

found 416.248; calc. for  $C_{32}H_{52}$ , 416.250;  $m/e$  416 ( $M^+$ , 58 %), 311 (14 %), 207 (72 %) and 104 (100 %). NMR: singlets at  $\delta=6.72$  (16 H) and  $\delta=2.85$  (16 H).

**Acknowledgements.** We thank prof. Martin Nilsson for his kind interest and the Swedish Natural Science Research Council for financial support.

1. Griffin, C. E. Martin, K. R. and Douglas, B. E. *J. Org. Chem.* 27 (1962) 1627.
2. Elix, J. A. *Aust. J. Chem.* 22 (1969) 1951.
3. Saikachi, H. and Muto, H. *Chem. Pharm. Bull.* 19 (1971) 959.
4. Tabushi, I., Yamada, H., Matsushita, K., Yoshida, Z., Kuroda, H. and Oda, R. *Tetrahedron* 28 (1972) 3381.
5. Errede, L. A., Gregorian, R. S. and Hoyt, J. M. *J. Amer. Chem. Soc.* 82 (1960) 5218.

Received November 8, 1974.

### Triterpenes. A Novel Acid Catalysed Double Bond Migration in $3\beta,28$ -Diacetoxy-lup-20(30)-ene (Betulin Diacetate)

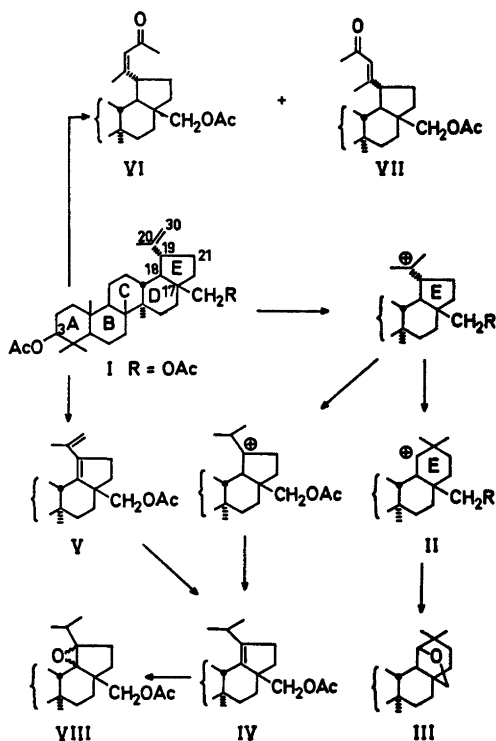
ELIAS SUOKAS and TAPIO HASE

Department of Chemistry, Helsinki University of Technology, SF-02150 Otaniemi, Finland

The acid catalysed rearrangement of  $\Delta^{20(30)}$ -derivatives in the lupane series has been reported<sup>1-3</sup> to proceed *via* the secondary carbocation (II). Subsequent reactions are highly dependent on the reaction conditions and on the nature of the function R at C-28. The common feature of the end products is the enlargement of the five-membered ring E to six-membered.

The acid catalysed rearrangement of betulin diacetate (I) has been performed by Vystrčil *et al.*<sup>3</sup> in  $H_2SO_4$ -AcOH-benzene mixture and by Pettit *et al.*<sup>3</sup> in HCl-EtOH- $CHCl_3$  mixture. Both reactions lead to the allobetulin ring system (III) with a six-membered ring E.

When we carried out the isomerisation of betulin diacetate (I) with HBr in AcOH- $Ac_2O$ -



benzene solution, another reaction pathway was observed. Instead of breaking the bond between C-19 and C-21, the hydrogen at C-19 was shifted, and the double bond migration product,  $\Delta^{18}$ -isomer (IV), was obtained. The  $\Delta^{18}$ -structure (IV) was confirmed by its identity (TLC, IR,  $^1H$  NMR, MS, m.p., mixed m.p.,  $[\alpha]_D$ ) with an authentic sample prepared by  $PtO_2$ -catalysed hydrogenation<sup>4</sup> of the mercuric acetate dehydrogenation product (V) of betulin diacetate (I). In addition, compounds (IV), obtained either by hydrogenation of diene (V) or by isomerisation of betulin diacetate (I), gave identical epoxides (VIII) with *m*-chlorobenzoic acid.

