CHAPTER III

HYDROBORATION OF β - HIMACHALENE AND SOLVOLYSIS OF HIMACHALOL p - NITROBENZOATE

HYDROBORATION OF β-HIMACHALENE AND SOLVOLYSIS OF HIMACHALOL p-NITROBENZOATE

Solvolysis of allohimachalol tosylate (I) has been shown[1] to furnish a mixture of α-himachalene (II)[2], β-himachalene (III)[2], himachalol (III)[3] and allohimachalol (V)[1]/ Fig.1. It was thought of interest to study the solvolysis of a suitable derivative of himachalol (IV) and epihimachalol (VI)[4]. It was envisaged that himachalol derivative (XIV) on solvolysis might give allohimachalol as one of the products which will constitute a biogenetic-type synthesis of allohimachalol (Fig.2). On the other hand epi-himachalol derivative can possibly lead to longiborane/longifolane skeletons[5] (Fig.3). In the first instance, we thought of preparing epi-himachalol from β-himachalene. In the first part of this chapter, are described the attempts directed towards the synthesis of epi-himachalol while in the second part we describe the solvolysis of himachalol p-nitrobenzoate.

Attempted preparation of epihimachalol from β-himachalene

In the reaction of β-himachalene with per acid, it is known[6] that fully substituted olefinic linkage is attacked preferentially. It was hoped that the hydroboration of β-himachalene with limited amount of diborane would generate olefinic alcohols, of which there would be at least some product development resulting from the

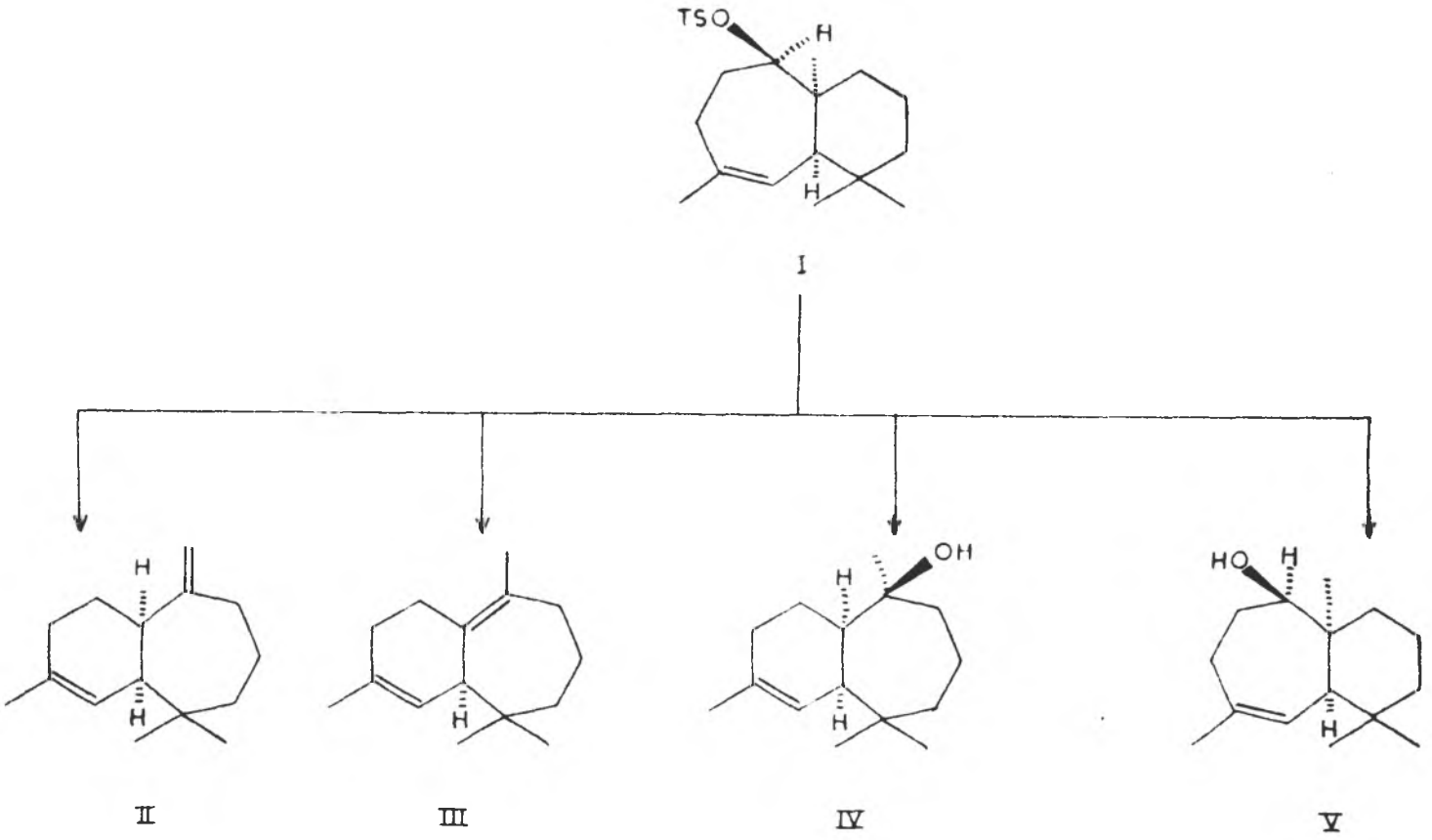


FIG. 1 SOLVOLYSIS PRODUCTS OF ALLOHIMACHALOL TOSYLATE(1)

