Supporting Information

Synthesis of [2-^{2}H]isopentenyl diphosphate (1).

(*R*)-Glyceraldehyde acetonide (5). Fifteen grams (57 mmol) of D-mannitol-1,2:5,6-bis-acetonide were dissolved in 150 mL CH_2Cl_2 and the vessel placed in a water bath at 25°C. $NaIO_4$ (28.3 g, 133 mmol) was added with vigorous stirring followed by 6 mL saturated $NaHCO_3$ solution. After 5 min, additional $NaHCO_3$ (2 g) was added and stirring was continued for 2 h. $MgSO_4$ (30 g) was added and the mixture stirred for 15 min. The reaction mixture was filtered and the cake washed with CH_2Cl_2 (2 x 30 mL). The solvent was removed by fractional distillation until the head temperature reached 40°C. The residue was then distilled at reduced pressure (*ca*. 20 mm Hg) collecting the fraction distilling at 53-54°C into four flasks. Each portion was analyzed by ^{1}H NMR and optical rotation measurements. The best fractions (typically 2 and 3) were combined affording 11g (85 mmol, 75%) of product; ^{1}H NMR ($CDCl_3$) δ (ppm):1.52 (3H, s), 1.43 (3H, s), 4.11 (1H, dd, 8.8 Hz, 4.8 Hz), 4.18 (1H, dd, 8.8 Hz, 7.5 Hz), 4.40 (1H, ddd, 8.8 Hz, 7.5 Hz, 2.1 Hz), 9.72 (1H, d, 2.1 Hz); ^{13}C NMR ($CDCl_3$) δ (ppm) 25.13, 26.24, 65.59, 79.83, 111.28, 201.9; $[\alpha]_D^{20}$: +64.3° (lit.[1] +64.9°).

(2*R*)-1,2,3-Butanetriol-1,2-acetonide (6). To a solution of **5** (11.1 g, 85 mmol) in 150 mL diethyl ether previously cooled to 0°C was slowly added a 3 N solution of methylmagnesium bromide in pentanes (35 mL, 105 mmol) over *ca.* 70 min with stirring. The ice bath was then removed and the mixture stirred at room temperature overnight. The reaction was poured onto ice/saturated NH_4Cl solution, and the aqueous layer was separated and extracted with diethyl ether (4 x 30 mL). The combined organic layers were dried with K_2CO_3 or Na_2SO_4 and concentrated at reduced pressure. The product (8.6g, 59 mmol, 70%) was a diastereomeric mixture of alcohols, which was used in the next step without further purification; ^{1}H NMR ($CDCl_3$) δ (ppm): 1.18 (3H, d, 6.5 Hz), 1.19 (3H, d, 6.3 Hz), 1.40 (3H, s), 1.47 (3H, s), 2.17 (1H, d, 3.3Hz), 2.45 (1H, d, 4.5Hz), 3.72 (1H, t, 6.3 Hz), 4.0 (7H, m); ^{13}C NMR ($CDCl_3$) δ (ppm): 18.49, 18.86, 25.21, 25.36, 26.48, 64.83, 66.06, 66.95, 68.79, 79.53, 80.45, 109.18, 109.53.

(*R*)-3,4-Dihydroxybutanone acetonide (7). Compound **7** was prepared following the oxidation protocol of Griffith *et al.*[2] with minor modifications. *N*-Methylmorpholine oxide (NMO) (10.35 g, 88 mmol) was dissolved in 400 mL CH_2Cl_2 and the solution treated with $MgSO_4$ for 20 min. After removal of the drying agent by filtration, molecular sieves and 8.6 g (59 mmol) (2*R*)-1,2,3-butanetriol-1,2-acetonide **6** were added and the solution stirred for 15 min prior to the addition of 340 mg (1.6% eq.) tetra-n-propylammonium perruthenate (TPAP). The reaction was stirred at room temperature for 6-7 h or until no more alcohol could be detected by TLC. The mixture was then passed through a 2 x 12 cm silica column to remove the catalyst. The eluent was washed with a saturated $CuSO_4$ solution, brine, and water. The organic layer was dried and the solvent removed at reduced pressure, maintaining P ≥ 40 mm Hg.[3] A clear oil (8.0 g, 94%) was obtained which was essentially pure by ^{1}H NMR; ^{1}H NMR ($CDCl_3$) δ (ppm): 1.40 (3H, s), 1.49 (3H, s), 2.27 (3H, s), 4.00 (1H, dd, 8.6 Hz, 5.7 Hz), 4.20 (1H, dd, 8.6 Hz, 7.5Hz), 4.42 (1H, dd, 7.8 Hz, 5.7 Hz); ^{13}C NMR ($CDCl_3$) δ (ppm): 25.03, 26.05, 26.33, 66.46, 80.47, 111.02, 209.20; $[\alpha]_D^{20}$: +64.5°; lit.[4] +65° (1.5, benzene).

