Regioselective and Stereospecific Azidation of 1,2- and 1,3-Diols by Azidotrimethylsilane via a Mitsunobu Reaction

Linli He, Meni Wanunu, 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

Received April 16, 1999

A one-pot regio- and stereospecific azidation reaction of 1,2- and 1,3-diols with azidotrimethylsilane (Me_3SiN_3) via a Mitsunobu reaction has been achieved. With 1,2- and 1,3-diols, the reaction of triphenylphosphine, diisopropyl azodicarboxylate, and Me_3SiN_3 in dichloromethane gave regioselective azidation at C-2 and C-3, respectively, in good yield (74−90% combined yield of **1a** + **1b** or of **2a** + **2b**). However, application of the same reaction conditions to a 1,4-diol led to the exclusive formation of the cyclic ether. The regioselectivity of this one-pot reaction is influenced by the solvent, the degree of steric bulk at C-2 of the 1,2-diol or at C-3 of the 1,3-diol, and the presence of electron-donating and electron-withdrawing groups near the secondary carbinol carbon. This selectivity is discussed in terms of the mechanistic model proposed by Mathieu-Pelta and Evans (Mathieu-Pelta, I.; Evans, S. A., Jr. *J. Org. Chem.* **1992**, *57*, 3409−3413), which involves reaction of the dioxaphospholane intermediate with Me_3SiN_3 to form oxyphosphonium ions **4** and **5**.

Introduction

A 2-amino-1-ol and 3-amino-1-ol substructure is a common component of many natural products. Chiral 1,2- and 1,3-amino alcohols are also versatile building blocks for the synthesis of a wide range of biologically important compounds and are precursors of ligands for asymmetric reaction catalysis.[1] Many synthetic methods are available for the direct installation of the amino alcohol functionalities into a substrate. Well-known methods for the preparation of amino alcohols are opening of epoxides[2] or cyclic sulfates[3] by amines, reduction of α- and β-amino acids,[4] and asymmetric aminohydroxylation of olefins.[5]

Azidohydrins are attractive precursors of amino alcohols because many efficient methods are known for the conversion of an azide to an amine (e.g., $Ph_3P/THF-H_2O$,[6] $LiAlH_4$, catalytic hydrogenation,[7] H_2S/pyridine,[8] $SnCl_2$,[9] SmI_2,[10] $Bu_3SnH/AIBN$[11]). This approach is particularly important since several powerful enantioselective methods can be used to prepare epoxides[12] and vicinal diols,[1d] which are facile precursors of azidohydrins. Moreover, azides can be converted in situ to carbamates,[13] amides,[14] and other derivatives.

Ring opening of epoxides by azide ion (NaN_3, LiN_3, or Me_3SiN_3) in the presence of a promoter (e.g., $LiClO_4$,[15a] $Al(i\text{-}PrO)_3$,[15b] $Ti(OPr\text{-}i)_4$,[15c,d] $BF_3{\cdot}Et_2O$,[15e] $MgSO_4$,[2a] and NH_4Cl[2a]) gives vicinal azidohydrins. However, in these reactions azide ion generally attacks the C-1 position of terminal epoxides and the C-3 position of 2,3-epoxy alcohols. Ring opening of cyclic sulfates by azide ion gives a similar regioselectivity.[3] These methods are thus not suitable when C-2 substitution is desired. The synthesis of C-2 monoazido alcohols from diols is usually achieved by a multistep reaction sequence involving selective protection, activation, azide substitution, and deprotection. In 1992, an efficient regioselective and stereospecific method was described for converting a 1,2-propanediol into a 2-azido-1-silyloxypropane.[16a] This reaction utilized formation of a 1,3,2-dioxaphospholane by reaction of 1,2-propanediol and $(EtO)_2PPh_3$ (generated by reaction of

* To whom correspondence should be addressed. Tel.: (718) 997-3279. Fax: (718) 997-3349. E-mail: robert_bittman@qc.edu.

(1) (a) Shioiri, Y.; Hamada, Y. *Heterocycles* **1988**, *27*, 1035−1050. (b) Barlow, C. B.; Bukhari, S. T.; Guthrie, R. D.; Prior, A. M. In *Asymmetry in Carbohydrates*; Dekker: New York, 1979; pp 81−99. (c) Blaser, H.-U. *Chem. Rev.* **1992**, *92*, 935−952. (d) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483−2547.

(2) (a) Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodward, S. S. *Pure Appl. Chem.* **1983**, *55*, 589−604. (b) Behrens, C. H.; Sharpless, K. B. *Aldrichim. Acta* **1983**, *16*, 67−79. (c) Askin, D.; Eng, K. K.; Rossen, K.; Purick, R. M.; Wells, K. M.; Volante, R. P.; Reider, P. J. *Tetrahedron Lett.* **1994**, *35*, 673−676. (d) Hanson, R. M. *Chem. Rev.* **1991**, *91*, 437−475. (e) Klunder, J. M.; Ko, S. Y.; Sharpless, K. B. *J. Org. Chem.* **1986**, *51*, 3710−3712.

(3) For a review, see: Lohray, B. B.; Bhushan, V. *Adv. Heterocycl. Chem.* **1997**, *68*, 89−180.

(4) (a) Gage, J. R.; Evans, D. A. *Org. Synth.* **1988**, *67*, 77−82. (b) Smith, G. A.; Gawley, R. E. *Org. Synth.* **1984**, *63*, 136−139. (c) Poindexter, G. S.; Meyers, A. I. *Tetrahedron Lett.* **1977**, *40*, 3527−3528. (d) Kokotos, G.; Noula, C. *J. Org. Chem.* **1996**, *61*, 6994−6996. (e) Coppola, G. M.; Schuster, H. F. *Asymmetric Synthesis: Construction of Chiral Molecules Using Amino Acids*; Wiley: New York, 1987.

(5) For asymmetric aminohydroxylation of olefins, see: Bruncko, M.; Schlingloff, G.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1483−1486 and references therein.

(6) For a review about the Staudinger reaction, see: Gololobov, Y. G.; Zhmurova, I. N.; Kasukhin, L. F. *Tetrahedron* **1981**, *37*, 437−472.

(7) Scriven, E. F. V.; Turnbull, K. *Chem. Rev.* **1988**, *88*, 297−368.

(8) (a) Adachi, T.; Yamada, Y.; Inoue, I. *Synthesis* **1977**, 45−46. (b) Becher, J.; Pluta, K.; Krake, N.; Brondum, K.; Christensen, N. J.; Vinader, M. V. *Synthesis* **1989**, 530−533.

(9) Maiti, S. N.; Singh, M. P.; Micetich, I. G. *Tetrahedron Lett.* **1986**, *27*, 1423−1424.

(10) (a) Huang, Y.; Zhang, Y.; Wang, Y. *Tetrahedron Lett.* **1997**, *38*, 1065−1066. (b) Goulaouic-Dubois, C.; Hesse, M. *Tetrahedron Lett.* **1995**, *36*, 7427−7430. (c) Benati, L.; Montevecchi, P. C.; Nanni, D.; Spagnolo, P.; Volta, M. *Tetrahedron Lett.* **1995**, *36*, 7313−7314.

(11) (a) Samano, M. C.; Robins, M. J. *Tetrahedron Lett.* **1991**, *32*, 6293−6296. (b) Pupeiko, N. E.; Prikota, T. I.; Mikhailopulo, I. A. *Synlett* **1991**, 342−342.

