CHAPTER I

FRAGMENTATION OF HOMOALLYLIC ALCOHOLS

SECTION I

CLEAVAGE OF HYDROXYSPIRO [BICYCLO(2.2.1)HEPTANE-2,1'-CYCLOPROPANE] DERIVATIVES

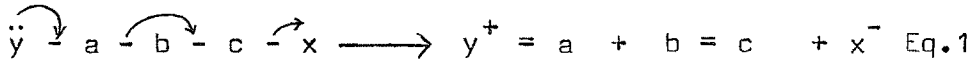
A B S T R A C T

A brief review of Grob's fragmentation and the related fragmentation of homoallylic alcohols reported by Sukh Dev and co-workers is presented. Synthesis of four spirocyclopropane derivatives, namely, 3,3-dimethylspiro-[bicyclo(2.2.1)heptane-2,1'-cyclopropane] (51), 6-exo/endo-hydroxy-3,3-dimethylspiro[bicyclo(2.2.1)heptane-2,1'-cyclopropane] (42/43) and methyl 6-exo-hydroxy-3,3-dimethylspiro-[bicyclo(2.2.1)heptane-2,1'-cyclopropane]-2'-carboxylate (46) is described. A byproduct formed in the Simmons-Smith reaction of 6-exo-acetoxycamphene (50) is characterised as 2,2-dimethyltricyclo[4.2.1.$0^{3,7}$]nonan-3-ol (56). The electrophile-induced fragmentation reactions of the above cyclopropane derivatives have been investigated and the products characterised.

CLEAVAGE OF HYDROXYSPIRO[BICYCLO(2.2.1)-HEPTANE-2,1'-CYCLOPROPANE] DERIVATIVES

INTRODUCTION

Grob Fragmentation: Systems such as ÿ-a-b-c-x, where x and y are normal nucleofuge and elctrofuge[1] respectively and a,b,c generally constitute a carbon chain but could also include atoms such as N,S,P or B etc., fragment easily under heterolytic conditions to form y^+ = a, b = c and x^- moieties (Eq. 1).

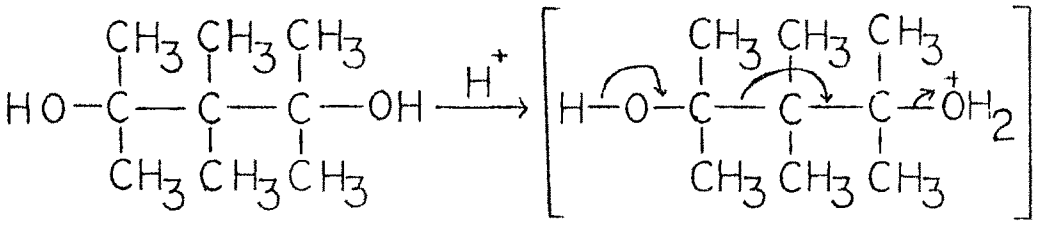


Eq.1

These reactions have been extensively studied[2] and the geometric and stereoelectronic requirements identified.[3] The unsaturated fragment, b = c can generally be (a) an olefin, (b) an alkyne, (c) an imine, (d) a nitrile or (e) a carbonyl compound. One or two illustrations for each type are given here:

(a) Acid-catalysed fragmentation of tetramethyl-2,4-pentane diol (1) gives acetone and dimethyl-2-butene (2)[4] (Eq. 2).

(b) Both cis- and trans-β-bromocinnamic acids give phenylacetylene when their salts are heated in water (Eq. 3).[5] The unstable benzyne is formed by mild decarboxylation of diazotised anthranilic acid[6] (Eq. 4).



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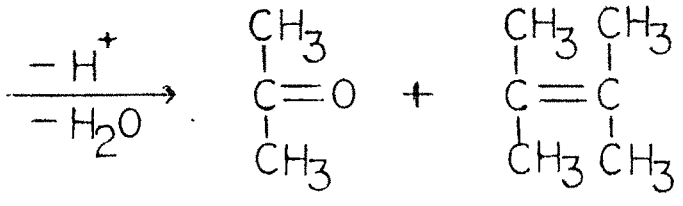
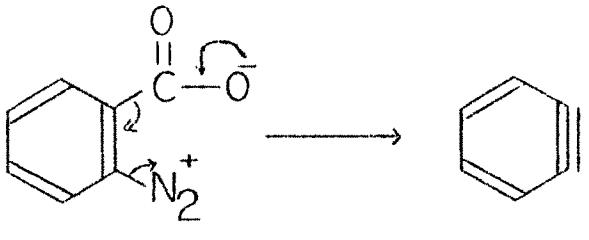


2

Eq.2

Eq.3



Eq.4

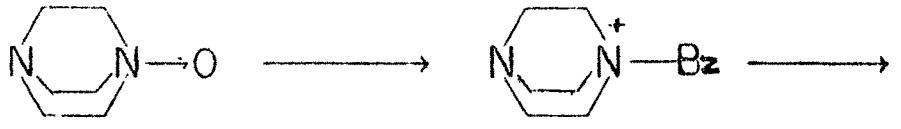
(c) Benzoylation of the N-oxide of 1,4-diazabicyclo-(2.2.2)octane (3) followed by hydrolysis yields piperazine (6) and formaldehyde.[7] The ammonium salt 4 fragments to the bisimonium salt 5, which further hydrolyses to 6 (Eq. 5).

(d) The compound 7 undergoes base-catalysed fragmentation to furnish the keto-nitrile 8[8] (Eq. 6).

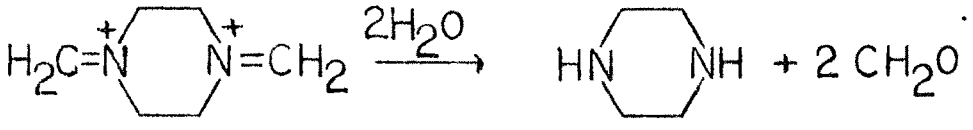
(e) α-Methylstyrene oxide (9) fragments with H_2O_2 into acetophenone and formaldehyde[9] (Eq. 7).

Geometric and stereoelectronic requirements: The heterolytic fragmentation reactions can proceed by either of two mechanisms, namely a two-step carbonium ion mechanism or a synchronous mechanism (Eq. 8). In the former mechanism, the C-X bond cleaves to give a carbonium ion of the type 10 which undergoes fragmentation. Specific geometry of the molecule is therefore not an essential condition for the fragmentation. The intermediate carbonium ion can also undergo other side reactions like elimination and substitution. For example, the carbonium, ion (12) derived from 3-(2'-chloro-2'-propyl)-quinuclidine (11) undergoes all the three types of reactions to give products[10] (Fig. 1).

In the synchronous mechanism, the cleavage of C-C bond is accompanied by simultaneous loss of X^- ion from the

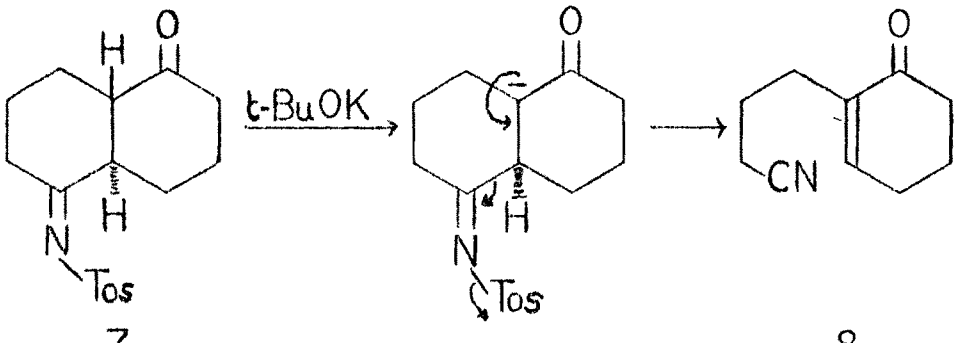


3 4



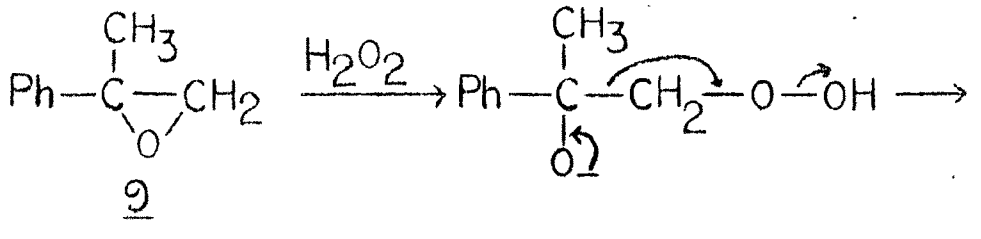
Eq·5

5 6

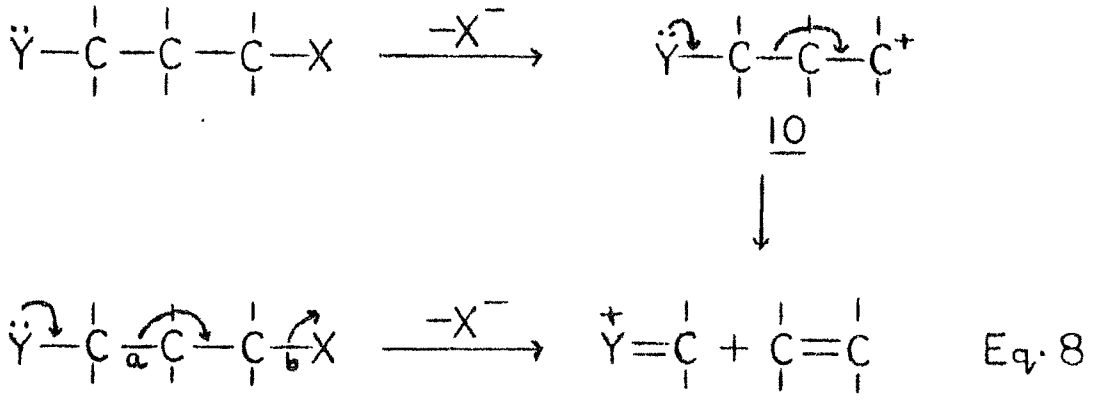


Eq·6

7 8



Eq·7



Eq. 8

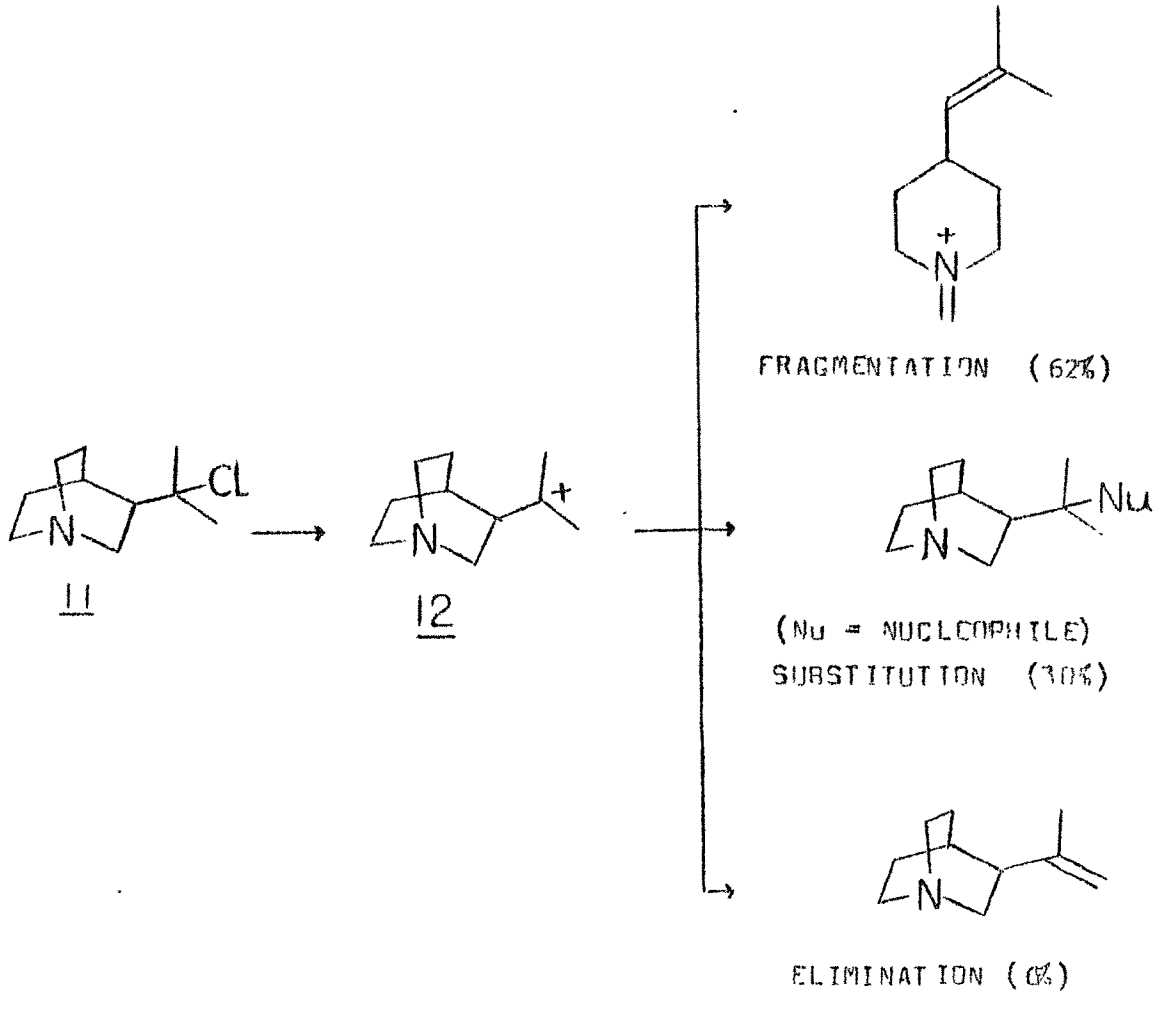


FIG. 1 : EXAMPLE OF TWO STEP NON-CONCERTED MECHANISM

α-carbon atom. Since five atomic centres are involved in the transition state, this mechanism would have certain structural requirements. The anti-periplanarity of the two breaking bonds a and b appears to be a primary requirement for this mode of fragmentation. Wharton and co-workers[3] studied the fragmentation reactions of the four 1,10-decalindiol monotosylates (13-16) with potassium t-butoxide and the results are summarised in Fig. 2. In the case of 13, in which the bonds a and b are necessarily synclinal, there was no appreciable reaction. Under drastic conditions, the product was a complex mixture containing no cis- or trans-5-cyclodecenones. In the case of 14 and 15, concerted breakage of the antiperiplanar bonds a and b gave trans-5-cyclodecenone (17) in high yields. Similarly, 16 gives cis-5-cyclodecenone (18) in quantitative yield.

Applications in Organic Synthesis: Such fragmentation reactions have often been made use of in stereospecific organic syntheses. Corey and co-workers,[11] in the synthesis of caryophyllene (20), generated the medium sized ring of the sesquiterpene, by an internal scission of the bond common to the six- and five-membered rings in the γ-hydroxy-p-toluene sulphonate (19) (Eq. 9). Edwards and co-workers[12] synthesised trans-cis-6-ethyl-10-methyldodeca-5,9-dien-2-one (24), a key intermediate in the synthesis of juvenile hormones, by a

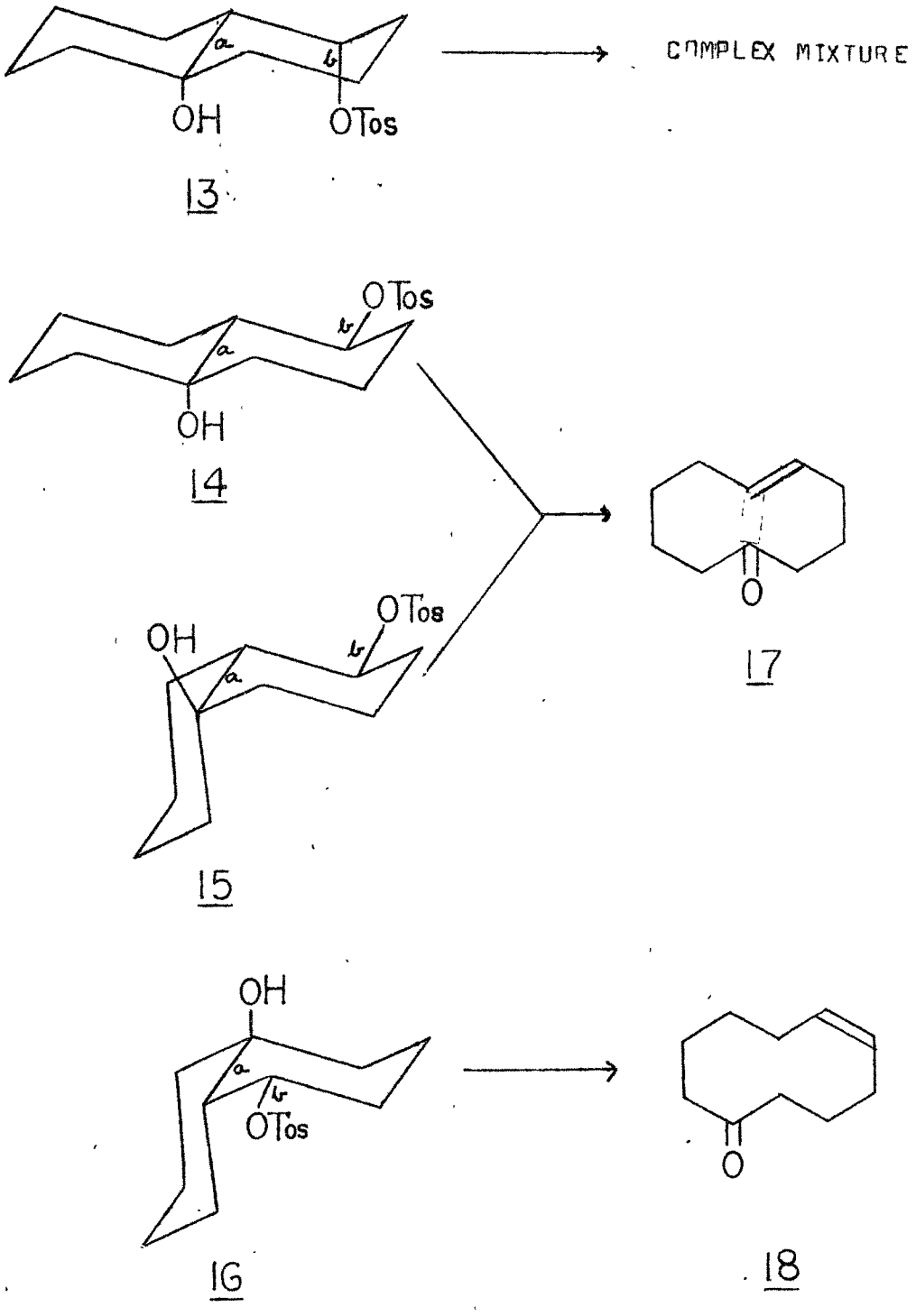
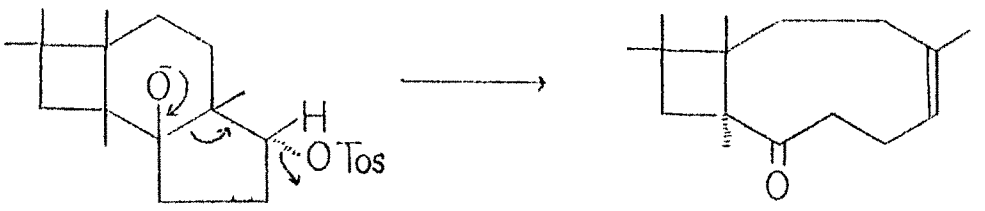


FIG. 2: GEOMETRIC REQUIREMENT IN THE FRAGMENTATION OF 1,10-DECALINDIOL MONOTOSYLATES



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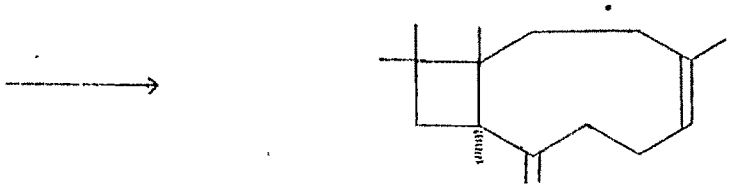

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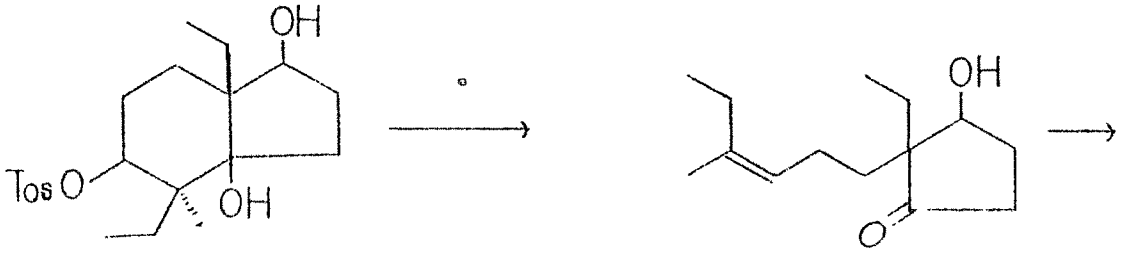
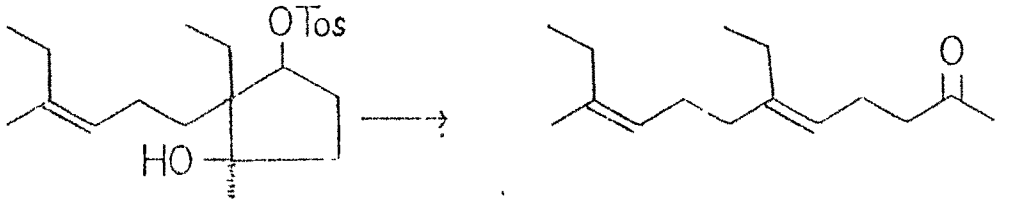
Eq.9

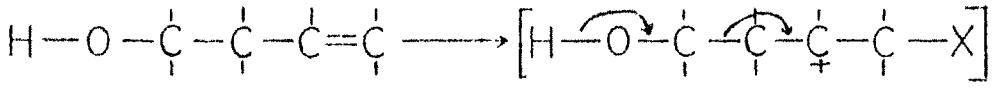


21 22



23 24

Eq.10



(X = Cl, OH)

Eq.11

sequential fragmentation of the bicyclic precursor (21), whereby it was possible to control the stereochemistry. Fragmentation of 21 with NaH/THF gave the cis-olefinic ketone 22, which was converted to another tosylate 23. The latter was again fragmented with NaH/THF to give 24 (Eq. 10).

Later, heterolytic fragmentation reactions have been utilised for the synthesis of a wide variety of natural products such as methyl dl-jasmonate,[13] "oropylure", the sex pheromone of the female pink ballworm moth[14], secolonganin aglycone O-methyl ether,[15] bissochlamic acid[16] and nootkatone.[17]

Fragmentation of Homoallylic Alcohols: Sukh Dev and co-workers[18] reported a related, yet novel cleavage of homoallylic alcohols 25, 26, 27 and 28, under conditions of electrophilic addition of chlorine or acid-catalysed ring-opening of the corresponding epoxides. In generalised terms, this fragmentation can be depicted as shown in Eq. 11.

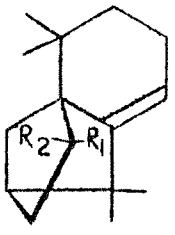
This cleavage was first encountered while studying the reactions of 25. The reaction differs from Grob fragmentations in producing allylic halides or alcohols, instead of olefins, and, in appropriate cases, this can be of distinct value for synthetic operations.

Reaction of 25 with chlorine in CCl_4 in the oresence of excess Li_2CO_3, yielded 29 in almost quantitative yield. The stereochemistry of C-Cl bond in 29 follows from the known propensity for endo-attack (with reference of norbornyl part) in isolongifolene derivatives.[19] Exposure of epoxide 32 to 0.35% $HClO_4$ in 90% aqueous dioxane furnished, in almost quantitative yield, a mixture of epimeric alcohols 30 and 31. The formation of both epimers rather than only 30 is ascribed to acid-catalysed epimerisation at C-8 under the reaction conditions.

Similarly, reaction of camphene alcohol (27) with Cl_2 in CCl_4 yielded quantitatively the cyclopentane derivative 33, which was characterised by reduction (LAH) to the known[20] α-camoholenic alcohol (34). Likewise, the homoallylic alcohol 28 on exposure to chlorine yielded the expected chloroaldehyde 35, while the derived epoxide on acid cleavage furnished the anticipated hydroxyaldehyde 36.

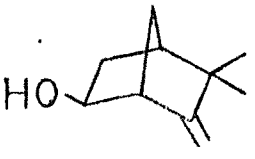
Configuration of the OH group appears to be inconsequential, as the epimeric alcohol 26 fragments with equal ease to give the same product 29.

Sukh Dev and co-workers[21] applied this novel fragmentation reaction for the synthesis of (-)-secolongifolene diol (37), an optical antipode of a metabolite of the fungus



25 : R_1=H, R_2=OH

26 : R_1=OH, R_2=H



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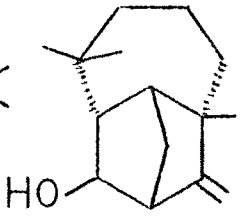

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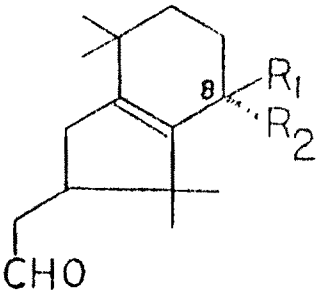
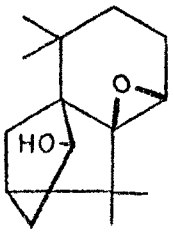


29 : R_1=Cl, R_2=H

30 : R_1=OH, R_2=H

31 : R_1=H, R_2=OH



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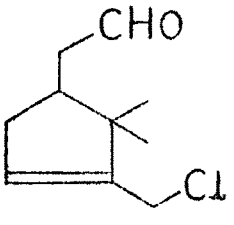

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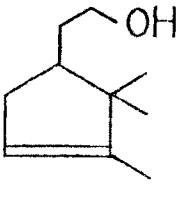

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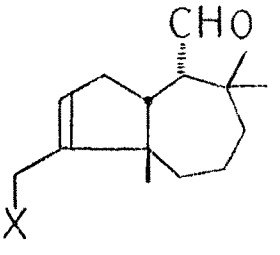
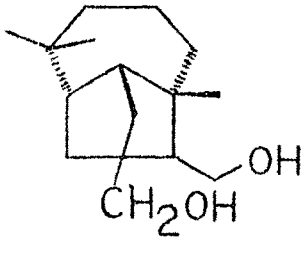


35 : X=Cl

36 : X=OH



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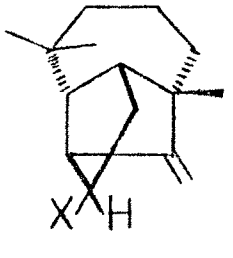
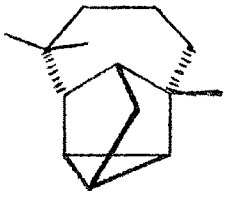


38 : X=Br

39 : X=OH



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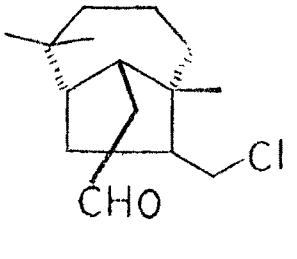

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Helminthosporium sativum.[22] The homoallylic alcohol 39, vital to the synthesis of 37 was prepared from longicyclene (40) by treatment with N-bromosuccinimide followed by hydrolysis of the bromide 38. Alcohol 39, when exposed to Cl_2 in CCl_4, in presence of Li_2CO_3, cleaved quantitatively into the chloroaldehyde 41, which on hydrolysis followed by $NaBH_4$ reduction gave(-)-secolongifolene diol (37).

PRESENT WORK

In continuation of studies on this fragmentation reaction, we planned to synthesise a few cyclopropanes incoroorated in bicyclo (2.2.1)heptane skeleton and investigate their fragmentation reactions with electrophiles. Since 1,3-cleavage of cyclopropane with electrophiles is well known,[23] it was thought interesting to study the homoallylic fragmentation by reolacing the double bond with a cyclooropane ring. Also, in the event of a clean fragmentation, the product (45) will be a higher homologue to the one which would arise from the corresponding olefin and this may be of synthetic importance. With this aim in mind, 6-exo-hydroxy-3,3-dimethylspiro-[bicyclo(2.2.1)heptane-2,1'-cyclopropane] (42) and the corresponding endo-epimer (43) were synthesised and subjected to fragmentation.

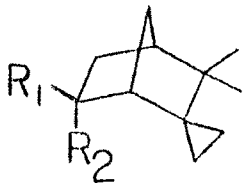
A further extension of the side-chain in the fragmented

product could be achieved if methyl 6-exo-hydroxy-3,3-dimethyl-soiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane]-2'-carboxylate (46) could be made to cleave. Cyclopropyl carbonyl compounds such as 48, in general, are prone to nucleophilic opening under acidic[24] as well as basic[25] conditions.

The ring opening of cyclopropanes activated by two geminally placed electronegative groups such as carbethoxy, cyano etc. is known to be particularly facile.[25,26] And vulnerability of ring cleavage with nucleophiles is further enhanced in spirocyclopropanes.[26,27] Ring opening in cyclopropanes containing only one activating group has also been observed in oxycyclopropyl carbonyl compounds (such as 48; R_1=OAc, R_2=$(CH_2)_4$ CH_3)[28] or in cases where cyclopropane ring is part of a particularly strained system.[29] In view of all this, it appeared worthwhile to synthesise 46 and attempt its fragmentation.

SYNTHESIS

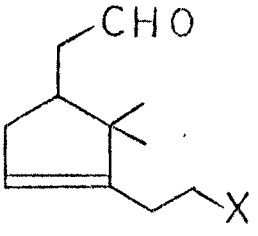
6-Hydroxy-3,3-dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropanes] (42/43): Both spirocyclopropane derivatives (42/43) were synthesised from 6-exo-hydroxycamphene (49),[30] which, in turn, was prepared in five steps from camphor by a known sequence.[30a]



42: R_1=OH, R_2=H

43: R_1=H, R_2=OH

44: R_1=OAc, R_2=H



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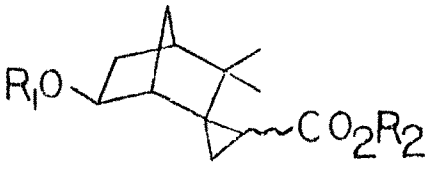
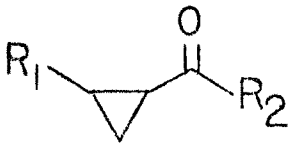


46: R_1=H, R_2=CH_3

47: R_1=Ac, R_2=C_2H_5



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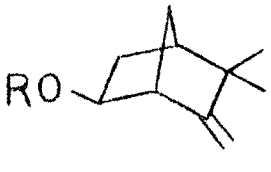
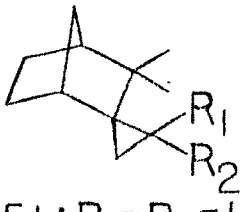


49: R=H

50: R=Ac



51: R_1=R_2=H

52: R_1=R_2=Cl

Initially, camphene itself was employed for cyclooropanation with an aim to obtain 3,3-dimethylspiro [bicyclo-(2.2.1)heptane-2,1'-cyclopropane] (51), which could be used to identify electrophile(s) suitable for efficient cleavage of cyclopropane ring in such systems. Compound 51 was prepared earlier by dehalogenation of 2',2'-dichloro-3,3-dimethylspiro-[bicyclo(2.2.1)heptane-2,1'-cyclopropane] (52) with sodium in liquid ammonia[31] or Zn/DMF[32] (25% yield). We were able to get 51 in 85% yield by Simmons-Smith reaction of camphene.

For the preparation of 42, it was felt at the outset that it should be possible to cyclopropanate 49 without protecting OH group. In fact, in many cases, a free OH group is known[33] to accelerate the reaction by complexing with, and thereby directing the approach of the 'Zinc reagent'. But reaction of 49 with CH_2I_2-Zn(Cu) in anhydrous ether always led to the formation of some decomposition products (Table 1). With higher mole ratios of the Zinc reagent, conversion of 49 increased, but at the same time the amount of decomposition products also increased. It appears that 42 as well as 49 are prone to fragmentation in presence of the Lewis acid, ZnI_2,[34] which is a by-product of the reaction. Even under the optimum conditions (Entry 2), it was found difficult to separate 42 and 49 by chromatography, as the two compounds have same R_f values. It was therefore deemed fit to protect the OH group

by acetylation. Surprisingly, however, in 6-exo-acetoxy-camphene (50), the olefinic bond was far less reactive than that in camphene. The reduced reactivity of 50 was also showed by its failure to undergo Prins (CH_2O/acetic acid) or Kharasch reaction (CCl_4/Bz_2O_2) ——— reactions which camphene undergoes readily.[35,36] Such a difference in the reactivity of substituted and unsubstituted terminal olefins is not unprecedented. For instance, out of 53, 54 and 55,

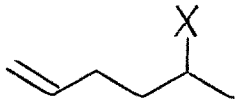
Table 1 : Simmons-Smith reaction of 6-exo-hydroxycamphene (49)

Entry	Molar ratio of[+] 49:Zinc reagent	Product composition[*](%)		
		49	42	Decomposition products
1	1:5	33	40	27
2	1:10	14	48	38
3	1:15	11	13	76
4	1:20	-	-	100

[+] Reaction time = 50 h. Temperature = 45-50°.

[*] Determined by GLC (10% carbowax, chromosorb W, 12', 200°, 60ml/min.)

only 53 undergoes Simmons-Smith reaction under normal conditions.[37]



53 : X = H

54 : X = Cl

55 : X = OH

By employing large excess of Simmons-Smith reagent (20 to 25 moles) and long reaction times (80 h), it was possible to achieve a complete conversion of 6-exo-acetoxycamphene (50). The GLC of the distilled product (10% carbowax, chromosorb W, 12', 200°, 60 ml/min) showed the presence of 6-exo-acetoxy-3,3-dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane] (44) (RRT, 0.93; 52%) and an alcohol A (RRT, 1.0; 15%) along with a number (10) of decomposition products (RRT, 0.06 to 0.5; 33%). Attempts to isolate 44 by fractional distillation were unsuccessful. So, the purification was deferred till the final stage.

The above mixture was hydrolysed with methanolic KOH at room temperature (~30°). The product containing the required

cyclopropane derivative 42 (RRT, 1.4) and alcohol A (RRT, 1.0), which remained unchanged, was systematically chromatographed (Al_2O_3, grade II) to get pure 42 in 45% yield (IR: OH 3290, 1095 cm^{-1}; cyclopropane 3060, 1040 cm^{-1}. PMR: cyclopropane CH_2, 4H, m, 0.24-0.40 ppm; CHOH, 1H, dd, 4.0 ppm, J_1=3Hz, J_2=6Hz) and pure alcohol A in 10% yield.

