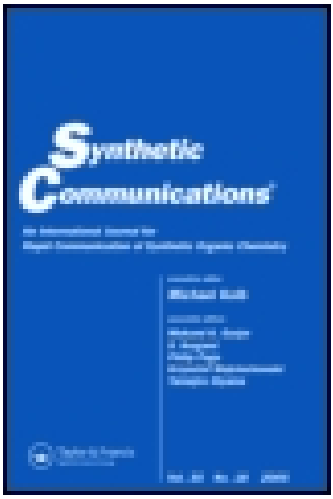

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Highly Enantiopure (tert-Butyldiphenylsilyloxymethyl)Ox from Barium Carbonate

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HIGHLY ENANTIOPURE (*tert*-BUTYLDIPHENYLSILYLOXYMETHYL)OXIRANES FROM BARIUM CARBONATE

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SUMMARY

Abstract: The synthesis of (2*R*)-(*tert*-butyldiphenylsilyloxymethyl)oxirane and the (2*S*)-enantiomer from barium carbonate was developed. Methyl glycolate or the hydroxamate analog was prepared and in turn reacted with (*S*)-(-)-methyl *p*-tolylsulfoxide or the (*R*)-enantiomer to make β-keto sulfoxides. From the sulfoxides, we made the diastereoisomeric alcohols in a highly selective sulfoxide group directed hydride reduction, and a Pummerer rearrangement reaction followed by deprotection yielded the enantiomeric diols. (2*R*)-(*tert*-Butyldiphenylsilyloxymethyl)oxirane and its (2*S*)-enantiomer were derived from these diols in an overall yield of 56 % from barium carbonate. This method was developed to provide a convenient access to isotope-labeled analogs of these compounds.

INTRODUCTION

In connection with the preparation of a carbon-isotope labeled version of (*R*)-(+)-α-[[(2-bromoethyl)amino]methyl]-2-nitro-1H-imidazole-ethanol monohydrobromide **1** for metabolic and pharmacokinetic study, we needed to make labeled (2*R*)-(*tert*-butyldiphenylsilyloxymethyl)oxirane **13**. From labeled **13** we planned to prepare the labeled version of compound **1**, a very potent hyposia selective cytotoxin that is being developed as a potential radiosensitizing agent in cancer therapy. Originally, this compound and the *S*-enantiomer were prepared

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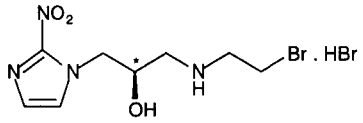
from commercial chiral glycidyl tosylate or epichlorohydrin [1] and these reagents formed the three-carbon chirality bearing moiety in **1**. Carbon-isotope, such as carbon-14, labeled forms of these reagents or a substitute such as **13** was found to be very expensive to obtain by custom synthesis. We have developed a sequence of reactions to both (2*R*) and (2*S*)-(tert-butyldiphenylsilyloxymethyl)oxirane from barium carbonate, a reagent that may be the source of desired label.



1

While this study was in progress, a method for preparing racemic epichlorohydrin from labeled glycerol was described.[2] However, this study is distinct in that it was aimed to achieve a concise, cost effective and practical synthesis of enantiomerically pure oxiranes. In the sequence that emerged we utilized (*S*)- and (*R*)-methyl *p*-tolylsulfoxide to install a β-keto sulfoxide group which is known to be capable of diastereotopic interaction with a reducing agent to produce chiral alcohol.[3] The method is a vastly superior synthesis to other strategies that we examined, and it furnished the desired product in very high optical purity and excellent yield. We wish to present the details of the reaction sequence leading from barium carbonate to both enantiomer of targeted oxirane. The application of this work to the radiolabeled synthesis of the compound **1** will be described elsewhere.

