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# TERPENOIDS FROM *CEDRUS DEODARA**

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**Key Word Index**—*Cedrus deodara*; Pinaceae; sesquiterpenes; himasecolone; himachalol; centdarol; diterpene; isopimaric acid.

**Abstract**—A new novel type of phenolic sesquiterpene, himasecolone, has been isolated in addition to isopimaric acid from the chloroform-soluble fraction extracted from *Cedrus deodara* and characterized on the basis of physico-chemical data.

## INTRODUCTION

In previous communications polyphenolic constituents belonging to lignans and dihydroflavonol groups were isolated from the butanol-soluble fraction of the extract of *Cedrus deodara* wood [1,2]. The studies on the chloroform-soluble fraction of the extract are now reported. It was found to be a very complex mixture of closely running compounds on TLC which could not be resolved. However, the separation of this fraction into acidic and neutral portions led to a reasonable resolution which resulted in the isolation of isopimaric acid and a new novel *seco*-sesquiterpene, named himasecolone, in addition to himachalol and centdarol [3] which have been reported earlier from the hexane-soluble fraction of the extract.

## RESULTS AND DISCUSSION

Himasecolone (substance B) was obtained as a colourless oil, homogenous by TLC and HPLC ($\mu$ porasil column using $C_6H_{14}$), optically inactive, with the molecular formula $C_{15}H_{22}O_2$ ($M^+$ *m/z* 234.162). The presence of absorptions for a carbonyl group (1700 $cm^{-1}$) and a phenolic hydroxyl group (3380, 1608, 1500 $cm^{-1}$) in its IR spectrum was corroborated with UV maxima at 280 nm which showed a bathochromic shift on addition of alkali. The $^1H$ NMR spectrum (270 MHz) (Table 1) displayed three singlets at $\delta$ 1.16 (6H), 2.02 (3H) and 2.23 (3H) corresponding to a *gem*-dimethyl, an acetyl-methyl and an aryl-methyl, respectively. A sharp doublet at 6.46, a double doublet at 6.97 and a broad singlet at 6.84 revealed the presence of 1,2,4-aromatic substitution. These data indicate the presence of an aromatic side chain ($C_8H_{15}O$) containing *gem*-dimethyl and keto groups in the molecule.

The $^1H$ NMR spectrum of himasecolone, recorded after addition of trichloroacetyl isocyanate (TAI), showed the signal of the carbamate proton at $\delta$ 9.17. Further, it exhibited the *gem*-dimethyls as non-equivalent (1.16, 1.20) and one aryl methine signal was shifted downfield suggesting the probable *ortho* disposition of the phenolic OH to the six-carbon side chain.

The mass spectrum of himasecolone (**1**) exhibited the most intense benzylic cleavage fragment ion at *m/z* 149. The presence of a terminal –COMe group in the side chain was suggested by the presence of a strong ion at *m/z* 43 and was confirmed by its $LiAlH_4$ reduction to a secondary carbinol **2a** whose $^1H$ NMR spectrum exhibited a doublet at $\delta$ 1.06 for a secondary methyl and a quartet at 3.64 due to a secondary carbinolic H which was established by decoupling experiments. The acetylation of **2a** yielded a diacetyl derivative **2b** whose IR spectrum demonstrated bands at 1758 and 1725 $cm^{-1}$ and whose $^1H$ NMR spectrum showed signals for an aliphatic and an aromatic acetoxy methyl at $\delta$ 1.78 and 2.14 respectively and a secondary methine H at 4.65. In the aromatic region, only one aryl methine showed an acetylation-induced paramagnetic shift of 0.1 ppm indicating that the other *ortho* and *para* positions with respect to the phenolic OH were occupied by the methyl group and the $C_6$ side chain. The absence of a free *para* position was also confirmed by a negative Gibb's test. The side chain was, thus, shown to be placed *ortho* to the phenolic hydroxyl. The mass spectral fragmentation pattern and the decoupling experiments when the irradiation at $\delta$ 2.30 in the 270 MHz spectrum showed a marked change in one of the methylene proton multiplets at $\delta$ 1.28, established the structure of the side chain as $-C(Me)_2CH_2CH_2CH_2COMe$.

