INVESTIGATIONS IN DIENAMINE CHEMISTRY

by

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(B.Sc.Hons.)

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Durban 1991

TO MY FAMILY, JOHN AND MEG SANDFORD

AND MY FIANCÉE JANINE

DECLARATION

The experimental work described in this thesis was carried out in the Department of Chemistry, University of Natal, Durban under the supervision of Prof. P. W. Hickmott.

These studies represent original work by the author and have not been submitted in any other form to another University. Where use was made of the work of others it has been duly acknowledged in the text.

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I hereby certify that the above statement is correct.

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ABSTRACT

Reaction of the pyrrolidine dienamines of $\Delta^{1,8a}$-2-octalones with methyl vinyl ketone is complex. In methanol as solvent, the reaction occurs primarily with the linear dienamine isomer and results in annulation of the 8,8a-positions and, to a lesser extent, the 1,2-positions to give the corresponding octahydro-1*H*-benzo[d]naphthalene-2,10(3*H*,11*H*)-dione and 3,4,5,6,7,8,8a,9-octahydrophenanthren-2(10*H*)-one respectively. In toluene the dienamines react mainly in their cross-conjugated form. Diels-Alder addition of methyl vinyl ketone occurs across the 3,8a-positions to give the corresponding 9-acetylperhydro-2,4a-ethanonaphthalen-3-one and annulation of the 2,3-positions gives the 4,4a,5,5a,6,7,8,9-octahydroanthracen-2(3*H*)-one.

The reaction of methyl vinyl ketone with the pyrrolidine dienamine of 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone is reported to give the aromatic product 3a,7-dimethyl-2,3,3a,4,5,6-hexahydrophenalen-3,6-dionearisingfromβ,δ-annulation and in a related investigation with dienamines derived from isophorone it was reported that only products of Stork alkylation and Diels-Alder cycloaddition were isolated, there being no evidence for the reaction of methyl vinyl ketone with either the endo- or exocyclic δ-positions of the dienamines.

In an attempt to ascertain the reason for the apparently random changes in the regioselectivity of these related reactions some of this work was repeated and the reaction of methyl vinyl ketone applied to two other dienamines derived from 5,6,7,7a-tetrahydroindan-5-one and 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone.

The reactions proved to be more complex than reported and several additional products have been isolated.

Finally, reaction of phenyl vinyl ketone with dienamines derived from $\Delta^{1,8a}$-2-octalone was investigated. With the exception of the reaction of the 4a-methyl dienamine, the main products isolated were those arising from addition of phenyl vinyl ketone across the 3,8a-position to give the corresponding 9-benzoylperhydro-2,4a-ethanonaphthalen-3-one. Reaction of the 4a-methyl dienamine with two equivalents of phenyl vinyl ketone gave a product tentatively assigned as the octahydrophenalenone.

The mechanism of formation and spectral properties of the various products are discussed.

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CHAPTER ONE

1. INTRODUCTION

1.1 FOREWORD

Since the first reports on enamine reactivity by Collie in 1883,[1] the field of enamine chemistry has progressed enormously. However it was not until the pioneering work of Gilbert Stork[2,3,4] and co-workers that the full synthetic potential of enamines was realised and their contributions to this field undoubtedly initiated the explosive development which subsequently occurred.

The Stork reaction,[5] as it became known, initially referred to the conversion of an aldehyde or ketone into a C-alkylated or C-acylated derivative *via* an enamine intermediate, but this definition was later extended by Hickmott[6] to include the "conversion of an aldehyde or ketone into a C-alkylated, C-acylated, carbocylic or heterocyclic derivative by reaction of an electrophile with an enamine intermediate". This extended definition indicates the scope of the reaction and it is not surprising that work in the field of enamine chemistry has become the subject of extensive publication. The chemistry of dienamines (enamines further conjugated with an additional carbon-carbon double bond) has in contrast received much less attention. One of the earliest preparations of a dienamine, reported in 1946, was by Bowden *et al.*[7] They

prepared 1-diethylaminobutadiene from crotonaldehyde and diethylamine, at -10°C in the presence of anhydrous potassium carbonate. Much of the initial interest in the field of dienamine chemistry however, focused on the preparation and reactivity of dienamines derived from 3-oxo-Δ^4-steroids and closely related compounds.[8,9,10]

Like simple enamines, the reactions of dienamines are often critically dependent on the experimental conditions employed, the course of the reaction being influenced by factors such as changes in solvent, amine moiety, temperature and catalysts to name but a few. The stereoselectivity and regioselectivity of dienamine reactions may also be altered by changes in experimental conditions leading to a diversity of products. During the course of this investigation into the chemistry of dienamines several interesting and unusual observations have been made. To place these recent developments in perspective it is necessary to consider certain aspects of dienamine chemistry in general.

1.2 PREPARATION OF DIENAMINES

The usual method of preparing dienamines is analogous to that commonly utilised for the preparation of simple enamines.[8,11] Thus α,β- or β,γ-unsaturated aldehydes or ketones undergo condensation with secondary amines in the presence of toluene-4-sulphonic acid, the reaction of α,β-unsaturated ketones generally being observed to be slower than the corresponding reaction of saturated ketones. The catalytic role of toluene-4-

sulphonic acid has been reported previously by Maas *et al.*[12] and by Marchese.[13] Secondary amines commonly employed are cyclic amines such as pyrrolidine, morpholine and piperidine. As noted for simple enamines, the rate of reaction depends on the ketone and amine employed, the more reactive pyrrolidine requiring a shorter reaction time (≈ 24 h.) compared to morpholine which requires between 1 and 6 days.

The yields obtained by azeotropic removal of the water formed, using a Dean and Stark head and benzene or toluene as the solvent, are in most cases satisfactory. Improved yields are however, usually obtained when, as demonstrated by Firrell,[14,15] the condensate is passed for an additional period over molecular sieves (4A). In reactions conducted on a small scale the water may be removed solely by the use of molecular sieves.

TABLE 1

Dienamine Preparations - Reaction Conditions and Yields

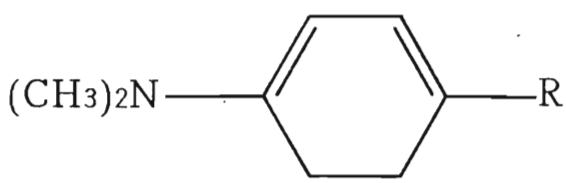
Ketone	2° Amine	Solvent	Reaction Time (h.)			Yield (%)
			Dean & Stark	Mol. Sieve	Total	
$\Delta^{1,8a}$-2-octalone	M	Toluene	40	16	56	90
$\Delta^{1,8a}$-2-octalone	P	Benzene	6	16	22	89
3-Me-$\Delta^{1,8a}$-2-octalone	M	Toluene	48	72	120	58
3-Me-$\Delta^{1,8a}$-2-octalone	P	Toluene	18	4	22	78
8-Me-$\Delta^{1,8a}$-2-octalone	M	Toluene	72	72	144	89
8-Me-$\Delta^{1,8a}$-2-octalone	P	Toluene	19	6	25	89
4a-Me-$\Delta^{1,8a}$-2-octalone	M	Toluene	20	-	20	77
4a-Me-$\Delta^{1,8a}$-2-octalone	P	Toluene	-	18	18	80

M = Morpholine P = Pyrrolidine

The reaction conditions and yields of dienamines derived from $\Delta^{1,8a}$-2-octalones as reported by Firrell are summarised in Table 1.

The preparation of dienamines of certain 3-oxo-Δ^4-steroids without the use of dehydrating conditions has also been reported.[9] The secondary amine was simply added to a hot solution of the steroid in methanol. Using this method, Firrell prepared the dienamine of cholest-4-en-3-one.[15]

Alternatively cyclic dienamines [1(a) and 1(b)] may be prepared by the Birch reaction by reduction of the corresponding aromatic tertiary amine with sodium in liquid ammonia.[16]

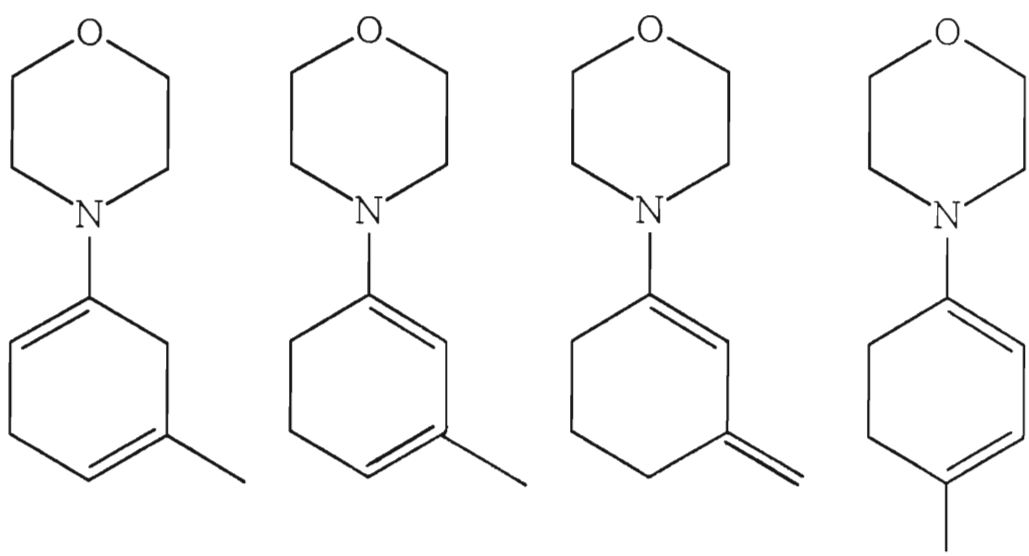


(a) R = H

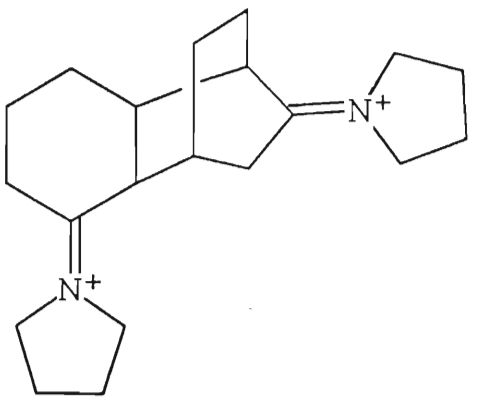
(b) R = CH_3

(1)

Similarly, the conjugated and non-conjugated dienamines (2 - 5) have also been prepared but using lithium and *t*-pentyl alcohol in liquid ammonia to carry out the reduction.[17,18]



The dienamines of isophorone are readily prepared[19] but dienamines derived from cyclohexenone cannot be isolated owing to preferential dimerisation to the tricyclic iminium salt (6) which gives (7) on hydrolysis.[20]



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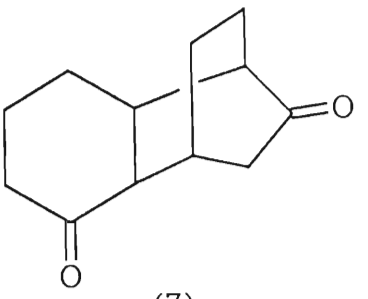
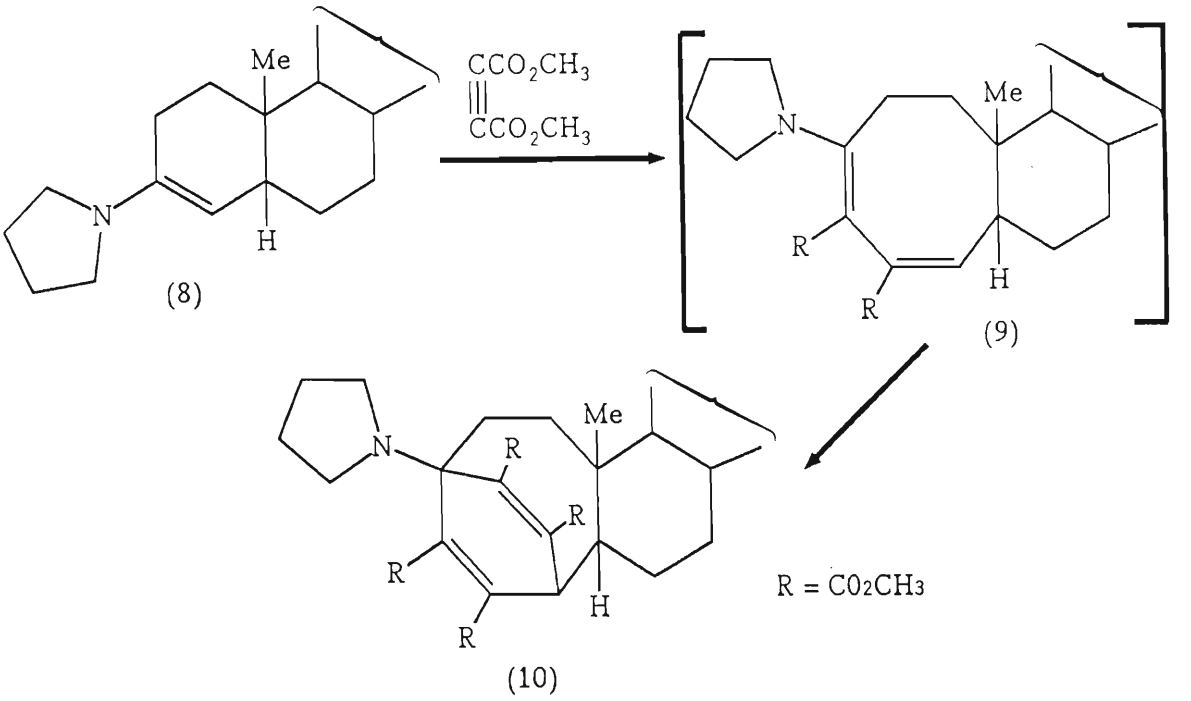


(7)

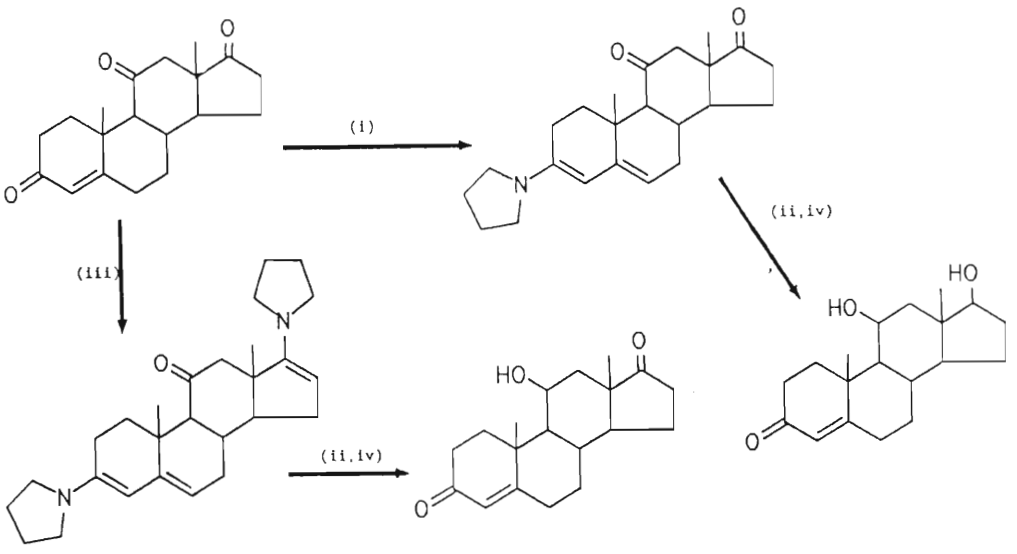
Dienamines have also been prepared by the reaction of enamines derived from cyclic ketones with acetylene esters.[21] The reaction proceeds *via* a thermally unstable cycloaddition product followed by ring enlargement to give a product containing two more carbon atoms than the starting enamine. The ring size of the starting ketone may be varied from 5 to 13 carbon atoms, and esters such as acetylene dicarboxylate,[21a-21d] phenyl[21d] and methyl propiolate,[21e] and methyl tetrolate[21f] have been employed. Usually a linear-conjugated dienamine is formed, as in the reaction of the pyrrolidine enamine of coprostan-3-one (8) with acetylene dicarboxylate[21d] (Scheme 1). In this case the s-*cis* dienamine (9) undergoes a Diels-Alder reaction with a further molecule of acetylene dicarboxylate to give adduct (10).

SCHEME 1



Reference has already been made to the fact that much of the early interest in dienamine chemistry was related to dienamines derived from steroids. Herr and Heyl[9] noted that by careful selection of secondary amine and reaction conditions, reaction could be promoted at a particular carbonyl functional group in a molecule containing several of these groups. Once "enaminized" these carbonyl groups were protected thus allowing nucleophilic reactions to be carried out elsewhere in the molecule. Their classical example[9] is illustrated in Scheme 2.

SCHEME 2



Reagents: (i) pyrrolidine (one equiv.); (ii) $LiAlH_4$; (iii) pyrrolidine (excess); (iv) hydrolysis.

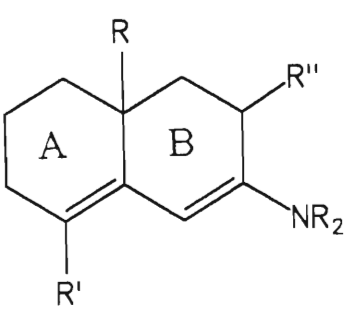
Other methods of dienamine preparation include condensation of amide acetals with alkynyl alcohols,[22] base catalysed isomerisation of propargylic amines with potassium *t*-butoxide[23] and condensation of aliphatic aldehydes with Fischer's base.[24]

1.3 STRUCTURE AND REACTIVITY OF DIENAMINES

The multitude of products commonly obtained from the reaction of dienamines with various electrophilic reagents is manifested in the reactivity and structure of these compounds. Owing to the $p\pi$-overlap between the nitrogen lone pair of electrons and the π-electrons of the extended conjugated system,

dienamines are polydentate nucleophilic reagents and can consequently undergo reaction at the nitrogen, and the β- or δ-carbon atoms, in contrast to simple enamines which have only two nucleophilic centres available for reaction. Although N-alkylation, N-acylation and N-protonation does occur, the majority of electrophilic reagents cause substitution at the β-position[14,25-31] and, to a lesser extent, at the δ-postition.[32-36] This is reflected in Huckel Molecular Orbital calculations which show that the electron density is greater at the β-position than at the δ-position of the dienamine system.[32] Reaction at the β-position is thus favoured under conditions of kinetic control. Where initial reaction at the nitrogen and the β-carbon is reversible, or when the transition state is product-like in character, the operation of thermodynamic control may lead to preferential or even complete reaction at the δ-position. As mentioned earlier the prevailing reaction conditions, particularly the choice of solvent, often dictates the regioselectivity of the reaction.[32,33,37]

Depending on the conditions under which the dienamines are prepared, they may exist as either cross-conjugated, non-conjugated, or linear double bond isomers. Frequently, a mixture of isomers is obtained. This is in fact the case for dienamines derived from $\Delta^{1,8a}$-2-octalones. The mixture in this instance was shown by Firrell to consist mainly of the linear exocyclic diene (11) together with the linear endocyclic diene (12).[19]



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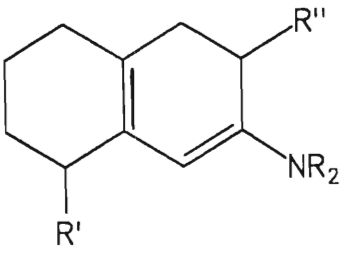
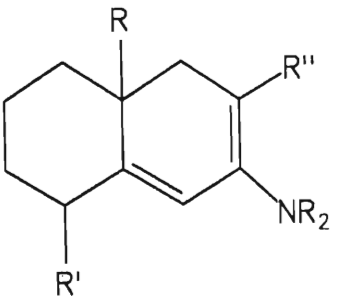


(12)

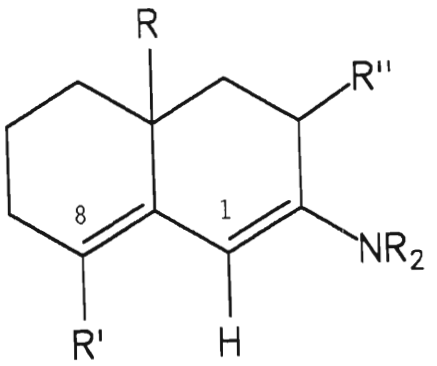


(13)

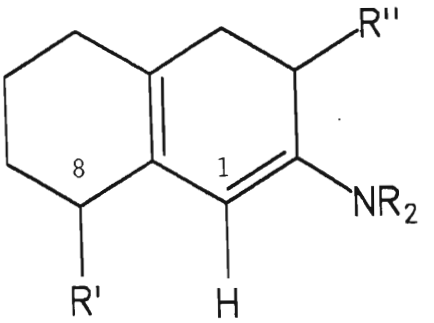
The presence of a methyl substituent (R'')[*a] at C-3 reduces the proportion of the diene (11) owing to 1,3-diaxial interactions but the proportion is increased by an 8-methyl substituent due to hyperconjugative stabilisation. A further factor which favours the exocyclic diene is the smaller deviation from coplanarity of the double bond system resulting in increased mesomeric stabilisation. Also of significance is the greater proportion of the *exo*-isomer when the dienamine is derived from pyrrolidine since orbital[39] interaction of the nitrogen lone pair would tend to enhance the mesomeric effect.

[*a]Quasi-axially oriented in order to reduce $A^{1,2}$-strain.[38]

TABLE 2



(11)



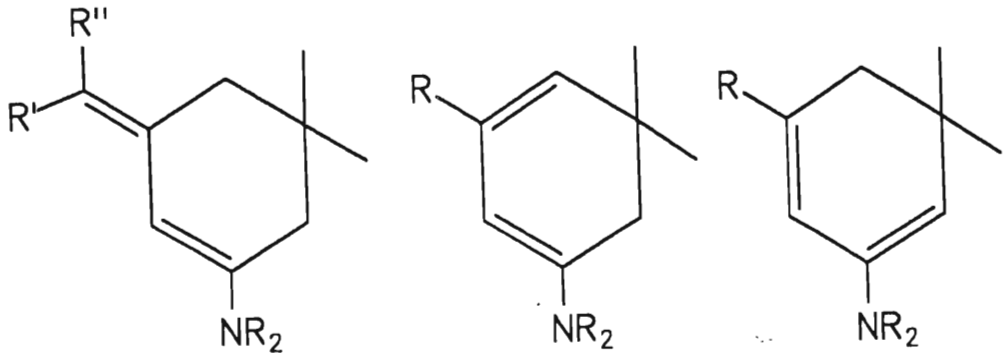
(12)

KETONE	AMINE	(11)			(12)	
		H_8	H_1	%	H_1	%
$\Delta^{1,8a}$-2-octalone (R,R',R"= H)	M	5,22	5,14	60	4,64	40
$\Delta^{1,8a}$-2-octalone (R,R',R"= H)	P	5,13	4,88	70	4,33	30
3-Me-$\Delta^{1,8a}$-2-octalone (R,R'=H;R"= Me)	M	5,28	5,17	45	4,68	55
3-Me-$\Delta^{1,8a}$-2-octalone (R,R'=H;R"= Me)	P	5,13	4,82	47	4,26	53
8-Me-$\Delta^{1,8a}$-2-octalone (R,R"=H;R'= Me)	M	-	5,48	85	4,83	15
8-Me-$\Delta^{1,8a}$-2-octalone (R,R"=H;R'= Me)	P	-	5,03	100		
4a-Me-$\Delta^{1,8a}$-2-octalone (R',R"=H;R'= Me)	M	5,24	5,16	100		
4a-Me-$\Delta^{1,8a}$-2-octalone (R',R"=H;R'= Me)	P	5,07	4,82	100		

Contrary to previous reports,[40,41] Firrell observed that none of the cross-conjugated diene (13) was present in the mixture and it was suggested that steric effects were responsible for this absence. The chemical shifts and

isomer distribution for the dienamines derived from $\Delta^{1,8a}$-2-octalones as reported by Firrell are shown in Table 2.

Similarly the pyrrolidine dienamine of isophorone was shown to exist mainly as the linear *exo*-isomer (14; 65%; R',R"= H) together with the linear *endo*-isomer (15; 35%; R = Me).[19]



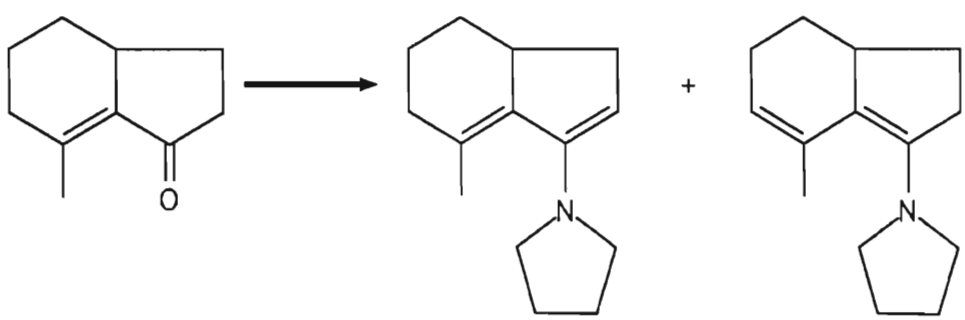
(14) (15) (16)

Only the linear *exo*-isomer (14) was formed when R = Et, *i*-Pr, $PhCH_2$ and only the linear *endo*-isomer (15) was formed when R = *t*-Bu.[42] For the dienamines derived from morpholine or piperidine it was shown that the main constituent of the mixtures was the linear *endo*-isomer (15; R = Me) with the *exo*-isomer (14) gradually increasing in proportion on prolonged standing and in some cases eventually exceeding the *endo*-isomer (15).[43] The cross-conjugated isomer (16) was only found to be present to the extent of 4 - 15 %[19,43] contradicting earlier reports by Nozaki *et al.* who proposed a 1:1 equilibrium mixture of the linear endocyclic and cross-conjugated isomers.[44]

Similar results were obtained with the N-methyl and N-phenyl piperazine dienamines of isophorone.[43,44] The corresponding dienamines derived from 3-methylcyclopent-2-enone however, were shown to exist mainly as the linear exo-isomer (90 %). This result would be expected owing to the greater stability of a double bond *exo* to a 5-membered ring.[43] It has also been shown that piperitone gives a mixture of the linear *exo*- and *endo*-pyrrolidine dienamines, non of the cross-conjugated isomers being observed.[45]

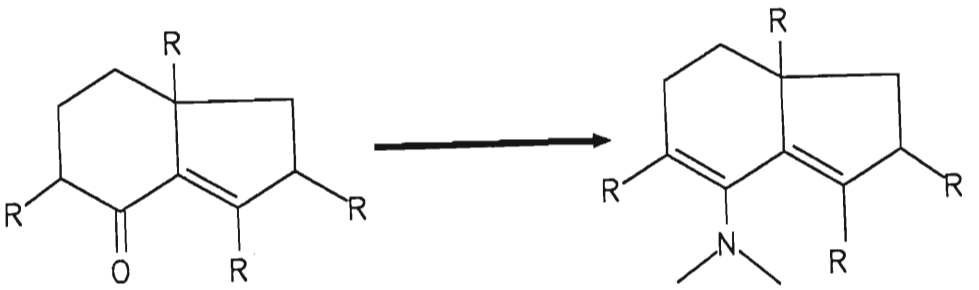
The fact that the cross-conjugated isomer is reported to be absent or only the minor component in the dienamine mixtures obtained from the condensation of $\Delta^{1,8a}$-2-octalones and isophorone with pyrrolidine and morpholine respectively is of particular interest in view of the experimental results obtained during the course of this investigation.

Although there is a preference for the formation of linear dienamines, the cross-conjugated dienamine is in some cases the major product. For example, when the α,β-unsaturated ketone is fixed in a cisoid arrangement of double bonds as in $\Delta^{4(9)}$-4-methylhydrinden-3-one (17), the cross-conjugated dienamine (18) is preferentially formed (80 - 90 %), depending on the reaction time. Only 10 - 20 % of the linear dienamine (19) is formed.[46]



(17) (18) (19)

In the case of $\Delta^{3(9)}$-hydrinden-4-ones (20) [R = H or Me] only the cross-conjugated dienamines (21) are formed.[47]



(20) (21)

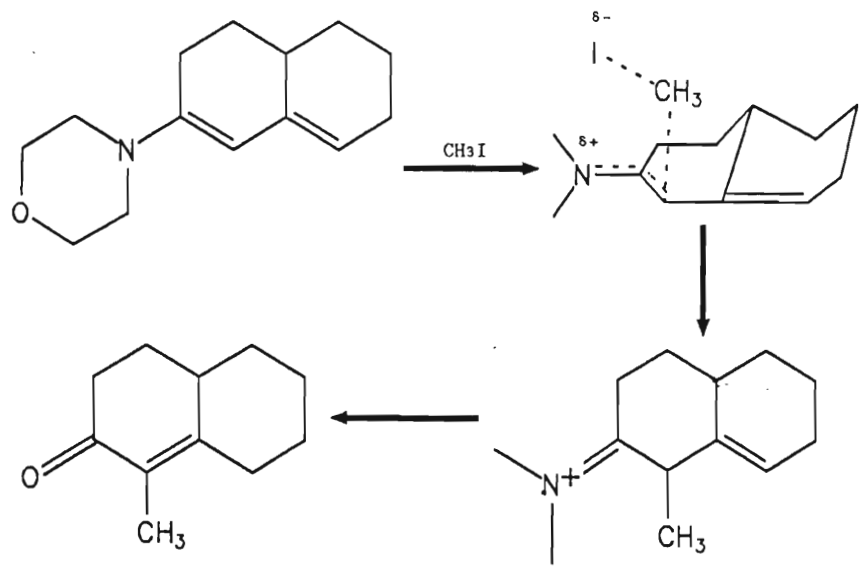
Despite the fact that the cross-conjugated isomer may appear to be absent from, or only the minor component of a dienamine mixture, in some cases the major product may be that derived from reaction of the cross-conjugated isomer. A few examples are discussed in Section 1.4.

1.4 REACTIONS OF DIENAMINES

Considering the properties of dienamines mentioned in section 1.3 it is not surprising that there is an abundance of examples of dienamines giving rise to products derived by reaction at the β-position. This is especially true in the case of the reaction of dienamines with alkylating agents.[25] Previous research in the early 60's showed that alkylation of dienamines derived from α,β-unsaturated ketones with methyl iodide,[26] ethyl α-bromoacetate[48] and 1,3-dichloro-2-butene[25g] resulted in preferential reaction at the β-position. In addition to the known fact that the electron density is higher at the β-position, Stork[26] also observed that there would be a lowering of the transition state

energy by release of the halide counter ion in close proximity to the developing positive charge of the intermediate iminium ion further promoting reaction at the β-position. The reaction of the morpholine dienamine of $\Delta^{1,8a}$-2-octalone with methyl iodide is illustrated in Scheme 3.

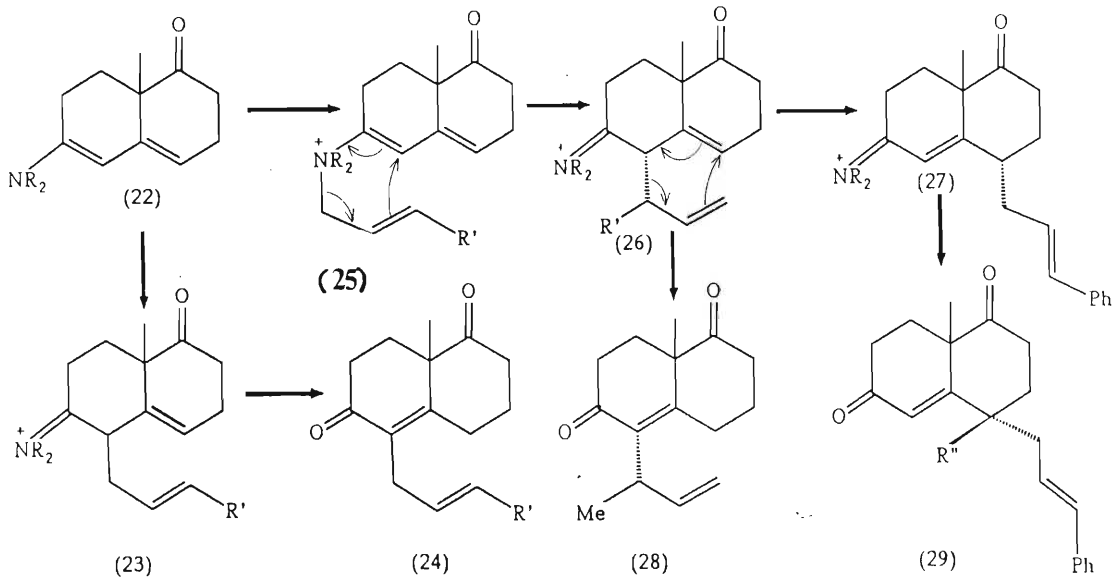
SCHEME 3



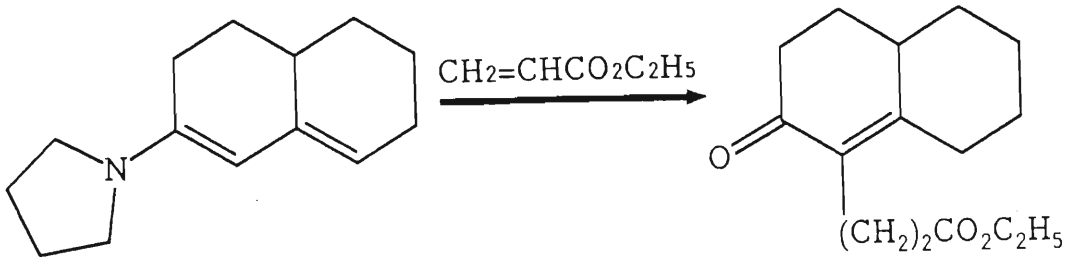
The reaction of dienamines with allylic halides is unusual since the path of the reaction depends both on the amine component and the allylic halide. Thus both crotyl and cinnamyl bromide react with the pyrrolidine dienamine (22) to give predominantly or exclusively products of direct C-alkylation [22 → (23) → 24]. The corresponding dienamines derived from morpholine and piperidine react with crotyl chloride to give mainly (28), and its Δ^5-double bond isomer but when treated with cinnamyl bromide the major products are (29; R" = H)

and (29; R" = $CH_2CH=CHPh$) which arise *via* double suprafacial [3,3] sigmatropic rearrangements [25 → 26 → 27 → 29 (R" = H); deprotonation and repetition of this process give (29; R" = $CH_2CH=CHPh$)] (Scheme 4).[49]

SCHEME 4



Alkylation of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone [a mixture of (11) and (12) (R,R',R" = H)] with ethyl acrylate gives (30).[25h]



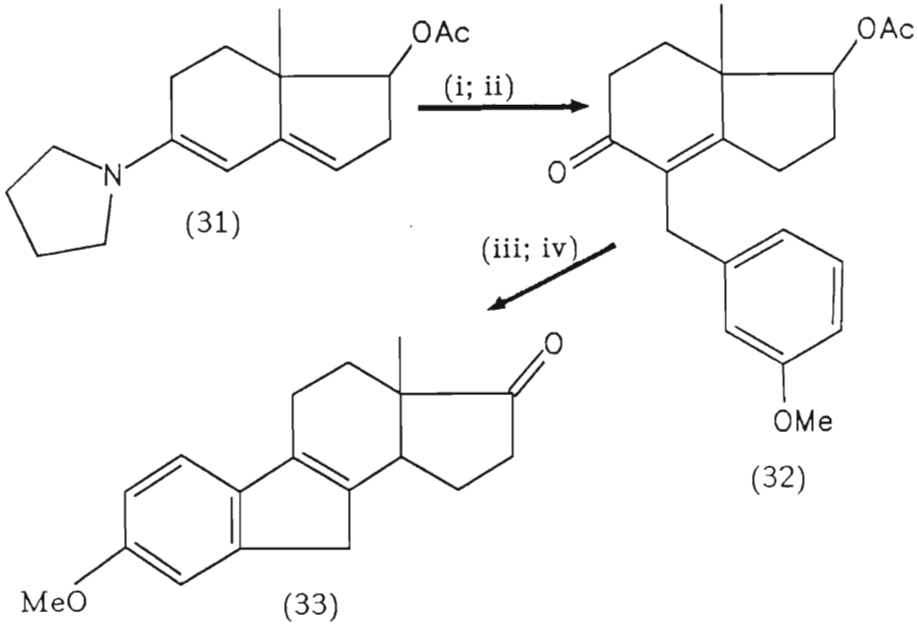
(30)

Similarly, methylation and benzylation of the pyrrolidine dienamine of 3-methyl-$\Delta^{1,8a}$-2-octalone [a mixture of (11) and (12) (R,R' = H; R" = Me)] gives only products derived from β-alkylation of the dienamine in both protic and aprotic solvents. The reaction with acrylonitrile and methyl acrylate has, however, been shown to be solvent dependent.[50] The solvent dependent regioselectivity of the reaction is discussed in detail in Section 2.1 of the discussion.

Solvent effects are also observed in the reaction of the pyrrolidine dienamines of 3-oxo-Δ^4-steroids with methyl iodide. In non-polar solvents mainly N-alkylated products result[10] whereas in more polar solvents β-alkylation[45,51] products arise.

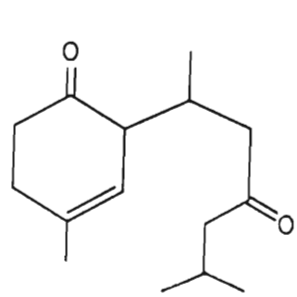
Alkylation of dienamine (31) with *m*-methoxybenzyl bromide gives (32), a precursor for B-norsteroid analogues (33)[25d] (Scheme 5).

SCHEME 5

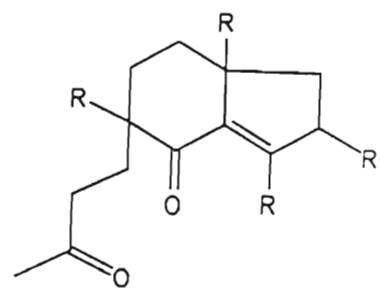


(i) *m*-methoxybenzyl bromide, DMF, Δ; (ii) hydrolysis; (iii) hydrolysis, oxidation; (iv) H_3PO_4 or P_2O_5.

Similarly endocyclic dienamines such as (1b) react with 6-methylhept-2-en-4-one to give (34),[18] and cross-conjugated dienamines such as (21) react with methyl vinyl ketone to give (35),[52] both products again arising from β-alkylation.

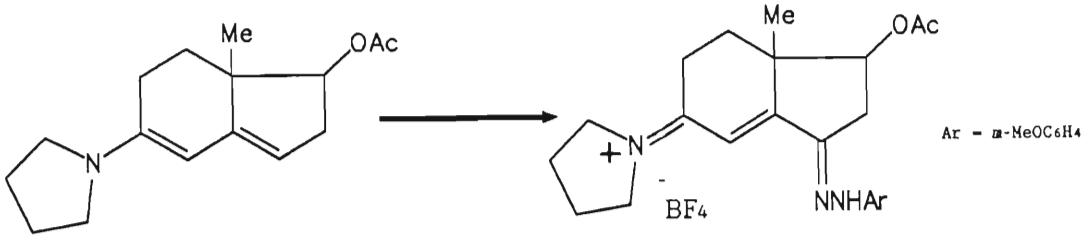


(34)



(35)

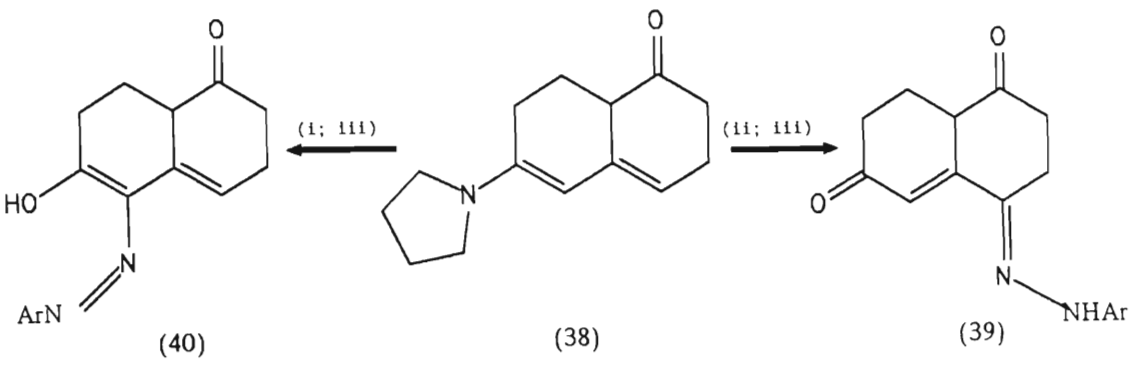
As mentioned earlier, dienamines react to a lesser extent at the δ-position. Consequently only a few examples are to be found in the literature. Pandit *et al.* have reported that the dienamine (36) gives the product (37) resulting from attack at the δ-position when treated with *m*-methoxyphenyl diazonium fluoroborate.[37]



(36) (37)

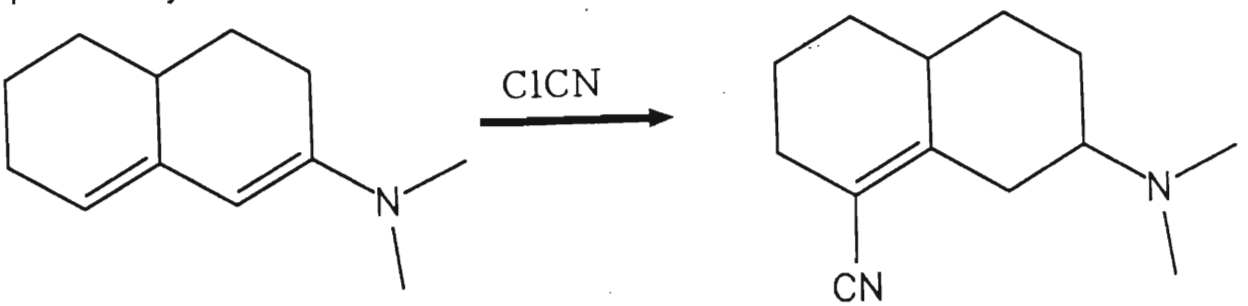
Nozoe has also shown that reaction of the tropylium ion with steroid dienamines occurs at the δ-position to give the 6-cycloheptatrienyl derivative.[34] Arenediazonium salts have been shown to couple with dienamines of the type (38) giving δ-substitution products (39) when the reaction is carried out in polar solvents. A change to less polar solvents interestingly alters the regioselectivity of the reaction resulting in β-substitution products[32a] (40) (Scheme 6).

SCHEME 6



(i) ArN_2BF_4, CH_2Cl_2 or $CHCl_3$ (ii) ArN_2Cl or ArN_2BF_4, DMF or H_2O (iii) hydrolysis

The reported[53] formation of (41) from the reaction of cyanogen chloride with dienamine (11; R,R'R" = H) is an unusual result in view of the low polarity solvent (dioxane) used. The product arising from β-substitution would presumably be the more obvious result.



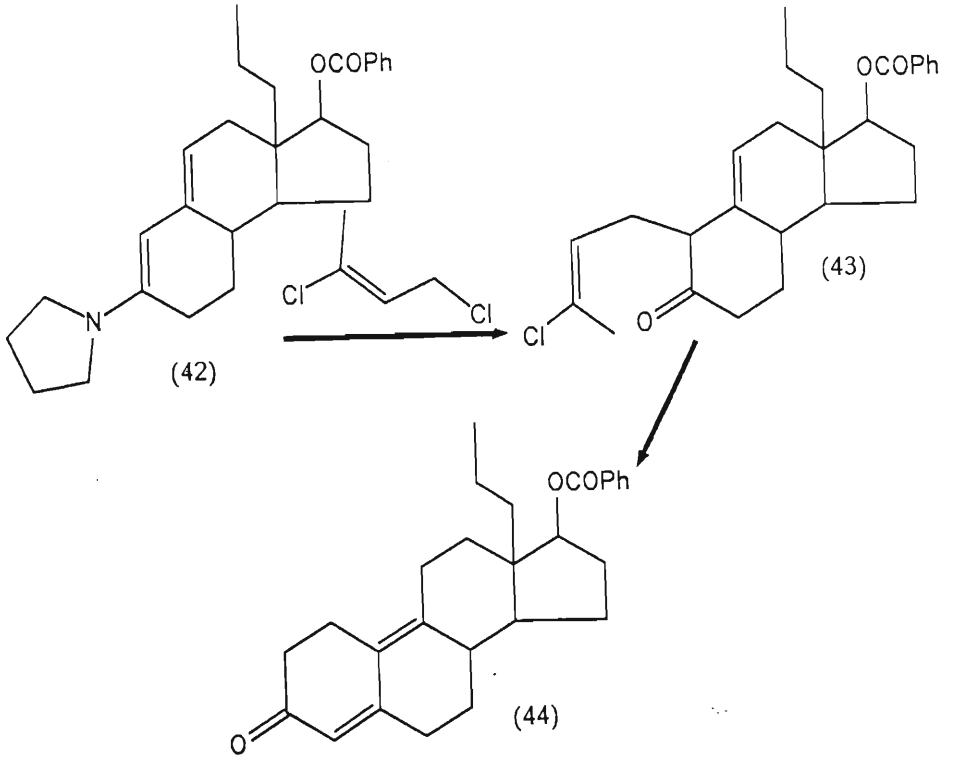
(11) (41)

Dienamine reactions have also proved to be of great value in carbocyclic synthesis. While examples of reactions giving rise to three, four, seven-membered and larger ring systems are to be found in the literature, those resulting in the formation of six-membered rings are of principle interest here.

The reaction of 1,3-dichloro-2-butene with the pyrrolidine dienamine (42) gives as mentioned previously, the β-alkylation product (43) which, following

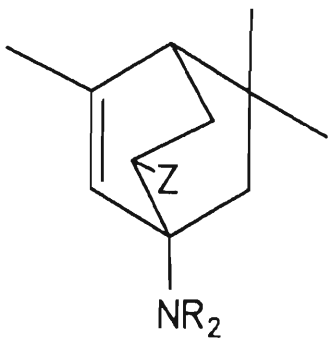
hydrolysis and subsequent cyclization yields the tetracyclic ketone (44)[25g] (Scheme 7).

SCHEME 7

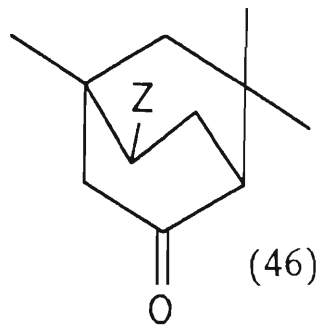


The Diels-Alder cycloaddition of cyclic linear dienamines with electrophilic olefins such as acrylonitrile, methyl acrylate and methyl vinyl ketone also results in the formation of six-membered rings, but the regioselectivity has been shown to be critically dependent on the reaction conditions. Opitz reported that the pyrrolidine dienamine of isophorone when treated with acrylonitrile gave the adduct (45) (R_2N = pyrrolidinyl; Z = CN), derived from the linear *endo*-isomer (15).[54] The corresponding reaction of the morpholine and piperidine dienamines was however, shown by Nozaki *et al.*[44] to give the adducts (45) (R_2N = piperidinyl, morpholinyl; Z = CN) as well as (in the case of the piperidine dienamine) cycloadduct (46) (Z = CN) and the alkylation product (47), both of which are derived from the cross-conjugated dienamine

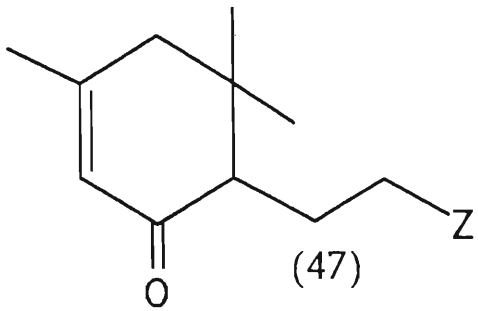
(16) which is the minor component of the dienamine mixture. This result presumably reflects the greater reactivity of the cross-conjugated dienamine and the ready acid-catalysed thermally accelerated dienamine interconversion. Similar results were obtained when the morpholine and piperidine dienamines were treated with methyl acrylate. The reaction with methyl vinyl ketone gave (46; Z = $COCH_3$) and (48).[44]



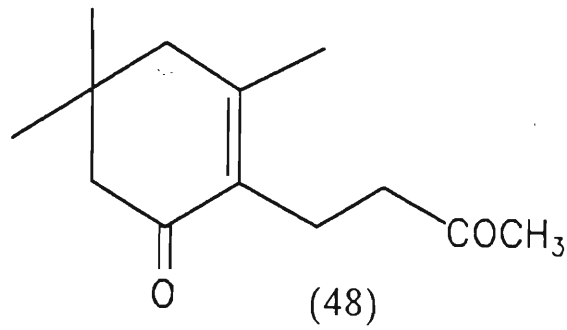
(45)



(46)



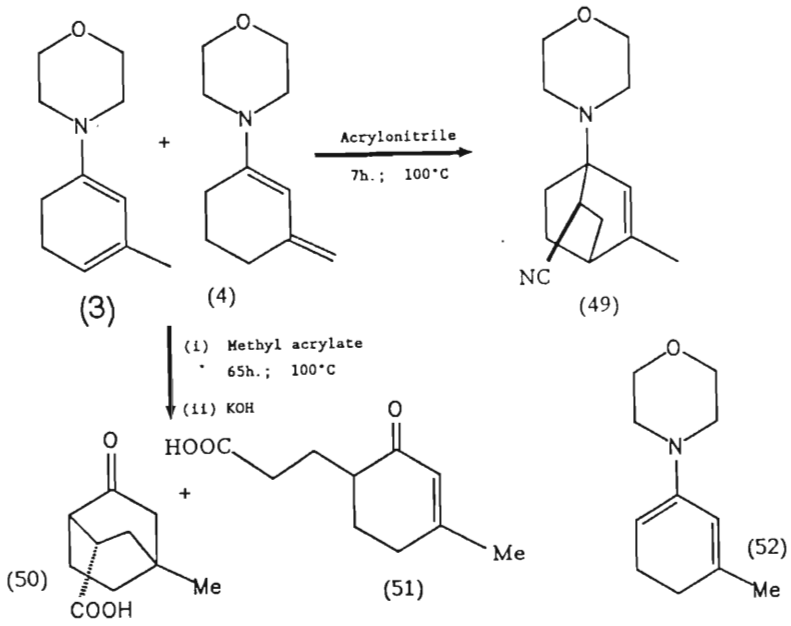
(47)



(48)

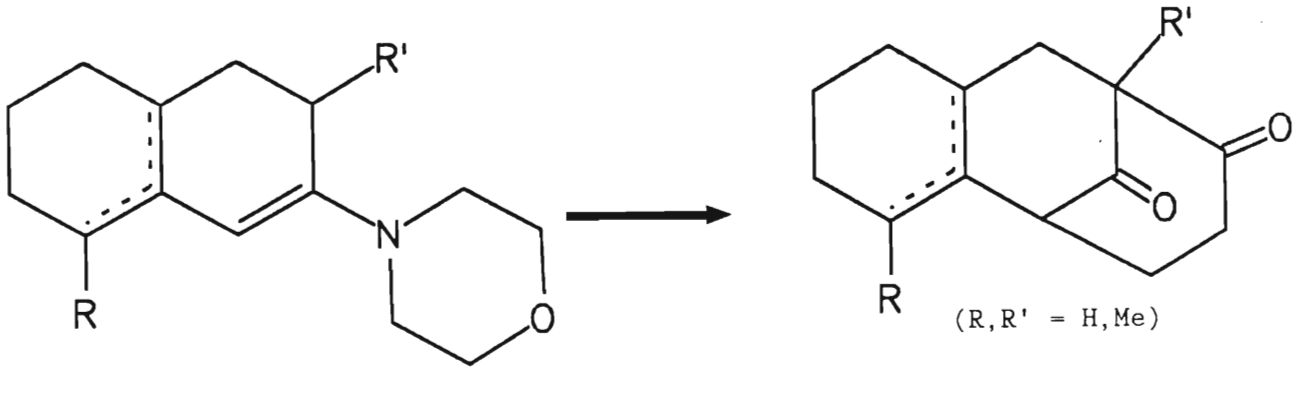
The Birch reduction products (3) and (4) react with acrylonitrile (Scheme 8) to give the cycloadduct (49) derived from the endo-isomer (3) only.

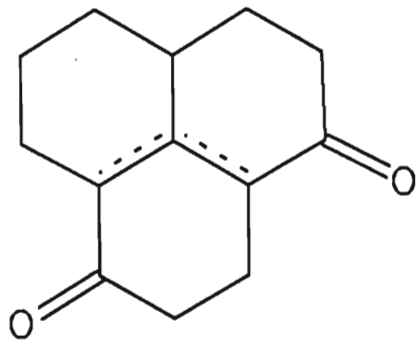
SCHEME 8



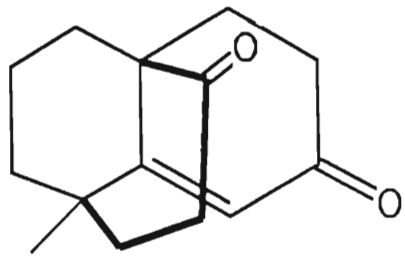
With methyl acrylate the products isolated following hydrolysis were (50) and (51) derived from the cross-conjugated dienamine (52) which was not present to any detectable extent in the original dienamine mixture.[55]

Six-membered rings have also been formed from the reaction of dienamines derived from $\Delta^{1,8a}$-2-octalones with acryloyl chloride as shown by Firrell.[14] The bridged bicyclic dione (53) (20 - 30 %) formed by initial reaction at C-1 followed by cyclization at C-3, was the major product of the reaction mixture. The 1,8- and 4a,8-bridged products (54) and (55) respectively were also isolated but in low yield.





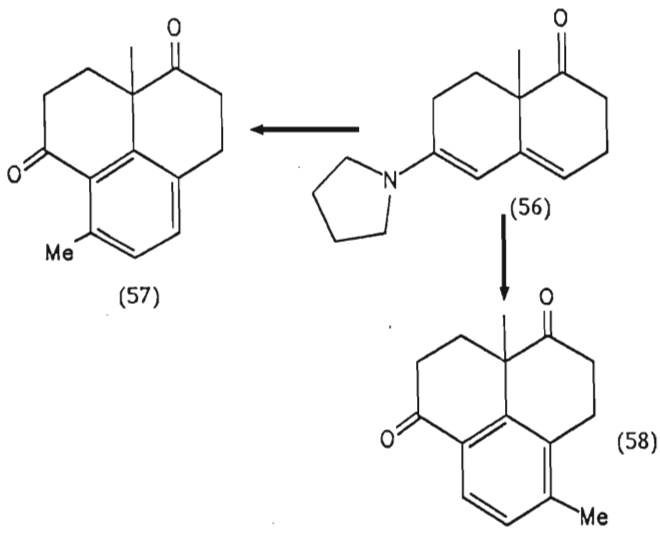
(54)



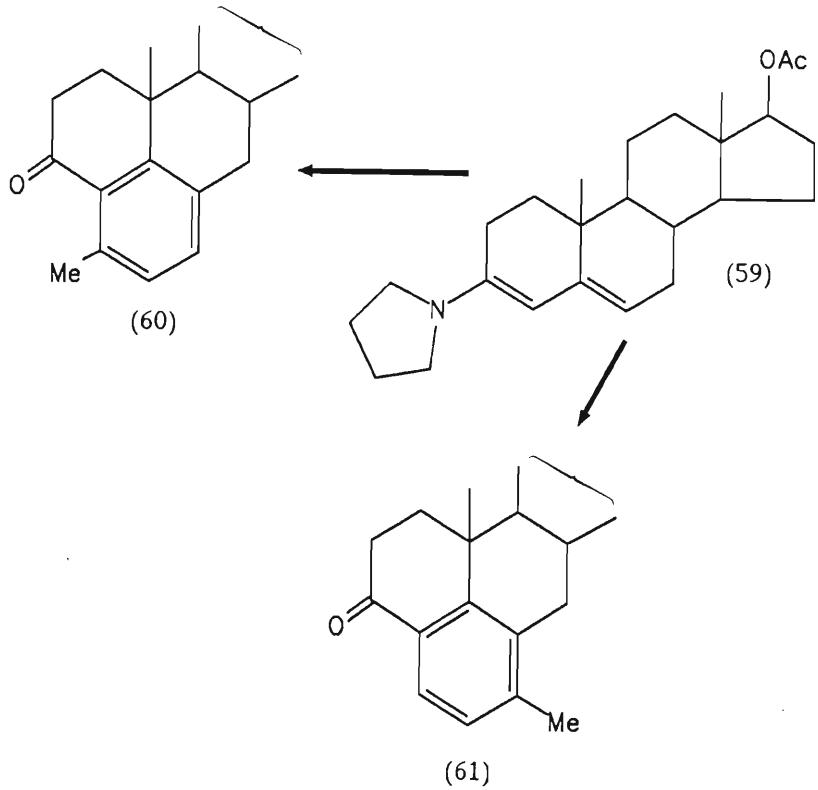
(55)

A particularly interesting reaction in view of the work presented in this thesis is the reported[56] condensation of both methyl vinyl ketone and crotonaldehyde with cyclic dienamines (56) to give products with fused aromatic ring systems (57) and (58) respectively *via* initial attack at the δ-position of the dienamine, followed by cyclization onto the β-position (Scheme 9).

SCHEME 9



This procedure has been applied to the facile conversion of steroidal dienamine (59) to benz[4,5,6]androstane derivatives (60) and (61).[57]



(60) (59) (61)

CHAPTER TWO

2. DISCUSSION

2.1 REACTION OF METHYL VINYL KETONE WITH DIENAMINES DERIVED FROM $\Delta^{1,8a}$-2-OCTALONES

As part of an ongoing investigation into the regioselective alkylation of dienamines, the reaction of methyl vinyl ketone (MVK) with a series of dienamines derived from $\Delta^{1,8a}$-2-octalones in protic and aprotic solvents has been studied. The reaction with MVK was of particular interest since although the Stork annulation[4] of substituted cyclohexanone enamines with MVK to give the corresponding $\Delta^{1,8a}$-2-octalones is well known, further annulation of $\Delta^{1,8a}$-2-octalones *via* the Stork reaction of their derived dienamines has not been investigated.

In view of the polydentate nucleophilic properties of dienamines, and the fact that dienamines derived from $\Delta^{1,8a}$-2-octalones exist as mixtures of the linear

exo- and endocyclic double bond isomers,[19] it was anticipated that the course of their reaction with MVK might well be complex.

In work already published,[50] the regioselectivity of reaction of the pyrrolidine dienamine of 3-methyl-$\Delta^{1,8a}$-2-octalone with methyl acrylate and acrylonitrile was, as mentioned earlier, shown to be solvent dependent. In protic solvents alkylation occurred at the β-carbon (C-1 of the dienamine), to give (64) (Z = CO_2Me; CN) on hydrolysis, whereas in aprotic solvents, reaction occurred at the δ-position (C-4a) to give (67) (Scheme 9•1).

The explanation offered for these results was based on the following principles:

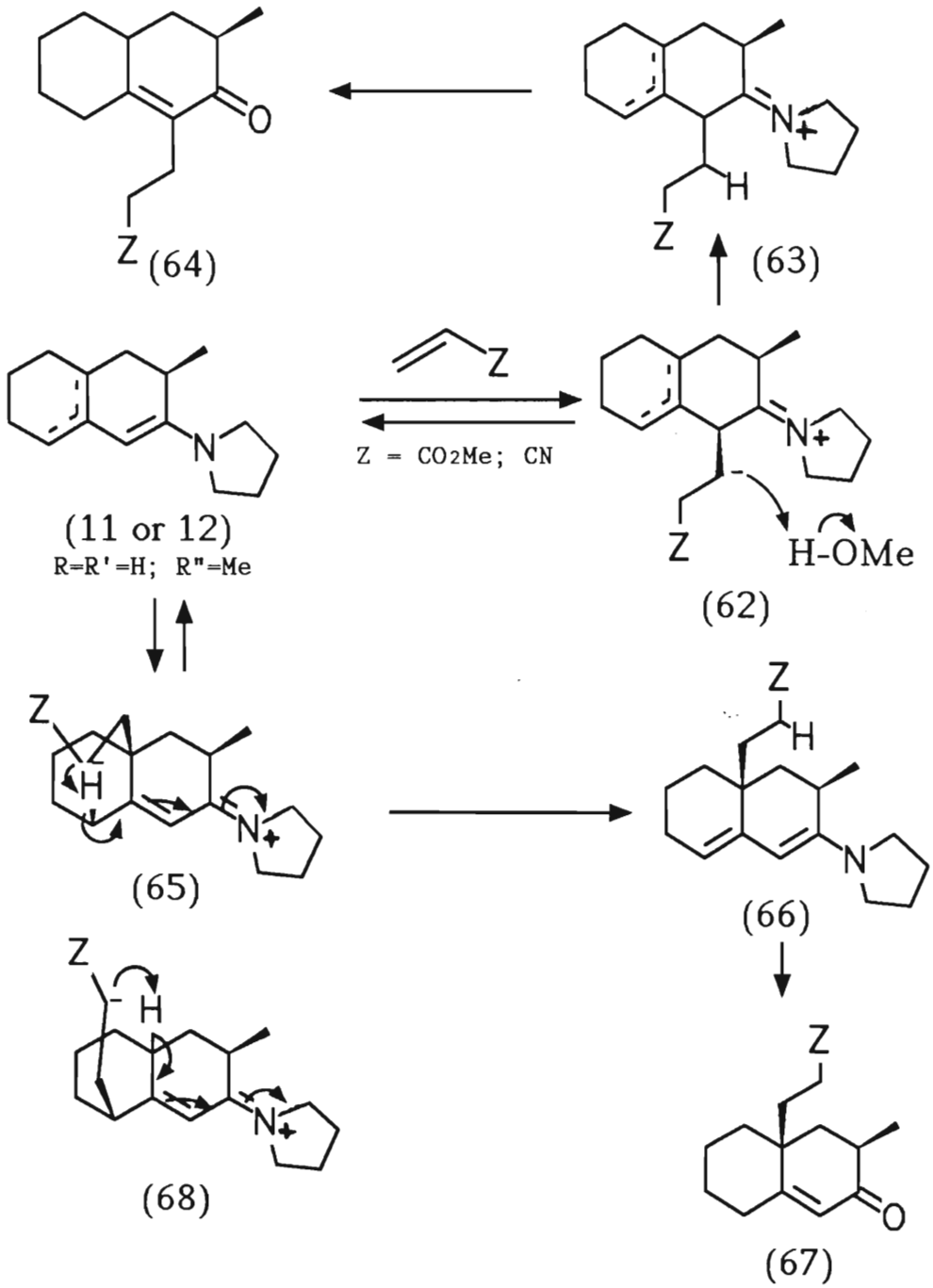
(i) the methyl group in (11 or 12; R,R' = H; R" = Me) was quasi-axial, rather than quasi-equatorial in order to minimise $A^{1,3}$-strain;[38]

(ii) reaction of an electrophilic alkene such as methyl acrylate or acrylonitrile with an enamine involved the reversible formation of a zwitterionic intermediate;[6]

(iii) formation of this zwitterionic intermediate may be rendered irreversible by subsequent protonation of the anionic centre, either by a protic solvent (methanol) or by transfer of an axial hydrogen, activated by the iminium group, to the anionic centre *via* a cyclic six-membered transition state;[6]

(iv) reaction at the β-position of the dienamine [*i.e.* C-1 in 11 or 12 (R,R' = H; R" = Me)] is a lower energy process than reaction at the δ-position (C-4a or C-8).

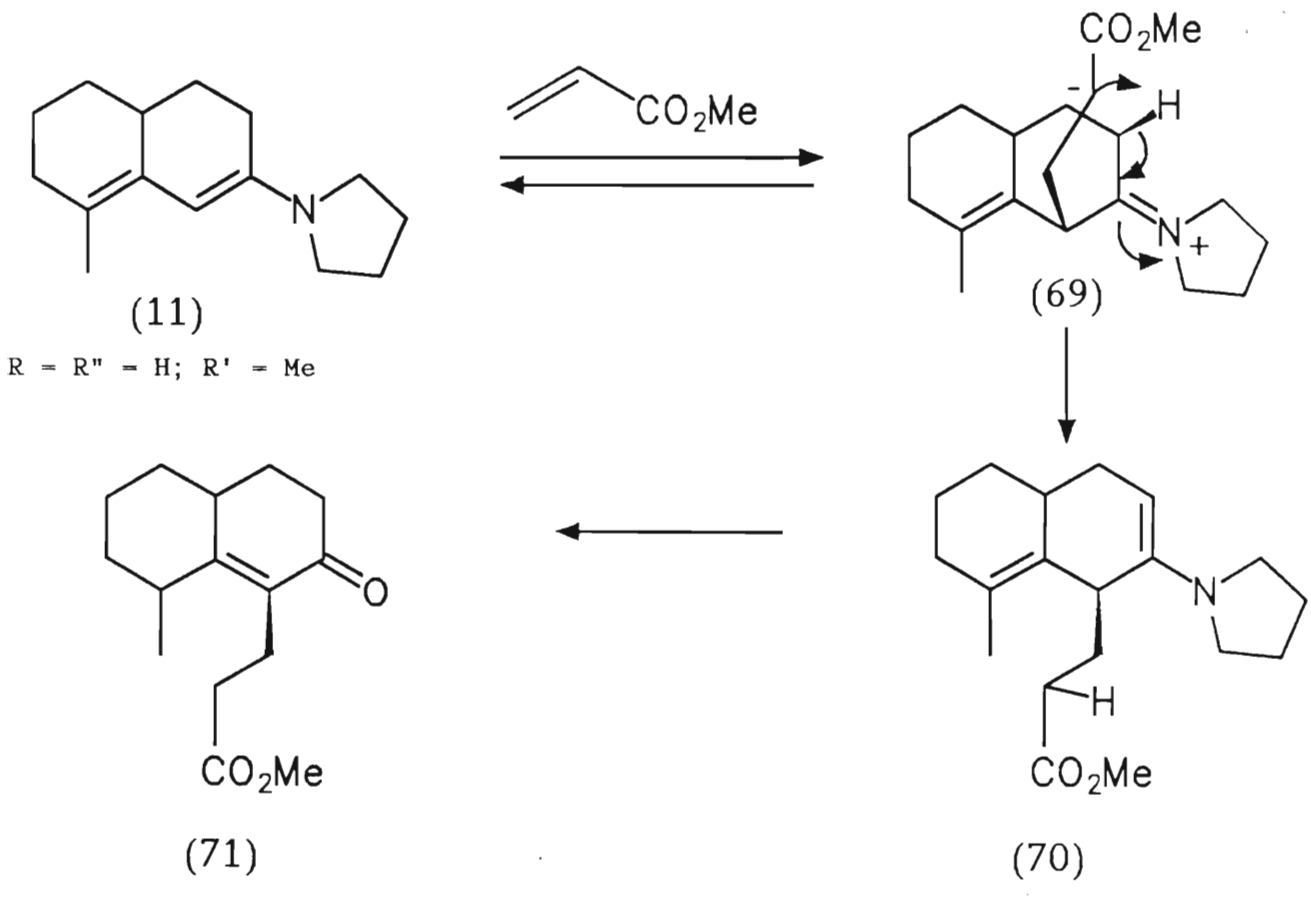
SCHEME 9·1


O
Z
(64)
N+
H
Z
(63)
Z
N
(11 or 12)
R=R'=H; R"=Me
Z = CO2Me; CN
N+
Z
H-OMe
(62)
Z
H
N+
(65)
Z
H
N
(66)
Z
H
N+
(68)
Z
O
(67)

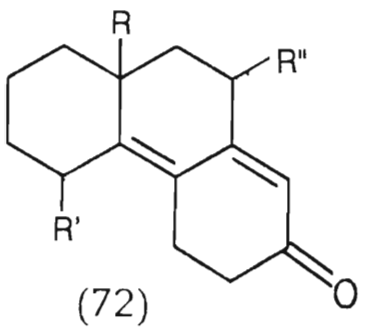
It was proposed that the zwitterionic intermediate (62) was formed initially, by axial attack syn to the methyl group, in both protic and aprotic solvents. In protic solvents this process may be rendered irreversible by protonation of the carbanionic centre by the solvent, thus leading to the iminium salt (63). Subsequent regeneration of the dienamine system and hydrolysis then gives the C-1 alkylated product (64). In aprotic solvents it was proposed that formation of (62) was reversible and did not lead to product formation. Since there is no acidic axial proton at C-3 (or C-1) which can be transferred to the carbanionic centre of the zwitterion (the equatorial hydrogens at these positions are less acidic than an axial hydrogen since the C-H bonds are orthogonal to the iminium group), elimination of methyl acrylate or acrylonitrile was the preferred mode of reaction. Reversion of (62) to starting dienamine therefore allowed thermodynamically favoured alkylation at C-4a or C-8 to compete with kinetically favoured alkylation at C-1. Alkylation at C-4a or C-8 can be rendered irreversible by stereoelectronically favoured transfer of an activated axial proton, vinylogous to the iminium group, from C-8 or C-4a, respectively, *via* a cyclic six-membered transition state as depicted in structures (65) and (68). The former gave dienamine (66) and thus the observed 4a-alkylation product (67) on hydrolysis. It was noted that formation of zwitterion (65) rather than (68) was surprising. Alkylation at C-8 would not be impeded by any developing 1,3-diaxial interactions with the C-3 methyl group, in contrast to alkylation at C-4a. Furthermore, the conjugated double bond system in an endocyclic dienamine is not coplanar[19] as it is in an exocyclic dienamine. Consequently the increase in the π-electron density

resulting from $p\pi$-conjugation would be expected to be greater at C-8 than at C-4a. Alkylation at C-4a was therefore presumed to have occurred because of the closer proximity of the negative charge to the 2-iminium group in the transition state leading to the intermediate zwitterion (65). Confirmation of this explanation was provided by alkylation of the dienamine (11; R,R" = H; R' = Me) (Scheme 10), in which the 3-methyl group was replaced by one at C-8. Only the β-alkylated product was obtained after hydrolysis, in both protic and aprotic solvents. Formation of the kinetically favoured zwitterion (69) would be rendered irreversible by stereoelectronically favoured transfer of the activated axial 3-proton thus leading to the dienamine (70) and the β-alkylated product (71) on hydrolysis.

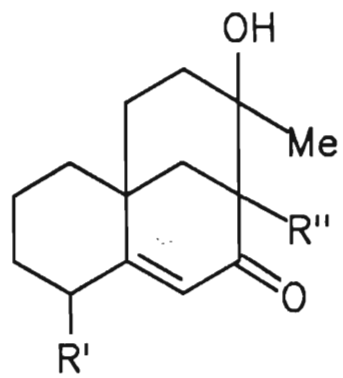
SCHEME 10



On the basis of these observations it would be anticipated that the reaction of MVK with dienamines derived from $\Delta^{1,8a}$-2-octalones would show similar solvent dependent regioselectivity. That is, dienamines (11 and 12; R" = H; R,R' = H,Me) would be expected to give β-alkylated products in both methanol and toluene, and dienamines (11 and 12; R" = Me; R,R' = H) should give the β-alkylated product in methanol but the δ-alkylated product in toluene. Furthermore, by analogy with Stork's synthesis of $\Delta^{1,8a}$-2-octalones, cyclisation of the β- or δ-alkylation products to give annulation products of the type (72 - 73; R,R',R" = H,Me) was another possibility to be considered.

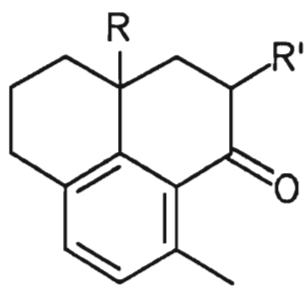


(72)



(73)

In addition the formation of (74; R,R' = H,Me) could not be ruled out, based on the reported synthesis of (57) from the corresponding reaction of MVK with the 5-oxodienamine (56).[56]



(74)

The reactions did in fact prove to be complex. Chromatographic analysis (GLC and TLC) of the crude reaction mixtures indicated the presence of several components. The gas chromatograms and thin layer chromatographic plates for the crude mixtures obtained from the reaction of MVK with the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone illustrate the complexity of the reaction (Figures 1 and 2).

FIGURE 1:

Gas chromatogram and thin layer chromatogram of the crude product obtained from the reaction between MVK and the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone in methanol.

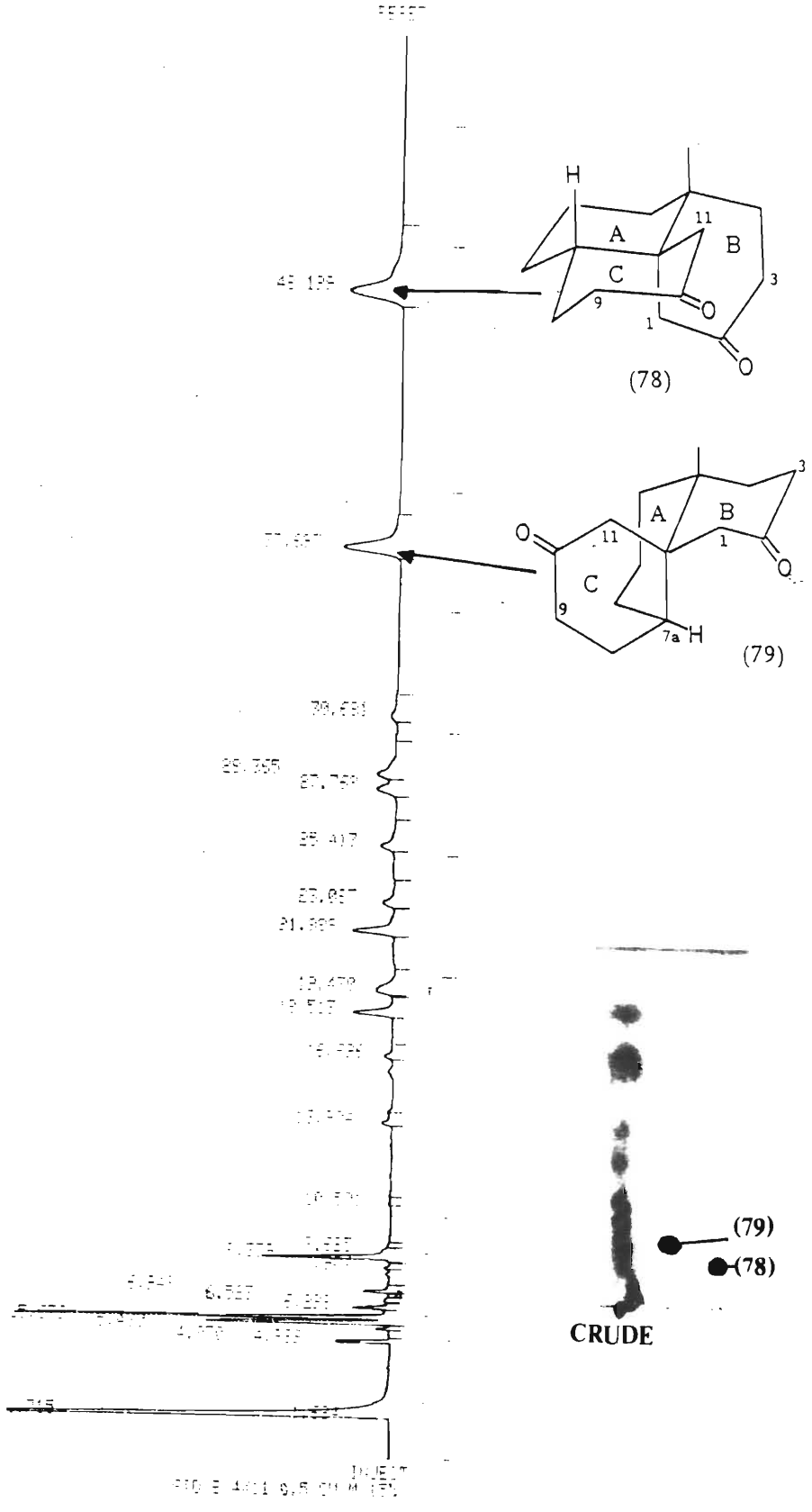
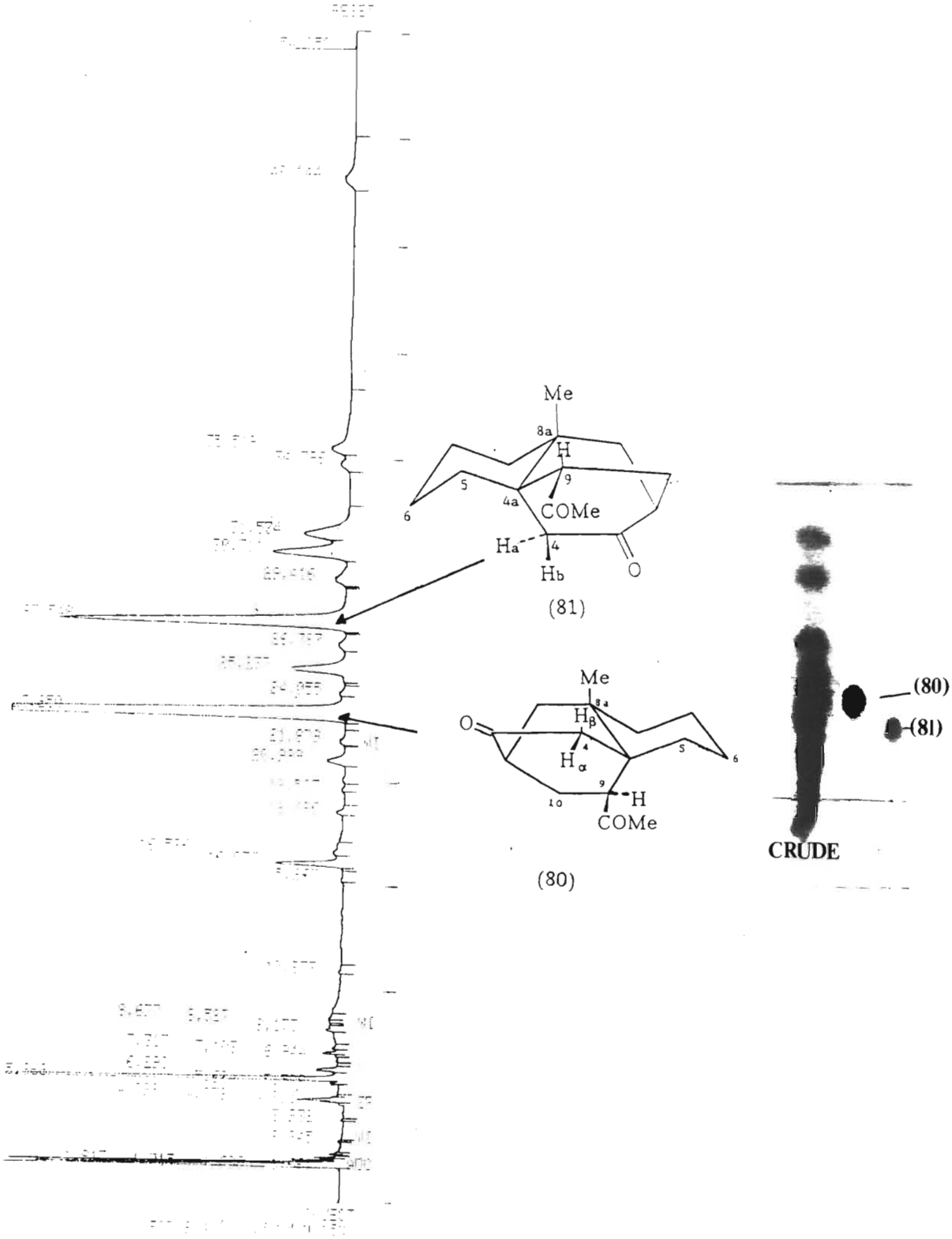
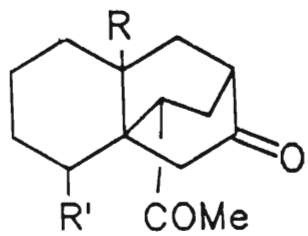


FIGURE 2:

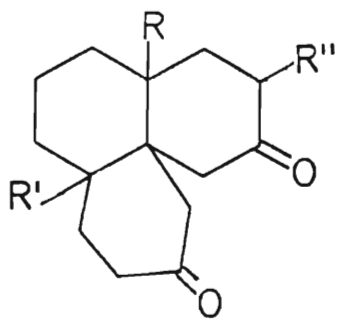
Gas Chromatogram and thin layer chromatogram of the crude product obtained from the reaction between MVK and the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone in toluene.



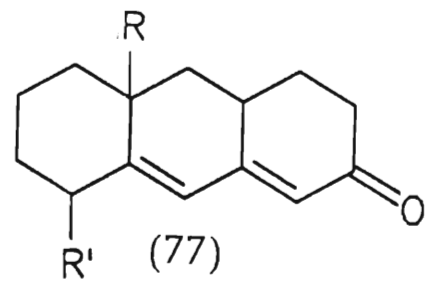
By judicious choice of eluant used in the flash chromatographic separation of these mixtures it was possible to isolate several compounds, many of them novel. During this investigation it also became apparent that the course of the reaction followed a particular solvent dependent pattern. In methanol the main products proved to be the 8,8a-annulation product (75; R,R',R" = H,Me) whereas in toluene the [4+2] cycloaddition product (76; R,R' = H, Me) was isolated as the major product. Structures of type (74; R,R' = H,Me) or the C-1, C-8 or C-4a alkylation products were not isolated from any of the reactions. Structures (72) and (77) were generally found to be the minor components of the complex reaction mixtures produced. These results were totally unexpected, especially the formation of structures (76) and (77) since they are both derived from the cross-conjugated dienamines (13) which, according to the work of Firrell[19] were not present to any detectable extent in the dienamine mixtures.



(76)



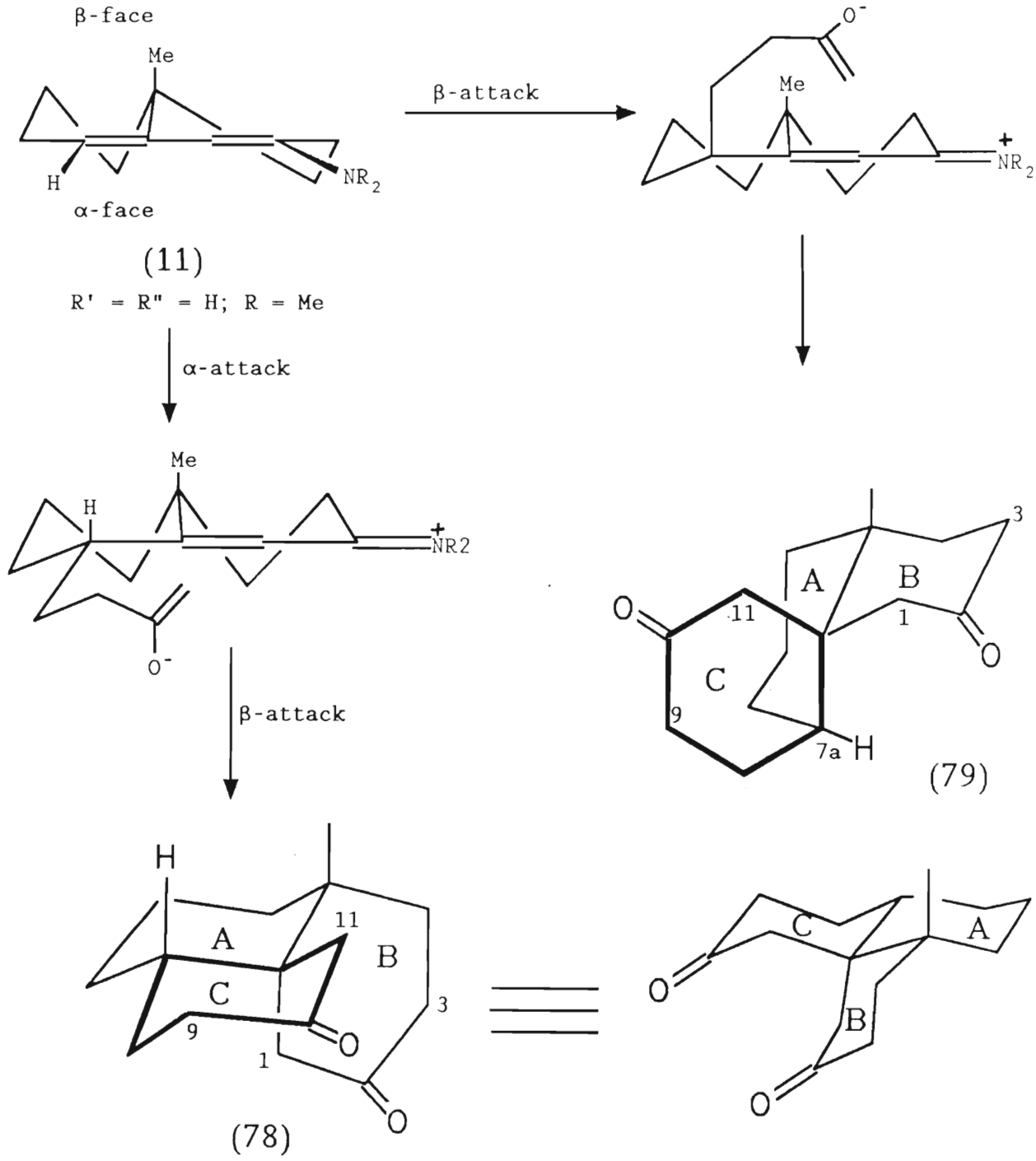
(75)



(77)

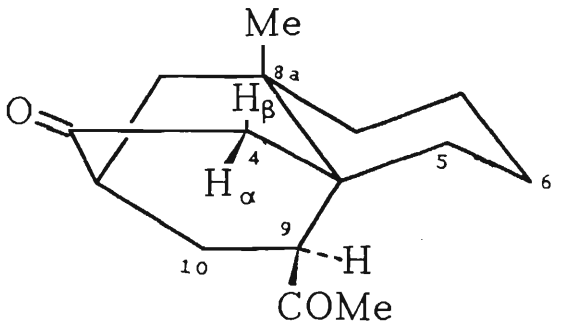
The first reaction investigated was that of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone since it was thought that this would exist only as the linear dienamine (11; R',R" = H; R = Me) and thereby simplify the course of the reaction. When the reaction was carried out in boiling methanol, the 50 MHz ^{13}C-nmr spectrum of the main product isolated showed the presence of two carbonyl groups (δ_c 210,43 and 210,61), one methyl group, and the absence of acetyl or tri- or tetra-substituted carbon-carbon double bonds. On the basis of these observations and mechanistic reasoning, structure (75; R',R" = H; R = Me) was proposed and subsequently confirmed by X-ray analysis of the crystal structure. The stereochemistry of the ring junctions are shown in structure (78) (Scheme 11). A second stereoisomer of this product was also isolated and later shown to be identical with the main product derived from the corresponding reaction of the pyrrolidine dienamine of 8-methyl-$\Delta^{1,8a}$-2-octalone (*vide infra*). The stereochemistry of this isomer is shown in structure (79) (Scheme 11). In each case the new ring which has been fused onto the existing bicyclic ring system is depicted in heavy lines. A third component was isolated in low yield (< 1%) from the complex reaction mixture and was tentatively identified as the angular annulation product 8a-methyl-3,4,5,6,7,8,8a,9-octahydrophenanthren-2(10*H*)-one (72; R',R" = H; R = Me) on the basis of the 60 MHz ^{1}H-nmr spectrum.

SCHEME 11

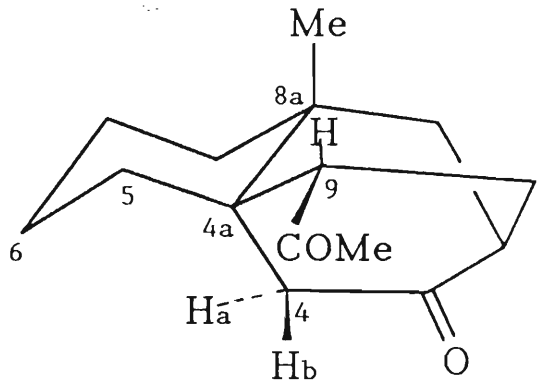

β-face
Me
H
NR2
α-face
β-attack
O-
Me
+
NR2
(11)
R' = R" = H; R = Me
α-attack
Me
H
+
NR2
O-
β-attack
A
B
C
3
11
1
9
7a
H
O
(79)
H
A
11
B
C
3
9
1
O
O
(78)
C
A
B
O
O

When toluene was employed as solvent the reaction took an entirely different route. The IR-spectrum of the main product isolated showed the presence of two carbonyl functions (ν_{CO} 1710 and 1730 cm^{-1}). The 50 MHz ^{13}C-nmr spectrum showed these two carbonyl functions at δ_C 212,60 and 216,56. In addition two methyl groups were detected (δ_H 0,94 and 2,3) but no carbon-carbon double bonds were observed. Thus structure (76; R' = H; R = Me) was assigned to this compound and subsequently confirmed by X-ray analysis. The stereochemistry of the ring junctions are shown in structure (80) in Scheme 12.

SCHEME 12

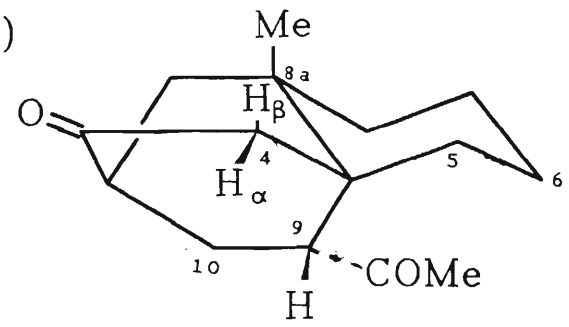


(80)



(81)

Me



(82)

A second product was isolated from the reaction in toluene and gave the same number of methine, methyl, methylene and quaternary signals in the ^{13}C-nmr spectrum as (80) and was thus assigned as a stereoisomer (81 or 82) of 9-acetyl-8a-methylperhydro-2,4a-ethanonaphthalen-3-one (80). No suitable X-ray analysis was obtained for this product owing to twinning of the crystals and thus the stereochemistry could not initially be assigned. The problem was later resolved in favour of (81) and the stereochemistry, together with that of the Diels-Alder adducts isolated during the course of this investigation, is discussed later.

A third product was isolated in low yield (4%) and assigned as the linear annulation product 5a-methyl-4,4a,5,5a,6,7,8,9-octahydroanthracen-2(3*H*)-one (77; R' = H; R = Me). The 200 MHz ^{1}H-nmr spectrum showed olefinic signals at δ 5,72 and 5,90 and the IR-spectrum showed the presence of an α,β-unsaturated carbonyl group at 1650 cm^{-1} as would be expected for this compound.

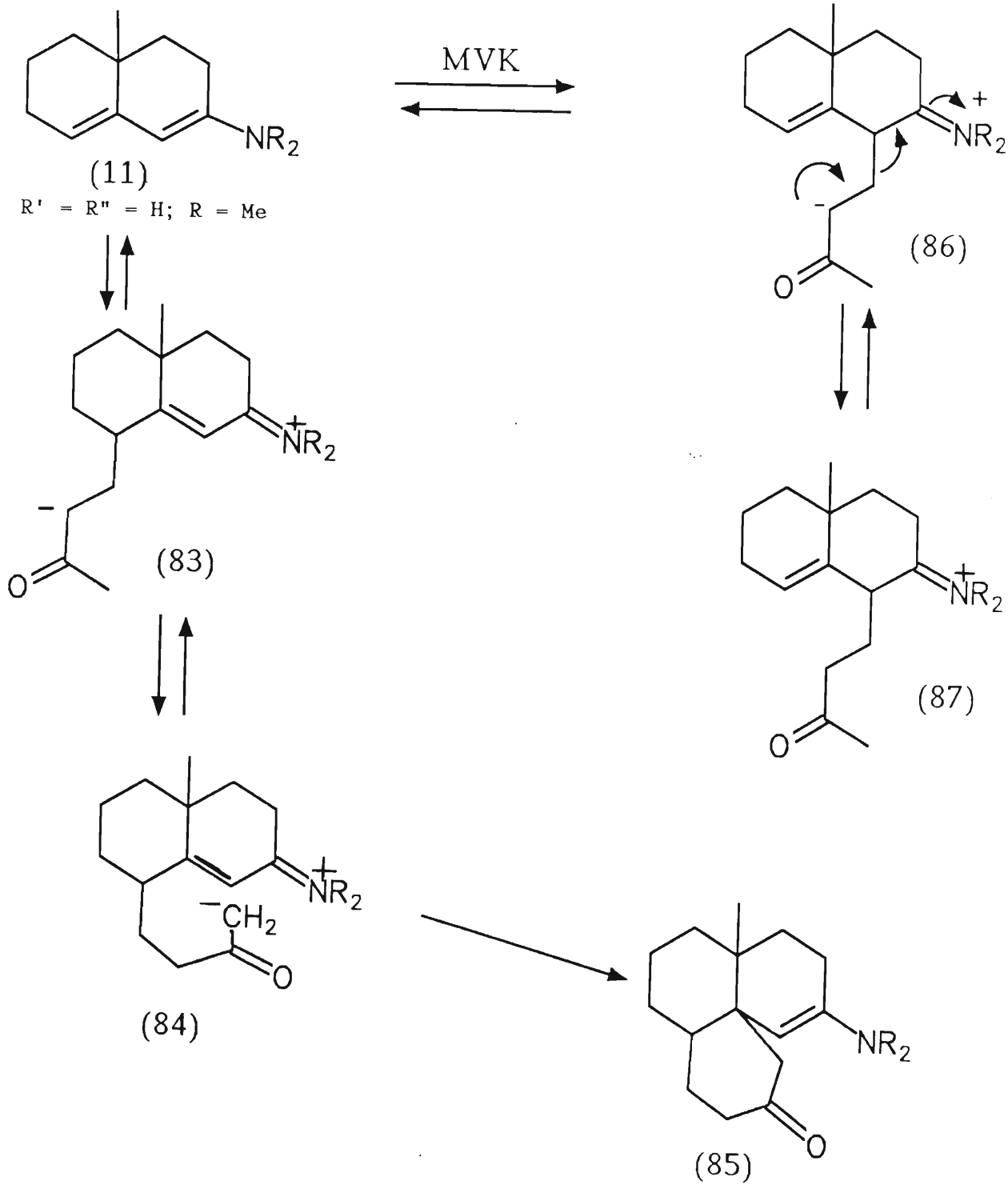
From the products isolated it is clear that in methanol the preferred course of reaction is *via* initial alkylation at the least reactive δ-position (C-8) of the linear exocyclic dienamine (11; R = Me; R',R" = H) to give (75; R = Me; R',R" = H) and to a much lesser extent *via* alkylation at the more reactive β-position (C-1) to give (72; R = Me; R',R" = H). The propensity for preferential reaction of MVK at what is undoubtedly the least reactive position of the dienamine is intriguing in view of the previously reported[50] results of the reaction of

dienamine (11 or 12; R,R' = H; R" = Me) (Scheme 9) with acrylonitrile and methyl acrylate which gave only the products of β-annulation (64) in protic solvents. The most plausible explanation that can be offered is that reaction at the β-position is reversible even in methanol.

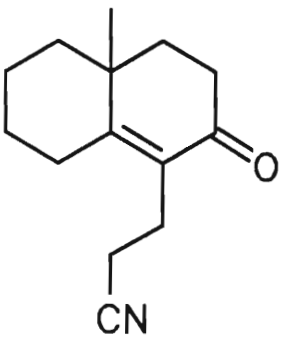
Pearson[58] has demonstrated that the anion stabilising power of electronegative substituents is SO_2 > CO > CO_2R > CN. The acidity of the α-protons must therefore also decrease in this order. This means that if the anionic centre of the initially formed zwitterion is protonated, the greater acidity of the protons alpha to the ketone carbonyl group with respect to those alpha to an ester carbonyl or nitrile, must result in an increased possibility for reversion to the zwitterion. The "push" of the anionic centre coupled with the "pull" of the positively charged iminium group then renders the reaction reversible. In the case of methyl acrylate and acrylonitrile the alpha protons are less acidic and once the anionic centre has been protonated, reversion to the zwitterion does not occur. Their β-site selectivity can therefore be attributed to an irreversible kinetically controlled reaction at the most reactive position of the dienamine. In the case of MVK, thermodynamic control presumably takes over. The conjugated eniminium zwitterion (83) will clearly be more stable than the non-conjugated one (86) (Scheme 13). Build up in concentration of the eniminium salt (83) then allows prototropic shift to (84) and cyclisation to the 8,8a-annulation product (85). Alternatively a *trans*-enamination process[6] could be involved in the conversion of (83) into the 8,8a-annulation product. Unfortunately it has not been possible to isolate any of the β-annulation product (87). Under the experimental conditions employed for this reaction

any β-alkylation intermediate formed which does not revert to starting material apparently undergoes cyclisation to give the angular annulation product (72; R',R" = H; R = Me).

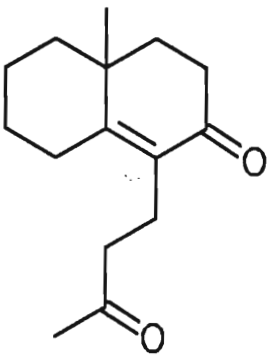
SCHEME 13



Some years ago Stork[59] reported that mono-alkylation of aldehydes and ketones could be achieved by making use of metalloenamines derived from the treatment of N-alkylamines with Grignard reagents. Stork[60] later demonstrated that the problem of mono-alkylation of α,β-unsaturated ketones could be resolved in the same manner. The procedure outlined by Stork[59] gave a reasonable yield (26%) of 1-(2-cyanoethyl)-4a-methyl-$\Delta^{1,8a}$-2-octalone (88) when the metalloenamine derived from ethylmagnesium bromide and the cyclohexylimine of 4a-methyl-$\Delta^{1,8a}$-2-octalone was treated with 3-bromopropionitrile.



(88)



(89)

The corresponding reaction using MVK was therefore carried out in an attempt to prepare the β-alkylated product 1-(3-oxobutyl)-4a-methyl-$\Delta^{1,8a}$-2-octalone (89). Analysis (GLC) of the crude product obtained from this reaction indicated that the attempt was unsuccessful. Only the starting octalone (52%[a]) was present to any significant extent, presumably because N-alkylation rather than C-1 alkylation had occurred. Another possibility to be considered is the formation of (89) *via* reaction of (88) with methyl magnesium bromide (after

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[a]Integrated GLC peak area.

first protecting the carbonyl function either as the ketal or the enamine) followed by acid hydrolysis. Time constraints however, have precluded efforts in this direction and further work is therefore necessary in order to substantiate the hypothesis proposed for the preferential reaction of MVK at the δ-position of the dienamine system.

The reaction of MVK with the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone in toluene to give (76 and 77; R = Me; R' = H) *via* the cross-conjugated dienamine (13; R',R" = H; R = Me) was also surprising since as reported by Firrell,[19] the cross-conjugated dienamine was not detected in the dienamine mixture. The explanation which we offer for this result is that in aprotic solvents of low dielectric constant, charge separation in the ground and transition states is less favoured and the reaction becomes orbital controlled. The activation energy for a [4+2] cycloaddition must therefore be less than that for the formation of zwitterionic intermediates in an aprotic solvent, and the equilibrium (11$\rightleftharpoons$13) is displaced as the cross-conjugated dienamine isomer (13) undergoes cycloaddition. Ring opening of the Diels-Alder adduct, initiated by the "push" of the enamine function and the "pull" of the acetyl group, could subsequently lead to a zwitterionic intermediate after the dienamine equilibrium (11$\rightleftharpoons$13) has been displaced and this gives the linear annulation product 5a-methyl-4,4a,5,5a,6,7,8,9-octahydroanthracen-2(3*H*)-one (77; R = Me; R' = H).

From the crystal structure of (78) (the main product in methanol) it is evident that initial attack by MVK has occurred from the least hindered α-face, *anti* to

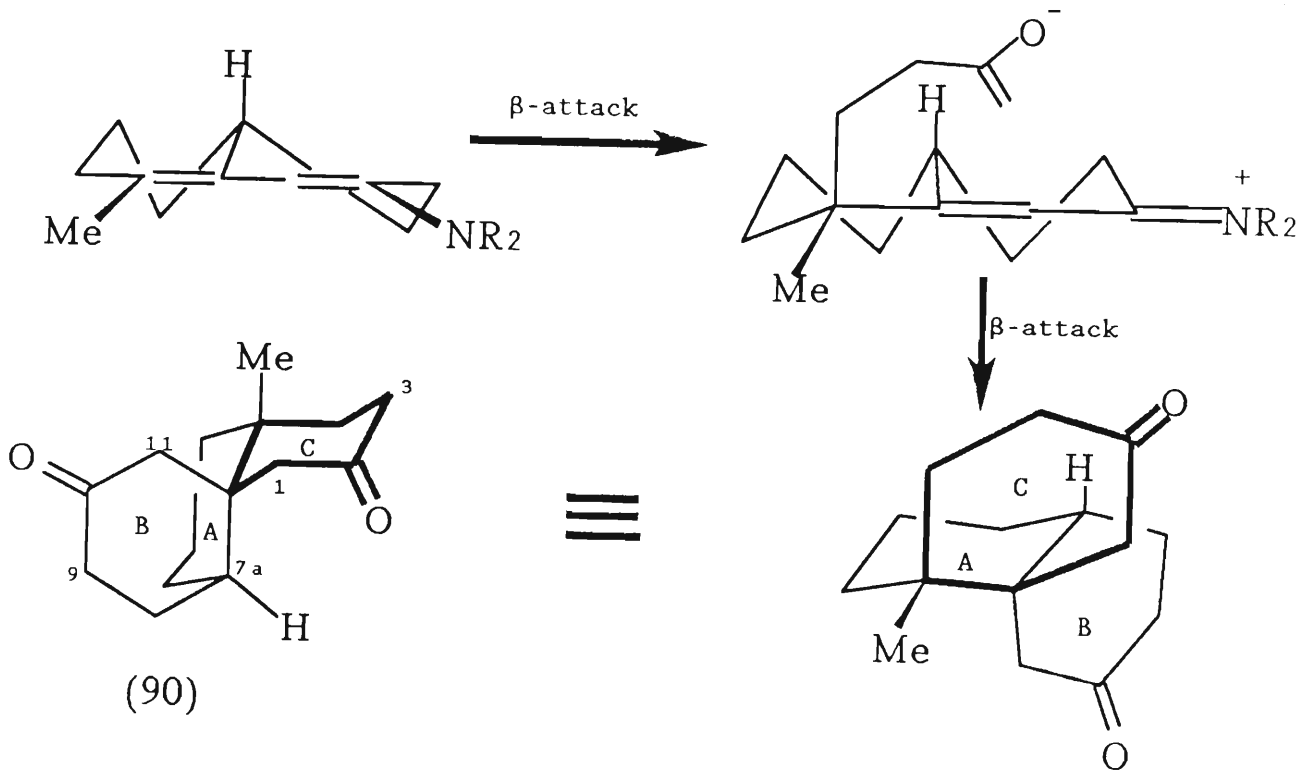
the C-4a methyl group, as would be expected on steric grounds, but cyclisation at C-8a has occurred *syn* to the angular methyl group (Scheme 11). Both newly formed carbon-carbon bonds are therefore equatorial to ring A of the starting dienamine and the original 1,8a bond has become axial to ring A. Thus the developing steric interactions with the angular methyl group are alleviated, the B-ring of the dienamine residue being cis-fused to the A-ring and the new ring introduced by reaction with MVK being trans-fused to the A-ring. The molecular framework is rigid with all three rings present as chairs with normal torsional angles. It thus appears that the transition state for the formation of the second bond is late and that significant re-hybridisation at C-8a has occurred to a significant extent in the transition state otherwise cyclisation would presumably have to occur from the less hindered α-face to give a cis-fused new ring. Developing sp^3 hybridised character at C-8a associated with a late or product-like transition state, as has previously been proposed in order to account for the relative stereoselectivity of protonation of enamines and enol ethers,[61] together with the 1,8a bond of the original dienamine becoming axial to ring-B would allow the terminal carbon atom of the MVK residue to approach the C-8a position at an angle to the C-4a-methyl bond and thus minimise developing steric interactions. The minor isomer (79) (Scheme 11) is, however, formed by initial attack at C-8 from the more hindered β-face, syn to the angular methyl group, followed by cyclisation at C-8a also from the β-face. The new ring introduced by reaction with MVK is thus cis-fused, being attached by an axial and an equatorial bond to the A-ring of the starting dienamine. The 1,8a bond has in this case however, not "dropped

away" to become axial to ring-A. Instead, the 8,8a bond has become axial to ring-B of the starting dienamine, again minimising steric interactions between the new ring and the angular methyl group.

The crystal structure (80) obtained for (76; R = Me; R' = H) (the main product in toluene) indicates that [4+2] cycloaddition to the dienamine (13; R',R" = H; R = Me) has occurred from the less hindered α-face. Both ring-B of the starting dienamine and the new ring formed by reaction with MVK, have adopted "boat" conformations. The "boats" are not ideal, but are slightly twisted in the same sense through a mean torsion angle of 13°. This effectively reduces the volume of this part of the molecule while simultaneously relieving the non-bonded H···H and C···H repulsions caused by eclipsing. Since it was not possible to obtain a crystal structure of the minor isomer isolated from the toluene reaction for the reasons mentioned earlier, it was initially uncertain in this case whether [4+2] cycloaddition had occurred from the more hindered β-face (syn to the 4a-methyl group) to give (81) or whether cycloaddition had again occurred from the less hindered α-face to give a diastereomer of (76; R = Me; R' = H) (*i.e.* structure 82). However, by closer examination of the ^{1}H-nmr spectra of these two isomers, assisted by two-dimensional COSY and HETCOR spectra it was possible to assign the minor isomer to structure (81). The reasons for this stereochemical assignment are discussed later.

The reaction of the pyrrolidine dienamine of 8-methyl-$\Delta^{1,8a}$-2-octalone with MVK produced similar results to the corresponding reaction of the 4a-methyl dienamine. In methanol a complex mixture was again obtained and shown to contain two isomeric forms of the tricyclic dione (75; R,R" = H; R' = Me). The major product of the reaction mixture was isolated by flash chromatography and purified by recrystallisation from hexane-ethyl acetate. X-ray analysis enabled this compound to be identified as (4aR*,7aR*,11aR*)-4a-methyloctahydro-1*H*-benzo[d]naphthalene-2,10(3*H*,1*H*)-dione (90; 25%; MP 158°C) (Scheme 14).

SCHEME 14

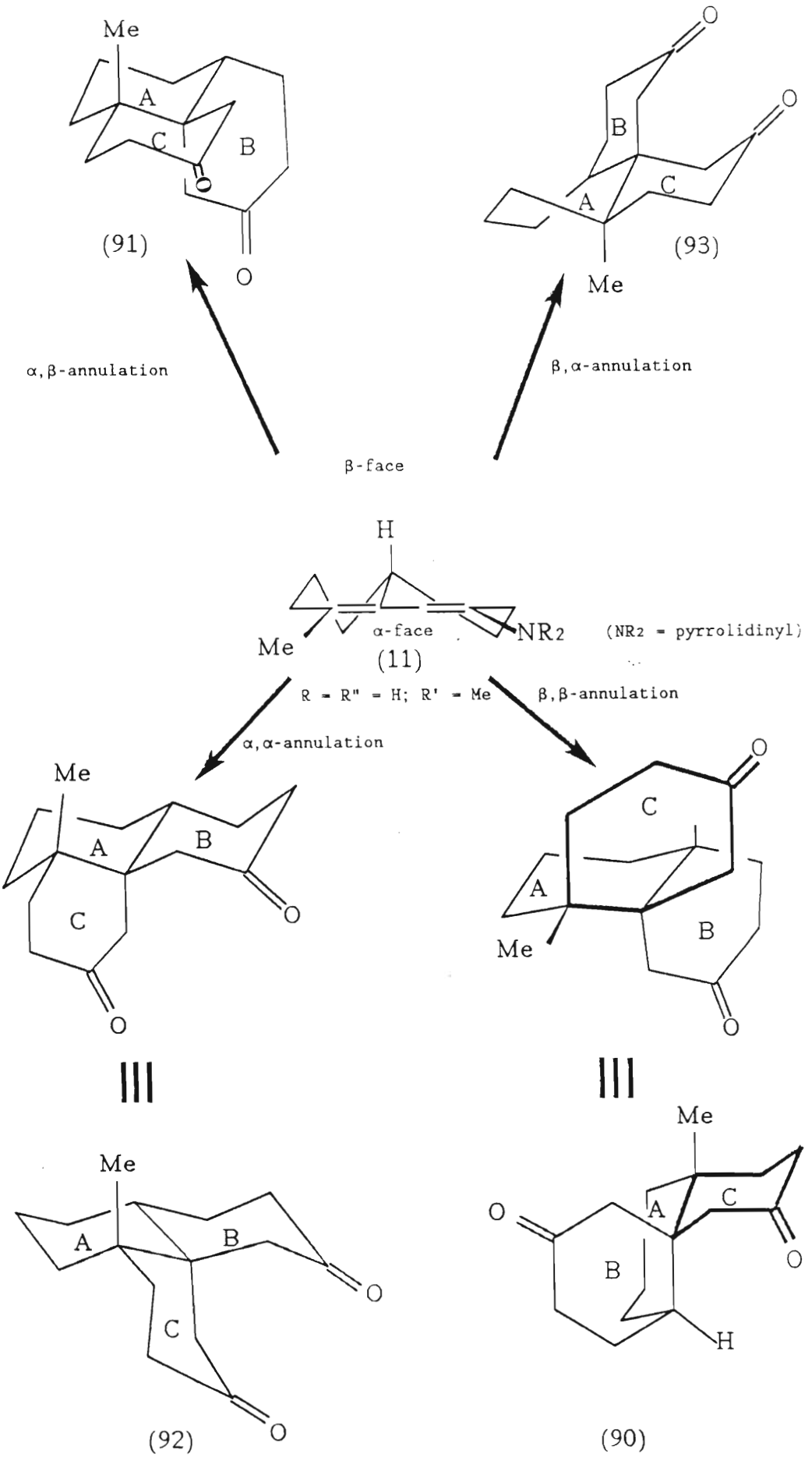


The crystal structure shows the molecular framework to be rigid with all three rings present as chairs with normal torsional angles. The spectral data for this compound was identical in every respect to that obtained for the minor isomer (79) isolated from the corresponding reaction of the 4a-methyl dienamine. Construction of the molecular models shows the two molecules (79) and (90) to be the same except for one subtle difference. The new cyclohexanone ring (C) which has been fused on in molecule (90) is the same as the existing cyclohexanone B-ring in the molecule (79) and *vice versa*. The difference in the isomer ratios of (79) and (90) from the two reactions can readily be explained in terms of steric and stereoelectronic effects. There are four stereochemical courses available for the 8,8a annulation of the 8-methyl dienamine (11; R,R" = H; R' = Me) with MVK and these are summarised in Scheme 15.

Initial attack of C-8 could occur from the α-face followed by cyclisation onto C-8a from the β-face (α,β-attack) to give the dione (91) on hydrolysis. This would result in the new ring (C) being joined by two equatorial bonds to the original A-ring of the dienamine and thus be expected to be thermodynamically favoured. Alternatively cyclisation onto C-8a could occur from the α-face (α,α-attack) to give dione (92)[a] in which the new ring is now joined to ring-A by an equatorial and an axial bond. However initial α-face attack at C-8 is stereoelectronically unfavourable since the transition state must involve a developing boat or twist-like conformation of ring-A with a consequent increase

[a]Enantiomer of (78).

SCHEME 15


Me
A
C
B
O
O
(91)
O
B
O
A
C
(93)
Me
α,β-annulation
β,α-annulation
β-face
H
Me
α-face
NR2
(NR2 = pyrrolidinyl)
(11)
R = R" = H; R' = Me
α,α-annulation
β,β-annulation
Me
A
B
C
O
O
C
A
Me
B
O
III
III
Me
A
B
C
O
O
Me
A
C
O
B
O
H
(92)
(90)

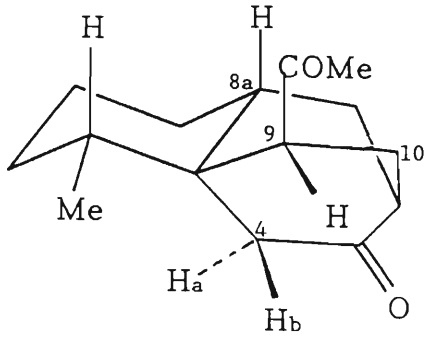
in the activation energy. A more stereoelectronically favourable process would therefore be initial β-face attack on C-8. The MVK residue would then be axially oriented with respect to ring-A and thus render cyclisation at C-8a sterically impossible from the α-face (β,α-attack) unless ring-A adopts a boat conformation, with consequent increase in activation energy and would result in dione (93) which would have a strained, deformed boat, and possibly chair, six-membered rings. A more favourable cyclisation would therefore be from the β-face at C-8a (β,β-attack) to give dione (90). The new ring (C) in (90) is attached to ring-A by an axial and an equatorial bond and each ring can exist as unstrained chair conformations. This would therefore be the most favourable process and would result in (90) being the major product. X-ray analysis proved this to be the case. In contrast, β-face approach by MVK in the corresponding reaction of the 4a-methyl dienamine is sterically impeded by the 4a-methyl group. Thus initial attack by MVK occurs at the least hindered α-face and is followed by cyclisation at C-8a from the β-face, as mentioned earlier, to give (78) as the major product.

The second product (2%) detected in the GLC of the crude reaction mixture, could not be isolated but by comparison of retention times was identified as the same product (78) isolated from the corresponding reaction of the 4a-methyl dienamine. Formation of this minor isomer (78) from the 8-methyl dienamine reaction would involve α-face attack at C-8 of the dienamine followed by cyclisation also from the α-face onto C-8a but, as discussed earlier this would be less favourable on stereoelectronic grounds (*i.e.* developing boat

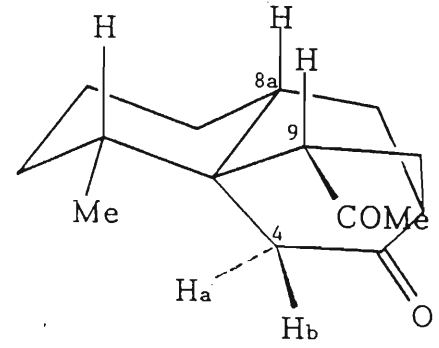
or twist-like conformations in the transition state), and would thus account for the low yield of this compound. The angular annulation product (72; R,R"=H; R' = Me) was also obtained in low yield (7%) from this reaction. The 80 MHz ^{1}H-nmr spectrum showed the presence of a single olefinic proton (δ_H 5,65) and the IR-spectrum showed the presence of an α,β-unsaturated carbonyl function at 1650 cm^{-1}. In addition the accurate mass measurement (M^+: 216,1520) was in agreement with this structure.

The reaction in toluene again showed the preferential formation of products derived from the cross-conjugated dienamine isomer (13; R,R" = H; R' = Me). The linear annulation product (77; R' = Me; R = H) and two isomers of the Diels-Alder adduct (76; R = H; R' = Me), structures (94) and (95) (Scheme 16) were isolated.

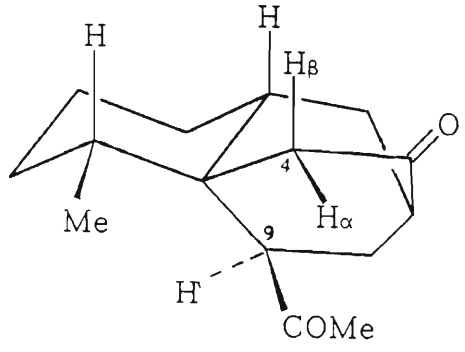
SCHEME 16



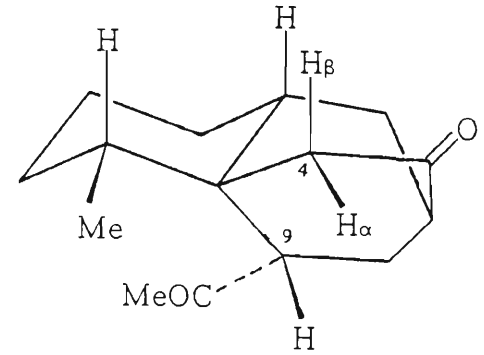
(94)



(95)



(96)



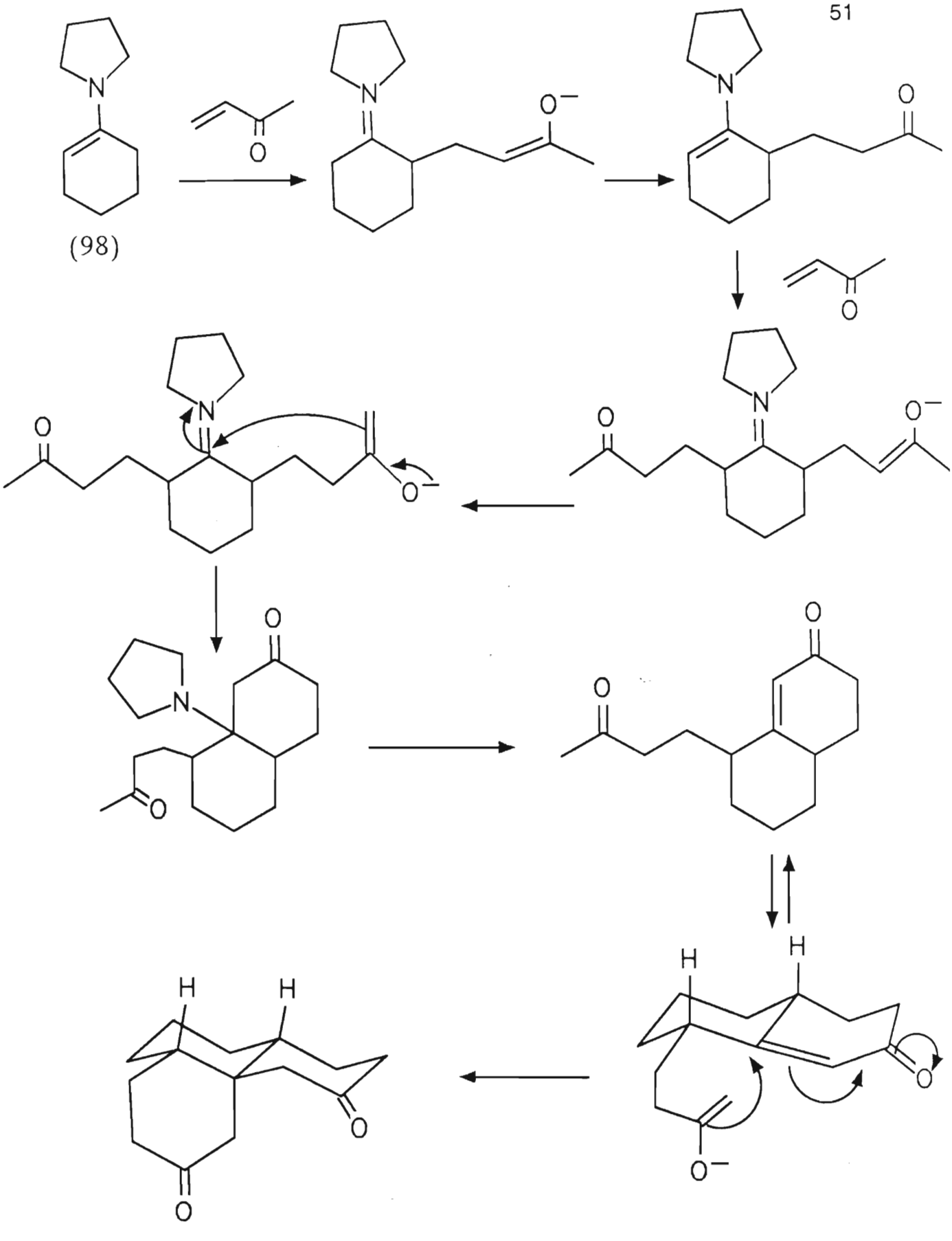
(97)

In this instance the linear annulation product proved to be the main component of the reaction mixture. This result differs from the corresponding reaction of the 4a-methyl dienamine but can readily be explained in terms of steric effects. The formation of (77; R = Me; R' = H) from the 4a-methyl dienamine is less favourable since β-face (axial) attack at C-3 is hindered by the 4a-methyl group and α-face (equatorial) attack is disfavoured on stereoelectronic grounds. However, β-face attack at C-3 of the 8-methyl dienamine is unimpeded resulting in an increased yield of the linear annulation product.

The reaction of MVK with the pyrrolidine dienamine of 3-methyl-$\Delta^{1,8a}$-2-octalone in methanol once again gave a complex mixture of products but it was possible to isolate the tricyclic dione (75; R" = Me; R,R' = H). The expected angular annulation product (72; R,R' = H; R" = Me) was not isolated from this reaction but once again steric and stereoelectronic effects could account for this. Since the methyl group at C-3 would be axially oriented to minimise $A^{1,2}$-strain,[38] reaction of MVK at C-1 would be impeded. Attack by MVK at the less reactive δ-position (C-8) would, however, not be impeded. The reaction in toluene was not investigated.

The last reaction of this series to be investigated was that of MVK with the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone. In methanol, two isomeric forms of the tricyclic dione (75; R,R',R" = H) were isolated [MP: 133 - 135°C (22%) and MP 165°C (3%)]. GLC showed the presence of a third product ($\simeq$ 20%) which

SCHEME 17



(98)

(75)

R, R', R" = H

was not isolated but from the observed trend in the course of the dienamine reactions is almost certainly the angular annulation product (72; R,R',R" = H). At this late stage of the investigation it was found that House *et al.*[40] had in fact already isolated the tricyclic dione (75; R,R',R" = H; MP: 160 - 162°C) as a by-product from the reaction of MVK with the pyrrolidine enamine of cyclohexanone in benzene. They proposed that their tricyclic dione was formed by 2,6-bis-alkylation of 1-N-pyrrolidinylcyclohexene (98) followed by a bis-cyclisation process (Scheme 17), rather than *via* the intermediacy of the dienamine.

The reaction was shown to give an increased yield in ethanol as expected since this solvent is known to promote the formation of 2,6-disubstituted products from cyclohexanone enamines,[62,63] thus further supporting their proposed pathway for diketone formation. They found no evidence for the formation of the diketone (75; R,R',R" = H) on reaction of dienamines (11 - 13; R,R',R" = H) with MVK in benzene or the reaction of $\Delta^{1,8a}$-2-octalone with MVK and pyrrolidine in benzene. The former reaction however, would be expected to give the linear annulation and [4+2] cycloaddition products as isolated in this investigation from the corresponding reaction in toluene, yet no mention of these products was made. The reaction of MVK with the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone in benzene, carried out in this investigation gave the expected Diels-Alder adducts (80) and (81) and the linear annulation product (77; R = Me; R' = H) in yields of 13, 4 and 10 % respectively. House *et al.* thus specifically excluded dienamines (11 - 13;

R,R',R" = H) and $\Delta^{1,8a}$-2-octalone as possible precursors to the tricyclic dione.

Despite the fact that their yield of the diketone increased considerably when the solvent was changed to ethanol, it is proposed that the tricyclic diones isolated throughout this investigation do not arise *via* a similar route since this would involve:

(i) hydrolysis of the dienamines under very mild conditions;

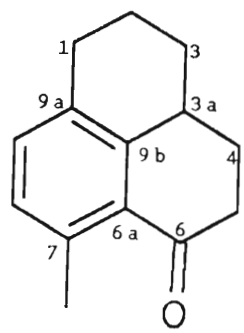
(ii) ring opening;

(iii) reformation of, in the case of the 4a- and 8-methyl dienamines, a 2,6- or a 2,2-disubstituted enamine; and

(iv) further alkylation to give the enamine or iminium salt of a trisubstituted ketone (*i.e.* 2-methyl-2,6-bis-3-oxobutylcyclohexanone).

Steps (iii) and (iv) for 2,2- or 2,6-disubstituted cyclohexanone enamines are rendered difficult, if not impossible, by developing $A^{1,3}$-strain[38] in a tertiary enamine, and would require forcing conditions. This is exemplified by the difficulty that was experienced in preparing the secondary enamine (imine) of a 2,2-disubstituted cyclohexanone[64] *via* the $TiC\ell_4$ method.[65] Furthermore the product isolated by House *et al.* corresponds to the minor isomer isolated here. If reversion of the dienamine to the mono-substituted cyclohexanone enamine had occurred, followed by further alkylation and recyclisation, then the isomer isolated by House *et al.* would also be the major product in this reaction. This is contrary to observation and confirms that tricyclic dione formation is occurring by δ-alkylation of the dienamines as shown in Schemes 11 and 14.

Further confirmation was provided by the results obtained when the reaction described by House *et al.* was repeated. Thus, when 1-N-pyrrolidinyl-cyclohexene was treated with MVK in ethanol, the main product isolated was again the tricyclic dione (75; R,R',R" = H; MP: 165°C; 38 %). The major product (75; R,R',R" = H; MP: 133 - 135°C) isolated from the reaction of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone with MVK was not isolated from this reaction but shown by GLC to be present in the crude reaction mixture to the extent of 5%.[a] Isothermal GLC (180°C) of the crude reaction mixture from the House reaction also showed products corresponding to the peaks at t_R 15,9 min. (6%[a]), 16,7 min., 17,4 min (4%[a]) and 26 min. (8%[a]) in addition to the two products just mentioned. The product corresponding to the peak at t_R 16,7 min. was isolated and shown to be 7-methyl-2,3,3a,4,5,6-hexahydrophenalen-6-one (99; 32%).



(99)

The product corresponding to the peak at t_R 26 min. could not be isolated but by comparison (GLC) with the crude reaction product obtained from the reaction of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone with MVK is most

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[a]Integrated GLC peak areas.

certainly the angular annulation product (72; R,R',R" = H). Both these products were not previously reported by House *et al.*

Also when the reaction of MVK with the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone was carried out in dry ethanol, the two isomeric forms of the tricyclic dione (75; R,R',R" = H; MP: 133 - 135°C and 165°C) were shown to be present to the extent of 11%[a] and 8%[a] respectively. The angular annulation product was present to the extent of 28%.[a]

The nmr spectra of the tricyclic products isolated during the course of this investigation were very complex, many of the spectra exhibiting surprising features which merit comment. Even at 500 MHz several regions of the ^{1}H-nmr spectrum consisted of overlapping areas of second order splitting so a completely unequivocal proton assignment could not be made. In structures (75) and (76) however, one or more of the protons alpha to the two carbonyl functions are sufficiently deshielded to appear outside the complex methylene envelope of the remaining protons thus making an unequivocal assignment possible. In addition to stereochemical assignments, this has led to the observation of some surprising variations in chemical shifts which have been attributed to long range shielding and deshielding effects associated with stereochemically rigid C-C and C-H sigma bonds.