Results and Discussion

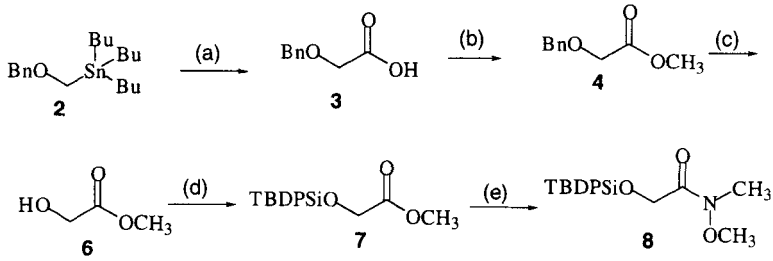
For our purpose, a peroxy acid oxidation of allyl alcohol or its derivative to a mixture of oxiranes was not a satisfactory option. On the other hand, our attempt at asymmetric epoxidation[4] of allyl alcohol was messy and the expected glycidyl tosylate could not be isolated in satisfactory yield. By combining AD-mix

dihydroxylation reaction with Sharpless' method for diol to epoxide[5] conversion we obtained improved result but the enantioselectivity (80 : 20) achieved was less than adequate. The option to explore chiral sulfoxide route to chiral diol was then considered. It was envisioned that we could construct these oxiranes enantioselectively by combining this method with the protocol for stereospecific diol to epoxide conversion.

The availability of methyl glycolate **6** was crucial to the success of this method. Fortunately, a procedure that could be applied to make carbon-isotope labeled glycolate from barium carbonate had indeed been reported.[6] We prepared compound **6** from (benzyloxymethyl)tributylstannane **2**, and **2** is in turn obtainable from benzyl chloromethyl ether[7] or tributyl(iodomethyl)stannane.[8] In our hands it was more easily prepared from tributyl(iodomethyl)stannane, and isolated in good yield by filtration through a short column of silica gel. Sequential transmetallation reaction of compound **2** with butyllithium at - 78 °C and addition of the carbon dioxide generated from barium carbonate provided 2-(benzyloxy)acetic acid **3**. The crude isolate **3** reacted with excess diazomethane, and the resulting methyl 2-(benzyloxy)acetate **4** was separated from the tetrabutylstannane by-product at this point by column chromatography to give pure **4**. It was found that the alternative acid-base extraction to obtain pure **3** prior to making the methyl ester derivative **4** must be handled in a minimum volume of aqueous solvent to obtain a comparable yield of product . Compound **4** was hydrogenolyzed in THF overnight in the presence of 20% Pd/C to give methyl glycolate **6**. Upon the treatment of compound **6** with *tert*-butylchlorodiphenylsilane (TBDPSCl) and imidazole in dimethylformamide (DMF) the silyl ether **7** was made in quantitative yield from **4**.

The β-keto sulfoxide **9** was prepared directly from compound **7** or a hydroxamate **8** that was derived from **7**. The hydroxamate was prepared in greater

Scheme 1

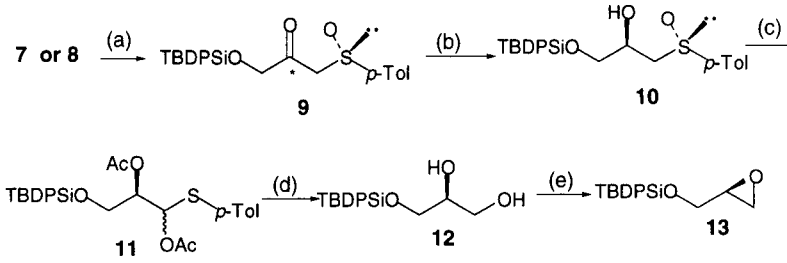


(a) BuLi, CO_2, -78°, H^+, 78%; (b) CH_2N_2, Quant.; (c) 20% Pd/C, H_2, Quant.
(d) TBDPSiCl, Imidazole, 96 %; (e) $AlEt_3$, $CH_3(CH_3O)NH.HCl$, 92 %

than 92 % yield from compound **7** by a reaction with N,O-dimethylhydroxylamine hydrochloride in the presence of triethylaluminum.[9] By this optional step we used a mole equivalent of the chiral sulfoxide to prepare β-keto sulfoxide **9**.

