

Characterization of an *abeo*-Taxane: Brevifoliol and Derivatives

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Brevifoliol is a natural diterpene isolated from *Taxus baccata* Nutt. A series of brevifoliol **1** derivatives, **2**–**8** and **10**, were prepared for characterization and semisynthesis purposes and included the introduction of acetyl, Troc, and TES groups at C-5 and C-13. Derivatives **16**–**20** of 5-acetylbrevifoliol **2** were obtained via esterification with cinnamic acid, with both 2*S*(–) and 2*R*(+)-3-phenyllactic acid, and with *N*-benzoyl-(2′*R*,3′*S*)-3′-phenylisoserine at C-13. Brevifoliol compounds **12**, **13**, and **15** with either 2*S*(–)-phenyllactate moieties at C-5 and C-13 or an *N*-benzoyl-(2′*R*,3′*S*)-3′-phenylisoserinyl at C-13 were also prepared. An *abeo*-taxane structure for **1** was clearly defined from the ¹³C NMR analysis of the 5-acetyl-13-oxo derivative **8** and from the conversion of **1** into **10**, a conformationally restrained compound having a C-13, C-15 oxygen bridge. The biological activity of each of these derivatives is being studied.

The diterpenoid paclitaxel (Taxol), originally isolated from the bark of *Taxus brevifolia*,¹ has stimulated intense research efforts in recent years because of its remarkable anticancer activity.^{2,3} Recently, a lot of attention has been focused on the search for other members of the taxane group⁴ that may be directly active or may serve as precursors for the semisynthesis of other active analogues.^{5–7} The following work describes a detailed characterization of brevifoliol **1**, a relatively abundant metabolite isolated from *Taxus brevifolia* needles (up to 0.30%). We have also been interested in the synthesis of brevifoliol derivatives for their biological activity, that is, microtubule disassembly and P-glycoprotein (P-gp) inhibition.

Brevifoliol had originally been proposed to have a taxa-4(20),11-diene system, **A**, similar to that of taxol⁸ (Figure 1). Lewis⁹ then proposed a taxane structure, **B**, for brevifoliol, while, later, Georg¹⁰ and Appendino¹¹ both revised the structure to an 11(15→1)-*abeo*-taxa-4(20),11-diene skeleton, **1**. These assignments were based solely on 1D and 2D NMR spectral data, and three key quaternary signals (i.e., C-1, C-8, and C-15) were missassigned.^{9,10} 11-(15→1)-*abeo*-Taxanes are, in general, difficult to characterize by NMR spectroscopy since they shift between different conformational isomers in solution.¹² In fact, most of the *abeo*-taxane structures reported in the literature needed to be confirmed by X-ray crystallography.^{11–13}

An X-ray crystal structure of **2** was obtained by one of the present coauthors (C.S.).¹⁴ It showed an 11(15→1)-*abeo*-taxane structure, but unfortunately, the crystals were unstable and its structure was obtained only after replacing the reflections measured during the first 30 h by a set of data taken at the end. Thus, the possibility of a skeletal rearrangement of brevifoliol to the 11(15→1)-*abeo*-taxane structure during the isolation and/or acetylation or during X-ray irradiation could not be ruled out. Indeed, there are examples of such chemical rearrangements in the literature.^{15,16}

Results and Discussion

An extract of the needles and twigs of *T. brevifolia* was obtained as previously described.⁸ We optimized the isolation

of brevifoliol from such extracts. An updated spectral characterization of brevifoliol, **1**, is given in Tables S1 and S2 (Supporting Information).

We began our investigation with the preparation of various derivatives with substituents at C-5 and C-13 (Figure 1). These included the mono- and bisacetyl, mono- and bis-2,2,2-trichloroethoxycarbonyl (Troc), and bis-triethylsilyl (TES) groups. Although 5-, 13-acetyl, and 5,13-bisacetyl-brevifoliol, **2**, **3**, and **4**,^{8,14} are known in the literature, they have not been adequately characterized. The Troc protecting group was introduced at C-5 with high selectivity by treatment of brevifoliol with Troc-Cl at –25 °C. Reactions at higher temperatures (i.e., 22 and 43 °C) afforded **5**, along with up to 27% of 5,13-bisTroc-brevifoliol **6**. In these reactions, the corresponding 13-Troc derivative could not be isolated. To our surprise, all attempts to prepare the 5-TES derivative gave only low yields of a single product, 5,13-TES-brevifoliol, **7**. However, **7** was obtained in good yield when 3.5 equiv of TESCl was used. Attempts to prepare the corresponding 5- and 13-FMOC (fluorenylmethyloxycarbonyl) derivatives by treating **1** with an excess of FMOC-Cl in pyridine resulted in the recovery of unreacted brevifoliol, even when the reaction mixture was heated to 50 °C. Similarly, the introduction of a benzyl group at C-13 of **5**, via the use of an excess of benzyl bromide in the presence of a catalytic amount of *n*-Bu₄NI and using dimethylamino pyridine (DMAP) as the base in pyridine, met with failure even when heated to 80 °C. All of these transformations illustrate unprecedented chemical behavior for **1**.

None of these derivatives afforded crystals suitable for X-ray analysis. Nonetheless, we were able to fully characterize all compounds synthesized. As mentioned above, 11-(15→1)-*abeo*-taxoids generally undergo a slow equilibration between two or more conformational isomers in solution, a characteristic of this type of diterpenoid structure.¹² Thus, the typical ¹H spectrum of an *abeo*-taxane usually displays a broadening of most of the signals and includes the appearance of many minor additional peaks.¹³ However, the room-temperature ¹H and ¹³C NMR spectra of **2**, **3**, and **5** were very similar to that of brevifoliol, **1**, being characterized by the same sharp, well-resolved first-order spectra with chemical shifts, multiplicities, and NOE effects as those of the taxanes. Also, a broad doublet for H-9 was observed in all derivatives, and in the cases of 5,13-disubstituted derivatives **4**, **6**, and **7**, additional broad peaks were noted for the protons assigned to H-5, -10, and

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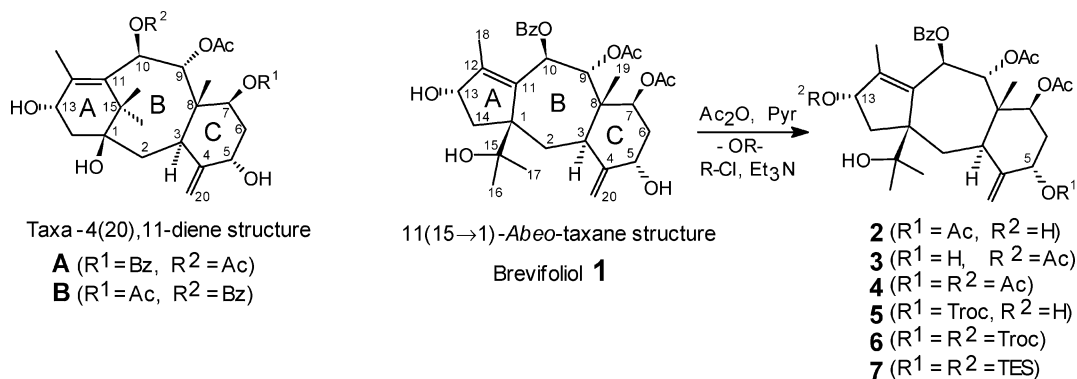


Figure 1. Proposed structures for brevifoliol and syntheses of C-5, C-13 derivatives **2**–**7**.

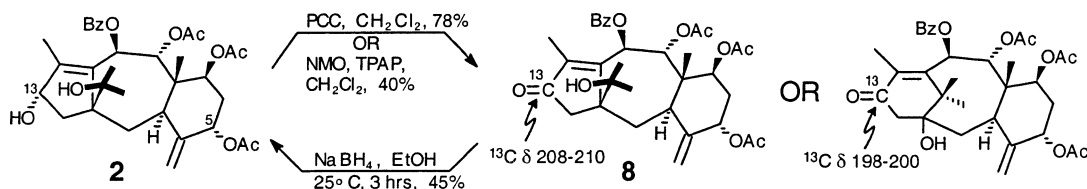


Figure 2. Oxidation of **2** to the conjugated ketone **8** and reduction back to **2**.

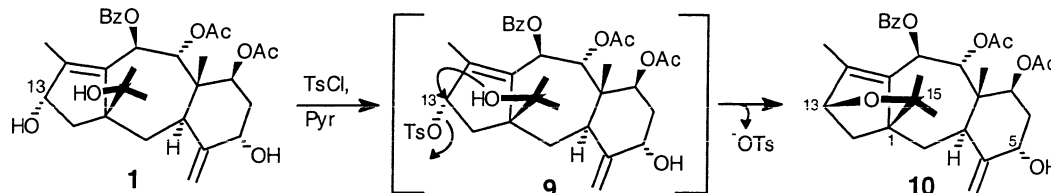


Figure 3. Conversion of brevifoliol **1** to the C-13, C-15 bridge ether compound **10**.

-13. The line broadening of these signals is consistent with an *abeo*-taxane structure for these derivatives.

