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Rearrangements of 14-Mesyloxy-*ent*-Beyer-15-enes

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Abstract: Rearrangement of *ent*-7α,18-diacetoxy-14β-mesyloxybeyer-15-ene (4) under several conditions gave 12(13→14)-*abeo* compounds (5 or 7), on some occasions in high yield, which evolved to 12(13→14),15(8→7)-di*abeo* compounds in acidic medium. Structures of rearranged products were established principally with the aid of INADEQUATE and other 2D-nmr experiments.

INTRODUCTION

Rearrangements of tetracyclic diterpenes have normally been achieved shifting leaving groups from C-12 of *ent*-kaurane[1] or *ent*-beyerane[2], from C-16 of *ent*-kaurane[3] and *ent*-beyerane[2a,4] and from C-13 of *ent*-atisane skeletons[1a]. On a few occasions the rearrangement processes were initiated by an electronic deficiency on C-15[5] of beyerane or on C-14 of *ent*-kaurane compounds[6].

We previously reported the influence of another functional group on the cycles to be rearranged in the solvolysis process, of 12,17-difunctionalized *ent*-beyeranes[7] compounds, and demonstrated the influence of some groups at C-14[8] on processes of rearrangement initiated on C-16 of *ent*-15α,16α-epoxybeyerane compounds. We now report the first rearrangement initiated at C-14 of *ent*-beyer-15-ene compounds.

RESULTS AND DISCUSSION

ent-14β,18-Dihydroxy-7α-acetoxybeyer-15-ene (7-acetylpusillatriol, 1) is a natural product isolated from *Sideritis* [9]. Acetylation of 1 under mild conditions[10] gave the diacetate 2 (75%) and triacetate 3 (20%). Mesylation of compound 2 gave mesylate 4 (95%), which was treated under several conditions to give, preferentially, rearranged products. Thus, treatment of 4 with $LiAlH_4$ under the normal conditions of demesylation gave principally product 5 (48%) and pusillatriol 6 (35%)[11]. Nmr spectra of product 5 (see Table 1 and experimental part) clearly indicated the presence of two unsaturated groups, one of which was an

exomethylene group, which was not possible in an *ent*-beyerene skeleton. Hence a rearrangement process might be involved, probably initiated at C-14 by the mesyloxy group. Product 4 was treated under AcOH/AcOK solvolysis conditions to demonstrate this possible rearrangement. In this case (pathway A in Figure 1) product 7 (with the same type of skeleton as product 5) was obtained in high yield (95%). A similar result (90%) was obtained when mesylate 4 was treated with Zn/EtOH (pathway B in Figure 1). Connectivity between the carbon atoms in rearranged product 7 was determined by INADEQUATE experiments (see Figure 2) done with a refocalization time of 0.0065 seconds, calculated for a value of 38.5 Hz for the C/C coupling constant, which is an average value for saturated carbons. Thus, as can be observed in Figure 2, all the connectivities could be determined with the exception of C-15/C-16 and C-13/C-16, which have estimated coupling constants of around 76 Hz[12].