Increasing concentrations of both HBr and AcOH cause a more rapid reaction. Acetic anhydride addition gives a milder reaction but results in the formation of an *E/Z*-mixture of ketones (VI) and (VII), due to the addition of  $CH_3CO^+$  to the double bond of betulin diacetate (I) followed by loss of a proton. Below 10 % HBr the reaction may demand months, while above 14 % HBr and 40 % AcOH all the starting material has reacted in a few hours or less and increasing amounts of less polar side products are formed. These side products were also obtained, when the  $\Delta^{18}$ -isomer (IV) was treated with HBr in AcOH- $Ac_2O$ -benzene solution. The  $^1H$  NMR-spectrum of this mixture

lacks the protons of the  $-\text{CH}_2\text{OAc}$  side chain at C-17.

The isomerisation of betulin diacetate (I) with *p*-toluenesulfonic acid in  $\text{AcOH}\text{-Ac}_2\text{O}$ -benzene solution gave as main products the preparatively inseparable *E/Z*-mixture of ketones (VI) and (VII), and the  $\Delta^{18}$ -compound (IV).

**Experimental.** Melting points are uncorrected PMR spectra were recorded on a Varian A-60 spectrometer in  $\text{CDCl}_3$  and related to internal TMS, the IR spectra on a Perkin-Elmer 125 spectrometer using KBr pellets, mass spectra on a Perkin-Elmer 270B mass spectrometer, specific rotations in  $\text{CHCl}_3$  solution on a Perkin-Elmer 141 polarimeter, and elemental analyses with a F & M 185 CHN-analyser.

**Isomerisation of betulin diacetate (I) with HBr.** (a) Betulin diacetate (1.0 g) in benzene (29.4 g) was added to a mixture of  $\text{Ac}_2\text{O}$  (15.0 g),  $\text{AcOH}$  (15.5 g), and 36.5 % HBr in  $\text{AcOH}$  (24.8 g) (resulting in 10.5 % HBr and 36.5 %  $\text{AcOH}$ ) and allowed to stand for two weeks at room temperature. The reaction was followed on silica plates impregnated with 10 %  $\text{AgNO}_3$ . The mixture was washed with water and  $\text{NaHCO}_3$ -solution, dried and the solvent evaporated. Crystallisation from EtOH gave  $3\beta,28$ -diacetoxy-lup-18-ene (IV) (0.87 g), m.p.  $215^\circ\text{C}$ ,  $[\alpha]_{\text{D}} +16^\circ$  (c 1.0) (Ref. 4, m.p.  $211^\circ\text{C}$ ,  $[\alpha]_{\text{D}} +15^\circ$ ), mixed m.p. with authentic sample <sup>4</sup>  $215^\circ\text{C}$ .  $M^+$  526;  $\delta$  4.45 (1 H, m), 4.0 (2 H, br.s), 3.15 (1 H, m), 2.1–2.7 (4 H, m), 0.83–1.07 (group of 7 Me).

(b) Betulin diacetate (1.0 g) in benzene (36.5 g),  $\text{Ac}_2\text{O}$  (15.0 g),  $\text{AcOH}$  (8.0 g), and 36.5 % HBr in  $\text{AcOH}$  (32.5 g) (resulting in 12.8 % HBr and 30.3 %  $\text{AcOH}$ ) was treated as above for 18 h. Work up and chromatography [silica gel dry column and 1:3  $\text{CHCl}_3$ -petroleum ether (b.p.  $60-80^\circ\text{C}$ ) eluent] gave a mixture of less polar side products (0.2 g) and  $3\beta,28$ -diacetoxy-lup-18-ene (IV) (0.7 g).

(c) Betulin diacetate (1.0 g) in benzene (27 g),  $\text{Ac}_2\text{O}$  (25 g), 36.5 % HBr in  $\text{AcOH}$  (16.5 g) (resulting in 8.7 % HBr, 15.2 %  $\text{AcOH}$ , and 36 %  $\text{Ac}_2\text{O}$ ) was treated as above for one month. According to TLC, the reaction mixture contained almost equal amounts of betulin diacetate (I),  $3\beta,28$ -diacetoxy-lup-18-ene (IV), and  $3\beta,28$ -diacetoxy-30-acetyl-lup-20(30)-ene *E/Z* isomers (VI + VII) characterised below.