Where it was preferred to make the β-keto sulfoxide **9** from the methyl ester **7**, the required excess (2.2 mole equivalent) of the chiral methyl *p*-tolylsulfoxide was not deleterious to the reaction. In every case product was made in greater than 85 % yield. The compound **7** or the hydroxamate analog **8** was taken through the sequence of reactions in scheme **2**. Accordingly, S*(*S*)-(+)-methyl *p*-tolylsulfoxide (*S*)-MPTS, (S* denotes chiral sulfur) was deprotonated with lithium diisopropylamide (LDA) at - 40 °C and reacted with compound **7** at - 78 °C to make the β-keto sulfoxide **9** in excellent isolated yield. A column purification was neccessary to remove excess sulfoxide when 2.2 mole equivalent of chiral methyl *p*-tolylsulfoxide was reacted with the methyl glycolate. The reduction of the β-keto sulfoxide **9** with diisobutylaluminum hydride (DIBAL-H) at - 78 °C furnished

Scheme 2



(a) (S)-MPTS, LDA, 85%; (b) DIBAL-H, -78°, 99 %; (c) Ac_2O, reflux; (d) $LiBH_4$, THF, 87 %; (e) $CH_3C(OCH_3)_3$, CH_3OBr, Amberlite, 92 %

(2*R*),S*(*S*)-alcohol **10** in 99% isolated yield. The optical purity of **10** was estimated by hplc to be greater than 96%. Contrary to the expectation of comparable result, a significantly lower optical purity (≥ 87 %) was achieved in the zinc chelated $NaBH_4$ reduction of **9** to make the (2*S*),S*(*S*)-alcohol. Consequently, the S*(*R*)-enantiomeric β-keto sulfoxide was prepared from S*(*R*)-(-)methyl *p*-tolylsulfoxide (*R*)-MPTS, and compound **7** in a manner similar to the preparation of **9**. From this compound the (2*S*),S*(*R*)-alcohol was obtained in greater than 96 % chiral purity, by reduction with DIBAL-H under similar reaction conditions.

By subjecting these β-hydroxy sulfoxides such as **10** in scheme **2** to standard Pummerer rearrangement reaction in refluxing acetic anhydride buffered with sodium acetate a mixture of acetoxy thioketals was formed. Deprotection of crude acetoxy thioketal isolates, such as **11**, by reduction with lithium borohydride gave 87% yield of the enantiomeric diol. Yields were comparable for both (*R*)- and the (S)-enantiomer. It is important to note that we chose *tert*-butyldiphenylsilyl protection of the glycolate **6** to afford **7** or **8** because we hoped it would survive the acidic workup condition in the reduction of **11** to **12**. Furthermore, the silyl

protecting group would serve to provide the 'bulk' that will permit easy handling of the low molecular weight **6** during labeled synthesis.

(2*R*)-*tert*-Butyldiphenylsilyloxymethyl oxirane **13** and its (2*S*)-enantiomer were made from these enantiomeric alcohols. Of the methods examined for making epoxides from diols, the procedure due to Sharpless[5] was the more effective. It involved the formation of cyclic orthoester by a transesterification with trimethyl orthoacetate, conversion of the latter to acetoxy halides followed by base mediated ring closure to the epoxide. The target epoxide **13** was made in 93% isolated yield from **12**. The chiral purity was estimated to be greater than 98%, and confirmed by the conversion of **13** to afford enantiopure **1**. We also investigated a Mitsunobu procedure in which a diol reacts with triphenylphosphine-diisopropyl azodicarboxylate as described by Abushanab *et al* [11] to make epoxide, but it was found to yield epoxides that were inferior (87%) in optical purity.

In conclusion, we have successfully developed a highly enantioselective synthesis of*tert*-butyldiphenylsilyloxymethyloxirane. The sequence took advantage of the stereo-directing influence of β-ketosulfoxide in metal hydride reduction of the carbonyl group to make a diol and the reaction method for the stereospecific generation of epoxide from 1,2-diol. We believe that the carbon-isotope labeled analogs of these chiral epoxides may now be more readily accessible by using the method described herein.

Experimental

General Methods.

Unless otherwise stated, materials were obtained from commercial sources and were used without purification. All glasswares were oven dried and reactions were carried out under argon atmosphere. Tetrahydrofuran (THF) was freshly

distilled from sodium-benzophenone. Analytical tlc were performed using 2.5 X 10 cm (250 μm) precoated silica gel plates from Analtech. NMR spectra were recorded on a Varian Gemini 200 MHz spectrometer. Proton chemical shifts (∂) are reported in ppm downfield from (TMS), and ^{13}C resonances were recorded using 77.0 ppm $CDCl_3$ resonanace of solvent as internal standard reference and are reported in ppm down field from TMS. MS and HRMS were performed on Finnigan MAT 900Q (Bremen, Germany), ESI , positive ion mode. HPLC analyses of final products were performed on a Water Associates 600E solvent delivery system with on line PDA 996 photodiode array detector. Purifications were by column chromatography on a Merck Kieselgel 60 (230μ) or by flash column chromatography on Biotage Flash 40 System.