In the 125 MHz ^{13}C-nmr spectrum of the tricyclic ketone (79; Scheme 11) the signals due to the C-1 and C-11 carbons can be assigned readily (δ_C: 45,10

and 45,15) since these are alpha to a carbonyl group and a quaternary centre and are therefore the lowest field methylene signals in the ^{13}C-nmr spectrum. The protons attached to these carbons (HETCOR) appear as doublets at δ 2,12; 2,24; 2,42 and 2,74 in the 500 MHz ^{1}H-nmr spectrum. The two doublets at high field, δ 2,12 and 2,24 are further split into weakly coupled triplets and doublets, respectively. The splitting arises from W-coupling and allows unequivocal assignment of the signals to be made. The doublet of triplets at δ 2,12 is assigned to be the equatorial proton at C-11 which is W-coupled to the C-9 equatorial proton and the methine proton at C-7a (δ 1,83). This assignment was confirmed by decoupling of the C-7a proton when the signal due to the C-11 equatorial proton collapsed to a doublet of doublets. The axial proton at C-11, to which the equatorial proton is geminally coupled (COSY), appears as a sharp doublet at **lower field** (δ_H 2,74) than the equatorial proton despite the latter being in the plane and under the deshielding influence of the adjacent carbonyl group ! Similarly at C-1, the equatorial proton is W-coupled to the equatorial proton at C-3 and is at higher field (δ_H 2,24) than the axial proton at C-1 which appears as a sharp doublet at δ_H 2,42.

The effect of alkyl substituents on the chemical shifts of cyclohexane ring protons has been summarised by Booth.[66] The introduction of an equatorial methyl group causes considerable upfield shifts (0,3 - 0,5 ppm) in the signals of both axial and equatorial protons on the adjacent carbon, whereas an axial methyl group causes an upfield shift of an adjacent equatorial proton ($\simeq$ 0,4

ppm) and a **downfield** shift of the adjacent axial proton (≃ 0,2 ppm). A 1,3-diaxial interaction between an axial methyl group and an axial proton causes a downfield shift of the latter (≃ 0,2 - 0,3 ppm).[67]

If it is assumed that a ring residue has a similar effect to a methyl group then the lowfield shifts of the axial protons at C-1 and C-11 relative to the equatorial protons at these positions can be attributed primarily to a shielding of the equatorial protons by the adjacent equatorially and axially oriented ring residues. This would reduce or cancel the deshielding influence of the neighbouring carbonyl group. Conversely the axial protons are deshielded by 1,3-diaxial interactions with ring residues (two for the C-11 axial proton) or 4a-methyl group (C-1 axial proton).

In the case of the [4+2] cycloaddition products [structures (80) and (81); Scheme 12] arising from the reaction of MVK with the dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone in toluene, the effect of nearby ring residues on proton chemical shifts is similar and perhaps more unusual. The structure of (80) was determined by X-ray analysis. The 200 MHz ^{1}H-nmr spectrum shows a lowfield signal at δ 3,57 as an overlaid quartet of doublets and is assigned to H-9. The splitting arises from vicinal coupling with the H-10 protons and W-coupling with the H_β-4 proton. At higher field there is a sharp doublet at δ 2,95 which shows no W-coupling and is therefore assigned to H_α-4 since it is deshielded by being 1,3-diaxial to the acetyl group at C-9. The H_α-4 proton is also geminally coupled (COSY) to a signal at δ 1,93 which appears as a doublet of doublets

and is therefore assigned to H_{β}-4. The structure of the stereoisomer (81) was assigned as shown since the H-9 signal again appeared as a quartet of doublets (δ 3,04) due to vicinal and W-coupling. The structure (82), a diastereomer of (80) which would have resulted from α-face attack on the dienamine at C-3 and C-8a, is positively ruled out since the H-9 proton in this structure would not show W-coupling with any other proton. In addition, the 200 MHz ^{1}H-nmr of (81) showed a doublet of doublets at δ 2,59 and a sharp doublet at δ2,14. The former signal is assigned to H_a-4 since it shows W-coupling (to H-9) and the latter to H_b-4. Thus the situation again arises where the proton (H_a-4) which is most distant from the deshielding effect of a carbonyl function, is at lower field than a proton (H_b-4) which is 1,3-diaxial to the acetyl group at C-9. The deshielding of H_a-4 is attributed to the axially oriented ring residue at C-8a and that at C-5 which has a similar 1,3-diaxial-type orientation to H_a-4. More specifically of course, the deshielding of the H_a-4 proton can be primarily attributed to intramolecular van der Waal's compression forces on H_a-4, similar to the mutual deshielding of axial protons at positions 2,4,6 and 8 in cis-decalin.[66,67] The H_{β}-4 proton signal in (80) is at higher field (δ 1,93) than the H_a-4 proton signal in (81) since the former is 1,3-diaxial to the C-8a methyl group whereas the latter (δ 2,59) is 1,3-diaxial to the two ring residues mentioned above. Perhaps even more surprising than this is the large difference in chemical shifts (0,81 ppm) between the two protons H_{α}-4 (δ 2,95) and H_b-4 (δ 2,14) 1,3-diaxial to the acetyl group in (80) and (81). This difference is attributed to the magnetic anisotropy of the 5-6 carbon-carbon bonds in the two isomers. The H_{α}-4 proton lies in the deshielding

"cone" of the 5-6 bond in (80), whereas the H_b-4 proton lies in the shielding region of the 5-6 bond in (81).

In the case of structure (78) both the equatorial and axial protons at C-1 and C-11 have a path for W-coupling, the former with the equatorial proton at C-3 or C-9, and the latter with each other. It was therefore not possible to distinguish between the two sets of protons by the presence or absence of long-range coupling and an unequivocal assignment of the ^{1}H-nmr signals was not attempted.

Four stereoisomers (94 - 97; Scheme 16) are possible for the [4+2] cycloaddition products arising from the 8-methyl-$\Delta^{1,8a}$-2-octalone dienamine, but only two isomers were isolated (as amber oils). Structures (94) and (95) would arise from β-face attack and structures (96) and (97) from α-face attack on the dienamine. The main difference to be expected in the ^{1}H-nmr spectra of these isomers is that in every case except (94) the H-9 proton should show evidence of W-coupling either to one of the H-4 protons or the H-8a proton. One of the isomers isolated gave a triplet at δ 3,07 which is assigned to H-9, vicinally coupled to the H-10 protons, and showing no splitting due to W-coupling. This isomer was therefore assigned the structure (94). The other isomer showed three lowfield signals [at δ 2,94 (dd); 2,8 qd, and 2,65 (dd)] due to the H-4 and H-9 protons. All three protons thus exhibit W-coupling. The only stereoisomer where this is possible is structure (95). In (96) H_α-4 would not be W-coupled, and in (97) neither of the H-4 protons would be W-

coupled. The magnitude of the geminal coupling constants (19 Hz) enabled the assignment of the signals at δ 2,94 and 2,65 to be assigned to the two H-4 protons of (95), and the magnitude of the W-coupling constants (2,0 and 1,5 Hz) means the latter δ 2,65 signal is due to H_a-4 (W-coupled to H-9) and the former (δ 2,94) is due to H_b-4 (W-coupled to H-8a).

Therefore both isomers have arisen by β-face attack, isomer (94) being slightly favoured over (95) presumably due to steric interactions between the C-9 acetyl group and the C-5 methyl group (presumed to be equatorial) in the latter.

In the case of the [4+2] cycloaddition of MVK to the unsubstituted $\Delta^{1,8a}$-2-octalone dienamine, only one stereoisomer of (76; R,R' = H) was isolated. The stereochemistry however, has not been assigned.

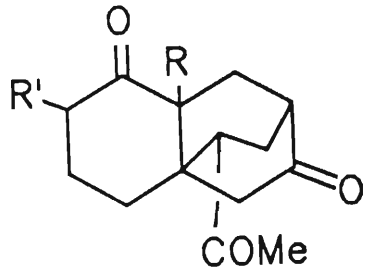
2.2 REACTION OF METHYL VINYL KETONE WITH DIENAMINES DERIVED FROM 5-OXO-$\Delta^{1,8a}$-2-OCTALONES, TETRAHYDRO-INDAN-5-ONE AND ISOPHORONE

As mentioned earlier (see Introduction, Section 1.4) Pandit *et al.*[56] reported that β,δ-annulation and aromatization occurred on reaction of methyl vinyl ketone (MVK) with the pyrrolidine dienamine of 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone (56) to give (58). As these authors pointed out, this must involve initial reaction at the less reactive[68] δ-position of the dienamine followed by cyclisation onto the more reactive β-position. This is surprising, particularly in view of the fact that in the investigation of the reaction of MVK with $\Delta^{1,8a}$-2-octalone dienamines (11 -13) no evidence for β,δ-annulation was found. The main products identified, depending on the solvent employed for the reaction were the γ,δ-annulation product (75) and the Diels-Alder adduct (76), and variable amounts of the linear (77) and angular (72) annulation products. In a related investigation with isophorone dienamines (14 - 16), Nozaki *et al.*[44] isolated only the products of Stork alkylation (48)[4,69] and Diels-Alder cycloaddition (46). There was no evidence for the reaction of MVK with either of the endo- or exocyclic δ-positions of the dienamines.

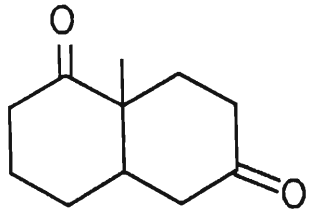
The apparent inconsistency in the regioselectivity of these related reactions is difficult to understand, particularly since the Diels-Alder products (76) and (46), and the linear annulation product (77) are derived from the cross-conjugated dienamines (13) and (16) which were not present to any detectable extent in the dienamine mixtures obtained by condensation of $\Delta^{1,8a}$-2-octalones and isophorone with pyrrolidine.[19] Some of this work was therefore repeated and the reaction of MVK applied to two other dienamines derived from 5,6,7,7a-tetrahydroindan-5-one and 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone, in an attempt to ascertain the reason for the apparently random changes in the regioselectivity of the reactions. The observations made by Pandit and Nozaki *et al.* were corroborated but the reactions were found to be more complex than their reports indicate and several additional products have now been isolated.

The reaction of MVK with the pyrrolidine dienamine of 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone in boiling toluene gave a multi-component mixture. Capillary GLC analysis (220°C) showed that there were four main components having retention times (min.) (and integrated peak areas) 3,7 (6%), 4,2 (19,5%, starting octalone), 9,2 (23%), and 9,9 (32%). Flash chromatographic purification resulted in the isolation of all the components except the starting octalone. The main component (t_R 9,9 min.) was identified as the [4+2] cycloaddition product (100; R = Me; R' = H). The nmr spectral and stereochemical assignments of this compound are discussed later. The second component isolated was the aromatized β,δ-annulation product (58)

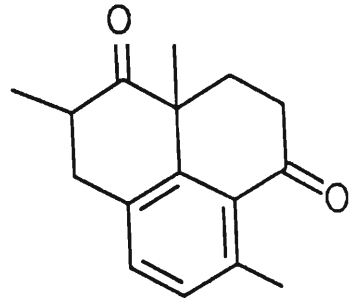
previously reported by Pandit *et al.*[56] The third product proved to be (101) [see Experimental Section 3.7] produced during the disproportionation process involved in the aromatization of the β,δ-annulation product.



(100)



(101)



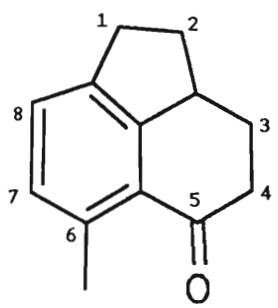
(102)

The reaction of MVK was then applied to the pyrrolidine dienamine of 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone. In this case GLC analysis (180°C) showed, apart from unchanged starting material, that the reaction mixture consisted of only three components, t_R 28 min. (4%), 29 min. (7%) and 32 min. (32%). The two minor components could not be isolated but GC-MS showed that they had the correct molecular ion (m/e 242) for the aromatized product (102). The main component again proved to be the [4+2] cycloaddition product (100; R,R' = Me) [*vide infra*].

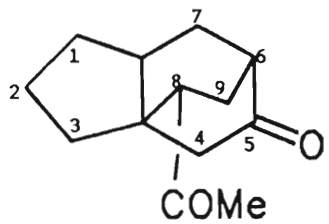
In neither reaction is there any evidence for the formation of the γ,δ-annulation products of type (75) or linear or angular annulation products of types (77) and

(72) although of course, one or more of these could have been produced to a small extent, particularly in the first reaction, but which could not be isolated.

Attention was then focused on the reaction of MVK with the pyrrolidine dienamine of tetrahydroindan-5-one. In this case the course of the reaction was investigated in methanol and toluene, as done previously for the corresponding reaction with dienamines derived from $\Delta^{1,8a}$-2-octalones. GLC analysis (180°C) showed the formation of an approximately fifteen component mixture, excluding unchanged staring materials ! The four main components gave peaks of retention times 10,6; 14,0; 18,4; and 28,9 min., and the variation in the component proportions with changes in the experimental conditions are summarised in Table 3. The first two components were isolated by flash chromatography and identified as the aromatized β,δ-annulation product (103a) and the [4+2] cycloaddition product (103b), respectively (see Experimental Section 3.9). The remaining two components of longer retention time could not be isolated in a sufficiently pure state for unambiguous identification are designated (A) and (B) in Table 3.



(103a)



(103b)

TABLE 3

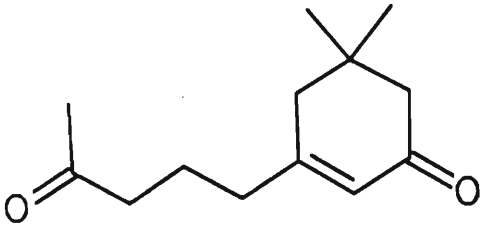
Main Products from 5,6,7,7a-tetrahydroindan-5-one.

SOLVENT	REACTION TIME (h)	PRODUCTS (%)*			
		103a	103b	A†	B†
Methanol	4	32	3	4	4
Methanol	4‡	14	6	18	13
Toluene	4	6	28	11	0,3
Toluene	50	5	18	18	2

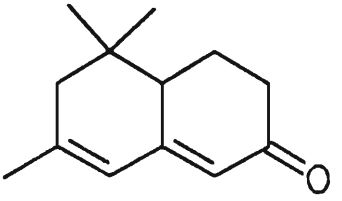
* GLC integrated peak areas.
† Unidentified.
‡ Second run.

As can be seen there are considerable variations in the component ratios, even when the same conditions are used. Nevertheless there appears to be a degree of solvent dependent regioselectivity in that initial reaction at the less reactive δ-position of the linear exocyclic dienamine is favoured in methanol leading to the aromatized β,δ-annulation product (103a) and cycloaddition across the β,β'-positions of the cross-conjugated dienamine is favoured in toluene, leading to (103b). This parallels the observations on the corresponding reaction with the dienamines derived form the $\Delta^{1,8a}$-2-octalones (see Section 3.3.2) except that initial δ-alkylation was followed by cyclisation at the γ-position, instead of the β-position, leading to the γ,δ-annulation product (75) instead of the aromatized product (103a). Although the changes are not so marked in the indanone reaction, the explanation offered for the solvent dependent regioselectivity is the same. That is, in aprotic solvents of low

dielectric constant, charge separation in the ground and transition states is less favoured and the reaction becomes orbital controlled. In other words, the activation energy for a [4+2] cycloaddition must be less than that for the formation of a zwitterionic intermediate in aprotic solvents. The corresponding solvent dependence of the 5-oxo-$\Delta^{1,8a}$-2-octalone dienamine reactions was not investigated.



(104)



(105)

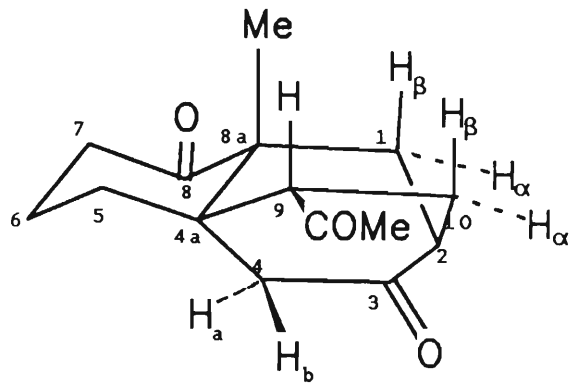
Finally, the investigation of Nozaki[44] into the reaction of MVK with isophorone dienamines was re-examined. In this case the morpholine dienamine was used. In addition to the two products reported by Nozaki [(46) and (48)] two new products were isolated from this reaction, namely the δ-alkylation product (104) and the naphthalenone (105) [see Experimental Section 3.10.1]. Surprisingly there was no evidence for the formation of a γ,δ- or β,δ-annulation product. The main products were those of β-alkylation (48) of the linear dienamine in methanol and [4+2] cycloaddition (46) in toluene.

The stereochemistry of the [4+2] cycloadducts produced from each of the dienamine reactions we have studied is now discussed. In each case cycloaddition may occur from the β-face or the α-face of the dienamine. In the absence of X-ray data, the stereochemical assignments have been based on 1D and 2D (COSY/HETCOR) spectral analysis.

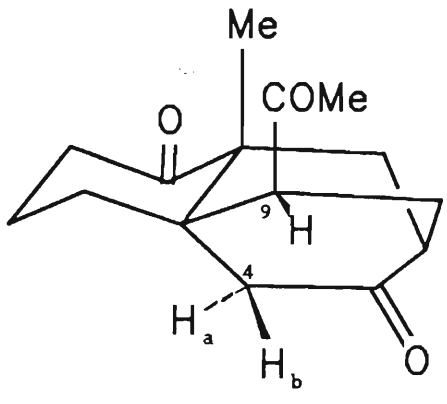
In the case of the cycloadduct (100;R = Me; R' = H) obtained from the 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone the $^{1}H/^{13}C$ assignments were made as follows. The lowest field doublet (δ_C 45,18) is assigned to C-9, deshielded by the adjacent carbonyl group and three α- and five β-carbons; H-9 appears at approximately δ_H 2,76 (HETCOR). The higher field doublet (δ 43,03) is therefore due to C-2, deshielded by three α- and three β-carbons, and H-2 is a multiplet at δ 2,46 (HETCOR). The lowest field triplet (δ_C 42,25) is assigned to C-4, deshielded by the adjacent carbonyl and two α- and four β-carbons; H-4 therefore appears as a doublet at δ 3,16 (J = 19,2 Hz) and a doublet of doublets at δ 2,22 (J = 19,2 and 2,3 Hz). The former signal is assigned to H_α-4 (being in a 1,3-diaxial relationship to the C-9 acetyl group) and the latter to H_β-4 W-coupled to H-9. The next two triplets appear at δ_C 36,68 and 33,08 and are assigned to C-7 and C-1, respectively, since C-7 is deshielded by the adjacent carbonyl group and two α- and two β-carbons, and C-1 is deshielded by two α- and five β-carbons. The assignment is supported by the associated proton coupling correlations; H_α-1 (δ_H 2,82) and H_β-1 (δ_H 1,36) are both coupled to H-2, and the high field signal (H_β-1) is W-coupled to H_b-10 (δ_H 1,6). The low field signal (δ_H 2,82) is assigned to H_α-1 since this proton lies closest

to the plane of the C-8 carbonyl group. The H-7 protons therefore appear at δ_H 2,64 and 2,36 (COSY/HETCOR). The highest field triplet (δ_C 22,13) is assigned to C-6, deshielded by two α- and two β-carbons. Both the remaining methylene carbons (C-5 and C-10 are deshielded by two α- and four β-carbons. However, W-coupling between H_β-1 and H_a-10 establishes the signal at δ_C 28,45 as C-10 and that at δ_C 26,84 is therefore due to C-5. The remaining proton signals are overlaid and approximate chemical shift assignments are given in the Experimental.

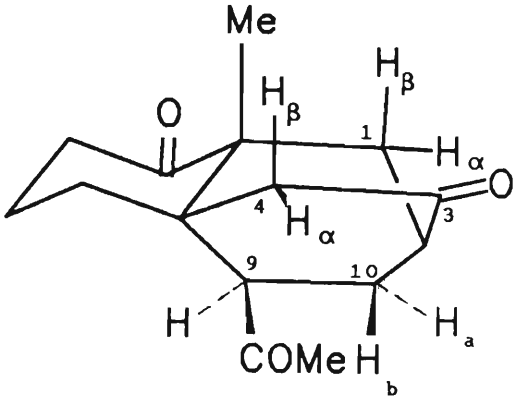
SCHEME 18



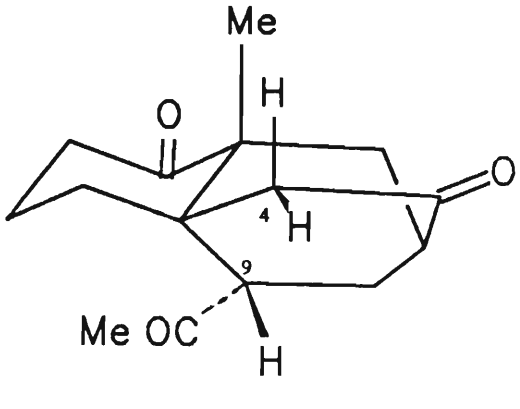
(106)



(107)



(108)

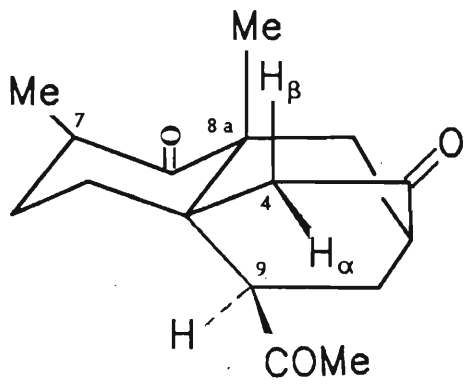


(109)

There are four stereoisomers (106 - 109) possible for this cycloadduct and these are depicted in Scheme 18. Structures (107) and (109) can be ruled out immediately since neither of the H-4 protons or the H-9 proton would show evidence of W-coupling. Assuming that the assignments of H_α-1 and H_β-1 signals are correct then the cycloadduct must be assigned structure (108) in which the **high field** H_β-1 proton (δ_H 1,36) is W-coupled to the H_b-10 proton. In structure (106) the **low field** H_α-1 proton would show W-coupling (to H_α-10) and is therefore ruled out. Formation of (106) is also less likely on theoretical grounds since cycloaddition would have to occur from the more hindered β-face, syn to the angular methyl group at C-8a, whereas (108) arises by cycloaddition to the less hindered α-face. The low field shift of the H_α-4 proton signal (δ_H 3,16 in (108) can also be attributed to the fact that it lies in the deshielding "cone" of the 5-6 carbon-carbon bond, in addition to it being 1,3-diaxial to the C-9 acetyl group, as was previously postulated for the H_α-4 proton (δ_H 2,95) in the corresponding cycloadduct (80) from the 4a-methyl-$\Delta^{1,8a}$-2-octalone pyrrolidine dienamine. In structure (106) the H_b-4 proton lies in the shielding "cone" of the 5-6 carbon-carbon bond and would be expected to give a signal to higher field ($\simeq \delta_H$ 2,14). One final point of interest is that the 2D (COSY) spectrum shows a weak coupling interaction between the **low field** H_α-1 proton (δ_H 2,82) and the C-8a methyl group which is not evident in the 1D spectrum. Such four bond coupling has been shown to be dependent on the H-C-C-C dihedral angle (ϕ) and is greatest when ϕ = 0° or 180°.[70] This observation suggests that the boat conformations are not ideal and have become twisted to alleviate non-bonded H···H and C···H

repulsion caused by eclipsing and thus make the H_{α}-1-C_1-C_{8a}-CH_3 dihedral angle more favourable for long-range coupling between H_{α}-1 and the methyl group.

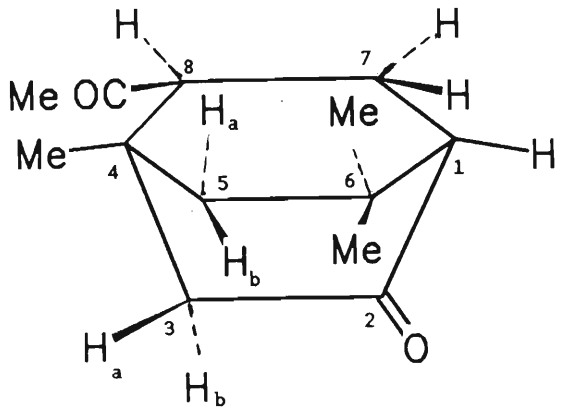
The $^1H/^{13}C$-nmr assignments for the 7,8a-dimethyl analogue(100; R,R' = Me) were made in similar manner. The main differences in the ^{13}C-nmr spectrum were the signals due to C-7 and C-6 which were shifted to lower field by approximately 3 and 9 ppm, respectively, owing to the α- and β-deshielding effects of the C-7 methyl group. Interestingly the low field H-1 proton (δ_H 2,88) again showed evidence of coupling to the C-8a methyl group (COSY). The remaining assignments are given in the Experimental (see Section 3.8). Based on the W-coupling evident between the high field H-1 proton and H-10 (COSY) the stereochemistry is assigned as for (108)(i.e. structure 110) with the C-7 methyl group equatorially oriented otherwise steric compression effects would be observable on carbons 5 and 8a, the chemical shifts of which are virtually unchanged from those of (108). W-coupling was also evident between H-9 and H_{β}-4. As expected on steric grounds cycloaddition has therefore again occurred from the less hindered α-face.



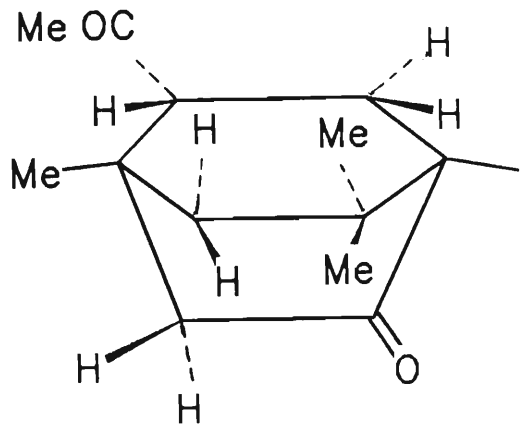
(110)

In the case of the cycloaddition to the isophorone dienamine, α-face attack merely gives the enantiomer of β-face attack. Hence only two structures have to be considered namely (111) and the diastereomer (112) (Scheme 19).

SCHEME 19



(111)

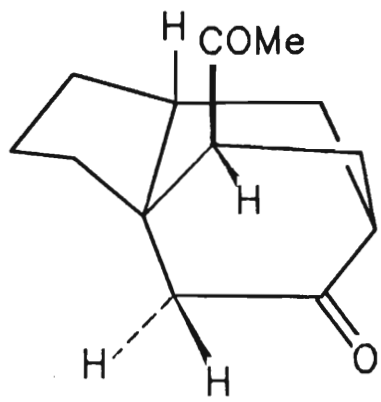


(112)

The $^1H/^{13}C$-nmr assignments are as follows. The C-1 and C-8 methine carbons have the same number of α- and β-substituents (3α, 5β) and each is α- to a carbonyl. However, H-8 will be more strongly coupled with the vicinal protons at H-7 (dihedral angles $\phi \simeq 0°$ and 120°) than is H-1 (dihedral angles $\phi \simeq 60°$ and 60°) and H-8 will be W-coupled with H_b-3 whereas H-1 has no W-coupling possible. The low field oqd (δ_H 2,77; δ_C 50,48) is therefore assigned to H-8 and the weakly coupled dd at δ_H 1,96 is assigned to H-1 (δ_C 54,25) (HETCOR). Of the methylene carbons C-5 has the most deshielding β-substituents (six) and is therefore assigned to the lowest field triplet (δ_C 51,3). This assignment is confirmed by the fact that the H-5 protons appear as a doublet at δ_H 1,25

assigned to H_b-5 which is only coupled to H_a-5, and a doublet of doublets at δ_H 1,41 assigned to H_a-5 which is also W-coupled to H_a-3. The C-3 signal therefore appears at δ_C 44,11 (HETCOR) and the H_b-3 proton at δ_H 1,7 as a doublet of doublets since this is W-coupled to H-8. The remaining methylene signal due to C-7 appears at δ_C 24,13 and the H-7 proton signals at δ_H 1,8 and 2,2 (HETCOR). From this proton assignment the stereochemistry of the cycloadduct is assigned as in structure (111). Structure (112) can be unequivocally ruled out since both H-5 protons would show W-coupling (to H-8 or H_a-3).

The ^{1}H-nmr spectrum of the cycloadduct derived from the indanone dienamine was extremely complex and the stereochemistry could not be assigned. Apart from the acetyl group, only signals due to H-6 (δ_H 2,33) and H-8 (δ_H 2,79) could be unequivocally assigned. The fact that the latter showed W-coupling did, however, rule out structure (113) since H-8 in this stereoisomer would not show any W-coupling.



(113)

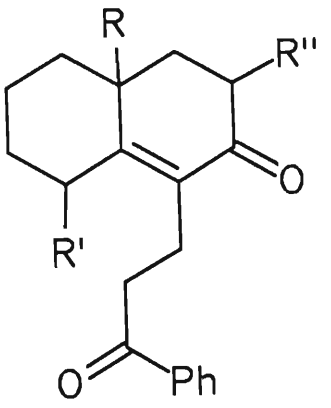
The $^{1}H/^{13}C$-nmr assignments for 6-methyl-1,2,2a,3,4,5-hexahydroacenaphthyl-en-5-one (103a) were based on the following reasoning. The proton H_a-2 is the only methine proton (HETCOR) and is therefore readily assigned to the multiplet at δ_H 3,31. The signal at δ_H 2,8 - 3,08 is assigned to the H-1 protons since the α-proton of indane is at lower field (δ_H 2,91) than the protons of the methylene group α- to the carbonyl group in α-tetralone (δ_H 2,58).[71] The only protons which H_a-2 and H-1 are both coupled to are the H-2 protons which are therefore assigned to the signals at approximately δ_H 2,4 (H_β-2) and δ_H 1,65 (H_α-2) (COSY). The only other signals due to the protons of one methylene group are those at δ_H 2,5 - 2,8 (HETCOR) and are therefore assigned to the H-4 protons, coupled to the H-3 protons at approximately δ_H 1,75 (H_α-3) and δ_H 2,55 (H_β-3). The H_α-2 and H_α-3 protons are further from the plane of the aromatic ring than the H_β-2 and H_β-3 protons and are therefore less deshielded. The ^{13}C-nmr assignments follow from the proton assignments (HETCOR) [see Experimental Section 3.9.1].

Although more light has been thrown on these complex dienamine reactions, the reason for the change from γ,δ-annulation in the case of $\Delta^{1,8a}$-2-octalone dienamines to β,δ-annulation in the case of 5-oxo-$\Delta^{1,8a}$-2-octalone and tetrahydroindan-5-one dienamines remains inexplicable. Presumably there are subtle conformational, steric or thermodynamic factors operating which are not immediately apparent.

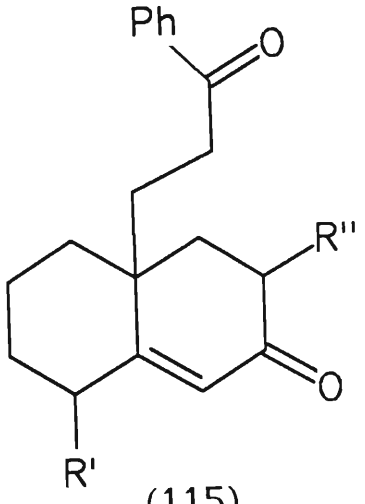
2.3 REACTION OF PHENYL VINYL KETONE WITH DIENAMINES DERIVED FROM $\Delta^{1,8a}$-2-OCTALONES

In an analogous manner to the reaction of MVK with the dienamines derived from $\Delta^{1,8a}$-2-octalones, the corresponding reactions using phenyl vinyl ketone (PVK) were investigated. For the same reasons discussed earlier (Section 2.1), it was anticipated that the course of the reaction of PVK would show similar solvent dependent regioselectivity as observed for the corresponding reactions of methyl acrylate and acrylonitrile,[50] even though we failed to isolate any of the β- or δ-alkylation products from the corresponding reactions using MVK. Thus dienamines (11 and 12; R" = H; R,R' = H, Me) would be expected to give the β-alkylation products (114; R,R',R" = H, Me) in both methanol and toluene, and dienamines (11 and 12; R" = Me; R,R' = H) should give the β-alkylation products (115 or 116; R,R',R" = H, Me) in toluene.

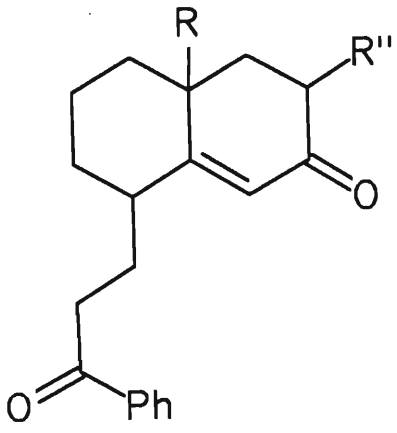
The formation of cycloadducts (117; R,R',R" = H, Me) from the reaction of PVK with the dienamines in toluene would again be expected based on the corresponding reactions of MVK.



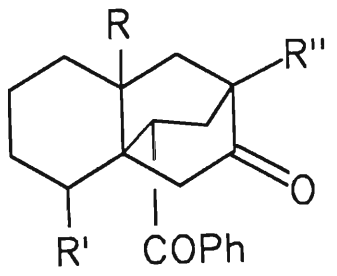
(114)



(115)



(116)



(117)

The first reaction studied was that of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone. The crude reaction products obtained from the reactions in boiling methanol and boiling toluene were both shown (GLC and TLC) to be complex multi-component mixtures. Two isomeric forms of the Diels-Alder adduct (117; R,R',R" = H) were isolated and shown by GLC to be present in both reaction mixtures, the reaction in methanol giving a slightly improved combined yield (35%). This result is remarkable since not only are the cycloadducts being formed *via* the cross-conjugated dienamine but are now the major products of the reaction in methanol, and in better yield compared to the reaction in

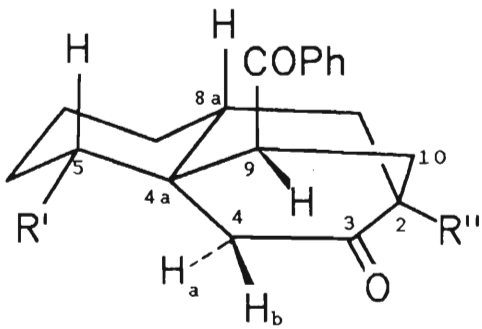
toluene. This is in stark contrast to the previously discussed reactions of MVK where it was proposed that the preferential formation of the cycloadducts in toluene and not methanol was due to the reaction being orbital controlled in a solvent of low dielectric constant. A possible explanation for this not being applicable to the PVK reactions is that δ-attack by MVK is rendered irreversible by β,δ- or γ,δ-annulation processes. In the case of PVK, γ,δ-annulation cannot occur, and the lower reactivity of the carbonyl group conjugated with the phenyl ring in PVK must make the β,δ-annulation process less favourable. δ-Attack by PVK could therefore be reversible thus allowing [4+2] cyclo-addition to become the most favoured process in both solvents. The only evidence for δ-attack by PVK has occurred in the reaction of the 4a-methyl-$\Delta^{1,8a}$-2-octalone dienamine and here δ-attack has apparently been rendered irreversible by capture of the initially formed zwitterion by a **second** molecule of PVK, followed by β,δ-annulation (*vide infra*).

The reaction of PVK with the pyrrolidine dienamines of the other $\Delta^{1,8a}$-2-octalones in methanol were subsequently investigated and with the exception of the reaction of the 4a-methyl dienamine, a similar trend was found. From the reaction of the 8-methyl dienamine one isomeric form of the Diels-Alder adduct (117; R' = Me; R,R" = H) was isolated and from the reaction of the 3-methyl dienamine two isomeric forms of the Diels-Alder adduct (117; R" = Me; R,R' = H) were isolated.

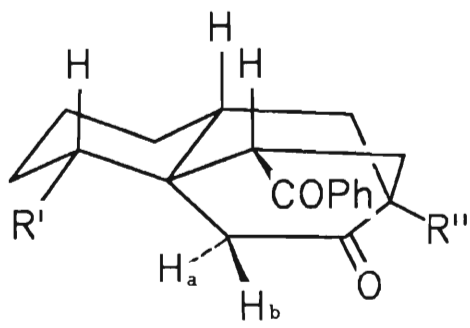
The NMR spectra of all the Diels-Alder adducts isolated were complex. In each case however, one or more of the protons were sufficiently deshielded to appear outside the complex methylene envelope of the remaining protons and showed the presence or absence of W-coupling thus making unequivocal proton and therefore stereochemical assignments possible.

There are four stereoisomers (118 - 121) possible for the cycloadducts arising from the reaction of PVK with the dienamines derived from $\Delta^{1,8a}$-2-octalones and these are depicted in Scheme 20. Structures (118) and (119) arise from β-face attack and structures (120) and (121) from α-face attack. The main difference to be expected in the spectra of these isomers is that in every case except (118) the H-9 proton should show evidence of W-coupling either to one of the H-4 protons or the H-8a proton.

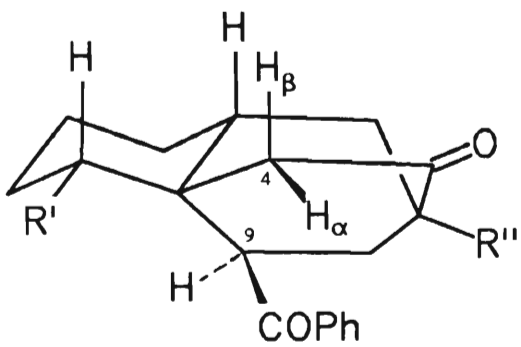
SCHEME 20

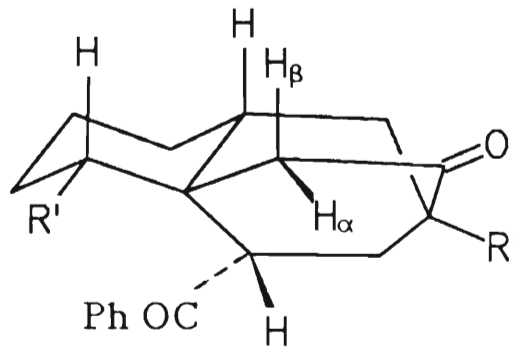


(118)



(119)





From the reaction of the dienamine derived from $\Delta^{1,8a}$-2-octalone one of the isomers of (117; R,R',R" = H) isolated gave a doublet of doublets at δ_H 3,65 and is assigned to H-9, vicinally coupled to the H-10 protons. The H-9 proton shows no W-coupling and therefore structure (118; R,R" = H) arising from β-face attack at C-3 and C-8a of the dienamine is assigned to this compound. The magnitude of the geminal coupling constants (19 Hz) enabled the signals at δ_H 1,86 and δ_H 2,85 to be assigned to the H-4 protons. The former signal is due to H_b-4 since it shows W-coupling (J = 1 Hz) to H-8a and the latter signal due to H_a-4 since there is no splitting due to W-coupling. The carbon assignments follow from the proton assignments (COSY/HETCOR) except for C-8a and C-2. The former is assigned to the signal at δ_C 29,51 since although it is subject to the deshielding effects of three α- and five β-carbons, there is a high field shift arising from the steric compression exerted by the C-9 benzoyl group. The C-2 carbon (δ_C 42,91) is deshielded by the alpha effect of the carbonyl group in addition to the three α- and three β- carbons. Assignment of C-2 thus enables the assignment (HETCOR) of the signal at δ_H 2,40 to H-2. The signal due to H-8a appears in the complex multiplet at δ_H 2,19 - 2,38.

The other isomer obtained from the reaction of the $\Delta^{1,8a}$-2-octalone dienamine, although not pure was assigned to structure (120; R',R" = H) on the basis of certain features evident in the ^{1}H-nmr spectrum. The low field signal (δ_H 3,61) is again attributed to the H-9 proton and appears as an overlaid triplet of doublets. The fact that this signal shows W-coupling immediately rules out

structure (118) in which the H-9 proton is not W-coupled to any other proton. The doublet at δ_H 2,10 and the doublet of doublets at δ_H 2,56 must arise from the H-4 protons. The latter signal is assigned to H_β-4 since it is W-coupled to H-9 and the former signal is therefore assigned to H_α-4 which shows no evidence of W-coupling. In structure (119) both H-4 protons would be W-coupled (H_a-4 to H-9 and H_b-4 to H-8a) whereas in structure (121) neither of the H-4 protons would be W-coupled. The assignment of this compound to structure (120), arising from α-face attack is therefore confirmed. The ^{13}C-nmr spectrum shows three methine signals at δ_C 39,02, 42,61 and 48,19 and these are assigned to C-8a, C-2 and C-9 respectively by virtue of the deshielding effects of the α- and β-substituents. There is only one fully substituted carbon and is thus assigned to C-4a. The lowest field methylene signal is assigned to C-4 since it is the only one α- to a carbonyl group.

From the reaction of the 8-methyl dienamine only one isomer of the Diels-Alder adduct (117; R' = Me; R,R" = H) was isolated. The ^{1}H-nmr spectrum shows a low field signal at δ_H 3,79 as a doublet of doublets and is assigned to the H-9 proton vicinally coupled to the H-10 protons. The signal shows no further splitting due to W-coupling. Once again the only structure where this is possible is (118; R' = Me; R" = H) arising from β-face attack on the dienamine at C-3 and C-8a. At higher field there is a sharp doublet at δ_H 2,53 and is assigned to H_a-4. This proton is geminally coupled (COSY) to a signal at δ_H 2,01 which appears as an overlaid doublet of doublets and is therefore assigned to H_b-4 (W-coupled to H-8a). The assignment of the lowest field

doublet at δ_C 44,29 (C-9) in the ^{13}C-nmr spectrum follows from the proton assignments and from the HETCOR spectrum. The three higher field doublets at δ_C 30,87; 34,98 and 43,27 are assigned to C-8a, C-5 and C-2 respectively since the C-2 carbon is deshielded by the carbonyl group and C-8a is shielded by the steric compression arising from the C-9 benzoyl group. The assignment of the signals at δ_H 2,66 and 2,40 to H-8a (1,3-diaxial to a benzoyl group) and H-2 (alpha to a carbonyl group) follow from the carbon assignments (HETCOR).

The preferred formation of structure (118; R' = Me; R" = H) can readily be explained in terms of steric effects. In structure (119; R' = Me; R" = H) there would be considerable steric interactions between the bulky benzoyl group and the C-5 methyl group (presumed to be equatorial) and therefore this structure would be disfavoured. Similarly structures (120) and (121) would be disfavoured due to steric interactions between the benzoyl group and the C-5 methyl group in structure (120) and the axial C-6 proton in structure (121).

The ^{1}H-nmr spectrum of the main component isolated from the reaction of the 3-methyl dienamine showed a low field signal at δ_H 3,67 as a triplet of doublets arising from the H-9 proton vicinally coupled to the H-10 protons and W-coupled to H_a-4. The only structure where this is possible is (119; R" = Me; R,R' = H) arising from β-face attack at C-3 and C-8a of the dienamine and is therefore assigned to this isomer. In structure (120) H_α-4 would not show W-coupling and in (121) neither of the H-4 protons would show W-coupling. At

higher field there is a quartet of doublets at δ_H 2,58 geminally coupled and W-coupled (COSY). This signal is assigned to the H-4 protons (H_a-4 is W-coupled to H-9 and H_b-4 is W-coupled to H-8a). The doublet of doublets at δ_H 2,04 is assigned to H_β-1 which is both geminally (COSY) and vicinally coupled to H-8a. At δ_H 1,91 there is a weakly split doublet arising from the two magnetically equivalent H-10 protons vicinally coupled to H-9. The splitting is due to H_α-10 being W-coupled to H_α-1. The carbon assignments follow from the proton assignments and from the HETCOR spectrum. The lowest field doublet at δ_C 49,11 is again assigned to C-9. The only other doublet at δ_C 39,94 must therefore be due to C-8a.

The other isomer isolated from the reaction of the 3-methyl dienamine gave a signal at δ_H 3,67 as a doublet of doublets and is assigned to H-9 vicinally coupled to the H-10 protons. There is no further splitting due to the H-9 proton being W-coupled and therefore this isomer is assigned as the diastereomer of (119) (i.e. structure 118; R" = Me; R' = H) also arising from β-face attack on the dienamine at C-3 and C-8a. At higher field there is a sharp doublet at δ_H 2,86 which shows no W-coupling and is therefore assigned to H_a-4. This proton is geminally coupled (COSY) to a signal at δ_H 1,89 which appears as a doublet of doublets and is therefore assigned to H_b-4 (W-coupled to H-8a). The signal at δ_H 2,35 is assigned to H-8a. This assignment correlates (HETCOR) with the assignment of the doublet at δ_C 30,35 to C-8a in the ^{13}C-nmr spectrum. Furthermore, the signal due to H-8a would be

expected to be downfield since it is 1,3-diaxial to the benzoyl group and therefore deshielded.

The reaction of the 4a-methyl-$\Delta^{1,8a}$-2-octalone dienamine differed from that of the other dienamines in that the only product isolated showed, from the mass spectrum (M^+ 410) and the ^{1}H-nmr integrals, that reaction had occurred with two equivalents of PVK. However the ^{13}C-nmr spectrum showed the presence of only two carbonyl absorptions (δ_C 200,21 and 200,61). The chemical shifts of these two carbonyl signals indicate that each is conjugated with a carbon-carbon double bond or a benzene ring. So it appears that one carbonyl group has been lost by a condensation process. Several alternative possibilities exist for this process but the one which we favour is shown in Scheme 21.

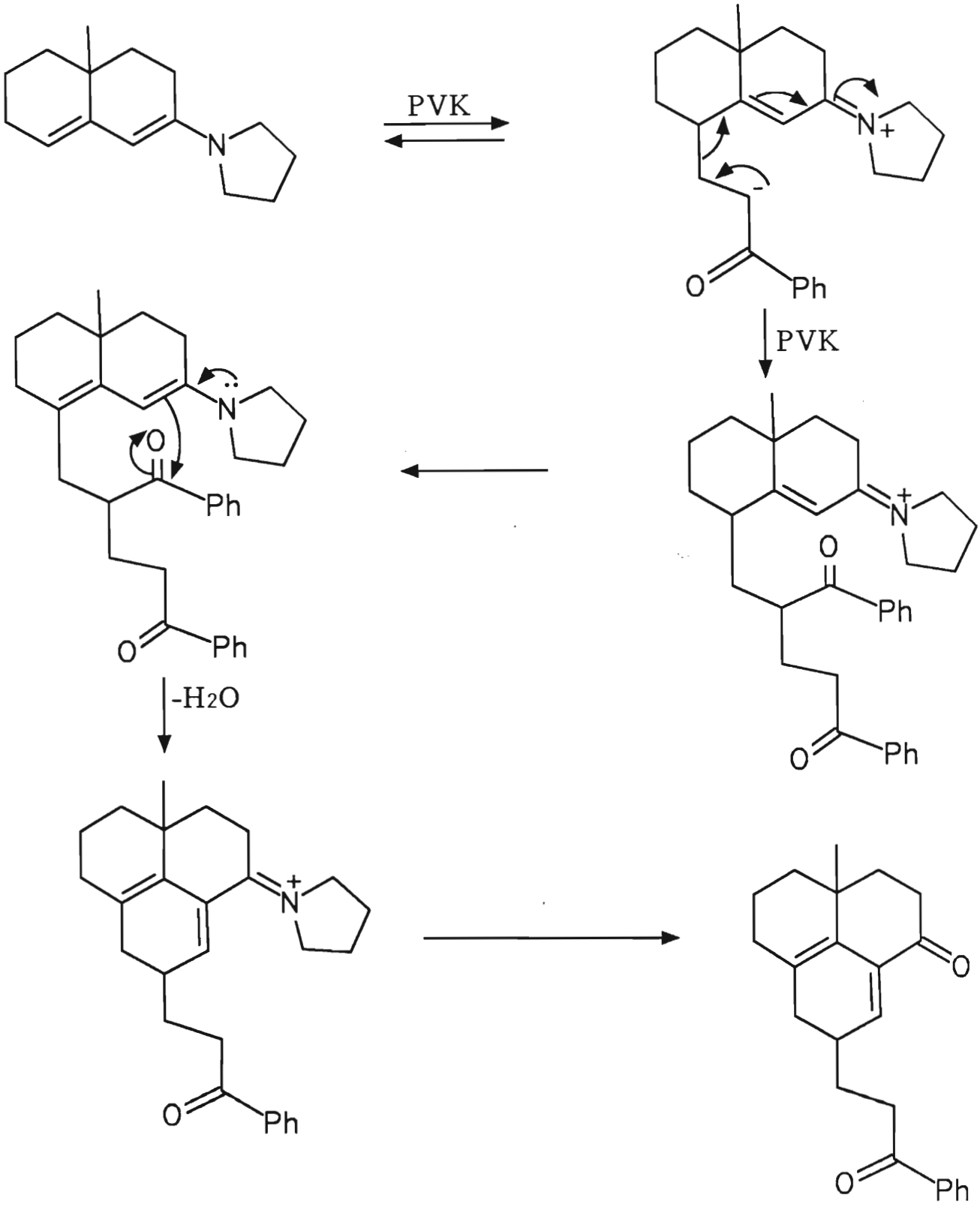
In this process initial δ-attack is reversible, as previously suggested, but in this case the initially formed zwitterion is captured by Michael addition to a second PVK molecule. This renders δ-attack irreversible and allows nucleophilic attack by the regenerated enamine system on the benzoyl group to take place. So in this case β,δ-annulation does occur, but *via* a stabilised intermediate which prevents reversion to starting material. Why this should apparently occur only with the 4a-methyl dienamine is at present inexplicable. The ^{13}C-nmr spectrum showed the current number of methyl, methylene, methine, and quaternary carbon signals as expected for the proposed octahydrophenalenone structure (122). Unfortunately the 200 MHz 1D ^{1}H-nmr and 2D (COSY) spectra were

extremely complex making unequivocal confirmation of the proposed structure impossible.

Products arising from [4+2] cycloaddition were not isolated from the reaction of PVK with the 4a-methyl dienamine. Although cycloaddition arising from β-face attack would not be anticipated due to the steric impediment of the 4a-methyl group, adducts arising from β-face attack could be expected, in view of the cycloaddition products isolated from the corresponding reaction with MVK. GLC of the crude reaction mixture did show peaks with similar retention times, t_R 35 min. (11%[a]) and 39 min. (5%[a]) to those of the cycloadducts isolated from the reaction of other $\Delta^{1,8a}$-2-octalone dienamines and could therefore possibly be attributed to products arising from α-face cycloaddition to the 4a-methyl dienamine.

[a]Integrated GLC peak areas.

SCHEME 21



(122)

CHAPTER THREE

3. EXPERIMENTAL

3.1 FOREWORD TO EXPERIMENTAL

^{1}H-nmr spectra were obtained using a Varian Associates T-60, CFT-20, CFT-20A or Gemini 200 spectrometer operating at 60, 80, 80 and 200 MHz respectively. A Bruker instrument was used to obtain the 500 MHz spectra. All spectra were recorded in deuteriochloroform ($CDCl_3$) using tetramethylsilane (TMS) as internal standard.

^{13}C-nmr spectra were recorded in $CDCl_3$ using a Varian Associates CFT-20A or Gemini 200 spectrometer operating at 20 and 50 MHz respectively. A Bruker instrument was used to obtain the 125 MHz spectra. The assignment of signals in both ^{1}H and ^{13}C-nmr spectra was in some cases aided by the use of two dimensional ^{1}H-^{1}H correlation (COSY) and ^{1}H-^{13}C correlation (HETCOR) spectra obtained with either the Gemini 200 or Bruker spectrometers.

The following abbreviations were used when assigning spectra:

s: singlet	q: quartet	J: coupling constant (Hz)
d: doublet	m: multiplet	b: broad
t: triplet	dd: doublet of doublets	td: triplet of doublets
qd: quartet of doublets		odd: overlaid doublet of doublets
c: complex		om: overlaid multiplet

IR-spectra were recorded with a Shimadzu IR 408 or Pye Unicam SP1000 spectrometer and were calibrated against the 1601 cm^{-1} peak of polystyrene film.

Gas-liquid chromatographic analyses were carried out using a Varian 3400 gas-liquid chromatograph, using ultra-high purity nitrogen as carrier gas (flow rate: 30 $cm.s^{-1}$), a 30 m glass capillary column (phase: PS 25S; film thickness: 0,53 μm) and a flame ionisation detector.

Experimental yields quoted are calculated from the masses of the crude reaction mixtures using GLC percentage (based on integrated peak areas) unless stated otherwise.

Microanalyses and gas chromatograph-mass spectral (GC-MS) determinations were carried out by the Chemistry Department of the University of Natal, Pietermaritzburg. Accurate mass measurements were carried out by the Mass Spectrometry Unit, Cape Town Technikon, and by the Processing and

Chemical Manufacturing Technology Division of the CSIR, Pretoria, together with some microanalyses. A Varian Associates MAT-212 spectrometer operating at 70 eV was used by the CSIR for accurate mass measurement.

Silica gel (0,2 mm) containing fluorescent indicator (F254) on aluminium backed plates (Merck: Art. 5554) were used for TLC and silica gel (Merck: Art. 9385) was used for flash chromatography.[72] Columns of diameter 40 mm and packed to a depth of ≈170 mm were used unless stated otherwise. Solvents used as eluant were distilled prior to use. TLC plates were developed using anisaldehyde-concentrated sulphuric acid-methanol (1:2:97) as spray reagent, followed by heating.

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

X-ray structure determinations were carried out by the X-ray Crystallographic Unit in the Department of Chemistry, University of Natal, Pietermaritzburg.

All products are optically inactive, enatiomeric or diastereoisomeric mixtures. Where an enantiomeric pair of isomers has been isolated, the relative configurations of the chiral centres of one enantiomer, where known has been given using the R^*/S^* symbolism or are as indicated in the corresponding structural formula given at the appropriate point in the experimental.

3.1.1 PURIFICATION AND DRYING OF SOLVENTS AND REAGENTS

The solvents were purified and dried by the following methods:

Methanol was dried following the method described in Vogel.[73] Magnesium turnings, washed with ether and dried (2,6 g), iodine (0,26 g) and methanol (50 ml) were heated under reflux, the condenser being fitted with a drying tube. After all the magnesium had been consumed, methanol (450 ml) was added and the mixture heated under reflux for a further hour. The methanol was then fractionally distilled (64,5 °C) with the exclusion of moisture and stored over molecular sieves (3A, BDH: Bead type). This "super-dry" methanol was used in the reactions described in the experimental section.

Benzene was allowed to stand over anhydrous calcium chloride for 24 h., and then distilled onto molecular sieves (5A), the fraction: 78 - 80 °C being collected.

Dioxane was allowed to stand over potassium hydroxide for 4 days prior to distillation onto molecular sieves (4A).

Toluene was dried by standing over anhydrous calcium chloride (24 h.), followed by distillation into a vessel containing molecular sieves (5A). Further drying prior to use was achieved by the addition of sodium wire.

Ether was dried by the addition of sodium wire.

Methyl vinyl ketone was distilled under reduced pressure from quinol and allowed to stand over molecular sieves (4A) for 12 h. prior to use.

Phenyl vinyl ketone was prepared according to the method outlined in the experimental section and dried by standing over molecular sieves (4A) for 12 h. prior to use.

Where molecular sieves were employed for drying purposes, between 50 and 70 g were added per litre of solvent or reagent. Activation of the sieves was achieved by heating in a muffle furnace at 350°C overnight and cooled in a desiccator.

3.1.2 GENERAL ABBREVIATIONS

^{1}H-nmr	-	proton nuclear magnetic resonance spectroscopy
^{13}C-nmr	-	carbon-13 nuclear magnetic resonance spectroscopy
TLC	-	thin layer chromatography
IR	-	infrared spectroscopy
BP	-	boiling point
MP	-	melting point
GLC	-	capillary gas-liquid chromatography
GC-MS	-	gas chromatography - mass spectrometry
$CDCl_3$	-	deuteriochloroform
TMS	-	tetramethylsilane
MVK	-	methyl vinyl ketone
PVK	-	phenyl vinyl ketone
HETCOR	-	heteronuclear correlation spectroscopy
COSY	-	correlation spectroscopy
Hz	-	hertz
ppm	-	parts per million
t_R	-	retention time (uncorrected)

3.2 STARTING MATERIALS

3.2.1 PREPARATION OF ENAMINES

The enamines were prepared by the general method of Stork *et al.*[4]

In most enamine or dienamine products small carbonyl absorptions were evident in the infra red spectra due to small amounts of unreacted ketone or hydrolysed enamine or dienamine. Attempts were not made to remove any carbonyl impurity since these have no affect on the course of the enamine/ dienamine reactions and attempts to do so could result in decomposition of the labile enamine/dienamine system.

3.2.1.1 1-N-PYRROLIDINYLCYCLOHEXENE

Cyclohexanone (31,36 g; 0,32 mol), pyrrolidine (34,08 g; 0,48 mol) and toluene-4-sulphonic acid (0,2 g) in dry benzene (200 ml) were heated under reflux using a Dean and Stark head until no further liberation of water was observed. Removal of the volatile fraction (benzene and excess pyrrolidine) *in vacuo* and distillation of the residue under reduced pressure gave 1-N-pyrrolidinylcyclohexene (98) (43,36 g; 89 %), BP. 64 °C / 0,2 mm Hg, (Lit.[74] 115 - 117 °C / 20 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

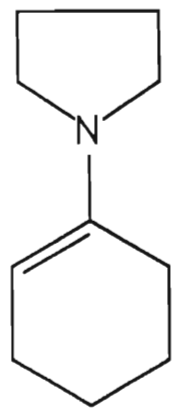
1 640 (C=C)

The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

1,36 - 2,33 (12H, complex methylene envelope)

2,96 (m, 4H, CH_2-N-CH_2)

4,21 (bs, 1H, =CH)



(98)

3.2.1.2 1-N-PYRROLIDINYL-6-METHYLCYCLOHEXENE

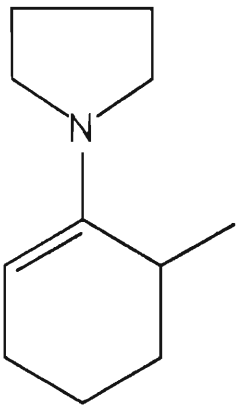
2-Methylcyclohexanone (30 g; 0,27 mol), pyrrolidine (29,11 g; 0,41 mol), and toluene-4-sulphonic acid (0,2 g) in benzene (200 ml) were heated under reflux for 48 h., the water liberated being collected using a Dean and Stark head. Removal of the volatile fractions *in vacuo* and distillation of the residue under reduced pressure gave 1-N-pyrrolidinyl-6-methylcyclohexene (30,96 g; 69%), BP. 64 - 66 °C/0,4 mm Hg, (Lit.[4] 112 - 114°C/15 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

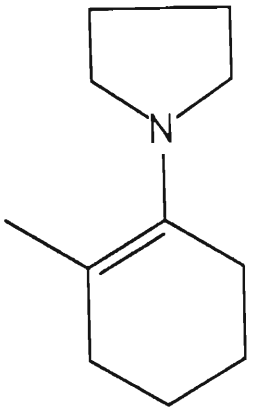
1 640 (C=C).

The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

1,13	(d, J = 6 Hz, CH_3)
1,43 - 2,39	(complex methylene envelope)
2,93	(m, 4H, CH_2-N-CH_2)
4,26	(t, 0,8H, =CH)



(125)



(126)

Integration of the olefinic signal shows that the product is a mixture of isomers, namely 1-N-pyrrolidinyl-6-methylcyclohexene (125) and 1-N-pyrrolidinyl-2-methylcyclohexene, (126) in the ratio of 4 : 1 respectively.

3.2.1.3 1-N-PYRROLIDINYLCYCLOPENTENE

Cyclopentanone (50 g; 0,59 mol), pyrrolidine (84,53 g; 1,18 mol), and toluene-4-sulphonic acid (0,2 g) in benzene (200 ml) were heated under reflux using a Dean and Stark head until the liberation of water had ceased. The solvent was removed *in vacuo* and the residue distilled under reduced pressure to give 1-N-pyrrolidinylcyclopentene (127) (65,07 g; 80 %), BP. 50 - 52 °C / 0,2 mm Hg, (Lit.[74] 97-98 °C / 20 mm Hg).

The IR-spectrum showed ν_{max}(film) cm^{-1}

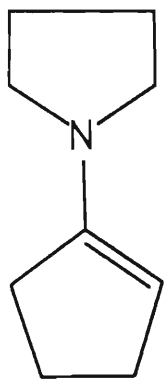
1 640 (C=C).

The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

1,67 - 2,67 (10H, complex methylene envelope)

3,0 (m, 4H, CH_2-N-CH_2)

4,0 (bs, 1H, =CH)



(127)

3.2.1.4 3-N-MORPHOLINO-2-PENTENE

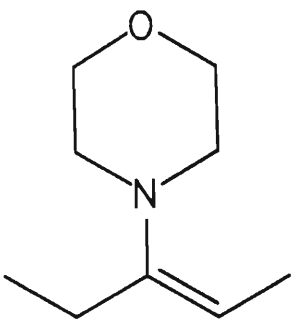
Diethyl ketone (134,30 g; 1,56 mol), morpholine (272,09 g; 3,12 mol) and toluene-4-sulphonic acid (0,2 g) in benzene (470 ml) were heated under reflux using a Dean and Stark head for approximately 24 h., followed by a further period of heating under reflux (≈ 24 h.) over molecular sieves (BDH; 4A). The volatiles were removed *in vacuo* and the residue distilled under reduced pressure to give 2-N-morpholino-2-pentene (128; 52,46 g; 22%), BP. 38 - 42°C/ 1 mm Hg, (Lit.[4] 77 - 78 °C / 9 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

1 645 (C=C).

The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

1,07	(t, 3H, J = 6 Hz, CH_3)
1,67	(d, 3H, J = 6 Hz, $=CHCH_3$)
2,20	(q, 2H, J = 6 Hz, CH_2)
2,73	(m, 4H, CH_2-N-CH_2)
3,70	(m, 4H, CH_2-O-CH_2)
4,38	(q, 1H, J = 6 Hz, =CH)



(128)

3.2.2 METHYL ISOPROPENYL KETONE

This was essentially prepared by the method of T. White.[75]

Ethyl methyl ketone (500 ml), paraformaldehyde (75 g) and a 2N methanolic solution of potassium hydroxide (2,5 ml) were gently heated to initiate the exothermic reaction. Occasional cooling was necessary. As the reaction proceeded, the alkalinity was maintained by further additions of 2N methanolic potassium hydroxide solution. After stirring for 24 h., at room temperature, (when the solution gave a negative test for formaldehyde using Fehling's

solution), the solution was neutralised with 2N-acetic acid. A small amount of quinol was added and the excess ketone removed by distillation up to 100 °C. The intermediate, 1-hydroxy-2-methylbutan-3-one was not isolated but dehydrated by adding iodine[15] (6,67 g) and the solution distilled using a Vigreaux column. The distillate was collected over the range 82 - 100°C. The lower aqueous layer was discarded and the crude vinyl ketone dried over anhydrous magnesium sulphate. A trace of quinol was added to the crude product which was then distilled to give methylisopropenyl ketone (129; 30,21 g; 7%). BP. 95 - 99 °C.

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 685 (CO)

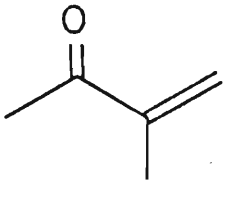
The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

1,84 (d, 3H, J = 1Hz, CH_3-C=C)

2,33 (s, 3H, CH_3CO)

5,77 (s, 1H, vinyl)

5,96 (s, 1H, vinyl)



(129)

3.2.3 2,4-DIMETHYLCYCLOHEXANE-1,3-DIONE

This was prepared using the method reported by Hargreaves.[76]

Acryloyl chloride (28,96 g; 0,32 mol) in dry benzene (100 ml) was added dropwise with stirring to a solution of 3-morpholino-2-pentene (49,63 g; 0,32 mol) in dry benzene (200 ml) at the boil over a period of 1 h. The mixture was then heated under reflux for 16 h. The solvent was decanted, leaving behind the intermediate product which was washed with dry benzene and hydrolysed by stirring with ice cold water (100 ml) for 3 h. The aqueous suspension was extracted with ether and dried (andydr. $MgSO_4$). Filtration and evaporation of the solvent gave 2,4-dimethylcyclohexane-1,3-dione (130; 17,86 g; 40%), MP. 116 - 118 °C (from benzene-petroleum), (Lit.[76] 117 - 118 °C).

The IR spectrum showed $\nu_{max}(CHCl_3)$ cm^{-1}

1 615 (C=C of enol)

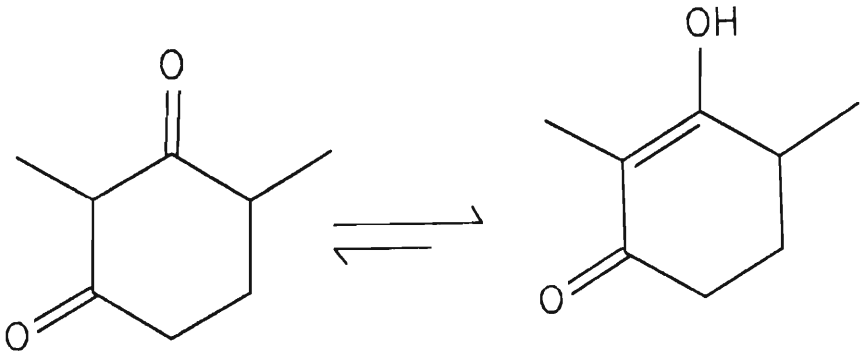
1 705 and 1 739 (CO)

The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

1,16 (d, J = 6 Hz, CH_3)

1,73 (s, $=CCH_3$ of enol form)

1,36 - 2,83 (complex methylene/methine envelope)



(130) (131)

^{1}H-nmr measurements indicated 2,4-dimethycyclohexane-1,3-dione to exist mainly as the enol form (131; ≈ 83 %). This compound is unstable,[76] and was therefore used immediately in the formation of 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone (141).

3.2.4 PREPARATION OF $\Delta^{1,8a}$-2-OCTALONE AND RELATED COMPOUNDS

3.2.4.1 $\Delta^{1,8a}$-2-OCTALONE

This was prepared by hydrolysis of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone obtained from the reaction of methyl vinyl ketone with 1-N-pyrrolidinyl-cyclohexene according to the method outlined by Stork *et al.*[4] The dienamine (3,98 g; 0,019 mol) was heated under reflux with a buffer solution[10] of sodium acetate (5 g) and acetic acid (10 ml) in water (10 ml) for 4 h. The mixture was extracted with ether (3 x 25 ml) and the combined extracts washed successively with 2N-hydrochloric acid (3 x 25 ml), saturated sodium bicarbonate solution (25 ml), and saturated sodium chloride solution (3 x 25 ml). The ether

layer was dried over anhydrous magnesium sulphate. Filtration and removal of the ether *in vacuo* gave a residue which was distilled under reduced pressure to give $\Delta^{1,8a}$-2- octalone (1,86 g; 63 %), BP. 82 - 40 °C/0,2 mm Hg, (Lit.[77] 101 - 102 °C / 2 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

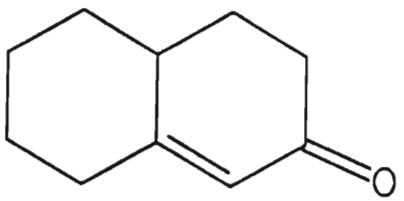
1 620 (C=C)

1 675 and 1 715 (CO).

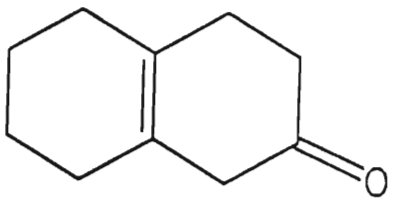
The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

1,10 - 2,63 (complex methylene/methine envelope)

5,68 (s; 0,8 H; =CH)



(132)



(133)

^{1}H-nmr measurements indicated the product to be a mixture of the α,β- and β,γ-unsaturated isomers (132) and (133) in the ratio of 4:1 respectively. This was confirmed by the IR spectrum which showed a non-conjugated carbonyl absorption at 1 715 cm^{-1}.

3.2.4.2 4a-METHYL-$\Delta^{1,8a}$-2-OCTALONE

This was prepared by the method of Ross and Levine.[78]

A solution of methyl vinyl ketone (12,6 g; 0,18 mol) in ether (90 ml) was added dropwise over 1 h. to a stirred solution of 2-methylcyclohexanone (40,04 g; 0,36 mol) and ethanolic potassium hydroxide [potassium hydroxide (1,51 g; 0,041 mol) in ethanol (5,1 ml)] in ether (100 ml) maintained at 0 °C. The reaction mixture was stirred for 1 h. at room temperature, poured onto crushed ice and acidified with concentrated hydrochloric acid. The mixture was extracted with ether, dried over anhydrous magnesium sulphate and filtered. Removal of the ether *in vacuo* and distillation of the residue under reduced pressure gave a mixture of 4a-methyl-$\Delta^{1,8a}$-2-octalone and 8a-hydroxy-4a-methyl-2-oxodecalin (134) and (135) (13,55 g; 45 %), BP. 96 - 120°C / 0,2 mm Hg, (Lit.[78] 110 - 120°C / 0,7 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

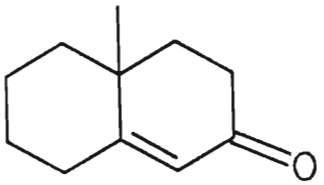
1 620	(C=C)
1 670, 1 715	(CO)
3 500	(OH)

The ^{1}H-nmr spectrum (60 MHz, $CDCl_3$) showed δ (ppm)

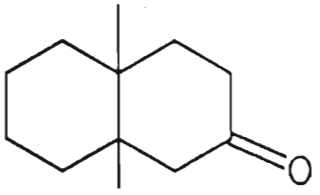
1,3 (s; 3H; CH3)

1,00 - 2,66 (complex methylene/methine envelope)

5,76 (s; =CH)



(134)



(135)

Separation of the mixture was not necessary since both compounds give the required dienamine on treatment with pyrrolidine.[15]

3.2.4.3 8-METHYL-$\Delta^{1,8a}$-2-OCTALONE

This was prepared by the method of Stork *et al.*[4]

Methyl vinyl ketone (10,58 g; 0,15 mol) was added dropwise to a stirred solution of 1-N-pyrrolidinyl-6-methylcyclohexene (25 g; 0,15 mol) in dry benzene (150 ml) and heating under reflux overnight. Hydrolysis was achieved by the addition of a buffer solution of sodium acetate (10 g) and acetic acid (20 ml) in water (20 ml) and heating under reflux for a further 4 h. The volatiles were removed *in vacuo* and the residue extracted with ether (3 x 50 ml). The

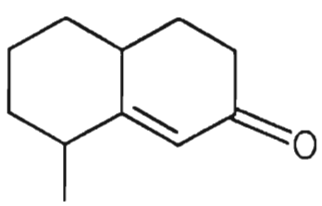
combined ether extracts were washed successively with 2N hydrochloric acid (3 x 50 ml), saturated sodium bicarbonate solution (50 ml), and saturated sodium chloride solution (3 x 50 ml). The ether layer was dried over anhydrous magnesium sulphate, filtered and the ether removed *in vacuo.* Distillation of the residue under reduced pressure gave 8-methyl-$\Delta^{1,8a}$-2-octalone (11,32 g; 46%), BP. 90 - 94 °C/0,2 mm Hg, (Lit.[77] 102 °C/0,2 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

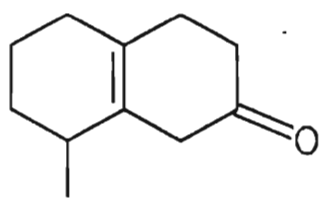
1 620	(C=C)
1 675 and 1 715	(CO).

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,00 and 1,13	(overlaid methyl doublets; J = 6 Hz, of the α,β- and β,γ-unsaturated isomers)
1,40 - 2,60	(complex methylene/methine envelope)
5,76	(s; 0,7 H; =CH)



(136)



(137)

^{1}H-nmr measurements indicated the product to be a mixture of the α,β- and β,γ-unsaturated isomers (136) and (137) in the ratio of 7 : 3 respectively. The

presence of the β,γ-isomer again being confirmed by the IR carbonyl absorption at 1 715 cm^{-1}.

3.2.4.4 3-METHYL-$\Delta^{1,8a}$-2-OCTALONE

This was prepared by the method of Stork *et al.*[4]

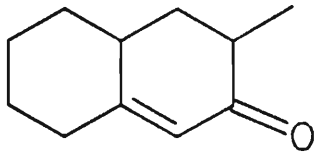
Methyl isopropenyl ketone (17,43 g; 0,20 mol) was added dropwise to a stirred solution of 1-N-pyrrolidinylcyclohexene (30,2 g; 0,20 mol) in dry dioxane (150 ml) and the solution heated under reflux for 18 h. Hydrolysis and work-up was as for 8-methyl-$\Delta^{1,8a}$-2 octalone followed by distillation of the residue under reduced pressure to give 3-methyl-$\Delta^{1,8a}$-2-octalone (12,75 g; 38 %), BP. 100°C/ 0,4 mm Hg, (Lit.[79] 100 - 105 °C/0,5 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

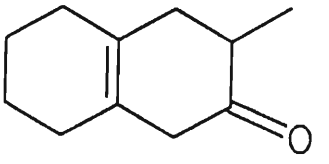
1 630	(C=C)
1 675 and 1 715	(CO)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,03 and 1,13	(overlaid methyl doublets; J = 1 Hz, of the α,β- and β,γ-unsaturated isomers)
1,2 - 2,7	(complex methylene/methine envelope)
5,83	(s; 0,8H; =CH)



(138)



(139)

^{1}H-nmr measurements indicated the product to be a mixture of the α,β- and β,γ-unsaturated isomers (138) and (139) in the ratio of approximately 80:20 respectively. The presence of the β,γ isomer was again confirmed by the non-conjugated carbonyl absorption at 1 715 cm^{-1} .

3.2.4.5 4a-METHYL-5-OXO-$\Delta^{1,8a}$-2-OCTALONE

This was prepared by the literature method.[80]

A solution of 2-methylcyclohexane-1,3-dione (25,20 g; 0,20 mol), methyl vinyl ketone (21,00 g; 0,30 mol) and potassium hydroxide (0,2 g) in methanol (100 ml) was heated under reflux until the dione dissolved ($\approx$ 3 h.). The solvent and excess methyl vinyl ketone were removed *in vacuo.* The intermediate 2-methyl-2-(3-oxobutyl)cyclohexane-1,3-dione was dissolved in benzene (100 ml) and a Dean and Stark head attached. Traces of water and methanol

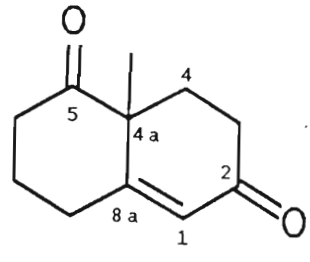
were removed by distillation of benzene (20 ml). The solution was cooled well below the boiling point, pyrrolidine (1,5 ml) added and the mixture heated under reflux until no further liberation of water was observed (≃30 min.) The water was removed and 50 ml of benzene distilled off. The reaction mixture was cooled to room temperature, diluted with ether and washed with water (40 ml) containing hydrochloric acid (6 ml; 10 %) and finally with water (40 ml). The combined aqueous phases were extracted with ether (2 x 50 ml) and the combined ether layers washed with water (3 x 50 ml), saturated sodium chloride solution (50 ml) and dried over anhydrous magnesium sulphate. The solvents were removed *in vacuo* and the residue distilled under reduced pressure. The fraction distilling at 108°C/0,1 mm Hg was collected (23,79 g), diluted with ether (5 ml) and left in the refrigerator overnight. The resulting crystals were collected, and washed with hexane (BP. 60 - 71°C) to give 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone (140; 16,82 g; 47 %), MP. 47 - 50°C (from ether), (from ether), (Lit.[80] 47 - 50 °C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 621	(C=C),
1 675	(CO; α,β-unsaturated)
1 715	(CO).

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,48	(s; 3H; methyl)
1,6 - 1,9	(m; 1H)
2,1 - 2,3	(m; 3H)
2,4 - 2,6	(m; 4H)
2,7 - 2,9	(m; 2H)
5,85	(s; 1H; H-1)



(140)

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

22,98 (t)	23,28 (q; CH_3)	29,71 (t)
31,79 (t)	33,67 (t)	37,71 (t)
50,70 (s; C-4a)	126,02 (d; C-1)	166,49 (s; C-8a)
198,71 (s; C-2)	211,58 (s; C-5)	

3.2.4.6 4a,6-DIMETHYL-5-OXO-$\Delta^{1,8a}$-2-OCTALONE

This was prepared using the methodology described in the previous preparation.

A solution of 2,4-dimethylcyclohexane-1,3-dione (17,38 g; 0,13 mol), methyl vinyl ketone (13,65 g; 0,20 mol) and potassium hydroxide (0,13 g) in methanol (100 ml) was heated under reflux for 3 h. The volatiles were removed *in vacuo*, benzene (100 ml) added and a Dean and Stark head attached. Traces of water and methyl vinyl ketone were again removed by distillation of 20 ml of benzene. The mixture was cooled, pyrrolidine (1 ml) added and the mixture heated under reflux for 30 minutes. Continuing as before gave a residue which was distilled under reduced pressure to give 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone as an orange oil (141; 16,14 g; 65 %), BP. 112 - 114°C/0,2 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

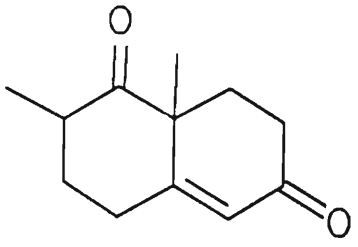
1 620	(C=C),
1 675	(CO)
1 695	(CO)
1 715	(CO)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,13 and 1,23 (overlaid methyl doublet and singlet)

1,26 - 3,23 (complex methylene/methine envelope)

5,73 (bs; H-1)



(141)

Although TLC (hexane-methylene chloride-ethyl acetate 12:3:1) of the product showed predominantly one spot, the IR and ^{1}H-nmr indicated the product to be impure. This impurity could possibly be attributed to the uncyclised compound 2,8a-dimethyl-2-(3-oxobutyl)cyclohexane-1,3-dione since this could account for the additional peak in the IR spectrum at 1 695 cm^{-1} and the signal at δ 2,1 expected for CH_3CO. In addition the GC-MS showed the presence of an impurity having the molecular ion (M^+) at m/e 210 as expected for the uncyclised product. Attempts to purify the product by flash chromatography were unsuccessful. The impure product was thus used in the preparation of the pyrrolidine dienamine.

3.2.5 PREPARATION OF 5,6,7,7a-TETRAHYDRO-INDAN-5-ONE

This was prepared using the method outlined by Stork *et al.*[4]

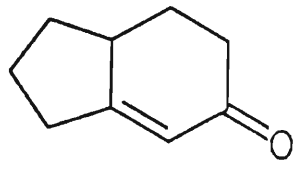
Methyl vinyl ketone (16,0 g; 0,23 mol) was added dropwise to a stirred solution of the pyrrolidine enamine of cyclopentanone (32,0 g; 0,23 mol) in dioxane (150 ml) and the mixture heated under reflux for 24 h. Continuing in the same manner as described previously for 8-methyl-$\Delta^{1,8a}$-2-octalone, gave 5,6,7,7a-tetrahydroindan-5-one (11,20 g; 36 %), BP. 70 - 72°C/0,2 mm Hg, (Lit.[4] 80 - 81°C/0,4 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

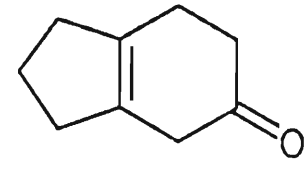
1 637	(C=C)
1 670 and 1 710	(CO).

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,0 - 3,0	(complex methylene/methine envelope)
5,83	(t; 0,7 H; =CH)



(142)



(143)

^{1}H-nmr measurements indicated the product to be a mixture of the α,β- and β,γ-unsaturated isomers (142) and (143) in the ratio of approximately 7:3 respectively. This was again confirmed by the non-conjugated IR carbonyl absorption at 1 710 cm^{-1}.

3.2.6 PREPARATION OF DIENAMINES

The dienamines were prepared essentially by the methods employed by Stork[4] and Firrell.[15]

3.2.6.1 DIENAMINES OF $\Delta^{1,8a}$-2-OCTALONE AND RELATED COMPOUNDS

3.2.6.1.1 PYRROLIDINE DIENAMINE OF $\Delta^{1,8a}$-2-OCTALONE

This was prepared directly from the reaction of methyl vinyl ketone with 1-N-pyrrolidinylcyclohexene. Methyl vinyl ketone (8,40 g; 0,12 mol) was added dropwise to a stirred solution of 1-N-pyrrolidinylcyclohexene (18,53 g; 0,12 mol) in dry toluene (100 ml) and the mixture heated under reflux for 24 h. The solvent was removed *in vacuo* and the residue distilled under reduced

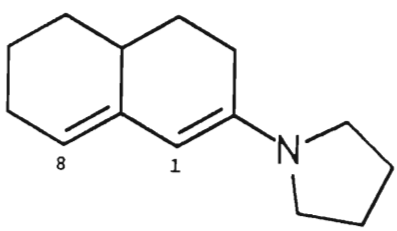
pressure to give the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone as a viscous oil (16,83 g; 69 %), BP. 124 - 126 °C/0,2 mm Hg, (Lit.[4] 146 - 150 °C / 0,3 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

1 600 and 1 630 (C=C)

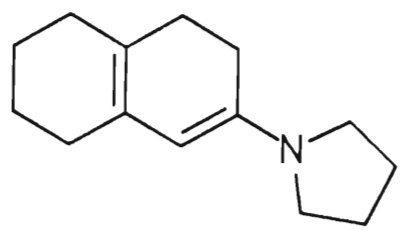
The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,1 - 2,5	(complex methylene/methine envelope)
3,20	(m; 4H; CH_2-N-CH_2)
4,26	(s; 0,3 H; H-1 endo)
4,8	(s; 0,7 H; H-1 exo)
5,1	(s; 0,7 H; H-8 exo)



(11)

R,R',R" = H



(12)

R,R',R" = H

^{1}H-nmr measurements indicated the dienamine to be a mixture of the exo- and endocyclic isomers (11) and (12) in the ratio of ≈7:3 respectively.

3.2.6.1.2 PYRROLIDINE DIENAMINE OF 4a-METHYL-$\Delta^{1,8a}$-2-OCTALONE

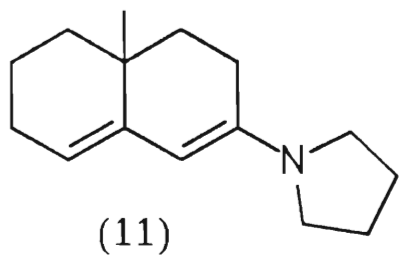
The mixture of 4a-methyl-$\Delta^{1,8a}$-2-octalone and 8a-hydroxy-4amethyl-2-oxo-decalin (10,0 g; 0,06 mol), pyrrolidine (11,0 g; 0,015 mol) and toluene-4-sulphonic acid (0,2 g) in toluene (120 ml) was heated under reflux for 24 h. using a Dean and Stark head, followed by an additional 24 h. period of reflux over molecular sieves (4 A). The solvent was removed *in vacuo* and the residue distilled under reduced pressure to give the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone pyrrolidine dienamine as a viscous amber oil (9,88 g; 76 %), BP 138 - 140 °C/0,3 mm Hg, (Lit.[15] oil bath temperature 120 - 138°C/0,2 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

1 607 and 1 635 (C=C)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,06	(s; 3H; Me)
1,26 - 2,56	(complex methylene envelope; 14H)
3,16	(m; 4H; CH_2-N-CH_2)
4,78	(s; 1 H; H-1)
5,03	(bs; 1 H; H-8)



(11)

R',R" = H; R = Me

^{1}H-nmr measurements indicated the dienamine to be only in the exocyclic form (11).

3.2.6.1.3 PYRROLIDINE DIENAMINE OF 8-METHYL-$\Delta^{1,8a}$-2-OCTALONE

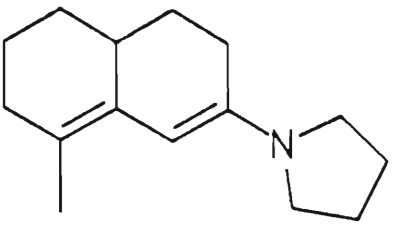
A solution of 8-methyl-$\Delta^{1,8a}$-2-octalone (10,0 g; 0,06 mol), pyrrolidine (11,0 g; 0,15 mol) and toluene-4-sulphonic acid (0,2 g) in toluene (120 ml) was heated under reflux using a Dean and Stark head for 24 h. The solvent was removed *in vacuo* and the residue distilled under reduced pressure to give the pyrrolidine dienamine of 8-methyl-$\Delta^{1,8a}$-2-octalone (8,71 g; 65 %), BP. 90 - 94°C / 0,2 mm Hg). On standing in the refrigerator, the viscous oil solidified to give a pale yellow solid.

The IR spectrum showed ν_{max}(film) cm^{-1}

1 600 and 1 635 (C=C)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,63	(s; overlaid Me)
1,00 - 2,36	(complex methylene/methine envelope)
3,16	(m; 4H; CH_2-N-CH_2)
5,00	(s; 1 H; H-1)



(11)

R,R" = H; R' = Me

^{1}H-nmr measurements indicated the dienamine to be mainly in the exocyclic form (11), but additional signals at δ_H 4,2 - 4,4 could be attributed to small amounts of the other double bond isomers.

In a separate experiment, distillation of the reaction mixture from the preparation of 8-methyl-$\Delta^{1,8a}$-2-octalone prior to the hydrolysis step gave the dienamine in 60 % yield, the product having analytical data identical in every respect with those given above.

3.2.6.1.4 PYRROLIDINE DIENAMINE OF 3-METHYL-$\Delta^{1,8a}$-2-OCTALONE

A solution of 3-methyl-$\Delta^{1,8a}$-2-octalone (15,59 g; 0,09 mol), pyrrolidine (17,85 g; 0,25 mol) and toluene-4-sulphonic acid (0,2 g) in toluene (150 ml) was heated under reflux using a Dean and Stark head for 24 h. followed by an additional 24 h. period heating under reflux over molecular sieves (4 A). The solvent was removed *in vacuo* and the residue distilled under reduced pressure to give the pyrrolidine dienamine of 3-methyl-$\Delta^{1,8a}$-2-octalone (15,69 g; 79 %), BP. 110 - 112°C / 0,2 mm Hg, (Lit.[15] 120 - 124°C / 0,6 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

1 590 and 1 630 (C=C)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

0,93 and 1,13 (methyl doublets of the endo- and exocyclic isomers; J = 7 Hz)

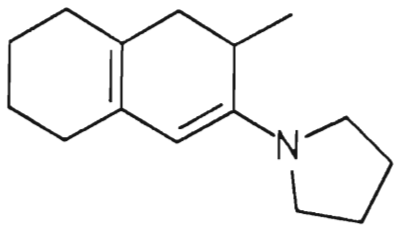
1,33 - 2,93 (complex methylene/methine envelope)

3,20 (m; 4H; CH_2-N-CH_2)

4,26 (s; 0,52 H; H-1 endo)

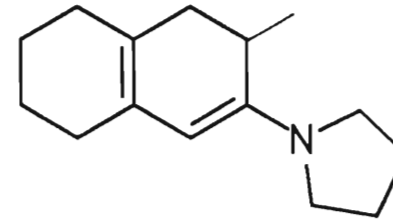
4,8 (s; 0,24 H; H-1 exo)

5,1 (bs; 0,24 H; H-8 exo)



(11)

R,R' = H; R" = Me



(12)

R,R' = H; R" = Me

^{1}H-nmr measurements indicated the dienamine to be a mixture of the exo- and endo-isomers (11) and (12) in the ratio of ≈ 48:52 respectively.

3.2.6.1.5 PYRROLIDINE DIENAMINE OF 4a-METHYL-5-OXO-$\Delta^{1,8a}$-2-OCTALONE

A solution of 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone (8,00 g; 0,045 mol), pyrrolidine (8,53 g; 0,12 mol) and toluene-4-sulphonic acid (0,2 g) in toluene (100 ml) was heated under reflux for 24 h. using a Dean and Stark head followed by an additional 24 h. period of reflux over molecular sieves (4 A). The volatiles were removed *in vacuo* and the residue distilled under reduced pressure to give the

pyrrolidine dienamine of 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone (56; 6,48 g; 62 %),

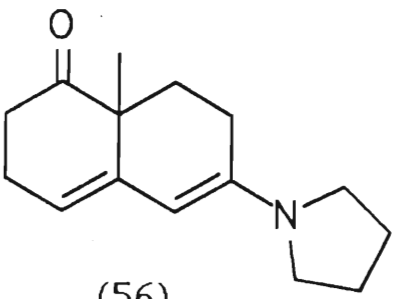
BP. 160 - 162°C / 0,5 mm Hg.

The IR spectrum showed ν_{max}(film) cm^{-1}

1 603 and 1 630	(C=C)
1 705	(CO)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,16	(s; 3H; Me)
1,36 - 2,63	(complex methylene/methine envelope)
3,10	(m; 4H; CH_2-N-CH_2)
4,73	(s; 1H; H-1)
5,13	(bs; 1H; H-8)



(56)

^{1}H-nmr measurements indicated the dienamine to be only in the exocyclic form (56).

3.2.6.1.6 PYRROLIDINE DIENAMINE OF 4a,6-DIMETHYL-5-OXO-$\Delta^{1,8a}$-2-OCTALONE

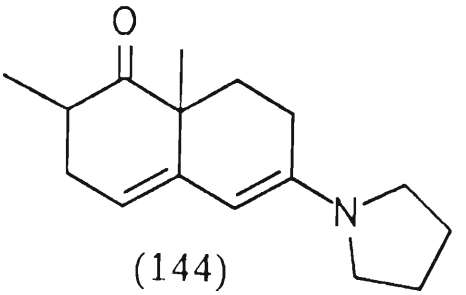
A solution of 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone (12,00 g; 0,063 mol), pyrrolidine (11,90 g; 0,17 mol) and toluene-4-sulphonic acid (0,2 g) in toluene (100 ml) was heated under reflux for 24 h. followed by an additional 24 h. period of reflux over molecular sieves (4A). The volatiles were removed *in vacuo* and the residue distilled under reduced pressure to give the pyrrolidine dienamine of 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone (144) as a viscous, dark red oil (8,67 g; 56 %), BP. 162 - 164 °C / 0,5 mm Hg.

The IR spectrum showed ν_{max}(film) cm^{-1}

1 603 and 1 630	(C=C)
1 707	(CO)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,1	(s; 3H; CH_3)
1,13 - 1,26	(2 x d; 3H each; CH_3-6; axial and equatorial)
1,40 - 2,67	(complex methylene/methine envelope)
2,90 - 3,40	(m; 4H; CH_2-N-CH_2)
4,83; 4,86; 5,10 and 5,33 -	olefinic signals of the two geometric isomers arising from the C-6 methyl group being axial or equatorial.



(144)

3.2.6.2 PYRROLIDINE DIENAMINE OF 5,6,7,7a-TETRAHYDRO-INDAN-5-ONE

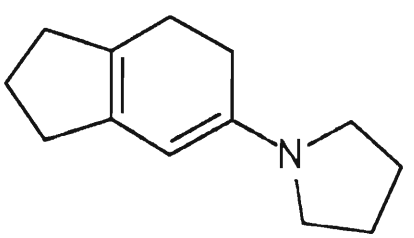
A solution of 5,6,7,7a-tetrahydroindan-5-one (9,9 g; 0,073 mol), pyrrolidine (12,98 g; 0,18 mol) and toluene-4 sulphonic acid (0,2 g) in toluene (100 ml) was heated under reflux for 24 h. using a Dean and Stark head, followed by an additional 24 h. period of reflux over molecular sieves (4 A). Removal of the solvent *in vacuo* and distillation of the residue under reduced pressure gave the pyrrolidine dienamine of 5,6,7,7a-tetrahydroindan-5-one (8,83 g; 64%), BP. 70 - 71°C / 0,2 mm Hg, (Lit.[4] 80 - 81 °C/0,4 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

1 580 and 1 625	(C=C)
3 050	(=CH)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

0,86 - 2,57	(14H; complex methylene envelope)
3,10	(m; 4H; CH_2-N-CH_2)
4,93	(s; 1H; =CH)



(145)

^{1}H-nmr measurements indicated that the dienamine was mainly in the endocyclic form (145), but additional signals at δ 4 - 4,5 could be attributable to small amounts of other double bond isomers.

3.2.6.3 MORPHOLINE DIENAMINE OF ISOPHORONE

This was prepared by the method of Firrell.[15]

A solution of isophorone (27,6 g; 0,2 mol), morpholine (24,0 g; 0,28 mol) and toluene-4-sulphonic acid (0,2 g) in benzene (125 ml) was heated under reflux for 112 h. using a Dean and Stark head. Removal of the volatiles *in vacuo* and distillation of the resulting oil under reduced pressure gave the morpholine dienamine of isophorone (19,77 g; 48 %), BP. 87 - 88°C / 0,12 mm Hg (Lit.[36] 107 - 110°C / 2 mm Hg).

The IR spectrum showed ν_{max}(film) cm^{-1}

1 590 and 1 620 (C=C)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

0,93 and 0,96 (2 x s; 3H each; CH_3)

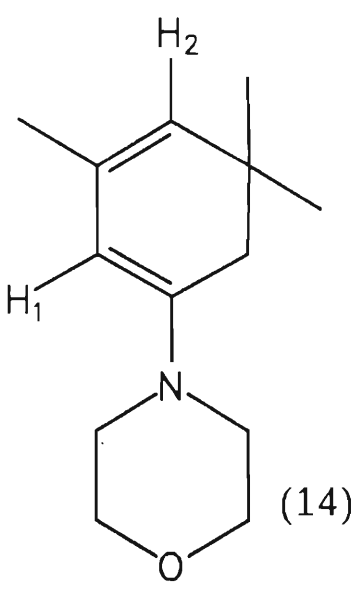
1,6 - 2,13 (methylene protons)

2,76 (m; 4H; CH_2-N-CH_2)

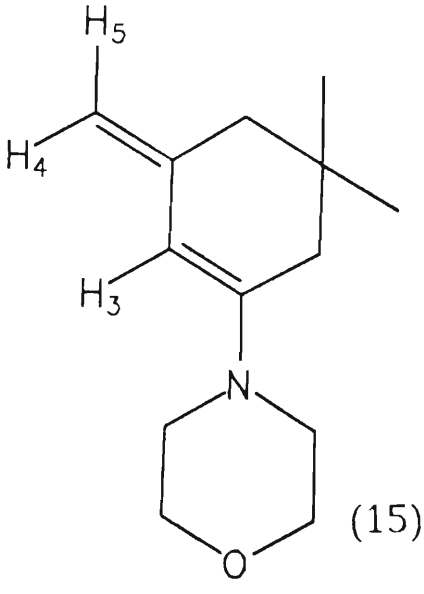
3,59 (m; 4H; CH_2-O-CH_2)

4,29; 4,43; 4,53; 4,66; 4,76; 5,19 and 5,49 (olefinic

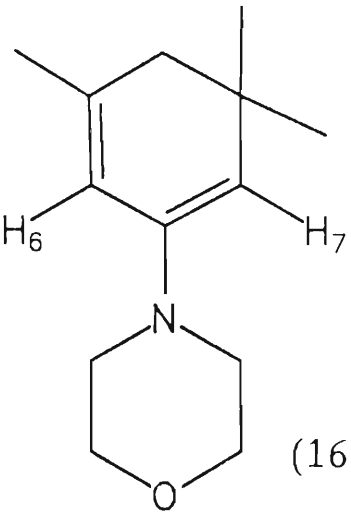
signals arising from protons H-7; H-5; H-4; H-1; H-2; H-3 and H-6 respectively).



(14)



(15)



(16)

^{1}H-nmr measurements indicated the product to be a mixture of the isomers (14), (15), and (16) in the approximate ratio of 38:50:12.

The lowfield signal δ_H 5,76 is attributed to a small amount of isophorone present as an impurity as indicated by comparison with the ^{1}H-nmr spectrum of pure isophorone. This is confirmed by the presence of the conjugated carbonyl absorption in the IR-spectrum at 1 657 cm^{-1}.

3.2.7 PREPARATION OF THE CYCLOHEXYL-IMINE OF 4a-METHYL-$\Delta^{1,8a}$-2-OCTALONE

A solution of cyclohexylamine (17,12 g; 0,17 mol), 4a-methyl-$\Delta^{1,8a}$-2-octalone (11,38 g; 0,07 mol) and toluene-4-sulphonic acid (0,2 g) in toluene (100 ml) was heated under reflux using a Dean and Stark head until no further separation of water was observed. The volatiles were removed *in vacuo* and the residue distilled under reduced pressure to give the cyclohexylimine of 4a-methyl-$\Delta^{1,8a}$-2-octalone (146; 13,4 g; 79%), BP 130 - 134°C/0,2 mm Hg, (Lit.[60] 125°C / 0,1 mm Hg).

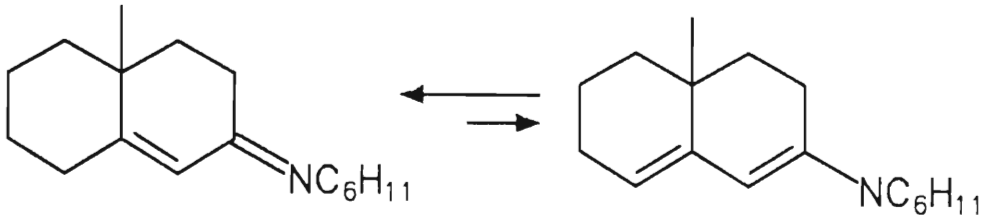
The IR spectrum showed ν_{max}(film) cm^{-1}

1 620	(C=C)
1 640	(C=N)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,03; 1,13 and 1,16	(3 x s; 3H each; 3 x CH_3; attributed to the exocyclic dienamine and syn and anti forms of the imine)
1,2 - 3,5	(complex methylene envelope)
4,86	(s; H-1 of the dienamine)
5,02	(t; H-8 of the dienamine)

5,8 and 6,06 (2 x s; olefinic signals of the syn- and anti-isomers of the imine)



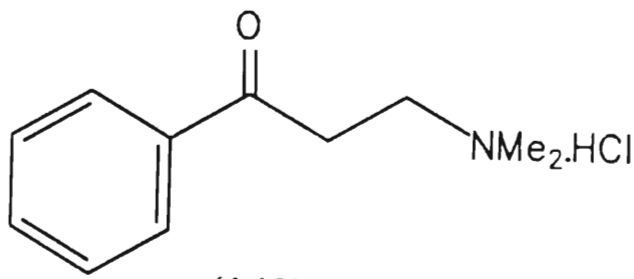
(146) (147)

The ^{13}C-nmr spectrum (50 MHz) showed the presence of ten signals in the region 94 - 166 ppm. The syn- and anti-isomers of the imine would give six signals (4 x singlets and 2 x doublets) and the dienamine would give four signals (2 x singlets and 2 x doublets) in this region. The ADEPT spectrum confirmed the presence of six singlets and four lowfield doublets and also the presence of three methyl signals δ_c 22,09; 22,60; and 23,38.

The GC-MS showed the molecular ion M^+ 245 as would be expected for this compound.

3.2.8 β-DIMETHYLAMINOPROPIOPHENONE HYDROCHLORIDE

Acetophenone (15,61 g; 0,13 mol), dimethylamine hydrochloride (8,16 g; 0,1 mol) predried in a vacuum oven at 70 °C overnight and paraformaldehyde (4,50 g; 0,05 mol) were added to a round bottomed flask. A mixture of concentrated hydrochloric acid (0,25 mol) in 95 % ethanol (30 ml) was then added and the contents of the flask heated under reflux for 1 h. A further portion of paraformaldehyde (3,00 g; 0,033 mol) was added and the mixture heated under reflux for 2 h. Acetone (250 ml) was added to the warm reaction mixture which was then allowed to cool to room temperature and finally placed in the refrigerator overnight. The crystals which separated were collected, washed with acetone and dried (70 °C) for 3 h. to give β-dimethyl-aminopropiophenone hydrochloride (148; 11,49 g; 54 %), MP. 156 °C (from ethanol), (Lit.[81] 155 - 156 °C).



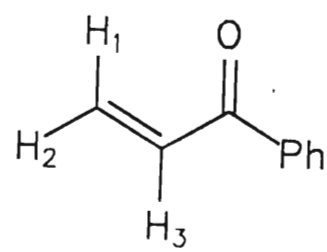
(148)

3.2.9 PREPARATION OF PHENYL VINYL KETONE (PVK)

β-Dimethylaminopropiophenone hydrochloride (20,00 g; 0,13 mol) was steam distilled until the distillate coming over no longer appeared cloudy ($\approx$ 4 - 8 h.). The distillate was then extracted with methylene chloride (3 x 50 ml) and the combined extracts dried over anhydrous magnesium sulphate. Filtration and removal of the solvent *in vacuo* gave phenyl vinyl ketone (149; 10,04 g; 59 %) as a pale yellow oil. Quinol was added to inhibit polymerisation of the phenyl vinyl ketone during the distillation and extraction processes. The phenyl vinyl ketone thus obtained was used as soon as possible in the reactions with the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone and related compounds.

The IR spectrum showed ν_{max}(film) cm^{-1}

1 610	(C=C)
1 670	(CO)



(149)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

5,87	(dd; H-2; J = 2; 10 Hz)
6,40	(dd; H-1; J = 2; 17 Hz)
7,30	(dd; H-3; partially overlaid by the aromatic signals)
7,3 - 8,3	(m; 5H; Ph-)

3.3 REACTION OF METHYL VINYL KETONE WITH DIENAMINES DERIVED FROM $\Delta^{1,8a}$-2-OCTALONES

3.3.1 GENERAL PROCEDURE

Methyl vinyl ketone (one equivalent) was added dropwise under nitrogen to a stirred solution of the dienamine in "super-dry" methanol or dry toluene (100 - 150 ml). After the addition was complete, the mixture was heated under reflux. In methanol, the mixture was heated under reflux for approximately 4 h. while in toluene, the period of reflux was increased to approximately 43 h. A positive pressure of nitrogen was maintained throughout the reaction. The mixture was hydrolysed by heating under reflux for 4 - 5 h. (unless otherwise stated) with a buffer solution[10] of anhydrous sodium acetate (5 g) and glacial acetic acid (10 ml) in water (10 ml). The volatiles were removed *in vacuo* and

the residue extracted with ether (3 x 50 ml). The combined ether extracts were washed successively with 2N-hydrochloric acid (3 x 50 ml), saturated sodium bicarbonate solution (50 ml) and saturated sodium chloride (3 x 50 ml). The ether layer was dried (anhydrous $MgSO_4$), filtered and evaporated under reduced pressure to give the crude product as a viscous amber to dark brown oil. GLC and TLC analysis showed the crude products to be complex multi-component mixtures. Purification was achieved by flash chromatography using eluant ratios detailed in each individual reaction. Fractions containing compounds with the same R_f value were combined and the solvent evaporated on a steam bath. If necessary, the combined fractions were further purified by the methods indicated in the description of individual experiments. In this way the following reactions were investigated:

3.3.2 REACTION OF THE PYRROLIDINE DI-ENAMINE OF 4a-METHYL-$\Delta^{1,8a}$-2-OCTALONE

3.3.2.1 IN METHANOL

Methyl vinyl ketone (1,61 g; 0,023 mol) was added dropwise to a stirred solution of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone (5 g; 0,023 mol) in "super-dry" methanol (100 ml), and heated under reflux for the specified period. Hydrolysis and work-up gave 3,66 g of crude product. A portion of the crude oil was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 42 fractions (≃50 ml each).

The eluant ratio was changed to 6:3:1 and an additional 31 fraction collected. Fraction 55 - 65 were combined on the basis of TLC and further purified by recrystallisation to give **(4aR*,7aS*,11aR*)-4a-methyloctahydro-1*H*-benzo[d]-naphthalene-2,10(3*H*,11*H*)-dione**[a] (78) as a white crystalline solid (0,67 g; 12%), MP 139 - 141 °C (from hexane-ethyl acetate).

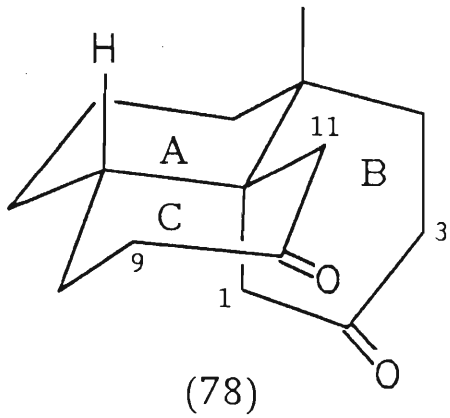
GLC of the crude oil showed this compound to be the main component, the pure sample giving a single peak, t_R 48,2 min (180°C).

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 715	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,1	(s; 3H; CH_3)
1,15 - 265	(19H; complex methylene/methine envelope)



(78)

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[a] Each product is a racemic mixture; R*/S* refer to the relative configuration of the chiral centres in one enantiomer.

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

21,16(t)	22,41(q; CH_3)	28,02(t)
28,10(t)	32,06(t)	35,78(s; C-4a)
35,92(t)	37,27(t)	38,04(d; C-7a)
40,84(t)	40,87(t)	46,80(t)
47,17(s; C-11a)	210,43 and 210,61 (s; C-2 and C-10)	

Analysis:

Found:	C, 76,8;	H, 9,6%;	M^+, 234
$C_{15}H_{22}O_2$ requires:	C, 76,9;	H, 9,5%;	M^+, 234

The stereoscopic drawing and crystal structure data for (78) are given in the Appendix.

Fractions 47 - 52 were combined and evaporated. Further purification by recrystallisation gave a **stereoisomer** of 4a-methyloctahydro-1*H*-benzo[d]-naphthalene-2,10(3*H*,11*H*)-dione (79) also as a white crystalline solid (0,48 g; 9%), MP 157 - 159°C (from hexane-ethyl acetate).

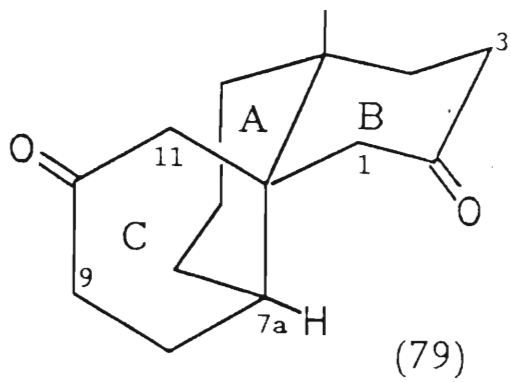
GLC showed one peak, t_R 37,7 min. (180°C).

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 705	(CO)

The ^{1}H-nmr spectrum (500 MHz; $CDCl_3$) showed δ (ppm)

1,10	(s; 3H; CH_3)
1,37	(m; 1H)
1,43	(m; 1H)
1,53-1,78	(complex; 5H)
1,79-1,89	(m; 2H)
2,10-2,32	(complex; 5H)
2,36	(quintet; 1H)
2,42	(d; 1H; J = 14 Hz)
2,5	(m; 2H)
2,74	(d; 1H; J = 14 Hz; axial H-11)



(79)

4aR*, 7aR*, 11aR*

The ^{13}C-nmr spectrum (125 MHz) showed δ (ppm)

20,44(t)	22,71(q; CH_3)	27,10(t)
27,24(t)	33,00(d, C-7a)	33,99(t)
34,78(t)	35,72(s; C-4a)	36,12(t)
39,97(t)	45,10(t)	46,15(t)
48,77(s; C-11a)	210,17 and 211,52 (s; C-2 and C-10)	

Analysis:

Found:	C, 76,5;	H, 9,55%;	M^+, 234
$C_{15}H_{22}O_2$ requires:	C, 76,9;	H, 9,5%;	M^+, 234

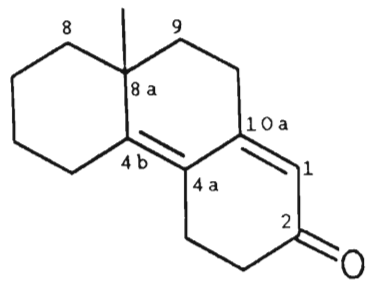
The spectral data and chromatographic properties are identical to that obtained for the compound (90) isolated from the corresponding reaction of the pyrrolidine dienamine of 8-methyl-$\Delta^{1,8a}$-2-octalone. The stereochemistry is commented upon in the discussion (Section 2.1).

A third product was isolated as an oil in very low yield (< 1%; GLC) from fractions 27-30 and was tentatively assigned as the angular annulation product **8a-methyl-3,4,5,6,7,8,8a,9-octahydrophenanthren-2(10*H*)-one** (72; R',R" = H; R = Me).

This compound gave a peak, t_R 31,5 min. (180°C), in the GLC of the crude reaction mixture.

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

0,73-2,93	(complex methylene envelope)
1,23	(s; 3H; CH_3)
6,16	(bs; 1H; =CH)



(72)

R', R" = H; R = Me

3.3.2.2 IN TOLUENE

Methyl vinyl ketone (1,61 g; 0,023 mol) was added dropwise to a stirred solution of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone (5 g; 0,023 mol) in dry toluene (100 ml) as outlined previously. This gave 3,94 g of crude product. A portion of this crude oil was subjected to flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 28 fractions. Thereafter, the eluant ratio was changed to 6:3:1 and an additional 18 fractions collected. Fractions 24-31 were combined, evaporated and washed with hexane. Further purification by recrystallisation gave **9-acetyl-8a-methylperhydro-2,4a-ethanonaphthalen-3-one** (80) as a white crystalline product (1,45 g; 28%), MP 95-97°C (from hexane-ethanol).

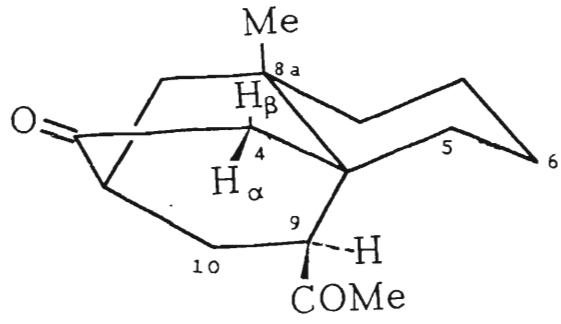
GLC of the crude oil indicated (80) to be the main component of the reaction mixture, the pure compound showing a single peak, t_R 23,2 min. (180°C).

The IR spectrum showed $\upsilon_{max}(CCl_4)$ cm^{-1}

1 710	(CH_3CO)
1 730	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

0,94	(s; 3H; CH_3)
1,30-1,85	(11H; complex methylene envelope)
1,93	(dd; 1H; J = 19 and 2 Hz; H_β-4)
2,08	(overlaid qd; 1H; J = 13, 10 and 4 Hz; H-10)
2,30	(s; 3H; CH_3CO)
2,35	(m; 1H; H-2)
2,95	(d; 1H; J = 19 Hz; H_α-4)
3,57	(overlaid qd; 1H; J = 10, 8 and 2 Hz; H-9)



(80)

2R*, 4aS*, 8aS*, 9S*

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

21,38(t)	21,56(t)	22,94(q; CH_3)
28,54(t)	29,03(t)	33,06(q; CH_3CO)
34,39(s; C-4a or C-8a)		36,79(t)
41,34(s; C-4a or C-8a)		43,27(t)
43,51(d and t)		43,69(d; C-9)
212,60 and 216,56 (s; C-3 and CH_3**C**O)		

Analysis:

Found:	C, 76,7;	H, 9,7%;	M^+, 234
$C_{15}H_{22}O_2$ requires:	C, 76,9;	H, 9,5%;	M^+, 234

The stereoscopic drawing and crystal structure data for (80) are given in the Appendix.

Fractions 38-46 were combined and evaporated. Further purification by washing with hexane and recrystallisation gave a **stereoisomer** (81) of 9-acetyl-8a-perhydro-2,4a-ethanonaphthalen-3-one as a white crystalline solid (0,68 g; 13%), MP 80-82°C (from hexane-ethanol).

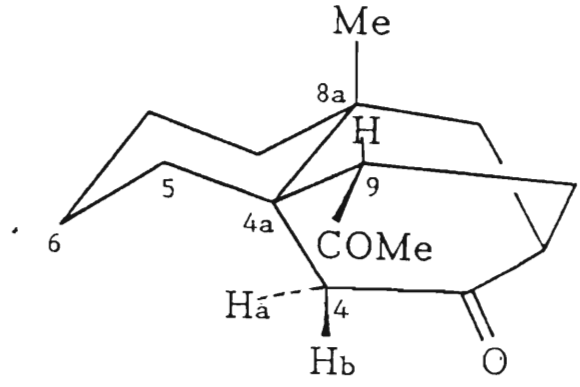
GLC showed one peak, t_R 27,5 min. (180°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 715	(CH_3CO)
1 730	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,21	(s; 3H; CH_3)
1,23-2,00	(12H; complex methylene envelope)
2,12	(s; 3H; CH_3CO)
2,13	(d; 1H; J = 19,5 Hz; H_b-4)
2,24	(quintet; 1H; J = 3 Hz; H-2)
2,59	(dd; 1H; J = 19,5 and 2 Hz; H_a-4)
3,04	(qd; 1H; J = 9,5 and 2 Hz; H-9)



(81)

$2R^{\ddagger}, 4aS^{\ddagger}, 8aR^{\ddagger}, 9S^{\ddagger}$

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

21,18(t)	21,47(t)	24,98(q; CH_3)
30,76(t)	33,08(s)	33,51(q; CH_3CO)
38,04(t)	39,62(t)	40,57(t)
41,70(s)	43,30(d; C-2)	49,07(d; C-9)

212,58 and 215,35 (s; C-3 and CH_3**C**O)

Analysis:

Found:	C, 76,9;	H, 9,6%;	M^+, 234,1615
$C_{15}H_{22}O_2$ requires:	C, 76,9;	H, 9,5%;	M^+, 234,1619

In this instance, it was not possible to obtain an X-ray analysis due to twinning of the crystals. The stereochemistry of (81) is commented on in the discussion (Section 2.1).

Fraction 22 gave on evaporation a low yield of the linear annulation product **5a-methyl-4,4a,5,5a,6,7,8,9-octahydroanthracen-2(3*H*)-one** (77; R = Me; R' = H; 0,2 g; 4%).

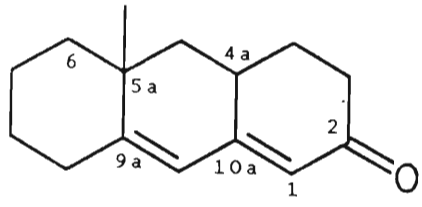
GLC of the crude oil indicated a peak t_R 30,7 min. corresponding to this compound.

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 585 and 1 615	(C=C)
1 650	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,20	(s; 3H; CH_3)
1,1-2,75	(complex methylene/methine envelope)
5,72	(d; 1H; J = 2,5 Hz; =CH)
5,90	(d; 1H; J = 1,8 Hz; =CH)



(77)

R = Me; R' = H

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

21,95(t)	23,24(q; CH_3)	27,79(t)
30,19(t)	31,87(d; C-4a)	32,77(t)
36,76(s; C-5a)		38,08(t)
42,06(t)	45,96(t)	
122,81 (d; C-1 and C-10)		201,06(s; C-2)

Accurate Mass Measurement:

Found: M^+, 216,1514

$C_{15}H_{20}O$ requires: M^+, 216,1514

3.3.2.3 In Benzene

The reaction in benzene was carried out in the same manner as the reaction in toluene. From the dienamine (2,0 g; 0,0092 mol) and methyl vinyl ketone (0,64 g; 0,0092 mol) in dry benzene (40 ml), 1,5 g of crude product was obtained. GLC (180°C) analysis of the crude product showed the presence of the same compounds (80; 13%), (81; 4%) and (77; R = Me; R' = H; 10%) isolated from the corresponding reaction in toluene.

3.3.3 REACTION OF THE PYRROLIDINE DI-ENAMINE OF 8-METHYL-$\Delta^{1,8a}$-2-OCTALONE

3.3.3.1 In Methanol

From MVK (1,61 g; 0,023 mol) and the pyrrolidine dienamine of 8-methyl-$\Delta^{1,8a}$-2-octalone (5 g; 0,023 mol) in "super-dry" methanol (100 ml), 6,13 g of crude product was obtained.

A portion of the crude oil was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (2:1:0,5) as eluant to collect 59 fractions (≃50 ml each). Fractions 30-40 were combined and treated with charcoal. The product, still impure was further purified by flash chromatography using the

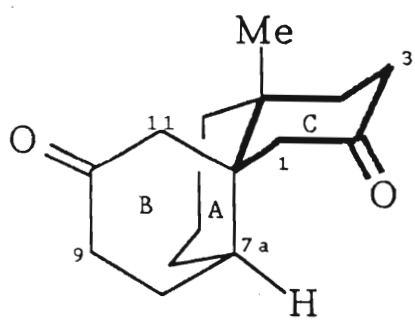
above solvents (in a 5:3:2 ratio) as eluant. Twenty fractions (≈30 ml each) were collected. Fractions 10-14 were combined and recrystallised to give **(4aR*,7aR*,11aR*)-4a-methyloctahydro-1*H*-benzo[d]naphthalene-2,10(3*H*,-11*H*)-dione**[b] (90) as a white crystalline product (2,10 g; 25%), MP 158°C (from hexane-ethyl acetate).

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 705	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,10	(s; 3H; CH_3)
1,3-1,9 and 2,1- 2,6	(complex methylene/methine envelope)
2,75	(d; 1H; J = 14 Hz; axial H-11)



(90)

[b]**One enantiomer.**

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

20,48(t)	22,77(q; CH_3)	27,15(t)
27,28(t)	33,03(d; C-7a)	34,04(t)
34,83(t)	35,76(s; C-4a)	36,18(t)
38,02(t)	45,14(t)	46,19(t)

48,82(s; C-11a)

210,25 and 211, 62 (s; C-2 and C-10)

Analysis:

Found:	C, 76,6;	H, 9,35%;	M^+, 234,1615
$C_{15}H_{22}O_2$ requires:	C, 76,9;	H, 9,5%	M^+, 234,1619

This compound (90) is identical to the stereoisomer (79) of (4aR*,7aS*,11aR*)-4a-methyloctahydro-1*H*-benzo[d]naphthalene-2,10(3*H*,11*H*)-dione(78)derived from the pyrrolidine dienamine of the 4a-methyl-$\Delta^{1,8a}$-2-octalone (see Experimental Section 3.3.2.1).

For comparison purposes, the ^{1}H-nmr and ^{13}C-nmr spectra for compound (79) were re-run at 200 and 50 MHz respectively. They were found to be superimposable on the ^{1}H- and ^{13}C-nmr spectra obtained for compound (90). There was no depression of MP on admixture and GLC of the mixture gave a single sharp peak, t_R 9,66 min. (230°C).

The stereoscopic drawing and crystal structure data for (90) are given in the Appendix.

GLC of the crude reaction mixture prior to flash chromatographic purification indicated the presence (<2%) of the other isomer (78) obtained from the reaction of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone [see Experimental Section 3.3.2.1].

A third product was isolated as an oil from fractions 18-22 and is tentatively assigned as the angular annulation product **5-methyl-3,4,5,6,7,8,8a,9-octahydrophenanthren-2(10*H*)-one** (72; R' = Me; R,R" = H; ≃7%).

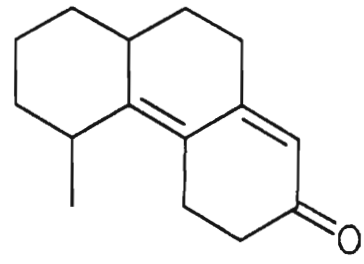
GLC of the crude oil showed this compound corresponded to the peak at t_R 31 min. (180°C).

The IR spectrum showed $\nu_{max}(CHCl_3)$ cm^{-1}

1 605	(C=C)
1 650	(CO)

The ^{1}H-nmr spectrum (80 MHz; $CDCl_3$) showed δ (ppm)

1,09	(d; 3H; CH_3)
1,0-3,45	(complex methylene/methine envelope)
5,65	(s; 1H; =CH)



(72)

R' = Me; R,R" = H

The ^{13}C-nmr spectrum (20 MHz) showed δ (ppm)

19,01(q; CH_3)	20,36(t)	25,05(t)
29,66(t)	30,52(t)	31,44(d)
32,97(t)	34,85(d)	35,25(t)
37,15(t)	121,92(d; =CH)	
124,28(s)	151,79(s)	158,56(s)
200,14(s; CO)		

Accurate Mass Measurement:

Found: M^+, 216,1520

$C_{15}H_{20}O$ requires: M^+, 216,1514

3.3.3.2 In Toluene

From MVK (1,61 g; 0,023 mol) and the pyrrolidine dienamine of 8-methyl-$\Delta^{1,8a}$-2-octalone (5 g; 0,023 mol) in dry toluene (100 ml), 5,26 g of crude product was obtained. Purification of the crude oil was achieved by flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 72 fractions (≃50 ml each). Fractions 19-28 appeared as one spot on TLC but GLC indicated a mixture with four components. GC-MS showed all four components to have the same molecular ion (M^+ 216). It was found possible to isolate only one component pure enough for analysis by combining fractions 19-28, evaporating off the solvent, washing the combined fractions with a small amount of hexane and recrystallising several times from hexane. This gave the main component of the crude product mixture which was identified as the linear annulation product **9-methyl-4,4a,5,5a,6,7,8,9-octahydroanthracen-2(3*H*)-one** (77; R' =Me; R = H; 0,86 g; 17%).

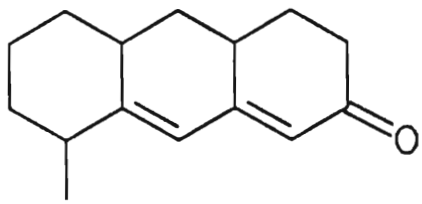
GLC showed one peak, t_R 31,4 min. (180°C).

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 585 and 1 610	(C=C)
1 650	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,14	(d; 3H; J = 8 Hz; CH_3)
1,01-2,48	(complex methylene/methine envelope)
5,79	(s; 1H; =CH)
6,02	(s; 1H; =CH)



(77)

R' = Me; R,R" = H

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

18,28(q; CH_3)	25,49(t)	29,93(t)
34,56(d)	35,66(t)	36,06(t)
37,52(d)	37,61(d)	37,86(t)
38,50(d)	120,46(d)	123,15(d)
159,55(s)	160,59(s)	201,05(s; C-2)

Accurate Mass Measurement:

Found: M^+, 216,1525

$C_{15}H_{20}O$ requires: M^+, 216,1514

Fraction 39 gave an amber oil which was identified as **9-acetyl-5-perhydro-2,4a-ethanonaphthalen-3-one** (94; 0,48 g; 9%).

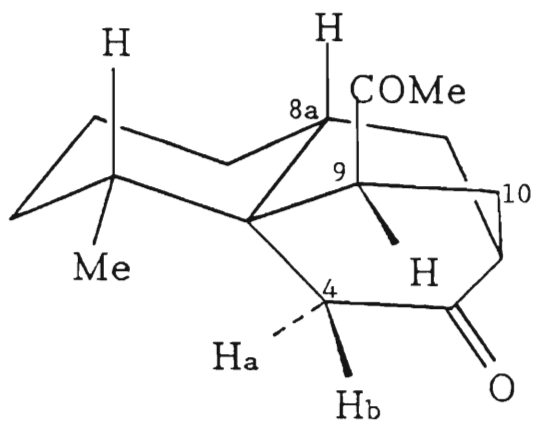
GLC of the crude oil showed this compound corresponded to the peak at t_R 20,1 min. (180°C).

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 710	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

0,94	(d; 3H; J = 8 Hz; CH_3)
1,05-2,8	(complex methylene/methine envelope)
2,25	(s; 3H; CH_3CO)
3,07	(t; 1H; J = 8,8 Hz; H-9)



(94) $2S^*, 4aS^*, 5R^*, 8aS^*, 9R^*$

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

16,52(q; CH_3)	25,49(t)	27,96(t)
31,06(d)	31,22(t)	31,64(t)
31,95(t)	33,18(q; **C**H_3CO)	
35,49(d)	38,80(t)	42,82(d)
43,43(s; C-4a)	49,97(d)	
212,67 and 217,12 (s; C-3 and CH_3**C**O)		

Accurate Mass Measurement:

Found: M^+, 234,1631

$C_{15}H_{22}O_2$ requires: M^+, 234,1620

Fraction 48 also gave an amber oil which was identified as a **diastereomer** of 9-acetyl-5-methylperhydro-2,4a-ethanonaphthalen-3-one (95; 0,32 g; 6%).

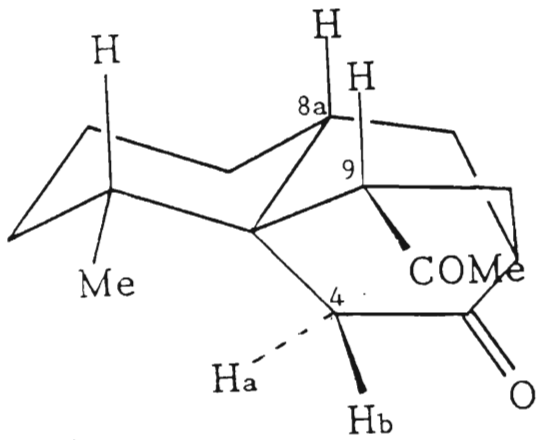
GLC of the crude oil prior to purification by flash chromatography showed this compound corresponded to the peak at t_R 25,3 min. (180°C).

The IR spectrum showed υ_{max}($CHCl_3$) cm^{-1}

1 710	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

0,89	(d; 3H; J = 8 Hz; CH_3)
0,93-2,4	(complex methylene/methine envelope)
2,18	(s; 3H; CH_3CO)
2,65	(dd; 1H; J = 19 and 2 Hz; H_a-4)
2,80	(overlaid qd; 1H; J = 11; 7 and 2 Hz; H-9)
2,94	(dd; 1H; J = 19 and 1,5 Hz; H_b-4)



$2S^{*}, 4aS^{*}, 5R^{*}, 8aR^{*}, 9S^{*}$

(95)

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

14,98(q; CH_3)	20,13(t)	28,14(t)
28,49(t)	30,62(q; **C**H_3CO)	
30,88(t)	31,48(d)	31,82(t)
32,48(d)	40,60(t)	40,98(s; C-4a)
42,78(d)	49,66(d)	

210,34 and 216,84 (s; C-3 and CH_3**C**O)

Accurate Mass Measurement:

Found: M^+, 234,1636

$C_{15}H_{22}O_2$ requires: M^+, 234,1620

The stereochemistry of compounds (94) and (95) are commented on in the discussion (Section 2.1).

3.3.4 REACTION OF THE PYRROLIDINE DI-ENAMINE OF 3-METHYL$\Delta^{1,8a}$-2-OCTALONE

3.3.4.1 In Methanol

From MVK (1,89 g; 0,027 mol) and the pyrrolidine dienamine of 3-methyl-$\Delta^{1,8a}$-2-octalone (6 g; 0,027 mol) in "super-dry" methanol (100 ml), 4,81 g of crude product was obtained.

