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STUDIES IN SESQUITERPENES—XXXII

STRUCTURE OF HIMACHALENE MONOHYDROCHLORIDE AND THE PREPARATION OF *TRANS*-HIMACHALENES*

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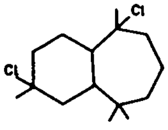
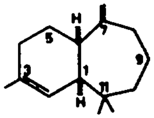
Abstract—The structure of himachalene monohydrochloride has been elucidated and it is shown that in the hydrochloride the ring-junction is *trans*. The products resulting from the dehydrohalogenation of this monohydrochloride have been fully characterized and one of them is shown to be *trans*-α-himachalene.

It has been mentioned earlier[1,2] that himachalene dihydrochloride (I) on mere recrystallization from methanol yields a monohydrochloride, for which several alternative structures are possible. Moreover, since both α-himachalene (II) and β-himachalene (III) furnish the same dihydrochloride, the stereochemistry at the ring-junction may or may not be the same as in α-himachalene. The work described in this communication was undertaken to settle these points.



I



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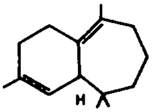
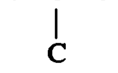


III

Structure of himachalene monohydrochloride

The monohydrochloride (m.p. 51–52°) contains a vinylidene group (IR spectrum: 887, 1635 and 3040 cm^{-1}. PMR spectrum: 2H s at 281 c/s) and three quaternary Me's, one of which must be attached to the C atom linked to chlorine (PMR spectrum: 3H s's at 48, 54 and 97 c/s). These data restrict the number of structures possible for the monohydrochloride to the two gross structures IV and V. The monohydrochloride on ozonolysis, followed by dehydrohalogenation (NaOAc–AcOH) yielded a mixture of two ketones (~1:1; GLC) which were separated by preparative GLC; the properties of these ketones are summarized in Table 1. It is clear from their PMR spectra (Table 1) that both the ketones contain the grouping  $\mathrm{Me{-}\underset{\underset{\textstyle C}{|}}{C}{=}CH{-}C}$ and since, both ketones remain unaffected by refluxing with t-butanolic $KOBu^t$, they

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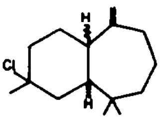
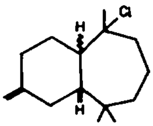
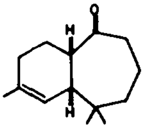


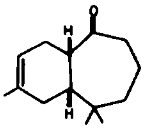
IV



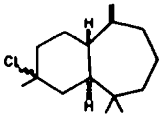
V



VI



VII



VIII

are not epimeric. These results can be explained only on the basis of structure IV for the monohydrochloride. Furthermore, because both the ketones are resistant to epimerization, they must posess the thermodynamically more stable ring-junction, which as has been discussed earlier[3] must be *trans*.* Thus, the two nor-ketones must be represented by VI and VII while the monohydrochloride should be VIII.†

The question, which of the structures VI, VII should be assigned to which nor-ketone, can now be considered. Examination of models (quasi-chair–twist chair conformations for the 6 and 7-membered rings respectively) reveals that in structure VI, the dihedral angle between the vinylic and the bridgehead protons is close to 90°, whence from Karplus equation[7] one would expect little coupling between them. On the other hand, in structure VII, the olefinic proton is flanked by a CH_2 group and hence, at least some coupling must occur. Actually, the vinyl proton signals for

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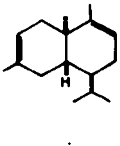
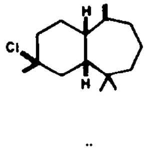
* It follows that himachalene dihydrochloride also must be *trans*-locked. Thus, during the formation of the dihydrochloride from α-himachalene an inversion at C_6 must occur *via* a hydride shift or else, prior isomerization to β-himachalene must take place.

