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SYNTHESIS OF 22,25-EPOXYFUROSTAN SAPOGENINS [1]

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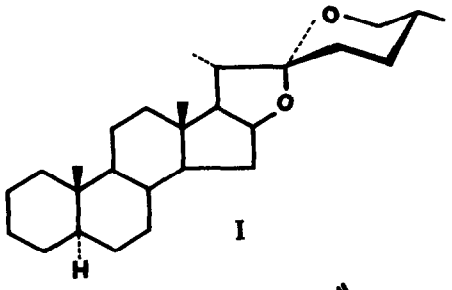
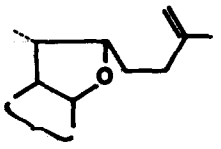
Several furostan sapogenins with oxygen bridge between C-22 and C-25 have been isolated, the stereochemistry of the side chain being 20S,22S,25S in cholegenin,[2] nuatigenin,[3] afurigenin,[4] funchaligenin[5] and androgenin A,[6] and 20S,22S,25R in androgenin B[6] and 25R-funchaligenin.[7] As no efficient syntheses of this type of compounds are known till now, we have prepared the 25S- and 25R-stereoisomers of (20S,22S)-furostan-22,25-epoxy-26-ol (IVa and IVb) from (25R)-5α-spirostan (I) by a simple method (overall yield 60%) which may easily be used to obtain other compounds of the same series.

Compound (I) was reduced with LAH/$AlCl_3$ in ether[8] to give (IIa) which via the tosylate (IIb) was transformed in (IIc). Elimination of the iodine with methanolic KOH gave the olefin (III), m.p. 82-83° (MeOH), $[\alpha]_D$ -8°, ν_{max}^{KBr} 3070, 1645 and 883 cm^{-1} (>C=CH_2); τ 5·30 (2H, m, $W_{1/2}$ 4 Hz, 2H-C_{26}), 8·29 (3H, s, $W_{1/2}$ 3 Hz, Me-C_{25}). Oxidation of (III) with OsO_4 in pyridine yielded an unseparable mixture of the isomer diols (IId) which was partially acetylated. The resulting monoacetates (IIe) could neither be separated and were therefore used without purification. Intramolecular cyclization of (IIe) (1 mmol) with $Pb(OAc)_4$ (3 mmol) and I_2 (1 mmol) in cyclohexane (10 ml) under reflux for 2 h gave a mixture of (IVc) and (IVd) which was saponified and separated by preparative column chromatography on silica gel (C_6H_6-EtOAc, 9:1), obtaining the desired compounds (IVa) and (IVb).

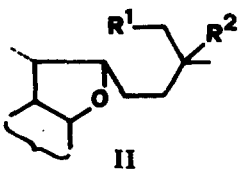
(IVa) has m.p. 156-158° (acetone), $[\alpha]_D$ -35°, $\nu_{max}^{CHCl_3}$ 3600 (OH), 1000, 975, 920 and 875 cm^{-1} (20S,22S,25S-furostan side chain); τ 6·58 (2H, m, $W_{1/2}$ 9 Hz, 2H-C_{26}), 8·86 (3H, s, Me-C_{25}). In the NMR spectrum of its acetate (IVc) [m.p. 210-212° (MeOH), $[\alpha]_D$ -46°] the chemical shift and shape of the signals corre-



I

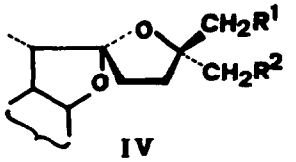


III



II

	R^1	R^2
a	OH	H
b	OTs	H
c	I	H
d	OH	OH
e	OAc	OH



IV

	R^1	R^2
a	H	OH
b	OH	H
c	H	OAc
d	OAc	H

sponding to the 2H-C_{26} (τ 5·82 and 6·05, AB, J 11 Hz) and Me-C_{25} (τ 8·84, s) coincide with those observed for 20S,22S,25S-epoxyfurostan sapogenins.[4-6]

(IVb), m.p. 170-173° (acetone), $[\alpha]_D$ -52°, $\nu_{max}^{CHCl_3}$ 3585 cm^{-1} (OH), τ 6·60 (2H, m, $W_{1/2}$ 4 Hz, 2H-C_{26}), 8·71 (3H, s, Me-C_{25}), gives the acetate (IVd), m.p. 191-193° (MeOH), $[\alpha]_D$ -41°, whose NMR signals for the 2H-C_{26} (τ 6·01 and 6·13, AB, J 11 Hz) and Me-C_{25} (τ 8·69, s) agree perfectly with those found for this type of furostan sapogenin acetates with 20S,22S,25R stereochemistry.[6,7]

All new compounds gave correct elemental analyses. Optical activities were determined in $CHCl_3$ and NMR spectra in $CDCl_3$ (60 MHz).

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