Catalytic Asymmetric Synthesis of New Halogenated Chiral Synthons

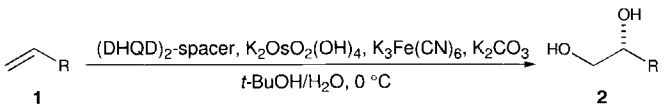
Koen P. M. Vanhessche and K. Barry Sharpless*

Abstract: Two-step and practical asymmetric syntheses of enantiomerically pure 4-trifluoromethyl-2,2-dioxo-1,3,2-dioxathiolane and 4-trichloromethyl-2,2-dioxo-1,3,2-dioxathiolane (>98% *ee*) have been achieved. Catalytic asymmetric dihydroxylation (AD) of 3,3,3-trifluoropropene and 3,3,3-trichloropropene, respectively, is followed by direct cyclic sulfate formation by reaction with sulfuryl chloride. Opening of the cyclic sulfates with various nucleophiles provides easy access to important chiral synthons.

Keywords
asymmetric catalysis · chiral synthons · cyclic sulfates · dihydroxylations · organofluorine compounds

Introduction

The high level of enantioselectivity and practicality reached in the Os-catalyzed asymmetric dihydroxylation (AD) of olefins has led to numerous synthetic applications.[1] Among chiral intermediates, C_3 and C_4 synthons have proven especially useful.[2] This fact along with the growing interest in fluorinated compounds in both the pharmaceutical[3] and material science[4] fields motivated us to investigate the synthesis of halogenated C_3 building blocks by means of the AD process (Scheme 1).



Scheme 1. Asymmetric dihydroxylation of propene analogues. Spacers: phthalazine (PHAL) or pyrimidine (PYR). DHQD = dihydroquinidinyl.

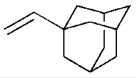
Results and Discussion

A number of 3,3,3-trisubstituted propene analogues were screened as AD substrates and the results with both phthalazine (PHAL) and pyrimidine (PYR) ligands are shown in Table 1.

Interestingly, the results with the pyrimidine (PYR) ligand seem to follow a simple steric trend: as the volume of the R substituent[6] increases, so does the enantioselectivity with the PYR ligand, in accord with earlier findings involving branching in that substituent.[7] Starting with 49% *ee* for propene (**1a**), the enantioselectivity increases rapidly, reaching 97% for 1-vinyladamantane (**1f**).[8]

In contrast, there is no clear trend with the phthalazine (PHAL) ligand where the outcome appears to be sensitive to an interplay of steric and electronic factors (e.g. substrate dipole?). Propene is dihydroxylated in 35% *ee*. The enantioselectivity rises to 63% for 3,3,3-trifluoropropene[9, 10] and reaches a maximum value of 70% for 3,3,3-trichloropropene.[10] When the branched substituents become larger, *ee* values drop again as seen for *tert*-butylethylene (**1d**, 64% *ee*)[7] and trimethylvinylsi-

Table 1. AD of 3,3,3-trisubstituted propene analogues.

	Olefin [a]	*ee* [%] [b] (config) [c] (DHQD)$_2$-PHAL [d]	(DHQD)$_2$-PYR [d,e]	R-group Volume [Å^3] [f]
1a	CH_3	35 (*R*)	49 (*R*)	26.9
1b	CF_3	63 (*S*)	64 (*S*)	37.6
1c	CCl_3	70 (*S*)	86 (*S*)	74.6
1d	$C(CH_3)_3$	64 (*R*)	92 (*R*)	77.7
1e	$Si(CH_3)_3$	46 (*R*)	89 (*R*)	91.9
1f		87 (*R*)	97 (*R*)	145.5

[a] Except for **1c**, for which the *buffered* AD mix [5] was employed (requiring 3 equiv of $NaHCO_3$ in addition to the usual 3 equiv K_2CO_3), all reactions were carried out with 3 equiv $K_3Fe(CN)_6$–K_2CO_3 and a 1 mol% ligand/0.5 mol% $K_2OsO_2(OH)_4$ catalyst loading in *t*BuOH/H_2O (1:1) at 0 °C. [b] *ee* determined by HPLC or GLC analysis of the diols or their derivatives; see Experimental Section. [c] The absolute configurations of the diols were determined by comparison of their optical rotations with literature values; see Experimental Section. [d] Only the DHQD-based ligands were used in this study. [e] All diol products, except 1,2-propanediol (**2a**), were raised to enantiopurity by a single recrystallization; see Experimental Section. [f] The volume of the R group was calculated with a modified MM2 force field (MacroModel V3.5x) [6].

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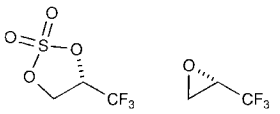
lane (**1e**, 46% *ee*),[11] presumably owing to disruption of the attractive interactions within the chiral binding pocket.[12] However, the high *ee* value (87% *ee*) found for 1-vinyladamantane (**1f**) clearly counters the above trend and is perhaps due to offsetting attractive interactions with the ligand at a greater distance from the reaction zone.

The synthetic utility of enantiopure 1,2-propanediol (**2a**)[13] and the use of the other diols in Table 1 [e.g. 1-trimethylsilyl-1,2-ethanediol (**2e**),[11] 1-(1-adamantyl)-1,2-ethanediol (**2f**),[8] and 3,3-dimethyl-1,2-butanediol[14]] as chiral auxiliaries have been previously reported. Hence, we focused on evaluating the potential of 3,3,3-trifluoro-1,2-propanediol (**2b**)[15] and 3,3,3-trichloro-1,2-propanediol (**2c**)[16] as chiral synthons.



3 **4**

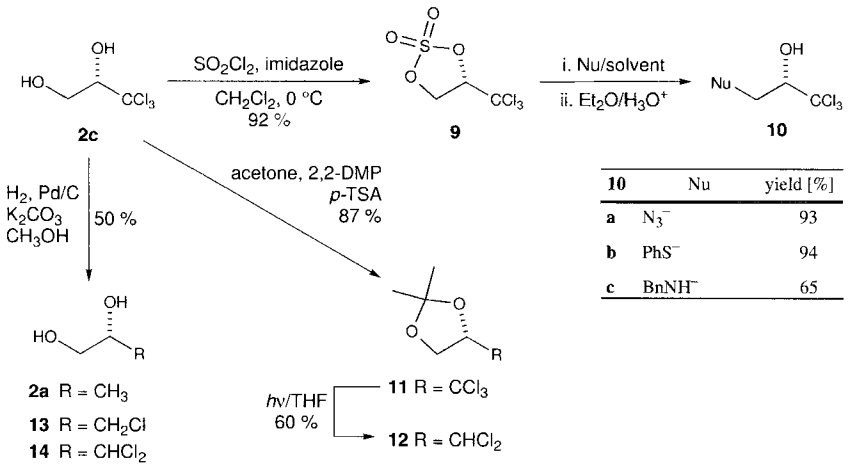
Several syntheses of the important fluorinated chiral building block (trifluoromethyl)oxirane (**4**), have appeared recently.[17, 18] This trifluoro analogue of propylene oxide undergoes regiospecific nucleophilic opening providing direct access to a series of substituted enantiomerically pure trifluoromethylcarbinol compounds.[17, 18] We report here that cyclic sulfate **3** is an attractive[19] synthetic equivalent of **4**.

