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Asymmetric Synthesis of D-*ribo*-Phytosphingosine from 1-Tetradecyne and (4-Methoxyphenoxy)acetaldehyde

Zheng Liu, Hoe-Sup Byun, and Robert Bittman*

Department of Chemistry and Biochemistry, Queens College of The City University of New York, Flushing, New York 11367-1597

robert.bittman@qc.cuny.edu

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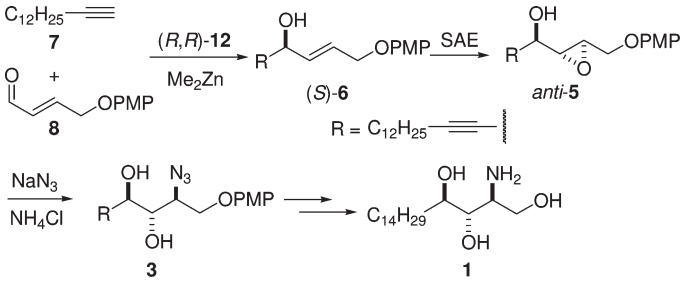

An asymmetric synthesis of D-*ribo*-phytosphingosine (**1**) was achieved by utilizing the ProPhenol (12)-catalyzed alkynylation of unsaturated aldehyde **8** to afford allylic propargylic alcohol (*S*)-**6** followed by asymmetric epoxidation and opening of propargylic epoxy alcohol *anti*-**5** with NaN_3/NH_4Cl. Deprotection and reduction of the resulting acyclic azide **3** then gave **1**. Alkyne−azide **3** was subjected to an intramolecular click reaction, generating a bicyclic triazole, which was found to have unexpected vicinal coupling constants. Application of the advanced Mosher method verified the configurations of the three contiguous stereogenic centers of **1**. An alkynyl azide analogue of **1**, which may be useful as a glycosyl acceptor in the synthesis of α-galactosylceramide derivatives, was also readily prepared by this route.

Introduction

(2*S*,3*S*,4*R*)-D-*ribo*-Phytosphingosine (4-D-hydroxysphinganine, PHS, **1**) is distributed ubiquitously, including in membranes of fungi, plants, bacteria, marine organisms, and mammalian tissues.[1] In addition to its structural role in membranes, **1** regulates cellular growth[2] and mediates the heat stress response of yeast.[3] Moreover, **1** serves as a metabolic precursor of important lipid mediators such as PHS 1-phosphate,[3b,4] inositol phosphorylceramide,[5] and KRN7000 (**2**, the α-anomer of galactosylceramide, an immunostimulant of invariant natural killer T (iNKT) cells) (Chart 1).[6]

Because of the biological importance of PHS, there has been considerable interest in the synthesis of **1** and its stereoisomers.[7] The construction of the three contiguous stereogenic centers poses an interesting and demanding challenge. Historically, natural chiral pools have played a significant role in their syntheses, but asymmetric reactions have emerged as a more favorable strategy for reasons of chirality economy and efficiency. Recently, the catalytic asymmetric alkynylation reaction developed by Trost et al. has been used

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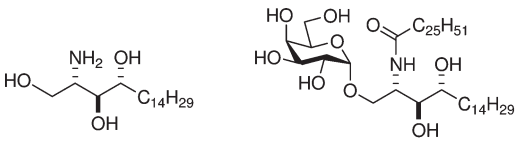
CHART 1. Structures of D-*ribo*-Phytosphingosine and α-Galactosylceramide (KRN7000)

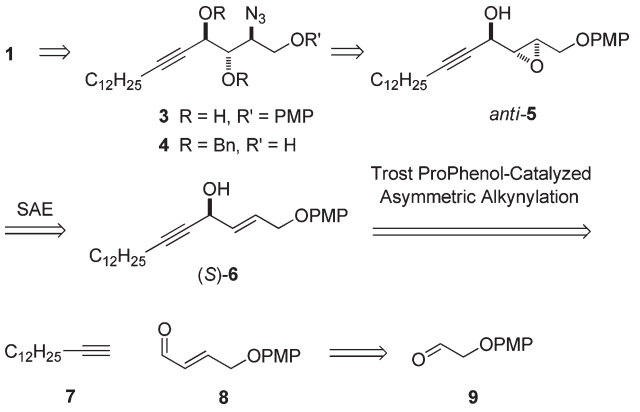


1 D-*ribo*-phytosphingosine **2** α-galactosylceramide (KRN7000)

as a key step in the syntheses of natural products.[8] As an extension of our previous studies on the synthesis of phytosphingolipids[7c,e,9] and of glycolipid-based iNKT cell agonists,[10] we describe here a stereocontrolled synthesis of **1** via a sequence of catalytic alkynylation and Sharpless asymmetric epoxidation (SAE)[11] reactions to generate the intermediate chiral propargylic epoxy alcohol **5** which was converted to **3** by ring-opening attack by azide ion. Although the ring-opening was expected to result in an inversion of configuration at C-2, the stereochemical outcome required verification because of a previous report of unexpected retention of configuration during a $Ti(O\text{-}i\text{-}Pr)_2(N_3)_2$-mediated epoxide ring-opening reaction.[12] To determine the relative configurations in azido diol **3**, we used an intramolecular click reaction[13] to form rigid bicyclic triazole **15**, which, however, proved to have unusual vicinal coupling constants. The configurations of the three contiguous stereogenic centers of **1** were instead determined by application of the advanced Mosher method.[14]

Interestingly, 2-azido alcohols have been found to be more favorable glycosyl acceptors than the corresponding 2-amido alcohols (ceramides).[15,16] Azido alkynyl alcohol **4** was readily obtained by the synthetic procedure described here. Thus, the route to **1** described herein may be used to prepare a glycosyl acceptor for the preparation of **2** and other galactosylceramide derivatives.[6,17]

SCHEME 1. Retrosynthetic Plan



Results and Discussion

Outline of the Synthetic Plan. As illustrated in Scheme 1, we envisaged **1** and **4** to be accessible from azido diol **3**. The 2*S*,3*S* configuration in **3** can be generated by SAE followed by opening of the resulting epoxy alcohol *anti*-**5** with NaN_3/NH_4Cl. SAE of (*S*)-**6** under kinetic resolution conditions can improve the diastereomeric excess of *anti*-**5**. Although the enantiomeric excess of (*S*)-**6** will not affect the subsequent stereoselectivity, it plays a key role in maximizing the yield of SAE. The enantiomeric excess of (*S*)-**6** can be enhanced via catalytic alkynylation of enal **8** with alkyne **7**. Asymmetric alkynylation of α,β-unsaturated aldehydes has been used in the synthesis of many complicated molecules with high efficiency[18] but often requires stoichiometric or catalytic titanium in addition to zinc. Trost and co-workers have recently simplified and expanded the scope of this reaction.[8a] We have employed the Trost protocol to make **6** starting with enal **8**, which was prepared from commercially available aldehyde **9** using our recently developed two-step HWE/AlH_3 reduction protocol.[19] This synthetic route may permit access to other stereoisomers of **1** because the catalytic alkynylation and SAE reactions can be used to generate