A portion of the crude oil was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (6:3:1) as eluant to collect 35 fractions (≃50 ml each). The eluant ratio was changed to (6:3:2) and a further 8 fractions collected. Fractions 17-20 were combined and shown by TLC (hexane-methylene chloride-ethyl acetate [6:3:1]) to be "one-spot" pure. GLC however, showed the presence of four components (1,38 g; 22%) (t_R 29,2; 31,0; 31,9 and 37,6 min.). Fractions 15-22 were combined and subjected to further flash chromatography using the same eluant as before but in the ration of 8:4:1. Thirty-one fractions were collected. Fraction 13-20, on standing, developed

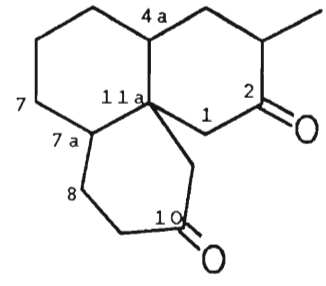
crystals surrounded by an oil. GC-MS showed four isomers, all having the molecular ion M^+ 234. Repeated recrystallisation from hexane-ethanol removed two components (t_R 29,2 and 37,6 min.) as indicated by GLC. Spectroscopic analysis of the remaining two component mixture was carried out.

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 705	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,00 and 1,01	(2xd; J = 6,45 Hz; 2xCH_3 from the two isomers)
1,48-2,6	(complex methylene/methine envelope)
1,93	(d; 1H; J = 13 Hz)
3,05	(dd; 1H; J = 1 and 13 Hz)



(75)

R,R' = H; R" = Me

3.3.5 REACTION OF THE PYRROLIDINE DI-ENAMINE OF $\Delta^{1,8a}$-2-OCTALONE

3.3.5.1 In methanol

Methyl vinyl ketone (5,26 g; 0,074 mol) was added dropwise with stirring to a solution of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone (15 g; 0,074 mol) in "super-dry" methanol (150 ml), following the general procedure outlined. After hydrolysis and hydrolytic work-up, this gave 9,13 g of crude product. A portion of the crude oil was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (5:3:2) as eluant to collect 44 fractions (≃ 50 ml each). Fractions 21-23 were combined on the basis of TLC, taken up in ethanol and treated twice with activated charcoal, to give a new **stereoisomer** of octahydro-1*H*-benzo[d]naphthalene-2,10-(3*H*,11*H*)dione (75; R,R',R" = H) as a white crystalline solid (3,58 g; 22%), MP 133-135°C (from hexane-ethyl acetate).

GLC analysis of the crude oil showed this to be the main component, the pure compound giving a single peak, t_R 28,7 min. (180°C).

The IR spectrum showed $\upsilon_{max}(CCl_4)$ cm^{-1}

1 720 (CO)

3.3.5 REACTION OF THE PYRROLIDINE DI-ENAMINE OF $\Delta^{1,8a}$-2-OCTALONE

3.3.5.1 In methanol

Methyl vinyl ketone (5,26 g; 0,074 mol) was added dropwise with stirring to a solution of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone (15 g; 0,074 mol) in "super-dry" methanol (150 ml), following the general procedure outlined. After hydrolysis and hydrolytic work-up, this gave 9,13 g of crude product. A portion of the crude oil was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (5:3:2) as eluant to collect 44 fractions (≃ 50 ml each). Fractions 21-23 were combined on the basis of TLC, taken up in ethanol and treated twice with activated charcoal, to give a new **stereoisomer** of octahydro-1*H*-benzo[d]naphthalene-2,10-(3*H*,11*H*)dione (75; R,R',R" = H) as a white crystalline solid (3,58 g; 22%), MP 133-135°C (from hexane-ethyl acetate).

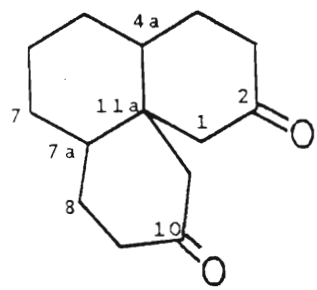
GLC analysis of the crude oil showed this to be the main component, the pure compound giving a single peak, t_R 28,7 min. (180°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 720	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,6 - 2,15	(14H; complex methylene/methine envelope)
2,0	(d; 2H; J = 14 Hz; H_{ax}-1 and H_{ax}-11)
2,35	(t; 4H; J = 7 Hz; 9-CH_2 and 3-CH_2)
2,75	(d; 2H; J = 14 Hz; H_{eq}-1 and H_{eq}-11)



(75)

R,R',R" = H

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

20,27(2xt)	26,52(2xt)	27,52(2xt)
35,84(d; C-7a and C-4a)		38,85(2xt)
46,95(s; C-11a)	50,02(2xt)	210,77(s; C-2 and C-10)

Analysis:

Found:	C, 76,1	H, 9,3%;	M^+, 220,1463
$C_{14}H_{20}O_2$ requires:	C, 76,3	H, 9,15%	M^+, 220,1463

A second portion of the crude oil was subjected to flash chromatography using hexane-methylene chloride-ethyl acetate (6:3:1) as eluant to collect 48 fractions (≃ 50 ml each). Fractions 37-41 were combined, evaporated and washed with a small amount of hexane using a pipette. These fractions contained a compound which was assigned as a stereoisomer of octahydro-1*H*-benzo[d]-naphthalene-2,10(3*H*,11*H*)-dione[a] (75; R,R',R" = H; 0,46 g; 3%), MP 164,9-165°C (from hexane-ethyl acetate), (Lit.[32] MP 161-162°C).

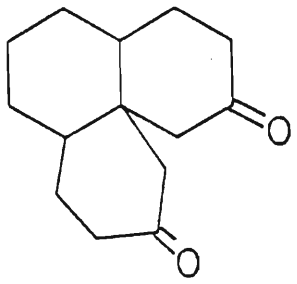
GLC analysis showed one peak t_R 34,1 min. (180°C).

The IR spectrum showed $\upsilon_{max}(CHCl_3)$ cm^{-1}

1 710 (CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,24 - 2,53 (complex methylene/methine envelope)



(75)

R,R',R" = H

[a] **The stereoscopic drawing and crystal structure data appear in the**

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

26,01(t) 26,62(t) 26,82(t)

28,16(t) 36,97(t) 40,38(t)

41,38(t) 41,84 and 44,21 (d; C-4a and C-7a)

45,14(s; C-11a) 52,05(t)

209,81 and 210,74 (s; C-2 and C-10)

Accurate Mass Measurement:

Found: M^+, 220,1453

$C_{14}H_{20}O_2$ requires: M^+, 220,1463

GLC (180°C) of the crude product showed a third component (t_R 26,3 min.) present to the extent of 20%. Attempts to isolate this component in a pure state by flash chromatography was unsuccessful. This component was tentatively assigned as the angular annulation product (72; R,R',R" = H) (see corresponding reaction in toluene).

3.3.5.2 In ethanol

The reaction in dry ethanol was carried out in the same manner as the reaction in methanol. From the dienamine (5,00 g; 0,025 mol) and methyl vinyl ketone (1,75 g; 0,025 mol) in ethanol (100 ml), 2,84 g of crude product was obtained. GLC (180°) analysis of the crude product showed the presence of the same two stereoisomers of the tricyclic ketone (75; R,R',R" = H) isolated from the

corresponding reaction in methanol [i.e. (75; R,R',R" = H; MP 133-135°C; 11%[c]) and (75; MP 165°C; 8%[c])]. A third component corresponding to the peak at t_R 26 min. was also present to the extent of 28%[c]. Once again, this is most probably the angular annulation product (72; R,R',R" = H) by virtue of the GLC retention time.

3.3.5.3 In toluene

Methyl vinyl ketone (2,45 g; 0,034 mol) was added dropwise with stirring to a solution of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone (7,00 g; 0,034 mol) in dry toluene (100 ml) according to the general procedure outlined. In this instance, the mixture was hydrolysed by heating under reflux overnight and after work-up gave 6,58 g of crude product. A portion of the crude oil was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 82 fractions (≃ 50 ml each). Fractions 35-56 were combined and washed with a small amount of hexane to give 9-acetylperhydro-2,4a-ethanonaphthalen-3-one (76; R,R' = H) as a white crystalline solid (2,02 g; 27%), MP 79-81°C (from hexane-ethanol).

GLC showed one peak, t_R 20,0 min (180°C).

---

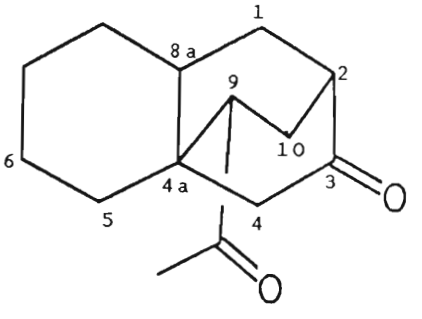
[c]**Integrated GLC peak areas.**

The IR spectrum showed $\upsilon_{max}(CCl_4)$ cm^{-1}

1 705	CH_3**CO**
1 720	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,17 - 2,20	(complex methylene envelope)
2,21	(s; 3H; CH_3CO)
2,28	(m; 1H)
2,41	(t; 1H)



(76)

R, R' = H

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

21,27(t)	25,41(t)	27,31(t)	30,35(t)
31,16(t)	33,05 (q; CH_3)		34,16(t)
37,48(t)	38,34 (d; C-8a)		39,09 (s; C-4a)

42,22 and 54,29 (d; C-2 and C-9)

212,23 and 215,48 (s; C-3 and CH_3CO)

Analysis:

Found:	C, 76,6	H, 9,3%;	M^+, 220
$C_{14}H_{20}O_2$ requires:	C, 76,3	H, 9,15%	M^+, 220

Fractions 10-27 were combined and subjected to further flash chromatography using hexane-methylene chloride-ethyl acetate (24:4:1) as eluant to collect 35 fractions (≃ 50 ml each). The eluant ratio was changed to (12:3:1) and a further 25 fractions collected. Fractions 31-50 were combined and again purified by flash chromatography using the same eluant ratio (12:3:1). Fractions 22-30 were combined and washed with a small amount of hexane using a pipette to give 4,4a,5,5a,6,7,8,9-octahydroanthracen-2(3*H*)-one (77; R,R' = H; 1,92; 28%), MP 103°C (from hexane-ethanol), (Lit.[82] MP 102-103°C).

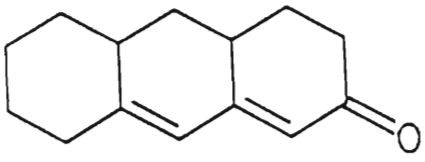
GLC showed on peak, t_R 26,9 min. (180°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 590, 1 625	C=C
1 670	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

0,95 - 2,53	(16H; complex methylene/methine envelope)
5,73	(s; 1H; =CH)
5,98	(s; 1H; =CH)



(77)

R,R' = H

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

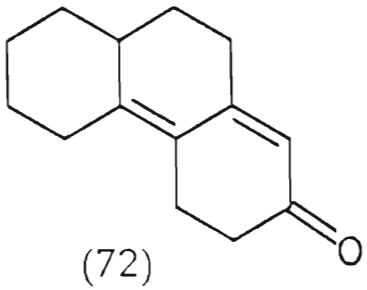
25,61(t)	27,02(t)	30,01(t)	34,86(t)
34,92(d)	35,15(t)	37,49(t)	37,90(t)
38,18(d)	122,64 and 123,22 (d; C-4a and C-5a)		
156,02 and 160,32 (s; C-9a and C-10a)			
200,95 (s; C-2)			

Analysis:

Found:	C, 82,9	H, 9,1%;	M^+, 202
$C_{14}H_{18}O$ requires:	C, 83,1	H, 9,0%	M^+, 202

A third component corresponding to the peak t_R 26,3 min. (17%) in the GLC of the crude reaction mixture was present in fraction 17 obtained from the column run of fractions 31-50. Although not pure, this compound is tentatively assigned as the angular annulation product 3,4,5,6,7,8,8a,9-octahydrophenanthren-2(10*H*)-one (72; R,R',R" = H) on the basis of the 200 MHz ^{1}H-nmr

spectrum which shows an olefinic signal at δ_H 5,7 and the GC-MS which gives the required molecular ion, M^+ 202.



(72)

R,R',R" = H

3.4 REACTION OF METHYL VINYL KETONE WITH 1-N-PYRROLIDINYLCYCLOHEXENE IN ETHANOL[40]

Methyl vinyl ketone (18,08 g; 0,3 mol) was added dropwise to a stirred solution of 1-N-pyrrolidinylcyclohexene (15,11 g; 0,1 mol) in absolute ethanol (35 ml) and the mixture heated under reflux for 4 hours. A buffer solution of anhydrous sodium acetate (5 g) and glacial acetic acid (10 ml) in water (10 ml) was added and the mixture heated under reflux for a further 2 hours. The volatiles were removed *in vacuo* and the residue diluted with water and extracted with ether (3 x 50 ml). The combined ether extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure to give 29,42 g of crude product which was shown by GLC (180°C) to be a complex mixture consisting of several components.

Recrystallisation of the crude product from isopropyl alcohol gave a white crystalline product (8,4 g; 38%), MP 165°C. This compound was shown to be identical with compound (75; R,R',R" = H; MP 164,9 - 165°C) obtained from the reaction of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone with MVK in methanol. There was no depression of the MP on admixture and GLC of the mixture (230°C) gave a single sharp peak, t_R 9,4 min.

The mother liquor was concentrated under reduced pressure to give a viscous oil. A portion of this oil was subjected to flash chromatography using hexane-

methylene chloride-ethyl acetate (10:10:0,5) as eluant to collect 20 fractions. Fraction 3 gave an oil (6,4 g; 32%) identified as 7-methyl-2,3,3a,4,5,6-hexa-hydrophenalen-6-one (99).

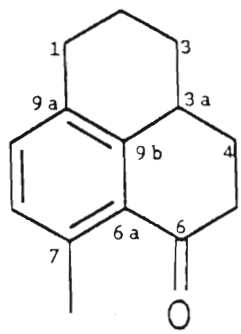
GLC (180°C) showed this compound corresponding to a peak at t_R 16,7 min in the crude reaction mixture.

The IR spectrum showed υ_{max}(film) cm^{-1}

1 675	CO

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,2 - 2,1 and 2,5 - 2,9	(complex methylene/methine envelope)
2,6	(s; 3H; CH_3)
6,98	(d; 1H; J = 8 Hz; H-8)
7,11	(d; 1H; J = 8 Hz; H-9)



(99)

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

22,28(t)	23,06(q; CH_3)	29,04(t)	30,34(t)
30,73(t)	36,80(q; C-3a)	40,51(t)	130,09(d; C-8 or C-9)
130,66(s)	133,31(d; C-8 or C-9)		138,77(s)
144,24(s)	200,89(s; C-6)		

Accurate Mass Measurement:

Found: M^+, 200.1215

$C_{14}H_{16}O$ requires: M^+, 200.1201

GLC of the crude product also showed the presence of the stereoisomer (75; R,R',R" = H; MP 133 - 135°C) (isolated from the reaction of the pyrrolidine dienamine of $\Delta^{1,8a}$-2-octalone with MVK in methanol) to the extent of 5%.[d]

Additional peaks at 15,9 min. (6%[d]), 17,4 min. (4%[d]) and 26 min. (8%[d]) were observed in the GLC of the crude reaction mixture but compounds corresponding to these could not be isolated. The peak at 26 min. most probably corresponds to the angular annulation product (72; R,R',R" = H).

---

[d]Integrated GLC peak areas.

3.5 PREPARATION OF 1-(2-CYANOETHYL)-4a-METHYL-$\Delta^{1,8a}$-2-OCTALONE

The methodology outlined by Stork[59] was used in this preparation.

Ethyl bromide (2,18 g; 0,02 mol) in dry THF (5 ml) was added dropwise under nitrogen to magnesium turnings (0,48 g; 0,02 mol) and iodine (trace amount) in THF (50 ml). After all the magnesium had been consumed, the cyclohexyl-imine of 4a-methyl-$\Delta^{1,8a}$-2-octalone (5,0 g; 0,02 mol) in dry THF (5 ml) was added to the stirred solution and the mixture heated under reflux for 24 hours. 3-Bromopropionitrile (2,68 g; 0,02 mol) in dry THF (5 ml) was then added dropwise with stirring and the mixture heated under reflux for a further 24 hours. Hydrolysis and work-up as outlined in the general procedure (Section 3.3.1) gave 3,46 g of the crude product. A portion of the crude product was subjected to flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 46 fractions. Fractions 23-29 were combined and subjected to further flash chromatography using the same eluant system to collect 28 fractions. Fraction 23 gave a yellow oil identified as 1-(2-cyanoethyl)-4a-$\Delta^{1,8a}$-2-octalone (88; 1,14 g; 26%).

The IR spectrum showed υ_{max}(film) cm^{-1}

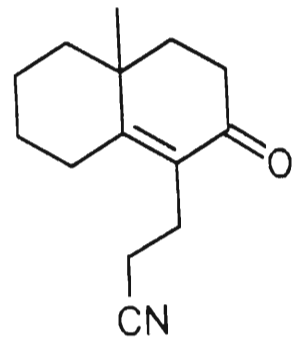
1 605	(C=C)
1 670	(CO)

2 250 (CN)

The ^{1}H-nmr spectrum (60 MHz; $CDCl_3$) showed δ (ppm)

1,26 (s; 3H; CH_3)

1,46 - 2,90 (16H; complex methylene envelope)



(88)

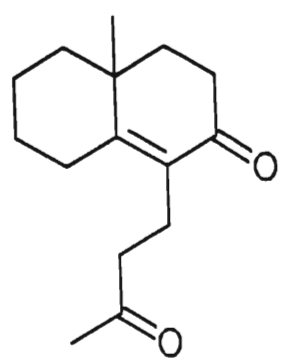
This compound has been reported previously[50].

3.6 ATTEMPTED PREPARATION OF 1-(3-OXO-BUTYL)-4a-METHYL-$\Delta^{1,8a}$-2-OCTALONE

In the same manner as the previous experiment, the reaction between MVK (1,4 g; 0,02 mol) and the magnesium salt of the cyclohexylimime of 4a-methyl-$\Delta^{1,8a}$-2-octalone gave on hydrolysis and work-up 2,19 g of crude product. GLC (180°C) analysis of the crude product showed the presence of 4a-methyl-$\Delta^{1,8a}$-2-octalone to the extent of 52% and no significant quantity of any other products.

The reaction was not further investigated.

The reaction of MVK with the cyclohexylimine of 4a-methyl-$\Delta^{1,8a}$-2-octalone also failed to give the desired C-1 alkylated product (89).



(89)

3.7 REACTION OF METHYL VINYL KETONE WITH THE PYRROLIDINE DIENAMINE OF 4a-METHYL-5-OXO-$\Delta^{1,8a}$-2-OCTALONE IN TOLUENE

From the reaction between methyl vinyl ketone (1,54 g; 0,022 mol) and the pyrrolidine dienamine of 4a-methyl-5-oxo-$\Delta^{1,8a}$-2-octalone (5,00 g; 0,022 mol) in dry toluene (100 ml), the crude product was obtained as a viscous, dark-brown oil (2,61 g). A portion of the crude oil was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 25 fractions ($\simeq$ 50 ml each). Thereafter, the eluant ratio was changed to (6:3:1) and a further 51 fractions collected. Fractions 12-14 were combined and evaporated, and recrystallised to give 3a,7-dimethyl-2,3,3a,4,5,6-hexahydrophenalen-3,6,dione (58) as a crystalline solid (0,45 g; 9%), MP 87 - 89°C (from cyclohexane); Lit.[56] MP 86 - 87°C.

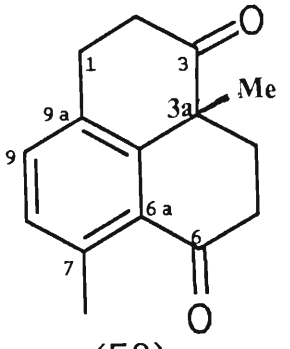
GLC showed one peak, t_R 8,9 min. (220°C).

The IR spectrum showed $\nu_{max}(CH_2Cl_2)$ cm^{-1}

1 670, 1 700 (CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,44	(s; 3H; CH_3)
2,0 - 3,68	(8H; complex methylene envelope)
2,62	(s; 3H; Ar-CH_3)
7,13	(d; 1H; J = 8 Hz; H-8)
7,29	(d; 1H; J = 8 Hz; H-9)



(58)

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

22,98 (q; CH_3)	23,39 (q; CH_3)	27,30 (t)	30,37 (t)
35,55 (t)	36,67 (t)	46,80 (s; C-3a)	
130,71 (s)	131,51 and 132,99 (d; C-8 and C-9)		
133,76 (s)	140,88 (s)	145,13 (s)	
199,96 (s; C-6)	214,38 (s; C-3)		

GLC showed a single sharp peak, t_R 9,2 min. (220°C).

GC-MS showed the molecular ion M^+ 228 as would be expected for this compound.

Fractions 55-67 were combined, evaporated and further purified by recrystallisation to give **9-acetyl-8a-methylperhydro-2,4a-ethanonaphthalen-3,8-dione** (108) as a white crystalline product (0,89 g; 16%), MP 97 - 99°C (from hexane ethanol).

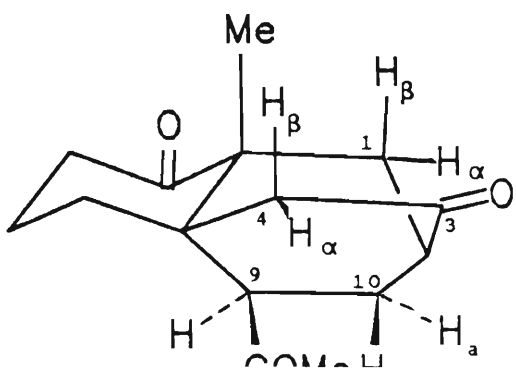
GLC showed one peak, t_R 9,9 min. (220°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 710, shoulders at 1 725 and 1 735 (CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,16	(s; 3H; CH_3-8_a)
1,36	(ddd; 1H; J = 14,2; 2,75; 2,75 Hz; H-1_β)
1,58 - 1,80	(c; 2H; H-6; H-10)
1,82 - 2,08	(c; 2H; CH_2-5; H-6)
2,12 - 2,42	(c; 3H; H-7; H-10)
2,46	(m; 1H; H-2)
2,20	(s; 3H; CH_3CO)
2,22	(dd; 1H; J = 19,2; 2,3 Hz; H-4_β)
2,76	(om; 1H; H-9)
2,58 - 2,80	(m; 3H; H-1; H-7; H-9)
3,16	(d; 1H; J = 19,2 Hz; H-4_α)



The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

22,13 (t; C-6)	22,66 (q; CH_3-8a)	26,84 (t; C-5)
28,45 (t; C-10)	32,06 (q; **C**H_3CO)	33,09 (t; C-1)
36,68 (t; C-7)	42,25 (t; C-4)	43,03 (d; C-2)
45,18 (s and d; C-4a and C-9)		50,72 (s; C-8a)
211,07 (s; CH_3**C**O)	214,57 and 214,93 (s; C-3 and C-8)	

Analysis:

Found:	C, 73,0;	H, 8,25%;	M^+, 248
$C_{15}H_{20}O_3$ requires:	C, 72,6;	H, 8,1%;	M^+, 248

A third product was obtained as an oil from fraction 29 and is assigned as *trans*-8a-methyldecahydronaphthalen-1,6-dione (100; 0,16g; 4%).

GLC of the crude oil showed this compound corresponded to the peak, t_R 3,7 min. (220°C).

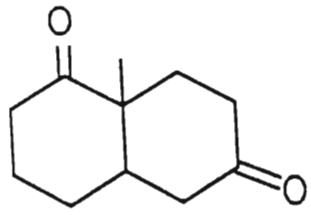
The IR spectrum showed ν_{max} (film) cm^{-1}

1 700	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,0 - 2,8 (complex methylene/methine envelope)

1,35 (s; 3H; CH_3)



(101)

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

22,96 (t) 23,97 (q; CH_3) 26,71 (t) 33,76 (t)

37,58 (t) 38,48 (t) 43,81 (t) 46,15 (d; C-4a)

48,64 (s; C-8a) 211,98 and 214,86 (s; C-1 and C-6)

GC-MS showed the molecular ion M^+ 180 as required for this compound.

Accurate Mass Measurement:

Found: M^+, 180,1149

$C_{11}H_{16}O_2$ requires: M^+, 180,1150

3.8 REACTION OF METHYL VINYL KETONE WITH THE PYRROLIDINE DIENAMINE OF 4a,6-DIMETHYL-5-OXO-$\Delta^{1,8a}$-2-OCTALONE IN TOLUENE

From the reaction between methyl vinyl ketone (1,75 g; 0,025 mol) and the pyrrolidine dienamine of 4a,6-dimethyl-5-oxo-$\Delta^{1,8a}$-2-octalone (6,13 g; 0,025 mol) in dry toluene (100 ml), the crude product was obtained as a viscous brown oil (4,85 g). A portion of the crude oil was subjected to flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 67 fractions (≃ 50 ml each). Fractions 46 - 62 were combined, evaporated and further purified by recrystallisation to give **9-acetyl-7,8a-dimethylperhydro-2,4a-ethanonaphthalen-3,8-dione** (110) as a white crystalline product (1,55 g; 24%), MP 121 - 122,5°C (from hexane-ethanol).

GLC showed one peak, t_R 32,2 min. (180°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

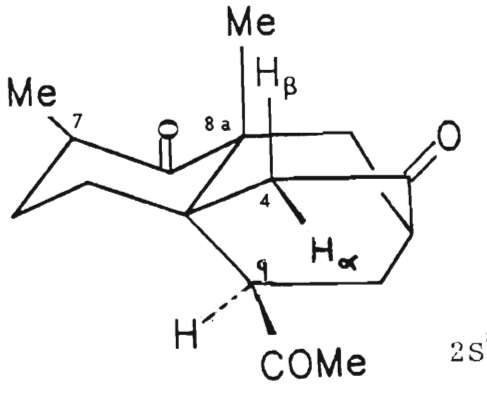
1 710, shoulders at 1 725 and 1 735 (CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,07	(d; 3H; J = 6,4 Hz; CH_3-7)
1,17	(s; 3H; CH_3-4a)
1,22 - 1,45	(m; 2H; H-1; H-6)
1,66	(m; 1H; H-10)
1,80 - 2,24	(m; 4H; CH_2-5; H-6; H-10)
2,20	(s; 3H; CH_3CO)
2,22	(dd; 1H; J = 19,0; 2,1 Hz; H_β-4)
2,45	(m; 1H; H-2)
2,67 - 2,87	(m; 2H; H-7; H-9)
2,88	(dd; 1H; J = 13,8 Hz; 1,7 Hz; H_α-1)
3,13	(d; 1H; J = 19,0 Hz; H_α-4)

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

15,05 (q; CH_3-7)	22,99 (q; CH_3-8a)	27,21 (t; C-5)
28,46 (t; C-10)	31,45 (t; C-6)	32,23 (q; **C**H_3CO)
33,28 (t; C-1)	39,38 (d; C-7)	42,22 (t; C-4)
42,99 (d; C-2);	45,03 (d; C-9)	45,84 (s; C-4a)
50,48 (s; C-8a)	211,22 (s; CH_3**C**O)	
215,02 and 215,42 (s; C-3; C-8)		



2S*, 4aR*, 7R*, 8aR*, 9R*

Analysis:

Found:	C, 72,98	H, 8,45%;	M^+, 262
$C_{16}H_{22}O_3$ requires:	C, 73,25;	H, 8,45%;	M^+, 262

3.9 REACTION OF METHYL VINYL KETONE WITH THE PYRROLIDINE DIENAMINE OF 5,6,7,7a-TETRAHYDROINDAN-5-ONE

3.9.1 In methanol

Methyl vinyl ketone (2,95 g; 0,042 mol) was added dropwise to a stirred solution of the pyrrolidine dienamine of 5,6,7,7a-tetrahydroindan-5-one (5,77 g; 0,042 mol) in "super-dry" methanol (100 ml) according to the general procedure outlined in Section 3.3.1. This gave 4,0 g of the crude product as a viscous oil, and was shown by GLC to be at least a fifteen component mixture. A portion of the crude oil was subjected to flash chromatography using hexane-methylene chloride - ethyl acetate (6:3:1) as eluant to collect 55 fractions (≃ 50 ml each). Fractions 3 - 6 contained the main component present to the extent of 32 % in the crude reaction mixture. These were combined and evaporated. Further purification by recrystallisation gave **6-methyl-1,2,2a,3,4,5-hexahydroacenaphthalen-5-one** (103a) as a waxy white solid (1,05 g; 13,5%); MP 54°C (from hexane).

GLC showed one peak, t_R 10,6 min. (180°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 680 (CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,54 - 1,85 (m; 2H; H_α-2; H_α-3)

2,21 - 2,48 (m; 2H; H_β-2; H_β-3)

2,62 (s; 3H; CH_3)

2,5 - 2,8 (m; 2H; $CH_2$4)

2,8 - 3,08 (m; 2H; CH_2-1)

3,11 - 3,31 (m; 1H; H-2a)

7,19 (d; 1H; J = 8 Hz; H-7)

7,27 (d; 1H; J = 8 Hz; H-8)

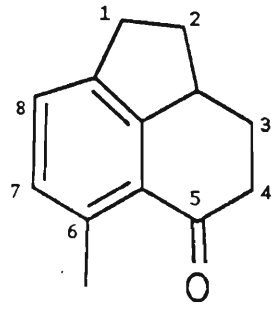
The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

21,77 (q; CH_3) 30,43 and 34,38 (t; C-2 and C-3)

32,37 (t; C-1) 40,97 (t; C-4) 42,63 (d; C-2a)

128,23 (s) 129,11 and 130,88 (d; C-7 and C-8)

138,23 (s) 141,41 (s) 154,02 (s) 200,48 (s; C-5)



(103a)

Analysis:

Found:	C, 83,6	H, 7,8%;	M^+, 186,1043
$C_{13}H_{14}O$ requires:	C, 83,8;	H, 7,6%;	M^+, 186,1045

Two other products present in the crude product mixture to the extent of 18%.[d] (GLC: t_R 18,4 min. at 180°C) and 13 % (GLC: t_R 28,9 min.) could not be isolated after repeated attempts in a sufficiently pure state to be identified.

3.9.2 In toluene

Methyl vinyl ketone (0,74 g; 0,01 mol) was added to a stirred solution of the pyrrolidine dienamine of 5,6,7,7a-tetrahydroindan-5-one (2,0 g; 0,01 mol), according to the general method. The crude product (0,64 g), shown by GLC again to be a complex multi-component mixture, was subjected to flash chromatography using hexane-methylene chloride-ethyl acetate (12:6:1) as eluant to collect 22 fractions (≃ 50 ml each). The eluant ratio was changed to (6:3:1) and a further 32 fractions collected. Fraction 32 gave **9-acetylperhydro-3a-6-ethanoinden-5-one** (103b) as a light yellow oil (0,11 g; 6%).

GLC of the crude mixture showed this compound corresponding to the peak at t_R 14,0 min. (180°C).

The IR spectrum showed ν_{max}(film) cm^{-1}

1 700 and 1 720 (CO)

---

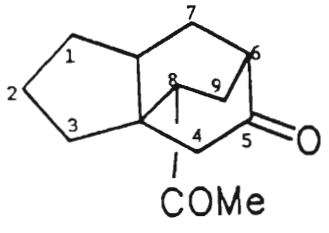
[d]Integrated GLC peak area.

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,16 - 2,24	(complex methylene/methine envelope)
2,19	(s; CH_3CO)
2,33	(m; 1H; H-6)
2,38 - 2,65	(complex; 2H; CH_2-4)
2,79	(4 x d; 1H; J = 10,5; 3,6; 1,5 Hz; H-8)

The ^{13}C-nmr spectrum (50 MHz) showed δ (ppm)

22,38 (t)	25,97 (t)	29,71 (t)	29,82 (t)
31,02 (q; **C**H_3CO);		34,52 (t)	39,66 (t)
42,67 and 42,90 (d; C-6 and C-8)			46,36 (s; C-3a)
55,26 (d; C-7a)		209,93 (s; CH_3**C**O)	
215,12 (s; C-5)			



(103b)

Accurate Mass measurement:

Found: M^+, 206,1301

$C_{13}H_{18}O_2$ requires: M^+, 206,1307

Three other products were present in the crude product mixture to the extent of 18,[a] 0,3[b] and 5[b] % [GLC (180°C): t_R 18,4; 28,9 and 10,6 min. respectively.] These are the same three products as formed in the methanol reaction. Reducing the reflux time in toluene from 50 to 4 h. caused the GLC peak areas to change as follows:

t_R (min.)	10,6	14,0	18,4	28,9
Yield (%)	6	28	11	2

Repeated attempts to isolate and purify these components proved unsuccessful.

[a]Integrated GLC peak areas.

3.10 REACTION OF METHYL VINYL KETONE WITH THE MORPHOLINE DI-ENAMINE OF ISOPHORONE

3.10.1 In Toluene

Methyl vinyl ketone (0,67 g; 0,0096 mol) was added dropwise to a stirred solution of the morpholine dienamine of isophorone (2,01 g; 0,0096 mol) in dry toluene (10 ml) and heated under reflux for 43 hours. Hydrolysis and work-up in the usual manner (see Section 3.3.1) gave the crude product as a viscous amber oil (1,23 g). A portion of the crude oil was subjected to flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:2) as eluant to collect 31 fractions (≃ 50 ml). The ratio of the eluant was changed to 12:5:3) and a further 10 fractions collected. Fractions 10-11 were combined on the basis of TLC and recrystallised from hexane to give **5,5,7-trimethyl-4,4a,5,6-tetrahydronaphthalen-2(3*H*)-one** (105; 0,21 g; 12%) MP 95-96°C.

GLC showed a single, sharp peak, t_R 24,8 min. (180°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

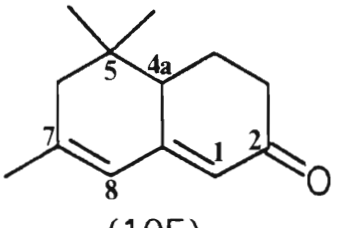
1 590 ; 1 632	(C=C)
1 665	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

0,89	(s; 3H; axial CH_3-5)
1,12	(s; 3H; equatorial CH_3-5)
1,32 -1,54	(m; 1H; H-4_{ax})
1,90	(br.s; 3H; CH_3-7)
1,90 - 2,03	(m; 1H; H-4_{eq})
2,22	(dd; J = 1,0; 15,9 Hz; H-6_{ax})
2,21 - 2,37	(m; 3H; H-3; H-4_a)
2,36	(dd; 1H; J = 0,8; 15,9 Hz; H-6_{eq})
5,73	(m; 1H; H-1)
6,06	(m; 1H; H-8)

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

20,16 (q; CH_3-5)	22,51 (t; C-4)	24,35 (q; CH_3-5)
28,96 (q; CH_3-7)	31,74 (t; C-6)	36,19 (s; C-5)
45,31 (d; C-4a)	54,07 (t; C-3)	122,27 (d; C-1)
125,64 (d; C-8)	150,63 (s; C-7)	157,44 (s; C-8a)
200,53 (s; C-2)		



(105)

Accurate Mass measurement:

Found:	C, 81,92	H, 9,65%	M^+, 190,1358
$C_{13}H_{18}O$ requires:	C, 82,06	H, 9,53%	M^+, 190,1339

Mass spectrometry:

The mass spectrum showed the following mass fragment ions (m/z):

190 (M^+); 175; 162; 134 (base peak); 119; 91; 77 and 65.

Fractions 13 and 14 were combined on the basis of TLC and further purified by recrystallisation from hexane to give 8-acetyl-4,6,6-trimethylbicyclo[2.2.2]-octan-2-one(111; 0,49 g; 27%), MP 71°C; Lit.[44] 71 - 72°C.

GLC showed a single, sharp peak, t_R 14,9 min. (180°C).

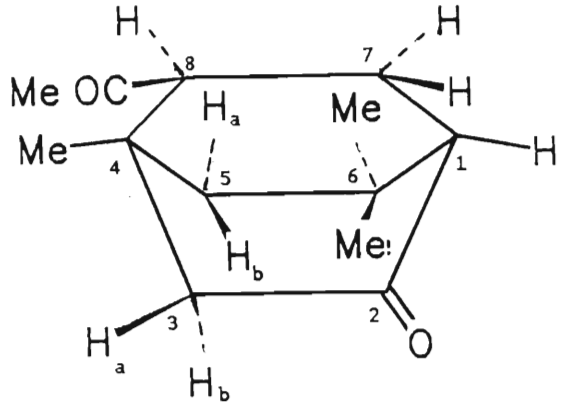
The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 718	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

0,93; 1,00 and 1,11	(s; 3x3H; CH_3-4 and 2xCH_3-6)
1,25	(d; 1H; J = 13,6 Hz; H_b-5)
1,41	(dd; 1H; J = 3,3; 13,6 Hz; H_a-5)
1,71	(dd; 1H; J = 17; 19,2 Hz; H_b-3)
1,80	(qd; 1H; J = 2; 7,4; 14,4 Hz; H_b-7)
1,96	(dd; 1H; J = 2; 7,4; 14,4 Hz; H-1)

2,20	(m; 1H; H_b-7)
2,23	(s; 3H; CH_3CO)
2,65	(dd; 1H; J = 3,3; 19,2 Hz; H_a-3)
2,77	(oqd; 1H; J = 1,7; 3,7 Hz; H-8)



(111)

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

24,13 (t; C-7)	24,67 (q; CH_3)	28,87 (q; CH_3)
31,59 (s; C-6)	31,92 (q; CH_3)	33,10 (q; $\mathbf{C}H_3CO$)
37,20 (s; C-4)	44,11 (t; C-3)	50,48 (d; C-8)
51,30 (t; C-5)	54,25 (d; C-1)	
212,42 and 215,45 (s; C-2 and $CH_3\mathbf{C}O$)		

Mass Spectrometry:

The mass spectrum showed the following mass fragment ions (m/z):

208 (M^+); 193; 175; 151; 138; 123 (base peak); 95; 81; and 69.

Fraction 19 gave a yellow oil which could not be isolated in a pure form. The main component was, however, identified as 2-(3-oxobutyl)-3,5,5-trimethyl-

cyclohex-2-enone (48; ≃12%) by comparison of the spectral data of the mixture with that of the pure compound isolated from the corresponding reaction in methanol (*vide infra)*; t_R 14,7 min. (150°C).

Fraction 29 gave 3-(4-oxopentyl)-5,5-dimethylcyclohex-2-enone (104) as a yellow oil (0,21 g; 10%).

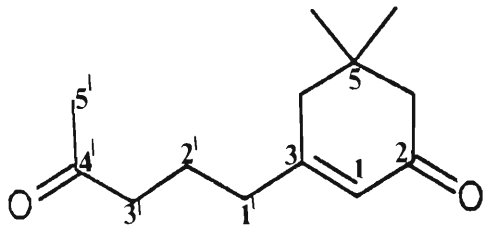
GLC showed one peak, t_R 24,2 min. (150°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 670; 1 718	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,04	(2xs; 6H; 2xCH_3)
1,76	(q; 2H; CH_2-2')
1,8 - 2,25	(m; 6H; CH_2-1';4;6)
2,15	(s; 3H; CH_3CO)
2,47	(t; 2H; CH_2-3')
5,87	(q; 1H; J = 3,8 Hz; H-2)



(104)

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

20,65 (t; C-2')	28,34 (q; 2xCH_3)	30,17 (q; C-5')
33,69 (s; C-5)	37,29 (t; C-1')	
42,68 and 43,84 (t; C-4 and C-3')		
51,17 (t; C-6)	125,28 (d; C-2)	163,57 (s; C-3)
200,63 (s; C-4')	208,64 (s; C-1)	

Accurate Mass Measurement:

Found: M^+, 208,1468

$C_{13}H_{20}O_2$ requires: M^+, 208,1463

Mass Spectrometry:

The mass spectrum showed the following mass fragment ions (m/z):

208 (M^+); 175; 151 (base peak); 135; 123; 94; 82; and 53.

3.10.2 In Methanol

The corresponding reaction in dry methanol (4h.; reflux) gave a complex mixture which was separated by flash chromatography into three components previously identified from the toluene reaction, namely (105; 2%), (46; 15%) and (104; 6%). A fourth product identified as 2-(3-oxobutyl)-3,5,5-trimethyl-cyclohex-2-enone (48; 23%) was isolated as the main component.

GLC showed one peak, t_R 14,7 min. (150°C).

The IR spectrum showed $\nu_{max}(CCl_4)$ cm^{-1}

1 665; 1 715	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

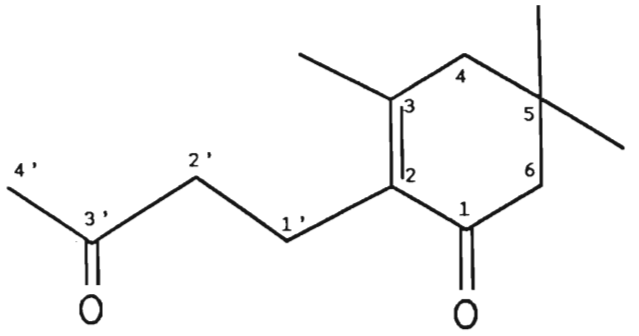
0,96	(2xs; 6H; 2xCH_3)
1,91	(3H; CH_3)
2,1	(3H; CH_3)
2,48	(m; 4H)

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

19,8 (t; C-1')	21,35 (q; CH_3-3)	28,2 (q; 2xCH_3-5)
29,8 (q; C-5')	32,7 (s; C-5)	42,7 (t)
47,1 (t)	51,35 (t)	133,2 (2; C-2)
154,3 (s; C-3)	199,5 (s; C-3')	209,3 (s; C-1)

Mass Spectrometry:

The mass spectrum showed the following mass fragment ions (m/z): 208 (M^+); 175; 165; 135; 123; 109 (base peak); 81; and 67. This compound has been reported previously.[44]



(48)

3.11 REACTION OF PHENYL VINYL KETONE WITH DIENAMINES DERIVED FROM $\Delta^{1,8a}$- 2-OCTALONES

The reactions of PVK (2 eq.) with dienamines derived from $\Delta^{1,8a}$-2-octalones were carried out following the same general procedure outlined for the corresponding reactions using MVK (see Experimental Section 3.3.1). In each case chromatographic (GLC and TLC) analysis showed the reaction products to be a complex multi-component mixture. Separation of the mixtures was again achieved by flash chromatography[72] the details of which are given in the description of individual experiments.

3.11.1 REACTION OF THE PYRROLIDINE DI-ENAMINE $\Delta^{1,8a}$-2-OCTALONE

3.11.1.1 In Methanol

A portion of the crude product (6,2 g) isolated as a viscous dark brown oil from the dienamine (5,0 g; 0,025 mol) was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (60:25:2) as eluant to collect 60 fractions (≃ 50 ml each). Fractions 22-24 were combined on the basis of TLC and evaporated to give an almost colourless oil. TLC [hexane-methylene chloride-ethyl acetate (12:3:1)] showed these fractions to be "one-spot" pure,

however, GLC indicated the presence of a small amount (≃ 3%) of an unknown impurity. The main component of fractions 22-24 was identified as **9-benzoylperhydro-2,4a-ethanonaphthalen-3-one** (118; R',R" = H; 0,73 g; 10%) by comparison of the spectral data with that of the pure compound isolated from the corresponding reaction in toluene (*vide infra*).

Fractions 42-45 were combined on the basis of TLC and evaporated to give a yellow oil. GLC analysis showed this oil to be predominantly one component. Repeated attempts to obtain this component in a pure state were unsuccessful but based on the spectral data obtained, is assigned as a **stereoisomer** of 9-benzoylperhydro-2,4a-ethanonaphthalen-3-one (120; R',R" = H; 1,79 g; 25%).

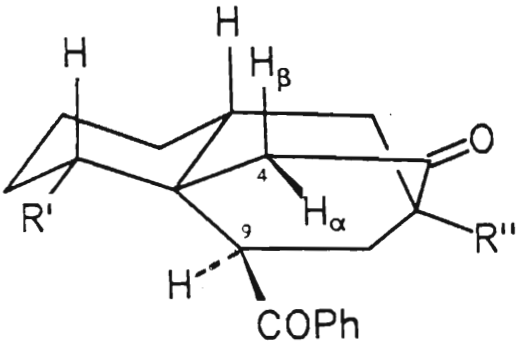
GLC analysis (10 min @ 180°C; 5°C/min - 230°C) of the crude reaction mixture showed this to be the main component and corresponded to a peak at t_R 39,7 min.

The IR spectrum showed ν_{max}(film)

1 595	(C=C)
1 675; 1 720	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,1 - 2,45	(complex methylene/methine envelope)
2,10	(o.d; 1H; J = 12,4 Hz; H_α-4)
2,56	(dd; 1H; J = 12,4 Hz; H_β-4)
3,61	(o.td; J = 1,2; 5,8 Hz; H-9)
7,05 - 8,05	(c; Ph)



(120)

2S*, 4aS*, 8aR*, 9R*

R, R" = H

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

21,37 (t)	25,64 (t)	28,68 (t)	30,62 (t)
31,47 (t)	34,65 (t)	38,0 (t; C-4)	39,02 (d; C-8a)
39,99 (s; C-4a)		42,61 (d; C-2)	
48,19 (d; C-9)		128,24 (2xd)	
128,79 (2xd)		133,27 (d)	138,61 (s)

203,98 and 216,13 (s; C-3 and Ph**C**O)

3.11.1.2 In Toluene

A portion of the crude product (7,05 g), once again isolated as a viscous brown oil from the dienamine (3,64 g; 0,018 mol) was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (60:25:2) as eluant to collect 28 fractions (≃ 50 ml each). The eluant ratio was changed (6:3:1) and a further 18 fractions collected. Fractions 22-28 were combined and subjected to further flash chromatography using hexane-methylene chloride-ethyl acetate (12:3:1) as eluant to collect 20 fractions. Fractions 11-13 were combined and recrystallised from hexane to give **9-benzoylperhydro-2,4a-ethanonaphthalen-3-one** (118; R',R" = H; 0,89 g; 18%) MP 107°C.

GLC gave s single, sharp peak, t_R 34,2 min. (10 min @ 180°C; 5°C/min - 230°C).

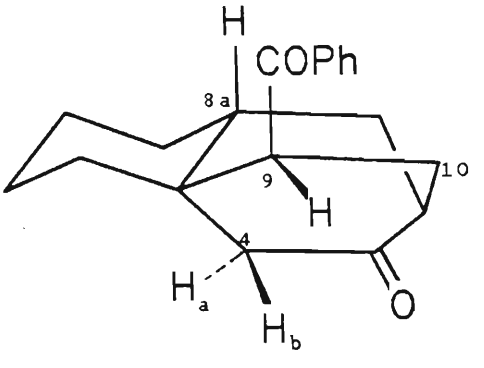
The IR spectrum showed $\nu_{max}(CCl_4)$

1 595	(C=C)
1 675; 1 725	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,0 - 1,5	(7H; complex methylene envelope)
1,56 - 1,68	(m; 2H)
1,86	(dd; 1H; J = 1; 19 Hz; H_b-4)
1,90 - 2,05	(c; 1H)
2,19 - 2,38	(c; 3H)

2,40	(m; 1H; H-2)
2,85	(d; 1H; J = 19 Hz; H_a-4)
3,65	(dd; 1H; J = 8; 10 Hz; H-9)
7,45 - 8,0	(m; 5H; Ph-)



(118) $2S^*, 4aR^*, 8aR^*, 9S^*$

R', R" = H

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

21,86 (t)	25,35 (t)	28,34 (t)	29,51 (d; C-8a)
31,36 (t)	31,61 (t)	35,01 (t)	40,50 (s; C-4a)
42,91 (d; C-2)		44,72 (t; C-4)	
47,12 (d; C-9)		128,23 (2xd)	128,71 (2xd)
133,24 (d)	138,70 (s)		
203,27 and 216,67 (s; C-3 and Ph**C**O)			

Analysis:

Found:	C, 80,85	H, 7,95%	M^+, 282,1594
$C_{19}H_{22}O_2$ requires:	C, 80,81	H, 7,85%	M^+, 282,1620

Fraction 32 gave an oil which although not pure gave spectral data consistent with the stereoisomer of 9-benzoylperhydro-2,4a-ethanonaphthalen-3-one (120; R',R" = H; 0,73 g; 14%) isolated from the corresponding reaction in methanol.

3.11.2 REACTION OF THE PYRROLIDINE DIENAMINE OF 8-METHYL-$\Delta^{1,8a}$-2-OCTALONE IN METHANOL

A portion of the crude product (9,46 g) isolated as a viscous dark brown oil from the dienamine (5,06 g; 0,023 mol) was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (60:25:2) as eluant to collect 43 fractions (≃ 50 ml each). Fractions 23 - 28 were combined on the basis of TLC, evaporated and further purified by repeated recrystallisation from hexane-ethanol to give **9-benzoyl-5-methylperhydro-2,4a-ethanonaphthalen-3-one** (118; R' = Me; R" = H; 2,01 g; 29%), MP 145°C.

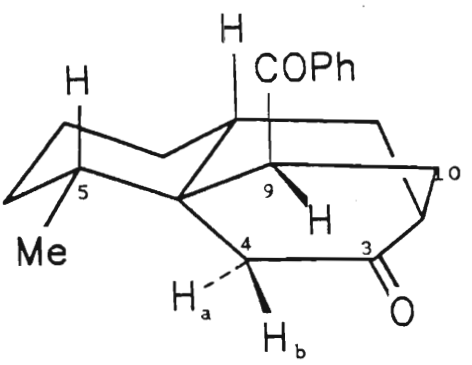
GLC of the crude reaction mixture showed this to be the major component. The pure compound gave a single, sharp peak at t_R 37,8 min. (10 min. @ 180°C; 5°C/min. - 230°C).

The IR spectrum showed $\nu_{max}(CCl_4)$

1 680; 1 725 (CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

0,62	(d; 3H; J = 7 Hz; CH_3)
1,04 - 1,42	(c; 5H)
1,54 - 1,68	(c; 3H)
1,92 - 2,31	(c; 3H)
2,01	(odd; 1H; J = 2; 19 Hz; H_b-4)
2,40	(m; 1H; H-2)
2,53	d; 1H; J = 19 Hz; H-4a)
2,66	(m; 1H; H-8a)
3,79	(dd; 1H; J = 8; 11 Hz; H-9)
7,40 - 7,95	(m; 5H; Ph-)



(118) $2S^{\ddagger}, 4aS^{\ddagger}, 5R^{\ddagger}, 8aR^{\ddagger}, 9R^{\ddagger}$

R' = Me; R" = H

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

16,28 (q; CH_3)	25,61 (t; C-7)	29,70 (t; C-10)
30,87 (d; C-8a)	31,18 and 31,86 (t; C-6 or C-8)	
32,12 (t; C-1)	34,98 (d; C-5)	39,39 (t; C-4)

43,27 (d; C-2) 43,96 (s; C-4a) 44,29 (d; C-9)

128,22 (2xd) 129,18 (2xd) 133,44 (d)

204,96 and 217,34 (s; C-3 and Ph**C**O)

Analysis:

Found:	C, 81,55	H, 8,36%	M_+, 296
$C_{20}H_{24}O_2$ requires:	C, 81,05	H, 8,16%	M^+, 296

3.11.3 REACTION OF THE PYRROLIDINE DI-ENAMINE OF 3-METHYL-$\Delta^{1,8a}$-2-OCTALONE IN METHANOL

A portion of the crude product (6,48 g) isolated as a viscous dark brown oil from the dienamine (4,0 g; 0,018 mol) was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (60:25:2) as eluant to collect 50 fractions (≃ 50 ml each). Fractions 12 - 15 were combined, evaporated and recrystallised from hexane-ethanol to give **9-benzoyl-2-methylperhydro-2,4a-ethanonaphthalen-3-one** (118; R" = Me; R' = H; 0,63 g; 12%), MP 151°C.

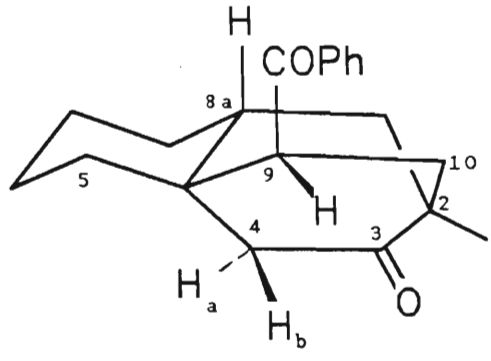
GLC gave a single, sharp peak at t_R 34,4 min. (10 min @ 180°C; 5°C/min. - 230°C).

The IR spectrum showed $\nu_{max}(CCl_4)$

1 580	(C=C)
1 675; 1 720	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,00	(s; 3H; CH_3)
1,01 - 1,49	(c; 7H)
1,50 - 1,80	(c; 3H)
1,89	(dd; 1H; J = 2; 19 Hz; H_b-4)
2,04 - 2,20	(c; 2H)
2,35	(m; 1H; H-8a)
2,86	(d; 1H; J = 19 Hz; H_a-4)
3,67	(dd; 1H; J = 8; 10 Hz; H-9)
7,45 - 8,0	(m; 5H; Ph-)



(118)

R" = Me; R' = H

2S*, 4aR*, 8aR*, 9R*

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

19,61 (q; CH_3)	21,91 (t)	25,32 (t)	30,35 (d; C-8a)
31,36 (t)	34,87 (t)	35,43 (t)	39,30 (t)
40,43 (s; C-4a)	43,28 (s; C-2)		44,56 (t; C-4)
47,88 (d; C-9)	128,20 (2xd)		128,69 (2xd)
131,19 (d)	138,69 (s)		
203,25 and 217,04 (s; C-3 and Ph**C**O)			

Analysis:

Found:	C, 80,83	H, 8,23%	M^+, 296
$C_{20}H_{24}O_2$ requires:	C, 81,04	H, 8,16%	M^+, 296

Fraction 21 was further purified by recrystallisation from hexane-ethanol to give a **diastereomer** of 9-benzoyl-2-methylperhydro-2,4a-ethanonaphthalen-3-one (119; R' = H; R" = Me; 1,45 g; 27%), MP 121°C.

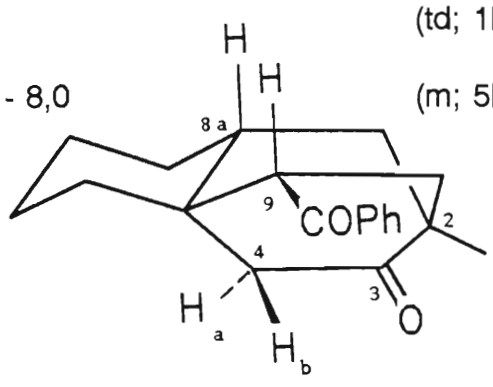
GLC showed this to be the main component of the complex reaction mixture. The pure compound gave a single, sharp peak at t_R 39,1 min. (10 min. @ 180°C; 5°C/min. - 230°C).

The IR spectrum showed ν_{max}(CCl_4)

1 595	(C=C)
1 675; 1 725	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,00	(s; 3H; CH_3)
1,10 - 1,48 and 1,52 - 1,84	(c; 10H)
1,91	(dd; 2H; J = 1; 8 Hz; H_α-10 and H_β-10)
2,04	(dd; 1H; J = 11; 14 Hz; H_β-1)
2,58	(qd; 2H; J = 1; 19 Hz; H_a-4 and H_b-4)
3,67	(td; 1H; J = 1; 7 Hz; H-9)
7,40 - 8,0	(m; 5H; Ph-)



(119)
R' = H; R" = Me

$2S^*, 4aR^*, 8aR^*, 9S^*$

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

19,77 (q; CH_3)	21,64 (t)	25,82 (t)	30,80 (t)
34,68 (t)	35,96 (t; C-10)		37,98 (t; C-4)
39,35 (t; C-1)	39,94 (d; C-8a)		40,20 (s; C-4a)
43,05 (s; C-2)	49,11 (d; C-9)		128,22 (2xd)
128,67 (2xd)	133,10 (d)		138,50 (s)

203,58 and 215,73 (s; C-3 and Ph**C**O)

Analysis:

Found:	C, 81,28	H, 8,36%	M^+, 296,1776
$C_{20}H_{24}O_2$ requires:	C, 81,04	H, 8,16%	M^+, 296,1791

3.11.4 REACTION OF THE PYRROLIDINE DI-ENAMINE OF 4a-METHYL-$\Delta^{1,8a}$-2-OCTALONE IN METHANOL

A portion of the crude product (9,05 g) isolated as a viscous dark brown oil from the dienamine (5,12 g; 0,024 mol) was purified by flash chromatography using hexane-methylene chloride-ethyl acetate (60:25:2) as eluant to collect 64 fractions (≃ 50 ml each). Fractions 24 - 31 were combined and subjected to further flash chromatography using a 20 mm diameter column and hexane-methylene chloride-ethyl acetate (70:25:4) as eluant to collect 18 fractions (≃ 30 ml each). Fractions 7 - 15 were combined, evaporated and recrystallised from hexane-ethanol to give a product tentatively assigned as the **octahydrophenalenone** (122; 0,75 g; 8%[f]),; cream coloured needles, MP 156°C.

GC-MS showed the molecular ion M^+ 410 as would be expected for this compound.

The IR spectrum showed $\nu_{max}(CH_2Cl_2)$

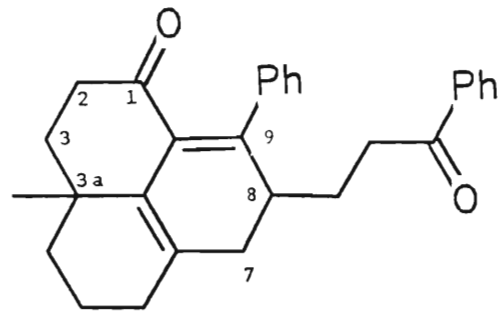
1 600; 1 640	(C=C)
1 650; 1 690	(CO)

The ^{1}H-nmr spectrum (200 MHz; $CDCl_3$) showed δ (ppm)

1,27	(s; 3H; CH_3)

[f] Percentage yield calculated from the mass of product isolated by flash chromatography.

1,34 - 2,45	(c; 12H; methylene envelope)
2,63 - 2,89	(c; 3H)
3,18 - 3,27	(m; 2H)
7,17 - 7,61 and 8,0 - 8,1	(c; 10H; 2xPh-)



(122)

The ^{13}C-nmr spectrum (50 MHz; $CDCl_3$) showed δ (ppm)

19,49 (t)	19,69 (t)	25,28 (q; CH_3)	25,89 (t)
28,07 (t)	30,37 (t)	34,96 (s)	36,49 (t)
38,87 (t)	41,58 (d)	44,64 (t)	126,92 (d)
127,93 (2xd)		128,09 (2xd)	128,19 (2xd)
128,54 (2xd)		129,68 (s)	132,92 (d)
136,92 (s)		141,72 (s)	142,22 (s)
157,85 (s)		200,21 (s)	200,61 (s)

Analysis:

Found:	C, 84,85	H, 7,53%
$C_{29}H_{30}O_2$ requires:	C, 84,84	H, 7,37%

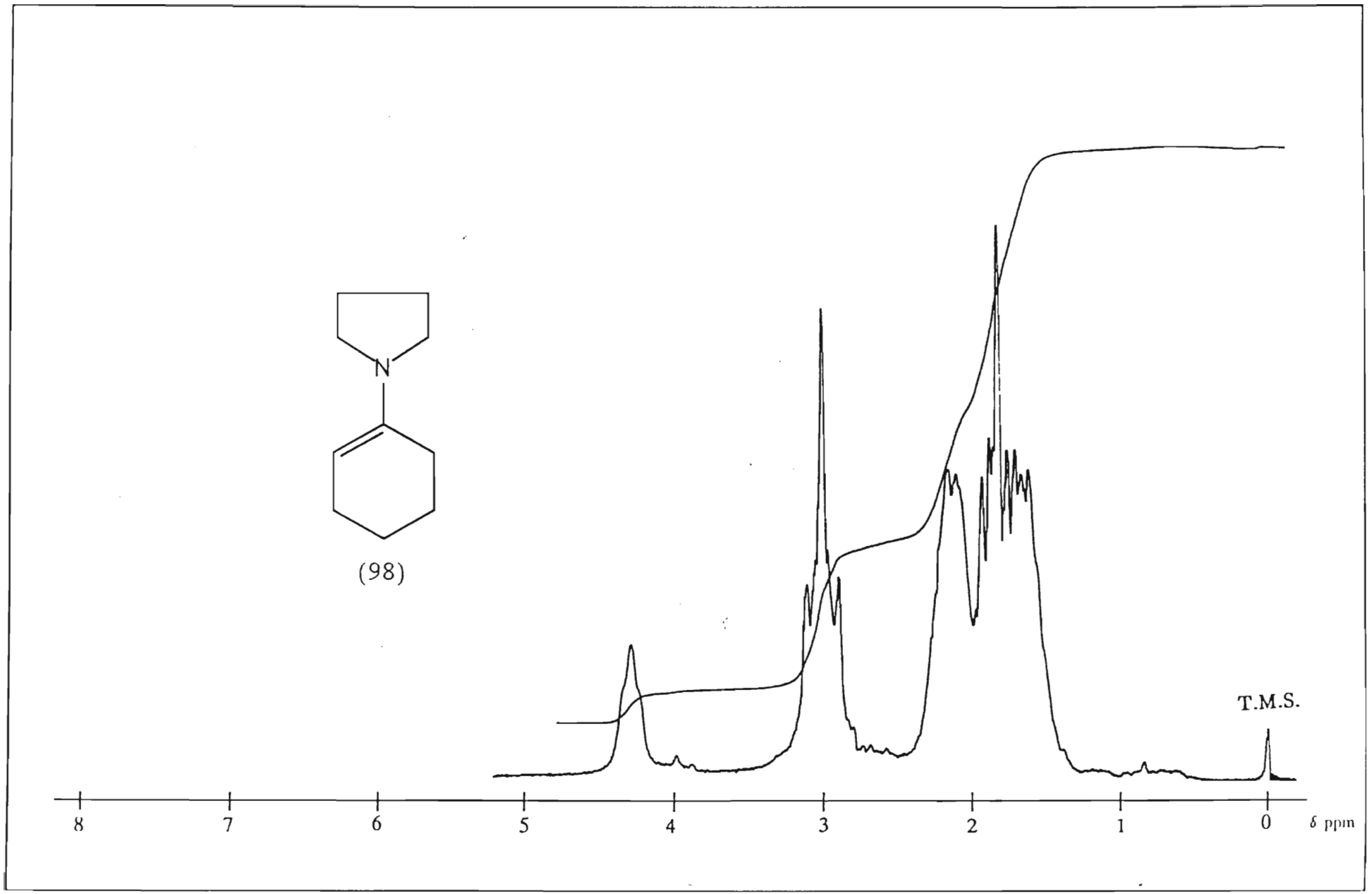
This product was not detected in the GLC of the crude reaction mixture under the operating conditions employed (10 min. @ 180°C; 5°C/min; - 230°C; 50 min.). The failure to elute is presumably due to the compound's high molecular mass. GLC did however show peaks at 35 min. (11%[g]) and 39 min (5%[g]) but products corresponding to these peaks were not isolated.

[g]Integrated GLC peak areas.

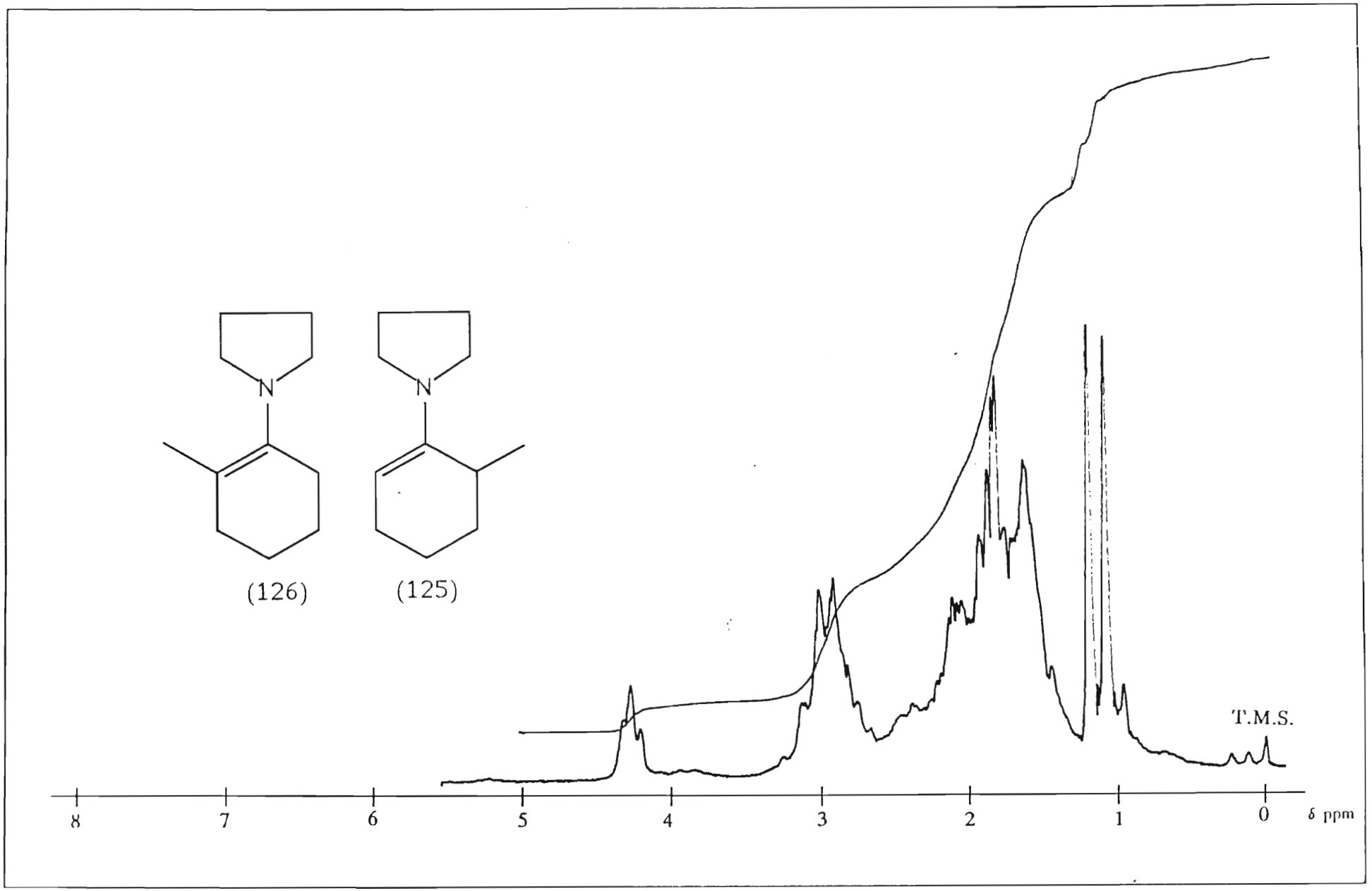
CHAPTER FOUR

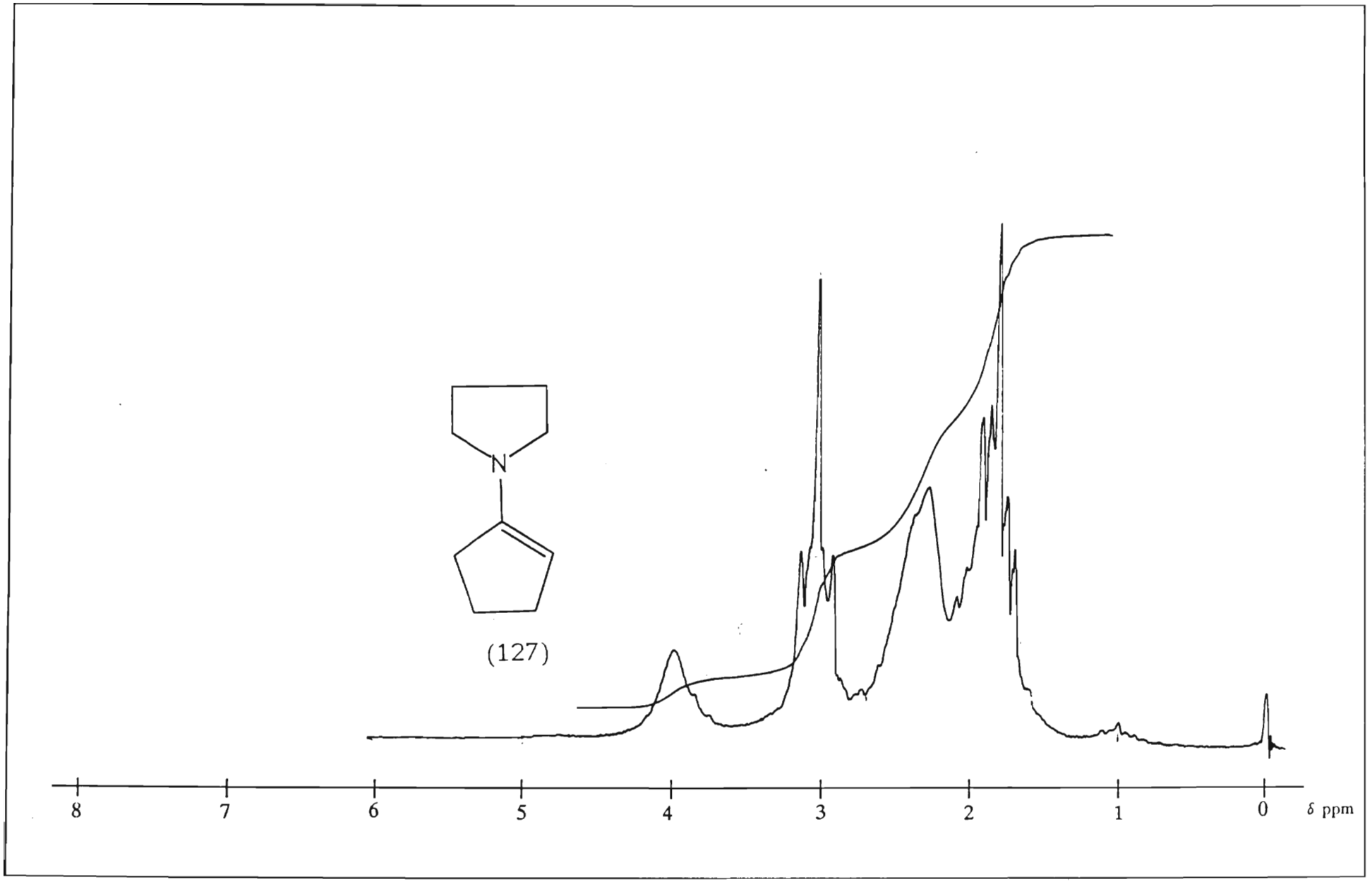
4. SPECTRA

The nmr spectra for each compound are grouped together for convenience and are labelled with the compound structure and number on the first ^{1}H-nmr spectrum which appears as the first spectrum of each set of spectra.

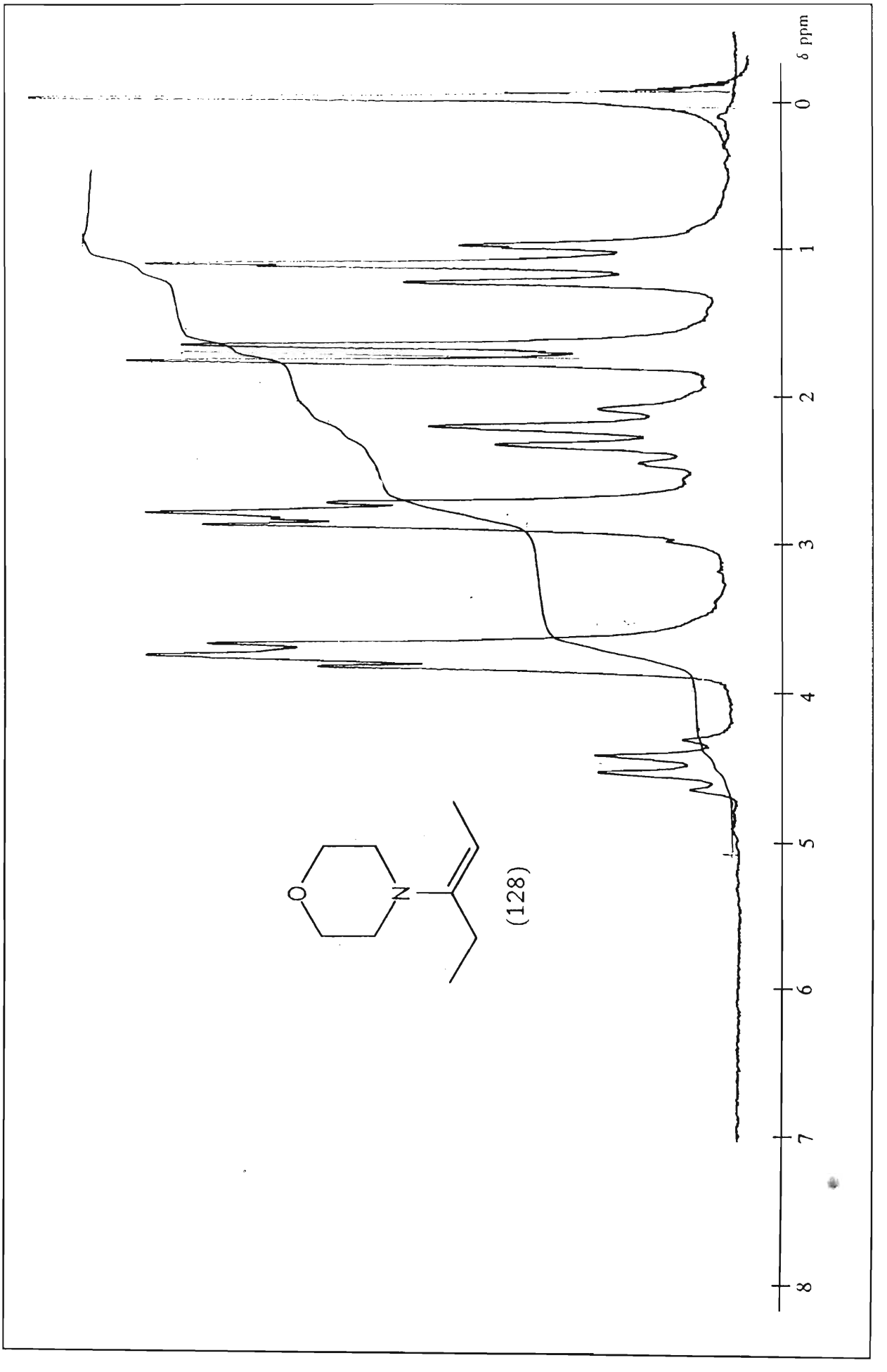


(98)

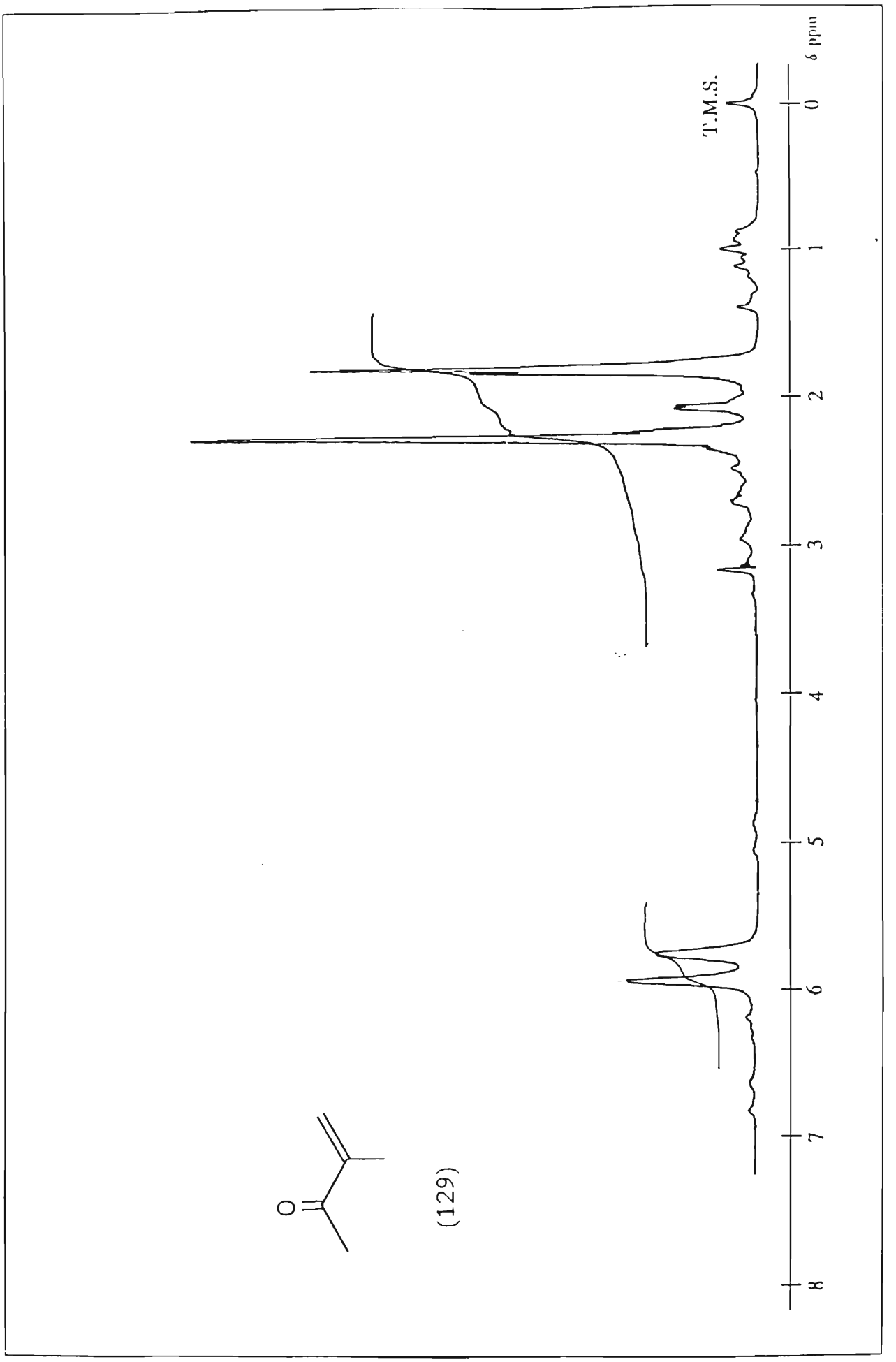

N
N
(126)
(125)
T.M.S.
8
7
6
5
4
3
2
1
0
δ ppm



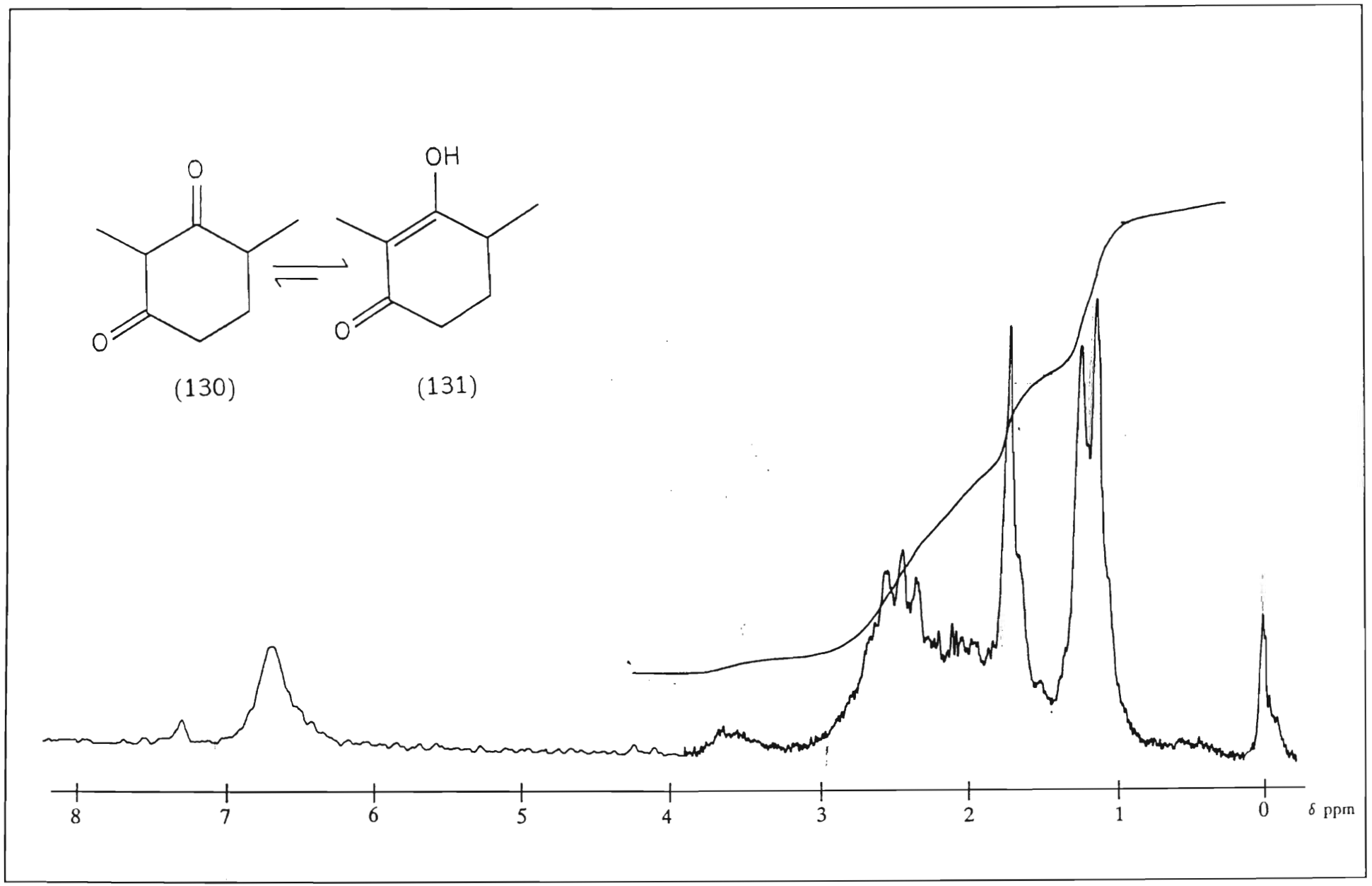
(127)

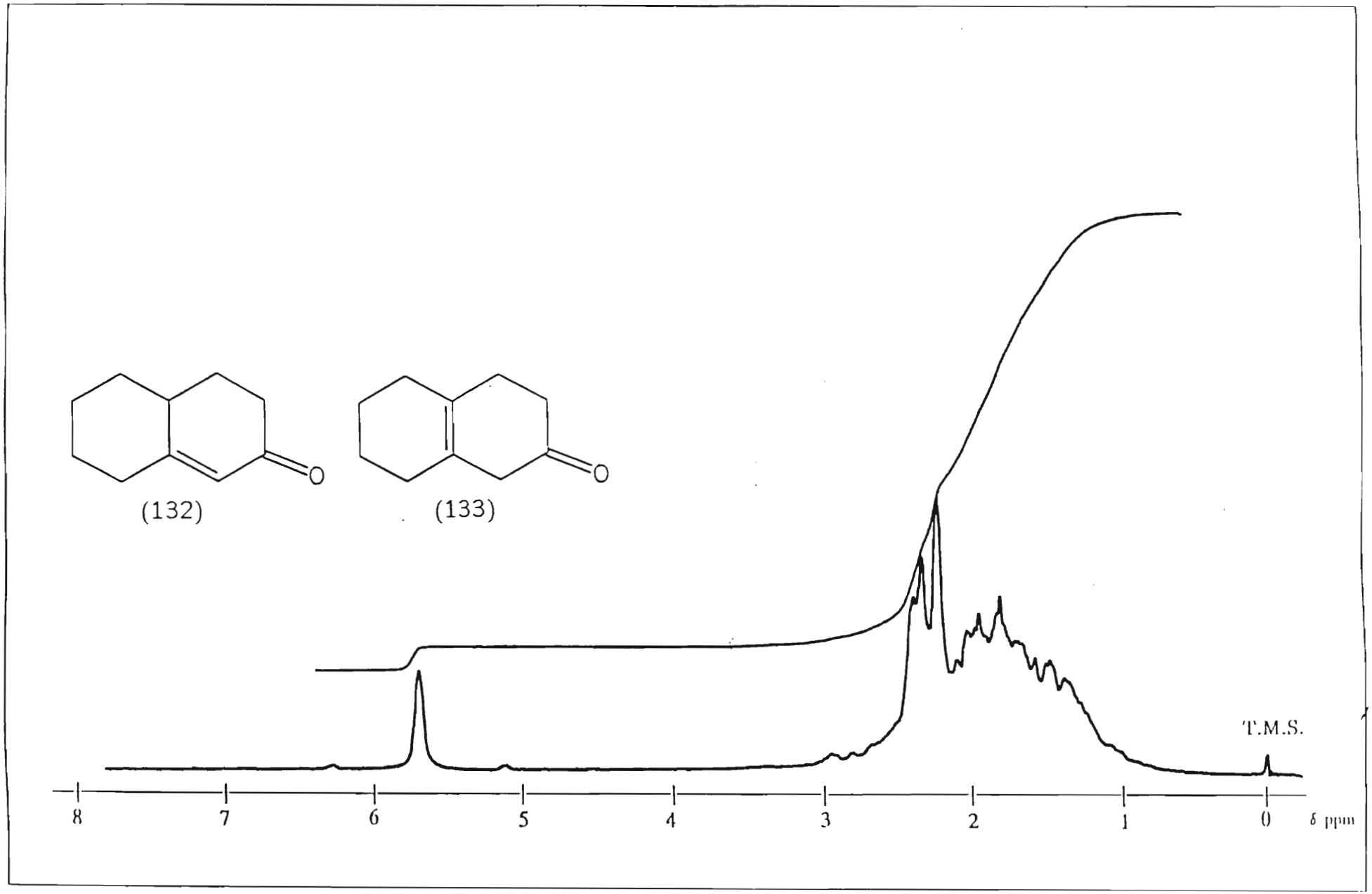


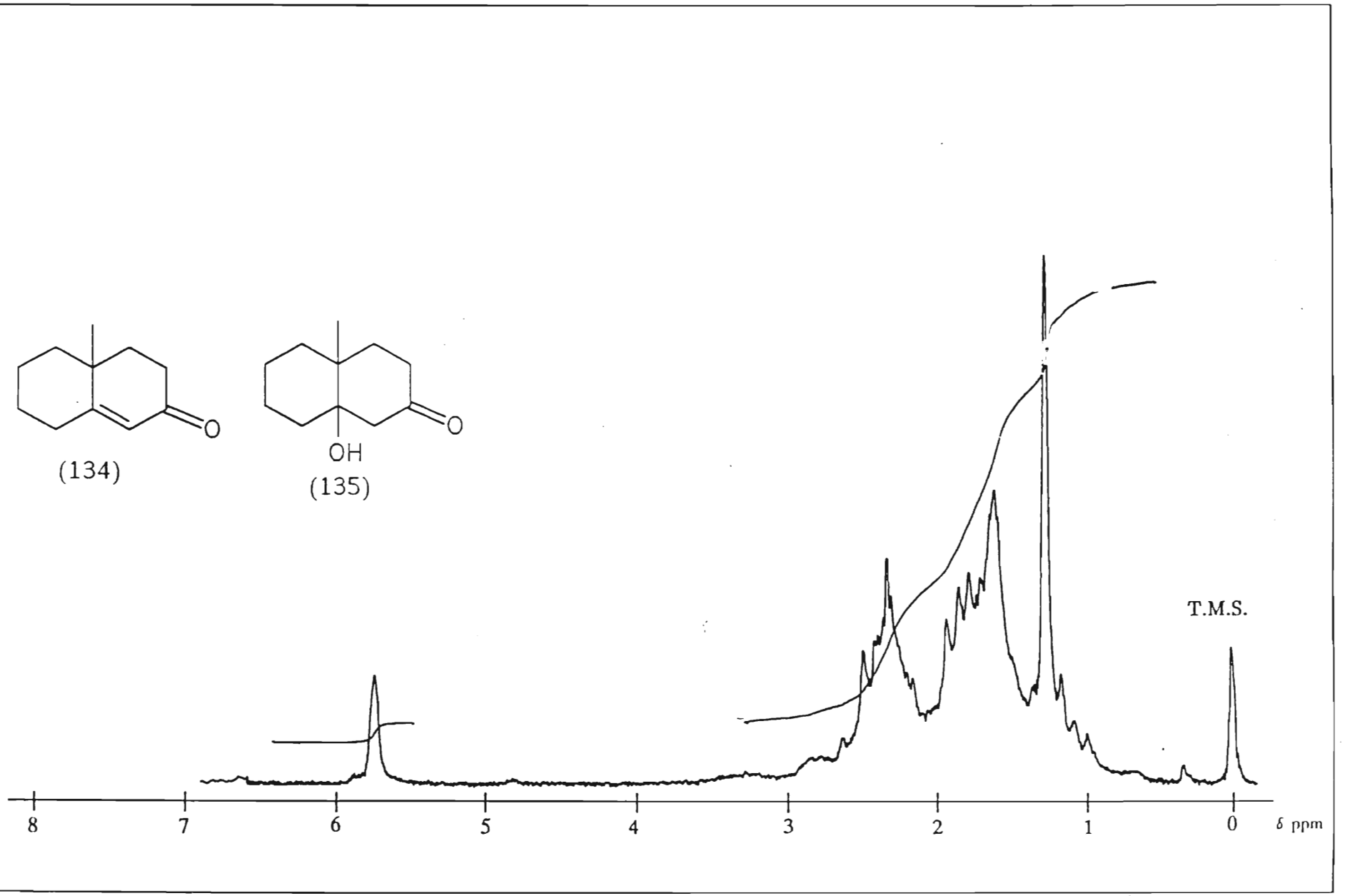
(128)

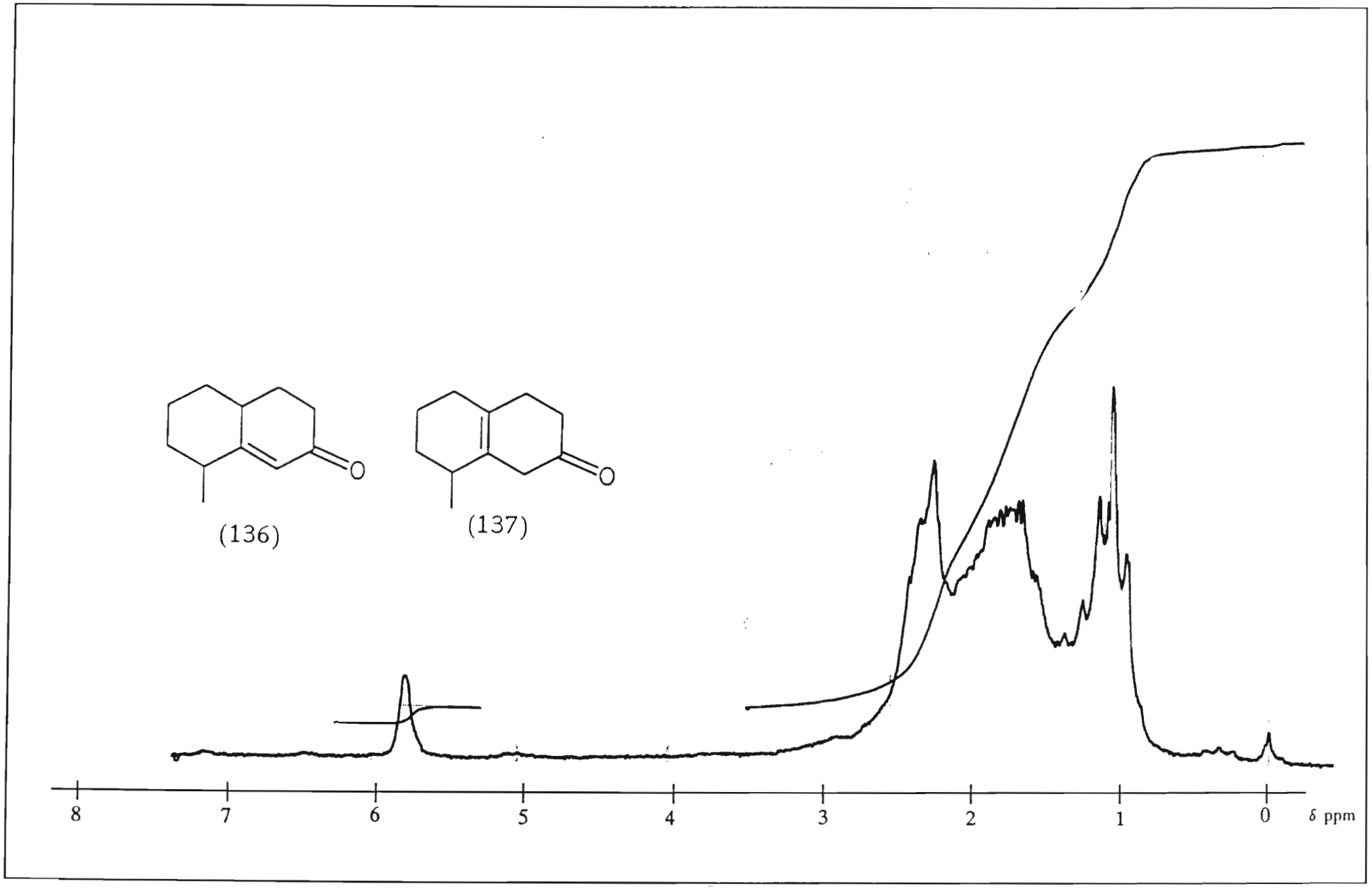


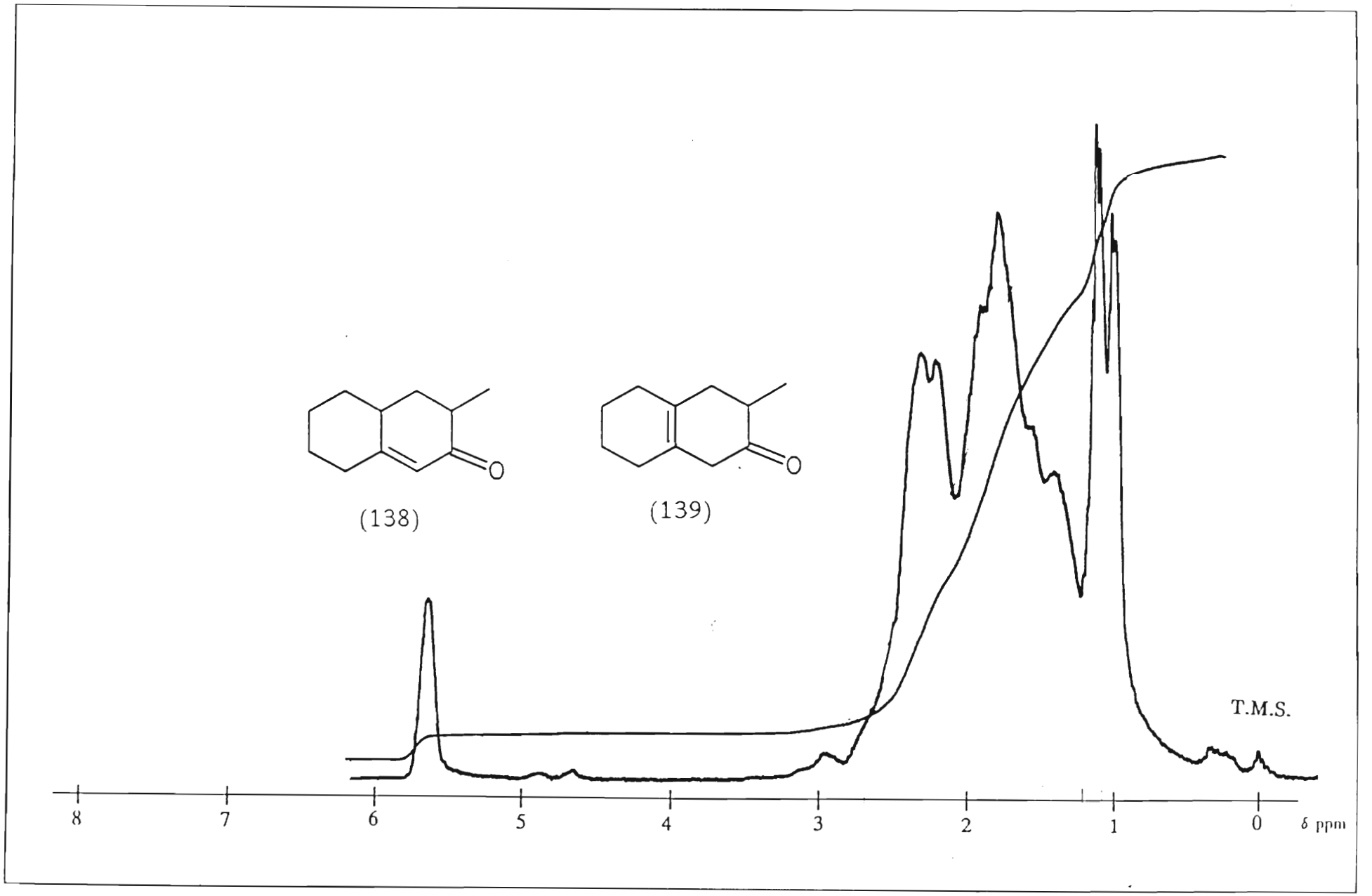
(129)


O
O
OH
O
(130)
(131)
8
7
6
5
4
3
2
1
0
δ ppm

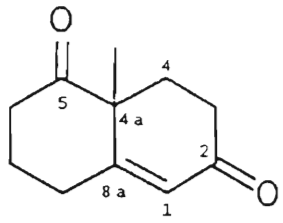

O
O
(132)
(133)
T.M.S.
8
7
6
5
4
3
2
1
0
δ ppm


O
(134)
OH
O
(135)
T.M.S.
8
7
6
5
4
3
2
1
0
δ ppm

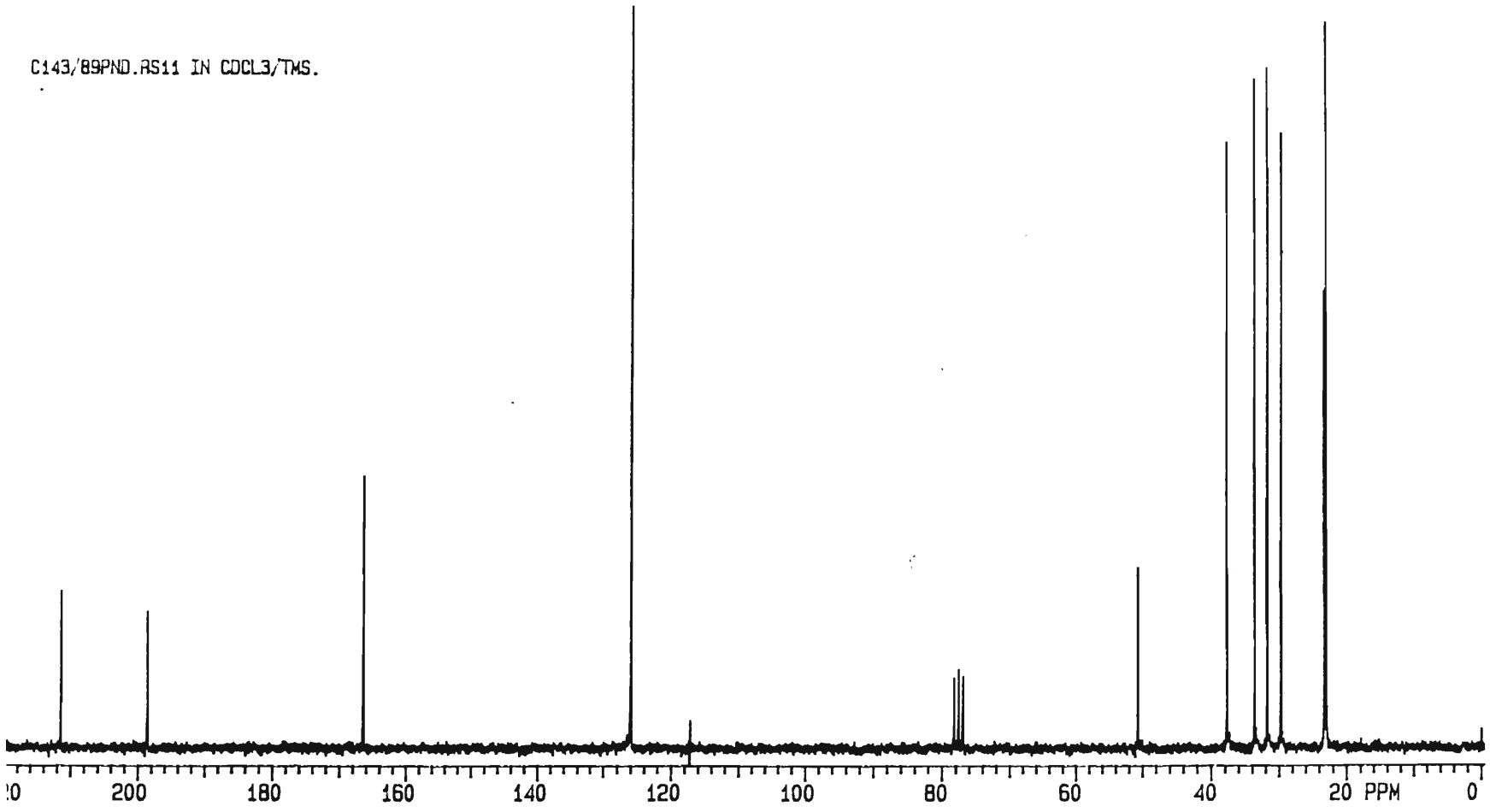

O
O
(136)
(137)
8
7
6
5
4
3
2
1
0
δ ppm

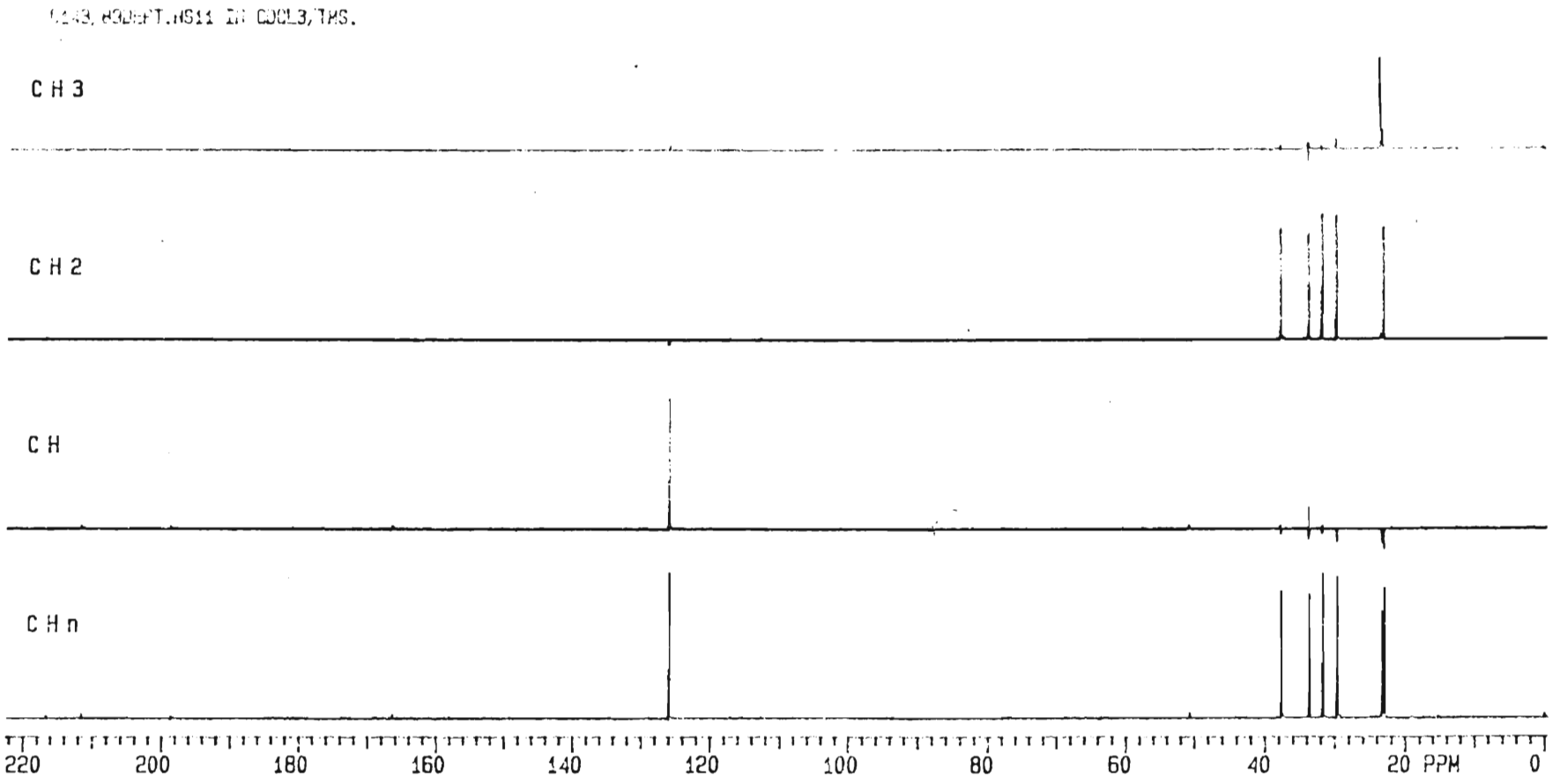

O
O
(138)
(139)
T.M.S.
8
7
6
5
4
3
2
1
0
δ ppm

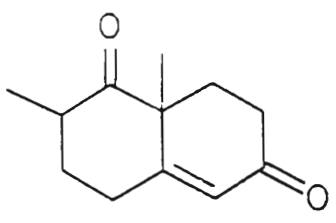
H143/89.AS11 IN CDCL3/TMS.



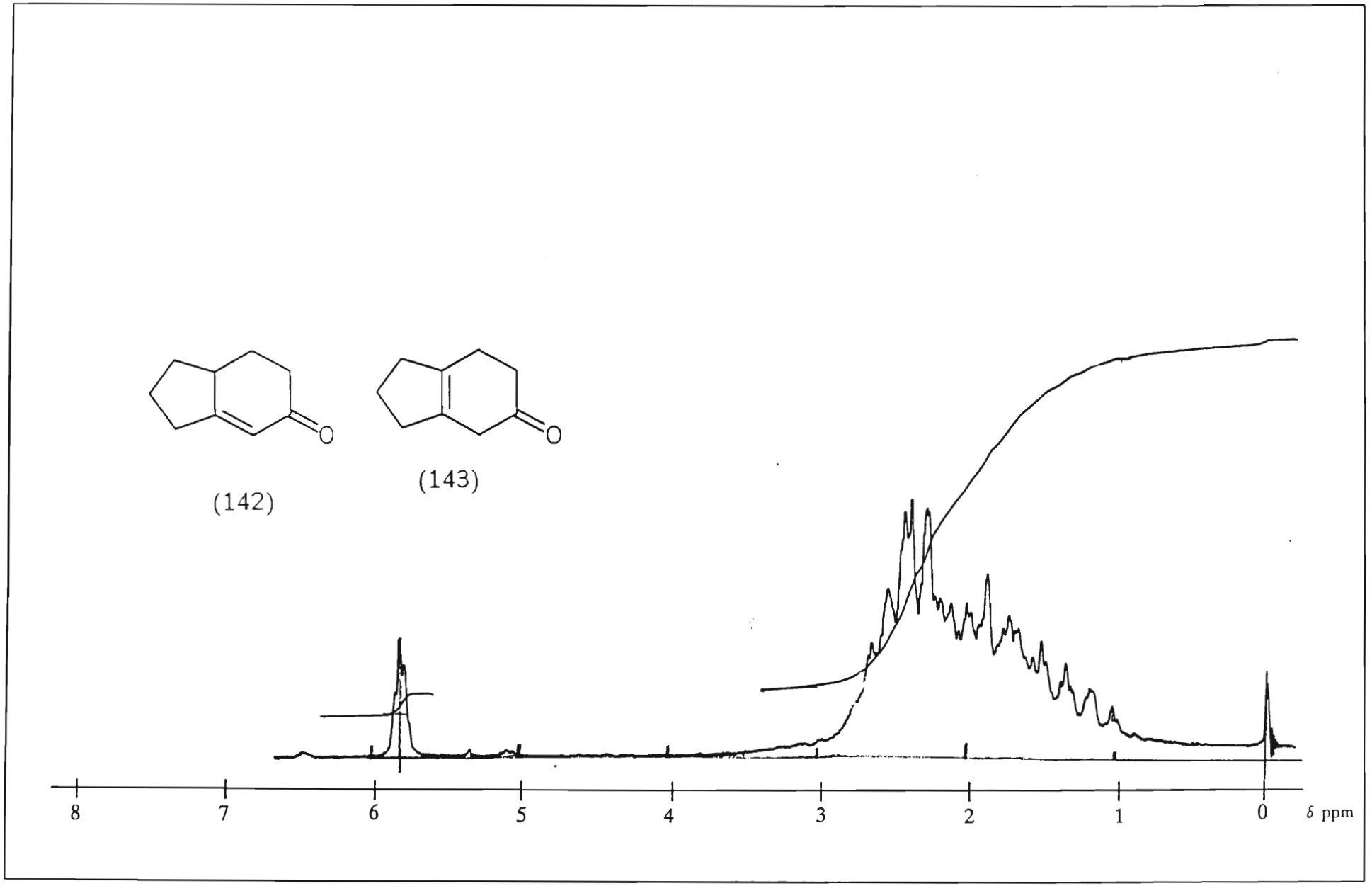
(140)

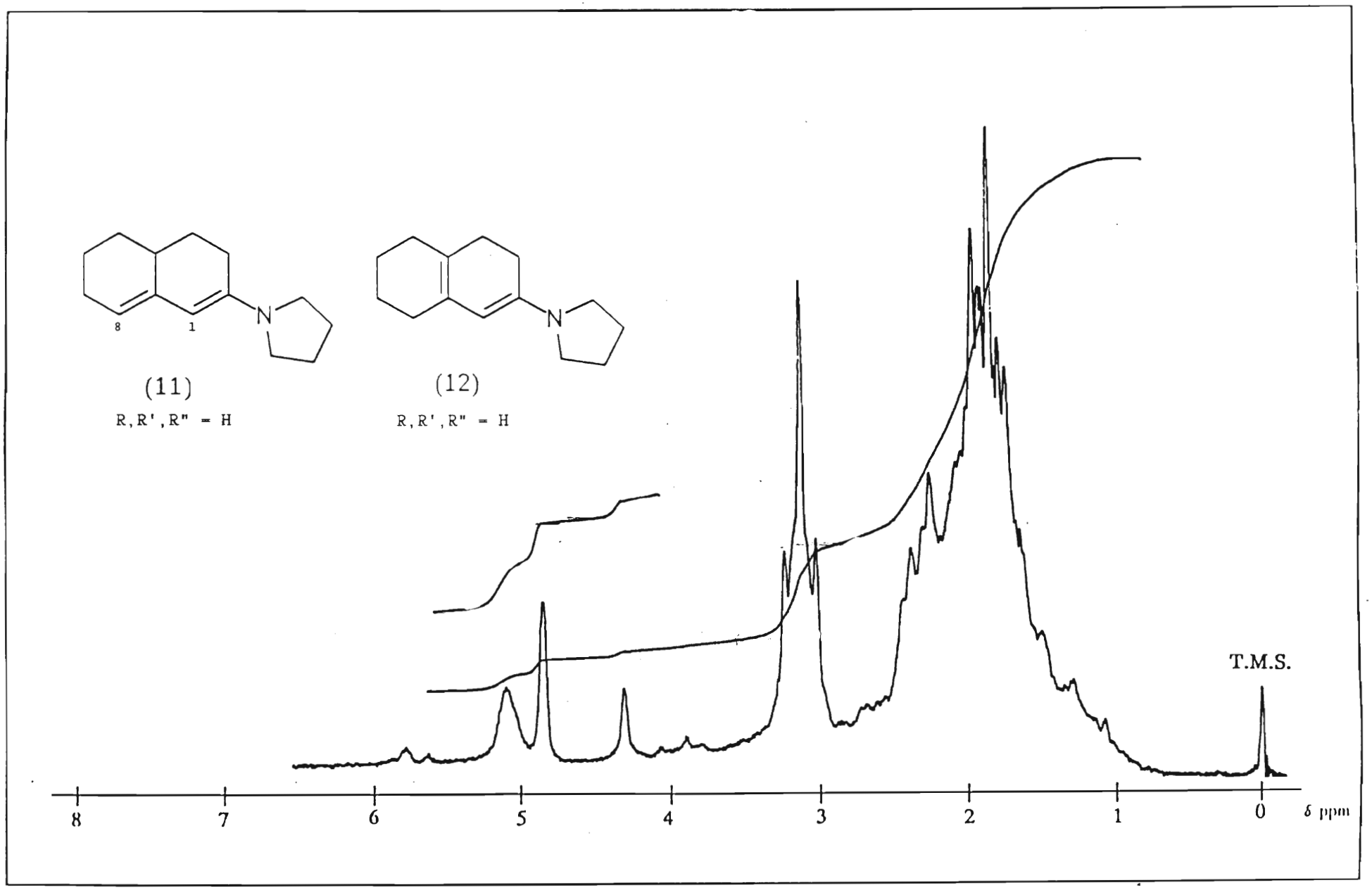

C143/89PND.RS11 IN CDCL3/TMS.
200
180
160
140
120
100
80
60
40
20 PPM
0

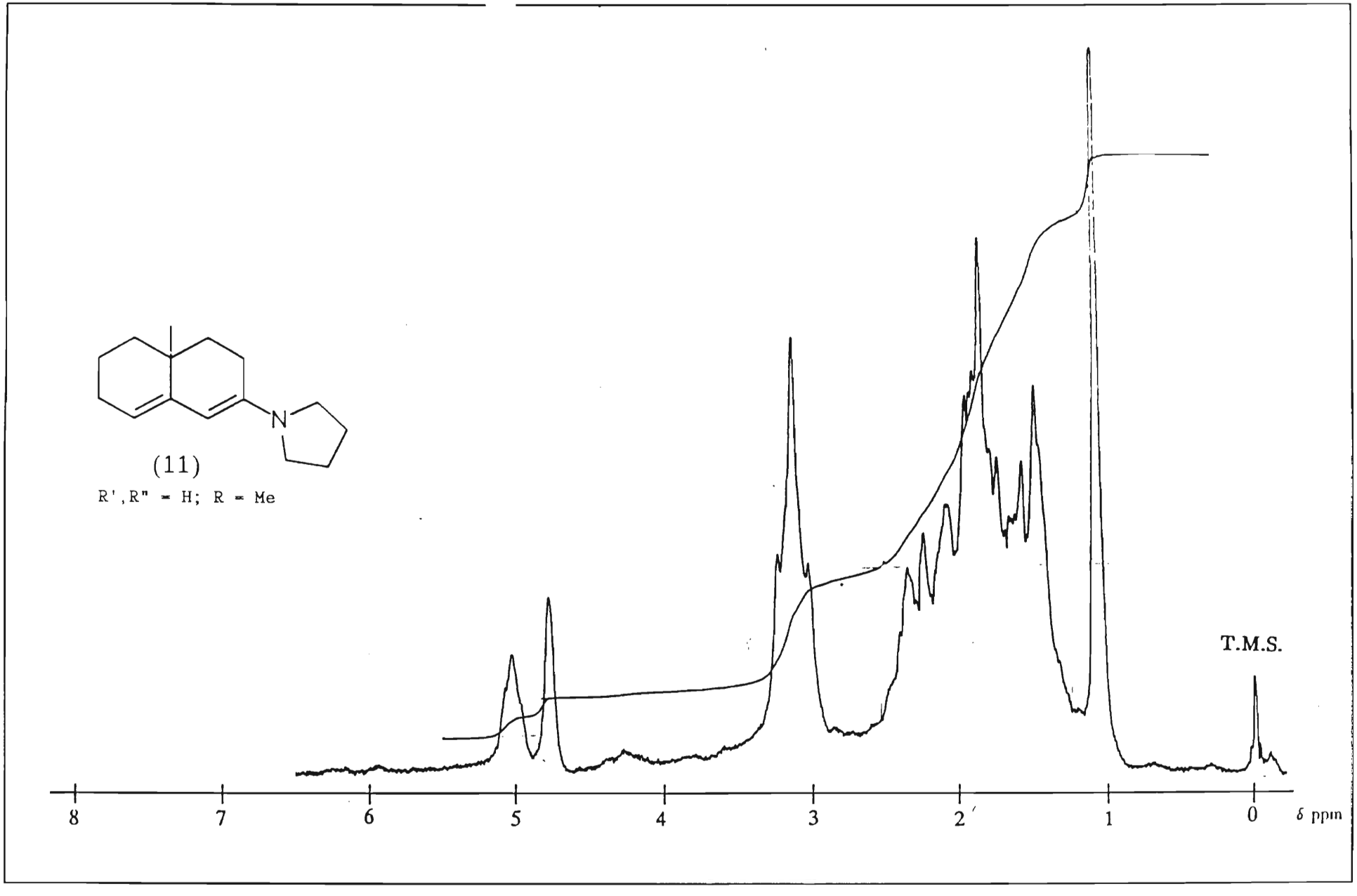

CH3
CH2
CH
CHn
220
200
180
160
140
120
100
80
60
40
20 PPM
0

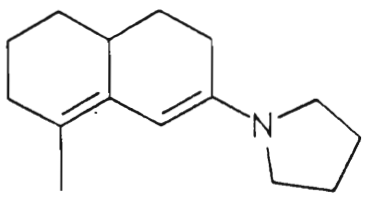


(141)


O
O
(142)
(143)
8
7
6
5
4
3
2
1
0
δ ppm

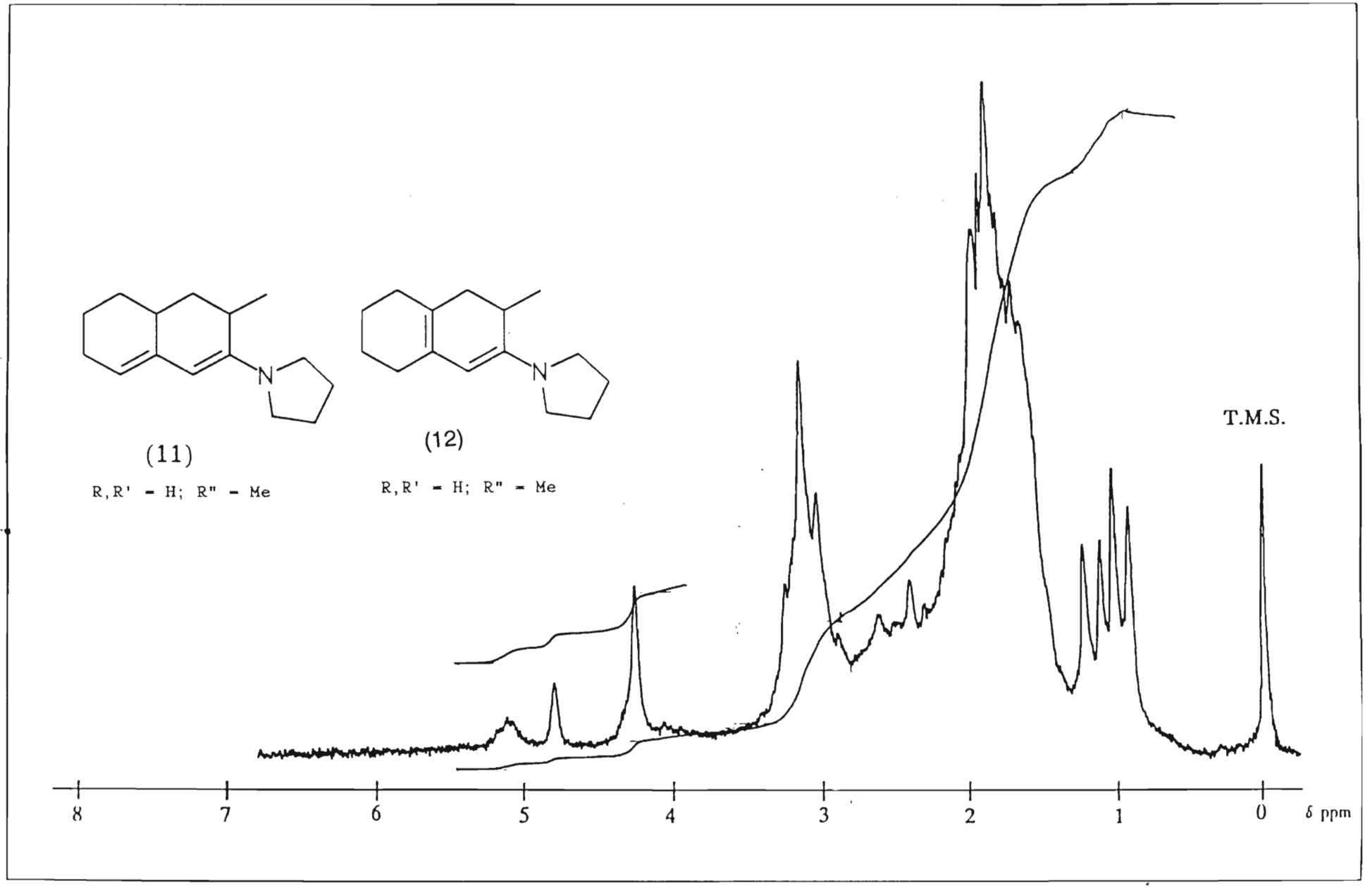

8
1
N
(11)
R,R',R" = H
N
(12)
R,R',R" = H
T.M.S.
8
7
6
5
4
3
2
1
0
δ ppm

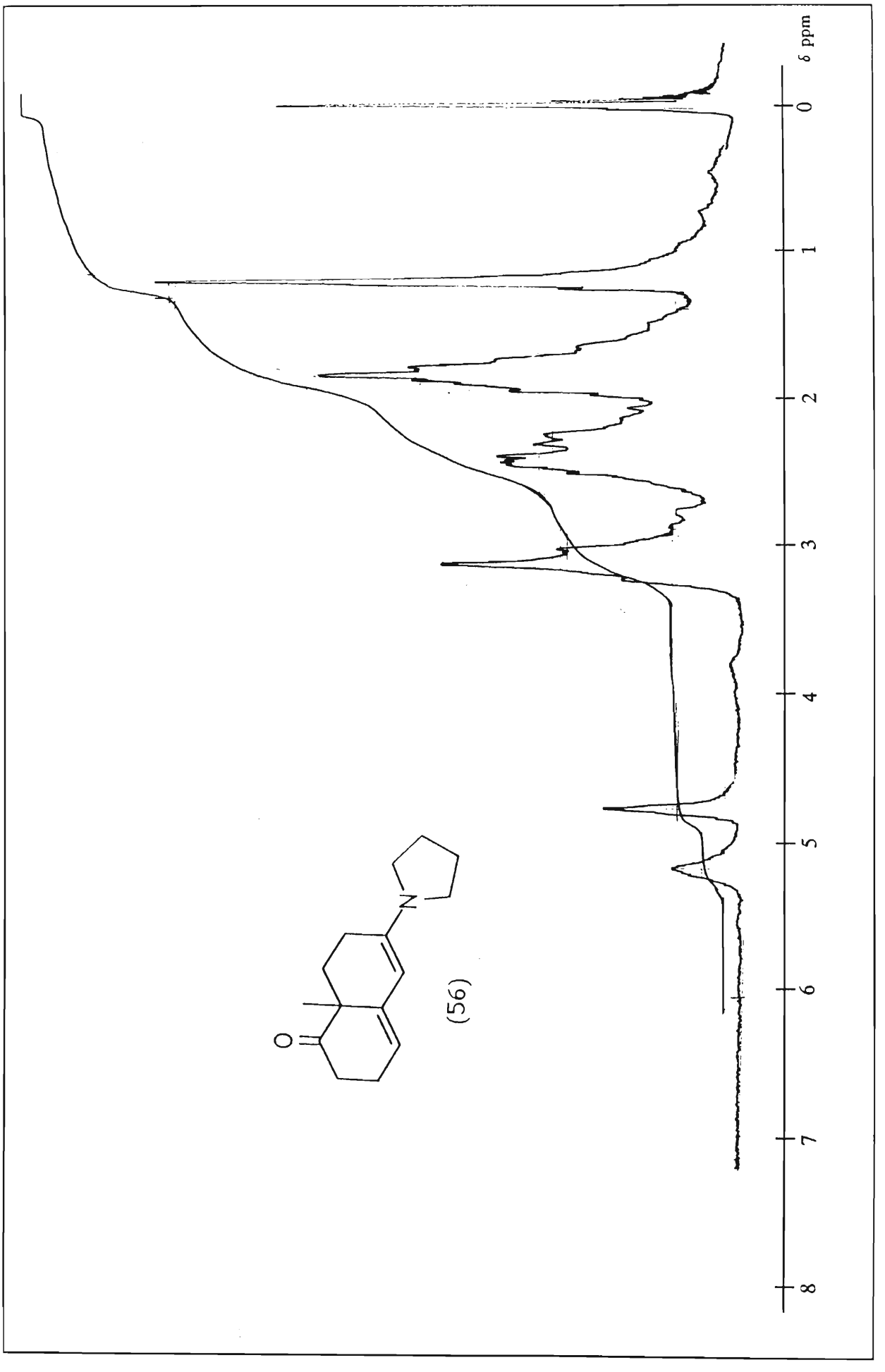

N
(11)
R',R" = H; R = Me
T.M.S.
8
7
6
5
4
3
2
1
0
δ ppm



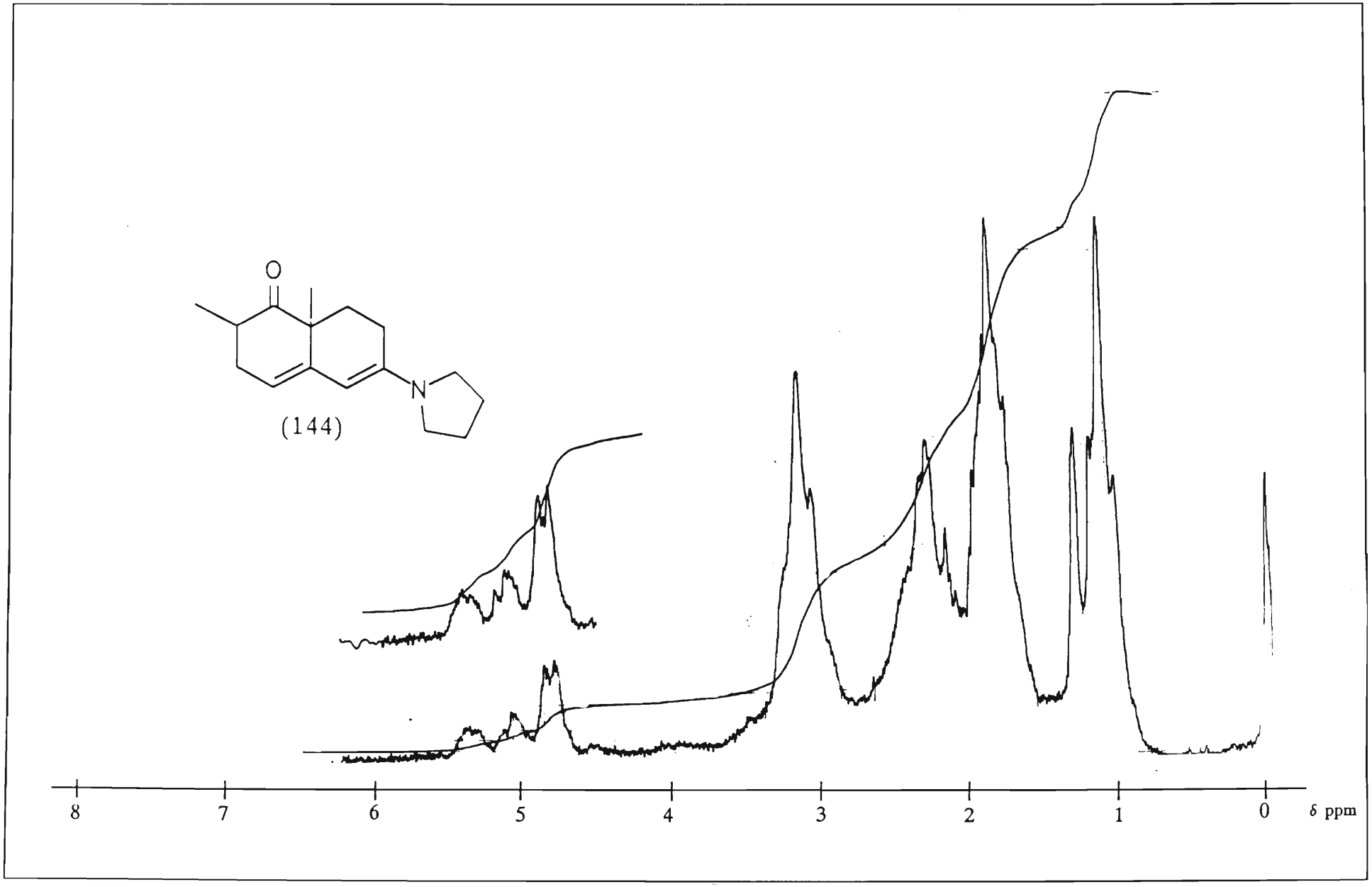
(11)

