Tetrahedron. Vol. 34, pp. 599 to 602. Pergamon Press, 1978. Printed in Great Britain

STUDIES IN SESQUITERPENES—LVIII

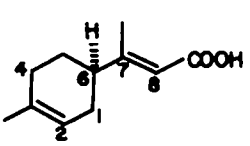
DEODARDIONE, A SESQUITERPENE DIOSPHENOL AND, LIMONENECARBOXYLIC ACID, A POSSIBLE NORSESQUITERPENE—COMPOUNDS FROM THE WOOD OF *CEDRUS DEODARA* LOUD.†‡

S. KRISHNAPPA and SUKH DEV*§
National Chemical Laboratory, Poona, India

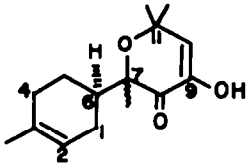
(*Received in UK 9 August 1975; Accepted for publication 30 August 1977*)

Abstract—Isolation and structure elucidation of a C_{11} mono-carboxylic acid, apparently a nor-sesquiterpene, and, a sesquiterpene diosphenol from the essential oil of *Cedrus deodara* Loud. are described.

In continuation of our studies[1] on the essential oil from the wood of *Cedrus deodara* Loud., we wish to report on the major constituents of the alkali-soluble fraction of the essential oil. The alkali-soluble fraction amounts to ~0.4% of the essential oil and has been investigated earlier (1916) by Roberts,[2] who reported the presence of an unidentified phenol. This, however, could not be substantiated by later (1922) workers.[3] We now find that this material is a complex mixture of $NaHCO_3$-soluble and NaOH-soluble compounds. From each of these fractions we have succeeded in isolating the major component, and have assigned structures 1 (limonenecarboxylic acid) and 2 (deodardione) respectively.



1

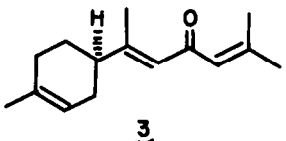


2

Limonenecarboxylic acid (1)

This compound was isolated from the $NaHCO_3$-soluble fraction by chromatography over silica gel. The compound, $C_{11}H_{16}O_2$ (M^+, *m/e* 180), m.p. 108–109°, $[\alpha]_D$ + 19.1° ($CHCl_3$), which must be an acid (equivalent wt., 180) from its method of isolation shows the following spectral/structural features: C=CH.COOH (λ_{max}^{EtOH} 225 nm, ϵ 9250. IR: 1688, 1635, 808 cm^{-1}. PMR: 1H, 5.67 ppm, *bs*), Me–C=C (PMR: 3H, *s*, 1.65 ppm; 3H, *s*, 2.19 ppm), –C=CH–CH_2 (PMR: 1H, 5.32 ppm, *m*).

From the above functionality and molecular formula, the compound must be monocarbocyclic. Gross structure implied in 1, appeared quite attractive as, it not only meets all the structural requirements, but has apparent relationship with atlantone (3),[1e] the chief oxygenated constituent of the *Cedrus deodara* essential oil.



3

This structure appears to be fully supported[4] by its mass spectrum, as the major fragments are readily rationalised (see 4, 5) in terms of 1. Furthermore, *E*-configuration shown in 1 is apparent from the chemical shift of the C(7)-Me, which occurs at 2.19 ppm, a position consistent only with the *cis* relationship of Me and the carbonyl function.[5]