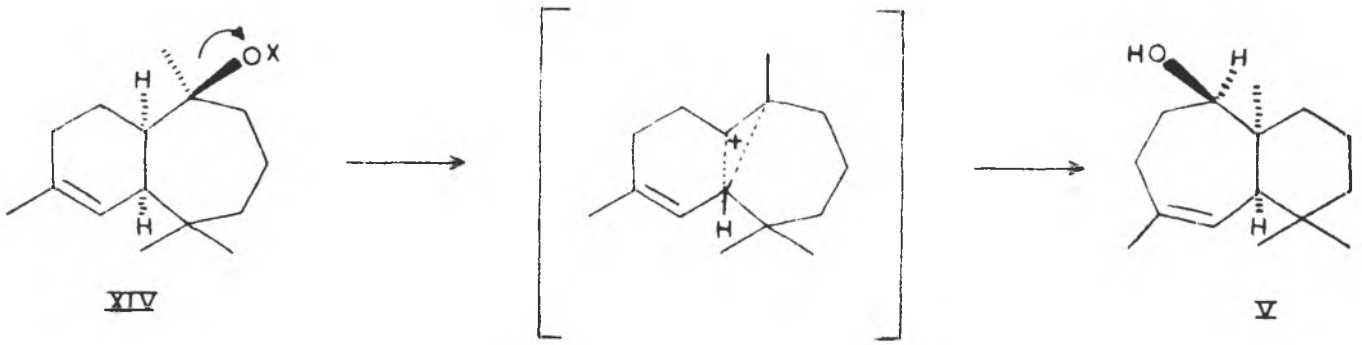


FIG. 2 POSSIBLE FORMATION OF ALLOHIMACHALOL FROM SOLVOLYSIS OF HIMACHALOL DERIVATIVE

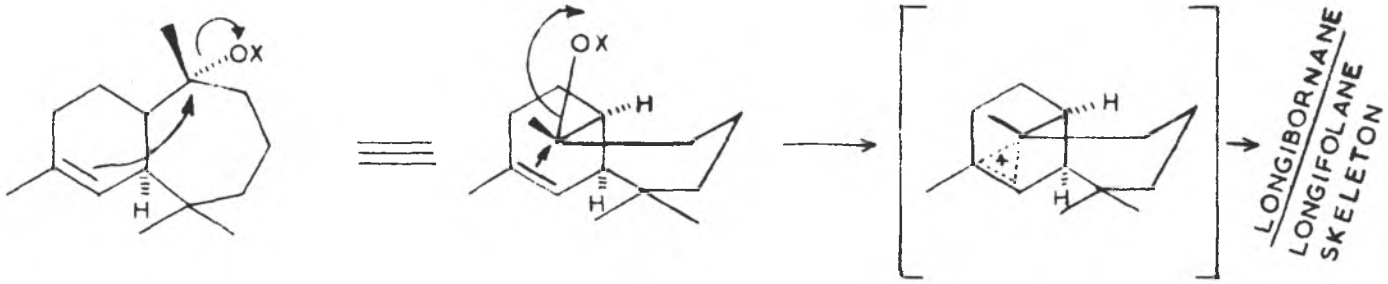
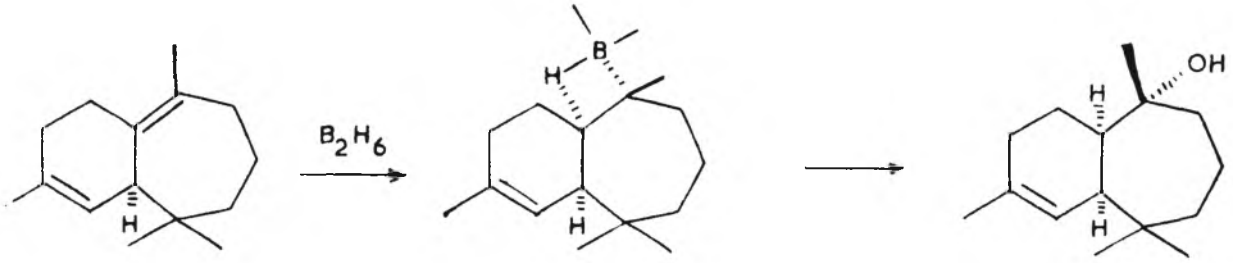


FIG. 3 – POSSIBLE PRODUCTS FROM SOLVOLSIS OF EPI-HIMACHALOL DERIVATIVE.

attack at the tetrasubstituted double bond. Thus it was conceived that monohydroboration of β-himachalene might possibly generate epihimachalol (Fig.4).

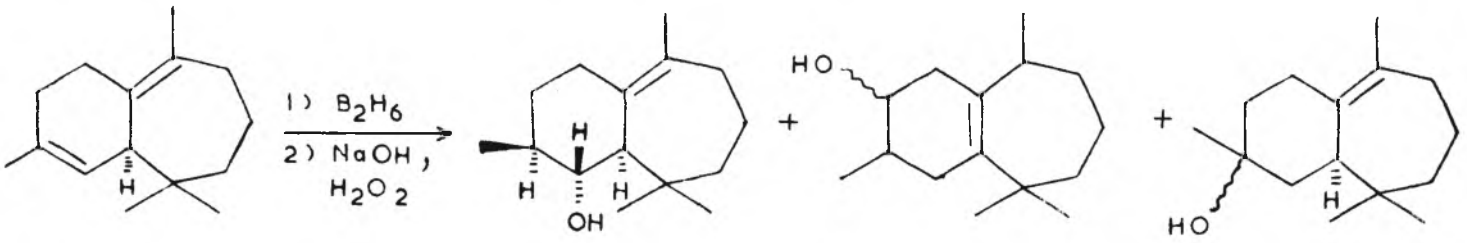
With the above objective monohydroboration[7] of β-himachalene was carried out with diborane (dissolved in THF) at 0° (ice bath) and the resulting organoborane was oxidised with alkaline hydrogen peroxide (30%), to furnish a mixture of mono alcohols and diols (IR, TLC). The total oxidised product was separated by chromatography into mono alcohols and diol cuts (TLC). The mono-alcohol fraction was further separated by systematic chromatography and three pure compounds were isolated. These are discussed below. The diol fraction was not investigated.

Alcohol-1 (RRf = 1.00), analyses for $C_{15}H_{26}O$ (M^+, m/e = 222) is an unsaturated alcohol (TNM test: yellow colour). IR spectrum (Fig.6): OH 3300, 1030 cm^{-1}. Its PMR spectrum (Fig.7) shows signals assignable to two quaternary Me's (two 3H, s, 0.82 and 1.05 ppm); $C\underline{H}_3.C=CH$ (3H, d, 1.66 ppm, J = 1 Hz); $C\underline{H}_3.CH$ (3H, d, 1.06 ppm, J = 8 Hz); $HOCH-C\underline{H}-\dot{C}=\dot{C}-$ (1H, d, 2.3 ppm, J = 8 Hz) and $-\dot{C}H-C\underline{H}OH-\dot{C}H-$ (1H, t, 3.28 ppm, J_1 = 9 Hz; J_2 = 8 Hz). From spectral characteristics, it appears this alcohol is clearly VII (Fig.5). The α-configuration of the hydroxyl group was established from the fact that the proton on the carbon bearing the