(2*R*)-3-(Trimethylsilyl)methyl-1,2,3-butanetriol 1,2-acetonide (8). To a vigorously stirred solution of **7** (5.11g, 35.4 mmol) in 250 mL diethyl ether at -78°C was slowly added 60 mL of (trimethylsilyl)methyllithium solution (1 M) in pentanes. The acetone/dry ice bath was removed and the reaction quenched by carefully adding 100 mL saturated NH_4Cl/NaCl solution. The aqueous phase was separated and extracted with diethyl ether (3 x 30 mL). The combined organic layers were washed with brine and water, dried with $MgSO_4$, and the solvent removed at reduced pressure. A colorless oil (7.27 g, 33.3 mmol, 94%) was obtained; ^{1}H NMR ($CDCl_3$) δ (ppm): diastereomeric mixture: 0.07 (9H, s), 0.1 (9H, s), 0.47 (1H, d, 13 Hz), 0.86 (1H, d, 13 Hz), 0.93 (1H, d, 15 Hz), 1.07 (1H, d, 15 Hz), 1.14 (3H, s), 1.27 (3H, s), 1.37 (3H, s), 1.40 (3H, s), 1.43 (3H, s), 1.47 (3H, s), 1.90 (1H, s), 3.80 (m), 3.95 (m); ^{13}C NMR ($CDCl_3$) δ (ppm): 0.63, 0.73, 24.61, 25.49, 25.60, 26.63, 26.80, 27.48, 30.32, 65.44, 65.47, 72.41, 72.49, 83.30, 83.43, 109.44, 109.56.

(*S*)-3-Methyl-3-butene-1,2-diol (9). 3N HCl (3 mL) was added to a solution of 7.27g (33.3 mmol) of the Peterson adduct **8** dissolved in 100 mL ethanol and the mixture refluxed for 1.5 h. After cooling to room temperature, the acid was neutralized by slowly adding solid $NaHCO_3$. The precipitated salts were filtered, washed with fresh ethanol, and the solvent evaporated under reduced pressure to give a viscous oil with some inorganic salts and residual water. The oil was redissolved in 3 mL methanol, and 100 mL diethyl ether were added with stirring. The precipitated salts were removed by filtration and the solvent evaporated affording 3.1 g crude product which contained a small amount of methanol and water. The crude product was distilled at 1.5 mm Hg in a Kuegelrohr apparatus obtaining 2.2 g (21.6 mmol, 65%) pure product; ^{1}H NMR ($CDCl_3$) δ (ppm): 1.74 (3H, s), 3.53 (1H, dd, 11.1 Hz, 7.2 Hz), 3.69 (1H, dd, 11.9 Hz, 3.6 Hz), 4.16 (1H, dd, 7.2 Hz, 3.6 Hz), 4.95 (1H, m), 5.05 (1H, m); ^{13}C NMR ($CDCl_3$) δ (ppm): 18.93, 65.24, 75.68, 111.97, 144.10; $[\alpha]_D^{20}$ = +13.7° (3.2, CH_2Cl_2); lit.[5] $[\alpha]_D^{23}$ = +13.96° (2.95, CH_2Cl_2).

