

of freshly recrystallized and dried  $\text{Me}_3\text{S}^+\text{I}^-$ , and 0.62 mmol of  $n\text{-BuLi}$  in 6.2 mL of THF at  $-78^\circ\text{C}$ . The reaction was stirred at  $0-5^\circ\text{C}$  for 3 h and then the THF was evaporated and the residue partitioned between  $\text{CH}_2\text{Cl}_2$  (20 mL) and  $\text{H}_2\text{O}$  (20 mL). The aqueous layer was extracted with EtOAc ( $1 \times 10$  mL). The combined organic extracts were dried ( $\text{Na}_2\text{SO}_4$ ), filtered, and evaporated to give 63 mg of crude product. This material was purified by preparative TLC (0.5-mm silica gel plate, 9:1 hexane-EtOAc, two elutions), giving 54 mg of an inseparable 3:1 mixture ( $^1\text{H}$  NMR analysis) of epoxide **10a** and the methylthio adduct **11a** ( $R_f$  0.29, 9:1 hexane-EtOAc). A portion of the above mixture (38 mg, 70% of total) was dissolved in 2 mL of dry THF and treated with  $\text{Bu}_4\text{NF}$  (0.08 mL, 0.08 mmol, 1 M in THF) at  $0^\circ\text{C}$ . After 2 h, the reaction was diluted with  $\text{Et}_2\text{O}$  (30 mL) and was washed with brine ( $1 \times 10$  mL). The organic phase was dried ( $\text{Na}_2\text{SO}_4$ ) and evaporated; the crude mixture (71 mg) was separated by preparative TLC (0.5-mm silica gel plate, three developments with 1:1 hexane-EtOAc) to give 8 mg (25%) of **13a** and 14.1 mg (52%) of **12a**: mp  $177-179^\circ\text{C}$ ;  $[\alpha]_D^{22} - 22.7^\circ$  ( $c$  1.04,  $\text{CHCl}_3$ );  $R_f$  0.16 (1:1 hexane-EtOAc);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3/\text{D}_2\text{O}$  washed)  $\delta$  4.64 (m, 1 H, THP), 4.26 (dd, 1 H,  $J = 1.7$ , 8.6 Hz,  $\text{H}_{10}$ ), 4.18 (m, 2 H,  $\text{H}_4$  and  $\text{H}_{11}$ ), 3.95 (m, 1 H, THP), 1.90 (br m, 1 H,  $\text{H}_3$ ), 3.77 (d, 1 H,  $J = 9$  Hz,  $\text{H}_{15a}$ ), 3.69 (dd, 1 H,  $J = 3.1$ , 9.3 Hz,  $\text{H}_{15b}$ ), 3.58 (m, 1 H, THP), 2.74 (d, 1 H,  $J = 4.2$  Hz,  $\text{H}_{13a}$ ), 2.44 (d, 1 H,  $J = 5$  Hz,  $\text{H}_{13b}$ ), 2.38 (m, 1 H), 2.27 (m, 1 H), 1.90-1.5 (m, 8 H), 1.28 (s, 3 H,  $\text{H}_{16}$ ), 0.66 (s, 3 H,  $\text{H}_{14}$ ); IR ( $\text{CHCl}_3$ ) 3600 (br), 2950, 2880, 1450, 1380, 1170, 1120, 1050, 1025, 965, 700 ( $\text{br}$ )  $\text{cm}^{-1}$ ; mass spectrum,  $m/e$  359, 361 ( $\text{M}^+ - \text{C}_5\text{H}_9\text{O}$ ).

Data for **13a**:  $[\alpha]_D^{23} - 29.8^\circ$  ( $c$  0.67,  $\text{CHCl}_3$ );  $R_f$  0.38 (1:1 hexane-EtOAc);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  4.63 (m, 1 H, THP), 4.3-4.2 (m, 3 H,  $\text{H}_4$ ,  $\text{H}_{10}$  and  $\text{H}_{11}$ ), 3.95 (m, 1 H, THP), 3.82 (dd, 1 H,  $J = 3$ , 5.5 Hz,  $\text{H}_3$ ), 3.73 (br s, 3 H,  $\text{H}_{15}$  and  $\text{H}_2$ ), 3.60 (m, 1 H, THP), 2.93 (d, 1 H,  $J = 14$  Hz,  $\text{H}_{13a}$ ), 2.87 (s, 1 H, OH), 2.79 (d, 1 H,  $J = 14$  Hz,  $\text{H}_{13b}$ ), 2.17 (s, 3 H, SMe), 1.9-1.5 (m, 10 H), 1.28 (s, 3 H,  $\text{H}_{16}$ ), 0.86 (s, 3 H,  $\text{H}_{14}$ ); IR ( $\text{CHCl}_3$ ) 3550 (br), 2960, 2880, 1450, 1380, 1350, 1200, 1150, 1120, 1060, 1050, 1025  $\text{cm}^{-1}$ .

**12-Epi-3 $\alpha$ -(tetrahydropyranyl)oxy]-12,13-epoxy-trichothec-9-ene-4 $\beta$ ,15-diol (14a).** To a solution of **12a** (11.0 mg, 0.025 mmol) in 2 mL of dry THF and 0.4 mL of dry EtOH were added six spatula scoops of freshly prepared Zn/Ag couple and 1 mL of dry  $\text{Et}_2\text{O}$ . This mixture was heated to  $45^\circ\text{C}$  for 12 h. Solvents were then evaporated, and the residue was suspended

in acetone and filtered through a 0.25-in. pad of silica gel overlaid with Celite. The filtrate was evaporated to give 11 mg of crude product that was purified by TLC (0.25-mm plate, two elutions with 2:1 EtOAc-hexane), giving 8.8 mg (96%) of **14a**: mp  $74-75^\circ\text{C}$ ;  $R_f$  0.20 (1:2 hexane-EtOAc);  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  5.50 (br dd, 1 H,  $J = 1.4$ , 3.4 Hz,  $\text{H}_{10}$ ), 4.71 (m, 1 H, THP), 4.51 (br s, 1 H,  $\text{H}_4$ ), 4.03 (d, 1 H,  $J = 5$  Hz,  $\text{H}_{11}$ ), 3.93 (m, 1 H,  $\text{H}_3$ ), 3.76 (d, 1 H,  $J = 12.2$  Hz,  $\text{H}_{15a}$ ), 3.70 (d, 1 H,  $J = 4.7$  Hz,  $\text{H}_2$ ), 3.58 (d, 1 H,  $J = 12.2$  Hz,  $\text{H}_{15b}$ ), 3.5 (s, 1 H, OH), 2.80 (d, 1 H,  $J = 4.6$  Hz,  $\text{H}_{13a}$ ), 2.70 (br s, 1 H, OH), 2.39 (d, 1 H,  $J = 4.6$  Hz,  $\text{H}_{13b}$ , overlapping with m, 1 H), 2.1-1.5 (m, 10 H), 1.70 (s, 1 H,  $\text{H}_{16}$ ), 0.95 (s, 3 H,  $\text{H}_{14}$ ); IR ( $\text{CHCl}_3$ ) 3600-3400 (br), 2940, 2860, 1450, 1375, 1345, 1200, 1165, 1125, 1070, 1020, 955, 899  $\text{cm}^{-1}$ ; FAB mass spectrum (glycerol- $\text{CH}_2\text{Cl}_2$ ),  $m/e$  367 ( $\text{M} + \text{H}^+$ ).

**12-Epianguidine (5).** To a solution of **14a** (12.6 mg, 0.025 mmol) in 1.0 mL of dry pyridine were added 4-DMAP (4 mg, 0.033 mmol) and acetic anhydride (0.04 mL, 0.42 mmol). The mixture was stirred for 2.5 h, and then the pyridine was removed by coevaporation with heptane ( $2 \times 50$  mL). The residue was dried in vacuo to afford the crude diacetate THP ether ( $R_f$  0.45, 1:1 hexane-EtOAc). This material was dissolved in 0.4 mL of THF, 0.2 mL of  $\text{H}_2\text{O}$ , and 0.4 mL of glacial HOAc and then heated at  $50^\circ\text{C}$  for 7 days. All volatile reaction components were then removed by coevaporation with heptane ( $3 \times 25$  mL). The crude product was purified by preparative TLC (0.25-mm silica gel plate, 1:1 hexane-EtOAc, two elutions) to give 4.4 mg of pure 12-epianguidine (**5**, 48% from **14a**):  $[\alpha]_D^{21} - 45^\circ$  ( $c$ , 0.17,  $\text{CHCl}_3$ );  $R_f$  0.16 (1:1 hexane-EtOAc);  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ )  $\delta$  5.53 (m, 1 H,  $\text{H}_{10}$ ), 5.16 (d, 1 H,  $J = 3.0$  Hz,  $\text{H}_4$ ), 4.17 (br d, 1 H,  $J = 5.0$  Hz,  $\text{H}_{11}$ ), 4.10 (d, 1 H,  $J = 12.0$  Hz,  $\text{H}_{15a}$ ), 4.00 (m, 2 H,  $\text{H}_3$ ,  $\text{H}_{15b}$ ), 3.70 (d, 1 H,  $J = 4.9$  Hz,  $\text{H}_2$ ), 3.02 (d, 1 H,  $J = 2$  Hz, OH), 2.79 (d, 1 H,  $J = 4.7$  Hz,  $\text{H}_{13a}$ ), 2.40 (d, 1 H,  $J = 4.7$  Hz,  $\text{H}_{13b}$ ), 2.13 (s, 3 H, OAc), 2.05 (s, 3 H, OAc), 1.70 (s, 3 H,  $\text{H}_{16}$ ), 0.83 (s, 3 H,  $\text{H}_{14}$ ); IR ( $\text{CHCl}_3$ ) 3580 (br), 2960, 2920, 1735 (br), 1445, 1435, 1400, 1370, 1240-1200 (br), 1070, 1030, 960  $\text{cm}^{-1}$ ; mass spectrum,  $m/e$  366 ( $\text{M}^+$ ); high resolution mass spectrum for  $\text{C}_{19}\text{H}_{26}\text{O}_7$ , calcd 366.1679, found 366.1679  $\pm$  0.0004.

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## Ruthenium-Catalyzed Rearrangements of 15,16-Epoxybeyerane Diterpenes Functionalized at C-14

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Several rearrangements, catalyzed by ruthenium acetylacetonate, of *ent*-18-acetoxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyeranes with exo- or endo-hydroxyl or exo- or endo-acetoxy groups at C-14 were carried out. In the case of the 14-endo-hydroxy compound, only *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16*R*)-kauran-15-one was isolated. However, the rearrangement of the exo-hydroxy compound gave *ent*-18-acetoxy-14 $\beta$ ,15 $\alpha$ ,16 $\beta$ -trihydroxybeyerane, *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16*S*)-kauran-15-one, *ent*-18-acetoxy-14 $\alpha$ ,15 $\beta$ -dihydroxykaur-16-ene, and *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16*S*)-atisan-15-one. Under the same conditions the exo-acetoxy compound yielded *ent*-15 $\beta$ ,18-diacetoxy-14 $\alpha$ -hydroxykaur-16-ene, *ent*-14 $\beta$ ,18-diacetoxy-15 $\alpha$ ,16 $\beta$ -dihydroxybeyerane, and *ent*-15 $\beta$ ,18-diacetoxy-14 $\alpha$ -hydroxy-(16*S*)-kaur-11-ene. On the other hand, the endo-acetoxy derivative yielded *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16*R*)-kauran-15-one, *ent*-15 $\alpha$ ,18-diacetoxy-14 $\alpha$ -hydroxykaur-16-ene, *ent*-14 $\alpha$ ,18-diacetoxy-15 $\alpha$ ,16 $\beta$ -dihydroxybeyerane, *ent*-15 $\alpha$ ,18-diacetoxy-14 $\alpha$ -hydroxy-(16*S*)-kaur-11-ene, and *ent*-14 $\alpha$ ,18-diacetoxy-beyer-9(11),15-diene. The stereochemistry of the rearrangement processes is discussed.

