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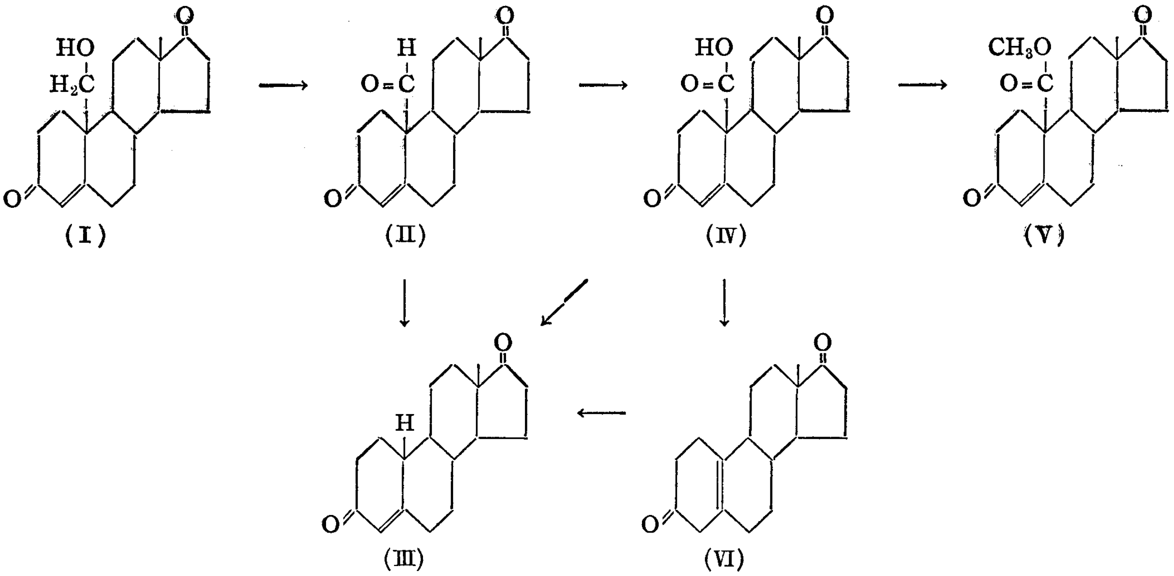
Syntheses of 19-Nor-3-ketosteroids

The present authors have shown that 19-hydroxylation of Reichstein's compound S is effected by *Corticium sasakii.*[1]

19-Nor-Δ^4-3-ketosteroids have been prepared from 19-hydroxy-Δ^4-3-ketosteroids by elimination of the hydroxymethyl group at C-10 by treatment with an alcoholic potassium hydroxide solution,[2] but in a very low yield.

In the present communication, a new approach to the synthesis of 19-nor-3-ketosteroids from 19-oxo- and 19-carboxy-Δ^4-3-ketosteroids is described.

Oxidation of 4-androsten-19-ol-3,17-dione (I) with chromium trioxide gave 4-androstene-3,17-dion-19-al[1] (II), m.p. 129~133°, the latter being converted by treatment with 4% NaOH solution at 5~10° into 19-nor-4-androstene-3,17-dione[3] (III), m.p. 169~171°; $[\alpha]_D^{25}$ +135° ($CHCl_3$); UV : λ_{max}^{EtOH} 238 mμ (ε 17,000); IR λ_{max}^{KBr} μ : 5.75, 6.00, 6.17. *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found : C, 79.06; H, 8.75. In an alternative procedure, (II) was oxidized with chromium trioxide-sulfuric acid in acetone[4] to give 4-androstene-3,17-dion-19-oic acid (IV), m.p. 155° (decomp.); IR λ_{max}^{Nujol} μ : 5.78 (17-CO), 5.85 (COOH), 6.00, 6.15 (4-ene-3-CO). *Anal.* Calcd. for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65. Found : C, 72.41; H, 7.81. Methyl ester (V) : m.p. 135~137°; $[\alpha]_D^{27}$ +273° (dioxane); IR λ_{max}^{Nujol} μ : 5.85, 6.02, 6.20. *Anal.* Calcd. for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93. Found : C, 72.45; H, 7.69. (IV) was led to (III) in almost quantitative yield by heating in methanolic hydrogen chloride solution.



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1) M. Nishikawa, H. Hagiwara : This Bulletin, **6**, 226 (1958).

2) A. S. Meyer : Experientia, **11**, 99 (1955); G. W. Barber, M. Ehrenstein : J. Org. Chem., **20**, 1253 (1955).

3) A.L. Wilds, *et al.* (J. Am. Chem. Soc., **75**, 5366 (1953)) reported m.p. 170~171°; $[\alpha]_D^{27}$ +137° ($CHCl_3$); λ_{max}^{EtOH} 239 mμ (ε 16,900).

4) Jones reagent (K. Bowden, *et al.* : J. Chem. Soc., **1946**, 39).

When heated in pyridine, however, (IV) gave in excellent yield 19-nor-5(10)-androstene-3,17-dione (VI), m.p. 142~145°; $[\alpha]_D^{24}$ +270° ($CHCl_3$); no absorption maximum at 220~340 mμ; $\lambda_{max}^{EtOH \cdot 1\% KOH}$ 238 mμ (ε 16,000); IR λ_{max}^{KBr} μ: 5.75 (5-membered ring C=O), 5.82 (6-membered C=O). *Anal.* Calcd. for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.32; H, 8.85. The structure of (VI) was confirmed by elementary analysis, UV and IR spectra, and by the fact that (VI) gives (III) in the presence of either alkali or mineral acid in a methanolic solution.

19-Nor-17α-hydroxyprogesterone[5] was also obtained from the corresponding 19-oxo-17α-hydroxyprogesterone in excellent yield by a similar method.

Transformation of other 19-hydroxy-Δ^4-3-ketosteroids to 19-nor-3-ketosteroids is under investigation.

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[5] The same compound was synthesized from 1,3,5(10)16-pregnatetraën-3-ol-20-one by A. Zaffaroni, *et al.* (J. Am. Chem. Soc., 80, 6110(1958)).