Oxonium Ion Intermediates in the Rearrangement of Thebaine

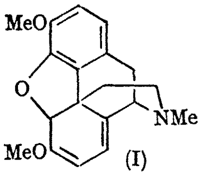
By R. T. CHANNON, G. W. KIRBY,* and S. R. MASSEY

(*Chemistry Department, University of Technology, Loughborough, Leicestershire*)

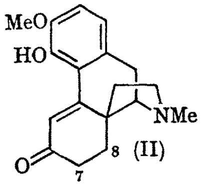
THEBAINE (I) gives a red solution in concentrated hydrochloric acid,[1] from which metathebainone (II)[1,2] can be isolated after catalytic hydrogenation or chemical reduction. Fleischhacker *et al.* have prepared[3] 7,8-dehydrometathebainone methoperchlorate (III; R = Me) by treatment of thebaine methoperchlorate with aqueous perchloric acid. We report a similar preparation and the identification of oxonium ion intermediates (IV), in the acid-catalysed rearrangement of thebaine and its quaternary salts. A convenient preparation of neodihydrothebaine [dihydro-(V)] is also described.

Thebaine methotrifluoroacetate readily dissolves in trifluoroacetic acid to give a solution which rapidly develops an intense absorption band at 420 nm.; this diminishes in intensity with time at ambient temperature and is eventually replaced by a broad band, λ_{max} 322 nm. (ϵ 7130). The n.m.r. spectrum of a freshly prepared solution showed the methoxonium ion (IV; $R^1 = R^2 =$ Me) to be the major species present. The 6-methoxy-group absorbed at lower field (s, τ 5·34) than the aromatic methoxy-group (s, τ 5·94) and the olefinic proton signals showed the expected H (5,7) and H (7,8) coupling constants of 2·2 and 10·1 Hz respectively. After *ca.* 1 hr. the solution, then yellow, gave an n.m.r. spectrum consistent with that expected for the dienone (III; R = Me). Evaporation of the solvent under reduced pressure and conversion of the residual salt into the chloride form by ion exchange gave 7,8-dehydrometathebainone methochloride (III; R = Me) as a yellow, amorphous solid, ν_{max} 1660 cm.$^{-1}$ (Nujol), λ_{max} (EtOH) 304 nm. (ϵ 8650). The same compound was obtained by treatment of thebaine methotrifluoroacetate with concentrated hydrochloric acid. This material was further characterised as a crystalline complex with Reinecke's anion. Addition of concentrated sulphuric acid (2%; v/v) to the dienone (III; R = Me) in trifluoroacetic acid generated the red hydroxonium ion (IV; R^1 = H, R^2 = Me), λ_{max} 407 nm. (ϵ 11,800) with appropriate changes in the n.m.r. spectrum.

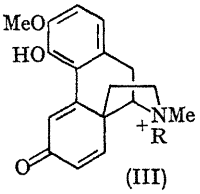
The conversion of the methoxonium ion (IV; $R^1 = R^2 = Me$) into the dienone (III; R = Me) was accelerated by addition of water and occurred only slowly in freshly dried trifluoroacetic acid. Treatment of thebaine methotrifluoroacetate directly with CF_3CO_2H–H_2SO_4 (composition as above) gave a solution of the pure methoxonium ion (IV; $R^1 = R^2 = Me$), λ_{max} 420 nm. (ϵ 14,800), which was stable for several hours at room temperature.



(I)

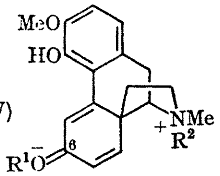


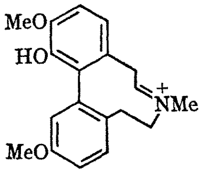
(II)



(III)

(IV)





(V)

Thebaine itself dissolved in trifluoroacetic acid to give the red ion (IV; $R^1 = Me$, $R^2 = H$) which rapidly decomposed, by loss of a proton from nitrogen, to give the imine (V). This was not itself characterised but was reduced in ethanol with sodium borohydride to the corresponding amine, neodihydrothebaine, in good yield. Two reports[4] have recently appeared of the synthesis of neodihydrothebaine by another route. A sample, kindly provided by Dr. K. W. Bentley, was found to be identical with our material. As expected, when thebaine was dissolved in $CF_3 \cdot CO_2H$–H_2SO_4 a stable solution of the ion (IV; $R^1 = Me$, $R^2 = H$), λ_{max} 420 nm. (ϵ 15,400), was obtained, the nitrogen atom being securely protonated in the presence of the mineral acid.

The red solution obtained from thebaine in concentrated hydrochloric acid appears, from its u.v.-visible spectrum, to contain the protonated dienone (III; R = H) and the hydroxonium ion (IV; $R^1 = R^2 = H$) in a ratio of *ca.* 3 : 1. Earlier failure[1] to isolate compounds of the type (III) from this solution after basification may be explained by the ready collapse of the dienone system to give the imine (V). Battersby *et al.*[5] have recently prepared a stable base of the structural type (III).

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