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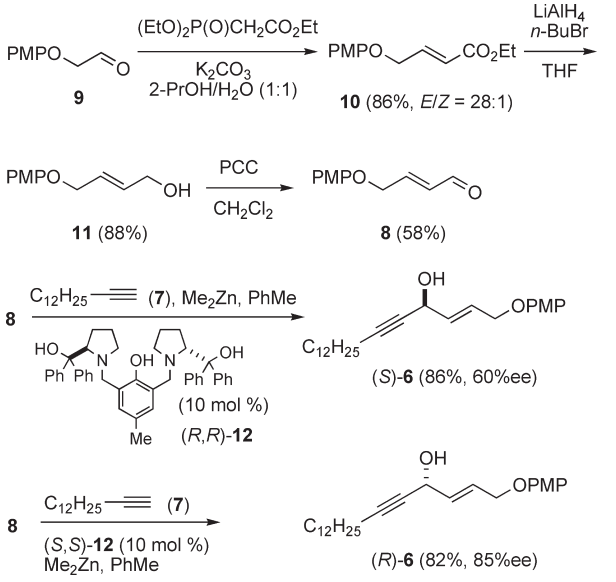
SCHEME 2. Synthesis of Allylic Propargylic Alcohols (*S*)-6 and (*R*)-6

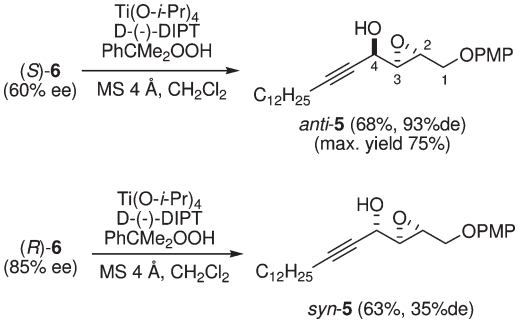


the opposite configurations by use of their counterpart ligands.

Asymmetric Synthesis of Enynol (*S*)-6. On the basis of the retrosynthetic analysis depicted in Scheme 1, the first target, the conjugated (*E*)-enynol (*S*)-**6**, can be prepared by coupling of enal **8** with **7** by catalytic alkynylation. As shown in Scheme 2, allylic alcohol **11** was prepared from (4-methoxyphenoxy)acetaldehyde (**9**)[20] via a two-step HWE/reduction protocol.[19] Previously, because it is difficult to achieve high *E*-selectivity by the HWE olefination reaction, (*E*)-α,β-unsaturated ester **10** was obtained by nucleophilic substitution of alkyl 4-bromocrotonate with 4-methoxyphenol.[21] HWE reaction of aldehyde **9** with triethyl phosphonoacetate in the presence of K_2CO_3 in H_2O/2-PrOH (1:1) produced ester **10** in 86% yield and high *E*-selectivity (*E*/*Z* = 28:1). Reduction of ester **10** by AlH_3 (generated from LAH and *n*-BuBr in THF and used in situ)[19] provided allylic alcohol **11** in 88% yield. Oxidation of allyl alcohol **11** with PCC gave (*E*)-α,β-unsaturated enal **8** in 58% yield.

Chiral allylic propargylic alcohols have been accessible with high ee either by reduction of the corresponding ketone with a stoichiometric amount of pinanylborane[22] or by lipase-catalyzed resolution of racemic allylic propargylic alcohols.[23] In our hands, alkynylation of enal **8** with 1-tetradecyne catalyzed by ProPhenol ligand (*R*,*R*)-**12**[24] reproducibly provided a high yield of the desired (*E*)-enynol (*S*)-**6** (86%), but the enantiomeric excess was only moderate at best (60% ee). Under degassed reaction conditions, the chemical yield was improved, but the enantioselectivity was not. However, to our surprise, ProPhenol zinc alkynylation of **8** with 1-tetradecyne catalyzed by (*S*,*S*)-**12** provided (*E*)-enynol (*R*)-**6** with a high enantioselectivity (85% ee).[25] The enantiomeric excess and absolute configuration of *E*-enynols (*S*)-**6** and (*R*)-**6** were determined by preparing the (*R*)- and (*S*)-MTPA esters and analyzing their ^{1}H NMR spectra by the subtraction protocol of the advanced Mosher method (see the Supporting Information).[14]

SCHEME 3. Synthesis of Epoxy Alcohols *anti*-5 and *syn*-5



Epoxidation of (*E*)-Enynol 6. As shown in Schemes 1 and 3, we intended to use SAE as one of the key steps to build the other two stereogenic centers from enynols (*S*)- and (*R*)-**6**. Under Sharpless kinetic resolution conditions, epoxidation of (*S*)-**6** (60% ee) with cumene hydroperoxide (CHP) in the presence of substoichiometric amounts of catalysts (D-(−)-DIPT, Ti(OPr-*i*)$_4$) and 4 Å molecular sieves gave epoxy alcohol *anti*-**5** in good yield (68%; the maximum yield was 75%). After the unreacted substrate was removed by chromatography, the desired propargylic epoxy alcohol *anti*-**5** was obtained in high diastereomeric excess (93% de). In contrast, epoxidation of (*R*)-**6** (85% ee) under the same conditions led to *syn*-**5** in a much lower diastereomeric excess (35% de), indicating that the *R* configuration eroded the diastereomeric induction dominated by the catalyst. This mismatched effect brought about by the acetylenic moiety may be more pronounced than that of the alkyl group.

Opening of Epoxy Alcohol *anti*-5. As shown in Scheme 4, opening of epoxy alcohol *anti*-**5** with NaN_3/NH_4Cl[26] provided azido diol **3** in 61% yield, together with other unidentified compounds. Although this reaction was not very clean, alternative methods, such as Ti(O-*i*-Pr)$_2$(N$_3$)$_2$,[27] were not attempted because in our prior experience this reagent gave rise to many unidentified compounds,[10,28] including the Ti-catalyzed semipinacol rearrangement product of α-hydroxy epoxides.[29]

Investigation of the Stereochemistry of the Azido Diols from *syn*- and *anti*-5 on the Basis of *J* Values of Bicyclic Derivatives. To verify the stereochemistry of azido diols **3**, propargylic epoxy alcohol *anti*-**5** was converted to bicyclic dihydroxy triazole **14** via a copper-free intramolecular click reaction in refluxing toluene for 48 h (Scheme 4).[13] Diol **14** was then converted to diacetate **15**. However, when *syn*-**5** (which has a low de) was subjected to the same reaction sequence, we obtained a mixture of diastereoisomer **15′** [4*S*,5*S*,6*S*] and *ent*-