(Benzyloxymethyl)tributylstannane **2**

Sodium hydride (60 % dispersion, 2.0 g, 50 mmol) was washed with pentane three times, and suspended in dry THF (100 mL). A solution of benzyl alcohol (d 1.045, 5.36 g, 49.6 mmol) in dry Tetrahydrofuran (20 mL) was added dropwise with stirring at room temperature. After 1 hr a solution of tributyl(iodomethyl)stannane (19.37 g, 45 mmol) in dry THF (20 mL) was added in one portion , and stirred for 48 hr at room temperature. The excess NaH was destroyed by the addition of methanol. Petroleum ether (400 mL) was added, and the mixture was washed with cold water (3 X 200 mL). Magnesium sulfate was added to dry the solution. After fitration, the solution was concentrated to a residue which was purified by chromatography on silica gel eluted with 5-10% acetone in hexane to give **2** (16.9 g, 92.0%). Product was shown by tlc (acetone : hexane 1 : 9) to be homogenous. Analytical sample was obtained by vaccum distillation (bp 140 - 142 °C /0.03 mm, Lit[7] 126 - 144 °C/ 0.1 mm) to give a colorless oil. NMR ($CDCl_3$) δ 7.32 (5H, aromatic); 4.43 (s, 2H, $C_6H_5C\underline{H}_2O$-); 3.75 (tr, 2H, -

$OC\underline{H}_2SnBu_3$); 1.52 and 1.33 (m, 12H $-SnC\underline{H}_2C\underline{H}_2CH_2CH_3$); 0.93 (m, 17H, $SnCH_2CH_2C\underline{H}_2C\underline{H}_3$). ^{13}C-NMR ($CDCl_3$) 139.1, 128.36, 127.68, 127.46, 77.41, 61.66, 29.34, 27.52, 13.91, and 9.18. IR (neat) 1450, 1375, 1085, 1065, and 725 cm^{-1} .

Methyl 2-(benzyloxy)acetate **4**

n-Butyllithium (1.6 M solution in THF, 10.5 mL, 16.8 mmol) was added dropwise to a solution of (benzyloxymethyl)tributylstannane (6.13 g, 15 mmol) in dry THF (50 mL) at -78 °C and stirred at -78 °C for 30 min under argon. The reaction was cooled in liquid nitrogen bath and transferred onto a vacuum manifold to which had been attached a carbon dioxide generator. Following a sequence of freeze-thaw to degas the reaction, the carbon dioxide generated by the addition of excess sulfuric acid to $BaCO_3$ (3.31 g, 16.8 mmoL) was transferred into the reaction vessel. The liquid nitrogen bath was replaced with acetone dry ice bath, the reaction was stirred for 15 min at -78 °C and another 1 hr at room temperature. Saturated NH_4Cl solution (10 mL) was added followed by acidification with 6.0M HCl (4.0 mL). It was extracted with ether (5 X 60 mL) and dried on $MgSO_4$. The solvent was evaporated, and the residue was taken up in anhydrous ether (60 mL). A solution of diazomethane in ether was added in portions until yellow coloration was permanent. This color, due to excess diazomethane, was discharged by the dropwise addition of acetic acid. The solvent was removed, and the product was purified by column chromatography on silica gel with 10% ethyl acetate in hexane to give **4** (2.10 g, 78%) as a colorless oil. NMR ($CDCl_3$) δ 7.35 (5H, $C_6\underline{H}_5CH_2O$-), 4.63 (2H, s, $C_6H_5C\underline{H}_2O$-), 4.10 (2H, $-OC\underline{H}_2COOCH_3$), 3.75 (3H, s, $OCH_2COOC\underline{H}_3$). ^{13}C-NMR ($CDCl_3$) 170.88, 137.08, 128.56, 128.14, 73.40, 67.13, and 51.91.

