Investigations Toward the Total Syntheses of Proaporphine and Homoproaporphine Alkaloids

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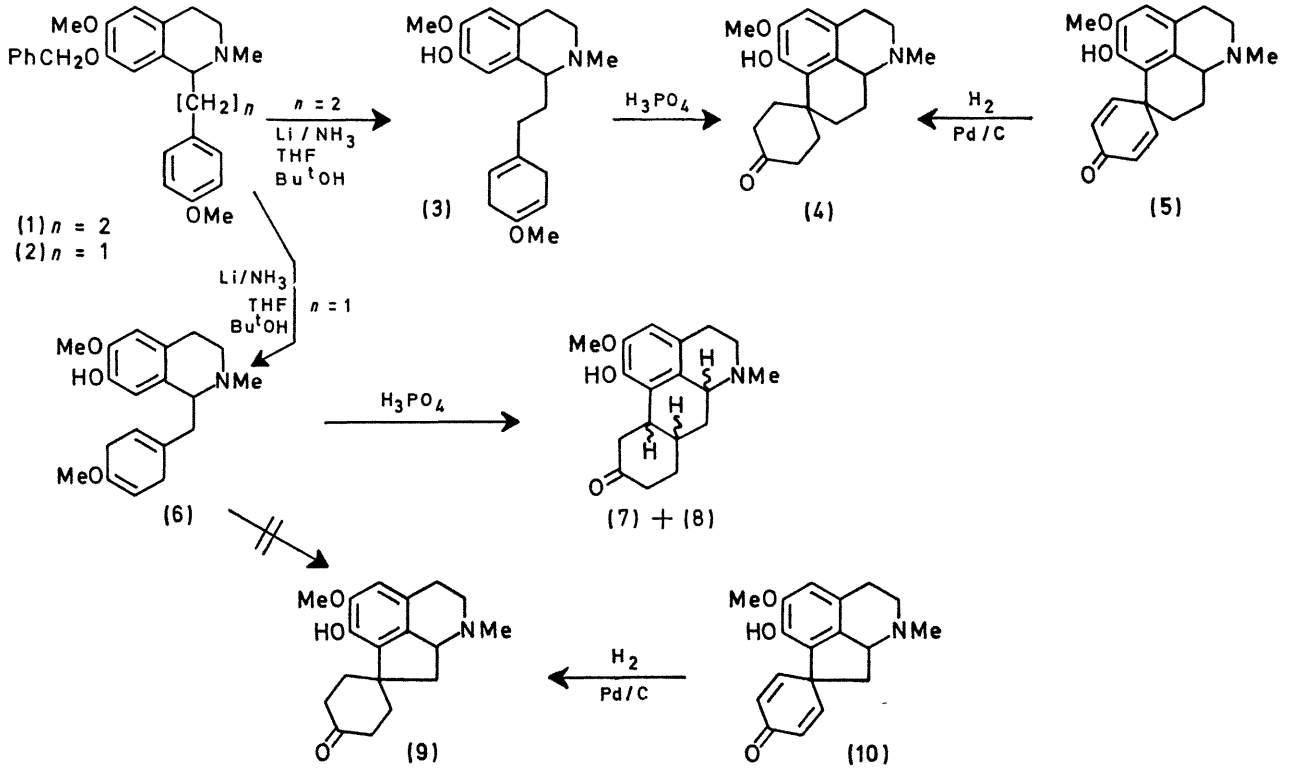
Summary A synthetic approach to the proaporphine and homoproaporphine alkaloids which was successful in the latter series is presented.

PROAPORPHINE and homoproaporphine alkaloids are an interesting group of isoquinoline type compounds which have only recently been described.[1] We describe a synthetic approach to these systems.[2]



Isoquinoline (**1**),[3] was subjected to the Dryden modification of the Birch reduction[4] to afford the white crystalline enol ether (**3**) (68%): m.p. 111—113·5°; i.r. ($CHCl_3$), 3540 (OH), 1670, and 1695 cm^{-1} (enol ether bands); n.m.r. ($CDCl_3$) δ 2·43 (s, 3H, NMe), 3·55 (s, 3H, enol OMe), 3·85 (s, 3H, ArO*Me*), 4·62 (m, 1H, olefinic H), 5·40 (m, 1H, olefinic H), 6·54 (s, 1H, Ar*H*), and 6·67 (s, 1H, Ar*H*) p.p.m. Treatment of (**3**) with hot phosphoric acid afforded (±)-tetrahydrohomoglaziovine (**4**) as the principal product: white crystals, m.p. 206—211° decomp.; i.r. (KBr) 1710 (C=O); n.m.r. ($CDCl_3$) δ 2·43 (s, 3H, NMe), 3·84 (s, 3H, COMe), and 6·50 (s, 1H, Ar*H*) p.p.m. The structure of this compound was unequivocally established since catalytic reduction of the previously described dienone (**5**)[5] gave the same compound (i.r. and t.l.c.).

The benzylisoquinoline (**2**)[6] was also converted into a crystalline enol ether (**6**) in good yield by a modified Birch reduction:[4] white crystals, m.p. 78—80°; i.r. ($CHCl_3$) 1660 and 1690 cm^{-1} (enol ether bands); n.m.r. ($CDCl_3$) δ 2·44 (s, 3H, NCH_3), 3·54 (s, 3H, enol OCH_3), 3·84 (s, 3H, aromatic OCH_3), 4·63 (m, 1H, olefinic H), 5·41 (m, 1H, olefinic H), 6·55 (s, 1H, Ar*H*), and 6·64 (s, 1H, Ar*H*) p.p.m. Treatment of this compound with hot phosphoric acid gave two compounds which were separated by liquid–liquid partition chromatography on Celite. Neither was (±)-tetrahydroglaziovine (**9**) as they were not identical to authentic (**9**) obtained by catalytic hydrogenation of (±)-glaziovine (**10**).[7] The two compounds (a major and minor isomer) have been assigned structures (**7**) and (**8**), having aporphine-type skeletons, but the available evidence does

TABLE. *Acid cyclization products from* (**6**)

	Major isomer	Minor isomer
Molecular ion (*m/e*)	301	301
i.r. ν($CHCl_3$)/cm^{-1}	3660, 1710, 1630	3660, 1710, 1625
u.v. λ_{max}(EtOH)/nm (ε)	288(3600)	288(3300)
δ (p.p.m. in $CDCl_3$)	2·47(3H, s, NMe)	2·54(3H, s, NMe)
	3·82(3H, s, OMe)	3·84(3H, s, OMe)
	6·50(1H, s, Ar)	6·52(1H, s, Ar)

not allow exact stereochemical formulation.† Their principal physical characteristics are listed in the Table. Both compounds exhibit only one unsplit aromatic proton proving that a Friedel–Crafts type cyclization has taken place. Other types of acid treatment on the enol ether (**6**) did not afford any of the spiro-compound (**9**). Further details will be presented elsewhere.

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† All structures reported with chiral centres are racemates.

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