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Ring-Opening of Glycidyl Derivatives by Silanes Mediated by Ti(O-*i*-Pr)$_4$ or Al(O-*i*-Pr)$_3$: Access to Versatile C_3 Building Blocks.

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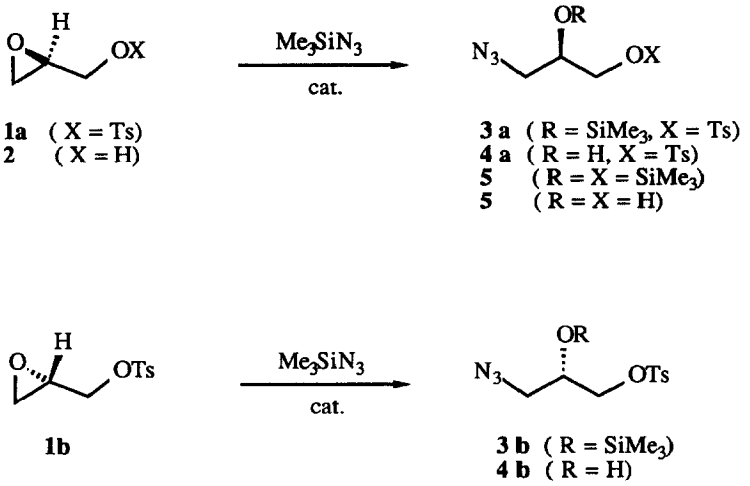
Abstract: Ring-opening of chiral glycidol or glycidyl tosylate by Me_3SiN_3 or Me_3SiCN catalyzed by Ti(O-*i*-Pr)$_4$ or Al(O-*i*-Pr)$_3$ occured in a regiospecific manner and with very high stereoselectivity, leading to new trifunctionalized chiral building blocks. The enantiomeric excess of the ring-opened products was 90-95 %, as determined by ^{1}H NMR of the Mosher ester derivatives, indicating that there was not significant loss of optical purity during the ring-opening. This methodology was applied for the one-pot synthesis of (*R*)-1-azido-3-naphthyloxy-2-hydroxypropane in 94 % ee, a precursor of analogs of propanolol.

Glycidol and related C_3-synthons have found widespread synthetic utility as chiral building blocks for asymmetric synthesis.[1] Noteworthy are the ease of preparation of these compounds and particularly the crystalline derivatives, and now their commercially avaibility in optically active form.[2] Stœchiometric amounts of Ti(O-*i*-Pr)$_4$ mediated the regio- and stereoselective attack of a variety of nucleophiles at C-3 of 2,3-epoxy alcohols under mild conditions.[3] However, this process failed to afford the desired opening of glycidyl derivatives without a free hydroxyl function like glycidyl tosylates. Recently, it was shown that ring-opening of glycidyl tosylates occured with high regio- and stereoselectivity with alcohols when BF_3 etherate was used as the catalyst.[4]

Following our continuing interest in the ring-opening of epoxides with trimethylsilyl compounds in the presence of a catalytic amount of Ti(O-*i*-Pr)$_4$ or Al(O-*i*-Pr)$_3$,[5] we report here the very high stereoselectivity observed in the ring-opening of the chiral glycidyl derivatives using these systems, leading to new trifunctional chiral building blocks.

Results and Discussion:

Ring-opening reactions of (*R*)- and (*S*)-**1** and (*R*)-**2** by Me_3SiN_3 with catalytic amounts of Ti(O-*i*-Pr)$_4$ or Al(O-*i*-Pr)$_3$ are outlined in Scheme 1 and the results are summarized in Table 1. As previously shown, ring-opening proceeded with very high regioselectivity, only the products **3a**, **3b** and **5**, arising from attack at C-1, being obtained with quite good chemical yields after purification.