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(25) The reason for the different ee values is not clear, but the ee of the ligands appear to differ based on our determination of their specific rotations: (*S*,*S*)-**12**: $[\alpha]^{25}_D$ +38.7 (*c* 0.63, $CHCl_3$), [lit.[24] $[\alpha]^{25}_D$ +49.8 (*c* 3.0, $CHCl_3$), Sigma-Aldrich catalog: $[\alpha]^{25}_D$ +50 (*c* 1.0, $CHCl_3$)]; (*R*,*R*)-**12**: $[\alpha]^{25}_D$ −40.9 (*c* 0.65, $CHCl_3$), [Sigma-Aldrich catalog: $[\alpha]^{25}_D$ −50 (*c* 1.0, $CHCl_3$)].
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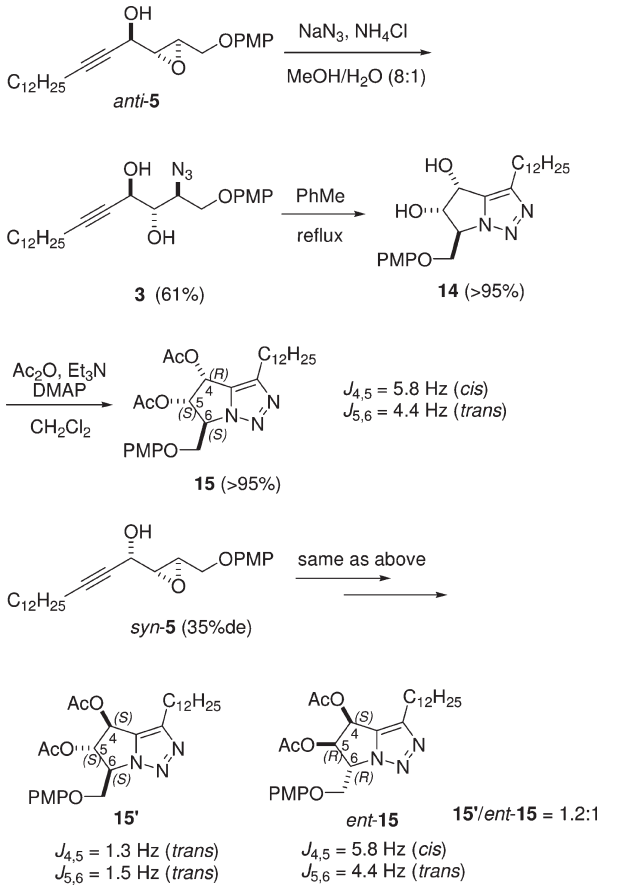
SCHEME 4. Opening of *anti*-5 and Unexpected Coupling Constants in Bicyclic Triazole Derivative 15



15 (the enantiomer of **15**, (4*S*,5*R*,6*R*)) in a ratio of 1.2:1 (Scheme 4). The partial ^{1}H NMR spectra of triazoles **15** and **15′** are reported in Figure 1.

In 2005, Kim et al. prepared bicyclic triazoles **16a**−**d** from chiral aziridines (Chart 2).[30a] The coupling constant in the *cis* relationship is 5.5−5.6 Hz, whereas that in the *trans* is 3.3−4.3 Hz. Although H-4 in diol **14** gave a doublet signal (J = 5.5 Hz) and H-6 gave a quartet signal (J = 3.4 Hz), H-5 demonstrated an abnormal doublet of doublets (4.3 and 5.0 Hz), probably because of intramolecular hydrogen bonding between the hydroxy groups. The coupling constants of **14** match those of **16a**−**d**; therefore, these data may tentatively confirm the relative configuration of the three contiguous stereogenic centers. However, it must be pointed out that the intramolecular hydrogen bonds in **14** and **16a**−**d** are different, which leads to uncertainty regarding the values of the coupling constants. Furthermore, because of the absence of the substituent at the 6 position, **16a**−**d** may adopt different conformations compared with **14**. In 1988, based on coupling constants,[30b] Ferris and Devades reported a conformational analysis in the pyrroloimidazole ring system **17a** and **17b**, which is very similar to our bicyclic triazole **15** (Chart 2). Since **17a** and **17b** were fully protected, the impact of intramolecular hydrogen bonds is avoided. Their

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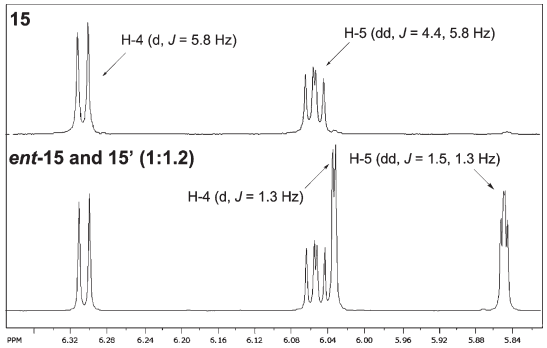
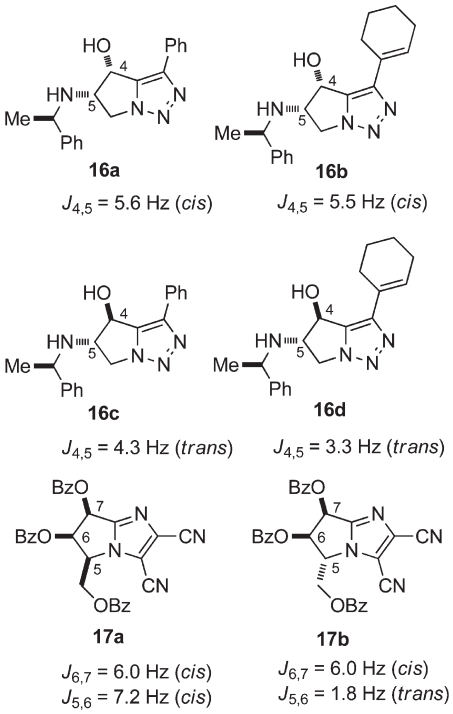


FIGURE 1. Partial ^{1}H NMR spectra of **15** (top) and *ent*-**15**/**15′** (ratio 1:1.2, bottom).

CHART 2. Reported Coupling Constants in Similar Bicyclic Systems[30a,b]



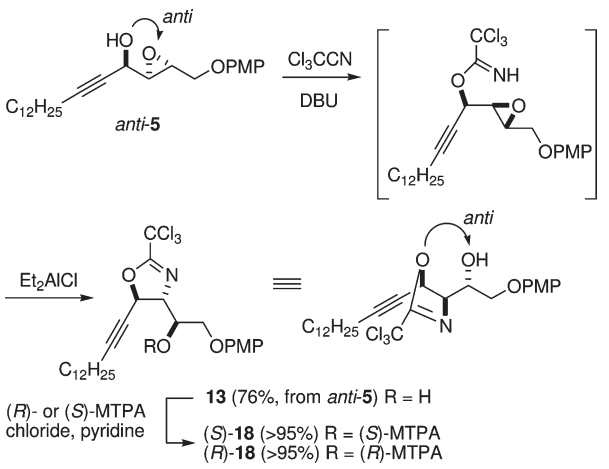
investigation revealed that the value of the *trans* coupling constant ($J_{5,6}$ in **17**) was 1.8 Hz, whereas the *cis* coupling constants ($J_{6,7}$ in **16** and **17**, $J_{5,6}$ in **16**) were 6.0 and 7.2 Hz, respectively.[30b]

The coupling constants of *cis* $J_{4,5}$ and *trans* $J_{5,6}$ in bicyclic triazole **15** (Figure 1) were expected to differ largely. However, to our surprise, we found that they have two very close J values ($J_{4,5}$ = 5.8 Hz and $J_{5,6}$ = 4.4 Hz). Furthermore, the two $J_{5,6}$ values of the *trans* coupling constants in **15** and **15′** are markedly different (4.4 Hz in **15**, 1.5 Hz in **15′**). On the basis of this analysis, it is possible that one of the known stereocontrolled steps did not proceed in the normal way. Therefore, we decided to verify the course of the construction of the three contiguous stereogenic centers by examining (1) the configuration at C-4 in *anti*-**5** to check which enynol reacted [(*S*)-**6** or (*R*)-**6**] in SAE, (2) the configurations at the C-2 and C-3 positions in *anti*-**5**, and (3) the opening of *anti*-**5** to verify the configuration at C-2 of **3**.

