# Ruthenium-Catalyzed Rearrangement of *ent*-14-(Benzoyloxy)-15,16-epoxybeyerane Diterpenes

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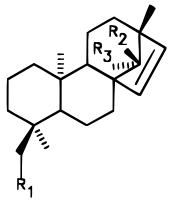
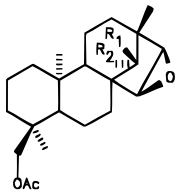
Rearrangements of *ent*-18-acetoxy-14α-(benzoyloxy)-15α,16α-epoxybeyerane and *ent*-18-acetoxy-14*β*-(benzoyloxy)-15α,16α-epoxybeyerane, catalyzed by ruthenium acetylacetonate, were carried out. With the 14-*endo*-(benzoyloxy) compound, *ent*-18-acetoxy-14α-(benzoyloxy)beyera-9,15-diene, *ent*-18-acetoxy-15α-(benzoyloxy)-14α-hydroxykaur-16-ene, *ent*-18-acetoxy-15α-(benzoyloxy)-14α-hydroxy-(16*S*)-kaur-11-ene, and *ent*-18-acetoxy-14α-hydroxy-(16*R*)-kauran-15-one were isolated. However, rearrangement of the 14-*exo*-(benzoyloxy) compound gave *ent*-18-acetoxy-15*β*-(benzoyloxy)-14α-hydroxykaur-16-ene, *ent*-18-acetoxy-15*β*-(benzoyloxy)-14α-hydroxyatis-16-ene, *ent*-18-acetoxy-14*β*-(benzoyloxy)-16*β*-chloro-15α-hydroxybeyerane, *ent*-18-acetoxy-15*β*-benzoyloxy)-14α-hydroxy-(16*S*)-kaur-11-ene, *ent*-18-acetoxy-15*β*-(benzoyloxy)-12α-chloro-14α-hydroxy-(16*S*)-kaurane, and *ent*-18-acetoxy-14*β*-(benzoyloxy)-12α-chloro-15α-hydroxybeyerane. The influence of the C-14 benzoyloxy substituent and its arrangement are discussed by comparison with other rearrangement processes reported previously.

## Introduction

Rearrangements of tetracyclic diterpenoids have been extensively studied and were carried out on epoxy compounds[1−9] or thiocarbonates[10] or through solvolytic reactions.[11−18] Recent papers[8,9] have demonstrated that oxygenated functions near the epoxy group participate in the rearrangement process. Moreover, stereochemistry of this function may also influence the course of the reaction.[8,9] In previous papers, ruthenium-catalyzed rearrangements of epoxybeyeranes with 14- or 12-hydroxy and 14- or 12-acetoxy groups were reported.[8,9] In this paper, we investigate the possible participation of a benzoyloxy group in the intermediate structures formed in the rearrangement process and in the yields of products obtained.




| | $R_1$ | $R_2$ | $R_3$ |
|---|---|---|---|
| 1 | OH | H | OAc |
| 2 | OH | H | OH |
| 3 | OAc | H | OH |
| 4 | OAc | =O | |
| 5 | OAc | OH | H |




| | $R_1$ | $R_2$ |
|---|---|---|
| 6 | OBz | H |
| 7 | H | OBz |

## Results and Discussion

Saponification of *ent*-14*β*-acetoxy-18-hydroxybeyer-15-ene (**1**), a natural product isolated from *Sideritis pusilla*,[19,20] gave tartesidiol (**2**),[8] which was acetylated to obtain 18-acetoxy derivative **3**.[8] Product **3** was oxidized with Jones' reagent, yielding ketone **4**, which was reduced with $NaBH_4$ to give *ent*-18-acetoxy-14α-hydroxybeyer-15-ene (**5**).[8] Treatment of product **5** with benzoyl chloride gave an *ent*-14α-(benzoyloxy) derivative, which was epoxidized with *m*-CPBA to obtain *ent*-18-acetoxy-14α-(benzoyloxy)-15α,16α-epoxybeyerane (**6**). Product **3** was treated with benzoyl chloride and afterwards with *m*-CPBA to give *ent*-18-acetoxy-14*β*-(benzoyloxy)-15α,16α-epoxybeyerane (**7**).

The reaction of *ent*-14*β*-(benzoyloxy)-15α,16α-epoxy derivative **6** with ruthenium acetylacetonate in a sealed tube at 140 °C for 7 h gave rise to a mixture of products **8** (5%), **9** (19%), **10** (8%), and **11** (15%) (Scheme 1). These rearranged products were similar to those obtained previously in which the starting material was the *ent*-14α-acetoxy-15α,16α-epoxy derivative.[8] Spectroscopic data of products **8**−**10** were very similar to those of the acetoxy derivatives isolated in previous work, with the expected differences produced by the benzoyloxy group at C-14 or C-15 in the *ent*-beyerene or *ent*-kaurene skeletons, respectively. Formation of these rearranged products from the benzoyloxy epoxy compound **6** has been explained through a process similar to that described for the acetoxy derivatives[8] (Scheme 2). As can be seen, the proposed mechanism assumed different pathways involving hydride shifts and/or the participation of a 14-*endo*-(benzoyloxy) group.

Treatment of epoxy compound **7** with ruthenium acetylacetonate under the above conditions gave **12** (4%), **13** (7%), **14** (10%), **15** (6%), **16** (5%), and **17** (16%) (Scheme 3). In this case, the rearrangement process gave rise to three new rearranged compounds (products **13**, **16**, and **17**). Moreover, other products differed only in the substituent at C-14 and C-15, now a benzoyloxy group instead of an acetoxy group.

Product **12** was similar to a product obtained from an epoxy acetoxy compound[8] and had an *ent*-15*β*-(benzoyloxy)-14α-hydroxykaur-16-ene skeleton. $^1H$ and $^{13}C$ NMR spectroscopic data of **12** confirmed this structure, and its formation was justified by the mechanism shown in Scheme 4. An opening of the epoxy group

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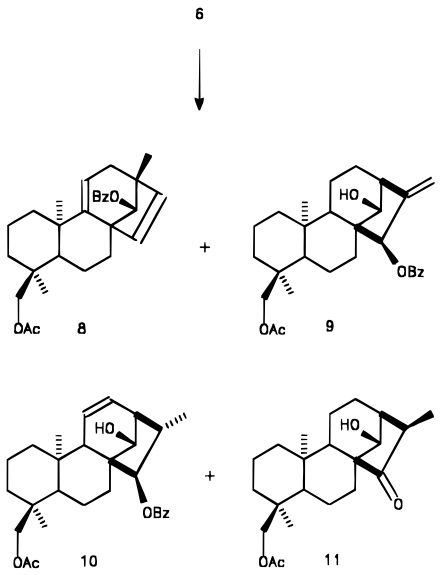
**Scheme 1.** Rearrangement of Product **6**




toward C-15 was assumed, and a concerted 12(13)→16 rearrangement could occur. Thus, the *ent*-kaurene skeleton with a carbocation at the original C-13 was formed (path a in Scheme 4). The participation of an *ent*-14$\beta$-(benzoyloxy) group gave an intermediate B, which by loss of a C-17 proton yielded product **12** (path b in Scheme 4).

