$CDCl_3$): δ 0.94 (d, CH_3, 6.8 Hz), 0.96 (d, CH_3 6.8 Hz), 0.99 (d, CH_3, 6.8 Hz), 1.58 (s, CH_3), 1.67 (s, CH_3), 1.73 (s, CH_3), 1.76 (s, CH_3), 1.77 (s, CH_3), 1.80 (s, CH_3), 2.00 (m, CH), 2.22 (t, CH_2), 2.35 (q, CH), 2.45 (t, CH), 3.05 (bs, OH), 3.44 (t, CH_2), 3.54 (t, CH_2), 3.59 (t, CH_2), 5.00 (t, CH olefinic). $^{13}C\{^1H\}$ NMR (67.5 MHz, $CDCl_3$): δ [9.9, 10.8, 10.9, 11.4, 11.5, 12.7, 13.9, 14.0, 19.0, 21.1] (CH_3), [21.9, 22.3, 22.5, 23.7] (CH_2 γ to OH in 4a and CH_2 β to OH in 4), [32.0, 32.3, 33.1] (CH_2 γ to OH in 4b and 4c, and CH_2 β to OH in 5), [62.2, 62.3, 62.6, 62.8] (CH_2 α to OH), [42.0, 49.2, 51.0, 51.3, 55.4] (CH), [110.7] (olefinic, CH in 5), [130.3, 133.2, 133.7, 134.6, 134.8, 135.5, 137.8, 137.9, 138.1, 138.4, 141.5, 143.5, 154.7] (olefinic). Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.84; H, 11.19.

Preparation of 3-(Tetramethylcyclopentadienyl)-1-(*p*-tolylsulfonyl)propanes, $[C_5(CH_3)_4H]CH_2CH_2CH_2OSO_2[p\text{-}CH_3(C_6H_4)]$ (6). Dry pyridine (400 mL) was added to 53.7 g (298 mmol) of **4** and **5** in a 1000-mL round-bottom flask. The resulting solution was stirred and cooled to 0 °C in an ice–water bath. To this solution was added 71.2 g (373 mmol) of *p*-toluenesulfonyl chloride. The flask was stoppered and placed in a refrigerator (approximately 3 °C). After 2 days, the solution had turned black and large crystals of pyridine hydrochloride had formed. The solution was then poured into a 1000-mL beaker containing 300 g of ice. The solution was stirred, and a purple oil formed. The oil was taken up in 300 mL of ether, and the water layer was separated from the organic layer. The aqueous layer was washed with 4 × 150 mL of diethyl ether. The combined organic phase was then washed with 2 × 200 mL of cold, 1:1 HCl/water. The yellow organic phase was then washed with H_2O until neutral. The organic layer was then washed once with aqueous saturated sodium chloride, dried over anhydrous magnesium sulfate, and filtered, and the solvent was removed under vacuum to give 74.1 g (222 mmol) of **6** (74% yield based on **4** and **5**) as a brown viscous oil. Compound **6** is thermally unstable; however, it may be stored at 0 °C for several weeks. This mixture was suitable for use without further purification. IR (neat): 2940 (vs), 2900 (vs), 2840 (vs), 1635 (w), 1590 (w), 1435 (s), 1350 (s), 1165 (vs), 1090 (m), 1020 (w), 955 (m), 910 (m), 805 (m), 655 (m). ^1H NMR (270 MHz, $CDCl_3$): δ 0.91 (d, CH_3, 5.4 Hz), 0.95 (d, CH_3, 5.4 Hz), 1.40–1.60 (m, CH_2), 1.65 (s, CH_3), 1.70 (s, CH_3), 1.75 (s, CH_3), 1.80 (s, CH_3), 2.40 (m, CH), 2.00 (s, CH_3), 3.90 (t, CH_2), 4.00 (t, CH_2), 6.90 (d, Ar-*m*, 10.8 Hz), 7.80 (d, Ar-*o*, 10.8 Hz). $^{13}C\{^1H\}$ NMR (67.8 MHz, $CDCl_3$): δ [10.7, 10.8, 11.3, 11.4, 13.7, 13.9, 21.1] (CH_3), [21.3] (CH_3 tosyl), [21.3] (CH_2 γ to tosyl 6a), [21.6, 22.7, 23.0] (CH_2 β to tosyl), [28.4, 29.2] (CH_2 γ to tosyl in 6b and 6c), [69.8, 70.0, 71.0] (CH_2 α to tosyl), [48.9, 51.2, 54.8] (CH), [133.6, 144.4] (Ar-*i*), [127.5] (CH, Ar-*o*), [129.5] (CH, Ar-*m*), [132.7, 133.0, 134.2, 135.6, 135.8, 136.3, 138.2, 138.3, 139.3, 139.6] (olefinic).

