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Tetracyclic Triterpenes. Part 5.[1]

The Synthesis of Epimeric 9,11-Epoxides in the Tri-, Hexa-, and Octa-Norlanostane Series

Short Communication

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Lanosterol was converted by degradation of the side chain followed by transformations within rings B and C into a series of 9,11-epoxy-7-oxo-4,4,14α-trimethylsteroids.

(Keywords: Stereochemistry of epoxidation; Steroidal 9,11-epoxides; 4,4,14α-Trimethylsteroids)

Tetrazyklische Triterpene. 5. Mitt.[1] Synthese von epimeren 9,11-Epoxiden in der Tri-, Hexa-, und Octa-Norlanostan-Reihe (Kurze Mitteilung)

Lanosterin wurde durch Abbau der Seitenkette und nachfolgende Transformationen innerhalb der Ringe B und C in die 9,11-Epoxy-7-oxo-4,4,14α-trimethylsteroidreihe umgewandelt.

In connection with synthetic efforts toward 19(10 → 9β) abeo compounds[2] we required 9,11-epoxy-7-oxo compounds with the lanostane-typ skeleton containing a partially degraded side chain. Introduction of the $\Delta^{9(11)}$-7-oxo moiety into the lanostane molecule has been described[3–6] although discrepancies exist both to the structure and to yield of products, and these seem to depend strongly on conditions of a particular reaction. Epoxidation of 3β-acetoxy-5α-lanost-9(11)-en-7-one has recently been published[7].

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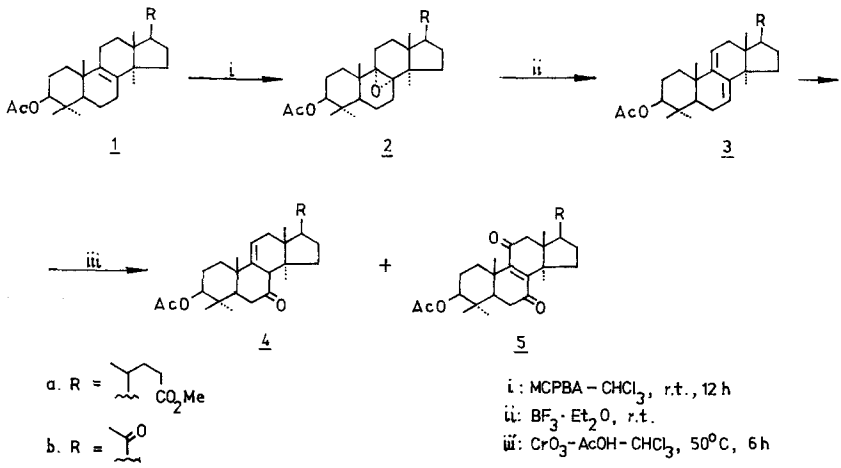
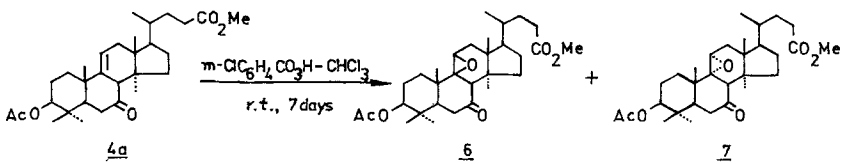
Scheme 1



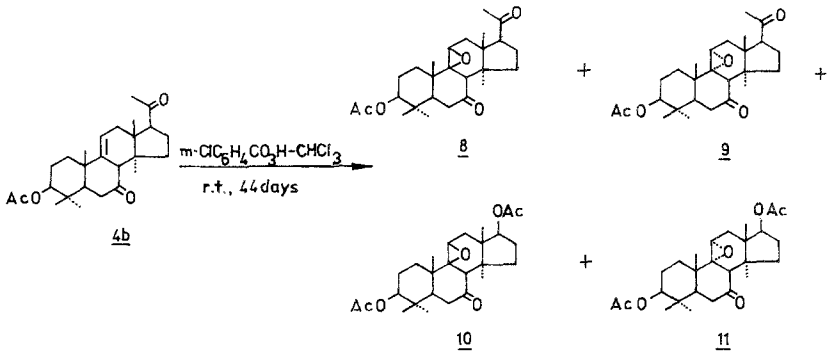
We report now the synthesis of steroidal 4,4,14α-trimethyl-7-oxo-9,11-epoxides with the side chain of various length.

