CHAPTER II

STRUCTURE OF AN ACETATE FROM SOLVOLYSIS OF 8-HALONEOISOLONGIFOLENE

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Abstract

Solvolysis of 8-haloneoislongifolene with sodium acetate/acetic acid gives, besides expected products, a rearranged tertiary acetate as the major component. The structure of the tert. acetate has been elucidated by its chemical transformation and spectral characteristics (PMR, NOE, LSR studies) and structure 6a has been assigned to it.

STRUCTURE OF AN ACETATE FROM SOLVOLYSIS OF 8-HALONEOISOLONGIFOLENE*

1. INTRODUCTION

ISOLONGIFOLENE[1] (1), on bromination, undergoes a rearrangement leading to the formation of 8-bromoneoisolongifolene[2] (3), which on solvolysis in refluxing acetic acid in the presence of sodium or potassium acetate, gives a mixture containing two hydrocarbons 4 (32.5%) and 5 (4.2%) and two acetates (50%) contaminated with their respective alcohols, besides some minor products. One of the acetates which was present as a minor product (ca, 1-2%) was identified as the expected secondary acetate 7a (vide infra). The major product was found to be a tertiary acetate whose structure has been elucidated as 6a (Chart I).

The total acetate mixture was saponified to the corresponding alcohols which were separated and isolated in pure state by systematic chromatography on silica gel. For the sake

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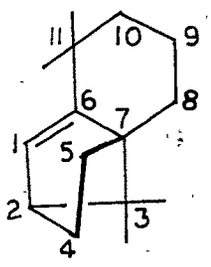
*We have designated monoolefinic hydrocarbon 2 derived from isolongifolene as neoisolongifolene. The following numbering has been followed in this chapter.



at 0.98, 1.15, 1.17 and 1.22 ppm; none of these signals arises from isopropyl group (J= 6-7Hz), since they appear at the same chemical shifts in the spectra recorded at 60MHz and 90MHz. Consequently, all four methyls are quaternary[4]. The PMR spectrum (Fig. 4) of alcohol B also reveals the presence of four quaternary Me's appearing as singlets at 0.93, 0.98, 1.20 and 1.27 ppm and one olefinic proton (1H, doublet centred at 5.30 ppm, J= 3Hz). The absence of any signal (between 3.4-4.5 ppm[5]) for a proton attached to a carbon linked to oxygen indicates that the alcohol must be tertiary. Its IR spectrum (Fig. 16) also clearly shows that it is an unsaturated alcohol (OH 3608, 3495 1188, 1061 cm^{-1}; C=C 1615, 821, 810 cm^{-1}). The presence of unsaturation is further indicated by the appearance of yellow colour with TNM.

3.1. Size of the Rings

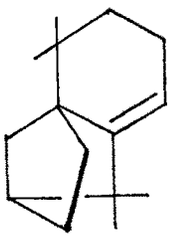
Alcohol B consumes one mole of peracid and the resulting epoxide gives no colour with TNM. Hence the alcohol is mono-olefinic and tricyclic (as it analyses for $C_{15}H_{24}O$). And since it contains only one olefinic proton (PMR) it must be a trisubstituted double bond.

The olefinic proton, in fact, appears as a doublet at 5.30 ppm similar in shape and magnitude of coupling

constant (J= 3Hz) to those of neoisolongifolene (2) and its derivatives 3, 7b, 8, 9 and 10 (Table 1). It suggests that olefinic proton is located in a ring of same size and environments, as existing in the above mentioned derivatives. That the double bond is exocyclic to a six-membered ring is revealed by the ozonalysis of the tert. acetate. The resulting ketoacid, after esterification with diazomethane, displays carbonyl frequencies at 1705, and 1735 cm^{-1} in the IR spectrum (Fig. 18). The absorption at 1705 cm^{-1} is assignable to a cyclohexanone derivative. On the basis of the data provided above, the tert. acetate may be assigned a partial structure 11 (Chart II).

Information about the relative positions of the olefinic bond and the hydroxyl group was obtained from the following observations.

Alcohol 8 when treated with aqueous sulfuric acid in dioxane isomerized to a saturated ketone (-ve TNM test) which shows carbonyl frequency at 1730 cm^{-1} in its IR spectrum (Fig.17), which is characteristics of cyclopentanone derivatives. Reduction of this ketone gave, as expected, the corresponding secondary alcohol, which displays a sharp singlet at 3.40 ppm for CHOH in its PMR spectrum (Fig. 7). The above data demand that this alcohol is flanked by tertiary carbon atoms on both



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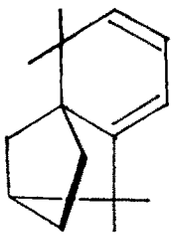

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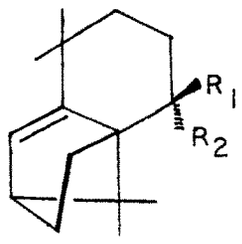

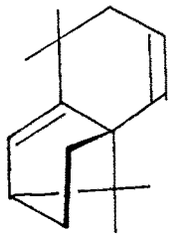

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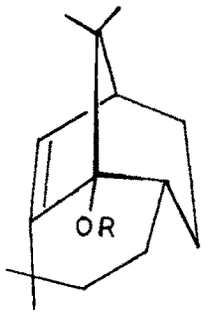
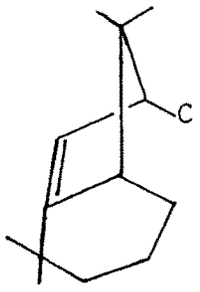


6a R=OAc
6b R=H

2 $R_1=R_2=H$
3 $R_1=Br$, $R_2=H$
7a $R_1=H$, $R_2=OAc$
7b $R_1=H$ $R_2=OH$
8 $R_1R_2=O$
9 $R_1=OH$, $R_2=H$
10 $R_1=Cl$ $R_2=H$

CHART I



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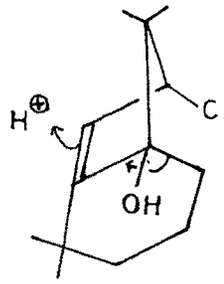
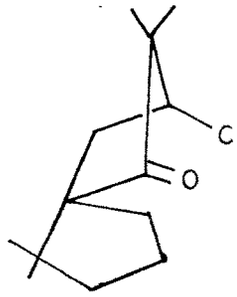


12a



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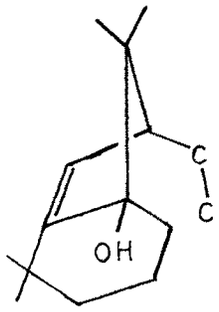
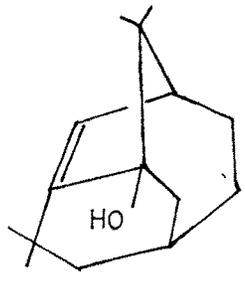


12 b



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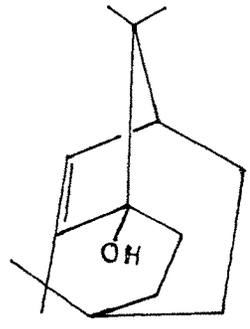

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CHART II

Table I: PMR and IR data of neoisolongifolene (2) and its derivatives having double bond in five membered ring

Sr. No.	Compounds	PMR chemical shift in δ ppm			IR frequencies for $-\overset{|}{C}=CH-$ (CM^{-1})
		Me[a]	to OH or Br(J, Hz)	olefinic protons[c](J,Hz)	
1.	2 $R_1=R_2=H$	0.73, 0.77, 1.02, 1.10	-	5.61 (4)	1610, 815
2.	3 $R_1=Br$, $R_2=H$	0.85, 0.97, 1.07, 1.11	4.28 (dd, 7.5, 8.0)	5.65 (4.0)	1610, 819, 810
3.	10 $R_1=Cl$, $R_2=H$	0.83, 0.93, 1.04, 1.08	4.11 (dd, 7.0, 9.0)	5.67 (3.5)	1608, 821, 811
4.	9 $R_1=OH$, $R_2=H$[b]	0.84, 0.93, 1.03, 1.09	3.83 (dd, 6.0, 7.0)	5.56 (4.0)	1608, 820, 810
5.	8 R_1, $R_2=O$	0.87, 1.03, 1.15, 1.18	-	5.70 (4.0)	1625, 822, 835
6.	7b $R_1=H$, $R_2=OH$[b]	0.95, 1.02, 1.05, 1.15	4.11 (idd, $W_H=9.5Hz$)	5.72 (3.5)	1610, 815, 810
7.	6a -	0.98, 1.15, 1.17, 1.22	-	5.37 (3.5)	1620, 820, 810
8.	6b -	0.93, 0.98, 1.20, 1.27	-	5.30 (3.5)	1615, 821, 810

[a] Each methyl signal appears as singlet

[b] PMR spectra were recorded in $CDCl_3$

[c] In all compounds olefinic proton appears as doublet.

sides, i.e. there is no vicinal hydrogen. The ready isomerization of this olefinic tert. alcohol to saturated ketone suggests allylic relationship of the hydroxyl and olefinic linkage[6], isomerization occurring through a 'pinacol-type' rearrangement. Thus, structure 11 may be elaborated to 12a which can rearrange to ketone 13, a cyclopentanone, as is indeed observed experimentally.

The expression 12a accounts for fourteen carbon atoms out of fifteen of alcohol B . Since alcohol B has only quaternary Me's (four in number) the fifteenth carbon must be attached to the carbon as shown in 12b. The question which still remains unresolved is the point of attachment of this dimethylene chain to form the third ring. The attachment of dimethylene chain at the positions C-9 and C-10 to give rise to structures 14 and 15 is ruled out as the genesis of these compounds from bromide 3 is not easily rationalized. This leaves 6b as the only plausible structure for alcohol B. This structure is fully consistent with mechanistic consideration.

3.2. Mechanistic Consideration

On the mechanistic consideration it is reasonable to assume that tert. acetate obtained by solvolysis of bromide 3 may have one of the three possible structures 6a, 16 and 17,

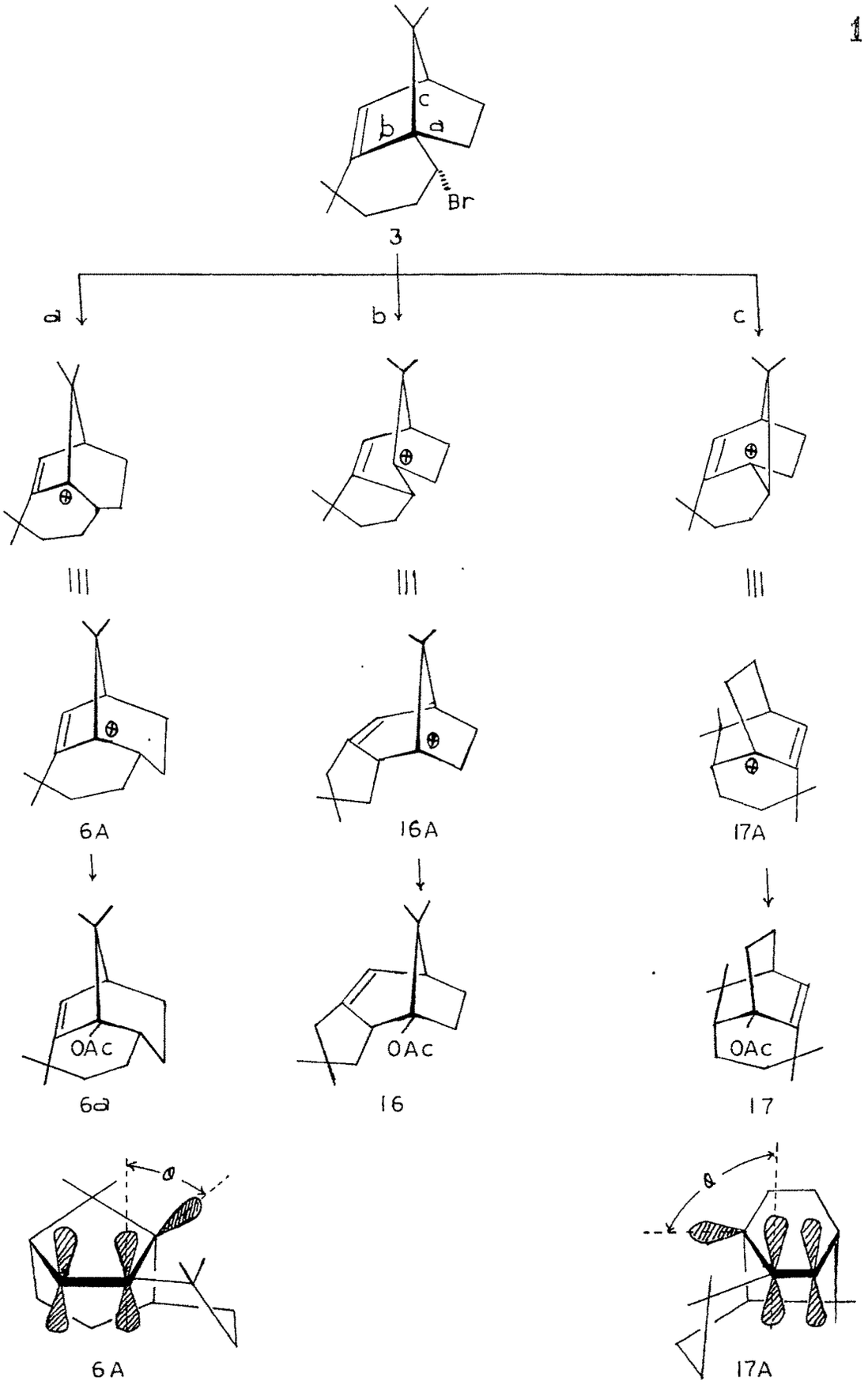

CHART III

arising from the Wagner Meerwein migration of the three different bonds adjacent to the carbon atom carrying the halogen as given in Chart III.

