Phenolic Oxidative Coupling of 1-(3-Phenylpropyl)isoquinoline Derivatives

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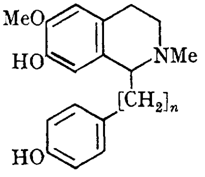
IN earlier Communications[1,2] we reported that phenolic oxidative coupling reactions of (±)-*N*-methylcoclaurine (Ia) and the homobenzylisoquinoline derivative (IIa) gave (±)-glaziovine[3] (Ib) and the homoproaporphine (IIb), respectively. Further research on the preparation of homoproaporphines has been carried out.[4–6]

We now report the synthesis of the dienone (IIIb) by phenolic oxidation of the 1-(3-phenylpropyl)isoquinoline derivative (IIIa) as a simple, though interesting, extension of the above dienone syntheses.

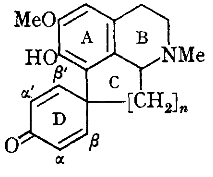
The best conditions for phenolic oxidation of 1,2,3,4-tetrahydro-7-hydroxy-1-[3-(4-hydroxyphenyl)propyl]-6-methoxy-2-methylisoquinoline (prepared according to the usual methods) involved a two-phase system of chloroform and aqueous potassium ferricyanide with ammonium acetate in ammonia.

By this method, the desired dienone (IIIb), $C_{20}H_{23}NO_3$, m.p. 153—154°, was obtained consistently in analytically pure state in about 1% yield after purification by column chromatography on silica gel.

The structure of the oxidation product was supported by the i.r. spectrum, which showed typical dienone absorptions at ν_{max} 1678 and 1620 cm.$^{-1}$ (in chloroform), and by the u.v. spectrum which showed λ_{max} 227, 273, and 307 mμ (in methanol) (log ϵ 4·37, 3·80, and 3·51 respectively).



(Ia) n=1
(IIa) n=2
(IIIa) n=3



(Ib) n=1
(IIb) n=2
(IIIb) n=3

Further, its n.m.r. spectrum† showed the expected N-methyl signal at τ 7·50 and O-methyl signal at τ 6·20 as two singlets, and a singlet at τ 3·50 (1H) was assigned to a single aromatic proton of the isoquinoline ring. In addition, it showed the signals of the olefinic protons at τ 3·60—4·10 (α and α') and τ 2·80—3·40 (β and β') as AA'BB'-type multiplets with fine structure. The α- and α'-protons show somewhat more complicated signals than those of β- and β'-protons because of the marked interaction across the ring. These spectral data and analytical values confirmed the structure of the oxidised product to be (IIIb).

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† N.m.r. spectrum was run at 60 Mc./sec. in $CDCl_3$ solution with Me_4Si as an internal standard.

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