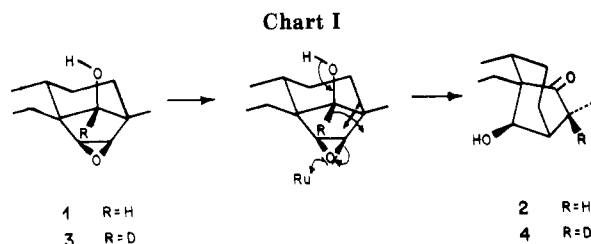
### Introduction

A considerable number of papers devoted to the study of rearrangements of the tetracyclic diterpenoids have been published. On some occasions, rearrangements of epoxy compounds were carried out.<sup>1-7</sup> Solvolytic reactions in

protic media<sup>8-12</sup> and rearrangements of thiocarbonates<sup>13</sup> have also been reported.

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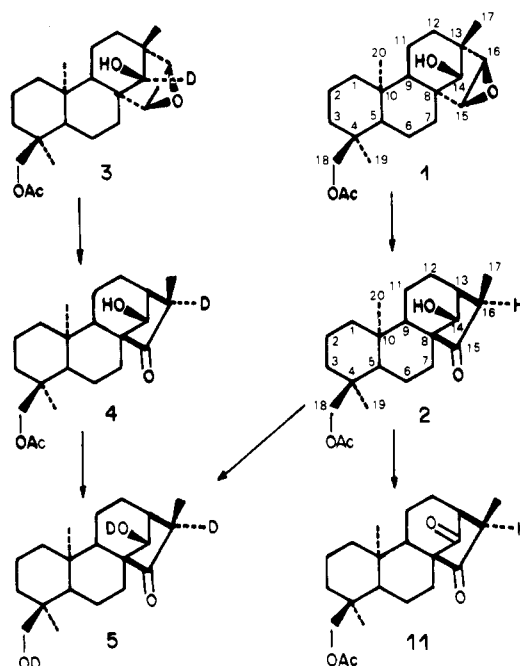
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The rearrangements of 15,16-epoxybeyeranes were usually carried out by treatment with  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  in anhydrous benzene or diethyl ether to give kaur-15-enes or kaur-16-enes, because isomerization of such products occurs easily in these conditions.<sup>1</sup> When substituents were present on the beyerene skeleton (i.e., at C-3 or C-19), the yield of the rearranged products was lower.<sup>1,2</sup> When rearrangement was performed in the presence of water, a hydroxyl group was introduced with a stereochemistry which indicated a concerted process.<sup>3</sup> The acid-catalyzed rearrangement of epoxybeyeranes in concentrated solutions leads to the expected kauranes and kaurenes in addition to a 8,13-*epi,epi*-beyerane.<sup>7</sup> The rearrangements<sup>1-12</sup> are in agreement with the biogenetic hypothesis for tetra- and pentacyclic diterpenes.<sup>14-18</sup> Biogenetic-like conversions of epoxykaurenes have also been performed to give *ent*-14 $\beta$ -hydroxybeyer-15-enes.<sup>19</sup> In the present paper we report a series of rearrangements of *ent*-15 $\alpha$ ,16 $\alpha$ -epoxybeyeranes with substitution at C-14 which in some cases provide evidence for stereochemistry of the previously described migrations and in other cases give products which have not been obtained before by rearrangement of epoxides or solvolytic reactions. To our knowledge, ruthenium acetylacetonate has not been used previously for epoxide rearrangements.

### Results and Discussion

The reaction of *ent*-18-acetoxy-14 $\alpha$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (1) with catalytic amounts of ruthenium acetylacetonate gave, after 1 h at 140 °C, only one product (2) which showed IR bands for hydroxyl, acetoxy, and keto groups. Its proton magnetic resonance (<sup>1</sup>H NMR) spectrum shows a singlet at  $\delta$  4.65 (1 H) and a doublet at  $\delta$  1.12 (3 H,  $J = 7$  Hz) in addition to an AB quartet ( $J = 12$  Hz, 2 H-18) and two methyl singlets (3 H each), C-19 and C-20 methyl groups. The presence of the methyl doublet signal suggested that product 2 had an *ent*-kauranic skeleton, since this type of rearrangement has been described previously for unsaturated<sup>1-3,5</sup> or C-16-functionalized systems.



This hypothesis was confirmed by the observation of a quintuplet at  $\delta$  2.72 (1 H,  $J_1 = J_2 = 7$  Hz) attributable to H-16. This signal indicated that H-16 is coupled with the C-17 methyl group (quartet,  $J = 7$  Hz), and also split by another  $J_{13/16} = 7$  Hz, which was proved by double resonance experiments. Thus, irradiation at  $\delta$  transformed the signal at  $\delta$  2.72 into a doublet ( $J = 7$  Hz). Examination of a Dreiding model indicated that this 7-Hz coupling is only compatible with *ent*-16 $\beta$ -H stereochemistry, because the dihedral angle of H-13 with *ent*-16 $\alpha$ -H must be 90°. <sup>13</sup>C NMR experiments confirmed the *ent*-kaurene structure for 2, which might be an *ent*-18-acetoxy-14 $\alpha$ -hydroxykauran-15-one with 16S or 16R configuration. If the rearrangement of 1 occurs in a concerted manner (see Chart I), a 16R configuration can be expected. In any case, the spectroscopic properties of compound 2 also suggested a 16R configuration. Thus, the chemical shift of the proton at C-16 ( $\delta$  2.72) as well as the chemical shift for methyl group at C-17 indicates the proximity of this C-16 proton to the *ent*-14 $\alpha$ -hydroxyl group of this molecule. The analysis of <sup>13</sup>C NMR data of 2 confirmed this 16R configuration because the chemical shift of the C-17 methyl group ( $\delta$  9.32) in 2 is in agreement with spectral data for *ent*-kaurene alkaloids ( $\delta$  10.1 for 16R and 15.9 for 16S derivatives<sup>20</sup>). We confirmed that the proton which appears at C-16 in 2 was originally at C-14 in the starting material 1. Thus the rearrangement of deuteriated 3 carried out under the same conditions as described above yielded a product (4) which had the same <sup>1</sup>H NMR spectrum as described for product 2, but with a C-17 methyl singlet signal at  $\delta$  1.12 (3 H) and without the quintuplet of the C-16 methylene group of 2. The <sup>13</sup>C NMR spectrum of product 4 confirmed the presence of deuterium only at C-16. Treatment of 2 with a deuteriated basic medium gave 5, identical with the product obtained from saponification of product 4. Its C-16 epimer was not detected.

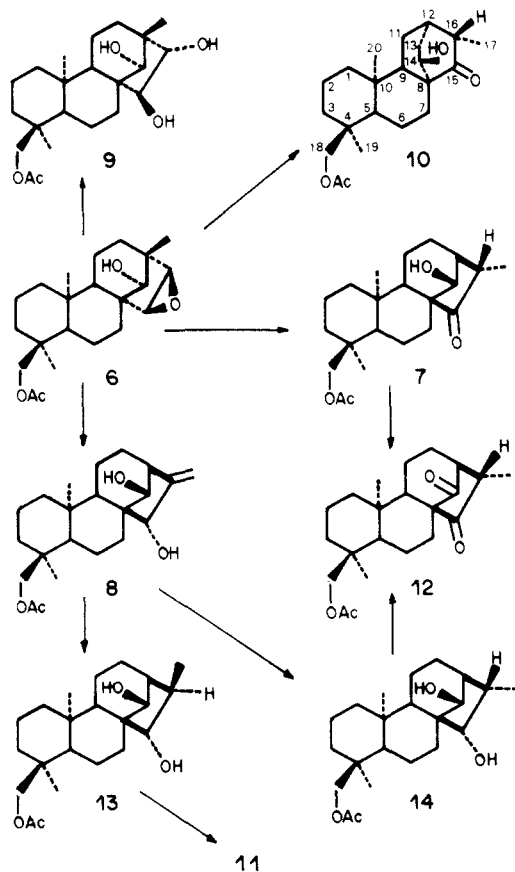
Concerted opening of the epoxy group, migration of trans-periplanar bond, which causes beyerane  $\rightarrow$  kaurane rearrangement, trans-periplanar migration of exo proton of C-14 to C-16 of the new kaurane compound and loss of the proton of original hydroxyl group at C-14 is a more reasonable mechanism for formation of 2 and 4 than

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pathways via the kaur-16-ene compounds as proposed in previous papers devoted to the study of  $\text{BF}_3 \cdot \text{Et}_2\text{O}$  catalyzed rearrangement of similar 15,16-epoxybeyerane compounds.<sup>1-3,5</sup> In the case of 1 and 3, the participation of the *ent*-14 $\alpha$ -hydroxyl group controls the course of the reaction in the manner described.

A similar experiment with *ent*-18-acetoxy-14 $\beta$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (6) was carried out to verify the influence of the stereochemistry at C-14. Structures of the five products 7-10 were deduced from spectroscopic data and chemical transformations. Product 7 (28% of isolated products) has the same molecular formula and a similar IR spectrum as 2. Since the  $^1\text{H}$  NMR spectrum of product 7 only differs from that of 2 in the chemical shifts of the methyl doublet (in this case at  $\delta$  1.21,  $J = 7$  Hz) and the H-16 methyne signal (in this case overlapping other signals at  $\delta$  2.20), we assumed that 7 is the C-16 epimer of 2. This assignment was confirmed by  $^{13}\text{C}$  NMR spectral data. Thus, the chemical shift for C-17 in 7 is  $\delta$  18.01, which is in agreement with that of *ent*-kaurane alkaloids<sup>20</sup> of the same configuration and very different from the one assigned by us earlier, for C-17 of 2 ( $\delta$  9.32). However, we believe that the assignments for C-11 and C-12 of the C-17 exo-methyl epimers of some *ent*-kauranic alkaloids<sup>20</sup> must be interchanged. The methyl group at C-17 produces a  $\gamma$ -effect on C-12 only in the case of endo epimer. Thus we conclude that 7 has the structure of *ent*-18-acetoxy-14 $\alpha$ -hydroxy-16(*S*)-kauran-15-one. Treatment of 7 with base leads to 2 (and with deuterated base to 5).



Product 8, also isolated from this reaction (18%), showed IR bands for hydroxyl, acetoxy, and exo-methylene groups. No ketone group was present. Its  $^1\text{H}$  NMR spectrum showed signals attributable to two exo-methylenic protons [ $\delta$  5.41 and 5.21 (1 H each)], an AB quartet [ $\delta$  3.91 and 3.65 ( $J = 12$  Hz, 2 H-18)], two protons geminal to hydroxyl groups [ $\delta$  4.22 (1 H, br s) and 3.80 (1 H, br s)], and methyl

singlet signals at  $\delta$  2.07 (3 H, acetoxy group at C-18), 1.03 (3 H), and 0.85 (3 H). These spectroscopic properties suggested an *ent*-kaur-16-ene structure, which could explain a signal at  $\delta$  2.82 (1 H, m,  $W_{1/2} = 8$  Hz) from a proton at C-13, and which must be functionalized further by a *ent*-14 $\alpha$ - and *ent*-15 $\beta$ -hydroxyl groups. The  $^{13}\text{C}$  NMR spectrum of 8 confirmed this structure, which has the configurations at C-14 and C-15 of the corresponding carbons in the *ent*-beyerane starting material 6. These configurations were confirmed after elucidation of the structures of other epimers as a result of other rearrangement processes to be discussed later in this paper. In addition, the  $^{13}\text{C}$  chemical shifts of product 8 are in agreement with those reported for a natural product similarly functionalized at C-14, C-15, and C-16.<sup>21</sup>

