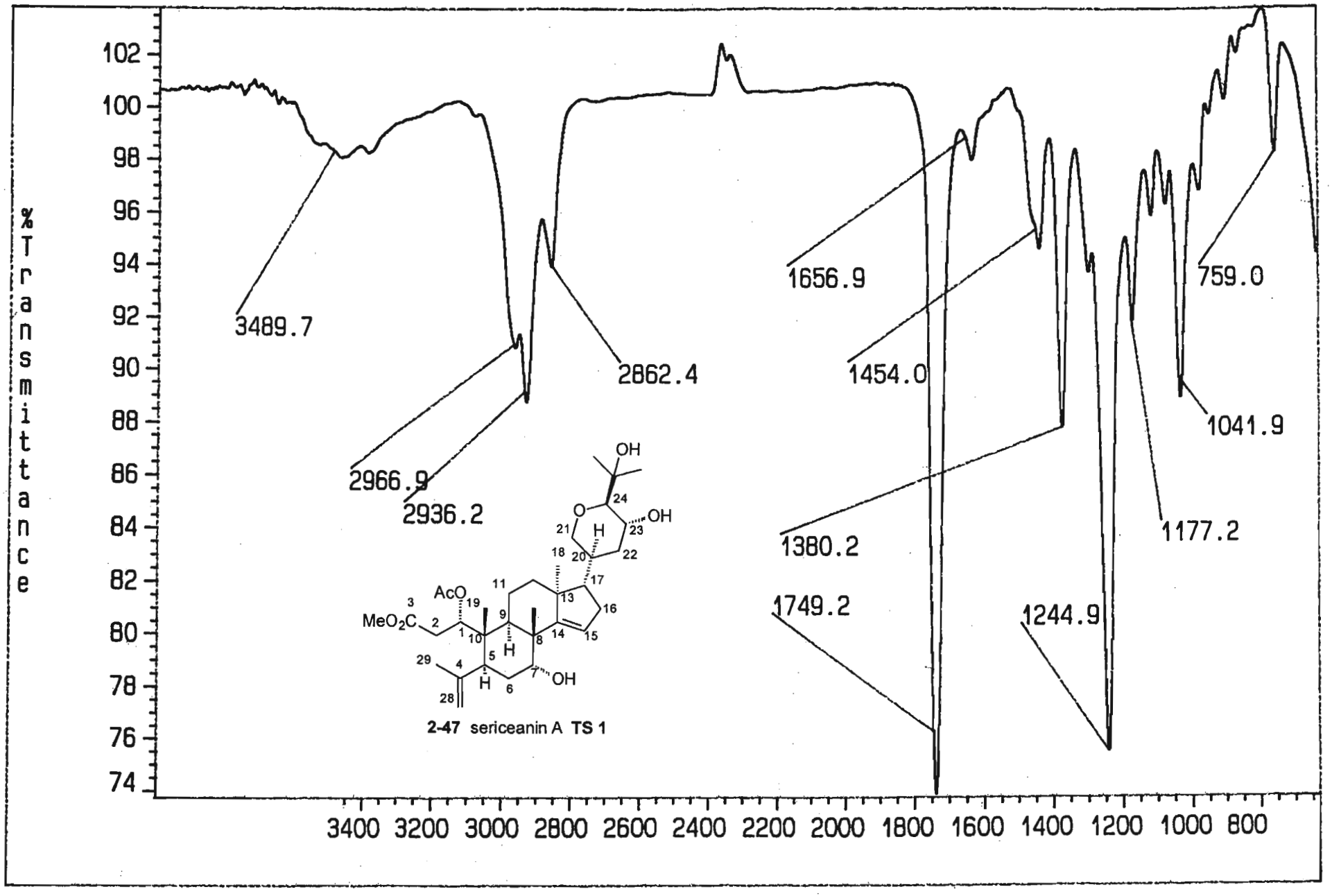


2-47 sericeanin A **TS 1**

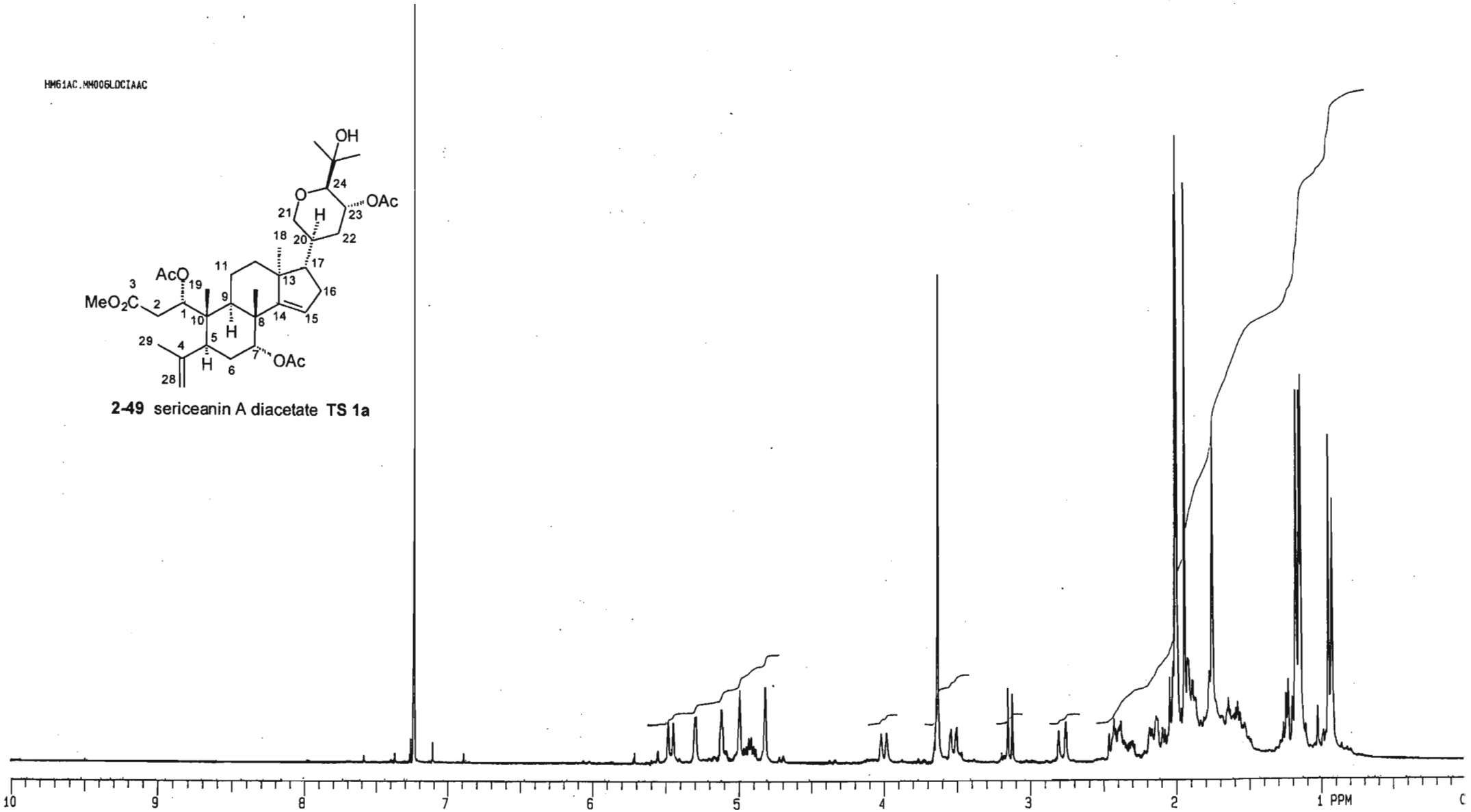
Spectrum TS 1.5: Expanded HETCOR Spectrum of sericeanin A TS 1



Spectrum TS 1.6: COSY Spectrum of sericeanin A TS 1



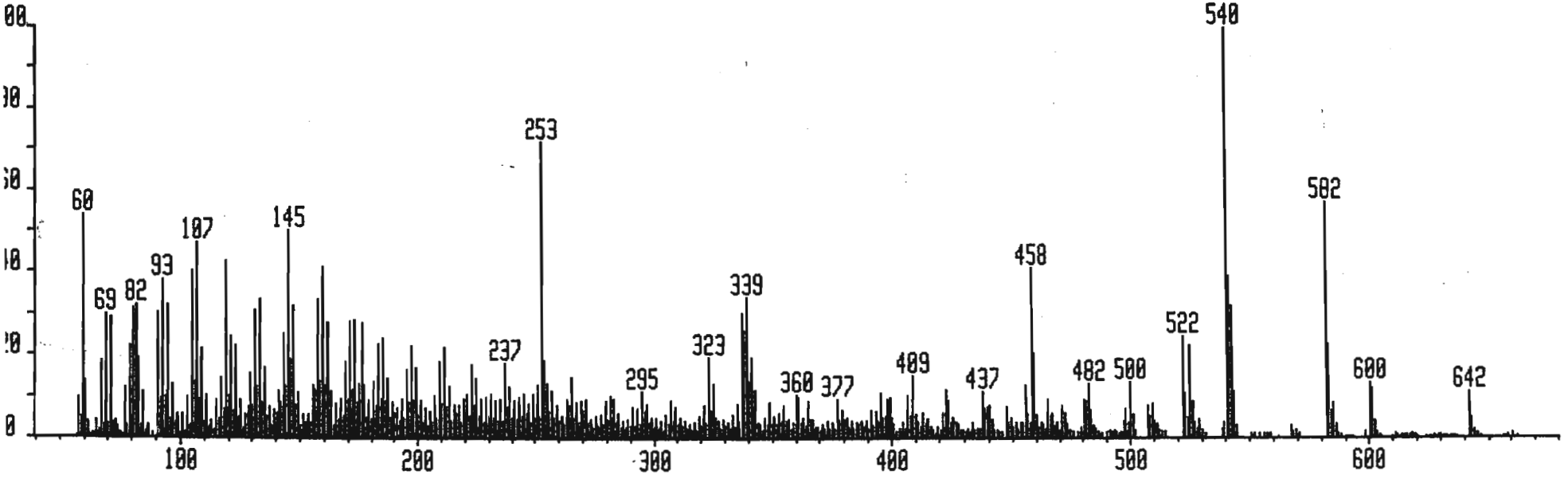
Spectrum TS 1.7: IR Spectrum of sericeanin A TS 1

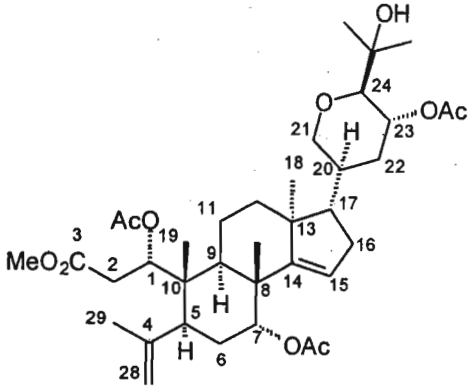


2-49 sericeanin A diacetate **TS 1a**

Spectrum TS 1.8: ^{1}H NMR Spectrum of sericeanin A diacetate TS 1a

PH1#24 x1 Bgd=11 6-AUG-97 16:03+0:03:03 70-250SEQ EI+
BpM=0 I=6.2v Hm=0 TIC=1646737024 Acnt: Sys:SYSTEMDEF HMR: 40713000
2 PT= 0° Cal:AUG06F MASS: 540

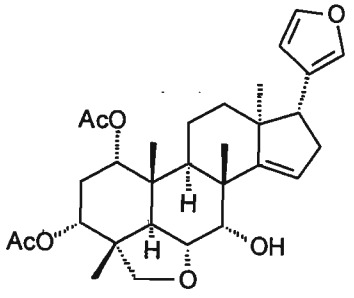




2-49 sericeanin A diacetate **TS 1a**

Spectrum TS 1.9: Mass Spectrum of sericeanin A diacetate TS 1a

Pulse Sequence: s2pul

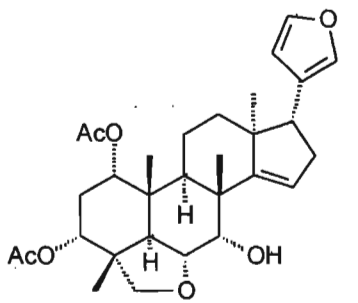


4-1 1,3-diacetylvilasinin **MA 1**

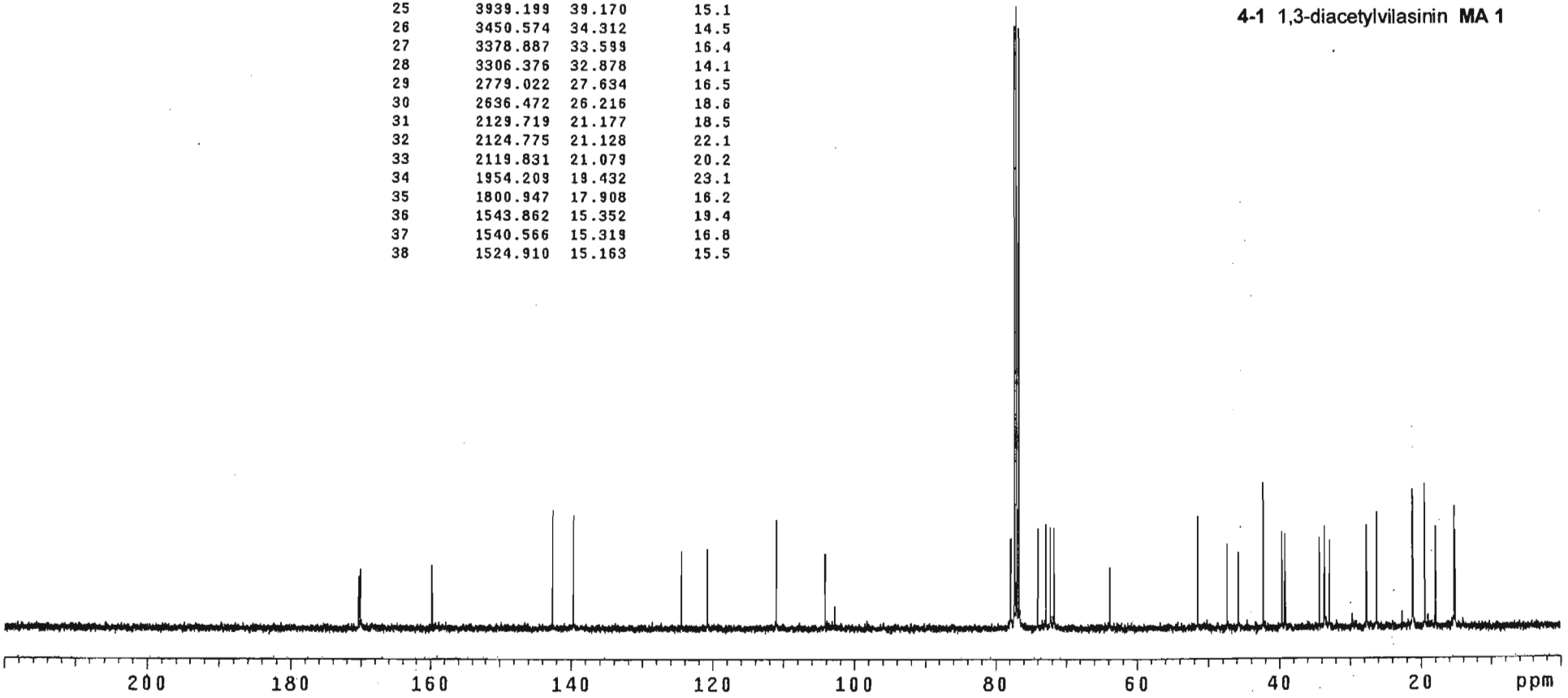
Spectrum MA 1.1: ^{1}H NMR Spectrum of 1,3-diacetylvilasinin MA 1

Pulse Sequence: s2pul

1	17134.567	170.382	8.5
2	17105.727	170.095	9.7
3	16070.796	159.804	10.3
4	14339.594	142.589	19.3
5	14048.726	139.697	18.4
6	12516.106	124.457	12.5
7	12146.134	120.778	12.9
8	11165.587	111.028	17.5
9	10476.732	104.178	12.1
10	7830.902	77.869	14.6
11	7775.694	77.320	96.8
12	7764.158	77.205	7.9
13	7743.559	77.000	100.0
14	7711.423	76.680	96.4
15	7440.331	73.985	16.2
16	7322.500	72.813	16.8
17	7263.997	72.231	16.2
18	7212.910	71.723	16.3
19	6416.936	63.808	9.8
20	5179.304	51.502	18.0
21	4761.541	47.348	13.6
22	4605.807	45.799	12.2
23	4250.667	42.268	23.3
24	3983.695	39.613	15.5
25	3939.199	39.170	15.1
26	3450.574	34.312	14.5
27	3378.887	33.599	16.4
28	3306.376	32.878	14.1
29	2779.022	27.634	16.5
30	2636.472	26.216	18.6
31	2129.719	21.177	18.5
32	2124.775	21.128	22.1
33	2119.831	21.079	20.2
34	1954.209	19.432	23.1
35	1800.947	17.908	16.2
36	1543.862	15.352	19.4
37	1540.566	15.319	16.8
38	1524.910	15.163	15.5

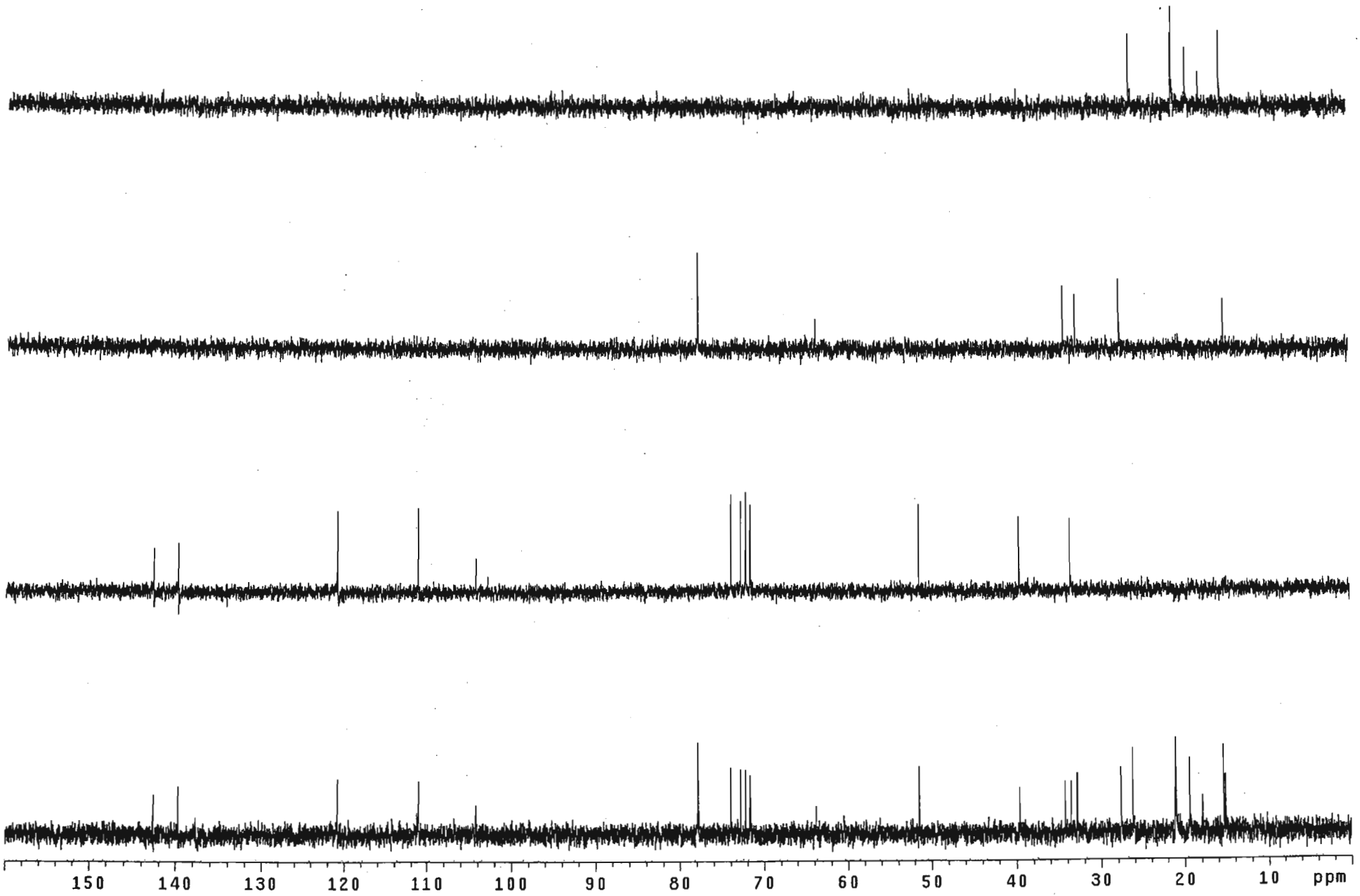


4-1 1,3-diacetylvilasinin **MA 1**



Spectrum MA 1.2: ^{13}C NMR Spectrum of 1,3-diacetylvilasinin MA 1

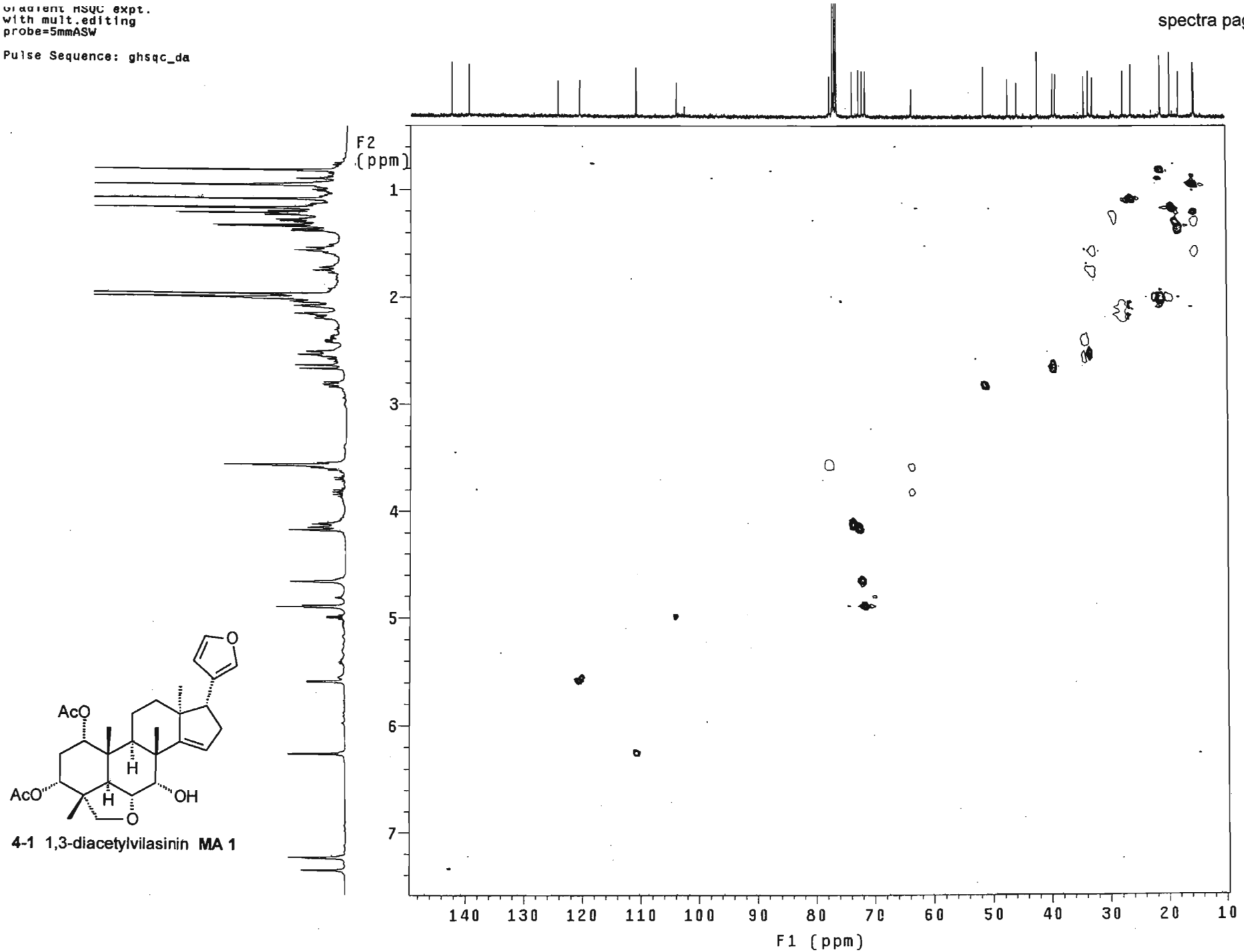
Pulse Sequence: dept



Spectrum MA 1.3: ADEPT Spectrum of 1,3-diacetylvilasinin MA 1

Gradient HSQC expt.
with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

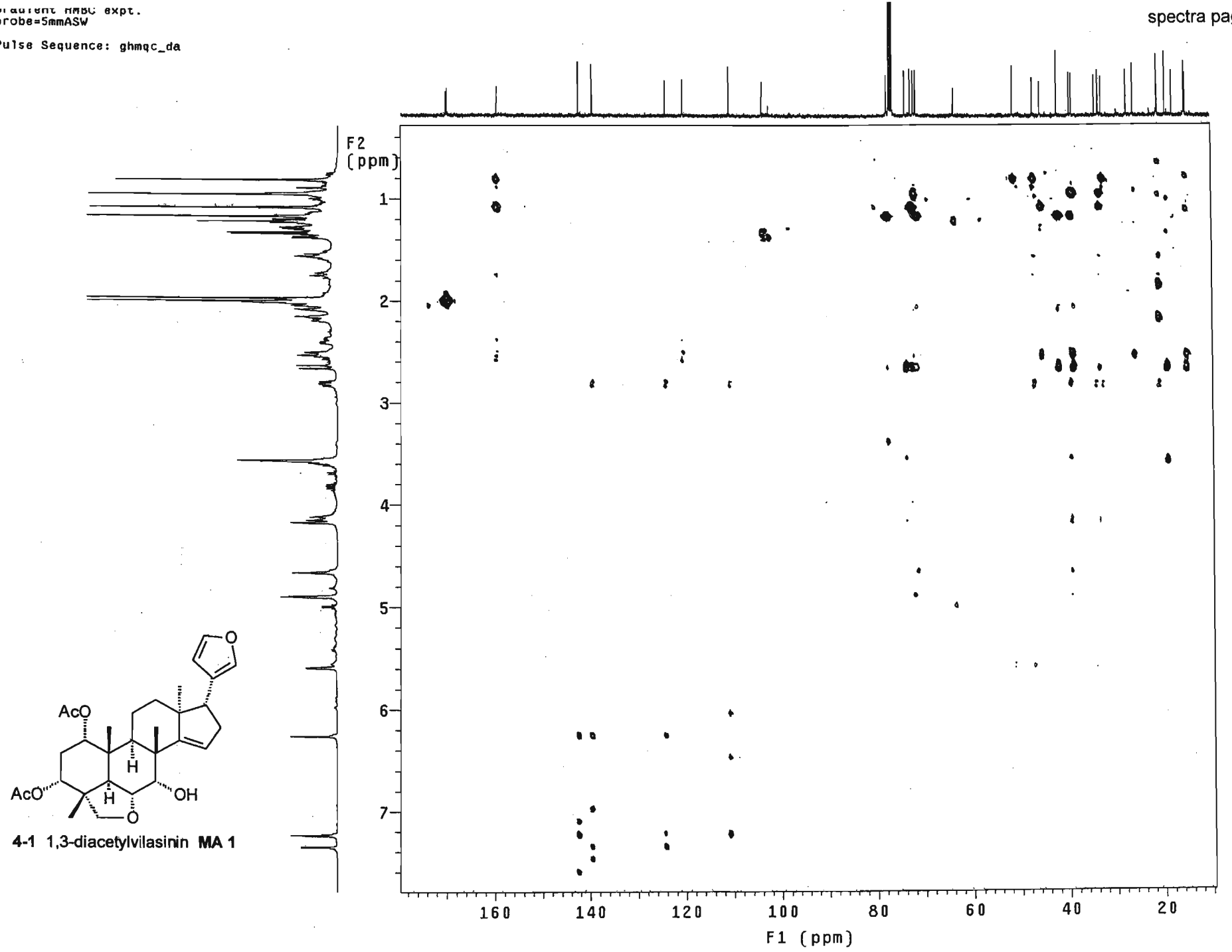


4-1 1,3-diacetylvilasinin **MA 1**

Spectrum MA 1.4: HSQC Spectrum of 1,3-diacetylvilasinin MA 1

Gradient HMBC expt.
probe=5mmASW

Pulse Sequence: ghmqc_da

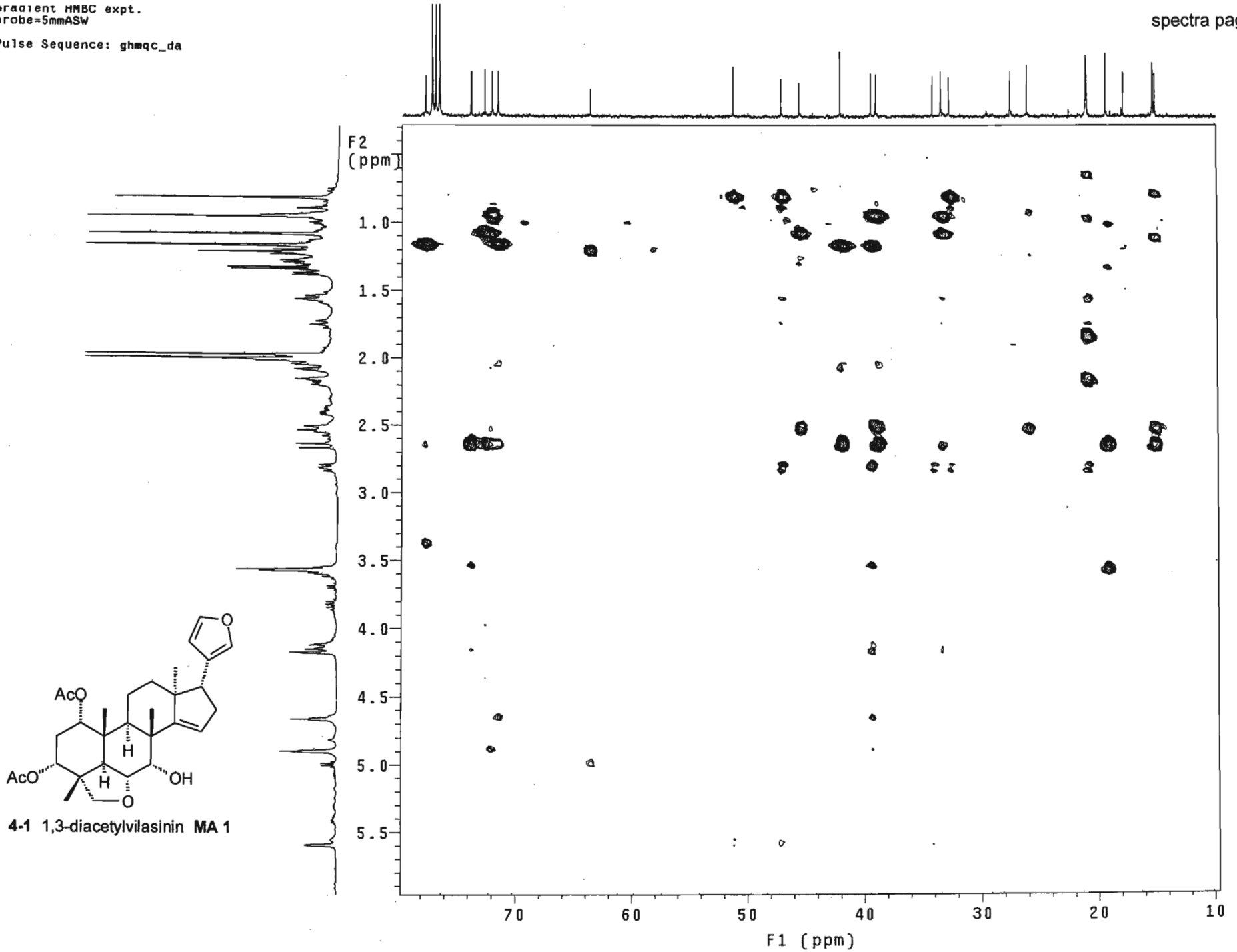


4-1 1,3-diacetylvilasinin **MA 1**

Spectrum MA 1.5: HMBC Spectrum of 1,3-diacetylvilasinin MA 1

Gradient HMBC expt.
probe=5mmASW

Pulse Sequence: ghmqc_da

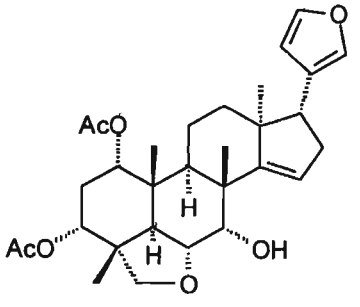


4-1 1,3-diacetylvilasinin **MA 1**

Spectrum MA 1.6: Expanded HMBC Spectrum of 1,3-diacetylvilasinin MA 1

probe=5mmASW

Pulse Sequence: relayh

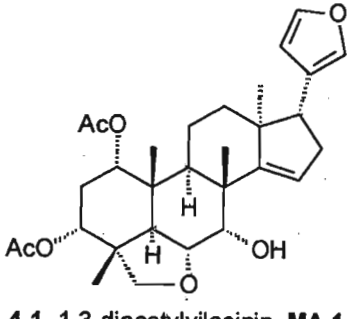


4-1 1,3-diacetylvilasinin **MA 1**

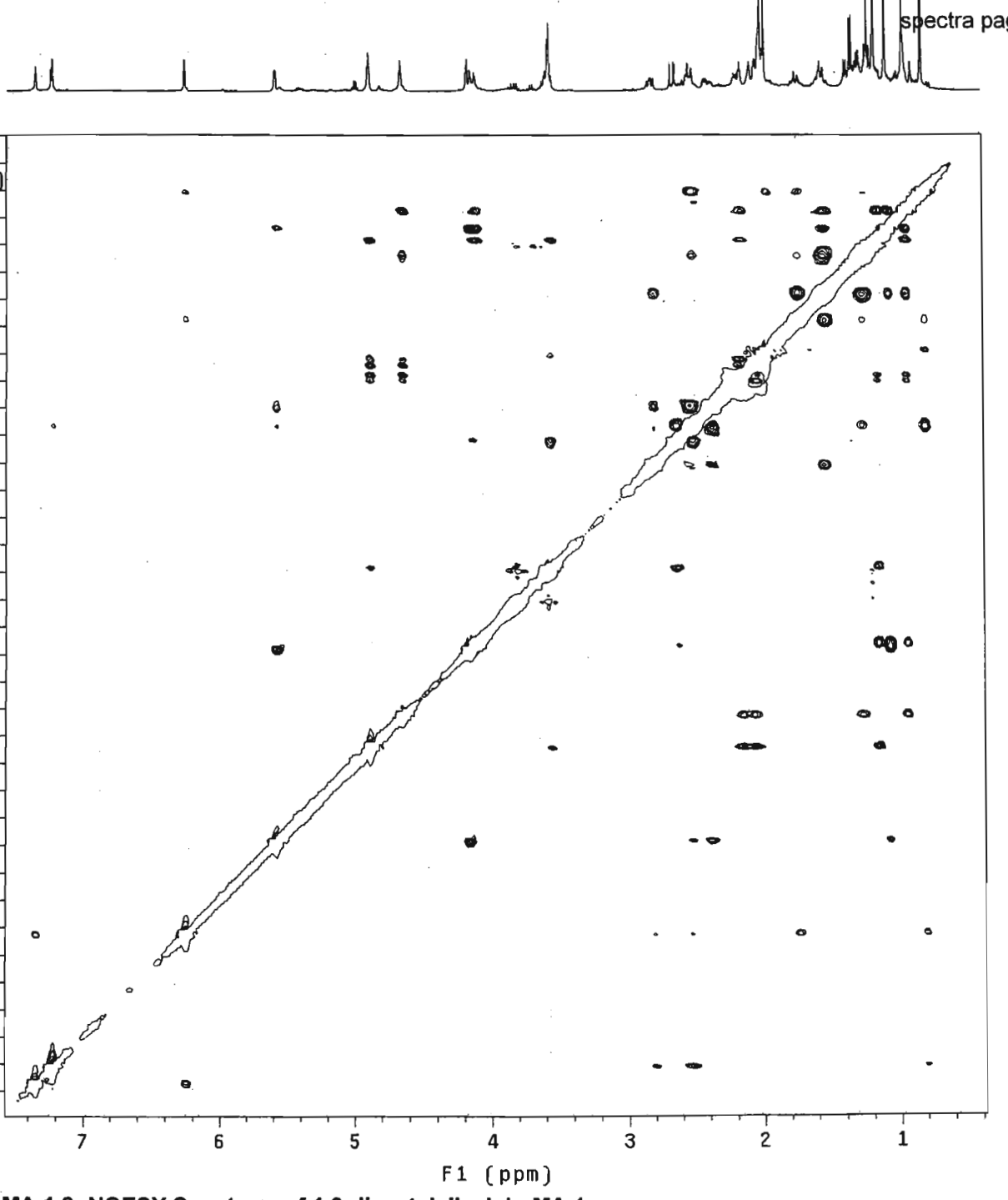
Spectrum MA 1.7: COSY Spectrum of 1,3-diacetylvilasinin MA 1

Gradient NOESY expt.
mix=1sec
probe=5mmASW

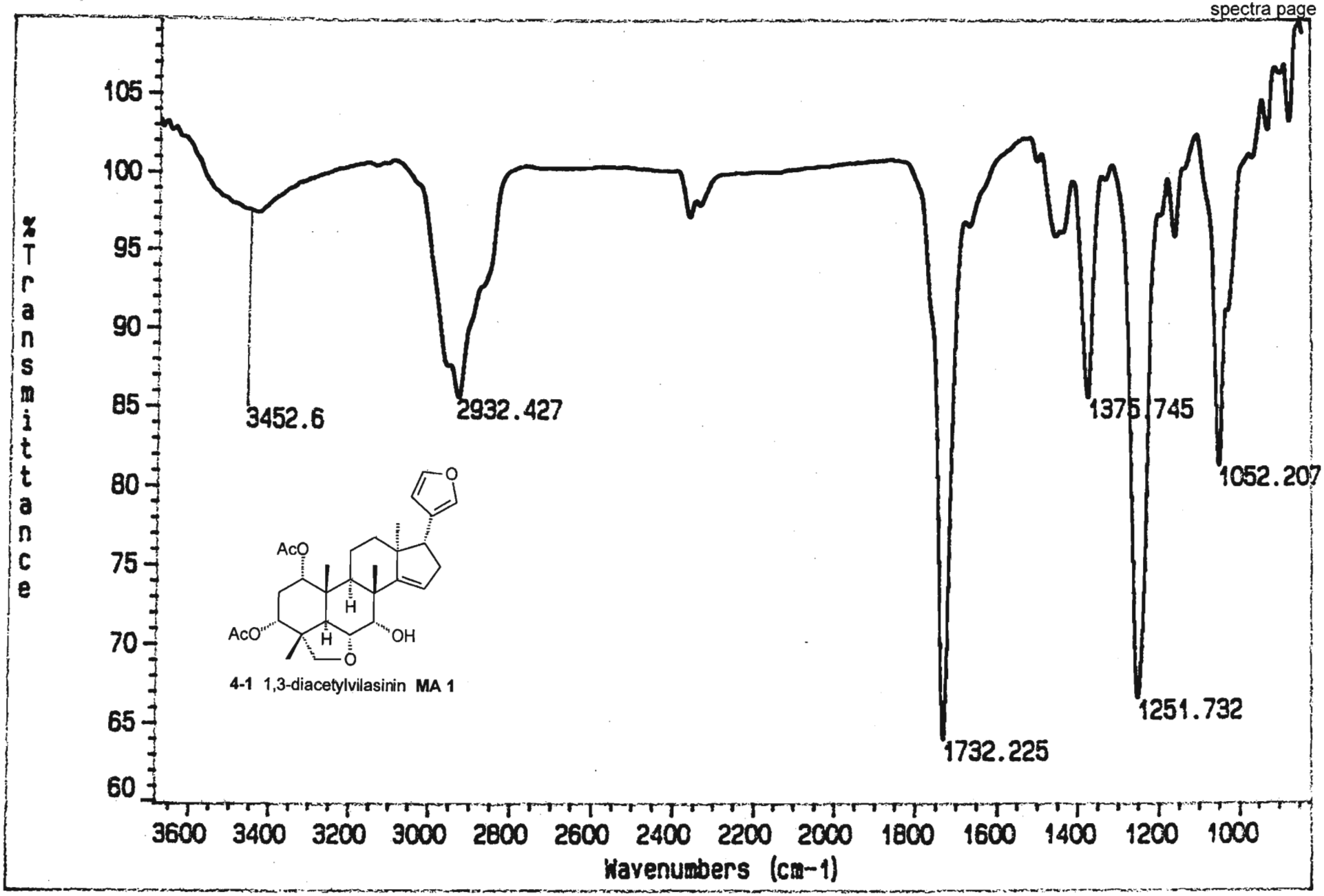
Pulse Sequence: noesy_da



4-1 1,3-diacetylvilasinin **MA 1**



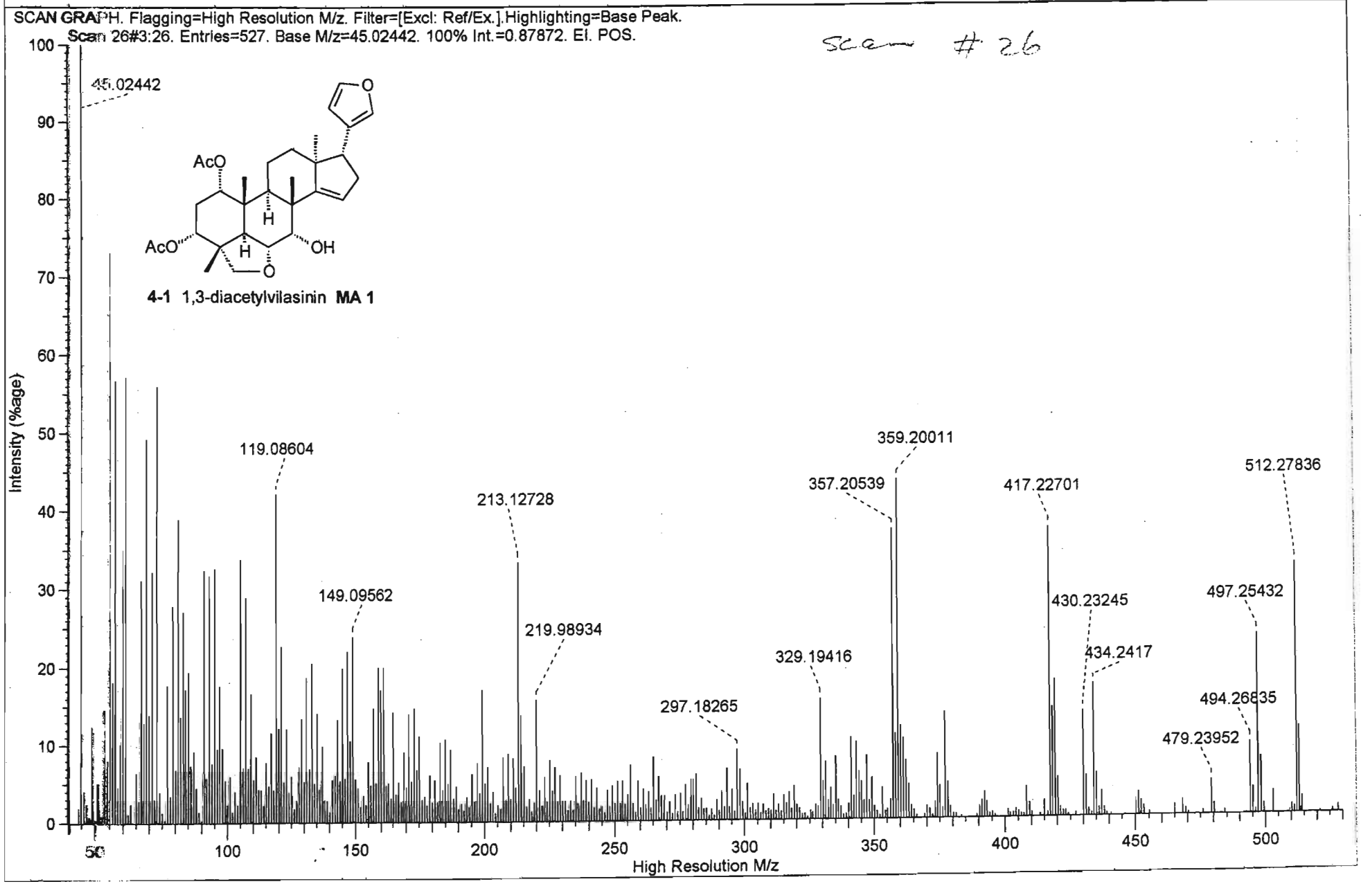
Spectrum MA 1.8: NOESY Spectrum of 1,3-diacetylvilasinin MA 1



4-1 1,3-diacetylvilasinin MA 1

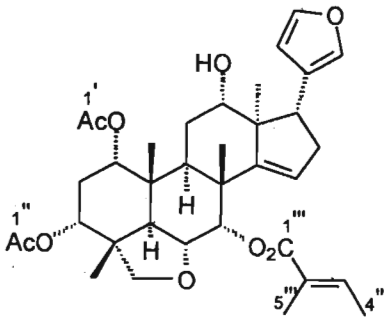
Spectrum MA 1.9: IR Spectrum of 1,3-diacetylvilasinin MA 1

File Name : C:\MASPEC\data\hc051824.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : 9doa1-12
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ



Spectrum MA 1.10: High Resolution Mass Spectrum of 1,3-diacetylvilasinin MA 1

Pulse Sequence: s2pul

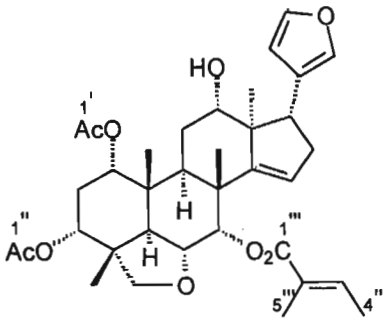


4-12 MA 2

Spectrum MA 2.1: ^{1}H NMR Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

Pulse Sequence: s2pul

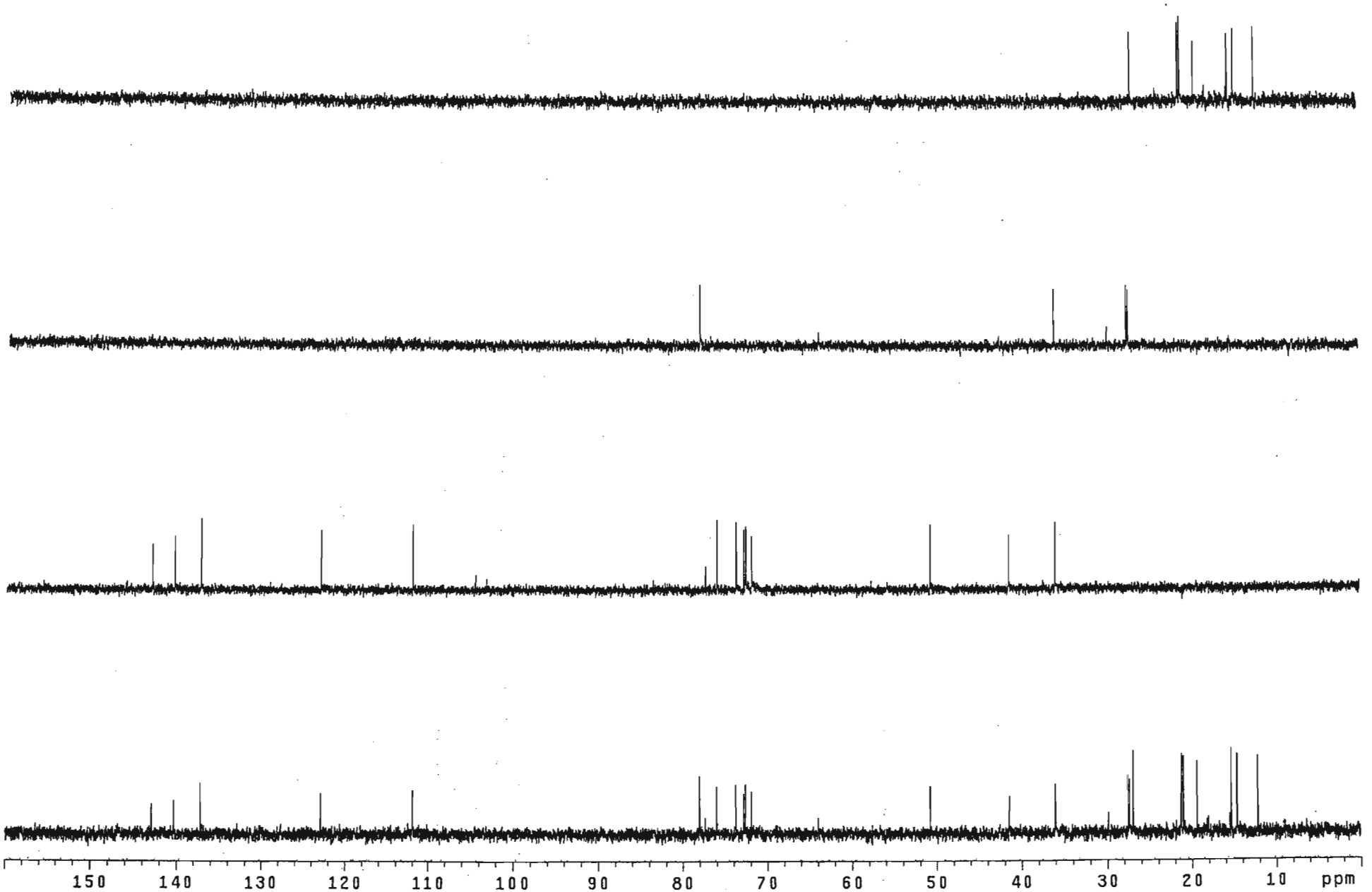
				INDEX	FREQUENCY	PPM	HEIGHT
1	17090.275	169.941	12.5	40	1469.907	14.616	18.1
2	17086.155	169.900	8.6	41	1226.830	12.199	17.0
3	16773.863	166.795	7.5				
4	15699.381	156.111	9.5				
5	14374.405	142.936	25.7				
6	14109.905	140.305	27.9				
7	13798.437	137.208	22.0				
8	12951.376	128.785	10.0				
9	12631.668	125.606	13.9				
10	12363.047	122.935	21.9				
11	11259.725	111.964	24.2				
12	7852.529	78.084	24.8				
13	7796.498	77.526	146.7				
14	7784.962	77.412	11.0				
15	7764.362	77.207	150.0				
16	7732.226	76.887	143.1				
17	7649.828	76.068	24.3				
18	7420.758	73.790	23.7				
19	7331.768	72.905	26.7				
20	7309.520	72.684	21.7				
21	7237.009	71.963	24.1				
22	5346.777	53.167	14.2				
23	5111.116	50.824	24.7				
24	4474.172	44.490	15.5				
25	4247.575	42.237	17.5				
26	4172.592	41.491	25.7				
27	3942.699	39.205	15.1				
28	3628.759	36.083	24.8				
29	3625.463	36.051	29.5				
30	3004.999	29.881	7.1				
31	2772.634	27.570	23.5				
32	2754.506	27.390	21.1				
33	2712.483	26.972	27.3				
34	2143.106	21.311	18.3				
35	2117.562	21.057	21.0				
36	1957.708	19.467	27.9				
37	1819.278	18.090	6.6				
38	1544.890	15.362	23.2				
39	1481.442	14.731	21.1				



4-12 MA 2

Spectrum MA 2.2: ^{13}C NMR Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

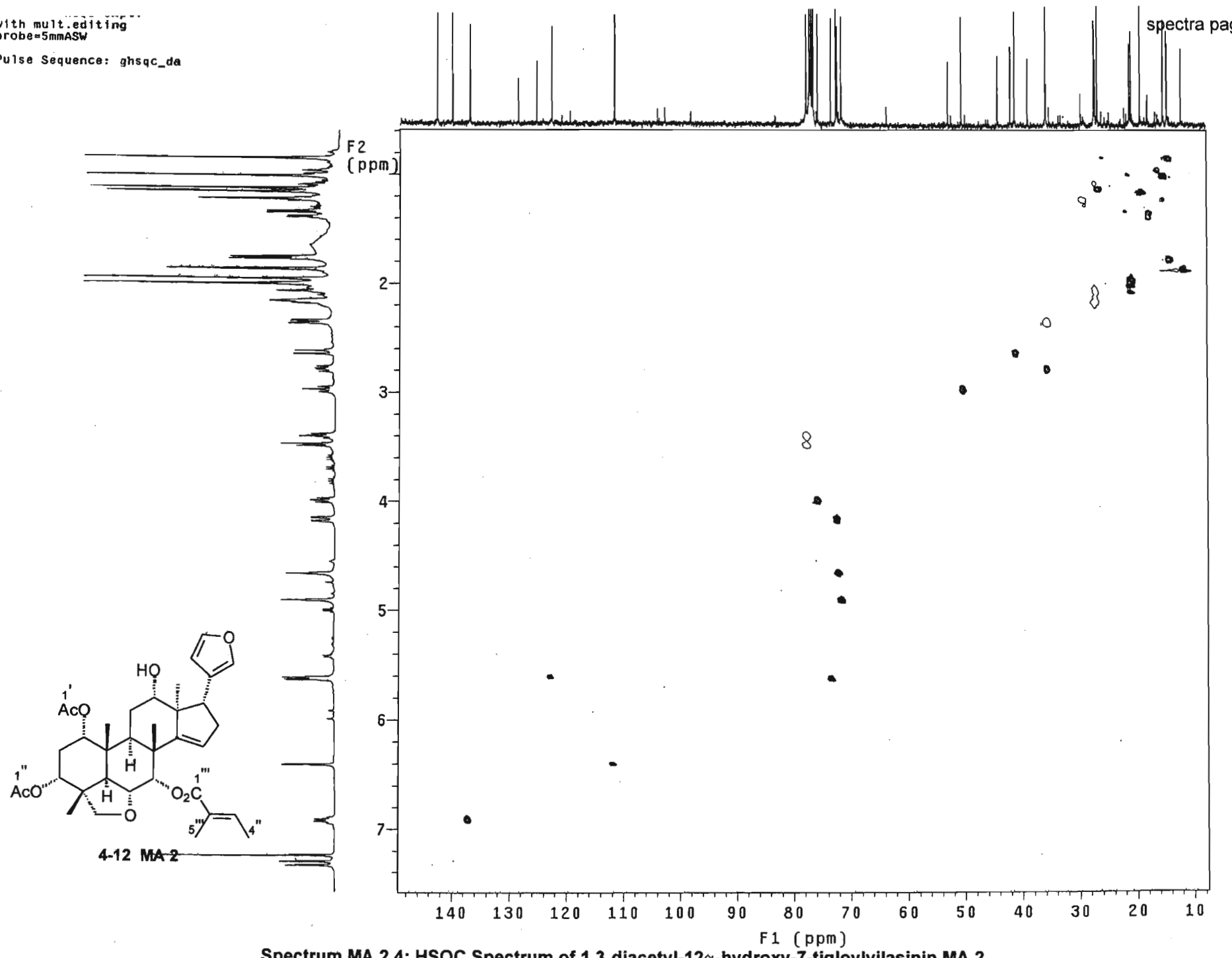
Pulse Sequence: dept



Spectrum MA 2.3: ADEPT Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

with mult.editing
probe=5mmASW

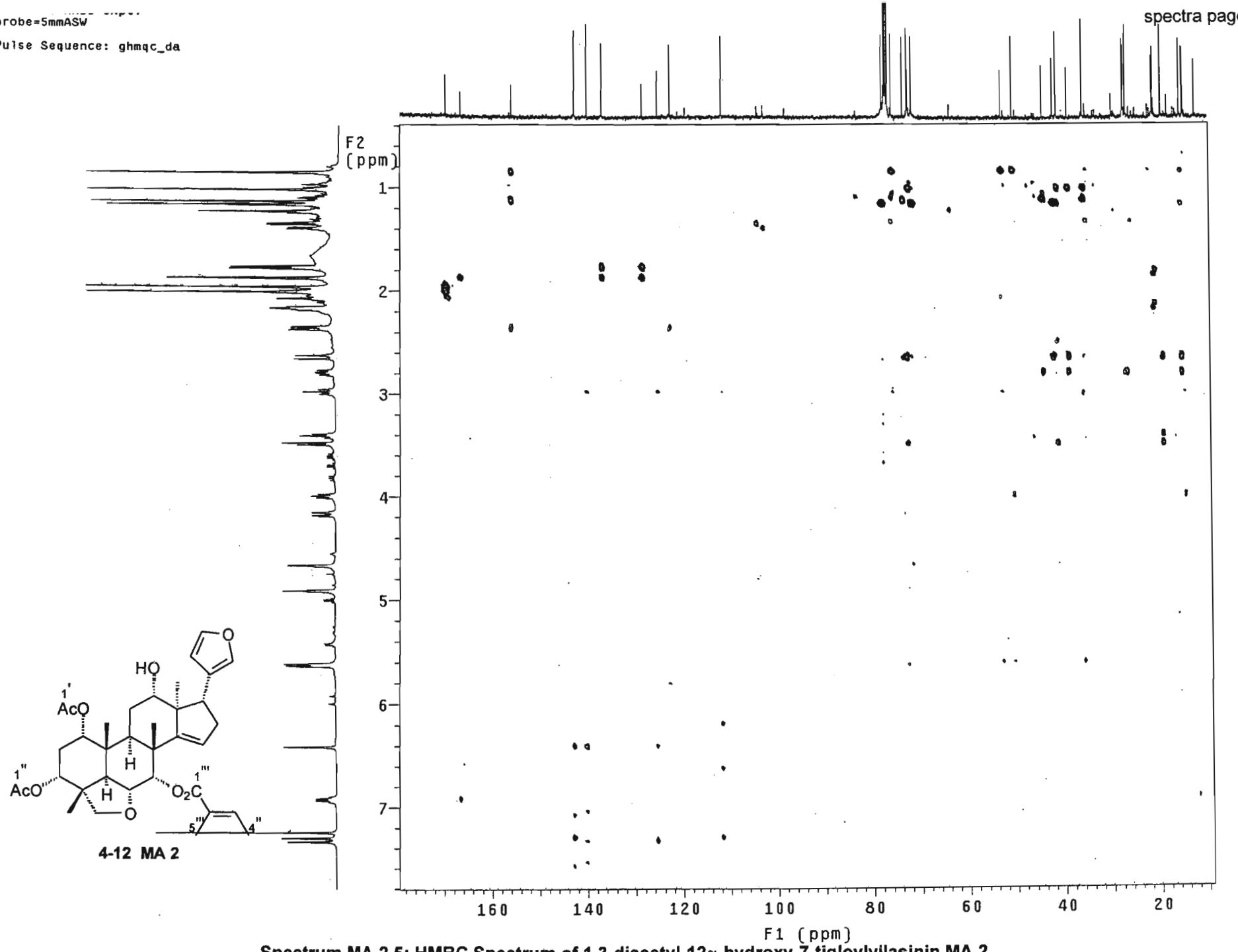
Pulse Sequence: ghsqc_da



Spectrum MA 2.4: HSQC Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

probe=5mmASW

Pulse Sequence: ghmqc_da

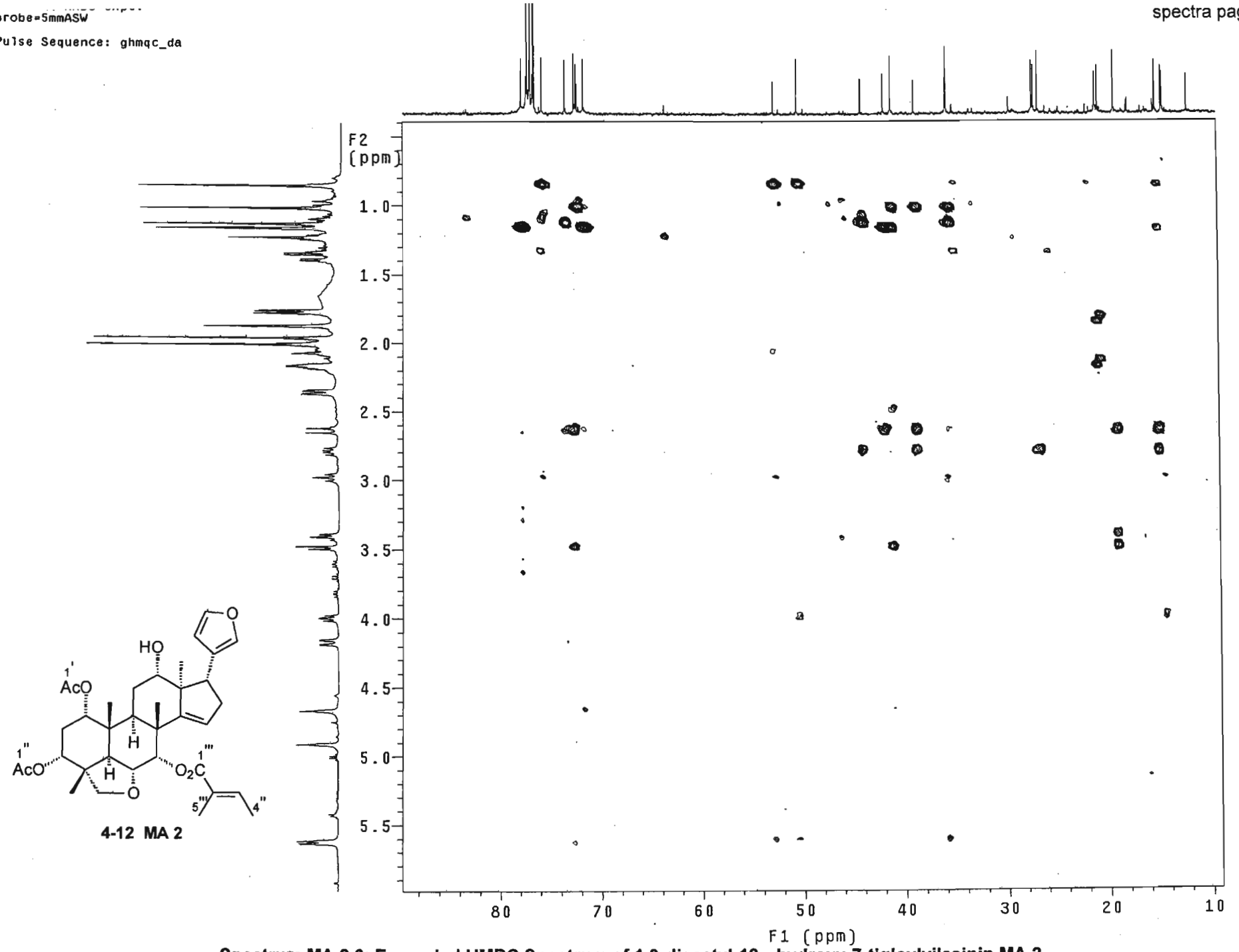


4-12 MA 2

Spectrum MA 2.5: HMBC Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

probe=5mmASW

Pulse Sequence: ghmqc_da

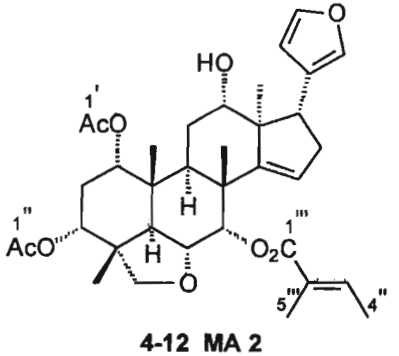


4-12 MA 2

Spectrum MA 2.6: Expanded HMBC Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

probe=5mmASW

Pulse Sequence: relayh



4-12 MA 2

F2 (ppm)

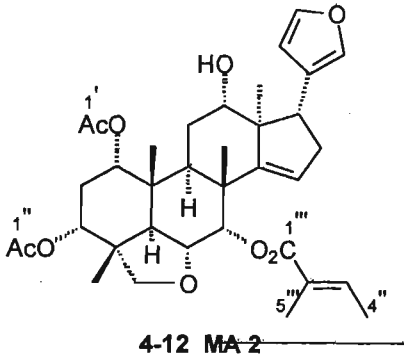
1 2 3 4 5 6 7

7 6 5 4 3 2 1

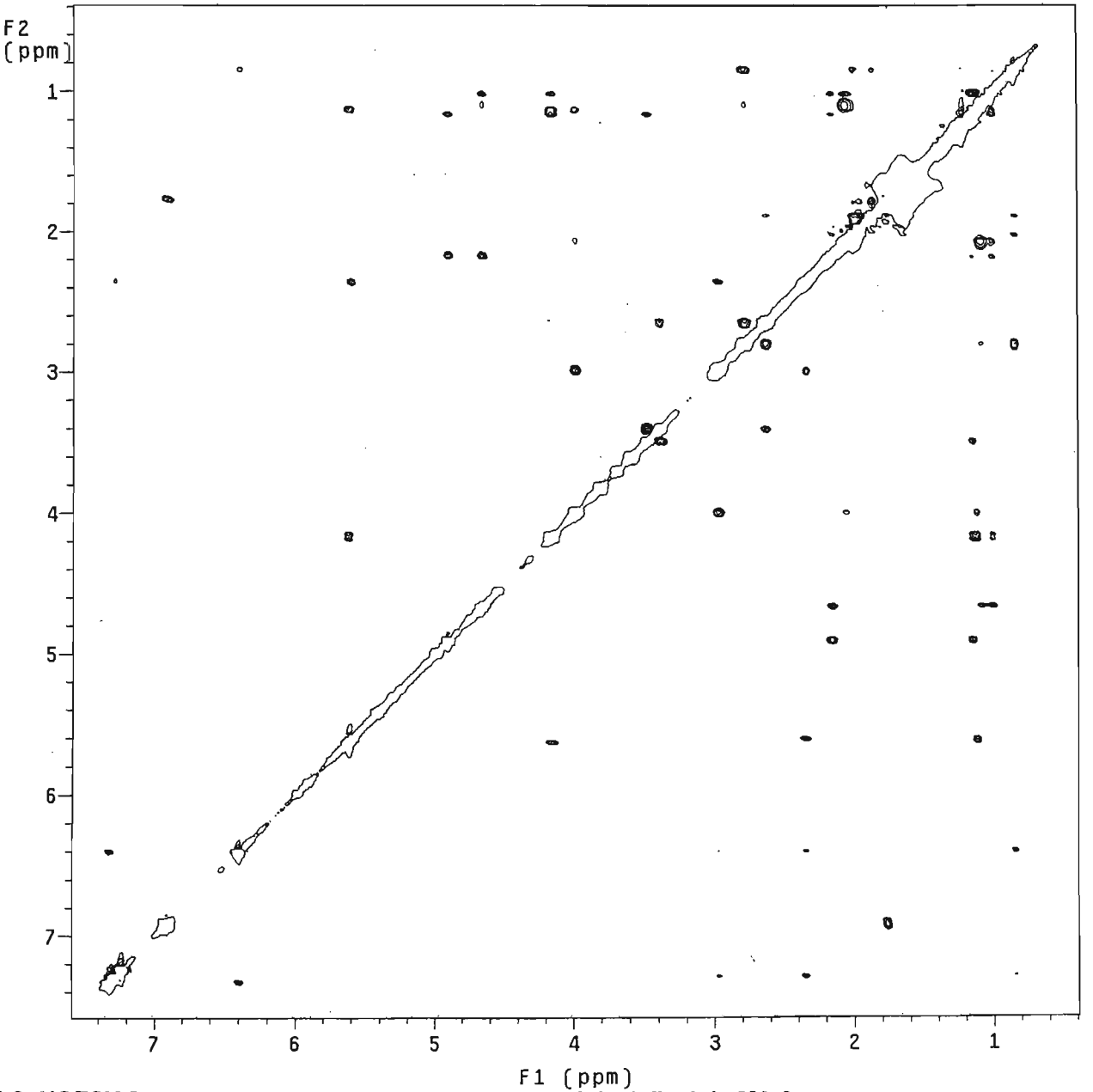
F1 (ppm)

Spectrum MA 2.7: COSY Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

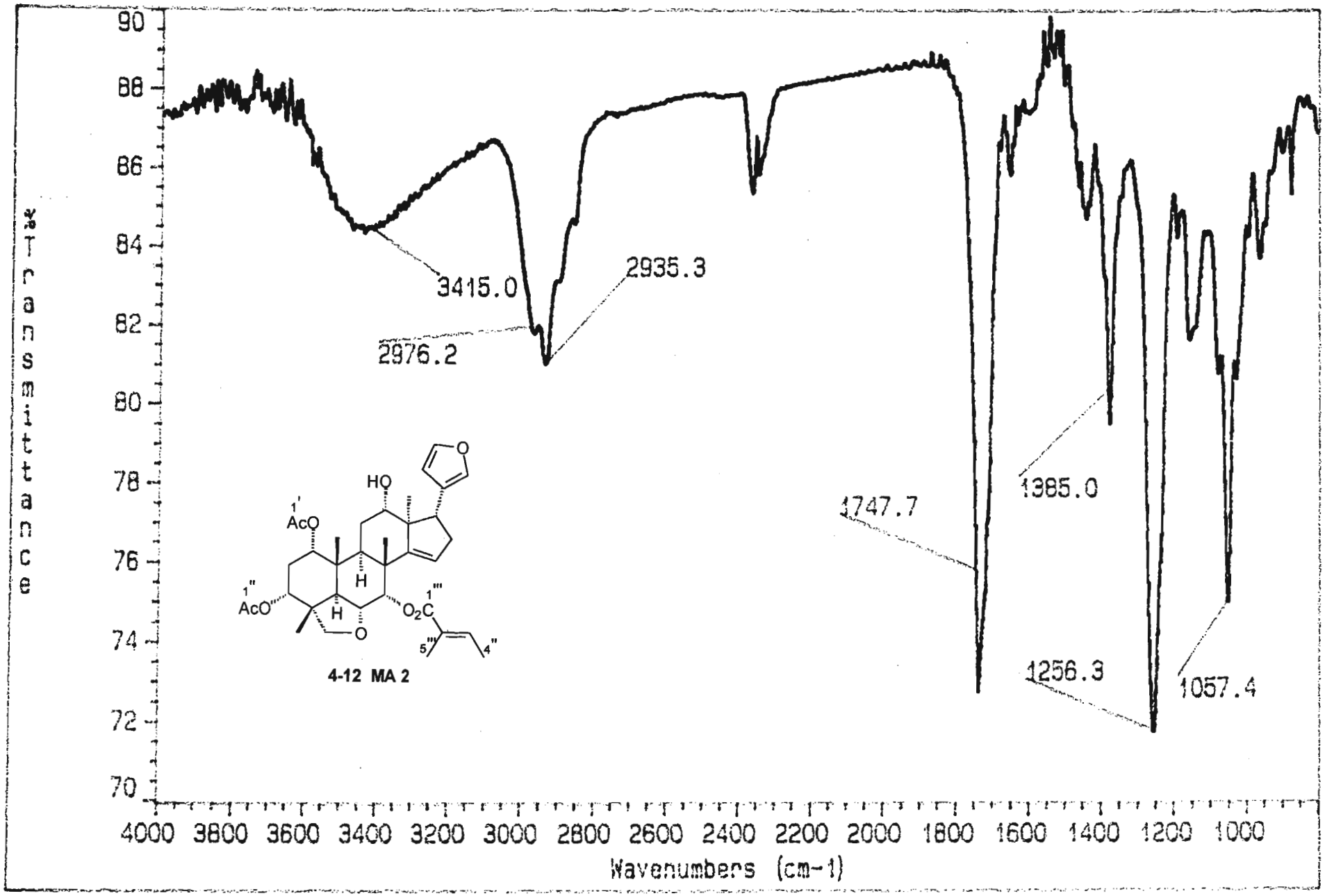
mix=1sec
probe=5mmASW
Pulse Sequence: noesy_da



4-12 MA 2



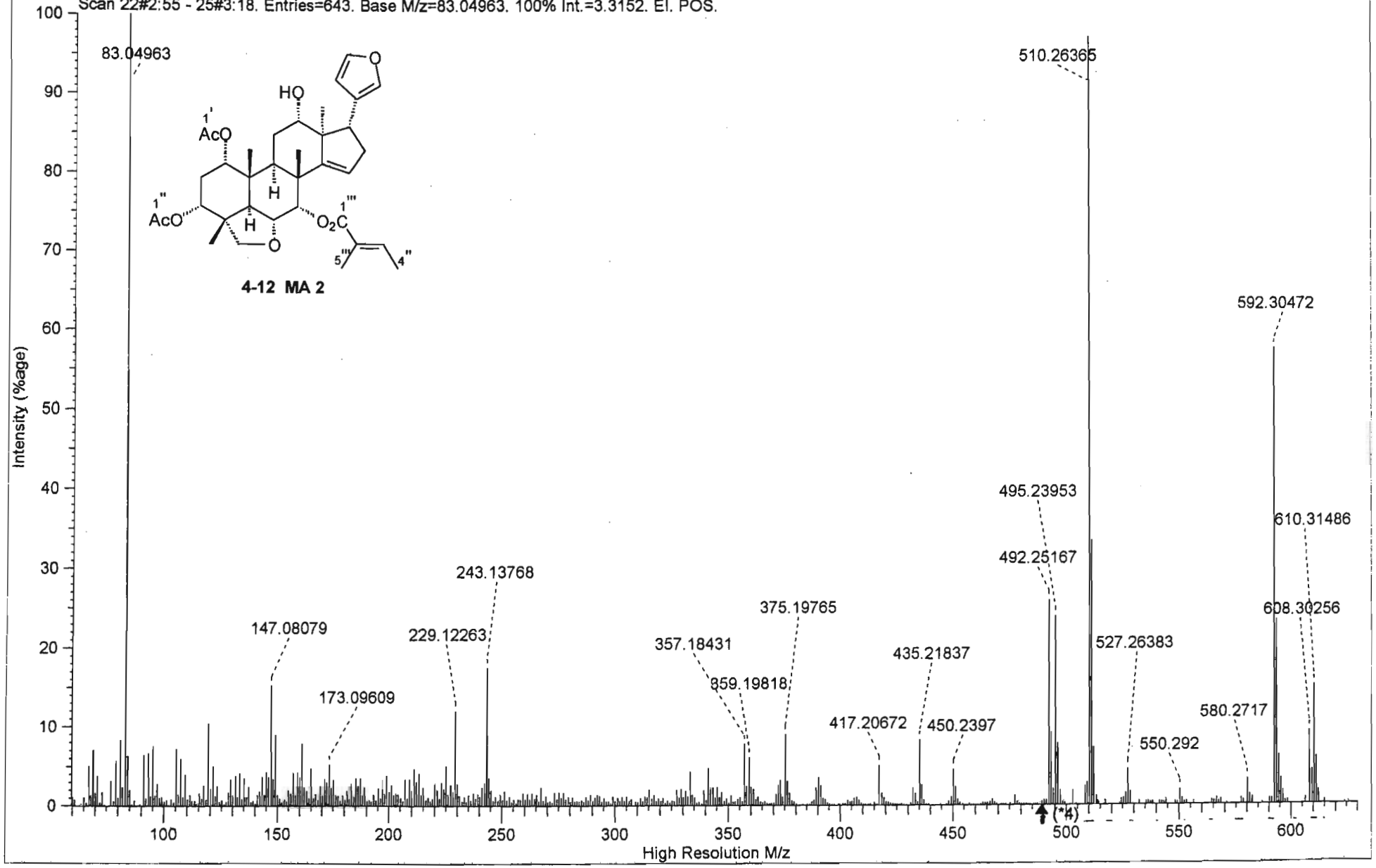
Spectrum MA 2.8: NOESY Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2



Spectrum MA 2.9: IR Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

File Name : C:\MASPEC\data\hc051823.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : 9dx-17/25-24/30
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

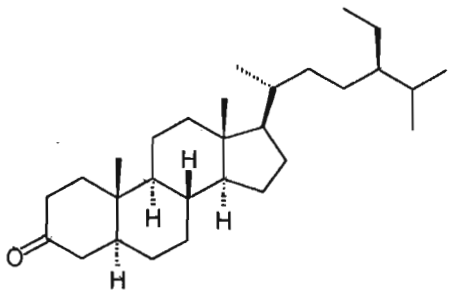
SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Range:0-620. Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 22#2:55 - 25#3:18. Entries=643. Base M/z=83.04963. 100% Int.=3.3152. EI. POS.