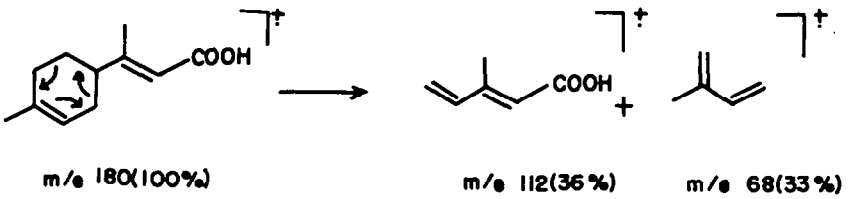
A survey of the literature showed that carboxylimonene (1, geometry not implied) has been obtained by two groups[6,7] of workers by the free radical-addition of CCl_4 to limonene, followed by alkaline hydrolysis. However, both these groups report a m.p. of 95–96°, with no comments on the geometry of the product; the latter authors[7] report $[\alpha]_D$ + 100°. At this stage a sample of this acid, synthesised by essentially the same method, became available through the courtesy of Prof. G. S. Krishna Rao,[8] for which these authors report m.p. 105–106°, $[\alpha]_D$ + 18.7°. A direct comparison (m.p., m.m.p., UV, IR, PMR) of the acid from *Cedrus deodara* with this sample, established their identity.[9] Almost at the same time another group of workers[10] reported an unambiguous synthesis of optically pure (+)-methyl ester of 1. The methyl ester of the acid isolated from the essential oil was identical (PMR) with the reported data except for its $[\alpha]_D$. Since, a value of + 79° has been reported for the optically pure ester and our ester has $[\alpha]_D$ + 25.6°, the material isolated from *Cedrus deodara*, is, thus, considerably racemised.[11,12] These comparisons also establish that 1 represents the absolute stereochemistry of the natural acid.[13] This also follows from the Absolute Stereochemistry Biogenetic Rule,[14] as the co-occurring (+)-atlantone, with which the C_{11} acid has obvious relationship, has the absolute stereochemistry[8,10] shown in 3.

Conceivably, the C_{11}-acid (1) may be a catabolic product[15] of atlantone (3) or another suitable bisabolene-based substrate. The possibility that this acid may be an artefact cannot be entirely ruled out, if one considers the possibility of auto-oxidation[16] of atlantone. However, the latter possibility is less likely as this acid is much *less* racemized than the atlantone present in the oil.

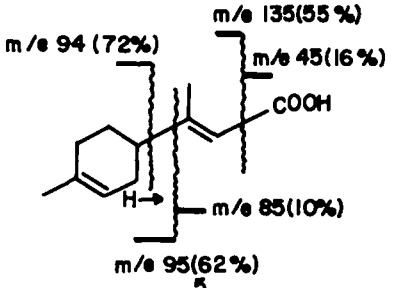
†Communication No. 2167, National Chemical Laboratory, Poona, India.

‡Presented at the Eighth I.U.P.A.C. Symposium on the Chemistry of Natural Products, New Delhi (1972). Abstract Book, p. C-90.

§Present address: Malti-Chem Research Centre, Nandesari, Vadodara, India.



4



5

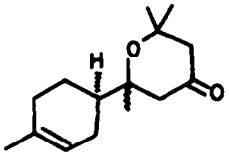
Deodardione (2)

This compound was isolated by chromatography of the NaOH-soluble fraction on silica gel: 5.4 kg of the essential oil furnished 103 mg of pure compound. The compound, m.p. 101–102°, $[\alpha]_D + 5.2°$, analyses for $C_{15}H_{22}O_3$ (M^+, *m/e* 250) and from its method of isolation, must be a phenol or an enol. From its absorption in the UV (λ_{max}^{EtOH} 269 nm, ϵ7120; $\lambda_{max}^{EtOH—NaOH_{aq}}$ 300 nm) it is clear that it is a diosphenol[17] and this is also supported by its IR[18] (3350, 1660, 1630 cm^{-1}) and PMR[19] spectra (CH=C–C=O: 1H, *s*, 5.90 ppm). The PMR spectrum shows following additional features: three Me–C–O (3H singlets at 1.40, 1.43 and 1.48 ppm), Me–C=C (3H, *bs*, 1.61 ppm) and Me–C–CH–CH_2– (1H, ill-resolved *m*, 5.30 ppm, $W_H = 8.5$ Hz). These features are quite reminiscent of the PMR spectrum of deodarone[1a] (6), which is a constituent of the *Cedrus deodara* essential oil, and hence, 2/7 appeared attractive as working structures.

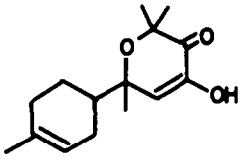
In order to adduce chemical evidence in support of the above conclusion, base-catalysed air oxidation[20] of deodarone (6) was carried out. The product was separated into $NaHCO_3$-soluble (50%), KOH-soluble (25%) and neutral (25%) fractions. The KOH-soluble fraction was shown by GLC to consist of two components (~2:1) of which the major component was shown by mixed GLC and PMR to be identical with the diosphenol from the essential oil. This transformation clearly leads to the formulation of deodardione as 2 or 7.

