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STUDIES IN SESQUITERPENES—LII[a]

ISOHIMACHALONE: A CONSTITUENT OF THE ESSENTIAL OIL FROM WOOD OF *CEDRUS DEODARA* LOUD.

R. SHANKARANARAYAN[b], S. KRISHNAPPA and SUKH DEV[b]*
National Chemical Laboratory, Poona, India

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Abstract—Isolation and structure elucidation of a new bicyclic sesquiterpene of a new carbo-skeleton, from the essential oil from the wood of *Credrus deodara* loud., is reported. The structure rests on a direct correlation with β-himachalene.

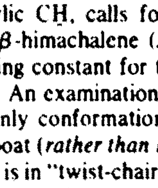
In continuation of our earlier studies[1-4] on the chemistry of *Cedrus deodara* loud., we report on the isolation and structure determination of a new bicyclic sesquiterpene ketone (1), which we call isohimachalone. This represents a new sesquiterpene carbon-skeleton and we propose the name isohimachalone for the parent fully saturated carbon frame-work.

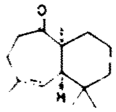
The new ketone is present to the extent of ~0.2% in the essential oil and is best isolated from atlantone-rich fractions (either fractional distillation cuts or chromatography cuts from a silica-gel column) by preparative GLC or by a chemical separation (Experimental) followed by distillation. With respect to this ketone, *cis*- and *trans*-atlantones[5] have RRT of 1.46 and 2.20 respectively (column: 10 ft, 5% diethylene glycol polysuccinate on chromosorb W; temp., 160°; gas, 70 ml H_2/min).

The new compound analyses for $C_{15}H_{24}O$ (M^+, *m/e* 220) and is clearly a non-conjugated olefinic ketone. IR (lig): $C{=}O$ 1695 cm^{-1}, $-\underset{|}{C}{=}CH$ 870 cm^{-1} (cf. IR spectra of himachalenes[2]); UV: no significant absorption above 220 nm; yellow color with tetranitromethane. Its PMR spectrum shows signals for: three tertiary methyls (3H singlets at 0.75, 0.98 and 1.13 ppm), one $M\underline{e}-C{=}C$ (3H, bs, 1.80 ppm, $W_H = 3$ Hz), $-COC\underline{H}_2CH_2$ (2H, m, 2.60 ppm), $Me-C{=}C\underline{H}-\underset{|}{C}H-$ (1H, bs, 5.50 ppm, J = 8.0 Hz). The PMR spectrum is fairly similar to that of allohimachalone (2),[7] a constituent of the *Cedrus deodara* essential oil. These findings, considered along with biogenetic reasonings,[8] suggested structure 1 (gross structure) as the likely structure of the new ketone. That this indeed is so, was established by its partial synthesis from β-himachalene (3).

β-Himachalene was conveniently monoepoxidised to 4[9] using peroxyacetimidic acid.[10] Exposure of this epoxide to BF_3-Et_2O, as expected,[11] led to isohimachalone (1) (identified by mixed GLC, IR, PMR and mass spectra), though only in 25% yield; no other ketone was formed, and much polymeric product resulted. Since, the stereochemistry of the oxide is well-secured,[9] that of isohimachalone, as depicted in 1, follows from the concerted nature of BF_3-induced oxirane ketone transformation.[12] It is conceivable that isohimachalone arises in Nature by a similar pathway from β-himachalene oxide, which has been recently identified in *Cedrus atlantica* Manet.[13]

The value J ~ 8 Hz for the coupling of the vinylic proton and the allylic C$\underline{H}$, calls for a brief comment, especially since in β-himachalene (3) and related compounds,[2-4] the coupling constant for these two protons is in the range 2–6 Hz. An examination of Drieding models for 1 reveals that only conformation 5, in which cyclohexene ring is half-boat (*rather than half-chair*)[14] and the cycloheptanone ring is in "twist-chair" conformation,[15] do the concerned protons, make an angle of ~30°, which is consistent[16] with the observed J value. This conformation also places one of the C_{11}-methyls in the shielding zone of the ethylenic linkage, so that this Me should resonate at higher field-strength, as is the case (δ = 0.75 ppm). Any attempt to convert cyclohexene half-boat into half-chair, immediately sets up increased non-bonded interaction

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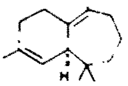
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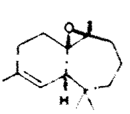
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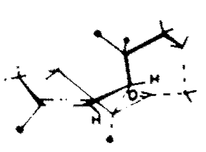

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[a] Communication No. 2004, National Chemical Laboratory, Poona.

[b] Present address: Malti-Chem Research Centre, Nandesari, Vadodara, India.

between the *endo*-methyl at C_{11} and the quasi-axial H at C_5, and this appears to be the reason for the preferred half-boat conformation for the cyclohexene ring.

