bonded nature of the 4-substituent—which means that if pyrrolosine was really **1** it would have to crystallize in the lactim form, which is itself improbable. The same data also indicate that the atom at position 5 does not serve as a hydrogen bond donor since the closest acceptor is more than 3.5 Å away. Such a feature is much more consistent with the existence of an oxygen atom at that position. In our crystal structure of 9-deazainosine, all hydrogen bond donors are accounted for, and a strong hydrogen bond is formed between N(5) and O(5′) of an associated molecule.

Because of the inconsistencies noted above between the crystallographic data and the reported structure of pyrrolosine, we have reanalyzed the X-ray intensity data obtained by Ikegami and co-workers. When the atom at position 5 was changed from N to O and the substituent atom at position 4 was changed from O to N, the crystallographic *R* factor dropped from 0.065 to 0.053. A second hydrogen atom attached to N(4) was located as the largest feature in a difference Fourier map and included in the model. All four hydrogen atoms associated with the solvent methanol were also located in the difference Fourier map and added. Finally, the disordered oxygen atom of the methanol molecule was replaced by a single anisotropic atom. After least-squares refinement, the *R* factor converged at 0.039.

All bond distances and angles in the reinterpreted model are consistent with the structure of the furo[3,2-*d*]pyrimidine C-nucleoside **2**. Furthermore, the hydrogen bonding scheme, which consists of five intermolecular and one intramolecular contact, accounts for all potential hydrogen bond donors.[16] The misinterpretation of their own X-ray data by Ikegami and co-workers in the structural determination of pyrrolosine illustrates the pitfall of relying too heavily on X-ray diffraction techniques without the corroboration of other synthetic and spectroscopic evidence.

The finding that the furo[3,2-*d*]pyrimidine C-nucleoside **2** is a natural product is of considerable interest given the fact that the compound has been obtained by synthesis in only modest overall yield via a demanding eight-step route starting with D-ribose.[13] Its natural occurrence also poses some interesting questions about its benefit to the organism that produces it and about its biosynthetic pathway. However, we suggest that future studies to investigate these questions should use a name other than "pyrrolosine" in order to more accurately reflect the actual structure of the compound.

Acknowledgment. Support of this work by funds from the American Cancer Society (Grants CH-305 and CH-213) and the U.S. Department of Health and Human Services (Grants CA-13330, CA-24634, and GM-38823) is gratefully acknowledged.

Registry No. **1**, 89458-19-5; **1**-H_2O, 137541-62-9; **2**, 86132-93-6; **2**-MeOH, 137623-78-0; 7-(hydroxymethyl)pyrrolo[3,2-*d*]pyrimidin-4-one, 104303-72-2.

Supplementary Material Available: Comparative perspective views of 9-deazainosine and "pyrrolosine" (Figure 5), tables of final atomic coordinates, thermal parameters, bond distances, bond angles, torsion angles, and hydrogen bonds for 9-deazainosine (**1**) (Tables 1–6), and corrected atomic coordinates, thermal factors, bond distances, bond angles, torsion angles, and hydrogen bonds for "pyrrolosine" (**2**) (Tables 8–13) (15 pages); listing of observed and calculated structure factors for **1** (Table 7) (7 pages). Ordering information is given on any current masthead page.

(16) The intramolecular contact is a 5′-OH···N(1) hydrogen bond. Coincidentally, the syn conformation of pyrrolosine (**2**) in the crystalline state is similar to that found for 9-deazainosine in solution in DMSO-d_6 (see footnote 12).

Stereochemistry of the Macrolactins

Scott D. Rychnovsky,*,†,[1] Donald J. Skalitzky,† Charles Pathirana,‡ Paul R. Jensen,‡ and William Fenical*,‡

Contribution from the Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455, and Scripps Institution of Oceanography, University of California at San Diego, La Jolla, California 92093-0236. *Received July 11, 1991*

Abstract: The macrolactins are a group of six 24-membered ring lactones isolated from a taxonomically-undefinable deep sea bacterium. Macrolactin A, the parent aglycone, shows a number of interesting biological activities, including the protection of T-lymphoblast cells against human HIV viral replication. Herein we report the stereochemistries of macrolactin B and macrolactin F, which were determined by a combination of ^{13}C-acetonide analysis using isotopically enriched acetone, oxidative degradation, and chemical correlation. Macrolactins B and F were found to have the same stereochemistry at each of the common stereogenic centers, and so we expect that macrolactin A, the aglycone of macrolactin B, has the stereochemistry 7*S*,13*S*,15*R*,23*R*.

The macrolactins are a group of six 24-membered ring lactones isolated from a taxonomically-undefinable deep sea bacterium.[2] Macrolactin A, the parent aglycone, shows selective antibacterial activity and inhibits B16–F10 murine melanoma cancer cells in in vitro assays.[2] Macrolactin A also shows significant inhibition of mammalian *Herpes simplex* viruses (types I and II) and protects T-lymphoblast cells against human HIV viral replication.[2] The structures of macrolactins A–F were determined by a combination of spectroscopic techniques that included extensive use of proton NMR spectroscopy. The macrolactins are not crystalline, and their derivatives are not suitable for X-ray analysis, so the absolute and relative stereochemistry of the macrolactins have remained undefined.[2] Unfortunately, fermentation of this deep sea bacterium has been unreliable, and macrolactin A is no longer available in significant yield. We turned to macrolactins B and F and report herein their complete stereochemistry, which was determined by a combination of ^{13}C-acetonide analysis, degradation, and chemical correlation (Figure 1).

^{13}C-Acetonide Analysis

The relative stereochemistry of 1,3-diols can be determined by preparing the acetonide derivative and inspecting the ^{13}C chemical shifts of the acetonide methyl groups.[3,4] As shown in Figure 2,

†University of Minnesota.
‡University of California at San Diego.

(1) Camille and Henry Dreyfus Teacher-Scholar, 1990–1995.
(2) Gustafson, K.; Roman, R.; Fenical, W. *J. Am. Chem. Soc.* **1989**, *111*, 7519–7524.

0002-7863/92/1514-671$03.00/0

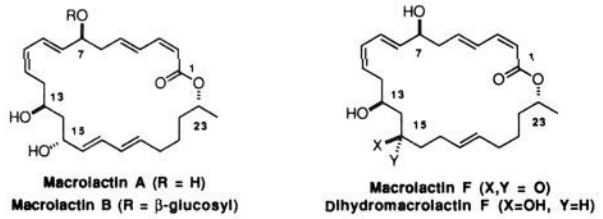


Figure 1. The structure and stereochemistry of selected macrolactins.

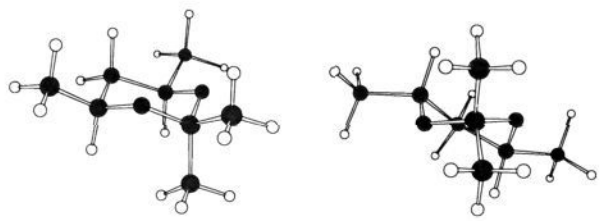
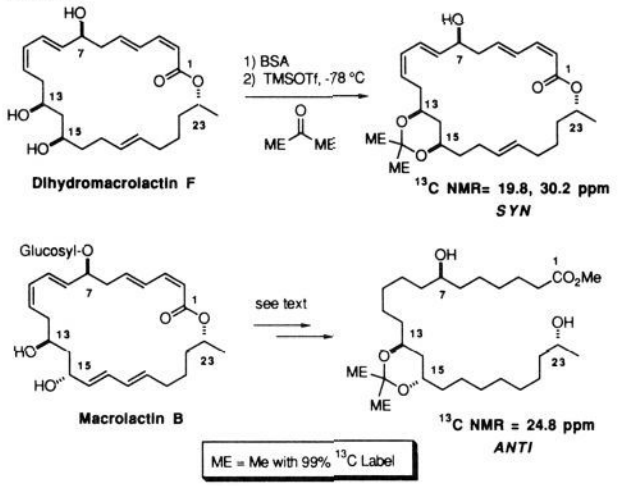


Figure 2. Global minima[5] for cis (syn) and trans (anti) 1,3-diol acetonides.

the acetonide from a *syn*-1,3-diol adopts a chair conformation[5] so that the equatorial methyl group appears at 30 ppm and the axial one appears at 20 ppm, as one would expect on the basis of the sensitivity of ^{13}C chemical shifts to steric hindrance.[6] In contrast, the acetonide from an *anti*-1,3-diol adopts a twist-boat conformation,[7] so the two methyl groups are in a steric environment midway between axial and equatorial and both appear at 25 ppm. Simple inspection of the ^{13}C NMR spectrum of a 1,3-diol acetonide allows the stereochemistry to be assigned. One apparent drawback to this technique is its lack of sensitivity. Even with the dramatic improvement in NMR spectrometer design in the last decade, several milligrams of a complex molecule may be required to measure the ^{13}C spectrum. This is an apparent rather than a real drawback because the nuclei of interest do not originate with the natural product but rather with acetone. *Using commercially available*[8] *99% ^{13}C-enriched acetone to prepare the acetonide gives an immediate 100-fold boost in sensitivity*. The ability to perform a ^{13}C-acetonide analysis on small samples was important because only limited quantities of macrolactin B (40 mg) and dihydromacrolactin F (9 mg) were available for study.

