20,23-Dihydroxyspirostans[1]

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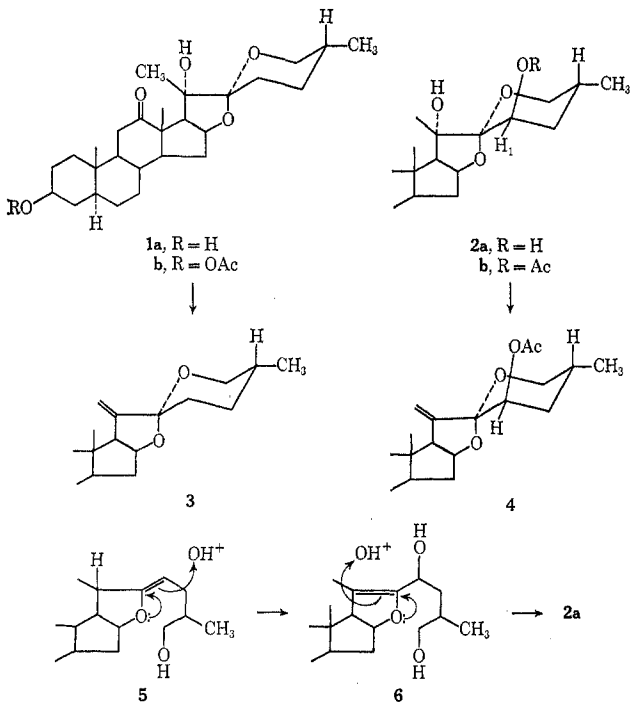
Chromic acid oxidation of 20-cyclopseudotigogenin[2] and pseudohecogenin[3,4] yields 20-hydroxyspirostans. This product is also produced by treatment of pseudosapogenins with peracids.[4,5]

During the preparation of 20-dehydrohecogenin acetate (**3**), we examined the oxidation of pseudohecogenin with *m*-chloroperbenzoic acid. Since the peracid product is difficult to purify as the diol **1a** and exhibits wide melting ranges,[4,6] the oxidation mixture was acetylated



and the C_3 acetate was removed by crystallization. Thin layer chromatographic analysis of the mother liquor then revealed the presence of a more polar material, **2b**. Careful chromatography on silica gel yielded **2b**, mp 288–289°, $[\alpha]D$ −21°, with an empirical composition in agreement with a hecogenin acetate derivative containing additional hydroxyl and acetoxyl substituents. This finding was substantiated by the ir hydroxyl band at 3510 cm^{-1} and the nmr signals for the acetate methyls at τ 7.92 and 8.02. The tertiary character of the hydroxyl group was indicated by its inability to be acetylated in pyridine with acetic anhydride, and its location at C_{20} was inferred by the appearance of the C_{21}-methyl signal in the nmr as a singlet at τ 8.67.

The polar material **2b** dehydrates to afford a 20-dehydrohecogenin acetate derivative **4** under conditions identical with those employed for the dehydration of **1b**.[2] The dehydrated material **4** retains the extra acetoxyl substituent.

The formation of an acetate and the appearance of a proton signal (H_1) at τ 5.23 in **2b** as a symmetrical triplet (J = 2.2 Hz) confirms the introduction of a secondary acetoxyl group into 20-hydroxyhecogenin acetate. The coupling constant is characteristic of diequatorial or equatorial–axial coupling, whereas diaxial coupling is 6–10 Hz.[7] The configuration of H_1 is therefore equatorial, to be consistent with the magnitude of the observed coupling of 2.2 Hz.

Based on the hydrogen-bonding interaction of the C_{20} hydroxyl with the C_{22} oxygen of sapogenins, Wall and Walens[5] have assigned C_{20} and C_{22} stereochemistry. Examination of the hydroxyl bands of **1b** and **2b** in carbon disulfide solutions showed intramolecular hydrogen bonding at 3510 cm^{-1}, indicating the *cis* C_{20}-hydroxyl and C_{22}-oxygen relationship. Support for the C_{22} (*R*) configuration is the observed negative rotation of **2b**, which is in accord with values previously found.[8] Thus the combined chemical and spectroscopic data are compatible with structure **2b**.

The reaction of 20-hydroxyhecogenin with *m*-chlorobenzoic acid and *m*-chloroperbenzoic acid was examined to establish whether **2a** comes from this route. This reaction yielded unidentified, more polar materials but did not give **2a**.

