

**MUTHI COMPOUNDS FROM INDIGENOUS
LAURACEAE AND RUBIACEAE SPECIES**

By

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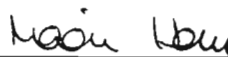
A thesis submitted in partial fulfilment of the
requirements for the degree of Master of Science

Department of Chemistry
University of Natal
Pietermaritzburg
December 1996

DECLARATION

I hereby certify that this research is the result of my own investigation, which has not already been accepted in substance for any degree and is not being submitted in candidature for any other degree.

Signed



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I certify that this statement is correct.

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December 1996

To my Mother, my husband and my sons.

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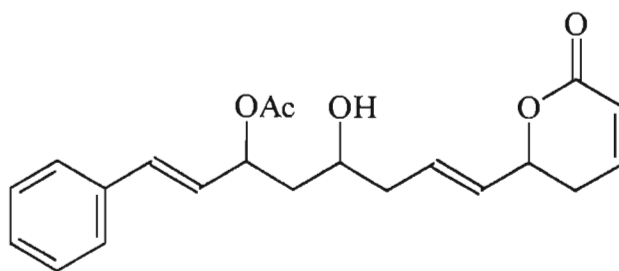
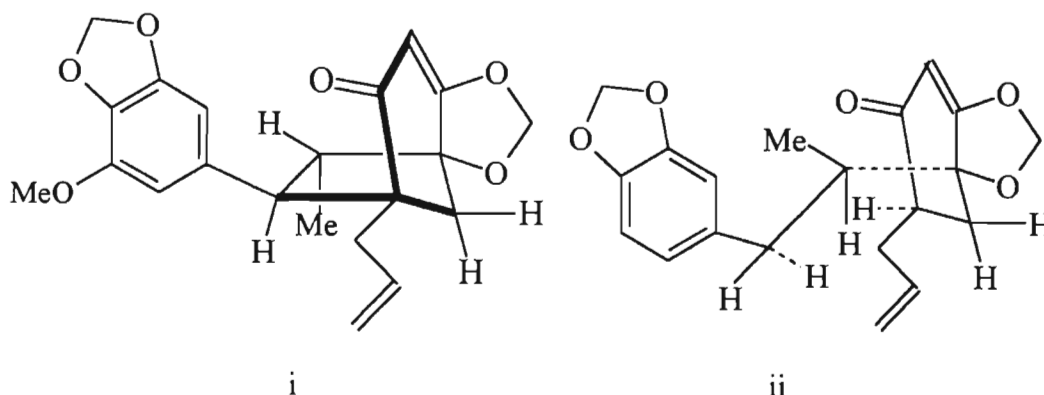
ABBREVIATIONS

CD	circular dichroism
CI-MS	chemical ionization mass spectrometry
COSY	homonuclear shift correlation
DEPT	distortionless enhancement of polarisation transfer
EtOAc	ethyl acetate
GCMS	gas chromatograph-mass spectrometry
HETCOR	heteronuclear chemical shift correlation
HRMS	high resolution mass spectrometry
IR	infra red
RT	room temperature
tlc	thin layer chromatography
TMS	trimethylsilyl

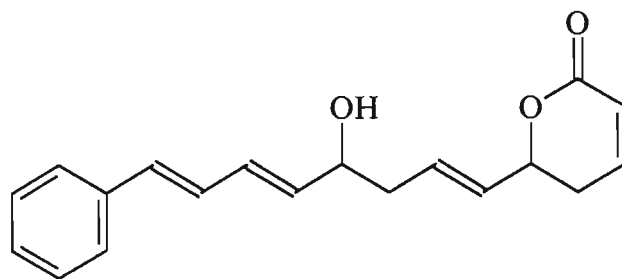
SUMMARY

The Lauraceae species indigenous to Southern Africa investigated were: *Ocotea bullata*, *Cryptocarya liebertiana*, *Cryptocarya latifolia*, *Cryptocarya wyliei* and *Cryptocarya myrtifolia*. The chemical constituents isolated from *Ocotea bullata* were neolignans (two known and two new, the new being i and ii). *Cryptocarya liebertiana* yielded 6-substituted α -pyrones (three known and two new, the new being iii and iv) and two known neolignans. *Cryptocarya latifolia* yielded 6-substituted α -pyrones (three known and three new, the new being v, vi, vii). *Cryptocarya wyliei* yielded 6-substituted α -pyrones (four known and one new, the new being viii). *Cryptocarya myrtifolia* yielded 6-substituted α -pyrones (one known and one new, being ix).

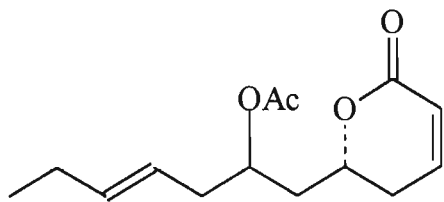
The Rubiaceae species indigenous to South Africa investigated, *Alberta magna* yielded iridoids (two novel), compounds x, xi and one known cyclopentyl dialdehyde.



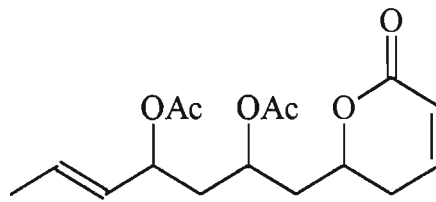
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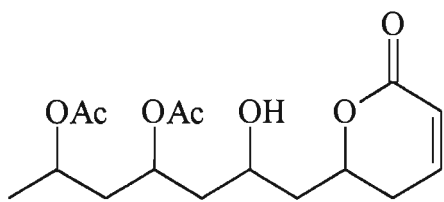
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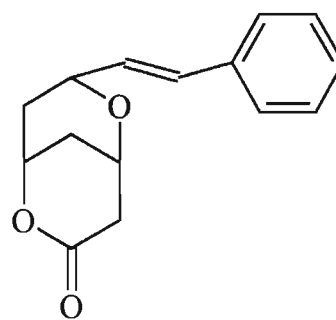
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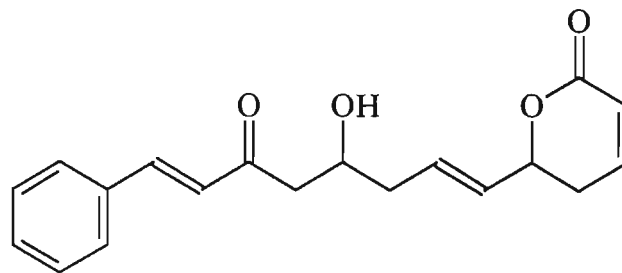
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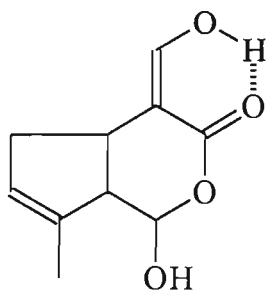
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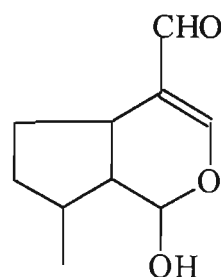
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ix



x

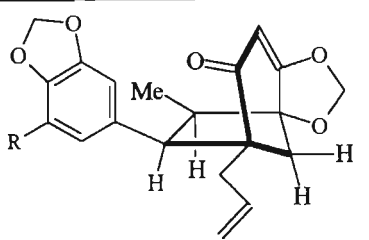
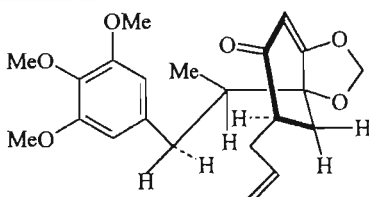
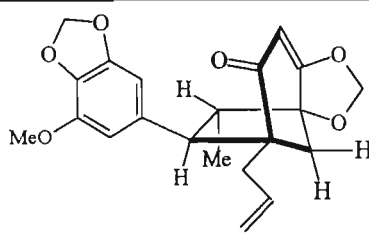
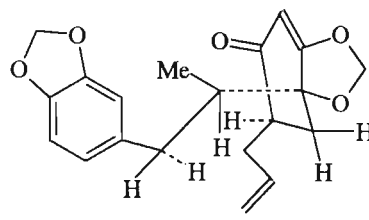
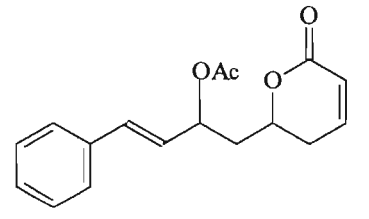
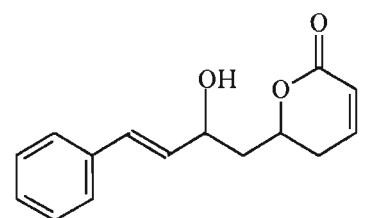
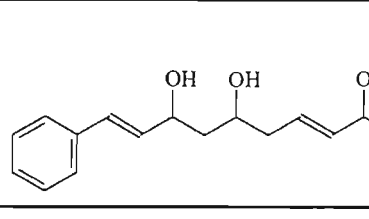


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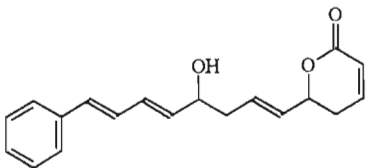
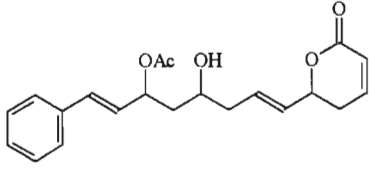
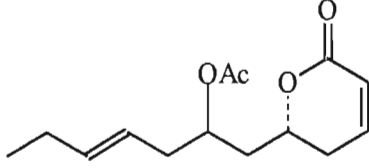
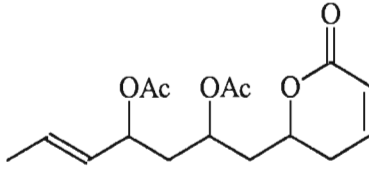
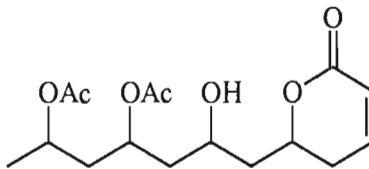
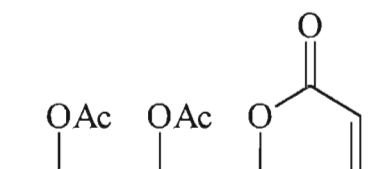
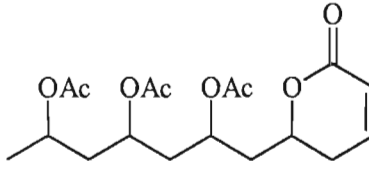
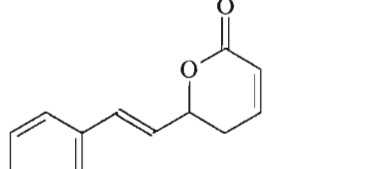
From the above investigation the following publications have resulted:

1. Drewes, S. E., Sehlapeo, B. M., Horn, M. M., Scott-Shaw, R. and Sandor, P. (1995) *Phytochemistry* **38**, 1427.
2. Drewes, S. E., Horn, M. M., Sehlapeo, B. M., Ramesar, N., Field, J. S., Scott-Shaw, R. and Sandor, P. (1995) *Phytochemistry* **38**, 1505.
3. Drewes, S. E., Horn, M. M. and Scott-Shaw, R. (1995) *Phytochemistry* **40**, 321.
4. Drewes, S. E., Horn, M. M. and Wijewardene, C. S. (1996) *Phytochemistry* **41**, 333.

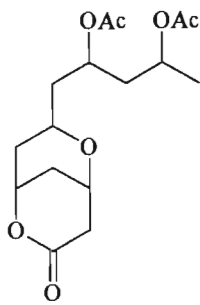
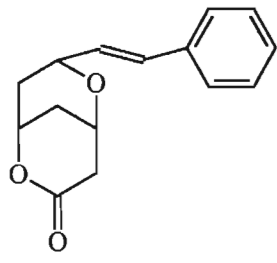
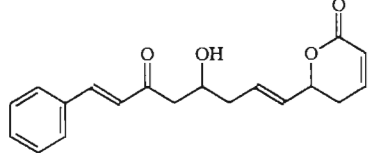
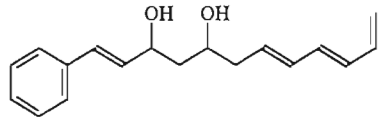
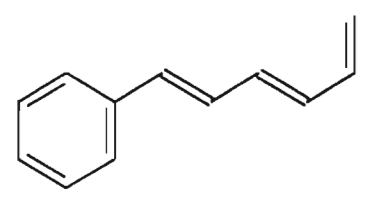
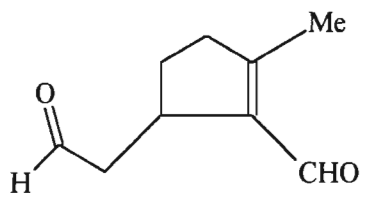
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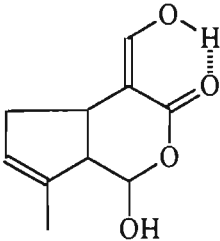
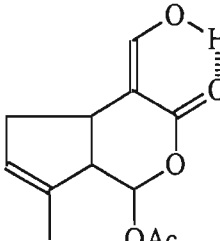
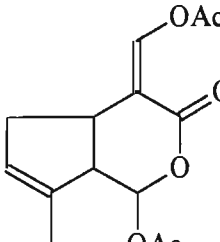
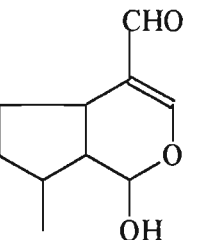
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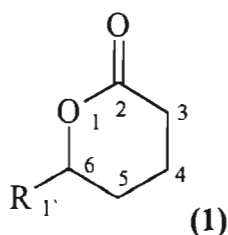
CHAPTER 1

INTRODUCTION

6-Substituted 5,6-dihydro- α -pyrones

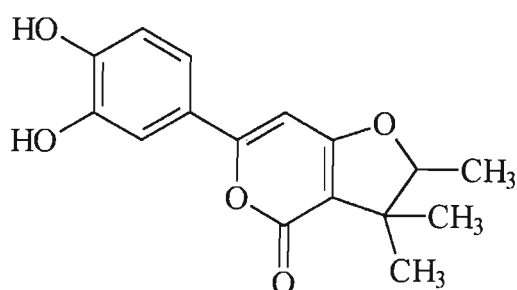
GENERAL

Pyran-2-ones (1) are fairly common in Nature. Pyran-2-one is the ketone derived from pyran, when the carbonyl group is α to the heteroatom. The presence of this group is the reason for the wide range of biological activities, e.g., antibiotic, antifungal, cytotoxic, neurotoxic, phytotoxic, insect antifeedant and plant growth inhibition. Pyrones are therefore an important group of compounds. The natural sources for pyrones are plants, animals, microorganisms and marine organisms. The occurrence of α -pyrones in plants is mainly in the Lauraceae, Annonaceae, Pipericeae and Lamiaceae families. 6-Substituted α -pyrones have been isolated from thirteen plant families and twenty fungal species. Pyrones can be fully unsaturated, partially saturated (dihydropyran-2-ones) or fully saturated δ -lactones. The 6-substituent is usually alkyl or styryl but many variations are possible. γ or 4-Pyrones, which are obviously related to the α -pyrones are widely distributed in plants in form of flavones and they are outside the scope of this introduction. Aryl and styryl substituted pyrones have been isolated from various Brazilian *Aniba* species [1] and from *Cryptocarya caloneura* (Scheff) [1]. 6-Styryl-5,6 dihydro-2-pyrone was also isolated from a species of Annonaceae [1], *Cryptocarya moshata* (Lauraceae) [2], *Mundulea sericea* (Leguminosae) [1]. A study of the α -pyrones present in plants leads to useful phytochemical information.



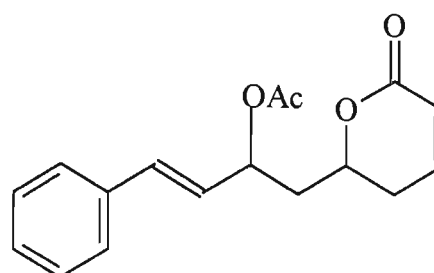
BIOLOGICAL ACTIVITY

Many of the biologically-active pyrones have been used for medicinal purposes. Saropyrone (**2**) was isolated from a Chinese herbal medicine *Hypericum japonicum* (Guttiferae) [3] together with nine anti microbially active compounds. The plant is used for the treatment of bacterial diseases, tumors and infectious hepatitis. Cryptocaryalactone (**3**) and deacetyl cryptocaryalactone (**4**) were isolated from *Cryptocarya moshata* [2] (Lauraceae) seeds from Uruguay. These compounds are effective against velvetleaf (*Abutilon theophrasti*), a weed that competes with soybeans and corn. Umuravumbolide (**5**) from *Tetradenia riparia* (formerly *Iboza*) (Labiatae) was proved to inhibit significantly growth of *Pseudomonas* species on potatoes. The plant is used in Rwanda against malaria, fevers, aches and diarrhoea[4]. Osmundalactone (**6**) seems to be the only 6-substituted 5,6-dihydro- α -pyrone that is insect antifeedant. It inhibits the feeding of the yellow butterfly larvae *Eurema hecabe mandarina* on *Osmunda japonicum* Thunberg [5]. The kawa lactones kawain (**7**) and methysticin (**8**) from different parts of *Piper methysticum* (Forst) [5] (called in the South Pacific kava or kawa) have such activities as smooth muscle relaxant, local anaesthetic, antipyretic, anti inflammatory, antimicotic and antioedemic. Goniotalamin (**9**) from *Goniotalamus macrophyllus* (Annonaceae) [5] is being used in the rural areas of Northern Malaysia as an abortifacient. α -Pyrones can also be phytotoxic, for example colletopyrone (**10**) that was isolated from microorganisms pathogenic on plants [6]. Calanolide A (**11**), isolated from Malaysian rain forest species *Calophyllum lanigerum*, has anti HIV activity [7].



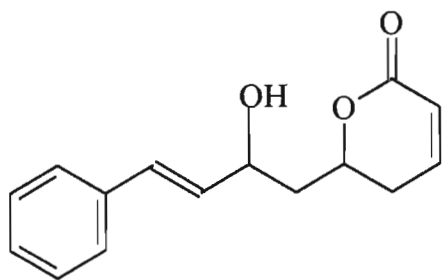
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saropyrone



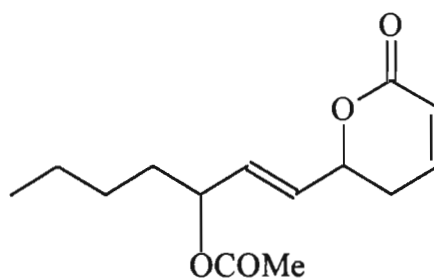
(3)

cryptocaryalactone



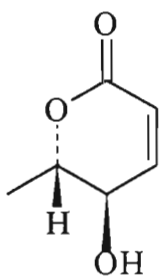
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deacetylcryptocalactone



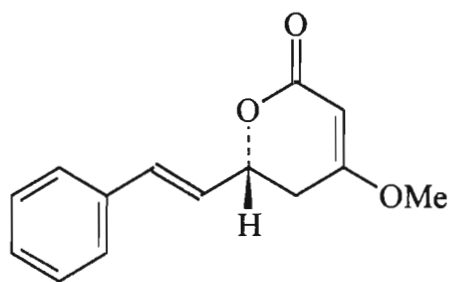
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umuravumbolide



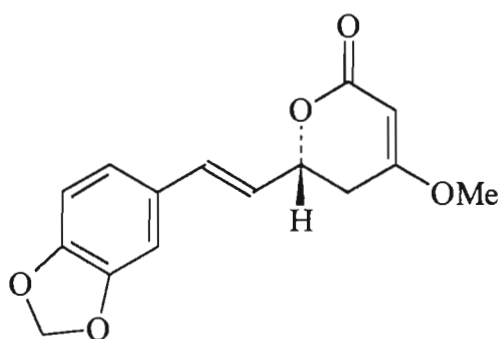
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osmundalactone



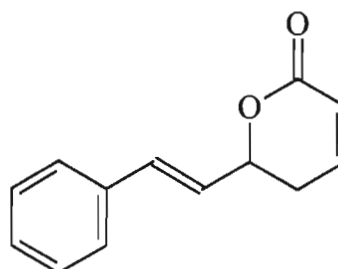
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kawain



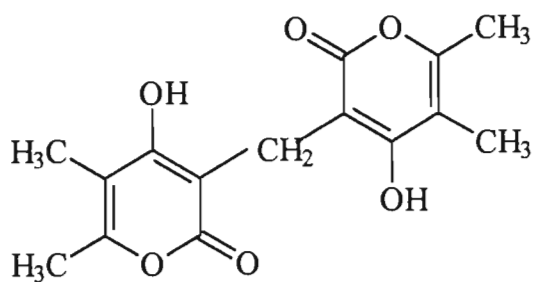
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metysticin



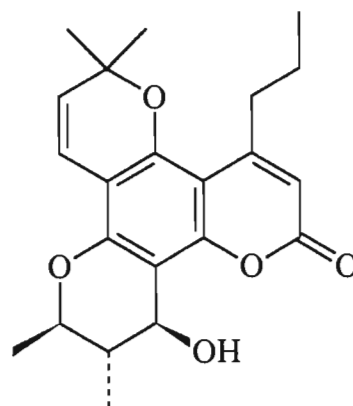
(9)

goniotalamin



(10)

colletopyrone



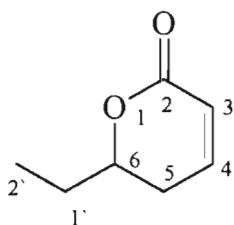
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calanolide A

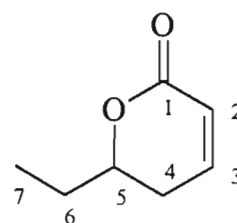
NOMENCLATURE

Lactones can be named in either of two ways. The first, recommended by IUPAC identifies the lactone with a corresponding heterocyclic nucleus. Thus, a substituted α - β -unsaturated δ -lactone is named as a substituted 5,6-dihydro-2H-pyran-2-one, for example: 6-ethyl-5,6-dihydro-2H-pyran-2-one(12). This is the most widely used procedure and is accepted by Chemical Abstracts. When there is no doubt in the nomenclature it is possible to omit the indicated hydrogen, and to reduce pyran-2-one to 2-pyrone. The term α -pyrone is synonymous with 2-pyrone. Side chain atoms are numbered with prime.

The second recommended nomenclature is based on replacement of the suffix 'oic' with 'olide' from the lactonization of a carboxylic acid at position C-5. Example: 2-hepten-5-olide or 5-ethyl-2-penten-5-olide (13).



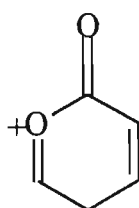
(12)



(13)

STRUCTURE DETERMINATION

When examining α -pyrones by physical methods such as ^1H NMR, ^{13}C NMR, IR, and Mass Spectrometry there are a few characteristic features that point to the presence of this moiety. In ^1H NMR H-3 is a doublet of triplets around 6ppm, H-4 is a multiplet at around 6.8 ppm. In ^{13}C NMR C-2 is around 164 ppm. In IR the carbonyl group appears at around 1730 cm^{-1} . In MS the fragment with a m/z value of 97 indicates the presence of a pyrone ring (**14**).



(14)

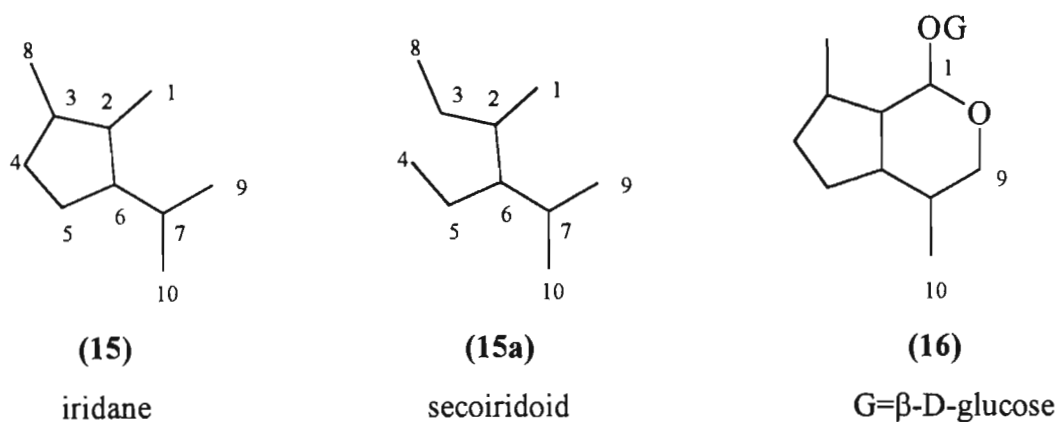
$m/z = 97$

Iridoids

GENERAL

Iridoids are monoterpenes with a cyclopentane moiety of the type (**15**), secoiridoids as shown in (**15a**). In many of the compounds there is a hemiacetal bridge linking C-1 and C-9 resulting in the formation of an α -hydroxytetrahydro, or dihydropyrane ring, fused to the cyclopentane ring. The hydroxyl group at the C-1 position has frequently a glucoside linkage as shown in (**16**). An alternate definition of iridoid can be an oxygen containing heterocyclic 6 membered ring fused to a cyclopentane ring [8]. Iridoids have been isolated as early as the late 1900 s, but the proposal for the nature of their skeleton was given in 1958 by Halpern and Schmid [9]. Naturally occurring iridoids are mainly isolated as the water soluble D-glucoside. Iridoids are present in plant tissue like leaves, seeds, bark and root. Insects are another source of iridoids. Indeed, the name of this class of compounds

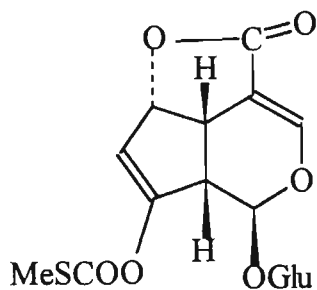
is derived from a genus of ants that secrete them, *Iridomyrmex*. Iridoids are distributed in about 50-70 Families, mainly in plants.



Most iridoids have a bitter taste and manifest some antifungal activity. It is interesting to note the relationship between plant and insect iridoids. There are some insect species that are able to sequester and store plant toxins. Iridoids of plant origin can be found in 10 species of aphids from three Lepidopteran families, as well as in aphids, leaf beetles, flies and grasshoppers [10]. Recently there have been findings that aliphatic lactones can be also sequestered by insects [10].

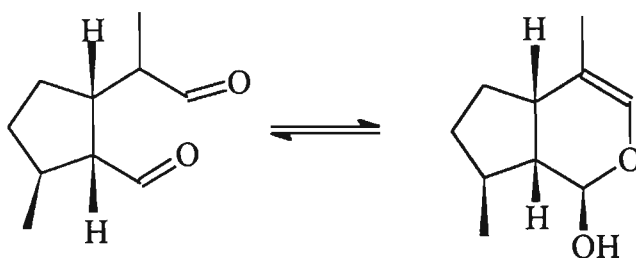
BIOLOGICAL ACTIVITY

The iridoid from *Paedria scandens* such as paederoside (17) is transferred to the aphid *Acyrtosiphon niponicus* by its feeding on the plant [10]. Paederoside is sequestered by the aphid, then hydrolysed to give methylmercaptan with an unpleasant smell. This in turn, protects it from the ladybird beetle *Harmonia oxyridis* [10]. Beetles from subtribe *Staphylinina* defend themselves against ants by the chemicals they have in the abdominal glands such as iridodial (18) nepatalactone (19) and monoterpenes [10]. In their defence mechanism they use a fixative agent, such as iridodial (18) and terpenes as repellent. Nepatalactone (19) has an odour that is attractive to cats and for this reason also called the catnip plant.



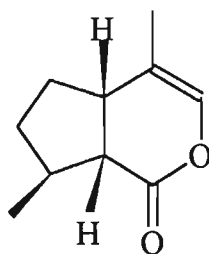
(17)

paederoside



(18)

iridodial



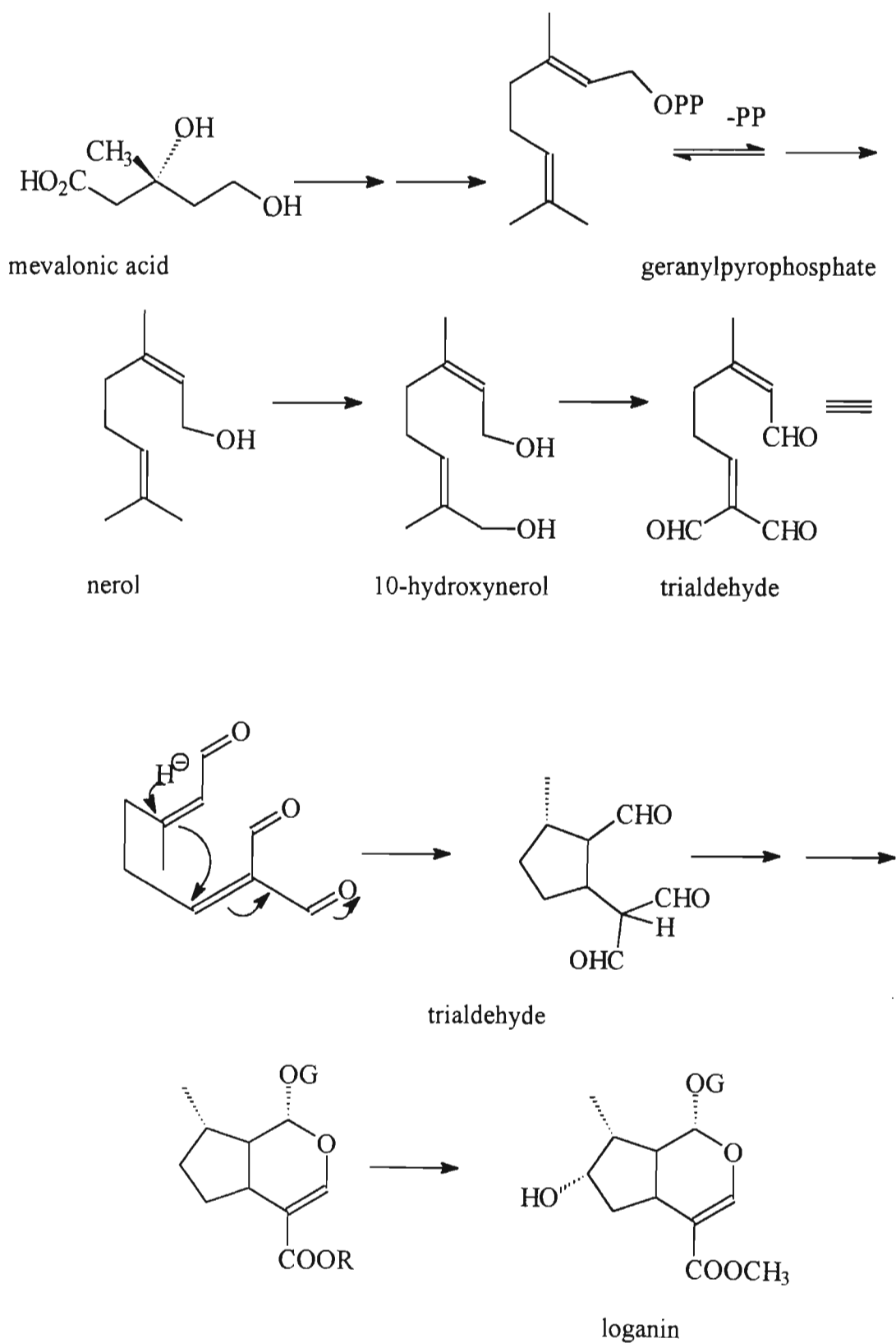
(19)

nepatalactone

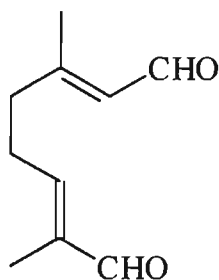
BIOSYNTHESIS

From biosynthetic studies carried out with labelled precursors the pathway from mevalonic acid to loganin via geranyl pyrophosphate, nerol, 10-hydroxynerol, and a trialdehyde (Arigoni [8]), was proposed. (Scheme 1). Loganin is the precursor of secoiridoids and of the terpene portion of indole alkaloids. From biogenetic point of view the iridoids are

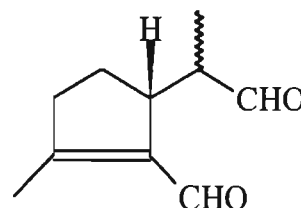
closely related to indole and isoquinoline alkaloids. 10 or 9 Carbons of the iridoid skeleton are found in these alkaloids.[8].



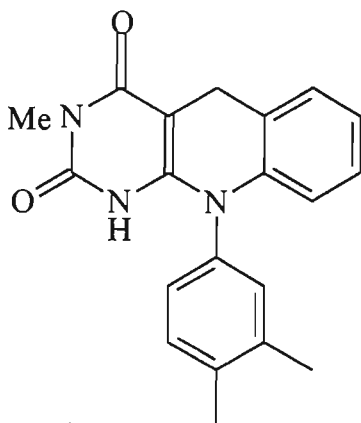
Synthetic studies on biogenetic precursors have been carried out on isomers of the dialdehyde (20). When reacted with 50 % HCO₂H it gives a racemic mixture of (21) [11]. Reduction of (21) using formic acid in the presence of coenzyme (22) gives iridodial (23). This example is analogous to the intramolecular Michael addition leading to the cyclopentane trialdehyde in the biosynthetic route. Aspects of the structure and significance of (21) will be considered further in the discussion section.



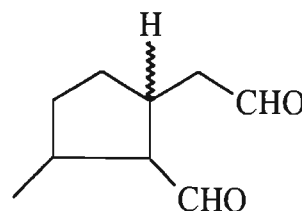
(20)



(21)



(22)



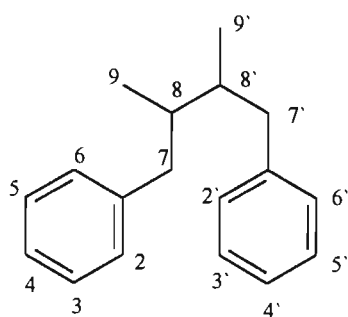
(23)

Neolignans

GENERAL

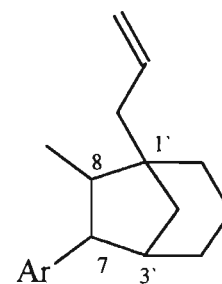
Lignans are compounds in which two propylbenzene residues are linked by at least one C-C bond between 8,8' carbons of the propyl side chain [12] (24). Most of the lignans fitting

this definition are the derivatives of coupling of an acid or an alcohol. Neolignan is the name proposed by Gottlieb [12] for compounds in which the two units are propenyl and/or allyl (25). The source of these compounds is plants, although in humans and several animals they are also present [13]. Lignans and neolignans have been used as folk medicines in many cultural societies. Some 400-600 Years ago the Himalayan natives and the American Indians of Maine separately discovered the poisonous activity of alcoholic extract of *Podophyllum* perennials [13]. The major ingredient of *Podophyllum peltatum* is podophyllotoxin (26). The alcoholic extract of the plant is called Podophyllin and is used in treatment of anogenital warts and nasal papillomas. The podophyllotoxin has a marked antitumor activity and it is in use in clinical preparations at present.

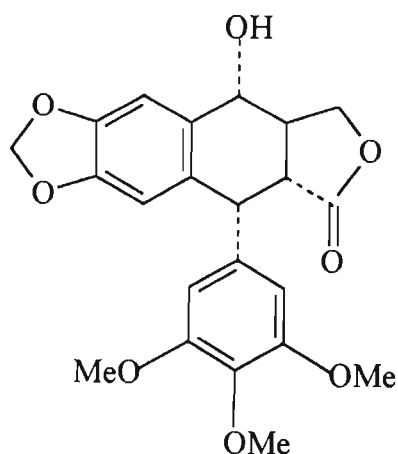


(24)

8,8' link



(25)

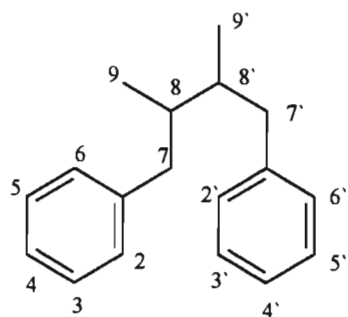


(26)

podophyllotoxin

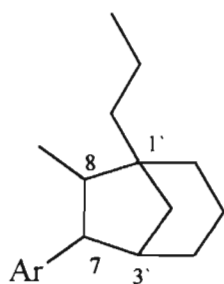
NUMBERING AND STRUCTURE

The neolignans have a diversity of structures, but basically they are part of a homogenous group of natural compounds. An example of an 8,8' lignan is **(24)**.

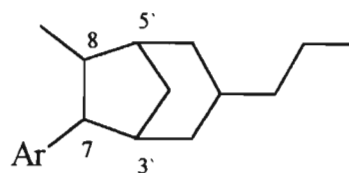


(24) 8,8' bond

Neolignans do have bonds other than 8,8' between their two units, examples given in Scheme 2.



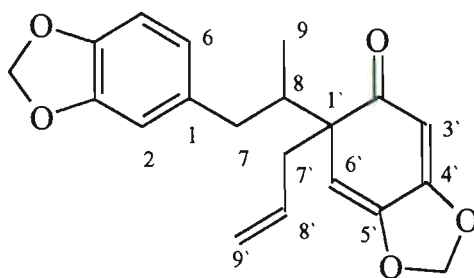
connecting bonds 7,3' and 8,1'



connecting bonds 7,3' and 8,5'

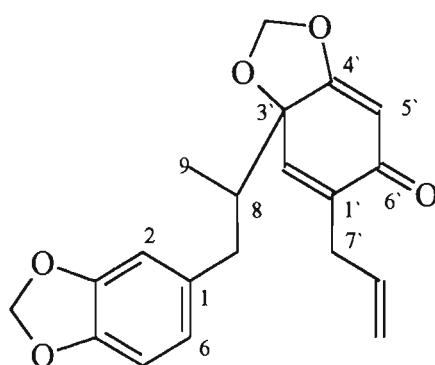
Scheme 2

The connection of the units to give a 8,1' linkage as in **(27)**, is the less common case. The most common neolignan is the 8,3' variety **(28)** [14].



(27)

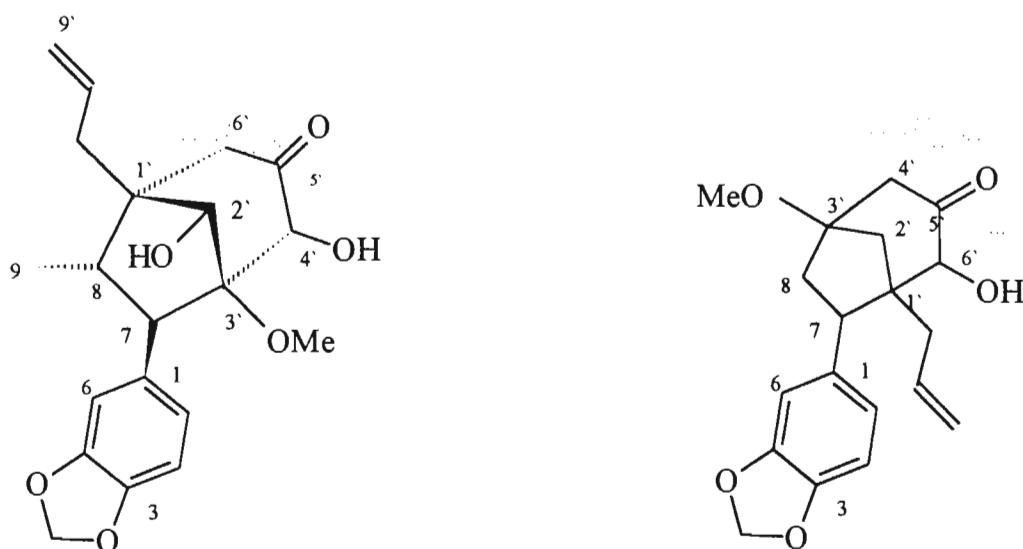
8,1' linkage



(28)

8,3' linkage

Another possibility of linkage gives rise to bicyclo [3,2,1] octanoids as seen in Scheme 2, in which the connecting bonds are as shown.



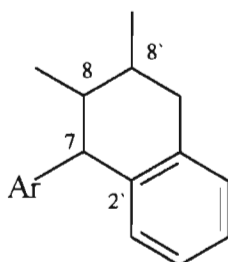
Connecting bonds 7,3' and 8,1'

Connecting bonds 7,1' and 8,3'

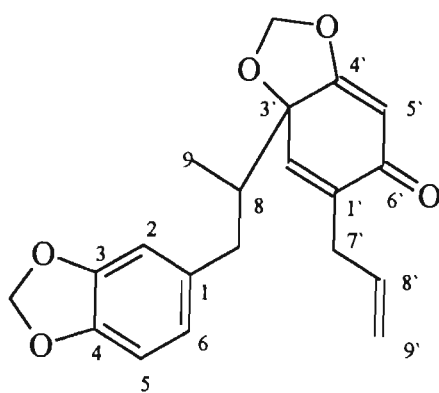
Scheme 3

These structures are formed when the C_6, C_3 and the C_6, C_3' units are doubly linked. There are two possible ways of linking as seen in the structures above. When the attachment of the carbon bearing the allyl group is to C-8 and thus forming the bicyclo system, the result is an 8,1' linkage. This is the less common case. Most common is the 8,3' linkage.

When numbering neolignans the first C_6, C_3 group is written on the lefthand side and labelled 1-9. The C_6, C_3' group is numbered with prime, 1'-9'. When the links between the units are direct links or oxygen linked, then the bridgehead position will receive the smallest possible number. For example: 7,2' and not 8,8'.



With the inclusion of the the substituents of the C_6 ring *e.g.* hydroxy, methoxy and methylenedioxy groups then the full name is complete. For example compound **(28)** is Δ 8'-3',6'-dihydro-3,4,3',4',-bis-methylenedioxy-6'-oxo-8,3' neolignan.

**(28)**

CHAPTER 2

DISCUSSION

Introduction

LAURACEAE

Species of Lauraceae family can be found in tropical and subtropical regions and over a wide range of temperature zones from Chile to southern Canada. Lauraceae species have been used for their timber as in the case of South African *Ocotea bullata*, Chinese *Persea nanmu* Oliv. and *Eusideroxylon zwageri* T. and B. from Indonesia. Edible fruit comes from avocado (*Persea americana* Miller), drugs (the coto bark) from *Aniba coto* (Kosterm), (demerara greenheart) drugs from *Ocotea rodiaei* Mez. from British Guyana and perfume oils from *Ocotea pretiosa* Mez from Brazil. The leaves of the bay *Laurus nobilis* L. were used by the ancient Greeks and Romans to make wreaths which were used to crown victorious warriors and athletes.

The ethnopharmacologist Lewin [21] asks: "In what mysterious way or with the aid of what instinct has man been able to select from the immense vegetable world the plant most suitable and desirable for his purposes?"

The Southern African *Lauraceae* species belonging to the *Ocotea* and *Cryptocarya* species have been used for traditional medicine, for their timber, and have a pleasant aroma and beauty. *Ocotea bullata* has been used for hundreds of years in traditional medicine, becoming very scarce as a result of intensive utilization. In 1974 it was declared a specially protected species in the province of Kwazulu-Natal. Ethnobotanists from Natal Parks Board and also Dr. A.T. Cunningham from (at that time) the Institute of Natural Resources observed in the late 1980's that traditional healers were substituting another species for *Ocotea bullata* for the same purpose (mostly magical). The alternative sources belong to the genus *Cryptocarya*, which is also part of the Lauraceae family.

Although *Ocotea bullata* has been known and used for so long, the chemical constituents have not been investigated until recently [16] in these laboratories.

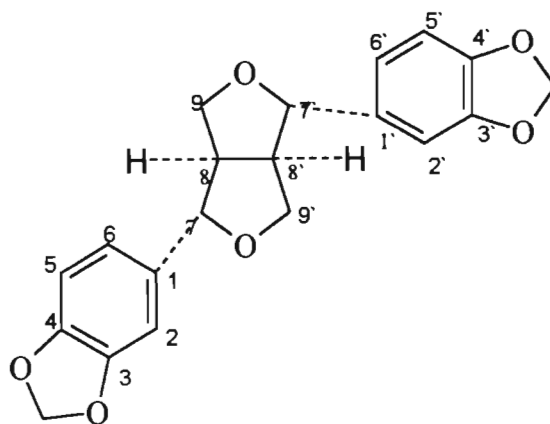
This fact, together with the shift of usage to *Cryptocarya* species, was the stimulus which provided the driving force for this investigation. Since the chemical constituents of these species are responsible for their biological activity, their isolation, characterisation and tests for biological activity could provide invaluable information both in traditional and conventional medicine. In addition it was hoped that comparison of the chemical constituents of *Ocotea bullata* with those in *Cryptocarya* species would show a chemical relationship thus “vindicating” the actions of the traditional healers.

The relationships in the family Lauraceae are shown in Table 1.

Family	LAURACEAE		
Genus	<i>Cryptocarya</i>	<i>Ocotea</i>	<i>Dahlgrenodendron</i>
Species	<i>liebertiana</i>	<i>bullata</i>	<i>natalense</i>
	<i>latifolia</i>	<i>usambarensis</i>	
	<i>wyliei</i>	<i>kenyensis</i>	
	<i>myrtifolia</i>		
	<i>woodii</i>		

Table 1

Ocotea usambarensis bark has been investigated by Carnmalm [19] and found to contain *d*-sesamin (29) as the major component. This finding was confirmed in these laboratories.



(29)

Dahlgrenodendron natalense (previous name *Beilschmiedia natalensis*) was also investigated in the present work. Preliminary findings indicate that it contains only one major component and that it does not belong to the α -pyrone nor to the neolignan class of compounds.

Cryptocarya woodii was investigated by Sehlapelo [16] and found to have traces of two 6-substituted pyrones.

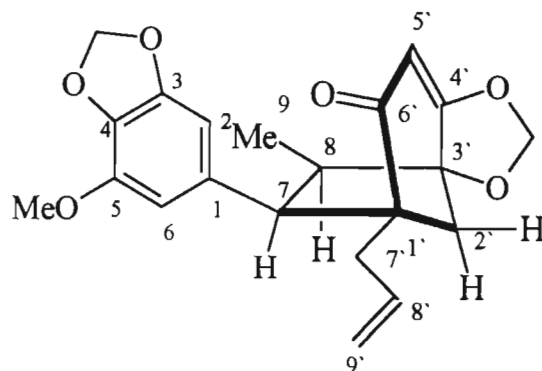
2.1. OCOTEA BULLATA

Distribution and uses.

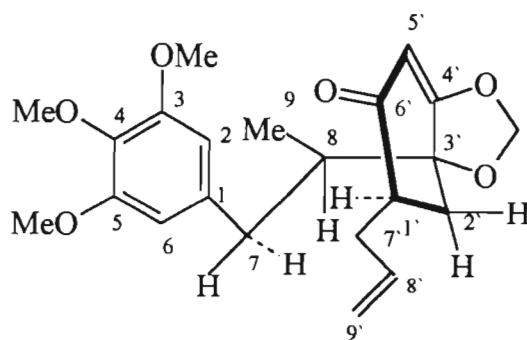
Ocotea bullata (black stinkwood, unukane). It is a tall evergreen tree (10-20 m) growing in the high forests of the Cape, Transkei, Natal midlands, Zululand, Swaziland and Mpumalanga. The leaves have characteristic raised hollow pockets "bubbles" (*bullata*). Ground bark is used for treatment of urinary infections when mixed with ginger and another muthi plant (called umahlabekufeni). The roots are used in a pulverized form when mixed with roots of *Secamone gerardii*, *Pterocelastrus rostratus* and *Sarcophyte sanguinea* and are applied to an incision made in the infected area of spinal disease. The bark is burned and the smoke snuffed or inhaled to treat headaches. Magic properties are attributed to this plant, for example it can operate as a charm to get a secure job or be lucky in one's love life.

Chemical constituents.

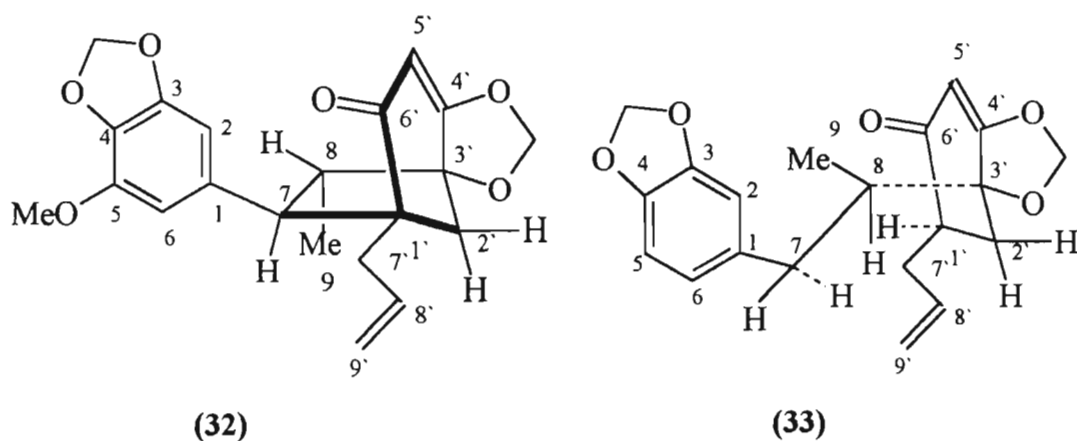
Ocotea bullata yielded four neolignans. *Rel*-(7*R*,8*R*,1'*R*,3'*R*)- Δ^8 -5-methoxy-3,4-methylenedioxy-3',4'-methylenedioxy-1',2',3',6'-tetrahydro-6'-oxo-7,1'.8,3'-neolignan (ocobullenone) (**30**) and Δ^8 -3,4,5-trimethoxy-3',6'-dihydro-3',4'-methylenedioxy-6'-oxo-8,3'-neolignan (bullatone) (**31**) have been isolated previously by Sehlapelo [16]. Two new neolignans have been isolated: a bicyclo [3.2.1] neolignan Δ^8 -5-methoxy-3,4-methylenedioxy-1',2',3',6'-tetrahydro-6'-oxo-7,1'.8,3'-neolignan named isoocobullenone (**32**) and Δ^8 -3,4-methylenedioxy-3',4'-methylenedioxy-1',2',3',6'-tetrahydro-6'-oxo-8,3'-neolignan (**33**) from the CHCl_3 extract of the bark.



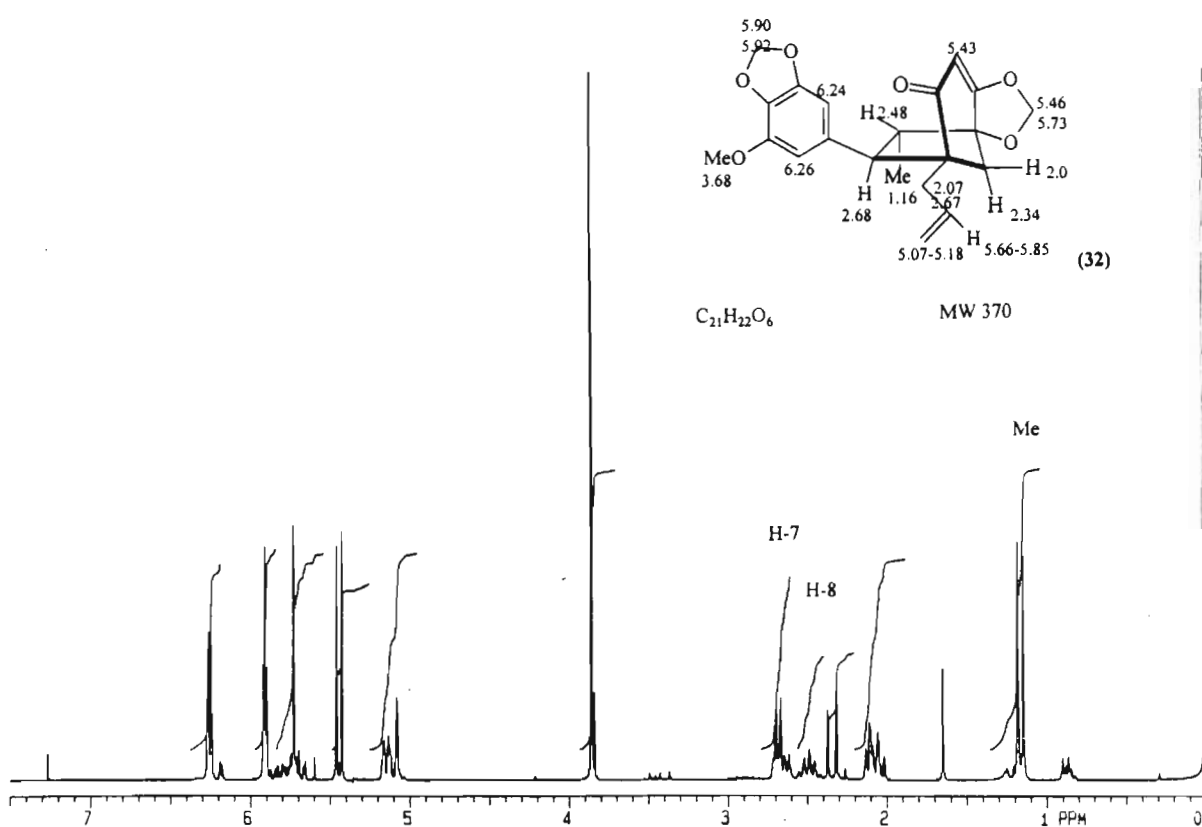
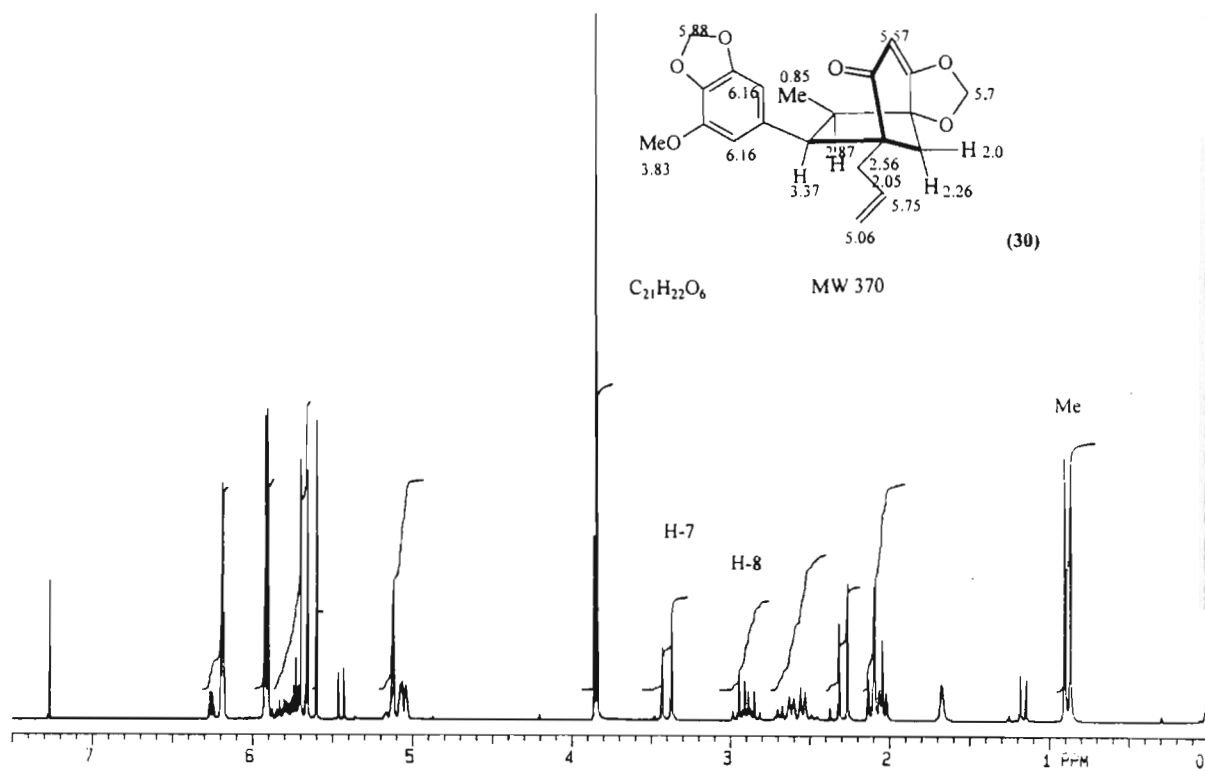
(30)



(31)

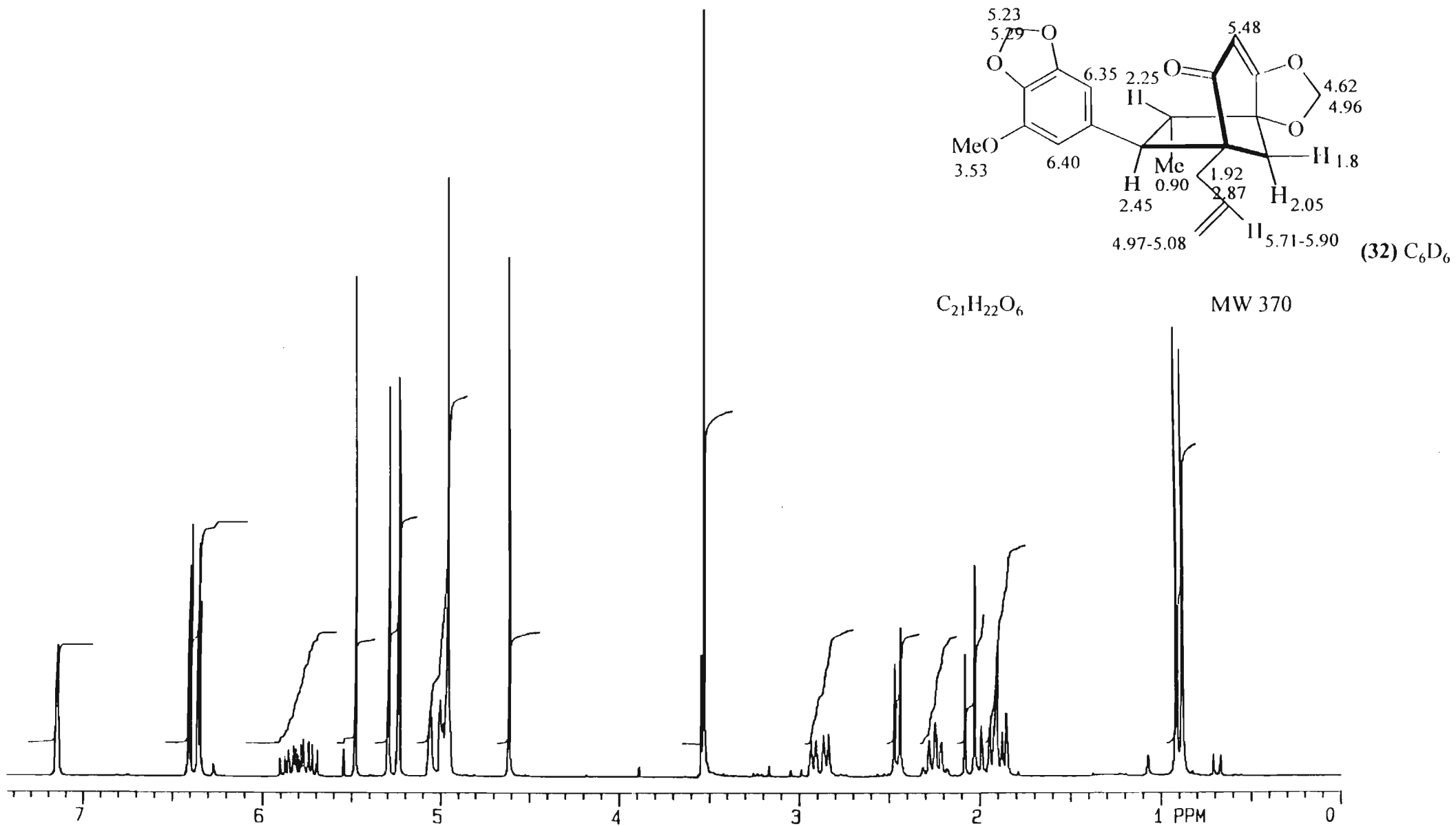


2.1.1. The isolation of isoocobullene (**32**) (Experimental, 3.1.1.) turned out to be a labour intensive task, due to its close chemical similarity to ocobullene *e.g.* they have almost identical R_f values on tlc. Isoocobullene eluted very close to ocobullene and repeated recycling of the impure isoocobullene (still containing traces of ocobullene) for chromatography was necessary. Comparison of ^1H NMR spectra of these two compounds run in CDCl_3 showed the differences were confined to the chemical shifts of the protons attached to C-7 and C-8 (see Insert 1). The differences in chemical shifts of the remaining protons were small. The same spectral data was compared using C_6D_6 as NMR solvent, where there was less of an overlap of peaks, facilitating allocation of protons (see Insert 2). GCMS showed that the $[\text{M}]^+$ was 370 mass units. HRMS confirmed the formula of $\text{C}_{21}\text{H}_{22}\text{O}_6$. The optical rotation of both compounds was positive, yet different in value. This led to the proposal that the compounds were diastereomers and this was confirmed by CD spectra which showed only a small difference in absorption at 226 nm (see Insert 3). X-Ray crystallography confirmed the proposed structure of isoocobullene (see Insert 4). From the crystal structure it was clear that ocobullene and isoocobullene had the same structure, with the configuration at three of the four stereocenters being identical. At C-8 the compounds have opposite configuration. In ocobullene, the C-9 methyl group, the benzene ring and the cyclohexanone ring all lie above the general plane of the cyclopentane ring, while in isoocobullene the methyl group is below the plane of the cyclopentane ring.

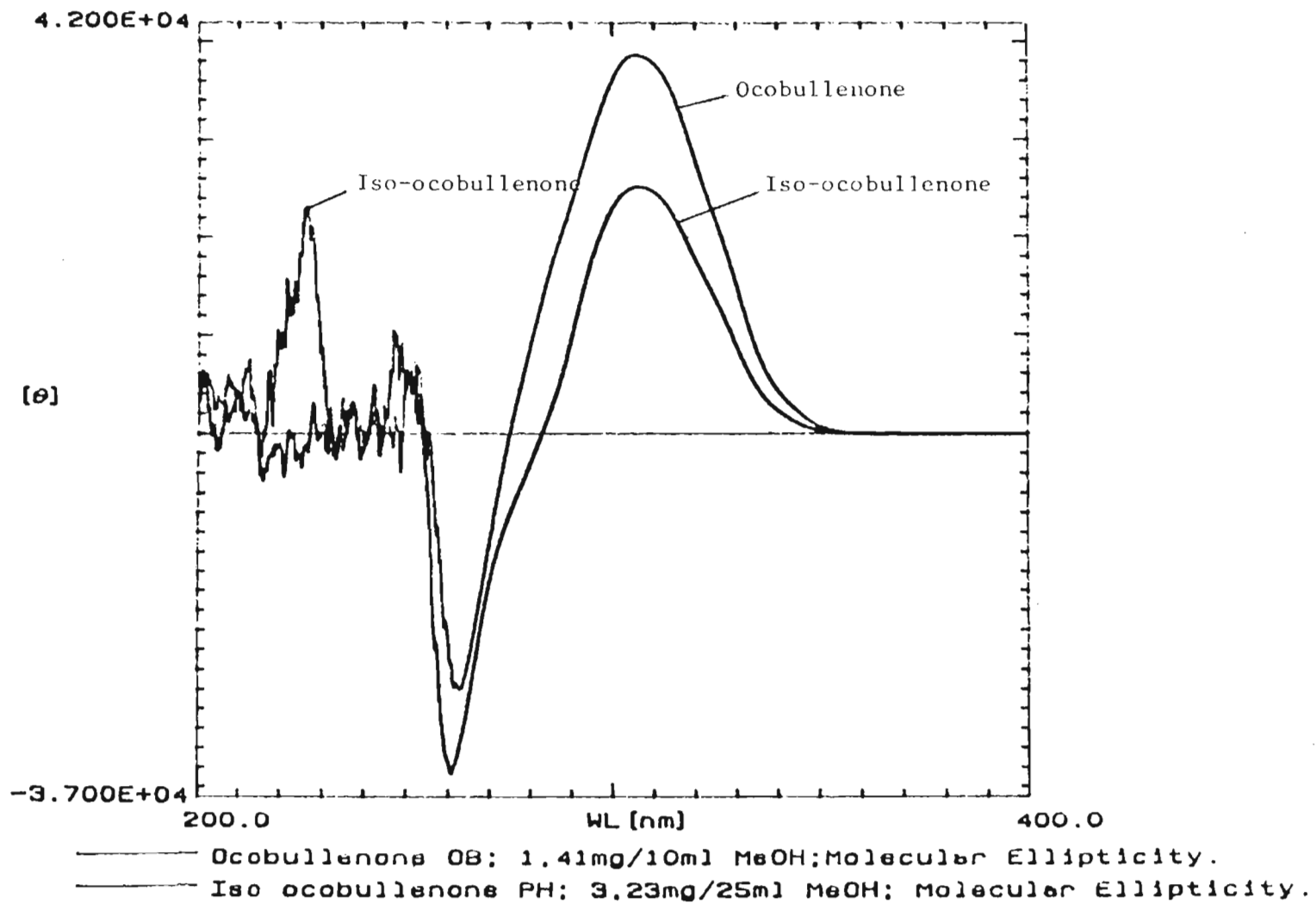


1H NMR in $CDCl_3$

Insert 1

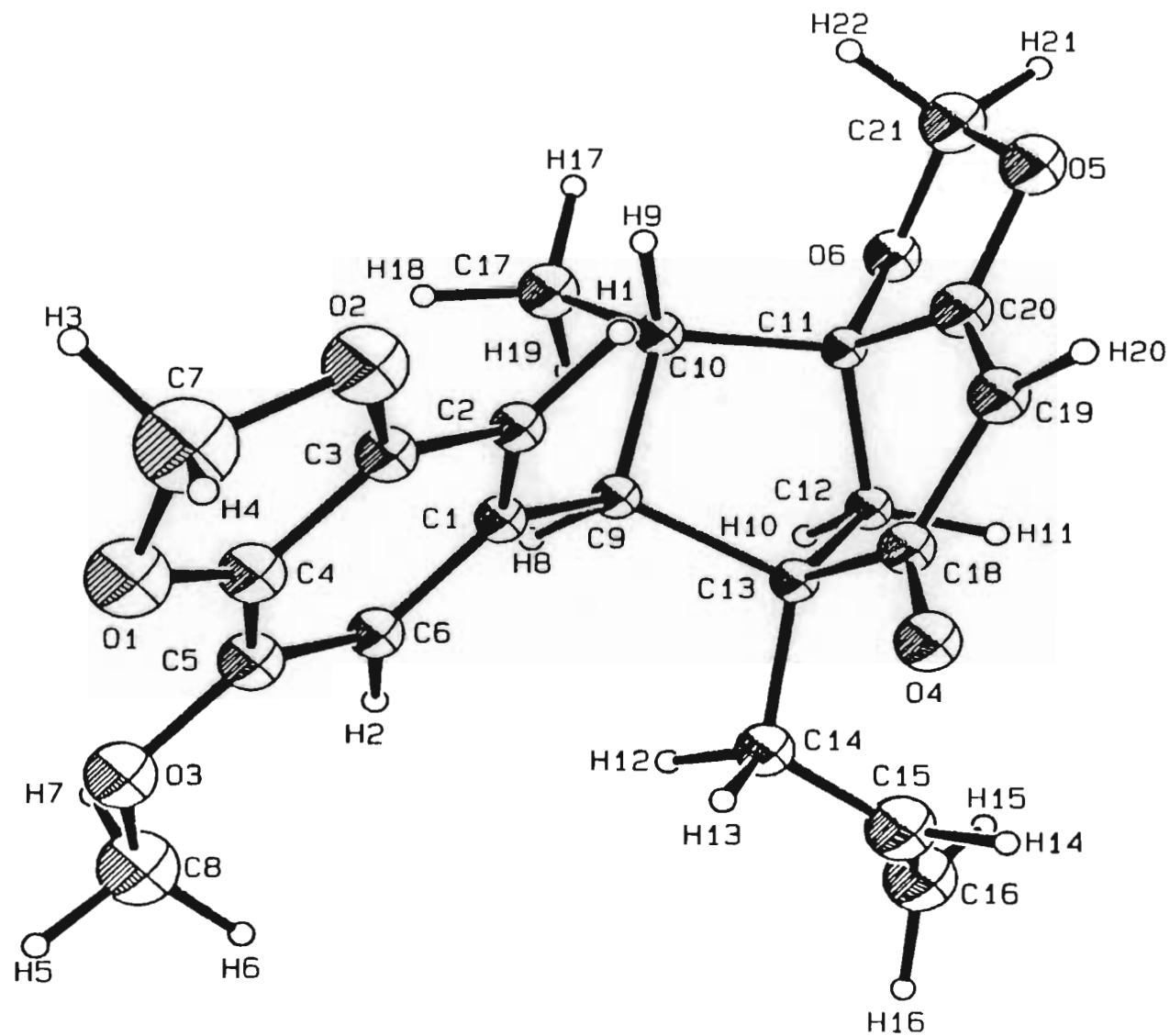


1H NMR of isocobullenone in C_6D_6

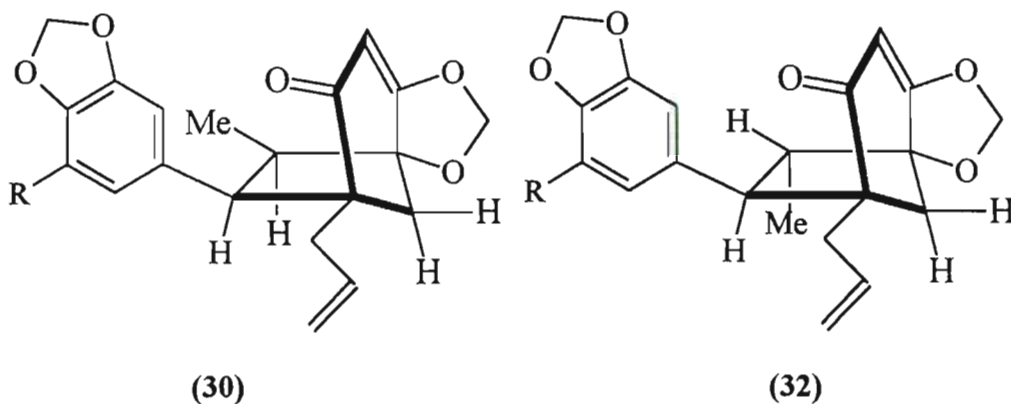


Circular dichroism spectra of ocobullenone (1) and iso-ocobullenone (2).