Table 1. $^1H$ NMR spectral data of himasecolone (270 MHz)

| Proton as assigned | Chemical shift ($\delta$) (multiplicity) | Coupling constants (Hz) |
|---|---|---|
| HO-1 | 4.82 (*br. s*) | — |
| H-2 | 6.46 (*d*) | 8.5 |
| H-3 | 6.79 (*dd*) | 2,8.5 |
| H-5 | 6.84 (*br. s*) | — |
| $H_2$-8 | 1.46 (*m*) | — |
| $H_2$-9 | 1.28 (*m*) | — |
| $H_2$-10 | 2.30 (*t*) | 7 |
| $H_3$-12 | 2.02 (*s*) | — |
| $H_3$-13,14 | 1.16 (*s*) | — |
| $H_3$-15 | 2.23 (*s*) | — |

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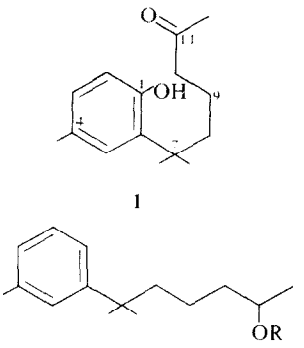
These findings and biogenetic considerations led to structure **1** for himasecolone. This was supported by the mass spectral fragmentation of **2b**, which exhibited intense ions at *m/z* 191 and 149 as a consequence of benzylic cleavage with and without loss of carbene from the phenoxyacetyl function which could easily stabilize as a tropylium or quinonoid ion by the loss of H. Additional confirmation was obtained by the $^{13}C$ NMR chemical shifts of the aromatic carbons and the $^{13}C$–$^{1}H$ coupling pattern observed in the NOE-enhanced single frequency spectrum which were consistent with the calculated values for structure **1** (Table 2). The chemical shifts of the side chain carbons were comparable with reported values in taylorione, which has a similar side chain [4].

So far the phenolic sesquiterpenoids in angiosperms have been represented by elvirol [5] and sesquichamaenol [6], which were believed to originate from their biogenetic precursors, sesquicarene [7] and δ-cadinene, by oxidative ring scission followed by aromatization. It may, however, be mentioned that a number of phenolic sesquiterpenes have also been reported from marine sources [8]. The present finding of himasecolone in *Cedrus deodara* is significant since it is the first report of the occurrence of a phenolic sesquiterpenoid in a gymnosperm. Obviously himasecolone has arisen by an analogous sequence of reactions from β-himachalene [9], i.e. oxidative cleavage of the C-10, C-11 olefinic bond followed by aromatization.

Substance D, mp 160°, $M^+$ at *m/z* 302, showed bands for a vinyl group (975 and 910 $cm^{-1}$), a trisubstituted double bond (840 $cm^{-1}$) and COOH (1695 $cm^{-1}$) in the IR spectrum. The presence of five terminal groups, namely three tertiary methyls giving signals at δ 0.75, 0.79 and 1.15, vinylidine protons exhibiting a typical ABX pattern, a carboxylic proton signal at 8.50 and an olefinic proton at 5.17 ($W_{\frac{1}{2}}$ = 8 Hz) in its $^{1}H$ NMR spectrum suggested




**2a** R = H
**2b** R = Ac

Fig. 1

the compound to be tricarbocyclic with an isopimaradiene skeleton. It formed a methyl ester, mp 61° (IR: 1725 and 1240 $cm^{-1}$; $^{1}H$ NMR: δ 3.53, –COOMe), which was reduced to a dihydro derivative on catalytic hydrogenation (IR, $^{1}H$ NMR) that still possessed the olefinic proton at δ 5.15 ($W_{\frac{1}{2}}$ = 8.5 Hz).

Substance D was identified as isopimaric acid and its $^{13}C$ NMR spectrum was also in agreement with the reported data [10]. No resin acid so far has been detected in the wood of *Cedrus* species, although it is rich in sesquiterpenes, mainly of the himachalene group. Resin acids of the abietane and pimarane types have been reported in cones of *C. atlantica* and *C. libani* [11]. This is the first report of the presence of a resin acid in *Cedrus* wood.

