Tetrahedron Letters No. 32, pp 3349 - 3352, 1972. Pergamon Press. Printed in Great Britain.

SELECTIVE DEACETYLATION AND STEREOSPECIFIC ACYL MIGRATION OF STEROID ACETATES ON ALUMINIUM OXIDE.

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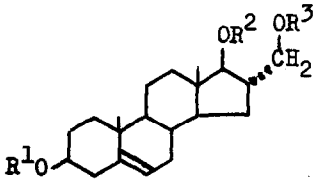
(Received in UK 26 May 1972; accepted for publication 6 July 1972)

Chromatography on aluminium oxide may be accompanied by side reactions[1]. Recently, we have observed a deacetylation reaction of high stereospecificity proceeding on alkaline aluminium oxide (pH 8-9) of activity IV (Reanal Fine Chemical Factory, Budapest). The isomers of 16-acetoxymethylandrost-5-en-3β, 17-diol 3,17-diacetates (Ia,IIa,IIIa,IVa) underwent selective deacetylation at the 16-function, when kept in the column under conditions of usual chromatography.

16α-Acetoxymethylandrost-5-en-3β,17β-diol 3,17-diacetate (Ia) kept 6-7 days on alkaline Al_2O_3 lost its primary acetoxy group, while the secondary acetoxy groups remained intact to give 16α-hydroxymethylandrost-5-en-3β,17β-diol 3,17-diacetate (Ib); m.p. 195-198, $[\alpha]_D = -20^\circ$ (c 0.5 $CHCl_3$). Under similar conditions, 16β-acetoxymethylandrost-5-en-3β,17α-diol 3,17-diacetate (IIa) containing again the 16,17 functional groups in <u>trans</u> orientation with respect to one another resulted 16β-hydroxymethylandrost-5-en-3β,17α-diol 3,17-diacetate (IIb); m.p. 167°, $[\alpha]_D = -30^\circ$ (c 0.5 $CHCl_3$).

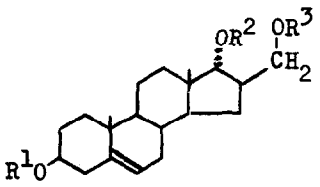
In order to confirm that the deacetylation occurred actually at the primary acetoxy group in both cases (Ia, IIa), the already known[2] Ic was selectively propionylated and the resulted Id acetylated to give the mixed propionate-acetate derivative (Ie); m.p. 117-120°, $[\alpha]_D = -24^\circ$ (c 0.5 $CHCl_3$) was prepared from IIc through IId.

Deacylation of the mixed propionate-acetate isomers (Ie,IIe) on alkaline Al_2O_3 gave rise to Ib and IIb, respectively, with loss of the propionyl group.



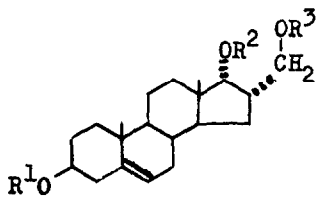
(I)

	R^1	R^2	R^3
a	Ac	Ac	Ac
b	Ac	Ac	H
c	Ac	H	H
d	Ac	H	Pr
e	Ac	Ac	Pr



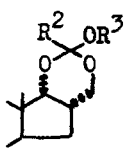
(II)

	R^1	R^2	R^3
a	Ac	Ac	Ac
b	Ac	Ac	H
c	Ac	H	H
d	Ac	H	Pr
e	Ac	Ac	Pr

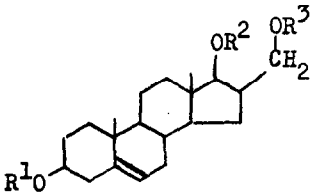


(III)

	R^1	R^2	R^3
a	Ac	Ac	Ac
b	Ac	Ac	H
c	Ac	H	Ac
d	Ac	H	H

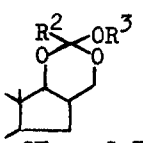


e Ac CH_3 C_2H_5



(IV)

	R^1	R^2	R^3
a	Ac	Ac	Ac
b	Ac	Ac	H
c	Ac	H	Ac
d	Ac	H	H



e Ac CH_3 C_2H_5

Under similar conditions, 16α-acetoxymethylandrost-5-en-3β,17α-diol 3,17-diacetate (IIIa), containing the 16,17 functional groups in cis orientation with respect to one another, underwent deacetylation to give 16α-hydroxymethylandrost-5en-3β,17α-diol 3,17-diacetate (IIIb). We had already prepared[3] this compound (IIIb) by treating the cyclic ortho-ester IIIe with methanol in the presence of p-toluenesulphonic acid. However, compound IIIb transformed further on the alkaline Al_2O_3 to IIIc; m.p.159-161°, $[\alpha]_D$= -61° (c o.5 $CHCl_3$), by acyl migration, followed by cleavage of the newly formed primary acetoxy group to give IIId.

16β-Acetoxymethylandrost-5-en-3β,17β-diol 3,17-diacetate (IVa) containing again the 16,17 functional groups in cis orientation behaved similarly to IIIa and gave IVb on alkaline Al_2O_3. Compound IVb, already prepared[3] by degradation of cyclic ortho ester IVe, proved to be unstable under experimental conditions and underwent acyl migration to give IVc ; m.p. 136-138°, $[\alpha]_D$ = -12° (c o.5 $CHCl_3$). Further deacetylation of IVc at the primary acetoxy function resulted IVd.

Accordingly, the isomers containing the 16,17 functional groups in trans orientation with respect to one another (Ia, IIa) undergo de-acetylation at the primary acetoxy group to give Ib and IIb, respectively, while in case of the other two isomers containing these functional groups in cis orientation (IIIa, IVa), the corresponding diacetates (IIIb, IVb) obtained by cleavage of the primary acetoxy groups react further to give monoacetates (IId, IVd) via an acyl migration and a second deacetylation.

The authors are indebted to the Chemical Works of Gedeon Richter (Budapest) for support of this work.

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