cis-PhCH=CHPh, 645-49-8; *trans*-PhCH=CHPh, 103-30-0; CH_2=$CH(CH_2)_5CH_3$ (epoxide), 2984-50-1; CH_2=$CH(CH_2)_5CH_3$ (oxide dimer), 95999-50-1; $(CH_3)_2\overline{COC}(CH_3)_2$, 5076-20-0; C_6H_6, 71-43-2; PhCHO, 100-52-7; PhCH=$CHCH_3$ (epoxide), 4436-22-0; PhCH=CHPh (*cis*-epoxide), 1689-71-0; PhCH=CHPh (*trans*-epoxide), 1439-07-2; PhC≡CPh, 501-65-5; $PhOCH_2\overline{CHOCH_2}$, 122-60-1; $Ph\overline{CHOCH_2}$, 96-09-3; $PhCH_2OC(CH_3)_3$, 3459-80-1; $PhCH_2Ph$, 101-81-5; $PhCH_3$, 108-88-3; Ph_2S, 139-66-2; Ph_2SO, 945-51-7; Ph_3P, 603-35-0; $PhCH_2OH$, 100-51-6; $PhCH_2Cl$, 100-44-7; $PhCO_2H$, 65-85-0; PhCOCl, 98-88-4; PhCOPh, 119-61-9; PhOH, 108-95-2; Ph_2SO_2, 127-63-9; Ph_3PO, 791-28-6; PhCOCOPh, 134-81-6; $\overline{CH_2OCH(CH_2)_3CH_3}$, 1436-34-6; cyclohexene, 110-83-8; 1,4-cyclohexadiene, 628-41-1; 1,3-cyclohexadiene, 592-57-4; cyclohexene epoxide, 286-20-4; (cyclohexene oxide)$_2$, 25500-50-9; 4,5-epoxy-1-cyclohexene, 6253-27-6; 3,4-epoxy-1-cyclohexene, 6705-51-7; cyclohexane, 110-82-7; cyclohexanol, 108-93-0; cyclohexyl chloride, 542-18-7; cyclohexanone, 108-94-1; 1-hexene oxide dimer, 96128-93-7.

Hiroshi Sugimoto, Donald T. Sawyer*

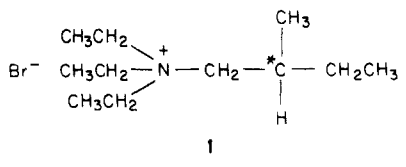
Department of Chemistry
University of California
Riverside, California 92521

Received January 21, 1985

Chiral Phase-Transfer Catalysis. Enantioselective Alkylation of Racemic Alcohols with a Nonfunctionalized Optically Active Phase-Transfer Catalyst

Summary: Racemic *sec*-phenethyl alcohol and 1-phenyl-1-propanol can be alkylated to produce optically active methyl ethers in a phase-transfer-catalyzed reaction with dimethyl sulfate when the optically active quaternary ammonium salt **1** is used as the phase-transfer agent.

Sir: Recent literature reports have demonstrated the viability of conducting asymmetric syntheses using the principle of chiral phase-transfer catalysis.[1] Virtually all of the work reported in this area has dealt with the use of highly functionalized quaternary ammonium salts derived from cinchonidine, ephidrine, quinine, and most commonly cinchonine.[2] An elegant ion pairing scheme based on crystal structure data and molecular modeling studies has been invoked to explain functional group interactions in intimate ion pairs and the efficiency of this chiarl phase-transfer agents.[3] We report the first example of asymmetric induction in the phase-transfer-catalyzed alkylation of racemic alcohols employing the simple, nonfunctionalized, chiral quaternary ammonium salt **1**.



