Novel Rearrangement of Homoproaporphine and the Configuration of Two Isomeric Homoproaporphines

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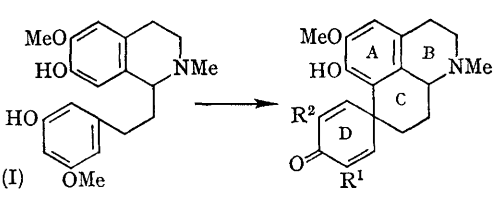
IN an earlier Communication,[1] we have described the synthesis and separation of two isomeric homoproaporphines [(IIa), m.p. 156—158° (decomp.), and (IIb), m.p. 193—195°] by phenolic oxidation of the phenethylisoquinoline (I), and the rearrangement of one of them (IIa) to homoaporphine (III)[1,2] has also been reported. Here we report a novel rearrangement of another dienone (IIb) under the same conditions.

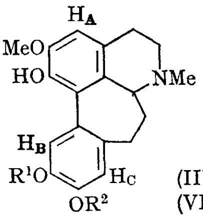
The dienone (IIb) was treated with concentrated hydrochloric acid in glacial acetic acid at 20° for 48 hr. with stirring in a current of nitrogen. A careful work-up involving silica gel chromatography using chloroform–methanol (99 : 1) as an eluent afforded three compounds, to which structures (IV), (V), and (VI) were assigned on the basis of the following evidence.

The first compound (IV), m.p. 197—198°,



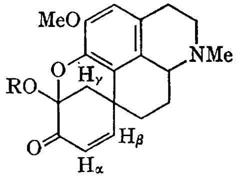
(I)

(IIa) R^1= OMe, R^2=H or *vice versa*
(IIb) R^1= H, R^2=OMe or *vice versa*
(VII) R^1=R^2=OMe

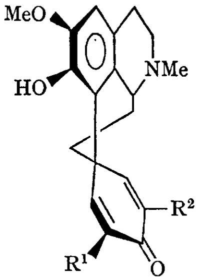


(III) R^1=H, R^2=Me
(VI) R^1=Me, R^2=H

obtained in 32·5% yield, had the molecular formula $C_{20}H_{23}O_4N$ (microanalysis and mass spectrometry, M^+ 341) and its i.r. [ν_{max} ($CHCl_3$) 1690, 1645 cm.$^{-1}$] and u.v. [λ_{max} (MeOH) 230, 275 mμ] spectra were in good accord with a cyclohexenone system. The n.m.r. spectrum (p.p.m. in $CDCl_3$) revealed three methyl resonances at 2·42 (NMe), 3·59 (aliphatic OMe), and 3·77 (aromatic OMe) as singlets, and one aromatic proton at 6·57 as a singlet. In addition, there appear two doublets (J = 11·0 c./sec.) at 5·98 and 6·90, both of which correspond to one proton, and are assigned to the H_α and H_β protons, respectively.[3] Furthermore, the doublet due to H_β proton suffers a further long-range coupling (J = 2 c./sec.) to H_γ proton through the ring, which is found at 2·28 as a doublet (J = 2·0 c./sec.).[3] The fact that these protons have the same chemical shift is attributed to competitive participation of the effect of the ring current of an aromatic ring and the anisotropy of the carbonyl group. The absence of a hydroxyl group in this compound was indicated by the i.r. spectrum and the u.v. spectrum showed no shift in an alkaline solution. This ketalisation might be due to direct protonation of the β-position in the enol–ether portion of the dienone (IIb) followed by attachment of the neighbouring phenolic oxygen.



(IV) R=Me
(V) R=H



(VIII) R^1=H, R^2=OMe
(IX) R^1=OMe, R^2=H

The second compound (V), m.p. 240° (decomp.), obtained in 13·5% yield, had the molecular formula $C_{19}H_{21}O_4N$ [microanalysis and mass spectrometry, M^+ 327; i.r.: ν_{max} (KBr) 3405, 1695, 1640 cm.$^{-1}$; u.v.: λ_{max} (MeOH) 230 sh., 276 mμ]. The n.m.r. spectrum was also similar to that of the first compound (IV), and showed the following signals, 2·21 (methylene protons in cyclohexenone, 2H, doublet, J = 2·0 c./sec.), 2·43 (NMe, 3H, singlet), 3·77 (OMe, 3H, singlet), 4·65 (hydroxyl, broad singlet, disappeared with D_2O), 6·06 (H_α, 1H, doublet, J = 11·0 c./sec.), 6·57 (aromatic proton, 1H, singlet), and 7·10 (H_β, 1H, a pair of doublets, $J_{\alpha\beta}$ = 11·0, $J_{\beta\gamma}$ = 2·0 c./sec.). Since the spectral data of this compound (V) are very similar to those of the first compound (IV) and one hydroxyl group is found in place of the methoxy-group in compound (IV), the structure of the second compound is (V).

Furthermore, hydrolysis of (IV) with 10% hydrochloric acid at room temperature afforded the compound (V), which showed the labile nature of methoxy-group.

The i.r. [ν_{max} ($CHCl_3$) 3475 cm.$^{-1}$] and u.v. [λ_{max} (MeOH) 264 and 293 mμ] spectra of the third compound (VI), m.p. 241—242°, obtained in 4·3% yield, were closely similar to those of homoaporphine (III).[1] The n.m.r. spectrum [p.p.m. in $(CD_3)_2SO$] showed three methyl signals at 2·31 (NMe), 3·72 (aromatic OMe) and 3·80 (aromatic OMe) as singlets and three aromatic protons at 6·67 (two protons, H_A and H_C) and 6·97 (one proton, H_B). On the other hand, the chemical shifts (p.p.m.) of aromatic protons of (III) in perdeuteriodimethyl sulphoxide are as follows: 6·63, 6·78, and 6·88. The chemical shifts of 6·63 in (III) and 6·67 in (VI) are assigned to H_A. The lowest signal in the aromatic proton region, namely, 6·88 in (III) and 6·97 p.p.m. in (VI), are assigned to H_B, because the half width of signals at 6·78 in (III) and 6·67 in (VI) is wider (*ca.*, 2×) than that of the lowest signal. The difference between the lowest signals of compound (III) and (VI), namely, 6·97 − 6·88 = 0·09 p.p.m. is in good agreement with that of the shielding constant between hydroxy- (0·50) and methoxy- (0·42) groups against the *ortho*-hydrogen, 0·50 − 0·42 = 0·08 p.p.m.[4] Therefore, the compound (III) has one hydroxyl group to the *ortho*-hydrogen showing the lowest chemical shift, and the compound (VI) has one methoxy-group at the same position. Moreover, the chemical shift of H_C between compounds (III) and (VI) showed a difference of 0·09 p.p.m., and this fact also confirmed the above result.

Treatment of the dienone (IIb) with concentrated hydrochloric acid in methanol under the same condition gave no reaction.

The dienone (VII), prepared independently by Kametani[1] and Battersby,[2] showed two *O*-methyl groups (3·51 and 3·63) (p.p.m. in $CDCl_3$) and two olefinic protons (5·84 and 6·0, doublet, J = 2·5 c./sec.) on the dienone system in different chemical shifts and, on the other hand, the dienones (IIa) and (IIb) showed the different chemical shifts in methyl groups (3·54 and 3·60).[1] This suggests that dienone ring is not at right angles to the benzene ring and the methoxy-groups are consequently in different environments in both cases. Considering the above results and the fact that ketalisation is possible only in dienone (IIb) but not in dienone (IIa), we assign the structure of dienone (IIa) as (VIII) and that of dienone (IIb) as (IX).

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