In the HMBC spectrum of **2**, the signals at δ 5.34 (s, H-5), 5.58 (dd, H-7), and 6.01 (d, H-9) were correlated to three acetyl carbonyl signals at δ 169.8, 170.9, and 170.1, which indicates that these acetyl groups are located at C-5, -7, and -9. Unfortunately, in all cases, the HMBC spectra, acquired at various evolution delays, did not show any key correlations between H-10 and C-15 nor between H-10 and C-1. Also, while a correlation between the signals for the protons of Me-16 and Me-17 with the peak assigned to C-15 was observed, key correlations of these protons with the resonances for the carbons at C-1 and C-11, usually observed in taxane structures, were either absent or buried within the background noise. Confronted with the persistent uncertainty surrounding the analyses of the various 2D NMR data of compounds **1**–**7**, we envisaged other simple chemical transformations that would enable us to establish a more clear-cut distinction between the 11-(15→1)-*abeo*-taxane structure and that of the taxanes, that is, between a five- and six-membered A ring, respectively. To this end, we reasoned that oxidation of the hydroxyl function at C-13 would convert the A ring into either a five- or six-membered enone, which should be easy to differentiate by ^{13}C NMR spectroscopy. Pyridinium chlorochromate (PCC) oxidation of 5-acetylbrevifoliol, **2**, yielded ketone **8** (Figure 2), for which the room-temperature ^1H and ^{13}C NMR spectra displayed many broad signals. The ^{13}C NMR spectrum was, nonetheless, quite informative. It is known that the carbonyl of the five-membered A ring enone typically resonates further downfield (δ 208–210)^{17,18} than that of the corresponding six-membered A ring enone in taxinines (δ 198–200).¹⁹ The ^{13}C NMR spectrum of enone **8** showed a single peak at δ 207, which suggests a five-membered enone and, thus, an 11(15→1)-*abeo*-taxane

structure. To verify that there had not been any skeletal rearrangement of **2** induced by PCC, which is an acidic reagent, another oxidation of **2** was carried out under neutral conditions²⁰ with tetrapropylammonium perruthenate (TPAP) and *N*-methylmorpholine *N*-oxide (NMO) as catalyst and co-oxidant, respectively. This reaction provided the same enone. Indeed, the reduction of enone **8** with NaBH_4 in EtOH produced **2** once again, thus ruling out the possibility of rearrangement of the A ring.

Although quite useful, this method is limited to substrates having only one free secondary hydroxyl (i.e., C-13). Another transformation would place a leaving group at C-13. In an *abeo*-taxane structure such as **9**, the angular tertiary C-15 hydroxyl group is well positioned to undergo an intramolecular nucleophilic substitution to form a bridge ether (Figure 3). Such a substitution reaction cannot take place with a taxane-type structure, but it should be possible to isolate derivatives substituted at C-5 and C-13. To our delight, treatment of brevifoliol with tosyl chloride provided a single new product, **10** (Figure 3). Both the ^1H and ^{13}C NMR spectra displayed sharp, well-resolved lines at room temperature, consistent with a conformationally fixed structure. A FABMS showed a parent peak at 538 amu for the $[\text{M}]^+$ ion, which corresponds to a dehydrated brevifoliol. The peak usually observed at δ 2.7 (OH at C-15) in **1** was also absent in **10**. The unusual shielding of the resonance for H-9 (0.85 ppm) is indicative of a change of conformation relative to **1**.¹² Furthermore, the ^{13}C resonances of all the carbons in ring A and those surrounding this ring were either shielded by an average of 3.5 ppm (C-2, -9, -10, and -12) or deshielded by 4.5 ppm on average (C-11, -13, -14, and -15) relative to those of **1** (Table S2). Thus, the conformational changes observed essentially affect ring A and the connecting parts of ring B. Together, these results are consistent with a substitution product having the

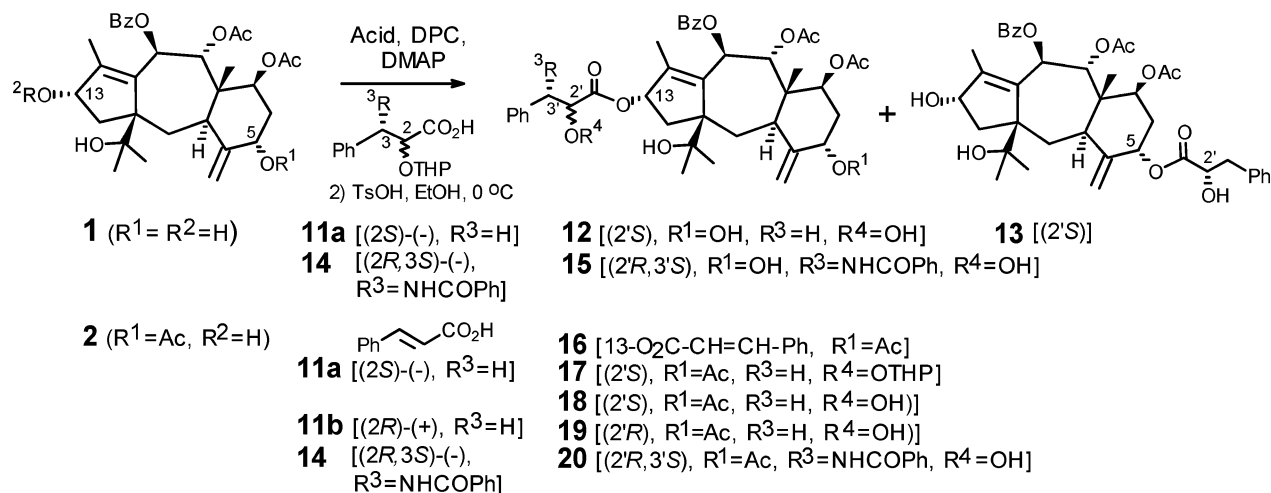


Figure 4. Synthesis of brevifoliol derivatives **12**, **13**, and **15–20**.

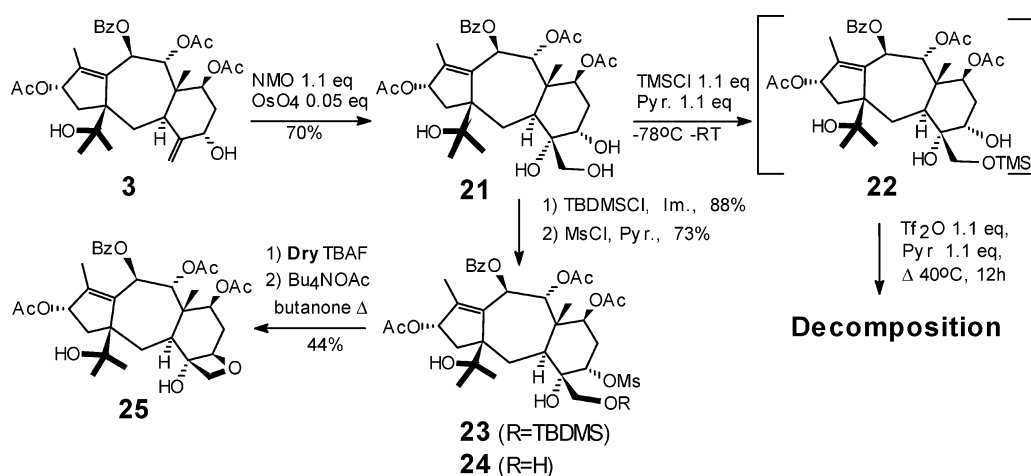


Figure 5. Construction of an oxetane D ring on derivative **3**.

bridge ether depicted for **10**. This structure was unambiguously confirmed by the detection of long-range correlations between H-13 and C-1, C-11, in the HMBC spectrum. Such correlations are not feasible for a taxane structure; therefore, brevifoliol has an 11(15→1)*abeo*-taxane structure. A consideration of the optical rotations provides an interesting side note since all known 13- α -hydroxylated 11(15→1)-*abeo*-taxane structures reported^{12,15,21} had negative rotations, while those derivatives having a C13–C15 oxygen bridge (i.e., 13- β oxygenated derivatives such as **10**) have positive ones.¹² The above findings agree with that reported for an *abeo*-taxane product having also a C13–C15 bridge ether which was isolated from *Taxus x media* Rehd. Cv Hicksii.¹²

Having firmly established a five-membered A ring for brevifoliol, **1**, we set out to further modify its structure in an attempt to enhance its biological activity profile. Over the past 10 years structure–activity relationship studies^{5–7,15,22} have revealed some structural elements that seem to be essential for the antitumor activity of the taxanes. More specifically, these elements include a C-13 phenylisoserine side chain, an oxetane D ring, a C-4 alkoxy group, and a C-2 aromatic ester or cyclohexanoate moiety. As for the inhibition of the drug transport activity of P-gp, the most active taxoids have in common a C-5 cinnamoyl moiety. The A ring could be five- or six-membered, and the C-13 was either substituted with an acetyl group or was a ketone.²³

Our initial objective was the introduction of a lateral side chain such as cinnamoyl, (*R*)- and (*S*)-phenyl lactate (which

may be considered to be deaminated derivatives of phenylisoserine or hydrated derivatives of the cinnamate moiety) and the phenylisoserinate at the C-13 and C-5 positions. A subsequent objective was the construction of an oxetane D ring.

Our first structural modification of brevifoliol, **1**, was to couple it to the propanoic acid (2*S*)-**11a** to give a mixture of isomers **12** and **13** having a C-13 side chain and a free C-5 hydroxyl group and vice versa (Figure 4). These esterifications were carried out using the coupling agent dipyrindyl carbonate (2-DPC).²⁴ An *N*-benzoyl-(2'*R*,3'*S*)-phenylisoserine moiety was introduced at C-13 of **1** via esterification of the corresponding *O*-tetrahydropyranyl (THP)-protected acid **14**,²⁵ and subsequent hydrolysis of the THP ether afforded the ester **15**.²⁶ 5-Acetylbrevifoliol, **2**, was coupled with cinnamic acid to provide ester **16**. Both phenyl lactate antipodal moieties were introduced at C-13 of **2**, via esterification of the corresponding *O*-THP-protected acids, (2*S*)-(-)-**11a** or (2*R*)-(+)-**11b**, and subsequent hydrolysis of the THP ether intermediate **17** produced the hydroxy ester derivatives **18** and **19**. Only the *S*-intermediate was isolated. An *N*-benzoyl-(2'*R*,3'*S*)-phenylisoserine moiety was also introduced via esterification of the corresponding acid, **14**, with the hydroxyl at the C-13 of **2** to provide **20**.

Our next goal was to place an oxetane D ring on the brevifoliol skeleton. Several methods to accomplish this transformation have been reported.^{7,27} A method developed by Danishefsky's group^{27c} was applied to compound **3**, but this led to complete decomposition of the starting material

(Figure 5). To close the oxetane ring, we adapted Potier's protocol.⁷ Thus, osmylation of **3** was carried out with *N*-methylmorpholine-*N*-oxide (NMO) and OsO₄ to produce the triol **21**. We protected the primary alcohol function as the *tert*-butyldimethylsilyl ether and then mesylated the secondary alcohol. This gave **23**, while subsequent removal of the silane function with dry TBAF gave the free primary alcohol **24**. Further treatment of **24** with tetrabutylammonium acetate produced the oxetane **25** (Figure 5).