Insert 3

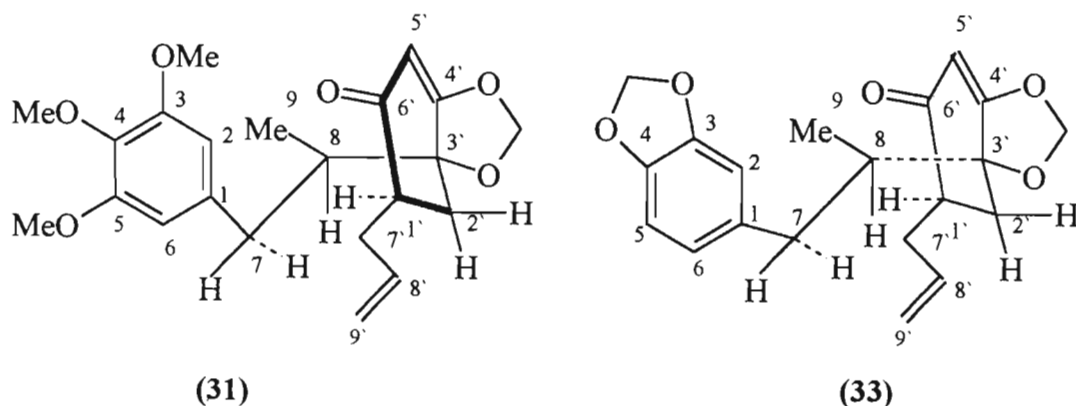


(32) X-Ray structure Note orientation of Me group on C-10



R=OMe

2.1.2. The structure of Δ^8 -3,4-methylenedioxy-3',4'-methylenedioxy-1',2',5',6'-tetrahydro-6'-oxo-8,3'-neolignan (33) (Experimental, 3.1.2.) was elucidated mainly by comparison with the structure of bullatone (31). The ^1H NMR spectra showed the absence of a OMe moiety and the presence of two protons each attached to both C-7 and C-1'. This led to the conclusion that the compound was a neolignan with a single linkage between the two arylpropanoid units at 8,3'. When the comparison with bullatone was done, the main difference was the absence of the OMe groups. GCMS gave $[\text{M}]^+$ 342 and HRMS confirmed the formula of $\text{C}_{20}\text{H}_{22}\text{O}_5$.



COMPARISON OF *OCOTEA BULLATA* SPECIES COLLECTED FROM DIFFERENT AREAS.

1. Bark and leaves were collected from a young tree growing in the Scottsville area of Pietermaritzburg. From the CHCl_3 extracts of both the bark and the leaves, ocobullenone

(30) was isolated and the presence of bullatone (31) was established by tlc spotting of the extracts.

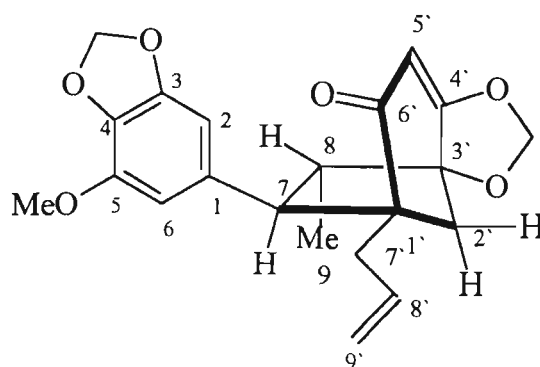
2. Bark, sapwood and heartwood of a mature tree growing in Weza forest in Southern Natal was investigated. An aliquot of each of the CHCl_3 extracts was subjected to GCMS analysis and showed the presence of ocobullenone (30), bullatone (31), isoocobullenone (32) and that of neolignan (33) in the bark and in the sapwood. The heartwood did not contain any of these compounds.

From this comparison it can be concluded that:

- there are no regional differences in the constituents,
- the components present in the bark are also found in the sapwood, but not in the heartwood.

Biological activity.

Isoocobullenone (32) was tested by The National Institute of Cancer in Washington D.C., U.S.A. against HIV and cancer. No activity was reported.



(32)

2.2. CRYPTO-CARYA LIEBERTIANA

Cryptocarya = “hidden nut” referring to calyx completely covering the fruit.

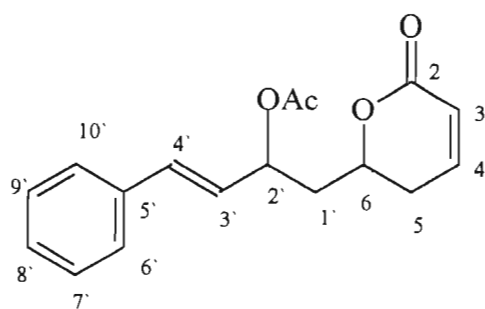
Distribution.

This species can be found from northern Kwazulu-Natal into tropical Africa.

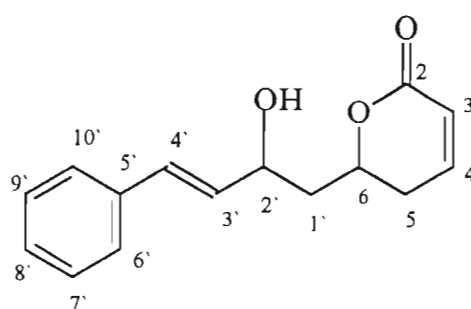
Chemical constituents.

Specimens of *Cryptocarya liebertiana* were collected at four different sites and each bark was screened for the chemical components.

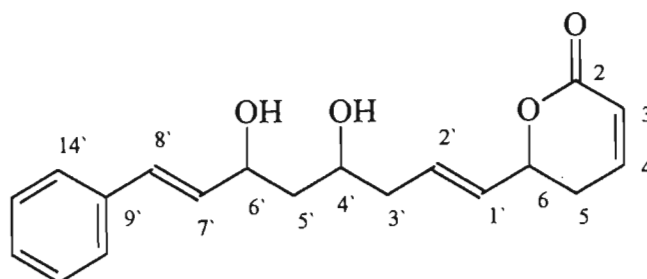
2.2.1.1. The sample collected from a tree growing in Ngoye forest in Natal was found to contain three known 6-substituted 5,6-dihydro- α -pyrones: 6-(2'-acetoxy-4'-phenylbuten-3'-yl)-5,6-dihydro-2H-pyran-2-one (cryptocaryalactone) [15] (34), 6-(2'-hydroxy-4'-phenylbuten-3'-yl)-5,6-dihydro-2H-pyran-2-one (deacetylcryptocaryalactone) (35) and 6-(4',6'-dihydroxy, 8'-phenyloct-1',7'-dienyl)-5,6-dihydro-2H-pyran-2-one (cryptofolione) (36).



(34)

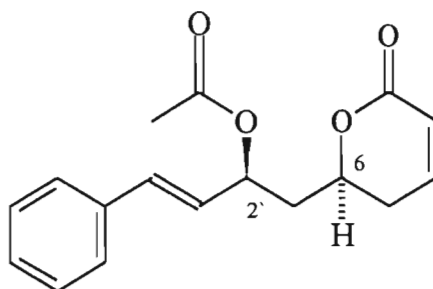


(35)



(36)

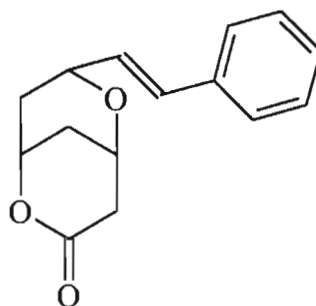
2.2.1.2. Cryptocaryalactone (34) was previously isolated from *Cryptocarya burdilloni* by Govindachari [15], reporting $[\alpha]_D^{25} +15.55^\circ$ and was also present in *Cryptocarya moshata* [2] reported by Spencer having $[\alpha]_D^{27} -20^\circ$. Cryptocaryalactone (34) isolated from the Ngoya specimen had (Experimental, 3.2.1.2.) $[\alpha]_D^{22} -19.7^\circ$. The identification was done on the basis of NMR data, showing very clearly the presence of the α -pyrone as well as the presence of the styryl moiety. The compound was synthesized by Meyer [22] (37), reporting a rotation of $+19^\circ$, and absolute configuration 6R, 2'S.



(37)

2.2.1.3. Deacetylcryptocaryalactone (35) was isolated from *Cryptocarya burdilloni* by Spencer [2], reporting $[\alpha]_D^{27} -94^\circ$. In the Ngoye specimen (Experimental, 3.2.1.3.) $[\alpha]_D^{22}$ was -82.1° . Deacetylcryptocaryalactone was acetylated (Experimental, 3.2.1.2.a.) to give cryptocaryalactone with $[\alpha]_D^{22} -16.8^\circ$. Similar acetylation was done by Spencer [2].

2.2.1.3a. ACTION OF BASE ON CRYPTOCARYALACTONE. The compound isolated from *Cryptocarya wyliei* cyclized under basic conditions to afford 7-styryl-2,6-dioxabicyclo [3,3,1] nonan-3-one.(48) (see section 2.4.4a.). The compound isolated from *Cryptocarya liebertiana* did not cyclize, but decomposed. This requires further investigation.

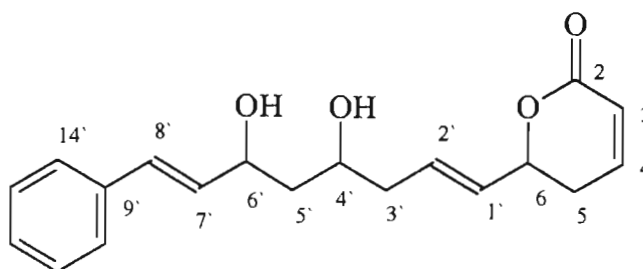


(48)

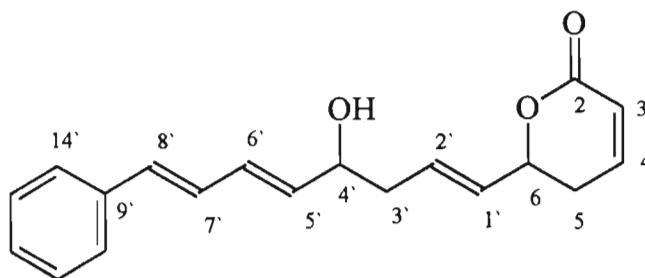
2.2.1.4. Cryptofolione (**36**) (Experimental, 3.2.1.4.) was identical by all spectroscopic data to the compound isolated by Sehlapelo [16] from *Cryptocarya latifolia* and from *Cryptocarya myrtifolia*. It was also present in *Cryptocarya wyliei* (see section 2.4.5.).

2.2.2. Bark from a mature *Cryptocarya liebertiana* tree growing in the Louis Trichardt area was investigated and found to contain two 6-substituted 5,6-dihydropyrones: cryptofolione (**36**) [16] and a new compound (+)-6-(4'-hydroxy-8'-phenyloct-1',5',7'-trienyl)-5,6-dihydro-2H-pyran-2-one (**38**). (liberfolione) C₁₉H₂₀O₃.

2.2.2.1. Liberfolione (Experimental, 3.2.2.1.) is the dehydration product of cryptofolione at the 5'-6' positions. The structure was deduced from comparison of NMR spectra with those of cryptofolione (see Table 2.)



(36)



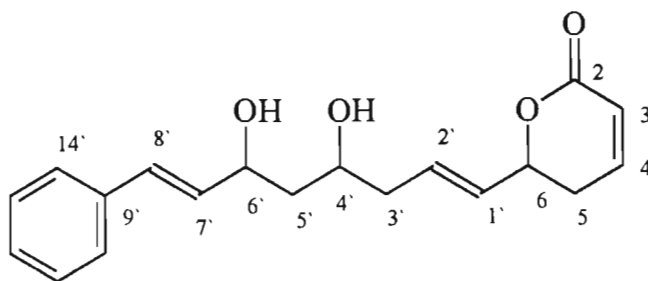
(38)

proton	(38)	(36)
H-3	6.03 <i>dt J</i> = 9.8, 1.9	6.00 <i>dt J</i> = 9.8, 1.6
H-4	6.86 <i>m</i>	6.83 <i>m</i>
H-5	2.30, 2.46 <i>m</i>	2.41 <i>m</i>
H-6	4.90 <i>q J</i> = 6.2	4.88 <i>m</i>
H-1'	5.66 <i>dd J</i> = 15.6, 6.2	5.63 <i>dd J</i> = 15.7, 6.3
H-2'	5.92 <i>m</i>	5.82 <i>m</i>
H-3'	2.30, 2.46 <i>m</i>	2.38 <i>m</i>
H-4'	4.30 <i>q J</i> = 6.3	4.05 <i>m</i>
H-5'	5.80 <i>m</i>	1.78 <i>m</i>
H-6'	6.35 <i>ddd J</i> = 15.2, 1.1	4.63 <i>m</i>
H-7'	6.76 <i>m</i>	6.23 <i>dd J</i> = 16.0, 5.8
H-8'	6.55 <i>d J</i> = 15.5	6.61 <i>dd J</i> = 16.0, 1.0

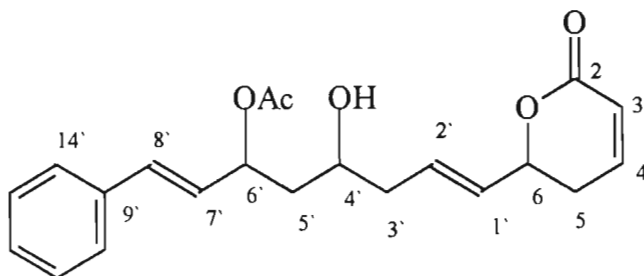
Table 2

Protons H-5' and H-6' of cryptofolione (**36**) have shifted downfield to 5.80 and 6.55 ppm respectively. Carbons C-5' and C-6' of cryptofolione have also shifted from 42.3 and 70.0 ppm to the sp^2 hybridized carbon region of 135.4 and 130.1 ppm respectively confirming the presence of a new double bond. The coupling constant of $J = 15.1$ Hz indicates the double bond to be *trans*. The compound was unstable, so that HRMS could not be done. GCMS gave $[M]^+$ 296 mass units.

2.2.3. Bark collected from a young tree of *Cryptocarya liebertiana* growing in Zimbabwe was found to contain (Experimental, 3.2.3.1.) two 6-substituted 5,6-dihydropyrones: cryptofolione (**36**) [16] and (+)-6-(6'-acetoxy-4'-hydroxy-8'-phenyloct-1',7'-dienyl)-5,6-dihydro-2H-pyran-2-one (called acetyl cryptofolione) (**39**).



(36)



(39)

2.2.3.1. The structure elucidation was done by comparison of NMR spectra of cryptofolione and acetyl cryptofolione (see Table 3.)

proton	(39)	(36)
H-3	6.03 <i>dt J</i> = 9.9, 1.9	6.00 <i>dt J</i> = 9.8, 1.6
H-4	6.87 <i>m</i>	6.83 <i>m</i>
H-5	2.48 <i>m</i>	2.41 <i>m</i>
H-6	4.90 <i>q J</i> = 6.8	4.88 <i>m</i>
H-1'	5.69 <i>m</i>	5.63 <i>dd J</i> = 15.7, 6.3
H-2'	5.89 <i>m</i>	5.82 <i>m</i>
H-3'	2.27 <i>t</i>	2.38 <i>m</i>
H-4'	3.68 <i>m</i>	4.05 <i>m</i>
H-5'	1.75 <i>m</i>	1.78 <i>m</i>
H-6'	5.69 <i>m</i>	4.63 <i>m</i>
H-7'	6.18 <i>dd J</i> = 15.9, 6.9	6.23 <i>dd J</i> = 16.0, 5.8
H-8'	6.62 <i>dd J</i> = 15.9, 7.0	6.61 <i>dd J</i> = 16.0, 1.0

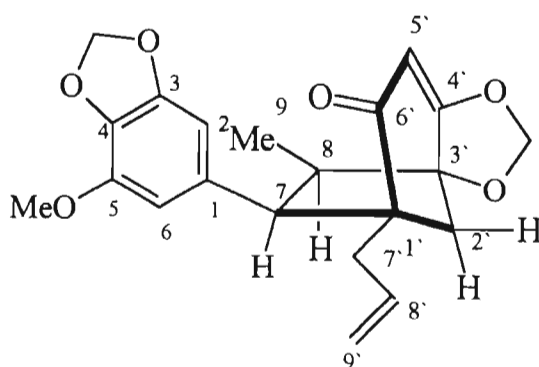
Table 3

The anticipated downfield signal shift of proton H-6' from 4.69 in cryptofolione (**36**) to 5.69 ppm and the new signal of acetyl group at 2.13 ppm confirms the structure of compound (**39**).

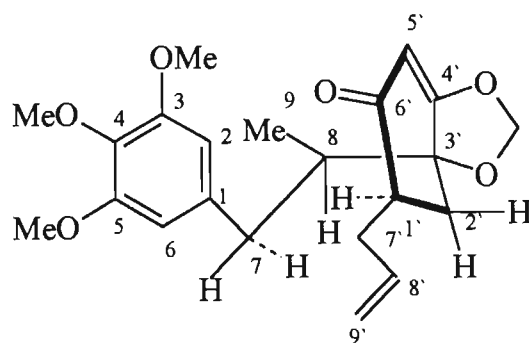
2.2.3.1a. The compound was also prepared from cryptofolione by acetylation (Experimental, 3.2.3.1a.) of cryptofolione. It resulted in a mixture of three compounds, two monoacetylated and one diacetylated cryptofolione. The NMR data of the naturally occurring and the synthetic compounds was identical, with a difference in the optical rotation, $[\alpha]_D^{22} +86.1^\circ$ for the naturally occurring one and $[\alpha]_D^{22} +101^\circ$ for the synthetic one.

2.2.4. Bark from a mature tree of *Cryptocarya liebertiana* growing in Zimbabwe in the same area as the immature one, was screened and found to contain no cryptofolione, but the two known neolignans isolated from *Ocotea bullata* [16]:

Δ^8 -5-methoxy-3,4-methylenedioxy-3',4'-methylenedioxy-1',2',5',6'-tetrahydro-6'-oxo-7,1'.8,3'-neolignan (ocobullenone) (**30**) [16] (experimental, 3.2.4.1.) and Δ^8 -3,4,5-methoxy-1',2',3',6'-tetrahydro-6'-oxo-8,3'-neolignan (bullatone) (**31**) [16] (Experimental, 3.2.4.2.).



(**30**)



(31)

The existence of this apparent phytochemical link between *Ocotea bullata* and *Cryptocarya liebertiana* was both unexpected and exciting. From the above mentioned information, regional variations of the constituents were observed, with cryptofolione being present in the specimen from Ngoye, Louis Trichard and in the bark of the young (immature) tree of *Cryptocarya liebertiana*. The latter was present both in the original and in the dehydrated and monoacetylated variations. From the previous investigation of other species of *Cryptocarya*, cryptofolione was isolated also from *Cryptocarya latifolia* [16], *Cryptocarya wyliei* and the compound was found in trace quantity in *Cryptocarya woodii* [16]. It certainly appears to be a phytochemical marker of the Southern African species. The absence of any 6-substituted-pyrones and the presence of the two neolignans in the above *Cryptocarya* species raises questions *e.g.* i) Does the cryptofolione present in the young bark and absent in the mature bark undergo transformation to ocobullenone and/or bullatone? ii) Do other Southern African *Cryptocarya* species perhaps contain mere traces of ocobullenone type neolignans? Only the screening of specimens collected from different regions and various stages of maturity of *Cryptocarya* species, will provide answers.

The spectral data of ocobullenone (30) and of bullatone (31) isolated from *Ocotea bullata* was identical to the data for the compound isolated from the mature bark of *Cryptocarya liebertiana* growing in Zimbabwe. The only differences are in the mp and rotations recorded. The “new” ocobullenone had a rotation of +158° (as opposed to +204°) and the mp was 136° (compared with 151°). This can be attributed to the presence of traces of isoocobullenone (32) (as seen in the ¹H NMR spectrum). The “new” bullatone was racemic and the mp was 128° (as opposed to 105°), but there is no doubt about the overall structure of these compounds and their relationship to one another.

2.3. CRYPTOARYA LATIFOLIA

Distribution and uses.

Cryptocarya latifolia (broad leafed quince, umhlangwenya.), is a tall forest tree (5-20 m) with spreading crown, growing along streams and rivers in Eastern Cape, Transkei and Zululand. When used for treatment of chest ailments, ground bark is mixed with crocodile fat. It is also used to treat muscular cramps and internal pains. Infusions made from finely ground bark are used in enemas, for urinary tract disease, uterine spasm and menstrual pain.

Chemical constituents.

Bark collected from mature tree growing in the Karkloof area, yielded on analysis seven 6-substituted α -pyrones (three new and four known):

6-(2'-acetoxihept-4'-enyl)-5,6-dihydro-2H-pyran-2-one (umuravumbolide isomer) **(40)**,

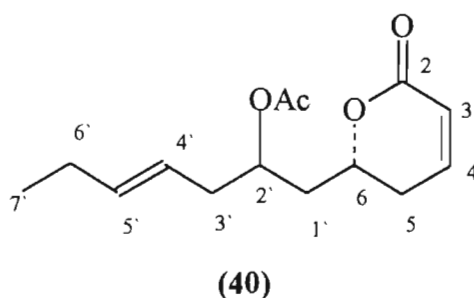
6-(2',4' diacetoxihept-5-enyl)-5,6-dihydro-2H-pyran-2-one **(41)**,

6-(4',6'-diacetoxi-2'-hydroxyheptyl)-5,6-dihydro-2H-pyran-2-one **(42)**,

6-(2',4'-diacetoxypentyl)-5,6-dihydro-2H-pyran-2-one (diacetate) [16] **(43)**,

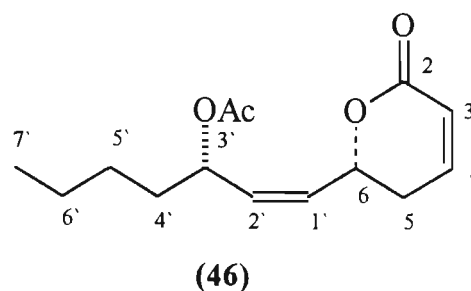
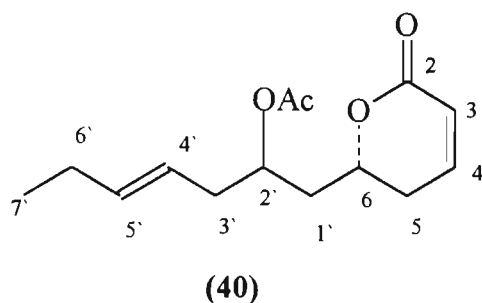
6-(2',4',6'-triacetoxiheptyl)-5,6-dihydro-2H-pyran-2-one (triacetate) [16] **(44)**,

6-styryl-5,6-dihydro-2H-pyran-2-one (goniothalamine) [17] **(45)** and cryptofolione [16] **(36)**.

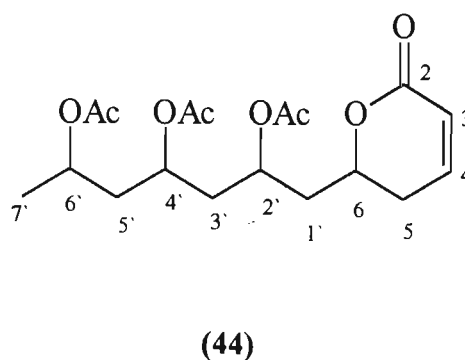
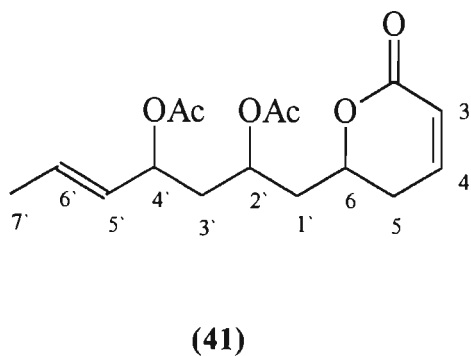


2.3.1. Structure elucidation of umuravumbolide isomer **(40)** (Experimental 3.3.1.) was done with the help of the ^1H NMR, ^{13}C NMR and DEPT. The presence of 6-substituted α -

pyrone was deduced from the presence of H-3 resonating at 6.02 ppm, H-4 resonating at 6.87 ppm, the lactone carbonyl C-2 at 164.0 ppm and the carbonyl IR signal at 1720 cm^{-1} . The protons attached to the sp^2 carbons at 5.31 and 5.56 ppm respectively indicated the presence of a double bond in the heptyl side chain. In the DEPT it was shown that there were four CH_2 groups. HR MS confirmed the formula of $\text{C}_{14}\text{H}_{20}\text{O}_4$. The spectral data were compared to those of umuravumbolide [4] **(46)**. The differences between the two compounds are in the position of the double bond in the heptyl side chain and in the position of the acetoxy group.



2.3.2. The structure of *6-(2',4' diacetoxyhept-5-enyl)-5,6-dihydro-2H-pyran-2-one* **(41)** was deduced by comparison to triacetate **(44)** (Experimental, 3.3.2.) (see Table 4.)

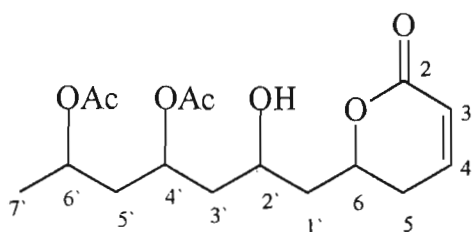


proton	(41)	(44)
H-3	6.02 <i>dq</i> $J = 9.7, 6.7$	6.01 <i>ddd</i> $J = 9.8, 2.5, 1.1$
H-4	6.88 <i>m</i>	6.89 <i>ddd</i> $J = 9.8, 5.7, 2.8$
H-5	2.20, 2.35 <i>m</i>	2.40 <i>m</i>
H-6	4.50 <i>m</i>	4.49 <i>dddd</i> $J = 11.6, 6.4, 4.0$
H-1'	1.95, 2.15 <i>m</i>	2.15 <i>m</i>
H-2'	5.06 <i>m</i>	4.83-5.13 <i>m</i>
H-3'	1.85 <i>m</i>	1.77 <i>m</i>
H-4'	5.27 <i>q</i> $J = 6.7$	4.83-5.13 <i>m</i>
H-5'	5.38 <i>ddd</i> $J = 14.9, 7.5, 1.6$	1.99 <i>m</i>
H-6'	5.73 <i>m</i>	4.83-5.14 <i>m</i>
H-7'	1.70 <i>dd</i> $J = 7.5, 1.1$ Me	1.23 <i>d</i> $J = 6.2$ Me

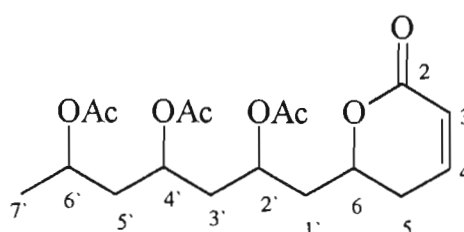
Table 4

The presence of the double bond on the heptyl side chain was deduced from the proton signals at 5.38 (H-5') and 5.73 (H-6') ppm, that were shifted from 1.99 (H-5') and 4.83-5.14 (H-6') ppm respectively. The correlation of the above protons as shown in the HETCOR was to the carbons resonating at 130.4 and 128.4 ppm respectively. The chemical shift of 1.70 ppm for the terminal Me group indicated it to be adjacent to the double bond.

2.3.3. The structure of (42) (Experimental, 3.3.3.) was deduced from comparison to triacetate (44), (see Table 5.) and was proved by derivatization (Experimental, 3.3.3a.).



(42)



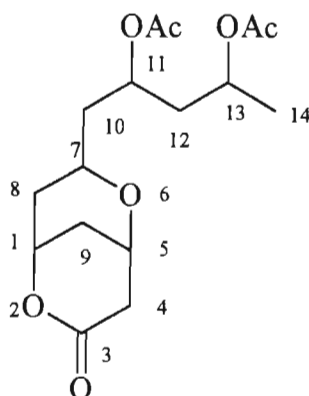
(44)

proton	(42)	(44)
H-3	6.03 <i>dt</i> $J=9.8, 1.8$	6.01 <i>ddd</i> $J=9.8, 2.5, 1.1$
H-4	6.90 <i>m</i> $J=9.8$	6.89 <i>ddd</i> $J=9.8, 5.7, 2.8$
H-5	1.80 <i>m</i>	2.40 <i>m</i>
H-6	3.8-3.9 <i>bm</i>	4.49 <i>dddd</i> $J=11.6, 6.4, 4.0$
H-1'	2.40 <i>m</i>	2.15 <i>m</i>
H-2'	4.95-5.22 <i>m</i>	4.83-5.13 <i>m</i>
H-3'	1.80 <i>m</i>	1.77 <i>m</i>
H-4'	4.55-4.65 <i>m</i>	4.83-5.13 <i>m</i>
H-5'	1.80 <i>m</i>	1.99 <i>m</i>
H-6'	4.95-5.22 <i>m</i>	4.83-5.14 <i>m</i>
H-7'	1.24 <i>m</i> Me	1.23 <i>d</i> $J=6.2$ Me

Table 5

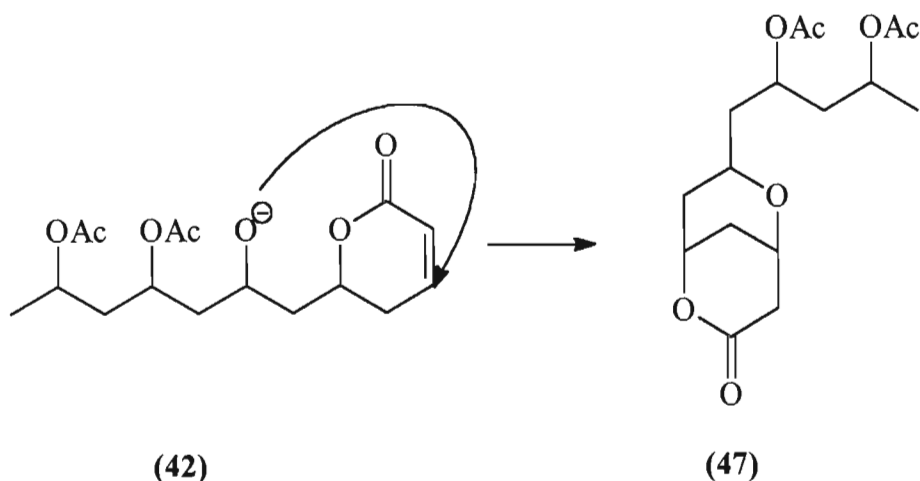
The upfield shift of proton H-2' in the triacetate (44) from 4.49 and ppm to 3.8-3.9 ppm indicated the presence an OH group linked to the same carbon as H-2'. Only two acetate signals were present in (42) compared to three in triacetate.

2.3.3a. CYCLIZATION OF (42) (Experimental, 3.3.3a.) to afford 7-(11, 13 Diacetoxypentyl)-2,6 dioxabicyclo[3,3,1] nonan-3-one [16] (47).



(47)

The mechanism of the cyclization is that of an intramolecular Michael type 1,4 addition taking place in basic environment with oxygen attacking C-4 of the pyrone ring, thus forming a bicyclo system. Compound (47) was isolated previously from this plant by Sehlapelo [16]. ^1H NMR and ^{13}C NMR data were identical to those for the compound isolated by Sehlapelo. The synthetic analogue had a rotation of $[\alpha]_{\text{D}}^{22} -21.7^\circ$ as opposed to -145° in the naturally-occurring compound.



Since **(42)** could only be isolated in an impure state, the cyclization confirmed the suggested structure.

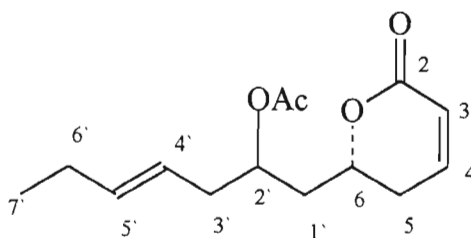
2.3.4. Diacetate **(43)** (Experimental, 3.3.4.) was identical to the one previously isolated by Sehlapelo [16].

2.3.5. Triacetate **(44)** (Experimental, 3.3.5.) was identical to the one previously isolated by Sehlapelo [16].

2.3.6 Goniotalamin **(45)** [17] (Experimental, 3.3.6.) was identical to the compound described in the literature.

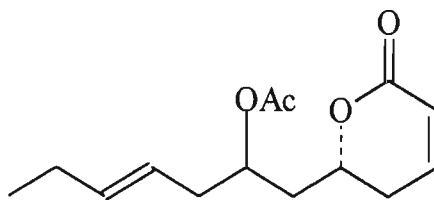
2.3.7 Cryptofolione **(36)** [16] (Experimental, 3.3.7.) was identical to the one isolated by Sehlapelo [16] and to the compounds present in *Cryptocarya liebertiana* (Ngoye, Louis Trichard and immature Zimbabwe specimen).

Biological activity.



(40)

Umuravumbolide (46) was reported by Van Puyvelde [4] to be active against *Pseudomonas* species on potatoes. The isomer of umuravumbolide (40) was tested by the Department of Microbiology and Plant Physiology at University of Natal, Pietermaritzburg for activity against *Pseudomonas* species. No growth inhibition was observed in well or in disk application.



(40)

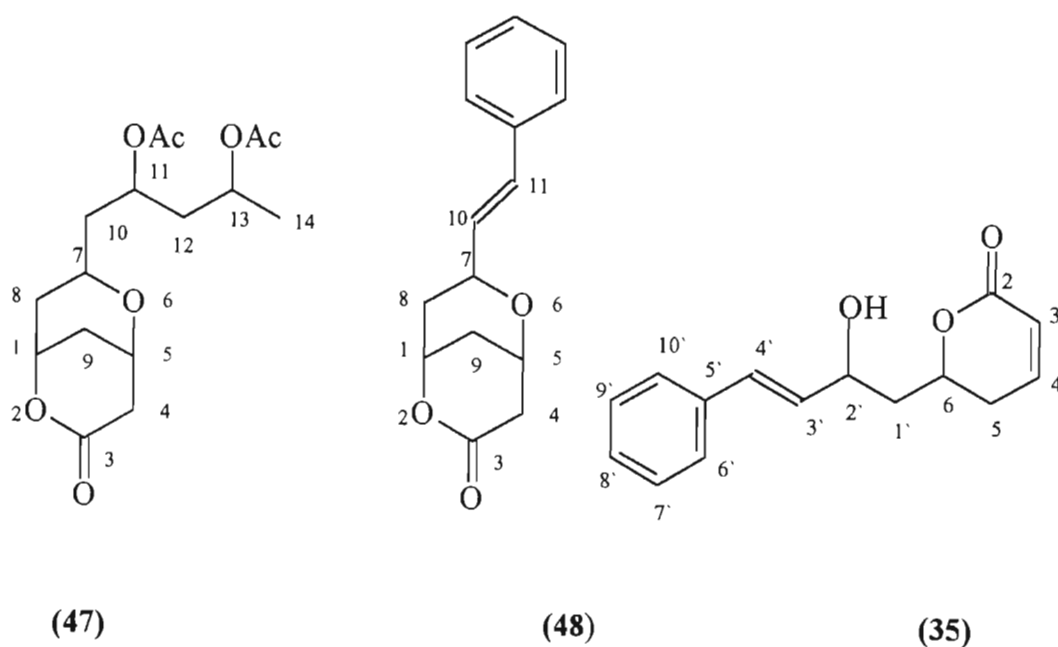
2.4. CRYPTO-CARYA WYLIEI

Distribution

It is a shrub or small tree (2-6m), endemic to Natal Group Sandstones with scattered distribution in forests of Kwazulu-Natal and Transkei.

The bark yielded upon investigation five 6-substituted pyrones (one new and four known): 7-styryl-2,6-dioxabicyclo-[3,3,1] nonan-3-one (**48**) (Experimental, 3.4.1.), goniotalamin (**45**) (Experimental, 3.4.2.) [17], cryptocaryalactone (**34**) (Experimental, 3.4.3.) [15], deacetylcryptocaryalactone (**35**) (Experimental 3.4.4.) [2], cryptofolione (**36**) (experimental, 3.4.5.) [16].

2.4.1. The structure of (**48**) was deduced by comparison of NMR spectra with those of deacetylcryptocaryalactone (**35**) and 7-(11, 13 diacetoxypentyl)-2,6 dioxabicyclo[3,3,1] nonan-3-one [16] (**47**).



The proton chemical shifts of all three compounds are listed in Table 6.

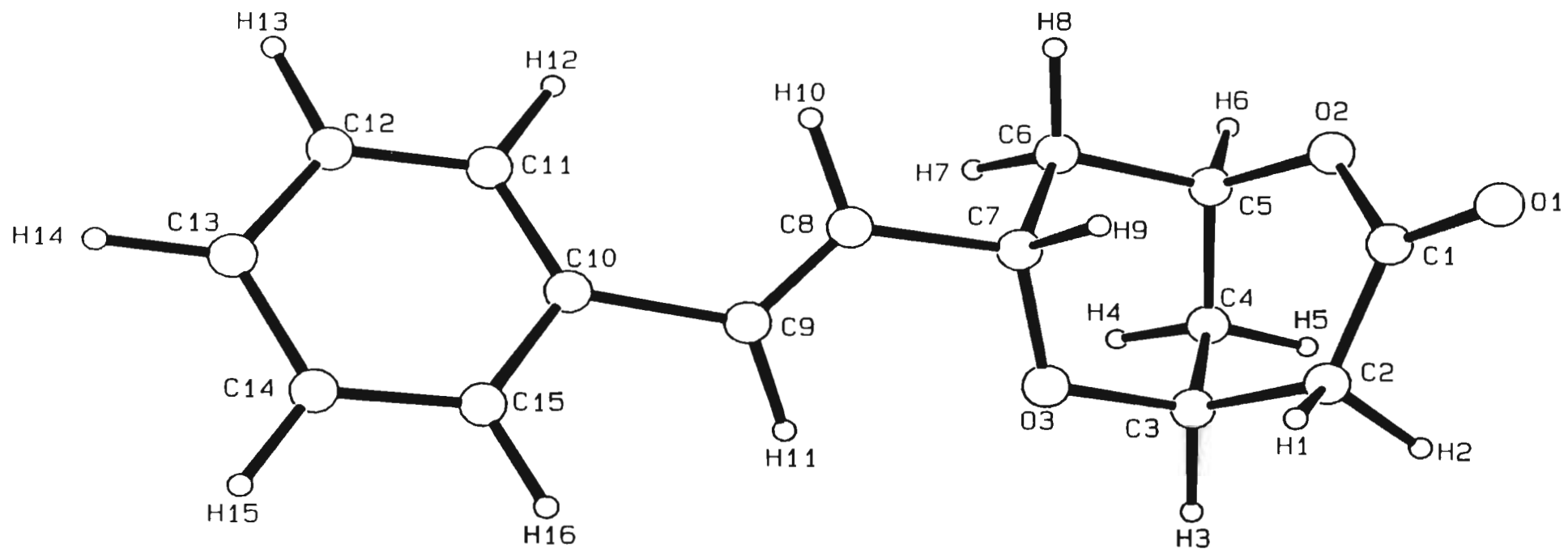
proton	(47)	(48)	proton	(35)
H - 4	2.81 <i>m</i>	2.83, 2.98 <i>dd J</i> 19.3	H-3	5.98 <i>m</i>
H - 5	4.90 <i>m</i>	4.45 <i>m</i>	H-4	6.85 <i>m</i>
H - 9	1.50-1.95 <i>m</i>	1.99 <i>m</i>	H-5	2.41 <i>m</i>
H - 1	4.33 <i>bs</i>	4.95 <i>m</i>	H-6	4.59 <i>m</i>
H - 8	1.50-1.95 <i>m</i>	1.77, 2.14 <i>ddd J</i> 14	H-1'	1.90, 2.20 <i>m</i>
H - 7	3.87 <i>m</i>	4.45 <i>m</i>	H-2'	4.59 <i>m</i>
H-10	1.50-1.95 <i>m</i>	6.14 <i>dd J</i> = 16, 6.1	H-3'	6.18 <i>dd J</i> = 15.9, 7.0
H-11	5.09 <i>m</i>	6.64 <i>dd J</i> = 16, 1.1	H-4'	6.63 <i>dd J</i> = 15.9

Table 6

The numbering of course did change for the bicyclic compounds and the comparison is done for the protons in all three compounds. The signals for H-3 and H-4 in deacetylcryptocaryalactone (35) have shifted upfield in (48) and they are not part of a double bond system any longer. There was only a slight change in the shifts of H-3' and H-4', their position has been retained. When comparing the two bicyclo compounds (47) and (48), protons H-4, H-5, H-9, H-1, H-8 and H-7 have similar chemical shift values, the two rings are the same, only the substituents at position 7 are different. HR-MS: $[M]^+$ 244.1086; calcd. for $C_{15}H_{16}O_3$ 244.1099 confirmed the proposed formula and crystal structure (see Insert 5) proved the structure.

2.4.2. The goniotalamin (45) isolated (Experimental, 3.2.2.) was identical in all aspects to the literature [17].

2.4.3. The cryptocaryalactone (34) isolated (Experimental, 3.4.3.) had a positive rotation of $+56.3^\circ$ compared to the one isolated from *Cryptocarya liebertiana* (Ngoye specimen) (see section 2.2.1.2.) that had negative rotation -19.7° . All other data were identical to the literature [15].



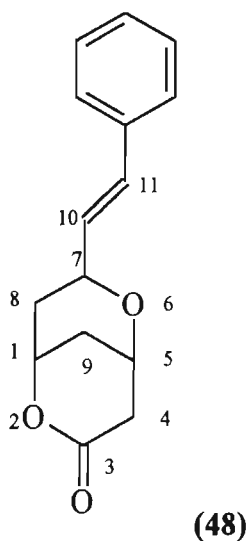
Crystal structure of 7-styryl-2,6-dioxabicyclo [3,3,1] nonan-3-one (48)

Insert 5

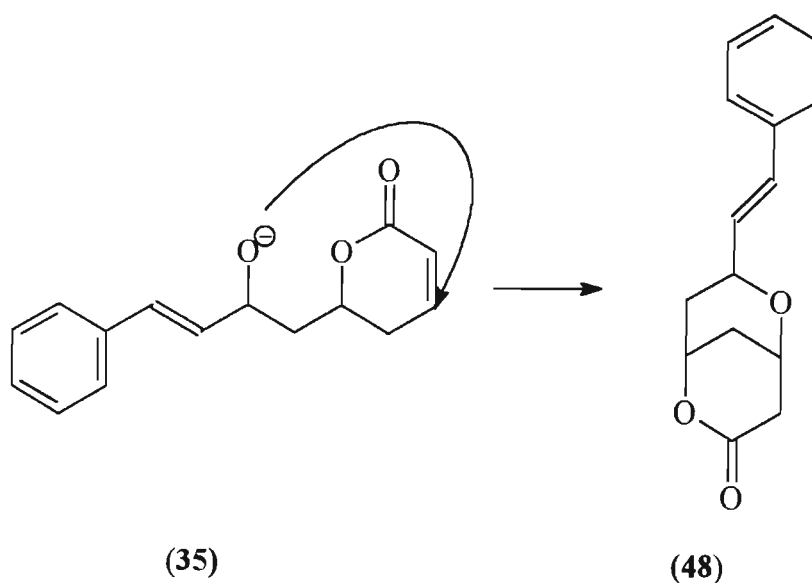
2.4.4. The deacetylcryptocaryalactone (**35**) isolated (Experimental 3.4.4.) was racemic, compared to the literature [2] -94° , and -82.1° in *Cryptocarya liebertiana* (Ngoye specimen) (see section 2.2.1.3.).

2.4.5. Cryptofolione (**36**) was identical to the literature [16].

2.4.4a. CYCLIZATION OF DEACETYLCRYPTOCARYALACTONE (Experimental, 3.4.4a.) to afford 7-styryl-2,6-dioxabicyclo [3,3,1] nonan-3-one. (**48**)



The mechanism is that of an intramolecular Michael type 1,4 addition, under basic conditions, similar to the one of 6-(4',6',-diacetoxy-2'-hydroxyheptyl)-5,6,-dihydro-2H-pyran-2-one (**42**), described in section 2.3.3a.



The naturally occurring and the synthetic compounds (**48**) were identical.

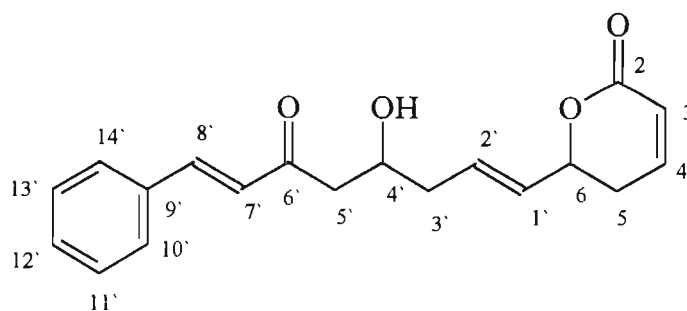
2.5. *CRYPTOCARYA MYRTIFOLIA* Stapf.

Distribution and uses.

Cryptocarya myrtifolia (camphor tree, igqeba, umngqabe) is a medium to tall tree (10-20 m) with scattered distribution in evergreen forests in Eastern Cape, Transkei and Kwazulu-Natal. Bark, twig and leaves smell of camphor. The bark is used as a substitute for *Ocotea bullata*.

Upon investigation two 6-substituted α -pyrones (one new and one known) were isolated: 6-(-4'-hydroxy-6'-oxo-8'-phenyloct-1',7'-dienyl)-5,6-dihydro-2H-pyran-2-one (**49**) and cryptofolione (**36**).

2.5.1. Compound (**49**) was very similar to cryptofolione. When NMR data of (**49**) were compared to cryptofolione, H-6' was absent, H-7' had shifted downfield from 6.23 to 7.57 ppm and C-6' was shifted from 70.0 to 200.5 ppm in the ^{13}C NMR spectrum. Although after repeated chromatographic separations (Experimental, 3.5.1.) it was still in an impure state the structure was identical to the synthetically derived oxidation product of cryptofolione [16].

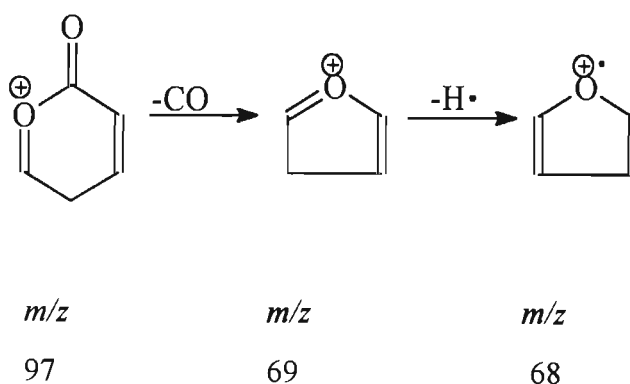


(**49**)

2.5.2. Cryptofolione (**36**) (Experimental, 3.5.2.) isolated from this plant was identical to the one isolated from the other *Cryptocarya* species.

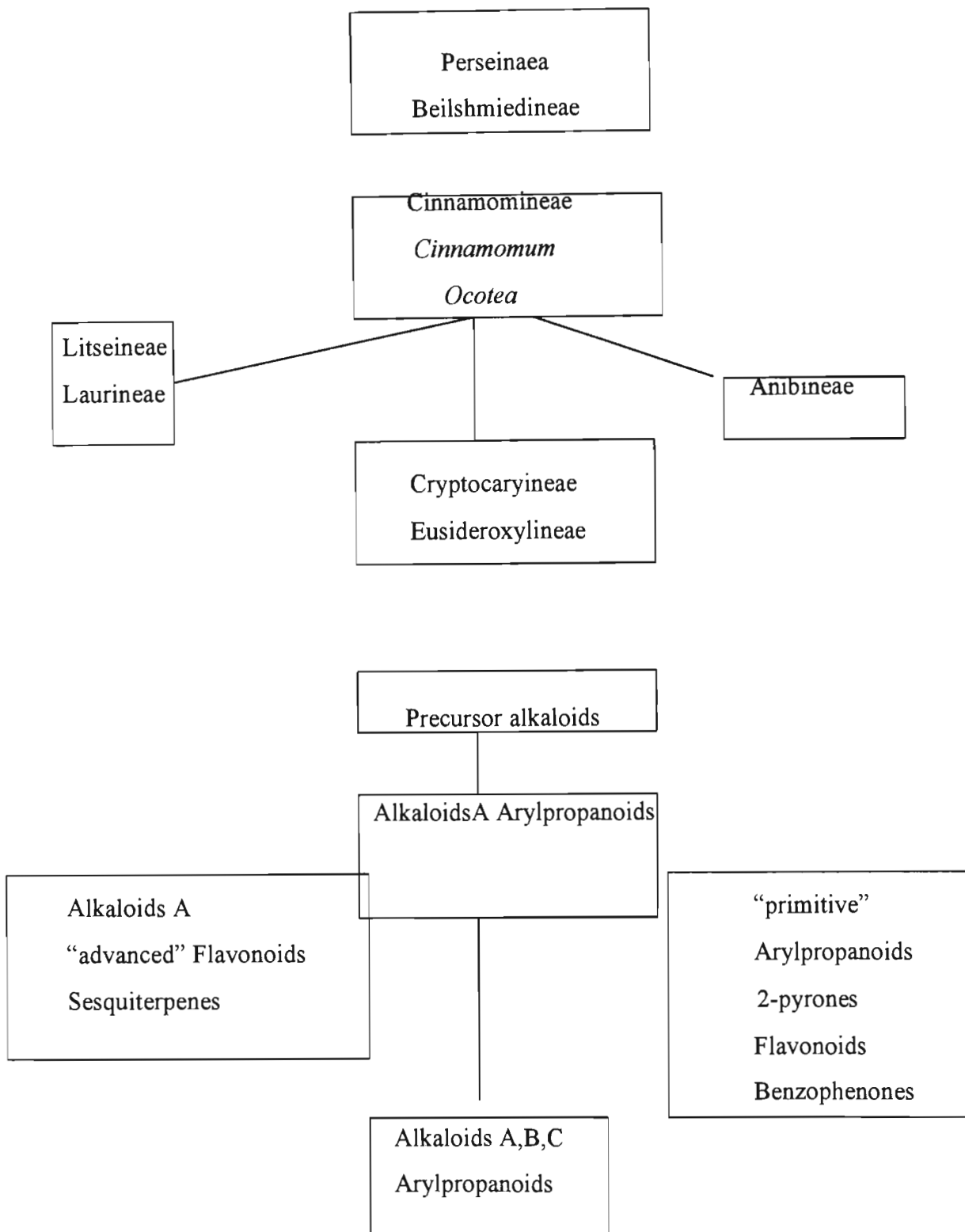
Summary.

Pyrones and neolignans are widely distributed among the different Lauraceae species [1]. Davies-Coleman [5] in his review summarised characteristic features of the naturally occurring 6-substituted α -pyrones. The compounds investigated were in accordance with those findings. In the ^1H NMR spectra, H-3 appears as a doublet of triplets at a chemical shift of 5.9-6.1 and is coupled to H-4 ($J = 9.7$ -10 Hz). This indicates the presence of a *cis* double bond next to a carbonyl. H-3 is also coupled to H-5 ($J = 2$ -6). In the ^{13}C NMR, C-2 is usually around 160-169 ppm and C-4 around 144-148 ppm. When examining the mass fragmentation of these pyrones there are 2 characteristic fragments of m/z 97 and m/z 68 that are formed from the cleavage of the side chain which was originally attached at position 6 to the ring.



In the IR spectrum the $\alpha\beta$ -unsaturated carbonyl group has a strong absorption band at 1710 - 1730 cm^{-1} . The absorption of the lactone double bond gives a much weaker signal around 1590 - 1640 cm^{-1} .

Gottlieb [1] in his review summarized the classification done by Kostermans for chronological evolution of subtribes of Lauraceae and the proposed chemical interrelationships, as shown in the following diagrams.



The question arises whether these interrelationships shed some light on the coexistence of 2-pyrones and neolignans.

Conclusions.

In the *Cryptocarya* species screened, cryptofolione (**36**) appears to be a phytochemical marker, present in all but the mature *Cryptocarya liebertiana* specimen from Zimbabwe. Cryptofolione in the species studied appears in the unchanged and in the derivatized form: e.g. dehydrated, acetylated and oxidized.

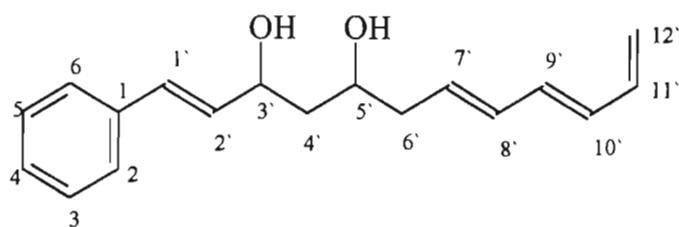
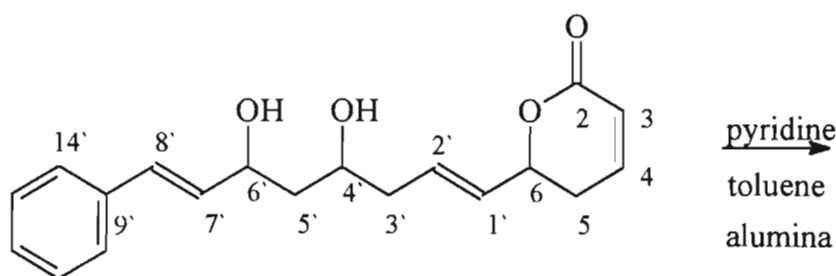
In more general terms, it can be said that these species are a rich source of 6-substituted 5,6- α -pyrones. In *Cryptocarya latifolia* diacetate (**43**) and triacetate (**44**) were present in high concentrations. There is a high degree of similarity between these compounds and cryptofolione. In the latter, the side chain substituted at the 6 position of the pyrone ring is a phenyloctyl one, while in diacetate (**43**) it is pentyl, in triacetate (**44**) and related compounds (**40**), (**41**) and (**42**) is heptyl.

The neolignans present in *Ocotea bullata* and in bark of mature *Cryptocarya liebertiana* together with the presence of cryptofolione in bark of young *Cryptocarya liebertiana* seem to be the connecting link between the *Ocotea* and *Cryptocarya* species investigated. This makes substitution of *Cryptocarya* for *Ocotea* species by the traditional healers a plausible one. Further investigation into biological activity of the various compounds isolated could strengthen these findings.

2.6. NOVEL REACTIONS OF α -PYRONES.

In an attempt to prepare the dehydrated cryptofolione (**49**) from cryptofolione a reaction was done using pyridine in the presence of activated alumina. The dehydration did not occur, instead a degradation of the pyrone ring involving loss of CO₂ took place. This sequence of events is discussed below.

2.6.1. Cryptofolione (**36**) was refluxed in toluene with pyridine, over activated neutral alumina. A novel reaction occurred and the pyrone ring was opened with loss of CO₂ to afford 3',5' dihydroxy-1',7',9',11' dodecatetraenylbenzene (**50**) (Experimental, 3.6.1.).



The ¹H NMR spectra were compared to that of cryptofolione in Table 7.

H	(50)	H	(36)
H- 1''	6.64 <i>dJ</i> 16.2	H-8'	6.61 <i>ddJ</i> 16.0, 1.0
H- 2''	6.31 <i>ddJ</i> 16.0, 5.9	H-7'	6.23 <i>ddJ</i> 16.0, 5.8
H- 3'	4.66 <i>m</i>	H-6'	4.63 <i>m</i>
H- 4'	1.80 <i>m</i>	H-5'	1.78 <i>m</i>
H- 5'	4.04 <i>bs</i>	H-4'	4.05 <i>m</i>
H- 6'	2.33 <i>ddJ</i> 7.0, 6.9	H-3'	2.29 <i>tJ</i> = 6.6
H- 7'	6.30 <i>m</i>	H-2'	5.82 <i>m</i>
H- 8'	6.30 <i>m</i>	H-1'	5.63 <i>ddJ</i> 15.7, 6.3
H- 9'	6.30 <i>m</i>	H-6	4.88 <i>ddJ</i> 14.5, 8.0
H-10'	6.30 <i>m</i>	H-5	2.41 <i>m</i>
H-11'	5.74 <i>m</i>	H-4	6.83 <i>m</i>
H-12'	5.16 <i>ddJ</i> 16.5, 9.9	H-3	6.00 <i>dtJ</i> 9.8, 3.1

Table 7

The major change was in the chemical shift of H-5, from a CH₂ group resonating at 2.41 ppm, to a CH group which was part of a double bond system and shifting downfield to 6.30 ppm. In the original pyrone ring the coupling constant of H-3 with H-4 was 9.9 Hz, indicating *cis* configuration, while in the newly formed system one of the terminal H-12' protons has a coupling constant of 16.5 Hz, indicating a *trans* coupling to H-11'. From [M]⁺ 270 it can be seen that there was a loss of 44 mass units compared to cryptofolione of 314 mass units. On account of small quantities of compound (50) it did not have all the spectroscopic data. HETCOR, COSY, HRMS would be necessary to confirm the proposed structure. It is a tentative proposal based on the data available.

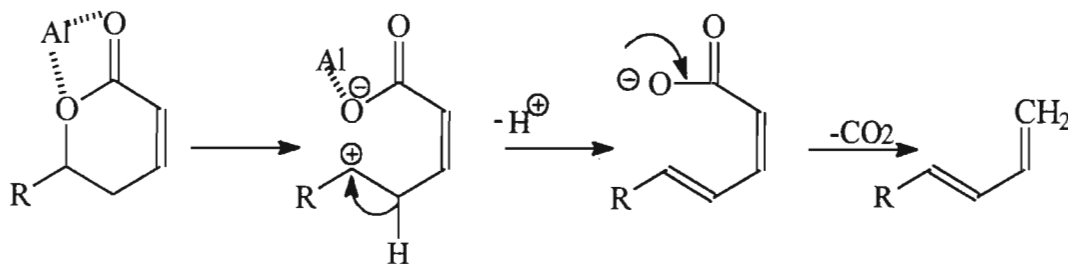
2.6.2. Goniotalamin (45) was subjected to a similar degradation as cryptofolione, yielding 1',3',5' hexatrienylbenzene (51) (Experimental, 3.6.2.).



In **(51)** H-6' (which originates from H-3 in goniotalamin), has shifted from 6.08 to 5.20 ppm, H-4' (originating from H-5) has shifted from 2.52 to 6.45 ppm. This parallels the situation in **(50)**. More data will be necessary to confirm this proposed structure.

Proposed mechanism.

The mechanism proposed involves coordination of the lactone oxygens to the alumina, ring opening, loss of proton leading to formation of double bond and final loss of CO₂, as seen in Scheme 3. This mechanism should be regarded as being only very tentative as more rigorous proof for the pathway is necessary.

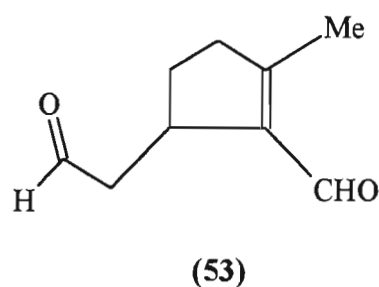
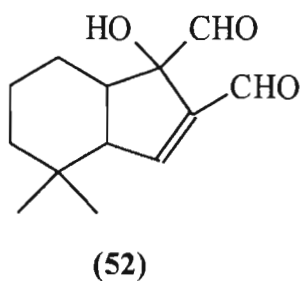


Scheme 3

2.7. ALBERTA MAGNA

Introduction.

Warburganal (**52**) previously isolated in these laboratories from *Warburgia salutaris* is similar in structure to the cyclopentyl dialdehyde (**53**) found in *Alberta magna*. Because of this similarity and the fact that *Alberta magna* bark is being used for medicinal purposes, it was investigated.



Alberta magna species is:

Family	RUBIACEAE
Genus	<i>Alberta</i>
Species	<i>magna</i>

Distribution and uses.

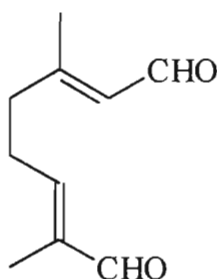
Alberta magna (Natal flame Bush, umCumane) is a medium size tree (5-10 m) found on forest margins, on rocky outcrops, usually near streams, with scattered distribution up to 1300 m in Natal and Pondoland (Transkei). Flowers are tubular (up to 30 mm long)

brilliant red, curved, in dense, branched terminal clusters. Flowers are spectacular and fruit and flowers grow slowly. Bark is used medicinally*.

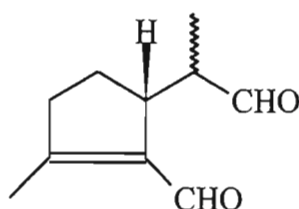
* Personal communication Mr. R. Scott-Shaw (Natal Parks Board).

Chemical constituents.

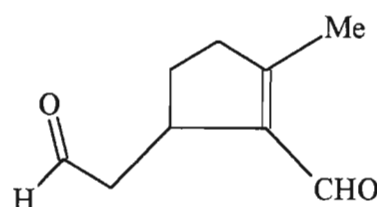
2.7.1 *2-Acetaldehyde-1-formyl-5-methylcyclopent-1-ene* [18] (**53**), (Experimental, 3.7.1.). This compound has been isolated from *Vitex rotundifolia* (Verbenaceae) in Japan [18] and reported to have insect repellent properties. The isolation of this compound and later that of an iridolactone (**55**) *4,4a,5,7a-tetrahydro-1-hydroxy-4-(hydroxymethylene)-7-methylcycopenta[c]pyran-3(1H)-one** (**55**) (Experimental, 3.7.2.) could explain the presence of iridoids in this plant, with (**53**) being a precursor to the iridoids. The proposed biosynthetic route from mevalonic acid, via geraniol, trialdehyde to loganin that was described in Scheme 1 of the introduction, assumes the existence of a trialdehyde. Thus, 10-hydroxynerol is oxidized to give either the trialdehyde or the dialdehyde (**20**). When (**20**) was reacted with 50% HCO₂H, [11] it afforded the dialdehyde (**21**) a C₁₀ compound that is very similar to (**53**) which is a C₉ compound.



(20)

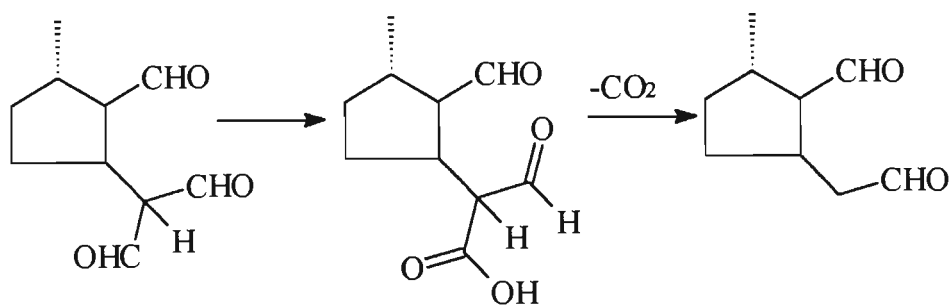


(21)



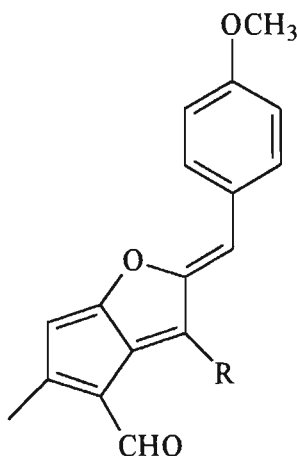
(53)

The cyclic trialdehyde described in the biosynthetic route can become a β -keto carbonyl that can lose CO₂ on heating, yielding the cyclopentyl dialdehyde (**54**) which is the saturated analogue of dialdehyde (**53**).



(54)

Our attention to this plant was drawn from the tlc spots of its ingredients that stain brilliant red with anisaldehyde. From a recent publication by Bianco [23] it is suggested that the iridoid complexes with anisaldehyde to give a characteristic chromatic reaction, as shown in the following compound.

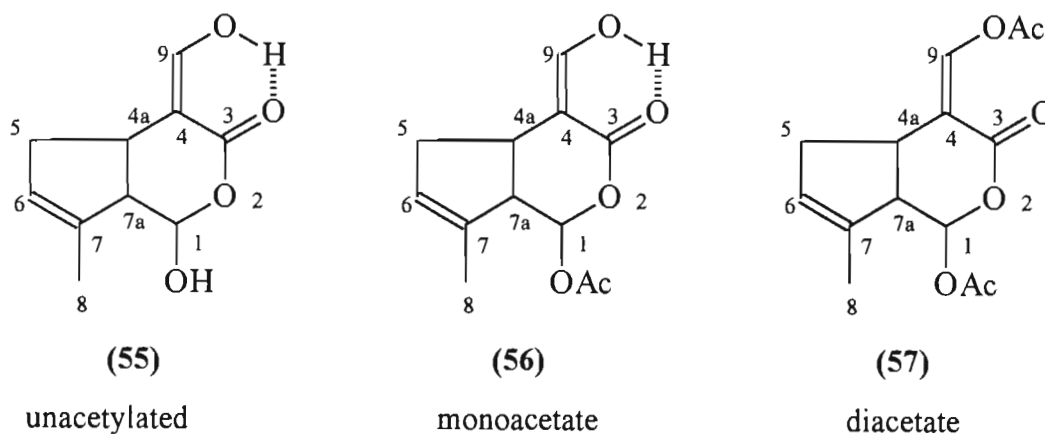


Under acidic hydrolysis, the iridoids form the corresponding unsaturated aldehydes. The aldehydes dehydrate to give the furan derivatives. Condensation of the furans with aromatic aldehydes lead to the compound shown above (this was investigated by Bianco [23] for 6-substituted hydroxy iridoids).

2.7.2. 4,4a,5,7a-Tetrahydro-1-hydroxy-4-(hydroxymethylene)-7-

methylcycopenta[c]pyran-3(1H)-one *(designated amagnalactone for brevity) **(55)** (Experimental, 3.7.2.). The elucidation of the structure of amagnalactone **(55)** was a stepwise procedure. The presence of two hydroxyl groups was verified by obtaining the *di*-TMS ether. GCMS *m/z* (rel.int) 340 [M]⁺ (5), 250 (63), 235 (38), 180 (92), 160 (100), 132 (7), 73 (55). The GCMS spectra also had the peak for the mono-TMS ether at 268 mass units and this suggested the molecular ion to be 196 mass units. The presence of a

lactone was deduced from the carbonyl resonating at 173.2 ppm in the ^{13}C NMR. The IR absorption of the carbonyl at 1684 cm^{-1} indicated the carbonyl being hydrogen bonded. During the process of purification, tlc indicated two spots with very similar R_f and same colouration on staining, possibly due to the existence of both axial and equatorial conformation of the hydroxyl group attached to C-1. Derivatization to obtain the acetylated compounds (Experimental, 3.6.2.aa. and 3.6.2.ab.) helped in allocating the protons attached to the carbons bearing the hydroxyl group, as summarized in Table 8.