A distinction between 2 and 7 could be readily made on the basis of electron-impact-induced fragmentation. An examination of structures 2 and 7 shows that only structure 2 is capable of undergoing the highly site-specific McLafferty rearrangement[21] (8), which should generate ion *m/e* 156. Indeed, the mass spectrum of deodardione shows a fairly strong (50%) signal at *m/e* 156. The base peak at *m/e* 141 conceivably arises from this ion by loss of CH_3 radical (9); this is supported by the presence of a metastable ion peak in the mass spectrum at *m/e* 127.5 (calc. 127.4). Thus, deodardione can be assigned the structure 2. Apparently, the compound exists completely in the enolic form, as is clear from its PMR spectrum (*vide supra*).

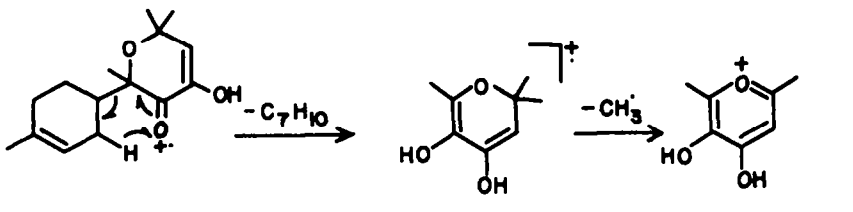
In order to cull further evidence in support of 2, deodardione was cleaved with alkaline H_2O_2[22] and the resulting dicarboxylic acid (10) purified as its dimethyl ester (11). The product, which had the expected features in its PMR spectrum, was



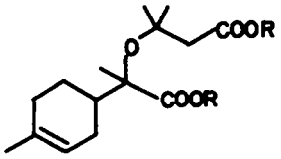
6



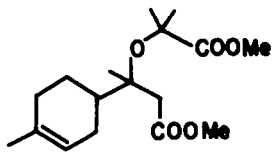
7



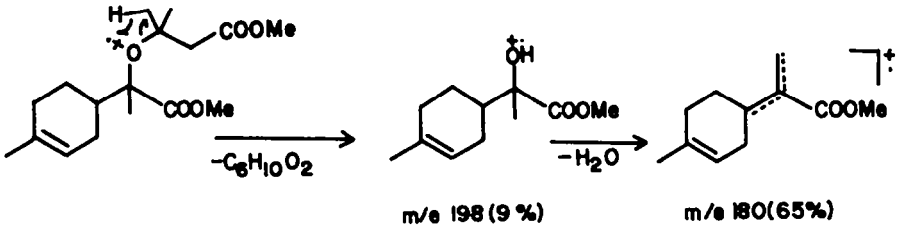
8 9



10: R=H
11: R=Me

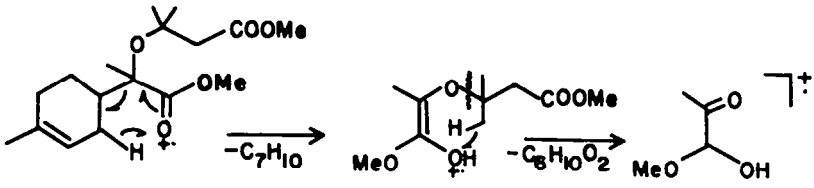


12



m/e 198 (9 %) m/e 180 (65%)

13



m/e 218 (13%) m/e 104 (60%)

14

examined for its mass spectral fragmentation, in order to identify ions which will be singularly characteristic of structure **11** and cannot be possibly derived from the alternative **12** based on **7**. Of several such fragmentations, only two will be pointed out. As can be seen from fragmentations **13** and **14**, the mass spectrum of the derived dimethyl ester clearly supports structure **2** for the *Cedrus deodara* diosphenol.

Like all other bisabolane-based sesquiterpenoids from the essential oil of *Cedrus deodara*, deodardione (**2**) must also be partially racemic. For remarks on absolute stereochemistry and configuration at C(7), reference is invited to our publication[18] on deodarone.

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light petrol refers to the fraction b.p. 60–80°. Optical rotations were measured in $CHCl_3$ at room temp. (30 ± 2°) on a Perkin–Elmer polarimeter model 141.