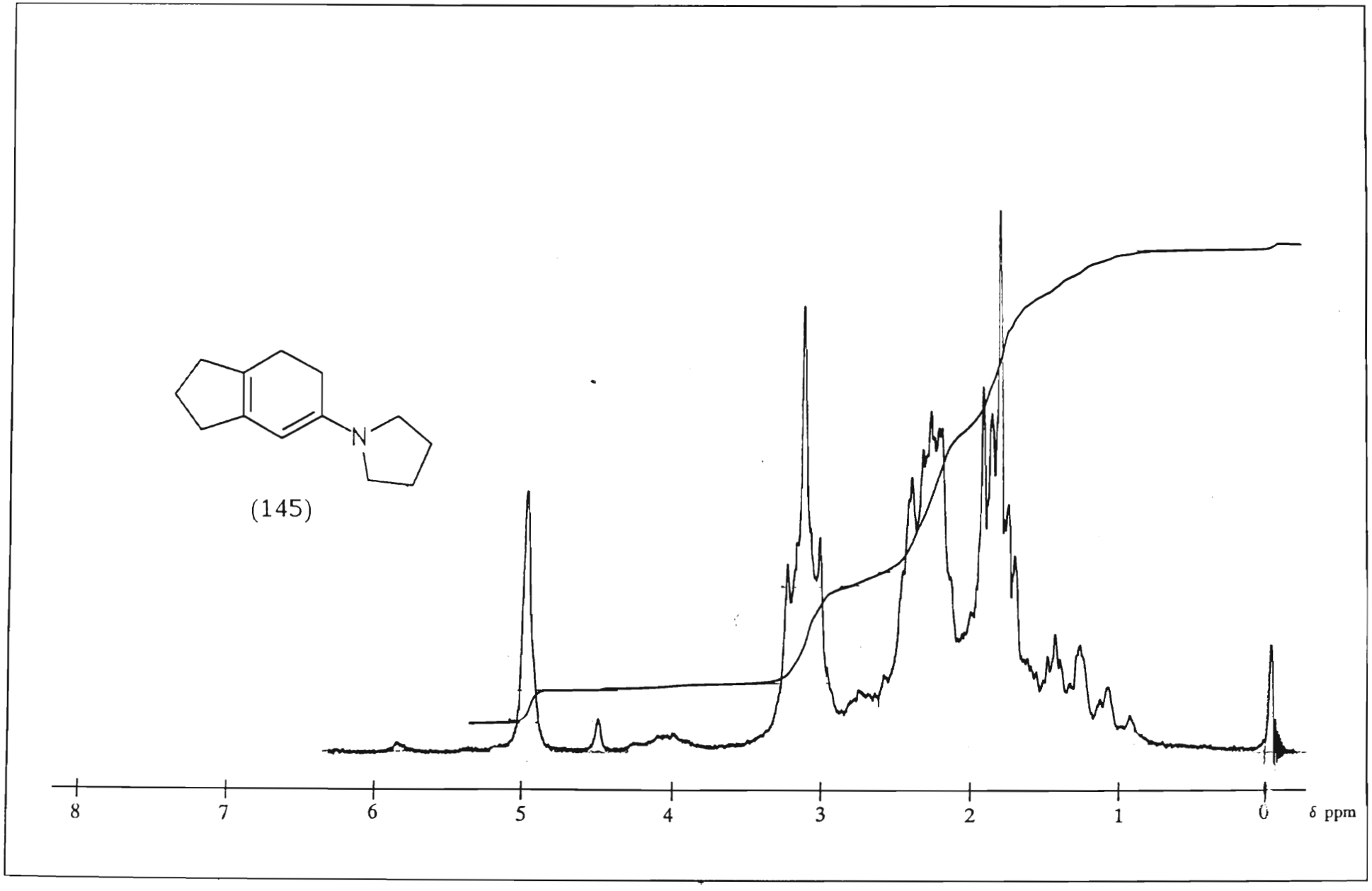
R,R" = H; R' = Me


(11)
R,R' = H; R" = Me
(12)
R,R' = H; R" = Me
T.M.S.
8
7
6
5
4
3
2
1
0
δ ppm

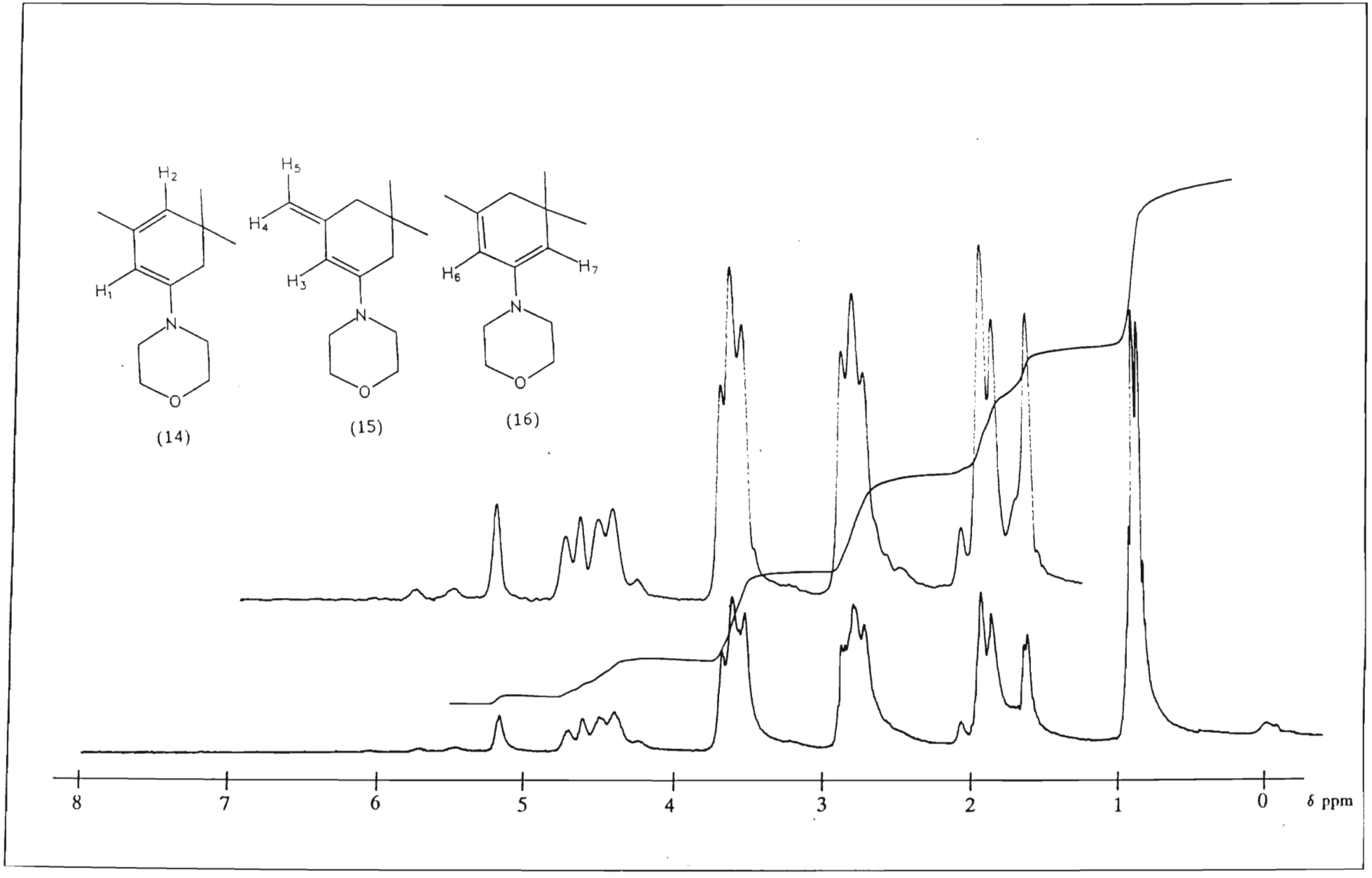


(56)

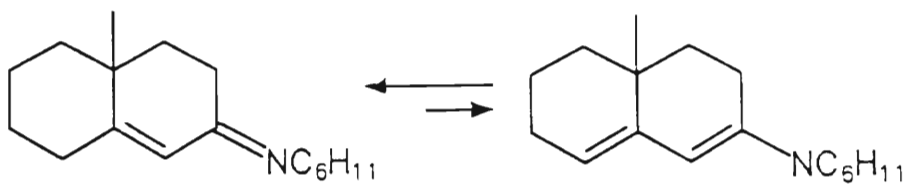

O
N
(144)
8
7
6
5
4
3
2
1
0
δ ppm



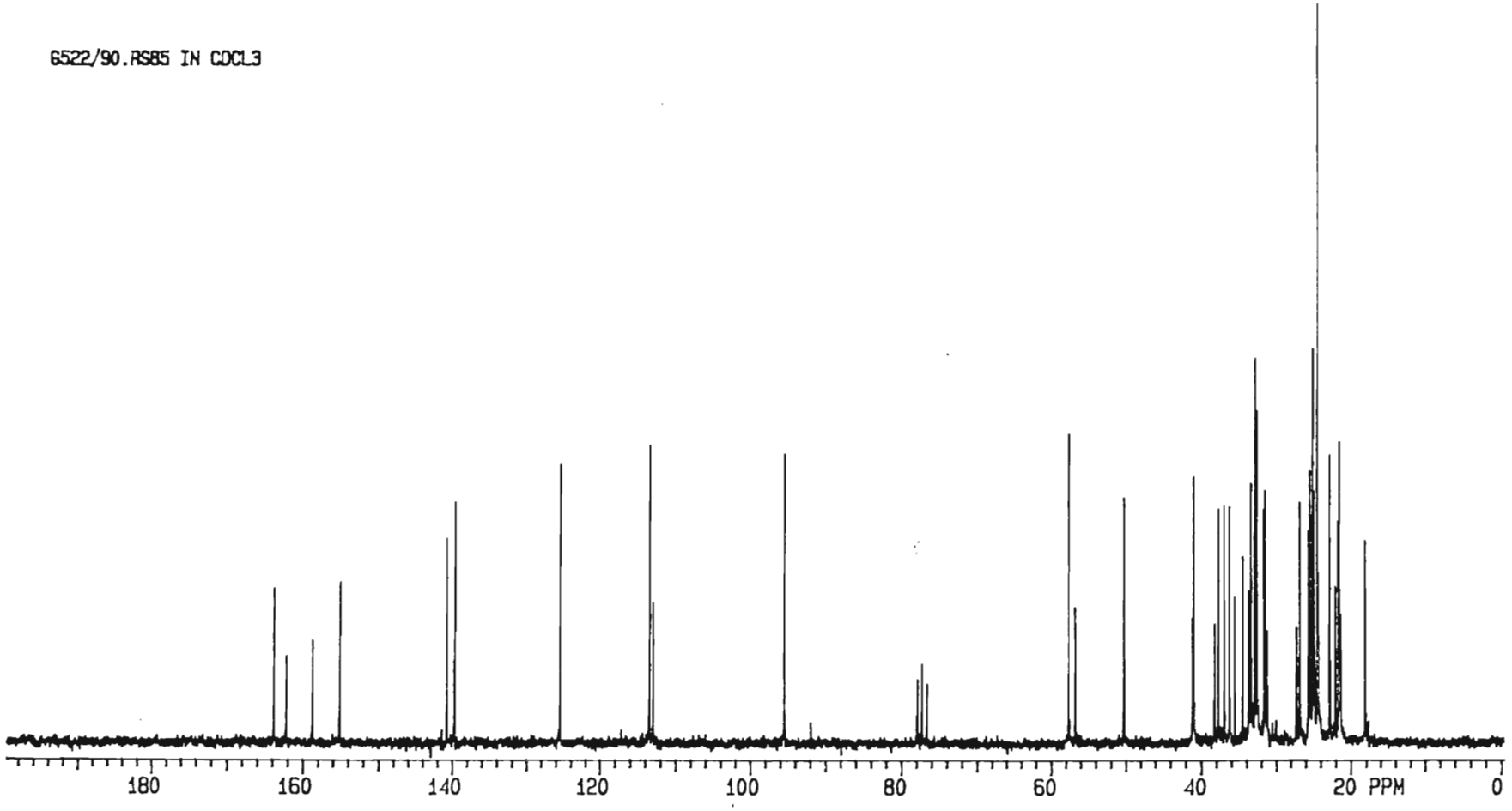
(145)

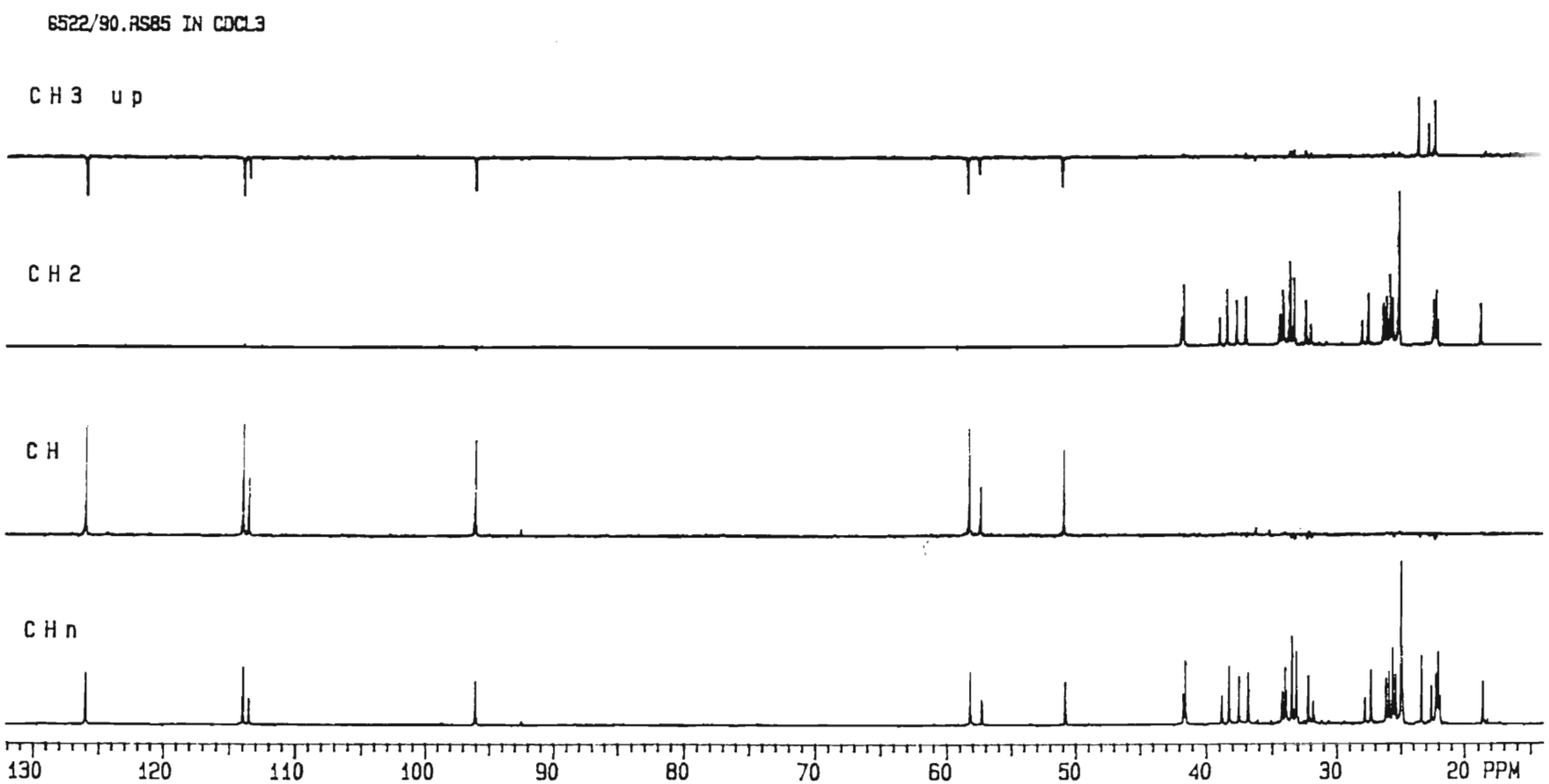

H2
H1
N
O
(14)
H5
H4
H3
N
O
(15)
H6
H7
N
O
(16)
8
7
6
5
4
3
2
1
0
δ ppm

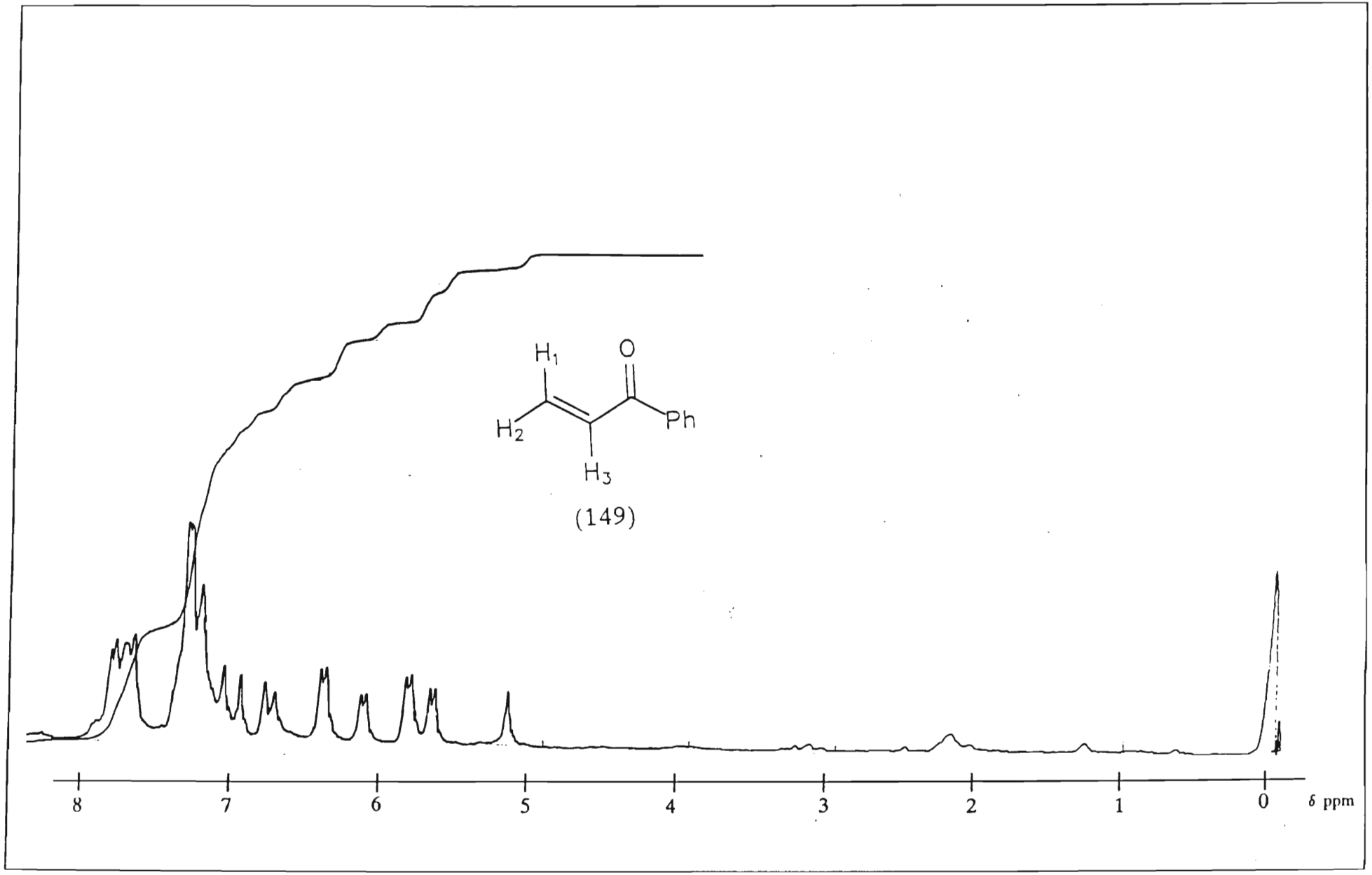
6522/90.RS85 IN CDCL3



(146) (147)

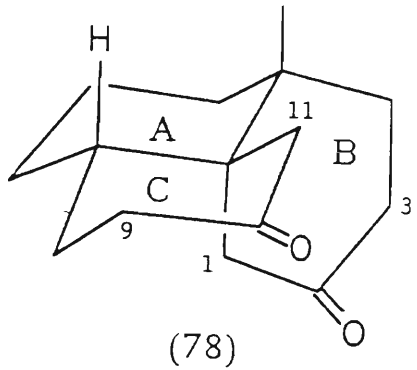

6522/90.RS85 IN CDCL3
180
160
140
120
100
80
60
40
20 PPM
0


6522/90.RS85 IN CDCL3
CH3 up
CH2
CH
CHn
130
120
110
100
90
80
70
60
50
40
30
20 PPM

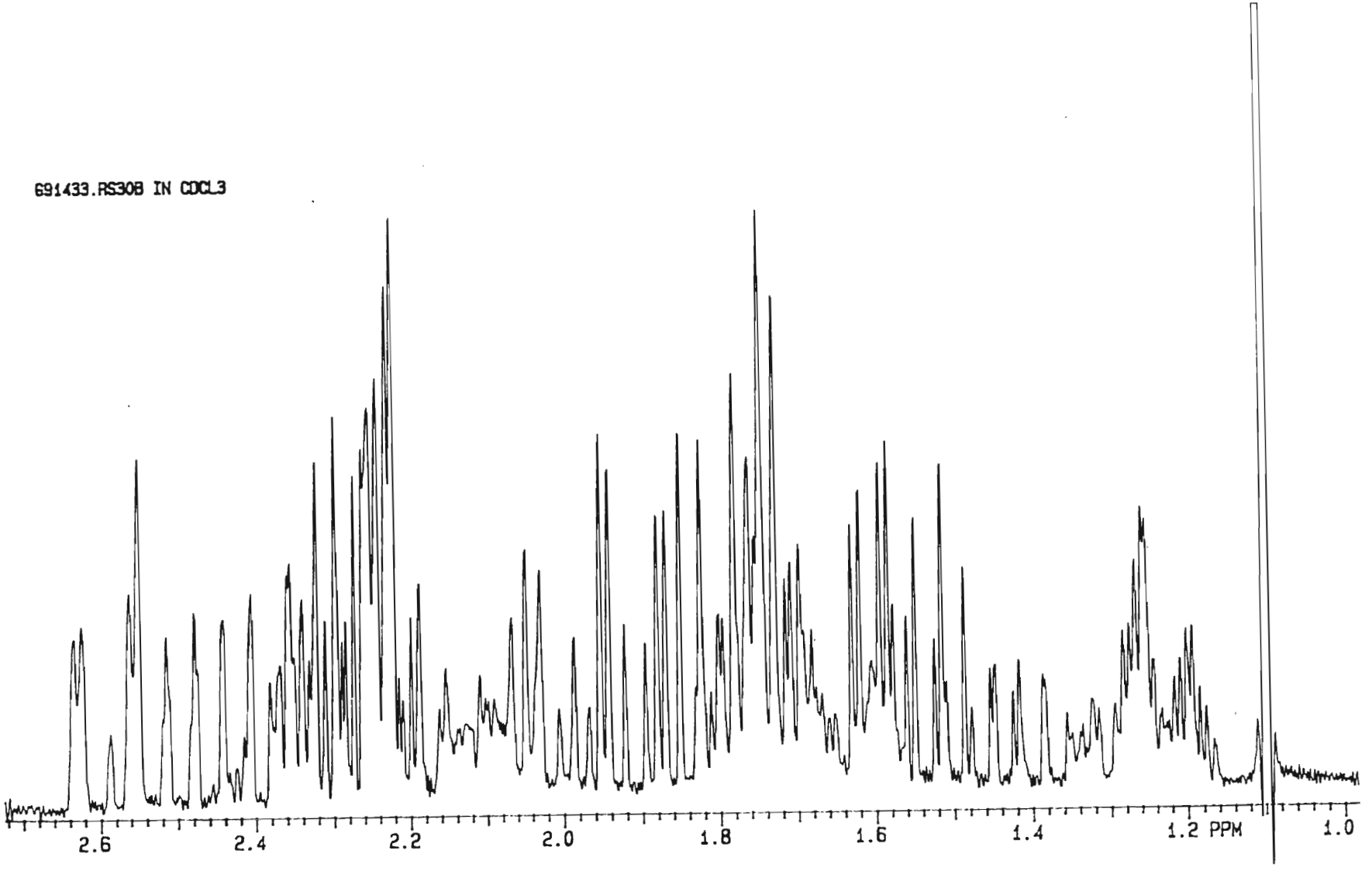


(149)

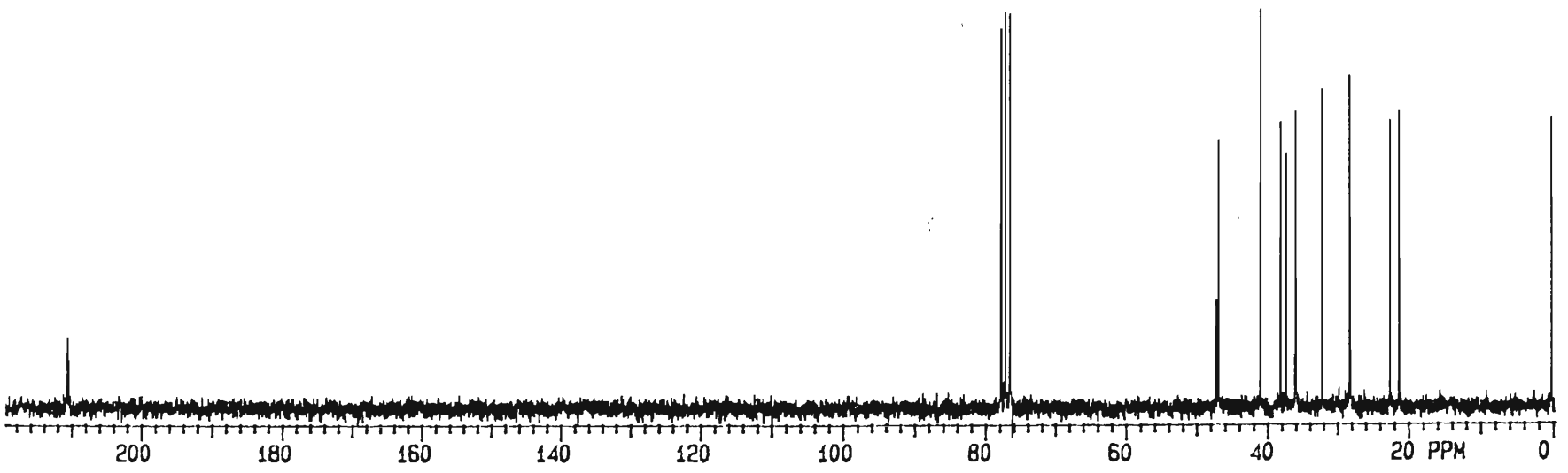
691433.RS308 IN CDCL3

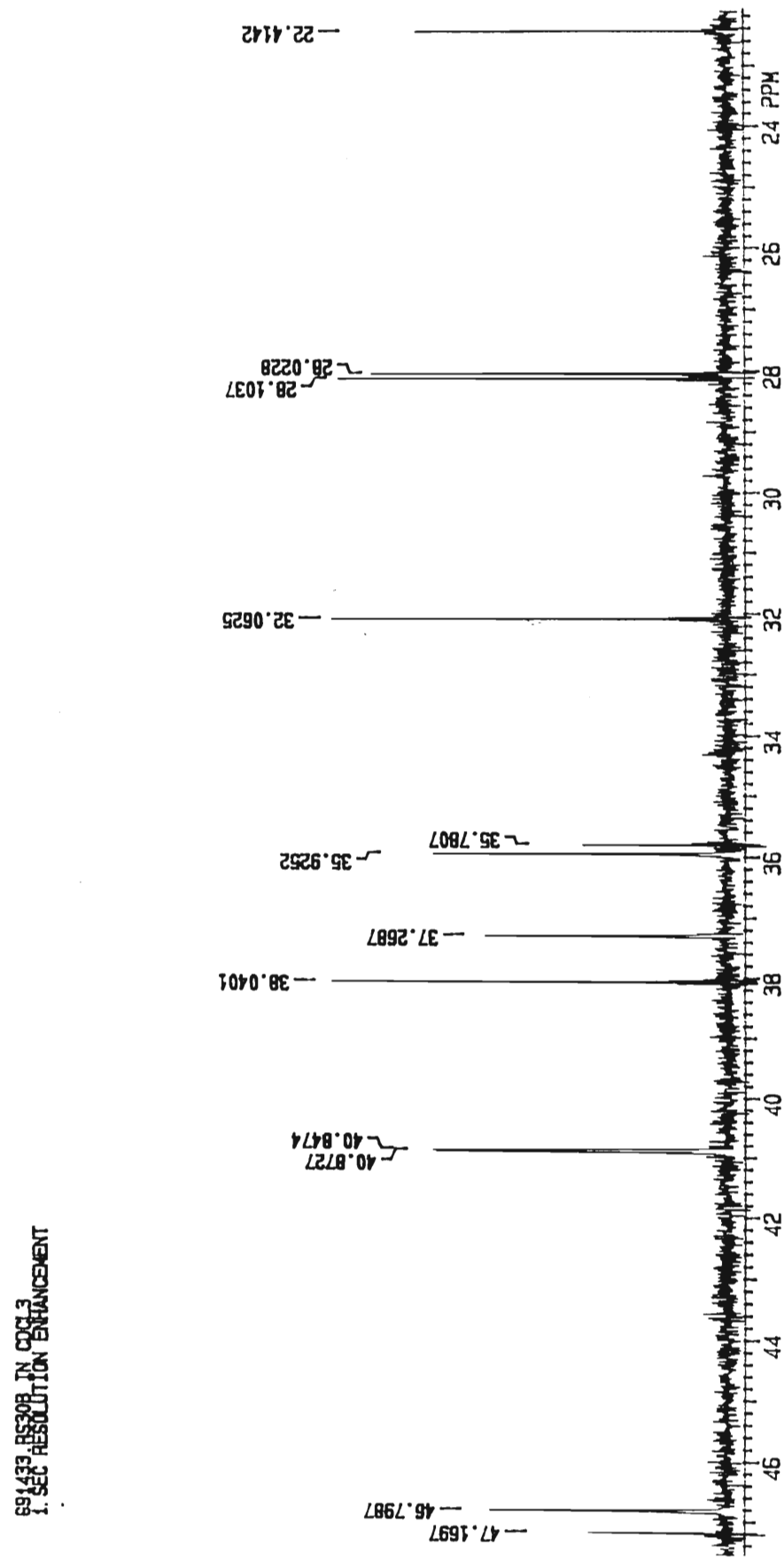


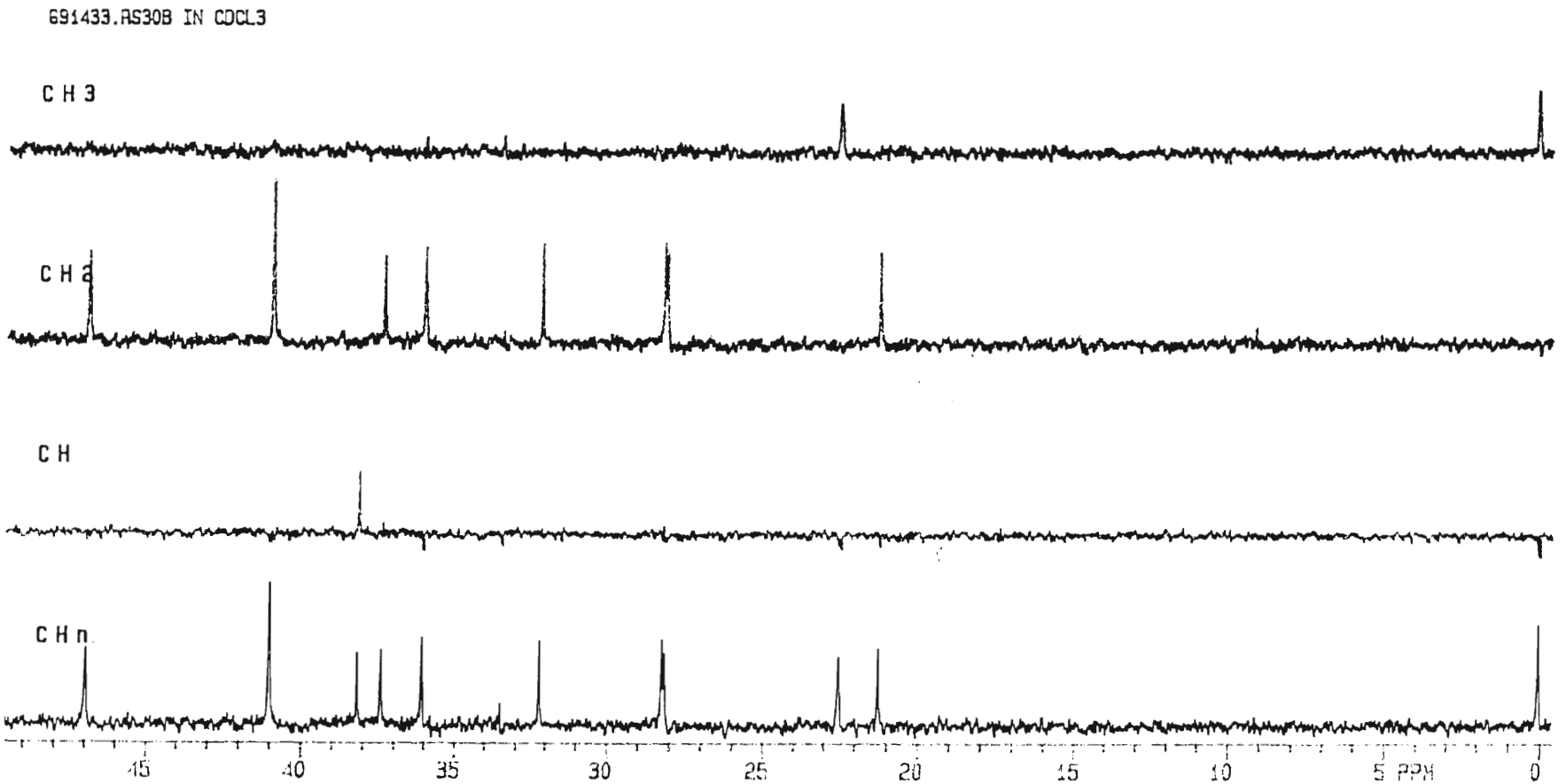
(78)

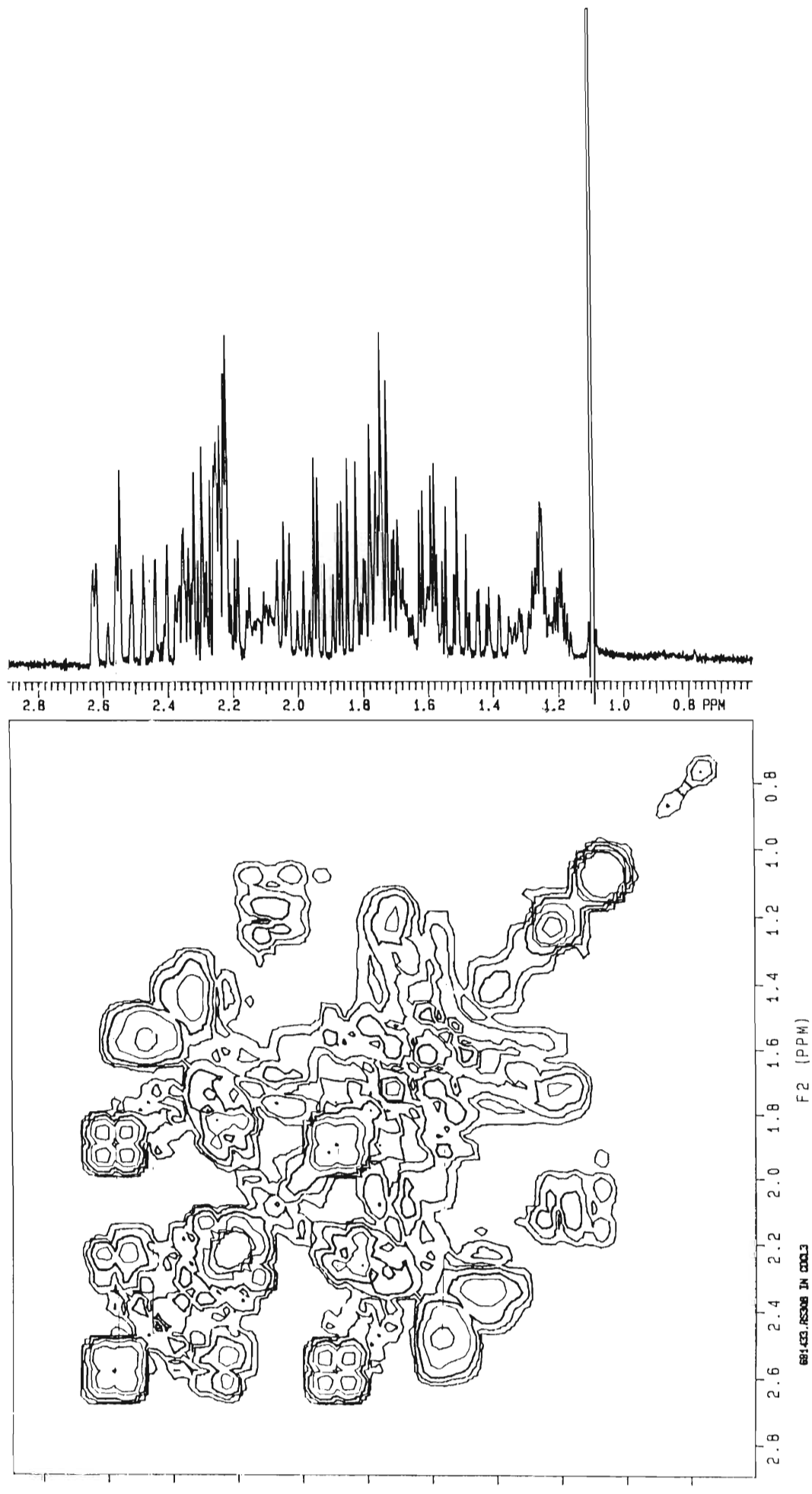

691433.RS308 IN CDCL3
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2 PPM
1.0

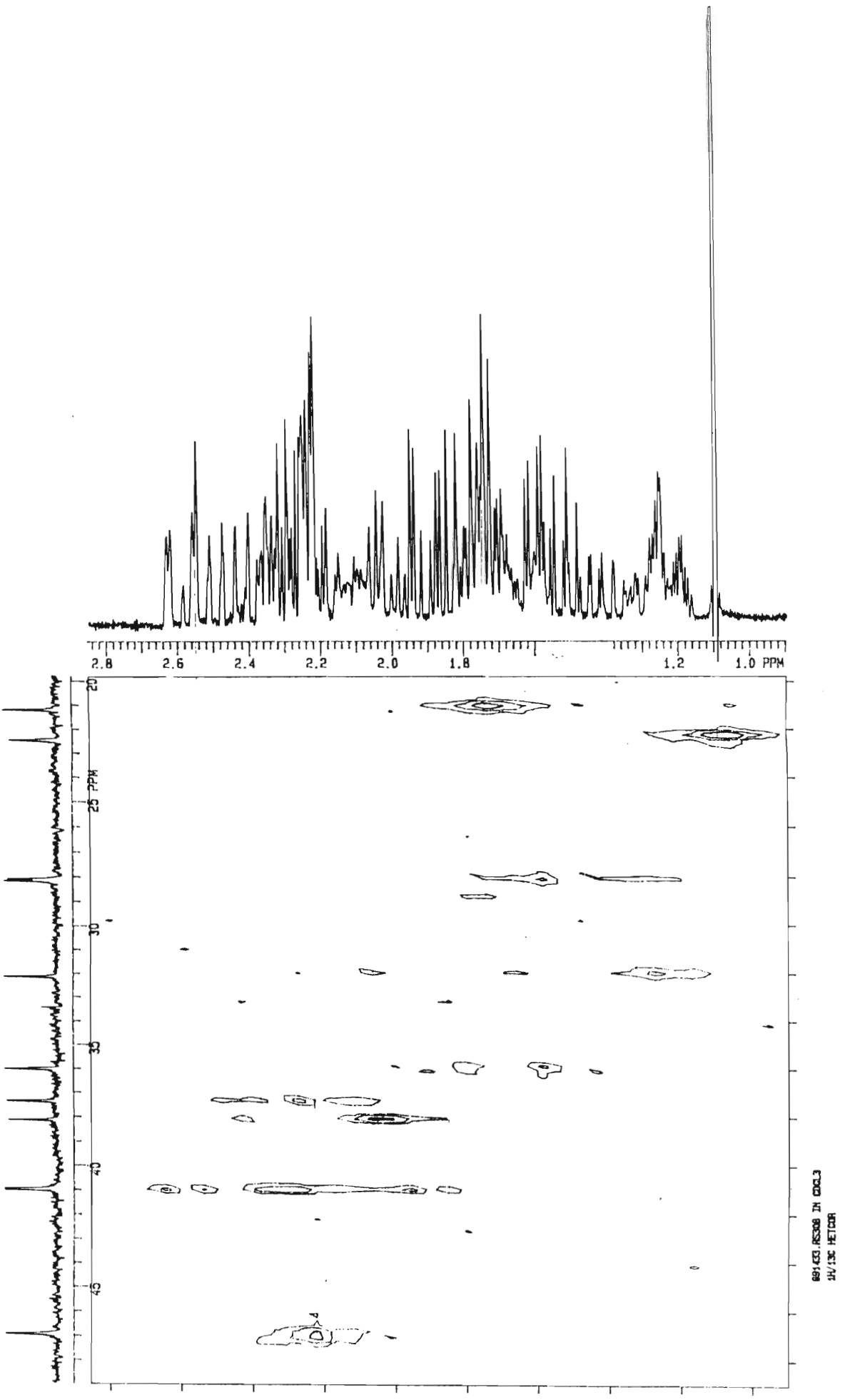
691433.RS30B IN CDCL3

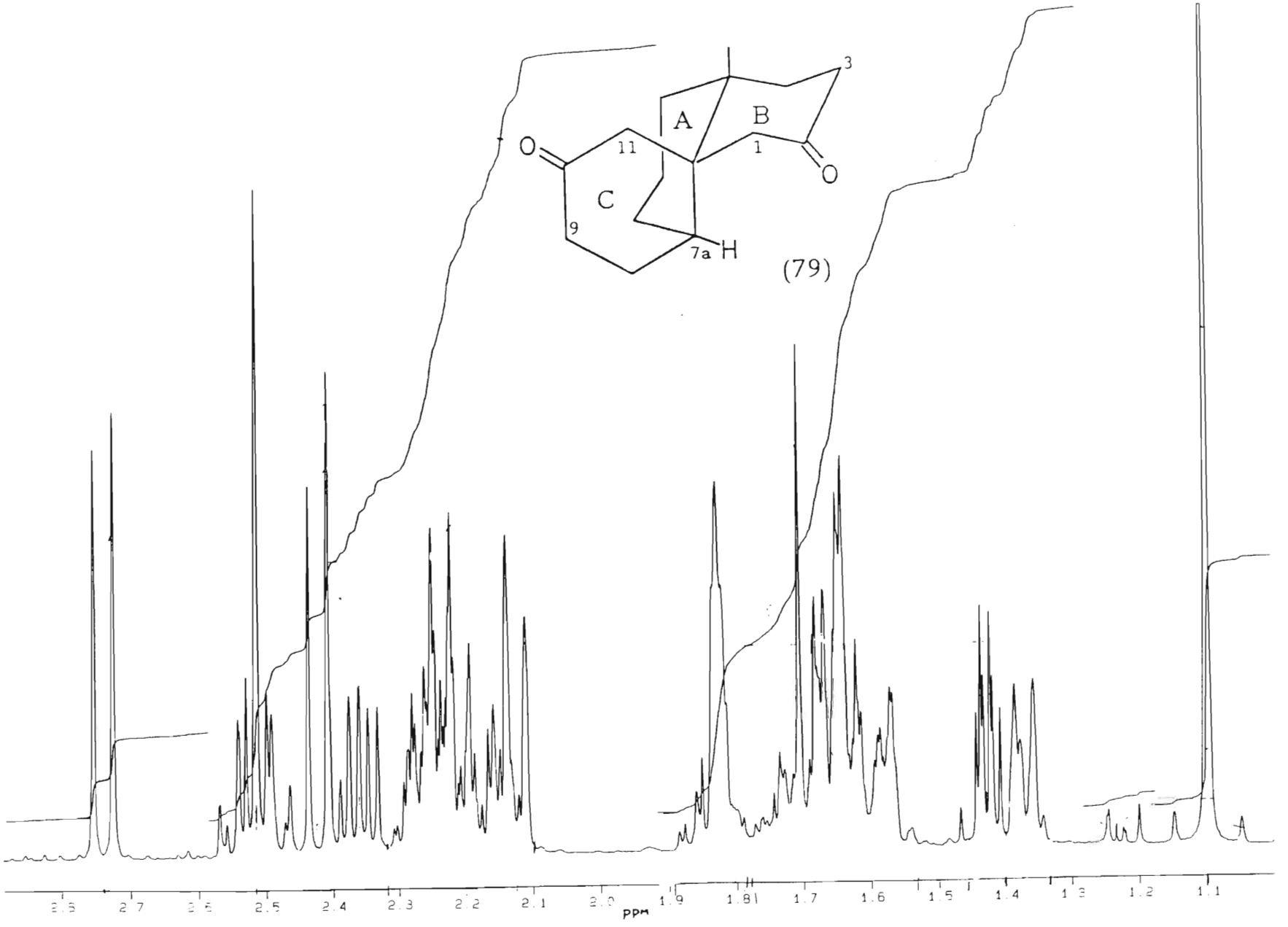



691433.BS308.IN.CDCL3
1.5EC RESOLUTION ENHANCEMENT
47.1697
46.7987
40.8727
40.8474
38.0401
37.2687
35.9252
35.7807
32.0625
28.1037
28.0228
22.4142
24 PPM
26
28
30
32
34
36
38
40
42
44
46


691433.RS30B IN CDCL3
C H 3
C H a
C H
C H n
45
40
35
30
25
20
15
10
5 PPM
0


2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8 PPM
F2 (PPM)
GB1433.RSOOB IN CDCL3
1H COSY-90

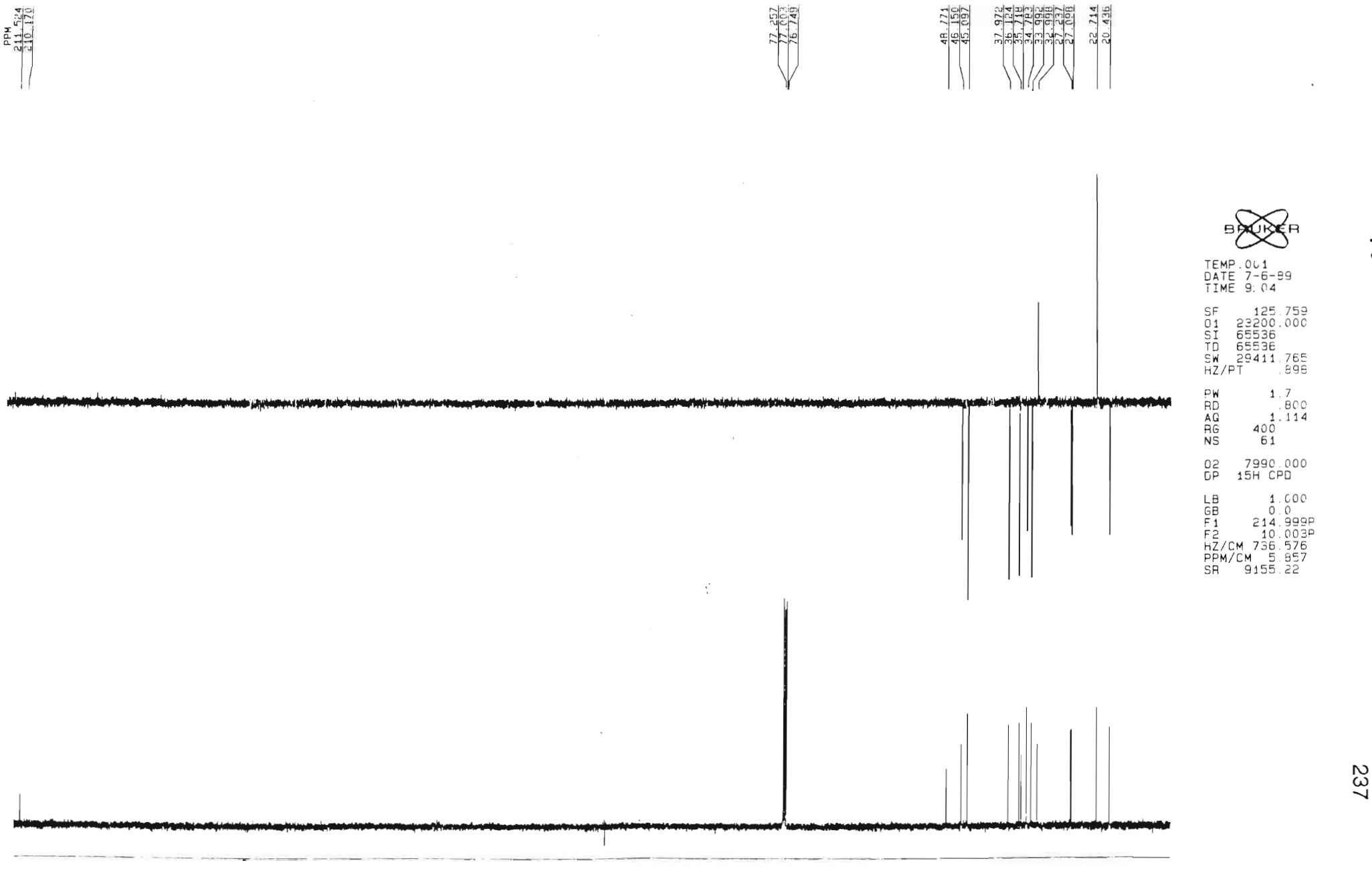

2.8
2.6
2.4
2.2
2.0
1.8
1.2
1.0 PPM
20
25 PPM
30
35
40
45
891CS3.RS300 IN CDCL3
1H/13C HETCOR



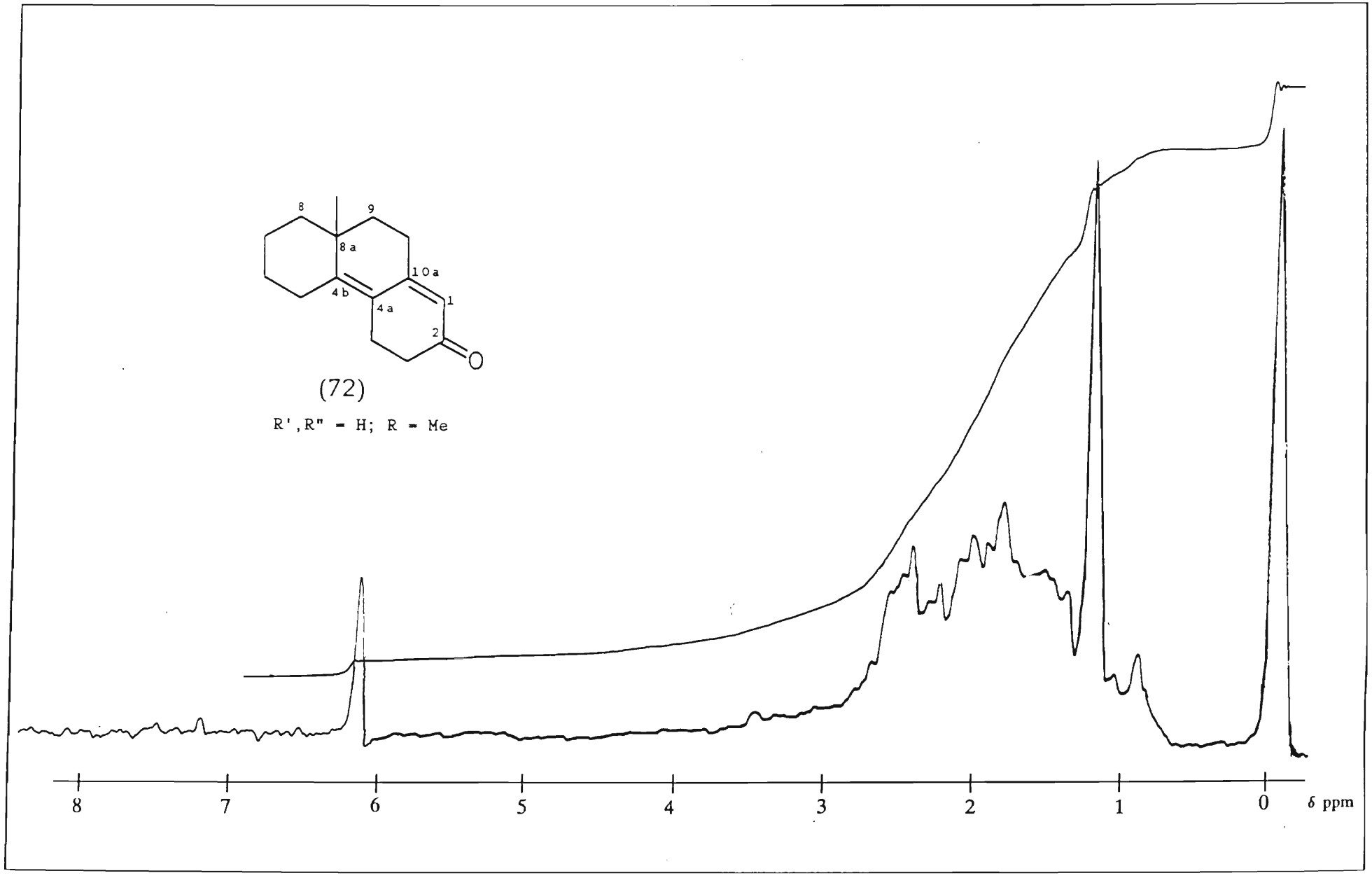
BRUKER

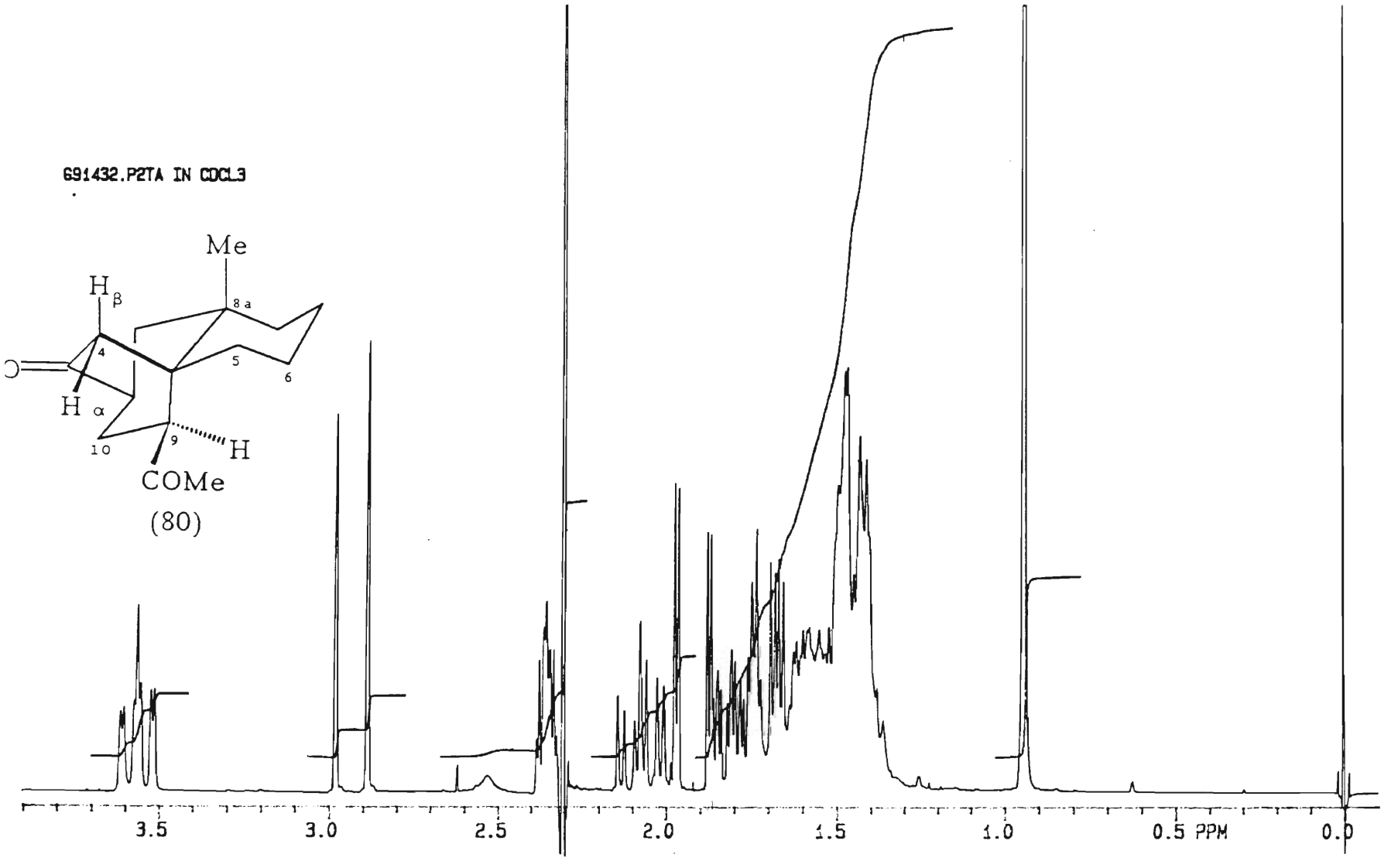
DATE 5-6-89
TIME 8.04

SF	500.135
O1	8470.020
SI	65536
TD	65536
SW	10000.000
HZ/PT	.305
PW	3.0
RD	0.0
AQ	3.277
RG	40
NS	52
O2	0.0
DP	63L PD
LB	.300
GB	0.0
F1	2.900P
F2	1.000P
HZ/CM	27.143
PPM/CM	.054
SR	5416.00

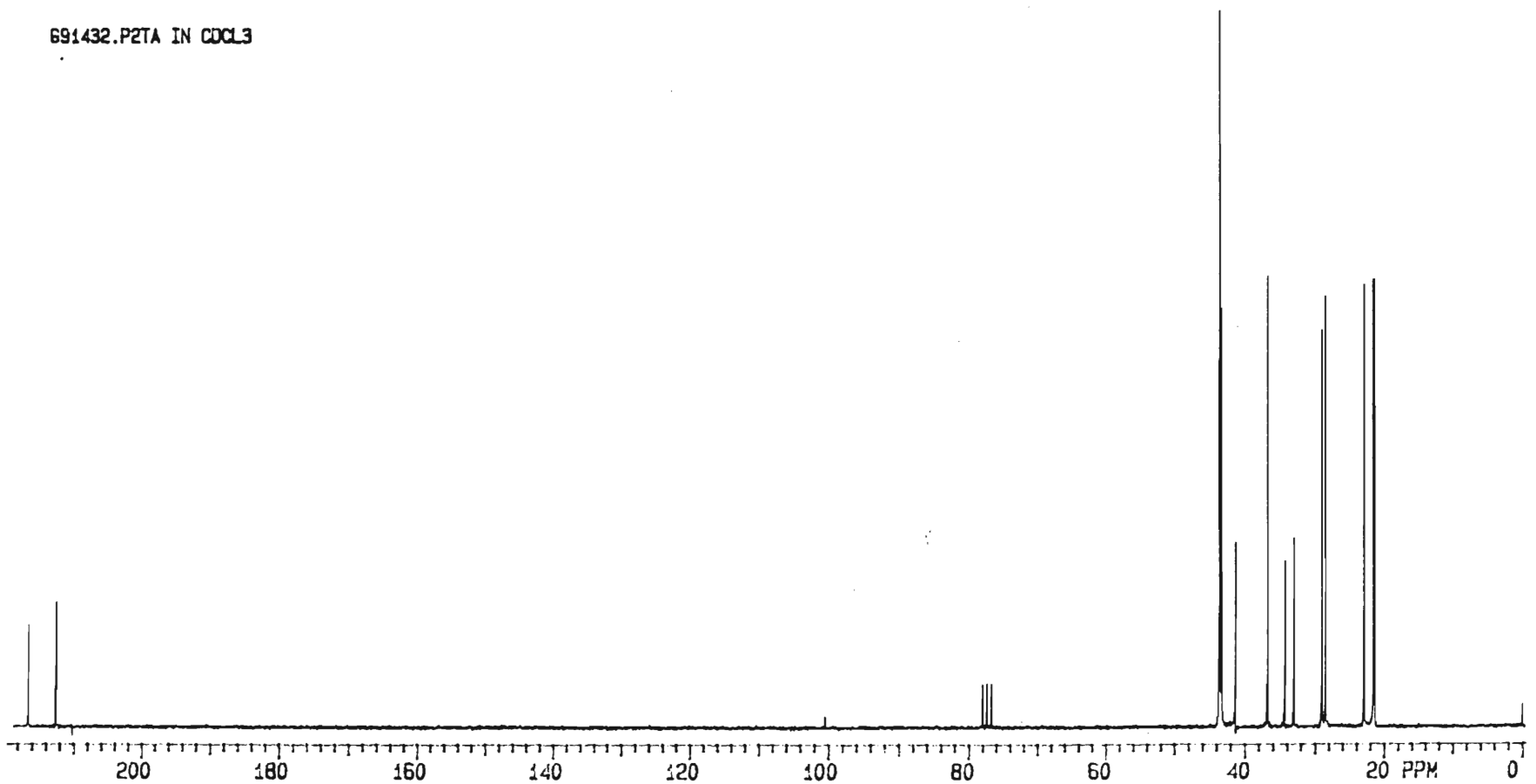

PPM
211.524
210.170
77.257
77.003
76.749
48.171
46.150
45.097
37.976
36.124
35.718
34.783
33.992
32.988
32.237
27.000
22.714
20.436
BRUKER
TEMP.001
DATE 7-6-89
TIME 9.04
SF 125.759
01 23200.000
SI 65536
TD 65536
SW 29411.765
HZ/PT .898
PW 1.7
RD .800
AQ 1.114
RG 400
NS 61
02 7990.000
DP 15H CPD
LB 1.000
GB 0.0
F1 214.999P
F2 10.003P
HZ/CM 736.576
PPM/CM 5.857
SR 9155.22

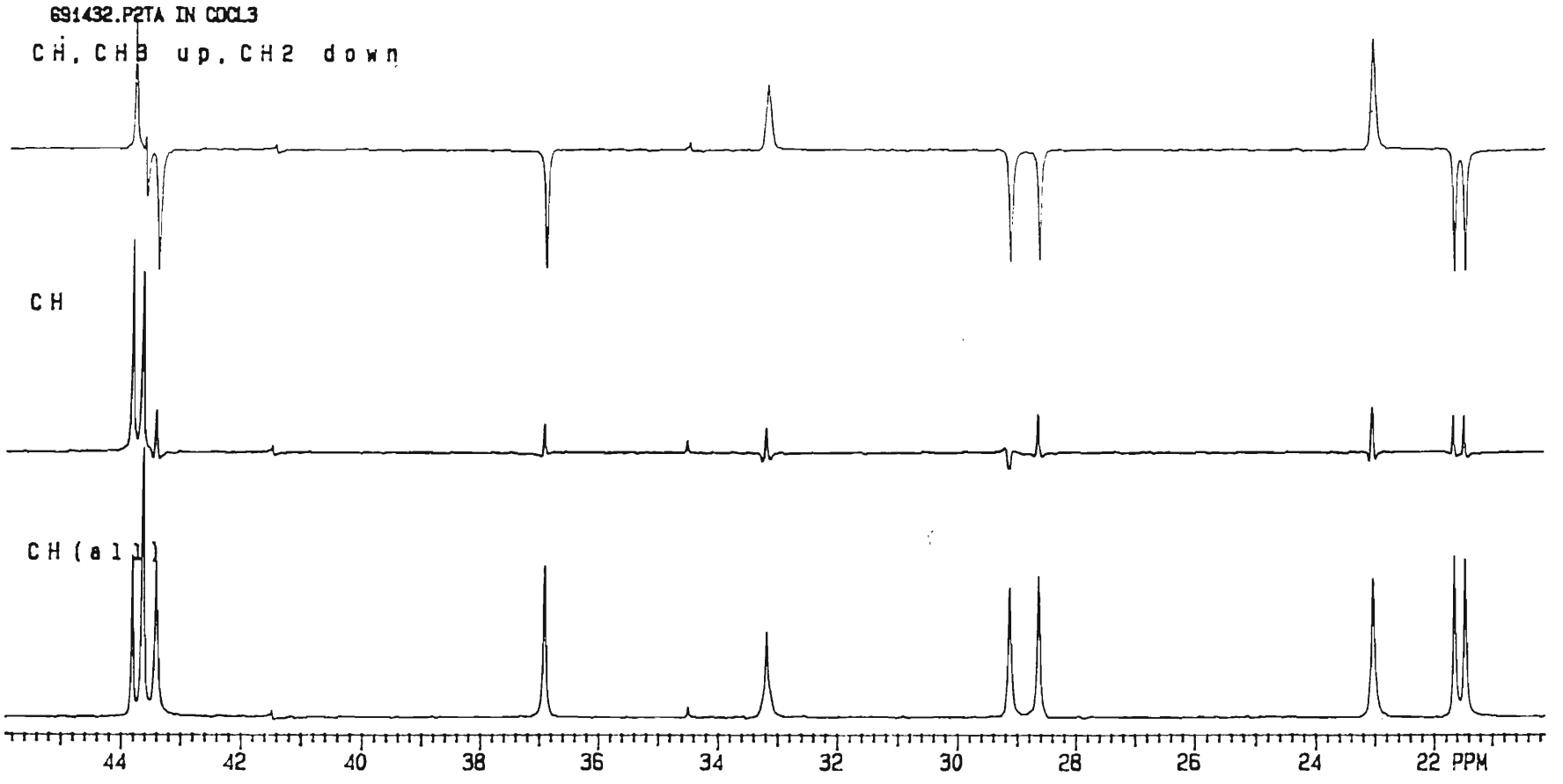
1.4
1.6
1.9
2.0
2.2
2.4
2.6
cm

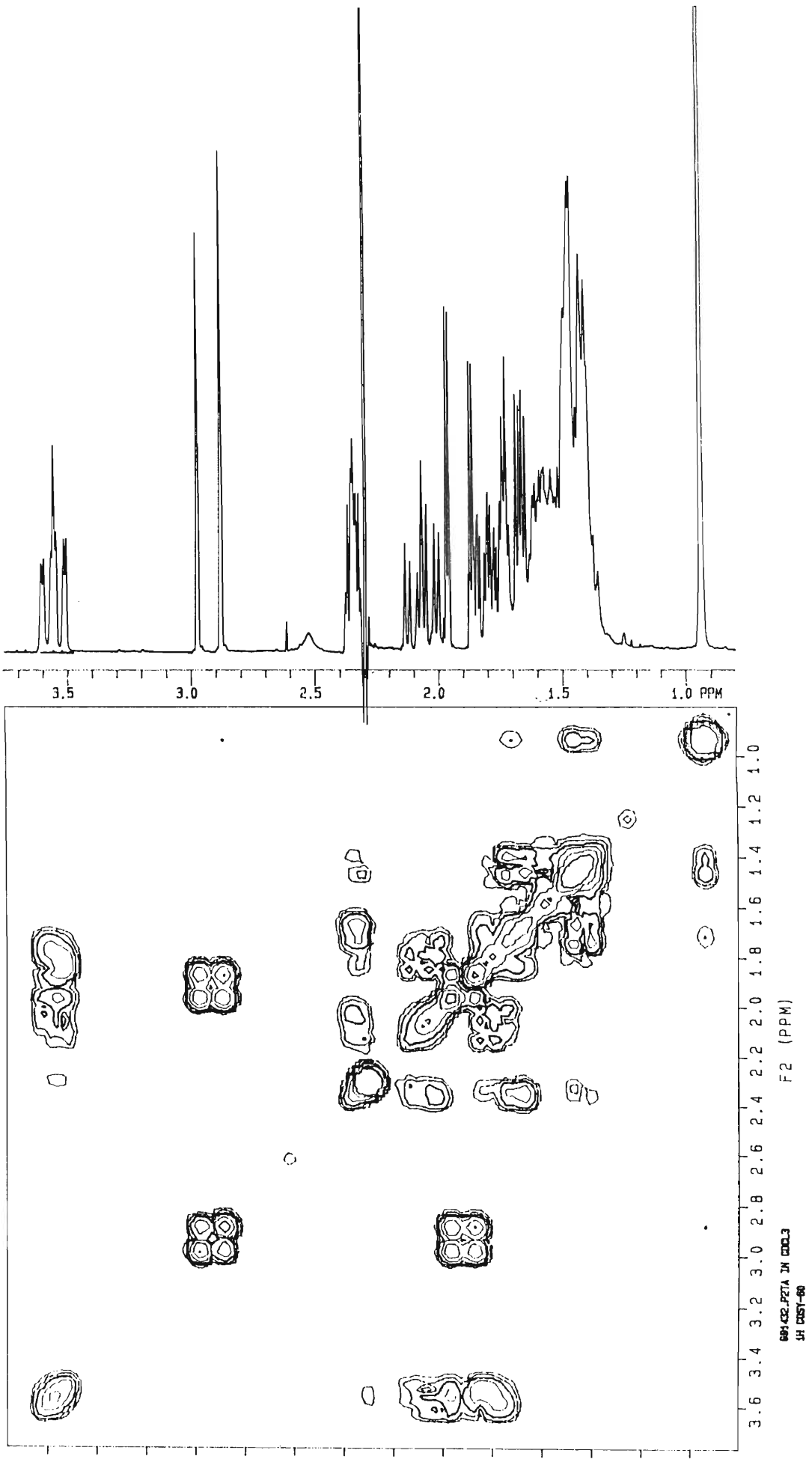

8
9
8a
10a
4b
4a
1
2
O
(72)
R',R" = H; R = Me
8
7
6
5
4
3
2
1
0
δ ppm

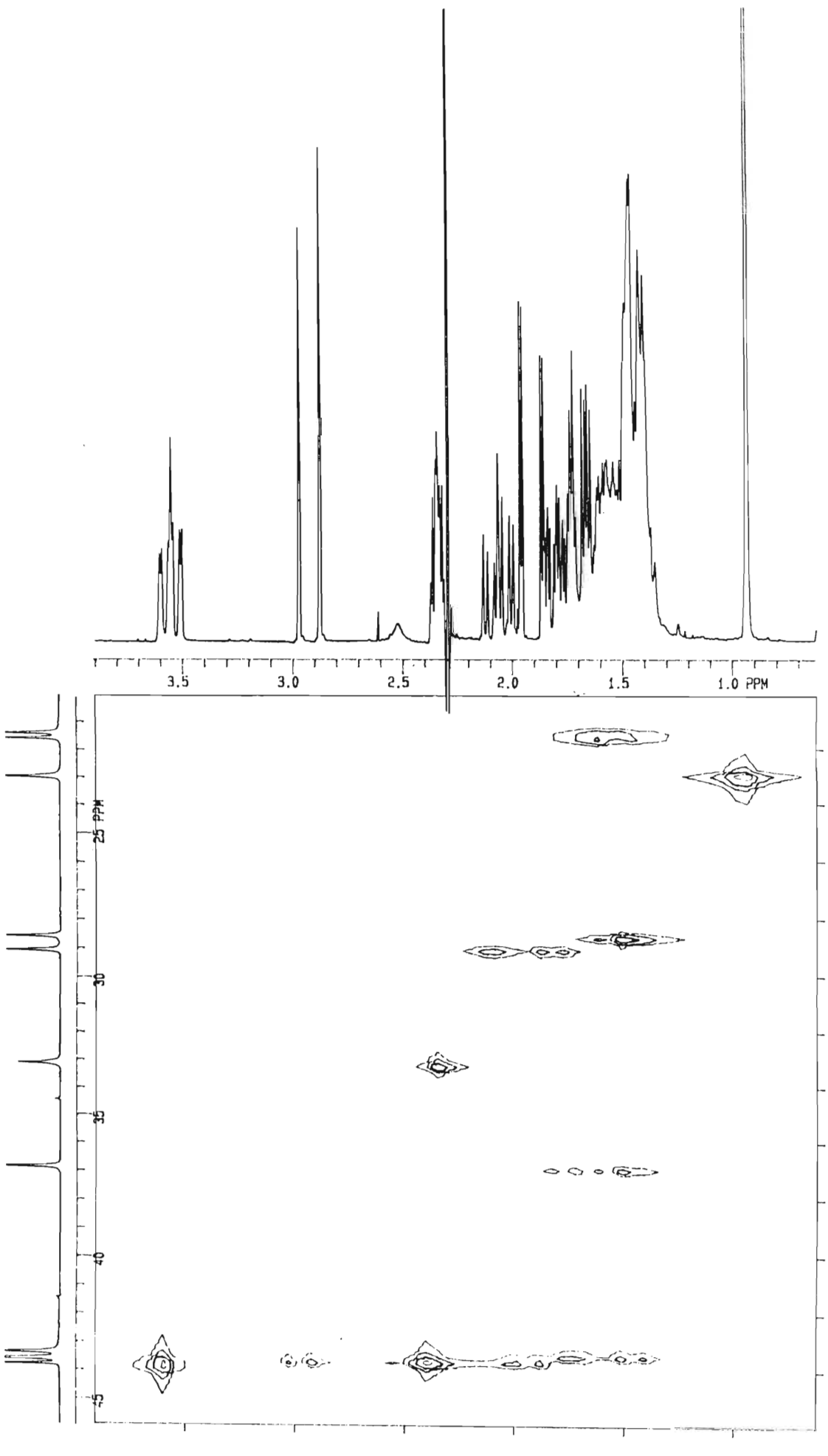

691432.P2TA IN CDCL3
Me
Hβ
8a
4
5
6
O
Hα
10
9
H
COMe
3.5
3.0
2.5
2.0
1.5
1.0
0.5 PPM
0.0

(80)

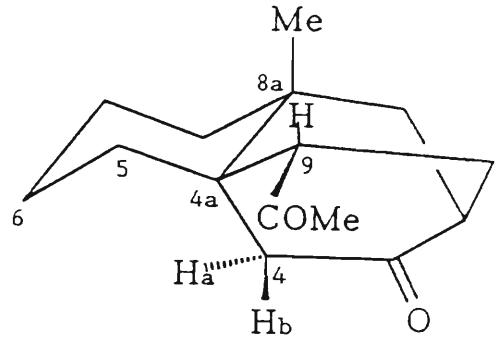

691432.P2TA IN CDCL3
200
180
160
140
120
100
80
60
40
20 PPM
0


691432.P2TA IN CDCL3
CH, CH3 up, CH2 down
CH
CH (all)
44
42
40
38
36
34
32
30
28
26
24
22 PPM

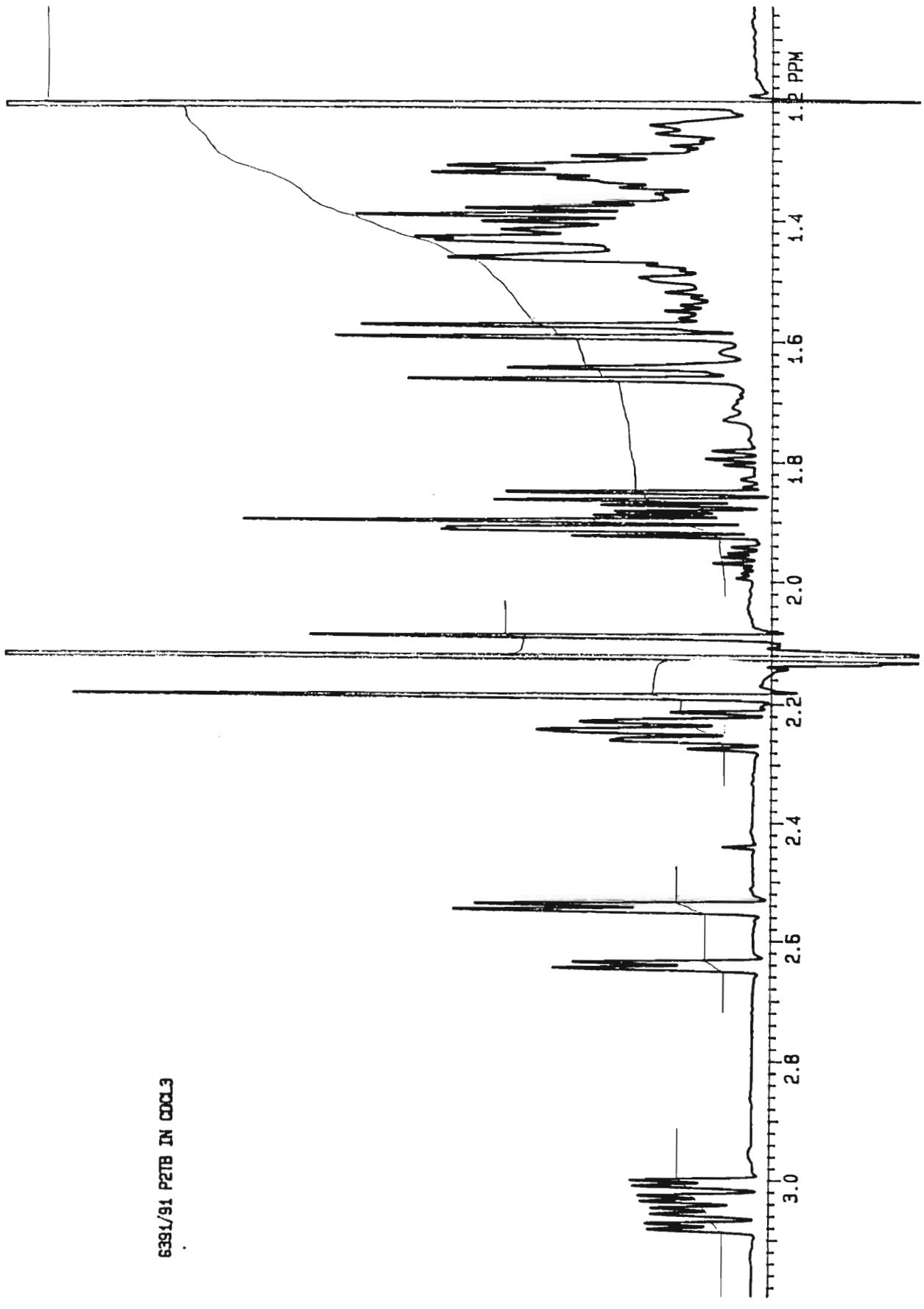

3.5
3.0
2.5
2.0
1.5
1.0 PPM
F2 (PPM)
3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
1H COSY-60

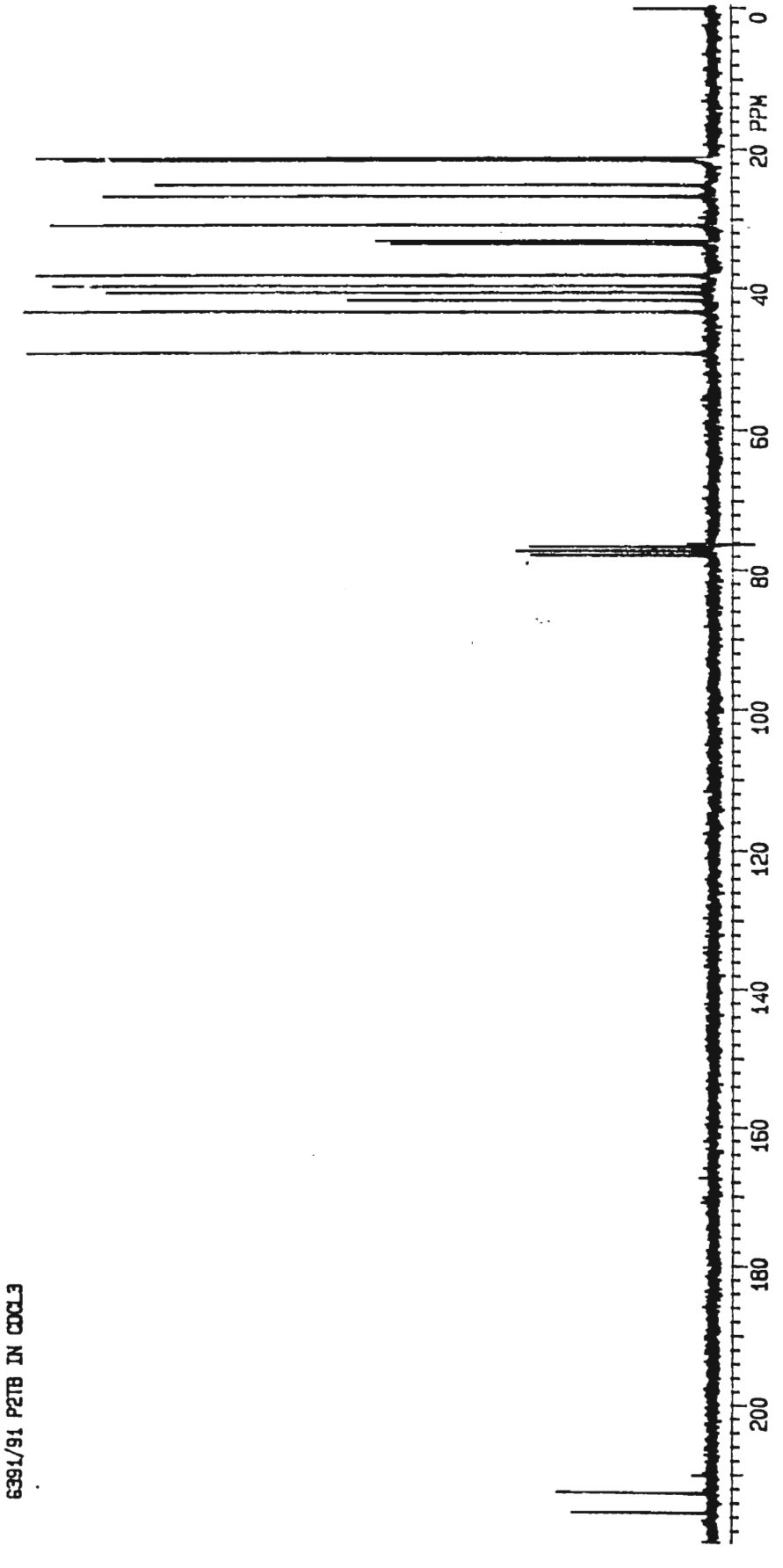

3.5
3.0
2.5
2.0
1.5
1.0 PPM
25 PPM
30
35
40
45

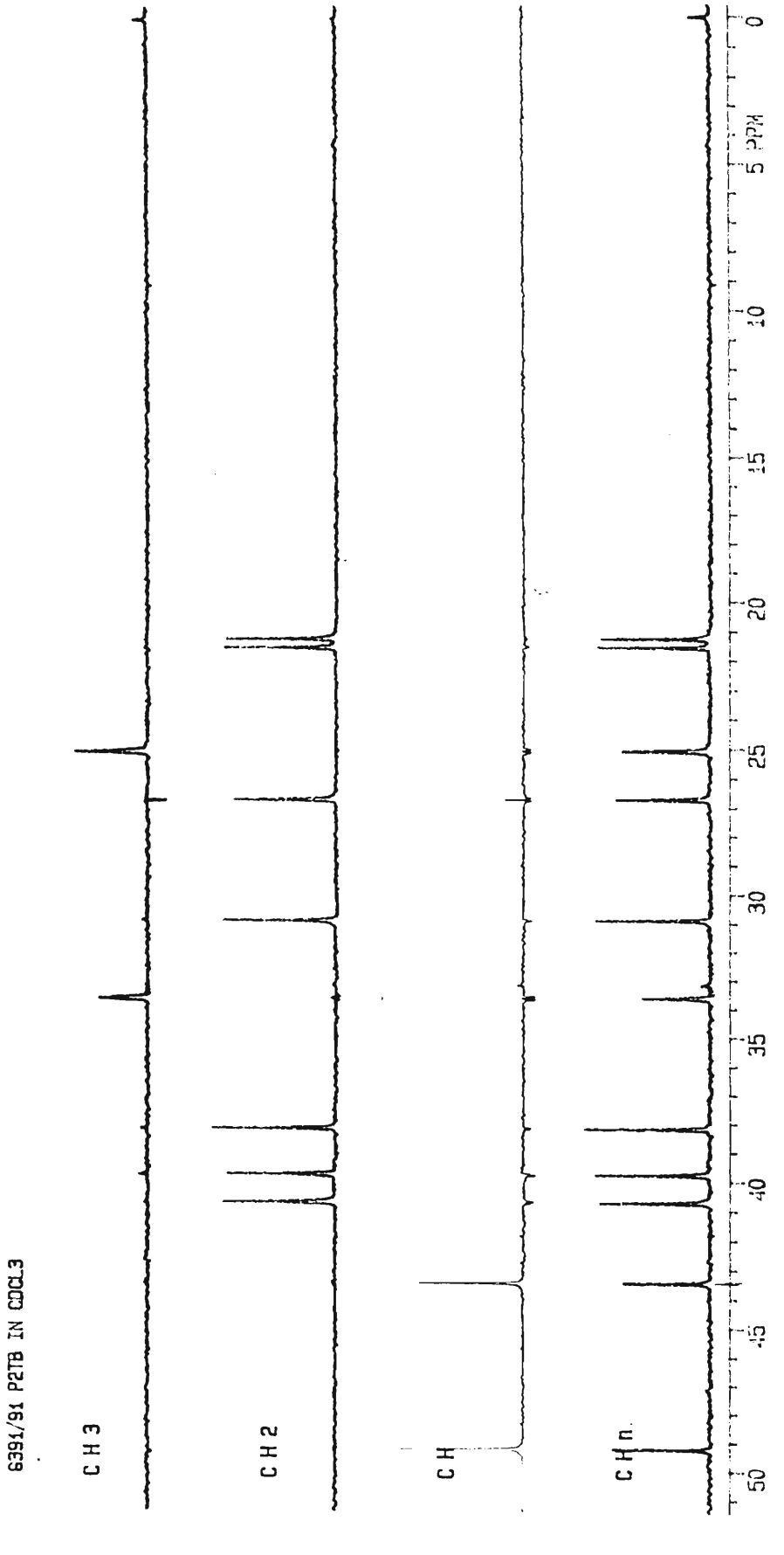
6391/91 P2TB IN CDCL3

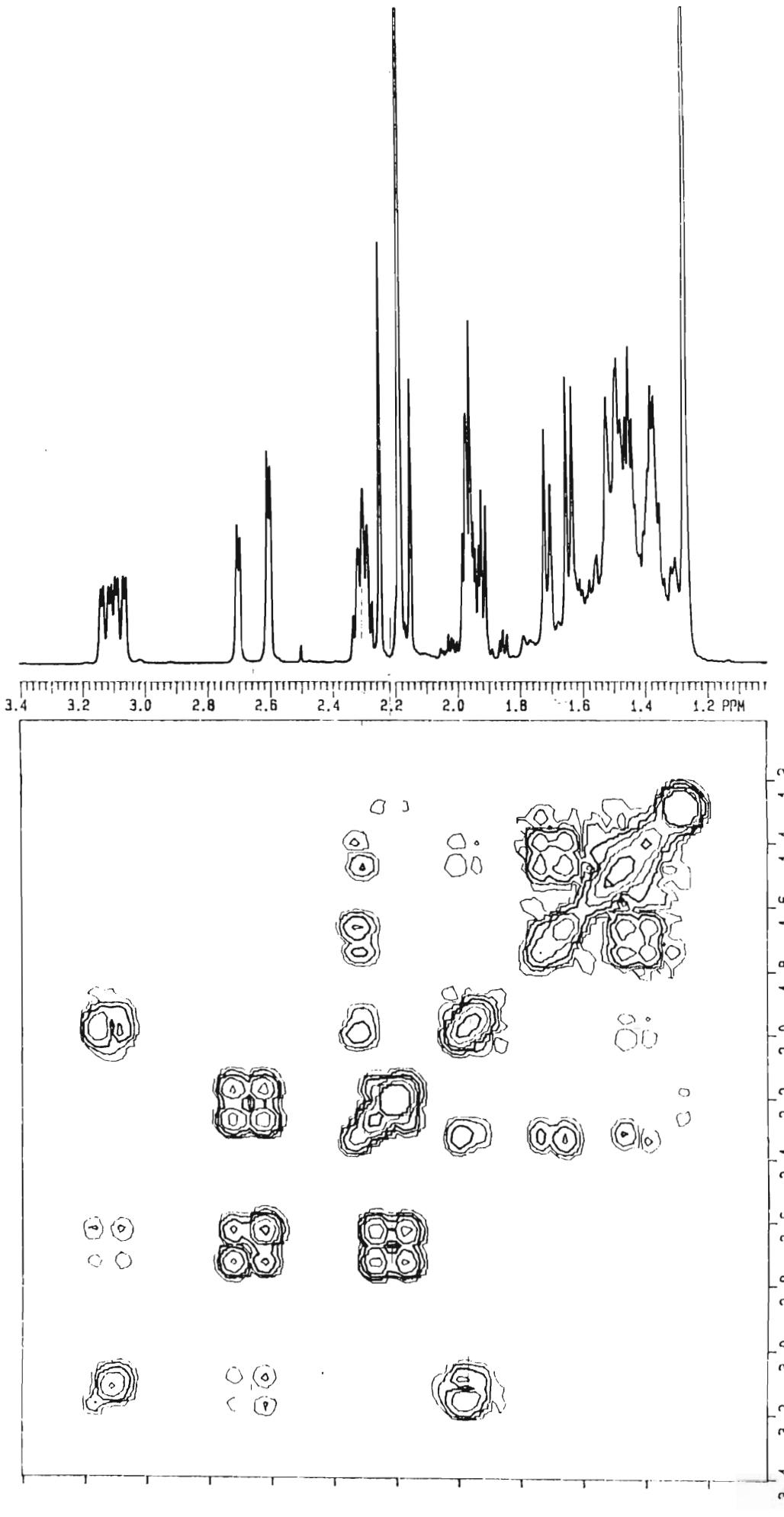


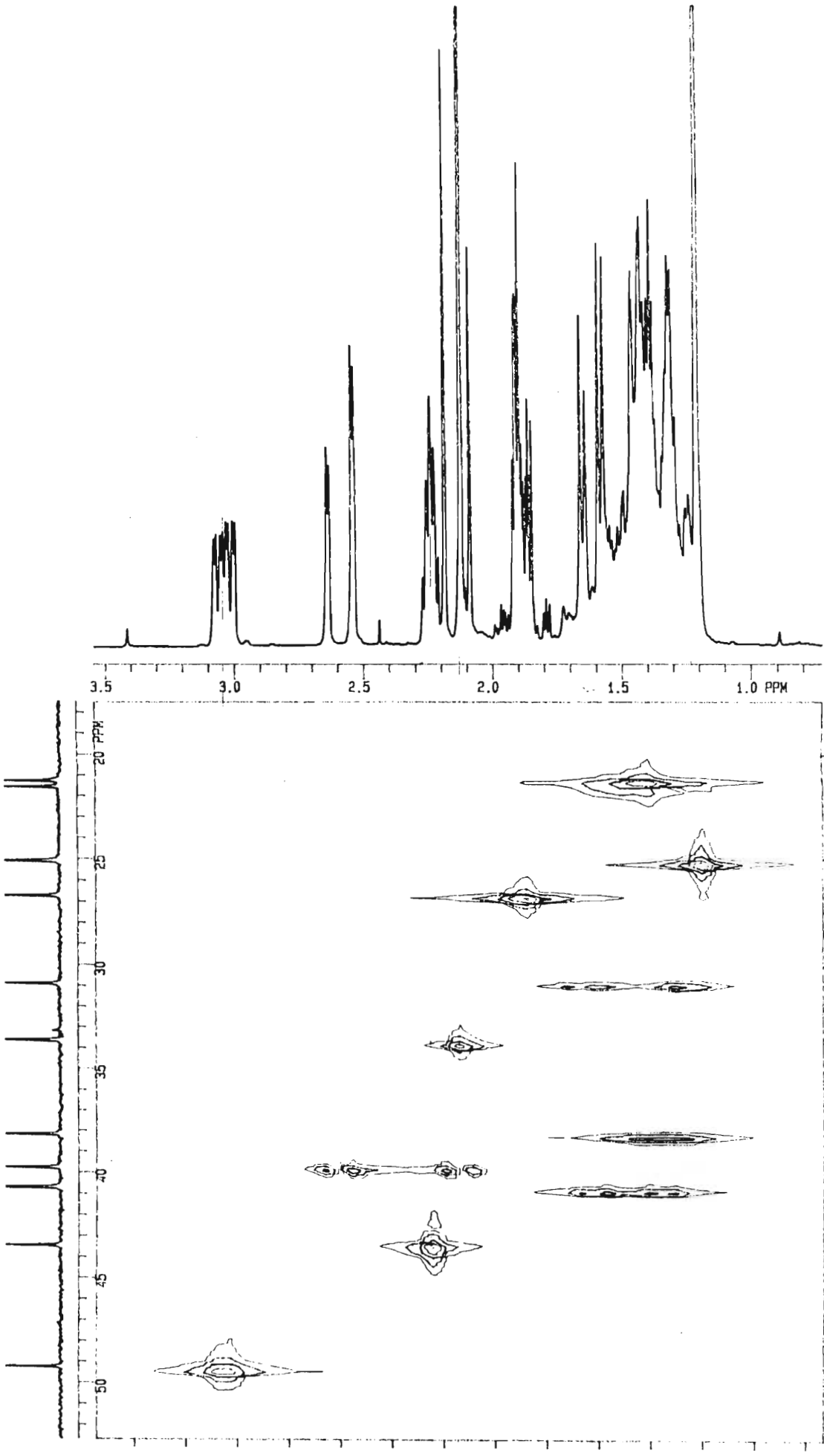
(81)


6391/91 P2TB IN CDCL3
1.2 PPM
1.4
1.6
1.8
2.0
2.2
2.4
2.6
2.8
3.0

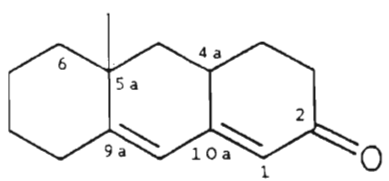

6391/91 P2TB IN CDCL3
0
20 PPM
40
60
80
100
120
140
160
180
200


6391/91 P2TB IN CDCL3
C H 3
C H 2
C H
C H n.
50
45
40
35
30
25
20
15
10
5 PPM
0


3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2 PPM
F2 (PPM)
E391/91 PCTB IN CDCL3
1H COSY-60

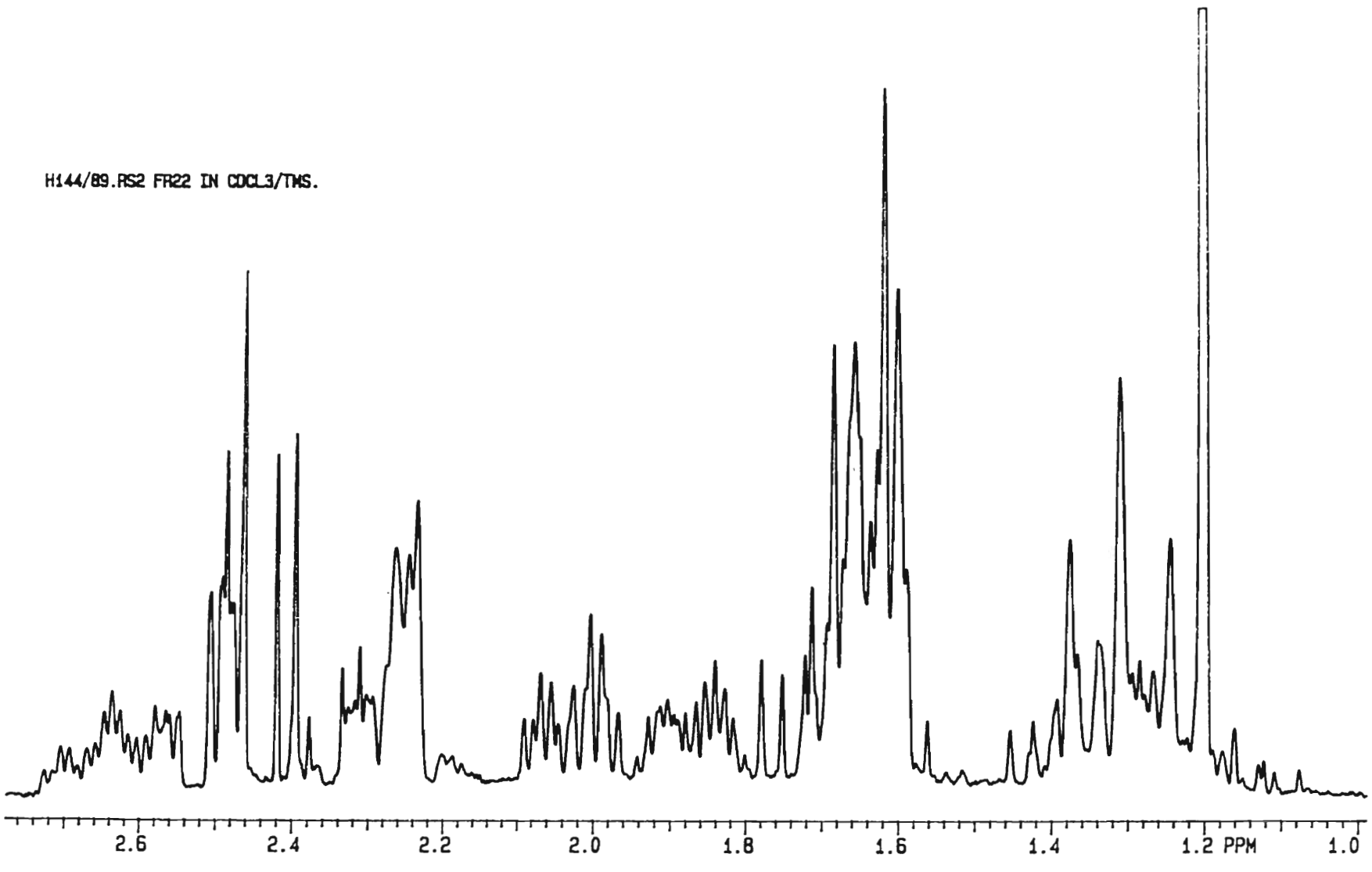

3.5
3.0
2.5
2.0
1.5
1.0 PPM
20 PPM
25
30
35
40
45
50
6381/91 PZTB IN CDCL3
1H/13C HETCOR

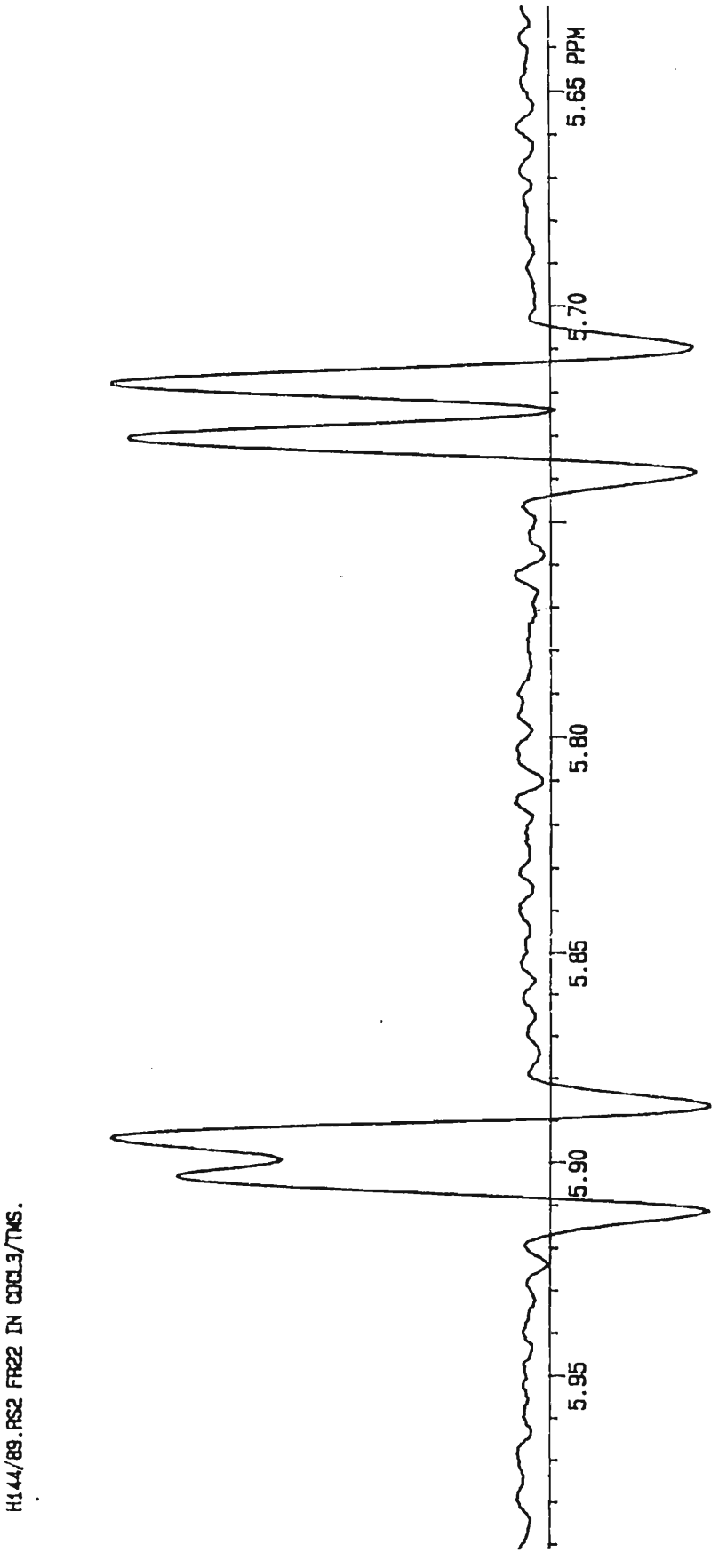
H144/89.RS2 FR22 IN CDCL3/TMS.



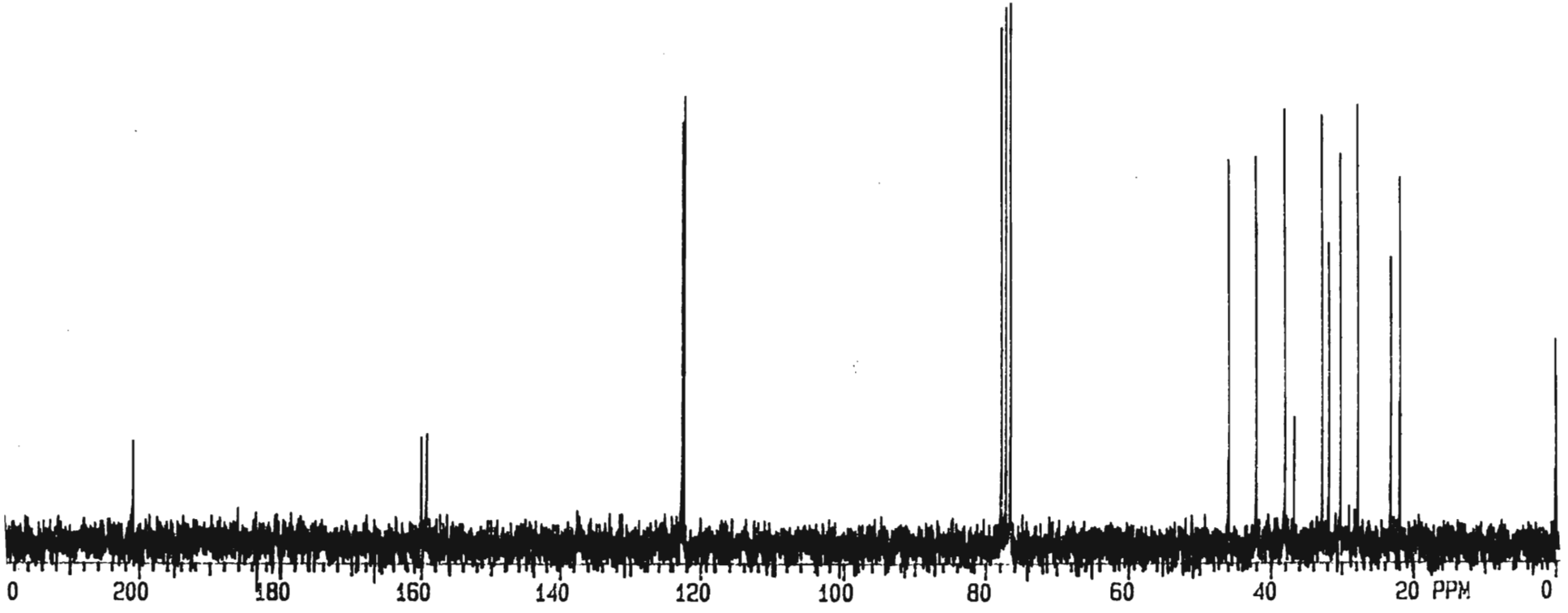
(77)

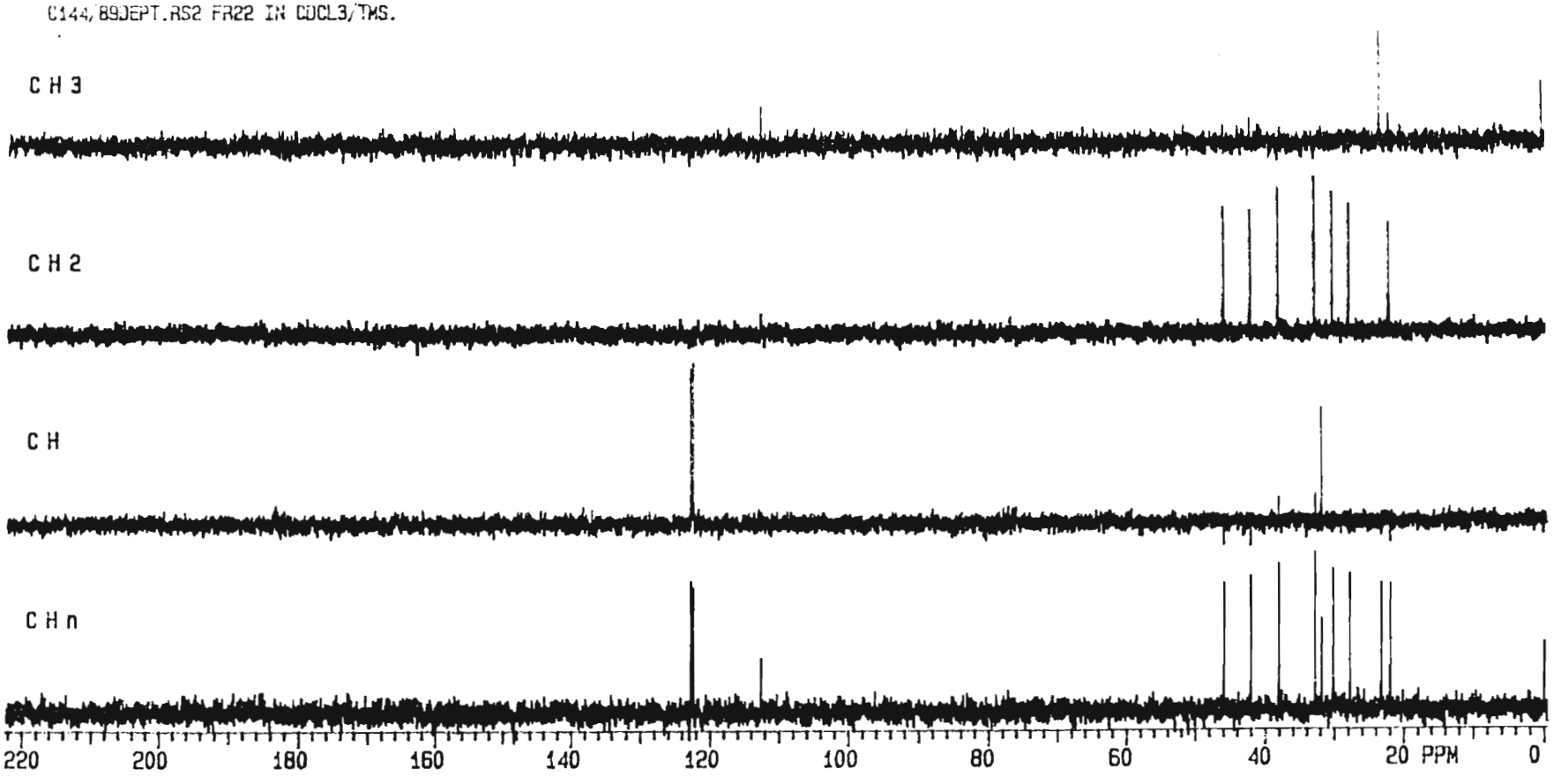
R = Me; R' = H


H144/89.RS2 FR22 IN CDCL3/TMS.
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2 PPM
1.0

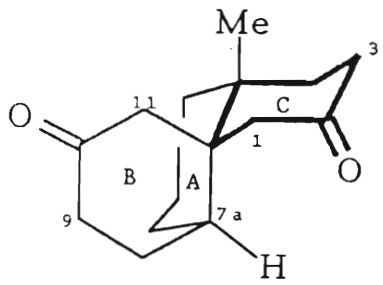

H144/89.RS2 FR22 IN CDCL3/TMS.
5.95
5.90
5.85
5.80
5.70
5.65 PPM

C144/89PNU.RS2 FR22 IN CDCL3/TMS.

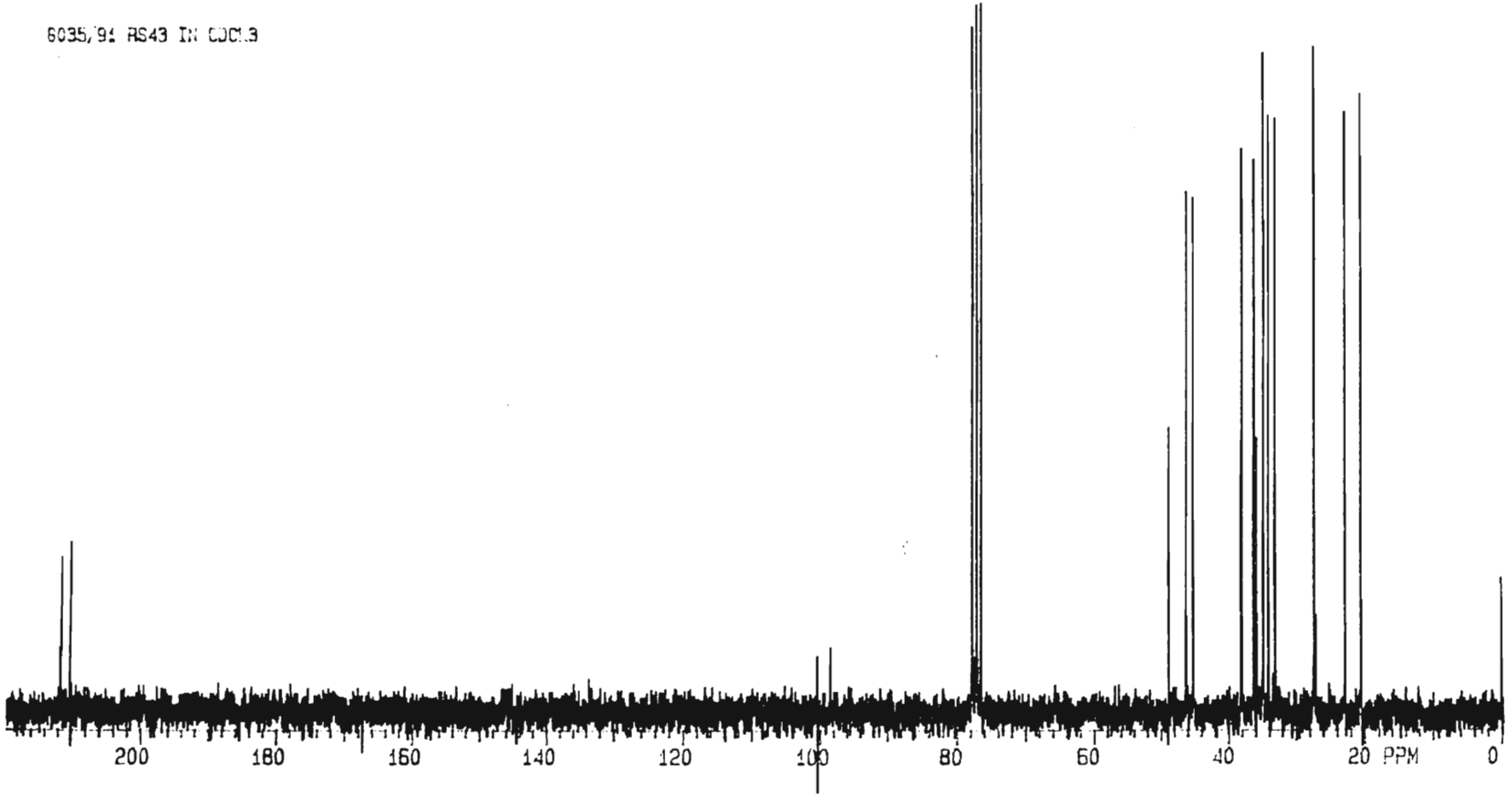


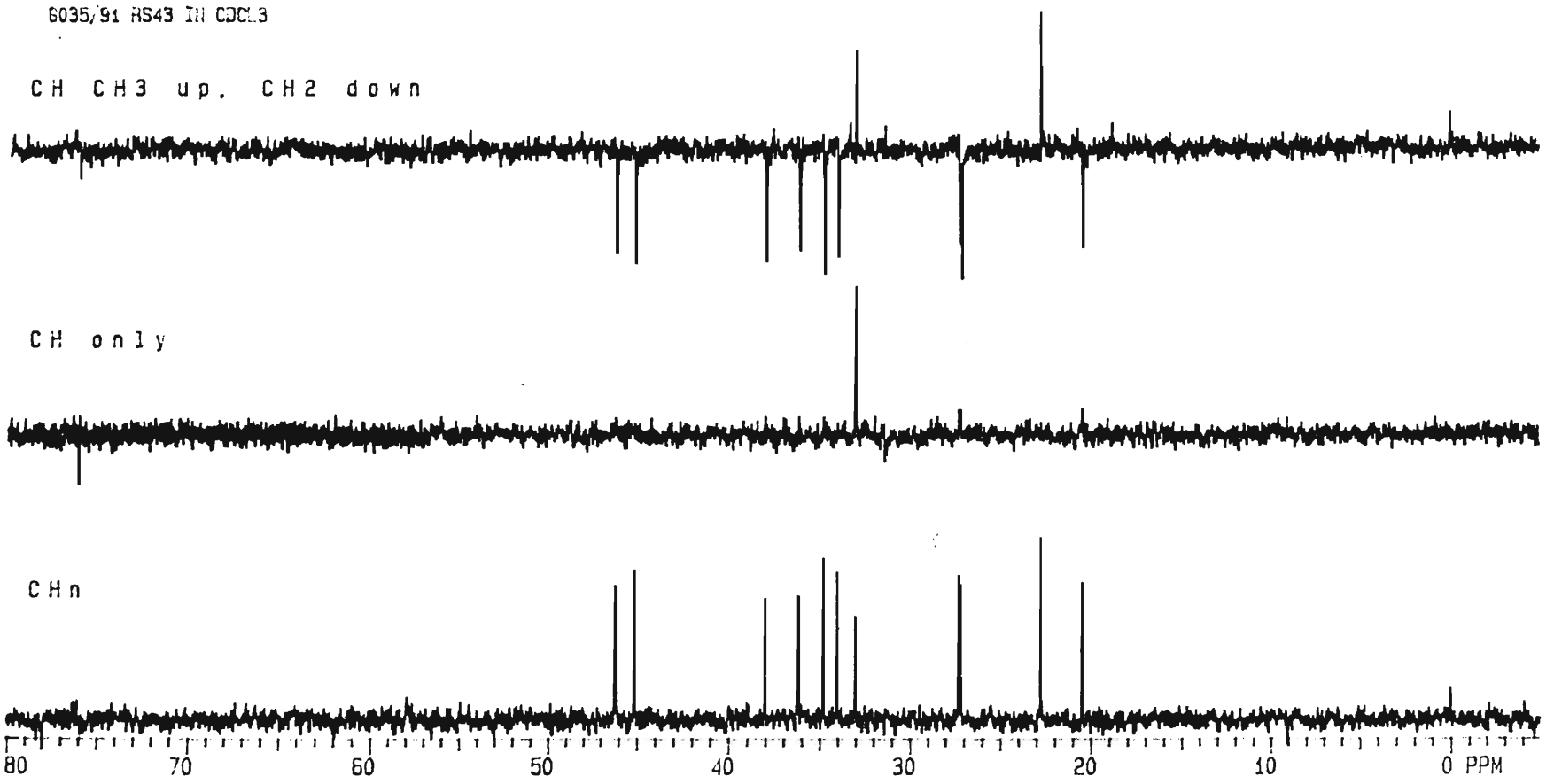

C144/89JEPT.RS2 FR22 IN CDCL3/TMS.
C H 3
C H 2
C H
C H n
220
200
180
160
140
120
100
80
60
40
20 PPM
0

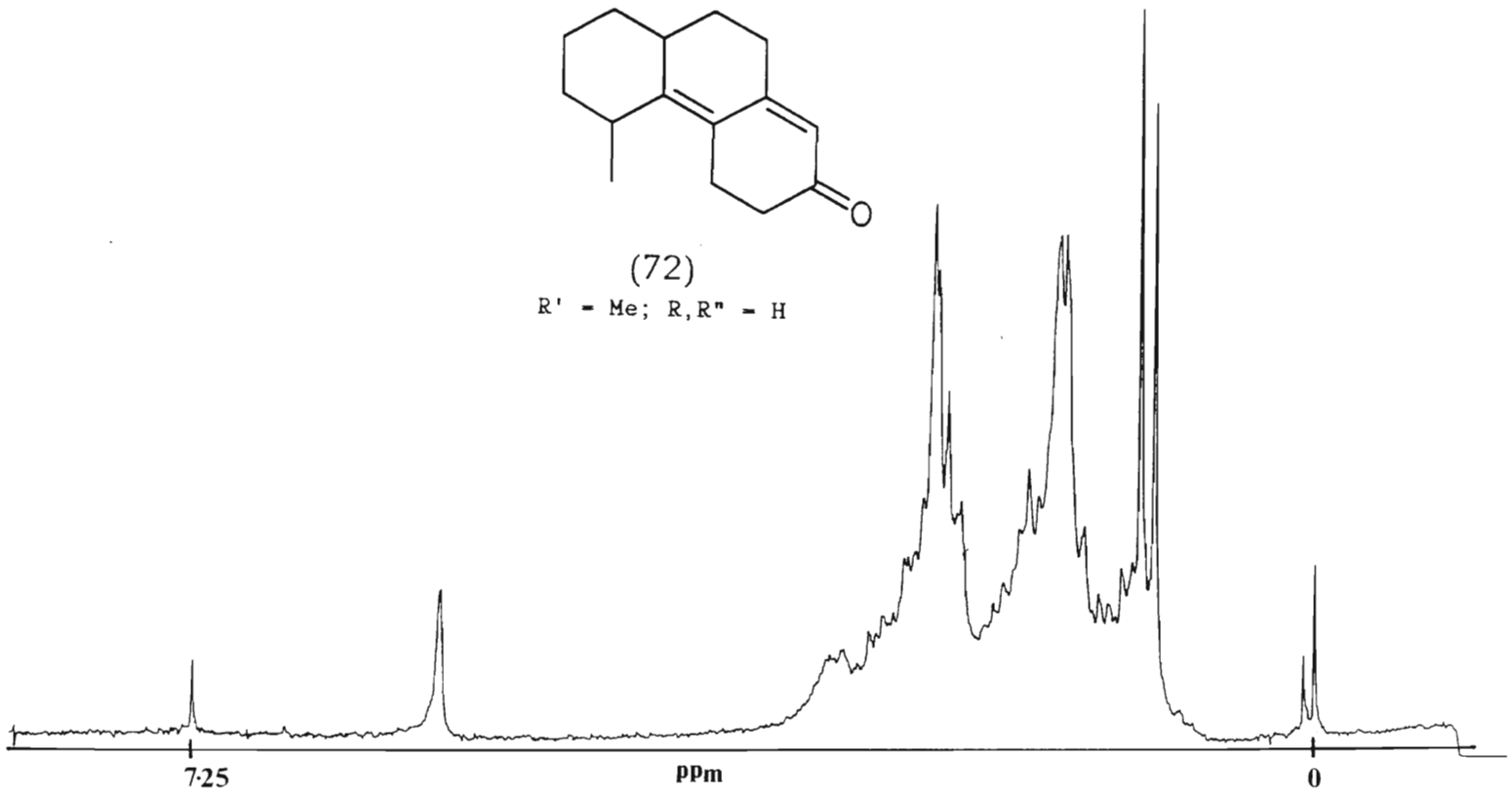
6035/91 RS43 IN CDCL3



(90)

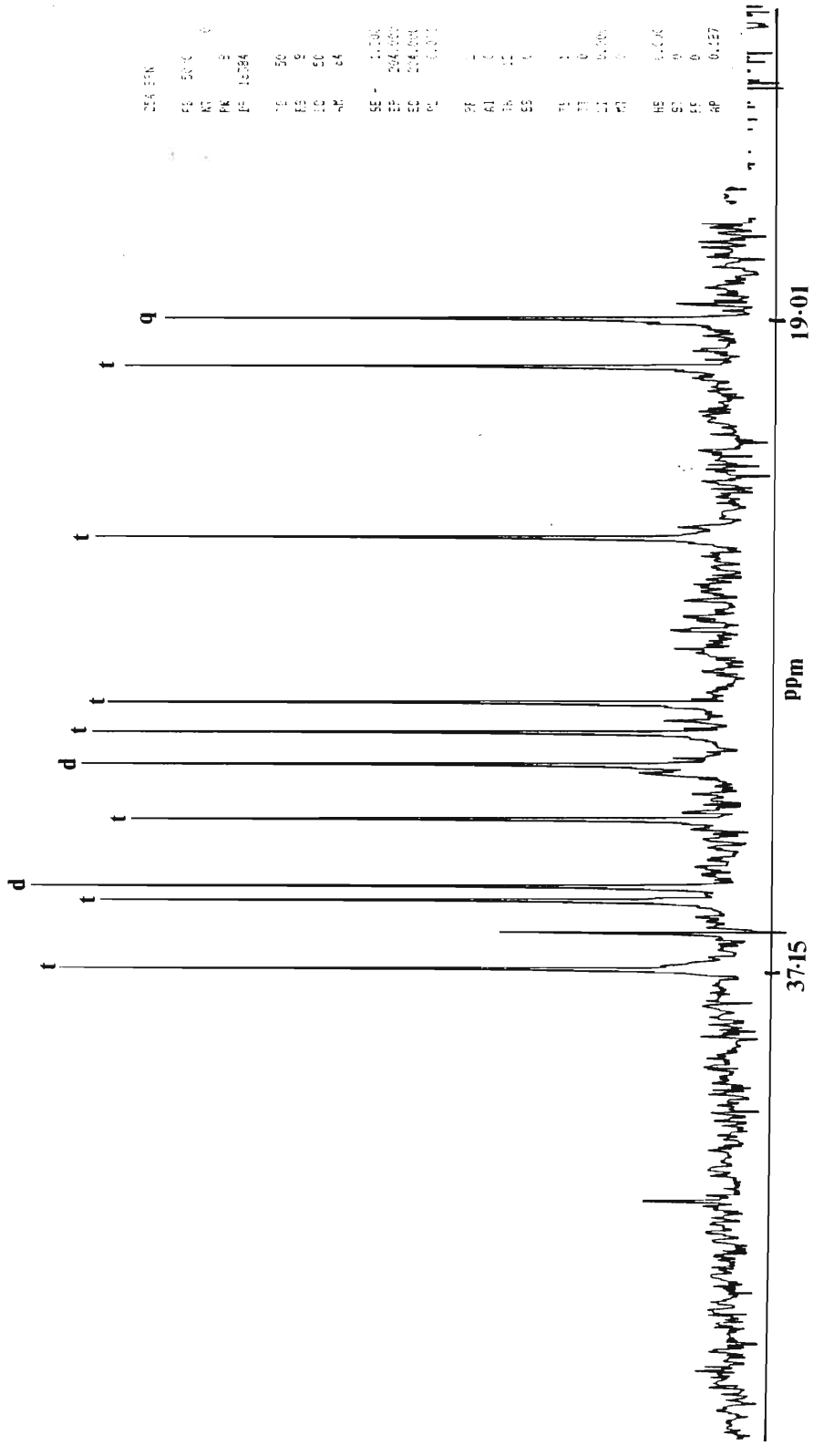

6035,91 RS43 IN CDCl3
200
180
160
140
120
100
80
60
40
20
PPM
0

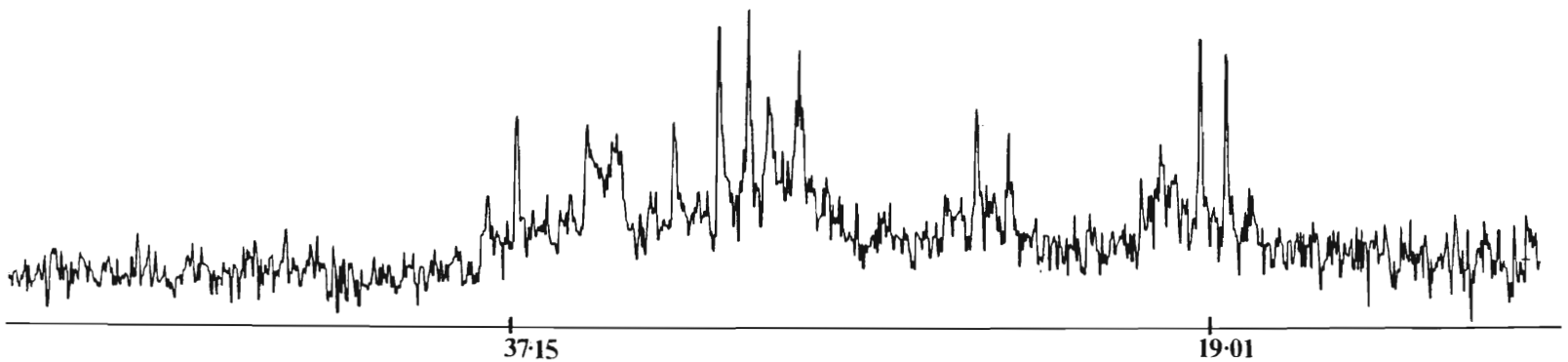

6035/91 RS43 IN CDCL3
CH CH3 up, CH2 down
CH only
CHn
80
70
60
50
40
30
20
10
0 PPM

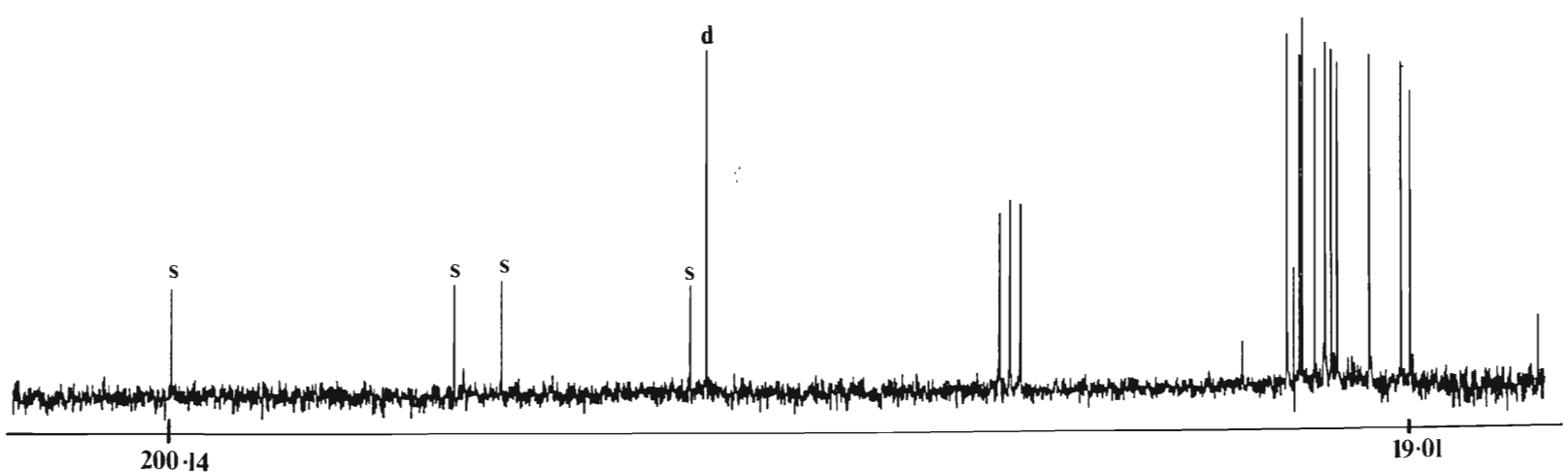


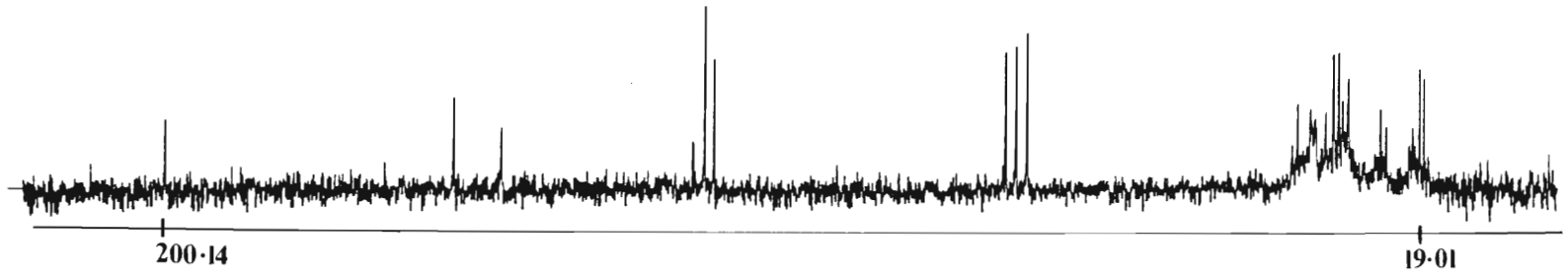
(72)

R' = Me; R,R" = H

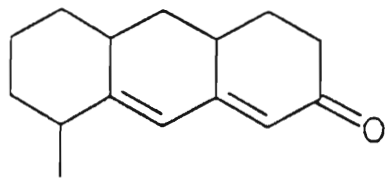

q
t
t
t
d
t
t
d
t
t
t
19·01
ppm
37·15


37·15
19·01


d
s
s
s
s
200·14
19·01


200·14
19·01

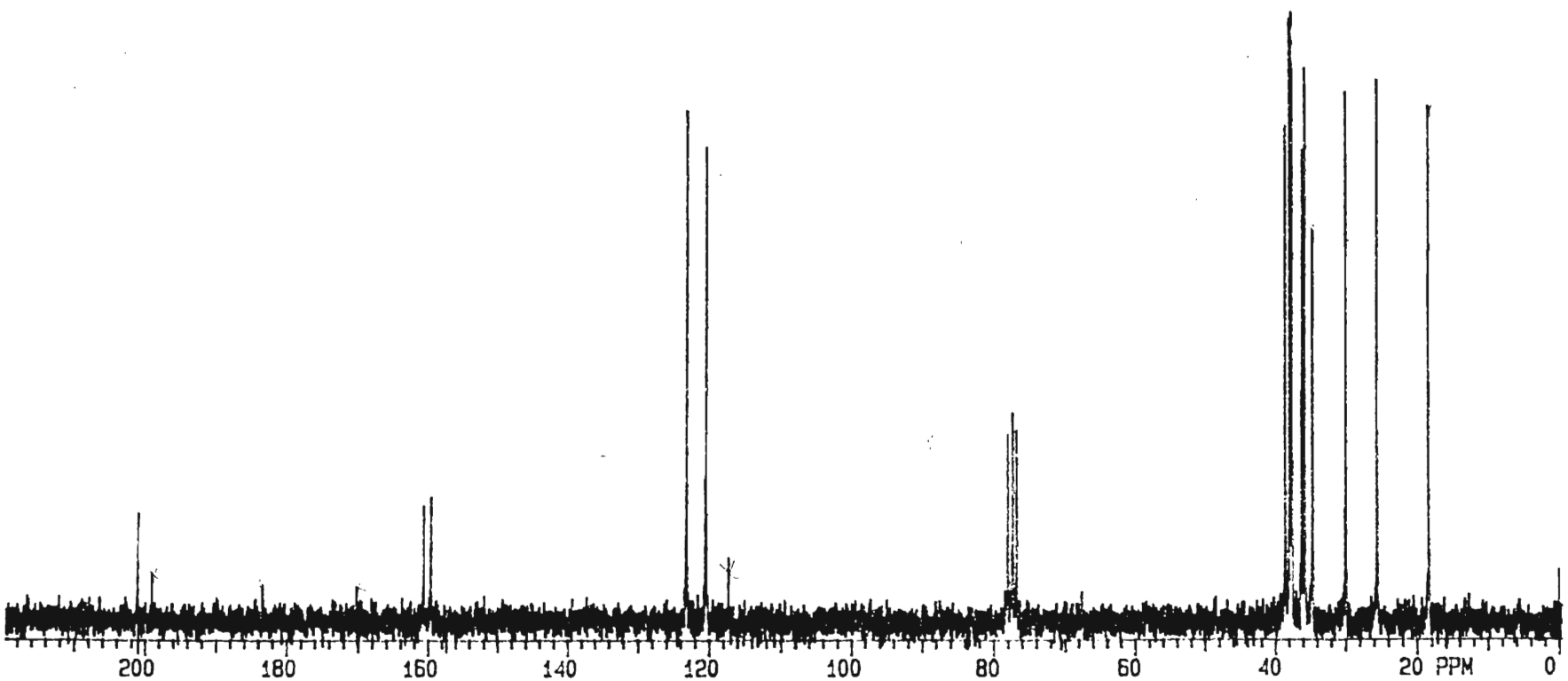
H89182.RS4FR21 IN CDCL3/TMS.