Structure of Alcohol A: Alcohol A (m.p. 97-99°) has a molecular formula $C_{11}H_{18}O$ (M^+, m/e 166). It is clearly a tertiary alcohol (IR:/$^{(nujol)}$OH 3600, 3440, 1135 cm^{-1}. PMR: no signal for CHOH) It has no olefinic linkage (no color with tetranitromethane; PMR; ^{13}C-NMR). These data can be accommodated by either of the two tricyclic tertiary alcohols 56 and 57. However, 56 was favoured over 57 for many reasons. It has been observed that as reaction progresses, the amount of alcohol A increases at the expense of the cyclopropane 44, indicating that the latter is a logical precursor for the former. Mechanistically, 56 can be derived from 44 by an initial opening of the cyclopropane ring by ZnI_2 (a Lewis acid formed in the reaction) followed by the formation of the tricyclic system by any of the two pathways a and b (Fig. 3). The intermediate carbonium ion 60 may either first add to $\bar{O}ZnI$ species which may be present in the reaction mixture and then cyclise or the ion-pair 60 may first cyclise to 61^+ and during hydrolytic

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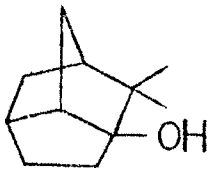
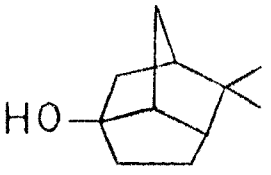
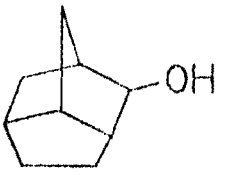
+ The minimum requirements for a bridge-head carbonium ion to form as a transitory intermediate are fulfilled by 61.[38]



56



57



58

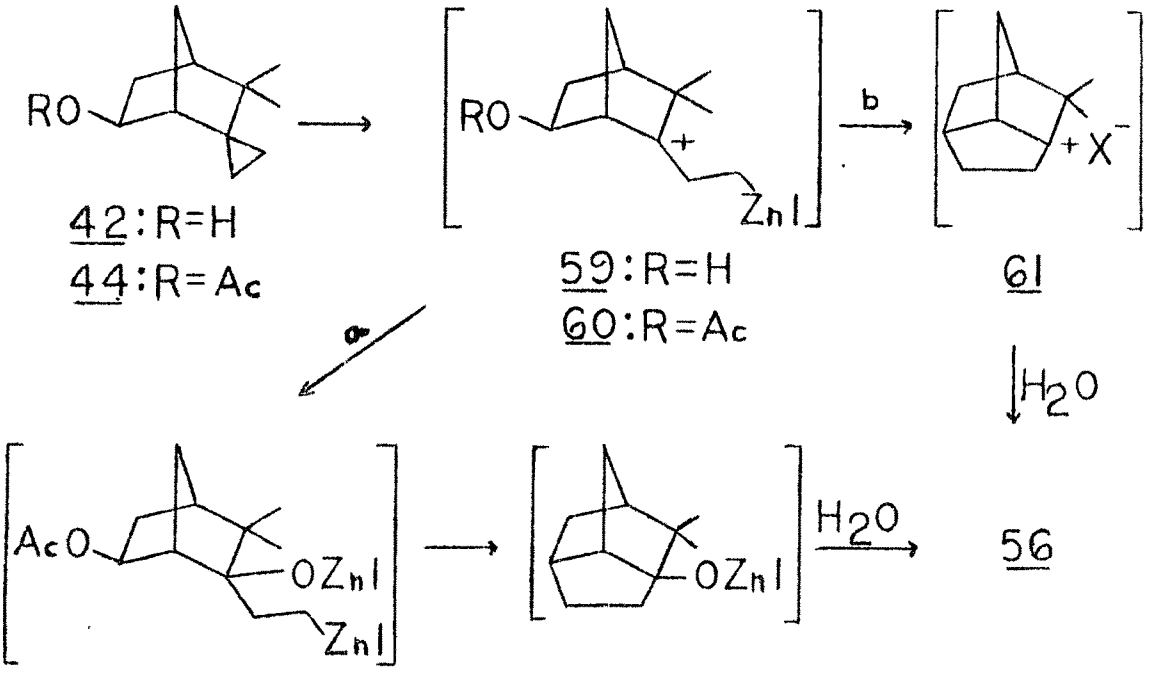
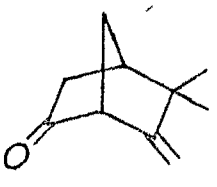
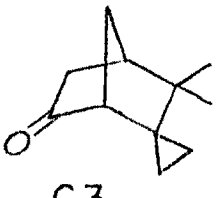


FIG. 3 : A POSSIBLE MECHANISM FOR THE FORMATION OF ALCOHOL A



62



63

work-up give 56. Such a mechanism would also explain the ready fragmentation of 42 under the conditions of Simmons-Smith reaction.

The structure 56 for alcohol A was also indicated by its mass fragmentation pattern, (a plausible rationalisation of which is provided in Fig. 4) and ^{13}C-NMR (Fig. 15). The assignment of ^{13}C-chemical shifts is based on comparison with those reported[39] for brendane derivative 58, coupled with general additivity principles.[40]

The placement of the OH group as in 56 was strongly indicated by lanthanide-induced shifts (LIS) study.[41] PMR spectra were recorded for alcohol A in $CDCl_3$ in presence of incremental quantities of $Eu(fod)_3$. A plot of $Eu(fod)_3$ / Alcohol A molar ratio *vs.* the observed shifts of C-2 *exo*-methyl*, C-2 *endo*-methyl and C_7-H gave three straight lines (Fig. 5). The slopes of these lines provide the magnitude of the shift parameter *s* for the respective nuclei. The distance *r* of the individual nuclei from the top of the lone pair of the oxygen of OH were measured for the structures 56 and 57, using Prentice-Hall Framework models. A plot of *s* *vs.* r^{-2} gave a straight line passing through origin in the case of structure 56 only (Fig. 6). This proves 56 as the structure of the alcohol A and rules out 57.

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* It is known[42] that *exo*-methyl in bornane systems appears downfield compared to *endo*-methyl.

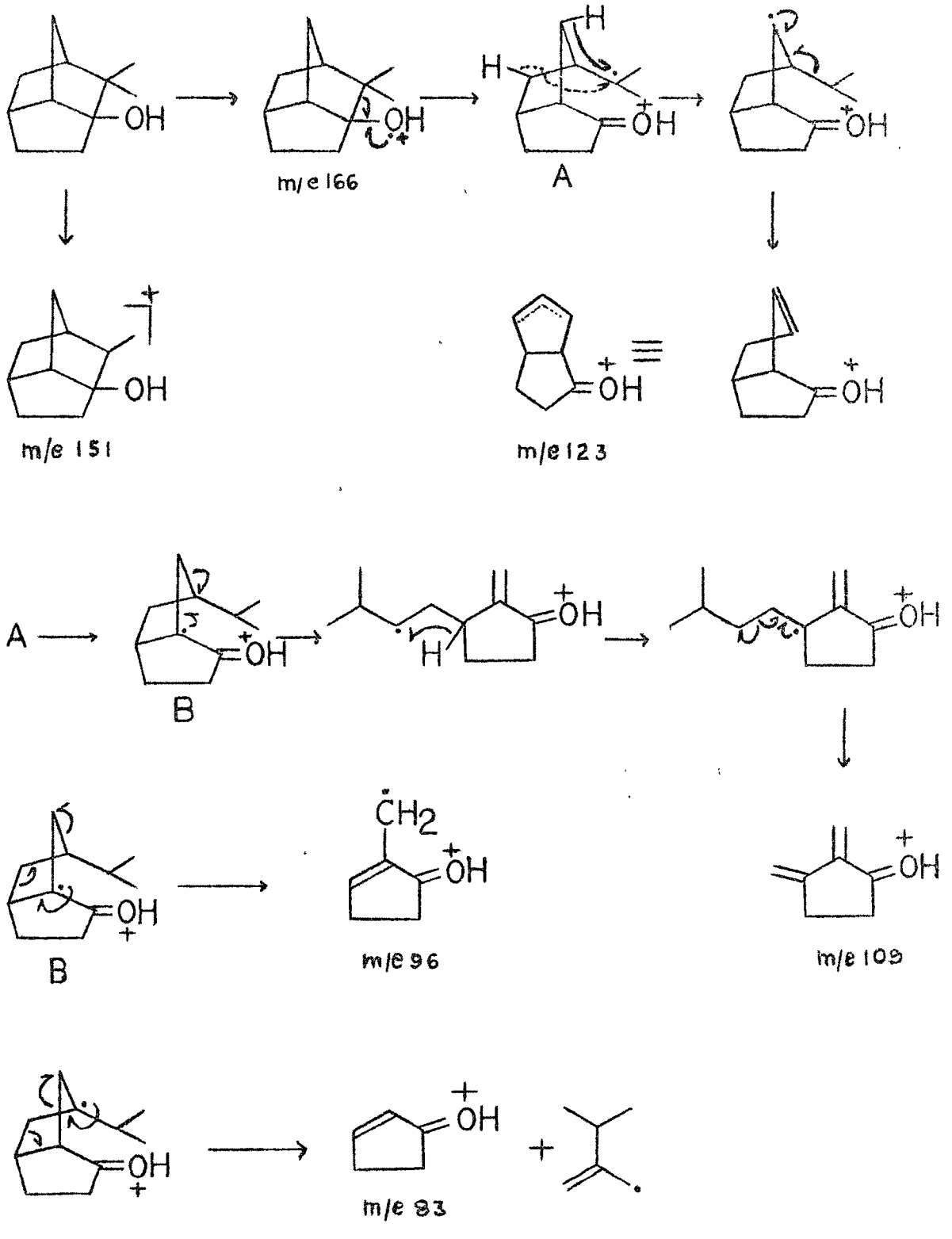


FIG. 4 : A PLAUSIBLE MASS SPECTRAL FRAGMENTATION PATTERN OF ALCOHOL A

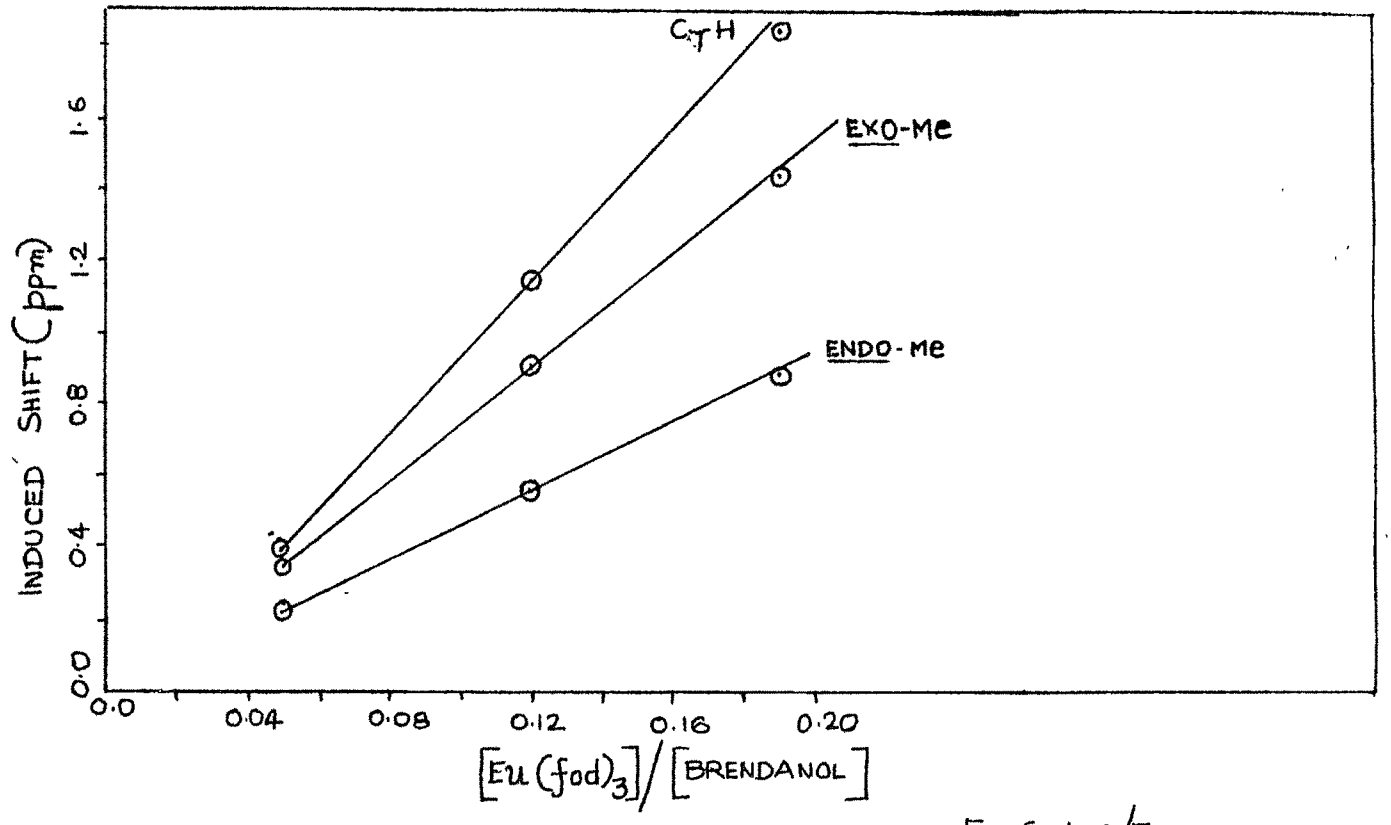


FIG.5: PLOT OF INDUCED SHIFT Vs. MOLAR RATIO OF $[Eu(fod)_3]/[BRENDANOL]$

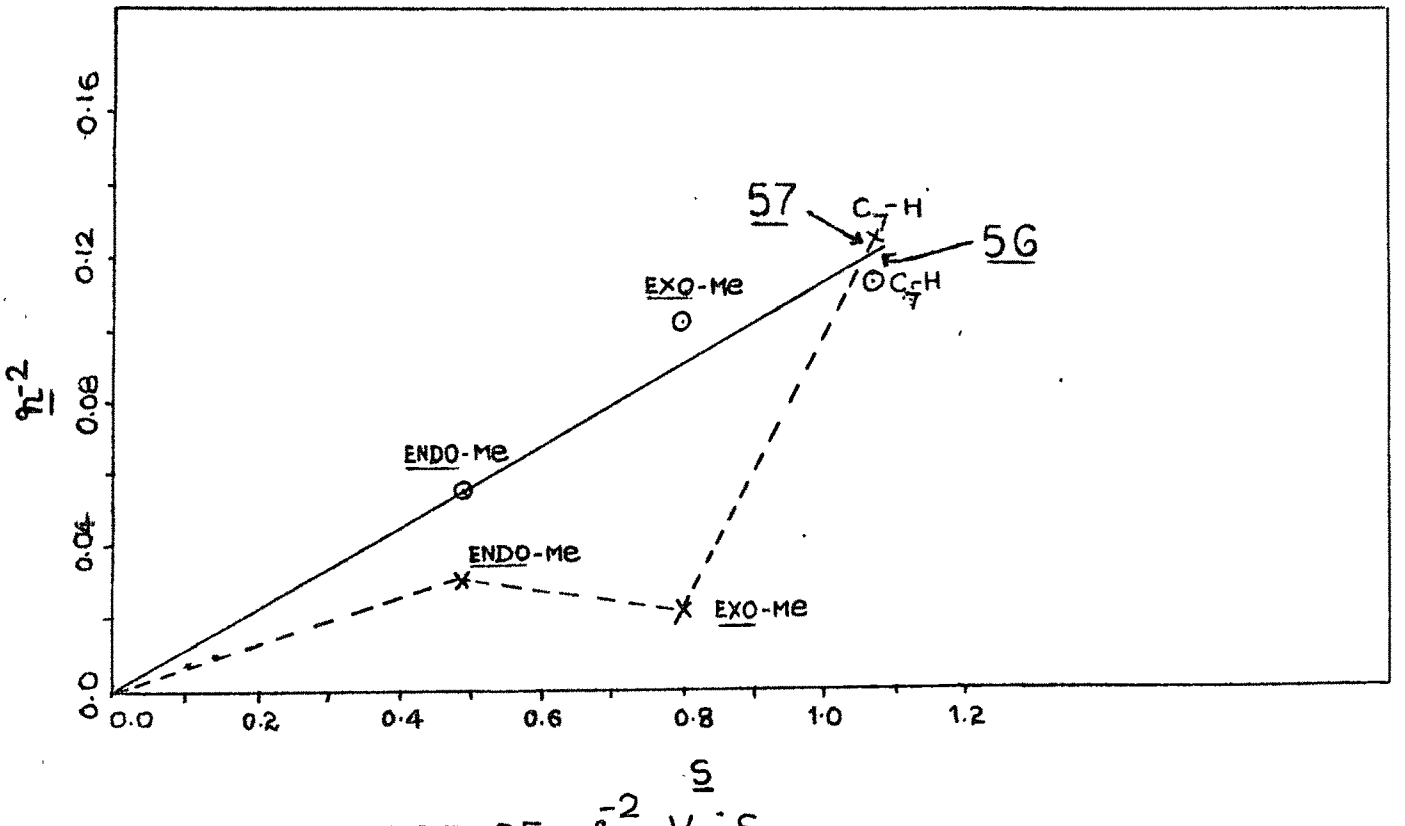


FIG.6: PLOT OF $\underline{r}^{-2}$ Vs $\underline{S}$

To our knowledge, excluding the rather common Wittig type products,[43] this is the first instance of the formation of such a cyclic product in Simmons-Smith reaction.

6-endo-Hydroxy-3,3-dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclooropane] (43): The endo-epimer 43 (IR: OH 3590, 3440, 1090 cm^{-1}; cyclopropane 3080, 1025 cm^{-1}. PMR: cyclopropane CH_2, 4H, m, 0.35 to 0.70 ppm; CHOH, 1H, m, 4.05 to 4.35 ppm) was prepared in 90% yield by the reduction of 6-keto-3,3-dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclooropane] (63) with lithium tri-t-butoxyaluminium hydride.[44] The ketone 63 was, in turn, prepared in two ways:

(i) Oxidation of 6-exo-hydroxycamphene (49) with pyridinium chromate-on-silica gel[45] in CH_2Cl_2 at room temperature (~30°) gave 6-ketocamphene (62) in 75% yield. Simmons-Smith reaction of 62 followed by chromatography on Al_2O_3 gave 63 in 59% yield (IR: CO 1745 cm^{-1}; cyclopropane 3065, 1020 cm^{-1}. PMR: C-Me's, 3H, singlets at 0.8, 1.0 ppm; cyclopropane CH_2, 4H, s, 0.45 ppm).

(ii) Oxidation of 6-exo-hydroxy epimer (42) with Py/CrO_3 gave 63 in 85% yield.

Methyl 6-exo-hydroxy-3,3-dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane]-2'-carboxylate (46): Reaction of 6-exo-acetoxy-camphene (50) with the carbene ($:CHCO_2Et$), generated thermally

from ethyl diazoacetate, in the presence of anhydrous $CuSO_4$ as catalyst,[46] gave a mixture containing the starting material (50), ethyl 6-exo-acetoxy-3,3-dimethylspiro [bicyclo-(2.2.1)heptane-2,1'-cyclopropane]-2'-carboxylate (47) and side products like diethyl maleate and diethyl fumarate. Fractionation failed to furnish the required product (47) in pure state. The mixture was hydrolysed with methanolic KOH. The product of the hydrolysis was separated into neutral and acidic parts. The neutral part was fairly pure 6-exo-hydroxycamphene (49), and could be recycled. The acidic part was esterified with diazomethane and systematic chromatography of the product on neutral Al_2O_3 gave the targeted compound 46 in an overall yield of 90% (IR: OH 3420, 1100cm^{-1}. PMR: C-Me's, 3H, singlets at 0.66, 0.91 ppm; cyclopropane CH_2, 1H, singlets at 0.74, 0.81 ppm; OCH_3, 3H, s, 3.69 ppm; CHOH, 1H, dd, 3.98 ppm).

In the cyclopropanation reactions described above, the progress of the reaction was conveniently monitored by the anisotropic effect of cyclopropane ring[47] on the PMR resonances of neighbouring methyl groups. The upfield shift caused by cyclopropane ring in such systems is recorded in Table 2.

Table 2 : Anisotroopic effect of cyclopropane ring in camphane derivatives

S.No.	Olefin	Gem-dimethyl signals (δ) (endo, exo)	Cyclopropane	Gem-dimethyl signals (δ) endo, exo	Upfield shift
1.	Camphene	1.02	51	0.72	0.30
		1.05		0.80	0.25
2.	6-exo-acetoxycamphene (50)	1.05	44	0.71	0.34
		1.075		0.85	0.22
3.	6-exo-hydroxycamphene (49)	0.96	42	0.66	0.30
		1.01		0.83	0.18
4.	" "	0.96	46	0.66	0.30
		1.01		0.91	0.10
5.	6-Ketocamphene (62)	1.11	63	0.80	0.31
		1.21		1.01	0.20
6.	6-endo-hydroxycamphene	1.10*	43	0.90*	0.20

* Both Me's have same resonance.

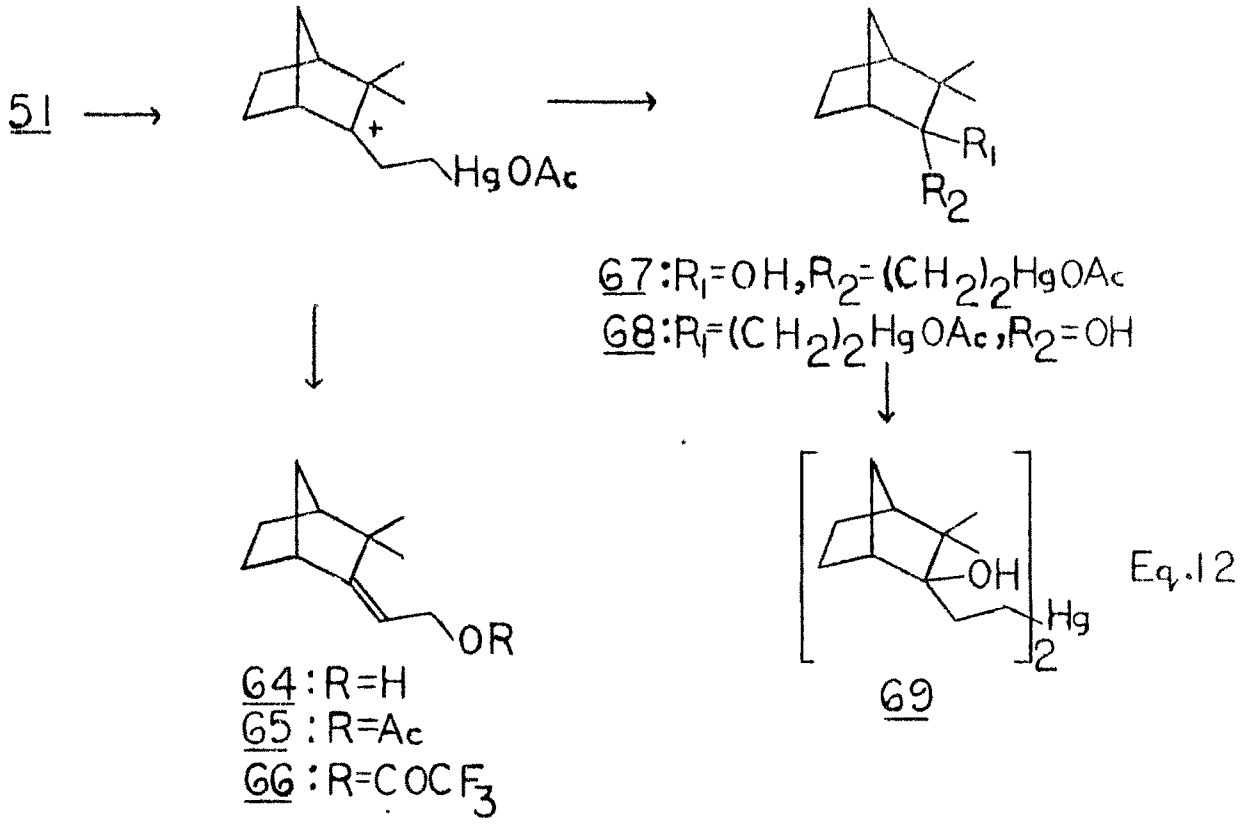
FRAGMENTATION REACTIONS

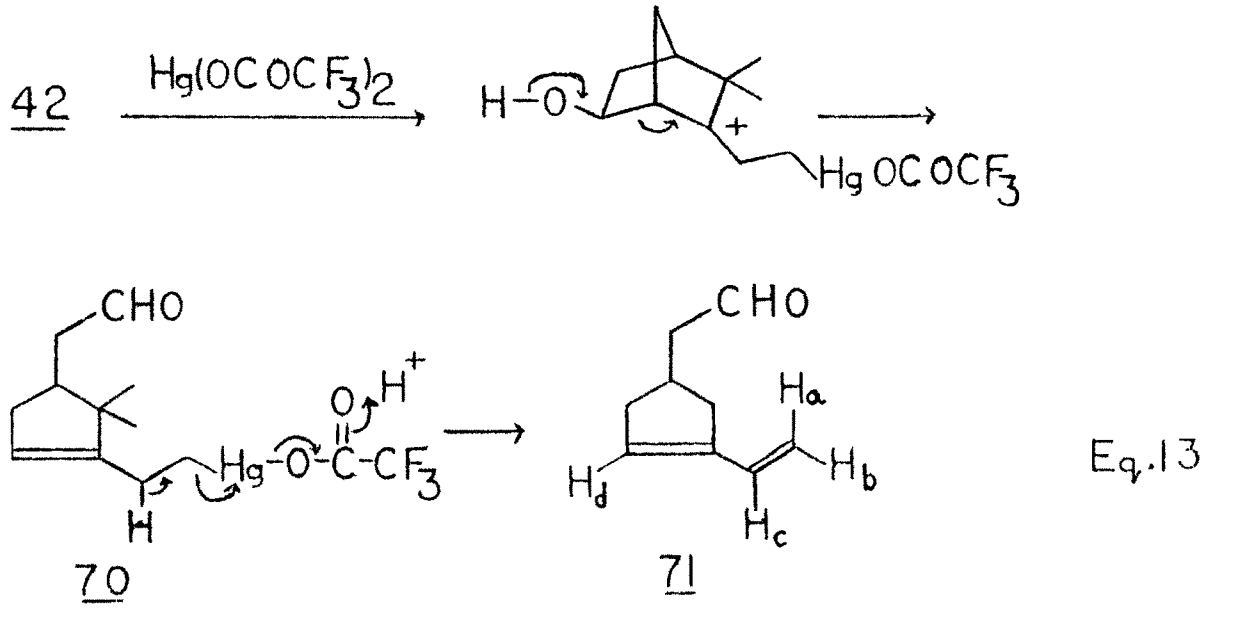
Cyclopropanes are susceptible to cleavage by electrophiles such as acids,[48] halogens,[49] mercuric salts[50] etc. In substituted cyclopropanes, with most electrophilic reagents, 1,2- and 1,3- scissions take place but mercuric salts cause predominantly 1,3-cleavage.[51] Our aim was to cleave the cyclopropane ring of the three alcohols 42/43 and 46, creating a tertiary carbonium ion at C-2 and thereby triggering the fragmentation reaction.

Cleavage of 3,3-dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane] (51): Cleavage of cyclopropane ring was first studied with 51. Reaction of 51 with methanolic HCl or bromine in CCl_4, gave a complex mixture of products but its reaction with $Hg(OAc)_2$ in THF/H_2O (1:1) gave two products which were separated easily. The first compound (b.p. 95-98°/2 mm) gave a negative spot test for mercury.[52] Based on its spectral data (IR: OH 3340, 1110 cm^{-1}; C=C 1675. cm^{-1}. PMR: C-Me's, 3H, singlets at 1.0, 1.02 ppm; CH_2OH, 2H, d, 3.99 ppm, J = 8Hz; C=CH, 1H, t, 5.12, J = 8 Hz), it is formulated as W-hydroxymethyl camphene (64) (Eq. 12). This structure was further confirmed by synthesising it from camphene. Prins reaction of camphene gave W-acetoxymethyl camphene (65), which was hydrolysed with methanolic KOH to give 64.[35]

The second compound (m.p. 143-5°) gave a positive spot test for mercury.[52] It is a tertiary alcohol (IR: 3320, 1085 cm^{-1}. No peak in PMR corresponding to C<u>H</u>OH) and contains HgOAc function (IR: 1610 cm^{-1}. PMR: COC<u>H</u>$_3$, 3H, s, 2.02 ppm). Accordingly, it is formulated as 1-[2'-<u>exo</u>-hydroxy-3',3'-dimethyl-bicyclo(2.2.1)heptan-2'-yl] ethan-2-yl mercury acetate (<u>67</u>). In view of the known[53] propensity for <u>exo</u>-attack in norbornane system, the OH group is given the <u>exo</u>-configuration. This is further established by LIS study using Eu(fod)$_3$. As described earlier, shift parameters <u>s</u> of the <u>endo</u>- and <u>exo</u>-methyl were plotted against <u>r</u>$^{-2}$. A straight line passing through origin was obtained for the structure <u>67</u> and not for the alternate configuration <u>68</u> (Fig. 7 and 8). Finally, reduction of <u>67</u> with $NaBH_4$ in NaOH aq gave the abnormal demercuration[54] product (<u>69</u>) (IR: OH 3600, 3480, 1130 cm^{-1}. PMR: C-<u>Me</u>'s, 6H, singlets at 0.92, 1.0 ppm).

Reaction of <u>51</u> with Hg(OCOCF$_3$)$_2$ in dry ether gave a single compound. Based on its spectral data (IR: OCOCF$_3$ 1780 cm^{-1}; C=C 1675, 910 cm^{-1}. PMR: C-<u>Me</u>'s, 3H, singlets at 1.03, 1.06 ppm; C<u>H</u>=C-C<u>H</u>, 1H, bs, 3.05 ppm, W_h=8Hz; C<u>H</u>$_2$OCOCF$_3$, 2H, d, 4.85 ppm, J = 8 Hz; =C<u>H</u>-CH$_2$-, 1H, t, 5.19 ppm, J = 8Hz), it is formulated as W-trifluoroacetoxymethyl camphene (<u>66</u>) and further confirmed by its hydrolysis with methanolic KOH to W-hydroxymethyl camphene (<u>64</u>). Compound (<u>51</u>) failed to react with PhSeBr. Thus, among the electrophilic reagents studied, only mercuric salts gave clean products.


51
HgOAc
R1
R2
67:R1=OH, R2=(CH2)2HgOAc
68:R1=(CH2)2HgOAc, R2=OH
OR
64:R=H
65:R=Ac
66:R=COCF3
OH
Hg
2
69
Eq.12


42
Hg(OCOCF3)2
H-O
HgOCOCF3
CHO
O
H+
Hg-O-C-CF3
H
70
CHO
Ha
Hb
Hc
Hd
71
Eq.13

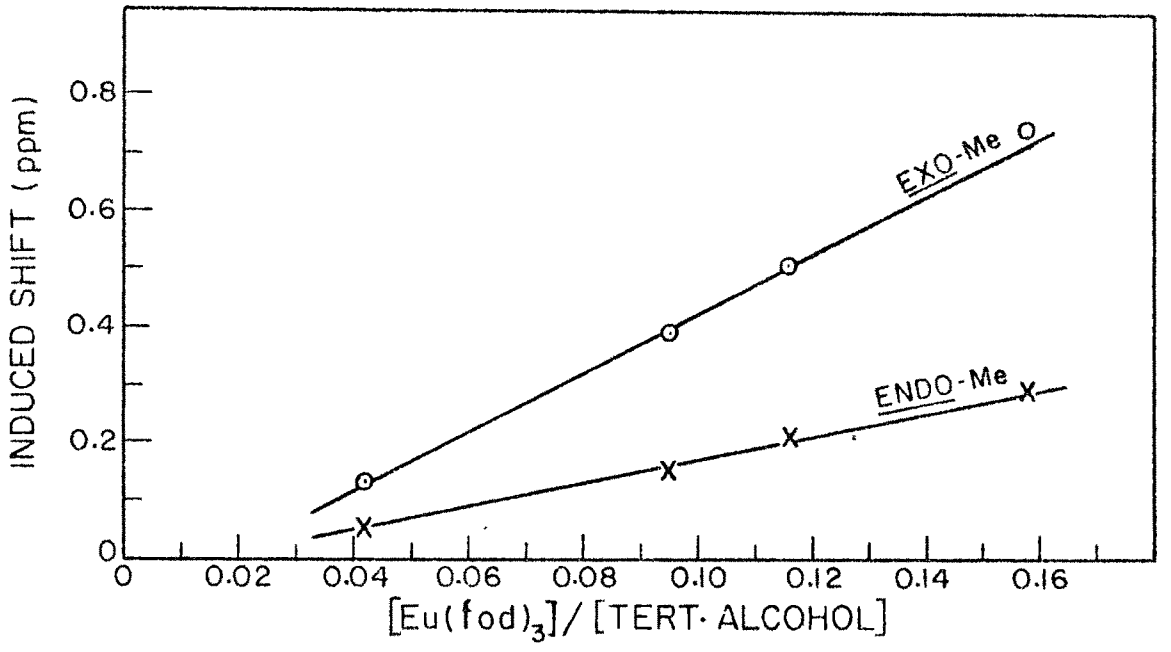


FIG. 7. PLOT OF INDUCED SHIFT VS. MOLAR RATIO OF $[Eu(fod)_3]/[TERT\cdot ALCOHOL]$

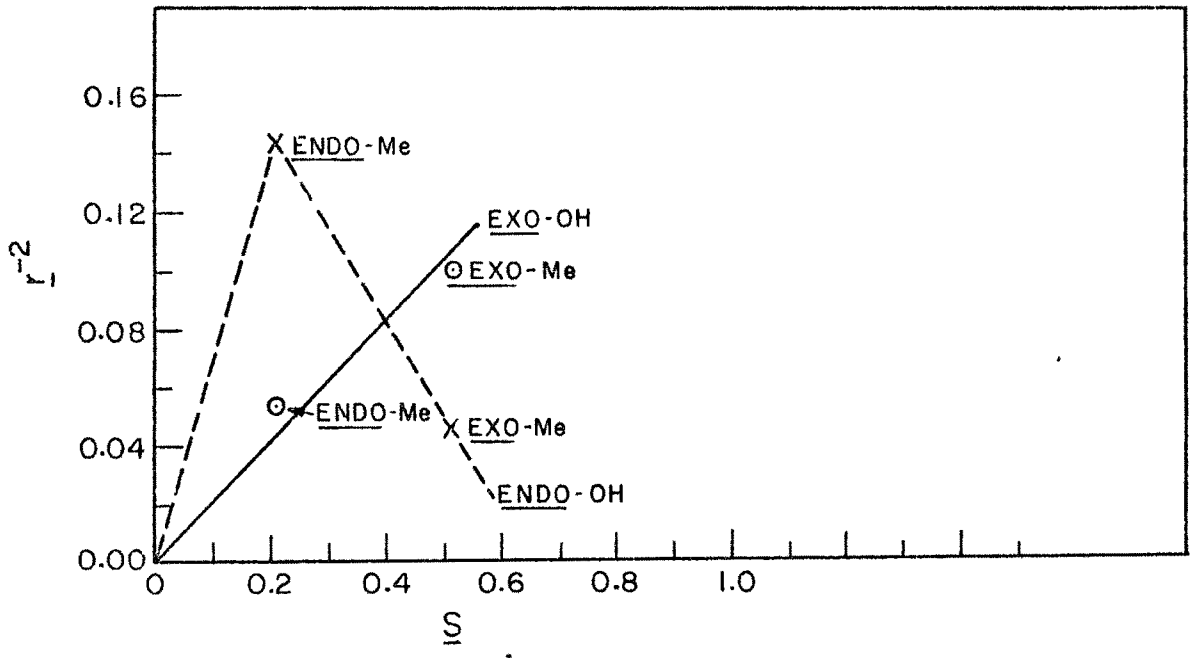


FIG. 8. PLOT OF $\underline{r}^{-2}$ VS. $\underline{S}$.

Fragmentation of 6-exo/endo-hydroxy-3,3-dimethylspiro-[bicyclo(2.2.1)heptane-2,1'-cyclopropane] (42/43): On reaction with $Hg(OCOCF_3)_2$, the alcohol 42 gave an unsaturated aldehyde, which, based on its spectral data (IR: CHO 2720, 1730 cm^{-1}; C=C 1630, 915 cm^{-1}. PMR: C-Me's, 3H, singlets at 0.92, 1.14 ppm; CH_2CHO, 2H, s, 2.45 ppm; H_b, 1H, d, 5.05 ppm, $J_{H_bH_c}$ = 10 Hz; H_a, 1H, d, 5.4 ppm, $J_{H_aH_c}$ = 17 Hz; H_d, 1H, s, 5.72 ppm; H_c, 1H, q, 6.25 ppm, $J_{H_cH_a}$ = 17 Hz, $J_{H_cH_b}$ = 10 Hz; CHO, 1H, t, 9.82 ppm, J = 1.5 Hz. Mass: m/e 164 (M^+), was assigned structure (71).

It is thus clear that the alcohol 42 undergoes the expected fragmentation, but the product (70) appears to be so unstable as to undergo instantaneous reductive elimination to give the olefinic aldehyde (71) (Eq. 13). Even this diene aldehyde itself is labile and on keeping tends to deteriorate.

Identical results were obtained with the epimeric alcohol (43).

Attempted fragmentation of methyl 6-exo-hydroxy-3,3-dimethyl-spiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane]-2'-carboxylate (46): All attempts to fragment 46 under acidic ($HClO_4$/dioxane), basic (NaH/THF or DMSO) conditions or with meruric salts were unsuccessful. It is evident that only one ester function even on a spiro-activated cyclopropane does not impart enough reactivity to induce fragmentation.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light petroleum refers to the fraction b.p. 60-80°. Optical rotations were measured in chloroform on a Schmidt-Haensch electronic polarimeter model Polartronic-I.

The following instruments were used for spectral analytical data: Perkin-Elmer Infrared Spectrophotometer, model 267 (IR); Perkin-Elmer spectrophotometer, model 402 (UV); Perkin-Elmer, model R-32 (90 MHz) spectrometer (PMR); Jeoul FX-100 spectrometer (^{13}C-NMR); Varian Mat. mass spectrometer, model CH-7 (mass; 70 eV, direct inlet system). While citing PMR data, the following abbreviations have been used: s(singlet), d(doublet), t(triplet), q(quartet), m (multiplet) and b(broad). While summarising mass spectral data, besides the molecular ion, ten most abundant ions (m/e) are reported with their relative intensities.