The acetonide analyses of dihydromacrolactin F, prepared as a mixture of major and minor isomers by sodium borohydride reduction of macrolactin F, and macrolactin B are shown in Scheme I. Approximately 0.7 mg of crude dihydromacrolactin F was derivatized using ^{13}C-enriched acetone to give ~0.1 mg of acetonide.[9] The ^{13}C NMR spectrum was acquired in only 25

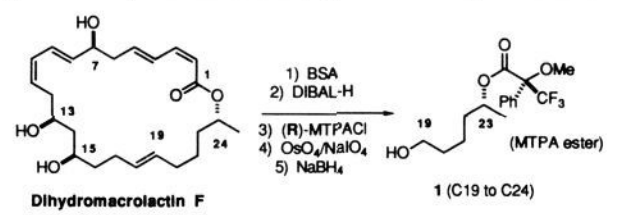
Scheme I



min and showed that the C13 and C15 alcohols in the major isomer of dihydromacrolactin F are syn. The glucose residue in macrolactin B can form several possible acetonides, and so the sugar was removed to simplify the analysis. Approximately 9 mg of crude macrolactin B was hydrogenated and then hydrolyzed in refluxing methanolic HCl to give ~1 mg of the corresponding acyclic ester. Acetonide formation using Noyori's procedure gave >0.1 mg of acetonide.[9] The ^{13}C NMR spectrum showed that the C13 and C15 alcohols in macrolactin B are anti. Thus, the C13,C15 relative stereochemistry of both macrolactin B and dihydromacrolactin F was determined using our ^{13}C-acetonide analysis with isotopically enriched acetone.

Degradation Studies

The degradations of dihydromacrolactin F and macrolactin B pose two problems. First, the oxidative degradation of macrolactins is not clean[10] and, second, the expected degradation fragments have low optical rotations, which makes the assignment of absolute configuration with small samples problematic.[11] The second problem can be overcome with a chiral derivatizing agent,[12] which produces diastereomeric degradation fragments rather than enantiomeric degradation fragments. Very small quantities of the diastereomeric degradation fragments can be identified and correlated by NMR spectroscopy. A trial degradation of dihydromacrolactin F (eq 1) began with silylation and DIBAL-H reduction to liberate the C23 hydroxyl group; deprotection and derivatization with (*R*)-Mosher's acid chloride ((*R*)-MTPACl)[12] gave the expected esterified polyene. Subsequent oxidative



(1)

(3) (a) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990**, *31*, 945–948. (b) Evans, D. A.; Rieger, D. L.; Gage, J. R. *Tetrahedron Lett.* **1990**, *31*, 7099–7100.

(4) Buchanan et al. have reported that the ^{13}C chemical shifts of acetal carbons are useful in distinguishing among 5-, 6-, and 7-membered acetonide rings. They discussed the conformation of several fused bicyclic acetonides derived from carbohydrates in relation to their ^{13}C chemical shifts. Although we were unaware of this work at the time of our previous publication, their analysis is consistent with the chemical shift correlations that we observed in acetonides derived from alternating polyol chains. Buchanan, J. G.; Edgar, A. R.; Rawson, D. I.; Shahidi, P.; Wightman, R. H. *Carbohydr. Res.* **1982**, *100*, 75–86.

(5) Global minima were calculated in a Monte Carlo conformational search using MacroModel V3.1X developed by Clark Still at Columbia University.

(6) Silverstein, R. M.; Bassler, G. C.; Morrill, T. C. *Spectrometric Identification of Organic Compounds*, 4th ed.; John Wiley & Sons: New York, 1981; pp 258–261. The γ-effect is attributed to steric compression.

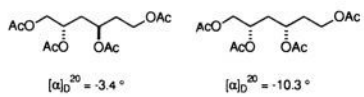
(7) Anteunis, M. J. O.; Borremans, F. *Heterocycles* **1976**, *4*, 293–371.

(8) [1,3-$^{13}C_2$]Acetone 99 atom % ^{13}C was purchased from Aldrich Chemical Company. Approximately 1–10 mg of enriched acetone was used for each acetonide formation.

(9) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357–1358. Very small scale acetonide preparations work best when *N,N*-bis(trimethylsilyl)trifluoroacetamide is added to the reaction; see the Experimental Section.

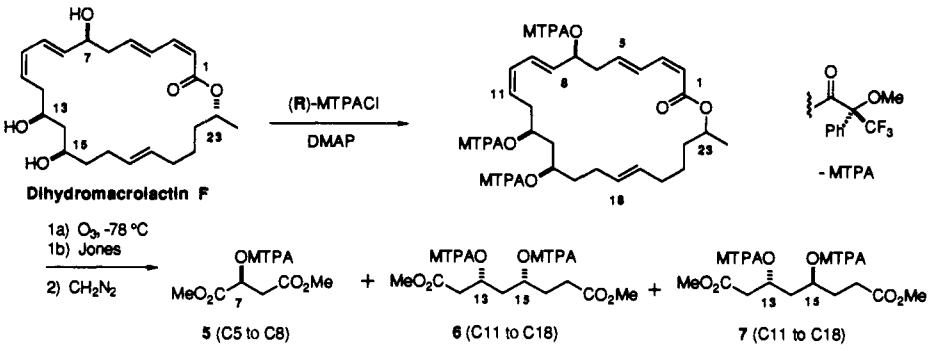
(10) These oxidative degradations were originally attempted on the peracetate of macrolactin A by ozonolysis and reductive workup, but they did not lead to the desired degradation fragments.

(11) The two optically pure tetraacetates shown below, which were prepared in the early stages of this investigation, had very small optical rotations. Assigning absolute configuration on samples of less than 1 mg in a 1-mL, 1-dm cell would require accurately measuring a rotation of $\alpha = 0.003°$.

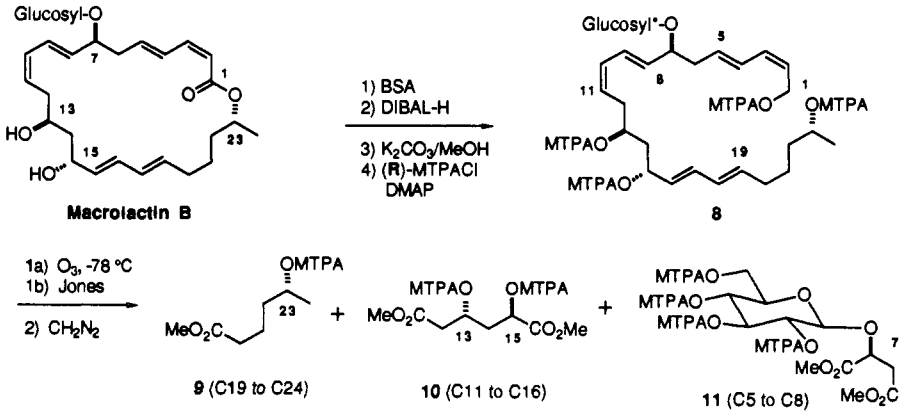


(12) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *9*, 2543–2549.

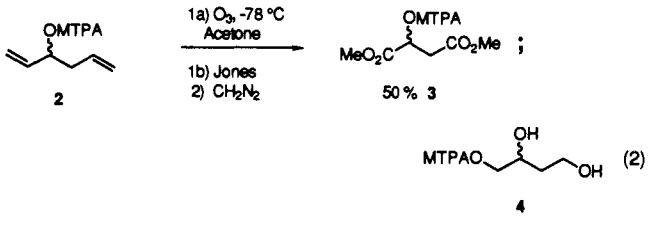
Scheme II



Scheme III



degradation ($OsO_4/NaIO_4$; $NaBH_4$) gave a C19–C24 fragment **1** in low yield but did not give any C5–C8 fragment or C11–C18 fragment. This degradation sequence gave only one of three desired degradation fragments expected from dihydromacrolactin F and was not satisfactory. We studied the oxidative degradation of model diene **2** to find a more efficient procedure. The oxidative degradation initially applied to dihydromacrolactin F ($OsO_4/NaIO_4$; $NaBH_4$) gave none of the desired product, but did give a small amount of compound **4** resulting from ester migration. The acyl migration is a facile process in this system and is a potential problem with any reductive workup. RuO_4 oxidation gave mainly tetrahydrofurans in accord with literature precedent.[13] The most successful procedure involved oxidation with ozone (acetone, −78 °C) and workup with Jones' reagent followed by diazomethane treatment to give dimethyl ester **3** in 50% yield (eq 2). With an effective oxidative degradation, we were ready to begin the degradation of dihydromacrolactin F and macrolactin B.



(2)

The initial degradation attempt with dihydromacrolactin F gave C19–C24 degradation fragment **1** containing the C23 stereogenic center, and so the new degradation only needed to give derivatized fragments containing the C7, C13, and C15 stereogenic centers. The dihydromacrolactin F was derivatized directly with (*R*)-Mosher's acid chloride, and the resulting triester was treated with ozone, Jones' reagent, and diazomethane according to the previously developed procedure (Scheme II). A C5–C8 fragment **5** and both a major C11–C18 fragment **6** and a minor C11–C18 fragment **7** were isolated by HPLC on silica gel. These fragments contain all of the remaining stereogenic centers of dihydromacrolactin F. Macrolactin B is a β-glucopyranoside, but there is no way to remove the sugar without destroying the remainder of the molecule, so the sugar was left intact in the degradation sequence. Macrolactin B was silylated and reduced with DIBAL-H to liberate the C23 alcohol (Scheme III). Hydrolysis and esterification with (*R*)-Mosher's acid chloride gave the esterified polyene **8**, which was degraded as before to give the three major degradation fragments **9**–**11**. Degradation of dihydromacrolactin F and macrolactin B each gave a set of fragments which contain all of the stereogenic centers present in the natural product, and whose proton NMR spectra were consistent with the proposed structures.