(*S*)-3-Methyl-3-butene-1,2-diol-1-yl tosylate (10). To a solution of 2.2 g (21.6 mmol) of the enediol in 40 mL dry pyridine at 0 °C was added 4.32 g (22.7 mmol) freshly recrystallized tosyl chloride dissolved in 15 mL dry

[1] Jackson, D. Y. *Synth. Commun.* **1988**, *18*, 337.
[2] Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D.*J. Chem. Soc., Chem. Commun.* **1987**, 1625.
[3] Concentration below 40 mm Hg leads to substantial loss of product.
[4] Tanner, D.; Somfai, P. *Synth. Commun.* **1986**, *16(12)*, 1517-1522.
[5] Wistuba, D.; Weigand, K.; Peter, H. *Chem. Res. Toxicol.* **1994**, *7*, 336.

pyridine. After 23 h at 0 °C, the mixture was poured onto ice-water and extracted with diethyl ether (4 x 20 mL). The combined organic layers were washed with dilute HCl followed by saturated $NaHCO_3$ solution, and brine, and dried over $MgSO_4$. Evaporation of the solvent afforded 4.65 g (18.1 mmol, 84%) of the product tosylate which was essentially pure by ^{1}H NMR. The oil crystallized after several days at 0 °C; ^{1}H NMR ($CDCl_3$) δ (ppm): 1.70 (3H, m), 2.46 (3H, s), 3.96 (1H, dd, 10 Hz, 7.8 Hz), 4.12 (1H, dd, 10 Hz, 3.4 Hz), 4.31 (1H, 7.8 Hz, 3.3 Hz), 4.97 (1H, m), 5.06 (1H, m), 7.36 (2H, dm, 6 Hz), 7.81 (2H, 8 Hz); ^{13}C NMR ($CDCl_3$) δ (ppm): 18.77, 21.85, 72.60, 73.10, 113.87, 128.14, 130.13, 132.80, 142.18, 145.29.

(*S*)-2-Isopropyledene oxirane (2). This procedure was similar to that reported for the synthesis of 2-vinyloxirane.[6] Finely powdered KOH (2 g) was placed in a 25 mL two-neck round bottom flask and cooled for 10 minutes in an ice bath. The tosylate oil **10** (1.26 g, 4.9 mmol) was then added and rapidly mixed. The reaction mixture was slowly warmed to 110-120°C and the product collected in a U-tube at -78°C. The volatile product contained a small amount of water and diethyl ether. Yields[7] varied from 60% to 80%; ^{1}H NMR ($CDCl_3$) δ (ppm): 1.63 (3H, m), 2.73 (1H, dd, 5.4 Hz, 2.7 Hz), 2.87 (1H, dd, 5.2 Hz, 4.1 Hz), 3.80 (1H, dd, 4.1 Hz, 3 Hz), 5.03 (1H, m), 5.17 (1H, m); ^{13}C NMR ($CDCl_3$) δ (ppm): 16.08, 46.71, 54.47, 114.61, 141.30.

(*R*)-[2-^{2}H]isopentenol (3). To a solution of 50 mg (0.59 mmol) of the oxirane **2**, sodium cyanoborodeuteride (78 mg, 1.19 mmol), and a small amount of bromocresol green in 4 mL diethyl ether at 0°C was added dropwise a BF_3-etherate solution, until a color change to yellow was observed. The mixture was stirred at 0 °C until no starting material was detected by ^{1}H NMR, typically 4-5 h. Periodical additions of BF_3 were necessary to maintain the acidity of the solution. The mixture was then diluted with brine and exhaustively extracted with diethyl ether. The combined ether extracts were dried over magnesium sulfate, the drying agent separated by filtration, and the solvent evaporated at P ≥ 100 mm Hg. The crude product was used in the next step without further purification. Yield: 40 mg (0.46 mmol), 78%;[8] ^{1}H NMR ($CDCl_3$) δ (ppm): 1.78 (3H, s), 2.28 (1H, broad t, 10 Hz), 3.72 (2H, d, 10 Hz), 4.8 (1H, broad s), 4.9 (1H, broad s); ^{13}C NMR ($CDCl_3$) δ (ppm): 22.19, 40.36 (t, $^1J_{C\text{-}D}$ = 18.8 Hz), 65.9, 112.70, 142.20.

(*R*)-[2-^{2}H]isopentenyl tosylate (11). (*R*)-[2-^{2}H]isopentenol **3** (75 mg, 0.86 mmol) was tosylated in CH_2Cl_2 by the method of Davisson *et al.*[9] A clear oil (110 mg, 0.43 mmol, 50%) was obtained. The product was purified by column chromatography (3:1 hexanes/Et_2O); ^{1}H NMR ($CDCl_3$) δ (ppm): 1.66 (3H, s), 2.34 (1H, broad t), 2.45 (3H, s), 4.11 (2H, m), 4.68 (1H, s), 4.80 (1H, s); ^{13}C NMR ($CDCl_3$) δ (ppm): 21.81, 22.47, 36.58 (t, $^1J_{C\text{-}D}$ = 11.3 Hz), 68.68, 113.30, 128.12, 130.03, 133.31, 140.30, 144.96.