Silica gel for column chromatography (-100, + 200 mesh) was washed with hot water till sulphate free, dried, activated at 125-30° for 6 h and standardised.[55] TLC was carried out on SiO_2-gel layers (0.25 mm) containing 15% gypsum and activated at 110-5° (2 h).

3,3-Dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane] (51).

Zinc-copper couple (couple II of Shank and Schechter;[56]

8.6 g, 0.13 g. atom) was taken in a 3-necked flask fitted with a condenser, a $CaCl_2$ guard tube and a dropping funnel. Dry ether (30 ml) and CH_2I_2 (1 g) were added followed by a crystal of iodine. The mixture was magnetically stirred and in 5 min. ether started refluxing due to heat of reaction. While the stirred suspension was kept under gentle reflux (by heat of reaction alone), a mixture of camphene (3 g, 0.022 mole) and CH_2I_2 (34 g, total 0.13 mole) in dry ether (30 ml) was added dropwise over a period of 1 hr. The reaction mixture was stirred and refluxed, till an aliquot worked up showed no starting material on GLC analysis (16 h). The ether solution was decanted from the couple into a separatory funnel containing cold saturated NH_4Cl solution (30 ml). The ethereal layer was washed with a second portion of NH_4Cl aq (15 ml), water (15 ml), 10% $NaHCO_3$ aq (10 ml x 2) and water (10 ml) and dried (Na_2SO_4). Solvent was removed and the resulting pale-yellow oil was distilled to give 51 (2.8 g, 85%) as a colorless oil, which solidified immediately. B.p. 51-56°/ 10 mm, m.p. 53-54° (lit.[32] m.p. 55°).

IR (nujol) (Fig. 9): Cyclopropane ring 3070, 1020 cm^{-1}.

PMR ($CDCl_3$) (Fig. 10): Cyclopropane protons, 4H, m, 0.15 to 0.50 ppm; C-Me's, 3H, singlets at 0.73, 0.79 ppm.

6-exo-Acetoxycamphene (50).

Freshly distilled acetic anhydride (15 g, 0.13 mole) was slowly added to a solution of 6-exo-hydroxycamphene (49)

(5 g, 0.033 mole) in dry pyridine (25 ml) at 15°, and left at room temperature (~30°) overnight. The reaction mixture was then poured into cold water (150 ml), left at 10° for 1 h, and extracted with ether (50 ml x 2). The combined ether extracts were washed with water (20 ml), cold 5% HCl aq (20 ml x 2), water (20 ml), 10% $NaHCO_3$ aq (20 ml x 2) and water (20 ml) and dried (Na_2SO_4). The solvent was stripped off and the resulting pale yellow oil distilled to get 50 (5.9 g, 82%), b.p. 95-98°/5 mm. n_D^{25} 1.4694.

IR (liq. film) (Fig. 11): OAc 1740, 1250 cm^{-1}; C=C 1660, 890 cm^{-1}.

PMR (CCl_4) (Fig. 12): C-Me's, 3H, singlets at 1.05, 1.075 ppm; $OCOCH_3$, 3H, s, 1.95 ppm; C_5-H_{endo}, 1H, octet, 2.25 ppm, J_1=3Hz, J_2=5Hz, J_3=13Hz; C=C-CH, 1H, bs, 2.73 ppm, W_h=5Hz; CHOAc, 1H, dd, 4.5 ppm, J_1=3Hz, J_2=7Hz; $C=CH_2$, 1H, singlets at 4.70, 4.95 ppm (lit.[30b] IR, PMR).

3,3-Dimethyl-6-exo-hydroxyspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane] (42) and 2,2-dimethyltricyclo [4.2.1.$0^{3,7}$]nonan-3-ol (56).

6-exo-Acetoxycamphene (1 g, 5.2 mmol) was reacted with Simmons-Smith reagent prepared from zinc-copper couple (5.06 g, 0.08 g atom) and CH_2I_2 (20.6 g, 0.08 mole) as described above. The reaction was complete in 60-80 h. Usual work-up gave a pale yellow oil (1.4 g), which was added to a solution of

KOH (1.7 g) in methanol (10 ml) and left overnight. The solution was then poured in cold water (100 ml) and extracted with ether (20 ml x 3). The combined ether extracts were washed with water (10 ml x 2) and dried. Removal of solvent furnished an oil (0.86 g), which was chromatographed over neutral alumina (26 g, II, 15 x 1.8 cm).

Fr. 1	Light petroleum	10 ml x 4	Mixture; 210 mg. Discarded.
	1% Ethylacetate in light petroleum	10 ml x 6	
	2% " "	10 ml x 8	
Fr. 2	2% " "	10 ml x 5	Crystalline solid (80 mg, 10%) (56, GLC, PMR).
Fr. 3	2% " "	10 ml x 2	Mixture, 30 mg (42 + 56)
	5% " "	10 ml x 2	
Fr. 4	5% " "	10 ml x11	Crystalline Solid (42, 0.5g, 45%, GLC, PMR).
	10% " "	10 ml x 3	

Fr. 2, m.p. 97-99° (crystallised from light petroleum) was the tricyclic alcohol (56).

IR ($CHCl_3$) (Fig. 13): OH 3360, 1090 cm^{-1}.

PMR ($CDCl_3$) (Fig. 14): C-Me's, 3H, singlets at 0.89, 0.99 ppm; OH, 1H, s, 1.17 ppm, exchangeable with D_2O.

Mass: m/e 166 (M^+, 29%), 151 (16%), 148 (2%), 123 (8%), 109 (10%), 105 (10%), 83 (100%), 79 (10%), 67 (10%) and 55 (9%).

Analysis: Found: C, 79.82; H, 10.64

$C_{11}H_{18}O$ requires: C, 79.52; H, 10.84%.

Fr. 4, m.p. 87-89° (crystallised from light petroleum) was the cyclopropane derivative (42).

IR (nujol) (Fig. 16): OH 3290, 1095 cm^{-1}; cyclopropane 3060, 1040 cm^{-1}.

PMR ($CDCl_3$) (Fig. 17): cyclopropane CH_2's, 4H, m, 0.35 ppm; C-Me's, 3H, singlets at 0.66, 0.83 ppm; OH, 1H, s, 1.55 ppm, exchangeable with D_2O; C_5-H_{endo}, 1H, octet, 2.3 ppm, J_1=3Hz, J_2=5Hz, J_3=13Hz; CHOH, 1H, dd, 4.0 ppm, J_1=3Hz, J_2=6Hz.

Mass: m/e 166 (M^+, 7%), 148 (37%), 133 (27%), 122 (29%), 107 (54%), 105 (47%), 95 (53%), 94 (100%), 83 (40%) and 79 (40%).

Analysis: Found: C, 79.74; H, 10.69

$C_{11}H_{18}O$ requires: C, 79.52; H, 10.84%.

6-Ketocamphene (62).

Oxidation of 6-exo-hydroxycamphene (49) with pyridinium chromate-on-silica gel according to the known[45] method gave 62 in 72% yield. m.p. 47-48° (lit.[45] m.p. 47-48°).

IR (CCl_4): C=O 1745 cm^{-1}; C=C 1650, 890 cm^{-1}.

PMR ($CDCl_3$): C-Me's, 3H, singlets at 1.1[redacted] and 1.21 ppm; C=C-CH, 1H, s, 3.14 ppm; $C=CH_2$, 1H, singlets at 4.88 and 5.12 ppm.

3,3-Dimethyl-6-oxospiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane] (63).

(a) Simmons-Smith reaction(as described earlier) of 6-ketocamphene (62) (1 g, 6.7 mmol) with zinc-copper couple (8.6 g, 0.14 g atom) and CH_2I_2 (37.5 g, 0.14 mole) followed by chromatography over Al_2O_3 gave 63 as a white crystalline solid (0.54 g, 59%), m.p. 48-50°.

IR (CCl_4) (Fig. 18): CO 1745 cm^{-1}; cyclopropane 3065, 1020 cm^{-1}.

PMR (CCl_4) (Fig. 19): C-Me's, 3H, singlets at 0.8 and 1.0 ppm; cyclopropane ring protons, 4H, s, 0.45 ppm.

Analysis: Found: C, 80.31; H, 9.90.

$C_{11}H_{18}O$ requires: C, 80.50; H, 9.757%.

(b) 3,3-Dimethyl-6-exo-hydroxyspiro [bicyclo(2.2.1)-heptane-2,1'-cyclopropane] (42) (55 mg, 0.33 mmol) in pyridine (0.4 ml) was added to a complex of CrO_3 (133 mg, 1.32 mmol) and pyridine (1.3 ml) and stirred at room temperature (~30°) for 20 h. The reaction mixture was poured in crushed ice and extracted with ether (20 ml x 3). The combined ether extracts were successively washed with water (10 ml), 5% HCl aq (10 ml x 2), water (10 ml), 5% $NaHCO_3$ aq (10 ml), water (10 ml) and brine (10 ml) and dried (Na_2SO_4). Removal of solvent furnished the ketone 63 (46 mg, 85%), m.p. 48-50°.

3,3-Dimethyl-6-endo-hydroxyspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane] (43).

A solution of the ketone 63 (100 mg, 0.6 mmol) in dry THF (5 ml) was added to a stirred solution of tri-t-butoxy lithium aluminium hydride (0.24 g, 1.2 mmol) in dry THF and stirred at room temperature (~30°) for 8 h. Water (20 ml) was added to the reaction mixture and it was extracted with ether (10 ml x 3). The combined ether extracts were washed with water (10 ml), brine (10 ml) and dried (Na_2SO_4). Removal of solvent gave 43 as a white solid (91 mg, 92%), m.p. 51-52°.

IR (nujol) (Fig. 20): OH 3590, 3440, 1090 cm^{-1}; cyclopropane 3080, 1025 cm^{-1}.

PMR ($CDCl_3$) (Fig. 21): cyclopropane protons 4H, m, 0.35 to 0.70 ppm; C-Me's, 6H, s, 0.9 ppm; OH, 1H, s, 2.05 ppm, exchangeable with D_2O; CHOH, 1H, m, 4.05 to 4.35 ppm.

Mass: m/e 166 (M^+, 4%), 148 (47%), 133 (57%), 122 (78%), 107 (70%), 105 (100%), 94 (48%), 91 (42%) and 79 (43%).

Analysis: Found: C, 79.70; H, 10.53.
$C_{11}H_{16}O$ requires: C, 79.52; H, 10.84%.

Methyl 3,3-dimethyl-6-exo-hydroxyspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane]-2'-carboxylate (46):

A solution of ethyl diazoacetate[57] (3.8 g, 0.03 mole) in cyclohexane (10 ml) was added dropwise over a period of 0.5 h

to a refluxing mixture of 6-exo-acetoxycamphene (0.6 g, 3.1 mmol) and anhydrous $CuSO_4$ (0.1 g) in cyclohexane (10 ml). After the mixture was stirred under reflux for a further 6 h, it was cooled and filtered. The solvent was removed under reduced pressure to furnish a brown oil (3.0 g). It was added to a solution of KOH (7.2 g) in water (5 ml) and methanol (60 ml) and left at room temperature ($\sim 30^{\circ}$) overnight. The reaction mixture was poured in cold water (100 ml) and extracted with ether (30 ml x 2). Work-up of the ether extract gave 6-exo-hydroxycamphene (49) (0.118 g). The aqueous layer was adjusted to pH 4 with 5% HCl aq and extracted with ether (20 ml x 3). The combined ether extracts were dried (Na_2SO_4). Removal of solvent gave a gummy solid (0.59 g), which was esterified with CH_2N_2 to give a red-colored viscous oil (0.67 g). The latter was chromatographed over alumina (20 g, II, 1.5 x 5 cms).

Fr. 1	Light petroleum	5 x 10 ml	Impurities
	5% Ethyl acetate in light petroleum	10 x 10 ml	
Fr. 2	10% EtOAc " "	10 x 10 ml	Pale yellow viscous oil, (46, GLC, PMR).

Fr. 2 was the compound 46 (0.49 g, 92%), b.p. 130-5°(bath)/0.4 mm.

IR (liq. film)(Fig. 22): OH 3420, 1100 cm^{-1}; C=O 1725 cm^{-1}; cyclopropane ring 1040 cm^{-1}.

PMR ($CDCl_3$)(Fig. 23): C-Me's, 3H, singlets at 0.66, 0.91 ppm;

cyclopropane CH_2, 1H, singlets at 0.74, 0.81 ppm; OH, 1H, s, 1.76 ppm, exchangeable with D_2O; C_5-H_{endo}, 1H, octet, 2.24 ppm, J_1=3Hz, J_2=6Hz, J_3=12Hz; OCH_3, 3H, s, 3.69 ppm; CHOH, 1H, dd, 3.98 ppm.

Mass: m/e 224 (M^+, 4%), 206 (2%), 192 (6%), 147 (10%), 138 (27%), 123 (19%), 105 (16%), 95 (46%), 94 (100%) and 79 (15%).

Analysis: Found: C, 69.43; H, 8.65.

$C_{13}H_{20}O_3$ requires: C, 69.65; H, 8.93%.

Reaction of 3,3-dimethylspiro [bicyclo(2.2.1)heptane-2,1'-cyclopropane] (51) with $Hg(OAc)_2$.

To a solution of 51 (1.5 g, 10 mmol) in THF/H_2O (1:1; 60 ml) was added $Hg(OAc)_2$ (3.18 g, 10 mmol) and stirred at 20° for 5 h. The reaction mixture was filtered. The filtrate was diluted with water (20 ml) and extracted with ether (20 ml x 3). The combined ether extracts were washed with 5% $NaHCO_3$ aq (20 ml), water (20 ml) and brine (20 ml) and dried. Removal of solvent gave a gum, which, when macerated with light petroleum, deposited the organomercurial compound 67 as a white solid (0.75 g, 18%), crystallised from ether/light petroleum; m.p. 143-5°.

IR(nujol)(Fig. 24): OH 3320, 1085 cm^{-1}; HgOAc 1610 cm^{-1}.

PMR ($CDCl_3$) (Fig. 25): C-Me's, 3H, singlets at 0.92, 1.0 ppm; $OCOCH_3$, 3H, s, 2.02 ppm; C(OH)CH, 1H, s, 2.1 ppm.

Analysis: Found: C, 37.01; H, 5.157.

$C_{13}H_{22}HgO_3$ requires: C, 36.57; H, 5.416%.

The above filtrate was evaporated to give ω-hydroxymethyl camphene (64) as a colorless oil (0.5 g, 31%); b.p. 100-105°(bath)/ 2 mm (lit.[35] b.p. 94-102°/1.7 mm).

IR (liq. film) (Fig. 26): OH 3340, 1110 cm^{-1}; C=CH 1675, cm^{-1}

PMR (CCl_4) (Fig. 27): C-Me's, 3H, singlets at 1.0, 1.02 ppm; OH, 1H, s, 1.35 ppm, exchangeable with D_2O; =C-CH, 1H, bs, 2.98 ppm, W_h = 8Hz; CH_2OH, 2H, d, 3.99 ppm, J= 8Hz; C=CH, 1H, t, 5.12 ppm, J = 8 Hz.

ω-Acetoxymethyl camphene (65).

Prins reaction of camphene according to the known[35] method gave 65 as a colorless oil, b.p. 110-8°/8 mm.

IR (liq. film): OAc 1740, 1240 cm^{-1}; C=CH 1680, 960 cm^{-1}.

PMR (CCl_4): C-Me's, 3H, singlets at 1.0, 1.04 ppm; $OCOCH_3$, 3H, s, 1.95 ppm; CH=C-CH-, 1H, bs, 3.05 ppm, W_h= 8Hz; CH_2OAc, 2H, d, 4.45 ppm, J = 8 Hz; C=CH, 1H, t, 5.05 ppm, J = 8 Hz.

Hydrolysis of 65 with methanolic KOH gave ω-hydroxymethyl camphene (64).

The dimer (69).

To a stirred and cooled (20°) mixture of the organomercurial acetate 67 (0.1 g, 0.23 mmol) and 3M NaOH (1.3 ml) was added dropwise 0.5 M $NaBH_4$ in 3M NaOH (1.3 ml). The stirring was continued at 20° for 6 h. The reaction mixture was diluted with water (5 ml) and extracted with light petroleum (10 ml x 3). The combined petroleum extracts were washed with water (5 ml) and brine (5 ml) and dried (Na_2SO_4). Removal of solvent gave 69 as a gummy solid (55 mg, 88%), which was homogeneous by TLC (15% EtOAc in light petroleum, R_f 0.55).

IR (nujol) (Fig. 28): OH 3600, 3480 cm^{-1}.

PMR (CCl_4) (Fig. 29): C-Me's, 6H, singlets at 0.92, 1.0 ppm.

Analysis: Found: C, 49.75; H, 6.902.

$C_{22}H_{33}HgO_2$ requires: C, 49.39; H, 7.109%.

ω-Trifluoroacetoxymethyl camphene (66).

To a solution of the spirocyclopropane (51) (0.2 g, 1.3 mmol) in dry benzene (15 ml) was added $Hg(OCOCF_3)_2$ (0.74 g, 1.7 mmol) and stirred at 60° for 12 h under anhydrous conditions. The reaction mixture was cooled to room temperature (≈30°) and filtered. The black residue was washed with benzene (10 ml). The filtrate was washed with 5% $NaHCO_3$ aq (10 ml x 2), water (10 ml) and brine (10 ml) and dried (Na_2SO_4). Removal of solvent followed by distillation gave ω-trifluoroacetoxymethyl

camphene (66) as a colorless oil (0.14 g, 50%); b.p. 110-5° (bath)/5 mm.

IR (liq. film) (Fig. 30): $OCOCF_3$ 1780 cm^{-1}; C=CH 1675 cm^{-1}.

PMR ($CDCl_3$) (Fig. 31): C-Me's, 3H, singlets at 1.03, 1.06 ppm; CH=C-CH-, 1H, bs, 3.05 ppm, W_h=8Hz; CH_2OCOCF_3, 2H, d, 4.85 ppm, J=8Hz; C=CH, 1H, t, 5.19 ppm, J = 8 Hz.

Analysis: Found: C, 59.26; H, 6.72.

$C_{13}H_{17}F_3O_3$ requires: C, 59.54; H, 6.49%.

Hydrolysis of the above ester in the usual fashion gave ω-hydroxymethyl camphene (64).

Fragmentation of 6-exo-hydroxy-3,3-dimethylspiro [bicyclo(2.2.1)-heptane-2,1'-cyclopropane] (42).

To a solution of 42 (50 mg, 0.3 mmol) in dry benzene (5 ml) was added $Hg(OCOCF_3)_2$ (140 mg, 0.33 mmol) and stirred at room temperature (~30°) under anhydrous conditions for 8 h. It was worked up as above to give the diene aldehyde (71) as a pale-yellow oil (31 mg, 63%).

UV (Ethanol): λ_{max} 237 nm; ϵ_{max} 5264.

IR (CCl_4) (Fig. 32): CHO 2720, 1730 cm^{-1}; C=C 1630, 915 cm^{-1}.

PMR ($CDCl_3$) (Fig. 33): C-Me's, 3H, singlets at 0.92, 1.14 ppm; CH_2CHO, 2H, s, 2.45 ppm; H_b, 1H, d, 5.05 ppm, J = 10 Hz; H_a, 1H, d, 5.4 ppm, J = 17 Hz; H_d, 1H, s, 5.72 ppm; H_c, 1H, q, 6.25 ppm, J_1 = 17 Hz, J_2 = 10 Hz; CHO, t, 9.82 ppm, J = 1.5 Hz.

Mass: m/e 164(M^+, 9%), 120 (100%), 105 (64%), 93 (17%), 91 (23%), 79 (21%), and 77 (19%).

Identical result was obtained with the endo-epimer 43 .

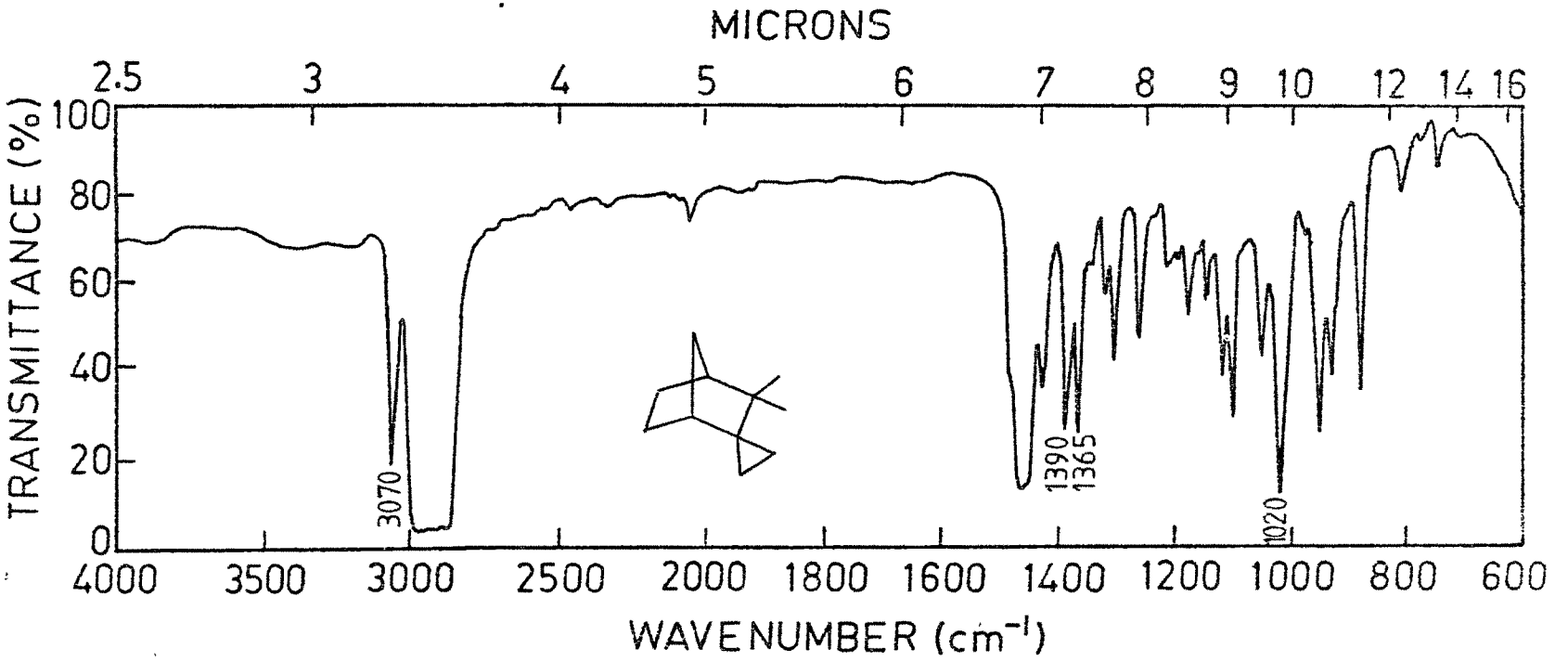


FIG. 9 -IR SPECTRUM OF 3,3-DIMETHYLSPIRO [BICYCLO (2.2.1) HEPTANE-2,1'-CYCLOPROPANE] (51)

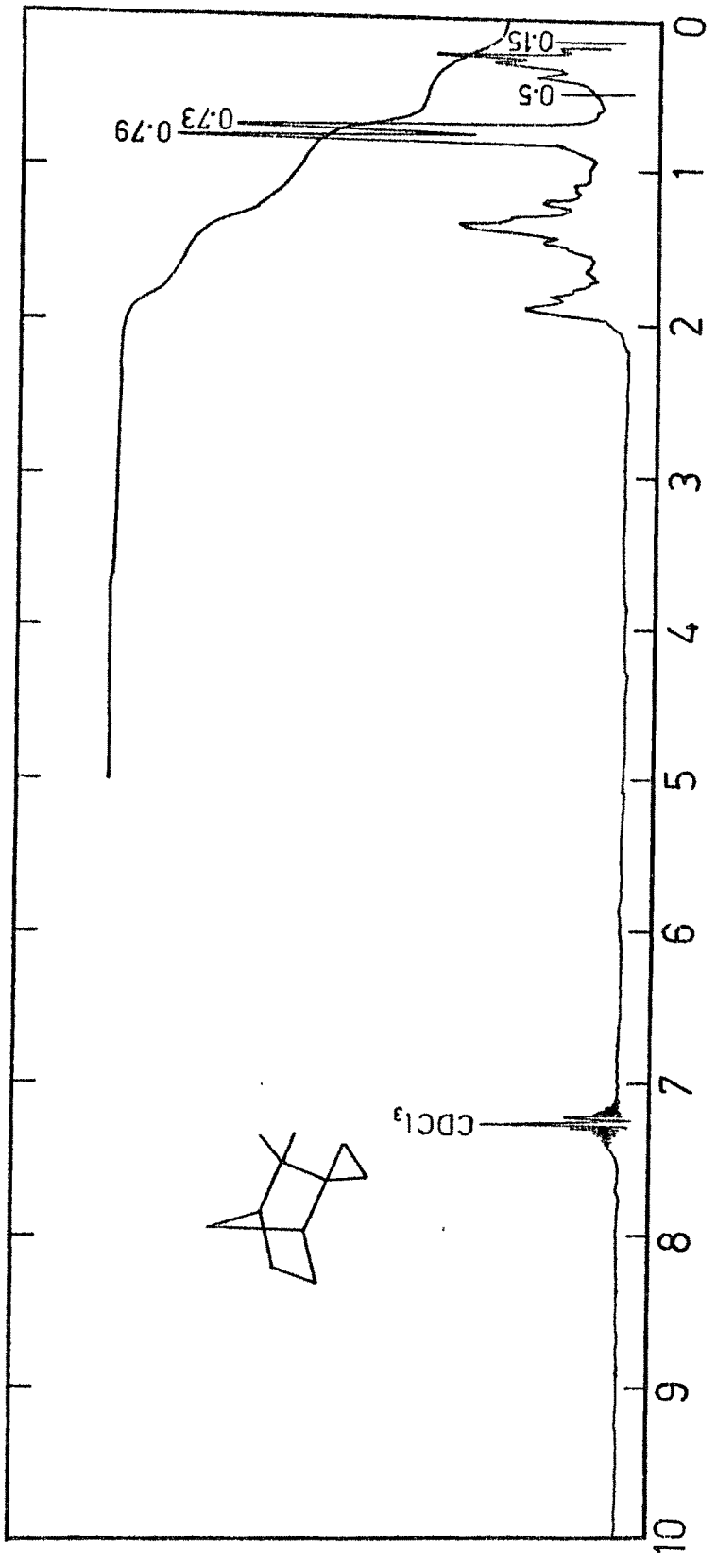


FIG. 10 -PMR SPECTRUM OF 3,3-DIMETHYLSPIRO [BICYCLO(2.2.1) HEPTANE-2,1'-CYCLOPROPANE] (51)

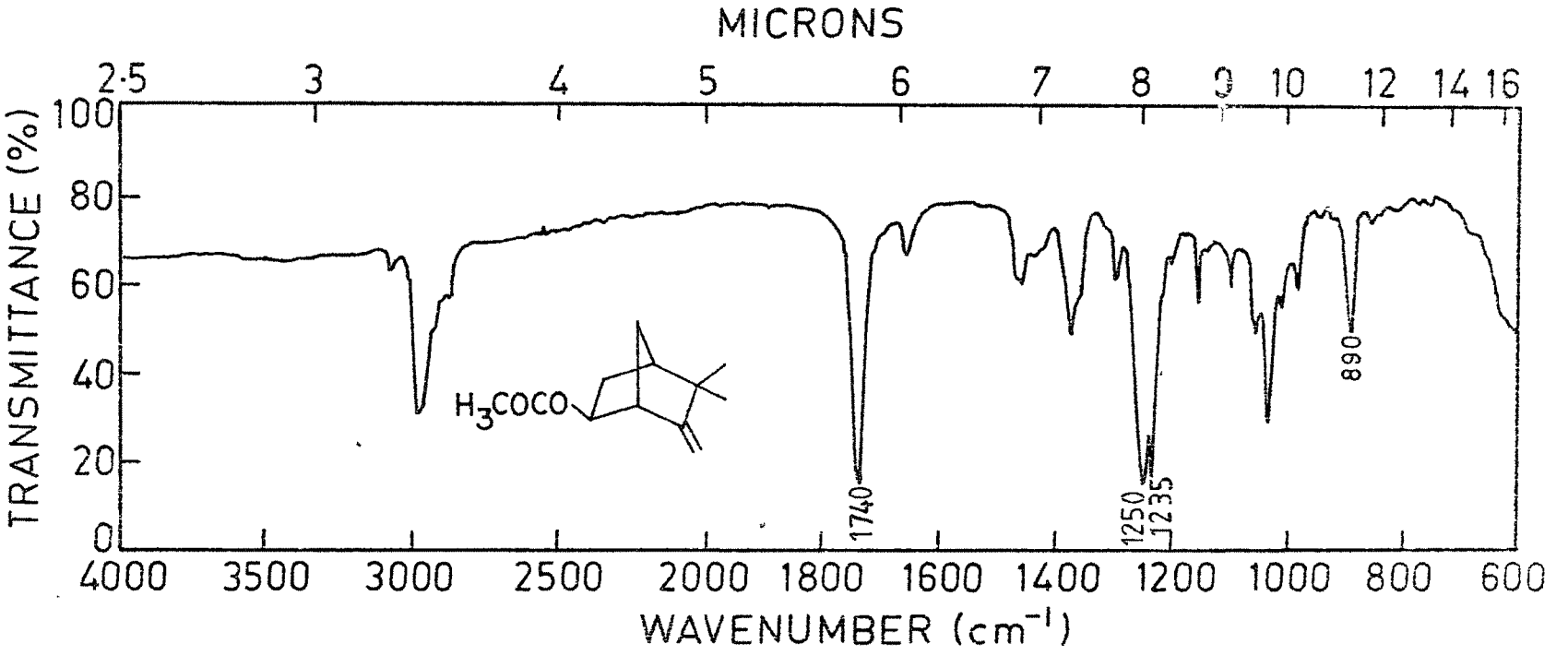


FIG.11 -IR SPECTRUM OF 6-EXO-ACETOXYCAMPHENE (50)

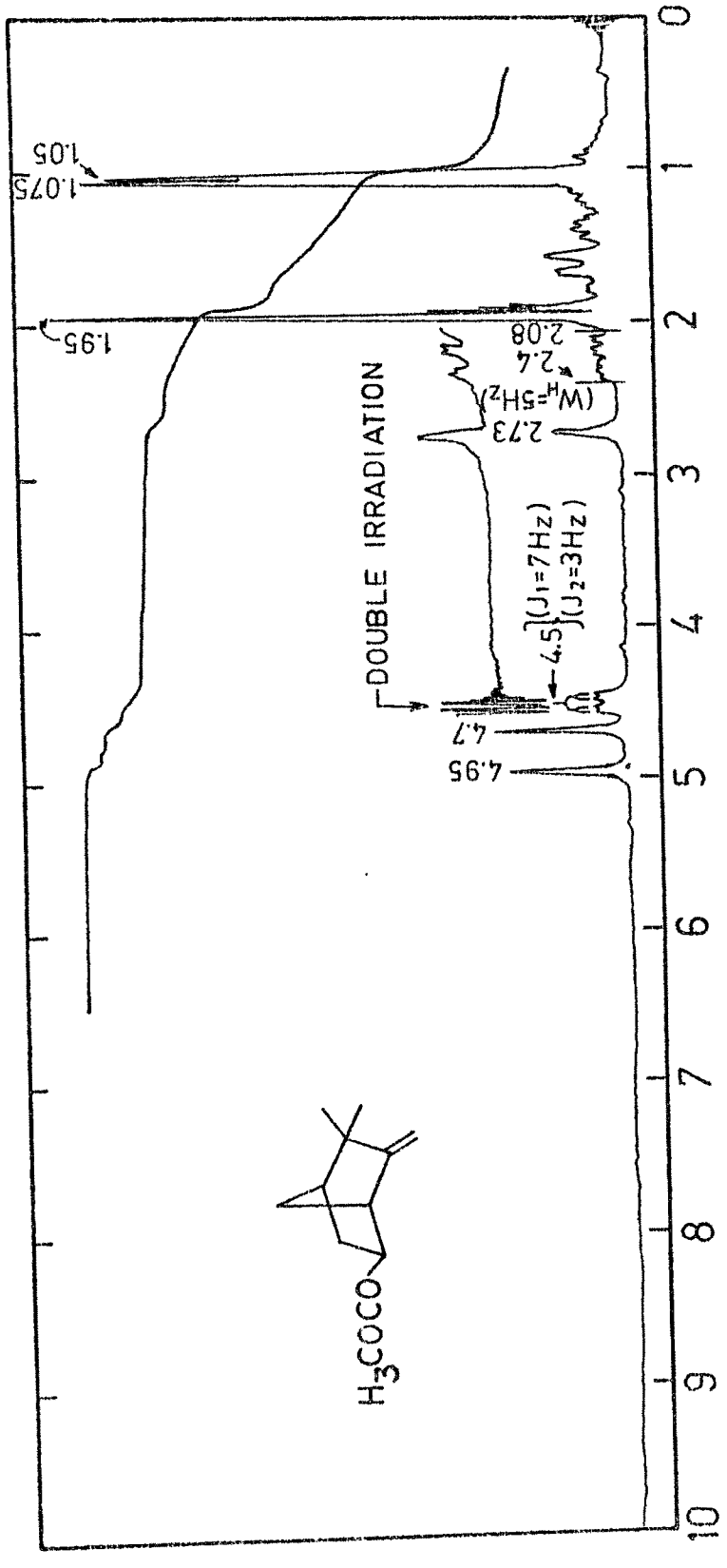


FIG.12 -PMR SPECTRUM OF 6-EXO-ACETOXYCAMPHENE (50)

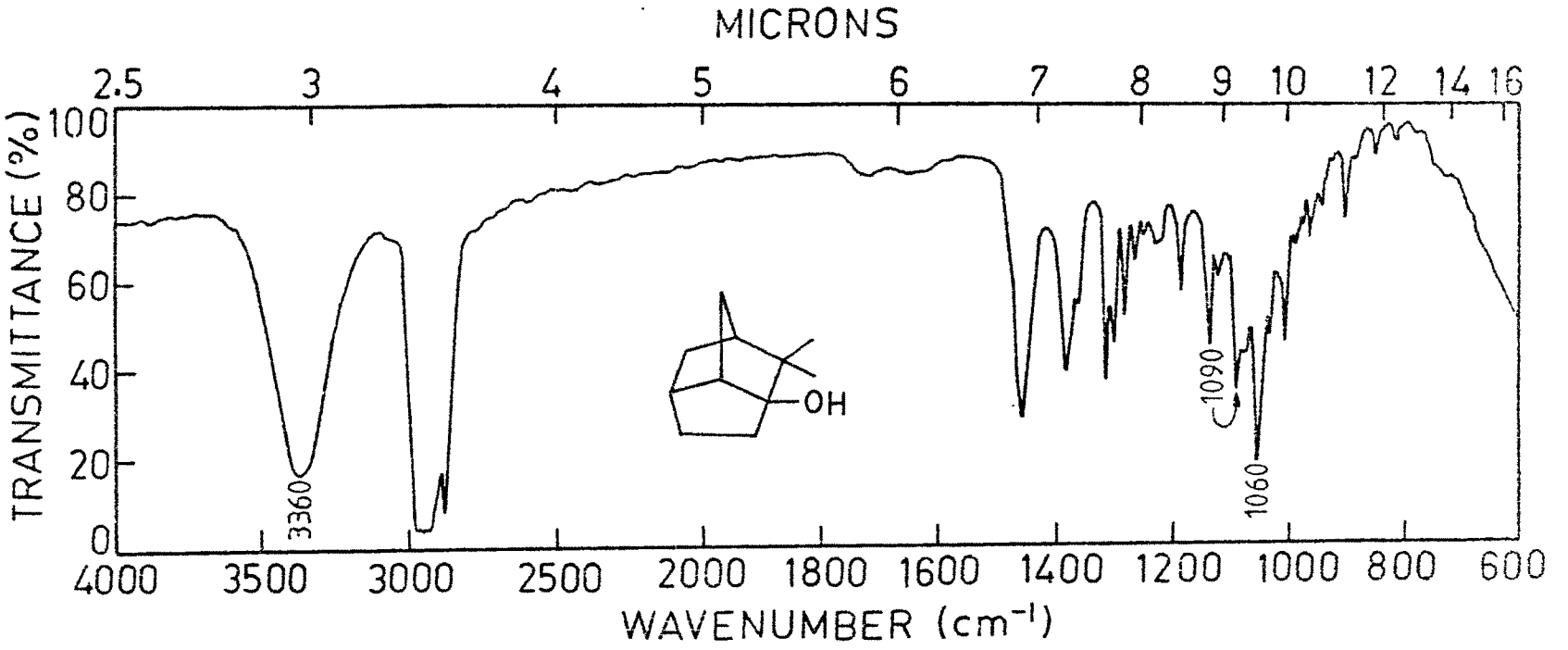


FIG.13 -IR SPECTRUM OF 2,2-DIMETHYLTRICYCLO [4.2.1.$0^{3,7}$] NONAN-3-OL (56)