Methyl 2-(*tert*-butyldiphenylsilyloxy)acetate **7**

To a solution of methyl 2-(benzyloxy)acetate (2.0 g, 11.11 mmol) in anhydrous THF (40 mL) was added 20 % Pd/C (200 mg, 10% w/w), and degassed. It was placed under an atmosphere of hydrogen contained in a balloon, and stirred overnight at room temperature. After it was filtered through a pad of Celite, the solvent was evaporated to give methyl glycolate (1.0 g, 11.0 mmol). *tert*-Butyldiphenylchlorosilane (3.29 g, 12 mmol) and imidazole (830 mg, 12.2 mmol) were added to a solution of this compound in DMF (15 mL), and the solution was stirred at room temperature overnight. Chloroform was added to the reaction mixture, and it was washed several times with cold water and dried. The solvent was evaporated to give **7** (3.5 g, 96%) as a colorless oil . NMR ($CDCl_3$) δ 7.70 and 7.41 (10H, m, aromatic), 4.24 (2H, s, $OC\underline{H}_2COOCH_3$), 3.67 (3H, s, -$OCH_2COOC\underline{H}_3$), 1.09 (9H, s, $(C\underline{H}_3)_3CSi$-). ^{13}C-NMR ($CDCl_3$) 172.17, 136.09, 133.28, 130.41, 128.30, 62.63, 52.16, 27.18, and 19.77. MS m/e 271 (M^+ - 57). Anal. Calcd for $C_{19}H_{22}O_3Si$: C, 69.47; H, 7.36. Found: C, 69.68; H 7.34.

S*(*S*)-3-*tert*-Butyldiphenylsilyloxy-1-tolylsulfinyl-2-propanone **9**

To a solution of diisopropylamine (2.22 g, 3.07 mL, 21.9 mmol) in dry THF (50 mL) at -40 °C was added n-butyllithium (1.6M solution in THF, 13.75 mL, 22 mmol) over 5 min under inert atmosphere. It was stirred for 30 min and (*S*)-(-)-methyl *p*-tolylsulfoxide (2.82 g, 18.29 mmol) in dry THF (10 mL) was added slowly and stirring was continued for another 30 min. The temperature was lowered to -78 °C, and a solution of methyl 2-(*tert*-butyldiphenylsilyloxy)acetate (3.0 g, 9.14 mmol) in dry THF (10 mL) was rapidly added. After 1 hr it was poured onto saturated ammonium chloride (40 mL). The organic phase was separated, and the aqueous phase was acidified with 1.0 M HCl (15 mL), and extracted with ethyl acetate (3 X 120 mL). The combined organic phase was

washed with water (40 mL), brine (60 mL), and dried. Solvent was removed to give the crude product. Purification by column on silica gel eluted with 10 % acetone in Pet ether, followed by crystallization from Pet ether gave **9** (3.5 g, 85%) mp 46 - 47 °C, $[\alpha]^{20}_{D}$ +104.9 (c 1.00, MeOH). NMR ($CDCl_3$) δ 7.54-7.26 (m, aromatic, 14H); 4.15 (s, -OC$\underline{H}_2$CO, 2H); 3.96 (q, OC$\underline{H}_2$SO-, 2H); 2.41 (s, p-C$\underline{H}_3C_6H_5SO$, 3H); 1.10 (s, $(CH_3)_3CSi$, 9H). ^{13}C-NMR 142.73, 140.55, 135.99, 132.65, 130.52, 128.43, 124.68, 71.02, 65.51, 27.23, 21.99 and 19.69 . Anal. Calcd. for $C_{26}H_{30}SiSO_3$: C, 69.29; H, 6.71; S, 7.11. Found C, 69.02; H, 6.82; S, 6.77; Si, 6.13