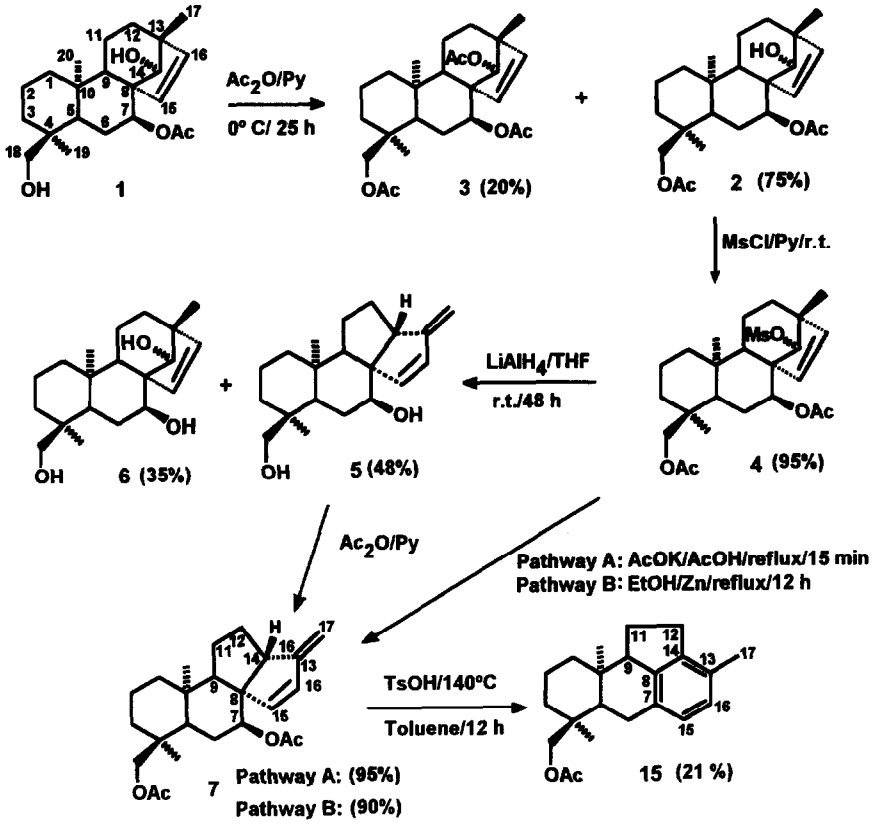


FIGURE 1

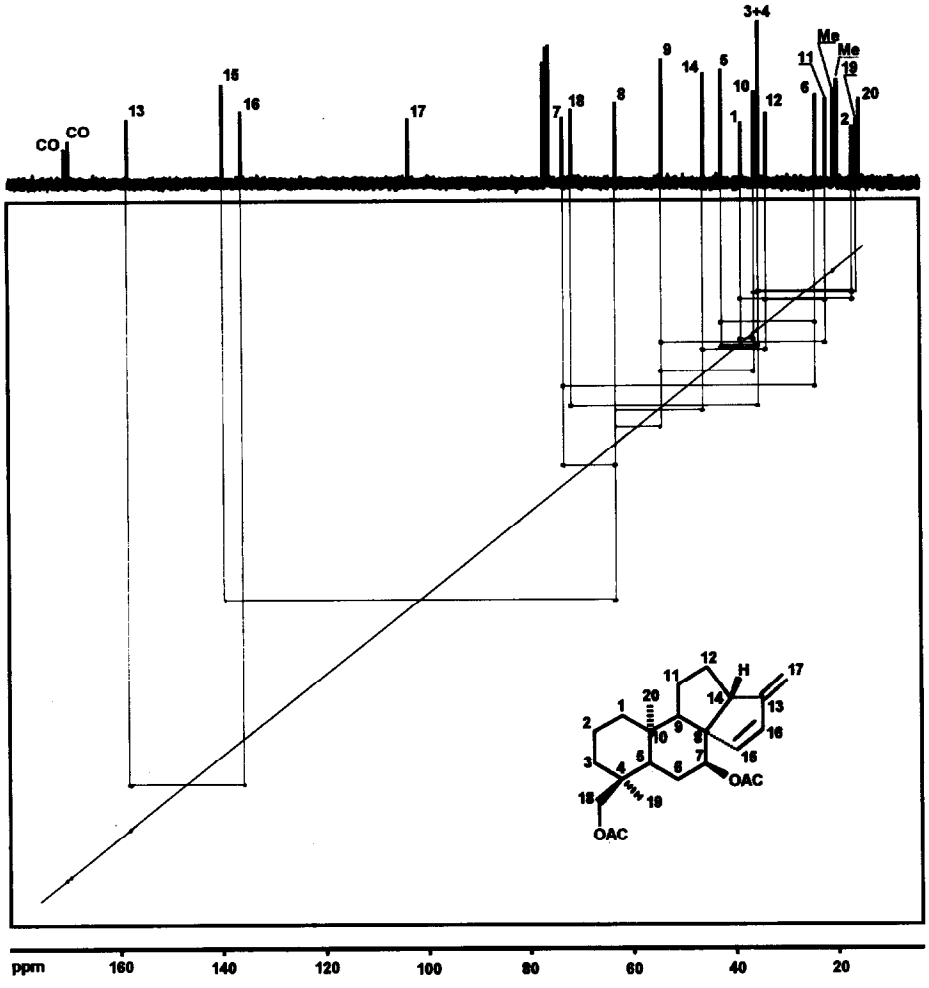
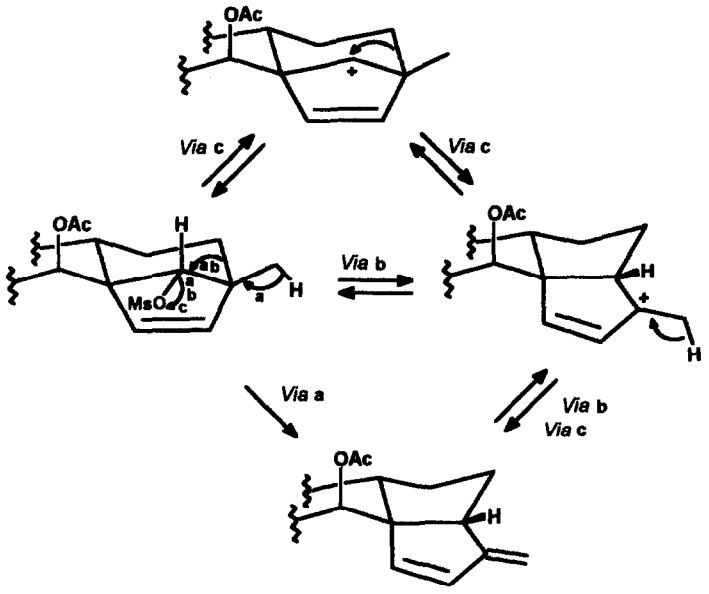


