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THE STRUCTURE AND STEREOCHEMISTRY OF LYRATOL A NEW C_{10} ALCOHOL FROM *CYATHOCLINE LYRATA*

O. N. DEVGAN and M. M. BOKADIA
Chemistry Department, Vikram University, Ujjain, India

and

AJAY K. BOSE

Department of Chemistry and Chemical Engineering
Stevens Institute of Technology, Hoboken, New Jersey 07030, U.S.A.

and

G. K. TRIVEDI and K. K. CHAKRAVARTI
National Chemical Laboratory, Poona, India

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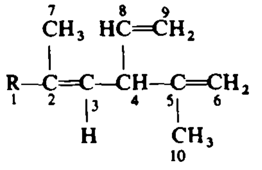
Abstract—Chemical reactions of lyratol are shown to confirm the modified isoprenoid structure 1 derived earlier mostly on the basis of spectral data. The stereochemistry of lyratol and the structure of its reduction products are deduced from a study of their NMR spectra.

IN A PRELIMINARY communication[1] the modified isoprenoid structure I was deduced for lyratol mainly on the basis of NMR spectral data but no stereochemical assignment was made. We report here chemical reactions of lyratol and information regarding its stereochemistry.

Lyratol, $C_{10}H_{16}O$ (I) and its acetate, $C_{12}H_{18}O_2$ (II) were isolated[2] from the essential oil of *Cyathocline lyrata* by repeated chromatography on alumina followed by chromatography on silica gel.



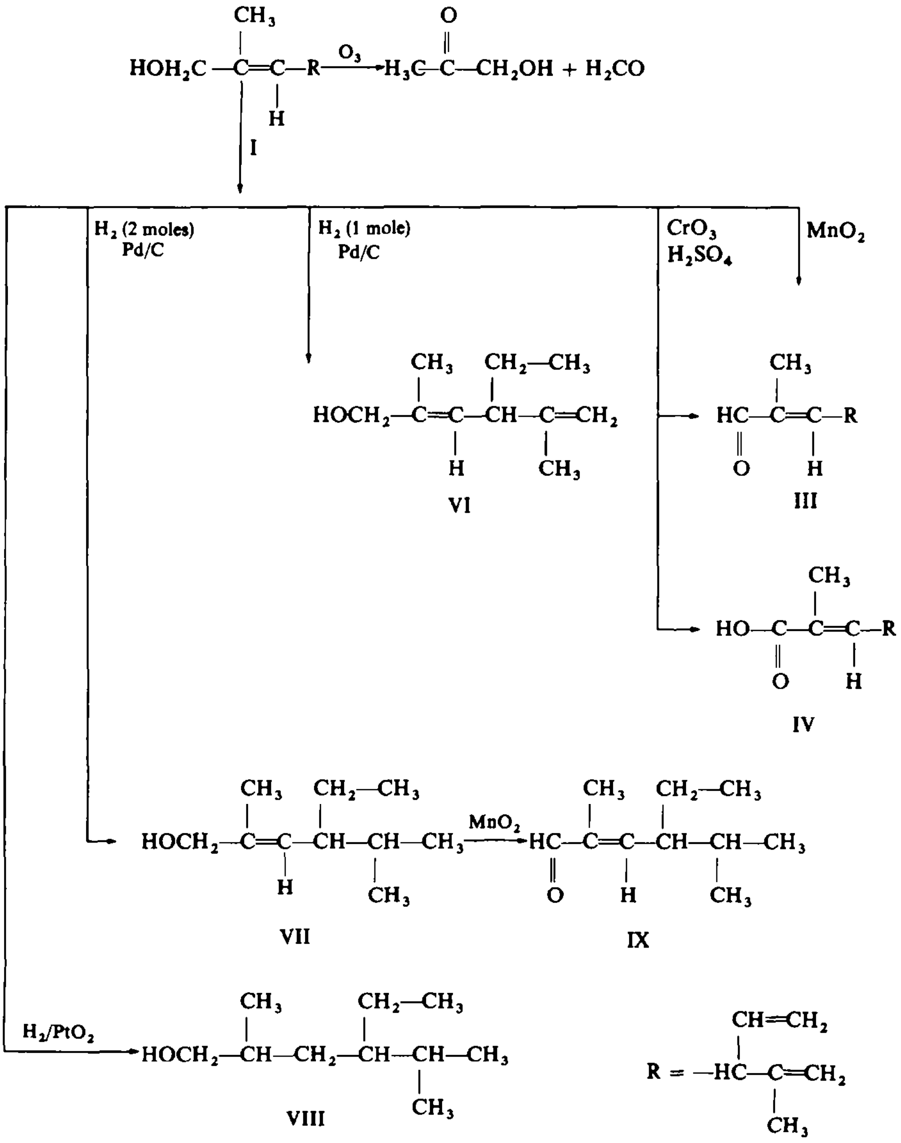
$$\underset{1}{R}{-}\overset{\overset{7}{CH_3}}{\overset{|}{\underset{2}{C}}}{=}\underset{\underset{H}{|}}{\overset{}{C}}{}^{3}{-}\overset{\overset{8\ \ \ 9}{HC=CH_2}}{\overset{|}{\underset{4}{CH}}}{-}\underset{\underset{\underset{10}{CH_3}}{|}}{\overset{5}{C}}{=}\underset{6}{CH_2}$$