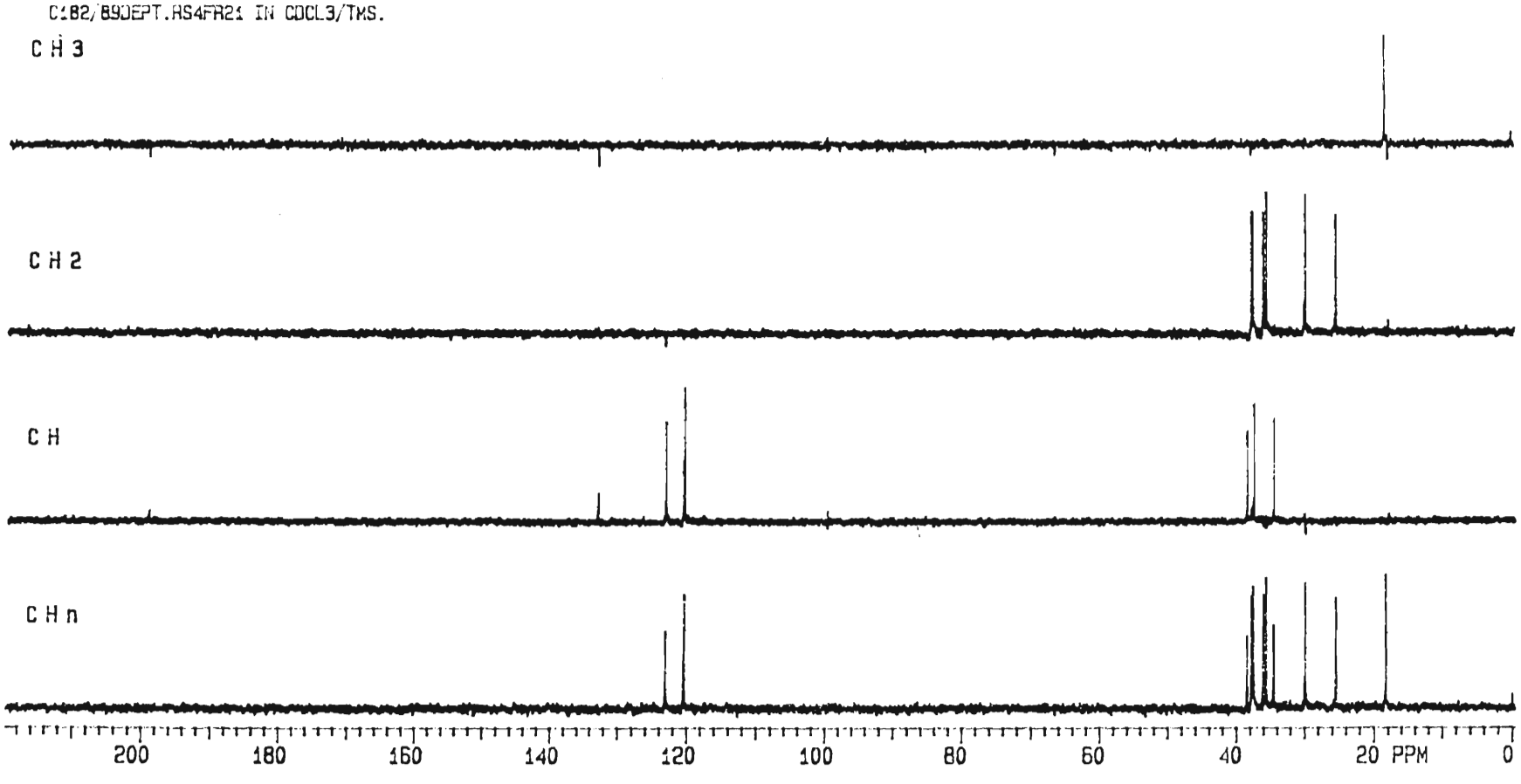


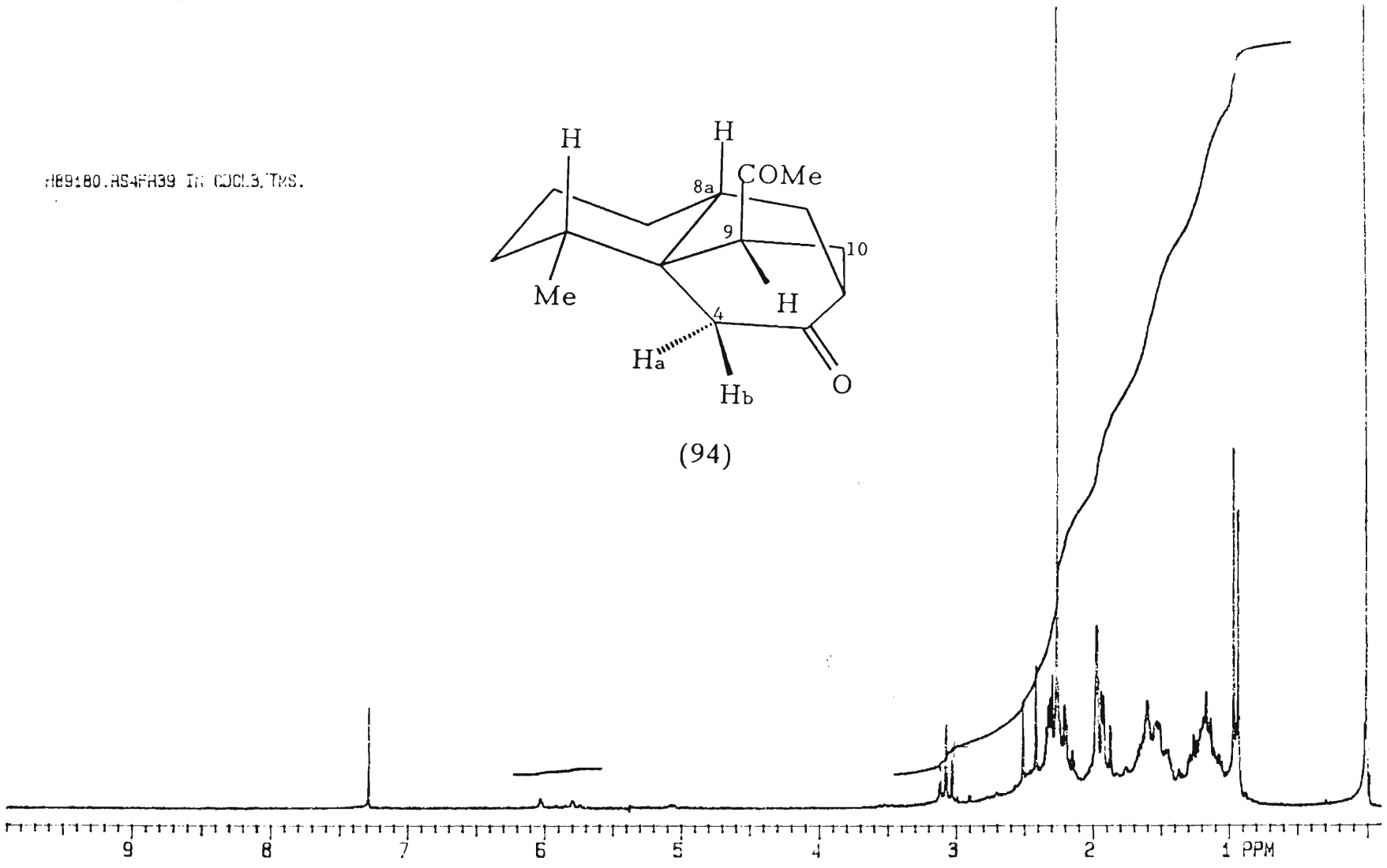
(77)

R' = Me; R,R" = H

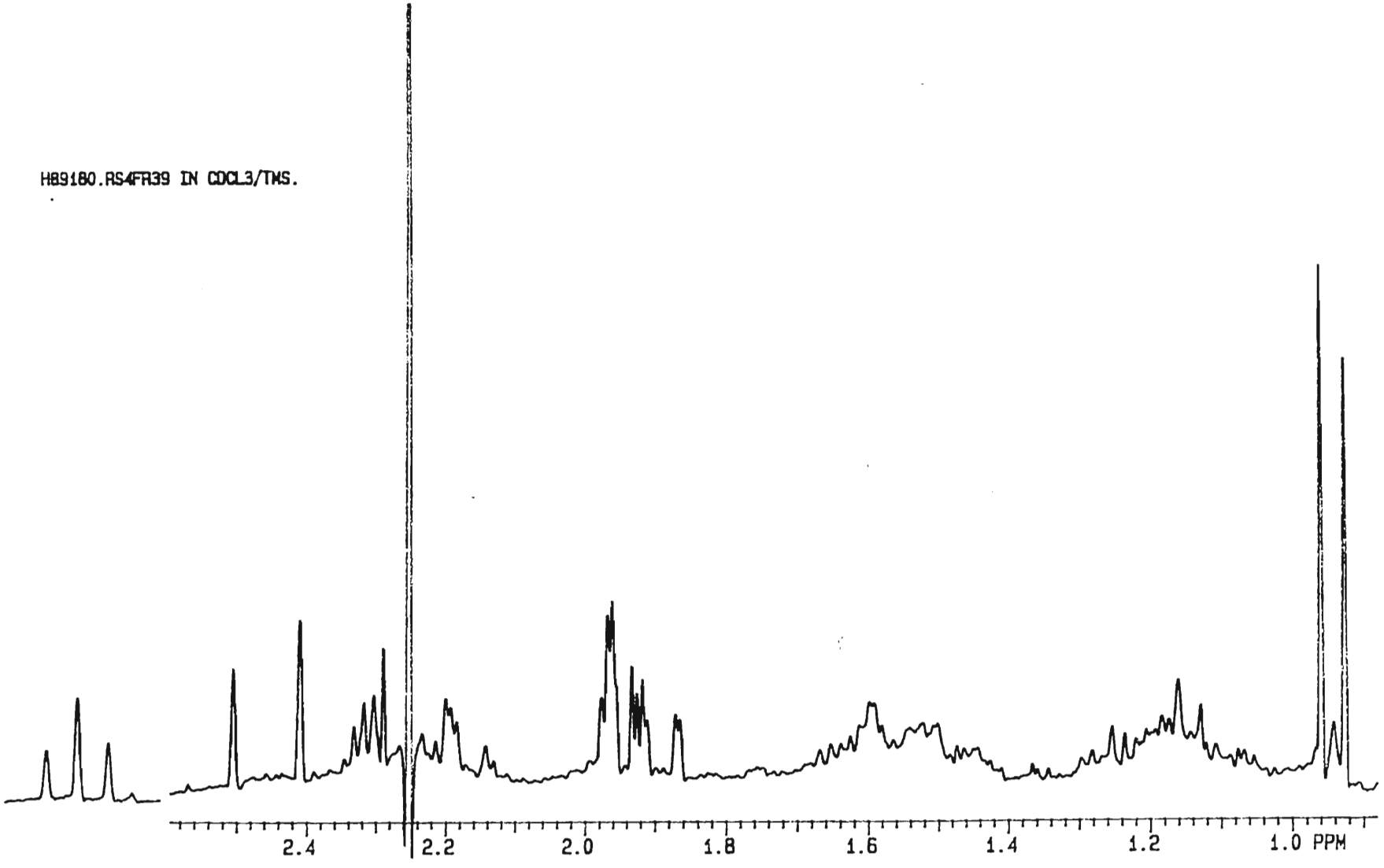
C182/89PND.RS4FR21 IN CDCL3/TMS.



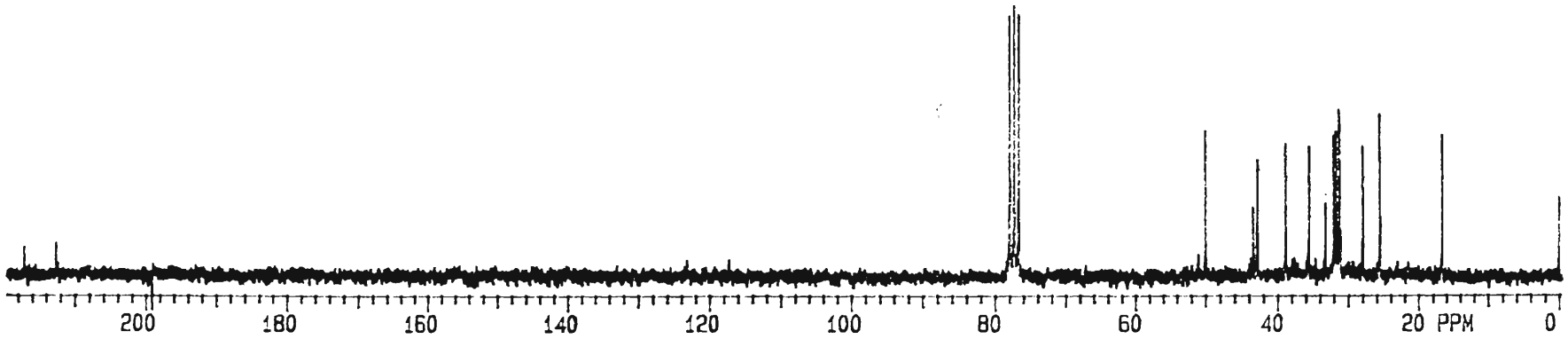

C182/89DEPT.RS4FR21 IN CDCL3/TMS.
C H 3
C H 2
C H
C H n
200
180
160
140
120
100
80
60
40
20 PPM
0


H89180.RS4FR39 IN CDCL3,TMS.
H
H
COMe
8a
9
10
Me
H
4
Ha
Hb
O
9
8
7
6
5
4
3
2
1 PPM

(94)

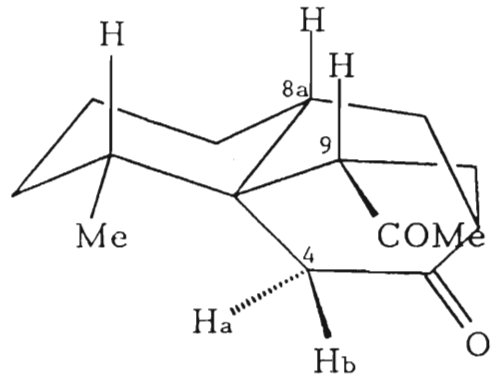

H89180.RS4FR39 IN CDCL3/TMS.
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM

C180/89PND.RS4FR39 IN CDCL3/TMS.

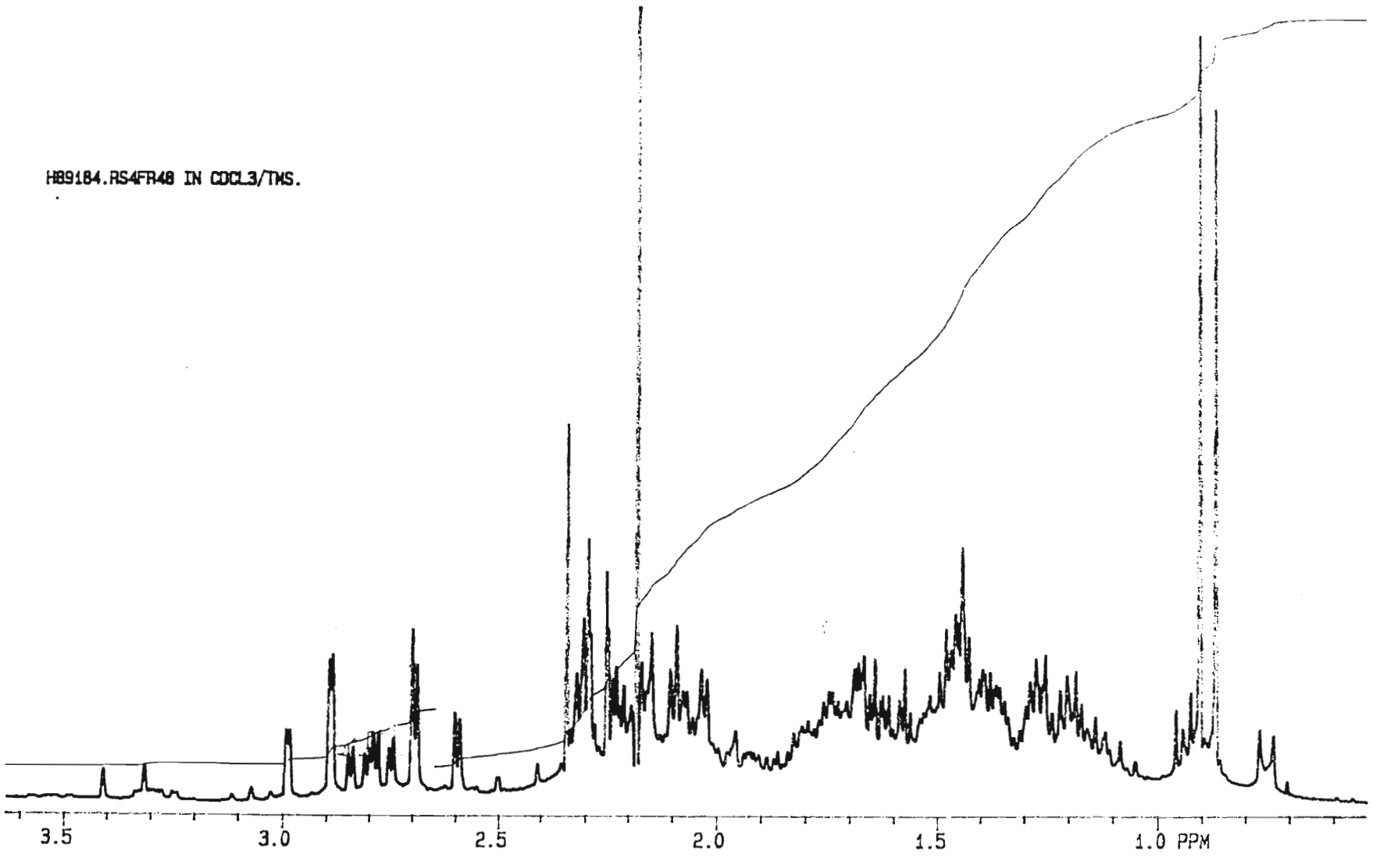


ALL CARBONS
C:80 89DEPT.AS:FH39 IH CDCL3; TMS
CH3
CH2
CH
CHn
55
50
45
40
35
30
25
20
15
10
5 PPM
0

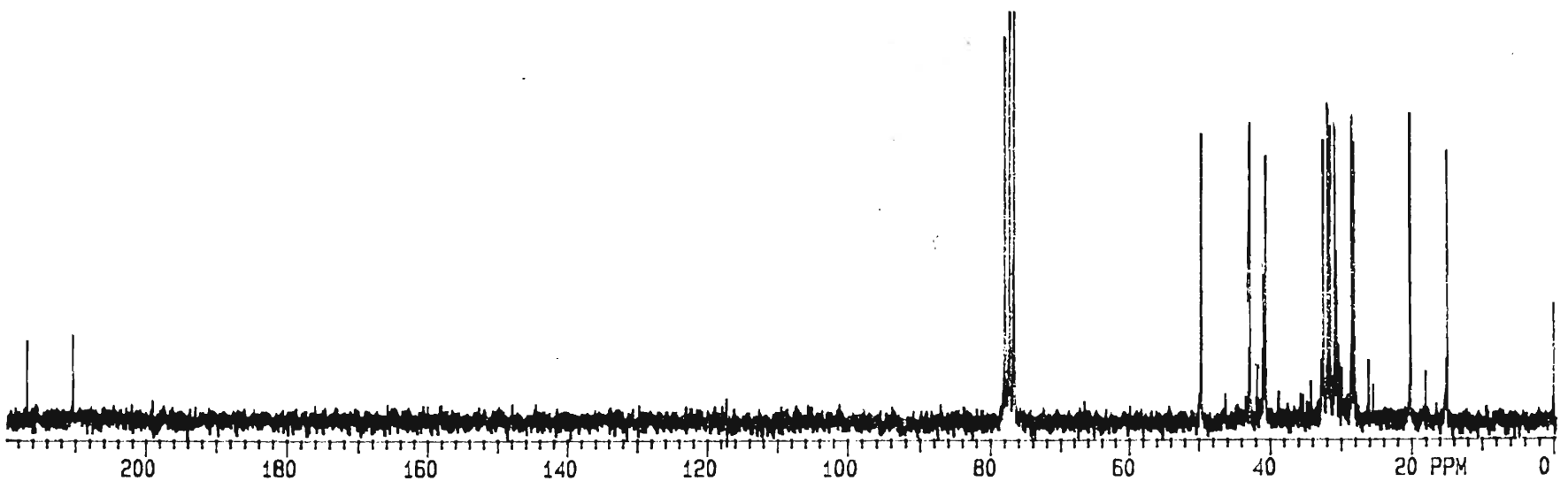
H89184.RS4FR48 IN CDCL3/TMS.

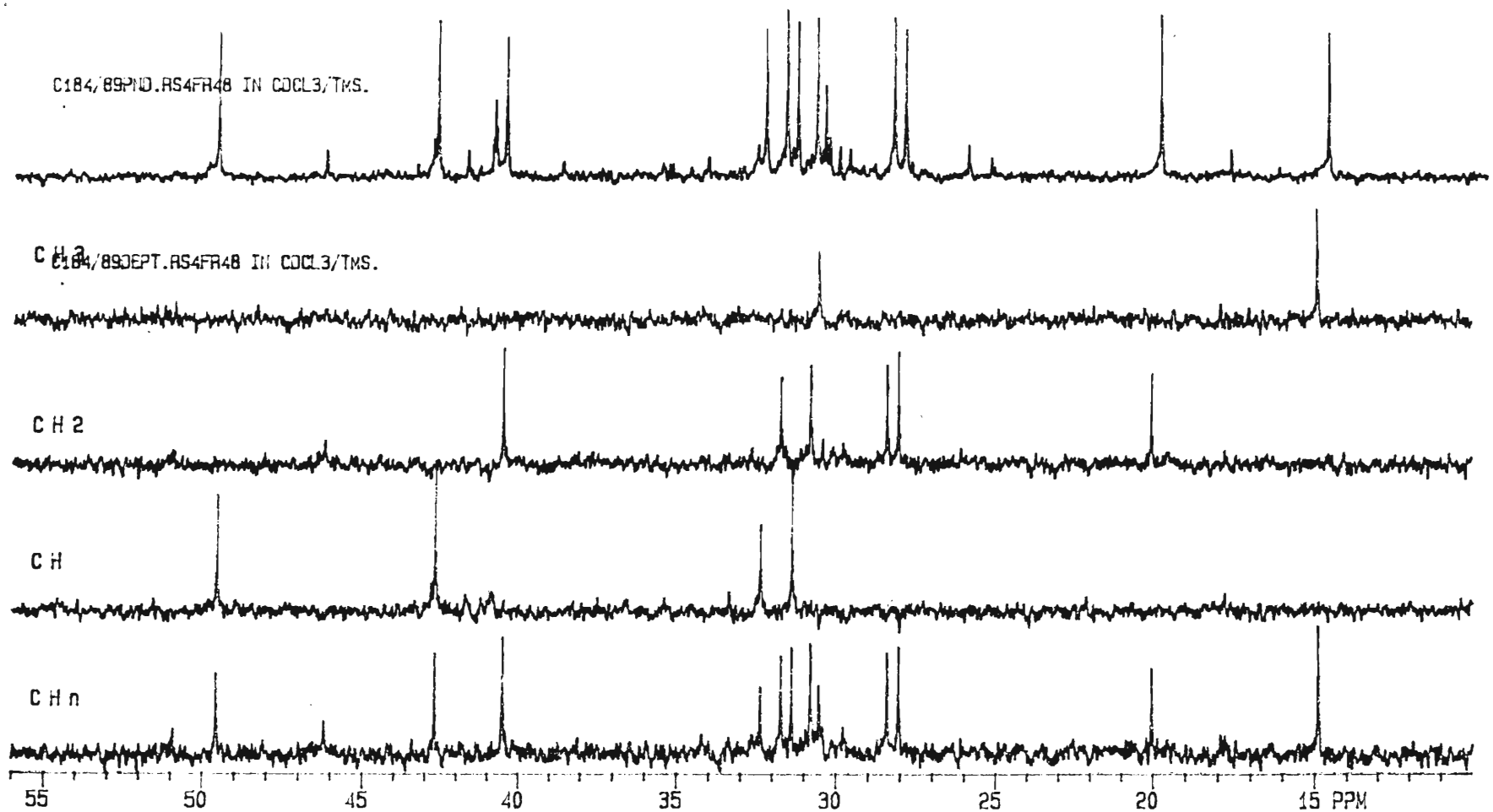


(95)

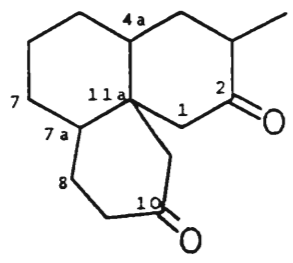

H89184.RS4FR48 IN CDCL3/TMS.
3.5
3.0
2.5
2.0
1.5
1.0 PPM

C184/89PND.RS4FR48 IN CDCL3/TMS.



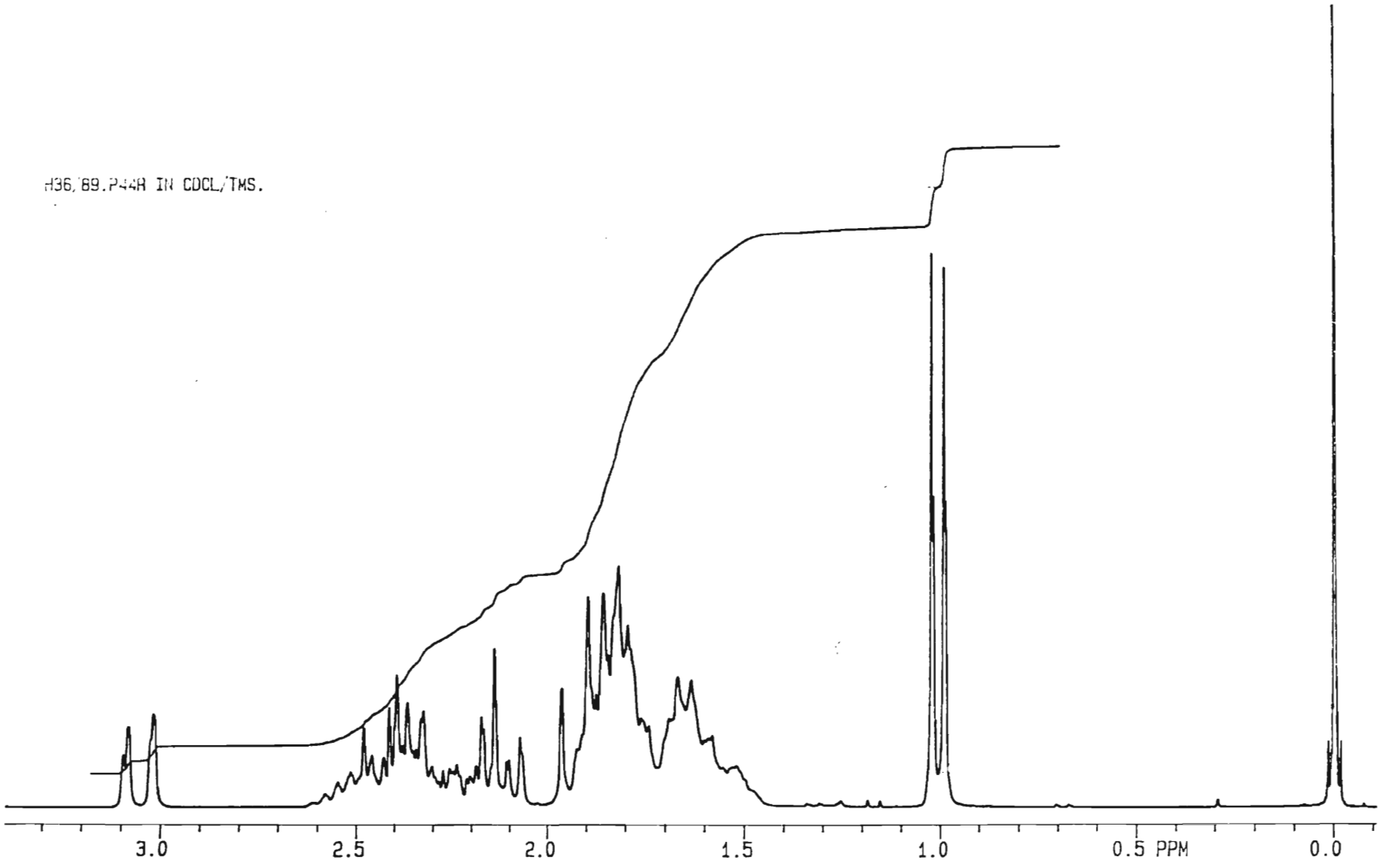

C184/89PND.RS4FR48 IN CDCL3/TMS.
C184/89DEPT.RS4FR48 IN CDCL3/TMS.
C H 3
C H 2
C H
C H n
55
50
45
40
35
30
25
20
15 PPM

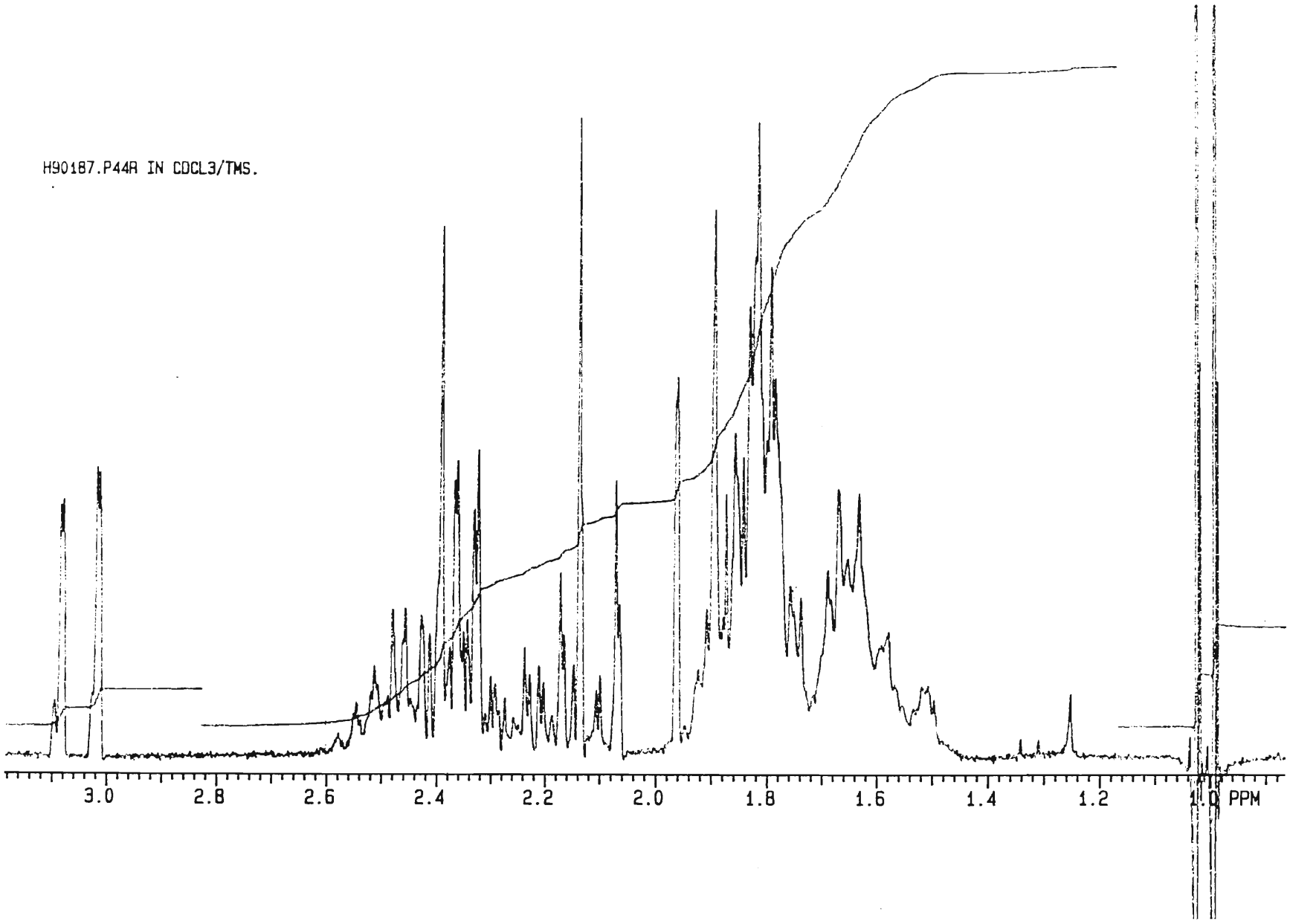
H90187.P44R IN CDCL3/TMS.



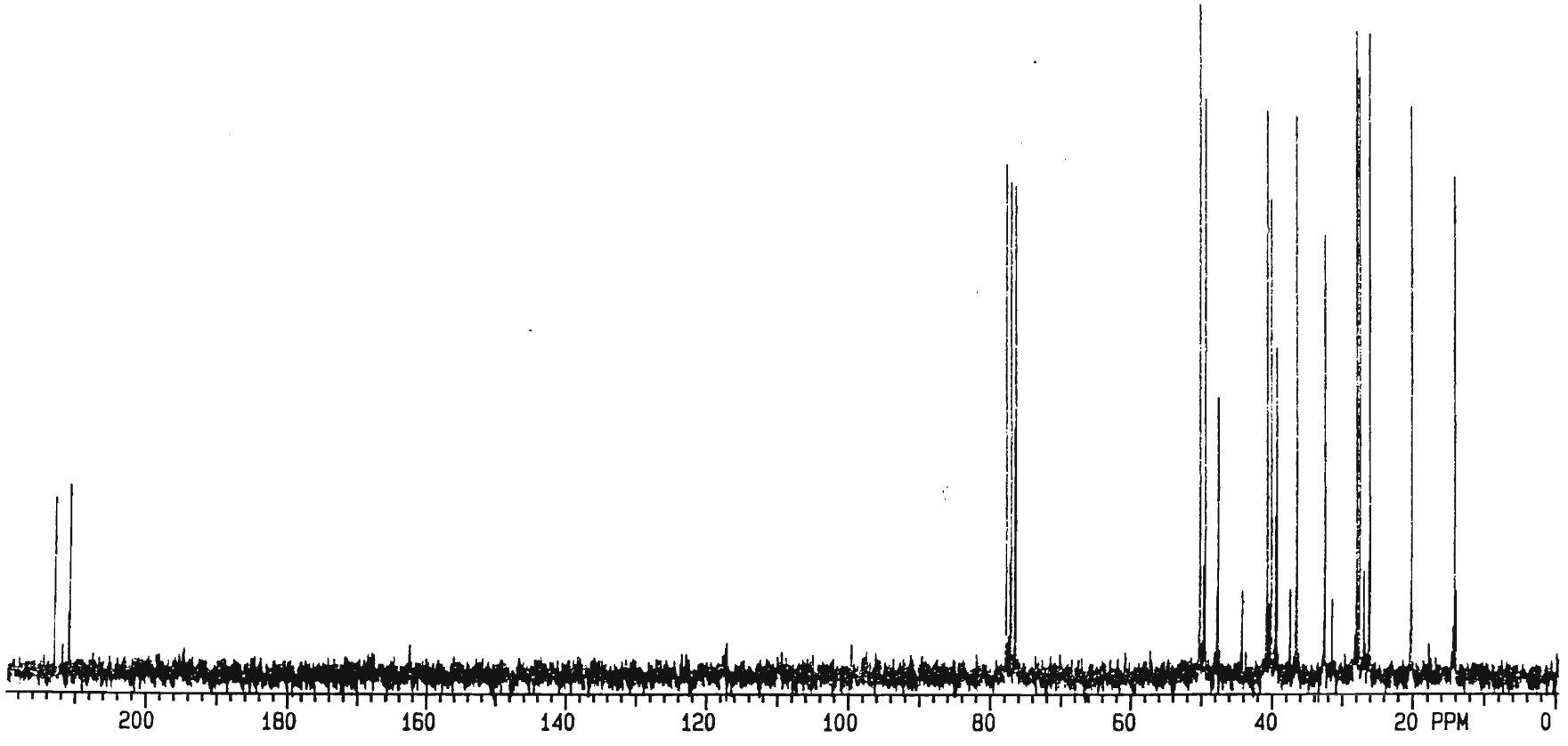
(75)

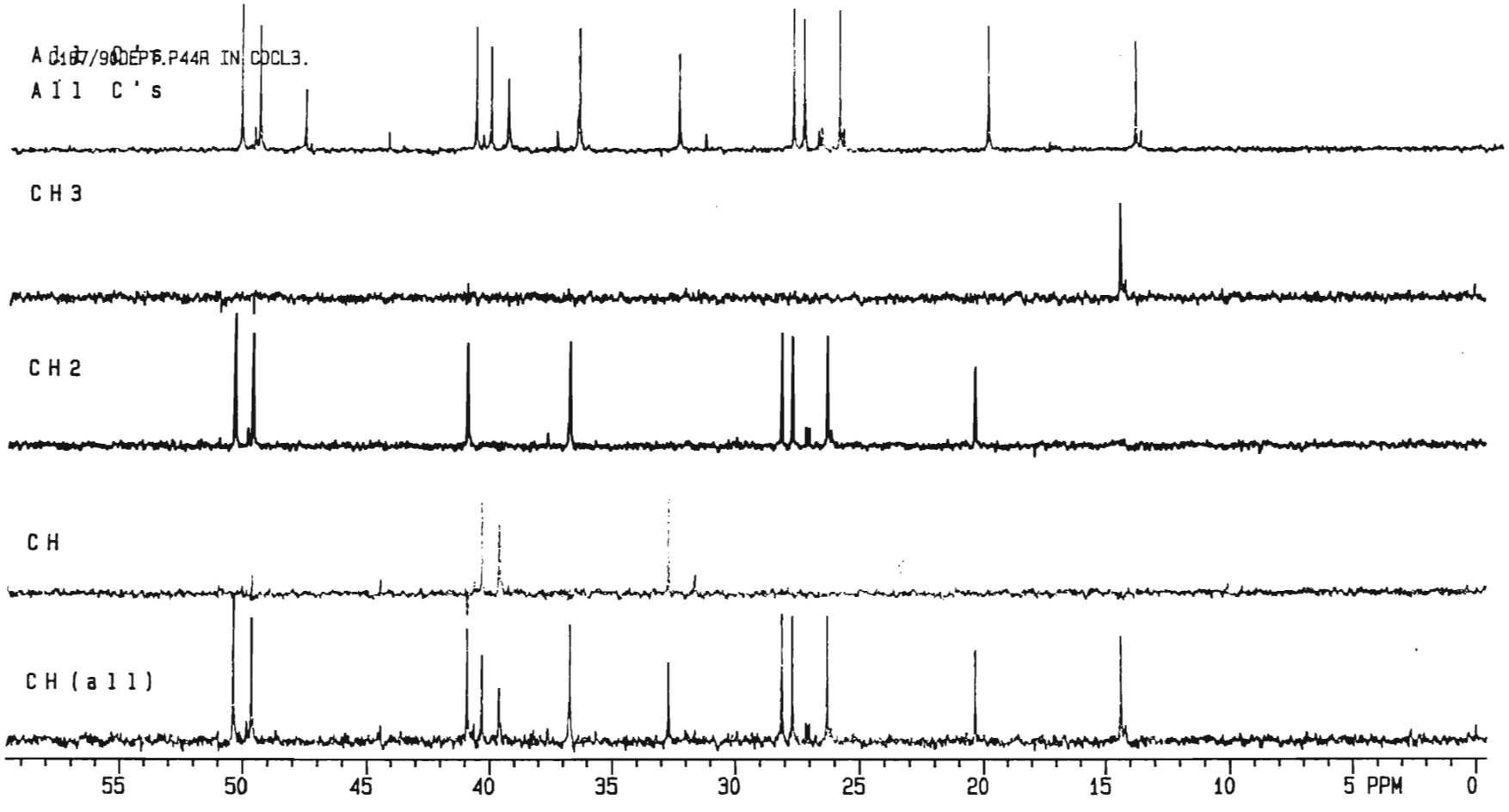
R,R' = H; R" = Me

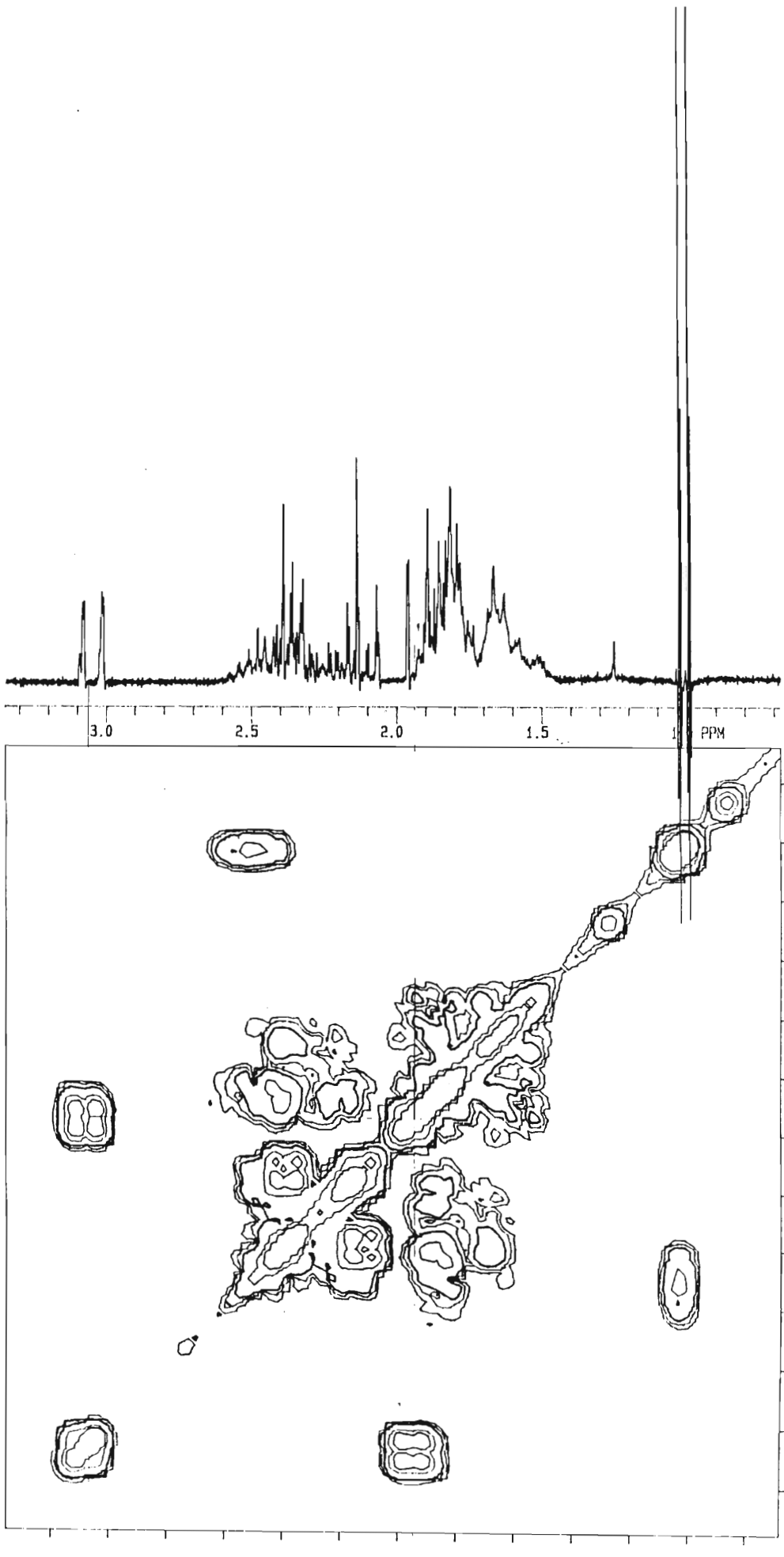

H36,89.P44R IN CDCL3/TMS.
3.0
2.5
2.0
1.5
1.0
0.5 PPM
0.0

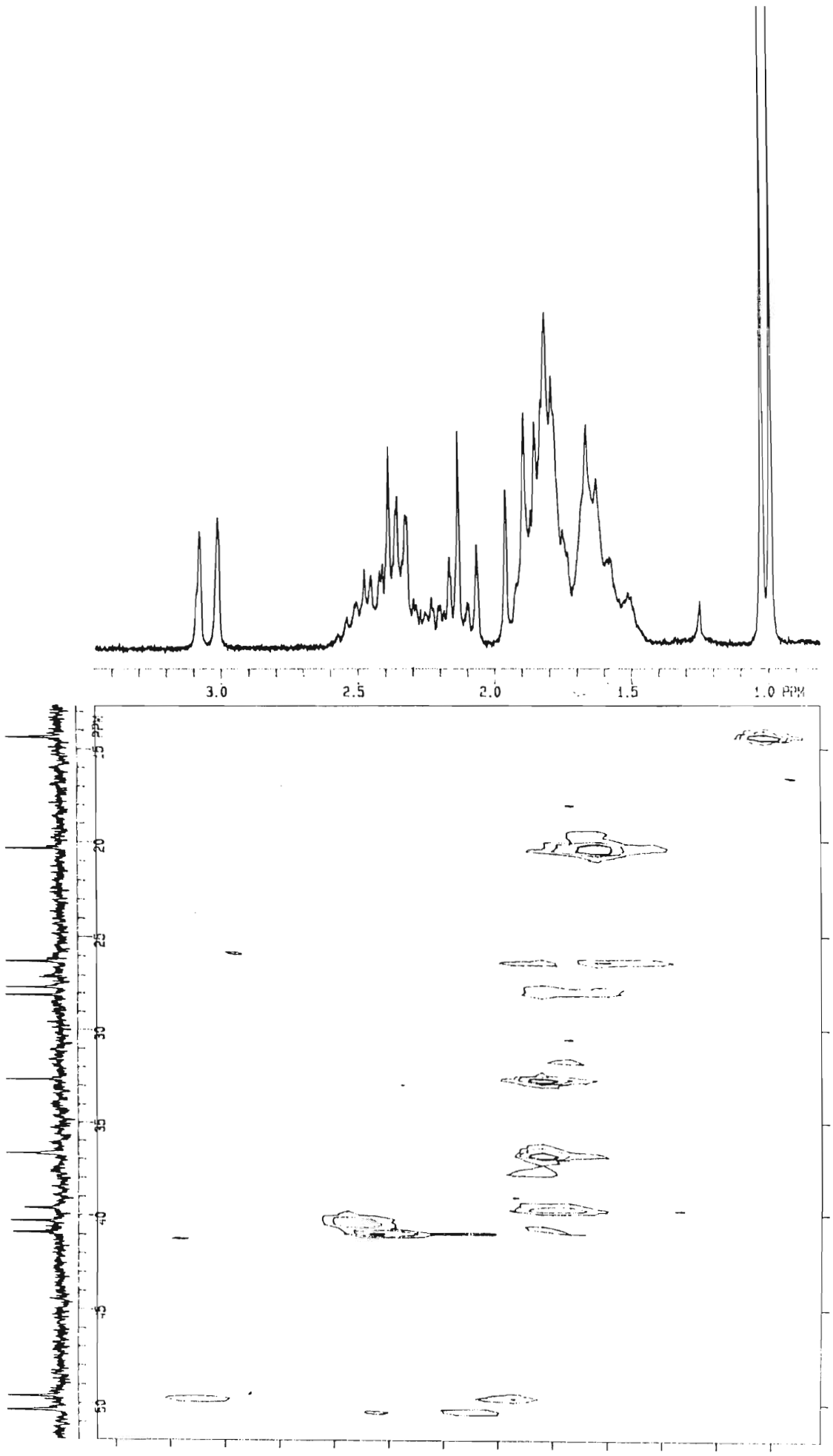

H90187.P44A IN CDCL3/TMS.
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM

C187/90PND.P44A IN CDCL3.

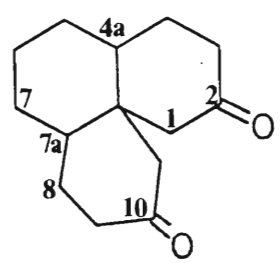



All C's
CH3
CH2
CH
CH(all)
55
50
45
40
35
30
25
20
15
10
5 PPM
0


3.0
2.5
2.0
1.5
PPM
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
F2 (PPM)
981435.P4#8 IN CDCL3
1H COSY-60


3.0
2.5
2.0
1.5
1.0 PPM
891125.P14R IN CDCL3
1H/13C METCOR

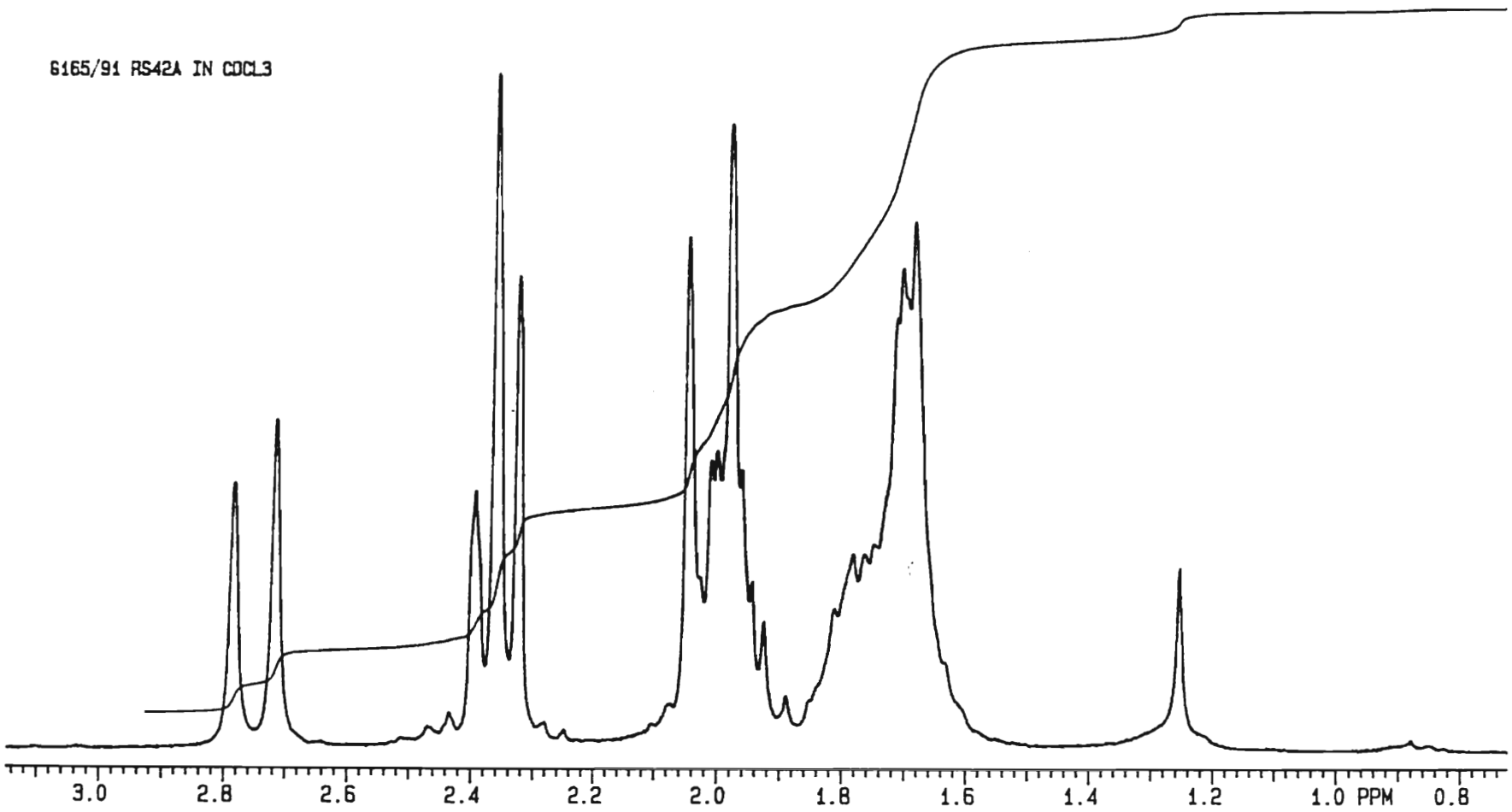
6165/91 RS42A IN CDCL3

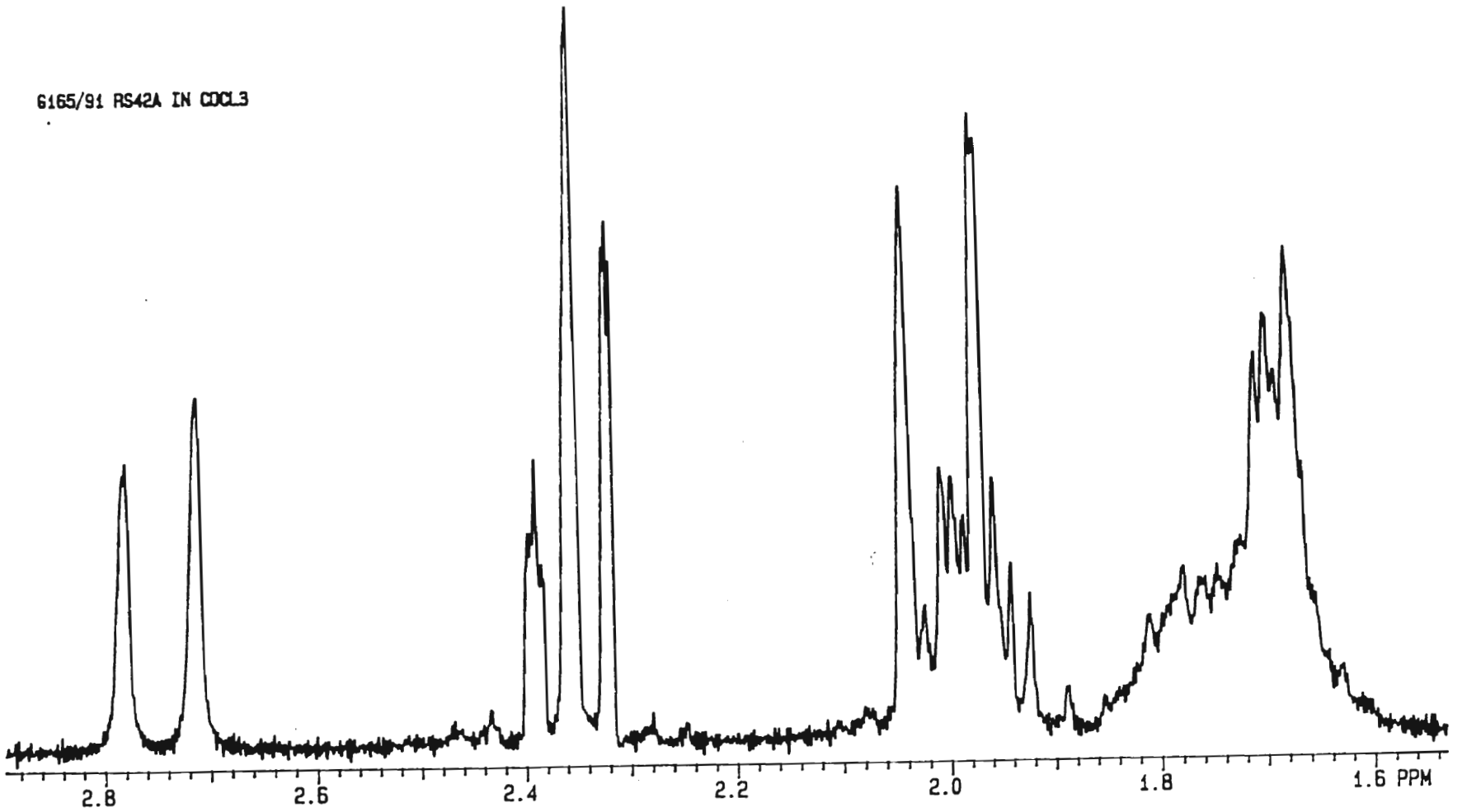


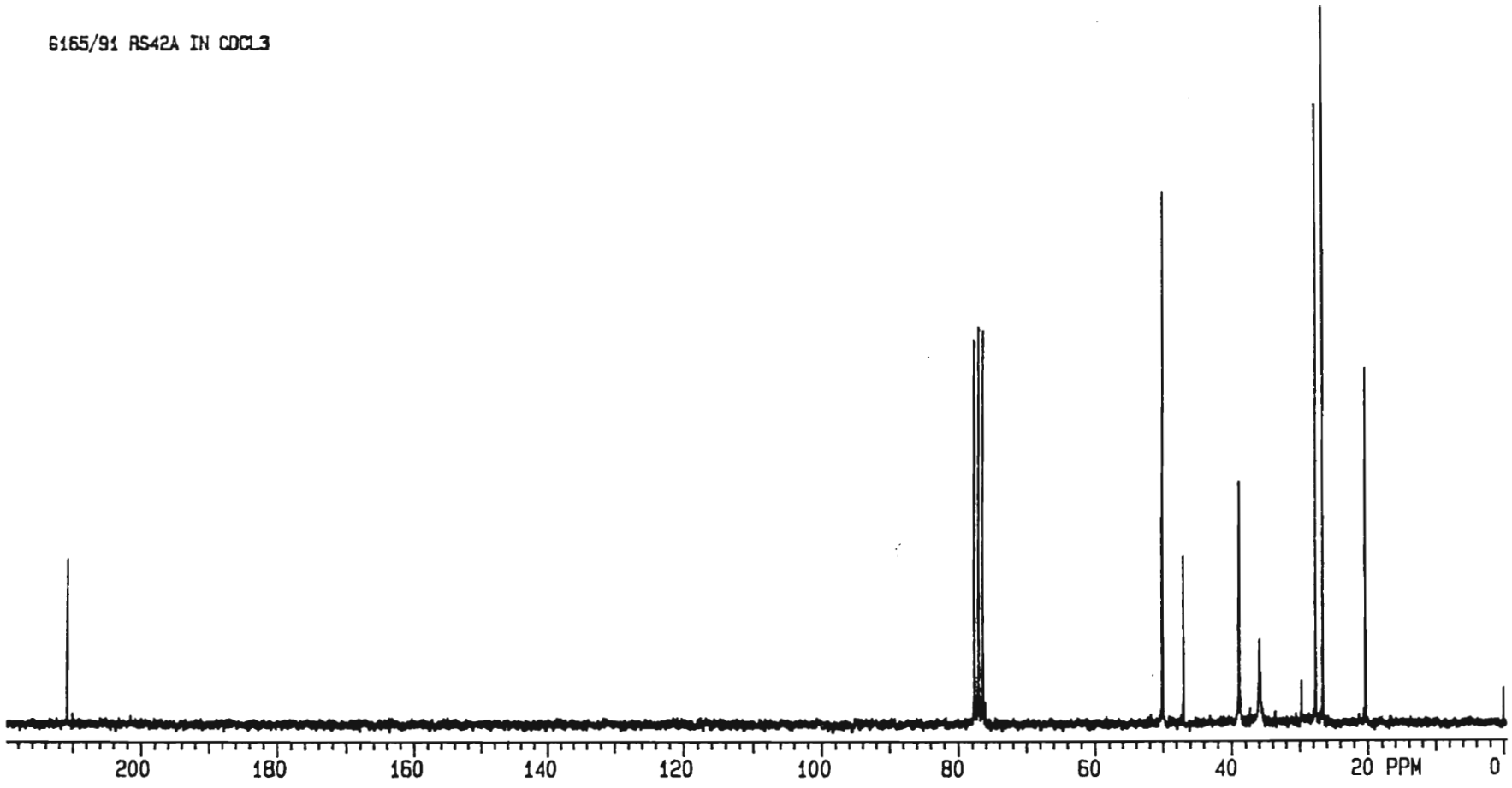
(75)

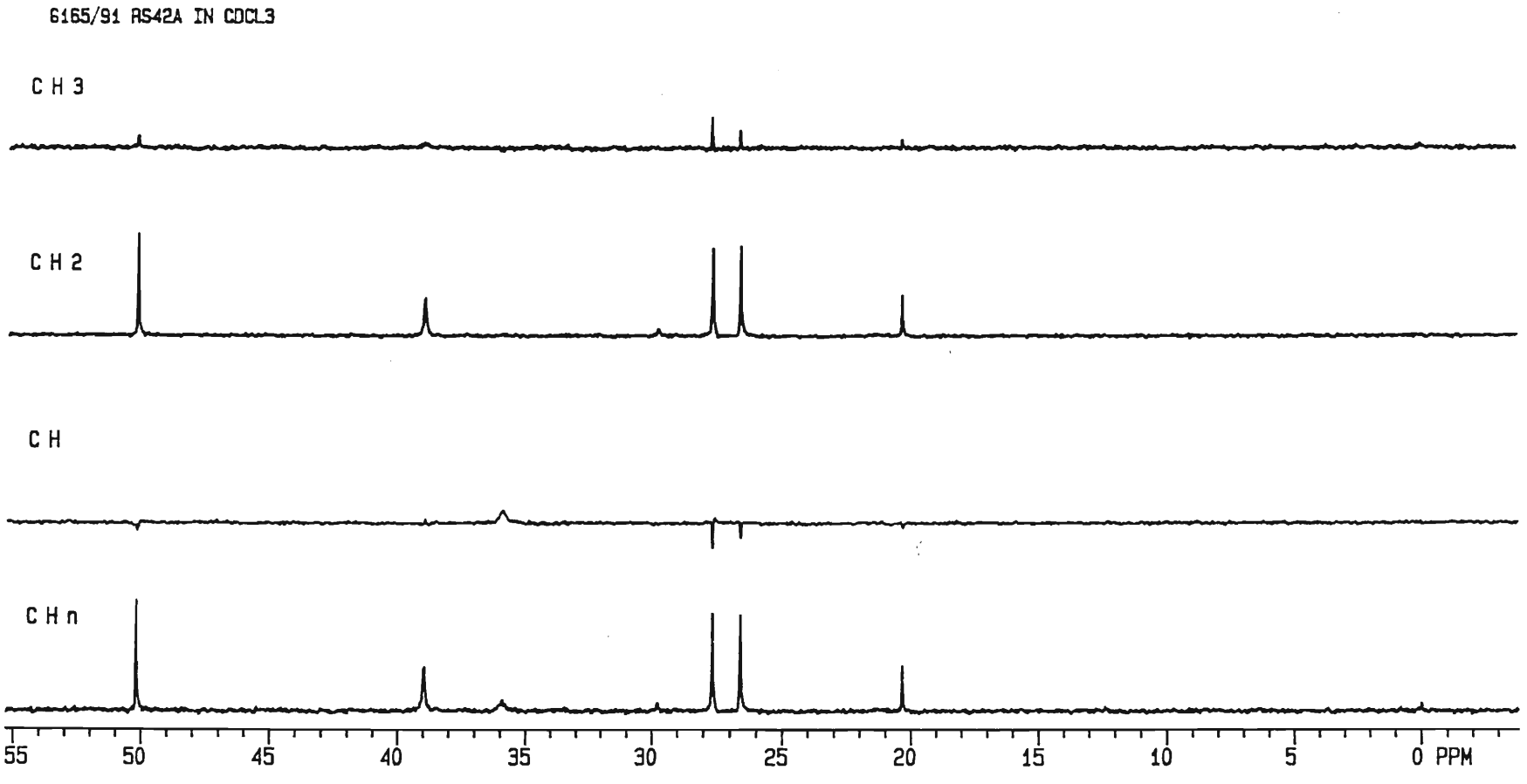
R,R',R" = H

MP 133-135°C

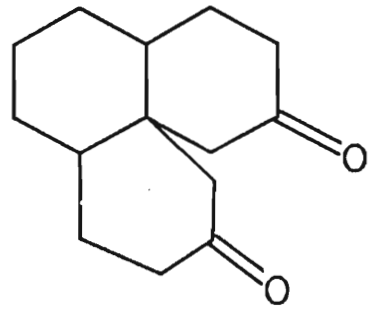

6165/91 RS42A IN CDCL3
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM
0.8


6165/91 RS42A IN CDCL3
2.8
2.6
2.4
2.2
2.0
1.8
1.6 PPM


6165/91 RS42A IN CDCL3
200
180
160
140
120
100
80
60
40
20 PPM
0


6165/91 RS42A IN CDCL3
C H 3
C H 2
C H
C H n
55
50
45
40
35
30
25
20
15
10
5
0 PPM

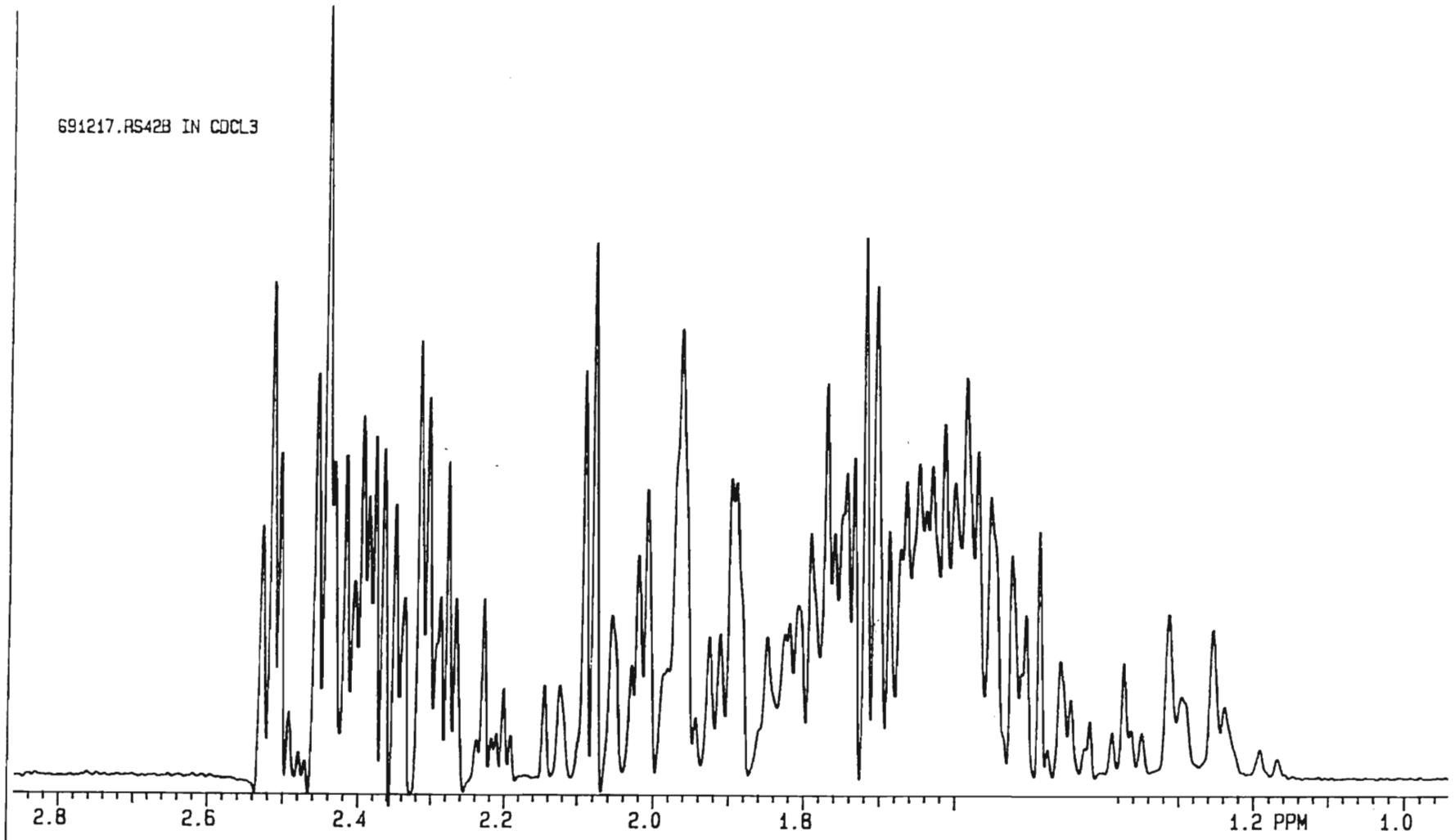
691217.RS42B IN CDCL3



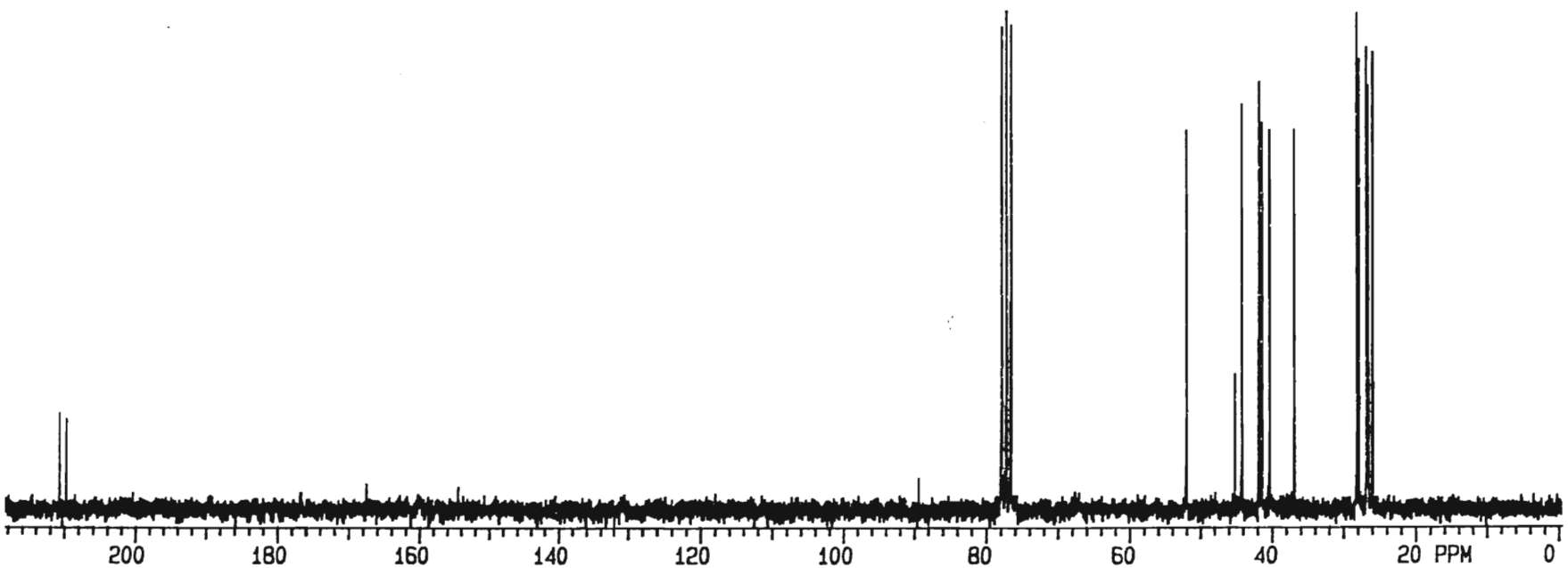
(75)

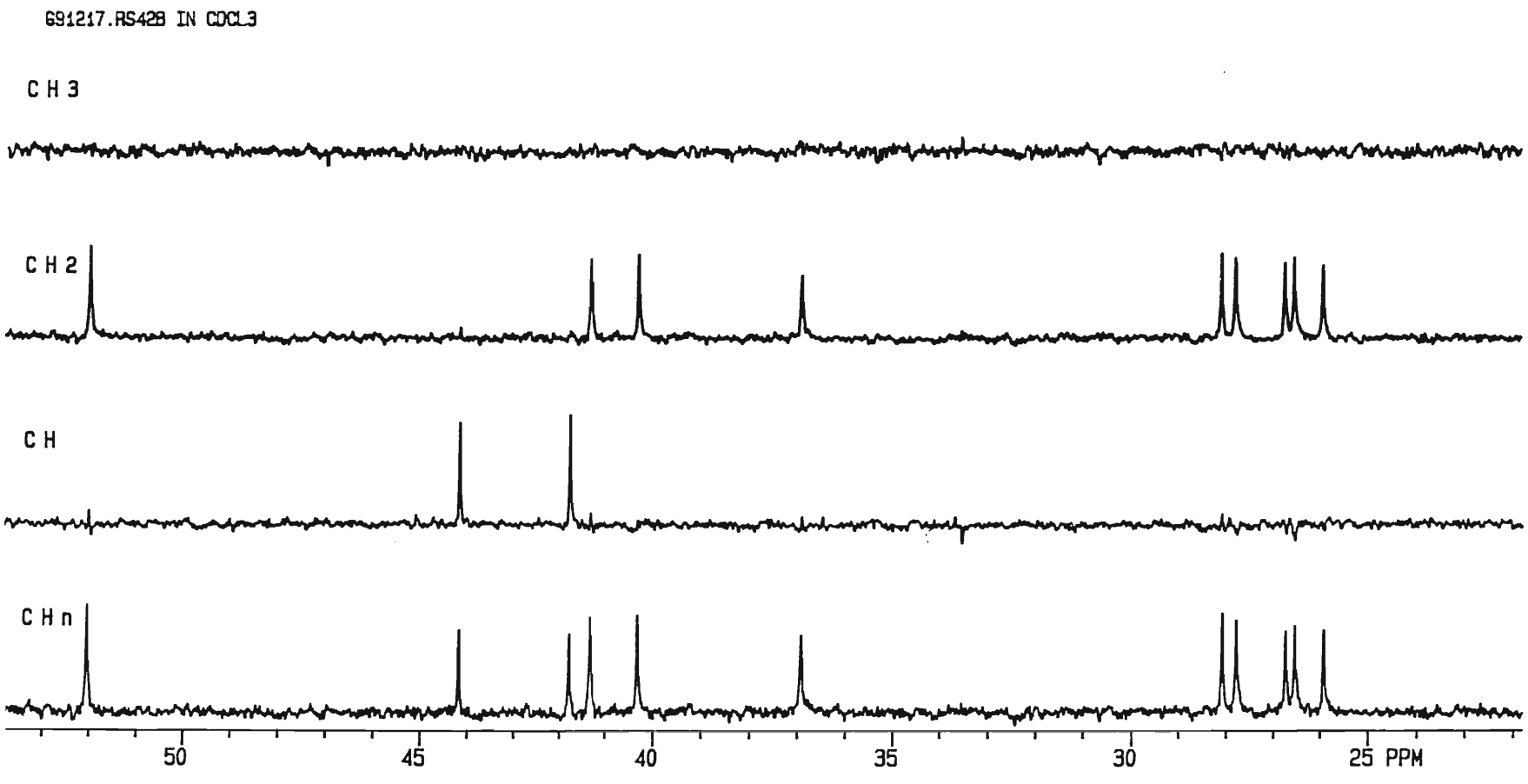
R,R',R" = H

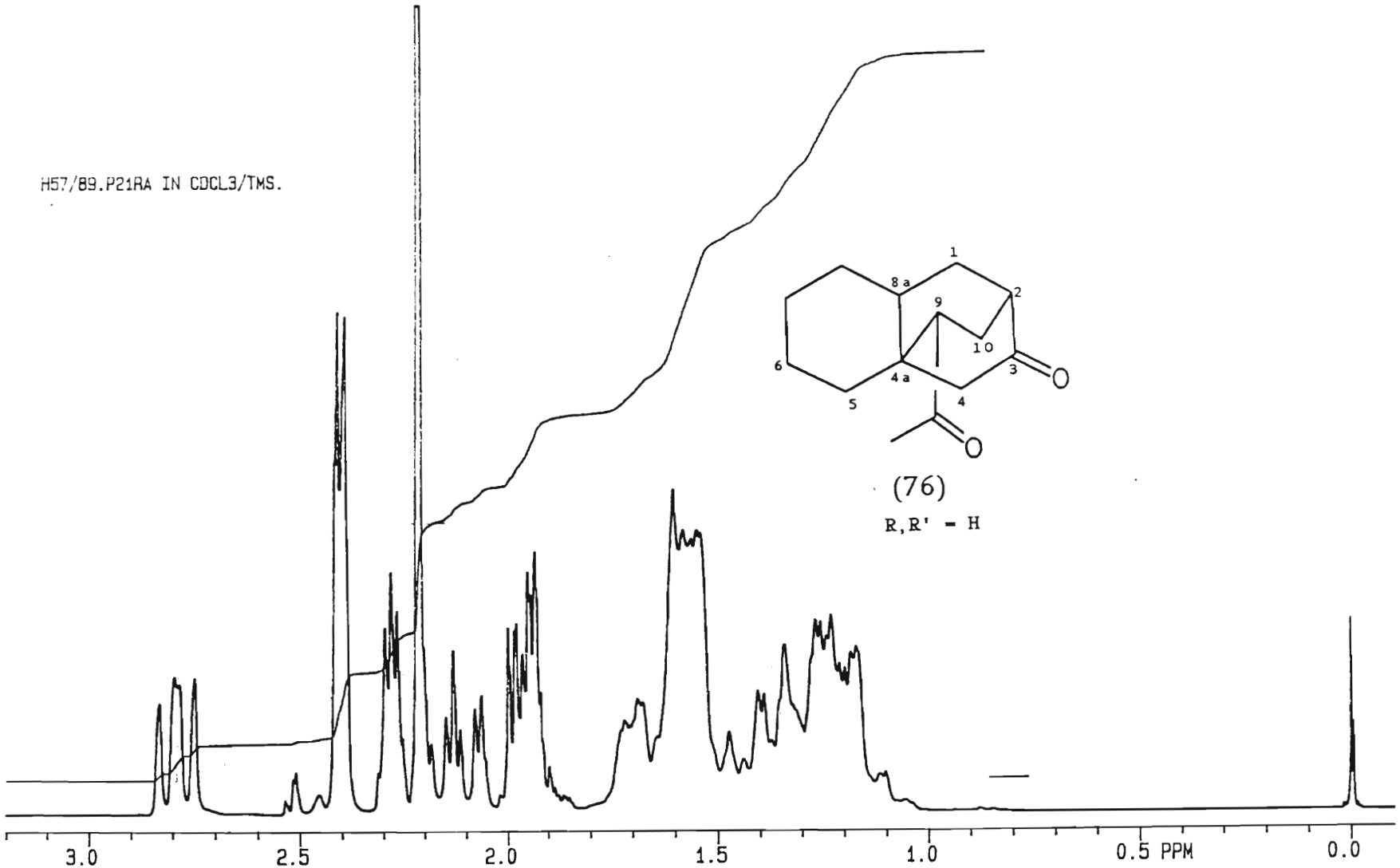
MP 164,9-165°C


691217.RS42B IN CDCL3
2.8
2.6
2.4
2.2
2.0
1.8
1.2 PPM
1.0

691217.RS42B IN CDCL3

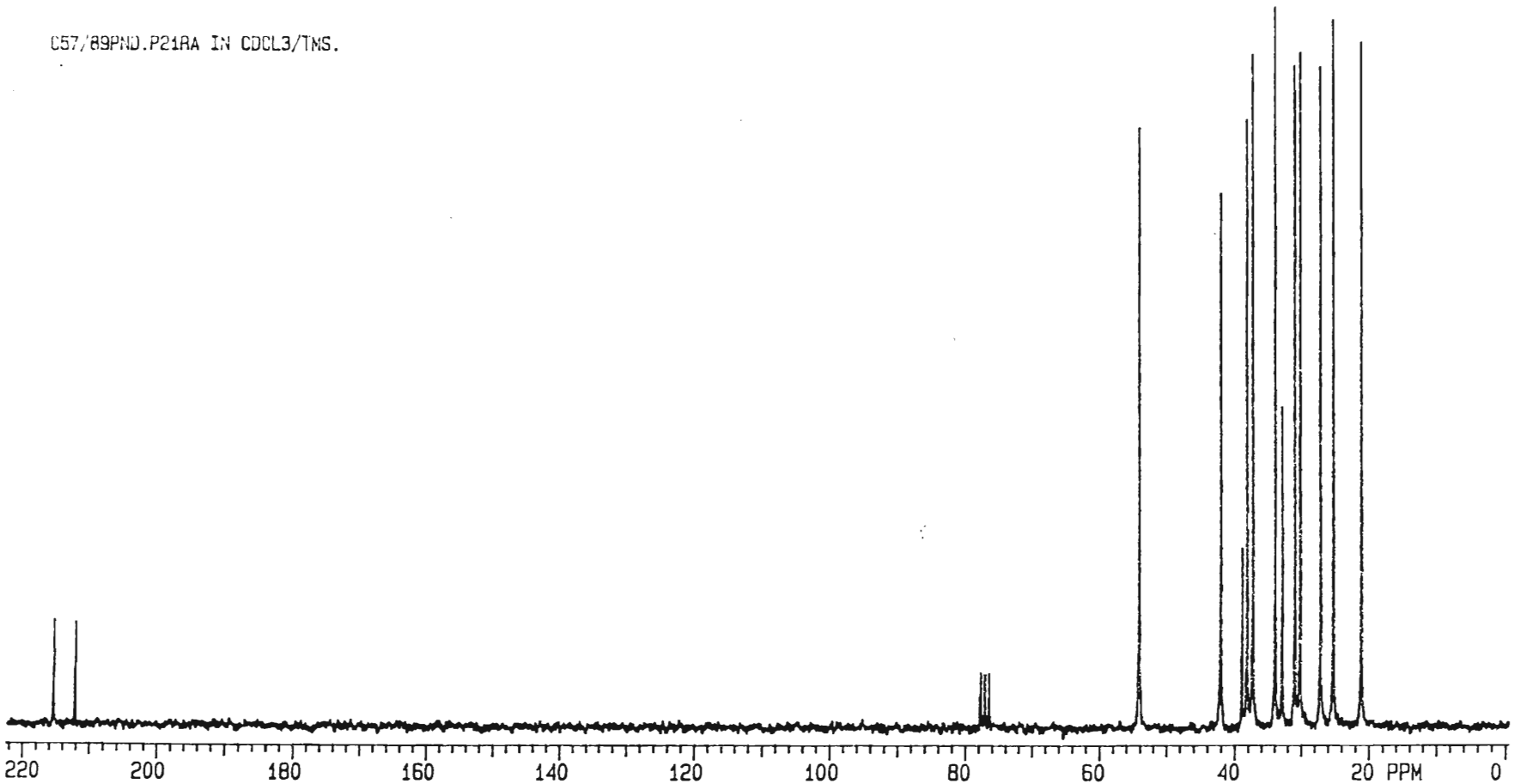


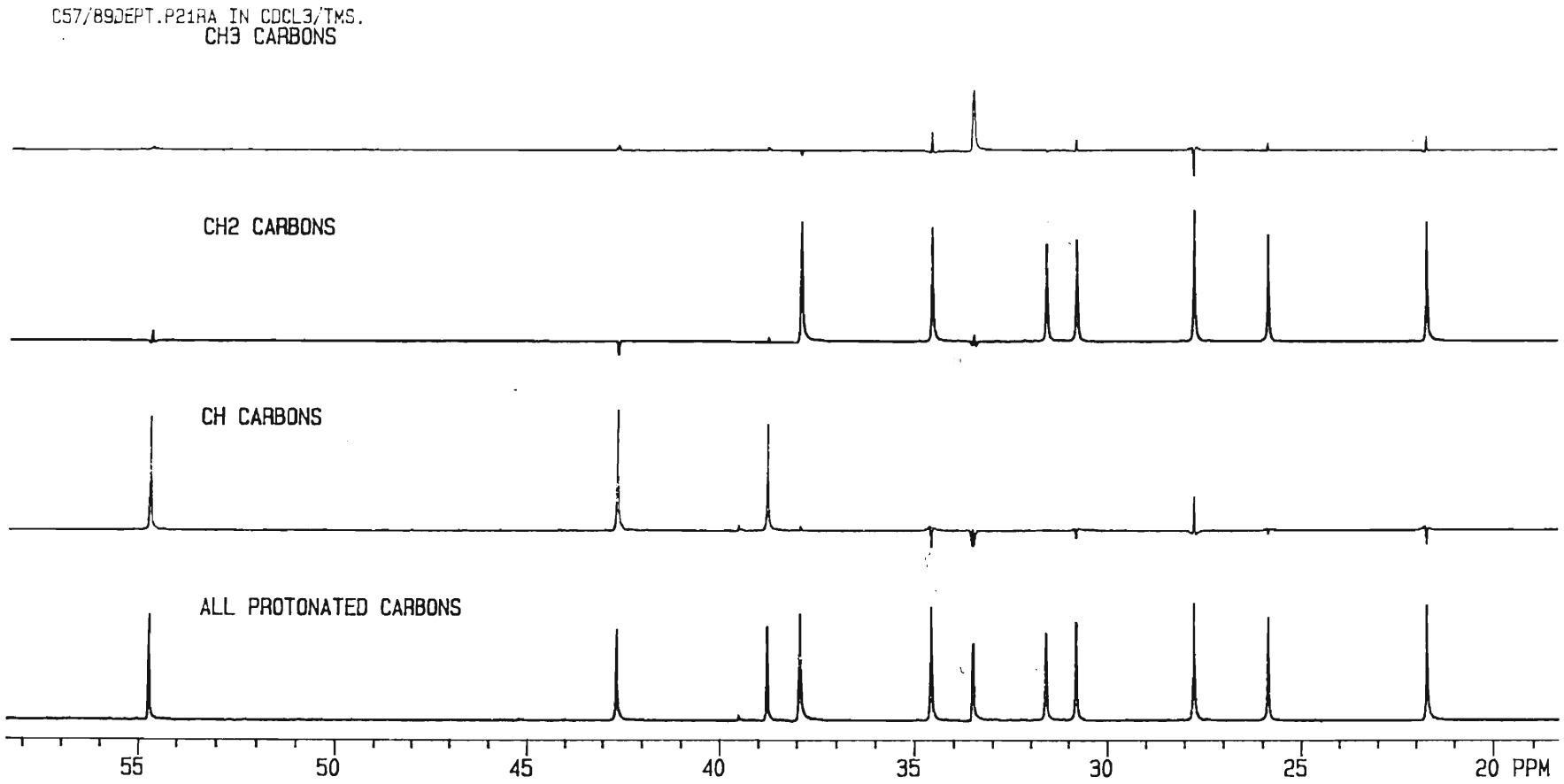

691217.RS428 IN CDCL3
CH3
CH2
CH
CHn
50
45
40
35
30
25 PPM

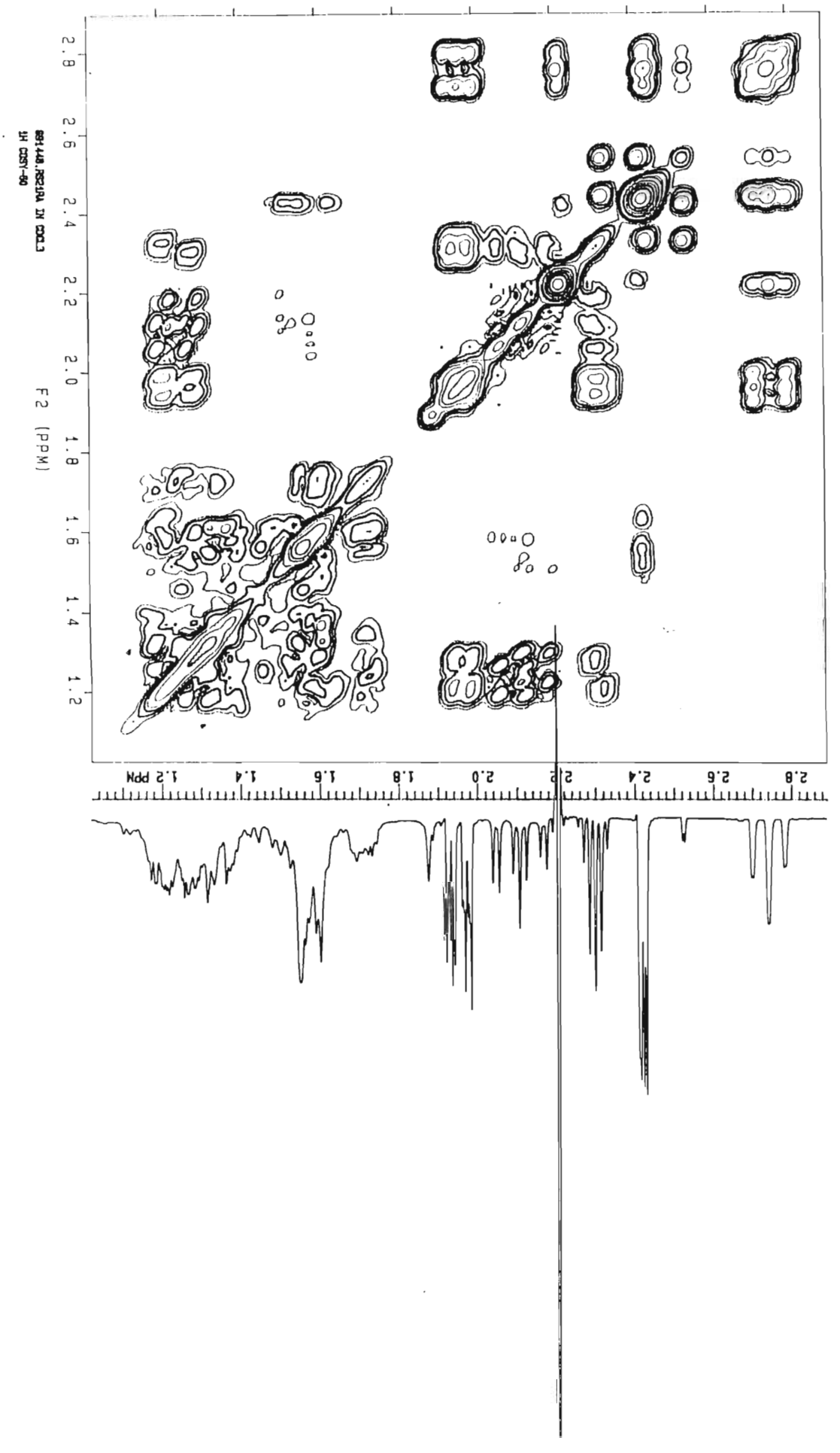

H57/89.P21RA IN CDCL3/TMS.
1
8a
2
9
10
6
4a
3
O
5
4
O
3.0
2.5
2.0
1.5
1.0
0.5 PPM
0.0

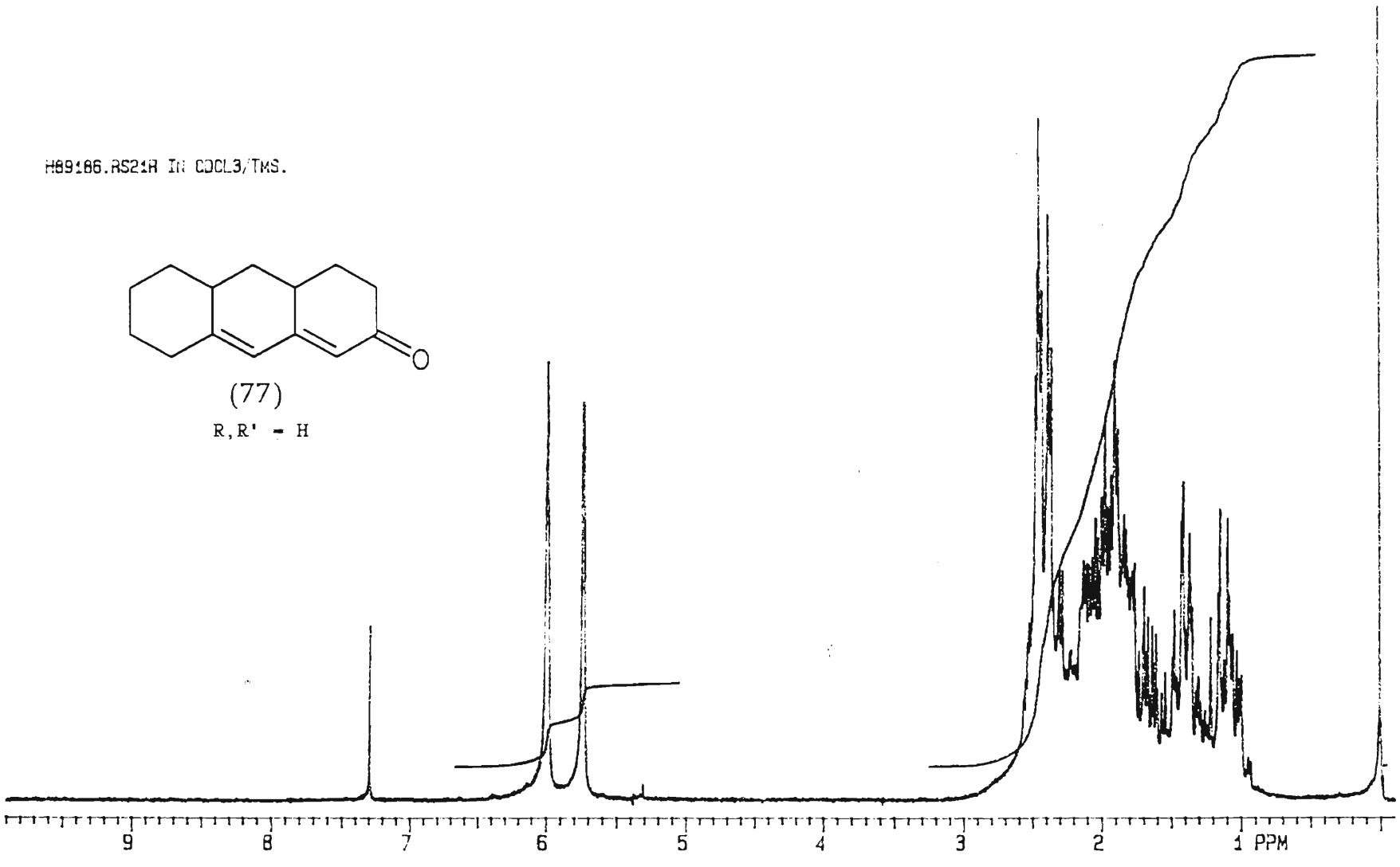
(76)

R,R' = H


C57/89PND.P21RA IN CDCL3/TMS.
220
200
180
160
140
120
100
80
60
40
20 PPM
0

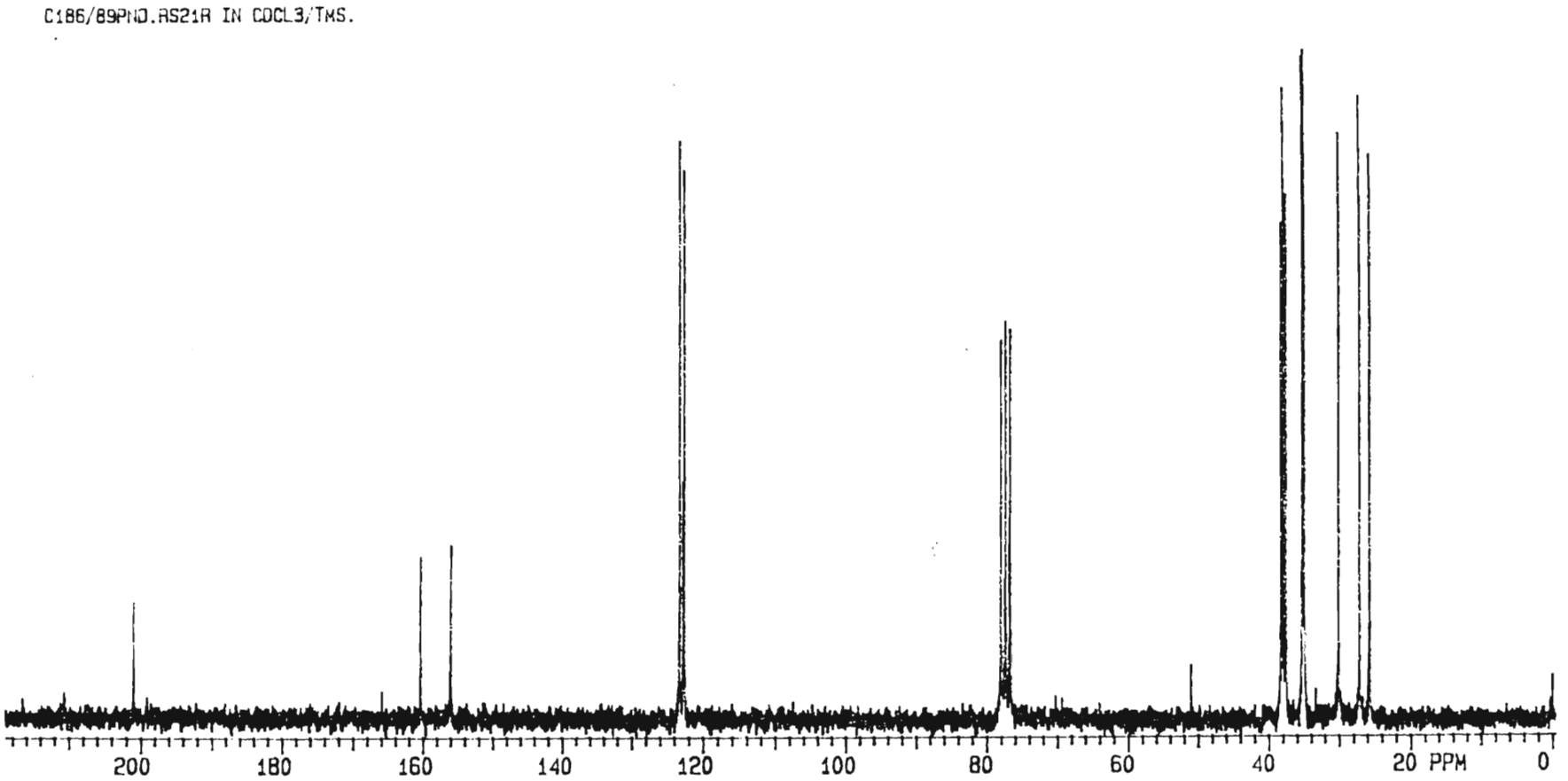

C57/89DEPT.P21RA IN CDCL3/TMS.
CH3 CARBONS
CH2 CARBONS
CH CARBONS
ALL PROTONATED CARBONS
55
50
45
40
35
30
25
20 PPM

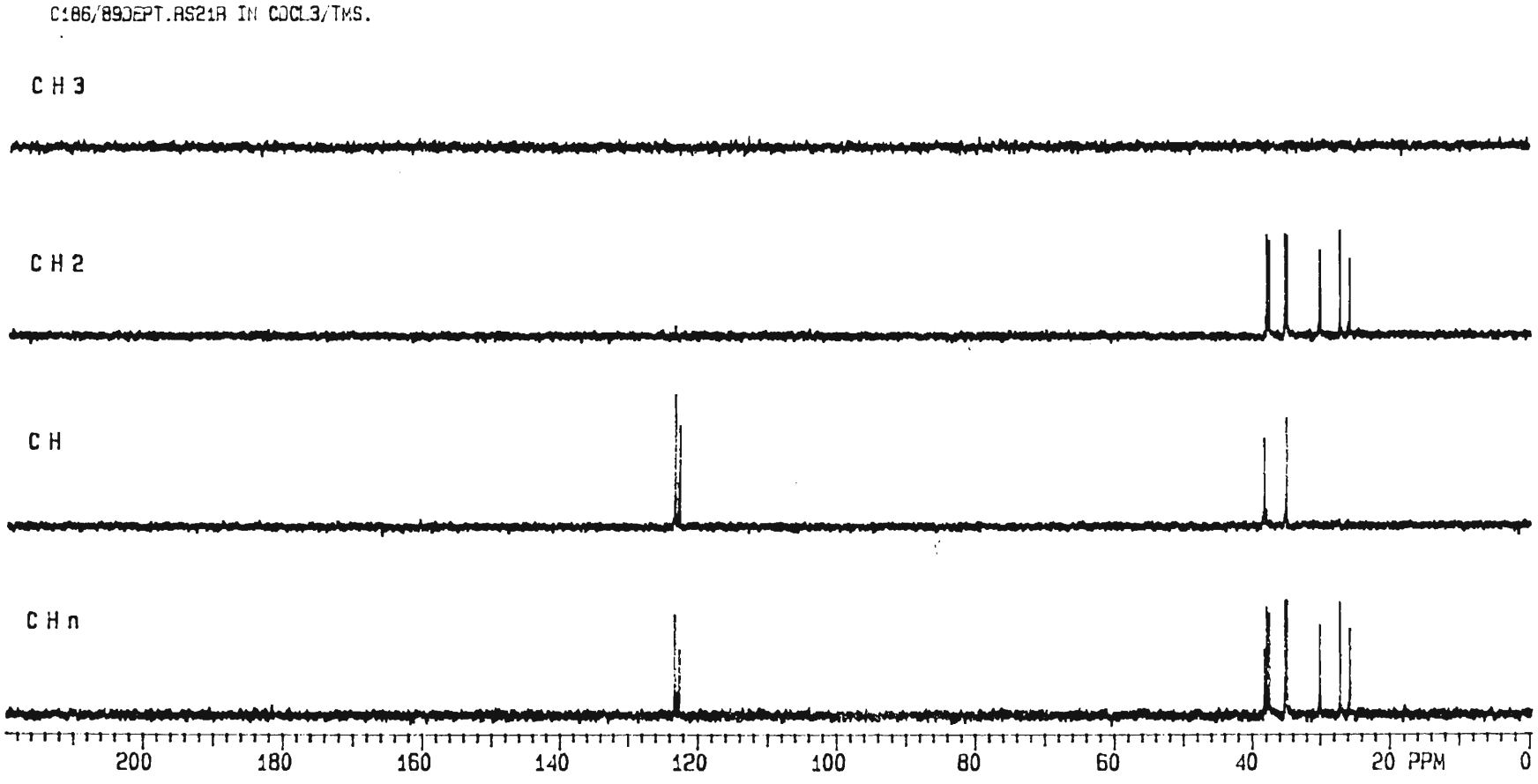

881448.RS2DA IN CDCL3
1H COSY-90
F2 (PPM)
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.2 PPM

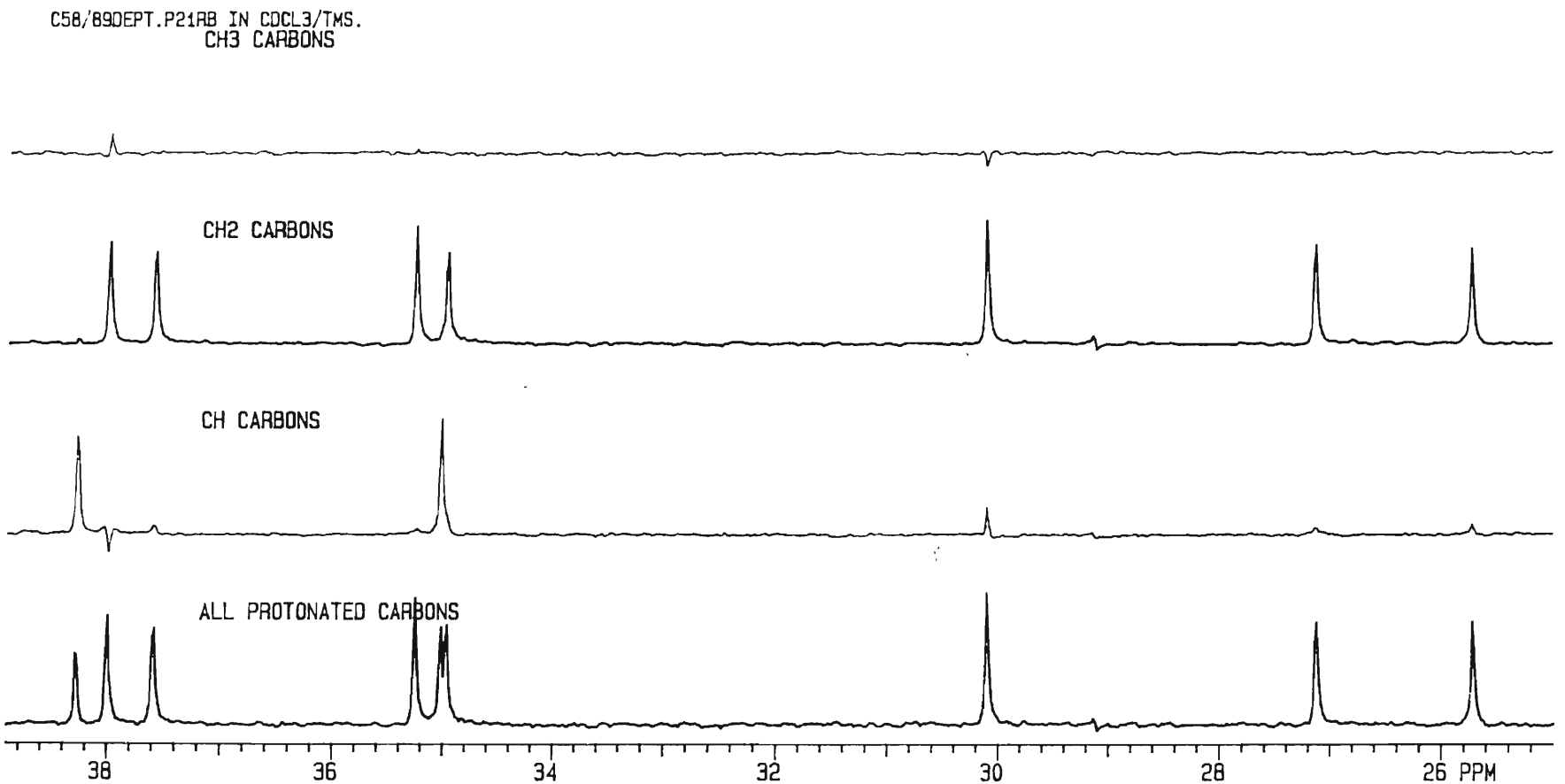


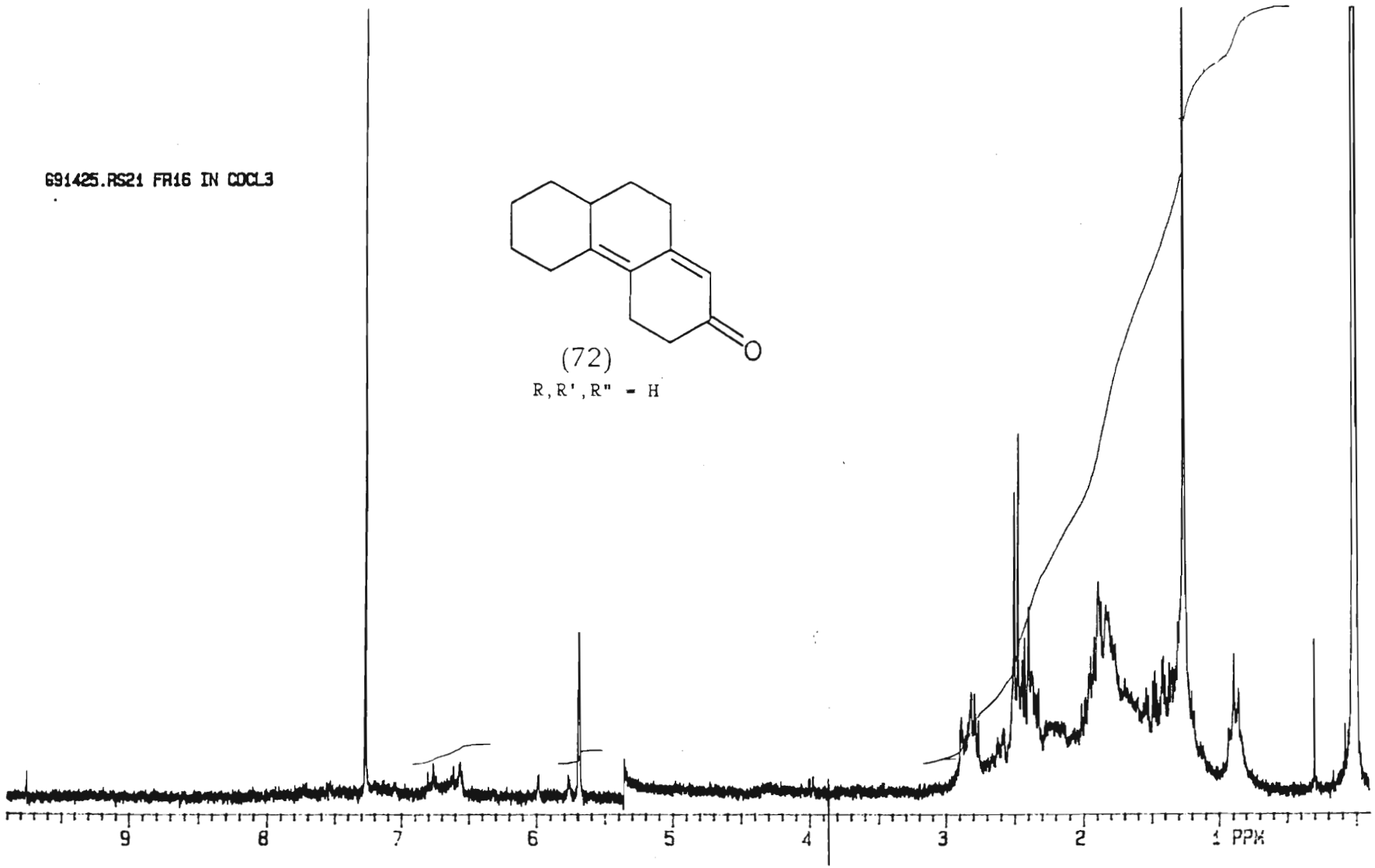
(77)

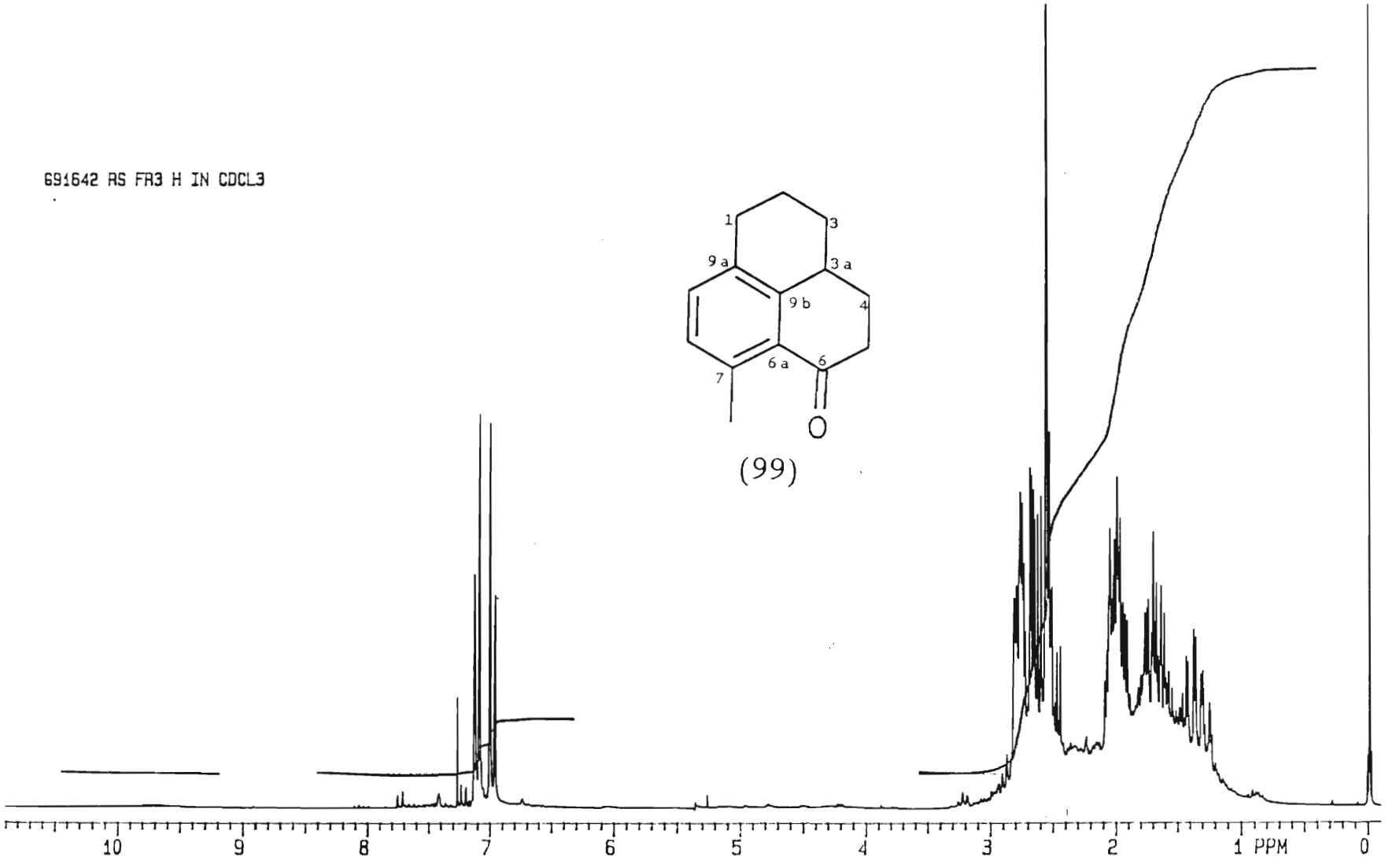
R,R' = H


C186/89PND.RS21R IN CDCL3/TMS.
200
180
160
140
120
100
80
60
40
20 PPM
0

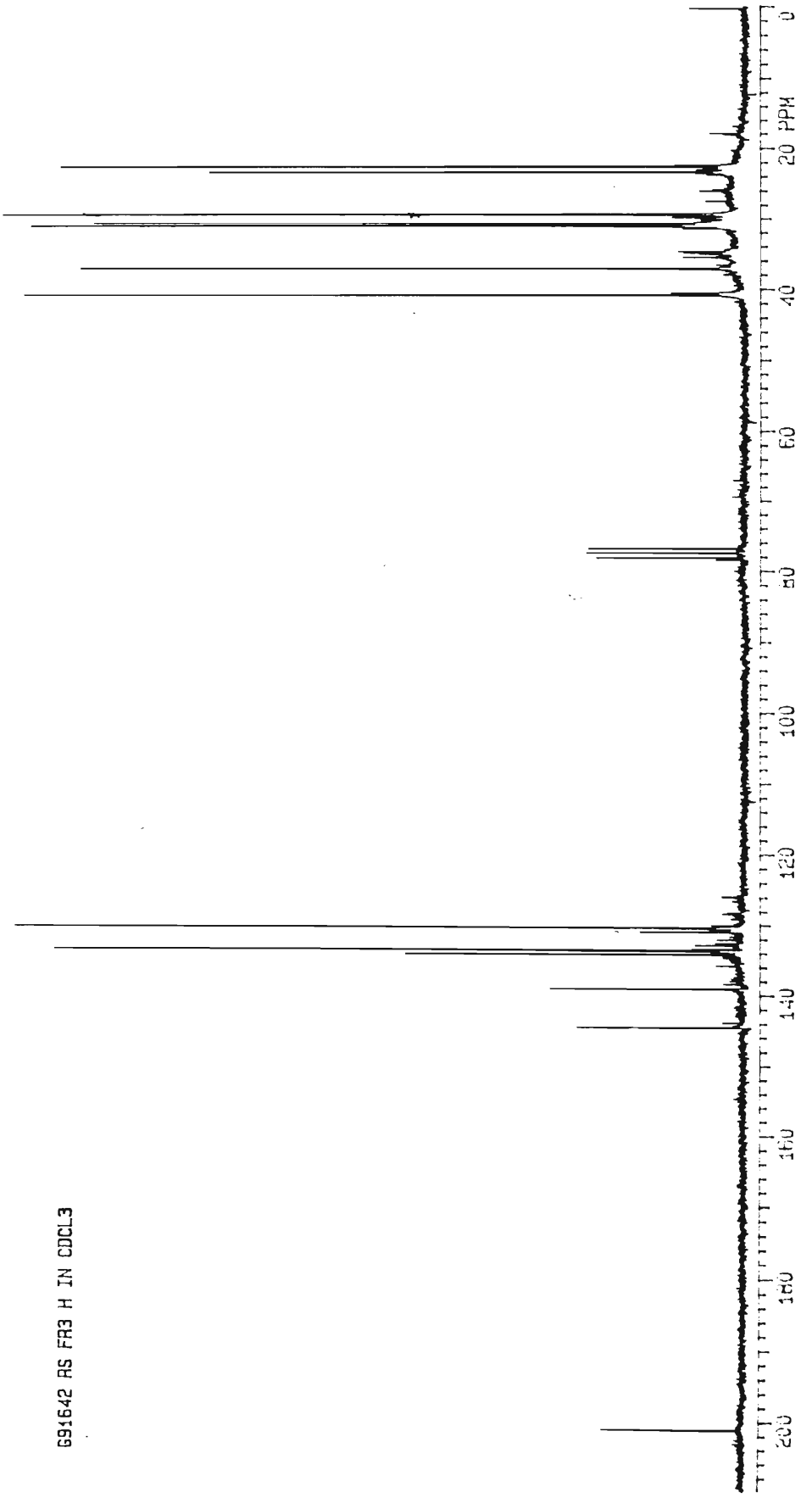

C186/89DEPT.AS21A IN CDCL3/TMS.
C H 3
C H 2
C H
C H n
200
180
160
140
120
100
80
60
40
20 PPM
0

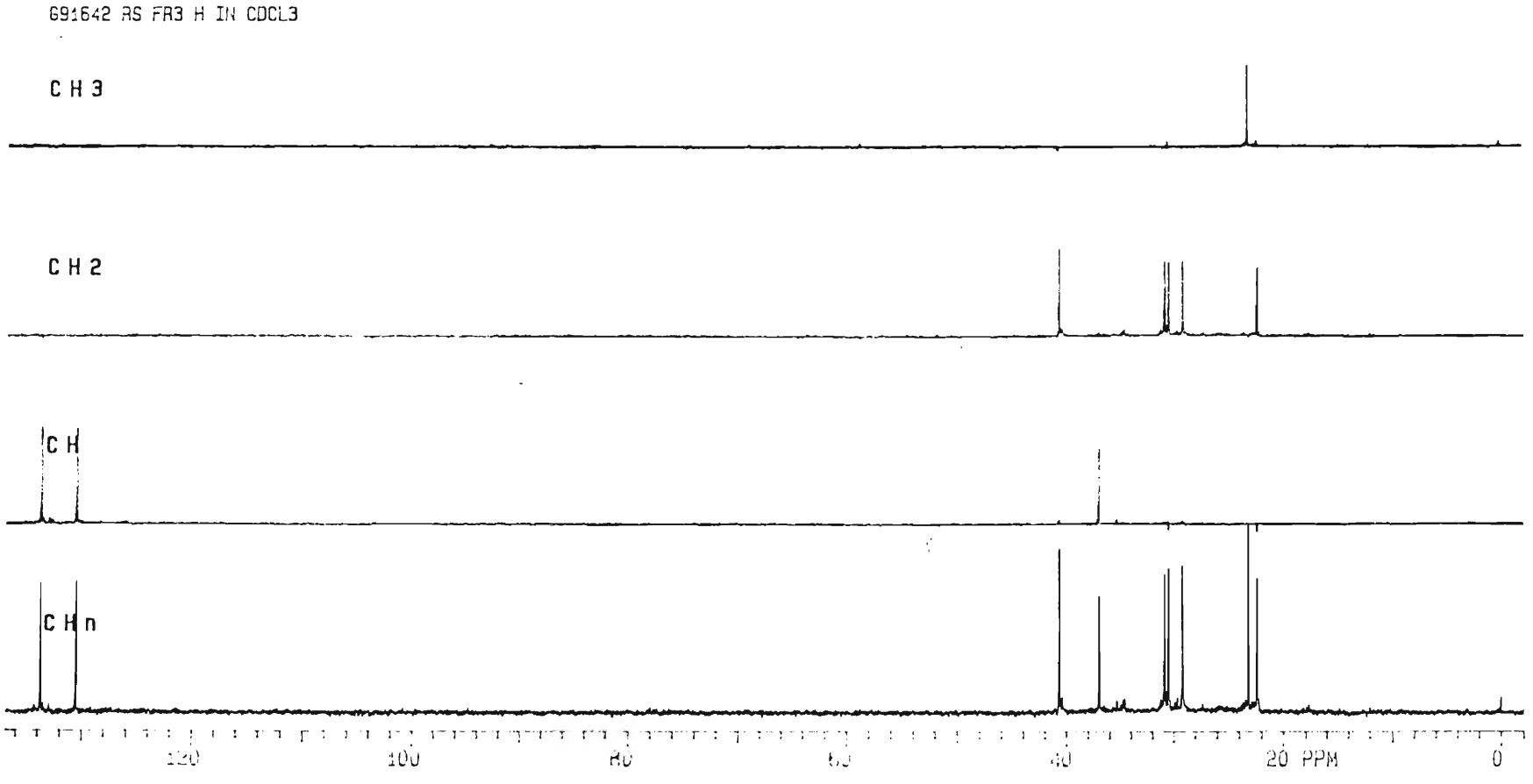

C58/89DEPT.P21RB IN CDCL3/TMS.
CH3 CARBONS
CH2 CARBONS
CH CARBONS
ALL PROTONATED CARBONS
38
36
34
32
30
28
26 PPM

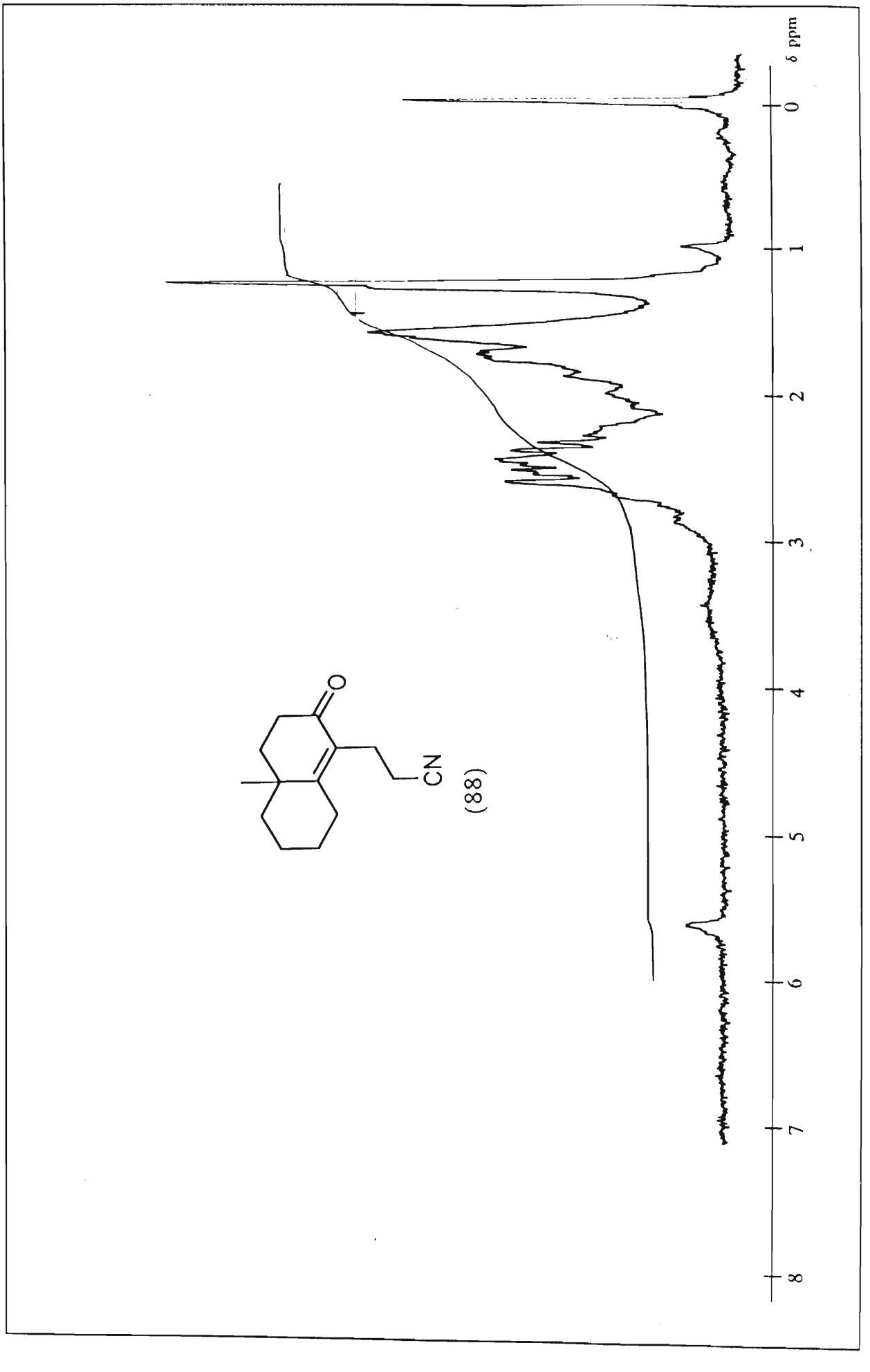

691425.RS21 FR16 IN CDCL3
O
(72)
R,R',R" = H
9
8
7
6
5
4
3
2
1 PPM



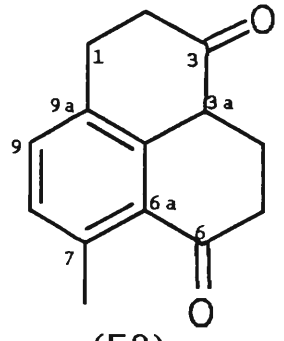
(99)


G91642 RS FR3 H IN CDCL3
200
180
160
140
120
100
80
60
40
20 PPM
0

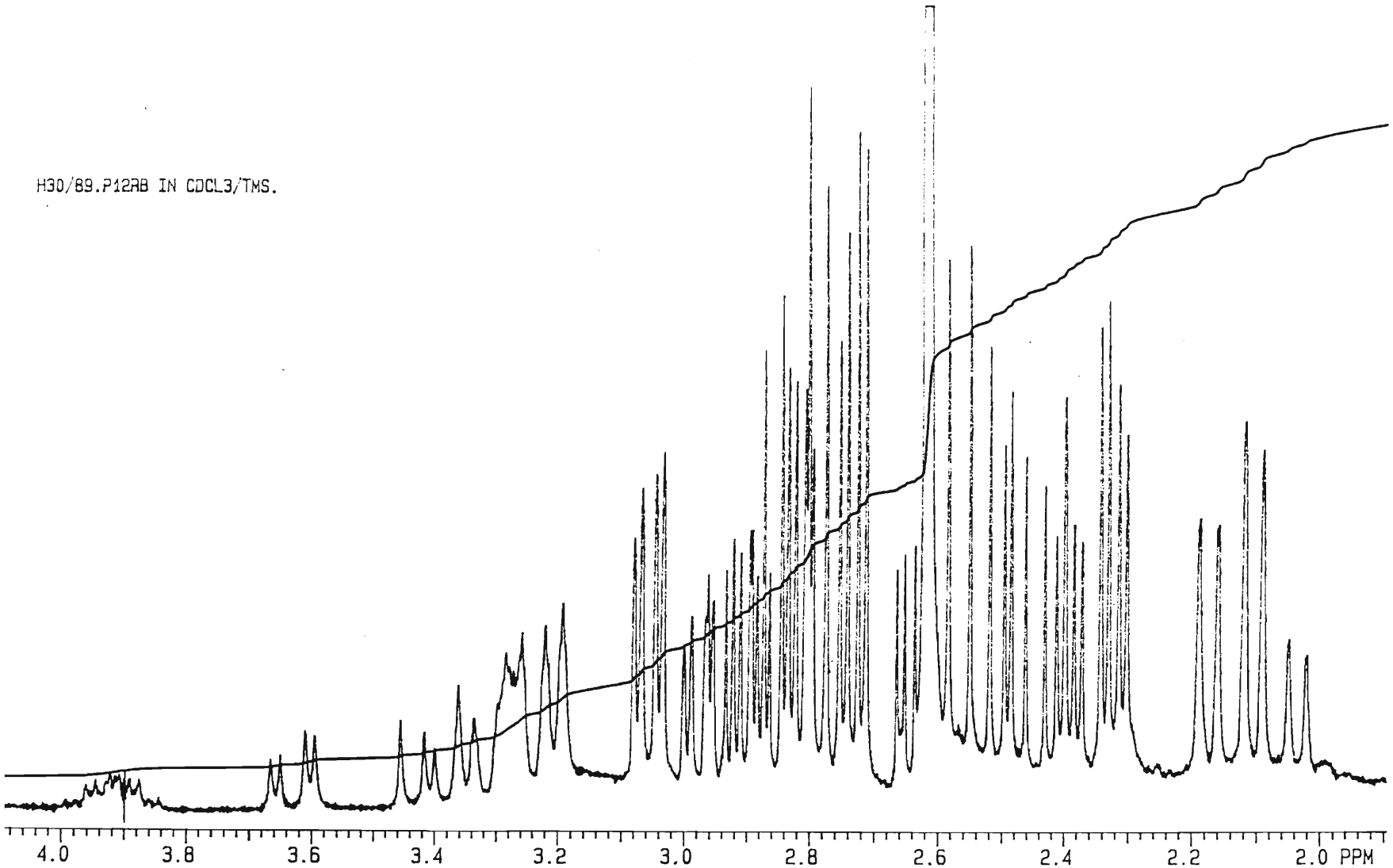

691642 AS FR3 H IN CDCL3
CH3
CH2
CH
CHn
120
100
80
60
40
20 PPM
0


O
CN
(88)
δ ppm
0
1
2
3
4
5
6
7
8

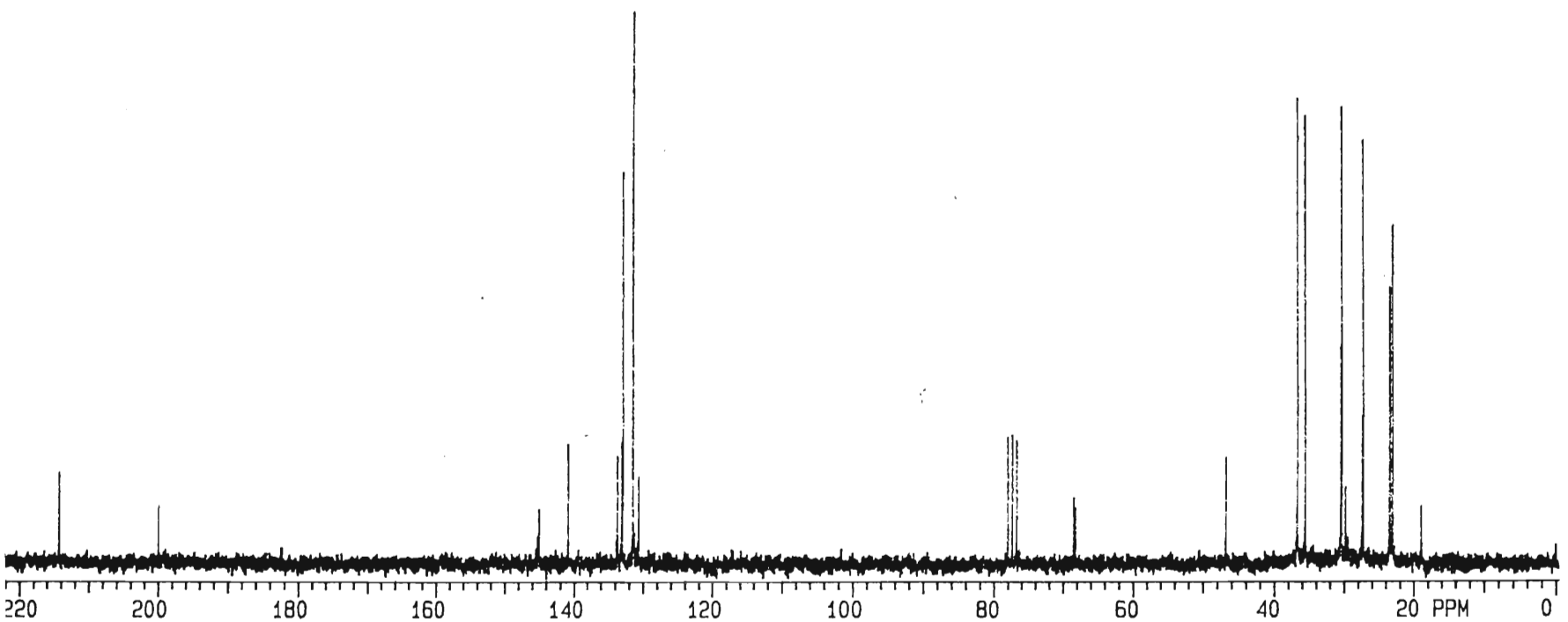
H30/89.P12RB IN CDCL3/TMS.

