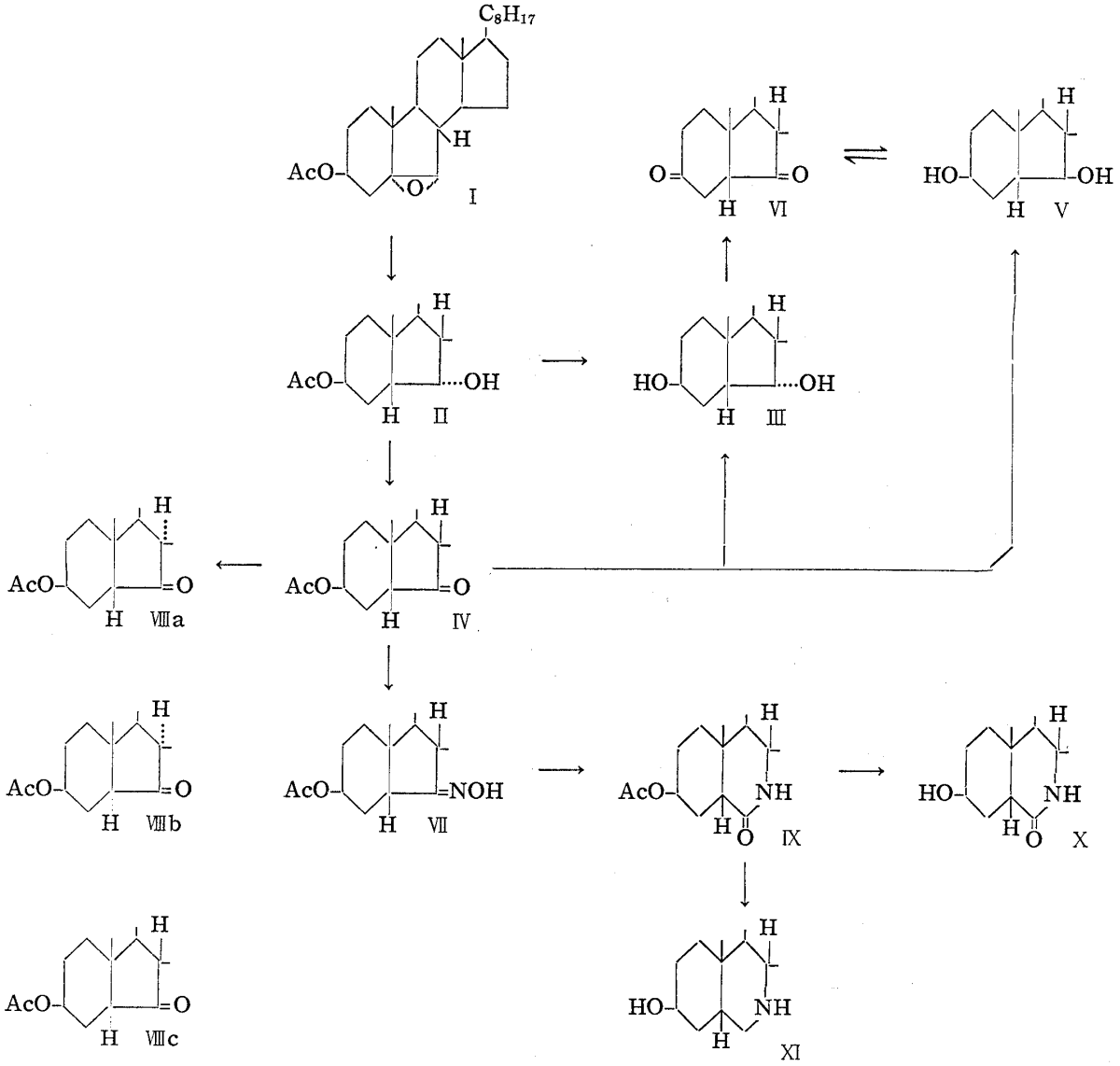
UDC 547.92

7-Aza-5β-cholestane Derivatives

Continuation of the study on B-norsteroids[1] naturally leads us to focus our attention to B-aza-steroids. The B-aza-steroids[2~11], which replaced the steroidal nuclear carbon atoms with nitrogen atoms might alternative biological activity of steroids. Furthermore possible therapeutic value enhanced our attention to prepare new 7-aza-5-cholestane



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derivatives.