We have prepared and characterized the C-5- and C-13-acetyl, **1–4**, Troc **5** and **6**, and TES, **7**, derivatives of brevifoliol, **1**. Two simple transformations (oxidation of the C-13 allylic alcohol to give **8** and formation of a C13–C15 ether bridge to give **10**) were used to unambiguously differentiate the abeo-taxane-type substrate from that of taxane. Spectroscopic data collected from 5-acetyl-13-oxobrevifoliol, **8**, and its ether, **10**, clearly and definitively established the structure of brevifoliol to be 9 α ,7 β -diacetoxy-10 β -benzoxy-11(15 \rightarrow 1)-abeo-taxane-4(20),11-dien-5 α ,13 α ,15-triol (**1**), in which ring A is five-membered. Derivatives **12** and **13**, having an *S*(–)-3-phenyllactate at C-5 and C-13 of brevifoliol, as well as brevifoliol-13-[*N*-benzoyl-2'-*R*, 3'-*S*]-3'-phenylisoserinate], **15**, were prepared. Derivatives with a cinnamoyl (**16**), both *S*(–) and *R*(+)-3-phenyllactate (**18**, **19**), and a [*N*-benzoyl-2'-*R*,3'-*S*]-3'-phenylisoserinate] (**20**) esterified at the C-13 of 5-acetyl-brevifoliol were also synthesized. We are currently evaluating these brevifoliol derivatives for microtubule assembly activity and for P-gp inhibition, and the results will be reported elsewhere.²⁸

Experimental Section

General Experimental Procedures. ¹H NMR spectra were recorded using a 500, 300BB, or 200 MHz spectrometer with either CD₂Cl₂ or CDCl₃ as solvent. Chemical shifts are reported in parts per million (δ) and are downfield from (CH₃)₄Si. ¹³C spectra were recorded at 75 or 125 MHz. Optical rotation data were recorded at 589 nm on a digital polarimeter. Melting points are uncorrected. Mass spectra were obtained using a VG Auto-SpecQ FAB⁺ Magnet BpI or a GC-MS (GCD plus gas chromatography-electron ionization detector) equipped with a 5% cross-linked PhMe silicone HP 19091 J-433 column, and the mass data are reported as *m/z*, with the intensity indicated in parentheses as a percent of the base peak. Silica gel 60 (230–400 mesh) was used for all column chromatography. Some separations were carried out on a centrifugally accelerated, radial, thin-layer chromatograph (Chromatotron) using silica gel PF-254 with CaSO₄· $\frac{1}{2}$ H₂O type 60 as adsorbent.

S(–)- and *R*(+)-3-phenyllactic acid, chlorotriethylsilane (TESCl), 2,2,2-trichloroethyl chloroformate (TrocCl), TsCl, DMAP, 4-methylmorpholine-*N*-oxide (NMO), tetrabutylammonium perruthenate(VII) (TPAP), imidazole, and *S*(+)-phenylglycine as well as all other inorganic reagents were used without further purification. The isolation of brevifoliol, **1**, from *T. brevifolia* needles⁸ and the syntheses of compounds **2–4**, **11a**, and **11b** are described in the Supporting Information section. (2*R*,3*S*)-(–)-2-(Tetrahydropyran-2-yloxy)-3-phenylmethanamido)propanoic acid, **14**, was prepared from *S*(+)-phenylglycine as previously described²⁵ with the exception that tetrahydropyranyl was used as a protecting group instead of an ethoxyethyl group. Di-2-pyridyl carbonate (2-DPC) was prepared as previously described.²⁴ Pyridine and triethylamine were freshly distilled over calcium hydride prior to use. Celite was used as a filtering agent. THF and diethyl ether were dried over sodium/benzophenone and distilled under a nitrogen atmosphere immediately prior to use. All reactions were carried out under nitrogen unless otherwise noted. Molecular sieves (4 Å-ms) were crushed and flame dried prior to use.

5-Troc-brevifoliol (5). 2,2,2-Trichloroethoxycarbonyl Troc-Cl (6.2 μ L, 0.045 mmol) was added to a brevifoliol (**1**, 50 mg,

0.090 mmol) solution in pyridine (1 mL) at –30 °C, containing 4 Å-ms (400 mg). The reaction mixture was stirred at –30 °C for 2 h. More Troc-Cl (6.2 μ L, 0.045 mmol) was added and stirred for an additional hour at –30 °C. The same quantity of Troc-Cl was added, and the mixture was kept at –20 °C for a 15 h period. One last portion of Troc-Cl was added and stirred at –20 °C for another 2 h. MeOH (50 μ L) was then added, and the reaction mixture was allowed to warm to room temperature. The salts that formed were filtered through Celite and washed with CH₂Cl₂ (4 mL) and EtOAc (4 mL), and the filtrate was concentrated under reduced pressure. The residue was purified by radial chromatography (2–5% EtOAc–CH₂Cl₂), giving 0.1 mg (0.1%) of 5,13-bis(Troc)brevifoliol **6** and 44.4 mg (68%) of **5** followed by 21 mg of impure **1**. The derivative **5** was obtained as a white powder: mp 110–112 °C; [α]_D²³ –35.0° (*c* 1.03, CH₂Cl₂); IR (KBr) ν_{\max} 3567, 2970, 1746, 1653, 1602, 1450, 1376, 1244, 1090, 1069, 1033, 904, 819, 784, 759, 712, 602, 572 cm^{–1}; ¹H NMR (CDCl₃, 500 MHz) δ 0.92 (3H, s, H-19), 1.02 (3H, s, H-16), 1.08 (1H, dd, *J* = 14.3, 6.7 Hz, H-14 α), 1.33 (3H, s, H-17), 1.40 (1H, s, OH (C-13)), 1.45 (1H, d, *J* = 13.9 Hz, H-2 α), 1.77 [3H, s, O₂CCH₃, (C-9 or C-7)], 1.93 (1H, td, *J* = 13.5, 3.9 Hz, H-6 β), 2.07 [3H, s, O₂CCH₃ (C-9 or C-7)], 2.15 (3H, s, H-18), 2.18 (1H, dd, *J* = 15.3, 5.2 Hz, H-6 α), 2.44 (1H, dd, *J* = 13.9, 8.9 Hz, H-2 β), 2.52 (1H, dd, *J* = 14.3, 7.4 Hz, H-14 β), 2.76 (1H, d, *J* = 8.9 Hz, H-3 α), 2.84 [1H, br s, OH (C-15)], 4.42 (1H, dd, *J* = 7.4, 6.7 Hz, H-13 β), 4.67, 4.86 (each 1H, d, *J* = 11.7 Hz, CCl₃CH₂O), 4.99 (1H, s, H-20a), 5.30 (1H, t, *J* = 3.9 Hz, H-5 β), 5.35 (1H, s, H-20b), 5.60 (1H, dd, *J* = 11.0, 5.2 Hz, H-7 α), 6.02 (1H, br d, *J* = 10.3 Hz, H-9 β), 6.62 (1H, d, *J* = 10.3 Hz, H-10 α), 7.43 (2H, t, *J* = 7.5 Hz, H_{m-Ph}), 7.55 (1H, t, *J* = 7.5 Hz, H_{p-Ph}), 7.87 (2H, d, *J* = 7.5 Hz, H_{o-Ph}); ¹³C NMR (CDCl₃, 125 MHz) δ 11.8 (CH₃, C-18), 12.8 (CH₃, C-19), 20.7 [CH₃, O₂CCH₃ (C-9 or C-7)], 21.3 [CH₃, O₂CCH₃ (C-7 or C-9)], 24.8 (CH₃, C-17), 27.0 (CH₃, C-16), 29.0 (CH₂, C-2), 33.5 (CH₂, C-6), 38.9 (CH, C-3), 44.7 (C, C-8), 48.1 (CH₂, C-14), 63.2 (C, C-1), 69.2 (CH, C-7), 70.7 (CH, C-10), 75.4 (C, C-15), 76.7 (CH₂, CH, CCl₃CH₂O and C-9), 77.6 (CH, C-13), 80.0 (CH, C-5), 94.2 (C, CCl₃C), 115.2 (CH₂, C-20), 128.8 (CH, C-3'), 129.2 (C, C-1'), 129.4 (CH, C-2'), 133.3 (CH, C-4'), 134.2 (C, C-11), 144.5 (C, C-4), 151.8 (C, C-12), 152.6 (C, CCl₃CH₂OCO₂), 164.1 (C, O₂CPh), 169.7 [C, O₂CCH₃ (C-9 or C-7)], 169.8 [C, O₂CCH₃ (C-7 or C-9)]; FABMS (NBA) *m/z* 713 [MH – H₂O]⁺, 609–615 [MH – PhCO₂H]⁺, 591 [MH – PhCO₂H – H₂O]⁺, 549–566 [MH – PhCO₂H – AcOH]⁺, 533 [MH – PhCO₂H – AcOH – H₂O]⁺.