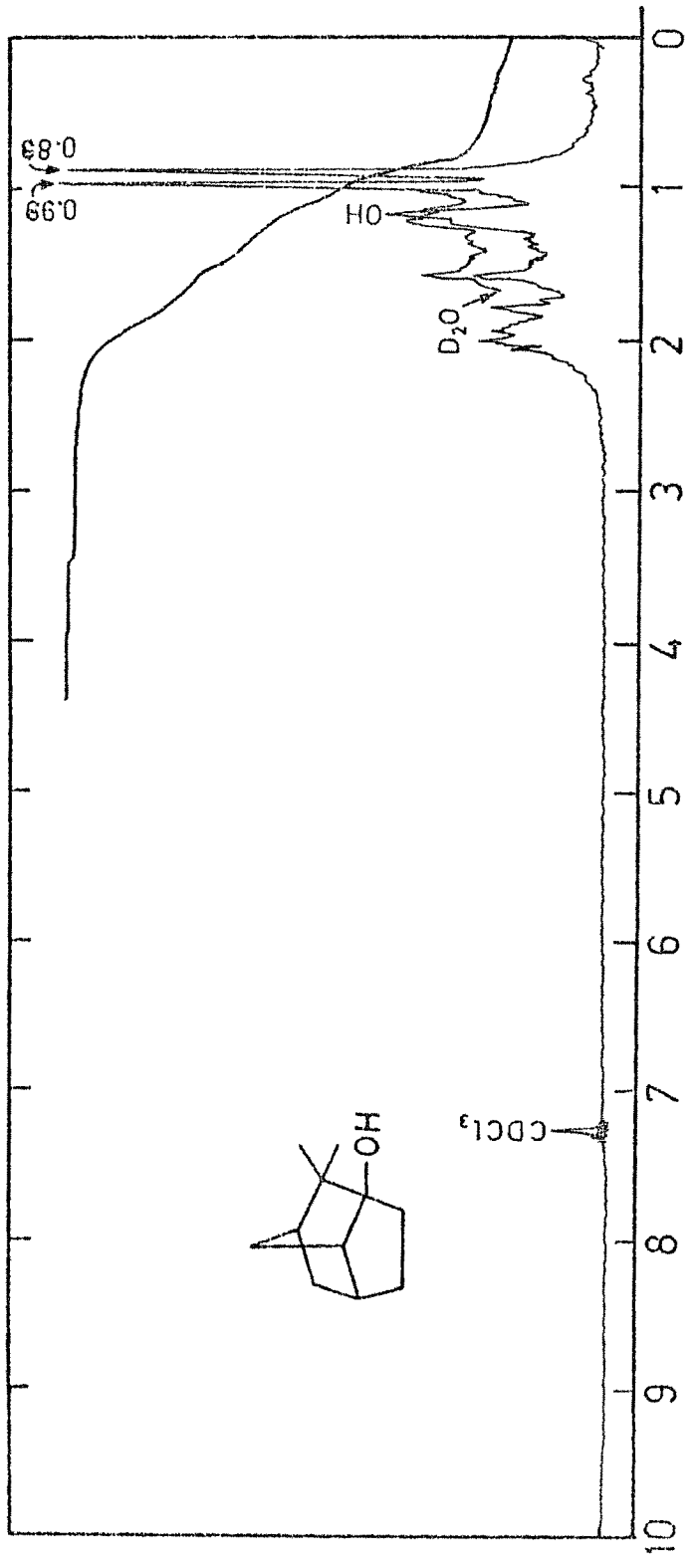


FIG.14 -PMR SPECTRUM OF 2,2-DIMETHYLTRICYCLO [4.2.1.$0^{3,7}$]NONAN-3-OL (56)

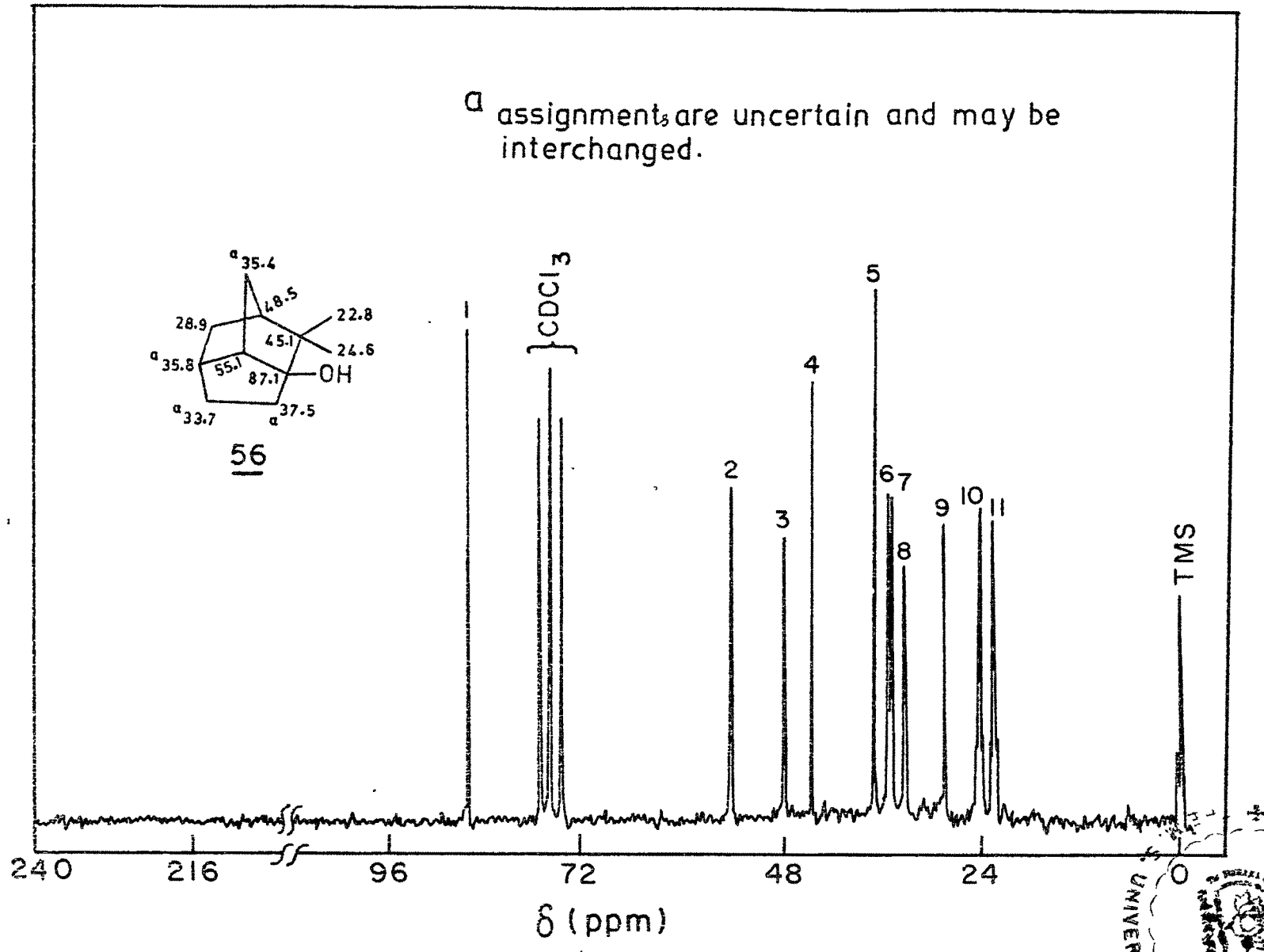


FIG.15-^{13}C-NMR SPECTRUM OF 2,2-DIMETHYLTRICYCLO [4.2.1.0^{3,7}]NONAN-3-OL

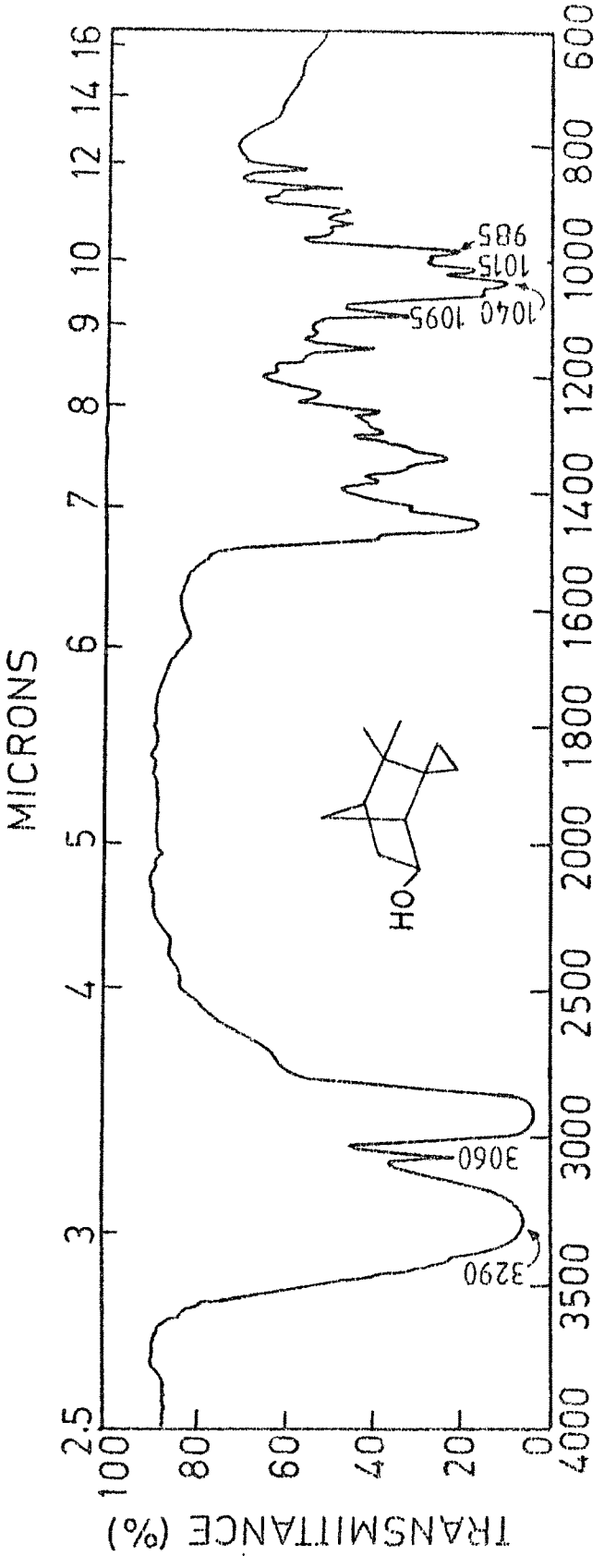


FIG.16 -IR SPECTRUM OF 6-EXO-HYDROXY-3,3-DIMETHYLSPIRO [BICYCLO(2.2.1) HEPTANE-2,1'-CYCLOPROPANE] (42)

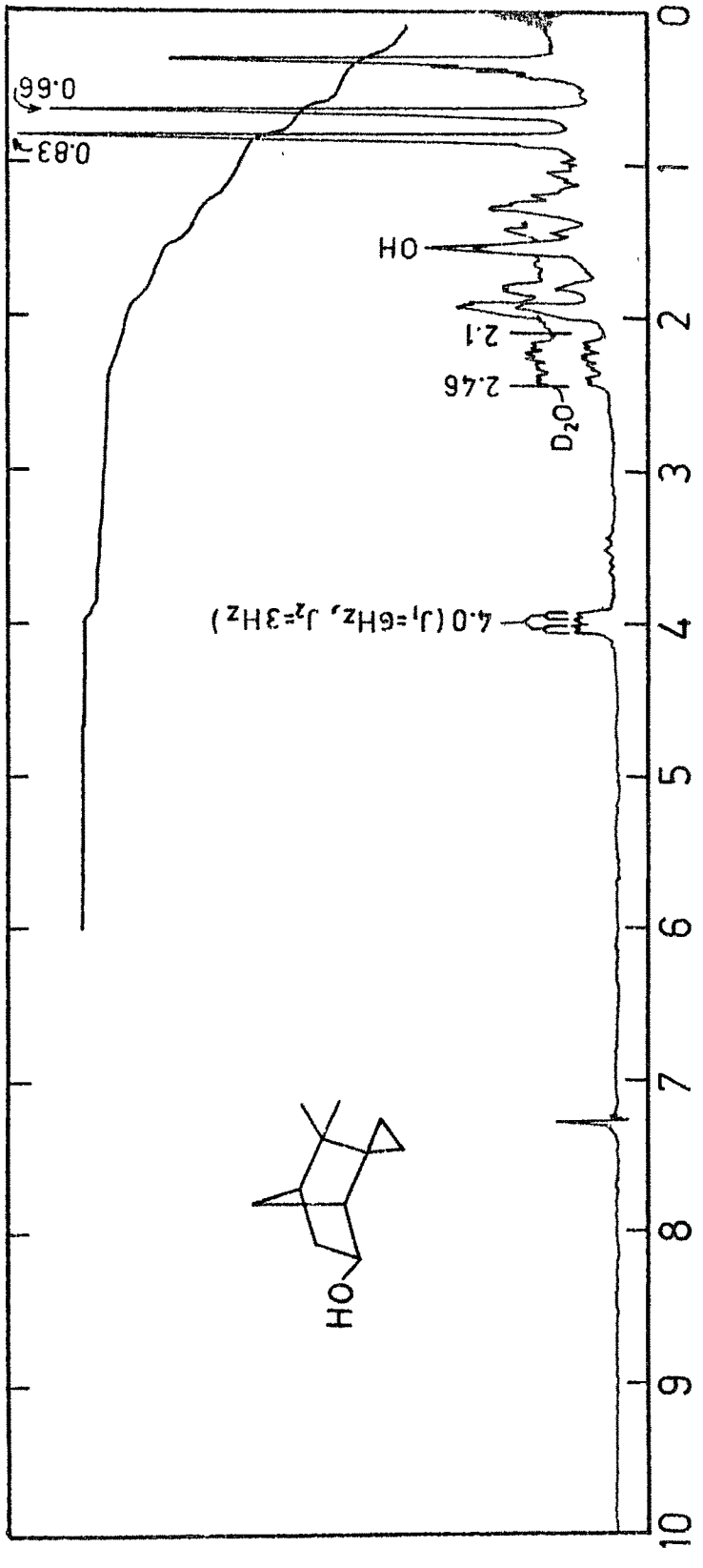


FIG.17 -PMR SPECTRUM OF 6-EXO-HYDROXY-3,3-DIMETHYLSPIRO [BICYCLO (2.2.1) HEPTANE-2,1'-CYCLOPROPANE] (42)

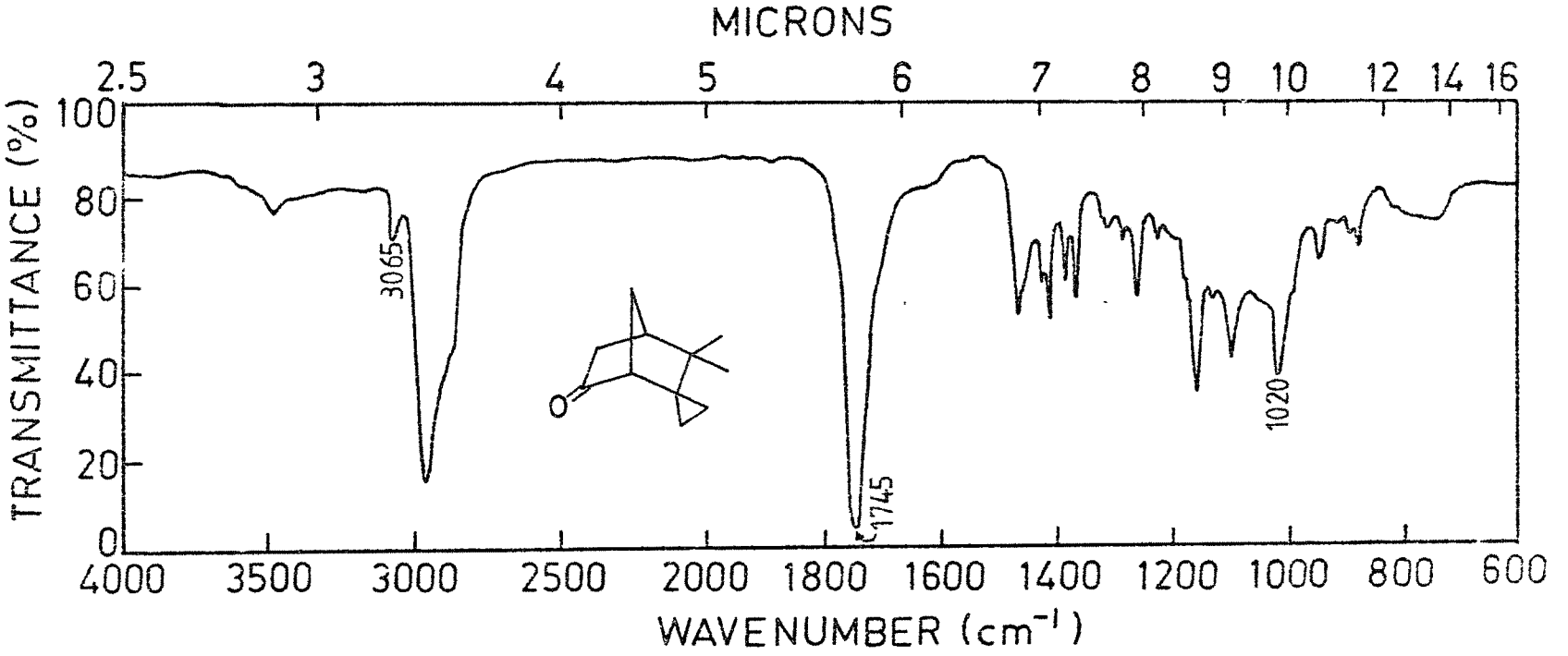


FIG. 18 -IR SPECTRUM OF 6-OXO-3,3-DIMETHYLSPIRO [BICYCLO (2.2.1) HEPTANE-2,1'-CYCLOPROPANE] (63)

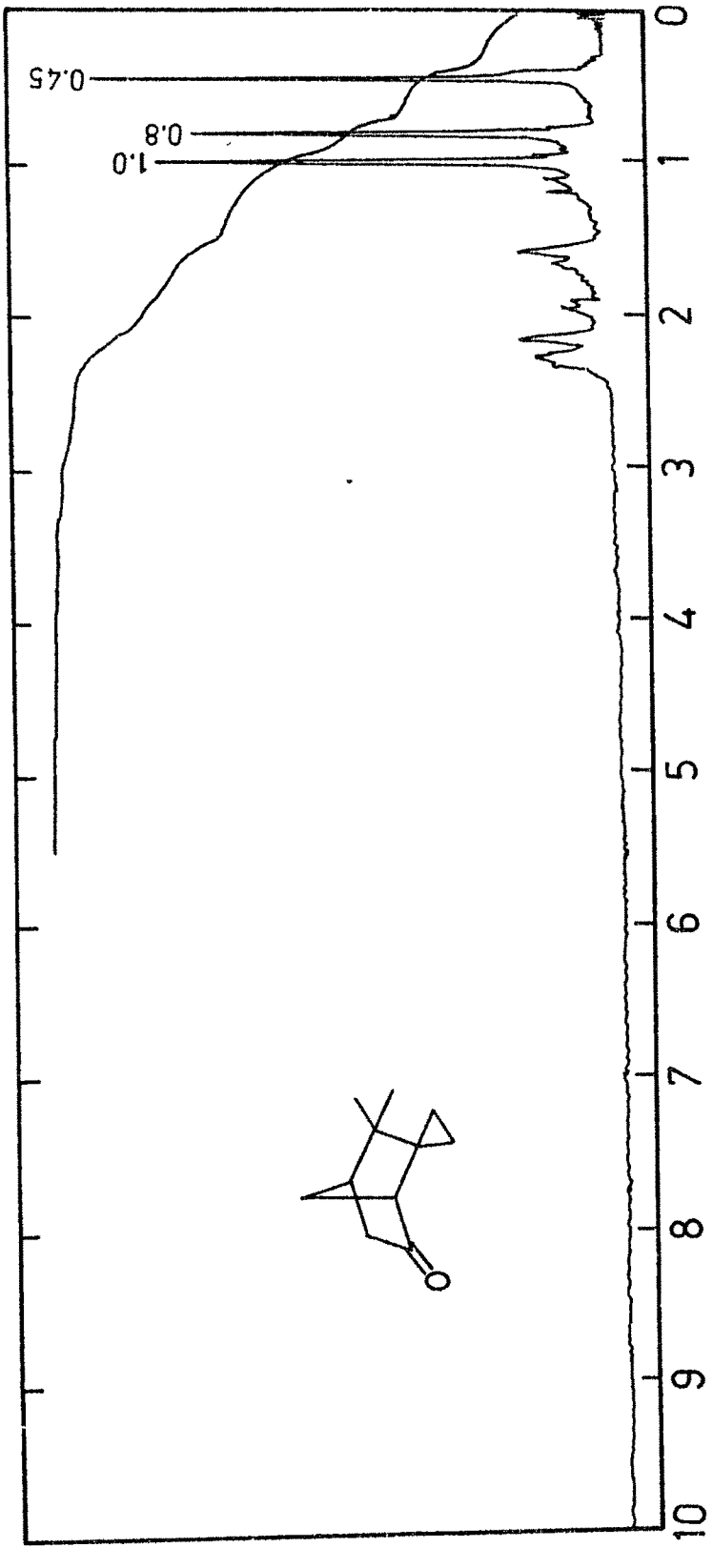


FIG. 19 - PMR SPECTRUM OF 6-OXO-3,3-DIMETHYLSPIRO[BICYCLO (2.2.1) HEPTANE-2,1'-CYCLOPROPANE] (63)

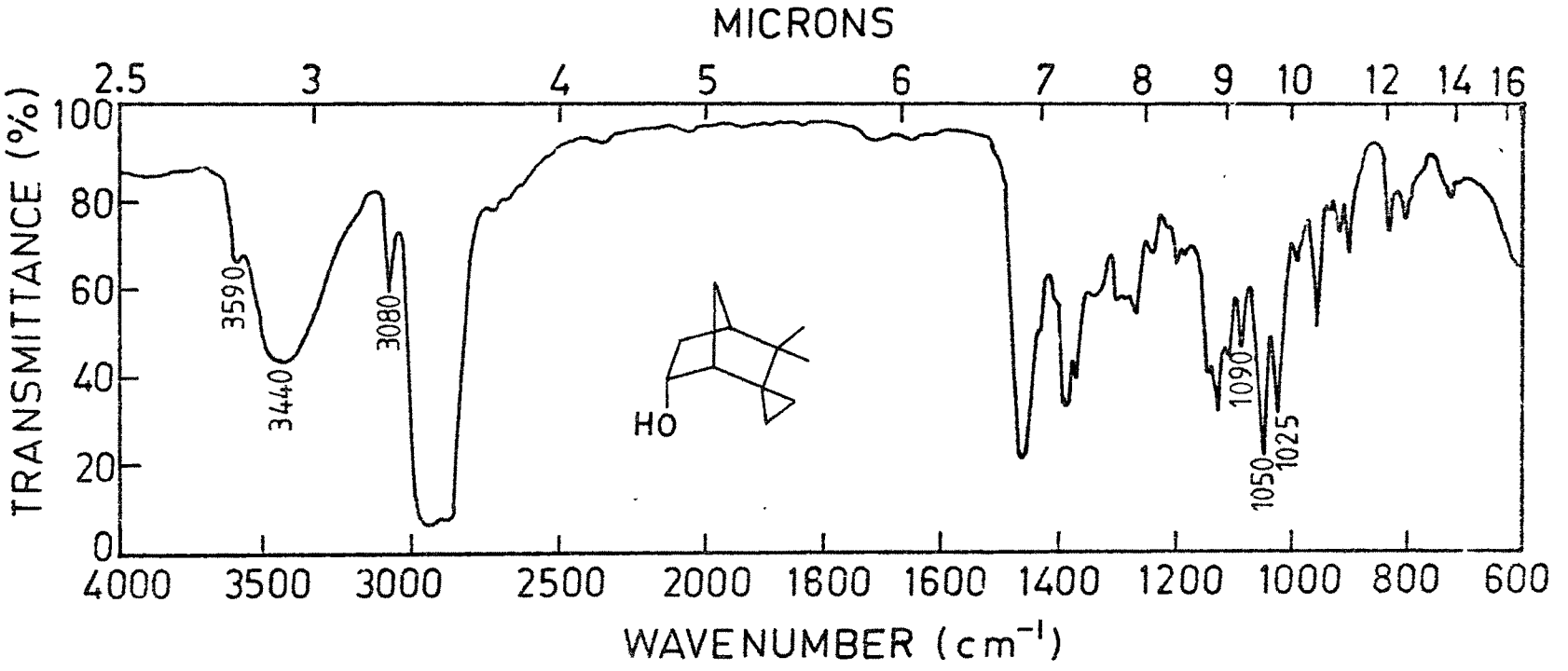


FIG. 20 - IR SPECTRUM OF 6-ENDO-HYDROXY-3,3-DIMETHYLSPIRO [BICYCLO (2.2.1) HEPTANE-2,1'-CYCLOPROPANE] (43)

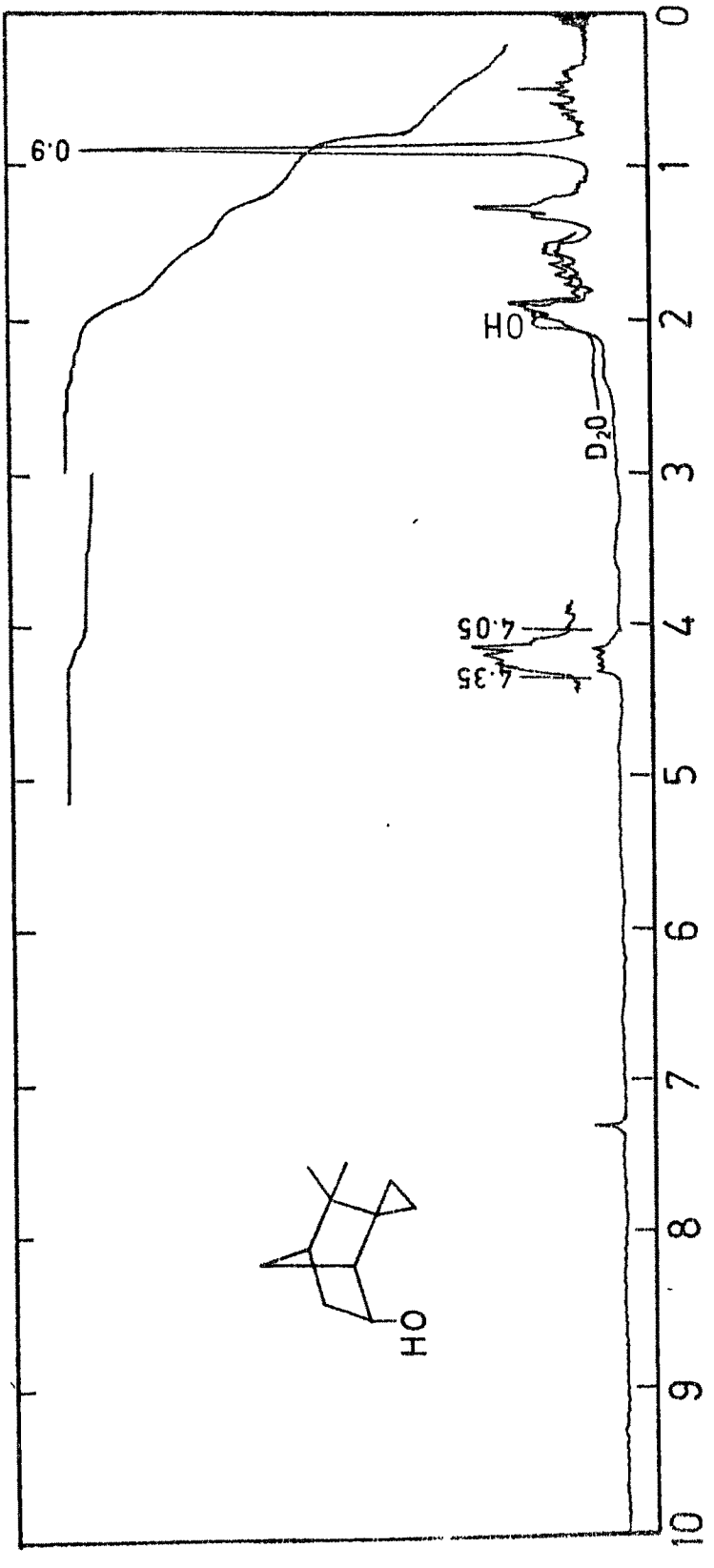


FIG. 21-PMR SPECTRUM OF 6-ENDO-HYDROXY-3,3-DIMETHYLSPIRO [BICYCLO(2.2.1)HEPTANE-2,1'-CYCLOPROPANE] (43)

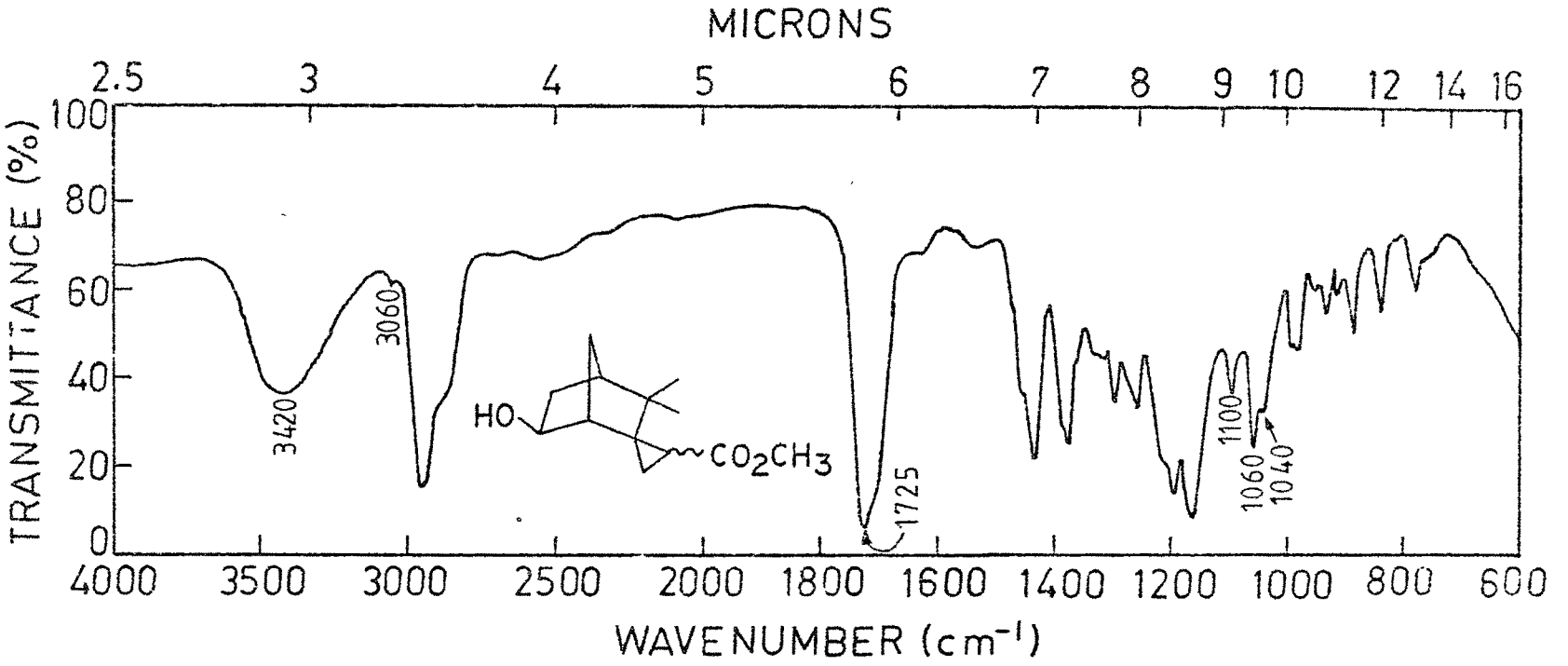


FIG.22 -IR SPECTRUM OF METHYL 6-EXO-HYDROXY-3,3-DIMETHYLSPIRO [BICYCLO (2.2.1) HEPTANE-2,1'-CYCLOPROPANE]-2'-CARBOXYLATE (46)

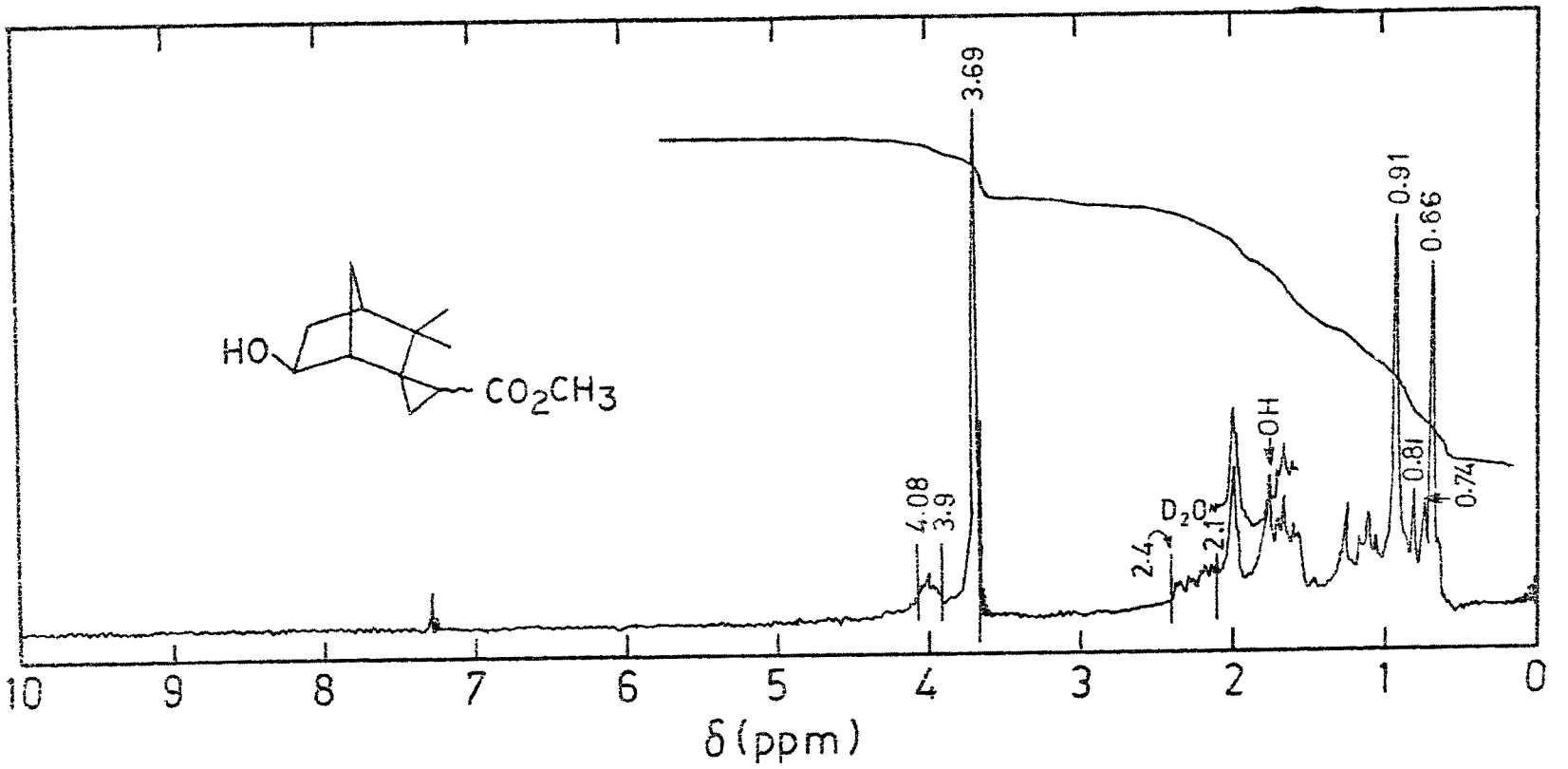


FIG. 23 -PMR SPECTRUM OF METHYL 6-EXO-HYDROXY-3,3-DIMETHYL-SPIRO [BICYCLO(2.2.1)HEPTANE-2,1'-CYCLOPROPANE]-2'-CARBOXYLATE (46)