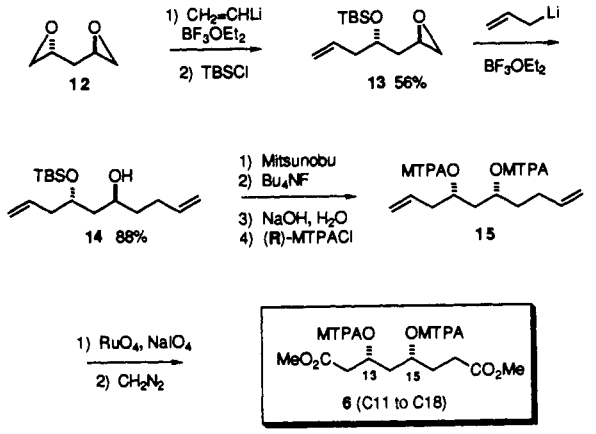
Chemical Correlation

The final step in the structure determination of dihydromacrolactin F was to correlate each degradation fragment with a synthetic sample of known structure using proton NMR spectroscopy in two solvents and one chromatographic method, either HPLC or GC. The stereochemical assignments depended upon distinguishing the diastereomeric Mosher's acid derivatives by NMR spectroscopy; to confirm this supposition *all possible diastereomers of dihydromacrolactin F fragments* ***1***, ***5***, ***6***, *and* ***7*** *were prepared and found to be easily distinguished by proton NMR spectroscopy*. The C5–C8 fragment **5** from dihydromacrolactin F was correlated with a synthetic sample prepared from (*S*)-malic acid and (*R*)-Mosher's acid chloride,[14] so the stereochemistry at C7 is *S*. The other diastereomer of **5** was prepared using (*S*)-Mosher's acid chloride, and the two diastereomers were easily distinguished by proton NMR spectroscopy. The C19–C24 fragment **1** from dihydromacrolactin F was correlated with a synthetic sample prepared from (*R*)-methyl 3-hydroxybutyrate and (*R*)-Mosher's acid chloride,[15] so the stere-

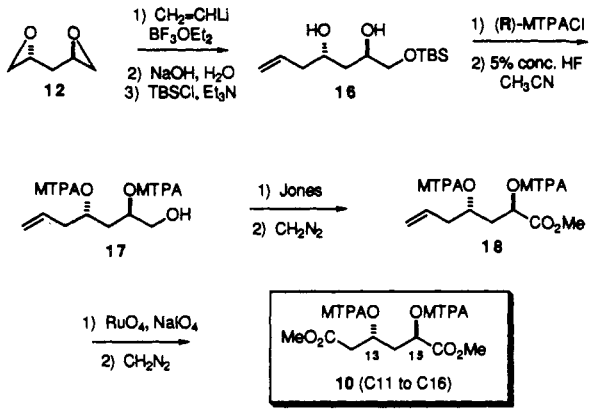
(13) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936–3938.

(14) Preparation of C5–C8 fragment **5** from (*S*)-malic acid: (a) MeOH, HCl; (b) (*R*)-MTPACl, DMAP. Experimental procedure and spectral data are given in the supplementary material.

Scheme IV

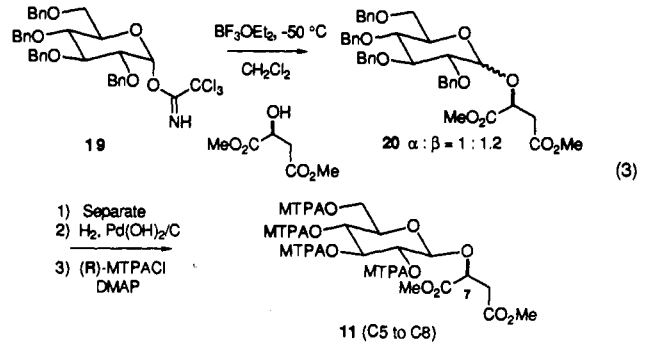


Scheme V



ochemistry at C23 is *R*. A mixture of diastereomers was prepared from racemic 1,5-hexanediol and (*R*)-Mosher's acid chloride, and the two distereomers of **1** were easily distinguished by proton NMR spectroscopy. A synthetic sample of the more complex C11–C18 fragments, **6** and **7**, was prepared by the stepwise addition of two alkyllithium reagents to the optically pure (2*R*,4*R*)-1,2:4,5-diepoxypentane (**12**) as shown in Scheme IV.[16] Monoaddition of vinyllithium, protection, and subsequent addition of allyllithium gave the monoprotected *anti*-1,3-diol **14**. Mitsunobu inversion, deprotection, and derivatization with (*R*)-Mosher's acid chloride gave the diene diester **15**. Oxidation with RuO_4 and esterification with diazomethane gave a dimethyl ester, which correlated with the major C11–C18 degradation product **6**, so the stereochemistry of the major isomer is C13-*S* and C15-*R*. The minor C11–C18 fragment **7** correlated with the dimethyl ester prepared from **14** without Mitsunobu inversion,[17] so the stereochemistry is C13-*S* and C15-*S*. The two remaining diastereomers of the C11–C18 fragments **6** and **7** were prepared by analogous routes using (*S*)-Mosher's acid chloride. All four diastereomers were easily distinguished by proton NMR spectroscopy, thus securing the stereochemical assignment. The complete stereochemistry of macrolactin F is 7*S*,13*S*,23*R*, and the stereochemistry of the major isomer of dihydromacrolactin F is 7*S*,13*S*,15*R*,23*R*.

The stereochemistry of macrolactin B was determined by correlation of each degradation fragment with a synthetic sample of known structure. The C5–C8 fragment **11** of macrolactin B was correlated with a synthetic sample prepared from (*S*)-malic acid and D-glucose (eq 3). The trichloro imidate **19** was coupled[18] with (*S*)-dimethyl malate to give a 1:1.2 mixture of α- and β-anomers. Chromatographic separation, debenzylation, and esterification with (*R*)-Mosher's acid chloride gave the synthetic C5–C8 fragment **11** of macrolactin B. The synthetic and natural samples of fragment **11** showed identical proton NMR spectra, demonstrating that the C7 stereochemistry is *S*. The C19–C24



fragment **9** from macrolactin B was correlated with a synthetic sample prepared[19] from (*R*)-methyl 3-hydroxybutyrate and (*R*)-Mosher's acid chloride, demonstrating that the C23 stereochemistry is *R*. Thus, the C7 and C23 stereochemistry is the same in macrolactin B and macrolactin F. The C11–C16 fragment **10** of macrolactin B was prepared from (2*R*,4*R*)-1,2:4,5-diepoxypentane (**12**) by monoaddition of vinyllithium, basic hydrolysis of the epoxide, and monosilylation to give diol **16** (Scheme V). To insure that the hydrolysis proceeded without rearrangement, the anti stereochemistry of diol **16** was confirmed by ^{13}C analysis of the corresponding acetonide.[3] Diol **16** was derivatized with (*R*)-Mosher's acid chloride, deprotected, and oxidized to give the synthetic C11–C16 fragment **10** of macrolactin B. The other anti diastereomer of the C11–C16 fragment **10** was prepared by a similar route using the (*S*)-Mosher's acid chloride. The natural C11–C16 fragment **10** showed identical NMR spectra with the synthetic (*R*)-Mosher's ester **10** and was easily distinguished from the synthetic (*S*)-Mosher's ester **10**. Thus, the stereochemistry at C13 is the same in macrolactin F and macrolactin B, and the complete stereochemistry of macrolactin B is 7*S*,13*S*,15*R*,23*R*.

Conclusions

The relative stereochemistry of the 1,3-diol unit of macrolactin B and the major isomer of dihydromacrolactin F was determined by preparing the acetonide with ^{13}C-enriched acetone and measuring the ^{13}C chemical shifts of the acetonide methyl groups. The complete stereochemistry of macrolactin B and both the major and minor isomers of dihydromacrolactin F were determined by preparing Mosher's ester derivatives and degrading the macrocyclic lactones to a set of diastereotopic fragments, which were characterized by proton NMR spectroscopy. Each fragment was correlated with a synthetic sample of known structure. Both of these methods can be performed with very small amounts of material and should be useful in other structure elucidation problems. Using these methods, macrolactin B and macrolactin F were found to have the same stereochemistry at each of the common stereogenic centers. It is reasonable to assume that this stereochemistry is maintained throughout the macrolactin family and, if so, the stereochemistry of macrolactin A is 7*S*,13*S*,15*R*,23*R*. Unfortunately, fermentation of this deep sea bacterium has been unreliable and macrolactin A is no longer available in significant yield. The structure determination of these

(15) C19–C24 **1** synthesis from (*R*)-methyl 3-hydroxybutyrate: (a) TIPSOTf, 2,6-lutidine; (b) DIBAL-H; (c) $Ph_3P{=}C(H)CO_2Me$; (d) H_2 Pd/C; (e) LAH; (f) DHP, CSA; (g) TBAF; (h) (*R*)-MTPACl; (i) CSA, MeOH. Experimental procedure and spectral data are given in the supplementary material.

(16) We have prepared (2*R*,4*R*)-1,2:4,5-diepoxypentane and its enantiomer for use as 1,3-diol synthons: Rychnovsky, S. D.; Griesgraber, G.; Zeller, S.; Skalitzky, D. J. *J. Org. Chem.* **1991**, *56*, 5161–5169. We would like to thank George Griesgraber and Sam Zeller for preparing the diepoxide used in this study.