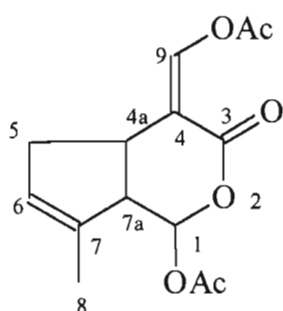


proton	(55)	(56)	(57)
H-1	4.90 $dJ=8.0$	5.95 $dJ=6.5$	6.60 $dJ=2.9$
H-9	7.59 $dJ=0.9$	7.55 $dJ=1.0$	8.24 $dJ=2.0$

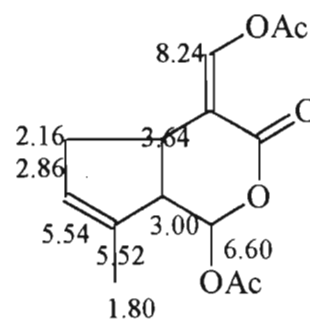
Table 8

* Name kindly supplied by Chemical Abstract Service, Columbus, Ohio, U.S.A.

The allocation of the other protons was done with the help of COSY and HETCOR. To elucidate further couplings, spin decoupling was done on (57) and the results are shown Table 9.



(57)

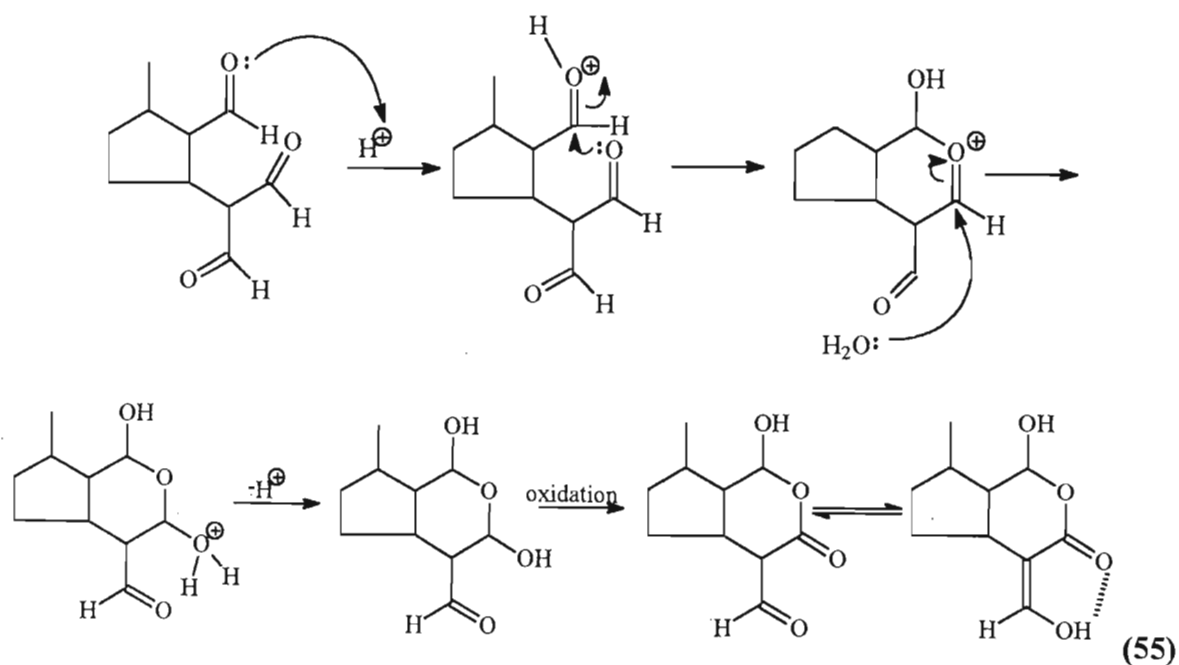


(57)

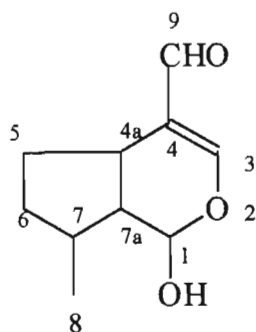
proton irradiated δ	protons affected- δ
Me 1.80	H-5 ₂ , 2.86, H-7a, 3.00, H-6, 5.54
H-4a, 3.64	H-5 ₂ , 2.86, H-7a, 3.00, H-9, 8.24
H-6, 5.54	Me, 1.80
H-9, 8.24	H-4a, 3.64

Table 9

The biosynthesis of (55) could follow the path to the trialdehyde, followed by protonation, intramolecular ring closure, addition of water molecule, loss of proton, oxidation and enol=keto tautomerism to get to the compound.



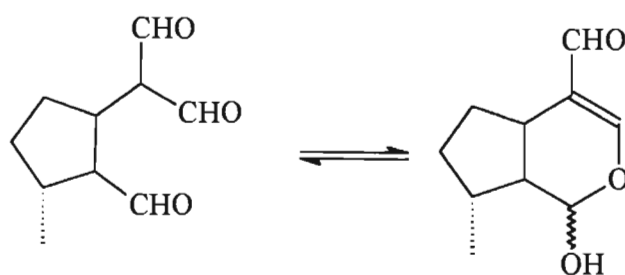
2.6.3. *Cyclopenta[*c*]pyran-4-carboxaldehyde, 1,4 α ,5,6,7,7 α -hexahydro-1-hydroxy-7-methyl (58)*, (Experimental, 3.6.3.).



(58)

The structure was deduced by interpreting the spectroscopic data and by comparison to the lactone (55). From the spectroscopic data it was found that the molecular ion was 182 mass units, the compound had one hydroxyl group that was derivatized to obtain the TMS ether with a molecular ion of 254 mass units. The presence of the aldehyde group was seen in the ^1H NMR H-9 resonating at 9.23 ppm and the aldehyde carbonyl in the ^{13}C NMR resonating at 190.7 ppm. HRMS confirmed the proposed formula of $\text{C}_{10}\text{H}_{14}\text{O}_3$.

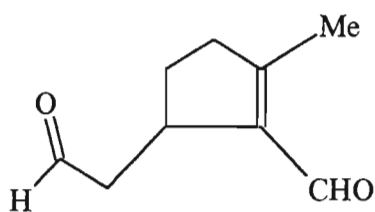
The glucoside of this compound has been isolated [24] from *Tecoma stans* (Bignoniaceae). The possible biosynthetic route could be the bicyclic form of the trialdehyde. Damtoft and coworkers [25] performed biosynthetic studies with deuterium labelled precursors. They state that the trialdehyde in the biosynthetic path can be either in the trialdehyde or the hydroxy aldehyde form.



(58)

Biological activity.

Cyclopentyl dialdehyde (**53**) was tested by the Malaria Unit in Durban (National Malaria Research Programme of the Medical Research Council) for mosquito repellency. The activity was compared to that of diethyltoluamide used as reference. For the first 24 hours it was as active as the reference compound. The activity deteriorated after 24 hours. This can be explained by the relatively high volatility of the compound, resulting in very little compound being left in the test site after 24 hours.

**(53)**

CHAPTER 3

EXPERIMENTAL

INSTRUMENTATION AND CHEMICALS.

Infrared spectra was recorded on Shimadzu FTIR-4300. Optical rotations were recorded on Perkin-Elmer 241 polarimeter. Mass spectra was performed on Hewlett-Packard gas chromatographic mass spectrometer (HP5988A) and a Varian high resolution mass spectrometer. NMR spectra were recorded on Varian Gemini 200 with tetramethylsilane as internal standard in deuterated chloroform, unless stated otherwise. Melting point recording was done on a Kofler hot-stage apparatus and the readings are uncorrected. Flash chromatography was done on silica gel columns (Merck 60, 230-400 mesh). Chromatotron runs were done on Harrison Research (Model 7924T) with silica coated plates (Merck 60, PF₂₅₄, 7749) using UV for detection. Separations and reactions were monitored by thin layer chromatography (tlc) using small strips of precoated Merck sheets (Kieselgel 60, F₂₅₄). Ultraviolet light and modified anisaldehyde stain [16] were used to detect components on tlc.

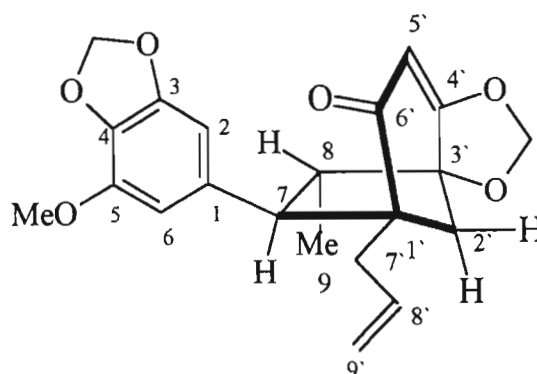
3.1. *OCOTEA BULLATA*

Plant material was collected in January 1994 from mature trees of *Ocotea bullata* growing in the Karkloof area. A voucher specimen was authenticated by Mr. Robert Scott-Shaw (Natal Parks Board) and was deposited in the CPF Herbarium, Queen Elizabeth Park, Pietermaritzburg.

Dry, milled bark (3 kg) was extracted successively with

1. Hexane for 2 weeks at RT -yielded 7.5 gr
2. CHCl₃ for 5 hours in Soxhlet apparatus -yielded 45.0 gr
3. EtOAc for 5 hours in Soxhlet apparatus -yielded 29.4 gr

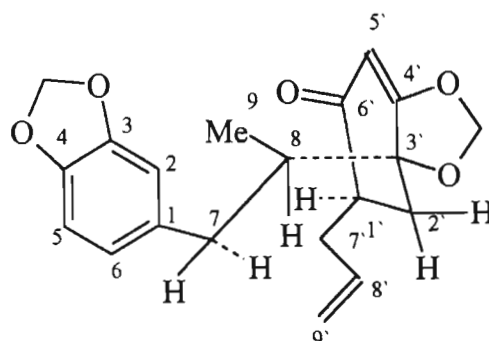
3.1.1. Δ^8 -5-Methoxy-3,4-methylenedioxy-3',4'-methylenedioxy-1',2',3',6'-tetrahydro-6'-oxo-7,1',8,3'-neolignan (isocobullenone) (32).



(32)

A portion of the CHCl_3 extract (11.4 gr) was fractionated on dry silica column, eluted with petrol ether (40-60°)- Et_2O (8:2), further purified on another column with petrol ether (40-60°)- Et_2O (7:3), yielding isocobullenone (18 mg), needles, mp 142-144°. $[\alpha]_D^{23} +122.8^\circ$ (CHCl_3 ; c 0021). IR $\nu^{\text{cm}^{-1}}$ 3000, 1651, 1640, 1612, 1512, 1455, 1408, 1320, 1180, 1096, 1049, 931, 924. ^1H NMR in (CDCl_3 200MHz) δ 1.16 (3H, d , $J = 6.90$ Hz, H-9), 2.07 (1H, dd , $J = 14.20, 8.88$ Hz, H-7_a), 2.08 (1H, dd , $J = 10.81, 1.28$ Hz, H-2_a), 2.34 (1H, d , $J = 10.81$ Hz, H-2_b), 2.48 (1H, dq , $J = 13.7$ Hz, H-8), 2.68 (1H, d , $J = 5.88$ Hz, H-7), 3.86 (3H, s , OMe), 5.07-5.18 (1H, m , H-9'), 5.43 (1H, s , H-5'), 5.46, 5.73 (2H, dd , $J = 0.32$ Hz, 3',4' methylenedioxy), 5.90, 5.92 (2H, dd , $J = 1.44$ Hz, 3,4 methylenedioxy), 6.24, 6.26 (2H, dd , $J = 1.65$ Hz, H-2, H-6). ^{13}C NMR (50 MHz, CDCl_3 ,): δ 16.9 (C-9), 37.1 (C-7'), 43.2 (C-2'), 43.6 (C-8), 56.7 (OMe), 58.2 (C-1'), 59.5 (C-7), 87.4 (C-3'), 97.0 (C-5'), 99.3 (aliph - OCH_2O -), 101.4 (arom - OCH_2O -), 102.2 (C-6), 108.7 (C-2), 118.5 (C-9'), 132.2 (C-1), 134.5 (C-8'), 134.5 (C-4), 142.9 (C-5), 148.8 (C-3), 179.1 (C-4'), 198.7 (C-6'). EI-MS m/z (rel. int.): 370 [M]⁺ (31), 325 (24), 270 (13), 219 (24), 178 (100), 137 (49) 115 (24). HR-MS calcd for $\text{C}_{21}\text{H}_{22}\text{O}_6$: 370.1415, found 370.1400.

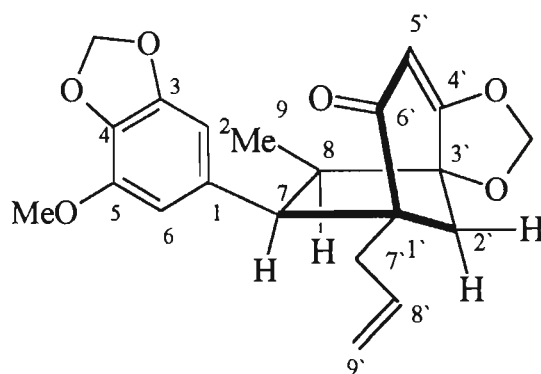
3.1.2. Δ^8 -3,4-Methylenedioxy-3',4'-methylenedioxy-1',2',3',6',-tetrahydro-6'-oxo-8,3'-neolignan (33).



(33)

A portion of the CHCl_3 extract (2 g) was partitioned between 2% citric acid (aq.) and Hexane, followed by partitioning between 2% citric acid and CHCl_3 . The organic layers were combined and purified twice on the chromatotron, using first Hexane- Et_2O (1:1), followed by Hexane- Et_2O (7:3) yielding the compound (16 mg), $[\alpha]_D^{22} +159.4^\circ$ (CHCl_3 ; c 0.16). ^1H NMR (200 MHz, CDCl_3): δ 0.96 (3H, *d*, $J = 7.0$ Hz, H-9), 1.80 (1H, *m*, H-2'), 2.10 (1H, *m*, H-8), 2.21 (1H, *d*, $J = 12.5$ Hz, H-7_b), 2.30 (1H, *m*, H-7_b), 2.38 (1H, *m*, H-1'), 2.55 (1H, *dd*, $J = 12.5, 5.3$ Hz, H-2'_a), 2.70 (1H, *m*, H-7'_a), 2.85 (1H, *dd*, $J = 12.4, 3.1$ Hz, H-7'_a), 5.07, 5.09, 5.13 (2H, *m*, H-9'), 5.59 (1H, *s*, H-5'), 5.60 (2H, *d*, $J = 1.1$ Hz, aliphatic- OCH_2O -), 5.70 (1H, *m*, H-8'), 5.92 (2H, *dd*, $J = 2.4, 0.5$ Hz, aromatic $\text{-OCH}_2\text{O}$ -), 6.51 (1H, *m*, H-2), 6.55 (1H, *d*, $J = 8.0$ Hz, H-5), 6.72 (1H, *dddd*, $J = 7.5, 3.8, 0.7$ Hz, H-6). ^{13}C NMR (50 MHz, CDCl_3): δ 13.1 (C-9), 35.6 (C-2'), 36.3 (C-7'), 38.1 (C-7), 41.4 (C-8), 42.4 (C-1'), 85.4 (C-3'), 99.9 (C-5'), 100.9 (2x- OCH_2O -), 108.2 (C-2), 109.2 (C-5), 117.7 (C-9'), 121.9 (C-6), 133.7 (C-1), 135.2 (C-8'), 146.0 (C-4), 147.6 (C-3), 175.8 (C-4'), 198.9 (C-6'). EI-MS *m/z* (rel.int.): 342 $[\text{M}]^+$ (7), 207 (7), 162 (100), 135 (92), 105 (21), 91 (6), 77 (33), 55 (38). HRMS calc. for $\text{C}_{20}\text{H}_{22}\text{O}_5$, 342.1467, found 342.1484.

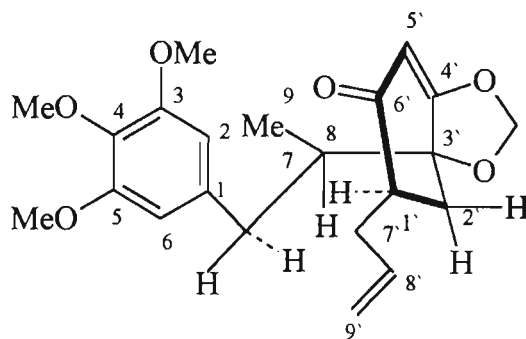
3.1.3. In the course of isolation of isoocobullenone (32) and Δ^8 -3,4-methylenedioxy-3',4'-methylenedioxy-1',2',3',6',-tetrahydro-6'-oxo-8,3'-neolignan (33), 200 mg ocobullenone [16] (30) and 27 mg bullatone [16] (31) were isolated.



ocobullenone (30)

Δ^8 -5-Methoxy-3,4-methylenedioxy-3',4'-methylenedioxy-1',2',3',6'-tetrahydro-6'-oxo-7,1'-8,3'-neolignan (ocobullenone) [16] (30).

Needles, mp 151°, $[\alpha]_D^{25} +204^\circ$ (CHCl₃, c0.16). EI-MS m/z (rel.int.): 370 [M]⁺ (15), 192 (11), 178 (100), 137 (29), 91 (27) and 69 (46). IR $\nu_{\max}^{\text{KBr}} \text{ cm}^{-1}$: 1641, 1510, 1427, 1363, 1205, 1176, 1049, 929. (Calc. for C₂₁H₂₂O₆: 370.1415, found: 370.1424). ¹H NMR (200 MHz, CDCl₃): δ 0.85 (3H, *d*, $J = 7.4$ Hz, H-9), 2.06 and 2.26 (2H, *dd*, $J = 10.5$ Hz, H-2'), 2.05 (1H, *dd*, $J = 14.18, 8.94$ Hz, H-7'_a), 2.56 (1H, *dddd*, $J = 14.11, 5.75, 1.35, 1.39$ Hz, H-7'_b), 2.87 (1H, *dq*, $J = 11.9, 7.4$ Hz, H-8), 3.37 (1H, *d*, $J = 11.9$ Hz, H-7), 3.83 (3H, *s*, OMe-5), 5.06 (2H, *m*, H-9'), 5.57 (1H, *s*, H-5'), 5.65 (2H, *dd*, $J = 0.33$ Hz, aliphatic-OCH₂O-), 5.75 (1H, *m*, H-8'), 5.88 (2H, *dd*, $J = 1.52$ Hz, aromatic-OCH₂O-), 6.16 (2H, *dd*, $J = 1.7$ Hz, H-2, 6). ¹³C NMR (50 MHz, CDCl₃): δ 14.2 (C-9), 37.7 (C-7'), 44.4 (C-8), 46.6 (C-2'), 54.0 (C-7), 56.6 (OMe), 59.8 (C-1'), 91.2 (C-3'), 98.4 (C-5'), 101.3 (aliph-OCH₂O), 101.5 (aromatic-OCH₂O-), 104.8 (C-6), 111.2 (C-2), 118.5 (C-9'), 129.8 (C-1), 134.4 (C-8', C-4), 142.7 (C-5), 148.5 (C-3), 177.5 (C-4'), 200.2 (C-6').



bullatone (31)

Δ^8 -3,4,5-Trimethoxy-3',6'-dihydro-3',4'-methylenedioxy-6'-oxo-8,3'-neolignan

(bullatone) [16] (31).

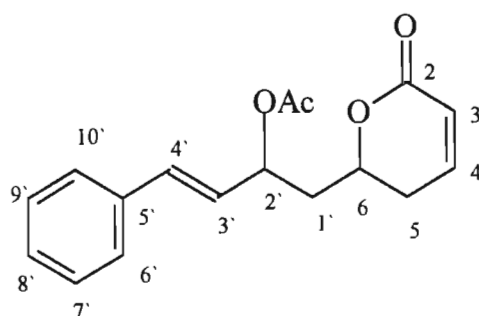
Needles, mp 105°. $[\alpha]_D^{25} +175^\circ$ (CH₂Cl₂, c 0.8). ¹H NMR (200 MHz, CDCl₃): δ 0.99 (3H, *d*, *J* = 6.7 Hz, Me-9), 1.78 (1H, *dd*, *J* = 12.7 Hz, H-2'_b), 2.09 (1H, *ddq*, *J* = 12.6, 6.8, 2.6 Hz, H-8), 2.25 (1H, *dd*, *J* = 12.6, 11.8 Hz, H-7'_b), 2.26 (1H, *m*, H-7'_b) 2.40 (1H, *m*, H-1'), 2.56 (1H, *dd*, *J* = 5.20 Hz, H-2'_a), 2.69 (1H, *m*, H-7'_a), 2.87 (1H, *dd*, *J* = 12.6, 2.4 Hz, H-7'_a), 3.80 (3H, *s*, OMe-4), 3.82 (6H, *s*, OMe, H-3, H-5), 5.07 (2H, *m*, H-9'), 5.55 (1H, *s*, H-5'), 5.60 (2H, *dd*, *J* = 7.9 Hz, -OCH₂O-), 5.70 (1H, *m*, H-8'), 6.27 (2H, *s*, H-2, H-6). ¹³C NMR (50 MHz, CDCl₃): δ 13.3 (C-9), 35.7 (C-2'), 36.3 (C-7'), 38.8 (C-7), 41.2 (C-8), 42.4 (C-1'), 56.2 (OMe-3, OMe-5), 60.8 (OMe-4), 85.4 (C-3'), 99.9 (C-5'), 100.0 (-OCH₂O-), 106.1 (C-2, C-6), 117.6 (C-9'), 135.2 (C-8'), 135.6 (C-1), 136.8 (C-4) 153.2 (C-3, C-5), 175.8 (C-4'), 198.8 (C-6'). EI-MS *m/z* (re.int.) 388 [M]⁺ (8), 209 (35), 208 (42), 193 (16), 182 (18), 181 (100), 148 (19), 137 (20). HR-MS calcd for C₂₂H₂₈O₆: 388.2886, found 388.1865.

Several batches of the EtOAc extract were subjected to purification by column chromatography, followed by chromatotron. Only minute quantities of ocobullenone and bullatone have been isolated.

3.2. *CRYPTOCARYA LIEBERTIANA*

3.2.1. Plant material was collected in May 1995 from *Cryptocarya liebertiana* growing in Ngoye forest in Natal. This was identified by Mrs. Anne Hutchings and a voucher specimen lodged in the Herbarium at the University of Zululand.

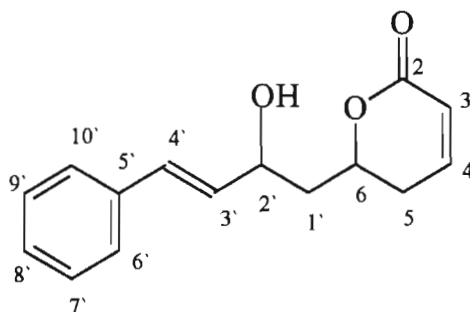
3.2.1.1. Cryptocaryalactone [15] (34).



(34)

Air dried milled bark (340 gr) was extracted at RT with CHCl_3 for three weeks, giving 3.91 gr extract.

The crude CHCl_3 extract was purified on dry silica column eluted with CH_2Cl_2 , followed by separation on the chromatotron with Hexane-EtOAc (1:1), affording crystalline solid (42 mg), m.p. 106-107°, lit (15) 124-126°. $[\alpha]_D^{22}$ -19.7° (CHCl_3 ; c 0.42), lit (15) +15.5°, lit. (2) -20°. ^1H NMR (200 MHz, CDCl_3): δ 2.03 (1H, *m*, H-1'a), 2.08 (3H, *s*, OAc), 2.39 (1H, *m*, H-1'b), 2.43 (2H, *m*, H-5), 4.52 (1H, *m*, H-6), 5.67 (1H, *m*, H-2'), 6.03 (1H, *m*, H-3), 6.11 (1H, *dd*, $J = 15.9, 7.6$ Hz, H-3'), 6.70 (1H, *dd*, $J = 10.6, 0.6$ Hz, H-4'), 6.88 (1H, *m*, H-4). 7.25-7.45 (5H, *m*, Ar-H). ^{13}C NMR (50 MHz, CDCl_3): δ 21.3 (OAc), 29.4 (C-5), 39.7 (C-1'), 71.2 (C-2'), 74.7 (C-6), 121.5 (C-3), 126.0 (C-3'), 126.7, 128.3, 128.6, 135.8 (Ar-C), 133.9 (C-4'), 144.6 (C-4), 163.8 (pyrone C=O), 170.1 (OCOMe). EI-MS m/z (rel.int.) $[\text{M}-43]^+$ 243 (286-43) (10), 226 (24), 181 (13), 159 (78), 131 (100), 104 (22), 97 (78), 57 (96).

3.2.1.2. Deacetylcryptocaryalactone [2] (**35**).**(35)**

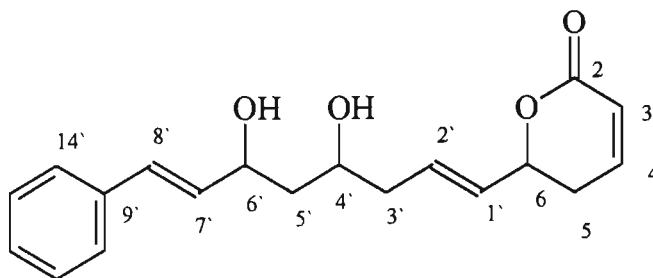
The crude CHCl_3 extract was purified on dry silica column eluted with CH_2Cl_2 , followed by chromatotron run with Hexane-EtOAc (1:1), affording an oil (25 mg), $[\alpha]_{\text{D}}^{22}$ (CHCl_3 ; c 0.24) -82.1° lit [2] -94° . ^1H NMR (200 MHz, CDCl_3): δ 1.90 (1H, *m*, H-1`a), 2.20 (1H, *m*, H-1`b), 2.41 (2H, *m*, H-5), 4.59 (2H, *m*, H-6 and H-2'), 4.78 (1H, *s*, OH), 5.98 (1H, *m*, H-3), 6.18 (1H, *dd*, $J = 15.9, 7.0$ Hz, H-3'), 6.63 (1H, *dd*, $J = 15.9$ Hz, H-4'), 6.85 (1H, *m*, H-4), 7.20-7.45 (5H, *m*, Ar-H). ^{13}C NMR (50 MHz, CHCl_3): δ 29.4 (C-5), 41.9 (C-1'), 69.6 (C-2'), 75.9 (C-6), 121.1 (C-3), 126.5, 127.9, 128.6 and 136.2 (Ar-C), 130.9 (C-3'), 131.3 (C-4'), 145.4 (C-4), 164.3 (pyrone C=O). EI=MS m/z (rel.int.) $[\text{M}]^+$ 244 (4), 184 (4), 158 (30), 131 (31), 104 (100), 97 (9), 89 (23), 71 (23).

3.2.1.2a. ACETYLATION OF DEACETYLCRYPTOCARYALACTONE (**34**).

Deacetylcryptocaryalactone (**35**) (60 mg) was dissolved in pyridine, acetic anhydride was added and stirred at RT for three hours. The mixture was poured over ice, acidified with 2N HCl, extracted with Et_2O and afforded crystalline cryptocaryalactone (28 mg) (**34**) ^1H NMR was identical to that of cryptocaryalactone isolated from this plant. $[\alpha]_{\text{D}}^{22}$ (CHCl_3 ; c 0.27) -16.8° , lit. [2] -20° . A similar acetylation was done by Spencer [2].

3.2.1.3. During the purification process 300 mg cryptofolione [16] (**36**) was

isolated. 6-(4',6'-Dihydroxy-8'-phenyloct-1',7'-dienyl)-5,6-dihydro-2H-pyran-2-one



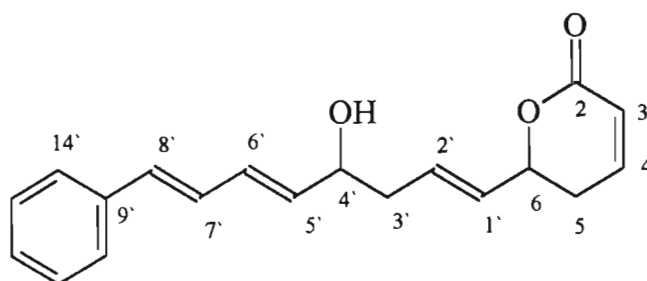
(36)

$\alpha]_D^{22} +57.0^\circ$ (CHCl_3 , c 0.52). IR ν_{max} cm^{-1} 3440, 2942, 1700, 1385, 1250, 1055, 975, 825, 755, 700. HRMS 314.1518 calcd. for $\text{C}_{19}\text{H}_{22}\text{O}_4$, found 314.1503. ^1H NMR (200 MHz, CDCl_3): δ 1.78 (2H, *m*, H-5'), 2.29 (2H, *t*, $J = 6.6$, Hz, H-3'), 2.41 (2H, *m*, H-5), 3.46 (2H, *m*, overlapping, OH-4', OH-6'), 4.05 (1H, *m*, H-4'), 4.63 (1H, *m*, H-6'), 4.88 (1H, *dd*, $J = 14.5, 8.0$ Hz, H-6), 5.63 (1H, *dd*, $J = 15.7, 6.3$ Hz, H-1'), 5.82 (1H, *m*, H-2'), 6.00 (1H, *dt*, $J = 9.8, 3.6$ Hz, H-3), 6.23 (1H, *dd*, $J = 16.0, 5.8$ Hz, H-7'), 6.61 (1H, *dd*, $J = 16.0, 1.0$ Hz, H-8'), 6.83 (1H, *m*, H-4), 7.23 (5H, *m*, overlapping, Ar-H). ^{13}C NMR (50 MHz, CDCl_3): δ 29.6 (C-5), 40.3 (C-3'), 42.3 (C-5'), 68.0 (C-4'), 70.0 (C-6'), 77.9 (C-6), 121.3 (C-3), 126.4 (C-10', C-14'), 127.5 (C-12'), 128.5 (C-11', C-13'), 129.6 (C-8'), 129.7 (C-1'), 131.3 (C-2'), 131.9 (C-7'), 136.6 (C-9'), 145.1 (C-4) 164.3 (C-2).

3.2.2. *CRYPTOCARYA LIEBERTIANA*

Plant material was collected in April 1995 at Hangklip Indigenous Forest Reserve near Louis Trichardt from *Cryptocarya liebertiana*. A voucher specimen no. 07934 was deposited by Prof. A.E. van Wyk (Pretoria University) in the H.G.W.J. Schweikerdt Herbarium in Pretoria.

3.2.2.1. (+) -6-(4'-Hydroxy, 8'-phenyloct-1', 5', 7' trienyl)-5,6-dihydro-2H-pyran-2-one (liberfolione) (**38**).



(**38**)

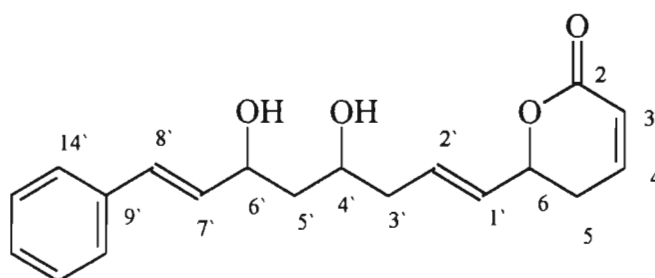
Air dried milled bark (600 gm) was extracted as follows:

1. CHCl_3 at RT for 4 weeks yielding 4.0 gm extract.
2. CH_3COCH_3 at RT for 4 weeks yielding 5.2 gm extract.

The CHCl_3 extract was purified on a dry silica plug using CHCl_3 -MeOH (94:6) as eluent. Further purification was done on the chromatotron with Hexane-EtOAc (1:1). After several runs under the same conditions, 14 mg (oil) compound was isolated. Additional 55 mg (oil) compound was isolated from the acetone extract. The extract was fractionated on dry silica column, followed by chromatotron purification using Hexane-EtOAc (1:2) as eluent. $[\alpha]_D^{22} +55.95^\circ$ (CHCl_3 ; c 0.55). IR ν_{max} cm^{-1} : 2254, 1718, 1382, 1253, 910. ^1H NMR (CDCl_3 , 200 MHz): δ 2.30-2.46 (4H, *m*, overlapping, H-3', H-5'), 4.30 (1H, *q*, $J = 6.3$ Hz, H-4'), 4.90 (1H, *q*, $J = 6.2$ Hz, H-6), 5.66 (1H, *dt*, $J = 6.2$ Hz, H-1'), 5.80 (1H, *m*, H-5'), 5.92 (1H, *m*, H-2'), 6.03 (1H, *dt*, $J = 9.8, 1.9$ Hz, H-3), 6.35 (1H, *ddd*, $J = 15.2, 1.08$ Hz, H-6'), 6.55 (1H, *d*, $J = 15.5$ Hz, H-8'), 6.76 (1H, *m*, H-7'), 6.86 (1H, *m*, H-4), 7.30 (5H, *m*, overlapping, H-10'-H-14'). ^{13}C NMR (50 MHz, CDCl_3): δ (29.7 (C-5), 40.1 (C-3'), 71.5 (C-4'), 77.8 (C-6), 121.5 (C-3), 126.4 (overlapping, C-10', C-14'), 127.6 (C-

12'), 128.0 (C-7'), 128.6 (overlapping, C-11', C-13'), 130.1 (C-6'), 130.6 (C-1'), 131.0 (C-2'), 133.0 (C-8'), 135.4 (C-5'), 137.0 (C-9'), 144.8 (C-4), 164.0 (C-2). MS *m/z* (rel.int.): 296 [M]⁺ (4), 207 (5), 181 (1), 159 (100), 129 (26), 97 (4), 91 (90), 81 (25), 77 (10).

3.2.2.2. During the course of isolation 410 mg cryptofolione [16] (**36**) was isolated.

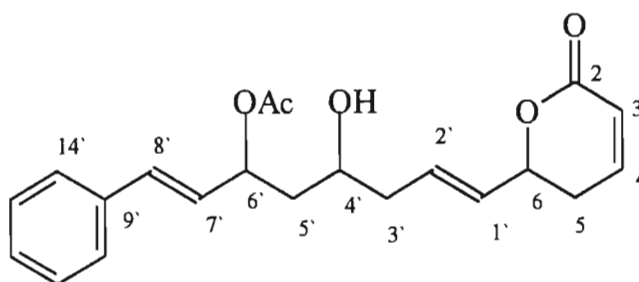


(36)

3.2.3. *CRYPTOCARYA LIBERTIANA*.

Plant material was collected in June 1995 from young trees of *Cryptocarya liebertiana* growing in Zimbabwe and was authenticated by Mr. Stephen Mavi. Voucher specimen no. 1096 was deposited in the National Herbarium in Harare.

3.2.3.1. (+)-6-(6'-Acetoxy, 4'-hydroxy, 8'-phenyloct-1', 7' dienyl)-5,6 -dihydro-2H-pyran-2- one (named acetyl cryptofolione) (**39**).



(**39**)

Air dried milled bark (220 gr) was extracted at RT successively with

1. CHCl_3 for three weeks- yielded 3.39 gr crude extract.
2. CH_3COCH_3 for 1 week-yielded 4.16 gr crude extract.

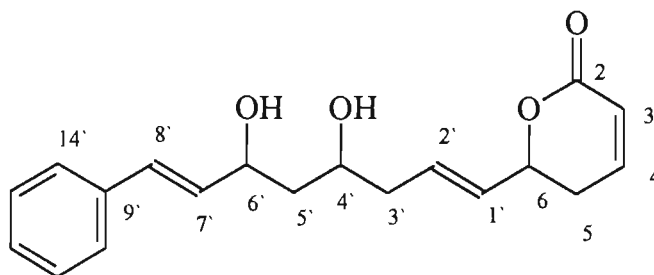
The crude CHCl_3 extract was fractionated. First a dry silica column eluted with CHCl_3 100%, followed by EtOAc 100%. Two main fractions have been collected: I and II. I was further purified on chromatotron using Hexane-EtOAc (1:1) as eluent, yielding an oil (32 mg) that tends to solidify upon standing, $[\alpha]_D^{23} +86.1^\circ$ (CHCl_3 , c 0.42). IR $\nu^{\text{cm}^{-1}}$ 3041, 2686, 2340, 1712, 1608, 1556, 1155, 903, 890. $^1\text{H NMR}$ (CDCl_3 , 200 MHz): δ 1.75 (2H, *m*, H-5'), 2.13 (3H, *s*, OAc), 2.27 (2H, *t*, $J = 6.5$ Hz, H-3'), 2.48 (2H, *m*, H-5), 2.92 (1H, *bs*, OH), 3.68 (1H, *m*, H-4'), 4.90 (1H, *q*, $J = 6.8$ Hz, H-6), 5.69 (2H, *m*, overlapping, H-1', H-6'), 5.89 (1H, *m*, H-2'), 6.03 (1H, *dt*, $J = 9.9, 1.9$ Hz, H-3), 6.18 (1H, *dd*, $J = 15.9, 6.9$ Hz, H-7'), 6.62 (1H, *dd*, $J = 15.9, 7.0$ Hz, H-8'), 6.87 (1H, *m*, H-4), 7.19-7.41 (5H, *m*, overlapping, H-10'-H-14'). $^{13}\text{C NMR}$ (CDCl_3 , 50 MHz): δ 21.3 (C-15'), 29.7 (C-5), 39.9 (C-3'), 42.5 (C-5'), 66.6 (C-4'), 71.9 (C-6'), 77.9 (C-6), 121.4 (C-3), 126.6 (overlapping C-10', C-14', aromatic), 127.2 (C-7'), 128.1 (C-12', aromatic), 128.6 (overlapping C-11', C-13', aromatic), 129.6 (C-1'), 131.3 (C-2'), 132.2 (C-8'), 136 (C-

9'), 144.8 (C-4), 164.1 (C-2), 171.5 (C-16'). GCMS -compound decomposing, the formula is $C_{21}H_{24}O_5$.

3.2.3.1a. PREPARATION OF ACETYL CRYPTOFOLIONE (39).

Cryptofolione (**36**) (300 mg), was acetylated overnight at RT in pyridine using equimolar amount of acetic anhydride. Acetyl cryptofolione was purified from the reaction mixture on the chromatotron using Hexane-EtOAc (1:2) affording the compound (**39**) (68 mg oil), $[\alpha]_D^{22} + 101^\circ$, compared to $[\alpha]_D^{22} + 86.1^\circ$ in the compound naturally occurring in the plant. The synthetic product had the same 1H NMR and ^{13}C NMR data as the naturally occurring compound.

3.2.3.2. Fraction II contained 520 mg of '(+)-6-(4',6'-dihydroxy-8'-phenyloct-1',7'-dienyl)-5,6 dihydro-2H-pyran-2-one (cryptofolione) [16] (**36**).

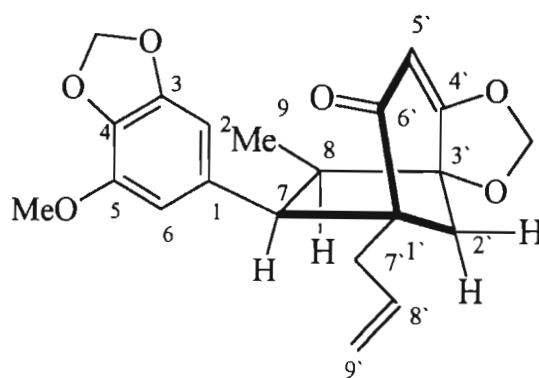


(36)

3.2.4. CRYPTOCARYA LIEBERTIANA

Plant material was collected in May 1995 in Zimbabwe from mature tree of *Cryptocarya liebertiana* and was authenticated by Mr. Stephen Mavi. A voucher specimen no. 1096 was deposited at the National Herbarium in Harare.

3.2.4.1. Δ^8 -5-Methoxy-3,4-methylenedioxy-3',4'-methylenedioxy-1',2',3',6'-tetrahydro-6'-oxo-7,1',8,3'-neolignan (ocobullenone) [16] (30).

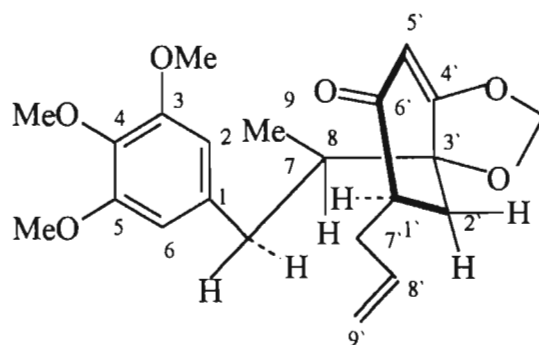


(30)

The second fraction from the CHCl_3 elution of the crude was purified on the chromatotron several times, run with Hexane- Et_2O (45:55) and (60:40) respectively, affording ocobullenone (41 mg), $[\alpha]_{\text{D}}^{22} +158.2^\circ$, (CHCl_3 ; c 0.11) lit. [16] $+204^\circ$. mp 136° , lit. (16) 158° .

The CH_3COCH_3 extract (7.4 gm) was dissolved in CHCl_3 (1.4 gm) This was purified on dry silica column eluted with CHCl_3 . Minute amounts of ocobullenone and bullatone were isolated, the rest of the extract was spotted on tlc and discarded.

3.2.4.2. Δ^8 -3,4,5-Methoxy-3',4'-methylenedioxy-1',2',3',6'-tetrahydro-6'-oxo-8,3'-neolignan (bullatone) [16] (31).



(31)

Air dried milled bark (380 gr) was extracted at RT successively with:

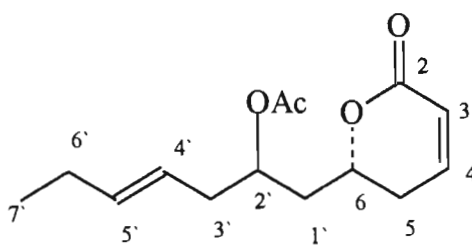
1. CHCl_3 for 1 month yielding 10 gr extract.
2. CH_3COCH_3 for 1 month yielding 7.4 gr extract.

The CHCl_3 was fractionated on dry silica plug, using CHCl_3 followed by Hexane-EtOAc (1:1) as eluent. Two fractions from the CHCl_3 elution were collected. The first fraction was further repeatedly purified on the chromatotron, using Hexane-Et₂O (1:1). White crystals were formed when the volume of eluant was reduced, the crystals were washed with Hexane-Et₂O, affording bullatone (29 mg), $[\alpha]_D^{22}$ 0.0°, CHCl_3 ; c 0.29), lit. [16] +175°. mp 128°, lit. [16] 105°.

3.3. *CRYPTOCARYA LATIFOLIA*

Plant material was collected in the Karkloof area from mature trees of *Cryptocarya latifolia*. A voucher specimen No. 6095, authenticated by Mr. Robert Scott-Shaw (Natal Parks Board) was deposited at the Killick Herbarium.

3.3.1. 6-(2'-Acetoxyhept-4'-enyl)-5,6-dihydro-2H-pyran-2-one (isomer of umuravumbolide) (40).



(40)

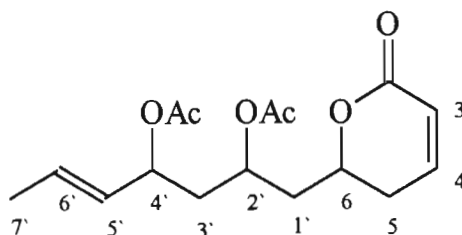
Air dried milled bark (4.39 kg) was extracted successively with:

1. Petrol-ether (60-80°) at RT for two weeks yielding 84 gr extract.
2. CH₂Cl₂ at RT for two weeks yielding 81 gr extract.
3. EtOAc at RT for two weeks yielding 35 gr extract.
4. EtOH at RT for two weeks yielding 9 gr extract.

A fraction of the CH₂Cl₂ extract (9 gr) was repeatedly purified on silica column with Petrol-ether-EtOAc (8:2), followed by another column eluted with Petrol-ether-EtOAc-CHCl₃ (16:3:1) affording impure compound. The impure compound was purified on the chromatotron using CH₂Cl₂, followed by Et₂O, affording the compound (14 mg oil), $[\alpha]_D^{28} +97.8^\circ$ (CHCl₃; c1.4). IR $\nu_{\max}^{\text{NaCl}} \text{cm}^{-1}$. 3350, 1720, 1480, 1350, 1040, 971. ¹H NMR (200 MHz, CDCl₃): δ 0.96 (3H, *t*, *J* = 7.5 Hz, H-7'), 2.04 (2H, *m*, H-6'), 2.04 (2H, *m*, H-1'_a, H-3'_a), 2.06 (3H, *s*, OAc), 2.22 (1H, *m*, H-1'_b), 2.30 (1H, *m*, H-5'_a), 2.32 (1H, *m*, H-3'_b), 2.47 (1H, *m*, H-5'_b), 4.49 (1H, *m*, H-6), 5.04 (1H, *m*, H-2'), 5.31 (1H, *dt*, *J* = 15.27, 6.98, 1.46 Hz, H-4'), 5.56 (1H, *dt*, *J* = 15.29, 6.23, 1.02 Hz, H-5'), 6.02 (1H, *ddd*, *J* = 9.8 Hz, H-3), 6.87 (1H, *m*, *J* = 9.8 Hz, H-4); ¹³C NMR (50 MHz, CDCl₃): δ 13.7 (C-7'), 21.1 (acetyl), 25.6 (C-6'), 29.1 (C-5), 37.7 (C-3'), 38.7 (C-1'), 70.0 (C-2'), 75.2

(C-6), 121.4 (C-3), 122.9 (C-4'), 136.4 (C-5'), 144.7 (C-4), 164.0 (C-2), 170.8 (acetyl); HREIMS: observed $m/z = 252.1329$, $C_{14}H_{20}O_4$ requires 252.1361.

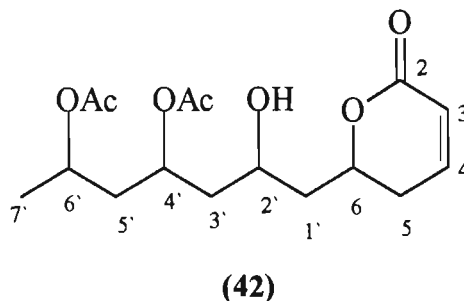
3.3.2. 6-(2', 4' Diacetoxyhept-5-enyl)-5,6-dihydro-2H-pyran-2-one (41).



(41)

A fraction of the CH_2Cl_2 (17 gr) extract was repeatedly purified on silica column with a gradient of Petrol-ether-EtOAc, starting with (8:2) and ending with (7:3). The impure compound was further purified twice on the chromatotron using Hexane-Et₂O (2:5), affording the compound (25 mg oil), $[\alpha]_D^{22} +91.5^\circ$ ($CHCl_3$ c0.25). IR ν_{max} cm^{-1} 1738, 1732, 1606, 1373, 1255, 1155, 1059, 968. ¹H NMR ($CDCl_3$, 200 MHz): δ 1.70 (3H, *dd*, $J = 7.5, 1.1$ Hz, H-7'), 1.85 (2H, *m*, H-3'), 1.95 (1H, *m*, H-1'a), 2.04 (3H, *s*, OAc), 2.07 (3H, *s*, OAc), 2.15 (1H, *m*, H-1'b), 2.20 (1H, *m*, H-5a), 2.35 (1H, *m*, H-5b), 4.50 (1H, *m*, H-6), 5.07 (1H, *m*, H-2'), 5.27 (1H, *q*, $J = 6.7$ Hz, H-4'), 5.38 (1H, *ddd*, $J = 14.9, 7.5, 1.6$ Hz, H-5') 5.73 (1H, *m*, H-6'), 6.02 (1H, *dq*, $J = 9.7, 6.7$ Hz, H-3), 6.88 (1H, *m*, H-4). ¹³C NMR, ($CDCl_3$, 50 MHz): δ 17.7 (C-7'), 21.1 (OAc), 21.3 (OAc), 29.2 (C-5), 39.1 (C-3'), 39.4 (C-1'), 67.2 (C-2'), 71.8 (C-4'), 74.9 (C-6), 121.3 (C-3), 128.4 (C-5'), 130.4 (C-6'), 144.8 (C-4), 163.9 (C-2), 170.2 (acetyl), 170.6 (acetyl). GCMS m/z (rel.int.) 268 $[M-42]^+$ (0.4), 250 (1), 232 (0.6), 190 (13), 162 (3), 141 (12), 123 (18), 97 (73), 68 (100). The formula is $C_{16}H_{22}O_6$.

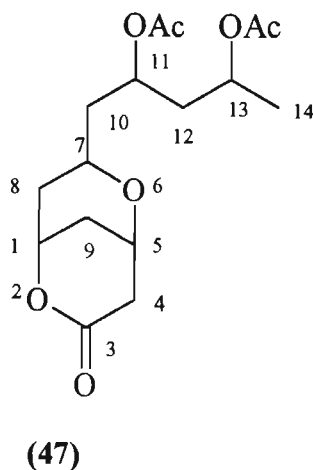
3.3.3. 6-(4',6' Diacetoxy-2'-hydroxyheptyl)-5,6-dihydro-2H-pyran-2-one (impure) (42).



A fraction of the CH_2Cl_2 extract (17 gr) was repeatedly purified on silica column with Hexane-EtOAc (7:3), followed by chromatotron separation using Hexane-EtOAc (75:25). This afforded the impure pyrone (70 mg oil), ^1H NMR (200 MHz, CDCl_3): δ 1.24 (3H, *m*, H-7'), 1.8 (6H, *m*, H-3', H-5, H-5'). 2.04, 2.05, (6H, *m*, OAcx2), 2.40 (2H, *m*, H-1'), 3.8, 3.9 (1H, *bm*, H-6), 4.55, 4.65 (1H, *m*, H-4'), 4.95, 5.08, 5.22 (2H, *m*, H-6' and H-2'), 6.03 (1H, *dt*, $J = 9.8, 1.8$ Hz, H-3), 6.90 (1H, *m*, $J = 9.8$ Hz, H-4). ^{13}C NMR (50 MHz, CDCl_3): δ 20.4 and 20.5 (C-7'), 21.6 (OAc), 21.7 (OAc), 29.5, 29.6 (C-5), 38.5, 38.8 (C-1', C-5'), 42.0, 42.4 (C-3'), 66.7 (C-2'), 67.0 (C-4'), 75.1, 75.4 (C-6), 121.3 (overlapping, C-3, C-6'), 145.7, 145.8 (C-4), 164.0 (C-2), 171.2 (acetyl).

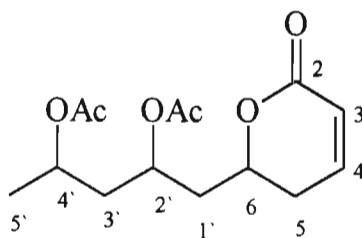
3.3.3a. CYCLIZATION OF 6-(4',6' Diacetoxy-2'-hydroxyheptyl)-5,6-dihydro-2H-pyran-2-one (42) to afford:

7-(11, 13 diacetylpentyl)-2,6 dioxabicyclo[3,3,1] nonan-3-one [16] (47).



The above compound (70 mg) was dissolved in CH_2Cl_2 , excess NaH added and left at RT for five minutes. The reaction was quenched with 2N HCl, the organic layer washed with water and then purified on the chromatotron with Et_2O affording the bicyclic compound (17 mg), $[\alpha]_D^{22} -21.7^\circ$ (CHCl_3 , c 0.17) lit. [16] -145° . IR. ^1H NMR (200 MHz, CDCl_3): δ 1.23 (3H, *d*, $J = 6.3$ Hz, Me), 1.50-1.95 (8H, *m*, overlapping, H-8, H-9, H-10, H-12), 2.03, 2.04 (OAc) 2.81 (2H, *m*, H-4), 3.87 (1H, *m*, H-7), 4.33 (1H, *bs*, H-1), 4.90 (1H, *m*, H-5), 4.96 (1H, *m*, H-13), 5.09 (1H, *m*, H-11). ^{13}C NMR (50 Hz, CDCl_3): δ 20.0 (C-Me), 21.2, 21.3 (2xCOMe), 29.5 (C-9), 36.1 (C-4), 36.9 (C-8), 39.7 (C-10), 39.9 (C-12), 63.1 (C-5), 67.9 (C-7), 68.4 (C-13), 68.8 (C-11), 72.9 (C-1), 169.7 (C-3), 170.5 (2x acetyl). GCMS m/z (rel.int.) 268 $[\text{M}-60]^+$ (1), 226 (8), 208 (100), 183 (10), 141 (66), 113 (21), 97 (21), 95 (21), 69 (18).

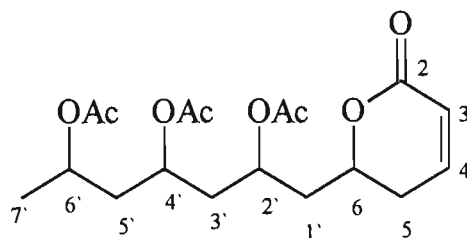
3.3.4. During the course of fractionation of the various extracts, 6-(2', 4'-Diacetoxy-pentyl)-5,6-dihydro-2H-pyran-2-one (diacetate) [16] (**43**), 6-(2', 4', 6'-Triacetoxy-heptyl)-5,6-dihydro-2H-pyran-2-one (triacetate) [16] (**44**), 6-(4', 6'-Dihydroxy, 8'phenyloct-1', 7'dienyl)-5,6-dihydro-2H-pyran-2-one (cryptofolione) [16] (**36**) and 6-(styryl-5,6-dihydro-2H-pyran-2-one (goniothalamine) [17] (**45**) were also isolated in gram quantities.



diacetate (**43**)

3.3.4. 6-(2', 4'-Diacetoxy-pentyl)-5,6-dihydro-2H-pyran-2-one (diacetate) [16] (**43**). $[\alpha]_D^{22} +55.8^\circ$ (CHCl_3 , c.016). IR $\nu_{\text{max}}^{\text{cm}^{-1}}$ 2950, 1733, 1435, 1375, 1245, 1040, 960, 820. ^1H NMR (200 MHz, CDCl_3): δ 1.26 (3H, *d*, $J = 6.29$ Hz, Me), 1.80, 2.06 (2H, *m*, H-3'), 1.96, 2.19 (2H, *m*, H-1'), 2.06 (6H, overlapping, *d*, OCOMe), 2.42 (2H, *m*, H-5), 4.52 (1H, *ddq*, $J = 12, 6.48, 4.48$ Hz, H-6), 4.98 (1H, *m*, H-4'), 5.13 (1H, *m*, H-2'), 6.00 (1H, *ddd*, $J = 9.76, 2.44, 0.96$ Hz, H-3), 6.91 (1H, *ddd*, $J = 9.76, 5.80, 2.27$ Hz, H-4). ^{13}C NMR (CDCl_3 , 50 MHz): δ 19.9 (Me), 21.0, 21.1 (2xOAc), 29.0 (C-5), 38.9 (C-1'), 40.2 (C-3'), 67.6 (C-2', C-4'), 74.8 (C-6), 121.0 (C-3), 145.0 (C-4), 163.7 (C-2), 170.3, 170.4

(2xOAc). CI-MS (CH_4) m/z (rel.int.): 285 $[\text{M}+\text{H}]^+$ (15), 265 (0.04), 253 (4), 226 (16), 225 (100), 193 (4), 165 (23). HR-MS: $[\text{M}]^+$ 284.1250; calcd. for $\text{C}_{14}\text{H}_{20}\text{O}_6$ $[\text{M}]^+$ 284.1260.

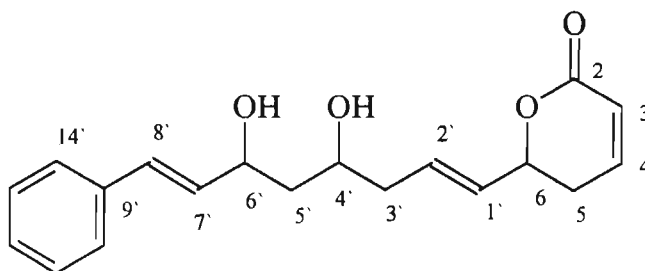


triacetate (**44**)

3.3.5. 6-(2',4',6'-Triacetoxy-heptyl)-5,6-dihydro-2H-pyran-2-one (triacetate) [16] (**44**).

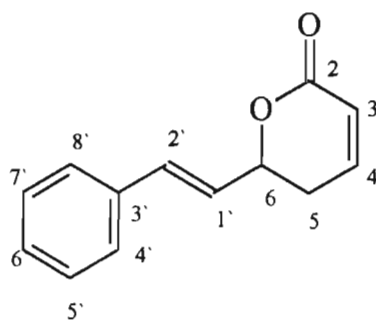
$[\alpha]_{\text{D}}^{22} +43.8^\circ$ (CHCl_3 , c 0.63). IR $\nu_{\text{max}}^{\text{cm}^{-1}}$ 2950, 1730, 1435, 1370, 1245, 1040, 960, 820. ^1H NMR (200 MHz, CDCl_3): δ 1.23 (3H, d , $J = 6.24$ Hz, Me), 1.77, 1.99, 2.15 (6H, overlapping, m , H-3', H-5', H-1'), 2.03 (3H, s , OCOMe), 2.07 (6H, s , OCOMe), 2.40 (2H, m , H-5), 4.49 (1H, $dddd$, $J = 11.60, 6.41, 4.01$ Hz, H-6), 4.83-5.13 (3H, m , H-2', H-4', H-6'), 6.01 (1H, ddd , $J = 9.76, 2.50, 1.16$ Hz, H-3), 6.89 (1H, ddd , $J = 9.80, 5.72, 2.80$ Hz, H-4). ^{13}C NMR (CDCl_3 , 50 MHz): δ 20.0 (Me), 21.1, 21.2, 21.3 (OAc), 29.1 (C-5), 39.0 (C-1', C-5'), 40.2 (C-3'), 67.6 (C-4'), 67.8 (C-2'), 68.1 (C-6'), 74.9 (C-6), 121.2 (C-3), 144.9 (C-4), 163.8 (lactone C=O), 170.4, 170.5, 170.6 (3xOAc). CI-MS (CH_4) m/z (rel.int.): 371 $[\text{M}+\text{H}]^+$ (4), 312 (12), 311 (100), 251 (6), 191 (10). HR-MS $[\text{M}]^+$ 370.1267; calc for $\text{C}_{18}\text{H}_{26}\text{O}_8$ $[\text{M}]^+$ 370.1625.

3.3.6. 6-(4', 6'-Dihydroxy, 8'phenyloct-1', 7' dienyl)-5,6-dihydro-2H-pyran-2-one (cryptofolione) [16] (**36**).



(**36**)

$[\alpha]_D^{22} +57.0^\circ$ (CHCl_3 , c 0.52). IR ν_{max} cm^{-1} 3440, 2942, 1700, 1385, 1250, 1055, 975, 825, 755, 700. HR MS 314.1518 calcd. for $\text{C}_{19}\text{H}_{22}\text{O}_4$, found 314.1503. ^1H NMR (200 MHz, CDCl_3): δ 1.78 (2H, *m*, H-5'), 2.29 (2H, *t*, $J = 6.6$, Hz, H-3'), 2.41 (2H, *m*, H-5), 3.46 (2H, *m*, overlapping, OH-4', OH-6'), 4.05 (1H, *m*, H-4'), 4.63 (1H, *m*, H-6'), 4.88 (1H, *dd*, $J = 14.5, 8.0, 6.6$ Hz, H-6), 5.63 (1H, *dd*, $J = 15.7, 6.3$ Hz, H-1'), 5.82 (1H, *m*, H-2'), 6.00 (1H, *dt*, $J = 9.8, 3.6$ Hz, H-3), 6.23 (1H, *dd*, $J = 16.0, 5.8$ Hz, H-7'), 6.61 (1H, *dd*, $J = 16.0, 1.0$ Hz, H-8'), 6.83 (1H, *m*, H-4). ^{13}C NMR (50 MHz, CDCl_3): δ 29.6 (C-5), 40.3 (C-3'), 42.3 (C-5'), 68.0 (C-4'), 70.0 (C-6'), 77.9 (C-6), 121.3 (C-3), 126.4 (C-10', C-14'), 127.5 (C-12'), 128.5 (C-11', C-13'), 129.6 (C-8'), 129.7 (C-1'), 131.3 (C-2'), 131.9 (C-7'), 136.6 (C-9'), 145.1 (C-4) 164.3 (C-2).



(45)

3.3.7. 6-(Styryl-5,6-dihydro-2H-pyran-2-one (goniotalamin) [17] (45). $[\alpha]_D^{22} +183.9^\circ$ (CHCl_3 ; c 0.71) lit. [17] $+170.3^\circ$. ^1H NMR (200 MHz, CDCl_3): δ 2.52 (2H, *m*, H-5), 5.09 (1H, *m*, H-6), 6.08 (1H, *ddd*, $J = 9.8, 3.7, 1.9$ Hz, H-3), 6.26 (1H, *dd*, $J = 15.9, 6.3$ Hz, H-1'), 6.72 (1H, *dd*, $J = 15.9, 1.3$ Hz, H-2'), 6.91 (1H, *ddd*, $J = 9.9, 4.2, 3.6$ Hz, H-4), 7.33 (5H, *m*, Ar-H). ^{13}C NMR (50 MHz, CDCl_3): δ 29.8 (C-5), 76.5 (C-6), 121.5 (C-3), 125.6 (C-1'), 126.7 (C-4', 8'), 128.3 (C-6'), 128.7 (C-5', 7'), 133.0 (C-2'), 135.7 (C-3'), 144.8 (C-4), 163.9 (C-2).

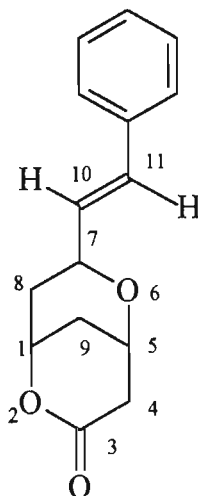
3.4. CRYPTOCARYA WYLIEI

Plant material was collected in Umtamvuma Nature reserve in May 1994 from *Cryptocarya wyliei* Stapf by Mr. Robert Scott-Shaw (Natal Parks Board). A voucher specimen no. 6084 was lodged in the Killick Herbarium.

Air dried milled bark (686 gr) was extracted successively under mild heat on a waterbath with:

1. Petrol ether 60-80° overnight yielding 2.02 gr extract.
2. CH₂Cl overnight yielding 6.24 gr extract.
3. EtOAc overnight yielding 4.34 gr extract.
4. EtOH 95% overnight yielding 29.60 gr extract.

3.4.1. 7-Styryl-2,6-dioxabicyclo [3,3,1] nonan-3-one. (48)

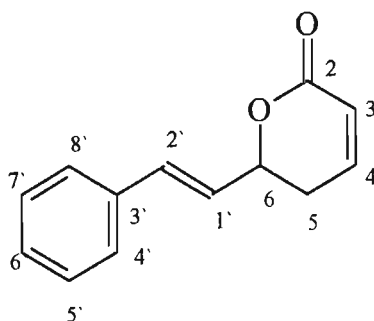


(48)

The CH₂Cl₂ extract (6.24 gr) was fractionated on dry silica column eluted with CH₂Cl₂ 100% (I), followed by Hexane-CHCl₃-EtOAc (4:2:4) (II), then EtOAc 100% (III). (I) Was further purified on chromatotron using CH₂Cl₂-EtOAc (90:10), affording the compound (18.6 mg), mp (CH₂Cl₂) 69°. [α]_D²² - 0.0°. IR ν_{\max} cm⁻¹: 1730 (C=O), 1608, 1341, 1218, 1080, 758. ¹H NMR (CDCl₃, 200 MHz): δ 1.77 (1H, *ddd*, *J* = 14.0, 2.2 Hz, H-8_a), 2.14 (1H, *m*, H-8_b), 1.99 (2H, *m*, H-9), 2.83 (1H, *dd*, *J* = 19.3, 5.0 Hz, H-4_a), 2.98 (1H, *m*, H-4_b), 4.45 (2H, *m*, H-5, H-7), 4.95 (1H, *m*, H-1), 6.14 (1H, *dd*, *J* = 16.0, 6.1 Hz, H-10), 6.64 (1H, *dd*, *J* = 16.0, 1.1 Hz, H-11), 7.23-7.41 (5H, *m*, Ar-H). ¹³C NMR (CDCl₃,

50 MHz): 29.5 (C-9), 36.5 (C-4), 37.2 (C-8), 66.1 and 66.8 (C-5, C-7 or reverse), 72.8 (C-1), 127.9 (C-10), 126.5, 128.1, 128.6, 136.2 (Ar-C), 131.6 (C-11), 169.6 (pyrone C=O). MS m/z (rel. int.): 244 (8), 184 (6), 158 (6), 131 (25), 115 (12), 104 (100), 91 (15), 77 (11), 70 (26). HR-MS: $[M]^+$ 244.1086; calcd. for $C_{15}H_{16}O_3$ 244.1099.

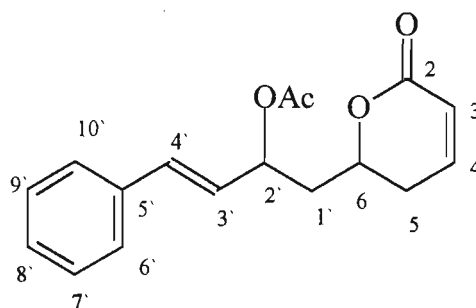
3.4.2. Goniotalamin [17] (45).



(45)

After combination of tubes from fraction (I), goniotalamin crystallized out (395 mg). $[\alpha]_D^{22}$ ($CHCl_3$; c 0.71) $+183.9^\circ$ lit. [17] $+170.3^\circ$. 1H NMR (200 MHz, $CDCl_3$): δ 2.52 (2H, *m*, H-5), 5.09 (1H, *m*, H-6), 6.08 (1H, *ddd*, $J = 9.8, 3.7, 1.9$ Hz, H-3), 6.26 (1H, *dd*, $J = 15.9, 6.3$ Hz, H-1'), 6.72 (1H, *dd*, $J = 15.9, 1.3$ Hz, H-2'), 6.91 (1H, *ddd*, $J = 9.9, 4.2, 3.6$ Hz, H-4), 7.33 (5H, *m*, Ar-H). ^{13}C NMR (50 MHz, $CDCl_3$): δ 29.8 (C-5), 76.5 (C-6), 121.5 (C-3), 125.6 (C-1'), 126.7 (C-4', 8'), 128.3 (C-6'), 128.7 (C-5', 7'), 133.0 (C-2'), 135.7 (C-3'), 144.8 (C-4), 163.9 (C-2).

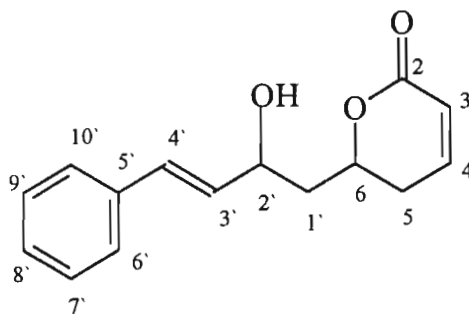
3.4.3. Cryptocaryalactone [15] (34).



(34)

Fraction (I) was further purified on dry silica column eluted with CH_2Cl_2 and the impure compound kept. A fraction of the Petrol-ether extract (900 mg) was purified on the chromatotron with CH_2Cl_2 and the impure compound kept. A fraction of the EtOAc extract (1.14 gr) was purified on chromatotron with CH_2Cl_2 keeping the impure compound. All the above impure fractions were combined and purified on a column with a gradient elution from CH_2Cl_2 -Petrol-ether (8:2) to CH_2Cl_2 -EtOAc (99:1), affording the compound (34.7 mg oil), $[\alpha]_D^{22} +56.3^\circ$, (CHCl_3 ; c 0.34) lit. $[\alpha] +15.55^\circ$. IR $\nu_{\text{max}}^{\text{cm}^{-1}}$ 1730, 1601, 1494, 1380, 1230, 1078, 1037, 968.

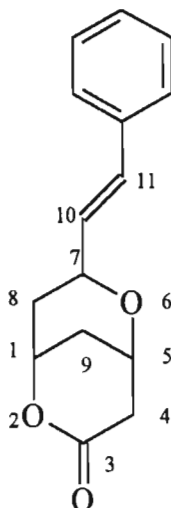
3.4.4. Deacetylcryptocaryalactone [2] (35).



(35)

Fraction (III) was purified twice on the chromatotron using CH_2Cl_2 -EtOAc (9:1) as eluent, affording the compound (210 mg) mp $65-67^\circ$, $[\alpha]_D^{22} - 0.0^\circ$, lit. (2) -90° . IR $\nu_{\text{max}}^{\text{cm}^{-1}}$ 3350 (OH), 1708 (C=O), 1394, 1269, 1010, 966, 756. ^1H NMR (CDCl_3 , 200 MHz): δ 1.90 (1H, *m*, H-1_a'), 2.20 (1H, *m*, H-1_b'), 2.41 (2H, *m*, H-5), 4.59 (2H, *m*, H-6 and H-2'), 4.78 (1H, *s*, OH), 5.98 (1H, *m*, H-3), 6.18 (1H, *dd*, $J = 15.9, 7.0$ Hz, H-3'), 6.63 (1H, *dd*, $J = 15.9$ Hz, H-4'), 6.85 (1H, *m*, H-4), 7.20-7.45 (5H, *m*, Ar-H). ^{13}C NMR (CDCl_3 , 50 MHz): δ 29.4 (C-5), 41.9 (C-1'), 69.6 (C-2'), 75.9 (C-6), 121.1 (C-3), 126.5, 127.9, 128.6, 136.2 (Ar-C), 130.9 (C-3'), 131.3 (C-4'), 145.4 (C-4), 164.3 (pyrone C=O). MS m/z (rel.int.): 244 $[\text{M}]^+$ (12), 158 (25), 133 (27), 104 (100) $[\text{C}_6\text{H}_5\text{CH}=\text{CH}_2^+]$, 97 (28), 94 (25), 91 (20), 77 (12). HR-MS: $[\text{M}]^+$ 244.1093; calcd. for $\text{C}_{15}\text{H}_{16}\text{O}_3$ 244.1099.

