Phase-Transfer-Catalyzed Oxidation and Reduction of Organosulfur Compounds with Dichlorocarbene. Mechanism and Synthetic Utility

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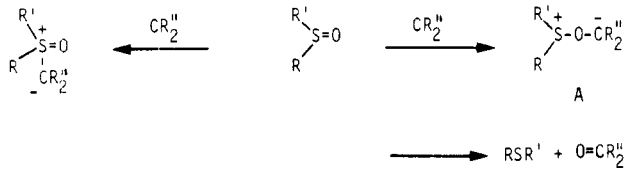
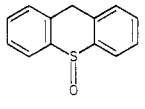
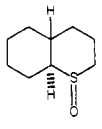
Diaryl and dialkyl sulfoxides undergo facile phase-transfer-catalyzed (PTC) deoxygenation with dichlorocarbene at 25 °C to afford excellent yields of sulfides. Comparisons of deoxygenation rates of dialkyl and diaryl sulfoxides suggest that *steric acceleration* occurs with the bulky sulfoxides while resonance interactions from aromatic rings retard the reduction. Less bulky sulfides also undergo the reverse reaction: addition of dichlorocarbene to the sulfide with hydrolysis of the dialkyl dichloromethylide with hydroxide ion to afford the corresponding sulfoxide. "Oxidation" of *trans*-thiadecalin by reaction with PTC dichlorocarbene addition followed by basic hydrolysis is highly stereoselective, affording 94% axial and 6% equatorial sulfoxide.

The preparation and reactions of sulfonium and oxosulfonium ylides via carbene additions to sulfides and sulfoxides, respectively, appear to be reasonably well established.[1] For example, photolysis or copper-catalyzed thermolysis of dimethyl diazomalonate in the presence of dialkyl or diaryl sulfides and the corresponding sulfoxides form stable sulfonium bis(carbomethoxy)methylides and oxosulfonium ylides, respectively.[2] In contrast to formation of oxosulfonium ylides by reaction of sulfoxides with carbenes, Oda et al.[3] have demonstrated that reaction of dichlorocarbene (CCl_2) with dimethyl sulfoxide (1) gives dimethyl sulfide (13).[4] In fact, carbenes prepared by alkaline cleavage of tosylhydrazones react with 1 to afford ketones and aldehydes in 12–67% yield.[3] Thus, it seems clear that sulfoxides are susceptible to attack by carbenes at either the oxygen or sulfur heteroatom.



While there exists considerable information on the factors which control carbene reactivity toward carbon–carbon multiple bonds,[5] detailed mechanistic input on carbene additions to highly polarized heteroatom–heteroatom multiple bonds (e.g., S=O,[3,4] N→O,[6,7] P=O, etc.) is scarce. It is evident, however, that electrophilic and/or nucleophilic reactivity characteristics of singlet carbenes[5] as well as reagent–substrate reactivity profiles,[8] will largely determine the site of initial carbene attack on sulfoxides.

Table I. Phase-Transfer Catalytic Reduction of Sulfoxides with Dichlorocarbene[a]

sulfoxide	% sulfide	equiv of base (OH^-)
$(CH_3)_2S=O$ (1)	52[b,c]	50
$(CH_3CH_2)_2S=O$ (2)	74	5
$[(CH_3)_2CH]_2S=O$ (3)	89	5
$[CH_3(CH_2)_3]_2S=O$ (4)	90	5, 10
$[CH_3(CH_2)_5]_2S=O$ (5)	90	5
$C_6H_5CH_2S(O)C_6H_5$ (6)	37	5
$[(CH_3)_3C]_2S=O$ (7)	93	5
$CH_2=CHCH_2S(O)CH_3$ (8)	0	1, 5
$(C_6H_5CH_2)_2S=O$ (9)	28[b]	5
$(C_6H_5)_2S=O$ (10)	95	5
 11	90[b]	5
 12	81	5

[a] In all of the reductions reported here, excess chloroform was used as reagent and solvent. Either sodium or potassium hydroxide was used as base. Tetrabutylammonium chloride (200–500 mg) was used as catalyst. Percent composition was determined by GLC analysis of an aliquot from the organic phase. [b] Percent composition determined by ^1H NMR integration of an aliquot from the organic phase. [c] The yield of dimethyl sulfide reported here results from sequential addition of a 50-equiv excess of potassium hydroxide in 10-equiv increments.

One of our initial goals was to establish whether phase-transfer-catalyzed (PTC) CCl_2 reductions of sulfoxides possessed synthetic utility and to gather information on factors which direct the course of the reduction. In this report, we present the results of reactions between CCl_2, generated under solid–liquid PTC[9] conditions, and dialkyl, aryl alkyl, and diaryl sulfoxides with either sodium or potassium hydroxide and chloroform as reagent and solvent. Tetrabutylammonium chloride (TBAC) was used

(1) (a) Trost, B. N.; Melvin, L. S., Jr. "Sulfur Ylides"; Academic Press: New York, 1975. (b) Ando, W. *Acc. Chem. Res.* **1977**, *10*, 179. (c) Block, E. "Reactions of Organosulfur Compounds"; Academic Press: New York, 1978.

(2) (a) Ando, W.; Yagihara, T.; Tozune, S.; Nakaido, S.; Migita T. *Tetrahedron Lett.* **1969**, 1979. (b) Diekmann, J. *J. Org. Chem.* **1965**, *30*, 2272.

(3) Oda, R.; Mieno, M.; Hayashi, Y. *Tetrahedron Lett.* **1967**, 2363.