Structure 16 is unlikely because it involves the migration of an olefinic bond*. This structure further stands ruled out by the results of ozonolysis of tert. acetate. The resulting product was substituted cyclohexanone derivative (vide supra) and not cyclopentanone as would arise from structure 16.

The tert. acetate was proposed to arise from carbonium ion 6A in preference to structure 17A for the following reasons:

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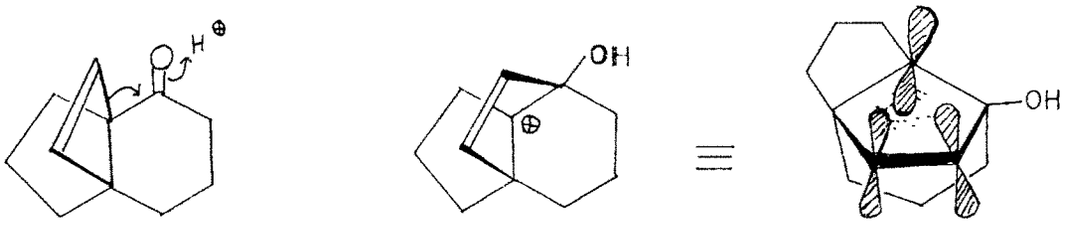
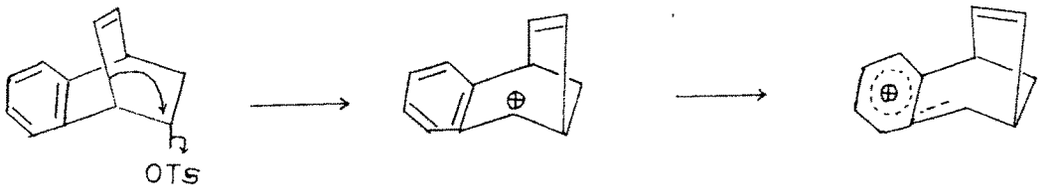
*Migration of allylic bonds has been reported in some cases. Tricyclo[4,3,2,$0^{1,6}$]undec-10-en-2-one[7] 18 undergoes an acid catalysed rearrangement via the migration of sp^2-sp^3 bond (allylic bond) to a substituted 8-bicyclo[3,2,1]octenyl type cation 19 which is stabilized by participation of π-bond[8]. Similarly, sp^2-sp^3 σ-bond migration in 20 may be due to highly stabilized benzylic cation[9] 21.

In case of i-steroid type rearrangement[10] it is believed that σ-bond delocalization (as in 24, path a) and not sp^2-sp^3 bond migration is involved as shown 22→23 (path b).

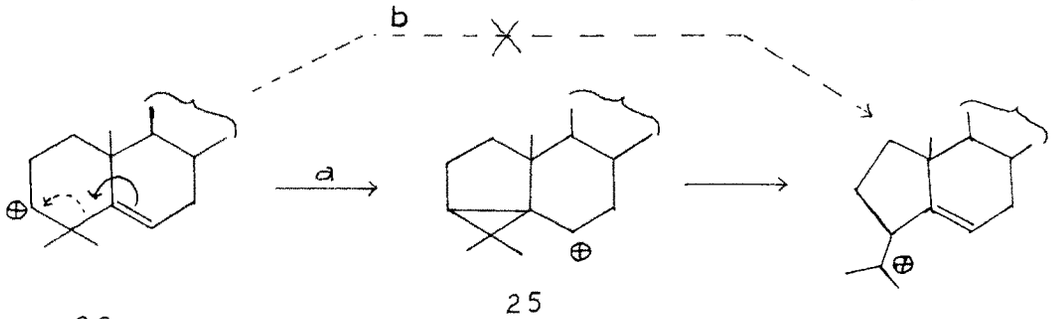
In 3 π-bond delocalization of the type shown in 26 (26a→26b⟶16A) is very improbable because of the geometry of the ring. Neither is the resulting carbonium ion 16A stabilized for such migration to occur (Chart IV).



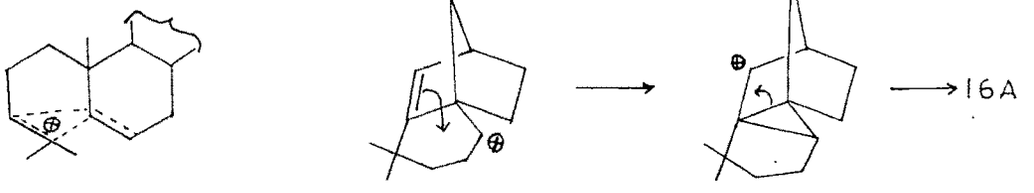
18 19



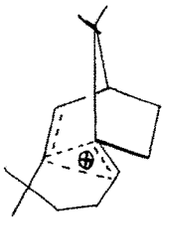
20 21



22 25 23



24 26a 26b



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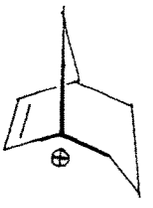

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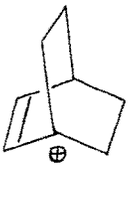

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CHART IV

(a) The size of the ring containing the olefinic bond remains unaltered and hence the similarity in the spectral characteristics of tert. acetate and alcohol 8 with neoisolongifolene derivatives (*vide supra*). In the two other alternative structures 16 and 17, there is a ring expansion from five to six-membered ring.

(b) An examination of framework molecular model (FMM) indicates that of these two ions 6A and 17A, 1-bicyclo[3,2,1] octenyl* type of cation (6A) leading to product 6a is capable of some allylic stabilization ($\theta \simeq 30^{o}$) while in 1-bicyclo[2,2,2]octenyl type cation (17A), that leads to product 17, such a stabilization is going to be minimal ($\theta \simeq 90^{o}$). Clearly, in 16A the possibility of allylic stabilization does not exist (Chart III).

The conclusion may be drawn here that ion 6A is more probable than ion 16A and more stable than ion 17A. Both

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*It has been reported that 1-bicyclo[3,2,1]ectenyl cation (27) has more allylic stabilization than 1-bicyclo[2,2,2]-octenyl cation[11](28)(Chart IV).

these factors could be reflected in the formation of the activated complex during rearrangement that leads to acetate or alcohol (6a or 6b) rather than its isomers 16 and 17.

Retrospectively, the product of ozonalysis of tert. acetate 6a can be designated as 30 and the saturated ketone obtained by the isomerization of alcohol 8 can be assigned structure 31 and the corresponding alcohol 32. The spectral characteristics are consistent with the proposed structures (Chart VI)

3.4. Mass spectral Evidence

The mass fragmentation pattern (Fig. 2) of this tert. acetate, briefly discussed below, is readily rationalized when structure 6a is assigned to the tert. acetate.

The base peak occurs at m/e 174 (29, $C_{13}H_{18}$). The fragmentation to this ion can be readily rationalized in view of the known preference for tropylium ion (given in Chart V).

The peaks at m/e 131,133 and 159 can be explained as those arising by loss of C_3H_7, C_3H_5 and CH_3 respectively from tropylium ion 31. The peaks at m/e 105 and 107 may be arising by loss of HC≡CH.

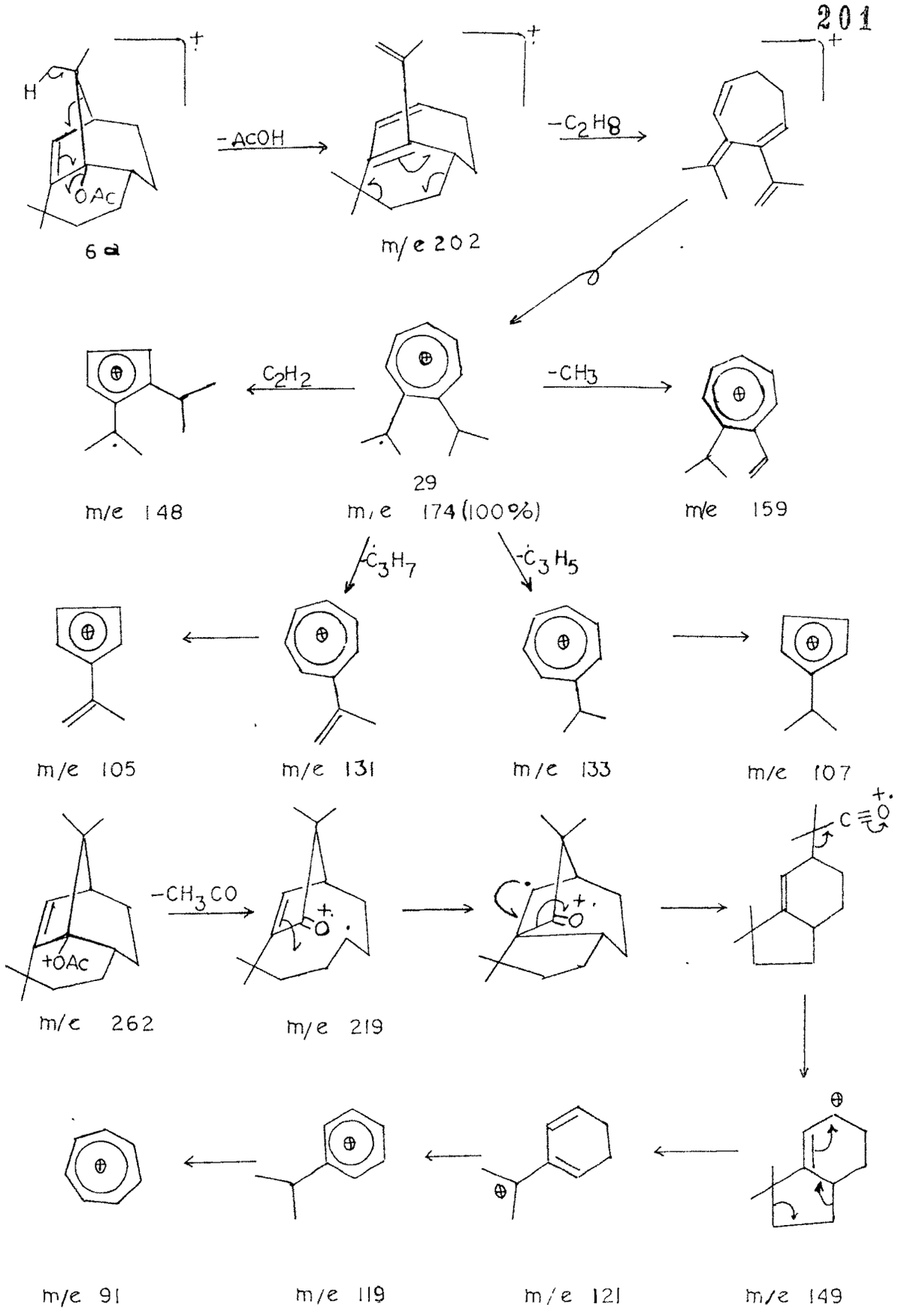

CHART V MASS SPECTRAL FRAGMENTS OF tert. ACETATE

The other major peaks at m/e 219, 149, 121, 119 and 91 are also rationalized as given in Chart V.