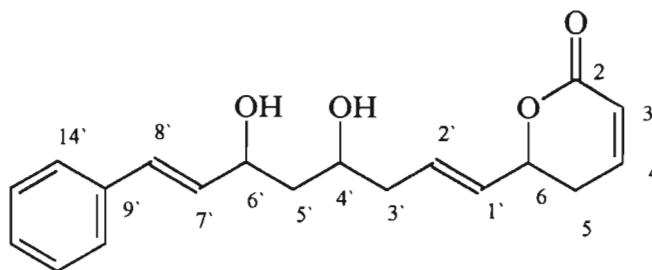
3.4.4a. CYCLIZATION OF DEACETYLCRYPTOCARYALACTONE to afford
7-styryl-2,6-dioxabicyclo [3,3,1] nonan-3-one (**48**)



(**48**)

Deacetylcryptocaryalactone (200 mg) in CH_2Cl_2 (5 ml) was treated with excess NaH. After 5 minutes at RT, the reaction was quenched (EtOAc) and the precipitate filtered off. The reaction mixture was purified on the chromatotron with CH_2Cl_2 , affording the compound (160 mg), mp 69° (Hexane/ CH_2Cl_2). The compound was identical to the one occurring naturally in the bark.

3.4.5. From the EtOAc and EtOH extracts 1.4 gr cryptofolione [16] (**36**) was isolated.



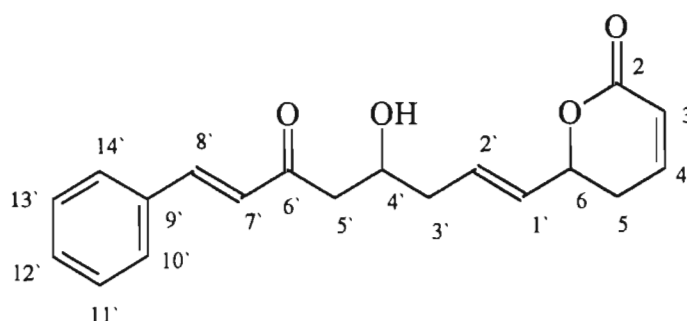
(**36**)

Air dried milled leaves (21.7 gr) from the same source as the bark were extracted at RT with CHCl_3 for two hours. The extract was spotted on tlc and compared to the bark extract, the same compounds as in the bark were present.

3.5. *CRYPTOCARYA MYRTIFOLIA*

Plant material was collected in May 1994 in the Karkloof Nature Reserve from *Cryptocarya myrtifolia* by Mr. Robert Scott-Shaw (Natal Parks Board). A voucher specimen no. 6083 was deposited in the Killick Herbarium.

3.5.1. 6-(4'-Hydroxy-6'-oxo-8'-phenyloct-1',7'-dienyl)-5,6-dihydro-2H-pyran-2-one.
(oxidized cryptofolione) (49).



(49)

Air dried milled bark (1.54 kg) was extracted successively under mild heat on a waterbath as follows:

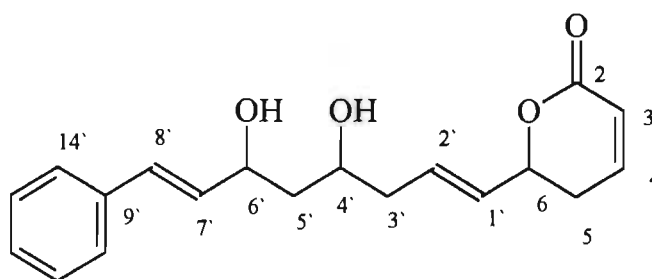
1. Hexane overnight yielding 1.85 gr extract.
2. CH₂Cl₂ overnight yielding 11.51 gr extract.
3. EtOAc overnight yielding 8.00 gr extract.
4. EtOH 95% for two days yielding 3.35 gr extract.

The CH₂Cl₂ and EtOAc extract were purified repeatedly on dry silica gel columns using a gradient of Hexane-EtOAc from (1:0) to (0:1). The impure compound from the columns was further purified on the chromatotron using Et₂O-EtOAc (7:0), yielding oxidized cryptofolione (120 mg oil), ¹H NMR (CDCl₃, 200 MHz): δ 2.35 (2H, *m*, H-3'), 2.45 (2H, *m*, H-5), 2.85 (2H, *m*, H-5'), 3.40 (1H, *bs*, OH), 4.22 (1H, *bm*, H-4'), 4.90 (1H, *q*, *J* = 7.9 Hz, H-6), 5.71 (1H, *dd*, *J* = 7.9, 6.4 Hz, H-1'), 5.91 (1H, *m*, H-2'), 6.03 (1H, *dt*, *J* = 9.9, 1.9 Hz, H-3), 6.74 (1H, *d*, *J* = 16.3 Hz, H-8'), 6.90 (1H, *m*, H-4), 7.49 (5H, overlapping, *m*, Ar-H), 7.57 (1H, *d*, *J* = 16.2 Hz, H-7'). ¹³C NMR (CDCl₃, 50 MHz): δ 29.6 (C-5), 39.3 (C-3'), 46.2 (C-5'), 67.2 (C-4'), 77.9 (C-6), 121.4 (C-3), 126.6 (C-7'), 128.4

(C-10',14'), 128.9 (C-11', 13'), 129.0 (C-1'), 130.8 (C-12'), 130.9 (C-2'), 134.1 (C-9'), 143.8 (C-8'), 144.9 (C-4), 164.1 (C-2), 200.5 (C-6').

This spectral data is in accordance with the synthetic compound that was the oxidation product of cryptofolione with pyridinium chloroformate [16].

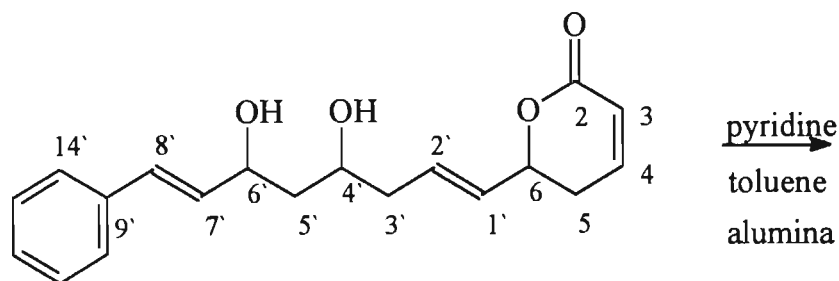
3.5.2. During the course of isolation of the above compound, 14 gr of cryptofolione (**36**) [16] was isolated.



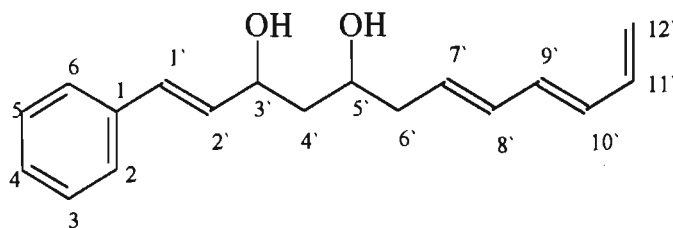
(36)

3.6. NOVEL REACTIONS OF α -PYRONES.

3.6.1. Ring opening in cryptofolione. 3',5' Dihydroxy- 1',7',9',11' dodecatetraenylbenzene (50).



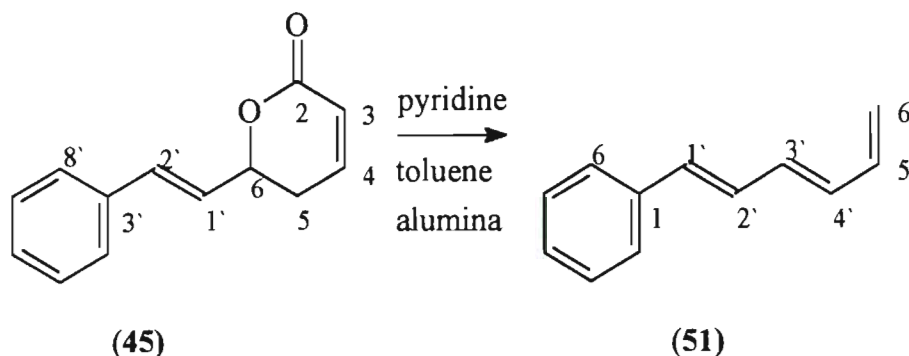
(36)



(50)

To cryptofolione (270 mg) in toluene, activated neutral alumina (heated to 350° and cooled for thirty minutes) was added, three drops of pyridine added and refluxed for one hour. The toluene was filtered off and the alumina was suspended in CHCl_3 . The alumina was extracted four times with CHCl_3 and the crude was purified on the chromatotron using CH_2Cl_2 yielding the compound (7mg). GCMS m/z (rel.int.) 270 $[\text{M}]^+$ (3), 252 (12), 234 (17), 207 (6), 165 (11), 159 (19), 131 (100), 91 (80), 57 (39). ^1H NMR (200 MHz, CDCl_3): δ 1.80 (2H, *m*, H-4'), 2.33 (2H, *t*, $J = 7.0$ Hz, H-6'), 4.04 (1H, *bs*, H-5'), 4.66 (1H, *m*, H-3'), 5.16 (1H, *dd*, $J = 16.5, 9.9$ Hz, H-12'), 5.74 (1H, *m*, H-11'), 6.30 (4H, *m*, H-7', H-8', H-9', H-10'), 6.31 (1H, *dd*, $J = 16.0, 5.9$ Hz, H-2'), 6.64 (1H, *d*, $J = 16.2$ Hz, H-1'), 7.20-7.41 (5H, *m*, Ar-H). ^{13}C NMR (50 MHz, CDCl_3): δ 41.1 (C-6'), 42.1 (C-4'), 68.5 (C-5'), 70.4 (C-3'), 117.2 (C-12'), 126.4 (overlapping, C-2, C-6), 127.6 (C-4), 128.5 (overlapping, C-3, C-5), 129.9 (C-1'), 130.3 (C-8'), 131.8 (C-2'), 132.4 (C-7'), 132.7 (C-9'), 133.6 (C-10'), 136.6 (C-1).

3.6.2. Ring opening of goniotalamin. 1',3',5' Hexatrienylbenzene (51).

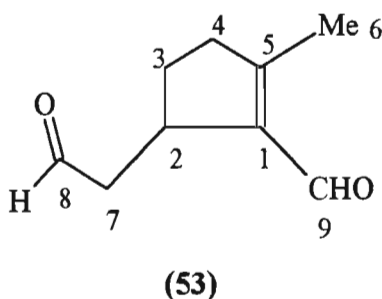


To goniotalamin (190 mg) in toluene, alumina (210 mg, activated at 400° for thirty minutes) was added and four drops of pyridine added. It was refluxed for one hour when four more drops of pyridine were added. After two hours reflux (from start), more alumina was added and left at RT overnight. Alumina was filtered off and the crude was purified on the chromatotron using CH₂Cl₂ yielding the product (10 mg). Goniotalamin (100 mg) was also recovered. ¹H NMR (200 MHz, CDCl₃): δ 5.20 (2H, *m*, H-6'), 6.45 (4H, overlapping, *m*, H-1', H-2', H-3', H-4'), 6.83 (1H, *m*, H-5'), 7.30 (5H, *m*, Ar-H). ¹³C NMR (50 MHz, CDCl₃): δ 117.5 (C-6'), 126.3 (overlapping, C-2, C-6), 127.5 (C-4), 128.6 (overlapping, C-3, C-5), 128.8 (C-1'), 132.9 (C-2'), 133.4 (C-3'), 133.7 (C-4'), 137.0 (C-5'), 137.2 (C-1).

3.7. ALBERTA MAGNA

Plant material was collected in July 1996 in the National Botanical Gardens in Pietermaritzburg from a mature tree of *Alberta magna*, identified and authenticated by the curator of the Gardens, Mr. Brian Tarr.

3.7.1 2-Acetaldehyde-1-formyl-5-methylcyclopent-1-ene [18] (53).



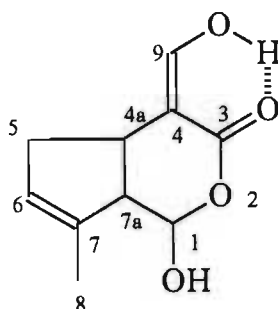
A batch of freshly collected milled leaves (922 gr) was extracted at RT as follows:

1. CH₂Cl₂ for two weeks yielding 12.10 gr extract.
2. EtOAc for one week yielding 11.80 gr extract.

The CH₂Cl₂ extract (12.1 gr), was fractionated on a dry silica column with CH₂Cl₂ and then repeatedly purified on the chromatotron with CH₂Cl₂ yielding an oil that solidifies (160 mg). $[\alpha]_D^{22} +81.2^\circ$ (CHCl₃, c 0.75). GCMS *m/z* (rel.int) 152 [M]⁺ (1), 134 (23), 124 (16), 108 (82), 95(42), 70 (100), 67 (29), 53 (44). ¹H NMR (200 MHz, CDCl₃): δ 1.50 (1H, *dddd*, *J* = 5.3, 4.6, 3.7, 3.4, 3.2 Hz, H-3_a), 2.15 (1H, *m*, H-3_b), 2.16 (3H, *dd*, *J* = 1.4, 1.3 Hz, Me), 2.34 (1H, *ddd*, *J* = 16.8, 9.8, 7.0, Hz, H-7_a), 2.56 (2H, *m*, H-4), 2.94 (1H, *ddd*, *J* = 16.8, 12.6, 4.2 Hz, H-7_b), 3.47 (1H, *m*, H-2), 9.76 (1H, *dd*, *J* = 1.6, 0.6 Hz, H-8), 9.98 (1H, *s*, H-9). ¹³C NMR (50 MHz, CDCl₃): δ 14.5 (C-6), 28.2 (C-3), 38.2 (C-2), 39.0(C-4), 47.8 (C-7), 139.1 (C-1), 164.0 (C-5), 188.0 (C-9), 202.0 (C-8).

Plant material was collected in May 1996 in the Winterskloof area of Pietermaritzburg and authenticated as before.

3.7.2. *4,4a,5,7a-Tetrahydro-1-hydroxy-4-(hydroxymethylene)-7-methylcyclopenta[c]pyran-3(1H)-one* *(amagnalactone) (**55**).



(**55**)

A batch of freshly collected milled leaves (200 gr) was extracted at RT with:

1. CH_2Cl_2 for twelve days yielding 1.97 gr extract.
2. EtOAc for one week yielding 1.50 gr extract.

A part (1.7 gr) of the EtOAc extract was purified on the chromatotron using CH_2Cl_2 , followed by Hexane-EtOAc (3:2) and then Hexane-EtOAc (1:1). The impure compound was then further purified on the chromatotron using Hexane-EtOAc (3:2) yielding the title compound (40 mg oil). More amagnalactone (65 mg) was obtained from another batch of leaves (665 mg) from the same source. $[\alpha]_{\text{D}}^{22} +138.1^\circ$, (CHCl_3 , c 0.19). IR $\nu_{\text{max}}\text{cm}^{-1}$ 3050, 3000, 1684 (H-bonded C=O), 1616, 1116. GCMS, not volatile enough to elute. TMS derivative GCMS m/z (rel.int) 340 $[\text{M}]^+$ (5), 250 (63), 235 (38), 180 (92), 160 (100), 132 (7), 73 (55). ^1H NMR (200 MHz, CDCl_3): δ 1.85 (3H, *d*, $J = 1.4$ Hz, Me), 2.10 (1H, *m*, H-5₁), 2.40 (1H, *dd*, $J = 8.0$ Hz, H-7a), 2.80 (1H, *m*, H-5₂), 3.16 (1H, *m*, H-4a), 4.90 (1H, *d*, $J = 8.0$ Hz, H-1), 5.54 (1H, *d*, $J = 0.9$ Hz, H-6), 7.59 (1H, *d*, $J = 0.9$ Hz, H-9). ^{13}C NMR (50 MHz, CDCl_3): δ 16.5 (Me), 35.4 (C-4a), 38.9 (C-5), 49.9 (C-7a), 96.8 (C-1), 110.5 (C-4), 127.5 (C-6), 139.1 (C-7), 154.1 (C-9), 173.2 (C-3).

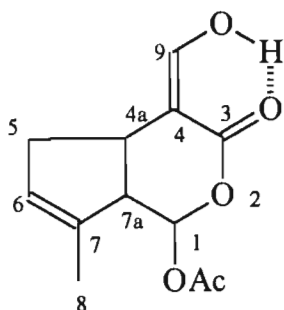
During the course of purification, 4-hydroxy-acetophenone was isolated in minute quantities.

* Name kindly supplied by Chemical Abstract Service, Columbus, Ohio, U.S.A.

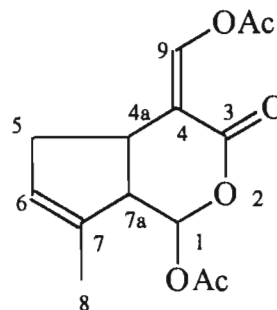
3.6.2a. ACETYLATION OF AMAGNALACTONE: two products.

3.6.2aa. *4,4a,5,7a-tetrahydro-1-acetoxy-4-(hydroxymethylene)-7-methylcyclopenta[c]pyran-3(1H)-one* (monoacetyl) (**56**).

3.6.2ab. *4,4a,5,7a-tetrahydro-1-acetoxy-4-(acetoxymethylene)-7-methylcyclopenta[c]pyran-3(1H)-one* (diacetyl) (**57**).



monoacetylamagnalactone (**56**)



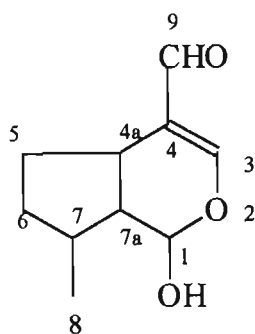
diacetylamagnalactone (**57**)

Amagnalactone (**55**), (90 gm) was dissolved in pyridine at RT, acetic anhydride added and left overnight. The reaction mixture was poured over ice, acidified with dil. HCl and extracted three times with EtOAc. The crude mixture was purified on the chromatotron using CH_2Cl_2 yielding monoacetyl lactone (**56**) (14 mg) and diacetyl lactone (**57**) (24 mg). Monoacetyl lactone (**56**) $[\alpha]_{\text{D}}^{22} +100^\circ$ (CHCl_3 , c 0.007). IR $\nu_{\text{max}} \text{ cm}^{-1}$ 3060, 2860, 1758, 1713 (H-bonded C=O), 1635, 1604, 1244, 1196, 929. GCMS not sufficiently volatile. ^1H NMR (200 MHz, CDCl_3): δ 1.77 (3H, *t*, $J = 0.7$, Hz, Me), 2.16 (3H, *s*, OAc), 2.05-2.22 (1H, *m*, H-5₁), 2.70 (1H, *m*, H-4a), 2.82 (1H, *m*, H-5₂), 3.22 (1H, *m*, H-7a), 5.54 (1H, *d*, $J = 1.5$ Hz, H-6), 5.95 (1H, *d*, $J = 6.5$ Hz, H-1), 7.55 (1H, *d*, $J = 1.0$ Hz, H-9). ^{13}C NMR (50 MHz, CDCl_3): δ 15.7 (C-8), 21.0 (OAc), 33.9 (C-7a), 38.5 (C-5), 47.8 (C-4a), 91.9 (C-1), 111.0 (C-4), 128.3 (C-6), 137.1 (C-7), 153.6 (C-9), 169.5 (OAc), 172.6 (C-3).

Diacetyl lactone (**57**) $[\alpha]_{\text{D}}^{22} +46.3^\circ$ (CHCl_3 , c 0.1). IR $\nu_{\text{max}} \text{ cm}^{-1}$ 1784, 1780, 1740, 1652, 1608. GCMS m/z (rel.int.) 220 $[\text{M}-60]^+$ (21), 192 (10), 178 (21), 150 (85), 122 (47), 108 (14), 80 (100), 53 (9). HR-MS calcd. for $\text{C}_{12}\text{H}_{12}\text{O}_4$ $[\text{M}-60]$ 220.0731, found 220.0731. ^1H NMR (200 MHz, CDCl_3): δ 1.80 (3H, *s*, Me), 2.11 (3H, *s*, OAc), 2.28 (3H, *s*, OAc), 2.16-2.26 (1H, *m*, H-5₁), 2.86 (1H, *m*, H-5₂), 3.00 (1H, *m*, H-7a), 3.64 (1H, *tt*, $J = 7.8, 6.0$,

2.2 Hz, H-4a), 5.52 (1H, *d*, $J = 1.5$ Hz, H-6), 6.60 (1H, *d*, $J = 2.9$ Hz, H-1), 8.24 (1H, *d*, $J = 2.0$ Hz, H-9). ^{13}C NMR (50 MHz, CDCl_3): δ 14.8 (C-8), 20.6 (OAc), 20.9 (OAc), 32.9 (C-4a), 39.7 (C-5), 48.7 (C-7a), 91.6 (C-1), 116.0 (C-4), 128.3 (C-6), 136.3 (C-7), 145.2 (C-9), 166.1 (2xOAc), 168.7 (C-3).

3.6.3. *Cyclopenta[c]pyran-4-carboxaldehyde, 1,4a,5,6,7,7a-hexahydro-1-hydroxy-7-methyl (58)*, (Experimental, 3.6.3.).



(58)

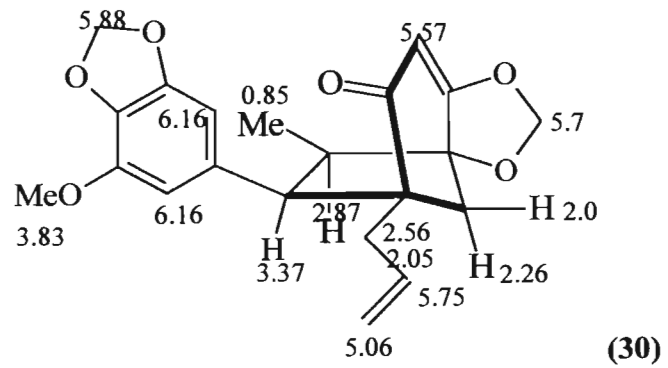
The EtOAc extract was purified on dry silica column with CH_2Cl_2 , followed by Et_2O . The Et_2O fraction was further purified on the chromatotron using CH_2Cl_2 - Et_2O (1:1) yielding the compound (57). GCMS 182 $[\text{M}]^+$ (20), 153 (23), 136 (30), 121 (21), 107 (39), 94 (59), 71 (98), 55 (100). GCMS of TMS derivative 254 $[\text{M}]^+$. HRMS calcdt. for $\text{C}_{10}\text{H}_{14}\text{O}_3$ 182.0939, found 182.0942. ^1H NMR (200 MHz, CDCl_3): δ 1.13 (3H, *d*, $J = 7.2$ Hz, Me), 1.30 (1H, *m*, H-6₁), 1.35 (1H, *m*, H-5₁), 2.06 (1H, *dd*, $J = 7.2$ Hz, H-7a), 2.30 (1H, *m*, H-5₂), 2.80 (1H, *m*, H-6₂), 2.90 (1H, *m*, H-4a), 5.25 (1H, *d*, $J = 7.1$ Hz, H-1), 7.19 (1H, *s*, H-3), 9.23 (1H, *s*, H-9). ^{13}C NMR (50 MHz, CDCl_3): δ 16.4 (Me), 30.4 (C-7), 31.7 (C-6), 32.5 (C-4a), 44.4 (C-7a), 95.9 (C-1), 127.4 (C-4), 161.7 (C-3), 190.7 (C-9).

REFERENCES

1. Gottlieb, O. R. (1972) *Phytochemistry* **11**, 1537.
2. Spencer, G. F., England, R. E. and Wolf, R. B. (1984) *Phytochemistry* **23**, 2499.
3. Ishiguro, K., Nagata, S., Fukomoto, H., Yamaki, M., Isoi, K. and Yamagat, Y. (1994) *Phytochemistry* **37**, 283.
4. Van Puyvelde, L., Dube, S., Uwimana, E., Uwera, C., Dommise, R.A., Esmans, E. L., Van Schoor, O. and Vlietinck, A.J. (1979) *Phytochemistry* **18**, 1215.
5. Davies-Coleman, M. T. and Rivett, D. E. A. (1989) *Progress Chem.Org.Nat.Products* **55**,1.
6. Dickinson, M. (1993) *Nat.Prod.Rep* **10**, 72.
7. Kashman, Y., Gustafson, K.R., Fuller, R.W., Cardelina, J.H., McMahon, J.B., Currens, M.J., Buckheit, R.W., Hughes, S.H., Cragg, G.M. and Boyd, M.R. (1992) *J.Med Chem.* **35**, 2735.
8. Mannito, P. (1981) *Biosynthesis of Natural Products*. Ellis Horwood Limited.
9. Halpern, O., Schmid, H. and Einleitung, A. (1958) *Helv.Chim.Acta* **41**, (123) 1109.
10. Harborne, J. B. (1993) *Nat.Prod.Rep.* **10**, 327.
11. Grayson, D.H. (1990) *Nat.Prod.Rep.* **7**, 327.
12. Gottlieb, O.R. (1978) *Prog.in the Chem.of Org.Nat.Prod.* **35**, 1.
13. Ayres, D.C. and Loike, J.D. (1990). *Lignans Chemical, biological and clinical properties*. Cambridge University Press.
14. Green, T. and Wiemer, D.F. (1991) *Phytochemistry* **30**, 3750.
15. Govindachari, T. R. and Parthasarathy, P. C. (1971) *Tetrahedron Letters* **37**, 3401.

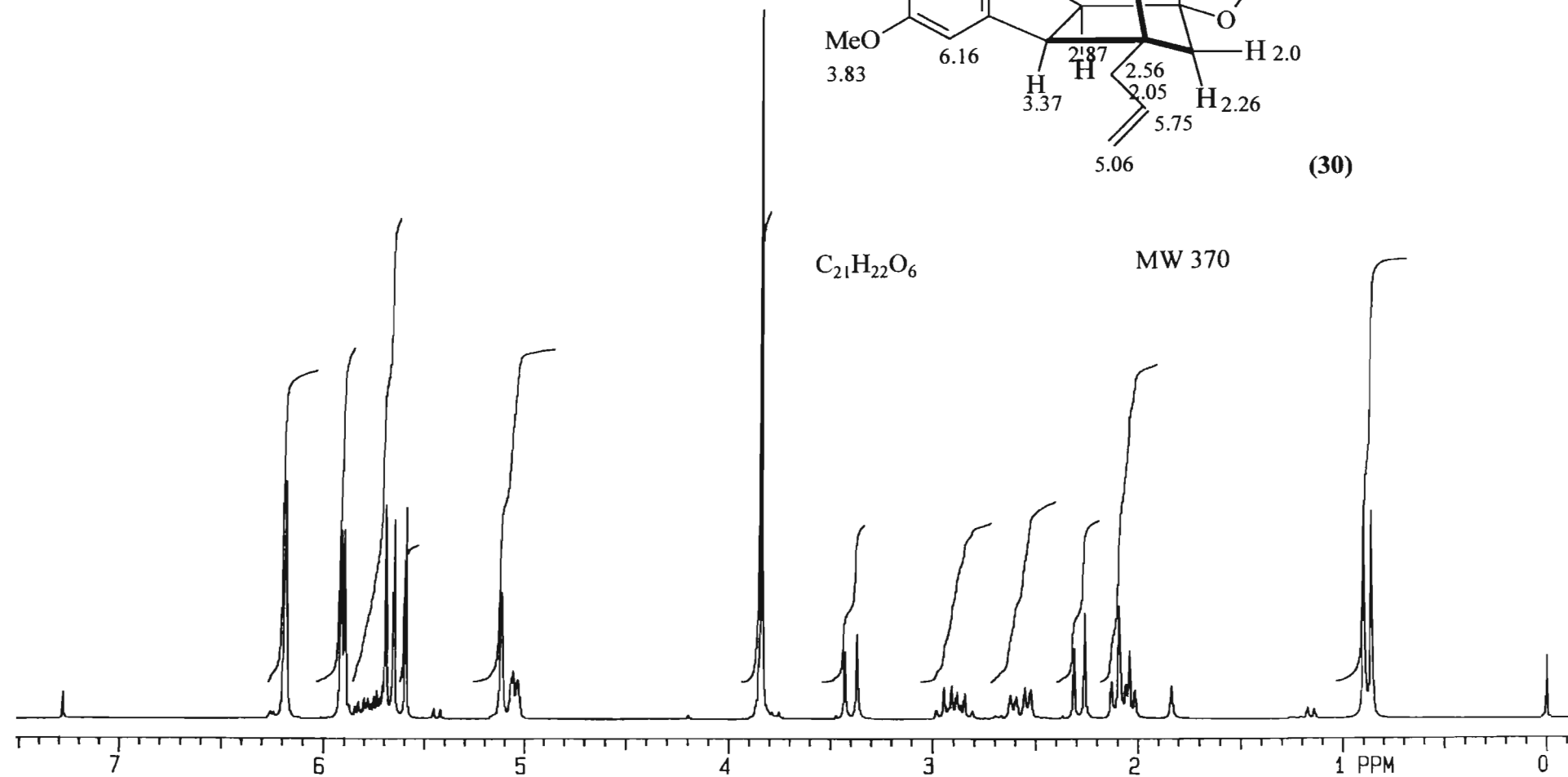
16. Sehlapelo, B.M. (1993) Ph.D. thesis , Department of Chemistry, University of Natal, Pietermaritzburg.
17. Jewers, K., Davis, J.B., Dougan, J., Manchanda, A. H., Bhenden, G., Kyi, A. and Wetchapinan, S. (1972) *Phytochemistry* **11**, 2025.
18. Japanese Patent JP 07010710-A 13/1/95.
19. Pooley, E. (1993) *The complete field guide to trees of Natal Zululand and Transkei*. Natal Flora Trust.
20. Hutchings, A. (1996) *Zulu Medicinal Plants an inventory*. University of Natal press Pietermaritzburg.
21. Beal, J.L. and Reinhard, E. (1980) *Natural Products as Medicinal Agents*. Hippokrates Verlag Stuttgart.
22. Meyer, H.H. (1984) *Liebigs. Ann. Chem.*, 977.
23. Bianco, A. (1994) *Pure & Appl. Chem.* **66**, 2335.
24. Bianco, A., Massa, M. Oguakwa, J.U. and Passacantilli, P. (1981) *Phytochemistry* **20**, 1871.
25. Damtoft, S., Jensen, S.R., and Weiergang, I. (1994) *Phytochemistry* **35**, 21.
26. Breinholt, J., Damtoft, S., Demuth, H., Jensen, S.R. and Nielsen, B.J. (1992) *Phytochemistry* **31**, 795.
27. Bianco, A., Guiso, M., Iavarone, C., Passacantilli, P. and Trogolo, C. (1977) *Tetrahedron* **33**, 851.
28. Xie, S., Uesato, S. Inouye, H., Fujita, T., Murai, F., Tagawa, M. and Shingu, T. (1988) *Phytochemistry* **27**, 49.
29. Ozaki, Y., Johne, S. and Hesse, M. (1979) *Helvetica Chimica Acta* **62**, 2708.

29. Ozaki, Y., Johne, S. and Hesse, M. (1979) *Helvetica Chimica Acta* **62**, 2708.
30. Bianco, A., Massa, M., Oguakwa, J.U. and Passacantilli, P. (1981) *Phytochemistry* **20**, 1871.
31. Achmad, S., Hoyer, T., Kjaer, A., Makmur, L. and Norrestam, R. (1987) *Acta Chem.Scand.* **B41**, 599.
32. Ward, R. S. (1993) *Nat.Prod.Rep.* **10**, 1.
33. Boros, C. A. and Stermitz, F. R. (1991) *J.Nat.Prod.* **54**, 1173.

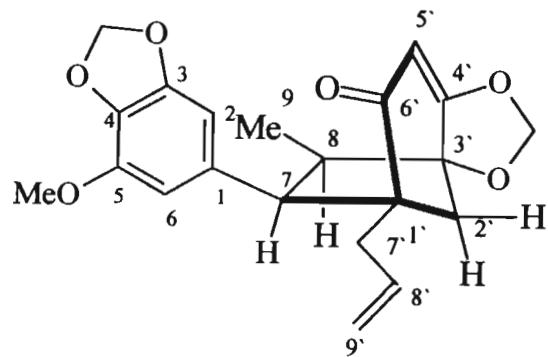


$C_{21}H_{22}O_6$

MW 370



(30) 1H NMR in $CDCl_3$

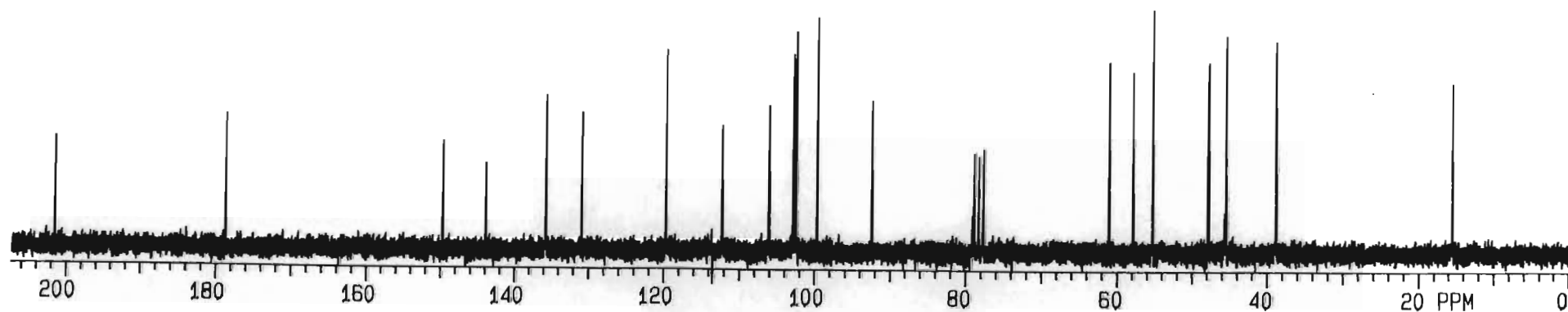


$C_{21}H_{22}O_6$

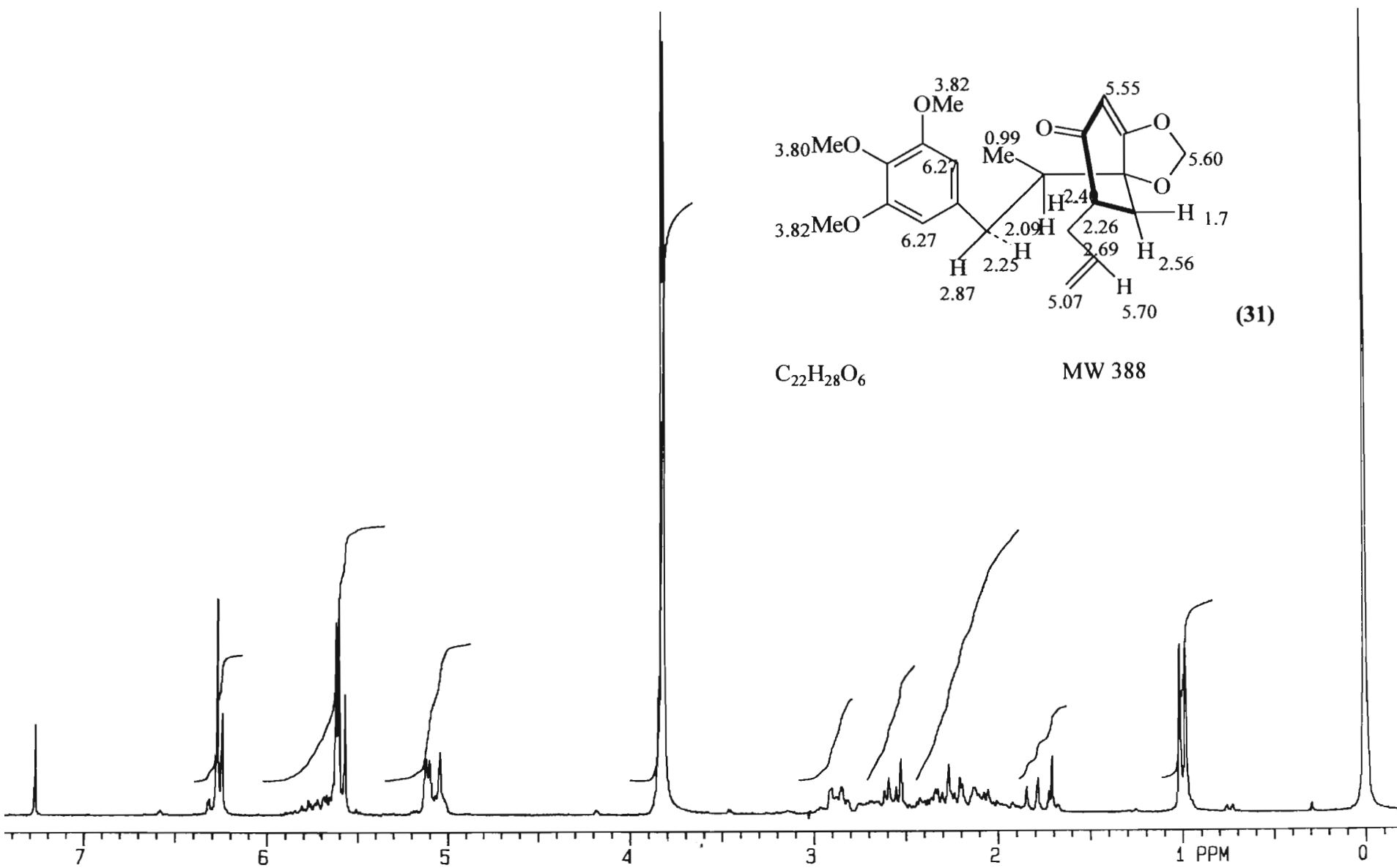
MW 370

(30)

carbon	δ	carbon	δ
C- 9	14.2	C- 6	104.8
C- 7	37.7	C- 2	111.2
C- 8	44.4	C- 9'	118.5
C- 2'	46.6	C- 1	129.8
C- 7	54.0	C- 8'	134.4
OMe	56.6	C- 4	134.4
C- 1'	59.8	C- 5	142.7
C- 3'	91.2	C- 3	148.5
C- 5'	98.4	C- 4'	177.5
OCH ₂ O	101.3	C- 6'	200.2
OCH ₂ O	101.5		



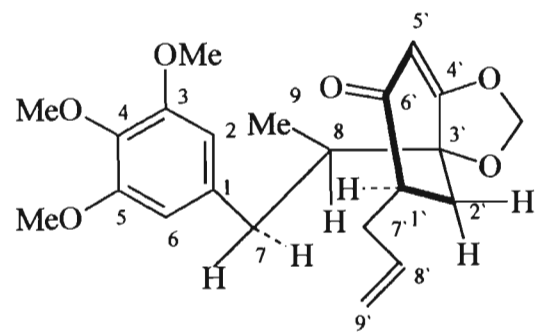
(30) ^{13}C NMR in $CDCl_3$



$C_{22}H_{28}O_6$

MW 388

(31) 1H NMR in $CDCl_3$

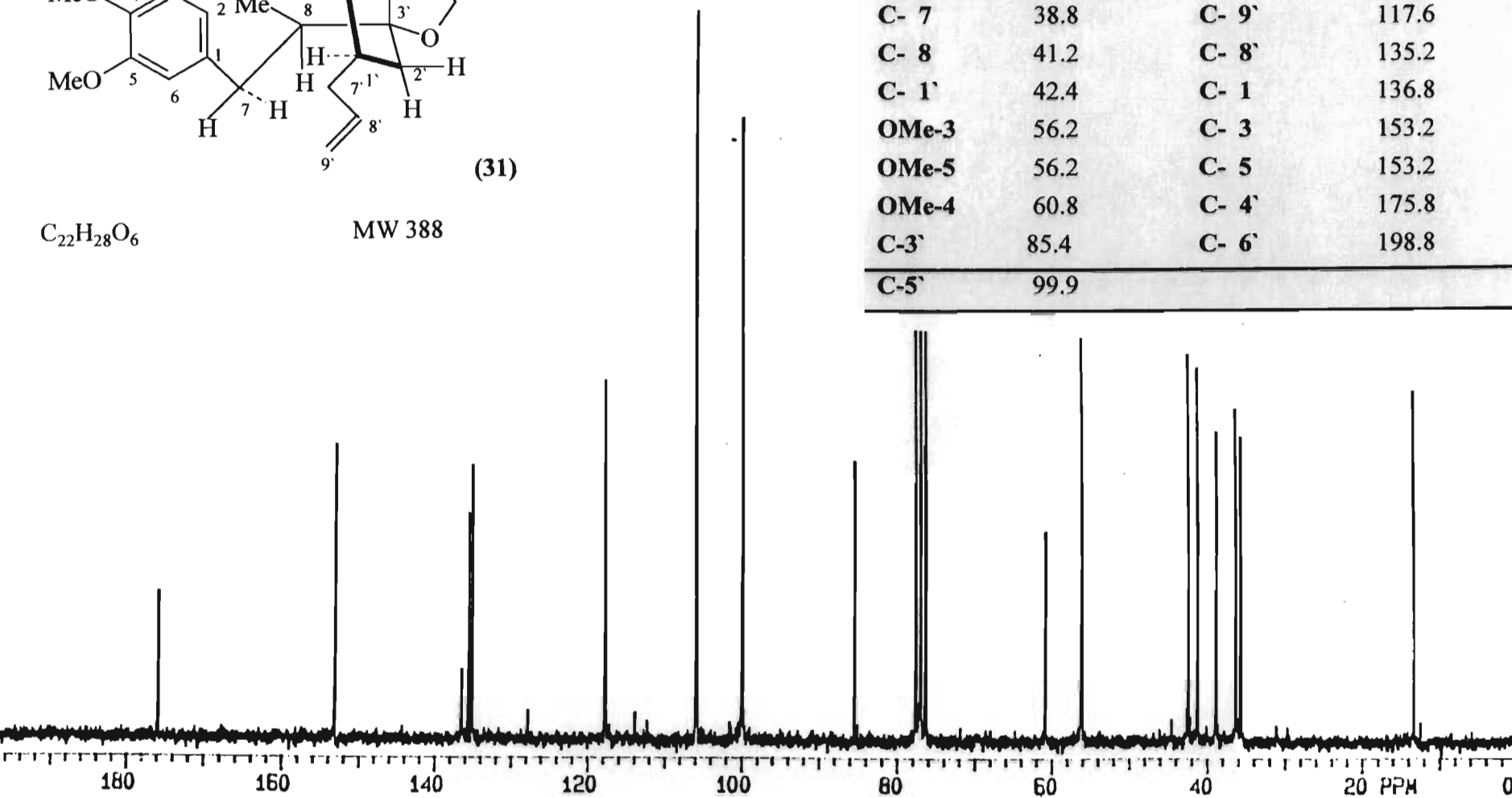


(31)

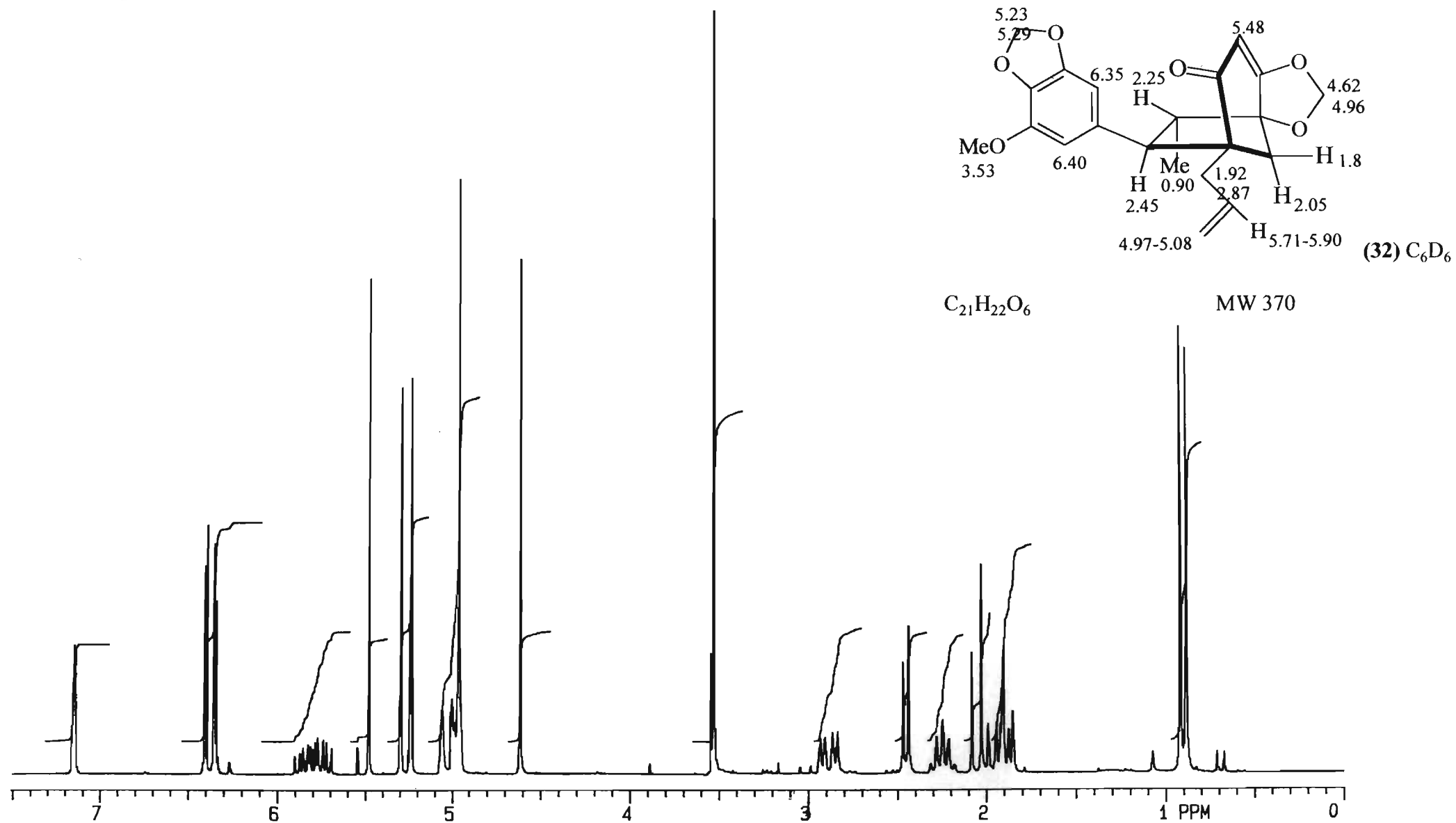
$C_{22}H_{28}O_6$

MW 388

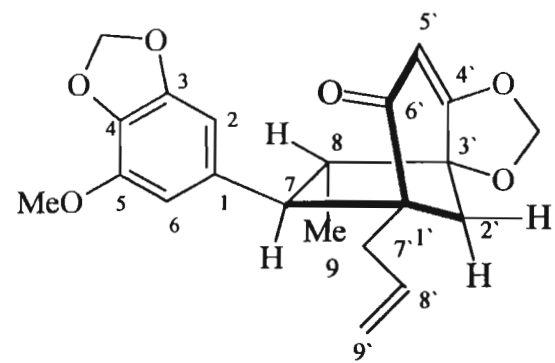
carbon	δ	carbon	δ
C- 9	13.3	OCH ₂ O	100.0
C- 2'	35.7	C- 2	106.1
C- 7'	36.3	C- 6	106.1
C- 7	38.8	C- 9'	117.6
C- 8	41.2	C- 8'	135.2
C- 1'	42.4	C- 1	136.8
OMe-3	56.2	C- 3	153.2
OMe-5	56.2	C- 5	153.2
OMe-4	60.8	C- 4'	175.8
C-3'	85.4	C- 6'	198.8
C-5'	99.9		



(31) ^{13}C NMR in $CDCl_3$



(32) 1H NMR in C_6D_6

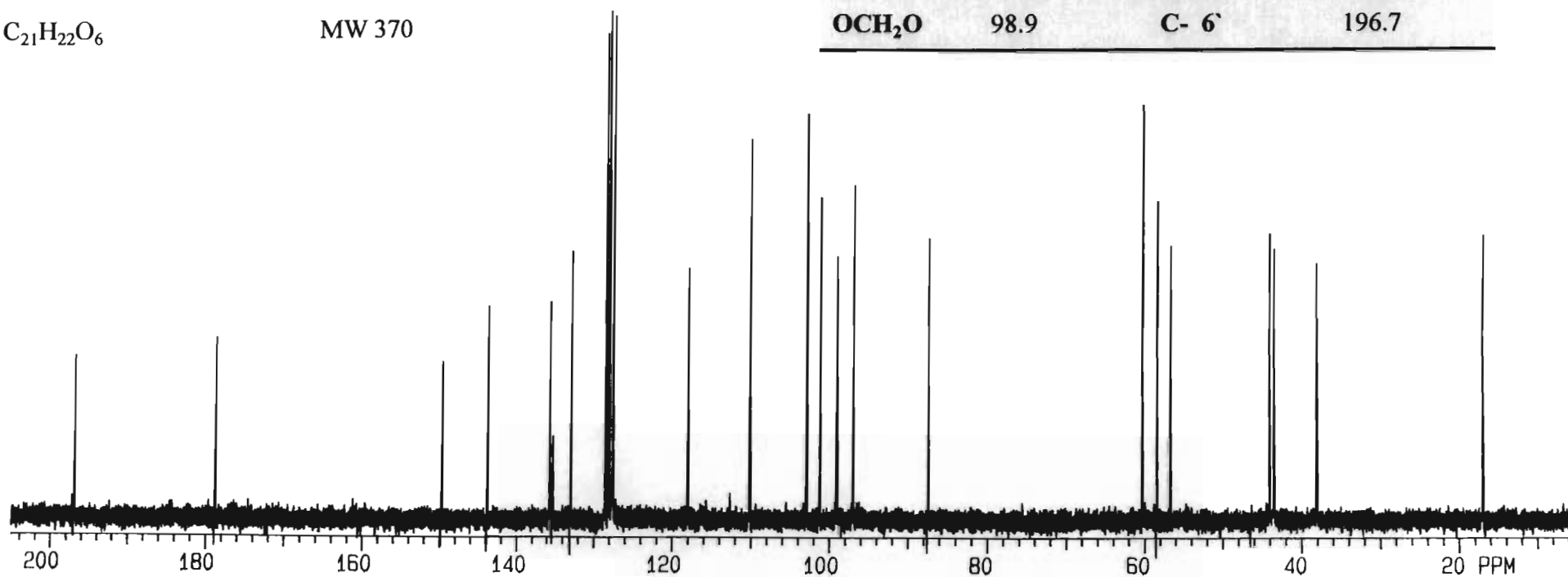


(32) C_6D_6

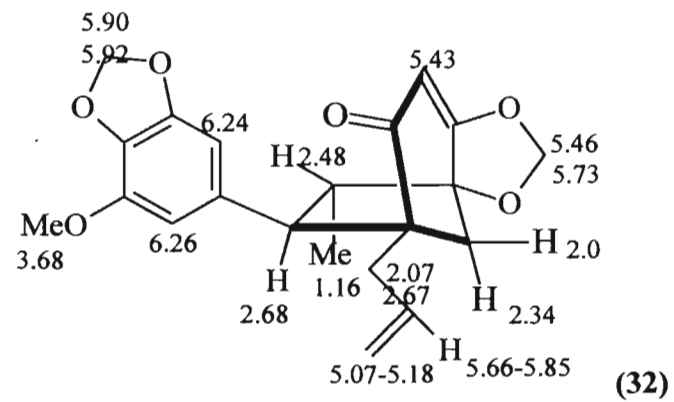
$C_{21}H_{22}O_6$

MW 370

carbon	δ	carbon	δ
C- 9	16.8	OCH ₂ O	101.2
C- 7'	38.0	C- 6	102.8
C- 2'	43.4	C- 2	110.2
C- 8	44.0	C- 9'	117.9
OMe	56.7	C- 1	132.8
C- 1'	60.2	C- 4	135.5
C- 7	60.2	C- 5	143.7
C- 3'	87.4	C- 3	149.6
C- 5'	97.0	C- 4'	178.8
OCH ₂ O	98.9	C- 6'	196.7

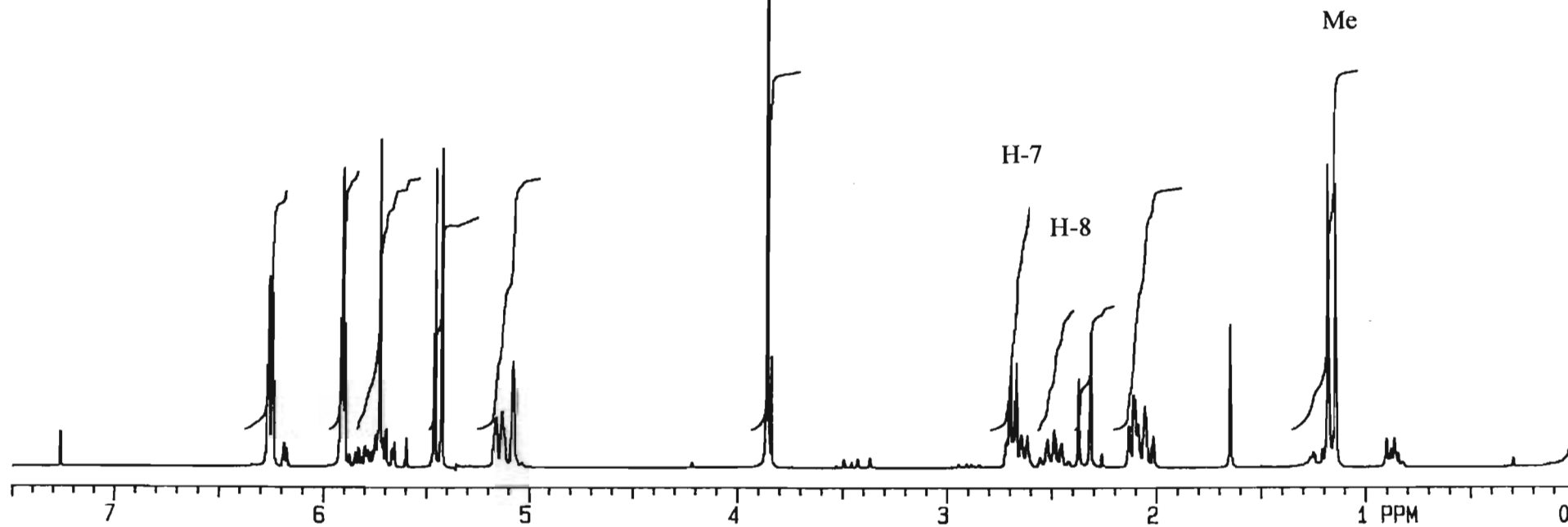


(32) ^{13}C NMR in C_6D_6

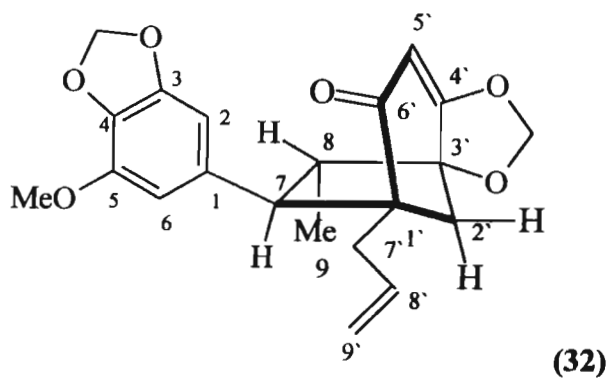


$C_{21}H_{22}O_6$

MW 370



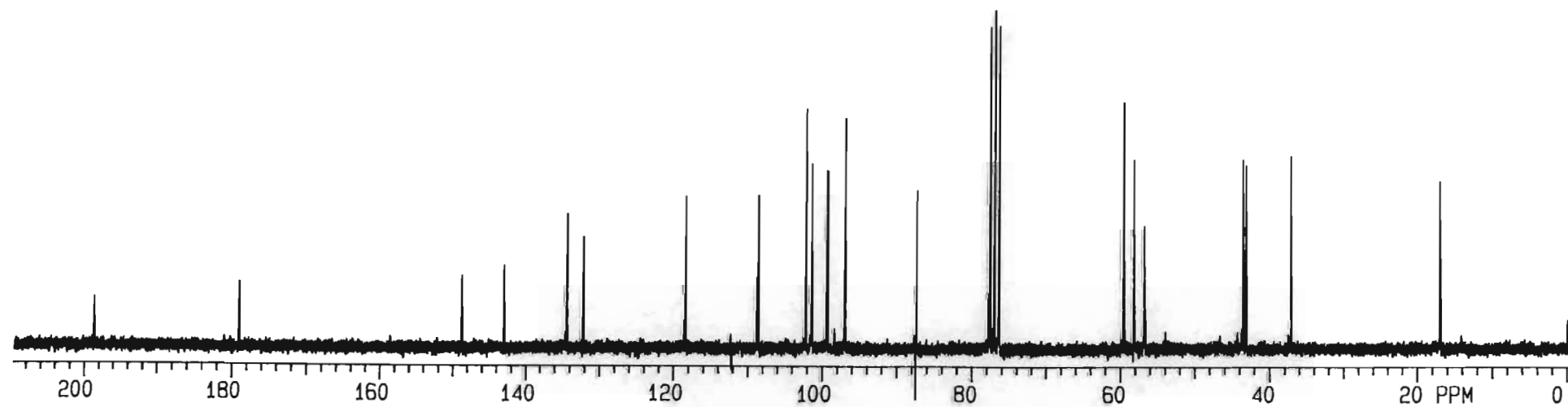
(32) 1H NMR in $CDCl_3$



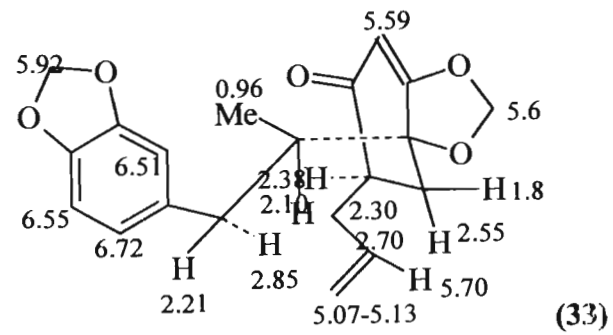
$C_{21}H_{22}O_6$

MW 370

carbon	δ	carbon	δ
C- 9	16.9	OCH ₂ O	101.4
C- 7'	37.1	C- 6	102.2
C- 2'	43.2	C- 2	108.7
C- 8	43.6	C- 9'	118.5
OMe	56.7	C- 1	132.2
C- 1'	58.2	C- 4	134.5
C- 7	59.5	C- 5	142.9
C- 3'	87.4	C- 3	148.8
C- 5'	97.0	C- 4'	179.1
OCH ₂ O	99.3	C- 6'	198.7

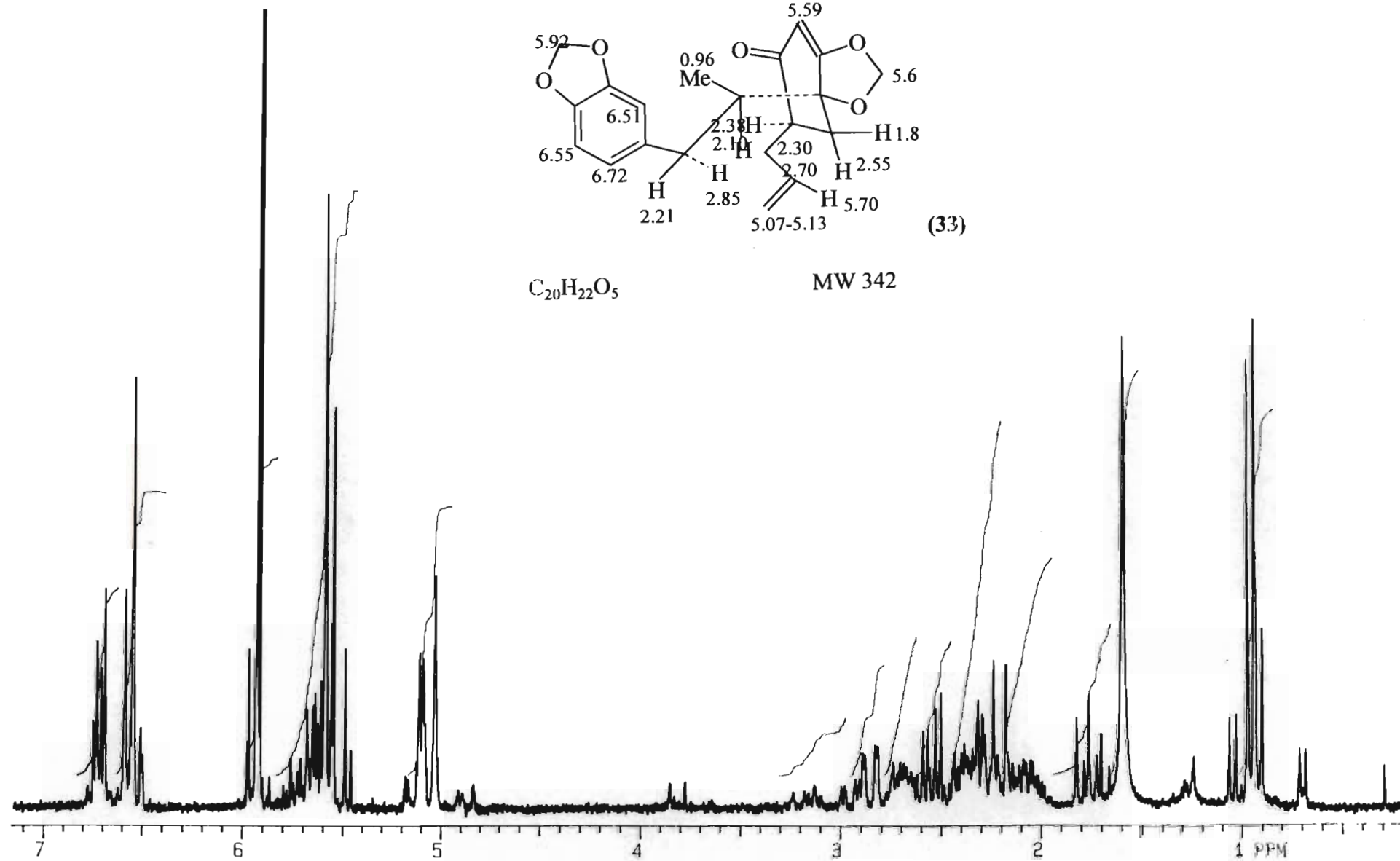


(32) ^{13}C NMR in $CDCl_3$

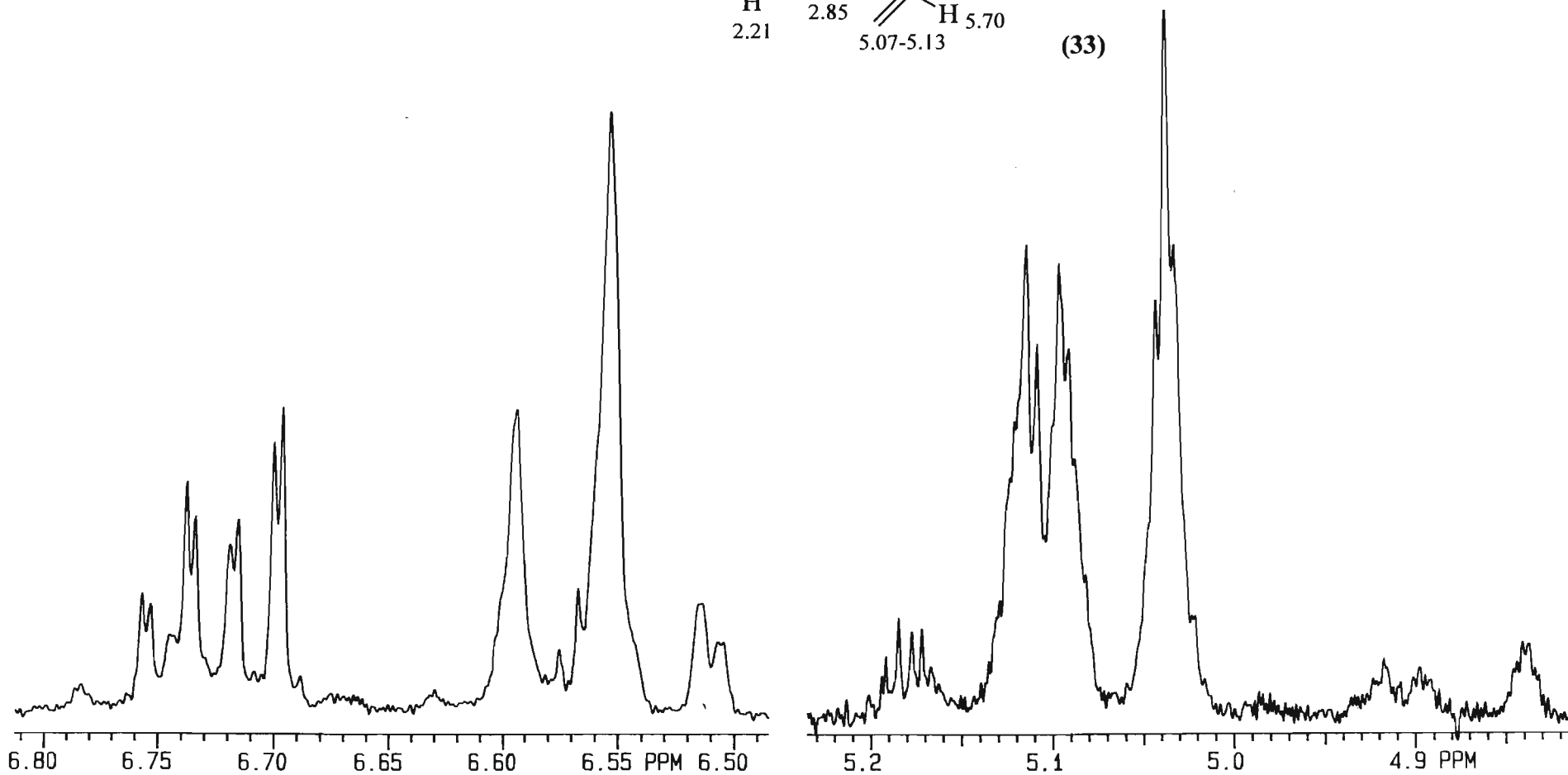
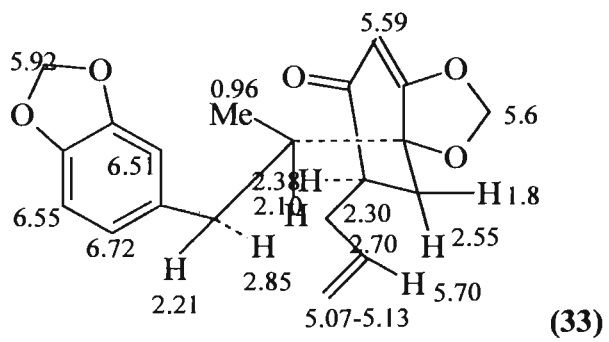