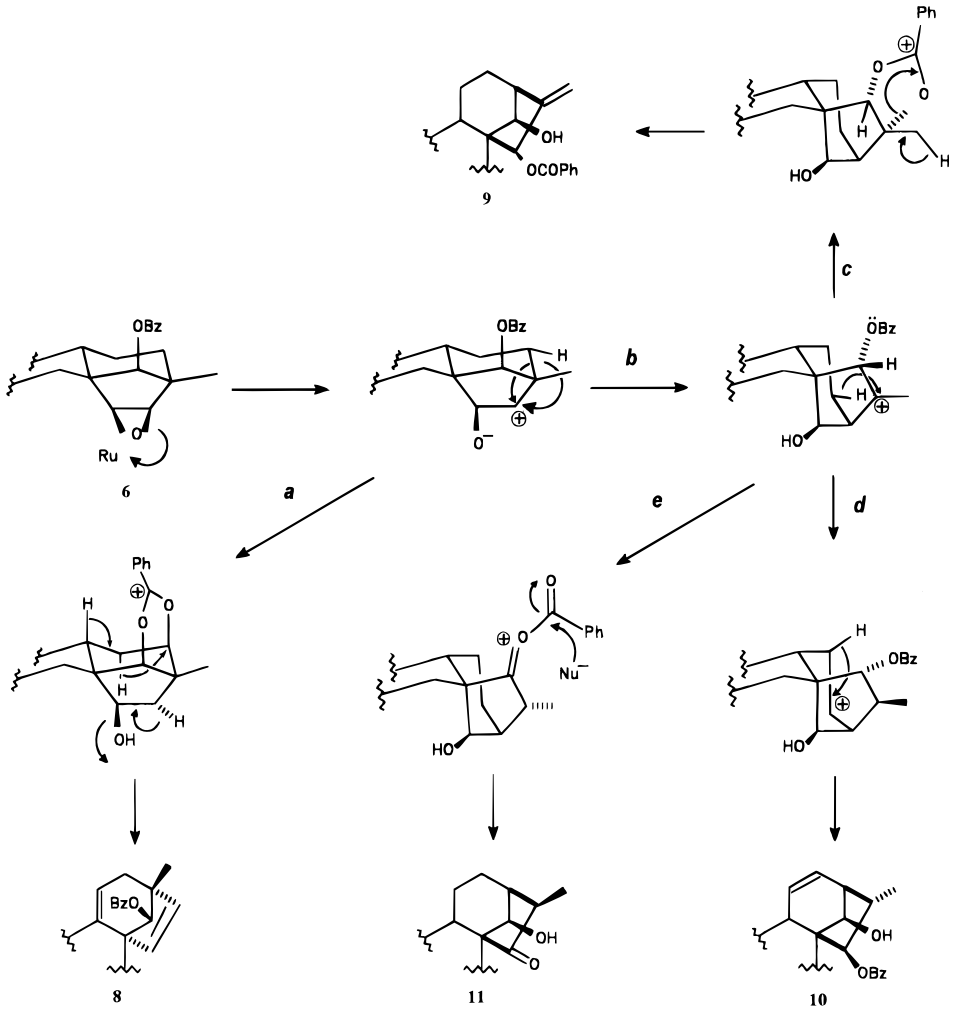
The $^1$H NMR data for rearranged product **13** showed signals similar to those of the previous *ent*-kaurene **12**. Thus, there were *exo*-methylene signals at $\delta$ 4.96 (1H, d, $J$ = 2.0 Hz) and at $\delta$ 5.03 (1H, d, $J$ = 2.0 Hz). The signals for geminal protons to oxygenated functions on C-14 ($\delta$ 4.21, 1H, br d) and C-15 ($\delta$ 5.53, 1H, dd, $J_1$ = 2.0 Hz, $J_2$ = 4.0 Hz) can be also observed. The structure of **13** was established using the C/H correlation and COSY experiments. These data suggested the existence of an *ent*-atis-16-ene skeleton functionalized at C-14 and C-15 using published data as a reference for this unfunctionalized skeleton.[21] Thus, the signals at $\delta$ 5.53 (H-15) and $\delta$ 4.21 (H-14) were correlated with the signals at 81.8 ppm (C-15) and 66.7 ppm (C-14) in the correlation C/H spectrum, respectively. Moreover, the H-17 signals were assigned to an *exo*-methylene group at $\delta$ 5.03 and $\delta$ 4.96 in the COSY spectrum. The H-14 signal was coupled to the signal at $\delta$ 2.32 (H-13), which was coupled to another at $\delta$ 2.50 (H-12) in the COSY spectrum. Furthermore, the $\gamma$, $\beta$, and $\alpha$ effects of the C-14 and C-15 substituents on the carbons of the C and D rings were taken into account to assign the chemical shifts in the $^{13}$C NMR spectrum of product **13**. Finally, oxidation of product **13** gave ketone **18**. Several $^1$H and $^{13}$C mono- and bidimensional NMR experiments were conducted on **13**, and these data were in agreement with published data for similar structures.[22] Therefore, product **18** was considered to be the 14-oxo derivative of **13**, which was *ent*-18-acetoxy-15$\beta$-(benzoyloxy)-14$\alpha$-hydroxyatis-16-ene. The formation of rearranged product **13** was explained according to path c in Scheme 4. Starting from intermediate A, intermediate C was obtained by a 12→16 hydride shift. The participation of an *ent*-14$\alpha$-(benzoyloxy) group is possible by the formation of an 1,3-dioxolan-2-ilio cation, and an 16-(13)→12 rearrangement could thus occur (path d in Scheme 4), leading to intermediate D. The process ended with five-membered ring opening and loss of an H-17 to give the *ent*-atis-16-ene structure **13**.

