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39. Steroids and Sex Hormones

Part 250[1]

Transformation of Dehydroabietic Acid into 14-Methyl-Steroids II

The Synthesis of 3-Oxo-17β-acetoxy-14α-methyl-Δ^4-8α,9β,10α,13α-estrene

Preliminary Communication[2]

by **Toni Wirthlin, Hansuli Wehrli,** and **Oskar Jeger**

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(8. I. 74)

Zusammenfassung. Im Rahmen der vorliegenden Mitteilung berichten wir über den partialsynthetischen Aufbau von 3-Oxo-17β-acetoxy-14α-methyl-Δ^4-8α,9β,10α,13α-östren (**12**), dessen Struktur anschliessend mittels dreidimensionaler Röntgenanalyse [2] sichergestellt worden ist. Als Ausgangsmaterial der Synthese diente die tricyclische Verbindung **2**, die, zusammen mit **3**, von uns (s. vorhergehende Mitt. [1]), aus Dehydroabietinsäure (**1**) dargestellt worden ist.

We have already described an 18-stage conversion of dehydroabietic acid (**1**) into a (1:4)-mixture of C/D-*cis*-compound **2** and C/D-*trans*-isomer **3**[3]. The minor isomer **2** served now as the starting material for the preparation of 3-oxo-17β-acetoxy-14α-methyl-Δ^4-8α,9β,10α,13α-estrene (**12**) along lines developed by *Velluz et al.*

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[1] For part 249, see [1].

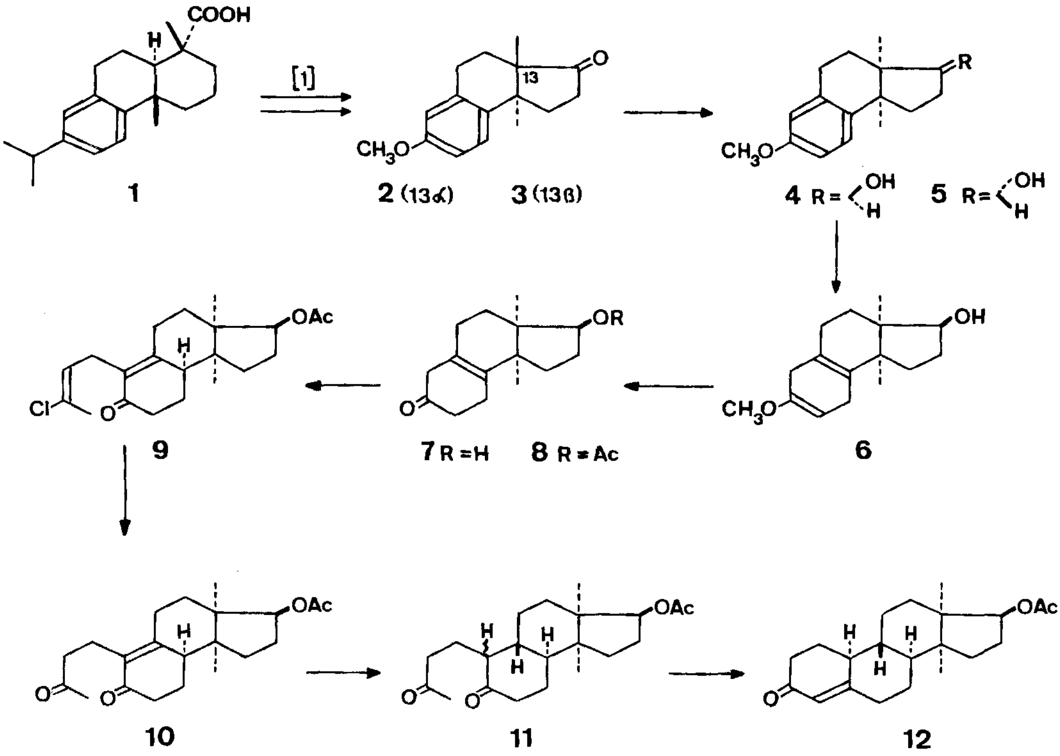
[2] Full paper: Helv., in preparation.

[3] The steric arrangement of the new compounds **2**–**12** follows from transformation into **12**, whose structure and configuration were established by X-ray analysis [2].

[3–5] in the course of earlier synthetic investigations in the 14-desmethyl-13β-steroid series.

Compound **2** was reduced with $NaBH_4$ in methanol at –30° to a (4:1)-mixture of the epimeric 17-alcohols **4** and **5**[4][5][6].