$C_{20}H_{22}O_5$

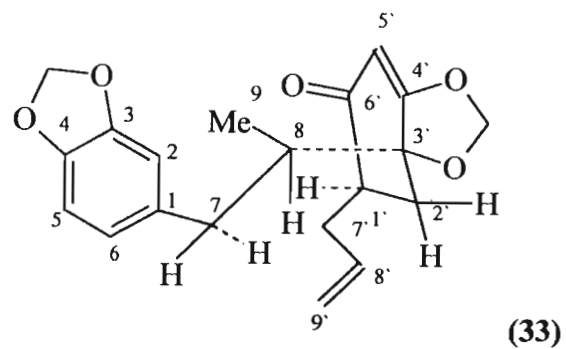
MW 342



(33) 1H NMR in $CDCl_3$



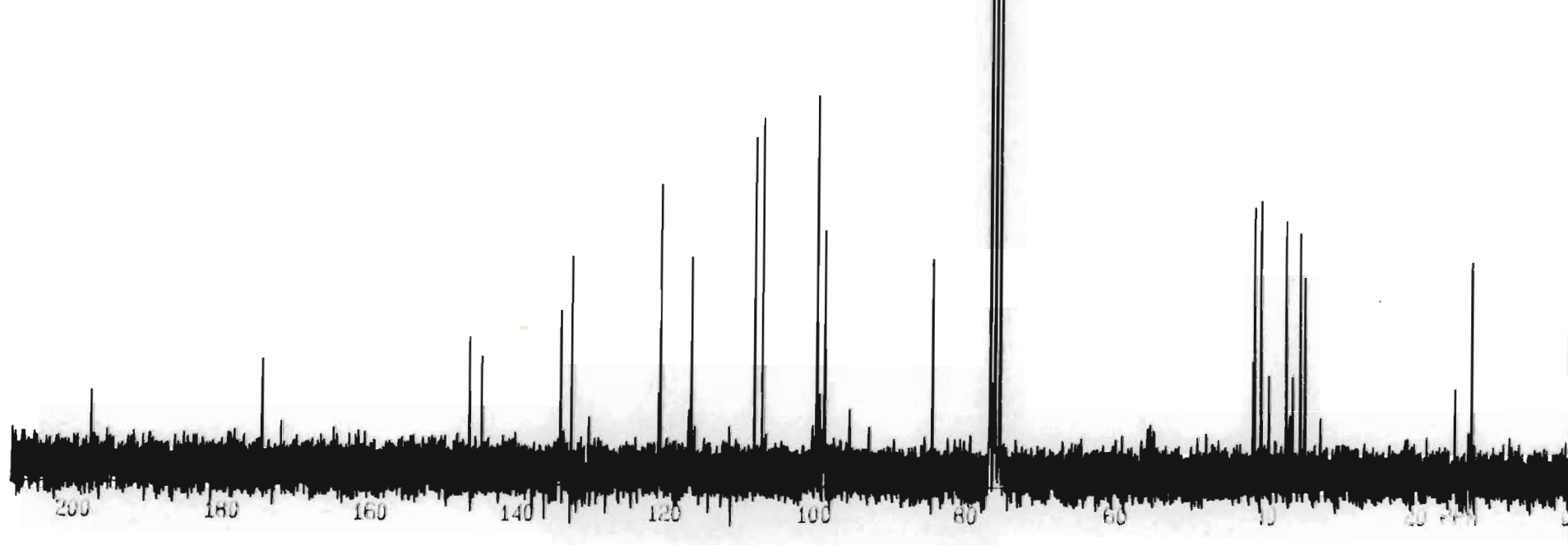
(33) ^1H NMR in CDCl_3



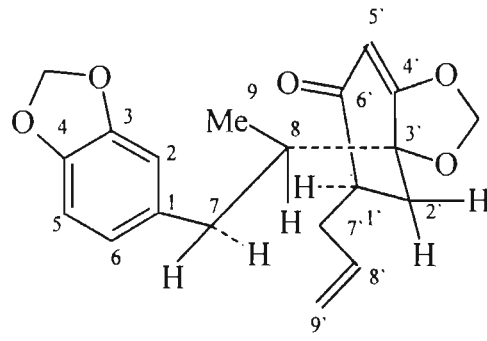
$C_{20}H_{22}O_5$

MW 342

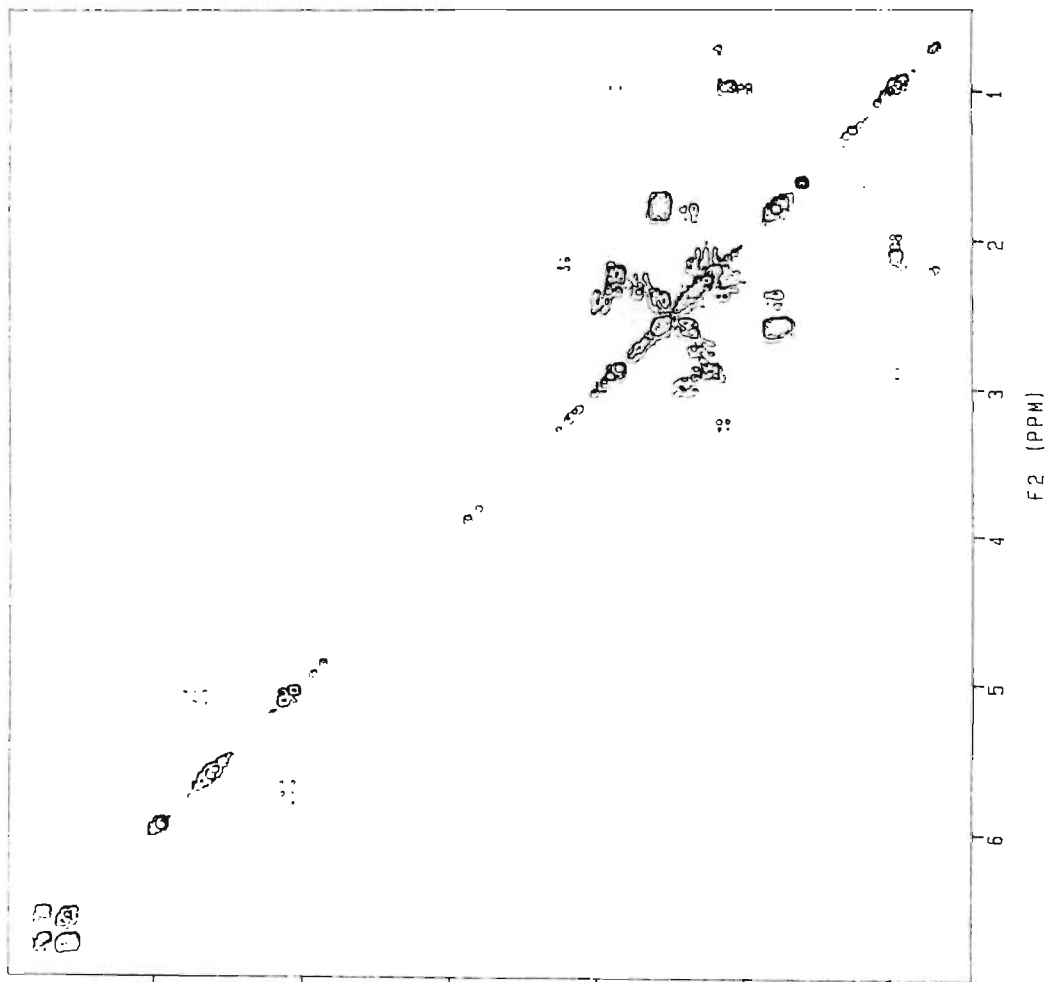
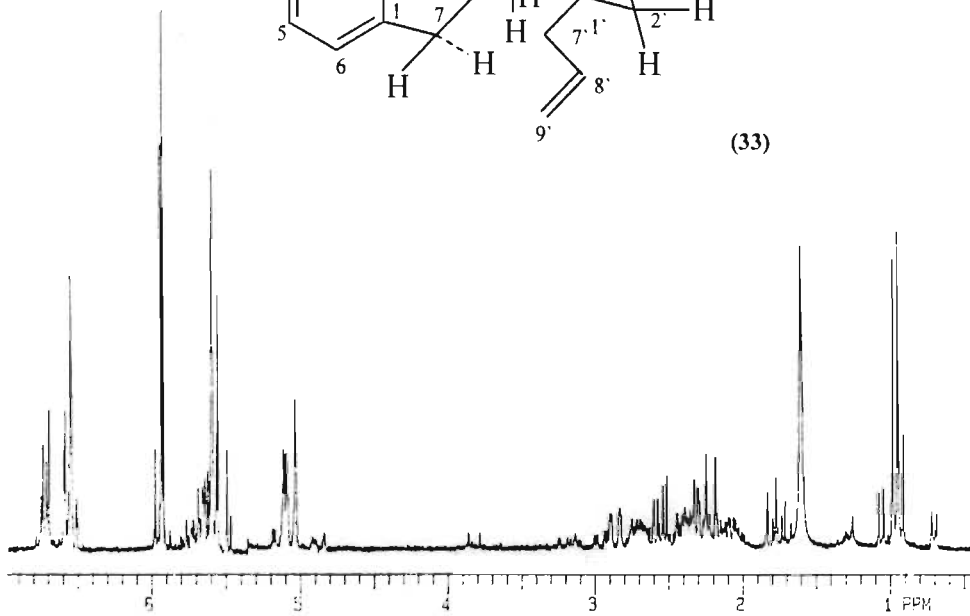
carbon	δ	carbon	δ
C- 9	13.1	C- 2	108.2
C- 2'	35.6	C- 5	109.2
C- 7'	36.3	C- 9'	117.7
C- 7	38.1	C- 6	121.9
C- 8	41.4	C- 1	133.7
C- 1'	42.4	C- 8'	135.2
C- 3'	85.4	C- 4	146.0
C- 5'	99.9	C- 3	147.6
OCH ₂ O	100.9	C- 4'	175.8
OCH ₂ O	100.9	C- 6'	198.9



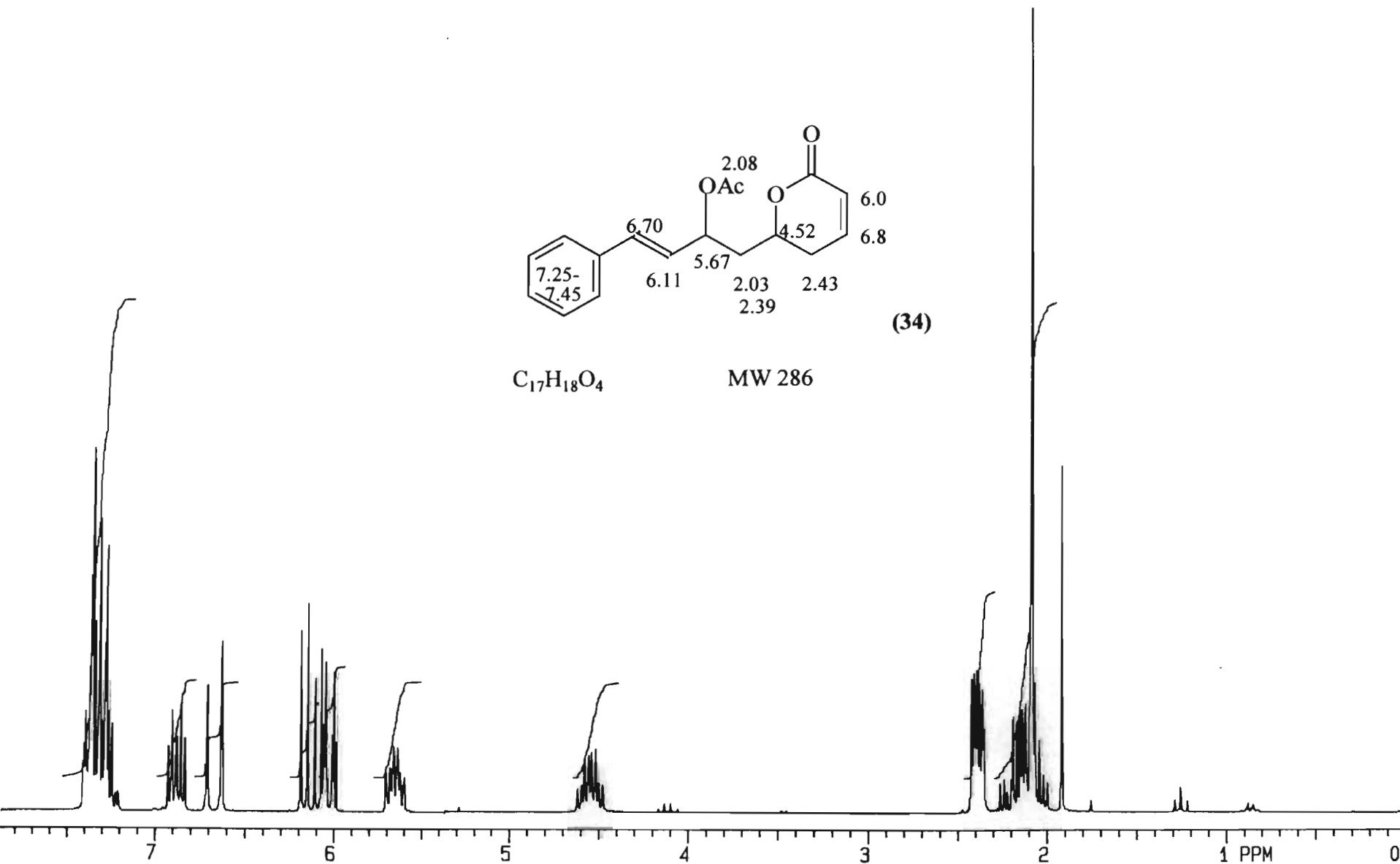
(33) ^{13}C NMR in $CDCl_3$



(33)

(33) COSY in CDCl₃

14-0271-92

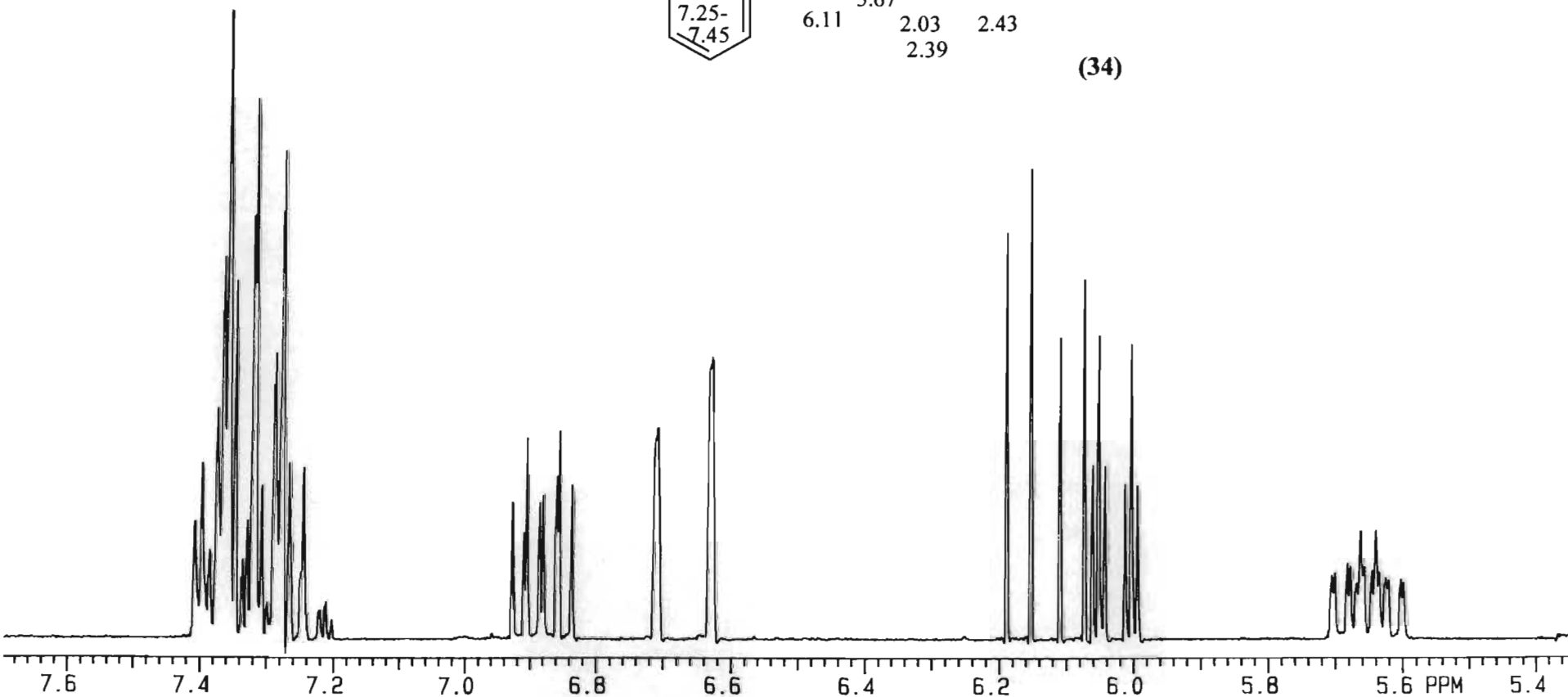
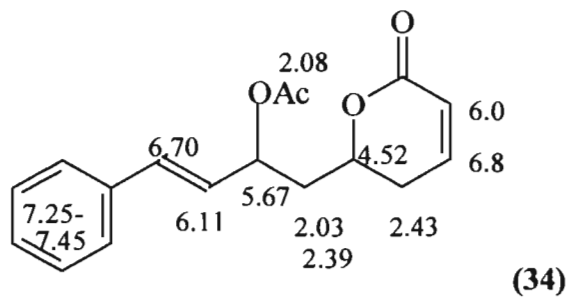


(34)

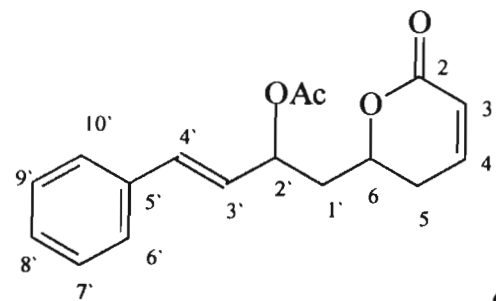
$C_{17}H_{18}O_4$

MW 286

(34) 1H NMR in $CDCl_3$



(34) ^1H NMR in CDCl_3

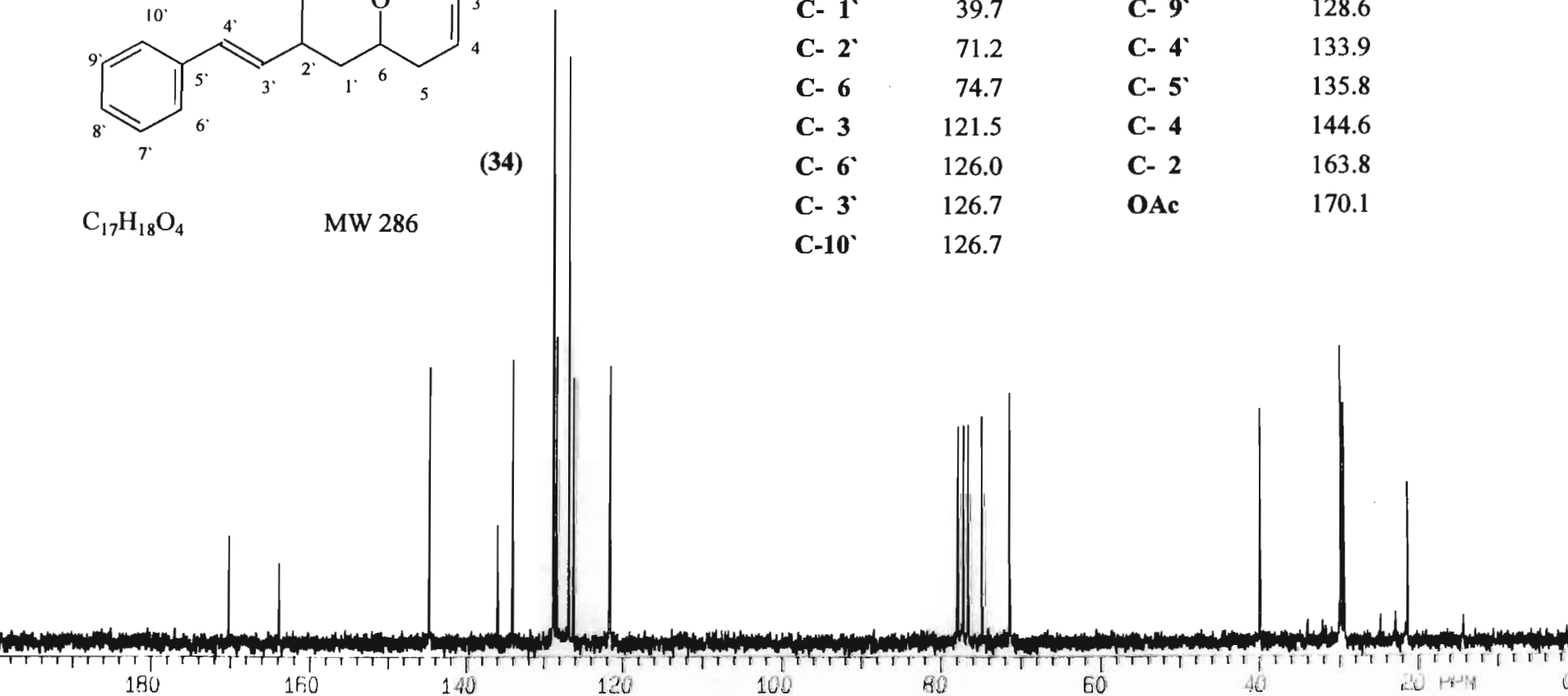


(34)

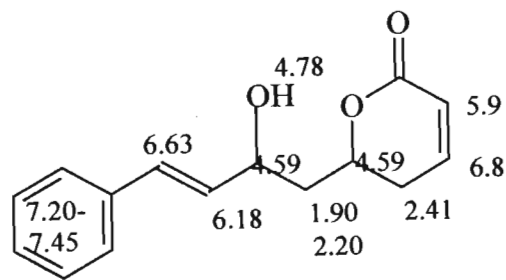
$C_{17}H_{18}O_4$

MW 286

carbon	δ	carbon	δ
OAc	21.3	C- 8'	128.3
C- 5	29.4	C- 7'	128.6
C- 1'	39.7	C- 9'	128.6
C- 2'	71.2	C- 4'	133.9
C- 6	74.7	C- 5'	135.8
C- 3	121.5	C- 4	144.6
C- 6'	126.0	C- 2	163.8
C- 3'	126.7	OAc	170.1
C-10'	126.7		



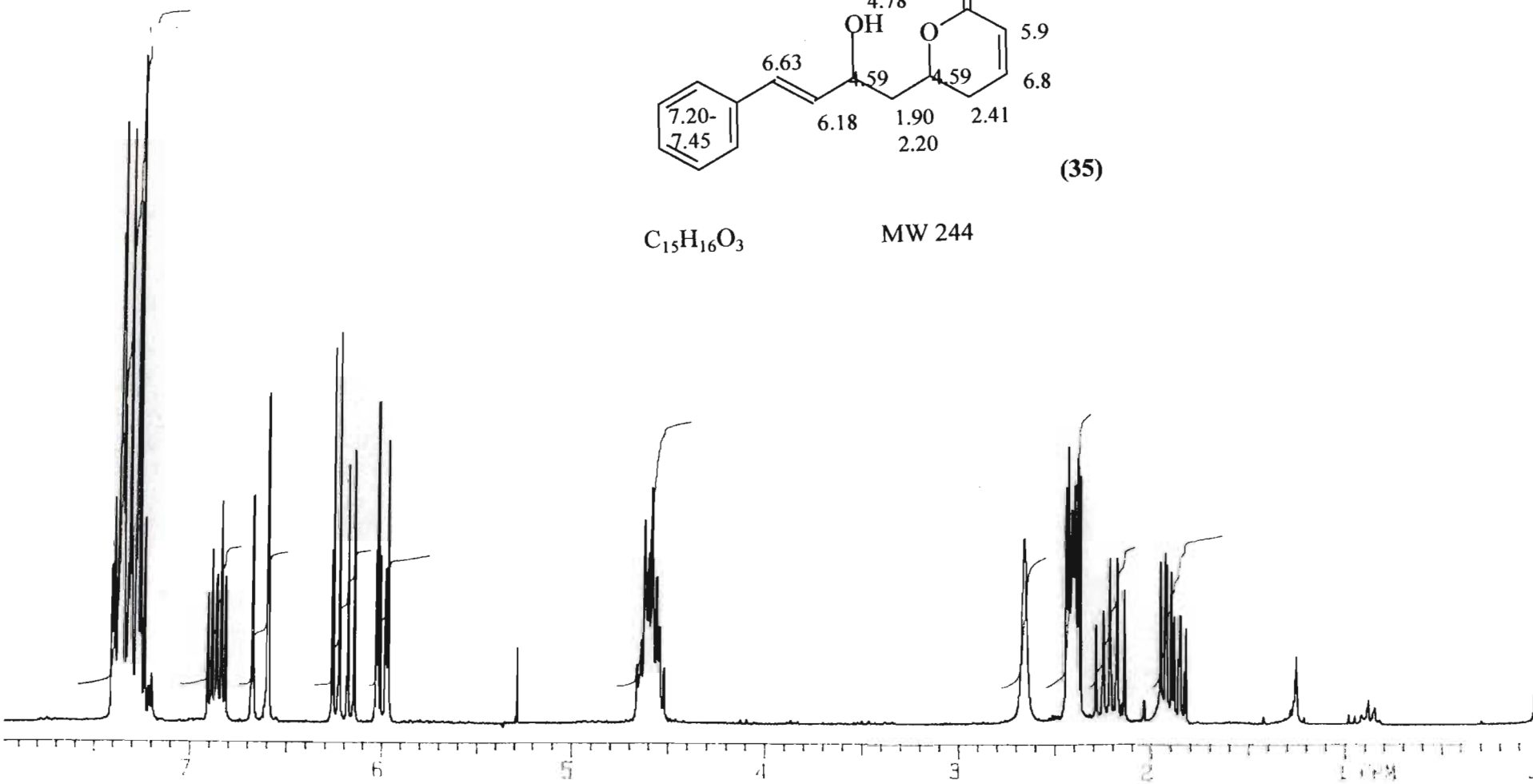
(34) ^{13}C NMR in $CDCl_3$



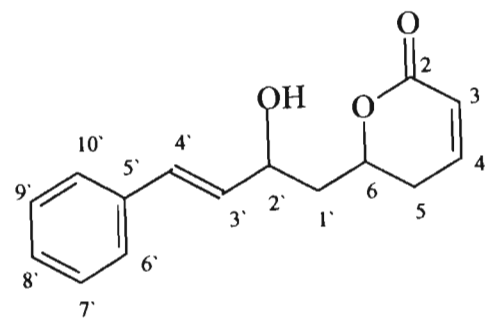
(35)

$\text{C}_{15}\text{H}_{16}\text{O}_3$

MW 244



(35) ^1H NMR in CDCl_3

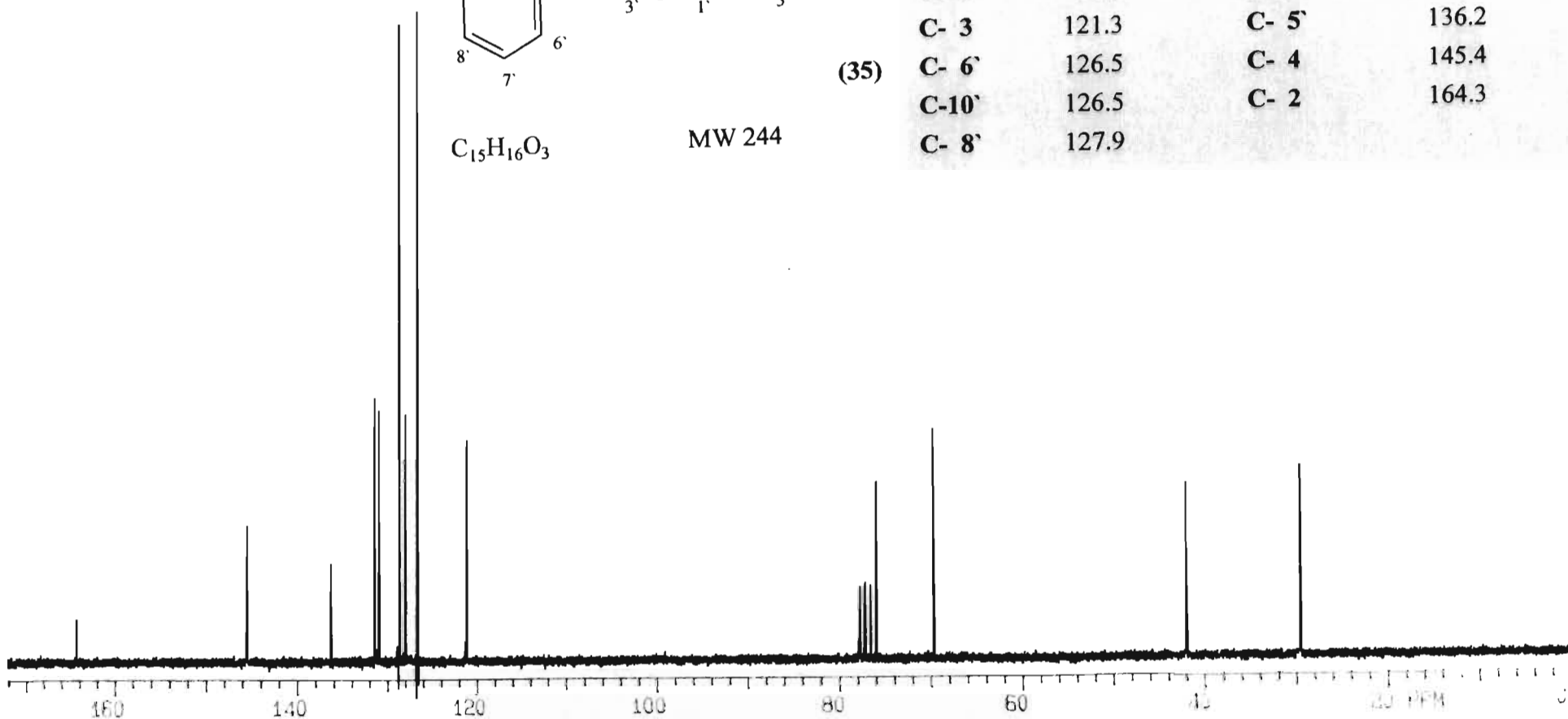


(35)

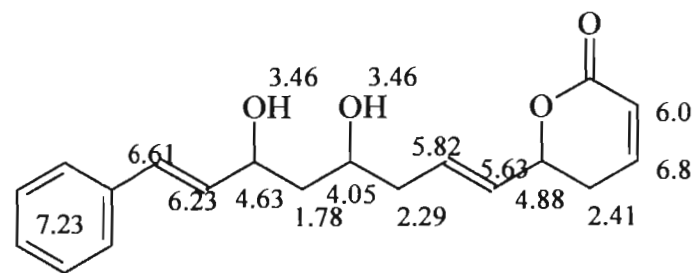
$C_{15}H_{16}O_3$

MW 244

carbon	δ	carbon	δ
C- 5	29.4	C- 7'	128.6
C- 1'	41.9	C- 9'	128.6
C- 2'	69.6	C- 3'	130.9
C- 6	75.9	C- 4'	131.3
C- 3	121.3	C- 5'	136.2
C- 6'	126.5	C- 4	145.4
C-10'	126.5	C- 2	164.3
C- 8'	127.9		



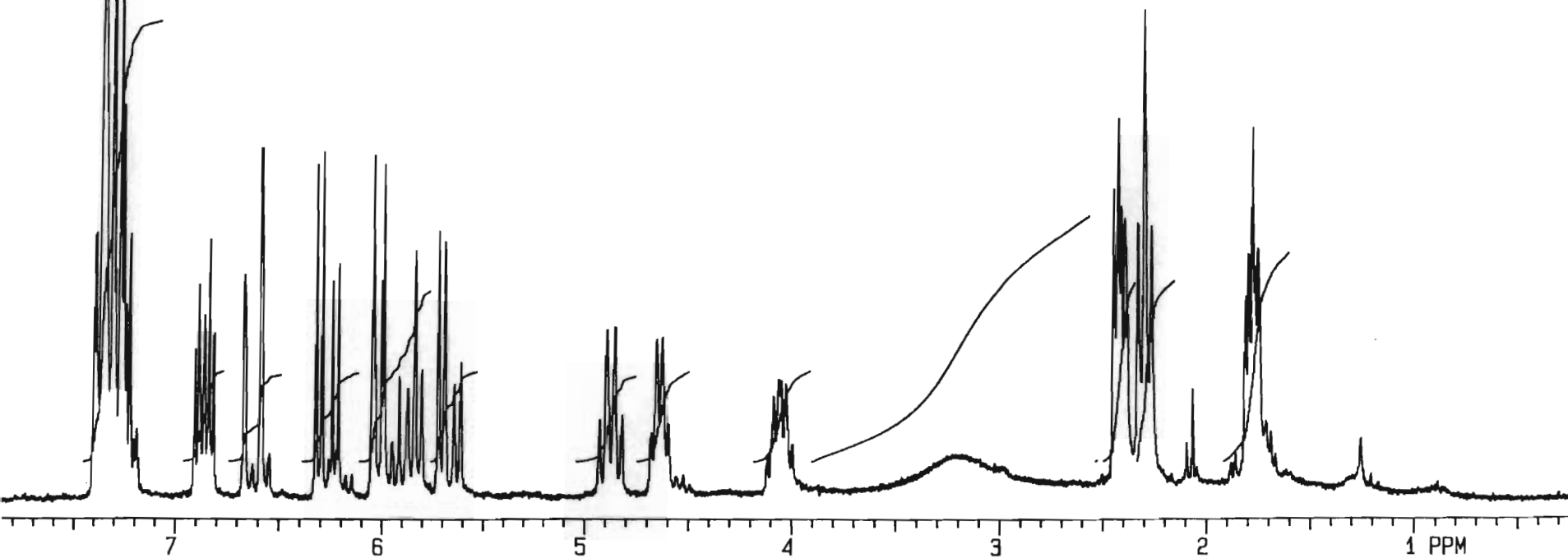
(35) ^{13}C NMR in $CDCl_3$



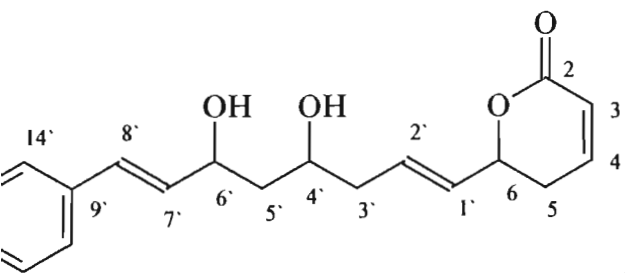
(36)

$\text{C}_{19}\text{H}_{22}\text{O}_4$

MW 314



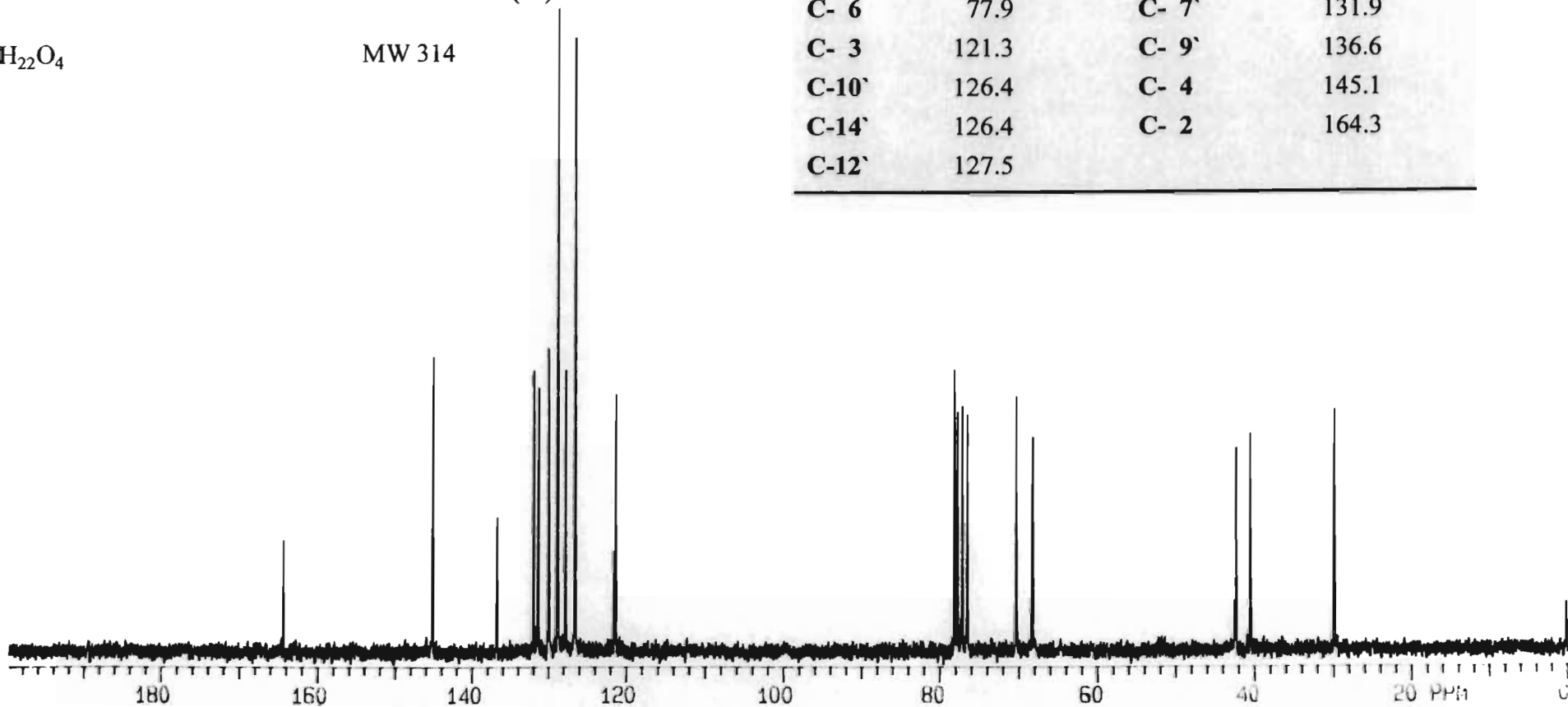
(36) ^1H NMR in CDCl_3



H₂₂O₄

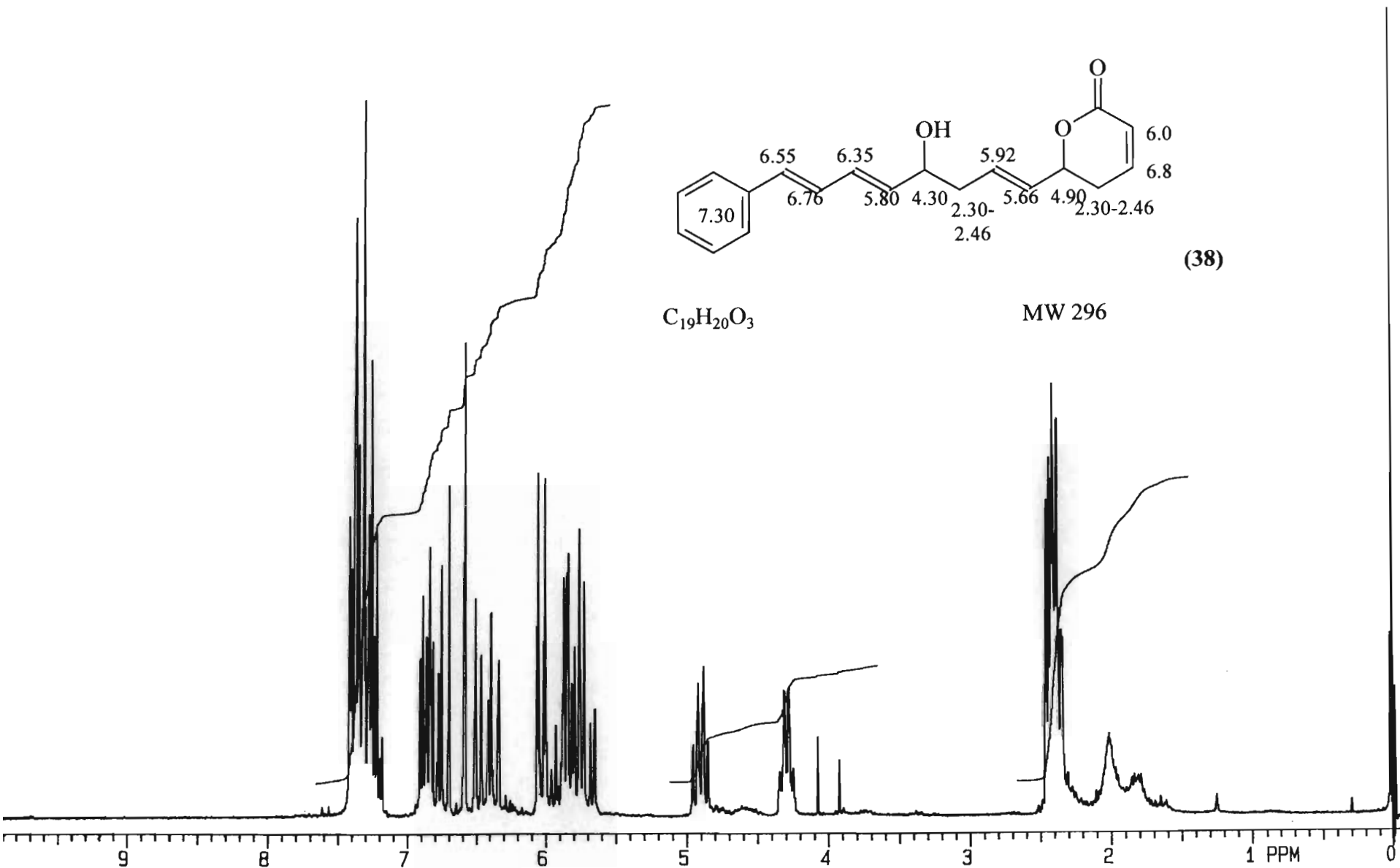
MW 314

(36)

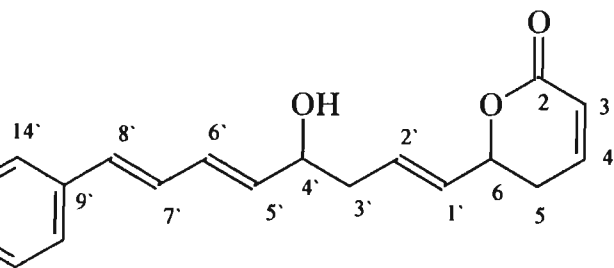


carbon	δ	carbon	δ
C- 5	29.6	C-11'	128.5
C- 3'	40.3	C-13'	128.5
C- 5'	42.3	C- 8'	129.6
C- 4'	68.0	C- 1	129.7
C- 6'	70.0	C- 2'	131.3
C- 6	77.9	C- 7'	131.9
C- 3	121.3	C- 9'	136.6
C-10'	126.4	C- 4	145.1
C-14'	126.4	C- 2	164.3
C-12'	127.5		

(36) ¹³C NMR in CDCl₃



(38) 1H NMR in $CDCl_3$

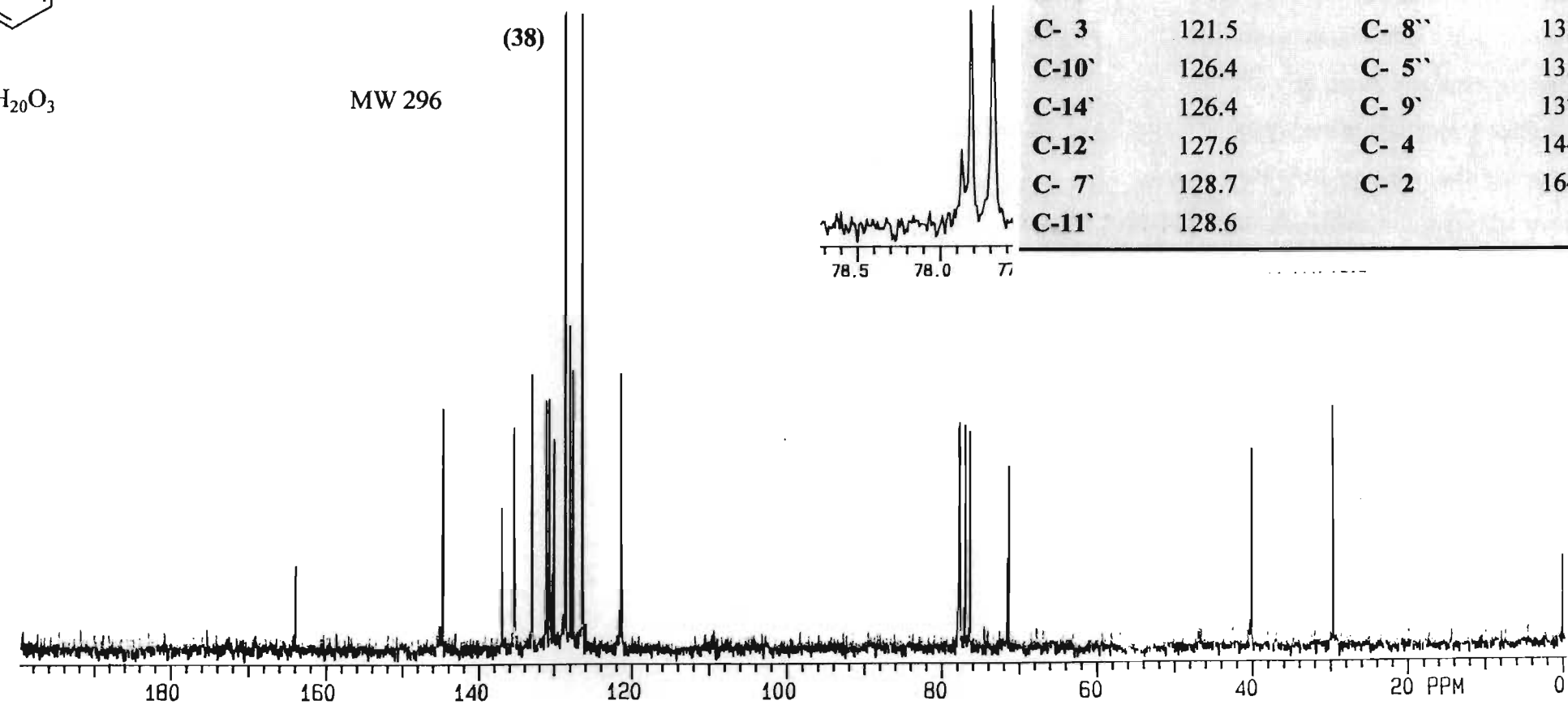
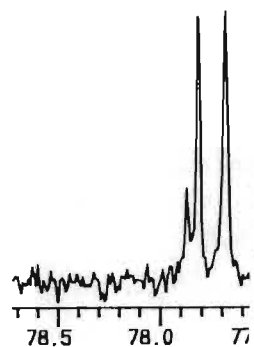


H₂O₃

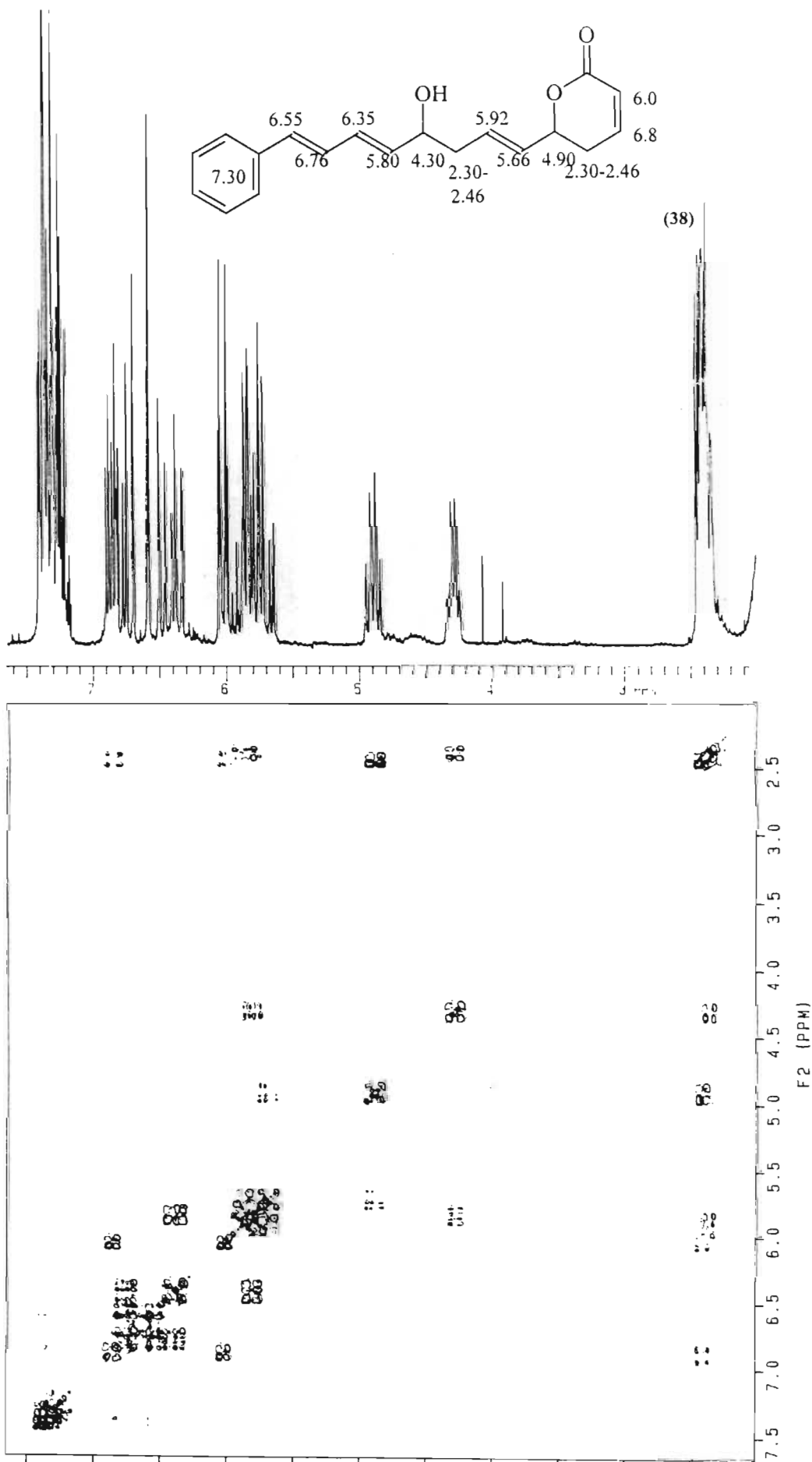
MW 296

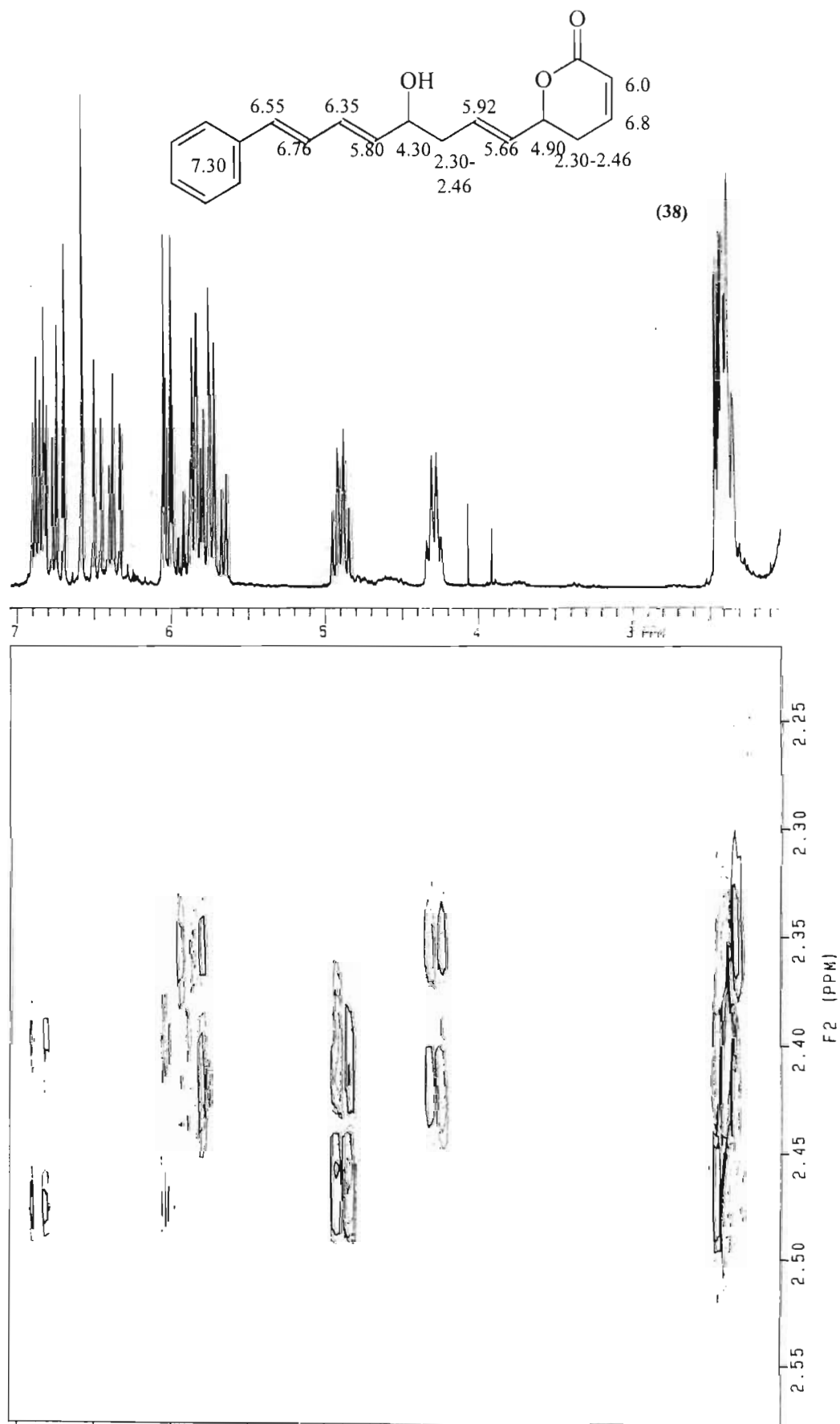
(38)

carbon	δ	carbon	δ
C- 5	29.7	C-13'	128.6
C- 3'	40.1	C- 6'	130.1
C- 4'	71.5	C- 1'	130.6
C- 6	77.8	C- 2'	131.0
C- 3	121.5	C- 8''	133.0
C-10'	126.4	C- 5''	135.4
C-14'	126.4	C- 9'	137.0
C-12'	127.6	C- 4	144.8
C- 7'	128.7	C- 2	164.0
C-11'	128.6		

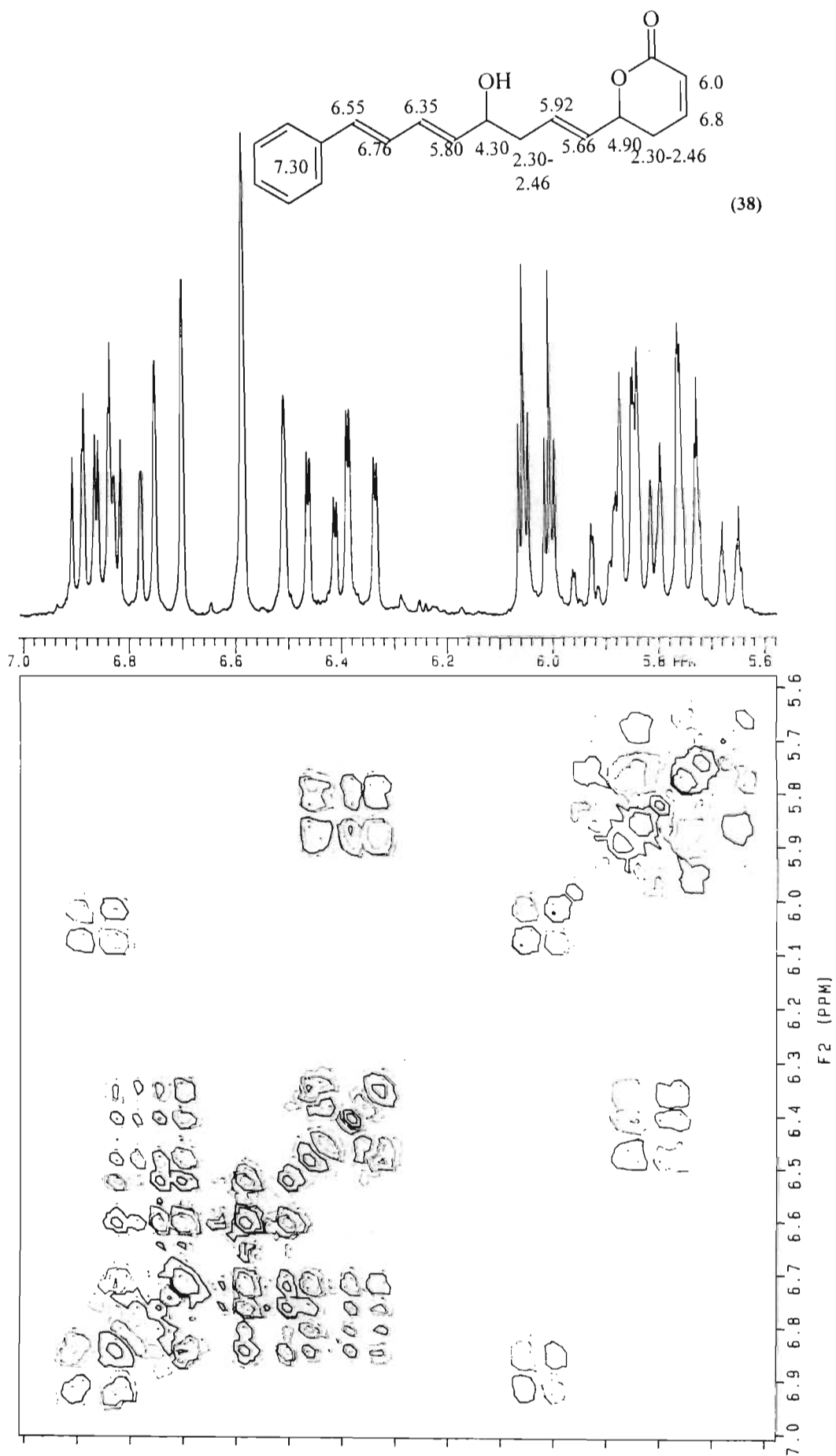


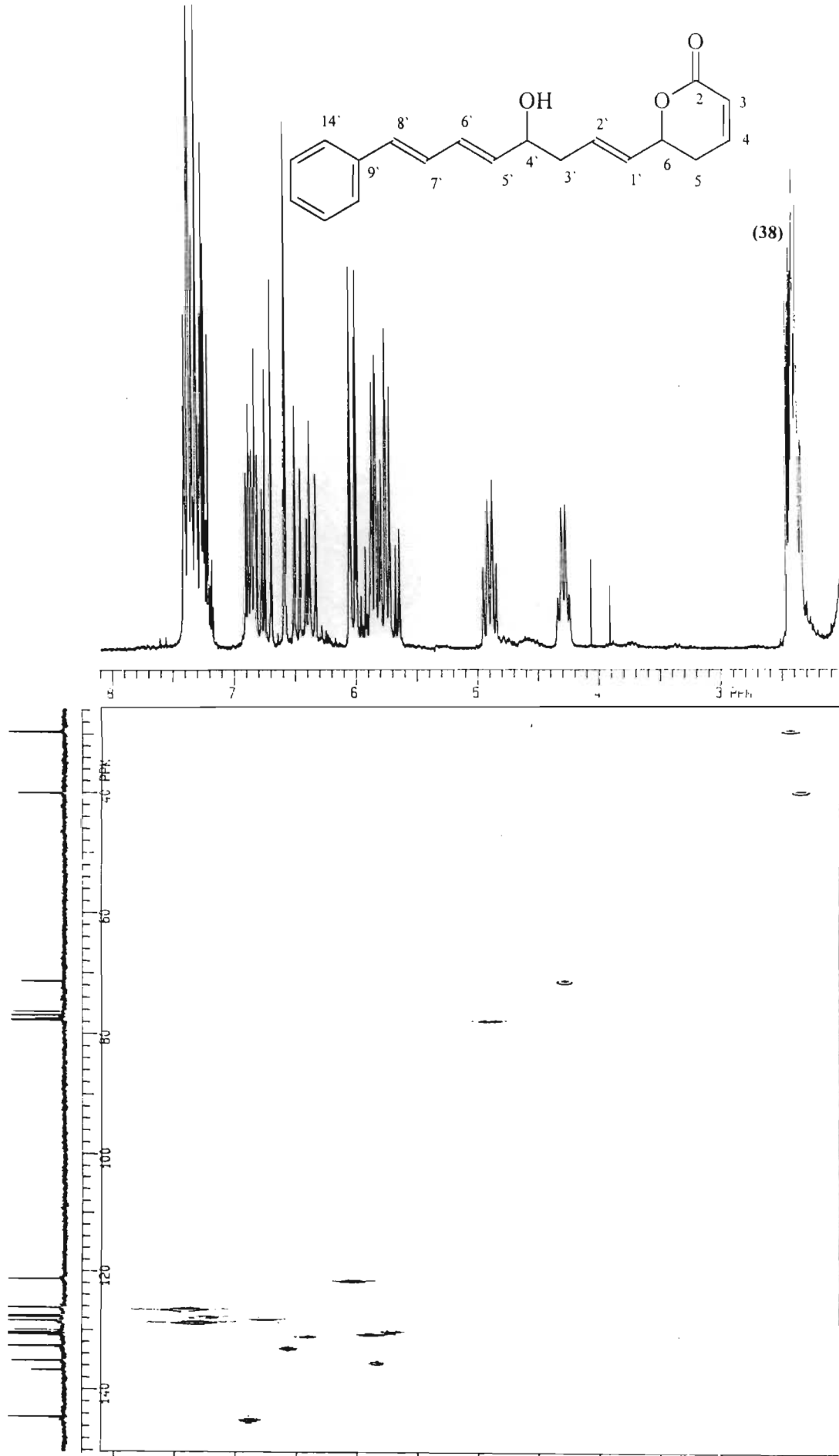
(38) ¹³C NMR in CDCl₃

(38) COSY in CDCl₃



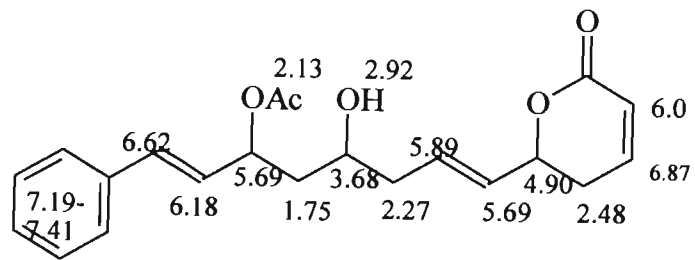
(38) COSY in CDCl₃

(38) COSY in CDCl_3



(38)

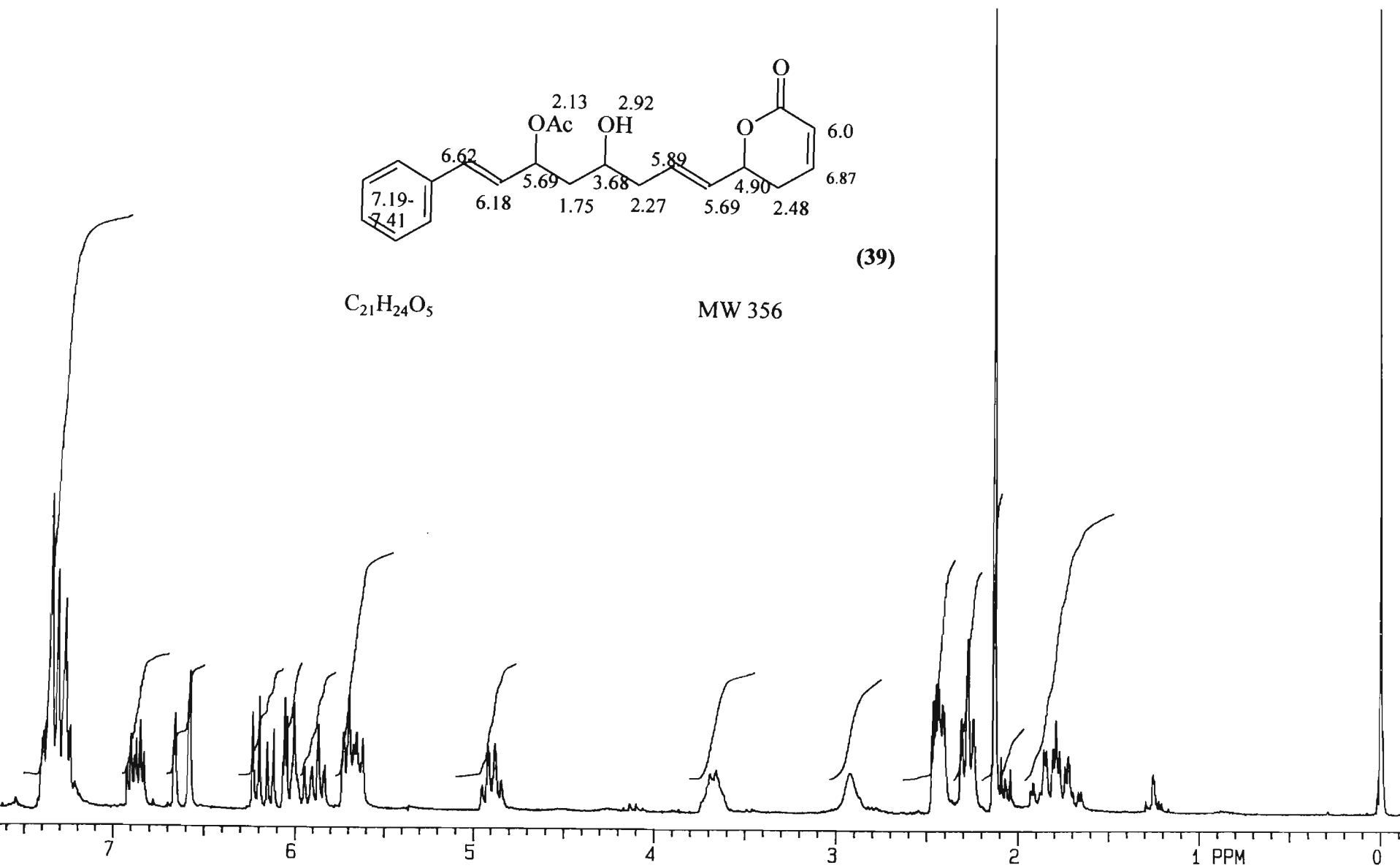
HETCOR in CDCl_3



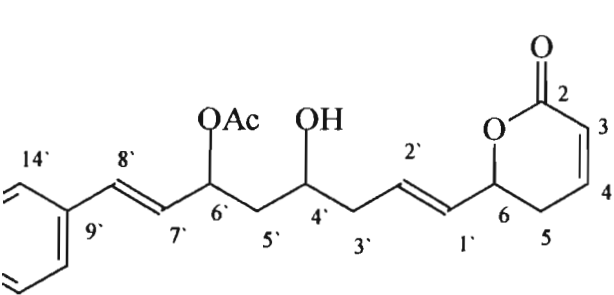
(39)

$C_{21}H_{24}O_5$

MW 356



(39) 1H NMR in $CDCl_3$

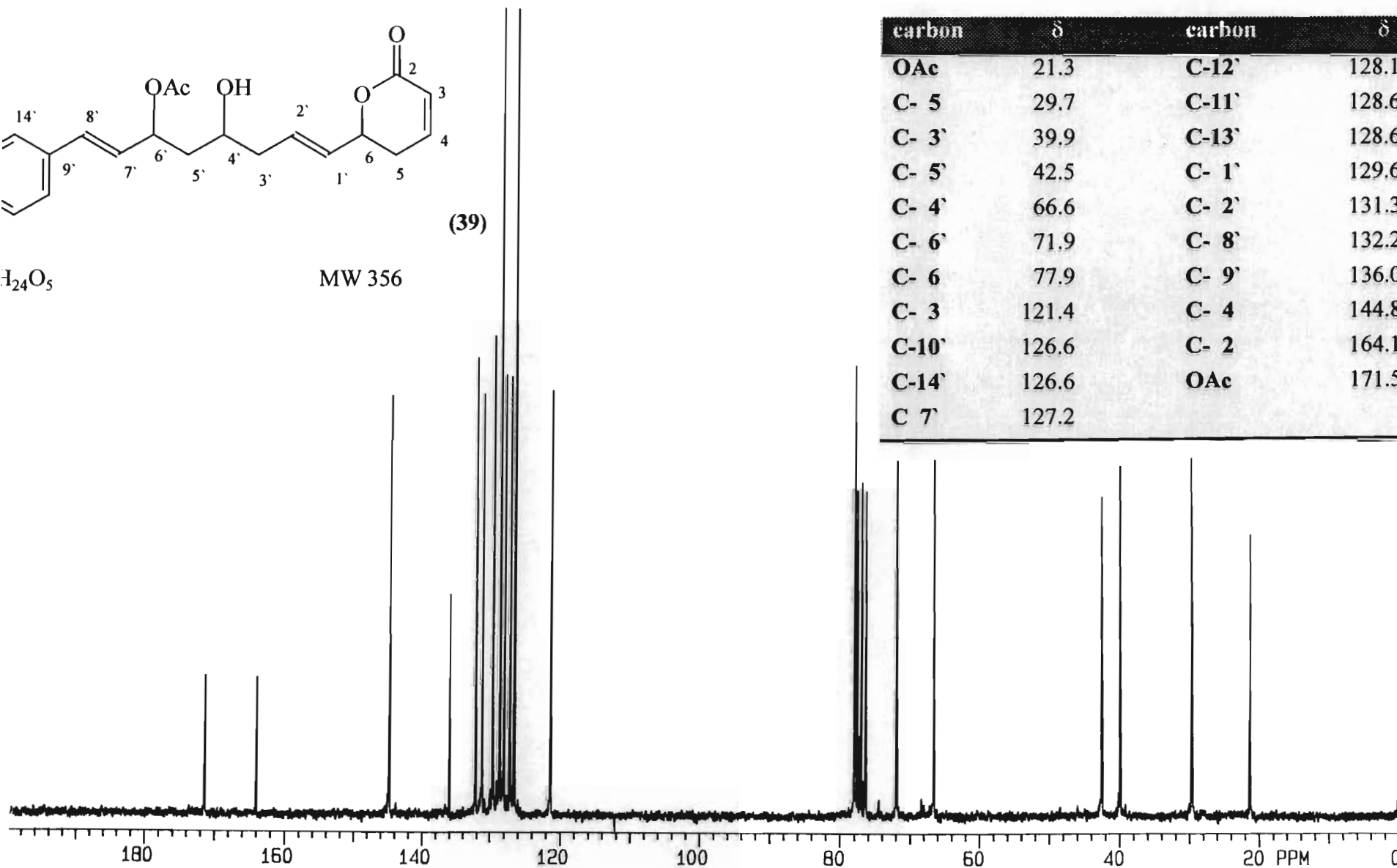


(39)