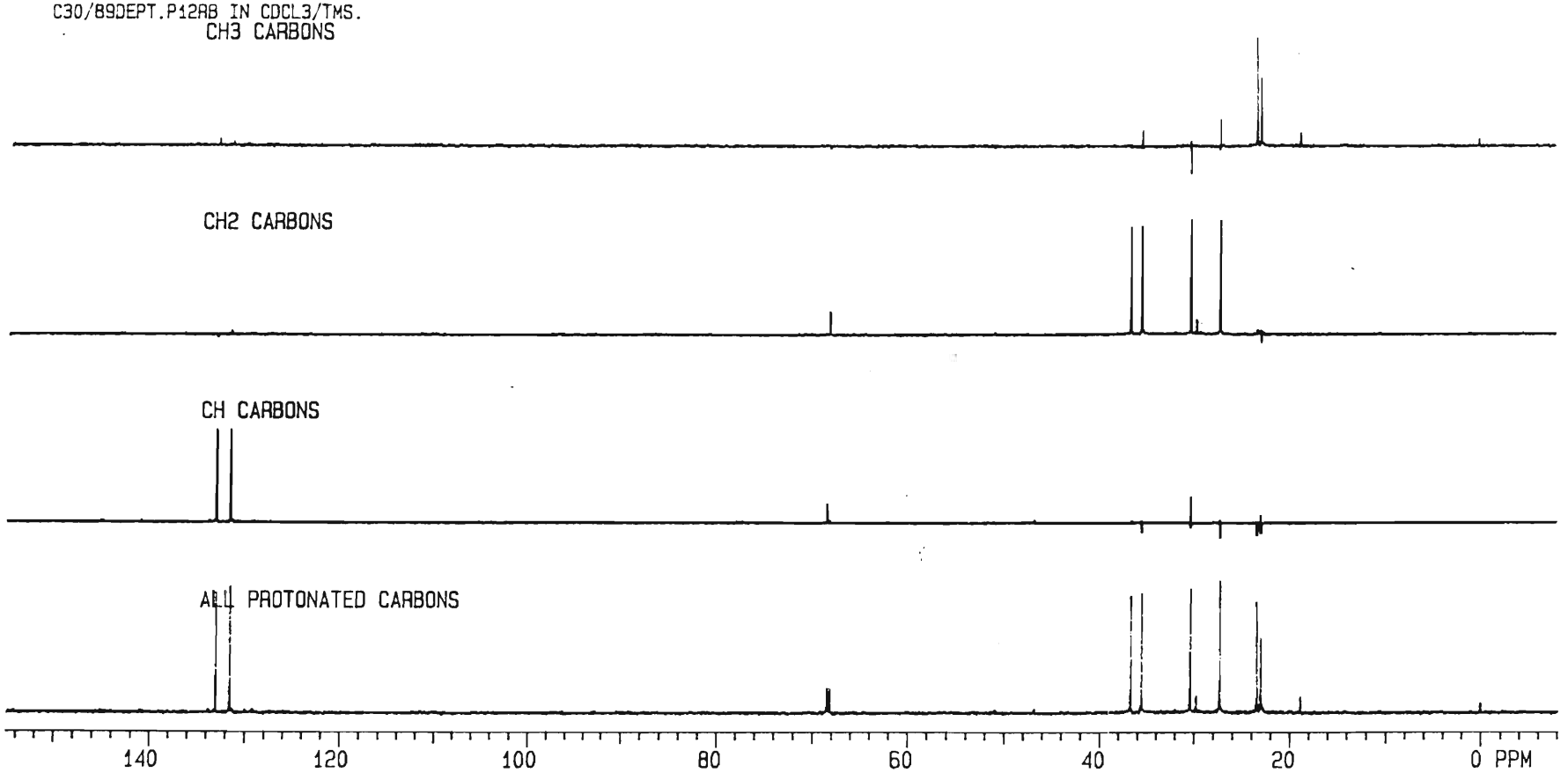


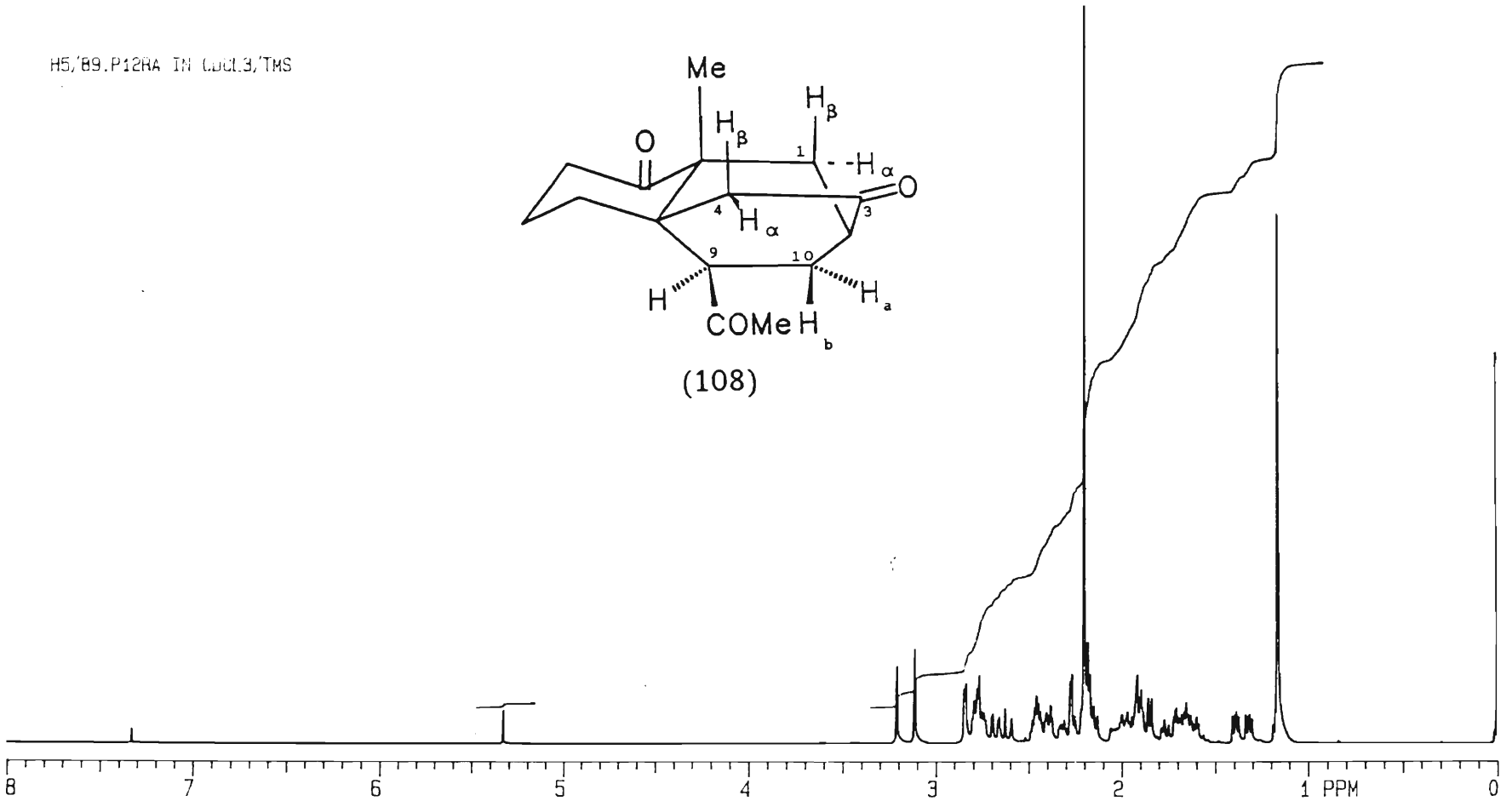
(58)


H30/89.P12RB IN CDCL3/TMS.
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0 PPM

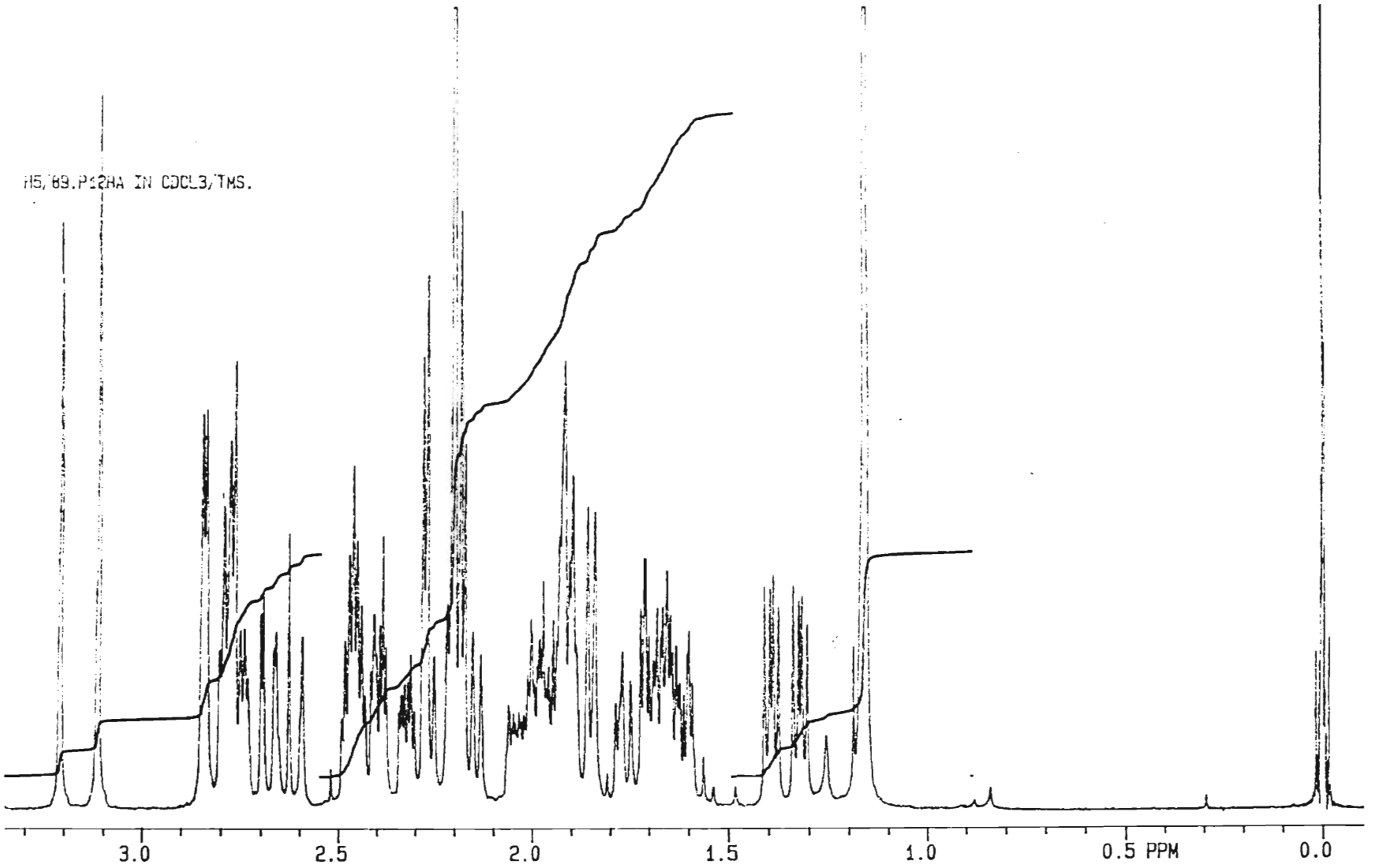
C30/89.P12RB IN CDCL3/TMS.

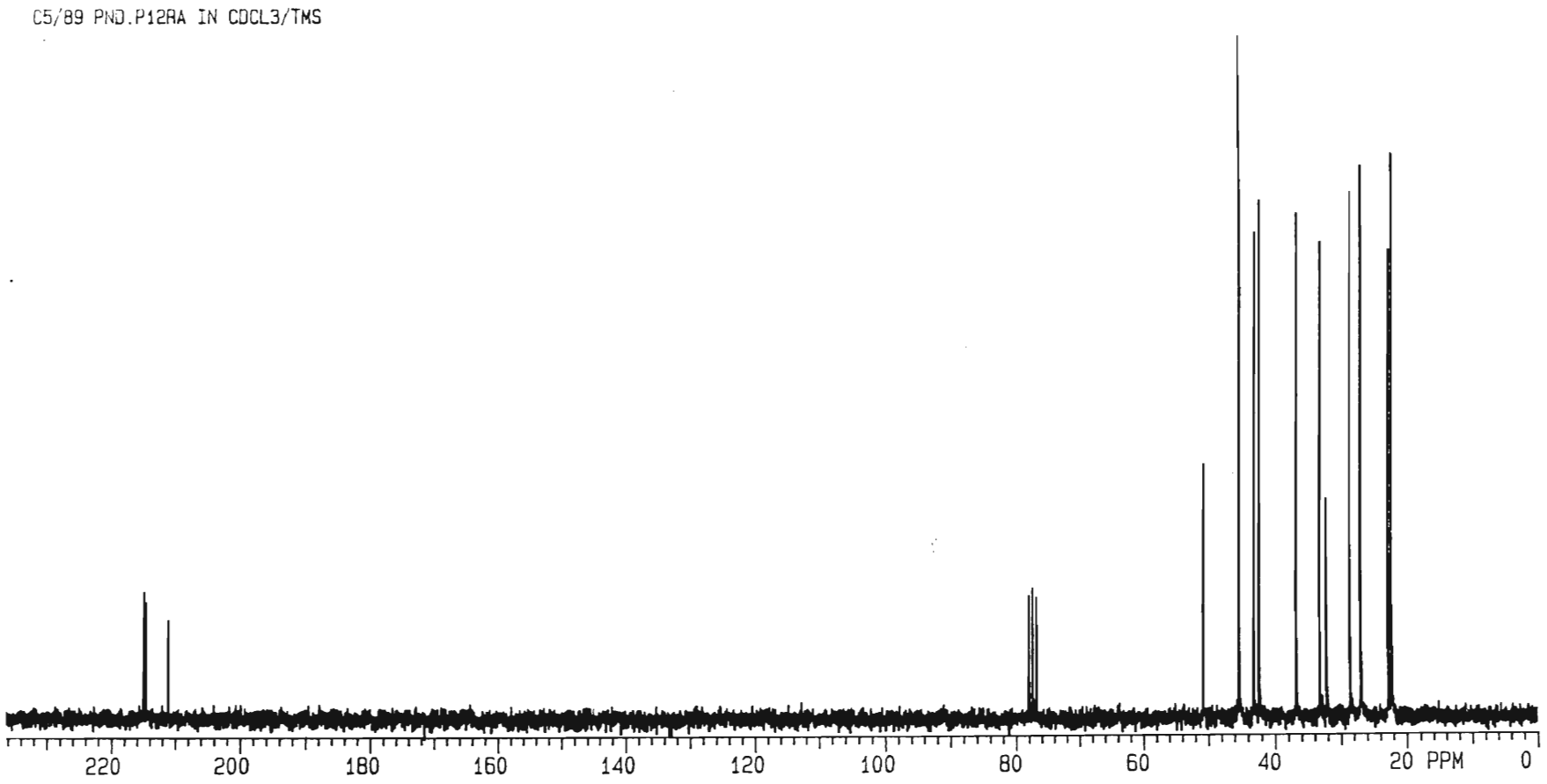


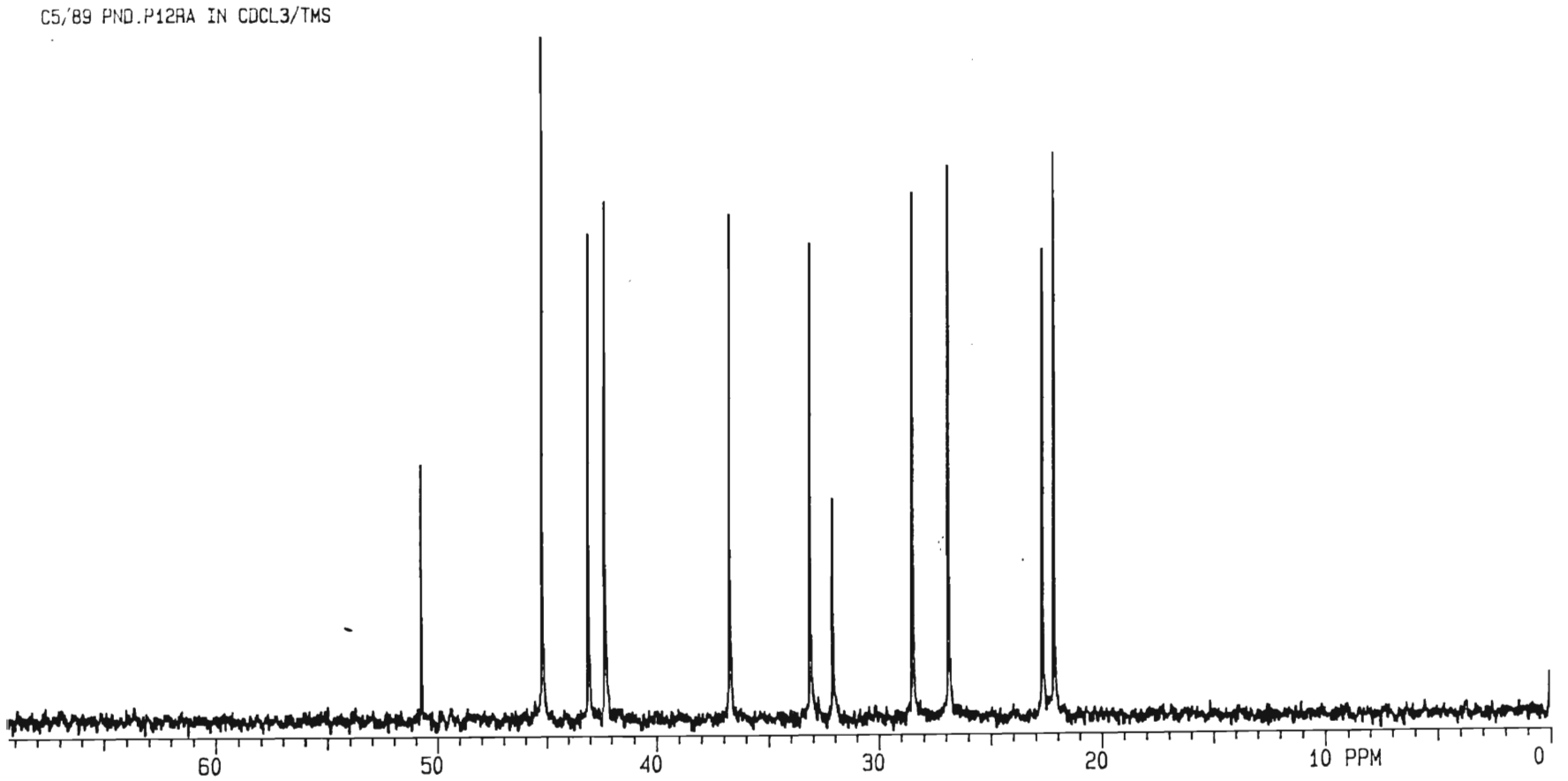

C30/89DEPT.P12RB IN CDCL3/TMS.
CH3 CARBONS
CH2 CARBONS
CH CARBONS
ALL PROTONATED CARBONS
140
120
100
80
60
40
20
0 PPM

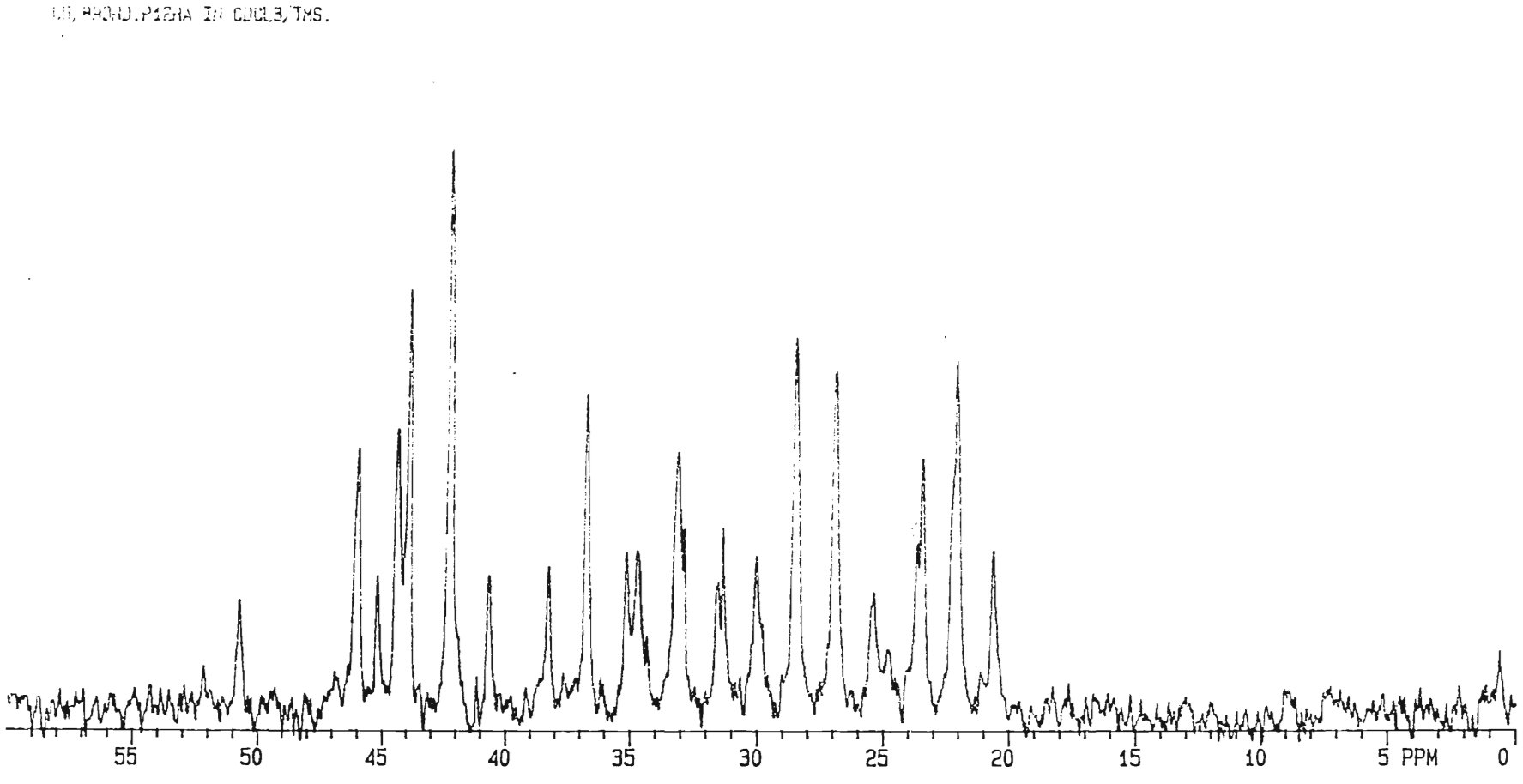

H5/89.P12RA IN CDCL3/TMS
Me
Hβ
Hβ
O
1
-Hα
O
4
Hα
3
9
10
H
Ha
COMe
Hb
8
7
6
5
4
3
2
1 PPM
0

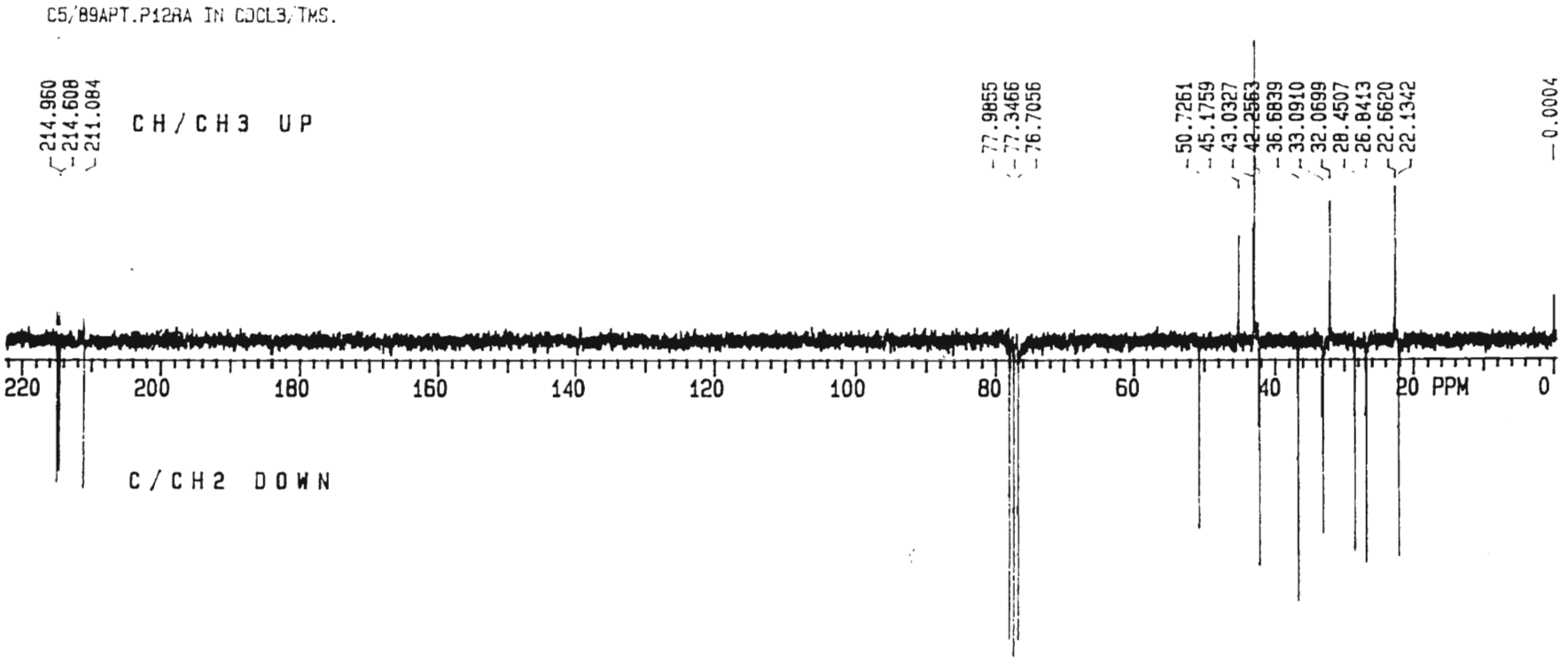
(108)

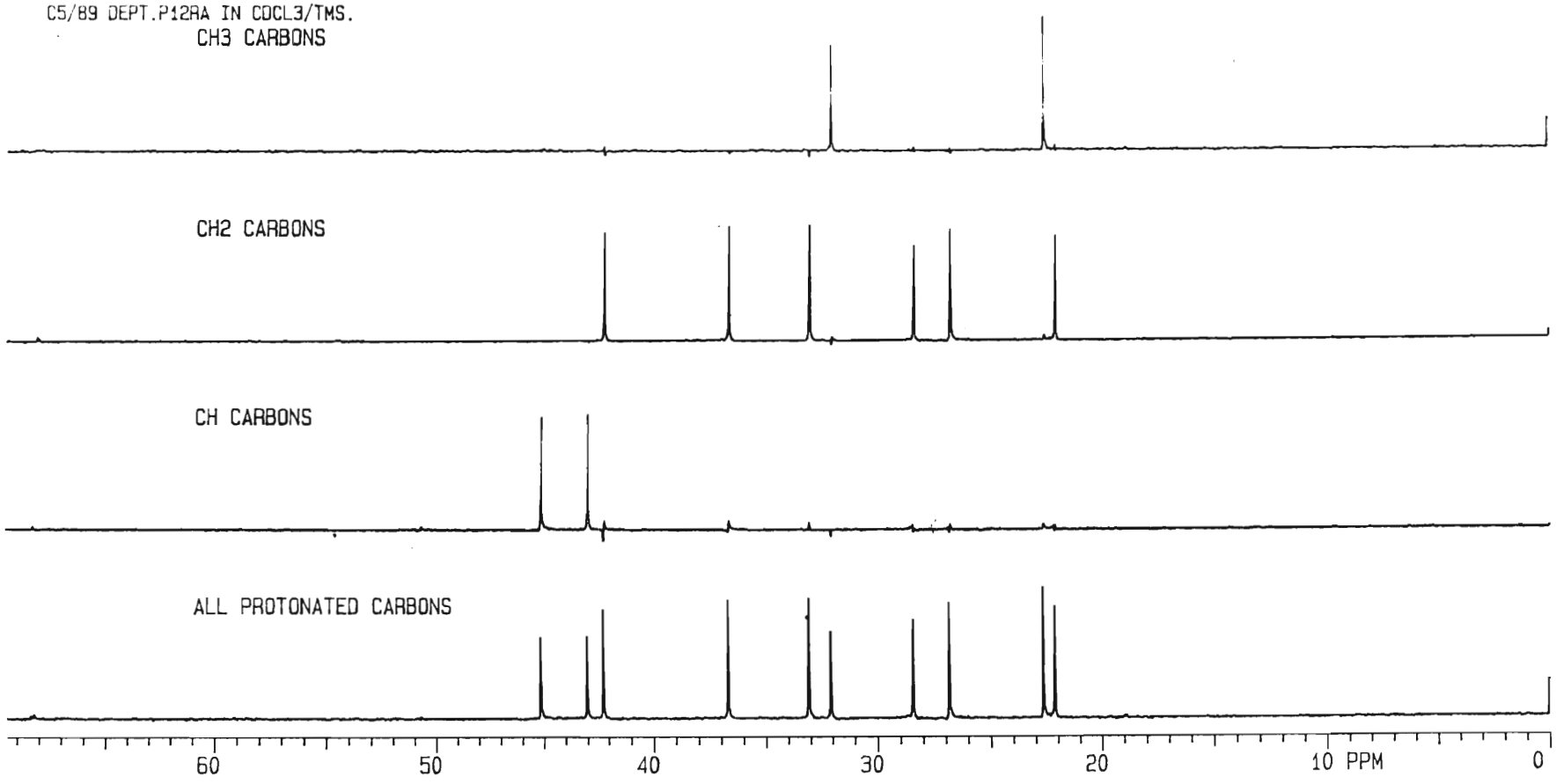

H5/89.P12HA IN CDCL3/TMS.
3.0
2.5
2.0
1.5
1.0
0.5 PPM
0.0

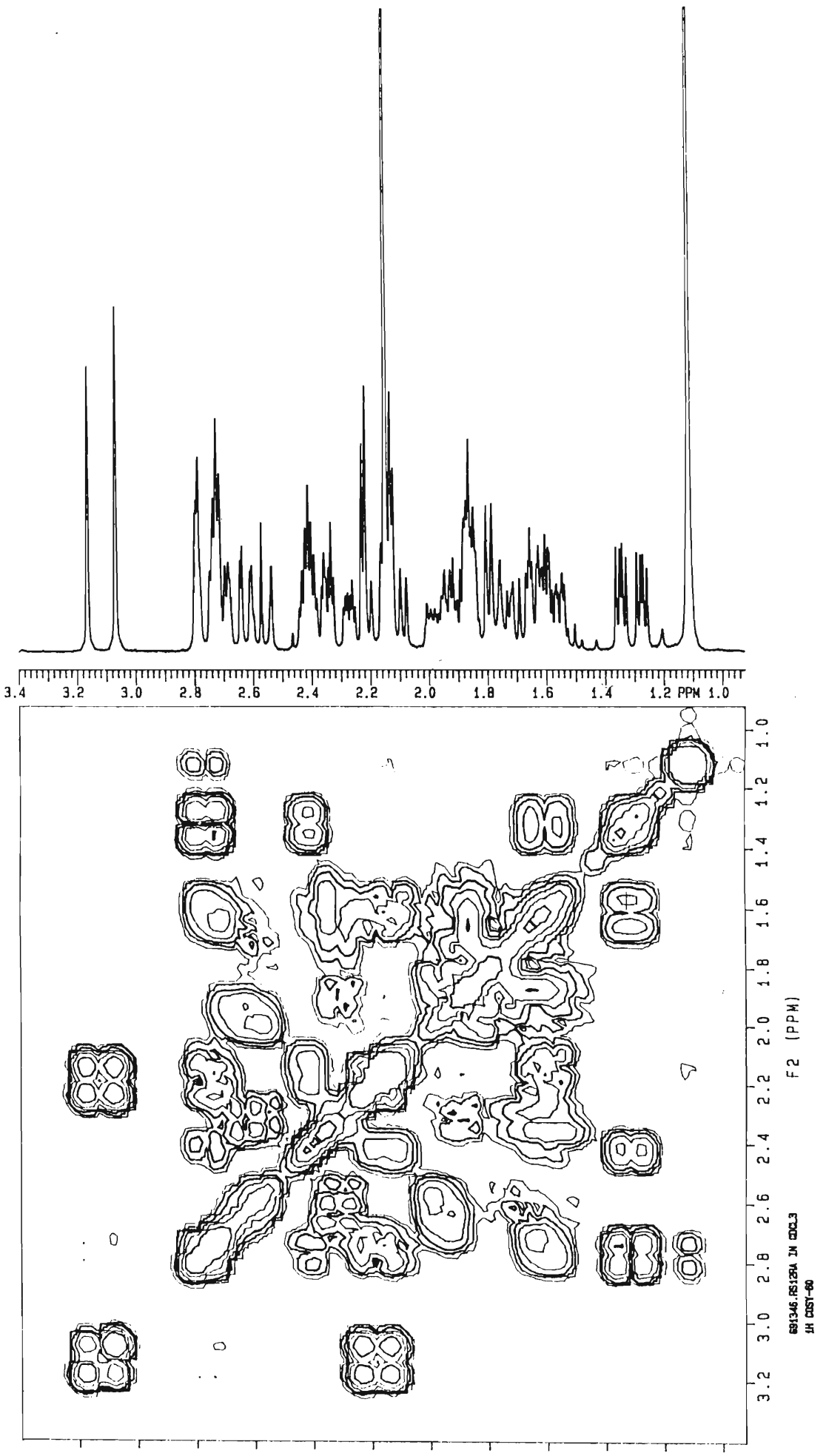

C5/89 PND.P12RA IN CDCL3/TMS
220
200
180
160
140
120
100
80
60
40
20 PPM
0

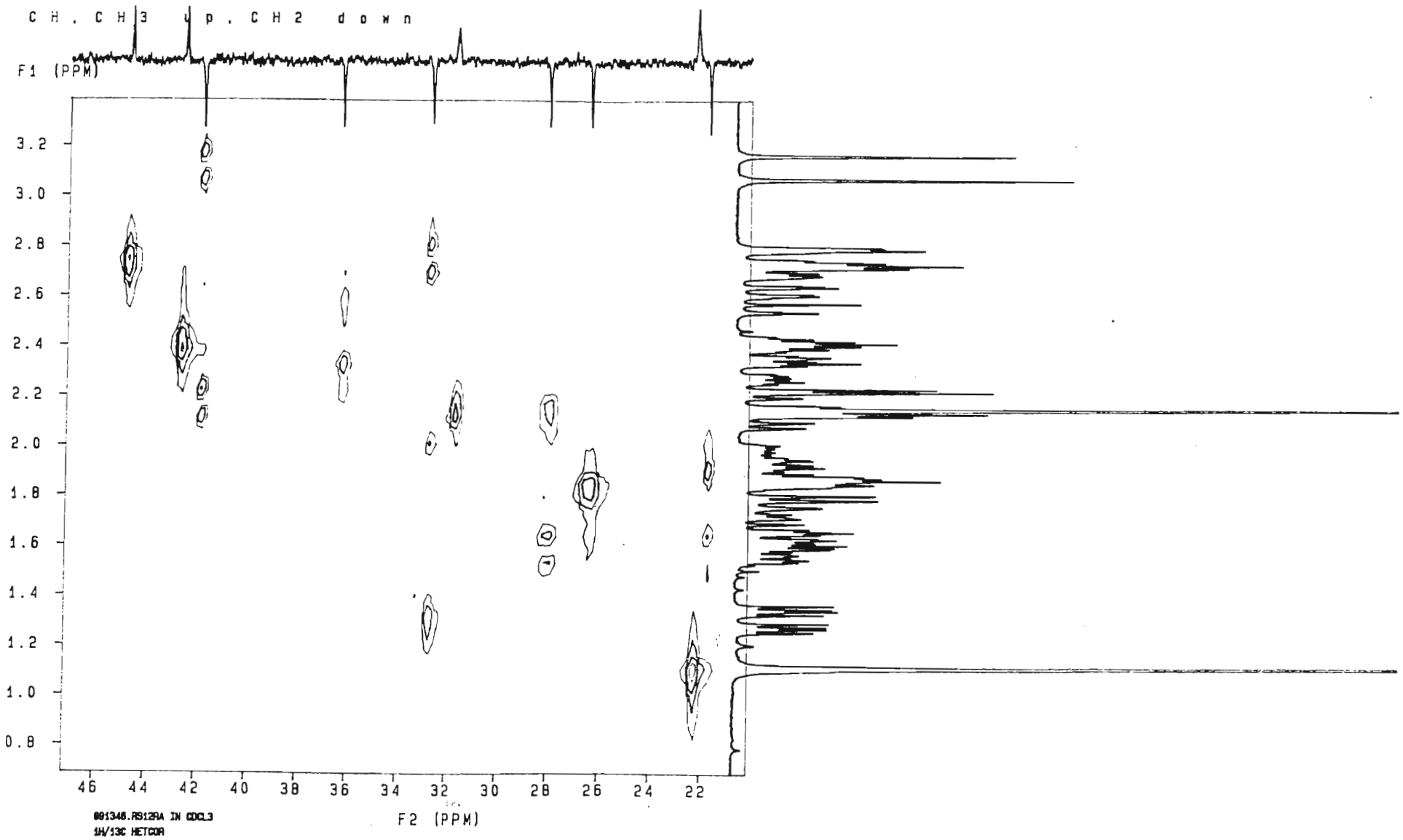

C5/89 PND.P12RA IN CDCL3/TMS
60
50
40
30
20
10 PPM
0


55
50
45
40
35
30
25
20
15
10
5 PPM
0

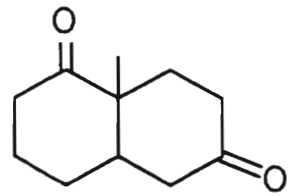

C5/89APT.P12RA IN CDCL3/TMS.
214.960
214.608
211.084
CH/CH3 UP
77.9855
77.3466
76.7056
50.7261
45.1759
43.0327
42.2563
36.6839
33.0910
32.0699
28.4507
26.8413
22.6620
22.1342
0.0004
220
200
180
160
140
120
100
80
60
40
20 PPM
0
C/CH2 DOWN


C5/89 DEPT.P12RA IN CDCL3/TMS.
CH3 CARBONS
CH2 CARBONS
CH CARBONS
ALL PROTONATED CARBONS
60
50
40
30
20
10 PPM
0

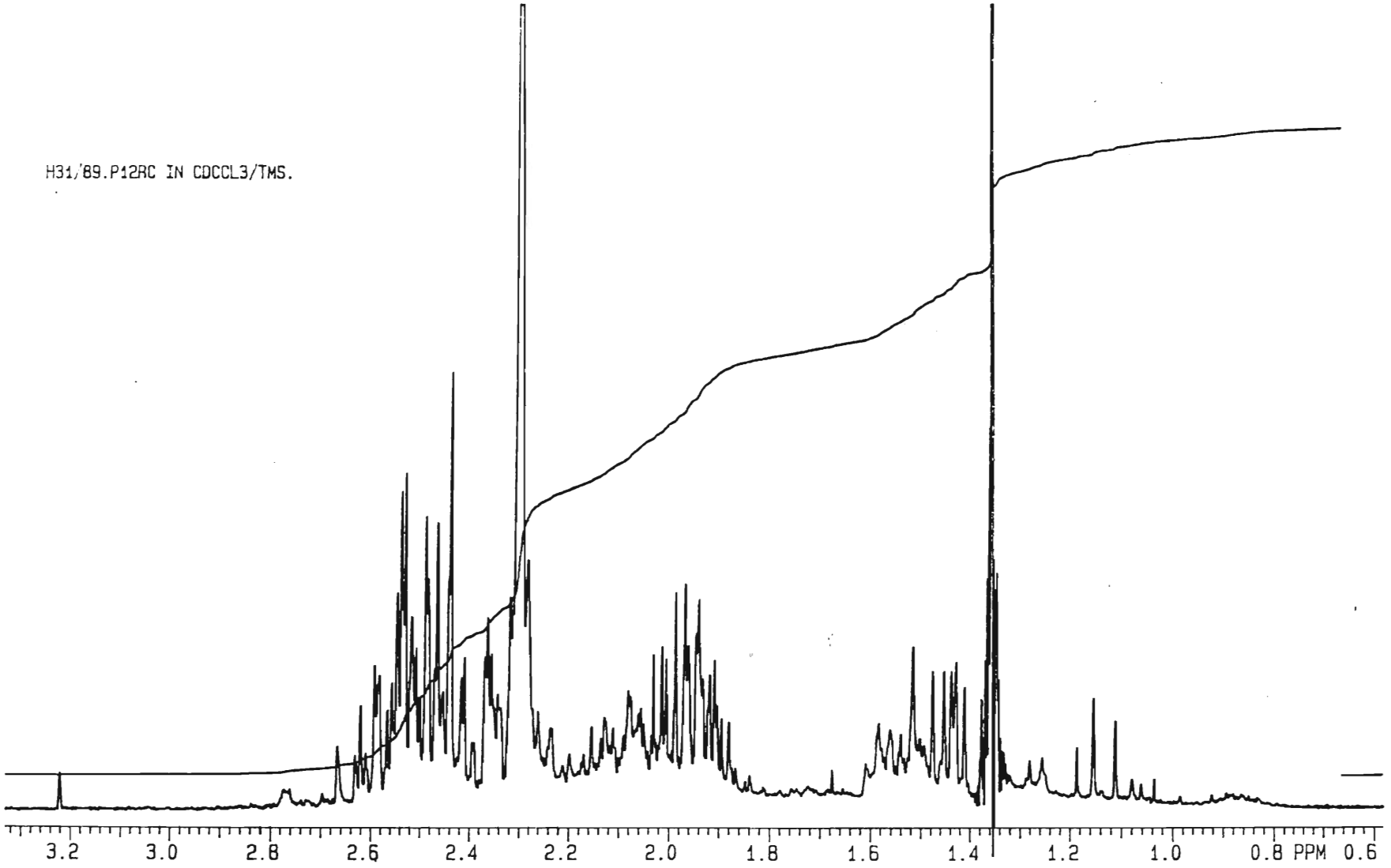

3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2 PPM 1.0
F2 (PPM)
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
691346.RS12PA IN CDCL3
1H COSY-90


C H , C H 3 u p , C H 2 d o w n
F1 (PPM)
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
46
44
42
40
38
36
34
32
30
28
26
24
22
F2 (PPM)
001348.RS128A IN CDCL3
1H/13C HETCOR

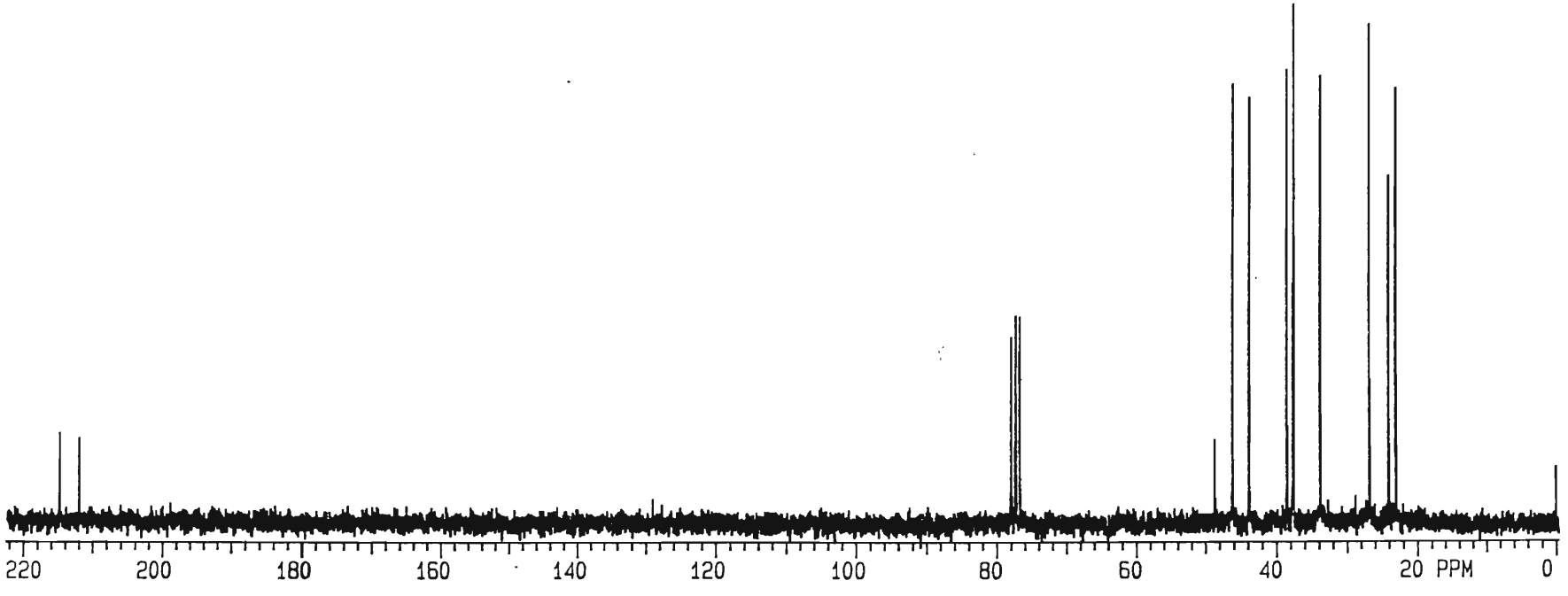
H31/89.P12RC IN CDCCL3/TMS.

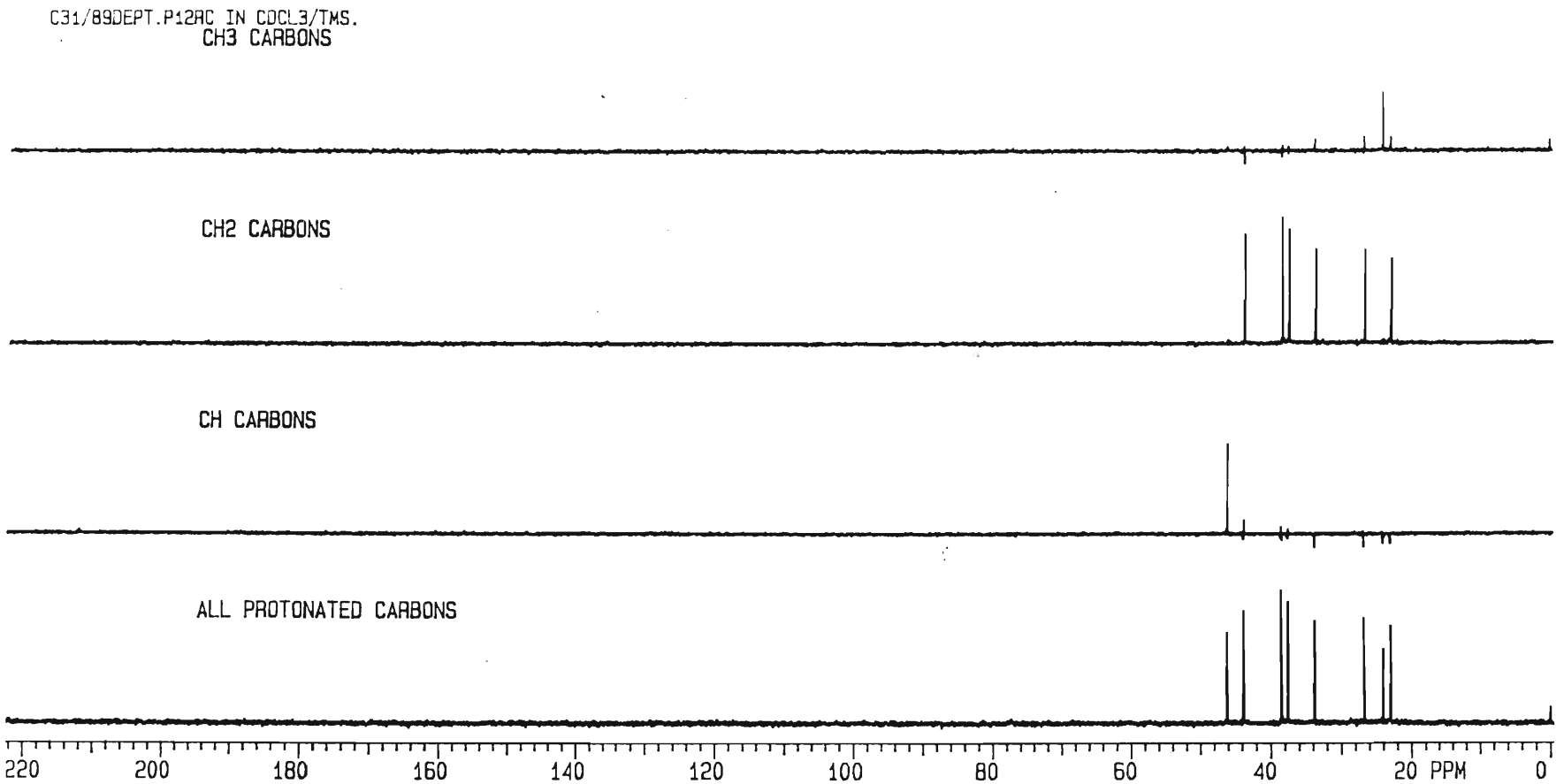


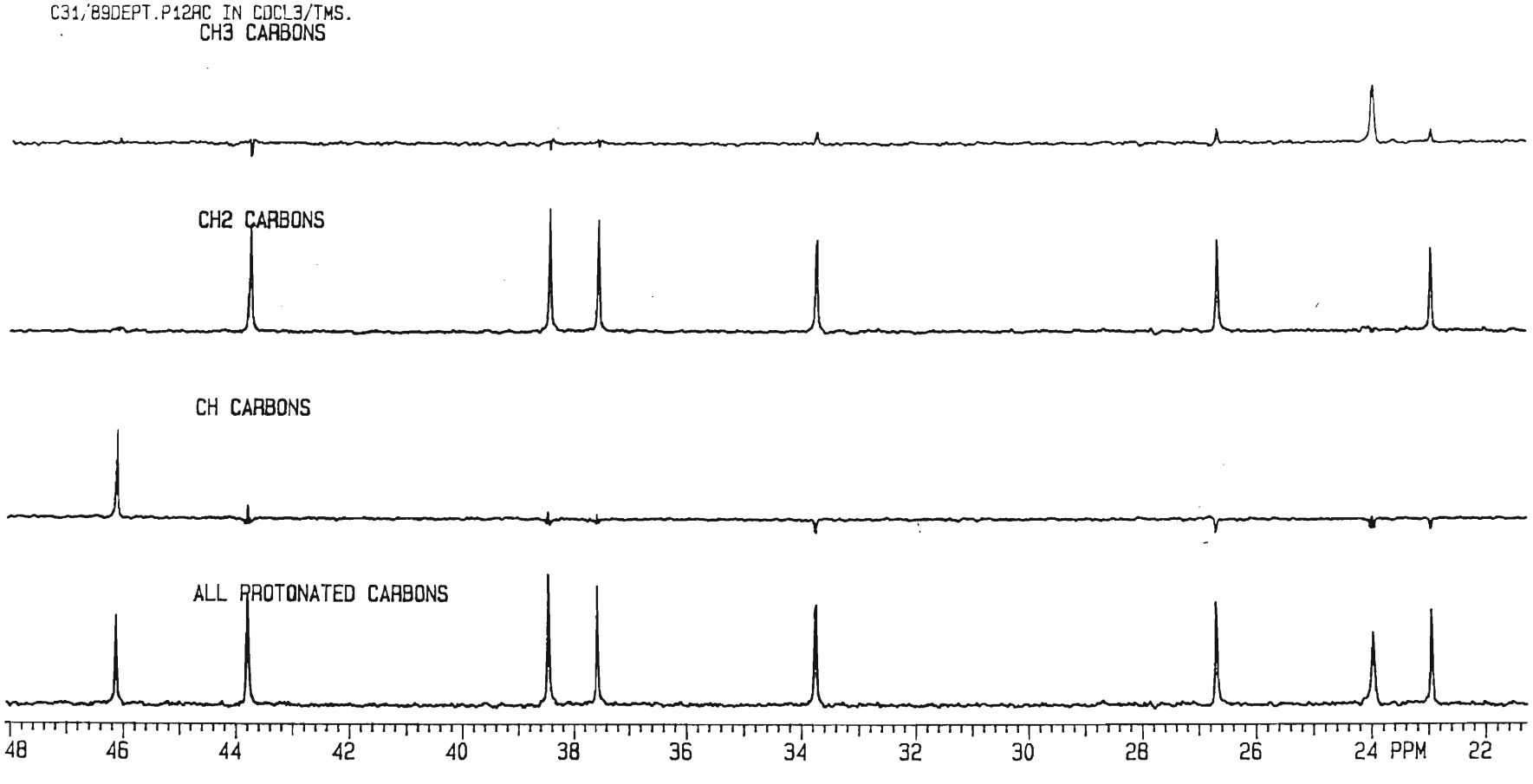
(101)


H31/'89.P12RC IN CDCCL3/TMS.
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8 PPM 0.6

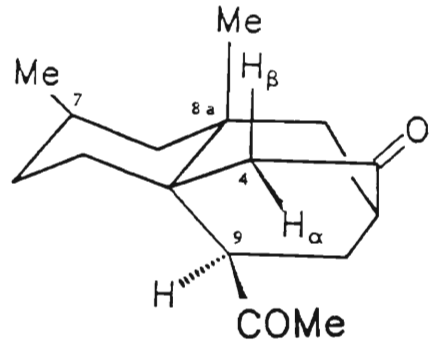
C31/89PND.P12RC IN CDCL3/TMS.



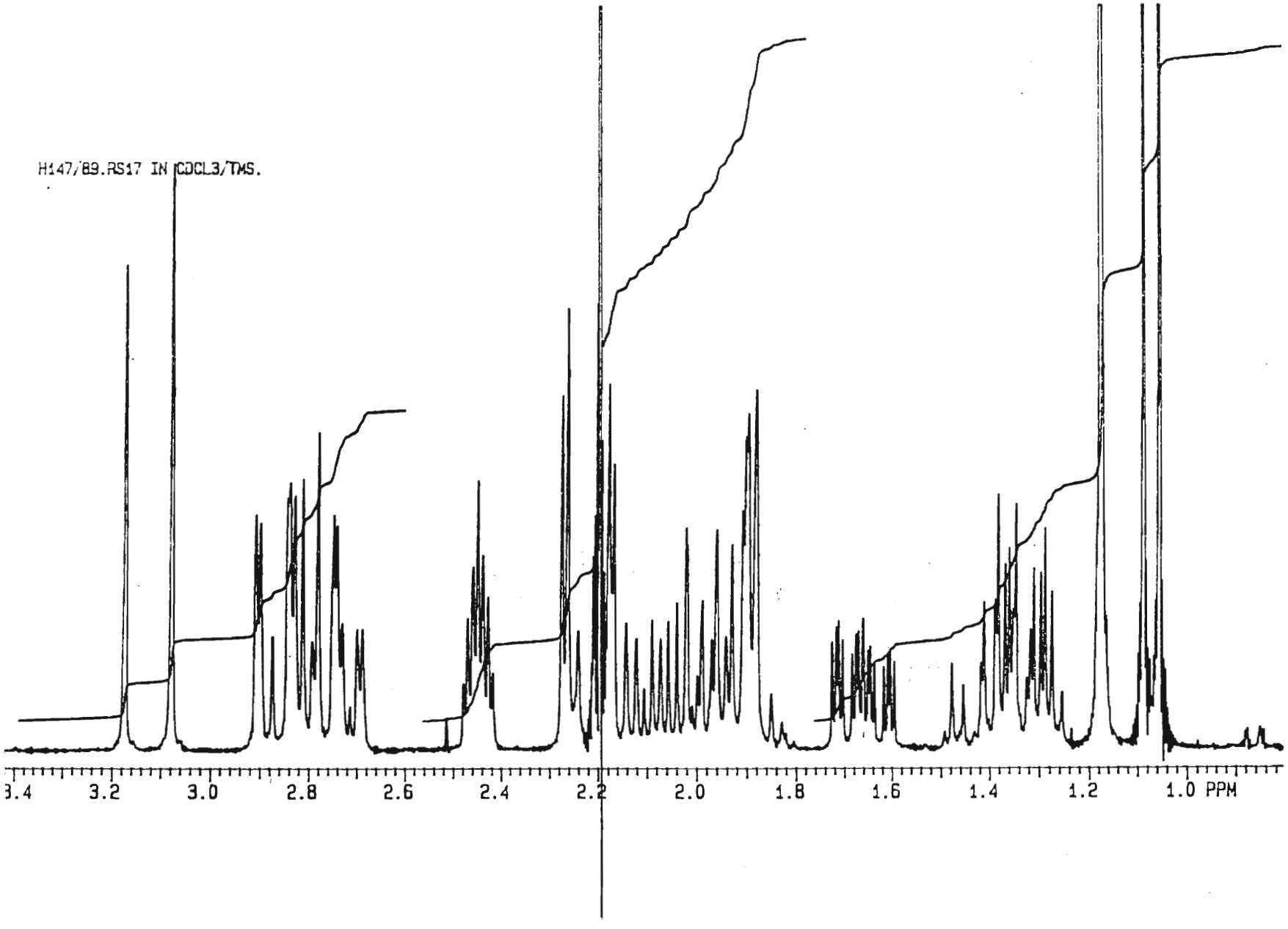

C31/89DEPT.P12AC IN CDCL3/TMS.
CH3 CARBONS
CH2 CARBONS
CH CARBONS
ALL PROTONATED CARBONS
220
200
180
160
140
120
100
80
60
40
20 PPM
0

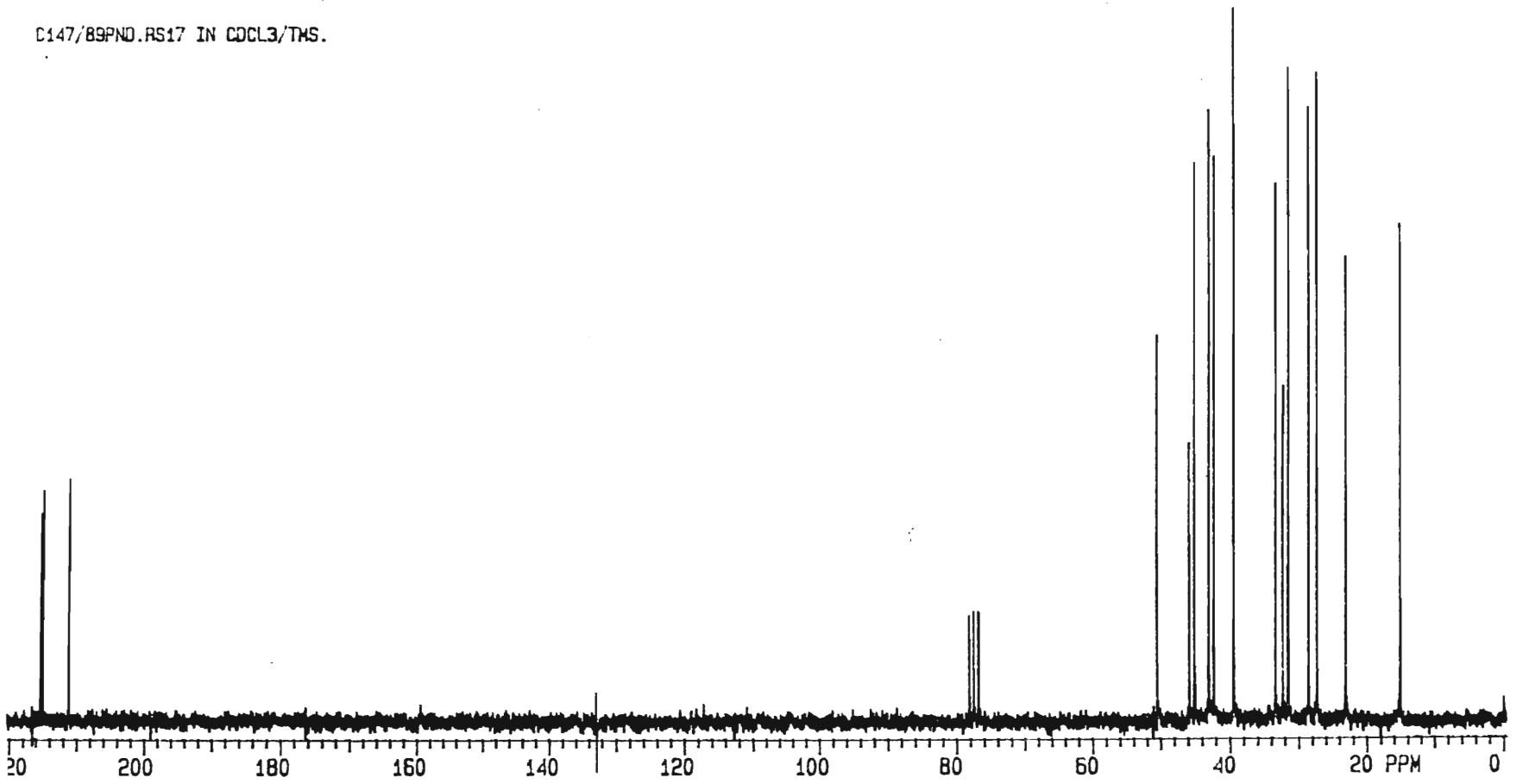

C31/89DEPT.P12AC IN CDCL3/TMS.
CH3 CARBONS
CH2 CARBONS
CH CARBONS
ALL PROTONATED CARBONS
48
46
44
42
40
38
36
34
32
30
28
26
24 PPM
22

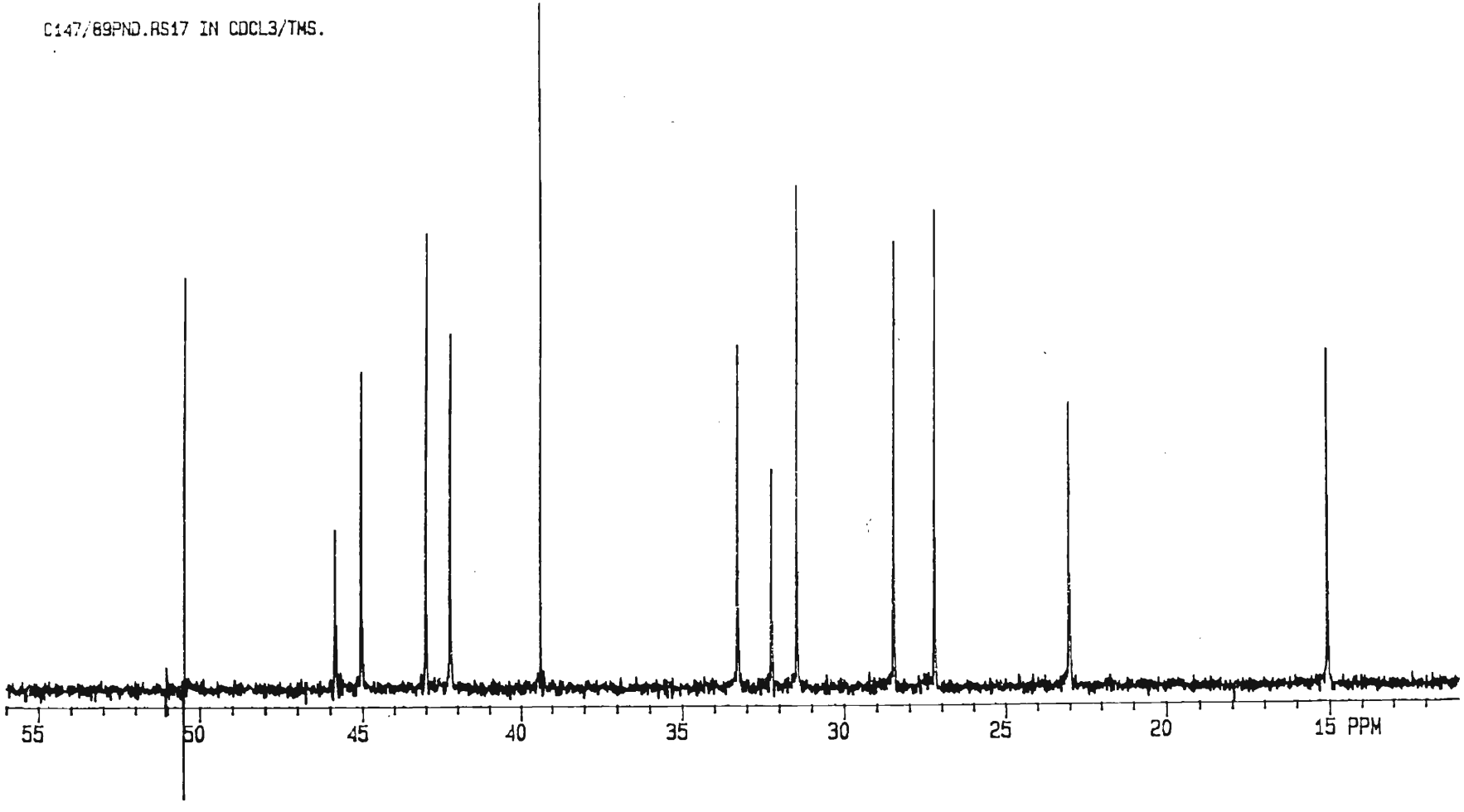
H147/89.RS17 IN CDCL3/TMS.

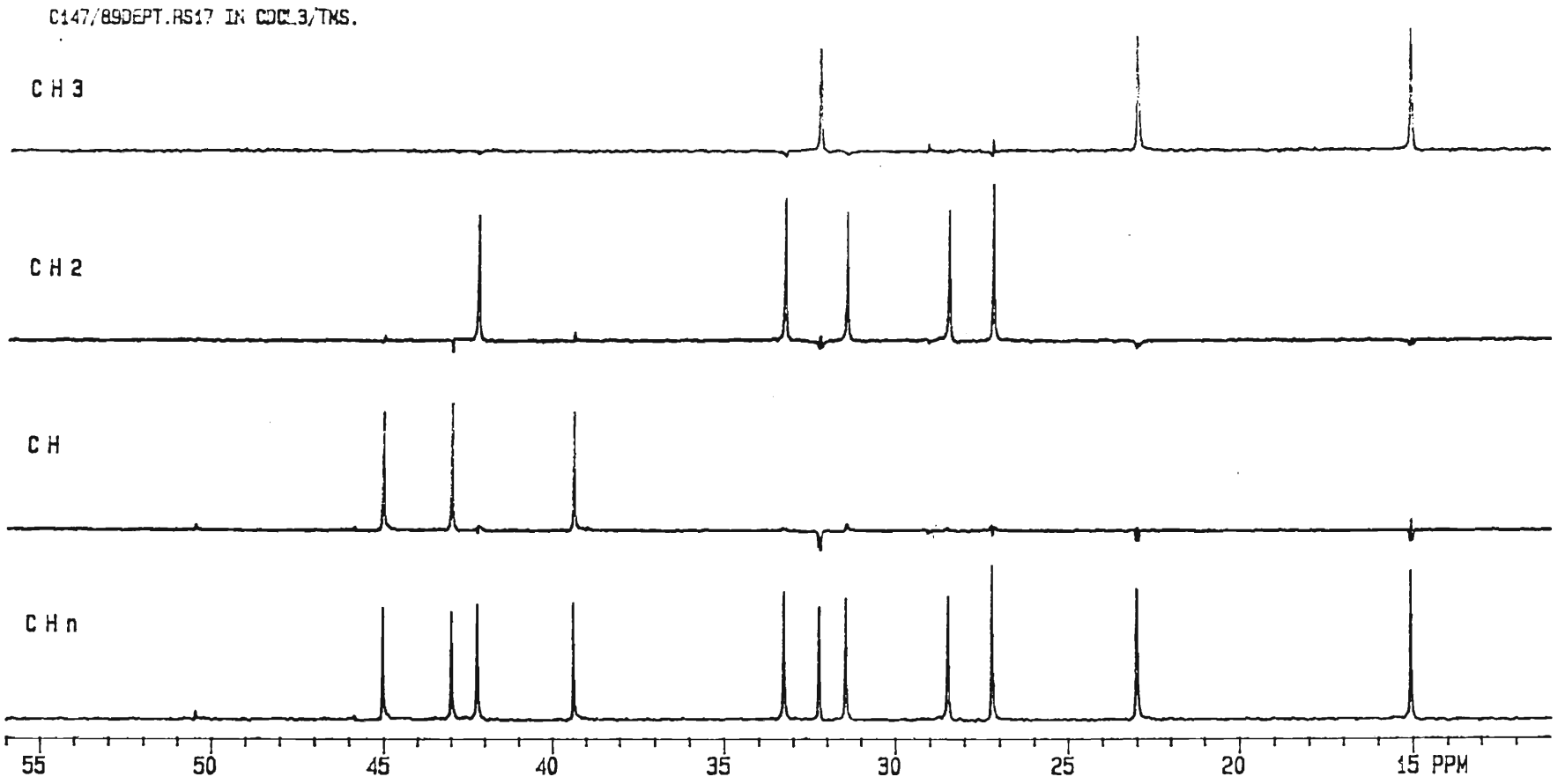


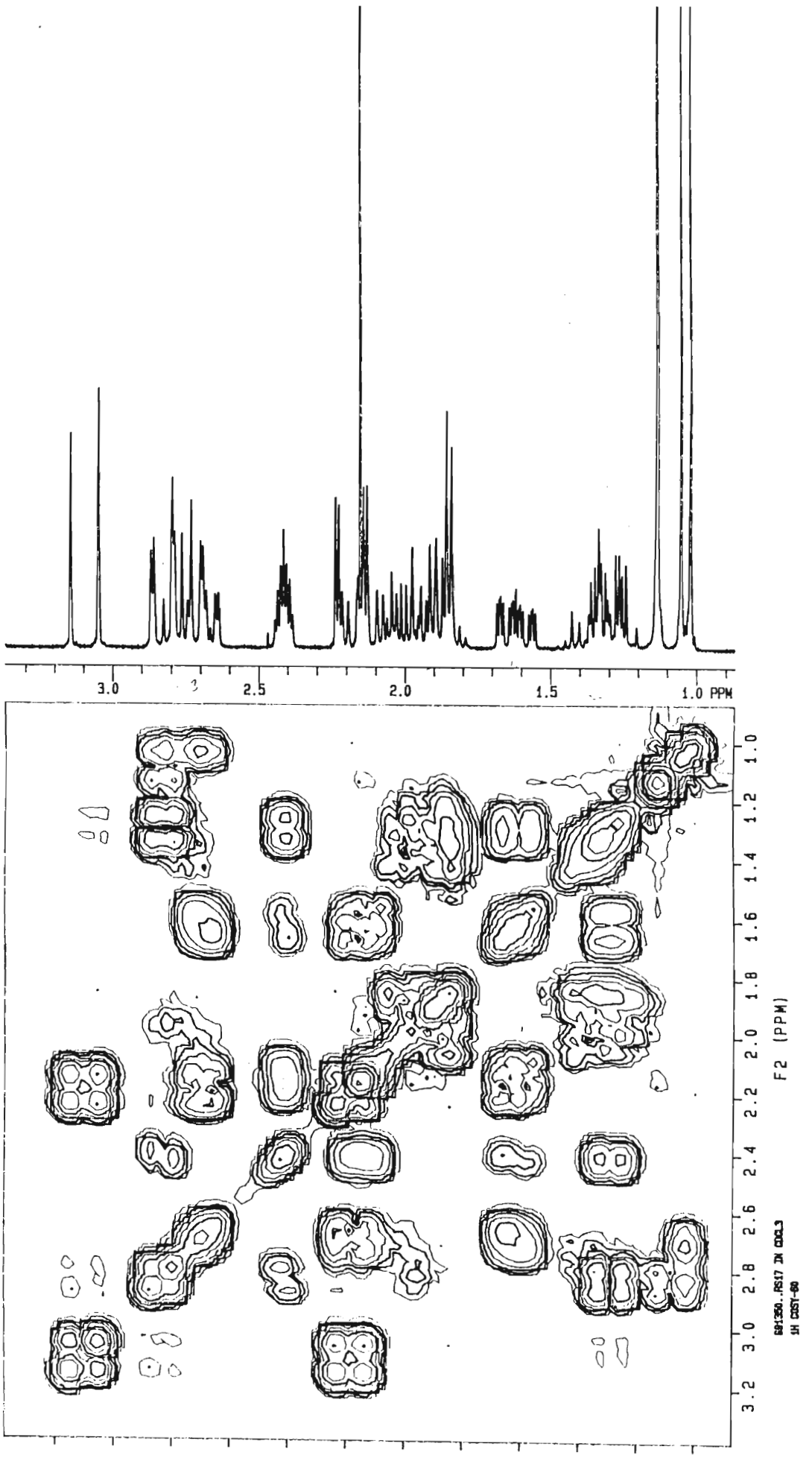
(110)

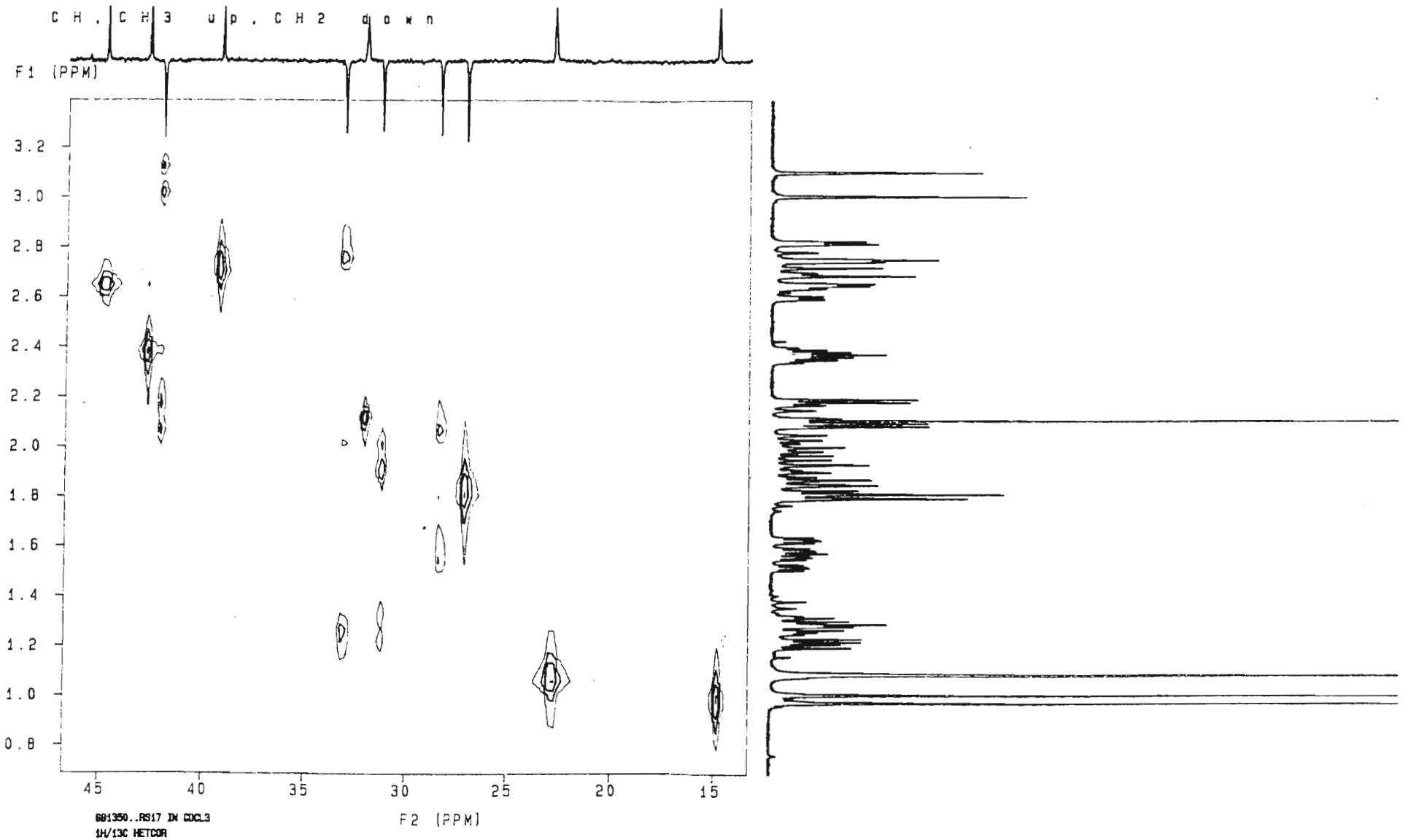

H147/89.RS17 IN CDCL3/TMS.
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM


C147/89PND.RS17 IN CDCL3/TMS.
220
200
180
160
140
120
100
80
60
40
20 PPM
0

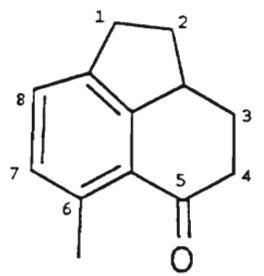

C147/89PND.RS17 IN CDCL3/TMS.
55
50
45
40
35
30
25
20
15 PPM


C147/89DEPT.RS17 IN CDCL3/TMS.
C H 3
C H 2
C H
C H n
55
50
45
40
35
30
25
20
15 PPM

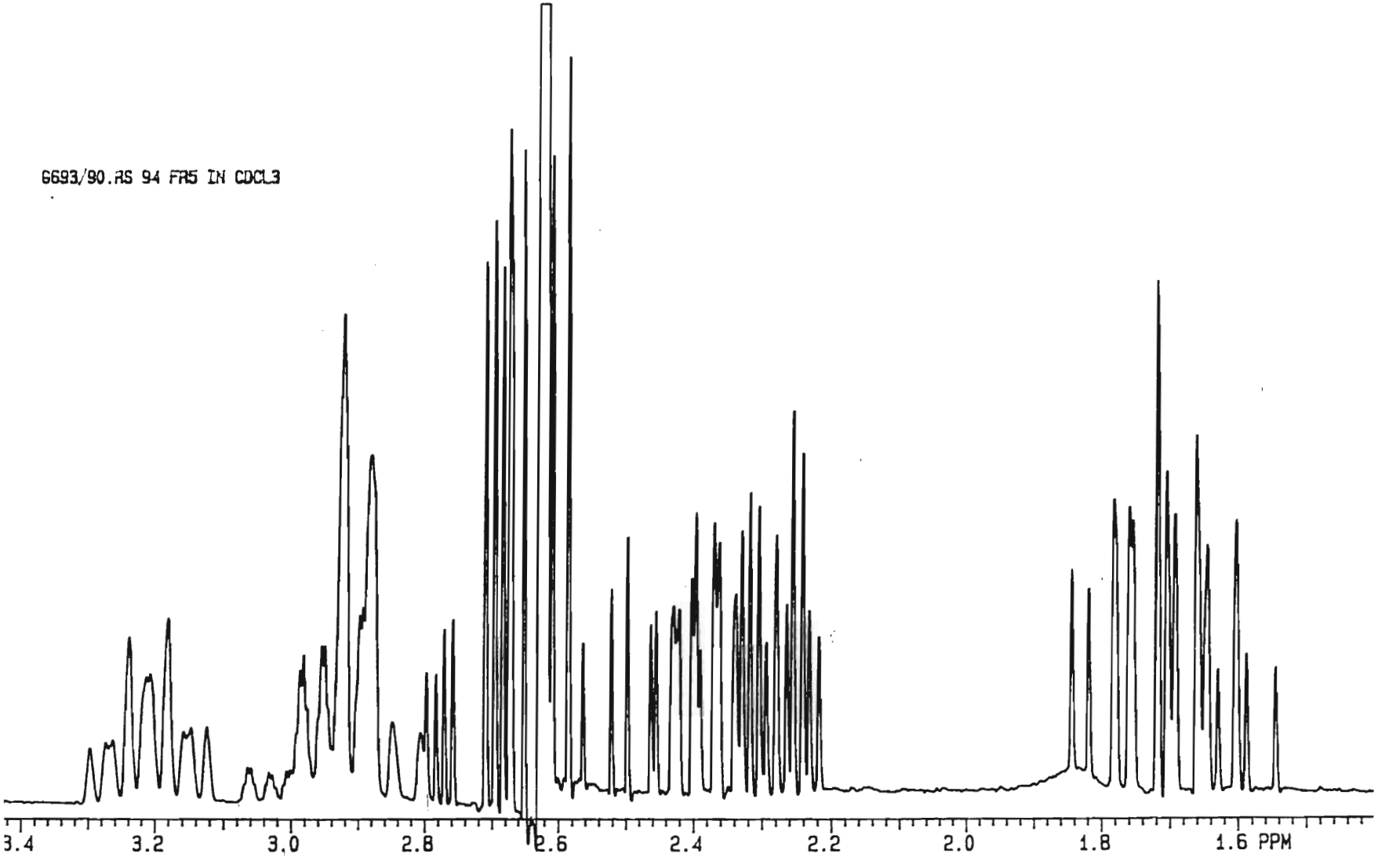

3.0
2.5
2.0
1.5
1.0 PPM
F2 (PPM)
3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
BRISO..RS17 IN CDCL3
1H COSY-90

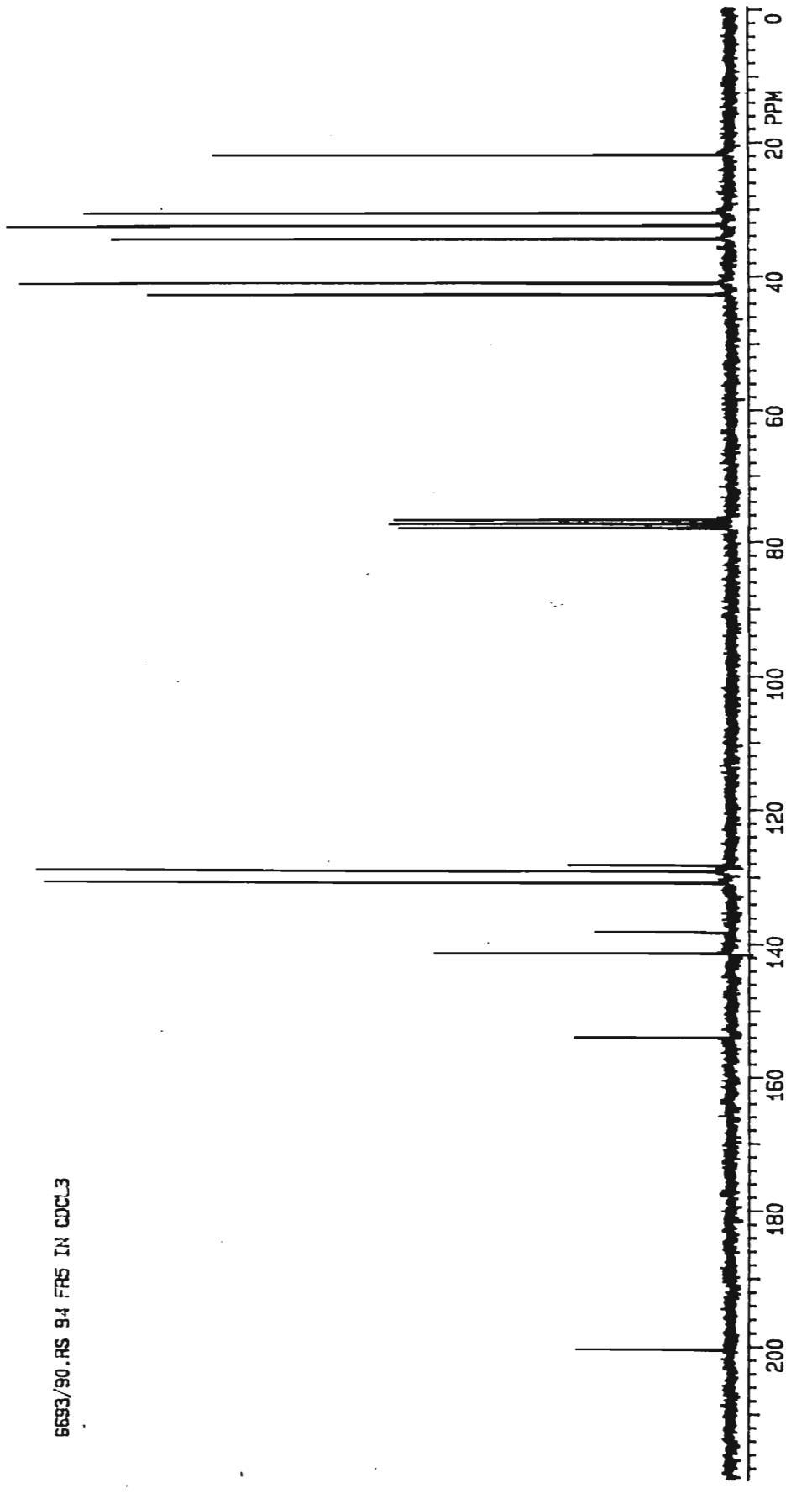

C H , C H 3 up , C H 2 down
F1 (PPM)
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
45
40
35
30
25
20
15
F2 (PPM)
691350..RS17 IN CDCL3
1H/13C HETCOR

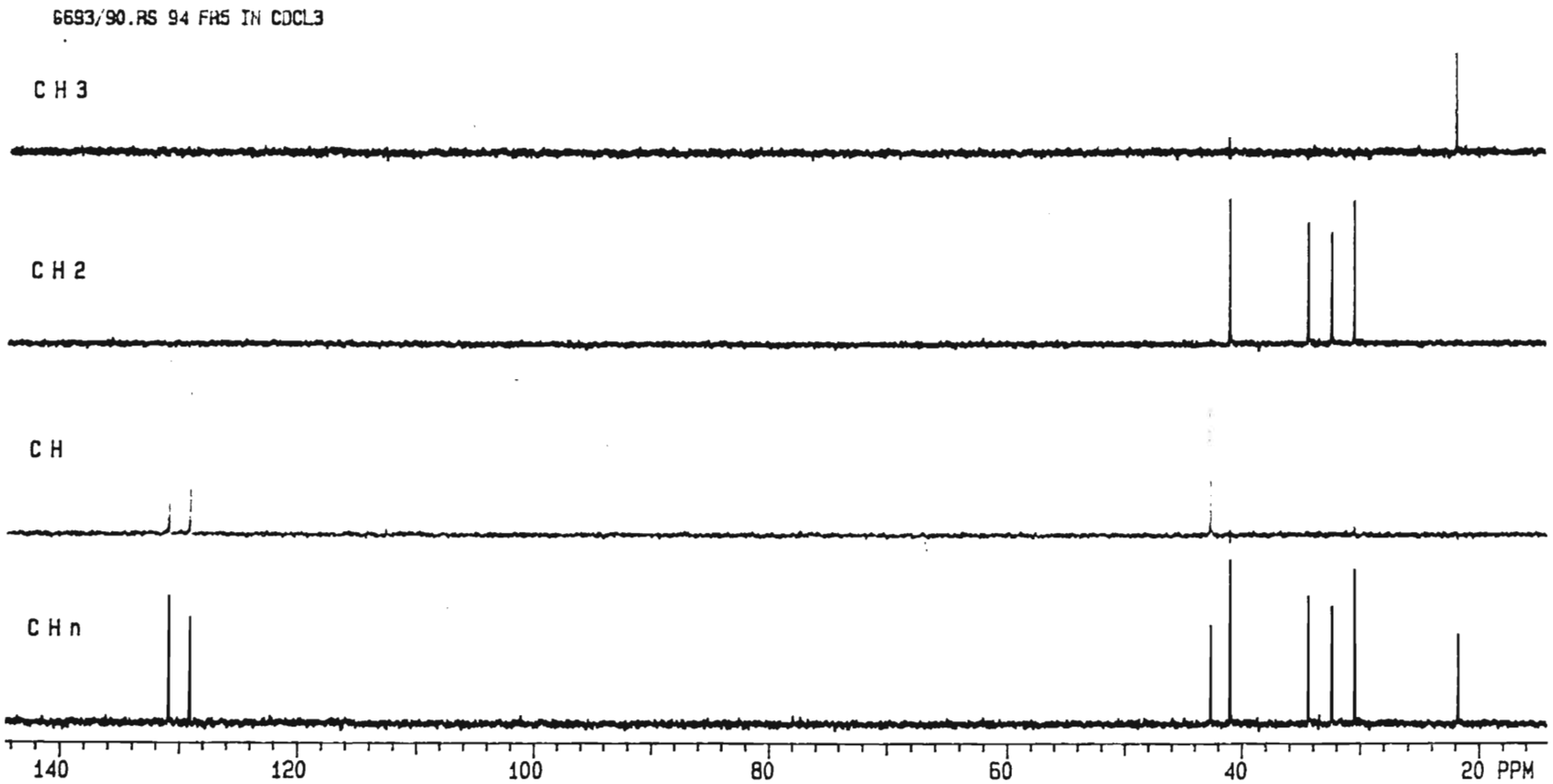
6693/90.RS 94 FR5 IN CDCL3

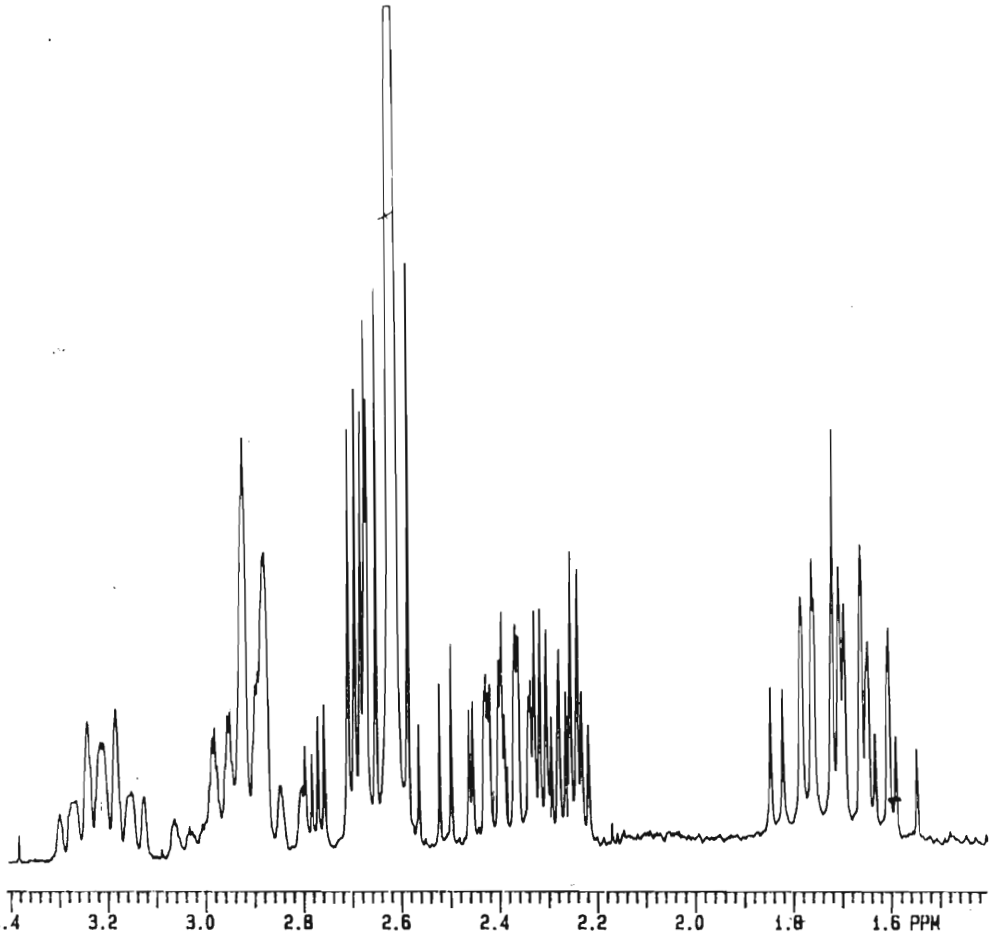


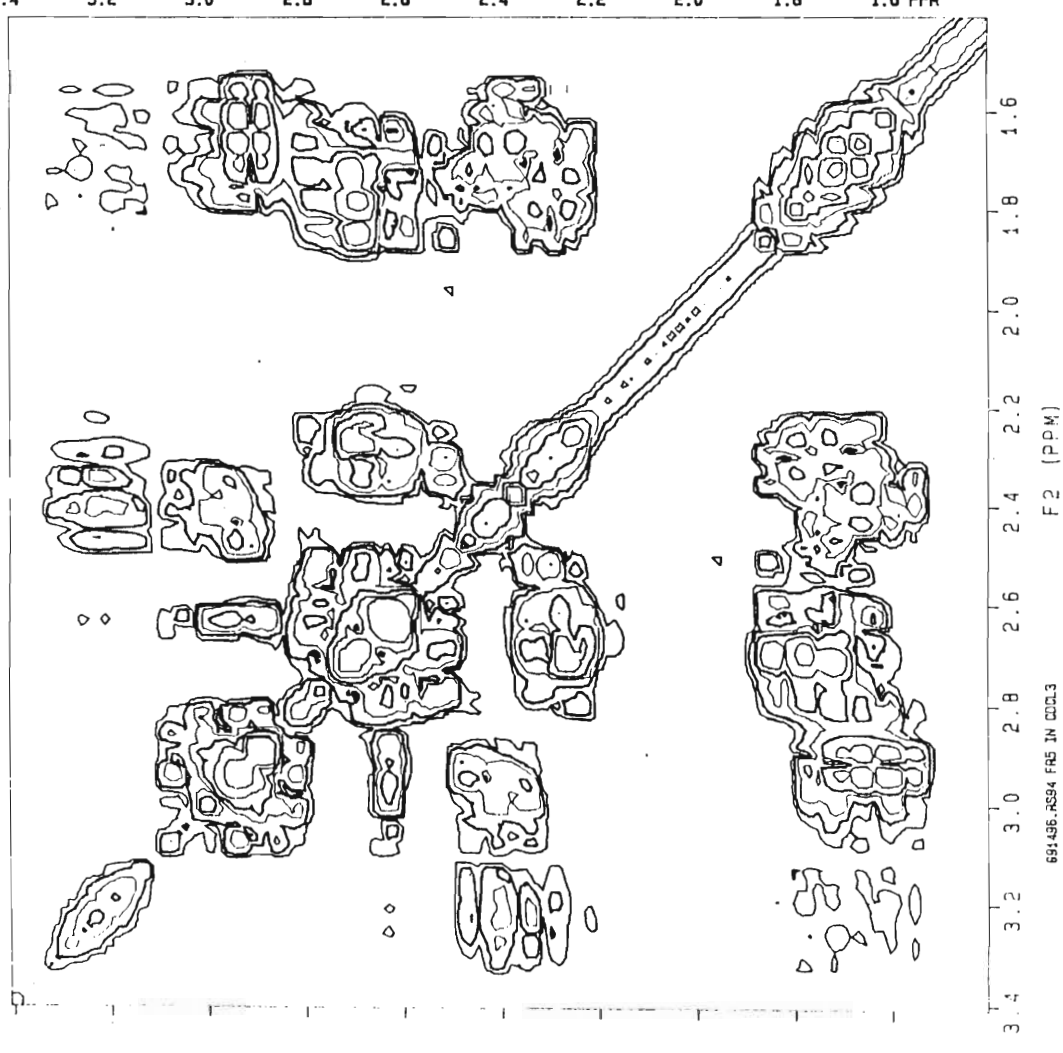
(103a)

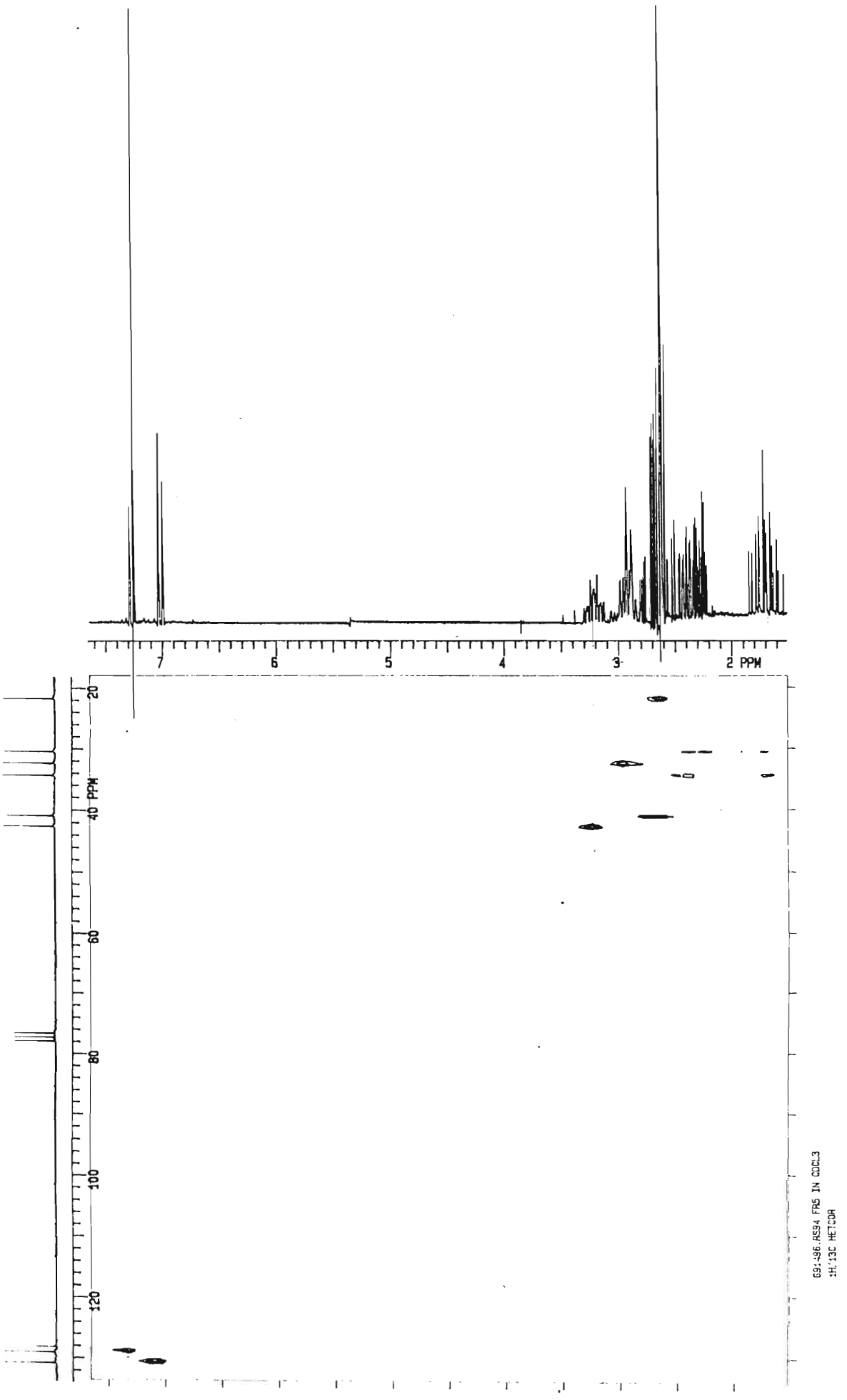

6693/90.RS 94 FR5 IN CDCL3
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6 PPM


6693/90.RS 94 FR5 IN CDCL3
0
20 PPM
40
60
80
100
120
140
160
180
200

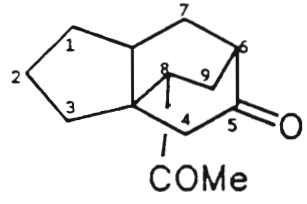

6693/90.RS 94 FR5 IN CDCL3
C H 3
C H 2
C H
C H n
140
120
100
80
60
40
20 PPM


3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6 PPM

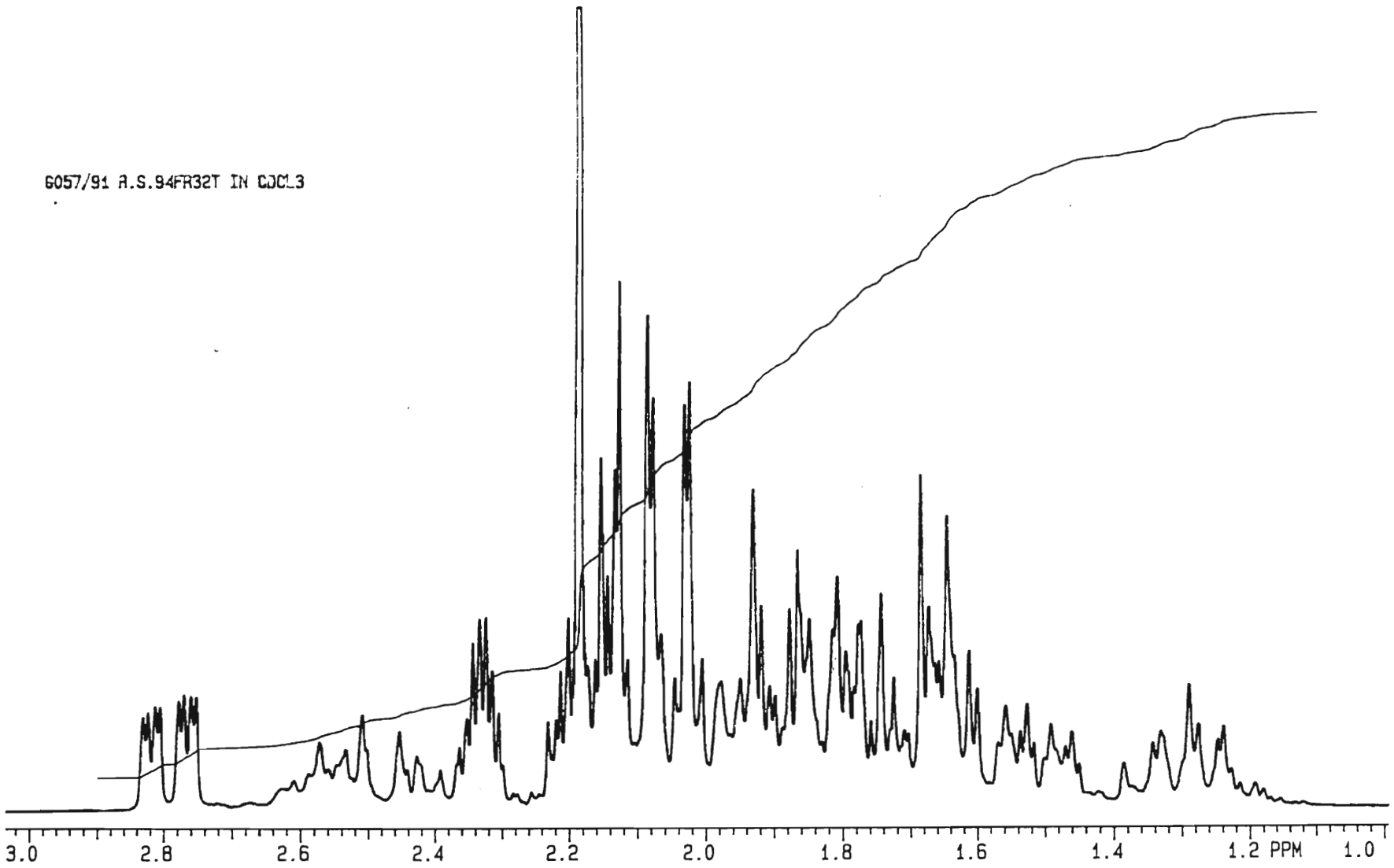

3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
F2 (PPM)
691436.RS94 FRS IN CDCL3
1H COSY-60

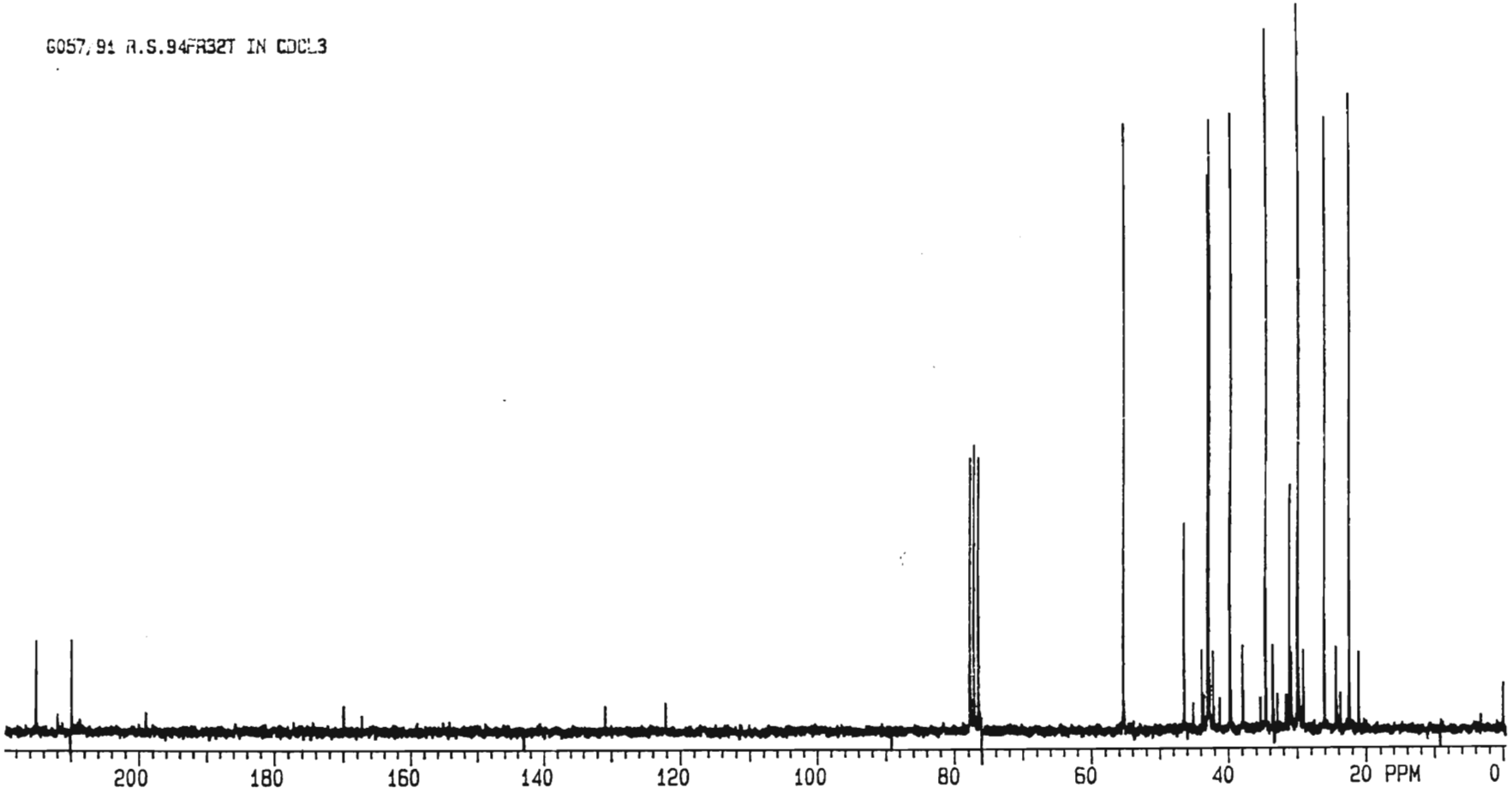

7
6
5
4
3
2 PPM
20
40 PPM
60
80
100
120
G9:496.RS94 FR5 IN CDCL3
1H/13C HETCOR

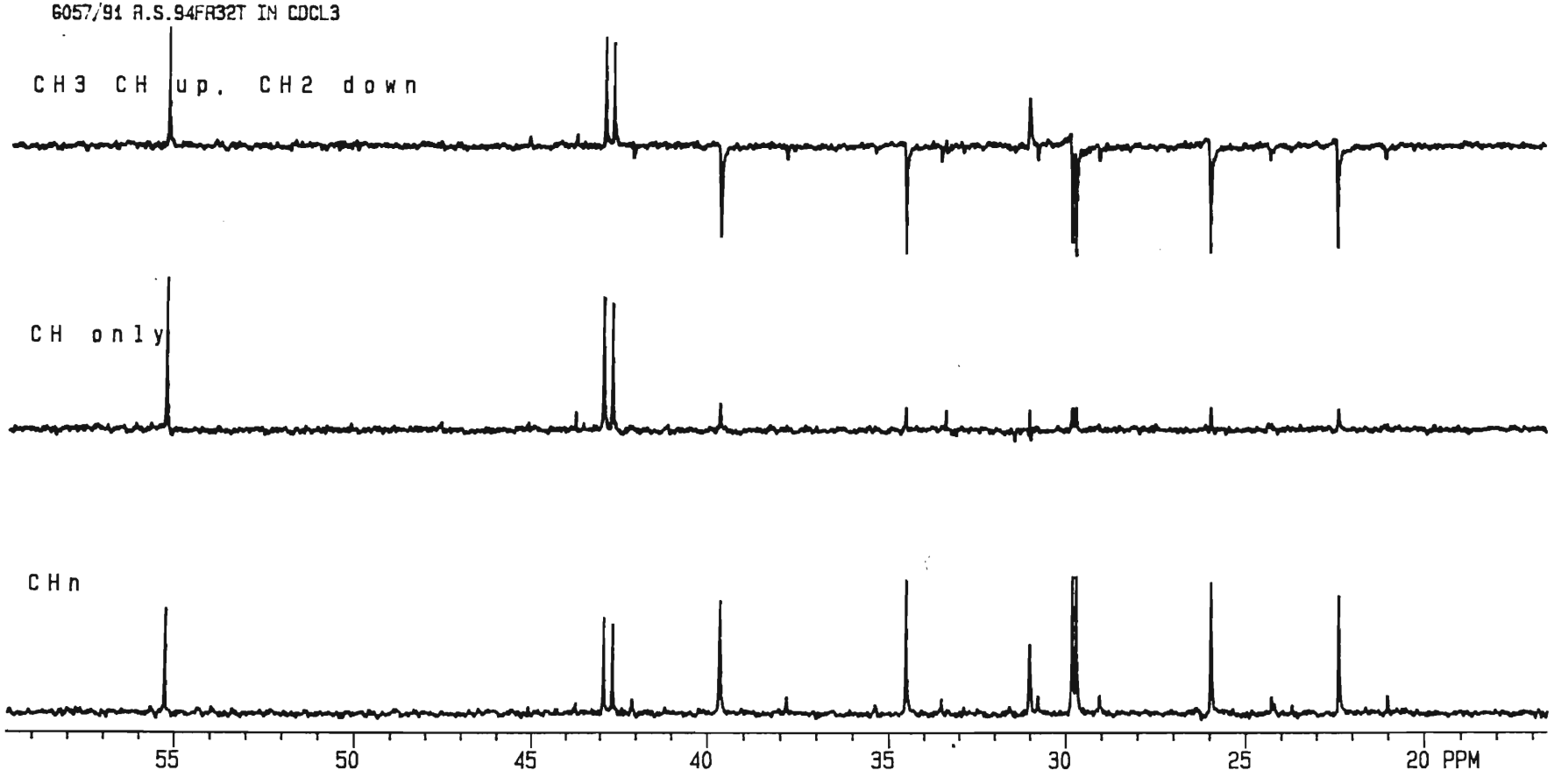
6057/91 R.S.94FR32T IN CDCL3



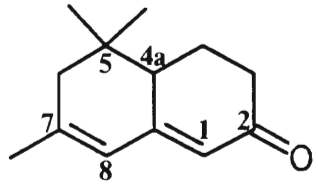
(103b)


6057/91 R.S.94FR32T IN CDCL3
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2 PPM
1.0

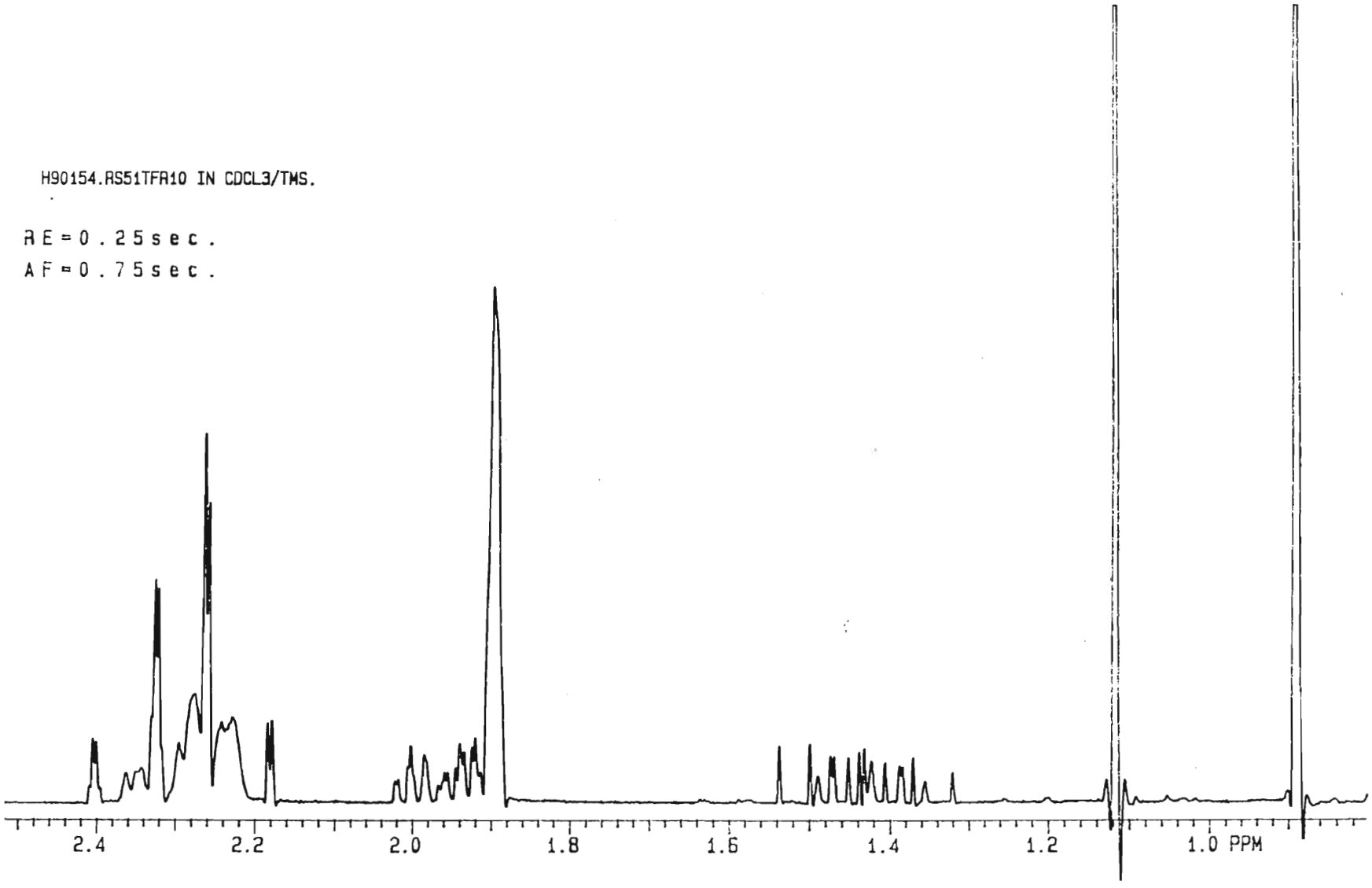

G057,91 R.S.94FR32T IN CDCL3
200
180
160
140
120
100
80
60
40
20 PPM
0


6057/91 R.S.94FR32T IN CDCL3
CH3 CH up, CH2 down
CH only
CHn
55
50
45
40
35
30
25
20 PPM

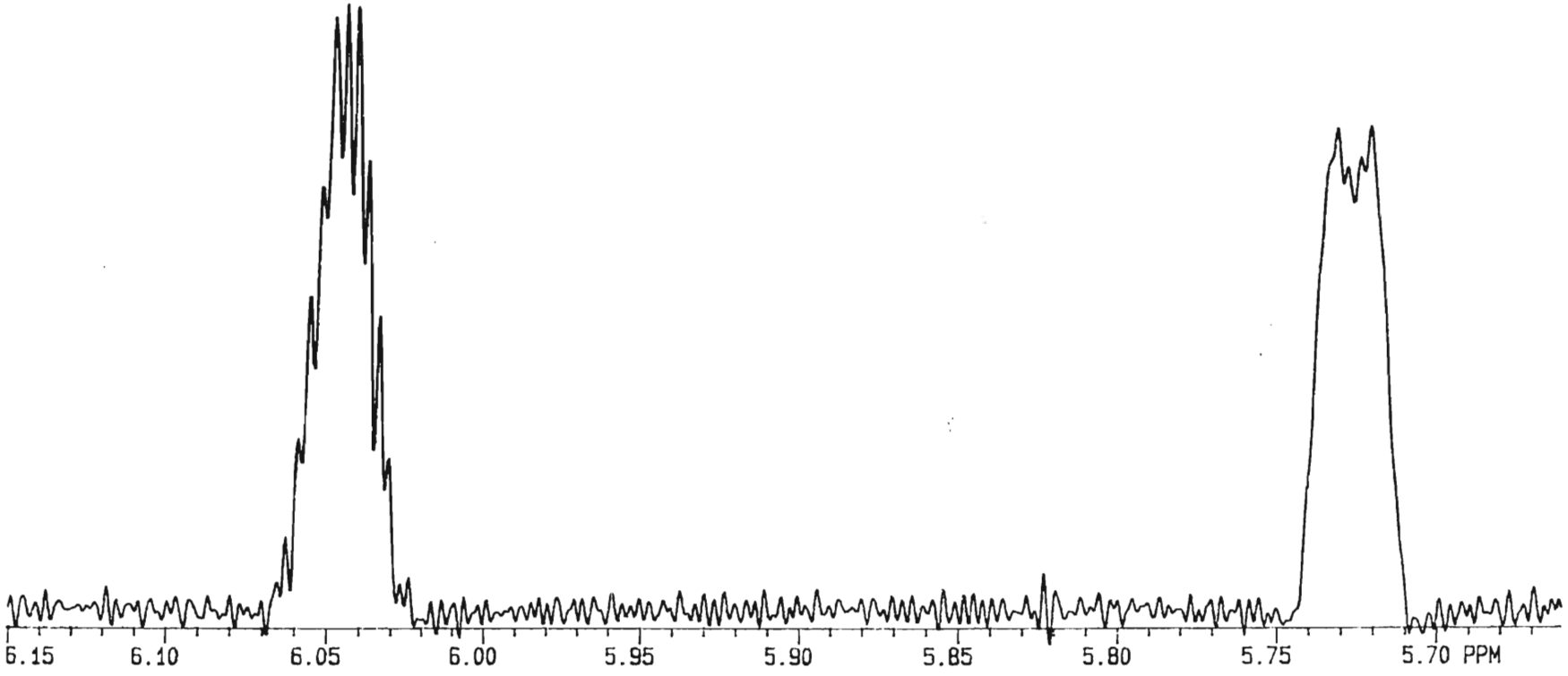
H90154.RS51TFR10 IN CDCL3/TMS.