Under conducting this work, Czechoslovakian group[12] reported fission of the epoxide (I) and their data showed almost the same result. Therefore this paper mainly concerns with the preparation of the new aza-steroid.

Hydrogenation of the epoxide (I) m.p. 113° with platinum oxide in acetic acid yielded B-nor-5β-cholestane-3β,6α-diol 3-acetate (II), m.p. 83° $[\alpha]_D$ 0°.*1 Treatment of II with lithium aluminum hydride furnished B-nor-5β-cholestane-3β,6α-diol (III), m.p. 144~145°, $[\alpha]_D$ +0.8° and with chromium trioxide, 3β-hydroxy-B-nor-5β-cholestan-6-one 3-acetate (IV), m.p. 90~91°, $[\alpha]_D$ +50.8°. The latter was reduced with lithium aluminum hydride to an epimeric pair of the diol (III) and B-nor-5β-cholestane-3β,6β-diol (V), m.p. 127°, $[\alpha]_D$ +43°, and V was identical with the authentic sample[13] prepared from Butenandt's diketone. These diols were oxidized separately with chromium trioxide in acetic acid into Butenandt's diketone.

The stereochemistry of the monool (II) was thus established by the routes described above and by the fact that the oxidation of the monool (II) with chromium trioxide in acetic acid to IV showed no change of its virtual configuration.

The ketone (IV) was isomerized by treatment with alkali or acid and followed by acetylation to 3β-hydroxy-B-nor-5β,8α-cholestan-6-one 3-acetate (VIII), m.p. 109~110°, $[\alpha]_D$ −41°, whose configuration was tentatively assigned by conformational analyses. That is to say, for this product three possible structures (VIIIa, VIIIb, and VIIIc) can be considered. VIIIb is almost impossible to exist because of the strong hindrance with 18-CH_3 and 19-CH_3. VIIIc exhibits very strong ring strain but if this compound would have existed, it should have not offered so great hindrance towards oximation (vide infra). VIIIa was easily composed, but Carbon 6 is covered both with 18-CH_3 in β-side and with A-ring in α-side. From these analyses VIIIa is most likely to exist.

Refluxing the ketone (IV) with hydroxylamine hydrochloride and sodium acetate in ethanol gave 3β-acetoxy-B-nor-5β-cholestan-6-one oxime (VII), m.p. 185~186°, $[\alpha]_D$ +43°, whose model indicates that the hydroxyl group of the oxime has no steric hindrance toward less bulky A-ring but considerably great hindrance toward D-rind. Under the same condition the ketone (VIIIa) gave no reaction product and the material isolated was merely the original ketone.

Beckmann rearrangement of VII afforded 3β-hydroxy-7-aza-5β-cholestan-6-one 3-acetate (IX), m.p. 217~219°, $[\alpha]_D$ +20.2°. Reduction of IX with lithium aluminum hydride in ether or tetrahydrofuran gave 3β-hydroxy-7-aza-5β-cholestan-6-one (X), m.p. 238~239°, $[\alpha]_D$ +1.3°, but in rather high-boiling solvent, dioxan the reduction successfully proceeded to give the desired compound, 7-aza-5β-cholestan-3β-ol (XI), m.p. 135~136°, $[\alpha]_D$ +41°.

New substances encountered in this work mentioned above were characterized by infrared spectra and conformational analyses. Satisfactory analytical data were obtained for all compounds. Elaboration of this work, together with extention to other steroid series is being carried on in this laboratories.

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*1 Rotations were measured in $CHCl_3$ solution.

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