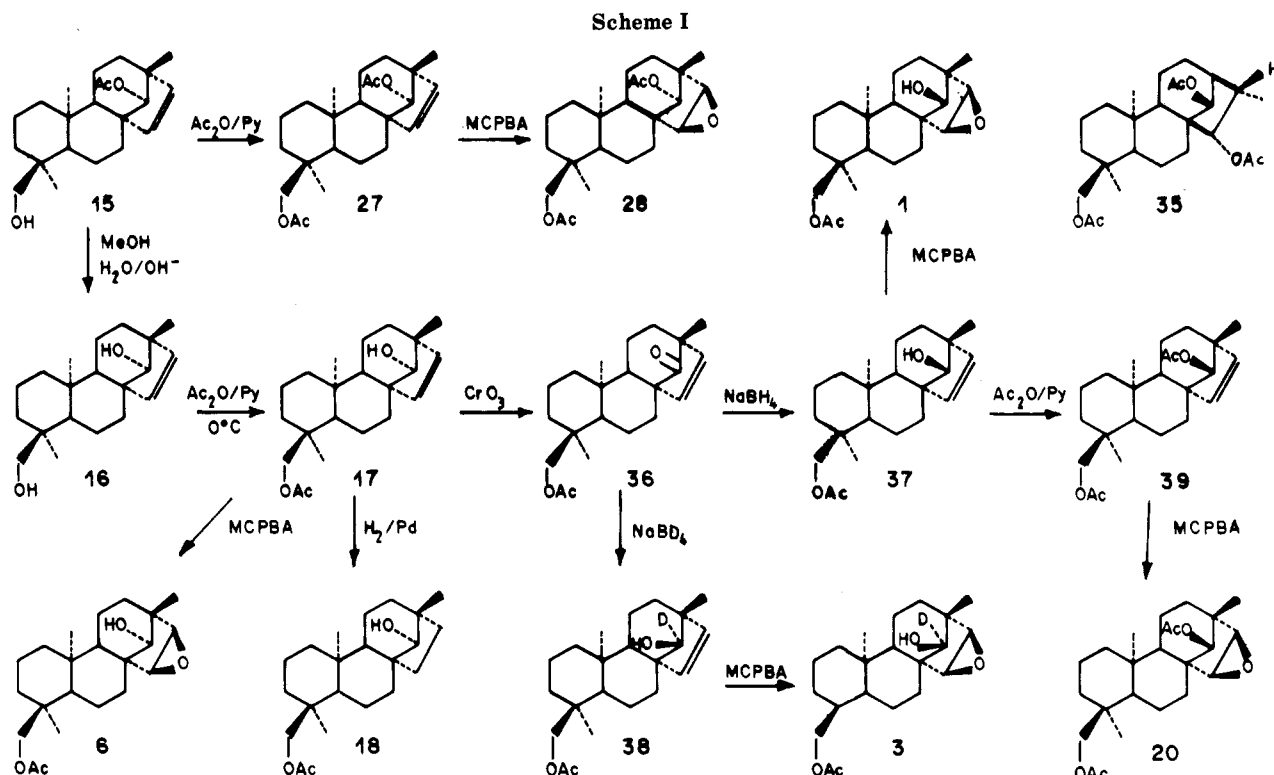
Further proof that 2 and 7 are epimers at C-16 was obtained by oxidation to the diketones 11 and 12. The  $^1\text{H}$  NMR spectra of 11 and 12 differ significantly in the signals of H-13 ( $\delta$  2.72 vs. 2.54), H-16 ( $\delta$  2.67 vs. 2.80) and H-17 ( $\delta$  1.32 vs. 1.05). The signals of H-16 in the diketones are also useful for distinguishing the two different configurations at C-16. Thus, in the  $^1\text{H}$  NMR spectrum at 12, H-16 appears as a sharp quartet ( $J = 7$  Hz) which indicates that  $J_{13/16} = 0$  (dihedral angle  $\approx 90^\circ$ ). However, H-16 of 11 is a quintuplet which overlaps the signal from H-13. Irradiation at  $\delta$  1.32 transforms this quintuplet into a doublet at  $\delta$  2.67 ( $J = 7$  Hz), which is in agreement with the assigned configuration of C-16 for 2, 7, 11, and 12. Also, the  $^{13}\text{C}$  NMR spectra provide additional support for the epimeric character of 11 and 12. Thus, chemical shifts of corresponding carbon atoms of the diketones are similar with the exception of those for C-12 and C-17 in 11 which appear upfield owing to steric compression. On the other hand the chemical shifts of these carbons in 12 indicate the absence of a  $\gamma$ -effect for C-12 and steric compression for C-17.

Chemical correlation of 8, 11, and 12 has also been achieved by hydrogenation of 8 to the epimers 13 and 14, which in turn yielded upon oxidation the previously described diketones 11 and 12. Usually, hydrogenation of *ent*-kaur-16-enes occurs from the *ent*- $\beta$ -side.<sup>20,22</sup> However, in this case the substituents at C-14 and C-15 hinder the  $\beta$ -face of the exocyclic methylene group, and a mixture of C-16 epimers is formed. Oxidation of 13 and 14 gave 11 and 12, respectively, as an additional proof of the epimeric character at C-16 of both compounds.

Another product (9, 12%) isolated from the mixture of rearrangement products from 6 was an *ent*-beyerane the structure of which was determined as follows. The  $^1\text{H}$  NMR spectrum of 9 shows three methyl singlet signals at  $\delta$  1.05, 1.01, and 0.85 (3 H each), which suggests that all three methyl groups are situated at nonoxygenated carbon atoms and indicates that the skeleton had remained unchanged. In addition to the AB quartet from the C-18 acetoxy methylene group, signals of another three protons attached to oxygenated carbons are evident. One of these signals [ $\delta$  3.22 (d,  $J = 2$  Hz)] can be assigned to H-14. The other two signals can be described as an AB quartet [ $\delta$  4.05 and 4.25 ( $J = 3.5$  Hz)] the doublet at  $\delta$  4.25 showing further weak coupling (possibly a  $W$  coupling). Taking into account the above spectroscopic evidence, it seemed reasonable to postulate the presence of an *ent*-beyerane with hydroxylation at C-14, C-15, and C-16 which resulted from nucleophilic opening of the original epoxy group by dorsal

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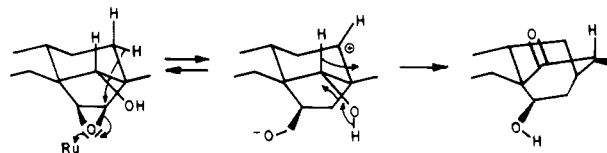


attack on C-16 to give an *ent*-14 $\beta$ ,15 $\beta$ ,16 $\beta$ -trihydroxy derivative. Dorsal attack on C-15 is difficult because the *ent*- $\beta$ -side of C-15 is spatially hindered.  $^{13}\text{C}$  NMR experiments confirmed the structure proposed for 9. For this purpose *ent*-14 $\beta$ -acetoxy-18-hydroxybeyer-15-ene (15) was saponified to give the dihydroxy derivative 16 (Scheme I). Acetylation at C-18 yielded 17, which was then hydrogenated to the dihydro derivative 18. A comparison of the chemical shifts of C-12 for 9 and 18 ( $\delta$  33.45 and 38.68, respectively) indicated a  $\gamma$ -effect for C-12 in 9 which is only compatible with *ent*- $\beta$ -disposition of the C-16 hydroxyl group of 9. On the other hand, the chemical shift of C-7 for 9 ( $\delta$  28.64) clearly indicates the presence of a  $\gamma$ -gauche effect from an *ent*-15 $\alpha$ -hydroxyl group ( $\delta$  35.21 for 18). Thus we conclude that the structure of 9 is *ent*-18-acetoxy-14 $\beta$ ,15 $\alpha$ ,16 $\beta$ -trihydroxybeyerane.

The minor product (10, 8%) isolated from the reaction was a ketone. The  $^1\text{H}$  NMR spectrum exhibited two methyl singlets [ $\delta$  0.97 and 0.86 (3 H each)] and one methyl doublet [ $\delta$  1.19 ( $J = 7$  Hz, 3 H)], was quite different from that of the *ent*-kaurane 7, which was also isolated from this same process, and suggested the presence of a secondary alcohol (presumably as a result of the opening of original epoxy group in 6) whose geminal proton gave a broad signal at  $\delta$  4.30 (1 H, br d,  $J = 8$  Hz). Treatment of 10 with NaOD/D $_2$ O to give 19 transformed the methyl doublet signal into a singlet. As described in previous papers, *ent*-kauranes and *ent*-beyeranes are related to *ent*-atisane systems<sup>10,11</sup> in Wenkert's biogenetic hypothesis.<sup>14,17</sup> All in all we believe that 10 has an *ent*-atisane structure, whose formation (Chart II) is the result of a 12  $\rightarrow$  16 hydride shift and subsequent conversion to an *ent*-(16*S*)-atisane structure if a concerted rearrangement is assumed.

The  $^{13}\text{C}$  NMR spectrum of 10 was also in agreement<sup>23-25</sup> with the structure of *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16*S*)-

Chart II



atisan-15-ene. Formation of atisanes from epoxybeyeranes has not been reported in previous papers<sup>1,3-5,7</sup> and we believe that the mobility of the proton at C-14 in product 6 is decisive for this rearrangement pathway.

In addition to the abovementioned products 7-10, 40 mg (20%) of starting material 6 was recovered.

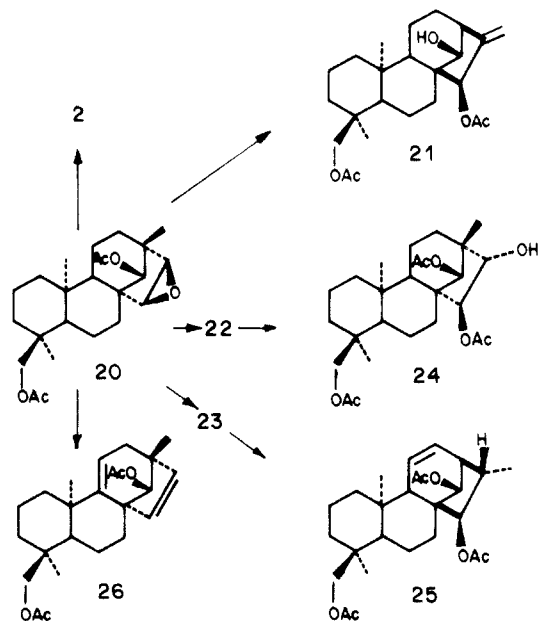
Additional rearrangements were carried out with *ent*-14 $\alpha$ ,18-diacetoxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (20) as starting material. Treatment of 20 with ruthenium acetylacetonate under conditions similar to those described for 1, 3, and 6 led to a mixture from which five products were isolated. One of these products (13%) was identical with 2. Another product (21, 12%) had  $^1\text{H}$  NMR signals attributable to an exo-methylene group and two methyl singlets at  $\delta$  1.05 and 0.85 (3 H each), which seemed to indicate that the skeleton of 21 was that of an *ent*-kaur-16-ene or an *ent*-atis-16-ene. Other significant resonances included a signal attributable to an allylic proton and geminal to an acetoxy group [ $\delta$  5.52 (1 H,  $W_{1/2} = 6$  Hz) which might be that of H-15 in both possible skeletons and a one-proton singlet at  $\delta$  4.27, similar to that found for H-14 in 2, 4, 5, 7, 8, 13, and 14. As this signal is characteristic of a proton geminal to an *ent*-14 $\alpha$ -hydroxyl group on an *ent*-kaurane skeleton we believe that 21 is an *ent*-18-acetoxy-14 $\alpha$ -hydroxykaur-16-ene which is also acetoxyated at C-15. The substantial deshielding for H-15 indicates that this proton is spatially close to the hydroxyl group at C-14 which is useful for deducing the configurations both at C-14 and C-15. The  $^{13}\text{C}$  NMR spectrum of 21 confirmed the proposed structure by comparison with spectral data published for some *ent*-15 $\alpha$ -acetoxykaur-16-enes.<sup>20</sup>

The rearrangement of 20 also gave a mixture of 22 and 23 whose separation proved unsuccessful with out chro-