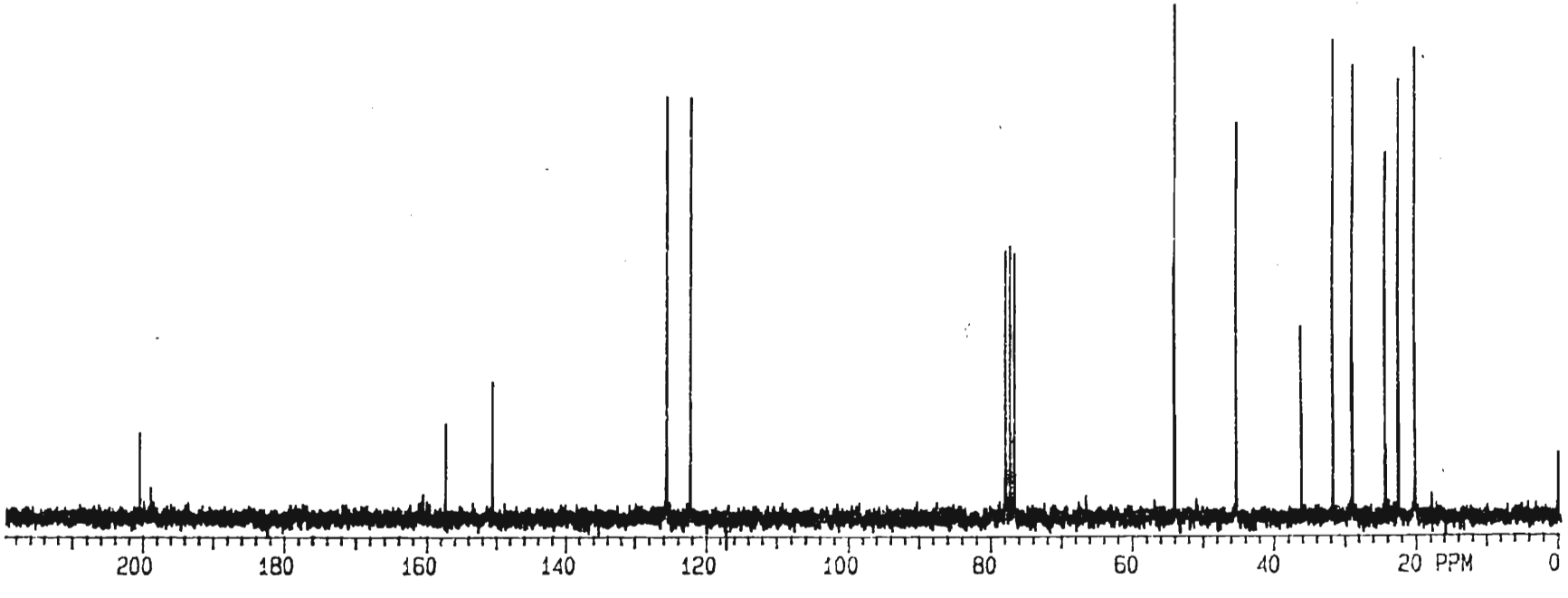
(105)

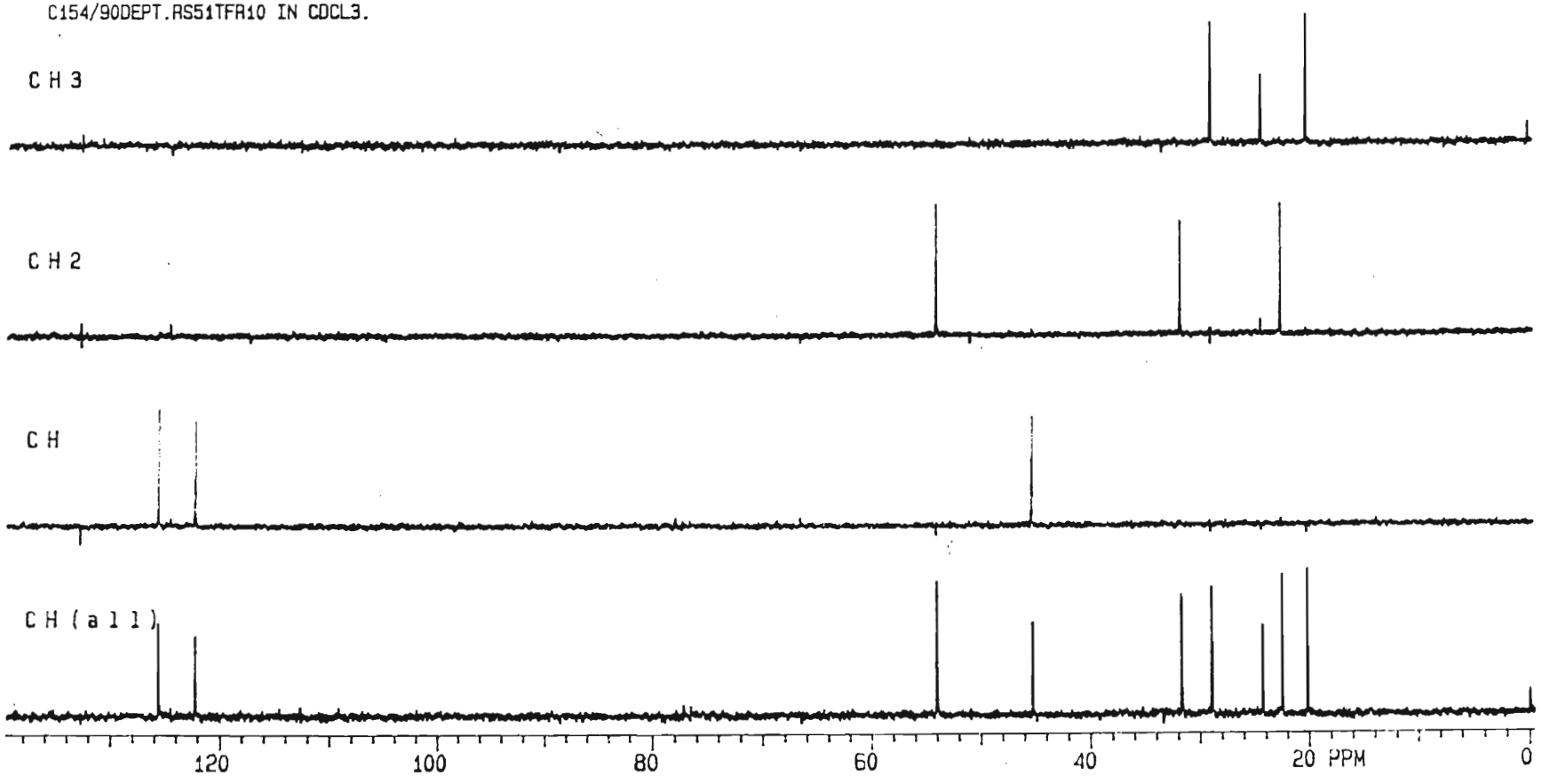

H90154.RS51TFR10 IN CDCL3/TMS.
RE=0.25sec.
AF=0.75sec.
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM

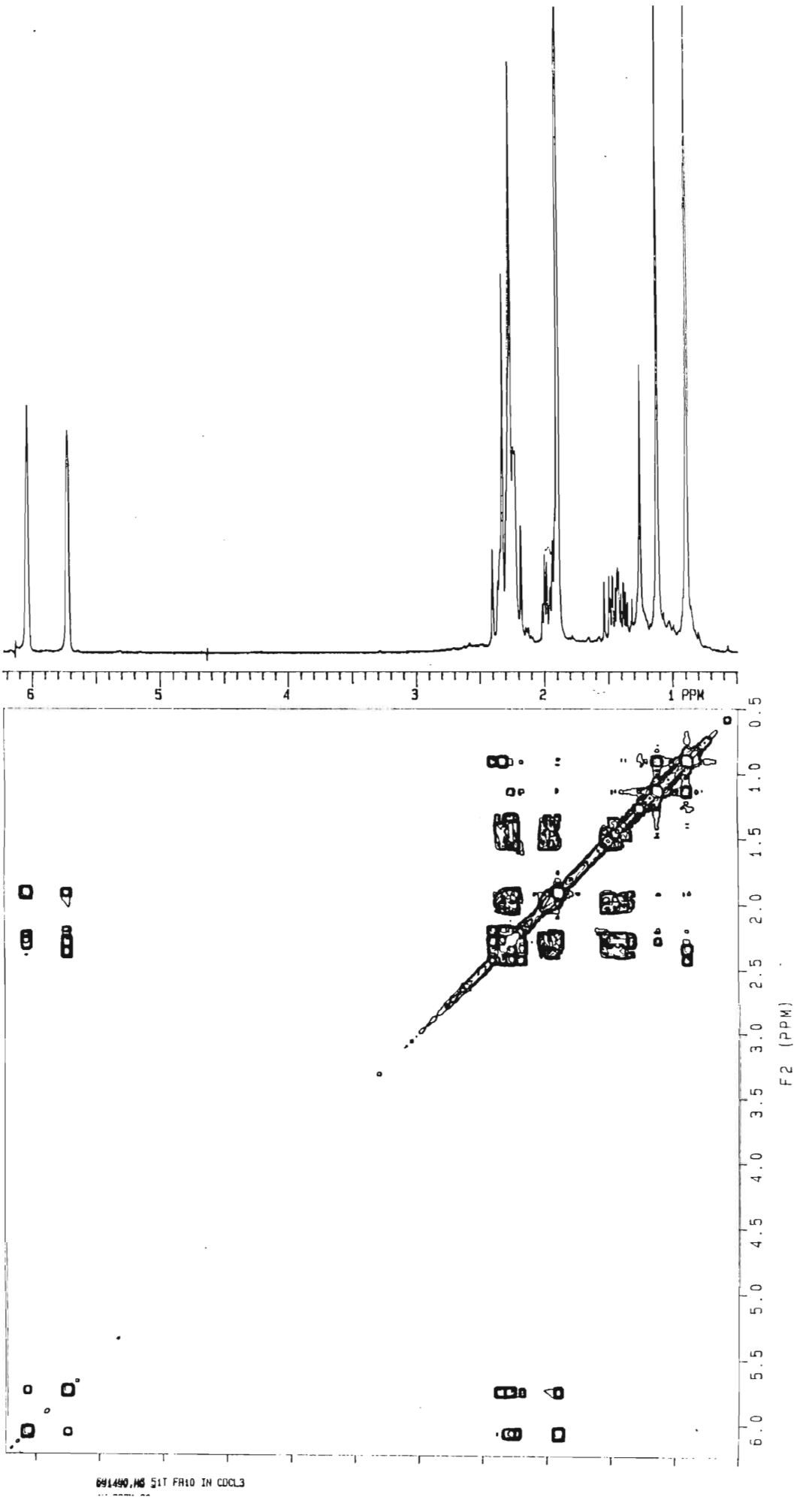
H90154.RS51TFR10 IN CDCL3/TMS.
Res.Enhancement=0,20sec.
Apod.Function=0,75sec.

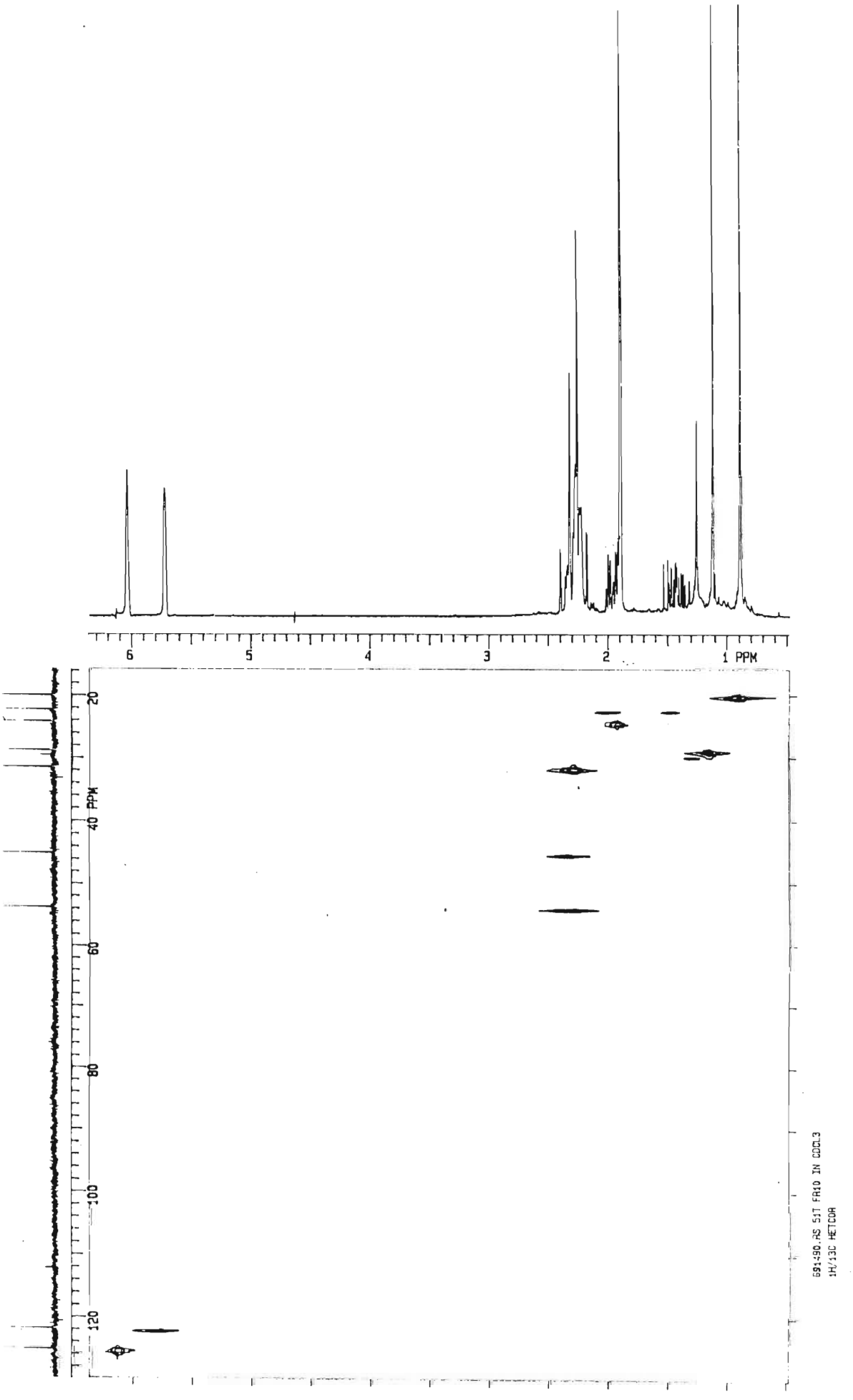


C154/90PND.RS51TFR10 IN CDCL3.

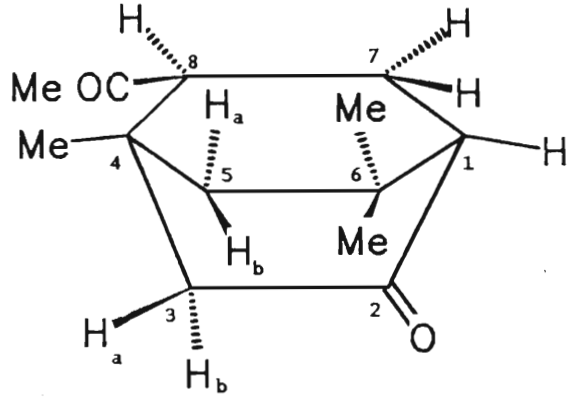



C154/90DEPT.RS51TFR10 IN CDCL3.
C H 3
C H 2
C H
C H (a l l)
120
100
80
60
40
20 PPM
0

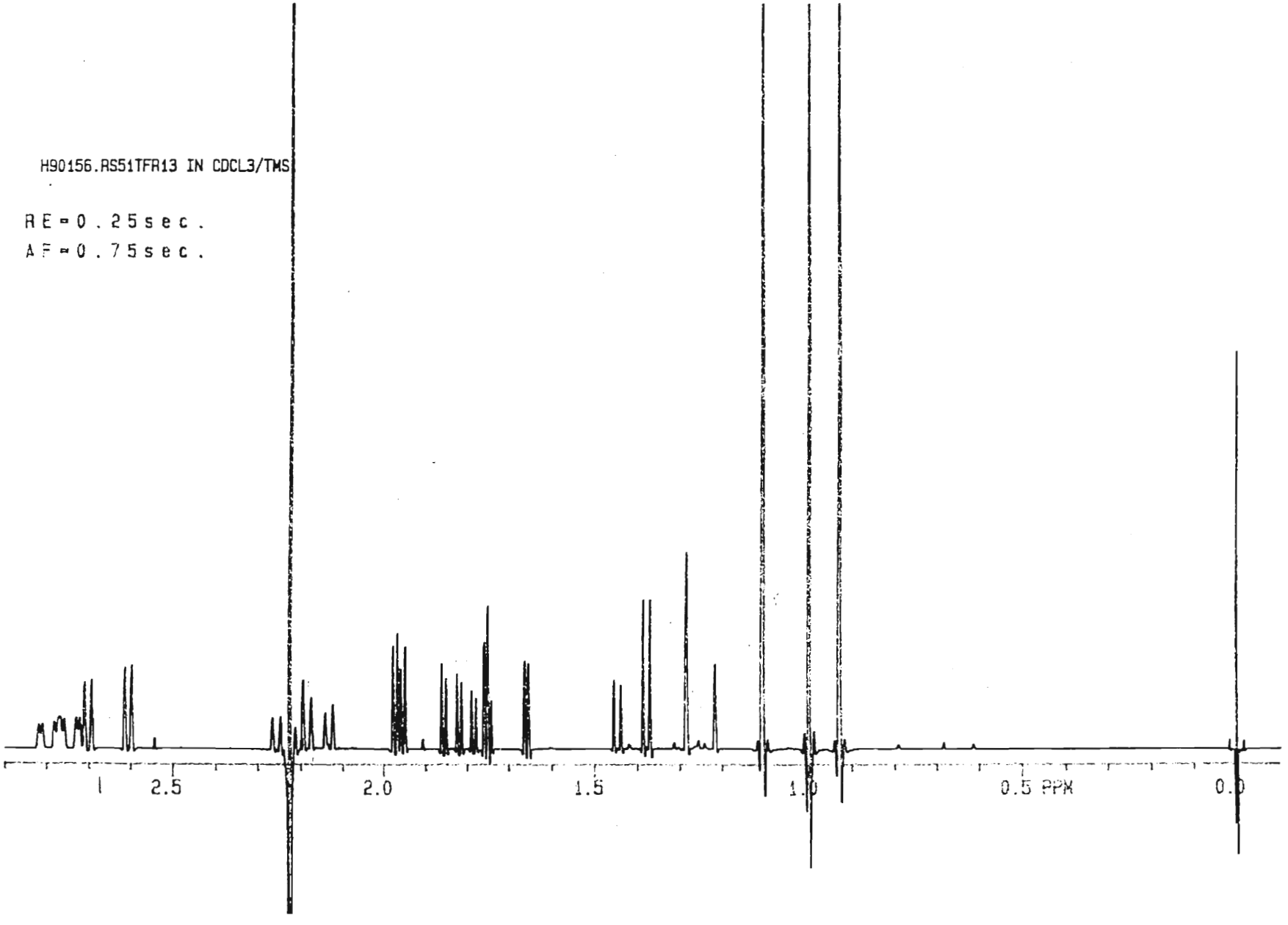

6
5
4
3
2
1 PPM
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
4.5
5.0
5.5
6.0
F2 (PPM)
691490,MS 51T FR10 IN CDCL3


6
5
4
3
2
1 PPM
20
40 PPM
60
80
100
120
691-90.AS 517 FA10 IN CDCL3
1H/13C HETCOR

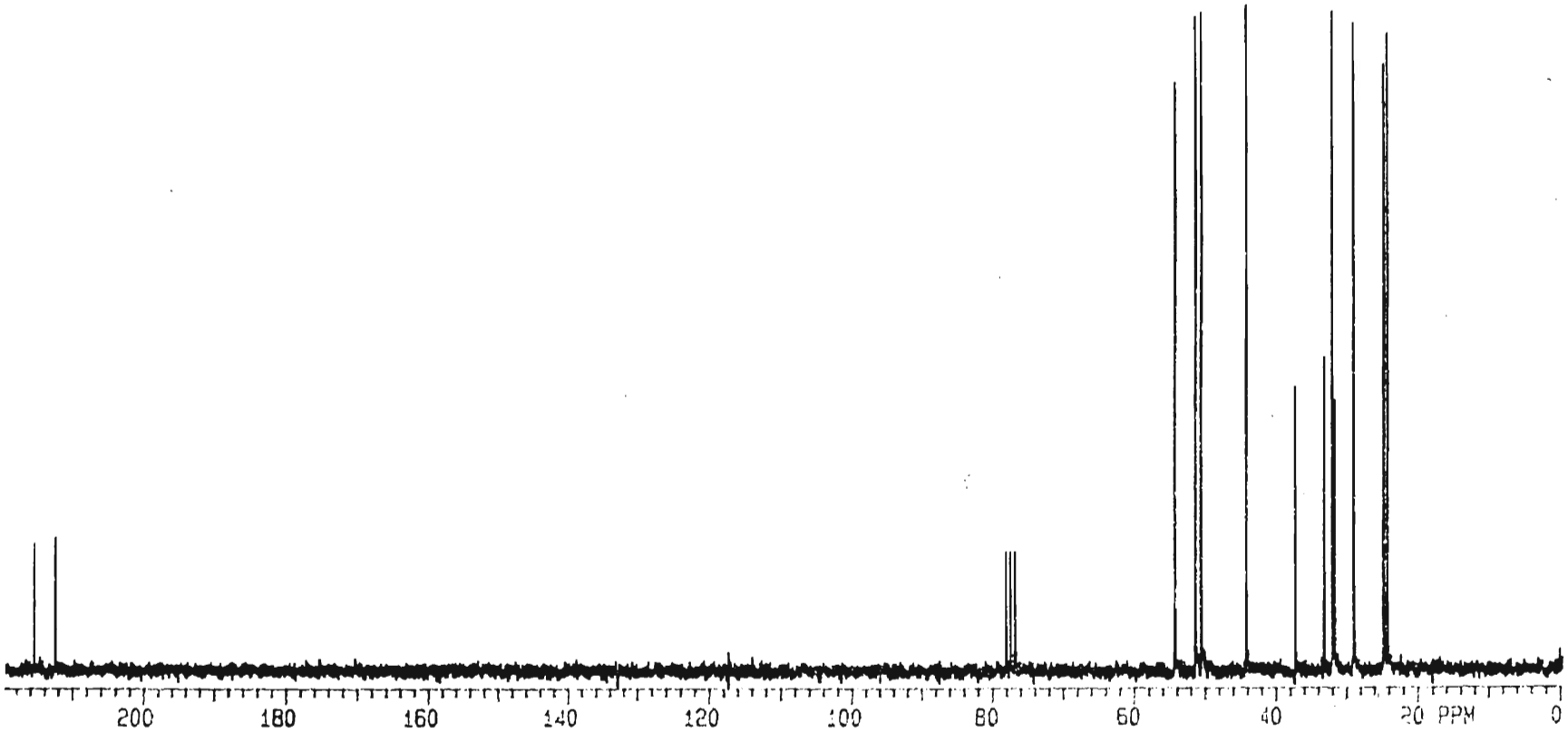
H90156.RS51TFR13 IN CDCL3/TMS.

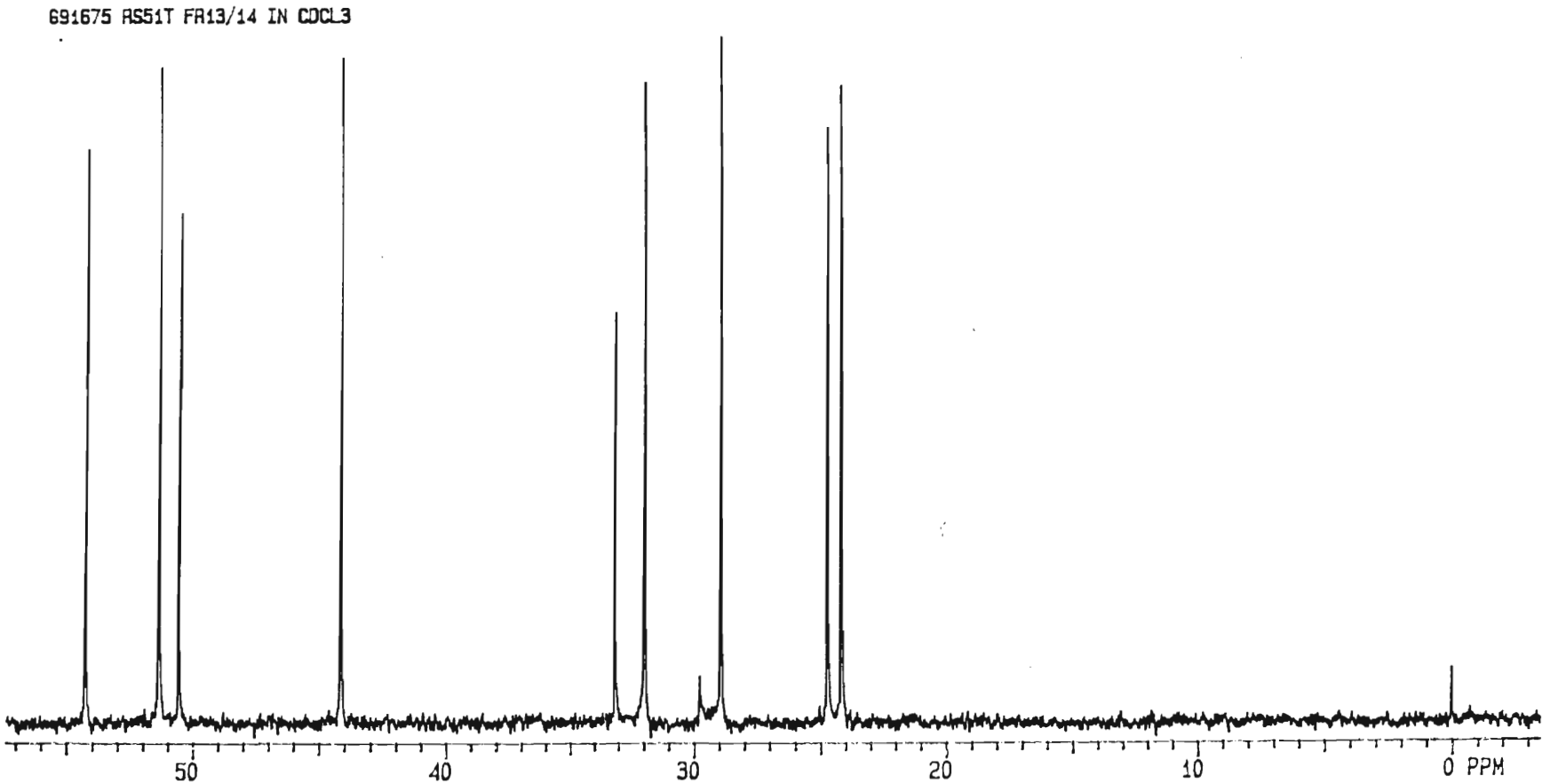


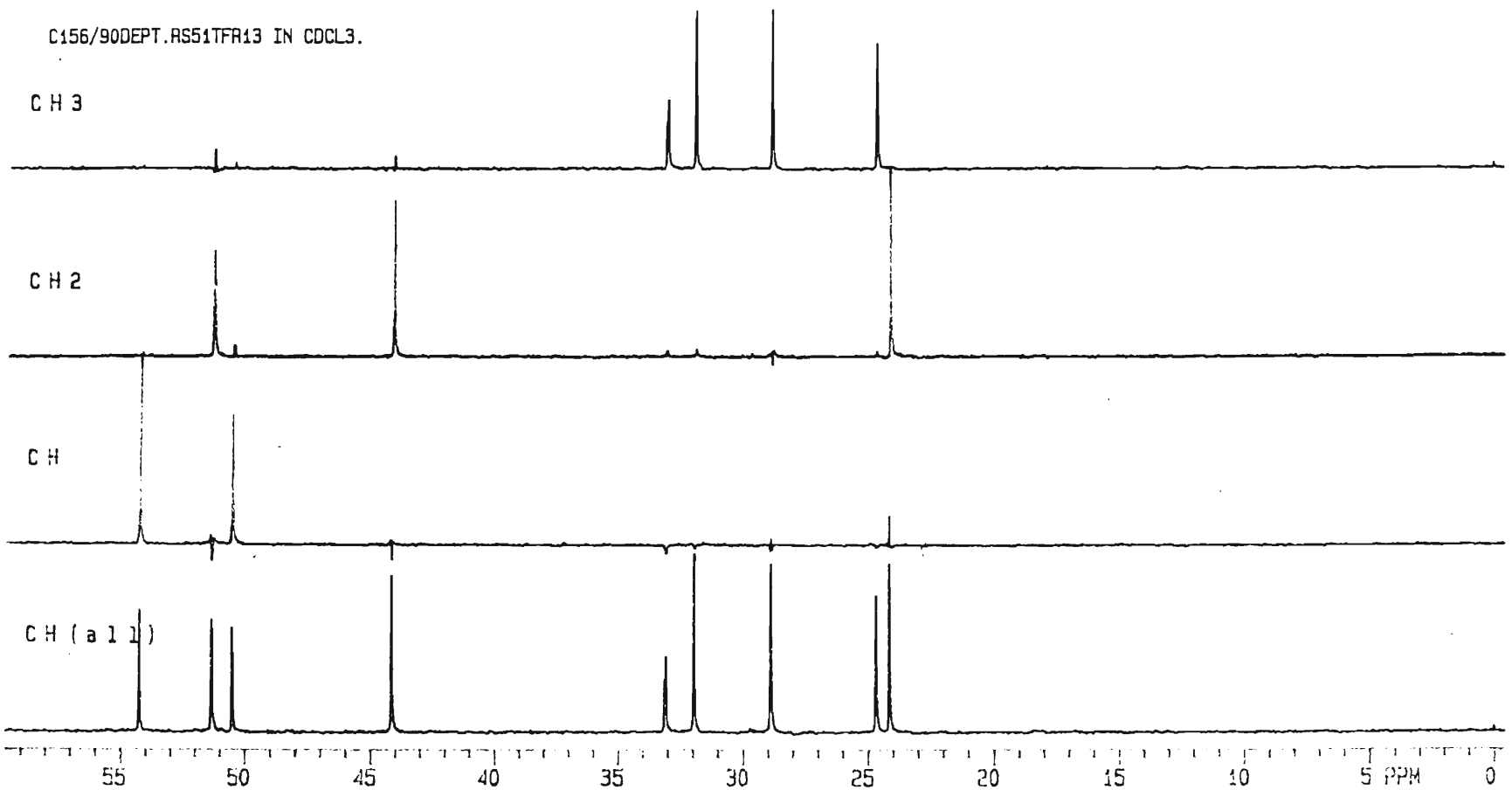
(111)

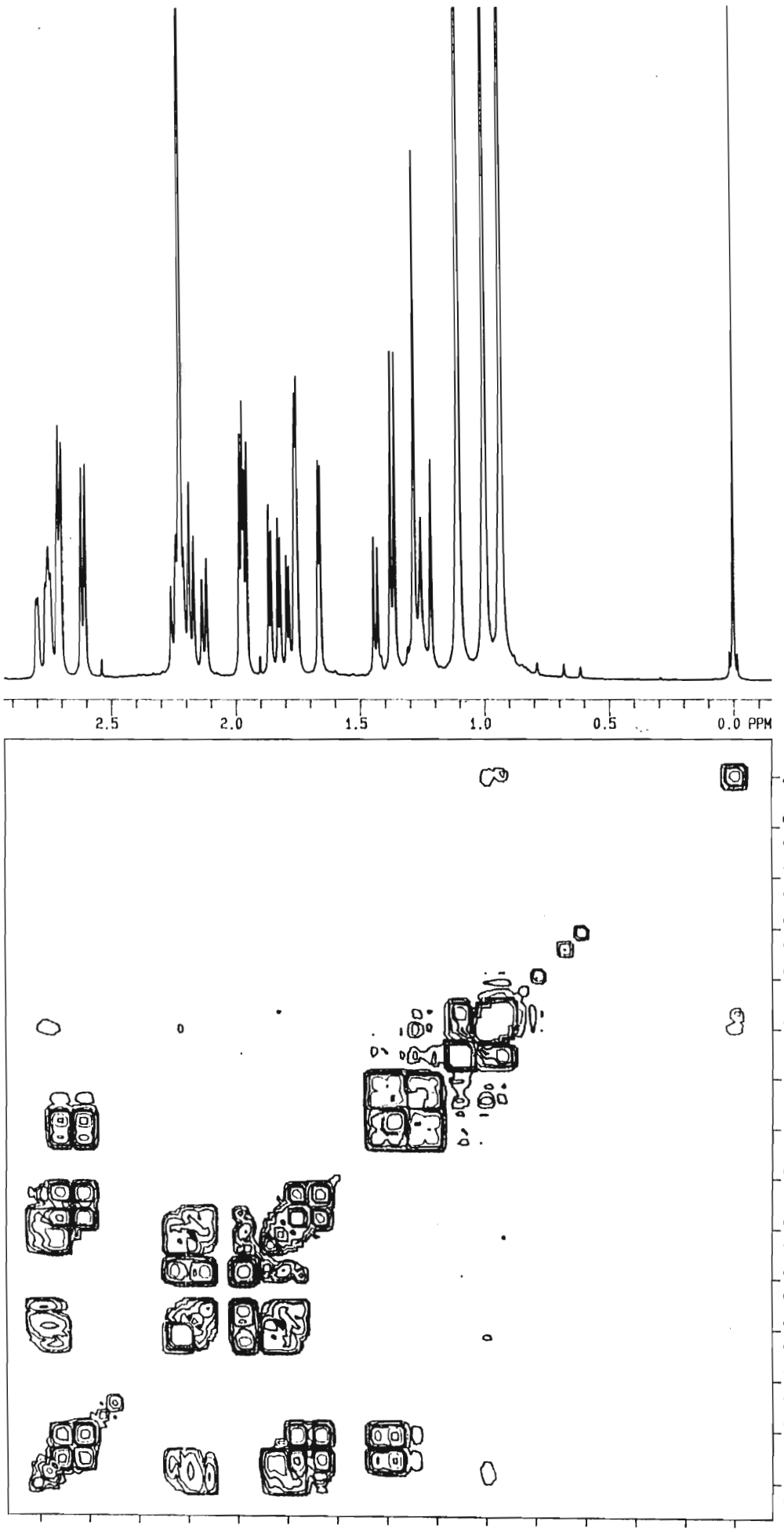

H90156.RS51TFR13 IN CDCL3/TMS
RE=0.25sec.
AF=0.75sec.
2.5
2.0
1.5
1.0
0.5 PPM
0.0

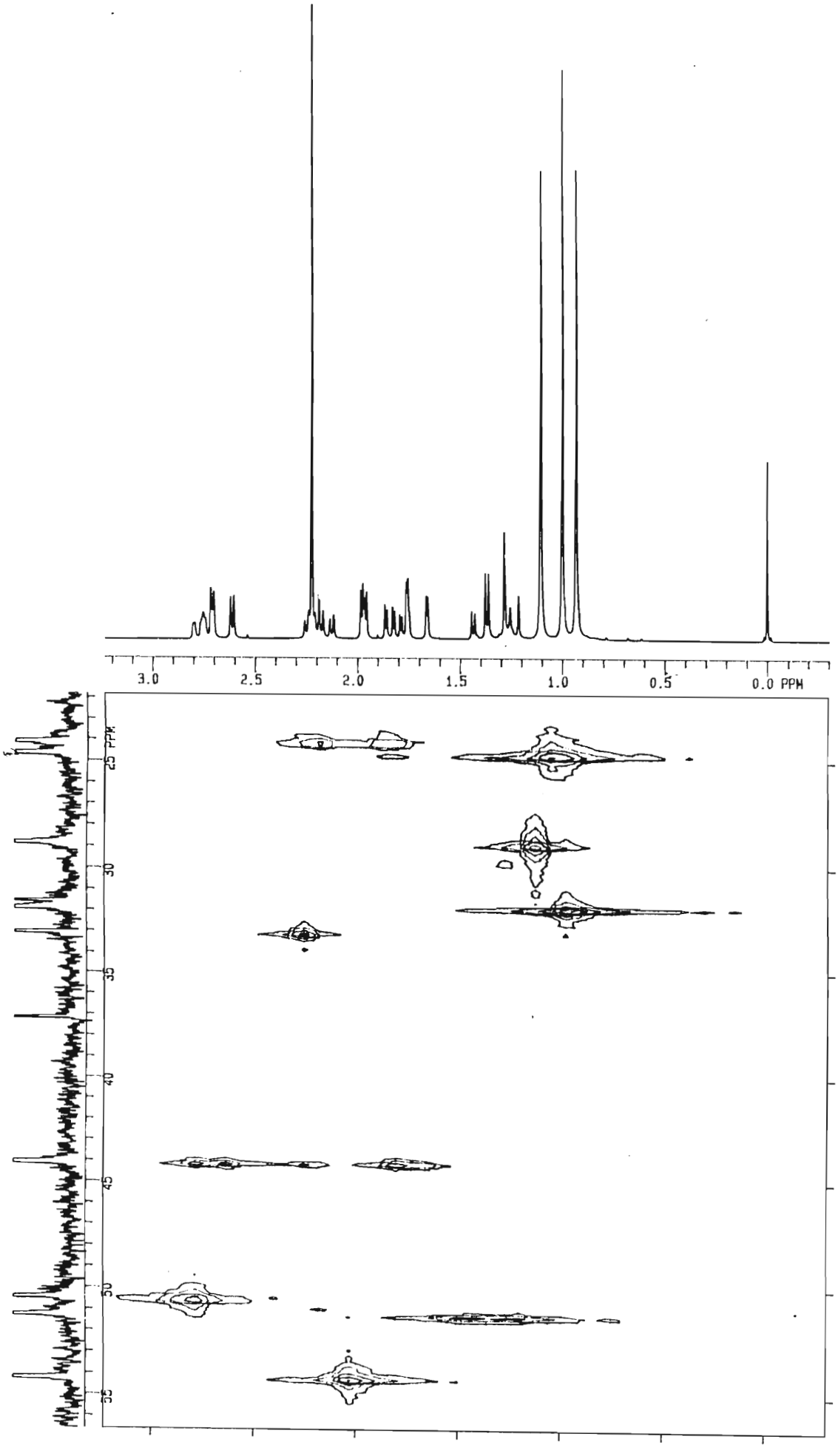
C156/90PND.RS51TFR13 IN CDCL3.



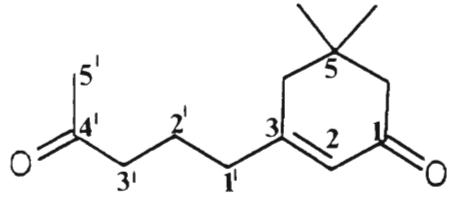

691675 RS51T FR13/14 IN CDCL3
50
40
30
20
10
0 PPM


C156/90DEPT.RS51TFR13 IN CDCL3.
C H 3
C H 2
C H
C H (a l l)
55
50
45
40
35
30
25
20
15
10
5 PPM
0

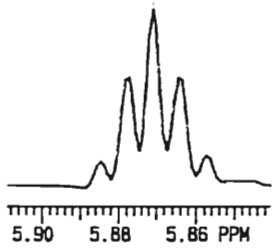

2.5
2.0
1.5
1.0
0.5
0.0 PPM
2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0
F2 (PPM)
891675 ASSIT FR13/14 IN CDCL3
1H-1H COSY 60


3.0
2.5
2.0
1.5
1.0
0.5
0.0 PPM
25 PPM
30
35
40
45
50
55
C:\56/90RND.RS\TFR13 IN CDCL3.
1H-13C HETCOR

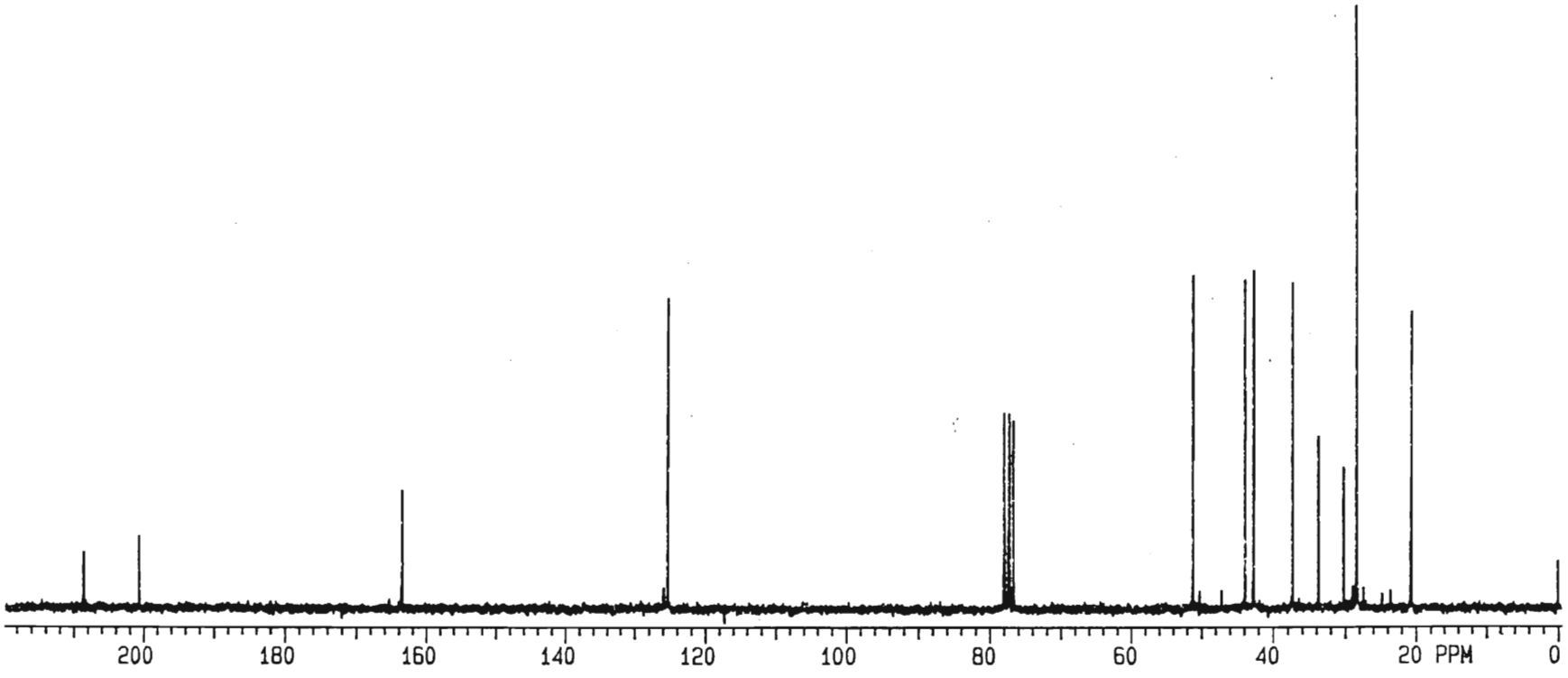
H90160.RS51TFR29 IN CDCL3/TMS.

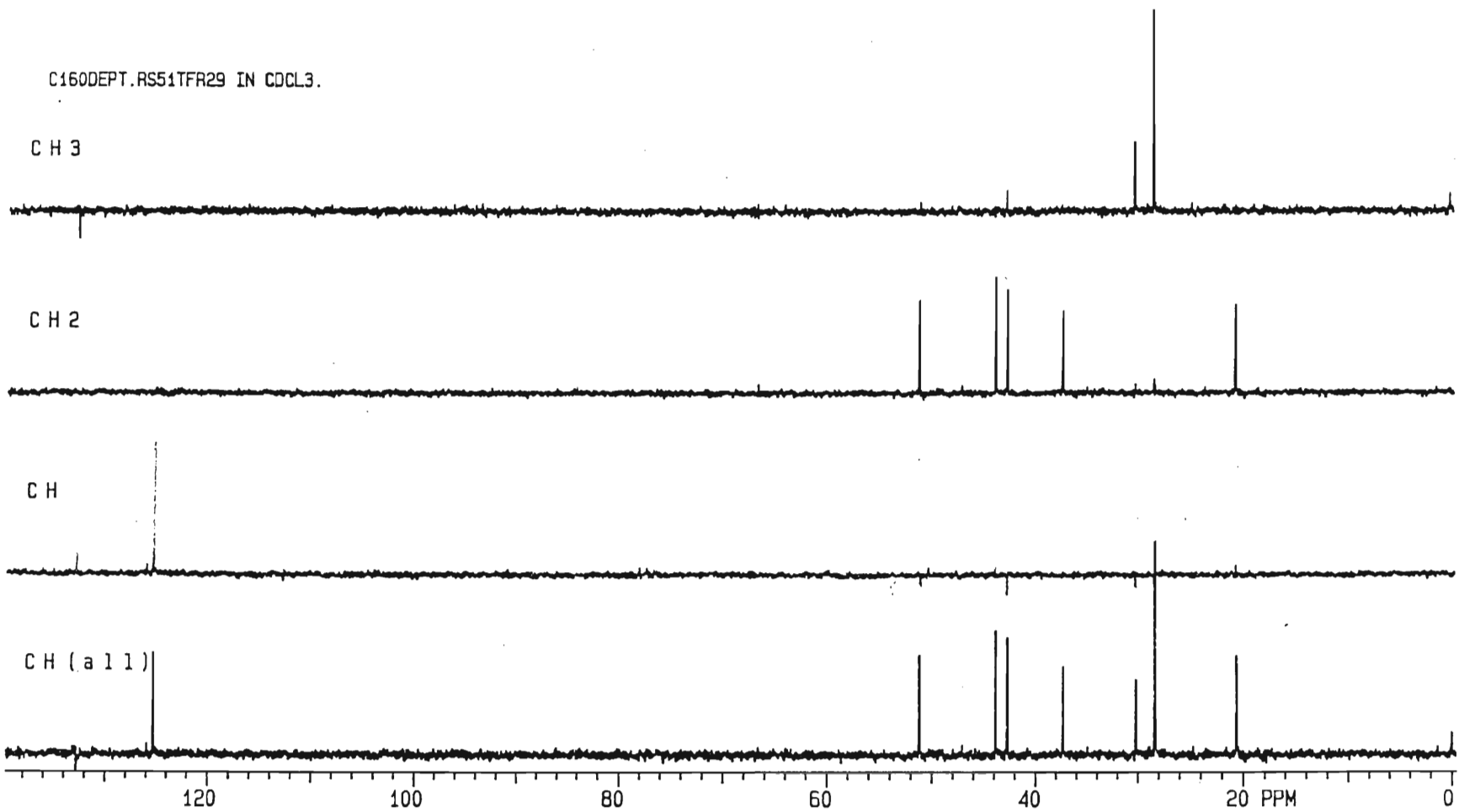


(104)

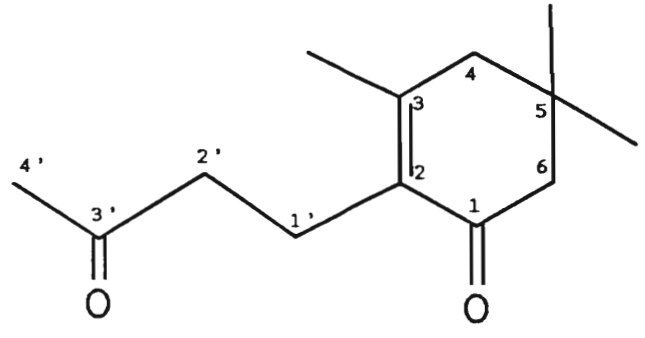


C160/90PND.RS51TFR29 IN CDCL3.

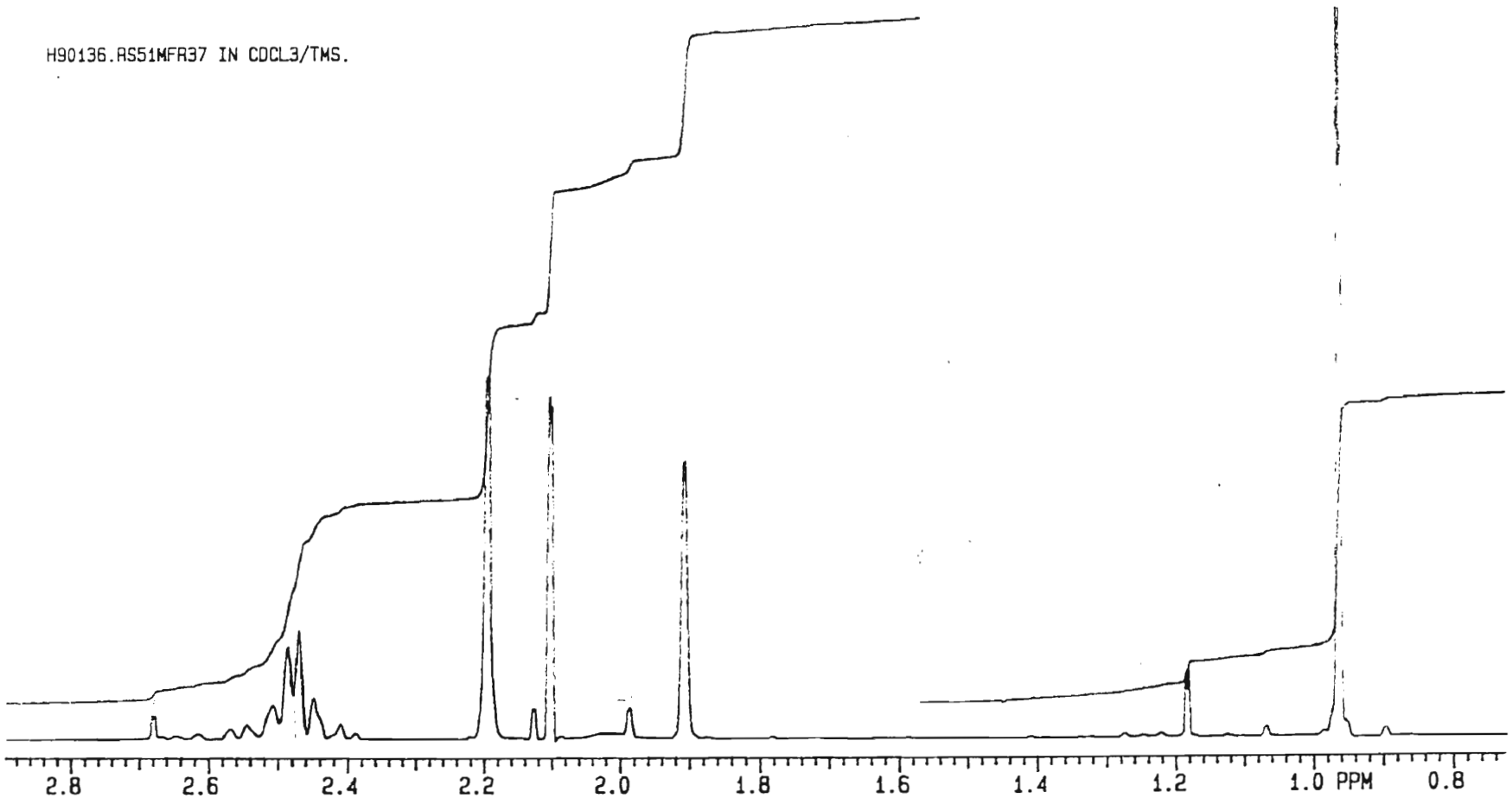


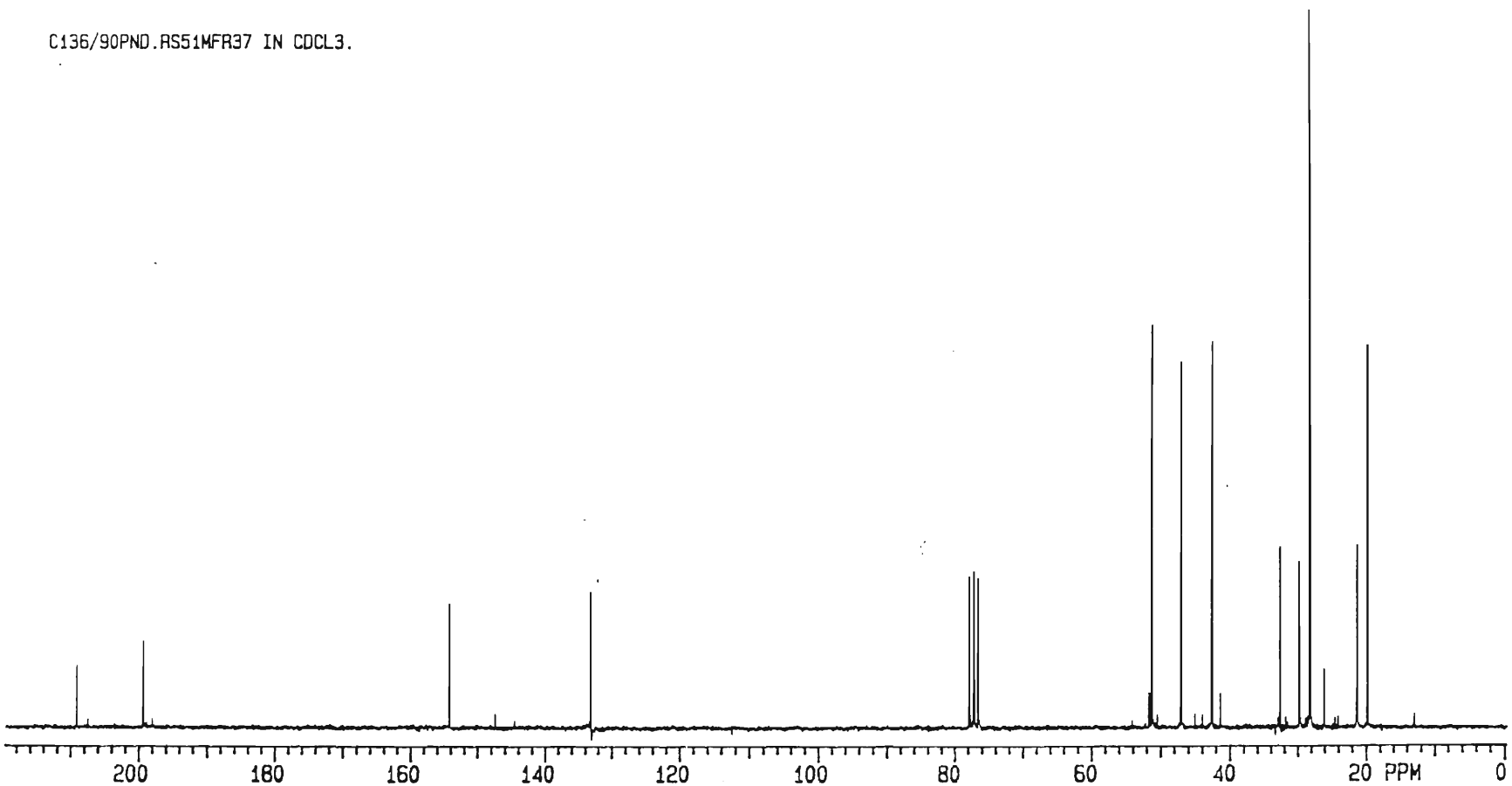

C160DEPT.RS51TFR29 IN CDCL3.
C H 3
C H 2
C H
C H (a l l)
120
100
80
60
40
20 PPM
0

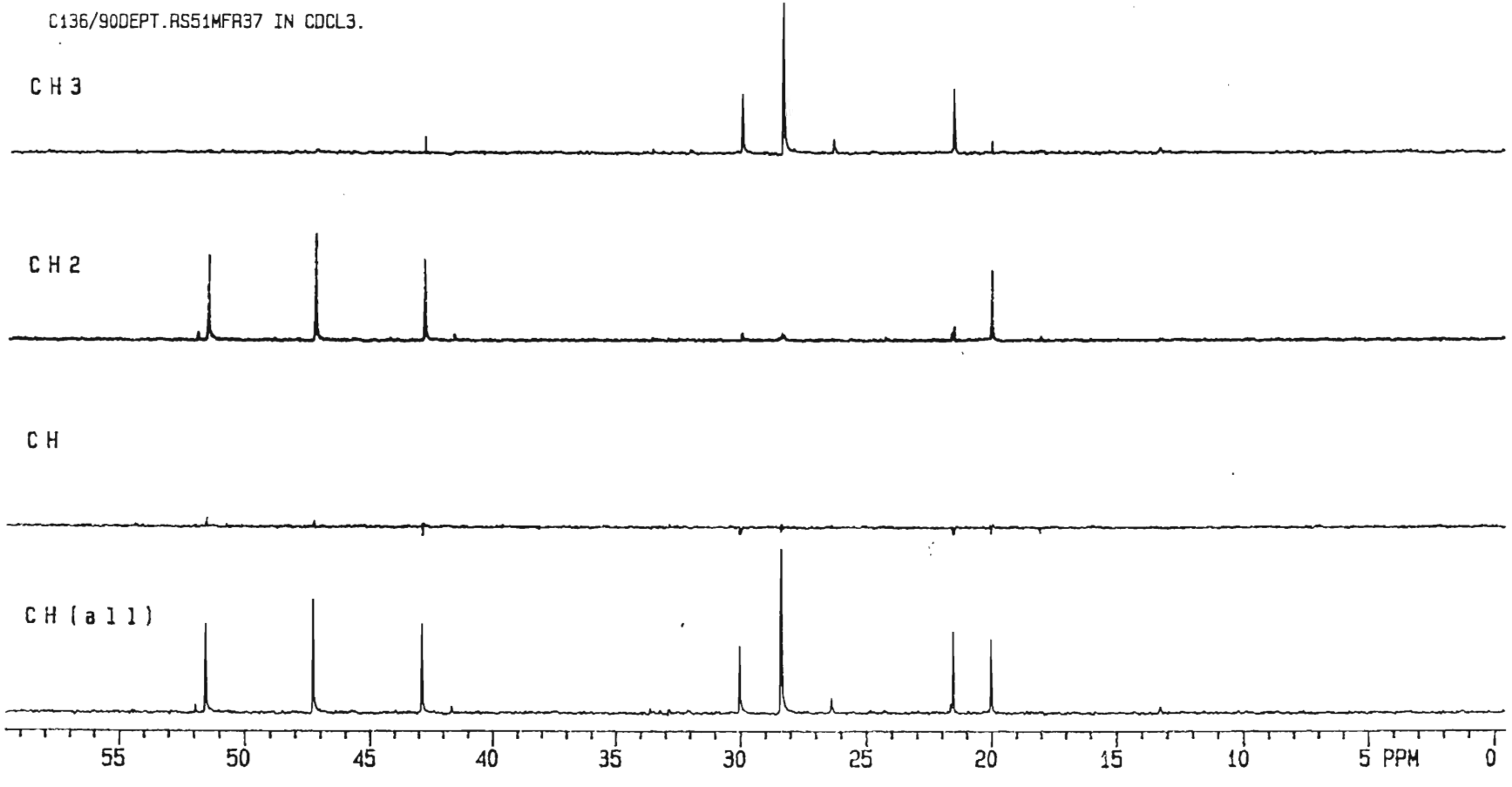
H90136.RS51MFR37 IN CDCL3/TMS.

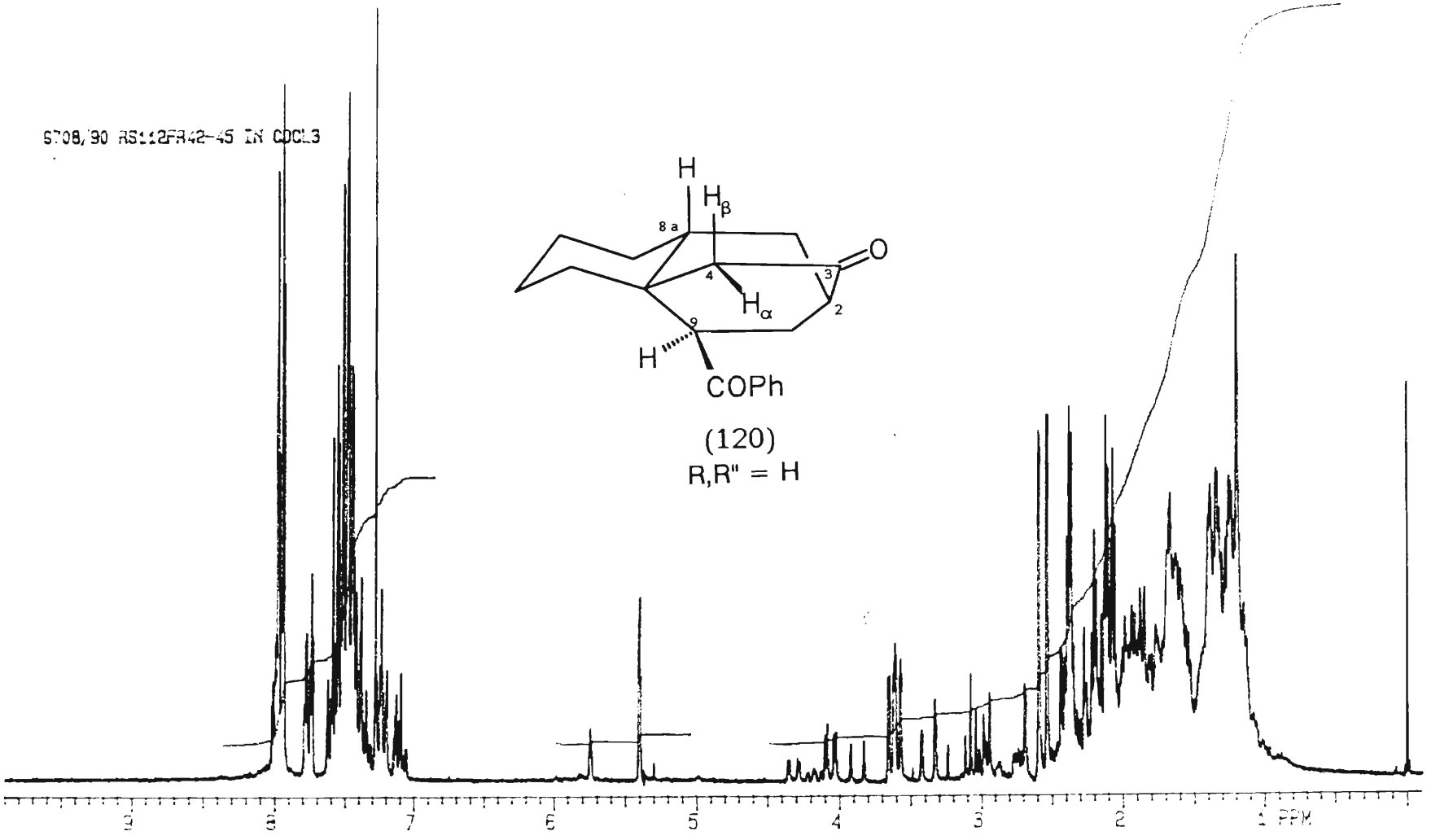


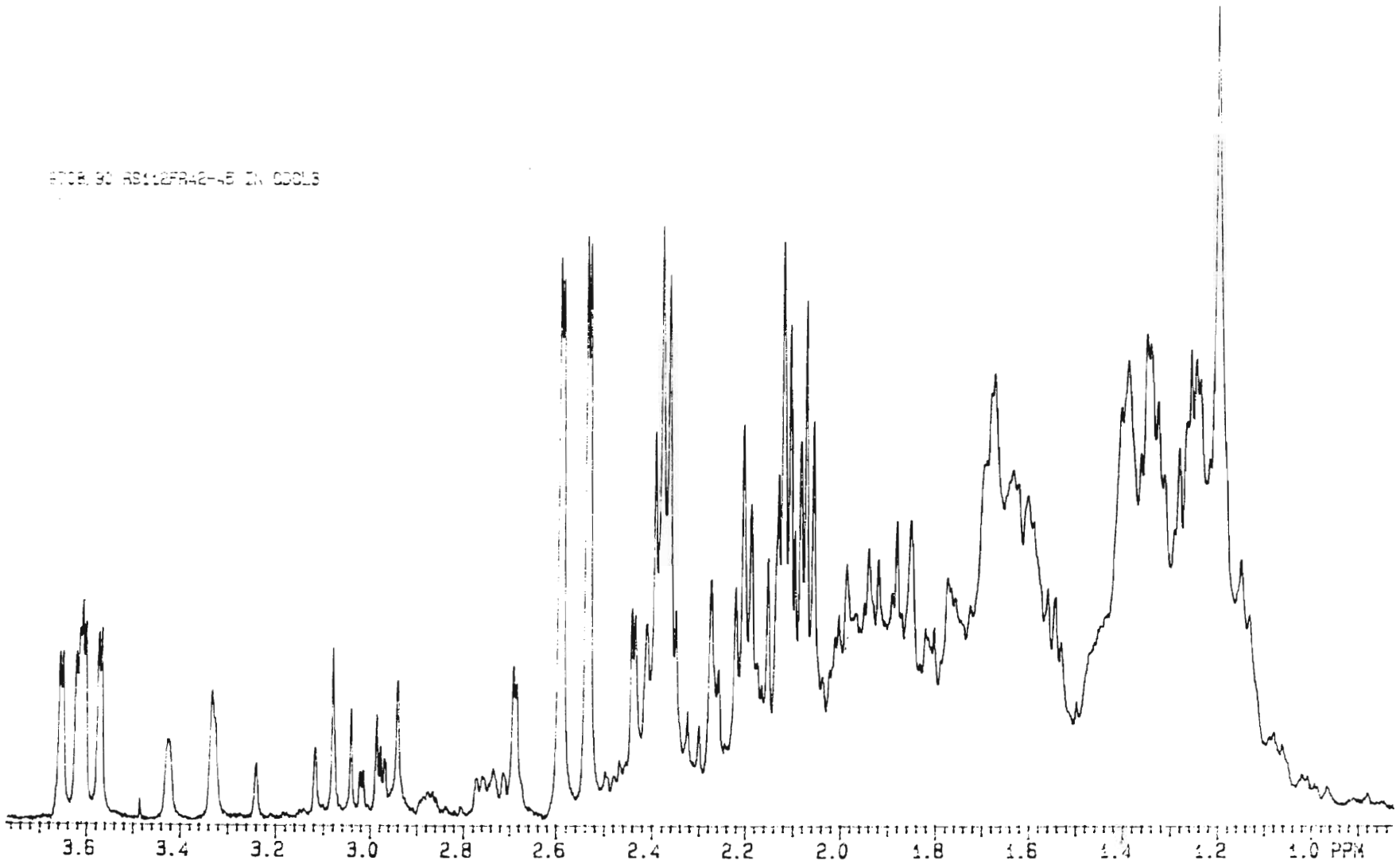
(48)

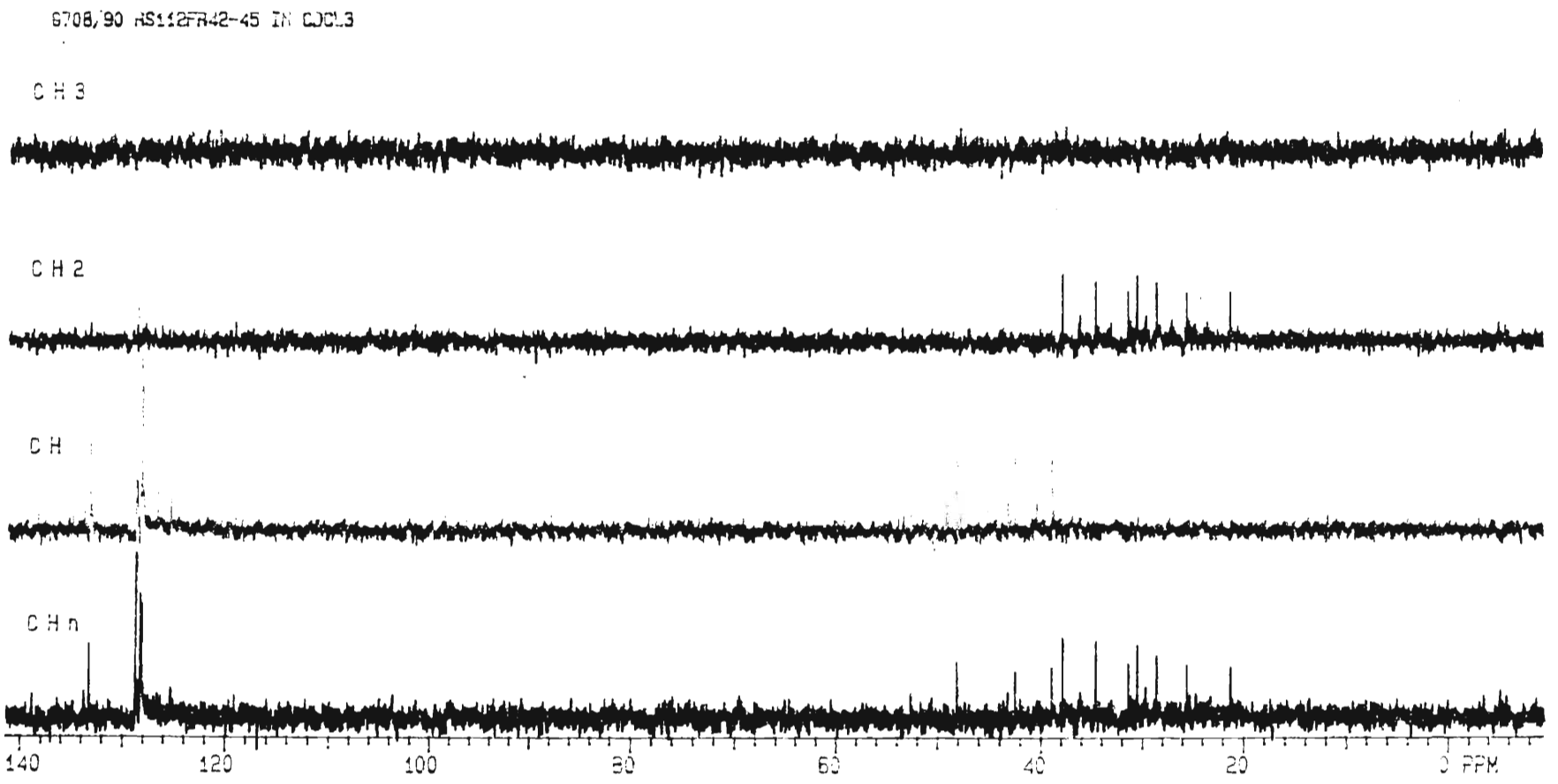

H90136.AS51MFR37 IN CDCL3/TMS.
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM
0.8

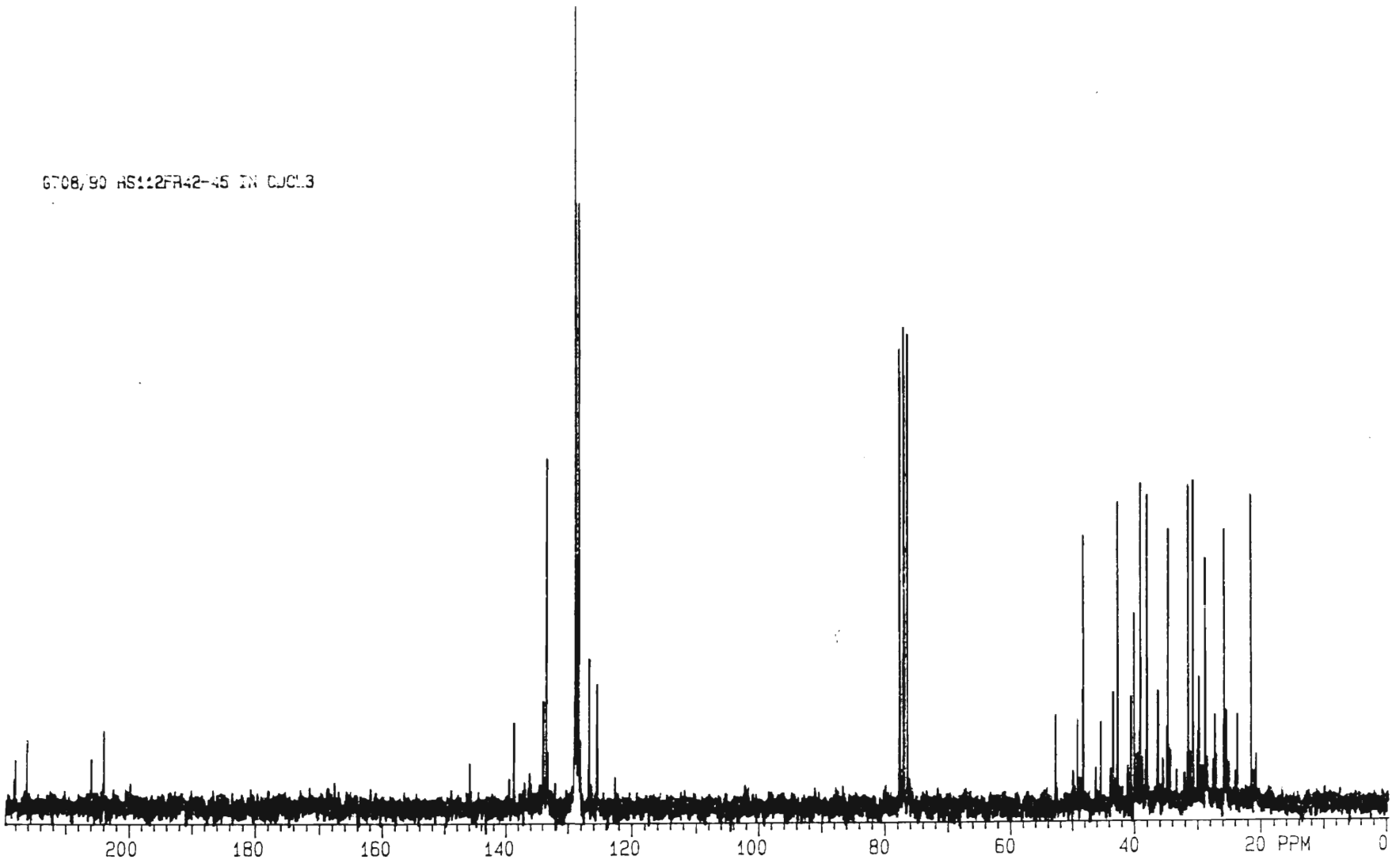

C136/90PND.RS51MFR37 IN CDCL3.
200
180
160
140
120
100
80
60
40
20 PPM
0

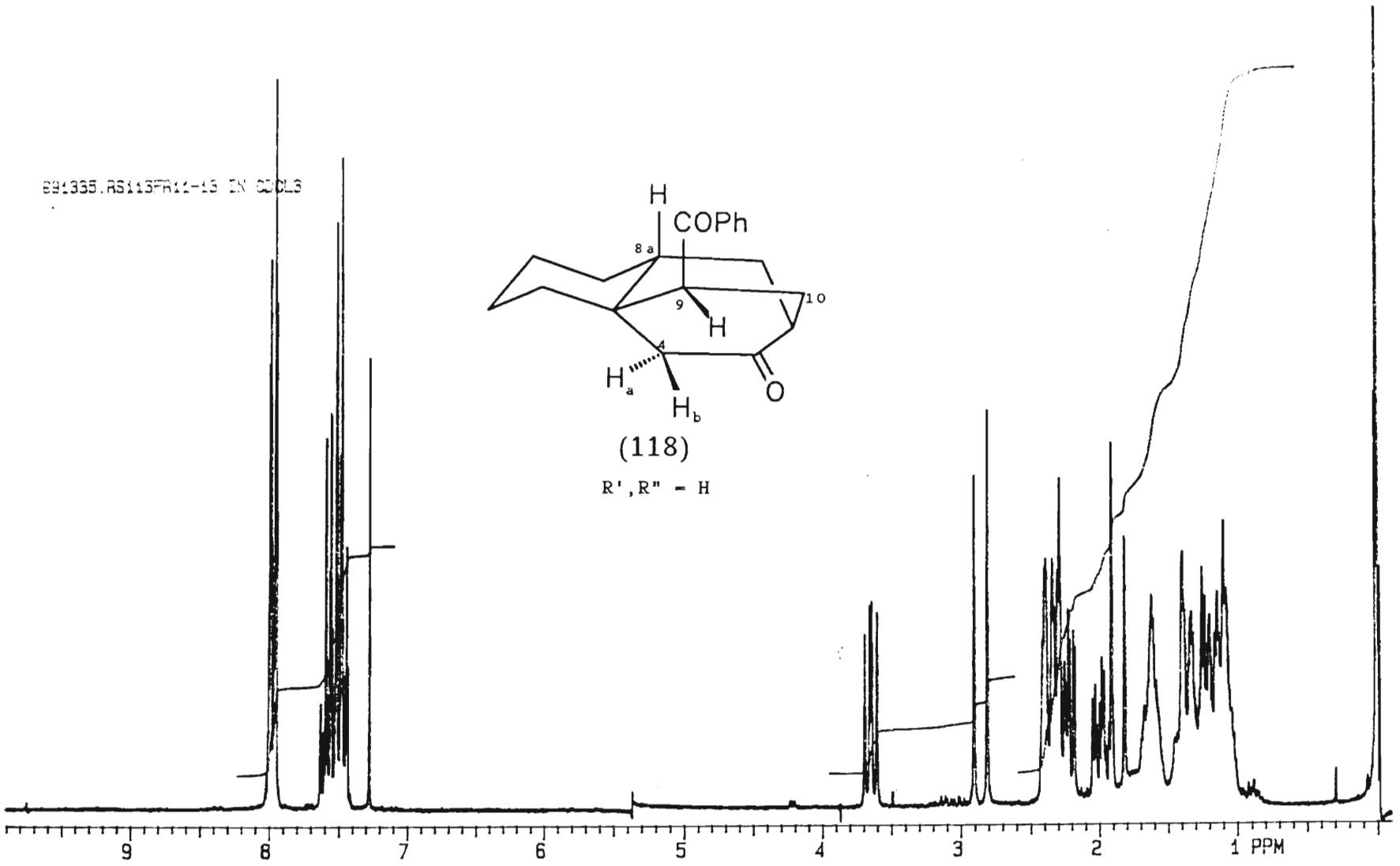

C136/90DEPT.RS51MFR37 IN CDCL3.
C H 3
C H 2
C H
C H (a l l)
55
50
45
40
35
30
25
20
15
10
5 PPM
0


S708/90 RS112FR42-45 IN CDCL3
H
Hβ
8a
O
4
3
Hα
2
9
H
COPh
(120)
R,R" = H
3
6
7
5
4
3
2
1 PPM


3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM

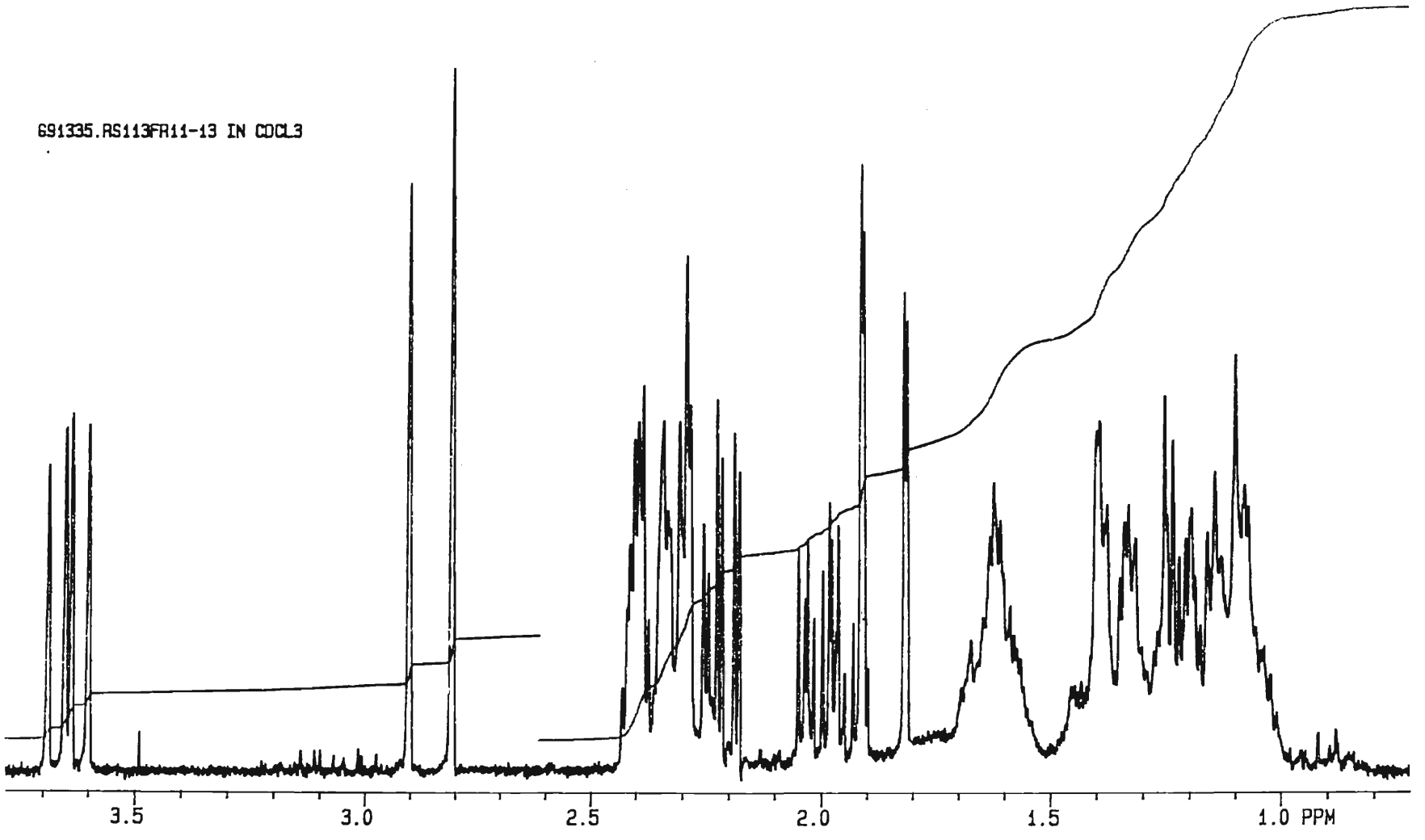

6708/90 HS112FR42-45 IN CDCL3
C H 3
C H 2
C H
C H n
140
120
100
80
60
40
20
0 PPM

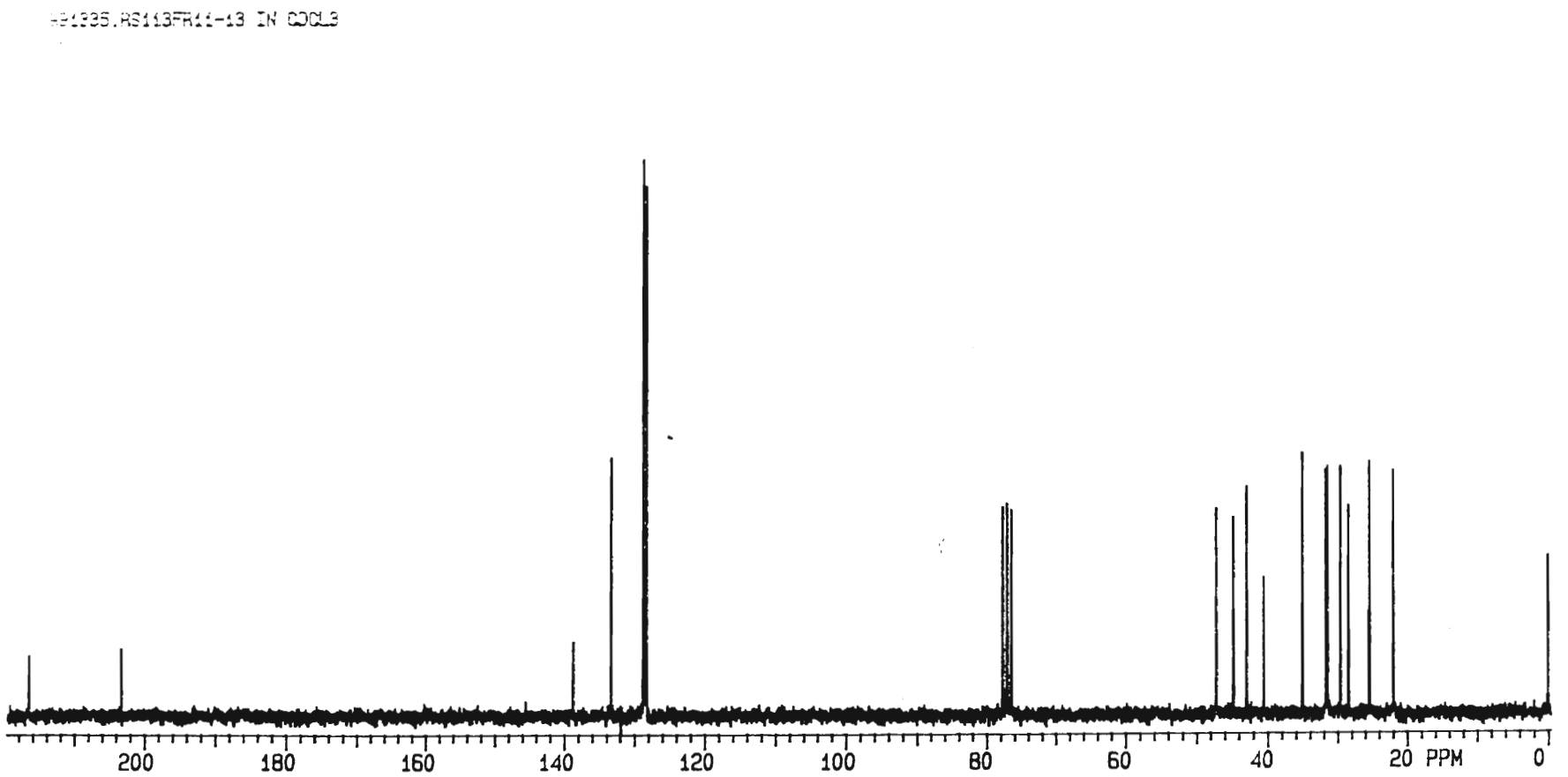

6708/90 HS112FR42-45 IN CDCL3
200
180
160
140
120
100
80
60
40
20 PPM
0

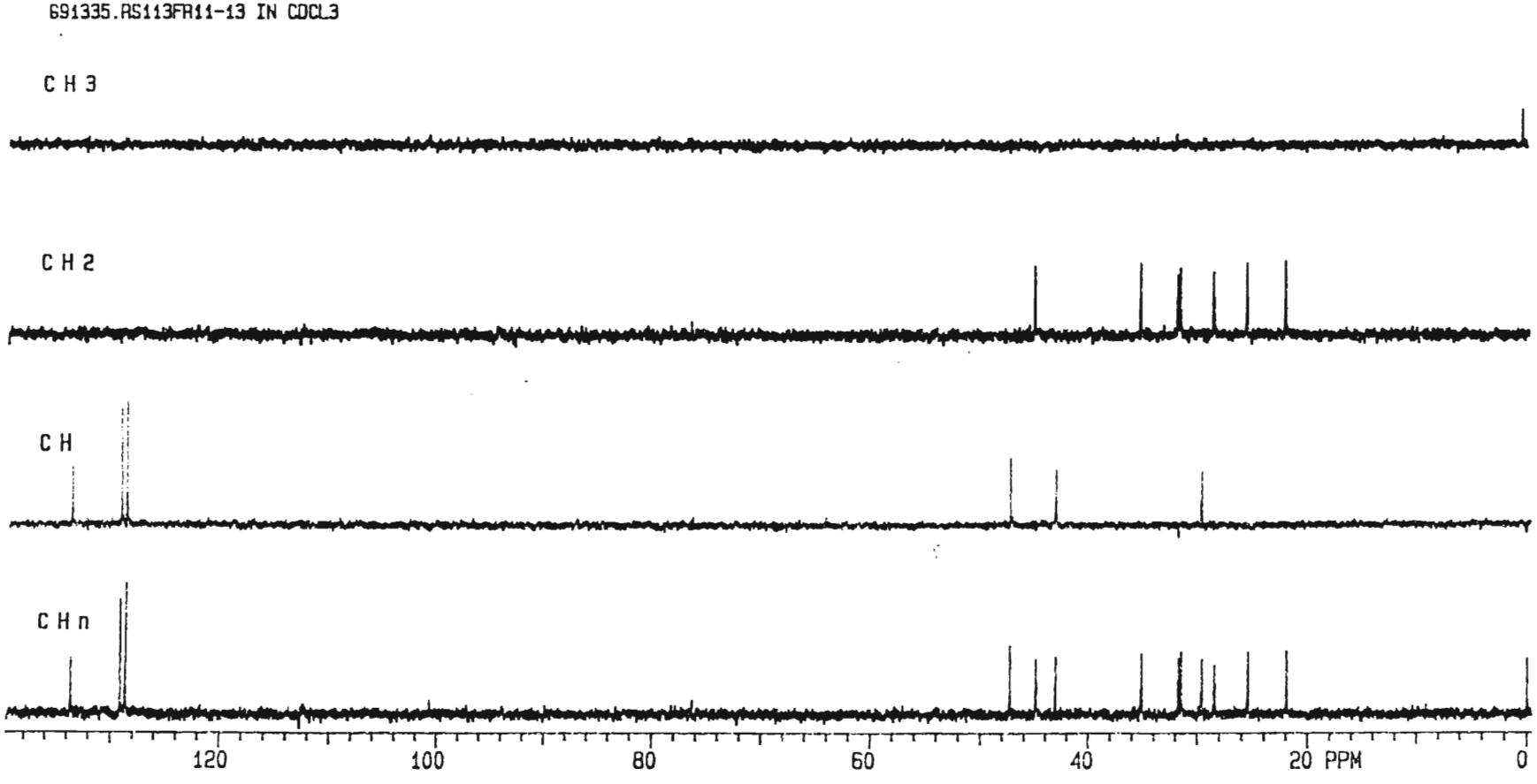

891365.RS113FR11-13 IN CDCL3
H
COPh
8a
9
10
H
4
H_a
H_b
O
9
8
7
6
5
4
3
2
1 PPM

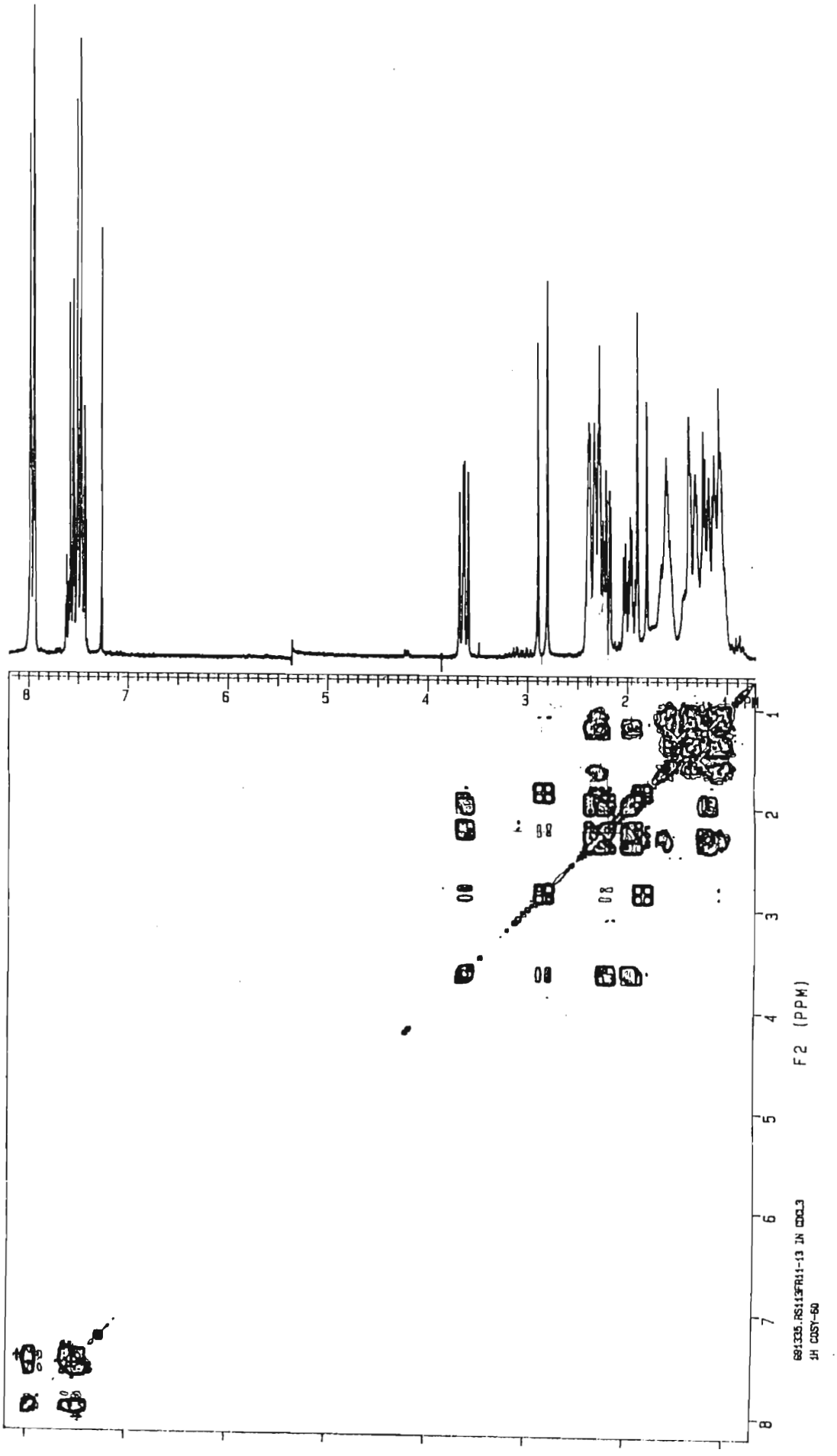
(118)

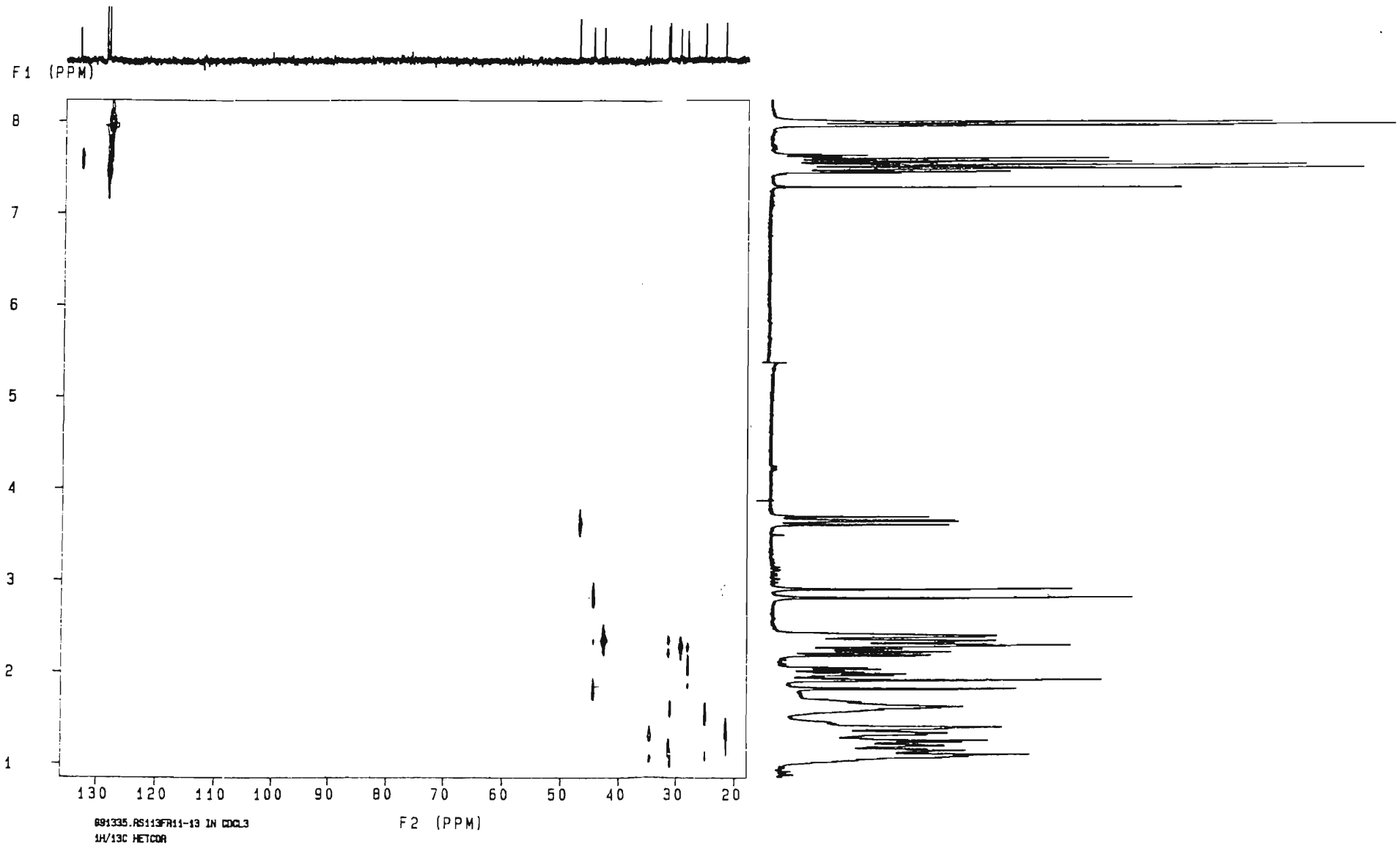
R',R" = H


691335.RS113FR11-13 IN CDCL3
3.5
3.0
2.5
2.0
1.5
1.0 PPM

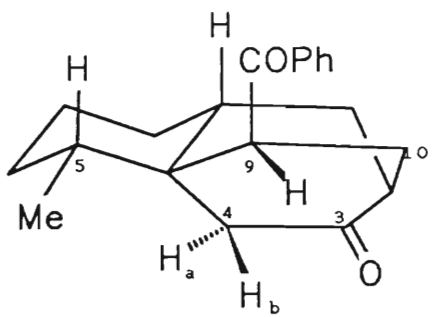

491335.RS113FR11-13 IN CDCL3
200
180
160
140
120
100
80
60
40
20 PPM
0


691335.RS113FR11-13 IN CDCL3
CH3
CH2
CH
CHn
120
100
80
60
40
20 PPM
0


8
7
6
5
4
3
2
PM
1
2
3
4
5
6
7
8
F2 (PPM)
881335.RS113FR11-13 IN CDCL3
1H COSY-60


F1 (PPM)
8
7
6
5
4
3
2
1
130
120
110
100
90
80
70
60
50
40
30
20
F2 (PPM)
691335.RS113FR11-13 IN CDCL3
1H/13C HETCOR

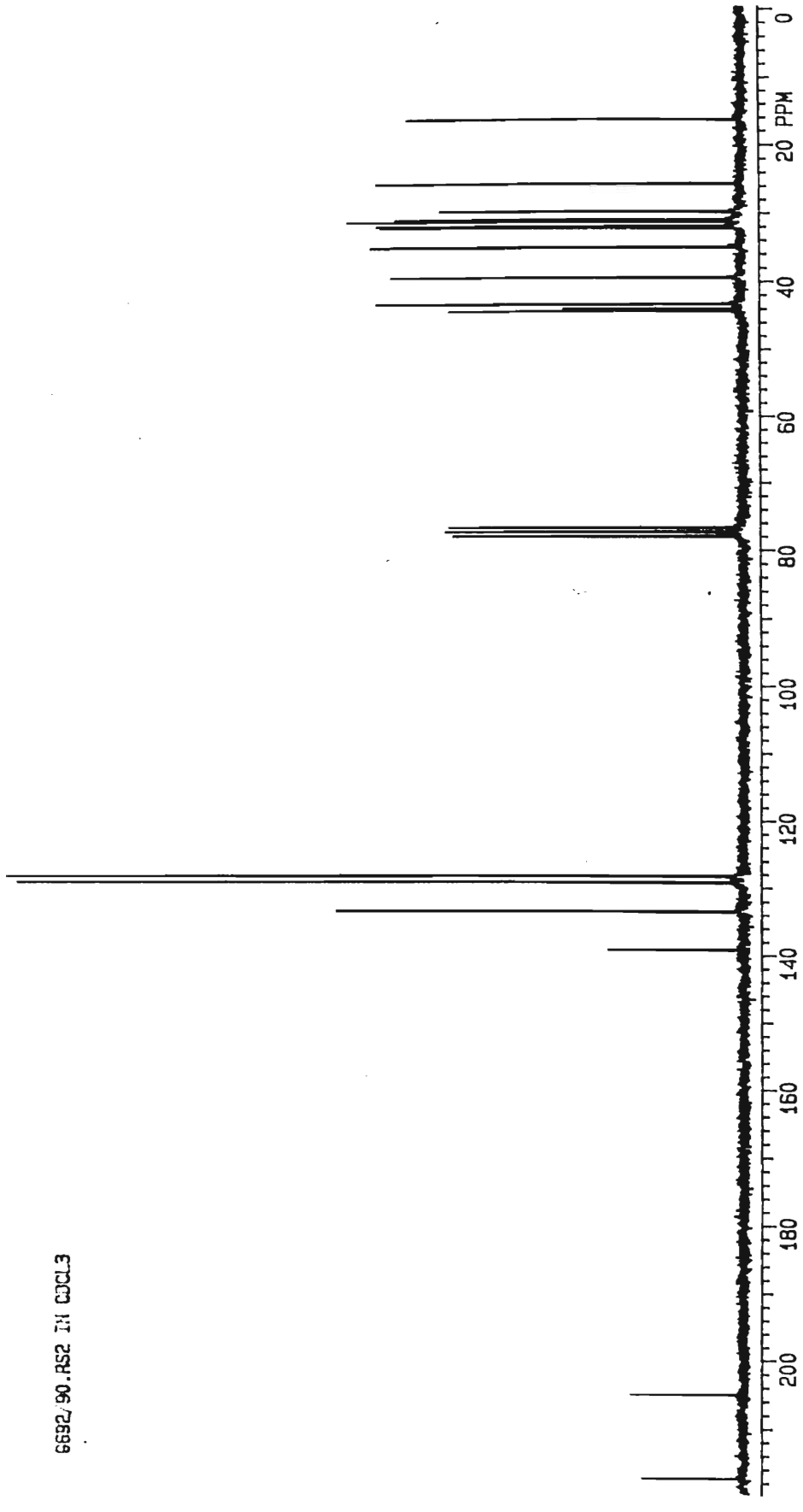
6692/90.RS2 IN CDCl3

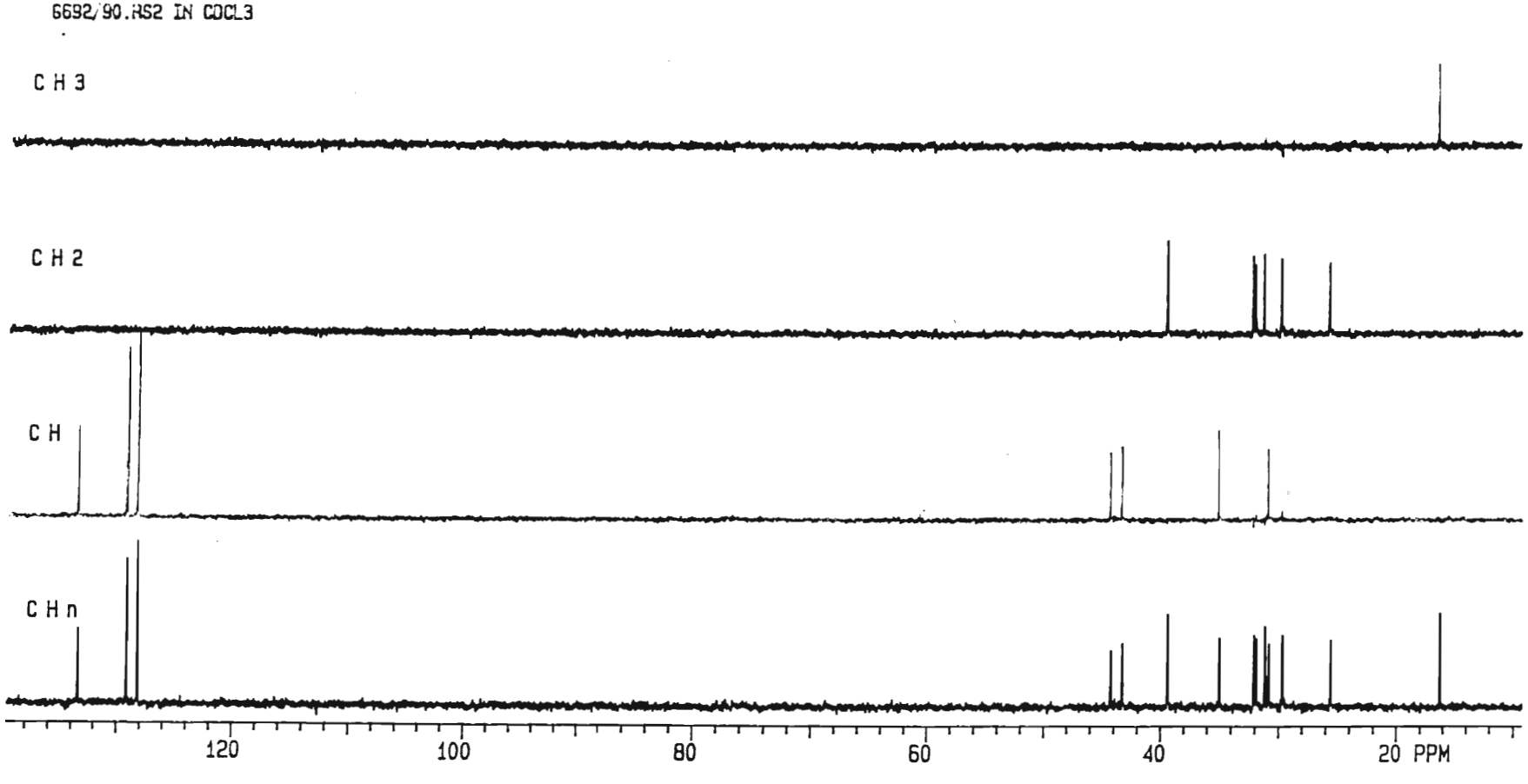


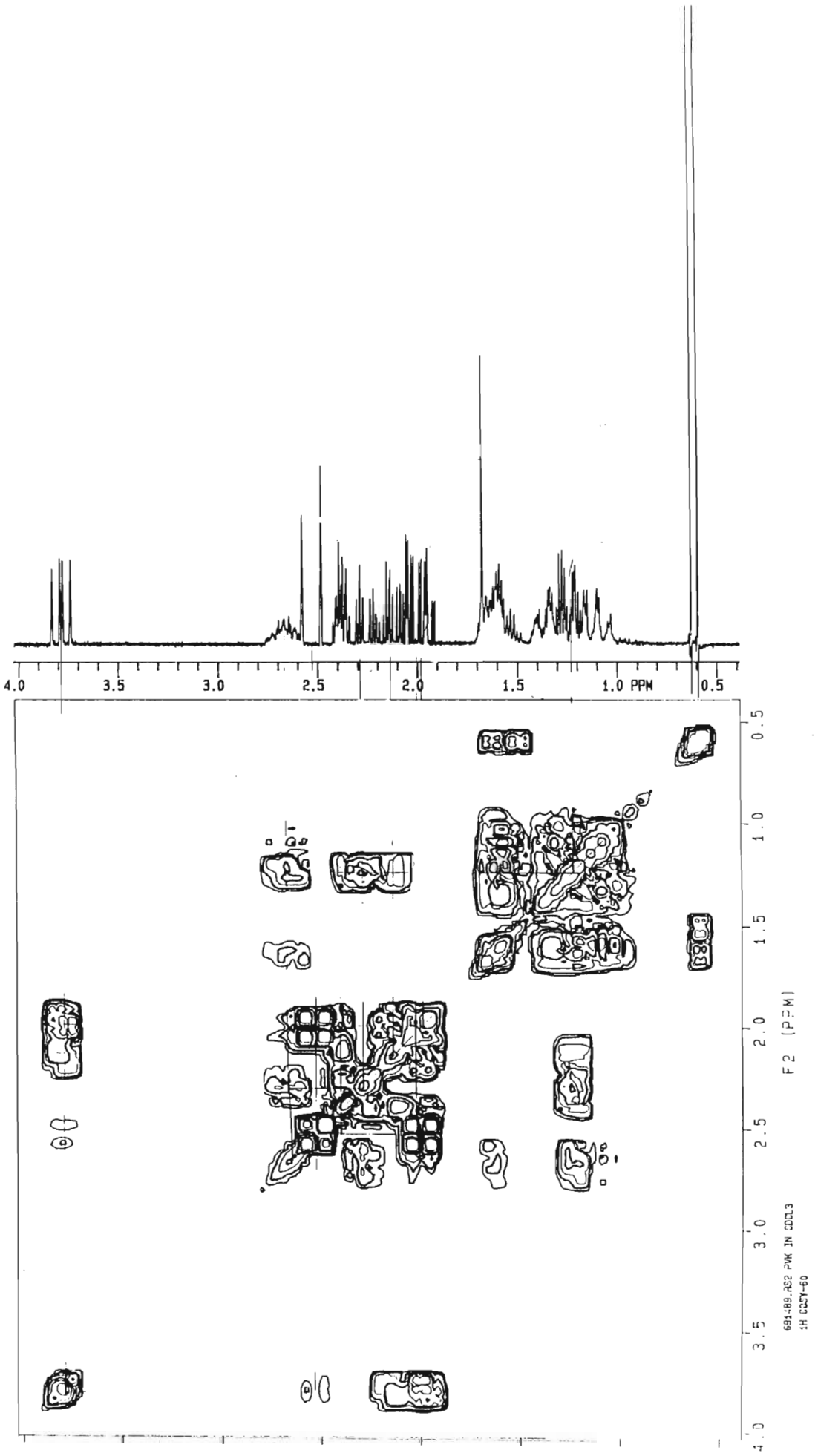
(118)

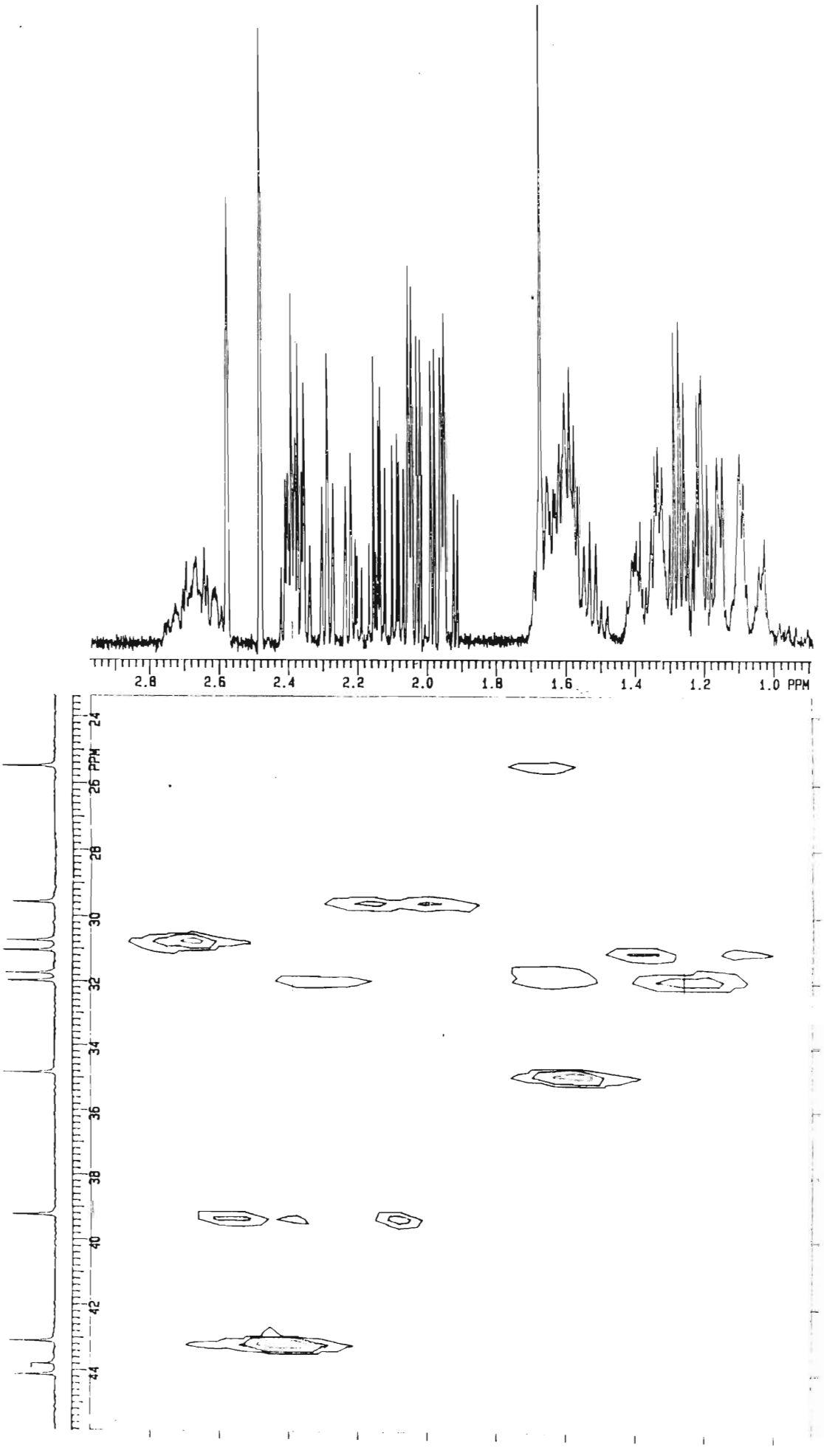
R' = Me; R" = H

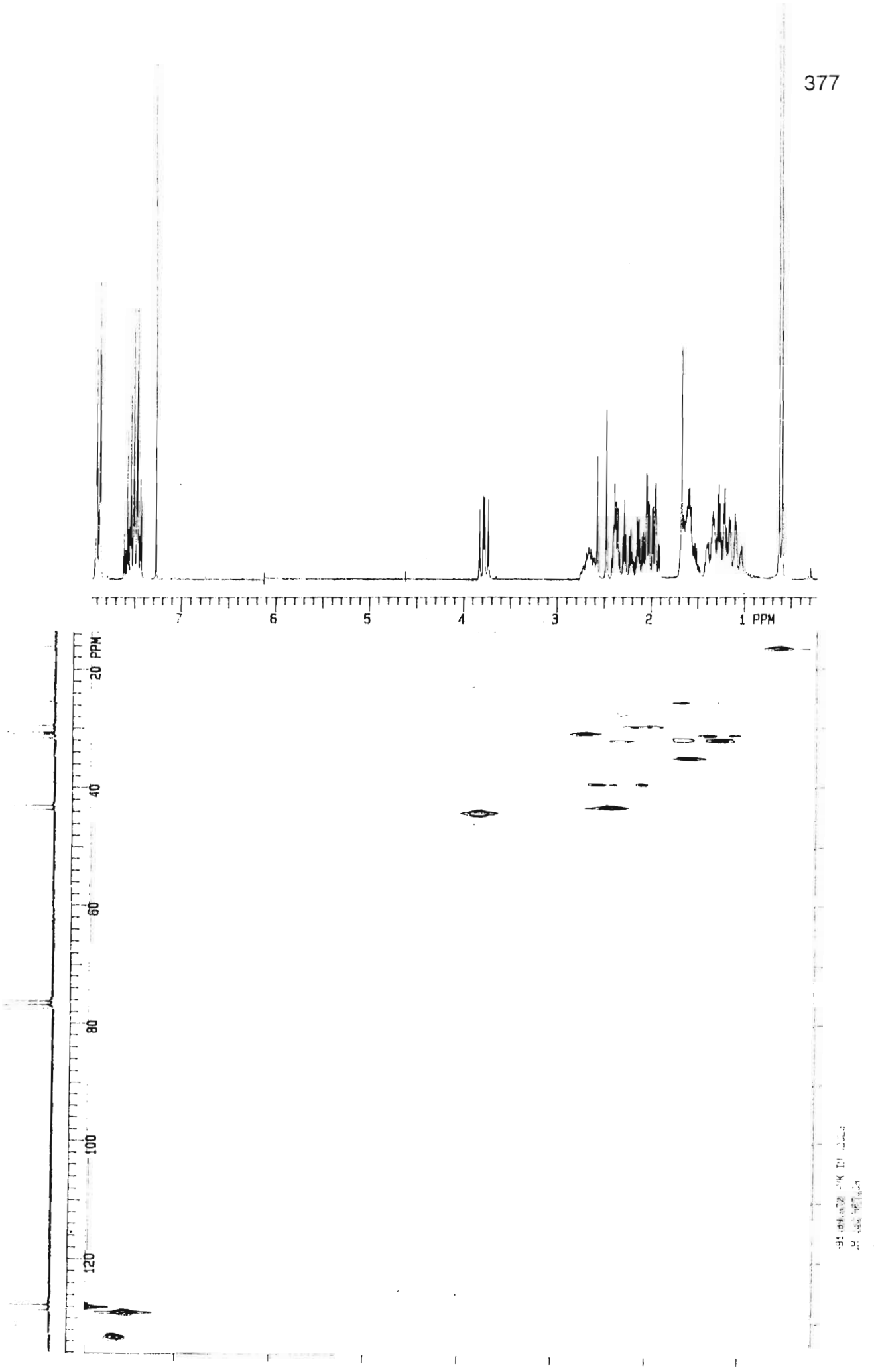
6693 90.RS2 IN CDCL3
7.9
7.8
7.7
7.6
7.5
7.4 PPM
4.0
3.9
3.8
3.7 PPM
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM

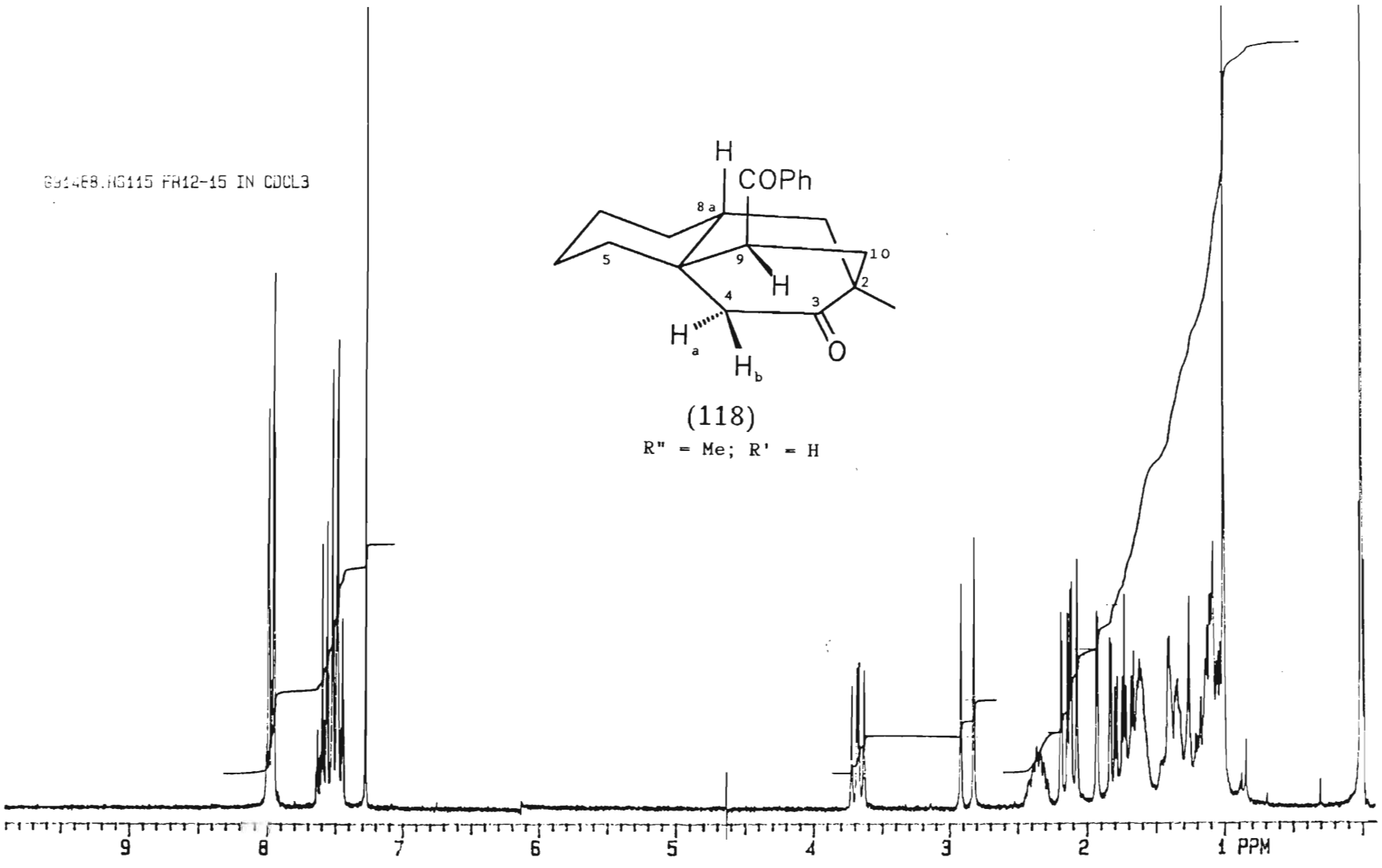

6692/90.RS2 IN CDCL3
0
20 PPM
40
60
80
100
120
140
160
180
200


6692/90.RS2 IN CDCL3
C H 3
C H 2
C H
C H n
120
100
80
60
40
20 PPM


4.0
3.5
3.0
2.5
2.0
1.5
1.0 PPM
0.5
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
F2 (PPM)
691-89.AS2 PWK IN CDCL3
1H COSY-60