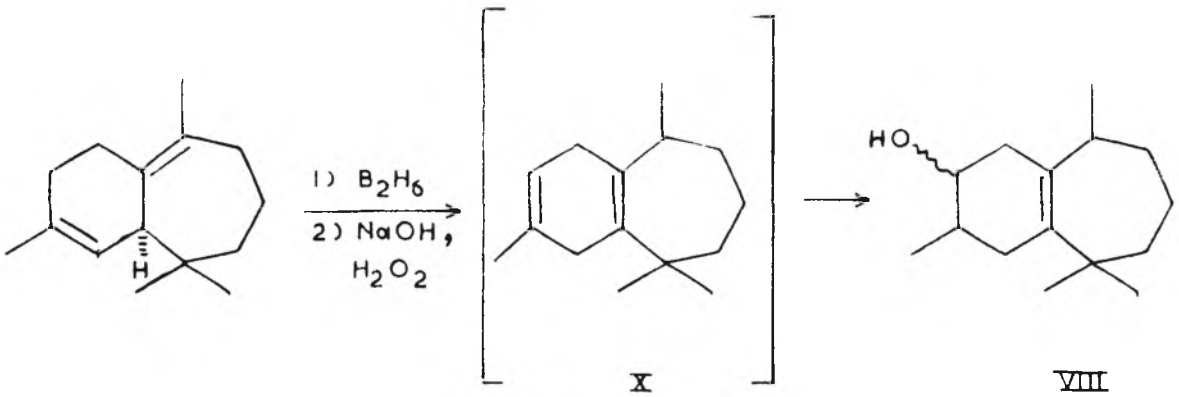
III VI

FIG. 4 – PREPARATION OF EPI-HIMACHALOL VIA HYDROBORATION OF β – HIMACHALENE



VII VIII IX

FIG 5 – MONOALCOHOLS FROM THE MONOHYDROBORATION OF β – HIMACHALENE



X VIII

FIG.10 – POSSIBLE FORMATION OF ALCOHOL – III (VIII) VIA X

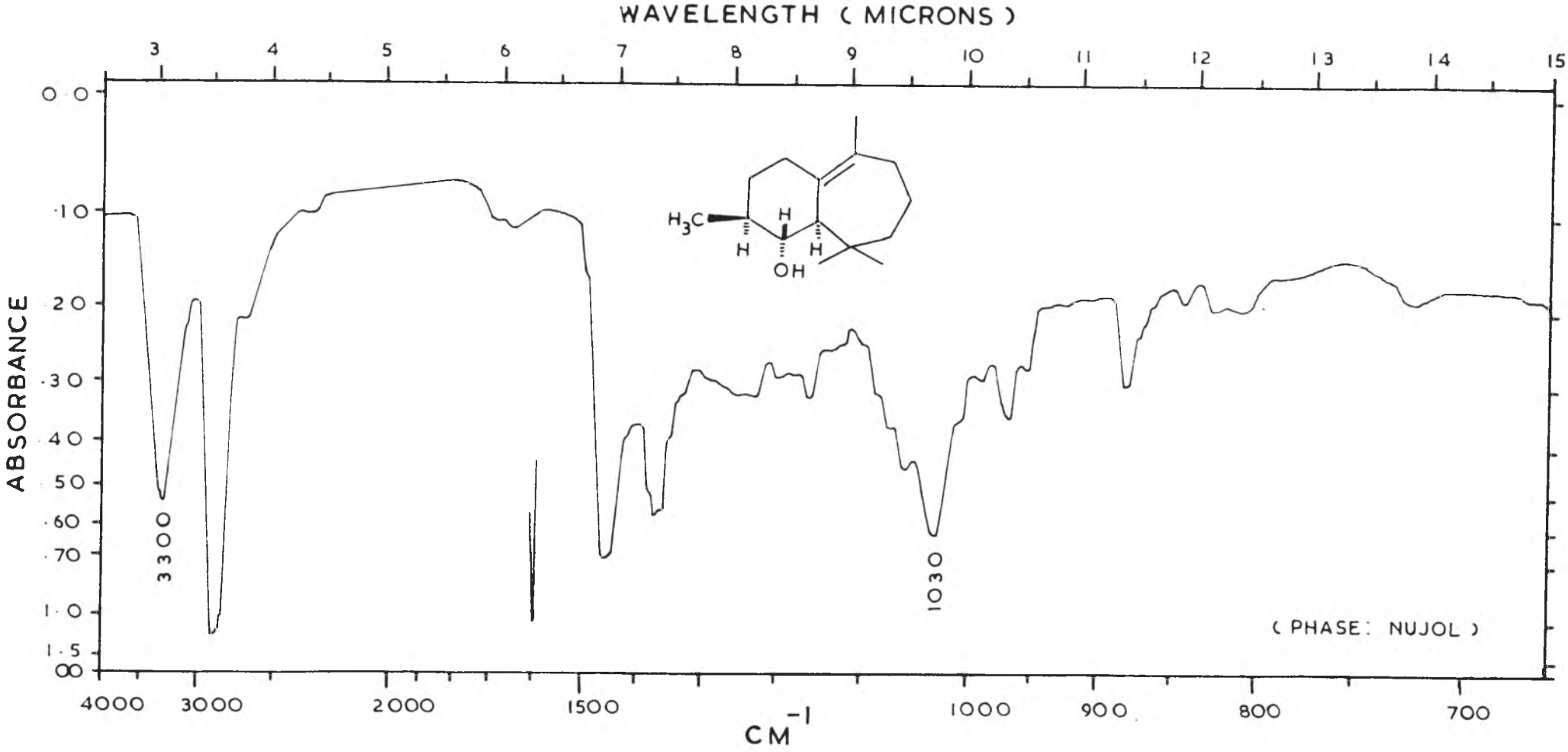


FIG. 6 IR SPECTRUM OF 2∝-HYDROXY-1∝-HIMACHAL-6-ENE (VII)