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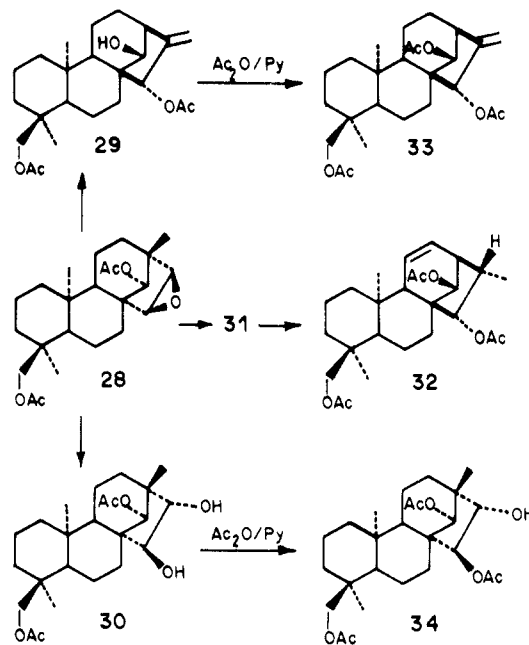
matographic procedures. After acetylation of the mixture, 24 and 25 were isolated in 4% and 9% yields, respectively. Product 24 retained the *ent*-beyerane skeleton as indicated by three methyl singlet signals together with three acetoxy groups. Two of the proton geminal to these acetoxy groups appeared as a sharp doublet at  $\delta$  5.58 (1 H,  $J = 4$  Hz) and a sharp singlet at  $\delta$  4.65 (1 H), respectively. Signals of an AB quartet (acetoxy-methylene group at C-18) partially overlapping a doublet signal at  $\delta$  3.70 (1 H,  $J = 4$  Hz) were also seen. Double resonance experiments confirmed that the doublet signals at  $\delta$  5.58 and 3.70 were those of an AB quartet. Taking into account the structure of starting material 20, we believe that product 24 is *ent*-14 $\alpha$ ,15 $\alpha$ ,18-triacetoxy-16 $\beta$ -hydroxybeyerane, which results from hydration of original epoxy group by dorsal attack on C-16 as found above in 9. The  $W$  coupling previously observed between H-14 and H-15 protons of 9 has not been observed for 24 which proves that 9 and 24 are C-14 epimers. In addition, the notable deshielding of H-14 in 24 shows the spatial proximity of this proton to the acetoxy group at C-15. The  $^{13}\text{C}$  NMR spectrum of 24 is also in agreement with the structure assigned.

The  $^1\text{H}$  NMR spectrum of the other triacetate (25), isolated from the mixture with 24, showed two methyl singlets and one methyl doublet which were indicative of an *ent*-kaurane or an *ent*-atisane skeleton. Double resonance experiments as outlined below allowed us to rule out the *ent*-atisane skeleton and led to formulation of 25 as an *ent*-kaur-11-ene on the basis of the following data: a one-proton at  $\delta$  6.07 signal (ddd,  $J_1 = 10$  Hz,  $J_2 = 7.5$  Hz,  $J_3 = 2$  Hz) may be attributed to the vinylic H-11 proton. Irradiation at  $\delta$  2.30 (1 H, presumably H-13) removes the third coupling constant which is due to  $W$  coupling between H-11 and H-13. This same irradiation transforms a one-proton signal at  $\delta$  5.40 (dd,  $J_1 = 10$  Hz,  $J_2 = 3.5$  Hz) into a sharp doublet ( $J = 10$  Hz) which is assigned to H-12. Moreover, a narrow multiplet at  $\delta$  5.51 (1 H, m,  $W_{1/2} = 4$  Hz) is transformed into a singlet which is assigned to H-14. A doublet at  $\delta$  4.70 (1 H, d,  $J = 4$  Hz) was unaltered by irradiation at H-13, and was assigned to H-15 geminal to an *ent*-15 $\alpha$ -acetoxy group. Besides, this stereochemistry is assumed when the acetoxy group is the original *ent*-14 $\alpha$ -acetoxy group in the starting material (20). The value of the coupling constant ( $J = 4$  Hz) indicated that if H-15 is *ent*- $\beta$ , H-16 (to which it is coupled) must be *ent*- $\alpha$  be-

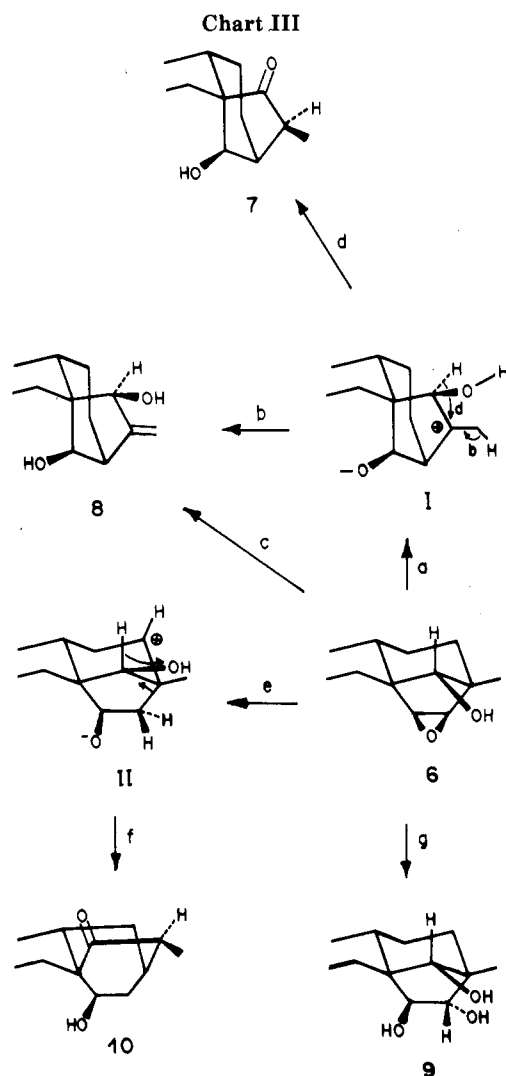
cause (after consideration of the influence of the electro-negative acetoxy group) a dihedral angle of  $120^\circ$  agrees best with this value.  $^{13}\text{C}$  NMR experiments on 25 confirmed the presence of the abovementioned groups<sup>26</sup> which led us to propose the structure of *ent*-14 $\alpha$ ,15 $\alpha$ ,18-triacetoxy-(16S)-kaur-11-ene for 25. Comparison with the  $^1\text{H}$  NMR spectrum of the original mixture of products before acetylation confirmed that the acetate group introduced on acetylation is the one situated at C-15 in 22 and at C-14 in 23.

The minor product isolated from the rearrangement of 20 was a diacetate (26, 4%) which had ( $^{13}\text{C}$  NMR) four ethylenic (three methyne and one quaternary) carbon atoms as well as four quaternary aliphatic carbons. As its  $^1\text{H}$  NMR spectrum showed three methyl singlets 26 was assumed to be an *ent*-beyer-9(11),15-diene, which was confirmed by the analysis of the other signals. Thus, in addition to vinylic signals, a one-proton singlet at  $\delta$  4.66 and an AB quartet [ $\delta$  3.90 and 3.65 ( $J = 12$  Hz)] indicated the presence of oxygenated functions similar to those shown by the starting material (20). Taking into account this spectroscopic evidence we obtained the structure of *ent*-14 $\alpha$ ,18-diacetoxybeyer-9(11),15-diene for product 26. Hydrogenation of  $\Delta^{9,11}$  with Pd on  $\text{BaSO}_4$  and Pt on carbon (5 atm) was unsuccessful (see Experimental Section).

Epoxidation of *ent*-14 $\beta$ ,18-diacetoxybeyer-15-ene (27) gave an epoxide (28) (Scheme I), which on treatment with ruthenium acetylacetonate under conditions similar to those indicated for 1, 3, 6, and 20 gave 29 (10%), 30 (9%), and 31 (as triacetate 32, 6%).



Product 29 shows IR bands for hydroxyl and acetoxy groups and an exo-methylene double bond. The  $^1\text{H}$  NMR spectrum had a signal at  $\delta$  5.25 (2 H, br s), indicative of an *ent*-kaur-16-ene system, which was confirmed by the presence of a signal at  $\delta$  2.83 (1 H, m,  $W_{1/2} = 8$  Hz) due to H-13. In addition to an AB quartet of the acetoxy-methylene group at C-18 [ $\delta$  3.85 and 3.62 ( $J = 12$  Hz)], a narrow multiplet at  $\delta$  4.12 (1 H, m,  $W_{1/2} = 4$  Hz), and another broad singlet at  $\delta$  5.37 (1 H) were present. Taking into account the structure of starting material 28, 29 must be *ent*-15 $\beta$ ,18-diacetoxy-14 $\alpha$ -hydroxykaur-16-ene which was confirmed by its  $^{13}\text{C}$  NMR spectrum, which had



chemical shifts similar to those of its C-15 spimer (21) with the exception of C-7 and C-9, and is therefore in agreement with the stereochemistry proposed for both 21 and 29. Acetylation of 29 gave 33 whose  $^1\text{H}$  NMR spectrum confirmed that the free hydroxyl of 29 was at C-14. Acetylation of 8 gave 33.

Product 30 was saturated (IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR), had three methyl singlet signals ( $^1\text{H}$  NMR), and seemed to be an *ent*-beyerane with an acetoxymethylene group at C-18 and a narrow doublet ( $^1\text{H}$  NMR) at  $\delta$  4.69 ( $J = 2$  Hz), possibly due to a proton geminal to an *ent*-14 $\beta$ -acetoxyl group. In addition, the  $^1\text{H}$  NMR spectrum of 30 showed a sharp doublet at  $\delta$  3.95 (1 H,  $J = 4$  Hz), practically unmodified in the acetate 34 (1 H, dd,  $J_1 = 4$  Hz,  $J_2 = 2$  Hz). That 30 was *ent*-14 $\beta$ ,18-diacetoxy-15 $\alpha$ ,16 $\beta$ -dihydroxybeyerane was confirmed by comparison of the  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra with those of 24, which indicated that 24 and 30 must be C-14 epimers.

Compound 31 was isolated in the form of its acetate 32, whose  $^1\text{H}$  NMR spectrum was similar to that of 25, showing signals of a C-11/C-12 double bond, an acetoxyl group at C-14, and a methyl doublet of C-17, as well as another signal, attributable to a proton at C-15 geminal to an acetoxyl group. Product 32 must be the C-15 epimer of 25 as H-15 at  $\delta$  4.95 is a doublet with  $J = 8$  Hz, showing that H-15 and H-16 are syn, in contrast with  $J = 4$  Hz for the corresponding signal of 25. Comparison of the  $^{13}\text{C}$  NMR spectrum of 32 with that of 25 confirmed this deduction. Hydrogenation of 32 gave 35, which was also obtained by acetylation of 14. Hence 32 is *ent*-

#### 14 $\alpha$ ,15 $\beta$ ,18-triacetoxy-(16*S*)-kaur-11-ene.

The rearrangement of 1 seems to occur in a concerted manner because there is an all-*trans* disposition of the migrating bonds. On the other hand, the stereochemistry at C-14 in starting material 6 is not appropriate for a concerted rearrangement, and hence a series of possibilities are open to give a series of very different products. Presumably, the catalyzed opening of the oxirane ring gives (via a in Chart III) carbocation I which may evolve toward the unsaturated compound 8 (via b) although this product (8) can also be obtained by a one-step process from 6 (via c). On the other hand, carbocation I may give 7 (via d) by migration of the H-15 proton which determines the configuration at C-16 of 7. Another pathway is opening of the oxirane ring and a 12  $\rightarrow$  16 hydride shift to give carbocation II in a manner similar to what was predicted in the case of solvolytic reactions.<sup>10,11</sup> The latter may evolve (via f) toward 10 by concerted migration of bond 16  $\rightarrow$  13 to 16  $\rightarrow$  12 on the *ent*- $\beta$ -side together with migration of H-14 to C-16 on the *ent*- $\alpha$ -side and loss of the hydroxylic proton to give the *ent*-*antis*-15-one (10). This concerted process (f) is decisive for the resulting configuration at C-16. The previously predicted, but not previously observed, formation of an *ent*-*atis*-anic compound from a beyerane functionalized at C-16<sup>10,11</sup> is of interest. Product 9 may be formed from 6 by dorsal attack on C-16 (via g) by a hydroxylic species.