4-12 MA 2

Spectrum MA 2.10: High Resolution Mass Spectrum of 1,3-diacetyl-12α-hydroxy-7-tigloylvilasinin MA 2

Pulse Sequence: s2pul

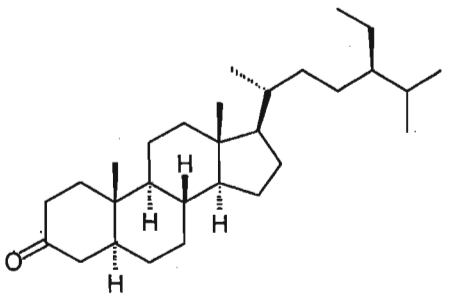


5-9 5α-stigmastan-3-one **SM 1**

Spectrum SM 1.1: ^{1}H NMR Spectrum of 5α-stigmastan-3-one SM 1

Pulse Sequence: s2pul

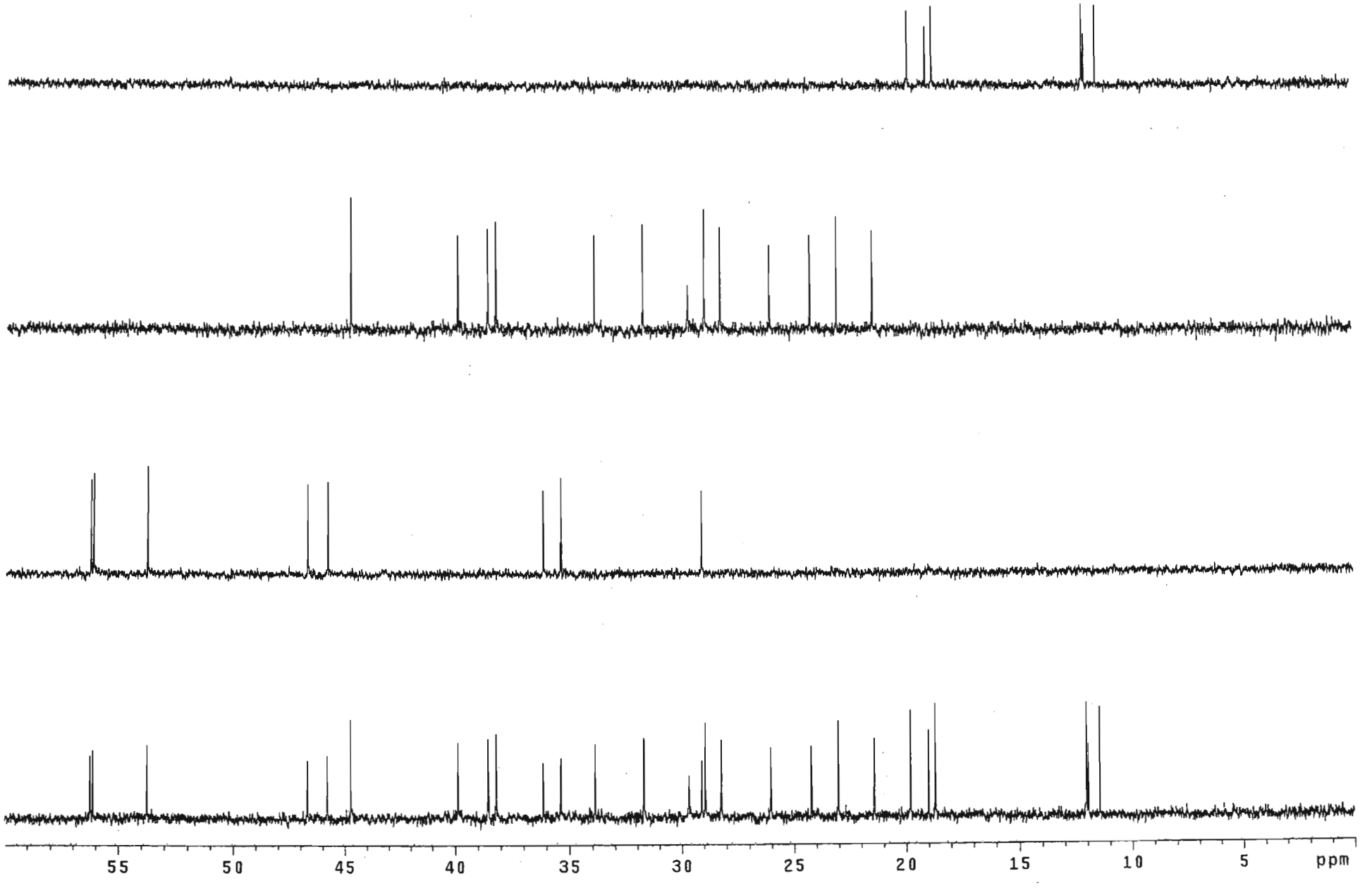
1	21350.097	212.300	8.1
2	7775.694	77.320	143.7
3	7764.158	77.205	10.1
4	7743.559	77.000	150.0
5	7711.423	76.680	144.2
6	5658.041	56.262	23.7
7	5645.682	56.139	21.2
8	5408.373	53.779	23.5
9	4696.446	46.700	28.1
10	4606.631	45.807	24.2
11	4498.688	44.734	27.6
12	4281.979	42.579	11.1
13	4010.886	39.883	24.3
14	3877.400	38.556	21.7
15	3841.145	38.195	23.8
16	3635.147	36.147	22.1
17	3583.236	35.631	18.8
18	3558.516	35.385	28.6
19	3407.726	33.886	22.6
20	3189.369	31.714	23.1
21	2985.844	29.690	12.9
22	2928.164	29.117	23.8
23	2912.508	28.961	28.9
24	2840.821	28.248	22.2
25	2619.168	26.044	26.0
26	2436.243	24.225	23.6
27	2316.764	23.037	23.6
28	2155.262	21.431	24.6
29	1992.112	19.809	20.7
30	1911.361	19.006	18.7
31	1881.698	18.711	25.6
32	1211.794	12.050	21.5
33	1202.730	11.960	18.8
34	1151.643	11.452	18.0