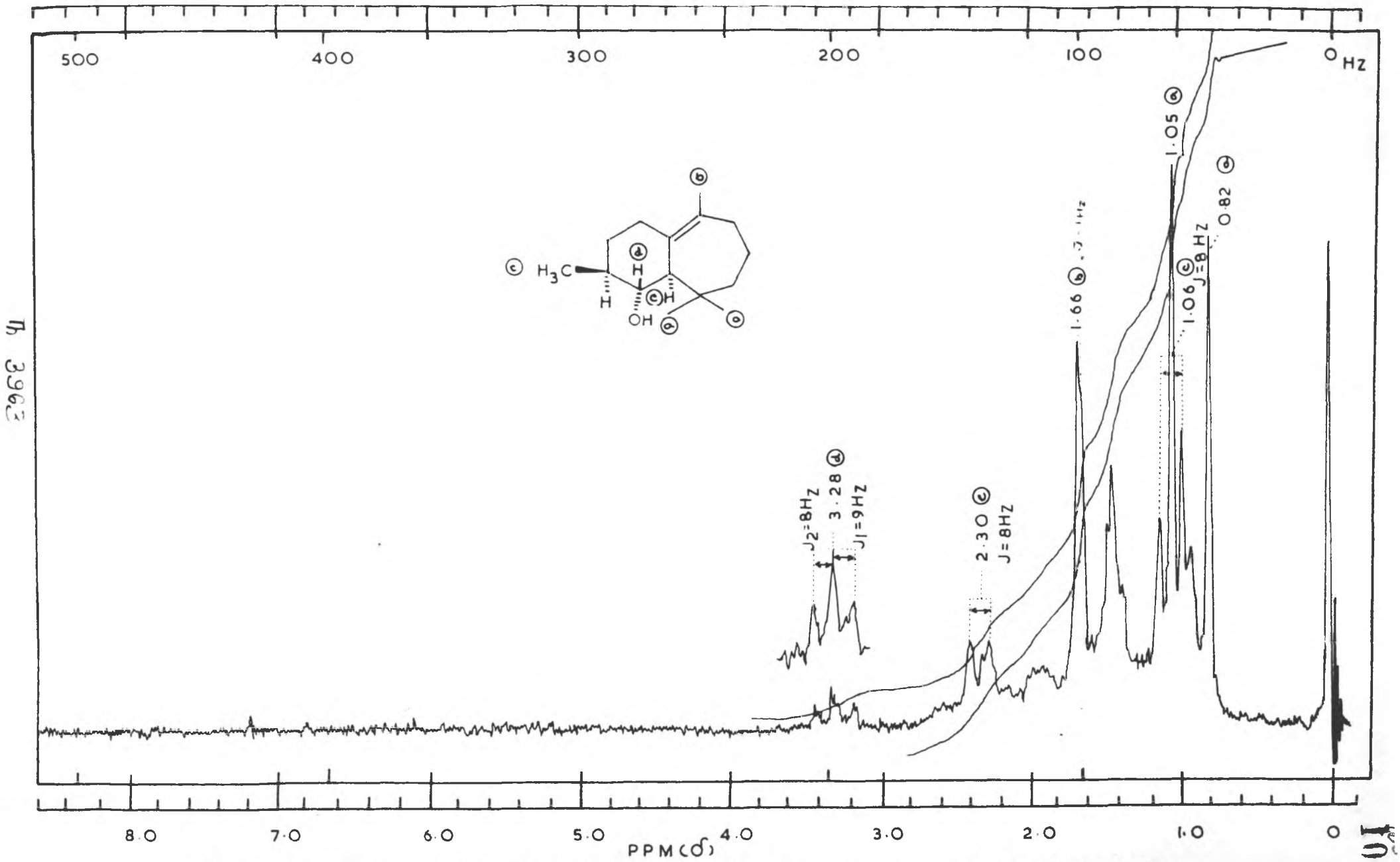


FIG.7 PMR SPECTRUM OF 2∝- HYDROXY -1∝- HIMACHAL -6-ENE (VII)

secondary hydroxyl, is experiencing two diaxial couplings as indicated by the magnitude of its coupling constant (J_1 = 9 Hz and J_2 = 8 Hz) (Fig.7). This alcohol (VII) arises via the anti-Markovnikov addition of diborane, on the trisubstituted double bond of β-himachalene.

Alcohol-II (RRf, 0.84), analyses for $C_{15}H_{26}O$ (M^+, m/e = 222), is an unsaturated alcohol (TNM test: orange colour). IR spectrum (Fig.8): OH 3300 and 1035 cm^{-1}. Its PMR spectrum (Fig.9) shows signals assignable to two quaternary Me's (two 3H, s, 1.00 and 1.10 ppm); two CH_3.CH (two 3H, d, 1.05 and 1.06 ppm, J = 7.5 and 6 Hz) and $CH_3.\dot{C}H\text{-}CHOH\text{-}\dot{C}H_2$- (1H, d,d, 3.51 ppm, J_1 = 8.5 Hz and J_2 = 3 Hz). From the spectral characteristics coupled with the magnitude of the coupling constant for CHOH proton (J_1 = 8 Hz and J_2 = 3 Hz; Fig.9), the most probable structure for this alcohol is given as VIII (Fig.5). The secondary nature of the hydroxyl group was confirmed by its oxidation to the corresponding ketone (IR, C=O 1705 cm^{-1}). The double bond and the carbonyl group in this ketone are not conjugated as is clear from its UV absorption: no high intensity absorption around 220 nm. The presence of CHOH grouping was further corroborated by the PMR spectrum of its formate which shows (1H, s, 7.98 ppm) assignable to CHOCOH proton.

It is obvious that the above structure can arise

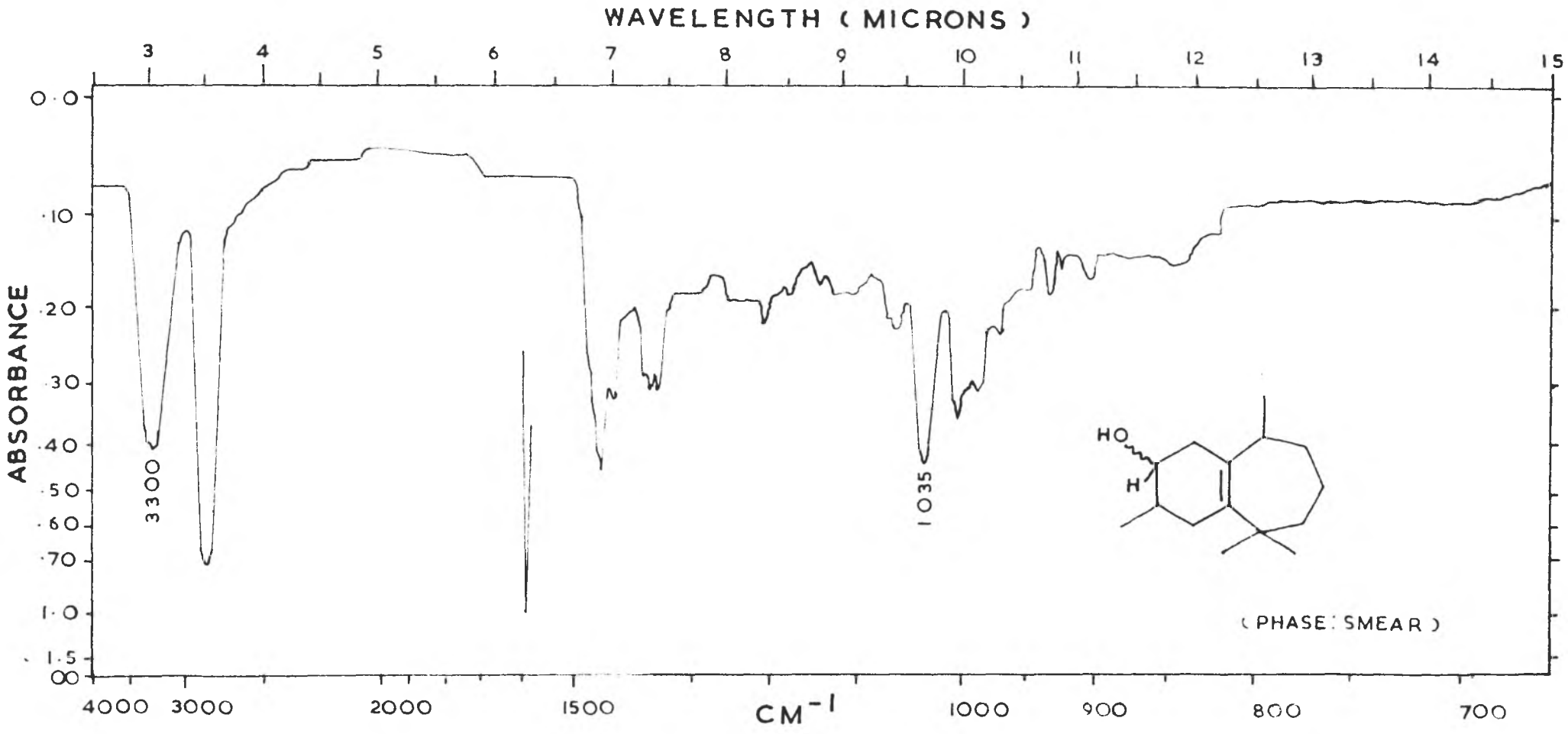


FIG.8 IR SPECTRUM OF 4-HYDROXY-HIMACHAL-I(6)-ENE. (VIII)

