

Note Added in Proof. While this paper was in press, two works—one related to a dimer-catalyzed decomposition of the σ -intermediate (Bamkole, T. O.; Hirst, J.; Onyido I. *J. Chem. Soc., Perkin Trans. 2* 1982, 889) and the other to mechanism II in the preceding paper (Banjoko, O.; Ezeani, C. *Ibid.* 1982, 1356)—appeared. Comments on these two papers as well as on the role of the third amine molecule in the dimer mechanism and a solvent effects study have been submitted for publication in this journal.

Acknowledgment. We are grateful to the National Research Council (CONICET) and to the Science and Technology Secretariat (SUBCYT), Argentina, for financial support. We also acknowledge IBM Argentina (Buenos Aires) for the computer calculations.

Registry No. 2,4-Dinitrofluorobenzene, 70-34-8; *o*-anisidine, 90-04-0; pyridine, 110-86-1.

Conversion of Sulfoxes to Sulfoxides via Hydride Reduction of (Aryloxy)sulfoxonium Salt Intermediates

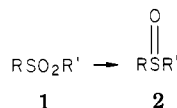
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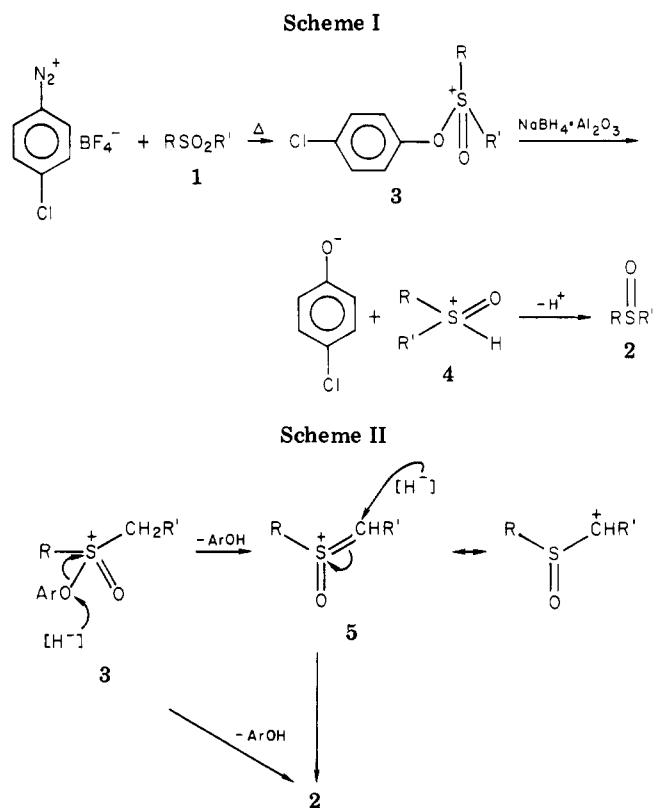
The conversion of sulfoxes into sulfoxides by a two-stage procedure, involving initial reaction of the sulfone with 4-chlorobenzenediazonium tetrafluoroborate to form an (aryloxy)sulfoxonium salt, $R_2^+S(O)OArBF_4^-$, and subsequent reduction of this with $NaBH_4 \cdot Al_2O_3$, has been investigated. Variations in the nature and amount of the diazonium salt used and its counterion, the temperature of the reaction, and solvent and concentration effects have been investigated in a largely unsuccessful attempt to improve significantly upon the yields in the first stage. It has been found, by using $NaBD_4$, that the hydride reduction of the (aryloxy)sulfoxonium salt in the second stage proceeds mainly by hydride attack at sulfur, rather than by a Pummerer-type mechanism. The latter mechanism, however, does occur when strong base is added to the (aryloxy)sulfoxonium salt prior to hydride reduction.

The procedure, recently reported in preliminary form,¹ for achieving the novel conversion of sulfone 1 \rightarrow sulfoxide 2 remains almost a unique method for achieving this



synthetic objective.² We were interested in carrying out a number of experiments aimed at improving yields, especially in the first stage of the reaction, the formation of an (aryloxy)sulfoxonium salt from the sulfone, which we found initially¹ gave rather modest, and sometimes variable, yields.