S*(*R*)-3-*tert*-Butyldiphenylsilyloxy-1-tolylsulfinyl-2-propanone

From methyl 2-(*tert*-butyldiphenylsilyloxy)acetate (3.98 g, 12 mmol) and (*R*)-(-)-methyl *p*-tolylsulfoxide (3.70 g, 24 mmol) by analogous reaction conditions, purification and crystallization from Pet ether to give S*(*R*)-3-*tert*-butyldiphenylsilyloxy-1-tolylsulfinyl-2-propanone (5.3 g, 98%), mp 54 - 56 °C, $[\alpha]^{20}_{D}$ -107.7 (c 1.00, MeOH). NMR ($CDCl_3$) δ 7.63 - 7.25 (m, aromatic, 14H); 4.14 (s, -OC$\underline{H}_2$CO, 2H); 4.07 (q, OC$\underline{H}_2$SO-, 2H); 2.40 (s, p-C$\underline{H}_3C_6H_5SO$, 3H); 1.08 (s, $(CH_3)_3CSi$, 9H). IR ($CHCl_3$) 1720, 1600, 1490, 1470, 1465, 1430, 1400, 1365, 1305. ^{13}C-NMR 201.36, 142.70, 140.63, 135.99, 132.66, 130.61, 128.43, 124.68, 71.02, 65.51, 27.27, 21.97 and 19.69 . Anal. Calcd. for $C_{26}H_{30}SiSO_3$: C, 69.29; H, 6.71; S, 7.11. Found C, 69.43; H, 6.83; S, 7.03; Si, 6.20.

[(2*R*),S*(*S*)]-3-(*tert*-Butyldiphenylsilyloxy)-1-p-tolylsulfinyl-2-propanol **10**

Diisobutylaluminum hydride (DIBAL-H) (1.5 M solution in toluene, 5.40 mL, 8 mmol) was added dropwise over 5 min to a solution of S*(*S*)-3-*tert*-butyldiphenylsilyloxy-1-tolylsulfinyl-2-propanone **9** (3.0 g, 6.66 mmol) in THF at

- 78 °C under argon atmosphere. It was stirred for 1 hr, and poured onto saturated solution of sodium tartrate (40 mL). The organic phase was separated, and the aqueous was extracted with ethyl acetate. The combined organic phase was washed with brine several times until the solution showed no more gelatinous constituent. After drying, the solution was concentrated and examined by Chiral hplc at room temperature on a Chiralcel OD 10 μ 4.6 X 250 mm column, eluted with 0.1 % diethylamine in hexanes:IPA 90:10 at a flow rate of 0.5 mL/min and detection by UV at 242 nm. The compound was shown to be 96% pure at a retention time of 11.52 min. Further purification by chromatographed on silica gel using 25 - 30 % acetone in Pet ether gave fractions that were combined, and concentrated to a residue that was crystallized from Pet ether -acetone to give white crystalline solid **10** (3.0 g, 99%), mp 92 - 94°C, $[\alpha]^{20}_{D}$ -118.9 (c 1.00, MeOH). NMR ($CDCl_3$) δ 7.61-7.28 (m, aromatic, 14H); 4.23 (m, -$OCH_2CHOHCH_2SO$-, 1H), 3.70 (brd, -CHOH-, exch. D_2O); 3.61 (m, -$OCH_2CHOHCH_2SO$-, 2H); 3.01 (dd, -OCH_2SO-, 1H, J 9.50, 13.5 Hz); 2.78 (dd, -OCH_2SO-, 1H, J 2.3, 13.5 Hz); 2.42 (s, p-$CH_3C_6H_5SO$, 3H); 1.01 (s, $(CH_3)_3CSi$, 9H). ^{13}C-NMR 142.05, 140.30, 135.85, 133.38, 133.33, 130.53, 130.37, 128.25, 124.48, 67.73, 67.22, 58.30, 27.28, 21.88 and 19.68. Anal. Calcd for $C_{26}H_{32}SiSO_3$: C, 68.98; H, 7.13; S, 7.08. Found C, 68.74; H, 7.08; S, 7.18; Si, 6.20 .

[(2*S*),S*(*R*)]-3-(*tert*-Butyldiphenylsilyloxy)-1-*p*-tolylsulfinyl-2-propanol

S*(*R*)-3-*tert*-butyldiphenylsilyloxy-1-tolylsulfinyl-2-propanone (5.3 g, 11.7 mmol) was similarly reduced with DIBAL-H (1.8 equiv) and afforded [(2*S*),S*(*R*)]-3-(*tert*-Butyldiphenylsilyloxy)-1-*p*-tolylsulfinyl-2-propanol (5.3 g, 99%). Examination by Chiral hplc at room temperature on a Chiralcel OD 10 μ 4.6 X 250 mm column, eluted with 0.1 % diethylamine in hexanes:IPA 90:10 at a flow rate of 0.5 mL/min and detected by UV at 242 nm showed the compound to be