(12) Katsuki, T.; Martin, V. *Org. React.* **1996**, *48*, 1−300.

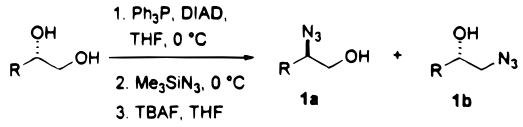
(13) Saito, S.; Nakajima, H.; Inaba, M.; Moriwake, T. *Tetrahedron Lett.* **1989**, *30*, 837−838.

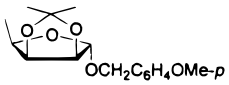
(14) Byun, H.-S.; Bittman, R. *J. Org. Chem.* **1996**, *61*, 8706−8708.

(15) (a) Chini, M.; Crotti, P.; Flippin, L. A.; Macchia, F. *J. Org. Chem.* **1990**, *55*, 4265−4272. (b) Emziane, M.; Lhoste, P.; Sinou, D. *Synthesis* **1988**, 541−544. (c) Caron, M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1557−1560. (d) Chong, J. M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 1560−1563. (e) Behrens, C. H.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 5696−5704.

10.1021/jo9906375 CCC: $18.00
Published on Web 07/16/1999

Table 1. Regioselective Azidation of 1,2-Diols via a Mitsunobu Reaction



Entry	R	Product Ratio[a] (1a/1b)	Combined Yield[b] of 1a and 1b (%)
1	*p*-$ClC_6H_4OCH_2$–	2.2:1	85
2	*p*-$MeOC_6H_4OCH_2$–	2:1	83
3	$C_6H_5CH_2OCH_2$–	6.3:1	78
4	$C_6H_5CH_2SCH_2$–	4.3:1	65[c]
5	*n*-$C_{18}H_{37}OCH_2$–	8.7:1	86
6	*n*-$C_{14}H_{29}$–	20:1	83
7	*n*-C_6H_{13}–	>50:1	74
8	*n*-$C_{13}H_{27}$–C≡CH_2–	7:1	78
9		1:22	92[d]

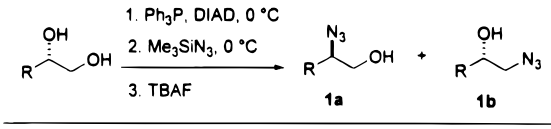
[a] The ratio was calculated from the isolated yields of **1a** and **1b**. [b] Isolated yield. [c] During the reaction, rearrangement takes place via an episulfenium ion intermediate to give (*S*)-3-azido-2-benzylthio-1-propanol.[26] [d] The reaction with Me_3SiN_3 was carried out at 70 °C.

Ph_3P with diethyl peroxide) to activate the alcohol and Me_3SiX (X = PhS, I, Br, Cl, CN, and N_3) as nucleophiles, mainly for the purpose of mechanistic study. In the course of our efforts to convert a hindered secondary hydroxy group to an azide under mild conditions, we found that addition of Me_3SiN_3 to a mixture of diisopropyl azodicarboxylate (DIAD), triphenylphosphine, and a 1,3-diol also provided the secondary azide in good yield and with excellent stereocontrol. The use of DIAD rather than the hazardous EtOOEt as the phosphine activator represents a significant advantage. In view of the potential importance of azidation of diols, a detailed study has been carried out, and herein we report some synthetic applications of this reaction.

Results

Azidation of 1,2-Diols (Derivatives of Propane-1,2-diol and Glycerol). Chiral 1,2-diols were prepared either by catalytic asymmetric dihydroxylation (entries 1, 2, and 6−8 of Table 1)[17] or by nucleophilic opening of chiral glycidol (entries 3−5).[18] The one-pot conversion of a 1,2-diol to its azido alcohol was performed by adding DIAD to a mixture of diol and Ph_3P in THF at 0 °C. After 3 h, Me_3SiN_3 was injected, and the reaction mixture was stirred at this temperature until azide substitution was completed. After desilylation (*n*-Bu_4NF in THF), the products were purified by column chromatography.

Table 2. Solvent Effects on the Regioselectivity of Azidation under Mitsunobu Conditions[a]



R	Solvent	Product Ratio (1a/1b)	Combined Yield of 1a and 1b (%)
p-$MeOC_6H_4OCH_2$–	THF	2:1	82
	CH_2Cl_2	3:1	81
	$PhCH_3$	4:1	84
n-$C_{14}H_{29}$–	THF	20:1	82
	CH_2Cl_2	32:1	80
	$PhCH_3$	47:1	89
n-$C_{13}H_{27}$–C≡CH_2–	THF	7:1	77
	CH_2Cl_2	10:1	80
	$PhCH_3$	12:1	74

[a] Typical reaction times required for the overall conversion of a diol to **1a** and **1b**: 7 h in THF and CH_2Cl_2, 12 h in $PhCH_3$.

The regioselectivity of the monoazidation of 1,2-diols is summarized in Table 1. With one exception, the diols shown in Table 1 gave 2-azido-1-ol **1a** as the major product. (Since the diol shown in entry 9 did not undergo azide substitution even at room temperature, the reaction mixture was heated to 70 °C; the primary azide **1b** of the protected mannose was obtained almost exclusively.) The highest C-2 regioselectivity was observed when R was *n*-hexyl (Table 1, entry 7). The possible reasons for the lower regioselectivity found with glycerol derivatives (Table 1, entries 1−5) and for the lower yield obtained from benzylthioglycerol (Table 1, entry 4) are discussed below.

Solvent Effect on the Azidation of 1,2-Diols. The influence of solvent on the reaction was studied. The three substrates shown in Table 2 were randomly selected, and three solvents commonly used in the Mitsunobu reaction[19] were tested. It is clear that the regioselectivity but not the yield of the reaction depends on the solvent, with the highest degree of regioselectivity taking place in toluene and the lowest in THF.

Azidation of 1,3- and 1,4-Diols. Similarly, the one-pot azidation reactions of 1,3- and 1,4-diols were carried out.[20] It is obvious that under the same conditions regioselective azide substitution also occurred at the more hindered C-3 position of the 1,3-diols shown in Table 3. However, with a 1,4-diol (R = *n*-$C_{14}H_{29}$) a tetrahydrofuran derivative was formed exclusively, presumably via an

(16) (a) Mathieu-Pelta, I.; Evans, S. A., Jr. *J. Org. Chem.* **1992**, *57*, 3409−3413. (b) Pautard, A. M.; Evans, S. A., Jr. *J. Org. Chem.* **1988**, *53*, 2300−2303.

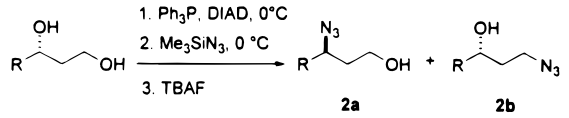
(17) Byun, H.-S.; Erukulla, R. K.; Bittman, R. *J. Org. Chem.* **1994**, *59*, 2630−2633.

(18) (a) Erukulla, R. K.; Byun, H.-S.; Locke, D. C.; Bittman, R. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2199−2200. (b) Byun, H.-S.; Bittman, R. *J. Org. Chem.* **1994**, *59*, 688−671.

(19) Hughes, D. V. *Org. React.* **1992**, *42*, 335−656.