(17) Preparation of **7** from **14**: (a) TBAF; (b) (*R*)-MTPACl; (c) RuO_4; (d) CH_2N_2.

(18) (a) Schmidt, R. R.; Stumpp, M. *Liebigs Ann. Chem.* **1983**, 1249–1256. (b) Schmidt, R. R.; Michel, J. *J. Carbohydr. Chem.* **1985**, *4*, 141–169.

(19) C19–C24 **9** synthesis from (*R*)-methyl 3-hydroxybutyrate: (a) TIPSOTf, 2,6-lutidine; (b) DIBAL-H; (c) $Ph_3P{=}C(H)CO_2Me$; (d) TBAF; (e) (*R*)-MTPACl; (f) H_2 Pd/$BaSO_4$. Experimental procedure and spectral data are given in the supplementary material.

macrolactins lays the groundwork for future synthetic and biological investigations.

Experimental Section

Combustion analyses were performed by M-H-W Laboratories (Phoenix, AZ). Unless otherwise noted, compounds were purified by flash chromatography[20] on E. Merck silica gel 60 (230–400 mesh), eluting with the indicated solvent system. Tetrahydrofuran and ether were distilled from benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Boron trifluoride etherate was distilled and stored under N_2. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen or argon using flame-dried glassware and standard syringe/septa techniques. Alcohol **14** was prepared by the previously described method.[16]

General Procedure for ^{13}C-Acetonide Formation. Approximately 1 mg of silylated diol was azeotropically dried with toluene. The sample was dissolved in 2.0 mL of CH_2Cl_2 with 20 μL of 0.844 M (in toluene) [1,3-$^{13}C_2$]acetone[8] and 5 μL of *N,N*-bis(trimethylsilyl)trifluoroacetamide. The reaction was cooled to −78 °C, and 7 μL of TMSOTf was added. After 3 h, the reaction was quenched with pyridine at −78 °C and warmed to room temperature. The reaction was concentrated under reduced pressure, the resulting crude oil was filtered through a small plug of silica gel with an appropriate solvent (ethyl acetate/hexanes), and the solvent was removed under reduced pressure.

Preparation of 7 [(*R*)-MTPA]. A. (4*R*,6*R*)-1,9-Decadiene-4,6-diol. The previously prepared[16] silyl ether **14** (46.1 mg, 0.16 mmol) was treated with 250 μL of TBAF (1.0 M, 0.25 mmol, 1.6 equiv) in 7.0 mL of THF for 12 h. The reaction was diluted with saturated NH_4Cl and extracted with ethyl acetate (3×). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 24.9 mg (0.15 mmol, 97%) of the product as a colorless oil: $[\alpha]^{24}_D = +16.0°$ (*c* = 1.06, $CHCl_3$); IR (neat) 3357, 3077, 2987, 2936, 1641, 1437, 1061, 994, 912, 831 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.97–5.75 (m, 2 H), 5.18–4.96 (m, 4 H), 4.09–3.90 (m, 2 H), 2.36–2.10 (m, 6 H), 1.70–1.49 (m, 2 H), 1.63 (d, *J* = 5.7 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C*H 138.3, 134.5, 68.6, 68.1, CH_2 118.0, 114.7, 41.9, 36.3, 30.0; HRMS (CI-CH_4) calcd for $C_{10}H_{19}O_2$ (M + H) 171.1385, found 171.1395.

B. Bis((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (4*S*,6*S*)-1,9-Decadiene-4,6-diol. The preceding diol (22.7 mg, 0.13 mmol, 1.0 equiv) and 54.1 mg of DMAP (0.44 mmol, 3.4 equiv) were dissolved in 5.0 mL of CH_2Cl_2. To this solution was added 60 μL of (*R*)-MTPACl (0.33 mmol, 2.5 equiv). After 2 h, the reaction was quenched with saturated $NaHCO_3$, and the mixture was diluted with 20 mL of Et_2O. The organic layer was washed with 1 N $NaHSO_4$ and saturated NaCl, dried ($MgSO_4$), and concentrated under reduced pressure to give 78.9 mg (0.13 mmol, 100%) of the product as a colorless oil: IR (neat) 2981, 2950, 1747, 1643, 1451, 1269, 1169, 1123, 1081, 1016, 994, 921, 765, 719, 697, 640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.55 (m, 4 H), 7.50–7.40 (m, 6 H), 5.74–5.51 (m, 2 H), 5.10–4.92 (m, 6 H), 3.60 (s, 6 H), 2.44–2.27 (m, 2 H), 1.95 (q, *J* = 7.4 Hz, 2 H), 1.84–1.54 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 166.2, 132.7, 123.6 (q, *J* = 289 Hz), 84.7 (q, *J* = 27 Hz), *C*H 136.9, 132.3, 129.8, 128.7, 128.7, 127.5, 127.5, 73.2, 72.7, CH_2 119.3, 115.8, 38.9, 37.7, 33.8, 29.2, CH_3 55.8; HRMS (CI-CH_4) calcd for $C_{30}H_{33}F_6O_6$ (M + H) 603.2181, found 603.2162.

C. Bis((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (3*R*,5*S*)-Dimethyl 3,5-Dihydroxyoctanedioate (7 [(*R*)-MTPA]). The preceding diene (66.6 mg, 0.11 mmol, 1.0 equiv) and 361.7 mg of $NaIO_4$ (1.69 mmol, 15.4 equiv) were dissolved in 2 mL of CH_3CN, 2 mL of CCl_4, and 3 mL of H_2O. $RuCl_3$-$3H_2O$ (5.0 mg, 0.02 mmol, 18 mol %) was added to the solution and, after 2 h, the reaction was poured into CH_2Cl_2/H_2O. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×). The organic layer was dried (Na_2SO_4) and then concentrated under reduced pressure. The resulting dark oil was redissolved in Et_2O and filtered through Celite. The solvent was removed under reduced pressure, and the oil obtained was treated with excess CH_2N_2 in Et_2O at 0 °C. The solvent and remaining reagent were removed under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 53.3 mg (0.08 mmol, 73%) of the product as a colorless oil: IR (neat) 2955, 2850, 1745, 1494, 1439, 1269, 1171, 1122, 1082, 1016, 921, 887, 819, 764, 718, 699, 639 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57–7.53 (m, 4 H), 7.44–7.39 (m, 6 H), 5.32–5.26 (m, 1 H), 4.99–4.93 (m, 1 H), 3.65 (s, 3 H), 3.62 (s, 3 H), 3.57 (s, 3 H), 3.56 (s, 3 H), 2.65 (dd, *J* = 15.6, 6.8 Hz, 1 H), 2.58 (dd, *J* = 15.6, 5.9 Hz, 1 H), 2.25–2.18 (m, 2 H), 1.95–1.89 (m, 4 H); ^{1}H NMR (500 MHz, C_6D_6) δ 7.80–7.76 (m, 4 H), 7.21–6.88 (m, 6 H), 5.46–5.41 (m, 1 H), 5.09–5.04 (m, 1 H), 3.51 (s, 3 H), 3.46 (s, 3 H), 3.27 (s, 3 H), 3.20 (s, 3 H), 2.28 (dd, *J* = 15.6, 6.8 Hz, 1 H), 2.14 (dd, *J* = 15.6, 5.9 Hz, 1 H), 2.05–1.94 (m, 2 H), 1.69–1.64 (m, 2 H), 1.53–1.50 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 172.8, 169.7, 166.3, 165.9, 132.3, 132.2, 123.5 (q, *J* = 288 Hz), 123.4 (q, *J* = 288 Hz), 84.7 (q, *J* = 28 Hz), 84.7 (q, *J* = 28 Hz), *C*H 129.9, 128.7, 128.7, 127.5, 72.5, 69.7, CH_2 39.0, 38.2, 29.5, CH_3 55.7, 52.1, 52.0; HRMS (CI-CH_4 with 1% NH_3) calcd for $C_{30}H_{36}F_6NO_{10}$ (M + NH_4) 684.2243, found 684.2237. Anal. Calcd for $C_{30}H_{32}F_6O_{10}$: C, 54.06; H, 4.84. Found: C, 54.16; H, 4.90.

Preparation of 7 [(*S*)-MTPA]. A. Bis((*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (4*S*,6*S*)-1,9-Decadiene-4,6-diol. (4*R*,6*R*)-1,9-Decadiene-4,6-diol (20.4 mg, 0.120 mmol) was treated with DMAP and (*S*)-MTPACl as above to give 69.1 mg (0.115 mmol, 96%) of the product as a colorless oil: IR (neat) 2980, 2949, 2848, 1746, 1641, 1451, 1270, 1170, 1121, 1081, 1016, 920, 818, 765, 719, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.50 (m, 4 H), 7.43–7.35 (m, 6 H), 5.72–5.46 (m, 2 H), 5.13–4.84 (m, 6 H), 3.54 (s, 6 H), 2.33 (t, *J* = 6.3 Hz, 2 H), 1.93–1.80 (m, 4 H), 1.77–1.55 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 165.9, 131.7, 123.1 (q, *J* = 288 Hz), 84.5 (q, *J* = 28 Hz), 84.4 (q, *J* = 28 Hz), *C*H 136.4, 131.5, 129.4, 128.3, 128.2, 127.2, 127.2, 72.6, 72.2, CH_2 118.8, 115.3, 38.0, 36.8, 32.9, 28.4, CH_3 55.15; HRMS (CI-CH_4) calcd for $C_{30}H_{33}F_6O_6$ (M + H) 603.2181, found 603.2193.