3.5. LSR and NOE Studies on tert. Alcohol

The structure of 6b was elucidated by careful study of its PMR spectrum. We have used $Eu(fod)_3$ complex with tert. alcohol for the assignment of its structure. For the pseudo-contact interaction of lanthanide complexes, the magnitude of LIS (lanthanide induced shift) of the nucleus is inversely proportional to the cube of the average distance from the lanthanide metal ion[12]. However, in almost all of the investigations, the precise location of the lanthanide nucleus (metal ion) has not been established. Hence, we adopted the method of Cockrill and coworkers[13]. These authors have suggested alternative approaches which obviate the need to know the precise location of the lanthanide nucleus. Measurements or calculations of r from a specific proton to the periphery of the coordinating pair of electrons gives the observed relationship of $s^* \propto r^{-2}$.

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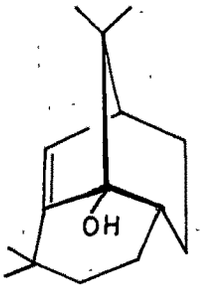
*The chemical shift of a particular hydrogen atom varies linearly with the molar ratio of $Eu(fod)_3$ to the substrate, for concentration of the shift reagent upto its equimolar amount. The slope of the lines has been defined as 's' i.e. the europium shift parameter.

The effect of incremental addition of $Eu(fod)_3$ upon the spectrum of tert. alcohol is shown graphically in Fig. 1. We have measured the distance r between the centre of the hydrogen nucleus and the perimeter of the lone pair of oxygen of hydroxyl group, using Prentice Hall Framework molecular models. The values of s (slope of line) for all the protons have been extracted from Fig. 1A. A graph plot between the shift parameter s and the inverse square of the separation (r^{-2}) gives a straight line as shown in Fig. 1B. Each of the possible conformations of the tert. alcohol was considered and the best fit for the plot of r^{-2} vs s gave a straight line for its structure and the conformation is as shown below:



From the molecular models of the tert. acetate it is clear that one of the methyl groups at position C-11 lies in the plane of π-bond and appears down-field in the PMR spectrum (Fig. 5). The spatial disposition of this methyl

group in relation to the hydroxyl group is also borne out by LIS study. This methyl group is expected to experience nuclear Overhauser effect from the olefinic proton. Irradiation of the low field methyl group, indeed, causes intensity-enhancement by 18%.

All the above data taken together provide ample evidence for structure 6a assigned to the tert. acetate.

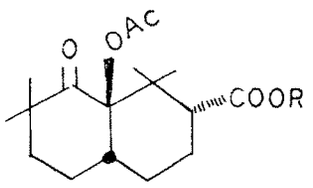
4. CHEMICAL TRANSFORMATION

In an early attempt to gain information about the structure of tert. alcohol (alcohol 8), the alcohol was exposed to perbenzoic acid in benzene for 5 days at 10°C. This reaction produced monoepoxide with the consumption of a molar equivalent of peracid. In the PMR spectrum (c.f. Fig 9) of the resulting epoxide the proton α to oxirane ring appears as a singlet at 3.08 ppm. In the epoxide 33b derived from 6b the dihedral angle of this proton with respect to the vicinal proton approaches 90°, whereas in the epoxide derived from 17 this dihedral angle would be ca 30°. Therefore, lack of vicinal coupling for the proton α-to the oxirane also supports structure 6b for the tert. alcohol.

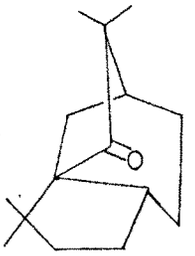
Treatment of tert. alcohol epoxide 33b with BF_3Et_2O in benzene gave a ketoalcohol (IR: CO 1730 cm^{-1}, OH 3460 cm^{-1}). Its PMR spectrum (Fig. 11) clearly indicates the absence of olefinic proton (TNM; negative test), but shows a signal for a proton on the carbon linked with oxygen (1H, singlet at 4.42 ppm). When the epoxyacetate 33a was treated with BF_3Et_2O under identical condition, an extra signal at 5.23 ppm (attributable to the proton α to acetoxy group) appeared as a singlet in the PMR spectrum of the product (Fig. 10). Hydrolysis of this ketoacetate afforded the same ketoalcohol obtained earlier from epoxyalcohol 33b. The appearance of a proton at the carbon bearing oxygen (secondary alcohol) suggests that a rearrangement has taken place.

These results are easily explained from structures 33a and 33b for the epoxides derived from tert. acetate 6a and alcohol 6b. The ketoacetate and ketoalcohol resulting from 33a and 33b can be assigned structures 34a and 34b respectively. The formation of the latter can be conceived as follows.

Treatment of epoxyalcohol 33b with BF_3Et_2O can generate a cation at C-6 (35) which, through a 'pinacol-type' rearrangement, can give rise to ketoalcohol 34b. The rearrangement is similar to the acid catalysed isomerization of tert. alcohol 6b to saturated ketone 31 (vide supra).



30 a R=H
30 b R=CH_3



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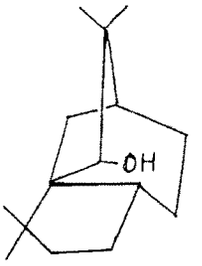

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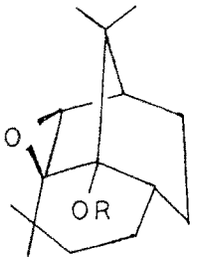
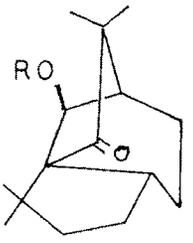
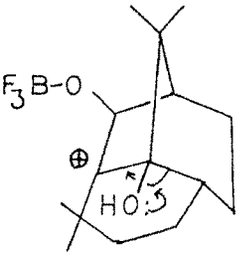


33 a R = Ac
33 b R = H



34 a R = Ac
34 b P = H



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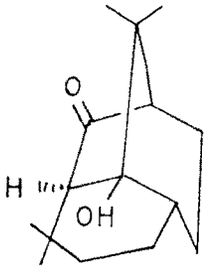

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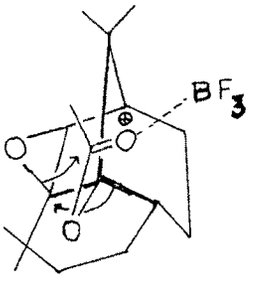

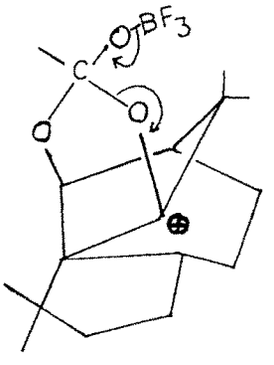

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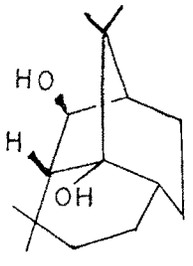

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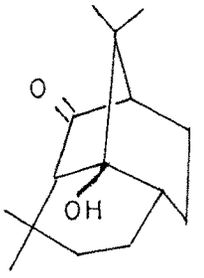

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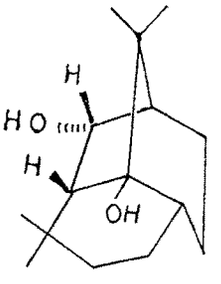

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CHART VI

One may expect the opening of epoxide 33a or 33b via endo-endo hydride migration from C-1 to C-6 leading to ketone 36, but such a process will be sterically very unfavourable due to angle distortion (inversion at C-6). This angle strain may be responsible for the epoxide 33a or 33b to follow an alternate route to form 34a and 34b.

The formation of ketoacetate 34a may be conceived to proceed through species 37 arising from the complexing of BF_3Et_2O with the oxygen of acetoxy carbonyl[14] followed by participation of the lone pair of electrons of epoxy oxygen with concomitant 'Wagner Meerwein' shift of C_8-C_7 bond in an S_N2-process, analogous to norbornyl cation[15]. The overall result is acyl group migration from one oxygen to another (Chart VI).

The hydroboration of 6b in tetrahydrofuran with one mole of diborane gave a diol 38 whose PMR (Fig. 38) shows resonance at 3.81 ppm (J= 6Hz) as a doublet for the proton α to OH. The diol 38 evidently arises from the tert. alcohol 6b by the attack of diborane from the less hindered side, i.e. exo-side. This diol was oxidized to ketoalcohol 39 with Jones reagent[16]. IR spectrum (Fig. 22) showed absorption corresponding to hydroxyl 3500 cm^{-1} and ketone 1727 cm^{-1}. The carbonyl frequency is

consistent with the value for substituted cyclopentanone derivatives. When ketone 39 was reduced with LAH, it affords an epimeric alcohol 40. The PMR spectrum (Fig. 14) shows a multiplet at 4.62 ppm for proton α to OH group. This signal collapsed into an expected double doublet (J_1= 7Hz, J_2= 10.5Hz), when PMR was recorded after adding a drop of trifluoroacetic acid. Simultaneously, the singlet at 1.04 ppm and the doublet at 1.43 ppm (J= 6.5 Hz) also disappear. It clearly dictates that proton α to OH group is coupled with nonexchangeable proton on hydroxyl. All these results nicely support the structure 6b for tert. alcohol (alcohol B).

5. EXPERIMENTAL

For general remarks refer Part B, Chapter I.

5.1. Alcohols A (7b) and B (6b)

These alcohols were prepared according to the procedure described earlier[2].

5.2. 8-Oxoneoisolongifolene (8)

Anhydrous CrO_3 (25 gm) was added portionwise into a stirred and cooled (5~10°) solution of pyridine (40 ml) in methylene chloride (300 ml) during 15 minutes and it was stirred for an additional 15 minutes. The unsaturated alcohol 9 (7.5 gm) in methylene chloride (100 ml) was added to this in one lot with efficient stirring and the mixture was stirred for an hour. Methylene chloride was evaporated under reduced pressure at room temperature (30-35°). The product was taken in di-isopropyl ether (20 ml x 10) and the organic extract was washed with water (30 ml x 3), 10% aq KOH (30 ml x 2), water (30 ml x 2), 5% aq HCl (40 ml x 2), 10% aq Na_2CO_3 (30 ml x 2) and water and then dried ($MgSO_4$). The residue after distillation gave ketone[3] 8 ;b.p. 84-86°/0.5 mm (5.1 gm). IR: CO, 1705, C=C 1625, 822, 815 cm^{-1} and PMR: $-\overset{|}{\underset{|}{C}}-Me$ (3H, s, 0.87 ppm; 3H, s, 1.03 ppm, 3H, s, 1.15 ppm; 3H, s, 1.18 ppm;); =CH (1H, d, 5.70 ppm, J= 3Hz).

5.3. 8 -Hydroxyneoisolongifolene (7b)

A solution of ketone 8 (4.02 gm) in ether (30 ml) was added dropwise to a stirred suspension of LAH (1.24 gm) in ether (30 ml) over a period of half an hour. The reaction mixture was stirred for an additional one hour and the product was worked up as usual. The residue (4.00 gm, m.p. 95-115°) obtained after solvent removal was chromatographed over silica gel (IIB, 115 gm, 2.5 cm x 50 cm).