The probable mode of formation of **2a** therefore appears to be *via* the attack of peracid on a Δ^{22}-furostene intermediate **5** formed initially to yield a 23-hydroxy derivative, **6**. Further reaction of the $\Delta^{20(22)}$-furostene **6** with peracid leads to **2a**. The formation of variable quantities of Δ^{22}-furostene derivatives, along with the more usual $\Delta^{20(22)}$-furostenes from the sapogenin ring F opening reactions, has been previously noted.[9]

Experimental Section

Infrared spectra were obtained on a Perkin-Elmer Infracord in Nujol and on a Beckman IR-4 in carbon disulfide solutions (0.0025 *M*). Nmr spectra were obtained on a Varian A-60A instrument using deuteriochloroform as a solvent and tetramethylsilane as an internal standard. Optical rotations were measured in 0.2–0.5% chloroform solutions at 23°. All extracts were dried over anhydrous sodium sulfate and evaporated at reduced pressure.

***m*-Chloroperbenzoic Acid Oxidation of Pseudohecogenin.**—To a solution of 10 g of pseudohecogenin in 1.8 l. of methylene chloride at 0° was added 9.7 g of *m*-chloroperbenzoic acid (80%). The solution was allowed to warm to room temperature and then stored in the dark. After 7 days, the solution was washed with sodium bisulfite and water and evaporated to yield a residue of 12.1 g. To 10 g of the residue in 10 ml of pyridine was added 10 ml of acetic anhydride. After 18 hr, water was added; the product was extracted with ether and washed with sodium bicarbonate and water. The residue was recrystallized from methanol to give 6.12 g of **1b**: mp 261–262°; $[\alpha]D$ −11°; ir ν_{max} 3510 cm^{-1} (OH) (lit.[4] mp 254–259°; $[\alpha]D$ −9°). The mother

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liquor was chromatographed on 300 g of silica gel. Nonpolar material was eluted with 50% benzene–ether to give 1.04 g of **1b**, followed by mixed fractions and, finally, 2.68 g of 3β-(23*R*)-diacetoxy-(20*S*)-hydroxy-(22*R*,25*R*)-5α-spirostan-12-one (**2b**), eluted with 20% chloroform–ether. An analytical sample was recrystallized from methanol: mp 288–289°; $[\alpha]_D$ −21°; ir ν_{max} 3510 cm^{-1} (OH), λ_{max} 2.86 (OH), 5.77, 8.10 ($OCOCH_3$), 5.85 (C=O), spiroketal bands, 10.78 (s), 10.99 (s), 11.10 (w), and 11.41 μ (w); nmr τ 9.22 (d, J = 6 Hz, CH_3-27), 9.10 (CH_3-19), 8.80 (CH_3-18), 8.67 (CH_3-21), 8.02 ($OCOCH_3$-3), 7.92 ($OCOCH_3$-23), and 5.08 (t, J = 2.2 Hz, H-23).

Anal. Calcd for $C_{31}H_{46}O_8$: C, 68.11; H, 8.48. Found: C, 68.49; H, 8.43.

3β-(23*R*)-Diacetoxy-(22*R*,25*R*)-5α-spirost-20(21)-en-12-one (4).—To a solution of 0.5 g of **2b** in 20 ml of pyridine at 0° was added 2.5 ml of thionyl chloride, dropwise with stirring. The mixture was allowed to stand at room temperature for 2 hr, poured over ice, extracted with ether, and washed with sodium bicarbonate and water. The residue was recrystallized from methanol to give 0.45 g of **4**: mp 281–283°; $[\alpha]_D$ −1.0°; ir λ_{max} 5.77, 8.10 ($OCOCH_3$), 5.85 (C=O), spiroketal bands, 10.81 (w), 10.91 (s), 11.02 (s), 11.14 (m), and 11.49 μ (m); nmr τ 9.20 (d, J = 6 Hz, CH_3-27), 9.09 (CH_3-19), 8.89 (CH_3-18), 8.01, ($OCOCH_3$-3), 7.92, ($OCOCH_3$-23), 5.08 (t, J = 2.2 Hz, H-23), and 4.58 (m, $=CH_2$-21).

Anal. Calcd for $C_{31}H_{44}O_7$: C, 70.43; H, 8.39. Found: C, 70.86; H, 8.58.

3β-Acetoxy-(22*R*,25*R*)-5α-spirost-20(21)-en-12-one (3).—The same procedure as the preparation of **4** was followed, using 0.5 g of **1b**, 20 ml of pyridine, and 2.5 ml of thionyl chloride. The residue was recrystallized from methanol to give 0.23 g of **3**: mp 229–232°; $[\alpha]_D$ +19°; ir λ_{max} 5.77, 8.10 ($OCOCH_3$), 5.85 (C=O), spiroketal bands, 10.22 (s), 10.95 (m), 10.87 (m), 11.04 (s) and 11.55 μ (m); nmr τ 9.20 (d, J = 6 Hz, CH_3-27), 9.09 (CH_3-19), 9.04 (CH_3-18), 8.00 ($OCOCH_3$-3), and 5.76 (m, $=CH_2$-21).