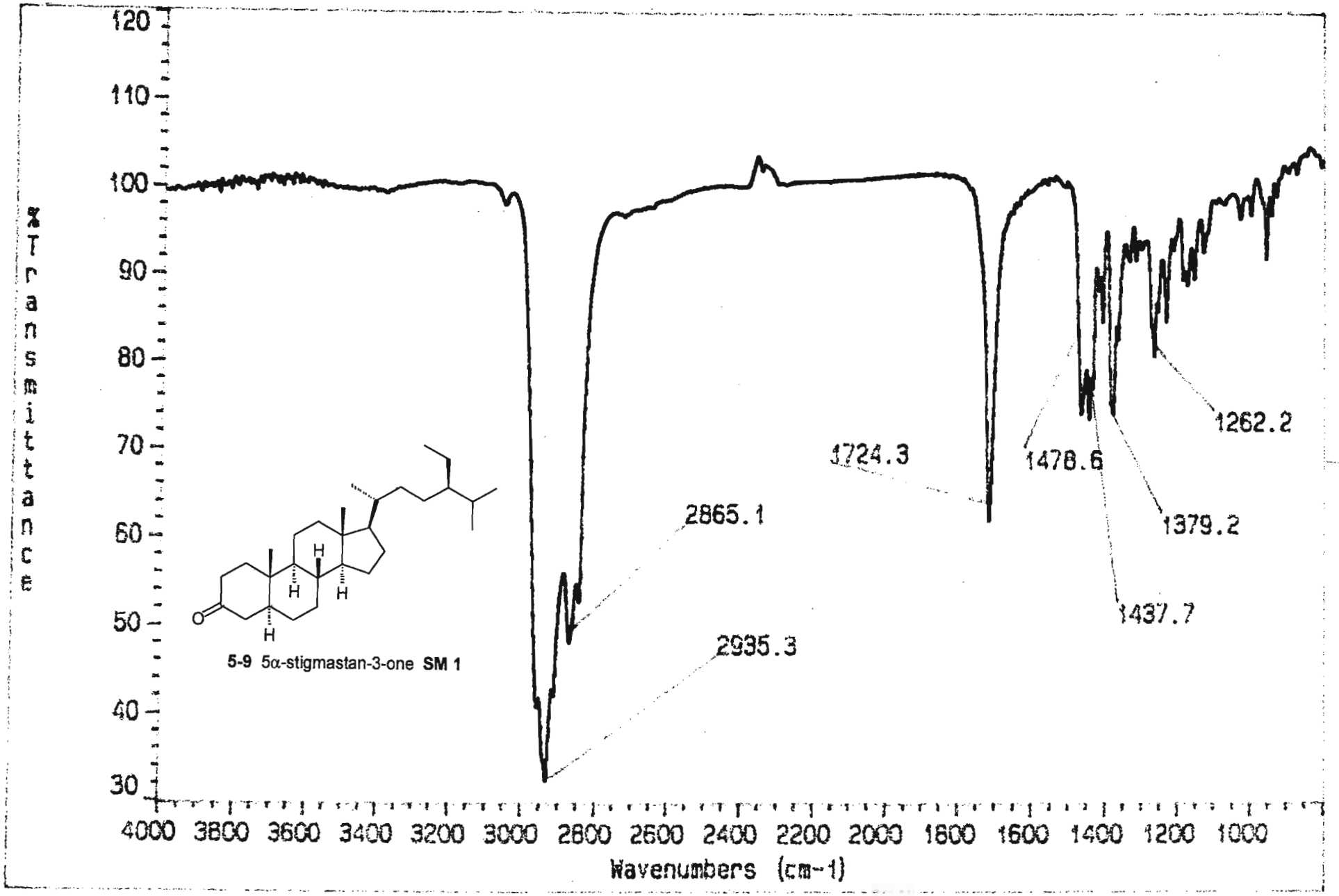
5-9 5α-stigmastan-3-one **SM 1**

Spectrum SM 1.2: ^{13}C NMR Spectrum of 5α-stigmastan-3-one SM 1

Pulse Sequence: dept



Spectrum SM 1.3: ADEPT Spectrum of 5α-stigmastan-3-one SM 1



Spectrum SM 1.4: IR Spectrum of 5α-stigmastan-3-one SM 1

```
File        : D:\PHIL\7F1.D
Operator    : Bret
Acquired    : 20 Jun 2001  11:18     using AcqMethod NEW
Instrument :   Instrumen
Sample Name: 7FL 6/7
Misc Info   : 1ul inject, 1:75 split, MeOH, 20dpm
Vial Number: 60
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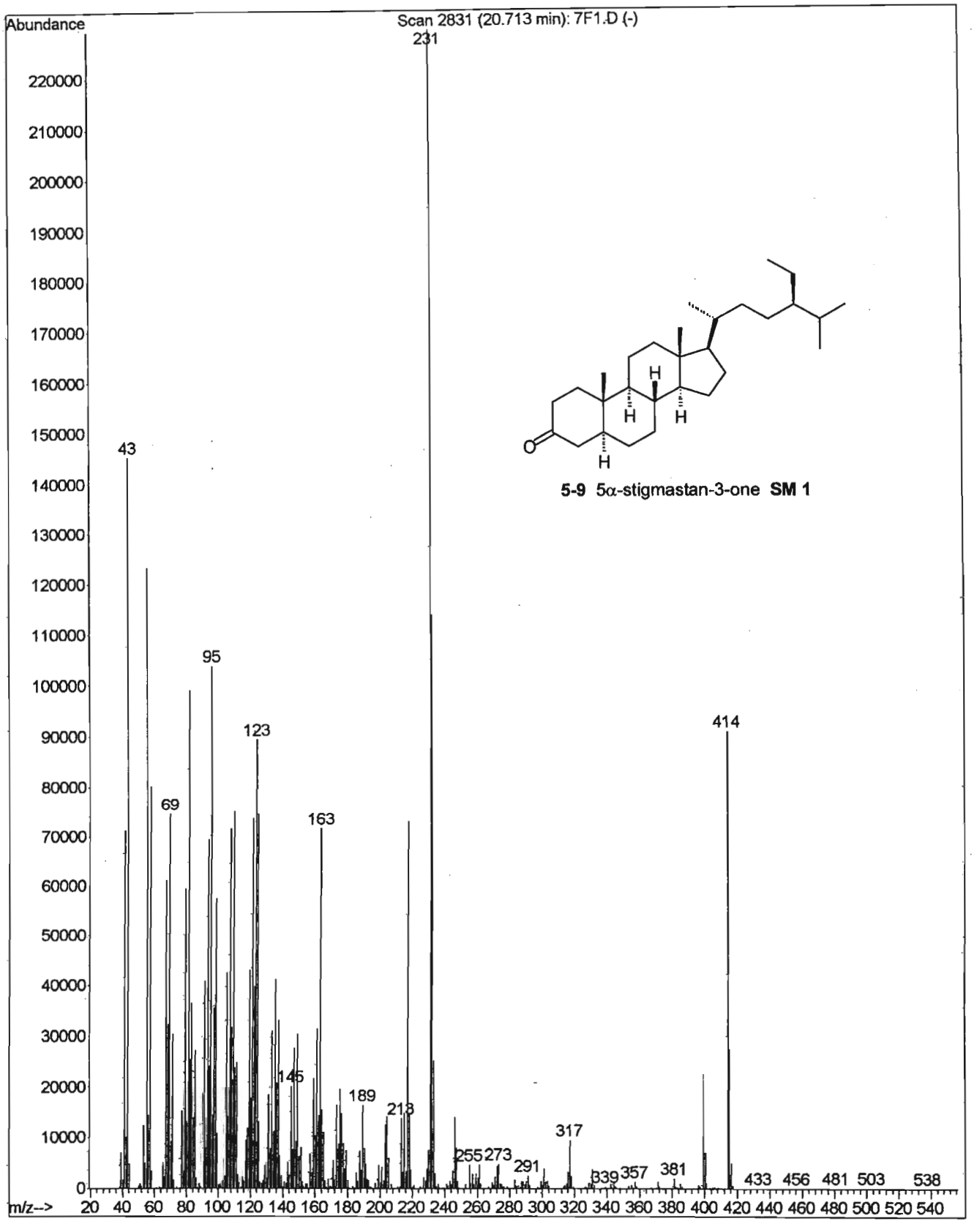
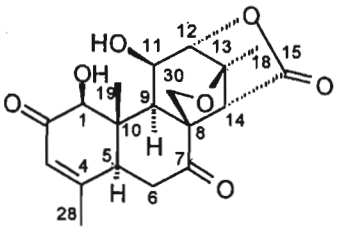


5-9 5α-stigmastan-3-one **SM 1**

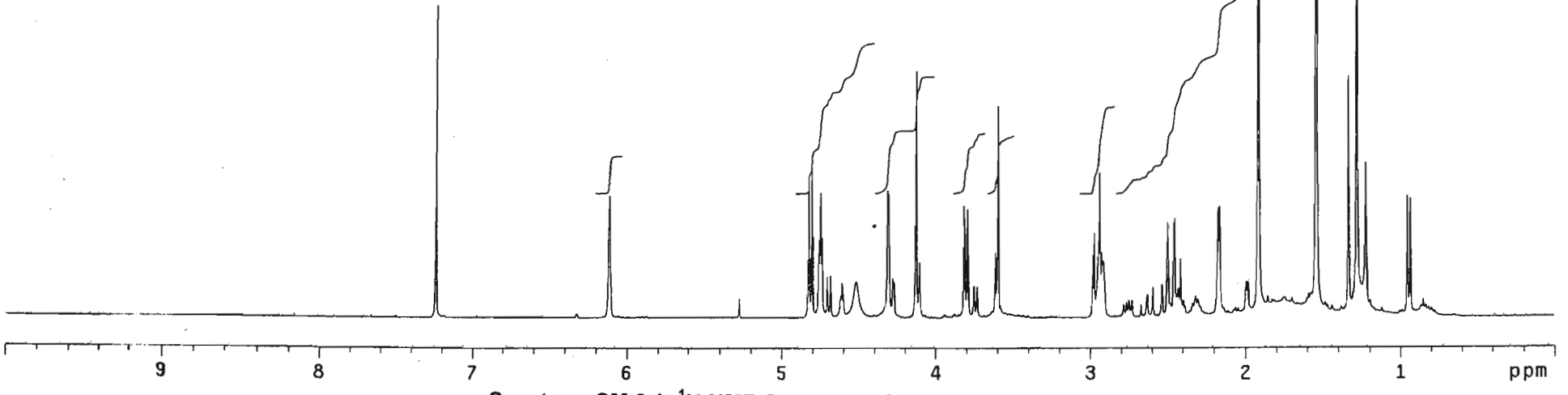
Spectrum SM 1.5: Mass Spectrum of 5α-stigmastan-3-one SM 1

Pulse Sequence: s2pul

1	2895.586	7.240	49.9	40	767.073	1.918	101.1
2	2446.003	6.116	19.7	41	617.823	1.545	150.0
3	1931.044	4.828	22.8	42	615.625	1.539	62.8
4	1922.803	4.808	23.9	43	534.682	1.337	38.9
5	1904.673	4.762	12.6	44	513.622	1.284	140.5
6	1900.827	4.753	20.2	45	490.731	1.227	24.9
7	1896.798	4.743	12.9	46	382.868	0.957	19.7
8	1882.697	4.707	6.7	47	375.176	0.938	19.2
9	1874.273	4.686	6.8				
10	1845.156	4.614	5.6				
11	1808.164	4.521	5.7				
12	1726.305	4.316	20.5				
13	1723.009	4.308	19.9				
14	1712.570	4.282	6.3				
15	1709.457	4.274	5.8				
16	1651.222	4.129	39.6				
17	1641.516	4.104	8.9				
18	1527.426	3.819	18.0				
19	1519.002	3.798	17.4				
20	1502.155	3.756	5.1				
21	1493.914	3.735	4.9				
22	1446.117	3.616	10.5				
23	1439.341	3.599	34.1				
24	1193.948	2.985	10.0				
25	1189.736	2.975	13.6				
26	1175.818	2.940	23.3				
27	1171.423	2.929	10.5				
28	1167.577	2.919	9.1				
29	1038.105	2.596	4.9				
30	1015.397	2.539	5.3				
31	999.464	2.499	15.4				
32	984.448	2.461	15.3				
33	981.335	2.454	16.0				
34	972.361	2.431	4.6				
35	966.318	2.416	9.4				
36	869.443	2.174	17.7				
37	865.780	2.165	17.9				
38	798.572	1.997	5.7				
39	794.726	1.987	5.8				



5-1 samaderine B **SM 2**

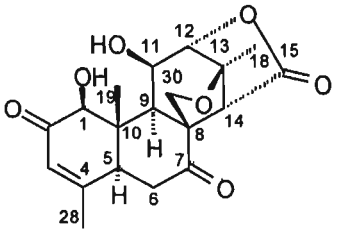


Spectrum SM 2.1: ^{1}H NMR Spectrum of samaderine B SM 2

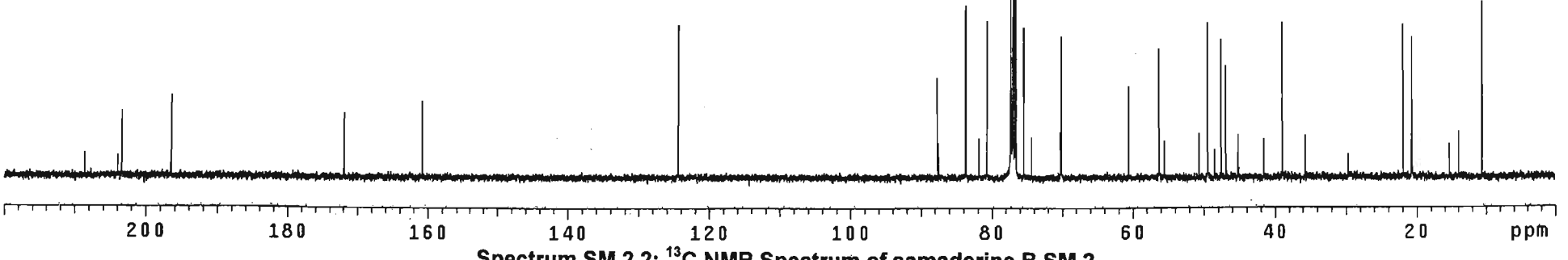
probe=5mmASW

Pulse Sequence: s2pul

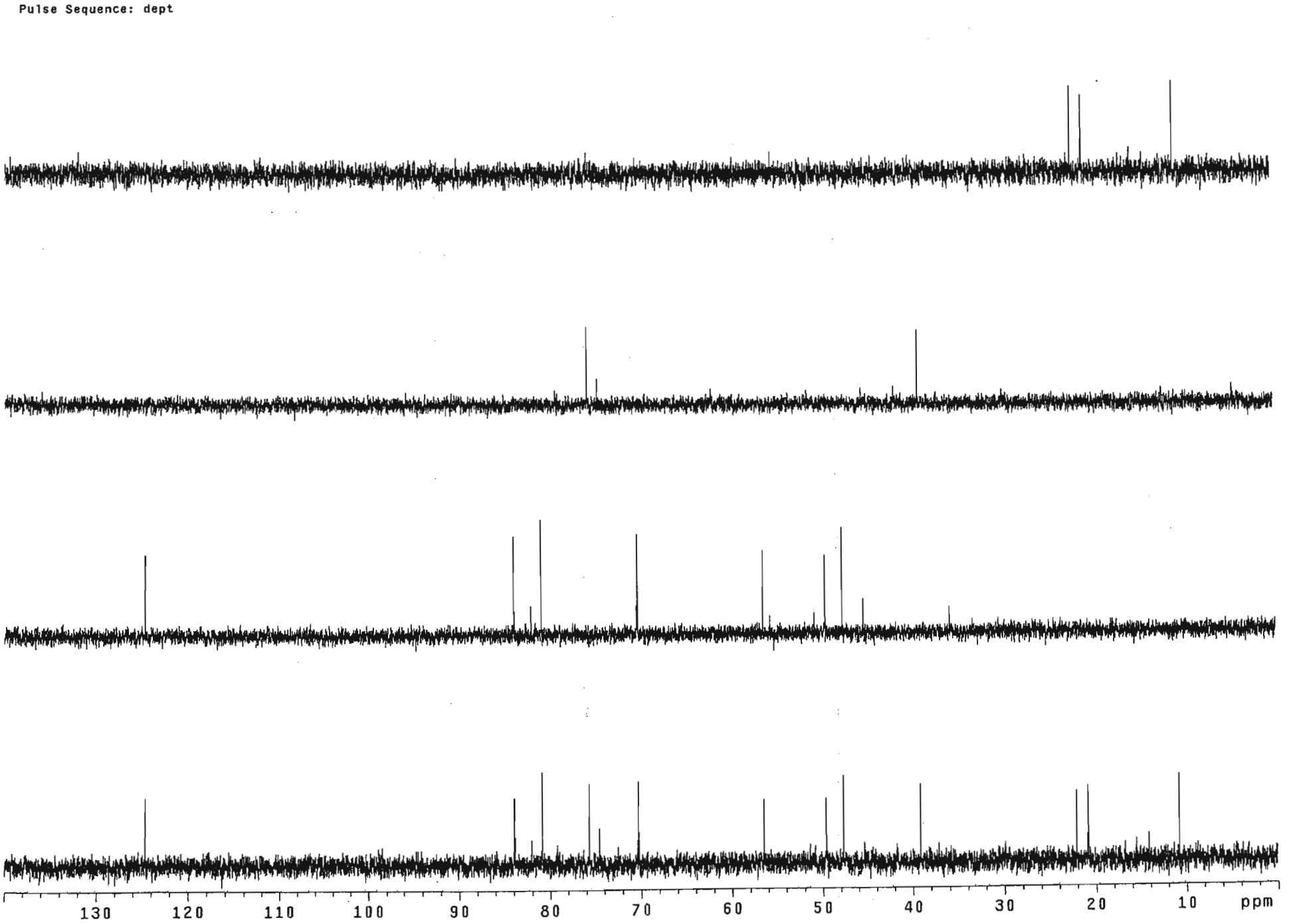
INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	20977.653	208.597	3.8	40	1401.312	13.934	7.4
2	20452.772	203.377	10.6	41	1063.476	10.575	28.1
3	19758.973	196.478	13.2				
4	17291.125	171.939	10.5				
5	16175.443	160.845	12.3				
6	12509.514	124.391	24.5				
7	8815.569	87.660	16.1				
8	8799.913	87.504	5.7				
9	8420.878	83.735	27.7				
10	8412.638	83.653	9.1				
11	8228.065	81.818	6.3				
12	8115.178	80.695	25.1				
13	7774.870	77.311	198.7				
14	7763.335	77.197	11.3				
15	7742.735	76.992	190.4				
16	7711.423	76.680	200.0				
17	7587.825	75.451	24.1				
18	7476.586	74.345	6.6				
19	7061.296	70.216	7.5				
20	7048.112	70.085	22.6				
21	6095.580	60.613	4.8				
22	6086.516	60.523	14.7				
23	5657.217	56.254	20.7				
24	5581.410	55.500	5.9				
25	5087.841	50.592	7.2				
26	4967.538	49.396	24.9				
27	4871.956	48.445	4.5				
28	4778.021	47.511	22.1				
29	4715.398	46.889	18.0				
30	4544.832	45.193	6.9				
31	4539.064	45.135	6.4				
32	4180.628	41.571	6.3				
33	3914.480	38.925	24.8				
34	3584.884	35.647	6.9				
35	2983.372	29.666	3.8				
36	2201.406	21.890	24.4				
37	2082.751	20.710	5.9				
38	2072.863	20.612	22.4				
39	1543.038	15.344	5.5				



5-1 samaderine B **SM 2**



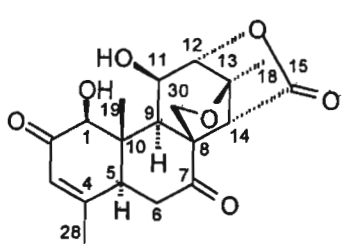
Spectrum SM 2.2: ^{13}C NMR Spectrum of samaderine B SM 2



Spectrum SM 2.3: ADEPT Spectrum of samaderine B SM 2

HQ/f1a./F1-12/19-1a in cdcl3
Gradient HSQC expt.
with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

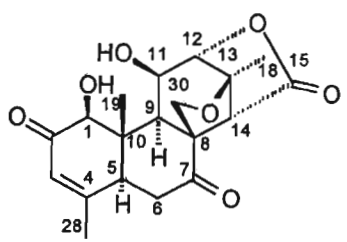


5-1 samaderine B **SM 2**

Spectrum SM 2.4: HSQC Spectrum of samaderine B SM 2

probe=5mmASW

Pulse Sequence: ghmqc_da

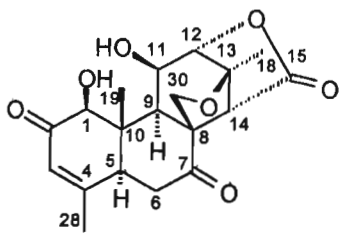


5-1 samaderine B **SM 2**

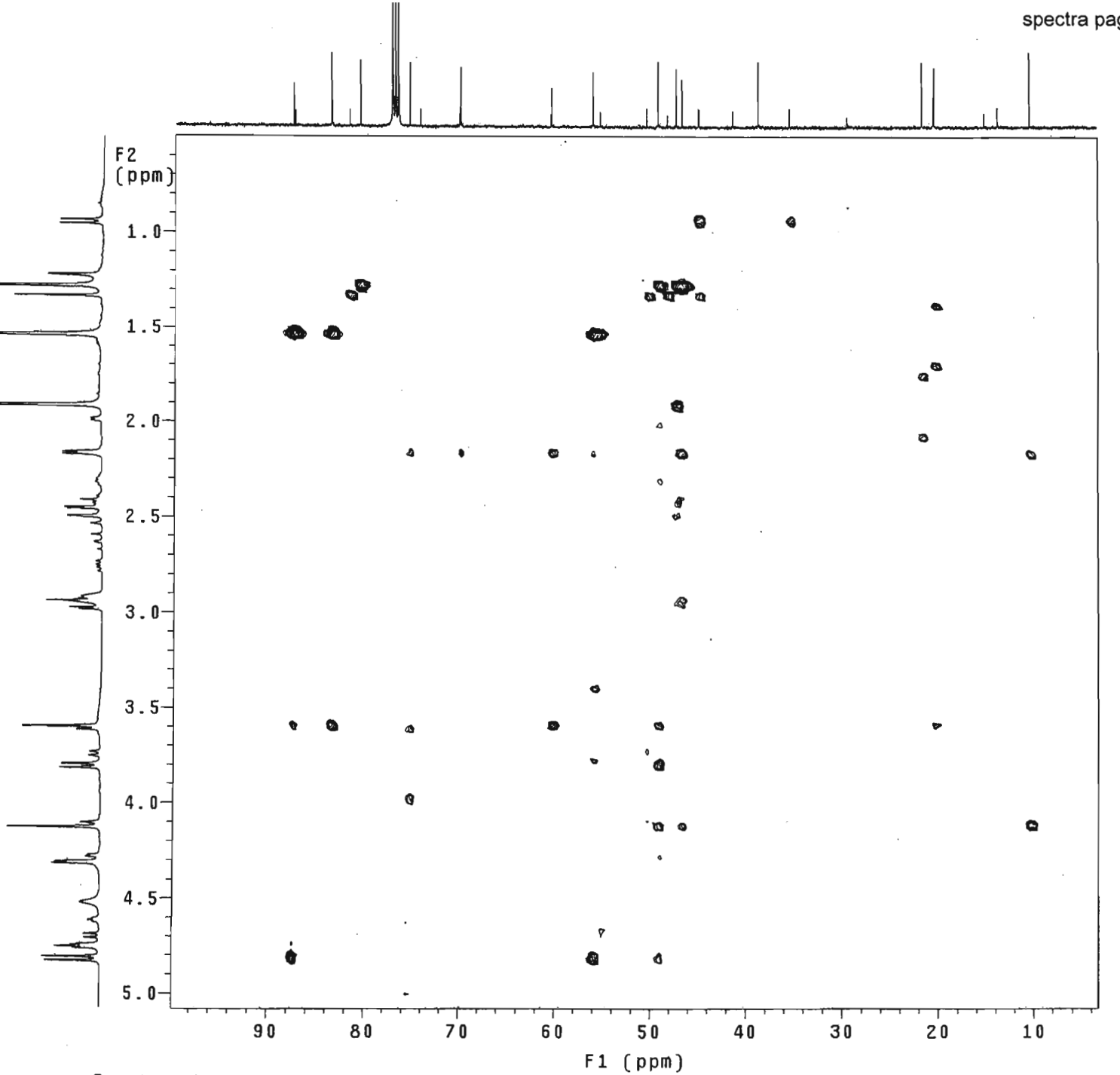
Spectrum SM 2.5: HMBC Spectrum of samaderine B SM 2

probe=5mmASW

Pulse Sequence: ghmqc_da



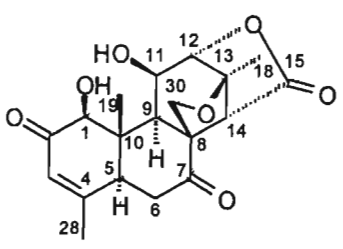
5-1 samaderine B **SM 2**



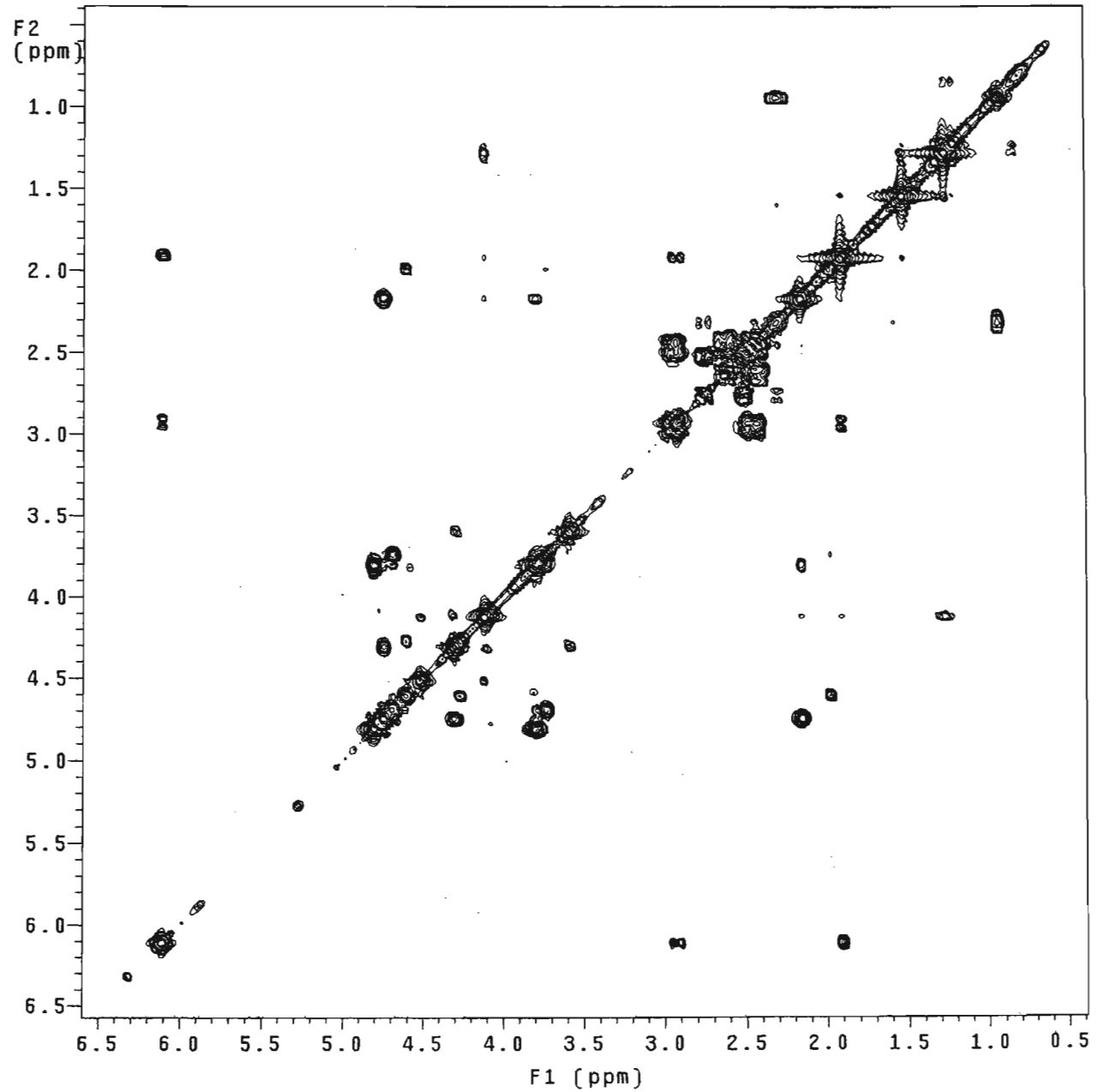
Spectrum SM 2.6: Expanded HMBC Spectrum of samaderine B SM 2

probe=5mmASW

Pulse Sequence: relayh



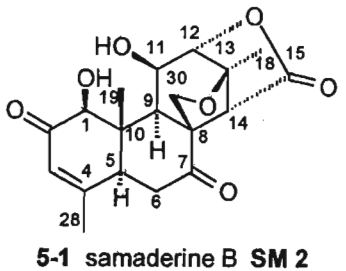
5-1 samaderine B **SM 2**



Spectrum SM 2.7: COSY Spectrum of samaderine B SM 2

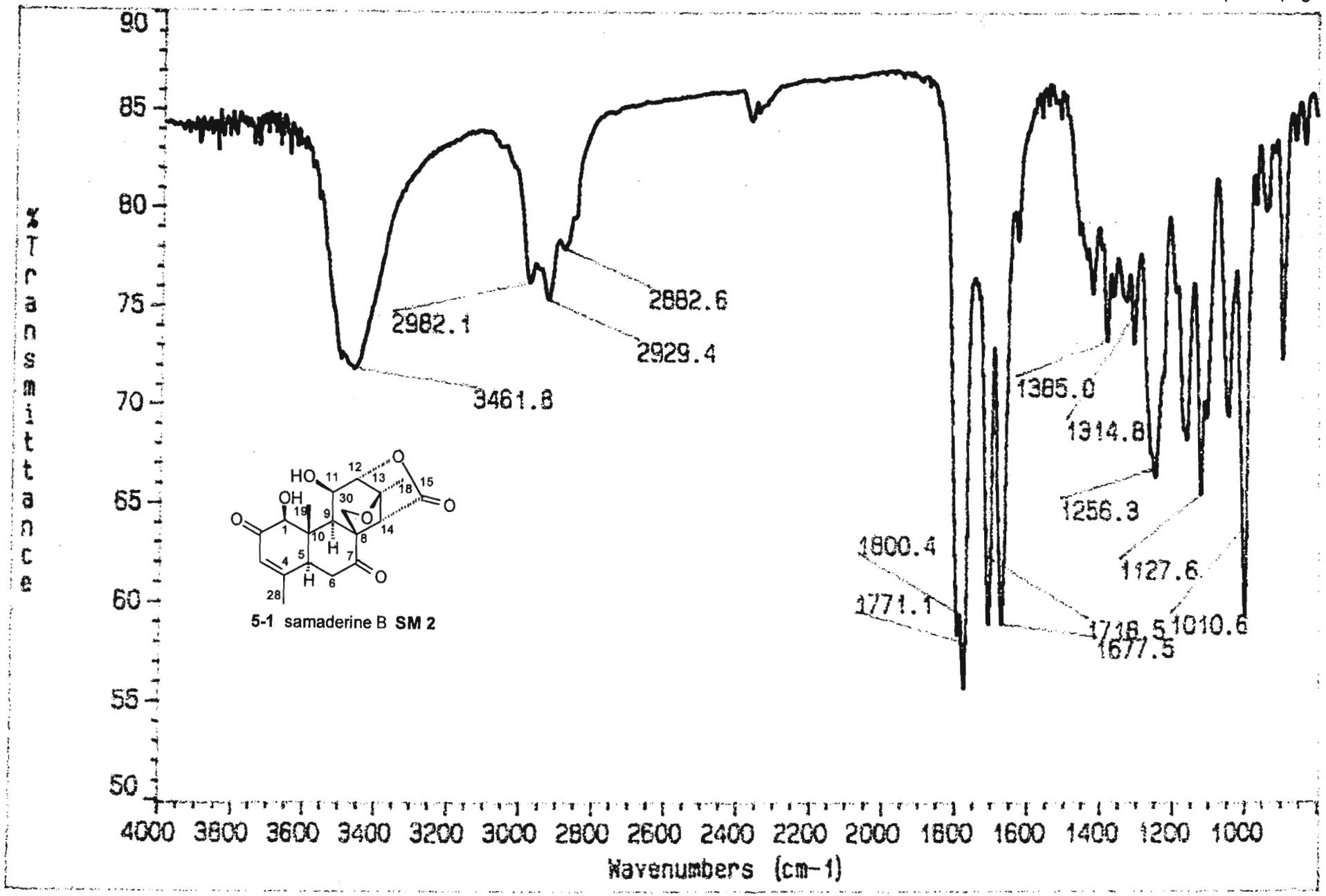
mix=1sec
probe=5mmASW

Pulse Sequence: noesy_da



5-1 samaderine B **SM 2**

Spectrum SM 2.8: NOESY Spectrum of samaderine B SM 2

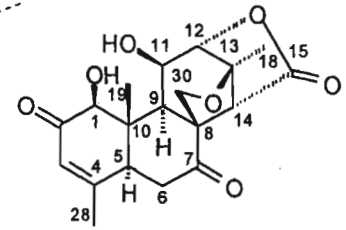


5-1 samaderine B **SM 2**

Spectrum SM 2.9: IR Spectrum of samaderine B SM 2

File Title : 7f1-12/19-1a
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

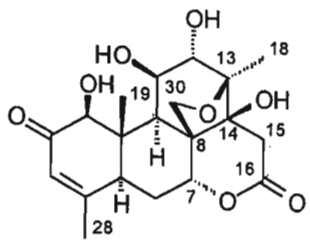
SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Int:0.2%. Range:0-365. Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 59#7:39 - 64#8:17. Sub=13#1:46,30#3:56 - 35#4:35,38#4:58 - 43#5:36,48#6:14 - 52#6:45. Entries=326. Base M/z=95.04982. 100%



5-1 samaderine B **SM 2**

Spectrum SM 2.10: High Resolution Mass Spectrum of samaderine B SM 2

Pulse Sequence: s2pul

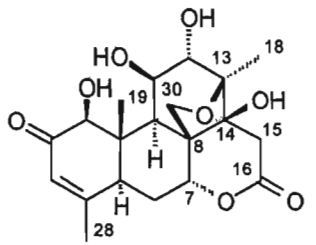


5-8 samaderine E **SM 3**

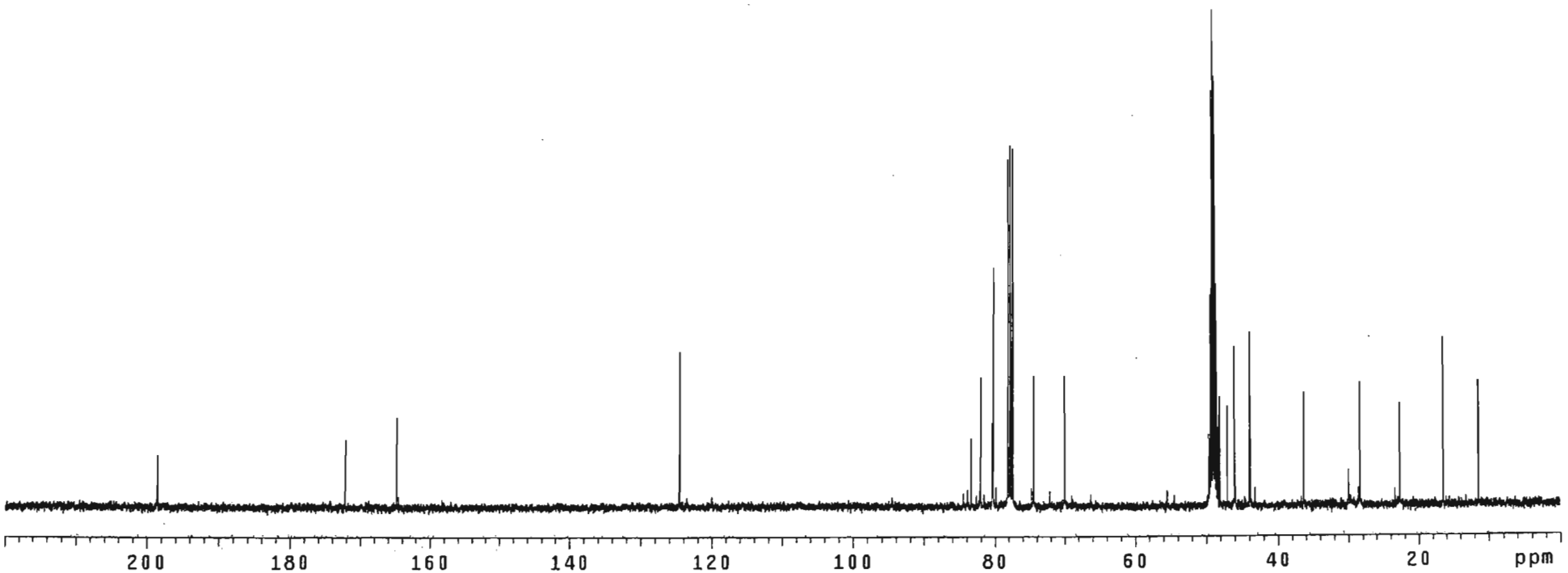
Spectrum SM 3.1: ^{1}H NMR Spectrum of samaderine E SM 3

Pulse Sequence: s2pul

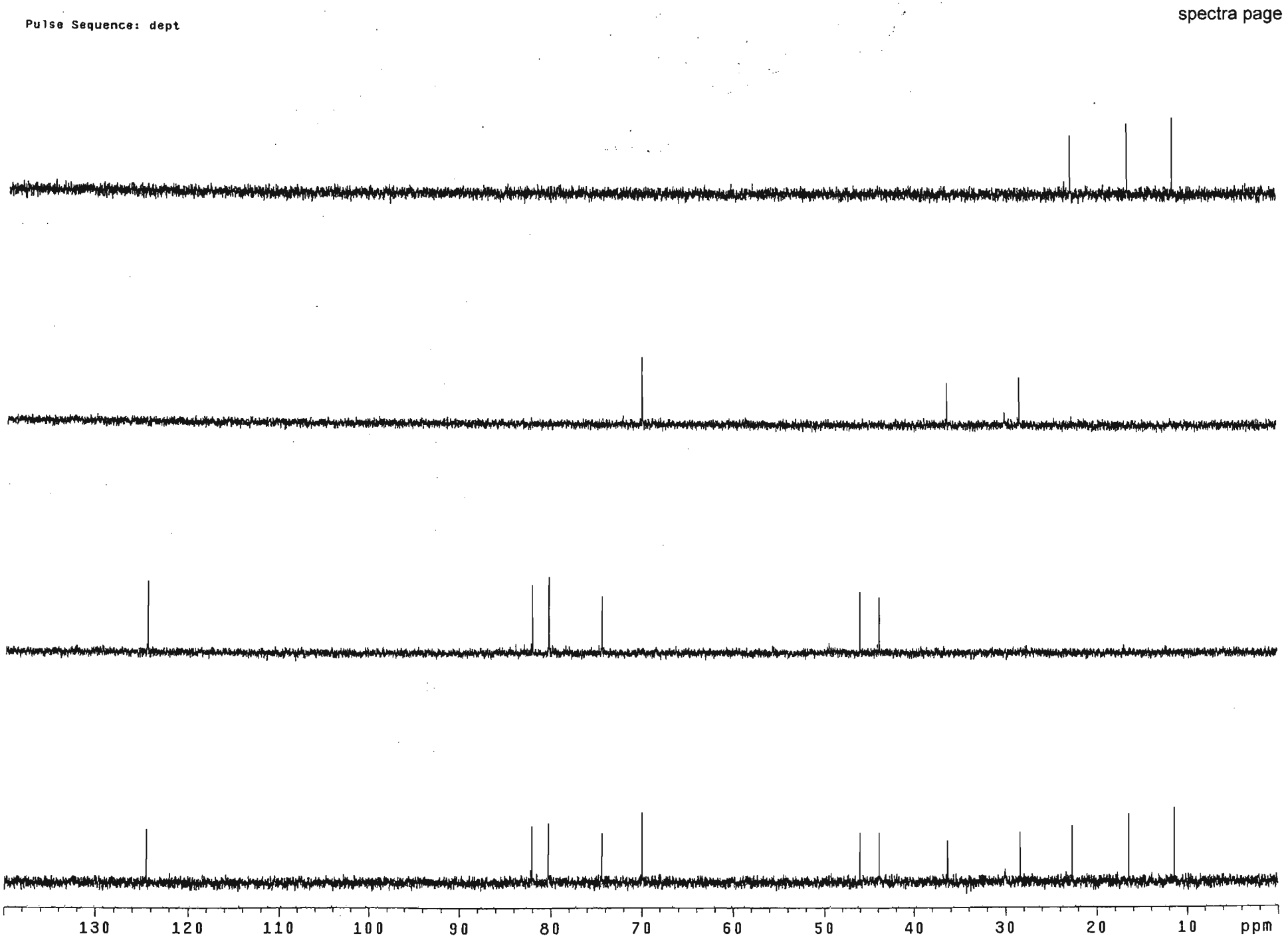
1	19964.720	198.523	8.4
2	17313.946	172.165	10.9
3	16576.475	164.832	14.4
4	12520.799	124.503	25.1
5	8382.724	83.355	11.0
6	8249.238	82.028	20.8
7	8087.736	80.422	13.6
8	8071.256	80.258	38.4
9	7857.019	78.128	55.9
10	7824.883	77.808	58.1
11	7792.748	77.489	57.5
12	7483.752	74.416	21.1
13	7036.325	69.967	21.2
14	4992.007	49.639	11.6
15	4970.584	49.426	34.1
16	4949.160	49.213	66.9
17	4926.912	48.992	80.0
18	4905.489	48.779	69.3
19	4884.065	48.566	35.8
20	4862.641	48.353	12.7
21	4839.569	48.123	17.6
22	4728.331	47.017	16.1
23	4629.452	46.034	25.7
24	4412.743	43.879	28.0
25	3651.377	36.308	18.4
26	2855.403	28.393	20.0
27	2282.730	22.699	16.5
28	1657.322	16.480	27.1
29	1148.921	11.425	20.1



5-8 samaderine E **SM 3**



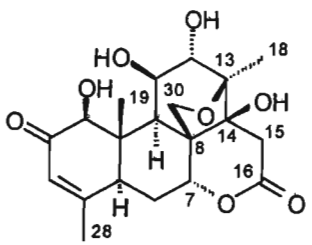
Spectrum SM 3.2: ^{13}C NMR Spectrum of samaderine E SM 3



Spectrum SM 3.3: ADEPT Spectrum of samaderine E SM 3

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

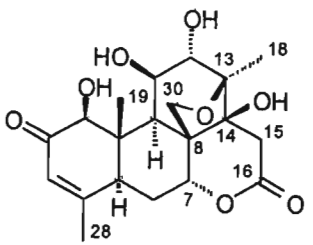


5-8 samaderine E **SM 3**

Spectrum SM 3.4: HSQC Spectrum of samaderine E SM 3

probe=5mmASW

Pulse Sequence: ghmqc_da

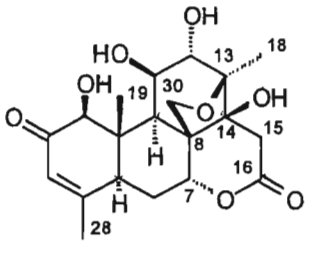


5-8 samaderine E **SM 3**

Spectrum SM 3.5: HMBC Spectrum of samaderine E SM 3

probe=5mmASW

Pulse Sequence: ghmqc_da



5-8 samaderine E **SM 3**

F2 (ppm)

1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0

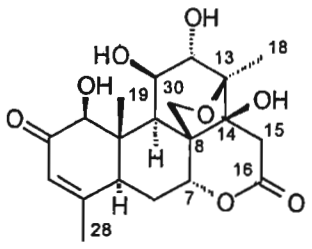
80 70 60 50 40 30 20 10

F1 (ppm)

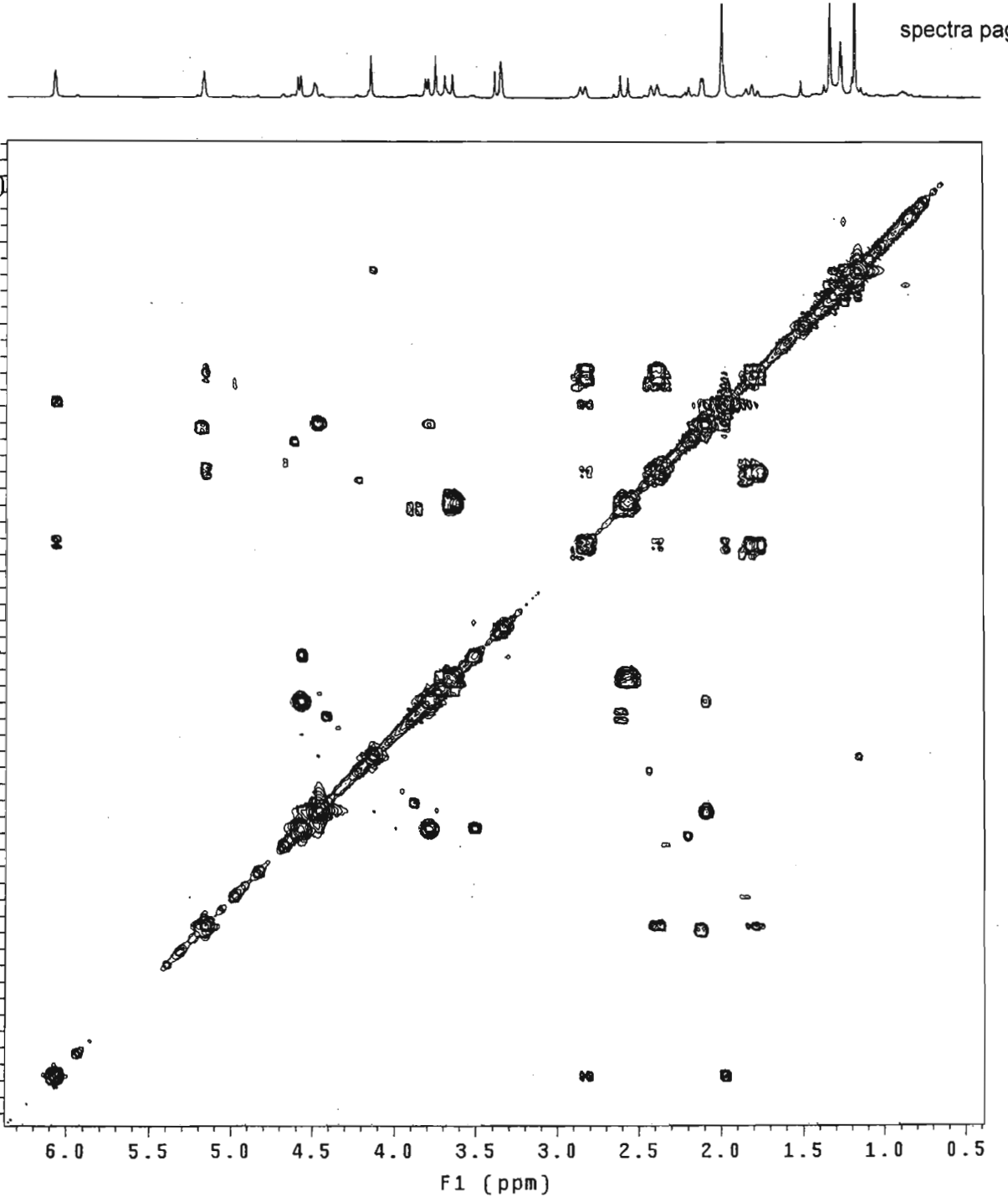
Spectrum SM 3.6: Expanded HMBC Spectrum of samaderine E SM 3

probe=5mmASW

Pulse Sequence: relayh



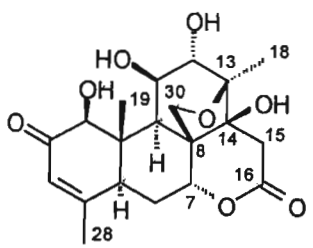
5-8 samaderine E **SM 3**



Spectrum SM 3.7: COSY Spectrum of samaderine E SM 3

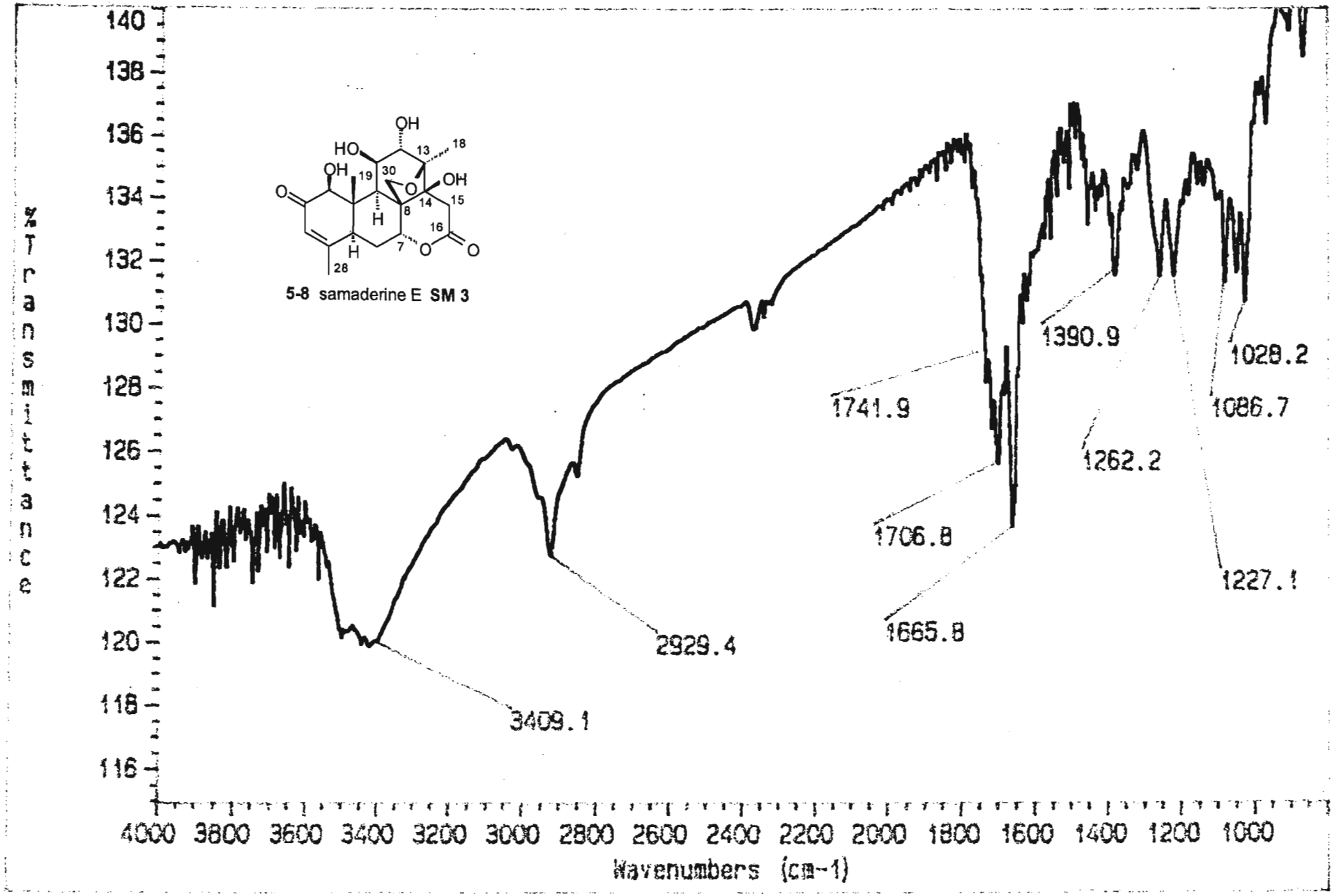
gradient NOESY expt.
using presat_h2o
mix=1sec
probe=5mmASW

Pulse Sequence: noesy_da



5-8 samaderine E **SM 3**

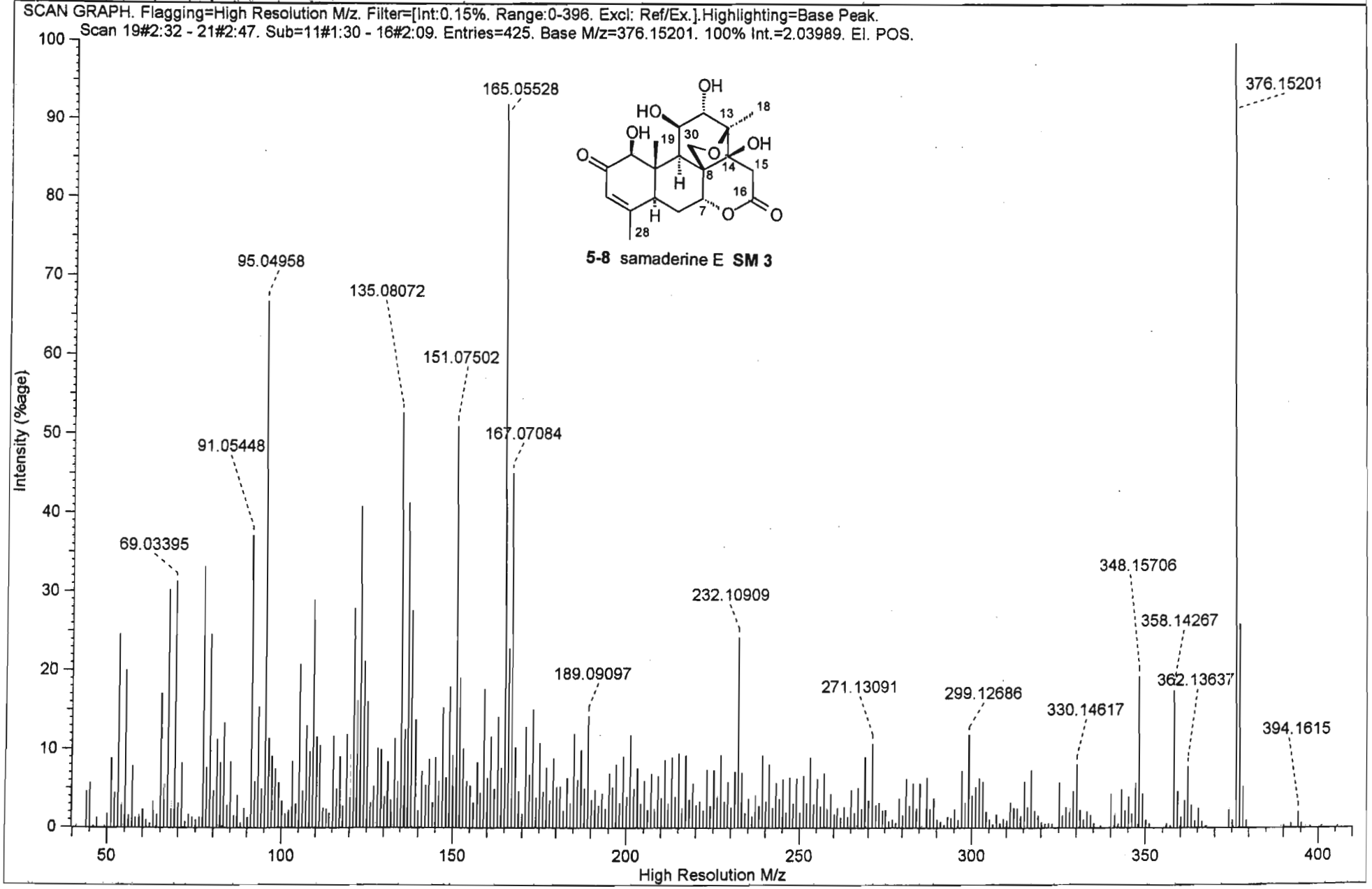
Spectrum SM 3.8: NOESY Spectrum of samaderine E SM 3



5-8 samaderine E **SM 3**

Spectrum SM 3.9: IR Spectrum of samaderine E SM 3

File Name : C:\MASPEC\data\hc052108.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : 7f1-54/60c-1a
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

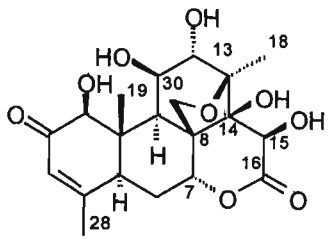


5-8 samaderine E **SM 3**

Spectrum SM 3.10: High Resolution Mass Spectrum of samaderine E SM 3

satpwr=-12
probe=5mmASW

Pulse Sequence: presat_da

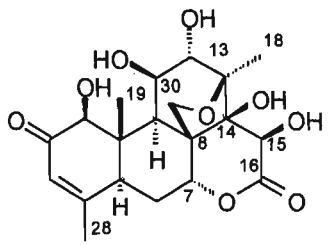


5-67 brucein D **SM 4**

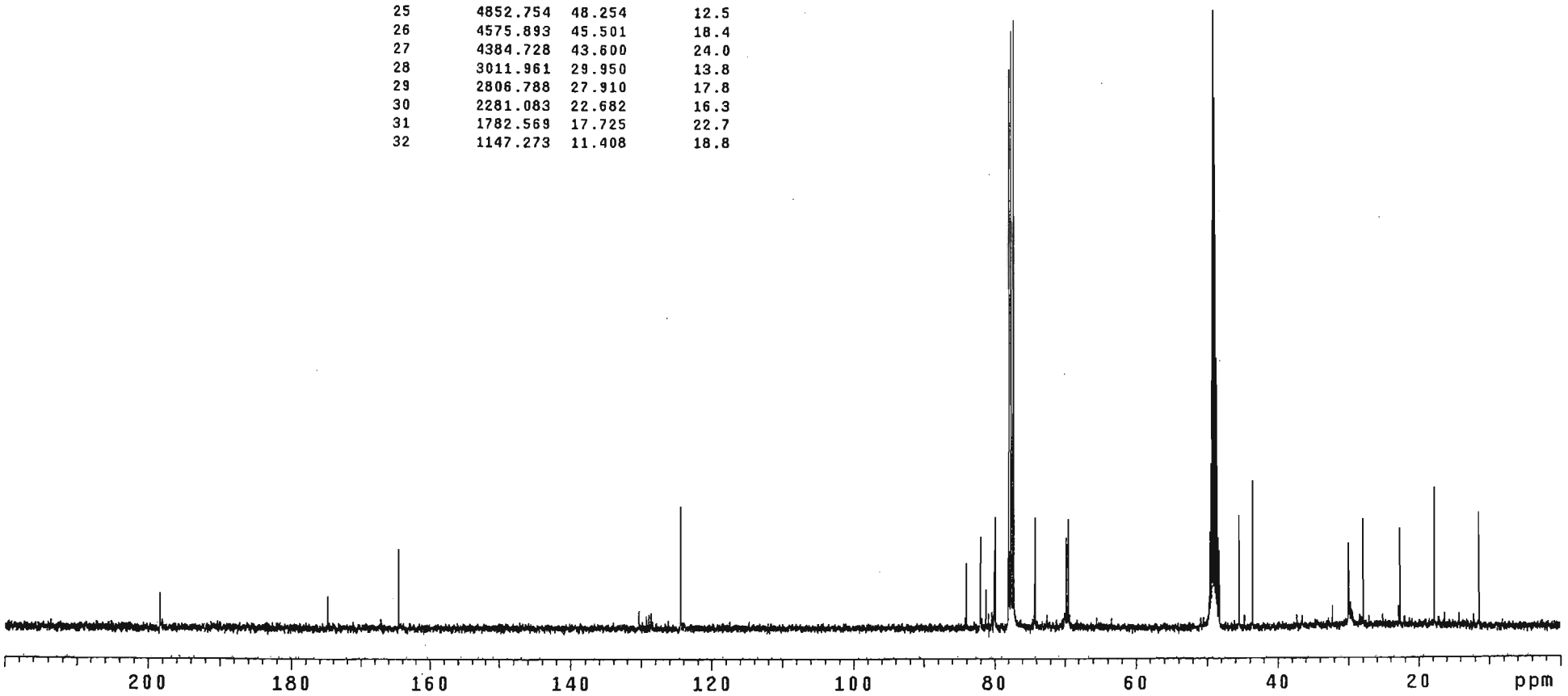
Spectrum SM 4.1: ^{1}H NMR Spectrum of brucein D SM 4

Pulse Sequence: s2pul

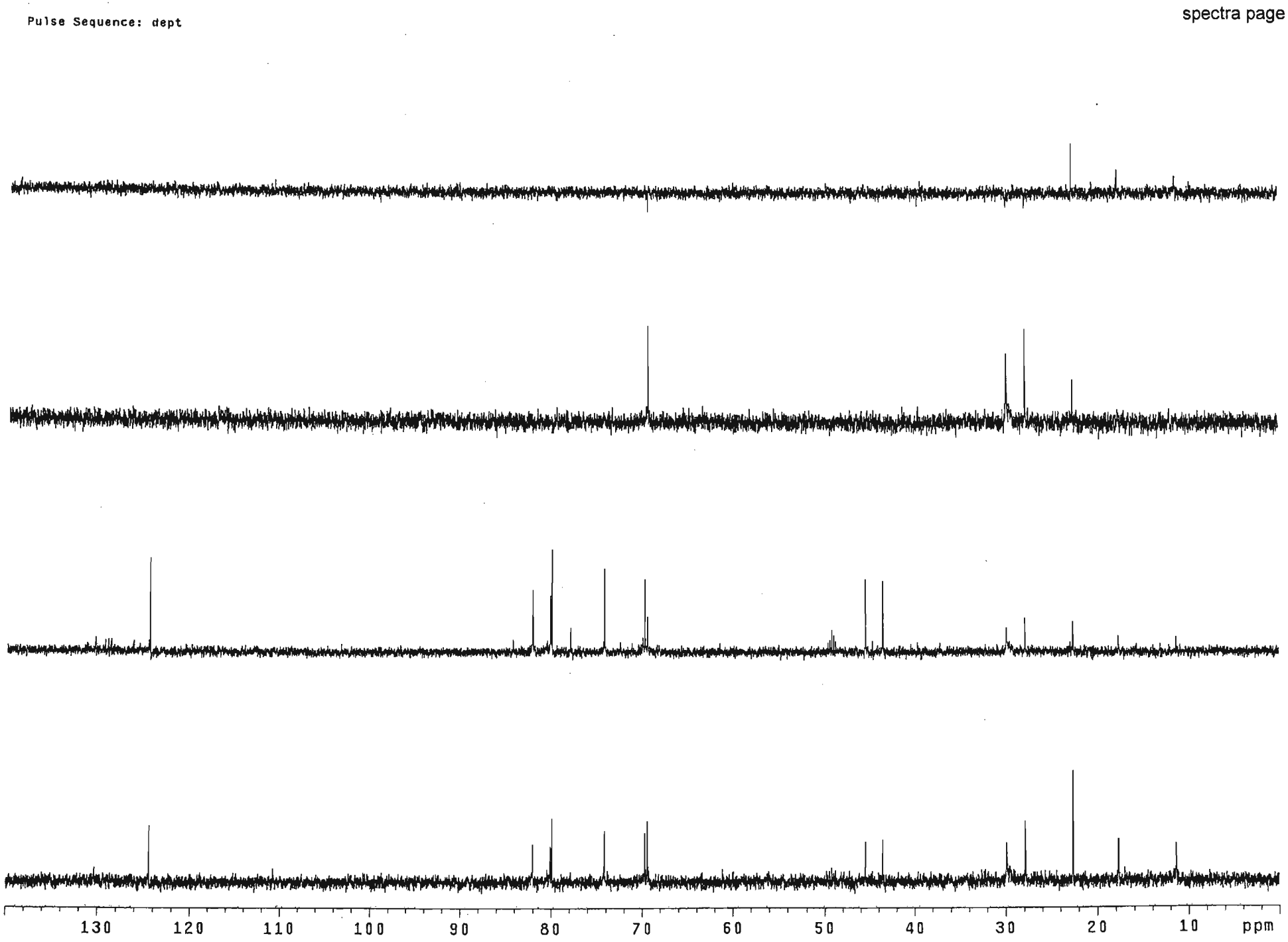
1	19948.240	198.360	5.7
2	17585.039	174.861	5.2
3	16550.932	164.578	12.9
4	12515.856	124.454	19.8
5	8449.468	84.019	10.7
6	8250.062	82.036	15.0
7	8172.607	81.266	6.2
8	8053.953	80.086	12.9
9	8036.649	79.914	18.1
10	7843.011	77.989	90.4
11	7830.651	77.866	9.5
12	7810.876	77.669	96.5
13	7778.740	77.350	98.4
14	7459.856	74.179	18.1
15	7015.726	69.762	14.8
16	6984.414	69.451	17.8
17	4992.008	49.639	15.8
18	4987.064	49.590	13.8
19	4970.584	49.426	42.9
20	4949.160	49.213	84.3
21	4927.737	49.000	100.0
22	4906.313	48.787	85.7
23	4884.889	48.574	43.5
24	4863.465	48.361	14.8
25	4852.754	48.254	12.5
26	4575.893	45.501	18.4
27	4384.728	43.600	24.0
28	3011.961	29.950	13.8
29	2806.788	27.910	17.8
30	2281.083	22.682	16.3
31	1782.569	17.725	22.7
32	1147.273	11.408	18.8



5-67 brucein D **SM 4**



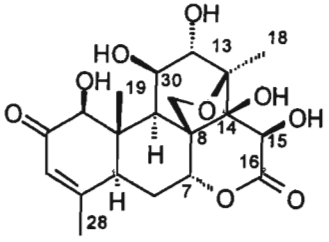
Spectrum SM 4.2: ^{13}C NMR Spectrum of brucein D SM 4



Spectrum SM 4.3: ADEPT Spectrum of brucein D SM 4

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

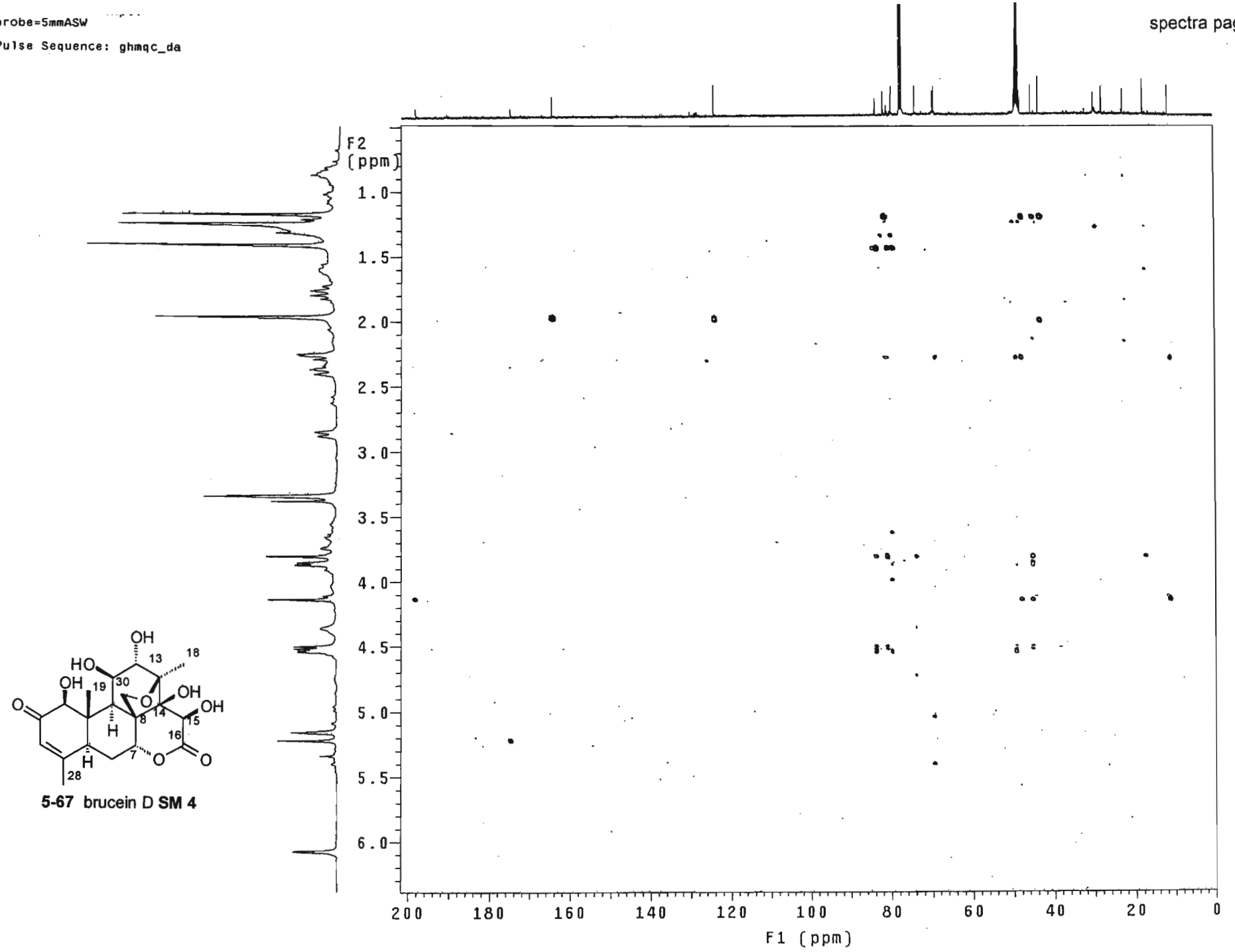


5-67 brucein D **SM 4**

Spectrum SM 4.4: HSQC Spectrum of brucein D SM 4

probe=5mmASW

Pulse Sequence: ghmqc_da

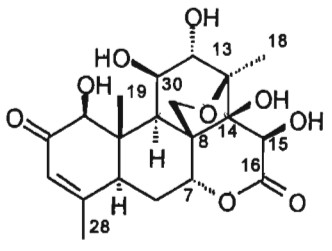


5-67 brucein D **SM 4**

Spectrum SM 4.5: HMBC Spectrum of brucein D SM 4

probe=5mmASW

Pulse Sequence: ghmqc_da

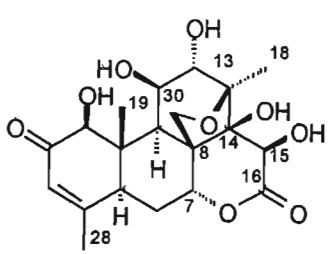


5-67 brucein D **SM 4**

Spectrum SM 4.6: Expanded HMBC Spectrum of brucein D SM 4

probe=5mmASW

Pulse Sequence: relayh

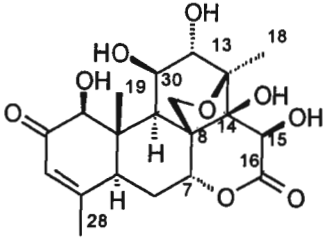


5-67 brucein D **SM 4**

Spectrum SM 4.7: COSY Spectrum of brucein D SM 4

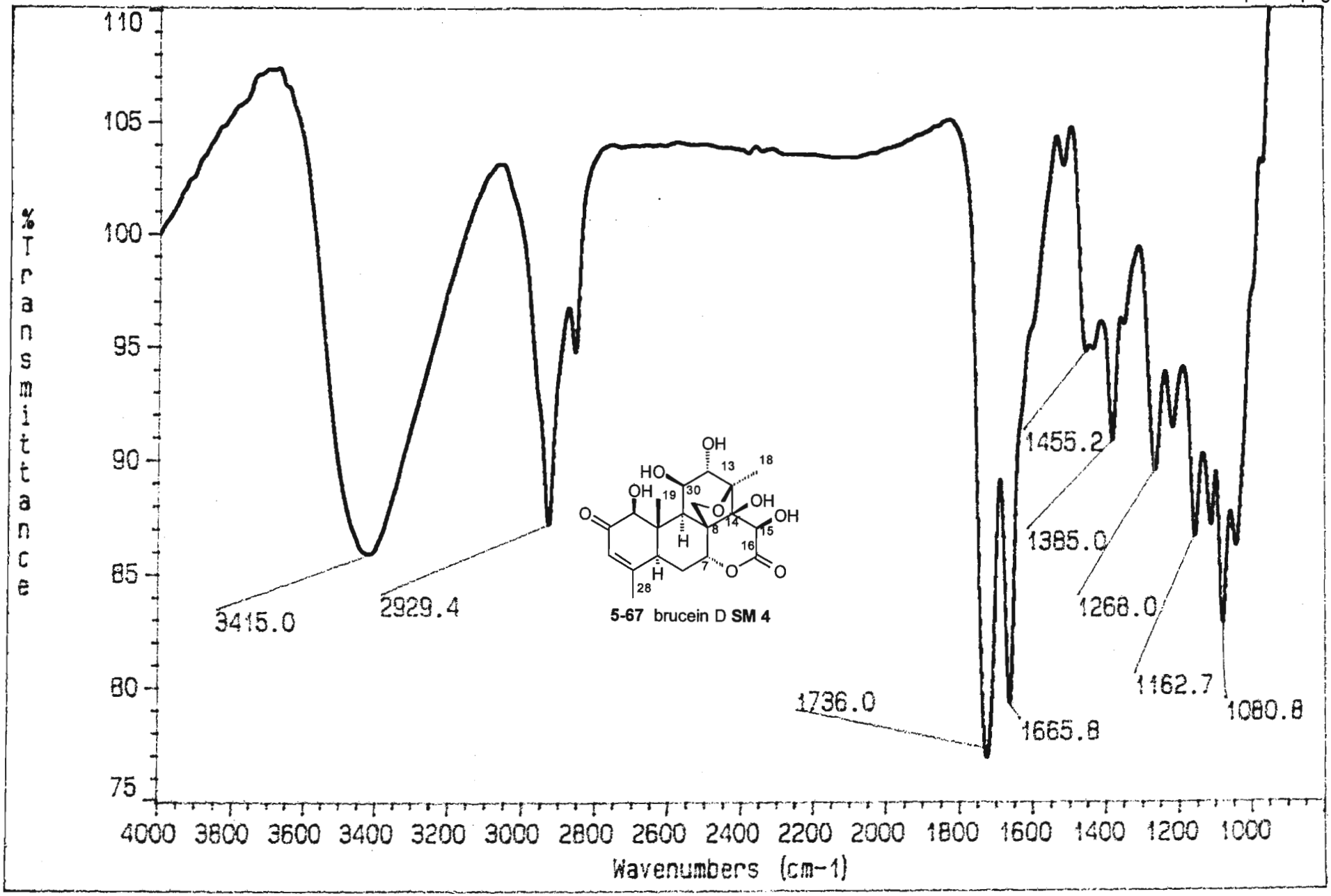
using presat_h2o
mix=1sec
probe=5mmASW

Pulse Sequence: noesy_da



5-67 brucein D **SM 4**

Spectrum SM 4.8: NOESY Spectrum of brucein D SM 4

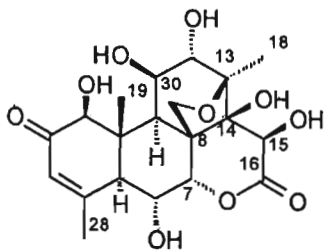


5-67 brucein D **SM 4**

Spectrum SM 4.9: IR Spectrum of brucein D SM 4

satpwr=-12
probe=5mmASW

Pulse Sequence: presat_da

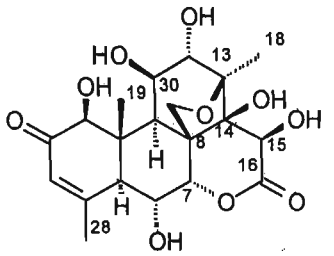


5-80 indaquassin X **SM 5**

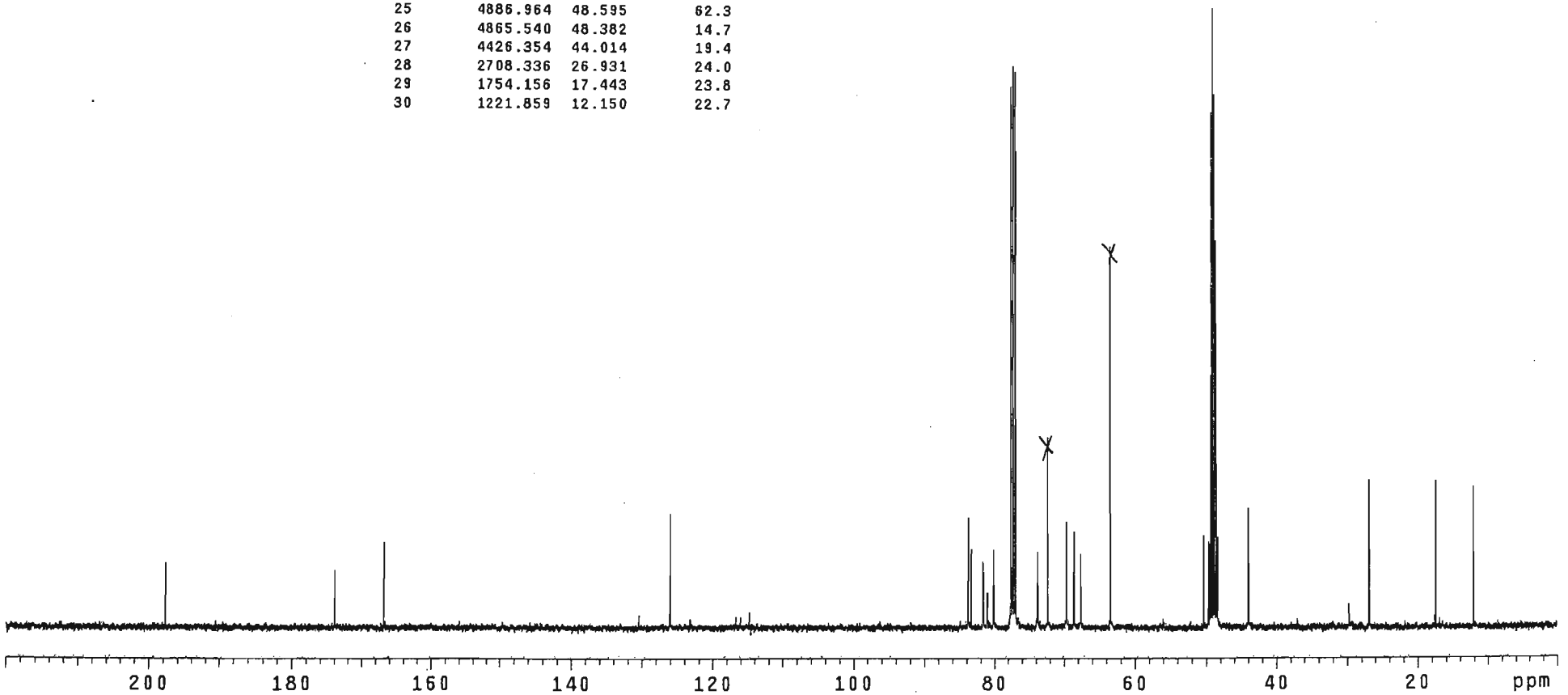
Spectrum SM 5.1: ^{1}H NMR Spectrum of indaquassin X SM 5

Pulse Sequence: s2pul

