Formation of the 3-Aza[4.4.4]propellane System by Rearrangement of a Bridged Isoquinoline

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Summary 6,8a-Ethano-1,2,3,4,6,7,8,8a-octahydroisoquinolyl carbinols (**3** and **4**, R = Et, Ph) undergo rearrangement in concentrated hydrochloric acid to give 3-aza[4.4.4]propellane derivatives (**7**, R = Et, Ph).

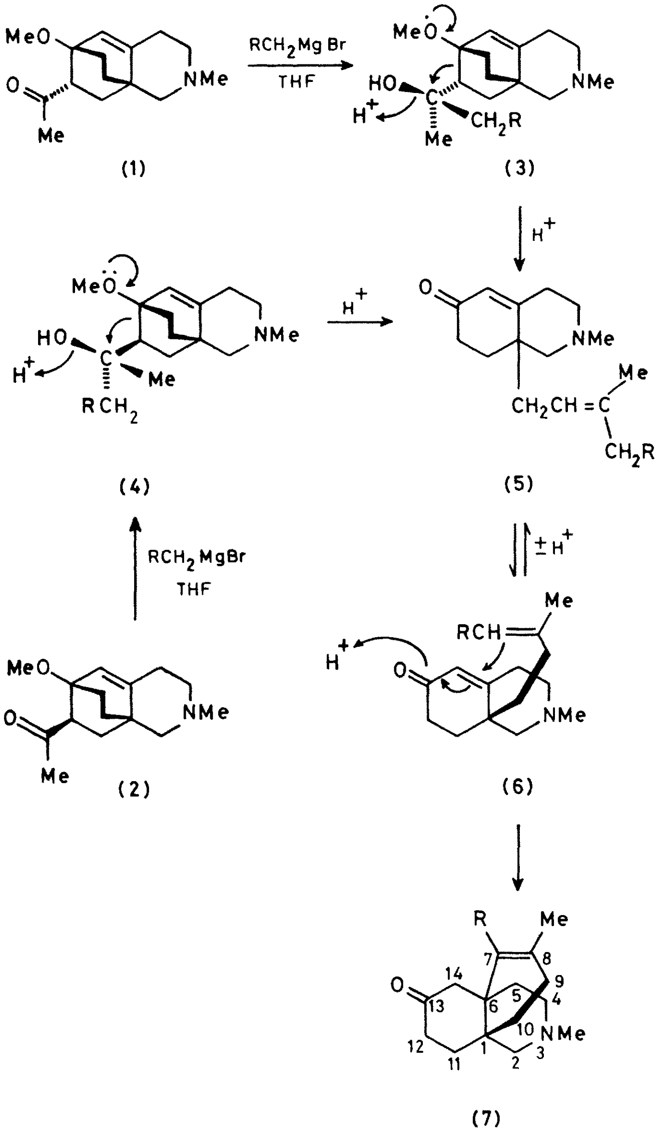
Propellane systems, which contain three rings fused to a single bond, have attracted attention as structures of chemical and synthetic interest,[1] and because of their presence in certain natural products such as the hasubanan alkaloids.[2] We report the formation of the little known[3] 3-aza[4.4.4]propellane system by novel rearrangement of a bridged isoquinoline.

The *endo*- and *exo*-ketones (**1** and **2**) are obtainable by Diels–Alder reaction of methyl vinyl ketone with 6-methoxy-2-methyl-1,2,3,4,7,8-hexahydroisoquinoline.[4] Grignard addition of n-propylmagnesium bromide to the *endo*-ketone (**1**) gives the carbinol (**3**, R = Et), m.p. 87—8 °C; its isomer (**4**, R = Et), b.p. 132—134 °C at 0·03 mm Hg, is likewise obtained from the *exo*-ketone (**2**). The stereoselectivity of the addition is similar to that reported in analogous cases.[5]

