Triterpenes. The HBr Catalysed Rearrangement of Lupenyl Acetate and Stereochemistry of the Epoxidation of the Products

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The acid catalysed rearrangement of lupenyl acetate (1a) is known to proceed via the skeletal rearranged carbocation 2. We reported previously an HBr catalysed rearrangement of betulin diacetate (1b), giving 3b, where the carbon skeleton is not altered. It was recently claimed that lupenyl acetate (1a) does not compound, identical with 4, is obtained in both cases. Compound 4 from these reactions gave the epoxide 5. X-Ray crystallographic measurements gave the 19α,19β-epoxy-19α(H)-structure 5 for this epoxide. This establishes the 19α(H)-structures for 4 and 6.

The epoxidation of 3a with m-chloroperbenzoic acid gives the β-epoxide 9a, also obtained from the corresponding betulin derivative 9b of known β-epoxy structure. Thus the isomeric epoxide obtained from 3a with ozone has α-epoxy structure 10a.

give 3a on HBr treatment. However, we have found that 3a is formed, when 1a is treated with HBr in Ac₂O-AcOH-benzene solution and can be isolated, but is also readily isomerised to 4.∗

Compound 3a has been reported previously as a component of the preparatively unseparable mixture of products from the PtO₂ catalysed hydrogenation of 5. We have now isolated and characterised 3a along with the tetrahydro derivative 12 from this mixture. Compound 3a has also been reported to occur in Nature but the reported physical data differ from those now obtained for 3a. The natural product is probably correctly formulated 3a but impure, according to the close similarity of the mass spectra.

When the diene 5 is first isomerised to the mixture of compounds 6* and 7, and these products hydrogenated, the same dihydro compounds identical with 4, is obtained in both cases. Compound 4 from these reactions gave the epoxide 5. X-Ray crystallographic measurements gave the 19α,19β-epoxy-19α(H)-structure 5 for this epoxide. This establishes the 19α(H)-structures for 4 and 6.

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Both epoxides 9a and 10a give the baccharane derivative 11 on a BF₃ treatment in analogy with the corresponding betulin epoxides 9b and 10b.∗

Experimental. Melting points are uncorrected.

1H NMR spectra were recorded on a Jeol JNM-PMX 60 spectrometer, IR spectra on a Perkin-Elmer 125 spectrometer using KBr pellets, mass spectra on a Perkin-Elmer 270 B mass spectrometer, specific rotations in CHCl₃ solution on a Perkin-Elmer 141 polarimeter.

* For the stereostructure at C-19 see below.

Isomerisation of lupenyl acetate (1a). (a) Lupenyl acetate (1a) (0.5 g) in benzene (17 g), Ac₂O (7 g), and 36 % HBr in AcOH (13 g) was allowed to stand at ambient temperature for 50 h. Work up and chromatography on 10 % AgNO₃ impregnated silica plates (eluent: CHCl₃–light petroleum b.p. 60–80 °C, 2:1) gave 3β-acetoxy-19α(H)-lup-13(18)-ene (4) (0.2 g), m.p. (EtOH) 177 °C, [α]D + 21° (c 0.82). (Ref. 6, m.p. 184–185 °C in vacuo, [α]D + 20.7°). v 1730, 1235. δ (CCL₄) 4.4 (1 H, m), 3.7–2.1 (3 H, m), 1.97 (3 H, s), 1.1–0.83 (8 methyls). m/e 468 (M⁺), 205 (100 %). (b) Lupenyl acetate (1a) (0.5 g) in benzene (17 g), Ac₂O (7 g), and 36 % HBr in AcOH (11 g) was allowed to stand at room temperature for ten days. The reaction is sensitive to the concentration of HBr. Work up and chromatography on 10 % AgNO₃ impregnated silica plates gave 3β-acetoxy-19α(H)-lup-13(18)-ene (4) (0.1 g) as above and 3β-acetoxy-lup-13(18)-ene (3a) (0.1 g), m.p. (EtOH) 228 °C, [α]D + 18° (c 1.0). (Ref. 5, m.p. 210–212 °C, [α]D + 6°). v 1730, 1245. δ (CCL₄) 4.4 (1 H, m), 3.05 (1 H, sept. J 7 Hz), 2.6–2.0 (4 H, m), 1.96 (3 H, s), 1.1–0.8 (8 methyls). m/e (% rel. int.) 468 (32, M⁺), 204 (94), 189 (100), 177 (64). This compound was identical (m.p., mixed m.p., [α]D, TLC, MS, IR, ¹H NMR) with the compound obtained from the hydrogenation of diene δ (see below).