Product **14**, also obtained from this rearrangement, presented a molecular peak of *m/z* 502 that indicated a molecular formula of $C_{29}H_{39}O_5Cl$. This product had an *ent*-beyerane skeleton, since its NMR spectrum showed three methyl singlet signals ($\delta$ 1.00, 0.93, and 0.79) and an AB quartet from the C-18 acetoxymethylene group. In addition, the *ent*-14$\beta$-(benzoyloxy) group also remained at this position, since the signal of its geminal proton appeared at $\delta$ 4.91 (1H, d, $J$ = 1 Hz). Moreover, the signals of protons geminal to functions on C-15 and C-16 were apparent at $\delta$ 4.41 (1H, m) and $\delta$ 4.14 (1H, d, $J$ = 3.9 Hz), respectively. These signals were similar to those observed for a previously described ent-16$\beta$-chloro-15$\alpha$-hydroxy derivative obtained from *trans* epoxy opening.[9] The $^{13}$C NMR data of **14** were also compatible with the mentioned substitution for similar compounds.[8,9] Product **14** was probably formed from intermediate A by dorsal attack of a chlorine ion on C-16 (path e in Scheme 4). Such chlorine entry was observed previously[9] and probably originated from the solvent ($CHCl_3$) in which the rearrangement process was conducted.

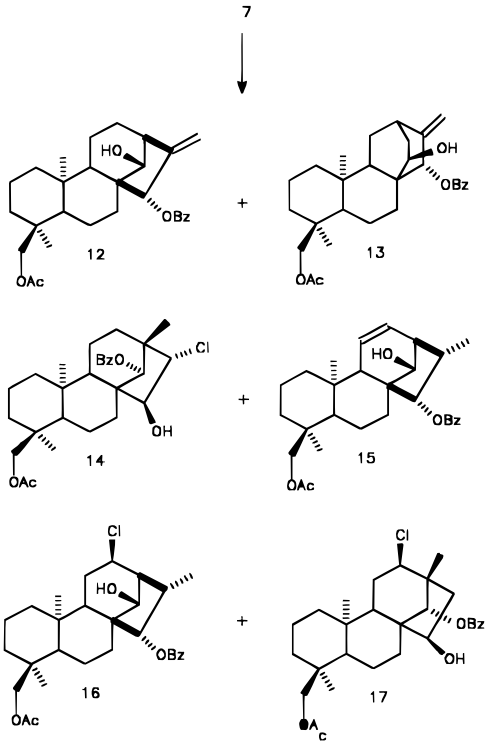
Rearranged product **15** had an *ent*-kaur-11-ene skeleton and was similar to a product obtained from the acetoxy epoxy compound rearranged previously.[8] Its formation was started from intermediate B by a 12→16 hydride shift (path f in Scheme 4) so that a carbonium ion was formed at C-12 (intermediate E). This cationic structure may undergo the loss of a C-11 proton with the formation of a C-11/C-12 double bond (path g in Scheme 4).

Product **16** also differed from derivatives previously obtained.[8] Its molecular ion peak (*m/z* 502) and the successive fragmentations observed indicated that a chlorinated compound was again formed, with a molecular formula of $C_{29}H_{39}O_5Cl$. The $^1$H NMR spectrum of **16** presented two singlet methyls ($\delta$ 0.97 and 0.79) and one doublet methyl ($\delta$ 1.10, $J$ = 8.0 Hz); in addition, a double quartet was observed at $\delta$ 2.73 (1H, dq, $J_1 = J_2$ = 8.0 Hz). These signals suggested that **16** had an *ent*-kaurane structure. Several bidimensional NMR experiments were done to establish the structure of this compound. At $\delta$ 5.22 there was a signal (1H, d, $J$ = 8.0 Hz) which was coupled with the signal at $\delta$ 2.73 (H-16); therefore, the $\delta$ 5.22 signal was due to the proton at C-15 geminal to a benzoyloxy group. Moreover, the signal of the *ent*-14$\beta$ proton geminal to hydroxyl group (1H, s) was located at $\delta$ 4.14. In addition, at 4.25 ppm we noted the signal of a proton coupled with three other protons (1H, ddd, $J_1$ = 12.0 Hz, $J_2$ = 6.2 Hz, $J_3$ = 2.3 Hz). Since there was a chlorine in the molecule, this signal must represent its geminal proton. From the COSY spectrum of **16** we deduced that the signal at $\delta$ 4.25 (*ent*-12$\beta$-H) was correlated with three proton signals at $\delta$ 2.32, 2.13, and 1.65. Therefore, a $CHCHXCH_2$ group must be present, an arrangement that is only possible if the chlorine atom is situated at C-11 or C-12. The C/H correlation spectrum of **16** was also studied and the $^{13}$C NMR chemical shifts were analyzed, assuming both possibilities. On the basis of these data and the $^{13}$C NMR chemical shifts for related *ent*-kaurane compounds,[8,23] we conclude that product **16** was *ent*-18-acetoxy-15$\beta$-(benzoyloxy)-12$\alpha$-chloro-14$\alpha$-hy-