Fr. 1	pet ether	(50 ml x 4)	nil
Fr. 2	20% benzene in pet ether	(40 ml x 7)	1.02 gm, solid m.p.41-43°
Fr. 3	20% benzene in pet ether	(40 ml x 3)	0.223 gm, solid mixture
Fr. 4	benzene	(40 ml x 6)	1.98 gm, solid m.p. 132-136°

Fr. 2. was crystallized upto constant m.p. 49.5-50.5°. IR (Fig. 15): ($CHCl_3$): OH 3520, 3460, C=C 1605, 811, 818 cm^{-1}; PMR (Fig. 3): ($CDCl_3$): $-\underset{|}{C}-Me$ (3H, s, 0.95 ppm; 3H, s, 1.04 ppm; 3H, s, 1.05 ppm; 3H, s, 1.17 ppm); CHOH (1H, illresolved triplet, 4.14 ppm, W_H = 9.5 Hz); =CH (1H, d, 5.73 ppm, J= 3Hz); microanalysis: $C_{15}H_{24}O$ requires C, 81.76; H, 10.98%; found C, 82.31; H, 11.10%, Mass: M^+(m/e)220. Its IR and PMR were superimposable with those of alcohol A obtained after solvolysis

of bromide 3 besides its mixed m.p. with alcohol A was not depressed.

Fr. 4 was crystallized from pet. ether; m.p. 141.5-142.5°. Its mixed m.p. with alcohol 9 was not depressed.

5.4. Treatment of tert. Alcohol with Acid.

tert. Alcohol 6b (815 mg) in 50% (v/v) aq. H_2SO_4 (1 ml) in dioxane (10 ml) was heated on a waterbath (95°C) for two hours under nitrogen atmosphere. When alcohol was isomerized completely (tlc), excess of dioxane (10 ml) was removed under reduced pressure, the residue was diluted with water (10 ml) and extracted with light petroleum ether (15 ml x 3). The organic extracts were washed with 5% aq. $NaHCO_3$ (10 ml x 2) followed by water and dried. Removal of solvent offered a free flowing liquid (805 mg), which was purified by passing through a column of silica gel. The resulting ketone 31 was distilled, b.p. 120-130° (bath)/2 mm (710 mg). IR (Fig.17): CO 1730 cm^{-1}. PMR (Fig. 6): $-\overset{|}{\underset{|}{C}}-Me$ each as singlet at 0.91, 0.99, 1.06 and 120 ppm; microanalysis: $C_{15}H_{24}O$ requires C, 81.76; H, 10.98%; found C, 81.17; H, 10.47%. Mass: M^+ (m/e) 220.

5.5. Reduction of Ketone 31 with LAH

The above ketone (31) (125 mg) in ether (10 ml) was

reduced with LAH in the usual manner. The usual work up offered a solid alcohol 32 (120 mg, m.p. 41-49°) which was crystallized from pet. ether (m.p. 69-70°, 50 mg). IR ($CHCl_3$): OH 3610 cm^{-1}. PMR (Fig. 7): $-\overset{|}{C}-Me$ each as singlet at 0.86, 0.95, 0.95, 1.02 ppm; CHOH (1H, bs, 3.40 ppm).

5.6. Ozonolysis of tert. Acetate (6a)

tert. Acetate (6a) (1.105 gm) was ozonized in MeOH (40 ml) at -7 ± 2° in 15 minutes. MeOH was removed under reduced pressure at room temperature (30 ± 1°). The ozonide was oxidized[17] in acetone with Jone's reagent (1 ml) at 0°. The reaction mixture was diluted with water (30 ml) and extracted with ether (25 ml x 3). The ether layer was washed with 10% aq. KOH (15 ml x 3) and then with water (15 ml x 3). The solvent was removed to offer a gummy neutral portion (780 mg). The aq. KOH portion after acidification with aq. phosphoric acid (50%) followed by extraction with ether (20 ml x 3) afforded an acid (m.p. 180-190°, 250 mg) which was further crystallized (MeCN) to get pure keto acid (30a) (m.p. 205-208°, 200 mg). IR: CO 1730, 1700 cm^{-1}. PMR ($CDCL_3$): $-\overset{|}{C}-CH_3$ 1.20, 1.20, 1.26, 1.31 ppm; CH_3CO (3H, s, 2.07 ppm), microanalysis: $C_{17}H_{26}O_2$ requires C, 65.80; H, 8.40%; found C, 65.76; H, 8.45%.

A small portion of the ketoacid (30a) (50 mg) was esterified with diazomethane in ether and the resulting ketoester was crystallized from petroleum ether m.p. 80-82°. IR (Fig. 18) (CCl_4): CO 1730, 1705 cm^{-1}. PMR (Fig. 8): $-\overset{|}{\underset{|}{C}}-Me$ each as singlet at 1.07, 1.07, 1.09, 1.20 ppm; CH_3CO (3H, s, 1.98 ppm); COOMe (3H, s, 3.58 ppm); microanalysis : $C_{18}H_{28}O_5$ requires C, 66.64; H, 8.70%; found C, 67.18, H, 9.11%.

5.7. Epoxidation of tert. Acetate (6a)

A solution of tert. acetate 6a (792 mg, 3.02 mmol.) in benzene (2 ml) was treated with perbenzoic acid (510 mg, 3.6 mmol.) in benzene (25 ml) at 10° and kept at this temperature for 8 days. When acetate was consumed completely (tlc), the benzoic acid was extracted with 10% aq. Na_2CO_3 (10 ml x 4). The organic phase was washed till neutral with water (10 ml x 2). Solvent removal under reduced pressure gave a residue (855 mg), which was distilled to give 33a (710 mg), b.p. 110-120° (bath)/ 0.5 mm. IR (Fig. 19): (liq.): CO 1740, epoxide 895, 878, 775 cm^{-1}. PMR (Fig. 9): $-\overset{|}{\underset{|}{C}}-Me$ each as singlet at 0.77, 1.04, 1.09, 1.15 ppm; CH_3CO (3H, s, 2.0 ppm); CHOO (1H, s, 3.07 ppm), 1H, m, spanned between 3.26-3.61 ppm. Microanalysis: $C_{17}H_{26}O_3$ requires C, 73.34; H, 9.35; found C, 73.06; H, 9.39%.

5.8. Epoxidation of tert. Alcohol

tert. Alcohol (6b) (600 mg) was treated with perbenzoic acid (500 mg) in benzene (20 ml) and kept at 10° for five days. The usual work up (as described above) gave a solid residue (605 mg, m.p. 82-88°) which was crystallized (pet. ether) to give epoxyalcohol (33b) (m.p. 101.5-102.5°, 580 mg). IR (CCl_4): 3510, 3400, epoxide 1250, 925, 910, 860 cm^{-1}. PMR: $-\overset{|}{C}-$Me each as singlet at 0.76, 0.83, 1.14, 1.28 ppm, CHOC (1H, s, 3.03 ppm). Microanalysis: $C_{15}H_{24}O_2$ requires C, 76.22; H, 10.24; found C, 76.72; H, 9.66%.

5.9. Action of $BF_3.Et_2O$ on tert. Acetate Epoxide (33a)

$BF_3.Et_2O$ (0.1 ml) was added to a cooled (10°) solution of tert. acetate epoxide 33a (410 mg) in benzene (5 ml) and kept at that temperature for one hour. The reaction was worked up by washing with 5% aq. Na_2CO_3 (5 ml x 3) followed by water (5 ml x 2). The residue (500 mg) obtained, after removal of solvent, was purified by passing through a column of alumina (N/III, 15 gm, 1 cm x 13 cm) to get pure keto acetate 34a (350 mg) which was crystallized (pet. ether) m.p. 111.5-112.5°; IR (Fig. 21): ($CHCl_3$): CO 1735, 1730, ester 1250 cm^{-1}. PMR (Fig. 10): $-\overset{|}{C}-$Me each as singlet at

0.90, 1.09, 1.11, 1.28 ppm; CH_3CO (3H, s, 2.0 ppm), CHOAc (H, s, 5.23 ppm). Microanalysis: $C_{17}H_{26}O_3$ requires C, 73.35; H, 9.35; found; C, 73.51; H, 9.56%.

5.10. Hydrolysis of Ketoacetate (34a)

Ketoacetate (34a) (105 mg) was refluxed with 10% alc. KOH in ethanol (2 ml) under nitrogen for four hours. The reaction mixture was neutralized with acetic acid, diluted with water (5 ml) and extracted with ether (5 ml x 3). The ethereal layer was washed with water and dried. The residue was crystallized (pet. ether and methylene chloride), m.p. 178-180°. Its PMR and IR were identical with those of the ketoalcohol (34b) derived from tert. alcohol epoxide (vide infra).

5.11. Action of $BF_3.Et_2O$ on tert. Alcohol Epoxide (33b).

To a cooled solution of epoxyalcohol (33b) (200 mg) in benzene (5 ml) was added a drop of $BF_3.Et_2O$ and the mixture was kept at 10° for 1 hour. The reaction mixture was washed with 5% aq. $NaHCO_3$ (2 ml x 2) and washed till neutral with water (2 ml x 2). It was crystallized (pet. ether methylene chloride) m.p. 178-180°. IR ($CHCl_3$): CO 1730, OH 3610, 3490, 1095, 1055 cm^{-1}. PMR (Fig. 11) ($CDCl_3$): $-\overset{|}{C}-Me$ each as singlet at 1.13, 1.14, 1.26, 1.36 ppm; CHOH (1H, s, 4.42 ppm). Microanalysis: $C_{15}H_{24}O_2$ requires C, 76.22; H, 10.24; found C, 75.84; H, 9.76%.

5.12. Hydroboration of tert. Alcohol (6b)

Diborane was generated by slow addition of $NaBH_4$ (1.5 gm) in diglyme (75 ml) to an agitated solution of BF_3Et_2O (15 ml) in diglyme (20 ml) at room temperature (35 ± 1°). The generated diborane was passed into a cold (0-5°) solution of tert. alcohol 6b (1.8 gm) in THF (30 ml) during 2.5 hours. After stirring for an additional one hour at room temperature, the excess diborane was destroyed by careful addition of water (5 ml). The boronane ester was oxidized by adding 3N. NaOH (5 ml) followed by 38% H_2O_2 (4 ml). It was stirred at room temperature for about 10 hrs, then diethyl ester (30 ml) was added and the organic layer was separated. The aqueous layer was saturated with sodium chloride and extracted twice with ether (20 ml x 2). The organic extracts were washed till neutral, with water and dried. The residue (1.9 gm, as sticky mass) was purified by passing through silica gel (II, A, 70 gm, 2 cm x 42 cm):

Frac. 1	pet ether	(20 ml x 2)	nil
Frac. 2	pet. ether: benzene(1:1)	(20 ml x 2)	nil
Frac. 3	benzene	(20 ml x 2)	10 mg rejected.
Frac. 4	benzene: ethylacetate (95:5)	(20 ml x 3)	230 mg solid
Frac. 5	benzene: ethyl-acetate (80:20)	(20 ml x 1)	15 mg rejected.

Frac. 6	benzene: ethyl-acetate (80:20)	(20 ml x 3)	1.48 gm, solid m.p. 85-90°

Frac. 4 is homogeneous on tlc, since it is neither soluble in $CDCl_3$ nor in CCl_4, its PMR could not be recorded.

Frac. 6 was crystallized (MeCN) to give diol 38; m.p. 90-92°, IR ($CHCl_3$): OH 3610, 3480, 1020 cm^{-1}. PMR (Fig.13) ($CDCl_3$): $-\overset{|}{\underset{|}{C}}-Me$ each as singlet at 0.90, 1.05, 1.13, 1.17 ppm; CHOH (1H, d, 3.81 ppm; J = 6Hz). Microanalysis: $C_{15}H_{26}O_2$ requires C, 75.58; H, 11.00; found C, 75.62; H, 10.18%.