The effectiveness of cyclic sulfates as epoxide equivalents has been amply demonstrated,[20] but they are used relatively infrequently, probably owing to the lack of direct preparative procedures of broad scope.[21] Acyclic 1,2-diols usually require a two-step procedure for their conversion to the corresponding cyclic sulfates (e.g. cyclic sulfite formation followed by ruthenium-catalyzed oxidation).[22] However, direct sulfate formation can often be achieved when the 1,2-diol unit is *syn* in a 5- or 6-membered ring, especially in carbohydrate systems.[23]

Treatment of diol **2b** (>98% *ee*)[24] with sulfuryl chloride and imidazole in dichloromethane at −20 °C afforded the dense ($\rho = 1.70\ g\,cm^{-3}$!) crystalline cyclic sulfate **3** in 82% yield (Scheme 2).[25] Presumably, the competing S_N2 displacement at carbon by chloride in the reactive intermediate(s) (C-OSO_2Cl) is suppressed by the strong electron withdrawing effect of the CF_3 group. This imidazole/SO_2Cl_2 procedure[26] for direct formation of cyclic sulfates is also highly efficient for certain other vicinal diols bearing electron withdrawing groups [e.g. vide infra, 1,1,1-trichloro-2,3-propanediol (**2c**) and (*S,S*)-1,4-dichloro-2,3-butanediol (**7**)[27]]. However, simple vicinal diols such as 5,6-decanediol, 1,2-decanediol, and 1-adamantyl-1,2-ethanediol (**2f**) gave complex mixtures.

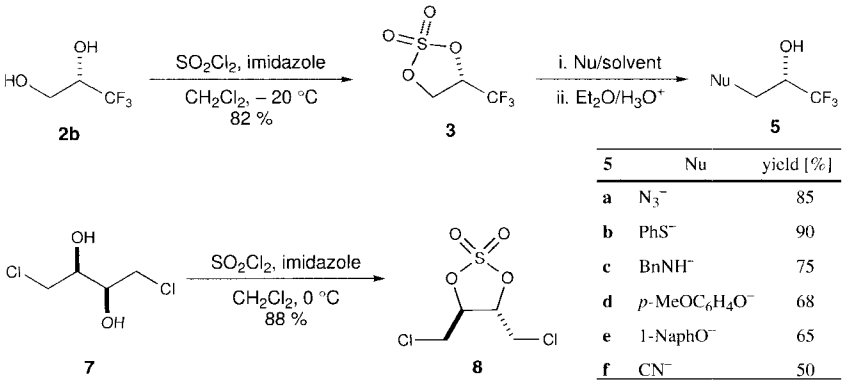
Reaction of cyclic sulfate **3** with a series of nucleophiles was studied (Scheme 2, **5a–f**). In all cases, nucleophilic opening took place exclusively at the terminal carbon atom. Azide (NaN_3) and thiophenoxide (NaSPh) both gave ring opening in excellent yield (85 and 90%, respectively). Benzylamine, *p*-methoxyphenoxide, and 1-naphthoxide afforded moderate yields (65–75%), while cyanide (NaCN) gave low yields (50%).

One recrystallization of the crude (86% *ee*) 3,3,3-trichloro-1,2-propanediol (**2c**) afforded enantiopure material (>98% *ee*).[28] Single-step sulfate formation under the above-mentioned conditions provided the crystalline cyclic sulfate **9**[29] in 92% isolated yield (Scheme 3). Nucleophilic opening of **9** was successful with NaN_3 (**10a**, 93%), NaSPh (**10b**, 94%), and benzylamine (**10c**, 65%), but reaction with other nucleophiles, such as CN^-, F^-, and $PhCOO^-$, led to decomposition, probably owing to the sensitivity of the trichloromethyl group towards reduction through attack of the nucleophile at a chlorine atom. The trichloromethylcarbinol moiety in **2c** and **10a–c** enables several further transformations[30] not readily available to the trifluoromethyl analogues **2b** and **5a–f**. Among the possibilities, we examined only the reductive removal of chlorine (Scheme 3). Catalytic hydrogenolysis[31] proved to be fast [10% Pd/C in methanol] yielding enantiopure (2*R*)-1,2-propanediol (**2a**) in 50% yield after distillation. Several attempts (Pt/C and Rh/Al_2O_3) to stop at the mono- or dichloride stage failed. On the other hand, selective monodechlorination was achieved by photo-



10	Nu	yield [%]
a	N_3^-	93
b	PhS^-	94
c	$BnNH^-$	65

Scheme 3. Reactions of 3,3,3-trichloro-1,2-propanediol (**2c**) (*p*-TSA = *p*-toluenesulfonic acid, 2,2-DMP = 2,2-dimethoxypropane).



5	Nu	yield [%]
a	N_3^-	85
b	PhS^-	90
c	$BnNH^-$	75
d	p-$MeOC_6H_4O^-$	68
e	1-$NaphO^-$	65
f	CN^-	50

Scheme 2. Syntheses of the cyclic sulfates of 3,3,3-trifluoro-1,2-propanediol (**2b**) and 1,4-dichloro-1,4-butanediol (**7**).

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chemical reduction[32] of the acetonide **11** in THF, giving the corresponding *gem*-dichloride **12** in 60% yield.

Selective electrochemical reductions of trichloromethylcarbinol-containing compounds have been well studied.[33] Electrochemical reduction of **2c** should enable one to obtain either 3-chloropropane-1,2-diol (**13**) or dichloro derivative **14**, which are formally glycidol and glyceraldehyde equivalents, respectively.[34] Reactions of alkyl trichloromethylcarbinols with nucleophiles under basic reaction conditions[30, 35] have been developed for the synthesis of optically active α-amino acids and α-hydroxy acids,[36] and may be applicable to derivatives such as **10a–c** in Scheme 3.

Conclusion

Practical preparations of the enantiopure 3,3,3-trifluoro- and 3,3,3-trichloro-1,2-propanediols (**2b** and **2c**) have been developed. The utility of these new C_3 chiral synthons is especially enhanced by their conversion to the corresponding cyclic sulfates (**3** and **9**) in a direct reaction with sulfuryl chloride.