B. Bis((*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (3*R*,5*S*)-Dimethyl 3,5-Dihydroxyoctanedioate (7 [(*S*)-MTPA]). The preceding diene (69.0 mg, 0.11 mmol) was treated with RuO_4 and CH_2N_2 as above to give, after purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes), 52.0 mg (0.078 mmol, 70%) of the product as a colorless oil: IR (neat) 2955, 2850, 1742, 1439, 1169, 1122, 1087, 1015, 820, 766, 719 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55–7.51 (m, 4 H), 7.43–7.25 (m, 6 H), 5.36–5.32 (m, 1 H), 5.13–5.09 (m, 1 H), 3.63 (s, 3 H), 3.60 (s, 3 H), 3.56 (s, 3 H), 3.53 (s, 3 H), 2.66 (dd, *J* = 15.6, 5.9 Hz, 1 H), 2.58 (dd, *J* = 15.6, 5.9 Hz, 1 H), 2.24–2.09 (m, 2 H), 2.01–1.94 (m, 3 H), 1.90–1.83 (m, 1 H); ^{1}H NMR (500 MHz, C_6D_6) δ 7.75–7.71 (m, 4 H), 7.22–6.99 (m, 6 H), 5.60–5.54 (m, 1 H), 5.33–5.27 (m, 1 H), 3.53 (s, 3 H), 3.52 (s, 3 H), 3.26 (s, 3 H), 3.19 (s, 3 H), 2.42 (dd, *J* = 15.6, 5.9 Hz, 1 H), 2.16 (dd, *J* = 15.6, 5.9 Hz, 1 H), 2.00–1.86 (m, 2 H), 1.75–1.51 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 172.8, 169.6, 166.5, 166.1, 132.0, 131.9, 123.4 (q, *J* = 288 Hz), 123.3 (q, *J* = 289 Hz), 84.8 (q, *J* = 28 Hz), *C*H 129.8, 128.7, 128.7, 127.7, 127.5, 72.2, 69.9, CH_2 38.6, 38.0, 29.8, 29.0, CH_3 55.6, 52.0, 51.9; HRMS (CI-CH_4 with 1% NH_3) calcd for $C_{30}H_{36}F_6NO_{10}$ (M + NH_4) 684.2243, found 684.2288. Anal. Calcd for $C_{30}H_{32}F_6O_{10}$: C, 54.06; H, 4.84. Found: C, 54.25; H, 5.08.

Preparation of 6 [(*R*)-MTPA]. A. (4*S*,6*R*)-4-*O*-((1,1-Dimethylethyl)dimethylsilyl)-6-*O*-benzoyl-1,9-decadiene-4,6-diol. The previously prepared[16] silyl ether **14** (110.4 mg, 0.39 mmol, 1.0 equiv), 63.1 mg of $PhCO_2H$ (0.52 mmol, 1.3 equiv), and 138.1 mg of Ph_3P (0.53 mmol, 1.3 equiv) were dissolved in 2.0 mL of THF. Diethyl azodicarboxylate was added to the mixture until a yellow color persisted. The reaction was stirred for 12 h, after which the solvent was removed under reduced pressure. Purification by flash chromatography (SiO_2, 5% tBuOMe/hexanes) gave 88.4 mg (0.22 mmol, 59%, 92% based on recovered starting material) of the product as a colorless oil: $[\alpha]^{24}_D = -2.9°$ (*c* = 1.03, $CHCl_3$); IR (neat) 3075, 2954, 2929, 2856, 1719, 1641, 1472, 1450, 1388, 1361, 1314, 1272, 1176, 1110, 1069, 1026, 1002, 913, 836, 807, 775, 711 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09–8.02 (m, 2 H), 7.60–7.51 (m, 1 H), 7.49–7.40 (s, 2 H), 5.95–5.75 (m, 2 H), 5.33–5.23 (m, 1 H), 5.09–4.94 (m, 4 H), 3.39–3.80 (m, 1 H), 2.33–2.08 (m, 4 H), 1.92–1.74 (m, 4 H), 0.88 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 165.2, 130.3, 17.8, *C*H 137.4, 134.4, 132.5, 129.3, 128.0, 71.5, 68.6, CH_2 117.0, 114.7, 41.1, 41.0, 33.6, 29.2, CH_3 25.6, −4.7, −4.9; HRMS (CI-CH_4) calcd for $C_{23}H_{37}O_3Si$ (M + H) 389.2511, found 389.2500.

B. (4*R*,6*S*)-1,9-Decadiene-4,6-diol. The preceding protected diol (102.3 mg, 0.26 mmol, 1.0 equiv) was dissolved in 5.0 mL of THF. To this solution was added 600 μL of 1.0 M TBAF (0.6 mmol, 2.3 equiv); the mixture was then heated to reflux for 30 min. The reaction was then cooled to room temperature and concentrated under reduced pressure. The crude oil was redissolved in Et_2O and filtered through a plug of silica gel, rinsing with 5% MeOH/ethyl acetate. The solvent was removed under reduced pressure and the crude oil was dissolved in 4 mL of MeOH and 1 mL of 2.0 M NaOH (2.0 mmol, 8 equiv). The reaction mixture was heated to reflux for 30 min, after which it was cooled to room temperature and neutralized with excess solid NH_4Cl. The aqueous layer was extracted with ethyl acetate (3×). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 40% ethyl acetate/hexanes) gave 37.7 mg (0.22 mmol, 85%) of the product as a colorless oil: $[\alpha]^{24}_D = +9.2°$ (*c* = 1.37, $CHCl_3$); IR (neat) 3356, 3077, 2978, 2936, 1640, 1438, 1328, 1084, 994,

(20) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.

912, 840 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.85–5.73 (m, 2 H), 5.12–4.93 (m, 4 H), 3.90–3.63 (m, 2 H), 3.39 (br s, 1 H), 3.24 (br s, 1 H), 2.24–2.10 (m, 4 H), 1.63–1.44 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C*H 138.3, 134.2, 72.2, 71.8, *C*H$_2$ 118.1, 114.7, 42.5, 42.2, 36.9, 29.6; HRMS (CI-CH_4) calcd for $C_{10}H_{19}O_2$ (M + H) 171.1385, found 171.1377.

C. Bis((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (4*S*,6*R*)-1,9-Decadiene-4,6-diol (15). The preceding diol (20.9 mg, 0.12 mmol) was treated with DMAP and (*R*)-MTPACl as above to give 72.7 mg (0.12 mmol, 100%) of the product as a colorless oil: IR (neat) 3078, 2952, 2850, 1747, 1643, 1497, 1451, 1256, 1168, 1123, 1081, 920, 823, 765, 719, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55–7.53 (m, 4 H), 7.41–7.33 (m, 6 H), 5.75–5.57 (m, 2 H), 5.21–5.01 (m, 4 H), 4.95–4.88 (m, 2 H), 3.55 (s, 3 H), 3.54 (s, 3 H), 2.52–2.36 (m, 2 H), 2.08–1.98 (m, 1 H), 1.93–1.78 (m, 3 H), 1.64–1.56 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 166.1, 132.1, 132.1, 123.4 (q, J = 286 Hz), 84.5 (q, J = 25 Hz), *C*H 136.8, 132.3, 129.7, 128.5, 128.5, 127.3, 73.0, 72.9, *C*H$_2$ 119.3, 115.6, 37.9, 37.2, 32.6, 28.8, *C*H$_3$ 55.5; HRMS (CI-CH_4) calcd for $C_{30}H_{33}F_6O_6$ (M + H) 603.2181, found 603.2204.

D. Bis((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (3*R*,5*R*)-Dimethyl 3,5-Dihydroxyoctanedioate (6 [(*R*)-MTPA]). Diene **15** (76.7 mg, 0.127 mmol) was treated with RuO_4 and CH_2N_2 as above to give, after purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes), 60.1 mg (0.09 mmol, 71%) of the product as a colorless oil: IR (neat) 2955, 2851, 1733, 1496, 1438, 1165, 1124, 1081, 1015, 922, 891, 828, 768, 715, 680 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54–7.48 (m, 4 H), 7.43–7.36 (m, 6 H), 5.50–5.43 (m, 1 H), 5.09–5.02 (m, 1 H), 3.65 (s, 3 H), 3.64 (s, 3 H), 3.54 (s, 3 H), 3.52 (s, 3 H), 2.77–2.65 (m, 2 H), 2.18–2.03 (m, 3 H), 1.98–1.86 (m, 2 H), 1.82–1.74 (m, 1 H); ^{1}H NMR (500 MHz, C_6D_6) δ 7.70 (d, J = 7.8 Hz, 2 H), 7.68 (d, J = 7.8 Hz, 2 H), 7.15–6.98 (m, 6 H), 5.66–5.58 (m, 1 H), 5.10–5.03 (m, 1 H), 3.48 (s, 3 H), 3.46 (s, 3 H), 3.25 (s, 3 H), 3.22 (s, 3 H), 2.50–2.38 (m, 2 H), 1.97–1.86 (m, 3 H), 1.74–1.66 (m, 1 H), 1.53–1.45 (m, 2 H); HRMS (CI-CH_4) calcd for $C_{32}H_{37}F_6O_{10}$ (M + C_2H_5) 695.2291, found 695.2306. Anal. Calcd for $C_{30}H_{32}F_6O_{10}$: C, 54.06; H, 4.84. Found: C, 54.09; H, 5.00.