(4) Soysa, H. S. D.; Weber, W. P. *Tetrahedron Lett.* **1978**, 1969.

(5) (a) Moss, R. A.; Fedorynski, M.; Shieh, W.-C. *J. Am. Chem. Soc.* **1979**, *101*, 4736. (b) Moss, R. A. In "Carbenes"; Jones, J. M., Jr., Moss, R. A., Eds.; Wiley: New York, 1973; Vol. 1, p 153 ff. (c) Hoffmann, R. W.; Reiffen, M. *Chem. Ber.* **1976**, *109*, 2565. (d) Moss, R. A. *Acc. Chem. Res.* **1980**, *13*, 58.

(6) Schweizer, E. E.; O'Neill, G. J. *J. Org. Chem.* **1963**, *28*, 2460.

(7) Weber, W. P. "Abstracts of Papers", 179th National Meeting of the American Chemical Society Houston, TX, Mar 24–28, 1980; American Chemical Society: Washington, DC, 1980; ORGN 35.

(8) (a) Ho, T. L. "Hard and Soft Acids and Bases Principle in Organic Chemistry"; Academic Press: New York, 1977; Chapter 9, p 142. (b) Wallenfals, K.; Friedrich, K.; Rieser, J.; Ertel, W.; Thieme, H. K. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 261–270.

(9) (a) Dockx, J. *Synthesis* **1973**, 441. (b) Dehmlow, E. V. *CHEMTECH* **1975**, *5*, 210. (c) Weber, W. P.; Gokel, G. W. "Phase Transfer Catalysis in Organic Synthesis"; Springer-Verlag: New York, 1977. (d) Starks, C. M.; Liotta, C. "Phase Transfer Catalysis—Principles and Techniques"; Academic Press; New York, 1978.

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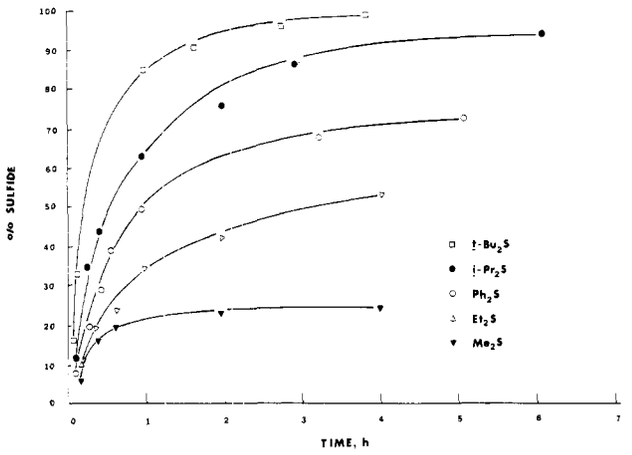


Figure 1. Percent PTC reduction of sulfoxides vs. time.

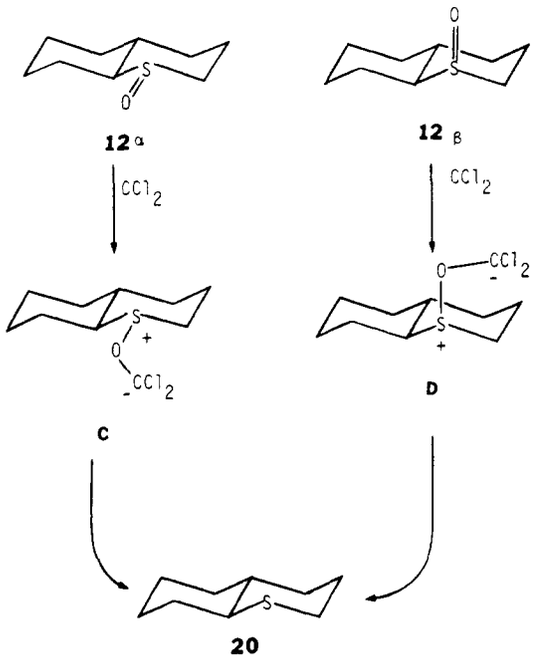
as the catalyst. We also report an interesting competing oxidation involving straight-chain dialkyl sulfides and CCl_2 under liquid–liquid PTC[9] conditions to afford the corresponding sulfoxides in low yield.

Results and Discussion

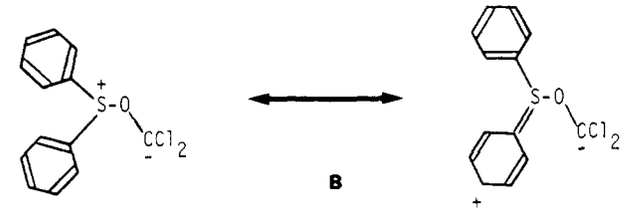
The CCl_2-promoted deoxygenations of dialkyl and diaryl sulfoxides under PTC conditions proceed smoothly (3–6 h at 25 °C), affording good to excellent yields of sulfides devoid of byproducts. However, for sulfoxides having either benzylic or allylic hydrogens α to the sulfinyl group (**6**, **8**, and **9**), the conversion of sulfoxide to sulfide is hampered by side reactions, and the desired sulfides are obtained only in 0–37% yield (vide infra). Good yields of sulfides can be obtained when at least 5 equiv of hydroxide ion are used (Table I). This excess is apparently necessary to ensure the conversion of the phosgene produced to bicarbonate ion and the competitive hydrolysis (H_2O) of CCl_2 to carbon monoxide followed by reaction of CO with hydroxide ion to form formate ion.[10] The yield of dimethyl sulfide (Table I) results from addition of 50 equiv of potassium hydroxide to the PTC medium in 10-equiv increments. This fact is of major importance in understanding the mechanism of *PTC oxidation* of sulfenyl sulfur with aliphatic substituents by CCl_2 and hydroxide ion (vide infra).