Preparation of 3-(Tetramethylcyclopentadienyl)-1-(diphenylphosphino)propanes, $[C_5(CH_3)_4H]CH_2CH_2CH_2P(C_6H_5)_2$ (7). To 30 g (90 mmol of **6** in 150 mL of THF in a 500-mL, three-necked, round-bottom flask equipped with a nitrogen inlet adapter, condenser, and a septum-capped, pressure-equalizing addition funnel was added at 0 °C 90 mmol of a lithium diphenylphosphide solution via the addition funnel, prepared from 16.1 mL (90 mmol) of chlorodiphenylphosphine in 20 mL of THF and 2.61 g (376 mmol) of Li shavings in 100 mL of THF. The yellow-brown reaction mixture was then stirred overnight at room temperature. The THF was then removed under vacuum. The resulting yellow oil was taken up in 250 mL of diethyl ether and then washed with 2 × 100 mL of deoxygenated H_2O. The aqueous layer was separated from the organic layer, dried over anhydrous calcium chloride, and filtered, and the solvent was removed under vacuum. The resulting yellow oil was dissolved in dry hexane and filtered through Celite, and the solvent was removed under vacuum. Diphenylphosphine formed during the reaction sequence was removed by vacuum distillation at 80 °C (1×10^{-3} Torr) to give 22.6 g (65 mmol) of **7** (72% yield) as a viscous yellow oil. IR (neat): 3040 (s), 2940 (vs), 2900 (vs), 2840 (vs), 1940 (w), 1875 (w), 1800 (w), 1640 (m), 1580 (m), 1470 (s), 1425 (vs), 1370 (s), 1325 (w), 1300 (w), 1250 (m), 1175 (m), 1090 (s), 1060 (m), 1020 (s), 995 (m), 960 (m), 800 (m), 735 (vs), 695 (vs). ^1H NMR (270 MHz, C_6D_6): δ 1.00 (d, CH_3, 8.0 Hz), 1.05 (d, CH_3, 8.0 Hz), 1.23 (m, CH_2), 1.40–1.50 (m, CH_2), 1.74 (s, CH_3), 1.78 (s, CH_3), 1.82 (s, CH_3), 1.85 (s, CH_3), 1.87 (s, CH_3), 2.00 (t, CH_2), 2.06 (t, CH_2), 2.09 (t, CH_2), 2.42 (t, CH), 2.50 (m, CH), 7.13 (s, aromatic), 7.50 (m, aromatic). $^{13}C\{^1H\}$ NMR (67.8 MHz, C_6D_6): δ [11.2, 11.4, 11.7, 11.8, 11.9, 14.3, 14.4] (CH_3), [20.7] (CH_2 β to phosphine 7a, $J_{^{31}P-^{13}C}$ = 17.0 Hz), [26.3, 27.2] (CH_2 β to phosphine 7b and 7c, $J_{^{31}P-^{13}C}$ = 17.0 Hz), [27.4, 27.9, 28.0, 28.8, 29.2, 29.4] (CH_2 α and γ to phosphine, $J_{^{31}P-^{13}C}$ = 13.6 Hz), [49.5, 51.8, 56.4] (CH), [128.6] (Ar-*m*, $J_{^{31}P-^{13}C}$ = 6.8 Hz), [128.7] (Ar-*p*), [132.5, 133.0, 133.1] (Ar-*o*, $J_{^{31}P-^{13}C}$ 17.1 Hz), [138.3, 139.8, 140.0] (Ar-ipso, $J_{^{31}P-^{13}C}$ = 14.6 Hz), [133.8, 134.2, 135.0, 135.3, 135.8, 138.0, 138.1, 141.8] (olefinic). $^{31}P\{^1H\}$ NMR (109.25 MHz, C_6D_6): δ −17.8, −17.9, −18.0. Anal. Calcd for $C_{24}H_{29}P$: C, 82.72; H, 8.39. Found: C, 82.84; H, 8.39.