(20) Chiral 1,3-diols were synthesized via the following sequence of reactions: (1) catalytic asymmetric dihydroxylation of α,β-unsaturated esters, (2) formation of cyclic sulfates, (3) opening of the cyclic sulfate with LiBr, (4) debromination of the α-bromide ester with Bu_3SnH/AIBN, and (5) ester reduction by DIBAL-H.

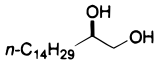
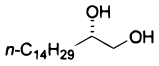
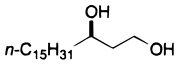
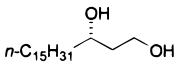
Table 3. Regioselective Azidation of 1,3-Diols via a Mitsunobu Reaction[a]



Entry	R	Solvent	Product Ratio[b] (2a/2b)	Combined Yield[c] of 2a and 2b (%)
1	n-$C_{16}H_{33}OCH_2$–	THF	7.4:1	78
2	n-$C_{13}H_{27}$–	CH_2Cl_2	18.7:1	90
3	n-$C_{15}H_{31}$–	THF	14.5:1	85

[a] The starting diols were prepared as outlined in ref 20. [b] The ratio was calculated from the isolated yields of **2a** and **2b**. [c] Isolated yield.

Table 4. Stereospecificity of Azidation

Entry	Diol	% ee of starting diol[a]	% ee of secondary azide product[b]
1		>99	97
2		97	96
3		96	94
4		94	94

[a] The enantiomeric excess of the starting diols was determined by analysis of the ^1H NMR spectra of the bis-MTPA esters. [b] The enantiomeric excess of the secondary azides was determined by analysis of the ^{13}C NMR spectra of the azido-MTPA ester (Figure 1).

intramolecular Mitsunobu reaction due to the facile formation of a five-membered ring.

Stereospecificity of Azidation. One representative example of a 1,2- and 1,3-diol was selected to evaluate the stereospecificity of the azidation. The enantiomeric excess of the starting diols was determined by analysis of the ^1H NMR spectra of the bis-MTPA esters, while for that of the azidohydrins, ^{13}C NMR analysis of the corresponding azido-MTPA ester was employed since baseline separations were not obtained in their ^1H NMR spectra. The excellent stereospecificity of the reaction is demonstrated in Table 4 and Figure 1. In each reaction, the chiral purity of the product was as high as that of the starting diol.

Discussion

Mechanism. Although the reaction conditions in the current study are different from those reported previously,[16a] our results support and extend the mechanism proposed by Mathieu-Pelta and Evans.[16a] Scheme 1 illustrates the following steps: (1) The reaction of an alkyl (*S*)-1,2-propanediol with triphenylphosphine and DIAD furnishes two conformational isomers, **3a** and **3b**, which undergo a rapid interconversion through a pseudorotation. (2) Silylation at the more basic P−O apical oxygen[21] leads to the formation of (silyloxy)phosphonium ions **4** and **5**, which was confirmed by ^{31}P NMR spectroscopy (δ 62.0 and 63.5 ppm, respectively[16b]). (3) The transition state leading to **3b′** experiences severe steric hindrance since the trimethylsilyl group is sandwiched between the C-4 alkyl group and the equatorial $P{=}C_6H_5$ groups in the trigonal-bipyramidal array. Thus, formation of C-2 siloxyphosphonium ion **4** is favored. (4) Subsequent S_N2 displacement of Ph_3PO by azide ion affords the C-2−N_3 regioisomer **1a** as the major product.

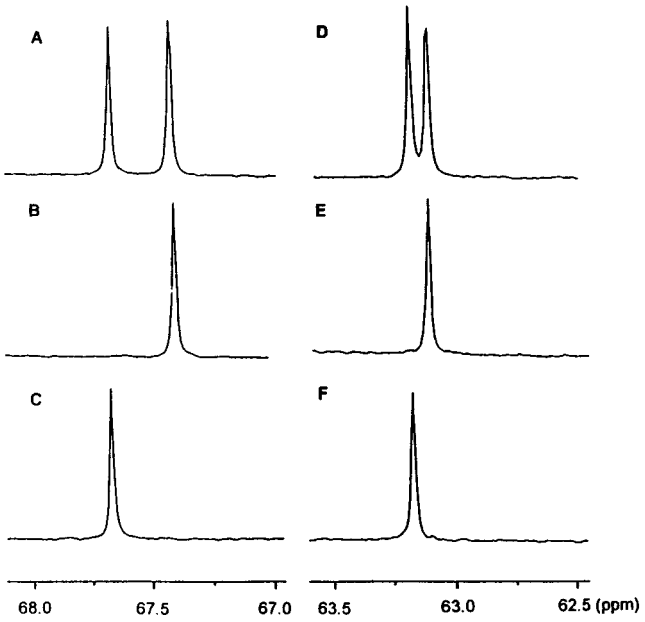
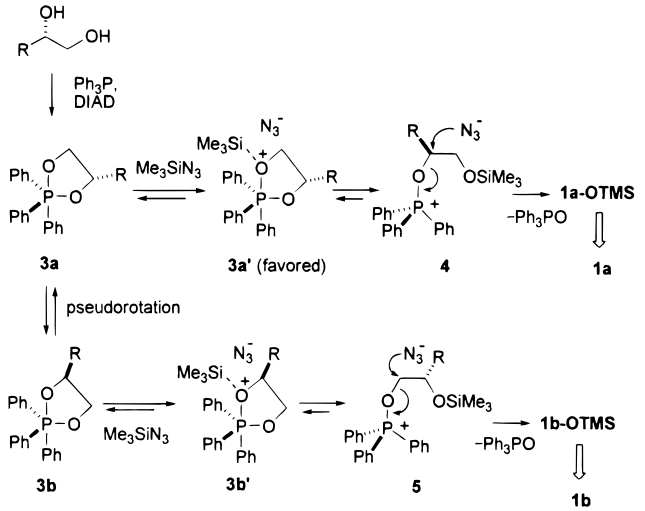


Figure 1. Partial ^{13}C NMR spectra of (*R*)-(−)-MTPA esters of 2-azido-1-hexadecanol (A−C) and 3-azido-1-octadecanol (D−F). Mosher esters derived from: (A) a 1.00:1.13 mixture of (*2R*)-2-azido-1-hexadecanol and (*2S*)-2-azido-1-hexadecanol; (B) (*2R*)-2-azido-1-hexadecanol; (C) (*2S*)-2-azido-1-hexadecanol; (D) a 1.19:1.00 mixture of (*2R*)-3-azido-1-octadecanol and (*2S*)-3-azido-1-octadecanol; (E) (*2R*)-3-azido-1-octadecanol; and (F) (*2S*)-3-azido-1-octadecanol.

Scheme 1. Suggested Mechanism for the Formation of 1a and 1b via 1,3,2λ^5-Dioxaphospholanes 3a and 3b



(21) Luckenbach, R. *Dynamic Stereochemistry of Pentacoordinated Phosphorus and Related Elements*; George Thieme: Stuttgart, FRG, 1973.

