Total Synthesis of 8,13-Diaza-steroids

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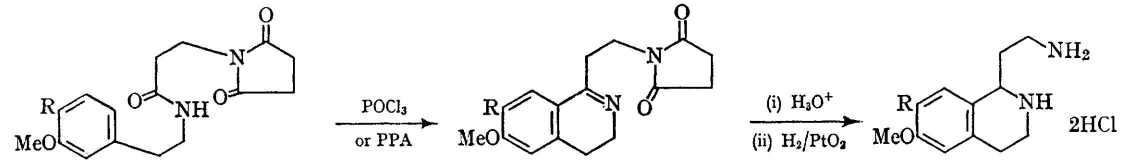
RECENT reports of the total synthesis of 13-aza-18-norequilenin methyl ether[1] prompt us to publish the total synthesis of a related 8,13-diaza-18-norœstrone system.[2]

3-Succinimido-*N*-(2-arylethyl)propionamides (Ia and b) in the Bischler–Napieralski reaction yielded the 3,4-dihydro-1-(2-succinimidoethyl)isoquinolines (IIa and b, m.p. 205°, decomp., and 196° decomp.), which were hydrolyzed and then catalytically reduced to the 1-(2-aminoethyl)-1,2,3,4-tetrahydroisoquinoline dihydrochlorides (IIIa and b), m.p. 233° decomp., and 277° decomp.

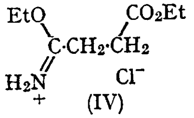


(Ia: R = H)
(Ib: R = OMe)

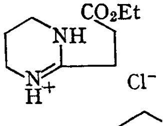
(IIa: R = H)
(IIb: R = OMe)

(IIIa: R = H)
(IIIb: R = OMe)

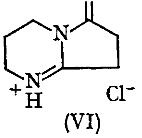
Propane-1,3-diamines are known to react with imidate hydrochlorides to give 2-substituted tetrahydropyrimidines.[3] In a related model synthesis, propane-1,3-diamine was allowed to react with ethyl 3-ethoxycarbonylpropionimidate hydrochloride (IV)[4] to afford 2-(2-ethoxycarbonylethyl)-3,4,5,6-tetrahydropyrimidine hydrochloride (V), m.p. 194—194·5°; ν_{max} (KBr) 1740 (ester C=O) and 1660 cm.$^{-1}$ (amidinium). When (V) was heated above its melting point and the melt was allowed to sublime, 2,3,4,6,7,8-hexahydro-6-oxopyrrolo[1,2-*a*]-pyrimidine hydrochloride (VI) was obtained, m.p. 181—182°. The infrared spectrum of (VI) revealed a medium band at 1775 cm.$^{-1}$, which is attributable to the strained lactam carbonyl group, and a strong band at 1660 cm.$^{-1}$, as a result of the immonium group.



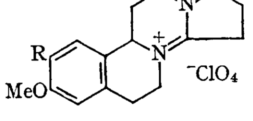
(IV)



(V)



(VI)



(VIIa: R = H)
(VIIb: R = OMe)

When (IIIa) and (IIIb) were separately treated with (IV) at 0° under dry CO_2-free nitrogen, the 3-methoxy-8,13-diazagona-1,3,5(10),8(14)-tetraen-17-ones (VIIa and b) were isolated in a single step procedure as the perchlorates, m.p. 231—232° decomp., and 276—277° decomp. Strained lactam carbonyl (1775 cm.$^{-1}$) and immonium (1660 cm.$^{-1}$) absorption were demonstrated as in the case of (VI).

Further synthetic studies involving (II) and (VII) are being pursued.

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[1] A. J. Birch and G. S. R. Subba Rao, *J. Chem. Soc.*, **1965**, 3007; S. V. Kessar, M. Singh, and A. Kumar, *Tetrahedron Letters*, 1965, 3245.

[2] Extracted from the Ph.D. thesis of H. N. Abramson, The University of Michigan, Ann Arbor, Michigan, U.S.A., 1966.

[3] J. A. Faust, A. Mori, and M. Sahyun, *J. Amer. Chem. Soc.*, 1959, **81**, 2214.

[4] M. Protiva, V. Rericka, and J. O. Jilek, *Chem. listy*, 1950, **44**, 231.