**Scheme 2.** Proposed Mechanism of Rearrangement of Epoxy Compound **6**



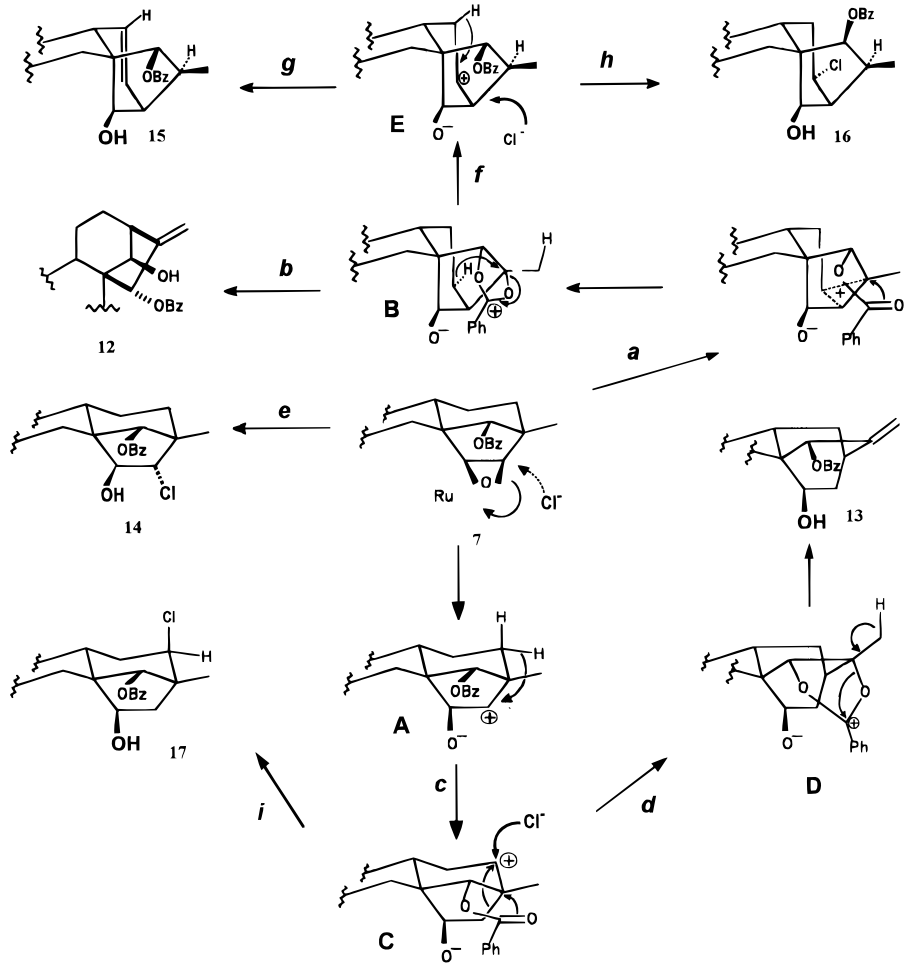

**Scheme 3.** Rearrangement of Product **7**




droxykaurane. The formation of **16** could be explained by an attack by chlorine ion on the intermediate E (path h in Scheme 4) only on the *ent*-α face because of marked steric hinderance on the *ent*-*β* face.

The last product isolated from this rearangement (**17**) also had a molecular formula of $C_{29}H_{39}O_5Cl$ (*m*/*z* 502). Product **17** had an *ent*-beyerane skeleton, since three methyl singlet signals at *δ* 1.12, 1.00, and 0.80 were observed in the $^1H$ spectrum. At *δ* 5.42 we noted a singlet signal corresponding to a proton geminal to the benzoyloxy group on C-14. Moreover, at 4.10 ppm (1H, narrow doublet, $J = 1.7$ Hz) and 4.35 ppm (1H, broad multiplet) we found the signals of two protons geminal to the hydroxy group and to the chlorine atom. The $^{13}C$ NMR data were not compatible with products formed from a *trans* or *cis* epoxy group opening. Various 2D-experiments (COSY, C/H, and INADEQUATE) were done to unequivocally establish the structure of compound **17**. An INADEQUATE spectrum study allowed us to determine the connectivity of all carbons of the molecule. An *ent*-beyerane skeleton was assumed for compound **17**, and its INADEQUATE spectrum showed that C-15 was oxygenated and that it was connected to a quarternary (C-8) and a methylenic carbon atom (C-16). Futhermore, C-16 was joined to a primary carbon (C-17), to a methynic carbon (C-12), and to the carbon which supported the benzoyloxy group (C-14). NOE effects were observed between H-17, H-12, and H-14; there was also a NOE effect between H-15 and H-20. Therefore, compound **17** is assumed to have an axial chlorine atom at C-12 and *ent*-15α-hydroxyl group at

**Scheme 4.** Proposed Mechanism of Rearrangement of Epoxy Compound **7**




C-15. We therefore conclude that **17** had a structure of *ent*-18-acetoxy-14$\beta$-(benzoyloxy)-12$\alpha$-chloro-15$\alpha$-hydroxybeyerane. The formation of compound **17** from **7** could easily be justified via intermediate C by an attack by chlorine ion at C-12 (path i in Scheme 4).

The results reported here indicate that rearrangement of the 14-(benzoyloxy) epoxy compounds **6** and **7** instead of the 14-acetoxy epoxy compounds[8] does not lead to a significant improvement in yield. However, in the case of *ent*-14$\beta$-(benzoyloxy) derivative **7**, the resulting products varied considerably. The *ent*-atis-16-ene product **13** is interesting because it can be used as a precursor for *ent*-14-oxo atis-16-enes. These *ent*-atisenes possess interesting biological properties and have been isolated from tropical plants.[24] In addition, the chlorinated compounds obtained allowed us to postulate a mechanism of formation of the products by capture of intermediates from the rearrangement process.

## Experimental Section

**General Experimental Procedures.** NMR spectra were done in $CDCl_3$ in a Bruker AM-300 Bruker and in a ARX-400. 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, were performed with pullprogrs from the Bruker library (COSY90, NOESYST, HXCO, and INAD respectively). A sample of 110 mg of product **17** in 0.5 mL of $CDCl_3$ 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 s and refocalization time of $1/4J = 0.0065$ s, in a week-end experiment. IR spectra were recorded on a Perkin-Elmer Model 983 G spectrometer or on a Nicolet 20SX FT-IR spectrometer. Mass spectra were determined with CI (methane) in a Hewlett-Packard Model 5988 A spectrometer. Optical rotations were measured on a Perkin-Elmer 241 polarimeter at 20 °C. Silica gel SDS 60 A CC (40−60 $\mu$m) 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 °C. Starting material for this work, *ent*-14$\beta$-acetoxy-18-hydroxybeyer-15-ene (**1**), was isolated from *Sideritis pusilla* (var.flavovirens).[19,20]

**Saponification of *ent*-14$\beta$-Acetoxy-18-hydroxybeyer-15-ene (1).** Seven hundred mg of **1** was dissolved in 25 mL of a MeOH/$H_2O$ solution (30/70) with 5% of KOH. The reaction was maintained at reflux for 6 h, after which time it was neutralized, extracted with $CH_2Cl_2$, dried with anhydrous $Na_2SO_4$, and purified by flash chromatography, yielding 600 mg of **2** (98%).[8]

**Acetylation of *ent*-14$\beta$,18-Dihydroxybeyer-15-ene (2).** Six hundred mg of **2** was acetylated with $Ac_2O$/Py (2:4 mL) for 1 h at 0 °C. Purification by flash chromatography provided 110 mg of monoacetylated product **3** (76%).[8]

**Oxidation of *ent*-18-Acetoxy-14$\beta$-hydroxybeyer-15-ene (3).** Three hundred mg of **3** was dissolved in acetone (10 mL) and oxidized with Jones' reagent for 30 min at 0 °C. Purification by flash chromatography gave 235 mg of **4** (79%).[8]