Me_3SiN_3 as a Source of Azide Ion. It is well known that cyclic sulfates are very reactive toward nucleophilic ring opening.[22] However, attempted reaction between Me_3SiN_3 and the cyclic sulfate of (*S*)-1-(4′-methoxyphenyl)glycerol revealed that little N_3^- was available from Me_3SiN_3 in THF and CH_2Cl_2, since no ring opening occurred at all, even after 48 h of reflux in THF (94% of the starting cyclic sulfate was recovered). This result suggests that dioxaphosphorane **3a** or **3b** first reacts with Me_3SiN_3 to form the ion pair **3a′** or **3b′**, which then generates (silyloxy)phosphonium ion **4** or **5** and azide ion.

Regioselectivity of Azidation. (a) Steric Effect. We propose that the regiochemistry of the reaction is controlled not only by steric congestion presented in the apical oxygen atom of dioxaphosphoranes **3a** and **3b** but also by the rate of the azide displacement reaction with **4** or **5**. As demonstrated in Tables 1 and 3, all of the azidation reactions (except that in entry 9, Table 1) showed a consistent attack of N_3^- at the more hindered secondary carbinol position. This result suggests that nucleophilic substitution by N_3^- is not the rate-determining step of the overall reaction. If so, **1b** instead of **1a** would be the major product (Curtin−Hammett principle).[23]

Steric hindrance in the R group causes the less hindered apical oxygen[21] of dioxaphosphorane **3a** to attack Me_3SiN_3 to give **3a′**; a similar attack after pseudorotation would yield the hindered ion pair **3b′**. After ring opening, oxyphosphonium ion **4** is favored over **5**. Therefore, C-2−N_3/C-3−N_3 becomes the major product (except in entry 9, Table 1). Although a bigger R group is expected to give a higher ratio of **4**/**5**, it would also slow the subsequent S_N2 reaction of **4** to a greater extent than it would for that of **5**. Hence, when the R group of the 1,2-diol is changed from CH_3[16a] to *n*-C_6H_{13} and to *n*-$C_{14}H_{29}$, the regioselectivity (**1a**/**1b** ratio) decreases from >99:1[16a] to >50:1 and to 20:1, since **4** can interconvert to **5** prior to undergoing direct reaction with N_3^-. When the R group in a diol is very bulky, the approach of N_3^- at the secondary carbinol carbon of **4** can be totally blocked. In this case, nucleophilic displacement can only take place at the primary position, and the C-1−N_3 derivative would become the major product. Entry 9 in Table 1 reflects such a situation, where R is bulky and molecular modeling indicates that one of the methyl groups in the isopropylidene moiety is positioned at the back of the leaving Ph_3PO.

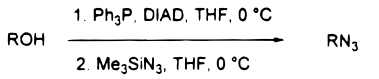
(b) Electronic Effect. The data presented in Tables 1 and 3 suggest that, in addition to the steric effect discussed above, a significant electronic effect is also observed in the azidation of 1,2- and 1,3-diols. Since the carbon atom bearing the leaving group is more electron-deficient in the S_N2 transition state than in the ground state,[24] most S_N2 reactions are retarded by the presence of electron-withdrawing substituents at the *β*-carbon atom.[25] For example, the relative S_N2 rate of XCH_2CH_2Br with PhSNa decreases from 1.0 to 0.18 and to 0.16 when X is changed from CH_3 to Cl and to F.[25a] This result may explain why the regioselectivities in entries 1−5 (Table 1) and entry 1 (Table 3) are lower than those in entries 6 and 7 (Table 1) and entries 2 and 3 (Table 3), respectively. The largest effect was observed in entries 1 and 2 (Table 1), where phenyloxy groups are stronger electron-withdrawing groups than benzyloxy and alkoxy groups (entries 3 and 5 of Table 1, respectively). Such *β*-carbon electronic effects are also known to take place in nucleophilic opening reactions of epoxides.[2]

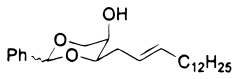
Finally, part of the oxyphosphonium ion **4** derived from benzylthioglycerol undergoes intramolecular displacement to form a sulfenium ion, which after ring opening by N_3^- leads to a 2-benzylthio-3-azide derivative (14%).[26] Therefore, the yield of **1a** is lower (entry 4, Table 1).

Solvent Effect. Although the solvent also plays a role in determining the regioselectivity of the reaction, and a nonpolar solvent seems to favor formation of the C-2-N_3 product (Table 2), it is worthwhile to point out that CH_2Cl_2 is the solvent of choice among the three studied here. All of the diols studied have poor solubility in toluene at 0 °C; therefore, prolonged reaction time is required, and sometimes reaction is incomplete.

Application of the Azidation to Simple Alcohols. Azidation of simple alcohols by the Mitsunobu reaction is well known using diphenylphosphoryl azide, hydrazoic acid, and zinc azide/pyridine complex.[19] Table 5 shows the results of azidation of simple alcohols with Ph_3P, DIAD, and Me_3SiN_3. Since Me_3SiN_3 needs to be activated prior to the azide substitution reaction, it was predictable that the maximum yield of the azido derivative that could be realized would be 50% (to get one N_3^- from Me_3SiN_3, one alcohol will be consumed to form Me_3SiOR). Azidation of cetyl alcohol proceeded in 46% yield, whereas a secondary alcohol bearing a 1,3-benzylidene group gave a poor yield. The failure of the azidation reaction with a tertiary alcohol (Table 5) may reflect the inability of this substrate to react with Ph_3P to form an oxyphosphonium ion.

Table 5. Azidation vs Silylation of Primary, Secondary, and Tertiary Alcohols with Me_3SiN_3 via a Mitsunobu Reaction



Entry	Alcohol	Yield of Product (%)	
		RN_3	$ROSiMe_3$
1	*n*-$C_{16}H_{33}OH$	46	51
2		28	25
3	*n*-$C_{13}H_{27}C(OH)(CH_3)_2$	trace	85

Conclusion

The one-pot regio- and stereospecific azidation of 1,2- and 1,3-diols with Ph_3P, DIAD, and Me_3SiN_3 under

(22) Gao, Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1988**, *110*, 7538−7539.

(23) For a discussion of the Curtin−Hammett principle, see: (a) Carey, F. A.; Sundberg, R. J. In *Advanced Organic Chemistry*; Plenum Press: New York, 1990; pp 215−216. (b) Seeman, J. I. *Chem. Rev.* **1983**, *83*, 83−134.

(24) Streitwieser, A., Jr. *Chem. Rev.* **1956**, *56*, 571−752.

(25) (a) Hine, J.; Brader, W. H., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 3964−3966. (b) Bordwell, F. G.; Brannen, W. T., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 4645−4650. (c) Winstein, S.; Allred, E.; Heck, R.; Glick, R. *Tetrahedron* **1958**, *3*, 1−13.

(26) Eames, J.; Warren, S. *Tetrahedron Lett.* **1996**, *37*, 3525−3528.

Mitsunobu conditions has been achieved in good yield. This mild method avoids a multistep protection and deprotection procedure and is compatible with a broad range of functional groups that may be present in the diol. The regioselectivity of the reaction appears to be sensitive to the size of the alkyl substituent, the electronic distribution of the substrate, and the polarity of the solvent. This reaction combination is not suitable for the conversion of a simple alcohol to its azido derivative because Me_3SiN_3 is a poor nucleophile.