Scheme 1

Table 1. Opening of Glycidyl Derivatives with Trimethylsilylderivatives in the Presence of Aluminium Isopropoxide and Titanium Isopropoxide.[a]

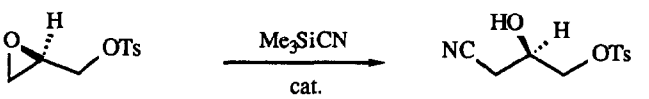
Entry	Epoxide	Silane	Catalyst	% Yield [b]	% ee [c]
1	**1a**	Me_3SiN_3	Ti(O-*i*-Pr)$_4$	83	93
2	**1a**	Me_3SiN_3	Al(O-*i*-Pr)$_3$	77	92
3	**1b**	Me_3SiN_3	Ti(O-*i*-Pr)$_4$	58	90
4	**1b**	Me_3SiN_3	Al(O-*i*-Pr)$_3$	50	93
5	**2**	Me_3SiN_3	Ti(O-*i*-Pr)$_4$	69	90
6	**2**	Me_3SiN_3	Al(O-*i*-Pr)$_3$	70	90
7	**1a**	Me_3SiCN	Ti(O-*i*-Pr)$_4$	70 [d]	85
8	**1a**	Me_3SiCN	Al(O-*i*-Pr)$_3$	40 [d]	90

[a] Ring-opening conditions are described in the Experimental Section.
[b] The percent yield refers to the product obtained after work-up and flash-chromatography.
[c] The % ee was determined by 300 MHz ^{1}H NMR analysis of the crude (*R*)-MTPA ester as described in the Experimental Section.
[d] The percent yield refers to the hydrolyzed product.

To determine the enantiomeric excess (ee) of the ring-opened products **3a** and **3b**, and so the stereoselectivity of the reaction, **3a** and **3b** were desilylated and the (*R*)-α-methoxy-α-(trifluoromethyl)phenyl acetic acid [(*R*)-MTPA] esters were prepared.[6] The diastereoisomeric ratio of the resulting mixture was analyzed by ^{1}H NMR (300 MHz). Figure 1A shows the ^{1}H NMR spectrum (δ 7.6-7.9) of (*R*)-MTPA ester of *rac*-**3**; the aromatic protons ortho to the -SO_2- group appear as a doublet for each diastereoisomer and show base-line separation.The lower field doublet (δ 7.76) is assigned to enantiomer **3a** and the higher-field doublet (δ 7.70) to **3b**. Integration of the two doublets in 1B and 1C gives a 95:5 ratio of the two diastereisomers, indicating that the optical purities of **3a** and **3b** are about 90-93 %, depending about the catalyst used. As we started from compound **1a** and **1b** having respectively 93 and 95 % ee, the ring-opening proceeded with very high stereoselectivity whatever the catalyst used.

For the determination of the optical purity of **5**, this compound was desilylated, and the bis-(*R*)-MTPA esters of **6** and *rac*-**6** were prepared. Figure 2A shows that the two CH_2-OMTPA signals exhibited by the bis-Mosher ester of *rac*-**6** are separated in the region δ 4.3-4.8. As the A proton doublet of the AB quartet of each diastereoisomeric CH_2-OMTPA group is readily separated (δ 4.58 and 4.70) and not the B proton doublet, the determination of the diastereomeric purity, and so the enantiomeric purity, was based on the A part. The integration of the signals in Figure 2B indicated 90 % ee for **6**. So, as we started from compound **2** with 90 % ee, the ring-opening of (*R*)-glycidol **6** proceeded without any significant loss of chiral purity.

Homologation by one carbon atom of chiral glycidyl tosylates would give ready access to important β-hydroxy butyric acids. To our knowledge, successful selective epoxide opening was only obtained using Nagata's[7] reagent, Et_2AlCN.[2b] However, epoxide ring-opening and homologation to (*R*)-**7** by introduction of a nitrile function was accomplished by treatment of **1a** with Me_3SiCN and a catalytic amount of Ti(O-*i*-Pr)$_4$ or Al(O-*i*-Pr)$_3$ (Scheme 2). The optical purity of (*R*)-**7** was analyzed by ^{1}H NMR of the (*R*)-MTPA ester. Figure 3A shows the ^{1}H NMR spectrum (δ 2.7-2.9) of *rac*-**7**; the CH_2-CN protons appear as a doublet at δ 2.77 in one diastereisomer, and as two doublets at δ 2.82 and 2.83, due probably to the presence of two rotamers, in the other diastereoisomer. Figure 3B shows the ^{1}H NMR observed in the ring-opening of (*R*)-**1a**; the integration of the two signals indicated 85 % and 90 %, respectively for Ti(O-*i*-Pr)$_4$ and Al(O-*i*-Pr)$_3$. As we started from compound **1a** with 93 % ee, the observed ring-opening using Me_3SiCN is again highly stereoselective, but a little lower than in the case of Me_3SiN_3.



