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TERPENOIDS*—XCIX

STRUCTURE AND ABSOLUTE CONFIGURATION OF KHUSINOLOXIDE, A NEW ANTIPODAL SESQUITERPENE EPOXY ALCOHOL FROM VETIVER OIL

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Abstract—A new laevorotatory epoxy alcohol, khusinoloxide, $C_{15}H_{24}O_2$, has been isolated from North Indian vetiver oil (*Vetiveria zizanioides*, Linn). Structure I has been assigned to it on the basis of IR and NMR spectra and its correlation with khusinol (II), of known absolute configuration. Khusinoloxide also belongs to the antipodal group of cadinenes.

IN PREVIOUS communications,[1-3] the isolation and characterisation of several antipodal cadinenic hydrocarbons and alcohols from North Indian vetiver oil (*Vetiveria zizaniodes*, Linn), have been described. Further investigation on the alcoholic fraction of the oil has led to the isolation of a new, crystalline epoxy alcohol, $C_{15}H_{24}O_2$, named khusinoloxide because of its structural relation with khusinol. Kushinoloxide was isolated in a pure state (TCL), free from other related components by extensive column chromatography over alumina and further purified by crystallization.

Evidence presented in this paper shows that khusinoloxide is represented by the structure I. Its IR spectrum (Fig. 1), exhibits bands at 3500 (OH group); 1650 and 833 (trisubstituted double bond) and at 1120, 1073 and 850 cm^{-1} (epoxide group). Khusinoloxide gives a positive tetranitromethane test and the presence of only one double bond is indicated by perbenzoic acid titrations. Reduction of khusinoloxide with LAH gives a crystalline diol, $C_{15}H_{26}O_2$, (IR spectrum, Fig. 1.), identified as khusinodiol (III) by mixed m.p. and comparison of the IR spectrum with that of an authentic sample recently prepared in our laboratory,[4] from khusinol by treatment with BF_3-ethereate. Thus khusinoloxide is a cadinenic epoxy alcohol and can be represented by one of the structures I, IV, and V. The NMR spectrum of khusinoloxide (Fig. 2), however, supports structure I. It shows signals at 9·32, 9·19, 9·13 and 9·02τ (6H), due to an isopropyl group; a signal at 8·35 τ (3H) is due to a Me group on a double bond; a doublet centred at 7·39 τ (J = 4 c/s, 2H), shows the presence of the protons on the epoxide ring; a broad triplet at 6·38 τ (1H) is due to the proton on the carbon atom bearing the secondary OH group; a signal at 5·65 τ (1H) can be attributed to the OH proton, which disappears on D_2O exchange; and a broad signal

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* Communication No. 944 from the National Chemical Laboratory, Poona 8, India.

[1] P. S. Kalsi, K. K. Chakravarti and S. C. Bhattacharyya, *Tetrahedron* **19**, 1073 (1963).

[2] C. C. Kartha, P. S. Kalsi, A. M. Shaligram, K. K. Chakravarti and S. C. Bhattacharyya, *Tetrahedron* **19**, 241 (1963).

[3] A. S. Rao, K. L. Surve, K. K. Chakravarti and S. C. Bhattacharyya, *Tetrahedron* **19**, 233 (1963).

[4] G. K. Trivedi, A. D. Wagh, S. K. Paknikar, K. K. Chakravarti and S. C. Bhattacharyya, *Tetrahedron* **22**, 1641 (1966).

at 4·55 τ (1H) is attributable to the proton on the trisubstituted olefinic linkage. The β-orientation of the epoxy group follows from the β-orientation of the OH group in the diol III.

A monoepoxide of khusinol (II) was prepared by treatment with one mol. of perbenzoic acid. It is interesting to note that the exocyclic double bond underwent epoxidation in preference to the trisubstituted double bond,[2,5] to afford an epoxy alcohol, $C_{15}H_{24}O_2$, identified as khusinoloxide by m.p. and mixed m.p. determination and comparison of the IR spectrum (Fig. 1) with that of the natural product. These reactions confirmed structure I for khusinoloxide.