Experimental Section

General Information. See refs 14 and 17 for general experimental protocols. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz on a Bruker spectrometer, respectively, and were referenced to the residual $CHCl_3$ at 7.24 (^1H) and 77.00 ppm (^{13}C). Deuterated chloroform ($CDCl_3$) was used as the only solvent for all of the NMR analysis. (*R*)-(−)-α-Methoxy-α-trifluoromethylphenylacetic acid chloride, DIAD, TBAF, and Me_3SiN_3 were purchased from Fluka, Lancaster, Aldrich, and Acros, respectively, and were used as provided commercially without further purification. Elemental analyses were carried out by Schwarzkopf Microanalytical Laboratory (Woodside, NY). Melting points are uncorrected.

General Procedure for the Azidation of 1,2- and 1,3-Diols. Method A (One-Pot Mode). To a solution of a diol (1.0 mmol) and Ph_3P (342 mg, 1.3 mmol) (both thoroughly dried overnight under vacuum of 0.7 Torr) in 18 mL of dry solvent (THF, CH_2Cl_2, or $PhCH_3$) was injected 311 μL (1.5 mmol) of DIAD[27] at 0 °C. After the yellow reaction mixture was stirred at this temperature for 3 h under nitrogen, 211 μL (1.3 mmol) of Me_3SiN_3 was injected. **CAUTION:** Me_3SiN_3 is sensitive to H_2O, releasing toxic hydrazoic acid on hydrolysis. Therefore, Me_3SiN_3 should be used only in a well-ventilated hood, and skin contact should be avoided. The reaction mixture (either a clear solution or sometimes a suspension) was stirred at the same temperature for 3 h and then allowed to warm to room temperature. After removal of the solvent, the residue was dissolved in 3 mL of THF and treated with 2.5 mL of a 1 M TBAF solution in THF containing 5 wt % of H_2O.[28] The brown reaction mixture was stirred at room temperature until all of the silyloxy azides **1a-OTMS** and **1b-OTMS** were consumed completely (TLC). Concentration gave a slurry, which was dissolved in CH_2Cl_2 and passed through a pad of silica gel in a sintered glass funnel to remove Ph_3PO and salts. The pad was washed with a mixture of hexanes−EtOAc (usually 6/1) depending on the polarity of the products. The crude products were purified by silica gel chromatography (elution first with 150 mL of hexanes−EtOAc 50/1 and then with the appropriate mixture of hexanes−EtOAc).

Method B (Two-Pot Mode). The only modification here is that after the completion of the reaction among a diol, Ph_3P, DIAD, and Me_3SiN_3 and concentration the yellow residue was dissolved in a minimum volume of CH_2Cl_2 and passed through a pad of silica gel in a sintered glass funnel instead of the direct addition of TBAF. The pad was rinsed with hexanes−EtOAc (100/1 or 50/1) to collect the silyloxy azides. The excess yellow DIAD served as an indicator, since silyloxy azides are less polar than DIAD (except for the sugar derivative), and therefore, they were eluted before DIAD. After concentration, the residue was dissolved in 3 mL of dry THF and treated with 2.5 mL of TBAF. After the same workup procedure as in the one-pot mode, the crude products were dissolved in a minimum volume of hexane and transferred to a silica gel column for chromatographic separation (elution first with 150 mL of hexanes−EtOAc 50/1, then with the appropriate mixture of hexanes−EtOAc).

(*S*)-2-Azido-3-*O*-(4′-chlorophenyl)-1,3-propanediol: mp 36.5−37.5 °C; $[\alpha]^{25}_D$ −22.1° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) 3611, 3442, 2125, 2110, 1511, 1235, 1040, 839 cm^{-1}; ^1H NMR δ 1.96 (br s, 1H), 3.75 (dd, 1H, *J* = 11.4, 5.9 Hz), 3.88 (m, 2H), 4.07 (dd, 1H, *J* = 9.7, 6.7 Hz), 4.12 (dd, 1H, *J* = 9.8, 4.7 Hz), 6.83 (d, 2H, *J* = 8.9 Hz), 7.23 (d, 2H, *J* = 8.9 Hz); ^{13}C NMR δ 61.99, 62.17, 68.07, 115.79, 126.40, 129.43, 156.68. Anal. Calcd for $C_9H_{10}O_2N_3Cl$: C, 47.48; H, 4.43; N, 18.64; Cl, 15.57. Found: C, 47.56; H, 4.21; N, 18.56; Cl, 15.27.

(*R*)-3-Azido-1-*O*-(4′-chlorophenyl)-1,2-propanediol: $[\alpha]^{25}_D$ +13.3° (*c* 1.4, $CHCl_3$); IR ($CHCl_3$) 3605, 3446, 2111, 1507, 1041, 830 cm^{-1}; ^1H NMR δ 2.24 (br s, 1H), 3.47 (dd, 1H, *J* = 12.7, 6.1 Hz), 3.52 (dd, 1H, *J* = 12.6, 4.6 Hz), 3.96 (d, 2H, *J* = 5.2 Hz), 4.14 (m, 1H), 6.80 (d, 2H, *J* = 8.9 Hz), 7.25 (d, 2H, *J* = 8.9 Hz); ^{13}C NMR δ 53.30, 69.19, 69.32, 115.79, 126.38, 129.45, 156.78.

(*S*)-2-Azido-3-*O*-(4′-methoxyphenyl)-1,3-propanediol: mp 52.5−53.0 °C; $[\alpha]^{25}_D$ −29.0° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) 3601, 3432, 2126, 2110, 1511, 1235, 1040, 825 cm^{-1}; ^1H NMR δ 1.92 (br s, 1H), 3.74 (dd, 1H, *J* = 11.1, 5.8 Hz), 3.75 (s, 3H), 3.85 (m, 2H), 4.05 (dd, 1H, *J* = 9.8, 6.4 Hz), 4.09 (dd, 1H, *J* = 9.8, 4.7 Hz), 6.83 (m, 4H); ^{13}C NMR δ 55.70, 62.12, 62.37, 68.58, 114.70, 115.60, 152.24, 154.33. Anal. Calcd for $C_{10}H_{13}O_3N_3$: C, 53.81; H, 5.87; N, 18.82. Found: C, 53.87; H, 5.72; N, 19.01.

(*R*)-3-Azido-1-*O*-(4′-methoxyphenyl)-1,2-propanediol: $[\alpha]^{25}_D$ +16.4° (*c* 4.3, $CHCl_3$); IR ($CHCl_3$) 3585, 3401, 2110, 1491, 1245, 1040, 820 cm^{-1}; ^1H NMR δ 2.40 (br s, 1H), 3.46 (dd, 1H, *J* = 12.7, 6.1 Hz), 3.52 (dd, 1H, *J* = 12.7, 4.7 Hz), 3.75 (s, 3H), 3.95 (m, 2H), 4.12 (m, 1H), 6.82 (s, 4H); ^{13}C NMR δ 53.36, 55.70, 69.38, 69.79, 114.71, 115.57, 152.32, 154.32.

(*S*)-2-Azido-3-*O*-benzyl-1,3-propanediol: $[\alpha]^{25}_D$ −29.9° (*c* 1.5, $CHCl_3$); IR ($CHCl_3$) 3460, 2120, 2097, 1261, 1096 cm^{-1}; ^1H NMR δ 2.31 (s, 1H), 3.60−3.73 (m, 5H), 4.55 (s, 2H), 7.29−7.36 (m, 5H); ^{13}C NMR δ 62.37, 62.61, 69.96, 73.47, 127.61, 127.84, 128.43, 137.37. Anal. Calcd for $C_{10}H_{13}O_2N_3$: C, 57.96; H, 6.32; N, 20.28. Found: C, 58.21; H, 6.24; N, 20.57.