The structures of the products isolated from the rearrangement of 20 are also in agreement with the postulate of a carbocation similar to II of Chart III, but in this case participation of the *ent*-14 $\alpha$ -acetoxyl group seems to be involved: this is diagrammed in Chart IV. Opening of

the oxirane ring (via a) gives carbocation III, which may evolve with (via b) or without participation of acetoxy group toward 21. Product 22 is the result of dorsal attack on C-16 in 20. In addition to skeletal rearrangements and nucleophilic addition, 20 gives 24, whose formation could be explained as follows: Opening of the oxirane ring produces in this case a 12 → 16 hydride shift (via c) to give a C-12 carbocation, which might be stabilized by the axial acetoxy group at C-14, through an 1,3-dioxan-2-ylum cation (as described in IV), which may evolve toward a  $\Delta^{9,11}$  derivative due to the transperiplanar disposition of the leaving groups. However, this double bond can also be obtained without participation of such axial acetoxy group as will be seen later. On the other hand, elimination may produce a  $\Delta^{15}$  double bond in a manner similar to that found in solvolytic reactions of 15-(tosyloxy)beyeranes.<sup>7</sup> Participation of the C-14 acetoxy group of 20 could also explain formation of 23. Thus, 20 gives III, which by a 12 → 16 hydride shift could produce (via d, giving V) the C-16 configuration of 23 and the elimination of the *ent*-11 $\beta$ -H because the ring C of the *ent*-kaurane species V has a certain mobility, thus allowing stabilization by means of a new 1,3-dioxepan-2-ylum cation (VI) in which there is a transperiplanar disposition of the leaving group and *ent*-11 $\beta$ -H. Formation of a  $\Delta^{9,11}$  derivative (23) can also be explained if one assumes opening of the oxirane ring by C-15<sup>7</sup> and elimination of H-9, although it is unlikely because no diterpenoid functionalized at C-12 has so far been isolated.<sup>7</sup> On the other hand, formation of 1,3-dioxan-2-ylum and related cations is well-known, and also its participation in similar processes is described in this paper.<sup>27</sup>

The formation of 2 could be explained as in Chart IV via e from III, which is in agreement with the C-16 configuration of 2.

As has been mentioned, the products isolated from the rearrangement of 28 are similar to those obtained from the rearrangement of its C-14 epimer (20). Thus we conclude that the *ent*-14 $\alpha$ -hydroxyl group determines the course of the rearrangement reaction. As concerns the other three types of C-14 substituents, the results are similar to some extent except for differences in the relative amounts of the products.

The rearrangements of C-14-substituted epoxybeyerenes described in this paper have led to several derivatives not reported in previous studies of such rearrangements.<sup>1-12</sup> The C and D rings functionalization of some of the products is similar to those of *ent*-kaurenoids isolated from *Pteris plumbaea*<sup>21</sup> and Japanese *Isodon*,<sup>28,29</sup> rastronols,<sup>30</sup> and grayanotoxins,<sup>31</sup> and the beyer-9(11),15-dienes are similar to those isolated from *Dimorphoteca aurantica*.<sup>32</sup>

### Experimental Section

Melting points (Koffler apparatus) are uncorrected. <sup>1</sup>H NMR measurements were made on CDCl<sub>3</sub> solutions at 80 MHz in a Bruker WP80SY spectrometer with Me<sub>4</sub>Si as internal standard. <sup>13</sup>C NMR measurements were made at 20.13 MHz, in CDCl<sub>3</sub> (which also provided the lock signal) and with Me<sub>4</sub>Si as internal

reference. Assignments of <sup>13</sup>C chemical shifts were made with the aid of distortionless enhancement by polarization transfer (DEPT) using a flip angle of 135°. IR spectra were recorded on a Perkin-Elmer 983 grating infrared spectrometer. The rotatory powers were measured on a Perkin-Elmer 240 polarimeter. Silica gel, Merck 7729 (less than 0.08 mm), was used for flash chromatography. The columns were pressurized to 1.00 atm with N<sub>2</sub> or air. Columns' size: column A, for 100–200 mg of mixture, i.d. 19 mm, 9 g of silica gel ( $\approx$ 4 cm); column B, for 30–100 mg of mixture, i.d. 17 mm, 7 g of silica gel ( $\approx$ 4 cm); column C, for 2–30 mg of mixture, i.d. 11.5 mm, 3 g of silica gel ( $\approx$ 4 cm). Eluents [rapid gradients of increasing polarity were used]: CH<sub>2</sub>Cl<sub>2</sub>/acetone, 100:1 to 2:1 mixtures according to polarity of products. Fractions of eluents: 6–8 fractions of 40 (column A), 30 (column B), and 20 mL (column C). Fractions of eluates:  $\approx$ 7 (column A),  $\approx$ 5 (column B), and  $\approx$ 3 mL (column C). Analytical plates (silica gel Merck G) were sprayed with H<sub>2</sub>O/H<sub>2</sub>SO<sub>4</sub>/AcOH (30:10:160) and then heated at 120 °C for 5 min. Unless otherwise mentioned solids were crystallized from hexane/chloroform.

**Isolation of Starting Product.** The *ent*-14 $\beta$ -acetoxy-18-hydroxybeyer-15-ene (tartresol, 15) utilized as starting product for this work was isolated from *Sideritis pusilla* subsp. *flavovirens*.<sup>33</sup>

**Preparation of *ent*-18-Acetoxy-14 $\alpha$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (1).** Product 15 (3 g) was dissolved in 100 mL of MeOH/H<sub>2</sub>O/KOH (70:30:5) and refluxed for 5 h, diluted with H<sub>2</sub>O (100 mL), neutralized with HCl (2 N), extracted with CH<sub>2</sub>Cl<sub>2</sub>, dried with MgSO<sub>4</sub>, and concentrated under vacuum. After column chromatography (CC) 2.7 g of *ent*-14 $\beta$ ,18-dihydroxybeyer-15-ene (16) was isolated: mp 183–185 °C; [ $\alpha$ ]<sub>D</sub><sup>20</sup> +15° (c 1.88, CHCl<sub>3</sub>); IR  $\nu_{\max}$  (KBr, cm<sup>-1</sup>) 3400, 3050, 1447, 1386, 1200, 1105, 1055, 960, and 745; <sup>1</sup>H NMR  $\delta$  5.45 and 5.70 (2 H, q<sub>AB</sub>, *J* = 6 Hz, H-15 and H-16), 3.10 and 3.42 (2 H, q<sub>AB</sub>, *J* = 12 Hz, 2 H-18), 2.95 (1 H, s, H-14), 1.05, 0.81, and 0.77 (3 H each, s, methyl groups). Anal. Found: C, 78.72; H, 10.99. Calcd for C<sub>20</sub>H<sub>32</sub>O<sub>2</sub>: C, 78.90; H, 10.59. Product 16 (2.7 g) was acetylated with Py/Ac<sub>2</sub>O (50:25 mL) for 2 h at 0 °C, after which it was poured onto cold water (200 mL) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 50 mL). The organic layer was washed with aqueous HCl (5%) (2 × 25 mL), water (25 mL), aqueous HNaCO<sub>3</sub> (5%) (25 mL), and water (25 mL), dried with MgSO<sub>4</sub>, and concentrated in vacuum. After CC *ent*-18-acetoxy-14 $\beta$ -hydroxybeyer-15-ene (17, 1.89 g, 61%) was obtained: mp 84–86 °C; [ $\alpha$ ]<sub>D</sub><sup>20</sup> +32° (c 1, CHCl<sub>3</sub>); IR  $\nu_{\max}$  (KBr, cm<sup>-1</sup>) 3500, 3055, 1735, 1450, 1385, 1260, and 740; <sup>1</sup>H NMR  $\delta$  5.66 and 5.45 (2 H, q<sub>AB</sub>, *J* = 6 Hz, H-15 and H-16), 3.90 and 3.62 (2 H, q<sub>AB</sub>, *J* = 12 Hz, 2 H-18), 2.97 (1 H, s, H-14), 2.06 (3 H, s, AcO group), 1.05, 0.85, and 0.80 (3 H each, s, methyl groups). Anal. Found: C, 75.92; H, 10.11. Calcd for C<sub>22</sub>H<sub>34</sub>O<sub>3</sub>: C, 76.26; H, 9.89. Product 17 (1.4 g) was dissolved in acetone (50 mL) and was oxidized with Jones's reagent,<sup>34</sup> stopped with a few drops of MeOH, diluted with H<sub>2</sub>O (100 mL), extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 50 mL), dried with MgSO<sub>4</sub> and evaporated under vacuum. After CC *ent*-18-acetoxybeyer-15-en-14-one (36, 1.2 g, 86%) was isolated: mp 146–148 °C. [ $\alpha$ ]<sub>D</sub><sup>20</sup> +13.3° (c 1, CHCl<sub>3</sub>); IR  $\nu_{\max}$  (KBr, cm<sup>-1</sup>) 3060, 1730, 1440, 1380, 1240, 1020, and 740; <sup>1</sup>H NMR  $\delta$  6.12 and 5.90 (2 H, q<sub>AB</sub>, *J* = 6 Hz, H-15 and H-16), 3.87 and 3.62 (2 H, q<sub>AB</sub>, *J* = 12 Hz, 2 H-18), 2.07 (3 H, s, AcO group), 1.05, 0.92, and 0.85 (3 H each, s, methyl groups). Anal. Found: C, 76.33; H, 9.81. Calcd for C<sub>22</sub>H<sub>32</sub>O<sub>3</sub>: C, 76.70; H, 9.36. Product 36 (850 mg) was dissolved in EtOH (20 mL), and NaBH<sub>4</sub> (200 mg) was added. The mixture was stirred at room temperature for 12 h. The solution was slowly acidified with HCl (2 N), diluted with H<sub>2</sub>O (50 mL), and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 50 mL). The organic layer was dried with MgSO<sub>4</sub> and concentrated under vacuum. After CC *ent*-18-acetoxy-14 $\alpha$ -hydroxybeyer-15-ene (37, 577 mg, 67%) was obtained: mp 142–144 °C; [ $\alpha$ ]<sub>D</sub><sup>20</sup> +14.7° (c 1, CHCl<sub>3</sub>); IR  $\nu_{\max}$  (KBr, cm<sup>-1</sup>) 3500, 3050, 1725, 1450, 1380, 1260, 1110, 960, and 745; <sup>1</sup>H NMR  $\delta$  5.75 and 5.52 (2 H, q<sub>AB</sub>, *J* = 6 Hz, H-15 and H-16), 3.86 and 3.65 (2 H, q<sub>AB</sub>, *J* = 12 Hz, 2 H-18), 3.02 (1 H, s, H-14), 2.05 (3 H, s, AcO group), 0.95, 0.82, and 0.80 (3 H each, s, methyl groups). Anal. Found: C, 76.30; H, 10.16. Calcd for C<sub>22</sub>H<sub>34</sub>O<sub>3</sub>: C, 76.20;

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Table I.  $^{13}\text{C}$  NMR Chemical Shifts ( $\delta$ ) of Products 1-4 and 11

C	1	2	3	4	11
1	38.71	38.93	38.85	38.92	38.94
2	17.82	17.78	17.80	17.76	17.68
3	35.75	35.64	35.85	35.62	35.69
4	36.39	36.51	36.54	36.49	36.49
5	49.57	49.36	49.65	49.36	50.30
6	19.48	18.37	19.55	18.37	18.21
7	29.82	25.67	29.93	25.66	24.86
8	44.72	58.04	44.75	58.04	60.86
9	46.14	54.87	46.32	54.86	63.68
10	36.91	39.79	37.07	39.76	39.99
11	17.68	17.78	17.80	17.76	17.51
12	27.86	25.67	27.94	29.28	25.66
13	40.11	42.53	40.16	42.43	48.48
14	75.85	73.73	75.11	73.66	214.52
15	55.26	223.29	55.36	223.50	219.94
16	58.92	41.83	58.99		48.48
17	19.14	9.32	19.20	9.22	8.60
18	73.20	72.66	73.24	72.67	72.62
19	17.45	18.23	17.62	18.21	17.51
20	16.02	17.46	16.16	17.44	15.66
MeCOO	20.89	21.10	21.05	21.07	21.06
MeCOO	171.25	171.43	171.41	171.42	171.22

H, 9.89. Product 37 (150 mg) was dissolved in  $\text{CHCl}_3$  (20 mL) and epoxidized with *m*-chloroperbenzoic acid (MCPBA) (150 mg) for 12 h at 0 °C. The mixture was diluted with  $\text{CHCl}_3$  (20 mL), washed with aqueous  $\text{FeSO}_4$  (10%) ( $2 \times 10$  mL), aqueous  $\text{HNaCO}_3$  (5%) ( $3 \times 20$  mL), and  $\text{H}_2\text{O}$  (20 mL), dried with  $\text{MgSO}_4$ , and concentrated under vacuum. After CC *ent*-18-acetoxy-14 $\alpha$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (1, 135 mg, 86%) was obtained: mp 157–159 °C;  $[\alpha]_D^{20} +5.4^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3520, 1730, 1455, 1380, 1230, 1085, 1030, 865, and 810;  $^1\text{H}$  NMR  $\delta$  3.82 and 3.58 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.48 and 3.07 (2 H,  $q_{\text{AB}}$ ,  $J = 4$  Hz, H-15 and H-16), 2.89 (1 H, s, H-14), 2.00 (3 H, s, AcO group), 0.97, 0.92, and 0.80 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR, see Table I. Anal. Found: C, 72.80; H, 9.50. Calcd for  $\text{C}_{22}\text{H}_{34}\text{O}_4$ : C, 72.89; H, 9.45.