† In an effort to fix configuration of the Cl at C_3, the IR spectra of himachalene mono- and dihydrochloride and (−)-cadinene dihydrochloride (of known absolute stereochemistry[4]) have been studied. Though it has been reported[5] that axial and equatorial C—Cl bonds can be distinguished by IR spectroscopy, the method could not be applied in the present instance, as even in the case of cadinene dihydrochloride in which the C—Cl bonds are known to be axial, there was no significant absorption in the expected region.

It is known that cadinene dihydrochloride on dehydrohalogenation gives essentially β-cadinene[6] (i). This is understandable as the halogen atoms are axially oriented. Since, in the dehydrohalogenation of the chloroketone, only VI, VII, both containing a trisubstituted olefinic linkage, are formed, one would infer axial configuration for the halogen in himachalene monohydrochloride (ii).



i



ii

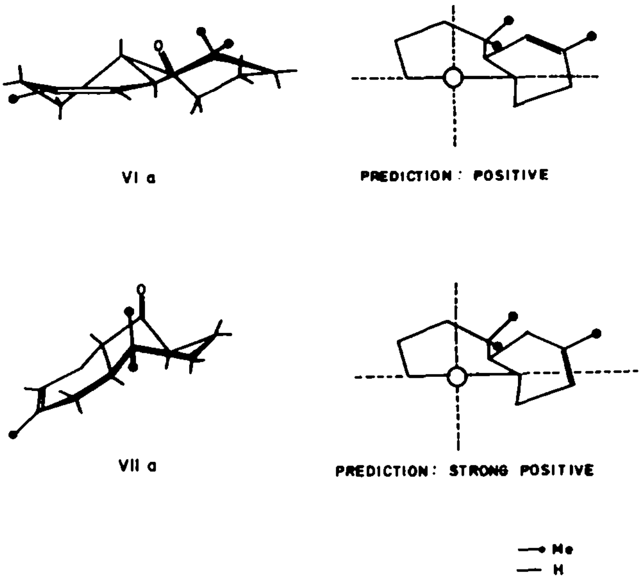
TABLE 1. SOME PROPERTIES OF THE NOR-KETONES VI AND VII

	Ketone-I	Ketone-II
RRT*	1	1·25
GLC purity (%)	97	95
B.p.	130° (bath)/1·5 mm	125–128° (bath)/1 mm
$[\alpha]_D$	−69·9°	+119·4°
$\nu^{C=O}$ (cm^{-1})	1705	1710
PMR spectrum:†		
$C\underline{H}_3$—C—	48 (s) 61 (s)	45 (s) 57 (s)
$C\underline{H}_3$—C=C	101 (b)	98 (b)
—$\underline{H}$C=C<	314 (b)	317 (b)

* Relative retention time; temp 175°, gas (H_2) 50 ml/min, 20% diethylene-glycol polysuccinate on Chromosorb W.

† Spectra are taken in CCl_4 and values are reported in c/s from TMS; s = singlet, b = broad singlet.

both the ketones occur with little splitting, but from the half-band widths* of these signals (3·5 and 7 c/s for ketone-I and ketone-II respectively) it is clear that the ketone-II, with the broader olefinic proton signal, should be VII. The octant rule[9]


VI a

PREDICTION : POSITIVE

VII a

PREDICTION : STRONG POSITIVE

FIG. 1 Octant diagrams of ketones VI and VII.

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* When coupling is not clear-cut to give a distinct pattern, half-band width of the signal has been used to check the extent of coupling.[8]

predicts (Fig. 1) a positive Cotton effect for the most likely conformations VIa and VIIa for the two ketones, VI and VII respectively and this is borne out from their CD curves (Fig. 2).