Acknowledgment. We thank the National Science Foundation (Grant RII-8011453) for partial support of this research. NMR spectra were recorded on an instrument supported by the National Science Foundation (Grant PRM 801143).

Communications

Studies on the Enantioselectivity in $Bu_4N[Fe(CO)_3NO]$-Catalyzed Nucleophilic Substitution of Optically Active Allylic Carbonates with Malonate

Summary: The stereochemical outcomes of optically active allylic carbonates **2**, **5**, and **9** with malonate in the presence of iron catalyst **1** were determined. It was found that in every case the nucleophile predominantly attacked at the carbon atom where the leaving group was attached, and the corresponding prevailing regioisomer **3**, **6**, or **10** was obtained with high retention of configuration at the chiral center.

Sir: Among the various carbon–carbon-bond-forming reactions promoted or catalyzed by transition metals, allylic alkylation has been one of the most aggressively sought after. Accordingly, in recent years, extensive studies have been devoted to the regio- and stereochemistry of these allylic alkylation reactions catalyzed by different metal complexes, such as palladium,[1] molybdenum,[2] tungsten,[3] nickel,[4] iron,[5] etc., and the wide applications of these re-

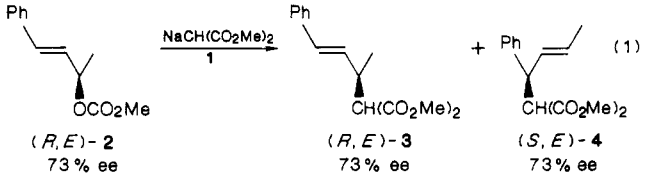
(1) Trost, B. M.; Verhoeven, T. R. *Compr. Organomet. Chem.* **1982**, *8*, 779. Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: Berlin, 1980.
(2) Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1982**, *102*, 5543; **1983**, *105*, 3343; **1987**, *109*, 1469; **1987**, *109*, 4817.
(3) Trost, B. M.; Hung, M. H. *J. Am. Chem. Soc.* **1983**, *105*, 7757.
(4) Cuvigny, T.; Julia, M. *J. Organomet. Chem.* **1983**, *350*, C21. Consiglio, G.; Morandini, F.; Piccolo, O. *J. Chem. Soc., Chem. Commun.* **1983**, 112.
(5) (a) Roustan, J. L.; Merour, J. Y.; Houlihan, F. *Tetrahedron Lett.* **1979**, 3721. (b) Xu, Y.; Zhou, B. *J. Org. Chem.* **1987**, *52*, 974. (c) Ladoulis, S. G.; Nicholas, K. M. *J. Organomet. Chem.* **1985**, *285*, C13. Silverman, G. S.; Strickland, S.; Nicholas, K. M. *Organometallics* **1986**, *5*, 2117.

0022-3263/88/1953-4419$01.50/0

actions in organic synthesis, especially in the case of palladium.

