

Tetracyclic Triterpenes. Part 5.¹
**The Synthesis of Epimeric 9,11-Epoxides in the Tri-, Hexa-,
and Octa-Norlanostane Series**

Short Communication

Zdzisław Paryzek* and **Roman Wydra**

Institute of Chemistry, A. Mickiewicz University,
60-780 Poznań, Poland

(Received 6 August 1980. Accepted 29 August 1980)

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-4,4,14 α -trimethylsteroids.

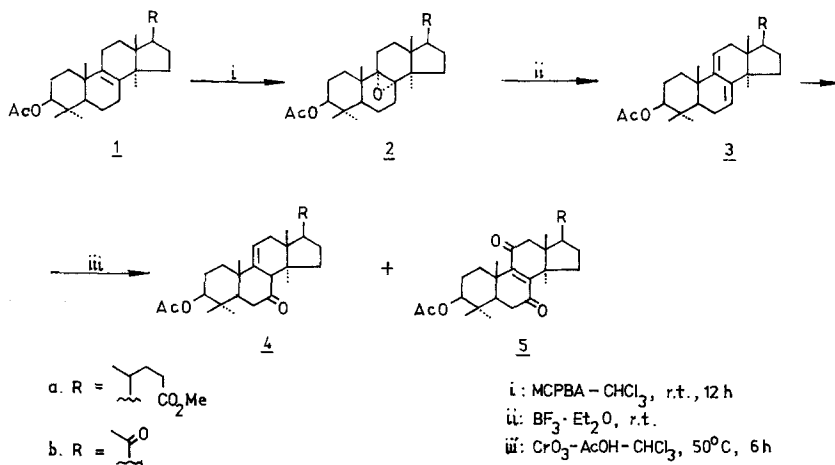
(Keywords: Stereochemistry of epoxidation; Steroidal 9,11-epoxides; 4,4,14 α -Trimethylsteroids)

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-4,4,14 α -trimethylsteroidreihe umgewandelt.

In connection with synthetic efforts toward 19(10 $\rightarrow$ 9 β) abeo compounds² we required 9,11-epoxy-7-oxo compounds with the lanostane-type skeleton containing a partially degraded side chain. Introduction of the $\Delta^{9(11)}$ -7-oxo moiety into the lanostane molecule has been described³⁻⁶ 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 3 β -acetoxy-5 α -lanost-9(11)-en-7-one has recently been published⁷.

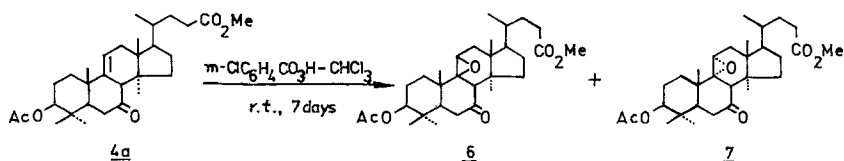
Scheme 1



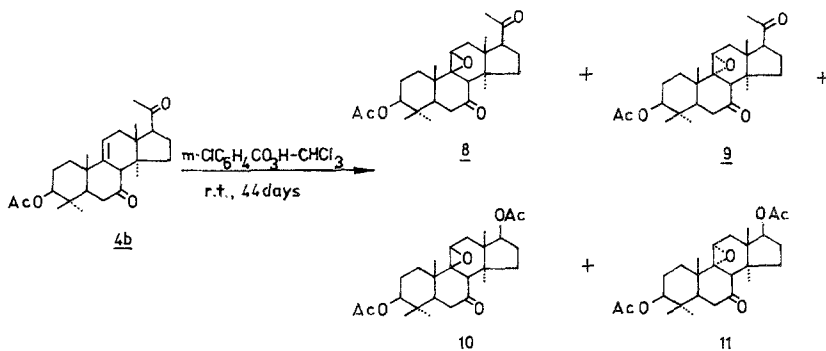
We report now the synthesis of steroidal 4,4,14 α -trimethyl-7-oxo-9,11-epoxides with the side chain of various length.

Olefins **1a** and **1b** 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 **2a** and **2b**, which gave dienes **3a** and **3b** upon treatment with acid. Oxidation of the dienes **3** with chromium trioxide in acetic acid—chloroform mixture⁵ was an unreproducible reaction. In all cases the 8 β -7-oxo-9(11)-olefins **4** and enediones **5** were the main products, the yields and ratios however varied considerably. In optimal experiments compounds **4a** and **5a** were obtained in 40 and 39% yield, while **4b** and **5b** 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 observations⁷. 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 rule⁷.

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 MeOH).

NMR (δ): 5.42 (q, J 3 Hz, $w_{1/2}$ 8 Hz, 11-H), 4.50 (m, $w_{1/2}$ 17 Hz, 3 α -H), 3.67 (s, 24-CO₂CH₃), 2.89 (br d, $w_{1/2}$ 8 Hz, 8 β -H), 2.48 (d, J 2 Hz, 6-H), 2.33 (s, 6-H), 2.05 (s, 3 β -OAc), 1.12, 0.94, 0.82, 0.76, and 0.67 (methyl groups).