Experimental Section

Materials and Methods: 3,3,3-Trichloropropene[37] and 3,3,3-trifluoropropene[38] were purchased from Coyote Chemicals and PCR, respectively. Propene, trimethylvinylsilane, 3,3-dimethylbutene, and sulfuryl chloride (97%) were all obtained from Aldrich. 1-Vinyladamantane was synthesized by Moffatt oxidation (SO_3–pyridine modification) of 1-adamantylmethanol (Aldrich) followed by Wittig methylenation. ^{1}H NMR spectra were recorded in $CDCl_3$ at 250 MHz (Bruker AC-250). Residual protic solvent $CHCl_3$ ($\delta_H = 7.26$) was used as internal reference. ^{13}C NMR spectra were recorded in $CDCl_3$ unless otherwise stated at 62.5 MHz, and the resonance of $CDCl_3$ ($\delta_C = 77.0$, t) was used as internal reference. FT-IR spectra were recorded on a Nicolet 510 FT-IR spectrometer. Flash column chromatography was performed on Merck Kieselgel 60 (230–400 mesh). Analytical thin-layer chromatography was performed with precoated glass-backed plates (Merck Kieselgel $60F_{254}$). HPLC was performed on Chiralcel *OB-H*, *OD*, or *OF* (25 cm × 4.6 mm i.d.) columns, and the products detected at 254 nm. GLC was performed on a J & W DB-5 (30 m × 0.32 mm i.d.) column.

(2*R*)-(−)-1,2-Propanediol [(−)-**2a**]: Propene gas[39] was bubbled for 30 min through a solution of $(DHQD)_2PHAL$ (390 mg, 1 mol%), $K_2OsO_2(OH)_4$ (92 mg, 0.5 mol%), $K_3Fe(CN)_6$ (49.4 g), and K_2CO_3 (20.7 g) in 1:1 *tert*-butyl alcohol/water (500 mL) at 0 °C. The mixture was stirred for 12 h at 0 °C. Sodium metabisulfite (40 g) was added slowly and stirring was continued for 2 h. The layers were separated and the aqueous layer was extracted with ethyl acetate (6 × 200 mL). The combined organic layers were washed with H_2SO_4 (5% aqueous solution, 100 mL) to extract the ligand, and the aqueous acid solution was reextracted with ethyl acetate (2 × 100 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (100 mL), dried over $MgSO_4$, and concentrated in vacuo yielding 2.9 g [47% yield based upon $K_3Fe(CN)_6$] of crude **2a**. The enantiomeric purity of the crude product was determined to be 36% *ee* by HPLC of the bisbenzoate derivative [Chiralcel OB-H column, 20% 2-propanol/hexane, 0.5 mL min^{-1}; (*R*)-**2a**: 19.4 min, (*S*)-**2a**: 27.1 min]. $[\alpha]_D^{23} = -10.7$ ($c = 6.5$ in H_2O) [lit.[40] enantiopure (−)-**2a**: −22 ($c = 7.5$ in H_2O)]; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.86$ (1H, ddq, $J = 7.9$, 6.4, 3.0 Hz), 3.57 (1H, dd, $J = 11.4$, 3.0 Hz), 3.35 (1H, dd, $J = 11.4$, 7.9 Hz), 1.12 (3H, d, $J = 6.4$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 68.2$, 67.7, 18.6.

(2*S*)-(−)-3,3,3-Trifluoro-1,2-propanediol [(−)-**2b**]: 3,3,3-Trifluoropropene gas[39] was bubbled for 20 min through a solution of $(DHQD)_2PHAL$ (470 mg, 1 mol%), $K_2OsO_2(OH)_4$ (110 mg, 0.5 mol%), $K_3Fe(CN)_6$ (59.2 g), and K_2CO_3 (24.8 g) in 1:1 *tert*-butyl alcohol–water (600 mL) at 0 °C. The mixture was stirred for 12 h at 0 °C. Sodium metabisulfite (50 g) was added slowly and stirring was continued for 2 h. The layers were separated and the aqueous layer was extracted with ethyl acetate (4 × 200 mL). The combined organic layers were washed with H_2SO_4 (5% aqueous solution, 100 mL) followed by saturated aqueous $NaHCO_3$ (100 mL), dried over $MgSO_4$, and concentrated in vacuo giving 9.2 g of crude **2b**. Distillation under reduced pressure (96 °C, 35 Torr) gave 8.8 g [75% yield based upon $K_3Fe(CN)_6$] of pure **2b**, which solidified upon standing. The enantiomeric purity of the crude product was determined to be 63% *ee* by HPLC of the bisbenzoate derivative [Chiralcel OD-column, 0.5% 2-propanol/hexane, 0.6 mL min^{-1}; (*S*)-**2b**: 16.9 min; (*R*)-**2b**: 19.4 min]. Recrystallization from dichloromethane yielded 5.3 g (45%) of enantiopure (>98% *ee*) (−)-**2b**. $[\alpha]_D^{23} = -12.3$ ($c = 4$ in MeOH) [lit.[18e] −10.95 ($c = 1.4$ in MeOH)]; m.p. 55 °C; b.p. 96 °C, 35 Torr; ^{1}H NMR (250 MHz, CD_3OD): $\delta = 3.96$ (1H, ddq, $J = 7.0$, 7.0, 4.0 Hz), 3.74 (1H, dd, $J = 11.8$, 3.9 Hz), 3.61 (1H, dd, $J = 11.8$, 7.0 Hz); ^{13}C NMR (62.5 MHz, [D$_6$]DMSO): $\delta = 124.2$ (q, $J_{C-F} = 282$ Hz), 70.4 (q, $J_{C-F} = 30$ Hz), 60.4; FT-IR (KBr): $\tilde{\nu} = 3550$–3220 (brs), 2954, 1381, 1277, 1177, 1138, 1068, 1038, 904, 856, 702, 609 cm^{-1}. Anal. Calcd for $C_3H_5F_3O_2$: C, 27.69; H, 3.85. Found: C, 27.63; H, 3.99.