Oda et al.[3] and more recently Soysa and Weber[4] have suggested the intermediacy of zwitterion A to explain the formation of sulfides from the reduction of sulfoxides (R′ = R = alkyl, aryl) with CCl_2 and their suggestion is supported by the results displayed in Figure 1. The graphic data in Figure 1 clearly show that formation of di-*tert*-butyl sulfide is considerably faster than formation of the lower homologues or diphenyl sulfide. More specifically, the data show that for dialkyl sulfoxides, the rate of formation of sulfides is a function of the steric bulk of the alkyl groups and thus is related to the propensity for elimination of RSR′ from zwitterion A. This trend in reactivity is consistent with the tenets of steric assistance[11] and argues against a mechanistic proposal involving initial attack by CCl_2 on sulfinyl sulfur in a rate-controlling step since such an attack would be hindered by the bulky alkyl groups.[12]

Scheme I



Interestingly, the influence of steric acceleration on zwitterion A is apparently more important than the stability of the departing sulfide. For example, one might have expected diphenyl sulfoxide (**10**) to show greater reactivity toward deoxygenation than sulfoxide **3** because diphenyl sulfide (**16**) is presumably a thermodynamically better leaving group than diisopropyl sulfide due to resonance stabilization of the sulfenyl sulfur lone-pair electrons.[13] The fact that reduction of **10** is actually *slower* than that of sterically similar **3** may have its origin in two opposing effects: (a) the steric assistance effect arising from the isopropyl groups is of larger magnitude than the phenyl groups, and as a consequence zwitterion A is severely destabilized for R = R′ = *i*-Pr; (b) resonance-stabilizing interactions with the alkoxy sulfonium sulfur in zwitterion B result in an increase in the activation energy



for deoxygenation of B where R = R′ = aryl or phenyl when compared to R = R′ = *i*-Pr. The net result of these factors is a lowering of the activation energy for collapse of $(i\text{-Pr})_2S^+\text{–O–C}^-Cl_2$ relative to $Ph_2S^+\text{–O–C}^-Cl_2$.

This conclusion seems viable because the general trend in increased reactivity of sulfoxides toward reduction with a number of reductants which ultimately involve alkoxy sulfonium salts indicates that dialkyl sulfoxides are more reactive than diaryl ones. Specifically, Brown,[14] Ho,[15]

(10) (a) Surprisingly, the reaction between dichlorocarbene and hydroxide ion appears to be kinetically insignificant compared to the reaction of dichlorocarbene with water. See: Robinson, E. A. *J. Chem. Soc.* **1961**, 1663. (b) See also: Makosza, M.; Wawrzyniewicz, M. *Tetrahedron Lett.* **1969**, 4569.

(11) Eliel, E. L.; Allinger, N. L.; Angyal, S. J.; Morrison, G. A. "Conformational Analysis"; Wiley: New York, 1965; p 81.

(12) It is conceivable that formation of sulfides may follow from a concerted decomposition of three-membered-ring intermediates containing tetravalent sulfur (σ-sulfurane), arising from cheletropic CCl_2 addition across the sulfinyl bond or by equilibration of zwitterion A. The experiments described here were not designed to provide useful insights to this interesting question. See: Jones, W. M.; Brinker, V. H. "Pericyclic Reactions"; Marchand, A. P., Lehr, R. E., Eds.; 1977; Vol. 1, Chapter 3, p 106.

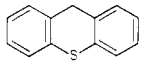
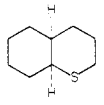
(13) Epstein, W. W.; Sweat, F. W. *Chem. Rev.* **1967**, *67*, 247.

Olah,[16] Drabowicz and Milolajczyk,[17] and Dreux et al.,[18] employing a range of synthetic procedures to deoxygenate a variety of sulfoxides, have shown that aliphatic sulfinyl compounds are more rapidly reduced than the aryl ones.[19]

We have also examined the reactivity of diastereoisomeric and conformationally homogeneous sulfoxides. In light of the results of Allinger's recent force field calculations[20a] concerning factors governing axial–equatorial preferences of the sulfinyl oxygen in six-membered rings, the observation that *trans*-1-thiadecalin 1β-oxide (**12**β) with the equatorial sulfinyl oxygen is reduced faster than the axial isomer **12**α (Scheme I) is not too surprising. Allinger et al. have suggested that the equatorial sulfinyl oxygen experiences two pairs of gauche hydrogen interactions which are sterically more severe than the interactions between the axial sulfinyl oxygen and the sum of the 1,3-synaxial and two gauche hydrogens.[20b,21] It does seem likely that the initial reaction between sulfoxide and CCl_2 to afford zwitterion A is probably not rate controlling. But while we imply from the foregoing that zwitterion C is probably less stable than zwitterion D, the small difference in half-lives ($t_{1/2}$ = 18 min for **12**β and $t_{1/2}$ = 28 min for **12**α) may arise from the collective energy differences between **12**α and **12**β, zwitterion C and D, and the appropriate transition states and, therefore, cannot be attributed entirely to steric acceleration.[23]