(*R*)-3-Azido-1-*O*-benzyl-1,2-propanediol: $[\alpha]^{25}_D$ +11.5° (*c* 1.1, $CHCl_3$); IR ($CHCl_3$) 3565, 3472, 2097, 1272, 1102 cm^{-1}; ^1H NMR δ 2.47 (br s, 1H), 3.30 (dd, 1H, *J* = 8.6, 6.1 Hz), 3.40 (dd, 1H, *J* = 8.6, 4.7 Hz), 3.47 (dd, 1H, *J* = 9.6, 6.1 Hz), 3.51 (dd, 1H, *J* = 9.6, 4.4 Hz), 3.94 (m, 1H), 4.54 (s, 2H), 7.27−7.37 (m, 5H); ^{13}C NMR δ 54.85, 71.09, 72.69, 74.96, 129.25, 129.39, 129.94, 138.93.

(*S*)-1-Azido-3-benzylthio-2-propanol: $[\alpha]^{25}_D$ +42.9° (*c* 1.9, $CHCl_3$); IR ($CHCl_3$) 3580, 3498, 2105, 1496, 1450, 702, 666 cm^{-1}; ^1H NMR δ 2.47 (m, 2H), 2.56 (s, 1H), 3.25 (dd, 1H, *J* = 12.6, 6.23 Hz), 3.32 (dd, 1H, *J* = 12.6, 4.0 Hz), 3.65−3.77 (m, 3H), 7.21−7.32 (m, 5H); ^{13}C NMR δ 35.50, 36.27, 55.10, 68.81, 127.25, 128.58, 128.78, 137.61.

(*R*)-2-Azido-3-benzylthio-1-propanol: $[\alpha]^{25}_D$ −5.0° (*c* 1.42, $CHCl_3$); IR ($CHCl_3$) 3500, 2110, 702, 666 cm^{-1}; ^1H NMR δ 1.71 (t, 1H, *J* = 5.9 Hz), 2.55 (dd, 1H, *J* = 13.8, 6.6 Hz), 2.60 (dd, 1H, *J* = 13.8, 6.7 Hz), 3.48 (m, 1H), 3.59 (m, 1H), 3.71 (m, 1H), 3.76 (s, 2H), 7.23−7.34 (m, 5H); ^{13}C NMR δ 31.79, 36.90, 63.35, 63.97, 127.36, 128.68, 128.94, 137.68. Anal. Calcd for $C_{10}H_{13}ON_3S$: C, 53.79; H, 5.87; N, 18.82. Found: C, 53.59; H, 5.65; N, 18.71.

(*S*)-3-Azido-2-benzylthio-1-propanol: $[\alpha]^{25}_D$ +16.6° (*c* 0.8, $CHCl_3$); IR ($CHCl_3$) 3478, 2105, 1496, 1455, 702, 666 cm^{-1}; ^1H NMR δ 1.87 (br s, 1H), 2.81 (m, 1H), 3.37 (dd, 1H, *J* = 12.6, 7.2 Hz), 3.42 (dd, 1H, *J* = 12.6, 6.4 Hz), 3.61 (dd, 1H, *J* = 11.5, 5.6 Hz), 3.67 (dd, 1H, *J* = 11.5, 5.4 Hz), 3.79 (s, 2H), 7.24−7.34 (m, 5H); ^{13}C NMR δ 35.87, 47.37, 52.57, 62.27, 127.46, 128.75, 128.80, 137.67.

(*S*)-2-Azido-3-*O*-octadecyl-1,3-propanediol: mp 46.8−47.4 °C; $[\alpha]^{25}_D$ +11.6° (*c* 1.78, $CHCl_3$); IR ($CHCl_3$) 3592, 2100, 1080 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, *J* = 7.0 Hz), 1.23 (m, 30H), 1.54 (m, 2H), 1.91 (br s, 1H), 3.45 (dt, 2H, *J* = 6.6, 1.5 Hz), 3.58−3.75 (m, 5H); ^{13}C NMR δ 14.10, 22.68, 25.97, 29.35, 29.41, 29.56, 29.59, 29.65, 29.68, 31.91, 62.18, 63.09, 71.01, 71.91.

(27) It is important to use an excess of DIAD (about 1.15 equiv) relative to Ph_3P; otherwise, an excess amount of Ph_3P can destroy the azide group in the products by the Staudinger reaction.

(28) The reaction was generally carried out in a one-pot mode. However, it is often helpful to pass the reaction mixture (before the addition of KF or TBAF) through a pad of silica gel to remove the more polar byproducts such as Ph_3PO, dihydro-DIAD, and unreacted diol. If this procedure is employed, it is also important to realize that the trimethylsilyloxy group is not stable, and therefore, the reaction mixture should not be allowed to remain in contact with silica gel for a prolonged time.

Anal. Calcd for $C_{21}H_{43}O_2N_3$: C, 68.25; H, 11.73; N, 11.37. Found: C, 68.13; H, 11.55; N, 11.44.

(*R*)-3-Azido-1-*O*-octadecyl-1,2-propanediol: mp 38.9−40.0 °C; $[\alpha]^{25}_D$ −5.2° (*c* 2.1, $CHCl_3$); IR ($CHCl_3$) 3580, 3440, 2105, 1045 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.23 (m, 30H), 1.53 (m, 3H), 3.30−3.48 (m, 6H), 3.91 (m, 1H); ^{13}C NMR δ 14.10, 22.67, 26.06, 29.35, 29.44, 29.53, 29.57, 29.60, 29.65, 29.68, 31.91, 53.46, 69.64, 71.69, 71.76.

(*S*)-2-Azido-1-hexadecanol: mp 45.0−45.5 °C; $[\alpha]^{25}_D$ +9.9° (*c* 1.2, $CHCl_3$); IR ($CHCl_3$) 3626, 3595, 2105 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.24−1.46 (m, 24H), 1.50 (dt, 2H, J = 14.0, 6.9 Hz), 1.71 (br s, 1H), 3.44 (m, 1H), 3.52 (dd, 1H, J = 11.2, 7.5 Hz), 3.67 (dd, 1H, J = 11.4, 3.5 Hz); ^{13}C NMR δ 14.10, 22.67, 26.00, 29.34, 29.41, 29.42, 29.51, 29.60, 29.64, 29.66, 30.56, 31.91, 64.49, 65.24; HRMS (FAB, MH^+) calcd for *m*/*z* $C_{16}H_{34}N_3O$ 284.2702, found 284.2712.

(*R*)-1-Azido-2-hexadecanol: mp 45.8−46.1 °C; $[\alpha]^{25}_D$ −3.3° (*c* 1.73, $CHCl_3$); IR ($CHCl_3$) 3621, 3421, 2105 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.24−1.48 (m, 24H), 1.70 (m, 2H), 3.22 (dd, 1H, J = 12.8, 7.6 Hz), 3.36 (dd, 1H, J = 12.8, 3.2 Hz), 3.74 (m, 1H); ^{13}C NMR δ 14.10, 22.49, 25.42, 29.34, 29.49, 29.54, 29.61, 29.64, 29.66, 31.90, 34.28, 57.13, 70.85.