FIGURE 2

After these assignations, heteronuclear C/H correlation and proton-proton homonuclear correlation (COSY90) were done to assign the proton signals of product **7**. This experiment allowed us to assign the skeleton indicated in structure **7**, and its stereochemistry was determined by phase sensitive NOESY, after assignation of the protons by heteronuclear C/H correlation. The dipolar correlation signal appeared between 3H-20 (δ 0.91) and the protons at C-15 (δ 6.00). Hence, the stereochemistry of the new cycles at C-8 was maintained in a rearrangement process that occurred by migration of bonds C-12/C-13 to C-12/C-14, as



SCHEME 1

shown in Scheme 1. Taking into account the *trans*-periplanar arrangement of the mesyloxy group and the bond, the process can be completely concerted (*pathway a*), although an allylic carbocation may also have been formed (*pathway b*). The configuration at C-14 can be fixed in route *a* or *b*. The calculated energy for the 14β-H configuration was 55.28 kcal/mol, and the calculated coupling constants (J_1=9.04 Hz, J_2=1.39 Hz) were in agreement with the experimental values (J=10.79 Hz, bd), although the program for the calculations

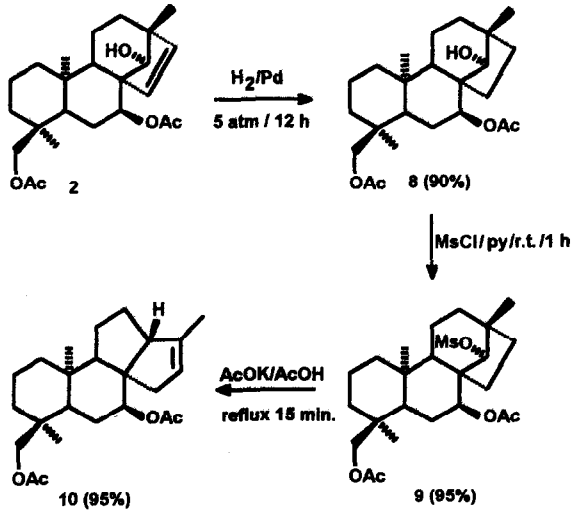
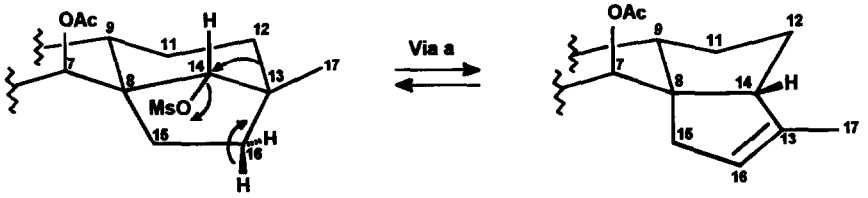


FIGURE 3

failed for conjugated system[13]. The other possible configuration at C-14 was not possible (133.8 kcal/mol). The high yield of the rearrangement (still 95%) seemed to indicate that the main pathway was *a* or *b*.

We also achieved the rearrangement of saturated compound **9** (Figure 3) under the same conditions as indicated for unsaturated product **4** to give, also in high yield, a rearranged product **10** with the same skeleton as that described for product **7**, although in this case the carbocation at C-13 was stabilised by loss of a proton from C-16 to give an *endo*-cyclic double bond (see Scheme 2, calculated energy was 47.18 kcal/mol for *endo*-cyclic double bond compound, and 50.97 kcal/mol for the *exo*-cyclic double bond product.