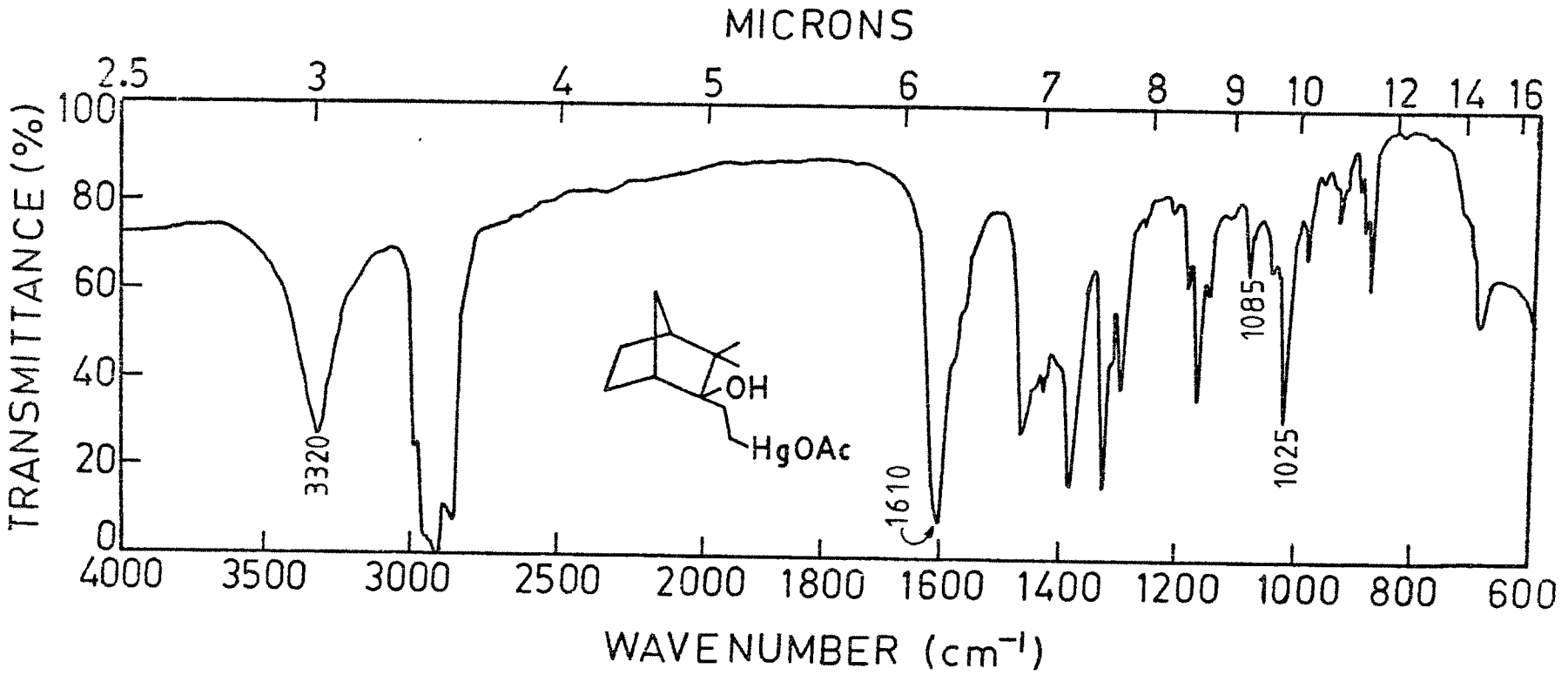
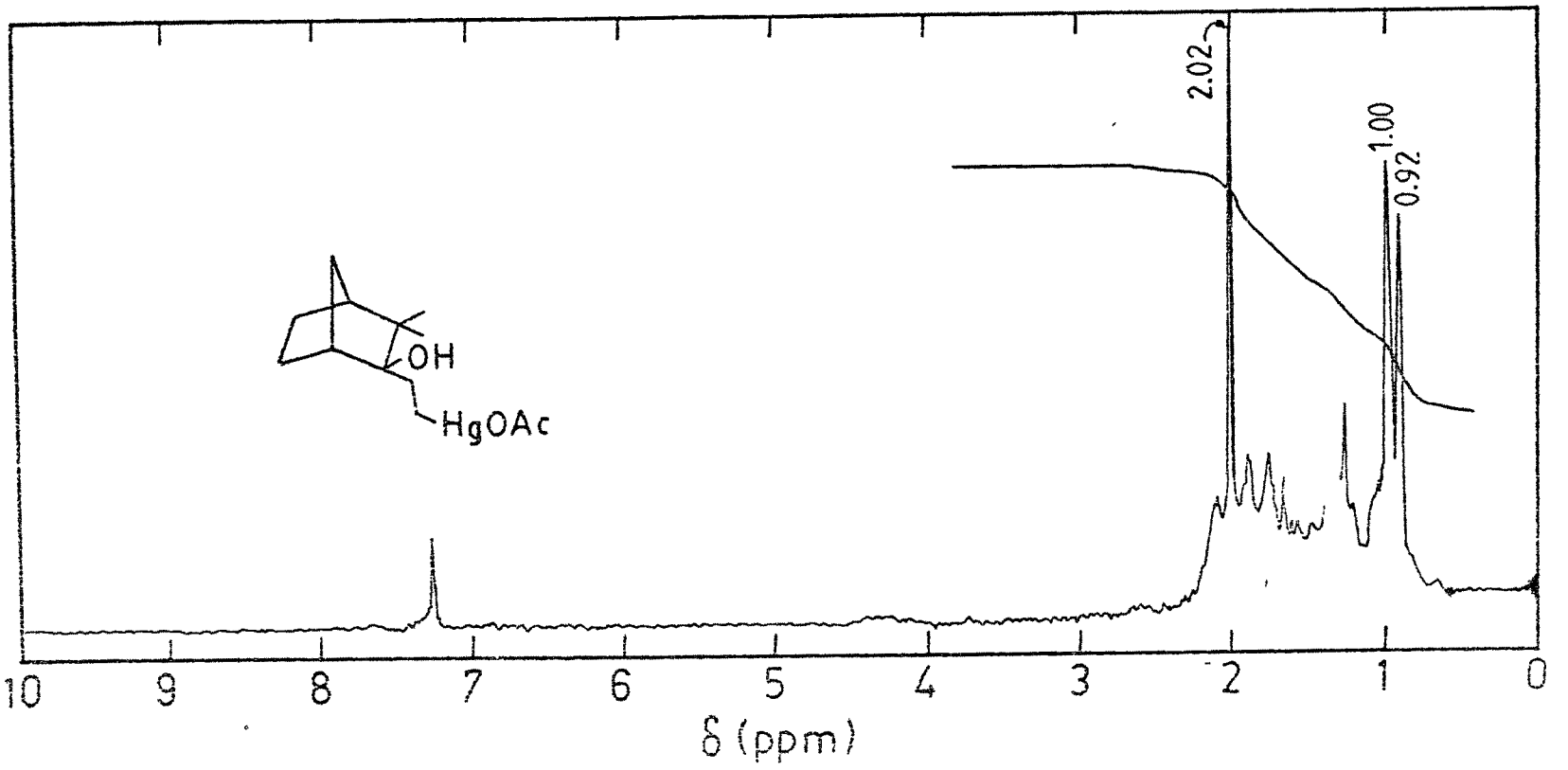


FIG. 24-IR SPECTRUM OF 1-[2'-EXO-HYDROXY-3',3'-DIMETHYLBICYCLO(2.2.1) HEPTAN-2'-YL]-ETHAN-2-YL MERCURY ACETATE (67)



F.G.25-PMR SPECTRUM OF 1-[2'-EXO-HYDROXY-3,3'-DIMETHYL BICYCLO (2.2.1) HEPTAN-2'-YL]-ETHAN-2-YL MERCURY ACETATE (E)

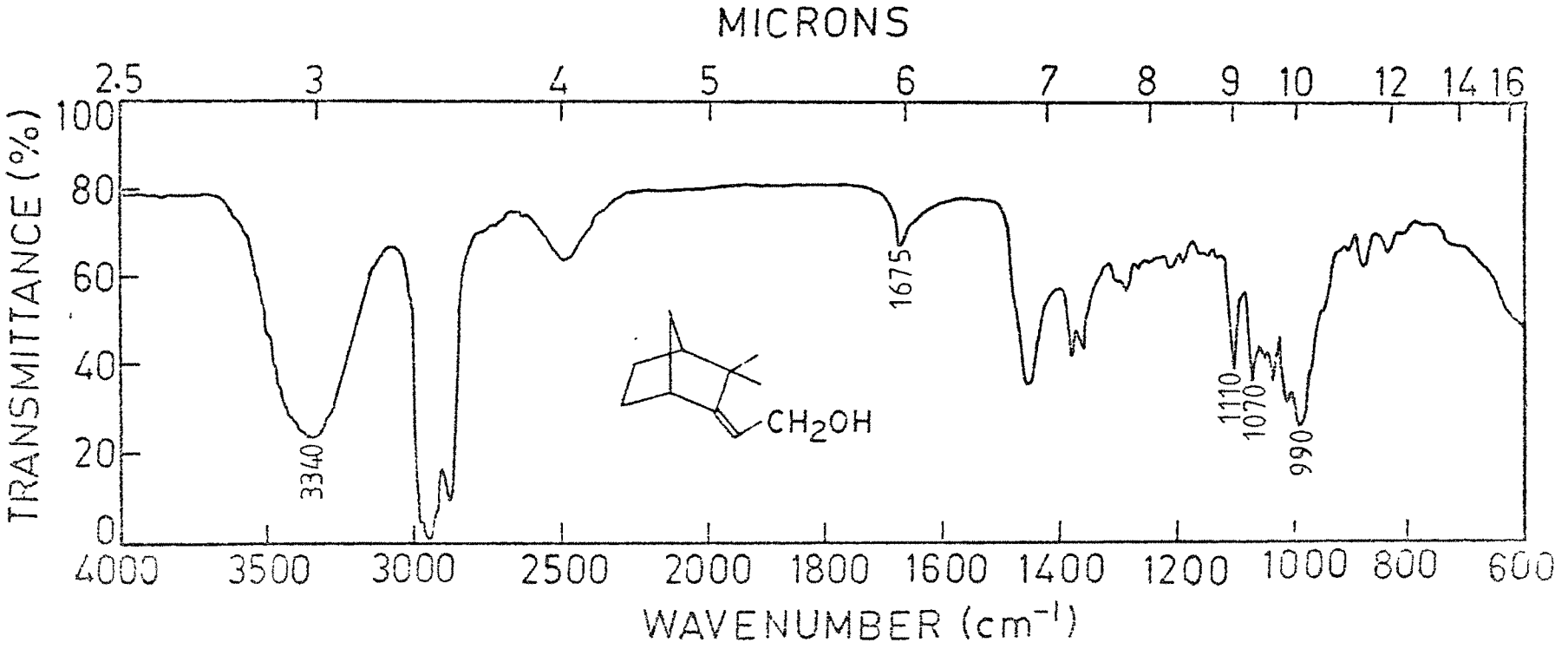


FIG. 26 -IR SPECTRUM OF ω-HYDROXYMETHYL CAMPHENE (64)

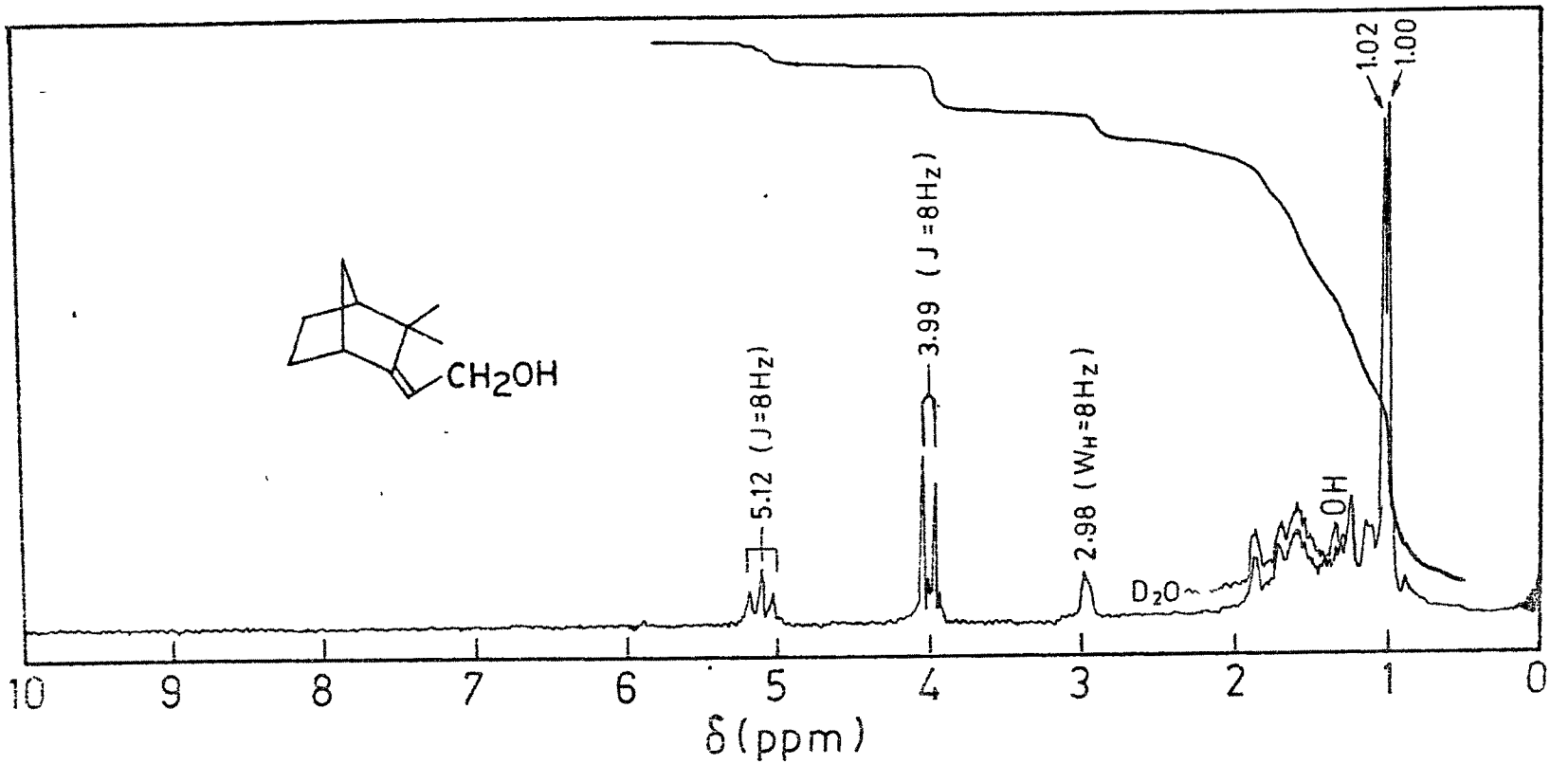


FIG. 27 -PMR SPECTRUM OF ω-HYDROXYMETHYL CAMPHENE (64)

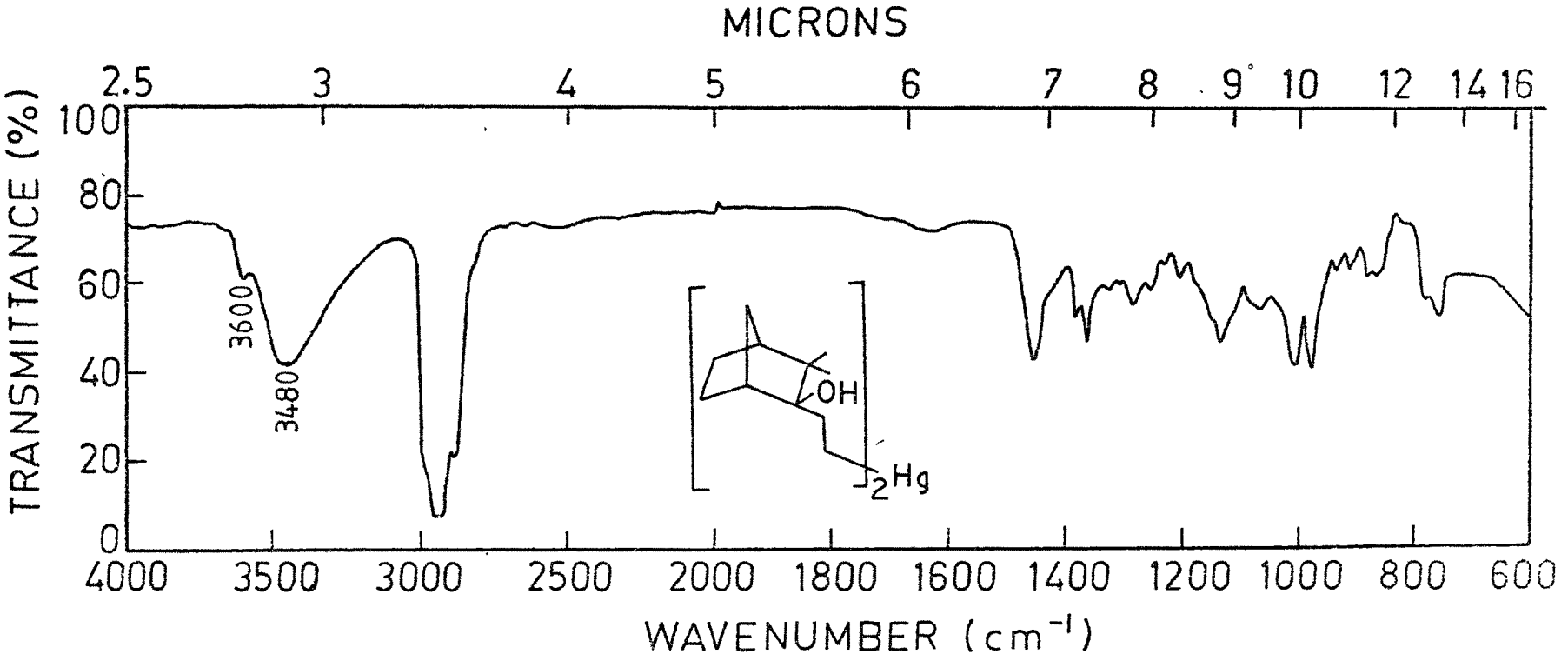


FIG. 28 -IR SPECTRUM OF THE DIMER (69)

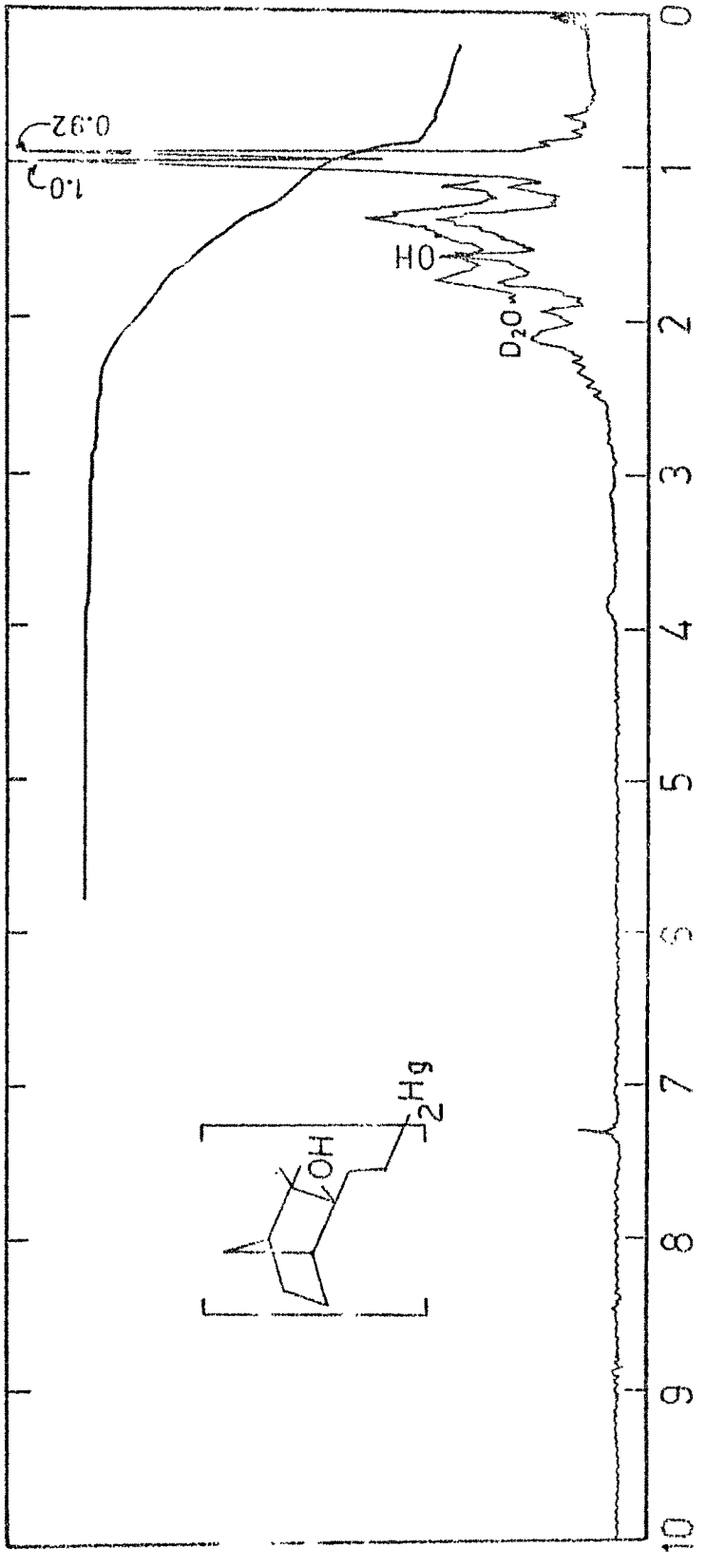


FIG. 29 -PMR SPECTRUM OF THE DIMER (69)

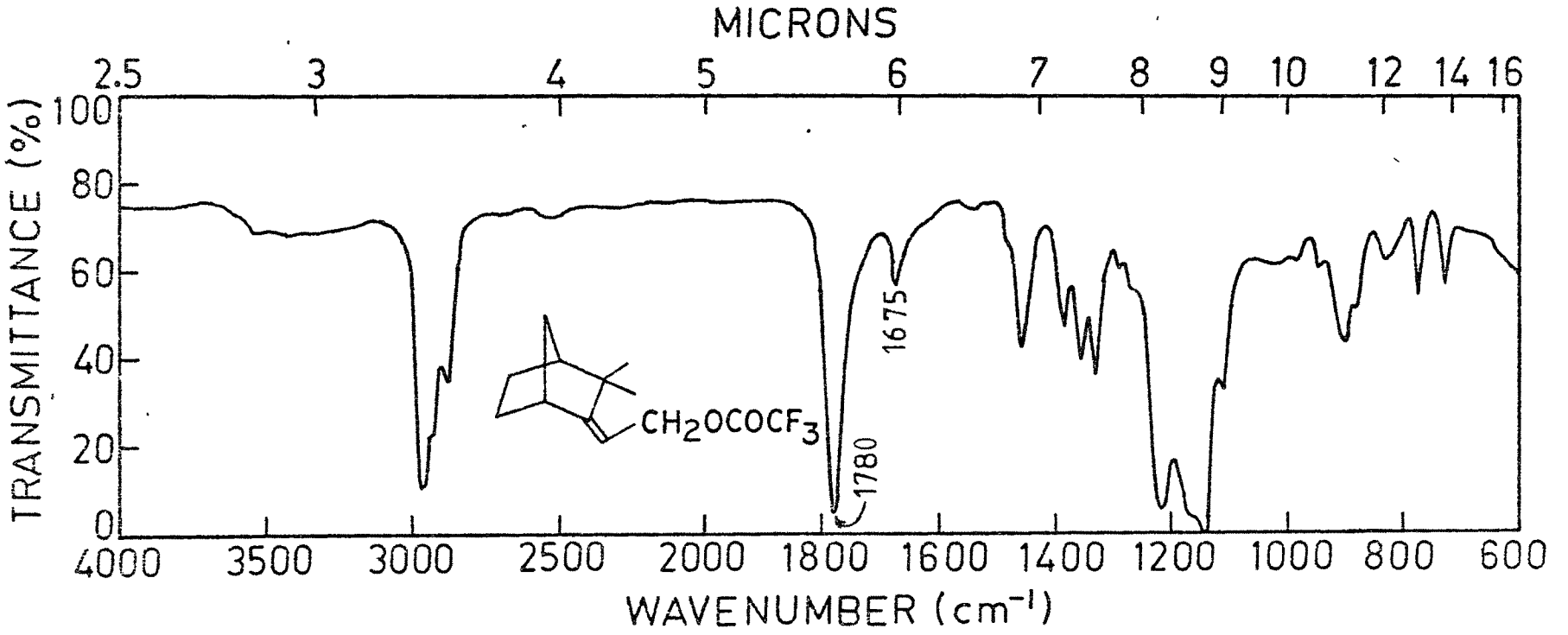


FIG. 30 -IR SPECTRUM OF ω-TRIFLUOROACETOXYMETHYL CAMPHENE (66)

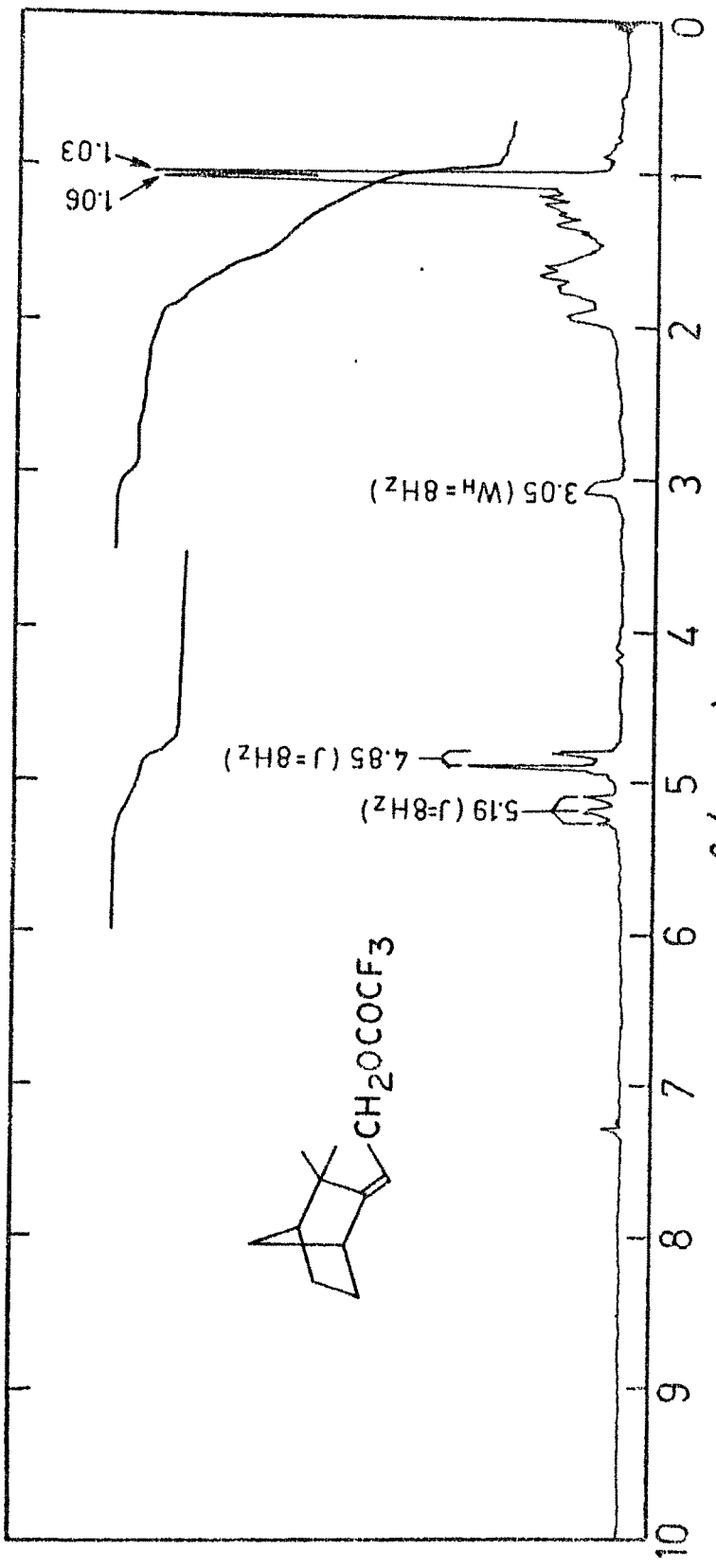


FIG. 31 -PMR SPECTRUM OF ω-TRIFLUOROACETOXYMETHYL CAMPHENE (66)

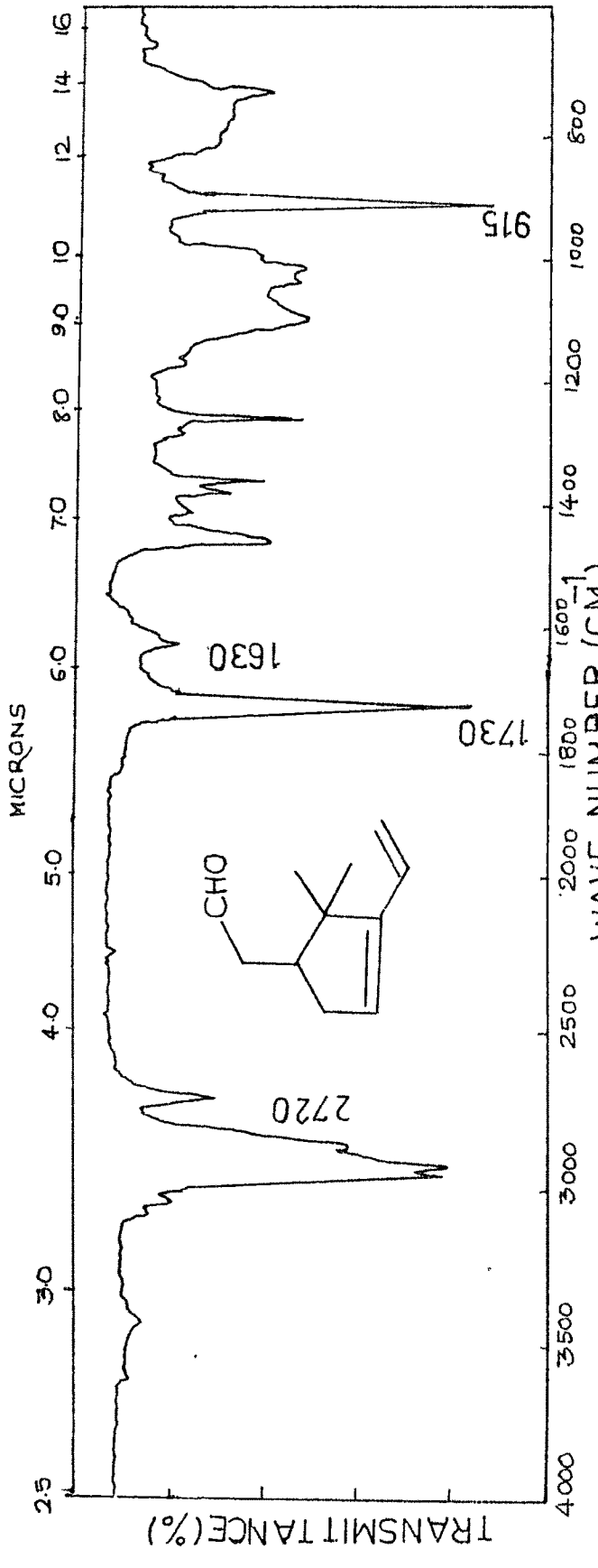


FIG.32:IR SPECTRUM OF THE DIENE ALDEHYDE 71

9.82
6.25
5.72
5.4(J=17Hz)
5.05(J=10Hz)
2.45
1.14
0.92
CHO
17Hz
10Hz
δ (ppm)

REFERENCES

1. J. Mathieu, A. Allais and J. Valls, Angew. Chem. 72 71 (1960).

2. G. Ohloff, J. Becker and K.H. Schulte-Elte, Helv. Chim. Acta. 50, 705 (1967); C.A. Grob and P.W. Schiess, Angew. Chem. Intern. Edit. 6, 1 (1967); W. Kraus and W. Rothenwohrer, Tetrahedron Letters 1007, 1013 (1968); P.G. Gassman and J.M. Hornback, J. Am. Chem. Soc. 91, 5817 (1969); C.A. Grob, Angew. Chem. Intern. Edit. 8, 535 (1969); J.A. Marshall and J.L. Belletire, Tetrahedron Letters 871 (1971); C.A. Grob, B. Schmitz, A. Sutter and A.H. Weber, ibid. 3551 (1975); A. Fischli, Q. Branca and J. Daly, Helv. Chim. Acta 59, 2443 (1976); H.O. House and V.L. Thomas, J. Org. Chem. 44, 2819 (1979); H.C. Brown, G.L. Buchanan and J. O'Donnell, J. Chem. Soc. Perkin I, 1740 (1979); J.F. Tietze, G. Kinast and H.C. Uzar, Angew. Chem. Intern. Edit. 18, 541 (1979); L.F. Tietz and U. Reichert, ibid. 19, 830 (1980).

3. P.S. Wharton and G.A. Hiegel, J. Org. Chem. 30, 3254 (1965).

4. A. Slawjanow, J. Russ. Phys. Chem. Soc. 39, 140 (1907); Chem. Abstr. 1, 2077 (1907).

5. C.A. Grob, J. Csapilla and G. Cseh, Helv. Chim. Acta 47, 1590 (1964).

6. M. Stiles and R.G. Miller, J. Am. Chem. Soc. 82, 3802 (1960).

7. R. Huisgen and W. Kolbeck, Tetrahedron Letters 783 (1965).

8. W. Eisele, C.A. Grob and E. Renk, Tetrahedron Letters 75 (1963).

9. J. Hoffmann, J. Am. Chem. Soc. 79, 504 (1957).

10. H.G. Enderle, Dissertation, Universital Basal (1967).

11. E.J. Corey, R.B. Mitra and H. Uda, J. Am. Chem. Soc. 86, 485 (1964).

12. R. Zurfluh, E.N. Wall, J.B. Siddall and J.A. Edwards, ibid. 90, 6224 (1968).

13. K. Sisido, S. Kurozumi and K. Utimoto, J. Org. Chem. 34, 2661 (1969).

14. M. Stoll and I. Flament, Helv. Chim. Acta. 52, 1996 (1969).

15. G. Kinast and L.F. Tietze, Chem. Ber. 109, 3626 (1976).

16. G. Stork, J.M. Tabak and J.F. Blount, J. Am. Chem. Soc. 94, 4735 (1972).

17. K.P. Dastur, ibid. 95, 6509 (1973).

18. J.S. Yadav, H.P.S. Chawla and Sukh Dev, Tetrahedron Letters 201 (1977).

19. J.A. McMillan, T.C. Paul, U.R. Nayak and Sukh Dev, ibid. 419 (1974).

20. V.S. Joshi, N.P. Damodaran and Sukh Dev, Tetrahedron 24, 5817 (1968).

21. J.S. Yadav, H.P.S. Chawla and Sukh Dev, Tetrahedron Letters 1749 (1977).

22. F. Dorn and D. Arigoni, Experientia 30, 851 (1974).

23. E.T. BcBee, A.B. Hass, R.M. Thomas, W.G. Toland, Jr. and A. Truchan, J. Am. Chem. Soc. 69, 944 (1947).

24. N. DiBello, L. Pellacani and P.A. Tardella, Synthesis 227 (1978).

25. S. Danishefsky, Accts. Chem. Res. 12, 66 (1979).

26. E.J. Corey and P.L. Fuchs, J. Am. Chem. Soc. 94, 4014 (1972); F. Klatte, U. Rosentretler and E. Winterfelt, Angew. Chem. Intern. Edit. 16, 878 (1977); B.M. Trost and W.J. Frajee, J. Am. Chem. Soc. 99, 6124 (1977).

27. T. Livinghouse and R.V. Stevens, ibid. 100, 6479 (1978).

28. See e.g.: E. Wenkert, Accts. Chem. Res. 13, 27 (1980); D.K.M. Due, M. Fetizon and E. Wenkert, Synth.Commun. 3, 277, 482 (1973).

29. J. Meinwald and J.K. Crandall, J. Am. Chem. Soc. 88, 1292 (1966); G.E. Koser and A.G. Relinyi, J. Org. Chem. 41, 1266 (1976).

30 (a) M. Gaitonde, P. Vatekencherry, and Sukh Dev, Tetrahedron Letters 2007 (1964); (b) M. Julia, D. Mansuy and P. Detraz, ibid. 2141 (1976); (c) N. Darby, N. Lamb and T. Money, Can. J. Chem. 57, 742 (1979).