1	19884.396	197.725	10.5
2	17490.707	173.923	9.3
3	16777.956	166.835	13.9
4	12676.136	126.048	18.4
5	8430.942	83.835	17.9
6	8386.447	83.392	12.8
7	8215.057	81.688	10.8
8	8061.795	80.164	12.8
9	7813.774	77.698	87.1
10	7781.639	77.378	90.4
11	7749.503	77.059	89.6
12	7422.379	73.806	12.3
13	7278.181	72.372	30.9
14	7008.737	69.693	17.3
15	6902.442	68.636	15.7
16	6806.035	67.677	12.0
17	6384.977	63.490	61.3
18	5064.122	50.356	15.0
19	5000.674	49.725	14.1
20	4994.082	49.660	13.6
21	4972.659	49.447	40.7
22	4951.235	49.234	83.2
23	4929.811	49.021	100.0
24	4908.388	48.808	86.0
25	4886.964	48.595	62.3
26	4865.540	48.382	14.7
27	4426.354	44.014	19.4
28	2708.336	26.931	24.0
29	1754.156	17.443	23.8
30	1221.859	12.150	22.7

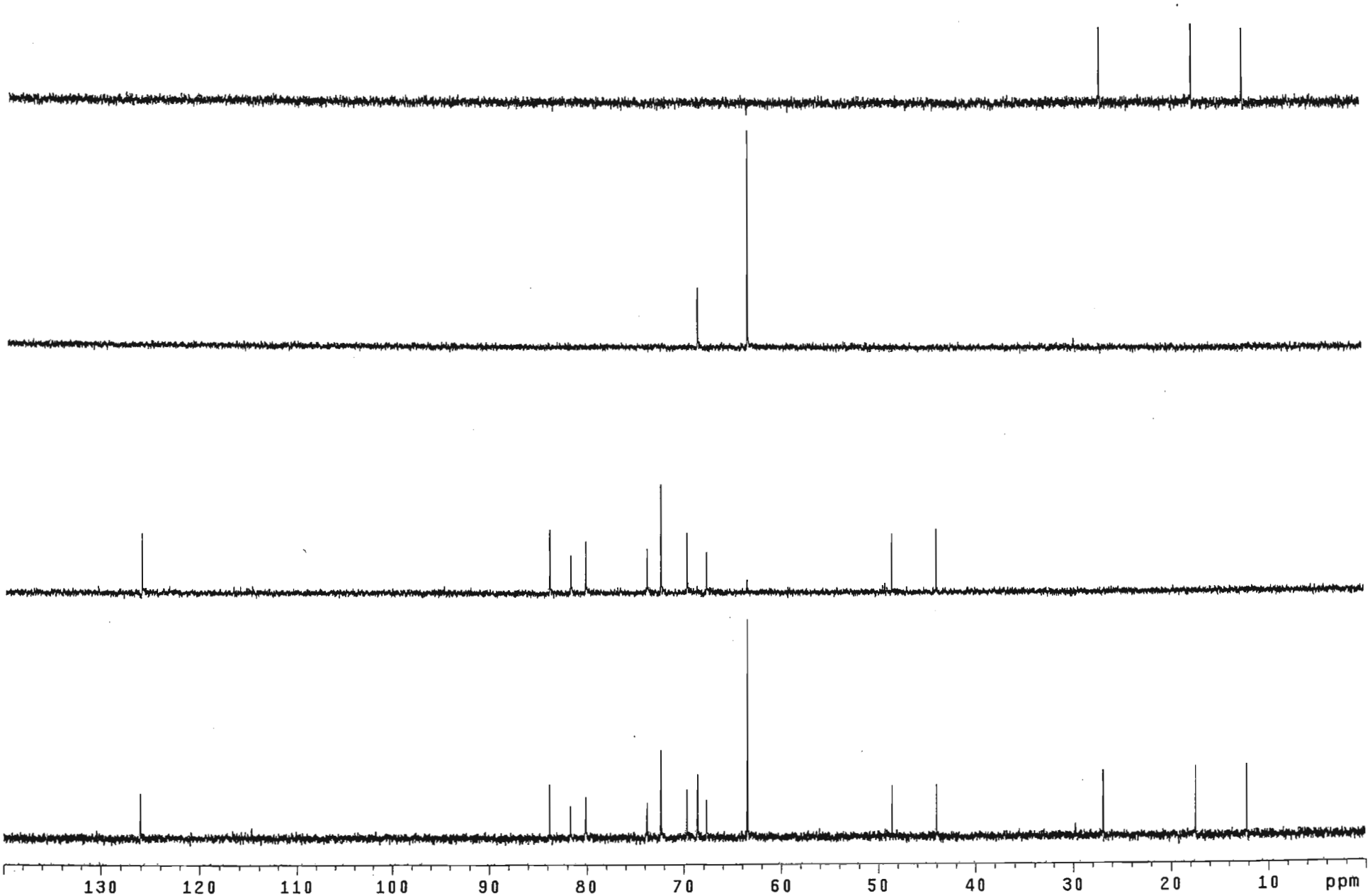


5-80 indaquassin X **SM 5**



Spectrum SM 5.2: ^{13}C NMR Spectrum of indaquassin X SM 5

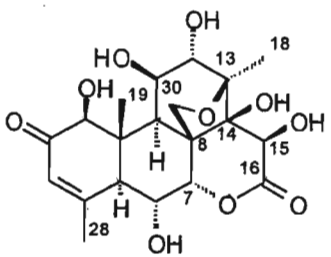
Pulse Sequence: dept



Spectrum SM 5.3: ADEPT Spectrum of indaquassin X SM 5

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

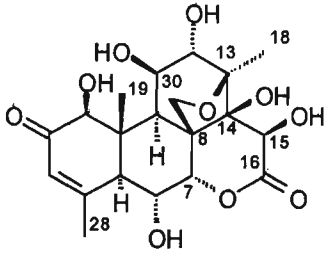


5-80 indaquassin X **SM 5**

Spectrum SM 5.4: HSQC Spectrum of indaquassin X SM 5

probe=5mmASW

Pulse Sequence: ghmqc_da



5-80 indaquassin X **SM 5**

F2 (ppm)

1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
6.5

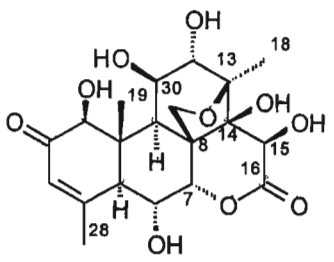
200 180 160 140 120 100 80 60 40 20 0

F1 (ppm)

Spectrum SM 5.5: HMBC Spectrum of indaquassin X SM 5

probe=5mmASW

Pulse Sequence: ghmqc_da

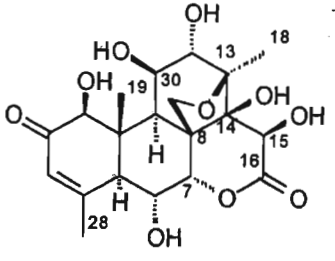


5-80 indaquassin X **SM 5**

Spectrum SM 5.6: Expanded HMBC Spectrum of indaquassin X SM 5

probe=5mmASW

Pulse Sequence: relayh



5-80 indaquassin X **SM 5**

F2 (ppm)

1 2 3 4 5 6 7

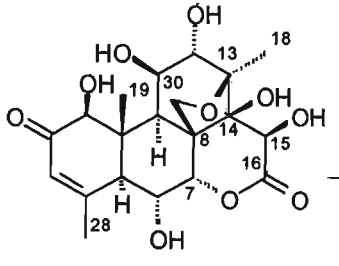
7 6 5 4 3 2 1

F1 (ppm)

Spectrum SM 5.7: COSY Spectrum of indaquassin X SM 5

using presat_da
mix=1sec
probe=5mmASW

Pulse Sequence: noesy_da



5-80 indaquassin X **SM 5**

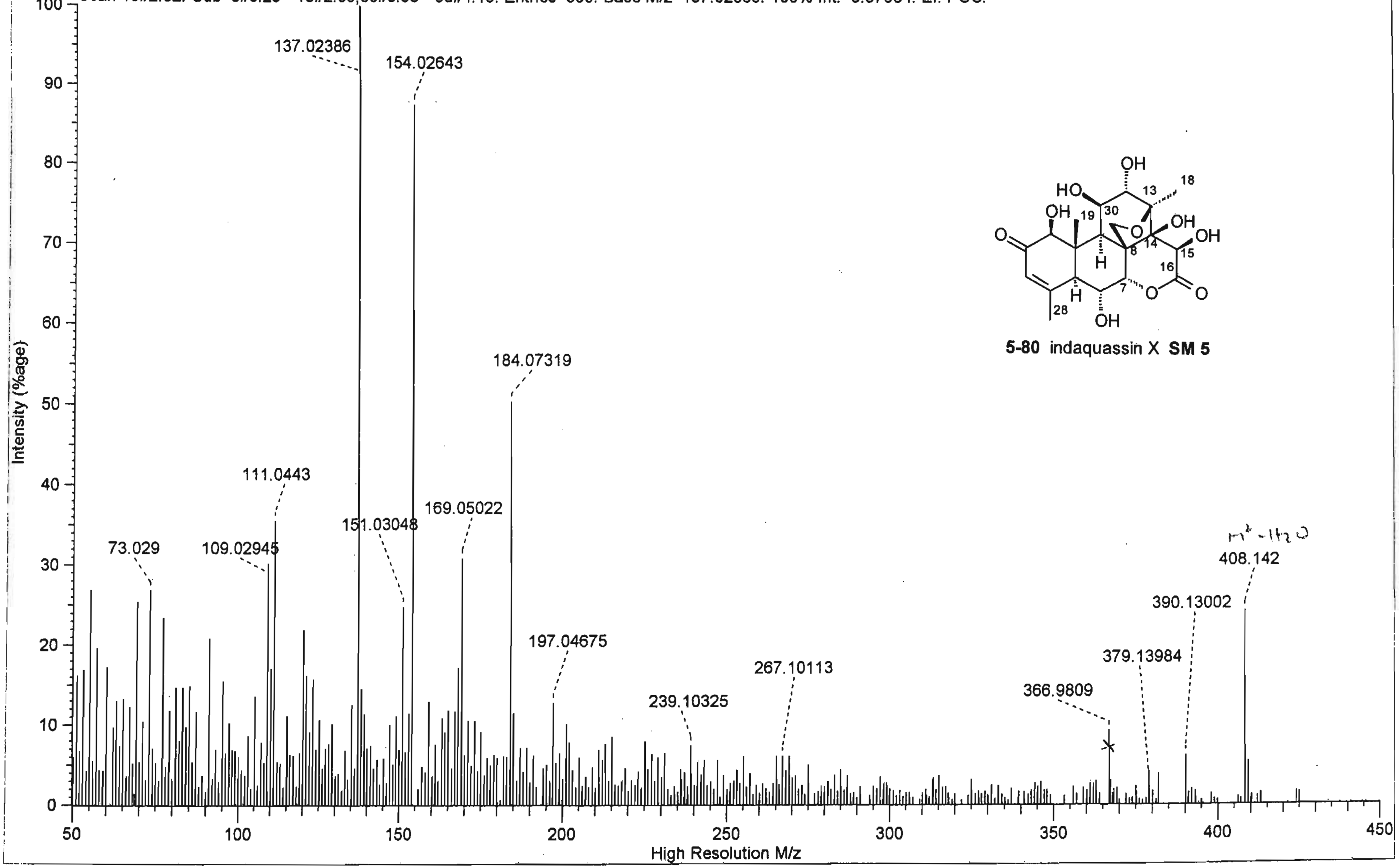
Spectrum SM 5.8: NOESY Spectrum of Indaquassin X SM 5

File Name	:	C:\MASPEC\data\hc052112.ms2
File Source	:	Acquired on MASPEC II system [II32/A002]
File Title	:	7f1-61/66-4
Operator	:	Dr. P. Boshoff
Instrument	:	VG70-SEQ

Cmp. too polar for EI. Bed-g could gel. will try FAB.

SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Int:0.5%. Range:0-430. Excl: Ref/Ex.].Highlighting=Base Peak.

Scan 19#2:32. Sub=3#0:29 - 16#2:09,30#3:56 - 33#4:19. Entries=530. Base M/z=137.02386. 100% Int.=0.57984. EI. POS.

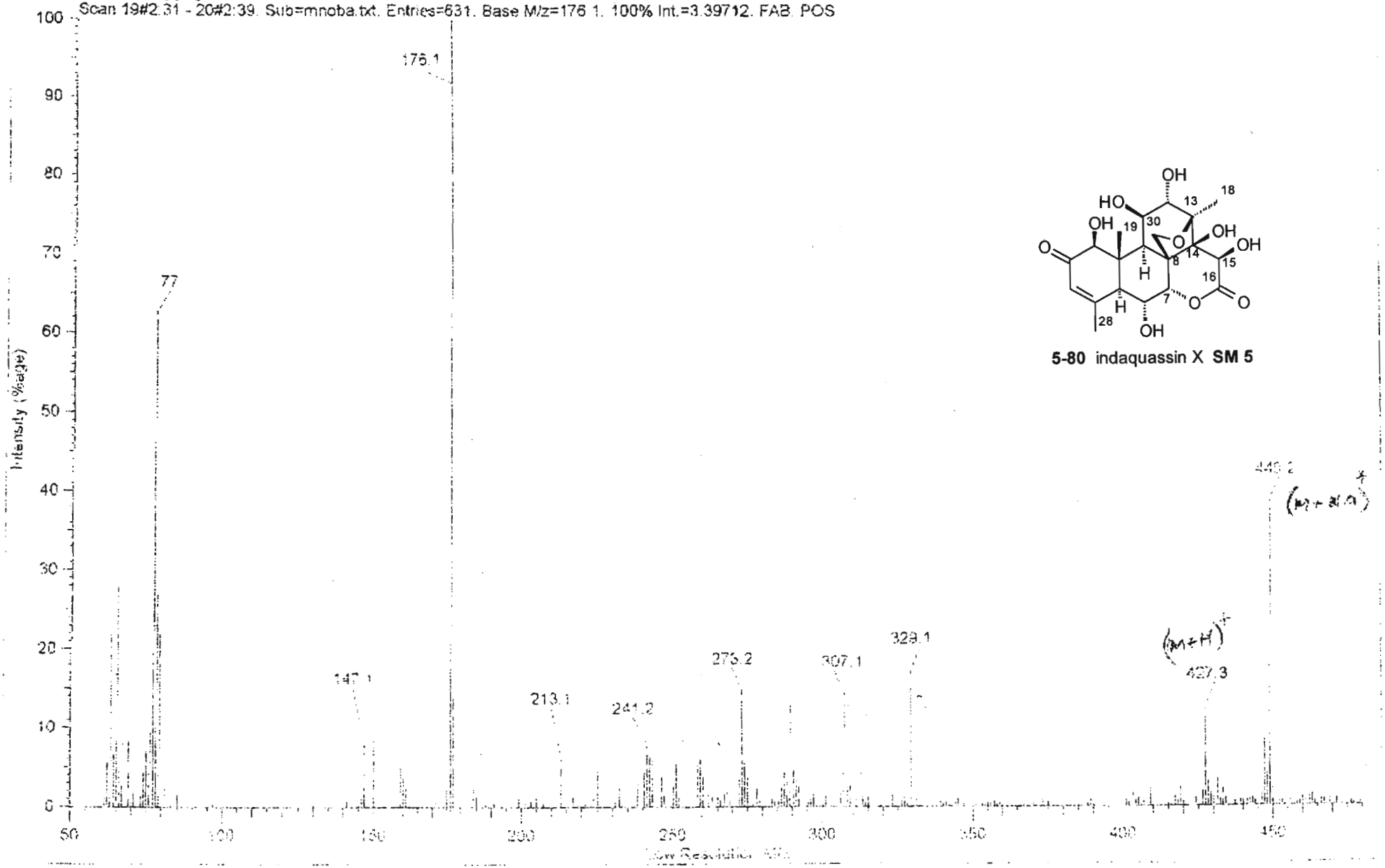


Spectrum SM 5.9: High Resolution Mass Spectrum of indaquassin X SM 5

FAB.

File Source	Acquired on MASPEC II system [II32/A002]
File Title	7F1-61/66-4
Operator	Dr. P. Boshoff
Instrument	VG70-SEQ

SCAN GRAPH. Flagging=Low Resolution M/z.
Scan 19#2:31 - 20#2:39. Sub=mnoba.txt. Entries=631. Base M/z=176.1. 100% Int.=3.39712. FAB. POS



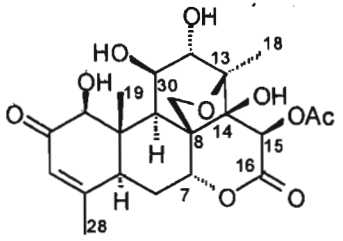
5-80 indaquassin X **SM 5**

Spectrum SM 5.10: Fast Atom Bombardment Spectrum of indaquassin X SM 5

probe=5mmASW

Pulse Sequence: presat_da

1	2984.118	7.461	20.8
2	2518.737	6.298	28.2
3	2431.445	6.079	14.6
4	2060.652	5.152	15.5
5	1820.666	4.552	15.8
6	1818.321	4.546	16.2
7	1813.630	4.535	24.9
8	1681.521	4.204	24.8
9	1545.502	3.864	12.7
10	1538.206	3.846	12.0
11	1499.121	3.748	25.3
12	1350.855	3.378	17.4
13	1335.742	3.340	31.7
14	1168.976	2.923	6.4
15	1156.469	2.892	6.8
16	968.336	2.421	13.6
17	962.604	2.407	12.7
18	957.653	2.394	9.5
19	870.883	2.178	83.3
20	787.760	1.970	63.0
21	728.871	1.822	5.2
22	726.786	1.817	5.3
23	714.018	1.785	8.9
24	641.058	1.603	6.3
25	548.816	1.372	83.4
26	500.350	1.251	200.0
27	477.420	1.194	7.9
28	467.518	1.169	77.8
29	452.144	1.131	6.2
30	354.169	0.886	11.3
31	347.915	0.870	18.8
32	340.880	0.852	11.3

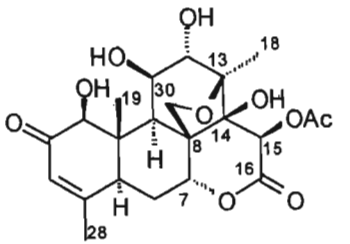


5-93 15-acetylbrucein D **SM 6**

Spectrum SM 6.1: ^{1}H NMR Spectrum of 15-acetylbrucein D SM 6

Pulse Sequence: s2pul

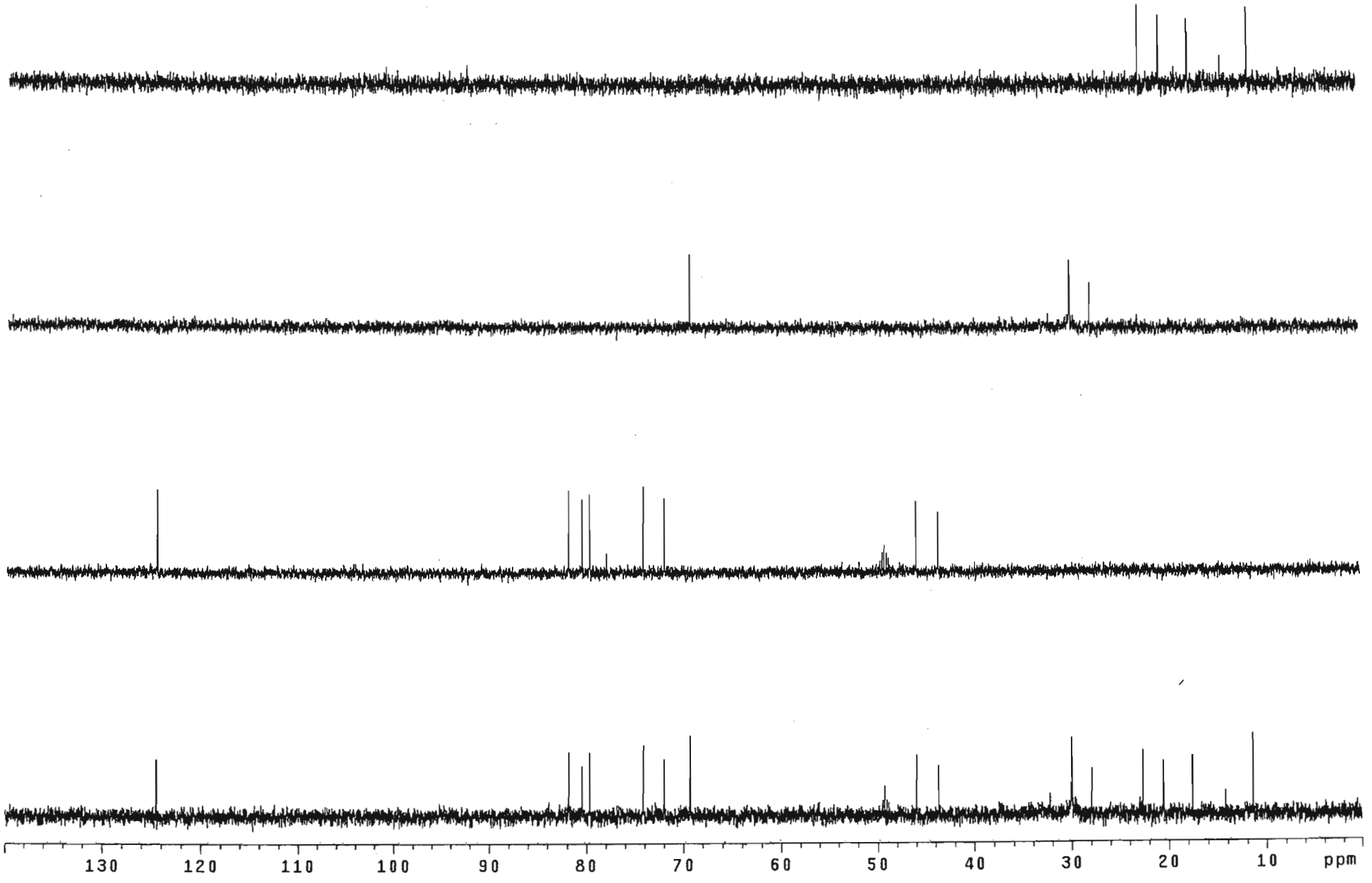
	FREQUENCY	PPM	HEIGHT
1	19951.536	198.392	7.8
2	17107.125	170.108	6.2
3	16527.860	164.348	9.4
4	12522.447	124.520	14.2
5	8420.628	83.732	12.9
6	8227.814	81.815	13.9
7	8153.655	81.078	8.2
8	8088.560	80.430	14.3
9	8010.281	79.652	14.2
10	7847.131	78.030	103.6
11	7833.947	77.899	6.8
12	7814.996	77.710	104.8
13	7782.860	77.391	99.2
14	7454.912	74.130	16.0
15	7236.555	71.958	13.0
16	6969.582	69.304	13.0
17	5072.759	50.442	13.6
18	4992.632	49.647	40.5
19	4971.408	49.434	108.9
20	4949.984	49.221	210.4
21	4927.737	49.000	250.0
22	4906.313	48.787	245.0
23	4884.889	48.574	125.6
24	4863.465	48.361	42.4
25	4848.634	48.213	15.3
26	4622.860	45.968	16.3
27	4392.143	43.674	17.3
28	3240.206	32.220	6.6
29	3017.729	30.007	19.2
30	3014.433	29.975	23.8
31	2808.436	27.926	12.0
32	2277.786	22.650	14.2
33	2061.901	20.503	15.6
34	1764.441	17.545	18.6
35	1144.801	11.384	16.4



5-93 15-acetylbrucein D **SM 6**

Spectrum SM 6.2: ^{13}C NMR Spectrum of 15-acetylbrucein D SM 6

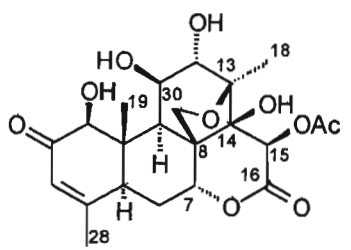
Pulse Sequence: dept



Spectrum SM 6.3: ADEPT Spectrum of 15-acetylbrucein D SM 6

Gradient HSQC expt.
with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

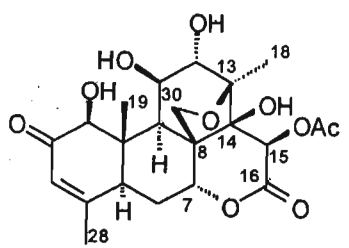


5-93 15-acetylbrucein D **SM 6**

Spectrum SM 6.4: HSQC Spectrum of 15-acetylbrucein D SM 6

probe=5mmASW

Pulse Sequence: ghmqc_da

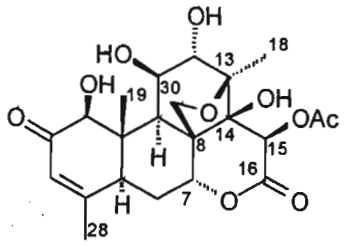


5-93 15-acetylbrucein D **SM 6**

Spectrum SM 6.5: HMBC Spectrum of 15-acetylbrucein D SM 6

probe=5mmASW

Pulse Sequence: ghmqc_da

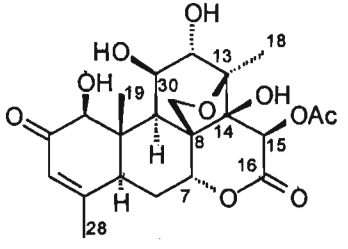


5-93 15-acetylbrucein D **SM 6**

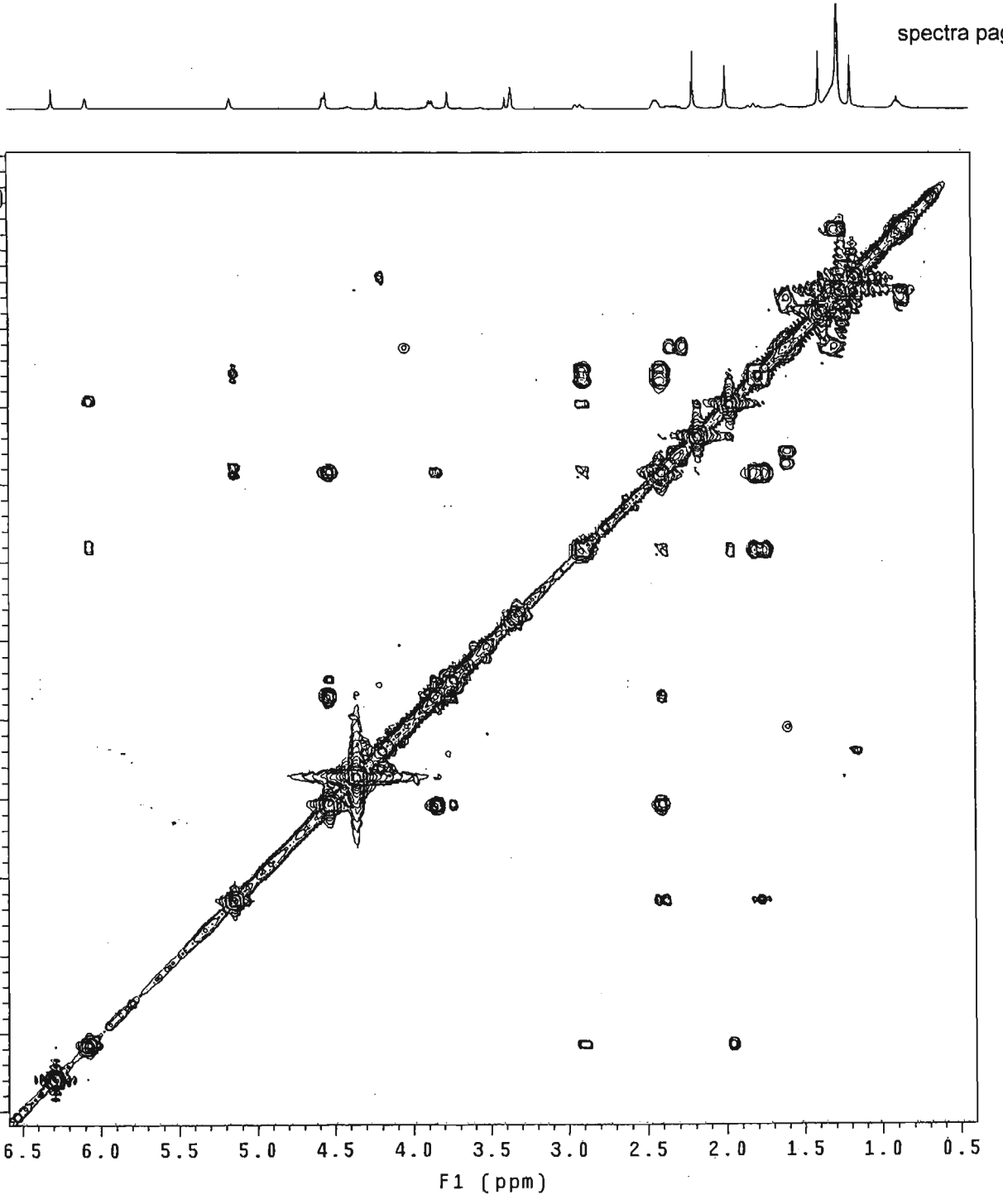
Spectrum SM 6.6: Expanded HMBC Spectrum of 15-acetylbrucein D SM 6

1H COSY-90
probe=5mmASW

Pulse Sequence: relayh



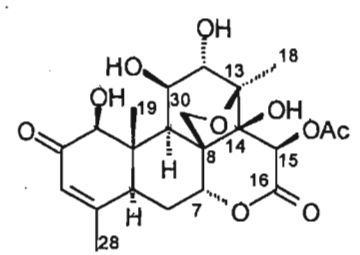
5-93 15-acetylbrucein D **SM 6**



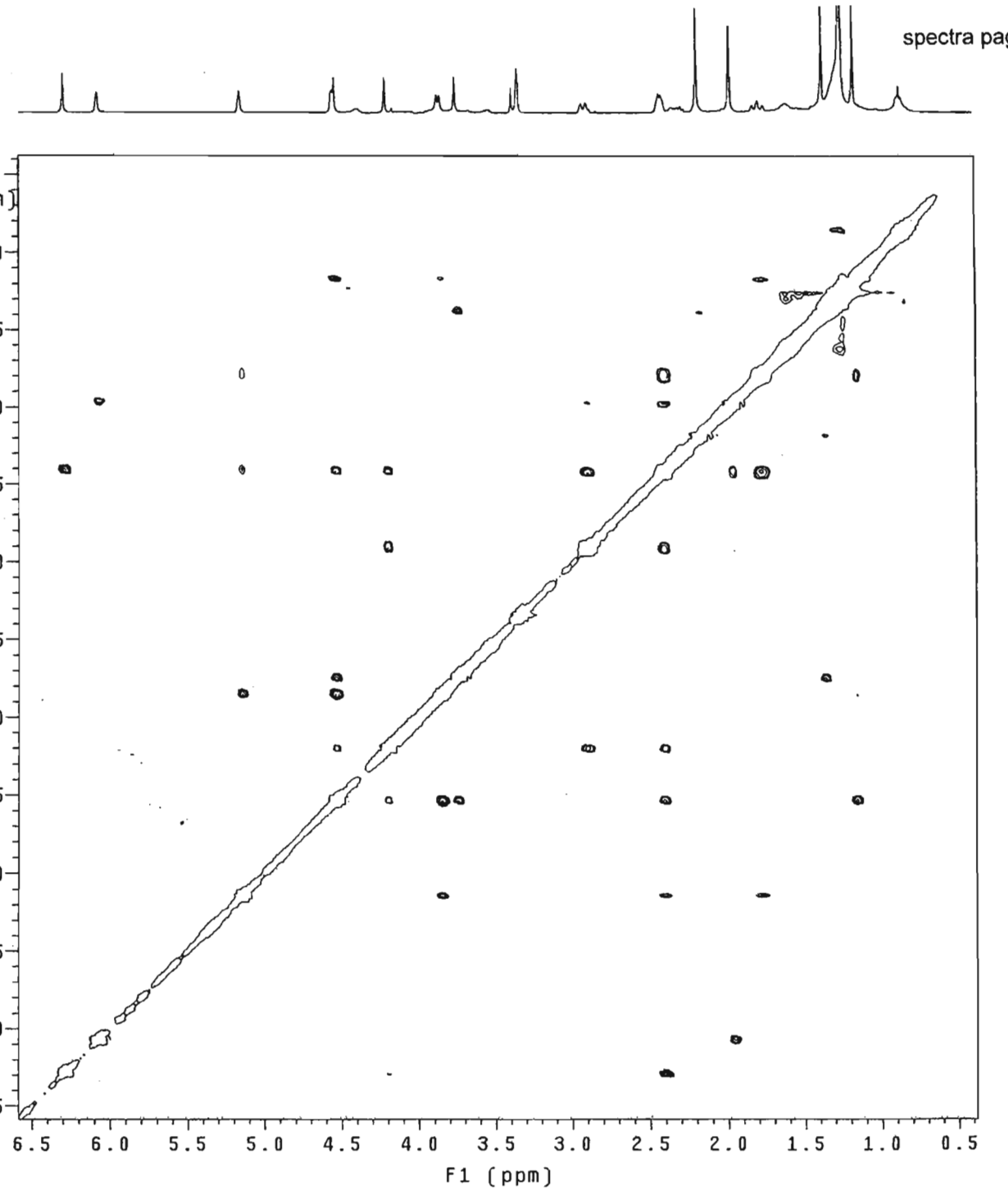
Spectrum SM 6.7: COSY Spectrum of 15-acetylbrucein D SM 6

gradient NOESY expt.
using presat_h2o
mix=1sec
probe=5mmASW

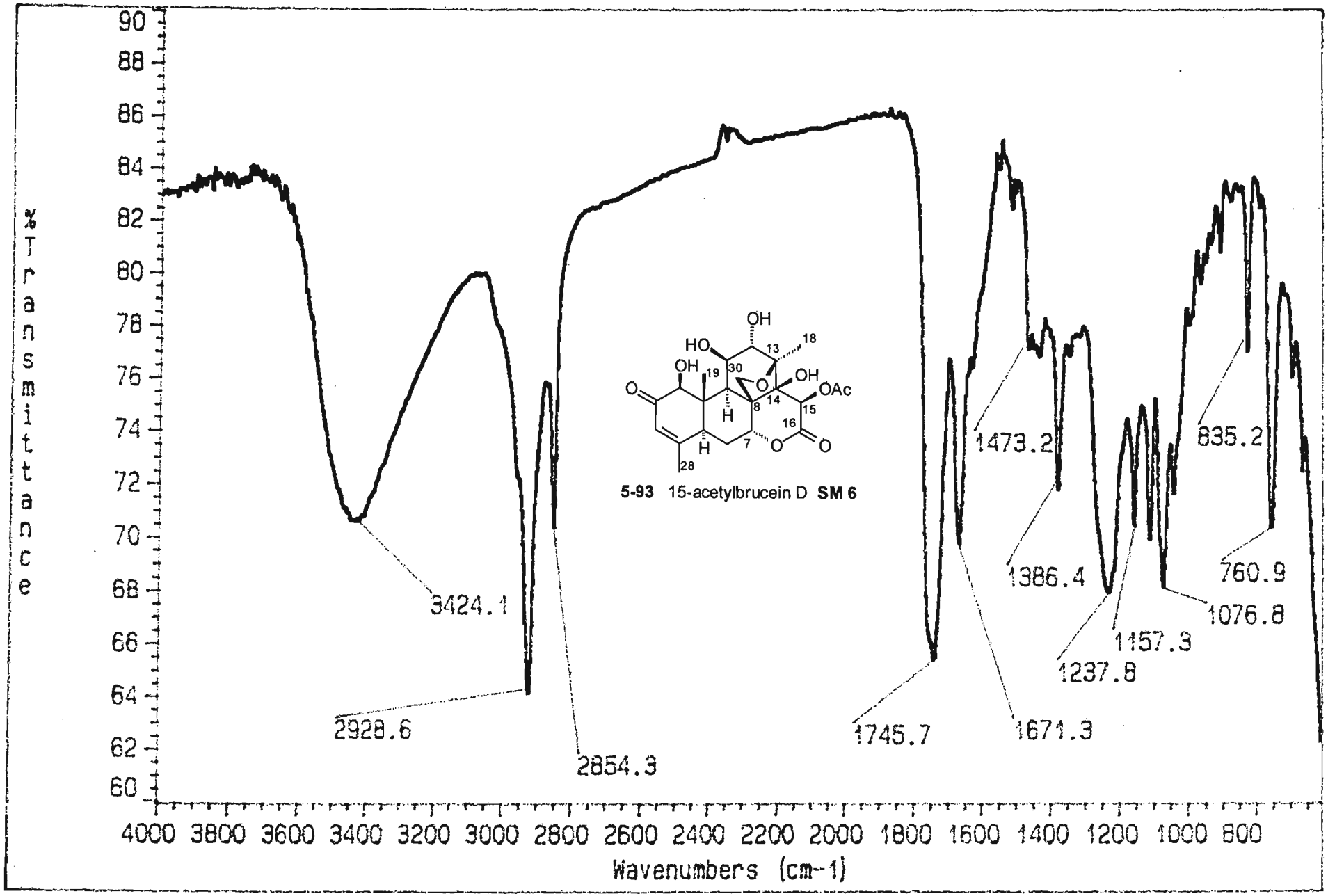
Pulse Sequence: noesy_da



5-93 15-acetylbrucein D **SM 6**



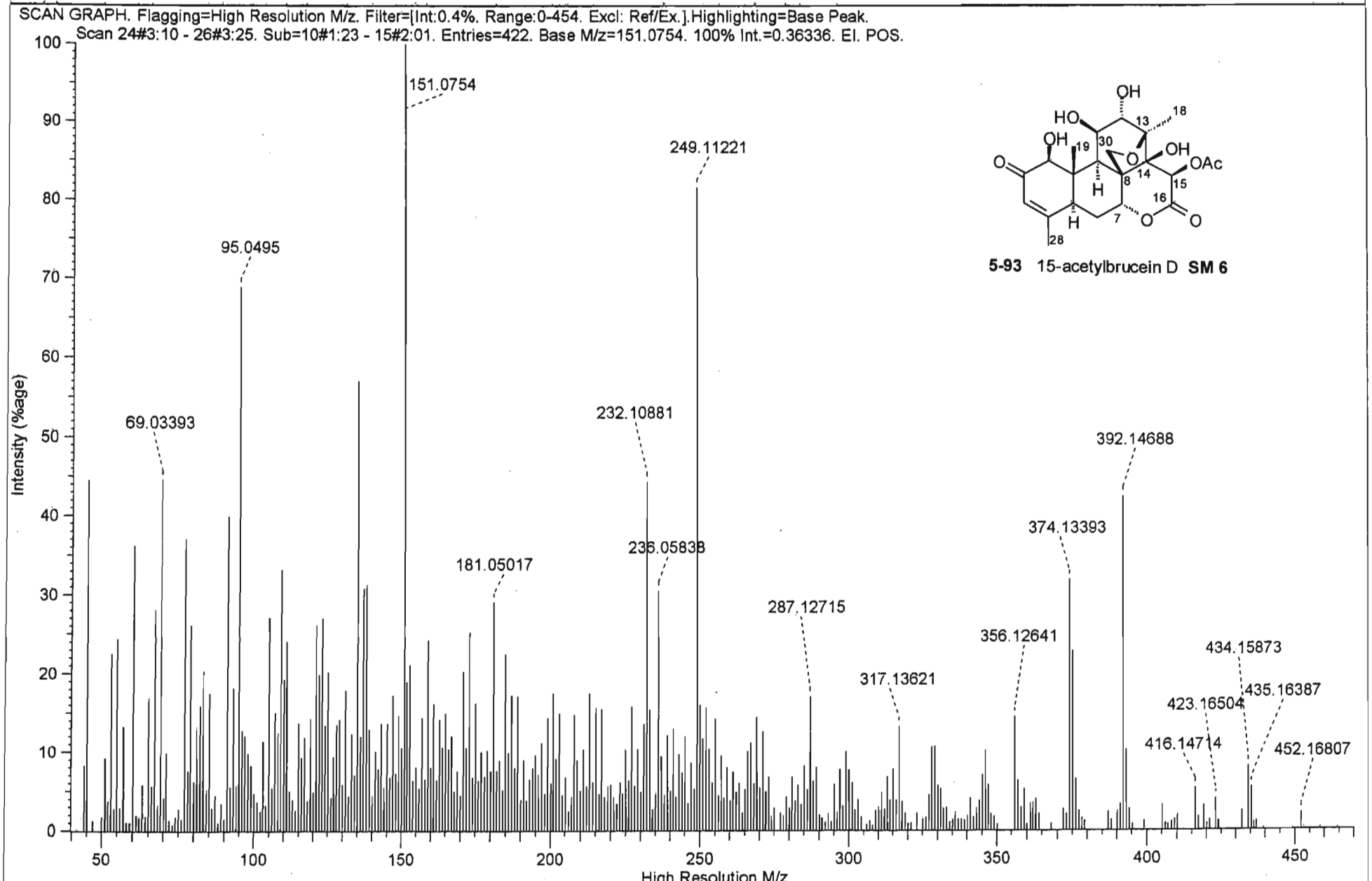
Spectrum SM 6.8: NOESY Spectrum of 15-acetylbrucein D SM 6



5-93 15-acetylbrucein D **SM 6**

Spectrum SM 6.9: IR Spectrum of 15-acetylbrucein D SM 6

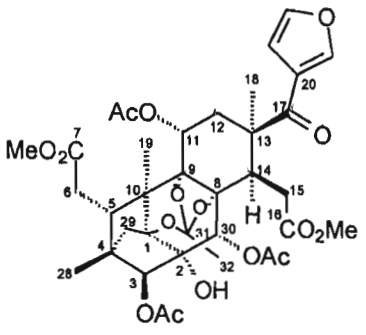
File Name : C:\MASPEC\data\hc052105.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : 7f1-47/50c-2
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ



5-93 15-acetylbrucein D **SM 6**

Spectrum SM 6.10: High Resolution Mass Spectrum of 15-acetylbrucein D SM 6

Pulse Sequence: s2pul



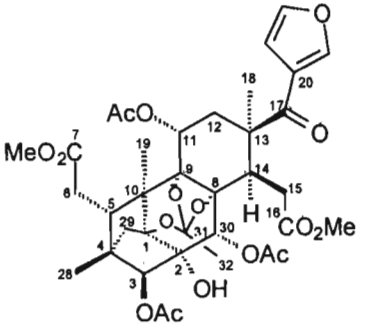
6-5 leandreanin A **NL 1**

9 8 7 6 5 4 3 2 1 ppm

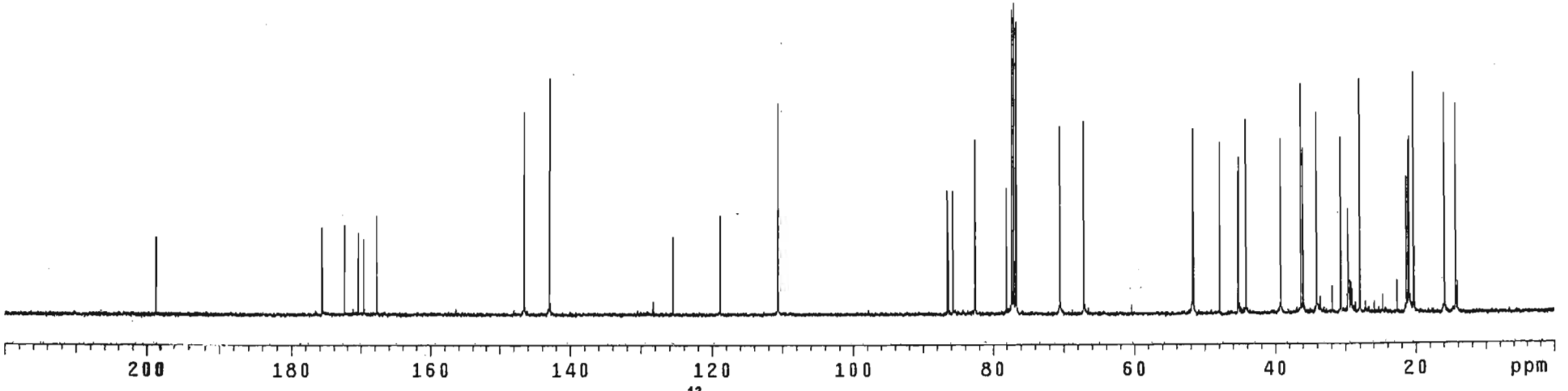
Spectrum NL1.1: ^{1}H NMR Spectrum of leandrianin A NL 1

Pulse Sequence: s2pul

	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	19972.386	198.600	12.3	40	1443.335	14.352	33.5
2	17667.688	175.683	14.1				
3	17342.212	172.447	14.4				
4	17139.511	170.431	13.2				
5	17062.880	169.669	12.1				
6	16873.362	167.784	16.0				
7	14739.229	146.563	32.6				
8	14377.498	142.966	38.0				
9	12622.400	125.514	12.5				
10	11954.145	118.869	15.8				
11	11127.683	110.651	34.0				
12	8704.331	86.554	19.9				
13	8687.027	86.382	17.1				
14	8623.580	85.751	19.9				
15	8306.344	82.596	28.1				
16	7851.501	78.073	20.3				
17	7775.694	77.320	49.0				
18	7743.559	77.000	50.0				
19	7711.423	76.680	47.0				
20	7090.135	70.503	30.3				
21	6753.947	67.160	31.1				
22	5202.375	51.731	29.4				
23	5190.015	51.608	29.8				
24	4813.452	47.864	27.6				
25	4558.840	45.332	22.8				
26	4540.712	45.152	25.3				
27	4441.009	44.160	31.2				
28	3939.199	39.170	28.2				
29	3651.627	36.311	36.9				
30	3619.492	35.991	26.5				
31	3425.854	34.066	32.4				
32	3086.370	30.690	28.3				
33	2982.548	29.658	16.8				
34	2815.278	27.994	37.6				
35	2144.550	21.325	21.9				
36	2116.535	21.046	27.7				
37	2106.647	20.948	28.3				
38	2040.728	20.292	38.7				
39	1601.541	15.925	35.2				



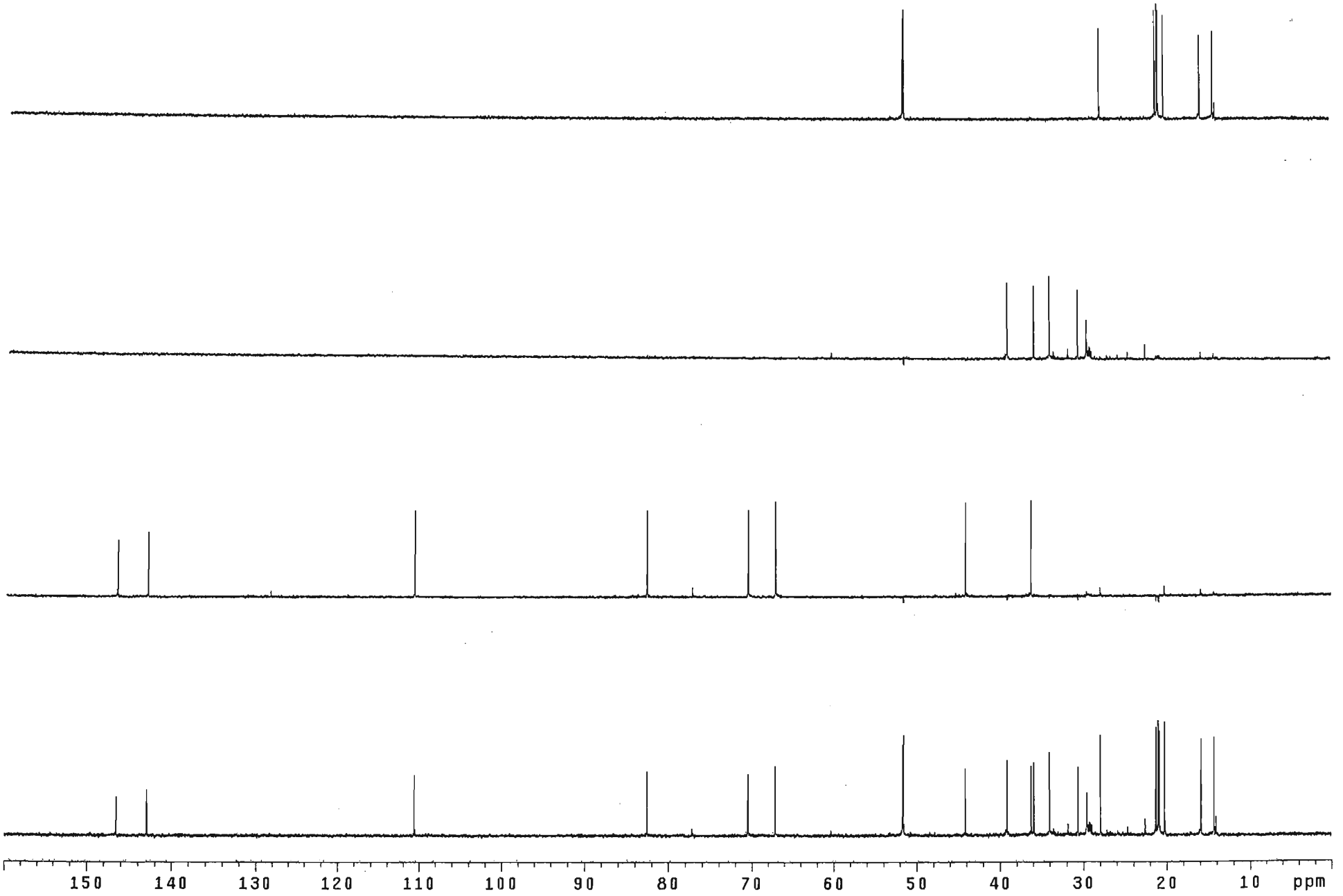
6-5 leandreanin A **NL 1**



Spectrum NL 1.2: ^{13}C NMR Spectrum of leandreanin A NL 1

Probe=5mmASW

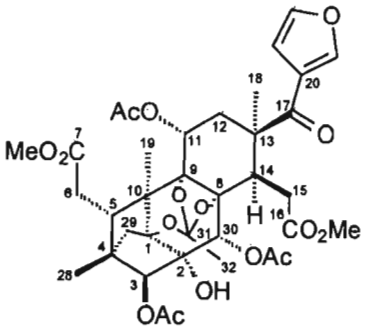
Pulse Sequence: dept



Spectrum NL 1.3: ADEPT Spectrum of leandreanin A NL 1

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

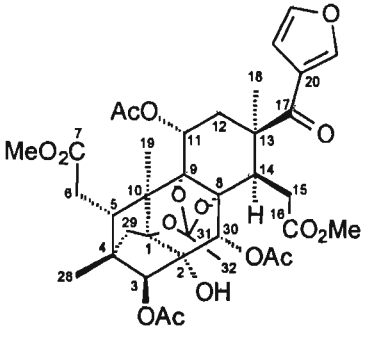


6-5 leandreanin A **NL 1**

Spectrum NL 1.4: HSQC Spectrum of leandreanin A NL 1

probe=5mmASW

Pulse Sequence: ghmqc_da

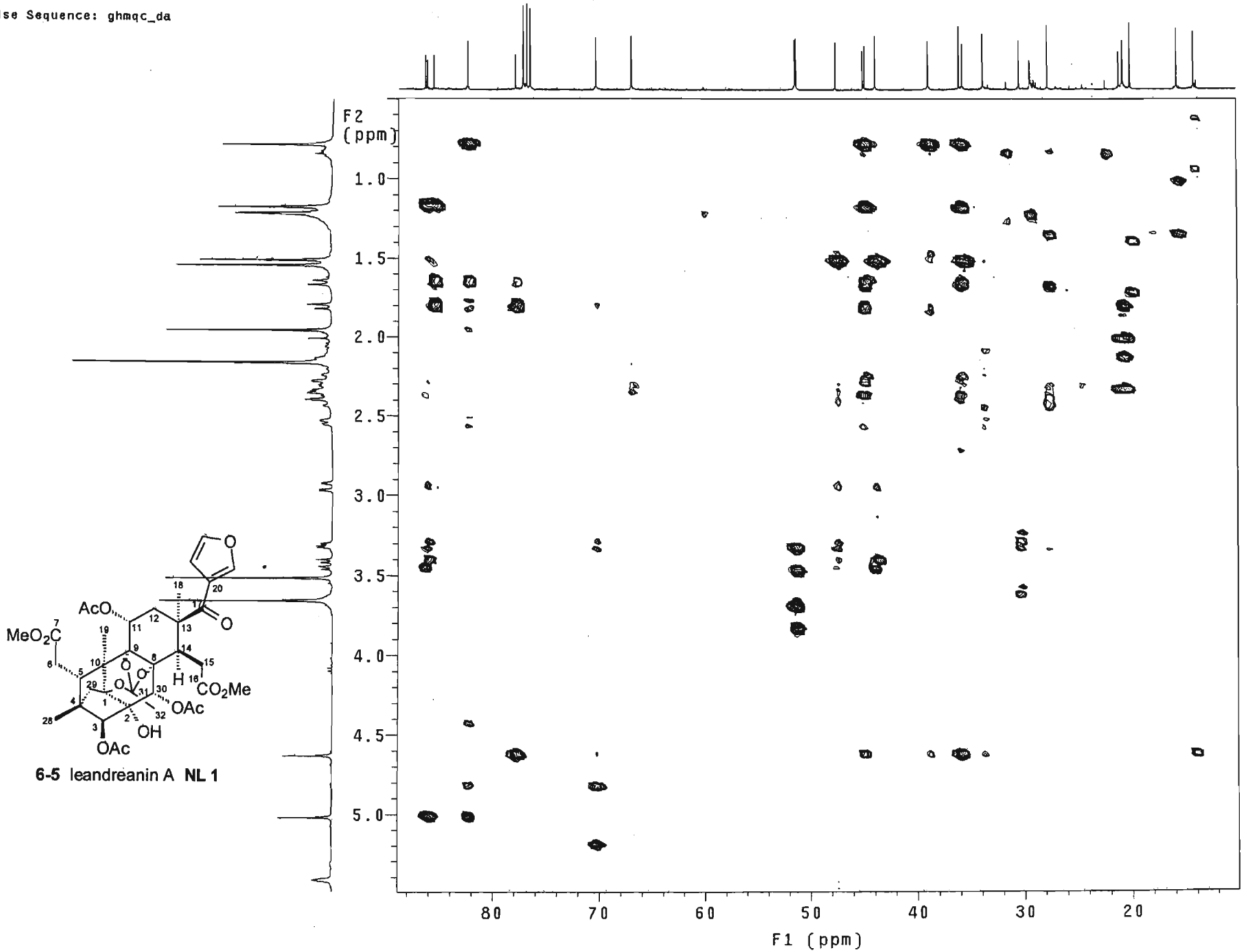


6-5 leandreanin A **NL 1**

Spectrum NL 1.5: HMBC Spectrum of leandreanin A NL 1

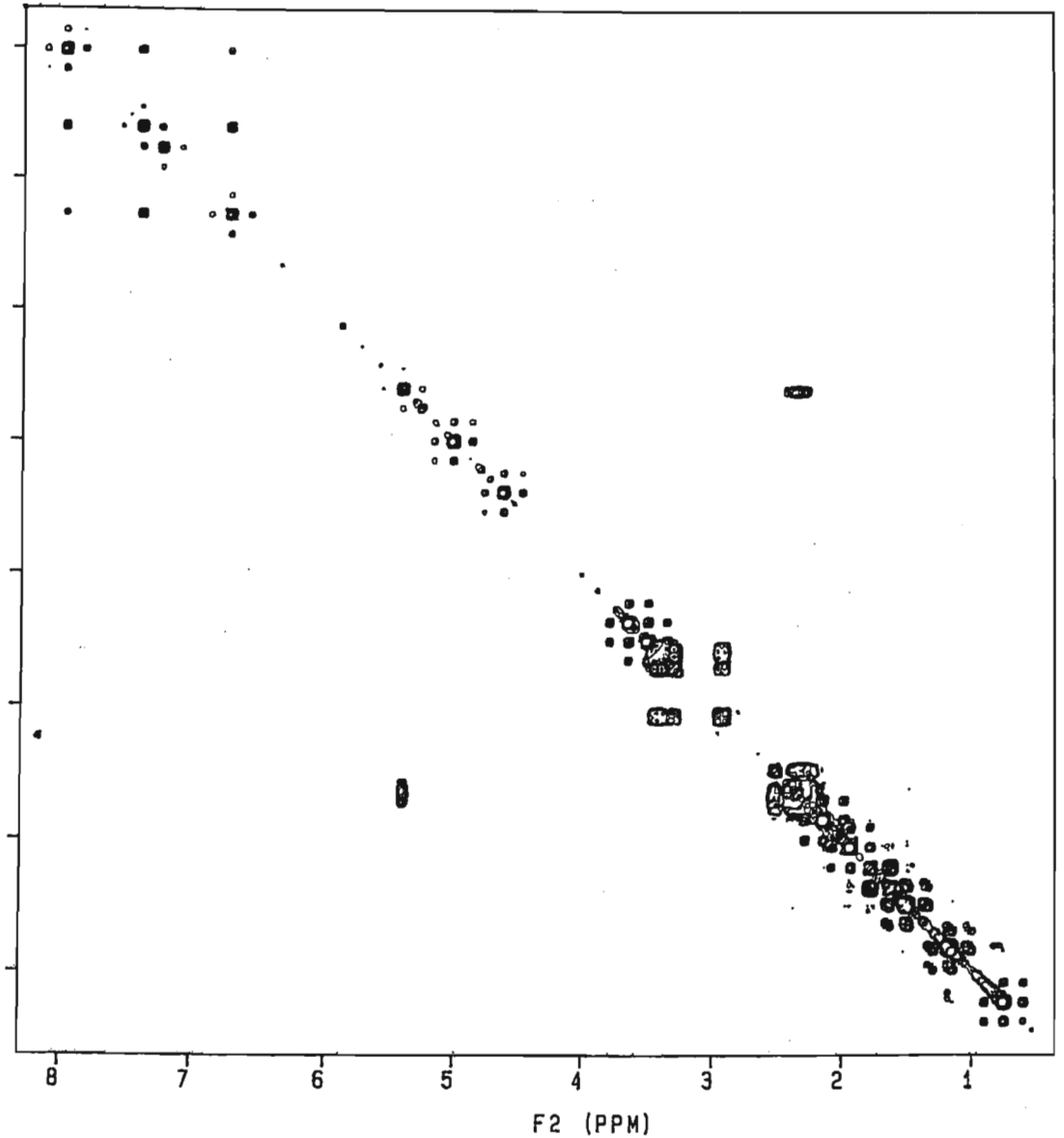
probe=5mmASW

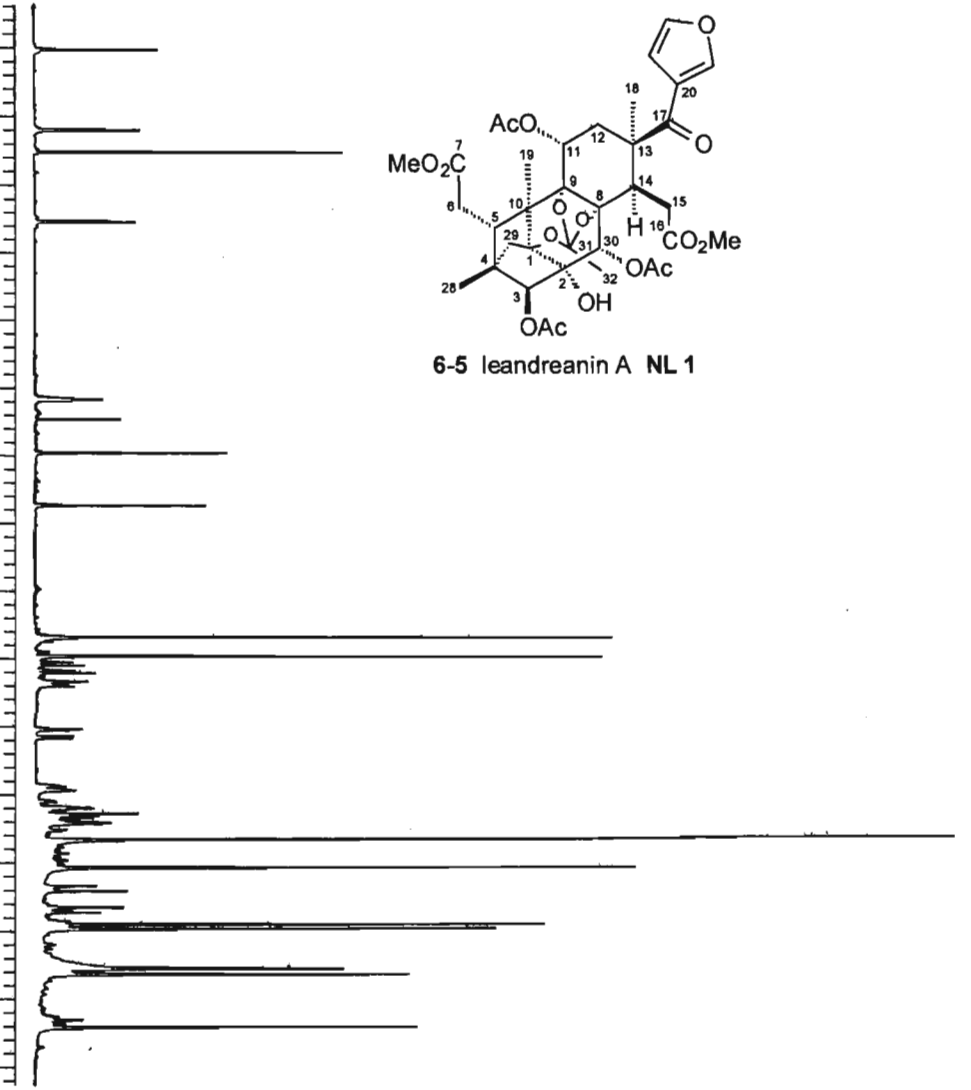
Pulse Sequence: ghmqc_da



6-5 leandreanin A **NL 1**

Spectrum NL 1.6: Expanded HMBC Spectrum of leandreanin A NL 1



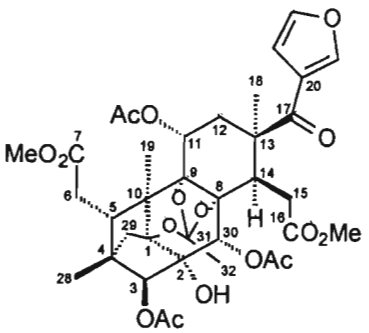


6-5 leandreanin A **NL 1**

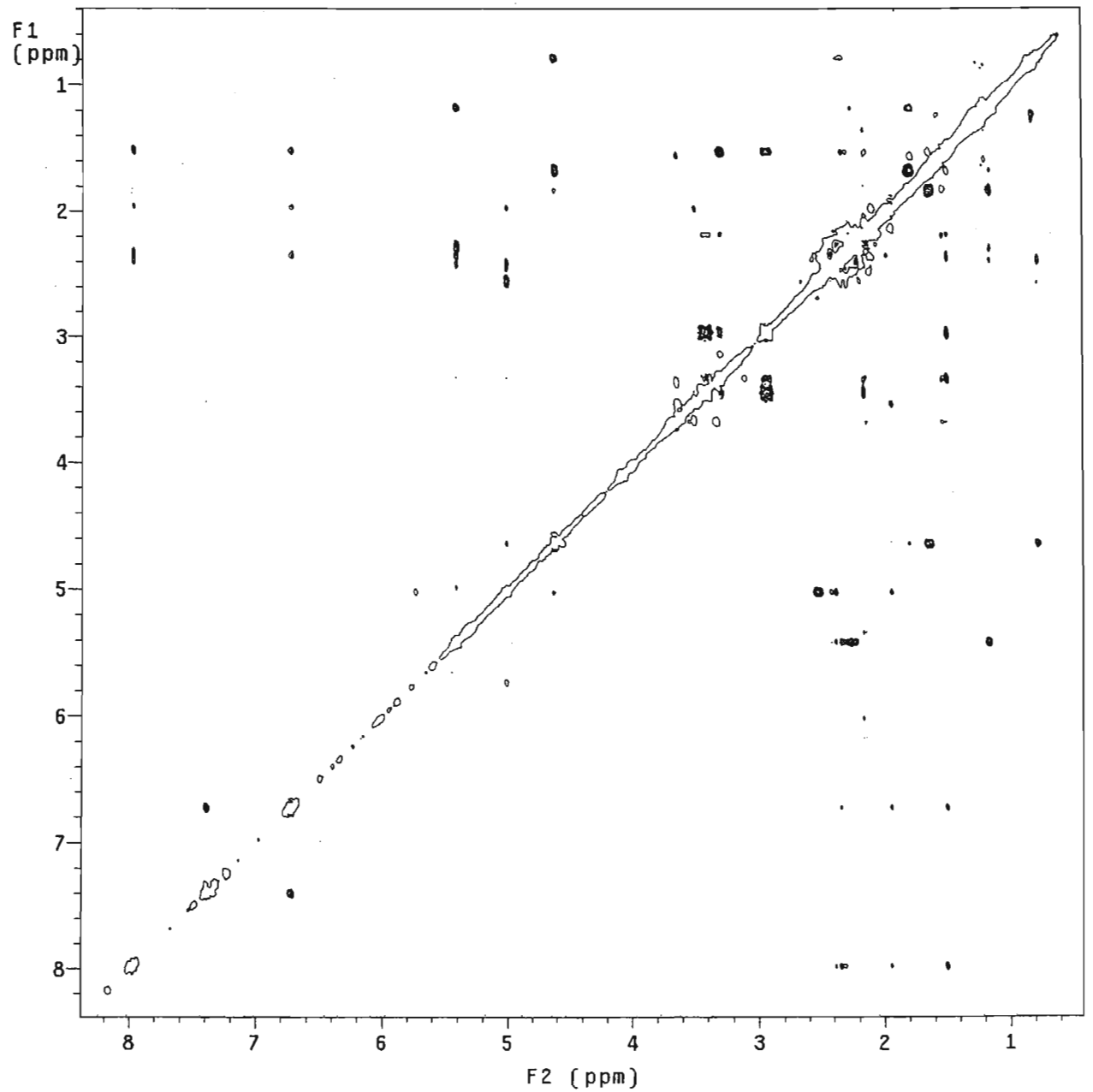
Spectrum NL 1.7: COSY Spectrum of leandreanin A NL 1

mix=1sec
probe=5mmASW

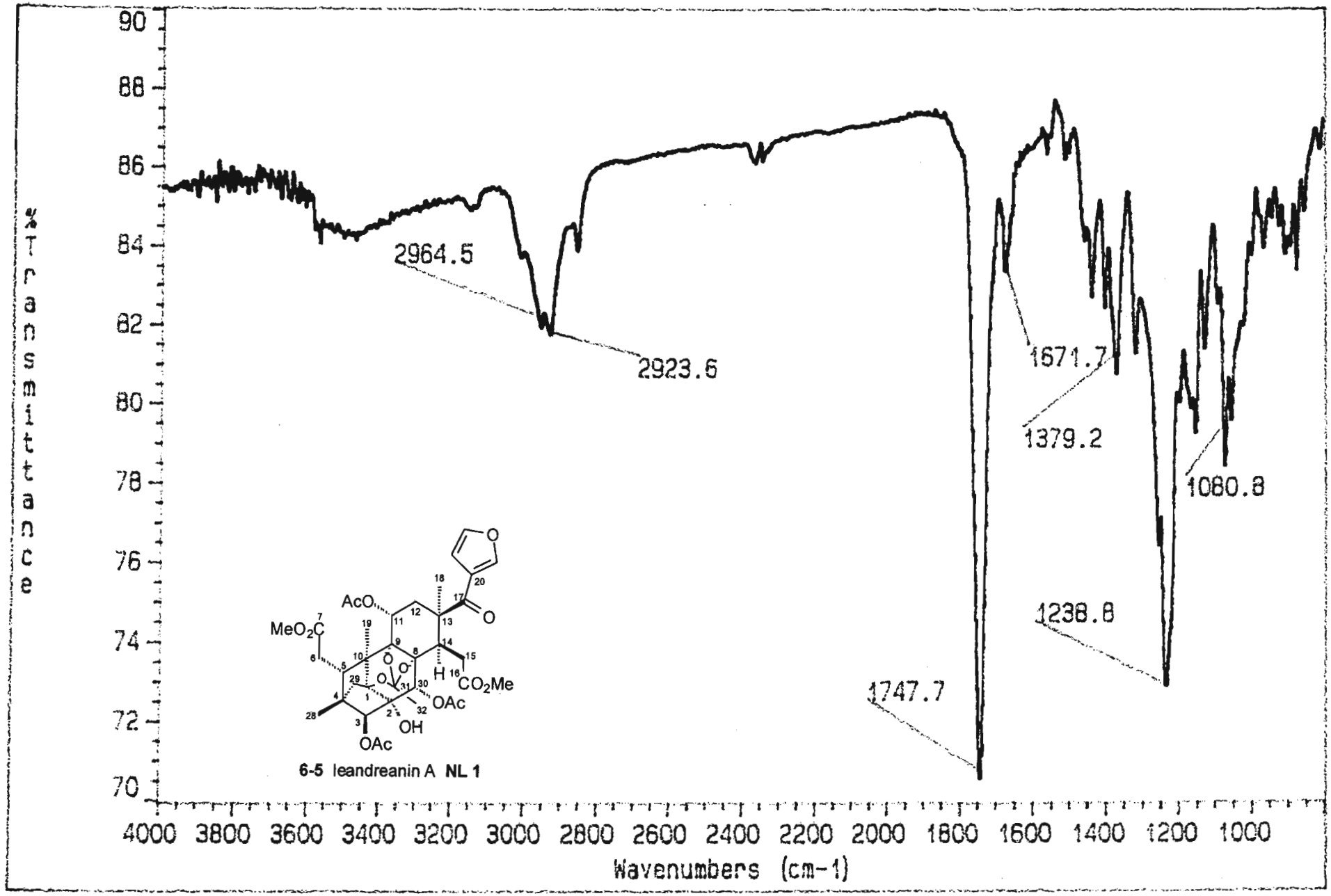
Pulse Sequence: noesy_da



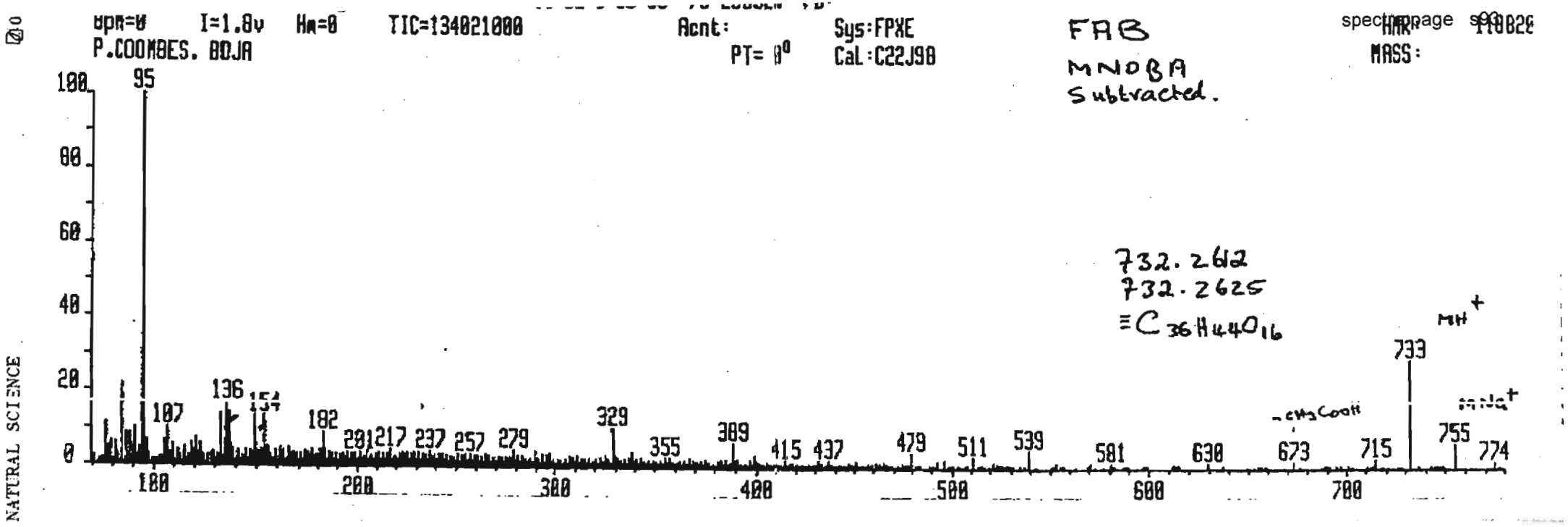
6-5 leandreanin A **NL 1**

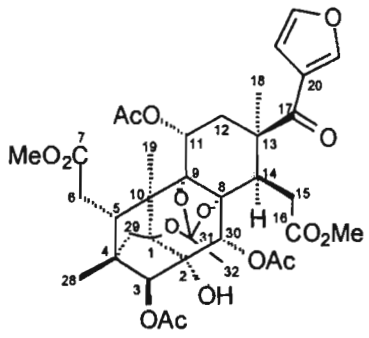


Spectrum NL 1.8: NOESY Spectrum of leandreanin A NL 1



Spectrum NL 1.9: IR Spectrum of leandreanin A NL 1

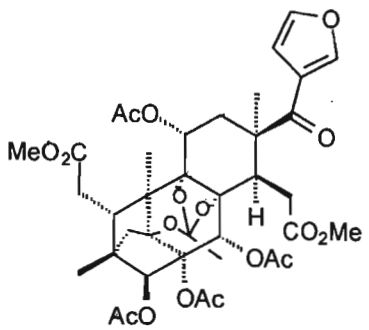




6-5 leandreanin A **NL 1**

Spectrum NL 1.10: Fast Atom Bombardment Mass Spectrum of leandreanin A NL 1

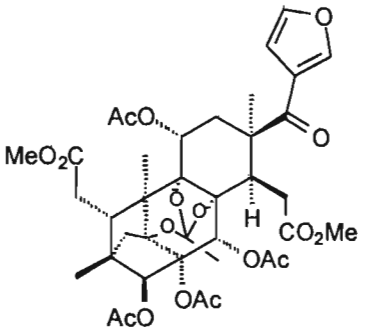
Pulse Sequence: s2pul



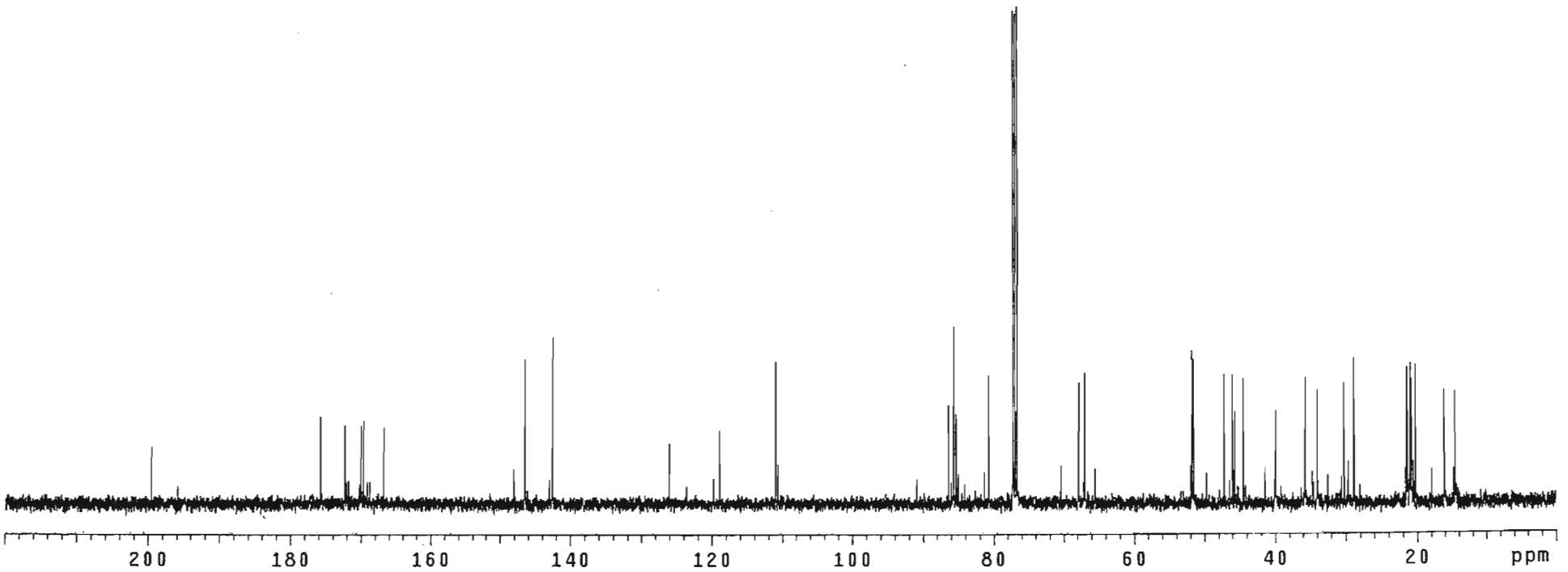
6-36 leandreanin B **NL 2**

Spectrum NL 2.1: ^{1}H NMR Spectrum of leandrianin B NL 2

Pulse Sequence: s2pul

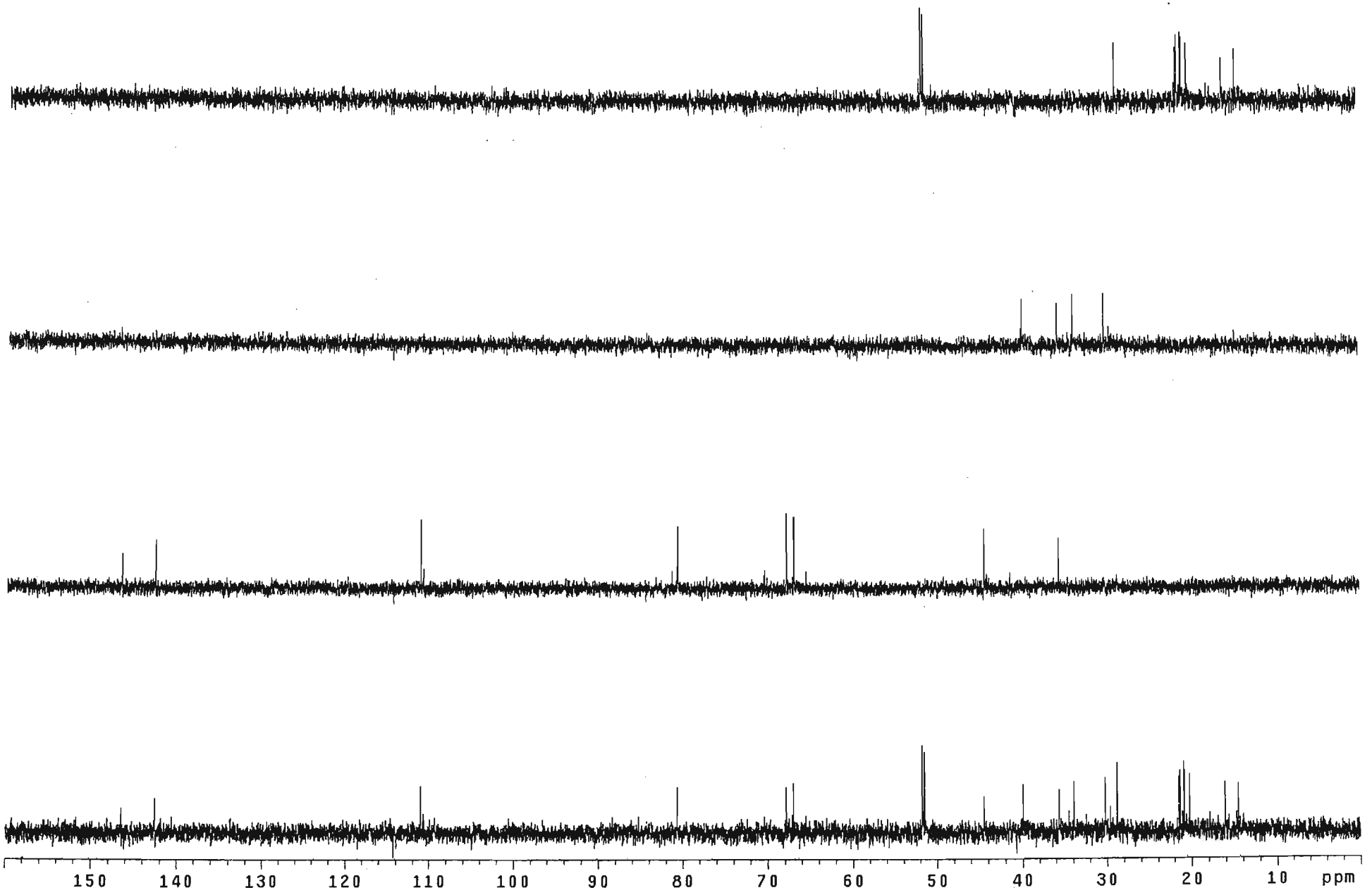


6-36 leandreanin B **NL 2**



Spectrum NL 2.2: ^{13}C NMR Spectrum of leandreanin B NL 2

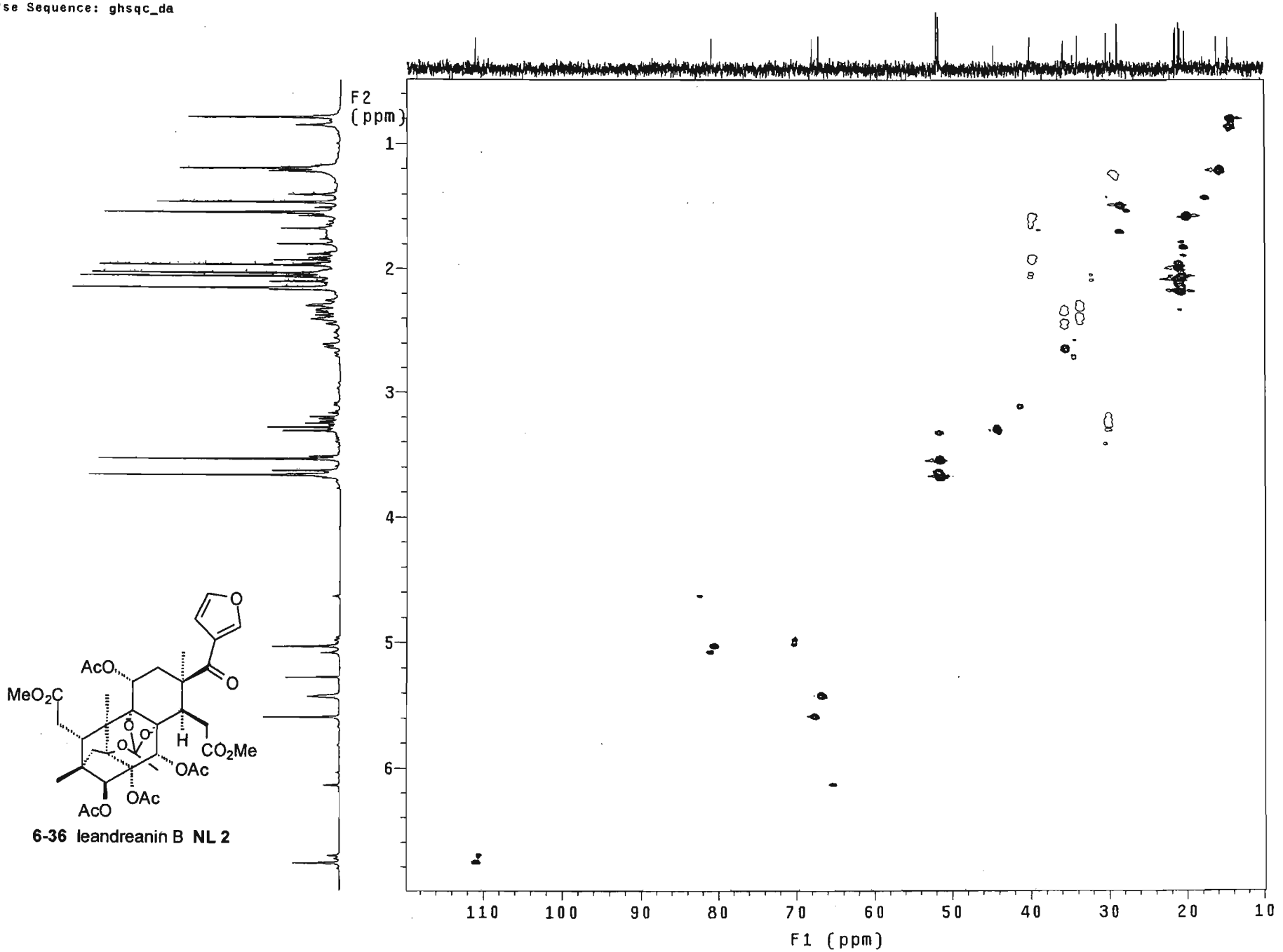
Pulse Sequence: dept



Spectrum NL 2.3: ADEPT Spectrum of leandreanin B NL 2

with mult.editing
probe=3mmID

Pulse Sequence: ghsqc_da

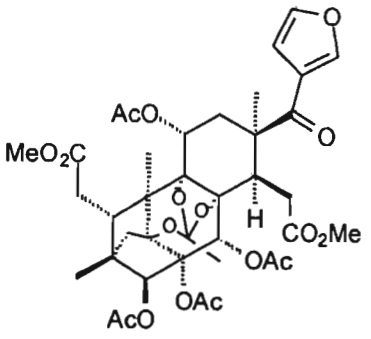


6-36 leandreanin B **NL 2**

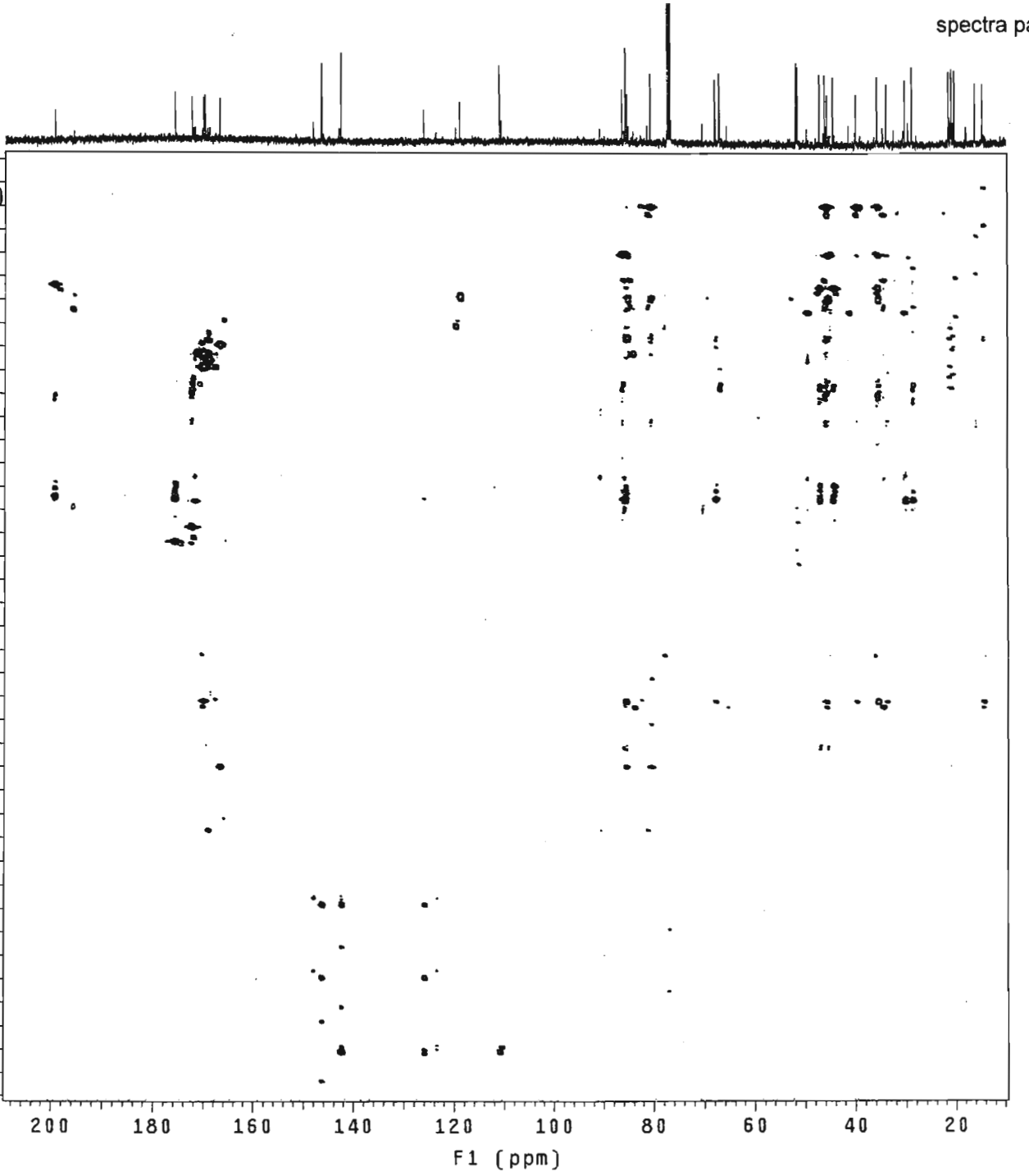
Spectrum NL 2.4: HSQC Spectrum of leandreanin B NL 2

probe=3mmID

Pulse Sequence: ghmqc_da