Verification of the Sharpless Kinetic Resolution. According to the empirical rule established by Sharpless and coworkers, the Sharpless kinetic resolution of secondary allylic alcohols favors the reaction in which the *R* enantiomer of the racemic mixture forms the epoxide, while the *S* enantiomer is recovered in an optically enriched form when D-(−)-DIPT is used.[31] For allylic propargylic alcohols, the *S* enantiomer should react faster with D-(−)-DIPT because the acetylenic moiety has a higher priority than the olefinic group. Allylic propargylic alcohols have already been proved to uphold the empirical rule,[32] although the acetylenic moiety would cause less steric crowding in the transition states for SAE in comparison with alkyl groups. However, the verification is limited to hydrocarbon substrates.[32] In order to confirm the Sharpless kinetic resolution in our case, the (*R*)- and (*S*)-MTPA esters of *anti*-**5** were prepared to verify the configuration at C-4 (see the Supporting Information). Analysis of the $\Delta\delta$ values of the protons indicates that the reacted allylic propargylic alcohol was in fact (*S*)-**6**, confirming the prediction made by the empirical rule.

Epoxide Configuration in *anti*-5. The absolute stereochemistry of an epoxide in chiral epoxy alcohols is generally assigned by the advanced Mosher method using (*R*)- and (*S*)-MTPA esters of the corresponding ring-opened diol or by established empirical mnemonics developed for different asymmetric epoxidation strategies.[33] Parker and Katsoulis[32c] determined the absolute configuration of the epoxide in propargylic epoxy alcohols by converting the epoxide to a 1,3-diol and analyzing the corresponding acetonide by the commonly used [^{13}C]-acetonide method developed by Rychnovsky et al.[34] This method needs a two-step derivatization. We selected the Et_2AlCl-catalyzed cyclization of epoxytrichloroacetimidates[35] to transfer the chiral information of the epoxide to the newly formed secondary hydroxy group in an oxazoline or dihydrooxazine (Scheme 5). Generally, cyclization takes place preferentially at the more polarized center of the epoxide with complete *inversion* of stereochemistry.[35] As a result, after this transformation, the newly formed hydroxy group and C-4 oxygen will retain the same relative configuration as that in the epoxy alcohol between the epoxide and C-4 hydroxy group. By determining the configuration of the newly formed hydroxy group, we can assign the stereochemistry of the epoxide in *anti*-**5**. Reaction of *anti*-**5** with trichloroacetonitrile in the presence of Et_2AlCl and DBU gave the corresponding 2,3-epoxy-1-trichloroacetimidate,

SCHEME 5. Conversion of *anti*-5 to (*S*)- and (*R*)-18



which delivered oxazoline **13** in a two-step yield of 76% (Scheme 5). The regiochemistry of cyclization was judged by analysis of the ^{1}H−^{1}H COSY spectrum of **13** (see the Supporting Information). Analysis of the (*R*)- and (*S*)-MTPA esters of **13** ((*R*)-and (*S*)-**18**) revealed the *anti* relationship between the C-2 hydroxy group and C-4 oxygen (Figure 2), indicating that SAE of enynol (*S*)-**6** followed the normal prediction made by Sharpless et al. for allylic alcohols bearing saturated alkyl groups.

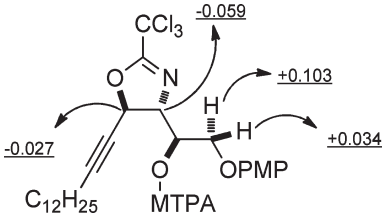


FIGURE 2. Absolute stereochemistry determination of **13** via the advanced Mosher method. $\Delta\delta$ values for the MTPA derivatives (*S*)-**18** and (*R*)-**18** ($\Delta\delta = \delta_S - \delta_R$ ppm, 500 MHz).

Configuration of C-2. At this stage, the stereochemistry of the opening of epoxy alcohol *anti*-**5** (the first step of Scheme 4) requires verification. For this purpose, we planned to determine the configuration at C-2 of **3** by preparing the (*R*)- and (*S*)-MTPA amides (Scheme 6). Reaction of diol **3** with BnBr and NaH in the presence of a catalytic amount of TBAI provided azide **19** in 63% yield. Several methods were explored for the reduction of azide **19**. We found that azide **19** was smoothly converted to the corresponding amine **20** by using 1,3-dithiopropane as the reducing agent.[36] In situ reaction of **20** with (*R*)- and (*S*)-MTPA chlorides gave the (*S*)- and (*R*)-MTPA amides ((*S*)- and (*R*)-**21**), respectively. Analysis of the two MTPA amides demonstrated the *syn* relationship between the azide at C-2 and oxygen at C-4, indicating that opening of epoxy alcohol *anti*-**5** took place by a simple S_N2 inversion (Figure 3). Therefore, the evidence showed that the construction of the three contiguous stereogenic centers was correct. The unexpected

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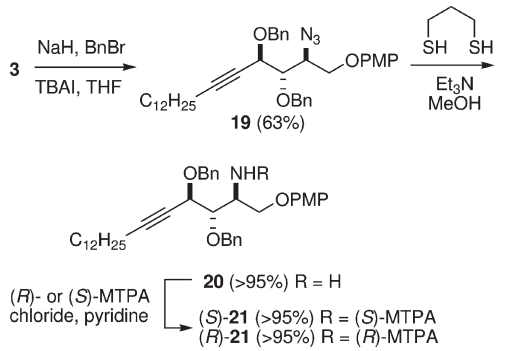
SCHEME 6. Conversion of Azido Diol 3 to (*S*)- and (*R*)-MTPA Amide 21



coupling constants in **15** and **15′** may result from the two different conformations they adopted. This result indicates the need for caution when coupling constants are used to judge the relative configuration in bicyclic triazole and related similar systems.

Completion of the Preparation of 1 and 4. As shown in Scheme 7, deprotection of the PMP group by CAN in **3** followed by hydrogenation of the resulting triol **22** using Pearlman's catalyst ($Pd(OH)_2/C$) in MeOH afforded **1**. Its ^1H and ^{13}C NMR spectra and specific rotation matched the previously reported data. The structure of **1** was further confirmed by conversion to its tetraacetyl derivative **23**.

In the synthesis of glycosylceramides, the choice of the glycosyl acceptor is a critical consideration (together, of course, with the selection of the glycosyl donor). A free amino group at the C-2 position of the sphingolipid is not a viable choice in the acceptor; moreover, the amide functionality of ceramide is not suitable because it deactivates the primary hydroxy group of the acceptor through unfavorable hydrogen bonding interactions.[15] Since an azide is apparently devoid of hydrogen-bonding interactions with the adjacent hydroxy group and can be readily converted to an amide in two steps after the glycosidation reaction,[16] we decided to prepare **4**. The saturated analogue of azido PHS **4** has been prepared from **1** by a tedious protecting group manipulation involving the conversion of an amino group to an azide by a diazo-transfer reaction.[37] In contrast, 2-azido carbinol **4**, which is accessible from *anti*-**5** via deprotection of **19**, is an attractive alternative glycosyl acceptor because the azido group is introduced into the phytosphingosine backbone at an early stage of the synthesis. Since modification of the lipid chain length in α-galactosylceramide analogues influences an array of cytokines release from activated iNKT cells and demonstrates a profound relationship between structure and activity,[38] the synthetic route described here allows modification of the chain length with ease.