31. J. Graefe, L.Q. Thah and M. Mehlstaedt, Z. Chem. 11, 304 (1971); Chem. Abstr. 75, 14099d (1971).

32. G. Mehta and S. Kapoor, J. Organomet. Chem. 80, 213 (1974).

33. S. Winstein, J. Sonnenberg and L. de Vries, J. Am. Chem. Soc. 81, 6523 (1959).

34. H.W. Wasserman and D.C. Clagett, Tetrahedron Letters 341 (1964).

35. U.R. Nayak, T.S. Santhanakrishnan and Sukh Dev, Tetrahedron 19, 2281 (1963).

36. G. DuPont, R. Dulou and G. Clement, Bull. Soc. Chim. Fr. 1002 (1951).

37. P.E. Peterson and G. Thomoson, J. Org. Chem. 33, 968 (1968).

38. G.L. Buchaman, Chem. Soc. Rev. 3, 41 (1974).

39. R.S. Bly, R.K. Bly, J.B. Hamilton, J.N.C. Hsu and P.K. Lillis, J. Am. Chem. Soc. 99, 216 (1977).

40. J.B. Stothers "Carbon-13 NMR Spectroscopy"; Academic Press, New York (1972).

41. A.F. Cockerill and D.M. Rackham, Tetrahedron Letters 5149 (1970).

42. L.M. Jackman and S. Sternhell, "Applications of N.M.R. Spectroscopy in Organic Chemistry", p. 84. Pergamon Press, Oxford (1972).

43. P. Turnbull, K. Syhora and J.H. Fried, J. Am. Chem. Soc. 88, 4764 (1966).

44. H.C. Brown and B.C. Subba Rao, ibid. 80, 5377 (1958).

45. R.P. Singh, H.N. Subbarao and Sukh Dev, Tetrahedron 35, 1789 (1979).

46. A.P. Meshcheryakov and I.E. Dolgii, Bull. Acad. Sci. USSR (Engl. Transl.) 1745 (1960); Chem. Abstr. 55, 13331 (1961).

47. K.B. Wilberg and B.J. Nist, J. Am. Chem. Soc. 83, 1226 (1961).

48. G.J. Karabastos, C. Zioudrou and S. Meyerson, ibid. 92, 5996 (1970).

49. J.B. Lambert and K. Kobayashi, J. Org. Chem. 41, 671 (1976).

50. A. Balsamo, C. Battistini, P. Crotti, B. Macchia and F. Macchia, ibid. 40, 3233 (1975).

51. R. Ya. Levina, V.N. Kostin and A. Tartakovskii, Zh. Obshch. Khim. 26, 2998 (1956); Chem. Abstr. 51, 8658h (1957).

52. Feigl "Spot tests in Organic Synthesis", 7th Ed., Elsevier, New York ((1971). p. 102

53. H.C. Brown, J.H. Kawakami and S. Ikegami, J. Am. Chem. Soc. 92, 6914 (1970).

54. J.M. Coxon, M.P. Hartshorn and A.J. Lewis, Tetrahedron 26, 3755 (1970).

55. R. Hermandez, R. Hernandez, Jr. and L.R. Axelrod, Anal. Chem. 33, 370 (1961).

56. R.S. Shank and H. Shechter, J. Org. Chem. 24, 1825 (1959).

57. F.B. LaForge, W.A. Gersdorff, N. Green and M.S. Schechter, ibid. 17, 381 (1952).

S E C T I O N II

SOME APPLICATIONS OF FRAGMENTATION OF HOMOALLYLIC ALCOHOLS

ABSTRACT

Fragmentation of homoallylic alcohols can be utilised to prepare cyclopentane-based synthons from bicyclo(2.2.1)-heptane precursors. cis-2-Oxabicyclo(3.3.0)oct-7-en-3-ol (13), a potential synthon for cyclopentane-based natural products, could be conveniently prepared by a one-step fragmentation of norborn-5-en-2-ol (6/7). 1-(2',2',3'-Trimethylcyclopent-3'-en-1'-yl)propan-2-one (18), a synthon for certain juvenile hormone analogues, was made by the fragmentation of 6-exo-methyl-6-endo-hydroxycamphene (24) followed by oxidation. Similarly, 6-exo-cyano-6-endo-hydroxycamphene (28) could also be fragmented to the acid nitrile 29, the reduction of which furnished the known α-campholenic alcohol (30).

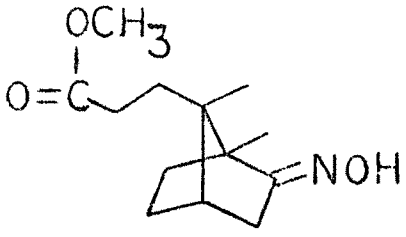
SOME APPLICATIONS OF FRAGMENTATION OF HOMOALLYLIC ALCOHOLS

INTRODUCTION

Bicyclo(2.2.1)heptane system has often served as a suitable precursor for the synthesis of chirally pure cyclopentane derivatives. For example, Stevens and co-workers[1] have taken advantage of the natural chirality of (-)-camphor and its topology to synthesise chirally pure steroids. Thus, camphor was converted to the oximino ester 1 by a six-step sequence. Exposure of 1 to p-toluenesulphonyl chloride in pyridine induces Beckmann fragmentation to give the cyclopentane derivative 2 (Eq. 1). By virtue of its functionalities, 2 could be utilised for the total synthesis of chirally pure steroids and the tedious process of resolution after derivatisation could be circumvented.

Similarly, Corey and co-workers[2] converted, by selective Baeyer-Villiger oxidation, bicyclic ketone 3 to bicyclic lactone 4, which on hydrolysis and iodolactonisation gave lactone 5, which has proved immensely useful in the synthesis of prostaglandins (Eq. 2).

In Section I, a description of the fragmentation of homoallylic alcohols —— a novel reaction reported by Sukh Dev



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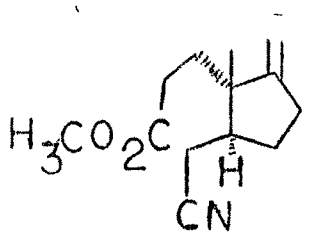

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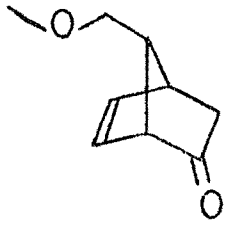
Eq. 1



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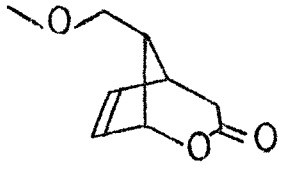

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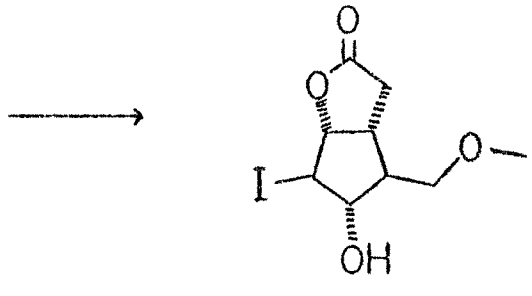

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Eq. 2

and co-workers was presented. Also described was the application of this reaction to synthesise naturally occuring secolongifolene diol.

This cleavage reaction appears to be well-suited for converting functionalised bicyclo(2.2.1)heptanes to substituted cyclopentanes, and is therefore potentially useful for making synthons for cyclopentane-containing natural products. Work undertaken in this direction is presented in this section.

PRESENT WORK

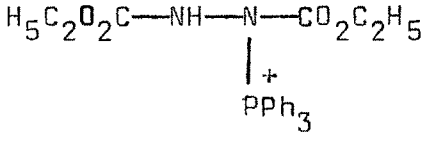
A. Synthesis of cis-2-oxabicyclo(3.3.0)oct-7-en-3-ol(13):

This lactol (13) is a potential synthon for making cyclopentane based natural products. It was envisioned that norborn-5-en-2-ol (6/7) or the derived epoxide (8/9) (Chart 1), when subjected to electrophile-induced fragmentation would lead to cyclopentane derivatives of the type 12, which can be easily transformed to the lactol 13 or cis-2-oxabicyclo(3.3.0)oct--7-en-3-one (14) by standard reactions.

A mixture of 2-endo-and 2-exo-hydroxy-5-norbornene (6/7) was obtained in 90% yield by saponification of a mixture of the corresponding acetates with methanolic KOH. The mixture

of epimeric acetates was obtained by a modification of the known[3] procedure. Instead of cyclopentadiene monomer, made just before use by cracking[4] of the commercially available dimer, the latter itself was directly used for Diels-Alder reaction with vinyl acetate —— thereby circumventing the tedious cracking step and realising a 10% improvement in the overall yield.

Attempts to obtain the alcohol mixture (6/7) rich in exo-OH by epimerising the above mixture (endo: exo = 3 : 1) by the method of Mitsunobu and co-workers[5] using molar as well as double the molar[6] quantities of triphenylphosphine, acetic or formic acid and diethyl azodicarboxylate[7] in anhydrous THF were unsuccessful. This may be due to the inability of the norbornenol molecule to attack the bulky phosphonium ion (17) because of steric hindrance. However, the above mixture of alcohols, when reacted with catalytic



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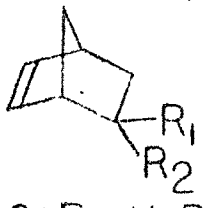
quantities of fluorenone[8] and sodium in refluxing toluene, yielded 6/7 in the ratio of 41 : 55 (GLC, 10% carbowax on

chromosorb W, 6', 170°, 60 ml/min; RRT 1.0, 1.2) in 36% yield.[9] This material was used to study the behaviour of the exo-alcohol 7.

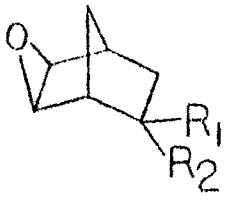
Epoxidation of the alcohols 6/7 with slight excess of peracetic acid at 10-15° for 1.5 h (monitored by TLC) gave the epoxyalcohols (8/9) in the corresponding ratio. Longer reaction times led to the formation of a ketonic impurity (IR: CO 1750 cm^{-1}), which was identified as 5,6-exo-epoxynorborn-2-one (10) by comparison with an authentic[10] sample. Oxidation of secondary alcohols to ketones with peracids is on record.[11]

Fragmentation reactions of 8/9: Treatment of the epoxides 8/9 with 0.5 to 2% $HClO_4$ in 90% dioxane aq failed to induce the expected cleavage and starting material was recovered. Reaction with 10% H_2SO_4 aq gave a very low yield of a complex mixture.

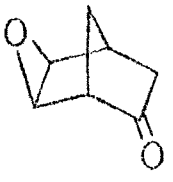
Treatment of 8/9 (3:1) with potassium t-butoxide in t-butanol at room temperature (≈30°) for 4 days gave 5-exo-hydroxynorbornane-2,6-endo-oxide (11) in 72% yield.[12] Formation of this oxetane was the basis for fixing exo-configuration for the epoxide.[12] When the same reaction was conducted with the material rich in exo-OH (8:9 = 41:55), a lot of black polymeric product was formed and the oxetane 11



6: R_1=H, R_2=OH
7: R_1=OH, R_2=H



8: R_1=H, R_2=OH
9: R_1=OH, R_2=H



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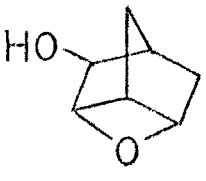

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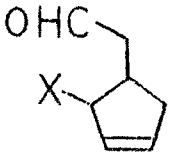

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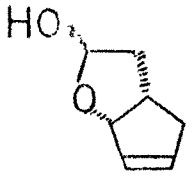

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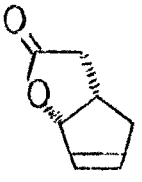

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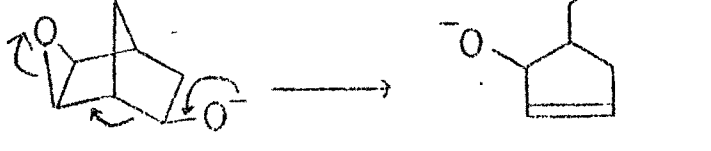
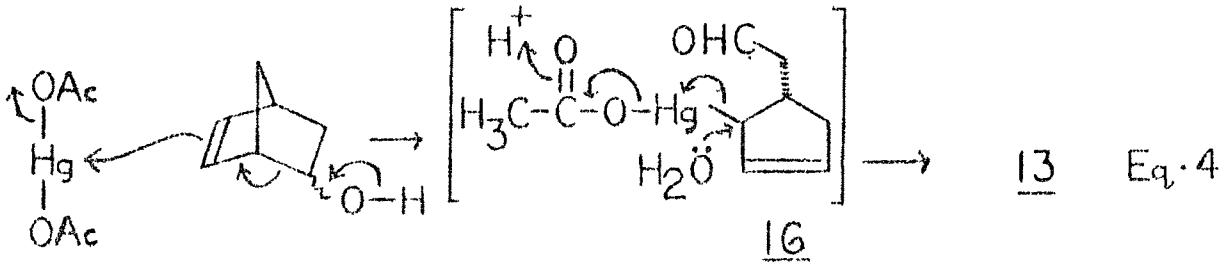


9 → 15 Eq·3



16 → 13 Eq·4

CHART I

was obtained in 40% yield only. It is probable that, while 8 rearranges to the oxetane 11, 9 fragments to the aldehyde 15 (Eq. 3), which under the conditions of reaction polymerises.

Fragmentation reactions of 6/7: Reaction of 6/7 with equimolar quantity of Br_2 in CCl_4 at -5^o in the presence of Na_2CO_3 as buffer afforded a complex mixture of bromides, which readily turned to a tar even at low temperatures.

However, treatment with $Hg(OAc)_2$ in THF/H_2O (1:1) at 20^o for 2 h gave a product from which the lactol 13 could be isolated in 45% yield (IR: OH 3400, 1070 cm^{-1}; C=C 1635, 895 cm^{-1}. PMR: CHOC, 1H, m, 5.15-5.38 ppm; CHOH, 1H, m, 5.43-5.63 ppm; CH=CH, 2H, m, 5.72-5.98 ppm). The structure of the lactol was further secured by oxidation with pyridinium chlorochromate[13] to the known lactone 14, prepared according to the method of Meinwald and co-workers.[10] A possible mechanism of formation of the above lactol is shown in Eq. 4. The allylic mercuric acetate (16) undergoes facile solvolytic demercuration[14] under the experimental conditions. Identical results were obtained with mercuric trifluoroacetate[15] and also with a mixture (41:55) of 6/7 in which 7 predominates.

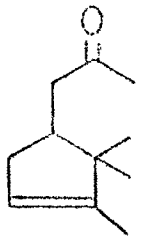
B. Synthesis of 1-(2',2',3'-trimethylcyclopent-3'-en-1'-yl)-propan-2-one (18): Cyclopentane derivative 18 (Chart 2) is a potential synthon for the preparation of juvenile hormone

analogues 19 and 20.[16] It was felt that fragmentation of homoallylic alcohols could be exploited for making this synthon. For this purpose, 6-exo-methyl-6-endo-hydroxy-camphene (24) was prepared and its fragmentation with electrophiles was studied.

Synthesis of 6-exo-methyl-6-endo-hydroxycamphene (24): Oxidation of 6-exo-hydroxycamphene (22) (see Section I) with pyridinium chromate-on-silica gel[17] in CH_2Cl_2 gave 6-ketocamphene (23) in 72% yield. Grignard reaction of 23 with a slight excess of MeMgI gave 24 in 81% yield (IR: OH 3530, 3480, 1060 cm^{-1}; $C=CH_2$ 1640, 940 cm^{-1}. PMR: C(OH) CH_3, 3H, s, 1.34 ppm; $CH_2=C-CH$, 1H, bs, 2.45 ppm, W_h = 4Hz; $C=CH_2$, 2H, s, 4.98 ppm). The stereochemistry of 24 at C-6 follows from the known[18] propensity of nucleophiles towards exo-attack in norbornane systems.

Fragmentation of the tertiary alcohol 24: Fragmentation of 24 with molar quantity of $Hg(OAc)_2$ in THF/H_2O (1:1) gave the anticipated allylic mercurial acetate (25) in quantitative yield (m.p. 104-6°; IR: CO 1705 cm^{-1}; HgOAc 1600 cm^{-1}. PMR: $HgOCOCH_3$, 3H, s, 2.02 ppm; $COCH_3$, 3H, s, 2.15 ppm; $C=CH$, 1H, bs, 5.4 ppm). This compound is unstable and demercuration with $NaBH_4$ gave a mixture containing compound 21 as the major component (PMR).

Reaction of the tertiary alcohol 24 with molar quantity of Br_2 in CCl_4, in presence of Na_2CO_3, gave the labile allylic



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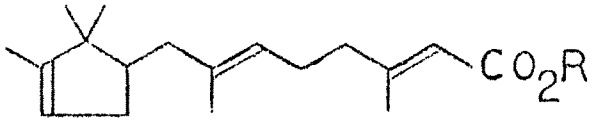
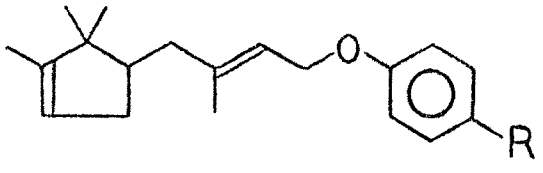
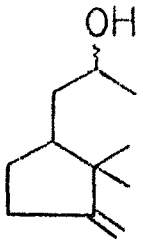


19: R = i-Pr, Bz



20: R = CH_3, Cl, Br, t-Bu



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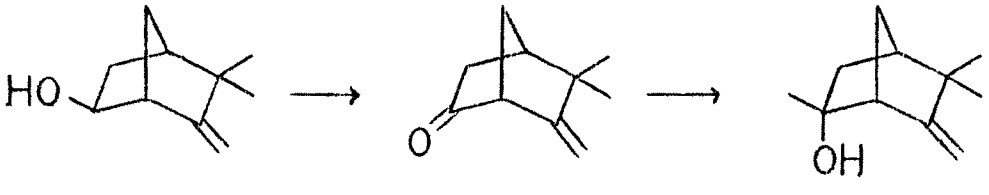
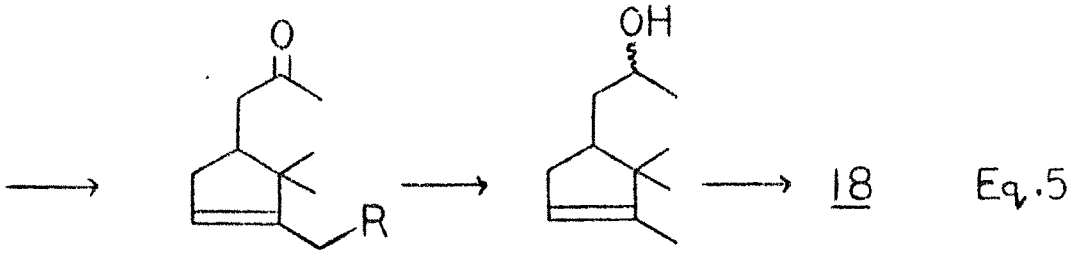


22 23 24



25: R = HgOAc
26: R = Br

27

18 Eq. 5

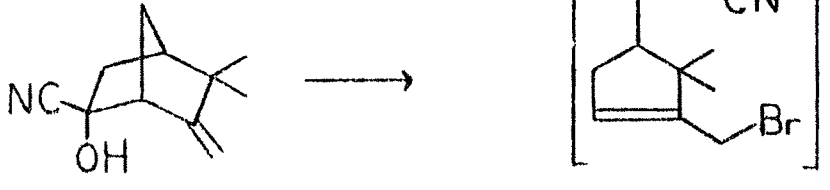
CHART 2

bromide 26, which was reduced with LAH to 1-(2',2',3'-trimethyl-cyclopent-3'-en-1'-yl)oroban-2-ols (27) (Eq. 5) in 90% yield (IR: OH 3360 cm^{-1}; C=C 1645 cm^{-1}. PMR: C-Me's, 3H, singlets at 0.78, 1.0 ppm; C(OH)CH_3, 3H, d, 1.21, 1.25 ppm, J = 6 Hz; C=C-CH_3, 3H, s, 1.62, 1.63 ppm; CHOH, 1H, m, 3.7-4.06 ppm; CH=C, 1H, bs, 5.28 ppm, W_h=6Hz. Mass: m/e 168 (M^+)). Oxidation of the epimeric alcohols 27 with Py/CrO_3 gave the targeted compound 18 in 85% yield (IR: CO 1710 cm^{-1}. PMR: C-Me's, 3H, singlets at 0.78, 1.0 ppm; C=C-CH_3, 3H, s, 1.62 ppm; $COCH_3$, 3H, s, 2.1 ppm: CH=C, 1H, bs, 5.24 ppm, W_h = 6 Hz. Mass: m/e 166 (M^+)).

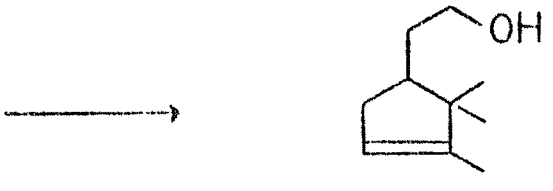
Fragmentation of the homoallylic alcohol 24 with ICl followed by LAH reduction gave identical result.

C. Fragmentation of 6-exo-cyano-6-endo-hydroxycamphene (28):

Reaction of 6-ketocamphene (23) with excess acetone cyanohydrin[19] gave the cyanohydrin 28 in 80% yield (IR: OH 3580, 3420, 1110 cm^{-1}; CN 2240 cm^{-1}; C=CH_2 1660, 900 cm^{-1}. PMR: C-Me's, 6H, s, 1.12 ppm; CH_2=C-CH, 1H, bs, 2.85 ppm, W_h = 4 Hz; C=CH_2, 1H, singlets at 4.98, 5.21 ppm. Mass: m/e 177 (M^+)).



28 29



30

Eq. G

Fragmentation of the cyanohydrin 28 with Br_2 in CCl_4 gave the unstable acid nitrile 29, which could be reduced *in situ* to the known[20,21] α-campholenic alcohol (30) (Eq. 6) in 90% yield (IR: OH 3350, 1060 cm^{-1}; C=C 1650, 805 cm^{-1}. PMR: C-Me's, 3H, singlets at 0.77, 0.97 ppm; C=C-CH_3, 3H, s, 1.6 ppm; CH_2OH, 2H, sextet, 3.69 ppm, J=6Hz; CH=C, 1H, bs, 5.25 ppm, W_h = 5 Hz).

EXPERIMENTAL

For general remarks, see Section I Experimental.

2-Acetoxynorborn-5-ene:

Dicyclopentadiene (30g, 0.23 mole) was mixed with freshly distilled vinyl acetate (45 g, 0.52 mole) in a glass-lined autoclave. The latter was sealed and heated to 170-80° for 24 h. The resulting light yellow liquid was fractionated to give 2-acetoxynorborn-5-ene as a colorless liquid (26.4 g, 38%); b.p. 85-87°/20 mm(lit.[3] b.p. 77-80°/13 mm); n_D^{25} 1.4604. IR (liq. film): OAc 1745, 1250 cm^{-1}. PMR ($CDCl_3$): $OCOCH_3$, s, 1.86 ppm for endo and 1.95 ppm for exo-isomer; C_1-H, bs, 2.80 ppm for endo- and 3.08 for exo-isomer; CHOAc, m, 4.55 ppm for exo- and 5.15 ppm for endo-isomer; C_5H, 1H, m, 5.90 ppm; C_6-H, 1H, m. 6.20 ppm.

Norborn-5-en-2-ol (6/7)

Hydrolysis of the above acetate with methanolic KOH gave 6/7 in 90% yield; m.p. 104-6° (lit.[3] m.p. 105-7°). IR (CCl_4): OH 3620, 3590, 3380, 1065 cm^{-1}; C=C 1630, 835 cm^{-1}. PMR(CCl_4): CHOH, bt, 4.35 ppm for endo- and bm, 3.75 for exo-alcohol; C_5-H, 1H, m, 5.97 ppm; C_6-H, 1H, m, 6.32 ppm.

5,6-exo-Epoxynorbornan-2-ol (8/9).

To a cooled (10°) solution of norborn-5-en-2-ol (2.02 g, 18.4 mmol) in $CHCl_3$ (20 ml) was added dropwise a solution of perbenzoic acid (3.17 g, 23 mmol) in $CHCl_3$ and stirring was continued at 10° for 1.5 h, when the olefin was totally consumed (TLC). The reaction mixture was quenched with 5% Na_2SO_3 aq (15 ml) and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (15 ml x 2). The combined $CHCl_3$ extracts were washed with 5% $NaHCO_3$ aq (20 ml x 2), water (15 ml) and brine (15 ml) and dried (Na_2SO_4). Removal of solvent furnished the epoxide as a white solid, crystallised from ether/light petroleum (2.078 g, 90%); m.p. 162-7° (lit.[12] m.p. 160-2°).

IR (CCl_4) (Fig. 1): OH 3675, 3420, 1050 cm^{-1}; epoxide 850 cm^{-1}.

PMR($CDCl_3$)(Fig. 2): $C_7\underline{H}_2$, 1H, septet, 2.0 ppm; O<u>H</u>, 1H, s, 2.4 ppm, exchangeable with D_2O; $C_4\underline{H}$, 1H, s, 2.47 ppm; C_1-<u>H</u>, 1H, ill-resolved q, 2.62 ppm; C_5-<u>H</u>, d, 3.0 ppm, J = 4 Hz for <u>exo</u>- and d, 3.3 ppm, J = 4 Hz for <u>endo</u>-alcohol; C_6-<u>H</u>, d, 3.09 ppm, J = 4 Hz for <u>exo</u>- and d, 3.47 ppm, J = 4 Hz for <u>exo</u>-alcohol; C_2-<u>H</u>, ill-resolved quartet, 3.87 ppm, J_1=8Hz, J_2 = 3Hz for <u>exo</u>- and sextet, 4.38 ppm, J_1= 8Hz, J_2=J_3 = 3Hz for <u>endo</u>-alcohol.

Mass: m/e 126 (M^+, 1%), 125 (2%), 108(2%), 83(100%), 82 (87%), 68(18%), 55(29%) and 42 (16%).

5-exo-Hydroxynorbornane-2,6-endo-oxide (11)

Treatment of the above epoxide with potassium t-butoxide according to the known method[12] gave the oxetane 11 in 72% yield; m.p. 175-6° (lit.[12] m.p. 173-6°).

IR ($CHCl_3$) (Fig. 3): OH 3600, 3400, 1070 cm^{-1}.

PMR (CCl_4) (Fig. 4): C_4-H, 1H, bs, 2.65 ppm; C_1-H, 1H, bs, 3.65 ppm; C_5-H, 1H, s, 3.90 ppm; C_2-H, 1H, m, 4.2 ppm; C_6-H, 1H, ill-resolved quartet, 4.55 ppm, J_1= 7Hz, J_2 = 4Hz.

Mass: m/e 126 (M^+, 6%), 108(3%), 97 (9%), 82 (100%), 79 (53%), 70 (33%), 67 (76%), 60(31%), 57(33%) and 41 (67%).

5,6-exo-Epoxynorbornan-2-one (10)

Oxidation of the epoxy alcohol 8/9 with Py/CrO_3 gave the epoxyketone 10, m.p. 134-6° (lit.[10] m.p. 139°).

IR (CCl_4) (Fig. 5): CO 1755 cm^{-1}; epoxide 850 cm^{-1}.

PMR (CCl_4)(Fig. 6): $COCH_2$, 2H, s, 2.62 ppm; C_5-H, 1H, d, 3.14 ppm, J = 4 Hz; C_6-H, 1H, d, 3.3 ppm, J = 4Hz.

Fragmentation of norborn-5-en-2-ol (6/7) with $Hg(OAc)_2$

A solution of norborn-5-en-2-ol (2 g, 18.2 mmol) in THF/H_2O (1:1, 50 ml) was cooled to 20° and $Hg(OAc)_2$ (5.8 g, 18.2 mmol) was added in portions during a period of 20 min,

while stirring the solution. Stirring was continued at 20° for another 2 h. The reaction mixture was diluted with cold water (50 ml) and extracted with ether (30 ml x 3). The combined ether extracts were washed with 5% $NaHCO_3$ aq (15 ml x 2) and brine (15 ml) and dried (Na_2SO_4). Removal of solvent gave a thick viscous liquid (1.99 g), which was chromatographed on alumina (II, 60 g, 19 x 2.5 cm).

Fr. 1	$CHCl_3$	15 ml x 5	60 mg, mixture.
	0.5% MeOH in $CHCl_3$	15 ml x 5	
Fr. 2	1% MeOH in $CHCl_3$	15 ml x 15	1.05 g
Fr. 3	5% MeOH in $CHCl_3$	15 ml x 5	Mixture.

Fr. 2 was distilled to give the lactol 13 (1.03 g, 45%), b.p. 120-5°/5 mm; n_D^{25} 1.4327.

IR (liq. film) (Fig. 7): OH 3400, 1070 cm^{-1}; C=C 1635, 895 cm^{-1}.

PMR ($CDCl_3$) (Fig. 8): C<u>H</u>OC, 1H, m, 5.15-5.38 ppm; C<u>H</u>OH, 1H, m, 5.43-5.63 ppm; C<u>H</u>=C<u>H</u>, 2H, m, 5.72-5.98 ppm.

Mass: m/e 126 (M^+, 1%), 125 (3%), 108 (13%), 80(100%), 79(91%), 70(13%), 66(28%), 57 (12%), 55(16%) and 41(25%).

~~Found:~~

Analysis: Found: C, 66.73; H, 8.005.

$C_7H_{10}O_2$ requires: C, 66.67; H, 7.94%.

cis-2-Oxabicyclo(3.3.0)oct-7-en-3-one (14)

(a) A solution of the lactol 11 (75 mg, 0.6 mmol) in anhydrous CH_2Cl_2 (4 ml) was added in one lot to a suspension of pyridinium chlorochromate (257 mg, 1.2 mmol) in CH_2Cl_2 (4 ml) and stirred at room temperature ($\sim 28^{\circ}$) for 1.5 h. Dry ether (20 ml) was added and the supernatent liquid was decanted from the black gum. The latter was washed thrice with dry ether (30 ml). The combined ether solution was passed through a small bed of deactivated alumina. Removal of solvent followed by distillation gave the lactone 14 (47 mg, 64%), b.p. 120-5°(bath)/5 mm (lit.[22] 55°/0.01 Torr); n_D^{25} 1.4100.

IR (CCl_4) (Fig. 9): CO 1770 cm^{-1}.

PMR (CCl_4) (Fig. 10): C<u>H</u>-O-, 1H, dd, 5.45 ppm, J_1= 8Hz, J_2= 1.5 Hz; C=C<u>H</u>-CH_2, 1H, m, 5.85 ppm; C=C<u>H</u>-CH-O , 1H, m, 6.05 ppm.

(b) Rearrangement of 5,6-<u>exo</u>-epoxynorbornan-2-one (10) with con.HCl by the known[10] method gave the same lactone (14).

6-<u>exo</u>-Methyl-6-<u>endo</u>-hydroxycamphene (24)

A solution of 6-ketocamphene (23) (0.45 g, 3 mmol) in ether (10 ml) was added dropwise to a chilled solution of MeMgI (6 mmol) in ether. The reaction mixture was stirred at room temperature ($\sim 30^{\circ}$) for 4 h and refluxed for 1 h. Then

it was decomposed with NH_4Cl aq and the ether layer was separated. The aqueous layer was once extracted with ether (20 ml). The combined ether extracts were washed with brine (15 ml) and dried (Na_2SO_4). Removal of solvent followed by distillation gave 24 as a colorless oil (0.398 g, 81%), b.p. 120°(bath)/5 mm.

IR (liq. film) (Fig. 11): OH 3530, 3480, 1060 cm^{-1}; $C=CH_2$ 1640, 940 cm^{-1}.

PMR ($CDCl_3$)(Fig. 12): C-Me's, 6H, s, 1.11 ppm; C(OH) CH_3, 3H, s, 1.34 ppm; OH, 1H, s, 2.2 ppm, exchangeable with D_2O; $CH_2=C-CH$, 1H, bs, 2.45 ppm, W_h= 4Hz; $C=CH_2$, 2H, s, 4.98 ppm.

Mass: m/e 166(M^+, 3%), 151 (4%), 133(4%), 123(7%), 108(100%), 107(20%), 93(52%), 91(14%), 81(9%) and 44(35%).

Analysis: Found : C, 79.21; H, 10.97

$C_{11}H_{18}O$ requires : C, 79.52; H, 10.84%.

Fragmentation of 6-exo-methyl-6-endo-hydroxy-camphene (24)

(a) With $Hg(OAc)_2$: $Hg(OAc)_2$ (0.203g, 0.64 mmol) was added to a solution of 24 (0.106 g, 0.64 mmol) in THF/H_2O (1:1, 5 ml) at 20° and stirred at the same temperature for 5 h. The reaction mixture was diluted with water (10 ml) and extracted with ether (10 ml x 3). The combined ether extracts were dried (Na_2SO_4). Removal of solvent gave a gum, which was crystallised from light petroleum to give the organomercurial

acetate 25 as a white solid (0.25 g, 98%), m.p. 104-6°.

IR ($CHCl_3$): CO 1705 cm^{-1}; HgOAc 1600 cm^{-1}.

PMR ($CDCl_3$): C-Me's, 3H, singlets at 0.92, 1.12 ppm; HgOAc, 3H, s, 2.02 ppm; $COCH_3$, 3H, s, 2.15 ppm; C=CH, 1H, bs, 5.4 ppm.

(b) With bromine: To a stirred mixture of a solution of the alcohol 24 (0.1 g, 0.6 mmol) in CCl_4 (2 ml) and Na_2CO_3 (0.1 g) at -5° was added dropwise a solution of Br_2 (0.096g, 0.6 mmol) in CCl_4 (2 ml). The bromine was instantaneously decolorised. The reaction mixture was filtered and the solvent was removed at reduced pressure. The residue was dissolved in dry ether, LAH (30 mg) was added and stirred at room temperature (~30°) for 5 h. The reaction mixture was decomposed with NH_4Cl aq and extracted with ether (10 ml x 3). The combined ether extracts were washed with brine (10 ml) and dried (Na_2SO_4). Removal of solvent followed by distillation gave 1-(2',2',3'-trimethyl-cyclopent-3'-en-1'-yl)propan-2-ol (27) as a colorless oil (90 mg, 90%), b.p. 90°(bath)/5 mm.

IR (liq. film) (Fig. 13): OH 3360 cm^{-1}; C=C 1645 cm^{-1}.

PMR ($CDCl_3$) (Fig. 14): C-Me's, 3H, singlets at 0.78, 1.0 ppm; C(OH)CH_3, 3H, d, 1.21, 1.25 ppm; J = 6Hz; C=C-CH_3, 3H, s, 1.62, 1.63 ppm; CHOH, 1H, m, 3.7-4.06 ppm; CH=C, 1H, bs, 5.28 ppm; W_h = 6 Hz.

Mass: m/e 168(M^+, 14%), 135 (28%), 120 (9%), 107(100%), 93(57%) and 91(51%).

Analysis: Found : C, 78.90; H, 12.11

$C_{11}H_{20}O$ requires : C, 78.57; H, 11.91%.

(c) With ICl: Fragmentation with ICl followed by LAH reduction gave identical result.

1-(2',2',3'-Trimethylcyclopent-3'-en-1'-yl)propan-2-one (18)

To the comolex prepared from CrO_3 (0.182 g, 1.8 mmol) and pyridine (1.8 ml) was added a solution of the alcohol 27 (0.078 g, 0.5 mmol) in pyridine (0.45 ml) and stirred at room temperature (~30°) for 20 h. The reaction mixture was poured in cold water (10 ml) and extracted with ether (10 ml x 3). The combined ether extracts were successively washed with water (5 ml), 5% HCl aq (5 ml x 2), water (5 ml), 5% $NaHCO_3$ aq (5 ml), water (5 ml) and brine (5 ml) and dried (Na_2SO_4). Removal of solvent followed by distillation gave the ketone 18 as a colorless liquid (0.066 g, 85%), b.p. 90°(bath)/3.5 mm (lit.[16] b.p. 82-5°/6 mm). n_D^{25} 1.4612.

IR (liq. film) (Fig. 15): CO 1710 cm^{-1}.

PMR (CCl_4) (Fig. 16): C-Me's, 3H, singlets at 0.78, 1.0 ppm; C=C-CH_3, 3H, s, 1.62 ppm; $COCH_3$, 3H, s, 2.1 ppm; CH=C, 1H, bs, 5.24 ppm, W_h = 6 Hz.

Mass: m/e 166(M^+, 6%), 123(9%), 108(100%), 93(66%), 80(30%) and 43(74%).

Analysis: Found : C, 79.38; H, 10.69

$C_{11}H_{18}O$ requires: C, 79.52; H, 10.84%.