**Reduction with $NaBH_4$ of *ent*-18-Acetoxybeyer-15-en-14-one (4).** Twenty mg of $NaBH_4$ was added to a stirred solution of 235 mg of **4** in EtOH (10 mL) at room temperature for 1 h. The reaction mixture was acidified with dilute HCl, extracted with $CH_2Cl_2$, dried, and evaporated. Purification by flash chromatography provided 228 mg of **5** (96%).[8]

**Benzoylation and Epoxidation of *ent*-18-Acetoxy-14$\alpha$-hydroxybeyer-15-ene (5).** Two hundred twenty-eight mg of **5** was treated with benzoyl chloride/Py (1:2 mL). After 12 h at room temperature, the mixture was diluted with $H_2O$, extracted with $CHCl_3$, washed with saturated $KHSO_4$, dried, and evaporated. Purification by flash chromatography gave *ent*-18-acetoxy-14$\alpha$-(benzoyloxy)beyer-15-ene. This benzoyloxy derivative was epoxidized with 200 mg of *m*-CPBA in 5 mL of $CHCl_3$ for 24 h at room temperature. The reaction mixture was then diluted with $CHCl_3$, washed with aqueous $FeSO_4$, aqueous $NaHCO_3$, and water, dried, and concentrated. Purification by flash chromatography provided *ent*-18-acetoxy-14$\alpha$-(benzoyloxy)-15$\alpha$,16$\alpha$-epoxybeyerane (**6**) (148 mg, 65%).

***ent*-18-Acetoxy-14$\alpha$-(benzoyloxy)-15$\alpha$,16$\alpha$-epoxybeyerane (6):** mp 45−47 °C; $[\alpha]^{20}_D$ −41° (*c* 0.5, $CHCl_3$); IR $\nu$(max) ($CHCl_3$) 1725, 1270, 1248; $^1$H NMR ($\delta$ $CDCl_3$) 8.09−7.45 (5H, PhCOO), 4.66 (1H, s, H-14), 3.81 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 3.63 (1H, d, $J$ = 3.5 Hz, H-15), 3.60 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 3.22 (1H, d, $J$ = 3.5 Hz, H-16), 1.84 (3H, s, MeCOO), 1.04, 1.01, 0.85 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.3 (C-1), 18.3 (C-2), 35.8 (C-3), 36.5 (C-4), 48.3 (C-5), 19.3 (C-6), 30.1 (C-7), 45.5 (C-8), 50.0 (C-9), 37.2 (C-10), 17.8 (C-11), 29.2 (C-12), 40.8 (C-13), 78.0 (C-14), 55.1 (C-15), 59.0 (C-16), 19.4 (C-17), 73.0 (C-18), 17.6 (C-19), 16.2 (C-20), 20.8 (*Me*CO), 171.2 (Me*CO*), 166.2 (Ph*COO*), 133.2, 130.5, 129.6, 128.6 (*Ph*COO); CIMS ($CH_4$) *m/z* 467 [M + 1]$^+$ (16), 407 (58), 345 (100), 285 (77). Anal. Calcd for $C_{29}H_{38}O_5$: C, 74.68; H, 8.15. Found: C, 74.5; H, 8.3.

**Benzoylation and Epoxidation of *ent*-18-Acetoxy-14$\beta$-hydroxybeyer-15-ene (3).** The procedure was the same as that described for the preparation of epoxy benzoyloxy derivative **6**. Thus, product **3** (200 mg) was converted into *ent*-18-acetoxy-14$\beta$-(benzoyloxy)-15$\alpha$,16$\alpha$-epoxybeyerane (**7**) (210 mg, 78%).

***ent*-18-Acetoxy-14$\beta$-(benzoyloxy)-15$\alpha$,16$\alpha$-epoxybeyerane (7):** mp 63−65 °C; $[\alpha]^{20}_D$ + 22° (*c* 0.5, $CHCl_3$); IR $\nu$(max) 1728, 1265, 1245; $^1$H NMR ($\delta$, $CDCl_3$) 8.11−7.39 (5H, PhCOO), 4.65 (1H, s, H-14), 3.79 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.61 (1H, dd, $J_1$ = 2.9 Hz, $J_2$ = 1.1 Hz, H-15), 3.61 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.19 (1H, dd, $J_1$ = 2.9 Hz, $J_2$ = 1.3 Hz, H-16), 2.03 (3H, s, MeCOO), 1.04, 0.99, 0.83 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.0 (C-1), 17.8 (C-2), 35.6 (C-3), 36.4 (C-4), 49.3 (C-5), 18.8 (C-6), 27.8 (C-7), 49.1 (C-8), 56.6 (C-9), 37.6 (C-10), 17.8 (C-11), 34.8 (C-12), 44.6 (C-13), 85.2 (C-14), 55.3 (C-15), 59.6 (C-16), 17.7 (C-17), 72.7 (C-18), 16.9 (C-19), 16.1 (C-20), 21.1 (*Me*CO), 171.3 (Me*CO*), 167.2 (Ph*COO*), 132.9, 130.3, 129.9, 128.4 (*Ph*COO); CIMS ($CH_4$) *m/z* 467 [M + 1]$^+$ (22), 345 (100), 285 (68). Anal. Calcd for $C_{29}H_{38}O_5$: C, 74.68; H, 8.15. Found: C, 74.8; H, 8.2.

**Rearrangement of *ent*-18-Acetoxy-14$\alpha$-(benzoyloxy)-15$\alpha$,16$\alpha$-epoxybeyerane (6).** Product **6** (140 mg) was dissolved in $CHCl_3$ (5 mL) in a sealed tube. Then, 14 mg of ruthenium acetylacetonate was added, and the mixture was heated at 140 °C for 7 h. The solution was concentrated, and after purification and separation by flash chromatography four products were obtained: **8** (7 mg, 5%), **9** (27 mg, 19%), **10** (11 mg, 8%), and **11** (8), (16 mg, 15%).