1 : R = CH_2OH
II : R = CH_2OAc
V : R = CO_2Me

Chemical transformations of lyratol

Treatment of I with acetic anhydride and pyridine converted it to a monoacetate II. Catalytic hydrogenation in presence of PtO_2 and acetic acid gave hexahydro lyratol VIII, $C_{10}H_{22}O$. The dihydro alcohol, VI, could be obtained by controlled hydrogenation using palladium on charcoal as the catalyst. Controlled hydrogenation of lyratol to tetrahydrolyratol, VII, was also successful.

CHART I



Jones oxidation of I produced a mixture of a conjugated aldehyde lyratal III and lyratic acid IV. The same aldehyde was obtained in quantitative yield by oxidizing lyratol with active MnO_2. Oxidation of tetrahydrolyratol with MnO_2 also afforded a conjugated aldehyde IX. Ozonization of lyratol gave rise to formaldehyde and hydroxyacetone.

All the reactions of lyratol described above support the structure I previously reported for this terpene. Structures for its various derivatives (Chart I) are readily assigned on the basis of chemical reactions and spectral data.

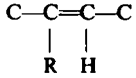
Spectral studies

Lyratol shows only end absorption in the UV region and is thus free of conjugated double bonds. The IR spectrum is indicative of —OH, vinylic double bond (913 cm^{-1}), unsymmetrical disubstituted double bond (888 cm^{-1}) and trisubstituted double bond (813 cm^{-1}). Since the absorption due to the vinyl double bond disappears in its IR spectrum, dihydrolyratol should have the structure VI. Tetrahydrolyratol possesses only the trisubstituted double bond (813 cm^{-1}) and, therefore, corresponds to VII. The NMR spectra of VI and VII are in accordance with the structures assigned to them. In the NMR spectrum of lyratol I, the long range coupling between the protons at C_3 and C_7 (the methyl protons) is slightly larger than that between the protons at C_3 and C_1 (the methylene protons of the alcohol group). This suggests that the C—H is *cis* to the carbinol group.

In a recent publication[3] an additivity rule has been proposed for the chemical shift of an olefinic proton [$\delta_{(\mathrm{H\ olefin})}$]. The geometry around a double bond can be predicted by using the equation:

$$\delta_{(\mathrm{H\ olefin})} = 5{\cdot}28 + \sum_i Z_i$$

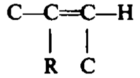
Pascual *et al.*[3] have collected an extensive Table of chemical shift increments Z_i due to various groups in geminal, *cis* or *trans* relationship to the olefinic proton under observation. An examination of this table shows that $Z_{\mathrm{CH_2OH}}$ is essentially the same for *cis* and *trans* positions. However, the conjugated aldehyde III and ester V are suitable for discrimination between *cis* and *trans* geometry around the C_2—C_3 double bond. The $\delta_{(\mathrm{H\ olefin})}$ computed from increment values given by Pascual *et al.*[3] are shown below: X, δ 6·42; XI, δ 6·67; XII, δ 6·58; XIII, δ 6·02. The C—H signal was a double of multiplets centered at δ 6·36 in the aldehyde IV and at δ 6·62 in the ester V. Clearly, the C_3—H in lyratol is *cis* to the alcohol group and *trans* to the Me group.



