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BIOGENETIC-LIKE BACKBONE REARRANGEMENT. A FORMATION OF D:C-FRIEDOBACCHAR-9(11)-ENE-3β,18β-DIYL DIACETATE FROM 13β,18β-EPOXYBACCHARAN-3β-YL ACETATE

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13β,18β-Epoxybaccharan-3β-yl acetate was treated with $BF_3 \cdot Et_2O$ in acetic anhydride to yield a complex mixture, in which the presence of D:C-friedobacchar-9(11)-ene-3β,18β-diyl diacetate (2) was shown; the product (2) was converted into 18-oxo-D:C-friedobacchar-9(11)-en-3β-yl acetate, the structure of which was confirmed by X-ray diffraction analysis.

On treatment with acid, protostene-type triterpenes undergo a sequential shift of methyl groups and hydrides in biogenetic direction to afford lanostene derivatives,[1,2] while reactions of oleanene-, lupene-, and baccharene-type triterpenes with acid do not give friedo-type triterpenes which would be produced by the biogenetic-like backbone rearrangement. Acid-catalyzed backbone rearrangement of these friedo-type triterpenes[1a,3,4] as well as migrated hopenes[5] proceed generally in the opposite direction from the biogenesis.

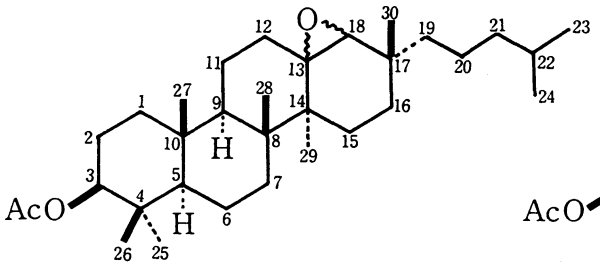
In order to bring about the energetically unfavorable rearrangements of these triterpenes, the reaction requires coupling to a free-energy releasing reaction which provides the thermodynamic driving force. Several investigations on these rearrangements have been reported so far;[1a,6] in these reactions, however, only one methyl group shifted towards biogenetic-like direction and a concomitant multigroup rearrangement did not occur.

As a continuation of our work on backbone rearrangement of triterpene epoxides,[4] we examined a reaction of 13β,18β-epoxybaccharan-3β-yl acetate (1)

with boron trifluoride etherate in acetic anhydride[6c] aiming at an occurrence of the biogenetic-like rearrangement. This communication describes a formation of D:C-friedobacchar-9(11)-ene-3β,18β-diyl diacetate (2), a biogenetic-like backbone rearranged product through a sequential shift of two methyl groups and one hydride, and structure elucidation of 18-oxo-D:C-friedobacchar-9(11)-en-3β-yl acetate (3) derived from 2 by X-ray diffraction analysis.

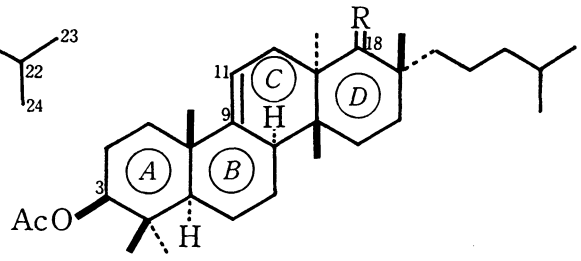
21-Oxobacchar-13(18)-en-3β-yl acetate (4)[7] prepared from lupeol was subjected to Huang-Minlon reduction followed by acetylation to afford bacchar-13(18)-en-3β-yl acetate (5). The 13(18)-ene acetate (5) was treated with hydrogen chloride in chloroform overnight to yield no backbone rearranged products, but an equilibrium mixture of 5 and bacchar-12-en-3β-yl acetate (6).[8]

Epoxidation of 5 with m-chloroperbenzoic acid in dichloromethane gave a 1:9 mixture of epoxides (7 and 1), which was separated by silica gel chromatography. The major epoxide (1)[9] exhibited a singlet signal due to $C_{(18)}$-H at δ 2.65, while the minor one (7)[10] at δ 2.3. These observations together with a preferential attack of the reagent from β-side of 5 lead to the conclusion that the major epoxide (1) should be 13β,18β-epoxide.[11]