1a **7**

Scheme 2

Finally we used this ring-opening for the "one-pot" synthesis of (*S*)-1-azido-3-naphtyloxy-2-hydroxy propane **8**, a precursor of propanolol derivatives (Scheme 3). Ring-opening of (*S*)-**1b** by Me_3SiN_3 in the presence of a catalytic amount of Ti(O-*i*-Pr)$_4$ followed by the treatment of the crude mixture with α-naphtoxysodium gives after hydrolysis compound **8** with 72 % overall yield. The optical purity of this compound was determined by ^{1}H NMR of its (*R*)-MTPA ester. Figure 4A shows the ^{1}H NMR spectrum (δ 4.2-4.4) of *rac*-**8**; the -CH_2O- protons appear as a doublet for each diastereoisomer respectively at 4.28 and 4.40 ppm. Figure 4B shows the

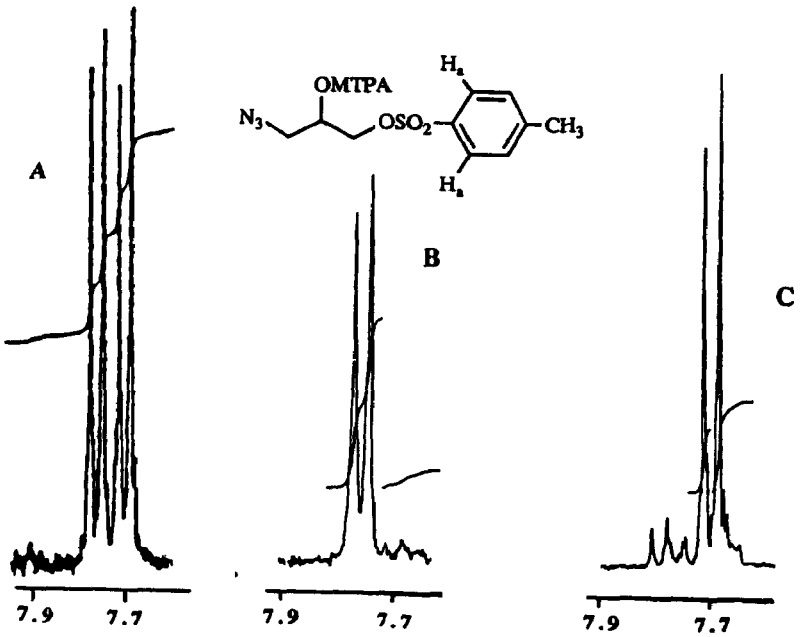


Figure 1. ^{1}H NMR spectra (300 MHz) of the (*R*)-MTPA esters of tosylate 4 corresponding to the aromatic proton H_a: (A) 1:1 mixture of (*R*)-**4a** and (*S*)-**4b** ; (B) (*R*)-**4a** ; (C) (*S*)-**4b** .