***ent*-18-Acetoxy-14$\alpha$-(benzoyloxy)beyera-9,15-diene (8)**: mp syrup; $[\alpha]^{20}_D$ + 35° (*c* 0.5, $CHCl_3$); IR $\nu$-(max) 1724, 1675, 1266; $^1$H NMR ($\delta$, $CDCl_3$) 8.06−7.42 (5H, PhCOO), 6.20 (1H, d, $J$ = 6.1 Hz, H-15), 5.40 (1H, dd, $J_1$ = $J_2$ = 3.5 Hz, H-11), 5.36 (1H, d, $J$ = 6.1 Hz, H-16), 4.91 (1H, s, H-14), 3.82 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.49 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 2.22 (1H, $Q_{AB}$, $J$ = 2.9 Hz, H-12), 2.16 (1H, $Q_{AB}$, $J$ = 2.9 Hz, H-12), 1.55 (3H, s, MeCOO), 1.11, 1.02, 0.83 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 37.8 (C-1), 18.3 (C-2), 35.7 (C-3), 36.8 (C-4), 44.9 (C-5), 19.3 (C-6), 33.1 (C-7), 49.2 (C-8), 152.1 (C-9), 38.7 (C-10), 116.0 (C-11), 31.6 (C-12), 43.1 (C-13), 83.1 (C-14), 142.1 (C-15), 132.4 (C-16), 22.3 (C-17), 72.2 (C-18), 17.9 (C-19), 25.3 (C-20), 20.3 (*Me*CO), 171.2 (Me*CO*), 166.8 (Ph*COO*), 133.0, 130.7, 129.7, 128.5 (*Ph*COO); CIMS ($CH_4$) *m/z* 449 [M + 1]$^+$ (6), 329 (100), 327 (10), 269 (23), 267 (8). Anal. Calcd for $C_{29}H_{36}O_4$: C, 77.68; H, 8.04. Found: C, 77.5; H, 7.9.

***ent*-18-Acetoxy-15$\alpha$-(benzoyloxy)-14$\alpha$-hydroxykaur-16-ene (9):** mp 68−70 °C; $[\alpha]^{20}_D$ −74° (*c* 0.5, $CHCl_3$); IR $\nu$(max) 3421, 1729, 1267, 1229; $^1$H NMR ($\delta$, $CDCl_3$) 8.11−7.46 (5H, PhCOO), 5.78 (1H, dd, $J_1$ = $J_2$ = 2.5 Hz, H-15), 5.13 (1H, br s, H-17), 5.11 (1H, d, $J$ = 2.5 Hz, H-17), 4.34 (1H, s, H-14), 3.78 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 3.64 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 2.74 (1H, br s, H-13), 1.94 (3H, s, MeCOO), 1.06, 0.82 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 40.3 (C-1), 18.1 (C-2), 35.7 (C-3), 36.6 (C-4), 50.8 (C-5), 19.5 (C-6), 29.9 (C-7), 51.7 (C-8), 50.4 (C-9), 39.2 (C-10), 17.8 (C-11), 33.7 (C-12), 49.6 (C-13), 75.2 (C-14), 79.9 (C-15), 151.8 (C-16), 110.0 (C-17), 73.4 (C-18), 18.5 (C-19), 17.5 (C-20), 19.3 (*Me*CO), 171.4 (Me*CO*), 166.8 (Ph*COO*), 133.2, 130.7, 129.9, 128.7 (*Ph*COO); CIMS ($CH_4$) *m/z* 467 [M + 1]$^+$ (1), 449 (26), 345 (16), 327 (18), 285 (100), 267 (15). Anal. Calcd for $C_{29}H_{38}O_5$: C, 74.68; H, 8.15. Found: C, 74.8; H, 8.0.

***ent*-18-Acetoxy-15$\alpha$-(benzoyloxy)-14$\alpha$-hydroxy-16(*S*)-kaur-11-ene (10):** mp 138−40 °C; $[\alpha]^{20}_D$ −133° (*c* 0.5, $CHCl_3$): IR $\nu$(max) 3515, 1716, 1274, 1237; $^1$H NMR ($\delta$, $CDCl_3$) 8.05−7.42 (5H, PhCOO), 6.09 (1H, ddd, $J_1$ = 9.7 Hz, $J_2$ = 7.0 Hz, $J_3$ = 1.7 Hz, H-12), 5.48 (1H, dd, $J_1$ = 9.7 Hz, $J_2$ = 3.6 Hz, H-11), 4.99 (1H, d, $J$ = 3.6 Hz, H-15), 4.47 (1H, br s, H-14), 3.82 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 3.64 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 2.47 (1H, dd, $J_1$ = 3.9 Hz, $J_2$ = 1.7 Hz, H-16), 2.29 (1H, dd, $J_1$ = 10.5 Hz, $J_2$ = 2.4 Hz, H-13), 2.12 (1H, d, $J$ = 7.1 Hz, H-9), 1.93 (3H, s, MeCOO), 1.35 (d, $J$ = 7.4 Hz, 3H-17), 0.98, 0.82 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.8 (C-1), 17.8 (C-2), 35.6 (C-3), 36.5 (C-4), 49.0 (C-5), 19.8 (C-6), 28.0 (C-7), 52.1 (C-8), 49.4 (C-9), 38.4 (C-10), 134.0 (C-11), 125.2 (C-12), 54.3 (C-13), 75.7 (C-14), 90.8 (C-15), 48.3 (C-16), 20.7 (C-17), 73.1 (C-18), 17.7 (C-19), 17.5 (C-20), 21.3 (*Me*CO), 171.3 (Me*CO*), 166.7 (Ph*COO*), 132.9, 131.0, 129.6, 128.5 (*Ph*COO); CIMS ($CH_4$) *m/z* 467 [M + 1]$^+$ (6), 345 (56), 327 (35), 285 (100), 267 (28). Anal.

Calcd for $C_{29}H_{38}O_5$: C, 74.68; H, 8.15. Found: C, 74.8, H, 8.0.

**Rearrangement of *ent*-18-Acetoxy-14$\beta$-(benzoyloxy)-15$\alpha$,16$\alpha$-epoxybeyerane (7).** Product **7** (837 mg) was dissolved in $CHCl_3$ (15 mL) in a sealed tube. Then, 80 mg of ruthenium acetylacetonate was added, and the mixture was heated at 140 °C for 7 h. The solution was concentrated, and after purification and separation by flash chromatography six products were obtained: **12** (33 mg, 4%), **13** (58 mg, 7%), **14** (85 mg, 9.5%), **15** (50 mg, 6%), **16** (45 mg, 5%), and **17** (143 mg, 16%).