(*R*)-[2-^{2}H]isopentenyl diphosphate (1). To a solution of 40 mg (0.155 mmol) (*R*)-**11** in 0.5 mL acetonitrile was added 0.422 g tris-n-butylammonium hydrogen diphosphate and the reaction mixture stirred overnight. The reaction was worked up as per Davisson *et al.*[9] Purification by column chromatography on cellulose gave 30 mg (0.1 mmol, 60%) of a fluffy white solid. ^{1}H NMR (D_2O) δ (ppm): 1.8 (3H, s), 2.40 (1H, broad t, 6.6 Hz), 4.09 (2H, t, 6.6 Hz); vinylic protons obscured by solvent peak. ^{13}C NMR ($CDCl_3$) δ (ppm): 23.91, 39.90 (broad),[10] 66.51 (d, $^2J_{C\text{-}P}$ = 5.6 Hz), 113.82, 146.00.

[6] Crawford, R. J.; Lutener, S. B.; Cockroft, R. D. *Can. J. Chem.* **1976**, *54*, 3364-3376.

[7] After correction for water and ether content based on ^{1}H NMR integrations.

[8] Yields varied from 50% to 80%.

[9] Davisson, V. J.; Woodside, A. B.; StremLer, K. E.; Neal, T.; Muelbacher, M.; Poulter, C. D. *J. Org. Chem.* **1986**, *51*, 4768.

[10] Due to coupling to deuterium and phosphorus; expected coupling constants *ca.* 10-15 Hz and 4-6 Hz, respectively.

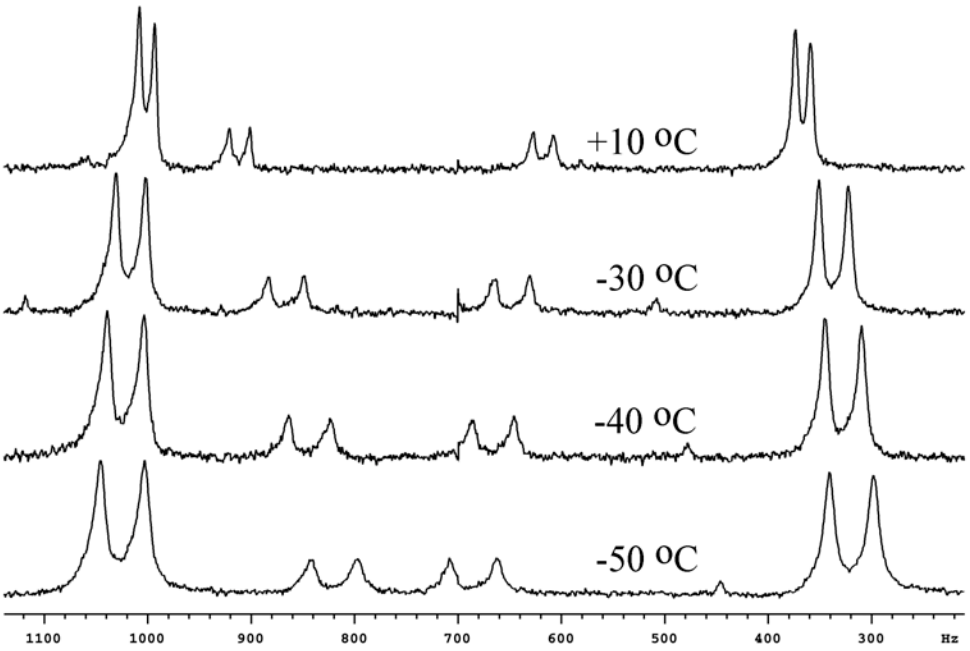

Figure 2. 46 MHz ^{2}H NMR spectra of racemic [2-^{2}H]isopentenyl tosylate in a 20% PBLG/CH_2Cl_2 liquid crystal. Dependence of the enantiotopic discrimination upon temperature.