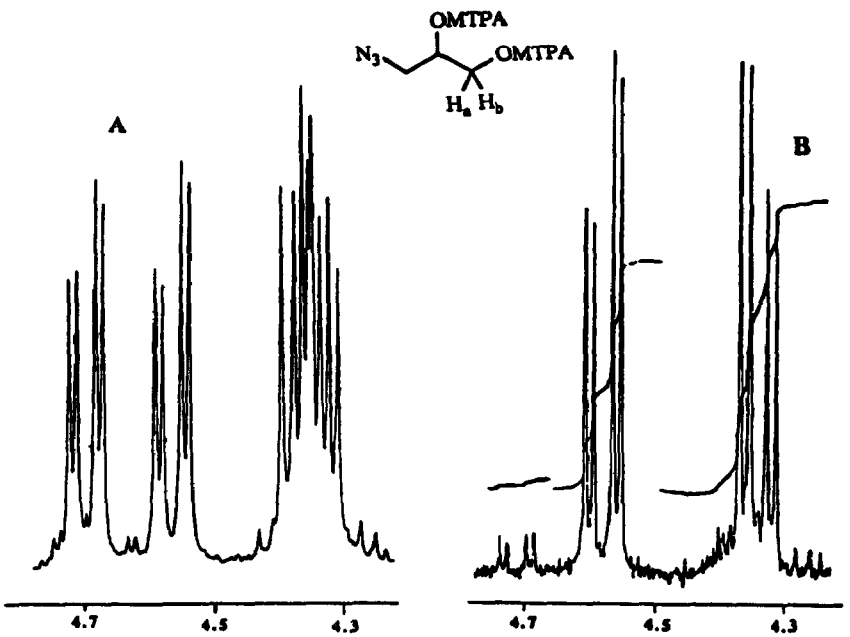


Figure 2. ^{1}H NMR spectra (300 MHz) of the bis-(*R*)-MTPA esters of diol **6** corresponding to the H_a and H_a protons: (A) 1:1 mixture of (*R*)-**6** and (*S*)-**6** ; (B) (*S*)-**6** .

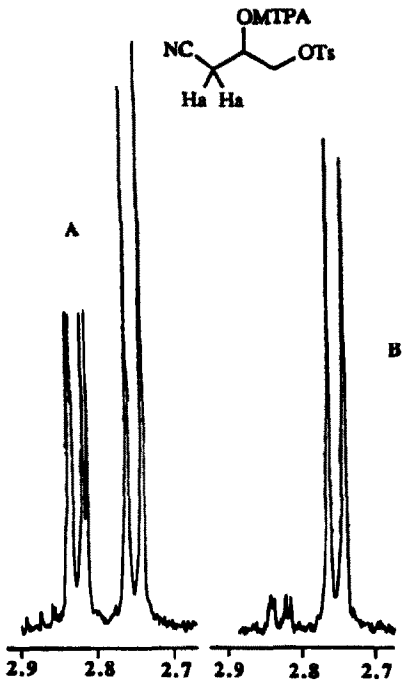


Figure 3

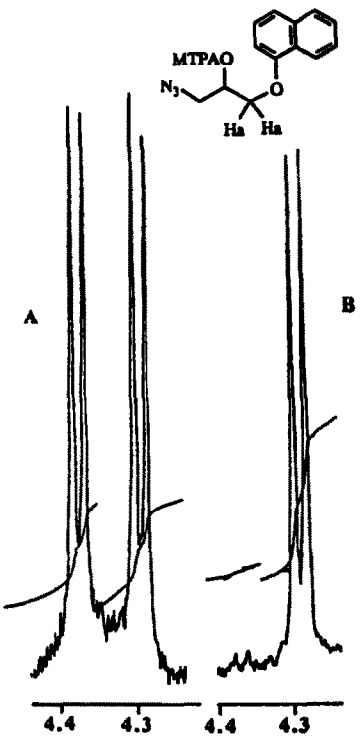
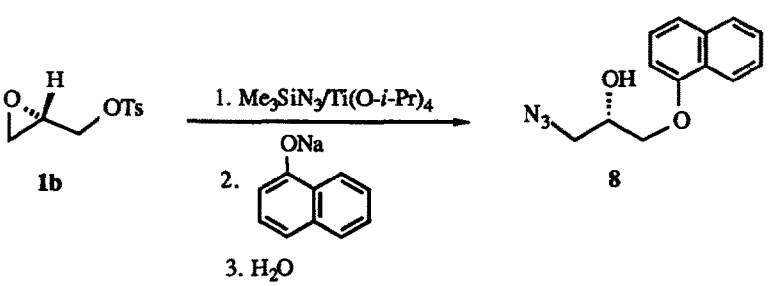