UV spectra were taken on Perkin–Elmer spectrophotometer, model 350, in 95% EtOH. IR spectra were recorded as smears (liquid) or as a mull in Nujol (solids) on a Perkin–Elmer Infracord model 137E. PMR spectra were taken in 10% soln in CCl_4 on a Varian A-60 spectrometer; signals are recorded in δ(ppm) relative to TMS as zero. While citing PMR data the following abbreviations have been used: *s*, singlet; *d*, doublet; *t*, triplet; *q*, quartet; *m*, multiplet; *b*, broad. Mass spectra were determined on a CEC mass spectrometer, model 21–110B using an ionizing voltage of 70 eV and a direct inlet system; besides the molecular ion, eight most abundant ions, above *m/e* 50 are reported with their relative intensities.

GLC analyses were carried out on "Aerograph" model A-350-B using Al columns (300 × 0.6 cm) packed with 20% diethyleneglycol polysuccinate on Chromosorb W (60–80 mesh); H_2 was used as the carrier gas.

SiO_2-gel for column chromatography (−100, +200 mesh) was activated at 125–130°/6–8 hr and standardised.[23] TLC was carried out on 0.3 mm layers of SiO_2-gel containing 15% gypsum; visualisation: 1% vanillin in 30% H_3PO_4 aq, followed by heating at ~110°/10 min.

Limonenecarboxylic acid (**1**)

The essential oil[24] (2.7 kg) diluted with an equal volume of light petrol, was extracted first with 10% $NaHCO_3$ aq (200 ml × 4) and then with 10% NaOH aq (200 ml × 4).

The $NaHCO_3$ extract was washed with ether (100 ml × 2) and then acidified with 30% H_3PO_4 aqueous to pH 2. The liberated acids were taken up in ether (100 ml × 3), washed with brine and dried (Na_2SO_4). The solvent was flashed off to furnish a product (4.2 g), a part (1.421 g) of which was chromatographed on SiO_2 gel/IIa (70 × 2 cm) with TLC monitoring (solvent: 10% acetone in $CHCl_3$) and using increasing amounts (0, 10, 15, 20, 25%) of $CHCl_3$ in C_6H_6 as eluant. 25% $CHCl_3$ in benzene (100 ml × 16) eluted 0.6 g of material in which one component

((TLC, R_f 0.42) predominated; all earlier fractions (total material ~ 0.8 g) were complex mixtures. This product (0.6 g) was rechromatographed (SiO_2-gel/IIa, 70 × 1.5 cm) as before, when 20% $CHCl_3$ in C_6H_6 (100 ml × 8) gave the product with R_f 0.42 in an essentially pure state, m.p. 97–105° (0.241 g). The product was recrystallised from light petrol to furnish colorless crystals (0.148 g), m.p. 108–109°, $[\alpha]_D$ + 19.1° (*c*, 0.9%). Mass: *m/e* 180 (M^+, 100%), 135 (55%), 121 (43%), 113 (47%), 111 (64%), 107 (55%), 95 (62%), 94 (74%), 79 (60%). (Found: C, 73.62; H, 8.89 $C_{11}H_{16}O_2$ Requires: C, 73.30: H, 8.95%).

Methyl ester (CH_2N_2 method): b.p. 130–135° (bath)/8 mm; $[\alpha]_D$ + 25.6° (*c*, 2.5%). PMR: two Me–C=C (3H singlets at 1.65, 2.15 ppm), COOMe (3H, *s*, 3.63 ppm), –C=CH–CH_2 (1H, *m*, 5.35 ppm), –C=CH.COOMe (1H, *s*, 5.62 ppm). (Found: C, 74.35: H, 9.26. $C_{12}H_{18}O_2$ requires: C, 74.19; H, 9.34%).