Anal. Calcd for $C_{29}H_{42}O_5$: C, 74.01; H, 8.99. Found: C, 73.79; H, 8.77.

Treatment of 3β-Acetoxy-(20*S*)-hydroxy-(22*R*,25*R*)-5α-spirostan-12-one with Peracid.—A solution of 0.4 g of **1a**, 0.4 g of *m*-chloroperbenzoic acid, and 0.4 g of *m*-chlorobenzoic acid in 50 ml of methylene chloride was stirred at room temperature, in the dark, for 5 days. The reaction was quenched by washing with a saturated sodium bisulfite solution, saturated sodium bicarbonate, and water. The residue (0.43 g) was acetylated in 2 ml of acetic anhydride and 10 ml of pyridine. The resulting acetate was recrystallized from methanol to afford 0.18 g of **1b**. The mother liquor was chromatographed on 15 g of silica gel. Upon elution with benzene–40% ether, 0.02 g of **1b** was obtained. Then 0.07 g of a mixed fraction was obtained, followed by 0.05 g of an unknown substance eluted with 20% chloroform–ether.

Registry No.—**2b**, 23405-42-7; **3**, 23405-43-8; **4**, 23405-44-9.

Thermal Decomposition of β-Hydroxy Esters. Ethyl-3-hydroxy-3-methylbutanoate

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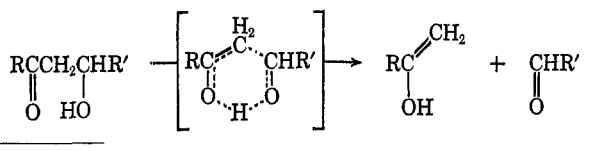
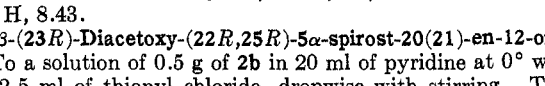
From recent studies[1] on the mechanism of the thermal decomposition of β-hydroxy ketones, it has been proposed that the reaction involves a cyclic six-membered transition state.



An obvious extension to this work would be to examine the thermal decomposition of β-hydroxy esters to see if they decompose by a similar mechanism. If such is the case, it would be predicted that the β-hydroxy ester ethyl 3-hydroxy-3-methylbutanoate would pyrolyze to acetone and ethyl acetate.



A literature search has indicated that, as far as can be ascertained, the thermal decomposition of β-hydroxy esters has not previously been studied. Accordingly, a study has been carried out on the thermal decomposition of ethyl 3-hydroxy-3-methylbutanoate, which was prepared by a Reformatsky reaction between ethyl bromoacetate and acetone.[2] The pyrolyses were carried out in xylene solution in sealed glass tubes that had been carefully washed to remove all traces of acid or base, and the products of the reaction were analysed by gas chromatography, using a 5-ft column of SE-30 on Chromosorb W.

It was found that in xylene solution ethyl 3-hydroxy-3-methylbutanoate did indeed decompose at temperatures of 180–250° to give acetone and ethyl acetate in yields of 90–95%. The products of the reaction were characterized both by their glpc retention times and in the case of acetone by the formation of a 2,4-dinitrophenylhydrazone, mp 127–8° (after crystallization), from the products of pyrolysis. (The reported melting point of the 2,4-dinitrophenylhydrazone of acetone is 128°.[3]) In the gas chromatography of the products of pyrolysis apart from the solvent peak (xylene) only peaks due to acetone and ethyl acetate were observed. The yields were calculated using glpc by comparison of the peak areas of the products of pyrolysis with those of a known mixture of ethyl acetate and acetone in xylene using benzene as an internal standard. In tubes that were not carefully washed some dehydration occurred as evidenced by the appearance of a new peak due to water in the gas chromatograph of the pyrolysis products.

The kinetics of the decomposition were followed by the methods used in the earlier study.[1a] The reaction was followed to at least two half-lives at 217.8 and 206.0° and one half-life at 191.4 and 179.4°. Good first-order kinetics were observed, the first-order plots being linear for all the periods during which the reaction was followed. The rate constants obtained are listed in Table I, and were found to be reproducible to within ±5%. Equal rate constants were obtained when the reaction was followed by the rate of appearance of the

TABLE I

RATE CONSTANTS FOR THE PYROLYSIS OF ETHYL 3-HYDROXY-3-METHYLBUTANOATE

	Temperature, °C			
	179.4	191.4	206.0	217.8
$k \times 10^6$, sec^{-1}	0.269	0.812	2.76	6.88

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