Since these transition-metal-catalyzed allylic alkylation reactions with carbon nucleophiles exhibit diverse regiochemical behaviors which are somewhat complementary to each other (for example, palladium catalysts generally lead to reaction at the less hindered terminus of the allyl fragment; molybdenum catalysts lead to reaction at the more hindered end with malonate as a nucleophile but not with more hindered nucleophiles; tungsten catalysts have shown a bias for reaction at the more hindered position regardless of nucleophile; and the iron catalyst $Bu_4N[Fe(CO)_3NO]$ (1) leads to reaction predominantly at the site where the leaving group was attached with malonate as the nucleophile[5b]), synthetically, there is plenty of room for choice of metal template. Diastereoselectivity in these reactions has also been investigated. Undoubtedly, future efforts will be the quest for enantioselectivity. Nevertheless, in contrast to the extensive studies on regio- and diastereochemical behaviors of these transition-metal-catalyzed allylic alkylations, enantioselectivity has only been rarely exploited. The stereochemical outcomes of palladium-catalyzed reaction of optically active allylic substrates with carbon nucleophiles were somewhat conflicting. For example, Hayashi et al.[6] reported that the reaction of optically active allylic acetates with a phenyl substituent with malonate proceeded with high retention of configuration while Cuvigny et al.[7] reported that the reaction of the optically active linalyl acetate with malonate led to alkylated product with complete racemization. Furthermore, to our knowledge, investigations on the stereochemistry of optically active allylic substrates with nucleophiles catalyzed by transition metals other than palladium are still lacking. Encouraged by the good regioselectivity, geometric selectivity, and diastereoselectivity exhibited in our $Bu_4N[Fe(CO)_3NO]$-catalyzed allylic alkylation,[5b] we determined to initiate a study on the enantioselectivity of this iron-catalyzed reaction. Herein, we wish to report the stereochemical outcomes[8] obtained from the reaction of several optically active allylic carbonates with malonate catalyzed by $Bu_4N[Fe(CO)_3NO]$.

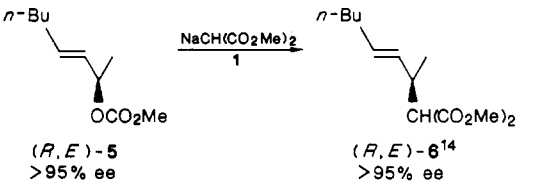
(*R,E*)-**2**[9] ($[\alpha]^{25}_D$ +89.2° (*c* 1.80, chloroform), 73% ee[10]) was allowed to react with 2 equiv of sodium dimethyl malonate in refluxing THF in the presence of 25 mol % of **1** under CO atmosphere for 12 h (eq 1). Workup[11]



(1)

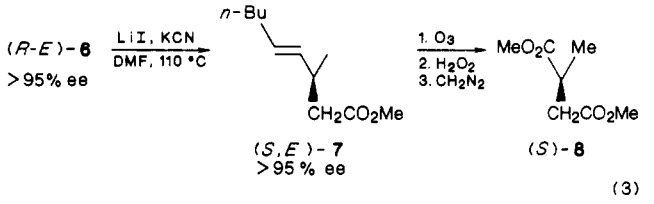
followed by flash chromatography on silica gel gave 78% yield of the alkylated products consisting of dimethyl [1-((*E*)-styryl)ethyl]malonate (**3**) and its regioisomer, dimethyl [1-phenyl-2(E)-butenyl]malonate (**4**), in a ratio of 93:7. The regioisomers **3** and **4** which could be isolated by preparative GLC were found to be an *R* isomer of 73% ee ($[\alpha]^{25}_D$ +50.4° (*c* 1.80, chloroform)) and an *S* isomer of 73% ee ($[\alpha]^{25}_D$ −29.0° (*c* 1.80, chloroform)), respectively. The configurations and enantiomeric excesses of **3** and **4** were determined by comparing the signs and values of optical rotation with those of known compounds[6] ((*S,E*)-**3**, 37% ee, $[\alpha]^{20}_D$ −25.2° (*c* 1.3, chloroform); (*R,E*)-**4**, 30% ee, $[\alpha]^{20}_D$ +12.0° (*c* 1.0, chloroform)).