Deodardione

The aqueous NaOH soluble extract, described under (1) above, was re-extracted with ether (100 ml × 2) and then acidified with 30% H_3PO_4 aqueous. The hazy soln was saturated with ammonium sulphate and extracted with ether (200 ml × 3). The combined ether extracts were washed with brine (100 ml × 2), dried (Na_2SO_4) and freed of solvent to give a product (7.8 g). Two such lots were combined and chromatographed on SiO_2-gel/IIB (70 × 5 cm) with TLC (solvent: 10% acetone in $CHCl_3$) monitoring and, using increasing amounts (0, 5, 15, 20 and 50%) of $CHCl_3$ in C_6H_6 as eluant; solvent cuts of 500 ml were made. 5% $CHCl_3$ in C_6H_6 (500 ml × 4) eluted 1.2 g (TLC: three spots with R_f 0.84, 0.79 and 0.76) of material in which component with R_f 0.79 predominated; material eluted (100 mg) before this fraction was rejected, while the material (~ 12 g) eluting after this was a complex mixture and failed to give any pure compound. The above 5% $CHCl_3$ in C_6H_6 fraction was rechromatographed (SiO_2-gel/IIB, 100 cm × 1.6 cm) as before to finally give a solid fraction (341 mg, m.p. 85–98°), which was twice recrystallized from light petrol to furnish pure 2 (103 mg), m.p. 101–102°, $[\alpha]_D$ + 5.2° (*c*, 1.1%). IR: 3350, 1660, 1630, 1230, 1140, 1032, 1010, 897, 852, 798, 787 cm^{-1}. Mass: *m/e* 250 (M^+, 10%), 156 (50%), 141 (100%), 95 (40%), 94 (9%), 83 (33%), 79 (9%), 67 (11%), 55 (10%). (Found: C, 72.09; H. 8.85. $C_{15}H_{22}O_3$ requires: C, 71.97; H, 8.86%).

Base-catalysed oxidation of deodarone

A soln of deodarone (118 mg) in *t*-BuOH (3 ml) was added to a soln of *t*-BuOK (84 mg) in *t*-BuOH (5 ml) and the reaction mixture stirred in oxygen atmosphere at room temp. (25°) and pressure (740 mm). Absorption of O_2 almost ceased after absorption of ~ 13.2 ml of the gas (~ 3 hr). The mixture was diluted with water (10 ml) and acidified with 30% H_3PO_4 aqueous. The product was taken up in ether (15 ml × 3) and separated into $NaHCO_3$-soluble (56 mg), KOH-soluble (32 mg) and neutral (38 mg) fractions in the usual manner. The KOH-soluble product was purified by PLC (solvent: 5% $CHCl_3$ in benzene). The major component showed on GLC two peaks having RRT of 1.0 and 1.7 (2:1).

Oxidative cleavage of deodardione

Deodardione (50 mg) in dioxane (5 ml) was mixed with KOH–methanolic (500 mg KOH in 5 ml MeOH) and heated under stirring to 50°. H_2O_2-aqueous (30%, 3 ml) was slowly added (15 min) with stirring at the same temp. Stirring was continued for an additional 30 min at 50°, and the mixture diluted with ice-water (10 ml) and acidified with 30% H_3PO_4 aqueous. The product was taken up in ether (15 ml × 3) and worked up in the usual manner to get the crude acid **10** (52 mg). This was converted into the *methyl ester* by CH_2N_2 in ether and the crude ester (50 mg) passed through a small column of SiO_2-gel/IIA, using benzene as eluant. The product (32 mg) was TLC (5% EtOAc in C_6H_6) pure: b.p. 134–136° (bath)/0.5 mm, n_D^{30} 1.5108. PMR: Me–C=O (3H singlets at 1.32, 1.38 and 1.41 ppm), Me–C=C (3H, *bs*, 1.63 ppm), COOMe (two 3H singlets at 3.56 and 3.72 ppm; there is evidence of small shoulders on each peak! C-7 diastereoisomer)?, =C=CH–CH_2 (1H, *m*, 5.29 ppm). Mass: *m/e* 253 $M^+ - 59$, 20%), 180 (65%), 139 (85%), 121 (40%), 115 (80%), 104 (60%), 95 (80%), 73 (100%), 55 (35%). (Found: C, 65.27; H, 8.88. $C_{17}H_{28}O_5$ requires: C, 65.36; H, 9.03%).

REFERENCES AND NOTES

[1a]G. S. Krishna Rao, Sukh Dev and P. C. Guha, *J. Indian Chem. Soc.* **29**, 721 (1952); [b]T. C. Joseph and Sukh Dev, *Tetrahedron* **24**, 3809, 3841, 3853 (1968); [c]R. C. Pandey and Sukh Dev, *ibid.* **24**, 3829 (1968); [d]S. C. Bisarya and Sukh Dev, *Ibid.* **24**, 3861, 3869 (1968); [e]B. S. Pande, S. Krishnappa, S. C. Bisarya and Sukh Dev, *Ibid.* **27**, 841 (1971); [f]R. Shankaranarayan, S. Krishnappa and Sukh Dev, *Ibid.* **33**, 885 (1977); [g]R. Shankaranaryan, S. Krishnappa, S. C. Bisarya and Sukh Dev, *Ibid.* **33**, (1977); [h]R. Shankaranarayan, S. C. Bisarya and Sukh Dev, *Ibid.* **33**, (1977).