EXPERIMENTAL

For general remarks see Part I.I.[8]

Isolation of isohimachalone (1)

Isohimachalone may be isolated from a suitable fractional distillation cut[4] or column chromatography cut.[5] On chromatography (SiO_2 gel) it is eluted (C_6H_6) immediately after *cis*-atlantone, but just before *trans*-atlantone (TLC, 5% EtOAc in C_6H_6; detection with 1% vanillan in 30% H_3PO_4 aq.,: isohimachalone gives a pink color in contrast to the green color given by atlantones) and hence further purification is best effected chemically. For example frac. 3 (1.0 g) of the column chromatography described earlier,[5] was mixed with MeOH (10 ml) and 30% H_2O_2 aq (1.6 ml), cooled to 5–10° and treated with 1.2 N NaOH aq (2.1 ml). After stirring for 2 hr at 15–20°, the mixture was worked up in the usual manner to give a product (1.0 g), now consisting of atlantone diepoxide (derived from atlantones; this conversion will be reported in detail in a later publication) and isohimachalone. This material can be readily separated by column chromatography over silica gel/IIB to furnish isohimachalone: b.p. 145–147° (bath/1.5 mm, n_D^{30} 1.5035, $[\alpha]_D$ + 101.4° (ç, 0.36% in $CHCl_3$). Mass: *m/e* 220 (M^+, 70%), 138 (100%), 137 (55%), 110 (44%), 109 (28%), 107 (32%), 93 (36%), 91 (36%), 77 (30%), 55 (46%), (Found: C, 81.36; H, 10.96. $C_{15}H_{24}O$ requires: C, 81.76; H, 10.98%).

β-Himachalone mono-epoxide (4)

A soln of *β*-himachalene (51.0 g, 0.25 mole) in MeOH (200 ml) containing CH_3CN (16.4 g, 0.4 mole), 30% H_2O_2 aq (45 ml, 0.4 mole), 0.5 N NaOH aq (20 ml) and 0.1 M Na_2HPO_4 aq (10 ml) was stirred at 50–55°, while additional quantities of 0.5 N NaOH aq (80 ml) were slowly introduced over a period of 5 hr, so as to maintain the pH of this mixture between 8 and 8.5. The mixture was stirred at the same temp for additional 5 hr, cooled to 25°, diluted with water (200 ml) and the product taken up in ether (100 ml × 3). The combined extract was washed with 2 N HCl aq (100 ml × 2), brine (100 ml × 2) and dried (Na_2SO_4) and freed of solvent. The product (52.0 g) is purified by fractional distillation or better chromatographed over SiO_2–gel/IIB (40 cm × 2.5 cm). Elution with C_6H_6 (200 ml × 3) gave unchanged *β*-himachalene (9.0 g), then some mixture (2.5 g), further elution with C_6H_6 (200 ml × 5) yielding the required oxide (38.0 g): b.p. 109–100°/3 mm, $[\alpha]_D$ + 177.4° (ç, 0.88% in $CHCl_3$); single peak on either SE-30 column (3%, 6 ft, 140°) or Carbowax (3%, 6 ft, 170). The product is identical (IR, PMR, $[\alpha]_D$) with the preparation reported earlier.[17]

Action of BF_3–Et_2O *on β-himachalene mono-epoxide*

To the above epoxide (10.5 g) in dry toluene (20 ml), cooled to 10°, was added (N_2) freshly distilled BF_3–Et_2O (25 ml) during 10 min. After stirring for 30 min at that temp, the mixture was poured into a satd $NaHCO_3$ aq (100 ml), the product taken up in light petrol (80 ml × 3), washed with brine (60 ml × 2) and dried (Na_2SO_4). Solvent was flashed off to give a product (10.45 g), which was chromatographed over SiO_2 gel/IIB (103 × 3.5 cm) with TLC monitoring (solvent: 5% EtOAc in C_6H_6):

Frac. 1	light petrol	200 ml	0.25 g, syrup ($C_{15}H_{24}$)
Frac. 2	light petrol	200 ml × 3	
	10% C_6H_6 in light petrol	200 ml × 15	
	25% C_6H_6 in light petrol	200 ml × 2	6.0 g, dark gum polymeric
	75% C_6H_6 in light petrol	200 ml × 6	
	C_6H_6	200 ml × 1	
Frac. 3	C_6H_6	200 ml × 5	2.5 g, isohimachalone
Frac. 4–6	5% EtOAc in C_6H_6	200 ml × 11	0.6 g, complex mixture

Frac. 3 above was distilled to give isohimachalone (1): b.p. 140-50°(bath)/1.5 mm, n_D^{30} 1.5038, $[\alpha]_D$ + 90.5° (ç, 0.66% in $CHCl_3$); GLC purity, 98% (column: 6 ft, 3% SE-30 on Chromasorb W; 140°; 60 ml H_2/min) (Found: C, 81.47; H, 10.82. $C_{15}H_{24}O$ requires: C, 81.76; H, 10.98%).

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