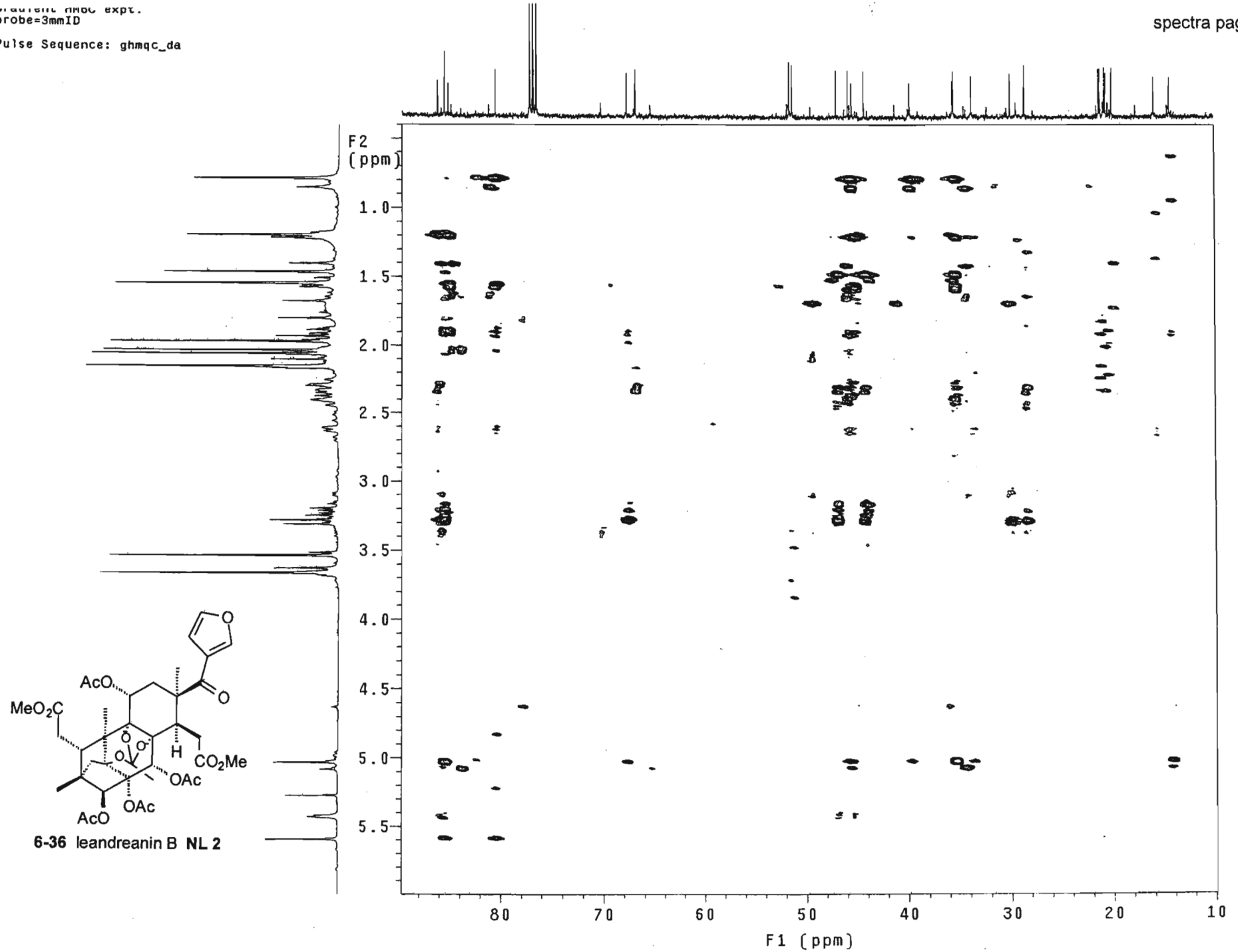
6-36 leandreanin B **NL 2**



Spectrum NL 2.5: HMBC Spectrum of leandreanin B NL 2

Gradient HMBC expt.
probe=3mmID

Pulse Sequence: ghmqc_da

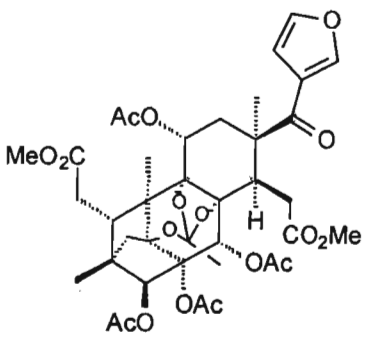


6-36 leandreanin B **NL 2**

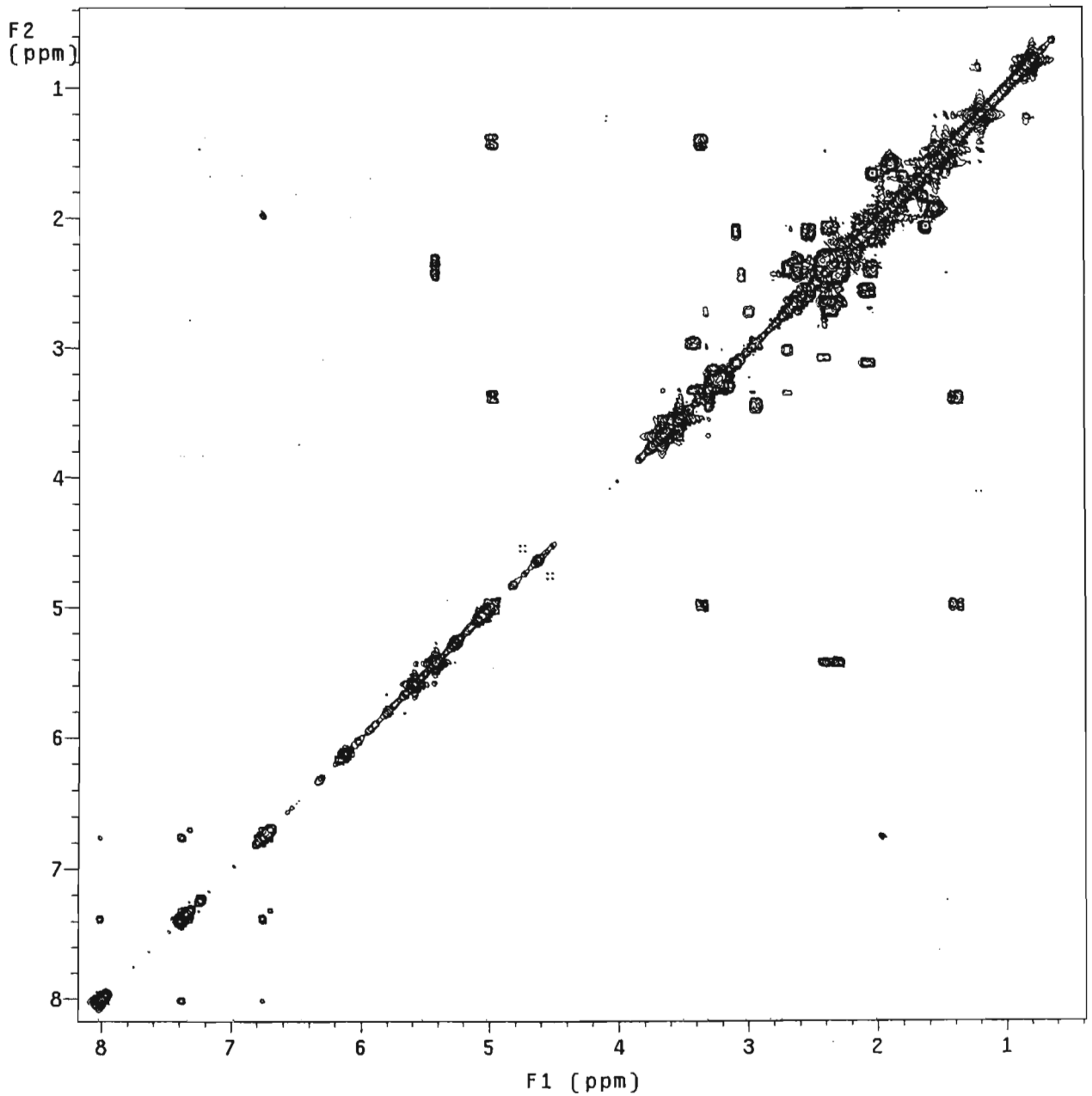
Spectrum NL 2.6: Expanded HMBC Spectrum of leandreanin B NL 2

1H COSY-90
probe=3mmID

Pulse Sequence: relayh



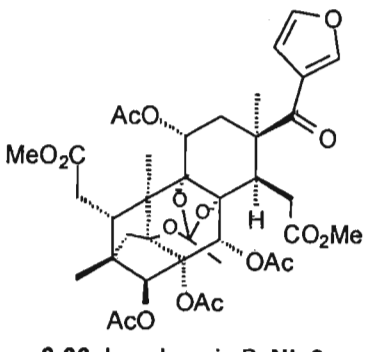
6-36 leandreanin B **NL 2**



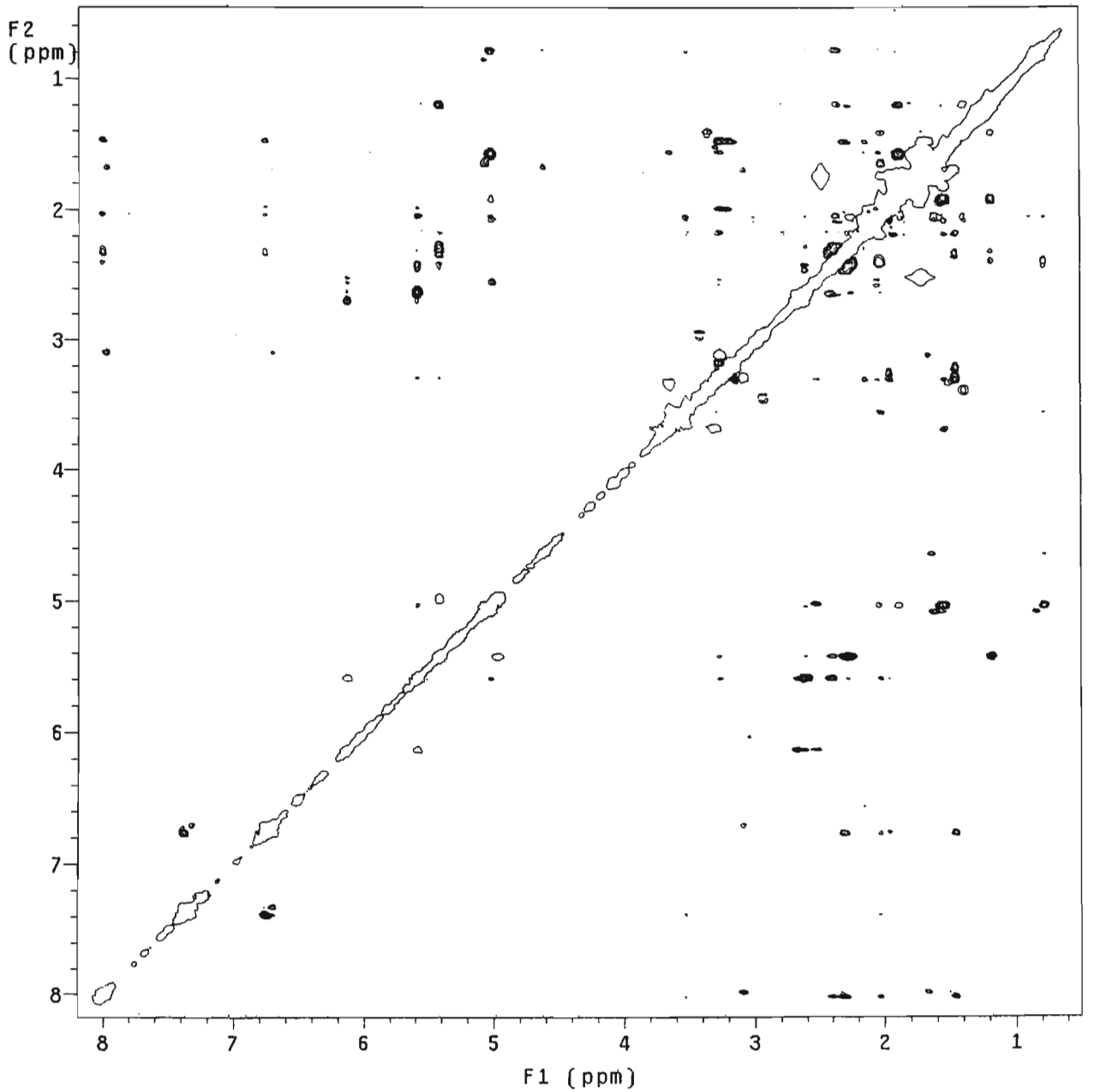
Spectrum NL 2.7: COSY Spectrum of leandreanin B NL 2

mix=1sec
probe=3mmID

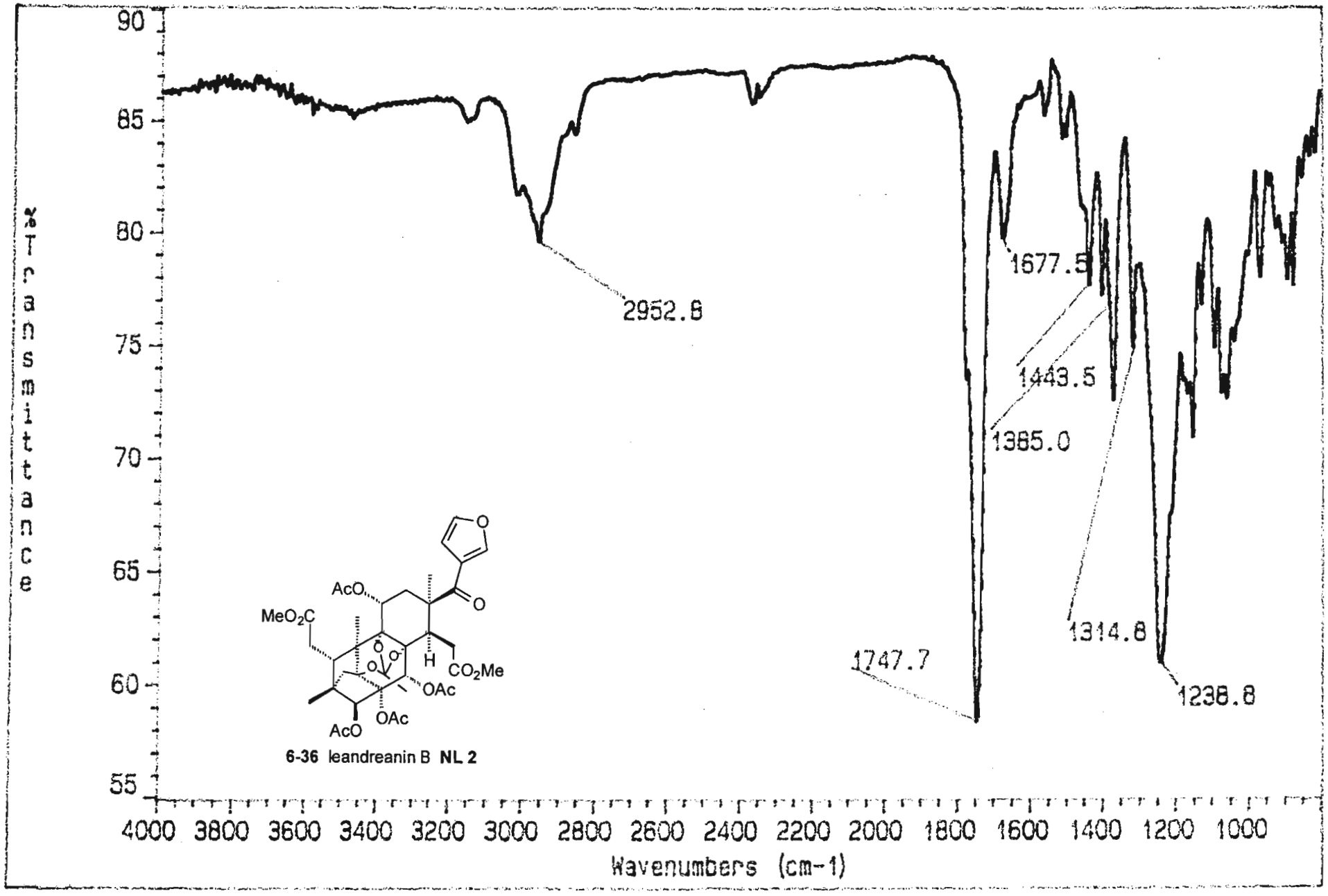
Pulse Sequence: noesy_da



6-36 leandreanin B **NL 2**

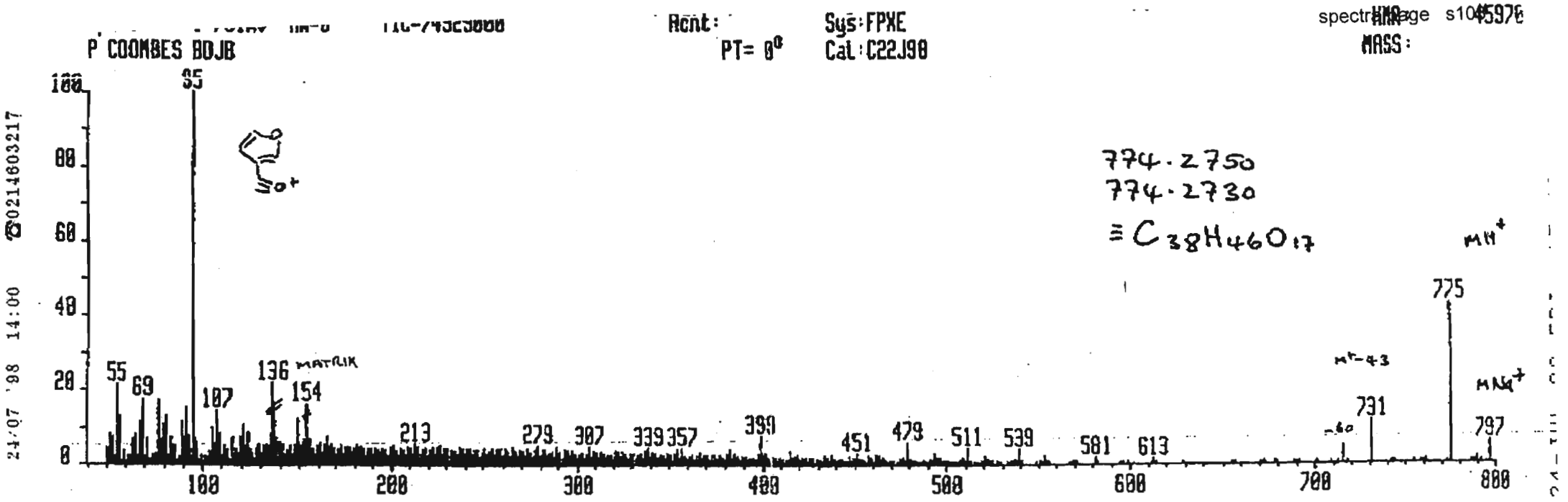


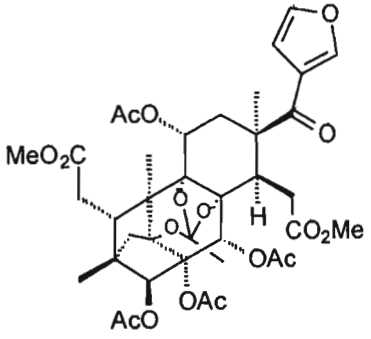
Spectrum NL 2.8: NOESY Spectrum of leandreanin B NL 2



6-36 leandreanin B **NL 2**

Spectrum NL 2.9: IR Spectrum of leandreanin B NL 2

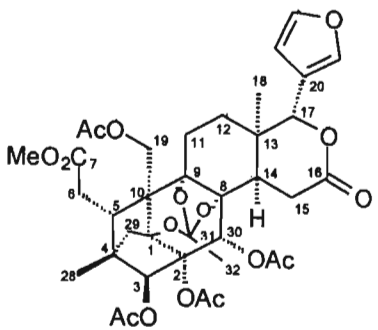




6-36 leandreanin B **NL 2**

Spectrum NL 2.10: Fast Atom Bombardment Mass Spectrum of leandreanin B NL 2

Pulse Sequence: s2pul



6-37 leandreanin C **NL 3**

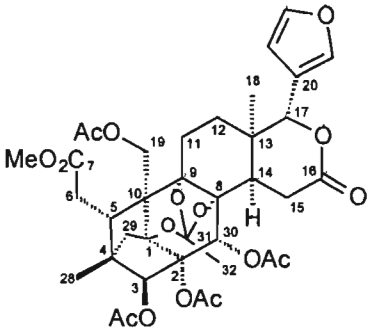
9 8 7 6 5 4 3 2 1 ppm

Spectrum NL 3.1: ^{1}H NMR Spectrum of leandrianin C NL 3

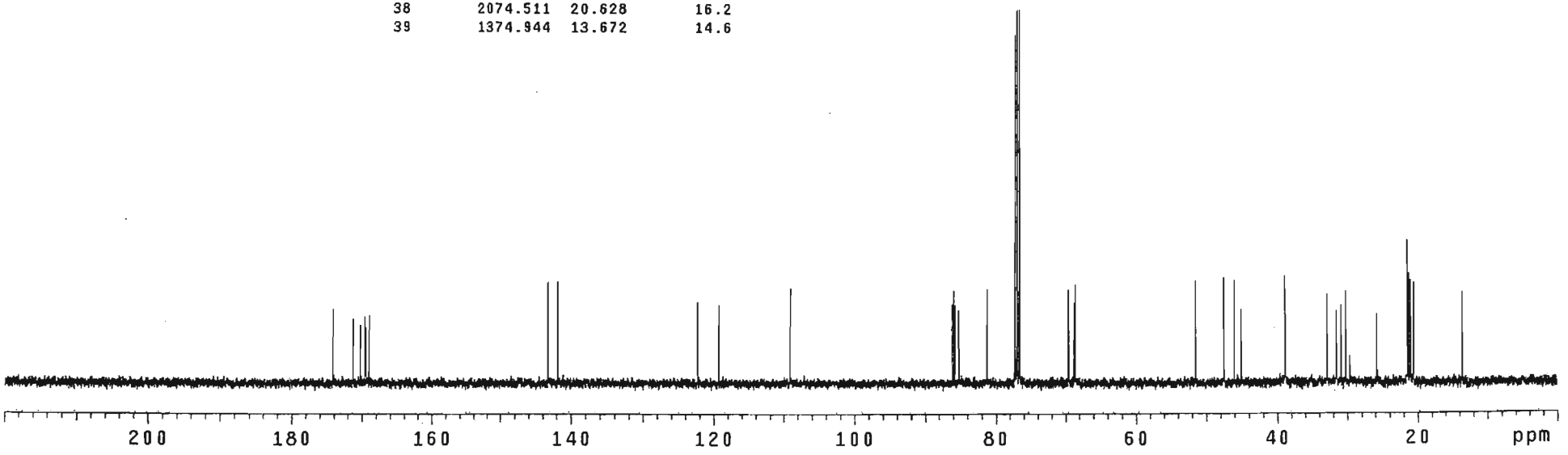
probe=5mm1D

Pulse Sequence: s2pul

INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	17511.954	174.134	12.2				
2	17230.149	171.332	10.5				
3	17124.679	170.283	9.5				
4	17065.352	169.694	10.8				
5	17039.808	169.440	9.1				
6	16998.608	169.030	11.1				
7	14411.282	143.302	16.4				
8	14271.203	141.909	16.6				
9	12296.101	122.269	13.2				
10	12002.760	119.352	12.7				
11	10971.950	109.102	15.5				
12	8665.603	86.169	12.8				
13	8643.355	85.947	15.1				
14	8621.932	85.734	12.7				
15	8567.548	85.194	12.0				
16	8173.681	81.277	15.3				
17	7775.694	77.320	56.0				
18	7743.559	77.000	59.8				
19	7711.423	76.680	60.0				
20	7001.968	69.626	15.1				
21	6920.393	68.815	13.0				
22	6902.266	68.634	16.0				
23	5184.248	51.551	16.6				
24	4780.493	47.536	17.1				
25	4634.647	46.086	16.6				
26	4539.064	45.135	12.0				
27	3915.304	38.933	17.4				
28	3906.240	38.843	12.5				
29	3308.848	32.902	14.5				
30	3177.009	31.591	11.7				
31	3106.146	30.887	12.7				
32	3039.403	30.223	15.0				
33	2597.745	25.831	11.1				
34	2167.622	21.554	23.1				
35	2156.086	21.440	16.7				
36	2142.903	21.308	17.8				
37	2118.183	21.063	16.6				
38	2074.511	20.628	16.2				
39	1374.944	13.672	14.6				

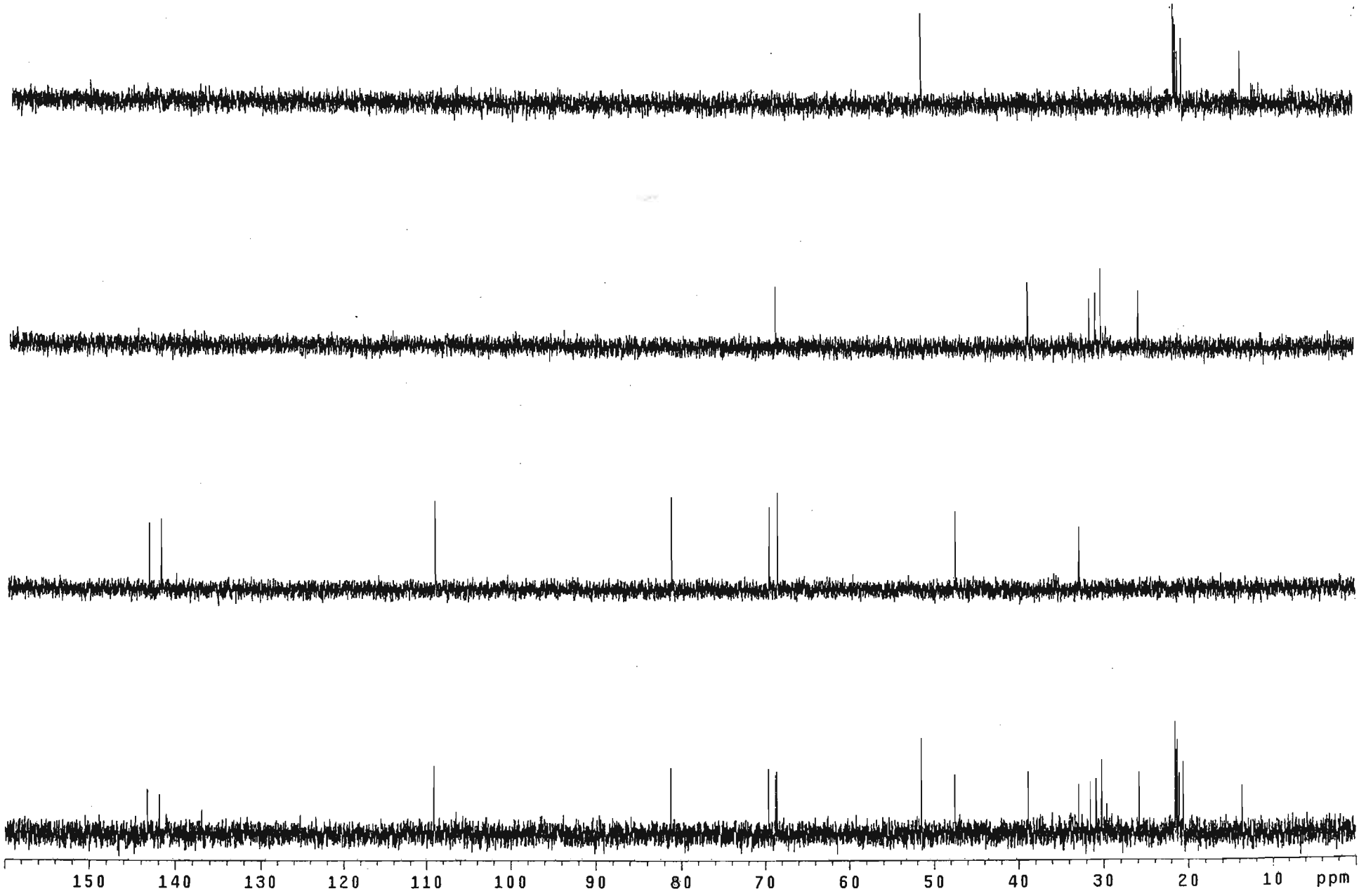


6-37 leandreanin C **NL 3**



Spectrum NL 3.2: ^{13}C NMR Spectrum of leandreanin C NL 3

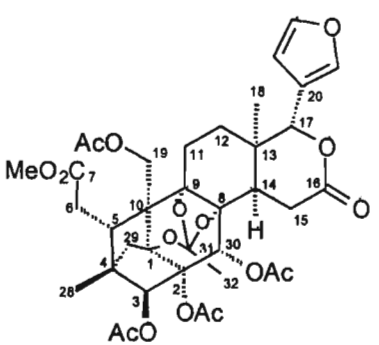
Pulse Sequence: dept



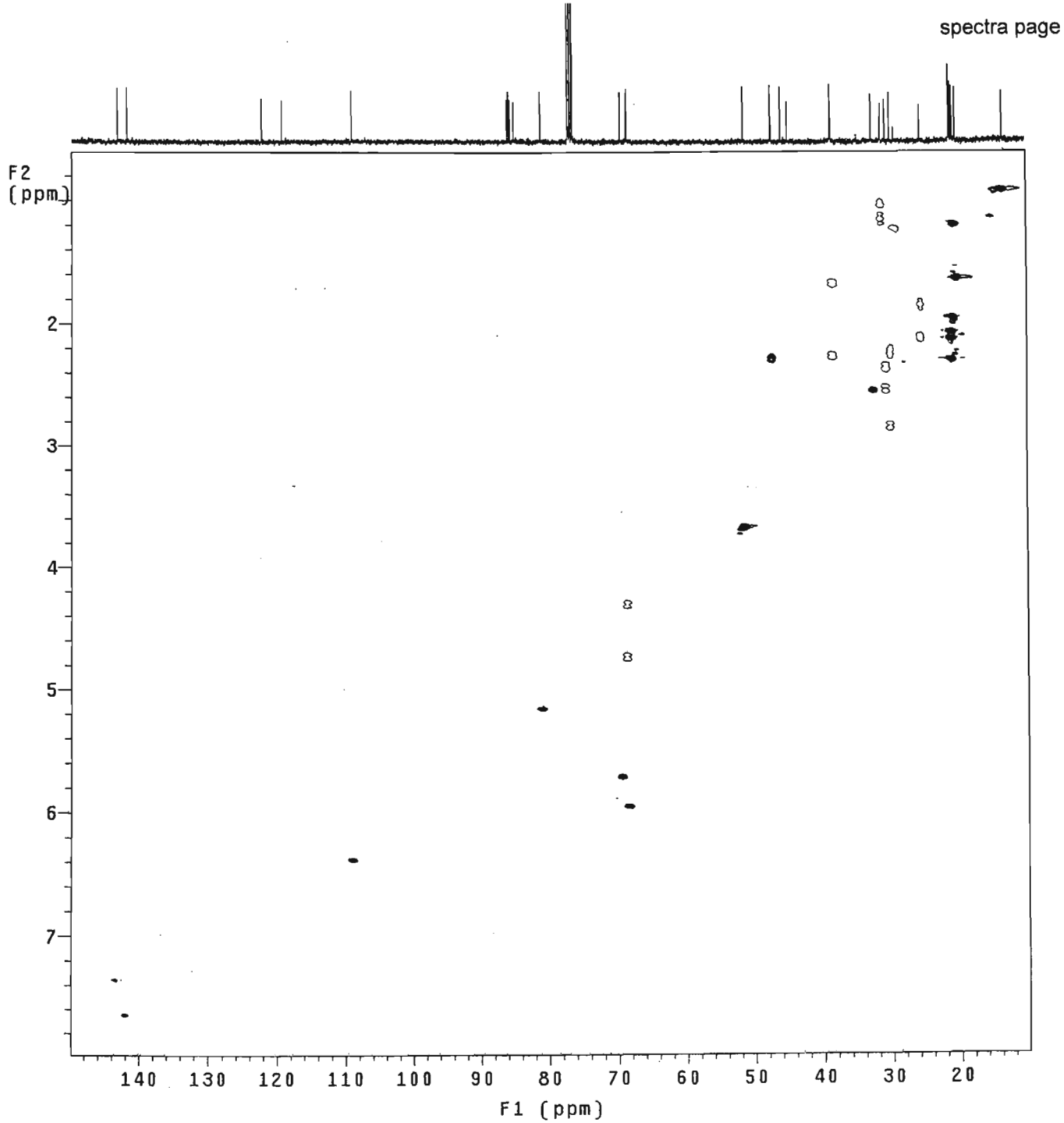
Spectrum NL 3.3: ADEPT Spectrum of leandreanin C NL 3

with mult.editing
probe=3mmID

Pulse Sequence: ghsqc_da



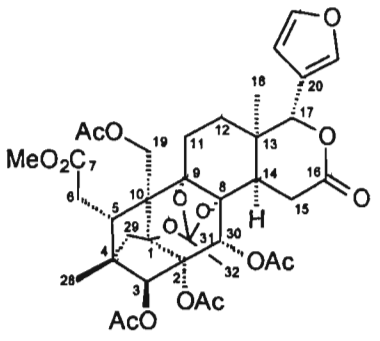
6-37 leandreanin C **NL 3**



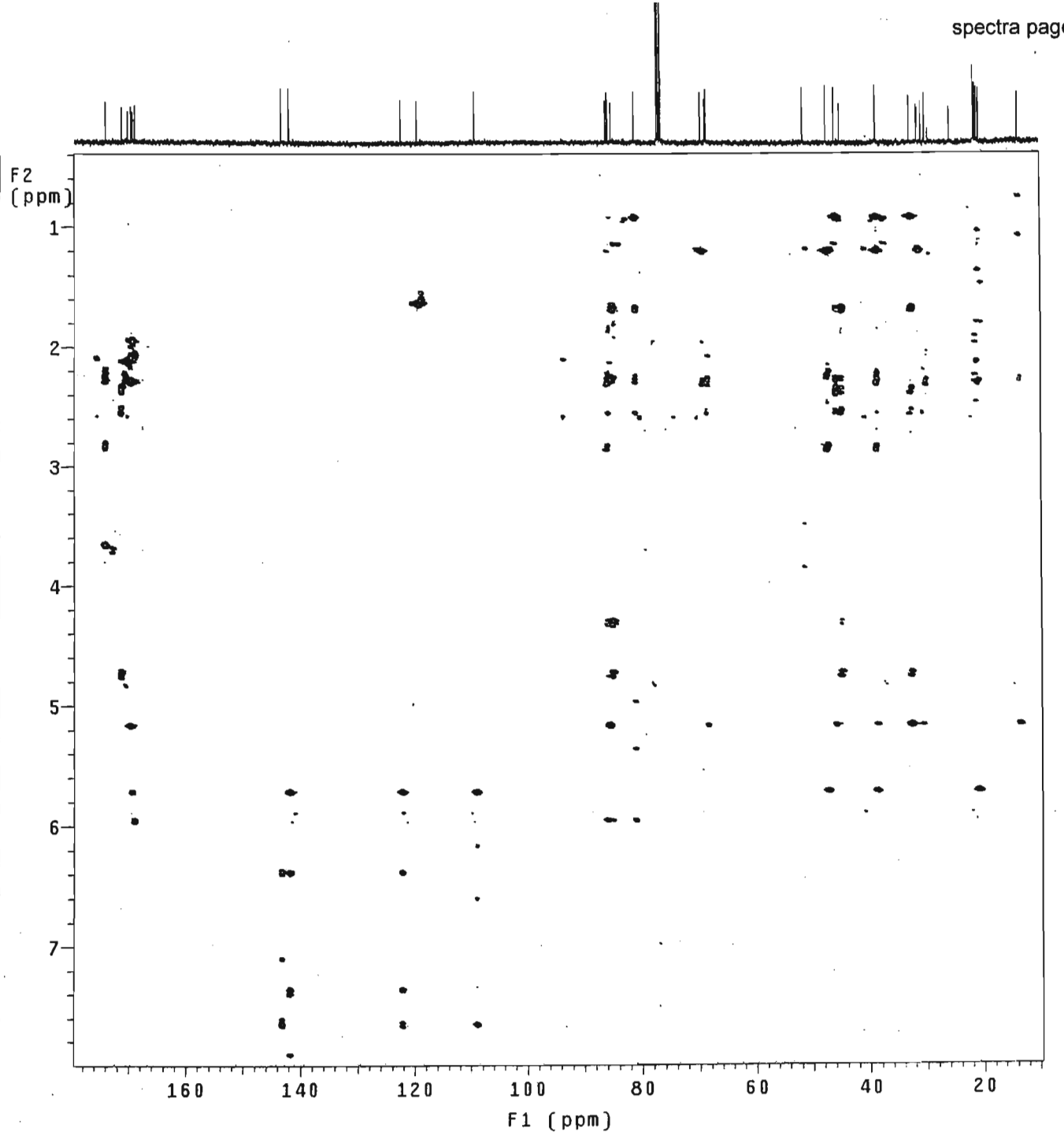
Spectrum NL 3.4: HSQC Spectrum of leandreanin C NL 3

Gradient HMBC expt.
probe=3mmID

Pulse Sequence: ghmqc_da



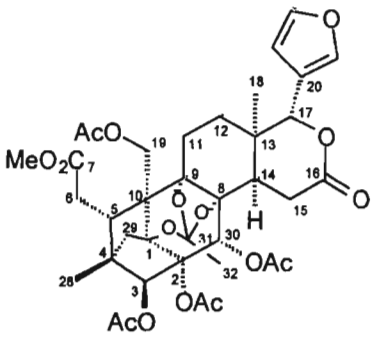
6-37 leandreanin C **NL 3**



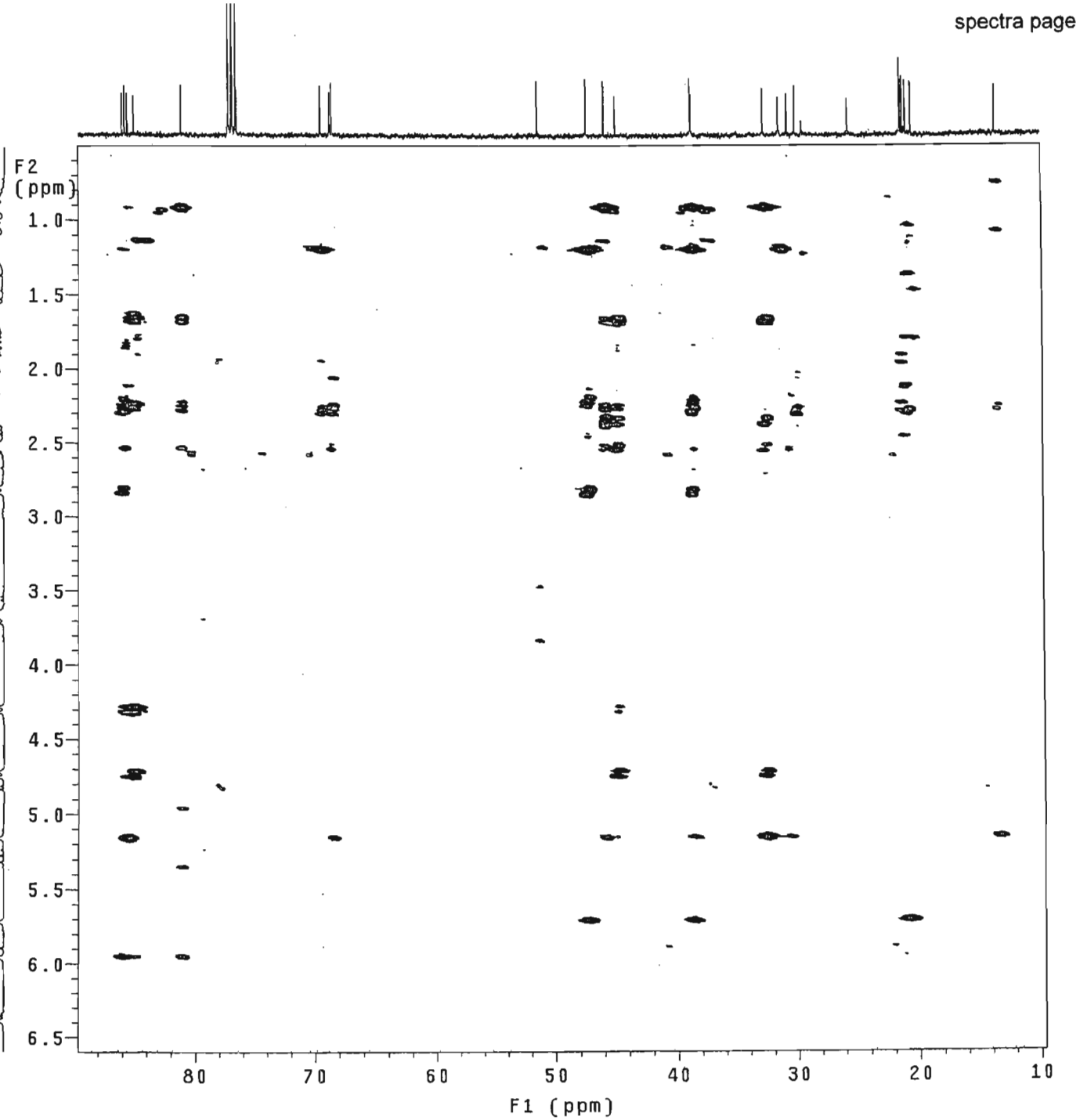
Spectrum NL 3.5: HMBC Spectrum of leandreanin C NL 3

probe=3mmID

Pulse Sequence: ghmqc_da



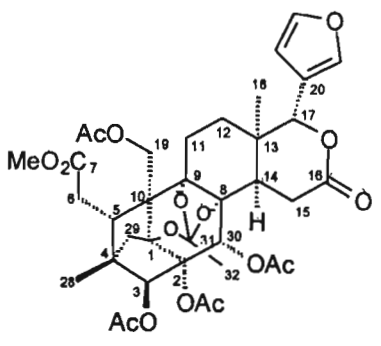
6-37 leandreanin C **NL 3**



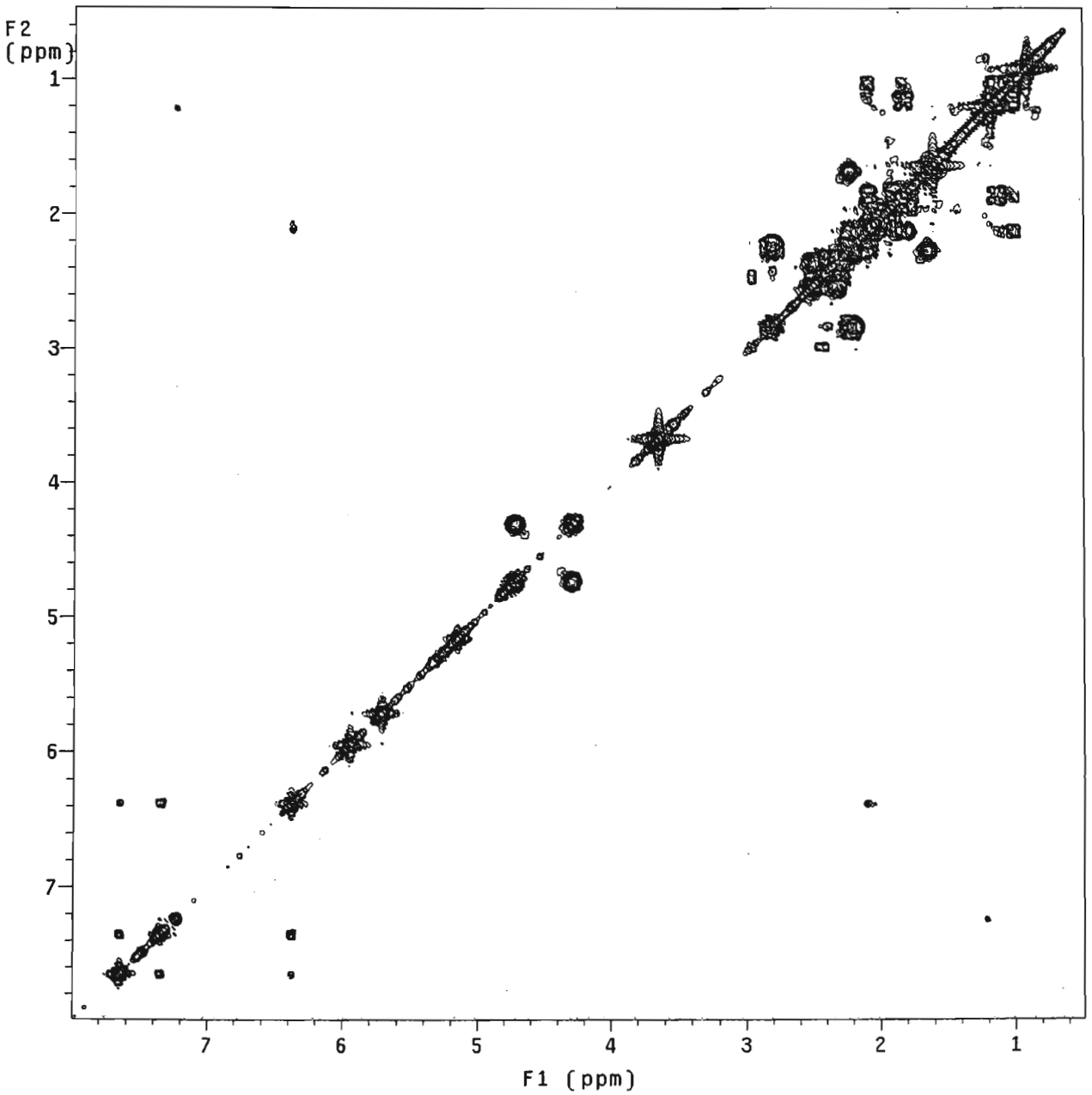
Spectrum NL 3.6: Expanded HMBC Spectrum of leandreanin C NL 3

probe=3mmID

Pulse Sequence: relayh



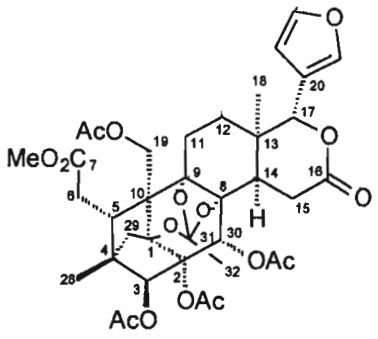
6-37 leandreanin C **NL 3**



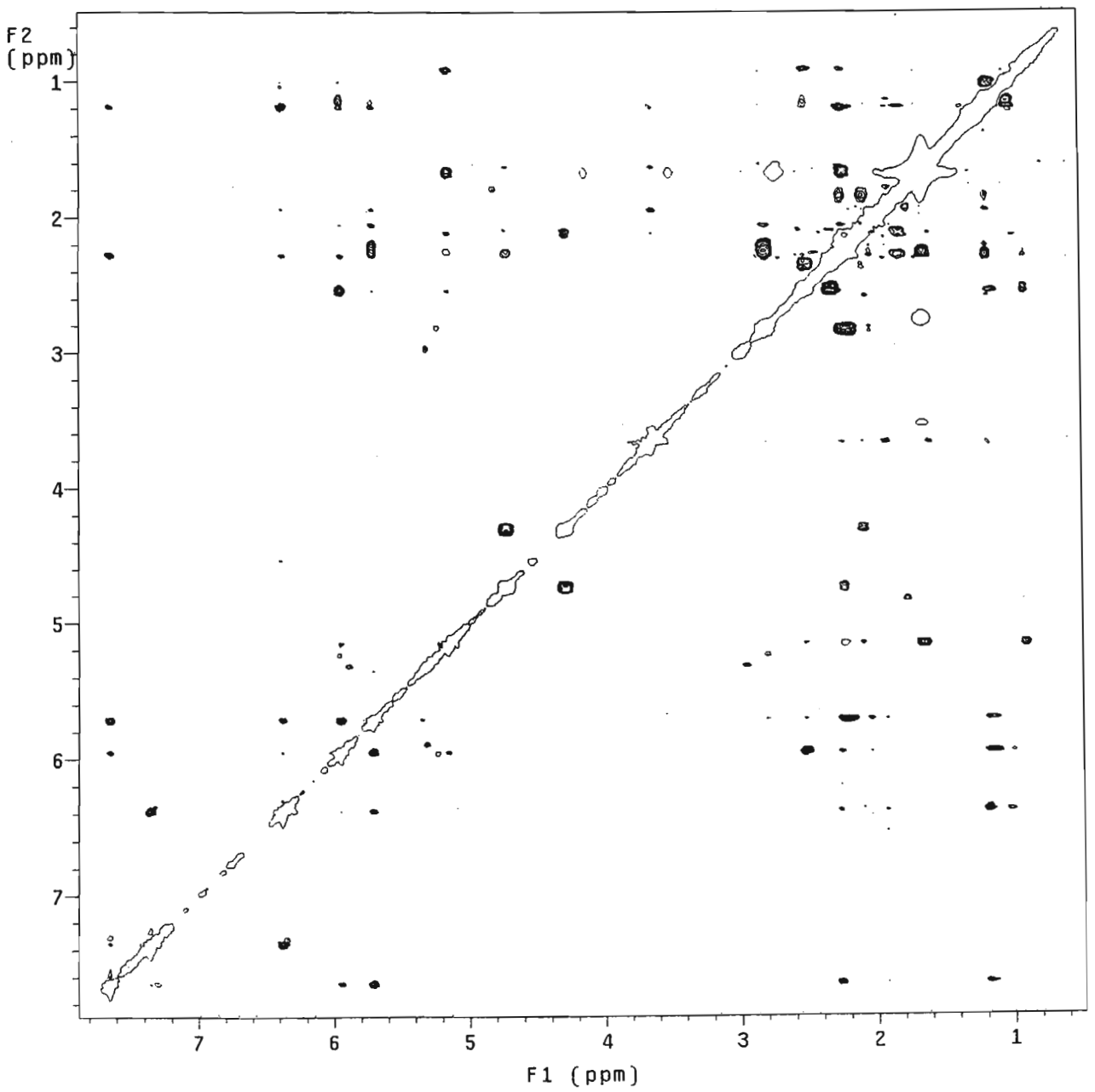
Spectrum NL 3.7: COSY Spectrum of leandreanin C NL 3

NOESY expt.
mix=1sec
probe=3mmID

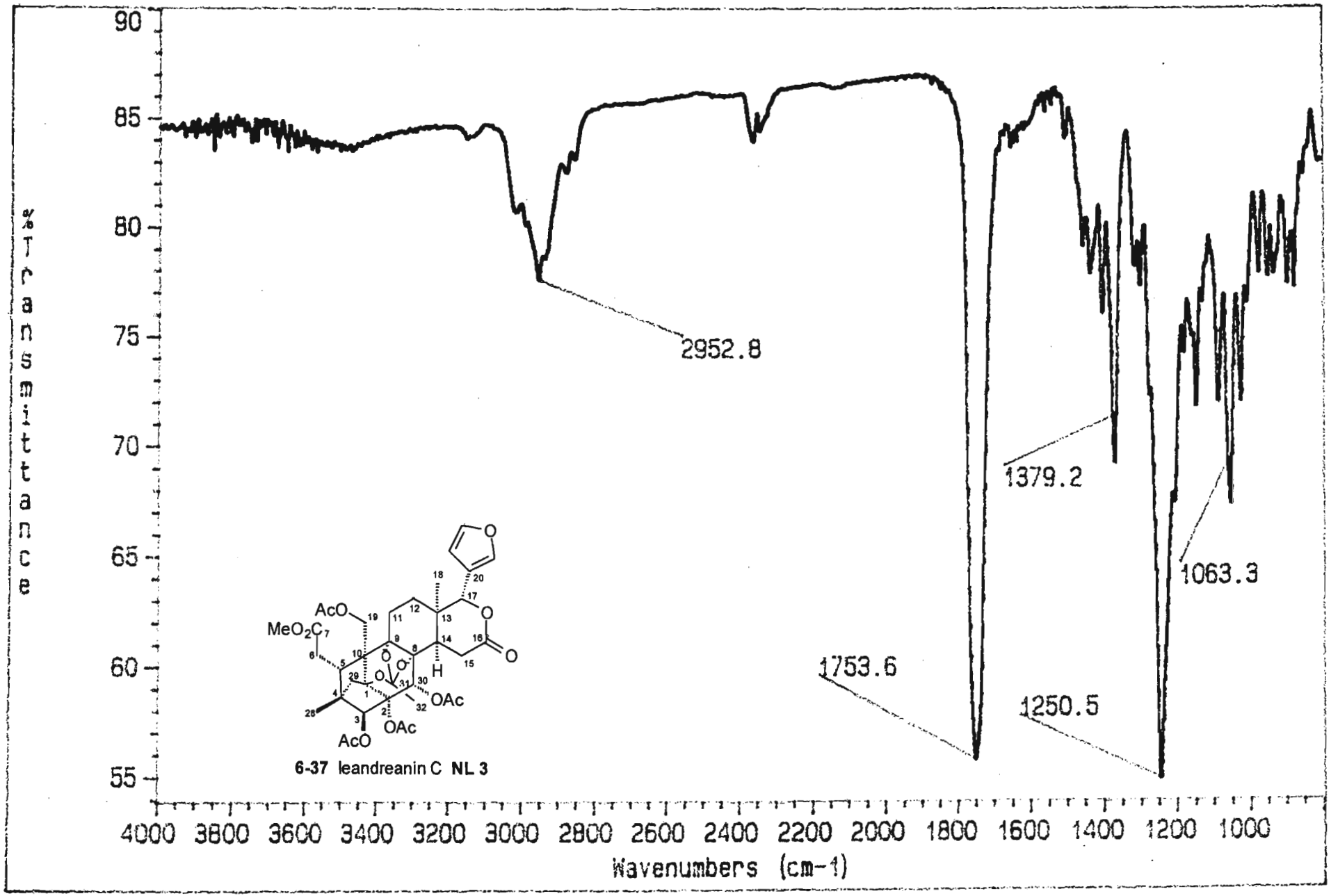
Pulse Sequence: noesy_da



6-37 leandreanin C **NL 3**



Spectrum NL 3.8: NOESY Spectrum of leandreanin C NL 3



Spectrum NL 3.9: IR Spectrum of leandreanin C NL 3

ATOMIC COMPOSITION REPORT (MANUAL)

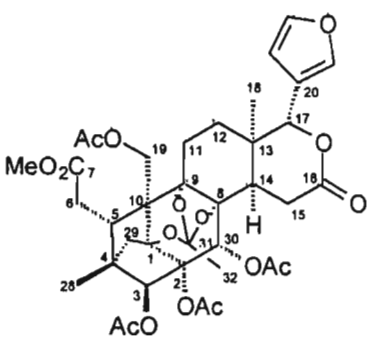
Selected Isotopes:

Symbol	Min	Max	Vcy	Name
C	0	37	4	Carbon-12
H	0	44	1	Hydrogen-1
O	0	16	2	Oxygen-16

Allowable error = minimum of 20.0 ppm, 2.8 mmu.
Ring/Double Bond limits = [0.5 : 100.0]

Mass	Calculated	ppm	mmu	R/DB	Formula
744.26308	744.26294	-0.2	-0.1	16.0	$C_{37}H_{44}O_{16}$

***** End of Atomic Composition Report *****



6-37 leandreanin C **NL 3**

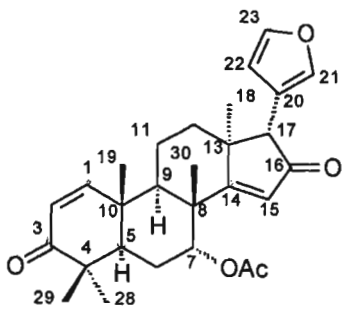
MRS K Mc Farland.
Chemistry.
BDBB. P. Coombes.

By peak matching
all 3 could do
MS is abit due
to heavy work load
Not being in service
Service until Tuesday.

Spectrum NL 3.10: High Resolution Mass Spectrum of leandreanin C NL 3

using presat mec12
satpwr=-12
probe=5mmASW

Pulse Sequence: presat_da

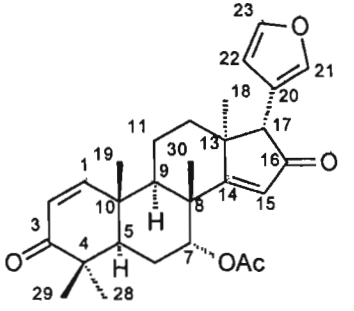


7-4 azadiradione **QP 1**

Spectrum QP 1.1: ^{1}H NMR Spectrum of azadiradione QP 1

Pulse Sequence: s2pul

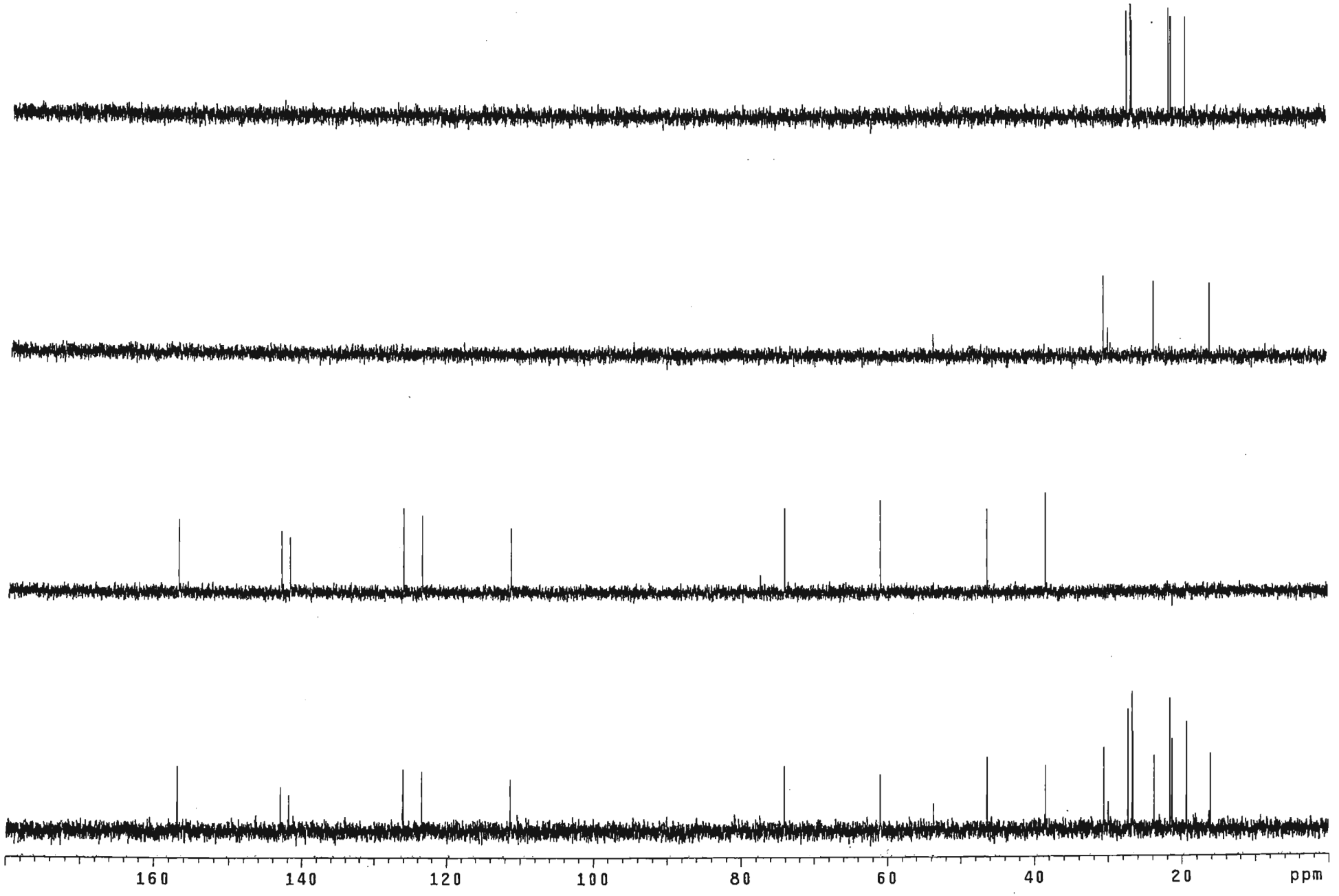
1	20623.964	205.076	8.9
2	20517.849	204.021	7.0
3	19344.819	192.357	7.7
4	17057.165	169.610	9.0
5	15763.213	156.743	12.4
6	14360.678	142.797	15.7
7	14243.868	141.635	16.4
8	12662.828	125.914	14.7
9	12397.128	123.272	13.0
10	11906.035	118.389	9.7
11	11174.743	111.117	12.8
12	7775.754	77.319	292.1
13	7764.237	77.204	13.4
14	7743.672	77.000	300.0
15	7711.591	76.681	289.8
16	7427.794	73.859	12.7
17	6105.051	60.706	14.1
18	5372.113	53.418	6.5
19	4825.083	47.979	13.0
20	4635.062	46.089	15.9
21	4477.945	44.527	10.5
22	4431.057	44.061	14.1
23	4019.756	39.971	13.3
24	3836.316	38.147	13.8
25	3043.328	30.262	12.2
26	2984.924	29.681	5.8
27	2712.643	26.973	15.1
28	2658.351	26.434	19.5
29	2644.367	26.295	14.7
30	2355.634	23.423	12.1
31	2139.290	21.272	14.9
32	2108.853	20.970	10.5
33	1913.074	19.023	16.6
34	1587.324	15.784	12.3



7-4 azadiradione **QP 1**

Spectrum QP 1.2: ^{13}C NMR Spectrum of azadiradione QP 1

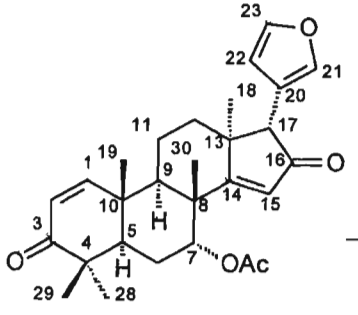
Pulse Sequence: dept



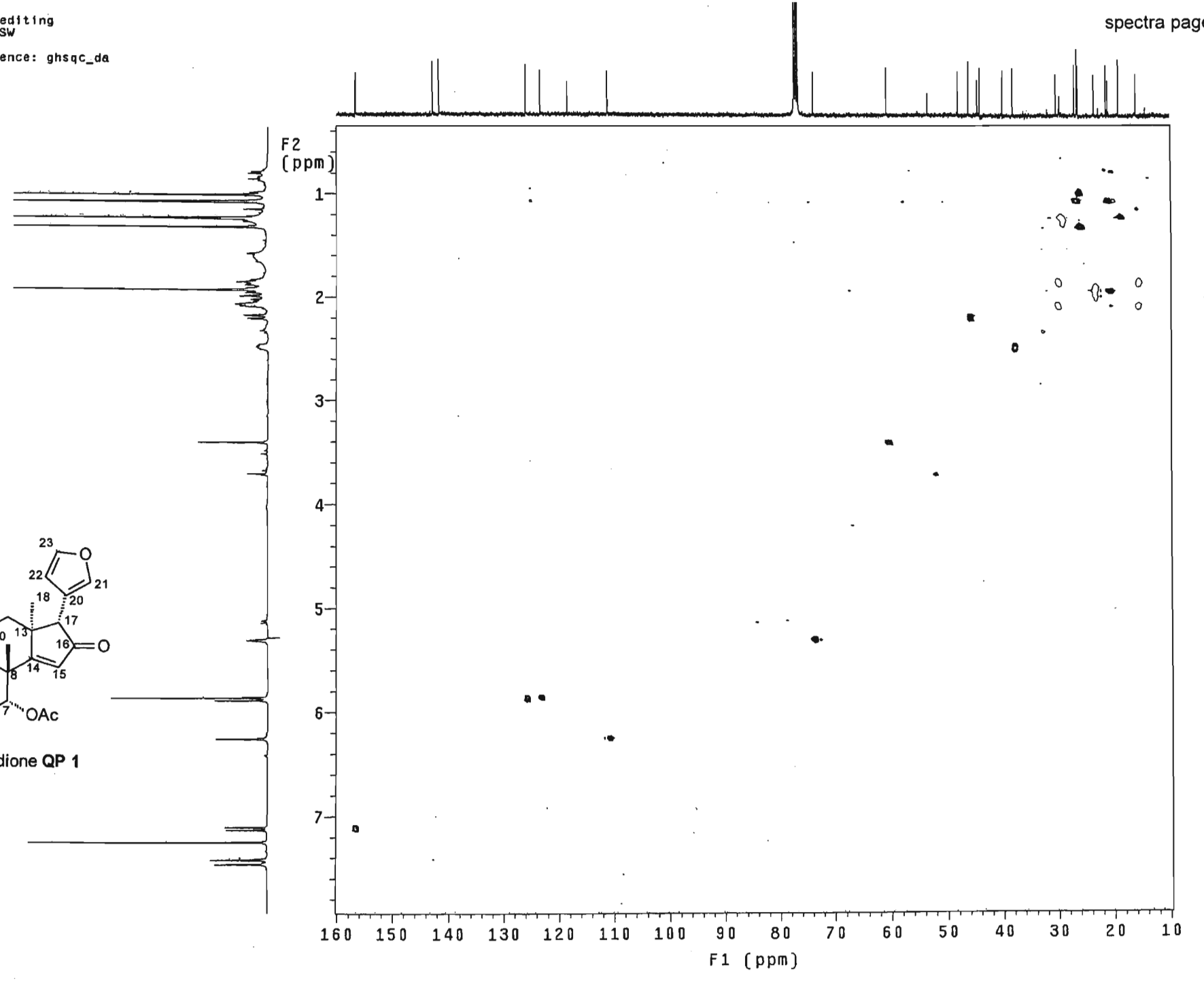
Spectrum QP 1.3: ADEPT Spectrum of azadiradione QP 1

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da



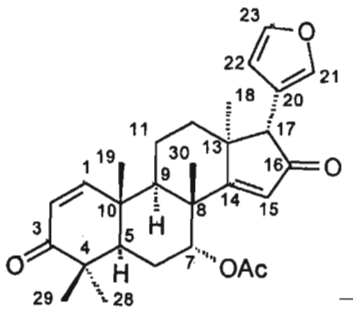
7-4 azadiradione **QP 1**



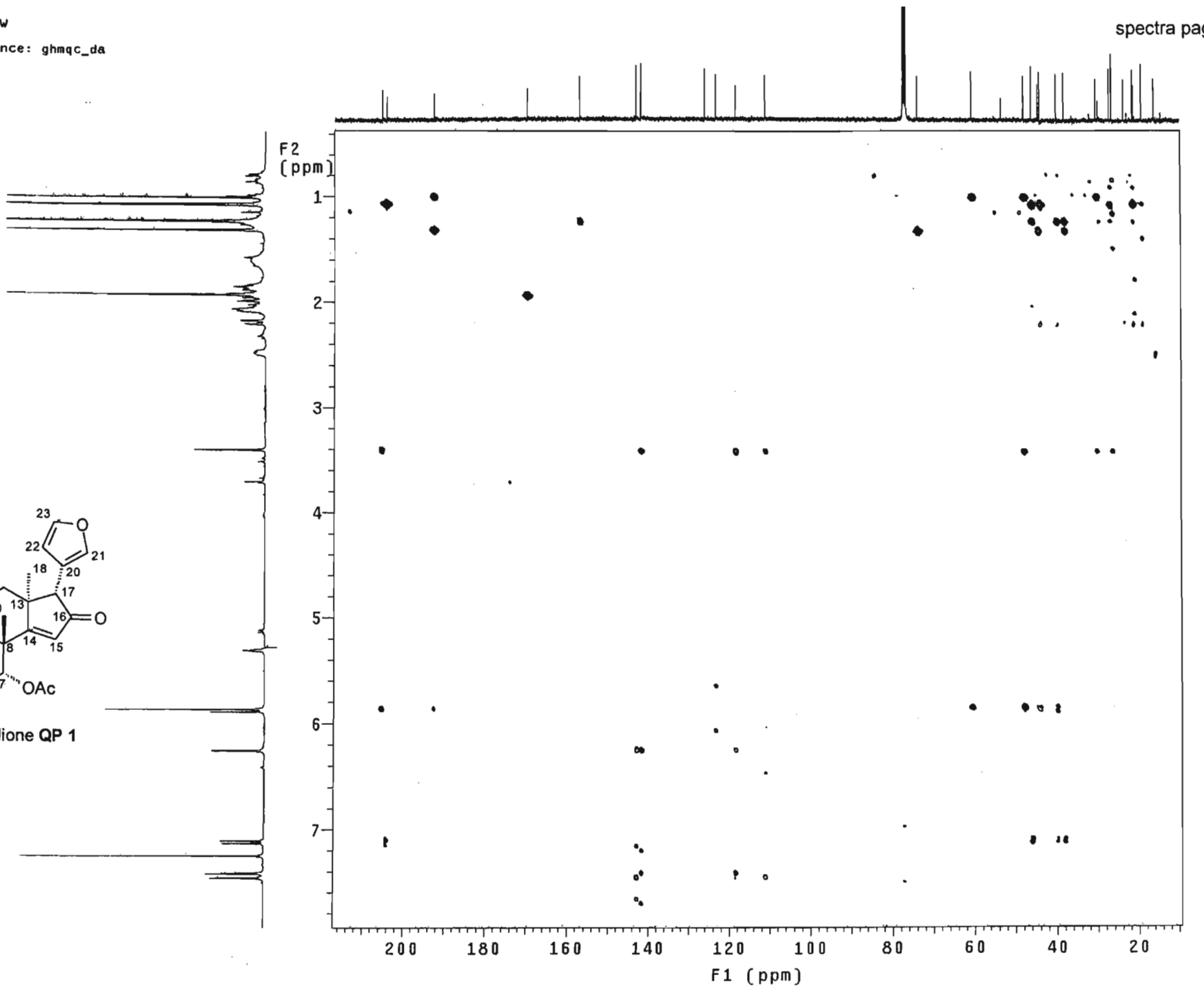
Spectrum QP 1.4: HSQC Spectrum of azadiradione QP 1

probe=5mmASW

Pulse Sequence: ghmqc_da



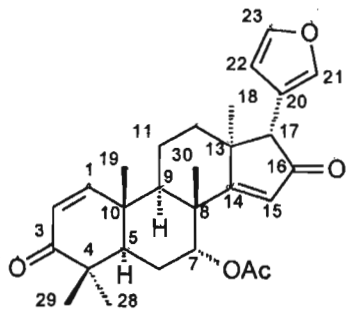
7-4 azadiradione **QP 1**



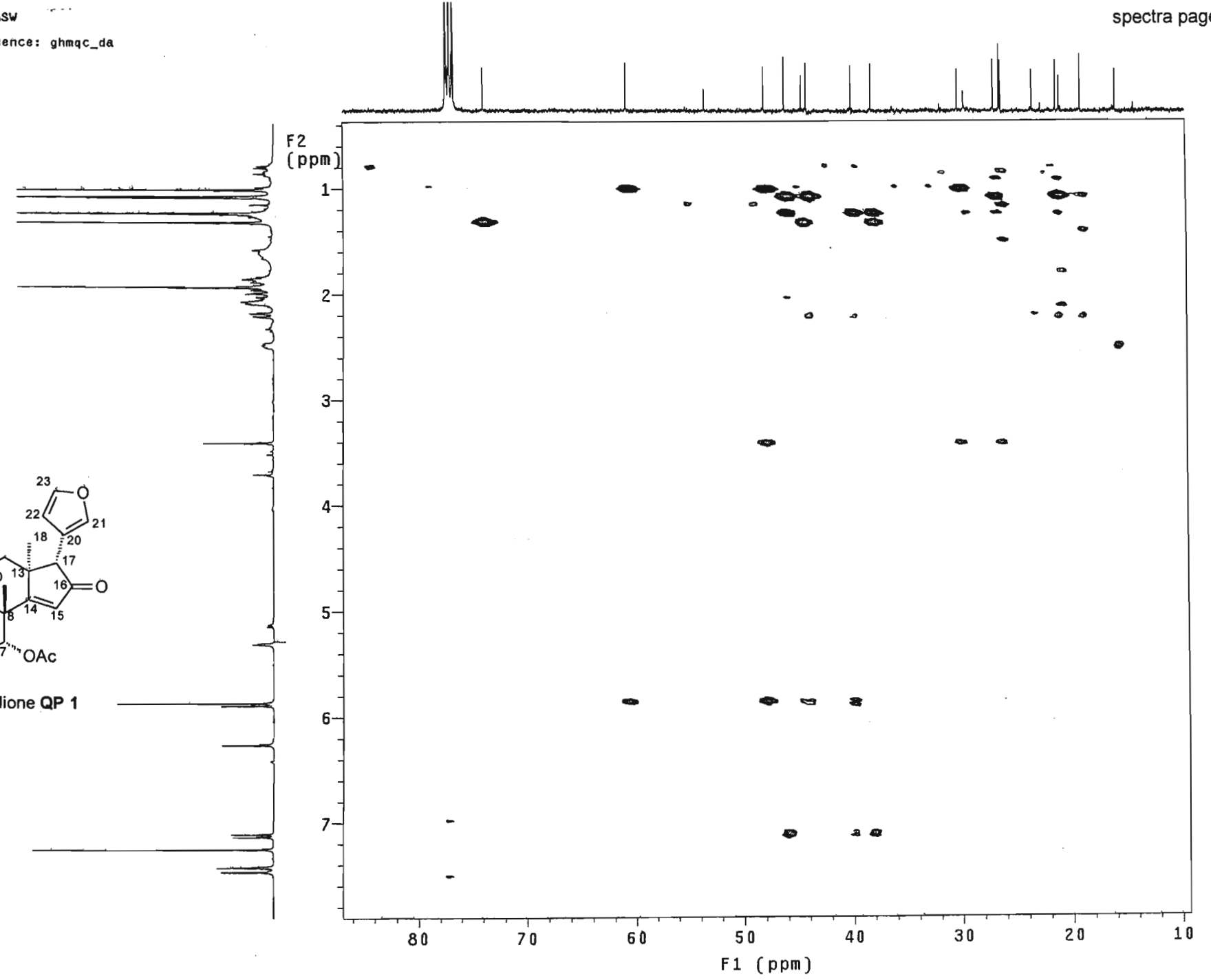
Spectrum QP 1.5: HMBC Spectrum of azadiradione QP 1

probe=5mmASW

Pulse Sequence: ghmqc_da



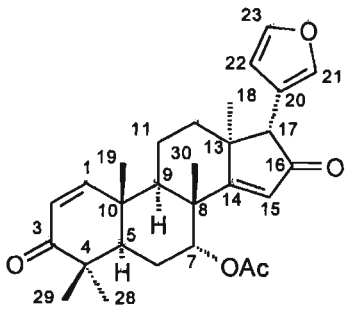
7-4 azadiradione **QP 1**



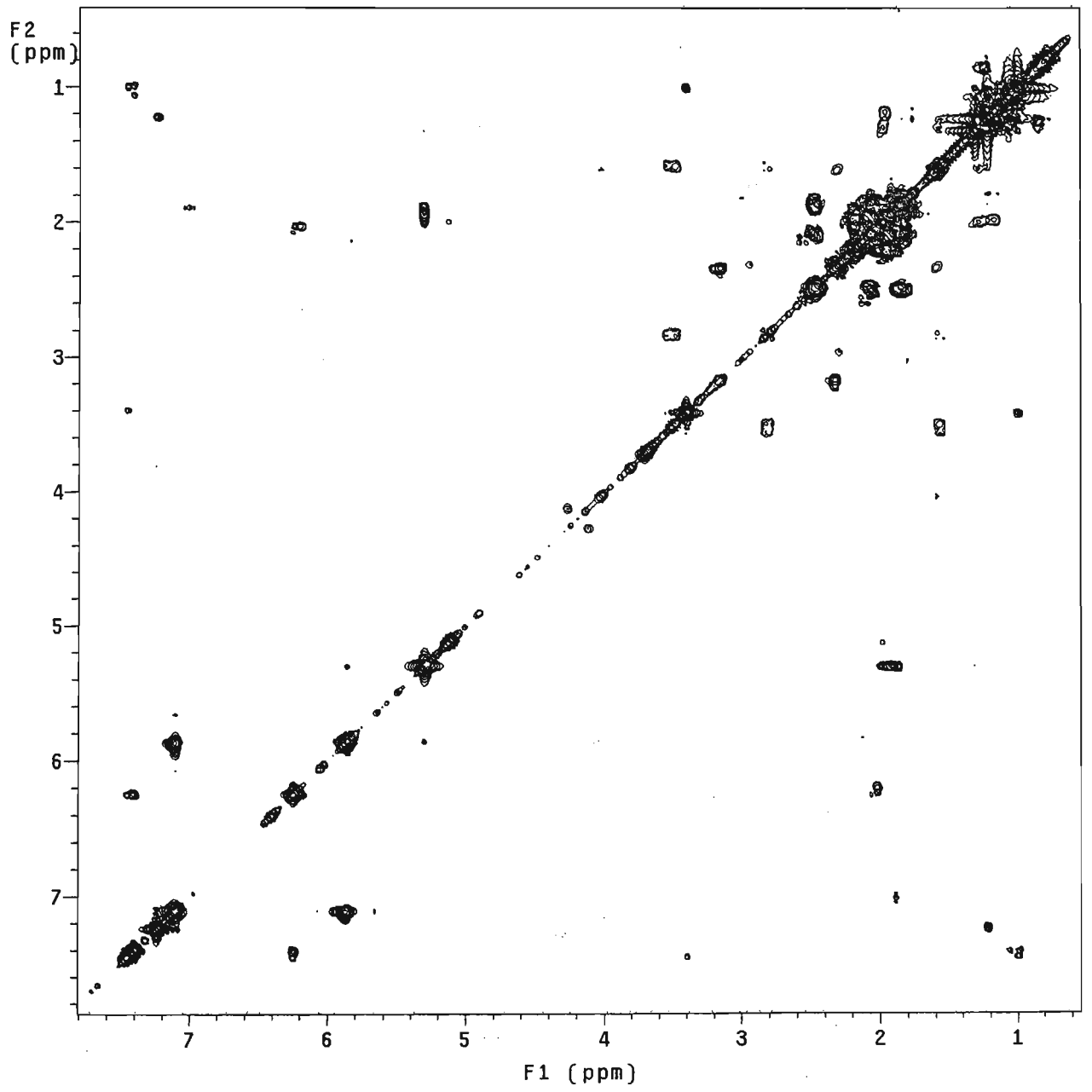
Spectrum QP 1.6: Expanded HMBC Spectrum of azadiradione QP 1

probe=5mmASW

Pulse Sequence: relayh



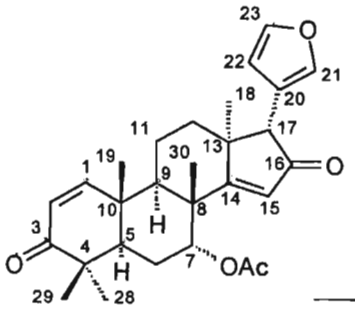
7-4 azadiradione **QP 1**



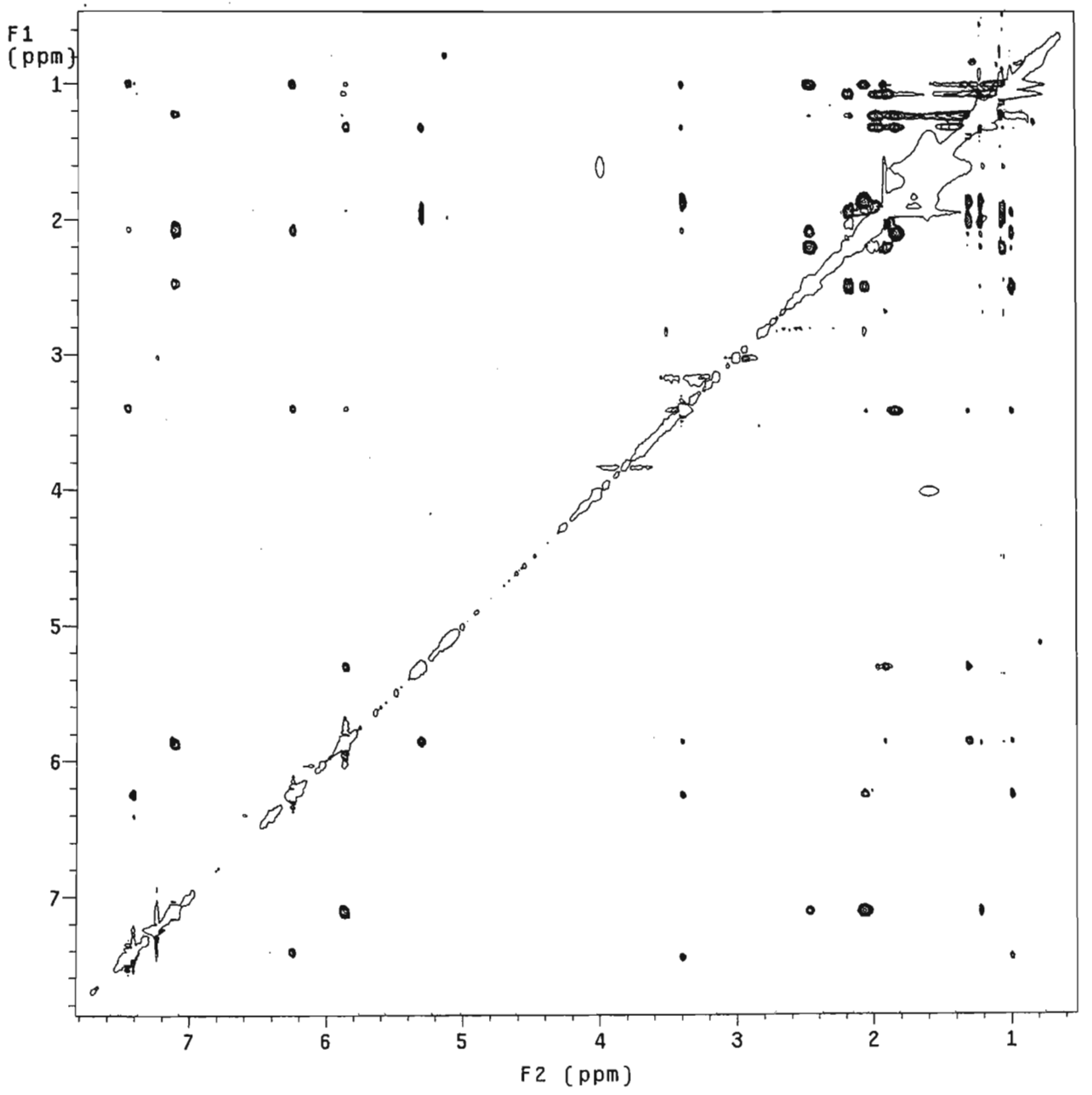
Spectrum QP 1.7: COSY Spectrum of azadiradione QP 1

using presat-mec12
mix=1sec
probe=5mmASW

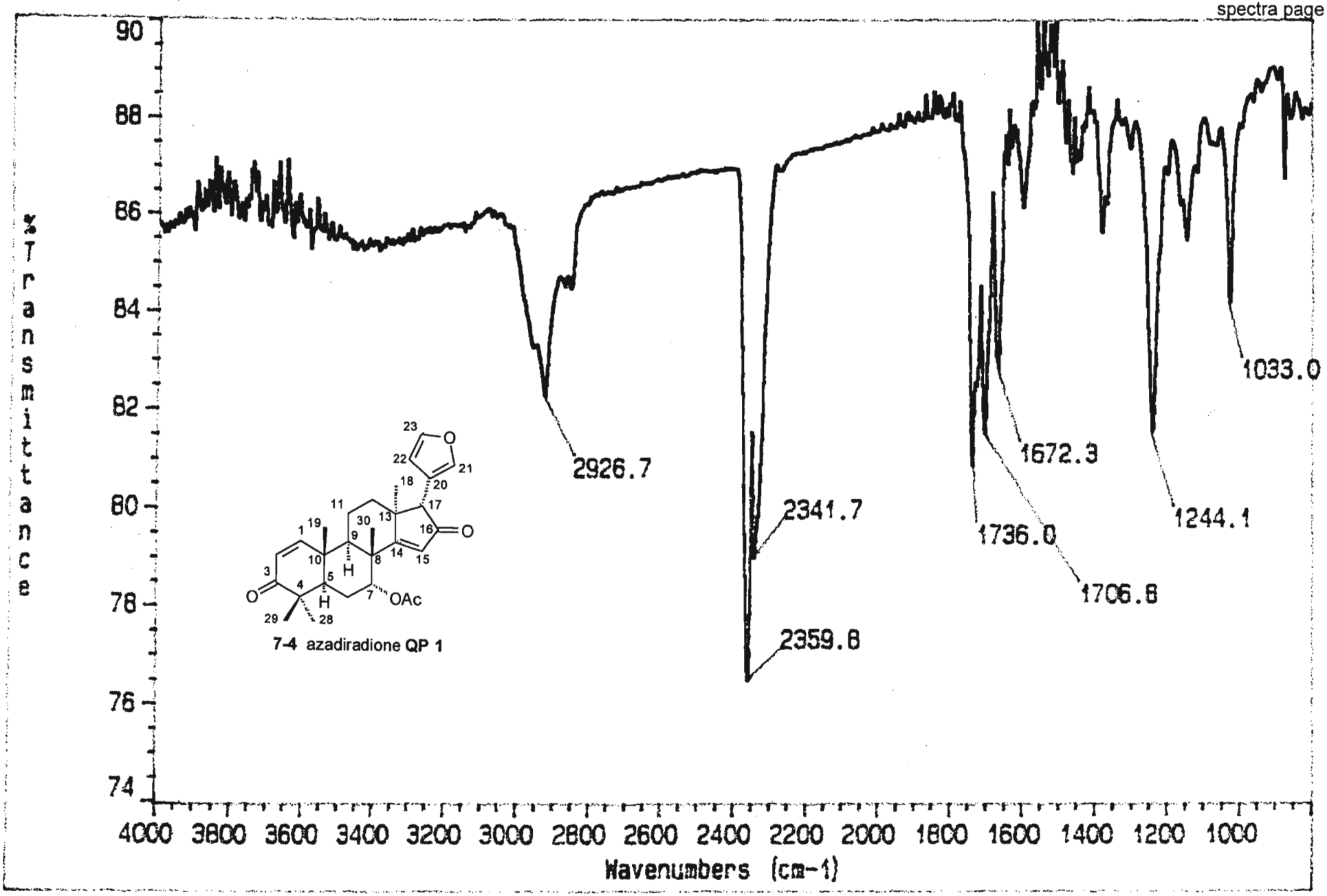
Pulse Sequence: noesy_da



7-4 azadiradione **QP 1**



Spectrum QP 1.8: NOESY Spectrum of azadiradione QP 1

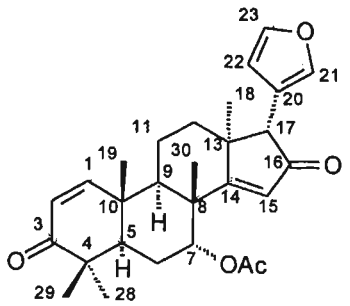


Spectrum QP 1.9: IR Spectrum of azadiradione QP 1

File Name	: C:\MASPEC\data\hc091417.ms2
File Source	: Acquired on MASPEC II system [II32/A002]
File Title	: QPK13a-3
Operator	: Dr. P. Boshoff
Instrument	: VG70-SEQ

(B a few reb peaks
just through.

SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Int:0.2%. Range:0-460. Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 47#6:07 - 50#6:30. Sub=36#4:42 - 38#4:58. Entries=459. Base M/z=450.24144. 100% Int.=3.51872. EI. POS.

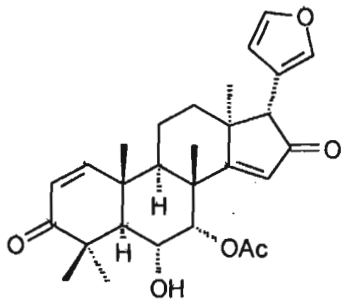


7-4 azadiradione **QP 1**

Spectrum QP 1.10: High Resolution Mass Spectrum of azadiradione QP 1

Probe=5mmASW

Pulse Sequence: s2pul



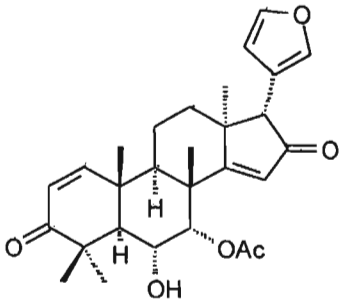
7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP2.1: ^{1}H NMR Spectrum of 6α-hydroxyazadiradione QP 2

probe=5mmASW

Pulse Sequence: s2pul

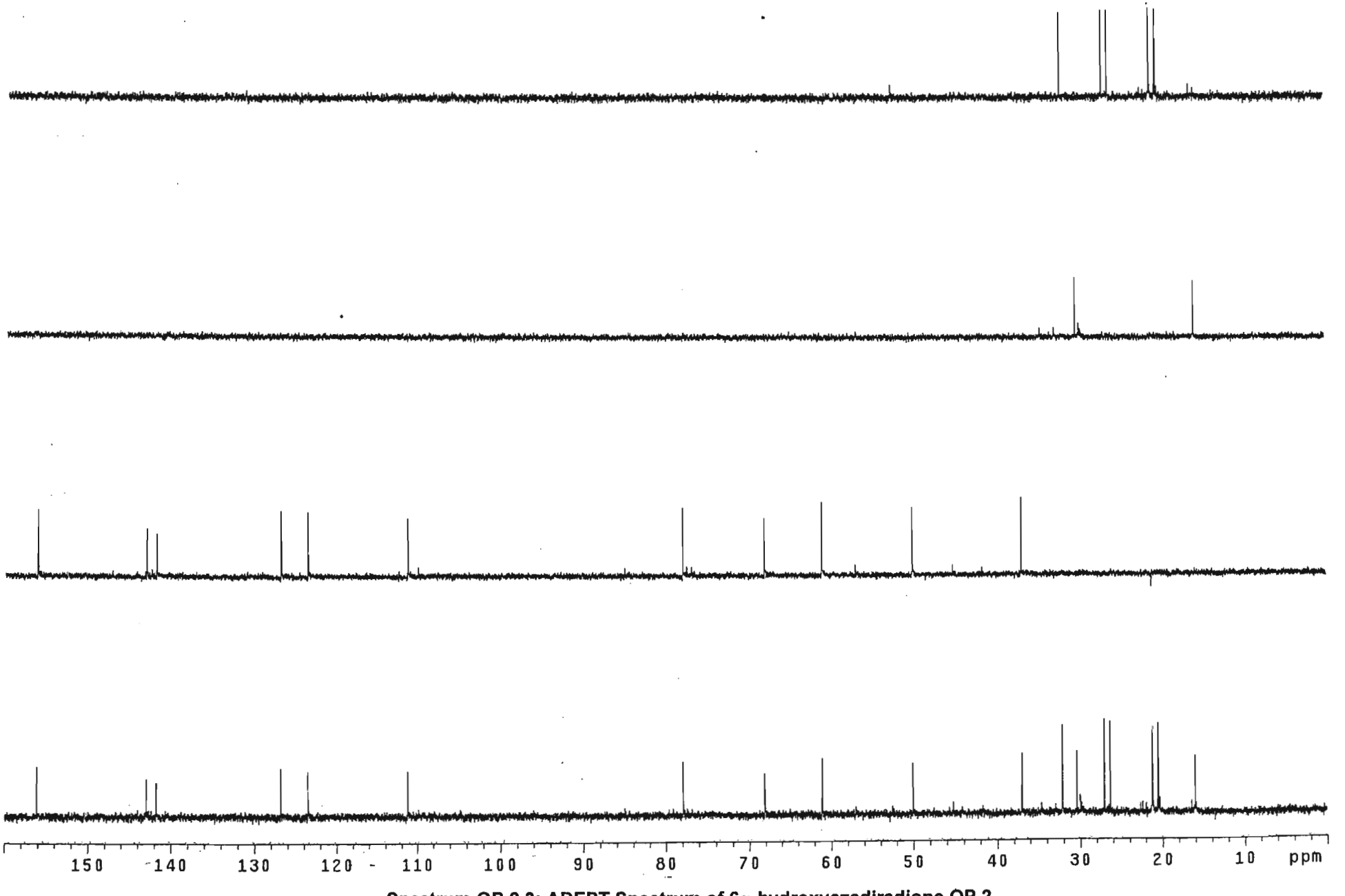
PEAK	FREQUENCY	PPM	HEIGHT
1	20665.260	205.487	5.0
2	20612.615	204.964	6.3
3	19269.801	191.611	6.0
4	17268.550	171.712	6.2
5	15702.187	156.136	9.2
6	14380.736	142.996	12.0
7	14261.713	141.813	10.4
8	12756.388	126.844	10.3
9	12430.603	123.605	10.1
10	11912.551	118.454	6.6
11	11190.025	111.269	10.6
12	7842.145	77.979	9.9
13	7802.471	77.585	143.9
14	7791.026	77.471	6.6
15	7770.426	77.266	150.0
16	7738.382	76.947	147.1
17	6853.345	68.147	8.6
18	6147.605	61.129	10.1
19	5036.731	50.083	10.5
20	4848.279	48.209	9.7
21	4600.316	45.744	11.0
22	4540.042	45.144	12.8
23	4104.391	40.812	13.6
24	3725.198	37.042	10.2
25	3236.902	32.186	11.0
26	3062.183	30.449	8.2
27	2724.191	27.088	10.3
28	2651.709	26.368	10.4
29	2143.576	21.315	12.1
30	2133.658	21.216	12.7
31	2067.280	20.556	12.4
32	1616.369	16.073	9.2



7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.2: ^{13}C NMR Spectrum of 6α-hydroxyazadiradione QP 2

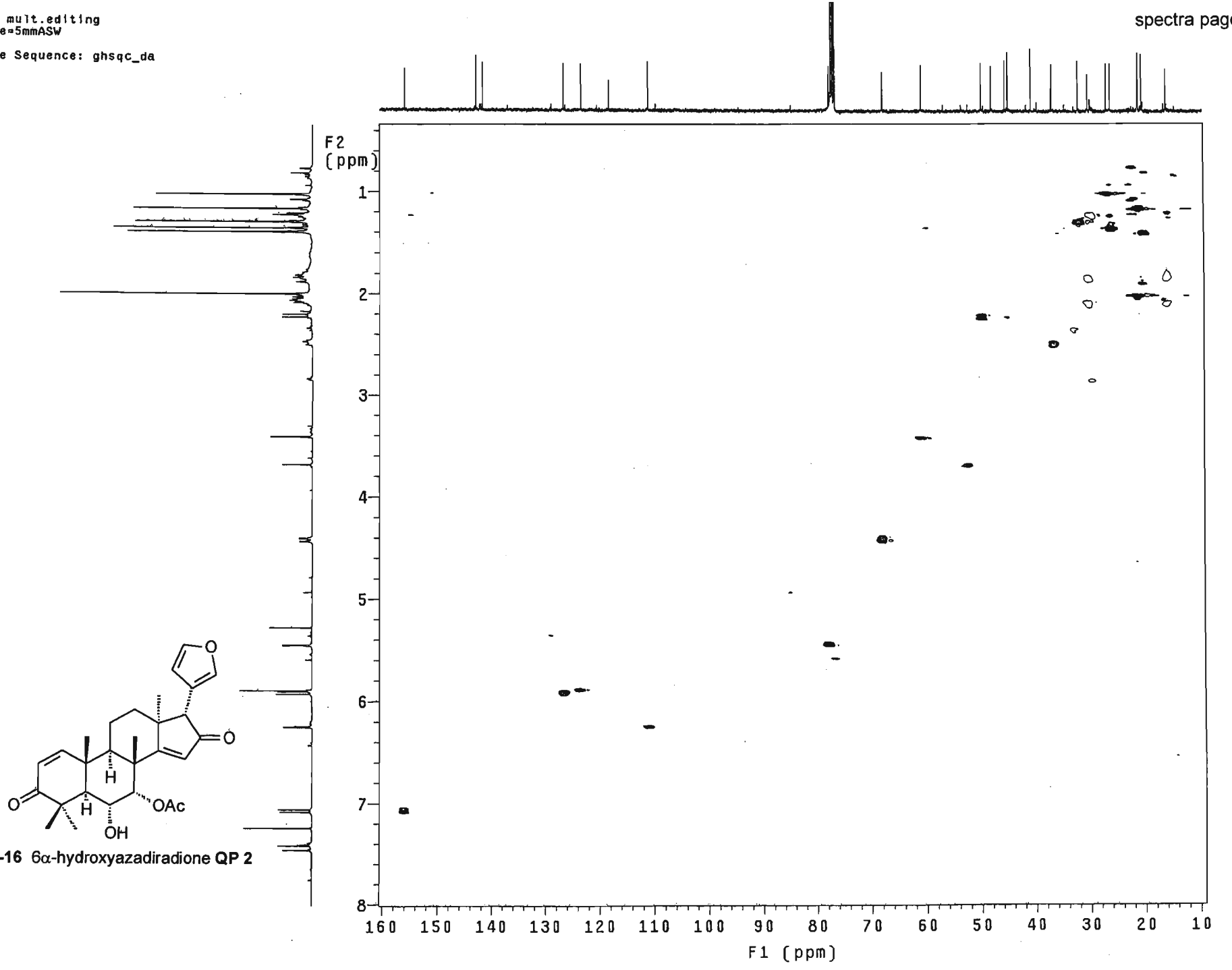
Pulse Sequence: dept



Spectrum QP 2.3: ADEPT Spectrum of 6α-hydroxyazadiradione QP 2

with mult.editing
probe=5mmASW

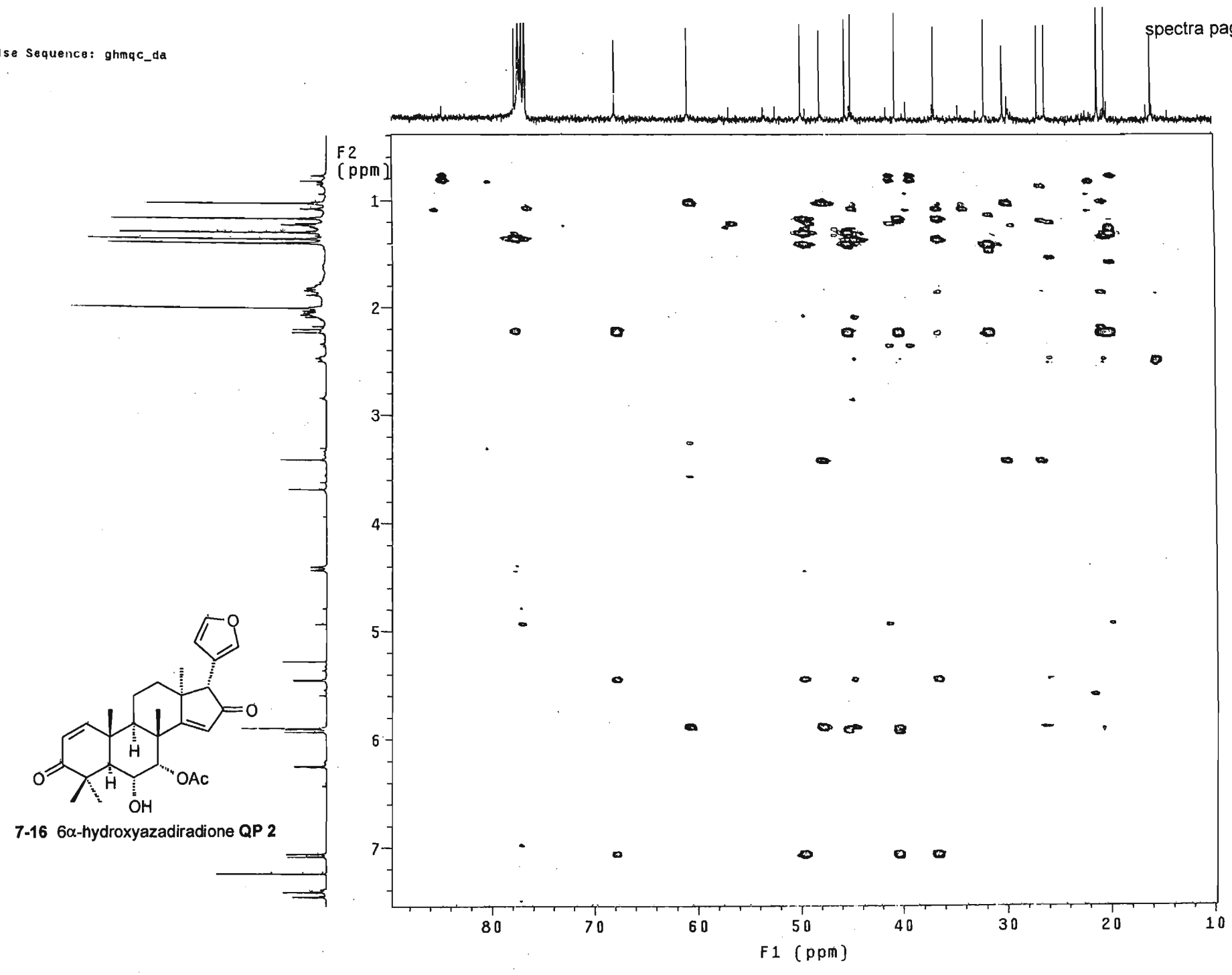
Pulse Sequence: ghsqc_da



7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.4: HSQC Spectrum of 6α-hydroxyazadiradione QP 2

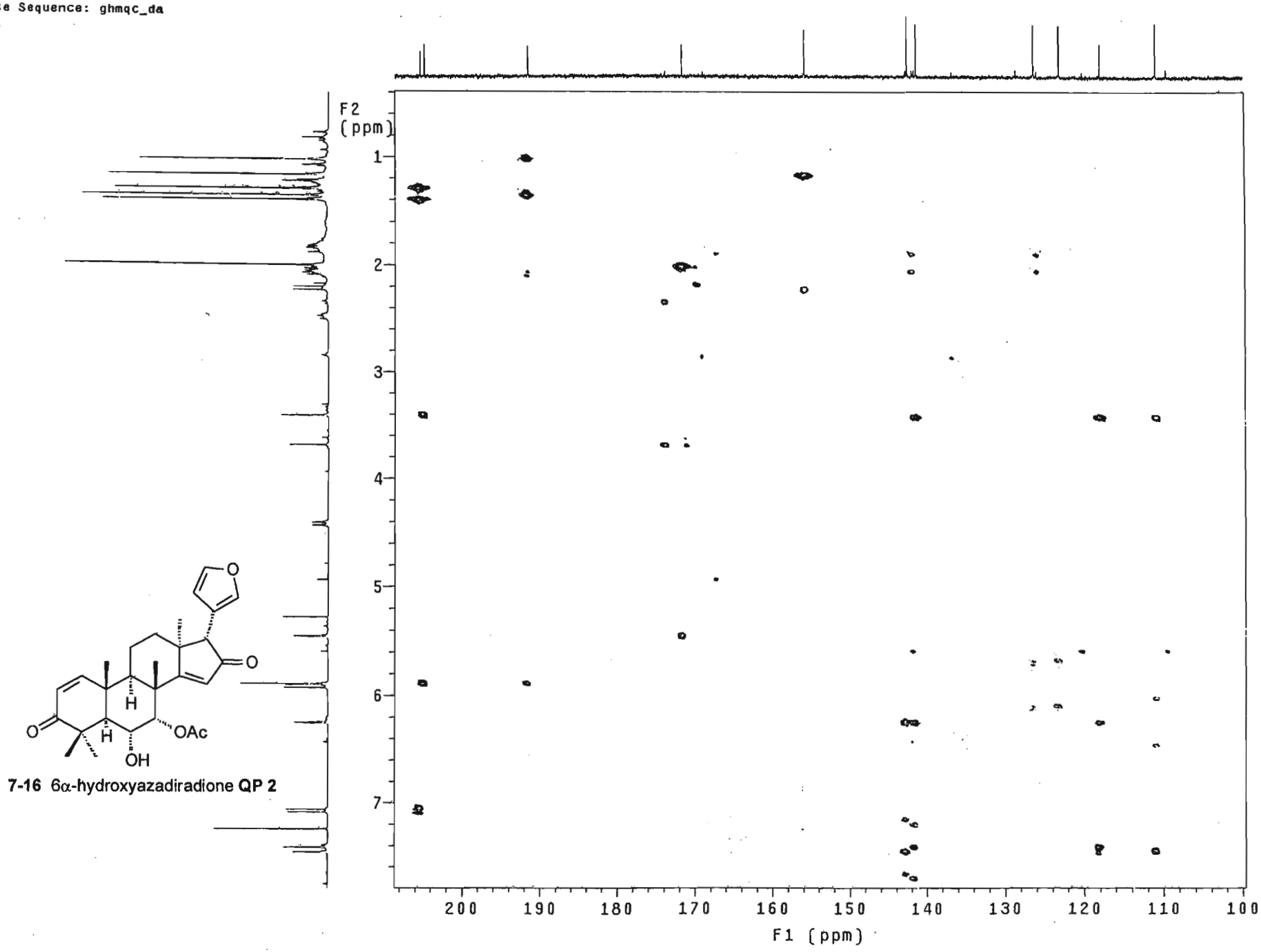
Pulse Sequence: ghmqc_da



7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.5: Expanded HMBC Spectrum of 6α-hydroxyazadiradione QP 2

Pulse Sequence: ghmqc_da

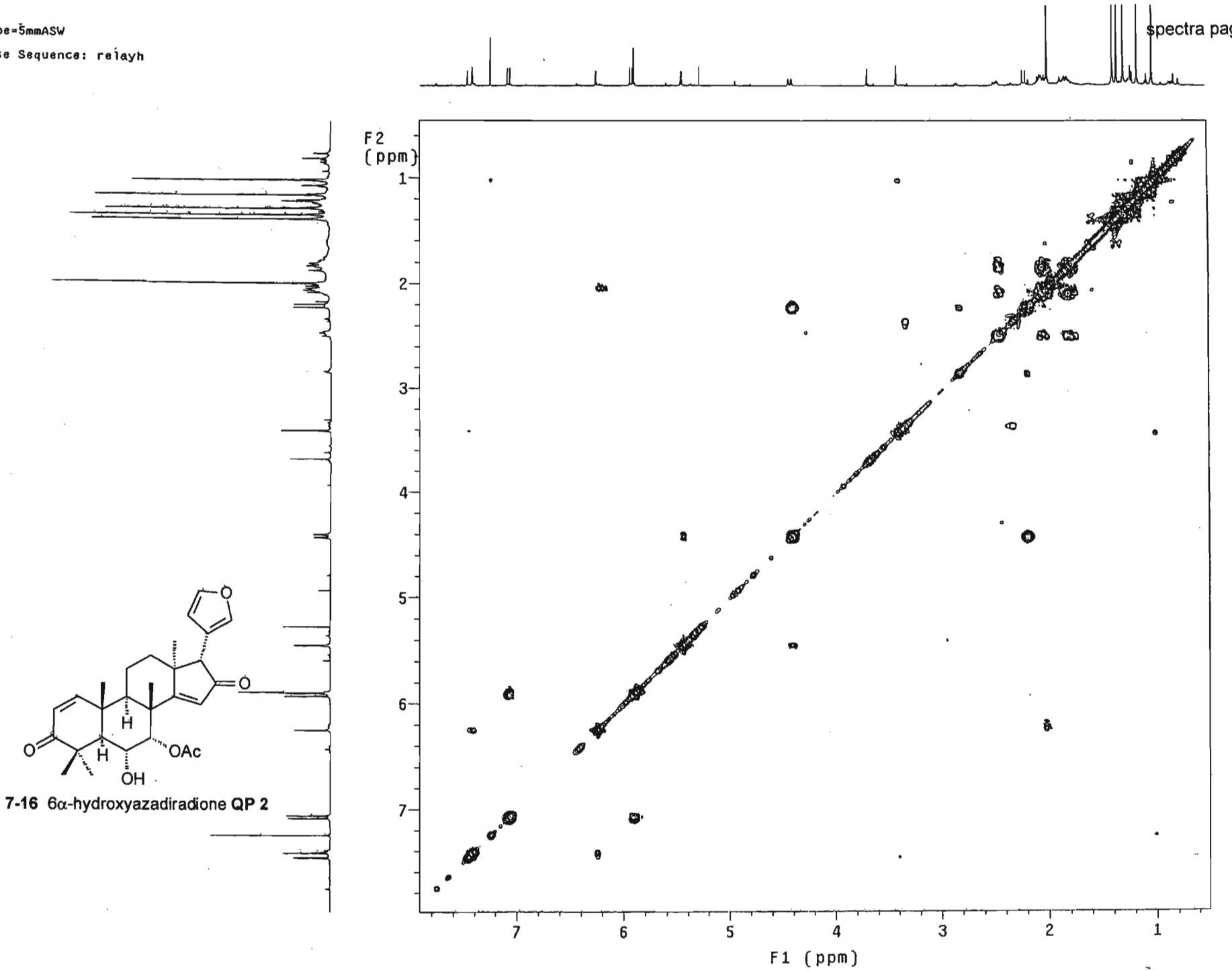


7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.6: Expanded HMBC Spectrum of 6α-hydroxyazadiradione QP 2

probe=5mmASW

Pulse Sequence: relayh

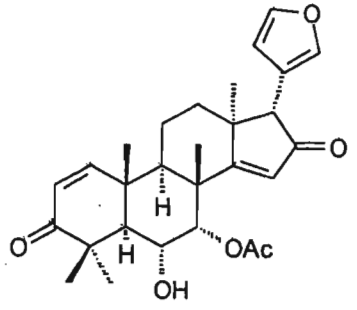


7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.7: COSY Spectrum of 6α-hydroxyazadiradione QP 2

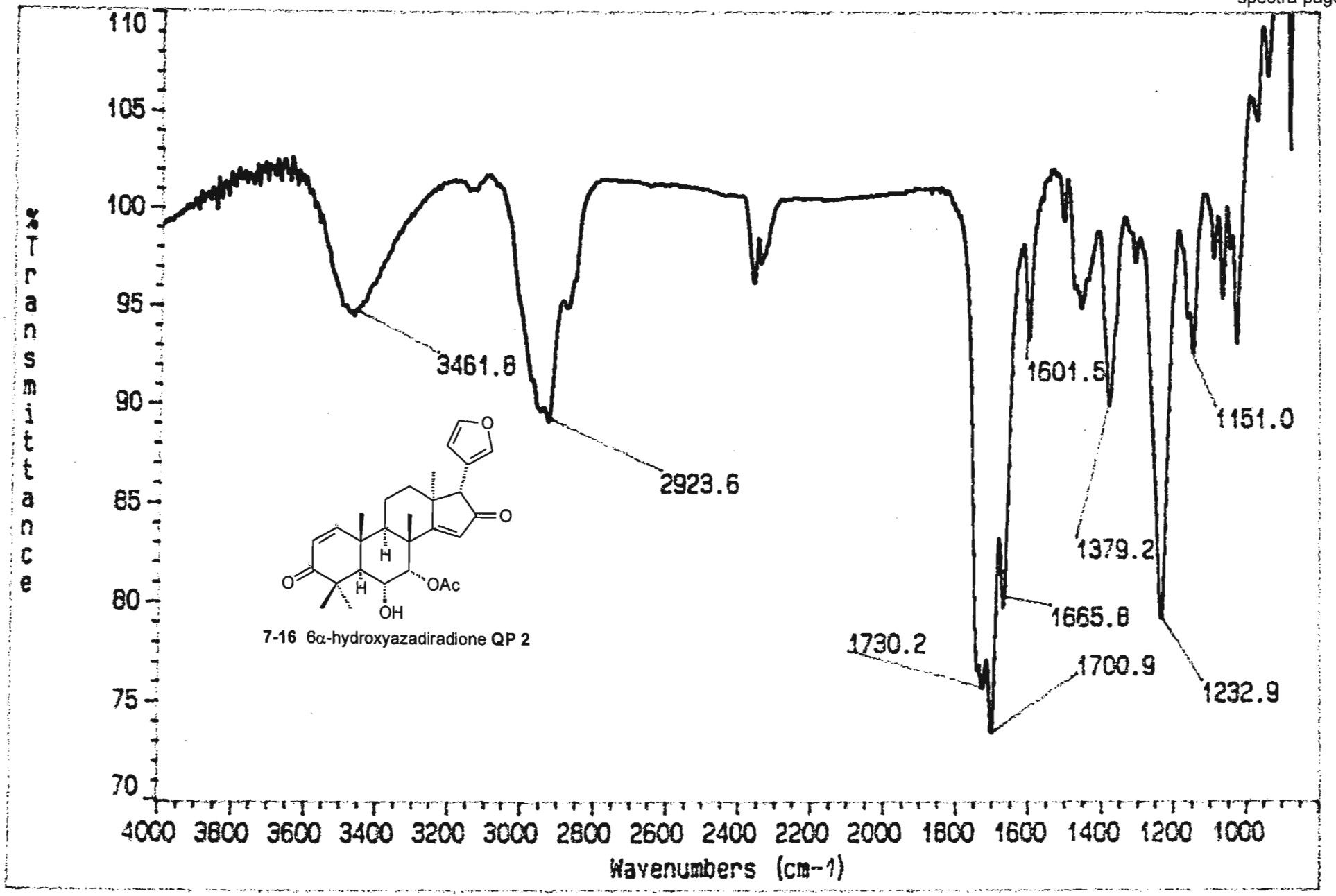
mix=1sec
probe=5mmASW

Pulse Sequence: noesy_da



7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.8: NOESY Spectrum of 6α-hydroxyazadiradione QP 2

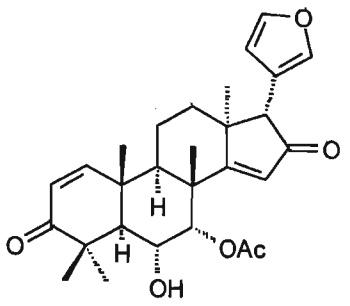


7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.9: IR Spectrum of 6α-hydroxyazadiradione QP 2

File Name : C:\MASPEC\data\hc050102.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPL8f/50-55