***ent*-18-Acetoxy-15$\beta$-(benzoyloxy)-14$\alpha$-hydroxykaur-16-ene (12):** mp 127−29 °C; $[\alpha]^{20}_D$ +5° (*c* 0.5, $CHCl_3$); IR $\nu$(max) 3424, 1712, 1273; $^1$H NMR ($\delta$, $CDCl_3$) 8.00−7.40 (5H, PhCOO), 5.62 (1H, s, H-15), 5.37 (1H, s, H-17), 5.28 (1H, s, H-17), 4.22 (1H, br s, H-14), 3.78 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 3.62 (1H, $Q_{AB}$, $J$ = 10.9 Hz, H-18), 2.02 (3H, s, MeCOO), 1.05, 0.81 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.8 (C-1), 17.9 (C-2), 35.6 (C-3), 36.5 (C-4), 49.8 (C-5), 18.8 (C-6), 27.1 (C-7), 53.2 (C-8), 56.7 (C-9), 39.6 (C-10), 18.4 (C-11), 33.1 (C-12), 51.4 (C-13), 76.7 (C-14), 82.7 (C-15), 152.7 (C-16), 114.8 (C-17), 72.8 (C-18), 17.9 (C-19), 17.5 (C-20), 21.2 (*Me*CO), 171.4 (Me*CO*), 166.4 (Ph*COO*), 133.2, 130.2, 129.8, 128.6 (*Ph*COO); CIMS ($CH_4$) *m*/*z* 467 $[M + 1]^+$ (1), 449 (7), 345 (14), 327 (15), 285 (100), 267 (16). Anal. Calcd for $C_{29}H_{38}O_5$: C, 74.68; H, 8.15. Found: C, 74.8; H, 8.1.

***ent*-18-Acetoxy-15$\beta$-(benzoyloxy)-14$\alpha$-hydroxyatis-16-ene (13):** mp 58−60 °C; $[\alpha]^{20}_D$ +45° (*c* 1, $CHCl_3$); $\nu$(max) 3420, 1718, 1269; $^1$H NMR ($\delta$, $CDCl_3$) 8.00−7.40 (5H, PhCOO), 5.53 (1H, dd, $J_1$ = 2.0 Hz, $J_2$ = 4.0 Hz, H-15), 5.03 (1H, d, $J$ = 2.0 Hz, H-17), 4.96 (1H, d, $J$ = 2.0 Hz, H-17), 4.21 (1H, br d, H-14), 3.81 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.63 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 2.50 (1H, m, H-12), 2.05 (3H, s, MeCOO), 0.96, 0.82 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.0 (C-1), 17.7 (C-2), 35.7 (C-3), 36.4 (C-4), 49.8 (C-5), 17.4 (C-6), 29.9 (C-7), 41.8 (C-8), 50.6 (C-9), 37.7 (C-10), 27.0 (C-11), 35.6 (C-12), 40.4 (C-13), 66.7 (C-14), 81.8 (C-15), 149.9 (C-16), 110.9 (C-17), 72.6 (C-18), 17.6 (C-19), 15.1 (C-20), 21.2 (*Me*CO), 171.4 (Me*CO*), 166.6 (Ph*COO*), 133.4, 130.0, 129.6, 128.8 (*Ph*COO); CIMS ($CH_4$) *m*/*z* 467 $[M + 1]^+$ (29), 449 (4), 345 (81), 327 (26), 285 (52). Anal. Calcd for $C_{29}H_{38}O_5$: C, 74.68; H, 8.15. Found: C, 74.4; H, 8.3.

***ent*-18-Acetoxy-14$\beta$-(benzoyloxy)-15$\alpha$-hydroxy-16$\beta$-chlorobeyerane (14):** mp 115−17 °C; $[\alpha]^{20}_D$ +17.2° (*c* 0.5, $CHCl_3$); IR $\nu$(max) 3497, 1718, 1272; $^1$H NMR ($\delta$, $CDCL_3$) 8.00−7.40 (5H, PhCOO), 4.91 (1H, d, $J$ = 1.7 Hz, H-14), 4.41 (1H, m, H-15), 4.14 (1H, d, $J$ = 3.9 Hz, H-16), 3.74 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.60 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 2.03 (3H, s, MeCOO), 1.00, 0.93, 0.79 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.0 (C-1), 17.5 (C-2), 35.5 (C-3), 36.3 (C-4), 49.5 (C-5), 18.5 (C-6), 27.7 (C-7), 49.4 (C-8), 55.7 (C-9), 37.9 (C-10), 19.0 (C-11), 33.1 (C-12), 47.0 (C-13), 91.2 (C-14), 80.5 (C-15), 77.0 (C-16), 19.4 (C-17), 72.8 (C-18), 17.8 (C-19), 15.2 (C-20), 21.1 (*Me*CO), 171.3 (Me*CO*), 166.0 (Ph*COO*), 133.3, 129.7, 129.7, 128.6 (*Ph*COO); CIMS ($CH_4$) *m*/*z* 503 $[M + 1]^+$ (2), 487 (3), 485 (7), 383 (3), 381 (9), 365 (23), 363 (65), 323 (33), 321 (100), 305 (37), 303 (98). Anal. Calcd for $C_{29}H_{38}O_5Cl$: C, 69.32; H, 7.57. Found: C, 69.2; H, 7.7.

***ent*-18-Acetoxy-15$\beta$-(benzoyloxy)-14$\alpha$-hydroxy-16(*S*)-kaur-11-ene (15):** mp 135−37 °C; $[\alpha]^{20}_D$ −12.5° (*c* 1, $CHCl_3$); IR $\nu$(max) 3502, 3012, 1715, 1279; $^1$H NMR ($\delta$, $CDCl_3$) 8.10−7.40 (5H, PhCOO), 6.02 (1H, ddd, $J_1$ = 9.7 Hz, $J_2$ = 7.1 Hz, $J_3$ = 1.6 Hz, H-12), 5.33 (1H, dd, $J_1$ = 9.7 Hz, $J_2$ = 3.6 Hz, H-11), 5.21 (1H, d, $J$ = 8.0 Hz, H-15), 4.35 (1H, s, H-14), 3.78 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.65 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 2.69 (1H, dq, $J_1$ = $J_2$ = 8.0 Hz, H-16), 2.02 (3H, s, MeCOO), 1.07 (d $J$ = 8.0 Hz, 3H-17), 0.96, 0.81 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.3 (C-1), 17.8 (C-2), 35.5 (C-3), 36.5 (C-4), 49.7 (C-5), 19.1 (C-6), 27.0 (C-7), 52.0 (C-8), 62.3 (C-9), 38.8 (C-10), 134.4 (C-11), 124.2 (C-12), 49.0 (C-13), 74.6 (C-14), 86.0 (C-15), 46.8 (C-16), 16.7 (C-17), 72.9 (C-18), 17.7 (C-19), 17.6 (C-20), 21.2 (*Me*CO), 171.5 (Me*CO*), 166.3 (Ph*COO*), 133.0, 130.4, 129.7, 128.6 (*Ph*COO); CIMS ($CH_4$) *m*/*z* 467 $[M + 1]^+$ (1), 345 (15), 285 (100), 267 (56). Anal. Calcd for $C_{29}H_{38}O_5$: C, 74.68; H, 8.15. Found: C, 74.9; H, 7.9.