$\mathrm{C{-}\underset{R}{\underset{|}{C}}{=}\underset{H}{\underset{|}{C}}{-}C}$

X: R = CHO

XII: R = CO_2CH_3



$\mathrm{C{-}\underset{R}{\underset{|}{C}}{=}\underset{C}{\underset{|}{C}}{-}H}$

XI: R = CHO

XIII: R = CO_2CH_3

The mass spectra of I, III and V have some interesting features. The molecular ion is insignificant in the spectrum of lyratol and absent in the spectra of the aldehyde III and ester V. In each case there is a small but significant $[M—CH_3]^+$ ion. The strong peak at *m/e* 121 common to all three spectra must correspond to the unsaturated hydrocarbon residue C_9H_{13} produced by the loss of the oxygen bearing C-1 fragment. Intense peaks at *m/e*; 119, 117 and doubly charged ions at *m/e* 61·5, 59·5 and 57·5 are also not unexpected. Some of these peaks may even correspond to aromatic systems generated by rearrangement of the polyenic hydrocarbon fragments. The aldehyde and the ester show strong peaks at *m/e* 47. Since a fragment corresponding to $(C_2H_7O)^+$ is quite unlikely to arise from III or V, this peak must correspond to a doubly charged ion $(C_7H_{10})^{++}$. Interestingly enough, lyratol does not show a peak at *m/e* 47, although a weak peak corresponding to $(M\text{-}47)^+$ is present. The strongest peak in the spectrum of I appear at *m/e* 93 and 79. The base peak in the spectra of both III and IV is at *m/e* 117.

EXPERIMENTAL

Rotations were measured in $CHCl_3$ soln. The UV spectra were obtained in EtOH soln. The IR spectra were recorded as liquid films on a Perkin–Elmer Infra-cord spectrophotometer, Model No. 137B. The NMR spectra were recorded with a Varian A-60 spectrometer operating at 60 MC using TMS as an internal standard. Mass spectra were determined on a C.E.C., 21-103C Mass Spectrometer, with direct insertion technique.

Lyratol I

Lyratol was isolated[2] from the essential oil of *Cyathocline Lyrata*. It has the following properties: b.p. 105° (bath)/2 mm; n_D^{30} 1·4761; $[\alpha]_D^{27}$ +62·3° (*c*, 4·6); IR bands at 3300, 1005 ($—CH_2OH$), 3030, 1625, 888 ($>C{=}CH_2$), 1815, 913 ($—CH{=}CH_2$) and 813 cm^{-1} ($>C{=}C<H$); NMR spectrum: s at 8·40 and 8·31 ($2CH_3$ on double bond), the peaks between 3·8 to 5·3 (6 olefinic H), m at 6·36 ($>CH$), s at 6·09 ($—C\underline{H}_2OH$) and s at 7·72 τ ($—CH_2O\underline{H}$); UV absorption at λ_{max}211 mμ, ε, 342. (Found: C, 78·48; H, 9·99; $C_{10}H_{16}O$ requires: C, 78·89; H, 10·59%).

Lyratol acetate, II. To a soln of lyratol (1·5 g) in pyridine was added Ac_2O (4 ml) and the mixture was refluxed for 6 hr. The reaction product was cooled and poured in ice cold dil HCl acid and extracted with ether. The ethereal extract was washed with water, $NaHCO_3$aq and then with water and dried (Na_2SO_4). After removal of solvent, the residue (1·3 g) was distilled b.p. 122° (bath)/8 mm when lyratol acetate was obtained; IR bands at 1748, 1235 cm^{-1} ($O—COCH_3$); NMR signals at 7·97 τ ($O—CO\cdot C\underline{H}_3$). (Found: C, 73·89; H, 9·54; $C_{12}H_{18}O_2$ require: C, 74·22; H, 9·28%).

Hexahydrolyratol, VIII. Lyratol (0·5 g) in glacial AcOH (25 ml) was hydrogenated using PtO_2 (0·09 g). The hydrogenation stopped after 6 hr and the absorption of H_2 (283 ml at 29°/708 mm) was equivalent to three double bonds. After filtering the catalyst, AcOH was removed under reduced press. The residue was taken in ether, washed with water and dried (Na_2SO_4). After removal of ether, the product was chromatographed on alumina and then distilled, b.p. 75° (bath)/2·5 mm, when hexahydrolyratol was obtained; n_D^{29} 1·4395 $[\alpha]_D^{28}$ ±0 (*c*, 3·2%), IR bands at 3378 and 1087 ($—CH_2OH$). (Found: C, 76·72; H, 14·82; $C_{10}H_{22}O$ requires: C, 75·85; H, 14·7%).