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

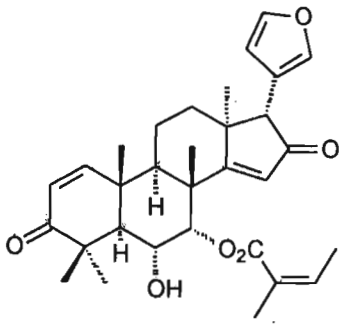
SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Int:0.5%. Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 28#6:29. Entries=344. Base M/z=466.23551. 100% Int.=0.96704. EI. POS.



7-16 6α-hydroxyazadiradione **QP 2**

Spectrum QP 2.10: High Resolution Mass Spectrum of 6α-hydroxyazadiradione QP 2

Pulse Sequence: s2pul

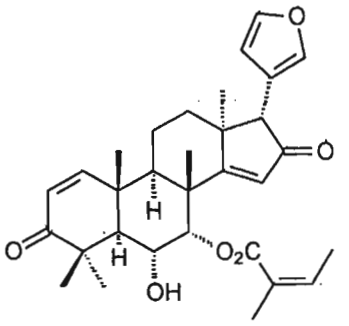


7-17 QP 3

Spectrum QP 3.1: ^{1}H NMR Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

Pulse Sequence: s2pul

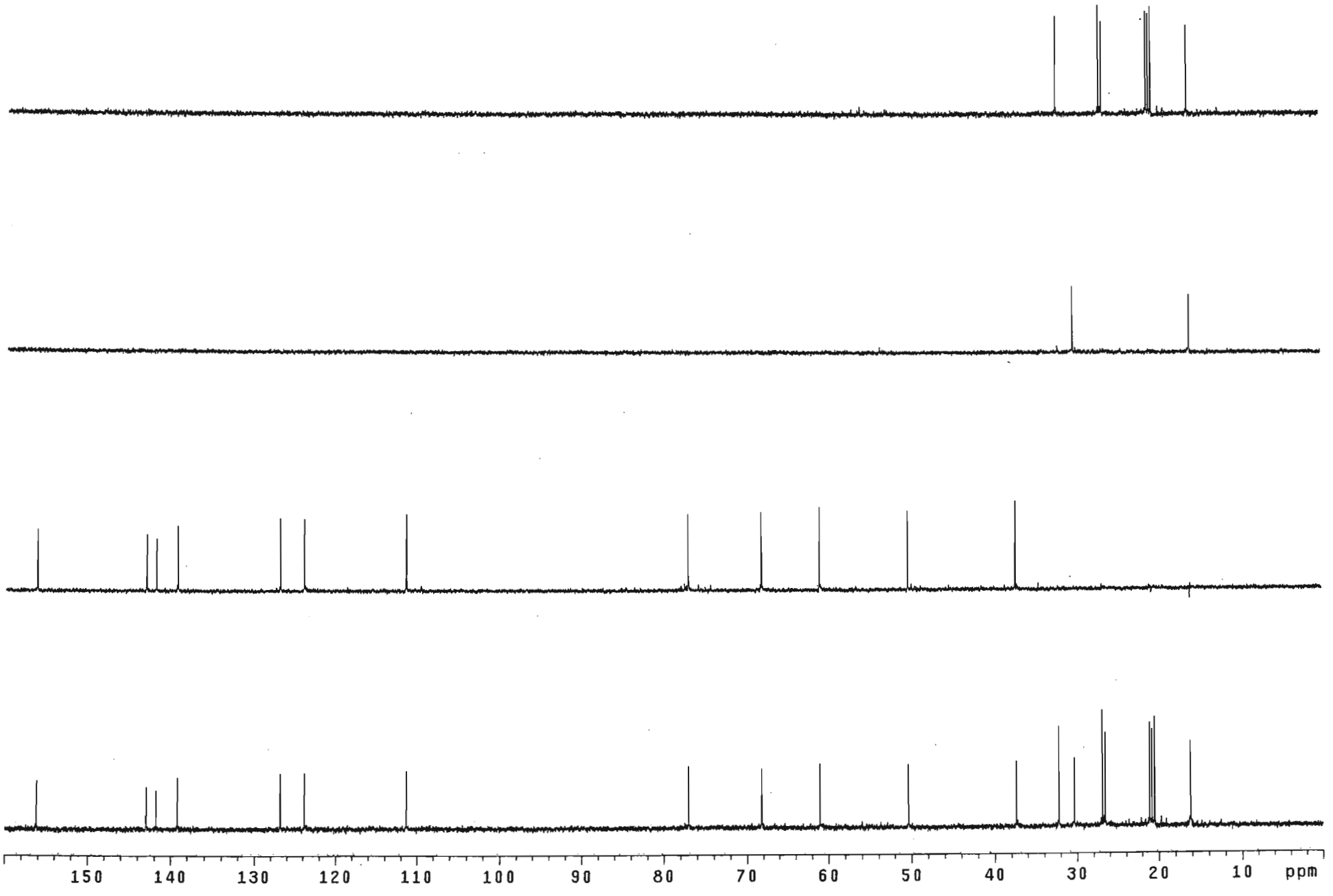
1	20665.260	205.487	10.1
2	20609.563	204.933	10.2
3	19233.179	191.247	10.0
4	16933.609	168.381	11.0
5	15706.765	156.182	15.3
6	14375.395	142.943	19.7
7	14259.425	141.790	19.8
8	13993.913	139.150	15.8
9	12799.877	127.277	11.3
10	12751.810	126.799	17.3
11	12453.492	123.833	15.4
12	11917.892	118.507	12.3
13	11193.840	111.307	17.9
14	7803.997	77.600	142.7
15	7771.952	77.281	149.1
16	7749.063	77.054	21.3
17	7739.908	76.963	150.0
18	6857.923	68.192	16.5
19	6140.738	61.061	16.8
20	5068.012	50.394	17.3
21	4858.198	48.308	17.6
22	4599.553	45.736	18.9
23	4548.435	45.228	18.7
24	4112.020	40.888	17.5
25	3761.820	37.406	17.6
26	3243.769	32.255	18.0
27	3053.028	30.358	14.9
28	2706.643	26.914	20.4
29	2672.309	26.572	18.9
30	2122.213	21.102	18.9
31	2094.747	20.829	18.0
32	2065.754	20.541	20.3
33	1631.628	16.224	17.6
34	1623.999	16.148	15.4



7-17 QP 3

Spectrum QP 3.2: ^{13}C NMR Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

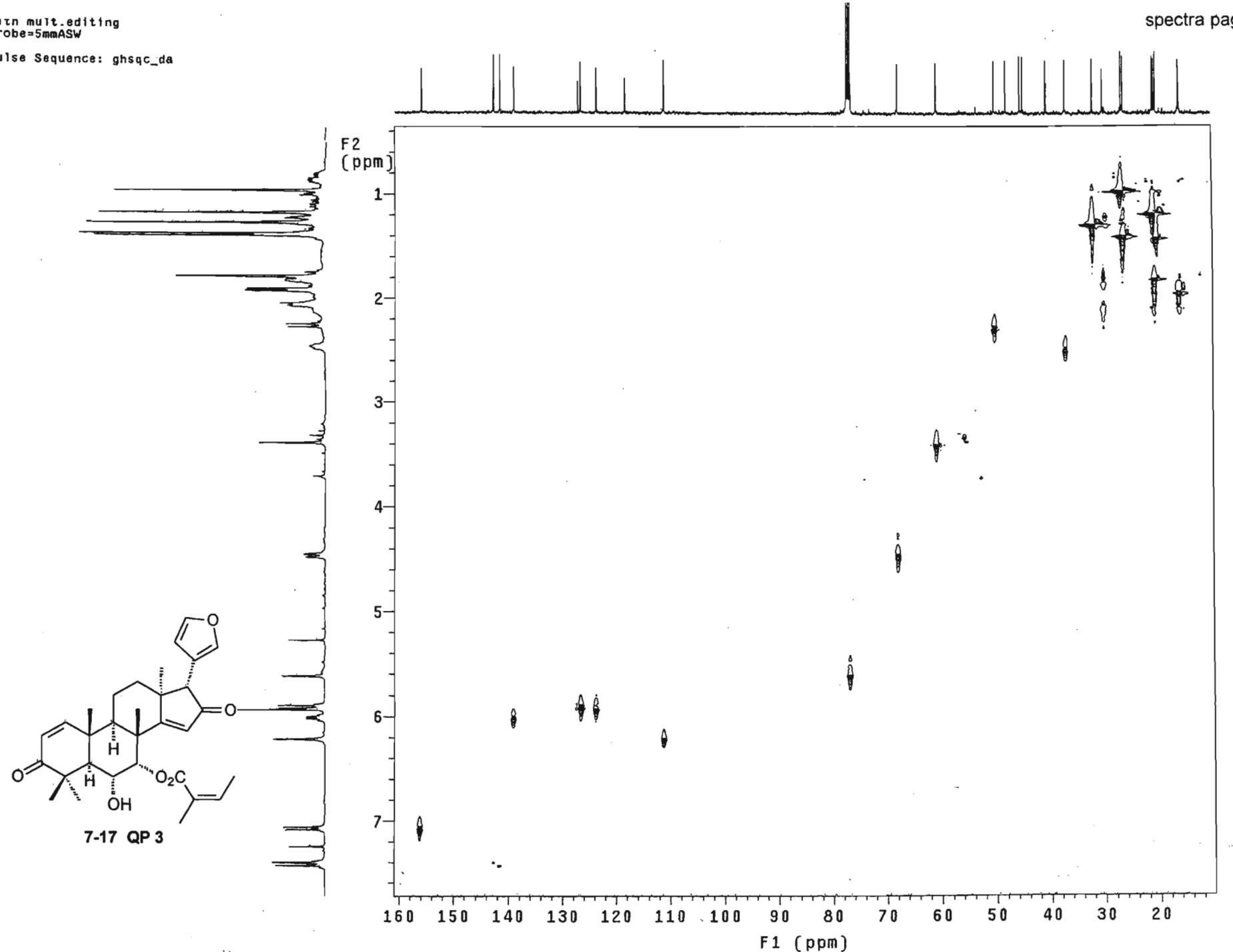
Pulse Sequence: dept



Spectrum QP 3.3: ADEPT Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

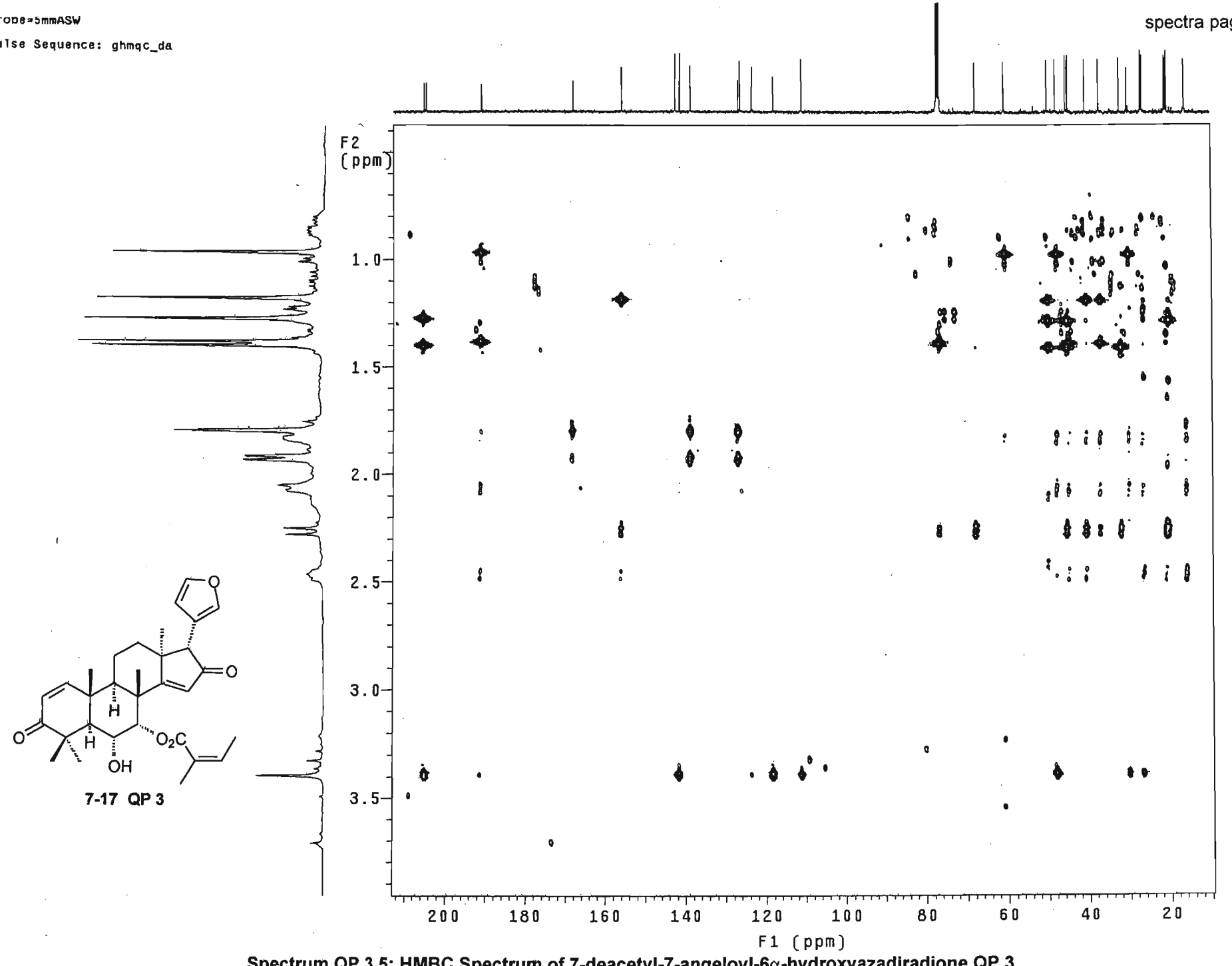


7-17 QP 3

Spectrum QP 3.4: HSQC Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

probe=5mmASW

Pulse Sequence: ghmqc_da

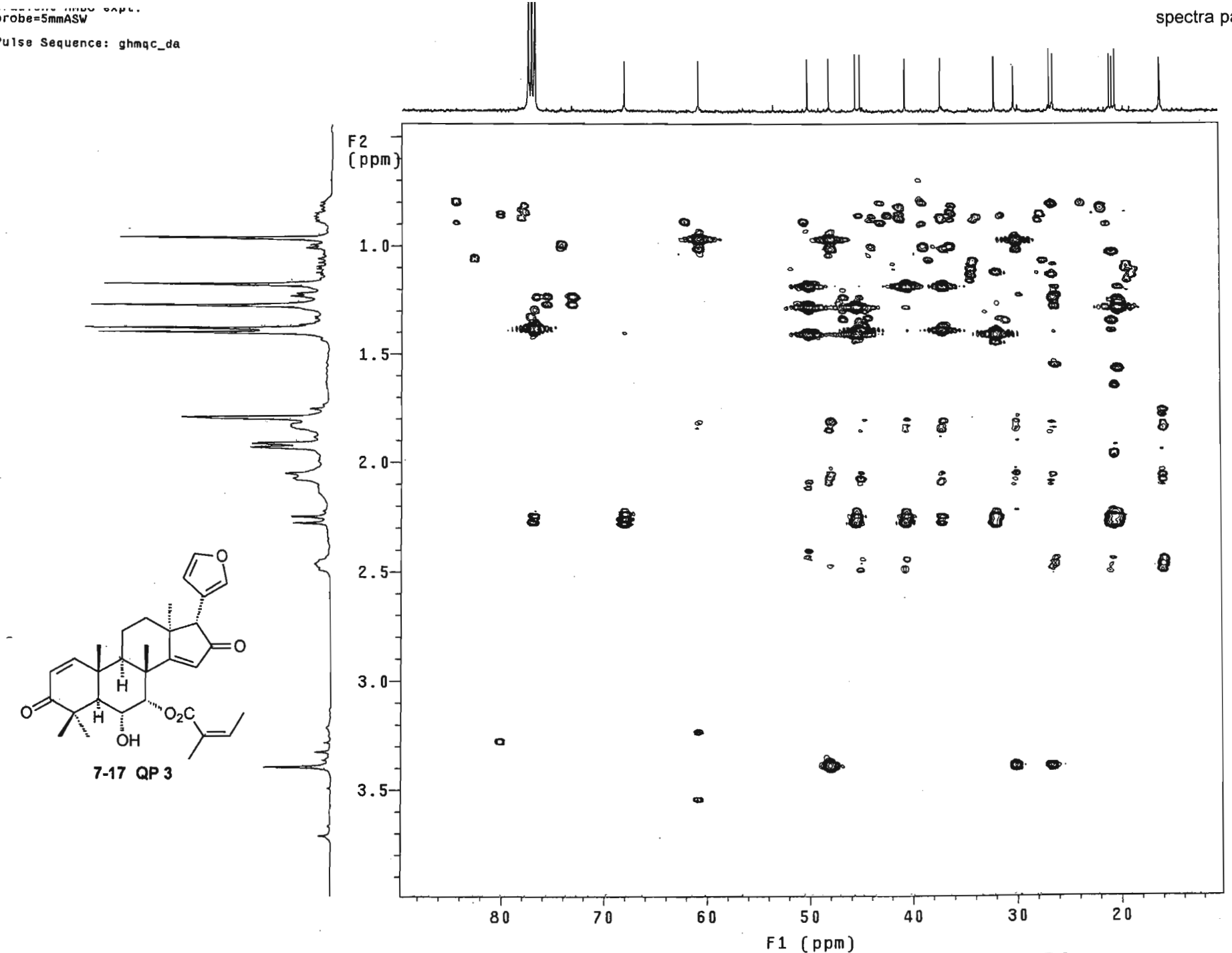


7-17 QP 3

Spectrum QP 3.5: HMBC Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

probe=5mmASW

Pulse Sequence: ghmqc_da

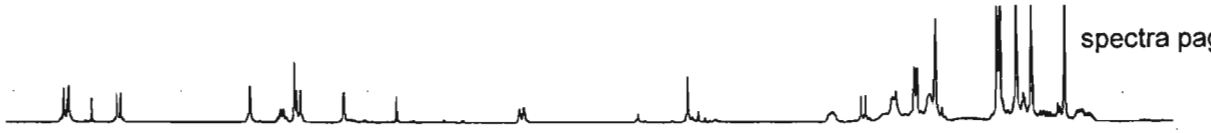


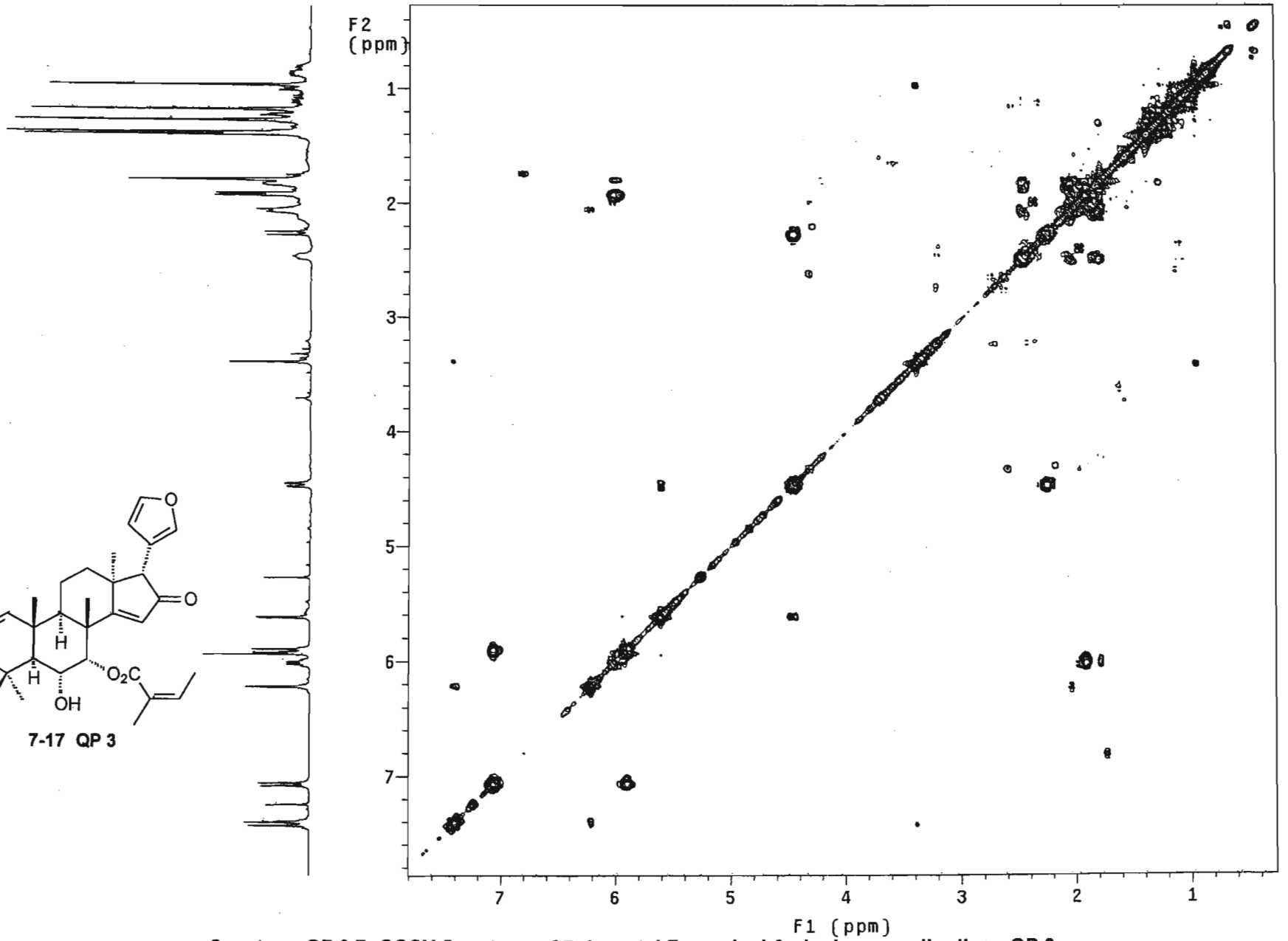
7-17 QP 3

Spectrum QP 3.6: Expanded HMBC Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

probe=5mmASW

Pulse Sequence: relayh



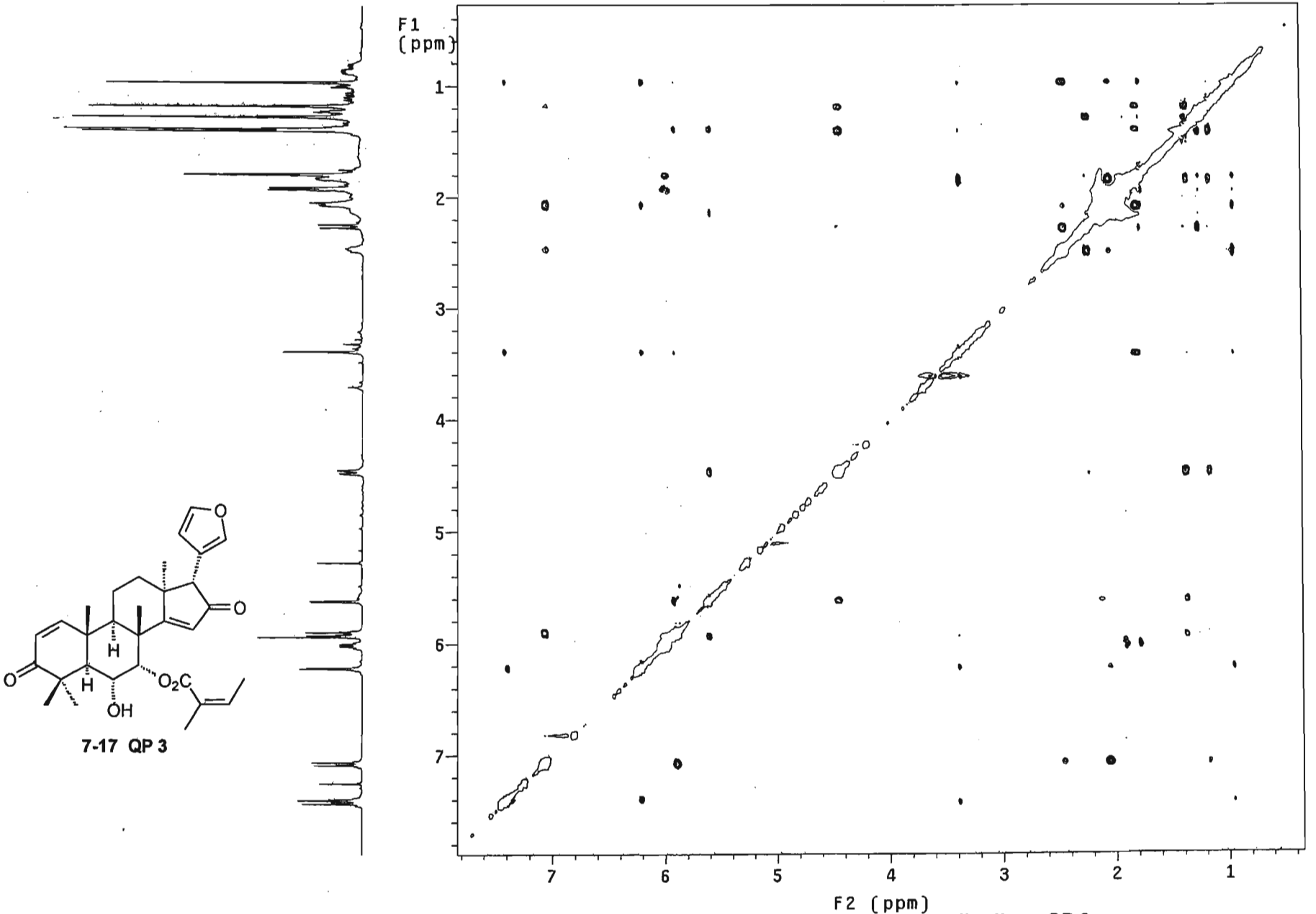


7-17 QP 3

Spectrum QP 3.7: COSY Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

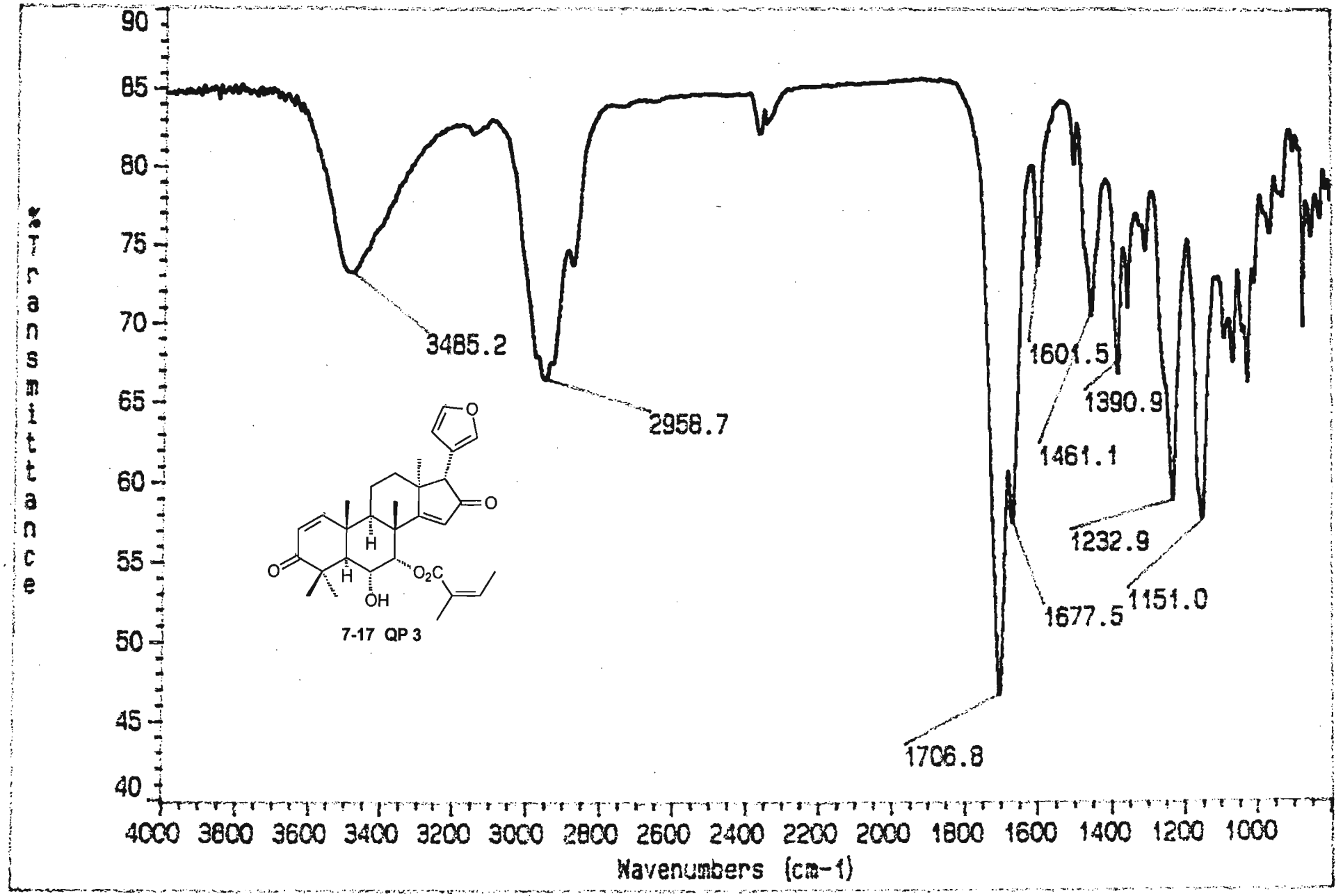
mix=1sec
probe=5mmASW

Pulse Sequence: noesy_da



7-17 QP 3

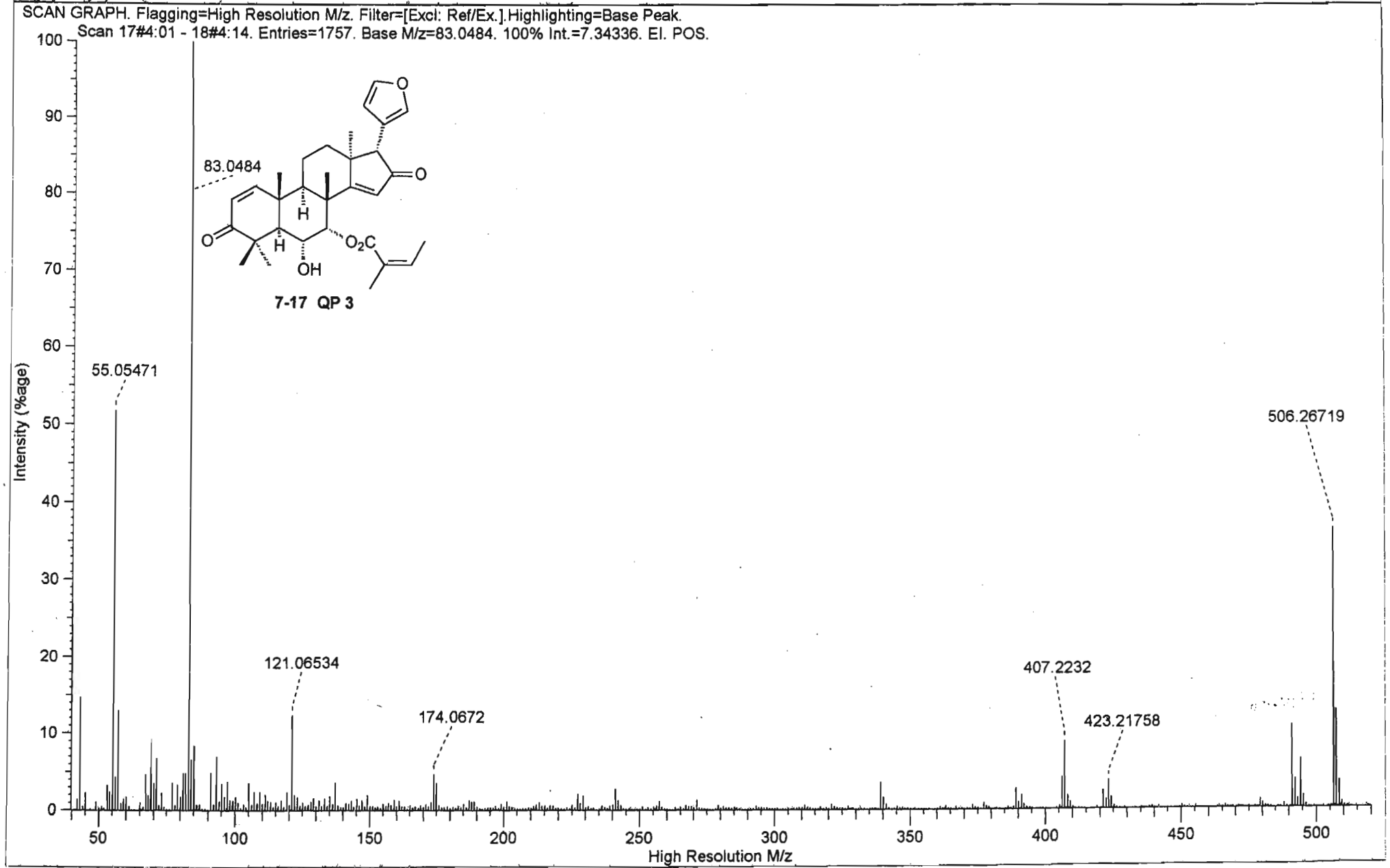
Spectrum QP 3.8: NOESY Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3



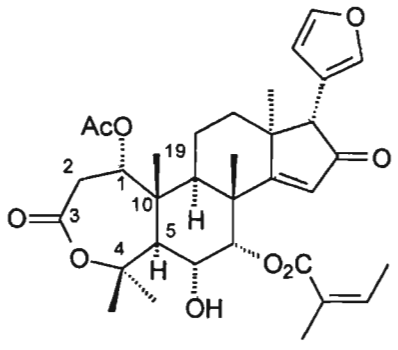
Spectrum QP 3.9: IR Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

File Name : C:\MASPEC\data\hc050106.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPL80/17-24
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

minor impurities.



Spectrum QP 3.10: High Resolution Mass Spectrum of 7-deacetyl-7-angeloyl-6α-hydroxyazadiradione QP 3

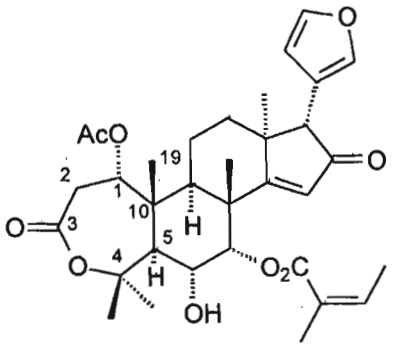


7-18 quivisianthone **QP 4**

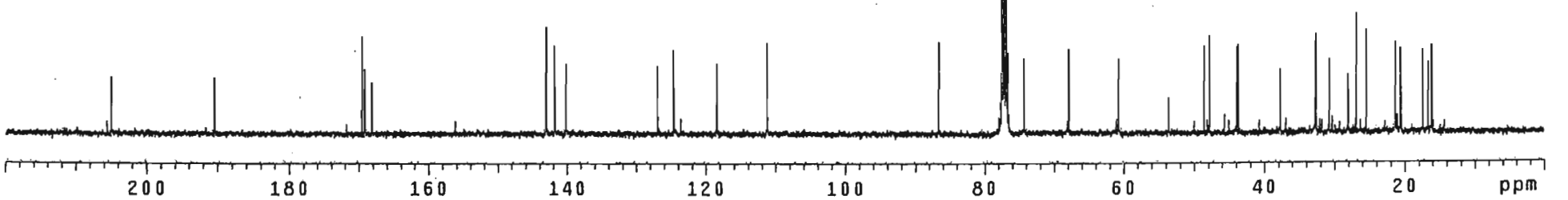
Spectrum QP 4.1: ^{1}H NMR Spectrum of quivisianthone QP 4

Pulse Sequence: s2pul

	Frequency	PPM	Height
1	20616.494	205.002	9.2
2	19153.909	190.459	9.2
3	17059.566	169.634	15.9
4	17017.613	169.216	10.6
5	16916.433	168.210	8.4
6	14386.934	143.058	17.5
7	14261.899	141.815	14.5
8	14094.088	140.146	11.5
9	12771.345	126.993	11.2
10	12536.081	124.654	13.8
11	11910.082	118.429	11.6
12	11187.015	111.239	15.0
13	8714.276	86.651	15.1
14	7799.543	77.556	327.3
15	7788.026	77.441	17.3
16	7767.461	77.237	349.0
17	7735.380	76.918	350.0
18	7705.766	76.623	13.3
19	7472.970	74.308	12.4
20	6829.696	67.912	14.0
21	6109.920	60.755	12.4
22	5395.079	53.647	5.9
23	4885.066	48.575	14.5
24	4809.387	47.823	16.1
25	4421.942	43.970	14.2
26	4397.264	43.725	14.8
27	3797.587	37.762	10.6
28	3295.801	32.772	14.2
29	3286.752	32.682	16.4
30	3094.263	30.768	12.2
31	2821.160	28.052	9.6
32	2704.350	26.891	19.6
33	2562.863	25.484	17.0
34	2150.740	21.386	14.9
35	2073.415	20.617	13.9
36	1750.133	17.403	13.7
37	1676.099	16.666	11.6
38	1625.920	16.168	14.4



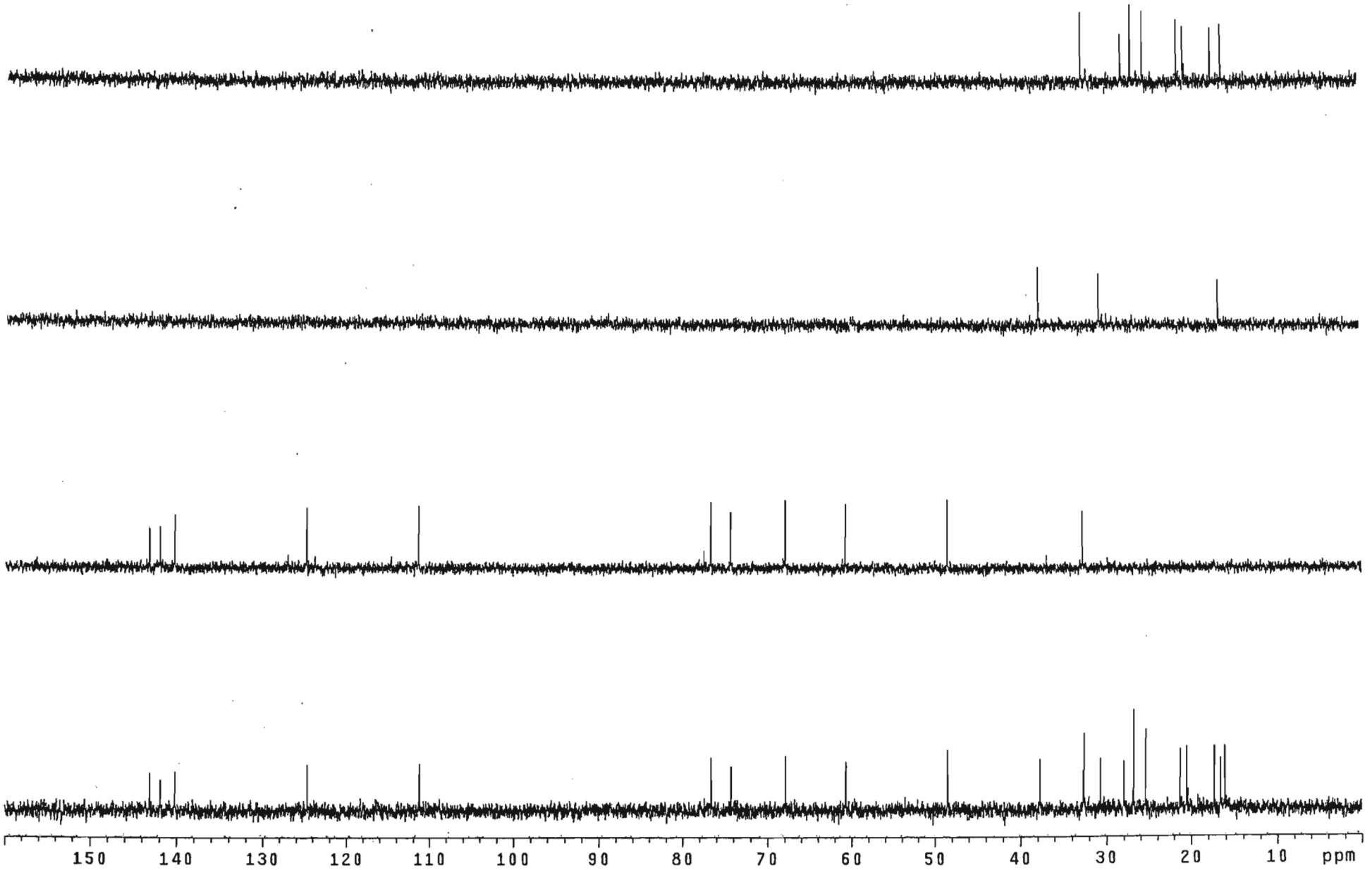
7-18 quivisianthone **QP 4**



Spectrum QP 4.2: ^{13}C NMR Spectrum of quivisianthone QP 4

probe=5mmASW

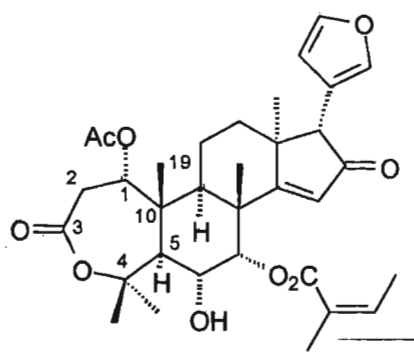
Pulse Sequence: dept



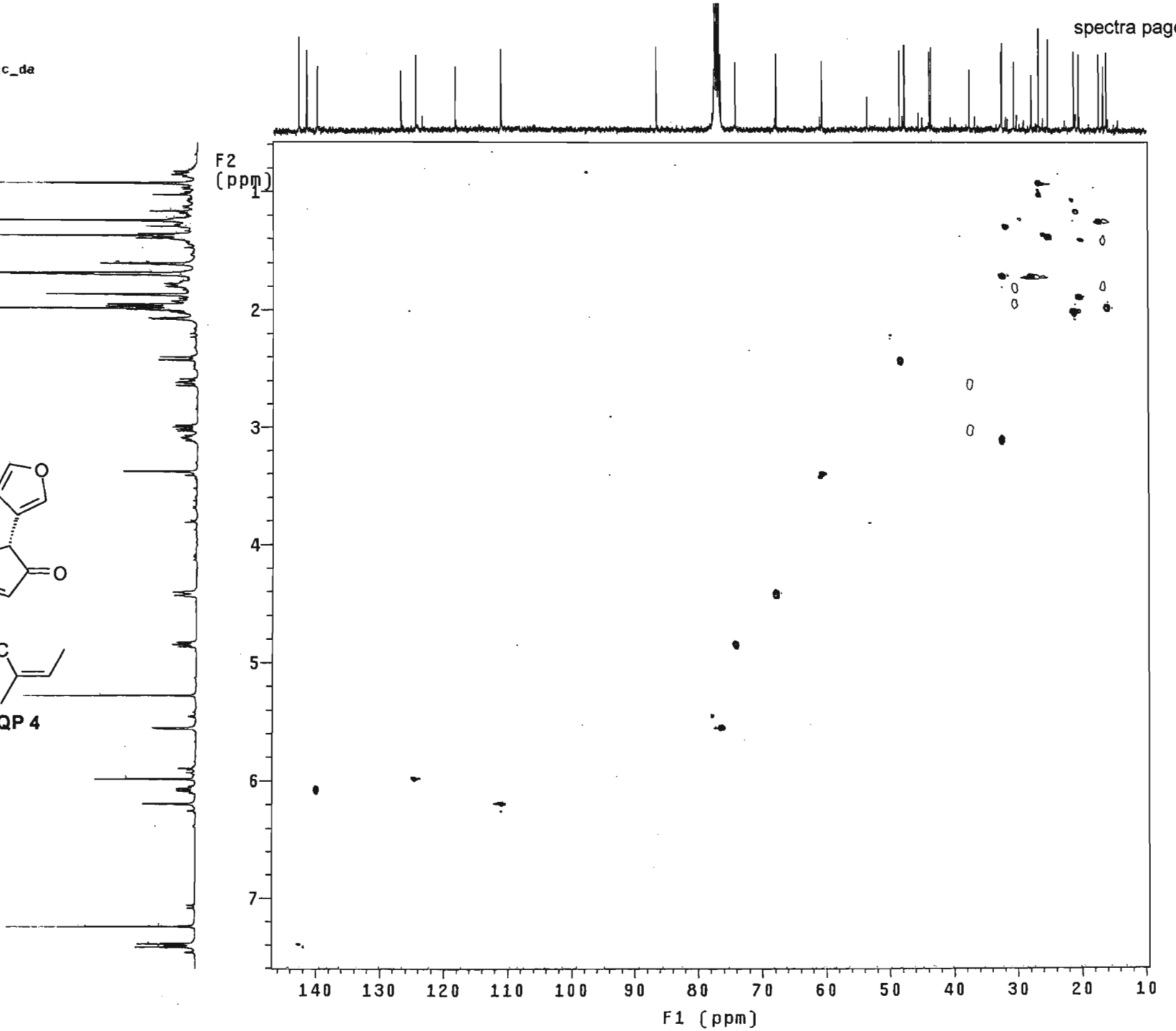
Spectrum QP 4.3: ADEPT Spectrum of quivisianthone QP 4

Gradient HSQC expt.
with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da



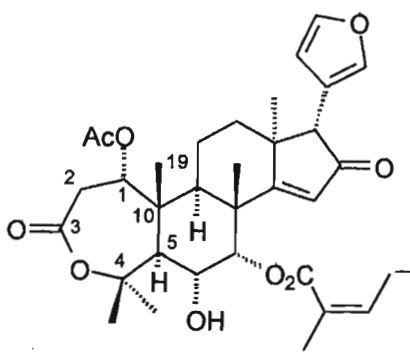
7-18 quivisianthone **QP 4**



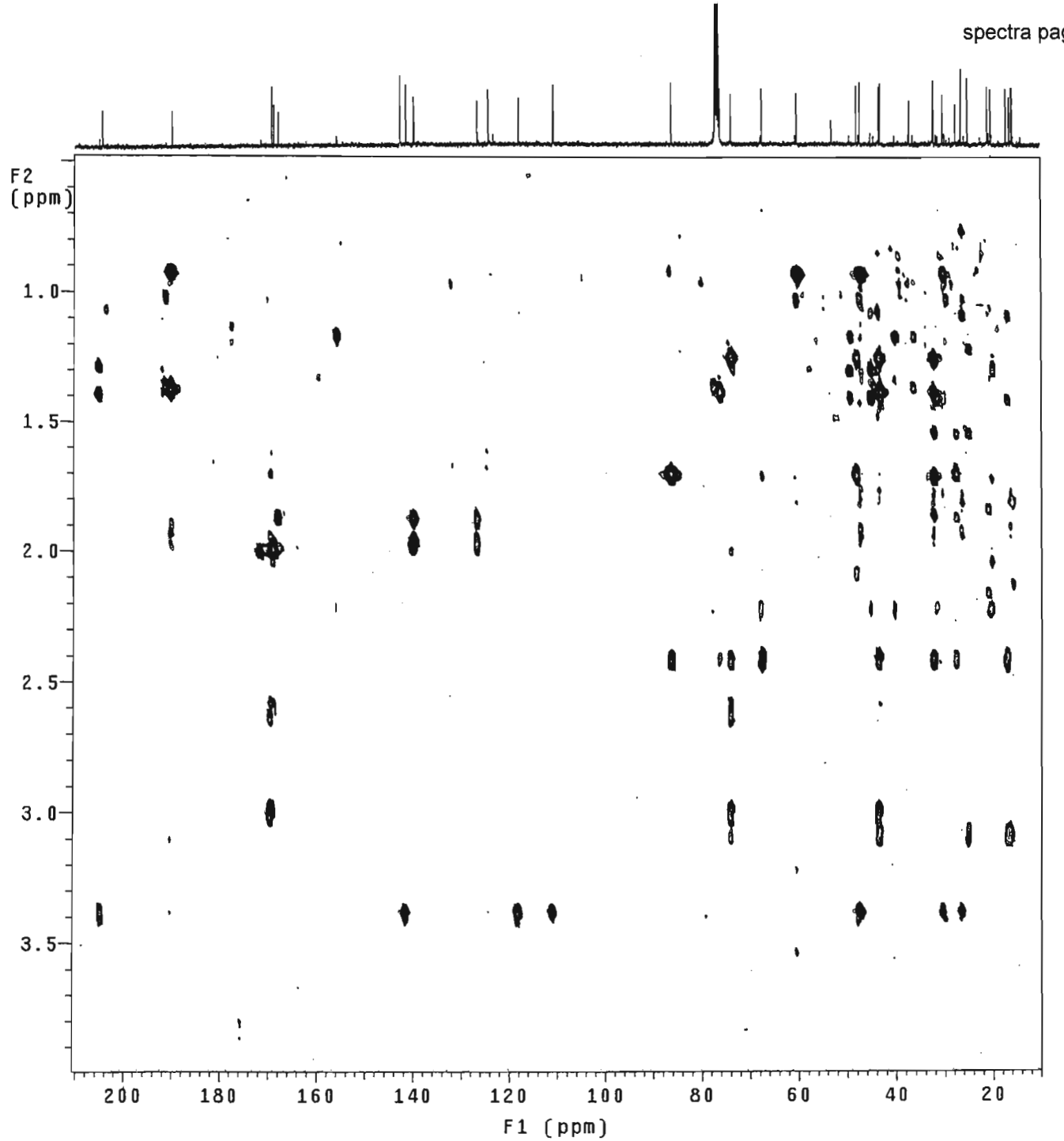
Spectrum QP 4.4: HSQC Spectrum of quivisianthone QP 4

probe=5mmASW

Pulse Sequence: ghmqc_da



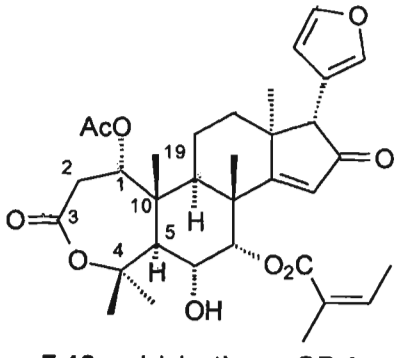
7-18 quivisianthone **QP 4**



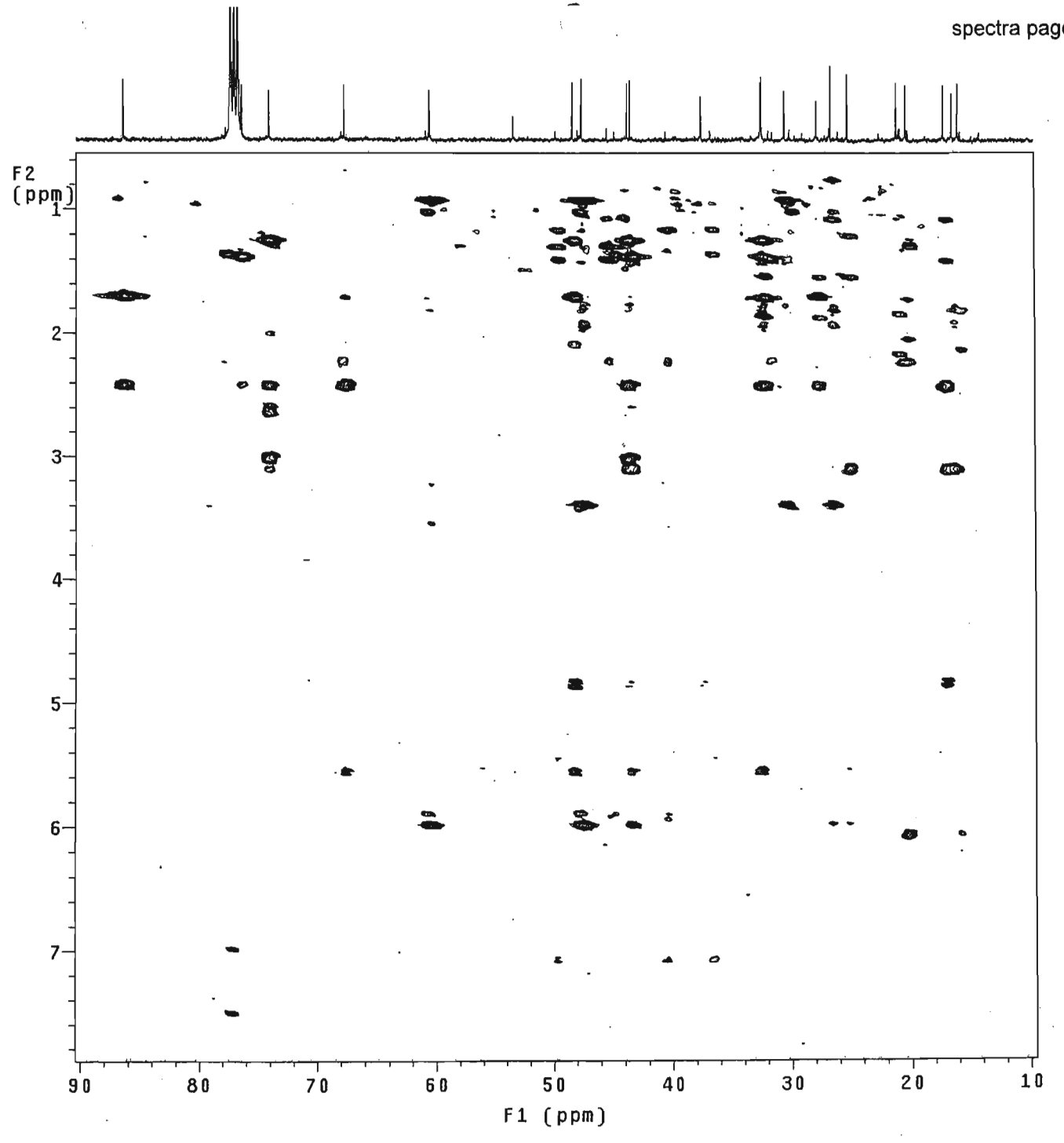
Spectrum QP 4.5: HMBC Spectrum of quivisianthone QP 4

Gradient HMBC expt.
probe=5mmASW

Pulse Sequence: ghmqc_da



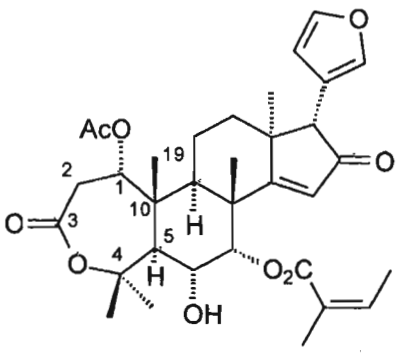
7-18 quivisianthone **QP 4**



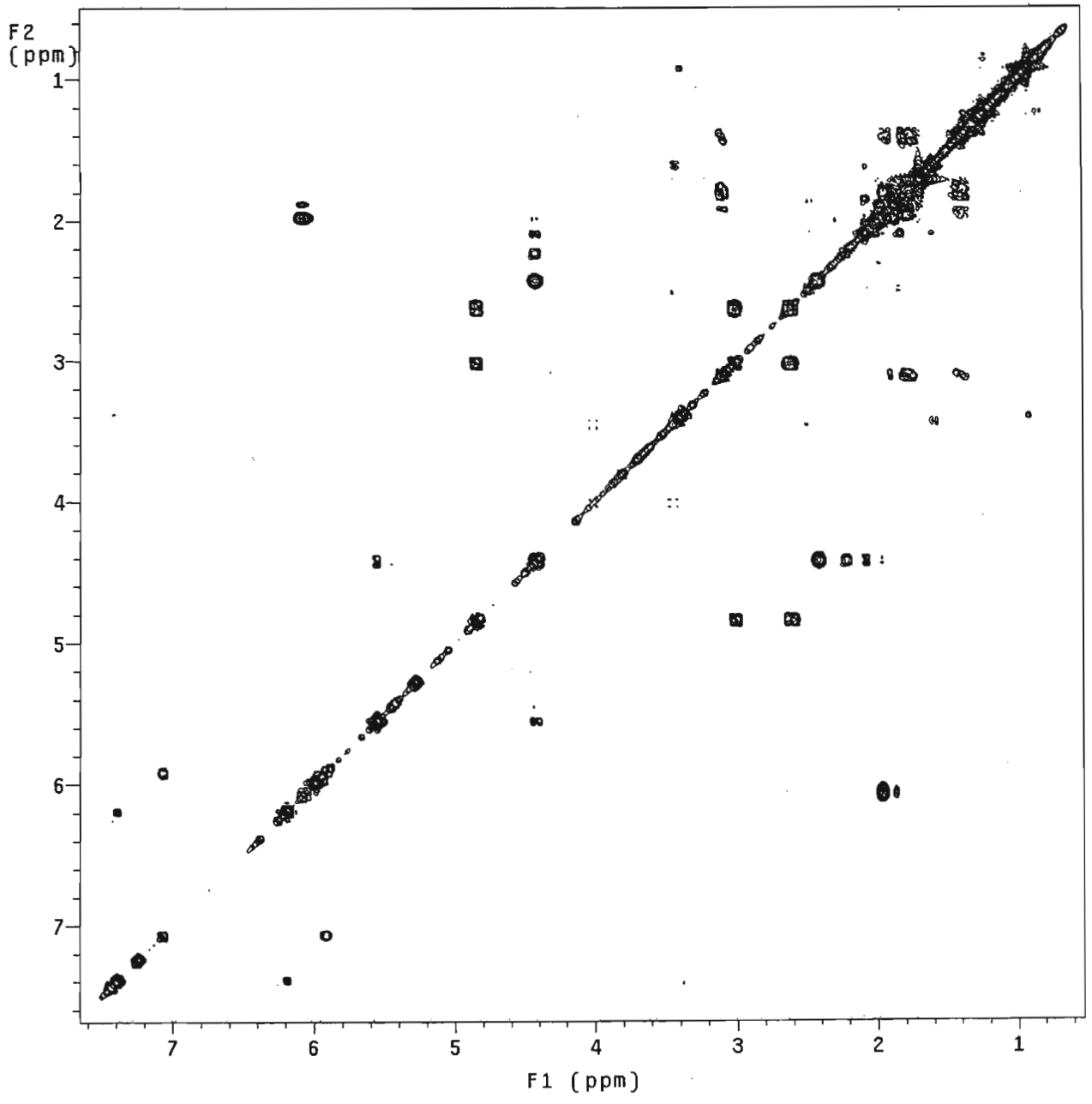
Spectrum QP 4.6: Expanded HMBC Spectrum of quivisianthone QP 4

1H COSY-90
probe=5mmASW

Pulse Sequence: relayh



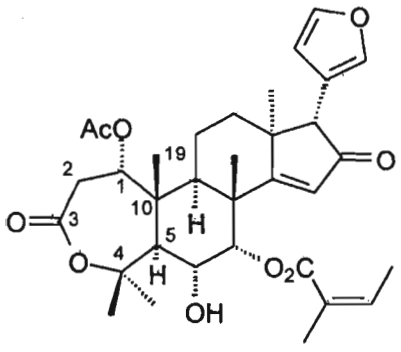
7-18 quivisianthone **QP 4**



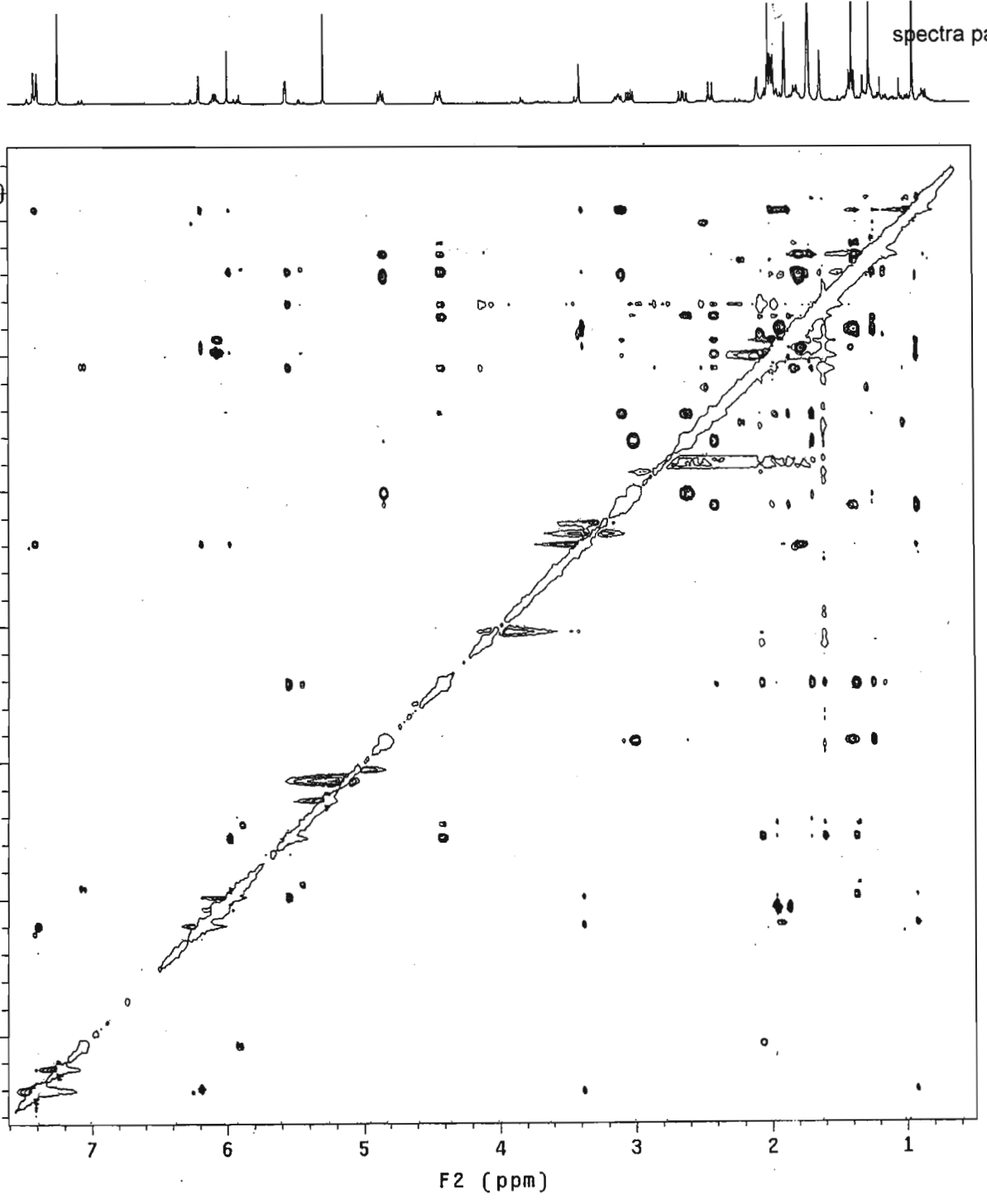
Spectrum QP 4.7: COSY Spectrum of quivisianthone QP 4

Gradient NOESY expt.
mix=1sec
probe=5mmASW

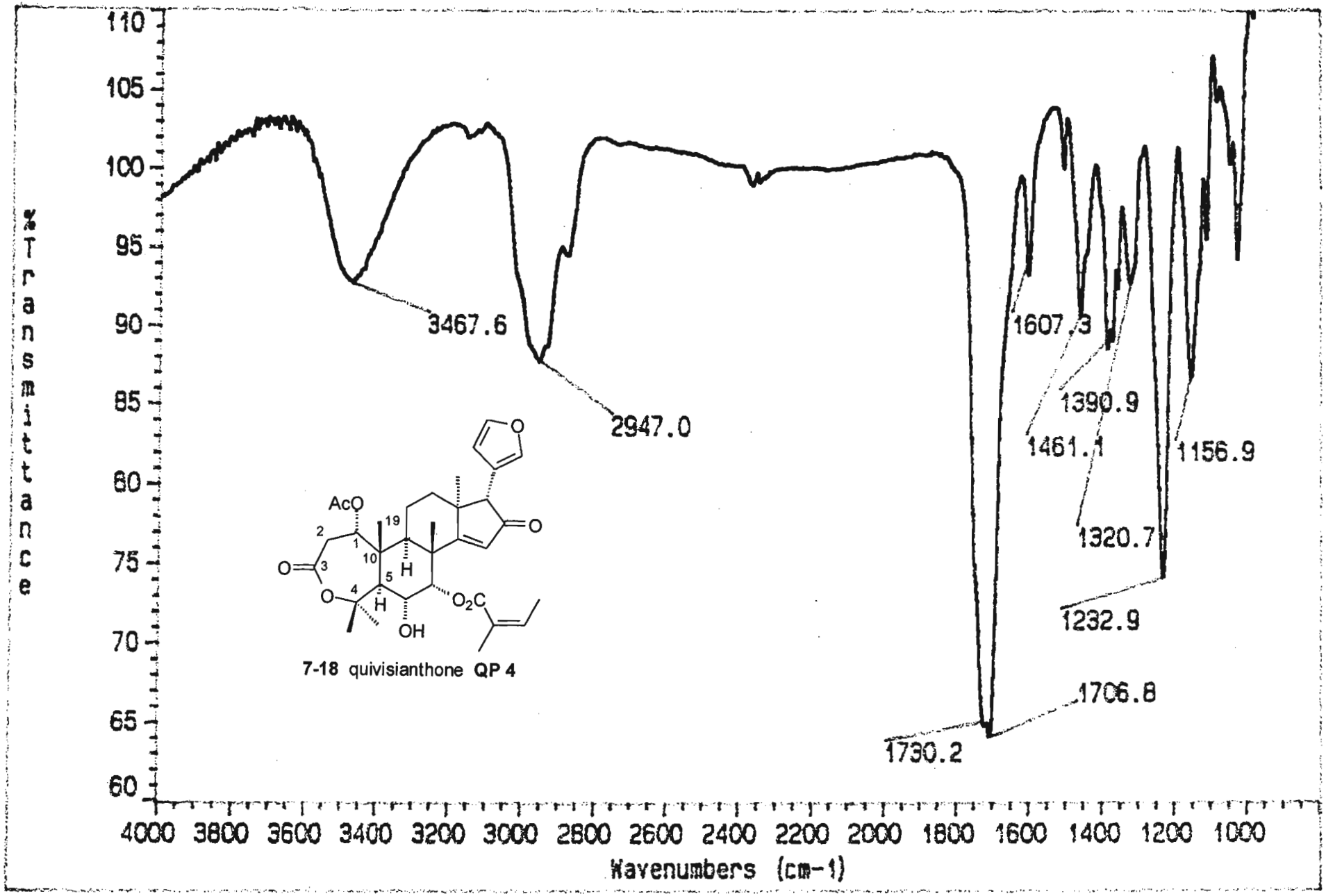
Pulse Sequence: noesy_da



7-18 quivisianthone **QP 4**



Spectrum QP 4.8: NOESY Spectrum of quivisianthone QP 4

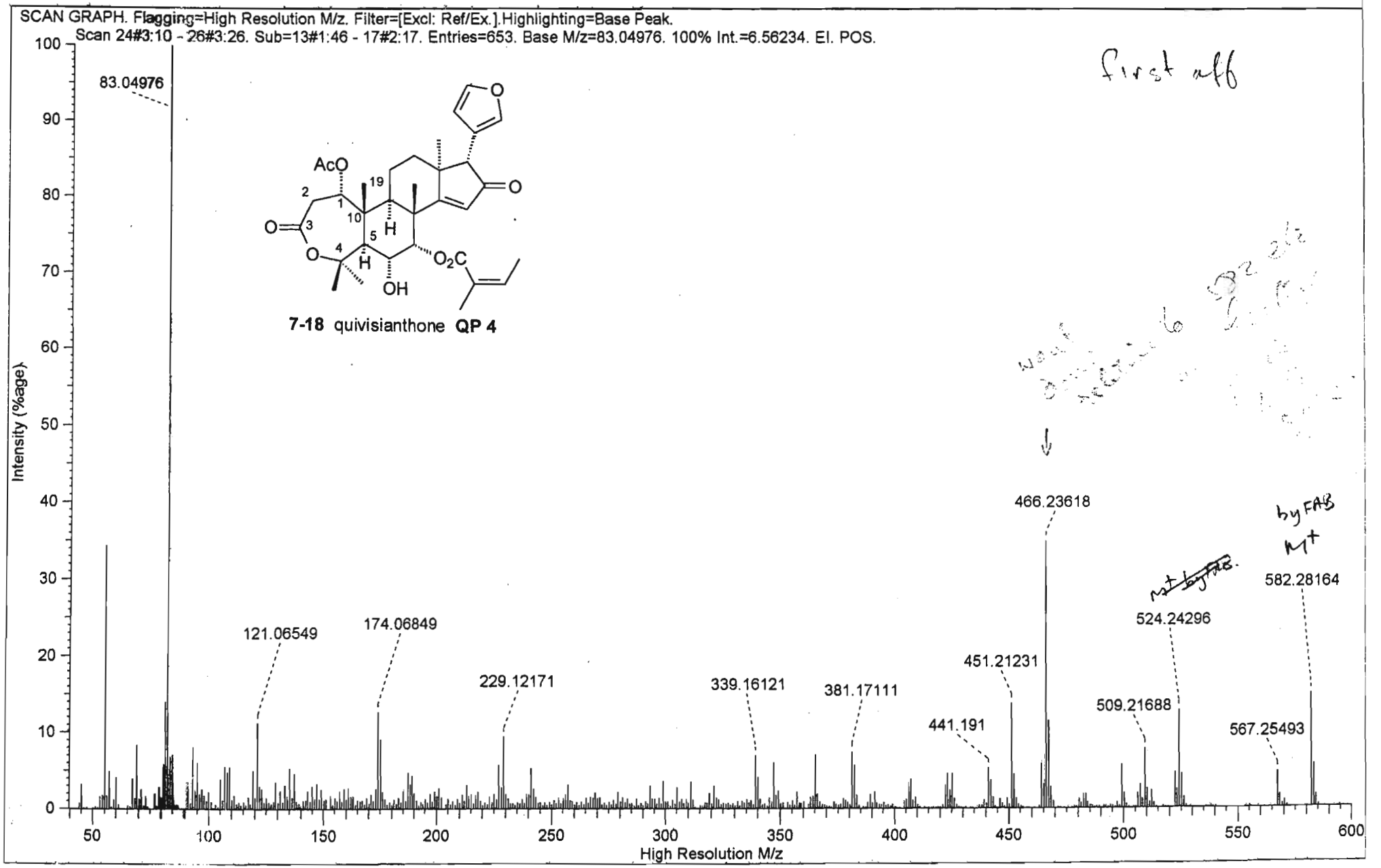


7-18 quivisianthone **QP 4**

Spectrum QP 4.9: IR Spectrum of quivisianthone QP 4

File Name : C:\MASPEC\data\hc091419.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPKbc-22/25
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

EI



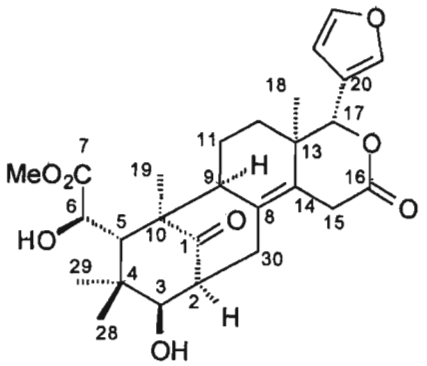
7-18 quivisianthone **QP 4**

first off

by FAB M+

Spectrum QP 4.10: High Resolution Mass Spectrum of quivisianthone QP 4

Pulse Sequence: s2pul



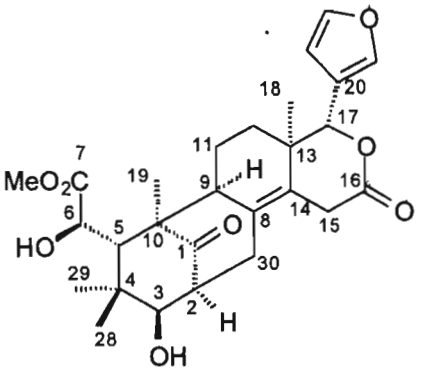
7-41 swietenolide **QP 5**

Spectrum QP 5.1: ^{1}H NMR Spectrum of swietenolide QP 5

probe=5mmASW

Pulse Sequence: s2pul

INDEX	FREQUENCY	PPM	HEIGHT
1	22117.041	219.923	10.5
2	17705.175	176.053	11.0
3	17252.534	171.552	12.2
4	14392.215	143.110	17.6
5	14207.141	141.270	17.1
6	13176.622	131.023	11.6
7	12999.242	129.259	14.8
8	12172.604	121.040	13.6
9	11065.577	110.032	15.4
10	8117.209	80.714	15.1
11	7921.877	78.772	14.8
12	7800.061	77.561	115.4
13	7768.432	77.246	120.0
14	7736.375	76.927	118.8
15	7420.509	73.787	14.9
16	5450.086	54.194	21.5
17	5379.561	53.492	16.6
18	5349.642	53.195	15.2
19	5045.316	50.169	13.7
20	4445.213	44.201	15.3
21	4010.524	39.879	22.0
22	3826.304	38.047	19.8
23	3419.824	34.005	12.2
24	3357.420	33.385	12.6
25	3007.361	29.904	6.7
26	2949.231	29.326	11.7
27	2397.427	23.839	12.2
28	2355.967	23.427	21.1
29	1907.600	18.968	12.4
30	1822.542	18.123	23.6

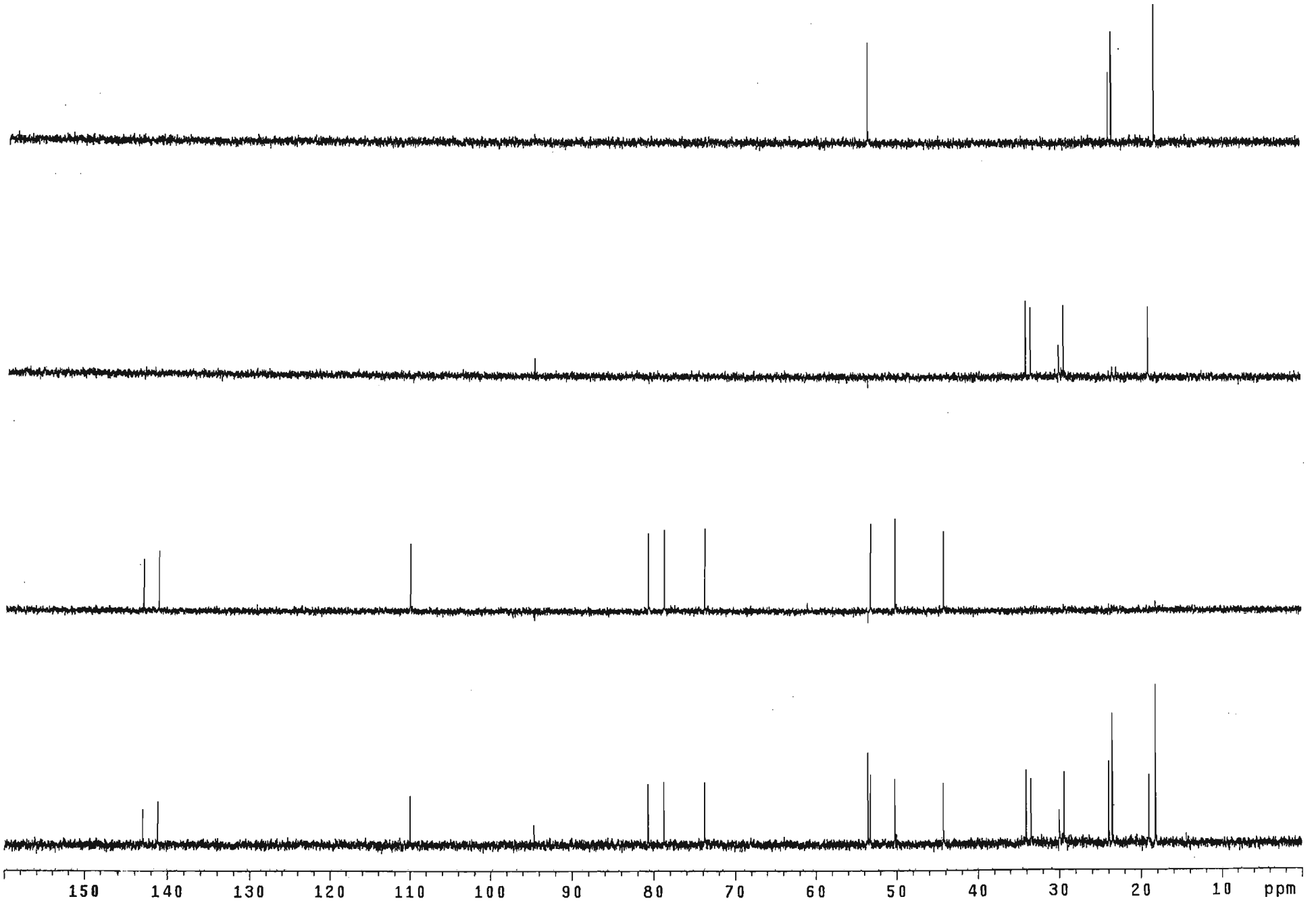


7-41 swietenolide **QP 5**

Spectrum QP 5.2: ^{13}C NMR Spectrum of swietenolide QP 5

probe=5mmASW

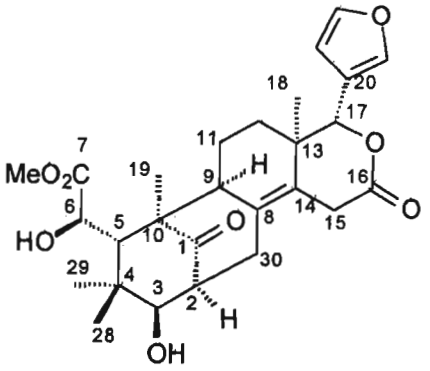
Pulse Sequence: dept



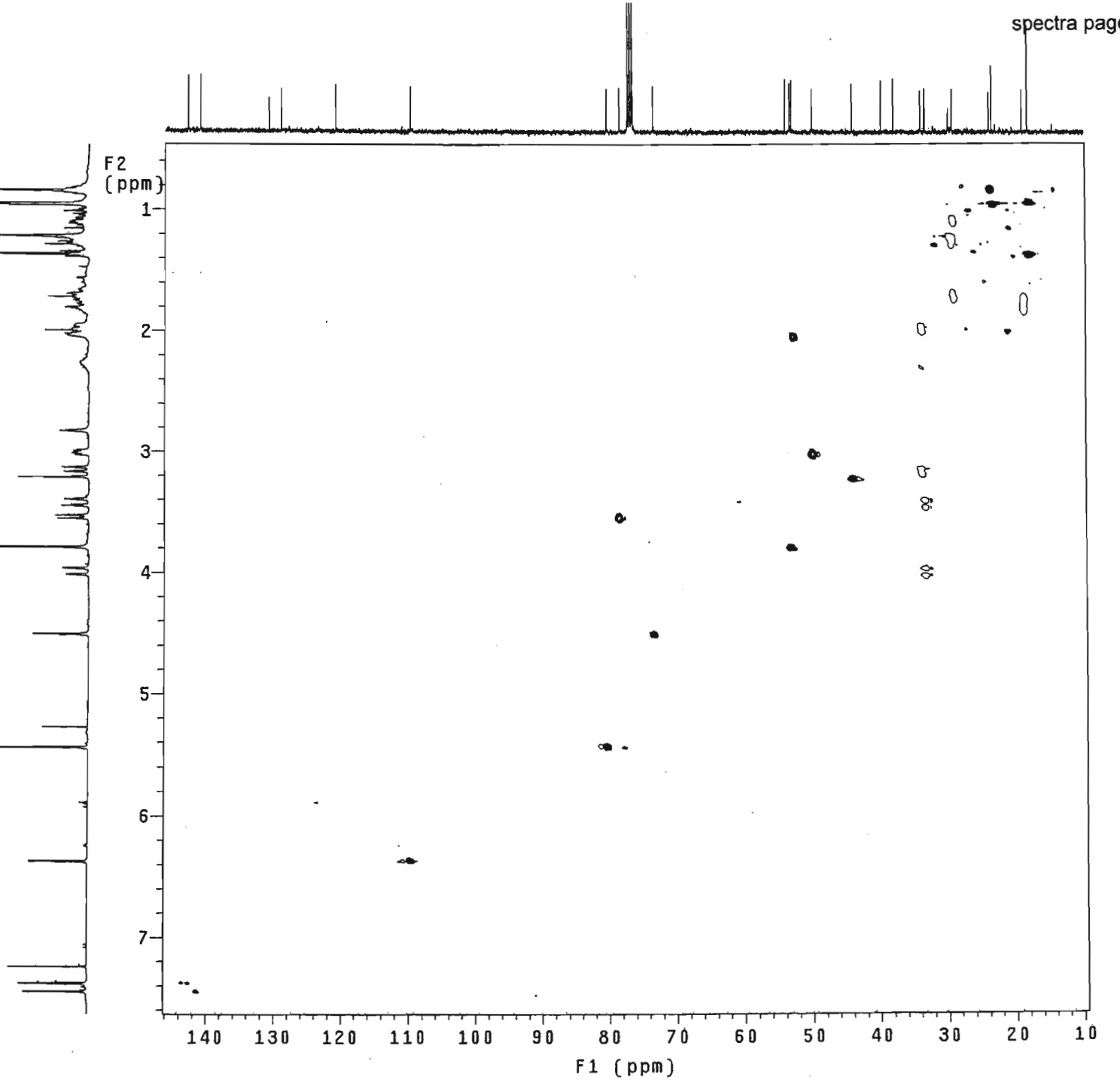
Spectrum QP 5.3: ADEPT Spectrum of swietenolide QP 5

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da



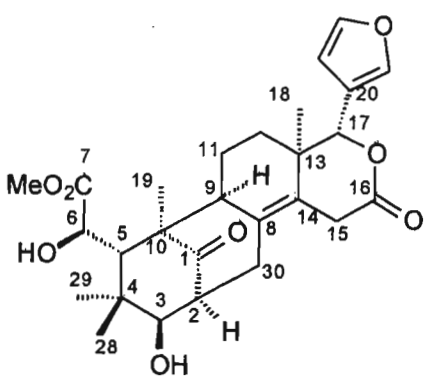
7-41 swietenolide **QP 5**



Spectrum QP 5.4: HSQC Spectrum of swietenolide QP 5

probe=5mmASW

Pulse Sequence: ghmqc_da

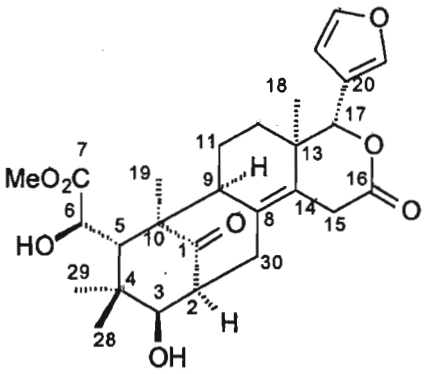


7-41 swietenolide **QP 5**

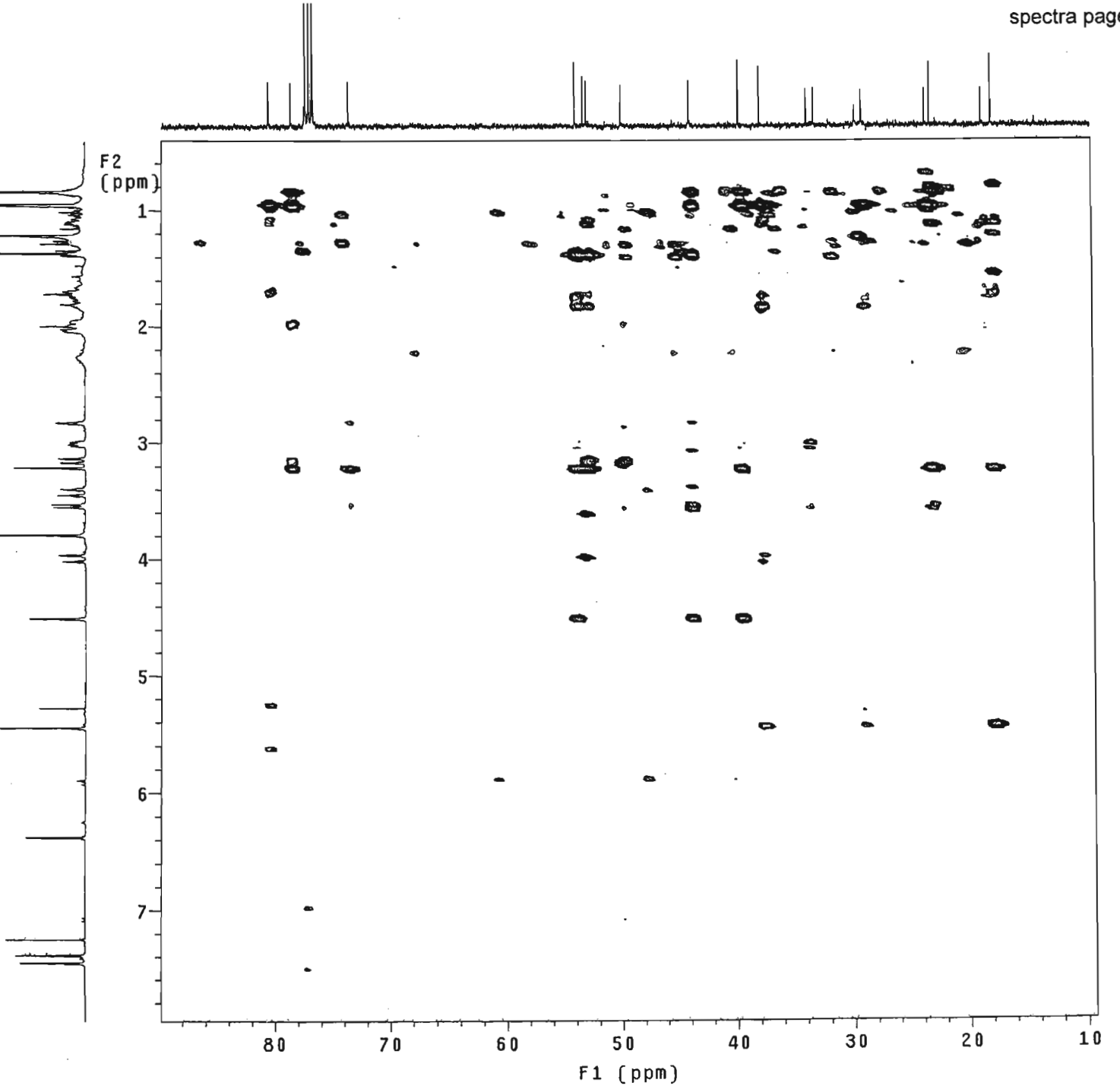
Spectrum QP 5.5: HMBC Spectrum of swietenolide QP 5

probe=5mmASW

Pulse Sequence: ghmqc_da



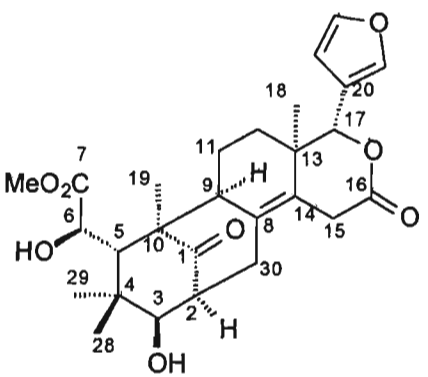
7-41 swietenolide **QP 5**



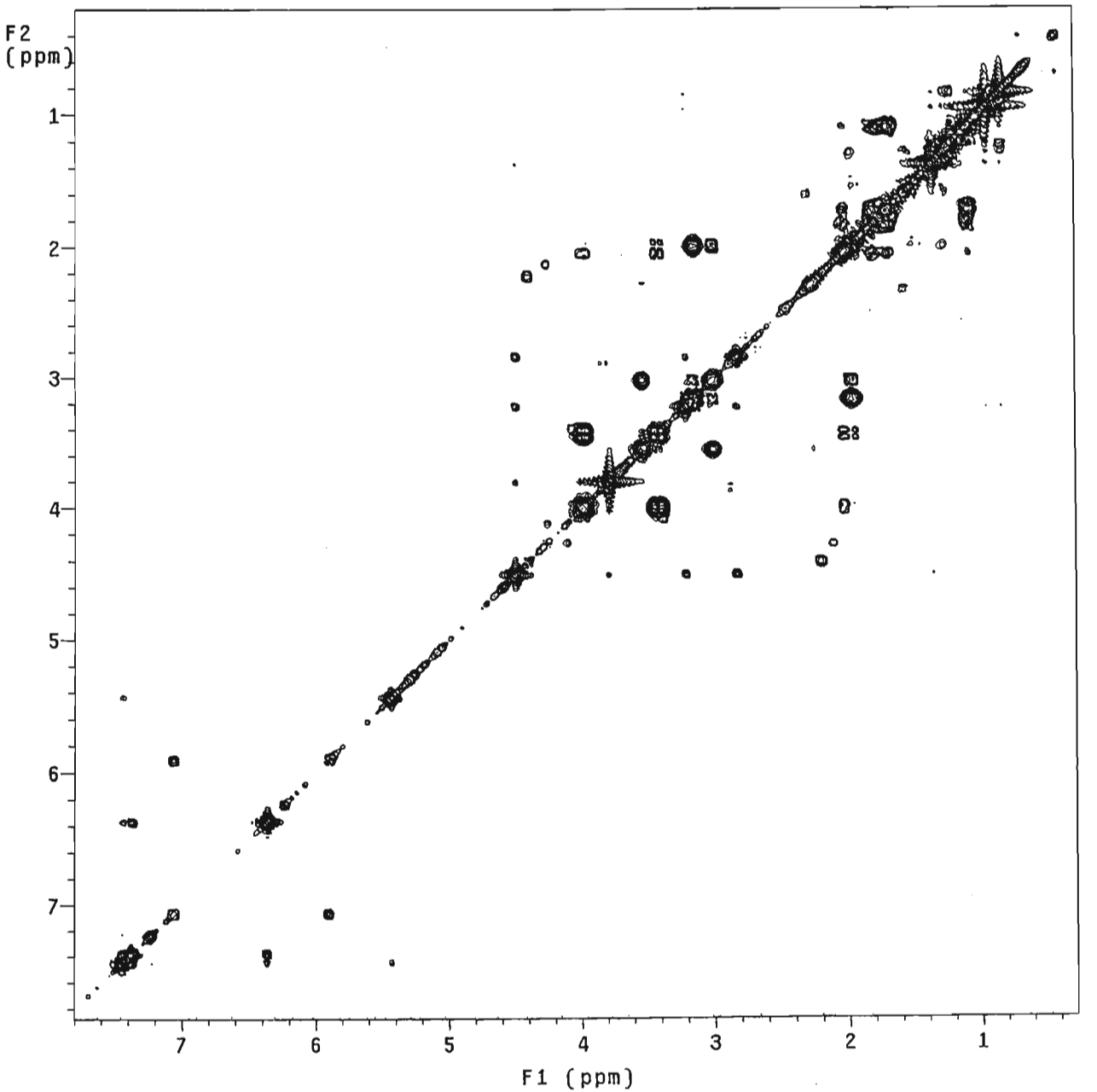
Spectrum QP 5.6: Expanded HMBC Spectrum of swietenolide QP 5

probe=5mmASW

Pulse Sequence: relayh



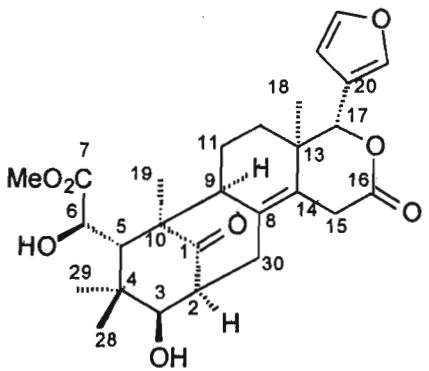
7-41 swietenolide **QP 5**



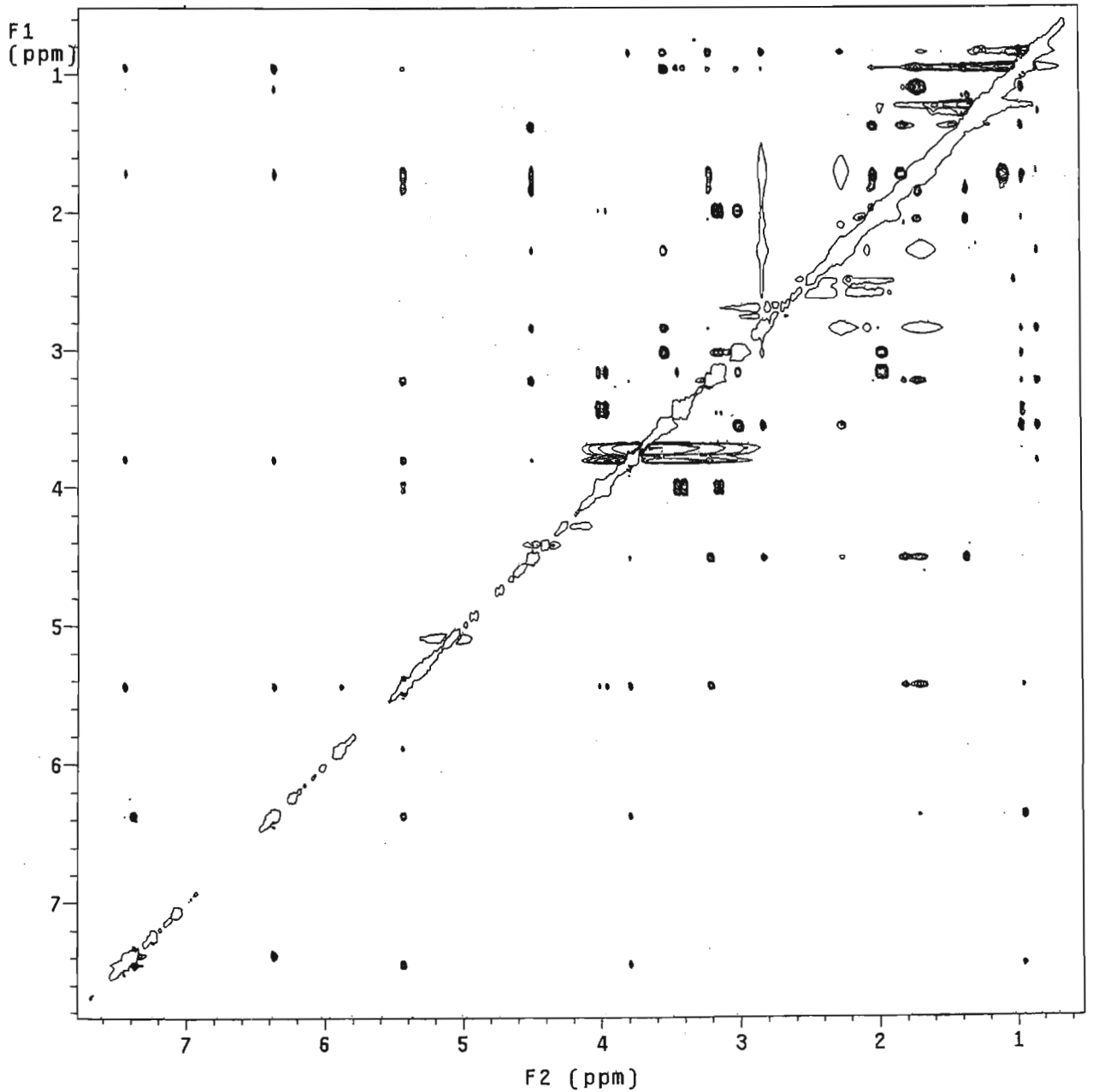
Spectrum QP 5.7: COSY Spectrum of swietenolide QP 5

Gradient NOESY expt.
mix=1sec
probe=5mmASW

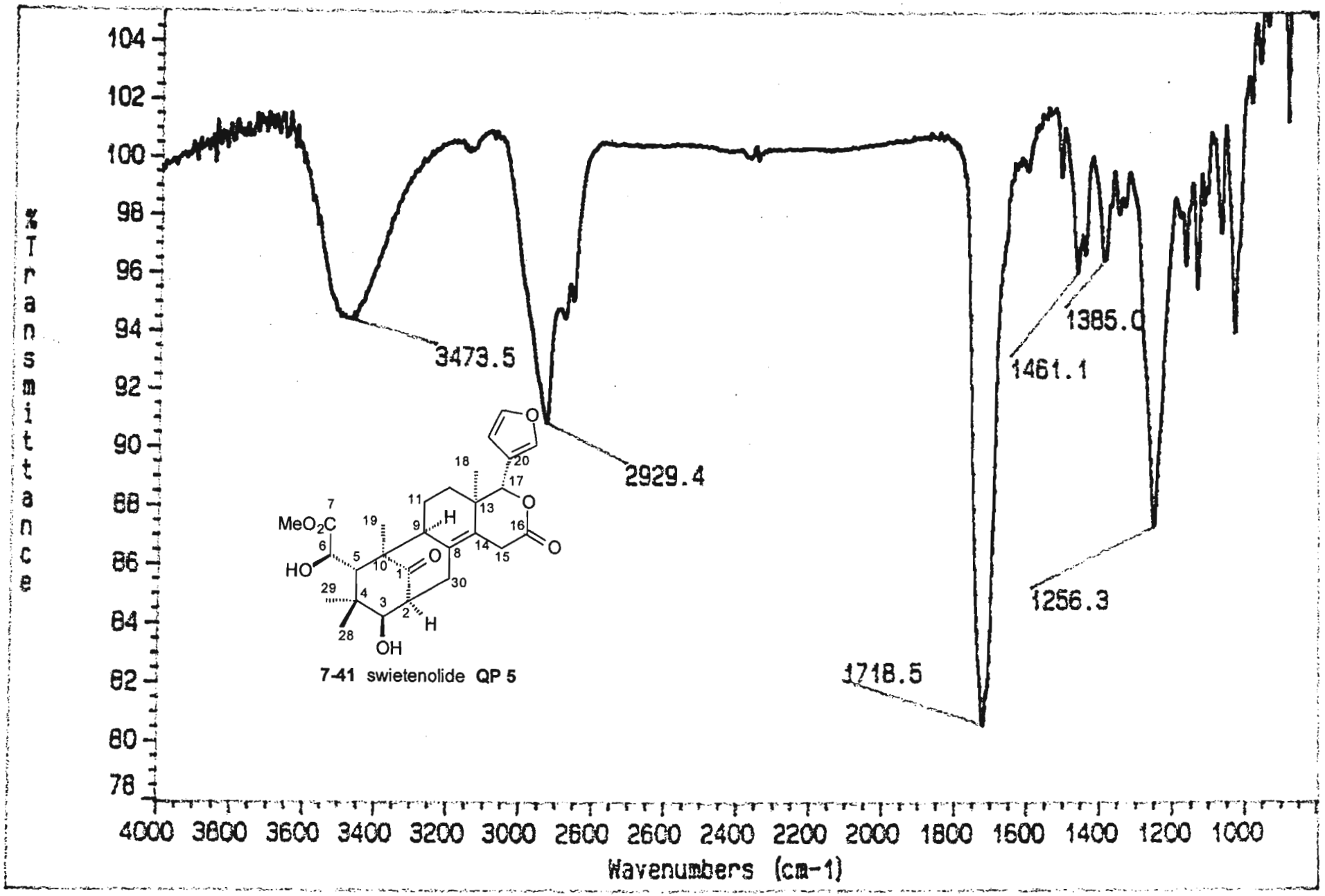
Pulse Sequence: noesy_da



7-41 swietenolide **QP 5**



Spectrum QP 5.8: NOESY Spectrum of swietenolide QP 5

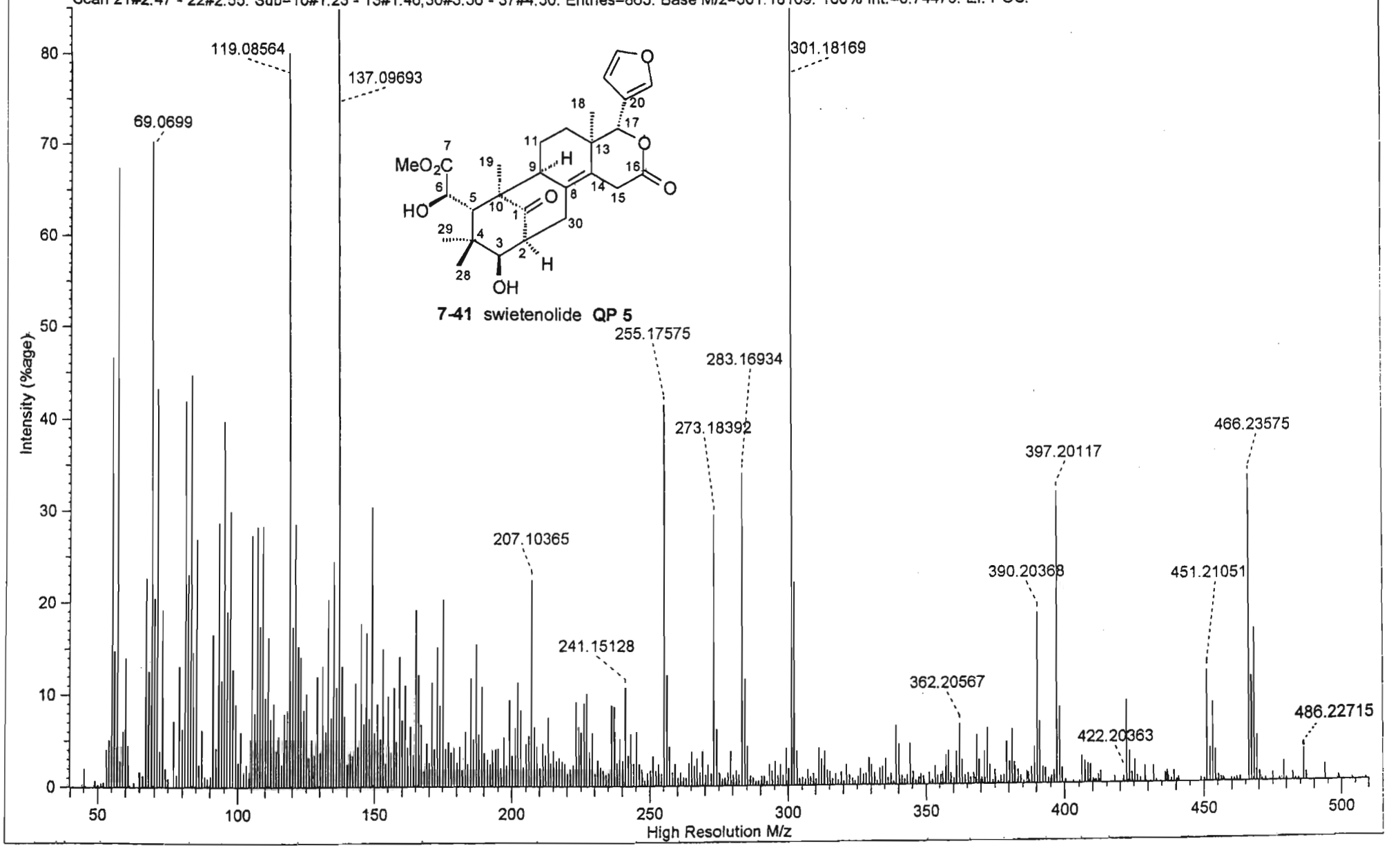


7-41 swietenolide **QP 5**

Spectrum QP 5.9: IR Spectrum of swietenolide QP 5

File Name : C:\MASPEC\data\hc091410.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPK10M-1
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

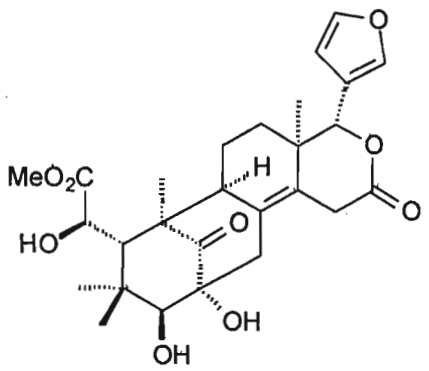
SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 21#2:47 - 22#2:55. Sub=10#1:23 - 13#1:46,30#3:56 - 37#4:50. Entries=865. Base M/z=301.18169. 100% Int.=0.74479. EI. POS.



7-41 swietenolide **QP 5**

Spectrum QP 5.10: High Resolution Mass Spectrum of swietenolide QP 5

Pulse Sequence: s2pul

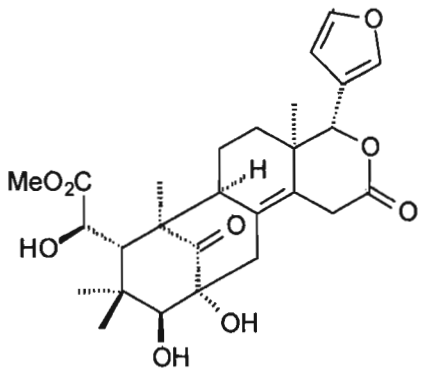


7-51 2α-hydroxyswietenolide **QP 6**

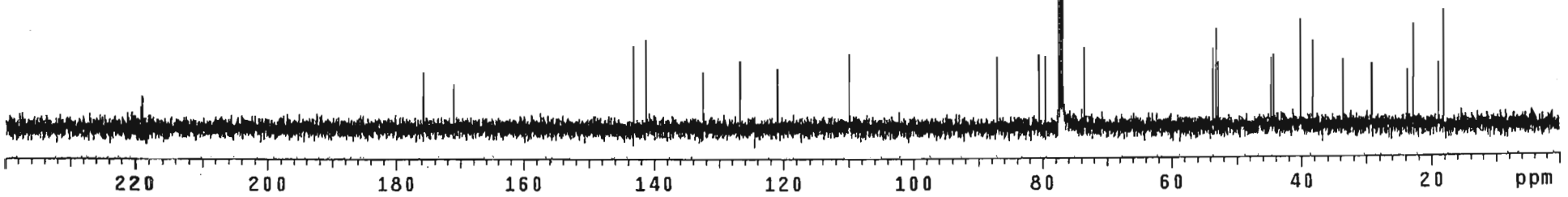
Spectrum QP 6.1: ^{1}H NMR Spectrum of 2α-hydroxyswietenolide QP 6

Pulse Sequence: s2pul

	FREQUENCY	PPM	HEIGHT
1	22023.436	218.992	5.2
2	17678.248	175.786	9.0
3	17211.074	171.140	7.1
4	14397.344	143.161	13.2
5	14209.278	141.291	14.3
6	13328.785	132.536	9.1
7	12747.917	126.760	10.7
8	12162.346	120.938	9.6
9	11063.013	110.006	11.8
10	8757.063	87.077	11.3
11	8102.677	80.570	11.6
12	8002.233	79.571	11.4
13	7799.206	77.552	242.0
14	7787.666	77.437	11.4
15	7767.150	77.233	250.0
16	7735.093	76.915	245.6
17	7396.146	73.544	12.8
18	5391.957	53.615	12.5
19	5342.803	53.127	15.7
20	5308.182	52.782	10.4
21	4493.085	44.677	11.0
22	4453.762	44.286	11.5
23	4038.306	40.155	17.2
24	3845.111	38.234	13.7
25	3373.235	33.542	10.7
26	2935.126	29.186	10.0
27	2382.040	23.686	9.0
28	2289.716	22.768	16.4
29	1901.188	18.905	10.1
30	1819.978	18.097	18.5



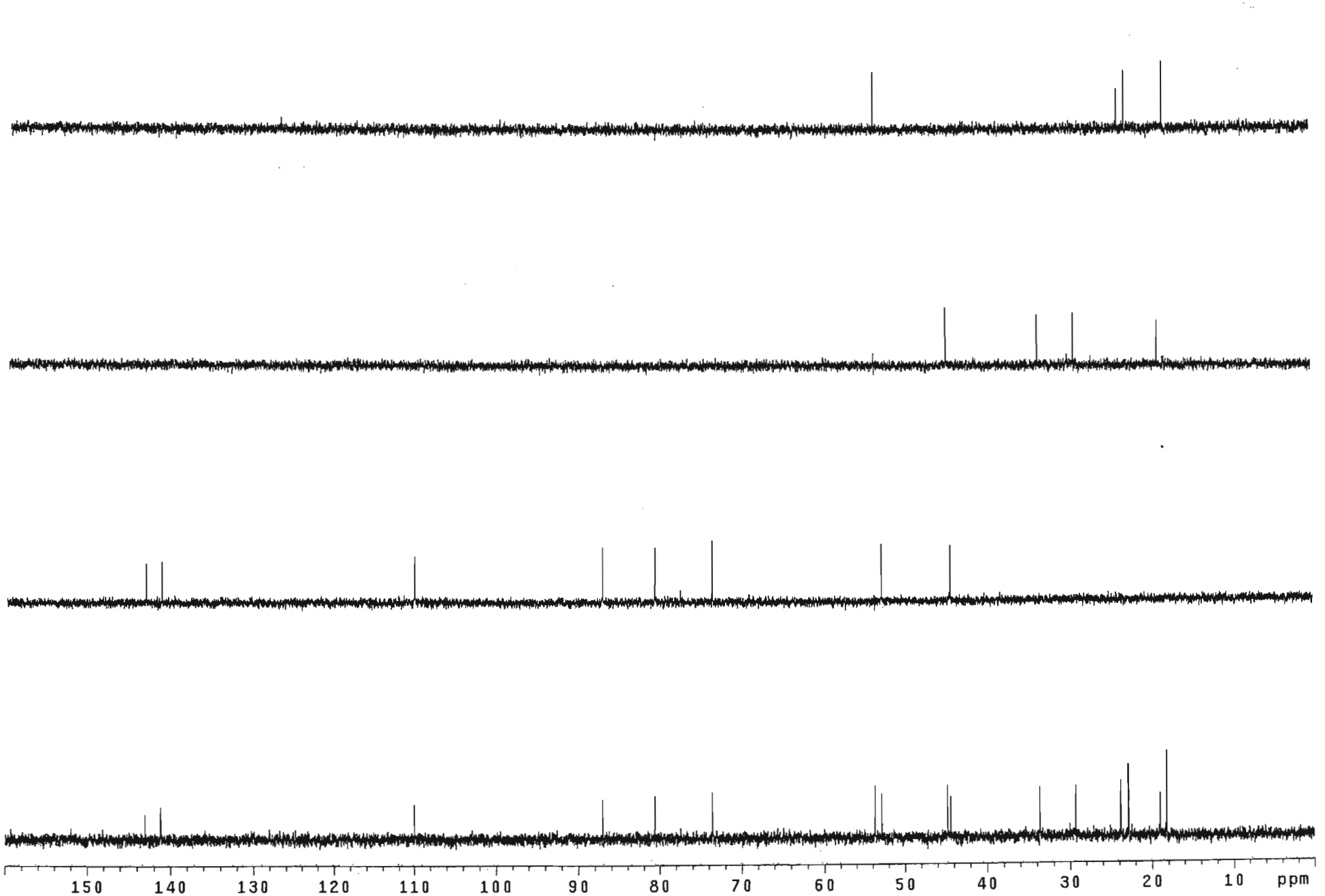
7-51 2α-hydroxyswietenolide **QP 6**



Spectrum QP 6.2: ^{13}C NMR Spectrum of 2α-hydroxyswietenolide QP 6

aqpu4:qpk3d-4 in cdcl3
probe=5mmASW

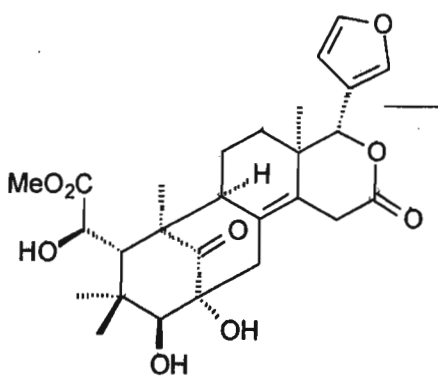
Pulse Sequence: dept



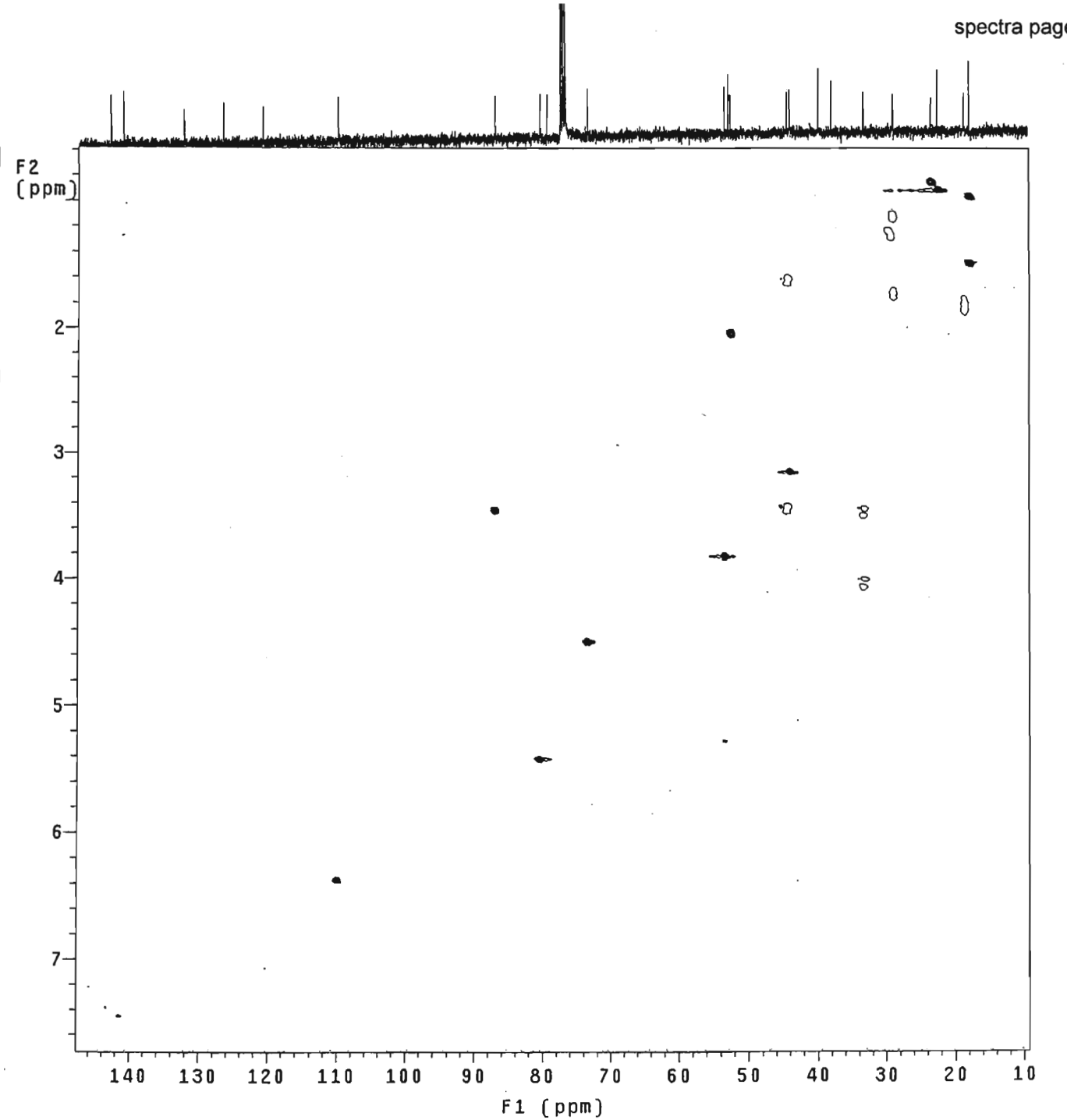
