Tetrahedron Letters No. 45, pp 4625 - 4626, 1972. Pergamon Press. Printed in Great Britain.

STEROIDS XXIII[1] MICHAEL REACTION WITH STEROIDAL 3-KETO-1,4,6-TRIENES

M. Kocór, M. Gumułka and T. Cynkowski

Institute of Organic Chemistry of the Polish Academy of Sciences, Warsaw

(Received in UK 21 September 1972; accepted for publication 4 October 1972)

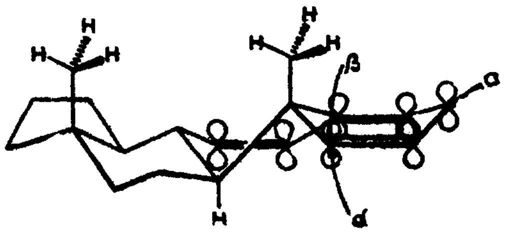
In the course of our investigations on the reactivity of steroidal 3-keto-1,4,6-trienes[2] we carried out more detailed studies on the Michael addition to this system. We found that the addition of nitromethane in t-butyl alcohol in the presence of tert-butoxide gives only one product IIa or IIb resp. in good yield (70%).

The homologous nitroalkanes react much slower; the yield not exceeding 10% in the case of nitropropanes, and the reaction mixture consists of two products isomeric on carbon atom 1. This rather unexpected result of the reaction can be explained on the basis of the recent studies on Michael reaction by Abramovitch at al.[3] in the following manner:

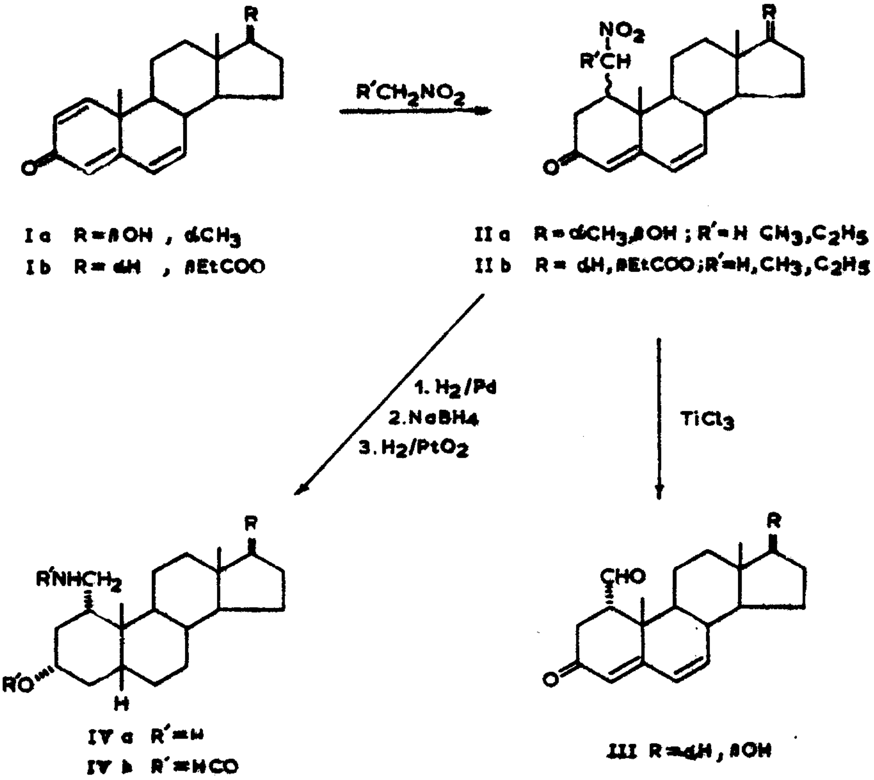
a) the initial approach of the nitroalkane anion to the almost coplanar ring A of 3-keto-1,4,6-triene will be in the direction perpendicular to the plane of ring A for maximum overlap of π orbitals.

b) Dreiding models indicate clearly, that there is only a very slight steric preference for approach from the α side (1,3 interaction with C-9 hydrogen) over approach from the β side (1,2 interaction with angular methyl group). However, this preference is sufficient in the case of nitromethane anion addition to cause the formation of one isomer only with the axial (α) orientation, and the yield of the reaction is good,

c) in the case of larger reactants i.e. nitroethane and nitropropanes the steric hinderance from both sides are comparably high, which consequently leads to the formation of both stereoisomers, but in much lower yield.



1α-nitromethyl-17α-methylandrosta-4,6-diene-17β-ol-3-one (IIa, R=H) did not give the Nef reaction, but the nitromethyl group could be converted into aldehyde group by the new method of McMurry with $TiCl_3$ in satisfactory yield giving III. We did not succeed in reducing the nitro group in unsaturated compounds II by standard methods, but after hydrogenation of both double bonds in the presence of palladium, followed by $NaBH_4$ reduction; hydrogenation in the presence of PtO_2 yielded the amine IVa, characterized as itself or N-formyl-formate IVb. All new compounds gave correct spectroscopic and analytical data.



Ia $R = \beta OH, \alpha CH_3$

Ib $R = \alpha H, \beta EtCOO$

IIa $R = \alpha CH_3, \beta OH; R' = H\ CH_3, C_2H_5$

IIb $R = \alpha H, \beta EtCOO; R' = H, CH_3, C_2H_5$

IVa $R' = H$

IVb $R' = HCO$

III $R = \alpha H, \beta OH$

The described Michael addition is a simple preparative method to obtain the 1-substituted steroids; full report with further Michael addition reactions will be published in the future. The authors are very much indebted to Prof. R. Abramovitch for helpful discussions.

References:

1) For Part XXII see Chem. Anal. 17, (1972) in press

2) See for example: M.Kocór and M.Gumułka, Roczn. Chem. 45, 1003 (1971)

3) R.A. Abramovitch, D.L. Struble, Tetrahedron 24, 357 (1968)

4) J.E. McMurry, J. Melton, J. Amer.Chem. Soc. 93, 5309 (1971).