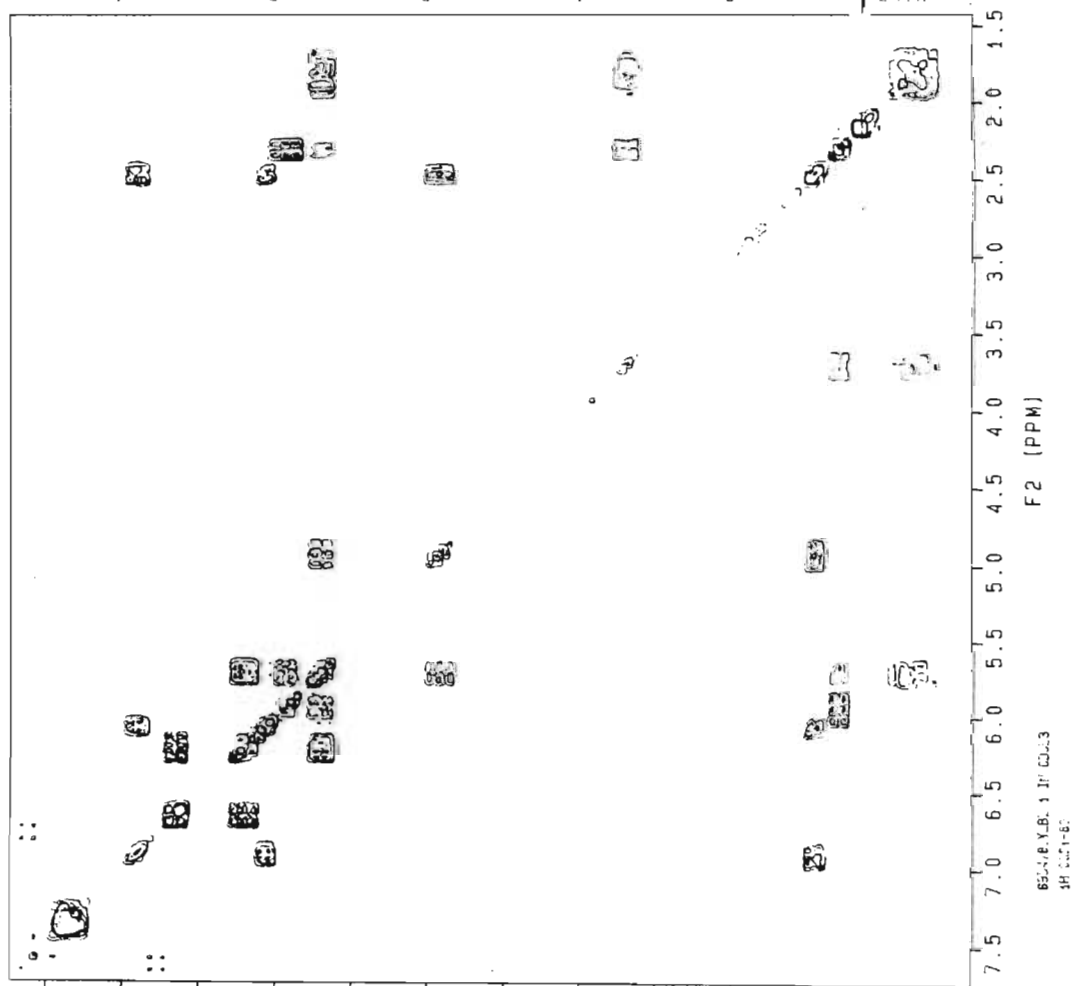
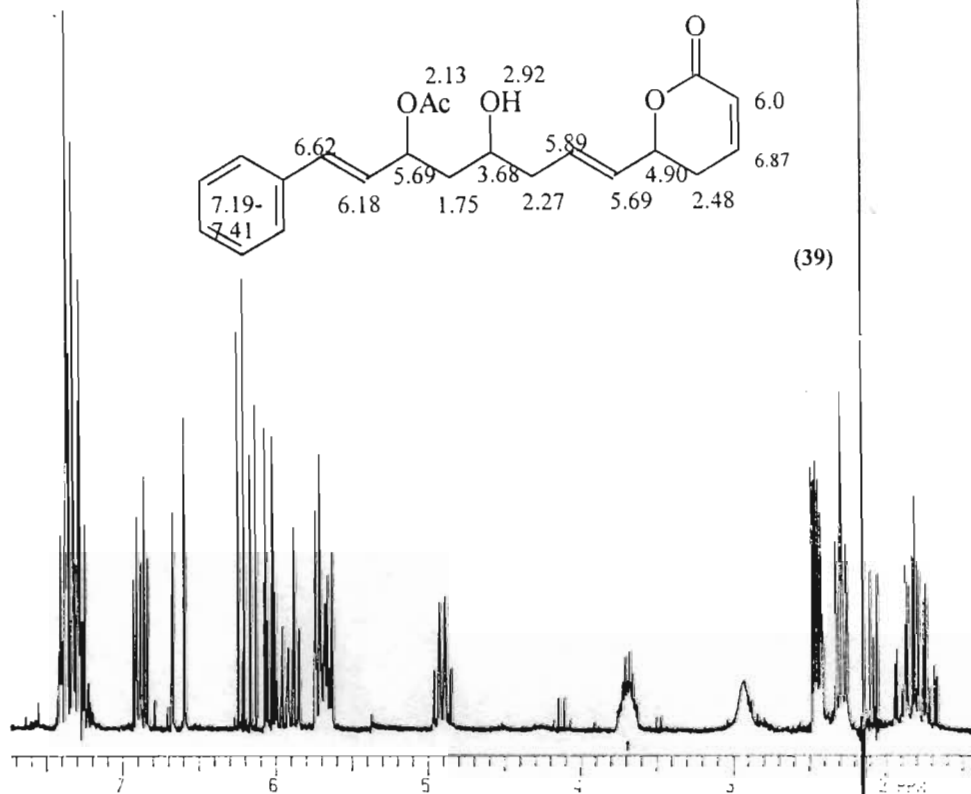
H₂₄O₅

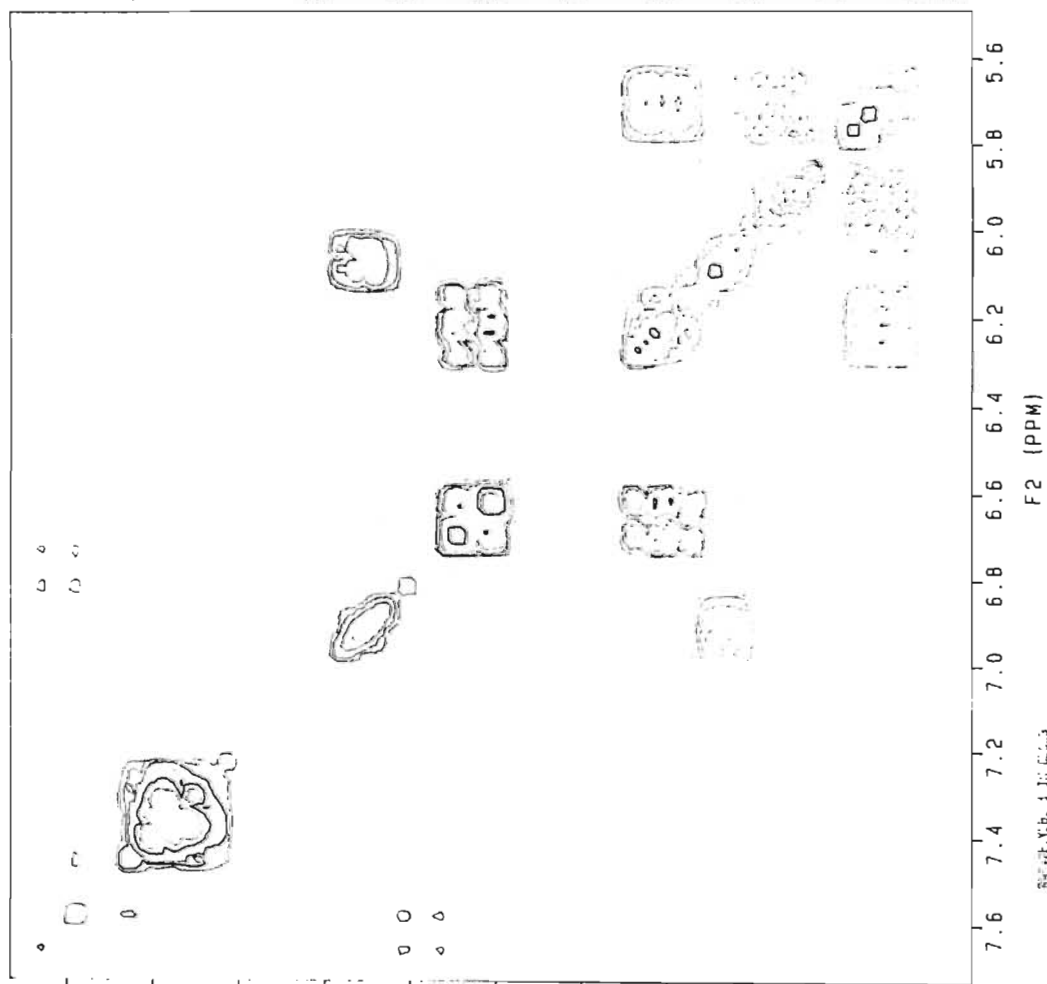
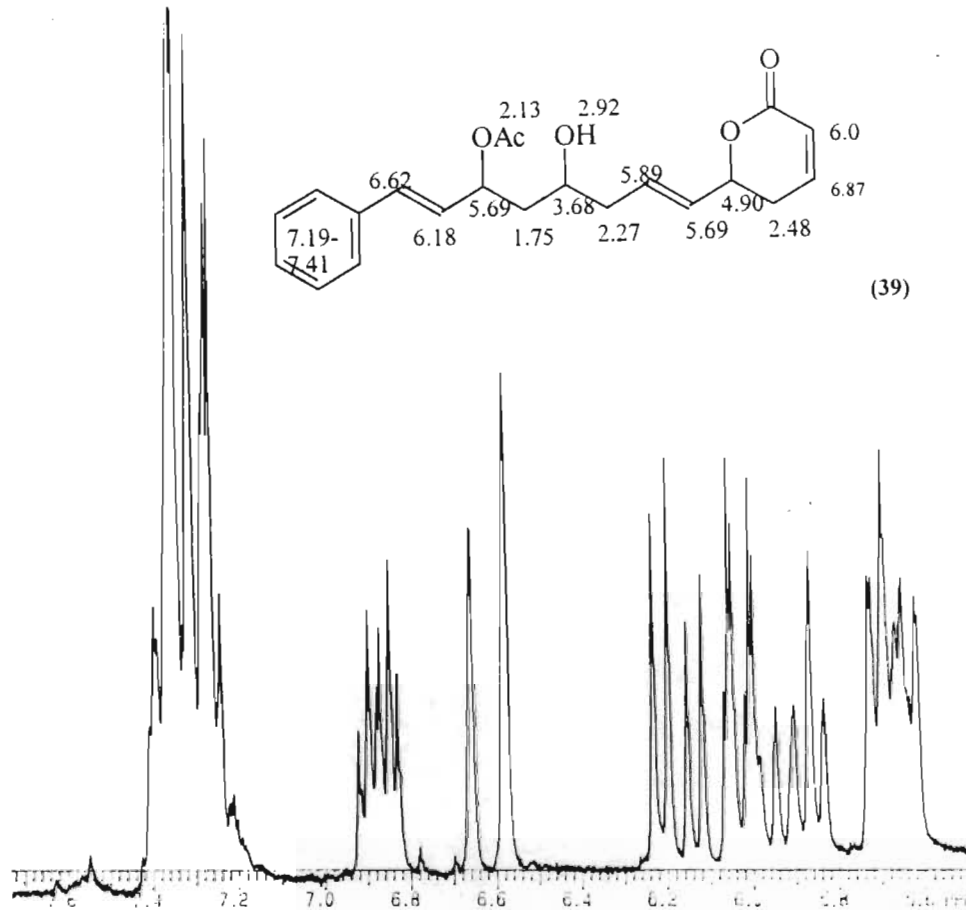
MW 356

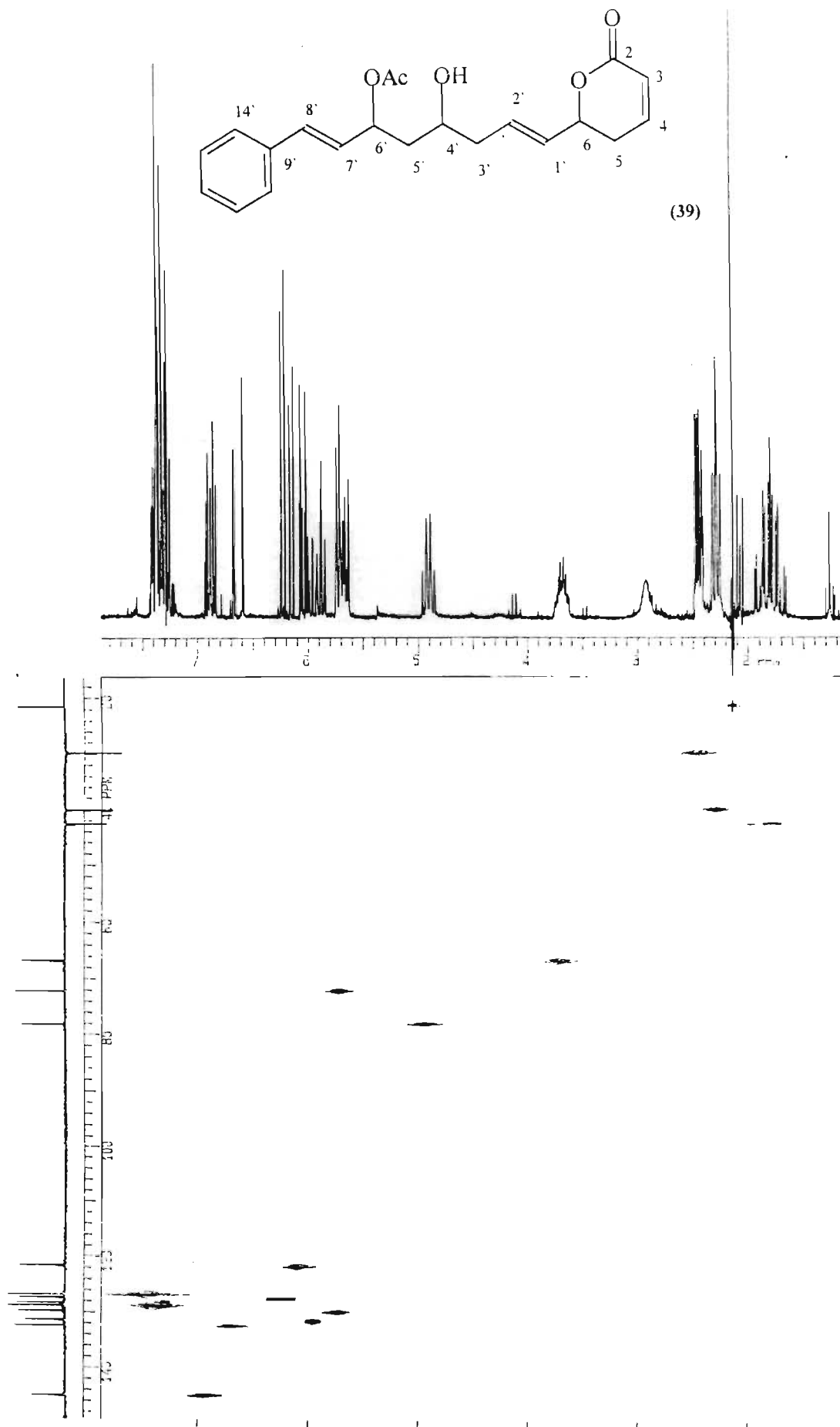
carbon	δ	carbon	δ
OAc	21.3	C-12'	128.1
C- 5	29.7	C-11'	128.6
C- 3'	39.9	C-13'	128.6
C- 5'	42.5	C- 1'	129.6
C- 4'	66.6	C- 2'	131.3
C- 6'	71.9	C- 8'	132.2
C- 6	77.9	C- 9'	136.0
C- 3	121.4	C- 4	144.8
C-10'	126.6	C- 2	164.1
C-14'	126.6	OAc	171.5
C 7'	127.2		

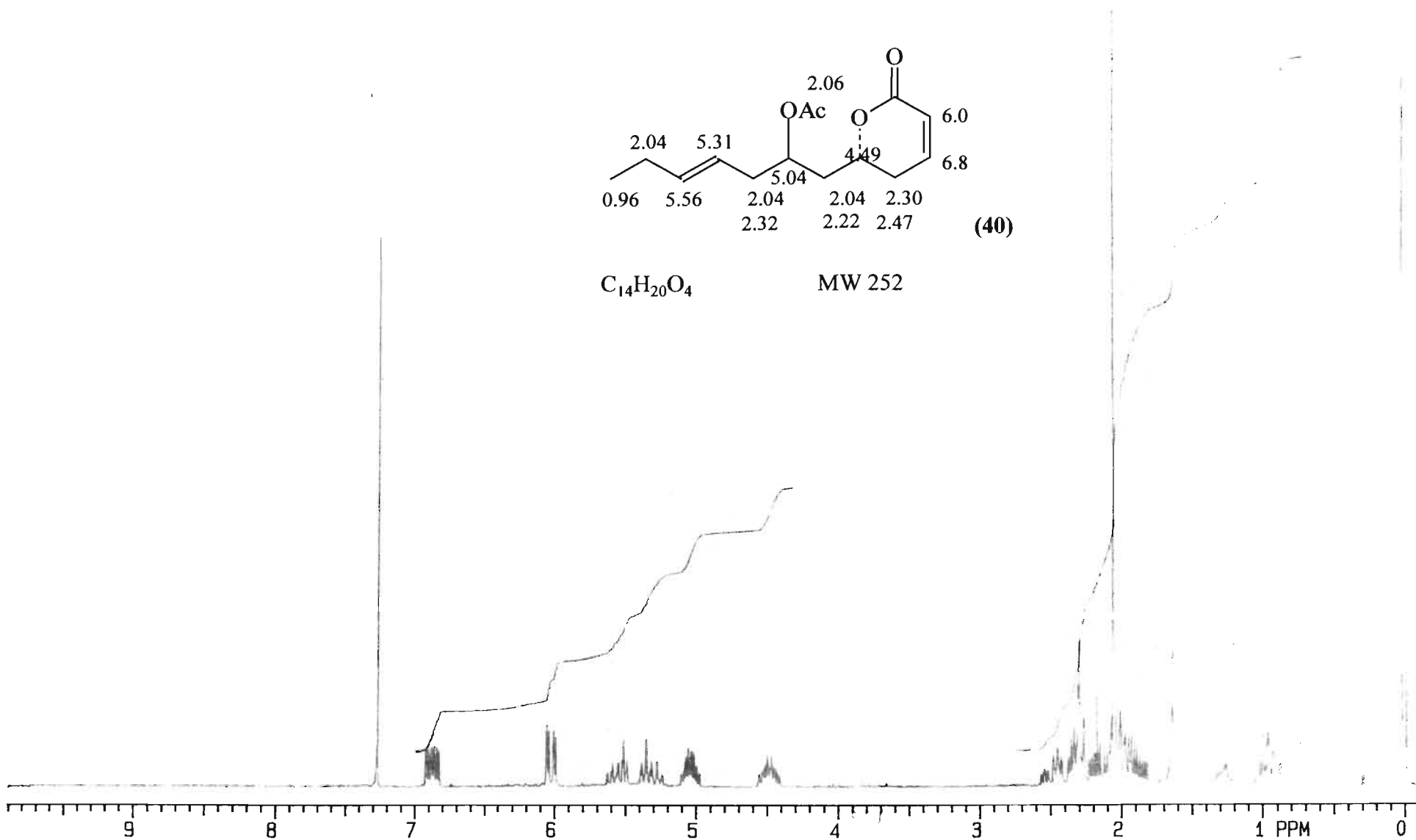


(39) ¹³C NMR in CDCl₃

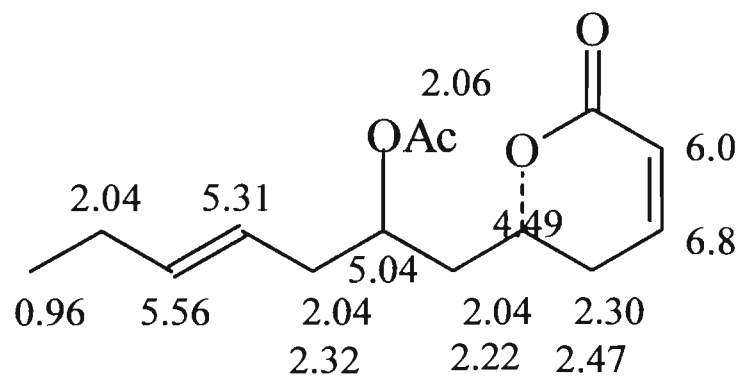
(39) COSY in CDCl_3

(39) COSY in CDCl_3

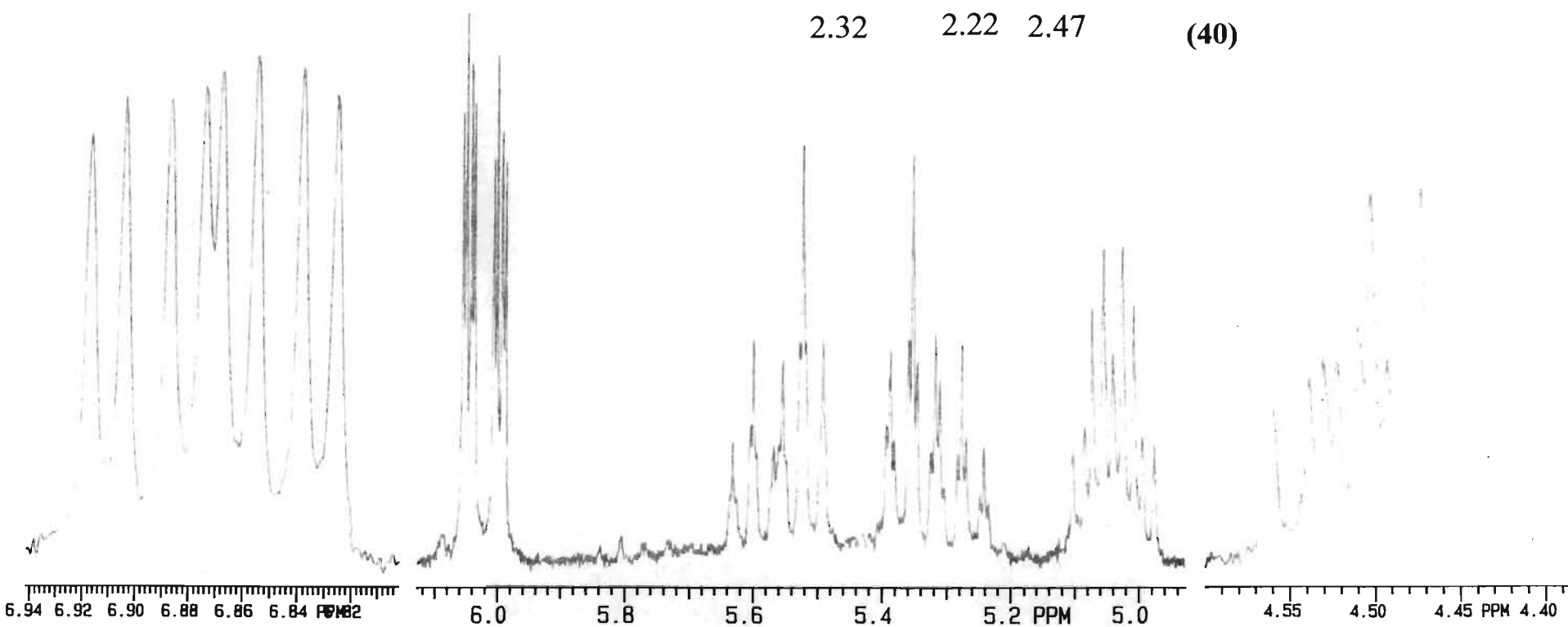
(39) HETCOR in CDCl₃



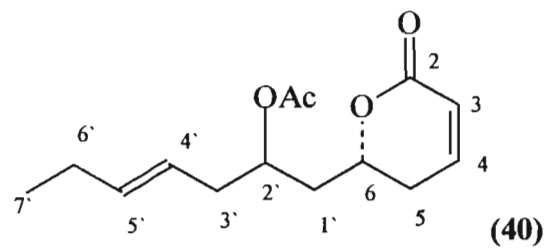
(40) ¹H NMR in CDCl₃



(40)



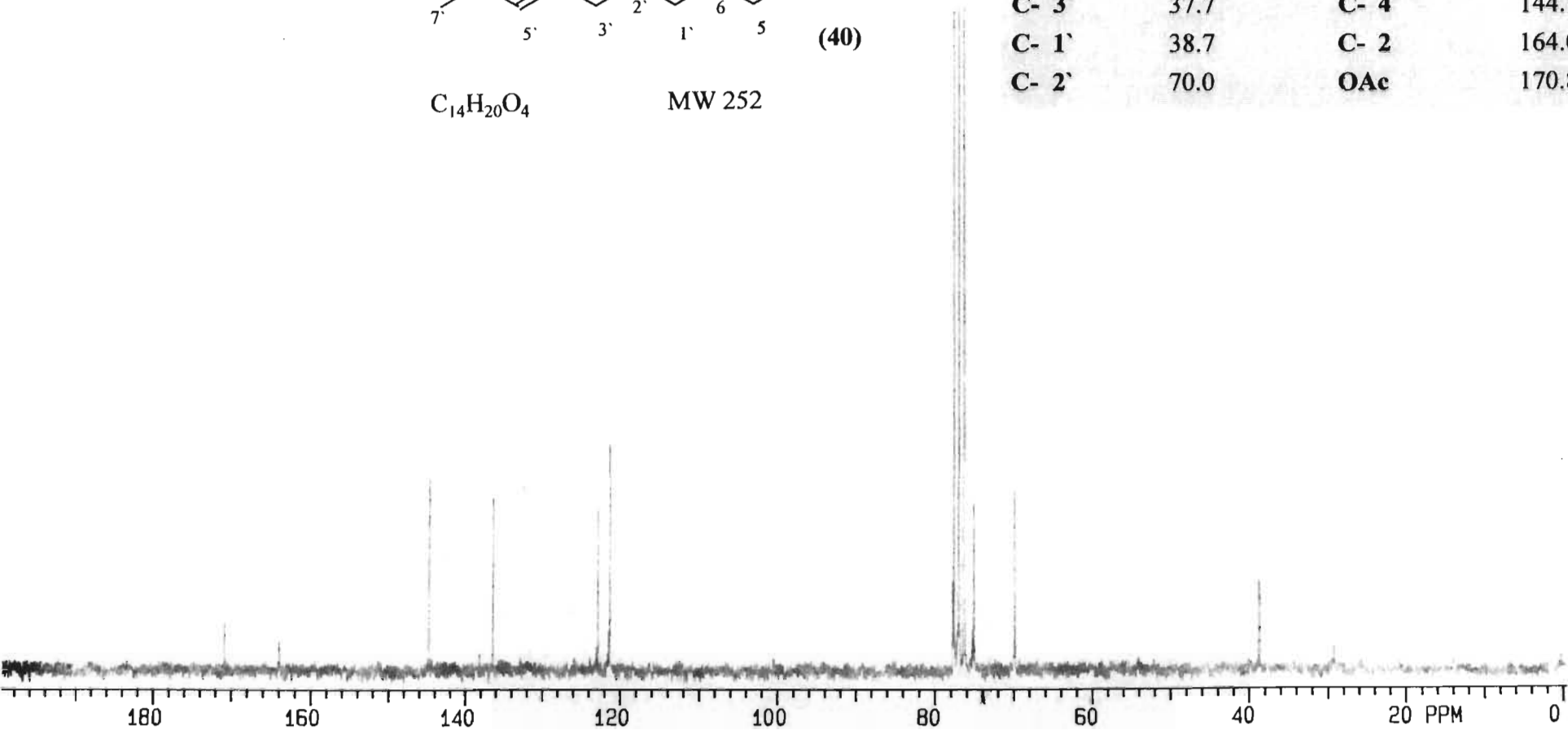
(40) ^1H NMR in CDCl_3



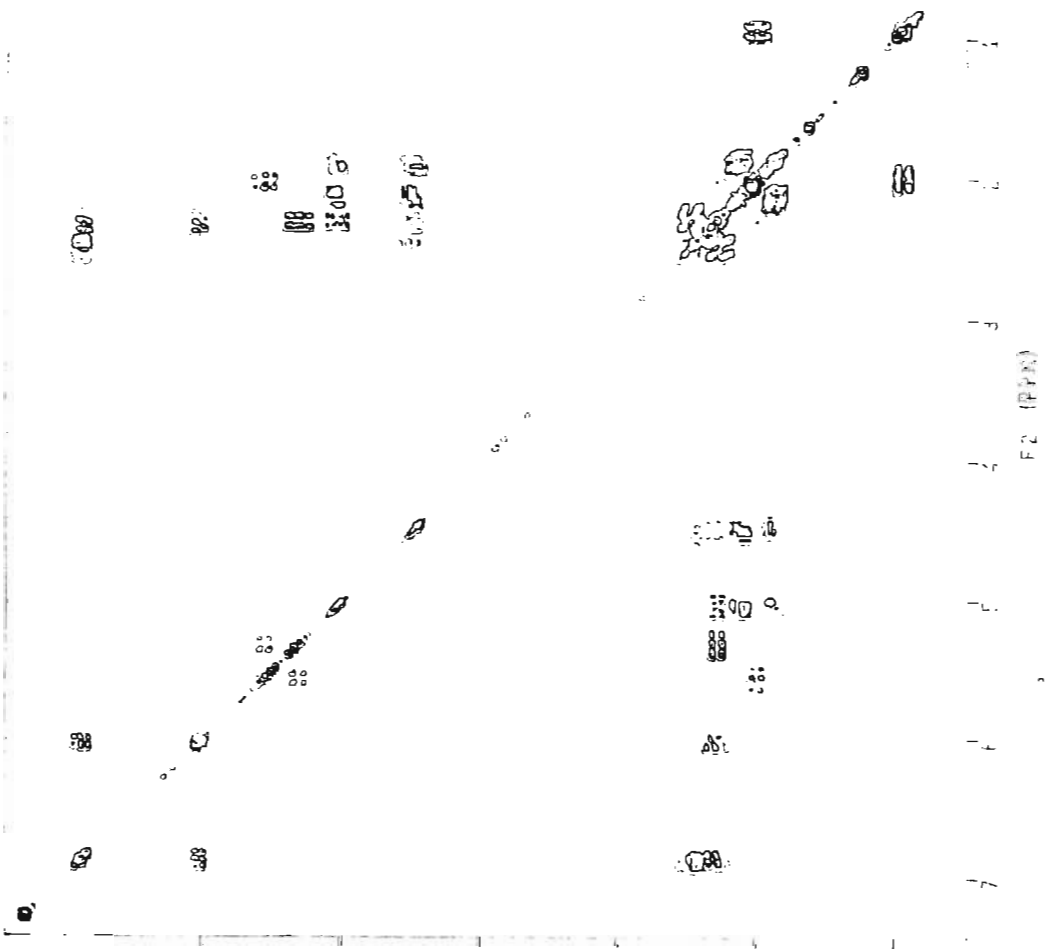
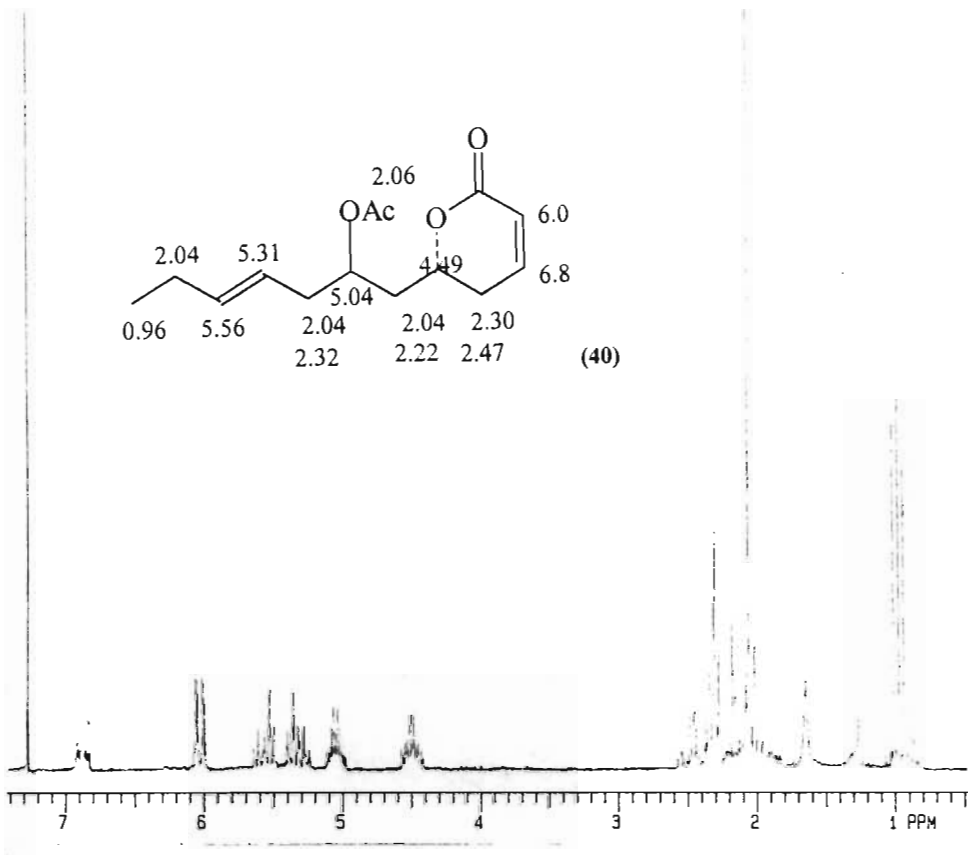
$C_{14}H_{20}O_4$

MW 252

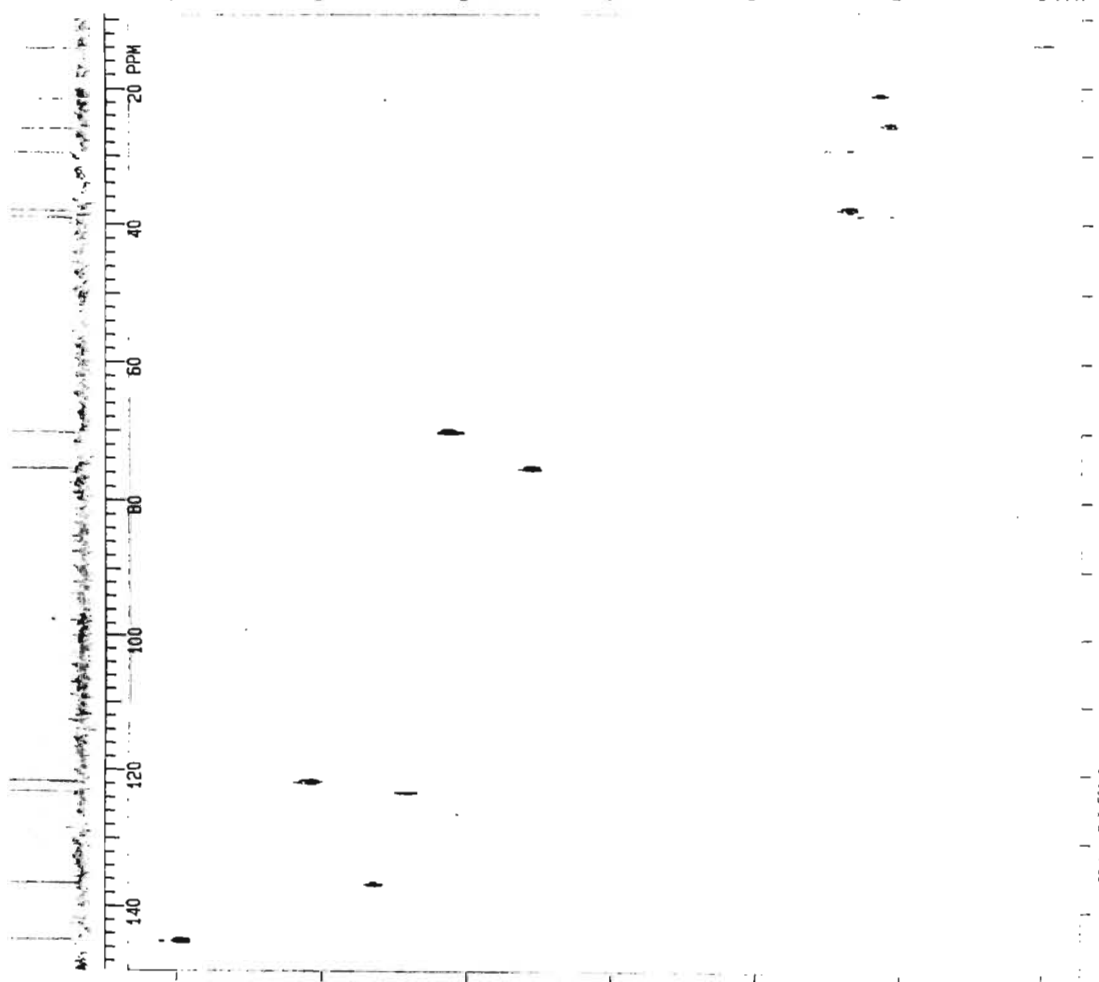
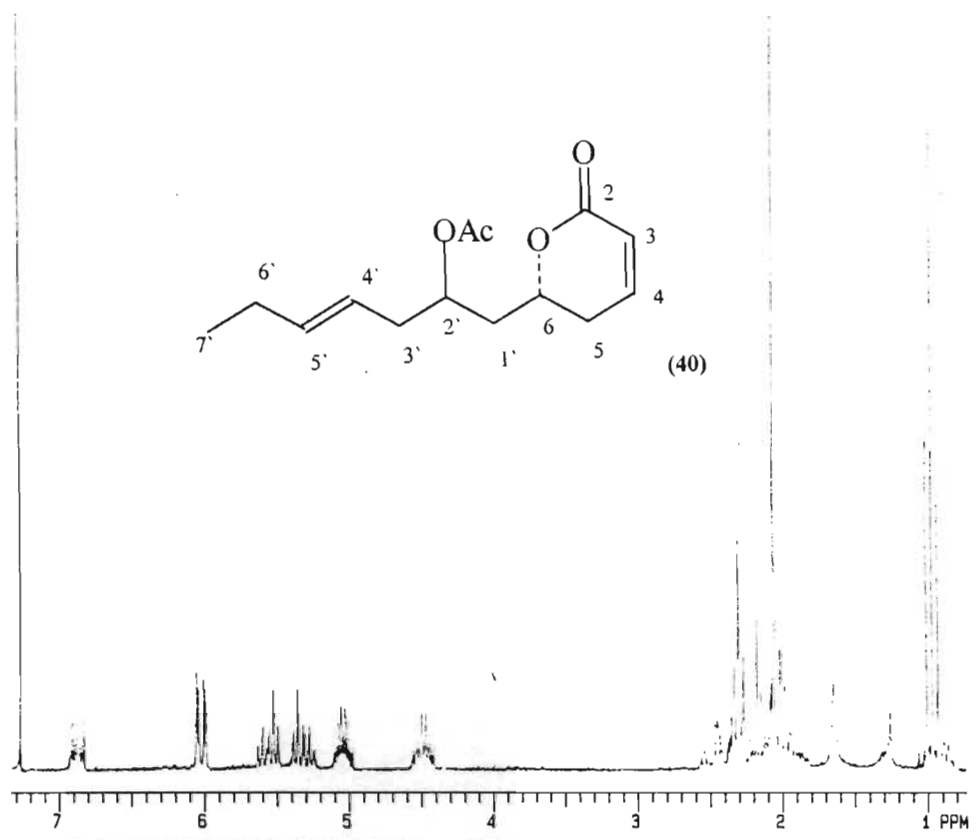
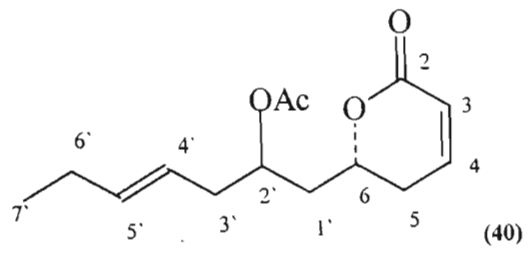
carbon	δ	carbon	δ
C- 7'	13.7	C- 6	75.2
OAc	21.1	C- 3	121.4
C- 6'	25.6	C- 4'	122.9
C- 5	29.1	C- 5'	136.4
C- 3'	37.7	C- 4	144.7
C- 1'	38.7	C- 2	164.0
C- 2'	70.0	OAc	170.8



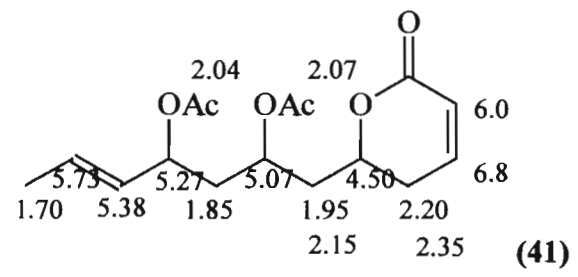
(40) ^{13}C NMR in $CDCl_3$



(40) COSY in CDCl₃

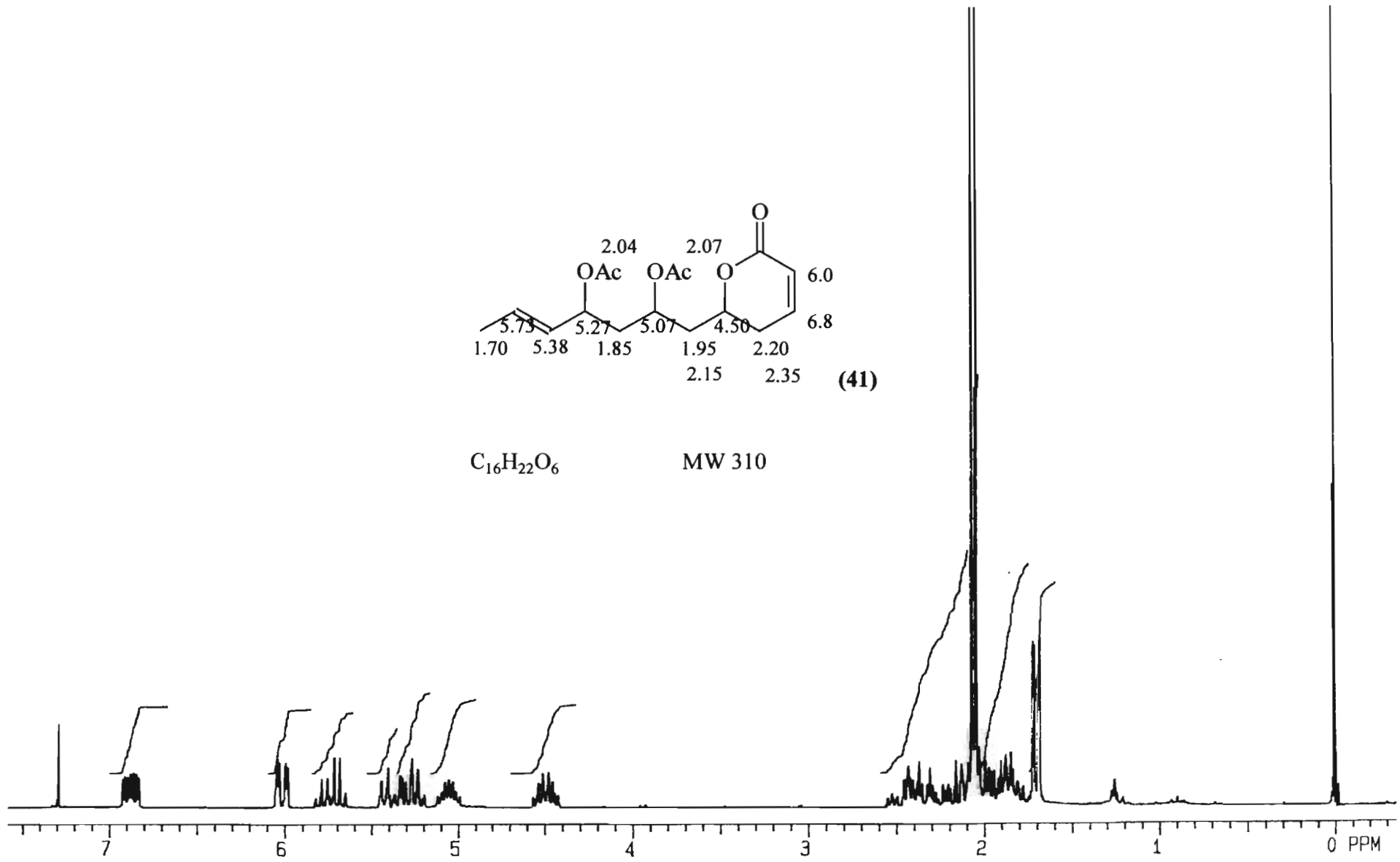


(40) HETCOR in CDCl₃

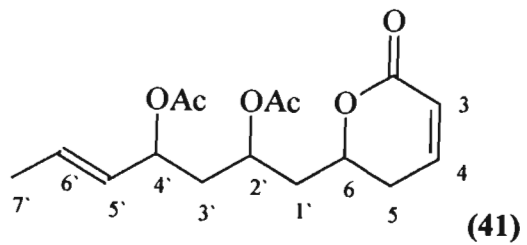


$C_{16}H_{22}O_6$

MW 310



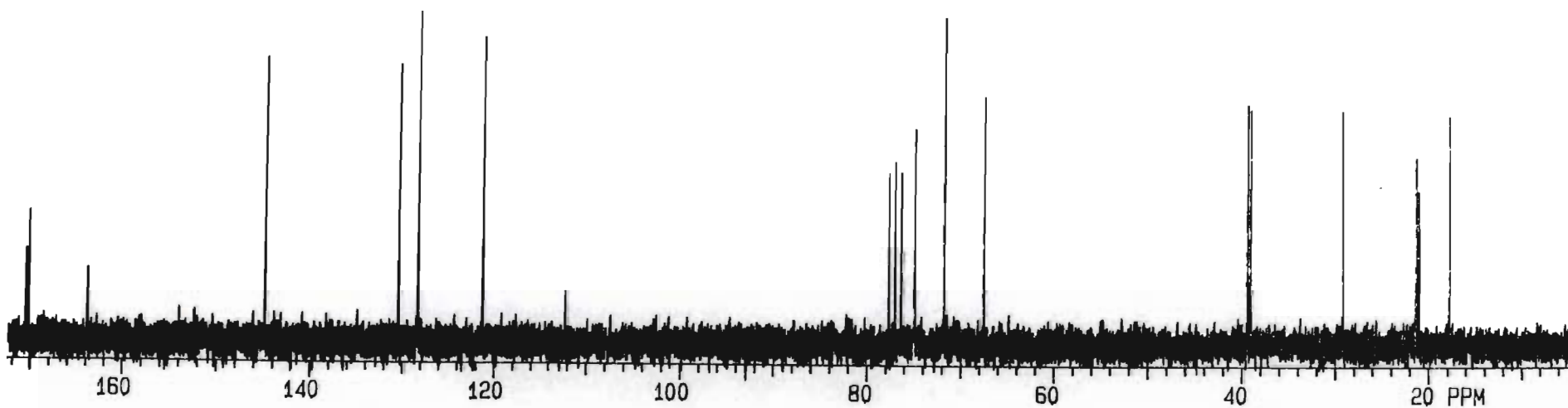
(41) 1H NMR in $CDCl_3$



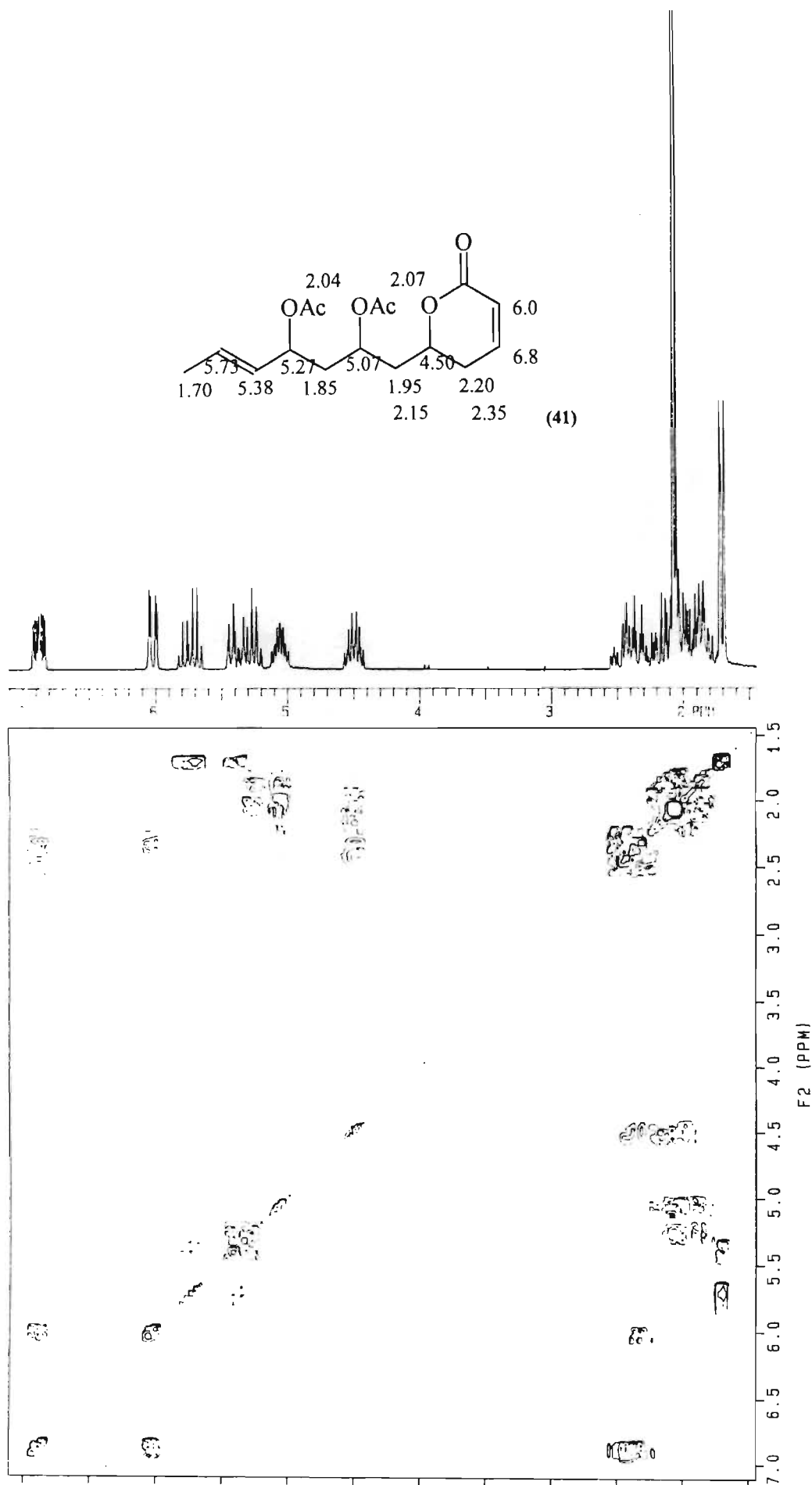
$C_{16}H_{22}O_6$

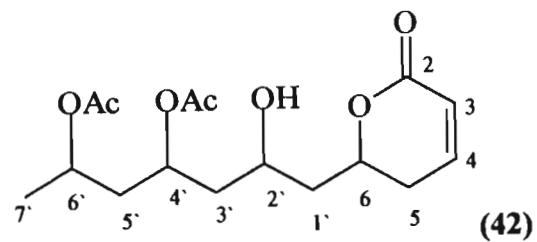
MW 310

carbon	δ	carbon	δ
C- 7'	17.7	C- 6	74.9
OAc	21.1	C- 3	121.3
OAc	21.3	C- 5'	128.4
C- 5	29.2	C- 6'	130.4
C- 3'	39.1	C- 4	144.8
C- 1'	30.4	C- 2	163.9
C- 2'	67.2	OAc	170.2
C- 4'	71.8	OAc	170.6



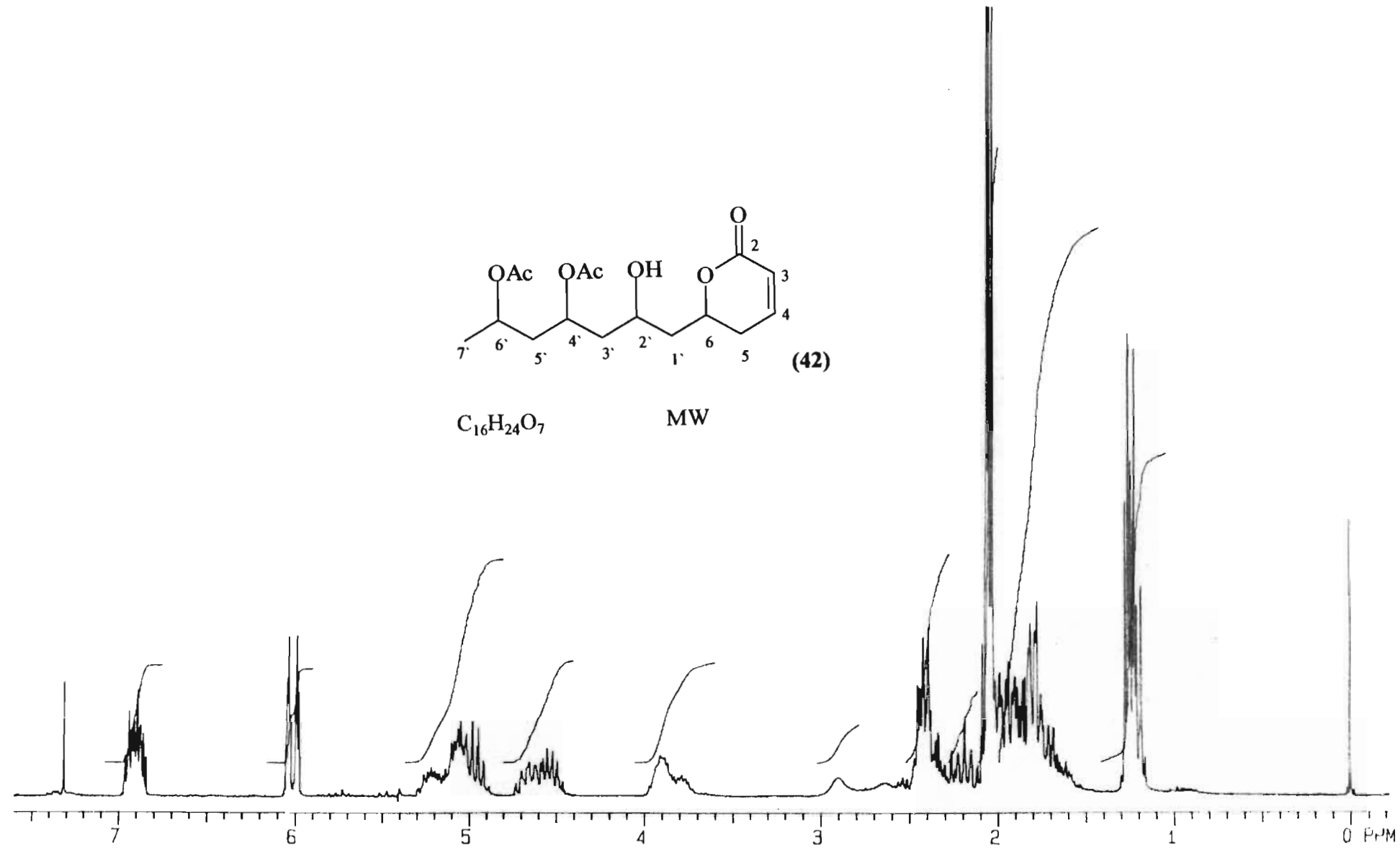
(41) ^{13}C NMR in $CDCl_3$



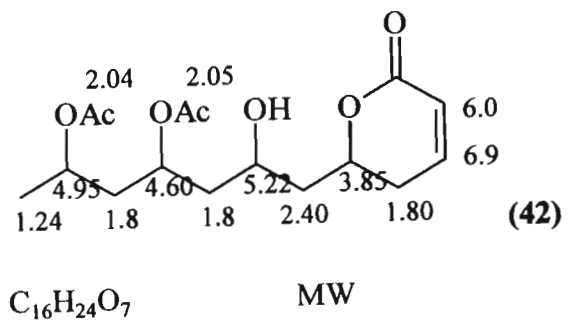


$C_{16}H_{24}O_7$

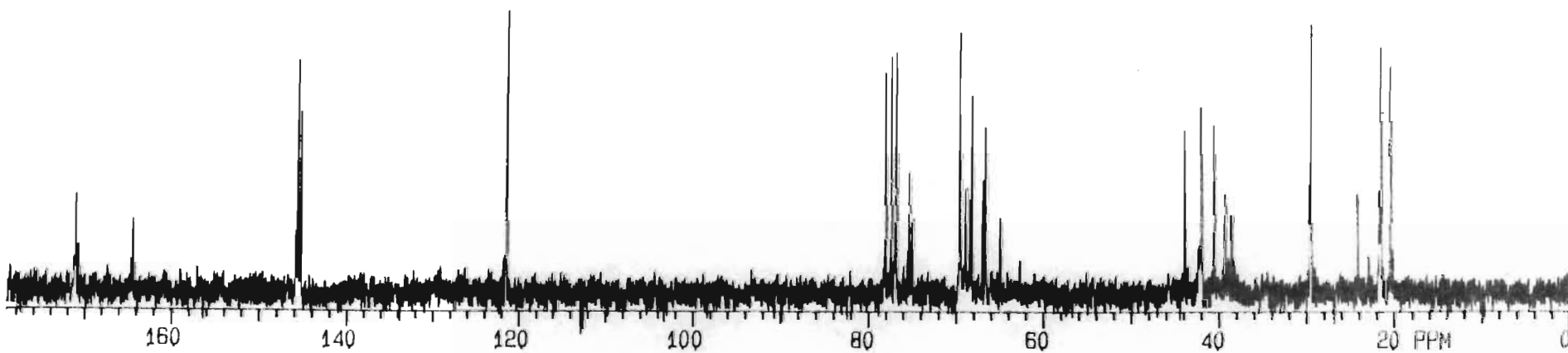
MW



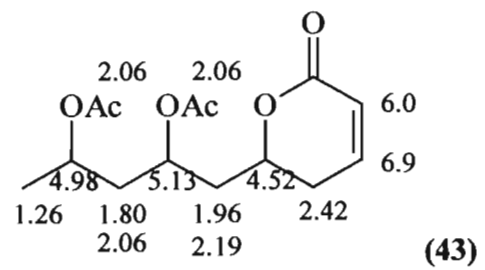
(42) 1H NMR in $CDCl_3$



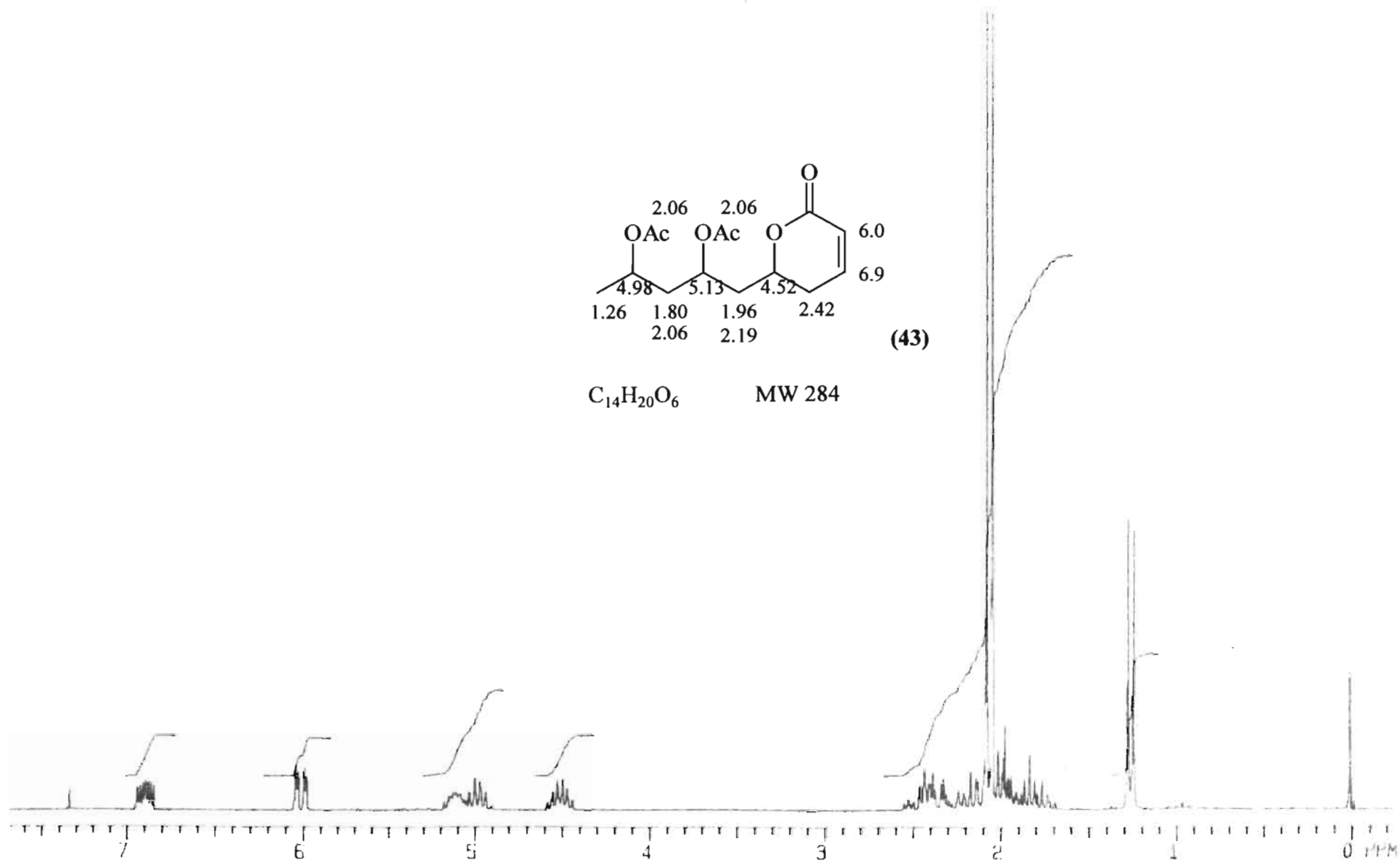
carbon	δ	carbon	δ
C- 7'	20.4	C- 4'	67.0
OAc	21.5	C- 6	75.1
OAc	21.6	C- 3	121.3
C- 5	29.5	C- 6'	121.3
C- 1'	38.5	C- 4	145.7
C- 5'	38.8	C- 2	164.0
C- 3'	42.0	OAc	171.2
C- 2'	66.7	OAc	171.2



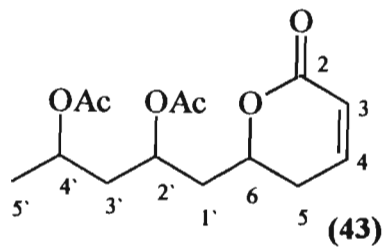
(42) ^{13}C NMR in $CDCl_3$



$C_{14}H_{20}O_6$ MW 284



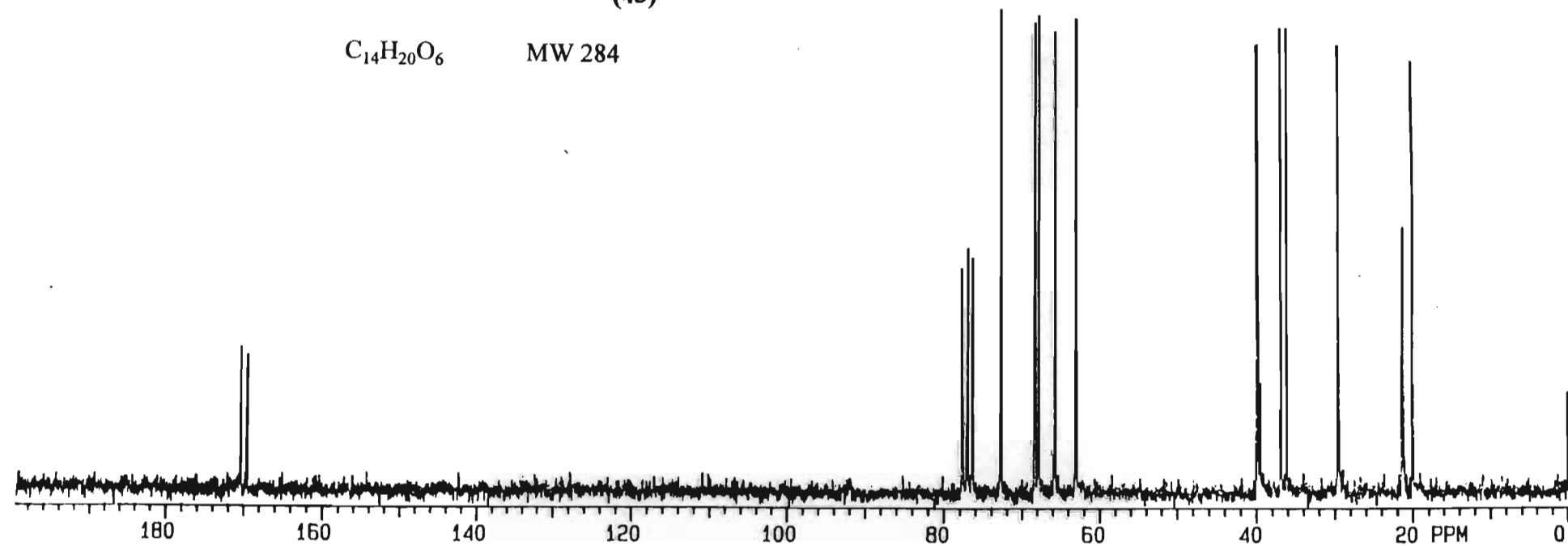
(43) 1H NMR in $CDCl_3$



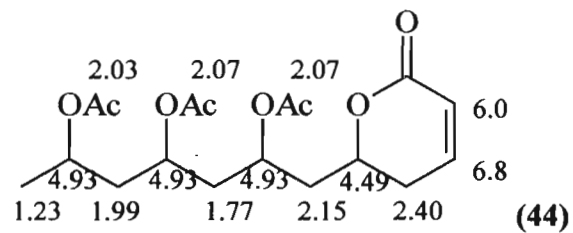
$C_{14}H_{20}O_6$

MW 284

carbon	δ	carbon	δ
Me	19.9	C- 4'	67.6
OAc	21.0	C- 6	74.8
OAc	21.1	C- 3	121.3
C- 5	29.0	C- 4	145.0
C- 1	38.9	C- 2	163.5
C- 3'	40.2	OAc	170.3
C- 2'	67.6	OAc	170.4

