Tetrahedron Letters No. 30, pp 2605 - 2606, 1975. Pergamon Press. Printed in Great Britain.

MERCURY(II) SALTS-CATALYSED REARRANGEMENT OF Δ^5-STEROIDS TO A-HOMO-B-NORDERIVATIVES

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(Received in UK 3 June 1975; accepted for publication 9 June 1975)

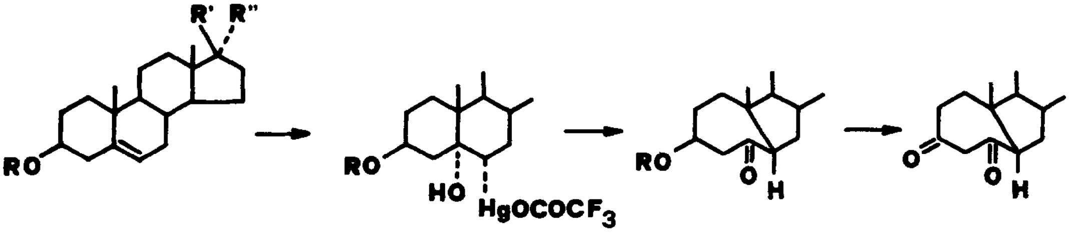
Recently several papers have appeared on the action of mercury(II) salts on olefinic compounds, although little work has been done on steroidal olefins.[1]

Here we report on the results obtained by reacting mercury(II) salts on Δ^5-steroids. Cholesterol Ia and $3\beta,17\beta$-dihydroxy-17α-methyl-androst-5-ene Ib were used as starting materials. In tetrahydrofuran-water solution (3:2), the reaction occurs with both mercury(II) trifluoroacetate and mercury(II) nitrate. Examination by thin layer chromatography of the reaction mixtures showed that, in addition to the expected organomercurial adducts, compounds Ia and Ib gave no mercurated derivatives. In order to examine these metal-free steroids, we proceeded directly to the separation of the reaction mixtures, omitting the demercuration step with sodium borohydride. The procedure was as follows: a solution of the steroid (1 mole) in tetrahydrofuran-water (3:2) containing mercury(II) trifluoroacetate (4 moles) was allowed to stand at room temperature for six days. Tetrahydrofuran was then evaporated under vacuum at room temperature and the aqueous solution was extracted with methylene chloride. The residue was chromatographed on silica gel.[2]

From the reaction carried out on cholesterol, compound IIIa was isolated (17% yield) together with 40% of starting material: [IIIa: 3β-hydroxy-A-homo-B-nor-6β-cholestan-5-one, $C_{27}H_{46}O_2$, m.p. 149-150°, (lit.[3] 148°); $[\alpha]_D$ +28.5° (c 1.0, $CHCl_3$) (lit.[3] +21°)]. The assigned structure was confirmed by comparison with an authentic sample prepared according to Jones and Marples.[3] By oxidation with CrO_3 ketol IIIa gave the corresponding diketone IVa: [IVa: A-homo-B-nor-6β-cholestan-3,5-dione, $C_{27}H_{44}O_2$, m.p. 146-147°, (lit.[3] 138-139°); $[\alpha]_D$ -43.6° (c 1.0, $CHCl_3$)].

When the reaction with mercury(II) trifluoroacetate was carried out on $3\beta,17\beta$-dihydroxy-17α-methyl-androst-5-ene Ib, 28% of the starting material was recovered together with ketol IIIb (15% yield). Structure IIIb was assigned on the basis of analytical data and of the c.d. spectrum of its acetyl derivative IIIc: [IIIb: 3β, 17β-dihydroxy-17α-methyl-A-homo-B-nor-6β-androstan-5-one, $C_{20}H_{32}O_3$, m.p. 217-219°; $[\alpha]_D$ -7.4° (c 1.79, MeOH); ν_{max}^{KBr} 1687, 1670 cm^{-1}; $\delta_{TMS}^{d_6-DMSO}$ 0.77 (18-Me), 1.12 ppm (19-Me and 17α-Me)]. [IIIc: 17β-hydroxy-3β-acetoxy-17α-methyl-A-homo-B-nor-6β-androstan-5-one, $C_{22}H_{34}O_4$, m.p. 137-138°; $[\alpha]_D$ +21.4° (c 0.56, MeOH); ν_{max}^{KBr} 1727, 1690, 1225 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 0.81 (18-Me), 1.18 (19-Me or 17α-Me), 1.19 ppm (19-Me or 17α-Me); c.d. (MeOH) λ_{max} 295 mμ, Δε +2.46]. By oxidation with CrO_3 of ketol IIIb diketone IVb was obtained : [IVb: 17β-hydroxy-17α-methyl-A-homo-B-nor-6β-androstan-3,5-dione, $C_{20}H_{30}O_3$, m.p. 159-160°; $[\alpha]_D$ -85.2° (c 1.0, $CHCl_3$); ν_{max}^{KBr} 1703, 1680 cm^{-1}; $\delta_{TMS}^{CCl_4}$ 0.81 (18-Me), 1.04 (19-Me), 1.21 ppm (17α-Me)].

The reported reaction proceeds probably trough a cis-addition with formation of a mercury intermediate such as II. A similar hydroxymercuration reaction has already been described for other strained olefinic compounds[4]. Specific addition of this type was also reported for Δ^5-steroids by utilizing other reagents[5]. The formation of compounds IIIa , IIIb by solvolysis of intermediate II is favoured by the coplanarity of the reaction centres involved in the rearrangement.



a) R=H, R'=C_8H_{17}, R"=H ;

b) R=H, R'=OH, R"=CH_3;

c) R=$COCH_3$, R'=OH, R"=CH_3

References and note.

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