Figure 4

Figure 3. ^{1}H NMR spectra (300 MHz) of the (*R*)-MTPAesters of tosylate **7** corresponding to the CH_2CN protons: (A) 1:1 mixture of (*R*)-**7** and (*S*)-**7** ; (B) (*R*)-**7**.
Figure 4. ^{1}H NMR spectra (300 MHz) of the (*R*)-MTPA esters of azido alcohol **8** corresponding to the CH_2O protons: (A) 1:1 mixture of (*R*)-**8** and (*S*)-**8** ; (B) (*S*)-**8**.

^{1}H NMR observed in the ring-opening of **1b**; the integration of the two signals indicated 94 % ee for (*S*)-**8**, indicating that the two-steps reaction occurs without loss of optical purity.



Scheme 3

Conclusion:

In summary, opening of (*R*)- and (*S*)-glycidol derivatives by Me_3SiN_3 or Me_3SiCN catalyzed by Ti(O-*i*-Pr)$_4$ or Al(O-*i*-Pr)$_3$ proceeds with regiospecificity and very high stereoselectivity. These derivatives are precursors of new functionalized optically active C_3 building blocks. The application of this methodology to the synthesis of biologically active compounds is in progress in our laboratory.

Experimental Section:

Column chromatography was carried out on silica gel GF_{254} (230-400 mesh Merck). Infrared spectra were obtained using a Perkin-Elmer 681 instrument. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. ^{1}H NMR spectra were recorded on either a Bruker AM 300 (300 MHz) or a Bruker W 80 (80 MHz) in $CDCl_3$ solution, the δ values calculated being based on δ 7.26 for $CHCl_3$ for the silylated products; ^{13}C-NMR spectra were obtained at 74.45 MHz on a Bruker AM 300 spectrometer, the δ values calculated being based on δ 77.0 ppm for $CDCl_3$ (central resonance) for the silylated products. All solvents were distilled from an appropriate drying agent and stored under an atmosphere of nitrogen. All air-sensitive reactions were performed under an atmosphere of nitrogen. Trimethylsilyl azide, titanium isopropoxide, aluminium isopropoxide, (*R*)-(-)-glycidyl tosylate **1a** {$[\alpha]^{19}_D$ -17.3 (*c* 2.7, chloroform), corresponding to 93 % ee}, (*S*)-(+)-glycidyl tosylate **1b** {$[\alpha]^{19}_D$ +17.7 (*c* 2.7, chloroform), corresponding to 95 % ee}, and (*R*)-(+)-glycidol **2** {$[\alpha]^{18}_D$ +12 (neat), corresponding to 91 % ee} are commercially available (Aldrich).

(*R*)-1-Azido-2-trimethylsilyloxy-3-tosyloxypropane 3a. To a mixture of Ti(O-*i*-Pr)$_4$ (11.4 mg, 0.04 mmol, 0.04 equiv) and $MeSiN_3$ (141 mg, 1.3 mmol, 1.3 equiv) in 3 mL of tetrahydrofuran was added the epoxide **1a** (228 mg, 1 mmol, 1 equiv). After 4 days at 40 °C, the catalyst was removed by flash-chromatography using a mixture of hexane and ethyle acetate (5:1) as the eluent to give 280 mg (83 %) of **3a**. $[\alpha]^{25}_D$ +10.4 (*c* 1.5, chloroform); IR (neat) ν 2090 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 9H, $SiMe_3$), 2.36 (s, 3H, CH_3), 3.12 (dd, *J* = 12.8, 5.5 Hz, 1H, H-1), 3.19 (dd, *J* = 12.8, 3.8 Hz, 1H, H-1'), 3.86 (dd, *J* = 9.3, 6.3 Hz, 1H, H-3), 3.88 (dd, *J* = 9.3, 4.7 Hz, 1H, H-3), 3.93 (m, 1H, H-2), 7.27 (d, 2H, Ar), 7.70 (d, 2H, Ar); ^{13}C NMR (75.45 MHz, $CDCl_3$) δ - 0.4 ($SiMe_3$), 21.4 (CH_3), 53.1 (C-1), 69.2 (C-2), 70.1 (C-3), 127.7, 129.7, 132.3, 144.9 (C_6H_4). Anal. Calcd for $C_{13}H_{21}N_3O_4SSi$: C, 45.46; H, 6.16. Found: C, 45.48; H, 6.23.