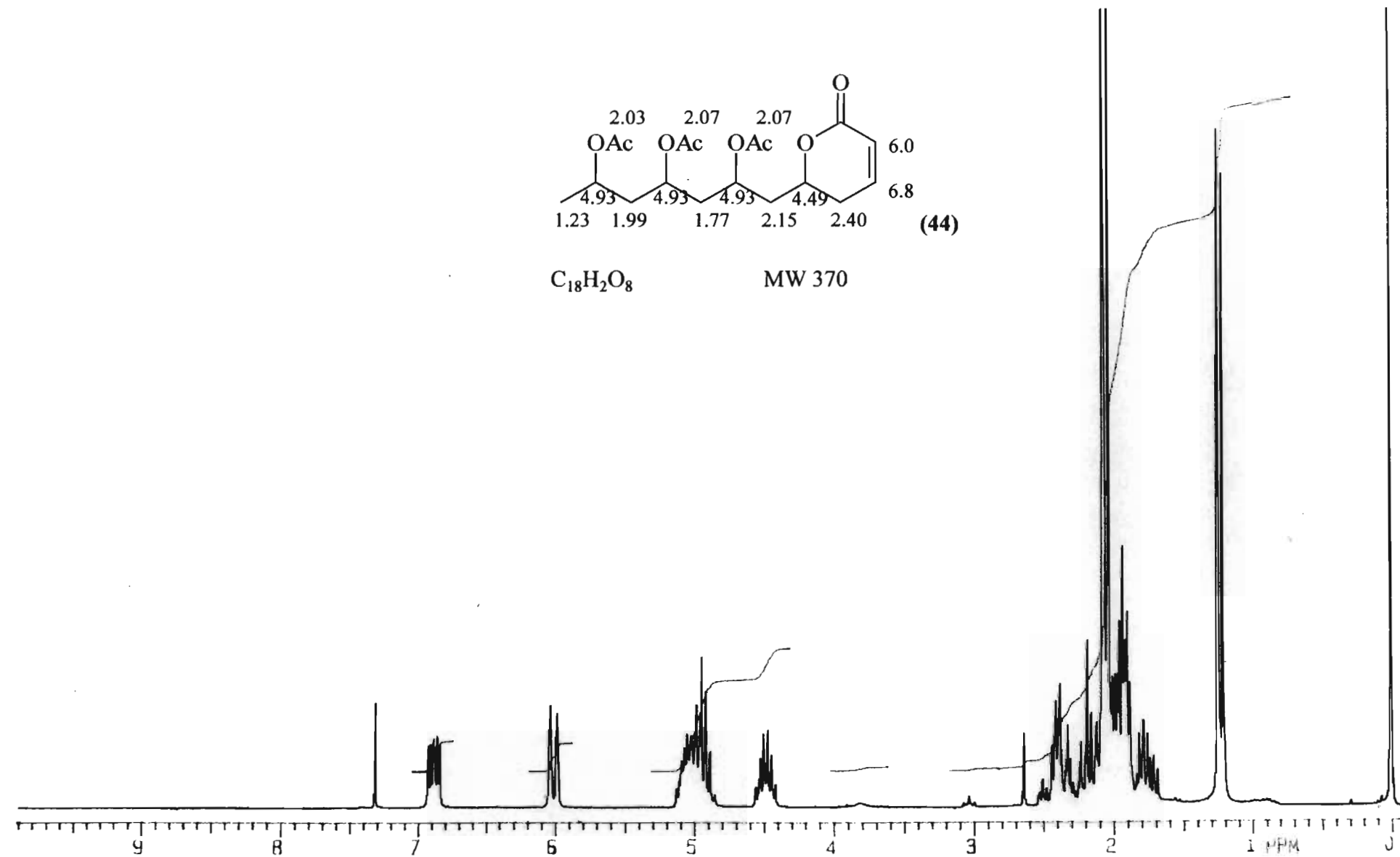


(43) ^{13}C NMR in $CDCl_3$

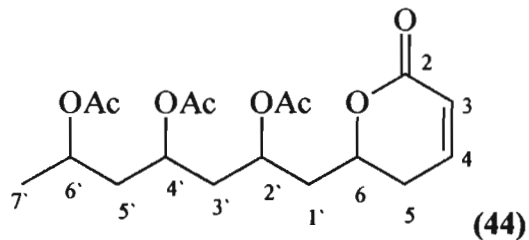


$C_{18}H_{20}O_8$

MW 370



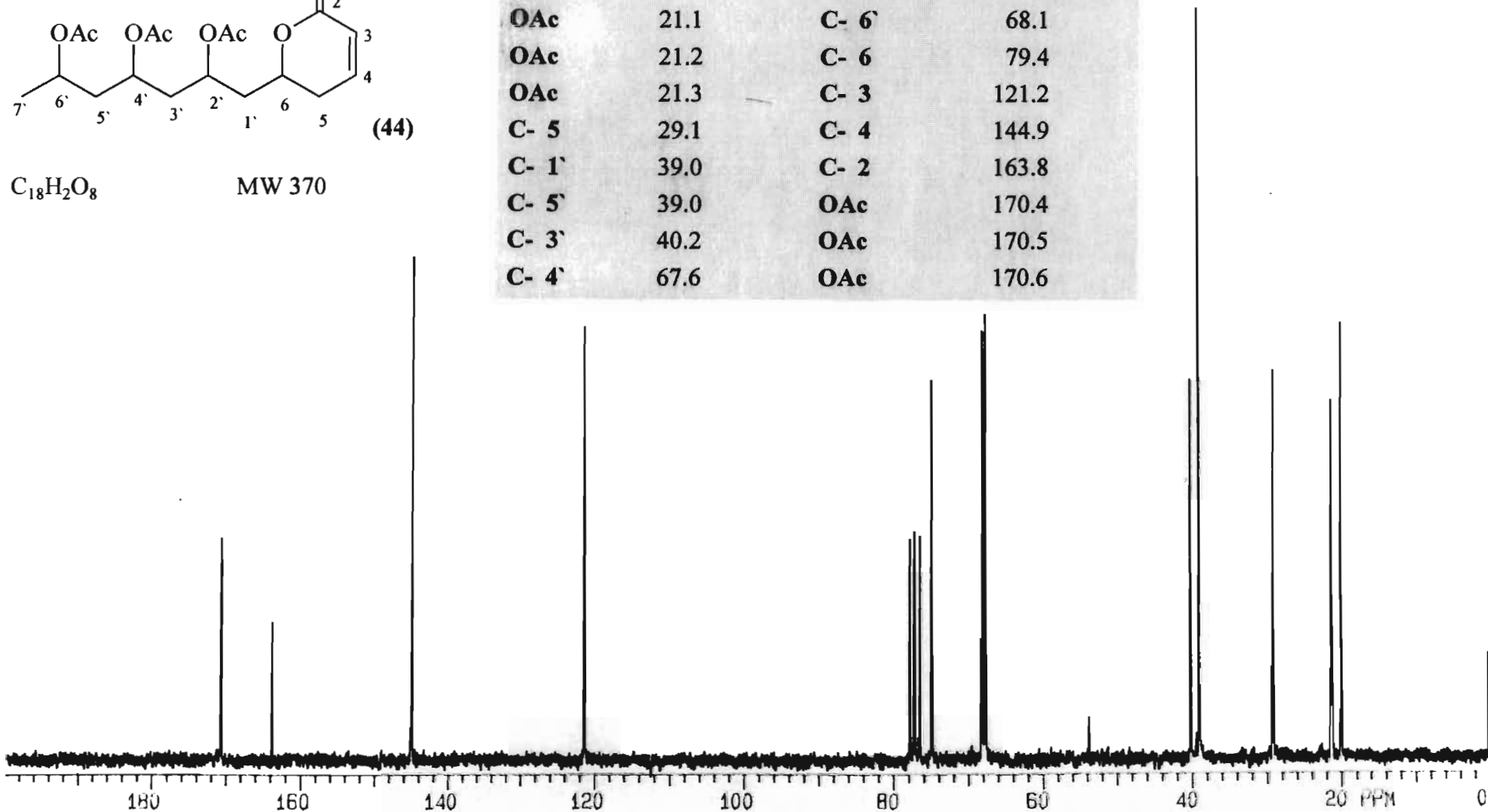
(44) 1H NMR in CDCl₃



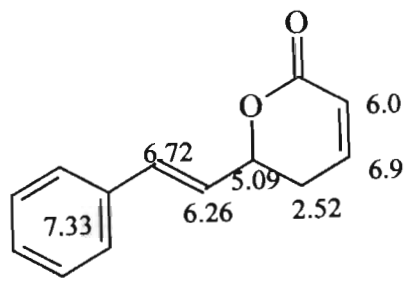
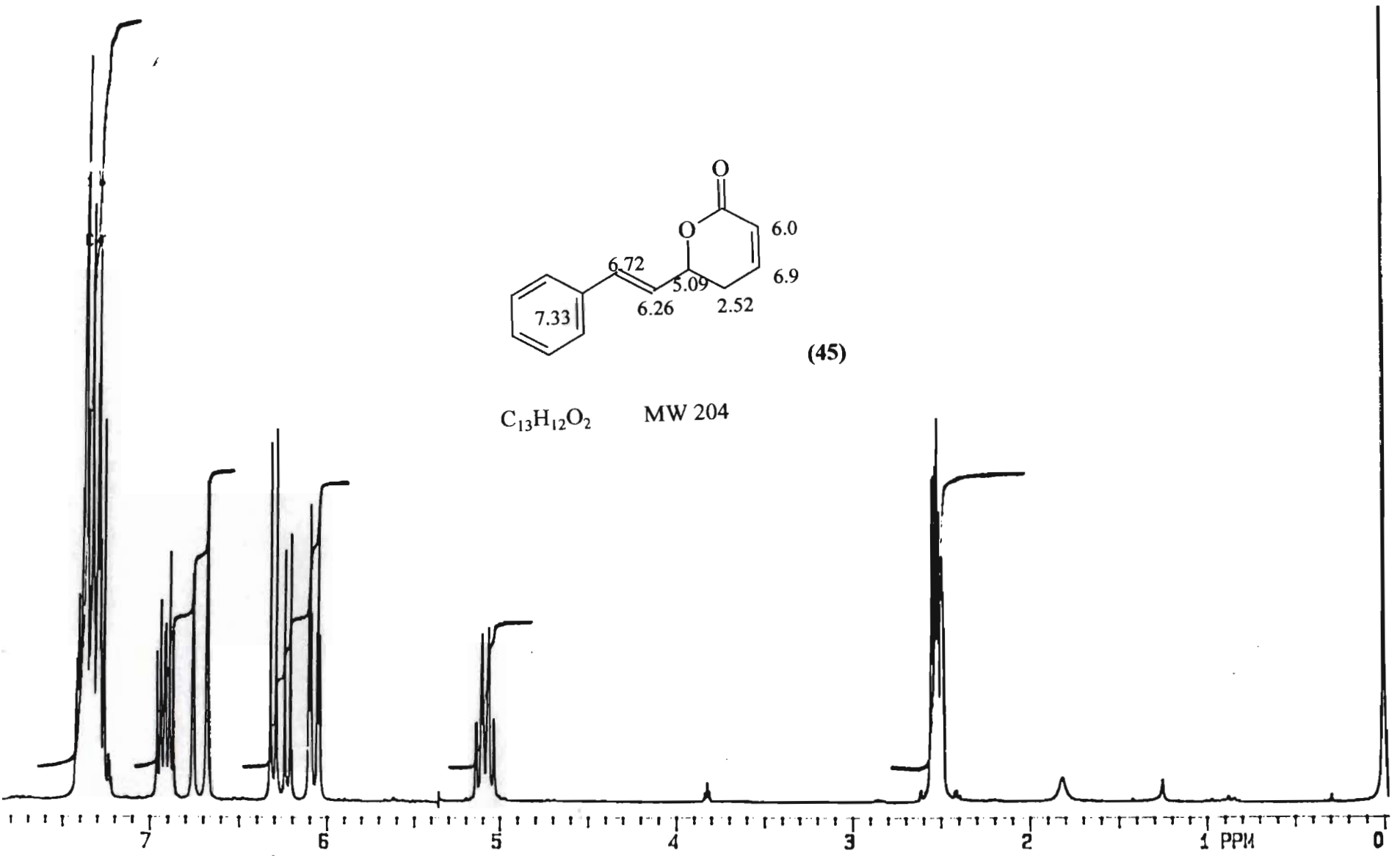
$C_{18}H_{20}O_8$

MW 370

carbon	δ	carbon	δ
Me	20.0	C- 2'	67.8
OAc	21.1	C- 6'	68.1
OAc	21.2	C- 6	79.4
OAc	21.3	C- 3	121.2
C- 5	29.1	C- 4	144.9
C- 1'	39.0	C- 2	163.8
C- 5'	39.0	OAc	170.4
C- 3'	40.2	OAc	170.5
C- 4'	67.6	OAc	170.6



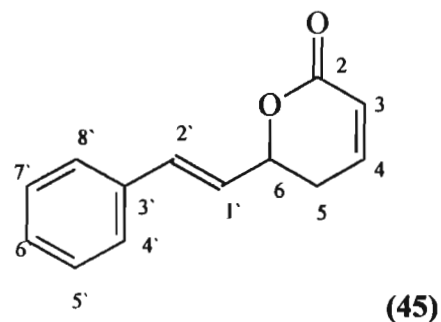
(44) ^{13}C NMR in $CDCl_3$



(45)

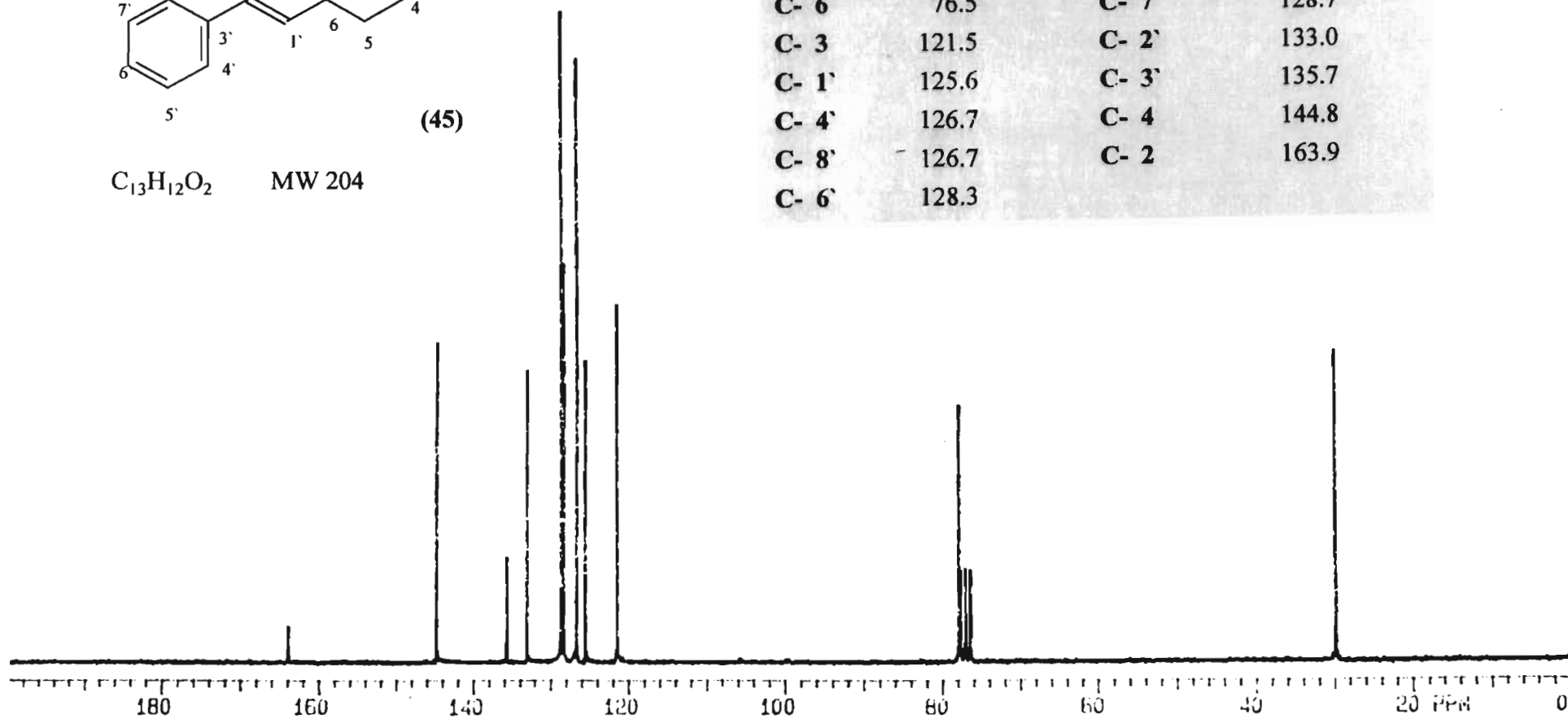
$C_{13}H_{12}O_2$ MW 204

(45) 1H NMR in $CDCl_3$

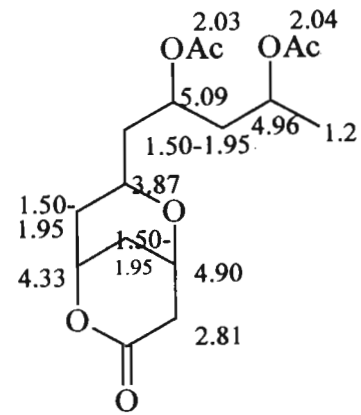


$C_{13}H_{12}O_2$ MW 204

carbon	δ	carbon	δ
C- 5	29.8	C- 5'	128.7
C- 6	76.5	C- 7'	128.7
C- 3	121.5	C- 2'	133.0
C- 1'	125.6	C- 3'	135.7
C- 4'	126.7	C- 4	144.8
C- 8'	126.7	C- 2	163.9
C- 6'	128.3		

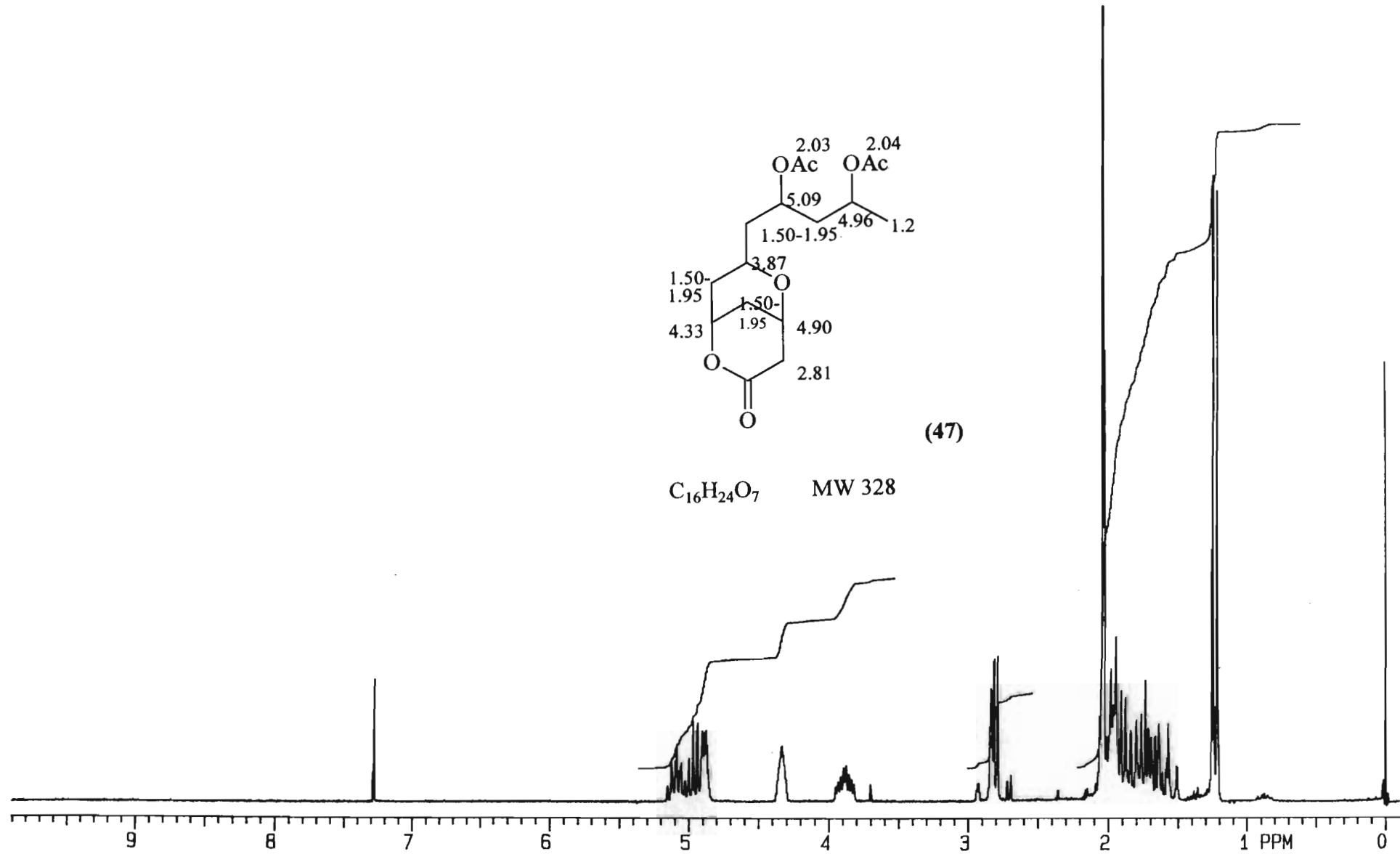


(45) ^{13}C NMR in $CDCl_3$

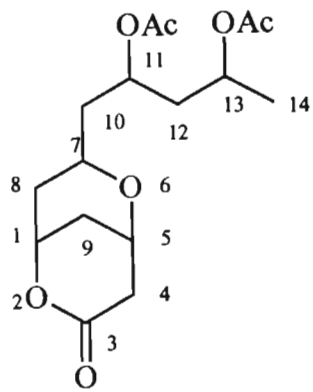


(47)

$\text{C}_{16}\text{H}_{24}\text{O}_7$ MW 328



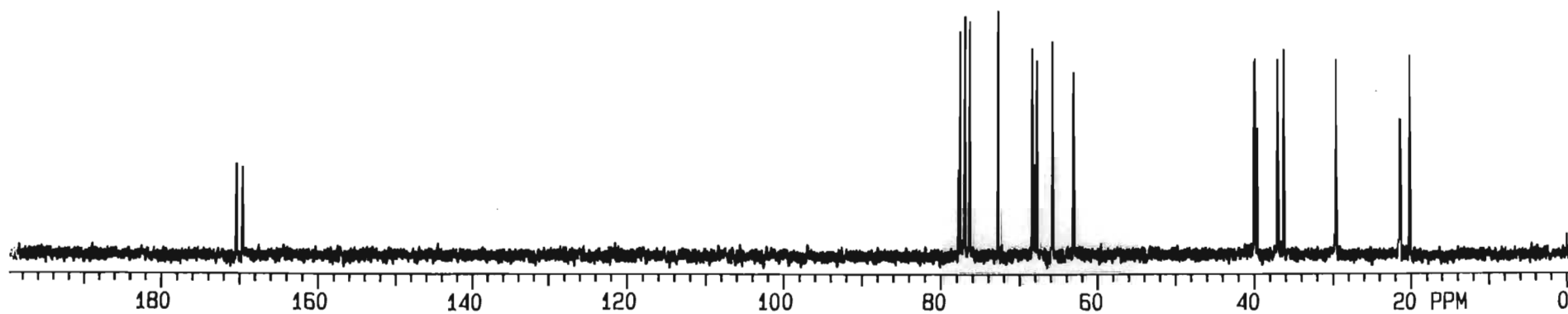
(47) ^1H NMR in CDCl_3



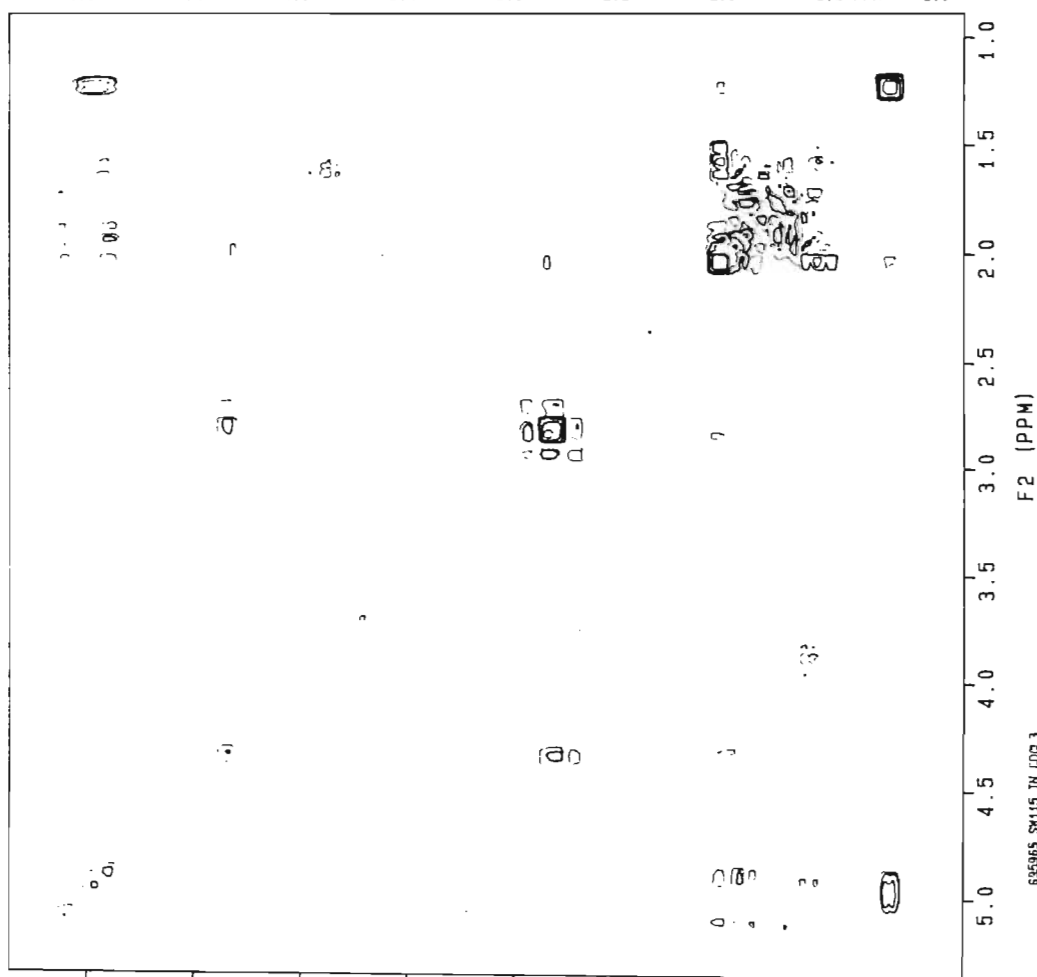
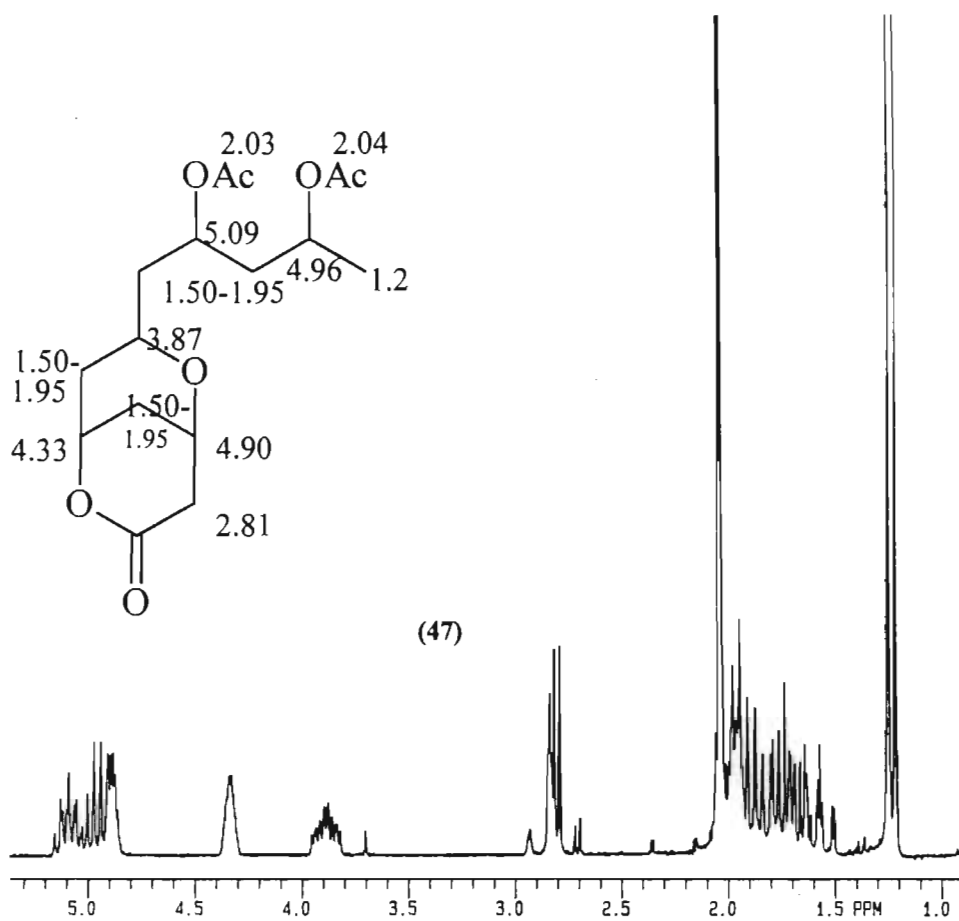
(47)

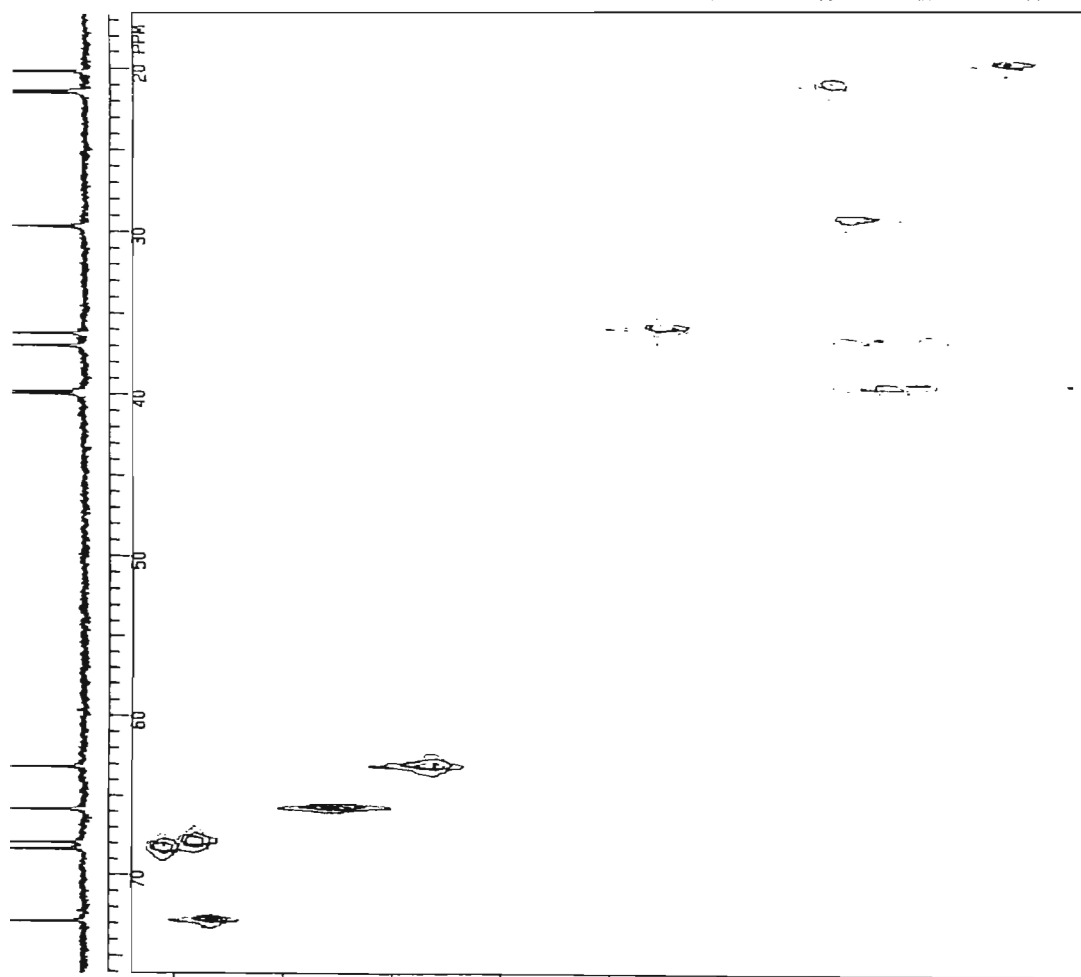
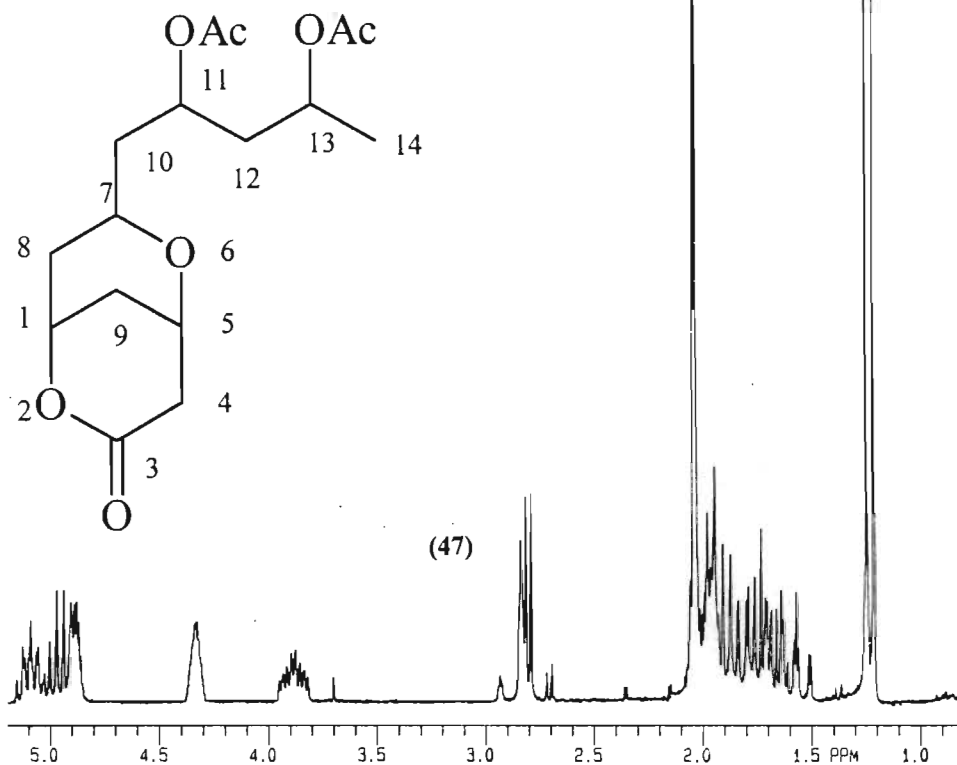
$C_{16}H_{24}O_7$ MW 328

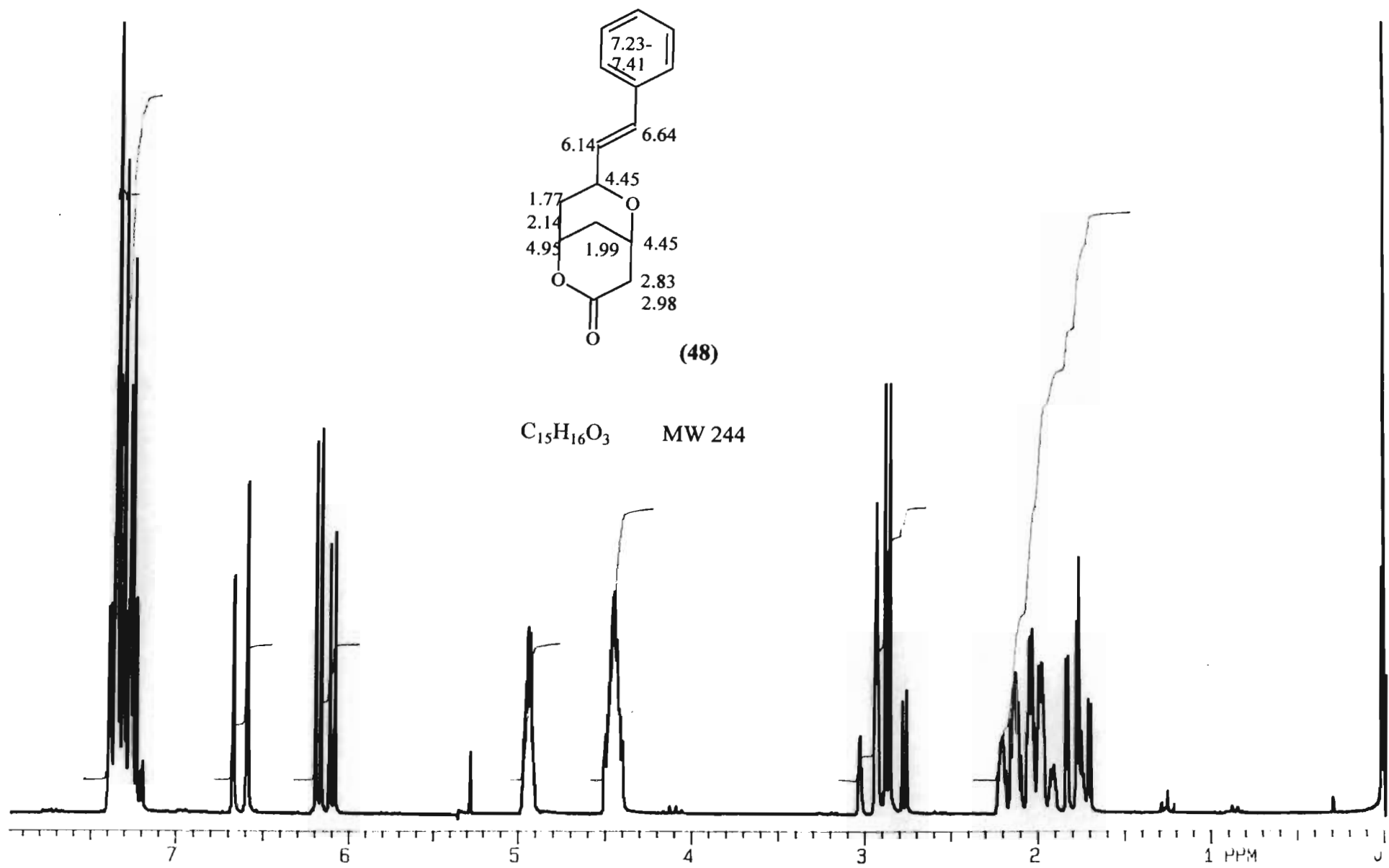
carbon	δ	carbon	δ
Me	20.0	C- 5	63.1
OAc	21.2	C- 7	67.9
OAc	21.3	C-13	68.4
C- 9	29.5	C-11	68.8
C- 4	36.1	C- 1	72.9
C- 8	36.9	C- 3	169.7
C-10	39.7	OAc	170.5
C-12	39.9	OAc	170.5



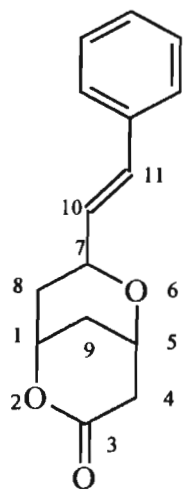
(47) ^{13}C NMR in $CDCl_3$



(47) HETCOR in CDCl₃



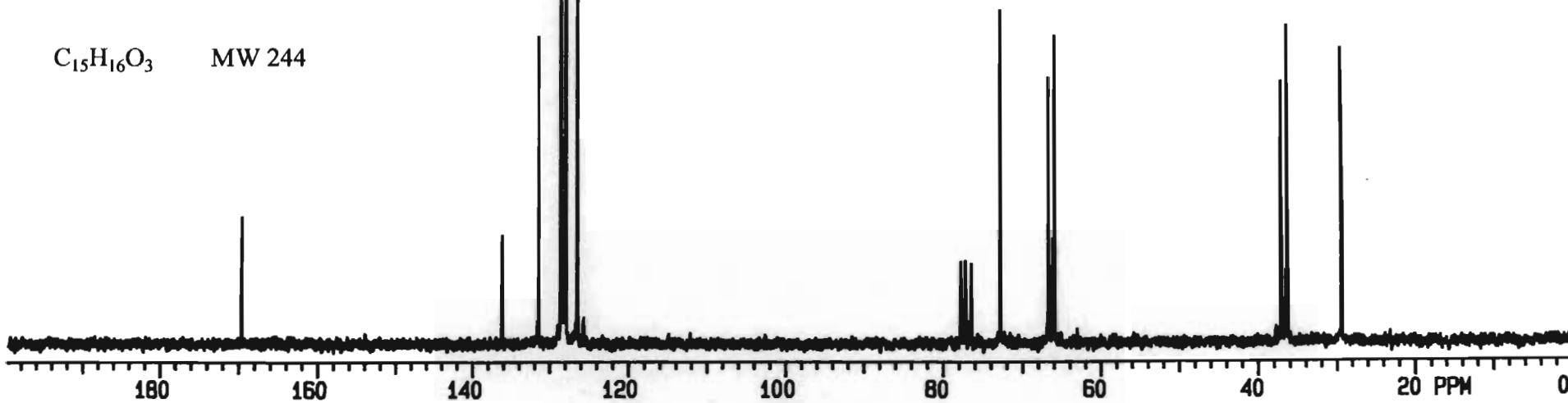
(48) 1H NMR in $CDCl_3$



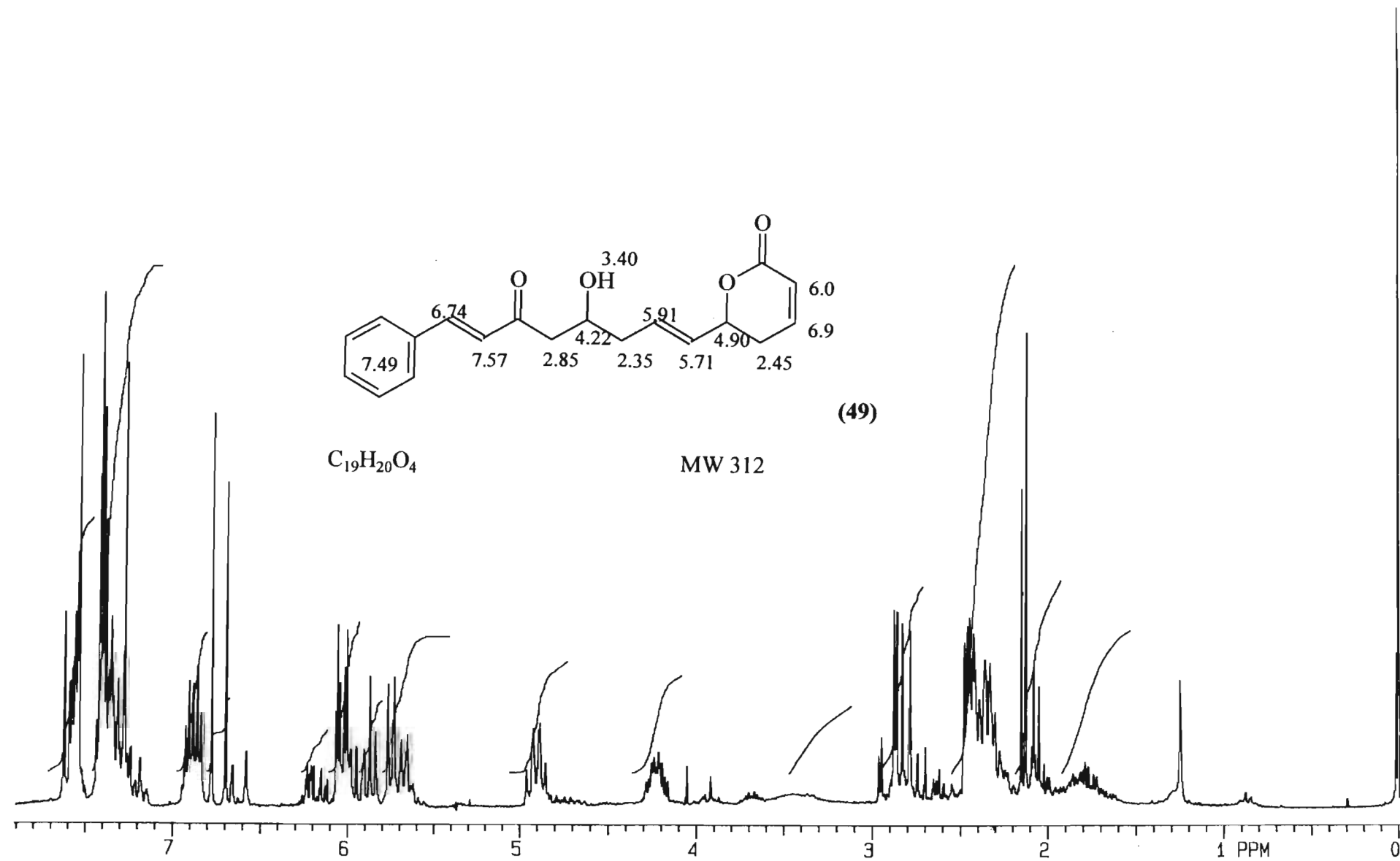
(48)

$C_{15}H_{16}O_3$ MW 244

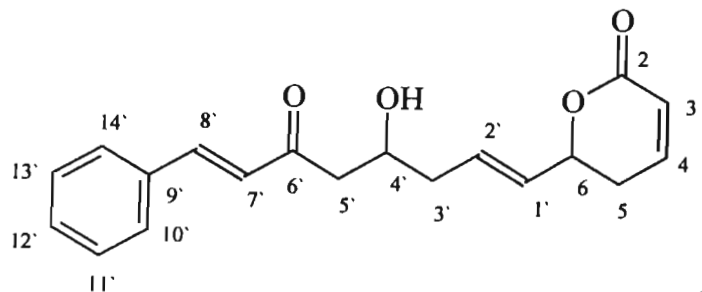
carbon	δ	carbon	δ
C- 9	29.5	C=13	126.5
C- 4	36.5	C-14	128.1
C- 8	37.2	C-15	128.6
C- 5	66.1	C-16	128.6
C- 7	66.8	C-11	131.6
C- 1	72.8	C-12	136.2
C-10	127.9	C- 3	169.6



(48) ^{13}C NMR in $CDCl_3$



(49) 1H NMR in $CDCl_3$

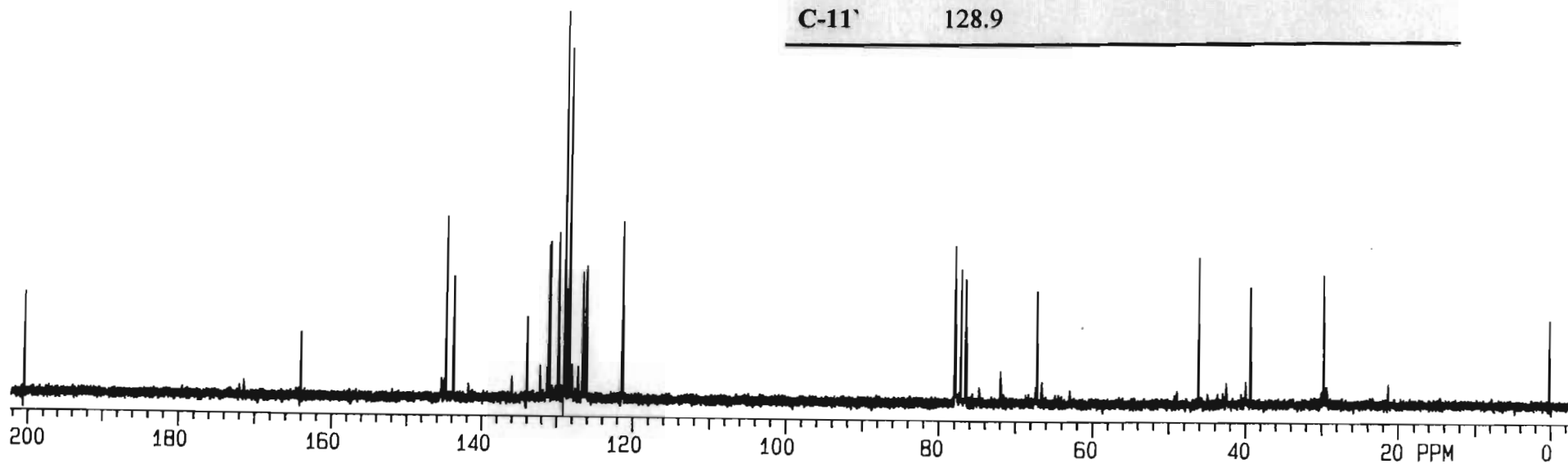


(49)

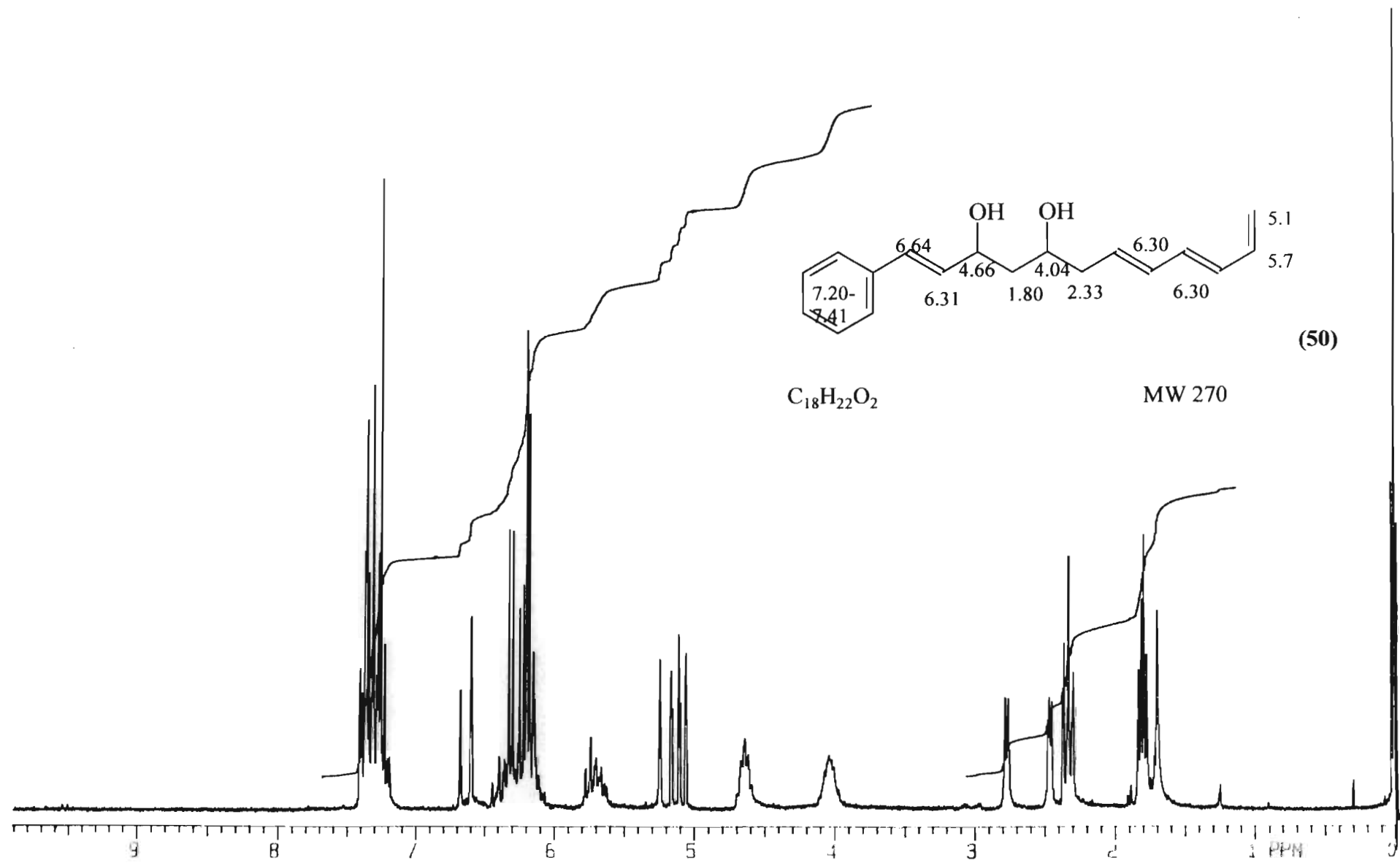
$C_{19}H_{20}O_4$

MW 312

carbon	δ	carbon	δ
C- 5	29.6	C-13'	128.9
C- 3'	39.3	C- 1'	129.0
C- 5'	46.2	C-12'	130.8
C- 4'	67.2	C- 2'	130.9
C- 6	77.9	C- 9'	134.1
C- 3	121.4	C- 8'	143.8
C- 7'	126.6	C- 4	144.9
C-10'	128.4	C- 2	164.1
C-14'	128.4	C- 6'	200.5
C-11'	128.9		



(49) ^{13}C NMR in $CDCl_3$

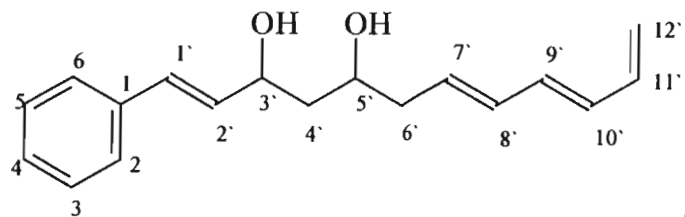


$C_{18}H_{22}O_2$

MW 270

(50)

(50) 1H NMR in $CDCl_3$

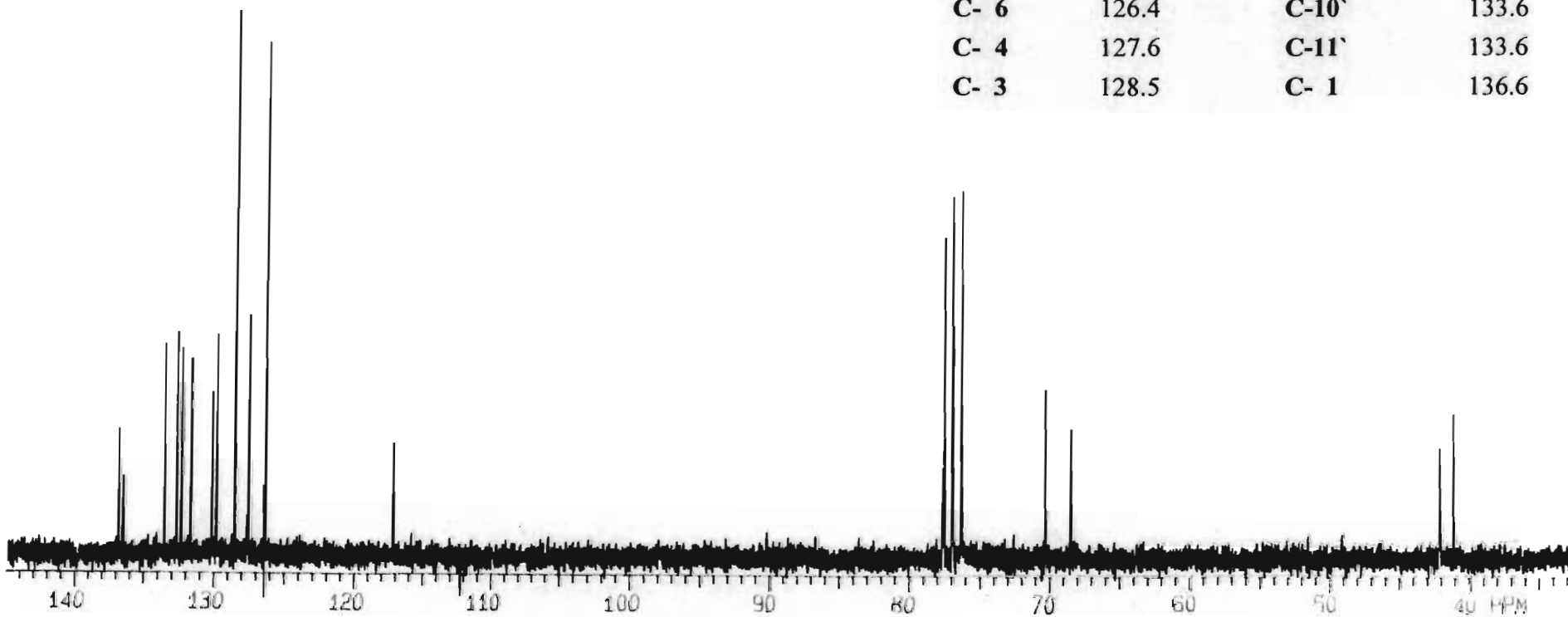


(50)

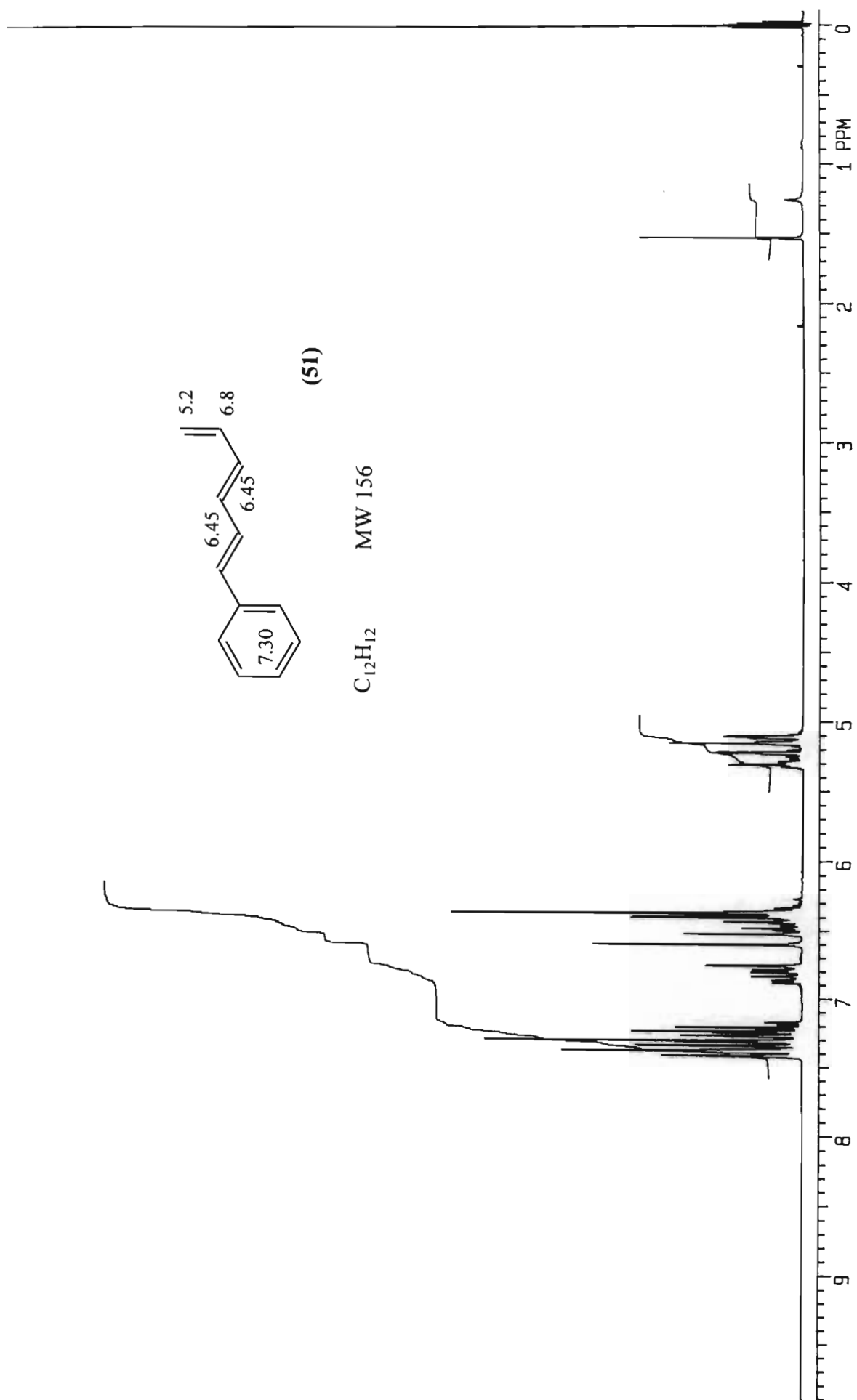
$C_{18}H_{22}O_2$

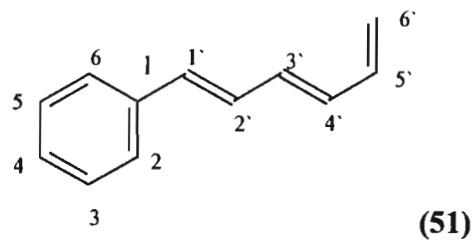
MW 270

carbon	δ	carbon	δ
C- 6'	41.1	C- 5	128.5
C- 4'	42.1	C- 1'	129.9
C- 5'	68.5	C- 8'	130.3
C- 3'	70.4	C- 2'	131.8
C-12'	117.2	C- 7'	132.4
C- 2	126.4	C- 9'	132.7
C- 6	126.4	C-10'	133.6
C- 4	127.6	C-11'	133.6
C- 3	128.5	C- 1	136.6



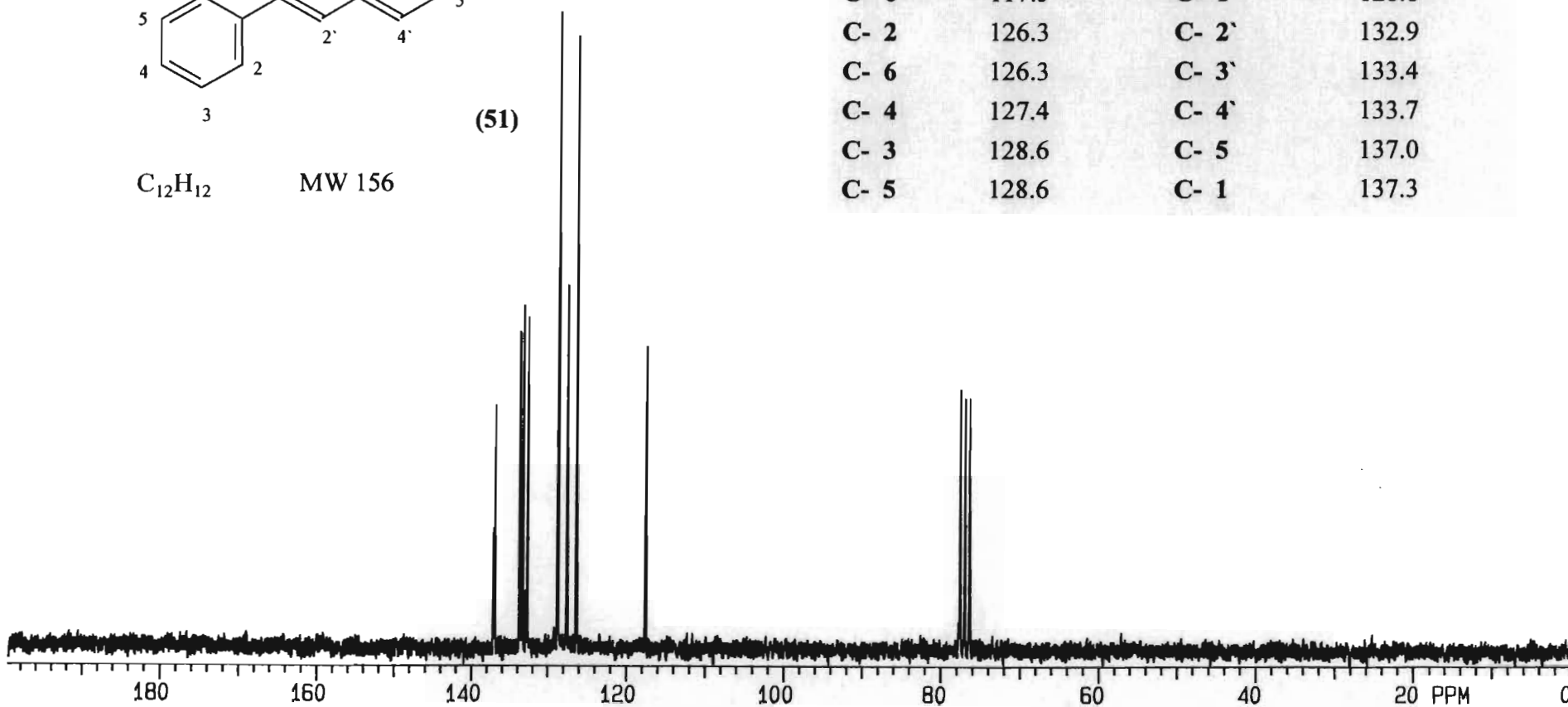
(50) ^{13}C NMR in $CDCl_3$

**(51)** $^1\text{H NMR}$ in CDCl_3

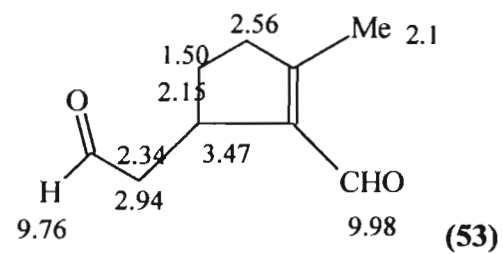


$C_{12}H_{12}$ MW 156

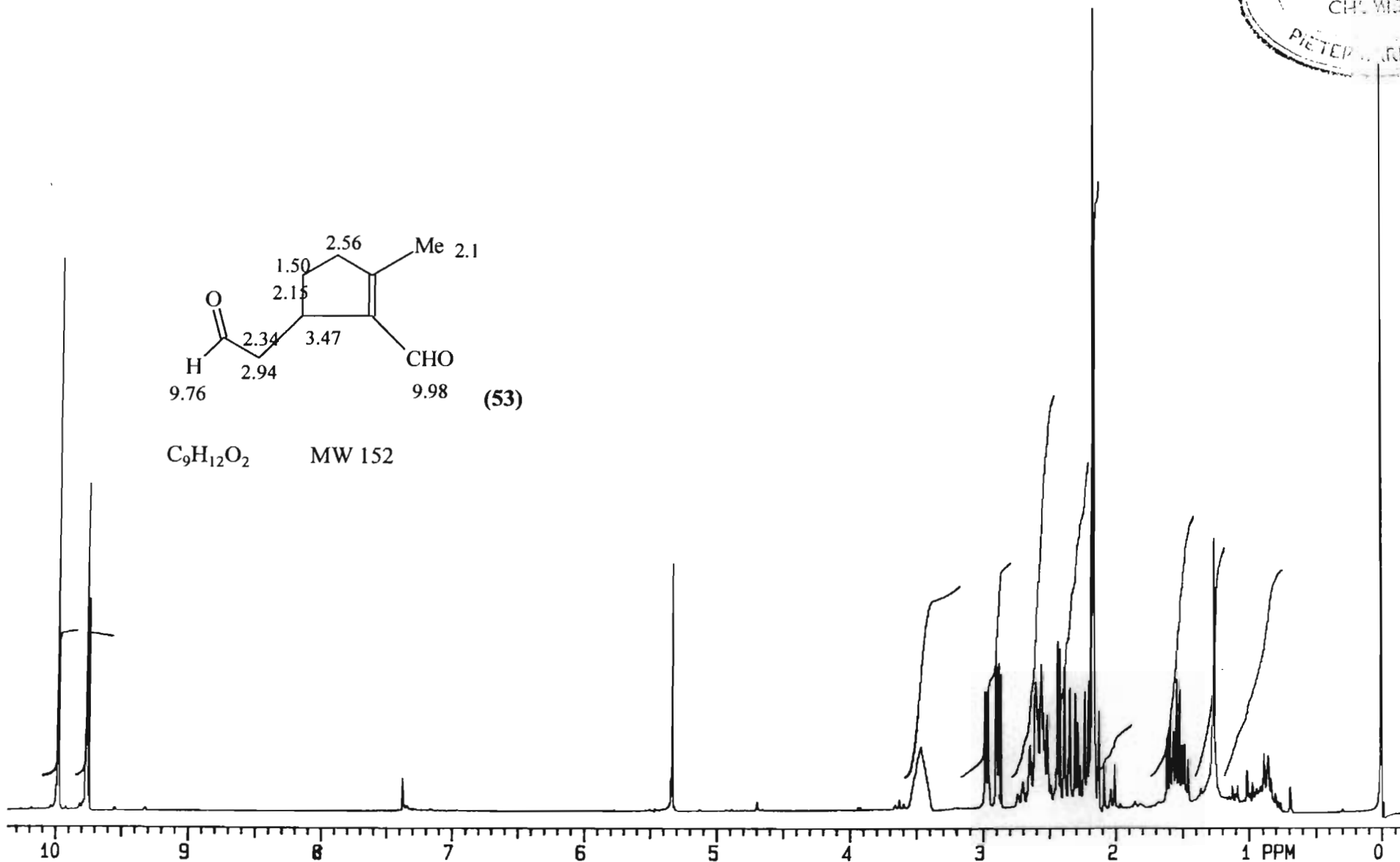
carbon	δ	carbon	δ
C- 6'	117.5	C- 1'	128.8
C- 2	126.3	C- 2'	132.9
C- 6	126.3	C- 3'	133.4
C- 4	127.4	C- 4'	133.7
C- 3	128.6	C- 5	137.0
C- 5	128.6	C- 1	137.3