Table 2. $^{13}C$ NMR spectral data of himasecolone*

| Carbon | Chemical shift (multiplicity) | $^{1}J_{CH}$ | $^{>1}J_{CH}$ | Calculated |
|---|---|---|---|---|
| C-1 | 151.42 (*S*, *dd*) | — | 7.25, 7.25 | 149.2 |
| C-2 | 114.35 (*D*) | 157.47 | — | 116.3 |
| C-3 | 124.27 (*D*, *d*) | 156.87 | 7.50 | 127.4 |
| C-4 | 128.36 (*br. S*) | — | — | 129.9 |
| C-5 | 128.36 (*D*, *d*) | 151.37 | 6.25 | 127.1 |
| C-6 | 141.15 (*S*, *dd*) | — | 7.25, 6.0 | 138.0 |
| C-7 | 44.17 (*S*) | — | | |
| C-8 | 29.82 (*T*) | 122.08 | | |
| C-9 | 19.41 (*T*) | 131.83 | | |
| C-10 | 44.36 (*T*) | 123.96 | | |
| C-11 | 201.16 (*S*) | — | | |
| C-12 | 32.01 (*Q*) | 126.98 | | |
| C-13 | 22.81 (*Q*) | 122.10 | | |
| C-14 | 29.09 (*Q*) | 122.10 | | |
| C-15 | 37.02 (*Q*) | 121.44 | | |

*Solvent $CDCl_3$, δ in ppm relative to TMS. Coupling constants in Hz.

Capital letters refer to the pattern resulting from directly bonded (C, H) couplings and small letters to that from (C, H) couplings over more than one bond. *S* = singlet, *D* or *d* = doublet, *T* = triplet, *Q* = quartet, *br.* = broad due to unresolved coupling.

## EXPERIMENTAL

Mps are uncorr. The $^{1}H$ NMR spectra were recorded in $CDCl_3$ with TMS as internal standard.

The $CHCl_3$ fraction (245 g) of the alcoholic extract of the plant wood [1] was resolved into acidic (169 g) and neutral (62 g) portions by shaking its ethereal soln with 5% aq. NaOH. A portion of the acidic fraction (100 g) was chromatographed on Si gel (3.5 kg) and the eluates were combined on the basis of their TLC patterns (Table 3).

Table 3. Chromatography of the acidic portion of the chloroform-soluble fraction of the extract of *C. deodara* wood

| Fraction No. | Eluant | Weight (g) | Constituents (TLC)* |
|---|---|---|---|
| 1 | $CHCl_3$ | 10.8 | — |
| 2 | $CHCl_3$–MeOH (99:1) | 12.0 | B,(+) |
| 3 | $CHCl_3$–MeOH (98:2) | 13.2 | B,(+) |
| 4 | $CHCl_3$–MeOH (96:4) | 7.2 | C,D,(+) |
| 5 | $CHCl_3$–MeOH (95:5) | 16.8 | (+) |
| 6 | $CHCl_3$–MeOH (90:10) | 9.6 | E,F,(+) |
| 7 | $CHCl_3$–MeOH (80:20) | 2.5 | H,J,(+) |
| 8 | $CHCl_3$–MeOH (75:25) | 4.5 | J,K,(+) |

*Solvent systems B–D: $C_6H_6$–EtOAc, 17:3; E–K: $CHCl_3$–MeOH–$H_2O$, 35:3:2. (+) = Complex mixture of compounds. Substances F–K have been described previously [1, 2].

The residue from fraction 3 was rechromatographed on Si gel and eluted with $C_6H_6$ containing increasing amounts of EtOAc. The $C_6H_6$–EtOAc (98:2) eluate residue (2 g) containing substance B showed some minor components and was therefore rechromatographed on Si gel and finally alumina in the same solvent system which furnished a colourless liquid (substance B), 0.25 g.

Similar chromatographic separations were also carried out with eluate 4 (7.2 g) on Si gel impregnated with $AgNO_3$ (10%). The $C_6H_6$–EtOAc (98:2 to 95:5) fractions yielded a residue (1.9 g) which crystallized from MeOH as rhombic flakes (substance D), 0.3 g, mp 160°.