***ent*-18-Acetoxy-15$\beta$-(benzoyloxy)-12$\alpha$-chloro-14$\alpha$-hydroxykaurane (16):** mp 156−58 °C; $[\alpha]^{20}_D$ +11.0° (*c* 0.5, $CHCl_3$); IR $\nu$(max) 3508, 1714, 1279; $^1$H NMR ($\delta$, $CDCl_3$) 8.03−7.40 (5H, PhCOO), 5.22 (1H, d, $J$ = 8.0 Hz, H-15), 4.25 (1H, ddd, $J_1$ = 12.0 Hz, $J_2$ = 6.2 Hz, $J_3$ = 2.3 Hz, H-12), 4.14 (1H, s, H-14), 3.77 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.60 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 2.01 (3H, s, MeCOO), 1.10 (d, $J$ = 8.0 Hz, 3H-17), 0.97, 0.79 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 39.8 (C-1), 17.9 (C-2), 35.4 (C-3), 36.4 (C-4), 49.4 (C-5), 18.9 (C-6), 27.1 (C-7), 53.1 (C-8), 58.4 (C-9), 39.2 (C-10), 30.1 (C-11), 60.8 (C-12), 56.0 (C-13), 76.8 (C-14), 84.4 (C-15), 35.0 (C-16), 17.2 (C-17), 72.6 (C-18), 18.4 (C-19), 17.5 (C-20), 21.1 (*Me*CO), 171.3 (Me*CO*), 166.0 (Ph*COO*), 133.2, 129.7, 128.6, 128.5, (*Ph*COO); CIMS ($CH_4$) *m*/*z* 503 $[M + 1]^+$ (1), 487 (2), 485 (5), 468 (4), 365 (4), 363 (10), 323 (33), 321 (100), 305 (12), 303 (33). Anal. Calcd for $C_{29}H_{38}O_5$-Cl: C, 69.32; H, 7.57. Found: C, 69.2; H, 7.7.

***ent*-18-Acetoxy-14$\beta$-(benzoyloxy)-12$\alpha$-chloro-15$\alpha$-hydroxybeyerane (17):** mp 129−31 °C; $[\alpha]^{20}_D$ +3.8° (*c* 1, $CHCl_3$); IR $\nu$(max) 3526, 1718, 1275; $^1$H NMR ($\delta$, $CDCl_3$) 8.00−7.40 (5H, PhCOO), 5.42 (1H, s, H-14), 4.35 (1H, m, H-15), 4.10 (1H, d, $J$ = 1.7 Hz, H-12), 3.78 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.61 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 2.07 (3H, s, MeCOO), 1.12, 1.00, 0.80 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 38.9 (C-1), 17.5 (C-2), 35.3 (C-3), 36.4 (C-4), 49.4 (C-5), 18.7 (C-6), 27.5 (C-7), 52.4 (C-8), 49.6 (C-9), 37.4 (C-10), 28.8 (C-11), 68.2 (C-12), 48.5 (C-13), 88.0 (C-14), 72.1 (C-15), 49.4 (C-16), 20.2 (C-17), 72.5 (C-18), 17.8 (C-19), 16.1 (C-20), 21.2 (*Me*CO), 171.4 (Me*CO*), 165.8 (Ph*COO*), 133.3, 129.9, 129.6, 128.7 (*Ph*COO); CIMS ($CH_4$) *m*/*z* 503 $[M + 1]^+$ (6), 487 (4), 485 (11), 383 (3), 381 (9), 365 (6), 363 (18), 323 (33), 321 (100). Anal. Calcd for $C_{29}H_{38}O_5Cl$: C, 69.32; H, 7.57. Found: C, 69.1; H, 7.6.

**Oxidation of *ent*-18-Acetoxy-15$\beta$-(benzoyloxy)-14$\alpha$-hydroxyatis-16-ene (13).** Product **13** (50 mg) was oxidized with Jones' reagent for 6 h as described above, and after flash chromatography *ent*-18-acetoxy-15$\beta$-(benzoyloxy)atis-16-en-14-one (**18**) was obtained (40 mg, 86%).

***ent*-18-Acetoxy-15$\beta$-(benzoyloxy)atis-16-en-14-one (18):** mp 66−68 °C; $[\alpha]^{20}_D$ −64.0° (*c* 0.5, $CHCl_3$); IR $\nu$(max) 2950, 1733, 1240; $^1$H NMR ($\delta$, $CDCl_3$) 7.95−7.38 (5H, PhCOO), 5.62 (1H, s, H-14), 5.19 (1H, s, H-17), 5.15 (1H, s, H-17), 3.80 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 3.60 (1H, $Q_{AB}$, $J$ = 11.0 Hz, H-18), 2.84 (1H, m, H-12), 2.04 (3H, s, MeCOO), 0.80, 0.77 (3H each, s); $^{13}$C NMR ($\delta$, $CDCl_3$) 38.4 (C-1), 17.4 (C-2), 35.7 (C-3), 36.3 (C-4),

48.9 (C-5), 18.6 (C-6), 28.0 (C-7), 51.8 (C-8), 48.9 (C-9), 38.0 (C-10), 28.6 (C-11), 37.2 (C-12), 44.2 (C-13), 213.2 (C-14), 79.1 (C-15), 147.8 (C-16), 114.0 (C-17), 72.6 (C-18), 17.8 (C-19), 14.2 (C-20), 21.2 (*Me*CO), 171.3 (Me*CO*), 166.3 (Ph*COO*), 133.3, 129.9, 129.8, 128.5 (*Ph*COO); CIMS ($CH_4$) *m/z* 465 $[M + 1]^+$ (5), 343 (100), 283 (80). Anal. Calcd for $C_{29}H_{36}O_5$: C, 75.00; H, 7.76. Found: C, 74.8; H, 8.0.

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