5.13. Oxidation of Diol 38 with Jone's Reagent

To the cooled solution of diol 38, (180 mg) in acetone (2 ml) was added Jone's reagent (0.2 ml) at 5°C and then kept at that temperature for 30 minutes. It was diluted with water and extracted with benzene: pet. ether (1:1, 15 ml x 3). The Organic layer was washed with aqueous $NaHCO_3$ and then with water till neutral. The removal of solvent followed by crystallization (pet. ether) gave ketoalcohol 39 (m.p. 135-137°, 175 mg). IR (Fig. 22) ($CHCl_3$): CO 1730, OH 3605, 3480, 1140, 1058 cm^{-1}. PMR (Fig. 12): $-\overset{|}{\underset{|}{C}}-Me$ each as singlet at 1.02, 1.07, 1.11, 1.26 ppm. Microanalysis: $C_{15}H_{24}O_2$ requires C, 76.22; H, 10.24; found C, 76.08; H, 10.13%.

5.14. Reduction of Ketoalcohol (39) with LAH

To a stirred slurry of LAH (150 mg) in ether (10 ml)

(at 10 ± 2°) was added dropwise a solution of ketoalcohol (39)(250 ml) in ether (15 ml) during 5 minutes. It was stirred for half an hour and worked up as usual to give diols 38 and 40 (210 mg). Both the alcohols were resolved over silica gel (10 mg, IIA, 0.7 cm x 14 cm) by eluting 40 (150 mg) with benzene (10 ml x 3) and 38 (m.p. 90-92°) (45 mg) with 20% ethyl-acetate in benzene (10 ml x 2). Alcohol 40 was crystallized, m.p. 133-135°. IR (nujol): OH 3400, 1040 cm^{-1}. PMR (Fig. 14): ($CDCl_3$): $-\overset{|}{\underset{|}{C}}-Me$ each as singlet at 0.90, 0.94, 1.16, 1.24 ppm; CHOH (1H, m, 4.62 ppm) (after trifluoroacetic acid treatment, multiplet at 4.62 resolved into dd, J_1 = 7 Hz, J_2 = 10.5 Hz and singlet at 1.04 ppm and doublet at 1.43 ppm, J = 6.5 Hz disappeared), microanalysis: $C_{15}H_{26}O_2$ requires C, 75.58, H, 11.0 found C, 75.43; H, 10.80%.

6. REFERENCES

1. (a) U.R. Nayak and Sukh Dev, Tetrahedron 8, 42 (1960).

   (b) R. Ranganathan, U.R. Nayak, T.S. Santhanakrishnan and Sukh Dev, Tetrahedron 26, 621 (1970).

2. See Part B, Chapter I [illegible].

3. T.S. Santhanakrishnan, R.R. Sobti, U.R. Nayak and Sukh Dev, Tetrahedron 26, 657 (1970).

4. (a) L.M. Jackman and S. Sternhell, Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry, pp. 115-116, Pergamon London (1969).

   (b) H.S. Gutowsky, V.D. Mochel and B.G. Sommers, J. Chem. Phys. 21, 279 (1953).

5. (a) see ref.(4a), pp. 163-164.

   (b) J.N. Shoolery and M.T. Rogers, J. Am. Chem. Soc. 80, 5121 (1958).

6. c_f (a) L.A. Yanavoskaya and Kh. Shakhidayatov. Russ. Chem. Rev. 39, 859 (1970).

   (b) Y. Sasson and G.L. Rempel, Tetrahedron Letters, 4133 (1974).

   (c) A.S. Dreiding and J.A. Hartman, J. Am. Chem. Soc. 78, 1216 (1956).

7. (a) R.L. Cargill and J.U. Crawford, J. Org. Chem. 35, 356 (1970).

   (b) R.L. Cargill, D.M. Pond and S.G. LeGrand, J. Org. Chem. 35, 359 (1970).

8. G.W. Klumpp, E. Ellen and F. Bickelhaupt, Rec. Trav. Chim. Pays. Bas. 88, 474 (1969).

9. H. Tanida, K. Tori and K. Hitahanoki, J. Am. Chem. Soc., 89, 3212 (1967).

10. (a) B. Capon, Quart. Rev. 18, 45 (1964).

(b) A.F. Thomas, Chem. Comm. 1054 (1970).

11. J.W. Wilts, C.T. Parsons, C.A. Schneider, D.G. Schultenover, S.J. and W.J. Wagner, J. Org. Chem. 33, 694 (1968).

12. For review see

(a) B.C. Mayo, Chem. Soc. Rev. 2, 49 (1973).

(b) Nuclear Magnetic Shift Reagents (Ed. R.E. Sievers), Academic Press, New York (1973).

13. A.F. Cockerill and D.M. Rockham, Tetrahedron Letters 5149, 5153 (1970).

14. For acetoxy group participation see

(a) S. Julia and B. Furer, Bull. Soc. Chim. Fr. 1106 (1966)

(b) N.S. Leads, D.K. Fukushima and T.F. Gallaghar, J. Am. Chem. Soc. 76, 2943 (1954).

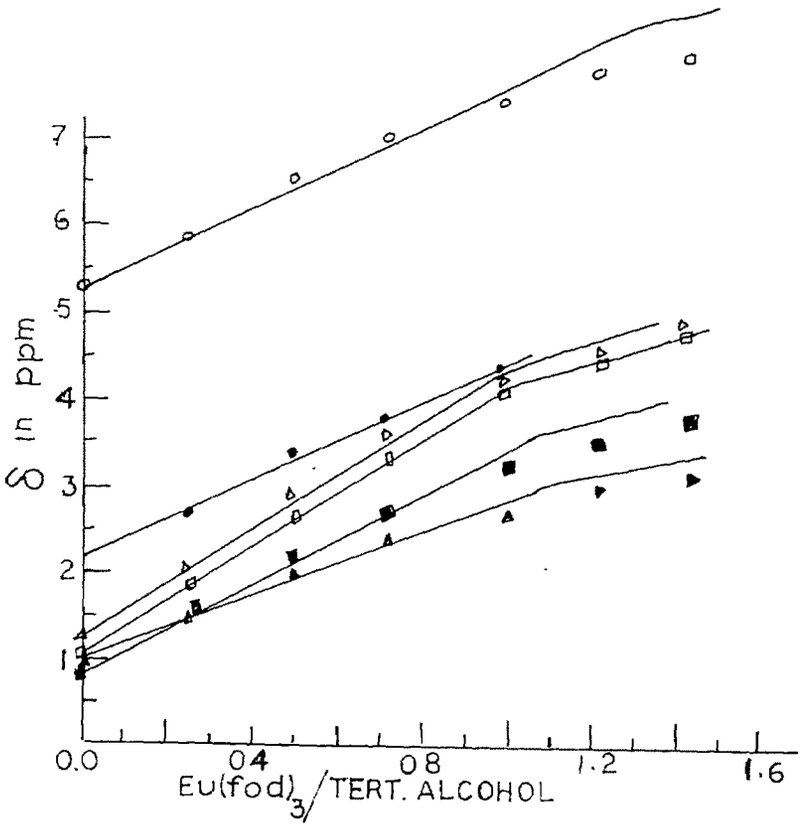
(c) A.H. Soloway, W.J. Considine, D.K. Fukusuma and T.F. Gallaghar, J. Am. Chem. Soc. 76, 2941 (1954).

(d) K.L. Williamson and W.S. Johnson, J. Org. Chem. 26, 4563 (1961).

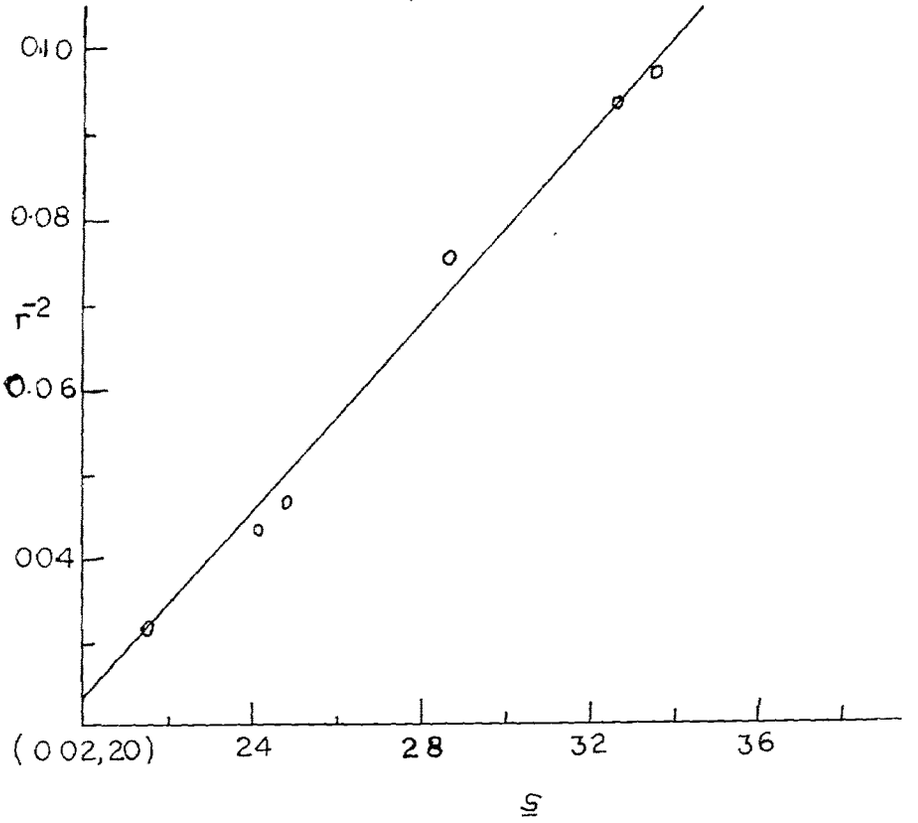
15. G.D. Sargent in Carbonium Ions (Eds. G.A. Olah and P.von R. Schleyer) vol III pp. 1099-1200, Wiley Interscience, New York (1972).

16. K. Bowden, I.M. Helbron, E.R.H. Jones and D.C.L. Weedon, J. Am. Chem. Soc. 39 (1946).

17. A.S. Narula, and Sukh Dev, Tetrahedron Letters, 1733 (1969).



A : THE RELATIONSHIP BETWEEN CHEMICAL SHIFT AND THE MOLAR RATIO OF $Eu(fod)_3$/TERT ALCOHOL(6b)



B. GRAPH r^{-2} VS S

FIG. 1

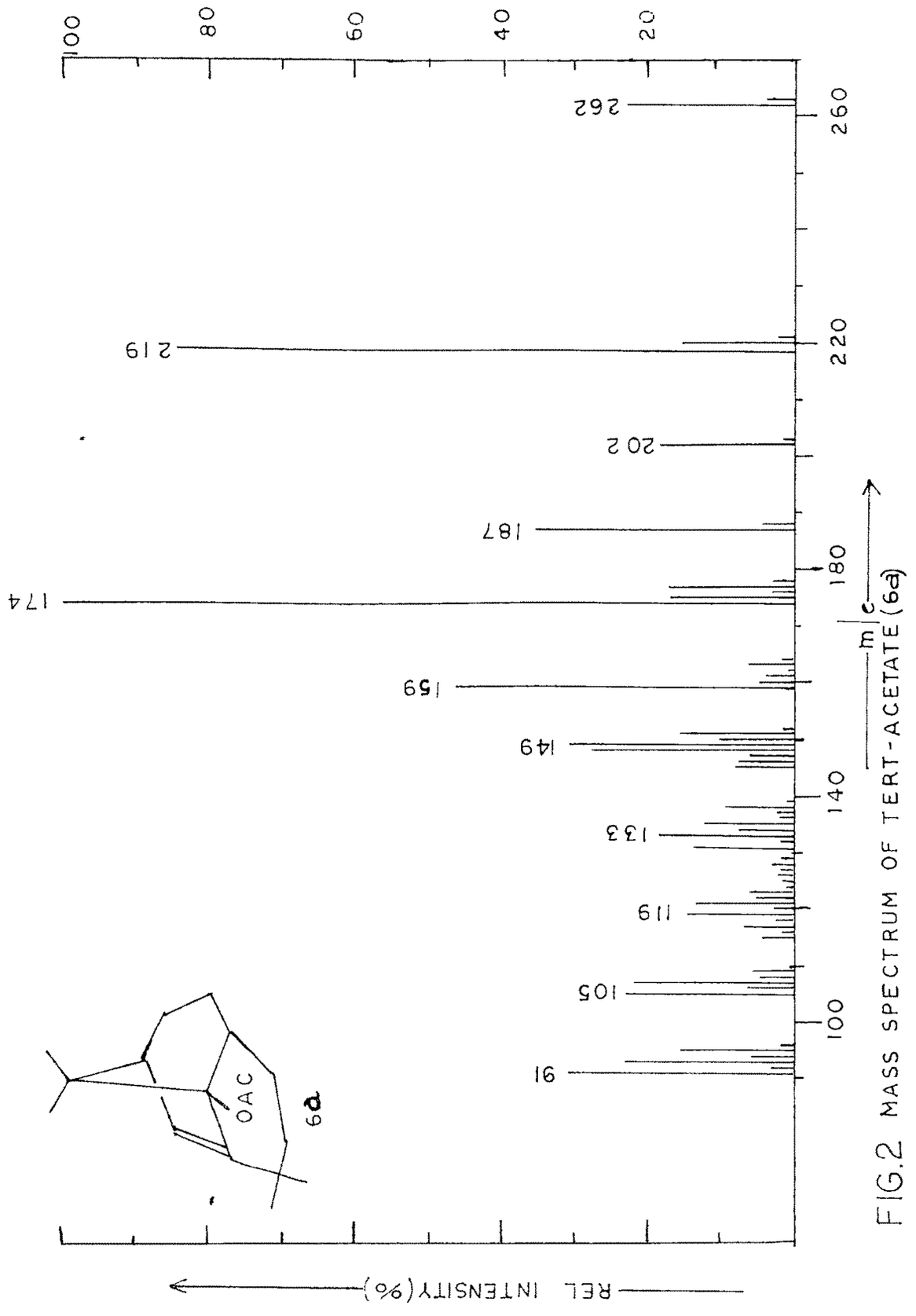


FIG.2 MASS SPECTRUM OF TERT-ACETATE (6a)