Sulfoxides **6**, **8**, and **9**, possessing allylic or benzylic hydrogens α to the sulfinyl group, react with CCl_2 under PTC conditions but do not afford good yields of sulfides (Table I). Under the experimental conditions, a number of components were evident from GLC analyses of reaction mixtures, and it seems reasonable to suggest that their existence is derived from base-catalyzed isomerization of the reactant sulfoxide especially in the case of **8**,[24] decomposition of zwitterion A by alternate pathways,[25] or subsequent reaction of the product sulfide.[26] For example, the reaction of allyl methyl sulfoxide with CCl_2 under PTC conditions gave material whose NMR spectral features were consistent with the structure, CH_2=CHCH=C(Cl)-SCH_3. Parham and Groen proposed a similar structure for the product arising from the reaction of allyl methyl sulfide and CCl_2.[26b]

Table II. Phase-Transfer-Catalyzed Oxidations of Organosulfur Compounds with Dichlorocarbene[a]

sulfide	% sulfoxide	equiv of NaOH
CH_3SCH_3 (13)	31[b]	5
$(C_4H_9)_2S$ (14)	23	6
$C_6H_5SCH_2C_6H_5$ (15)	5	10
$C_6H_5SC_6H_5$ (16)	0	7, 25, 75
$C_6H_{13}SC_6H_{13}$ (17)	7 (16)[c]	10 (30)
$[(CH_3)_2CH]_2S$ (18)	0	10
 19	0	10, 20
 20	20	10

[a] The PTC CCl_2 reaction mixtures consisted of equal volumes but an excess of chloroform and water, TBAC (125–500 mg) as PTC catalyst, and either sodium or potassium hydroxide. Percent composition was determined by GLC analyses of aliquots taken directly from the reaction mixture. [b] This reaction mixture is identical in all respects with the one described for the deoxygenation of sulfoxides in Table I. Percent composition was determined by ^{1}H NMR integration of aliquots taken from the organic phase with cyclohexane as an internal standard. [c] The product yield was increased to 16% after addition of 20 equiv of hydroxide to the reaction mixture.

PTC CCl_2 Oxidation of Sulfides to Sulfoxides. In contrast to the reduction of sulfoxides, the PTC oxidation of sulfides with CCl_2 and hydroxide ion occurs slowly (20–48 h at 25 °C) and affords relatively low yields (Table II). It is, however, remarkable that this particular oxidation reaction occurs simultaneously with the reduction. Although the yields are low, the sulfoxides are the *only* products of the reaction as evidenced by GLC and ^{1}H and ^{13}C NMR analyses of the reaction mixtures (see Experimental Section).

The initial step in the oxidation is probably formation of the sulfonium dichloromethylide E (see Scheme III). This would be consistent with the results of previous studies by Parham and Konocos[26a] as well as Andrews and

(14) Brown also suggests that the deoxygenation of aliphatic sulfoxides with dichloroborane may follow a similar route. See: Brown, H. C.; Ravindran, N. *Synthesis* **1973**, 42.

(15) (a) Ho, T. L.; Wong, C. M. *Synth. Commun.* **1973**, *3*, 37. (b) Ho, T. L.; Wong, C. M. *Synthesis* **1973**, 207. From the results of our work, it is entirely unwarranted to invoke *two* different mechanisms to explain the rate differences in the reduction of aliphatic and aromatic sulfoxides as reported in this reference.

(16) (a) Olah, G. A.; Gupta, B. G. B.; Namata, S. C. *Synthesis* **1977**, 583. (b) Olah, G. A.; Gupta, B. G. B.; Narang, S. C. *Ibid.* **1978**, 137.

(17) (a) Drabowicz, J.; Mikolajaczyk, M. *Synthesis* **1978**, 138. (b) Drabowicz, J.; Mikolajaczyk, M. *Ibid.* **1978**, 542.

(18) Dreux, M.; Leroux, Y.; Savignac, P. *Synthesis* **1974**, 506.

(19) It is noteworthy that when sulfoxides are acylated in the presence of iodide ion with subsequent decomposition to the sulfide, sterically hindered sulfoxides react slowly. This is presumably due to steric hindrance encountered during nucleophilic attack by I^- on the (acyloxy)-sulfonium sulfur. See: Allenmark, S. *Acta. Chem. Scand.* **1966**, *20*, 910.

(20) (a) Allinger, N. L.; Kao, J. *Tetrahedron* **1976**, *32*, 529. (b) Claus et al. have demonstrated that electronic factors are important in determining the conformation equilibria of thian-1-arylimides. See: Claus, P. K.; Vierhapper, F. W.; Willer, R. L. *J. Org. Chem.* **1979**, *44*, 2863–2871.

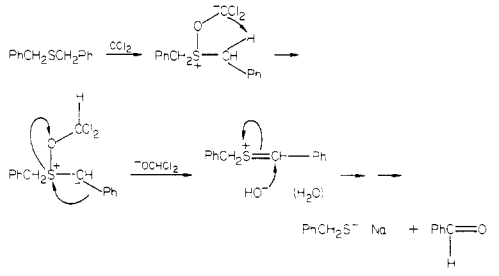
(21) Support for this contention comes from results obtained from pk_{BH^+} studies of sulfoxides in aqueous sulfuric acid.[22] The results indicate that the preference for the axial conformation for the sulfinyl oxygen in 4-*tert*-butylthiane 1-oxide is not only maintained in aqueous acid but actually *enhanced* by 0.3 kcal/mol. Apparently, the interactions between the vicinal hydrogens and the new oxygen hydrogen single bond (e.g., S^+–O–H) further destabilize the equatorial conformation of the conjugate acid.

(22) Curci, R.; Furia, F. D.; Levi, A.; Lucchini, V.; Scorrano, G. *J. Chem. Soc., Perkin Trans. 2* **1975**, 341.