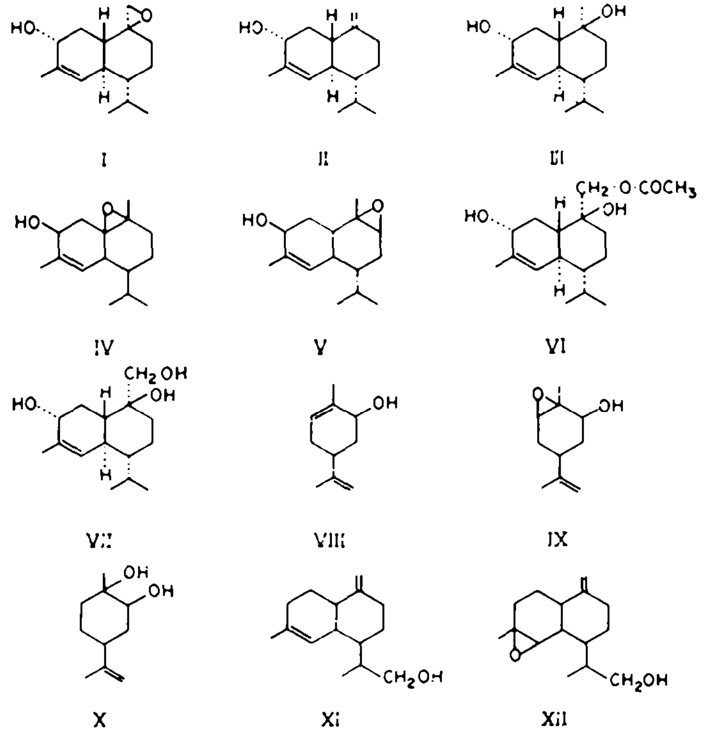

Fig. 1

Khusinoloxide, on treatment with glacial acetic acid at room temperature, furnishes a hydroxy acetate VI, $C_{17}H_{28}O_4$, (IR spectrum, Fig. 1). The NMR spectrum is in agreement with this structure for the hydroxy acetate, which, on hydrolysis, furnishes the corresponding triol, $C_{15}H_{26}O_3$ (VII).

In order to investigate the unusual behaviour of khusinol towards one mole of perbenzoic acid, whereby it forms a monoepoxide at the exocyclic double bond in preference to the trisubstituted double bond, carveol (VIII), which has a comparable structural feature, was treated with one mol. of perbenzoic acid under identical conditions. However, in the case of VIII, the trisubstituted double bond was observed to undergo epoxidation in preference to the end methylenic double bond.

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[5] C. C. Kartha and K. K. Chakravarti, *Tetrahedron* 21, 139 (1965).

The monoepoxide (IX), obtained from carveol, shows absorption at 1634, 892 cm^{-1} for an end methylene group and at 847 cm^{-1} for an oxide linkage, in its IR spectrum. The NMR spectrum was in conformity with this structure. On LAH reduction, this epoxide yielded the corresponding diol X, the structure of which was proved by a comparison of its physical properties with those reported in the literature.[6]