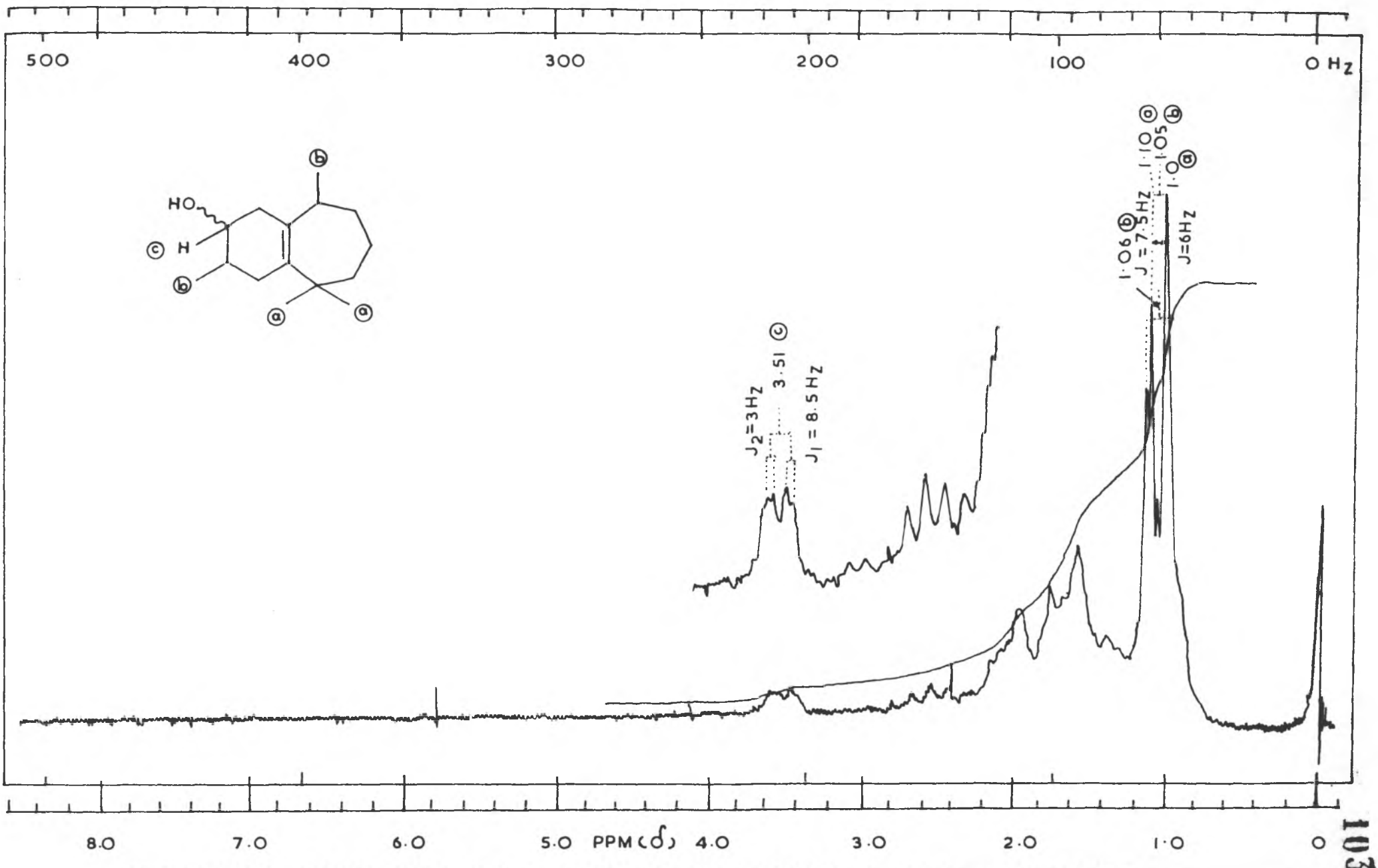


FIG. 9 PMR SPECTRUM OF 4-HYDROXY HIMACHAL-I-(6)-ENE (VIII)

only if β-himachalene undergoes isomerisation* to olefin (X), during the hydroboration conditions which may again undergo hydroboration followed by oxidation to furnish alcohol (Fig.10).

Alcohol-III (RRf. 0.80), analyses for $C_{15}H_{26}O$ (M^+, m/e 222), is an unsaturated alcohol (TNM test), IR spectrum (Fig.11): OH 3268 cm^{-1}. Its PMR spectrum (Fig.12) shows signals assignable to two quaternary Me's (two 3H, s, 0.80 and 0.85 ppm); CH_3-C(C)(C)-OH (3H, s, 1.08 ppm) and CH_3-C(C)(C)-O<u>H</u> (1H, bs, 0.95 ppm). From spectral characteristics this alcohol was assigned structure IX (Fig.5), which arises via the Markovnikov addition of diborane, on the trisubstituted double bond in β-himachalene. Hydroboration is known[7] to result in (4-6%) of Markovnikov products.

From the above results, it is clear that monohydroboration of β-himachalene takes place on the trisubstituted double bond of β-himachalene instead of its addition on the tetrasubstituted double bond, which

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*The observed isomerisation of original double bonds in β-himachalene to X, remains unaccountable. Isomerisation of double bond is known[8] to take place during hydroboration only if the organoborane is heated to 160°, before oxidation.