Conclusion

A stereocontrolled synthetic route to **1** from aldehyde **9** and 1-tetradecyne (**7**) has been developed. HWE reaction of aldehyde **9**[19] and AlH_3 reduction provided allylic alcohol **11**, and PCC oxidation afforded α,β-unsaturated aldehyde **8**. Catalytic alkynylation of **8** with **7** and SAE of (*S*)-**6** followed by regioselective NaN_3/NH_4Cl opening of the resulting propargylic epoxy alcohol *anti*-**5** delivered (2*S*,3*S*,4*R*) azido diol **3** with the desired three contiguous stereogenic centers in good yield and high stereoselectivity. Deprotection of **3** with CAN and catalytic hydrogenation gave **1**. A key intermediate, alkynyl-azido **3**, can be readily converted to glycosyl acceptor **4** via *O*,*O*-dibenzylation and CAN deprotection. An advanced Mosher method clarified the unexpected values of the coupling constants in bicyclic triazoles **15** and **15′** generated by a copper-free intramolecular click reaction of **3** and confirmed the configurations of the stereogenic centers.

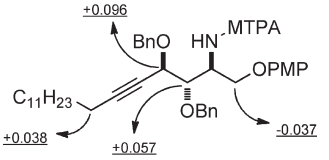
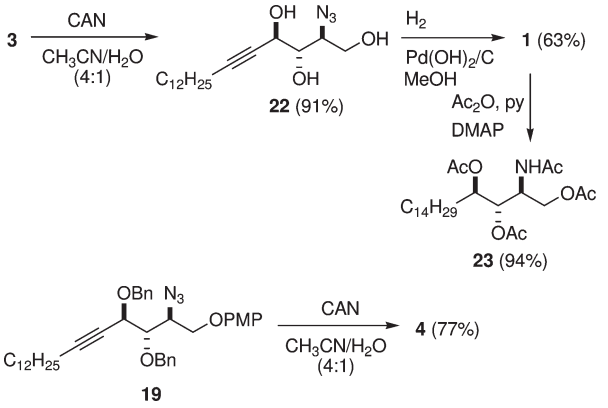


FIGURE 3. Absolute stereochemistry determination of **20** by the advanced Mosher method. $\Delta\delta$ values for the MTPA amides (*S*)-**21** and (*R*)-**21** ($\Delta\delta = \delta_S - \delta_R$ ppm, 500 MHz).

SCHEME 7. Completion of the Syntheses of 1 and 4 from 3 and 19, Respectively



Experimental Section

(*E*)-4-(4′-Methoxyphenoxy)-2-butenal (8). To a cooled, rapidly stirred suspension of PCC (15.0 g, 69.6 mmol) and Celite (16 g) in 250 mL of CH_2Cl_2 was added alcohol **11** (8.44 g, 43.5 mmol) in one portion. After the mixture had stirred for 3 h at rt, the resulting dark mixture was diluted with 150 mL of Et_2O. Filtration through a pad of Florisil left a dark solid residue that was washed with Et_2O. The combined filtrates were concentrated, and the residue was purified by flash chromatography (a gradient of hexane/EtOAc 6:1 to 3:1) to afford **8** (5.5 g, 58%) as a slightly yellow solid: ^1H NMR (400 MHz, $CDCl_3$) δ 3.77 (s, 3H), 4.76 (dd, J = 1.9, 4.0 Hz, 2H), 6.46 (ddt, J = 15.8, 7.8, 1.9 Hz, 1H), 6.82−6.87 (m, 4H), 6.94 (dt, J = 15.8, 4.0 Hz, 1H), 9.62 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 55.7, 67.1, 114.7, 115.6, 132.2, 151.3, 151.9, 154.3, 193.0.

(4*S*,2*E*)-1-(4′-Methoxyphenoxy)-2-octadecen-5-yn-4-ol ((*S*)-6). A flame-dried, round-bottom flask was charged with the commercially available ProPhenol ligand (*R*,*R*)-**12** (1.0 g, 1.57 mmol), alkyne **7** (9.2 g, 47.1 mmol), and 300 mL of toluene. A solution of Me_2Zn (39.3 mL, 1.2 M in toluene, 47.1 mmol) was added rapidly via syringe. The reaction mixture was stirred

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for 90 min at rt, and gas slowly evolved. A solution of α,β-unsaturated aldehyde **8** (3.0 g, 15.6 mmol) in a minimal amount of toluene was added via syringe over ~10 s. The reaction mixture was sealed and cooled to 4 °C for 4 days without stirring. The reaction mixture was then slowly quenched with aqueous saturated NH_4Cl solution, and the layers were separated. The aqueous layer was extracted with EtOAc (3 × 200 mL), and the combined organic layers were dried (Na_2SO_4), filtered, and concentrated. Purification of the residue by flash chromatography (a gradient of hexane/EtOAc 6:1 to 7:2) provided (*S*)-**6** (5.2 g, 86%, 60% ee): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.19−1.40 (m, 18H), 1.46−1.54 (m, 2H), 2.21 (dt, *J* = 2.0, 7.2 Hz, 2H), 2.45 (d, *J* = 4.3 Hz, 1H), 3.74 (s, 3H), 4.46−4.49 (m, 2H), 4.88−4.92 (m, 1H), 5.95 (ddt, *J* = 5.3, 15.4, 1.4 Hz, 1H), 6.08 (ddt, *J* = 1.2, 15.4, 5.3 Hz, 1H), 6.78−6.85 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.0, 18.6, 22.6, 28.5, 28.8, 29.0, 29.3, 29.4, 29.5, 29.6, 31.8, 55.5, 62.3, 68.0, 78.8, 87.2, 114.5, 115.5, 127.1, 132.4, 152.5, 153.7; ESI-HRMS $[M + Na]^+$ calcd for *m*/*z* $C_{25}H_{38}NaO_3^+$ 409.2713, found 409.2717.

(4*R*,2*E*)-1-(4′-Methoxyphenoxy)-2-octadecen-5-yn-4-ol ((*R*)-6). (*R*)-**6** was prepared in 82% yield and 85% ee according to the procedure used to prepare (*S*)-**6**. The ^{1}H and ^{13}C NMR spectra were identical to those of (*S*)-**6**: ESI-HRMS $[M + Na]^+$ calcd for $C_{25}H_{38}NaO_3^+$ 409.2713, found 409.2715.

General Preparation and Analysis of MTPA Esters or Amide. The reactions were generally run on a 0.02-mmol scale. A mixture of pyridine (4.0 equiv) and substrate (1.0 equiv) in CH_2Cl_2 (0.6 mL) was treated with neat (*R*)- or (*S*)-MTPA chloride (3.0 equiv). The solution was stored in a desiccator until no starting material was observed by TLC. It is important to monitor the reaction by TLC to ensure complete reaction because kinetic resolution of an incomplete reaction may significantly alter the ee or de measurements. The reaction mixture was passed through a short plug of silica gel to remove polar impurities, and the plug was washed with EtOAc/hexane (the ratio made the R_f = 0.5). After the filtrate was concentrated, the residue was dried under high vacuum (0.2 Torr, 1 h) and dissolved in $CDCl_3$. The (*S*)- and (*R*)-MTPA esters and amides were prepared by using (*R*)- and (*S*)-MTPA chlorides, respectively.