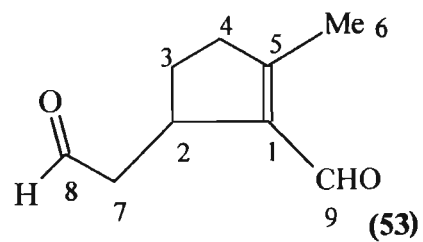
(51) ^{13}C NMR in $CDCl_3$



$\text{C}_9\text{H}_{12}\text{O}_2$ MW 152

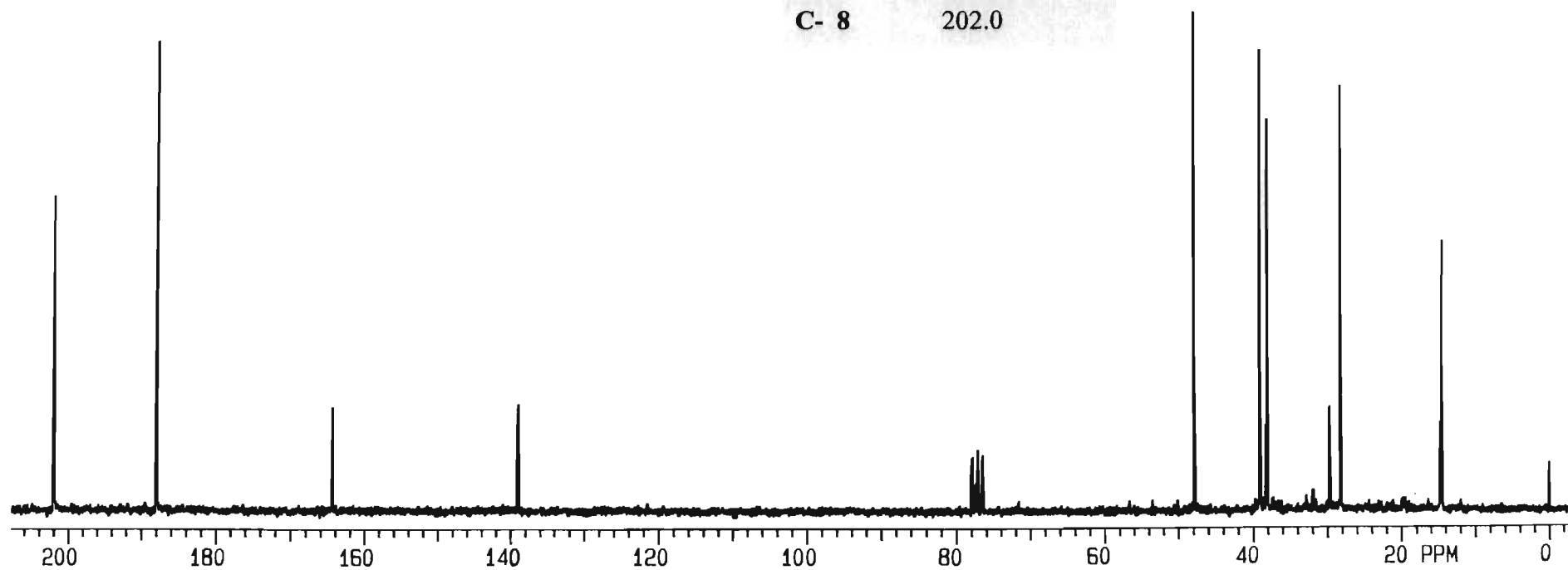


(53) ^1H NMR in CDCl_3

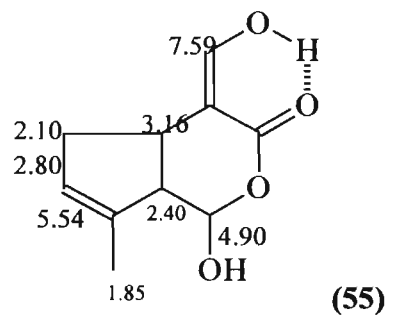


$C_9H_{12}O_2$ MW 152

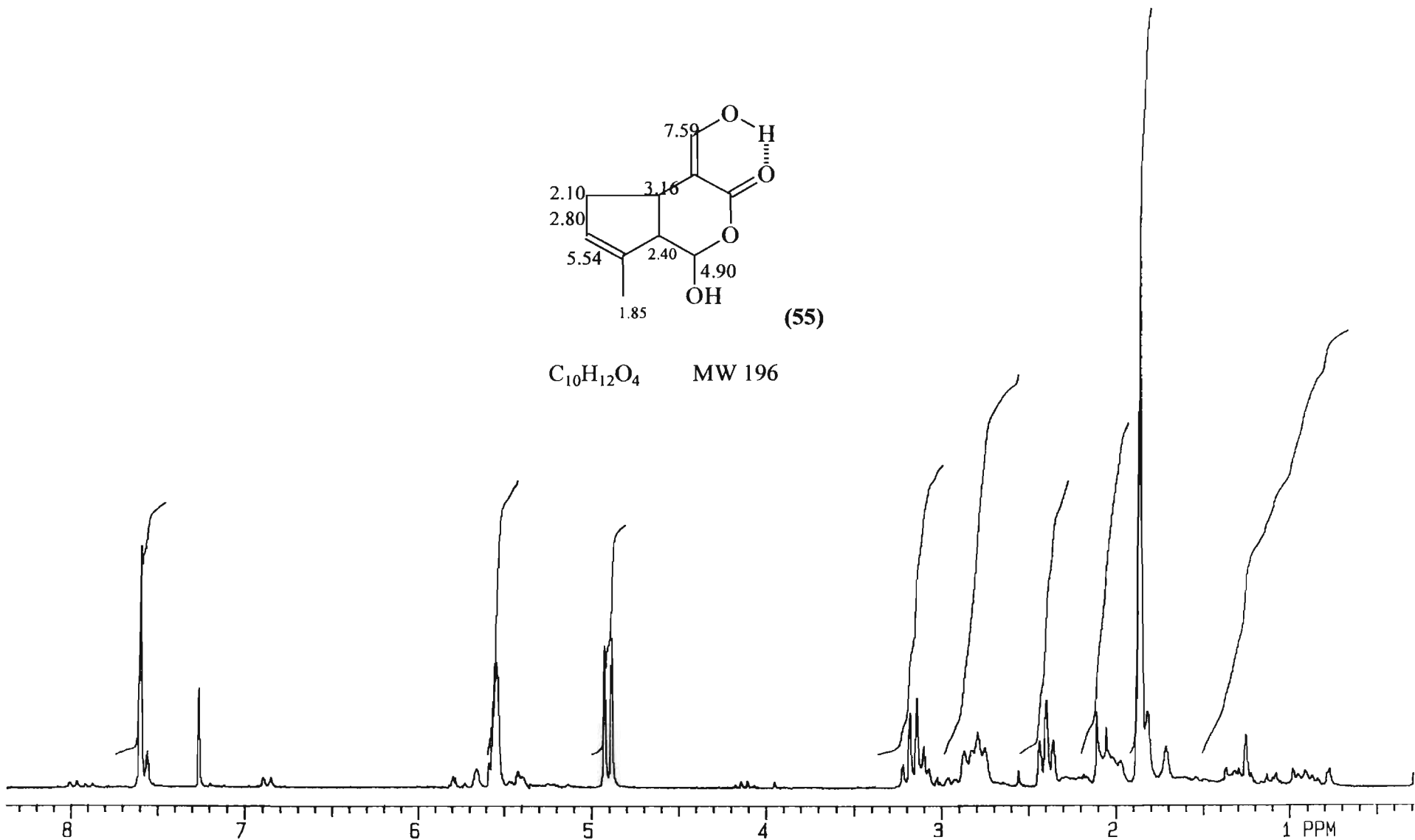
carbon	δ
C- 6	14.5
C- 3	28.2
C- 2	38.2
C- 4	39.0
C- 7	47.8
C- 1	139.1
C- 5	164.0
C- 9	188.0
C- 8	202.0



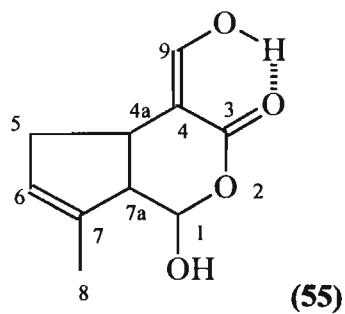
(53) ^{13}C NMR in $CDCl_3$



$C_{10}H_{12}O_4$ MW 196

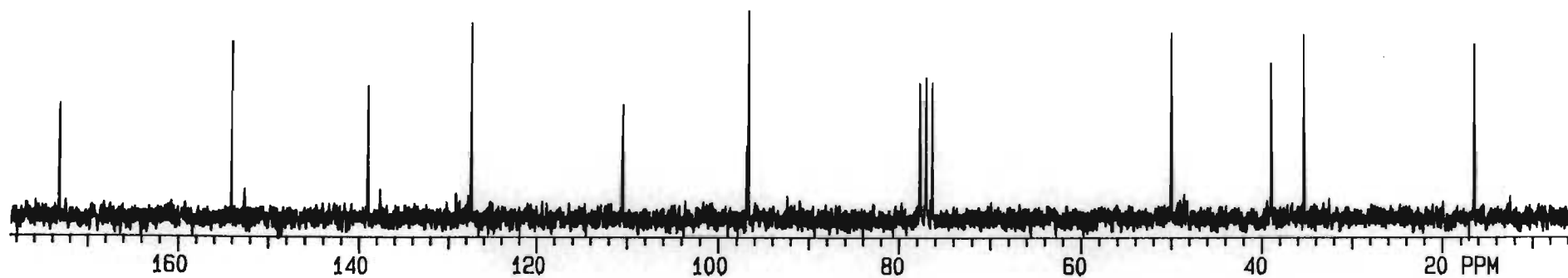


(55) 1H NMR in $CDCl_3$

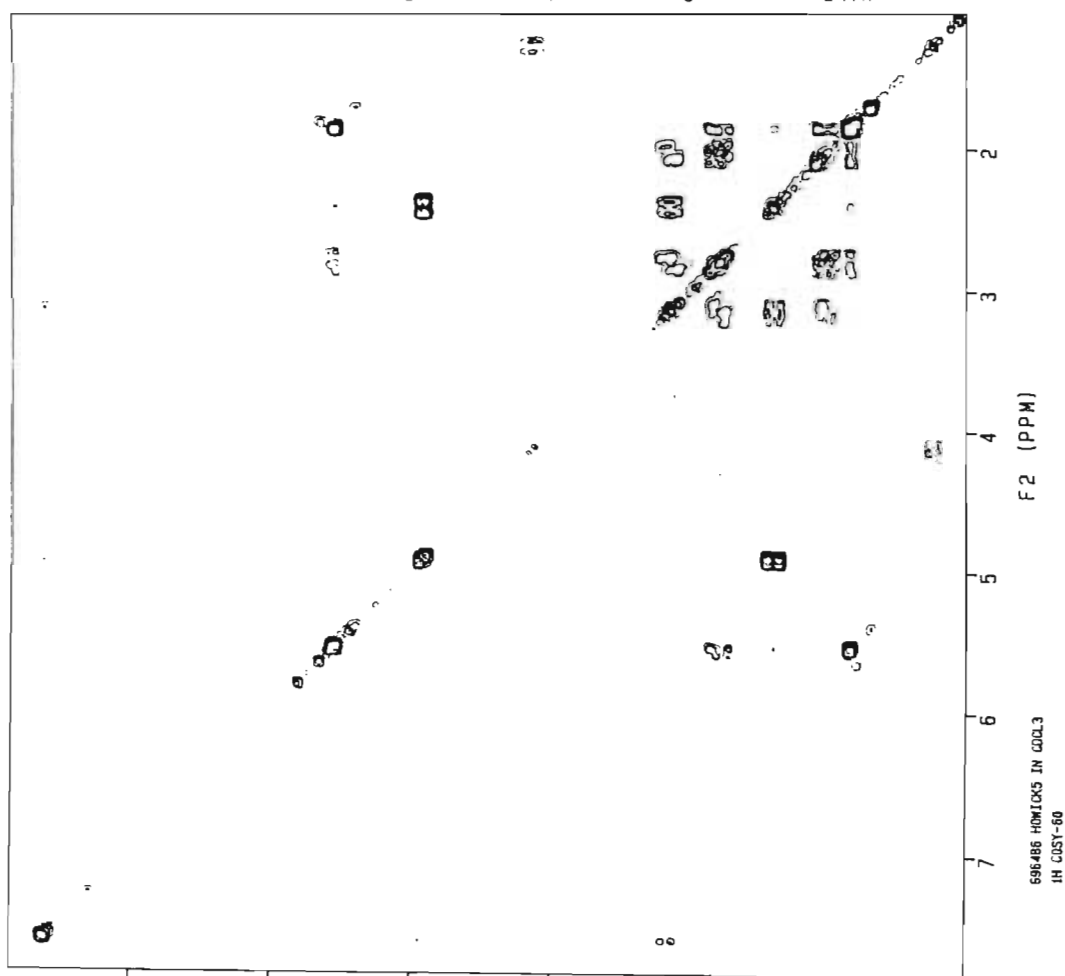
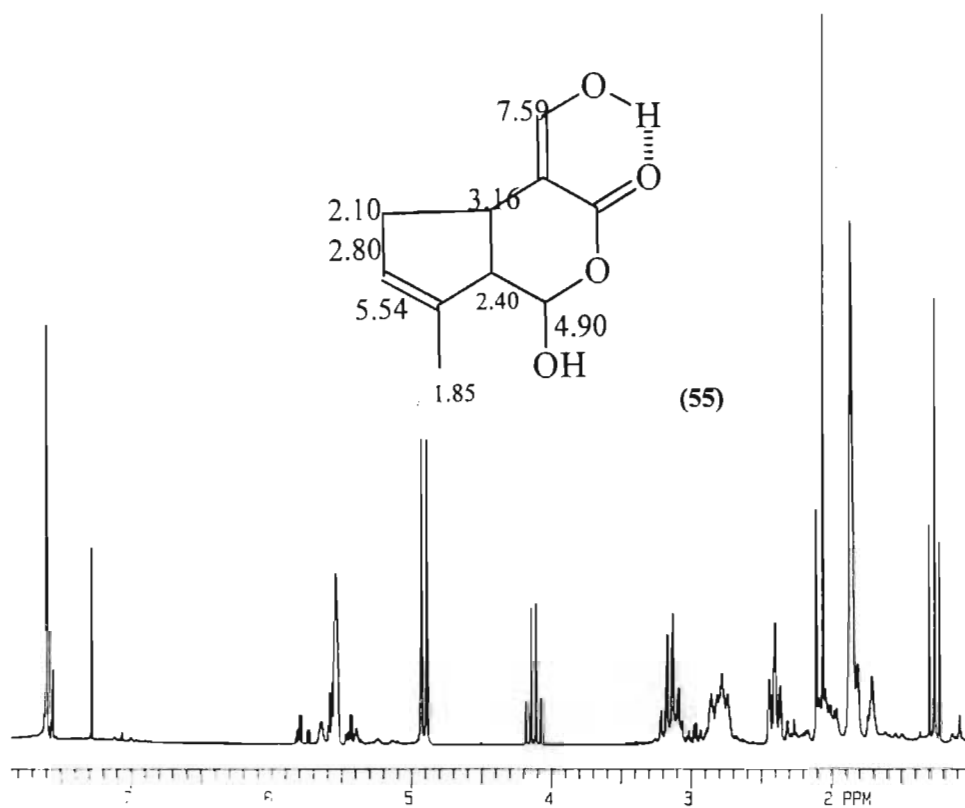


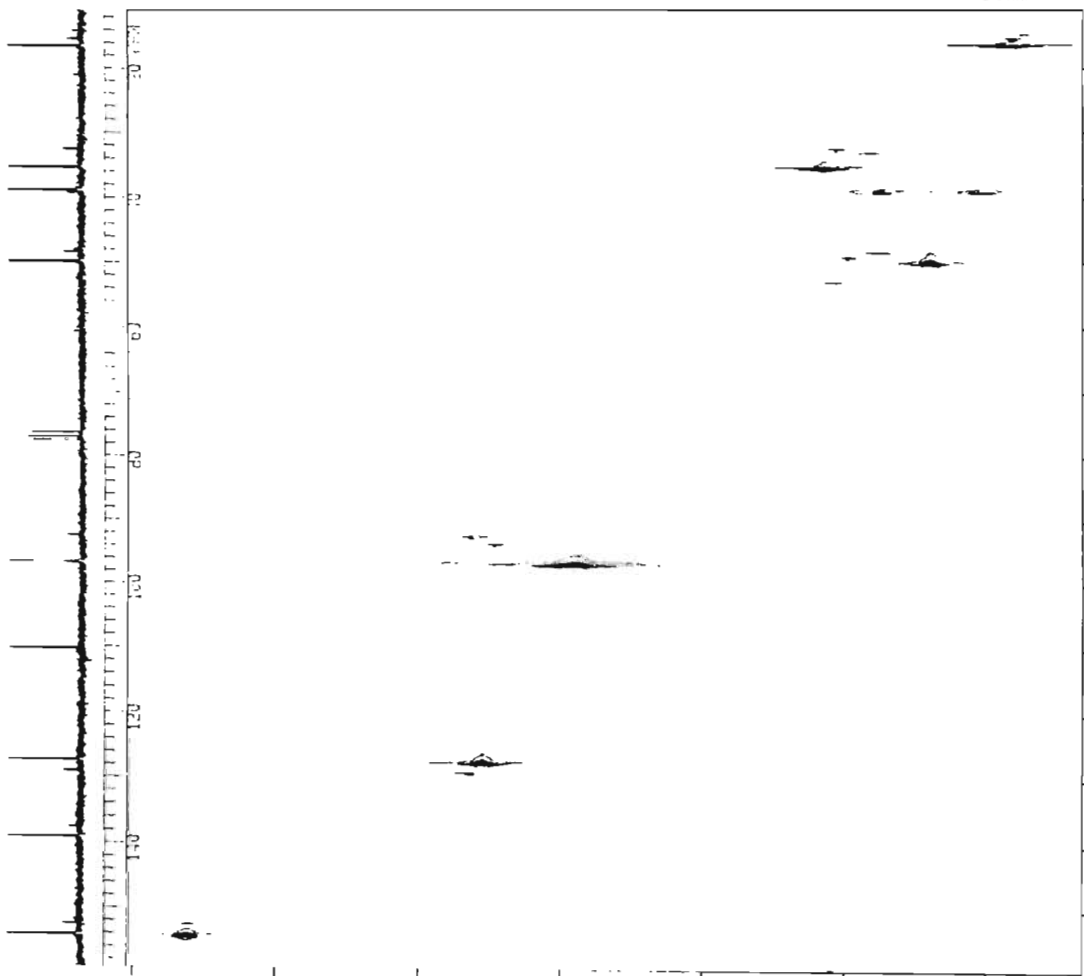
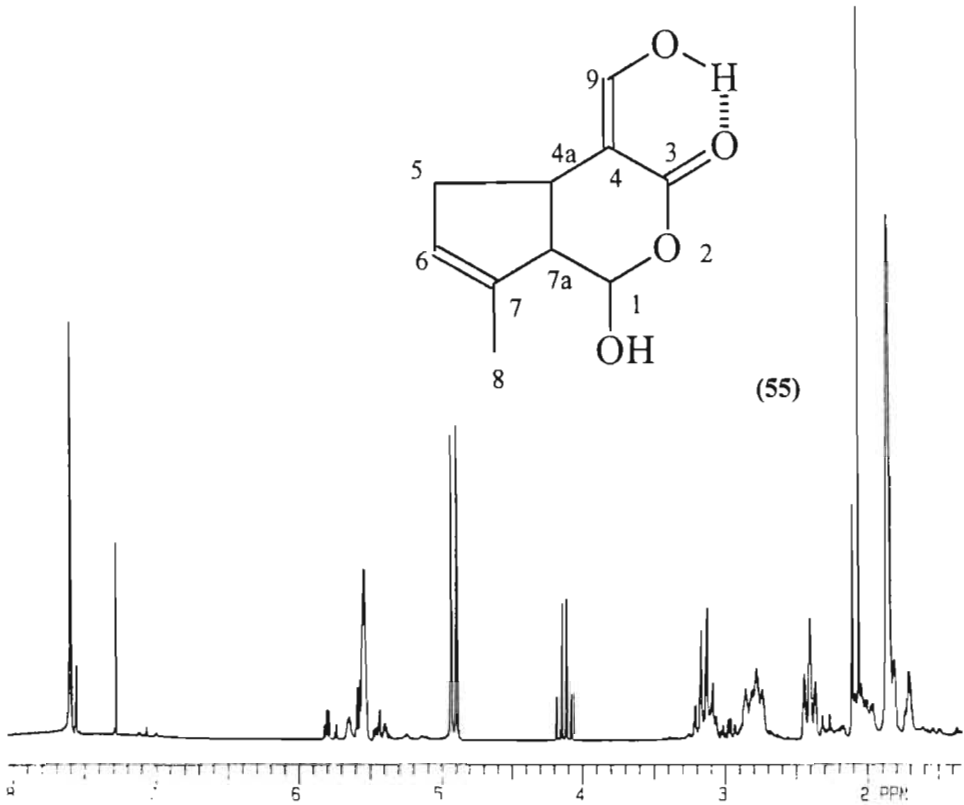
$C_{10}H_{12}O_4$ MW 196

carbon	δ
Me	16.5
C- 4a	35.4
C- 5	38.9
C- 7a	49.9
C- 1	96.8
C- 4	110.5
C- 6	127.5
C- 7	139.1
C- 9	154.1
C- 3	173.2

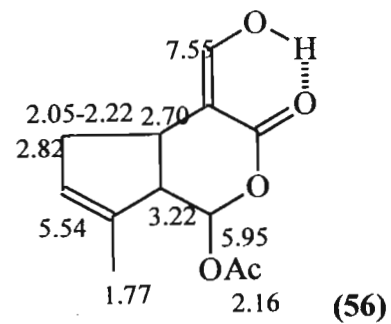


(55) ^{13}C NMR in $CDCl_3$

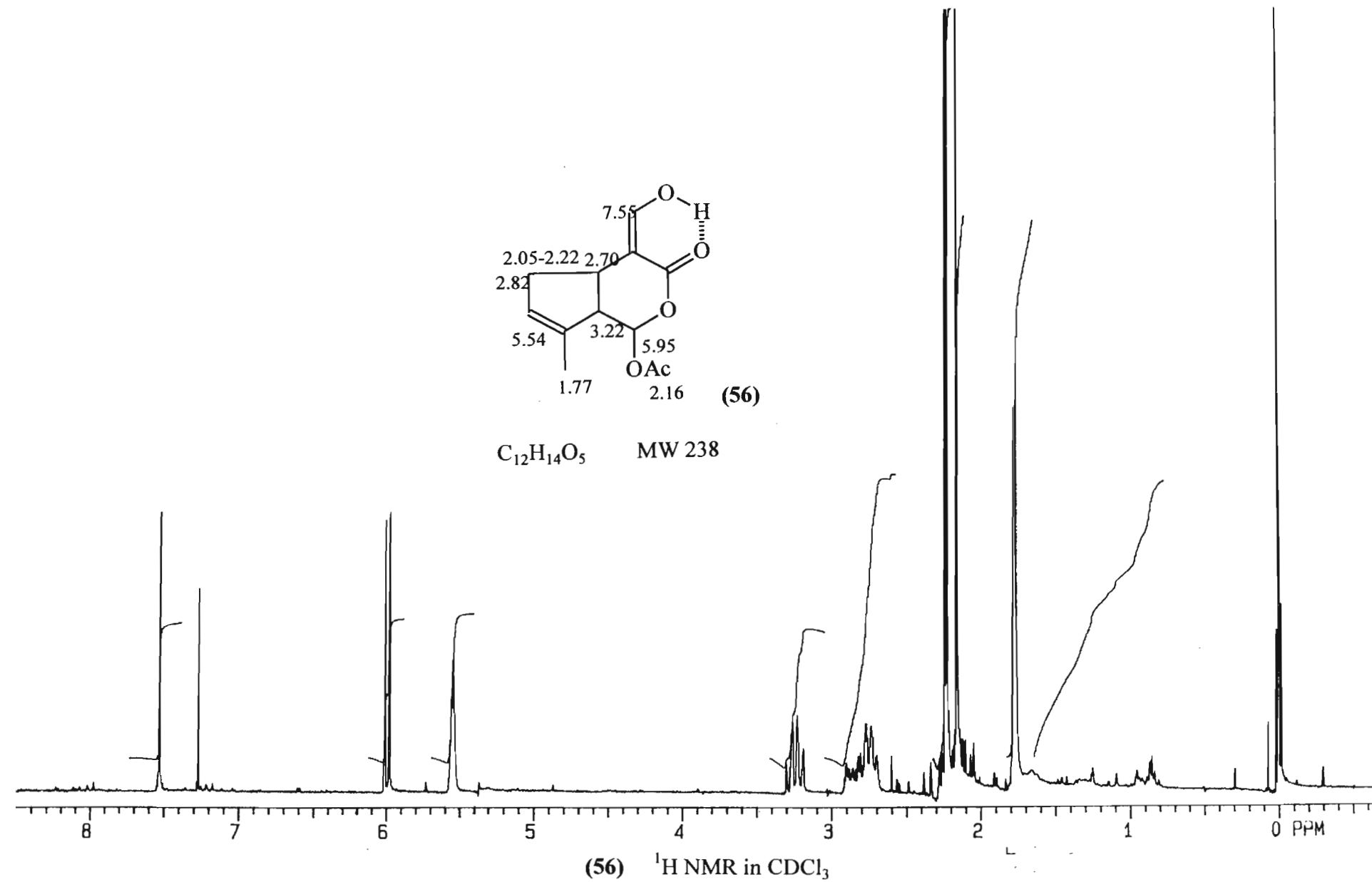
(55) COSY in CDCl₃

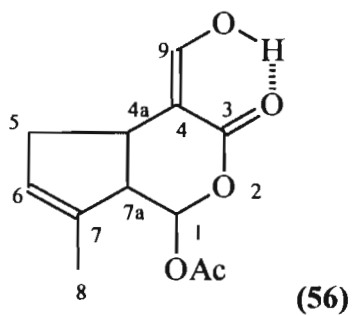


(55) HETCOR in CDCl₃



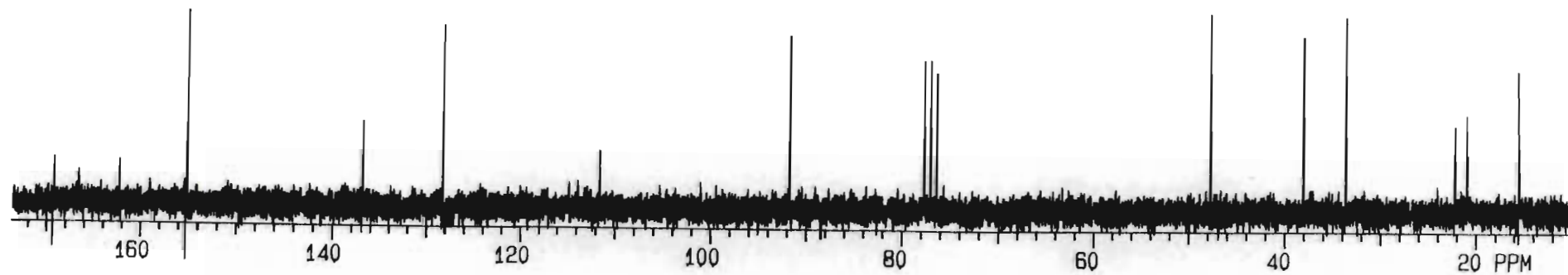
C₁₂H₁₄O₅ MW 238



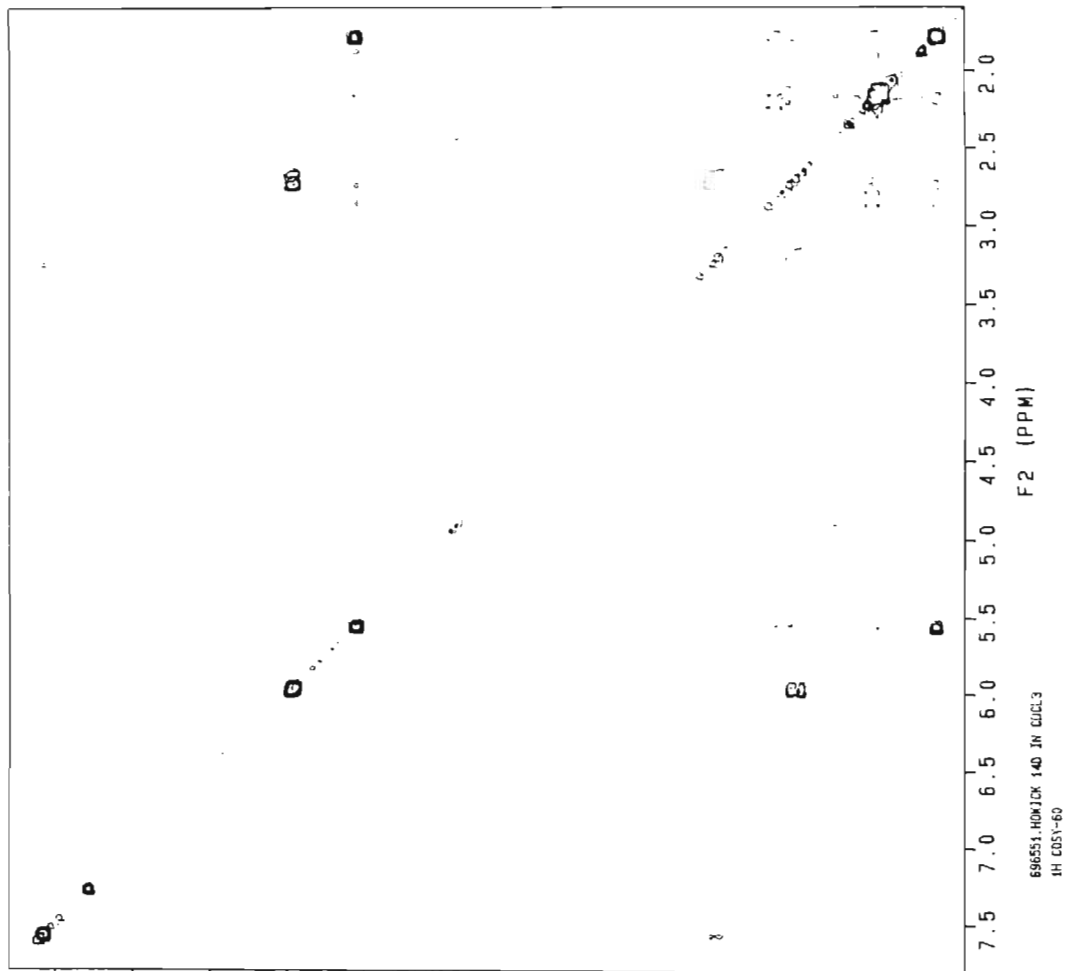
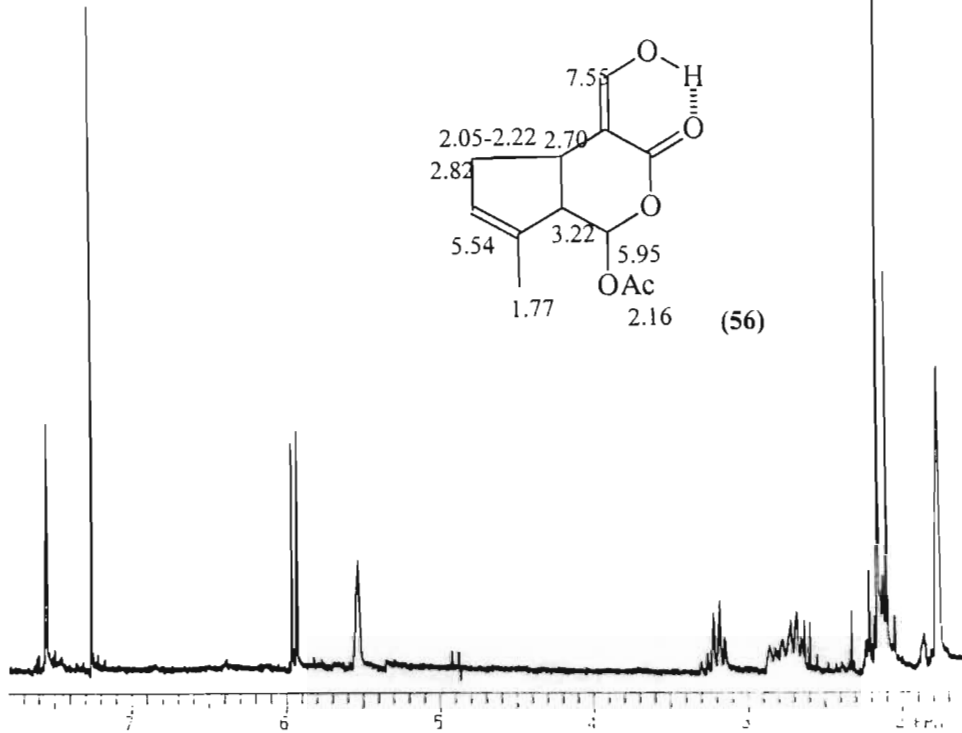


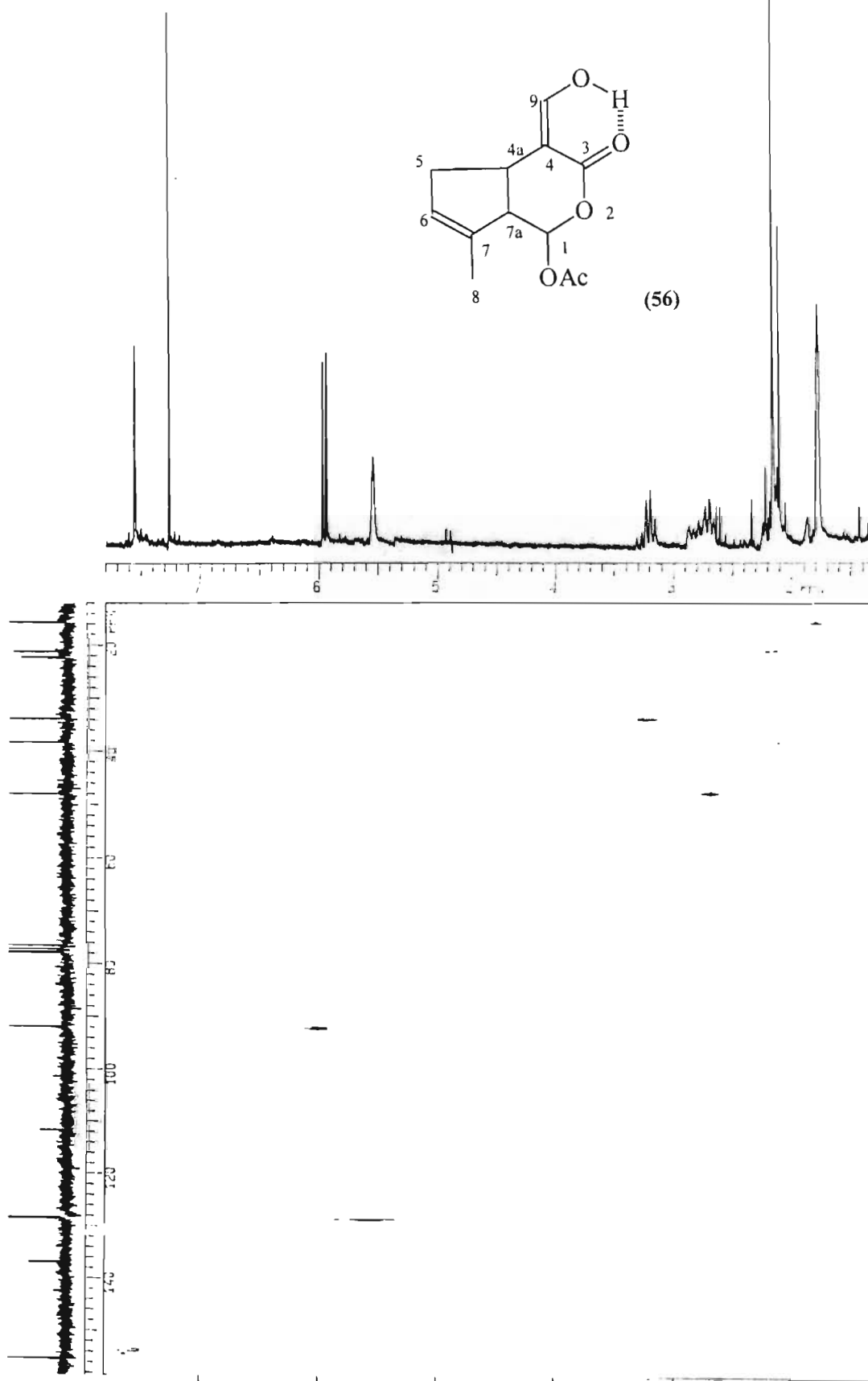
$C_{12}H_{14}O_5$ MW 238

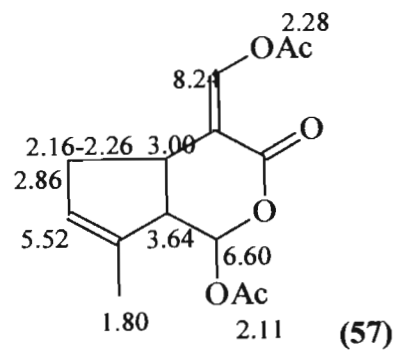
carbon	δ	carbon	δ
C- 8	15.7	C- 4	111.0
OAc	21.0	C- 6	128.3
C- 7a	33.9	C- 7	127.1
C- 5	38.5	C- 9	153.6
C- 4a	47.8	OAc	169.5
C- 1	91.9	C- 3	172.6



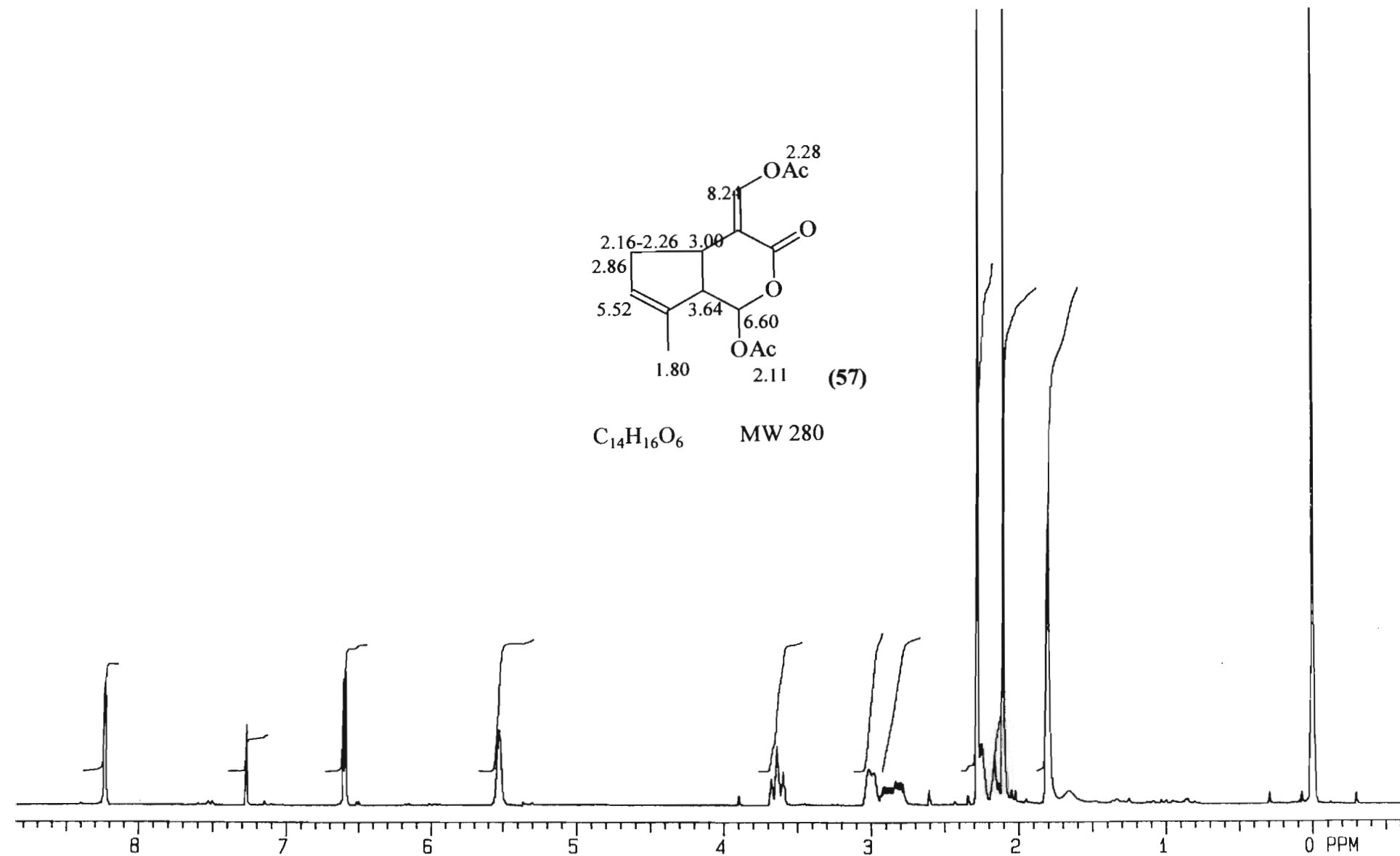
(56) ^{13}C NMR in $CDCl_3$

(56) COSY in CDCl₃

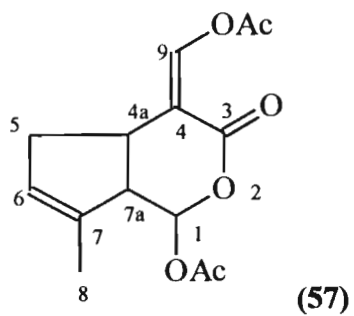
(56) HETCOR in CDCl₃



$C_{14}H_{16}O_6$ MW 280

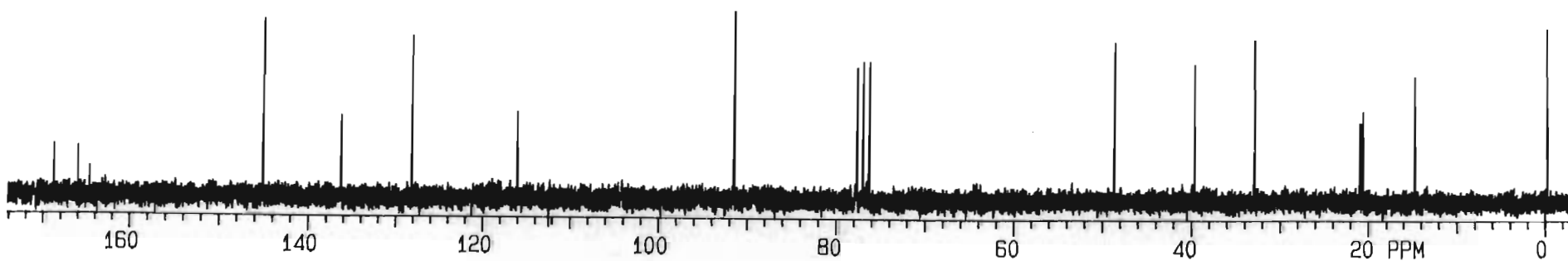


(57) 1H NMR in $CDCl_3$

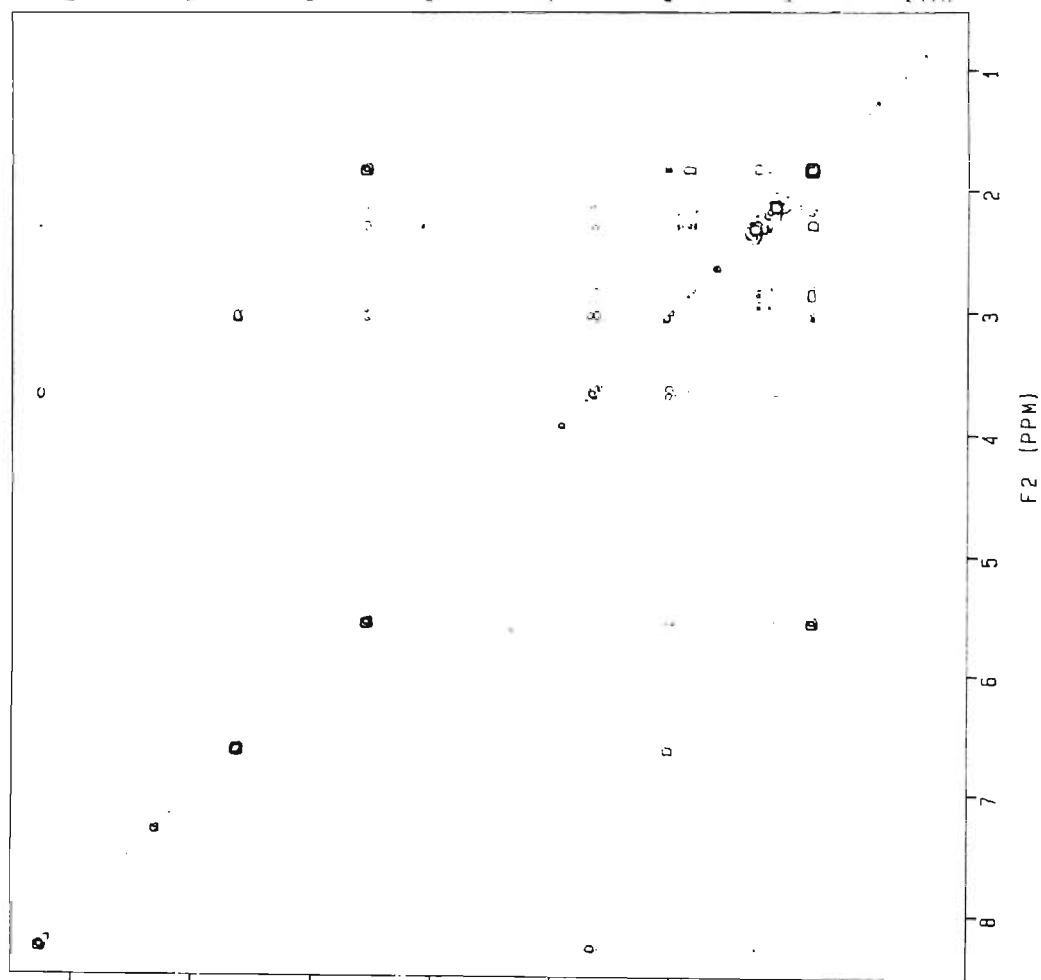
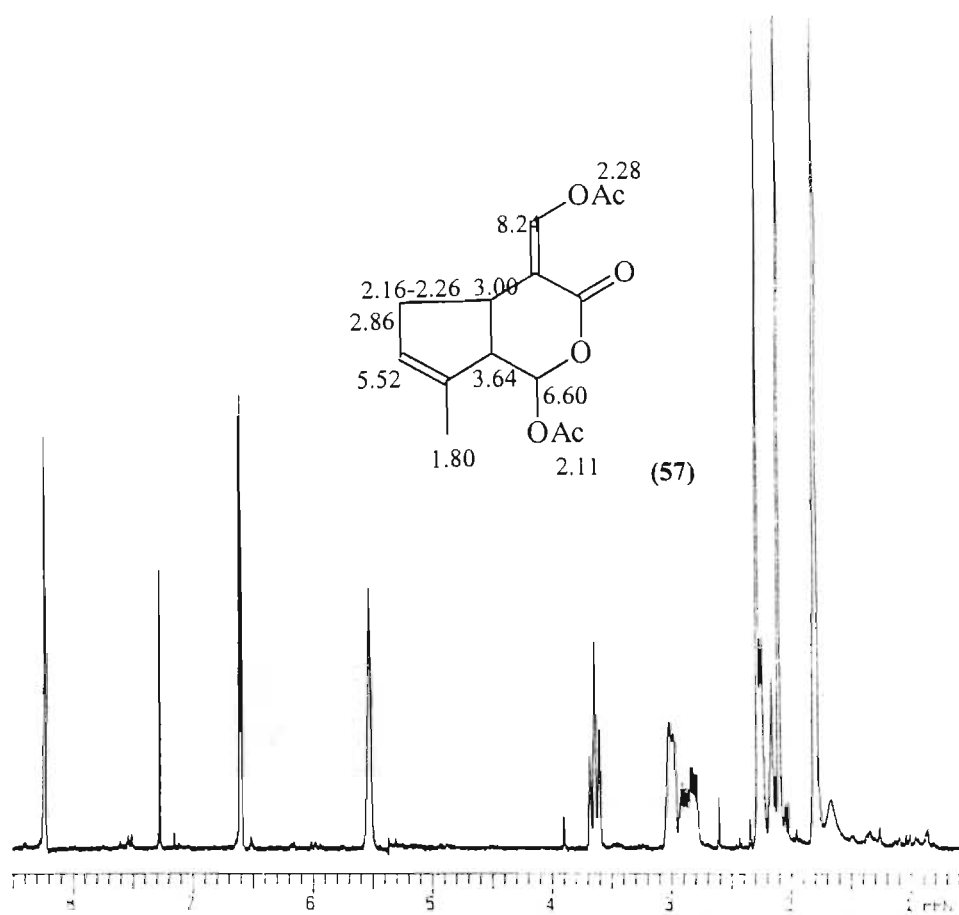


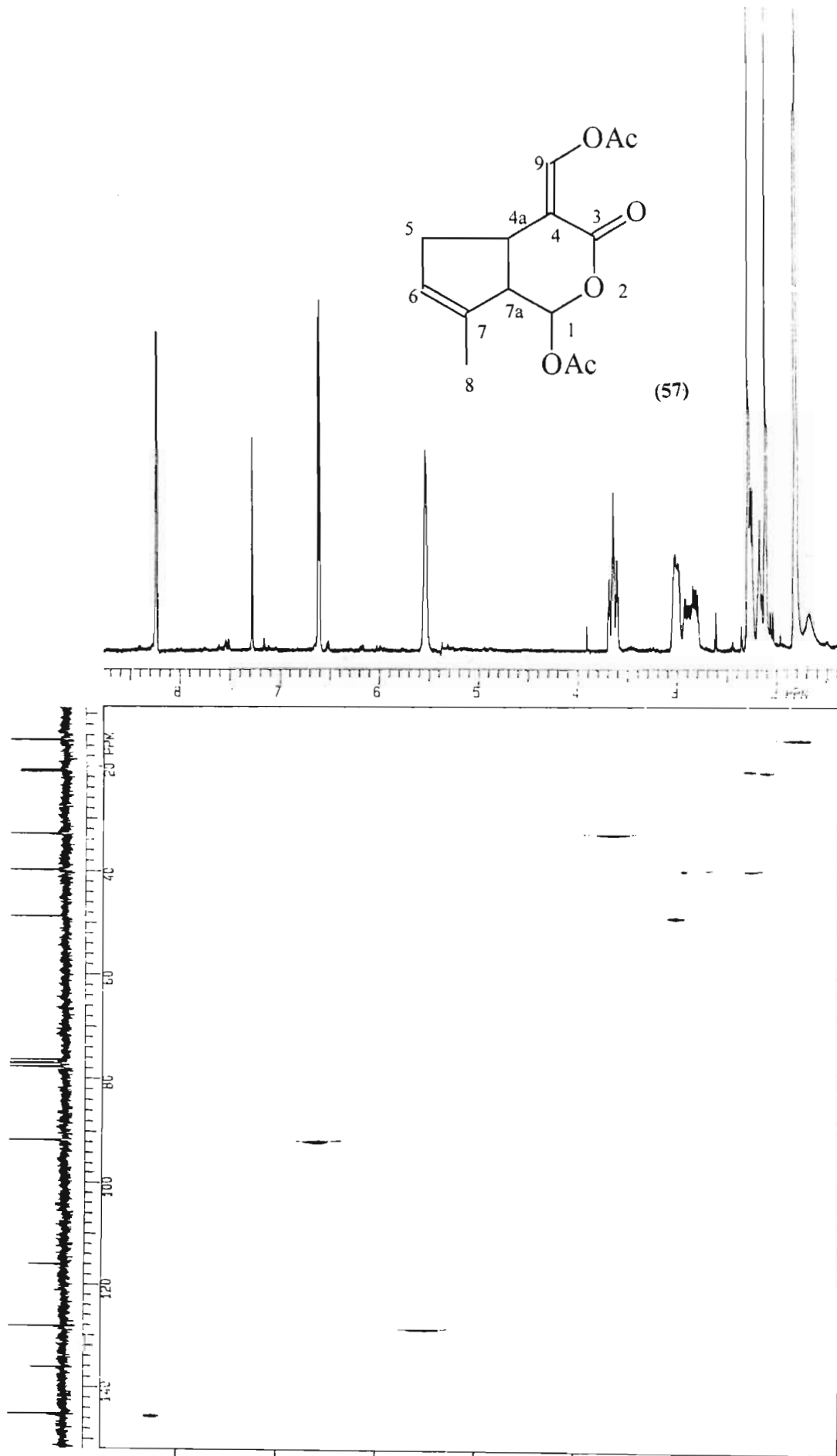
$C_{14}H_{16}O_6$ MW 280

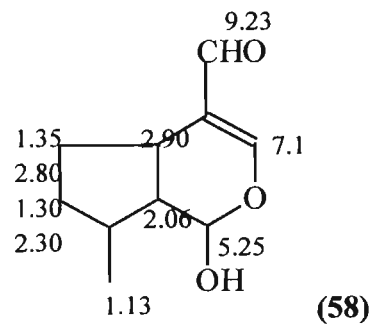
carbon	δ	carbon	δ
C- 8	14.8	C- 4	116.0
OAc	20.6	C- 6	128.3
OAc	20.9	C- 7	136.3
C- 4a	32.9	C- 9	145.2
C- 5	39.7	OAc	166.1
C- 7a	48.7	OAc	166.1
C- 1	91.6	C- 3	168.7



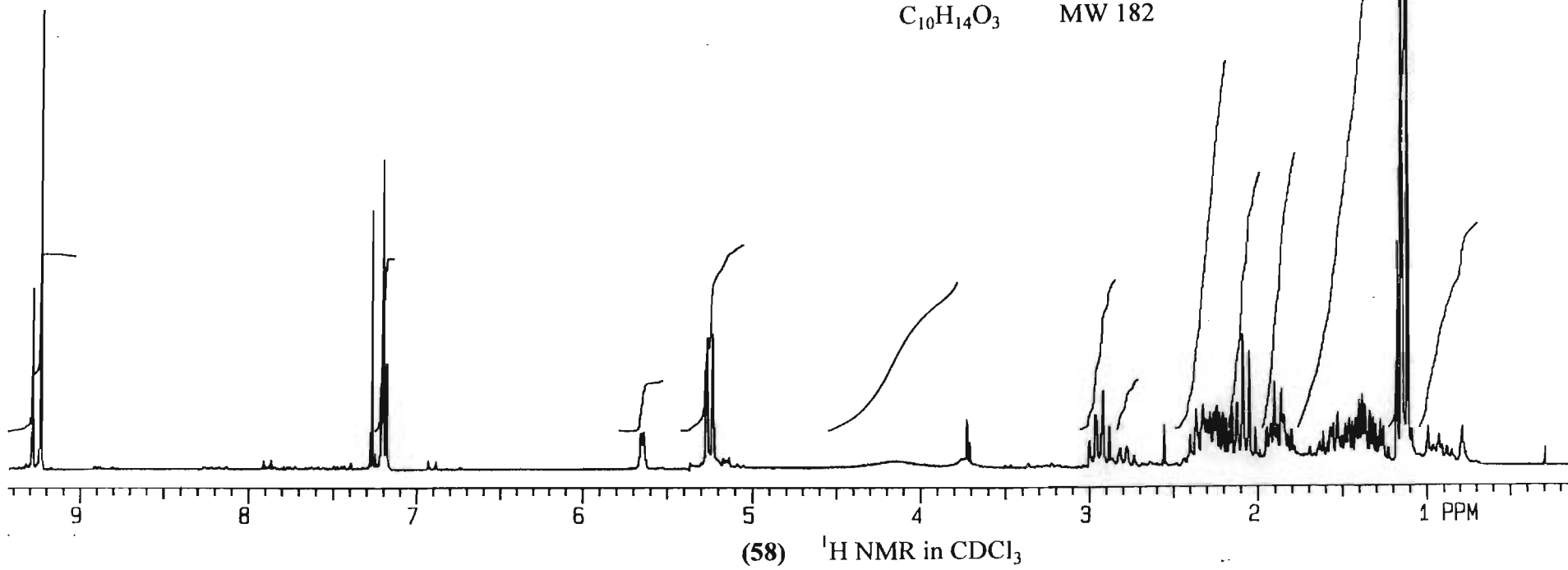
(57) ^{13}C NMR in $CDCl_3$

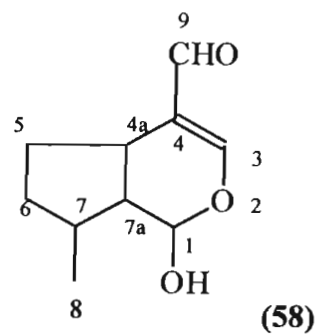
(57) COSY in CDCl₃

(57) HETCOR in CDCl_3



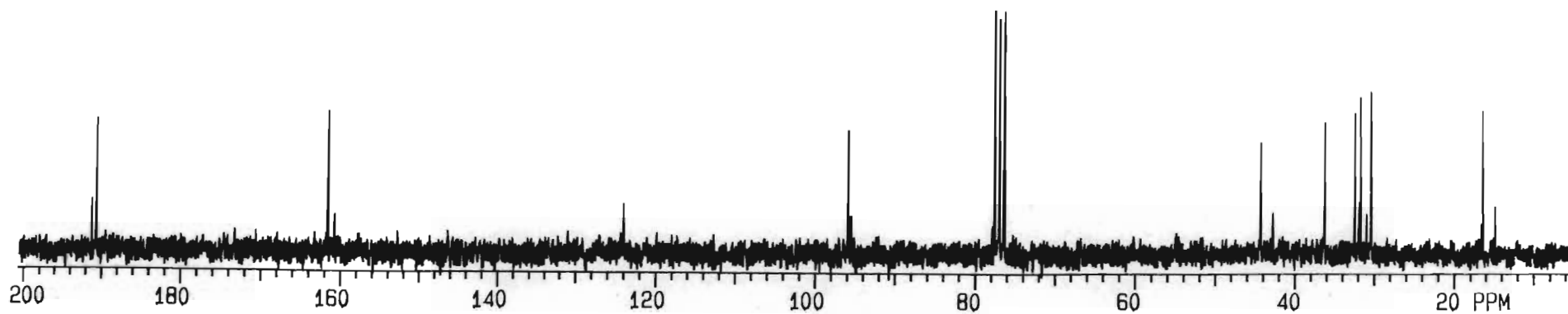
$C_{10}H_{14}O_3$ MW 182



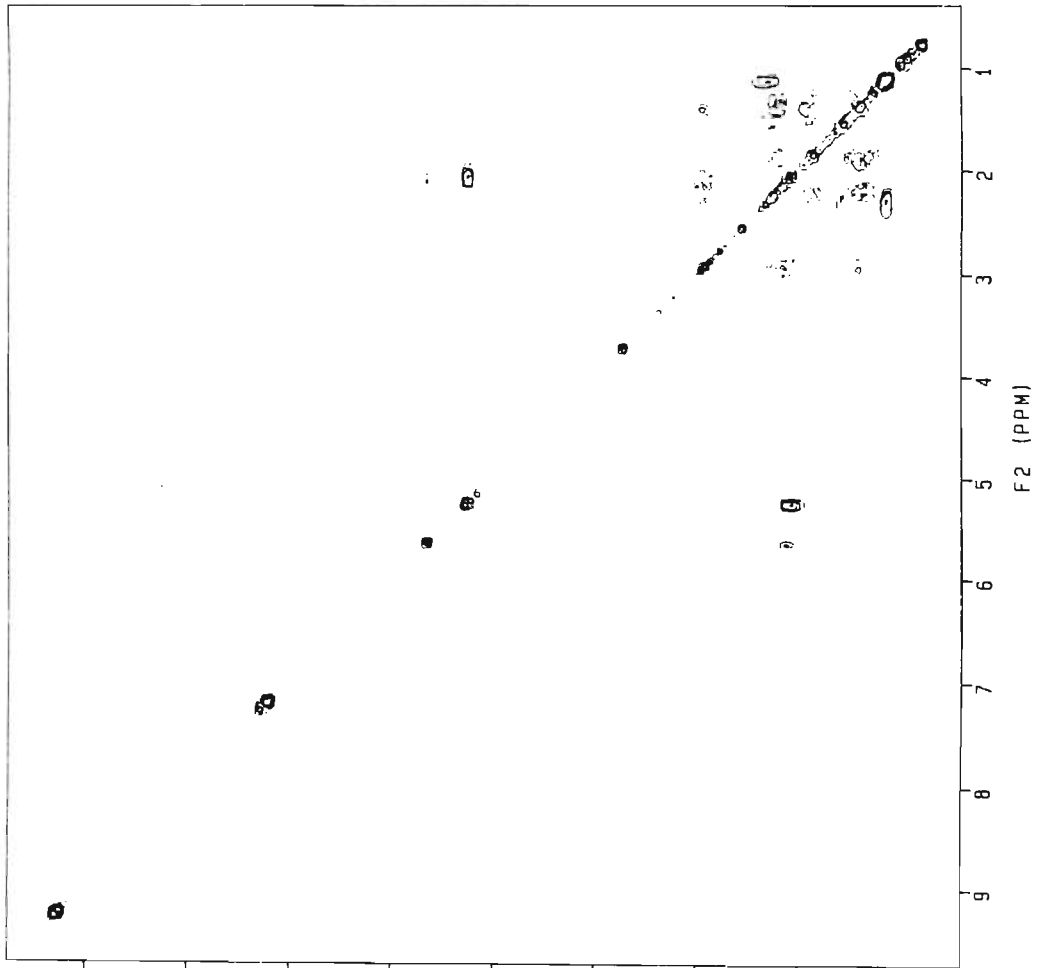
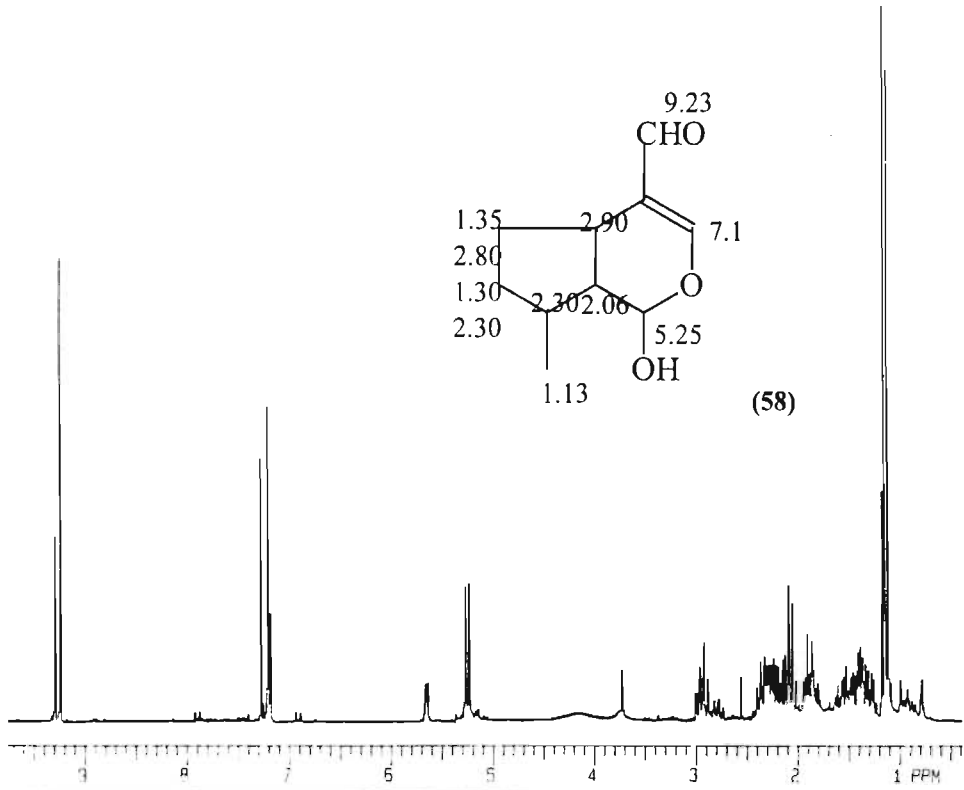


$C_{10}H_{14}O_3$ MW 182

carbon	δ
Me	16.4
C- 5	30.4
C- 6	31.7
C- 4a	32.5
C- 7	36.4
C- 7a	44.4
C- 1	95.9
C- 4	127.4
C- 3	161.7
C- 9	190.7

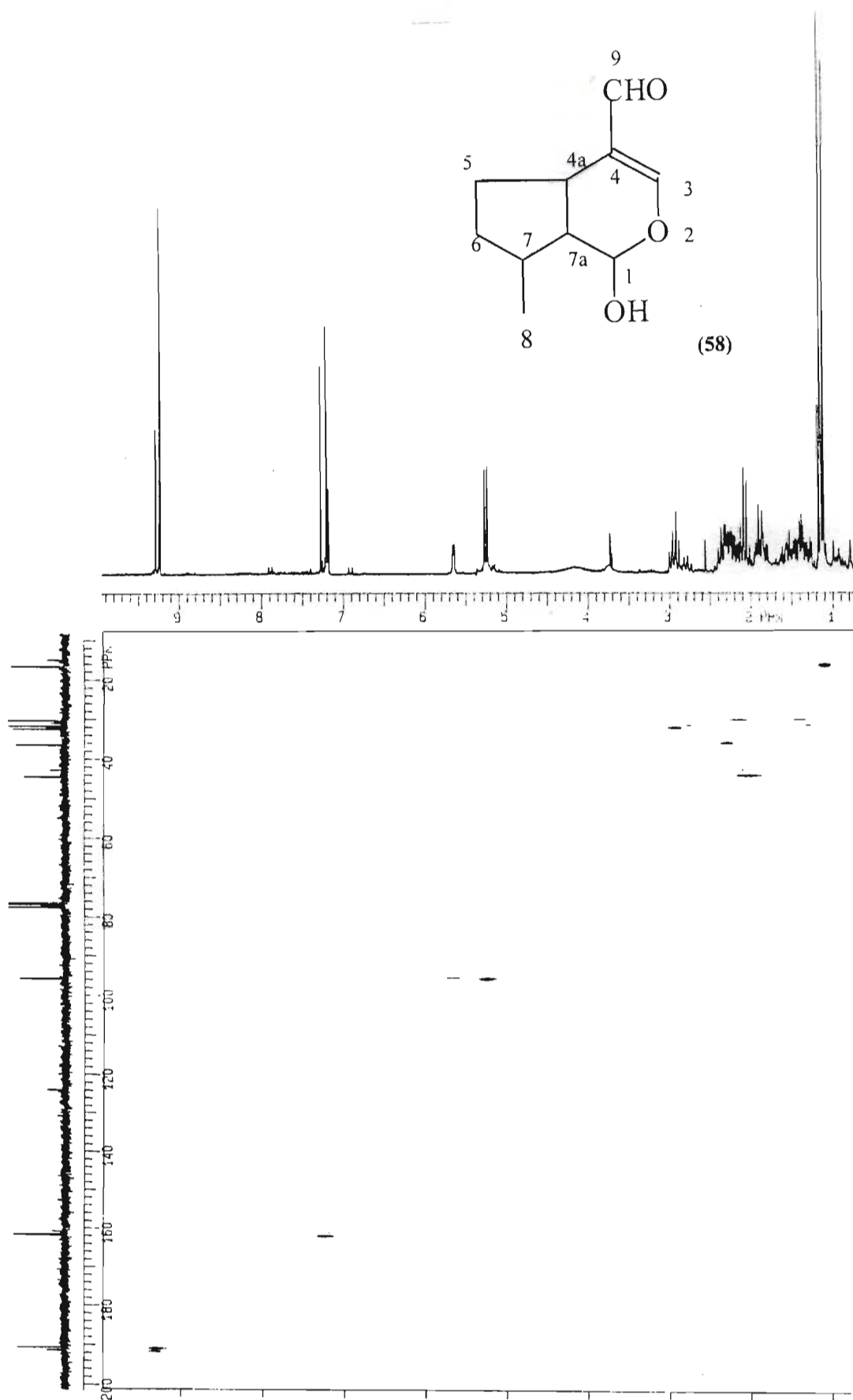


(58) ^{13}C NMR in $CDCl_3$



(58)

COSY in CDCl₃



(58)

HETCOR in CDCl₃