Isomerisation of 3β-acetoxy-lup-18-ene (3a). 3β-Acetoxy-lup-18-ene (3a) was treated with lupenyl acetate (1a) above with an HBr–Ac₂O–AcOH–benzene mixture. Work up gave 3β-acetoxy-19α(H)-lup-13(18)-ene (4), identical with the compound obtained above. Hydrogenation of 3β-acetoxy-lup-18,20(29)-diene (5). 3β-Acetoxy-lup-18,20(29)-diene (5) (1 g) was hydrogenated over PtO₂ according to Ref. 4. Chromatography on 10 % AgNO₃ impregnated silica plates (eluent: CHCl₃–light petroleum b.p. 60–80 °C, 3:1) gave 3β-acetoxy-18(18)H,19α(H)-lupane② (12) (0.25 g), m.p. (EtOH) 271 °C, [α]D + 21° (c 1.0). (Ref. 6, m.p. 272–274 °C, [α]D + 24°) and 3β-acetoxy-lup-18-ene (3a) (0.63 g) identical with the compound from the isomerisation of lupenyl acetate (1a). Epoxidation of 3β-acetoxy-19α(H)-lup-13(18)-ene (4). 3β-Acetoxy-19α(H)-lup-13(18)-ene (4) (0.2 g) from the isomerisation of 1a, or from the hydrogenation of the dienes δ and 7 was stirred with NaHCO₃ (0.5 g) and m-chloroperbenzoic acid (0.15 g) in CH₂Cl₂ (10 ml) for 30 min. The mixtures were washed with water and Na₂SO₄ solution, dried and chromatographed on silica plates (CHCl₃ eluent). Each reaction gave the same product 3β-acetoxy-13α,18α-epoxy-19α(H)-lupane (9) (80–100 mg), m.p. (EtOH) 194 °C, [α]D + 25° (c 0.92). v 1730, 1245, 1095, 1010, 980, 870. δ (CCL₄) 4.45 (1 H, m), 1.98 (3 H, s), 1.16–0.84 (8 methyls). m/e 484 (M⁺), 140 (100 %).

3β-Acetoxy-18β,19β-epoxy-lupane (9a). (a) 3β-Acetoxy-lup-18-ene (3a) was epoxidised with m-chloroperbenzoic acid as described above to give 3β-acetoxy-18β,19β-epoxy-lupane (9a), m.p. (EtOH) 235 °C, [α]D + 37° (c 1.0). (Ref. 6, m.p. 236–238 °C, [α]D + 32°).

(b) 3β,28-Diacehtoxy-18β,19β-epoxy-lupane (9b) (1.0 g) and KOH (0.12 g) in EtOH (100 ml) were refluxed for 1 h. Work up and chromatography gave as the main product 3β-acetoxy-28-hydroxy-18β,19β-epoxy-lupane (9c) (0.52 g), m.p. (EtOH) 246 °C, [α]D + 38° (c 1.0).

Hydroxyacetate 9c (0.2 g), p-toluenesulfonyl chloride (0.4 g), and pyridine (3 g) were stirred overnight and worked up. Chromatography on a silica plate gave 3β-acetoxy-28-tosyloxy-18β,19β-epoxy-lupane (9d) (0.14 g), m.p. (EtOH) 160 °C (decomp.), [α]D + 12° (c 1.1). δ (CCL₄) 7.78 and 7.30 (2 H, d, J 8 Hz), 4.4 (1 H, m), 4.3 and 3.77 (2 H, d, J 9 Hz), 2.45 (3 H, s), 2.05 (3 H, s), 1.1–0.8 (8 methyls).

Tosylate 9d (100 mg), Na₂[B]₂ (220 mg), Zn (300 mg), [Me₂N]PO (2 ml), and MeOCH₂CH₂OMe (2 ml) were kept at 80 °C overnight (cf. Ref. 11). Work up and crystallisation from EtOH gave 3β-acetoxy-18β,19β-epoxy-lupane (9a), identical (m.p., mixed m.p., [α]D, IR, ¹H NMR, TLC) with the compound above.

