A Simple Synthesis of 6,7-Diaza-steroids

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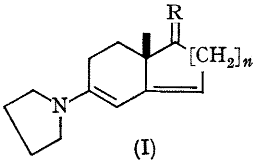
Summary Treatment of dienamine (I) with *m*-methoxydiazonium fluoroborate yields the 6,7-diaza-steroid (II) in one practical step.

REACTIONS of dienamines of type (I) with a variety of electrophiles have been investigated with a view to developing a new general approach to ring-A- and/or -B-modified steroids. We report here the synthesis of the 6,7-diazasteroidal system (II).

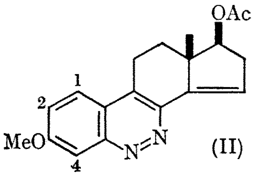
Treatment of (I; $n = 1$; R = β-OAc,α-H)† with *m*-methoxyphenyldiazonium fluoroborate, at −70°, in methylene chloride or chloroform, followed by heating under reflux for 4 hr., gave a mixture of products which represented both β- and δ-substitution of the dienamine.‡ Chromatographic separation yielded the steroid (II) (17%) m.p. 226—228°, hydrazone (III) (15%) m.p. 83—85·5° and the salt (IV) (35%) m.p. 232—234°. When the mixture was not warmed after the initial reaction, the azo-derivative (V) m.p. 163—165°, λ_{max} (KBr) 1730 and 1520 cm.$^{-1}$; δ (CDCl$_3$; 100 Mc./sec.) 1·03 (s, H$_3$, CH_3), 2·07 (s, H$_3$, OCO·CH_3), 3·79 (s, H$_3$, OCH_3), 3·65—3·95 (m, H$_4$, CH_2NCH$_2$), 7·01 (t, H$_1$, J 2·5 c./sec., =C–H) and 6·6—7·4 (m, H_4, aromatic)] was formed at the expense of the steroid (II).

The structure of (II) was indicated by its analytical and spectral data; [λ_{max} (KBr) 1720, 1640, and 1620 cm.$^{-1}$; δ (CDCl$_3$; 60 Mc./sec.) 1·07 (s, H$_3$, CH_3), 2·15 (s, H$_3$, OCO·CH_3), 4·01 (s, H$_3$, OCH_3), 6·82 (t, H$_1$, J 2·5 c./sec.; =C–H), 7·32 (q, H$_1$, J 9 and 2·5 c./sec.; 2-H), 7·71 (d, H$_1$, J 2·5 c./sec.; 4-H) and 7·83 (d, H$_1$, J 9 c./sec.; 1-H).

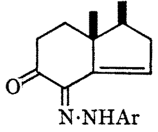
While attempts to cyclize (III) to (II) failed,§ the perchlorate of (V) was quantitatively converted into the diaza-steroid (II) by heating its solution under reflux in ethanol for 1 hr. The direct formation of (II) in the reaction of (Ia) with the diazonium salt is therefore visualized as proceeding *via* the following steps; (a) electrophilic substitution at the β-position of the dienamine to give intermediate (VI),¶ (b) intramolecular attack of the aromatic moiety on the iminium function in (VI), followed by (c) elimination of pyrrolidine, and completion of the process through aromatization of ring B.



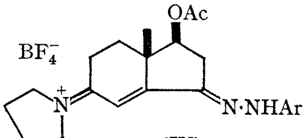
(I)



(II)

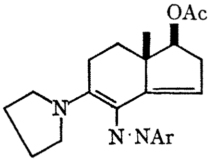


(III)

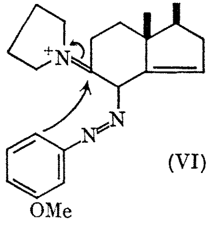


(IV)

[Ar=*m*-MeO·C$_6$H$_4$]



(V)



(VI)

(*Received, February* 26*th*, 1969; *Com.* 275.)

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† The compounds described gave elemental analyses and spectral data in agreement with the assigned structures.

‡ A discussion on the mechanism of electrophilic substitution of dienamines will be presented elsewhere.

§ Reaction of (III) with acids takes an unexpected course, involving cyclization with loss of a nitrogen atom. This will be reported in a forthcoming publication.

¶ Cyclization can also involve the corresponding hydrazone form of (VI); however, we have no evidence at present that allows us to distinguish between these two possibilities.