Spectrum OP 6.3: ADEPT Spectrum of 2α-hydroxyswietenolide OP 6

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da



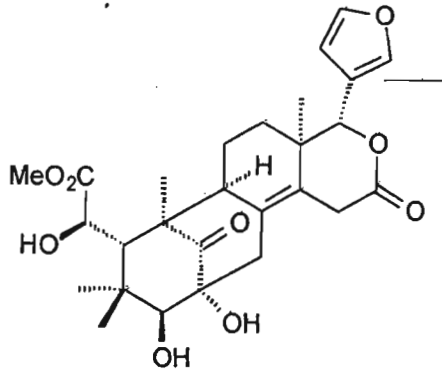
7-51 2α-hydroxyswietenolide **QP 6**



Spectrum QP 6.4: HSQC Spectrum of 2α-hydroxyswietenolide QP 6

probe=5mmASW

Pulse Sequence: ghmqc_da

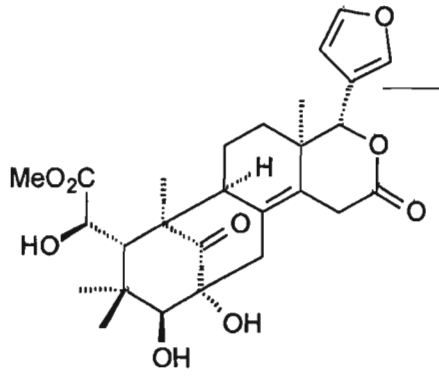


7-51 2α-hydroxyswietenolide **QP 6**

Spectrum QP 6.5: HMBC Spectrum of 2α-hydroxyswietenolide QP 6

probe=5mmASW

Pulse Sequence: ghmqc_da

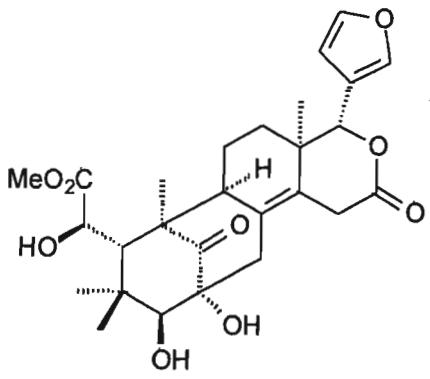


7-51 2α-hydroxyswietenolide **QP 6**

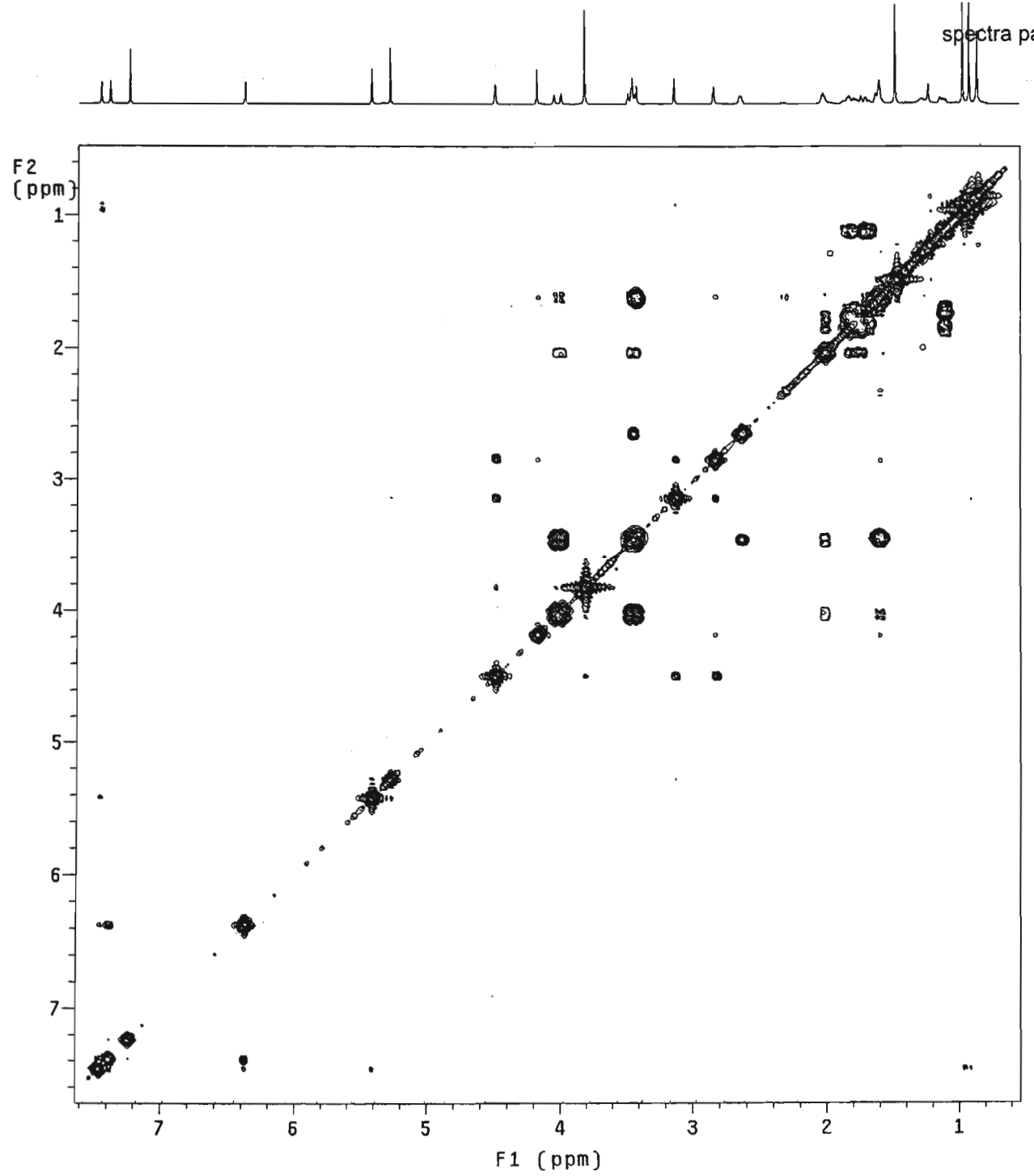
Spectrum QP 6.6: Expanded HMBC Spectrum of 2α-hydroxyswietenolide QP 6

probe=5mmASW

Pulse Sequence: relayh



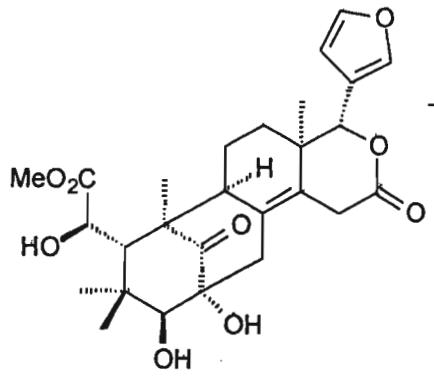
7-51 2α-hydroxyswietenolide **QP 6**



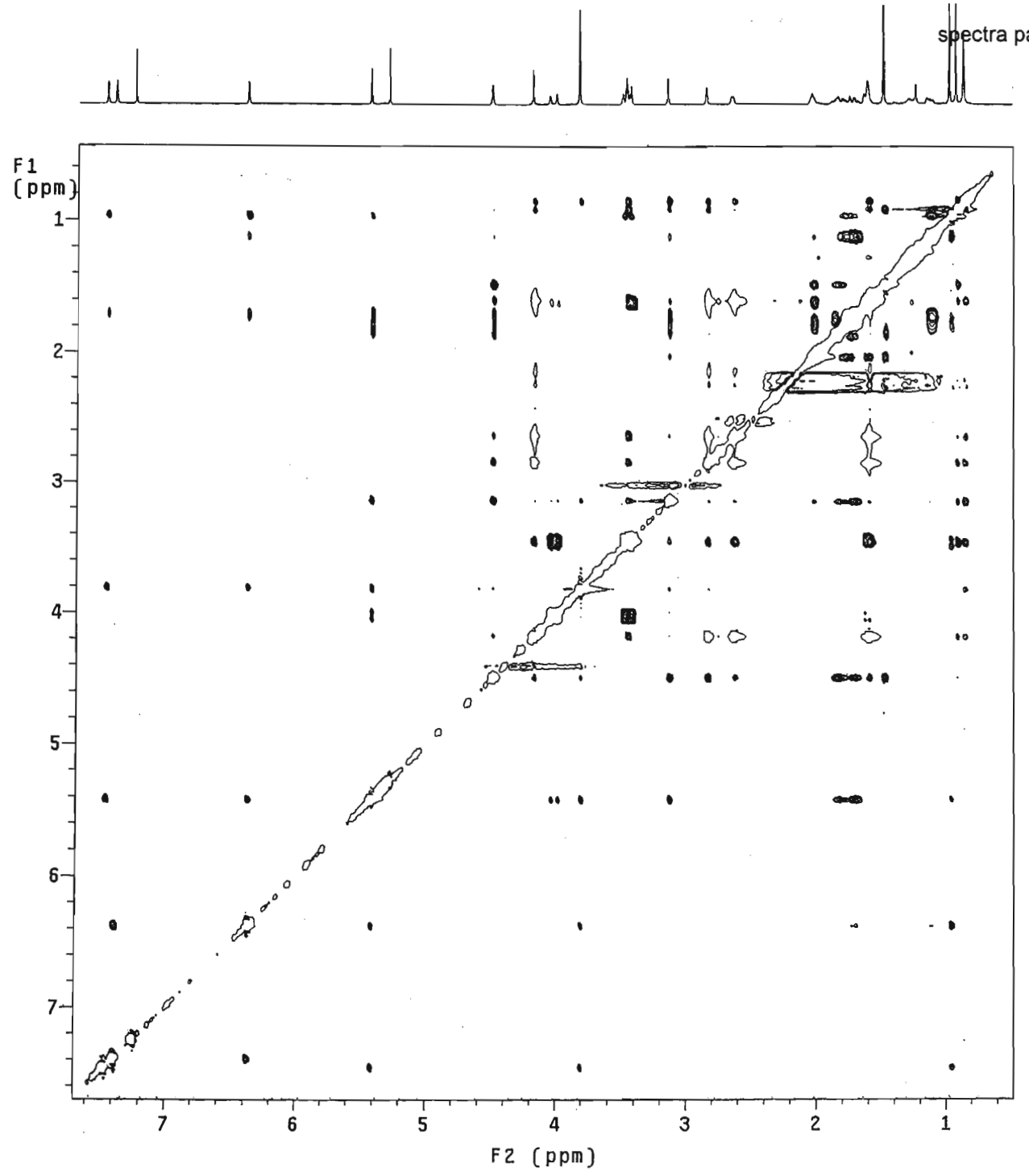
Spectrum QP 6.7: COSY Spectrum of 2α-hydroxyswietenolide QP 6

mix=1sec
probe=5mmASW

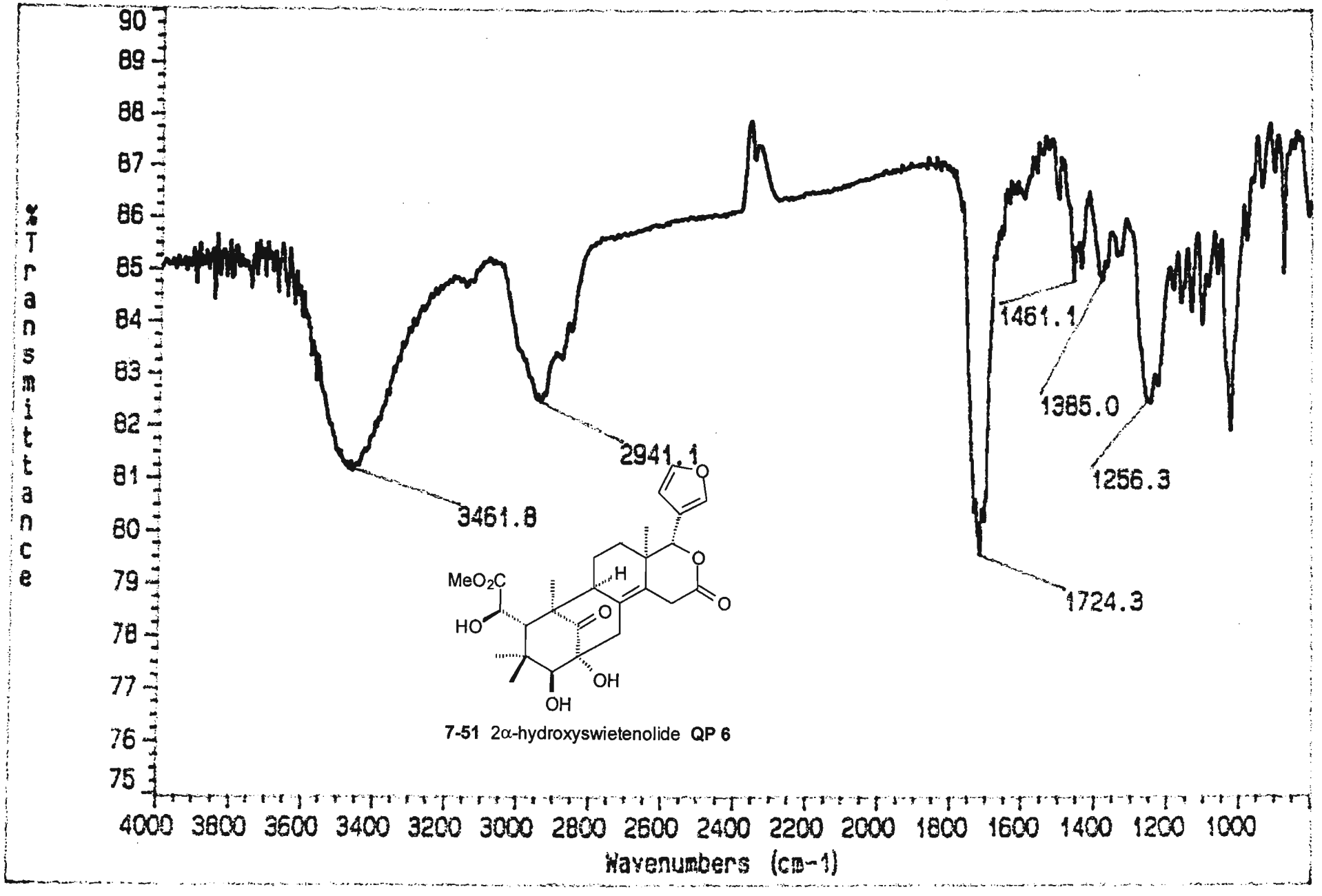
Pulse Sequence: noesy_da



7-51 2α-hydroxyswietenolide **QP 6**



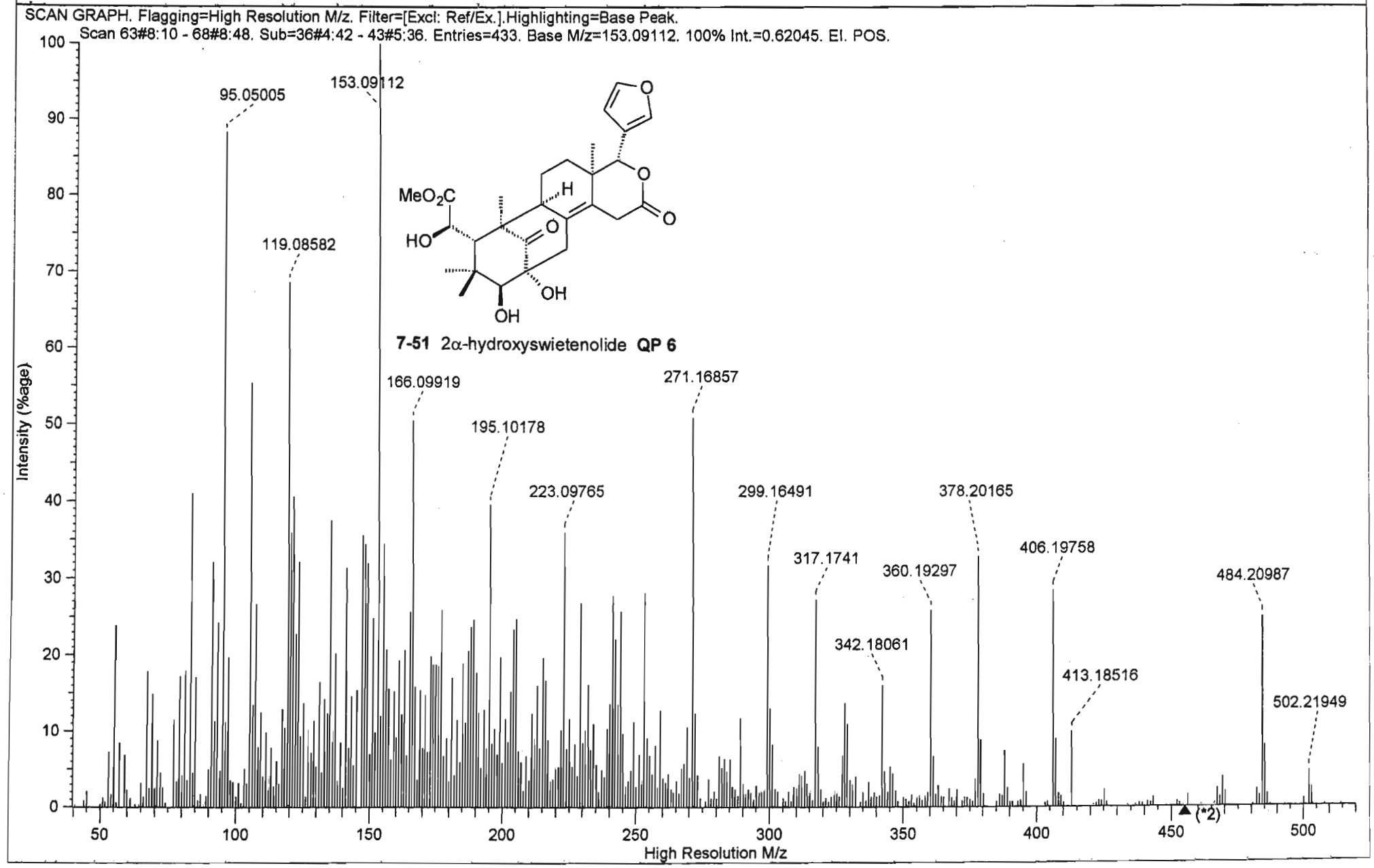
Spectrum QP 6.8: NOESY Spectrum of 2α-hydroxyswietenolide QP 6



7-51 2α-hydroxyswietenolide **QP 6**

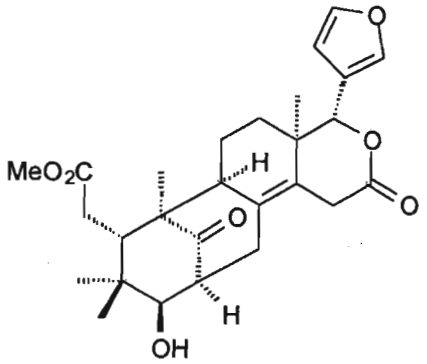
Spectrum QP 6.9: IR Spectrum of 2α-hydroxyswietenolide QP 6

File Name : C:\MASPEC\data\hc091415.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPK9d-4
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ



Spectrum QP 6.10: High Resolution Mass Spectrum of 2α-hydroxyswietenolide QP 6

Pulse Sequence: s2pul



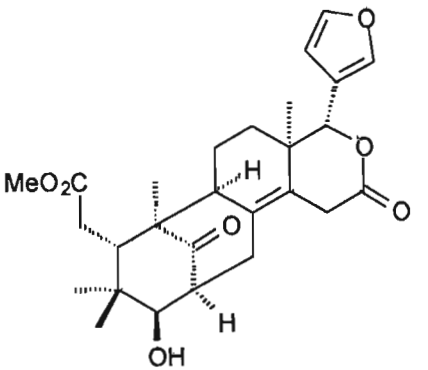
7-52 proceranolide **QP 7**

Spectrum QP 7.1: ^{1}H NMR Spectrum of proceranolide QP 7

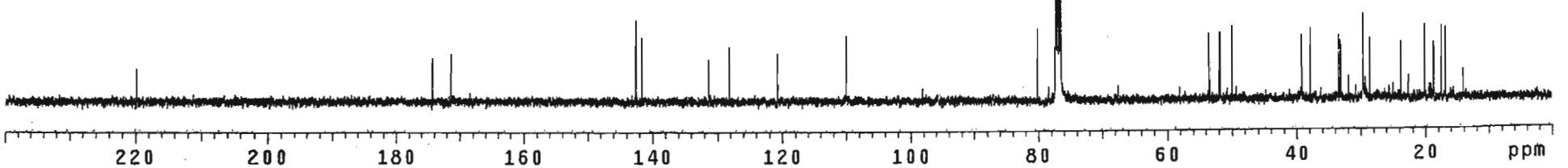
Pulse Sequence: s2pul

	Frequency	PPM	Height
1	22114.518	219.898	5.3
2	17532.628	174.337	7.1
3	17239.782	171.426	7.7
4	14341.758	142.609	13.1
5	14250.449	141.701	10.3
6	13212.326	131.378	6.8
7	12889.866	128.172	8.8
8	12146.235	120.777	7.8
9	11070.272	110.078	10.6
10	8065.310	80.198	11.7
11	7774.931	77.311	478.4
12	7762.592	77.188	25.2
13	7743.672	77.000	485.1
14	7711.591	76.681	500.0
15	5388.565	53.582	10.7
16	5228.158	51.987	10.9
17	5207.593	51.782	10.9
18	5026.620	49.983	11.9
19	3949.012	39.267	10.3
20	3945.722	39.235	9.7
21	3811.638	37.901	11.5
22	3370.724	33.517	10.3
23	3345.223	33.264	9.5
24	3325.481	33.067	8.7
25	3208.671	31.906	3.7
26	2984.924	29.681	13.8
27	2874.695	28.585	9.8
28	2393.473	23.800	9.1
29	2279.954	22.671	3.8
30	2025.771	20.143	11.8
31	1882.638	18.720	9.1
32	1764.183	17.542	11.7
33	1699.198	16.896	11.4
34	1418.691	14.107	4.6

34

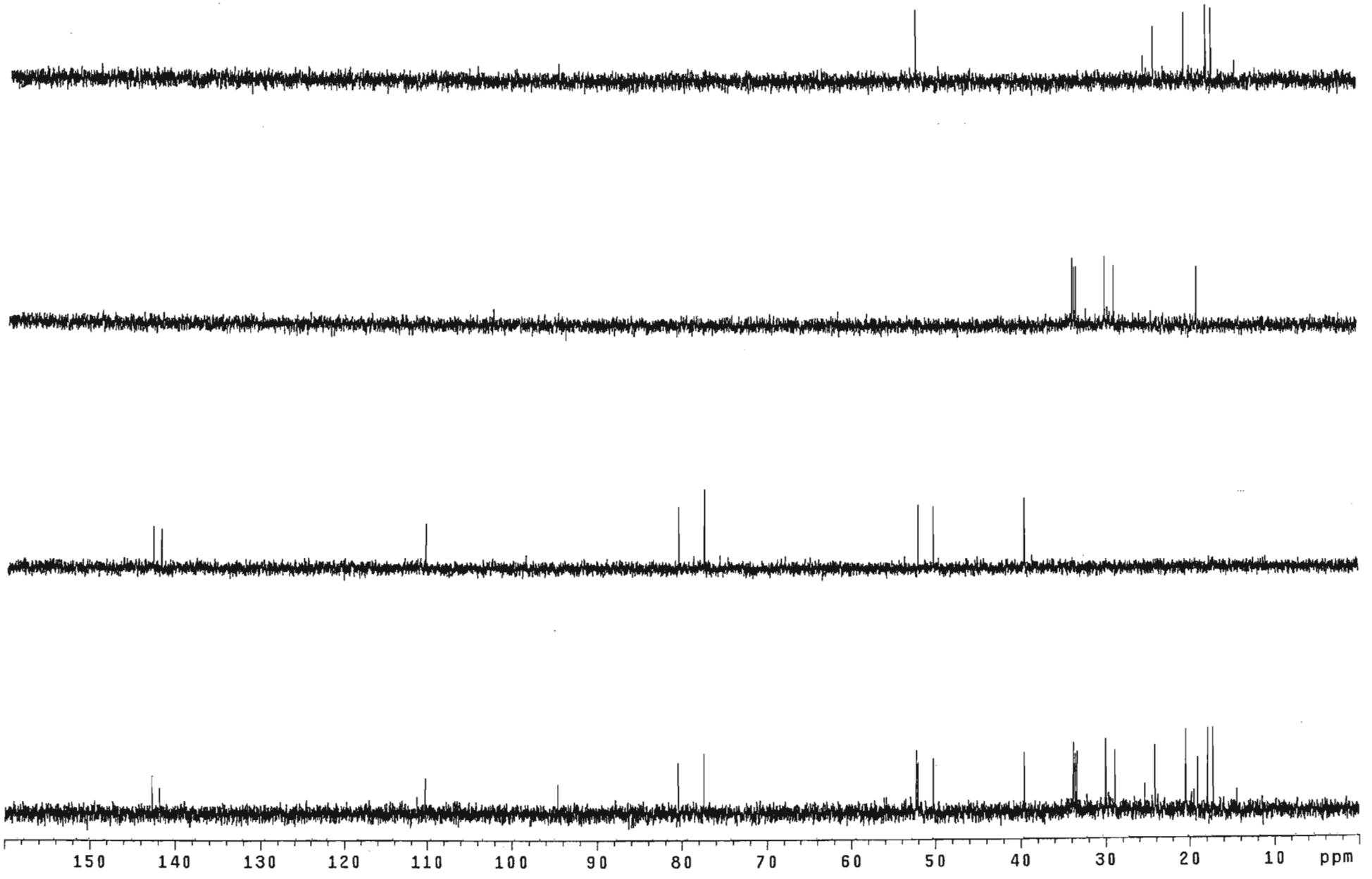


7-52 proceranolide **QP 7**



Spectrum QP 7.2: ^{13}C NMR Spectrum of proceranolide QP 7

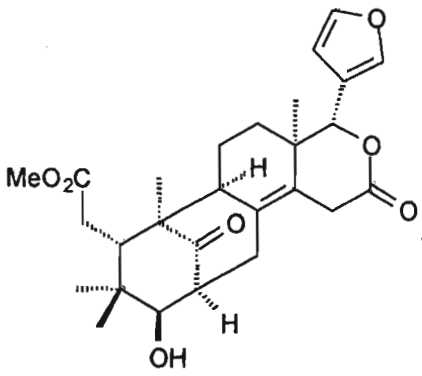
Pulse Sequence: dept



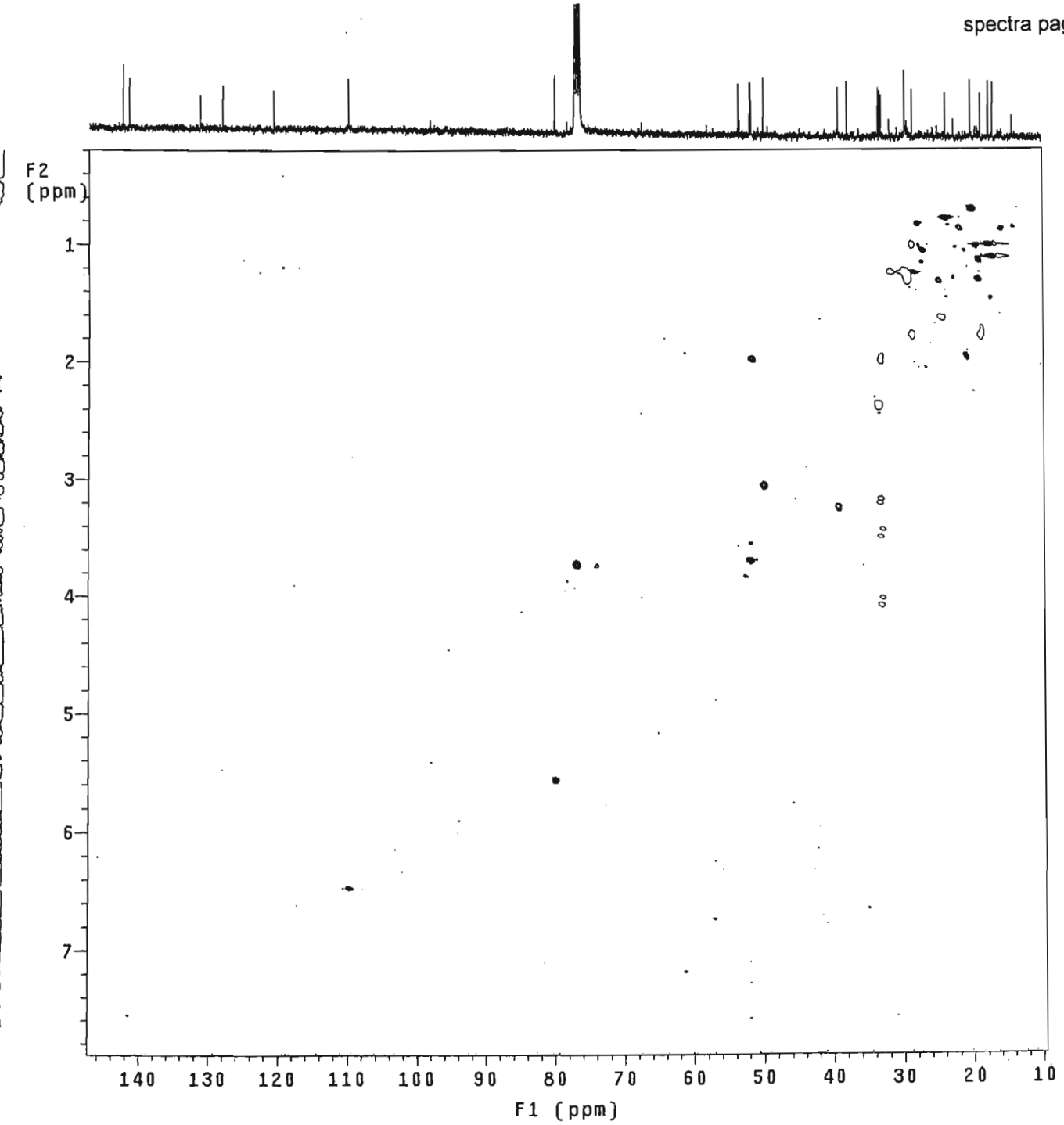
Spectrum QP 7.3: ADEPT Spectrum of proceranolide QP 7

probe=5mmASW

Pulse Sequence: ghsqc_da



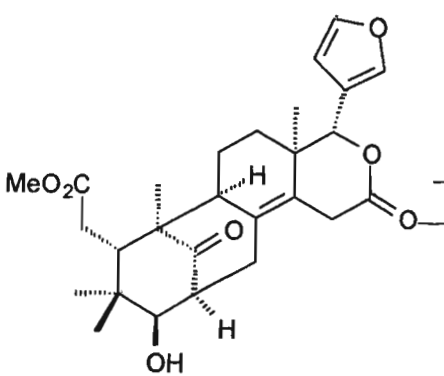
7-52 proceranolide **QP 7**



Spectrum QP 7.4: HSQC Spectrum of proceranolide QP 7

Gradient HMBC expt.
probe=5mmASW

Pulse Sequence: ghmqc_da

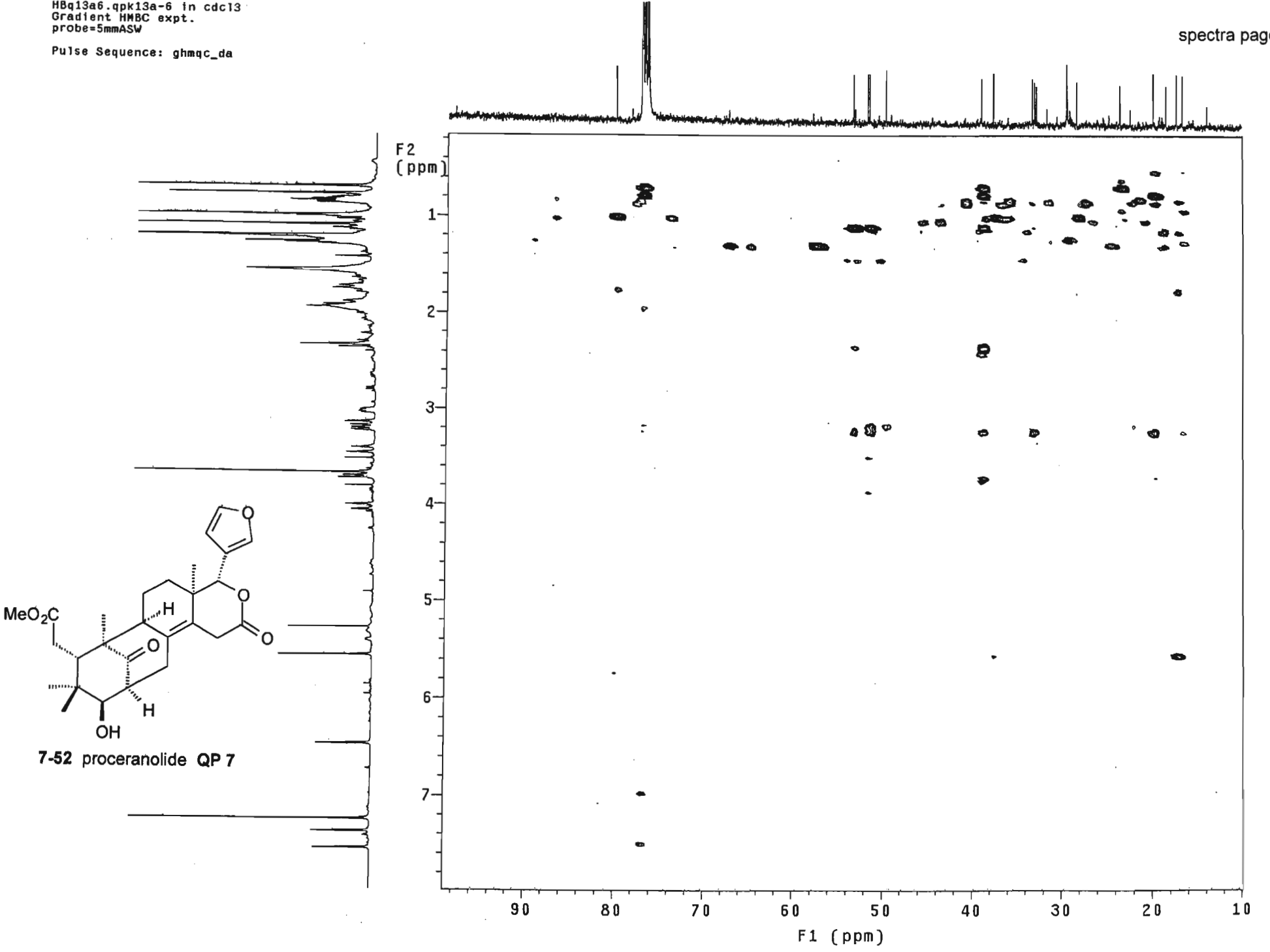


7-52 proceranolide **QP 7**

Spectrum QP 7.5: HMBC Spectrum of proceranolide QP 7

HBq13a6.qpk13a-6 in cdcl3
Gradient HMBC expt.
probe=5mmASW

Pulse Sequence: ghmqc_da

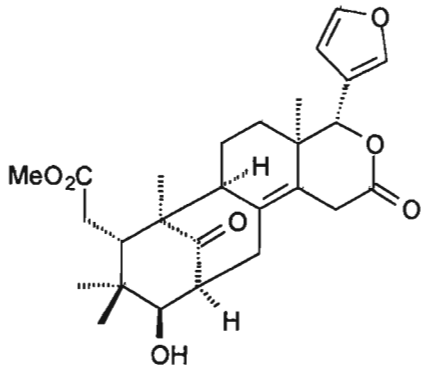


7-52 proceranolide **QP 7**

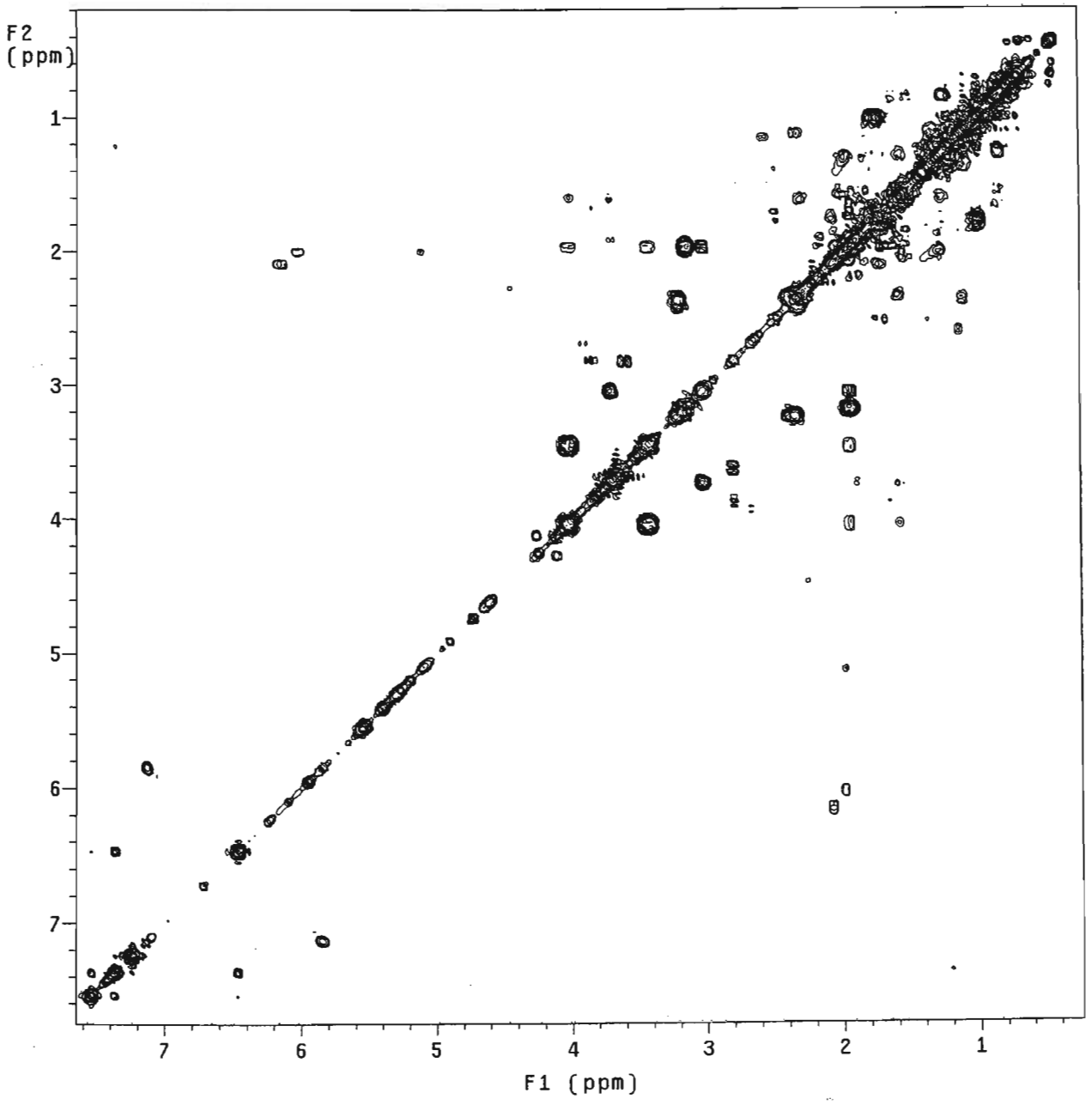
Spectrum QP 7.6: Expanded HMBC Spectrum of proceranolide QP 7

cyq13a6.qpk13a-6 in cdcl3
1H Cosy-90
probe=5mmASW

Pulse Sequence: relayh

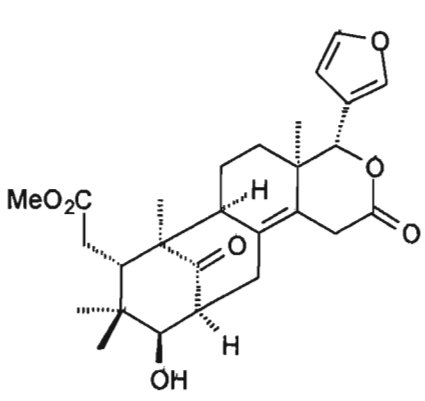


7-52 proceranolide **QP 7**

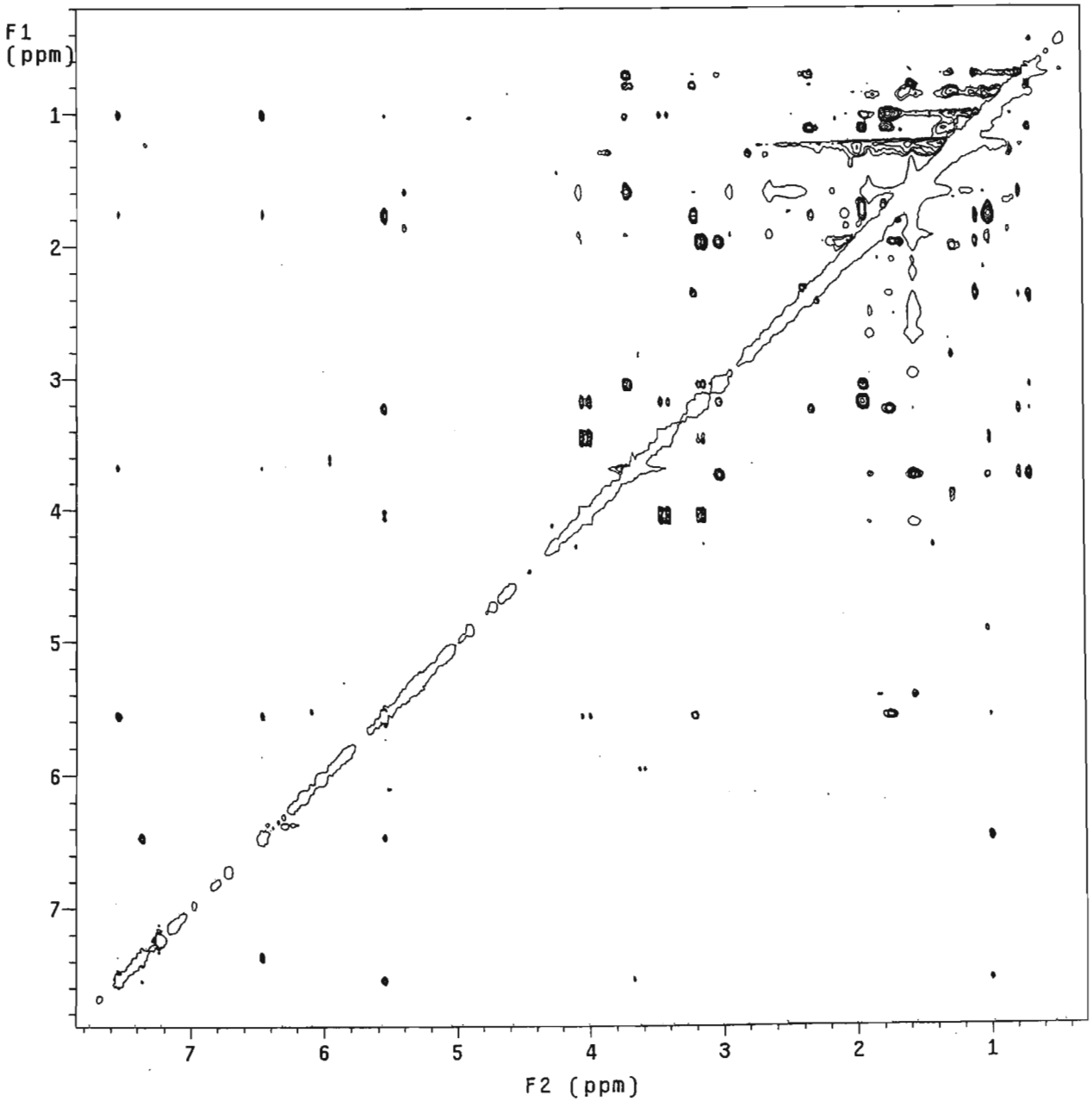


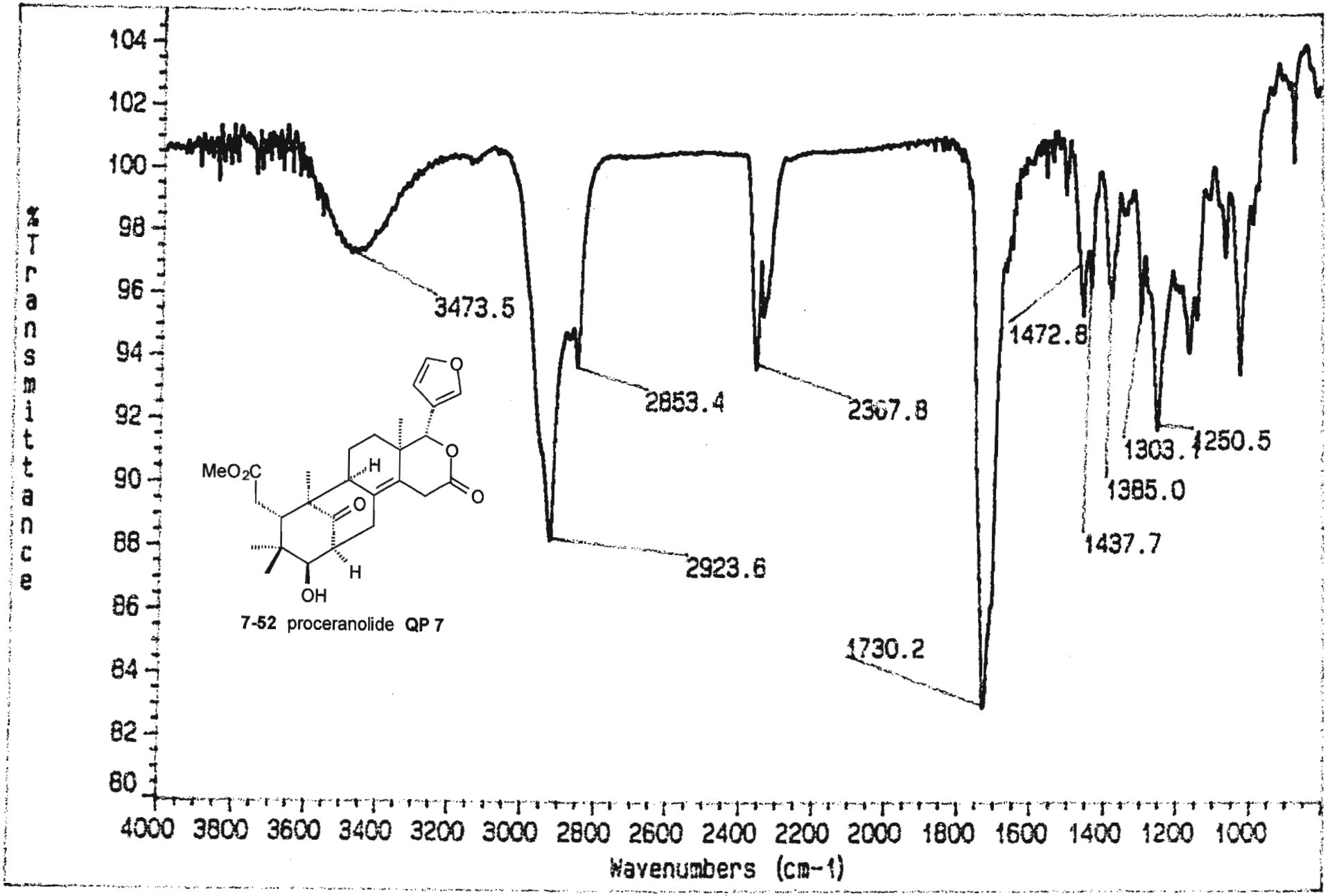
NOq13a6.qpk13a-6 in cdcl3
Gradient NOESY expt.
mix=1sec
probe=5mmASW

Pulse Sequence: noesy_da



7-52 proceranolide **QP 7**





7-52 proceranolide **QP 7**

File Name : C:\MASPEC\data\hc112807.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPK 13a-6
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Int:0.3%. Excl: Ref/Ex.].Highlighting=Base Peak.
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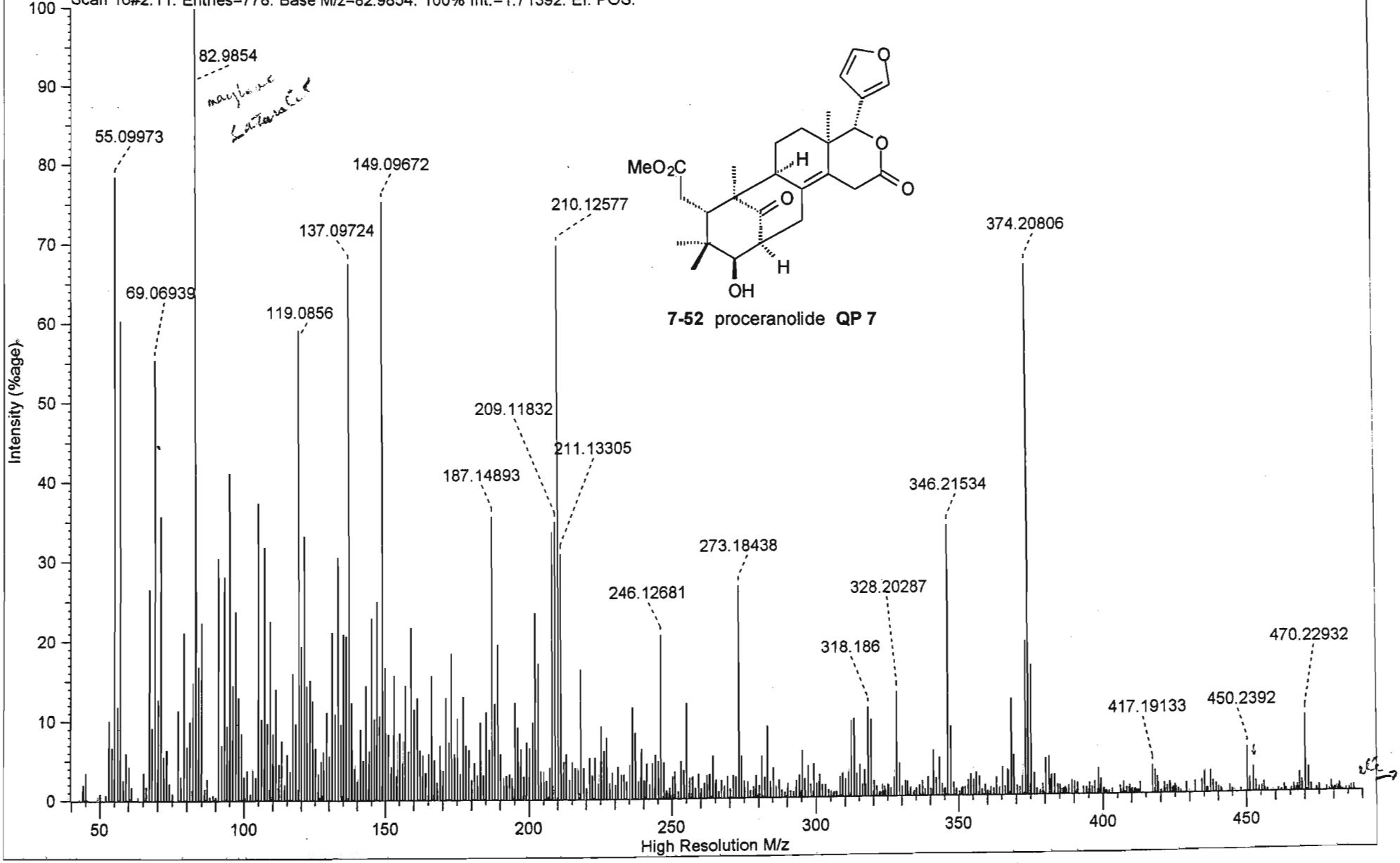
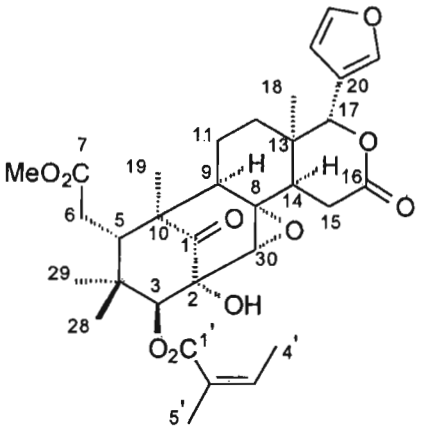


7-52 proceranolide **QP 7**


MeO2C
O2C
OH
H
H16
O
O
O
O
O
O
1
2
3
5
6
7
8
9
10
11
13
14
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18
19
20
29
28
30
1'
4'
5'

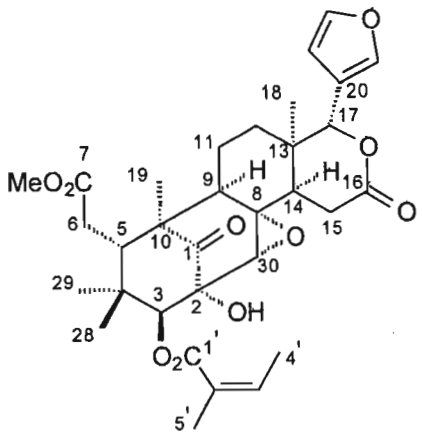
7-59 QP 8

9
8
7
6
5
4
3
2
1
ppm

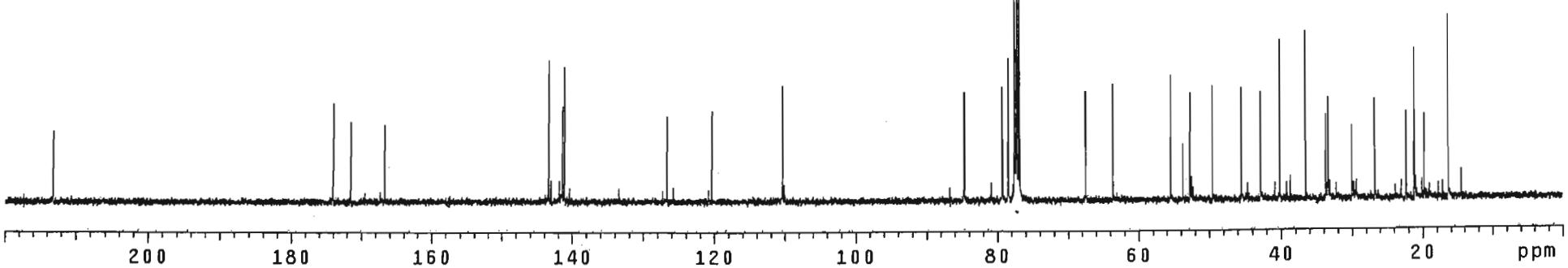
probe=5mmASW

Pulse Sequence: s2pul

INDEX	FREQUENCY	PPM	HEIGHT
1	21445.282	213.243	11.4
2	17496.950	173.983	15.9
3	17252.802	171.555	12.9
4	16767.558	166.730	12.4
5	14418.395	143.371	22.7
6	14220.025	141.398	15.2
7	14191.033	141.110	21.7
8	12739.877	126.680	13.8
9	12107.381	120.391	14.6
10	11101.033	110.384	18.6
11	8518.405	84.704	17.5
12	7977.464	79.325	18.3
13	7897.353	78.528	22.7
14	7805.034	77.610	269.0
15	7793.590	77.496	10.8
16	7772.990	77.292	269.4
17	7740.946	76.973	254.3
18	6792.583	67.543	17.6
19	6399.657	63.636	18.7
20	5579.472	55.480	20.1
21	5404.754	53.743	9.2
22	5303.280	52.734	17.3
23	4976.732	49.487	18.4
24	4573.124	45.473	18.0
25	4307.613	42.833	17.3
26	4040.576	40.178	25.6
27	3677.406	36.567	27.0
28	3395.873	33.767	13.6
29	3365.354	33.464	16.4
30	3355.436	33.365	16.1
31	3020.495	30.035	11.9
32	2696.236	26.810	16.2
33	2246.851	22.342	14.0
34	2130.881	21.189	16.6
35	2126.303	21.143	24.1
36	1990.495	19.793	13.7
37	1646.399	16.371	29.3



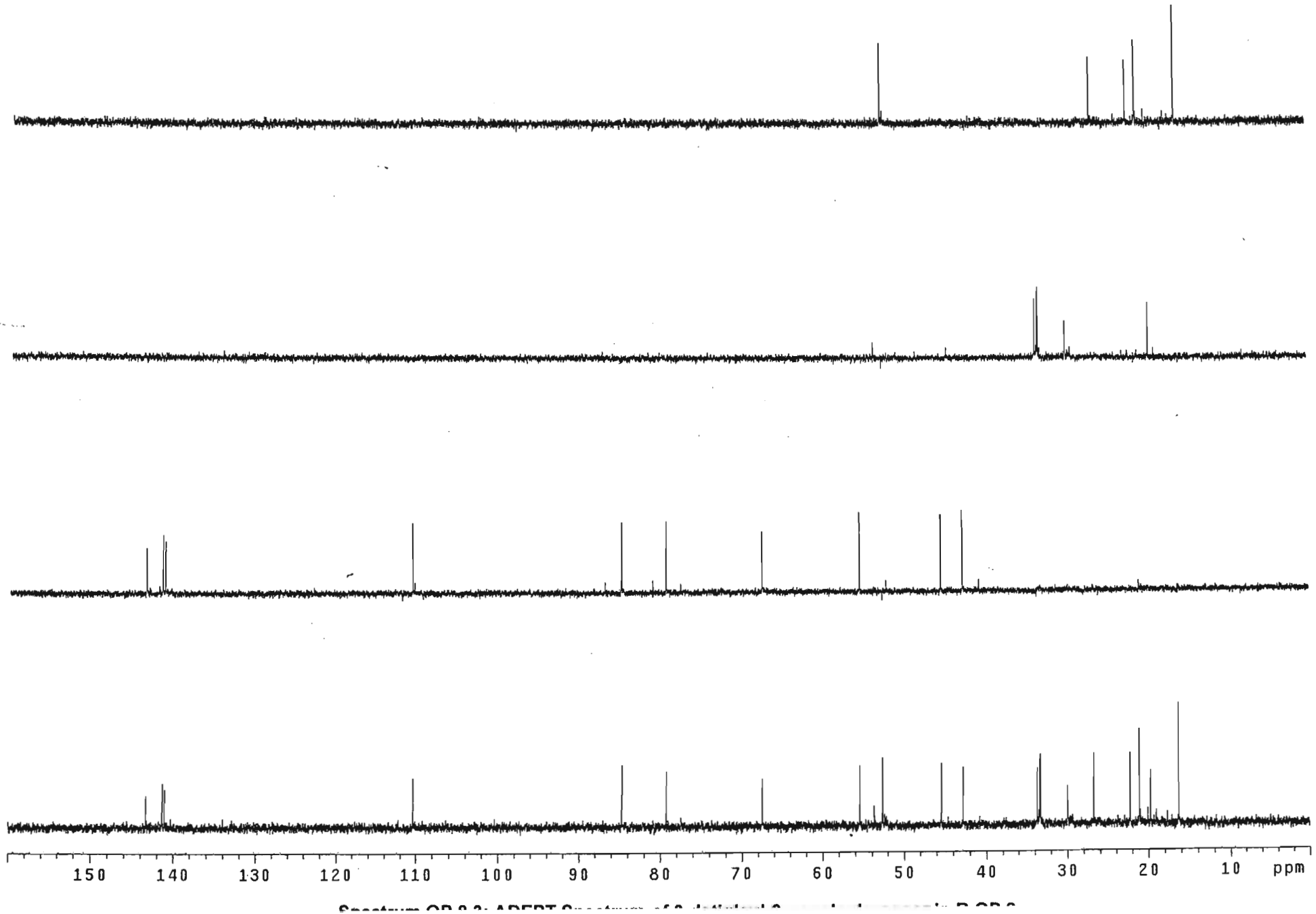
7-59 QP 8



Spectrum QP 8.2: ^{13}C NMR Spectrum of 3-deticloyl-3-angeloylrugeganin B QP 8

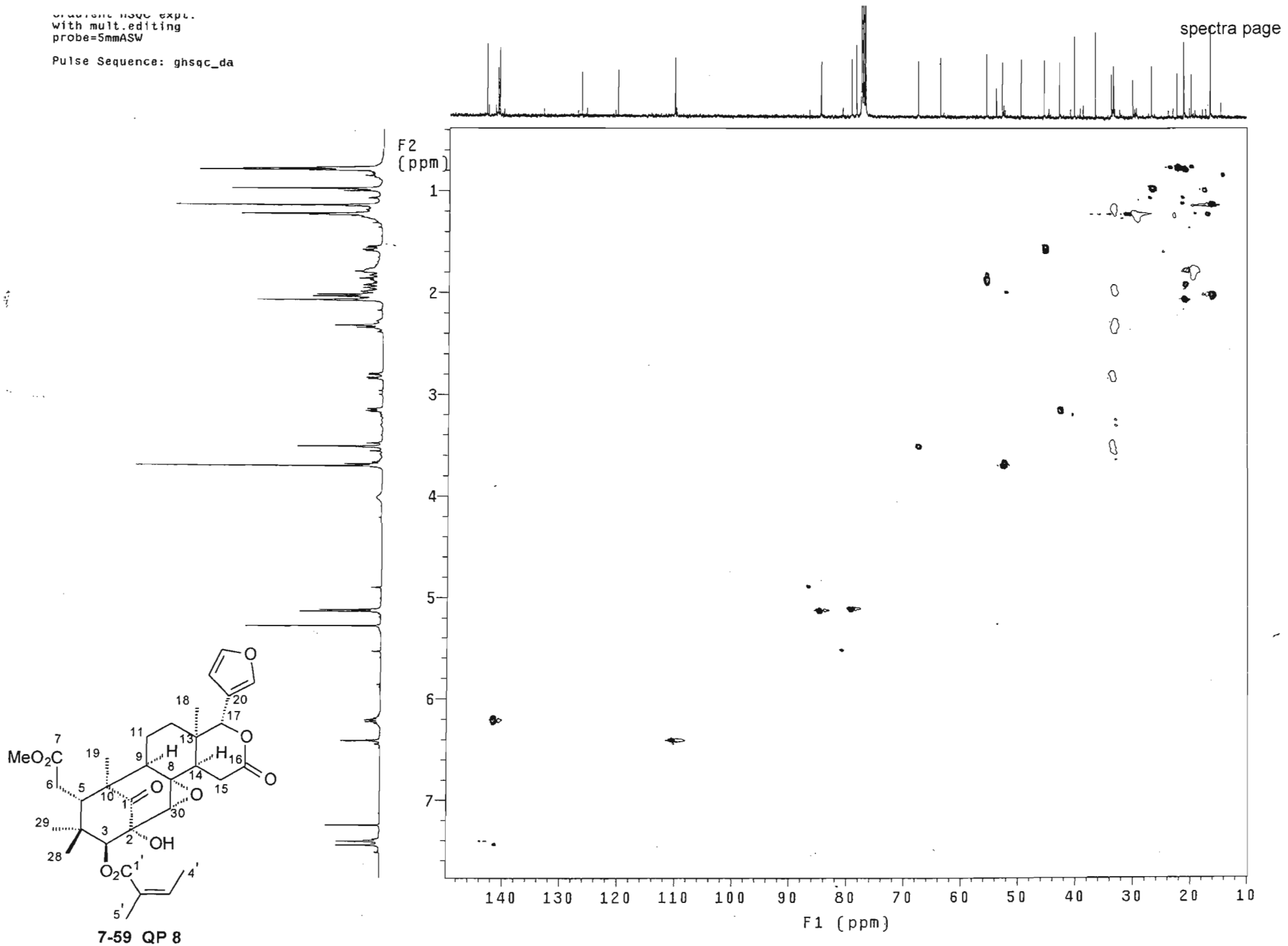
dk14c1.qpk14c_1 in cdcl3
probe=5mmASW

Pulse Sequence: dept



Gradient HSQC expt.
with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

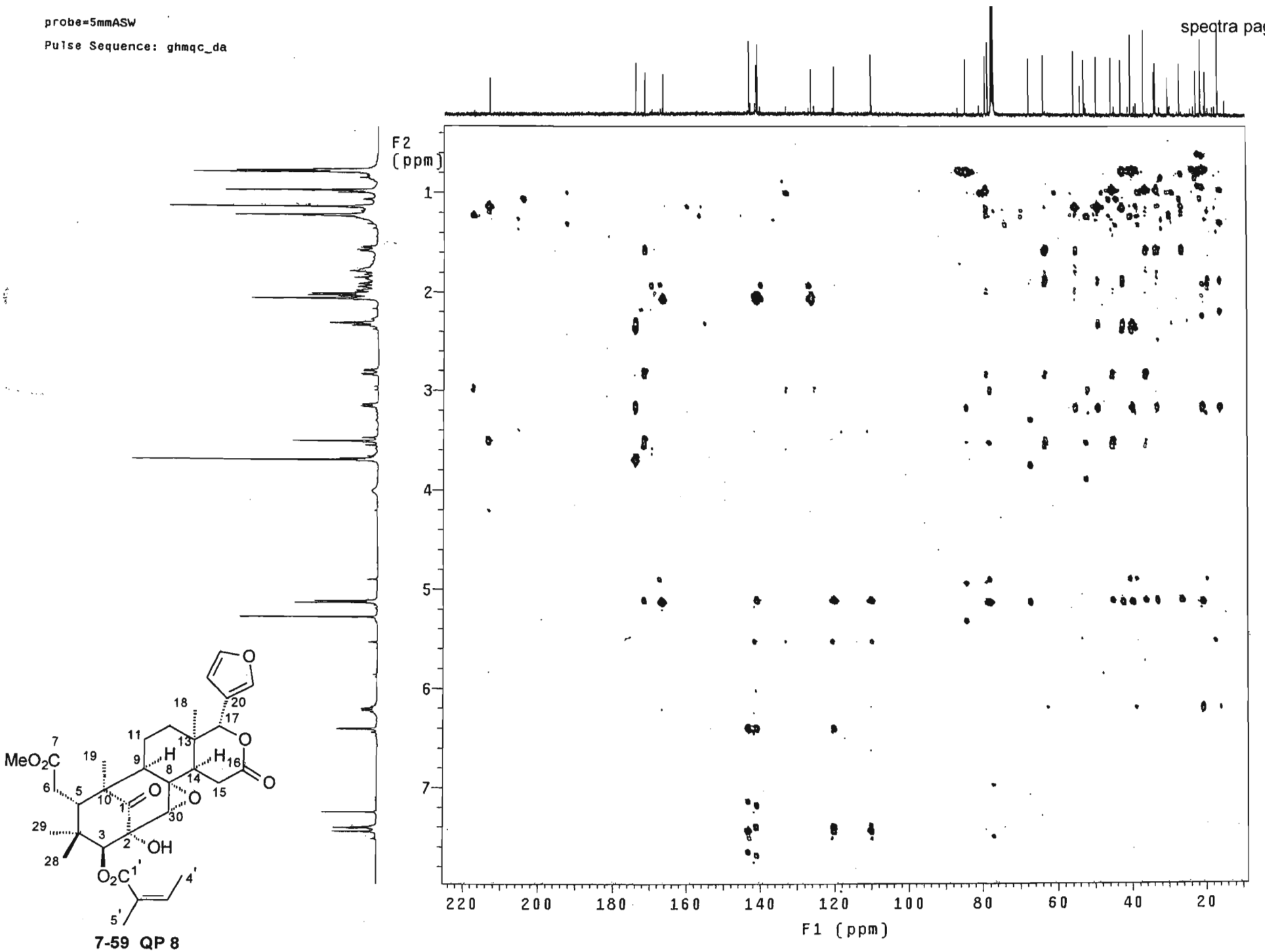


7-59 QP 8

Spectrum QP 8.4: HSQC Spectrum of 3-detigloyl-3-angeloylruageanin B QP 8

probe=5mmASW

Pulse Sequence: ghmqc_da

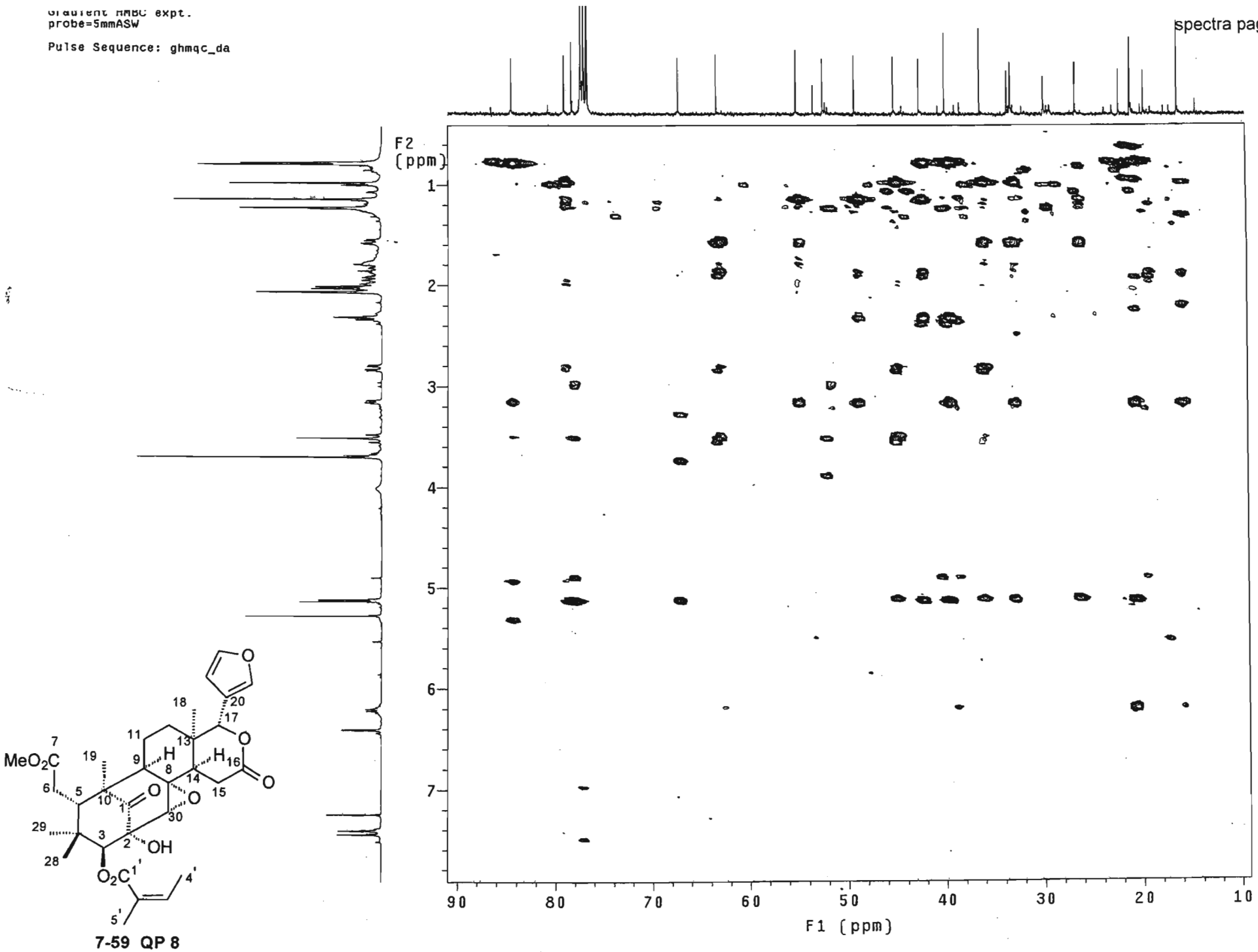


7-59 QP 8

Spectrum QP 8.5: HMBC Spectrum of 3-detigloyl-3-angeloylruageanin B QP 8

Gradient HMBC expt.
probe=5mmASW

Pulse Sequence: ghmqc_da

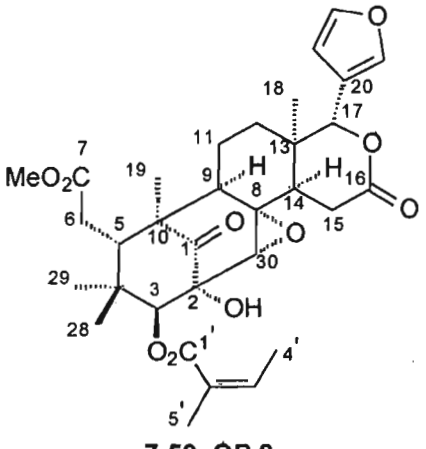


7-59 QP 8

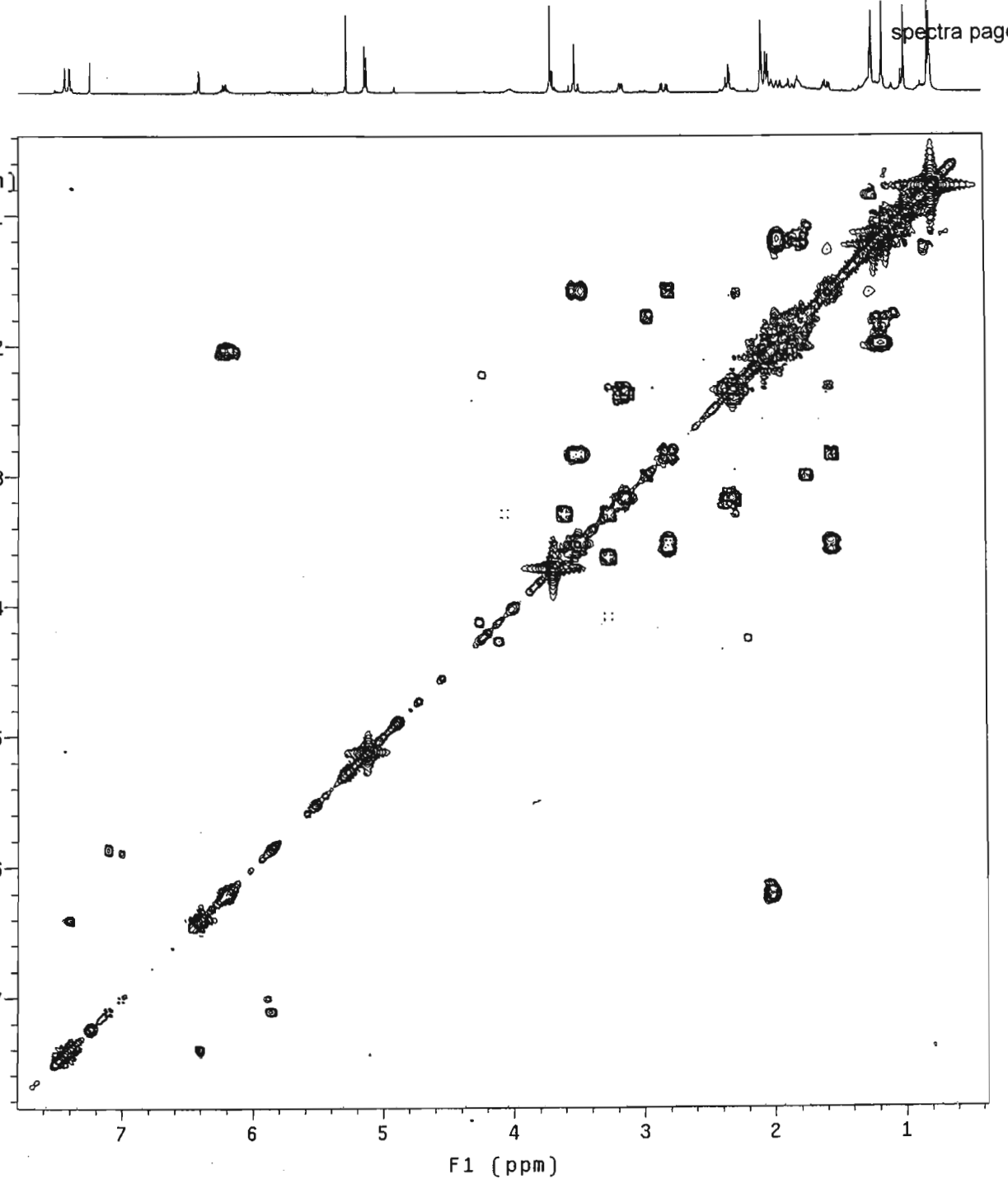
Spectrum QP 8.6: Expanded HMBC Spectrum of 3-detigloyl-3-angeloylruageanin B QP 8

probe=5mmASW

Pulse Sequence: relayh



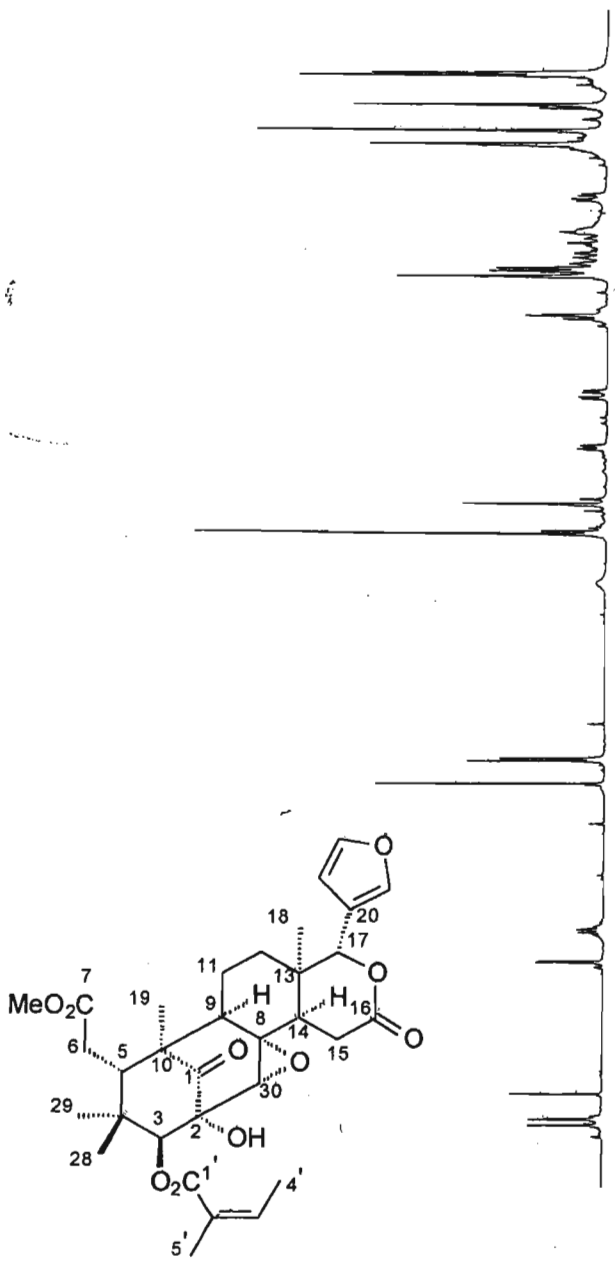
7-59 QP 8



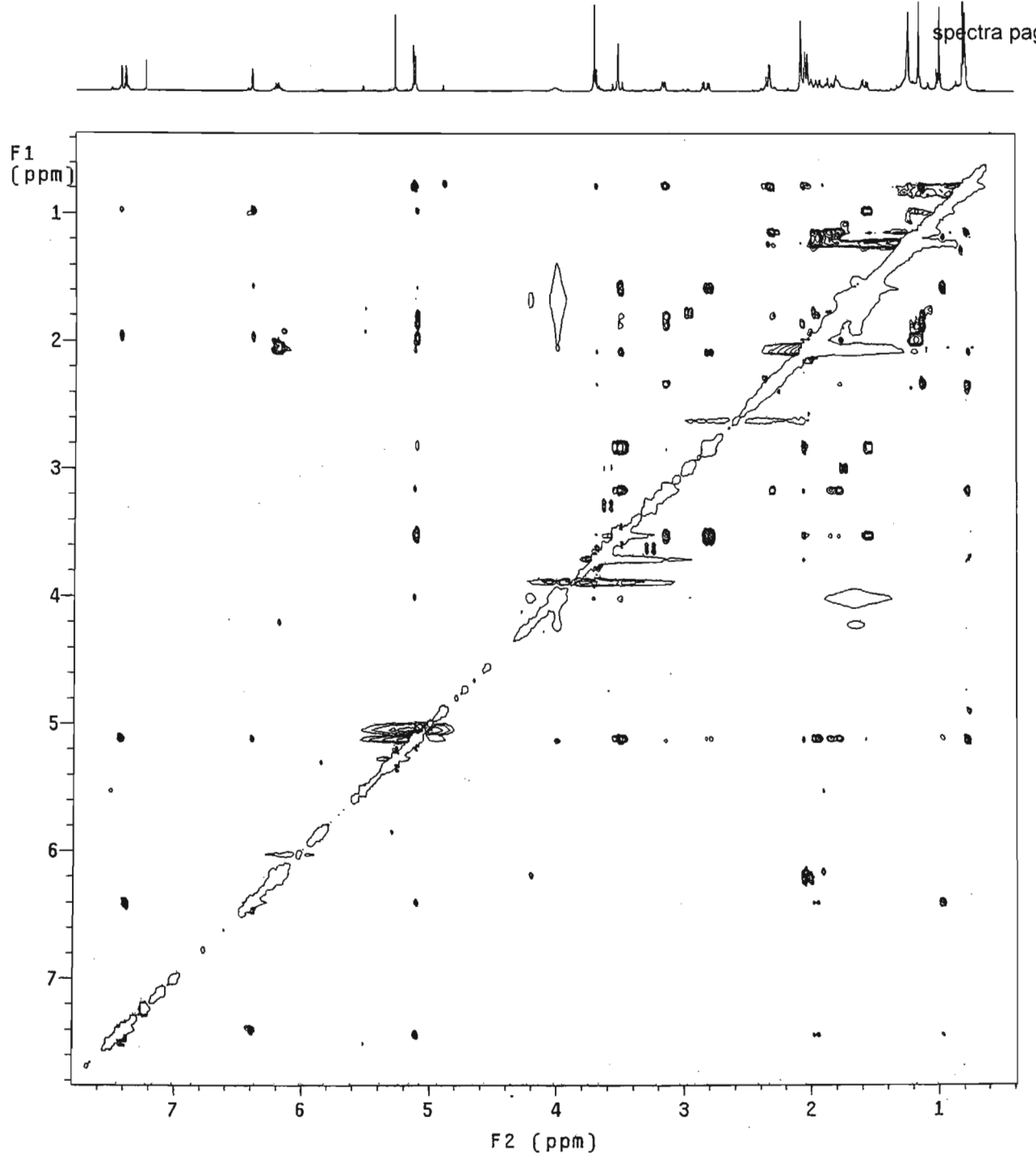
Spectrum QP 8.7: COSY Spectrum of 3-detigloyl-3-angeloylruageanin B QP 8

mix=1sec
probe=5mmASW

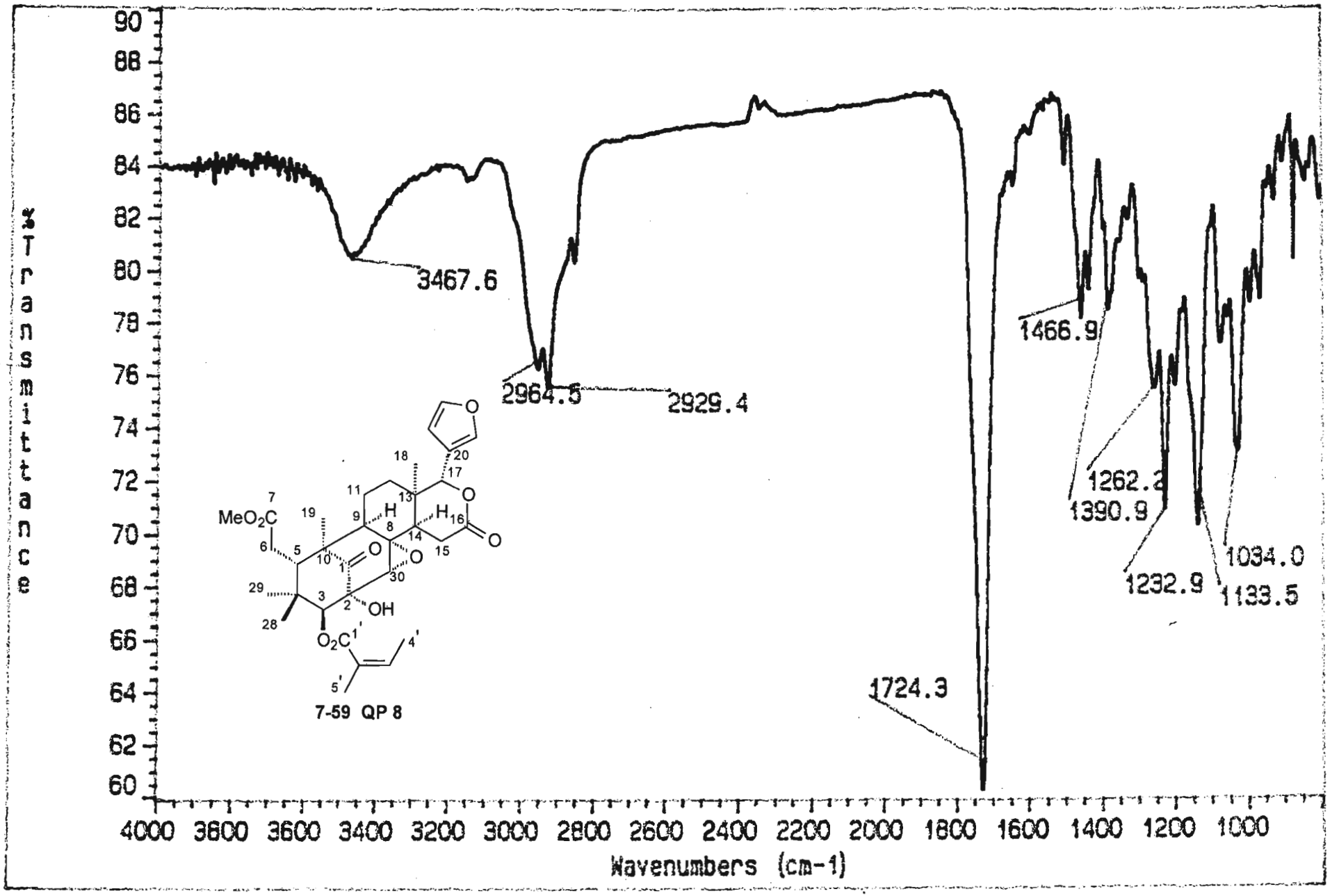
Pulse Sequence: noesy_da



7-59 QP 8



Spectrum QP 8.8: NOESY Spectrum of 3-detigloyl-3-angeloylruageanin B QP 8

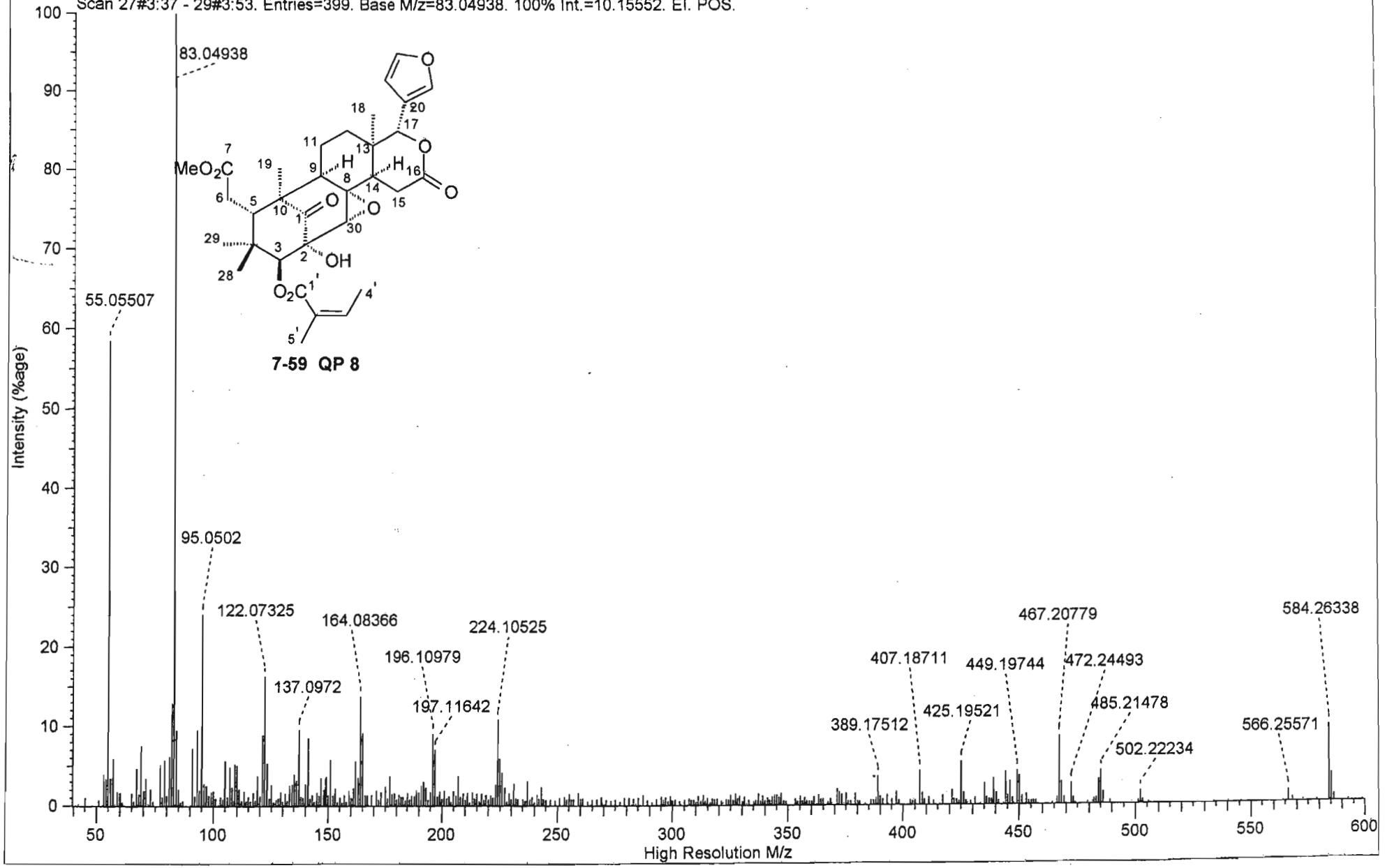


Spectrum QP 8.9: IR Spectrum of 3-detigloyl-3-angeloylruageanin B QP 8

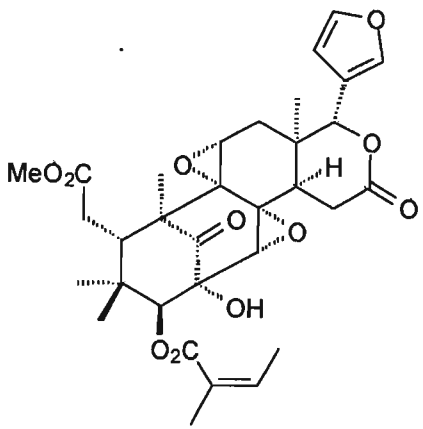
File Name : C:\MASPEC\data\hc112801.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPK 14c-1
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

Some Background.

SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Int:0.4%. Range:0-590. Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 27#3:37 - 29#3:53. Entries=399. Base M/z=83.04938. 100% Int.=10.15552. EI. POS.



Spectrum QP 8.10: High Resolution Mass Spectrum of 3-detigloyl-3-angeloylrugeanin B QP 8



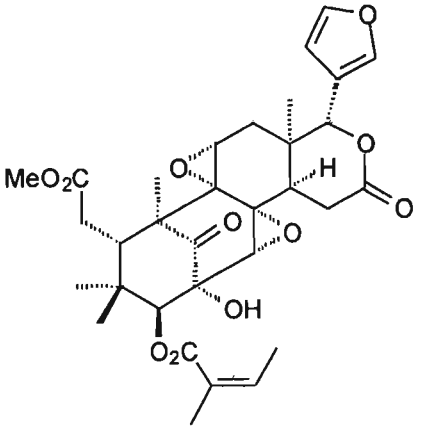
7-78 quivisianolide A **QP 9**

Spectrum QP 9.1: ^{1}H NMR Spectrum of quivisianolide A QP 9

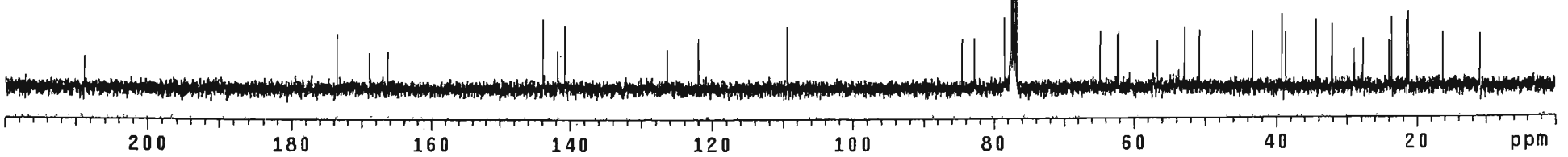
probe=5mmASW

Pulse Sequence: s2pul

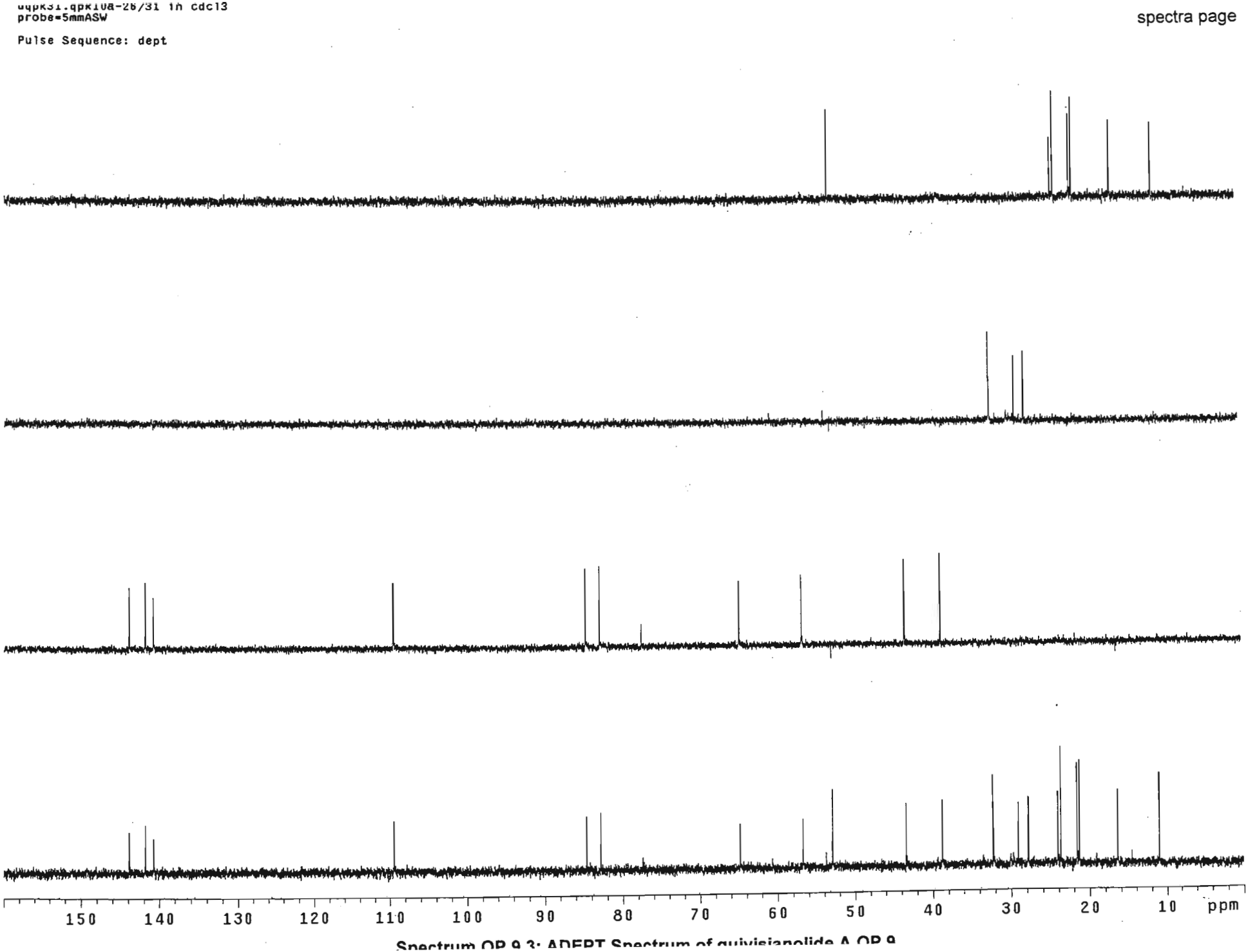
INDEX	FREQUENCY	PPM	HEIGHT
1	21005.740	208.873	5.1
2	17456.415	173.580	8.9
3	16997.790	169.019	5.8
4	16732.787	166.384	6.0
5	14475.563	143.939	11.3
6	14265.698	141.852	6.1
7	14163.116	140.832	10.3
8	12714.150	126.424	6.4
9	12267.493	121.983	8.1
10	11007.448	109.454	10.0
11	8507.020	84.590	7.9
12	8328.357	82.814	8.0
13	7893.667	78.492	11.5
14	7799.207	77.552	246.3
15	7788.094	77.442	10.4
16	7767.150	77.233	250.0
17	7735.093	76.915	242.6
18	6516.508	64.798	9.1
19	6270.312	62.350	8.5
20	6244.667	62.095	9.2
21	5697.137	56.650	7.4
22	5316.730	52.867	9.6
23	5103.446	50.747	9.1
24	4354.600	43.300	9.1
25	3945.128	39.229	11.8
26	3887.426	38.655	8.8
27	3454.018	34.345	10.9
28	3231.758	32.135	10.3
29	2913.328	28.969	6.2
30	2787.238	27.715	7.8
31	2410.250	23.967	7.4
32	2370.927	23.576	11.1
33	2161.917	21.497	10.7
34	2131.143	21.191	12.1
35	1637.468	16.282	8.7
36	1092.076	10.859	8.5



7-78 quivisianolide A **QP 9**



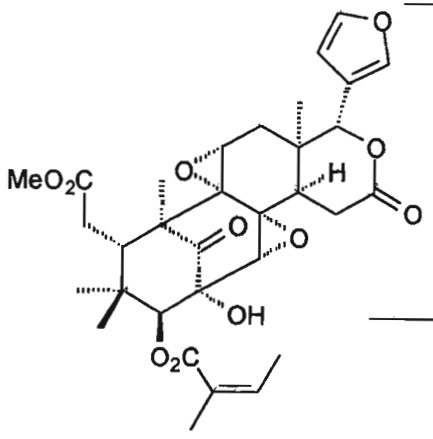
Spectrum QP 9.2: ^{13}C NMR Spectrum of quivisianolide A QP 9



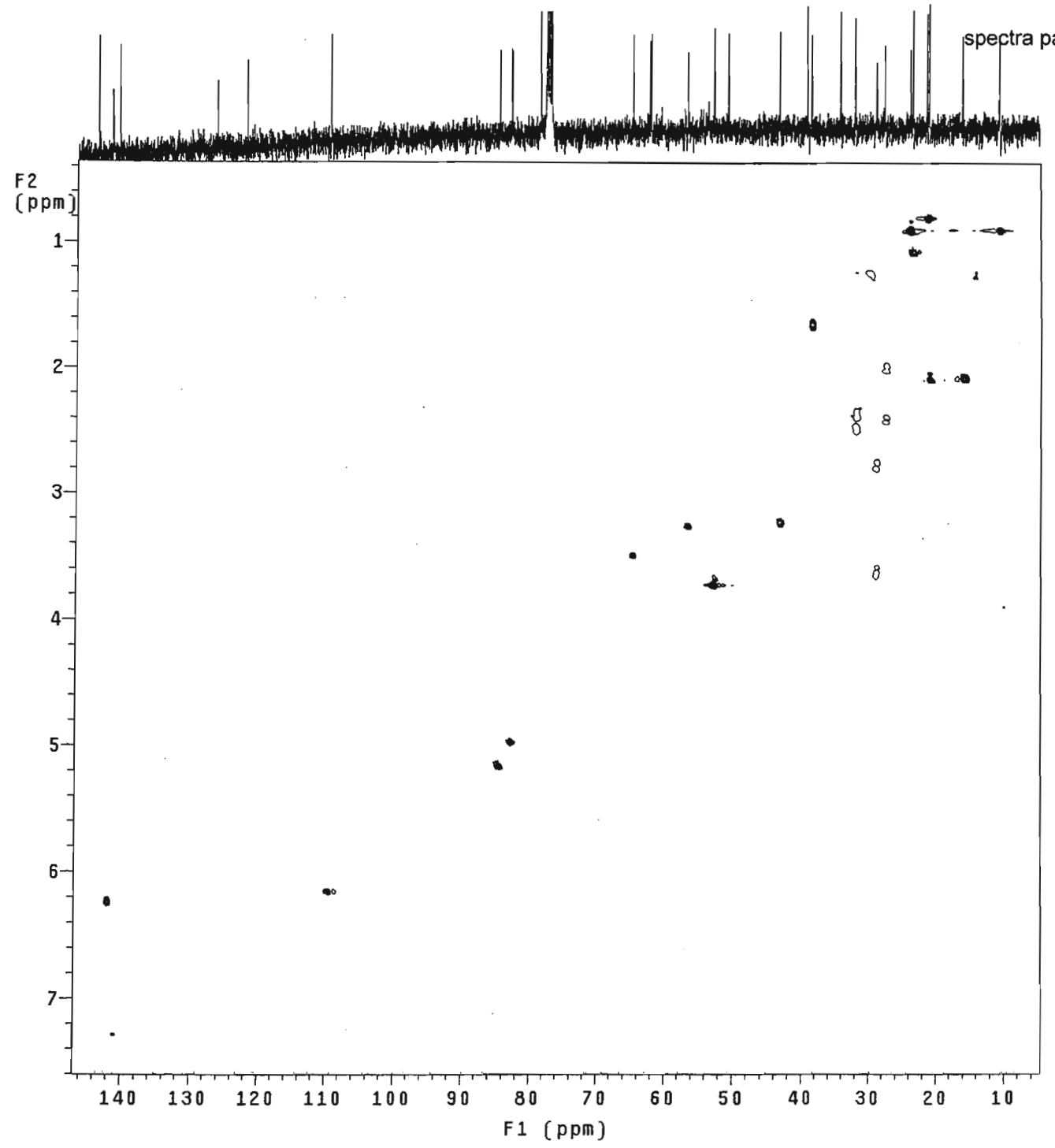
Spectrum OP 9.3: ADEPT Spectrum of quivisianolide A OP 9

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da



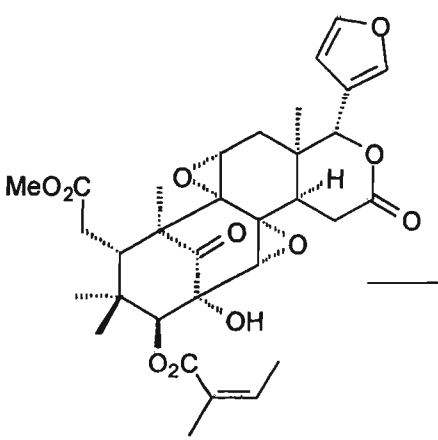
7-78 quivisianolide A **QP 9**



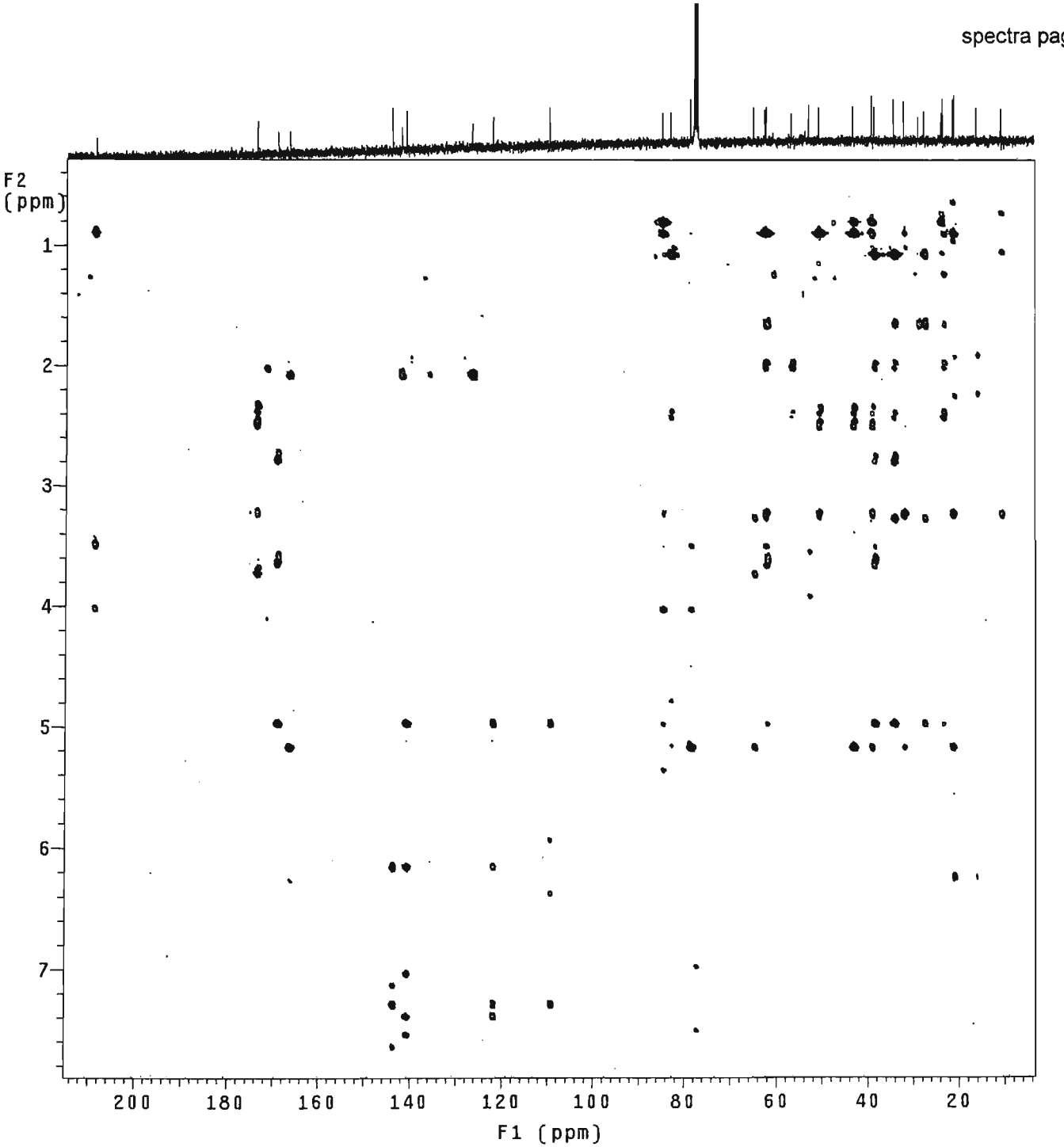
Spectrum QP 9.4: HSQC Spectrum of quivisianolide A QP 9

probe=5mmASW

Pulse Sequence: ghmqc_da



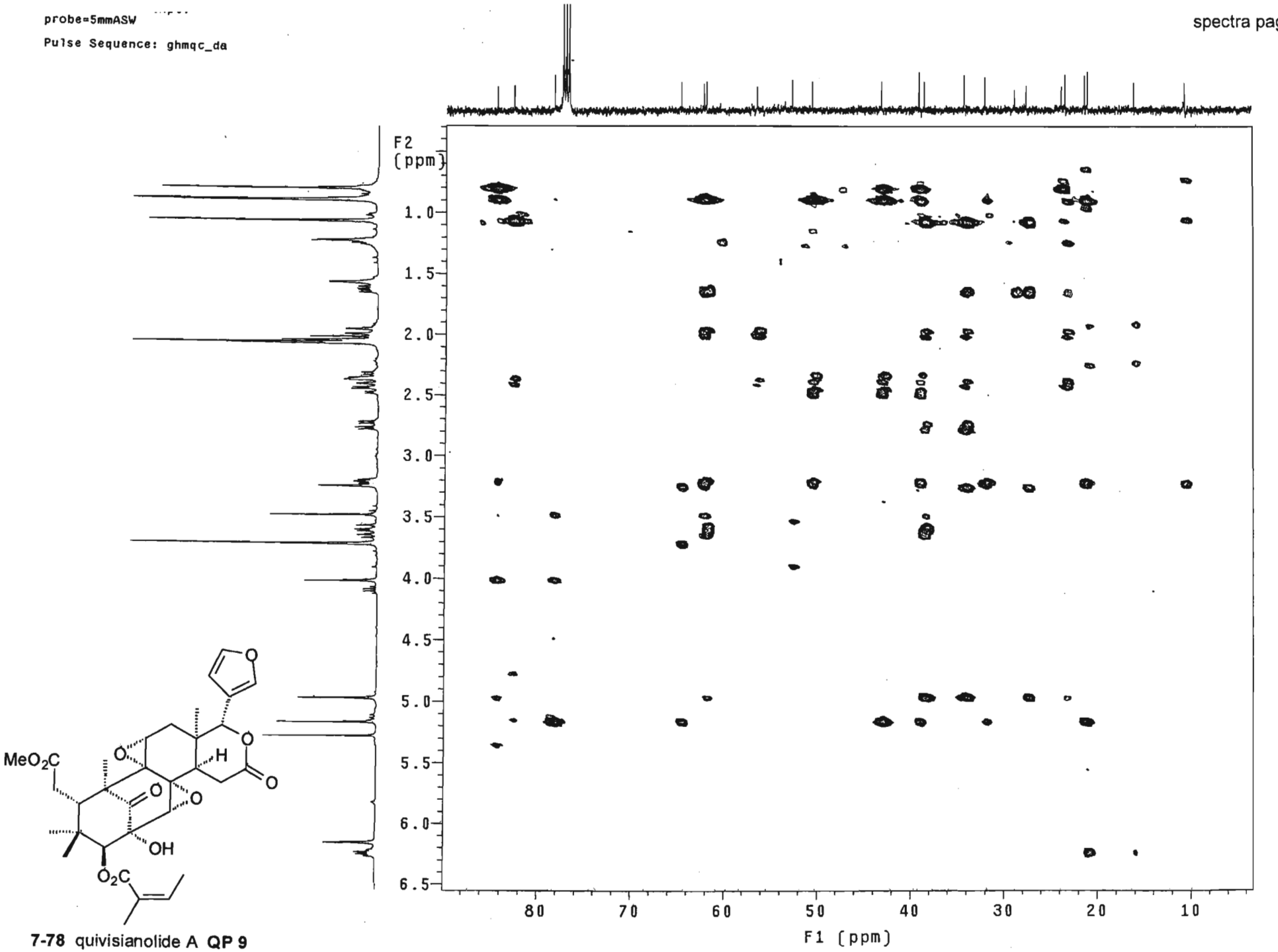
7-78 quivisianolide A **QP 9**



Spectrum QP 9.5: HMBC Spectrum of quivisianolide A QP 9

probe=5mmASW

Pulse Sequence: ghmqc_da

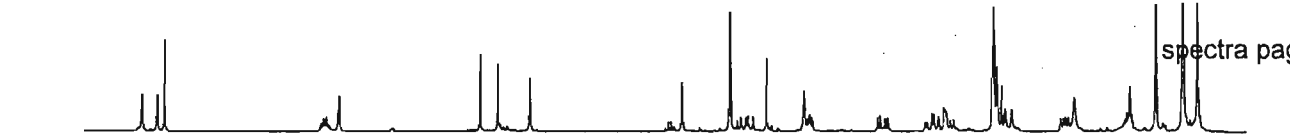


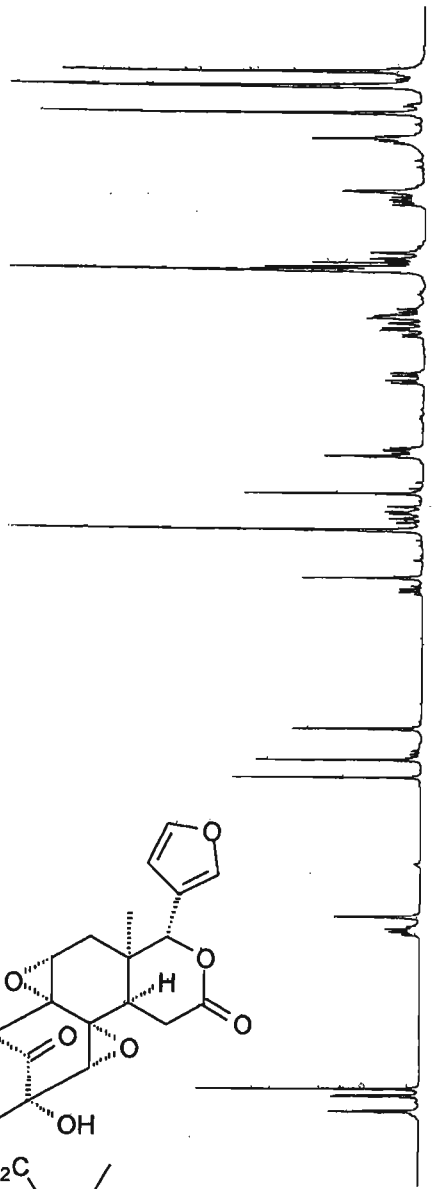
7-78 quivisianolide A **QP 9**

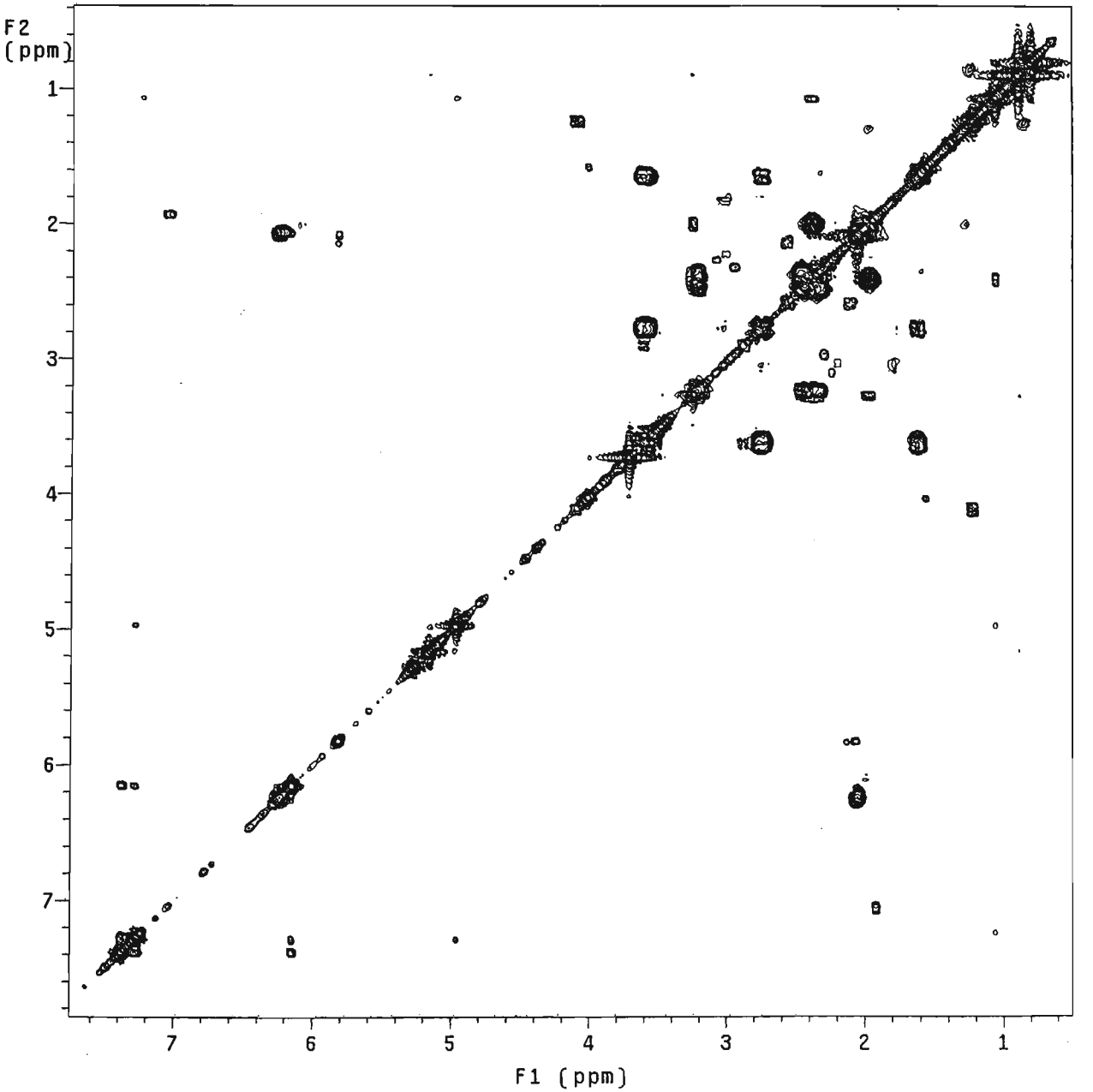
Spectrum QP 9.6: Expanded HMBC Spectrum of quivisianolide A QP 9

probe=5mmASW

Pulse Sequence: relayh





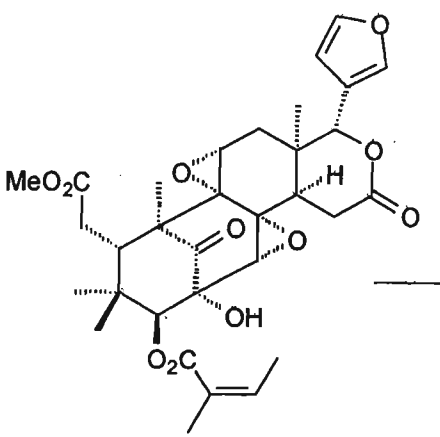


7-78 quivisianolide A **QP 9**

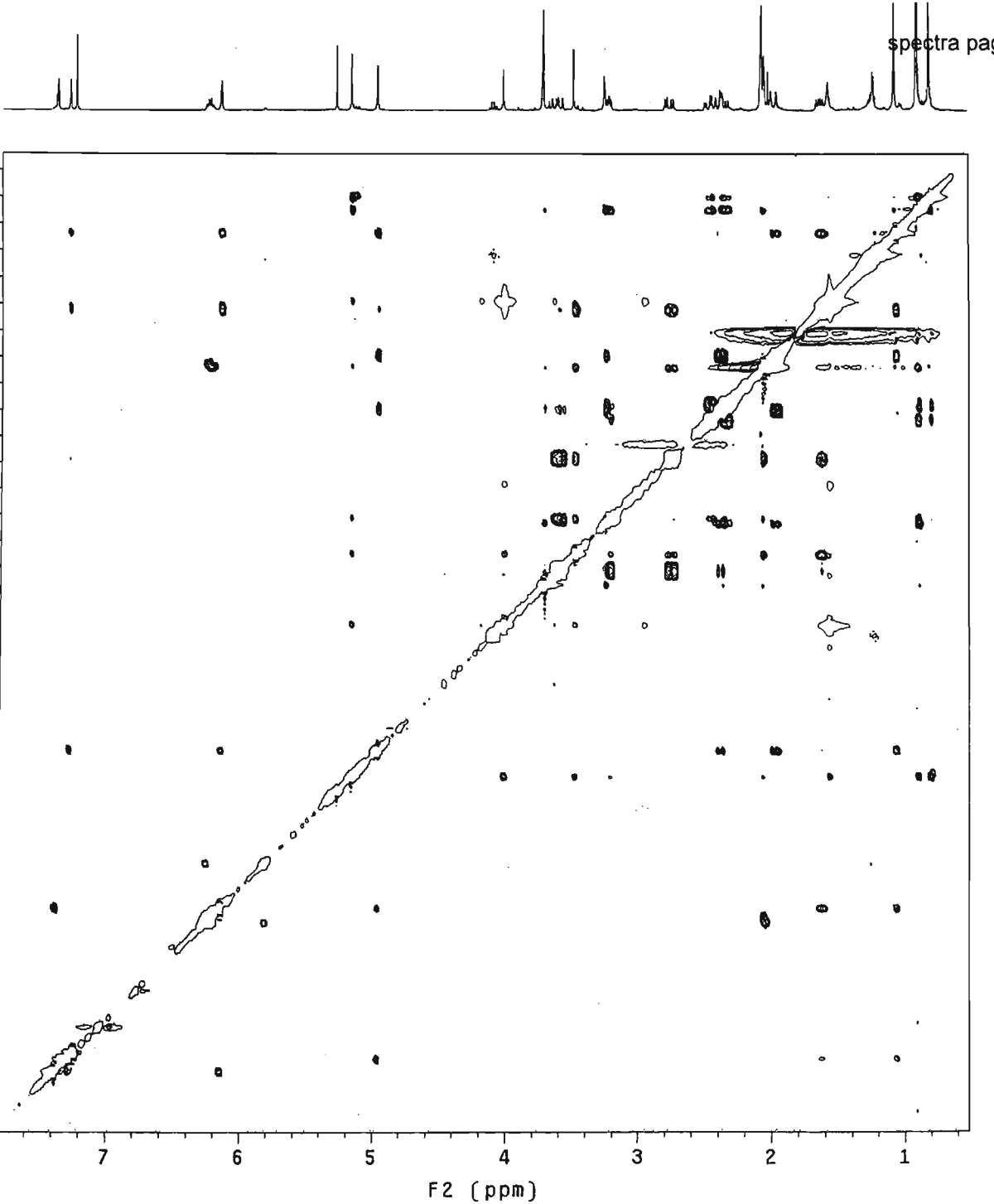
Spectrum QP 9.7: COSY Spectrum of quivisianolide A QP 9

mix=1sec
probe=5mmASW

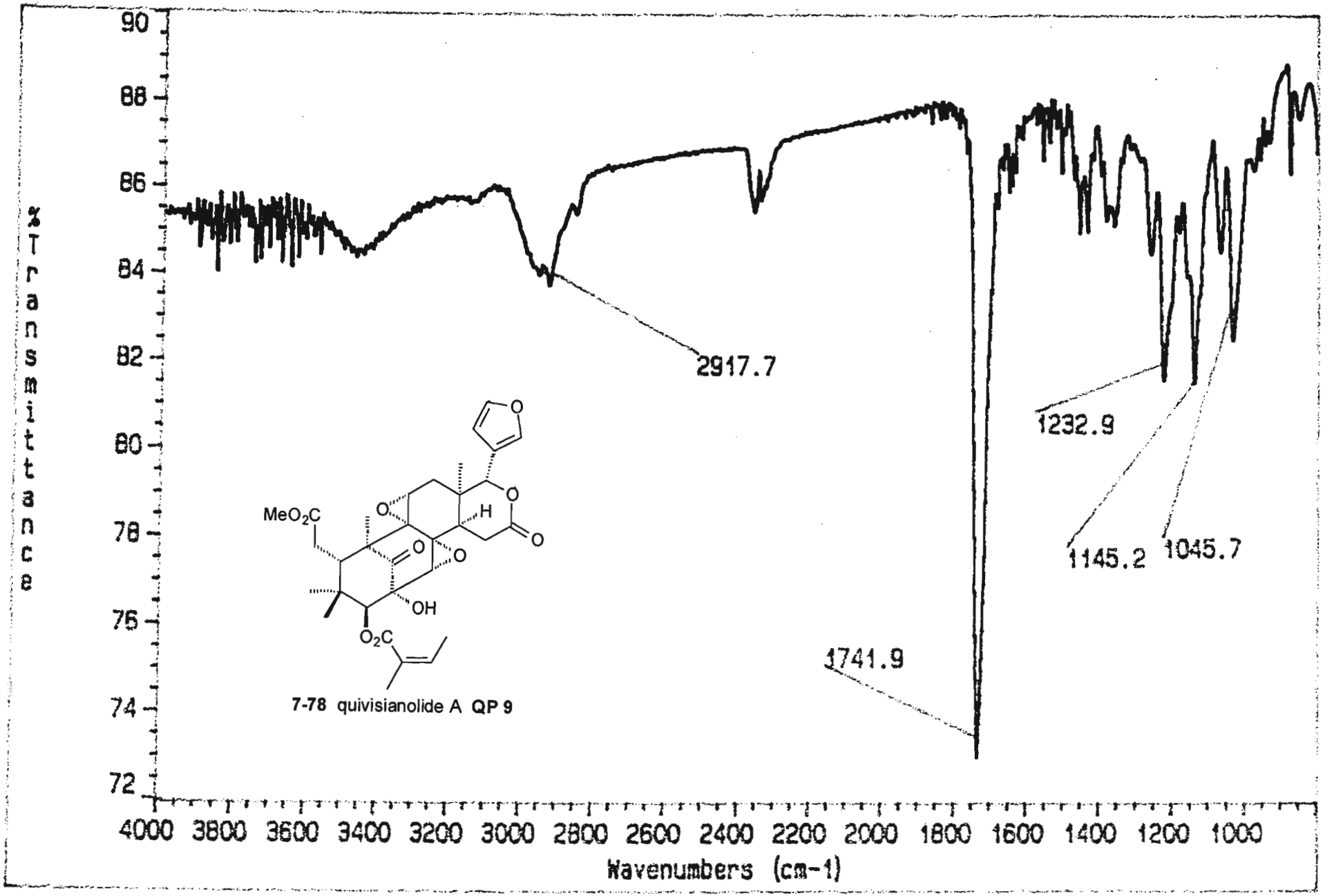
Pulse Sequence: noesy_da



7-78 quivisianolide A **QP 9**



Spectrum QP 9.8: NOESY Spectrum of quivisianolide A QP 9



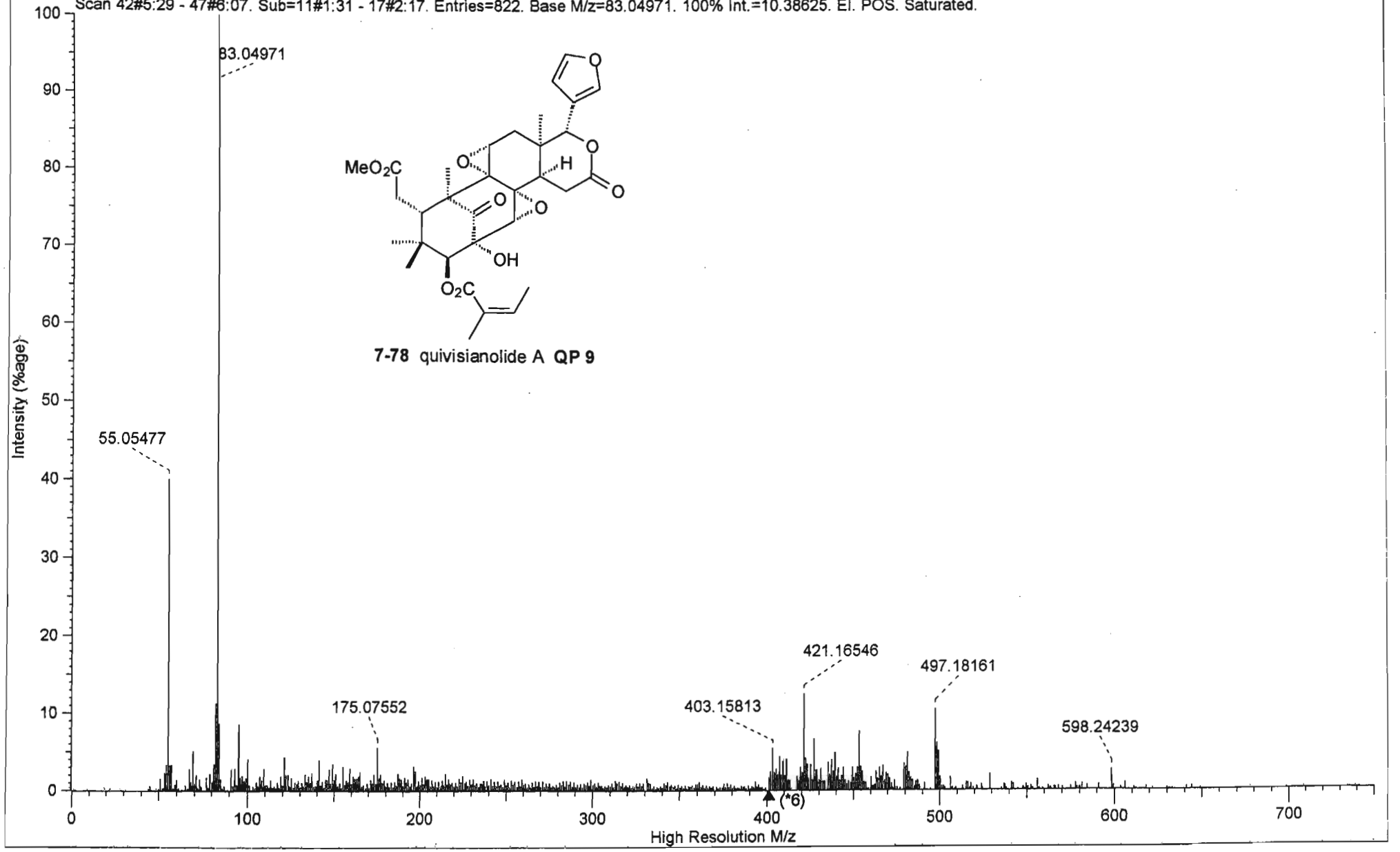
7-78 quivisianolide A **QP 9**

Spectrum QP 9.9: IR Spectrum of quivisianolide A QP 9

File Name : C:\MASPEC\Data\hc091423.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPK10a-26/31
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

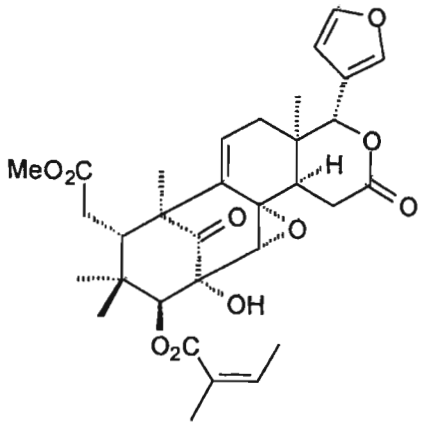
EI

SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 42#5:29 - 47#6:07. Sub=11#1:31 - 17#2:17. Entries=822. Base M/z=83.04971. 100% Int.=10.38625. EI. POS. Saturated.



7-78 quivisianolide A **QP 9**

Spectrum QP 9.10: High Resolution Mass Spectrum of quivisianolide A QP 9

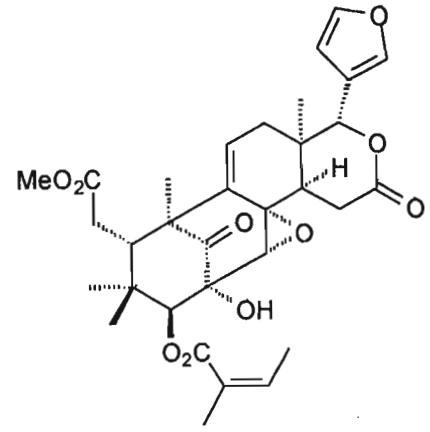


7-82 quivisianolide B **QP 10**

Spectrum QP 10.1: ^{1}H NMR Spectrum of quivisianolide B QP 10

Pulse Sequence: s2pul

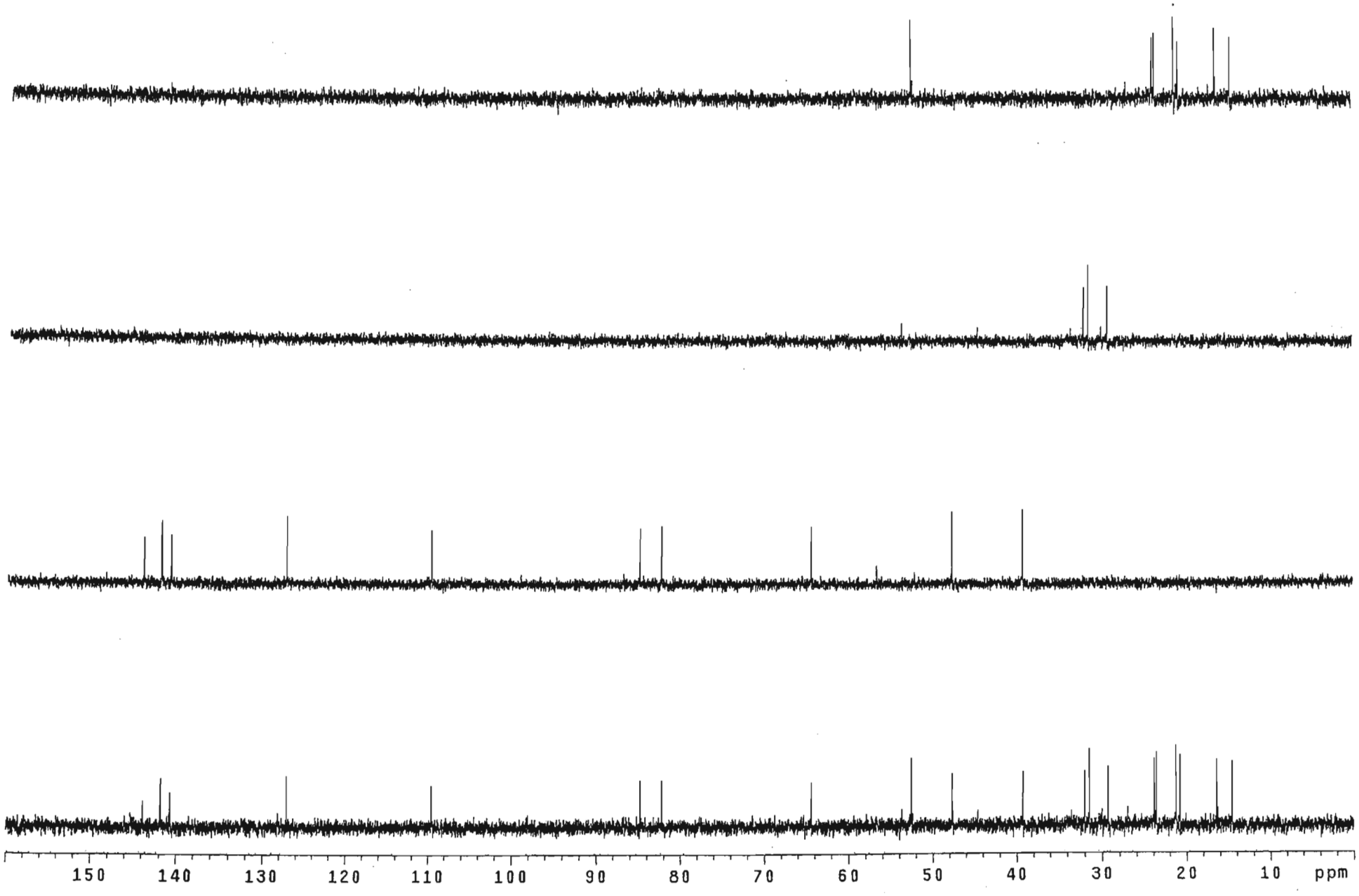
1	21134.733	210.155	7.6
2	17409.994	173.118	9.4
3	17045.582	169.495	11.1
4	16732.993	166.386	6.6
5	14469.194	143.876	14.7
6	14268.479	141.880	12.2
7	14156.606	140.768	18.7
8	13766.693	136.891	11.2
9	12784.507	127.124	15.2
10	12721.989	126.502	9.1
11	12275.316	122.061	11.9
12	11018.382	109.562	14.5
13	8524.254	84.762	12.1
14	8265.135	82.185	14.5
15	7964.885	79.200	18.9
16	7799.543	77.556	183.1
17	7767.461	77.237	197.1
18	7735.380	76.918	200.0
19	6475.977	64.395	14.1
20	6176.550	61.417	11.6
21	5395.079	53.647	6.8
22	5279.915	52.501	14.7
23	5202.590	51.732	19.4
24	4787.999	47.610	15.8
25	3967.866	39.455	18.8
26	3939.897	39.177	12.6
27	3561.500	35.414	13.8
28	3212.718	31.946	13.2
29	3155.958	31.382	13.3
30	2939.614	29.230	12.7
31	2392.584	23.791	10.6
32	2362.970	23.496	13.0
33	2126.884	21.149	16.1
34	2081.641	20.699	17.8
35	1637.436	16.282	16.3
36	1453.173	14.450	12.7



7-82 quivisianolide B **QP 10**

Spectrum QP 10.2: ^{13}C NMR Spectrum of quivisianolide B QP 10

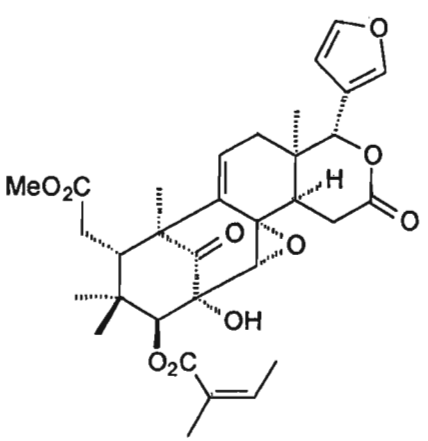
Pulse Sequence: dept



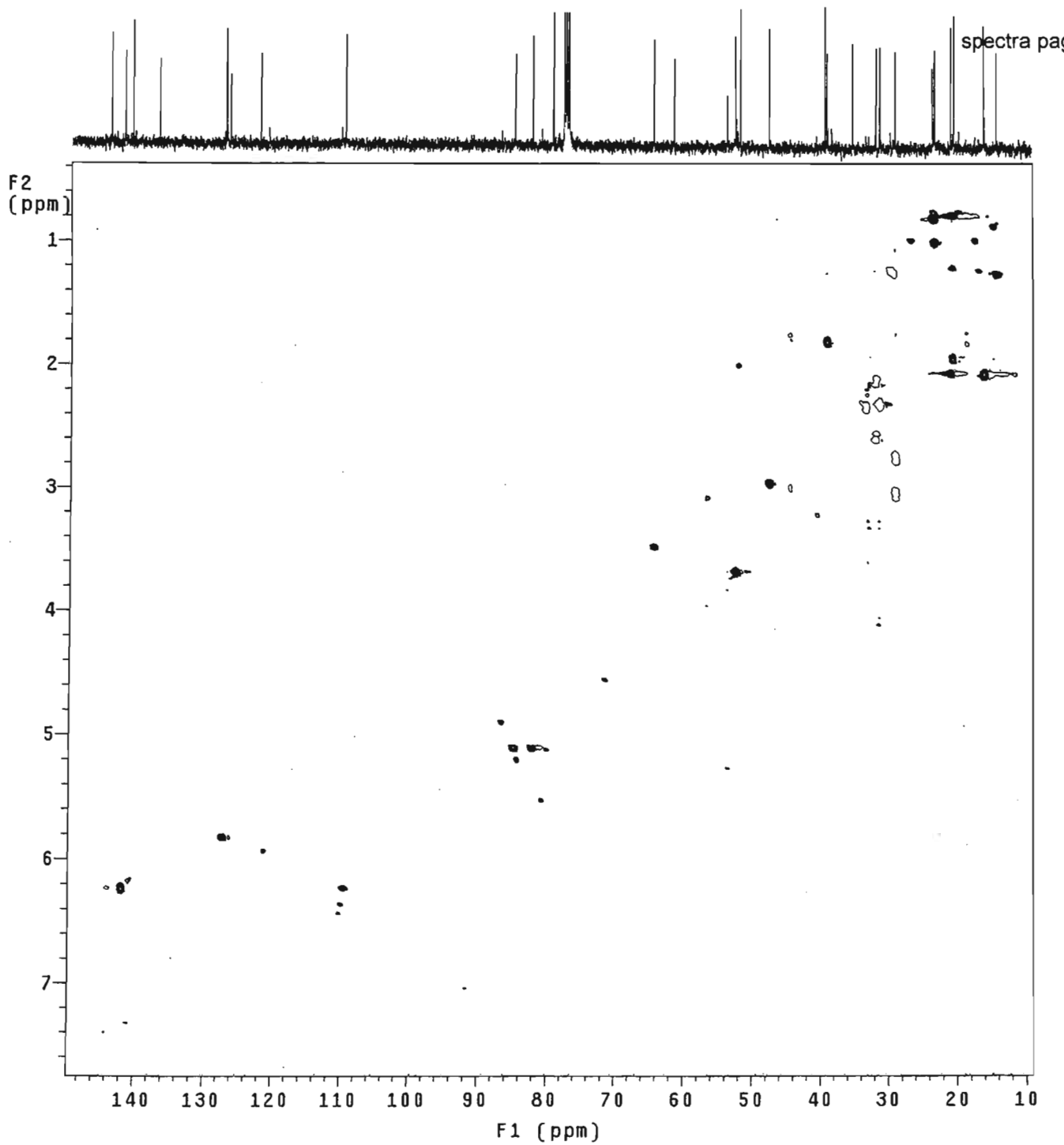
Spectrum QP 10.3: ADEPT Spectrum of quivisianolide B QP 10

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da

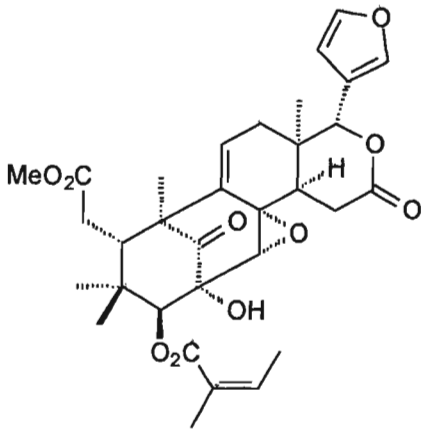


7-82 quivisianolide B **QP 10**

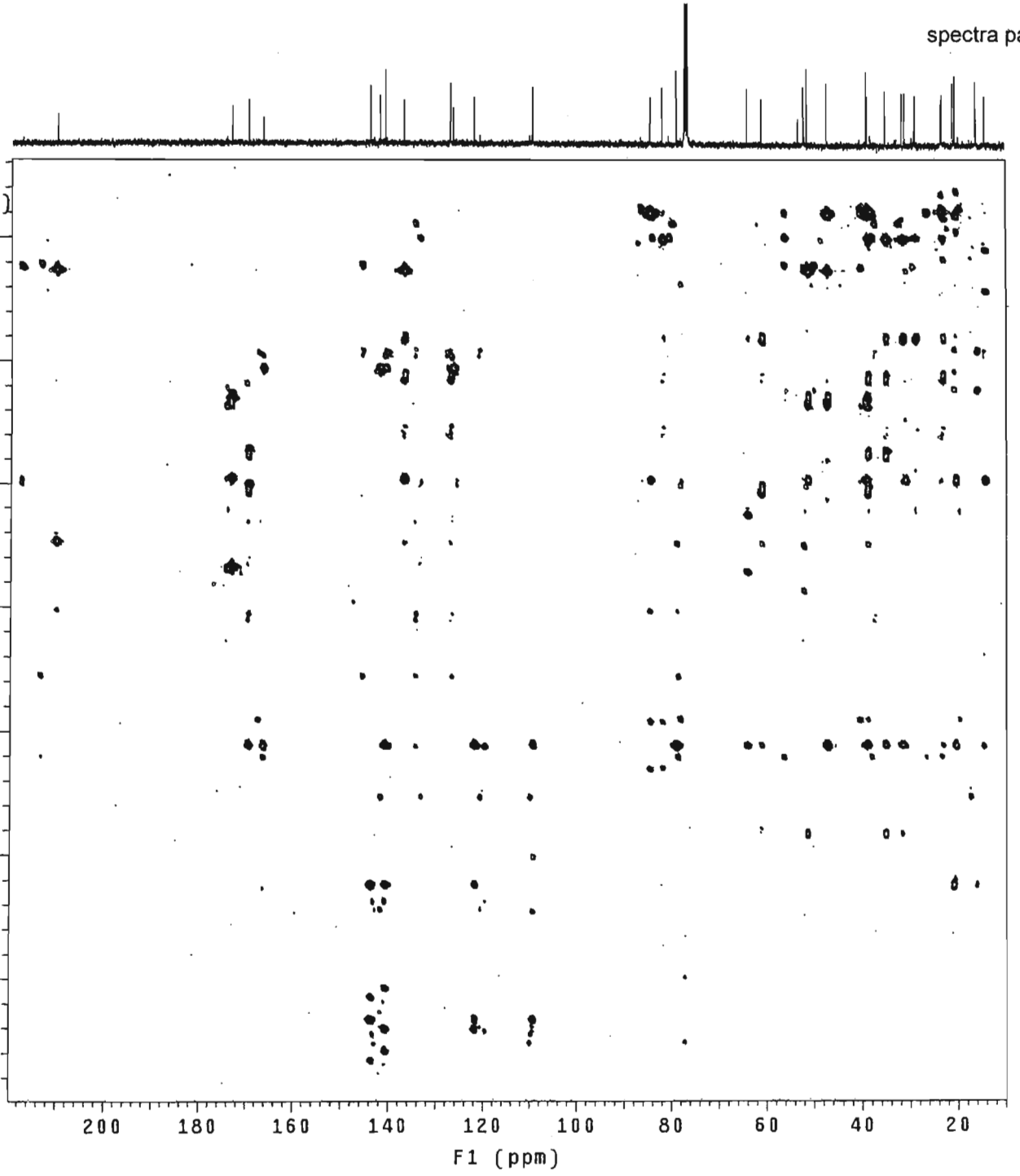


Spectrum QP 10.4: HSQC Spectrum of quivisianolide B QP 10

Pulse Sequence: ghmqc_da



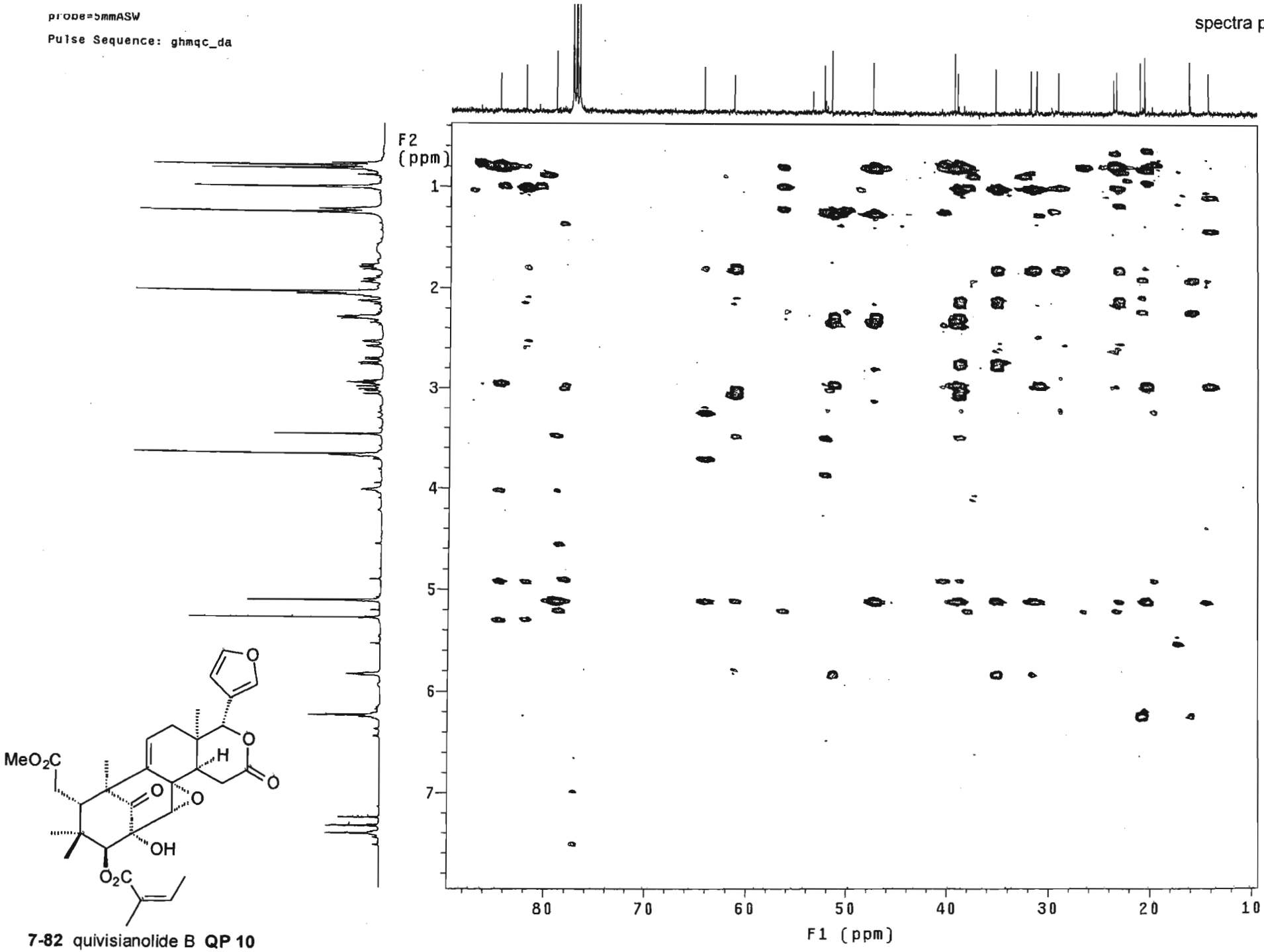
7-82 quivisianolide B **QP 10**



Spectrum QP 10.5: HMBC Spectrum of quivisianolide B QP 10

probe=5mmASW

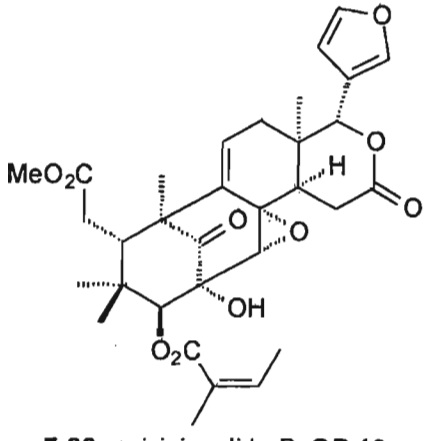
Pulse Sequence: ghmqc_da



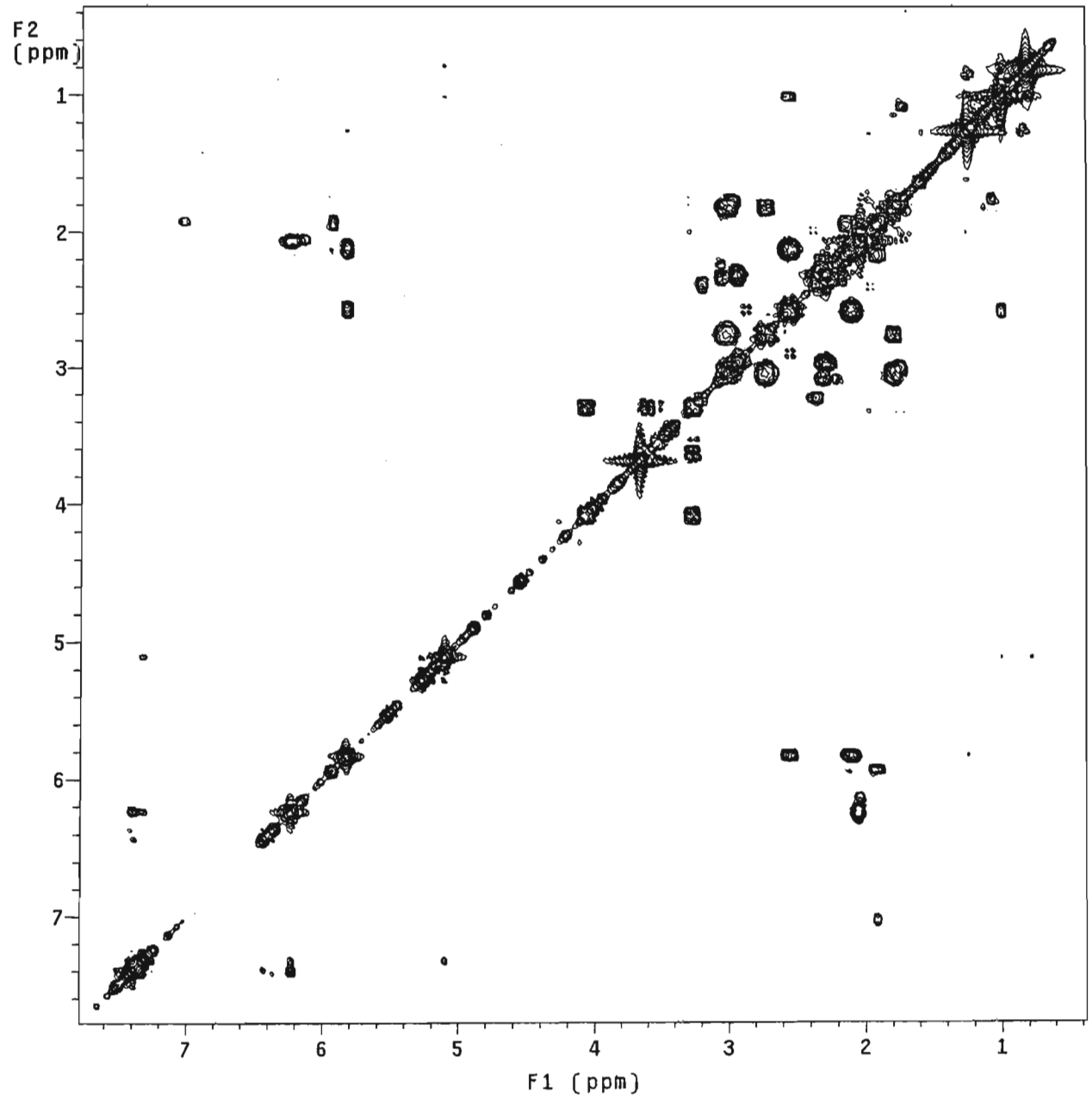
7-82 quivisianolide B **QP 10**

Spectrum QP 10.6: Expanded HMBC Spectrum of quivisianolide B QP 10

Pulse Sequence: relayh



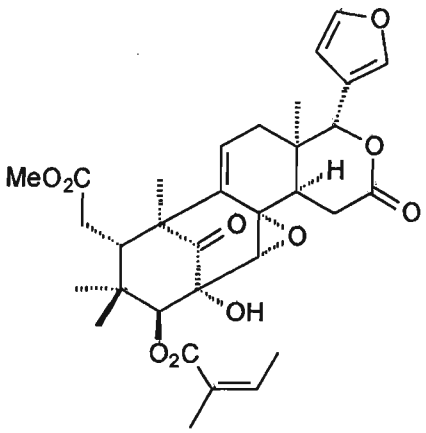
7-82 quivisianolide B **QP 10**



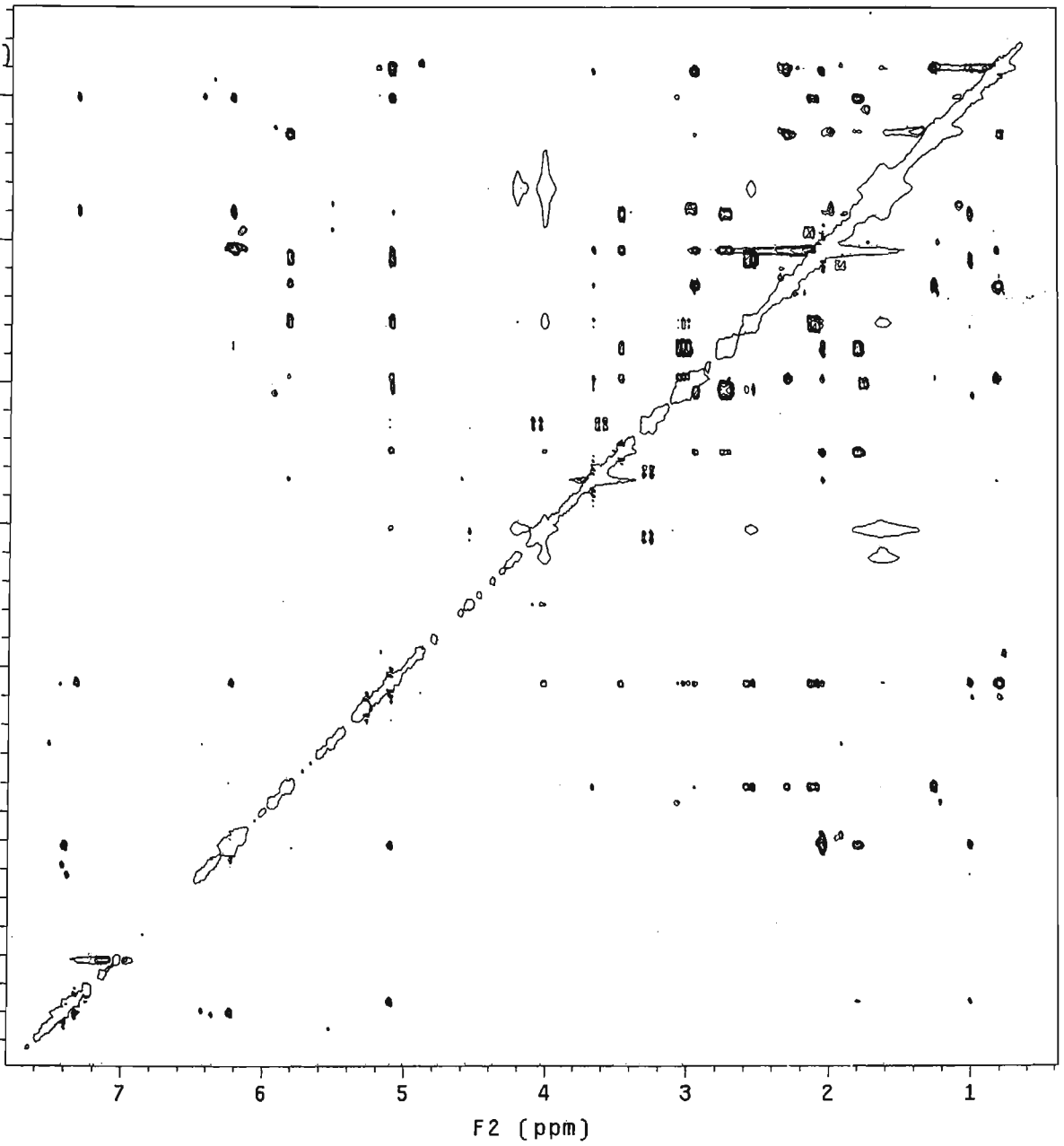
Spectrum QP 10.7: COSY Spectrum of quivisianolide B QP 10

probe=5mmASW

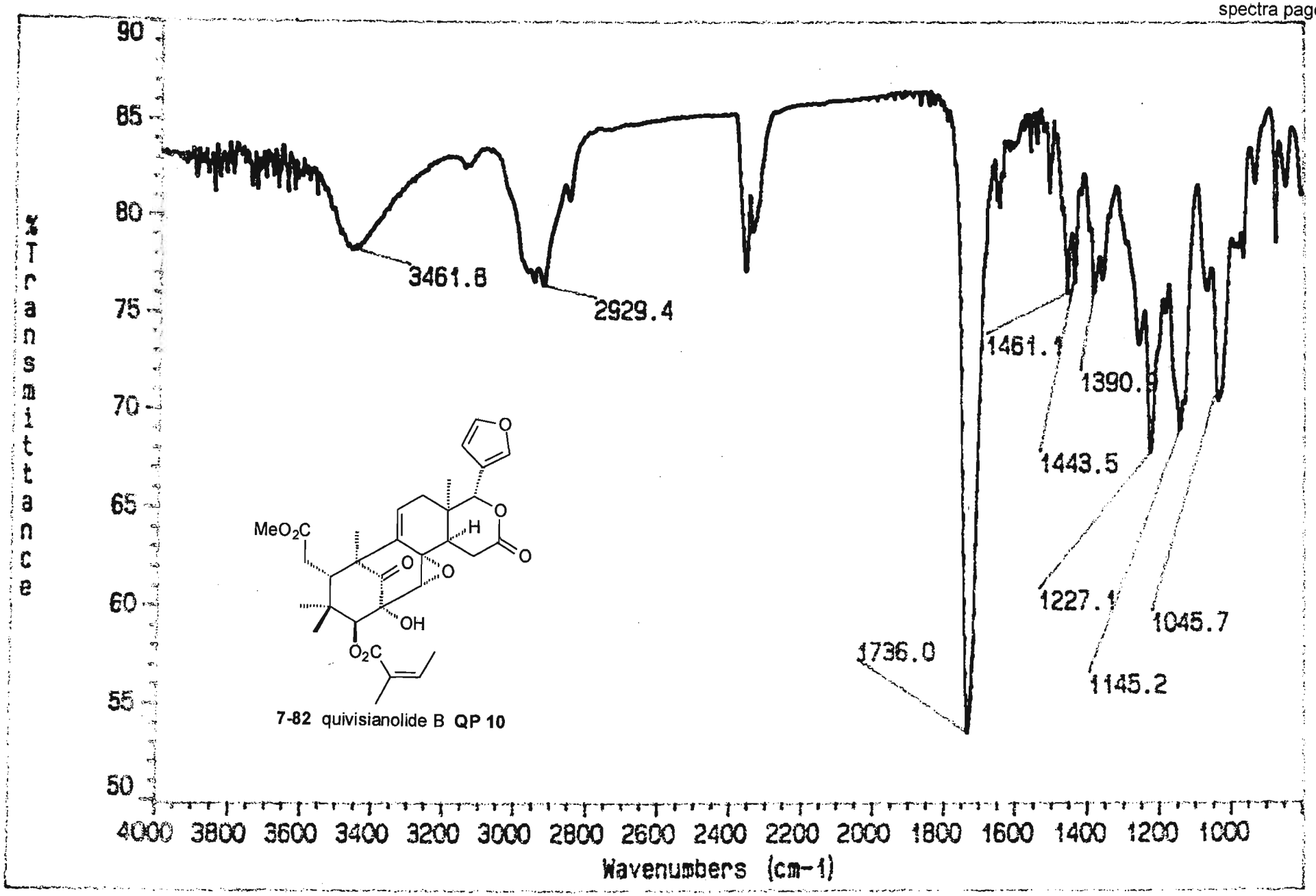
Pulse Sequence: noesy_da



7-82 quivisianolide B **QP 10**



Spectrum QP 10.8: NOESY Spectrum of quivisianolide B QP 10

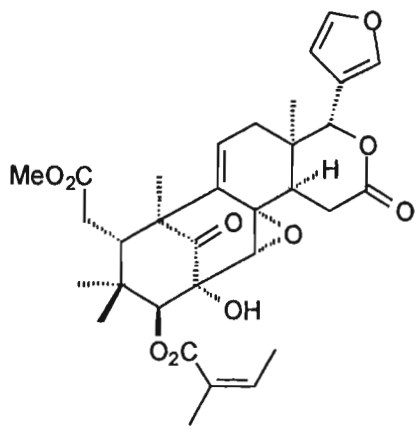


7-82 quivisianolide B **QP 10**

Spectrum QP 10.9: IR Spectrum of quivisianolide B QP 10

File Name : C:\MASPEC\data\hc112804.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPJ1f-1
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ

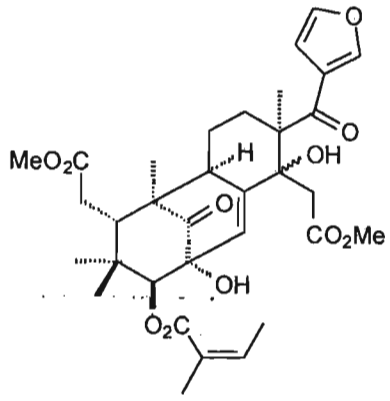
SCAN GRAPH. Flagging=High Resolution M/z. Filter=[Int:0.7%. Range:0-590. Excl: Ref/Ex.].Highlighting=Base Peak.
Scan 53#7:00 - 54#7:08. Sub=7#1:01 - 10#1:24,84#11:02. Entries=525. Base M/z=83.04964. 100% Int.=10.4832. EI. POS. Saturated.



7-82 quivisianolide B **QP 10**

Spectrum QP 10.10: High Resolution Mass Spectrum of quivisianolide B QP 10

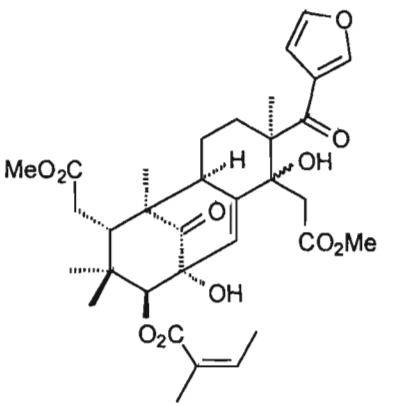
Pulse Sequence: s2pul



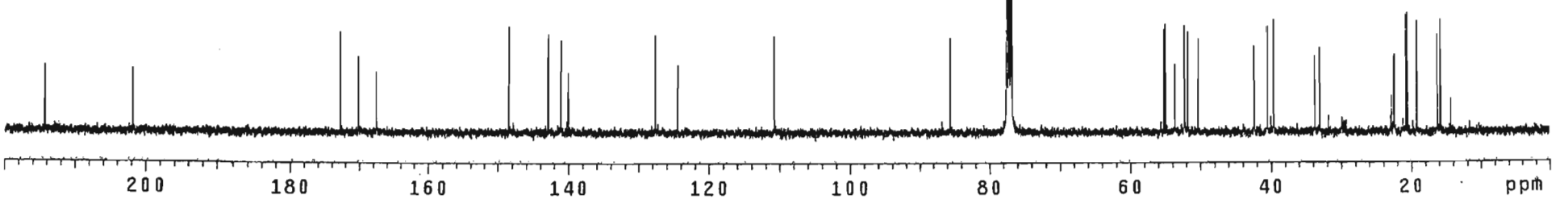
7-85 quivisianone **QP 11**

Spectrum QP 11.1: ^{1}H NMR Spectrum of quivisianone QP 11

Pulse Sequence: s2pul

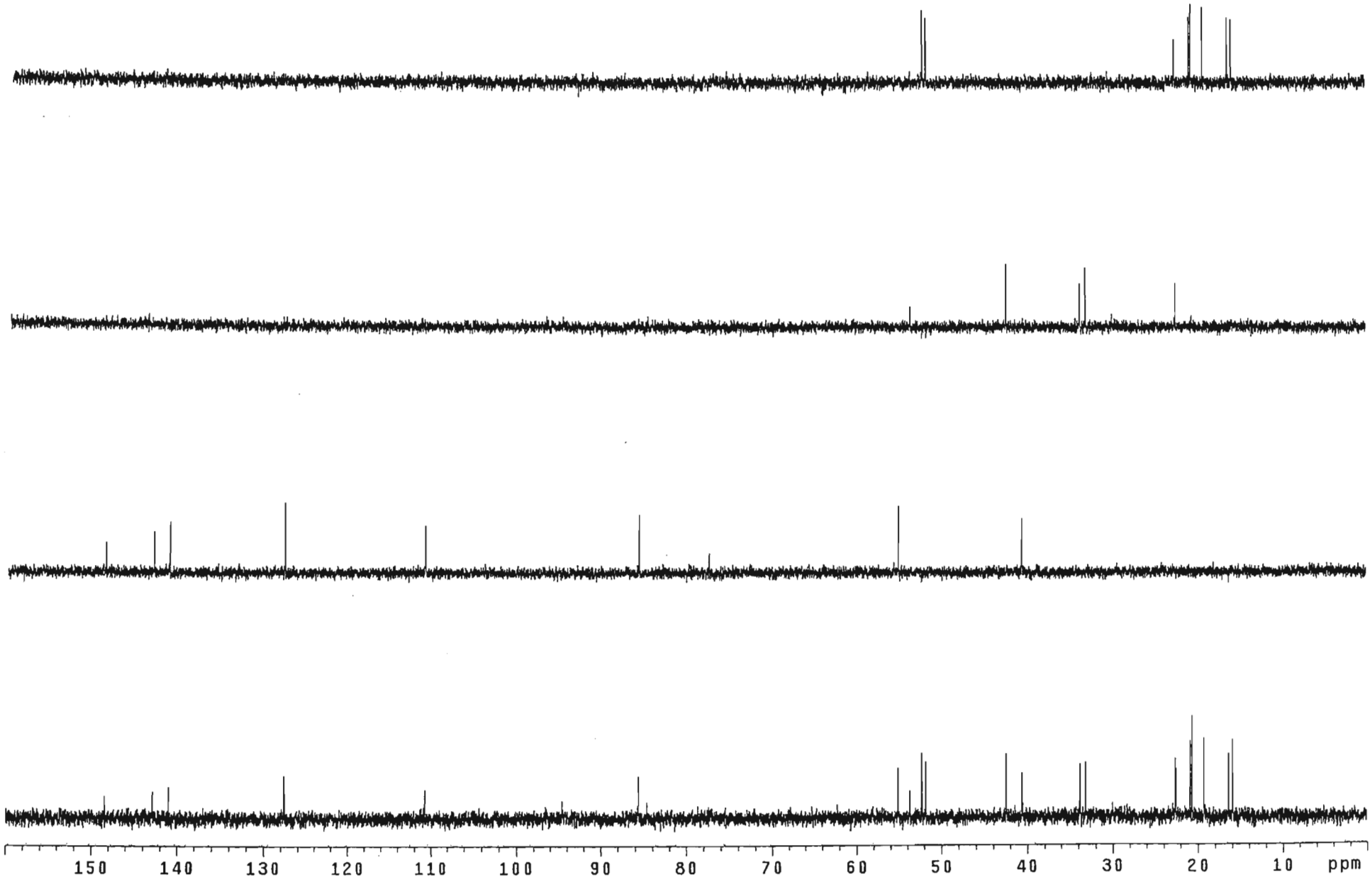


7-85 quivisianone **QP 11**



Spectrum QP 11.2: ^{13}C NMR Spectrum of quivisianone QP 11

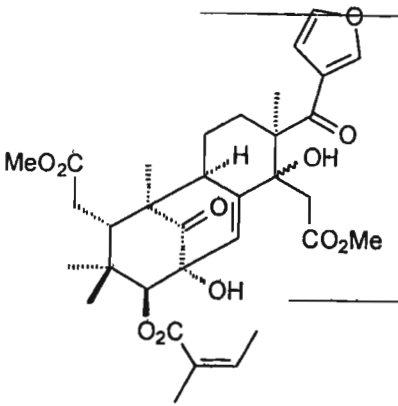
Pulse Sequence: dept



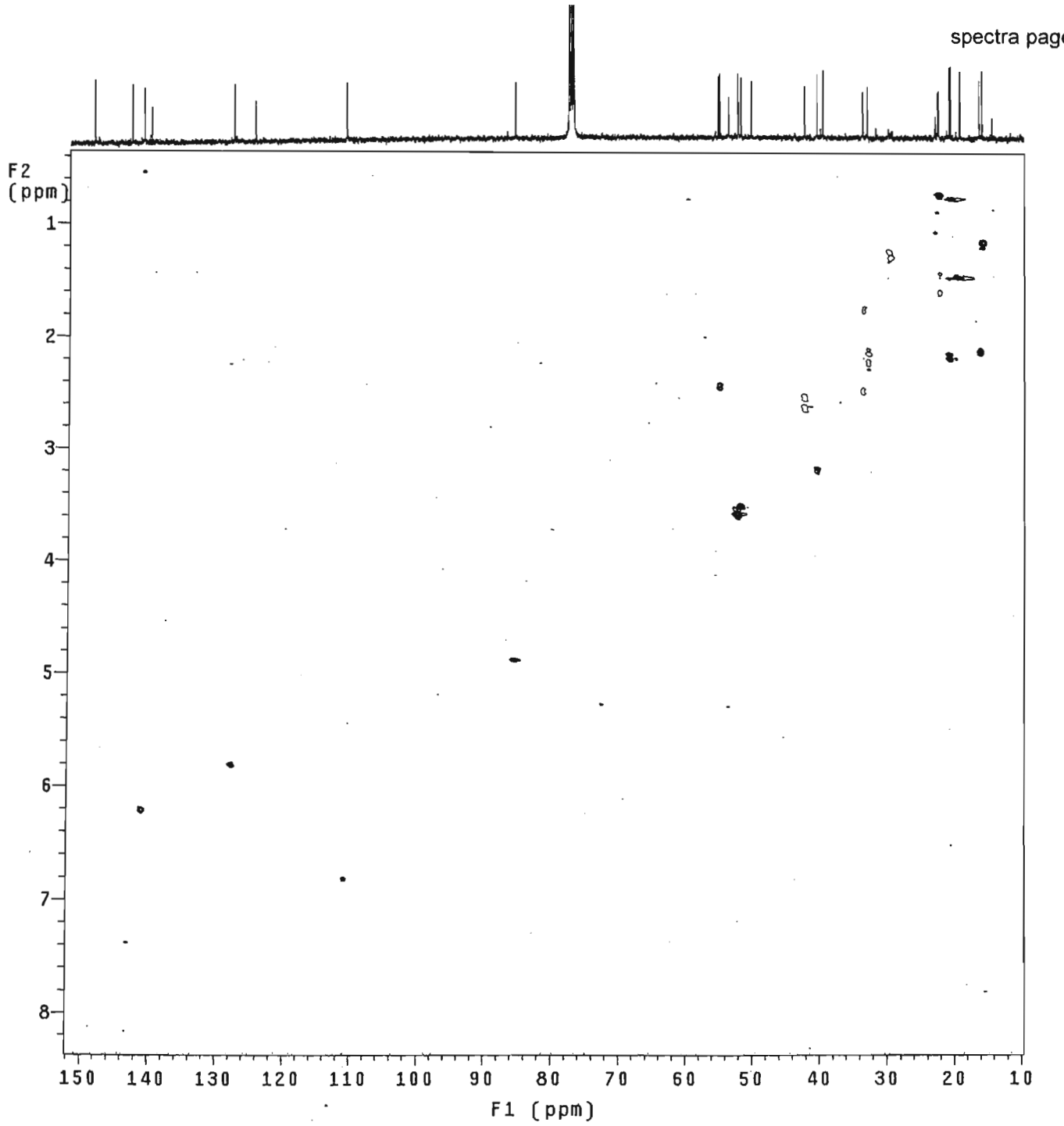
Spectrum QP 11.3: ADEPT Spectrum of quivisianone QP 11

with mult.editing
probe=5mmASW

Pulse Sequence: ghsqc_da



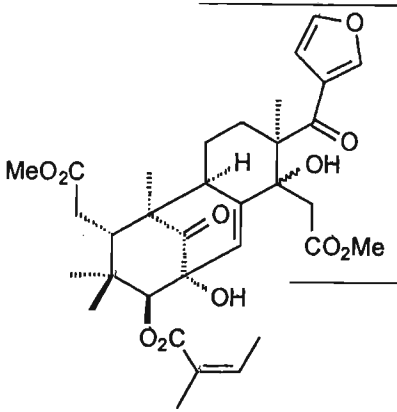
7-85 quivisianone **QP 11**



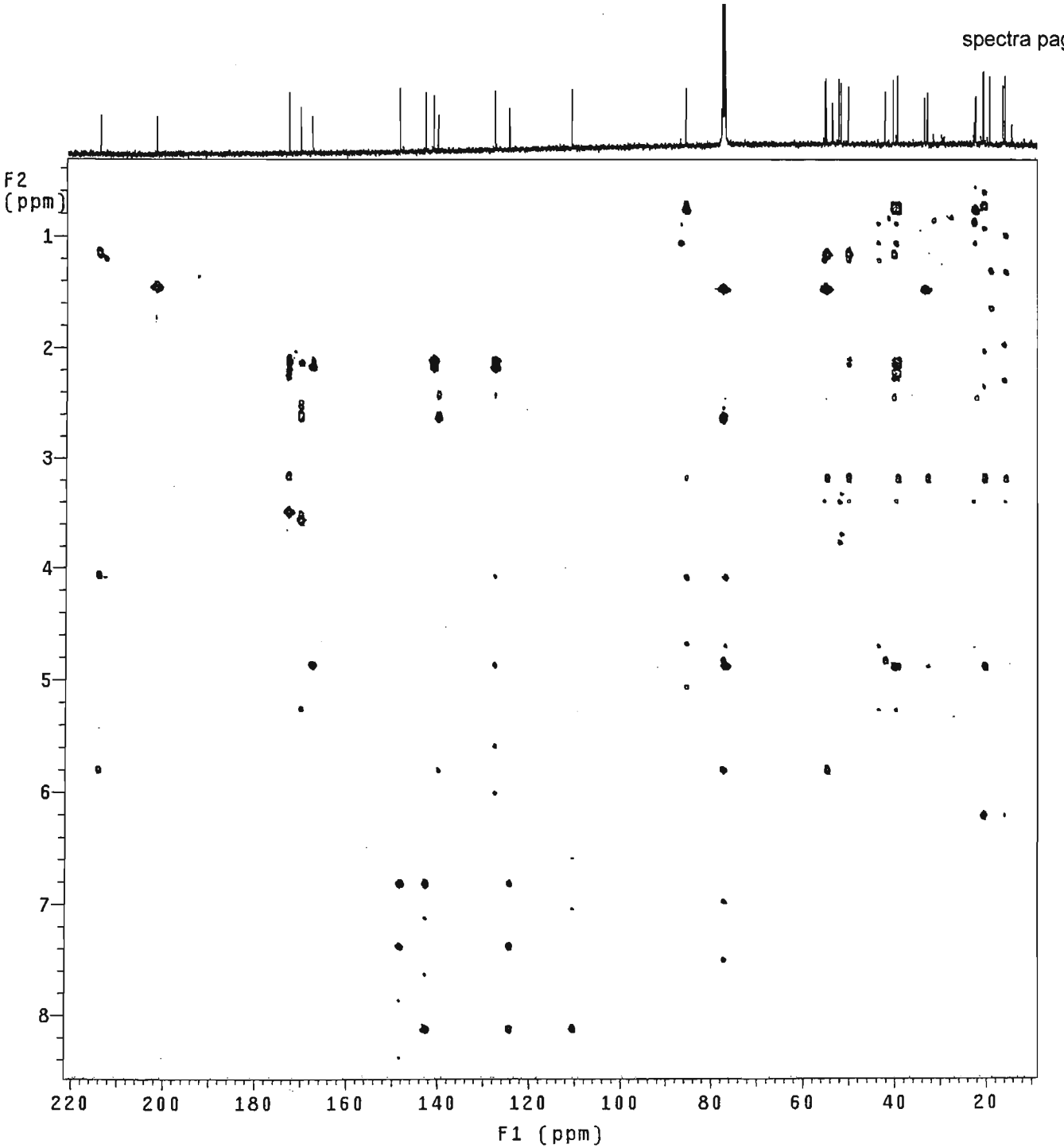
Spectrum QP 11.4: HSQC Spectrum of quivisianone QP 11

probe=5mmASW

Pulse Sequence: ghmqc_da



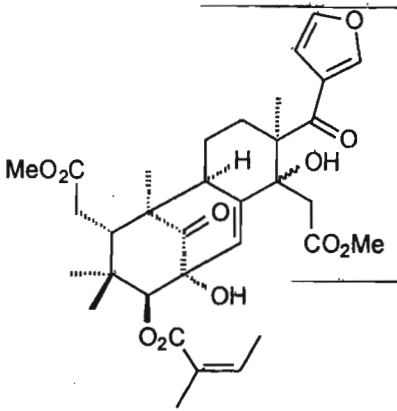
7-85 quivisianone **QP 11**



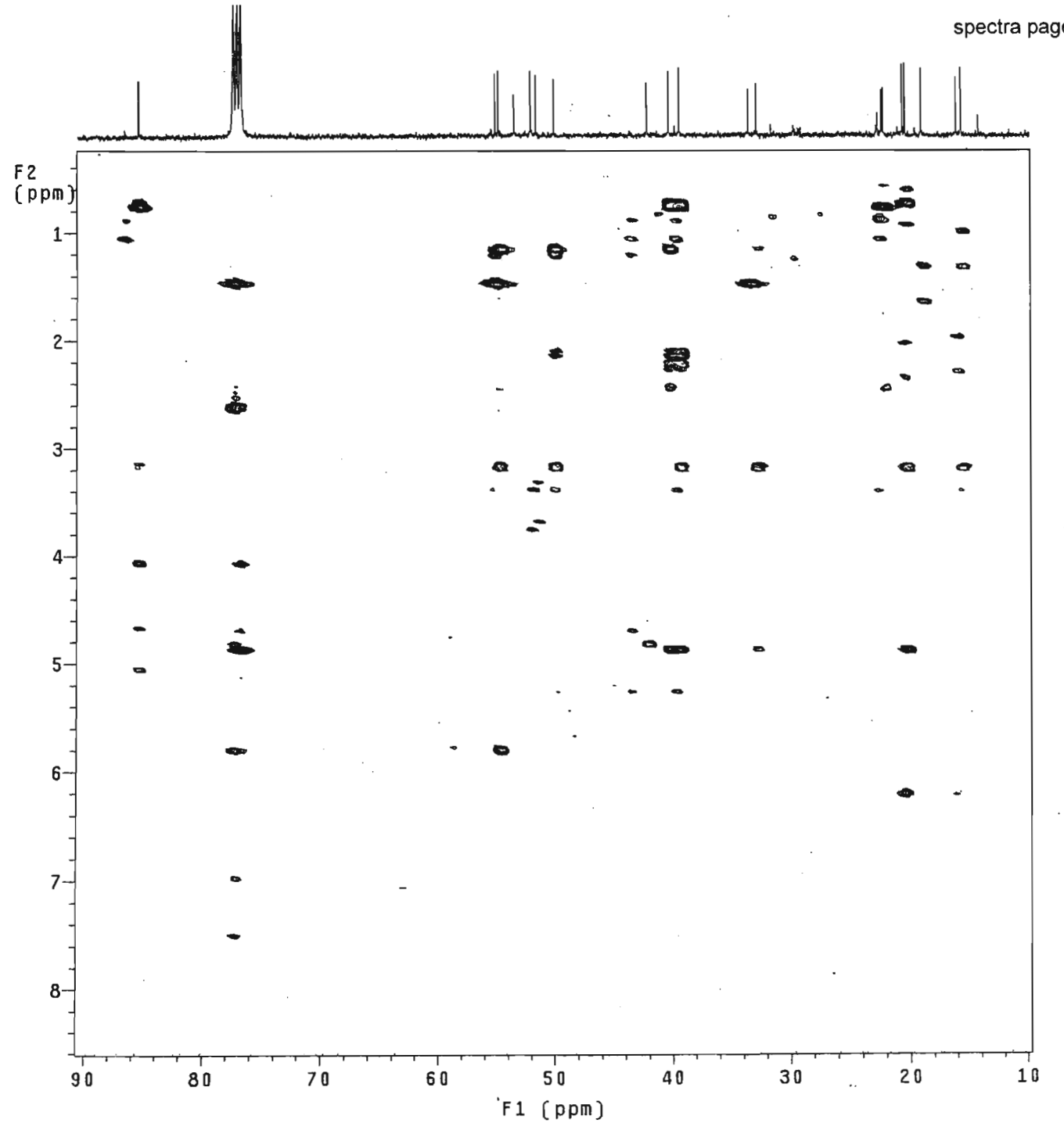
Spectrum QP 11.5: HMBC Spectrum of quivisianone QP 11

probe=5mmASW

Pulse Sequence: ghmqc_da

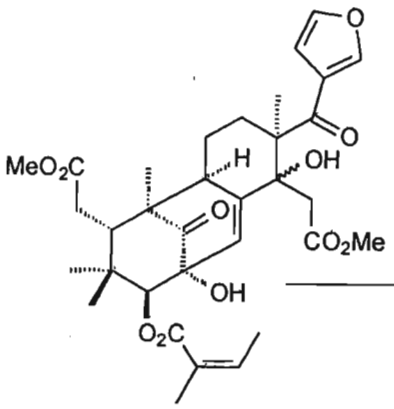


7-85 quivisianone **QP 11**

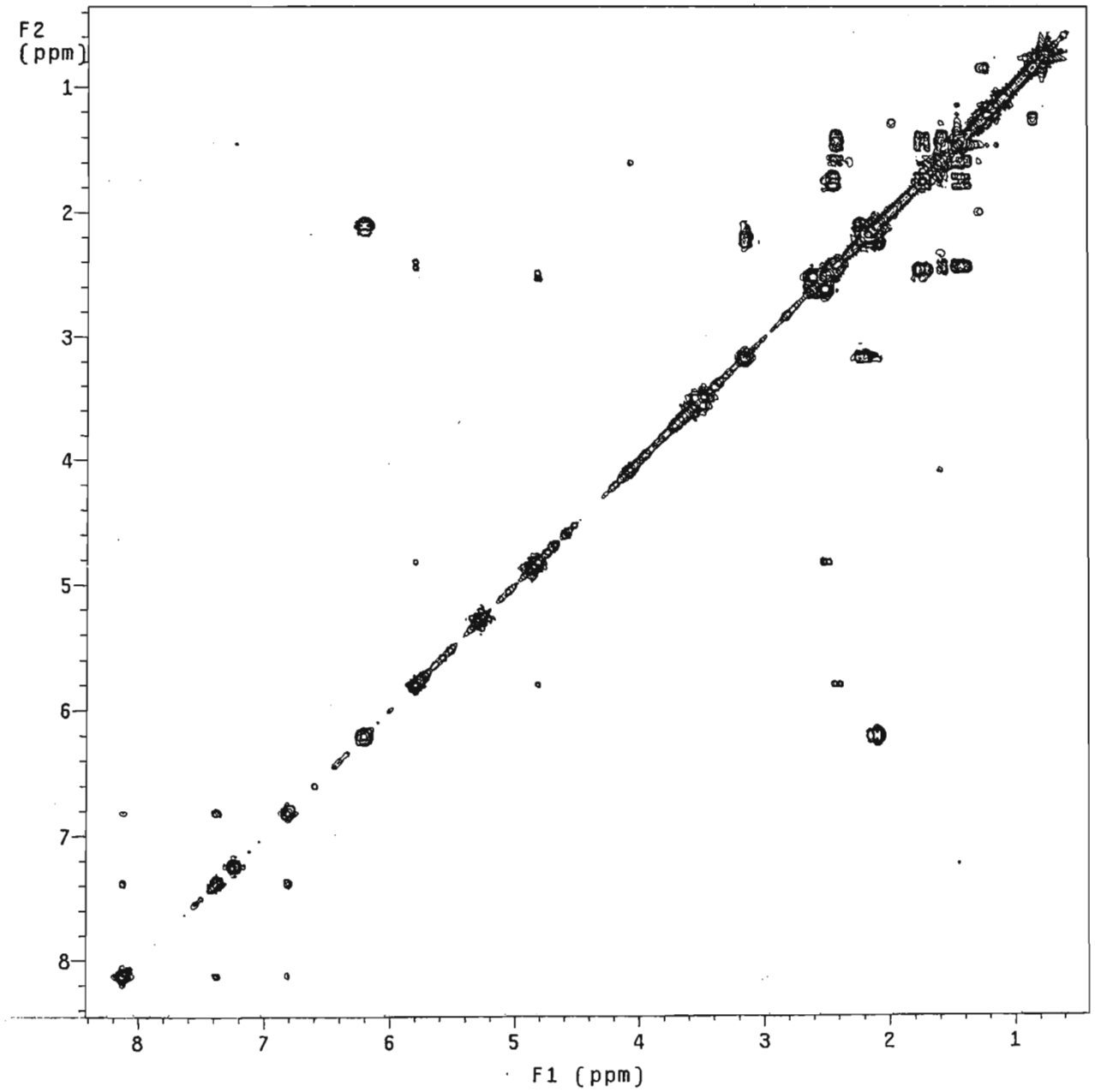


Spectrum QP 11.6: Expanded HMBC Spectrum of quivisianone QP 11

Pulse Sequence: relayh



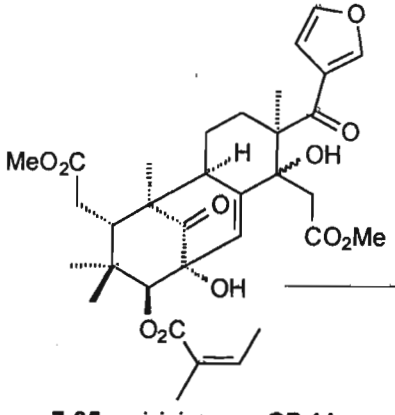
7-85 quivisianone **QP 11**



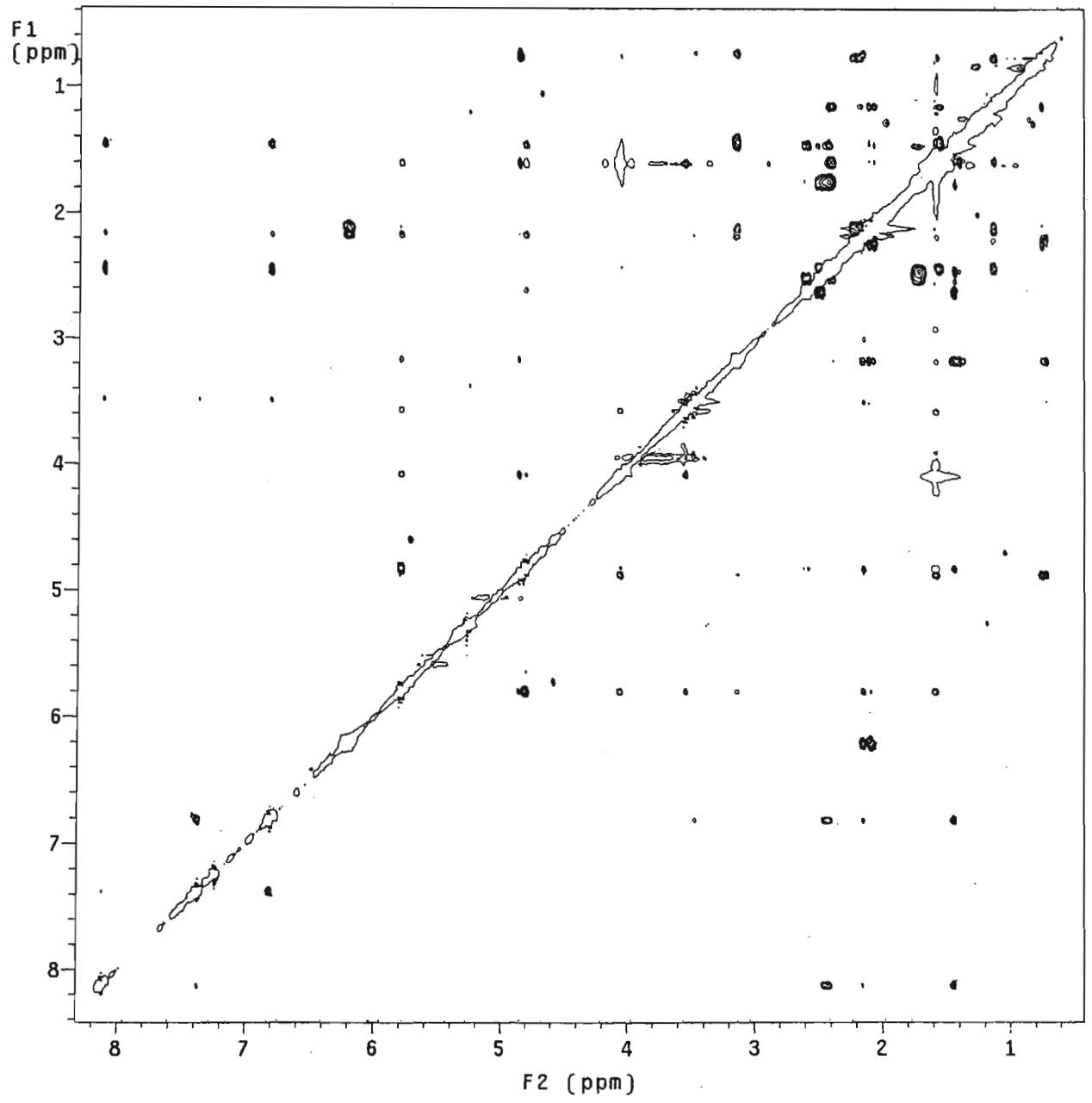
Spectrum QP 11.7: COSY Spectrum of quivisianone QP 11

mix=1sec
probe=5mmASW

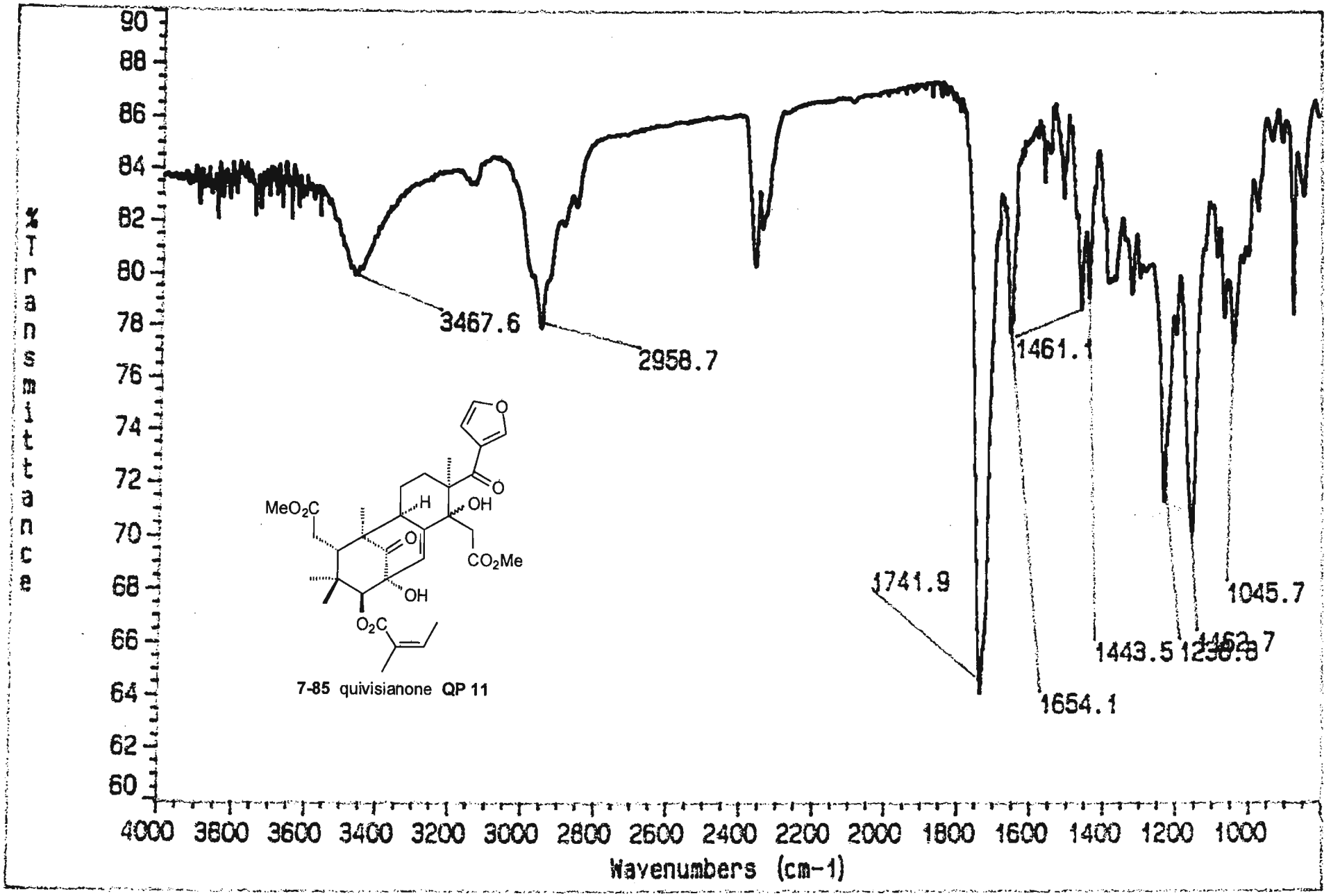
Pulse Sequence: noesy_da



7-85 quivisianone **QP 11**



Spectrum QP 11.8: NOESY Spectrum of quivisianone QP 11



7-85 quivisianone QP 11

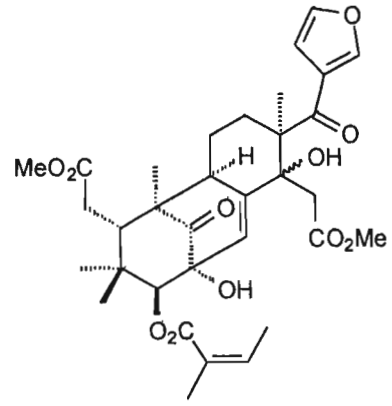
Spectrum QP 11.9: IR Spectrum of quivisianone QP 11

Selected Isotopes:

Symbol	Min	Max	V'cy	Name
C	0	48	4	Carbon-12
H	0	56	1	Hydrogen-1
O	0	14	2	Oxygen-16

Allowable error = minimum of 20.0 ppm, 5.0 mmu.
Ring/Double Bond limits = [0.5 : 100.0]

Mass	Calculated	ppm	mmu	R/DB	Formula
614.27346	614.27271	-1.2	-0.7	13.0	$C_{33}H_{42}O_{11}$
572.21688	572.21402	-5.0	-2.9	31.0	$C_{44}H_{28}O$
	572.21989	5.3	3.0	22.0	$C_{37}H_{32}O_6$
540.23404	540.23593	3.5	1.9	13.0	$C_{30}H_{36}O_9$
	540.23006	-7.4	-4.0	22.0	$C_{37}H_{32}O_4$
514.22081	514.22028	-1.0	-0.5	12.0	$C_{28}H_{34}O_9$

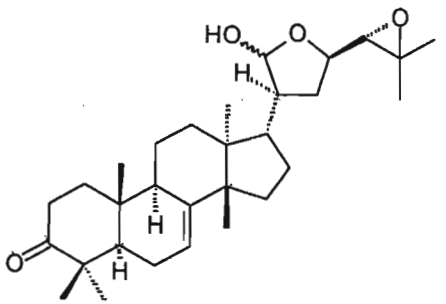


7-85 quivisianone **QP 11**

***** End of Atomic Composition Report *****

Spectrum QP 11.10: High Resolution Mass Spectrum of quivisianone QP 11

Pulse Sequence: s2pul

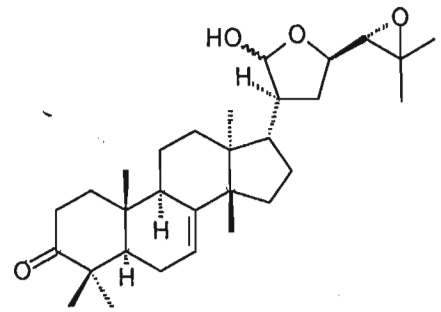


7-86 melianone **QP 12**

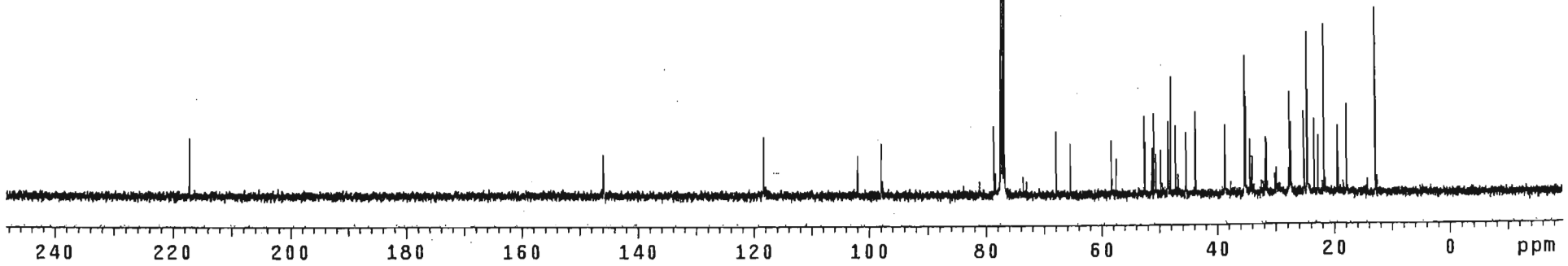
Spectrum QP 12.1: ^{1}H NMR Spectrum of melianone QP 12

Pulse Sequence: s2pul

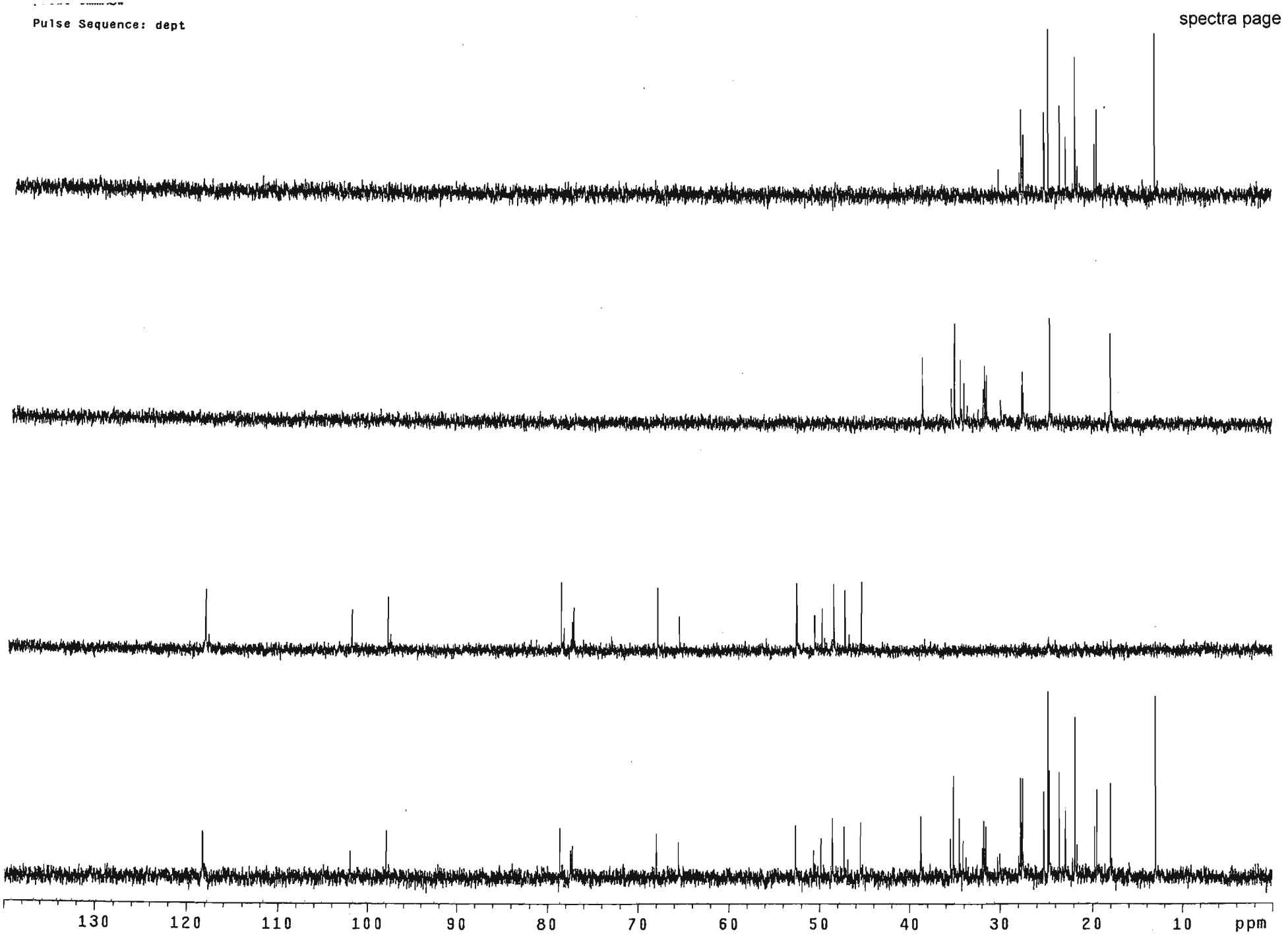
	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	21841.347	217.182	9.4	40	3168.297	31.504	8.2
2	21834.767	217.116	5.2	41	2782.497	27.668	16.5
3	14675.667	145.929	6.6	42	2766.868	27.513	8.1
4	14658.392	145.757	5.4	43	2761.109	27.455	11.5
5	11905.968	118.388	5.9	44	2535.717	25.214	13.3
6	11896.097	118.290	9.5	45	2527.491	25.132	8.5
7	10258.298	102.004	6.4	46	2485.538	24.715	26.1
8	9853.578	97.980	8.5	47	2471.554	24.576	16.9
9	7910.594	78.660	11.2	48	2360.503	23.472	12.0
10	7798.720	77.547	197.5	49	2296.340	22.834	9.4
11	7787.204	77.433	18.5	50	2190.224	21.779	27.2
12	7766.638	77.228	200.0	51	1974.703	19.636	8.9
13	7734.557	76.909	189.7	52	1951.670	19.407	11.0
14	6833.809	67.953	10.2	53	1801.134	17.910	14.4
15	6589.496	65.523	8.3	54	1301.815	12.945	29.9
16	5863.962	58.309	8.8				
17	5784.169	57.515	5.9				
18	5291.431	52.616	12.7				
19	5284.028	52.542	8.9				
20	5152.411	51.234	7.4				
21	5127.733	50.988	13.1				
22	5091.539	50.628	6.5				
23	5008.456	49.802	7.2				
24	4882.598	48.551	11.7				
25	4877.663	48.502	8.9				
26	4836.533	48.093	18.9				
27	4751.805	47.250	11.1				
28	4570.010	45.442	10.0				
29	4421.119	43.962	8.8				
30	4401.376	43.766	13.3				
31	4396.441	43.716	7.2				
32	3892.186	38.702	11.2				
33	3561.500	35.414	5.8				
34	3550.807	35.308	22.3				
35	3531.887	35.120	15.6				
36	3464.434	34.449	8.8				
37	3422.481	34.032	6.0				
38	3205.314	31.872	5.5				
39	3188.039	31.701	9.1				



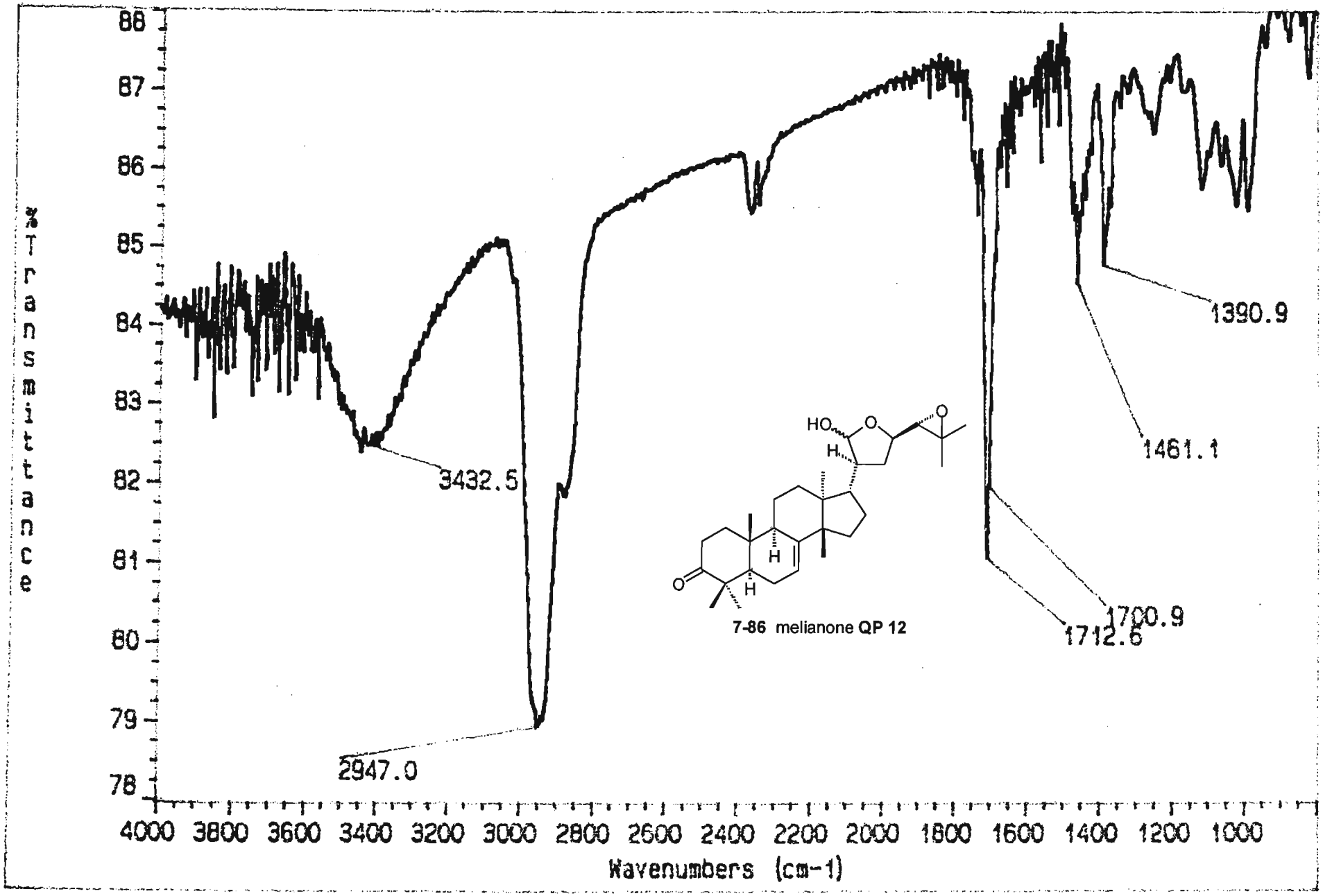
7-86 melianone **QP 12**



Spectrum QP 12.2: ^{13}C NMR Spectrum of melianone QP 12

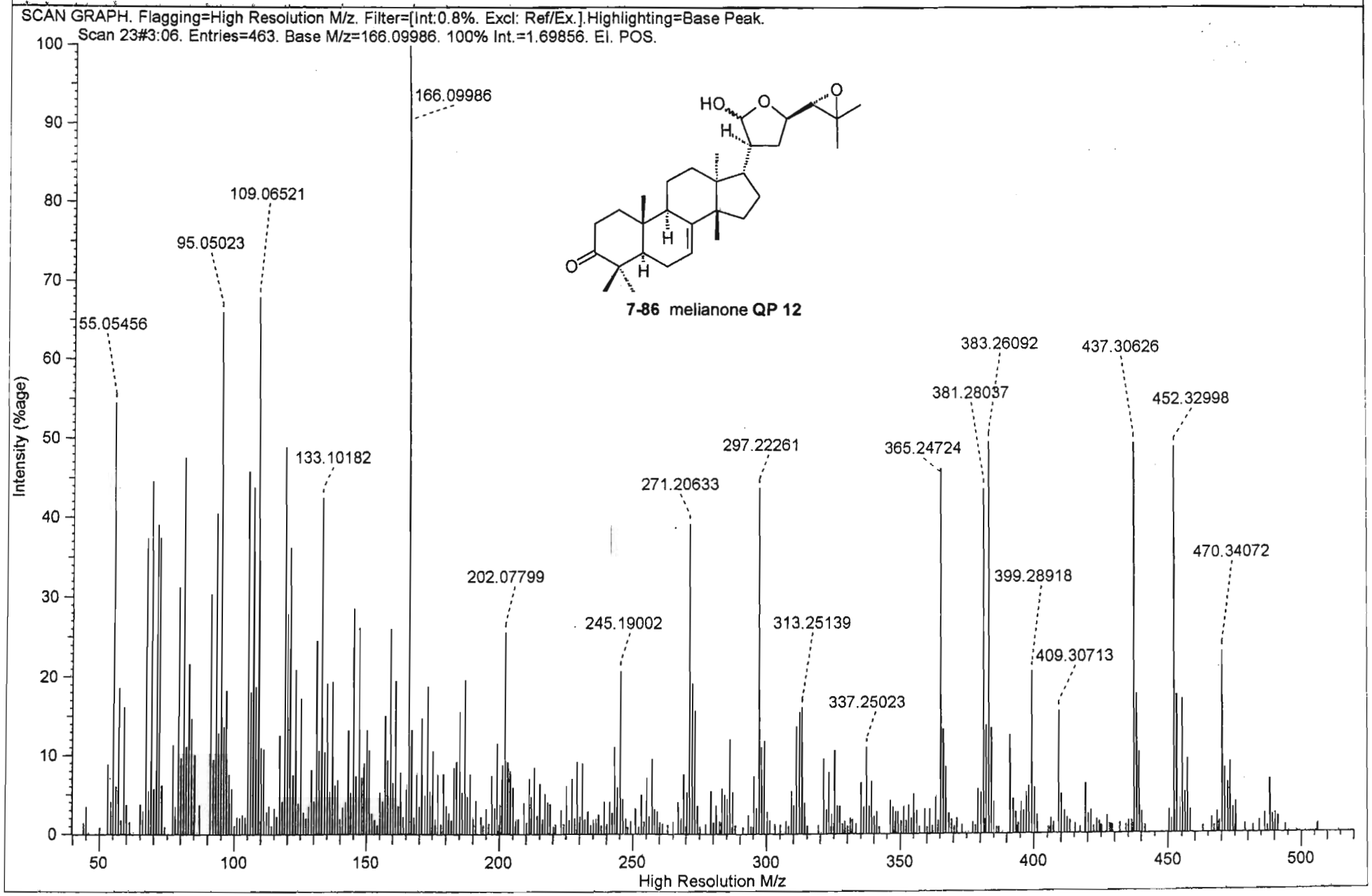


Spectrum QP 12.3: ADEPT Spectrum of melianone QP 12



Spectrum QP 12.4: IR Spectrum of melianone QP 12

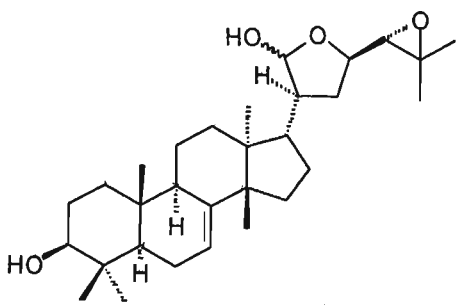
File Name : C:\MASPEC\data\hc112710.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPK 18-2
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ



Spectrum QP 12.5: High Resolution Mass Spectrum of melianone QP 12

satpwr=-12
probe=5mmASW

Pulse Sequence: presat_da



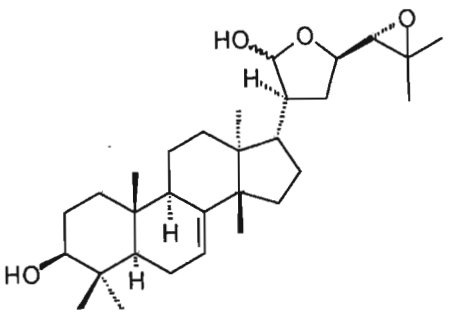
7-97 melianol **QP 13**

Spectrum QP 13.1: ^{1}H NMR Spectrum of melianol QP 13

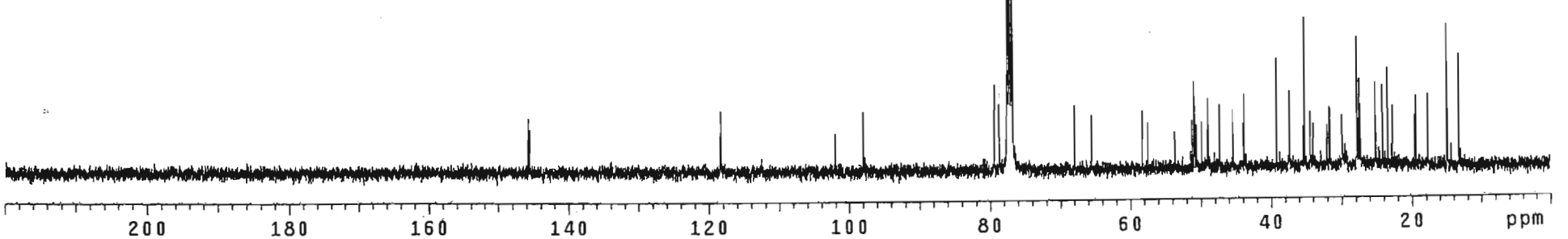
probe=5mmASW

Pulse Sequence: s2pul

INDEX	FREQUENCY	PPM	HEIGHT	INDEX	FREQUENCY	PPM	HEIGHT
1	14660.038	145.774	8.8	40	3007.890	29.909	8.3
2	14642.763	145.602	7.0	41	2801.417	27.856	15.7
3	11912.550	118.454	6.7	42	2795.659	27.799	20.9
4	11902.678	118.356	9.9	43	2781.675	27.660	7.6
5	10260.766	102.029	6.1	44	2770.158	27.545	10.3
6	9857.691	98.021	9.7	45	2766.045	27.504	14.1
7	7988.741	79.437	13.9	46	2745.480	27.300	10.0
8	7984.628	79.396	8.2	47	2537.362	25.231	13.5
9	7915.530	78.709	10.7	48	2528.314	25.141	8.8
10	7798.720	77.547	684.7	49	2430.424	24.167	13.0
11	7787.204	77.433	28.8	50	2355.567	23.423	15.8
12	7766.639	77.228	700.0	51	2291.404	22.785	9.7
13	7734.557	76.909	675.7	52	1975.525	19.644	8.2
14	6834.632	67.961	10.4	53	1952.493	19.415	11.4
15	6589.496	65.523	8.9	54	1783.037	17.730	11.6
16	5859.849	58.268	9.4	55	1500.062	14.916	22.8
17	5782.524	57.499	7.5	56	1333.896	13.264	18.0
18	5395.079	53.647	6.0				
19	5149.121	51.201	7.9				
20	5124.443	50.955	14.0				
21	5119.508	50.906	12.6				
22	5113.750	50.849	8.7				
23	5091.539	50.628	7.0				
24	5015.037	49.868	7.6				
25	4926.196	48.984	11.3				
26	4922.083	48.943	9.5				
27	4758.386	47.316	10.2				
28	4569.187	45.434	9.4				
29	4423.587	43.986	7.3				
30	4404.667	43.798	11.9				
31	3939.075	39.169	17.6				
32	3755.635	37.345	12.3				
33	3563.146	35.431	6.6				
34	3542.581	35.226	24.1				
35	3462.789	34.433	9.0				
36	3420.013	34.007	7.1				
37	3220.944	32.028	6.8				
38	3188.040	31.701	9.7				
39	3181.459	31.635	9.4				

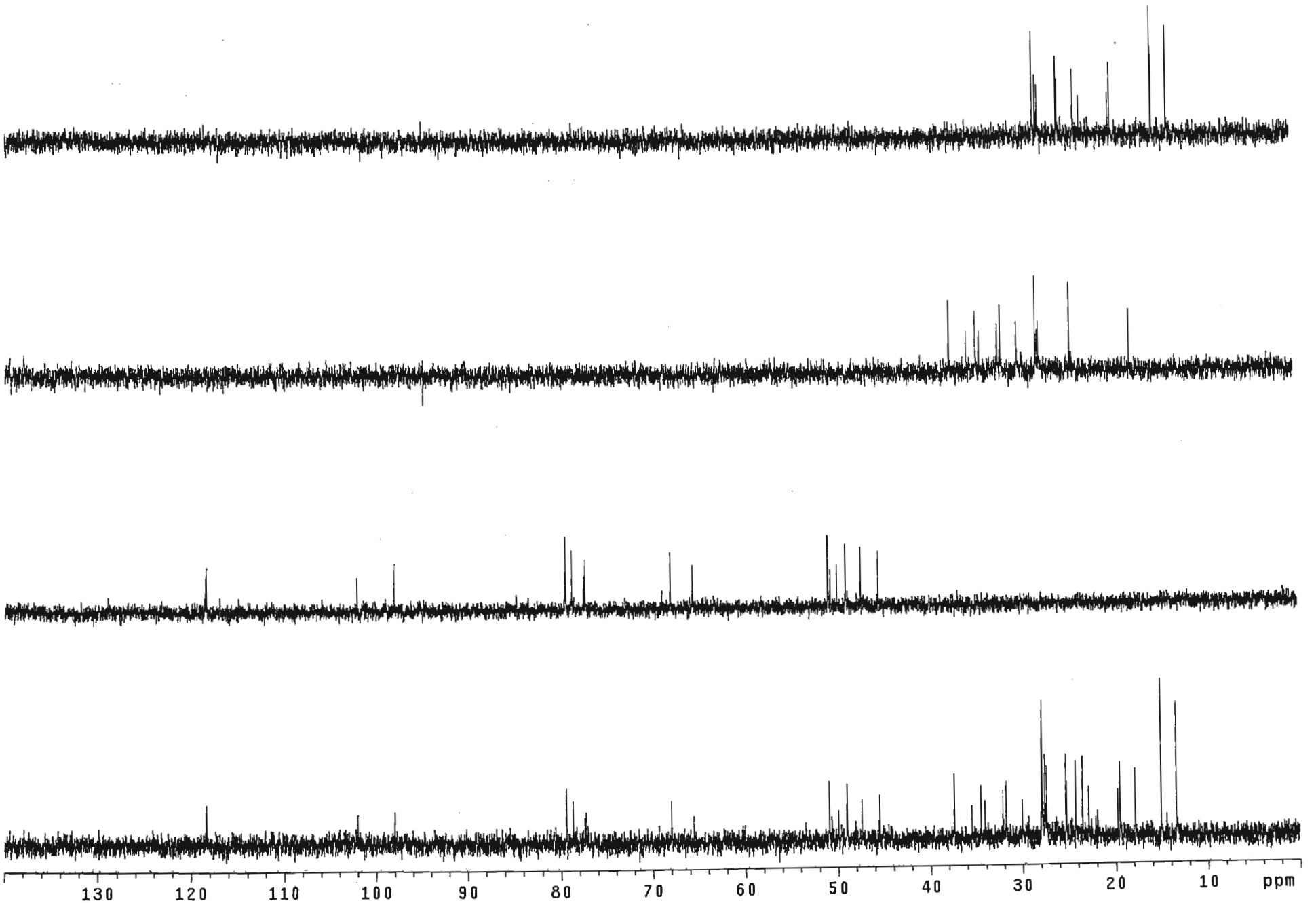


7-97 melianol **QP 13**

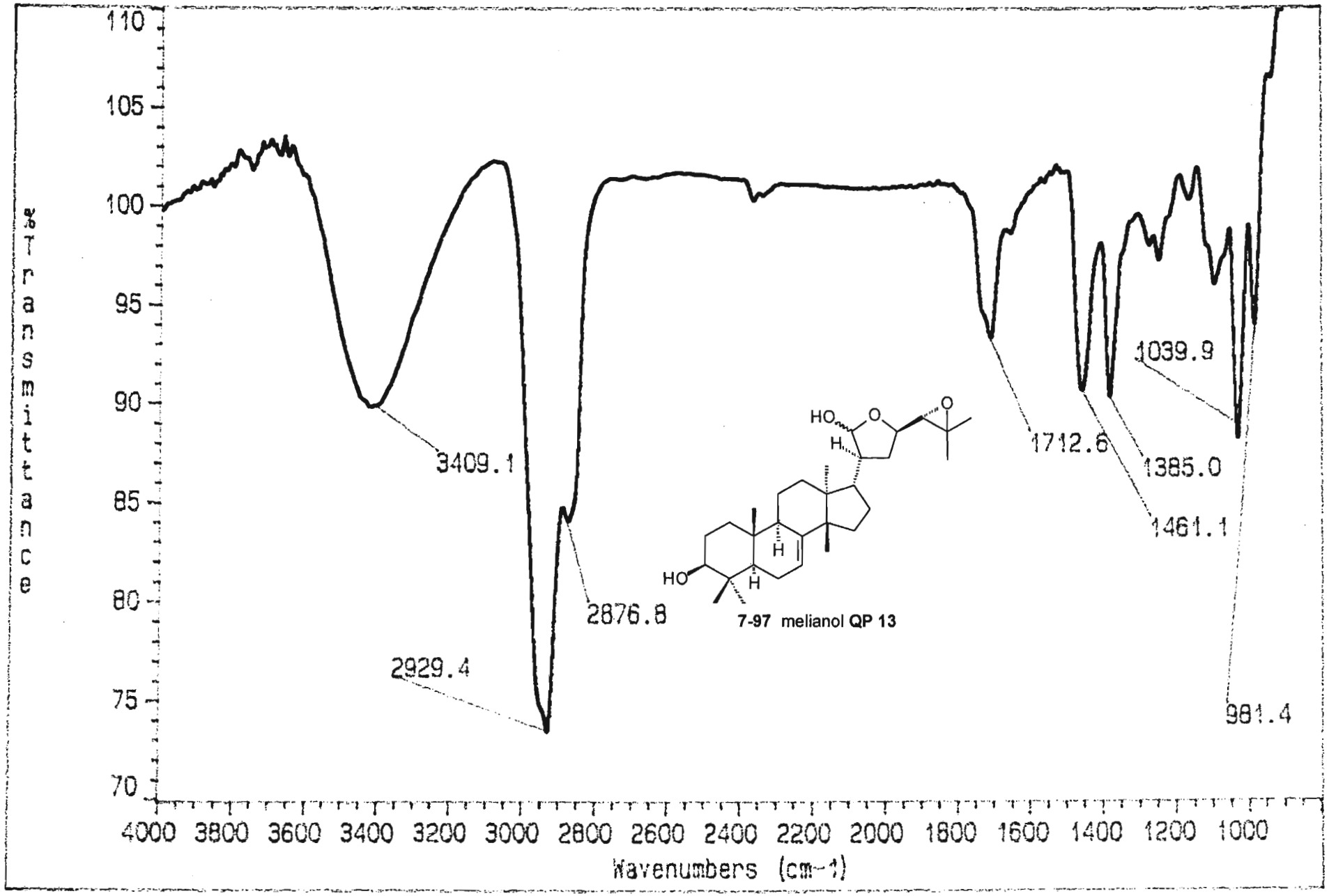


Spectrum QP 13.2: ^{13}C NMR Spectrum of melianol QP 13

Pulse Sequence: dept

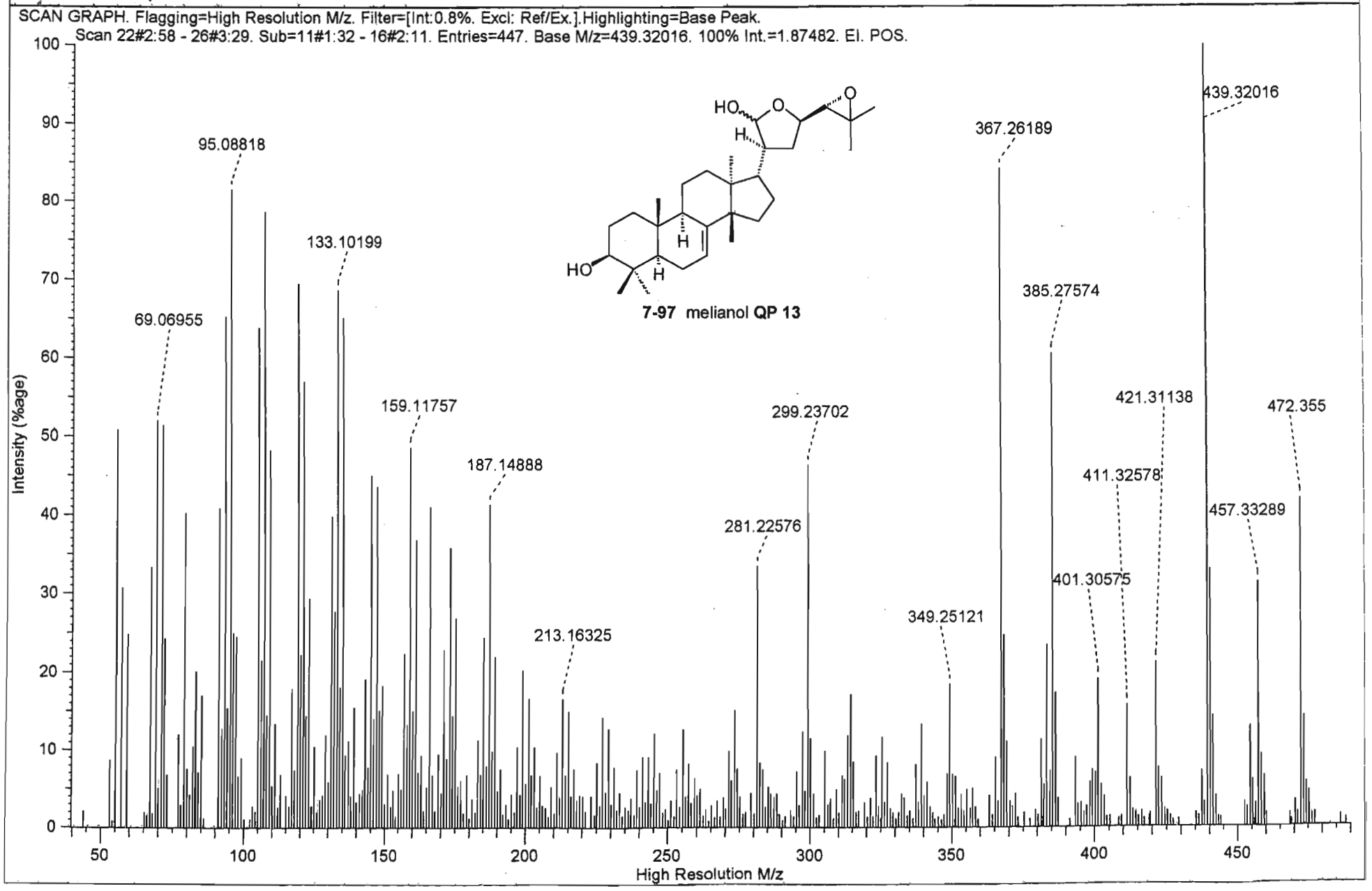


Spectrum QP 13.3: ADEPT Spectrum of melianol QP 13



Spectrum QP 13.4: IR Spectrum of melianol QP 13

File Name : C:\MASPEC\data\hc112712.ms2
File Source : Acquired on MASPEC II system [II32/A002]
File Title : QPK 16b1
Operator : Dr. P. Boshoff
Instrument : VG70-SEQ



Spectrum QP 13.5: High Resolution Mass Spectrum of melianol QP 13