(23) The entropy of activation, ΔS^*, may also be an influential factor in the differences in half-lives.

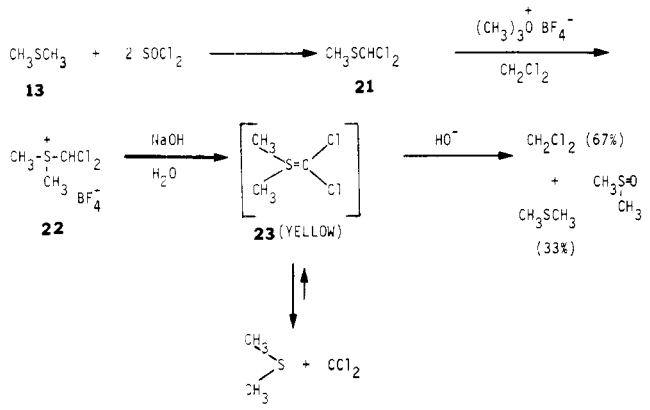
(24) O'Connor, D. E.; Broaddus, C. D. *J. Am. Chem. Soc.* **1964**, *86*, 2267.

(25) For example, we envision the following scheme for the CCl_2-promoted fragmentation of **9**. See also: Tuleen, D. L. *J. Org. Chem.* **1967**, *32*, 4006.

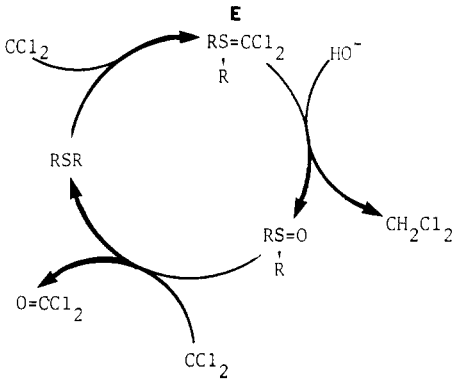


(26) (a) Parham, W. E.; Koncos, B. *J. Am. Chem. Soc.* **1961**, *83*, 4034. (b) Parham, W. E.; Groen, S. H. *J. Org. Chem.* **1965**, *30*, 3181.

Scheme II



Scheme III



Evans[27] where it has been shown that CCl_2 exhibits a relatively high propensity for the sulfenyl lone pair electrons.

To our knowledge, there have been no definitive studies on the isolation and characterization of dialkylsulfonium dichloromethylides. We attempted to prepare a solution of dimethyl- and di-*n*-butylsulfonium dichloromethylide by adding MeLi, *n*-BuLi, or *t*-BuLi to an ethereal solution of the sulfide with chloroform at −78 °C. The solution turned yellow, presumably indicative of $R_2S{=}CCl_2$ since no such coloration was evident in the absence of sulfide.[28] Similar coloration has been reported for the triphenylphosphonium dichloromethylide.[30] However, when we quenched the yellow solution with water or hydroxide ion, the sulfoxide was not formed; only sulfide was observed. If the yellow color is attributable to the dichloromethylides, then this latter observation implies that they are in equilibrium with "free" dialkyl sulfides and CCl_2. Recovery of only sulfide indicates not only that the equilibrium constant, K_f, is very large but also that the equilibrium is rapidly established and, of course, may be controlled by the continuous hydrolysis of CCl_2.

$$R_2S{=}CCl_2 \overset{K_f}{\rightleftharpoons} R_2S + CCl_2$$

When diisopropyl sulfide (18) or diphenyl sulfide is examined in the presence of PTC dichlorocarbene, no yellow color is evident, and evidence for the corresponding sulfoxide is also absent. Large alkyl groups are expected to destabilize formation of dialkylsulfonium dichloromethylides by steric hindrance while the phenyl groups in 16 also reduce the nucleophilic character of sulfenyl sulfur's lone-pair electrons through the delocalization. This rational is supported, in part, by the report that competitive attack of carbenes on dimethyl sulfide is 5 times faster than attack on diisopropyl sulfide.[31] The resistance of other carbenes (and nitrenes) to form ylides with sterically hindered or aryl sulfides has been adequately noted.[32] It seems clear that our inability to react the dialkylsulfonium dichloromethylides with hydroxide ion directly to form sulfoxides is due simply to an insufficient concentration of $R_2S{=}CCl_2$ and perhaps its questionable reactivity toward basic hydrolysis.[33]

We have obtained valuable information on these points by preparing the dialkylsulfonium dichloromethylide directly in the presence of hydroxide ion *before* equilibrium concentrations of CCl_2 and sulfide could be established. Dimethyl sulfide can be dichlorinated with thionyl chloride to afford α,α-dichloromethyl methyl sulfide (21)[34] which can be treated with trimethyloxonium tetrafluoroborate in dichloromethane to give α,α-dichloromethyl dimethylsulfonium tetrafluoroborate (22) in 52% yield (Scheme II). When dimethylsulfonium salt 22 is treated with aqueous hydroxide, a transient yellow color appears for ~3 s. Immediate extraction with deuteriochloroform followed by ^1H and ^{13}C NMR analysis of the organic phase confirmed the presence of dimethyl sulfoxide, dichloromethane (67%), and dimethyl sulfide (33%). The percentage of 1 is slightly less than the percentage of CH_2Cl_2 and variable due to its solubility in aqueous media. We interpret these data in the following way. Proton abstraction from sulfonium salt 22 gives dichloromethylide 23 which apparently undergoes attack by hydroxide ion through possibly a σ-sulfurane,[1a] followed by proton transfer and elimination of dichloromethylide to afford the sulfoxide. Simultaneously, disproportionation of 24 to sulfide 13 and CCl_2 also occurs.