**Preparation of *ent*-18-Acetoxy-14 $\beta$ -deuterio-14 $\alpha$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (3).** Product 36 (310 mg) was dissolved in EtOH (10 mL), and 150 mg of  $\text{NaBD}_4$  was added. The mixture was stirred at room temperature for 2 h. After CC *ent*-18-acetoxy-14 $\beta$ -deuterio-14 $\alpha$ -hydroxybeyer-15-ene (38, 175 mg, 56%) was isolated: mp 140–142 °C.  $[\alpha]_D^{20} +16.3^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3500, 3050, 1725, 1448, 1380, 1108, 963, and 745;  $^1\text{H}$  NMR  $\delta$  5.67 and 5.45 (2 H,  $q_{\text{AB}}$ ,  $J = 6$  Hz, H-15 and H-16), 3.80 and 3.57 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.00 (3 H, s, AcO group), 0.90, 0.79, and 0.75 (3 H each, s, methyl groups). Anal. Found: C, 76.08; H, 10.32. Calcd for  $\text{C}_{22}\text{H}_{33}\text{DO}_3$ : C, 76.04;

H, 10.15. Product 38 (100 mg) was dissolved in  $\text{CHCl}_3$  (10 mL) and epoxidized with MCPBA (100 mg) for 12 h at room temperature, yielding, after CC, 73 mg of *ent*-18-acetoxy-14 $\beta$ -deuterio-14 $\alpha$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (3, 70%): mp 156–158 °C;  $[\alpha]_D^{20} +4.5^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3500, 1735, 1450, 1380, 1240, 1075, 1030, 870, and 810;  $^1\text{H}$  NMR  $\delta$  3.88 and 3.65 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.65 and 3.15 (1 H each, d,  $J = 3$  Hz, H-15 and H-16), 2.06 (3 H, s, AcO group), 1.03, 0.97, and 0.87 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR, See Table I. Anal. Found: C, 72.50; H, 9.83. Calcd for  $\text{C}_{22}\text{H}_{33}\text{DO}_4$ : C, 72.69; H, 9.70.

**Preparation of *ent*-18-Acetoxy-14 $\beta$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (6).** Product 17 (270 mg) was dissolved in  $\text{CHCl}_3$  (25 mL), and MCPBA (200 mg) was added. After 2 h at room temperature and CC *ent*-18-acetoxy-14 $\beta$ -hydroxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (6, 230 mg, 81%) was isolated: mp 131–133 °C;  $[\alpha]_D^{20} +16.7^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3520, 1730, 1455, 1380, 1230, 1085, 1030, 865, and 810;  $^1\text{H}$  NMR  $\delta$  3.92 and 3.65 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.67 (1 H, dd,  $J_1 = 3$  Hz,  $J_2 = 2$  Hz) (H-15 and H-16), 2.72 (1 H, br s, H-14), 2.06 (3 H, s, AcO group), 1.16, 0.97, and 0.87 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table II. Anal. Found: C, 72.77; H, 9.57. Calcd for  $\text{C}_{22}\text{H}_{34}\text{O}_4$ : C, 72.89; H, 9.45).

**Preparation of *ent*-14 $\alpha$ ,18-Diacetoxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (20).** Product 37 (350 mg) was acetylated with  $\text{Py}/\text{Ac}_2\text{O}$  (6:3 mL) and refluxed for 2 h. After CC *ent*-14 $\alpha$ ,18-diacetoxybeyer-15-ene (39, 332 mg, 84%) was isolated: mp 118–120 °C;  $[\alpha]_D^{20} +25^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3060, 1739, 1441, 1369, 1237, 1045, and 757;  $^1\text{H}$  NMR  $\delta$  5.76 and 5.52 (2 H,  $q_{\text{AB}}$ ,  $J = 6$  Hz, H-15 and H-16), 4.45 (1 H, s, H-14), 3.86 and 3.68 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.12 and 2.05 (3 H each, s, AcO groups), 0.90, 0.86, and 0.82 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR, see Table III. Anal. Found: C, 74.02; H, 9.48. Calcd for  $\text{C}_{24}\text{H}_{36}\text{O}_4$ : C, 74.19; H, 9.34. Product 39 (325 mg) was epoxidized with MCPBA (300 mg) in  $\text{CHCl}_3$  (20 mL) for 2 days at room temperature. After CC *ent*-14 $\alpha$ ,18-diacetoxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (20, 300 mg, 88%) was obtained: gum;  $[\alpha]_D^{20} +13.3^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 1740, 1445, 1380, 1220, and 870;  $^1\text{H}$  NMR  $\delta$  4.41 (1 H, s, H-14), 3.90 and 3.67 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.59 and 3.16 (1 H each, d,  $J = 3$  Hz, H-15 and H-16), 2.14 and 2.06 (3 H each, s, AcO groups), 1.00 (6 H, s, methyl groups), 0.90 (3 H, s, methyl group);  $^{13}\text{C}$  NMR, see Table III.

**Preparation of *ent*-14 $\beta$ ,18-Diacetoxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (28).** Product 15 (300 mg) was acetylated with  $\text{Py}/\text{Ac}_2\text{O}$  (6:3 mL) and refluxed for 2 h. After CC *ent*-14 $\beta$ ,18-diacetoxybeyer-15-ene (27, 275 mg, 82%) was isolated: mp 150–152 °C;  $[\alpha]_D^{20} +25.4^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 1735, 1450, 1380, 1230, 1085, 1030, and 865;  $^1\text{H}$  NMR  $\delta$  5.67 and 5.44 (2 H,  $q_{\text{AB}}$ ,  $J = 6$  Hz, H-15 and H-16), 4.51 (1 H, s, H-14), 3.87 and 3.60 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.09 and 2.05 (6 H, s, AcO groups), 0.96, 0.85, and 0.82 (3 H each, s, methyl groups). Anal. Found: C,

Table II.  $^{13}\text{C}$  NMR Chemical Shifts ( $\delta$ ) of Products 6–12 and 18

C	6	7	8	9	10	12	18
1	38.94	39.27	39.92	39.11	38.65	39.24	39.42
2	17.74	17.84	18.01	17.62	17.60	17.73	17.67
3	35.65	35.60	35.68	35.66	35.72	35.69	35.74
4	36.35	36.48	36.54	36.42	36.36	36.49	36.39
5	49.28	49.25	50.81	50.00	49.20	49.34	49.96
6	19.00	28.44	19.01	19.32	17.60	18.10	19.71
7	28.12	25.20	27.37	28.64	28.86	24.90	35.21
8	48.33	59.04	52.34	50.00	51.63	60.89	48.73
9	56.49	53.77	56.39	55.59	45.94	63.51	56.05
10	37.37	39.98	39.52	37.98	35.72	40.18	37.62
11	28.91	17.84	17.64	18.75	25.40	17.59	19.46
12	34.59	31.07	32.70	33.45	32.99	34.64	38.68
13	43.78	44.89	50.00	46.86	32.38	53.63	43.65
14	86.16	76.32	77.10	90.83	67.35	214.64	91.99
15	57.95	224.47	83.02	81.46	217.30	219.95	31.07
16	62.08	44.52	157.79	77.79	46.92	48.46	35.21
17	17.63	18.01	111.68	19.32	15.16	17.59	21.53
18	72.62	72.67	72.89	73.19	72.55	72.64	73.12
19	16.91	18.01	18.30	17.71	17.60	16.63	17.67
20	15.84	17.55	17.64	15.28	14.07	15.86	15.73
MeCOO	20.84	21.09	21.05	21.11	21.04	21.06	20.93
MeCOO	171.30	171.39	171.32	171.33	171.29	171.24	171.11



Table III.  $^{13}\text{C}$  NMR Chemical Shifts ( $\delta$ ) of Products 20, 21, 24-26, and 38

C	20	21	24	25	26	38
1	38.81	40.09	39.12	39.40	37.25	38.57
2	17.99	17.99	17.63	17.79	18.22	17.73
3	35.69	35.79	35.82	35.74	35.80	35.91
4	36.34	36.60	36.45	36.51	36.82	36.43
5	50.07	50.49	50.64	49.14	45.64	50.06
6	19.28	19.48	19.36	19.85	19.42	19.65
7	29.83	29.78	29.51	30.67	32.83	33.17
8	44.91	51.17	48.15	54.15	48.88	49.30
9	47.53	50.32	47.28	47.92	151.68	45.34
10	36.98	39.10	37.29		38.65	36.89
11	17.58	17.56	18.29	133.38	115.68	19.04
12	28.77	33.55	27.70	125.50	31.41	26.65
13	40.18	49.48	45.06	50.72	42.75	44.47
14	77.10	75.00	78.68	78.33	82.52	83.50
15	54.73	79.36	78.68	89.69	142.29	133.95
16	58.65	151.93	70.59	46.66	132.24	134.17
17	19.10	109.38	22.13	20.78	22.24	22.10
18	73.21	73.51	73.49	73.47	73.06	73.48
19	17.41	18.44	17.71	17.44	17.76	17.57
20	16.00	17.46	15.03	17.44	25.44	16.05
MeCOO	21.10	21.36	21.05	21.27	21.29	21.24
MeCOO	20.75	21.01	20.95	21.00	20.89	20.88
MeCOO			20.95	20.78		
MeCOO	170.91	171.25	171.13		171.48	171.04
MeCOO	170.34	171.25	171.13		171.48	170.75
MeCOO			169.61			

74.15; H, 9.40. Calcd for  $\text{C}_{24}\text{H}_{36}\text{O}_4$ : C, 74.19; H, 9.34. Product 27 (250 mg) was epoxidized with MCPBA (250 mg) in  $\text{CHCl}_3$  (20 mL) for 48 h at room temperature. After CC *ent*-14 $\beta$ ,18-diacetoxy-15 $\alpha$ ,16 $\alpha$ -epoxybeyerane (28, 215 mg, 83%) was isolated: gum;  $[\alpha]_D^{20}$  -7.2° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 1735, 1430, 1360, 1230, 1030, 870, 820, and 720;  $^1\text{H}$  NMR  $\delta$  4.40 (1 H, br s, H-14), 3.85 and 3.60 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.50 (1 H, overlapping to a doublet of the  $q_{\text{AB}}$  system) and 3.10 (1 H, dd,  $J_1 = 3$  Hz,  $J_2 = 1.5$  Hz) (H-15 and H-16), 2.02 (6 H, s, AcO groups), 1.00, 0.95, and 0.85 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table IV.