We were also interested in the mechanistic question of how the sodium borohydride reduction of the intermediate (aryloxy)sulfoxonium salt 3 took place. Our earlier proposal was that this involved hydride attack directly on the positively charged sulfur atom in 3, which is well precedented,^{3,4} and is proposed by Whiting et al.³ to involve initial addition and then elimination, leading via the S-protonated sulfoxide 4 to the sulfoxide (Scheme I). Venier et al.,⁵ however, recently suggested that hydride attack was more likely to occur at the α -carbon of a sulfinylcarbenium ion, 5, via a Pummerer-like elimination-addition sequence (Scheme II). A third, albeit less likely, mechanistic possibility is also shown in Scheme II, namely, hydride



attack at the oxygen atom in 3.

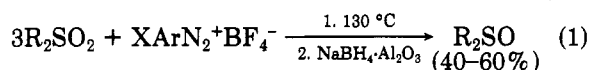
The results of both aspects of this investigation will now be presented.

Results and Discussion

The first stage in the reaction involves thermal decomposition of an arenediazonium salt at 130 °C in the pres-

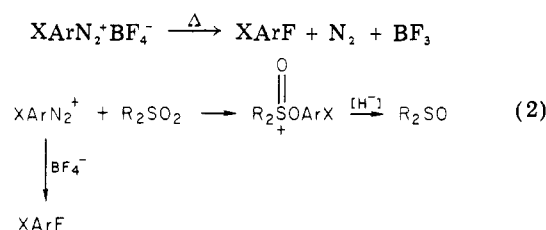
(1) Still, I. W. J.; Szilagy, S. *Synth. Commun.* 1979, 9, 923.
 (2) For a single earlier example, cf.: Anastassiou, A. G.; Wetzel, J. C.; Chao, B. Y. C. *J. Am. Chem. Soc.* 1975, 97, 1124. We thank Professor E. Block, SUNY (Albany), for bringing this paper to our notice.
 (3) Chalkley, G. R.; Snodin, D. J.; Stevens, G.; Whiting, M. C. *J. Chem. Soc., Perkin Trans. 1* 1978, 1580.
 (4) Shimagaki, M.; Tsuchiya, H.; Ban, Y.; Oishi, T. *Tetrahedron Lett.* 1978, 3435.
 (5) Venier, C. G.; Wing, F. A., Jr.; Barager, H. J. *Tetrahedron Lett.* 1980, 21, 3159.

ence of an excess of the sulfone 1, generally in the absence of solvent. For our purely synthetic investigations, we retained the 3:1 ratio of sulfone to diazonium salt (eq 1),



as we have found that significant departures from this ratio lead to increasing amounts of black, tarry decomposition products. The excess sulfone used can, in any event, be recovered and recycled without difficulty. The effects of attempting to vary the structure of the arenediazonium salt, the counterion used, and solvent/temperature conditions have been examined.

Various arenediazonium salts have been tried in place of 4-chlorobenzenediazonium tetrafluoroborate, all bearing one or more electron-withdrawing groups such as NO₂, CN, F, or CF₃, as well as Cl, in an attempt to enhance the electrophilic reactivity of the (presumed) arylcarbenium ion intermediate. We have also tried the effect of using hexafluorophosphate or hydrogen sulfate as counterions in the diazonium salt. The hexafluorophosphate salt was no more effective than the tetrafluoroborate in avoiding the competing Schiemann reaction^{6,7} (eq 2). Ortho sub-

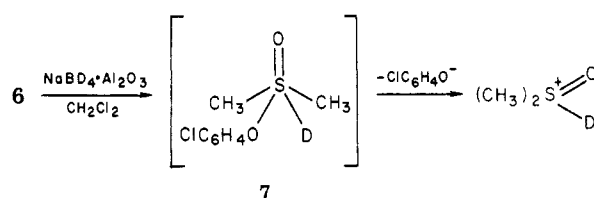


stitution in the arenediazonium salt had a particularly deleterious effect on the yield of the sulfoxide product, suggesting that steric factors are important in the initial formation of the (aryloxy)sulfoxonium salt. From these considerations, and also on general grounds of safety, the 4-chlorobenzenediazonium tetrafluoroborate salt remains the most effective electrophile we have found so far.