(*S*)-2-Azido-1-octanol: $[\alpha]^{25}_D$ +12.7° (*c* 2.05, $CHCl_3$; ∼85% ee); IR ($CHCl_3$) 3616, 3427, 2125, 2105 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.23−1.42 (m, 8H), 1.49 (dt, 2H, J = 14.3, 7.2 Hz), 2.00 (br s, 1H), 3.43 (m, 1H), 3.52 (dd, 1H, J = 11.2, 7.4 Hz), 3.66 (dd, 1H, J = 11.2, 3.5 Hz); ^{13}C NMR δ 64.46, 65.19. Anal. Calcd for $C_8H_{17}ON_3$: C, 56.11; H, 10.01; N, 24.54. Found: C, 55.91; H, 9.60; N, 24.35.

(*S*)-2-Azido-4-octadecyn-1-ol: mp 36.8−37.7 °C; $[\alpha]^{25}_D$ +12.8° (*c* 1.71, $CHCl_3$); IR ($CHCl_3$) 3611, 3406, 2121, 2110 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.23−1.44 (m, 20H), 1.46 (m, 2H), 1.75 (br s, 1H), 2.12 (tt, 2H, J = 7.1, 2.3 Hz), 2.44 (dt, 2H, J = 6.5, 2.1 Hz), 3.61 (m, 2H), 3.76 (m, 1H); ^{13}C NMR δ 14.11, 18.68, 21.41, 22.67, 28.71, 28.87, 29.12, 29.34, 29.52, 29.64, 31.90, 62.50, 64.26, 74.64, 83.69. Anal. Calcd for $C_{18}H_{33}ON_3$: C, 70.31; H, 10.82; N, 13.67. Found: C, 70.24; H, 10.96; N, 13.13.

(*R*)-1-Azido-4-octadecyn-2-ol: $[\alpha]^{25}_D$ −7.24° (*c* 1.98, $CHCl_3$); IR ($CHCl_3$) 3570, 3386, 2105 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.23−1.35 (m, 20H), 1.46 (m, 2H), 2.14 (tt, 2H, J = 7.1, 2.3 Hz), 2.41 (dt, 2H, J = 6.1, 2.3 Hz), 3.35 (dd, 1H, J = 12.5, 6.4 Hz), 3.41 (dd, 1H, J = 12.4, 4.2 Hz), 3.86 (m, 1H); ^{13}C NMR δ 14.09, 18.67, 22.66, 24.92, 28.85, 28.89, 29.11, 29.33, 29.51, 29.63, 29.66, 31.90, 55.44, 69.29, 74.41, 84.12.

1-*O*-(4′-Methoxybenzyl)-2,3-*O*-isopropylidene-6-azido-6-deoxy-D-mannofuranose: $[\alpha]^{25}_D$ +64.8° (*c* 2.62, $CHCl_3$); IR ($CHCl_3$) 3507, 2097, 1513, 1249, 1079 cm^{-1}; ^1H NMR δ 1.30 (s, 3H), 1.44 (s, 3H), 2.59 (br s, 1H), 3.42 (dd, 1H, J = 12.7, 6.36 Hz), 3.53 (dd, 1H, J = 12.7, 3.1 Hz), 3.78 (s, 3H), 3.93 (dd, 1H, J = 8.4, 3.8 Hz), 4.08 (m, 1H), 4.38 (d, 1H, J = 11.4 Hz), 4.55 (d, 1H, J = 11.4 Hz), 4.61 (d, 1H, J = 5.9 Hz), 4.82 (dd, 1H, J = 5.9, 3.9 Hz), 5.06 (s, 1H), 6.86 (d, 2H, J = 8.6 Hz), 7.22 (d, 2H, J = 8.6 Hz); ^{13}C NMR δ 24.51, 25.84, 54.31, 55.23, 68.77, 69.49, 79.34, 79.74, 84.79, 104.99, 112.70, 113.84, 129.14, 129.74, 159.36. Anal. Calcd for $C_{17}H_{23}O_6N_3$: C, 55.88; H, 6.35; N, 11.50. Found: C, 56.06; H, 6.50; N, 11.68.

1-*O*-(4′-Methoxybenzyl)-2,3-*O*-isopropylidene-5-azido-5-deoxy-D-mannofuranose: $[\alpha]^{25}_D$ +62.2° (*c* 1.62, $CHCl_3$); IR ($CHCl_3$) 3585, 3457, 2105, 1608, 1511, 1245, 1076 cm^{-1}; ^1H NMR δ 1.26 (s, 3H), 1.43 (s, 3H), 1.98 (t, 1H, J = 6.1 Hz), 3.69 (m, 1H), 3.78 (s, 3H), 3.86 (m, 2H), 4.14 (dd, 1H, J = 8.9, 3.4 Hz), 4.42 (d, 1H, J = 11.3 Hz), 4.60 (d, 1H, J = 1.1 Hz), 4.62 (d, 1H, J = 4.0 Hz), 4.69 (dd, 1H, J = 5.8, 3.5 Hz), 5.07 (s, 1H), 6.85 (d, 2H, J = 8.6 Hz), 7.24 (d, 2H, J = 8.6 Hz); ^{13}C NMR δ 24.69, 25.97, 55.27, 62.13, 63.29, 68.62, 79.52, 80.04, 85.32, 104.61, 112.77, 113.89, 129.02, 129.93, 159.41.

(*S*)-3-Azido-4-*O*-hexadecyl-1,4-butanediol: $[\alpha]^{25}_D$ +27.8° (*c* 2.21, $CHCl_3$); IR ($CHCl_3$) 3580, 2095 cm^{-1}, ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.23 (m, 26H), 1.55 (m, 2H), 1.71 (m, 2H), 2.29 (br s, 1H), 3.44 (m, 2H), 3.47 (dd, 1H, J = 10.1, 6.6 Hz), 3.54 (dd, 1H, J = 10.0, 4.1 Hz), 3.72 (m, 3H); ^{13}C NMR δ 14.08, 22.66, 25.96, 29.34, 29.41, 29.56, 29.58, 29.63, 29.67, 31.90, 33.70, 59.02, 59.42, 71.67, 73.51. Anal. Calcd for $C_{16}H_{33}ON_3$: C, 67.56; H, 11.62; N, 11.82. Found: C, 67.70; H, 11.75; N, 11.79.

(*R*)-4-Azido-1-*O*-hexadecyl-1,2-propanediol: mp 33.5−34.0 °C; $[\alpha]^{25}_D$ −5.7° (*c* 0.84, $CHCl_3$); IR ($CHCl_3$) 3562, 2097 cm^{-1}, ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.23 (m, 26H), 1.54 (m, 2H), 1.68 (dt, 2H, J = 6.9, 6.8), 1.96 (br s, 1H), 3.28 (dd, 1H, J = 9.5, 7.5 Hz), 3.41−3.51 (m, 5H), 3.89 (m, 1H); ^{13}C NMR δ 14.11, 22.68, 26.10, 29.36, 29.46, 29.60, 29.66, 29.69, 31.92, 32.29, 48.12, 67.72, 71.60, 74.61.