**Ruthenium-Catalyzed Rearrangement Procedure.** The starting material of each process (100 mg) were dissolved in  $\text{CHCl}_3$  (5 mL), and ruthenium acetylacetonate (10 mg) was added. The mixture was heated at 140 °C in a sealed tube, until extinction of starting material or nonevolution of resulting mixture (TLC). When reaction is achieved the initial orange-red color changes to deep-purple. Then, when the solution cools to room temperature, it is concentrated and directly chromatographed.

**Rearrangement of Product 1.** Product 1 (100 mg) was treated as indicated above for 1 h. After CC only *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16R)-kauran-15-one (2, 72 mg, 72%) was isolated: mp sublime;  $[\alpha]_D^{20}$  -82.3° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3479, 1734, 1713, 1382, 1244, and 1043;  $^1\text{H}$  NMR  $\delta$  4.65 (1 H, s, H-14), 3.87 and 3.62 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.72 (1 H, quintuplet,  $J_{13/16} = J_{16/17} = 7$  Hz, H-16), 2.47 (1 H, m,  $W_{1/2} = 8$  Hz, H-13), 2.09 (3 H, s, AcO group), 1.12 (3 H, d,  $J = 7$  Hz, 3 H-17), 1.07 and 0.82 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table I. Anal. Found: C, 72.94; H, 9.61. Calcd for  $\text{C}_{22}\text{H}_{34}\text{O}_4$ : C, 78.89; H, 9.45.

**Rearrangement of Product 3.** Product 3 (50 mg) was treated for 1 h. After CC only *ent*-18-acetoxy-16 $\beta$ -deuterio-14 $\alpha$ -hydroxykauran-15-one (4, 32 mg, 64%) was obtained: mp sublime;  $[\alpha]_D^{20}$  -84.8° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3500, 1734, 1713, 1380, 1245, and 1020.  $^1\text{H}$  NMR  $\delta$  4.62 (1 H, s, H-14), 3.87 and 3.62 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.10 (3 H, s, AcO group), 1.12, 1.07, and 0.84 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table I. Anal. Found: C, 72.76; H, 9.77. Calcd for  $\text{C}_{22}\text{H}_{33}\text{DO}_4$ : C, 72.69; H, 9.70.

**Rearrangement of Product 6.** Product 6 (200 mg) was treated for 3 h and yielded these products after CC: *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16S)-kauran-15-one (7, 55 mg, 28%), *ent*-18-acetoxy-14 $\alpha$ ,15 $\beta$ -dihydroxykaur-16-ene (8, 36 mg, 18%), *ent*-18-acetoxy-14 $\beta$ ,15 $\alpha$ ,16 $\beta$ -trihydroxybeyerane (9, 25 mg, 12%), *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16S)-atisan-15-one (10, 16 mg, 8%), and the starting product 6 (40 mg, 20%). Order of elution: 6, 7, 10, 9, and 8. Product 7: mp 178-179 °C;  $[\alpha]_D^{20}$  -66.6° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3450, 1730, 1720, 1380, 1245, and 1040;  $^1\text{H}$

Table IV.  $^{13}\text{C}$  NMR Chemical Shifts ( $\delta$ ) of Products 28-30 and 32

C	28	29	30	32
1	38.76	39.81	39.07	39.17
2	17.45	17.52	17.53	17.75
3	35.69	35.61	35.55	35.62
4	36.19	36.53	36.40	36.48
5	49.13	49.98	49.47	49.04
6	18.56	18.81	18.48	19.20
7	27.38	26.31	27.77	27.36
8	48.53	52.64	49.09	50.46
9	56.53	56.66	55.87	63.11
10	37.29	39.58	38.00	38.77
11	18.56	18.35	19.04	133.77
12	34.62	33.06	33.15	124.35
13	44.00	51.32	46.60	46.18
14	84.56	76.70	91.01	76.82
15	54.79	82.33	80.80	84.92
16	59.15		77.10	47.39
17	17.44	113.96	19.34	15.67
18	72.36	72.96	72.83	73.02
19	16.42	17.86	17.78	17.60
20	15.76	17.86	15.12	17.60
MeCOO	20.75	21.31	21.11	21.12
MeCOO	20.75	21.11	20.86	21.12
MeCOO				20.89
MeCOO	171.52	171.95	171.34	171.35
MeCOO	170.76			170.88
MeCOO				170.56

NMR  $\delta$  4.55 (1 H, br s, H-14), 3.87 and 3.66 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.20 (1 H, m,  $W_{1/2} = 10$  Hz, H-13), 2.09 (3 H, s, AcO group), 1.27 (3 H, d,  $J = 7$  Hz, methyl group at C-17), 1.06 and 0.82 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table II. Anal. Found: C, 72.57; H, 9.73. Calcd for  $\text{C}_{22}\text{H}_{34}\text{O}_4$ : C, 72.89; H, 9.45. Product 8: gum;  $[\alpha]_D^{20}$  -40.3° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3400, 1737, 1640, 1240, and 890;  $^1\text{H}$  NMR  $\delta$  5.41 and 5.21 (1 H each, s, 2 H-17), 4.22 (1 H, br s, H-14), 3.91 and 3.65 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.80 (1 H, br s, H-15), 2.82 (1 H, m,  $W_{1/2} = 8$  Hz, H-13), 2.07 (3 H, s, AcO group), 1.03 and 0.85 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table II. Product 9: mp 145-147 °C;  $[\alpha]_D^{20}$  -3.2° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3479, 1720, 1450, 1380, 1254, and 1039;  $^1\text{H}$  NMR  $\delta$  4.25 (1 H, m,  $W_{1/2} = 6$  Hz, H-15), 4.05 (1 H, d,  $J = 3.5$  Hz, H-16), 3.89 and 3.36 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.22 (1 H, d,  $J = 2$  Hz, H-14), 2.06 (3 H, s, AcO group), 1.05, 1.01, and 0.85 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table II. Anal. Found: C, 69.53; H, 9.73. Calcd for  $\text{C}_{22}\text{H}_{36}\text{O}_5$ : C, 69.44; H, 9.53. Product 10: mp 173-175 °C;  $[\alpha]_D^{20}$  -10° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3450, 1736, 1721, 1382, 1246, and 1033;  $^1\text{H}$  NMR  $\delta$  4.30 (1 H, br d,  $J = 8$  Hz, H-14), 3.87 and 3.62 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.07 (3 H, s, AcO group), 1.19 (3 H, d,  $J = 7$  Hz, 3 H-17), 0.97 and 0.86 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table II. Anal. Found: C, 72.52; H, 9.58. Calcd for  $\text{C}_{22}\text{H}_{34}\text{O}_4$ : C, 72.89; H, 9.45.

**Rearrangement of Product 20.** Product 20 (300 mg) was treated for 1 h, yielding five products which were isolated after CC: *ent*-15 $\alpha$ ,18-diacetoxy-14 $\alpha$ -hydroxykaur-16-ene (21, 35 mg, 13%), *ent*-14 $\alpha$ ,18-diacetoxybeyer-9(11),15-diene (26, 10 mg, 4%), *ent*-18-acetoxy-14 $\alpha$ -hydroxy-(16R)-kauran-15-one (2, 36 mg, 14%), and a mixture of two products which, after acetylation and CC, rendered *ent*-14 $\alpha$ ,15 $\alpha$ ,18-triacetoxy-16 $\beta$ -hydroxybeyerane (24, 15 mg, 4%) and *ent*-14 $\alpha$ ,15 $\alpha$ ,18-triacetoxy-(16S)-kaur-11-ene (25, 30 mg, 9%). Order of elution: 26, nonacetylated 24 and 25 (22 and 23, respectively), 21 and 2. Product 21: gum;  $[\alpha]_D^{20}$  -53.9° (c 0.75,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3454, 3060, 1738, 1665, 1250, 910, and 890;  $^1\text{H}$  NMR  $\delta$  5.52 (1 H, m,  $W_{1/2} = 6$  Hz, H-15), 5.07 (2 H, m,  $W_{1/2} = 4$  Hz, 2 H-17), 4.27 (1 H, br s, H-14), 3.86 and 3.67 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 2.17 and 2.05 (3 H each, s, AcO groups), 1.05 and 0.85 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table III. Product 24: gum;  $[\alpha]_D^{20}$  -9.5° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3450, 1744, 1445, 1369, 1228, and 1100;  $^1\text{H}$  NMR  $\delta$  5.58 (1 H, d,  $J = 4$  Hz, H-15), 4.65 (1 H, s, H-14), 3.85 and 3.61 (2 H,  $q_{\text{AB}}$ ,  $J = 12$  Hz, 2 H-18), 3.70 (1 H, d,  $J = 4$  Hz, H-16), 2.17, 2.14 and 2.05 (3 H each, s, AcO groups), 1.09, 0.90, and 0.82 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table III. Product 25: gum;  $[\alpha]_D^{20}$  -76° (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 1738, 1650, 1445,

1378, 1234, 1042, and 910;  $^1\text{H}$  NMR  $\delta$  6.07 (1 H, ddd,  $J_1 = 10$  Hz,  $J_2 = 7.5$  Hz,  $J_3 = 2$  Hz, H-11), 5.51 (1 H, m,  $W_{1/2} = 4$  Hz, H-14), 5.40 (1 H, dd,  $J_1 = 10$  Hz,  $J_2 = 3.5$  Hz, H-12), 4.70 (1 H, d,  $J = 3.5$  Hz, H-15), 3.87 and 3.64 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.30 (1 H, ddd,  $J_1 = 3.5$  Hz,  $J_2 = 2.5$  Hz,  $J_3 = 1.5$  Hz, H-13), 2.10 (6 H, s, AcO groups), 2.06 (3 H, s, AcO group), 1.22 (3 H, d,  $J = 7$  Hz, methyl group at C-17), 1.06 and 0.85 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR see Table III. Product 26: gum;  $[\alpha]_D^{20} +38.7^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3080, 1738, 1452, 1373, 1238, 1045, and 796;  $^1\text{H}$  NMR  $\delta$  6.17 and 5.30 (2 H,  $q_{AB}$ ,  $J = 6$  Hz, H-15 and H-16), 5.25 (1 H, m,  $W_{1/2} = 8$  Hz, H-11), 4.66 (1 H, s, H-14), 3.90 and 3.65 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.10 and 2.05 (3 H each, s, AcO groups), 1.10, 0.96, and 0.87 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR, see Table III.

**Rearrangement of Product 28.** Product 28 (200 mg) was treated for 2 h, yielding three products which were isolated after CC: *ent*-15 $\beta$ ,18-diacetoxy-14 $\alpha$ -hydroxykaur-16-ene (29, 20 mg, 10%), *ent*-14 $\beta$ ,18-diacetoxy-15 $\alpha$ ,16 $\beta$ -dihydroxybeyerane (30, 18 mg, 9%) and *ent*-14 $\alpha$ ,15 $\beta$ ,18-triacetoxy-(16S)-kaur-11-ene (32, 14 mg, 6%; isolated after acetylation of impurified 31). Product 29: gum;  $[\alpha]_D^{20} -27.8^\circ$  (c 0.5,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3450, 3060, 1736, 1454, 1369, 1242, 1032, 904 and 829;  $^1\text{H}$  NMR  $\delta$  5.37 (1 H, br s) and 5.25 (2 H, m,  $W_{1/2} = 4$  Hz) (H-15 and 2 H-17), 4.12 (1 H, m,  $W_{1/2} = 4$  Hz, H-14), 3.85 and 3.62 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.83 (1 H, m,  $W_{1/2} = 8$  Hz, H-13), 2.08 and 2.05 (3 H each, s, AcO groups), 1.02 and 0.82 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR; see Table IV. Product 30: gum;  $[\alpha]_D^{20} -16^\circ$  (c 0.5,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3455, 1737, 1454, 1378, 1241, and 1033;  $^1\text{H}$  NMR  $\delta$ , 4.69 (1 H, d,  $J = 2$  Hz, H-14), 4.30 (1 H, m,  $W_{1/2} = 8$  Hz, H-15), 3.95 (1 H, d,  $J = 4$  Hz, H-16), 3.85 and 3.60 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.10 and 2.06 (3 H each, s, AcO groups), 1.00, 0.90, and 0.82 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR, see Table IV. Product 32: gum;  $[\alpha]_D^{20} -33.8^\circ$  (c 0.5,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3065, 1740, 1235, 1042, and 910;  $^1\text{H}$  NMR  $\delta$  6.00 (1 H, ddd,  $J_1 = 10$  Hz,  $J_2 = 8$  Hz,  $J_3 = 2$  Hz, H-11), 5.40 (1 H, m,  $W_{1/2} = 4$  Hz, H-14) [overlapping to a signal centered at  $\delta$  5.34 (1 H, ddd,  $J_1 = 10$  Hz,  $J_2 = 3.5$  Hz,  $J_3 = 1.5$  Hz, H-12)], 4.95 (1 H, d,  $J = 8$  Hz, H-15), 3.85 and 3.62 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.60 (1 H, quintuplet,  $J = 8$  Hz, H-16), 2.35 (1 H, dd,  $J_1 = 8$  Hz,  $J_2 = 1.5$  Hz, H-9), 2.06 (9 H, s, AcO groups), 1.05 (3 H, s, methyl group), 0.95 (3 H, d,  $J = 8$  Hz, 3 H-17), 0.82 (3 H, s, methyl group);  $^{13}\text{C}$  NMR, see Table IV.