The neutral portion (62 g) mentioned above was fractionated on a neutral alumina column and the residue of combined $C_6H_{14}$–$C_6H_6$ (80:20) fractions 5–7 (6.96 g) was rechromatographed on Si gel (300 g) when the $C_6H_{14}$–$C_6H_6$ (95:5) eluate residue (2.4 g) yielded rhombic crystals from acetonitrile, 1.2 g (himachalol), mp 68°. The $C_6H_6$ fraction 10 on rechromatography on an alumina column in $C_6H_6$ containing increasing amounts of EtOAc yielded a fraction which crystallized from $C_6H_{14}$ as needles, 0.2 g (centdarol), mp 87°.

*Substance B (himasecolone).* $R_f$ 0.60 ($C_6H_6$–EtOAc, 9:1), UV $\lambda_{max}^{MeOH}$ nm: 280 (log ε 3.20); $\lambda_{max}^{MeOH-NaOH}$ nm: 289, 297 (log ε 3.59, 3.68). IR $\nu_{max}^{Neat}$ $cm^{-1}$: 3380 (OH), 2940, 1700 (C=O), 1608, 1500 (aromatic), 1450, 1410, 1408, 1358, 1260, 1124, 1038, 830. MS *m/z*: 234.162 ($M^+$), 161, 150, 149, 148, 133, 121, 109, 91, 43. (Found: C, 76.85; H, 8.15. $C_{15}H_{22}O_2$ requires: C, 76.90; H, 8.03%).

$LiAlH_4$ *reduction of substance B.* The substance (40 mg) was refluxed in dry dioxane (5 ml) with $LiAlH_4$ (100 mg) for 2 hr and the reaction product was chromatographed on Si gel ($C_6H_6$–EtOAc, 9:1) to yield a colourless syrup of **2a** (20 mg), $R_f$ 0.28 ($C_6H_6$–EtOAc, 9:1). $^1H$ NMR: δ 1.06 (3 H, *d*, *J* = 6 Hz, Me), 1.21 (6 H, *s*, 2 × Me), 1.20–1.75 (6 H, *m*, 3 × $CH_2$), 2.17 (3 H, *s*, Me), 3.64 (1 H, *q*, *J* = 6,12 Hz, –CHO–), 6.55 (1 H, *d*, *J* = 9 Hz, ArH–2), 6.87 (1 H, *dd*, *J* = 1.5,9 Hz, ArH-3), 6.91 (1 H, *d*, *J* = 1.5 Hz, ArH-5).

The $LiAlH_4$-reduced product yielded a diacetate **2b** ($Ac_2O$–pyridine). IR $\nu_{max}^{Neat}$ $cm^{-1}$: 2940, 1758, 1725, 1608, 1500, 1445, 1365, 1238, 1210, 1020, 907, 830. $^1H$ NMR: δ 1.05 (3 H, *d*, *J* = 6 Hz, Me), 1.20 (6 H, *s*, 2 × Me), 1.25–1.65 (6 H, *m*), 1.78 (3 H, *s*, OCOMe), 2.06 (3 H, *s*, OCOMe), 2.14 (3 H, *s*, Me), 4.65 (1 H, *q*, *J* = 6,12 Hz, –CHOAc), 6.65 (1 H, *d*, *J* = 9 Hz, ArH-2), 6.80–7.00 (2 H, *m*, ArH-3,5). MS *m/z*: 320 ($M^+$), 279, 278, 218, 203, 192, 191, 161, 150, 149 (base), 148, 135, 133, 129, 121, 109, 107, 91.

*Substance D (isopimaric acid).* Rhombic flakes (MeOH), mp 160°, $[\alpha]_D$ +5° (*c*, 1.2, MeOH). It gave a violet-red colour with the Liebermann–Burchard reagent. $^1H$ NMR: δ 0.75 (3 H, *s*, Me-20), 0.79 (3 H, *s*, Me-17), 1.15 (3 H, *s*, Me-19), 4.71, 4.76, 5.67 ($J_{AB}$ = 2 Hz, $J_{AX}$ = 10 Hz, $J_{BX}$ = 17 Hz, –CH=$CH_2$), 5.17 (1 H, *m*, $W_{\frac{1}{2}}$ = 8 Hz, H-7), 8.50 (1 H, $D_2O$ exchangeable). MS *m/z*: 302 ($M^+$), 287, 273, 257, 241, 187, 173, 159, 148, 145, 131, 129, 121, 119, 117, 109, 107, 105 (base), 94, 93, 91, 81, 77.

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