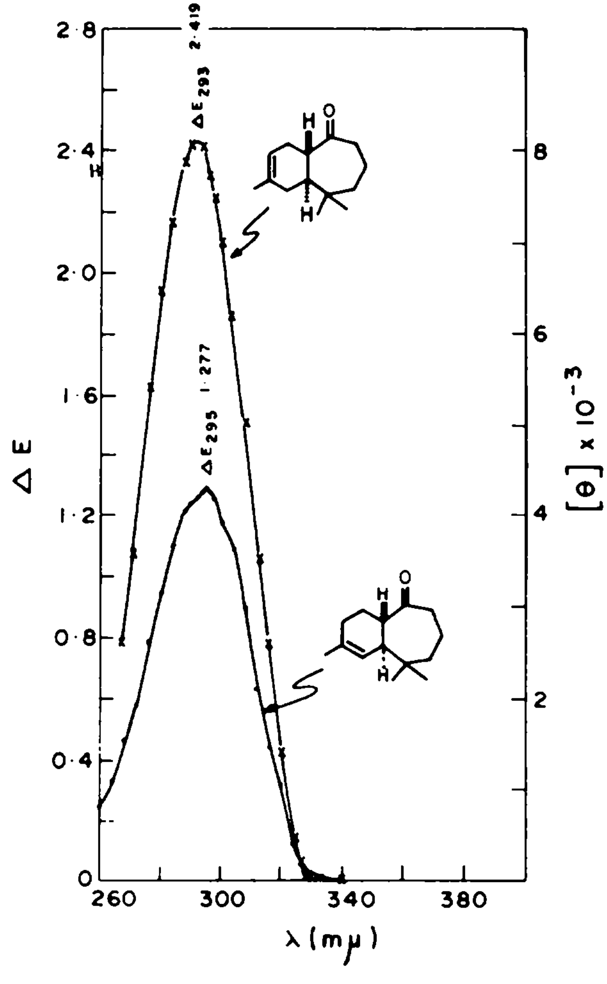


FIG. 2 CD Curves of ketones VI and VII.

When VI is treated with aqueous oxalic acid in dioxan, it is partly (15%) isomerized to VII.

trans-*Himachalenes*

The results reported in the preceding paper,[3] provide sufficient basis for the *cis*-fusion of the rings in α-himachalene (II). This is further supported by the demonstration that ketones VI, VII are stable to epimerization as was anticipated for a *trans*-ring junction in this bicyclo-system. The derivation of the structure of himachalene monohydrochloride as VIII, offers a unique possibility of preparing *trans*-α-himachalene (IX) which should be distinct from α-himachalene. This has been experimentally verified.

Dehydrohalogenation of himachalene monohydrochloride with either Al_2O_3 or with NaOAc–AcOH, resulted in a mixture, from which the three major components (A, B, C) could be isolated by chromatography over SiO_2 gel–$AgNO_3$.[10] Table 2 summarizes the important characteristics of these hydrocarbons.

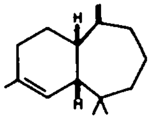
TABLE 2. HYDROCARBONS FROM THE DEHYDROHALOGENATION OF HIMACHALENE MONOHYDROCHLORIDE

	Component			α-Himachalene
	A		C	
R_{dye}*	3·44	2·44	1·77	4·00
GLC purity (%)	100	95	100	100
B.p. (bath)/mm	120–124°/3·5	124–127°/3·5	115–118°/3	93–94°/2 mm
n_D^{30}	1·5060	1·5038	1·5055	1·5082/25°
$[\alpha]_D$	+ 146·1°	− 39·5°	− 201·5°	− 192·3°
Position of *gem*-dimethyl groups in the PMR spectrum (c/s)	51, 53	43, 58	48, 59	58, 60

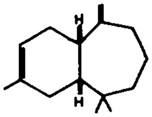
* $R_{dye} = \dfrac{\text{movement of the substance from start in mm}}{\text{movement of azobenzene in mm}}$; solvent (10% benzene in pet. ether) front 10 cm; TLC over SiO_2 gel–$AgNO_3$[12].