5,13-Bis(Troc)brevifoliol (6). Troc-Cl (12 μ L, 0.087 mmol) was added to a solution of **1** (26 mg, 0.047 mmol) in pyridine (0.5 mL) containing 4 Å-ms (200 mg). The reaction mixture was stirred at room temperature for 3 h. More Troc-Cl (12 μ L, 0.087 mmol) was added, and the mixture was stirred for an additional 15 h. The salts that formed were filtered through Celite and washed with CH₂Cl₂ (2 mL) and EtOAc (2 mL), and the filtrate was concentrated under reduced pressure. The residue was purified by radial chromatography (2–5% EtOAc–CH₂Cl₂), giving 15.4 mg (36%) of **6** and 16.4 mg (48%) of **5**, as white powders. The derivative **6** had the following physical characteristics: mp 177–179 °C; [α]_D²³ –17.0° (*c* 0.91, CH₂Cl₂); IR (KBr) ν_{\max} 3578, 2976, 1752, 1663, 1600, 1438, 1374, 1248, 1132, 1090, 1067, 1033, 938, 920, 882, 822, 788, 714, 602, and 570 cm^{–1}; ¹H NMR (CDCl₃, 500 MHz) δ 0.94 (3H, s, H-19), 1.12 (3H, s, H-16), 1.35–1.45 (1H, m, H-14 α), 1.38 (3H, s, H-17), 1.53 (1H, d, *J* = 14 Hz, H-2 α), 1.76 (3H, s, O₂CCH₃, C-9 or C-7), 1.95 (1H, td, *J* = 14, 3.5 Hz, H-6 β), 2.07 [3H, s, O₂CCH₃ (C-7 or C-9)], 2.09 (3H, s, H-18), 2.20 (1H, dd, *J* = 14, 4.2 Hz, H-6 α), 2.45 (1H, dd, *J* = 14, 9 Hz, H-2 β), 2.54 (1H, dd, *J* = 13.9, 7.4 Hz, H-14 β), 2.70 [1H, br s, OH (C-15)], 2.73 (1H, d, *J* = 9 Hz, H-3 α), 4.68 [1H, d, *J* = 11.8 Hz, CCl₃CH₂O (C-5 or C-13)], 4.79 [2H, br dd, CCl₃CH₂O (C-5 or C-13)], 4.99 [2H, br s, H-20a + CCl₃CH₂O (C-5 or C-13)], 5.27 (1H, t, *J* = 3.5 Hz, H-5 β), 5.38 (1H, s, H-20b), 5.53 (1H, br t, *J* = 7.4 Hz, H-13 β), 5.65 (1H, dd, *J* = 10, 4.2 Hz, H-7 α), 6.15 (1H, br d, *J* = 10.3 Hz, H-9 β), 6.67 (1H, br d, *J* = 10.3 Hz, H-10 α), 7.45 (2H, t, *J* = 7.5 Hz, H_{m-Ph}), 7.55 (1H, t, *J* = 7.5 Hz, H_{p-Ph}), 7.88 (2H, d, *J* = 7.5 Hz, H_{o-Ph}); ¹³C NMR (CDCl₃, 75 MHz) δ 11.9 (CH₃, C-18), 12.8 (CH₃, C-19), 20.7 [CH₃, O₂CCH₃ (C-9) or

(C-7)], 21.3 [CH₃, O₂CCH₃ (C-7) or (C-9)], 25.1 (CH₃, C-17), 27.2 (CH₃, C-16), 29.3 (CH₂, C-2), 33.7 (CH₂, C-6), 38.4 (CH, C-3), 43.7 (CH₂, C-14), 44.8 (C, C-8), 62.6 (C, C-1), 69.2 (CH, C-7), 69.5 (CH, C-10), 75.6 (C, C-15), 76.4 (CH₂, Cl₃CH₂O), 76.7 [CH, CH₂, C-9 and Cl₃CH₂O], 79.2 (CH, C-5), 84.2 (CH, C-13), 94.5, (C, CCl₃C), 94.8 (C, CCl₃C), 115.4 (CH₂, C-20), 128.8 (CH, C-3'), 129.1 (C, C-1'), 129.5 (CH, C-2'), 133.4 (CH, C-4'), 136.9 (C, C-11), 144.2 (C, C-4), 146.7 (C, C-12), 153.0 (C, CCl₃CH₂OCO₂), 154.2 (C, CCl₃CH₂OCO₂), 164.0 (C, O₂CPh), 169.6 [C, O₂CCH₃ (C-7 or C-9)], 169.9 [C, O₂CCH₃ (C-9 or C-7)]; FABMS (thioglycerol) *m/z* 904 [MH]⁺, 787 [MH - PhCO₂H]⁺, 767 [MH - PhCO₂H - H₂O]⁺, 727 [MH - PhCO₂H - AcOH]⁺.

5,13-Bis(TES)breviolifol (7). TESCl (80 μ L, 0.48 mmol) was added to a solution of **1** (106 mg, 0.19 mmol) and pyridine (40 μ L) in CH₂Cl₂ (1 mL). The reaction mixture was stirred for 2 h, and TESCl (16 μ L, 0.096 mmol) and pyridine (8 μ L) were added. After stirring 1.5 h, more TESCl (32 μ L, 0.19 mmol) and pyridine (16 μ L) were added, and the mixture was stirred for 18 h. The reaction mixture was diluted with CH₂Cl₂ (2 mL), cooled to 5 °C for 22 h, and filtered through a pad of Celite (0.5 cm). The solids were washed with EtOAc (2 mL), and the combined filtrate was evaporated. The residue was separated by radial chromatography (EtOAc-Hex, 1:4) to afford 104 mg (69%) of **7** as a white powder: mp 121–123 °C; [α]_D²³ -10.2° (c 1.0, CH₂Cl₂); IR (KBr) ν_{\max} 3559, 2956, 1741, 1664, 1601, 1458, 1375, 1263, 1089, 1028, 1002, 907, 826, 742, 709, 605 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 0.59 [12H, q, *J* = 7.6 Hz, 2 Si(CH₂CH₃)₃], 0.92 (3H, s, H-19), 0.95 [18H, t, *J* = 7.6 Hz, 2 Si(CH₂CH₃)₃], 1.09 (3H, s, H-16), 1.36–1.43 (2H, m, H-2 α + H-14 α), 1.37 (3H, s, H-17), 1.77 (3H, s, O₂CCH₃ (C-9 or C-7)), 1.65–1.79 (1H, m, H-6 β), 1.82 (1H, m, H-6 α), 1.98 (3H, s, H-18), 2.04 [3H, s, O₂CCH₃ (C-7 or C-9)], 2.21 (1H, dd, *J* = 13.2, 6.8 Hz, H-14 β), 2.32 (1H, br t, *J* = 13 Hz, H-2 β), 2.70 [1H, br s, OH (C-15)], 3.01 (1H, d, *J* = 9.1 Hz, H-3 α), 4.25 (1H, br s, H-5 β), 4.48 (1H, br t, *J* = 6.8 Hz H-13 β), 4.69 (1H, br s, H-20 α), 5.00 (1H, s, H-20 β), 5.70 (1H, dd *J* = 10.7, 5.5 Hz, H-7 α), 6.08 (1H, br d, *J* = 10.4 Hz, H-9 β), 6.63 (1H, br d, *J* = 10.4 Hz, H-10 α), 7.43 (2H, t, *J* = 7.5 Hz, H_{m-Ph}), 7.55 (1H, t, *J* = 7.5 Hz, H_{p-Ph}), 7.89 (2H, br d, *J* = 7.5 Hz, H_{o-Ph}); ¹³C NMR (CDCl₃, 75 MHz) δ 4.65 (CH₂, SiCH₂), 4.75 (CH₂, SiCH₂), 6.77 (CH₃, SiCH₂CH₃), 6.86 (CH₃, SiCH₂CH₃), 11.8 (CH₃, C-18), 12.8 (CH₃, C-19), 20.7 [CH₃, O₂CCH₃ (C-9 or C-7)], 21.4 [CH₃, O₂CCH₃ (C-7 or C-9)], 25.1 (CH₃, C-17), 27.4 (CH₃, C-16), 29.7 (CH₂, C-2), 37.0 (CH, C-3), 37.9 (CH₂, C-6), 45.0 (C, C-8), 47.8 (CH₂, C-14), 61.6 (C, C-1), 70.0 (CH, C-7), 70.7 (CH, C-10), 72.6 (CH, C-5), 76.0 (CH, C-13), 76.9 (CH, C-9), 77.2 (C, C-15), 109.3 (CH₂, C-20), 128.6 (CH, C-3'), 129.4 (CH, C-2'), 129.6 (C, C-1'), 132.7 (C, C-11), 133.0 (CH, C-4'), 151.1 (C, C-4), 151.8 (C, C-12), 164.1 (C, O₂CPh), 169.6 [C, O₂CCH₃ (C-7 or C-9)], 169.9 [C, O₂CCH₃ (C-9 or C-7)]; FABMS (thioglycerol) *m/z* 785 [MH]⁺, 725 [MH - AcOH]⁺, 663 [MH - PhCO₂H]⁺, 645 [MH - PhCO₂H - H₂O]⁺, 603 [MH - PhCO₂H - AcOH]⁺, 545 [MH - PhCO₂H - 2 AcOH]⁺.

5-Acetyl-13-oxobrevifol (8). (a) **From PCC Oxidation.** Pyridinium chlorochromate (PCC, 36 mg, 0.17 mmol) was added to a solution of **2** (100 mg, 0.17 mmol) in CH₂Cl₂ (2 mL). The reaction mixture was stirred for 16 h, and diethyl ether (10 mL) was added. The solids were filtered through a pad of Florisil (1.5 cm) and washed with ether (3 \times 3 mL) and CH₂Cl₂ (5 mL), and the combined filtrate was concentrated. The residue was purified by radial chromatography (2% MeOH-CH₂Cl₂, EtOAc-Hex, 1:1) to give 78 mg (78%) of enone **8** as a white powder: mp 215–219 °C, [α]_D²³ -2.9° (c 1.0, CH₂Cl₂); IR (KBr) ν_{\max} 3570, 2972, 1753, 1740, 1716, 1664, 1599, 1451, 1372, 1242, 1087, 1070, 1024, 959, 824, 807, 720, 668 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz at 23 °C) δ 0.88 (3H, s), 0.98 (3H, s), 1.21–1.28 (3H, m), 1.36 (3H, s), 1.64–1.70 (4H, br s), 1.7–2.30 (8H, m), 2.35–2.60 (2H, s), 2.70 (2H, d, *J* = 14 Hz), 2.79 [1H, br s, OH (C-15)], 4.94 (1H, br s), 5.30 (1H, s), 5.37 (1H, br s), 5.49 (1H, br s), 6.24 (1H, br d), 6.79 (1H, br s), 7.43 (2H, t, *J* = 7.5 Hz, H_{m-Ph}), 7.58 (1H, t, *J* = 7.5 Hz, H_{p-Ph}), 7.91 (2H, br d, *J* = 7.5 Hz, H_{o-Ph}); ¹H NMR (CDCl₃, 500 MHz at -10 °C) δ 0.88 (3H, s), 0.94 (3H, s), 1.25 (3H, s), 1.37 (3H, s), 1.81 (3H, s), 1.91 (3H, s), 2.10 (3H, s), 2.15 (3H, s), 2.42–2.66 (4H, m), 2.79 [1H, br s, OH (C-15)], 4.94 (1H, br s), 5.30 (1H, s), 5.37