Preparation of 6 [(*S*)-MTPA]. A. Bis((*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (4*S*,6*R*)-1,9-Decadiene-4,6-diol. (4*R*,6*S*)-1,9-Decadiene-4,6-diol (16.2 mg, 0.095 mmol) was treated with DMAP and (*S*)-MTPACl as above to give 56.0 mg (0.093 mmol, 98%) of the product as a colorless oil: IR (neat) 3078, 2950, 2849, 1746, 1641, 1497, 1450, 1269, 1170, 1122, 1081, 1017, 920, 823, 765, 719, 697 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54–7.51 (m, 4 H), 7.41–7.38 (m, 6 H), 5.79–5.65 (m, 1 H), 5.59–5.46 (m, 1 H), 5.15–4.96 (m, 6 H), 3.55 (s, 3 H), 3.53 (s, 3 H), 2.38–2.20 (m, 2 H), 2.09–1.97 (m, 3 H), 1.90–1.71 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 166.3, 166.0, 132.1, 123.4 (q, J = 288 Hz), 84.7 (q, J = 28 Hz), *C*H 136.8, 132.0, 129.8, 129.7, 128.6, 128.5, 127.5, 127.4, 73.2, 72.8, *C*H$_2$ 119.2, 115.9, 37.8, 37.1, 32.8, 29.3, *C*H$_3$ 55.6; HRMS (CI-CH_4) calcd for $C_{30}H_{33}F_6O_6$ (M + H) 603.2181, found 603.2162.

B. Bis((*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (3*R*,5*R*)-Dimethyl 3,5-Dihydroxyoctanedioate (6 [(*S*)-MTPA]). The preceding diene (52.0 mg, 0.863 mmol) was treated with RuO_4 and CH_2N_2 as above to give, after purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes), 37.2 mg (0.056 mmol, 65%) of the product as a colorless oil: IR (neat) 2955, 2850, 1747, 1438, 1256, 1170, 1122, 1082, 1016, 921, 891, 826, 767, 717, 681, 649, 618 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.53–7.48 (m, 4 H), 7.42–7.38 (m, 6 H), 5.44–5.38 (m, 1 H), 5.17–5.10 (m, 1 H), 3.66 (s, 3 H), 3.56 (s, 3 H), 3.52 (s, 3 H), 3.51 (s, 3 H), 2.63–2.53 (m, 2 H), 2.39–2.28 (m, 2 H), 2.16–2.08 (m, 2 H), 2.00–1.91 (m, 2 H); ^{1}H NMR (500 MHz, C_6D_6) δ 7.71 (d, J = 7.8 Hz, 2 H), 7.66 (d, J = 7.8 Hz, 2 H), 7.15–6.97 (m, 6 H), 5.55–5.48 (m, 1 H), 5.23–5.16 (m, 1 H), 3.47 (s, 3 H), 3.37 (s, 3 H), 3.28 (s, 3 H), 3.16 (s, 3 H), 2.32 (dd, J = 16.6, 7.8 Hz, 1 H), 2.25 (dd, J = 16.6, 4.9 Hz, 1 H), 2.18–2.06 (m, 2 H), 2.00–1.89 (m, 2 H), 1.74–1.66 (m, 1 H), 1.58–1.52 (m, 1 H); HRMS (CI-CH_4) calcd for $C_{32}H_{37}F_6O_{10}$ (M + C_2H_5) 695.2291, found 695.2265. Anal. Calcd for $C_{30}H_{32}F_6O_{10}$: C, 54.06; H, 4.84. Found: C, 53.92; H, 4.93.

Preparation of 10 [(*R*)-MTPA]. A. (2*R*,4*S*)-1-*O*-((1,1-Dimethylethyl)dimethylsilyl)-6-heptene-1,2,4-triol (16). (2*R*,4*R*)-1,2:4,5-Dianhydro-3-deoxypentitol (226.0 mg, 2.26 mmol, 1.0 equiv) and a crystal of 1,10-phenanthroline indicator were dissolved in 11.0 mL of THF at −78 °C. To this solution was added 1.0 M vinyllithium until a brown color persisted, and then 2.74 mL more (2.74 mmol, 1.2 equiv) followed by 365 μL of BF_3·Et_2O (2.97 mmol, 1.3 equiv). After 30 min, the reaction was quenched at −78 °C with MeOH followed by saturated $NaHCO_3$. The resulting mixture was warmed to room temperature and extracted with Et_2O (4×). The organic layer was dried ($MgSO_4$) and concentrated under reduced pressure at 0 °C. The resulting oil was then heated to 100 °C for 48 h in a solution of 10 mL of 0.5 N NaOH and 2.0 mL of tBuOH. The reaction was cooled to room temperature and neutralized with Amberlite MB-3 mixed bed resins. The resins were filtered and washed thoroughly with MeOH. The solvent was removed under reduced pressure (<0.5 Torr). The crude product was treated with 33.0 mg of DMAP (0.27 mmol, 12 mol %), 1.0 mL of Et_3N (7.17 mmol, 3.2 equiv), and 518 mg of TBDMSCl (2.44 mmol, 1.5 equiv) in 10 mL of CH_2Cl_2. After 2 h, the reaction was quenched with saturated $NaHCO_3$, extracted (ethyl acetate, 3×), dried (Na_2SO_4), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 252.1 mg (0.97 mmol, 43%) of the product as a colorless oil: $[\alpha]^{24}_D$ = +7.5° (c = 1.10, $CHCl_3$); IR (neat) 3383, 3077, 2930, 2858, 1640, 1471, 1437, 1362, 1255, 1087, 1005, 914, 837, 778 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.89–5.74 (m, 1 H), 5.14–5.08 (m, 2 H), 3.98–3.91 (m, 2 H), 3.60 (dd, J = 9.9, 3.9 Hz, 1 H), 3.46 (dd, J = 9.9, 7.5 Hz, 1 H), 2.75 (d, J = 3.3 Hz, 1 H), 2.58 (d, J = 4.1 Hz, 1 H), 2.29–2.23 (m, 2 H), 1.66–1.47 (m, 2 H), 0.88 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 18.3, *C*H 134.8, 69.3, 67.9, *C*H$_2$ 117.9, 67.2, 42.19, 38.4, *C*H$_3$ 25.9, −5.3, −5.4; HRMS (CI-CH_4) calcd for $C_{13}H_{29}O_3Si$ (M + H) 261.1886, found 261.1879. Anal. Calcd for $C_{13}H_{28}O_3Si$: C, 59.95; H, 10.84. Found: C, 59.76; H, 10.68.

B. (2*R*,4*S*)-1-*O*-((1,1-Dimethylethyl)dimethylsilyl)-2,4-*O*-(1-methylethylidene)-6-heptene-1,2,4-triol. Diol **16** (66.0 mg, 0.25 mmol, 1.0 equiv) was dissolved in 4.0 mL of acetone and 1.0 mL of 2,2-dimethoxypropane. To this solution was added 3.0 mg of CSA (0.013 mmol, 5 mol %). The reaction was stirred overnight and then quenched with excess Et_3N. The volatile components were removed in vacuo. Purification by flash chromatography (SiO_2, 5% tBuOMe/hexanes) gave 69.7 mg (0.23 mmol, 92%) of the product as a colorless oil. The ^{13}C NMR spectrum confirmed the anti stereochemistry: $[\alpha]^{24}_D$ = +31.2° (c = 1.11, $CHCl_3$); IR (neat) 2987, 2930, 2857, 1642, 1472, 1378, 1253, 1224, 1175, 1141, 1114, 1025, 913, 837, 777 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.79 (dddd, J = 17.0, 10.2, 6.8, 6.8 Hz, 1 H), 5.11–5.02 (m, 2 H), 3.90–3.81 (m, 2 H), 3.62 (dd, J = 10.8, 5.7 Hz, 1 H), 3.54 (dd, J = 10.8, 5.1 Hz, 1 H), 2.34–2.27 (m, 1 H), 2.22–2.16 (m, 1 H), 1.64–1.53 (m, 2 H), 1.35 (s, 3 H), 1.33 (s, 3 H), 0.88 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 100.1, 18.3, *C*H 134.4, 67.7, 66.2, *C*H$_2$ 116.7, 66.1, 40.1, 33.9, *C*H$_3$ 25.8, 25.0, 24.9, −5.2, −5.3; HRMS (EI) calcd for $C_{15}H_{29}O_3Si$ (M − CH_3) 285.1885, found 285.1880. Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.73. Found: C, 63.92; H, 10.68.

C. Bis((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (2*R*,4*S*)-1-*O*-((1,1-Dimethylethyl)dimethylsilyl)-6-heptene-1,2,4-triol. Diol **16** (58.1 mg, 0.22 mmol) was treated with DMAP and (*R*)-MTPACl as above to give 156.4 mg (0.22 mmol, 100%) of the product as a colorless oil: IR (neat) 2954, 2932, 2858, 1749, 1644, 1497, 1452, 1391, 1361, 1258, 1170, 1123, 1082, 1019, 964, 922, 837, 779, 765, 718, 697, 641 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65–7.58 (m, 4 H), 7.46–7.40 (m, 6 H), 5.58 (dddd, J = 17.0, 10.3, 6.9, 6.9 Hz, 1 H), 5.08–5.01 (m, 4 H), 3.74–3.48 (m, 2 H), 3.65 (s, 3 H), 3.61 (s, 3 H), 2.44–2.30 (m, 2 H), 1.96–1.75 (m, 2 H), 0.89 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 166.1, 132.8, 132.6, 123.6 (q, J = 288 Hz), 84.7 (q, J = 28 Hz), 18.3, *C*H 132.2, 129.8, 129.7, 128.6, 127.5, 127.4, 73.4, 72.5, *C*H$_2$ 119.2, 64.2, 38.9, 34.6, *C*H$_3$ 55.7, 25.8, −5.45, −5.5; HRMS (CI-CH_4) calcd for $C_{29}H_{33}F_6O_7Si$ (M − C_4H_9) 635.1900, found 635.1907.