(*R*)-3-Azido-1-hexadecanol: mp 37.0−37.5 °C; $[\alpha]^{25}_D$ −23.8° (*c* 1.89, $CHCl_3$); IR ($CHCl_3$) 3610, 3460, 2105 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.20−1.24 (m, 22H), 1.50−1.70 (m, 4H), 1.76 (m, 1H), 3.47 (m, 1H), 3.76 (t, 2H, J = 5.5 Hz); ^{13}C NMR δ 14.10, 22.67, 26.02, 28.93, 29.34, 29.40, 29.48, 29.53, 29.61, 29.63, 29.66, 31.91, 34.56, 36.81, 59.85, 60.18. Anal. Calcd for $C_{16}H_{33}ON_3$: C, 67.80; H, 11.73; N, 14.82. Found: C, 67.78; H, 11.79; N, 14.88.

(*S*)-1-Azido-3-hexadecanol: mp 42.1−43.1 °C; $[\alpha]^{25}_D$ +7.5° (*c* 0.5, $CHCl_3$); IR ($CHCl_3$) 3600, 2100 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.20−1.45 (m, 24H), 1.56−1.65 (m, 2H), 1.72 (m, 1H), 3.45 (m, 2H), 3.72 (m, 1H); ^{13}C NMR δ 14.11, 22.68, 25.53, 29.35, 29.57, 29.64, 29.65, 29.68, 31.92, 35.97, 37.75, 48.62, 69.49.

(*R*)-3-Azido-1-octadecanol: mp 43.7−44.5 °C; $[\alpha]^{25}_D$ −23.3° (*c* 1.59, $CHCl_3$); IR ($CHCl_3$) 3621, 2105 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.20−1.45 (m, 26H), 1.46−1.69 (m, 4H), 1.76 (m, 1H), 3.48 (m, 1H), 3.75 (t, 2H, J = 5.3 Hz); ^{13}C NMR δ 14.10, 22.67, 26.03, 29.35, 29.40, 29.49, 29.53, 29.61, 29.64, 29.67, 31.91,34.57, 36.81, 59.83, 60.17; HRMS (FAB, MH^+) calcd for *m*/*z* $C_{18}H_{38}N_3O$ 312.3015, found 312.3015.

(*S*)-1-Azido-3-octadecanol: mp 49.3−50.3 °C; $[\alpha]^{25}_D$ +7.1° (*c* 0.4, $CHCl_3$); IR ($CHCl_3$) 3615, 2100 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.20−1.47 (m, 28H), 1.50−1.71 (m, 2H), 1.74 (m, 1H), 3.44 (m, 2H), 3.71 (m, 1H); ^{13}C NMR δ 14.11, 22.69, 25.53, 29.36, 29.57, 29.65, 29.69, 31.92, 35.97, 37.75, 48.62, 69.50.

(*S*)-3-Azido-1-octadecanol: mp 43.5−44.5 °C; $[\alpha]^{25}_D$ +23.7° (*c* 1.73, $CHCl_3$); IR ($CHCl_3$) 3612, 2105 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.20−1.45 (m, 26H), 1.46−1.69 (m, 4H), 1.76 (m, 1H), 3.48 (m, 1H), 3.75 (t, 2H, J = 5.3 Hz); ^{13}C NMR δ 14.11, 22.69, 26.04, 29.36, 29.41, 29.49, 29.54, 29.62, 29.65, 29.68, 31.92, 34.58, 36.82, 59.88, 60.20.

(*R*)-1-Azido-3-octadecanol: mp 49.5−50.2 °C; $[\alpha]^{25}_D$ −7.2° (*c* 1.27, $CHCl_3$); IR ($CHCl_3$) 3608, 2100 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.20−1.47 (m, 28H), 1.50−1.71 (m, 2H), 1.74 (m, 1H), 3.44 (m, 2H), 3.71 (m, 1H); ^{13}C NMR δ 14.10, 22.69, 25.52, 29.36, 29.58, 29.65, 29.69, 31.93, 35.97, 37.75, 48.62, 69.50.

2-Tetradecyltetrahydrofuran: IR ($CHCl_3$) 1460, 1050 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.23 (m, 22H), 1.41 (m, 2H), 1.54 (m, 1H), 1.79−1.95 (m, 3H), 3.68 (dd, 1H, J = 7.3, 6.5 Hz), 3.75 (m, 1H), 3.83 (dt, 1H, J = 7.4, 7.1 Hz); ^{13}C NMR δ 14.11, 22.68, 25.72, 26.41, 29.36, 29.60, 29.62, 29.67, 29.76, 31.38, 31.92, 35.75, 67.58, 79.47.

(2*S*,3*R*)-2-Azido-(1,3-*O*-benzylidene)hexadec-(5*E*)-ene-1,3-diol: $[\alpha]^{25}_D$ +7.63° (*c* 2.7, $CHCl_3$); IR ($CHCl_3$) 2260, 1162, 735, 692 cm^{-1}; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.24 (m, 20H), 2.02 (dt, 2H, J = 7.0, 6.8 Hz), 2.39 (dt, 1H, J = 14.4, 6.7 Hz), 2.55 (dt, 1H, J = 14.9, 4.6 Hz), 3.50 (m, 1H), 3.59 (m, 1H), 3.60 (dd, 1H, J = 10.4, 5.0 Hz), 4.34 (dd, 1H, J = 10.8, 5.0 Hz), 5.44 (s, 1H), 5.56 (m, 2H), 7.33−7.45 (m, 5H); ^{13}C NMR δ 14.11, 56.35, 68.99, 80.51, 101.03, 123.93, 126.00, 128.26, 129.01, 134.66, 137.50; HRMS [FAB, MH^+] calcd for $C_{25}H_{40}N_3O_2$ *m*/*z* 414.3120, found 414.3119 (40); [FAB, $MH^+ - N_2$] calcd for $C_{25}H_{40}NO_2$ *m*/*z* 386.3059, found 386.3055 (100).

1-Azidohexadecane: IR ($CHCl_3$) 2105 cm^{-1} [lit.[29] IR (film) 2100 cm^{-1}]; ^1H NMR δ 0.86 (t, 3H, J = 7.0 Hz), 1.24 (m, 26H), 1.50 (m, 2H), 3.23 (t, 2H, J = 7.0 Hz); ^{13}C NMR δ 14.11, 22.69, 25.83, 26.71, 28.84, 29.11, 29.28, 29.30, 29.45, 29.62, 29.68, 31.92, 51.49.

(29) Rolla, F. *J. Org. Chem.* **1982**, *47*, 4327−4329.

Hexadecyltrimethylsilyl ether: IR ($CHCl_3$) 1040 cm^{-1}; ^1H NMR δ 0.09 (s, 9H), 0.86 (t, 3H, $J = 7.0$ Hz), 1.24 (m, 26H), 1.58 (m, 2H), 3.55 (t, 2H, $J = 6.8$ Hz); ^{13}C NMR δ −0.46, 14.11, 22.68, 25.83, 26.73, 29.15, 29.36, 29.46, 29.48, 29.54, 29.66, 19.68, 32.75, 62.76.

Acknowledgment. This work was supported by National Institutes of Health Grant HL 16660. We thank the mass spectrometry facility at Michigan State University for the HR-FAB MS. We gratefully acknowledge support from the National Science Foundation (CHE-9408535) for funds for the purchase of the 400-MHz NMR spectrometer.

Supporting Information Available: Copies of ^1H and ^{13}C NMR spectra for compounds **1a** + **1b** and **2a** + **2b** in Tables 1 and 3. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9906375