SCHEME 2

We also did 2D-nmr experiments in addition to monodimensional pmr and cmr (see Table 1) to determine the stereochemistry of rearranged product **10**. After assignation of the largest proton signals by C/H correlation, we detected (NOESY) dipolar correlation between the geminal proton of C-7 and of the allylic protons of C-15 (δ 2.48). The other allylic protons of C-15 (δ 1.68) showed a dipolar correlation with the methyl group of C-20 (δ 0.83). The configuration at C-14 was also defined by the rearrangement process. Calculated energy for product **10** was 54.45 kcal/mol (rather than 85.72 for its C-14 epimer) and the calculated coupling constants (J_1=10.20 Hz, J_2=2.90 Hz) were in agreement with the experimental values (J=10.40 Hz, bd), rather than calculated values (J_1=12.24 Hz, J_2=4.94 Hz) for its 14β-epimer.

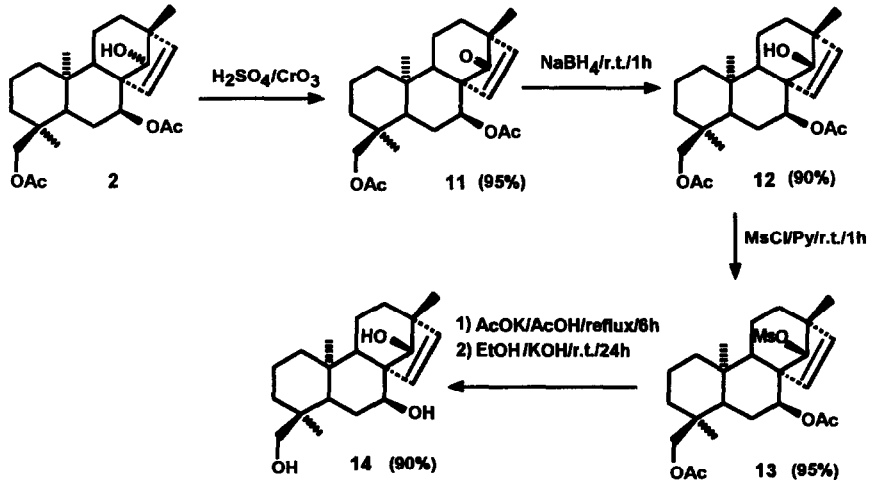
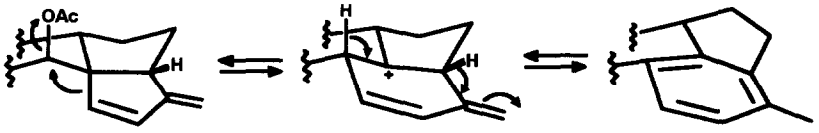


FIGURE 4

The result of the rearrangement of this saturated product **8** seems to indicate that these rearrangements are not dependent of the formation of an allylic carbocation, hence pathway *a*, with participation of a proton at C-17 in the case of product **4** or at C-16 in the case of product **9**, was preferred.

We also obtained the epimer mesylate compound at C-14 of starting product **13** to confirm the type of these rearrangements. Oxidation of diacetate compound **2** (see Figure 4) gave ketone compound **11** (95%), which was treated with $NaBH_4$ to give compound **12** (90%). Product **12** was mesylated as usual (see experimental part) to give product **13** (93%). Acetolysis of product **13**, inclusive under higher energetic



SCHEME 3

conditions than those indicated above for mesylate **4**, produced only a inseparable mixture of *ent*-14α-acetoxy or *ent*-14α-hydroxy derivatives, which was saponified to give *ent*-7α,14α,18-trihydroxybeyer-15-ene (**14**, 90%). These reactions ruled out *pathway c* for the rearrangement of products **4** and **9** (see Scheme 1).When we treated rearranged product **7** and **10** with acid, product **7** evolved toward an aromatic product (**15**, 21 %) with participation of the acetoxy group at C-7. Acid treatment of product **10** did not lead to any rearrangement (see Scheme 3).