(1H, br s), 5.50 (1H, br s), 6.25 (1H, d, *J* = 10.7 Hz), 6.88 (1H, d, *J* = 10.7 Hz), 7.43 (2H, t, *J* = 7.5 Hz, H_{m-Ph}), 7.58 (1H, t, *J* = 7.5 Hz, H_{p-Ph}), 7.91 (2H, br d, *J* = 7.5 Hz, H_{o-Ph}), in a 4:1 ratio with δ 8.03), 8.03 (2H, br d, *J* = 7.5 Hz, H_{o-Ph}); ¹³C NMR (CDCl₃, 75 MHz) δ 8.8, 12.5, 14.0, 26.6 (4 CH₃, C-16, C-17, C-18, and C-19), 20.7, 21.1, 21.2 [3 CH₃, O₂CCH₃ (C-5, C-7, and C-9)], 27.5, 33.6 (2 CH₂, C-2 + C-6), 39.0 (CH, C-3), 45.1 (C, C-8), 49.6 (CH₂, C-14), 59.0 (C, C-1), 69.5, 70.1, 74.0, 77.2 (4 CH, C-5, C-7, C-9, and C-10), 75.2 (C, C-15), 114.3 (CH₂, C-20), 128.8, 129.5 (2 CH, C-2' + C-3'), 129.4 (C, C-1'), 133.5 (CH, C-4'), 145.0, 147.0 (2 C, C-4 + C-12), 163.6 (C, O₂CPh), 163.9 (C, C-11), 169.5, 169.8, 169.9 [3 C, O₂CCH₃ (C-5, C-7 + C-9)], 207.3 [C, C=O (C-13)]; FABMS (NBA) *m/z* 597 [MH]⁺, 579 [MH - H₂O]⁺, 537 [MH - AcOH]⁺, 475 [MH - PhCO₂H]⁺, 457 [MH - PhCO₂H - H₂O]⁺, 415 [MH - PhCO₂H - AcOH]⁺, 357 [MH - PhCO₂H - 2 AcOH]⁺.

(b) **From NMO-TPAP Oxidation.**²⁰ Tetrapropylammonium perruthenate (TPAP, 3 mg, 0.59 mmol) and *N*-methylmorpholine-*N*-oxide (NMO, 45 mg, 0.38 mmol, 2.3 equiv) were added to a solution of **2** (96 mg, 0.16 mmol) in CH₂Cl₂ (2.5 mL) containing 4 Å-ms (500 mg). The reaction mixture was stirred at room temperature for 2 h, and the disappearance of the starting material, **2**, was monitored by TLC analysis. TPAP (1 mg, 0.20 mmol) was added, and the mixture was stirred for 2 h. One last addition of TPAP (1 mg, 0.20 mmol) was required, and after 1.5 h of stirring, the reaction mixture was filtered in a sintered glass funnel. The solids were washed with EtOAc (2 mL), and the combined filtrate was concentrated and applied on a pad of silica gel (1 cm, Pasteur pipet) and eluted with EtOAc (10 mL). The eluent was removed under reduced pressure, and the residue was purified by radial chromatography (PE:Et₂O, 1:3) to give 38.4 mg (40%) of enone **8**. This material has the same physical properties as that described above.

C-13, C-15 Oxygen Bridge Compound 10. A solution of **1** (26 mg, 0.047 mmol) and *p*-toluenesulfonyl chloride (TsCl, 20 mg, 0.10 mmol) in pyridine (1 mL) containing 4 Å-ms (250 mg) was stirred at room temperature for 6 h. An additional portion of TsCl (5 mg, 0.03 mmol) was added, and the mixture was stirred for another 17 h. The reaction mixture was then filtered through a sintered glass funnel, and the filtrate was concentrated. The crude product was purified by radial chromatography (PE:CH₂Cl₂-EtOH, 15:4:1) to give 10.9 mg (44%) of compound **10** as a white powder: mp 122–123 °C; [α]_D²³ 6.5° (c 0.49, CH₂Cl₂); IR (KBr) ν_{\max} 3447, 2957, 1734, 1653, 1601, 1457, 1368, 1267, 1245, 1092, 1067, 1026, 980, 910, 826, 803, 712 cm⁻¹; ¹H NMR (CDCl₃, 500 MHz) δ 0.85 (3H, s, H-17), 1.22 (3H, s, H-19), 1.30 (3H, s, H-16), 1.75 (1H, ddd, *J* = 13.5, 12.1, 2.8 Hz, H-6 β), 1.80–2.30 [4H, m, H-2 α , H-14 α , H-14 β + OH (C-5)], 1.88 (3H, s, H-18), 1.99 [3H, s, O₂CCH₃ (C-7)], 2.04 [3H, s, O₂CCH₃ (C-9)], 2.08 (1H, ddd, *J* = 13.5, 4.9, 2.8 Hz, H-6 α), 2.22 (1H, dd, *J* = 14.4, 11.1 Hz, H-2 β), 3.07 (1H, d, *J* = 11.0 Hz, H-3 α), 4.40 (1H, distorted t, *J* = 7.7 Hz, H-13 α), 4.45 (1H, t, *J* = 2.5 Hz, H-5 β), 4.96 (1H, s, H-20 α), 5.20 (1H, s, H-20 β), 5.22 (1H, d, *J* = 6.0 Hz, H-9 β), 5.55 (1H, dd, *J* = 12.1, 4.9 Hz, H-7 α), 6.25 (1H, d, *J* = 6.0 Hz, H-10 α), 7.47 (2H, t, *J* = 7.5 Hz, H_{m-Ph}), 7.57 (1H, t, *J* = 7.5 Hz, H_{p-Ph}), 8.0 (2H, d, *J* = 7.5 Hz, H_{o-Ph}); ¹³C NMR (CDCl₃, 75 MHz) δ 11.3 (CH₃, C-19), 11.8 (CH₃, C-18), 20.6 [CH₃, O₂CCH₃ (C-9)], 21.0 [CH₃, O₂CCH₃ (C-7)], 24.8 (CH₂, C-2), 25.3 (CH₃, C-17), 26.4 (CH₃, C-16), 34.1 (CH₂, C-6), 36.3 (CH, C-3), 46.1 (C, C-8), 51.4 (CH₂, C-14), 61.6 (C, C-1), 67.3 (CH, C-10), 70.6 (CH, C-7), 73.1 (CH, C-9 or C-5), 73.2 (CH, C-5 or C-9), 79.4 (C, C-15), 82.9 (CH, C-13), 112.3 (CH₂, C-20), 128.5 (CH, C-3'), 129.5 (CH, C-2'), 129.8 (C, C-1'), 133.0 (CH, C-4'), 137.3 (C, C-11), 146.8 (C, C-12), 150.8 (C, C-4), 165.2 (C, O₂CPh), 169.6 [C, O₂CCH₃ (C-9)], 170.5 [C, O₂CCH₃ (C-7)]; FABMS (NBA) *m/z* 538 M⁺, 537 [M - H]⁺, 417 [MH - PhCO₂H]⁺, 359 [MH - PhCO₂H - AcOH]⁺, 298 [MH - PhCO₂H - 2 AcOH]⁺; *anal.* C 68.98%, H 7.08%, calcd for C₃₁H₃₈O₈, C 69.13%, H 7.11%.

Esterification: General Procedure. To a solution containing the alcohol (1 equiv), dipyrilidyl carbonate²⁴ (2-DPC, 6 equiv), and dimethylamino pyridine (DMAP, 2 equiv) in dry toluene at room temperature was added the appropriate substituted acid (6 equiv), and the reaction mixture was stirred

overnight. The solvent from the reaction mixture was evaporated under reduced pressure to dryness (without heating) to give a crude mixture. Separation of this mixture with silica gel (1 mm), using the specified eluents, gave the desired ester.

13 α - and 5 α -[(2'*S*)-3-Phenyllactate]brevifoliol (12 and 13). Following the general procedure, the (*S*)-(-)-acid, **11a** (48 mg, 0.19 mmol), was coupled with **1** (18 mg, 0.032 mmol), and the reaction mixture was stirred at rt for 24 h to give a mixture of the corresponding C-13 (25% yield) and C-5 esters (35% yield) as white solids, which after hydrolysis of the THP group gave **12** and **13**, both in 50% yield as white solids.

13 α -[(2'*S*)-3-Phenyllactate]brevifoliol (12): IR (KBr) ν_{\max} 3550–3300, 2979, 1742, 1640, 1604, 1450, 1373, 1262, 1104, 1093, 1028, 713 cm^{-1} ; ^1H NMR (CDCl_3 , 500 MHz) δ 0.92 (3H, br s, H-19), 1.15 (3H, s, H-16), 1.19 (1H, dd, $J = 14$, 7 Hz, H-14 α), 1.35 (3H, s, H-17), 1.45 (1H, d, $J = 14$ Hz, H-2 α), 1.62 [1H, br s, OH (C-5)], 1.75 (3H, br s, O_2CCH_3), 1.80 (1H, dd, $J = 14$, 11 Hz, H-6 β), 1.96 (3H, br s, H-18), 1.98 (1H, dd, $J = 14$, 5 Hz, H-6 α), 2.05 (3H, s, O_2CCH_3), 2.10 [1H, s, OH (C-2')], 2.36 (1H, br dd, $J = 14$, 8 Hz, H-2 β), 2.55 (1H, dd, $J = 14$, 7 Hz, H-14 β), 2.58–2.65 [1H, br s, OH (C-15)], 2.69 (1H, d, $J = 8$ Hz, H-3 α), 2.92 (1H, dd, $J = 14$, 8 Hz, H-3'), 3.00 (1H, dd, $J = 14$, 4 Hz, H-3'), 4.02 (1H, dd, $J = 8$, 4 Hz, H-2'), 4.46 (1H, br s, H-5 β), 4.86 (1H, s, H-20a), 5.25 (1H, s, H-20b), 5.45 (1H, br t, $J = 7$ Hz, H-13 β), 5.56 (1H, dd, $J = 11$, 5 Hz, H-7 α), 6.01–6.12 (1H, br m, H-9 β), 6.58–6.62 (1H, br d, $J = 10$ Hz, H-10 α), 7.12 (2H, d, $J = 7.5$ Hz, $\text{H}_{\text{O-Ph}}$), 7.15–7.25 (3H, m, H_{Ar}), 7.40 (2H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.54 (1H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.84 (2H, d, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$); *anal.* C 68.08%, H 6.88%, calcd for $\text{C}_{40}\text{H}_{48}\text{O}_{11}$, C 68.16%, H 6.86%.