FIG. 3

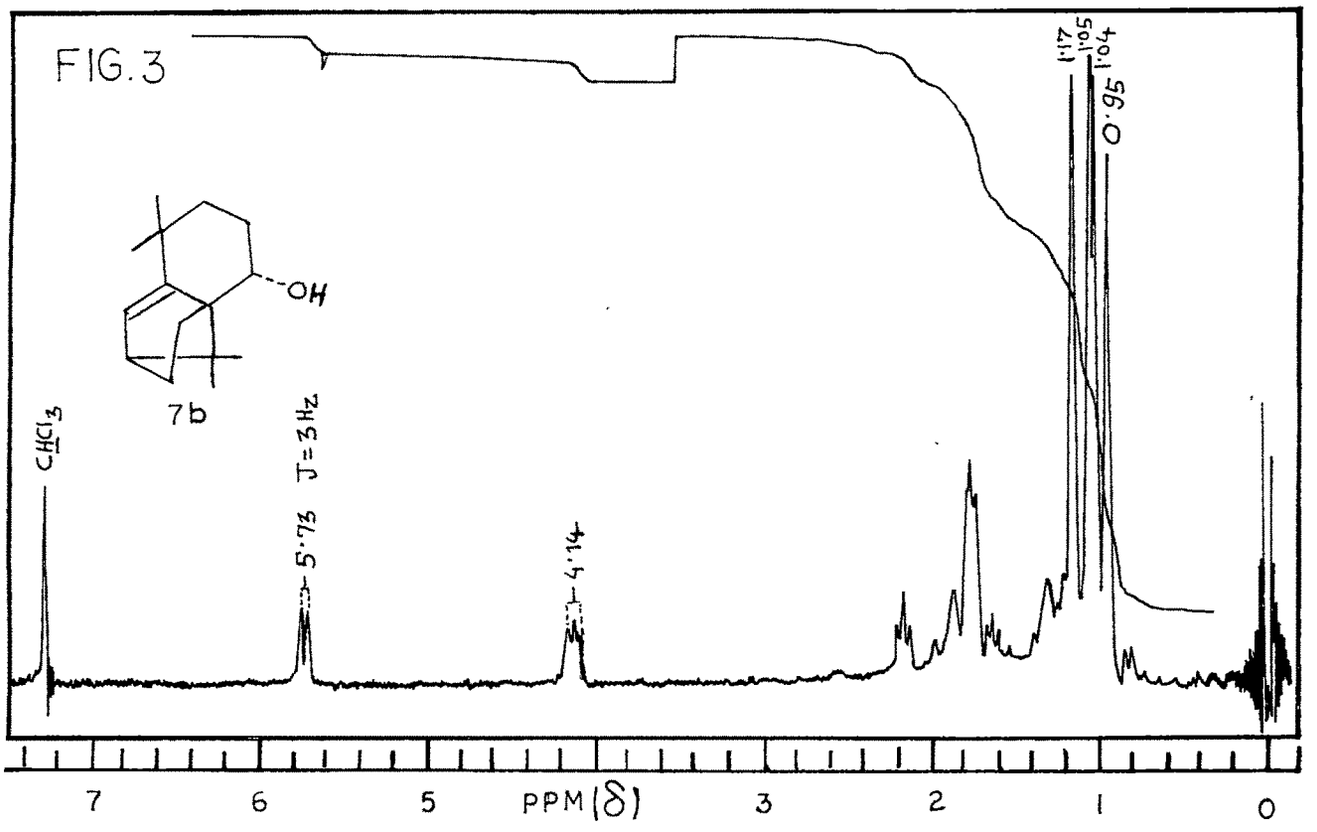

OH
7b
CHCl3
5·73 J=3Hz
4·14
1·17
1·05
1·04
0·95
7
6
5
PPM(δ)
3
2
1
0

FIG. 4

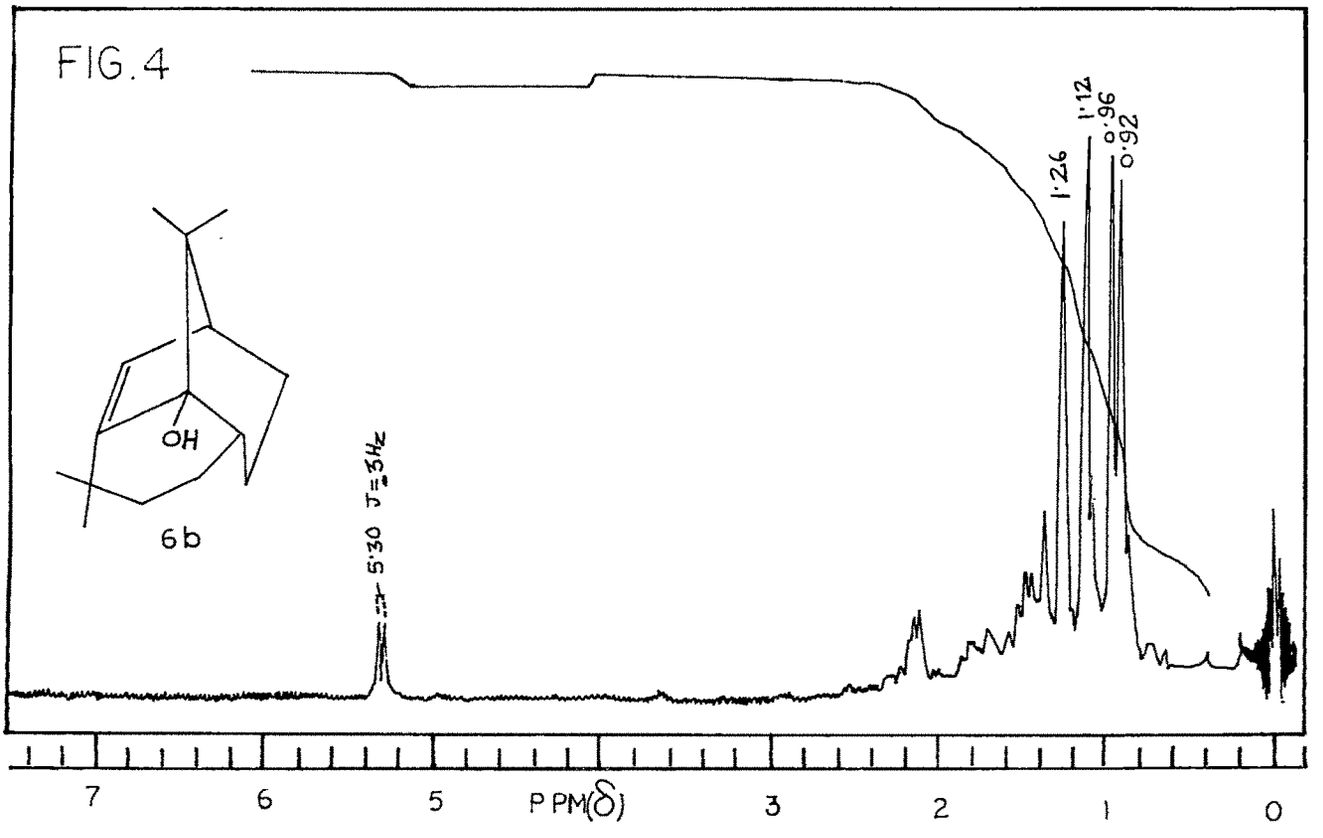
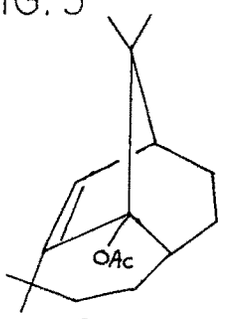

OH
6b
5·30 J=3Hz
1·26
1·12
0·96
0·92
7
6
5
PPM(δ)
3
2
1
0

FIG. 5



6a

FIG 6

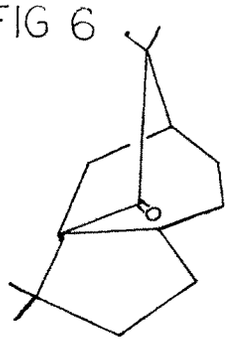


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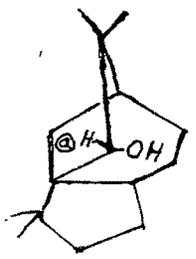
FIG. 7



32

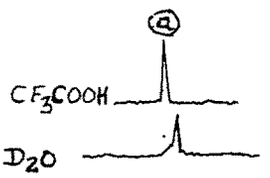
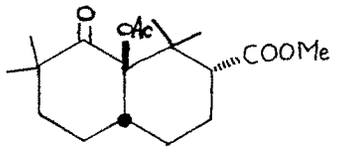
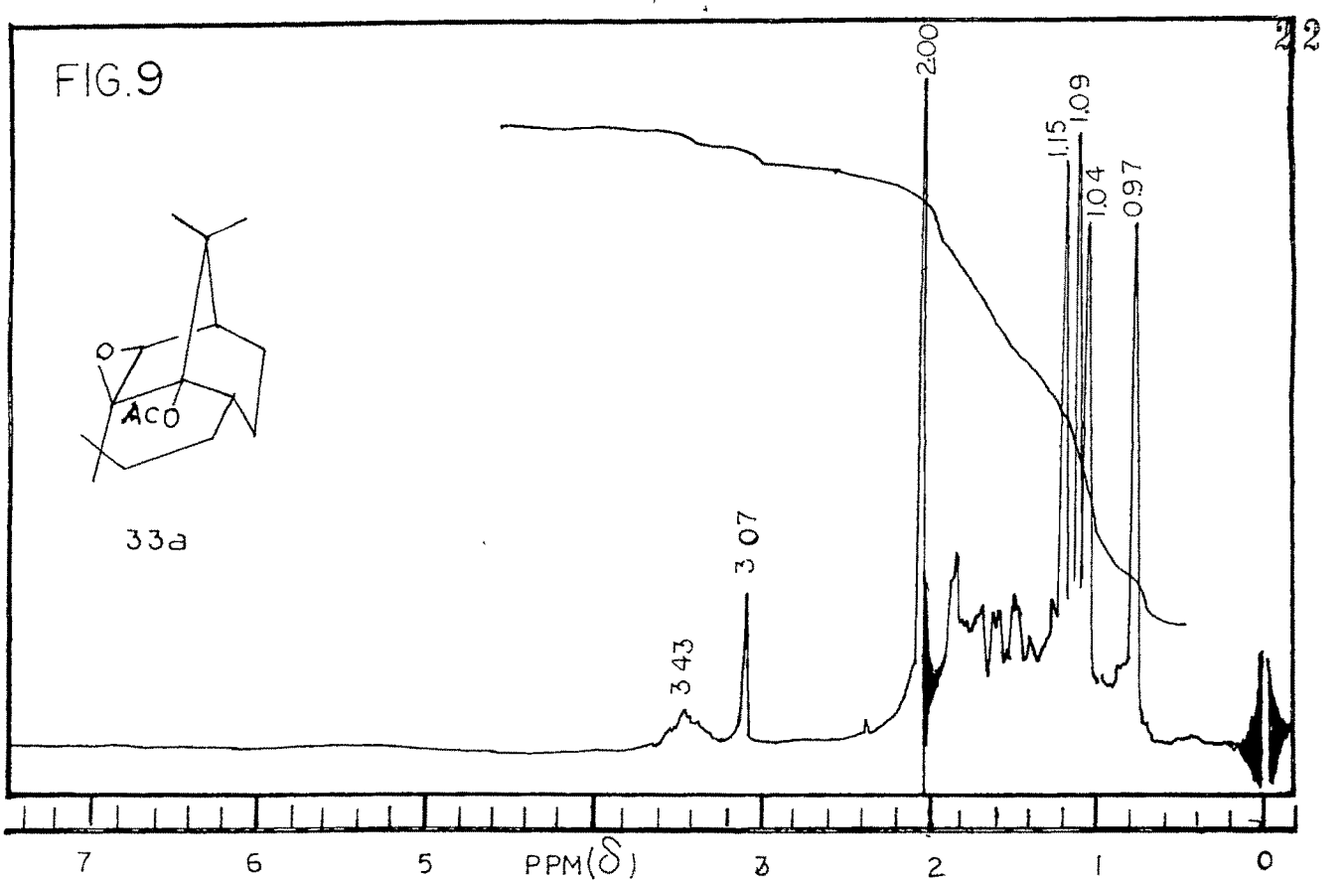