TABLE 1

C	4	5	6	7	8	9	10	12	13	14	15
1	38.3	39.6	38.7	39.4	39.3	39.0	39.1	38.5	38.5	38.6	39.1
2	17.6	17.9	18.0	17.6	17.8	17.5	17.6	17.7	17.6	18.0	17.6
3	35.2	35.5	35.0	36.0	36.5	35.1	36.1	35.7	35.5	35.2	36.1
4	36.1	37.1	37.0	35.9	35.1	36.1	35.9	36.8	37.2	36.8	36.9
5	41.4	46.5	47.7	43.3	45.4	41.3	43.6	42.0	41.9	39.7	43.6
6	23.7	27.1	26.2	24.9	25.0	23.4	24.1	25.1	25.3	27.6	24.1
7	70.9	71.6	68.8	73.8	130.4	74.8	73.6	78.4	74.9	75.2	73.6
8	57.3	65.7	59.0	63.7	142.0	52.4	57.3	51.9	51.9	52.1	57.3
9	47.6	53.8	47.7	54.8	57.0	51.2	55.1	41.0	41.2	38.9	55.1
10	37.6	37.2	37.2	36.9	36.6	38.0	37.1	36.2	36.1	37.2	37.1
11	18.8	23.2	19.2	22.9	26.8	18.8	23.4	18.6	18.5	18.6	23.4
12	31.9	34.5	32.5	34.5	30.2	29.1	30.3	25.6	26.5	25.8	30.3
13	49.0	159.2	49.0	158.4	130.2	43.9	143.0	45.7	45.7	43.3	143.0
14	98.4	40.5	90.8	46.7	141.6	97.7	53.1	84.1	90.1	84.9	53.1
15	129.7	142.2	131.6	140.1	124.9	34.4	39.6	131.0	131.7	132.0	39.6
16	134.7	135.5	135.1	136.4	127.2	37.8	122.1	136.6	134.8	136.2	122.1
17	22.0	103.4	19.3	104.0	18.3	23.6	15.8	21.8	22.6	21.9	15.8
18	72.3	71.2	70.1	72.3	72.5	72.5	72.5	72.6	72.9	70.1	72.5
19	17.8	17.4	18.0	17.0	17.4	17.8	17.2	17.7	17.8	18.2	17.2
20	15.5	16.7	15.4	16.7	14.1	15.8	15.4	15.8	16.1	15.8	15.4
CH_3	21.0			20.9	20.8	22.2	21.5	21.6	22.1		21.1
CH_3	21.1			21.1		21.2	21.1	21.1	21.1		21.5
CH_3	38.7					38.7			40.1		
CO	171.0			170.0	170.9	171.0	171.0	169.7	171.0		171.0
CO	170.9			170.8		171.0	170.4	170.9	171.2		170.5

EXPERIMENTAL

Measurements of NMR spectra (400.13 MHz ^1H and 100.62 MHz ^{13}C) were done in $CDCl_3$ (which also provided the lock signal) in a Bruker ARX-400 apparatus. The assignments of ^{13}C chemical shifts were done with the aid of distortionless enhancement by polarization transfer (DEPT) using a flip angle of 135°. 2D-nmr experiments: COSY90, NOESY, direct C/H correlation and INADEQUATE, performed with pullprogrs from the Bruker library (COSY90, NOESYST, HXCO and INAD respectively). A sample of 130 mg of product 7, in 0.5 mL $CDCl_3$ in a 5 mm diameter probe was used for INADEQUATE, which was acquired by 512 experiences of 192 scans, with relaxation delay between scans of 2.2 sec, and refocalization time of 1/4J=0.0065 sec, in a week-end experiment. Infrared spectra were recorded on a Perkin-Elmer mod. 983 G spectrometer or on a Nicolet 20SX FT-IR spectrometer. Mass spectra were determined with CI (methane) or EI (70 eV) in a Hewlett-Packard mod. 5988 A spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 20°. Elemental analyses were performed on a Fisons EA 1108 Elementar Analyzer. Silica gel SDS 60 A CC (40-60 μm) was used for flash chromatography. CH_2Cl_2 or $CHCl_3$ containing increasing amounts of Me_2CO was used as the eluent. Analytical plates (silica gel, Merck 60 G) were rendered visible by spraying with H_2SO_4/AcOH, followed by heating to 120°.

Acetylation of product 1

Product 1 (500 mg) isolated of *Sideritis pusilla* subsp. *flavovirens* according to reference 9 was dissolved in Ac_2O/Py (1:2) with stirring for 25 h at 25°C. The reaction mixture was diluted with water, extracted with CH_2Cl_2, washed with saturated $KHSO_4$ and dried with anhydrous Na_2SO_4. Chromatography over silica gel yielded 376 mg of *ent*-7α,18-diacetoxy-14β-hydroxybeyer-15-ene (**2**, 75%)[10] and 100 mg of *ent*-7α,14β,18-triacetoxybeyer-15-ene (**3**, 20%)[10].