**Deuteration of Products 2, 7, and 10.** Product 2 (15 mg) was dissolved in  $(\text{CD}_3)_2\text{CO}$  (0.5 mL) and  $\text{D}_2\text{O}/\text{DO}^-$  (0.5 mL, 5%). The mixture was stirred for 2 h, after which it was concentrated under vacuum and extracted with  $\text{CH}_2\text{Cl}_2$ . After CC *ent*-16 $\beta$ -deuterio-14 $\alpha$ ,18-dihydroxykaur-15-ene (5, 9 mg, 60%) was isolated: mp sublime;  $[\alpha]_D^{20} -35.4^\circ$  (c 0.5, EtOH); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3437, 1715, 1450, 1380, and 1047;  $^1\text{H}$  NMR  $\delta$  4.65 (1 H, d,  $J = 2$  Hz, H-14), 3.68 and 3.11 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 1.10, 1.07, and 0.77 (3 H each, s, methyl groups). In the same conditions, product 7 (10 mg) yielded 5 (6 mg, 60%) and product 10 (10 mg) yielded *ent*-16 $\alpha$ -deuterio-14 $\alpha$ ,18-dihydroxykaur-15-ene (19, 6 mg, 60%):  $^1\text{H}$  NMR  $\delta$  4.35 (1 H, br d,  $J = 8$  Hz, H-14), 3.42 and 3.12 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 1.12 (3 H, s, 3 H-17), 0.97 and 0.80 (3 H each, s, methyl groups).

**Saponification of Product 4.** Product 4 (10 mg) was saponified in a  $(\text{CD}_3)_2\text{CO}/(\text{D}_2\text{O}/\text{DO}^-)$  (0.5:0.5 mL (5%)) medium for 2 h, after which it rendered product 5 (7 mg, 69%) by CC.

**Hydrogenation of Products 8, 17, and 32.** Product 8 (25 mg) was dissolved in EtOH (5 mL), and Pd on  $\text{BaSO}_4$  (5 mg, 5%) was added. The hydrogenation was carried out at 5 atm for 12 h. The mixture of reaction was filtered and washed with EtOH. The EtOH solutions were concentrated to give, after CC, *ent*-18-acetoxy-14 $\alpha$ ,15 $\beta$ -dihydroxy-(16R)-kaurane (13, 11 mg, 44%) and *ent*-18-acetoxy-14 $\alpha$ ,15 $\beta$ -dihydroxy-(16S)-kaurane (14, 12 mg, 48%). Product 13:  $^1\text{H}$  NMR  $\delta$  4.24 (1 H, br s, H-14), 3.90 and 3.64 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 3.02 (1 H, br d,  $J = 4$  Hz, H-15), 2.07 (3 H, s, AcO group), 1.18 (3 H, d,  $J = 7$  Hz, methyl group at C-17), 1.92 and 0.85 (3 H each, s, methyl groups). Product 14:  $^1\text{H}$  NMR  $\delta$  4.12 (1 H, br s, H-14), 3.87 and 3.62 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 3.57 (1 H, br d,  $J = 8$  Hz, H-15), 2.07 (3 H, s, AcO group), 1.12 (3 H, d,  $J = 7$  Hz, 3 H-17), 0.97 and 0.82 (3 H each, s, methyl groups). In similar conditions, product 17 (100 mg)

rendered *ent*-18-acetoxy-14 $\beta$ -hydroxybeyerane (18, 92 mg, 91%), whose data were as follows: mp 87–89 °C;  $[\alpha]_D^{20} +2.7^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 3450, 1740, and 1250;  $^1\text{H}$  NMR  $\delta$  3.90 and 3.62 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.97 (1 H, s, H-14), 2.07 (3 H, s, AcO group), 1.00 (6 H, s, methyl groups), 0.85 (3 H, s, methyl group);  $^{13}\text{C}$  NMR, see Table II. Anal. Found: C, 75.64; H, 10.86. Calcd for  $\text{C}_{22}\text{H}_{36}\text{O}_3$ : C, 75.82; H, 10.41. Product 32 (8 mg) yielded 35 (6 mg, 75%): gum;  $[\alpha]_D^{20} -16^\circ$  (c 0.5,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 1735, 1240, and 1038;  $^1\text{H}$  NMR  $\delta$  5.30 (1 H, m,  $W_{1/2} = 4$  Hz, H-14), 4.97 (1 H, d,  $J = 8$  Hz, H-15), 3.82 and 3.57 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.07 (6 H, s, AcO groups), 2.05 (3 H, s, AcO group), 1.10 (3 H, s, methyl group), 0.97 (3 H, d,  $J = 7$  Hz, 3 H-17), 0.82 (3 H, s, methyl group).

**Oxidation of Products 2, 7, 13, and 14.** Product 2 (28 mg) was dissolved in acetone (5 mL) and oxidized with Jones's reagent.<sup>34</sup> After CC, *ent*-18-acetoxy-(16R)-kauran-14,15-dione (11, 25 mg, 90%) was obtained: mp 204–206 °C;  $[\alpha]_D^{20} -98.7^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 1761, 1723, 1464, 1380, 1246, and 1027;  $^1\text{H}$  NMR  $\delta$  3.87 and 3.62 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.67 (1 H, quintuplet,  $J = 7$  Hz, H-16), 2.72 (1 H, m,  $W_{1/2} = 7$  Hz, H-13), 2.07 (3 H, s, AcO group), 1.32 (3 H, d,  $J = 7$  Hz, 3 H-17), 0.95 and 0.85 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR, see Table I. Anal. Found: C, 73.05; H, 9.10. Calcd for  $\text{C}_{22}\text{H}_{32}\text{O}_4$ : C, 73.30; H, 8.95. In the same way product 7 (20 mg) afforded *ent*-18-acetoxy-(16S)-kauran-14,15-dione (12, 16 mg, 80%): mp 178–180 °C;  $[\alpha]_D^{20} -68.7^\circ$  (c 1,  $\text{CHCl}_3$ ); IR  $\nu_{\text{max}}$  (KBr,  $\text{cm}^{-1}$ ) 1760, 1725, 1465, 1382, 1250, and 1030;  $^1\text{H}$  NMR  $\delta$  3.87 and 3.62 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.80 (1 H, q,  $J = 7$  Hz, H-16), 2.54 (1 H, m,  $W_{1/2} = 8$  Hz, H-13), 2.07 (3 H, s, AcO group), 1.05 (3 H, d,  $J = 7$  Hz, 3 H-17), 0.95 and 0.85 (3 H each, s, methyl groups);  $^{13}\text{C}$  NMR, see Table II. Anal. Found: C, 73.21; H, 9.27. Calcd for  $\text{C}_{22}\text{H}_{32}\text{O}_4$ : C, 73.30; H, 8.95. Oxidation of product 13 (6 mg) yielded 11 (4 mg, 67%), and oxidation of 14 (7 mg) gave 12 (4 mg, 58%).

**Acetylation of Products 8, 14, 29, and 30.** Product 8 (10 mg) was dissolved in Py/ $\text{Ac}_2\text{O}$  (1:0.5 mL) and refluxed for 2 h. Product 33 (8 mg, 65%) was isolated after CC. Product 14 (5 mg) refluxed for 2 h with Py/ $\text{Ac}_2\text{O}$  (1/0.5 mL) gave 35 (4 mg, 65%). Product 29 (8 mg) was dissolved in Py/ $\text{Ac}_2\text{O}$  (1/0.5 mL) and refluxed for 2 h. After CC, *ent*-14 $\alpha$ ,15 $\beta$ ,18-triacetoxykaur-16-ene (33, 6 mg, 68%) was isolated: gum;  $[\alpha]_D^{20} -29.6^\circ$  (c 0.5,  $\text{CHCl}_3$ ); IR,  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3065, 1732, 1630, 1370, 1238, 1034, 905, and 820;  $^1\text{H}$  NMR  $\delta$  5.37 (2 H, m,  $W_{1/2} = 4$  Hz) and 5.16 (2 H, m,  $W_{1/2} = 6$  Hz) (H-14, H-15, and 2 H-17), 3.85 and 3.57 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.80 (1 H, m,  $W_{1/2} = 8$  Hz, H-13), 2.10 and 2.06 (3 H and 6 H, respectively, s, AcO groups), 1.12 and 0.82 (3 H each, s, methyl groups). Product 30 (10 mg) was acetylated as described above for product 29 to give, after CC, *ent*-14 $\beta$ ,15 $\alpha$ ,18-triacetoxy-16 $\beta$ -hydroxybeyerane (34, 8 mg, 73%): gum;  $[\alpha]_D^{20} -9.4^\circ$  (c 0.5,  $\text{CHCl}_3$ ); IR,  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3400, 1739, 1453, 1372, 1232, and 1024;  $^1\text{H}$  NMR  $\delta$  5.60 (1 H, dd,  $J_1 = 4$  Hz,  $J_2 = 2$  Hz, H-15), 4.70 (1 H, d,  $J = 2$  Hz, H-14), 4.02 (1 H, d,  $J = 4$  Hz, H-16), 3.85 and 3.56 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.12, 2.10, and 2.06 (3 H each, s, AcO groups), 1.08, 0.92, and 0.80 (3 H each, s, methyl groups).

**Treatment in Basic Medium of 7.** Product 7 (10 mg) was treated in basic medium (5 mL) [ $\text{MeOH}/\text{H}_2\text{O}/\text{KOH}$  (3.5:1.5:0.25)] in similar conditions to those described for the deuteration of 7. Product 2 (7 mg, 70%) was isolated after CC.

**Hydrogenation of Product 26.** Product 26 (5 mg) was dissolved in EtOH (5 mL), and Pd on  $\text{BaSO}_4$  (5 mg, 5%) was added. The hydrogenation was carried out at 5 atm for 24 h. After CC *ent*-16 $\alpha$ ,18-diacetoxybeyer-9(11)-ene (40, 4 mg, 80%) was isolated: IR  $\nu_{\text{max}}$  (neat,  $\text{cm}^{-1}$ ) 3080, 1738, 1452, 1373, 1242, and 1047;  $^1\text{H}$  NMR  $\delta$  5.35 (1 H, dd,  $J_1 = 6$  Hz,  $J_2 = 2$  Hz, H-11), 4.57 (1 H, s, H-14), 3.87 and 3.62 (2 H,  $q_{AB}$ ,  $J = 12$  Hz, 2 H-18), 2.07 and 2.00 (3 H each, s, AcO groups), 0.17, 0.95, and 0.85 (3 H each, s, methyl groups). Product 40 (4 mg) was dissolved in EtOH (5 mL), and Pt on carbon (5 mg) was added. The hydrogenation was carried out at 5 atm for 24 h, after which product 40 was recovered unaltered.

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