D. 2,4-*O*-Bis((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (2*R*,4*S*)-6-Heptene-1,2,4-triol (17). The preceding silyl ether (156.4 mg, 0.22 mmol, 1.0 equiv) was dissolved in 6.0 mL of 5% concentrated HF/CH_3CN. After 1 h, saturated $NaHCO_3$ was added and the aqueous layer was extracted with CH_2Cl_2 (3×). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give 125.9 mg (0.217 mmol, 96%) of the product as a colorless oil: IR (neat) 3530, 2953, 2851, 1749, 1643, 1495, 1451, 1269, 1169, 1123, 1082, 1017, 925, 818, 766, 718, 698 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62–7.57 (m, 4 H), 7.51–7.40 (m, 6 H), 5.57 (dddd, J = 17.0, 10.4, 6.9, 6.9 Hz, 1 H), 5.15–5.00 (m, 4 H), 3.69–3.48 (m, 2 H), 3.60 (s, 3 H), 3.58 (s, 3 H), 2.45–2.27 (m, 2 H), 2.01–1.75 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 166.2, 165.7, 132.1, 123.1 (q, J = 289 Hz), 84.33 (q, J = 28 Hz), 84.2 (q, J = 28 Hz), *C*H 131.6, 129.4, 129.4, 128.3, 128.2, 127.0, 127.0, 73.3, 72.2, *C*H$_2$ 118.9, 63.8, 38.4, 34.0, *C*H$_3$ 55.3; HRMS (CI-CH_4 with 1% NH_3) calcd for $C_{27}H_{32}F_6NO_7$ (M + NH_4) 596.2083, found 596.2073.

E. Bis((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (2*R*,4*R*)-Dimethyl 2,4-Dihydroxyhexanedioate (10 [(*R*)-MTPA]). The unsaturated alcohol **17** (123.4 mg, 0.213 mmol, 1.0 equiv) was dissolved in 4.0 mL of acetone and treated with 2.0 mL of 0.6 M Jones' reagent (1.2 mmol, 5.6 equiv) for 20 h. Excess oxidant was quenched with iPrOH, and the dark solid that formed was dissolved with H_2O. The aqueous layer was extracted with Et_2O (3×). The organic layer was

dried ($MgSO_4$) and concentrated under reduced pressure. The crude oil obtained was treated with excess CH_2N_2 in Et_2O at 0 °C. After the solvent and excess CH_2N_2 were removed under reduced pressure, the resulting crude oil was dissolved in 2 mL of CH_3CN, 2 mL of CCl_4, and 3 mL of H_2O. $NaIO_4$ (500 mg, 2.34 mmol, 10 equiv) and $RuCl_3 \cdot 3H_2O$ (5.0 mg, 0.02 mmol, 10 mol %) were added to the solution; after 2 h the reaction was poured into CH_2Cl_2/H_2O. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3×). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. The resulting dark oil was redissolved in Et_2O and filtered through Celite. The solvent was removed under reduced pressure, and the oil obtained was treated with excess CH_2N_2 in Et_2O at 0 °C. The solvent and remaining reagent were removed under reduced pressure. Purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes) gave 63.4 mg (0.099 mmol, 46%) of the product as a colorless oil: IR (neat) 2957, 2853, 1756, 1495, 1440, 1171, 1121, 1082, 1016, 921, 821, 766, 720 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.67–7.63 (m, 2 H), 7.52–7.48 (m, 2 H), 7.45–7.39 (m, 6 H), 5.32–5.26 (m, 1 H), 5.03 (dd, J = 11.7, 2.0 Hz, 1 H), 3.74 (s, 3 H), 3.66 (s, 3 H), 3.61 (s, 3 H), 3.53 (s, 3 H), 2.66 (dd, J = 15.6, 6.8 Hz, 1 H), 2.56 (dd, J = 15.6, 5.9 Hz, 1 H), 2.33 (ddd, J = 14.7, 9.7, 2.0 Hz, 1 H), 2.13 (ddd, J = 14.7, 11.7, 2.9 Hz, 1 H); ^1H NMR (500 MHz, C_6D_6) δ 7.92 (d, J = 7.8 Hz, 2 H), 7.70 (d, J = 7.8 Hz, 2 H), 7.24–6.98 (m, 6 H), 5.46–5.40 (m, 1 H), 5.21 (dd, J = 10.7, 2.0 Hz, 1 H), 3.69 (s, 3 H), 3.43 (s, 3 H), 3.16 (s, 3 H), 3.09 (s, 3 H), 2.14 (dd, J = 16.6, 6.8 Hz, 1 H), 2.06 (ddd, J = 15.7, 9.8, 2.0, 1 H), 2.03 (dd, J = 16.6, 6.8 Hz, 1 H), 1.74 (ddd, J = 15.7, 10.7, 2.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 169.2, 168.7, 165.9, 165.7, 131.9, 131.8, 123.1 (q, J = 288 Hz), 84.4 (q, J = 28 Hz), *C*H 129.7, 129.6, 128.5, 128.4, 127.4, 127.1, 70.1, 69.0, CH_2 38.5, 35.2, CH_3 55.6, 55.3, 52.7, 51.9; HRMS (CI-CH_4 with 1% NH_3) calcd for $C_{28}H_{32}F_6NO_{10}$ (M + NH_4) 656.1930, found 656.1913. Anal. Calcd for $C_{28}H_{28}F_6O_{10}$: C, 52.67; H, 4.42. Found: C, 52.79; H, 4.66.

Preparation of 10 [(*S*)-MTPA]. A. Bis((*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (2*R*,4*S*)-1-*O*-((1,1-Dimethylethyl)dimethylsilyl)-6-heptene-1,2,4-triol. Diol **16** (57.6 mg, 0.22 mmol) was treated with DMAP and (*S*)-MTPACl as above to give 155.2 mg (0.22 mmol, 100%) of the product as a colorless oil: IR (neat) 2953, 2858, 1748, 1643, 1497, 1451, 1390, 1361, 1256, 1170, 1121, 1082, 1017, 922, 837, 779, 765, 719, 695, 642 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.56–7.52 (m, 4 H), 7.46–7.39 (m, 6 H), 5.57 (dddd, J = 17.0, 10.3, 7.0, 7.0 Hz, 1 H), 5.27–4.99 (m, 4 H), 3.67–3.46 (m, 2 H), 3.55 (s, 3 H), 3.53 (s, 3 H), 2.40–2.35 (m, 2 H), 2.00–1.91 (m, 2 H), 0.84 (s, 9 H), 0.00 (s, 3 H), –0.01 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 166.0, 165.9, 131.7, 131.6, 123.0 (q, J = 288 Hz), 84.6 (q, J = 28 Hz), 84.5 (q, J = 29 Hz), 17.8, *C*H 131.5, 129.3, 128.2, 127.3, 127.2, 73.2, 72.2, CH_2 118.8, 63.3, 38.1, 33.9, CH_3 55.2, 55.0, 25.4, –6.0; HRMS (CI-CH_4) calcd for $C_{29}H_{33}F_6O_7Si$ (M – C_4H_9) 635.1900, found 635.1906.

B. 2,4-Bis((*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (2*R*,4*S*)-6-Heptene-1,2,4-triol (17 [(*S*)-MTPA]). The preceding silyl ether (151.4 mg, 0.218 mmol) was treated with HF/CH_3CN as above to give 123.4 mg (0.213 mmol, 98%) of the product as a colorless oil: IR (neat) 3568, 3070, 2951, 2849, 1747, 1643, 1497, 1451, 1270, 1170, 1121, 1082, 1016, 926, 819, 763, 720, 698, 640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.55–7.53 (m, 4 H), 7.47–7.40 (m, 6 H), 5.56 (dddd, J = 17.1, 10.1, 7.0, 7.0 Hz, 1 H), 5.18–4.97 (m, 4 H), 3.70 (dd, J = 12.3, 3.6 Hz, 1 H), 3.55–3.50 (s, 1 H), 3.54 (s, 6 H), 2.37 (t, J = 6.6 Hz, 2 H), 2.00 (ddd, J = 15.4, 10.0, 2.7 Hz, 1 H), 1.90 (ddd, J = 15.4, 10.4, 3.3 Hz, 1 H), 1.71 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 166.5, 166.2, 131.8, 131.8, 123.2 (q, J = 288 Hz), 84.8 (q, J = 28 Hz), 84.7 (q, J = 28 Hz), *C*H 131.5, 129.7, 129.7, 128.6, 128.5, 127.4, 127.3, 73.8, 72.4, CH_2 119.3, 63.8, 38.3, 33.8, CH_3 55.5; HRMS (CI-CH_4 with 1% NH_3) calcd for $C_{27}H_{32}F_6NO_7$ (M + NH_4) 596.2083, found 596.2035.