The principal component, the 17β-alcohol **4** [m.p. 75–78°; – $[\alpha]_D = +9°$ $(CHCl_3)$] was then converted in three stages by Li/NH_3-reduction [6], oxalic acid treatment and acetylation *via* enolether **6** [NMR.: among other signals δ = 3.46, *s*, 5-OCH_3; 4.47, b*m*, CH(6) $(CDCl_3)$][7] and hydroxyketone **7**[7] into the β,γ-unsaturated acetoxyketone **8** [NMR.: among other signals δ = 0.94 + 1.04, 2*s*, CH_3(18) + 14-CH_3; 2.03, *s*, 17-$OCOCH_3$; 5.04, *m*, CH(17) $(CDCl_3)$; – MS.: $M^+ = 276$ $(C_{17}H_{24}O_3)$], which has not so far been crystallized. Alkylation of **8** with 1,3-dichloro-butene-(2) according to *Conia* [7] (sodium-*t*-amylate in toluene) followed by acid treatment (HCl in acetic acid) gave the so far amorphous chloroderivative **9** [IR.: 1738, 1670, 1612, 1245 (CCl_4); – NMR.: among other signals δ = 2,07, bs, CH_3(4); 5.20, b*m*, CH(2) + CH(17) $(CDCl_3)$][3], which was transformed (H_2SO_4/CH_2Cl_2) into diketone **10** [IR.: among others 1720, 1670, 1610 (CCl_4); – NMR.: among other signals δ = 1.05 + 1.09, 2*s*,



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[4] The 17α-alcohol **5** was reoxidized to **2** by CrO_3.

[5] The new compounds were characterized by IR., NMR., and MS., and, if crystalline, by optical rotations.

[6] The numbering of carbon atoms in this paper corresponds to that of steroids.

[7] The unstable compounds **6** and **7** were not isolated in pure form.

$CH_3(18)$ + 14-CH_3; 2.07, *s* $CH_3(4)$ ($CDCl_3$); – not yet crystallized]3)). Finally, **8** was converted by catalytic hydrogenation [5%-Pd/C in ethanol/triethylamine; → **11** 3))] and cyclisation [HCl in acetic acid] into 3-oxo-17β-acetoxy-14α-methyl-Δ^4-8α,9β,10α,13α-estrene (**12**) [m.p. 86–88°; – $[\alpha]_D = +1°$ ($CHCl_3$). – IR.: 1729, 1665, 1620, 1255 ($CHCl_3$); – UV.: 245 nm ($\varepsilon = 14500$ in ethanol). – NMR.: 0.98 + 0.99, 2*s*, $CH_3(18)$ + 14-CH_3; 1.98, *s*, 17-$OCOCH_3$; 5.05, b*m*, CH(17); 5.70, b*s*, CH(4) ($CDCl_3$). – MS.: $M^+ = 330$ ($C_{21}H_{30}O_3$). – CD.: 320 nm ($\Delta\varepsilon = 1.37$ in ethanol)]. The structure of **12** was subsequently confirmed by three-dimensional X-ray diffraction; in addition the 8α,9β,10α,13α,14α-configuration of this steroid like derivative **12** was also established by the X-ray results8)).

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8) We wish to express our sincerest thanks to Dr. *G. Koyama* for the structure determination by X-ray analysis [2].

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40. The Crystal and Molecular Structure of 3-Oxo-17β-acetoxy-Δ^4-14α-methyl-8α,9β,10α,13α-estrene

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(8. I. 73)

Summary. The crystal and molecular structure of 3-oxo-17β-acetoxy-Δ^4-14α-methyl-8α,9β,10α,13α-estrene, $C_{21}H_{30}O_3$, has been determined by X-ray diffraction analysis. The crystals belong to the orthorhombic space group $P2_12_12_1$, with the cell dimensions $a = 12.093$ Å, $b = 19.667$ Å, $c = 7.746$ Å; Z = 4. Intensity data were collected at room temperature with an automatic four-circle diffractometer. The structure was solved by direct methods and the parameters were refined by least-squares analysis. All the hydrogen atoms were included in the refinement. The final R value was 0.038 for 1413 observed reflections. The conformation of ring A is intermediate between a half-chair and a 1,2-diplanar form. The hydrogens at C(9) and C(10) are *anti*, the B/C ring junction is *trans*, and rings B and C adopt chair conformations. Ring D is *cis* fused and is halfway between C_2 and C_s forms.

The transformation of dehydroabietic acid into a 14α-methyl steroid product is described in the preceding communications [1]. Since the configurations at C(8),

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