The effects of varying other parameters in the first stage of the sulfone reduction were also explored. Attempted catalysis of the initial reaction by metallic copper led to greatly diminished yields of the sulfoxide ultimately, perhaps because of competing catalysis of the Schiemann reaction. Following a recent report in the literature on the beneficial effects of using crown ether catalysts in reactions involving diazonium salts,⁸ we also explored the effects of adding dibenzo-18-crown-6 and 18-crown-6, with and without the presence of chlorobenzene as solvent, at temperatures up to 130 °C, without success. Since similar lack of success was found when using chlorobenzene alone, or chlorobenzene with 10% acetonitrile, as solvent *without* the phase-transfer catalyst, we have concluded that any dilution of the reagents in the first step of eq 1 is deleterious, since it lowers the rate of the desired intermolecular reaction between the sulfone and the diazonium salt and hence indirectly favors the competing intramolecular (Schiemann) process.

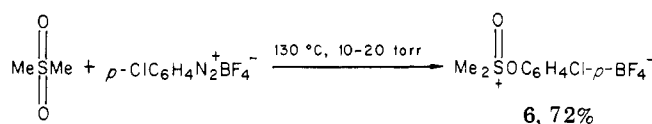
A similar effect is probably occurring when the diazonium salt is decomposed in the neat sulfone. Initially, the Schiemann product will form in competition with O-arylation. But as the reaction proceeds the fluorobenzene formed acts as a diluent, decreasing the inter-

Scheme III



molecular reaction with the sulfonyl oxygen and increasing the chance of the "intramolecular" (or ion pair) Schiemann reaction. This suggested to us that if the Schiemann product were removed by distillation as soon as it is formed, a higher yield of O-arylation and hence ultimately of the reduction product should be observed.

We decided to test this reasoning in one specific case, namely, that of dimethyl sulfone. One equivalent of the diazonium salt was mixed together with dimethyl sulfone and a vacuum distillation apparatus assembled. The solid mixture was stirred and heated under vacuum to about 130 °C, by which time the diazonium salt was rapidly decomposing. The Schiemann product was removed by distillation as soon as it formed. A significantly higher yield of the corresponding (aryloxy)sulfoxonium salt 6 could be



obtained in this way although we have not attempted to extend this approach to the general synthetic method. The properties of 6 (see Experimental Section) were fully in accord with those reported earlier for a related salt by Whiting et al.⁹

In summary, our investigation of a variety of diazonium salts, derived mainly from commercially available anilines, has shown that the best yields of sulfoxide may be obtained with 4-chlorobenzenediazonium tetrafluoroborate. The reaction seems to be distinctly subject to steric effects in the diazonium cations. The most significant reaction parameter, apart from temperature, seems to be the solvent effect, whether of an added solvent or of the fluorobenzene formed in situ by the competing Schiemann reaction.

Mechanistic Investigation. In order to try to settle the question of the mechanism of hydride reduction of the (4-chlorophenoxy)sulfoxonium salt intermediate 3 (Ar = 4-ClC₆H₄) as outlined in the introduction, we decided to carry out the reduction step by using sodium borodeuteride adsorbed on alumina, under otherwise identical reaction conditions. If the mechanism involves direct (S_N2) displacement of 4-chlorophenolate ion by hydride (deuteride) attack at the positively charged sulfur atom in 6 or perhaps more likely according to the ¹H NMR evidence obtained by Whiting et al.³ via initial hydride *addition* to form the 12-S-5 species 7,¹⁰ then no incorporation of hydrogen (deuterium) in the product sulfoxide should result (Scheme III). Should the mechanism suggested by Venier et al.⁵ be in effect, then hydrogen (deuterium) exchange via an intermediate of type 5 would be observable in the product sulfoxide. In the case of the third mechanistic possibility outlined earlier, namely, hydride attack at the oxygen atom in 3 (Scheme II), again this would not involve hydrogen