[2]O. D. Roberts, *J. Chem. Soc.* **109**, 791 (1916).

[3]J. L. Simonsen and M. G. Rau, *Indian Forest Records* **9**, 123 (1922); *J. Soc. Chem. Ind.* **42**, A 29 (1923).

[4]See e.g. Ref. 1*e*.

[5]See e.g. L. M. Jackman and S. Sternhell, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, pp. 222–225. Pergamon, Oxford (1969); H. N. A. Al-Jallo and E. S. Waight, *J. Chem. Soc.* (B) 75 (1966); Ref. 1*e*.

[6]S. Israelashvili and E. Diamant, *J. Am. Chem. Soc.* **74** 3185 (1952).

[7]G. Dupont, R. Dulou and G. Clement, *C. R. Acad. Sci.* **236**, 2512 (1953).

[8]J. Alexander and G. S. Krishna Rao, *Abstract Book, Eighth IUPAC Symp. Chem. Natural Products* p. C–40, New Delhi (1972); *Indian J. Chem.* **11**, 859 (1973).

[9]We are grateful to Prof. G. S. Krishna Rao for supply of an authentic sample.

[10]R. J. Crawford, W. F. Erman and C. D. Broaddus, *J. Am. Chem. Soc.* **94**, 4298 (1972).

[11]It may be pointed out here that all bisabolane-based sesquiterpenoids isolated so far from *Cedrus deodara* Loud. are considerably racemized; e.g. see Ref. 1*g*.

[12]This would also mean that the preparation of Alexander and Rao[8] is also considerably racemized. Different extent of racemization might account for the difference in the m.ps of the acid of these authors and that of earlier workers.[6,7]

[13]Obviously, the reference is to be optically active acid, which should be present to the extent of some 30% in the product. This value may not be very reliable as the values of $[\alpha]_D$ reported for the two preparations are in different solvents: EtOH[10], $CHCl_3$ (present work).

[14]A. H. Kapadi, R. R. Sobti and Sukh Dev, *Tetrahedron Letters* 2729 (1965).

[15]Cf. e.g.: D. R. Adams, S. P. Bhatnagar and R. C. Cookson, *J. Chem. Soc.* Perkin I 1502 (1975). These authors report a C_{12}–ketone, based on atlantone, in the essential oil from *Cedrus atlantica* Manet; however, see Ref. 1*g*.

[16]See e.g. autoxidation of $\alpha\beta$-unsaturated ketones: E. G. E. Hawkins, *J. Chem. Soc.* 3288 (1955).

[17]See, e.g. A. Melera and C. R. Noller, *J. Org. Chem.* **26**, 1213 (1961).

[18]See, e.g. W. H. Baarschers, D. H. S. Horn and L. R. F. Johnson, *J. Chem. Soc.* 4046 (1962).

[19]C. R. Noller, A. Melera, M. Gut, J. N. Shoolery and L. F. Johnson, *Tetrahedron Letters* No. 15, 15.

[20]D. H. R. Barton, E. J. Bailey and J. Elks, *Proc. Chem. Soc.* 214 (1960); B. Camerino, B. Patelli and R. Sciaky, *Tetrahedron Letters* 554 (1961).

[21]H. Budzikiewics, C. Djerassi and D. H. Williams, *Mass Spectrometry of Organic Compounds*, pp. 155–162. Holden-Day, San Francisco (1967).

[22]See, e.g. E. Kyburz, B. Riniker, H. R. Schenk, H. Heusser and O. Jeger, *Helv. Chim. Acta* **36**, 1891 (1953).

[23]R. Hernandez, R. Hernandez, Jr. and L. R. Axelrod, *Analyt. Chem.* **33**, 370 (1961).

[24]The essential oil of *Cedrus deodara* was obtained from Standard Essential Oil Distillers, Kanpur.