In the case of the ring-opening catalyzed by Al(O-*i*-Pr)$_3$, a mixture of Al(O-*i*-Pr)$_3$ (30 mg, 0.15 mmol, 0.15 equiv) and $MeSiN_3$ (220 mg, 1.9 mmol, 1.9 equiv) in 2 mL of dichloromethane was stirred at room temperature for 2 h. The epoxide **1a** (228 mg, 1 mmol, 1 equiv) was added to the mixture and the solution was stirred at 40 °C for 3 days. The product **3a** was obtained as described above in 77 % yield.

(*S*)-1-Azido-2-trimethylsilyloxy-3-tosyloxypropane 3b. This title compound was prepared from **1b** in 58 % yield [Ti(O-*i*-Pr)$_4$] or 50 % [Al(O-*i*-Pr)$_3$] by the same procedure used to prepare **3a**. $[\alpha]^{25}_D$ -10.4 (*c* 1.5, chloroform); IR, ^{1}H and ^{13}C NMR were identical with those obtained for (*R*)-**3a**.

General Procedure for Preparation of Mosher Esters. A solution of **3a** (or **3b**) (1.7 mmol) in 10 mL of methanol containing a trace of HCl was stirred at room temperature for 4 h. After neutralisation using Amberlite IRA 68 (20-50 mesh), removal of the solvent gave the crude hydrolyzed product **4a** (or **4b**) in quantitative yield. To 20 mg (0.07 mmol) of the crude azido alcohol [**4a** or **4b**] in 1 mL of pyrydine was added 50 µL of neat (*R*)-(+)-MTPA chloride. The mixture was stirred at 50 °C for 12 h. Ether was then added (10 mL), the ether layer was washed with water (3x5 mL) and dried (Na_2SO_4). Concentration afforded the crude

Mosher ester.

Mosher Ester of 4a. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H, $CH_3C_6H_4$-), 3.52 (s, 3H, CH_3O-), 3.40-3.60 (m, 2H, H-1), 4.17 (dd, *J* = 11.0, 5.8 Hz, 1H, H-3), 4.23 (dd, *J* = 11.0, 3.8 Hz, 1H, H-3'), 5.29 (m, 1H, H-2), 7.35 (d, *J* = 8.1Hz, 2H, Ar), 7.4-7.5 (m, 5H, Ar), 7.76 (d, *J* = 8.3 Hz, 2H, Ar).

Mosher Ester of 4b. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45 (s, 3H, $CH_3C_6H_4$-), 3.50 (s, 3H, CH_3O-), 3.55 (dd, *J* = 13.3, 6.1 Hz, 1H, H-1), 3.62 (dd, *J* = 13.3, 4.6 Hz, 1H, H-1'), 4.08 (dd, *J* = 11.0, 5.6 Hz, 1H, H-3), 4.16 (dd, *J* = 11.0, 4.3 Hz, 1H, H-3'), 5.30 (m, 1H, H-2), 7.32 (d, *J* = 8.1 Hz, 2H, Ar), 7.4-7.5 (m, 5H, Ar), 7.70 (d, *J* = 8.3 Hz, 2H, Ar).

(*R*)-1-Azido-2,3-dihydroxypropane 6. Ring-opening of (*R*)-glycidol **2** using the procedure described in the presence of 2.6 equiv of Me_3SiN_3 gave the (*R*)-1-azido-2,3-bis(trimethylsilyloxy)propane **5** which was immediatly hydrolyzed in methanol (5 mL) containing a trace of HCl. Removal of the solvent gave a residue that was purified by flash-chromatography (elution with 2:1 AcOEt/hexane) to yield compound **6** (70 %). $[\alpha]^{20}_D$ +0.69 (*c* 1, chloroform); IR (neat) ν 3400, 2100 cm^{-1}; ^{1}H NMR (80 MHz, $CDCl_3$) δ 3.4 (m, 3H), 3.7 (m, 4H).