Component-A clearly has one vinylidenic (IR spectrum: 885, 1642 cm^{-1}; PMR spectrum: 2H s at 278 c/s) and one trisubstituted (IR spectrum: 849 cm^{-1}. PMR spectrum: 1H broad s at 317 c/s, W_H 9 c/s) olefinic bond and one vinylic Me (PMR spectrum: 3H signal at 98 c/s). Component-B, also, shows the same structural features: $>C{=}CH_2$ (IR spectrum: 890, 1650, 3070 cm^{-1}. PMR spectrum: two 1H s's at 281 and 285 c/s), $\overset{Me}{>}C{=}CH$— (IR spectrum: 820 cm^{-1}. PMR spectrum: 3H s at 100 c/s; 1H s centred at 316 c/s, W_H 3·5 c/s).

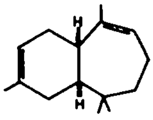
The above hydrocarbons can clearly be formulated as IX and X, which have



IX



X



XI

properties, distinct from those of α-himachalene (Table 2). Of the two structures, component-A can be represented by X, while structure IX can be assigned to the other hydrocarbon on the basis of the half-band widths[8] (W_H) of their trisubstituted olefinic proton signals. Support for these assignments is forthcoming from a comparison of molecular rotational differences of the pair of ketones VII–VI

[$\Delta M_{(VII)-(VI)}$ +549·4°] and those of hydrocarbons [$\Delta M_{(X)-(IX)}$ +378·7°] which are of the same sign and magnitude.

The third hydrocarbon (component-C) has clearly two linkages of type: Me—C═CH— (PMR spectrum: 6H s at 101 c/s; 1H t at 330 c/s, $J = 4$ c/s; 1H, b at 317 c/s) and is preferentially formulated as XI, in view of the W_H (7·5 c/s) of the 317 c/s olefinic proton signal.

EXPERIMENTAL

For general remarks see Parts XXIX and XXXI of this series.

Ozonolysis of himachalene monohydrochloride

A soln of himachalene monohydrochloride (6·8 g) in $CHCl_3$ (60 ml) was ozonized at −10° by bubbling ozonized O_2 (~160 mg/hr) till it escaped freely (17 hr, KI-boric acid test). The solvent was removed under reduced press (50 mm) at room temp and the crude ozonide warmed gently with water (60 ml), first at 60° (1 hr) and finally at reflux (2 hr). After cooling, the reaction mixture was saturated with $(NH_4)_2SO_4$ and the product extracted with pet. ether (65 ml × 4), the extract washed with $NaHCO_3$aq and dried. Removal of solvent gave a gum (6·7 g) which was directly dehydrohalogenated.

Dehydrohalogenation of ozonolysis product of VIII

The above product (6·7 g) in gl. AcOH (25 ml) containing fused NaOAc (7 g) was heated on a steam bath for 4 hr. The reaction mixture was cooled, diluted with water (100 ml) and extracted with ether (30 ml × 4). The combined extracts were washed with water, $NaHCO_3$aq and dried. The solvent was flashed off and the residue distilled to get a liquid (4·4 g), b.p. 112–116°/2 mm, shown by GLC (Table 1) to be ~1:1 mixture of two components.

The above mixture (3·8 g) was separated by preparative GLC on a column (2·5 cm × 3 meters) of 20% diethyleneglycol polysuccinate on Chromosorb W (60–80 mesh), at 200° in lots of 0·5 ml and using N_2 (15 psi) as the carrier gas.

Ketone-I (VI). The earlier cut (1·1 g), b.p. 130°/1·5 mm, was converted into its *semicarbazone* (pyridine method), which crystallized from EtOH in white, shining flakes, m.p. 210–211°. (Found: C, 68·29; H, 9·19. $C_{15}H_{25}ON_3$ requires: C, 68·40; H, 9·57%).

The above semicarbazone (0·8 g) was treated with aqueous oxalic acid–heptane in the usual manner[11] to get pure ketone-I with characteristics recorded in Table 1. (Found: C, 81·7; H, 11·06. $C_{14}H_{22}O$ requires: C 81·50; H, 10·75%).