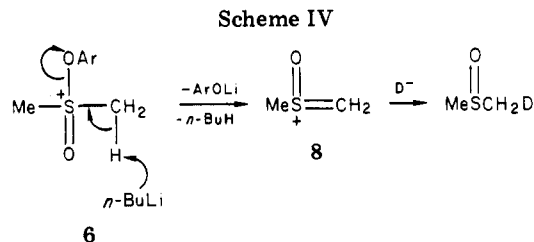
(9) Chalkley, G. R.; Snodin, D. J.; Stevens, G.; Whiting, M. C. *J. Chem. Soc. C* 1970, 682.

(10) Perkins, C. W.; Martin, J. C.; Arduengo, A. J.; Lau, W.; Alegria, A.; Kochi, J. K. *J. Am. Chem. Soc.* 1980, 102, 7753. These authors have persuasively argued the adoption of this convenient system of nomenclature for hypervalent compounds.

(6) Roe, A.; Hawkins, G. F. *J. Am. Chem. Soc.* 1947, 69, 2443.

(7) Newman, M. S.; Galt, R. H. B. *J. Org. Chem.* 1960, 25, 214.

(8) Korzeniewski, S. H.; Leopold, A.; Beadle, J. R.; Ahern, M. F.; Sheppard, W. A.; Khanna, R. K.; Gokel, G. W. *J. Org. Chem.* 1981, 46, 2153.



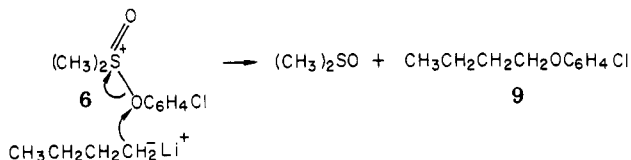
(deuterium) incorporation in the sulfoxide. We feel that this mechanism however, is less likely on general intuitive grounds and by comparison with the other two well-precedented routes.

In order to study the mechanism more effectively in this way, we have used the pure (aryloxy)sulfoxonium salt 6, isolated as described above.

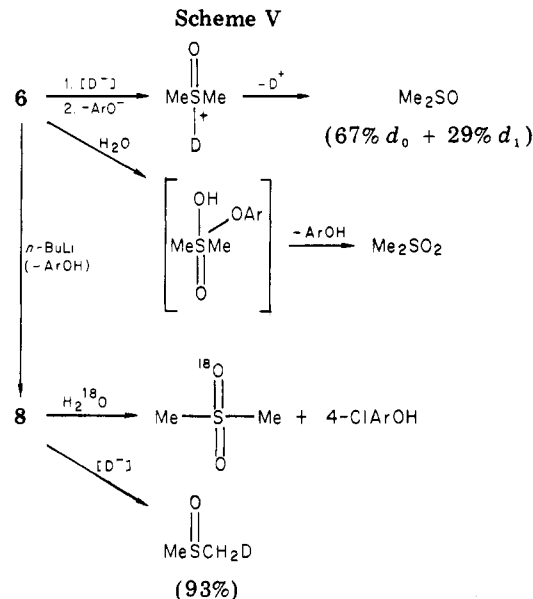
When the (4-chlorophenoxy)sulfoxonium salt 6 was reduced with the sodium borodeuteride—aluminum oxide reagent,¹ dimethyl sulfoxide was obtained with 29% *d*₁ labeling and 67% *d*₀ (after correction for natural isotopic abundances). To take account of the possibility of base-catalyzed exchange in the sulfoxide formed, as discussed by Kabalka et al.,¹¹ dimethyl sulfoxide itself was treated, in a control experiment, with either D₂O·Al₂O₃ or the NaBD₄·Al₂O₃ reducing agent above. The resulting *d*₁ incorporation was never greater than 5%. This strongly suggests that the *upper limit* for hydride (deuteride) attack at carbon, via a carbenium ion species such as 8, as suggested by Venier,⁵ is of the order of 25%. A gratifyingly similar result, providing additional support for this proposal, was found for the reduction of 6 with LiAlD₄¹² in 1,2-dimethoxyethane at 25 °C, with 22% *d*₁ incorporation being observed. In both reductions, it appears that the *major* mechanistic pathway is that of Scheme III, resulting in no deuterium incorporation.