Since the reactions of optically active alkyl substituted allylic substrates are more interesting and synthetically important, the stereochemical outcomes of (*R,E*)-**5** and (*R*)-**9** were determined. Reaction of (*R,E*)-**5**[12] ($[\alpha]^{14}_D$ +53.2° (*c* 1.08, chloroform), 95% ee[13]) in a similar manner to that of (*R,E*)-**2** gave (*R*)-dimethyl [1-methyl-2(*E*)-heptenyl]malonate, (*R,E*)-**6** ($[\alpha]^{15}_D$ +24.5° (*c* 3.34, chloroform), 95% ee), in 80% yield (eq 2), which was contaminated with



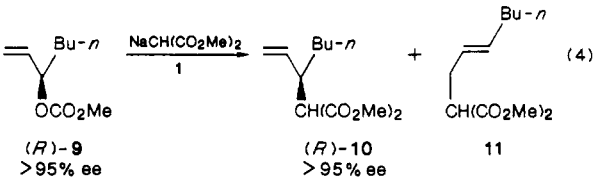
(2)

4% of its regioisomer, dimethyl [1-*n*-butyl-2(*E*)-butenyl]malonate, as revealed by capillary GC. However, we failed to isolate the latter by either preparative TLC or preparative GLC. The ee value of **6** was determined by ^1H NMR of its decarboxylated product (*S,E*)-**7** in the presence of $Eu(dcm)_3$, and the configuration of **6** was determined by conversion of (*S,E*)-**7** into the (*S*)-dimethyl methylsuccinate, (*S*)-**8** ($[\alpha]^{22}_D$ −4.48° (*c* 0.98, chloroform)), by a sequence of reactions shown in eq 3. The antipode of (*S*)-**8** was known[15] ($[\alpha]^{29}_D$ +4.1° (*c* 4.1, chloroform)).



(3)

The reaction of (*R*)-**9**[16] ($[\alpha]^{20}_D$ +14.6° (*c* 1.65, chloroform), 95% ee[17]), an optically active allylic carbonate with a terminal double bond, was also carried out (eq 4). The



(4)

alkylated products (*R*)-dimethyl (1-ethenyl-*n*-pentyl)-malonate, (*R*)-**10** ($[\alpha]^{25}_D$ +4.03° (*c* 1.24, chloroform), 95% ee) and dimethyl 2(*E*)-heptenylmalonate (**11**, devoid of chirality) were obtained in 76% yield after a reaction time of 14 h. The ratio of the regioisomer **10** and **11** was 80:20. The configuration and ee value of **10** were determined by

(6) Hayashi, T.; Yamamoto, A.; Hagihara, T. *J. Org. Chem.* **1986**, *51*, 723.

(7) Civigny, T.; Julia, M.; Rolando, C. *J. Organomet. Chem.* **1985**, *285*, 395.

(8) All new compounds have been fully characterized spectrally (^1H NMR, IR, MS), and elemental composition has been determined by combustion analysis.

(9) (*R,E*)-**2** was prepared by Sharpless kinetic resolution of (±)-1-((*E*)-styryl)ethanol with $Ti(OPr\text{-}i)_4$, (+)-DIPT and *t*-BuOOH, followed by treatment with methyl chloroformate in the presence of pyridine.

(10) The ee value was determined by ^1H NMR in the presence of $Eu(dcm)_3$.

(11) The reaction mixture was treated with an ethereal solution of I_2, followed by washing with an aqueous solution of $Na_2S_2O_3$; see the Experimental Section of ref 5b.

(12) (*R,E*)-**5** was prepared from (±)-3(*E*)-octen-2-ol via a procedure similar to that in the case of (*R,E*)-**2**.

(13) Determined by ^1H NMR using $Eu(dcm)_3$.