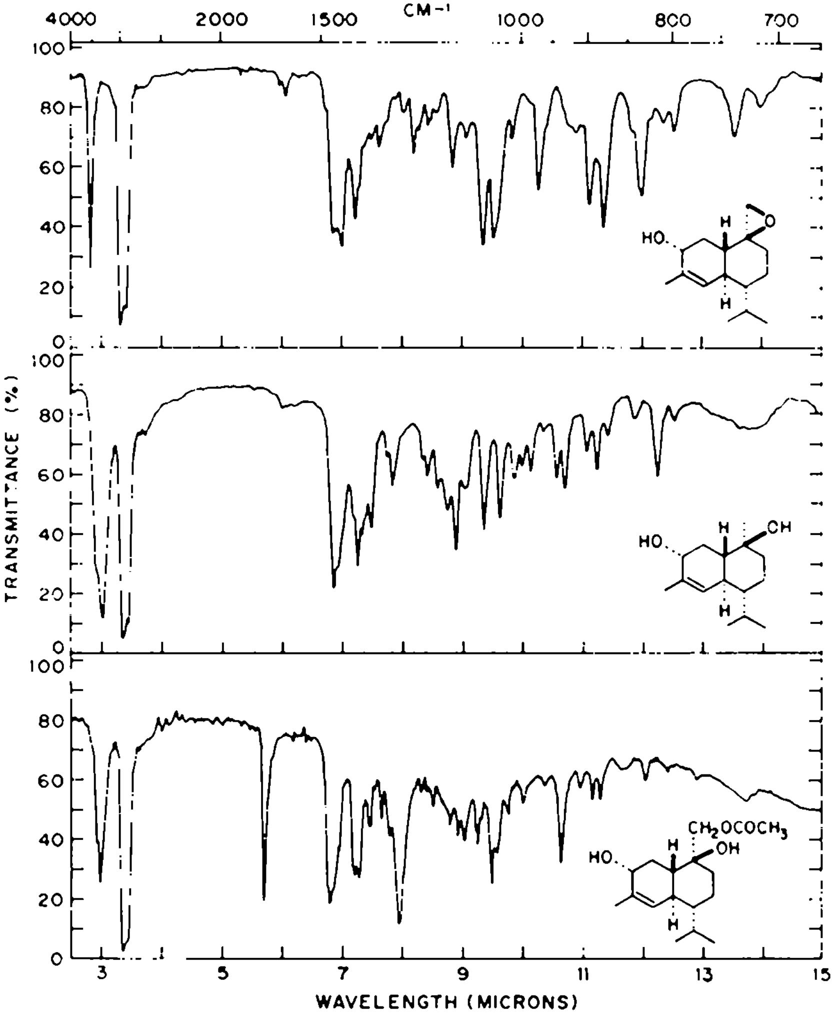

FIG. 2

The IR spectrum of the diol showed that the end methylenic double bond was in tact (bands at 1652, 882 cm^{-1}) and revealed the presence of OH groups (bands at 3283, 1064, 1014 cm^{-1}). The structure was further confirmed by a study of its NMR spectrum. Thus, carveol undergoes normal expected epoxidation of the trisubstituted double bond.

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[6] William F. Newhall, *J. Org. Chem.* **29**, 185 (1964).

Khusol (XI) also, on treatment with one mol. of perbenzoic acid, under identical conditions, gives the monoepoxide (XII), as revealed by its IR and NMR spectra. $\left(893\ \text{cm}^{-1};\ 5{\cdot}38 \text{ and } 5{\cdot}45\ \tau;\ \begin{smallmatrix}\diagdown\\ \ \\ \diagup\end{smallmatrix}\!C{=}CH_2\right)$

Thus, khusinol exhibits an apparently abnormal behaviour, which may deserve further scrutiny.