In contrast to the above findings, when the sulfoxonium salt 6 was first treated with *n*-butyllithium and then with borodeuteride, 93% *d*₁-labeled sulfoxide was obtained. These results add further support to the view that when hydride/deuteride is the only base/nucleophile present, the reduction proceeds mainly via *S-attack* (addition-elimination mechanism), unless a stronger base is present, when the 10-*S*-3 (or methylsulfinyl carbenium ion) species 8 may play an important role as an intermediate, via the elimination-addition mechanism (Scheme IV). The intervention of an additional (ylide) intermediate, CH₃⁺S(O)(OAr)CH₂, here, as suggested by Whiting et al.,³ cannot be ruled out.

A minor side product in the above reaction with *n*-butyllithium is *n*-butyl 4-chlorophenyl ether (9), isolated in



about 5% yield. No halomethyl methyl sulfoxide was isolated or detected, although this was reported to be a major product of the reaction between *n*-butyllithium and a phenoxy-sulfoxonium salt by Shimagaki et al.^{4,13} Our result



can most simply be rationalized as involving *n*-butyl carbanion attack on the O atom of the aryloxy unit in 6, with displacement of dimethyl sulfoxide. Since both H⁻ and R⁻ are considered to be soft bases,¹⁴ we cannot rule out the further possibility that a small amount of the unlabeled sulfoxide derived from the borodeuteride reduction experiment described above may also arise by this minor pathway.

As expected from the results of Whiting et al.,³ when the (aryloxy)sulfoxonium salt 6 was hydrolyzed with water, dimethyl sulfone was formed almost quantitatively. Similarly, when the methylsulfinyl carbenium ion 8 was generated with *n*-butyllithium and hydrolyzed with ¹⁸O-labeled water, the sulfone was again obtained quantitatively, with 100% ¹⁸O label incorporation in the sulfone and none in the 4-chlorophenol. These results are summarized in Scheme V.

The labeling experiments demonstrate clearly that S attack by hydride is the most important pathway for hydride reduction of the intermediate, unless a strong base is present, when the major pathway seems to involve alkylsulfinyl carbenium ion formation (via an ylide) before attack by hydride at the α-carbon atom. These results make it likely that all of the (aryloxy)sulfoxonium salts in our original study, both with and without α-hydrogen atoms, react by the same mechanistic pathway, i.e., by nucleophilic hydride attack at sulfur. It is of interest to note that a similar mechanistic conclusion concerning the related reduction of *alkoxysulfoxonium* salts with sodium borohydride was reached by Johnson and Phillips.¹⁵

Experimental Section

¹H NMR spectra were recorded on a Varian EM-360 spectrometer. Mass spectra were recorded on a Bell and Howell 21-490 instrument, correcting for natural abundance where appropriate. The NaBD₄ and LiAlD₄ used were supplied by MSD Isotopes, Dorval, Quebec. Melting points are uncorrected. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, DK-2730, Herlev, Denmark.

(4-Chlorophenoxy)dimethylsulfoxonium Tetrafluoroborate (6). Dimethyl sulfone (11.54 g, 0.123 mol) was admixed

(11) Kabalka, G. W.; Pagni, R. M.; Bridwell, P.; Walsh, E.; Hassaneen, H. M. *J. Org. Chem.* 1981, 46, 1513.

(12) While NaBH₄ alone, in either CH₂Cl₂ or DME at 25 °C, was ineffective as a reducing agent for the (aryloxy)sulfoxonium salt, LiAlH₄ was found to give the sulfoxide almost quantitatively in DME at 25 °C. It can therefore be assumed that other, more reactive hydride reducing agents may also be used successfully in this reaction.