6-exo-Cyano-6-endo-hydroxycamphene (28)

A mixture of 6-ketocamphene (23) (0.396 g, 2.7 mmol), acetone cyanohydrin (1.125 g, 13.2 mmol) and a drop of 10% K_2CO_3 aq was stirred at room temperature (~30°) for 2 h. The reaction mixture was poured in water (50 ml) and extracted with light petroleum (10 ml x 3). The combined petroleum extracts were washed with brine (10 ml) and dried (Na_2SO_4). Removal of solvent gave a colorless oil, which was adsorbed on a small bed of silica gel (4 g). Eluting with $CHCl_3$ (10 ml) removed the impurity. Elution with 10% ethyl acetate in $CHCl_3$ gave the cyanohydrin 28 as a colorless liquid (0.371 g, 80%), b.p. 150-5°(bath)/ 2.5 mm.

IR (CCl_4) (Fig. 17): OH 3580, 3420, 1110 cm^{-1}; CN 2240 cm^{-1}; $C=CH_2$ 1660, 900 cm^{-1}.

PMR ($CDCl_3$) (Fig. 18): C-Me's, 6H, s, 1.12 ppm; $CH_2=C-CH$, 1H, bs, 2.85 ppm, W_h= 4Hz; OH, 1H, bs, 3.1 ppm, exchangeable with D_2O; $C=CH_2$, 1H, singlets at 4.98, 5.21 ppm.

Mass: m/e 177 (M^+, 8%), 162(8%), 121 (21%), 118 (100%), 93(91%), 79(12%) and 77(17%).

Analysis: Found : C, 74.81; H, 8.19; N, 7.62

$C_{11}H_{15}NO$ requires: C, 74.57; H, 8.474; N, 7.909%.

Fragmentation of cyanohydrin 28

A solution of Br_2 (0.27 g, 1.7 mmol) in CCl_4 (2.25 ml) was added dropwise to a cooled (-5°) and stirred mixture of a solution of the cyanohydrin 28 (0.3 g, 1.7 mmol) in CCl_4 (5 ml) and Na_2CO_3 (0.1 g). Usual work up followed by LAH reduction gave α-camoholenic alcohol (30) (0.232 g, 90%), b.p. 90-95°(bath)/3.5 mm (lit.[20] b.p. 90°/3 mm). n_D^{25} 1.4690.

IR (liq. film) (Fig. 19): OH 3350, 1060 cm^{-1}; C=C 1650, 805 cm^{-1}.

PMR ($CDCl_3$) (Fig. 20): C-Me's, 3H, singlets at 0.77, 0.97 ppm; C=C-CH_3, 3H, s, 1.6 ppm; OH, 1H, s, 2.0 ppm, exchangeable with D_2O; CH_2OH, 2H, sextet, 3.69 ppm, J = 6 Hz; CH=C, 1H, bs, 5.25 ppm, W_h = 5 Hz.

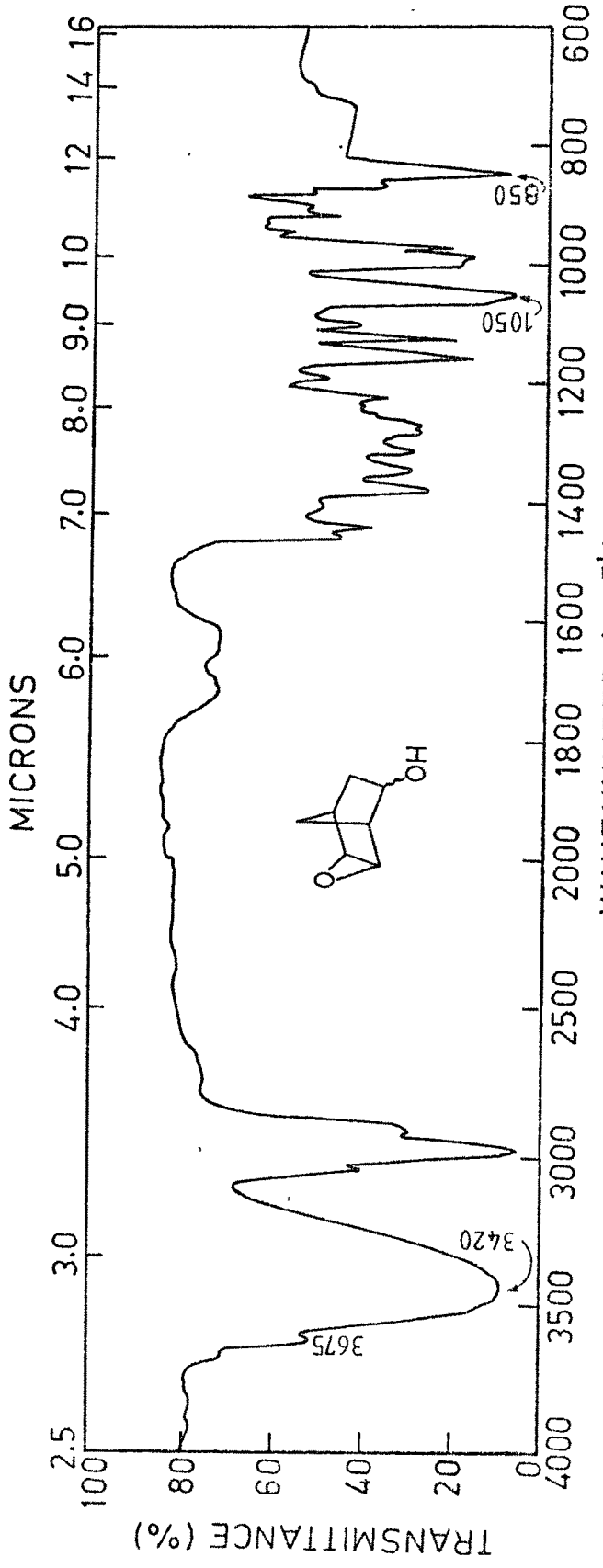


FIG. 1 -IR SPECTRUM OF 5,6-EXO-EPOXY-2-NORBORNANOL (8/9)

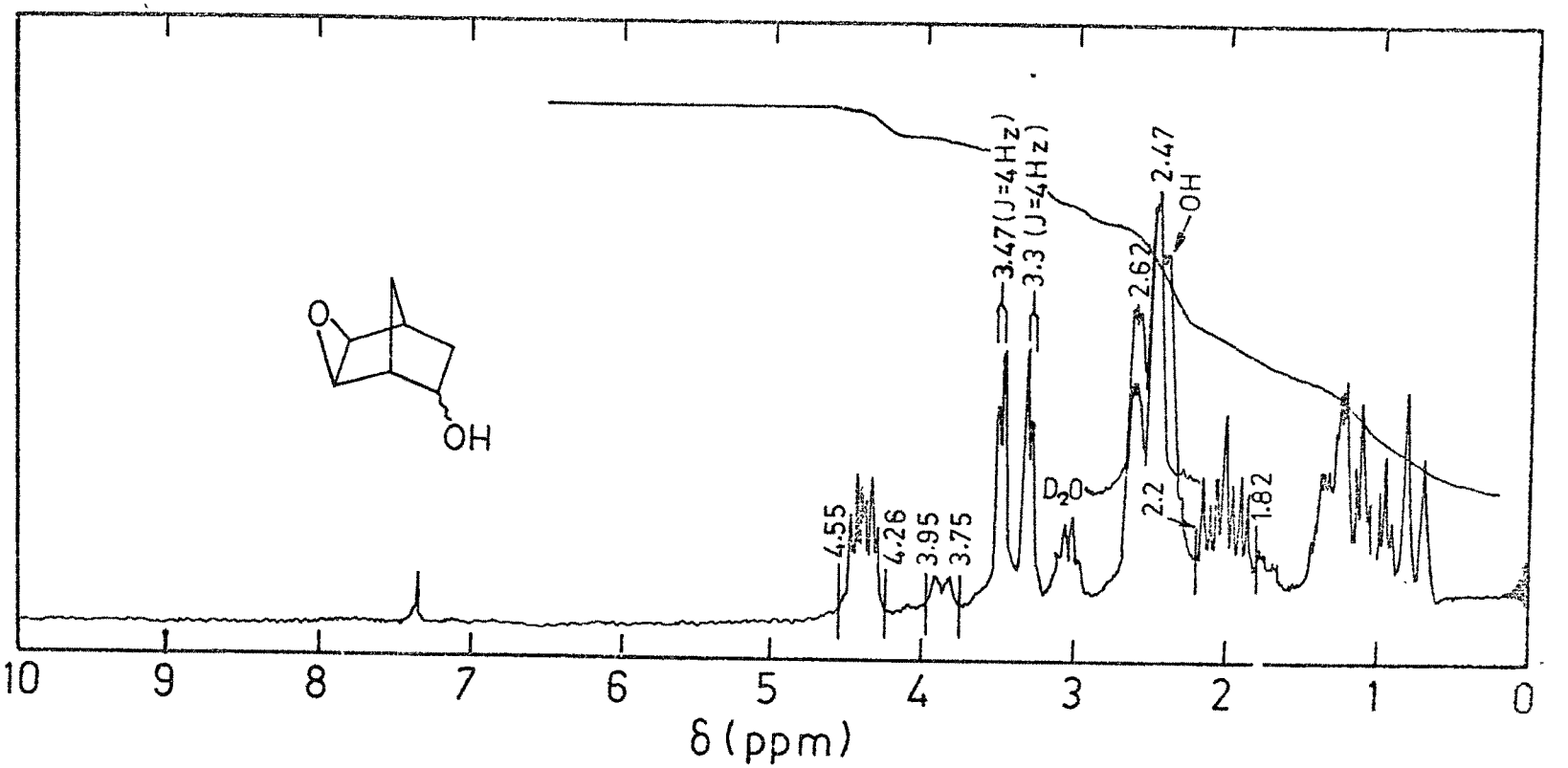


FIG. 2 - PMR SPECTRUM OF 5,6-EXO-EPOXY-2-NORBORNANOL (8/9)

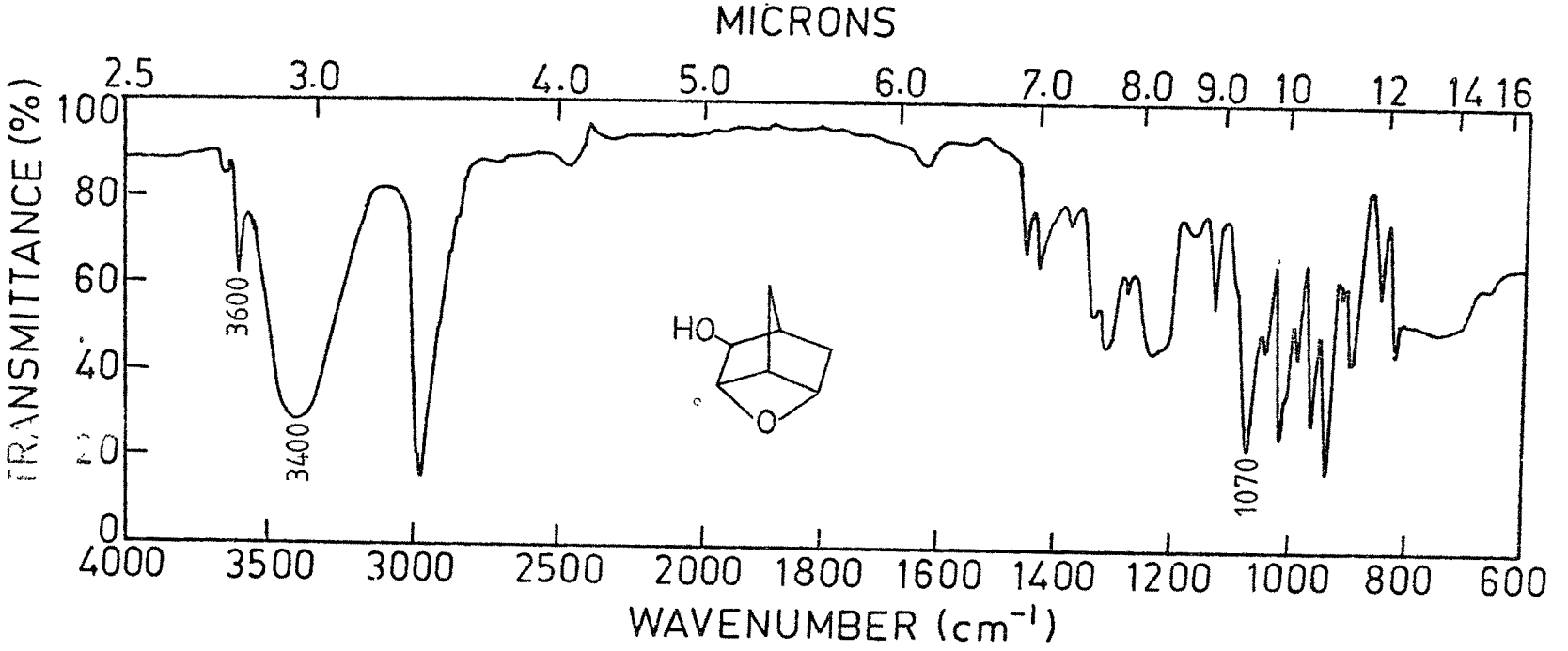


FIG. 3 -IR SPECTRUM OF 2,6-ENDO-EPOXY-5-EXO-NORBORNANOL (11)

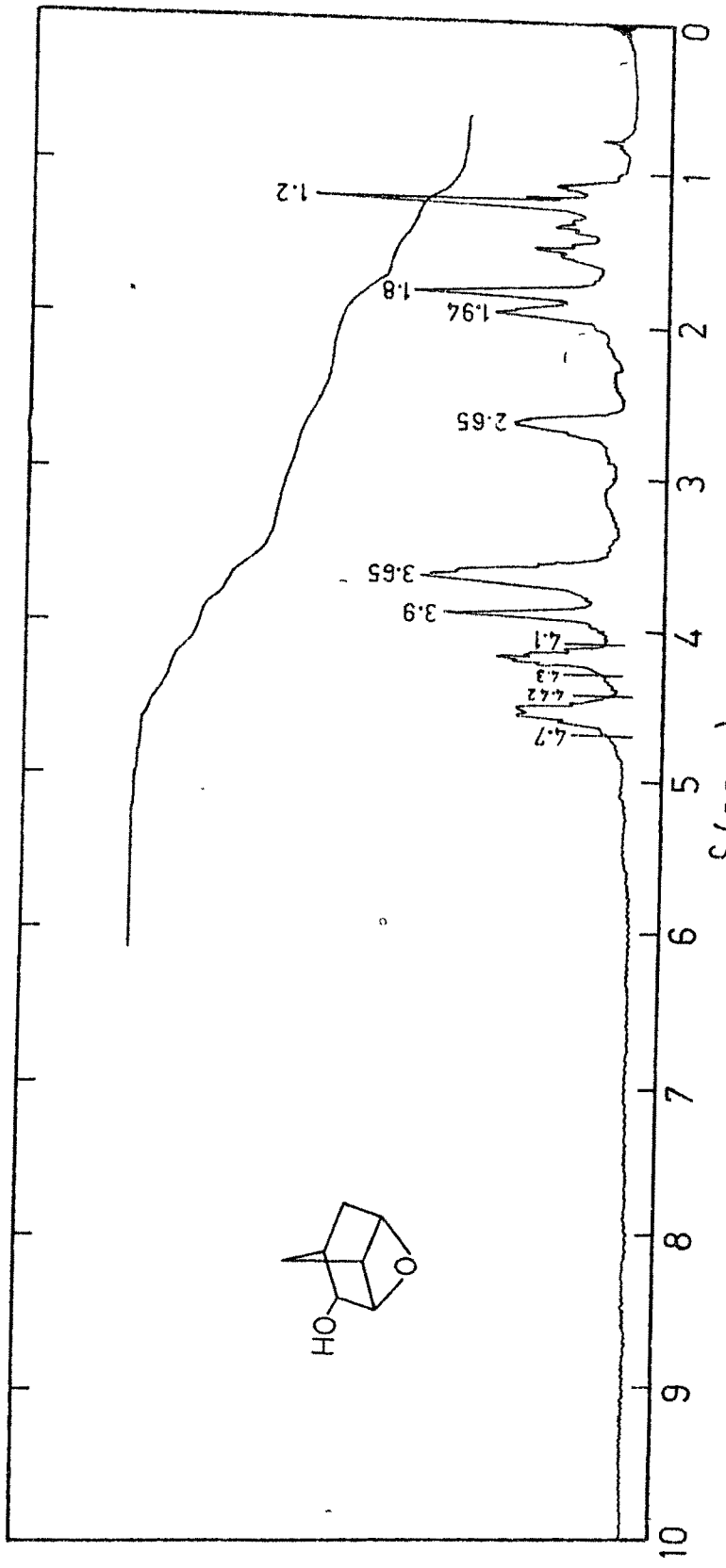


FIG. 4 - PMR SPECTRUM OF 2,6-ENDO-EPOXY-5-EXO-NORBORNANOL (11)

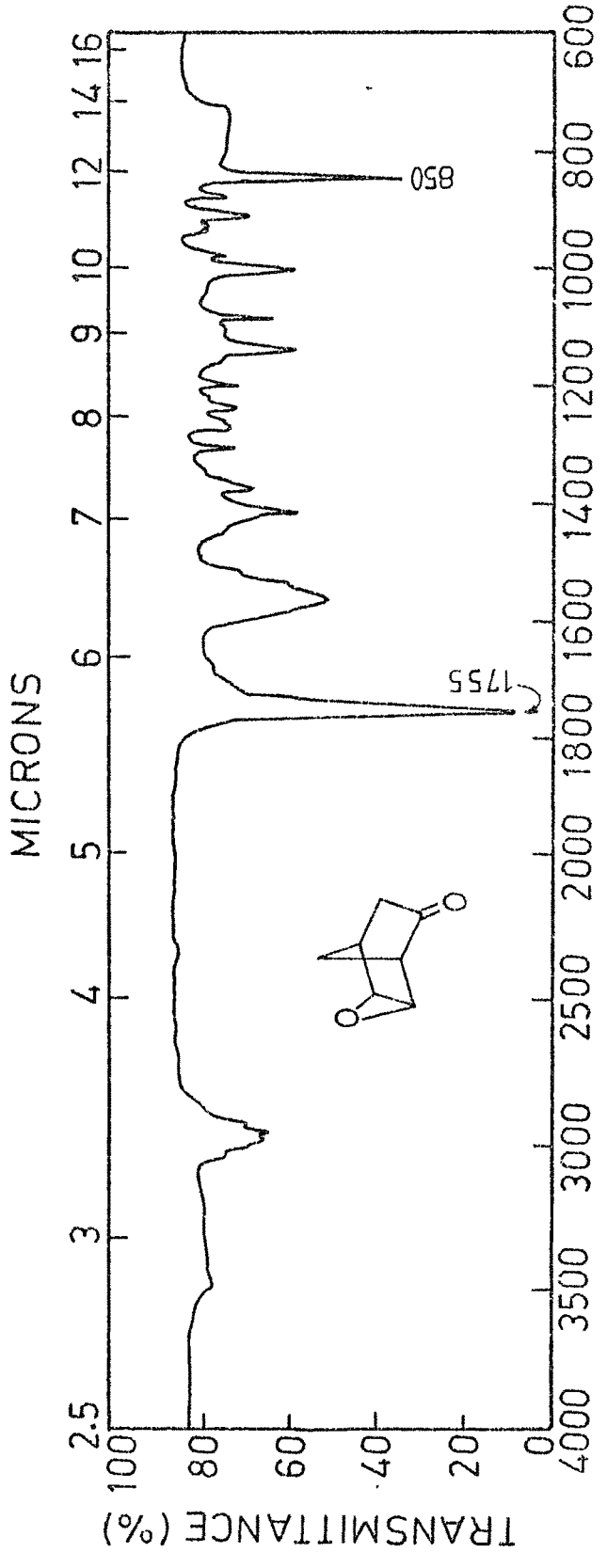


FIG. 5 -IR SPECTRUM OF 5,6-EXO-EPOXY-2-NORBORNANONE (10)

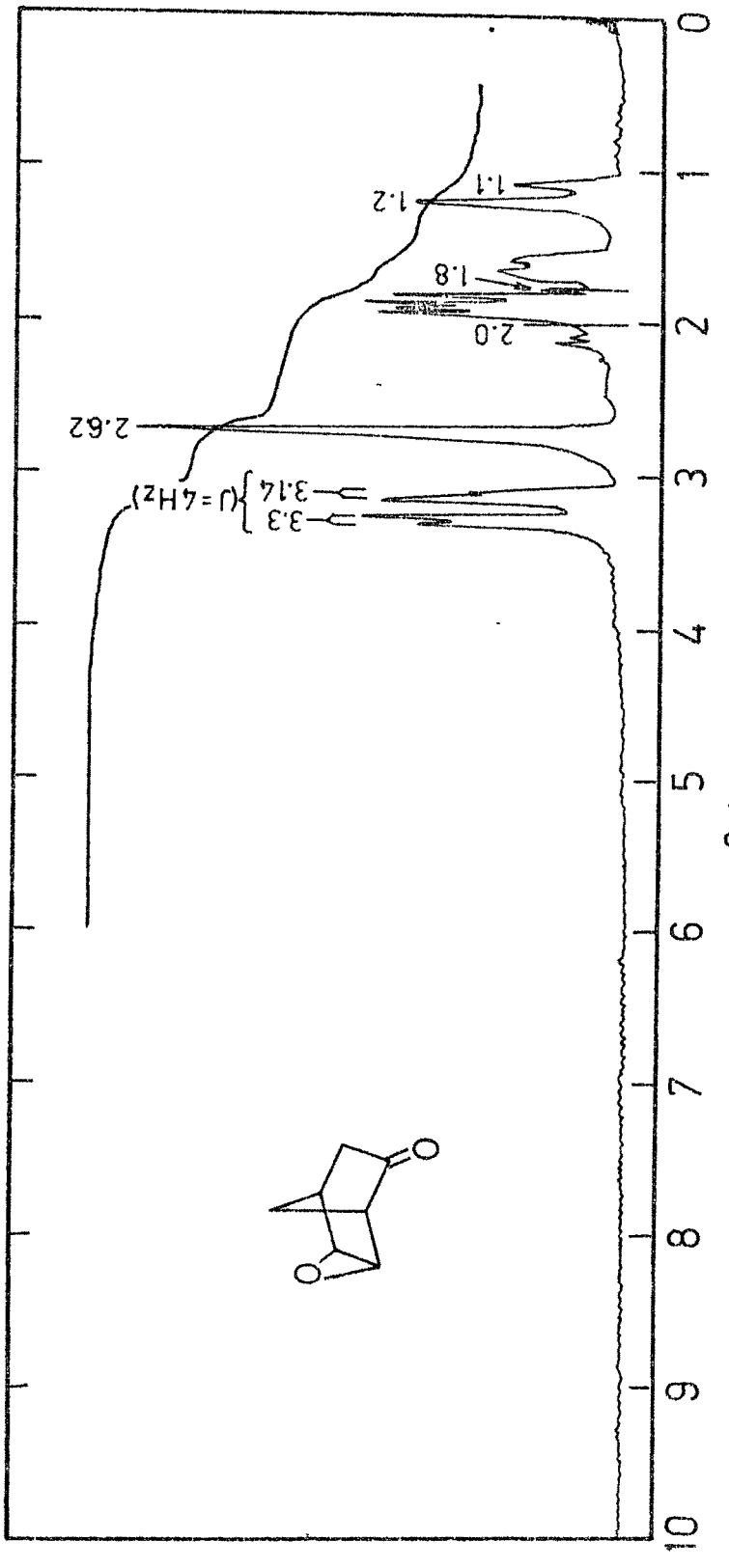


FIG. 6 -PMR SPECTRUM OF 5,6-EXO-EPOXY-2-NORBORNANONE (10)

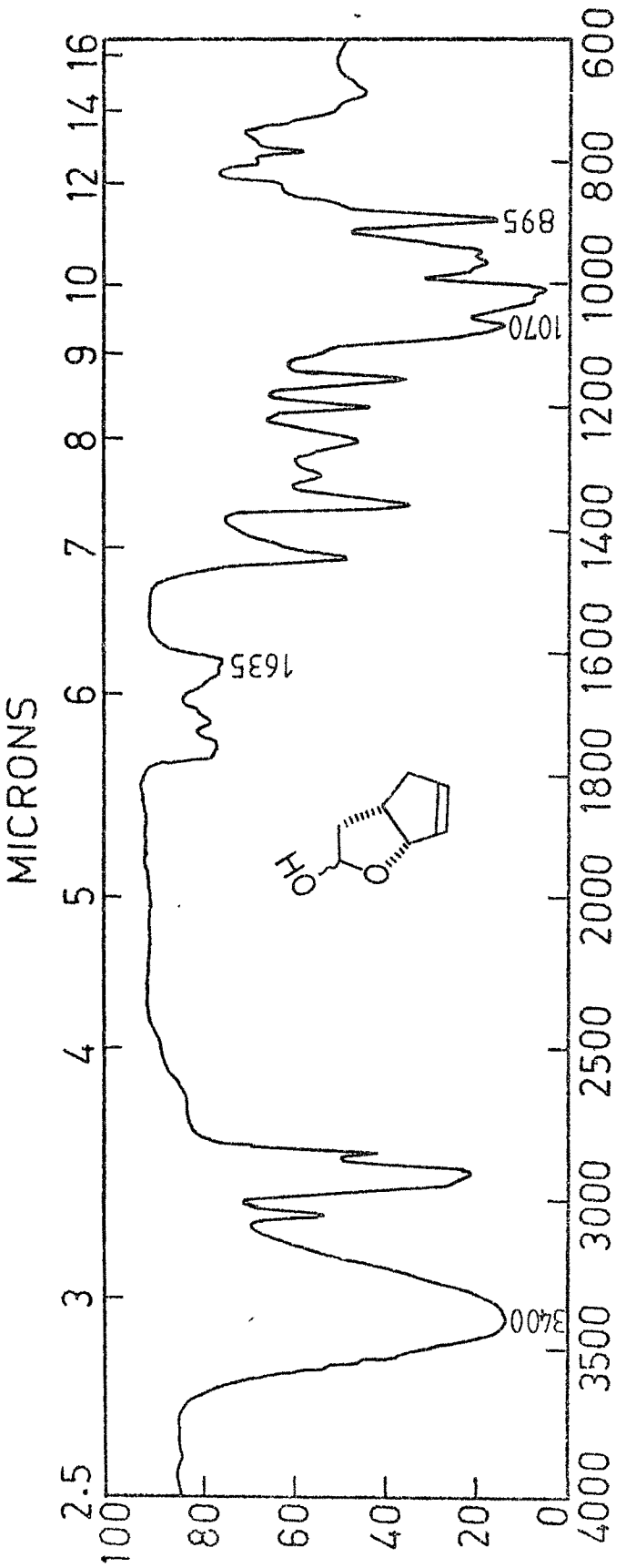


FIG. 7 -IR SPECTRUM OF THE LACTOL 13

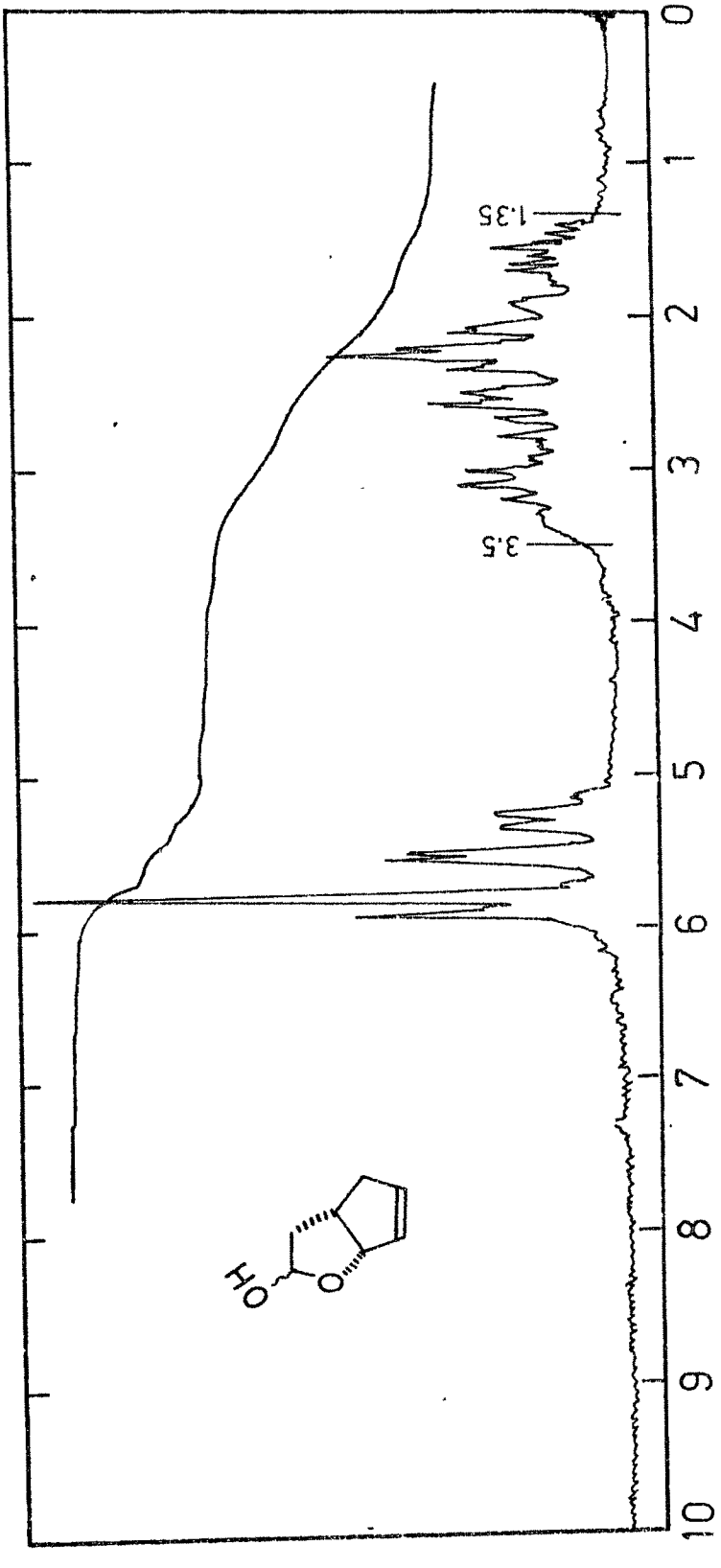


FIG. 8 -PMR SPECTRUM OF THE LACTOL 13

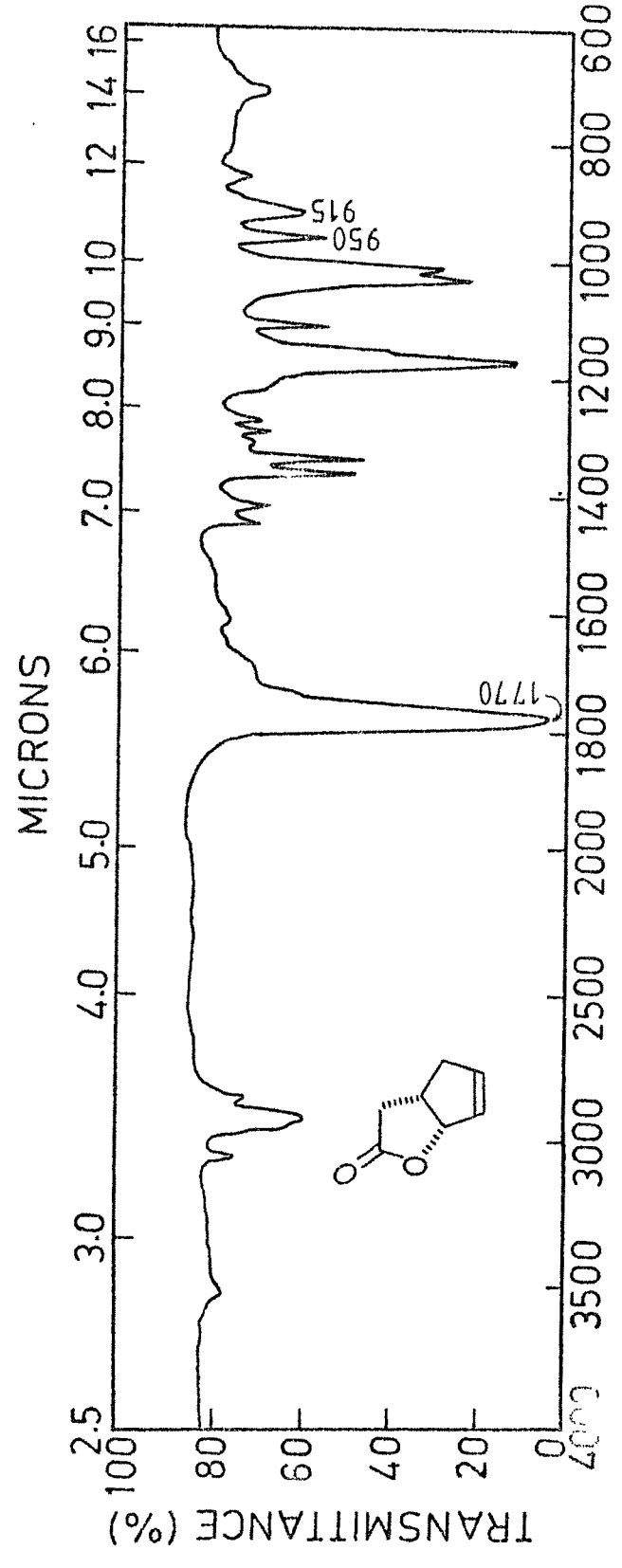


FIG. 9 -IR SPECTRUM OF THE LACTONE 14

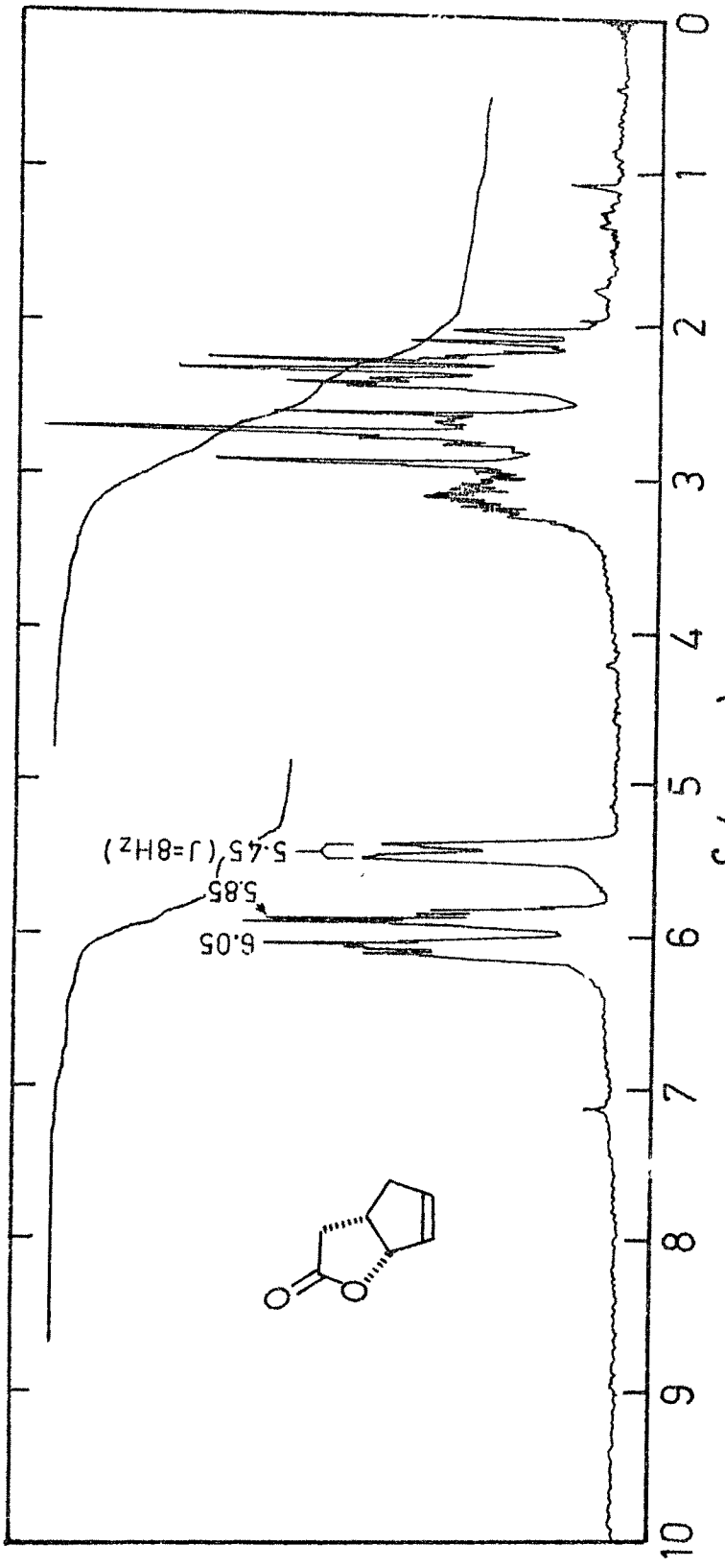


FIG. 10 - PMR SPECTRUM OF THE LACTONE 14

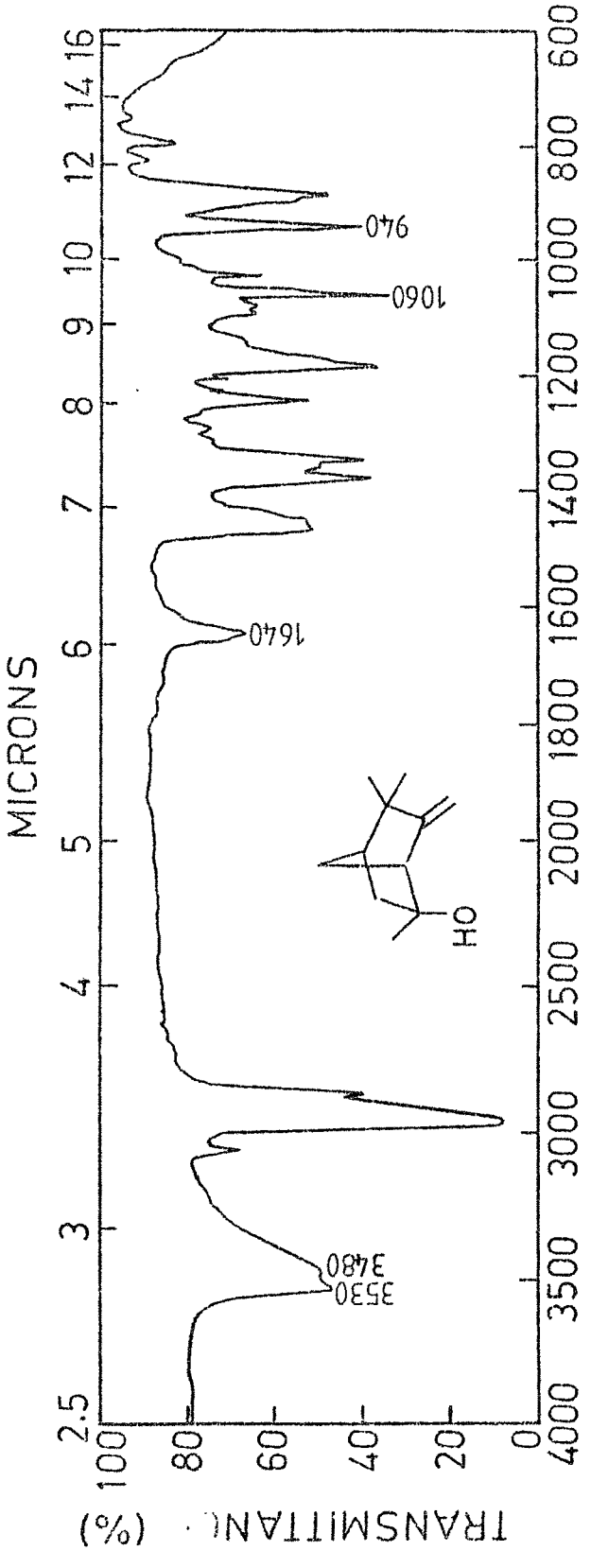


FIG. 11 -IR SPECTRUM OF 6-EXO-METHYL-6-ENDO-HYDROXYCAMPHENE (24)