Bis-Mosher Ester of *rac*-6 and (*R*)-6. To a solution of the diol **6** (0.15 mmol) in 2 mL of pyridine was added 80 µL of neat (*R*)-(+)-MTPA chloride. After stirring at 50 °C for 12 h., work-up was as described above. ^{1}H NMR (300 MHz, $CDCl_3$) of **bis-Mosher ester of (*R*)-6**: δ 3.41 (bs, 3H, CH_3O-), 3.49 (bs, 3H, CH_3O-), 3.49 (dd, *J* = 13.1, 6.5 Hz, 1H, H-1), 3.55 (dd, *J* = 13.1, 5.0 Hz, 1H, H-1'), 4.34 (dd, *J* = 12.4, 4.4 Hz, 1H, H-3), 4.58 (dd, *J* = 12.4, 3.7 Hz, 1H, H-3'), 5.35 (m, 1H, H-2), 7.3-7.5 (m, 10H, Ar).^{1}H NMR (300 MHz, $CDCl_3$) of **bis-Mosher ester of (*S*)-6** (determined on *rac*-**6a**): δ 3.39 (bs, 3H, CH_3O-), 3.48 (bs, 3H, CH_3O-), 3.35-3.55 (m, 2H, H-1), 4.37 (dd, *J* = 12.5, 5.5 Hz, 1H, H-3), 4.70 (dd, *J* = 12.5, 3.4 Hz, 1H, H-3'), 5.35 (m, 1H, H-2), 7.3-7.5 (m, 10H, Ar).

(*R*)-1-Cyano-2-hydroxy-3-tosyloxypropane 7. To a solution of 0.23 g (1 mmol) of (*R*)-**1a** in 3 mL of CH_3CN were added 5.7 mg (0.02 mmol) of Ti(O-*i*-Pr)$_4$ and 19.8 mg (2 mmol) of Me_3SiCN. After the mixture was stirred at 60 °C for 6 days, 2 mL of water containing a trace of HCl was added. The solvent was removed under reduced pressure, and the residue was extracted with 20 mL of ether; evaporation of the solvent followed by flash-chromatography (elution with 2:3 hexane/EtOAc) gave 178 mg (70 % overall yield) of compound **7** as an oil; $[\alpha]^{25}_D$ + 2.7 (*c* 1, chloroform).

In the case of ring-opening using Al(O-*i*-Pr)$_3$, the catalyst (20.4 mg, 0.1 mmol) and Me_3SiCN (19.8 mg, 2 mmol) were stirred in 3 mL CH_3CN for 2h; after addition of the epoxide (0.23 g, 1 mmol), the mixture was allowed to stirr at 50 °C for 10 days. The same treatment gave 102 mg (40 % overall yield) of compound (*R*)-**7** as an oil; $[\alpha]^{25}_D$ + 2.4 (*c* 0.5, chloroform).

IR (neat) ν 3400, 2250 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.42 (s, 3H, CH_3), 2.54 (dd, *J* = 16.9, 6.5 Hz, 1H, H-1), 2.61 (dd, *J* = 16.9, 5.4 Hz, 1H, H-1'), 4.00 (dd, *J* = 10.3, 3.2 Hz, 1H, H-3), 4.00 (bs, 1H, OH), 4.03 (dd, *J* = 10.3, 5.1 Hz, 1H, H-3'), 4.18 (m, 1H, H-2), 7.30 (d, 2H, Ar), 7.70 (d, 2H, Ar) in agreement with the litterature[8]; ^{13}C NMR (75.45 MHz, $CDCl_3$) δ 21.8 (CH_3), 22.3 (C-1), 65.2 (C-2), 69.5 (C-3), 116.8 (CN), 127.9, 130.1, 131.8, 145.6 (Ar).