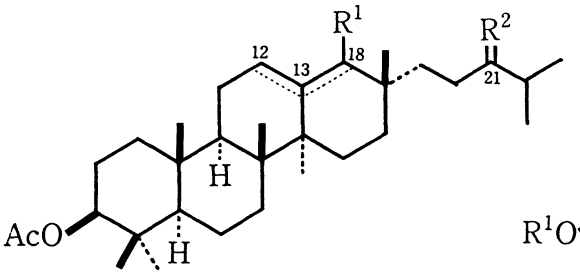
1 13β,18β-epoxide

7 13α,18α-epoxide



2 R = α-H, β-OAc

3 R = O

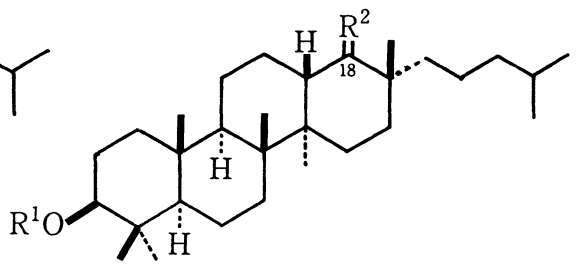


4 R^1 = H; R^2 = O; $\Delta^{13(18)}$

5 R^1 = H; R^2 = H_2; $\Delta^{13(18)}$

6 R^1 = H; R^2 = H_2; Δ^{12}

10 R^1 = OAc; R^2 = H_2; $\Delta^{13(18)}$



8 R^1 = H; R^2 = α-OH, β-H

9 R^1 = Ac; R^2 = O

13β,18β-Epoxybaccharan-3β-yl acetate (1; 84 mg) in acetic anhydride (17 ml) was treated with boron trifluoride etherate (0.8 ml) at 0 °C for 2 h and the reaction was stopped by pouring into saturated sodium hydrogencarbonate solution. The reaction mixture of diacetates, after the usual work-up, was treated with lithium aluminium hydride to give a mixture of diols, which was subjected to separation by HPLC.[12] Two components (ca. 28 mg, R_t 21.3 min and ca. 4.2 mg, R_t 25.0 min) were isolated from the complex mixture. One component with R_t 21.3 min was identified to be baccharane-3β,18α-diol (8)[13] by comparison with an authentic sample prepared from 18-oxobaccharan-3β-yl acetate (9).[7] Therefore the original diacetate is deduced to be bacchar-13(18)-ene-3β,18-diyl diacetate (10).[13] The other diol with R_t 25.0 min was subjected to monoacetylation followed by Jones oxidation to give keto acetate (3),[14] which was shown to be a trisubstituted olefin by the ^{1}H NMR spectrum (δ 5.38, m). Since, however, further information on the skeletal feature of the keto acetate (3) could be obtained by neither NMR nor mass spectrum, X-ray diffraction analysis of 3 was carried out. The single crystal of 3, crystallized from methanol solution, belongs to a monoclinic space group $P2_1$ with the cell parameters of a=17.273(9), b=11.981(5), and c=7.323(3) Å, β=99.13(3)°, z=2, and D_c=1.08 g·cm^{-3}. The current R-value is 5.6%. Figure 1 shows a computer-generated perspective drawing of 3. Thus the structure of the keto acetate (3) being shown to be 18-oxo-D:C-friedobacchar-9(11)-en-3β-yl acetate, the original diacetate formed in the BF_3·Et_2O-catalyzed rearrangement is formulated as D:C-friedobacchar-9(11)-ene-3β,18β-diyl diacetate (2).

The formation of diacetate (2) constitutes the first example of energetically unfavorable rearrangement of triterpenes involving a sequential shift of the 14α-Me, 8β-Me, and 9α-H to 13α-Me, 14β-Me, and 8α-H, respectively. Further investigation on the structures of the reaction products other than 2 and 10 is now in progress.

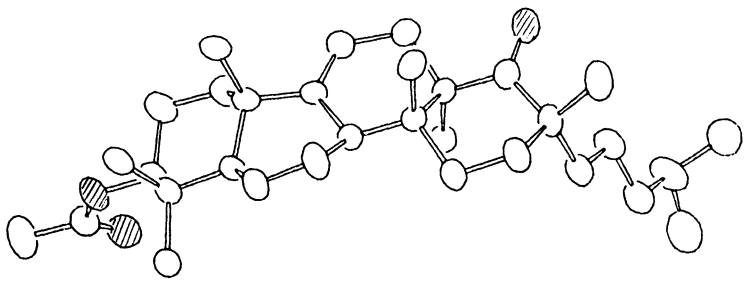


Figure 1. A computer-generated perspective drawing of 3, shaded circles indicating oxygen atoms.

References

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6) e.g., a) I. Agata, E. J. Corey, A. G. Hortmann, J. Klein, S. Proskow, and J. J. Ursprung, J. Org. Chem., 30, 1698 (1965); b) G. V. Baddeley, H. J. Samaan, J. J. H. Simes, and T. H. Ai, J. Chem. Soc., Perkin Trans. I, 1979, 7; c) Z. Paryzek, ibid., 1979, 1222.

7) E. Suokas and T. Hase, Acta Chem. Scand., 25, 2359 (1971); B 31, 633 (1977).

8) Friedelene, glutinene, and olean-12-ene are all converted into the equilibrium mixture of olean-13(18)-ene and 18α-olean-12-ene under a variety of acidic conditions.[3)]

9) ^{1}H NMR ($CDCl_3$) δ 2.0 (3H, s; -OAc), 2.65 (1H, s; $C_{(18\alpha)}$-H), and 4.5 (1H, m; $C_{(3\alpha)}$-H); MS m/e (%) 486 (M^+; 35), 469 (92), and 383 (100).

10) ^{1}H NMR ($CDCl_3$) δ 2.0 (3H, s; -OAc), 2.3 (1H, s; $C_{(18\beta)}$-H), and 4.5 (1H, m; $C_{(3\alpha)}$-H); MS m/e (%) 486 (M^+; 63), 468 (21), and 383 (23).

11) This conclusion was confirmed by ^{1}H NMR pseudo-contact shift induced by $Eu(fod)_3$ using 3-deacetoxyl derivatives of 7 and 1.

12) HPLC separation was carried out on a Waters Liquid Chromatograph ALC/GPS 202/401 at room temperature with RI detector (column: μPORASIL; solvent system: 25% ether-hexane; flow rate: 2 ml/min).

13) Since the mass spectrum of the rearrangement product showed an intense peak at m/e 528 due to diacetate(s) but no peak at m/e 486 due to keto acetate (9), formation of diol (8) would be explicable as follows; epoxide (1) afforded enol acetate (10) under the rearrangement conditions, which was converted into 3β,18α-diol (8) on treatment with lithium aluminium hydride.

14) Mp 117-119 °C; IR (film) 1740, 1692, and 1245 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.05 (3H, s; -OAc), 4.47 (1H, dd, J=6 Hz and 10 Hz; $C_{(3\alpha)}$-H), and 5.38 (1H, m; $C_{(11)}$-H); MS m/e (%) 484 (M^+; 51), 469 (31), 409 (53), 400 (47), 344 (62), and 343 (100).

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