(2*S*)-(−)-3,3,3-Trichloro-1,2-propanediol [(−)-**2c**]: 3,3,3-Trichloropropene (8.73 g; 60 mmol) was added to a solution of $(DHQD)_2PHAL$ (470 mg, 1 mol%), $K_2OsO_2(OH)_4$ (110 mg, 0.5 mol%), $K_3Fe(CN)_6$ (59.2 g), K_2CO_3 (24.8 g), and $NaHCO_3$ (15.1 g) in 1:1 *tert*-butyl alcohol–water (600 mL) at 0 °C. The mixture was stirred for 12 h at 0 °C. Sodium metabisulfite (75 g) was added slowly and stirring was continued for 2 h. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 200 mL). The combined organic layers were washed with H_2SO_4 (5% aqueous solution, 50 mL) followed by saturated aqueous $NaHCO_3$ (100 mL), dried over $MgSO_4$, and concentrated in vacuo giving 9.26 g (86%) of crude **2c**. The enantiomeric purity of the crude product was determined to be 86% *ee* by HPLC of the bisbenzoate derivative [Chiralcel OF column, 1% 2-propanol/hexane, 1 mL min^{-1}; (*R*)-**2b**: 10.8 min; (*S*)-**2b**: 13.0 min]. Recrystallization from dichloromethane/ethyl acetate (120 mL/15 mL) gave enantiomerically pure (>98% *ee*) (−)-**2c** as colorless needles (7.54 g, 70%). $R_f = 0.21$ (hexane/ethyl acetate 70/30). $[\alpha]_D^{23} = -29.7$ ($c = 2.3$ in EtOH); m.p. 110 °C (lit.[16] 84.6–85 °C for *rac*-**2c**); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 4.23$ (1H, dd, $J = 7.3$, 3.3 Hz), 4.12 (1H, dd, $J = 11.8$, 3.3 Hz), 3.86 (1H, dd, $J = 11.8$, 7.3 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 101.0$, 81.7, 61.5; MS (EI): *m/z*: 183, 181, 179, 154, 143, 130, 125, 116, 113 (100%), 107, 102, 97, 83, 79, 76; FT-IR (KBr): $\tilde{\nu} = 3457$ (brs), 3212 (brs), 2973, 1381, 1109, 1051, 893, 816, 781, 648 cm^{-1}. Anal. Calcd for $C_3H_5Cl_3O_2$: C, 20.07 and H, 2.78%. Found: C, 20.07 and H, 2.86%.

(2*R*)-(−)-3,3-Dimethyl-1,2-butanediol [(−)-**2d**]: see ref. [7,14].

(1*R*)-(+)-(Trimethylsilyl)-1,2-ethanediol [+)-**2e**]: Vinyltrimethylsilane (1.0 g, 10 mmol) was added to a solution of $(DHQD)_2PHAL$ (77.9 mg, 1 mol%), $K_2OsO_2(OH)_4$ (18.4 mg, 0.5 mol%), $K_3Fe(CN)_6$ (9.87 g), and K_2CO_3 (4.14 g) in 1:1 *tert*-butyl alcohol–water (100 mL) at 0 °C. The mixture was stirred for 12 h at 0 °C. Sodium metabisulfite (10 g) was added slowly and stirring was continued for 1 h. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with H_2SO_4 (5% aqueous solution, 15 mL), followed by saturated aqueous $NaHCO_3$ (20 mL), dried over $MgSO_4$, and concentrated in vacuo giving 1.12 g (83%) of crude **2e**. The enantiomeric purity of the crude product was determined to be 89% *ee* by GC analysis of the *bis*-(*R*)-MTPA derivative [DB-5 capillary column; 210 °C isothermal, (*R*)-**2e**: 33.3 min, (*S*)-**2e**: 34.3 min]. Recrystallization from hexane gave enantiopure (>98% *ee*) (+)-**2e** as colorless needles (715 mg, 55%). $R_f = 0.25$ (hexane/ethyl acetate 50/50); $[\alpha]_D^{23} = +1.8$ ($c = 1.1$ in CCl_4) [lit.[11a] +0.8 ($c = 0.1$ in CCl_4)]; m.p. 50 °C (*rac*-**2e** is an oil); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.74$ (1H, d, $J = 11.6$, 3.6 Hz), 3.67 (1H, dd, $J = 11.6$, 9.0 Hz), 3.44 (1H, dd, $J = 9.0$, 3.6 Hz), 3.15 (1H, brs), 2.90 (1H, brs), 0.05 (9H, s); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 67.7$, 65.1, −3.8; FT-IR (KBr): $\tilde{\nu} = 3356$, 2954, 1653, 1418, 1249, 1168, 1064, 996, 952, 839, 749 cm^{-1}. Anal. Calcd for $C_5H_{14}SiO_2$: C, 44.78 and H, 10.45%. Found: C, 44.82 and H, 10.13%.

(1*R*)-(+)-(1-Adamantyl)-1,2-ethanediol [(+)-**2f**]: 1-Vinyladamantane (810 mg, 5 mmol) was added to a solution of $(DHQD)_2PHAL$ (39 mg, 1 mol%), $K_2OsO_2(OH)_4$ (9.2 mg, 0.5 mol%), $K_3Fe(CN)_6$ (4.94 g), and K_2CO_3 (2.07 g) in 1:1 *tert*-butyl alcohol–water (50 mL) at 0 °C. The mixture was stirred for 12 h at 0 °C. Sodium metabisulfite (5 g) was added slowly and

stirring was continued for 30 min. The layers were separated and the aqueous layer was extracted with ethyl acetate (2 × 30 mL). The combined organic layers were washed with H_2SO_4 (5% aqueous solution, 10 mL) followed by saturated aqueous $NaHCO_3$ (20 mL), dried over $MgSO_4$, and concentrated in vacuo giving 834 mg (85%) of crude **2f**. The enantiomeric purity of the crude product was determined to be 97% *ee* by GC analysis of the *bis*-(*R*)-MTPA derivative [DB-5 capillary column; 250 °C isothermal; (*R*)-**2f**: 53.7 min, (*S*)-**2f**: 55.6 min]. Recrystallization from hexane/ethyl acetate (95/5) gave enantiopure (>98% *ee*) (+)-**2f**. $R_f = 0.32$ (hexane/ethyl acetate 50/50). $[\alpha]_D^{23} = +19.0$ ($c = 1.1$ in EtOH) [lit.[8] +19.2 ($c = 1.0$ in EtOH)]; m.p. 124–125 °C (lit.[8] 125–127 °C); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 3.74$ (1H, dd, $J = 10.9$, 2.9 Hz), 3.54 (1H, dd, $J = 10.9$, 9.4 Hz), 3.21 (1H, dd, $J = 9.4$, 2.9 Hz), 2.49 (2H, brs), 1.98 (3H, brs), 1.5-1.85 (12H, m). ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 80.0$, 62.2, 38.2, 37.1, 28.2. HRMS (FAB): Calcd: 219.1361 ($M + Na^+$); Found: 219.1353.