The above ketone (50 mg) was refluxed (5 hr) in t-BuOH (5 ml), in which 0·2 g K had been earlier dissolved, and then worked up in the usual manner to give a product (21 mg, $[\alpha]_D$ −70·1°) identical (IR, GLC) with the starting ketone.

Ketone-II (VII). The second cut (0·95 g, 85% pure by GLC) was converted into its *semicarbazone*, m.p. 190–191° (EtOH). (Found: C, 68·29; H, 9·56. $C_{15}H_{25}ON_3$ requires: C, 68·40; H, 9·57%).

Regeneration of the ketone from the above semicarbazone furnished a liquid having properties recorded in Table 1. (Found: C, 81·62; H, 11·00. $C_{14}H_{22}O$ requires: C, 81·50; H, 10·75%).

The ketone (75 mg) when treated with t-butanolic $KOBu^t$, as above, was recovered (34 mg) unchanged ($[\alpha]_D$, IR, GLC).

Isomerization of ketone-I. Ketone-I (90 mg) was refluxed with a soln of oxalic acid (0·5 g) in water (1 ml) and dioxan (4 ml) for 10 hr (N_2) and then worked up (dilution with water and extraction with ether) to give, after distillation, a product (56 mg), b.p. 120–122° (bath)/1 mm, n_D^{30} 1·5037, $[\alpha]_D$ −37·1°. GLC showed the product to consist of ketone-I and ketone-II in the ratio 85:15.

Dehydrohalogenation of himachalene monohydrochloride

(i) *By alumina.* Himachalene monohydrochloride (1·1 g) in pet. ether (15 ml) was placed on a column of Al_2O_3 (Basic/I, 2 cm × 15 cm) and the product eluted with excess pet. ether after 20 hr. The product (0·9 g), b.p. 100–102°/2·5 mm, n_D^{30} 1·5054, was shown by SiO_2 gel–$AgNO_3$ TLC[12] to consist of three major components which were separated by chromatography over SiO_2 gel–$AgNO_3$ (1·2 g of the mixture;

column: 2·5 cm × 28 cm), while following the separation by TLC (solvent system: 10% benzene in pet. ether):

Fraction 1	Pet. ether	50 ml × 8	340 mg	Mixture
Fraction 2	5% C_6H_6 in pet. ether	30 ml × 3	40 mg	Mixture
Fraction 3	5% C_6H_6 in pet. ether	50 ml × 1	185 mg	95% pure A
Fraction 4	5% C_6H_6 in pet. ether	30 ml × 4	163 mg	Pure A
Fraction 5	10% C_6H_6 in pet. ether	50 ml × 4	110 mg	Mixture
Fraction 6	25% C_6H_6 in pet. ether	25 ml × 1	31 mg	Mixture
Fraction 7	25% C_6H_6 in pet. ether	25 ml × 2	80 mg	95% pure B
Fraction 8	25% C_6H_6 in pet. ether	30 ml × 2	25 mg	Mixture
Fraction 9	50% C_6H_6 in pet. ether	25 ml × 3	73 mg	Pure C
Fraction 10	C_6H_6	50 ml × 5	40 mg	Mixture

Fractions 4, 7 and 9, on distillation gave pure components A, B and C respectively and, had characteristics recorded in Table 2. (Found for A: C, 88·45; H, 11·88. Found for C: C, 88·41; H, 11·92. $C_{15}H_{24}$ requires: C, 88·16; H, 11·84%).

(ii) *By sodium acetate–acetic acid.* To a soln of the monohydrochloride (3 g) in gl. AcOH (12 ml) at ~100°, fused NaOAc (3 g) was added in two lots at an interval of 10 min. After heating the reaction mixture on the steam bath for 3·5 hr, the product was isolated by dilution with water, extraction with pet. ether and washing the extract with $NaHCO_3$aq and drying. Removal of solvent and distillation of the residue yielded a colourless liquid (1·93 g), b.p. 100–102°/2·5 mm, n_D^{30} 1·5050; TLC of this material was essentially identical with that of the product from (i) above.

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