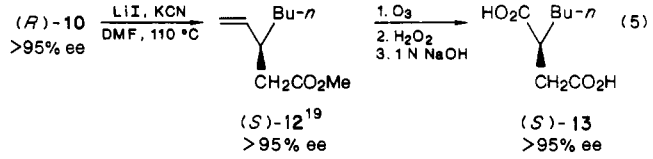
converting it into (*S*)-*n*-butylsuccinic acid ((*S*)-**13**) (eq 5) and comparing the sign and value of optical rotation of the latter ($[\alpha]^{29}_D$ −21.5° (*c* 1.49, water) with that reported in the literature[18] ($[\alpha]^{25}_D$ −22.5°, water).



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 $Eu(hfc)_3$.

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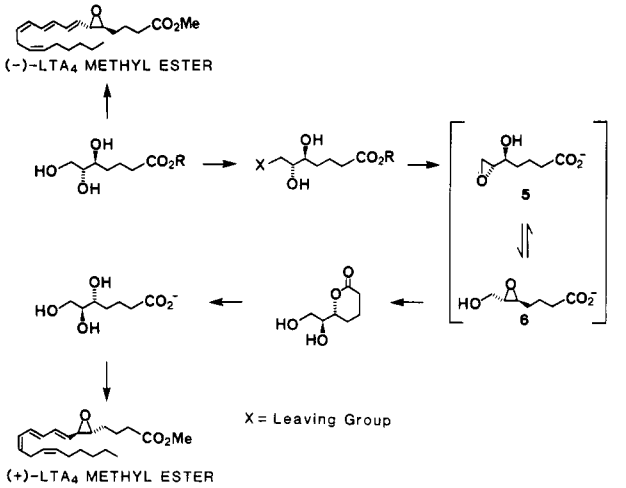
Inversion of Configurations of Contiguous Carbinol Centers

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.

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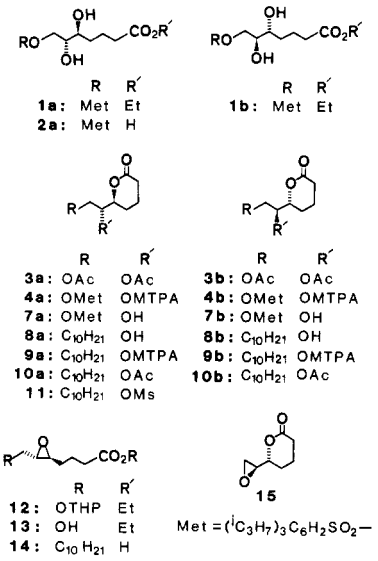
the isolated product had >98% ee, whereas the ee of product derived from the unprotected alcohol **13** was found to be only 68%. It is evident then that anhydrous conditions are essential in order to eliminate side reactions and to obtain high enantiomeric purity. Consequently the acid **2a**[10] was treated with freshly prepared NaOEt in anhydrous EtOH for 18 h, and the product was acetylated to afford the diacetate **3b** [88% yield, $[\alpha]_D$ −55° (*c* 0.9, $CHCl_3$)] whose optical purity was found to be >98% ee. Thus a simple procedure for effecting the inversion of configuration of two contiguous carbinol centers was achieved in high yield with high optical purity. This allows a direct access to the antipode of LTA_4[11] and a general entry to the synthesis of lipoxin A family of compounds in which the stereochemistry of the diol at C-5 and C-6 is critical for biosynthetic studies.[17]



This new methodology was also found to be useful for the synthesis of the oviposition attractant pheromone of the mosquito *Culex pipiens fatigans*, **10b**, and its enantiomer, **10a**,[12] from the same chiral starting material. Hydrolysis of the acetate **3b** with K_2CO_3/EtOH followed by sulfonylation (MetCl/pyr/0 °C) gave **1b** (91% yield). Heating this ester in THF containing 1 M HCl caused hydrolysis of the ester, which upon evaporation of the solvent lactonized to yield the lactone **7b** [78% yield, mp 131–132 °C $[\alpha]_D$ −30° (*c* 1, $CHCl_3$)]. Treatment of lactone **7b** with NaH in THF containing a catalytic amount of DMSO gave the epoxy lactone **15** [90% yield, $[\alpha]_D$ −41° (*c* 1, $CHCl_3$)] as an oil. Selective opening of the epoxide with $H_{21}C_{10}MgBr$ was achieved with 10 mol % of Li_2CuCl_4 as catalyst (THF, −78 °C, 20 min)[13] to afford the alcohol **8b** in 75% yield, which possessed similar physical data to that reported in the literature.[14] Finally, acetylation (Ac_2O/DMAP/CH_2Cl_2) gave the natural product **10b** in quantitative yield.[15,16]

