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# THE REDUCTION OF STEROIDAL 3-KETO-1,4-DIENES

Masato Tanabe, James W. Chamberlin and Patricia Y. Nishiura
Life Sciences Division,
Stanford Research Institute, Menlo Park, California

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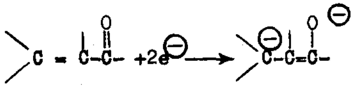
THE concept[1,2] of the two electron additions to α, β unsaturated ketones undergoing reduction by dissolving metals in ammonia, has led to some novel reduction products of steroidal ring A-3-keto-1,4-dienes,



by utilization of the reactive carbanion beta to the carbonyl generated during the reduction of these steroids.

The reduction of prednisone BMD[3] (I) with lithium and ammonia leads in good yield to a 9//10 seco product (II), m.p. 235-239°; $[\alpha]_D$ -5; $^{\text{MeOH}}_{\text{max}}$ 280 mμ, $\epsilon = 2600$; $\lambda^{\text{MeOH}}_{\text{infl.}}$ 285 mμ, $\epsilon = 2445$, by a concerted two electron addition process.

Analogous phenolic 9//10 seco compounds of this type have been prepared by the pyrolysis of ring A unsaturated C.3-ketones.[4] In a similar manner, lithium and ammonia reduction of 1,4-androstadiene-3,11,17-trione affords the 9//10 seco product, 3-hydroxy-9//seco-1,3,5(10) androstatriene-11,17-dione, m.p. 210-213°; $[\alpha]_D$ + 80; $\epsilon^{\text{MeOH}}_{\text{max}}$ 280 mμ, = 2370.[5]

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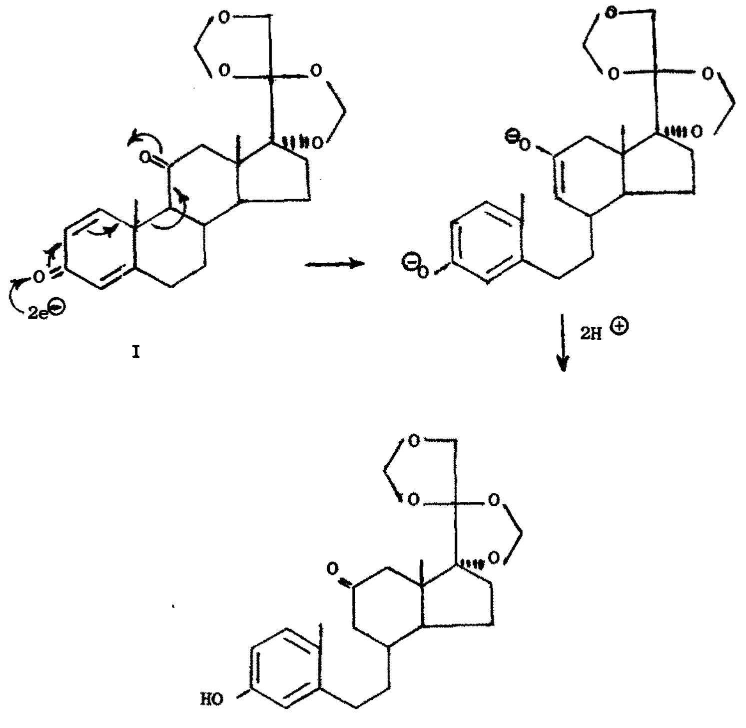
[1] A.J. Birch, Quart.Rev. 4, 69 (1950).

[2] D.H.R. Barton and C.R. Robinson, J.Chem.Soc. 3045 (1954).

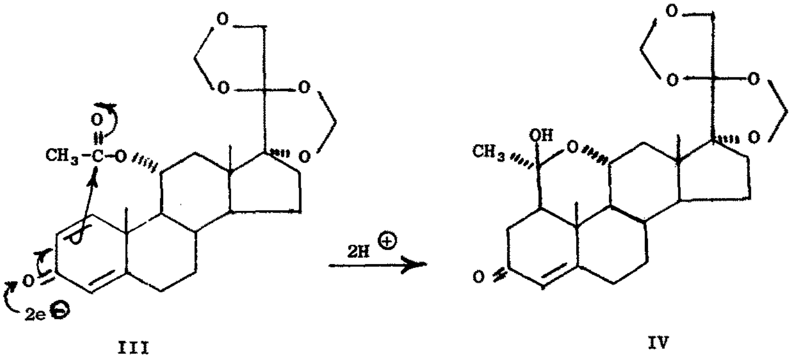
[3] R.E. Beyler, R.M. Moriarty, Frances Hoffman and L.H. Sarett, J.Amer.Chem.Soc. 80, 1517 (1958).

[4] B.J. Magerlein and J.A. Hogg, Tetrahedron 2, 80 (1958).



I

II



III

IV

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[5] These physical constants are in agreement with the published values of ref. 4. Satisfactory analyses have been obtained for all new compounds herein described. Rotations are in chloroform and the melting points are uncorrected.

Reduction with lithium and ammonia of ring A-3-keto-1,4-dienes having a neighboring 11α-acetoxy substituent leads to intramolecular acylation of the incipient β-carbanion generated at C.1. Thus the controlled lithium and ammonia reduction of 11α-acetoxy-17α; 20:20, 21-bismethylenedioxy-1,4-pregnadiene-3-one (III); m.p. 199-203°; $\lambda_{max}^{MeOH}$ 245 mμ, ε = 15,000; $\lambda_{max}^{Nujol}$ 5.78, 6.0, 6.15, 6.25, 8.5μ leads to a 1,2-dihydro-1-acetyl derivative (IV),[6] m.p. 210-213°; $[\alpha]_D$ - 8.0; $\lambda_{max}^{MeOH}$ 242 mμ, ε = 10,800; $\lambda_{max}^{Nujol}$ 3.05, 6.0, 6.15, 9.15μ.

The 1-acetyl derivative (IV) exists as the cyclic hemiketal tautomer as evidenced by the absence of saturated carbonyl absorption and the presence of hydroxyl absorption in the infra-red spectrum.

The cyclic hemiketal structure implies that the configuration of the masked 1-acetyl group is β-oriented. This allows the preferred accommodation of the fused tetrahydropyran ring in the more stable chair conformation.

The configuration at the hemiketal carbon C.1 presumably has the larger methyl substituent equatorial and α-oriented.

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[6] A similar intramolecular acylation of a carbanion produced during Birch reduction of 11β-acetoxy-estrone-3-methyl ether has been reported; see B.J. Magerlein and J.A. Hogg, J.Amer.Chem.Soc. **80**, 2223 (1955). The intramolecular discharge by alkylation of a beta-carbanion generated by lithium and ammonia reduction of an eneone has been recently reported; see G. Stork and J. Tsuji, Ibid. **83**, 2783 (1961).