5 α -[(2'*S*)-3-Phenyllactate]brevifoliol (13): IR (KBr) ν_{\max} 3565, 2970, 1741, 1715, 1663, 1601, 1445, 1380, 1305, 1250, 1134, 1088, 1070, 963, 805, 759, 716 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.90 (3H, br s, H-19), 1.03 (3H, s, H-16), 1.05–1.16 (1H, m, H-14 α), 1.34 (3H, s, H-17), 1.35–1.55 [3H, m, H-2 α , OH (C-2') + OH (C-13)], 1.75 (3H, br s, O_2CCH_3), 1.86–1.98 (1H, m, H-6 α), 2.04 (3H, s, O_2CCH_3), 2.09 (3H, br s, H-18), 2.15 (1H, br d, $J = 14$ Hz, H-6 β), 2.42 (1H, br dd, $J = 14$, 9 Hz, H-2 β), 2.52 (1H, dd, $J = 14$, 7 Hz, H-14 β), 2.76 (1H, d, $J = 8$ Hz, H-3 α), 2.83 [1H, br s, OH (C-15)], 2.94 (1H, dd, $J = 14$, 8 Hz, H-3'), 3.12 (1H, dd, $J = 14$, 6 Hz, H-3'), 4.22 (1H, dd, $J = 8$, 6 Hz, H-2'), 4.42 (1H, br t, $J = 7$ Hz, H-13 β), 4.94 (1H, s, H-20a), 5.31 (1H, br s, H-5 β), 5.35 (1H, s, H-20b), 5.59 (1H, dd, $J = 11$, 5 Hz, H-7 α), 5.97–6.07 (1H, br d, $J = 10$ Hz, H-9 β), 6.62 (1H, d, $J = 10$ Hz, H-10 α), 7.14 (2H, d, $J = 7.5$ Hz, $\text{H}_{\text{O-Ph}}$), 7.17–7.28 (3H, m, H_{Ar}), 7.42 (2H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.54 (1H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.86 (2H, d, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$); *anal.* C 67.94%, H 6.83%, calcd for $\text{C}_{40}\text{H}_{48}\text{O}_{11}$, C 68.16%, H 6.86%.

13 α -Phenylisoserinatebrevifoliol (15). Following the general procedure, (2*R*,3*S*)-(-)-2-(tetrahydropyran-2-yloxy)-3-phenylmethanamido)propanoic acid, **14**²⁵ (34 mg, 0.092 mmol), was coupled with compound **1** (10 mg, 0.018 mmol) to give the corresponding C-13 ester (13.7 mg, 86% yield). Hydrolysis of the THP group (13.7 mg, 0.016 mmol) with the *p*-toluenesulfonic acid in EtOH gave the alcohol derivative **15** (6.8 mg, 51% yield): mp 150–152 °C; IR (KBr) ν_{\max} 3499, 3435, 3017, 2933, 1731, 1660, 1651, 1450, 1370, 1120, 1080, 969, 805, 735 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.87 (3H, br s, H-19), 1.04 (3H, s, H-16), 1.14 (1H, dd, $J = 14$, 8 Hz, H-14 α), 1.23 (3H, s, H-17), 1.27 [1H, d, $J = 4.0$ Hz, OH (C-5)], 1.73 (3H, s, O_2CCH_3), 1.78 (1H, d, $J = 14$ Hz, H-2 α), 1.92–2.00 (2H, m, H-6 α , H-6 β), 2.05 (3H, s, O_2CCH_3), 2.09 (3H, s, H-18), 2.28 (1H, dd, $J = 14$, 9 Hz, H-2 β), 2.44 (1H, dd, $J = 14$, 7 Hz, H-14 β), 2.64 [1H, br s, OH (C-15)], 2.98 (1H, d, $J = 9$ Hz, H-3 α), 3.34 [1H, d, $J = 3.0$ Hz, OH (C-2')], 4.37 (1H, br s, H-5 β), 4.72 (1H, t, $J = 3$ Hz, H-2'), 5.10 (1H, s, H-20a), 5.33 (1H, s, H-20b), 5.48 (1H, br t, $J = 7$ Hz, H-13 β), 5.64–5.72 (2H, m, H-7 α + H-3'), 5.97 (1H, br d, $J = 10$ Hz, H-9 β), 6.53 (1H, d, $J = 10$ Hz, H-10 α), 7.11 (1H, d, $J = 9.4$ Hz, N–H), 7.30–7.61 (11H, m, H_{Ar}), 7.72 (2H, d, $J = 7.5$ Hz, H_{Ar}), 7.85 (2H, d, $J = 8.0$ Hz, H_{Ar}); *anal.* C 68.28%, H 6.50%, N 1.70%, calcd for $\text{C}_{47}\text{H}_{53}\text{NO}_{12}$, C 68.50%, H 6.48%, N 1.69%.

5 α -Acetyl-13 α -cinnamoylbrevifoliol (16). Following the general procedure described above, cinnamic acid (30 mg, 0.20

mmol) was coupled with compound **2** (30 mg, 0.050 mmol) in boiling CH_2Cl_2 for 20 h. Workup and chromatography (CH_2Cl_2 – Et_2O , 85:15) gave **16** (16 mg, 53% yield) as a white solid: mp 124–125 °C; IR (KBr) ν_{\max} 3581, 2981, 1742, 1718, 1639, 1451, 1373, 1313, 1238, 1093, 1027, 713 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.90 (3H, br s, H-19), 1.12 (3H, s, H-16), 1.31 (1H, dd, $J = 14$, 7 Hz, H-14 α), 1.35 (3H, s, H-17), 1.46 (1H, d, $J = 14$ Hz, H-2 α), 1.73 (3H, br s, O_2CCH_3), 1.88 (1H, td, $J = 14$, 4 Hz, H-6 β), 1.98 (1H, ddd, $J = 14$, 5, 2 Hz, H-6 α), 2.03 (3H, s, O_2CCH_3), 2.05 (3H, s, O_2CCH_3), 2.08 (3H, s, H-18), 2.41 (1H, br dd, $J = 14$, 8 Hz, H-2 β), 2.62 (1H, dd, $J = 14$, 7.4 Hz, H-14 β), 2.70 [1H, br s, OH (C-15)], 2.73 (1H, d, $J = 8$ Hz, H-3 α), 4.88 (1H, s, H-20a), 5.26 (1H, s, H-20b), 5.38 (1H, dd, $J = 4$, 2 Hz, H-5 β), 5.57 (1H, br t, $J = 7.4$ Hz, H-13 β), 5.63 (1H, dd, $J = 11.0$, 5.0 Hz, H-7 α), 6.09 (1H, br d, $J = 10.5$ Hz, H-9 β), 6.32 (1H, d, $J = 16$ Hz, H-1'), 6.68 (1H, br d, $J = 10.5$ Hz, H-10 α), 7.35–7.47 (7H, m, H_{Ar}), 7.54 (1H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.65 (1H, d, $J = 16$ Hz, H_2), 7.86 (2H, d, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$); *anal.* C 69.37%, H 6.66%, calcd for $\text{C}_{42}\text{H}_{48}\text{O}_{11}$, C 69.21%, H 6.64%.

5 α -Acetyl-13 α -[(2'*S*)-O-(tetrahydropyran-2-yl)-3-phenyllactate]brevifoliol (17). Following the general procedure described above, the (*S*)-(-)-acid, **11a** (33 mg, 0.13 mmol), was coupled with compound **2** (13 mg, 0.021 mmol). Workup and chromatography (Hex–EtOAc, 7:3) gave **17** (10 mg, 55% yield) as a white solid: ^1H NMR (CDCl_3 , 400 MHz) δ 0.85 (3H, br s, H-19), 1.08 (3H, s, H-16), 1.20–1.30 (1H, m, H-14 α), 1.35 (3H, s, H-17), 1.40–1.60 (7H, br m, H-2 α + $(\text{CH}_2)_3$), 1.73 (3H, br s, O_2CCH_3), 1.75–1.95 (2H, m, H-6 α , H-6 β), 1.97 (3H, br s, H-18), 2.03 (3H, s, O_2CCH_3), 2.05 (3H, s, O_2CCH_3), 2.35 (1H, br dd, $J = 13.9$, 9.1 Hz, H-2 β), 2.51 (1H, dd, $J = 13.9$, 7.4 Hz, H-14 β), 2.64 [1H, br s, OH (C-15)], 2.68 (1H, d, $J = 9.1$ Hz, H-3 α), 2.92 (1H, dd, $J = 14$, 6 Hz, H-3'), 3.00 (1H, dd, $J = 14$, 7.5 Hz, H-3'), 3.32–3.41 (1H, m, OCH_2), 3.75–3.85 (1H, m, OCH_2), 4.25 (1H, dd, $J = 7.5$, 6 Hz, H-2'), 4.40 (1H, t, $J = 3$ Hz, R– OCHO –R), 4.88 (1H, s, H-20a), 5.28 (1H, s, H-20b), 5.35–5.40 (1H, br s, H-5 β), 5.45 (1H, t, $J = 7.4$ Hz, H-13 β), 5.56 (1H, dd, $J = 11.0$, 5.0 Hz, H-7 α), 6.06 (1H, br d, $J = 10$ Hz, H-9 β), 6.65 (1H, d, $J = 10.4$ Hz, H-10 α), 7.10–7.25 (5H, m, H_{Ar}), 7.45 (2H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.54 (1H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.87 (2H, d, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$); *anal.* C 67.72%, H 6.99%, calcd for $\text{C}_{47}\text{H}_{58}\text{O}_{13}$, C 67.92%, H 7.04%.