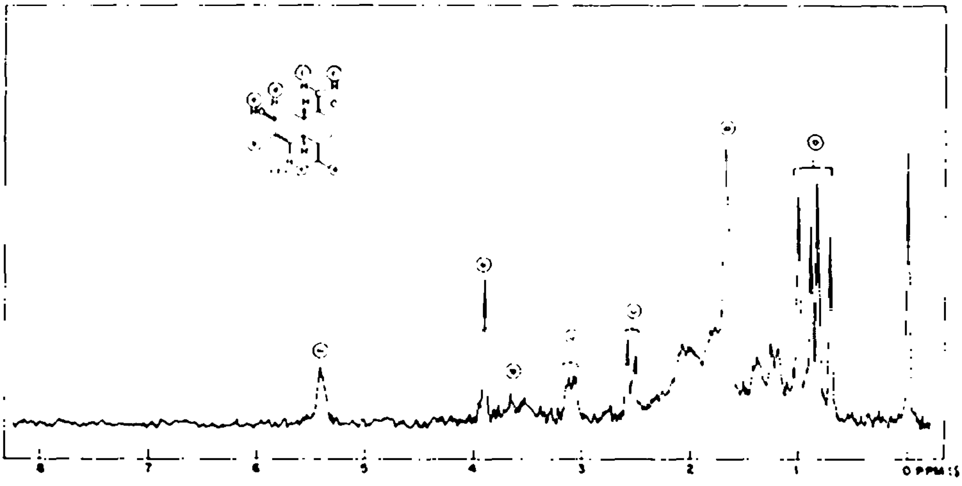

FIG. 3

EXPERIMENTAL

All m.ps are uncorrected. Pet. ether refers to the fraction b.p. 60–80°. Optical rotations were taken in chf. IR spectra were recorded in nujol suspension on a Perkin-Elmer infracord spectrophotometer (Model No. 137B). NMR spectra were recorded with a Varian A-60 spectrophotometer operating at 60 MC, TMS being used as an internal standard. Microanalyses were carried out in the Microanalytical Section of the Laboratory.

Alumina used for chromatography was acid-washed, activated and graded according to the Brockman scale[7,8] of activity. TLC analysis was carried out on silica-gel containing 15% gypsum according to standard procedures.

Isolation of khusinoloxide (I). Vetiveroil (1 kg), obtained from Bharatpur in North India, was chromatographed on alumina (Gr. III, 20 kg) and eluted successively with pet. ether (40 l.), benzene (45 l.) and ether (30 l.). The product (350 g), obtained by elution with benzene, deposited crystals of khusinol[9] on cooling. Khusinol was filtered and the filtrate on storing at 0° furnished more of khusinol. The filtrate was then further chromatographed on alumina (Gr. II, 16 kg) and eluted successively with benzene (40 l.), benzene–ether (1:1, 50 l.) and ether (20 l.). The benzene–ether fraction was extensively chromatographed on Gr. II alumina (25 to 30 times) to furnish I (0·9 g; TLC pure). It was crystallized from pet. ether when long shining needles deposited, m.p. 113°, $[\alpha]_D^{30}$ −24·9° (*c*, 1·9). (Found: C, 75·60; H, 10·63. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%.)

Khusinodiol (III) *from khusinoloxide* (I). A soln of khusinoloxide (100 mg) in dry ether (5 ml) was added dropwise to a stirred suspension of LAH (25 mg) in dry ether (20 ml). The mixture was stirred for 10 hr under reflux and excess of LAH was decomposed with water, followed by cold dil. HCl. After extraction with ether, the product obtained was crystallized from pet. ether to yield khusinodiol (88 mg), m.p. 130°, [α] +22·7° (*c*, 3·12). (Found: C, 75·13; H, 10·85. $C_{15}H_{26}O_2$ requires: C, 75·58; H, 11·00%.)

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[7] H. Brockman and H. Schödder, *Ber. Dtsch. Chem. Ges.* 74, 73 (1941).

[8] F. Lederer and M. Lederer, *Chromatography* p. 26, Elsevier, N.Y. (1957).

Khusinoloxide (I) *from khusinol* (II). A soln of khusinol (1·23 g) in chf (50 ml) was treated with one mole perbenzoic acid (12 ml, 0·93N) in chf solution at 0°. After 24 hr, the chf solution was washed with $NaHCO_3$aq, water and dried (Na_2SO_4). Evaporation of the solvent gave an epoxy alcohol, which was crystallized several times from pet. ether, m.p. and mixed m.p. with I, 113°, $[\alpha]_D$ −24·0°. (Found: C, 76·13; H, 10·85. $C_{15}H_{24}O_2$ requires: C, 76·22; H, 10·24%.)

Hydroxy acetate VI *from khusinoloxide* (I). Khusinoloxide (0·5 g) was mixed with glacial AcOH (1·5 ml) and kept at the room temp for 48 hr. Excess of acetic acid was removed under reduced pressure, the residue taken up in ether, washed with Na_2CO_3aq and water, dried (Na_2SO_4) and solvent removed to furnish the crude VI (0·58 g). It was chromatographed on alumina (Gr. II, 20 g). Pet. ether–ether (1:1, 50 ml) eluted the unreacted epoxide (0·10 g). Pure (TLC) hydroxy acetate (0·39 g) was eluted with acetone. It was crystallized from ether, m.p. 143°, $[\alpha]_D$ +18·0° (*c*, 3·20).