With excess hydroxide ion and CCl_2, the oxidation and reduction reactions should, in principle, be competitive. However, some important aspects of the reaction conditions may serve to minimize the importance of oxidation during reduction or vice versa. In the oxidation sequence, equal volumes of chloroform and aqueous hydroxide solution were employed as the two-phase liquid medium while in the reduction sequence only chloroform in dichloromethane solvent with solid potassium hydroxide represented the reaction medium. We reason that the dialkylsulfonium dichloromethylides are produced in low, steady-state concentrations, and the relatively small quantities of sulfoxides which are formed (16–23%) suggest that the newly formed sulfoxide is "insulated" from CCl_2 and the ensuing "rapid" reduction. It is conceivable that the sulfoxide is simply solubilized in the aqueous phase and only undergoes slow deoxygenation at the liquid–liquid

(27) Andrews, G. A.; Evans, D. A. *Tetrahedron Lett.* **1972**, 5121.

(28) Treatment of di-*n*-butyl sulfide with CCl_2 (from *n*-butyllithium and deuteriochloroform) gave a yellow solution with an intense ^{13}C NMR absorption at δ 128.69. We have tentatively assigned this absorption to "free" CCl_2 since the relative intensity and chemical shift of this signal are not consistent with the $R_2S{=}CCl_2$ structure. Seebach et al.[29] reported the observation of an absorption at δ 151 which they attributed to CBr_2 arising from reaction of alkyllithiums with bromoform.

(29) (a) Seebach, D.; Siegel, H.; Mullen, K.; Hiltbrunner, K. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 784. (b) Siegel, H.; Hiltbrunner, K.; Seebach, D. *Ibid.* **1979**, *18*, 785.

(30) Speizale, J. *J. Am. Chem. Soc.* **1962**, *84*, 854.

(31) Ando, W.; Yagihara, T.; Tozune, S.; Imai, I.; Suzuki, J.; Toyama, T.; Nakaido, S.; Migita, T. *J. Org. Chem.* **1972**, *37*, 1721.

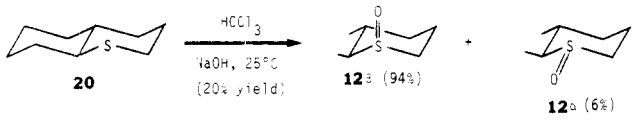
(32) Appleton, D. C.; Bull, D. C.; McKenna, J. M.; Walley, A. R. *J. Chem. Soc., Chem. Commun.* **1974**, 140.

(33) The stability of sulfonium ylides contrasts with the relative ease of hydrolysis of nonstabilized phosphorus ylides to afford phosphine oxides and hydrocarbons. See: Johnson, A. W.; LaCount, R. B. *J. Am. Chem. Soc.* **1961**, *83*, 417.

(34) Truce, W. E.; Birum, G. H.; McBee, E. T. *J. Am. Chem. Soc.* **1952**, *74*, 3594.

interface or in the chloroform solvent. Scheme III summarizes our mechanistic interpretations.

We have also discovered a rather high stereoselection in the PTC oxidation of *trans*-thiadecalin with CCl_2. It was anticipated that attack of CCl_2 on the conformationally homogeneous sulfide **20** might occur from the equatorial



20 **12β** (94%) **12α** (6%)

face of sulfenyl sulfur in a manner characteristic of other electrophiles.[35] McKenna has reported a preference for equatorial attack on 4-*tert*-butylthiane with a stabilized carbene.[32] Our results [94% axial sulfoxide (**12β**), 6% equatorial sulfoxide (**12α**)] are consistent with a preference for electrophilic attack by CCl_2 at the equatorial position with subsequent displacement by hydroxide ion to afford the sulfoxide. The equatorial approach by CCl_2 is also consonant with the orbital arguments of Klein and Stollar.[35]

Experimental Section[36]

Dimethyl, diethyl, diisopropyl, di-*n*-butyl, dihexyl, di-*tert*-butyl, diphenyl, dibenzyl, and allyl methyl sulfide as well as thioxanthene were obtained from Aldrich Chemical Co. and used without prior purification. Benzyl phenyl sulfide was synthesized by the procedure developed by Dockx.[37]

Dimethyl sulfoxide was obtained from Fisher Scientific, distilled over calcium hydride under a nitrogen atmosphere, and finally stored over 4-Å molecular seives. Chloroform was washed with an equimolar amount of water and distilled over phosphorus pentoxide under a nitrogen atmosphere.[38]

All of the sulfoxides were prepared by oxidation of the corresponding sulfides with mCPBA in dichloromethane solvent at 0–5° (ice bath).[39] Neutralization with a saturated aqueous sodium bicarbonate solution and removal of dichloromethane gave the crude sulfoxides. Di-*n*-butyl sulfoxide [mp 31–33 °C (lit.[40] mp 32 °C)], di-*n*-hexyl sulfoxide [mp 58.0–59.5 °C; 76% yield (lit.[41] mp 60 °C)], di-*tert*-butyl sulfoxide [mp 62–64 °C; 50% yield (lit.[42] mp 63.5–65.0 °C)], and diphenyl sulfoxide [mp 70 °C; 70% yield; (lit.[43] mp 71 °C)] were recrystallized from hexane–dichloromethane solution and sublimed. Thioxanthene 10-oxide [mp 116–118 °C; 65% yield (lit.[44] mp 109 °C)], benzyl phenyl sulfoxide [mp 119–120 °C; 82% yield (lit.[45] mp 120.5 °C)], and dibenzyl sulfoxide [mp 133–134 68% yield (lit.[46] mp 133 °C)] were recrystallized from hexane–dichloromethane solvents. Diethyl sulfoxide [bp 77–79 °C (2.4 torr); 87% yield; lit.[47] bp 45–47 °C (0.15 torr)] and diisopropyl sulfoxide [bp 35–36 °C (0.10 torr); 66% yield; lit.[48] bp 50 °C (0.1 torr)] were distilled at reduced pressure by using a microdistillation apparatus.