Dihydrolyratol, VI. Lyratol (0·95 g) in EtOH (25 ml) was hydrogenated over 5% Pd–C (0·2 g). The hydrogenation was stopped when H_2 (69 ml/27°/709 mm) equivalent to one double bond was absorbed. After filtering the catalyst, ethanol was removed under reduced press. The residue was chromatographed and then distilled b.p. 95° (bath)/0·2 mm when dihydrolyratol was obtained; n_D^{29} 1·4704; $[\alpha]_D^{28}$ +23·27 (*c*, 3·95); IR bands at 3333, 1010 ($—CH_2OH$), 3049, 1637, 909 ($C{=}CH_2$), 813 ($>C{=}C<_H$); NMR a triplet centered at 9·16 (3H, $—CH_2C\underline{H}_3$) *J*, 7 c/s) and signals at 5·3 τ ($>C{=}C\underline{H}_2$). (Found: C, 78·56; H, 11·80; $C_{10}H_{18}O$ requires: C, 77·86; H, 11·76%).

Tetrahydrolyratol, VII. Lyratol (0·97 g) in EtOH (30 ml) was hydrogenated in the presence of Pd–C (0·39, 5%) when H_2 (350 ml/27°/709 mm) equivalent to two double bonds was absorbed, the hydrogenation was stopped. Working in the usual manner, the product was chromatographed and then distilled [105° (bath)/3 mm] when tetrahydrolyratol was obtained; $n_D^{3\ 0}$ 1·4750; IR bands at 3390, 1013 ($—CH_2OH$), 819 cm^{-1} ($>C{=}C<_H$); NMR signals centered at 8·37 (3H, Me on a double bond) and signals at 8·04 to 9·24 (9H, three Me's) and at 4·7 τ (one olefinic proton). (Found: C, 76·01; H, 13·1; $C_{10}H_{20}O$ requires: C, 76·80; H, 12·90%).

Lyratal, III

(a) *Jones oxidation of lyratol*. To a soln of lyratol (1 g) in dry acetone (60 ml) chromic acid soln was added dropwise at room temp till the soln was slightly reddish colour. The mixture was diluted with water (40 ml) and the reaction product extracted with ether. The ethereal extract was washed with $NaHCO_3$ aq, water and dried (Na_2SO_4). The residue (0·54 g) after removal of ether was chromatographed on alumina (Gr. 111, 15 g) and the pet ether eluent gave lyratal (TLC pure) after removal of pet ether. The product was distilled b.p. 60° (bath)/1 mm; $n_D^{9\cdot5}$ 1·4838; $[\alpha]_D^{29\cdot5}$ +37·4 (*c*, 3·87); IR bands at 3040, 2778, 2703, 1681, 1631, 1437, 1399, 1370, 1351, 1258, 1193, 1117, 990, 927, 904 and 803 cm^{-1}; UV absorption at λ_{max}^{232} mμ, ε, 16,390. (Found: C, 79·67; H, 9·31; $C_{10}H_{14}O$ requires: C, 80·00; H, 9·30%).

(b) *Oxidation of lyratol with* MnO_2. Lyratol (1 g) was shaken for 24 hr with a suspension of active MnO_2 (15 g) in $CHCl_3$ (50 ml). The reaction mixture was filtered and the solvent removed by distillation. Lyratal (0·8 g) was distilled, b.p. 60° (bath)/1 mm. Its IR spectrum was superimposable with lyratal obtained by Jones oxidation of lyratol. (Found: C, 79·81; H, 9·02; $C_{10}H_{14}O$ requires: 80·00; H, 9·3%).

Lyratic acid, IV

The $NaHCO_3$ extract obtained by washing the Jones oxidation product of lyratol was acidified with HCl. The acidified soln was extracted with ether and the ether extract washed with water and dried. After removal of ether, the acid was distilled under reduced press, b.p. 103° (bath)/6 mm; IR bands at 3030, 1695, 1620, 1449, 1403, 1232, 1247, 917 and 892 cm^{-1}. (Found: C, 72·6; H, 8·1; $C_{10}H_{14}O_2$ requires: C, 72·3; H, 8·4%).

Tetrahydrolyratal, IX. Tetrahydrolyratol (0·6 g) was shaken for 24 hr with a suspension of active MnO_2 (10 g) in $CHCl_3$ (40 ml). The reaction mixture was filtered and the solvent removed. The residue (0·5 g) was chromatographed over alumina (Gr. 111, 10 g) and the pet eluent was distilled, b.p. 60° (bath)/3 mm, when tetrahydrolyratal was obtained; IR bands at 2703, 1695, 1460, 1374, 833 and 781 cm^{-1}; UV absorption λ_{max} 232 mμ, ε, 13·812. (Found: C, 77·41; H, 12·01; $C_{10}H_{18}O$ requires: C, 77·92; H, 11·69%).

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