5 α -Acetyl-13 α -[(2'*S*)-3-phenyllactate]brevifoliol (18). Hydrolysis of compound **17** (10 mg) was carried out in EtOH (1 mL) in the presence of *p*-toluenesulfonic acid. The reaction mixture was stirred at room temperature for 16 h, after which time the solvent was removed under reduced pressure, leaving a crude residue. Separation of this mixture with silica gel (CH_2Cl_2 – Et_2O , 85:15) gave compound **18** (5 mg) in 56% yield as a white solid: mp 87–88 °C; IR (KBr) ν_{\max} 3560–3300, 2980, 1742, 1452, 1373, 1236, 1093, 1028, 713 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.90 (3H, br s, H-19), 1.10 (3H, s, H-16), 1.19 (1H, dd, $J = 14$, 7 Hz, H-14 α), 1.24 [1H, s, OH (C-2')], 1.35 (3H, s, H-17), 1.45 (1H, d, $J = 14$ Hz, H-2 α), 1.73 (3H, br s, O_2CCH_3), 1.78–1.92 (2H, m, H-6 α , H-6 β), 1.96 (3H, br s, H-18), 2.02 (3H, s, O_2CCH_3), 2.05 (3H, s, O_2CCH_3), 2.38 (1H, br dd, $J = 14$, 8 Hz, H-2 β), 2.56 (1H, dd, $J = 14$, 7.4 Hz, H-14 β), 2.53–2.66 [1H, br s, OH (C-15)], 2.64 (1H, d, $J = 8$ Hz, H-3 α), 2.95 (1H, dd, $J = 14$, 8 Hz, H-3'), 3.08 (1H, dd, $J = 14$, 4 Hz, H-3'), 4.29 (1H, dd, $J = 8.0$, 4 Hz, H-2'), 4.88 (1H, s, H-20a), 5.27 (1H, s, H-20b), 5.35–5.40 (1H, br s, H-5 β), 5.43–5.48 (1H, br t, $J = 7.4$ Hz, H-13 β), 5.58 (1H, dd, $J = 11.0$, 5.0 Hz, H-7 α), 6.01–6.12 (1H, br m, H-9 β), 6.58–6.65 (1H, br d, $J = 10$ Hz, H-10 α), 7.14–7.25 (5H, m, H_{Ar}), 7.42 (2H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.54 (1H, t, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$), 7.86 (2H, d, $J = 7.5$ Hz, $\text{H}_{\text{COO-Ph}}$); FABMS m/z 746 ($\text{M}^+ - \text{PhCO} - \text{CH}_3$), 626, 540, 401, 358, 341, 221, 239, 220, 185, 184, 148, 105, 91; *anal.* C 67.45%, H 6.68%, calcd for $\text{C}_{42}\text{H}_{50}\text{O}_{12}$, C 67.54%, H 6.75%.

5 α -Acetyl-13 α -[(2'*R*)-3-phenyllactate]brevifoliol (19). Following the general procedure, the coupling of the (2*R*)-(+)-acid, **11b** (62.5 mg, 6 equiv), with compound **2** (24.8 mg, 1 equiv) and subsequent hydrolysis of the THP ether (12.5 mg, 36% yield) gave the corresponding free alcohol **19** (9.2 mg, 86.7% yield), as a white solid: mp 91–92 °C; IR (KBr) ν_{\max} 3575–3400, 3000–2900, 1742, 1453, 1372, 1236, 1094, 1027, 915, 755 cm^{-1} ; ^1H NMR (CDCl_3 , 400 MHz) δ 0.93 (3H, br s,

H-19), 1.11 (3H, s, H-16), 1.23–1.339 (1H, m, H-14 α), 1.35 (3H, s, H-17), 1.48 (1H, br d, J = 14 Hz, H-2 α), 1.73 (3H, br s, O₂CCH₃), 1.78–2.07 (2H, m, H-6 α , H-6 β), 1.92 (3H, br s, H-18), 2.02 (3H, s, O₂CCH₃), 2.05 (3H, s, O₂CCH₃), 2.36–2.44 [2H, br dd, J = 14, 8 Hz, H-2 β + OH (C-2)], 2.54–2.64 (2H, br dd, J = 14, 7 Hz, H-14 β + OH (C-15)], 2.67 (1H, d, J = 8 Hz, H-3 α), 2.92 (1H, dd, J = 14, 8 Hz, H-3'), 3.06 (1H, dd, J = 14, 6 Hz, H-3'), 4.38 (1H, dd, J = 8, 6 Hz, H-2'), 4.94 (1H, s, H-20a), 5.30 (1H, s, H-20b), 5.36–5.44 (1H, br s, H-5 β), 5.53–5.67 (2H, m, H-7 α and H-13 β), 6.05–6.16 (1H, br m, H-9 β), 6.60–6.66 (1H, br d, J = 10 Hz, H-10 α), 7.15 (2H, d, J = 7.5 Hz, H_{CO-Ph}), 7.18–7.20 (3H, m, H_{Ar}), 7.42 (2H, t, J = 7.5 Hz, H_{CO-m-Ph}), 7.55 (1H, t, J = 7.5 Hz, H_{CO-p-Ph}), 7.86 (2H, d, J = 7.5 Hz, H_{CO-o-Ph}); FABMS m/z 746 (M^+ - PhCO, -CH₃), 626, 540, 401, 358, 341, 238, 221, 220, 185, 184, 148, 105, 91; anal. C 67.68%, H 6.72%, calcd for C₄₂H₅₀O₁₂, C 67.54%, H 6.75%.

5 α -Acetyl-13 α -phenylisoserinatebrevifoliol (20). The acid **14**²⁵ (37 mg, 0.1 mmol) was coupled with compound **2** (10 mg, 0.0167 mmol) as above to give the corresponding C-13 ester (15.6 mg, 45% yield). Hydrolysis of the THP group (4.7 mg, 6.8×10^{-2} mmol) with the *p*-toluenesulfonic acid in EtOH gave the alcohol derivative **20** (1.5 mg, 35% yield): IR (KBr) ν_{\max} 3437, 2983, 1739, 1713, 1601, 1445, 1320, 1240, 1145, 1070, 955, 809, 729 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 0.92 (3H, br s, H-19), 1.10 (3H, s, H-16), 1.20–1.32 (1H, m, H-14 α), 1.35 (3H, s, H-17), 1.51 (1H, d, J = 14 Hz, H-2 α), 1.68–1.78 (3H, br s, O₂CCH₃), 1.82–2.00 (2H, m, H-6 α , H-6 β), 1.90 (6H, s, 2 \times O₂CCH₃), 2.05 (3H, s, H-18), 2.30–2.45 (2H, m, H-2 β + H-14 β), 2.55–2.66 [1H, br s, OH (C-15)], 2.70 (1H, d, J = 9 Hz, H-3 α), 3.24 [1H, d, J = 6.0 Hz, OH (C-2)], 4.63 (1H, dd, J = 6.0, 2.7 Hz, H-2'), 4.94 (1H, s, H-20a), 5.30 (1H, s, H-20b), 5.39–5.42 (1H, br s, H-5 β), 5.56 (1H, dd, J = 11.0, 5.0 Hz, H-7 α), 5.62 (1H, dd, J = 9.4, 2.7 Hz, H-3'), 5.68–5.75 (1H, br t, J = 7.4 Hz, H-13 β), 6.05–6.12 (1H, br d, J = 10 Hz, H-9 β), 6.58–6.64 (1H, br d, J = 10 Hz, H-10 α), 6.95 (1H, d, J = 9.4 Hz, N-H), 7.30–7.60 (11H, m, H_{Ar}), 7.72 (2H, d, J = 7.5 Hz, H_{Ar}), 7.84 (2H, d, J = 8.0 Hz, H_{Ar}); anal. C 68.04%, H 6.47%, N 1.59%, calcd for C₄₉H₅₅NO₁₃, C 67.96%, H 6.40%, N 1.62%.

13 α -Acetyl-4 α ,20-dihydroxybrevifoliol (21). Compound **3** (87 mg, 0.15 mmol) was dihydroxylated with OsO₄ (1.8 mg, 0.0071 mmol, 0.05 equiv) and *N*-methylmorpholine-*N*-oxide (18.7 mg, 1.1 equiv) in acetone (1.5 mL) and water-*t*-BuOH (6:1). The reaction mixture was stirred at room temperature overnight. Once the reaction was complete, Fluorisil (40 mg), sodium hydrosulfite (25 mg), and water (2 mL) were added. Extraction was carried out in ethyl acetate (6 \times 15 mL) and diethyl ether (7 \times 5 mL). The combined extracts were dried over MgSO₄ and filtered, and then the solvent was removed under reduced pressure to leave a crude material (85 mg). Separation of this material with silica gel (CH₂Cl₂-MeOH, 95:5; 9:1) gave 65.7 mg (72%) of pure triol **21**, which crystallized upon drying under vacuum: mp 134–135 °C; IR (KBr) ν_{\max} 3575–3331, 2980, 1733, 1375, 1251, 1031, 714 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 1.05 (3H, br s, H-19), 1.23–1.26 (1H, m, H-14 α), 1.28 (3H, s, H-16), 1.75–1.90 (10H, br s, H-17, H-2 α , + 2 \times O₂CCH₃), 2.00 (3H, s, O₂CCH₃), 1.95–2.10 (2H, m, H-6 β + H-6 α), 2.05 (3H, s, H-18), 2.15–2.23 (1H, br s, OH), 2.23–2.34 (2H, m, H-2 β + H-3 α), 2.38 (1H, dd, J = 14, 7.4 Hz, H-14 β), 2.50–2.55 (1H, br s, OH), 3.25–3.35 (1H, m, OH), 3.62–3.75 (3H, br m, H-20 + OH), 4.40 (1H, br s, H-5 β), 5.43–5.51 (1H, m, H-9 β), 5.51–5.60 (2H, m, H-7 α + H-13 β), 6.32–6.44 (1H, br s, H-10 α), 7.44 (2H, t, J = 7.5 Hz, H_{CO-m-Ph}), 7.54 (1H, t, J = 7.5 Hz, H_{CO-p-Ph}), 7.90 (2H, br d, J = 7.5 Hz, H_{CO-o-Ph}); anal. C 62.78%, H 6.99%, calcd for C₃₃H₄₄O₁₂, C 62.64%, H 7.01%.