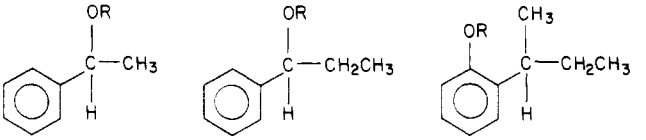
1

Table I. Methylation of *sec*-Phenethyl Alcohol in the Presence of 1[a]

solvent	methyl ether product **5** $[\alpha]^{25}_D$, deg	ee, %	yield, %	uncatalyzed yield[b] of **5**, %
pentane	+18.4	48	84	0.0
toluene	+15.8	39	88	0.5
dichloromethane	+3.2	8	87	5.0

[a] 1.0 mol % catalyst on the basis of starting alcohol was used. [b] Yield of methyl ether after 1 h at 25 °C.

Alkylation of triethylamine with (*S*)-(+)-1-bromo-2-methylbutane, $[\alpha]^{25}_D$ +3.80° (acetonitrile), in refluxing acetonitrile for 24 h followed by evaporation to dryness and washing with ethyl acetate afforded a 91% yield of the optically active quaternary ammonium salt **1** $[\alpha]^{25}_D$ +3.15° (acetonitrile), as colorless needles, mp 97–98 °C.[4] The methylation of 1.0 equiv (4.88 g) of racemic **2** with 0.5



2, R = H
5, R = Me

3, R = H
6, R = Me

4, R = H
7, R = Me

equiv (2.52 g) of dimethyl sulfate in a two-phase system (50% aqueous NaOH, 10.0 g/pentane, 40.0 g) with 0.1 g (1.0 mol %) of **1** as a phase-transfer catalyst was performed at 25 °C for 1 h. Neutralization of the reaction mixture with 8 mL of 50% NH_4OH followed by aqueous extraction, drying (Na_2SO_4), and evaporation produced an 84% yield of the crude methyl ether as an oil contaminated with a trace of acetophenone.[5] Purification by column chromatography (CH_2Cl_2/silica gel) afforded (*R*)-(+)-1-phenyl-1-methoxyethane (**5**) in 48% ee in 75% overall yield.[6] Attempts to verify the enantiomeric excesses by ^1H NMR with chiral shift reagents were unsuccessful as the enantiomers of **5** were not resolved. However, the unreacted alcohol recovered from the aqueous phase by acidification afforded (*S*)-(−)-*sec*-phenethyl alcohol in 40% ee. These results were most surprising in view of the absence of functional groups in the chiral phase-transfer catalyst **1**. In control reactions, only unreacted starting material was recovered in the absence of a phase-transfer catalyst while the product obtained from a methylation reaction employing tetrabutylammonium bromide as a catalyst exhibited no optical activity. Similarly, the methylation of racemic 1-phenyl-1-propanol (**3**) in the presence of **1** afforded, after isolation and purification, a 73% yield of 1-phenyl-1-methoxypropane (**6**), $[\alpha]^{25}_D$ +13.6° (acetonitrile). In contrast the methylation of racemic 2-*sec*-butylphenol (**4**) in the presence of the chiral phase-transfer catalyst yielded only the racemic methyl ether **7**. We first thought that this result might suggest that the chiral center located three bonds away from the reaction site had reduced the ability of the catalyst to differentiate

(1) (a) Saigo, K.; Koda, H.; Nohira, H. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 3119. (b) Julia, S.; Ginabreda, A. *Tetrahedron Lett.* **1979**, 2171. (c) Colonna, S.; Fornasier, R.; Pfeiffer, U. *J. Chem. Soc., Perkin Trans. 1* **1978**, 8. (d) Colonna, S.; Fornasier, R. *J. Chem. Soc., Perkin Trans. 1* **1978**, 371. (e) Julia, S.; Ginebreda, A.; Guixer, J. *J. Chem. Soc., Chem. Commun.* **1978**, 742. (f) Balcells, J.; Colonna, S.; Fornasier, R. *Synthesis* **1976**, 266.