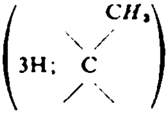
NMR spectrum shows the presence of an isopropyl group (9·31, 9·20, 9·15 and 9·04 τ; 6H); a Me group on a double bond (8·35 τ; 3H); an acetate Me group on a carbon atom carrying an oxygen atom (7·9 τ, 3H; $—O—CO—CH_3$); a proton attached to a carbon carrying the OH group (6·0 τ, 1H; $—CH$OH); two methylenic protons on the carbon atom carrying an acetoxy group (5·66 τ, 2H; $—CH_2—O—CO—CH_3$) two OH groups (5·15, 5·55 τ; 2H; which disappear on D_2O exchange); a proton on a trisubstituted olefinic linkage (a broad singlet at 4·58 τ, 1H). (Found: C, 69·00; H, 9·77. $C_{17}H_{28}O_4$ requires: C, 68·89; H, 9·52%.)

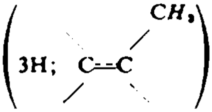
Triol VII *from the hydroxy acetate* VI. Hydroxy acetate (0·1 g), on saponification with alcoholic potash, gave VII as a pale yellow glassy material. It was filtered and dried.

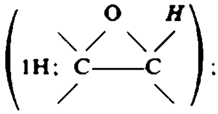
IR bands (in nujol suspension) at: 3571, 3300, 1389, 1370, 1100, 1058, 926, 843, 820, 800 cm⁻¹. (Found: C, 70·50; H, 10·45. $C_{15}H_{26}O_3$ requires: C, 70·83; H, 10·30%.)

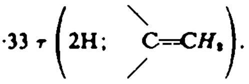
Carveol monoepoxide (IX) *from carveol* (VIII). Carveol (1·75 g), obtained by LAH reduction of carvone, in chf (10 ml), was treated with perbenzoic acid (20 ml, 1·2N; 1·02 moles) at 0° and the mixture was kept at the same temp for 24 hr. The product (1·8 g) was worked up as usual. IR and TLC analyses showed the presence of a small amount of unreacted carveol. Pure carveol monoepoxide was obtained by preparative TLC.

IR bands (liq. film) at: 3396, 3063, 1634, 1052, 892, 847 cm⁻¹.

NMR spectrum shows signals at 8·64 τ 

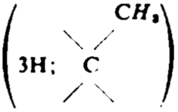
; 8·34 τ 

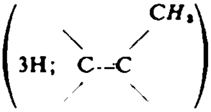
; 7·27 τ (1H; $—CH$OH); a doublet centred at 7·03 τ 

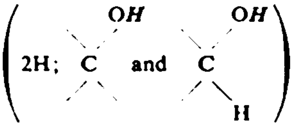
: a sharp singlet at 5·33 τ 

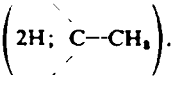
. (Found: C, 70·94; H, 9·86. $C_{10}H_{16}O_2$ requires: C, 71·39; H, 9·59%.)

Diol X *from carveol monopoxide* (IX). Carveol monepoxide (1·0 g) in dry ether (20 ml) was added slowly to a stirred suspension of LAH (0·2 g) in dry ether (25 ml) and refluxed for 6 hr. The product was worked up as usual to get the crude diol (1·1 g) which was chromatographed on alumina (Gr. II, 40 g). Pet. ether (100 ml) eluted a liquid component (150 mg). Pure diol (TLC) was obtained in a crystalline form in the end fractions of ether elution, m.p. 68–70°C (lit.[4] m.p. of *trans*-1,2-*trans*-1,4,p-meth-8-ene-1,2-diol, 70–71·6°) IR bands (in nujol suspension) at: 3283, 1652, 1370, 1165, 1147, 1068, 1014, 939, 882 cm⁻¹.

NMR spectrum shows signals at 8·82 τ 

8·32 τ 

; 7·70 τ (1H; $—CH$OH); 7·15 and 7·37 τ 

; 5·32 τ 

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(Found: C, 70·23; H, 10·64. $C_{10}H_{18}O_2$ requires: C, 70·54; H, 10·66%.)