FIG. 8



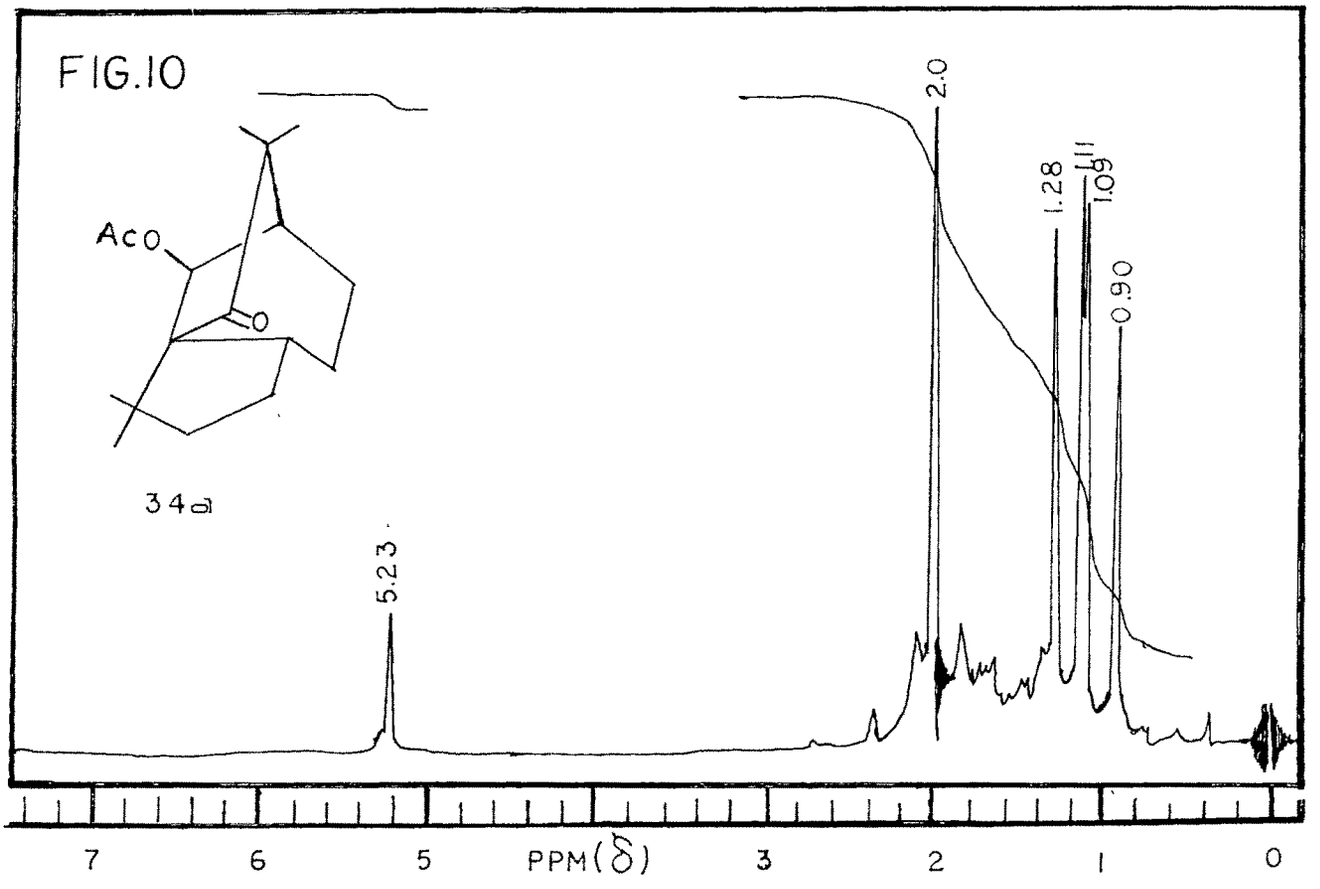
30a

FIG.9



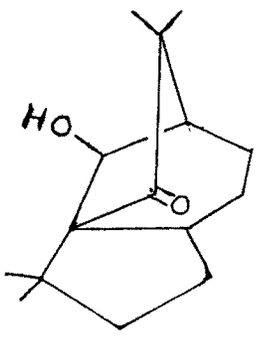
33a

FIG.10



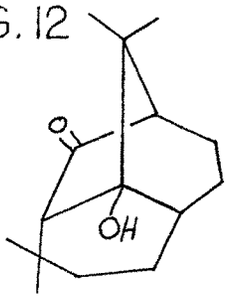
34a

FIG. 11



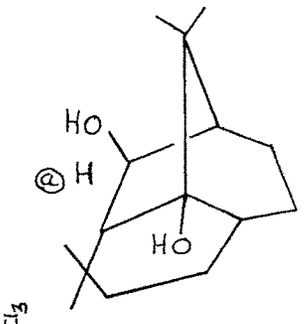
34b

FIG. 12



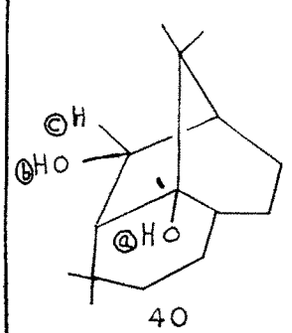
39

FIG. 13

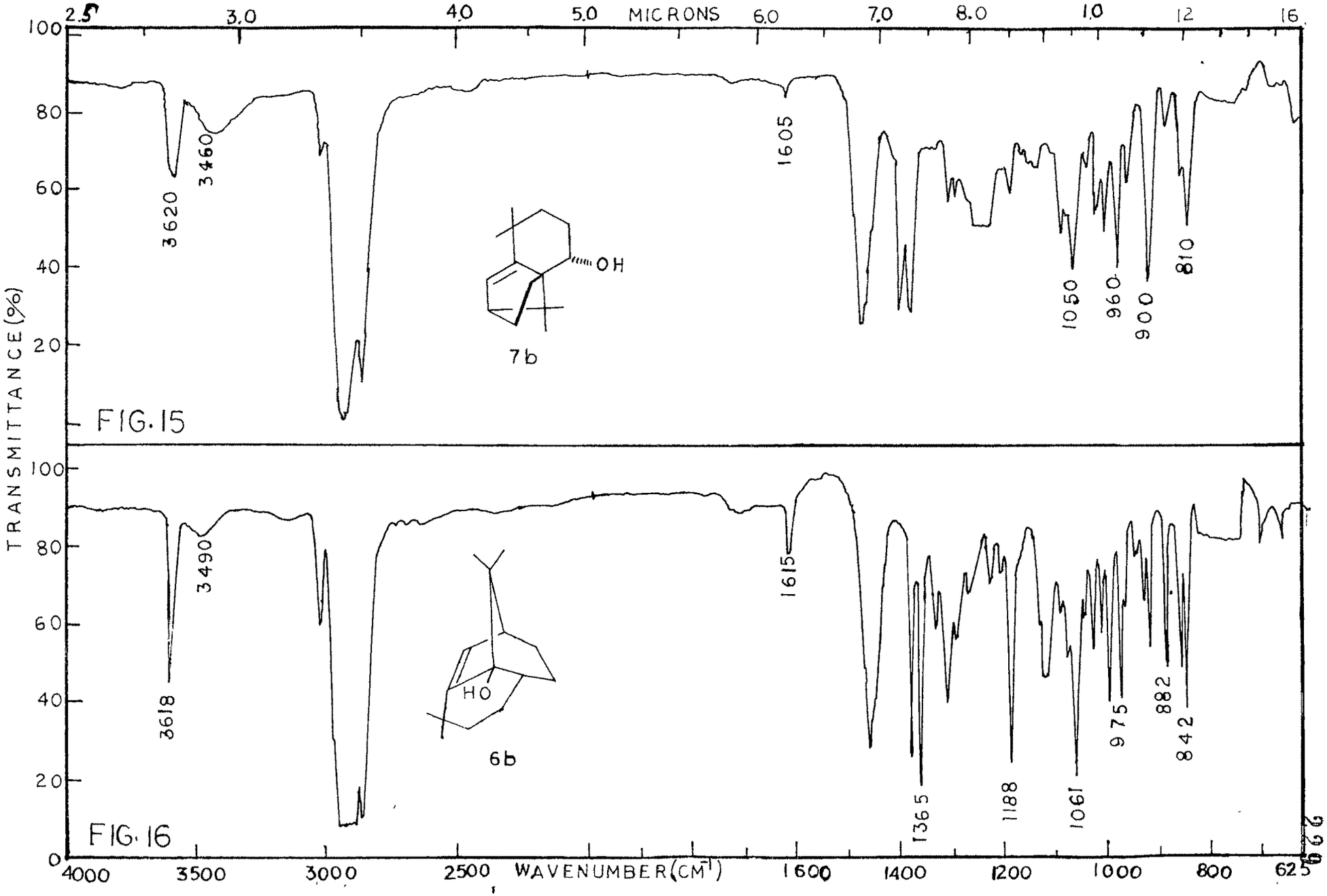


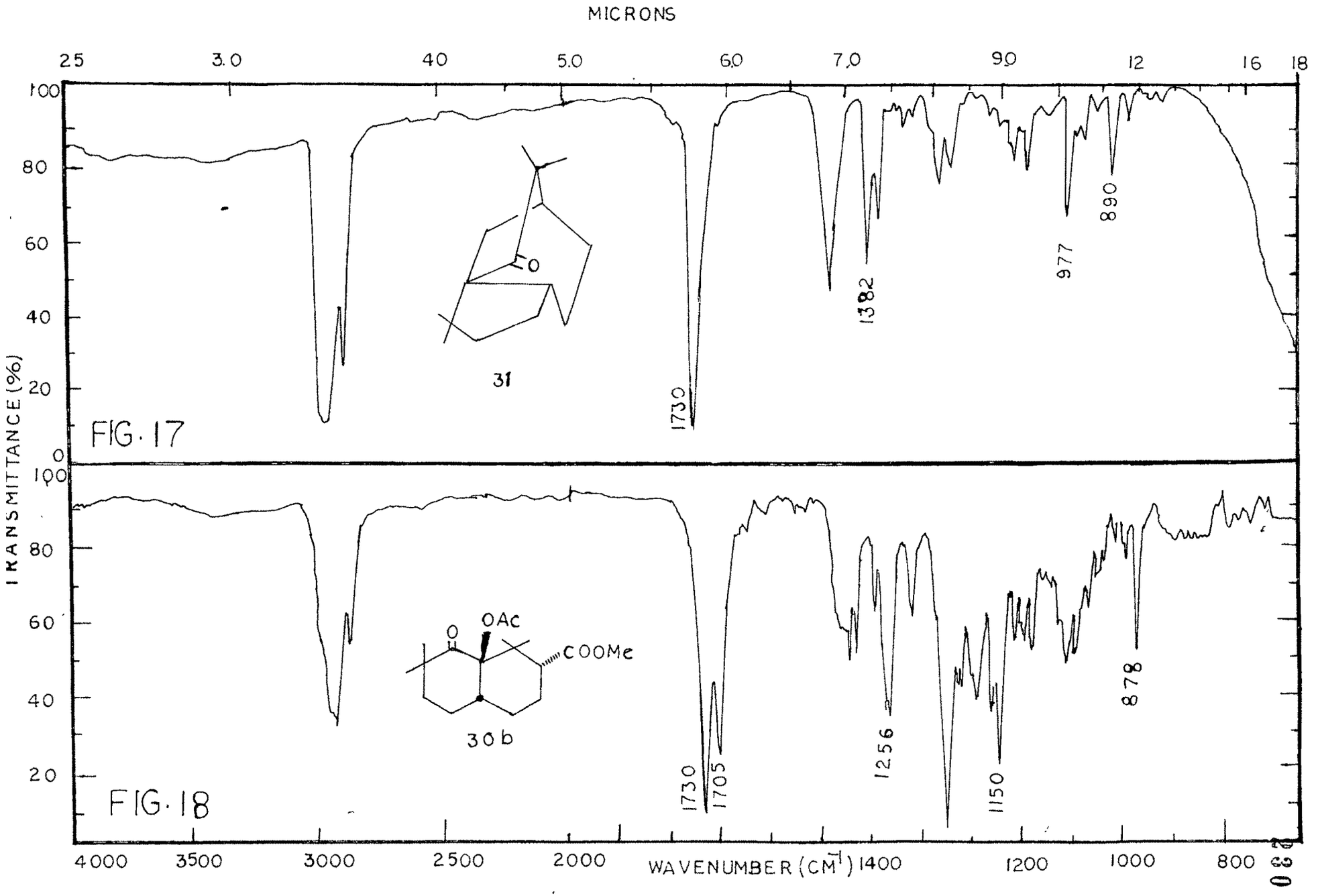
38

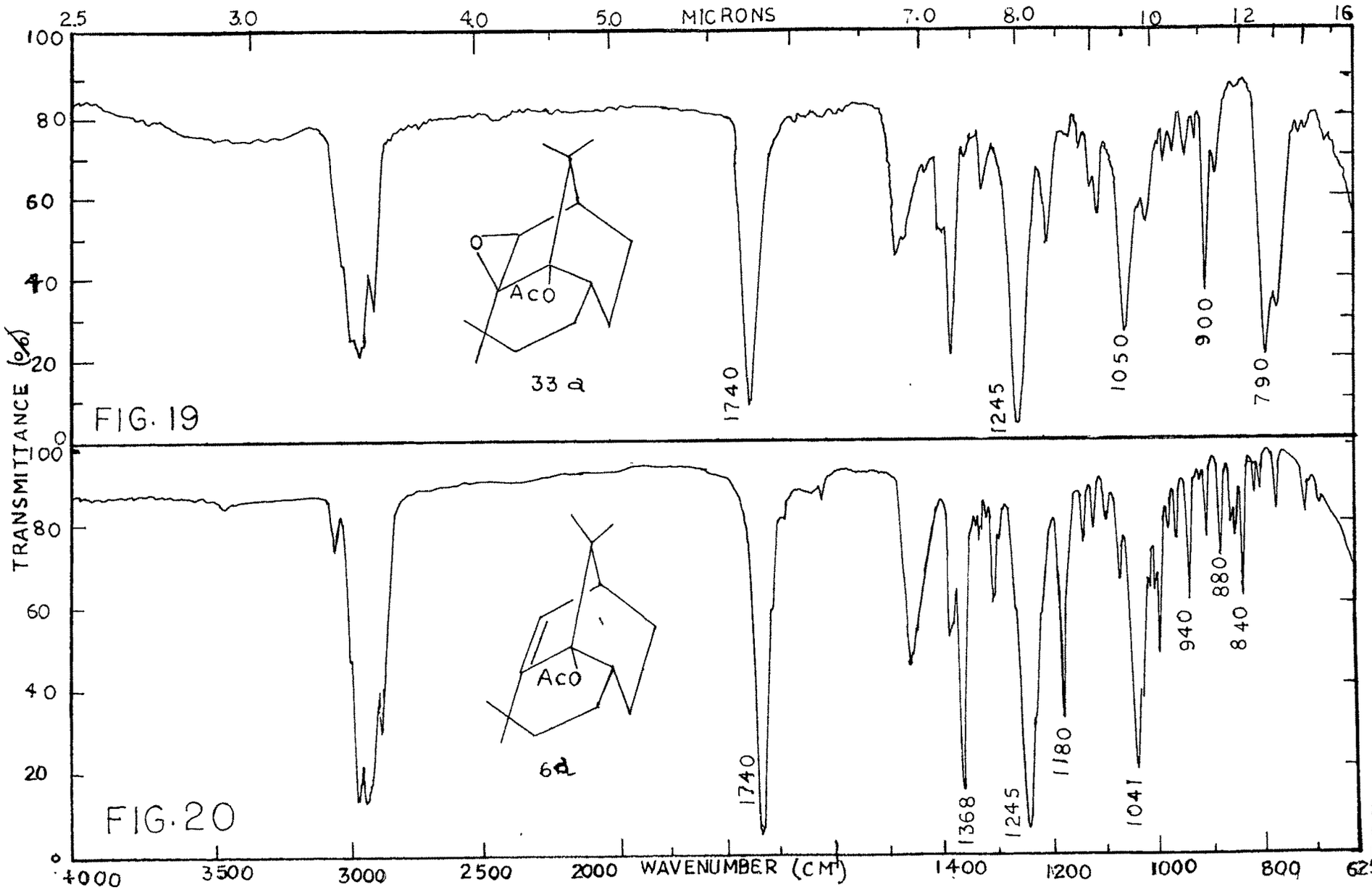
FIG 14

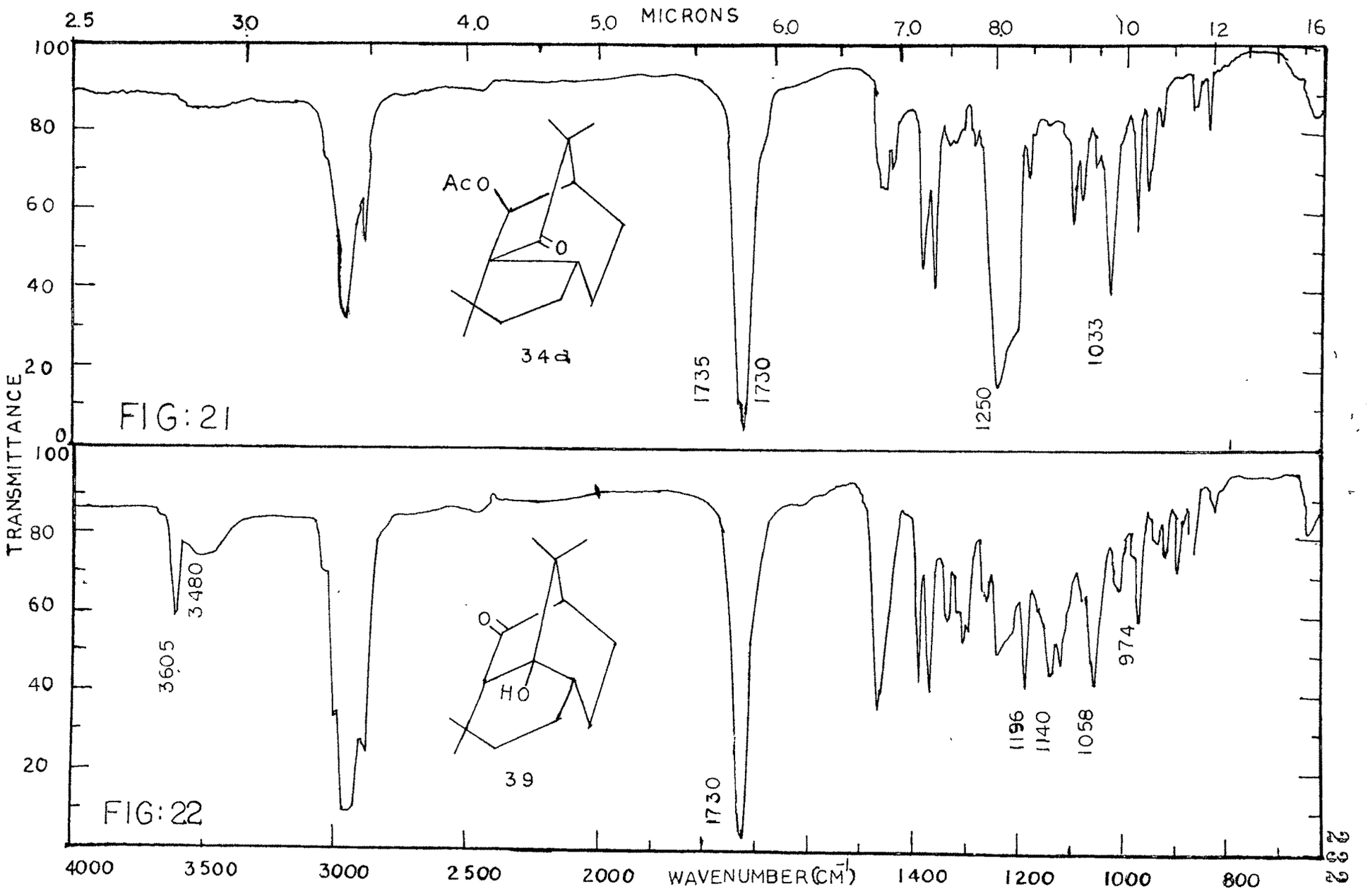


40


2.5
3.0
4.0
5.0
MICRONS
6.0
7.0
8.0
10
12
16
100
80
60
40
20
TRANSMITTANCE (%)
3620
3460
1605
1050
960
900
810
OH
7b
FIG. 15
3618
3490
1615
1365
1188
1061
975
882
842
HO
6b
FIG. 16
0
4000
3500
3000
2500
WAVENUMBER (CM⁻¹)
1600
1400