(4*S*)-(+)-4-Trifluoromethyl-2,2-dioxo-1,3,2-dioxathiolane [(+)-**3**]: Sulfuryl chloride (8.51 g, 5.06 mL, 63 mmol) was added dropwise to a cooled (−20 °C) solution of diol **2b** (7.8 g, 60 mmol) and imidazole (10.2 g, 150 mmol) in dichloromethane (100 mL). A precipitate formed gradually upon addition. When the addition was completed, the mixture was allowed to warm to room temperature. The mixture was further diluted with dichloromethane (100 mL). Sulfuric acid (5% aqueous solution, 15 mL) was added and the organic layer was separated. The organic phase was washed with saturated aqueous $NaHCO_3$ (25 mL) and brine, dried over $MgSO_4$, and concentrated in vacuo to give 9.91 g (86%) of crude **3**. Further purification by vacuum distillation (b.p. 48 °C, 2.4 Torr) gave 9.45 g (82%) of analytically pure (+)-**3** as an oil (*rac*-**3**, m.p. 34–35 °C). $[\alpha]_D^{23} = +17.0$ ($c = 2.2$ in CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 5.14$ (1H, ddq, $J = 7.1$, 5.7, 4.8 Hz), 4.90 (1H, dd, $J = 9.8$, 7.1 Hz), 4.79 (1H, dd, $J = 9.8$, 4.8 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 121.3$ (q, $J_{C-F} = 174$. Hz), 74.8 (q, $J_{C-F} = 23.1$ Hz), 66.0; FT-IR (KBr): $\tilde{\nu} = 1408$, 1289, 1219, 1165, 1069, 1028, 997, 951, 837, 800, 658 cm^{-1}. Anal. Calcd for $C_3H_3F_3SO_4$: C, 18.75; H, 1.56; and S, 16.67%. Found: C, 18.77; H, 1.52; and S, 16.77.

(2*S*)-(+)-1-Azido-3,3,3-trifluoro-2-propanol [(+)-**5a**]: A solution of cyclic sulfate **3** (1.15 g; 6 mmol) and sodium azide (780 mg, 12 mmol) in acetone (6 mL) and water (6 mL) was stirred for 4 h at room temperature. After removal of the solvent in vacuo, ether (10 mL) and sulfuric acid (20% aq. solution, 10 mL) were added, and the mixture was stirred for 30 min. Powdered potassium carbonate was added until neutral and the mixture was extracted with ether (2 × 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by bulb-to-bulb distillation yielding 792 mg (85%) of azido alcohol **5a** as an oil.[41] $[\alpha]_D^{23} = +30.0$ ($c = 1.8$ in MeOH) [lit.[18c] +12.87 ($c = 1.9$, MeOH)]; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 4.15$ (1H, m), 3.54 (2H, m), 2.98 (1H, d, $J = 6.2$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 123.7$ (q, $J_{C-F} = 281$ Hz), 69.9 (q, $J_{C-F} = 31.1$ Hz), 50.2; FT-IR (neat): $\tilde{\nu} = 3418$, 2942, 2110 (s), 1623, 1448, 1391, 1270, 1137, 1058, 944, 896, 850, 700, 655 cm^{-1}.

(2*S*)-(−)-3,3,3-Trifluoro-1-phenylthio-2-propanol [(−)-**5b**]: Cyclic sulfate **3** (403 mg, 2.1 mmol) was added slowly to a solution of thiophenol (242 mg, 2.2 mmol) and potassium *tert*-butoxide (246 mg, 2.2 mmol) in dry tetrahydrofuran (5 mL) at room temperature. The mixture was stirred for 2 h at ambient temperature and the solvent was then removed under reduced pressure. The residue was dissolved in ether (3 mL), and sulfuric acid (20% aqueous solution, 3 mL) was added. The mixture was then slowly neutralized with powdered potassium carbonate until neutral. The aqueous phase was extracted with ether (2 × 15 mL), washed with 2M NaOH (2 × 10 mL), followed by brine, and dried over $MgSO_4$. Concentration in vacuo afforded 570 mg (90%) of **5c** as an oil. $R_f = 0.33$ on silica gel (hexane/ethyl acetate 90/10). $[\alpha]_D^{23} = -67.6$ ($c = 1.6$ in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.37$ (5H, m), 3.98 (1H, m), 3.34 (1H, dd, $J = 14.3$, 2.8 Hz), 3.02 (1H, dd, $J = 14.3$, 10.0 Hz), 2.82 (1H, brs); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 130.8$, 129.4, 127.6, 124.3 (q, $J_{C-F} = 281$ Hz), 68.4 (q, $J_{C-F} = 31.3$ Hz), 35.3; FT-IR (neat): $\tilde{\nu} = 3444$, 3061, 1583, 1482, 1440, 1412, 1372, 1276, 1166, 1025, 1003, 866, 741 cm^{-1}. HRMS (EI): Calcd: 222.0326 (M^+); Found: 222.0319.

(2*S*)-(−)-1-Benzylamino-3,3,3-trifluoro-2-propanol [(−)-**5c**]: Benzylamine (470 μL, 4.31 mmol) was added slowly to a solution of cyclic sulfate **3** (413 mg, 2.15 mmol) in dry tetrahydrofuran (3 mL) at room temperature. After addition of the amine (exothermic), the mixture was stirred for 2 h at ambient temperature. The solvent was removed in vacuo, the residue dissolved in ether (10 mL), and sulfuric acid (20% aqueous solution, 5 mL) added. A precipitate formed immediately and the suspension was stirred for 1 h. The precipitate was filtered, washed with ether, and resuspended in sulfuric acid (20% aqueous solution). The suspension was heated at 85 °C. After 20 min the solution became clear. Heating was continued for 15 min. The mixture was then cooled to room temperature and slowly neutralized with powdered potassium carbonate until neutral. The aqueous phase was extracted with ether (30 mL), washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was recrystallized from hexane/ethyl acetate (80/20) yielding 352 mg (75%) of analytically pure **5c**. $R_f = 0.31$ on silica gel (hexanes/ethyl acetate 50/50); $[\alpha]_D^{23} = -8.3$ ($c = 1.6$ in $CHCl_3$); m.p. 102 °C; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 7.31$ (5H, m), 3.96 (1H, m), 3.83 (2H, s), 2.98 (1H, dd, $J = 13.0$, 6.0 Hz), 2.88 (1H, dd, $J = 13.0$, 4.7 Hz), 2.85 (1H, brs); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 138.8$, 128.7, 128.1, 127.5, 124.9 (q, $J_{C-F} = 281$ Hz), 67.7 (q, $J_{C-F} = 29.6$ Hz), 53.6, 46.8; FT-IR (KBr): $\tilde{\nu} = 3420$, 1653, 1559, 1266, 1130, 746 cm^{-1}. Anal. Calcd for $C_{10}H_{12}F_3NO$: C, 54.79; H, 5.48; and S, 6.39%. Found: C, 54.56; H, 5.34; and S, 6.36. HRMS (FAB): Calcd: 220.0949 ($M + H^+$); Found: 220.0942.