Mesylation of product 2

Methanesulfonyl chloride (MsCl, 0.8 mL) was added to a solution of 450 mg of product 2 dissolved in 1.6 mL pyridine. The reaction mixture was stirred at room temperature for 1 h. Then the reaction mixture was diluted with CH_2Cl_2, washed with water and with saturated aqueous $KHSO_4$, and concentrated in vacuum. Chromatography on a silica gel column yielded 428 mg of *ent*-7α,18-diacetoxy-14β-mesyloxybeyer-15-ene (**4**, 95%); m.p.: 178 °C; $[\alpha]_D$= 29.1° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 1735, 1340, 1248 and 738 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 5.54 and 5.50 (2H, Q_{AB}, J=5.2 Hz, H-15 and H-16), 4.95 (1H, dd, J_1=2.1 Hz, J_2=3.5 Hz, H-7), 4.58 (1H, bs, H-14), 3.77 and 3.56 (2H, Q_{AB}, J=11.2 Hz, 2H-18), 2.94 (3H, s, CH_3-SO_2-), 2.08 and 2.04 (3H each, s, AcO groups at C-18 and C-7); 1.15, 0.81 and 0.80 (3H, each, s, Me groups at C-17, C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M+1]^+$ 483 (0.05), 423 (0.2), 387 (1.3), 363 (1.6), 327 (59.7), 267 (100). Anal. Found: C, 62.17; H, 8.02; S, 6.41. Calcd. for $C_{25}H_{38}O_7S$: C, 62.22; H, 7.94; S, 6.64.

Reduction of product 4

Product 4 (100 mg) was dissolved in THF (10 mL) and treated with $LiAlH_4$ (10 mg) at room temperature for 48 h. The reaction mixture was diluted with aqueous diethyl ether, extracted with CH_2Cl_2, dried with anhydrous Na_2SO_4 and evaporated in vacuum to dryness. Chromatography over silica gel gave 48 mg of *ent*-7α,18-dihydroxy-12(13)→14-*abeo*beyer-13,15-diene (**5**, 48%); m.p.: 225 °C; $[\alpha]_D$= 70.4° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 3378, 1460, 754cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 6.14 and 6.04 (2H, Q_{AB}, J=5.7 Hz, H-15 and H-16), 4.79 and 4.75 (1H each, s, 2H-17), 3.72 (1H, dd, J_1=J_2=2.9 Hz H-7), 3.46 and 2.96 (2H, Q_{AB}, J=11.3 Hz, 2H-18), 2.81 (1H, d, J=11.1 Hz, H-14), 0.90 and 0.73 (3H each, s, Me groups at C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M+1]^+$ 303 (13), 285 (53), 267 (14), 57 (100). Anal. Found: C, 79.22; H, 10.08. Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00; and 35 mg of *ent*-7α,14β,18-trihydroxybeyer-15-ene (**6**, 35%)[11]; $IR_{\nu max}$

($CHCl_3$): 3383, 1456, 750 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 5.49 and 5.47 (2H, Q_{AB}, J=6.6 Hz, H-15 and H-16), 4.02 (1H, dd, $J_1=J_2=3.0$ Hz, H-7), 3.50 and 2.92 (2H, Q_{AB}, J=11.4 Hz, 2H-18), 1.06, 0.76 and 0.70 (3H each, s, Me groups at C-17, C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M+1]^+$ 321 (1), 303 (25), 285 (100), 267 (36).

Solvolysis of product 4: Pathway A: Acetolysis

Mesylate 4 (100 mg) was treated with AcOK/AcOH 0.5 N (4 mL). The reaction mixture was refluxed for 15 min and then neutralised with $NaHCO_3$, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4 and evaporated in vacuum to dryness. The crude product was chromatographed on a silica gel column to give 95 mg of *ent*-7α,18-diacetoxy-12(13)→14-*abeo*beyer-13,15-diene (**7**, 95%); m.p.: 93-95 °C; $[\alpha]_D$= 72.9° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 3076, 1739, 1635, 1247, 1039 and 757 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 6.18 and 6.00 (2H, Q_{AB}, J=5.7 Hz, H-15 and H-16), 4.80 and 4.71 (1H each, s, 2H-17), 4.80 (1H, bs, H-7), 4.28 and 3.65 (2H, Q_{AB}, J=11.1 Hz, 2H-18), 2.60 (1H, bd, J=10.8 Hz, H-14), 2.07 and 2.03 (3H each, s, AcO groups at C-18 and C-7), 0.91 and 0.84 (3H each, s, Me groups at C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M+1]^+$ 387 (1), 327 (21), 269 (100), 267 (49). Anal. Found: C, 74.32; H, 8.94. Calcd. for $C_{24}H_{34}O_4$: C, 74.58; H, 8.87.

Solvolysis of product 4: Pathway B: Treatment with EtOH/Zn

Zinc dust (100 mg) was added to a solution of 100 mg of product **4** in 10 mL EtOH, then the reaction mixture was heated to reflux for 12 h, and the solvent was removed in vacuum. The residue was extracted with CH_2Cl_2, and the organic layer was washed with $NaHCO_3$ solution, dried over anhydrous sodium sulphate and evaporated in vacuum. Chromatography on a silica gel column yielded 90 mg of the product **7** (90%).