3β-Acetoxy-18α,19α-epoxy-lupane (10a). 3β-Acetoxy-lup-18-ene (3a) (200 mg) was ozonised in CH₂Cl₂ (20 ml) at −75 °C until the solution remained faintly blue. Excess ozone was driven off with a nitrogen stream and the solution allowed to reach room temperature. Chromatography on a silica plate (CHCl₃ eluent) gave 3β-acetoxy-18α,19α-epoxy-lupane (10a) (150 mg), m.p. (MeOH) 242 °C, [α]D + 4° (c 0.8). (Ref. 9, m.p. 238 °C, [α]D + 4°). v 1730, 1240, 1150, 1100, 1023, 1000, 980. δ (CCL₄) 4.5 (1 H, m), 2.3–2.0 (4 H, m), 2.05 (3 H, s), 1.1–0.85 (8 methyls). M⁺ 484.

Rearrangement of 3β-acetoxy-18,19-epoxy-lupanes (9a) and (10a). Both 3β-acetoxy-18α,19α-epoxy-lupane (10a) and 18β,19β-epoxy isomer (9a) (0.2 g) were treated with BF₃ etherate (5 drops) in dry benzene (3 ml) for 5 min. Work up and chromatography on silica plates (CHCl₃ eluent) gave 3β-acetoxy-18,19-seco-lup-13(18)-ene-19-one (11) (yields 80–95 %), m.p. (EtOH) 130 °C, [α]D − 5° (c 0.72). v 1725, 1710, 1245. δ (CCL₄) 4.96 (1 H, br. s), 4.53 (1 H, m), 2.9–2.0 (7 H, m), 2.04 (3 H, s), 1.16–0.85 (8 methyls). M⁺ 484.

The Formation of Barbaralone Derivatives from the Reaction between Triazolinediones and Cyclocatetraene-iron Tricarbonyl

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Coordination of a polyene to a metal center can lead to drastic modification of its reactivity. Thus cyclocatetraene (COT) cycloadds to tetracyanoethylene (TCNE) via its [4.2.0]-bicyclic valence isomer in classic Diels-Alder fashion, while the iron tricarbonyl complex I yields a 1,3-addition product containing an Fe-C σ bond. The even more powerful dienophile 4-phenyl-1,2,4-triazoline-3,5-dione (2, R = Ph, PTAD) is reported to combine with I in low yield at 25 °C to give the 1,4-adduct 3. Apart from the Fe(CO)₅ moiety the reaction appears to be completely analogous to that between PTAD and COT under ambient conditions. We have reinvestigated the transformation with both MTAD and PTAD (2, R = CH₃, Ph) and have found that the barbaralone derivative 4 is formed along with complex 3. The result implies carbonyl insertion into an intermediate 1,3-addition product.

Mixing of equimolar quantities of MTAD and I (in CH₂Cl₂, 25 °C, 30 min) followed by chromatography (silica gel, ethyl acetate) leads to the isolation of three compounds. Besides unreacted I (22%), 3 (R = CH₃, 34%, m.p. 185 °C, dec.) the barbaralone derivative 4 was obtained (R = CH₃, 16%, m.p. 214–215 °C). The latter gave a satisfactory elemental analysis and molecular weight (MS). The presence of the keto group was substantiated by derivatization (2,4-DNP) and IR (CHCl₃): 1750 (m), 1772 (s) and 1714 (s) cm⁻¹ (C=O and N-CO-N). 1H NMR spectroscopy (90 MHz, CDCl₃) established the symmetry and structure of 4 by revealing six signals readily analyzable by spin decoupling. The absorption at lowest field is an AB quartet showing additional fine structure (δ 6.41 (2 H, H-3 and H-5) 5.99 (2 H, H-2 and H-6); J₅₆ = J₄₅ = 9 Hz; J₄₅ = J₃₄ = 4 Hz; J₃₄ = J₃₅ = 6.5 Hz; J₃₅ = J₃₆ = 1 Hz). The bridgehead protons α to nitrogen resonate at δ 5.11 (2 H, H-1 and H-7, dd, J₅₆ = J₅₇ = 8 Hz). At high field the remaining absorption consists of two doublets of triplets centered at δ 3.68 (1 H, H-8, J₄₅ = 2 Hz) and 3.39 (1 H, H-4) and a singlet at δ 3.08 (N-CH₃). The broad band decoupled ¹³C NMR spectrum (22.03 MHz, CDCl₃) is in complete agreement with structure 4 exhibiting only eight peaks:

δ 201.1, 156.2, 134.5, 126.2, 61.7, 50.9, 45.3 and 25.8.

The corresponding reaction with PTAD yielded I (22%), the previously characterized 3 (R = Ph, 33%, m.p. 156–157 °C; lit. m.p. 155 °C) and the barbaralone system 4 (R = Ph, 14%, m.p. 225–226 °C). The N-phenylbarbaralone was characterized as above, its spectro-


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