IR ($\nu_{\max}$): 1,725, 1,700 sh, and 1,255 cm^{-1} .

CD ($\Delta\epsilon$): -0.53 (298 nm).

MS (m/z): 486 (M^+).

4b: Mp. 254–256 °C (from *MeOH*).

NMR (δ): 5.47 (m, $w_{1/2}$ 10 Hz, 11-H), 4.49 (m, $w_{1/2}$ 17 Hz, 3 α -H), 2.85 (m, $w_{1/2}$ 9 Hz, 8 β - and 17 α -H), 2.49 (br s, 6-H), 2.35 (s, 6-H), 2.12 (s, 21-CH₃), 2.05 (s, 3 β -OAc), 1.13, 0.92, 0.84, and 0.59 (methyl groups).

IR ($\nu_{\max}$): 1,725, 1,705, and 1,255 cm^{-1} .

CD ($\Delta\epsilon$): $+2.31$ (290 nm).

MS (m/z): 414 (M^+).

6: Mp. 219–221 °C (from *MeOH*).

NMR (δ): 4.54 (m, $w_{1/2}$ 18 Hz, 3 α -H), 3.64 (s, 24-CO₂CH₃), 3.60 (br s, 11 α -H), 2.82 (s, 8 β -H), 2.54 (d, J 4 Hz, 6-H), 2.38 (s, 6-H), 2.03 (s, 3 β -OAc), 0.98, 0.96, 0.88, and 0.85 (methyl groups).

IR ($\nu_{\max}$): 1,725, 1,695, and 1,250 cm^{-1} .

CD ($\Delta\epsilon$): $+1.74$ (303 nm).

MS (m/z): 502 (M^+).

7: Mp. 193–195 °C (from *MeOH*).

NMR (δ): 4.46 (m, $w_{1/2}$ 18 Hz, 3 α -H), 3.62 (s, 24-CO₂CH₃), 3.13 (d, J 5 Hz, 11 β -H), 2.80 (s, 8 β -H), 2.49 (s, 6-H), 2.34 (d J 2 Hz, 6-H), 2.03 (s, 3 β -OAc), 1.31, 1.00, 0.87, 0.82, and 0.75 (methyl groups).

IR ($\nu_{\max}$): 1,725 and 1,255 cm^{-1} .

CD ($\Delta\epsilon$): -0.60 (297 nm).

MS (m/z): 502 (M^+).

8: Mp. 288–290 °C (from CHCl₃-*MeOH*).

NMR (δ): 4.56 (m, $w_{1/2}$ 17 Hz, 3 α -H), 3.70 (br s, $w_{1/2}$ 6 Hz, 11 α -H), 2.81 (s, 8 β -H), 2.57 (d, J 3 Hz, 6-H), 2.40 (s, 6-H), 2.14 (s, 21-CH₃), 2.08 (s, 3 β -OAc), 1.01, 0.97, 0.94, 0.87, and 0.84 (methyl groups).

IR ($\nu_{\max}$): 1,725, 1,705, and 1,250 cm^{-1} .

CD ($\Delta\epsilon$): $+4.04$ (293 nm).

MS (m/z): 430 (M^+).

9: Mp. 258–260 °C (from CHCl₃-*MeOH*).

NMR (δ): 4.50 (m, $w_{1/2}$ 18 Hz, 3 α -H), 3.24 (d, J 6 Hz, 11 β -H), 2.84 (s, 8 β -H), 2.55 (s, 6-H), 2.40 (d, J 3 Hz, 6-H), 2.09 (s 21-CH₃), 2.04 (s, 3 β -OAc), 1.35, 1.12, 0.90, 0.87, and 0.76 (methyl groups).

IR ($\nu_{\max}$): 1,725 sh, 1,705, and 1,260 cm^{-1} .

CD ($\Delta\epsilon$): $+1.81$ (290 nm).

MS (m/z): 430 (M^+).

10: Mp. 234–236 °C (from *MeOH*).

NMR (δ): 5.01 (m, $w_{1/2}$ 16 Hz, 17 α -H), 4.47 (m, $w_{1/2}$ 17 Hz, 3 α -H), 3.67 (br s, $w_{1/2}$ 4.5 Hz, 11 α -H), 2.84 (s, 8 β -H), 2.58 (d, J 4 Hz, 6-H), 2.42 (s, 6-H), 2.09 and 2.07 (two s, 3 β - and 17 β -OAc), 1.04, 1.00, 0.97, and 0.90 (methyl groups).

IR ($\nu_{\max}$): 1,725, 1,700, and 1,255 cm^{-1} .

CD ($\Delta\epsilon$): $+1.66$ (303 nm).

MS (m/z): 446 (M^+).

11: Mp. 230–232 °C (from *MeOH*).

NMR (δ): 4.98 (m, $w_{1/2}$ 16 Hz, 17 α -H), 4.48 (m, $w_{1/2}$ 18 Hz, 3 α -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 -OAc), 1.35, 1.10, 0.91, and 0.86 (methyl groups).

IR ($\nu_{\max}$): 1,725 and 1,255 cm^{-1} .

CD ($\Delta\epsilon$): -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., Ulrich, W., Ann. **1976**, 1199.