Acetylation of product 5

Product **5** (20 mg) was dissolved in Ac_2O/Py (0.5:1 ml) and refluxed for 12 h. The reaction mixture was diluted with water, extracted with CH_2Cl_2, washed with saturated $KHSO_4$ and dried with anhydrous Na_2SO_4. Chromatography over silica gel yielded 18 mg of diacetate **7** (72%).

Acid treatment of product 7

A very small amount (5 mg) of TsOH (p-toluenesulfonic acid) was added to a solution of product **7** (50 mg) in toluene (5 mL) and the reaction mixture was heated at 140°C for 12 h in a sealed tube. The reaction mixture was cooled to room temperature, evaporated in vacuum and chromatographed on a silica gel column. This yielded 35 mg of starting product and 11 mg of *ent*-18-acetoxy-12(13)→14,15(8)→7-*diabeo*beyer-7,13,15-triene (**15**, 21%); m.p.: syrup; $[\alpha]_D$= 5° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 1741, 1454, 1237 and 804 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 6.90 and 6.84 (2H, Q_{AB}, J=7.5 Hz, H-15 and H-16), 3.93 and 3.74 (2H, Q_{AB}, J=11.0 Hz, 2H-18), 2.23 (3H, s, Me group at C-17), 2.06 (3H, s, AcO groups at C-18), 1.00 and 0.88 (3H each, s, Me groups at C-19 and C-20), ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M+1]^+$ 327 (2), 297 (4), 267 (36), 51 (100). Anal. Found: C, 80.56; H, 9.54. Calcd. for $C_{22}H_{30}O_2$: C, 80.94; H, 9.26.

Hydrogenation of product 2

Product **2** (150 mg) was hydrogenated according to reference 14 to give 135 mg of *ent*-7α,18-diacetoxy-14β-hydroxybeyerane (**8**, 90%)[14].

Mesylation of product 8

Methanesulfonyl chloride (0.2 mL) was added to a solution of 120 mg of product **8** dissolved in 0.4 mL pyridine. The reaction mixture was stirred at room temperature for 1 h. Then the reaction mixture was diluted with CH_2Cl_2, washed with water and with saturated aqueous $KHSO_4$, and concentrated in

vacuum. Chromatography on a silica gel column yielded 114 mg of *ent*-7α,18-diacetoxy-14β-mesyloxybeyerane (**9**, 95%); m.p.: 140-2°C; $[\alpha]_D$= 82.7° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 1732, 1335, 1250, 1172 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): 4.81 (1H, dd, J_1=1.9 Hz, J_2=3.9 Hz, H-7), 4.61 (1H, bs, H-14), 3.78 and 3.54 (2H, Q_{AB}, J=11.2 Hz, 2H-18), 2.99 (3H, s, CH_3-SO_2-), 2.08 and 2.04 (3H each, s, AcO groups at C-18 and C-7), 1.10, 0.99 and 0.80 (3H, each, s, Me groups at C-17, C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M+1]^+$ 485 (0.3), 425 (0.2), 365 (1.6), 330 (7.8), 329 (31.8), 269 (100). Anal. Found: C, 61.65; H, 8.54; S, 6.27. Calcd. for $C_{25}H_{40}O_7S$: C, 61.96; H, 8.32; S, 6.62.

Acetolysis of product 9

Mesylate **9** (100 mg) was treated with AcOK/AcOH 0.5 N (4 mL). The reaction mixture was refluxed for 15 min and then neutralised with $NaHCO_3$, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4 and evaporated in vacuum to dryness. The crude product was chromatographed on a silica gel column to give 95 mg of *ent*-7α,18-diacetoxy-12(13)→14-*abeo*beyer-16-ene (**10**, 95%); m.p.: 116-118°C; $[\alpha]_D$= 57.3° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 1738, 1247; ^1H nmr (400 MHz, $CDCl_3$): δ 5.04 (1H, bs, H-16), 4.82 (1H, dd, J_1=J_2=2.5 Hz, H-7), 3.70 and 3.62 (2H, Q_{AB}, J=11.1 Hz, 2H-18), 2.48 (1H, dd, J_1=16.4 Hz J_2=4.6 Hz, H-15), 2.28 (1H, bd, J=10.4 Hz, H-14), 2.05 and 2.03 (3H each, s, AcO groups at C-18 and C-7), 1.60 (3H, bs, Me group at C-17), 0.83 and 0.80 (3H each, s, Me groups at C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M+1]^+$ 389 (21), 329 (21), 269 (100). Anal. Found: C, 73.89; H, 9.02. Calcd. for $C_{24}H_{36}O_4$: C, 74.19; H, 9.34.

Oxidation of product 2

Product **2** (200 mg) was oxidized by the Jones method according to reference 14, and 190 mg of *ent*-7α,18-diacetoxy-14-oxo-beyer-15-ene (**11**, 95 %)[14] were obtained.