13 α -Acetyl-20-(*t*-butyldimethylsilyloxy)-4 α -hydroxybrevifoliol (21a). The primary alcohol of triol **21** (17 mg, 0.027 mmol) was treated with *tert*-butyldimethylsilyl chloride (22.2 mg, 0.147 mmol, 5.5 equiv) and imidazole (24.5 mg, 0.36 mmol, 13.5 equiv) in CH₂Cl₂ (2 mL) containing 4 Å-ms (100 mg). The reaction mixture was stirred at rt for 18 h (TLC analysis) and filtered through Celite and then the solvent was removed under reduced pressure. Separation of the crude material with silica gel (Hex-EtOAc, 1:1) gave 17.8 mg (88% yield) of the silyl ether derivative **21a**: mp 111–112 °C; IR (KBr) ν_{\max} 3450,

2947, 1731, 1370, 1220, 1162, 1065, 845 cm⁻¹; ¹H NMR (CD₂Cl₂, 400 MHz) δ 0.09 (3H, s, SiCH₃), 0.12 (3H, s, SiCH₃), 0.90 (3H, s, H-19), 0.92 (9H, s, Si(CH₃)₃), 1.07 (3H, s, H-16), 1.00–1.10 (1H, m, H-14 α), 1.25 (1H, d, J = 14 Hz, H-2 α), 1.28 (3H, s, H-17), 1.60–1.75 (3H, m, H-6 β , H-6 α + OH), 1.89 (3H, br s, O₂CCH₃), 1.96–2.03 (6H, br s, 2 \times O₂CCH₃), 2.06 (3H, s, H-18), 2.22 (1H, m, H-2 β), 2.33 (1H, d, J = 8 Hz, H-3 α), 2.62 (1H, dd, J = 14, 7.4 Hz, H-14 β), 2.85 [1H, br s, OH (C-15)], 3.43–3.50 (1H, br s, OH), 3.55, 3.66 (each 1H, br d, J = 10 Hz, H-20), 3.8 (1H, br s, H-5 β), 5.47–5.55 (2H, m, H-13 β + H-9 β), 5.57 (1H, dd, J = 14, 5.0 Hz, H-7 α), 6.36–6.47 (1H, br s, H-10 α), 7.42 (2H, t, J = 7.5 Hz, H_{CO-m-Ph}), 7.54 (1H, t, J = 7.5 Hz, H_{CO-p-Ph}), 7.90 (2H, br d, J = 7.5 Hz, H_{CO-o-Ph}).

13 α -Acetyl-20-*tert*-butyldimethylsilyloxy-5-methanesulfonyl-4 α -hydroxybrevifoliol (23). The above alcohol precursor (13 mg, 0.0174 mmol) was treated with mesyl chloride (6.75 mL, 0.087 mmol, 5 equiv) in pyridine (3 mL) and 3 Å molecular sieves (50 mg). The reaction mixture was stirred at room temperature for 24 h, then filtered through Celite and rinsed with CH₂Cl₂. Evaporation of the solvents under reduced pressure followed by separation of the crude material with silica gel (CH₂Cl₂-EtOAc, 8:2) gave the mesylated product **23** (31.1 mg, 73% yield): mp 109–110 °C; IR (KBr) ν_{\max} 3505, 2933, 1741, 1452, 1372, 1245, 1179, 1086, 1034, 841 cm⁻¹; ¹H NMR (CD₂Cl₂, 400 MHz) δ 0.08 (3H, s, SiCH₃), 0.09 (3H, s, SiCH₃), 0.88 (3H, s, H-19), 0.90 (9H, s, Si(CH₃)₃), 1.07 (3H, s, H-16), 1.04–1.13 (1H, m, H-14 α), 1.25–1.30 (1H, d, J = 14 Hz, H-2 α), 1.30 (3H, s, H-17), 1.70–2.05 (3H, br m, H-6 β , H-2 β + OH), 1.80 (3H, br s, O₂CCH₃), 1.85 (3H, s, O₂CCH₃), 2.00 (3H, br s, O₂CCH₃), 2.02 (3H, s, H-18), 1.88 (1H, dt, J = 14, 4 Hz, H-6 α), 2.23 [1H, s, OH (C-15)], 2.25 (1H, d, J = 8 Hz, H-3 α), 2.37 (dd, J = 14, 7.4 Hz, 1H, H-14 β), 3.15 (3H, s, O₂SCCH₃), 3.52–3.62 (1H, br s, H-20), 3.73 (1H, d, J = 10 Hz, H-20), 5.00 (1H, br s, H-5 β), 5.40–5.50 (1H, br m, H-9 β), 5.48 (1H, br d, J = 14 Hz, H-7 α), 5.56 (1H, br s, H-13 β), 6.30–6.43 (1H, br s, H-10 α), 7.42 (2H, t, J = 7.5 Hz, H_{CO-m-Ph}), 7.54 (1H, t, J = 7.5 Hz, H_{CO-p-Ph}), 7.89 (2H, br s, H_{CO-o-Ph}); anal. C 58.35%, H 7.37%, calcd for C₄₀H₆₀O₁₄SSi, C 58.23%, H 7.33%.

13 α -Acetyl-4 α ,20-dihydroxy-5-methanesulfonylbrevifoliol (24). Deprotection of the primary alcohol group of **23** (8 mg, 0.01 mmol) with TBAF (dry, 1.0 M solution in THF, 14.5 μ L) in THF (1.0 mL) gave derivative **24** (3 mg, 66% yield, based on recovered starting material): IR (KBr) ν_{\max} 3455, 2928, 1734, 1446, 1375, 1340, 1220, 1170, 1056, 1048, 843 cm⁻¹; ¹H NMR (CD₂Cl₂, 400 MHz) δ 1.09 (3H, s, H-19), 1.18 (3H, s, H-16), 1.16–1.26 (1H, m, H-14 α), 1.30 (3H, s, H-17), 1.53 (1H, d, J = 14 Hz, H-2 α), 1.70–1.95 (3H, br m, H-6 β , H-2 β + OH), 1.77 (3H, br s, O₂CCH₃), 1.89 (3H, s, O₂CCH₃), 1.92 (3H, br s, O₂CCH₃), 1.99 (3H, s, H-18), 2.05 [1H, s, OH (C-15)], 2.15 (1H, dt, J = 14, 4 Hz, H-6 α), 2.20 (1H, br d, J = 8 Hz, H-3 α), 2.33 (1H, dd, J = 14, 7.4 Hz, H-14 β), 3.11 (3H, s, O₂SCCH₃), 3.57, 3.66 (each 1H, d, J = 11 Hz, H-20), 4.51 (1H, s, OH), 5.07 (1H, br s, H-5 β), 5.24 (1H, dd, J = 14, 5.0 Hz, H-7 α), 5.34–5.41 (1H, m, H-9 β), 5.51 (1H, br t, J = 7.4 Hz, H-13 β), 6.19–6.34 (1H, br s, H-10 α), 7.37 (2H, t, J = 7.5 Hz, H_{CO-m-Ph}), 7.52 (1H, t, J = 7.5 Hz, H_{CO-p-Ph}), 7.76–7.86 (2H, br s, H_{CO-o-Ph}).

Compound 25. Compound **24** (3.0 mg, 0.0044 mmol) was treated with tetrabutylammonium acetate (12 mg, 9 equiv) in butanone (1.0 mL). The reaction mixture was stirred under reflux for 19 h. Separation of this crude mixture with silica gel (CH₂Cl₂-Et₂O, 4:1) gave the hydroxyoxetane derivative **25** (1.2 mg, 44% yield): IR (KBr) ν_{\max} 3550, 2958, 1728, 1708, 1445, 1385, 1226, 1171, 1046, 863 cm⁻¹; ¹H NMR (CD₂Cl₂, 400 MHz) δ 1.09 (3H, s, H-19), 1.20 (3H, s, H-16), 1.28 (3H, s, H-17), 1.30 (1H, dd, J = 14, 7 Hz, H-14 α), 1.39 (1H, d, J = 14 Hz, H-2 α), 1.65 (3H, br s, O₂CCH₃), 1.67–1.84 (2H, br m, H-6 β , + OH), 2.01 (3H, s, O₂CCH₃), 2.03 (3H, s, O₂CCH₃), 2.04 (3H, s, H-18), 2.05–2.10 (1H, m, H-6 α), 2.30 (1H, br dd, J = 14, 8 Hz, H-2 β), 2.58 (1H, dd, J = 14, 7 Hz, H-14 β), 2.77 (1H, br d, J = 8 Hz, H-3 α), 2.92 [1H, s, OH (C-15)], 4.36 (1H, d, J = 8.1 Hz, H-20a), 4.52 (1H, d, J = 8.1 Hz, H-20b), 5.15 (1H, br s, H-5 α), 5.37 (1H, dd, J = 14, 5.0 Hz, H-7 α), 5.60 (1H, br t, J = 7 Hz, H-13 β), 6.98 (1H, br d, J = 10.5 Hz, H-9 β), 7.15 (1H, br d, J = 10.5 Hz, H-10 α), 7.46 (2H, t, J = 7.5 Hz, H_{CO-m-Ph}), 7.62 (1H, t, J = 7.5 Hz, H_{CO-p-Ph}), 8.04 (2H, d, J = 7.5 Hz, H_{CO-o-Ph});

FABMS (NBA) m/z 555 ($M^+ - \text{CH}_3\text{CO}_2$), 531, 515, 484; *anal.* C 64.39%, H 6.90%, calcd for $\text{C}_{33}\text{H}_{42}\text{O}_{11}$, C 64.48%, H 6.89%.

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Supporting Information Available: Procedures for isolation of **1** and for the preparation of compounds **2–4**; Tables S1 of ^1H and S2 of ^{13}C NMR spectral data for compounds **1–7** and **10**, copies of IR spectra for compounds **1–4**, **8**, and **10**, and 300 or 500 MHz ^1H and ^{13}C NMR spectra for compounds **1**, **8**, and **10** and 2D NMR spectra for **10**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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