1200
1000
800
625


MICRONS
2.5
3.0
4.0
5.0
6.0
7.0
9.0
12
16
18
100
80
60
40
20
0
TRANSMITTANCE (%)
1730
1382
977
890
O
31
FIG. 17
OAc
O
COOMe
30b
1730
1705
1256
1150
878
FIG. 18
4000
3500
3000
2500
2000
WAVENUMBER (CM⁻¹)
1400
1200
1000
800


2.5
3.0
4.0
5.0
MICRONS
7.0
8.0
10
12
16
100
80
60
40
20
0
TRANSMITTANCE (%)
AcO
O
33 a
1740
1245
1050
900
790
FIG. 19
AcO
6a
1740
1368
1245
1180
1041
940
880
840
FIG. 20
4000
3500
3000
2500
2000
WAVENUMBER (CM⁻¹)
1400
1200
1000
800
625


2.5
3.0
4.0
5.0
MICRONS
6.0
7.0
8.0
10
12
16
100
80
60
40
20
0
TRANSMITTANCE
AcO
O
34d
1735
1730
1250
1033
FIG: 21
3605
3480
O
HO
39
1730
1196
1140
1058
974
FIG: 22
4000
3500
3000
2500
2000
WAVENUMBER (CM⁻¹)
1400
1200
1000
800