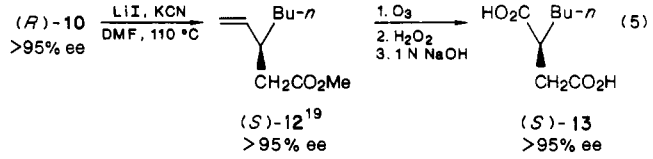
(14) Contaminated with 4% of its regioisomer, dimethyl [1-*n*-butyl-2(*E*)-butenyl]malonate, of unknown configuration, as revealed by capillary GC by comparison with an authentic sample of this compound.

(15) Cohen, S. G.; Milovanovic, A. *J. Am. Chem. Soc.* **1968**, *90*, 3495.

(16) (*R*)-**9** was prepared from (±)-1-hepten-3-ol via a procedure similar to that in the case of (*R,E*)-**2**.

(17) Determined by ^1H NMR using $Eu(hfc)_3$.

converting it into (*S*)-*n*-butylsuccinic acid ((*S*)-**13**) (eq 5) and comparing the sign and value of optical rotation of the latter ($[\alpha]^{29}_D$ −21.5° (*c* 1.49, water) with that reported in the literature[18] ($[\alpha]^{25}_D$ −22.5°, water).



The above results reveal that $Bu_4N[Fe(CO)_3NO]$-catalyzed nucleophilic substitution reactions of optically active allylic carbonates, including those with a phenyl substituent or an alkyl substituent and also the one with a terminal double bond with malonate, occurred with high regioselectivity, the nucleophile predominantly attacked at the carbon atom where the leaving group was attached. In every case, the prevailing regioisomer of the alkylated products possessed the same configuration as that of the starting allylic carbonate and high retention of enantiomeric purity throughout the reaction was observed. This stereochemical outcome might stem from two consecutive S_N2-like processes: backside displacement of the carbonate from the iron complex results in an initial inversion, and a nucleophilic attack occurs on the side opposite iron with a second inversion at the carbon.

We expect that the high enantioselectivity coupled with the good regioselectivity, geometric selectivity, and diastereoselectivity of this $Bu_4N[Fe(CO)_3NO]$-catalyzed allylic alkylation should make the reaction find its synthetic utilities in natural product synthesis. Syntheses of sex pheromones and other natural products via this strategy are in progress and will be reported in due course.

Acknowledgment. Financial support from the National Natural Science Foundation of China and from Academia Sinica is gratefully acknowledged.

(18) Matell, M. *Ark. Kemi* **1953**, *5*, 17.

(19) (*S*)-(−)-**12** ($[\alpha]^{25}_D$ −2.04° (*c* 1.27, chloroform)). (±)-**12** failed to show any chemical shift nonequivalences of the two enantiomers in the presence of either $Eu(dcm)_3$ or $Eu(hfc)_3$.

Bo Zhou, Yuanyao Xu*

Shanghai Institute of Organic Chemistry
Academia Sinica, 345 Lingling Lu, Shanghai
People's Republic of China

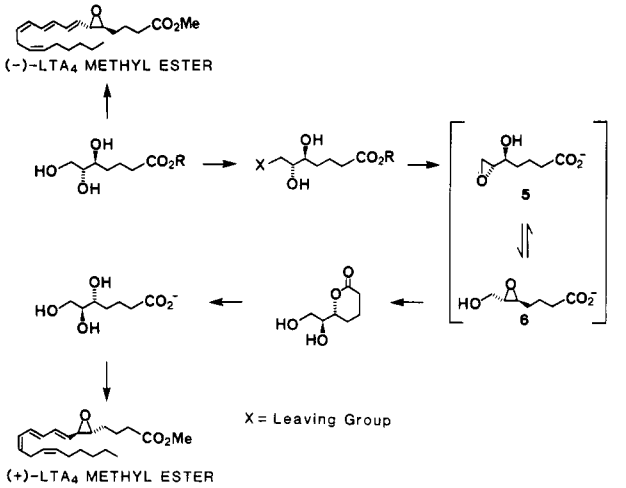
Received April 29, 1988

Inversion of Configurations of Contiguous Carbinol Centers

Summary: A simple method for effecting the inversion of configuration of two contiguous carbinol centers in a diol and triol chain, thus affording the opposite enantiomer, has been developed. Application of this methodology to the synthesis of an LTA_4 intermediate and its enantiomer and the oviposition attractant pheromone of the mosquito *Culex pipiens fatigans* and its enantiomer from the same enantiomerically pure starting material are described.