(2*S*)-(−)-1-(4-Methoxyphenyloxy)-3,3,3-trifluoro-2-propanol [(−)-**5d**]: Cyclic sulfate **3** (384 mg, 2 mmol) was added slowly to a solution of *p*-methoxyphenol (273 mg, 2.2 mmol) and potassium *tert*-butoxide (246 mg, 2.2 mmol) in dry tetrahydrofuran (3 mL) at room temperature. The mixture was stirred for 2 h at ambient temperature and the solvent then removed in vacuo. The residue was dissolved in ether (10 mL) and sulfuric acid (20% aqueous solution, 10 mL) was added. The mixture was then slowly neutralized with powdered potassium carbonate until neutral. The aqueous phase was extracted with ether (20 mL), washed with 2M NaOH (2 × 10 mL), followed by brine and dried over $MgSO_4$. Concentration in vacuo afforded 320 mg (68%) of **5d** as an oil. $R_f = 0.35$ on silica gel (hexane/ethyl acetate 90/10); $[\alpha]_D^{23} = -15.0$ ($c = 1.6$ in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 6.87$ (4H, m), 4.35 (1H, m), 4.21 (1H, dd, $J = 10.1$, 3.4 Hz), 4.12 (1H, dd, $J = 10.1$, 6.3 Hz), 3.79 (3H, s), 2.93 (1H, brs.); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 154.7$, 124.2 (q, $J_{C-F} = 257$ Hz), 115.8, 114.8, 69.4 (q, $J_{C-F} = 31.3$ Hz), 66.8, 55.7; FT-IR (neat): $\tilde{\nu} = 3441$, 2942, 2838, 1509, 1466, 1444, 1231, 1177, 1142, 1046, 878, 826, 748, 691 cm^{-1}. HRMS (FAB): Calcd: 236.0660 (M^+); Found: 236.0660.

(2*S*)-(−)-1-(1-Naphthyloxy)-3,3,3-trifluoro-2-propanol [(−)-**5e**]: Cyclic sulfate **3** (768 mg, 4 mmol) was added slowly to a solution of 1-naphthol (864 mg, 6 mmol) and potassium *tert*-butoxide (672 mg, 6 mmol) in dry tetrahydrofuran (8 mL) at room temperature. The mixture was stirred overnight at room temperature and the solvent was then removed in vacuo. The residue was dissolved in ether (10 mL) and sulfuric acid (20% aqueous solution, 10 mL) was added. The mixture was then slowly neutralized with powdered potassium carbonate until neutral. The aqueous phase was extracted with ether (40 mL), washed with 2M NaOH (2 × 15 mL), followed by brine, and dried over $MgSO_4$. Concentration in vacuo afforded 664 mg (65%) of **5e**. $R_f = 0.23$ on silica gel (hexanes/ethyl acetate 90/10); $[\alpha]_D^{23} = -13.1$ ($c = 2.2$ in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 8.23$ (1H, m), 7.84 (1H, m), 7.53 (3H, m), 7.40 (1H, m), 6.85 (1H, m), 4.3-4.6 (3H, m), 2.92 (1H, d, $J = 6.8$ Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 134.5$, 127.6, 126.7, 126.3, 125.7, 125.6, 125.3, 121.6, 121.5, 105.1, 69.5 (q, $J_{C-F} = 31.4$ Hz), 66.2; FT-IR (neat): $\tilde{\nu} = 3574$, 3055, 2986, 1597, 1581, 1509, 1459, 1396, 1265, 1243, 1177, 1147, 1105, 1069, 793, 774, 732, 705 cm^{-1}. HRMS (FAB): Calcd: 256.0711 (M^+); Found: 256.0722.

(2*S*)-(−)-1-Cyano-3,3,3-trifluoro-2-propanol [(−)-**5f**]: A solution of cyclic sulfate **3** (3.84 g; 20 mmol) and sodium cyanide (1.18 g, 24 mmol) in acetone (20 mL) and water (20 mL) was stirred overnight at room temperature. The solvent was then removed in vacuo. Ether (20 mL) and sulfuric acid (20% aqueous solution, 20 mL) were added and the mixture was stirred for 30 min. Powdered potassium carbonate was added until neutral and the mixture was extracted with ether (2 × 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by bulb-to-bulb distillation (60 °C, 10 Torr) yielding 1.40 g (50%) of cyanoalcohol **5f** as an oil. $[\alpha]_D^{23} = -19.5$ ($c = 1.6$ in MeOH) [lit.[18c] −16.78 (c 1.9; MeOH)]; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 4.34$ (1H, m), 3.65 (1H, d, $J = 5.9$ Hz), 2.78 (2H, m); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 123.8$ (q, $J_{C-F} = 279$ Hz), 115.5, 66.6 (q, $J_{C-F} = 33.2$ Hz), 20.1; FT-IR

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(neat): $\tilde{\nu}$ = 3409, 2984, 2267 (s), 1661, 1422, 1393, 1275, 1221, 1111, 947 cm^{-1}.

(4*S*,5*S*)-(+)-4,5-Bis(chloromethyl)-2,2-dioxo-1,3,2-dioxathiolane [(+)-**8**]: Sulfuryl chloride (4.46 g, 2.65 mL, 33 mmol) was added dropwise to a cooled (0 °C) solution of enantiopure (>98% *ee*) (*S*,*S*)-diol **7**[27] (4,74 g, 30 mmol) and imidazole (5.1 g, 75 mmol) in dichloromethane (85 mL). A precipitate formed gradually upon addition. When the addition was completed, the mixture was allowed to warm to room temperature. The mixture was further diluted with dichloromethane (100 mL). Sulfuric acid (5% aqueous solution, 30 mL) was added and the organic layer was separated. The organic phase was washed with saturated aqueous $NaHCO_3$ (30 mL) and brine, dried over $MgSO_4$, and concentrated in vacuo to give 5.82 g (88%) of crude solid **8**. Recrystallization from toluene/hexane yielded analytically pure (+)-**8**. $[\alpha]_D^{23}$ = + 62.0 (*c* = 1.6 in EtOH); m.p. 54 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.01 (2H, m), 3.92 (4H, m); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 81.1, 41.7; FT-IR (KBr): $\tilde{\nu}$ = 1385, 1302, 1212, 1180, 1057, 1019, 985, 897, 856, 828, 799, 761, 654 cm^{-1}. Anal. Calcd for $C_4H_6SO_4Cl_2$: C, 21.72; H, 2.72; and S, 14.48%. Found: C, 21.60; H, 2.73; and S, 14.33%.