Table III. ^{13}C NMR Spectral Data for the Three Isolated Components from the PTC Reaction of Di-*n*-butyl Sulfide and CCl_2

compd	^{13}C NMR shifts,[a] δ			
	C_β	C_γ	C_δ	C_ϵ
di-*n*-butyl sulfide (14)	31.96	31.96	22.14	13.74
di-*n*-butyl sulfoxide (4)	52.18	22.11	24.66	13.70
tetrabutylammonium chloride	58.97	24.18	19.79	13.70

[a] C_β is attached directly to the heteroatom (S, N) and β to oxygen or the lone pair.

***trans*-Thiadecalin 1-Oxides (12α,β).** The synthesis of the diastereomeric sulfoxides of *trans*-thiadecalin have been previously reported.[49] In this present work, the isomeric sulfoxides were prepared by sodium *m*-periodate oxidation of the corresponding sulfide in methanol–water medium at approximately −15 °C to give 69% axial and 31% equatorial sulfoxides. This mixture was examined under deoxygenation conditions.

Kinetic Analysis of the Reduction. The sulfoxide (2.5 mmol) was added to a rapidly stirring mixture of ethanol-free chloroform (0.5 mL), TBAC (125 mg), finely ground potassium hydroxide (860 mg, 12.5 mmol), and dichloromethane solvent (20 mL). Aliquots were quenched in approximately 1 mL of 2 N hydrochloric acid, and the concentration of sulfide and sulfoxide was determined by GLC analyses. The values reported in Table I are averages taken from several GLC peak integrations, and they are considered accurate to ±3%. For the reaction involving **1**, the percent yield of sulfide was determined by ^1H NMR integration of absorptions at δ 2.1 (dimethyl sulfide) and 2.5 (dimethyl sulfoxide).

PTC CCl_2 Reduction of Sulfoxides. All of the sulfoxides for which reaction profiles were determined (Figure 1) were subjected to identical PTC reaction conditions. The experimental procedure described below for reduction by phase-tranfer catalysis should be viewed as representative.

Diisopropyl Sulfide (18). A solution of diisopropyl sulfoxide (0.34 g, 2.5 mmol) in 20 mL of dichloromethane was combined with finely ground potassium hydroxide (0.82 g, 13 mmol) and a solution of TBAC (125 mg) in 0.50 mL of chloroform. GLC analyses were performed on aliquots from the reaction mixture which had been quenched in approximately 1 mL of 2 N hydrochloric acid.

General PTC CCl_2 Reduction of Sulfoxides. The procedure shown below should be considered typical for the reduction of sulfoxides with PTC CCl_2 as a synthetic procedure.

Thioxanthene (19). A solution of thioxanthene 1-oxide (540 mg, 2.5 mmol) in 20 mL of chloroform was added to sodium hydroxide pellets (1.00 g, 25.0 mmol) and then stirred rapidly to effect thorough mixing. Tetrabutylammonium chloride (200 mg) was added to the reaction mixture, and the entire mixture was stirred overnight. The organic phase was washed with water (3 × 20 mL), dried (magnesium sulfate), and concentrated to dryness (rotary evaporator) to give a yellow solid. ^1H NMR analysis indicated the presence of **19** (90%) and **11** (10%).

Oxidation of Sulfides with PTC CCl_2. All of the sulfides except **13** were oxidized under identical reaction conditions, and the experimental procedure described below for **14** should be viewed as typical except that isolation of separate components of the reaction mixture by column chromatography was not

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(36) Melting points were obtained in a Mel-Temp melting point apparatus with an open capillary tube and are uncorrected. ^1H NMR spectra were recorded on the Perkin-Elmer Model R24B and Varian Model XL-100-12 NMR spectrometers controlled by a 620/f computer. All Fourier transform spectra were obtained at ambient temperatures (approximately 30 °C), and Fourier transforms were based on 8K data points with off-resonance and noise decoupling. The ^1H and ^{13}C NMR chemical shifts of samples as deuteriochloroform ($CDCl_3$) solutions are presented in parts per million (δ) downfield from internal tetramethylsilane (Me_4Si), and these values are considered accurate to ±0.03 ppm unless otherwise indicated. The coupling constants are in hertz. Gas–liquid chromatographic (GLC) analyses were performed on a Hewlett-Packard Model 5754B research gas chromatograph using a 12 ft × 0.025 in. (i.d.) stainless-steel column packed with 10% DC-550 on Chromosorb W and a 6 ft × 0.025 in. stainless-steel column packed with 1% DC-550 on Chromosorb W. Cyclohexane was used as internal reference standard on GLC analyses.
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performed on all reaction mixtures.

