The Preparation of Bentley and Robinson's "Dihydrothebaine" and Proof of its Structure

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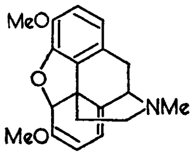
The action of phenylmagnesium bromide on thebaine (I) gives phenyldihydrothebaine, shown by Bentley and Robinson[1] to have the structure (II; R=Ph). By treating thebaine with anhydrous magnesium iodide Bentley and Robinson[1] hoped to prepare the unsubstituted "dihydrothebaine" (II; R=H), which Schmid and Karrer[2] had also tried to make by direct reduction of thebaine. Bentley and Robinson obtained a light brown solid, for which they tentatively suggested structure (III); reduction with lithium aluminium hydride gave a gas (assumed to be methane) and what appeared to be a phenolic secondary amine from which they could obtain no crystalline derivatives. They considered that demethylation accompanying reduction might have given (IV).

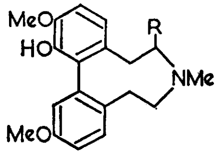
We have reinvestigated these reactions and have now shown that the main product of the lithium aluminium hydride reduction is the tertiary amine, (+)-2,3,8,9-tetrahydro-4′-hydroxy-3′,2″-dimethoxy-*N*-methyl-4,5 : 6,7-dibenzazonine (II; R=H). We were unable to detect methane among the gases evolved during the reduction and could find no evidence for the presence of the secondary amine (IV). The reaction with nitrous acid on which Bentley and Robinson based their assignment is probably a *C*-nitrosation of the phenolic aromatic ring.

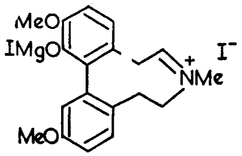
The azonine (II; R=H) was obtained as a crystalline solid, m.p. 103·5—104·5°. Infrared and nuclear magnetic resonance spectra are consistent with the suggested structure, both showing the presence of a hydroxyl and an *N*-methyl group. The methiodide, the methyl ether (V), and the methyl ether methiodide (VI; X=I) have all been prepared and characterised. The methyl ether methobromide (VI; X=Br) has an ultraviolet spectrum (λ_{inf} 225 mμ, λ_{max} 280·5, ϵ_{max} 4145) closely resembling that of phenyldihydrothebaine methyl ether methobromide (λ_{inf} 230 mμ, λ_{max} 282, ϵ_{max} 4290) both in 96% ethanol.

Two Hofmann degradations of the methyl ether methiodide (VI; X=I) gave a nitrogen-free product, considered to be (VII), which polymerised readily and could be hydrogenated to (+)-6,6′-diethyl-2,3,2′-trimethoxybiphenyl (VIII). This compound and the azonine methyl ether (V) racemise on heating in solution at rates consistent with their hindered biphenyl structures.

We conclude that the secondary amine (IV) is


(I)


(II)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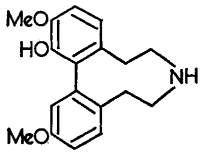
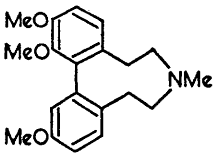
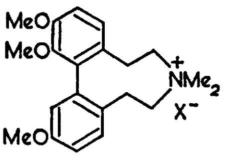
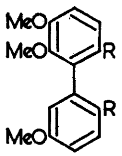
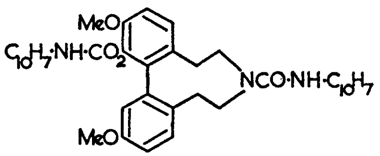

(IV)


(V)


(VI)


(VII) R=CH:CH$_2$
(VIII) R=Et


(IX)

absent from the lithium aluminium hydride reduction product for the following reasons: (*a*) we failed to separate the product into two components, (*b*) we were unable to detect any of the substituted urea (IX), when the crude reduction product was treated with α-naphthyl isocyanate, although the α-naphthylurethane of (II; R=H) was readily obtained, and (*c*) we did not observe any shifts in the infrared spectrum after treatment of the sodium salt of (II; R=H) with deuterium oxide; the phenol itself readily underwent *O*-deuteration under the same conditions.

Full details, including a study of the optical stability of (V), will be published elsewhere.

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[1] K. W. Bentley and R. Robinson, *J. Chem. Soc.*, 1952, 947.
[2] H. Schmid and P. Karrer, *Helv. Chim. Acta*, 1950, **33**, 863.