(*R*)-1-[(2′*R*,3′*R*)-3′-[(4″-Methoxyphenoxy)methyl]oxiran-2′-yl]-pentadec-2-yn-1-ol (*anti*-5). Molecular sieves (4 Å, the amount is not critical if the allyl propargyl alcohol, CH_2Cl_2, and cumene hydroperoxide are predried) were added to a solution of D-(−)-DIPT (363 mg, 1.55 mmol) in 50 mL of dry CH_2Cl_2. The mixture was stirred at rt for 30 min before it was cooled to −40 °C. Ti(OPr-*i*)$_4$ (367 mg, 1.29 mmol) was added to the reaction mixture, which was stirred for 30 min. After cumene hydroperoxide (590 mg, 80% technical grade, 3.10 mmol) was added, the reaction mixture was stirred for 30 min. A solution of (*S*)-**6** (1.33 g, 3.45 mmol, 60% ee) in a minimal amount of dry CH_2Cl_2 was added, and the reaction mixture was sealed and stored at −20 °C without stirring for 3 days. An aqueous precooled (0 °C) solution of tartaric acid (10 mL, 10% w/v) was added dropwise, and the mixture was allowed to warm to rt over 1 h, after which time the solution became transparent. The organic layer was separated, washed with brine, and concentrated. The residue was dissolved in Et_2O at 0 °C, and the solution was treated with a solution (4 mL) of 30% w/v NaOH in saturated brine. The two-phase mixture was stirred vigorously for 1 h at 0 °C. The phases were separated, the aqueous layer was extracted with Et_2O, and the combined organic layers were dried over Na_2SO_4. The solvent was evaporated, and the residue was purified by flash chromatography (hexane/EtOAc 5:1 to 4:1) to afford *anti*-**5** (949 mg, 68% (maximum yield, 75%), 93% de): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.20−1.41 (m, 18H), 1.47−1.55 (m, 2H), 2.03 (br s, 1H), 2.22 (dt, *J* = 7.2, 1.9 Hz, 2H), 3.30 (t, *J* = 2.5 Hz, 1H), 3.50−3.53 (m, 1H), 3.77 (s, 3H), 3.99 (dd, *J* = 11.5, 5.3 Hz, 1H), 4.26 (dd, *J* = 11.5, 2.7 Hz, 1H), 4.65−4.68 (m, 1H), 6.80−6.88 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 18.7, 22.7, 28.4, 28.9, 29.1, 29.3, 29.5, 29.63, 29.65, 31.9, 53.8, 55.7, 57.4, 60.8, 68.0, 76.0, 88.1, 114.6, 115.8, 152.5, 154.2; ESI-HRMS $[M + NH_4^+]$ calcd for $C_{25}H_{42}NO_4^+$ 420.3108, found 420.3114.

(*S*)-1-[(2′*R*,3′*R*)-3′-[(4″-Methoxyphenoxy)methyl]oxiran-2′-yl]-pentadec-2-yn-1-ol (*syn*-5). Compound *syn*-**5** was prepared in 63% yield and 35% de from (*R*)-**6** (85% ee) according to the procedure used to prepare *anti*-**5**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.22−1.40 (m, 18H), 1.47−1.55 (m, 2H), 2.22 (dt, *J* = 7.2, 1.9 Hz, 2H), 3.27 (dd, *J* = 2.2, 4.1 Hz, 1H), 3.40−3.43 (m, 1H), 3.77 (s, 3H), 3.98 (dd, *J* = 11.5, 5.3 Hz, 1H), 4.23 (dd, *J* = 11.5, 2.9 Hz, 1H), 4.38−4.42 (m, 1H), 6.81−6.88 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 18.7, 22.7, 28.4, 28.9, 29.1, 29.3, 29.5, 29.62, 29.64, 31.9, 54.2, 55.7, 58.2, 60.4, 61.8, 76.9, 87.6, 114.6, 115.7, 152.5, 154.2.

(1*S*)-2-(4′-Methoxyphenoxy)-1-[(4′*R*,5′*R*)-2′-(trichloromethyl)-4′,5′-dihydro-5′-(tetradec-1″-ynyl)oxazol-4′-yl]ethanol (13). To an ice-cold solution of *anti*-**5** (30 mg, 74.5 μmol) in 1 mL of CH_2Cl_2 were added DBU (1.1 μL, 7.5 μmol) and trichloroacetonitrile (15 μL, 149 μmol). After being stirred at 0 °C until no starting material was observed on TLC, the reaction mixture was diluted with CH_2Cl_2 (10 mL), quenched with saturated NH_4Cl solution (5 mL), and extracted with CH_2Cl_2. The combined organic extracts were washed with saturated aqueous NH_4Cl solution, dried (Na_2SO_4), and concentrated. The residue was dissolved in Et_2O and passed through a short column packed with anhydrous Na_2SO_4 and silica gel. Evaporation of Et_2O gave a residue that was dried under high vacuum (0.2 Torr, overnight) and used directly in the subsequent cyclization reaction without further purification.

To an ice-cold solution of epoxy trichloroacetimidates in CH_2Cl_2 (1 mL) was added Et_2AlCl (37.3 μL, 1.0 M solution in hexane, 37.3 μmol). After being stirred at rt until no starting material was observed on TLC, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ solution. The reaction mixture was diluted with Et_2O, washed with water, dried, and evaporated. The residue was purified by flash chromatography (hexane/EtOAc 5:1) to afford oxazoline **13** (31 mg, 76%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.21−1.36 (m, 18H), 1.43−1.50 (m, 2H), 2.21 (dt, *J* = 1.9, 7.1 Hz, 2H), 2.48 (d, *J* = 4.8 Hz, 1H), 3.77 (s, 3H), 4.05 (dd, *J* = 6.0, 9.5 Hz, 1H), 4.12 (dd, *J* = 4.2, 9.5 Hz, 1H), 4.15−4.20 (m, 1H), 4.46 (dd, *J* = 5.8, 7.0 Hz, 1H), 5.61 (dt, *J* = 1.9, 7.0 Hz, 1H), 6.81−6.90 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 18.8, 22.7, 28.2, 28.8, 29.1, 29.3, 29.5, 29.62, 29.63, 29.66, 31.9, 55.7, 69.5, 70.5, 74.9, 75.8, 76.1, 91.2, 114.7, 115.6, 152.3, 154.3, 162.7; ESI-HRMS $[M + H]^+$ calcd for $C_{27}H_{38}Cl_3NO_4^+$ 546.1939, found 546.1944.