**Treatment of  $3\beta,28$ -diacetoxy-lup-18-ene (IV) with HBr.**  $3\beta,28$ -Diacetoxy-lup-18-ene (IV) (0.2 g) in benzene (6.7 g) was added to a mixture of  $\text{Ac}_2\text{O}$  (1.0 g),  $\text{AcOH}$  (5.0 g), and 36.5 % HBr in  $\text{AcOH}$  (8.7 g) (resulting in 14.5 % HBr and 49 %  $\text{AcOH}$ ) and kept for 7 h at room temperature and worked up. According to TLC, the complex mixture contained no starting material. The  $^1\text{H}$  NMR spectrum of this mixture of un-separated compounds lacks the protons of the  $-\text{CH}_2\text{OAc}$  side chain at C-17.

**Treatment of betulin diacetate (I) with TsOH.** Betulin diacetate (3.0 g) in benzene (30 g),

$\text{AcOH}$  (50 g),  $\text{Ac}_2\text{O}$  (10 g), and  $\text{TsOH}\cdot\text{H}_2\text{O}$  (3.0 g) was stirred for 4 days at  $60^\circ\text{C}$ . The mixture was treated with water and  $\text{NaHCO}_3$ -solution, dried and the solvent evaporated. Chromatography [silica gel dry column and 1:2  $\text{CHCl}_3$ -petroleum ether (b.p.  $60-80^\circ\text{C}$ ) eluent] gave  $3\beta,28$ -diacetoxy-lup-18-ene (IV) (0.6 g) with physical constants identical to those given above, and  $3\beta,28$ -diacetoxy-30-acetyl-lup-20(30)-ene (VI) and (VII) (1.2 g) as an inseparable mixture of (*E*)- and (*Z*)-isomers.  $M^+$  568;  $\lambda_{\text{max}}$  (EtOH) 244nm,  $\epsilon$  15 500;  $\nu$  1735, 1725, 1680, 1600;  $\delta$  6.15+6.0 (1 H), 4.7–3.6 (3 H, m), 2.5 (1 H, m), 2.13, 2.08, 2.04 [ $3 \times (3 \text{ H, s})$ ], 1.85 (3 H, br. s), 1.03, 0.96 [ $2 \times (3 \text{ H, s})$ ], 0.83 (9 H, s). (Found: C 75.61; H 9.96. Calc. for  $\text{C}_{38}\text{H}_{58}\text{O}_5$ : C 76.01; H 9.92).

**Epoxydation of  $3\beta,28$ -diacetoxy-lup-18-ene (IV).**  $3\beta,28$ -Diacetoxy-lup-18-ene (IV) (1.0 g), either from the isomerisation of betulin diacetate (I) or from the hydrogenation of diene (V), was stirred for 1 h in  $\text{CHCl}_3$  (30 ml) with *m*-chloroperbenzoic acid (0.6 g) and  $\text{Na}_2\text{CO}_3$  (1.0 g). The mixtures were treated with water,  $\text{NaHSO}_3$ , and  $\text{NaHCO}_3$ -solutions, dried and the solvent evaporated. Crystallisations from EtOH gave  $3\beta,28$ -diacetoxy-18 $\xi$ ,19 $\xi$ -epoxy-lupane (VIII) (0.8 g), m.p.  $222^\circ\text{C}$ ,  $[\alpha]_{\text{D}} +25.5^\circ$  (c 1.7);  $M^+$  542;  $\delta$  4.53 (1 H, d 11 Hz), 4.42 (1 H, m), 3.88 (1 H, d 11 Hz), 1.12–1.08 (4 Me groups), 0.89–0.83 (3 Me groups). (Found: C 75.39; H 10.09. Calc. for  $\text{C}_{34}\text{H}_{54}\text{O}_5$ : C 75.23; H 10.03).

1. de Mayo, P. *The Higher Terpenoids*, Interscience, New York 1959.
2. Vystržil, A., Stejskalová-Vondrášková, E. and Černý, J. *Collect. Czech. Chem. Commun.* 24 (1959) 3279.
3. Pettit, G. R., Green, B. and Bowyer, W. J. *J. Org. Chem.* 26 (1961) 2879.
4. Suokas, E. and Hase, T. *Acta Chem. Scand.* B 23 (1974) 793.

Received October 30, 1974.