(2) (a) Wynberg, H.; Helder, R.; Hummelen, J.; Laane, R.; Wiering, J. *Tetrahedron Lett.* **1976**, 1831. (b) Wynberg, H.; Hummelen, J. *Tetrahedron Lett.* **1978**, 1089. (c) Julia, S.; Ginebreda, A.; Guixer, J.; Tomas, A. *Tetrahedron Lett.* **1980**, 21, 3709.

(3) Dolling, U.; Davis, P.; Grabowski, E. *J. Am. Chem. So.* **1984**, *106*, 446.

(4) ^1H NMR ($CDCl_3$): δ 1.25 (18 H, m), 3.25 (2 H, d), 3.55 (6 H, q); ^{13}C NMR (ppm) 8.70, 11.07, 19.75, 29.09, 29.70, 46.13, 54.04, 64.12; high resolution atom bombardment ionization mass spectra, M (*m/e*) calcd, 172.2065, obsd 172.2044, quaternary ammonium ion.

(5) Optically pure (*R*)-(+)-1-phenyl-1-methoxyethane, $[\alpha]^{25}_D$ +38.3° (acetonitrile), was synthesized from optically pure (*R*)-(+)-*sec*-phenethyl alcohol, $[\alpha]^{25}_D$ +39.5° (acetonitrile), via phase-transfer-catalyzed methylation with dimethyl sulfate.

(6) The isolated product was identified by comparison with an authentic sample and gave satisfactory spectral analyses. Enantiomeric excesses were measured by optical rotation and comparison with an authentic sample.

0022-3263/85/1950-1786$01.50/0

between enantiomers. However, an uncatalyzed control reaction quickly revealed that the methylation of **4** is quite rapid even in the absence of a phase-transfer catalyst.

The use of more polar organic solvents such as toluene or dichloromethane lead to reduced enantioselectivity in the phase-transfer-catalyzed methylation of racemic *sec*-phenethyl alcohol (Table I). This observation is consistent with reported solvent effects on the chiral phase-transfer process. However, Fiaud[7] has reported that the alkylation of β-diketones under conditions of chiral phase-transfer catalysis afforded greater asymmetric induction when dichloromethane was used as a solvent in place of hexane. In order to investigate the source of the observed solvent effects, racemic *sec*-phenethyl alcohol was methylated in a series of control experiments in which no phase-transfer catalyst was employed. The results obtained (Table I) show that the solvent related enantioselectivity observed in the phase-transfer-catalyzed methylation of *sec*-phenethyl alcohol is inversely related to the rate of the uncatalyzed reaction in the two-phase system. In addition to preventing indiscriminate uncatalyzed reactions from occurring, the choice of the organic solvent may affect the intimacy of the chiral ion pair and, therefore, the extent of chiral recognition. Thus, the selection of the organic solvent in chiral phase-transfer-catalyzed reactions is a key parameter in the optimization of this enantioselective process. The importance of other parameters in these reactions is currently under investigation.

In summary, we have demonstrated that asymmetric induction can be achieved with a high degree of enantioselectivity when optical isomers of a racemic alcohol are alkylated in a two-phase system with a nonfunctionalized optically active quaternary ammonium salt as a phase-transfer catalyst.

Acknowledgment. We thank S. Dorn and P. Donahue for spectral analyses and Dr. J. Cella for many helpful discussions.

(7) Fiaud, J. *Tetrahedron Lett.* **1975**, 3495.

J. W. Verbicky, Jr.,* E. A. O'Neil
Corporate Research and Development Center
General Electric Company
Schenectady, New York 12301
Received January 22, 1985

Highly Selective Direct Oxidation of Thioethers to Sulfoxides Using Molecular Oxygen

Summary: Dialkyl sulfides are converted to sulfoxides in high yield by use of molecular oxygen, ~40-atm pressure, and polar solvents.