Mosher Ester of (*R*)-7. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.48 (s, 3H, CH_3), 2.77 (d, *J* = 6.1 Hz, 2H, H-1), 3.46 and 3.53 (2xbs, 3H, CH_3O- corresponding to two rotamers), 4.05- 4.26 (m, 2H, H-3), 5.46 (m, 1H, H-2), 7.2-7.8 (m, 9H, Ar). **Mosher Ester of (*S*)-7** (determined on the racemic mixture of 7). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.48 (s, 3H, CH_3), 2.82 and 2.83 (2xd, *J* = 6.3, 6.3 Hz, 2H, H-1 corresponding

to two rotamers), 3.53 (bs, 3H, C*H*$_3$O-), 4.05- 4.26 (m, 2H, H-3), 5.46 (m, 1H, H-2), 7.2-7.8 (m, 9H, Ar).

(*S*)-1-Azido-3-naphtyloxy-2-hydroxypropane 8. To a solution of 1g (4mmol) of (*S*)-**1b** in 5 mL of tetrahydrofuran under argon were added 79.6 mg (0.28 mmol) of Ti(O-*i*-Pr)$_4$ and 0.92 g (8 mmol) of Me_3SiN_3. After the mixture was stirred at 50 °C for 4 days, a solution of 1.2 g (8 mmol) of α-naphtoxysodium in 5 mL of tetrahydrofuran was added and the mixture was allowed to stirr at room temperature for 2 days. After hydrolysis using 5 mL of water containing a trace of HCl, the solvent was removed under reduced pressure to give a residue which was extracted by 30 mL of ether. Evaporation of the solvent followed by flash-chromatography (elution with 3:1 hexane/EtOAc) gave 700 mg (72 % overall yield) of compound (*S*)-**8** as an oil; $[\alpha]^{25}_D$ - 12.4 (*c* 1, chloroform): IR (neat) ν 3400, 3060, 2100 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.50 (s, 1H, OH), 3.62 (dd, *J* = 12.6, 6.0 Hz, 1H, H-1), 3.68 (dd, *J* = 12.6, 4.6 Hz, 1H, H-1'), 4.20 (d, *J* = 4.9 Hz, 2H, H-3), 4.33 (ddt, *J* = 6.0, 4.6, 4.9 Hz, 1H, H-2), 6.85 (d,1H, Ar), 7.40 (d, 1H, Ar), 7.55 (m, 3H, Ar), 7.85 (d, 1H, Ar), 8.25 (d, 1H, Ar); ^{13}C NMR (75.45 MHz, $CDCl_3$) δ 53.7 (C-1), 69.2 (C-3), 69.5 (C-2), 105.1, 121.1, 121.5, 125.4, 126.6, 127.6, 127.7, 134.5, 153.8 (Ar). Anal. Calcd for $C_{13}H_{13}N_3O_2$: C, 64.18; H, 5.39. Found: C, 64.44; H, 5.83.

Mosher Ester of (*S*)-8. ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.55 (bs, 3H, C*H*$_3$O-), 3.79 (dd, *J* = 13.1, 6.1 Hz, 1H, H-1), 3.84 (dd, *J* = 13.1, 4.5 Hz, 1H, H-1'), 4.28 (d, *J* = 5.0 Hz, 2H, H-3), 5.65 (ddt, *J* = 6.1, 4.5, 5.0 Hz, 1H, H-2), 6.70 (d, 1H, Ar), 7.1-7.9 (m, 3H, Ar), 8.09 (d, 1H, Ar), 8.35 (d, 1H, Ar).**Mosher Ester of (*R*)-8** (determined on the racemic mixture of **8**). ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.55 (bs, 3H, C*H*$_3$O-), 3.6-3.8 (m, 2H, H-1), 4.4 (d, *J* = 4.8 Hz, 2H, H-3), 5.65 (m, 1H, H-2), 6.8 (d, 1H, Ar), 7.1-7.9 (m, 3H, Ar), 8.19 (d, 1H, Ar), 8.40 (d, 1H, Ar).

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