Thus far the strategy involved inverting all the stereocenters of the starting material **2a** to give its enantiomer, which was then further elaborated to give the natural product. An alternative strategy would be to invert the two contiguous asymetric centers later in the synthetic sequence after all the structual elements of the desired compound are in place, for example the conversion of **8a** to **8b**. This variant of the approach would have the added attraction that both enantiomers **10a** and **10b** can be prepared in fewer steps. This would be particularly useful in cases where long syntheses are involved. Following the latter strategy, it was anticipated that mesylation of the masked vicinal diol **8a** followed by saponification should lead directly to its enantiomer **8b** via the epoxide **14** with carboxylate opening at C-5 of **14** competing favorably with random opening by hydroxide anion (cf. saponification of **12**).[9,17] Indeed, when the mesylate **11** was treated with aqueous NaOH followed by acidification with AcOH, **8b** was obtained in 82% yield and 98% ee.[18] Acetylation of the alcholol **8b** gave the natural product as before.[19]

In summary, the chemistry described represents a convenient way to invert the stereochemistry of vicinal hydroxyl groups in a diol and triol chain, thus affording the opposite enantiomer. Further studies on the scope of this methodology, including the effect of additional hydroxymethyl units, and the relative stereochemistry of hydroxy groups are in progress.

Acknowledgment. We thank Dr. Michael Bernstein for ^{19}F NMR measurements.

Supplementary Material Available: Experimental data for compounds **2a**, **3**, **4a,b**, **8**, **9a,b**, **10**, **11**, and **15** (2 pages). Ordering information is given on any current masthead page.

(9) Noyori described a similar reaction: Suzuki, M.; Morita, Y.; Yanakisawa, A.; Noyori, R. *J. Am. Chem. Soc.* **1986**, *108*, 5021.

(10) The acid **2a** was prepared by a slight variation of our published method[3] with $Ph_3P{=}CHCO_2CH_2Ph$ followed by hydrogenolysis.

(11) Compound **1b** was converted to the enantiomer of epoxide **13**, $[\alpha]_D$ +34° (*c* 0.9, $CDCl_3$) [lit.[3] $[\alpha]_D$ +35° (*c* 2.4, $CDCl_3$)], which has been converted (+)-LTA_4 methyl ester.[3]

(12) (a) Laurence, B. R.; Pickett. J. A. *J. Chem. Soc., Chem. Commun.* **1982**, *59*. (b) Mori, K.; Otsuka, T. *Tetrahedron Lett.* **1983**, *29*, 3267. (c) Quo-qiang, L.; Hai-jian, X.; Bi-chi, W. *Tetrahedron Lett.* **1985**, *26*, 1233. (d) Fuganti, C.; Grasselli, P.; Servi, S. *J. Chem. Soc., Chem. Commun.* **1982**, 1285.

(13) The use of other catalysts required longer time and higher temperature and gave lower yields.

(14) Literature data:[12b] mp 67–68 °C, $[\alpha]^{20}_D$ −12.5° (*c* 5.4, $CHCl_3$); observed mp 68–69 °C, $[\alpha]^{20}_D$ −13.9° (*c* 0.4, $CHCl_3$).

(15) Literature data:[12b,c] $[\alpha]_D$ −38.5° (*c* 0.51, $CHCl_3$); observed $[\alpha]_D$ −38.1° (*c* 0.4, $CHCl_3$).

(16) The synthesis of the enantiomer of the natural product **10a** was achieved in a similar fashion by starting from the acid **2a** to yield **10a**, $[\alpha]_D$ +38.0° (*c* 1, $CHCl_3$) [lit.[12b,c] $[\alpha]_D$ +38.4° (*c* 1.41, $CHCl_3$)].

(17) Adams, J.; Fitzsimmons, B. J.; Girard, Y.; Leblanc, Y.; Evans, J. F.; Rokach, J. *J. Am. Chem. Soc.* **1985**, *107*, 464.

(18) ^1H NMR ($CDCl_3$) for OMe signals of (−)-MTPA derivatives: (**9b**) δ 3.51; (**9a**) δ 3.57. ^{19}F NMR ($CDCl_3$): (**9b**) δ 4.63; (**9a**) δ 4.69.

(19) $[\alpha]_D$ −37.5° (*c* 0.8, $CHCl_3$).

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Novel Amide-Directed Hydrocarbonylation and Double Carbonylation of *N*-Allylamides

Summary: The rhodium-catalyzed hydroformylation and palladium-catalyzed hydroesterification of *N*-allylamides give isoaldehyde (**1**) and isoester (**5**), respectively, with good regioselectivity through chelation control while the rhodium- and $Co_2Rh_2(CO)_{12}$-catalyzed reactions of an *N*-methallylamide give a novel double carbonylation product (**10**) and a pyrrolidine (**11**), respectively, with excellent selectivity.

Sir: Chelation-controlled regioselective and stereoselective reactions have extensively been studied in the field of

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