Sir: We have recently reported that tertiary amines can be directly converted to their corresponding *N*-oxides with molecular oxygen under high pressures (>50 bar) and in polar solvents.[2] We have extended our studies to another class of electron-rich substrates, thioethers, and find that they too will react directly with molecular oxygen in a selective manner producing sulfoxides. This reaction does not require a catalyst, an initiator, or a photosensitizer and light. In addition, there is very little oxidation of the product sulfoxides to sulfones; thus high sulfoxide/sulfone ratios result. This high selectivity for sulfoxide formation in an autoxidation reaction is unprecedented. Previous studies of thioether autoxidations have led to the conclusion that the autoxidation occurs primarily by abstraction of the α-hydrogen and sulfoxides are produced in low yields by reaction of the unreacted thioethers with the intermediate α-hydroperoxides.[3-5] Unactivated (saturated) thioethers have been found to be fairly inert toward autoxidation in the absence of an initiator.[3]

A critical parameter in the thioether autoxidations presented here is the polarity of the solvent. The reaction does not occur in solvents of low polarity, such as benzene. In addition, the reaction does not occur in decalin, where the oxygen concentration in solution is high,[6] indicating that while a high O_2 pressure (concentration) is important, high oxygen concentrations alone are not sufficient to promote this oxidation. There is also a marked increase in sulfoxide yield as a percentage of converted sulfide when the solvent polarity is increased. For example, in the oxidation of benzyl methyl sulfide at 117 °C and 72 bar in various polarity solvent sytstems, we observe after 6 h the following ratios of sulfoxide/thioether converted: acetone, 0.29; acetonitrile, 0.41; and 60% acetonitrile/40% water, 0.67. At the same time, the reaction rates decrease as the specificity increases (K_{rel} = 1.00 in acetone, 0.104 in CH_3CN, and 0.097 in 60:40 CH_3CN/H_2O), indicating either a change in the mechanism or a suspension of the nonselective pathway in the more polar solvents.

The high pressure autoxidations of thioethers proceed at rates that are slow, similar to the reactions of O_2 with trialkylamines under the same conditions.[2] The observed kinetics for the oxidation of thioethers are also similar to those observed with trialkylamines. Since methionine is soluble in water, its oxidation was studied in water at 119 °C in order to eliminate any added complication arising from solvent oxidation. The reaction is first order in sulfide at constant oxygen pressure (72 bar). The rate constant is also linearly dependent on oxygen pressure over the range studied (18–54 bar). Analysis of these data by a standard ln–ln plot is first order in oxygen within experimental error.

As with tertiary amines, the structure of the thioether affects the rate of reaction and the product distribution. Aliphatic thioethers can be converted to the corresponding sulfoxides in high yield. This includes the functionalized thioether methionine. Phenyl substitution on thioether reduces the reactivity substantially. The failure of diphenyl sulfide to react extensively even at more highly elevated temperatures is typical of the inertness of the phenyl-substituted thioethers.

The similarity in the broad characteristics between the oxidation of tertiary amines and thioethers suggests that both reactions proceed by a similar mechanism. The strong dependence on solvent polarity and the elevated temperatures required are consistent with an initial reversible endothermic one electron transfer from the thioether to oxygen (eq 1).[7] This electron transfer is less

$$R_2S + O_2 \rightleftarrows \underset{1}{R_2S^{+}\cdot} + O_2^{-}\cdot \qquad (1)$$

favorable than that for tertiary amines but still attainable

(1) Present address: Monsanto Co., 800 N. Lindbergh Boulevard, St. Louis, MO 63167.
(2) Riley D. P.; Correa, P. E., *J. Org. Chem.*, in press.
(3) Bateman L.; Cuneen, J. I. *J. Chem. Soc.* **1955**, 1596–1603.
(4) Bateman, L.; Cuneen, J. I.; Ford, J. *J. Chem. Soc.* **1956**, 3056–3064.
(5) Bateman L.; Cuneen, J. I.; Ford, J. *J. Chem. Soc.* **1957**, 1539–1544.
(6) Wesseler, E. P.; Iltis, R.; Clark, L. C. Jr. *J. Fluorine Chem.* **1977** *9*, 137–146.

0022-3263/85/1950-1787$01.50/0