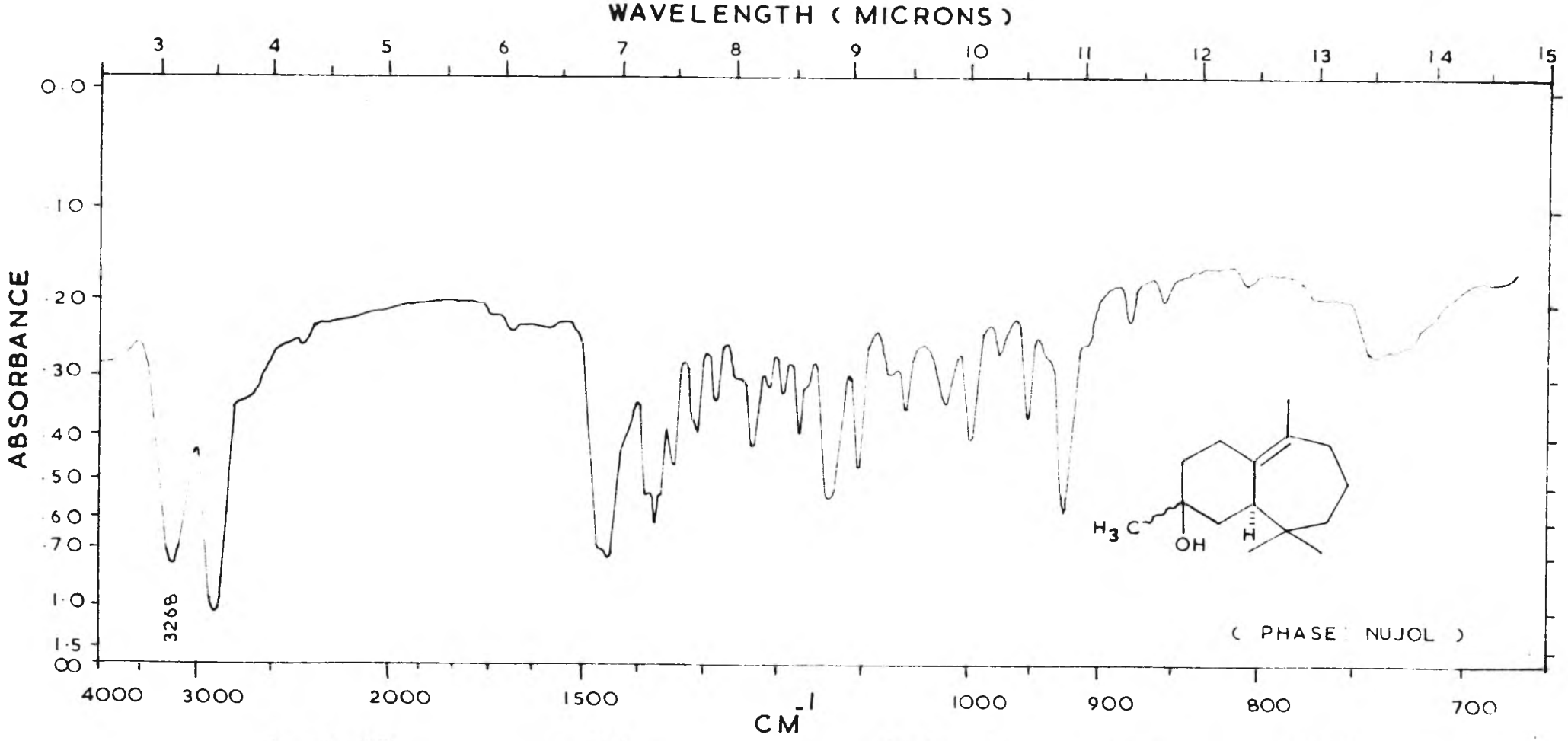

FIG. II IR SPECTRUM OF 3-HYDROXY-1 ∝-HIMACHAL-6-ENE (IX)

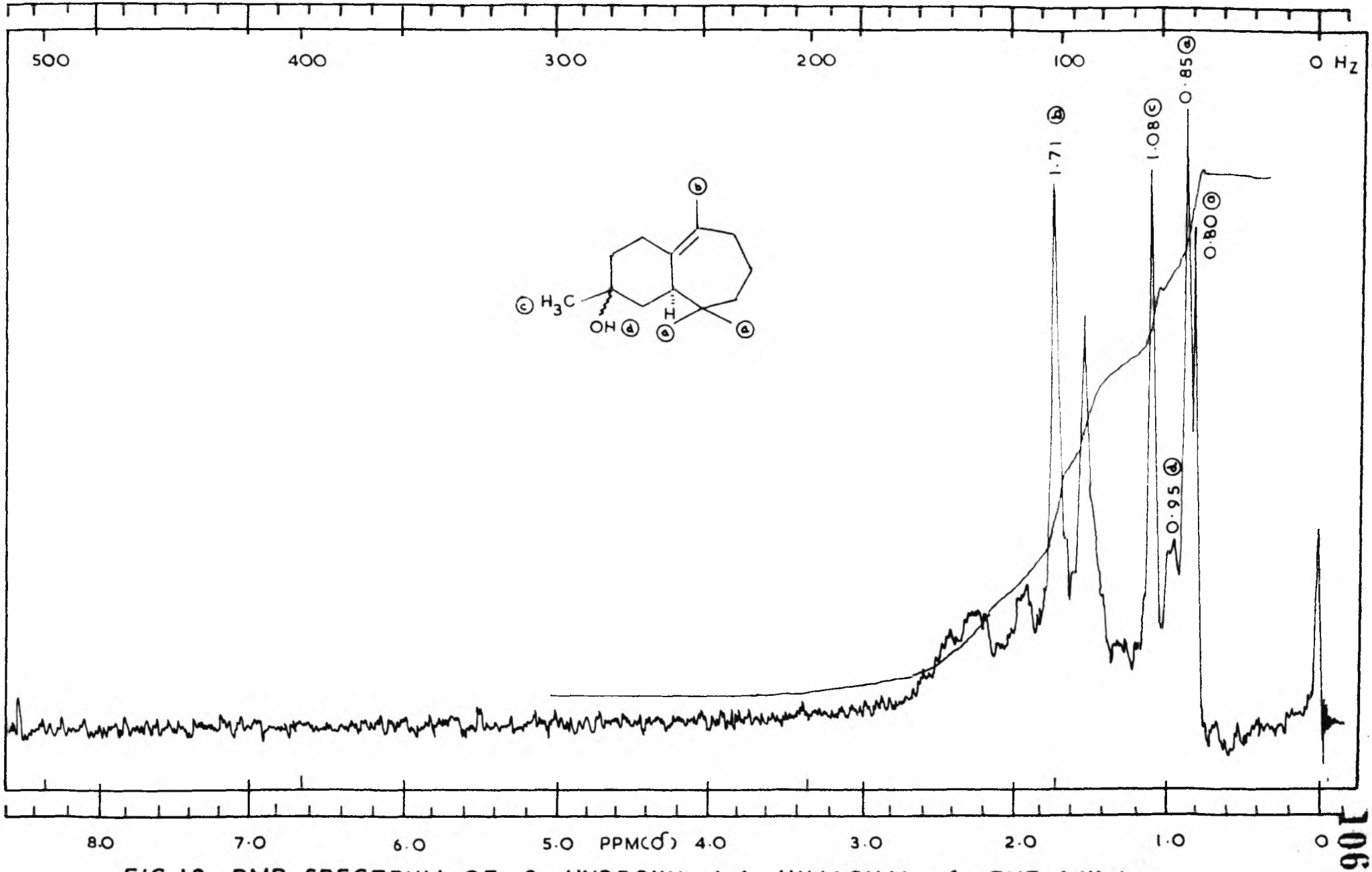

FIG.12 PMR SPECTRUM OF 3-HYDROXY-1∝-HIMACHAL-6-ENE (IX)

was envisaged and hence no epihimachalol was obtained*.