(13) Shimagaki et al.⁴ prepared organolithium reagents from which no attempt was made to remove halide ion. We could find no indication of the halide ion content of our (commercial) *n*-butyllithium.

(14) Pearson, R. G.; Songstad, J. *J. Am. Chem. Soc.* 1967, 89, 1827.

(15) Johnson, C. R.; Phillips, W. G. *J. Org. Chem.* 1967, 32, 3233. We are grateful to Professor Johnson for drawing this work to our attention.

with 4-chlorobenzenediazonium tetrafluoroborate¹ (30.20 g, 0.133 mol) in a 250-mL round-bottomed flask, which was assembled into a vacuum distillation apparatus. The flask was heated to 130 °C at 10–20 torr, when vigorous decomposition of the diazonium salt occurred. The resulting black mass was cooled and, some unchanged sulfone (5.44 g, 47%) was removed by vacuum sublimation.

The dark residue was shown by ¹H NMR to be >90% **6**, and repeated recrystallization from dry ethyl acetate afforded white prisms: mp 127 °C; ¹H NMR (acetone-*d*₆) δ 4.35 (s, 6 H), 7.46 (s, 4 H). Further crops of salt, with somewhat depressed melting point, could be recovered upon concentration of the mother liquor. Anal. Calcd for C₈H₁₀BClF₄O₂S: C, 32.85; H, 3.45; Cl, 12.12; S, 10.96. Found: C, 32.90; H, 3.51; Cl, 12.22; S, 11.13.

Reactions of (4-Chlorophenoxy)dimethylsulfoxonium Tetrafluoroborate (6). A. NaBD₄ Reduction.¹ Sulfoxonium salt **6** (0.61 g, 2.1 mmol) was dissolved in 10 mL of dry DME, and NaBD₄/alumina¹⁶ (5.00 g) was stirred in with evolution of gas. After 18 h the mixture was filtered and solvent removed to yield a white solid (0.37 g) containing sulfoxide and phenol, which was dissolved in 5 mL of 0.1 M sodium hydroxide solution. Extraction with dichloromethane, drying (Na₂SO₄), and removal of solvent yielded dimethyl sulfoxide (0.13 g, 76%), which low-resolution mass spectrometry indicated to be 67% *d*₀, 29% *d*₁, and 3% *d*₂ in composition.

B. LiAlD₄ Reduction. Sulfoxonium salt **6** (0.94 g, 3.2 mmol) was dissolved in 10 mL of dry DME, and LiAlD₄ (0.09 g, 2.1 mmol) was added cautiously. After 22 h of stirring, ethyl acetate (1.0 mL) was added. The resulting slurry was filtered and solvent removed to yield 0.61 g of an oil containing dimethyl sulfoxide and *p*-chlorophenol. Dimethyl sulfoxide was obtained by dissolving the oil in 10% sodium hydroxide solution and extracting with dichloromethane.

Low-resolution mass spectrometry indicated a dimethyl sulfoxide composition of 77% *d*₀, and 22% *d*₁.

C. *n*-Butyllithium/Borodeuteride Reduction. Sulfoxonium salt **6** (1.34 g, 4.6 mmol) was dissolved in 10 mL of dry DME, and butyllithium (90% in hexane, 0.40 mL, 5.5 mmol) was added under a nitrogen atmosphere at -11 °C, with gas evolution. The solution was warmed to 25 °C and the borodeuteride/alumina reagent (4.0 g) added with stirring.

After 10 h the mixture was filtered and solvent removed to yield a wet solid (1.59 g), which was extracted with dichloromethane to yield 4-chlorophenol and dimethyl sulfoxide (1.05 g). Dimethyl sulfoxide was isolated by chromatography on silica thick-layer plates (E. Merck, 2.0 mm), eluting with 20% acetone/dichloromethane. Low-resolution mass spectrometry indicated 93% *d*₁ labeling.