Reduction of product 11

$NaBH_4$ (15 mg) was added to a solution of product **11** (150 mg) in MeOH (10 mL) and the mixture was stirred at room temperature for 1 h. The reaction mixture was acidified with dil. HCl, extracted with CH_2Cl_2, dried with anhydrous Na_2SO_4 and concentrated in vacuum. Chromatography on a silica gel column yielded 135 mg of *ent*-7α,18-diacetoxy-14α-hydroxybeyer-15-ene (**12**, 90%) m.p.: 162-4°C; $[\alpha]_D$= 12.6° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 3590, 1737, 1248 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$):δ 5.58 and 5.49 (2H, Q_{AB}, J=5.2 Hz, H-15 and H-16), 4.90 (1H, dd, J_1=2.2 Hz, J_2=3.4 Hz, H-7), 3.70 and 3.65 (2H, Q_{AB}, J=11.0 Hz, 2H-18), 3.35 (1H, bs, H-14), 2.07 and 2.04 (3H each, s, AcO groups at C-18 and C-7), 0.98 (3H, s, Me group at C-17), 0.82 (6H, s, Me groups at C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M]^+$ 404 (0.5), 344 (16.6), 284 (11.0), 269 (15.0), 43 (100). Anal. Found: C, 71.20; H, 8.86. Calcd. for $C_{24}H_{36}O_5$: C, 71.26; H, 8.97.

Mesylation of product 12

Methanesulfonyl chloride (0.2 mL) was added to a solution of 120 mg of product **12** dissolved in 0.4 mL of pyridine. The reaction mixture was stirred at room temperature for 1 h. Then, the reaction mixture was diluted with CH_2Cl_2, washed with water and with saturated aqueous $KHSO_4$ and concentrated in vacuum. Chromatography on a silica gel column yielded 114 mg of *ent*-7α,18-diacetoxy-14α-mesyloxybeyerane (**13**, 95%); m.p.: 145-7°C; $[\alpha]_D$= 56° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 1732, 1362, 1246, 1174 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 5.56 (2H, collap. Q_{AB}, H-15 and H-16), 4.89 (1H, dd, J_1=J_2=2.5 Hz, H-7), 4.41 (1H, bs, H-14), 3.69 and 3.62 (2H, Q_{AB}, J=11.1 Hz, 2H-18), 3.07 (3H, s, CH_3-SO_2-), 2.11 and 2.04 (3H each, s, AcO groups at C-18 and C-7), 1.08, 0.83 and 0.82 (3H, each, s, Me groups at C-17, C-19 and C-20); ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M]^+$ 482 (0.1), 422 (0.2), 387 (0.3), 362 (0.6), 327 (1.7), 267 (1.6), 43 (100). Anal. Found: C, 61.85; H, 8.04; S, 6.32. Calcd. for $C_{25}H_{38}O_7S$: C, 62.22; H, 7.94; S, 6.64.

Acetolysis of product 13

Mesylate **13** (100 mg) was treated with AcOK/AcOH 0.5 N (4 mL). The reaction mixture was refluxed for 6 h and then neutralised with $NaHCO_3$, extracted with CH_2Cl_2, dried over anhydrous Na_2SO_4 and evaporated in vacuum to dryness. The crude product was chromatographed on a silica gel column to give a very difficult separation mixture of two products. This mixture was saponified with alcoholic KOH at room temperature for 24 hours to yield 90 mg of *ent*-7α,14α,18-trihydroxybeyer-15-ene (**14**, 90%); m.p.: 177-79 °C; $[\alpha]_D$= +41.2° ($CHCl_3$, c 1); $IR_{\nu max}$ ($CHCl_3$): 3351, 3051 cm^{-1}; ^1H nmr (400 MHz, $CDCl_3$): δ 5.53 and 5.48 (2H, Q_{AB}, J=6.3 Hz, H-15 and H-16), 3.83 (1H, dd, $J_1=J_2=2.7$ Hz, H-7), 3.45 (1H, bs, H-14), 3.44 and 2.93 (2H, Q_{AB}, J=11.1 Hz, 2H-18), 0.98, 0.79 and 0.70 (3H, each, s, Me groups at C-17, C-19 and C-20) ; ^{13}C nmr (100 MHz, $CDCl_3$): see Table 1; ms, m/z(%): $[M]^+$ 320 (0.1), 302 (15.0), 284 (8.0), 43 (100). Anal. Found: C, 74.82; H, 9.91. Calcd. for $C_{20}H_{32}O_3$: C, 74.96; H, 10.06.

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