Solvolysis of Himachalol p-nitrobenzoate

Himachalol p-nitrobenzoate (XIV, X = $COC_6H_4NO_2$) was prepared by treating lithium alkoxide of himachalol with p-nitrobenzoyl chloride in petroleum ether. It was found that some amount of himachalol always remained unreacted even though a large excess of n-BuLi and p-nitrobenzoyl chloride were used, in order to complete the reaction. This product was found to be labile and hence the crude ester [IR (smear): -COO 1720 cm^{-1}; NO_2 1528 and 1350 cm^{-1}; PMR (CCl_4): two quaternary Me's (6H,

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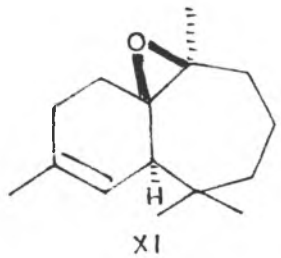
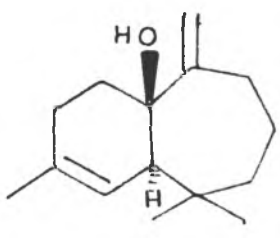
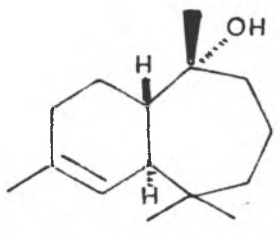
*It was also attempted to prepare epihimachalol by the oxymercuration-demercuration[9] of β-himachalene. Only 10-12% of β-himachalene undergoes hydration in above reaction conditions and the resulting product was found to be a very complex mixture by TLC (solvent: 10-15% EtOAc in C_6H_6, a streak is obtained). Epihimachalol or himachalol was not formed under these conditions, however, three products could be isolated with great difficulty and were identified as β-himachalene epoxide (XI)[6], a known[6] allylic alcohol (XII) and a trans-alcohol (XIII). No attempt was made to identify the other products formed.



XI



XII



XIII

s, 0.93 ppm); $C\underline{H}_3$-OCO$C_6H_4NO_2$ (3H, s, 1.73 ppm); CH_3-C=C$\underline{H}$-CH, ill-defined d, 5.58 ppm, J = 4.5 Hz and -OCO $C_6\underline{H}_4.NO_2$ (4H, q, 8.24 ppm); these bonds have been selected from the IR and PMR of the crude ester] was subjected to solvolysis with 80% aq. acetone at 70-80°. This furnished a hydrocarbon mixture.

This hydrocarbon mixture was shown to consist of only two components (7.5 : 92.5) by GLC; the components were found to be α-himachalene (II)[2] and β-himachalene (III)[2] from their retention times, IR and PMR and this was confirmed by the study of specific rotation and IR and comparing with those of a mixture of the same composition prepared from authentic samples of pure α and β-himachalenes. Thus in this reaction, a simple elimination rather than rearrangement took place, unlike the case of allohimachalol tosylate (I).

E X P E R I M E N T A L

For general remarks, see p. 78 . Analytical GLC were recorded on Hewlet-Packard 5700A gas chromatograph (column: 180 cm x 3 mm; 3% carbowax on chromosorb W 60-80; H_2 as carrier gas).

Monohydroboration of β-himachalene (III): In a dry flask (250 ml), equipped with septum inlet, pressure equalizing dropping funnel and a magnetic stirrer, under a positive N_2 pressure dry THF (25 ml) and (10.2, 0.05 mole) of β-himachalene were taken and cooled to 0° (ice-H_2O bath). Hydroboration was achieved by the dropwise addition of (29 ml, 0.4590 g; 0.0166 mole) of 1M solution of diborane in THF. The solution was stirred for 30 minutes at 0° and 15 hr at room temperature (~ 30°). (10 ml) of H_2O was then added very slowly and cautiously to destroy excess of diborane, followed by (50 ml) of 1M NaOH and (50 ml) of 30% H_2O_2 and stirred for two hr. The reaction mixture was poured into (300 ml) of H_2O and saturated with NaCl. The organic layer was separated from the aqueous layer, the aqueous layer extracted with Et_2O (100 ml x 4), washed with H_2O (30 ml x 3), brine (30 ml x 3), dried and the solvent distilled off to give 12.7 g of the hydroboration mixture. TLC (solvent: 15% EtOAc in C_6H_6) indicated the presence of some very polar compounds besides unreacted β-himachalene and mono-alcohols.

BROAD SEPARATION

The hydroboration mixture (11.78 g) was chromatographed on alumina (grade III, 350 g; 43 cm x 3.5 cm) with TLC (solvent: 15% EtOAc in C_6H_6) monitoring.

TABLE 1

Fr.No.	Eluent	Vol. collected	Wt.	Remarks
1	Pet. ether	400 ml	-	-
2	" "	300ml x2	2.80 g	β-himachalene
3	10% C_6H_6 in pet.ether	300ml x8	5.1840g	Corresponds to mixture of mono-alcohols.
4	C_6H_6	400ml x8		
5	5% MeOH in C_6H_6	400ml x6	2.8488g	Corresponds to mixture of diols.

Fr.2 (Table 1, 2.80 g), was distilled to give pure β-himachalene (1.8434 g); b.p. 107°/1.5 mm and was further identified by TLC and PMR [Lit.[2]: b.p. 121-122°/4 mm, PMR].

Fr.5 (Table 1, 2.8488 g), TLC (solvent 15% EtOAc in C_6H_6) indicated the presence of most polar compounds, probably diols which were not investigated further.

Chromatography of mono-alcohols. Fr.3 - Fr.4 (Table 1, 5.184 g), TLC (solvent 15% EtOAc in C_6H_6) indicated the presence of three alcohols, corresponding to RRf of 1.00, 0.84 and 0.80 respectively. This mixture (5.00 g) was

chromatographed on Al_2O_3 (grade III, 500 g; 109 cm x 2.5 cm) with TLC monitoring.

TABLE 2

Fr.No.	Eluent	Vol. collected	Wt.	Remarks
1	Pet.ether	500 ml	0.0578 g	Unreacted β-himachalene
2	10% C_6H_6 in pet. ether	100ml x3	-	-
3	" "	75ml x3	0.1584 g	Mixture β-himachalene + compound of RRf = 1.00.
4	" "	100ml x14	0.8399 g	Corresponds to pure compound of RRf = 1.00
5	10% C_6H_6 in pet. ether	100ml x12	0.8609 g	Mixture of compounds with RRf = 1.00 and 0.84
6	" "	100ml x5	0.3628 g	Compound with RRf = 0.84
7	" "	100ml x5	0.5301 g	Mixture of compounds with RRf = 0.84 and 0.80
8	" "	100ml x15	1.1698 g	Major (0.80) + traces of compound (RRf = 0.84)
9	15% " "	100ml x7		
10	C_6H_6	100ml x2	-	-

Alcohol-I [RRf, 1.00; 2β-hydroxy-1α-himachal-6-ene (VII)]:

Fr.4 (Table 2, 0.8399 g), was distilled to give pure VII,

b.p. 140° (bath)/0.4 mm which became solid on keeping, $[\alpha]_D$ +9.5° (c, 2.02%). IR spectrum (Fig.6). PMR spectrum (Fig.7). Mass spectrum: m/e 222 (M^+, 71%), 41(100%), 82 (87%), 135 (79%), 111 (64%), 55 (59%), 43 (55%), 109 (45%), 95 (45%) and 93 (43%). (Found: C, 81.17; H, 11.82. $C_{15}H_{26}O$ requires: C, 81.02; H, 11.79%).