95% at a retention time of 10.57 min. The compound was further purified and crystallized from Pet ether - ether as described for compound **10** to give white solid mp 89 - 90°C, $[\alpha]^{20}_D$ +116.1 (c 1.01, MeOH). NMR ($CDCl_3$) δ 7.61-7.29 (m, aromatic, 14H); 4.25 (m, -$OCH_2C\underline{H}OHCH_2SO$-, 1H); 3.65 (m, -$OC\underline{H}_2CHOHCH_2SO$-, 2H); 3.60 (brd, -$CH\underline{OH}$-, exch. D_2O); 3.02 (dd, -$OC\underline{H}_2SO$-, 1H, J 9.50, 13.5 Hz); 2.78 (dd, -$OC\underline{H}_2SO$-, 1H, J 1.3, 13.5 Hz); 2.42 (s, *p*-$C\underline{H}_3C_6H_5SO$, 3H); 1.00 (s, $(CH_3)_3CSi$, 9H). IR ($CHCl_3$) 3600, 3420, 1610, 1600, 1500, 1480, 1480, 1435, 1400, 1120, 1090 cm^{-1}. ^{13}C-NMR 142.00, 140.28, 135.87, 133.38, 133.33, 130.54, 130.37, 128.25, 124.48, 67.72, 67.22, 59.30, 27.28, 21.88 and 19.68. Anal. Calcd for $C_{26}H_{32}SiSO_3$: C, 68.98; H, 7.13; S, 7.08. Found C, 69.03; H, 7.15; S, 7.16; Si, 6.22.

(2*R*)-3-(*tert*-Butyldiphenylsilyloxy)-1,2-propanediol **12**

Sodium acetate (5.44 g, 66.37 mmol) was added to a solution of **10** (3.0 g, 6.66 mmol) in acetic anhydride (50 mL), and the solution was refluxed for 5 hr. It was cooled to room temperature, toluene (120 mL) was added to the reaction, and the solvent was evaporated under reduced pressure. Following two additional azeotrope with toluene, the residue was suspended in ether (300 mL) and filtered. The solid cake was washed with ether, and the combined ether solution was evaporated. After product **11** was dried on a vacuum pump for 2 hr, it was re-dissolved in THF (30 mL), $LiBH_4$ (2.0 M solution in THF, 133.2 mL, 266.4 mmol) was added, and stirred at room temperature overnight. The temperature was reduced and maintained at - 40 °C, and 1.0 M HCl was cautiously added till solid precipitate was formed. It was filtered, evaporated and purified by column chromatography on silica eluted with 35% acetone in hexane to give **12** (1.90 g, 87%), $[\alpha]^{20}_D$ -7.35 (c 1.05, MeOH). NMR ($CDCl_3$) δ 7.72 (d, aromatic-4H); 7.45 (m, aromatic, 6H); 3.82 (m, -$OCH_2C\underline{H}OHCH_2OH$, 1H); 3.74- 3.60 (m, -

$OCH_2CHOHCH_2OH$, 4H); 2.20 (br , OH-, exch. D_2O); 1.10 (s, $(CH_3)_3CSi$, 9H). ^{13}C-NMR ($CDCl_3$) 135.54, 129.95, 127.86, 71.90, 65.25, 63.87, 26.87 and 19.24. Anal. Calcd for $C_{19}H_{26}SiO_3$: C, 69. 05; H, 7.93 . Found C, 68.97; H, 7.95, Si, 8.42.

(2*S*)-3-(*tert*-Butyldiphenylsilyloxy)-1,2-propanediol

[(2*S*),S*(*R*)]-3-(*tert*-Butyldiphenylsilyloxy)-1-*p*-tolylsulfinyl-2-propanol (4.67 g, 10.33 mmol) was analogously converted to crystalline (2*S*)-3-(*tert*-butyldiphenylsilyloxy)-1,2-propanediol (2.0 g, 62.5 %), mp 56 - 58°C, $[\alpha]^{20}_D$ +7.40 (c 1.05, MeOH). NMR ($CDCl_3$) δ 7.70 - 7.35 (m, aromatic, 10H); 3.82 - 3.61 (m, $-OCH_2CHOHCH_2OH$, 5H); 2.50 (br , OH-, exch. D_2O); 1.10 (s, $(CH_3)_3CSi$, 9H). ^{13}C-NMR ($CDCl_3$) 136.02, 133.41, 133.37, 130.42, 128.34, 72.32, 65.69, 64.19, 27.35 and 19.71. Anal. Calcd for $C_{19}H_{26}SiO_3$: C, 69. 05; H, 7.93 . Found C, 68.89; H, 7.93; Si, 8.46