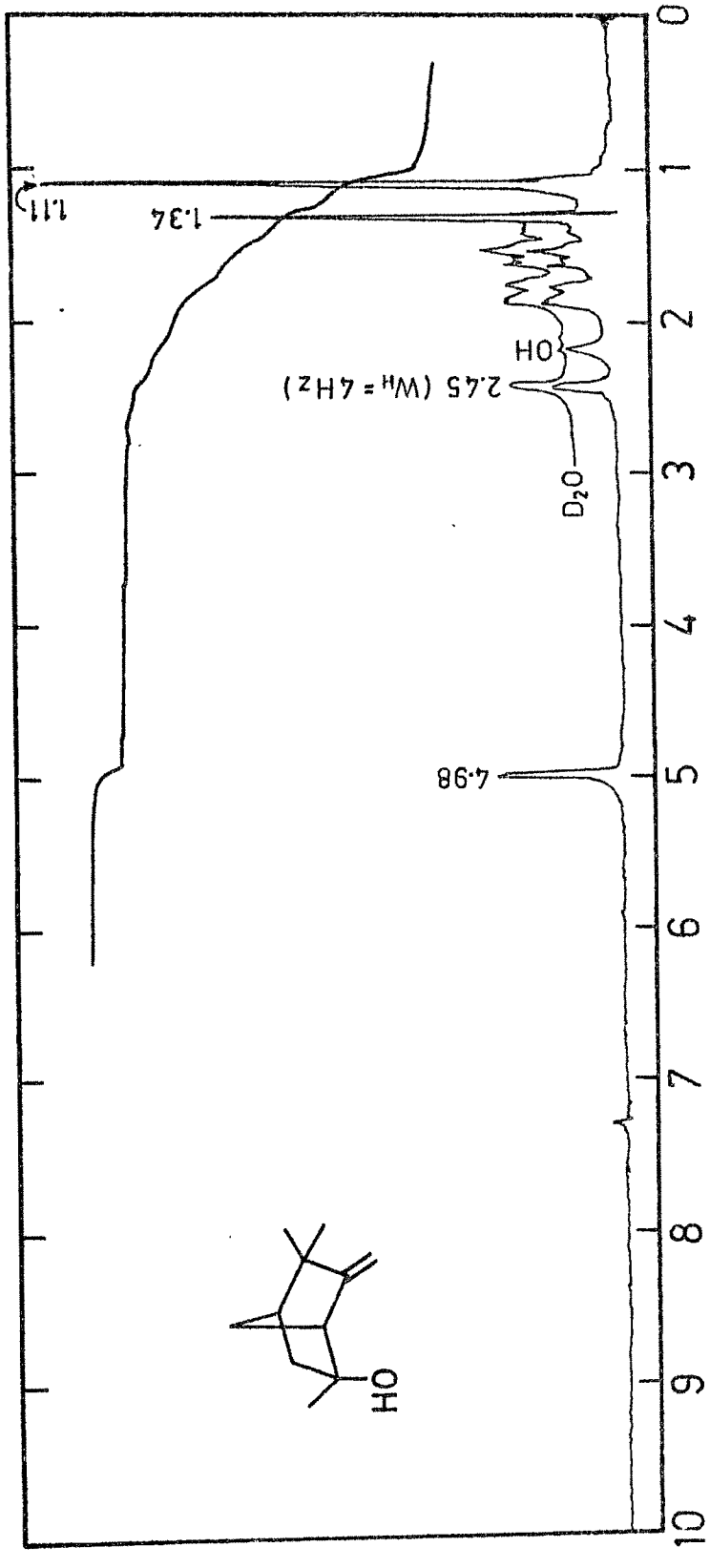


FIG. 12 -PMR SPECTRUM OF 6-EXO-METHYL-6-ENDO-HYDROXYCAMPHENE (24)

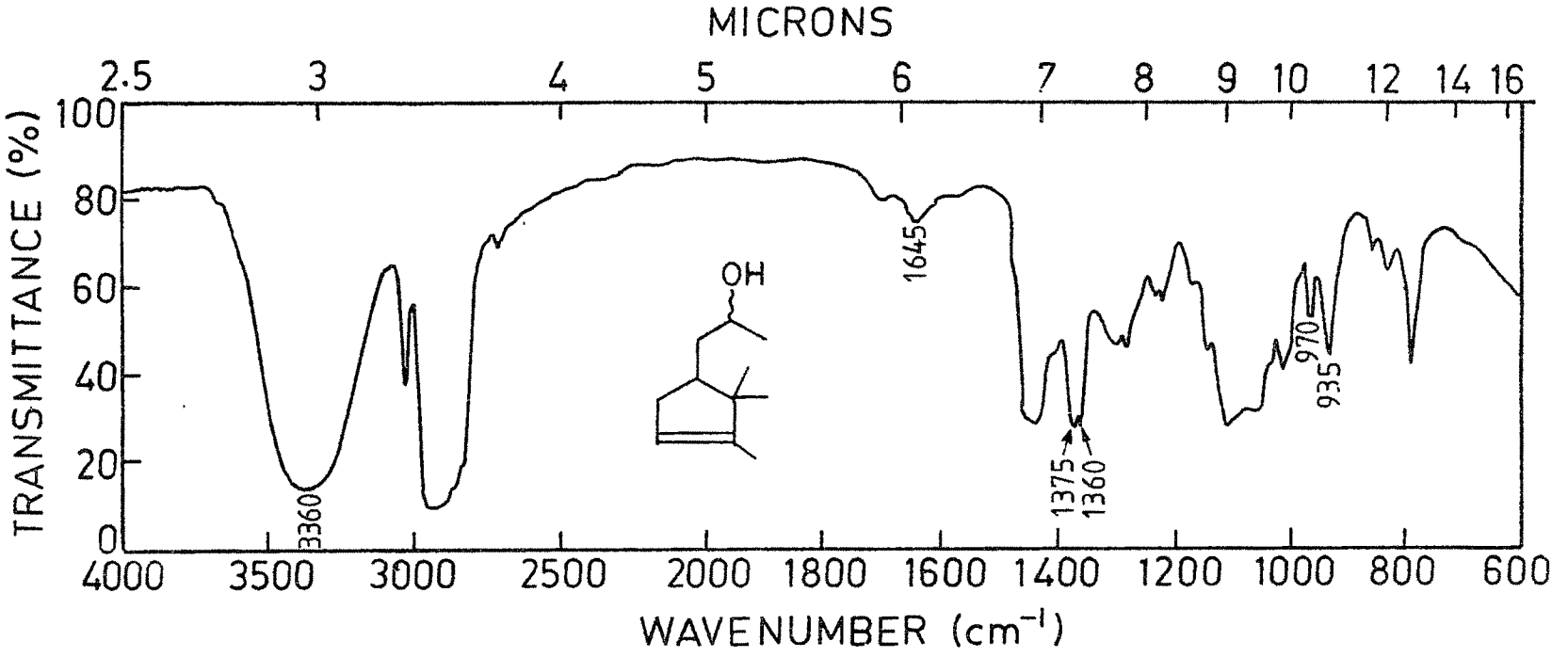


FIG. 13 - IR SPECTRUM OF 1- [2',2',3'-TRIMETHYLCYCLOPENT-3'-EN-1'-YL]-2-PROPANOL (27)

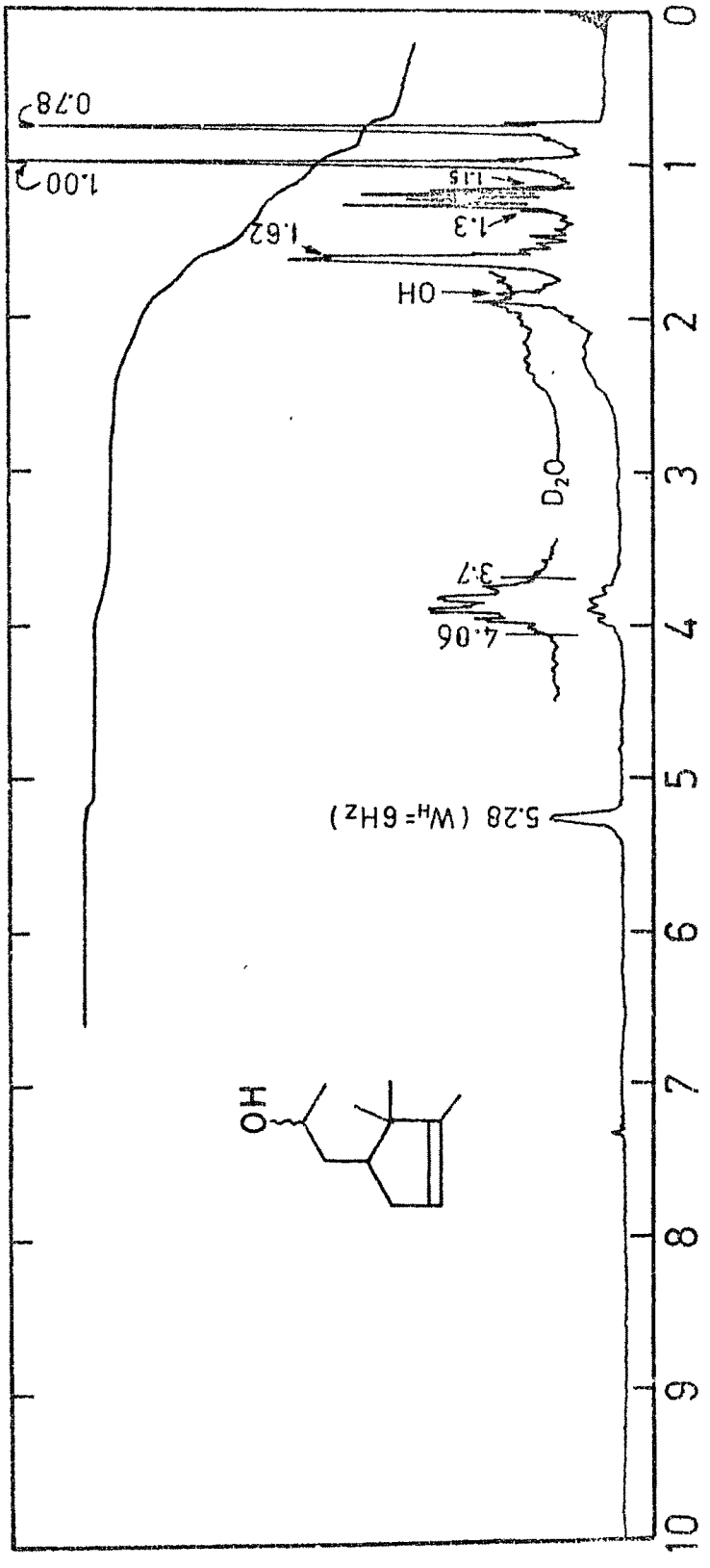


FIG. 14 -PMR SPECTRUM OF 1-[2',2,3'-TRIMETHYLCYCLOPENT-3'-EN-1'-YL]-2-PROPANOL (27)

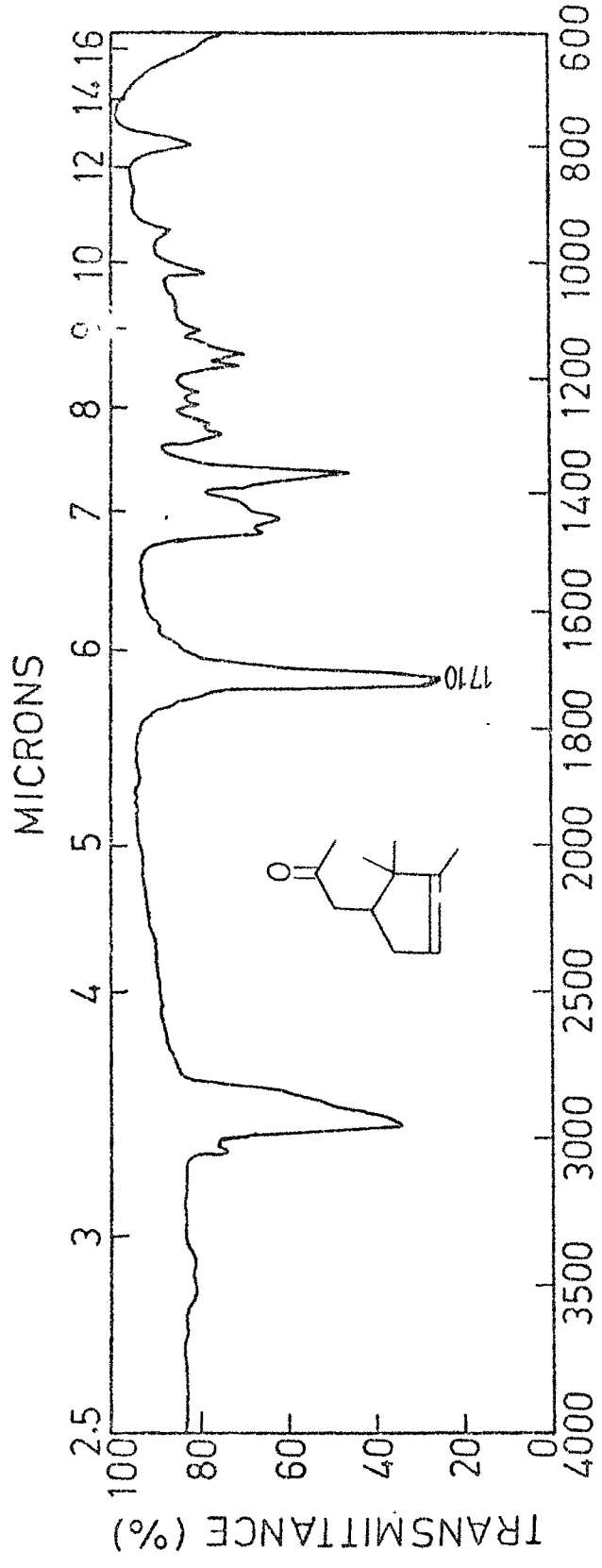


FIG. 15 -IR SPECTRUM OF 1-[2',2',3'-TRIMETHYLCYCLOPENT-3'-EN-1'-YL]-2-PROPANONE (18)

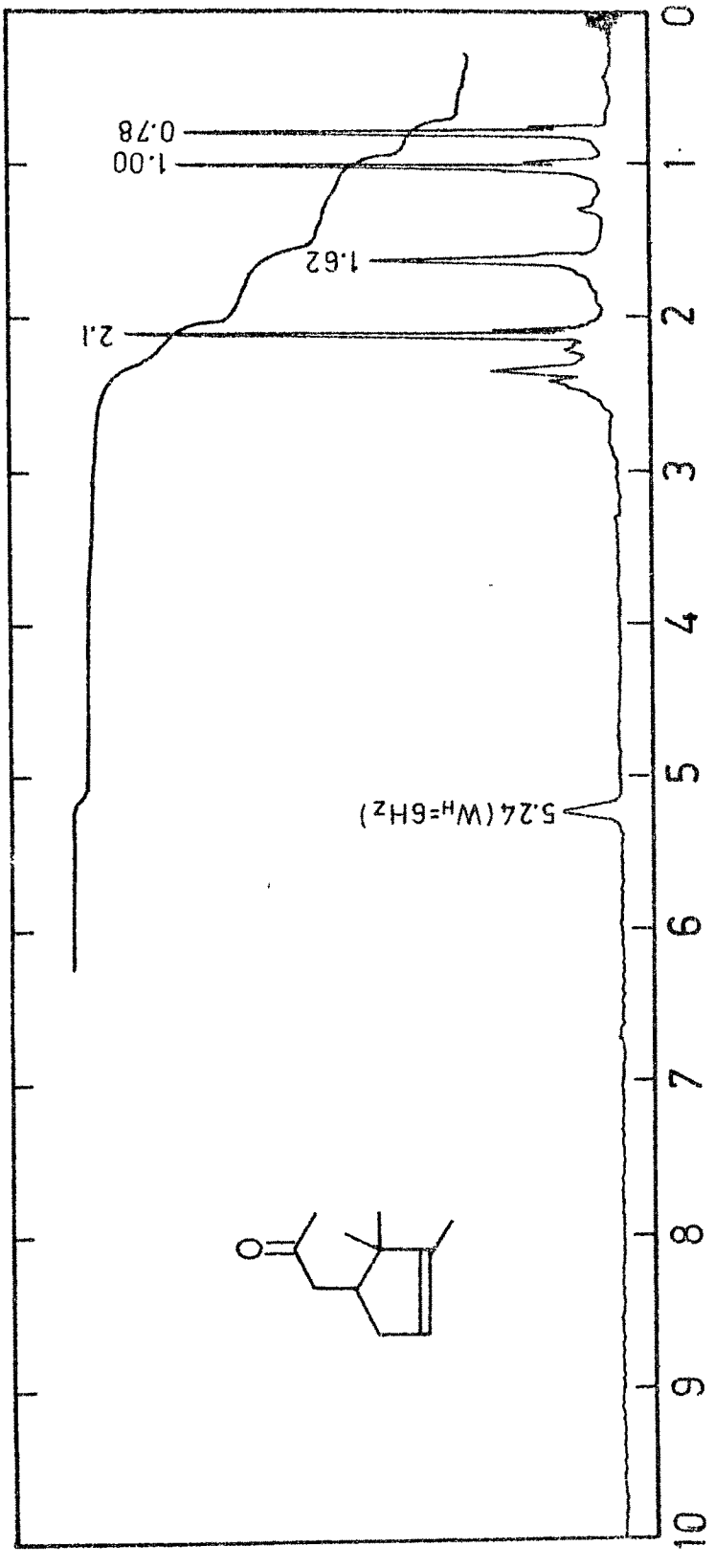


FIG. 16 - PMR SPECTRUM OF 1-[2',2',3'-TRIMETHYLCYCLOPENT-3'-EN-1'-YL] -2-PROPANONE (18)

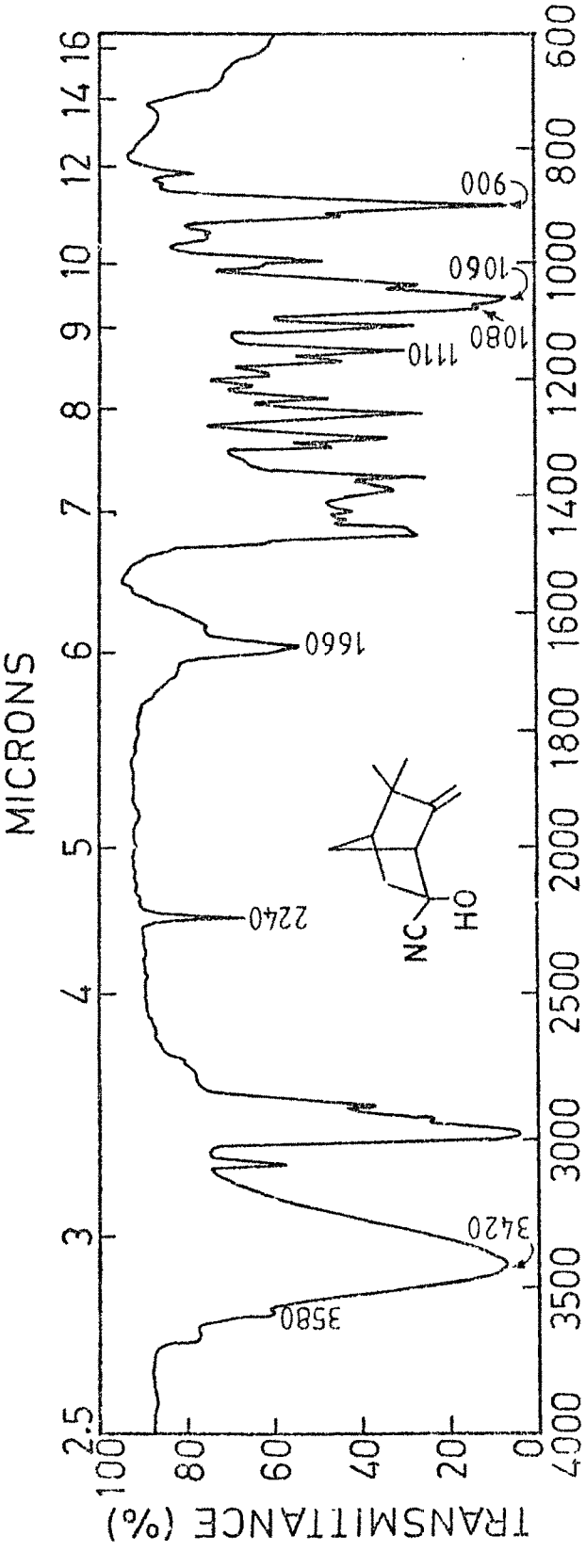


FIG.17 -IR SPECTRUM OF 6-EXO-CYANO-6-ENDO-HYDROXYCAMPHENE (28)

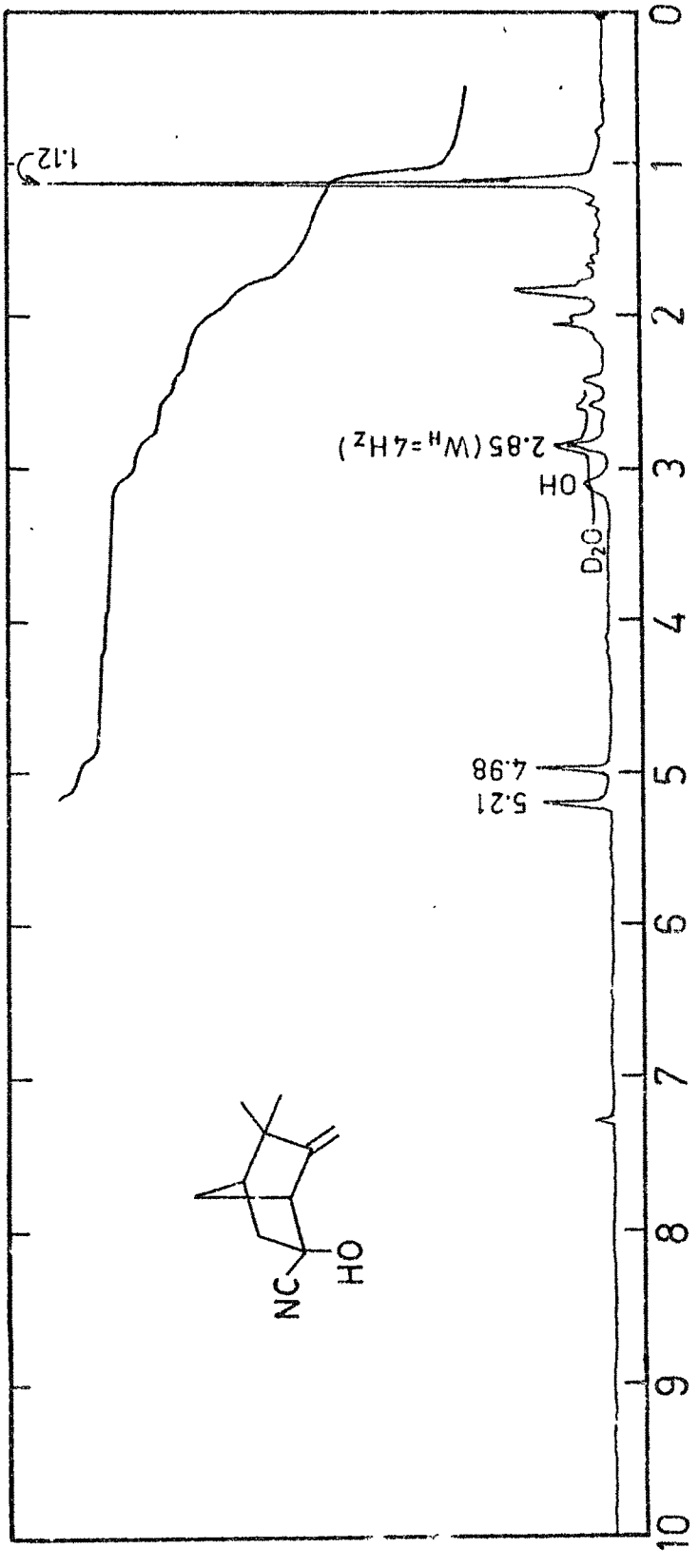


FIG. 18 -PMR SPECTRUM OF 6-EXO-CYANO-6-ENDO-HYDROXYCAMPHENE (28)

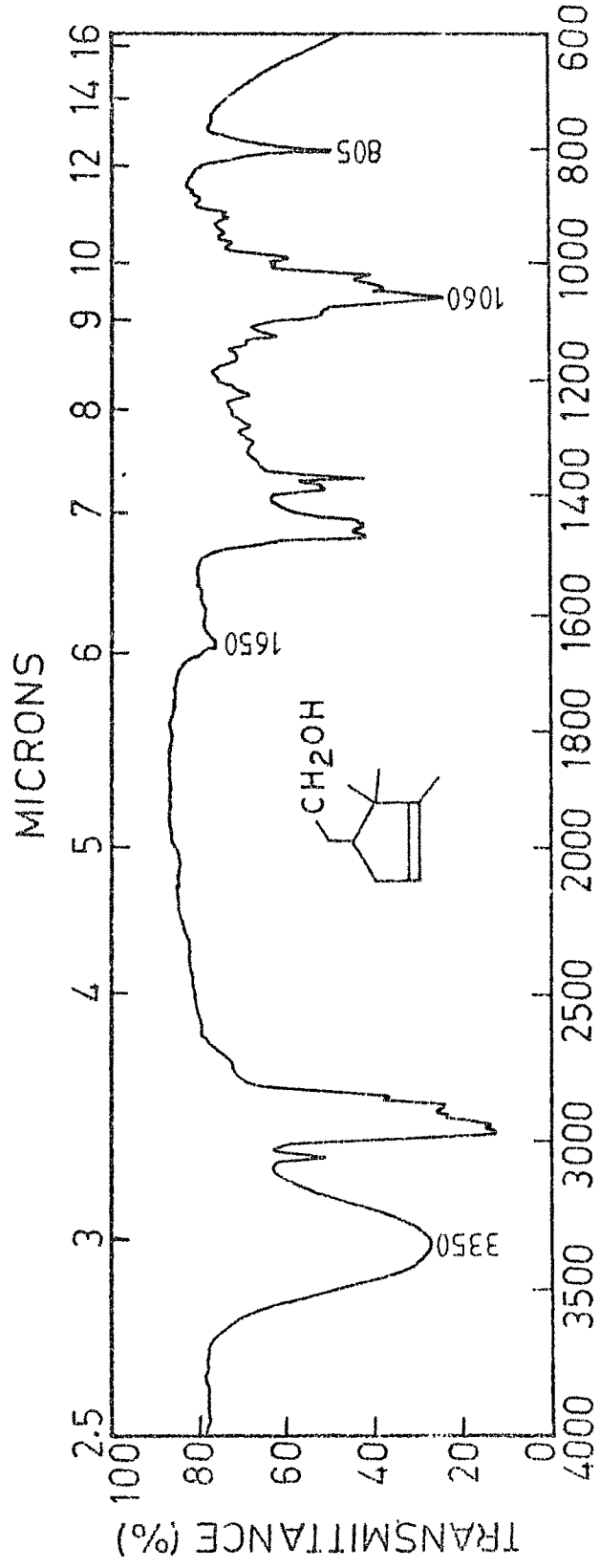


FIG. 19 -IR SPECTRUM OF α-CAMPHOLENIC ALCOHOL (30)

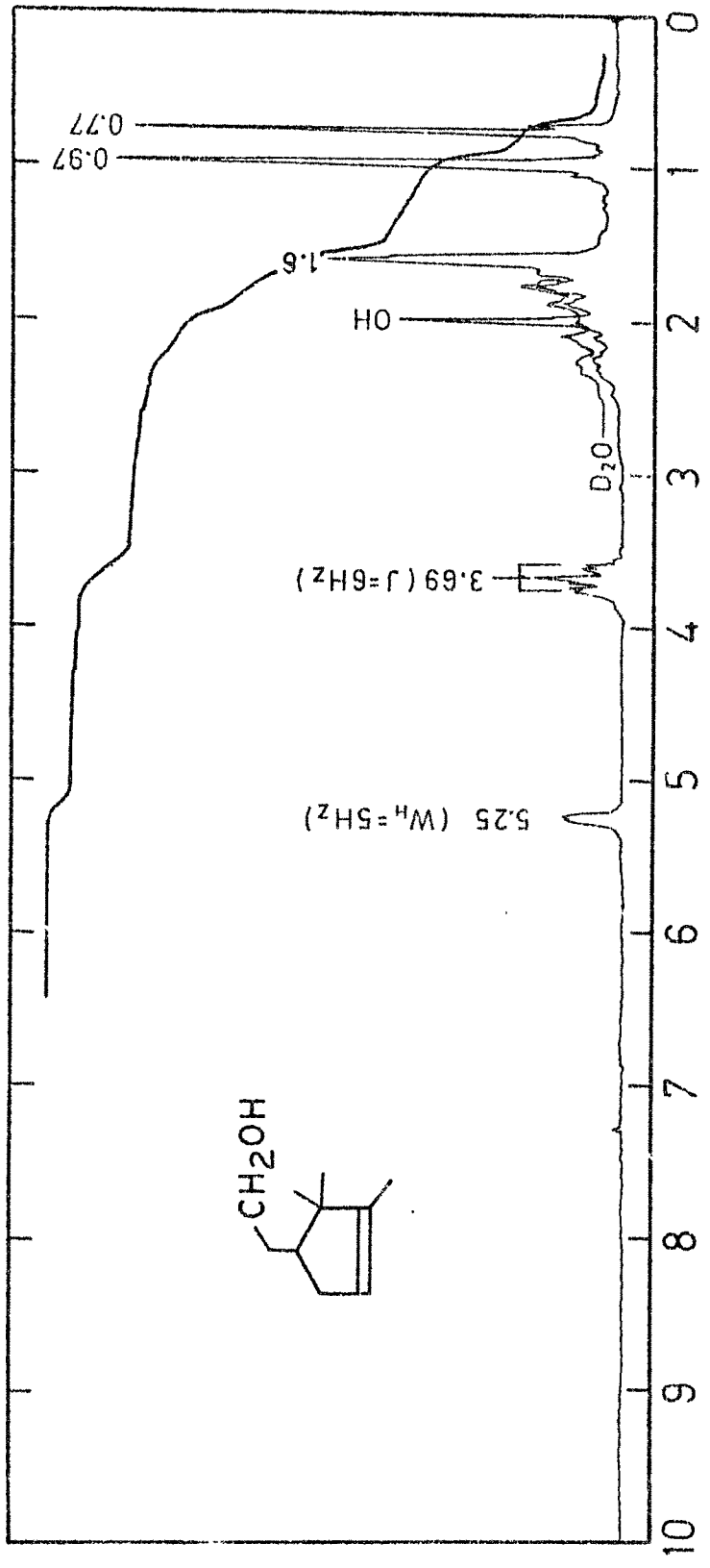


FIG. 20 -PMR SPECTRUM OF α-CAMPHOLENIC ALCOHOL (30)

REFERENCES

1. R.V. Stevens and F.C.A. Gaeta, J. Am. Chem. Soc. 99, 6105 (1977).
2. E.J. Corey, N.M. Weinshenker, T.K. Schaaf and W. Huber, ibid. 91, 5675 (1969).
3. D.A. Lightner and W.A. Beavers, ibid. 93, 2677 (1971).
4. R.B. Moffett, Org. Syn. Coll. Vol. IV, p. 238. John Wiley, New York (1967).
5. O. Mitsunobu and M. Eguchi, Bull. Chem. Soc. Jap. 44, 3427 (1971); O. Mitsunobu, Synthesis 1 (1981).
6. A.K. Bose, B. Lal, W.A. Hoffmann III and M.S. Manhas, Tetrahedron Lett. 1619 (1973).
7. N. Rabjohn, Org. Syn. Coll. Vol. III, p. 375. John Wiley, New York (1967).
8. E.H. Huntress and H. Cliff, J. Am. Chem. Soc. 53, 2720 (1931).
9. J.D. Roberts, E.R. Trumbull, Jr., W. Bennett and R. Armstrong, ibid. 72, 3116 (1950).
10. J. Meinwald and B.C. Cadoff, J. Org. Chem. 27, 1539 (1962).
11. Y. Ogata, K. Tomizawa and K. Takagi, Tetrahedron 29 47 (1973).
12. Henbest and Nicholls, J. Chem. Soc. 221 (1959).
13. E.J. Corey and J.W. Suggs, Tetrahedron Lett. 2647 (1975).
14. See e.g. P.D. Sleezer, S. Winstein and W.G. Young, J. Am. Chem. Soc. 85, 1890 (1963).
15. H.C. Brown and M. Rei, ibid. 91, 5646 (1969).
16. A. Siewinski, J. Dmochowska-Gladysz, T. Kolch, A. Zabra and K. Derdzinski, Tetrahedron 35, 1409 (1979).

17. R.P. Singh, H.N. Subba Rao and Sukh Dev, Tetrahedron 35, 1789 (1979).

18. H.C. Brown, J.H. Kawakami and S. Ikegami, J. Am. Chem. Soc. 92, 6914 (1970).

19. A. Eredi and P. De Ruggieri, ibid. 75, 650 (1953).

20. V.S. Joshi, N.P. Damodaran and Sukh Dev, Tetrahedron 24, 5817 (1968).

21. A.F. Thomas, Helv. Chim. Acta 55, 815 (1972).

22. T.K. Das Gupta, D. Felix, U.M. Kempe and A. Eschenmoser, ibid. 55, 2198 (1972).