Di-*n*-butyl Sulfoxide (4). Sodium hydroxide pellets (13.9 g, 287 mmol) were added to a mixture containing water (50 mL), chloroform (50 mL), and TBAC (500 mg). Di-*n*-butyl sulfide (4.2 g, 290 mmol) was added to the mixture at ambient temperature which was stirred vigorously for 23 h. GLC analysis of an aliquot of the organic layer indicated the presence of 4 (18%) and a number of minor components arising from catalyst (TBAC) degradation within the injection port and on the GLC column. Separation of these components was accomplished with column chromatography. The dark red-brown chloroform solution was concentrated to dryness (rotary evaporator), and a 5-mL aliquot was pipetted onto a column (1 in. o.d. × 15 in.) containing neutral aluminum oxide (50 g). Elution with a mixture of hexanes afforded homogeneous **14**; elution with chloroform gave pure **4**; elution with methanol gave TBAC. The identity of each substance was confirmed by ^{13}C NMR (Table III) and GLC retention time comparisons with authentic samples.

Dichloromethyl Methyl Sulfide (21). Dimethyl sulfide (31.7 g, 50 mmol) was added to a dry 500-mL, three-necked flask equipped with an addition funnel (250 mL), an overhead stirrer, a condenser, and a drying tube (Drierite). The reaction flask was cooled to approximately −10 °C (ice–salt bath), and thionyl chloride (119 g, 71.9 mL, 100 mmol) was added dropwise over a 3-h period. The solution was then heated to reflux (steam bath) and allowed to stir overnight. The remaining yellow liquid was decanted from a yellow solid and distilled to afford 42.3 g of a liquid. A second distillation (8-in. Vigreux column) gave 14.0 g (21%) of a yellow homogeneous liquid: bp 130–133 °C [lit.[34] bp 137 °C (742 torr)], ^1H NMR (neat) δ 2.70 (s, 3 H, SCH_3), 7.08 (s, 1 H, Cl_2CHS).

(Dichloromethyl)dimethylsulfonium Tetrafluoroborate (22). A solution of **21** (6.5 g, 50 mmol) in 20 mL of dichloromethane was added to a dry, round-bottomed flask fitted with a reflux condenser and a drying tube. Methyl iodide (7.1 g, 3.1 mL, 50 mmol) was added in one portion, and the solution was heated to reflux (steam bath) for 12 h. An ^1H NMR analysis of an aliquot indicated that no reaction had occurred. Trimethyloxonium tetrafluoroborate (7.4 g, 50 mmol) was added, and the solution was again heated to reflux for 2 h. The lower brown viscous phase was pipetted into 50 mL of anhydrous diethyl ether where it crystallized. Recrystallization of this solid from a 1:1 solution of diethyl ether and acetone gave 6.1 g (52%) of a colorless solid: mp 45 °C; ^1H NMR (D_2O) δ 3.4 (s, 6 H, $S(CH_3)_2$), 7.6 (s, 1 H, Cl_2CHS). Anal. Calcd for $C_3H_7SCl_2BF_4$: C, 17.19; H, 3.03. Found: C, 17.27; H, 3.16.

(Dichloromethyl)dimethylsulfonium Tetrafluoroborate in Aqueous Sodium Hydroxide. A solution of **22** (2.33 g, 10.0 mmol) in 5 mL of water was added to a round-bottomed flask equipped with a reflux condenser. A solution of 50% aqueous sodium hydroxide (0.50 mL, 13 mmol) was added in one portion with rapid stirring. A transient yellow color appeared immediately following the addition, and in less than 3 s the solution turned dark brown. The solution was extracted in approximately 2 mL of $CDCl_3$ and analyzed by NMR: ^1H NMR ($CDCl_3$) δ 2.11 (0.33 H, CH_3SCH_3), 2.52 ($CH_3S(O)CH_3$), 5.3 (0.67 H, CH_2Cl_2).

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Registry No. **1**, 67-68-5; **2**, 70-29-1; **3**, 2211-89-4; **4**, 2168-93-6; **5**, 2180-20-3; **6**, 833-82-9; **7**, 2211-92-9; **8**, 21892-75-1; **9**, 621-08-9; **10**, 945-51-7; **11**, 10133-81-0; **12** (isomer 1), 67530-09-0; **12** (isomer 2), 67530-10-3; **13**, 75-18-3; **14**, 544-40-1; **15**, 831-91-4; **16**, 139-66-2; **17**, 6294-31-1; **18**, 625-80-9; **19**, 261-31-4; **20**, 54340-73-7; **21**, 2032-76-0; **22**, 62425-75-6; diethyl sulfide, 352-93-2; di-*tert*-butyl sulfide, 107-47-1; dibenzyl sulfide, 538-74-9; dichlorocarbene, 1605-72-7; tetrabutylammonium chloride, 1112-67-0.

Synthesis of Substituted Crown Ethers from Oligoethylene Glycols

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A convenient synthetic method for preparing 12-crown-4, 15-crown-5, 18-crown-6, and 21-crown-7 bearing various substituents by intramolecular cyclization of the corresponding substituted oligoethylene glycols in high yields is described. Substituents include modifiable pendent groups such as phenyl and hydroxymethyl, as well as various alkyl groups. Stability constants for the new substituted crown ethers with sodium and potassium ions in methanol were determined by potentiometric titration. The absolute effect of pendent groups on stability constants was insignificant.

Since the discovery of macrocyclic polyethers and their complexing ability toward metal and ammonium cations, numerous papers and books have been published on their synthesis, properties, and applications.[1-4] For the most part, interest has been directed to the synthesis of new macrocyclic compounds with higher complexing ability and selectivity, rather than more practical methods suitable for their industrial production.

Although some of the alkyl crown ethers reported in this study have already been synthesized and reported to be effective as phase-transfer catalysts,[5-8] they were previously

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