(2*S*,3*S*,4*R*)-1-(4′-Methoxyphenoxy)-2-azidooctadec-5-yne-3,4-diol (3). To epoxy alcohol *anti*-**5** (95 mg, 0.246 mmol) in 4.5 mL of MeOH/H_2O (8:1) were added NH_4Cl (66 mg, 1.23 mmol) and NaN_3 (160 mg, 2.46 mmol). The reaction mixture was heated at reflux for 48 h. The reaction mixture was allowed to cool to rt, and the solvents were evaporated. The residue was extracted with CH_2Cl_2 (3 × 10 mL). The combined extracts were dried (Na_2SO_4) and concentrated. Purification of the residue by flash chromatography (elution with EtOAc/hexane, 5:1 to 3:1 to 5:2) afforded **3** (68 mg, 62%): $[\alpha]^{25}_D$ +22.8 (*c* 1.2, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.19−1.33 (m, 16H), 1.33−1.41 (m, 2H), 1.48−1.56 (m, 2H), 2.25 (dt, *J* = 2.0, 7.1 Hz, 2H), 2.53 (br s, 1H), 2.60 (br s, 1H), 3.76−3.80 (m, 4H), 3.85−3.90 (m, 1H), 4.18 (dd, *J* = 7.1, 10.0 Hz, 1H), 4.42 (dd, *J* = 3.3, 10.0 Hz, 1H), 4.67−4.71 (m, 1H), 6.82−6.91 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 14.1, 18.7, 22.7, 28.5, 28.9, 29.1, 29.3, 29.5, 29.6, 29.7, 31.9, 55.7, 62.2, 64.4, 69.1, 72.7, 76.1, 89.3, 114.7, 115.7, 152.3, 154.3; ESI-HRMS $[M + Na]^+$ calcd for $C_{25}H_{39}N_3NaO_4^+$ 468.2833, found 468.2834.

(4*R*,5*S*,6*S*)-6-[(4′-Methoxyphenoxy)methyl]-3-dodecyl-5,6-dihydro-4*H*-pyrrolo[1,2-*c*][1,2,3]triazole-4,5-diol (14). A solution of 20 mg (45 μmol) of diol **3** in 2 mL of toluene was stirred at 90 °C for 48 h. The solvent was evaporated, and the residue was purified by column chromatography (elution with hexane/EtOAc 1:1 to 2:3) to provide **14** (19 mg, 95%): $[\alpha]^{25}_{D}$ −20.8 (*c* 0.48, MeOH); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 3H), 1.19−1.39 (m, 16H), 1.53−1.65 (m, 4H), 1.66−1.75 (m, 2H), 2.71 (t, *J* = 7.7 Hz, 2H), 3.75 (s, 3H), 4.42−4.46 (m, 1H), 4.48−4.53 (m, 1H), 4.73 (q, *J* = 3.4 Hz, 1H), 4.96−4.99 (m, 1H), 5.21 (d, *J* = 5.5 Hz, 1H), 6.72−6.80 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 22.7, 25.4, 29.1, 29.4, 29.62, 29.65, 29.68, 31.9, 55.7, 64.5, 64.8, 66.9, 77.9, 114.7, 115.9, 137.8, 143.3, 152.0, 154.6; ESI-HRMS $[M + H]^+$ calcd for $C_{25}H_{40}N_3O_4^+$ 446.3013, found 446.3006.

(4*R*,5*S*,6*S*)-6-[(4′-Methoxyphenoxy)methyl]-3-dodecyl-5,6-dihydro-4*H*-pyrrolo[1,2-*c*][1,2,3]triazol-4,5-diyl Acetate (15). To a solution of 10 mg (22 μmol) of **14** in 1 mL of CH_2Cl_2 was added 100 μL (717 μmol) of Et_3N and 50 μL (530 μmol) of Ac_2O. The solution was stirred overnight at rt. After the solvent was removed, the residue was further dried under high vacuum (0.7 Torr) for 1 h, dissolved in a minimal amount of CH_2Cl_2, and filtered through a pad of silica gel in a buret. The pad was rinsed with 10 mL of hexane/EtOAc 4:1. Concentration gave diacetate **15** (11 mg, 98%) as a colorless syrup: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.20−1.37 (m, 18H), 1.61−1.70 (m, 2H), 2.13 (s, 3H), 2.14 (s, 3H), 2.73 (t, *J* = 7.7 Hz, 2H), 3.75 (s, 3H), 4.48 (dd, *J* = 2.7, 10.4 Hz, 1H), 4.59 (dd, *J* = 3.0, 10.4 Hz, 1H), 4.87 (dt, *J* = 4.3, 2.9 Hz, 1H), 6.05 (dd, *J* = 4.3, 5.7 Hz, 1H), 6.31 (d, *J* = 5.8 Hz, 1H), 6.73−6.81 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 20.4, 20.5, 22.7, 25.3, 29.2, 29.3, 29.4, 29.57, 29.62, 29.64, 29.7, 31.9, 55.6, 62.2, 64.6, 66.4, 76.8, 114.6, 116.1, 134.6, 143.7, 151.7, 154.7, 169.5, 169.6.

(4*S*,5*S*,6*S*)-6-[(4′-Methoxyphenoxy)methyl]-3-dodecyl-5,6-dihydro-4*H*-pyrrolo[1,2-*c*][1,2,3]triazol-4,5-diyl Acetate (15′). Compound **15′** was prepared from *syn*-**5** (35% de) according to the same sequence used to convert *anti*-**5** to **15** and was contaminated with **15** (ratio of **15′**/*ent*-**15** = 1.2:1): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.20−1.37 (m, 18H), 1.61−1.70 (m, 2H), 2.14 (s, 3H), 2.15 (s, 3H), 2.69−2.72 (m, 2H), 3.76 (s, 3H), 4.51−4.53 (m, 2H), 4.72−4.75 (m, 1H), 5.85 (dd, *J* = 1.5, 1.9 Hz, 1H), 6.03 (d, *J* = 1.3 Hz, 1H), 6.73−6.81 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 20.4, 20.5, 22.7, 25.3, 29.2, 29.3, 29.4, 29.57, 29.62, 29.64, 29.7, 31.8, 55.6, 64.0, 67.0, 69.4, 84.3, 114.6, 115.8, 134.9, 143.6, 151.9, 154.5, 169.7, 169.8.

(2*S*,3*S*,4*R*)-1-(4′-Methoxyphenyl)-2-azido-3,4-benzyloxy-5-octadecyne-1,3,4-triol (19). To a mixture of 222 mg (5.56 mmol) of NaH (60%) and 620 mg (1.39 mol) of diol **3** in 10 mL of freshly distilled THF were added 343 μL (6.95 mmol) of benzyl bromide and 3 mg (8 μmol) of TBAI at rt. The mixture was stirred at rt overnight and then was quenched with 5 mL of MeOH. The reaction mixture was poured into a mixture of ice and EtOAc. The organic layer was separated, washed with aqueous 1 M HCl, water, saturated aqueous $NaHCO_3$ solution, and brine, and then dried (Na_2SO_4). The solvent was evaporated, and the residue was purified by flash chromatography (hexane/EtOAc 40:1) to afford **19** (546 mg, 63%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.1 Hz, 3H), 1.20−1.30 (m, 12H), 1.37−1.44 (m, 2H), 1.51−1.60 (m, 2H), 2.28 (dt, *J* = 1.6, 7.0 Hz, 2H), 3.77 (s, 3H), 3.82 (t, *J* = 4.9 Hz, 1H), 4.00−4.06 (m, 2H), 4.18−4.23 (m, 1H), 4.40−4.42 (m, 1H), 4.51 (d, *J* = 11.6 Hz, 1H), 4.65 (d, *J* = 11.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 18.9, 22.7, 28.6, 29.0, 29.2, 29.4, 29.55, 29.64, 29.66, 31.9, 55.7, 61.5, 68.3, 70.0, 70.8, 74.3, 75.6, 80.1, 89.1, 114.6, 115.6, 127.8, 128.0, 128.2, 128.3, 128.4, 137.6, 137.8, 152.5, 154.1; ESI-HRMS $[M + Na]^+$ calcd for $C_{39}H_{51}N_3O_4Na^+$ 648.3772, found 648.3776.