Alcohol-II [RRf, 0.84; 4-hydroxyhimachal-1(6)-ene (VIII)]. Fr.6 (Table 2, 0.3628 g), was distilled to give pure VIII, b.p. 130-135° (bath)/0.7 mm; $[\alpha]_D$ -147.6 (c, 1.97%). IR spectrum (Fig.8). PMR spectrum (Fig.9). Mass spectrum: m/e 222 (M^+, 86%), 41 (100%), 161 (95%), 189 (78%), 55 (67%), 81 (64%), 153 (59%), 148 (48%) and 105 (44%). [Found: C, 80.91; H, 11.73. $C_{15}H_{26}O$ requires: C, 81.02; H, 11.79%].

Jones oxidation of (VIII): (0.2040 g) of this alcohol was taken up in (25 ml) of dry Et_2O and treated with (1.2 ml) of Jones reagent[10] [stock solution: CrO_3 (133 g), conc. H_2SO_4 (115 ml), H_2O (385 ml)] at (0-5°C and stirred for 2.5 hrs. After usual work up (0.200 g) of the corresponding ketone was obtained which was distilled; b.p. 130-135° (bath)/0.3 mm; TNM test: +ve. UV absorption: λ_{max}^{EtOH} 214 and 245 nm (ε 180.7 and 110.5).

Formate of (VIII): The above alcohol (0.190 g) on treatment with acetic-formic anhydride[11] (2 ml) at 30°/12 hr (N_2), furnished (0.211 g) of the required formate, after usual work up. b.p. 115°(bath)/0.5 mm. Mass spectrum: m/e 250 (M^+, 8%), 204 (100%), 176 (85%), 55 (76%), 105 (75%),

91 (72%), 161 (66%), 43 (53%), 119 (48%) and 79 (48%).

Fr.8 - Fr.9 (Table 2, 1.1698 g), TLC (solvent: 15% EtOAc in C_6H_6) indicated it to be mixture of two compounds with RRf of 0.84 (minor) and 0.80 (major). The major compound was isolated pure by inverted dry column chromatography[12] on SiO_2-gel (250 g, 25 cm x 4.7 cm; solvent: 15% EtOAc in C_6H_6).

Alcohol-III [RRf, 0.80; 3-hydroxy-1α-himachal-6-ene (IX)]: The major compound, isolated from above IDCC was crystallised from MeCN to give silky crystals, m.p. 125-126°, $[\alpha]_D$ +14.6° (c, 1.24%). IR spectrum (Fig.11). PMR spectrum (Fig.12). Mass spectrum: m/e 222 (M^+, 48%), 135 (100%), 93 (83%), 41 (65%), 42 (52%), 55 (45%), 79 (43%), 148 (42%), 122 (41%), 95 (38%) and 107 (35%). (Found: C, 80.37; H, 11.7. $C_{15}H_{26}O$ requires: C, 81.02; H, 11.79%).

Himachalol p-nitrobenzoate (XIV, X = $COC_6H_4.NO_2$): In a flame dried flask, flushed with N_2, were taken dry pet. ether (6 ml), himachalol (0.2336 g, 0.001 mole) and (1.4 ml) of n-BuLI solution[13] (0.096 g; 0.0015 mole) and the mixture stirred at room temperature (29°) for 1 hr. To this solution was added an ethereal solution of p-nitrobenzoyl chloride, through a septum and the mixture stirred for 2 hr/29°. The solution was separated from the precipitated lithium chloride and the crude product (0.2630g), was recovered from the filtrate and used as such for solvolysis.

Solvolysis of himachalol p-nitrobenzoate: To the freshly prepared crude himachalol p-nitrobenzoate (0.2630 g) in acetone (2 ml), H_2O (8 ml) was added and the reaction mixture was stirred under N_2 at 70-80° for 42 hr. The solid separated was filtered off and the aq. phase extracted with pet. ether (25 ml x 3). Pet. ether extract was washed with $NaHCO_3$, H_2O, brine, dried and freed from the solvent to give a product, which was identified as follows.

α- and β-Himachalene. The above product was found to be a hydrocarbon (TLC) which was filtered through a small alumina column(Grade II, 20 g; 20 cm x 1 cm) using pet.ether for elution. (0.0910 g) of hydrocarbon was obtained and distilled. b.p. 110-120° (bath)/1 mm, $[\alpha]_D$ +155.8 (c, 0.38%). GLC (temp. 130°; gas flow 60 ml/min] showed it to consist of two components in the percentages of 7.5 : 92.5 and having RRT 1.1 and 1.3 respectively, and these were identified (IR, PMR) as α and β-himachalenes respectively.

SUMMARY

Monohydroboration of β-himachalene has been studied with a view to prepare epi-himachalol. Solvolysis of himachalol p-nitrobenzoate gives α and β- himachalenes.

REFERENCES

1 S.C. Bisarya and Sukh Dev, Tetrahedron 24, 3869 (1968).

2 T.C. Joseph and Sukh Dev, Tetrahedron 24, 3809, 3841 (1968).

3 S.C. Bisarya and Sukh Dev, Tetrahedron 24, 3861 (1968).

4 K. Naemura and E. Wenkert, Syn. Comm. 3, 45 (1973).

5 W. Parker, J.S. Roberts and R. Ramage, Quart. Rev. 21, 331 (1967).

6 V.S. Joshi, N.P. Damodaran and Sukh Dev, Tetrahedron 27, 459 (1971).

7 H.C. Brown, "Hydroboration",W.A. Benjamin Inc., New York, N.Y. 1962.

8 a) H.C. Brown and B.C. Subba Rao, J. Amer. Chem. Soc. 81, 6434 (1959); (b) H.C. Brown and G. Zweifel, ibid. 88, 1433 (1966); ibid. 89, 561 (1967).

9 H.C. Brown, P.J. Geoghegan, Jr., G.J. Lynch and J.T. Kurek, J. Org.Chem. 37, 1941 (1972).

10 K. Bowden, I.M. Heilbron, E.R.H. Jones and B.C.L. Weedon, J. Chem. Soc. 39 (1946).

11 E. Guenther, The Essential Oils, Vol.1, p.276, D van Nostrand, New York (1948). Also see: L. Muramatsu, M. Murakami, T. Yoneda and A. Hagitani, Bull. Chem. Soc. Japan 38, 244 (1965).

12 V.K. Bhalla, U.R. Nayak and Sukh Dev, J. Chromatog. 26, 54 (1967).

13 H.C. Brown, F.J. Chloupek and M.H. Rei, J. Amer. Chem. Soc. 86, 1248 (1964).