C. Bis((*S*)-α-methoxy-α-(trifluoromethyl)phenylacetate) of (2*R*,4*R*)-Dimethyl 2,4-Dihydroxyhexanedioate (10 [(*S*)-MTPA]). The preceding unsaturated alcohol (123.4 mg, 0.213 mmol) was treated with Jones' reagent and RuO_4 as above to give, after purification by flash chromatography (SiO_2, 30% ethyl acetate/hexanes), 58.0 mg (0.091 mmol, 43%) of the product as a colorless oil: IR (neat) 3066, 2956, 2850, 2748, 1496, 1440, 1357, 1269, 1172, 1121, 1082, 1014, 919, 822, 763, 721, 699, 641 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.60–7.56 (m, 2 H), 7.50–7.46 (m, 2 H), 7.44–7.36 (m, 6 H), 5.51–5.44 (m, 1 H), 5.15 (dd, J = 10.7, 2.9 Hz, 1 H), 3.74 (s, 3 H), 3.60 (s, 3 H), 3.59 (s, 3 H), 3.49 (s, 3 H), 2.70 (dd, J = 15.6, 6.8 Hz, 1 H), 2.61 (dd, J = 15.6, 5.9 Hz, 1 H), 2.42 (ddd, J = 14.7, 10.7, 2.9 Hz, 1 H), 2.23 (ddd, J = 14.7, 11.7, 2.9 Hz, 1 H); ^1H NMR (500 MHz, C_6D_6) δ 7.85 (d, J = 7.8 Hz, 2 H), 7.63 (d, J = 7.8 Hz, 2 H), 7.20–6.98 (m, 6 H), 5.68–5.62 (m, 1 H), 5.33 (dd, J = 10.7, 2.9 Hz, 1 H), 3.62 (s, 3 H), 3.38 (s, 3 H), 3.15 (s, 6 H), 2.26 (dd, J = 15.6, 6.8 Hz, 1 H), 2.13 (ddd, J = 14.7, 10.7, 2.9 Hz, 1 H), 2.09 (dd, J = 15.6, 5.9 Hz, 1 H), 1.83 (ddd, J = 14.7, 11.7, 2.9 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 169.2, 168.5, 166.0, 131.5, 123.1 (q, J = 288 Hz), 84.7 (q, J = 28 Hz), *C*H 129.8, 128.6, 128.3, 127.6, 127.2, 70.2, 69.1, CH_2 38.3, 34.9, CH_3 55.7, 55.4, 52.8, 51.9; HRMS (CI-CH_4 with 1% NH_3) calcd for $C_{28}H_{32}F_6NO_{10}$ (M + NH_4) 656.1930, found 656.1926. Anal. Calcd for $C_{28}H_{28}F_6O_{10}$: C, 52.67; H, 4.42. Found: C, 52.82; H, 4.49.

Preparation of 11 [(*R*)-MTPA]. A. (2*S*)-Dimethyl 2-*O*-(2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl)malate (20). The previously reported[18] *O*-(2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl) trichloro imidate **19** (267.7 mg, 0.39 mmol, 1.0 equiv) and 116.1 mg of (*S*)-dimethyl malate (0.71 mmol, 1.8 equiv) were dissolved in 5.0 mL of CH_2Cl_2 at –50 °C. To this solution was added 5 μL of $BF_3 \cdot Et_2O$ (0.04 mmol, 10 mol %). After 1 h, the reaction was quenched with solid $NaHCO_3$, H_2O was added, and the mixture was extracted (CH_2Cl_2 × 3). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 5% tBuOMe/95% (1:1 CH_2Cl_2/hexanes)) gave 95.8 mg (0.14 mmol, 36%) of the α-anomer as a colorless oil and 115.1 mg (0.17 mmol, 44%) of the β-anomer as a colorless oil. β-Anomer: $[\alpha]^{24}_D$ = –1.61° (c = 1.68, $CHCl_3$); IR (neat) 3063, 3030, 2951, 2867, 1743, 1497, 1438, 1400, 1360, 1279, 1209, 1169, 1070, 1028, 912, 899, 753, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.14 (m, 20 H), 5.03 (d, J = 10.7 Hz, 1 H), 4.93 (d, J = 10.7 Hz, 1 H), 4.80 (d, J = 10.7 Hz, 1 H), 4.76 (d, J = 10.7 Hz, 1 H), 4.73 (t, J = 6 Hz, 1 H), 4.67 (d, J = 10.7 Hz, 1 H), 4.63–4.56 (m, 2 H), 4.54 (s, 1 H), 4.53 (d, J = 10.7 Hz, 1 H), 3.71 (s, 3 H), 3.66 (s, 3 H), 3.70–3.55 (m, 4 H), 3.46 (t, J = 8 Hz, 1 H), 3.41 (ddd, J = 8.8, 2.9, 2.9 Hz, 1 H), 2.98 (d, J = 6 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 170.9, 170.2, 138.6, 138.5, 138.1, *C*H 128.3, 128.3, 128.2, 127.9, 127.8, 127.6, 127.6, 127.5, 102.8, 84.4, 81.7, 77.4, 74.8, 72.9, CH_2 75.6, 74.9, 74.4, 73.4, 68.7, 37.9, CH_3 52.2, 51.8; HRMS (FAB) calcd for $C_{40}H_{43}O_{10}$ (M – H) 683.2856, found 683.2850.

B. (*S*)-Dimethyl 2-*O*-[2,3,4,6-Tetra-*O*-((*R*)-α-methoxy-α-(trifluoromethyl)phenylacetyl)-α-D-glucopyranosyl]malate (11 [(*R*)-MTPA]). A solution containing 113.3 mg of the preceding β-glycoside (0.17 mmol, 1.0 equiv), 10 mg of 20% $Pd(OH)_2/C$, and 6.0 mL of EtOH was stirred under hydrogen for 4 h, filtered through Celite, and concentrated under reduced pressure. The resulting crude oil was suspended in 5.0 mL of CH_2Cl_2, to which were added 206.7 mg of DMAP (1.69 mmol, 10 equiv) and 185 μL of (*R*)-MTPACl (1.0 mmol, 6.0 equiv). After 2 h, the reaction was quenched with saturated $NaHCO_3$ and diluted with 20 mL of Et_2O. The organic layer was washed with 1 N $NaHSO_4$ and saturated NaCl, dried ($MgSO_4$), and concentrated under reduced pressure. Purification by flash chromatography (SiO_2, 25% ethyl acetate/hexanes) gave 174.4 mg (0.15 mmol, 89%) of the product as a colorless oil: IR (neat) 3066, 3008, 2956, 2850, 1766, 1495, 1452, 1440, 1411, 1372, 1170, 1123, 1082, 1015, 920, 850, 827, 806, 762, 724, 698, 667, 637 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.52–7.28 (m, 20 H), 5.43 (t, J = 7.3 Hz, 1 H), 5.31 (dd, J = 9.8, 7.8 Hz, 1 H), 5.21 (t, J = 6.8 Hz, 1 H), 5.04 (d, J = 6.8 Hz, 1 H), 4.68 (t, J = 6.3 Hz, 1 H), 4.18–4.12 (m, 1 H), 3.73–3.67 (m, 2 H), 3.64 (s, 3 H), 3.60 (s, 3 H), 3.49 (s, 3 H), 3.47 (s, 3 H), 3.43 (s, 3 H), 3.35 (s, 3 H), 2.79 (dd, J = 16.6, 4.9 Hz, 1 H), 2.69 (dd, J = 16.6, 6.8 Hz, 1 H); ^1H NMR (500 MHz, C_6D_6) δ 7.72–7.61 (m, 8 H), 7.30–6.98 (m, 12 H), 5.46 (t, J = 7 Hz, 1 H), 5.44 (t, J = 7.8 Hz, 1 H), 5.26 (dd, J = 10.8, 7.8 Hz, 1 H), 4.67–4.64 (m, 1 H), 4.63 (t, J = 6.8 Hz, 1 H), 3.86 (d, J = 12.7 Hz, 1 H), 3.55 (dd, J = 12.7, 5.9 Hz, 1 H), 3.51 (s, 3 H), 3.43 (s, 36 H), 3.35 (s, 3 H), 3.25 (s, 3 H), 3.24 (s, 3 H), 2.77–2.58 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ *C* 170.0, 170.0, 165.8, 165.3, 165.0, 164.9, 131.7, 131.5, 131.2, 130.5, 123.3, (q, J = 288 Hz), 122.9 (q, J = 288 Hz), 84.8 (q, J = 28 Hz), 84.2 (q, J = 28 Hz), *C*H 130.0, 129.9, 129.8, 129.8, 128.6, 128.4, 127.9, 127.8, 127.5, 126.8, 96.9, 74.5, 72.6, 70.9, 70.9, 69.9, CH_2 62.8, 37.0, CH_3 56.0, 55.3, 55.1, 55.0, 52.3, 52.0; HRMS (CI-CH_4) calcd for $C_{52}H_{47}F_{12}O_{18}$ (M – H) 1187.2571, found 1187.2559. Anal. Calcd for $C_{52}H_{48}F_{12}O_{18}$: C, 52.33; H, 4.07. Found: C, 52.51; H, 4.16.

Acknowledgment. We gratefully acknowledge support provided by the Searle Scholars Program (SDR) and the National Institutes of Health, National Cancer Institute, under Grant CA44848 (WF).

Supplementary Material Available: Experimental procedures for the remaining correlation compounds as well as proton NMR spectra of the (*R*)-Mosher's esters **6** and **7** and the corresponding (*S*)-Mosher's ester derivatives (9 pages). Ordering information is given on any current masthead page.