D. Reaction with *n*-Butyllithium/H₂¹⁸O. Sulfoxonium salt **6** (1.00 g, 3.4 mmol) was dissolved in 10 mL of dry DME. The flask was cooled in an acetone-ice bath to -11 °C under nitrogen

and butyllithium (90% in hexane, 0.25 mL, 3.4 mmol) added. The yellow solution was warmed to 0 °C and H₂¹⁸O added (0.60 mL, 17.5% ¹⁸O). The solution was warmed to 25 °C and solvent evaporated. Extraction of the residue with dichloromethane yielded an oil (0.43 g). Chromatography on silica thick-layer plates (dichloromethane) yielded 4-chlorophenol (0.35 g, 79%) and butyl 4-chlorophenyl ether (0.03 g, 5%), characterized by ¹H NMR and MS analyses. Dimethyl sulfone was recovered quantitatively as the dichloromethane-insoluble hydrate. Low-resolution mass spectrometry indicated 100% ¹⁸O-labeling incorporation in the sulfone.

Deuteration of Dimethyl Sulfoxide (Control Experiments). A. With D₂O-Al₂O₃. Deuterium oxide (1.00 mL) was admixed with alumina (4 g, Merck I, 70–230 mesh), which had been activated for 24 h at 320 °C. The alumina was then dried 24 h at 20 torr (22 °C).

Dimethyl sulfoxide (0.52 g, 6.7 mmol) was dissolved in 20 mL of dry dichloromethane and the alumina reagent (4.04 g) stirred in for 18 h. Filtration and removal of solvent yielded 97% *d*₀- and 3% *d*₁-labeled dimethyl sulfoxide (as determined by low-resolution mass spectrometry).

B. With NaBD₄·Al₂O₃·D₂O. Dimethyl sulfoxide (0.52 g, 6.7 mmol) was dissolved in 20 mL of dry dichloromethane and stirred with NaBD₄·Al₂O₃ (5.0 g) for 24 h. The slurry was filtered and solvent removed to yield 0.30 g of sulfoxide. Low-resolution mass spectrometry indicated 95% *d*₀ and 5% *d*₁ labeling. On repeating this experiment, a value of 2% *d*₁ labeling in the sulfoxide was found.

Attempted Phase-Transfer Arylation of Methyl Phenyl Sulfone. The two procedures below are representative of the methods tried.

A. Methyl phenyl sulfone (1.15 g, 7.4 mmol) was refluxed with 4-chlorobenzenediazonium tetrafluoroborate (1.00 g, 4.4 mmol) in 40 mL of dry chlorobenzene for 5 h. The solution was cooled and sodium borohydride/alumina (4.00 g) added, followed by 20 h stirring. No reduction could be detected by ¹H NMR monitoring of the resulting solution. The same result was obtained with the addition of 0.10 g of dibenzo-18-crown-6.

B. Methyl phenyl sulfone (1.39 g, 8.9 mmol) was mixed with dibenzo-18-crown-6 (0.06 g) and 4-chlorobenzenediazonium tetrafluoroborate (0.67 g, 3.0 mmol) and the mixture heated to 130 °C to effect diazonium salt decomposition. The resulting purple oil was cooled and dissolved in 40 mL of dry dichloromethane, and borohydride/alumina (5.00 g) was added with stirring. After 20 h, solvent was removed and a 25% yield of sulfoxide was estimated by ¹H NMR.

Acknowledgment. We gratefully acknowledge continuing support of this work by the Natural Sciences and Engineering Research Council of Canada and by the con-naught Fund of the University of Toronto. It is a pleasure to acknowledge valuable discussions with Dr. G. W. Kutney of CIL, Sheridan Park, Mississauga, Ontario.

Registry No. **1** (R = R' = Me), 67-71-0; **1** (R = Me; R' = Ph), 3112-85-4; **2** (R = R' = Me), 67-68-5; **6**, 73040-88-7; *p*-ClC₆H₄N₂⁺BF₄⁻, 673-41-6.

(16) The reducing agent is prepared shortly before use in the ratio NaBD₄·D₂O:Al₂O₃ = 1:1:10 (w/w). This represents a *maximum* concentration (in the somewhat unlikely absence of hydrolysis, or destruction of the reducing agent by >AlOH groups) of ca. 11 mmol of the reducing agent.