(4*S*)-(+)-4-Trichloromethyl-2,2-dioxo-1,3,2-dioxathiolane [(+)-**9**]: Sulfuryl chloride (891 mg, 6.6 mmol, 530 µL) was added dropwise to a stirred solution of enantiopure diol (−)-**2c** (1.07g, 6 mmol) and imidazole (980 mg, 14.4 mmol) in dichloromethane (10 mL) at 0 °C. A precipitate formed gradually upon addition. When the addition was completed, the mixture was allowed to warm to room temperature. The mixture was further diluted with dichloromethane (20 mL). Sulfuric acid (5% aqueous solution, 5 mL) was added and the organic layer was separated. The organic phase was washed with saturated aqueous $NaHCO_3$ (10 mL) and brine, dried over $MgSO_4$, and concentrated in vacuo to give crude **9** (1.33 g, 92%). Recrystallization from ethyl acetate/hexane (75/25) gave analytically pure **9** as colorless needles. R_f = 0.25 (hexane/ethyl acetate 90/10); $[\alpha]_D^{23}$ = + 24.8 (*c* = 1.7 in CH_2Cl_2); m.p. 122–123 °C (*rac*-**9**, m.p. 89 °C); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.32 (1H, dd, *J* = 6.9, 5.6 Hz), 4.93 (1H, dd, *J* = 9.8, 6.9 Hz), 4.83 (1H, dd, *J* = 9.8, 5.6 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 94.4, 85.2, 68.6; MS (EI): *m*/*z*: 245, 243, 241, 209, 207, 205, 147, 145, 143, 123 (100%), 111, 97, 83; FT-IR (KBr): $\tilde{\nu}$ = 2991, 1399, 1206, 1054, 1005, 980, 888, 808, 785, 650 cm^{-1}. Anal. Calcd for $C_3H_3Cl_3SO_4$: C, 14.9; H, 1.2; and S, 13.3%. Found: C, 15.3; H, 1.4; and S, 13.0%.

***(R)*-(−)-1,2-Propanediol** [(−)-**2a**]: A solution of enantiopure (2*S*)-(−)-3,3,3-trichloro-1,2-propanediol **2c** (897 mg, 5 mmol), potassium carbonate (1.4 g, 10 mmol), and 10% palladium on carbon (200 mg) in methanol (10 mL) was hydrogenated (1 atm) at room temperature. After 4 h, the suspension was filtered over Celite and concentrated in vacuo. Bulb-to-bulb distillation (60 °C, 10 Torr) yielded 192 mg (50%) of pure (−)-1,2-propanediol (**2a**). $[\alpha]_D^{23}$ = − 21.5 (*c* = 7.0 in H_2O) [lit.[40] enantiopure (−)-**2a**: −22 (*c* = 7.5 in H_2O)]. Spectroscopic data, vide supra.

(4*S*)-(−)-4-Trichloromethyl-2,2-dimethyl-1,3-dioxolane [(−)-**11**]: A solution of diol **2c** (3.59 g, 20 mmol) and *p*-toluenesulfonic acid (76 mg, 2 mol%) in 2,2-dimethoxypropane (20 mL) and acetone (20 mL) was stirred for 12 h at room temperature. Pulverized potassium carbonate (280 mg, 10 mol%) was added and the suspension was stirred for an additional 2 h. The mixture was filtered and concentrated in vacuo. The crude product was distilled under reduced pressure (b.p. 70–71 °C, 8 Torr) yielding 3.82 g (87%) of acetonide **11**. $[\alpha]_D^{23}$ = − 0.9 (*c* = 2.2 in THF); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.69 (1H, dd, *J* = 6.8, 4.6 Hz), 4.27 (1H, dd, *J* = 9.7, 6.8 Hz), 4.19 (1H, dd, *J* = 9.7, 4.6 Hz), 1.60 (3H, s), 1.43 (3H, s); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 112.9, 99.3, 86.1, 67.0, 25.9, 25.0; FT-IR (neat): $\tilde{\nu}$ = 2990, 2889, 1457, 1384, 1374, 1262, 1212, 1155, 1119, 1083, 1052, 964, 896, 856, 799, 733 cm^{-1}. HRMS (EI): Calcd: 202.9433 ($M^+ - CH_3$); Found: 202.9442.

(4*S*)-(−)-4-Dichloromethyl-2,2-dimethyl-1,3-dioxolane (−)-12: A Pyrex tube was charged with trichloroacetonide **11** (658 mg, 3 mmol) and dry tetrahydrofuran (20 mL). The solution was irradiated with a mercury lamp (254 nm) for 6 h. The solution was concentrated in vacuo. Bulb-to-bulb distillation (60 °C, 10 Torr) gave 332 mg (60%) of pure dichloroacetonide **12**. $[\alpha]_D^{23}$ = − 9.1 (*c* = 1.4 in CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 5.63 (1H, d, *J* = 6.4 Hz), 4.42 (1H, ddd, *J* = 6.4, 6.4, 4.8 Hz), 4.18 (1H, dd, *J* = 9.3, 6.4 Hz), 4.09 (1H, dd, *J* = 9.3, 4.8 Hz), 1.49 (3H, s), 1.38 (3H, s); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 111.5, 80.1, 72.3, 66.3, 26.5, 25.1; FT-IR (neat): $\tilde{\nu}$ = 2990, 2890, 1480, 1383, 1374, 1255, 1217, 1154, 1074, 962, 851, 775 cm^{-1}; MS (EI): *m*/*z*: 169, 119, 101, 83, 73, 59, 49, 43 (100%).

(2*S*)-(+)-1-Azido-3,3,3-trichloro-2-propanol [(+)-**10a**]: A solution of cyclic sulfate **9** (966 mg, 4 mmol) and sodium azide (520 mg, 8 mmol) in *N*,*N*-dimethylformamide (10 mL) was stirred for 4 h at 90 °C. The solvent was carefully removed by distillation under reduced pressure. Tetrahydrofuran (10 mL), water (72 µL) and sulfuric acid (392 mg) were added and the resulting suspension was stirred for 30 min. Saturated aqueous $NaHCO_3$ (5 mL) was added and the solution was stirred for 10 min. Water (10 mL) was added and the mixture was extracted with ethyl acetate (2 × 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (hexane/ethyl acetate: 80/20) yielding 760 mg (93%) of azidoalcohol **10a**. R_f = 0.39 (hexane/ethyl acetate 90/10); $[\alpha]_D^{23}$ = + 41.4 (*c* = 2.3 in CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.31 (1H, dd, *J* = 8.1, 2.6 Hz), 3.73 (1H, dd, *J* = 13.0, 2.6 Hz), 3.62 (1H, dd, *J* = 13.0, 8.1 Hz), 3.31 (1H, brs); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 100.4, 81.9, 51.9; MS (EI): *m*/*z*: 179, 168, 149, 136, 121, 105, 100 (100%); FT-IR (neat): $\tilde{\nu}$ = 3359, 2931, 2096 (s), 1624, 1313, 1114, 1017, 898 cm^{-1}.