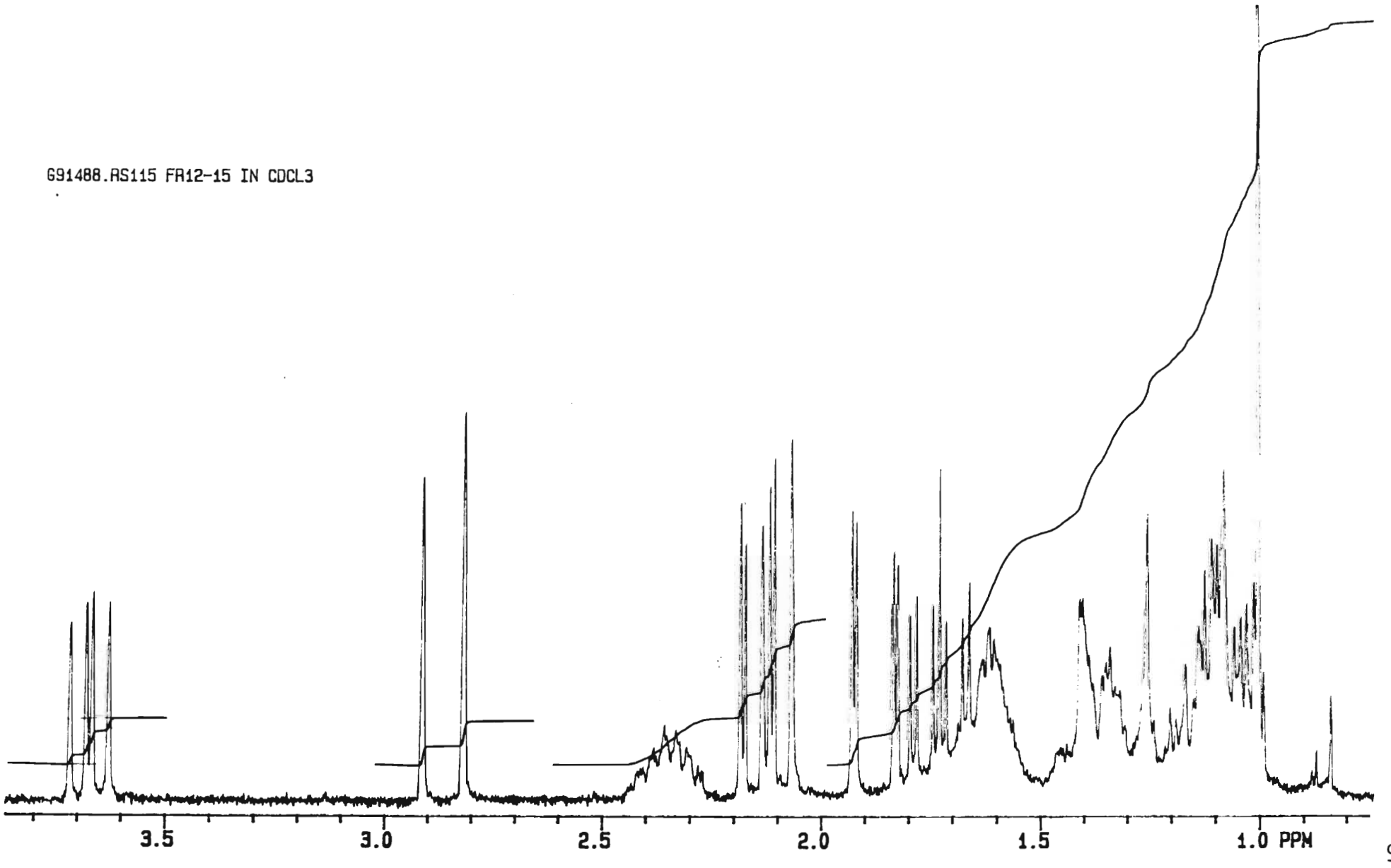

2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0 PPM
24
26 PPM
28
30
32
34
36
38
40
42
44


7
6
5
4
3
2
1 PPM
20 PPM
40
60
80
100
120

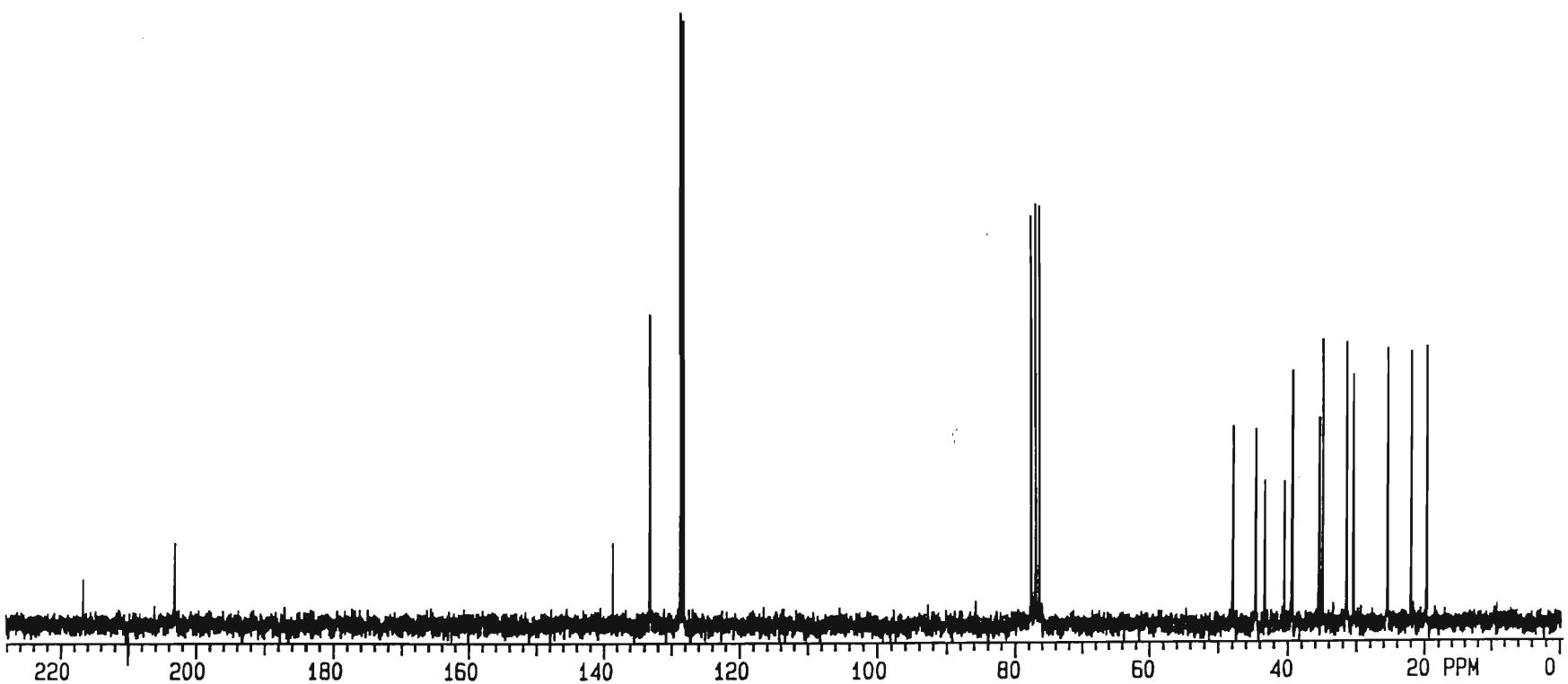

GB1468.NS115 FR12-15 IN CDCL3
H
COPh
8a
5
9
10
2
3
4
H
H a
H b
O
9
8
7
6
5
4
3
2
1 PPM

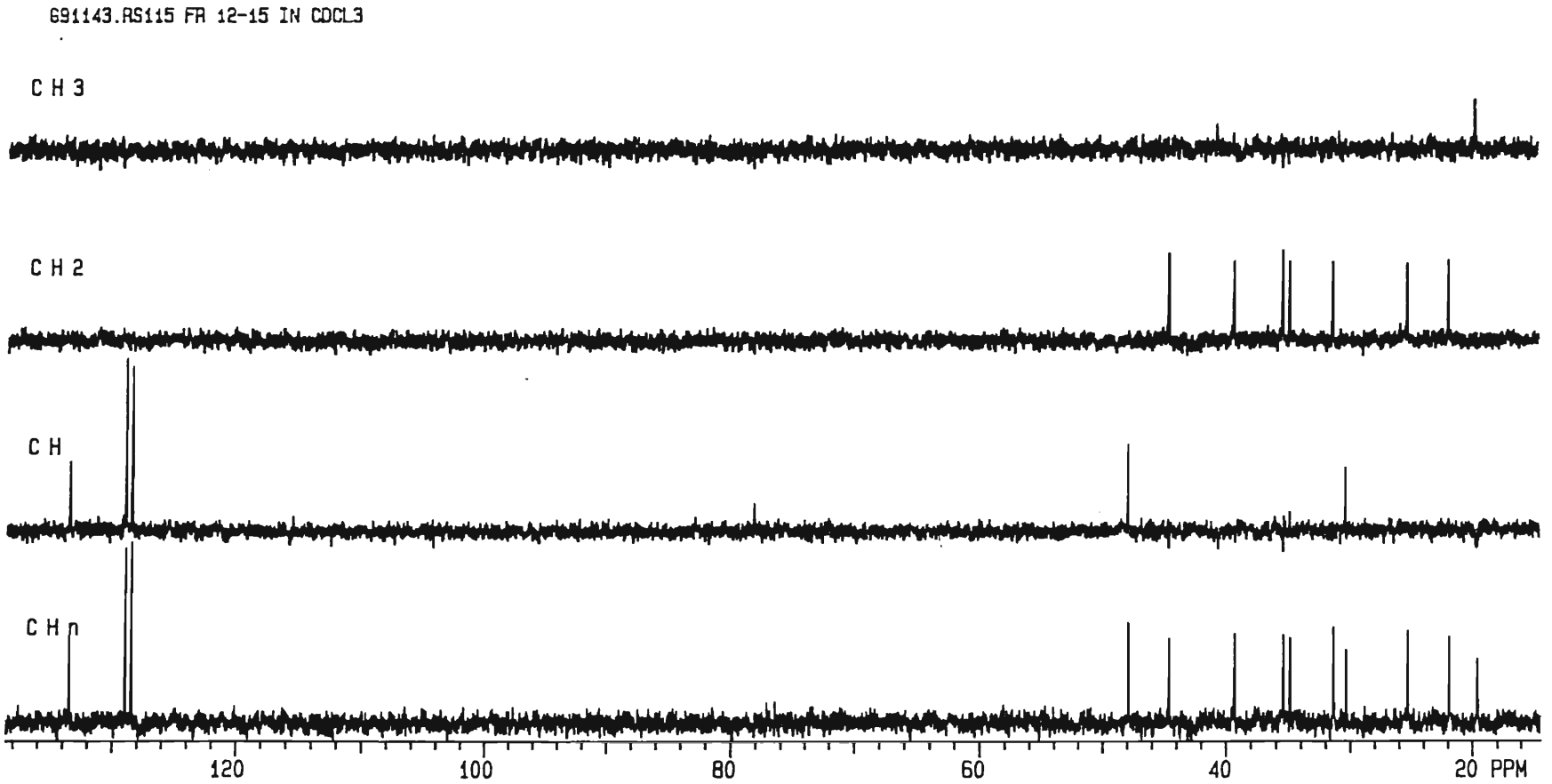
(118)

R" = Me; R' = H


G91488.RS115 FR12-15 IN CDCL3
3.5
3.0
2.5
2.0
1.5
1.0 PPM

691143.RS115 FR 12-15 IN CDCL3

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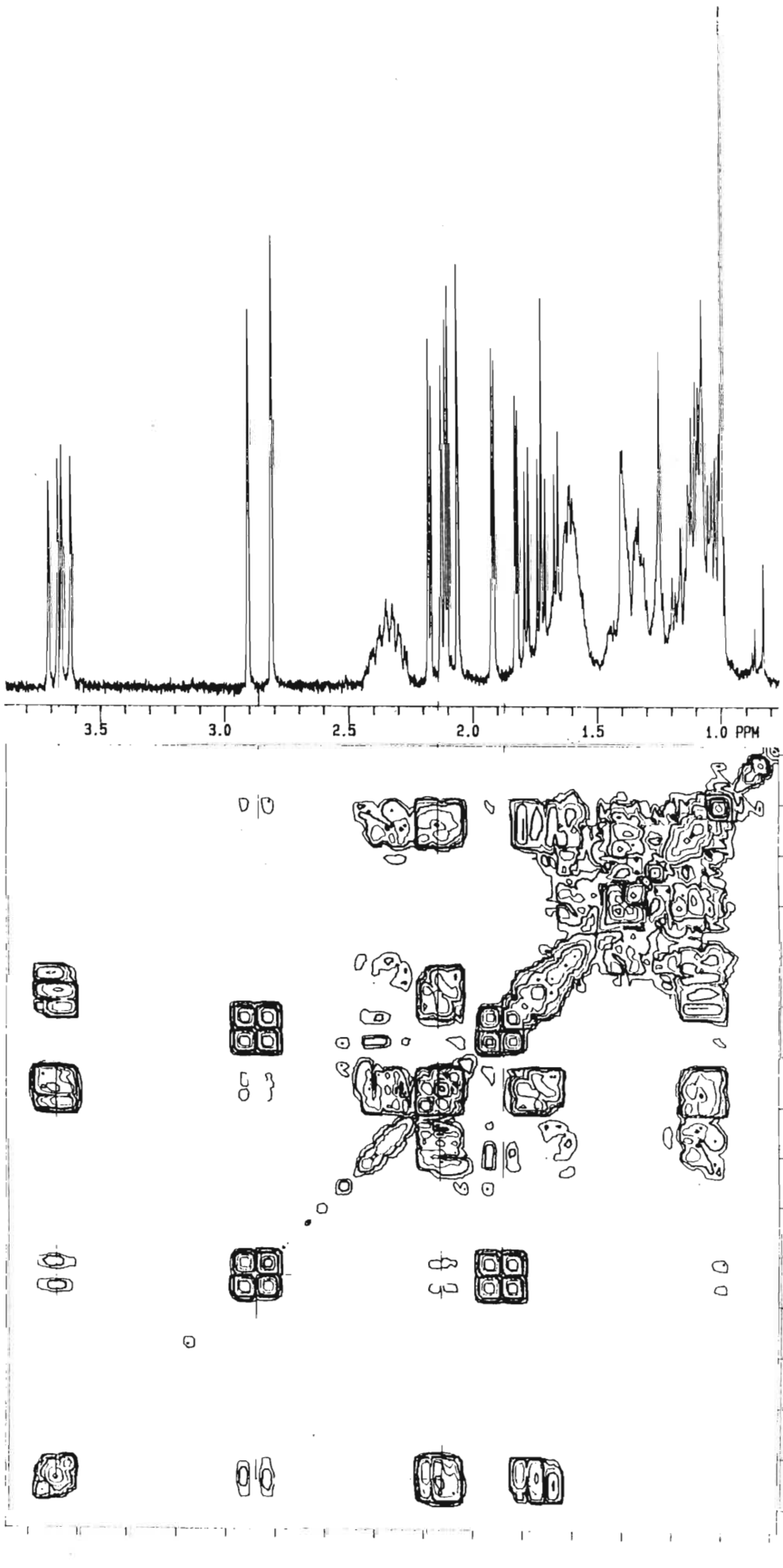
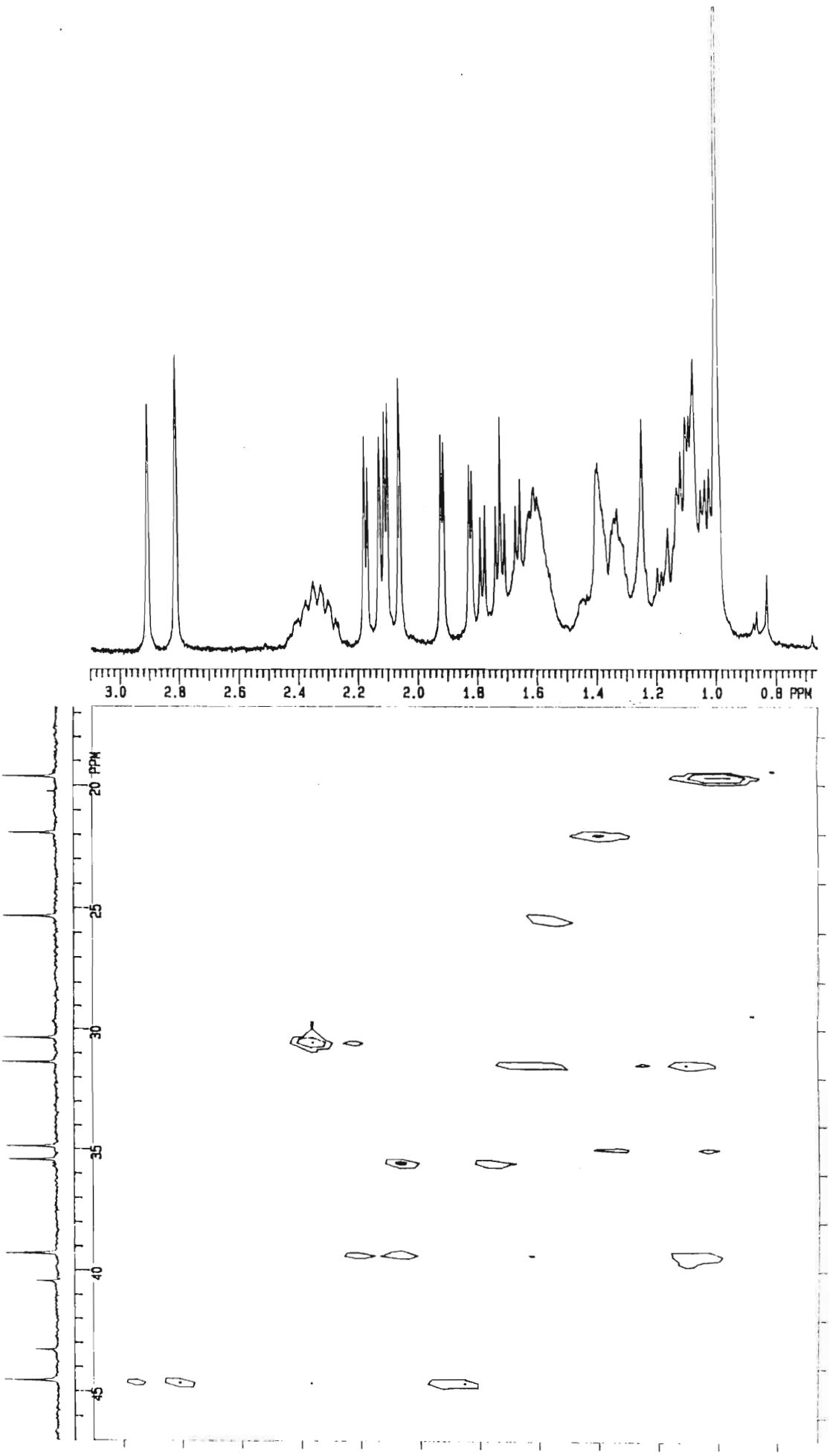
C H 3
C H 2
C H
C H n
120
100
80
60
40
20 PPM


3.5
3.0
2.5
2.0
1.5
1.0 PPM
F2 (PPM)
691:BB.AS115 FA12-15 IN CDCL3
1H COSY-60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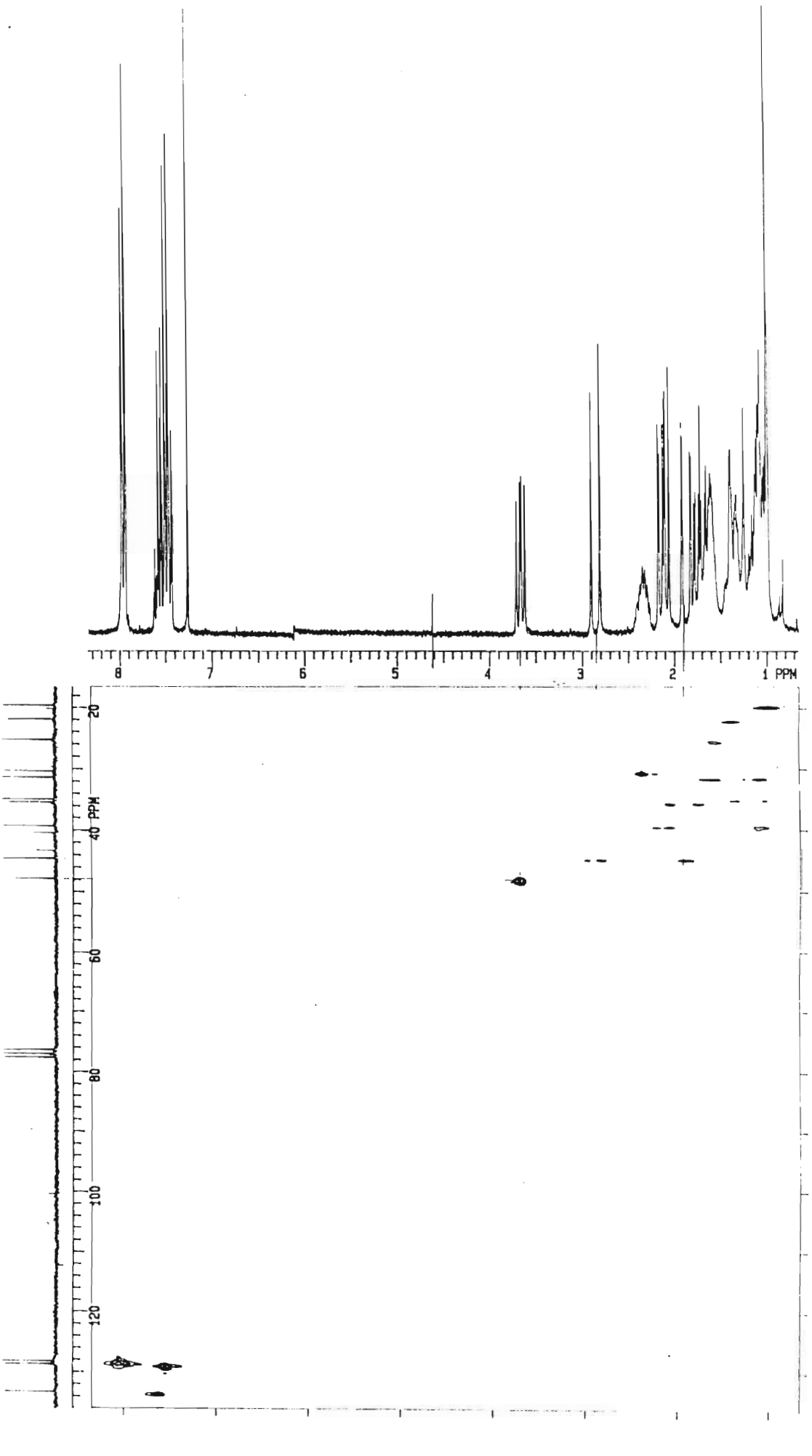
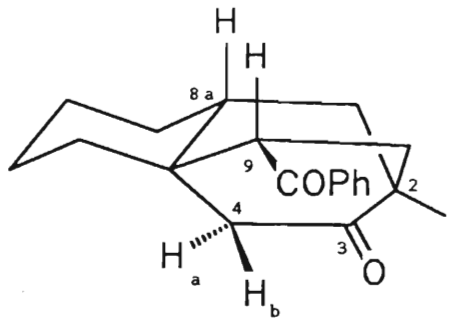
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8 PPM
20 PPM
25
30
35
40
45
691408.NS115 FA12-15 IN CDCL3
1H/13C HETCOR

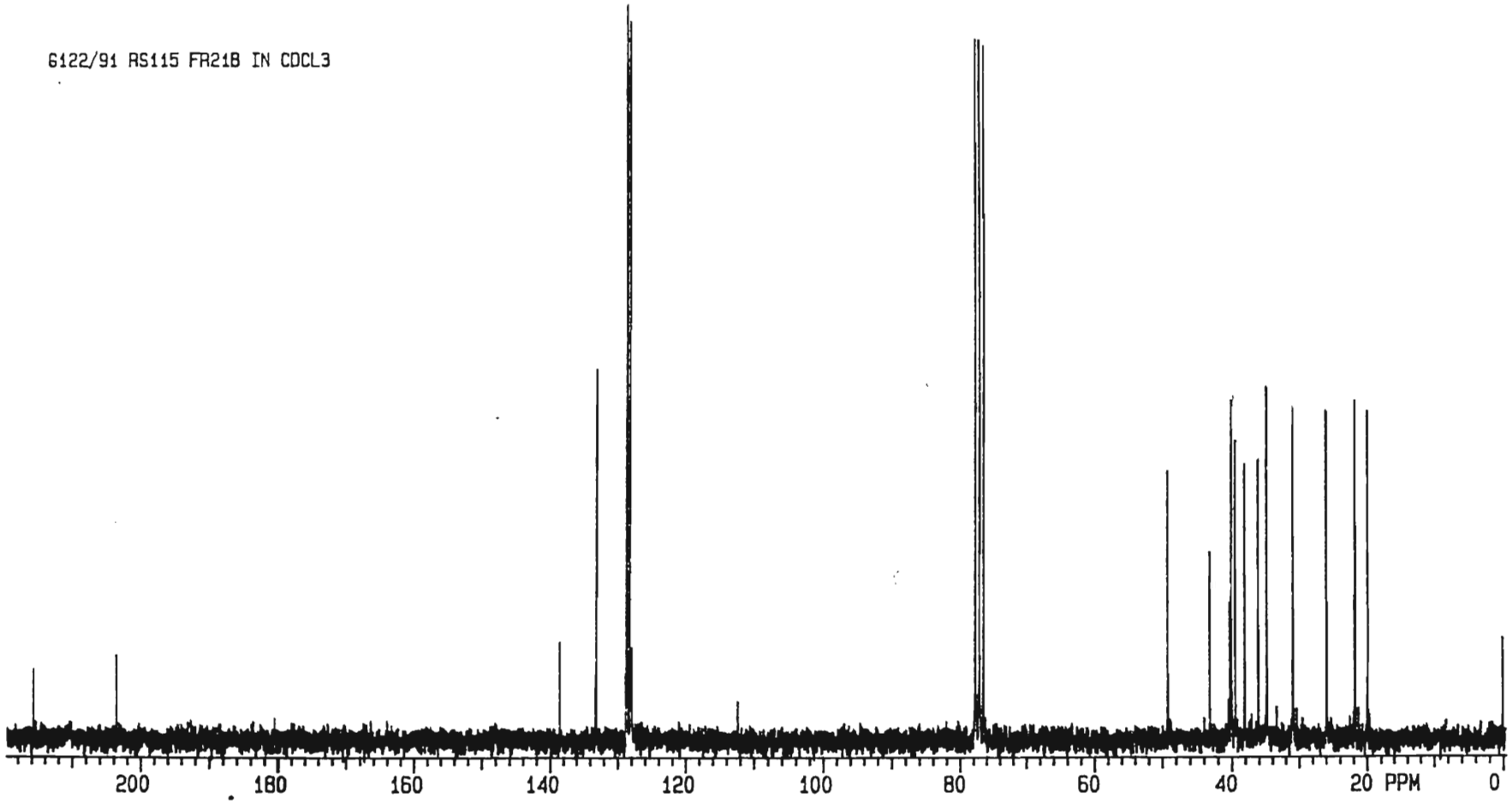

8
7
6
5
4
3
2
1 PPM
20
40 PPM
60
80
100
120

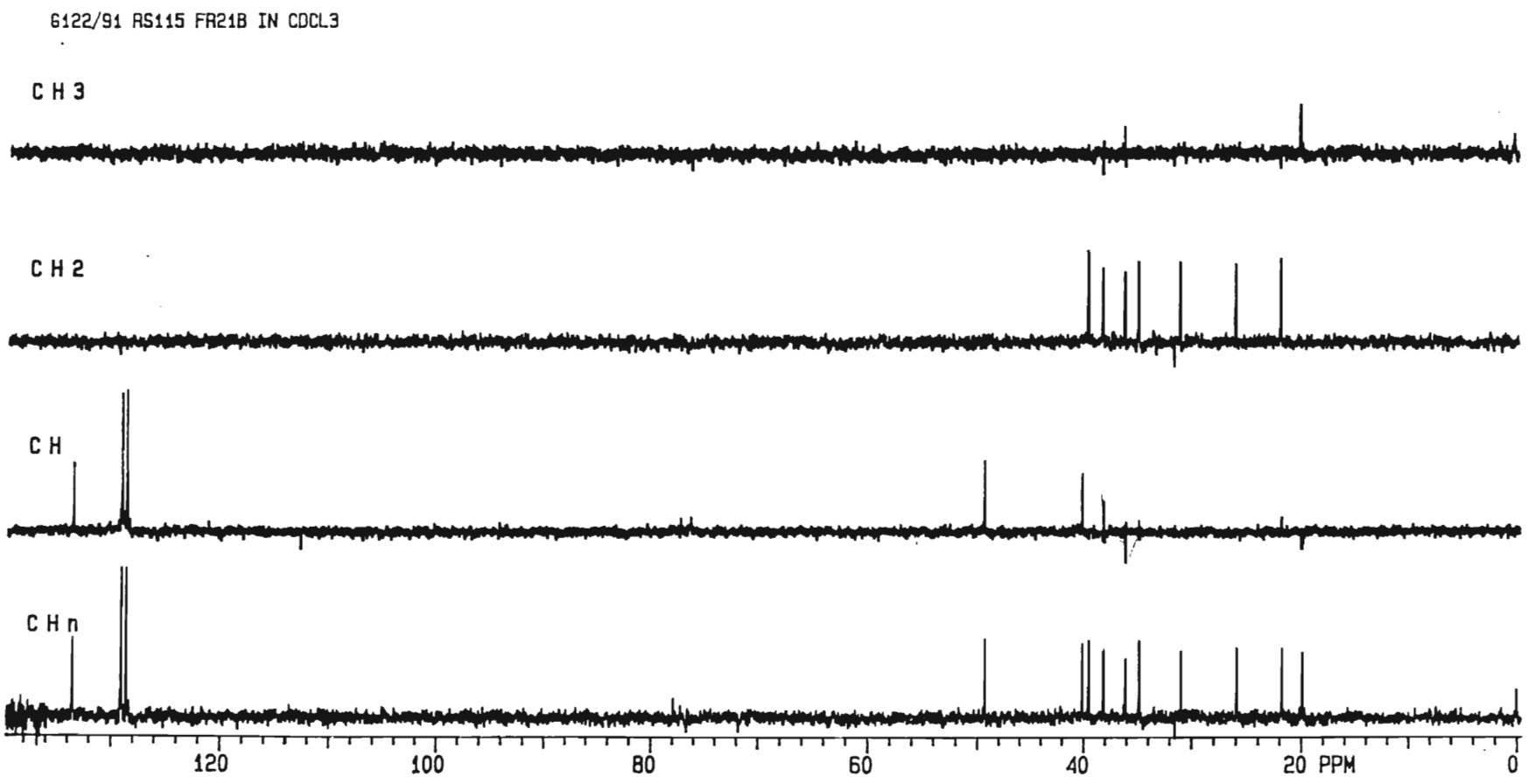
6122/91 AS115 FR21B IN CDCL3

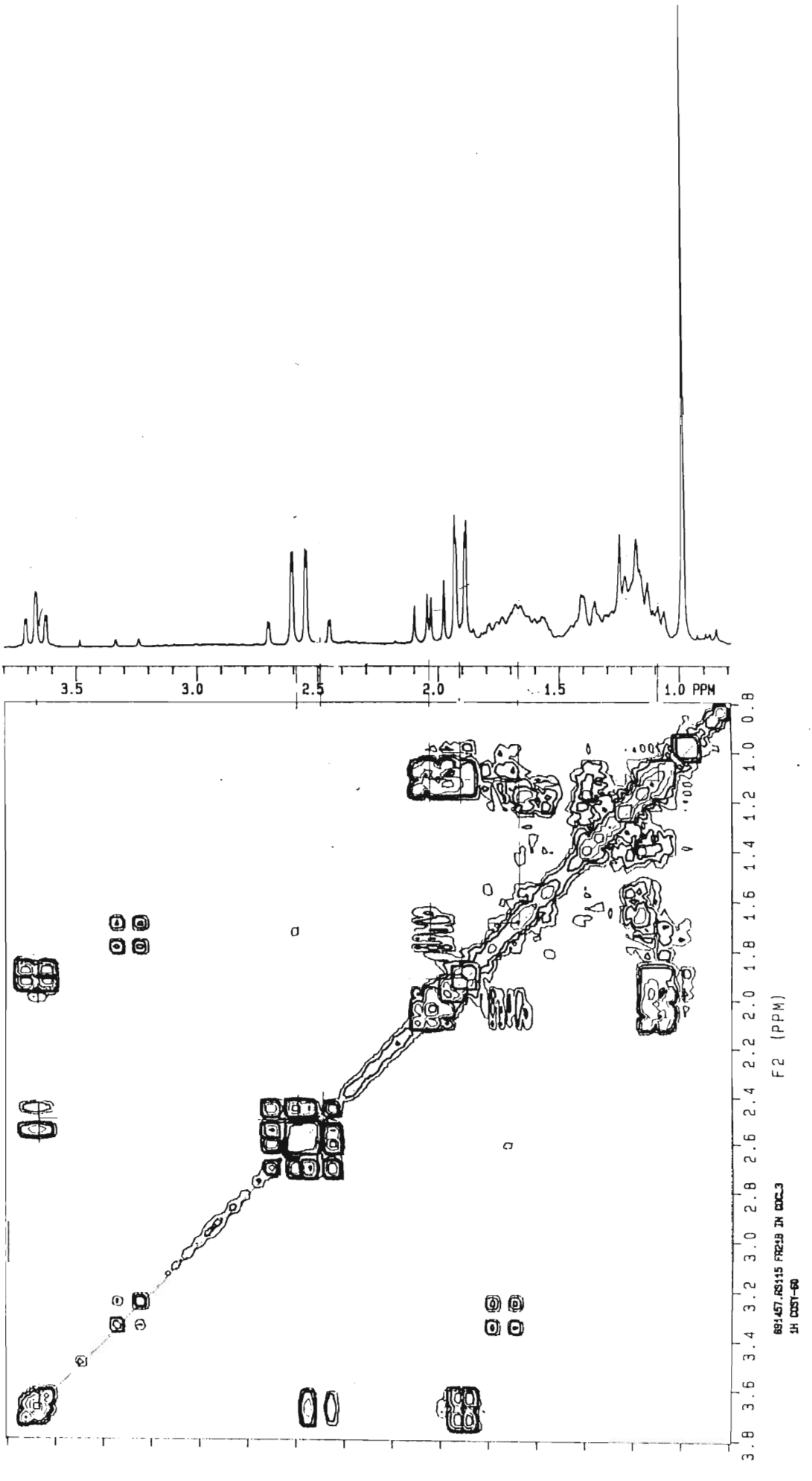


(119)

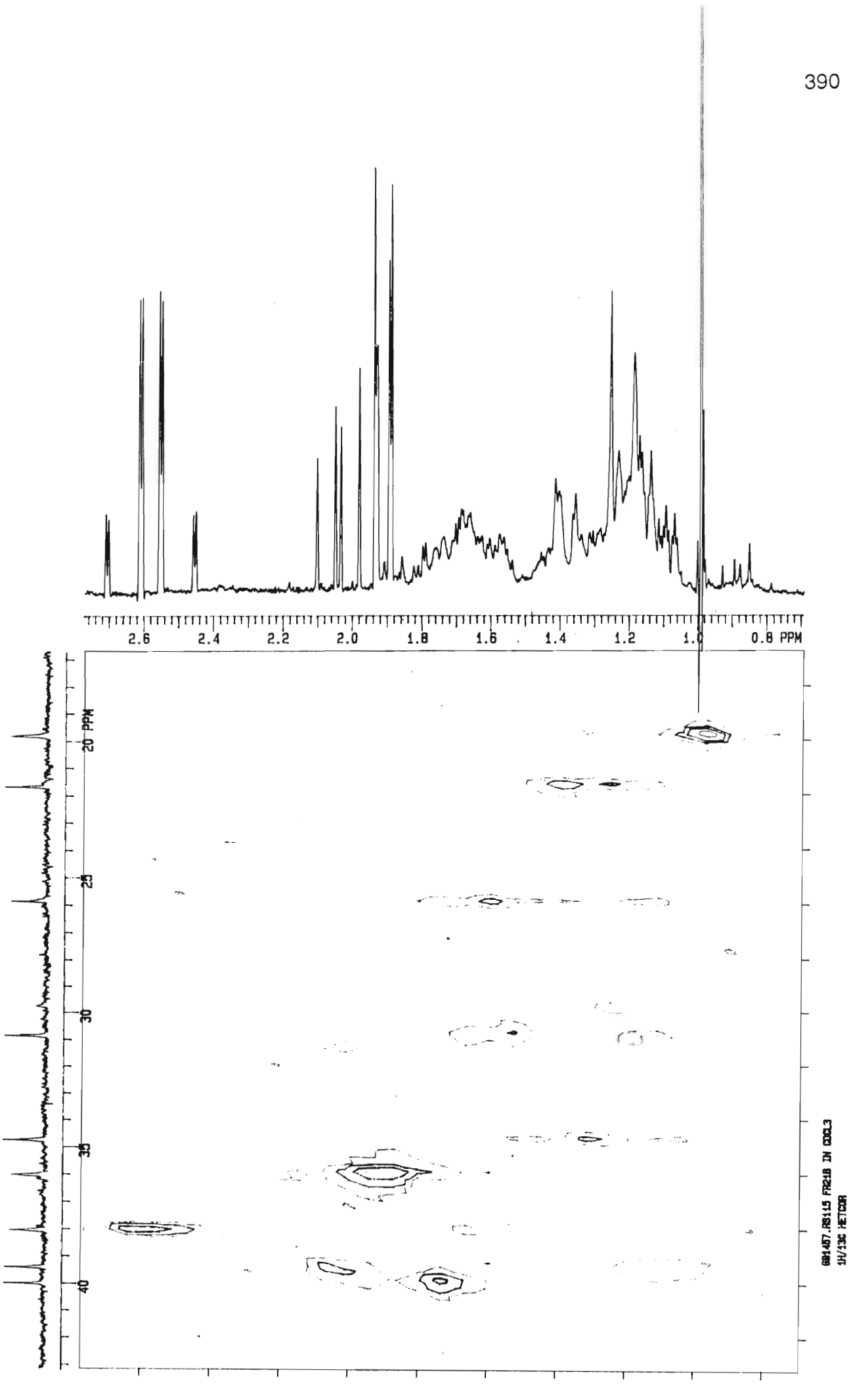
R' = H; R" = Me

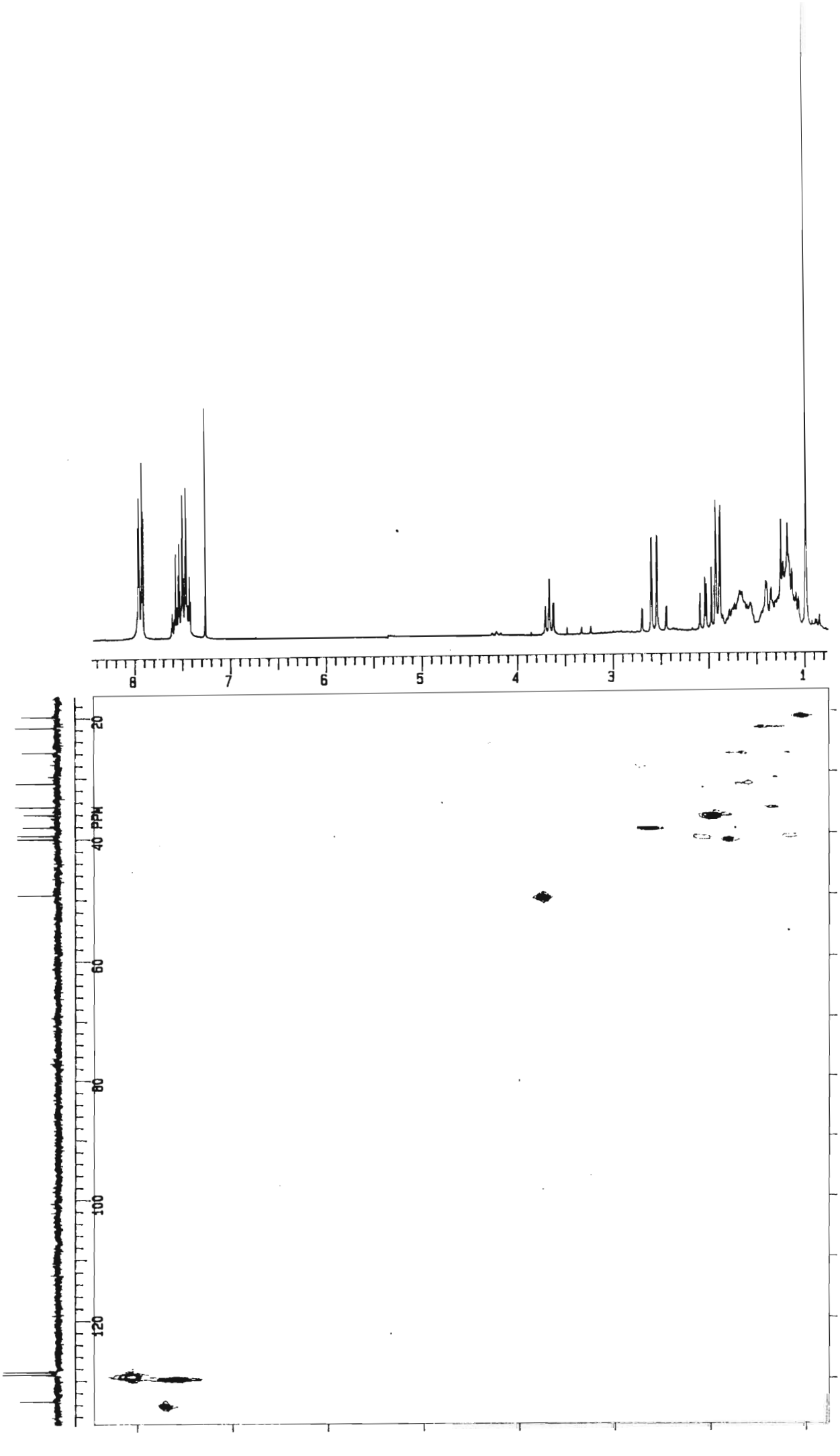

6122/91 RS115 FR21B IN CDCL3
200
180
160
140
120
100
80
60
40
20 PPM
0

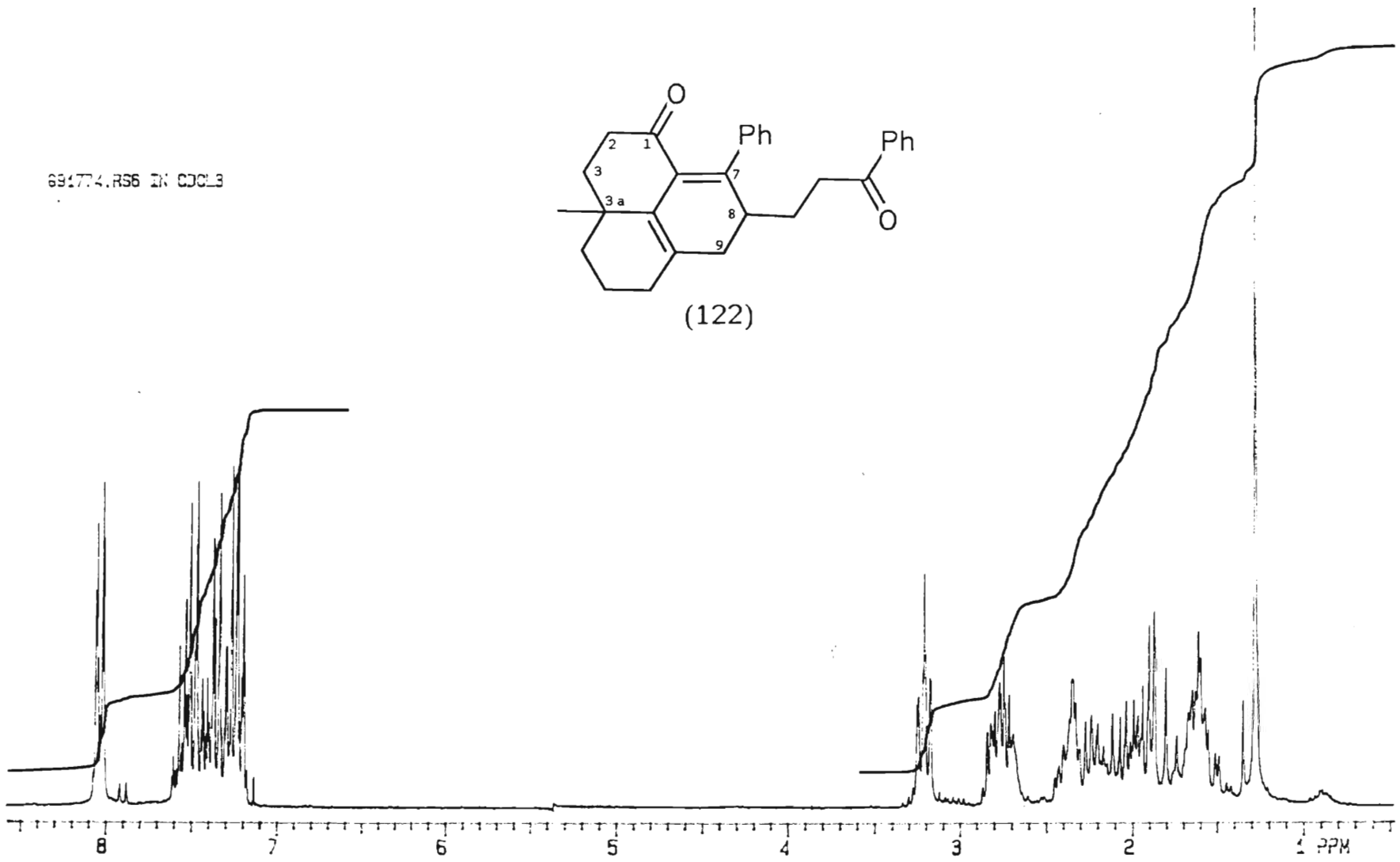

6122/91 RS115 FR21B IN CDCL3
C H 3
C H 2
C H
C H n
120
100
80
60
40
20 PPM
0


3.5
3.0
2.5
2.0
1.5
1.0 PPM
F2 (PPM)
891457.RS115 FR21B IN CDC-3
1H COSY-60

8
7
6
5
4
3
2
1 PPM
F2 (PPM)
891457.AS15 FR218 IN CDCL3
1H COSY-90

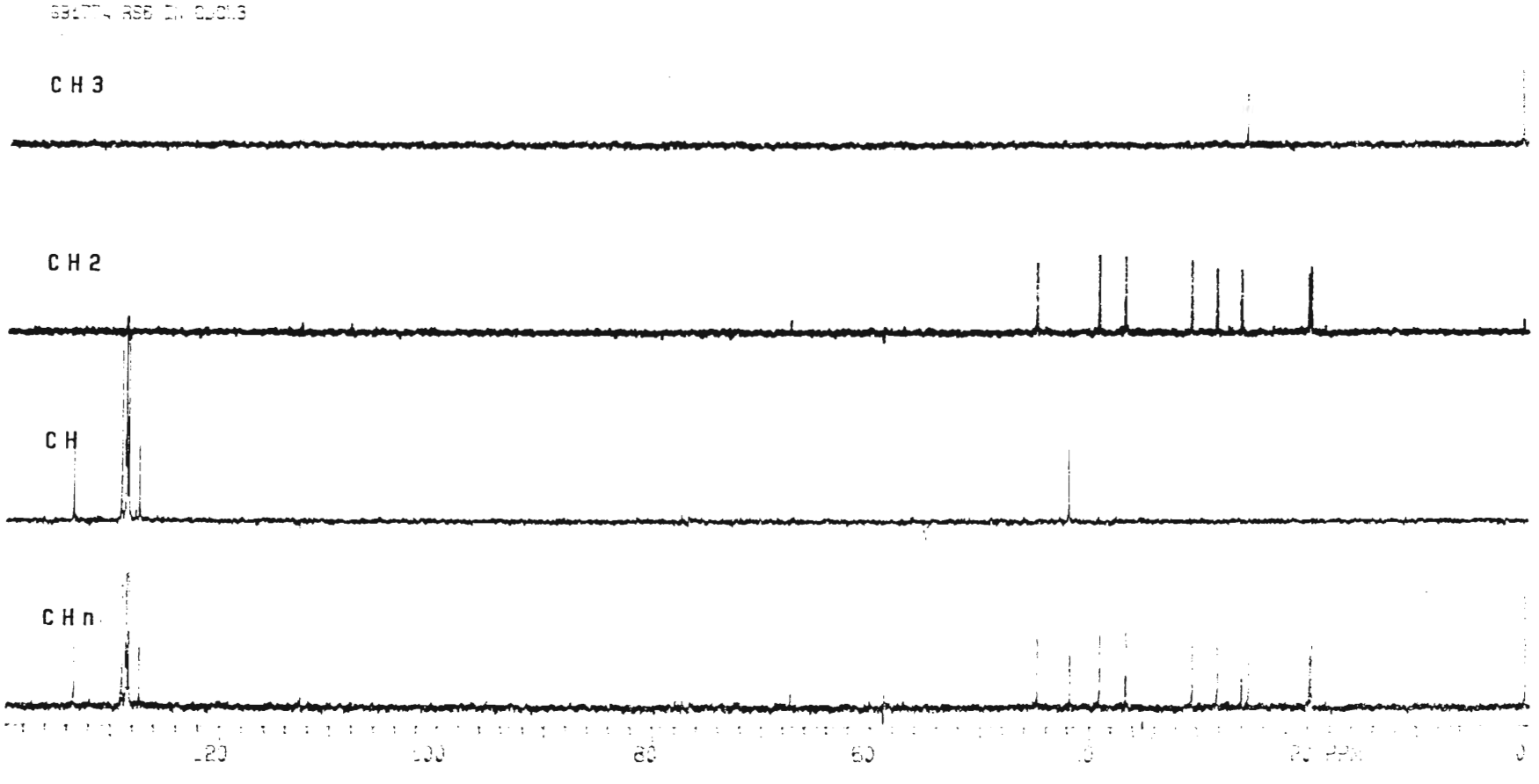

2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8 PPM
20 PPM
25
30
35
40
981467.RS115 FR218 IN CDCL3
1H/13C METCOR


8
7
6
5
4
3
1
20
40 PPM
60
80
100
120
891457.RS115 FR248 IN CDCL3
1H/13C HETCOR



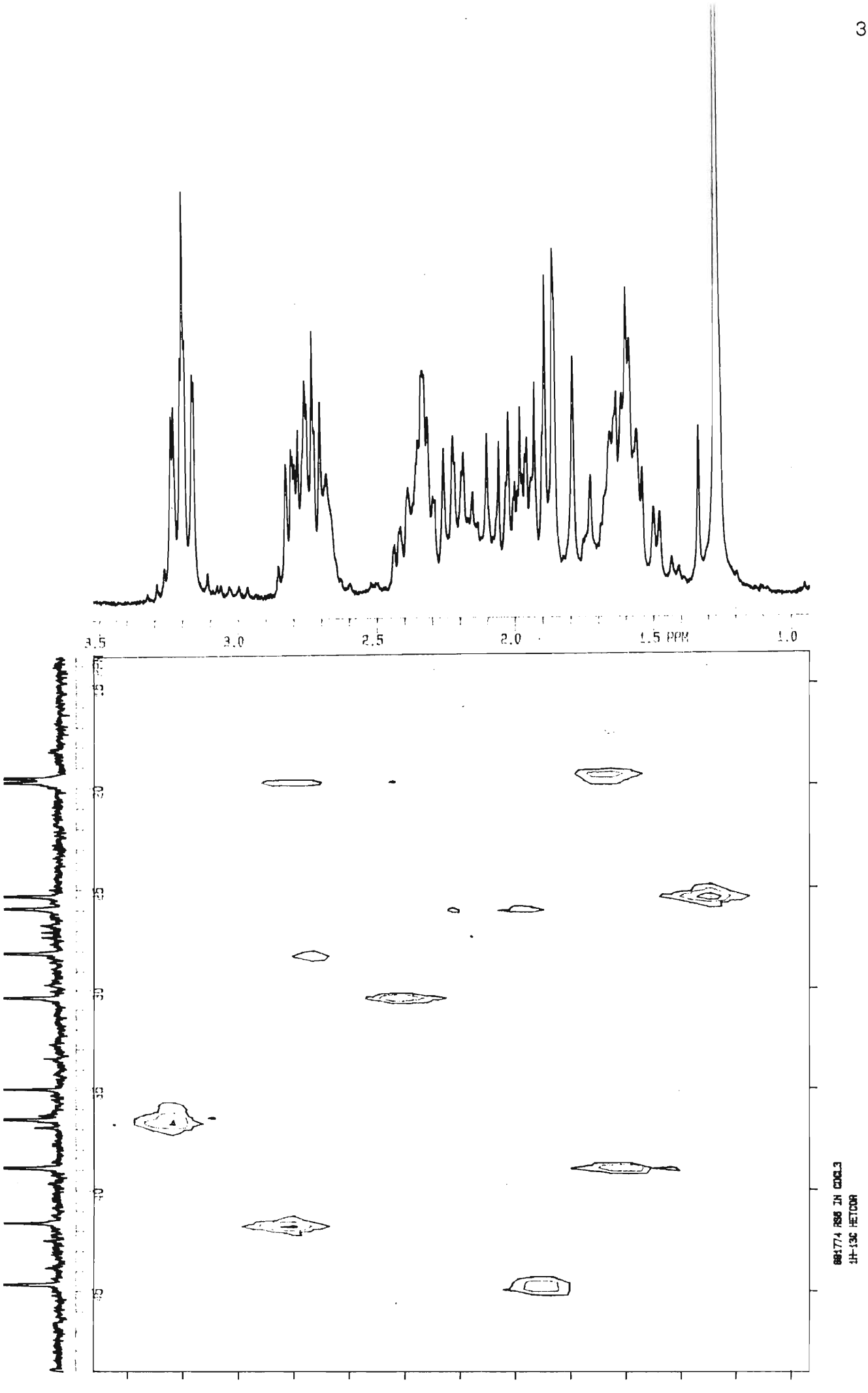
(122)

0
20 PPM
40
60
80
100
120
140
160
180
200


CH3
CH2
CH
CHn

3.0
2.5
2.0
1.5
1.0 PPM
3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8
F2 (PPM)
881774 RS6 IN CDCL3

8
7
6
5
4
3
2 PPM
1
F2 (PPM)
1
2
3
4
5
6
7
8
891774 RS6 IN CDCL3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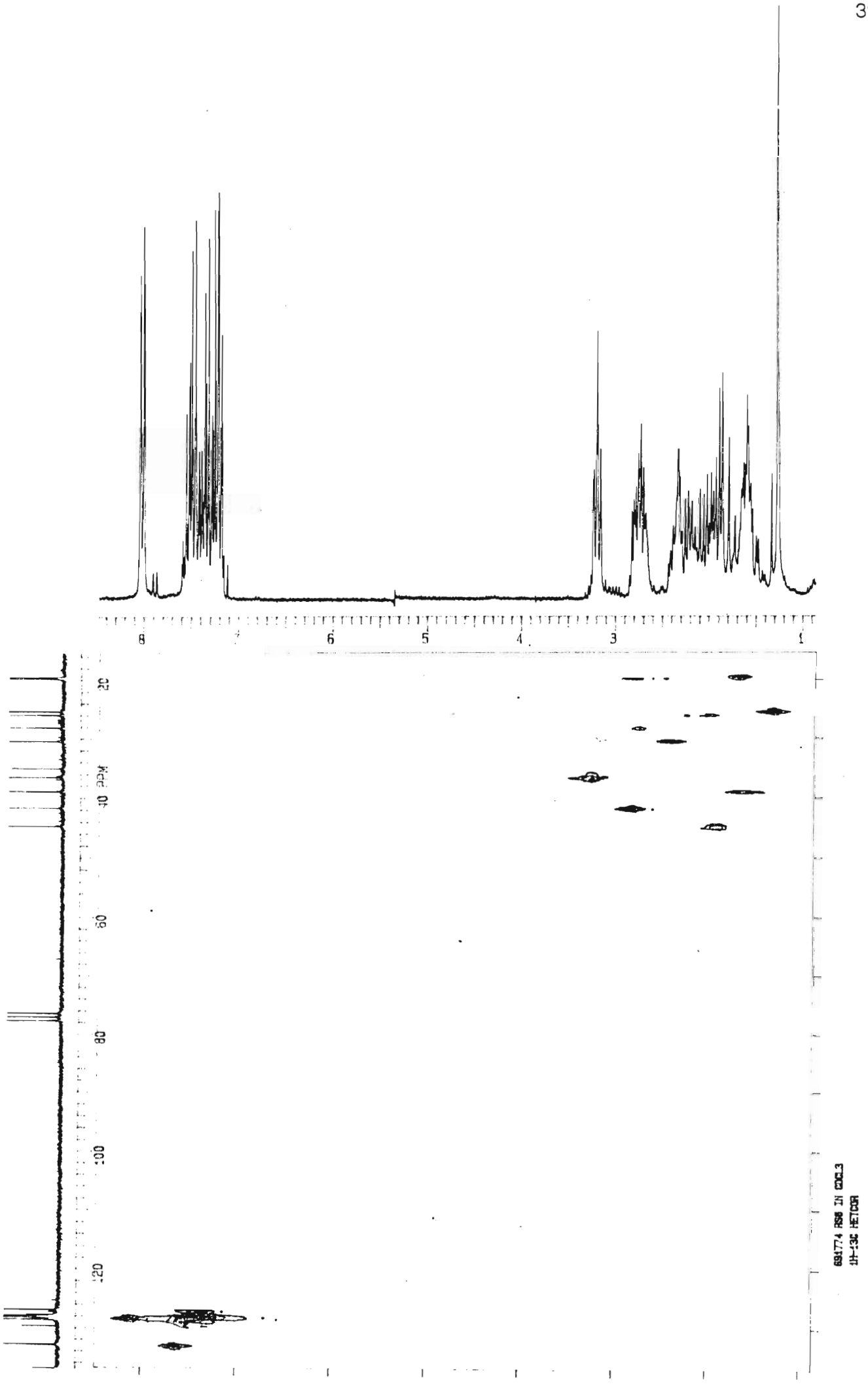
3.0
2.5
2.0
1.5 PPM
1.0
981774 R86 IN CDCL3
1H-13C HETCOR


8
6
5
4
3
1
20
40
60
80
100
120
PPM
691774 RS6 IN CDCL3
1H-13C HETCOR

CHAPTER FIVE

5. REFERENCES

[1] Collie, J.N., *Liebigs Ann. Chem.*, 1884, **266**, 316.

[2] Stork, G., Terrell, R. and Szmuzkovicz, *J. Am. Chem. Soc.*, 1954, **76**, 2029.

[3] Stork, G. and Landesman, *Ibid.*, 1956, **78**, 5128.

[4] Stork, G., Brizzolara, A., Landesman, H., Szmuzkovicz, J. and Terrell, R., *Ibid.*, 1963, **86**, 207.

[5] Surrey, A. R., *Name Reactions in Organic Chemistry*, 231, Academic Press, New York, 1961.

[6] Hickmott, P. W., *Tetrahedron*, 1982, **38**, 1975.

[7] Bowden, K., Braudl, E. A., Jones, E.R.H. and Weedon, *J. Chem. Soc.*, 1946, 45.

[8] Heyl, F.W. and Herr, M.E., *J. Am. Chem. Soc.*, 1953, **75**, 1918.

[9] Herr, M.E. and Heyl, F.W., *Ibid.*, 1953, **75**, 5927.

[10] Johnson, J.L., Herr, M.E., Babcock, J.C., Fonken, A.E., Stafford, J.E. and Heyl, F.W., *Ibid.*, 1956, **78**, 430.

[11] Hickmott, P.W., *Tetrahedron*, 1982, **38**, 2050.

[12] Maas, W., Janssen, M.J., Stamhuis, E.J. and Wynberg, H., *J. Org. Chem.*, 1967, **32**, 1111.

[13] Marchese, J.S., *Ph.D. Thesis*, Uinversity of Maryland, 1964.

[14] Firrell, N.R. and Hickmott, P.W., *J. Chem. Soc. (C)*, 1968, 2320.

[15] Firrell, N.R., *Ph.D. Thesis*, University of Salford, 1970.

[16] Birch, A.J., *J. Chem. Soc.*, 1946, 593.

[17] Birch, A.J., Hutchinson, E.J. and Subba Rao, G., *J. Chem. Soc. (C)*, 1971, 637.

[18] Birch, A.J., Hutchinson, E.J. and Subba Rao, G., *Chem. Commun.*, 1970, 657.

[19] Firrell, N.R. and Hickmott, P.W., *J. Chem. Soc. (B)*, 1969, 293.

[20] Leonard, N.J. and Musliner, W.J., *J. Org. Chem.*, 1966, **31**, 639.

[21a] Berchold, G.A. and Uhlig, G.F., *J. Org. Chem.*, 1963, **28**, 1459.

[21b] Brannock, K.C., Burpitt, R.D., Goodlett, V. W. and Thweatt, J.G., *J. Org. Chem.*, 1963, **28**, 1464.

[21c] Heubner, C.F., Dorfman, L., Robinson, M.M., Pierson, W.G. and Strachan, P., *J. Org. Chem.*, 1963, **28**, 3134.

[21d] Bose, A.K., Mina, G., Manhaus, M.S. and Rzucidlo, E., *Tetrahedron Letters*, 1963, 1467.

[21e] Brannock, K.C., Burpitt, R.D., Goodlett, V. W. and Thweatt, J.G., *J. Org. Chem.*, 1964, **29**, 818.

[21f] Yoshii, E. and Kimoto, S., *Chem. Pharm. and Bull.*, (Japan), 1969, **17**, 629.

[22a] Parker, K.A. and Kosley, R.W., *Tetrahedron Letters*, 1975, 3039.

[22b] Parker, K.A. and Kosley, R.W., Buchwals, S.L. and Petraitis, J.J., *J. Am. Chem. Soc.*, 1976, **98**, 7104.

[22c] Ref. 11, Scheme 23.

[23] Farmer, M.L., Billups, W.E., Greenlee, R.B. and Kurtz, A.N., *J. Org. Chem.*, 1966, **31**, 2885.

[24] Hubschwerlen, C., and Fleury, J.P., *Tetrahedron*, 1977, **33**, 761.

[25a] Julia, M., Julia, S. and Jeanmart, C., *Compt. Rend.*, 1960, **251**, 249.

[25b] Julia, M., Julia, S., Jeanmart, C. and Langlois, M., *Bull. Soc. Chim. Fr.*, 1962, 2243.

[25c] Bucourt, R., Tessier, J. and Nominé, G., *Bull. Soc. Chim. Fr.*, 1963, 1923.

[25d] Pandit, U.K., de Jonge, K., Erhardt, E. and Huisman, H.O., *Tetrahedron Letters*, 1969, 1207.

[25e] Malhotra, S.K. and Ringold, H.J., *J. Am. Chem. Soc.*, 1963, **85**, 1538.

[25f] Ringold, H.J. and Malhotra, S.K., *Ibid.*, 1962, **84**, 3042.

[25g] Velluz, L., Nominé, G., Bucourt, R., Pierdet, A. and Dufray, P., *Tetrahedron Letters*, 1961, 127.

[25h] Brizzolara, A.A., *Ph.D. Thesis*, Columbia University, 1960.

[26] Stork, G. and Birnbaum, *G., Tetrahedron Letters*, 1961, 313.

[27] Könst, W.N.B., Witteveen, J.G. and Boelens, H., *Tetrahedron*, 1976, **32**, 1415.

[28] Huffman, J.W., Roewe, C.D. and Matthews, F.J., *J. Org. Chem.*, 1982, **47**, 1438.

[29] Marshall, J. and Johnson, W.S., *J. Org. Chem.*, 1963, **28**, 421.

[30] Johnson, W.S., Bauer, V.J. and Franck, R.W., *Tetrahedron Letters*, 1961, 72.

[31] Millward, B.B., *J. Chem. Soc.*, 1960, 26.

[32a] Pollmann, M.J.M., Reus, H.R., Pandit, U.K. and Huisman, H.O., *Rec. Trav. Chim.*, 1970, **89**, 929.

[32b] Mazarguil, H. and Lattes, A., *Bull. Soc. Chim. Fr.*, 1972, 1880.

[33] Yoxall, C.T., *Ph.D. Thesis*, University of Salford, 1971.

[34] Nozoe, T., *Pure Appl. Chem.*, 1971, **28**, 239.

[35] Sciaky, R., Pallini, U. and Consonni, A., *Gazz. Chim. Ital.*, 1966, **96**, 1284.

[36] Opitz, G. and Merz, *Liebigs Ann. Chem.*, 1962, **652**, 158.

[37] Pandit, U.K., Pollmann, M.J.M. and Huismann, H.O., *Chem. Commun.*, 1969, 527.

[38a] Johnson, F. and Malhotra, S.K., *J. Am. Chem. Soc.*, 1965, **87**, 5492.

[38b] Johnson, F., *Chem. Rev.*, 1968, **68**, 375.

[39] Gurowitz, W.D. and Joseph, M.A., *Tetrahedron Letters*, 1965, 4433.

[40] House, H.O., Trost, B.M., Magin, R.W., Carlson, R.G., Frank, R.W. and Rasmusson, G.H., *J. Org. Chem.*, 1965, **30**, 2513.

[41] Cook, A.G. (Ed.), *Enamines: Synthesis, Structure and Reactions*, Marcel Dekker, New York, 1969.

[42] Firrell, N.F. and Hickmott, P.W., *J. Chem. Soc. (C)*, 1970, 716.

[43] Mazarguil, H. and Lattes, A., *Bull. Soc. Chim Fr.*, 1971, 112.

[44] Nozaki, H., Yamaguti, T., Ueda, S. and Kondo, K., *Tetrahedron*, 1968, **24**, 1445.

[45] Bessiere, Y. and Derguini-Boumechal, F., *J. Chem. Res. (S)*, 1977, 204.

[46] Dana, G., Weisbuch, F. and Yamagami, C., *Bull. Soc. Chim. Fr.*, 1973, 1109.

[47] Yamagami, C., Weisbuch, F. and Dana, G., *Tetrahedron*, 1971, **27**, 2967.

[48] Julia, M., Julia, S. and Jeanmart, C., *Acad. Sci., Paris*, 1960, **251**, 249.

[49] Houdewind, P. and Pandit, U.K., *Tetrahedron Letters*, 1974, 2359.

[50] Hickmott, P.W., Papaphilippou, A., Pienaar, D.H., Soelistyowati, R.D. and Yoxall, C.T., *S. Afr. J. Chem.*, 1988, **41**, 75.

[51] Szmuszkovicz, J., *Ad. Org. Chem.*, 1963, **4**, 1.

[52] Weisbuch, F. and Dana, G., *Tetrahedron*, 1974, **30**, 2873.

[53] Kuehne, M.E. and Nelson, J.A., *J. Org. Chem.*, 1970, **35**, 161.

[54] Opitz, G. and Merz, W., *Liebigs Ann. Chem.*, 1962, **652**, 163.

[55] Birch, A.J. and Hutchinson, E.J., *J. Chem. Soc. Perkin I*, 1973, 1757.

[56] Houdewind, P., Lappiere Armande and Pandit, U.K., *Tetrahedron Letters*, 1974, 591.

[57a] Manhas, M.S., Brown, J.W., Pandit, U.K. and Houdewind, P. *Tetrahedron*, 1975, **31**, 1325.

[57b] Manhas, M.S., Brown, J.W. and Pandit, U.K., *Heterocycles 3*, 1975, 117.

[58] Pearson, R.G. and Dillon, D.L., *J. Am. Chem. Soc. (C)*, 1971, 1385.

[59] Stork, G. and Dowd, S., *J. Am. Chem. Soc.*, 1963, **85**, 2178.

[60] Stork, G. and Benaim, J. *J. Am. Chem. Soc.*, 1971, **93**, 5938.

[61] Hickmott, P.W. and Woodward, K.N., *J. Chem. Soc. Chem. Commun.*, 1974, 275.

[62a] Augustine, R.L. and Cortez, H.B., *Chem. Ind. (London).*, 1963, 490.

[62b] Spencer, T.A. and Schmeigel, A.K., *Ibid.*, 1963, 1765.

[63a] Westman, T.L., Peredes, R. and Berg, W.S., *J. Org. Chem.*, 1963, **28**, 3512.

[63b] Westman, T.L. and Kober, A.E., *Ibid.*, 1964, **29**, 2448.

[63c] Mandell, L., Hall, B.A. and Singh, K.P., *Ibid.*, 1964, **29**, 3067.

[64] Hickmott, P.W. and Rae, B., Unpublished results.

[65a] White, W.A. and Weingarten, H., J. Org. Chem., 1967, **32**, 213.

[65b] Weingarten, H., Chupp, J.P. and White, W.A., *Ibid.*, 1967, **32**, 3246.

[65c] Carlson, R and Nilsson, A., *Acta Chem. Scand.*, 1984, **B38**, 49.

[65d] Carlson, R and Nilsson, A., *Ibid.*, 523.

[66] Booth, H., *Tetrahedron*, 1966, **22**, 615.

[67] Jackman, L. and Sternhell, S., *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 237, Pergamon Press, Oxford, 1969.

[68] Hickmott, P.W., *Tetrahedron*, 1984, **40**, 2989.

[69] Ref. 6, 3363.

[70] Ref. 67, 337.

[71] Ref. 67, 197.

[72] Still, W.C., Kahn, M. and Mitra, A., *J. Org. Chem.*, 1978, **43**, 2932.

[73] Furniss, B.S., Hannaford, A.J., Rogers, V., Smith, P.W.G. and Tatchell, A.R., *Vogel's Textbook of Practical Organic Chemistry*, 1053, Longmans, London, 1978.

[74] Terrel, R., *Ph.D. Dissertation*, Columbia University, 1954.

[75] White, T., *J. Chem. Soc.*, 1943, 238.

[76] Hargreaves, J.R., Hickmott, P.W. and Hopkins, B.J., *J. Chem. Soc. (C)*, 1968, 2599.

[77] Robinson, R., du Feu, E.C. and M_cQuillin, F.J., *J. Chem. Soc.*, 1937, 53.

[78] Ross, N.C. and Levine, R., *J. Org. Chem.*, 1964, **29**, 2341.

[79] Colonge, J., *Bull. Soc. Chim. Fr.*, 1954, 1406.

[80] Ramchandran, S. and Newman, M.S., *Organic Syntheses, Coll. Vol. V*, 486, Wiley and Sons, New York, 1973.

[81] Organic Reactions, **1**, 303, Wiley and Sons, New York, 1942.

[82] Birch, A.J., Murray, A.R. and Smith, H., *J. Chem. Soc.*, 1951, 1945.

[83] Field, J.S. and Ramesar, N., Personal Communication.

CHAPTER SIX

6. APPENDIX

6.1 CRYSTAL STRUCTURE DATA AND STEREOSCOPIC DRAWING FOR (4aR*,7aS*,11aR*)-4a-METHYLOCTA-HYDRO-1*H*-BENZO[d]NAPHTHALENE-2,10(3*H*,11*H*)-DIONE[a] (78)

Formula	$C_{15}H_{22}O_2$
M	234
Space group	$P2_1/c$
a/Å	7,171(1)
b/Å	15,610(1)
c/Å	11,481(1)
β/°	94,60
U/Å^3	1281,2
Z	4
Dc/g.cm^{-3}	1,21

Crystal data were collected on an Enraf-Nonius CAD4 diffractometer with graphite-monochromated M_o-K_α radiation (λ = 0,7107 Å). From 4027 reflections measured for 2,0 < θ < 30°, 2753 observed reflections (final residual R = 0,063) with F > 2σF were used in the structure solution [direct methods (MULTAN)] and refinement (block diagonal least squares). The stereoscopic drawing (Figure 3) was calculated with the ORTEP programme.

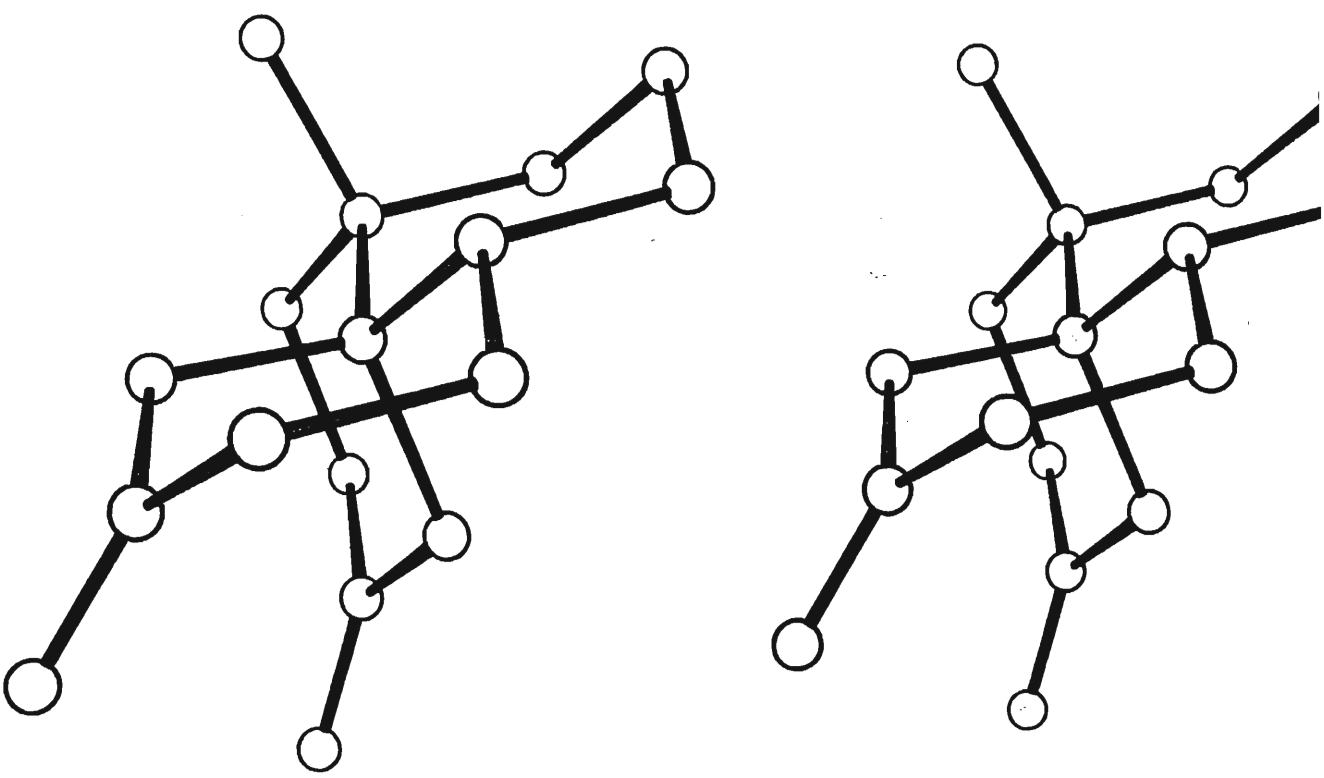
---

[a]Relative configurations of one enantiomer.

The bond lengths are given in Table 4[b], the bond angles in Table 5 and the ring torsion angles in Table 6.

FIGURE 3

The stereoscopic drawing of (4aR*,7aS*,11aR*)-4a-methyloctahydro-1*H*-benzo[d]naphthalene-2,10(3*H*,11*H*)-dione (78)



[b] **Full crystallographic data have been deposited at the Cambridge Crystallographic Data Centre.**

TABLE 4

BOND LENGTHS (Å) FOR (78)

	Bond Lengths (Å)
C1-C2	1,557
C1-C6	1,552
C1-C10	1,559
C1-C14	1,552
C2-C3	1,507
C3-C4	1,495
C3-O1	1,209
C4-C5	1,531
C5-C6	1,527
C6-C7	1,539
C7-C8	1,520
C8-C9	1,527
C9-C10	1,545
C10-C11	1,541
C10-C15	1,540
C11-C12	1,521
C12-C13	1,495
C13-C14	1,504
C13-O2	1,210

TABLE 5

BOND ANGLES (°) FOR (78)

	Bond Angles (°)
C1-C2-C3	111,5
C2-C1-C6	107,8
C1-C6-C5	112,5
C1-C6-C7	112,6
C2-C1-C10	111,2
C6-C1-C10	110,3
C1-C10-C9	109,8
C1-C10-C11	110,9
C1-C10-C15	113,2
C2-C1-C14	107,2
C6-C1-C14	110,7
C10-C1-C14	109,5
C1-C14-C13	114,2
C2-C3-C4	115,2
C2-C3-O1	122,1
C3-C4-C5	111,7
C4-C3-O1	122,7
C4-C5-C6	111,5
C5-C6-C7	111,1
C6-C7-C8	111,5
C7-C8-C9	110,9
C8-C9-C10	113,4
C9-C10-C11	109,3
C9-C10-C15	107,8
C10-C11-C12	115,1
C11-C10-C15	105,7
C11-C12-C13	111,8
C12-C13-C14	115,8
C12-C13-O2	122,5
C14-C13-O2	121,7

TABLE 6

TORSIONAL ANGLES (°) FOR (78)

Atom 1	Atom 2	Atom 3	Atom 4	Angle (°)	Error
C6	C1	C2	C3	- 55	0
C10	C1	C2	C3	-176	0
C14	C1	C2	C3	64	0
C2	C1	C6	C5	57	0
C2	C1	C6	C7	-176	0
C10	C1	C6	C5	179	0
C10	C1	C6	C7	- 55	0
C14	C1	C6	C5	- 60	0
C14	C1	C6	C7	67	0
C2	C1	C10	C9	173	0
C2	C1	C10	C11	- 66	0
C2	C1	C10	C15	53	0
C6	C1	C10	C9	54	0
C6	C1	C10	C11	175	0
C6	C1	C10	C15	- 67	0
C14	C1	C10	C9	- 68	0
C14	C1	C10	C11	53	0
C14	C1	C10	C15	171	0
C2	C1	C14	C13	69	0
C6	C1	C14	C13	-174	0
C10	C1	C14	C13	- 52	0
C1	C2	C3	C4	54	0
C1	C2	C3	O1	-126	0
C2	C3	C4	C5	- 51	0
O1	C3	C4	C5	129	0
C3	C4	C5	C6	51	0
C4	C5	C6	C1	- 56	0
C4	C5	C6	C7	177	0
C1	C6	C7	C8	55	0
C5	C6	C7	C8	-178	0
C6	C7	C8	C9	- 54	0
C7	C8	C9	C10	56	0
C8	C9	C10	C1	- 56	0
C8	C9	C10	C11	-177	0
C8	C9	C10	C15	68	0
C1	C10	C11	C12	- 53	0
C9	C10	C11	C12	68	0
C15	C10	C11	C12	-176	0
C10	C11	C12	C13	49	0
C11	C12	C13	C14	- 46	0
C11	C12	C13	O2	137	0
C12	C13	C14	C1	50	0
O2	C13	C14	C1	-133	0

6.2 CRYSTAL STRUCTURE DATA AND STEREOSCOPIC DRAWING FOR 9-ACETYL-8a-METHYLPERHYDRO-2,4a-ETHANONAPHTHALEN-3-ONE (80)

Formula	$C_{15}H_{22}O_2$
M	234
Space group	$P2_1/n$
a/Å	6,702(2)
b/Å	13,074(2)
c/Å	14,505
β/°	92,19
U/Å^3	1270
Z	4
Dc/g.cm^{-3}	1,22

Crystal data were collected on an Enraf-Nonius CAD4 diffractometer with graphite-monochromated M_o-K_α radiation (λ = 0,7107 Å). From 3990 reflections measured for $2 < \theta < 30°$, 2816 observed reflections (final residual R = 0,067) with $F > 2\sigma F$ were used in the structure solution [direct methods (MULTAN)] and refinement (block diagonal least squares). The stereoscopic drawing (Figure 4) was calculated with the ORTEP programme. The bond lengths are given in Table 7[c], the bond angles in Table 8 and the ring torsion angles in Table 9.

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[c] **Full crystallographic data have been deposited at the Cambridge Crystallographic Data Centre.**

FIGURE 4

Stereoscopic drawing of 9-acetyl-8a-methyl-perhydro-2,4a-ethanonaphthalen-3-one (80)

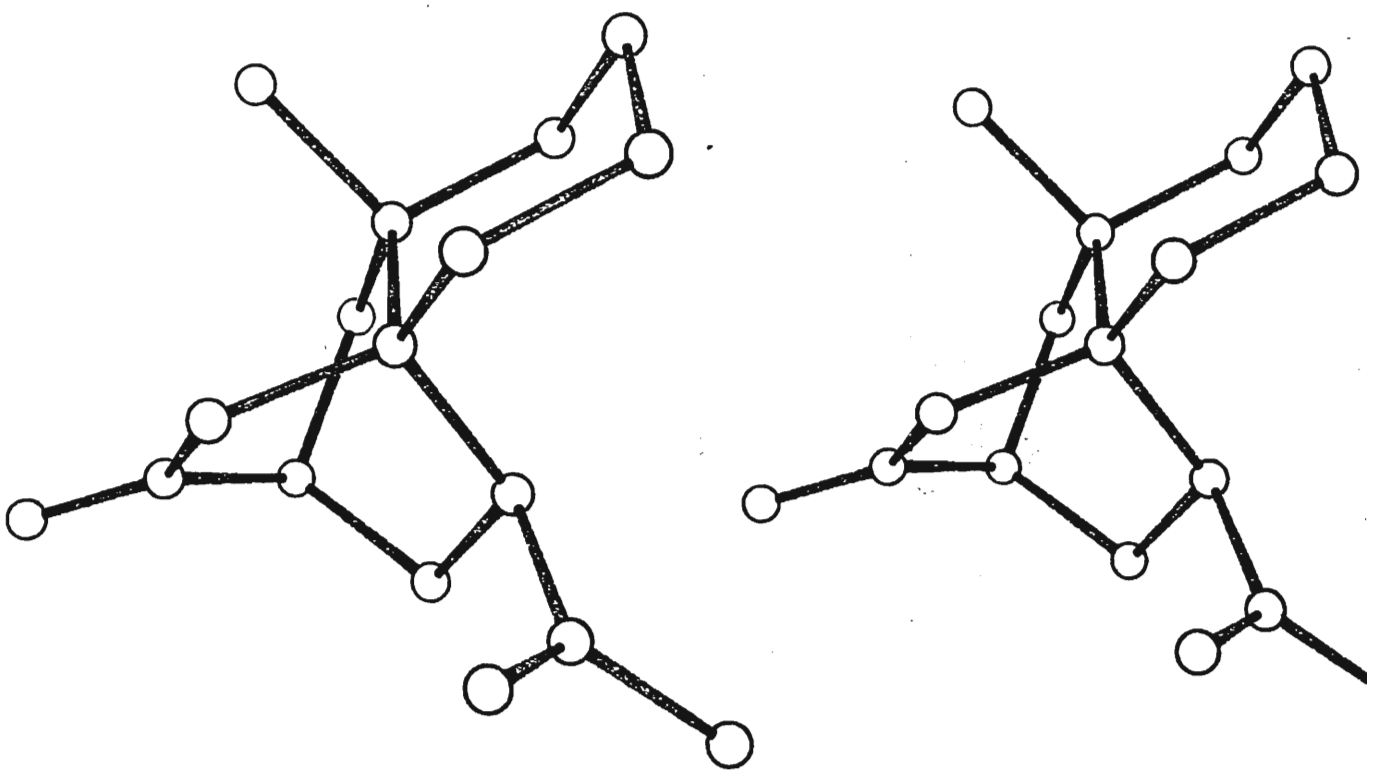

TABLE 7

BOND LENGTHS (Å) FOR (80)

	Bond Lengths (Å)
C1-C2	1,557
C1-C3	1,569
C1-C11	1,537
C1-C13	1,548
C2-C4	1,560
C2-CE	1,519
C3-C5	1,552
C3-C6	1,541
C3-Me12	1,551
C4-CG	1,536
C5-CG	1,539
C6-C9	1,526
C9-C10	1,524
C10-C11	1,515
CG-CB	1,509
CB-C13	1,516
CB-O1	1,209
CE-CF	1,523
C5-O2	1,215

TABLE 8

BOND ANGLES (°) FOR (80)

	Bond Angles (°)
C1-C2-C4	110,5
C1-C2-CE	117,0
C2-C1-C3	107,4
C1-C3-C5	108,4
C1-C3-C6	110,4
C1-C3-Me12	111,5
C2-C1-C11	111,9
C3-C1-C11	110,8
C1-C11-C10	112,8
C2-C1-C13	107,3
C3-C1-C13	108,5
C11-C1-C13	110,8
C1-C13-CB	109,9
C2-C4-CG	109,1
C4-C2-CE	107,2
C2-CE-CF	115,1
C2-CE-O2	124,3
C3-C5-CG	111,4
C5-C3-C6	110,0
C3-C6-C9	113,2
C5-C3-Me12	108,3
C6-C3-Me12	108,3
C4-CG-C5	108,0
C4-CG-CB	106,7
C5-CG-CB	109,7
C6-C9-C10	111,2
C9-C10-C11	111,7
CG-CB-C13	112,4
CG-CB-O1	124,4
C13-CB-O1	123,2
CF-CE-O2	120,6

TABLE 9

TORSIONAL ANGLES (°) FOR (80)

Atom 1	Atom 2	Atom 3	Atom 4	Angle (°)	Error
C3	C1	C2	C4	- 67	0
C3	C1	C2	CE	170	0
C11	C1	C2	C4	171	0
C11	C1	C2	CE	48	0
C13	C1	C2	C4	49	0
C13	C1	C2	CE	- 74	0
C2	C1	C3	C5	50	0
C2	C1	C3	C6	- 70	0
C2	C1	C3	Me12	169	0
C11	C1	C3	C5	173	0
C11	C1	C3	C6	52	0
C11	C1	C3	Me12	- 68	0
C13	C1	C3	C5	- 66	0
C13	C1	C3	C6	174	0
C13	C1	C3	Me12	54	0
C2	C1	C11	C10	66	0
C3	C1	C11	C10	- 54	0
C13	C1	C11	C10	-175	0
C2	C1	C13	CB	- 64	0
C3	C1	C13	CB	52	0
C11	C1	C13	CB	174	0
C1	C2	C4	CG	14	0
CE	C2	C4	CG	143	0
C1	C2	CE	CF	-159	0
C1	C2	CE	O2	24	0
C4	C2	CE	CF	76	0
C4	C2	CE	O2	-101	0
C1	C3	C5	CG	14	0
C6	C3	C5	CG	135	0
Me12	C3	C5	CG	-107	0
C1	C3	C6	C9	- 53	0
C5	C3	C6	C9	-173	0
Me12	C3	C6	C9	69	0
C2	C4	CG	C5	51	0
C2	C4	CG	CB	- 67	0
C3	C5	CG	C4	- 68	0
C3	C5	CG	CB	48	0
C3	C6	C9	C10	55	0
C6	C9	C10	C11	- 55	0
C9	C10	C11	C1	56	0
C4	CG	CB	C13	54	0
C4	CG	CB	O1	125	0
C5	CG	CB	C13	- 63	0
C5	CG	CB	O1	118	0
CG	CB	C13	C1	11	0
O1	CB	C13	C1	-170	0

6.3 CRYSTAL STRUCTURE DATA AND STEREOSCOPIC DRAWING SHOWING THE CRYSTALLOGRAPHIC NUMBERING FOR (4aR*,7aR*,11aR*)-4a-METHYLOCTA-HYDRO-1*H*-BENZO[d]NAPHTHALENE-2,10(3*H*,11*H*)-DIONE[d] (90)

Formula	$C_{15}H_{22}O_2$
M	234
Space group	$P\bar{1}$
a/Å	7,583(1)
b/Å	8,284(2)
c/Å	10,938(2)
α/°	88,56(2)
β/°	84,47(1)
γ/°	69,01(2)
U/Å^3	638,5(2)
Z	2
Dc/g.cm^{-3}	1,227
λ/Å	0,71069
F(000)	256
μ(M_o-K_α)/cm^{-1}	0,43

[d]Relative configurations of one enantiomer.

Intensity data were collected from a crystal of 0,56 x 0,13 x 0,09 mm on an Enraf-Nonius CAD4 diffractometer using the ω - 2θ scan method ($\theta \leq 30°$). From 3172 unique measured reflections corrected for Lorentz and polarisation effects but not for absorption, 2460 with $I > 3\sigma(I)$ were used in the structure solution (direct methods[e]) and refinement[f] which converged at R and R_ω values of 0,047 and 0,058 respectively.

The atomic co-ordinates are given in Table 10[g] and the ring torsion angles are listed in Table 11. The atomic numbering and molecular structure are given in Figure 5.

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[e] Sheldrick, G.M., SHELX76, Program for crystal structure solution and refinement, University of Cambridge, 1976.

[f] Sheldrick, G.M., SHELX86, Program for crystal structure solution, University of Göttingen, 1986.

[g] Full crystallographic data have been deposited as supplementary material, available on request from: Reference Section, CSIR Library Division, NII, P.O. Box 396, Pretoria, 0001.

FIGURE 5

Stereoscopic drawing of (4aR*,7aR*,11aR*)-4a-methyl-octahydro-1*H*-benzo[d]naphthalene-2,10(3*H*,11*H*)-dione (90) showing the crystallographic numbering.

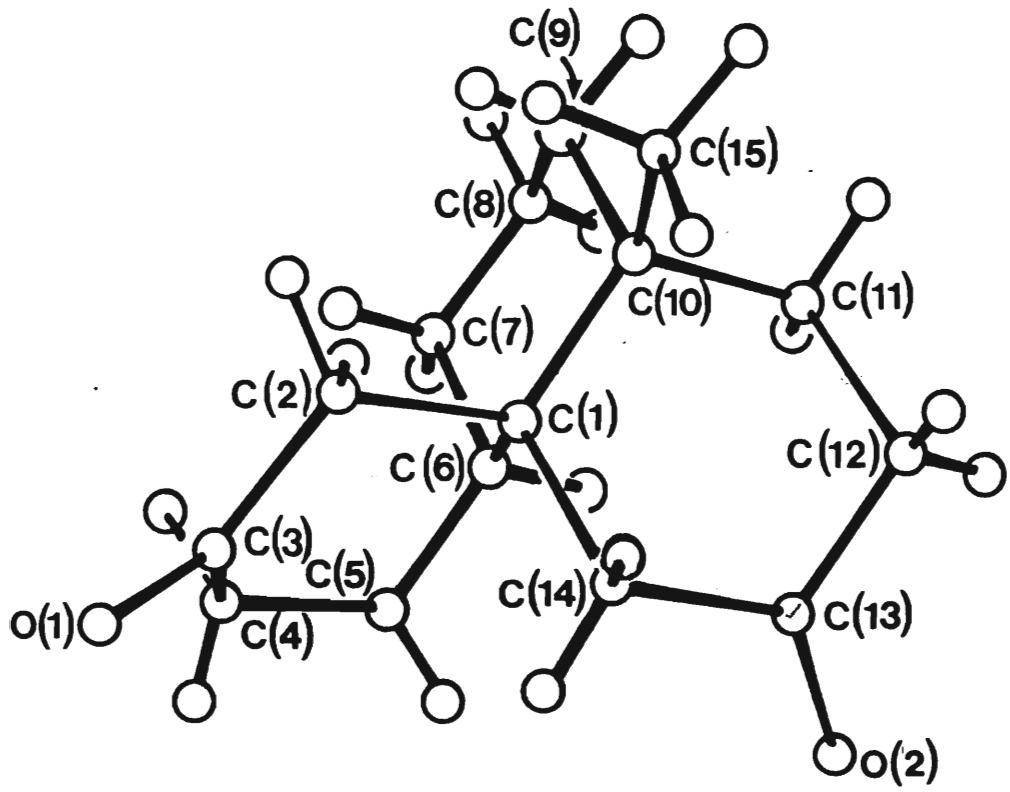


TABLE 10

Fractional coordinates ($x10^4$) for structure (90).

Atom	x/a	y/b	z/c
O1	7167(2)	6377(2)	4468(1)
O2	6109(2)	10912(2)	8571(1)
C1	4151(2)	8183(1)	7166(1)
C2	4436(2)	7295(2)	5895(1)
C3	6479(3)	6242(2)	5498(1)
C4	7547(3)	5008(2)	6414(2)
C5	7221(2)	5800(2)	7703(2)
C6	5115(2)	6794(2)	8108(1)
C7	4067(2)	5519(2)	8382(1)
C8	2000(2)	6459(2)	8841(2)
C9	1028(2)	7803(2)	7925(2)
C10	1994(2)	9131(2)	7586(1)
C11	1764(2)	10260(2)	8729(2)
C12	2780(3)	11568(2)	8578(2)
C13	4820(2)	10688(2)	8117(2)
C14	5134(2)	9543(2)	7011(1)
C15	909(3)	10275(2)	6579(2)

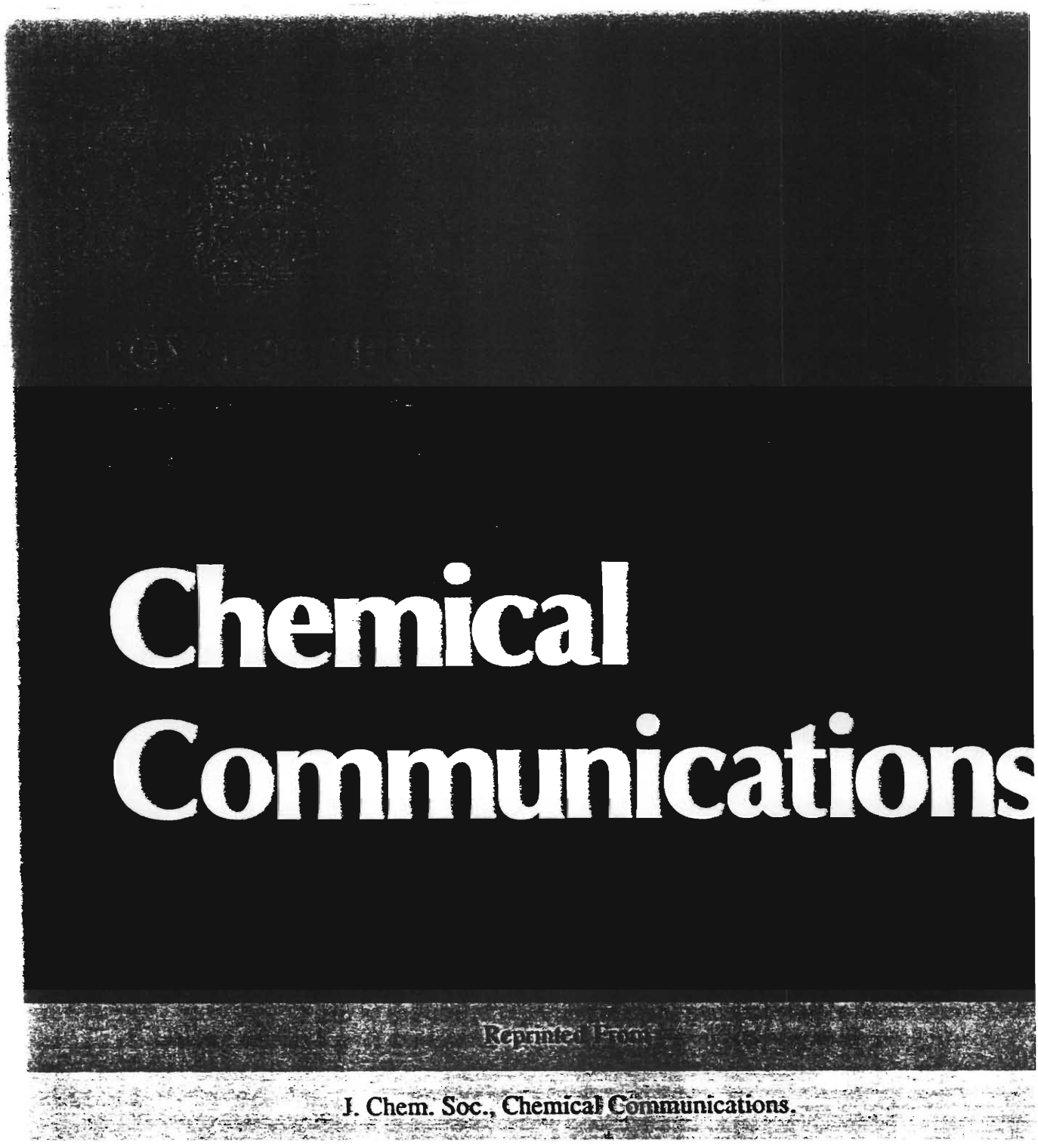
TABLE 11

Ring Torsion Angles (°) in (90).

RING A	Torsion Angles (°)
C10-C1-C6-C7	53,6(2)
C6-C7-C8-C9	56,1(2)
C8-C9-C10-C1	56,2(2)
C1-C6-C7-C8	-56,8(2)
C7-C8-C9-C10	-55,5(2)
C9-C10-C1-C6	-50,3(2)
RING B	
C6-C1-C2-C3	-52,8(2)
C2-C3-C4-C5	-45,1(2)
C4-C5-C6-C1	-53,8(2)
C1-C2-C3-C4	49,4(2)
C3-C4-C5-C6	46,9(2)
C5-C6-C1-C2	55,5(2)
RING C	
C11-C10-C1-C14	-52,9(2)
C1-C14-C13-C12	-52,8(2)
C13-C12-C11-C10	-52,2(2)
C10-C1-C14-C13	53,2(2)
C14-C13-C12-C11	49,8(2)
C12-C11-C10-C1	55,0(2)

CHAPTER SEVEN

7. PUBLICATIONS



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Remarkable Solvent Dependent Cyclisation of Methyl Vinyl Ketone across the 8,8a and 3,8a Positions of $\Delta^{1,8a}$-2-Octalone Dienamines. First Syntheses of the Tricyclo[8.4.0.0^{1,6}]tetradecane and Tricyclo[6.2.2.0^{1,6}]dodecane Ring Systems. Crystal Structures

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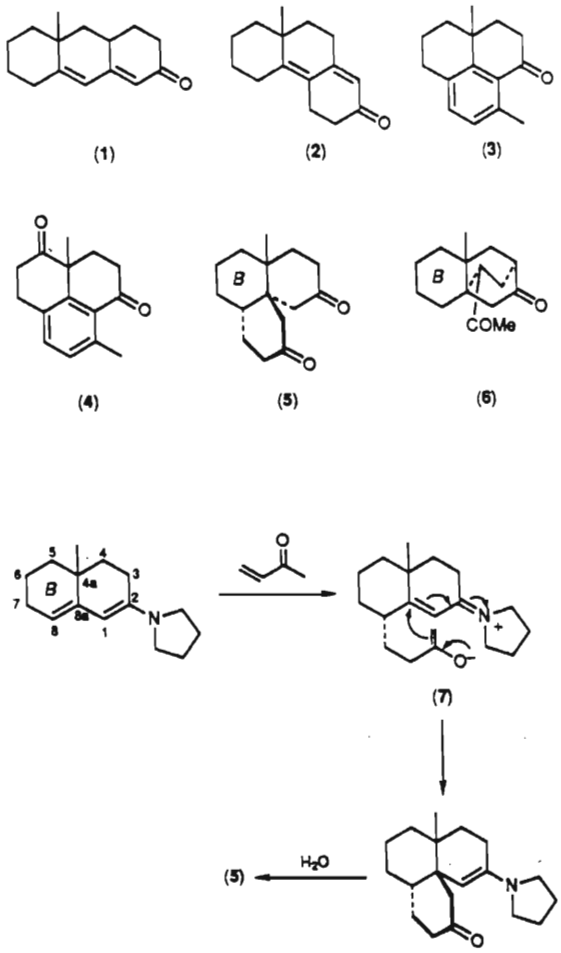
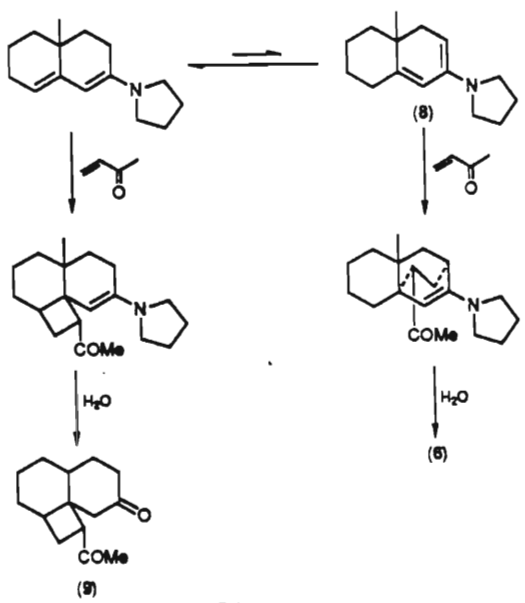
Reaction of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone with methyl vinyl ketone occurs primarily across the 8,8a-positions in methanol to provide the first synthesis of 10-methyltricyclo[8.4.0.0^{1,6}]tetradecane-3,13-dione (**5**), whereas in toluene reaction occurs across the 3,8a-positions to give 11-acetyl-6-methyltricyclo[6.2.2.0^{1,6}]dodecan-9-one (**6**), the stereochemistry of both structures being determined by *X*-ray analysis.

Recently we have reported that the alkylation of the pyrrolidine dienamine of 3-methyl-$\Delta^{1,8a}$-2-octalone with methyl propenoate and propenenitrile is solvent dependent;[1] in protic medium the reaction occurred at C-1 whereas in aprotic medium reaction occurred at C-4a. In an extension of this investigation we now report our preliminary observations on the reaction of the pyrrolidine dienamine of 4a-methyl-$\Delta^{1,8a}$-2-octalone with methyl vinyl ketone (MVK).

This reaction was expected to give either the linear (**1**) or angular (**2**) annulation product, as an extension of Stork's



Scheme 1



Scheme 2

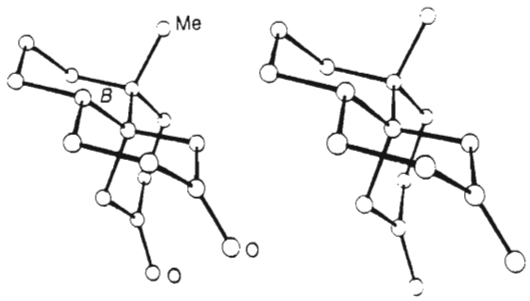


Figure 1

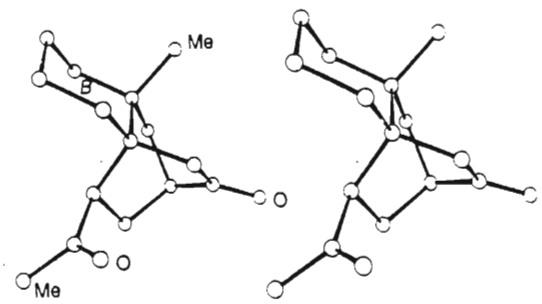


Figure 2

synthesis of $\Delta^{1,8a}$-2-octalones,[2] or (**3**) by analogy with the reported synthesis of (**4**) from the corresponding 5-oxodienamine.[3] In fact only compound (**1**) was produced in any detectable amount (by GC MS). The reaction was carried out initially in boiling methanol followed by hydrolytic work-up producing a complex mixture from which the 8,8a-cycloadduct [(**5**); 21%]† was isolated as the main component, and separated by flash chromatography into two stereoisomers. In boiling toluene the 3,8a-cycloadduct [(**6**); 28%]† was the main component of the complex mixture, together with a small amount (<5%) of the linear condensation product (**1**).

These results are remarkable and could not have been anticipated from previous work on related systems.[1,4] In methanol reaction occurs primarily at the less reactive δ-position[4b] of the dienamine, in stark contrast to the corresponding reaction with methyl propenoate and propenenitrile where reaction with this dienamine occurs at the more reactive β-position (C-1) in all solvents.[1] The mechanism of the subsequent cyclisation is not proved but probably involves a prototropic shift in the initially formed enolate anion to give (**7**), and subsequent cyclisation onto C-8a of the eniminium salt (Scheme 1) thus producing the quaternary centre. This provides access to the novel [8.4.0.$0^{1,6}$]tetradecane ring system for the first time.

The second result is also surprising, not only for the apparently inexplicable change in the regioselectivity of the reaction, but also as both products [(**1**) and (**6**)] must arise from the cross-conjugated dienamine [(**8**); Scheme 2] which we have shown previously[5] was not present in any detectable amount in the starting dienamine! To the best of our knowledge, this is the first synthesis of the tricyclo-[6.2.2.$0^{1,6}$]dodecane ring system. Formation of the alternative tricyclic structure [(**9**), Scheme 2] by [2 + 2]cycloaddition across the 8,8a-positions is mechanistically more plausible.

† No attempts have yet been made to optimise yields. All new compounds gave the expected microanalytical, IR, NMR, and mass spectral data.

Cycloadduct (**9**) would give the same number of methine, methyl, methylene, and quaternary carbon signals in the ^{13}C NMR spectrum as (**6**) but has been ruled out from the *X*-ray crystal structure analysis.‡

The ^{13}C NMR spectrum of both isomers of (**5**) showed one methyl, two carbonyl, two quaternary carbon, one methine, nine methylene, and no alkenic signals. On this basis we assigned the tricyclo[8.4.0.$0^{1,6}$]tetradecane structure to both isomers. This was subsequently confirmed by a single crystal *X*-ray structure determination of the major isomer. The stereoscopic drawing of the enantiomer of (**5**)§ (Figure 1) shows that initial attack at C-8 occurred from the α-face of the dienamine, *anti* to the C-4a methyl group, as would be expected on steric grounds, but cyclisation at C-8a occurred *syn* to the angular methyl group. Both newly formed carbon–carbon bonds are therefore equatorial to ring *B* of the starting dienamine, and the original 1,8a-bond has become axial to ring *B*. The molecular framework is rigid with all three rings present as chairs with normal torsion angles.

The stereoscopic drawing of the enantiomer of (**6**)§ (Figure 2) shows that [4 + 2]cycloaddition to the dienamine (**7**) has again occurred from the less hindered α-face. The 'boats' in the tricyclo[2.2.2]octane residue are not ideal, but are all slightly twisted in the same sense through a mean torsion angle of 13°. This effectively reduces the volume of this part of the molecule while simultaneously relieving the non-bonded H · · · H and C · · · H repulsions caused by eclipsing.

The application of this reaction to this and other cyclic, acyclic, and heterocyclic dienamines is being actively pursued. The effect of experimental conditions and substituents on the yield and course of the reaction is also being determined.

We thank Dr J. S. Field of the University of Natal, Pietermaritzburg, for *X*-ray data collection, and the Foundation for Research Development for financial support.

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‡ However another as yet unidentified component (m.p. 80—82 °C; 13%) was isolated from this reaction which could be a stereoisomer of (**6**) or a regioisomer such as (**9**).

§ *Crystal data* for $C_{15}H_{22}O_2$ (**5**): white crystals, m.p. 139—141 °C (from hexane–ethyl acetate), M = 234, monoclinic, space group $P2_1/c$, a = 7.171(1), b = 15.610(1), c = 11.481(1) Å, β = 94.60°. U = 1281.2 Å^3, Z = 4, D_c = 1.21 g cm^{-3}, 4027 reflections measured for 2.0 < θ < 30.0°, final residual R = 0.063 for 2753 observed reflections ($F > 2\sigma F$). *Crystal data* for $C_{15}H_{22}O_2$ (**6**): white crystals, m.p. 95—97 °C (from hexane–ethanol), M = 234, monoclinic, space group $P2_1/n$, a = 6.702(2), b = 13.074(2), c = 14.505(2) Å, β = 92.19°, U = 1270.1 Å^3, Z = 4, D_c = 1.22 g cm^{-3}, 3990 reflections measured for 2.0 < θ < 30.0°; final residual R = 0.067 for 2816 observed reflections ($F > 2\sigma F$). All crystal data were collected on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromated Mo-K_α radiation (λ = 0.7107 Å). Both structures were solved by direct methods (MULTAN) and refined by block-diagonal least squares. The stereoscopic drawings were calculated with the ORTEP program. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

References

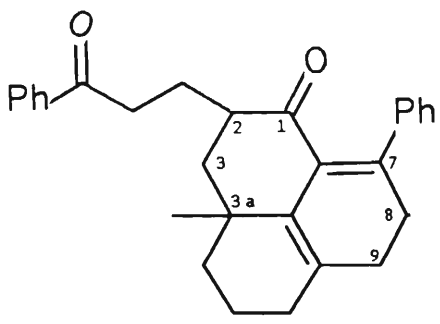
1 P. W. Hickmott, A. Papaphilippou, D. H. Pienaar, R. D. Soelistyowati, and C. T. Yoxall, *S. Afr. J. Chem.*, 1988, **41**, 75.
2 G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, and R. Terrell, *J. Am. Chem. Soc.*, 1963, **85**, 207.
3 P. Houdewind, J. C. Lapierre Armande, and U. K. Pandit, *Tetrahedron Lett.*, 1974, 591.
4 (a) P. W. Hickmott, *Tetrahedron*, 1982, **38**, 2050; 3363; (b) 1984, **40**, 2989.
5 N. F. Firrell and P. W. Hickmott, *J. Chem. Soc.* (*B*), 1969, 293.

CHAPTER EIGHT

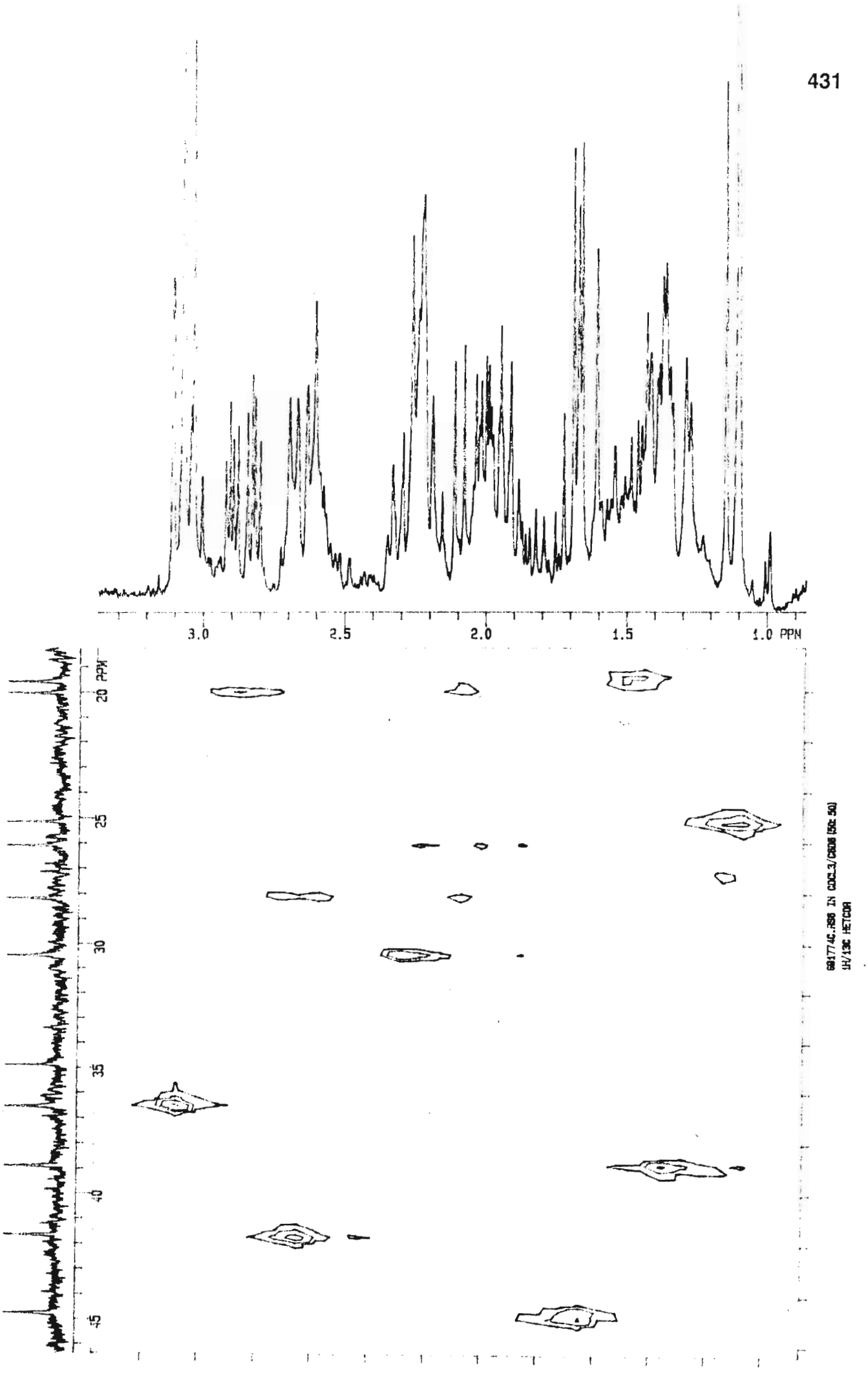
8. POSTSCRIPT

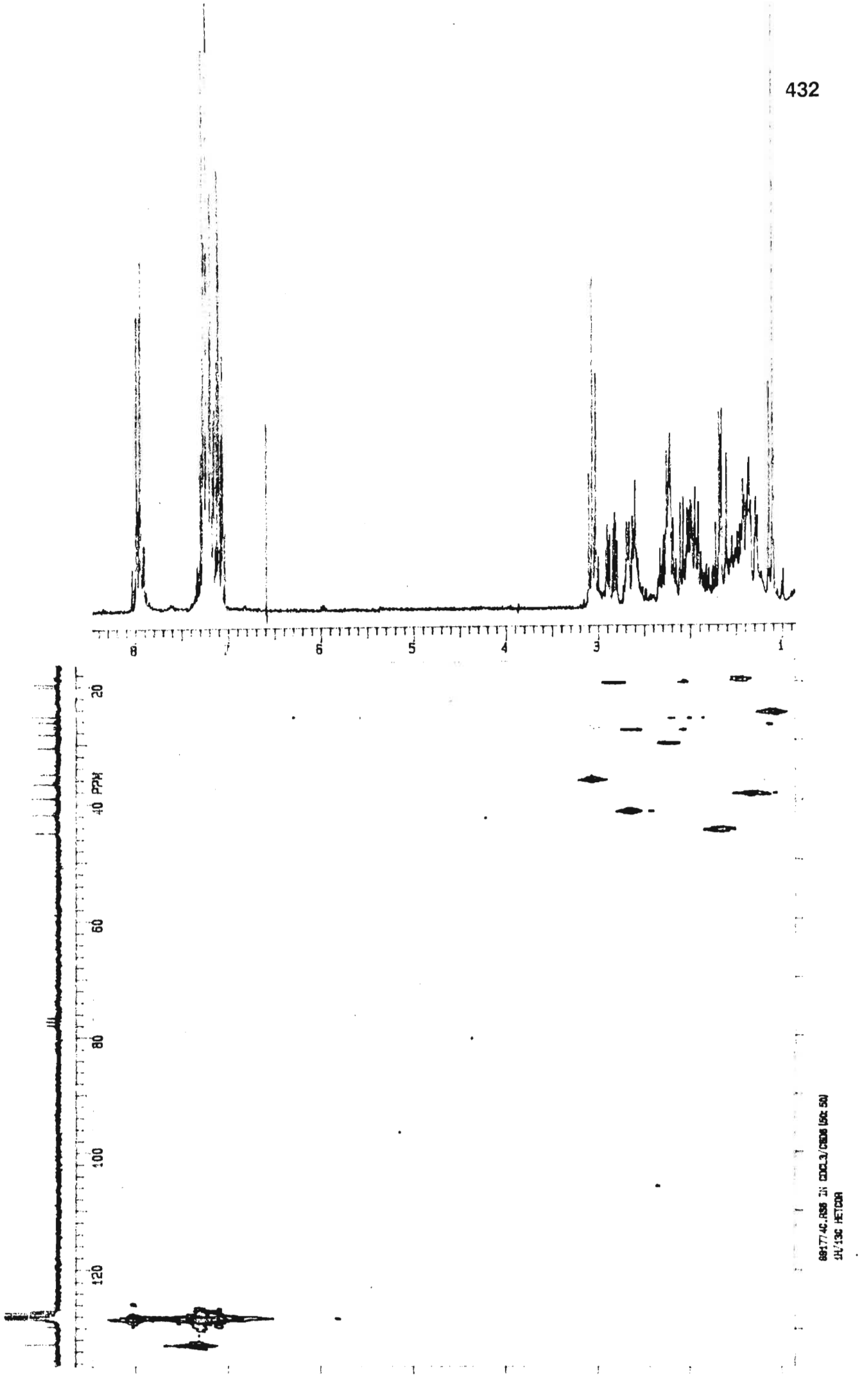
8.1 CONFIRMATION OF STRUCTURE(122)

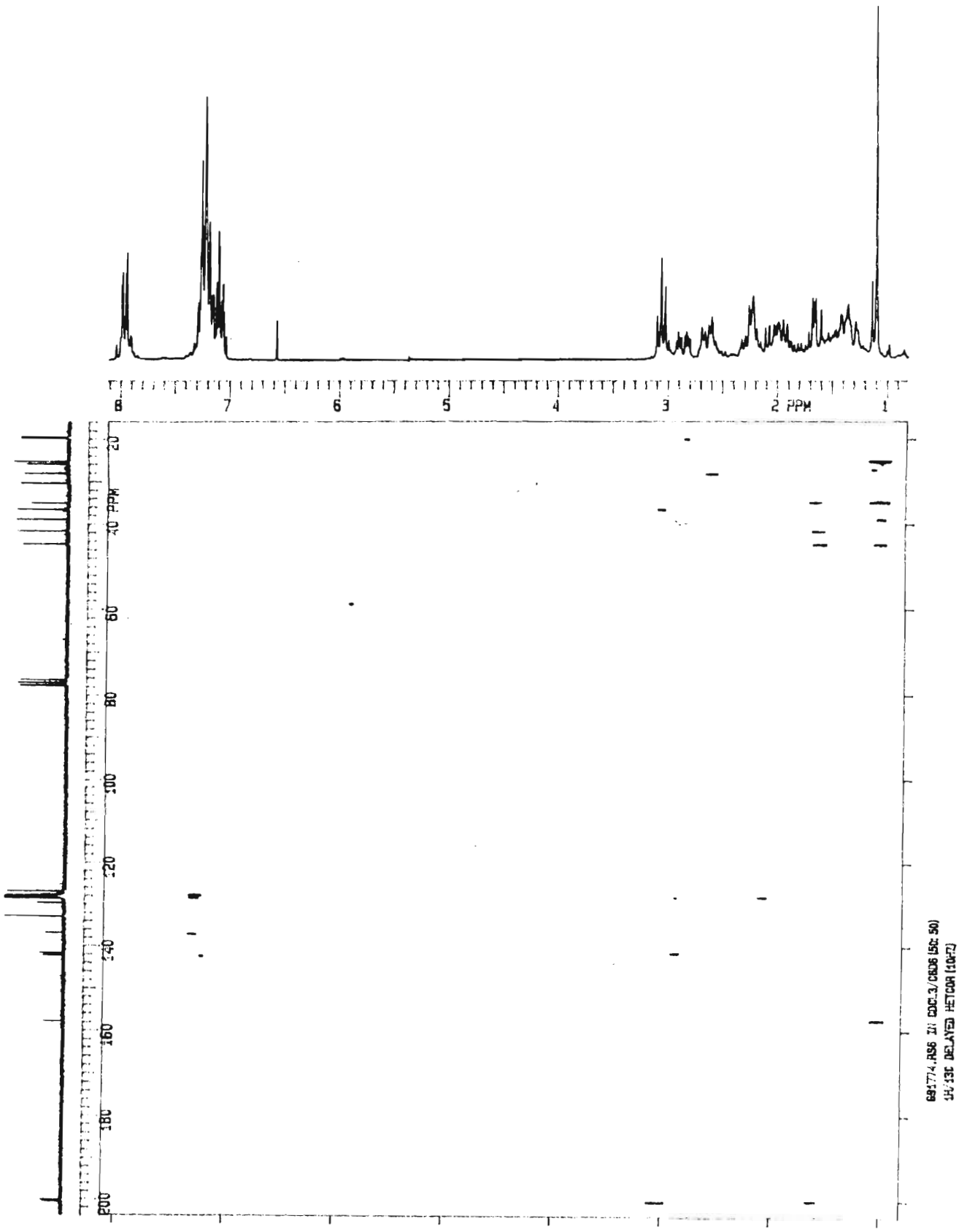
As mentioned in Section 2.3 structure (122) could not be confirmed due to the complexity of the 1D and 2D spectra.The HETCOR spectrum was re-run using a mixed solvent [$CDCl_3/C_6D_6$(50:50].The multiplet at δ 2.75 was resolved to give two multiplets centred at δ 2.65 and δ 2.85. The signal due to the proton of the CH group remained in the multiplet centred at δ 2.65 and shows no long range coupling to the carbonyl groups in the DELAYED HETCOR spectrum which would be expected for the possible structure (123). Long range coupling between the carbonyl groups and the CH_2 protons at δ 1.65 and δ 3.05, is however evident in the DELAYED HETCOR spectrum thus confirming structure (122). The spectra appear on pages 431-433.



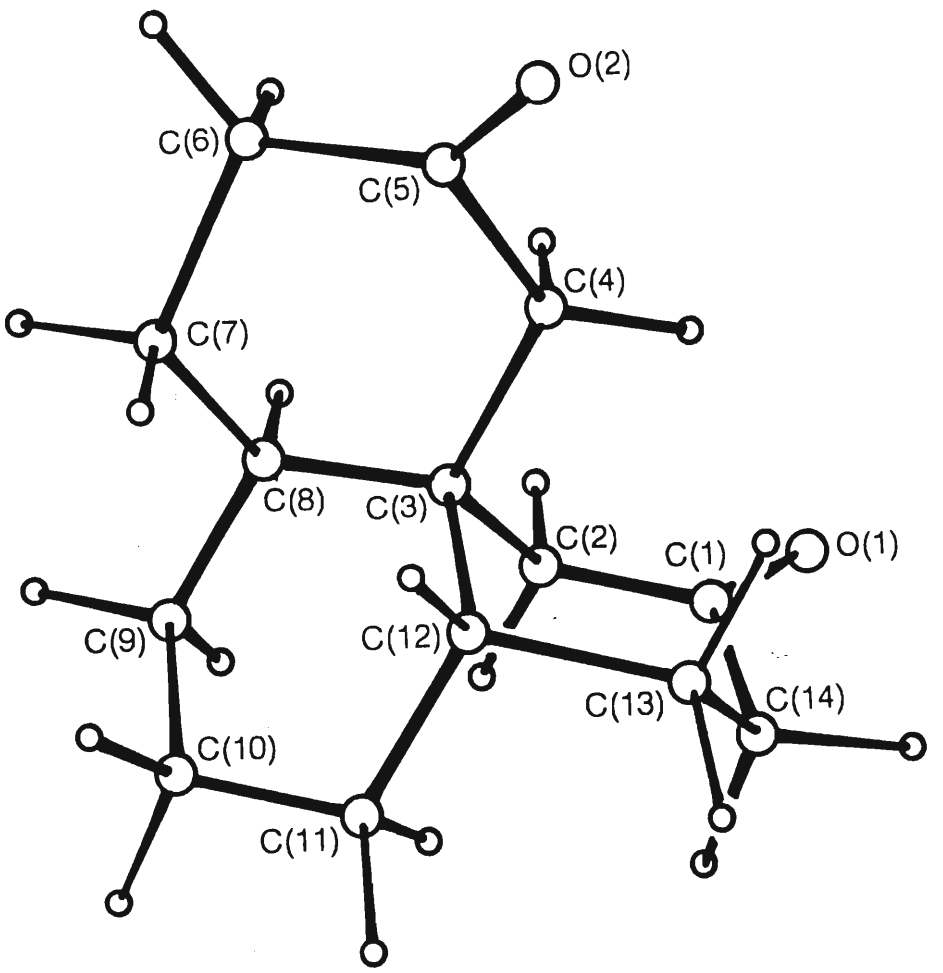
(123)


3.0
2.5
2.0
1.5
1.0 PPM
20 PPM
25
30
35
40
45
GB1774C.R90 IN CDCL3/CDOD (50: 50)
1H/13C HETCOR


8
7
6
5
4
3
1
20
40 PPM
60
80
100
120


8
7
6
5
4
3
2 PPM
1
20
40 PPM
60
80
100
120
140
160
180
200
981774.A56 IN CDCL3/C6D6 (5C 50)
1H/13C DELAYED HETCOR (10Hz)

8.2 CRYSTAL STRUCTURE DATA AND STEREOSCOPIC DRAWING FOR OCTAHYDRO-1 H-BENZO[d]NAPHTHALENE-2,10-(3H,11H)-DIONE(75;MP 164.9-165^{0}C)[83]



.J.S. Field and N. Ramesar, personal communication. Crystal data. - $C_{14}H_{20}O_2$, M = 221,74; space group = $Pna2_1$; a = 14,171 (3), b = 7,952(5), c = 21,241(2) Å; Z = 8, Mo-Kα radiation (λ = 0.71069Å). Final R = 0,050; Rw = 0,060 for 1501 unique reflections and 289 variables. The two independent molecules in the asymmetric unit are geometrically equivalent.