(2*R*)-(+)-(*tert*-Butyldiphenylsilyloxymethyl) oxirane **13**

To a solution of (2*R*)-3-(*tert*-butyldiphenylsilyloxy)-1,2-propanediol (1.90 g, 5.75 mmol) in dichloromethane (5 mL) was added trimethyl orthoacetate (0.944, 928 μL, 7.29 mmol) followed by pyridinium *p*-toluenesulfonate (PPTS) (14.3 mg, 0.0575 mmol). It was stirred at room temperature for 20 min, and the volatiles were removed by rotary evaporation. It was redissolved in methylene chloride (5 mL), and triethylamine (90 μL) was added. It was cooled to 0 °C and acetyl bromide was added dropwise with stirring. After additional 90 min, saturated sodium bicarbonate was added, and the mixture was stirred vigorously for a few minutes. Methylene chloride was added, and the organic phase was separated. The aqueous phase was extracted with methylene chloride and the combined organic extract was washed with brine and dried. The solvent was evaporated, and the

residue was washed through a plug of silica gel with 10 % ether in pentane. Following evaporation, the residue was taken up in anhydrous methanol and Amberlite 410 RP (pre washed with 2.0 N NaOH and dried) was added. The mixture was stirred vigorously for 5 hr, filtered, and evaporated. The residue was redissolved in 10% ether in pentane and filtered through a plug of silica gel to give **13** (1.65 g 92%); $[\alpha]_D^{25}$ + 2.60 ° (c 9.07, $CHCl_3$); (lit.[5c] $[\alpha]_D^{25}$ + 2.40° (c 9.07, $CHCl_3$). NMR ($CDCl_3$) δ 7.67 - 7.71 (m, 5 H), 7.35 - 7.45 (m, 5 H), 3.86 (dd, J = 2.9, 12,5 Hz, 1 H), 3.70 (dd, J = 4.4, 12.5 Hz, 1 H), 3.10 - 3.13 (m, 1 H), 2.73 (dd, J 3.3, 5.8 Hz, 1 H), 2.60 (dd, J = 3.3, 5.1 Hz, 1 H), 1.06 (s, 9 H). ^{13}C-NMR ($CDCl_3$) 136.12, 133.78, 130.24, 128.22, 64.81, 52.77, 44.94, 27.26 and 19.75. IR ($CHCl_3$) 2968, 2962, 2940, 1365, 1110 cm^{-1}

(2*S*)-(-)-(*tert*-Butyldiphenylsilyloxymethyl) oxirane

By similar conditions to those described for **13**, (2*S*)-3-(*tert*-butyldiphenylsilyloxy)-1,2-propanediol (2.0 g, 6.06 mmol) was converted to the compound (2*S*)-(-)-(*tert*-butyldiphenylsilyloxymethyl) oxirane (1.72 g, 91 %), $[\alpha]_D^{25}$ - 2.56°(c 9.07, $CHCl_3$); (lit.[5c] $[\alpha]_D^{25}$ - 2.28° (c 9.07, $CHCl_3$). NMR ($CDCl_3$) δ 7.67 - 7.71 (m, 5 H), 7.35 - 7.45 (m, 5 H), 3.86 (dd, J = 2.9, 12,5 Hz, 1 H), 3.70 (dd, J = 4.4, 12.5 Hz, 1 H), 3.10 - 3.13 (m, 1 H), 2.73 (dd, J 3.3, 5.8 Hz, 1 H), 2.60 (dd, J = 3.3, 5.1 Hz, 1 H), 1.06 (s, 9 H). ^{13}C-NMR ($CDCl_3$) 136.12, 133.78, 130.24, 128.22, 64.81, 52.77, 44.94, 27.26 and 19.75. IR ($CHCl_3$) 2968, 2962, 2940, 1365, 1110 cm^{-1} .

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