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STUDIES ON CATALYTIC HYDROGENATION OF 16-FURFURYLIDENE-17β-HYDROXY STEROIDS.

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Condensation of androstenolone (1) with furfural in the presence of sodium hydroxide under nitrogen, afforded in quantitative yield 16-furfurylidene-androstenolone (2) - m.p. 190°; $[\alpha]_D^{20} = -107°$ (c=0,57 in $CHCl_3$); UV-Spectrum: λ_{max} = 327 nm (ε = 26,000); IR-Spectrum: ν_{max} = 3509, 1724, 1640, 1563, 1026, 1010, 892, 752 cm^{-1}.

Acetylation of (2) with Ac_2O/Py gave the corresponding 3β-acetate (3) - m.p. 196°; $[\alpha]_D^{20} = -165°$ (c=0,58 in $CHCl_3$); UV-Spectrum: λ_{max} = 325 nm (ε = 27,600); IR-Spectrum: ν_{max} = 1724, 1626, 1550, 1250, 1026, 1010, 885, 746 cm^{-1}; NMR-Spectrum**: δ = 7,60/d (J=1,8)/(1); ca.7,2/m/(1); 6,64/d (J=6,3)/(1);

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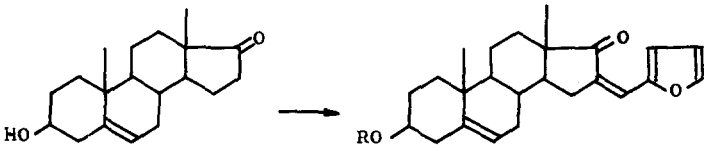
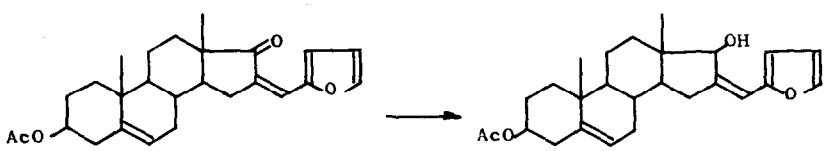
** Chemical shifts are given in ppm and coupling constants in cps; symbols d, t, q and m indicate doublett, triplett, quartett and multiplett, respectively; the numbers in parentheses represent the number of protons of the corresponding peak.

6,52/q (J=3,6 and 1,8)/(1); 5,44/d (J=4,0)/(1); ca.4,6/m (broad)/(1); 2,02/s/(3); 1,09/s/(3); 0,96/s/(3).



(1) (2) R = H
(3) R = Ac

Reduction of (3) with sodium borohydride in methanol at 0°, gave a 90% yield of 3β-acetoxy-16-furfurylidene-17β-hydroxy-Δ^5-androstene (4) - m.p. 214°; $[\alpha]_D^{20} = -160°$ (c=0,64 in $CHCl_3$); UV-Spectrum: λ_{max} = 271 nm (ε = 24,700); IR-Spectrum: ν_{max} = 3425, 1724, 1626 (shoulder), 1550, 1258, 1026, 1010, 879, 742 cm^{-1}; NMR-Spectrum: δ = 7,39/d (J=1,75)/(1); ca.6,4/m/(2); ca.6,2/d (J=3,0)/(1); 5,40/d (J=4,0)/(1); ca.4,6/m (broad)/(1); ca.4,0/s (broad)/(1); 2,02/s/(3); 1,06/s/(3); 0,70/s/(3).



(3) (4)

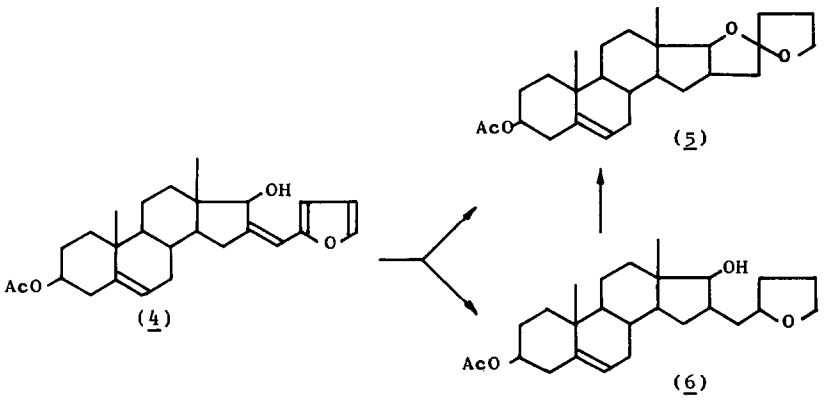
An ethylacetate solution of (4) was hydrogenated under normal pressure using PtO_2 as catalyst. After 6 hours the

absorption of hydrogen ceased and the resulting mixture was chromatographed on a silica-gel column. The following products were isolated and identified:

(a) Spiro-ketal (5) - m.p. 170°; $[\alpha]_D^{20} = 0°$ (c=1,00 in $CHCl_3$); UV-Spectrum: no absorption; IR-Spectrum: ν_{max} = 1722, 1233, 1096, 1080, 1064, 1046, 1017, 990, 975, 920, 903 cm^{-1}; NMR-Spectrum: δ = 5,36/d (J=4,6)/(1); ca.4,6/m (broad)/(1); 4,05/d (J=9,8)/(1); ca.3,9/m/(2); 2,02/s/(3); 1,04/s/(3); 0,74/s/(3).

(b) 3β-Acetoxy-16β-tetrahydrofurfuryl-17β-hydroxy-Δ^5-androstene (6) - m.p. 210°; $[\alpha]_D^{20} = -61°$ (c=1,00 in $CHCl_3$); UV-Spectrum: no absorption; IR-Spectrum: ν_{max} = 3356, 1720, 1235, 1070 cm^{-1}; NMR-Spectrum: δ = 5,40/d (J=4,0)/(1); ca.4,6/m (broad)/(1); ca.3,8/m/(4); 3,3/s (broad)/(1); 2,02/s/(3); 1,04/s/(3); 0,78/s/(3).

Oxidation of (6) with lead tetraacetate in benzene gave the spiro-ketal (5).

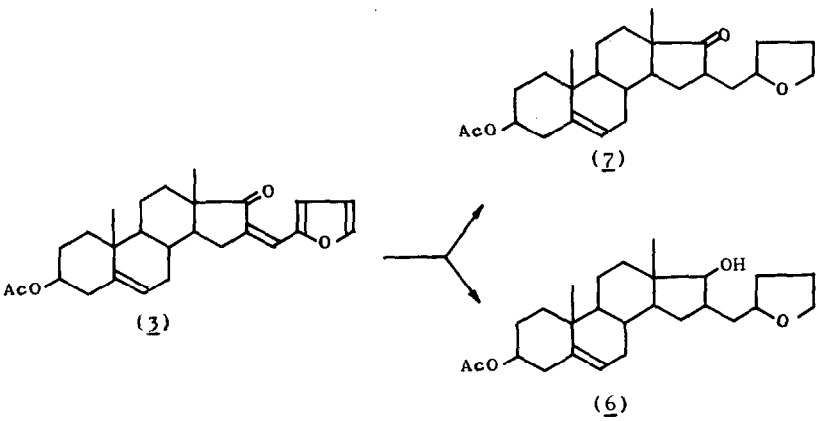


Hydrogenation of 3β-acetoxy-16-furfurylidene-androstenolone (3) under the same experimental conditions yielded the following products:

(a) 3β-Acetoxy-16β-tetrahydrofurfuryl-17-oxo-Δ^5-androstene (7) - m.p. 176°; $[\alpha]_D^{20}$ = +25° (c=0,60 in $CHCl_3$); UV-Spectrum: no absorption; IR-Spectrum: ν_{max} = 1736, 1250, 1080 cm^{-1}; NMR-Spectrum: δ = 5,40/d (J=4,0)/(1); ca.4,6/m (broad)/(1); ca. 3,8/m/(3); 2,02/s/(3); 1,06/s/(3); 0,80/s/(3).

(b) 3β-Acetoxy-16β-tetrahydrofurfuryl-17β-hydroxy-Δ^5-androstene (6).

In this case no spiro-ketal was obtained.



Hydrogenation of (3) in ethylacetate under normal pressure with Raney-nickel as catalyst afforded the same products as above, the yield of (7) being higher.

The intramolecular cyclisation of β-furylacrolein derivatives was carried out under a pressure of 100-200 atm. at 160° and with Raney-nickel on Kieselgur as catalyst[1,2]. In our case, however, the intramolecular cyclisation of (4) into the spiro-ketal (5) occurs by hydrogenation at room temperature with PtO_2 as catalyst. This is probably due both to the rigid conformation of the D-ring and to the cis-configuration of the 17β-hydroxy and 16β-dihydrofurfuryl groups (probable intermediate in the reaction), which allows close enough approach of the reacting centers*.

REFERENCES

1. H.E.Burdick & H.Adkins, J.Am.chem.Soc. 56, 438 (1934)
2. M.Farlow, H.E.Burdick & H.Adkins, J.Am.chem.Soc. 56, 2498 (1934)

* Cyclisation of furfurylidene derivatives of cyclohexanone also requires the conditions proposed by Adkins[1,2].