

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<sup>7</sup> has reported that the alkylation of  $\beta$ -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.

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### 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.<sup>2</sup> 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

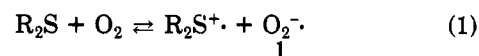
not require a catalyst, an initiator, or a photosensitizer and light. In addition, there is very little oxidation of the product sulfoxides to sulfones; thus high sulfoxide/sulfone ratios result. This high selectivity for sulfoxide formation in an autoxidation reaction is unprecedented. Previous studies of thioether autoxidations have led to the conclusion that the autoxidation occurs primarily by abstraction of the  $\alpha$ -hydrogen and sulfoxides are produced in low yields by reaction of the unreacted thioethers with the intermediate  $\alpha$ -hydroperoxides.<sup>3-5</sup> Unactivated (saturated) thioethers have been found to be fairly inert toward autoxidation in the absence of an initiator.<sup>3</sup>

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,<sup>6</sup> indicating that while a high O<sub>2</sub> 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 systems, 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<sub>3</sub>CN, and 0.097 in 60:40 CH<sub>3</sub>CN/H<sub>2</sub>O), 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<sub>2</sub> with trialkylamines under the same conditions.<sup>2</sup> 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).<sup>7</sup> This electron transfer is less



favorable than that for tertiary amines but still attainable

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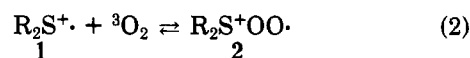
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Table I

substrate (concn, N)	solvent	P <sub>O<sub>2</sub></sub> , bar	temp, °C	time, h	products <sup>a</sup>
dimethyl sulfide (0.55)	42% H <sub>2</sub> O/MeOH	72	105	40	92% Me <sub>2</sub> SO
decyl methyl sulfide (0.21)	4:1 EtOH/H <sub>2</sub> O	72	100	64	88% sulfoxide, 2% sulfide
decyl methyl sulfide (0.16)	4:1 EtOH/H <sub>2</sub> O	72	110	40	60% sulfoxide <sup>b</sup>
decyl methyl sulfide (0.41)	2:1 BuOH/H <sub>2</sub> O	72	100	16	24% sulfoxide, 75% sulfide
tetrahydrothiophene (0.23)	4:1 EtOH/H <sub>2</sub> O	72	120	30	78% sulfoxide, 0.5% sulfone
methionine (0.14)	H <sub>2</sub> O	72	130	21.5	93% sulfoxide
diphenyl sulfide (0.11)	MeOH	72	145	30	<0.3% sulfoxide, >99% sulfide

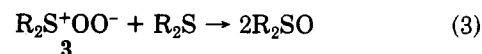
<sup>a</sup> For all reactions the conversions were in excess of 95% unless stated otherwise and the reactions were analyzed by capillary GC with FID. <sup>b</sup> Isolated yield after crystallization from hexane.

under the reaction conditions.<sup>8</sup> To support this the temperature dependence (105–145°C) of the O<sub>2</sub> oxidation of benzyl methyl sulfide was studied in 60:40 CH<sub>3</sub>CN/H<sub>2</sub>O and gave an activation energy of 21.3 kcal.<sup>9</sup> A second key step is the oxygenation of the radical cation with <sup>3</sup>O<sub>2</sub> to yield an oxygenated radical cation, **2** (eq 2). Such a step



would explain the lack of reactivity of phenyl sulfides, since the spin density on a phenyl sulfide radical cation would be highly delocalized. This would slow the rate of combination with <sup>3</sup>O<sub>2</sub>. The conversion to the observed sulfoxide products can be accomplished by reduction of the oxygenated radical cation **2** to a zwitterion **3** with either

superoxide or another molecule of thioether (generating a chain process). This would be followed by a bimolecular reaction of **3** with thioether substrate to generate two molecules of sulfoxide (eq 3).<sup>10</sup> Certainly the initiation



of such selective autoxidations may be possible if these reactions proceed by a chain process. Further studies are under way to discern between these mechanistic possibilities.

**Registry No.** Me<sub>2</sub>SO, 67-68-5; dimethyl sulfide, 75-18-3; decyl methyl sulfide, 22438-39-7; tetrahydrothiophene, 110-01-0; methionine, 63-68-3; diphenyl sulfide, 139-66-2; decyl methyl sulfide, 3079-28-5; tetrahydrothiophene S-oxide, 1600-44-8; methionine S-oxide, 454-41-1.

(7) A reviewer noted the possibility of a heavy atom induced generation of singlet oxygen by the sulfide. The solvent polarity effect is more consistent with the ion-radical mechanism proposed.

(8) The oxidation potential for benzyl methyl sulfide has been measured by cyclic voltammetry in 60% MeCN/40% H<sub>2</sub>O (0.1 M TBATFB vs. Ag<sup>+</sup>/AgCl) to be E<sub>p</sub> = 1.08 V. The reduction of O<sub>2</sub> under similar conditions gives E<sub>p</sub> = -0.4 V. This gives an energy gap of 1.48 V (34 kcal/mol).

(9) This is considerably smaller than the measured energy gap of 34 kcal/mol (ref 8). It must be noted that the redox potentials were from irreversible peak measurements and that the true thermodynamic values could result in a smaller energy difference. In addition, corrections for the higher O<sub>2</sub> concentration and interaction energy between the ions should reduce the measured energy gap further.

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