Treatment of either the *endo*-carbinol (**3**, R = Et) or *exo*-carbinol (**4**, R = Et) with concentrated hydrochloric acid for 3 h at 100 °C gives in high yield, as a viscous oil, a product, $C_{17}H_{27}NO$, formulated as the 3-aza[4.4.4]propellane (**7**, R = Et), hydrochloride m.p. 242—243 °C, methiodide m.p. 261—264 °C.† The free base shows ν_{max} 1705 cm^{-1} in the i.r. spectrum and in the ^1H n.m.r. spectrum, methyl groups

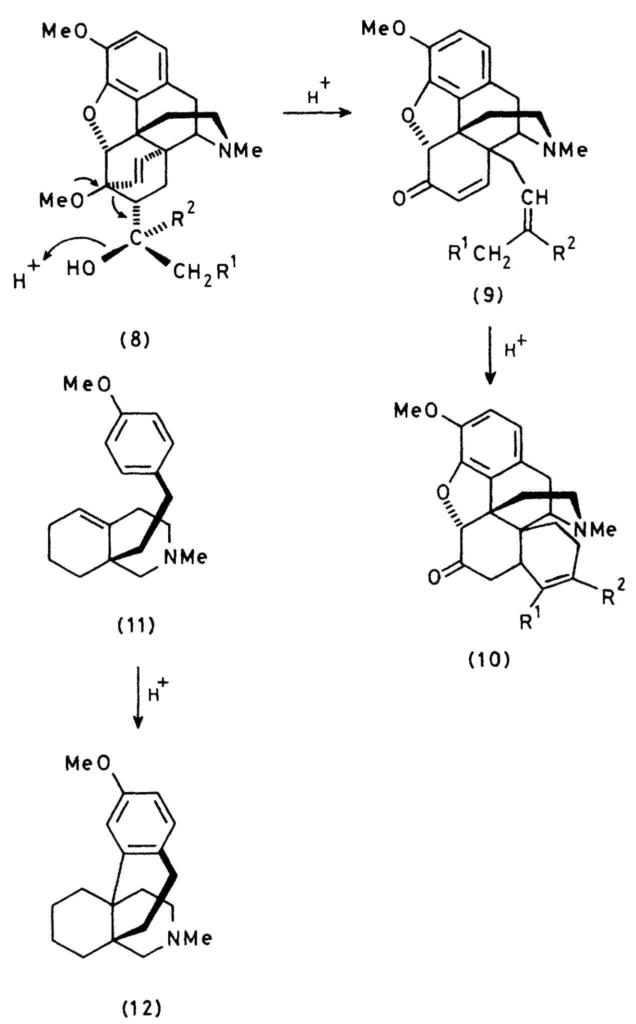
† All new products provided satisfactory microanalytical data.

appear at δ 1 0 (3H, t, *Me*CH$_2$), 1 65 [3H, s C(8) Me], and 2 2 (3H, s, NMe), and no olefinic proton signals are present Use of benzylmagnesium bromide in the Grignard addition gives the *endo*- and *exo*-carbinols (**3** and **4**, R = Ph) which undergo similar rearrangement on treatment with concentrated hydrochloric acid to provide the 3-aza[4 4 4]propellane (**7**, R = Ph), though in lower yield (25%)



SCHEME THF = tetrahydrofuran

A possible pathway for the reaction is shown in the Scheme It is somewhat analogous to the behaviour of the bridged thebaine carbinol system (**8**, R^2 = Me, R^1 = Me or Bu^t) in strong acid[6] The first-formed alkenylcodeinone (**9**) undergoes prototropic equilibration and cyclisation to (**10**) and an isomer Also, the benzo-3-aza[4 4 4]propellane (**12**) results from cyclisation in HBr of the octahydroisoquinoline (**11**)[3] The ring opening step from carbinols (**3**) and (**4**) is similar to that postulated as occurring with 2N hydrochloric acid at 100 °C in an analogous case, where R = H and 6-EtO replaces 6-MeO[5] Under these more dilute conditions, however, the enone intermediate (**5**, R = H) only undergoes hydration of the side-chain double bond[5]



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