Olefins **1 a** and **1 b** were obtained if the side chain of lanosterol was degraded according to the described conditions[8, 9]. These olefins were transformed (Scheme 1) to epoxides **2 a** and **2 b**, which gave dienes **3 a** and **3 b** upon treatment with acid. Oxidation of the dienes **3** with chromium trioxide in acetic acid—chloroform mixture[5] was an unreproducable reaction. In all cases the 8β-7-oxo-9(11)-olefins **4** and enediones **5** were the main products, the yields and ratios however varied considerably. In optimal experiments compounds **4 a** and **5 a** were obtained in 40 and 39% yield, while **4 b** and **5 b** were obtained in 22 and 48% yield, respectively.

Scheme 2



Scheme 3



The enone **4a** slowly reacted with peracid (Scheme 2) giving two isomeric epoxides **6** and **7** with 65 and 20% yield, respectively. Epoxidation of the enone **4b** was a very slow reaction (Scheme 3), probably as a result of intramolecular inhibition exerted by carbonyl groups at C-7 and C-20. This result confirmed our previous observations[7]. From the complex mixture of reaction products five pure compounds were isolated by combining crystallization and preparative layer chromatography. Epoxides **8** and **9** were obtained with 33 and 14%, respectively. Two other epoxides **10** and **11** (10 and 7% yield, respectively) resulted from epoxidation of the 9,11-double bond and simultaneous *Bayer-Villiger* oxidation of the C-20 carbonyl group. Isolated were also the substrate **4b** (5%) and two minor products of unidentified structure (total yield about 6%).

Both β-keto olefins **4a** and **4b** gave epoxides resulting from predominant attack of the peracid from the β direction. These reactions are new examples of epoxidation of β-keto olefins confirming the recently proposed rule[7].

Structures of all new compounds were confirmed by their spectral properties.

Spectral data (the analytical values for C, H were in all cases in agreement with the proposed structures; for instruments and conditions see Ref.[7])

4a: Mp. 175–177 °C (from *Me*OH).
NMR (δ): 5.42 (q, *J* 3 Hz, $w_{1/2}$ 8 Hz, 11-H), 4.50 (m, $w_{1/2}$ 17 Hz, 3α-H), 3.67 (s, 24-CO_2CH_3), 2.89 (br d, $w_{1/2}$ 8 Hz, 8β-H), 2.48 (d, *J* 2 Hz, 6-H), 2.33 (s, 6-H), 2.05 (s, 3β-O*Ac*), 1.12, 0.94, 0.82, 0.76, and 0.67 (methyl groups).

IR (ν_{max}): 1,725, 1,700 sh, and 1,255 cm^{-1}.
CD ($\Delta\varepsilon$): —0.53 (298 nm).
MS (*m/z*): 486 (M^+).

4b: Mp. 254–256 °C (from *Me*OH).
NMR (δ): 5.47 (m, $w_{1/2}$ 10 Hz, 11-H), 4.49 (m, $w_{1/2}$ 17 Hz, 3α-H), 2.85 (m, $w_{1/2}$ 9 Hz, 8β- and 17α-H), 2.49 (br s, 6-H), 2.35 (s, 6-H), 2.12 (s, 21-CH_3), 2.05 (s, 3β-O*Ac*), 1.13, 0.92, 0.84, and 0.59 (methyl groups).
IR (ν_{max}): 1,725, 1,705, and 1,255 cm^{-1}.
CD ($\Delta\varepsilon$): + 2.31 (290 nm).
MS (*m/z*): 414 (M^+).

6: Mp. 219–221 °C (from *Me*OH).
NMR (δ): 4.54 (m, $w_{1/2}$ 18 Hz, 3α-H), 3.64 (s, 24-CO_2CH_3), 3.60 (br s, 11α-H), 2.82 (s, 8β-H), 2.54 (d, *J* 4 Hz, 6-H), 2.38 (s, 6-H), 2.03 (s, 3β-O*Ac*), 0.98, 0.96, 0.88, and 0.85 (methyl groups).
IR (ν_{max}): 1,725, 1,695, and 1,250 cm^{-1}.
CD ($\Delta\varepsilon$): + 1.74 (303 nm).
MS (*m/z*): 502 (M^+).