(2*S*)-(−)-3,3,3-Trichloro-1-phenylthio-2-propanol [(−)-**10b**]: Cyclic sulfate **9** (87 mg, 0.36 mmol) was added slowly to a solution of thiophenol (42 mg, 0.38 mmol) and potassium *tert*-butoxide (45 mg, 0.4 mmol) in dry tetrahydrofuran (2 mL) at room temperature. The mixture was stirred for 2 h at ambient temperature and the solvent was then removed under reduced pressure. The residue was dissolved in ether (3 mL) and sulfuric acid (20% aqueous solution, 3 mL) was added. The mixture was then slowly neutralized with potassium carbonate until neutral. The aqueous phase was extracted with ether (15 mL), washed with 2 M NaOH (2 × 5 mL), followed by brine, and dried over $MgSO_4$. Concentration in vacuo afforded 92 mg (94%) of **10b**. R_f = 0.28 on silica gel (hexane/ethyl acetate 90/10); $[\alpha]_D^{23}$ = − 91.3 (*c* = 1.1 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.45 (2H, m), 7.30 (3H, m), 4.16 (1H, ddd, *J* = 9.7, 3.7, 2.0 Hz), 3.68 (1H, dd, *J* = 14.2, 2.0 Hz), 3.28 (1H, d, *J* = 3.7 Hz), 3.10 (1H, dd, *J* = 14.2, 9.7 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 130.3, 129.3, 127.2, 80.8, 36.8; FT-IR (neat): $\tilde{\nu}$ = 3450, 3059, 2916, 1583, 1480, 1439, 1409, 1278, 1217, 1177, 1087, 1025, 980, 804, 738, 690 cm^{-1}. HRMS (FAB): Calcd: 269.9440 (M^+); Found: 269.9431.

(2*S*)-(−)-1-Benzylamino-3,3,3-trichloro-2-propanol [(−)-**10c**]: Benzylamine (545 µL, 5 mmol) was added slowly to a solution of cyclic sulfate **9** (600 mg, 2.15 mmol) in dry tetrahydrofuran (3 mL) at room temperature. After addition of the amine (exothermic), the mixture was stirred for 2 h at ambient temperature. Diethyl ether (10 mL) and sulfuric acid (20% aqueous solution, 5 mL) were added. A precipitate formed immediately and the suspension was stirred for 1 h at room temperature. The precipitate was filtered and washed with ether and resuspended in sulfuric acid (20% aqueous solution, 6 mL). The suspension was heated at 85 °C. After 20 min the solution became clear. Heating was continued for 15 min. The mixture was then cooled to room temperature and slowly neutralized with powdered potassium carbonate until neutral. The aqueous phase was extracted with ether (30 mL), washed with brine, dried over $MgSO_4$, and concentrated in vacuo. The crude product was recrystallized from CH_2Cl_2 yielding 375 mg (65%) of **10c**. R_f = 0.29 on silica gel (hexane/ethyl acetate 50/50); $[\alpha]_D^{23}$ = − 13.8 (*c* = 1.6 in $CHCl_3$); m.p. 144 °C; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.34 (5H, m), 4.17 (1H, dd, *J* = 6.8, 4.7 Hz), 3.89 (1H, d, *J* = 13.9 Hz), 3.83 (1H, d, *J* = 13.9 Hz), 3.15 (1H, dd, *J* = 13.1, 4.7 Hz), 3.06 (1H, dd, *J* = 13.1, 6.8 Hz); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 139.0, 128.6, 128.1, 127.5, 102.3, 79.3, 53.7, 48.7; FT-IR (KBr): $\tilde{\nu}$ = 3407, 1651, 1455, 1422, 1340, 1214, 1135, 1038, 749, 704, 627 cm^{-1}. HRMS (FAB): Calcd: 268.0063 ($M+H^+$); Found: 268.0053. Anal. Calcd for $C_{10}H_{12}Cl_3NO$: C, 44.69; H, 4.47 and N, 5.21%. Found: C, 44.59; H, 4.41 and N, 4.91%.

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[24] The fact that **2b** (63% *ee*) is raised to enantiopurity by a single recrystallization and that *rac*-**2b** is an oil at room temperature suggests that **2b** crystallizes as a conglomerate. Dihydroxylation of **1b** using $(DHQ)_2$-PYR afforded *ent*-**2b** in 63% *ee*, which also crystallized to enantiopurity.

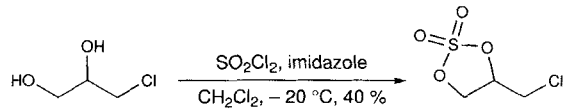
[25] Analytically and enantiomerically pure **3** is obtained by distillation under reduced pressure and is an oil at room temperature (cf. *rac*-**3**, m.p. 34–35 °C).

[26] Preliminary control experiments suggest that sulfuryl diimidazole is not an intermediate in this process. The use of other bases such as NEt_3 and pyridine or other solvents (e.g. EtOAc) gave inferior results.

[27] For a synthesis of enantiopure **7**, see: K. P. M. Vanhessche, Z.-M. Wang, K. B. Sharpless, *Tetrahedron Lett.* **1994**, *35*, 3469.

[28] Again, as for diol **2b**, **2c** (86% *ee*) is raised to enantiopurity by a single recrystallization and the difference in melting points between *rac*-**2c** (84.6–85 °C, ref. [16]) and enantiopure **2c** (110 °C) suggests that this diol also crystallizes as a conglomerate. Dihydroxylation of **1c** using $(DHQ)_2$-PYR, afforded *ent*-**2c** in 77% *ee* (which is also raised to enantiopurity by one recrystallization).

[29] A related compound, cyclic sulfate **15**, was earlier described as an epichlorohydrin equivalent (prepared in two steps from 3-chloro-1,2-propanediol): V. Massonneau, X. Radisson, M. Mulhauser, N. Michel, A. Buforn, B. Botannet, *New J. Chem.* **1992**, *16*, 107. We found that treatment of 3-chloro-1,2-propanediol with SO_2Cl_2/imidazole in CH_2Cl_2 at −20 °C afforded **15** in one step (Scheme 4), albeit in only 40% yield.



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Scheme 4.

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[37] 3,3,3-Trichloropropene is prepared by dehydrochlorination of 1,1,1,3-tetrachloropropane, see: R. N. Haszeldine, *J. Chem. Soc.* **1953**, 3371.

[38] Smaller quantities (25 g) of 3,3,3-trifluoropropene can also be purchased from Aldrich (for a synthesis, see: R. N. Haszeldine, *J. Chem. Soc.* **1952**, 2504).

[39] With the gaseous AD substrates, an excess of olefin is introduced by continuous bubbling, and the yield is calculated based upon the amount of $K_3Fe(CN)_6$ used. For large scale reactions, a closed system may be employed.

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[41] Reduction of **5a** (H_2, Pd/C, MeOH) afforded the corresponding amino alcohol, $[\alpha]_D^{23} = -20.1$ ($c = 1.4$ in MeOH) [lit.[18e] -19.5 ($c = 1.3$ in MeOH)].

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