(2*S*,3*S*,4*R*)-1-(4′-Methoxyphenoxy)-3,4-bis(benzyloxy)octadec-5-yn-2-amine (20). To a solution of **19** (23 mg, 37 μmol) in MeOH (1 mL) were added Et_3N (102 μL, 0.73 mmol) and 1,3-dithiopropane (73 μL, 0.73 mmol). The reaction mixture was stirred overnight at 50 °C. The white precipitate was removed by filtration and washed twice with MeOH. After the solvent was evaporated, the residue was dried under high vacuum (0.2 Torr, overnight) and used directly in the subsequent MTPA ester analysis without further purification.

(2*S*,3*S*,4*R*)-2-Azidooctadec-5-yne-1,3,4-triol (22). Diol **3** (75 mg, 0.17 mmol) was dissolved in 2.5 mL of CH_3CN/H_2O (4:1) at rt, and CAN (461 mg, 0.84 mmol) was added. The mixture was stirred at rt until completion of the reaction as monitored by TLC (about 1 h) and diluted with $CHCl_3$. The resulting solution was washed with H_2O and brine. The organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (hexane/EtOAc 3:2) to afford triol **22** (52 mg, 91%): $[\alpha]^{25}_{D}$ +43.2 (*c* 0.5, MeOH); ^{1}H NMR (500 MHz, CD_3OD) δ 0.90 (t, *J* = 7.1 Hz, 3H), 1.23−1.35 (m, 16H), 1.39−1.46 (m, 2H), 1.49−1.56 (m, 2H), 2.25 (dt, *J* = 2.0, 7.0 Hz, 2H), 3.52−3.57 (m, 2H), 3.69 (dd, *J* = 7.2, 11.5 Hz, 1H), 3.96−4.00 (m, 1H), 4.45−4.47 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 18.7, 22.7, 28.5, 28.9, 29.1, 29.3, 29.5, 29.62, 29.65, 31.9, 62.7, 63.9, 64.2, 73.7, 76.2, 89.3; ESI-HRMS $[M + Na]^+$ calcd for $C_{18}H_{33}N_3O_3Na^+$ 362.2414, found 362.2412.

D-*ribo*-Phytosphingosine (1). To a solution of 34 mg (0.10 mmol) of triol **22** in 5 mL of MeOH was added 11 mg (0.020 mmol) of 20% $Pd(OH)_2/C$. The resulting suspension was degassed three times and was stirred with a balloon filled with H_2 overnight. The crude reaction mixture was filtered through a short pad of Celite, which was washed with 30 mL of MeOH. The combined filtrates were concentrated and purified by flash chromatography ($CHCl_3$/MeOH/concd NH_4OH 130:25:4) to afford **1** (20 mg, 63%) as a white solid. The product was dissolved in a minimum volume of $CHCl_3$ and passed through a 0.45-μm filter to remove the suspended silica gel: mp 99−101 °C (lit.[9] mp 98.5−101.5 °C); $[\alpha]^{25}_{D}$ +8.0 (*c* 0.8, C_5H_5N) [lit.[9] $[\alpha]^{25}_{D}$ +7.3 (*c* 0.9, C_5H_5N)]; ^{1}H NMR (500 MHz, CD_3OD) δ 0.89 (t, *J* = 7.1 Hz, 3H), 1.22−1.41 (m, 24H), 1.49−1.60 (m, 1H), 1.68−1.77 (m, 1H), 2.94−2.97 (m, 1H), 3.33 (dd, *J* = 5.4, 7.8 Hz, 1H), 3.47−3.52 (m, 1H), 3.55 (dd, *J* = 6.8, 10.9 Hz, 1H), 3.75 (dd, *J* = 4.1, 10.9 Hz, 1H); ^{13}C NMR (125 MHz, CD_3OD) δ 14.4, 23.8, 26.6, 30.5, 30.79, 30.82, 31.0, 33.1, 34.8, 55.8, 64.0, 74.4, 76.4; ESI-HRMS $[M + Na]^+$ calcd for $C_{18}H_{39}NNaO_3^+$ 340.2822, found 340.2823.

D-*ribo*-Phytosphingosine Tetraacetate (23). Compound **23** was prepared from **1** according to ref 9: $[\alpha]^{25}_{D}$ +22.6 (*c* 0.7, $CHCl_3$) [lit.[39] $[\alpha]^{20}_{D}$ +21.9 (*c* 1.1, $CHCl_3$)]; ^{1}H NMR (500 MHz, $CHCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 3H), 1.16−1.39 (m, 24H), 1.57−1.72 (m, 2H), 2.03 (s, 1H), 2.05 (s, 6H), 2.09 (s, 3H), 4.00 (dd, *J* = 2.8, 11.7 Hz, 1H), 4.29 (dd, *J* = 4.7, 11.7 Hz, 1H), 4.44−4.51 (m, 1H), 4.93 (t, *J* = 9.9, 2.8 Hz, 1H), 5.11 (dd, *J* = 2.8, 8.4 Hz, 1H), 6.06 (d, *J* = 9.4 Hz, 1H); ^{13}C NMR (125 MHz, $CHCl_3$) δ 14.1, 20.75, 20.78, 21.1, 22.7, 23.3, 25.5, 28.0, 29.28, 29.34, 29.5, 29.57, 29.61, 29.64, 29.66, 31.9, 47.5, 62.8, 71.8, 73.0, 169.8, 170.1, 170.9, 171.2.

(2*S*,3*S*,4*R*)-2-Azido-3,4-bis(benzyloxy)octadec-5-yn-1-ol (4). Compound **19** (546 mg, 0.872 mmol) was dissolved in 25 mL of CH_3CN/H_2O (4:1) at rt, and CAN (2.39 g, 4.36 mmol) was added. The mixture was stirred at rt until completion, as monitored by TLC (about 1 h), and was then diluted with $CHCl_3$. The resulting solution was washed with H_2O and brine. The organic layer was dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (elution with hexane/EtOAc 10:1 to 6:1) to afford 349 mg (77%) of alcohol **4** as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.1

(39) Shirota, O.; Nakanishi, K.; Berova, N. *Tetrahedron* **1999**, *55*, 13643–13658.

Hz, 3H), 1.20−1.33 (m, 16H), 1.36−1.45 (m, 2H), 1.50−1.58 (m, 2H), 2.28 (dt, J = 1.9, 7.1 Hz, 2H), 2.32 (br s, 1H), 3.72−3.81 (m, 3H), 3.81−3.87 (m, 1H), 4.37−4.40 (m, 1H), 4.50 (d, J = 11.8 Hz, 1H), 4.63 (d, J = 11.4 Hz, 1H), 4.81 (d, J = 11.4 Hz, 1H), 4.86 (d, J = 11.8 Hz, 1H), 7.26−7.38 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 18.8, 22.7, 28.6, 28.9, 29.1, 29.3, 29.5, 29.60, 29.63, 31.9, 62.1, 63.0, 69.6, 70.7, 73.9, 75.3, 80.8, 89.3, 127.85, 127.89, 128.0, 128.1, 128.38, 128.39, 137.3, 137.5; ESI-HRMS $[M + Na]^+$ calcd for $C_{32}H_{45}N_3NaO_3^+$ 542.3353, found 542.3356.

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Supporting Information Available: Copies of ^{1}H NMR and ^{13}C NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.