7: Mp. 193–195 °C (from *Me*OH).
NMR (δ): 4.46 (m, $w_{1/2}$ 18 Hz, 3α-H), 3.62 (s, 24-CO_2CH_3), 3.13 (d, *J* 5 Hz, 11β-H), 2.80 (s, 8β-H), 2.49 (s, 6-H), 2.34 (d *J* 2 Hz, 6-H), 2.03 (s, 3β-O*Ac*), 1.31, 1.00, 0.87, 0.82, and 0.75 (methyl groups).
IR (ν_{max}): 1,725 and 1,255 cm^{-1}.
CD ($\Delta\varepsilon$): —0.60 (297 nm).
MS (*m/z*): 502 (M^+).

8: Mp. 288–290 °C (from $CHCl_3$-*Me*OH).
NMR (δ): 4.56 (m, $w_{1/2}$ 17 Hz, 3α-H), 3.70 (br s, $w_{1/2}$ 6 Hz, 11α-H), 2.81 (s, 8β-H), 2.57 (d, *J* 3 Hz, 6-H), 2.40 (s, 6-H), 2.14 (s, 21-CH_3), 2.08 (s, 3β-O*Ac*), 1.01, 0.97, 0.94, 0.87, and 0.84 (methyl groups).
IR (ν_{max}): 1,725, 1,705, and 1,250 cm^{-1}.
CD ($\Delta\varepsilon$): + 4.04 (293 nm).
MS (*m/z*): 430 (M^+).

9: Mp. 258–260 °C (from $CHCl_3$-*Me*OH).
NMR (δ): 4.50 (m, $w_{1/2}$ 18 Hz, 3α-H), 3.24 (d, *J* 6 Hz, 11β-H), 2.84 (s, 8β-H), 2.55 (s, 6-H), 2.40 (d, *J* 3 Hz, 6-H), 2.09 (s 21-CH_3), 2.04 (s, 3β-O*Ac*), 1.35, 1.12, 0.90, 0.87, and 0.76 (methyl groups).
IR (ν_{max}): 1,725 sh, 1,705, and 1,260 cm^{-1}.
CD ($\Delta\varepsilon$): + 1.81 (290 nm).
MS (*m/z*): 430 (M^+).

10: Mp. 234–236 °C (from *Me*OH).
NMR (δ): 5.01 (m, $w_{1/2}$ 16 Hz, 17α-H), 4.47 (m, $w_{1/2}$ 17 Hz, 3α-H), 3.67 (br s, $w_{1/2}$ 4.5 Hz, 11α-H), 2.84 (s, 8β-H), 2.58 (d, *J* 4 Hz, 6-H), 2.42 (s, 6-H), 2.09 and 2.07 (two s, 3β- and 17β-O*Ac*), 1.04, 1.00, 0.97, and 0.90 (methyl groups).
IR (ν_{max}): 1,725, 1,700, and 1,255 cm^{-1}.
CD ($\Delta\varepsilon$): + 1.66 (303 nm).
MS (*m/z*): 446 (M^+).

11: Mp. 230–232 °C (from *Me*OH).
NMR (δ): 4.98 (m, $w_{1/2}$ 16 Hz, 17α-H), 4.48 (m, $w_{1/2}$ 18 Hz, 3α-H), 3.18 (d,

J 6 Hz, 11β-H), 2.88 (s, 8β-H), 2.52 (s, 6-H), 2.39 (d, J 3 Hz, 6-H), 2.03 (s, 3β- and 17β-O*Ac*), 1.35, 1.10, 0.91, and 0.86 (methyl groups).
IR (ν_{max}): 1,725 and 1,255 cm^{-1}.
CD ($\Delta\varepsilon$): —0.41 (298 nm).
MS (m/z): 446 (M^+).

References

[1] Part IV. *Paryzek, Z., Wydra, R.*, Bull. Acad. Polon. Sci., Ser. sci. chim. **26**, 591 (1978).
[2] *Paryzek, Z.*, J. Chem. Soc. Perkin I **1979**, 1222.
[3] *Cavalla, J. F., McGhie, J. F.*, J. Chem. Soc. **1951**, 744.
[4] *Briggs, L. H., Bartley, J. P., Rutledge, P. S.*, J. Chem. Soc. Perkin I **1972**, 581.
[5] *Lassak, E. V., Pinhey, J. T., Simes, J. J. H.*, Australian J. Chem. **26**, 1051 (1973).
[6] *Elks, J., Evans, R. M., Long, A. G., Thomas, G. H.*, J. Chem. Soc. **1954**, 451.
[7] *Paryzek, Z.*, J. Chem. Soc. Perkin I **1978**, 329.
[8] *Narula, A. S., Dev, S.*, Tetrahedron **27**, 1119 (1971).
[9] *Kreiser, W., Urlich, W.*, Ann. **1976**, 1199.