Sir: The inversion of configuration of a carbon bearing a hydroxyl group is a strategy routinely used in organic synthesis.[1] However, methods for inverting several such centers at the same time are rare. Paulsen reported a method for cyclic peracetylated carbohydrates via a cyclic acyloxonium ion rearrangement using $SbCl_5$.[2] Presently, no method exists for inverting several adjacent carbinol centers on an acyclic backbone. Such a process would provide a rapid and efficient means for converting one enantiomer into the other.

Scheme I



We reported a synthesis of LTA_4 methyl ester and its antipode from 2-deoxy-D-ribose.[3] The antipode was prepared by a less direct route, which required protecting group chemistry in order to invert the desired stereocenter. Herein, we report a novel, conceptually simple solution that obviates such needs.

It was envisioned that the inversion of configuration of several contiguous carbinol centers should be possible via sequential epoxide formation, Payne's rearrangement,[3,4] and lactonization as illustrated in Scheme I. In principle this should be a one-pot process. The equilibrating epoxides would be intercepted by the anticipated irreversible lactonization followed by hydrolysis to yield the enantiomer of the starting triol.

In order to test the viability of this approach, ester **1a** was treated with aqueous NaOH in various solvents (EtOH, THF, DMSO) at various temperatures, conditions which allowed simultaneous hydrolysis of the ester and rearrangement. The product of the reaction was isolated as its acetate **3a** and **3b**[5] after neutralization and acetylation. The enantiomeric purity of the product obtained under a variety of conditions was found to be in the range of 50–60% ee with **3b** predominating as determined by analysis of the 250 and 300 MHz ^1H NMR and ^{19}F NMR spectra of the corresponding (−)-MTPA ester **4a** and **4b**.[6,7]

The loss of optical purity presumably comes from a competing hydroxide anion opening at C-1 of the 1,2-epoxy alcohol **5** in the equilibrium.[8] This hypothesis was substantiated when the protected 2,3-epoxy alcohol **12** was used as a substrate under the same conditions.[9] After the base treatment, removal of the THP ether, and acetylation,

(1) Mitsunobu, O. *Synthesis* **1981**, 1.

(2) Paulsen, H. *Adv. Carbohydr. Chem. Biochem.* **1971**, 127.

(3) Rokach, J.; Lau, C. K.; Zamboni, R.; Guindon, Y. *Tetrahedron Lett.* **1981**, *22*, 2759, 2763.

(4) (a) Payne, G. B. *J. Org. Chem.* **1962**, *27*, 3819. The position of the equilibrium is highly substrate dependent. (b) For recent work on epoxide cascades: Hoye, T. R.; Suhadolnik, J. C. *Tetrahedron* **1986**, 2855.

(5) All new compounds gave satisfactory ^1H NMR (250 MHz) and combustion analysis.

(6) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. ^1H NMR ($CDCl_3$) for OMe signals: (**4a**) δ 3.58; (**4b**) δ 3.46. ^{19}F NMR ($CDCl_3$, CF_3CO_2H as internal standard): (**4a**) δ 4.04; (**4b**) δ 4.42.

(7) Conversion of **3** to **4** was accomplished by deacetylation, sulfonylation, and lactonization to give **7**, which was then treated with (−)-MTPA-Cl in CH_2Cl_2 in the presence of DMAP.

(8) For work on opening of epoxy alcohols: (a) Behrens, C. H.; Ko, S. Y.; Sharpless, K. B.; Walker, F. J. *J. Org. Chem.* **1985**, *50*, 5687. (b) Behrens, C. H.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 5696.

0022-3263/88/1953-4421$01.50/0