Nucleophilic Displacements on Halogen Atoms. III. Reduction of α,α-Dichlorobenzyl Benzyl Sulfoxide to α-Chlorobenzyl Benzyl Sulfoxides

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Attempted dichlorination (with SO_2Cl_2) of the α-carbon atom of either dibenzyl sulfoxide or benzyl phenyl sulfoxide led only to cleavage of the carbon–sulfur bond. Dibenzyl sulfide could be dichlorinated at the α position, but treatment of benzyl phenyl sulfide with 2 equiv of SO_2Cl_2 gave carbon–sulfur bond cleavage. Several α,α-dichlorobenzyl benzyl sulfoxides were made from the corresponding sulfides by oxidation with peracid. Reduction of α,α-dichlorobenzyl benzyl sulfoxide (**2a**) to a mixture of diastereomeric α-chlorobenzyl benzyl sulfoxides was carried by (a) $(Me_2N)_3P$ in aqueous solvents and (b) chromous ion in aqueous solvents. Variations in the ratios of diastereomers obtained were studied as a function of solvent and reducing agent. Little variation in product ratios was observed with $(Me_2N)_3P$ but product ratios in the reduction of **2a** with chromous ion varied a great deal.

In the past few years, a number of reports dealing with α-halo sulfoxides have appeared. Up until recently, these compounds were relatively unknown; now there exist a number of methods for their synthesis.[2] Since the sulfinyl group is capable of asymmetry, many of these α-halo sulfoxides [*e.g.*, $R^1R^2CXS(O)R^3$] are diastereomeric (and/or optically active) and therefore an added structural feature is naturally present.

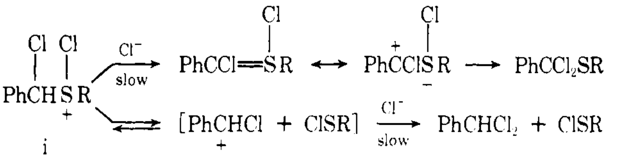
A number of workers have observed that α-chlorination of sulfoxides may stereoselectively lead to one of two possible diastereomeric α-chloro sulfoxides.[2c,f,g,i,j,3] Furthermore, α-chlorination of sulfides followed by oxidation also may give α-chloro sulfoxides with a high degree of stereoselectivity.[2m] We sought an alternate and perhaps complementary synthetic pathway to the stereoselective synthesis of α-chloro sulfoxides based on reductions of α,α-dichloro sulfoxides. Analogy for such a reaction can be found in the reductions of α-halo sulfones.[4]

Results and Discussion

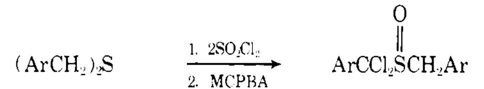
We tried two principal routes into α,α-dichloro sulfoxides: dichlorination of sulfoxides and dichlorination of sulfides followed by oxidation to the desired sulfoxides. Of these methods, only the latter was successful.

Initially, we attempted to synthesize α,α-dichlorobenzyl phenyl sulfoxide. However, attempted dichlorination of either benzyl phenyl sulfide or benzyl phenyl sulfoxide by the usual procedures[5] led only to cleavage of the benzylic carbon–sulfur bond. Monochlorination of either benzyl phenyl sulfide or benzyl phenyl sulfoxide to give the corresponding α-chlorination products proceeds in high yields. However, treatment of these α-chloro sulfides or sulfoxides with an additional 1 equiv of chlorinating agent (*e.g.*, sulfuryl chloride) under a variety of conditions invariably led to cleavage products (benzal chloride) and no α,α-dichlorobenzyl phenyl sulfide or α,α-dichlorobenzyl phenyl sulfoxide were observed. It appears that one of the driving forces for cleavage of the carbon–sulfur bond is the increased stability of the benzylic cation possessing an α-chlorine atom.[6] As evidence of this, dichlorination of *p*-nitrobenzyl phenyl sulfide and *p*-cyanobenzyl phenyl sulfide (but not the corresponding sulfoxides) followed by oxidation with *m*-chloroperbenzoic acid (MCPBA) led to the *p*-nitro-α,α-dichlorobenzyl phenyl sulfoxide and *p*-cyano-α,α-dichlorobenzyl phenyl sulfoxide, respectively, in good yields. Unfortunately, these compounds were extremely difficult to handle owing to their sensitivity to moisture and protic solvents. The chemistry of these sulfoxides will be the subject of a separate article.

The proposed mechanism for α-chlorination of sulfides[5b] suggests that cleavage products and α-chloro sulfides result from competitive second-order reactions of the intermediate chlorosulfonium ions (i) with chloride ion. The scheme we propose combines certain ideas previously presented.[5] This scheme explains why cleavage becomes more favored when an α-chlorine atom is already present, since the resulting carbonium ion will be more stable.[6] Nucleophilic displacement on the α-carbon atom in i by Cl$^-$ [5b] seems less likely since the α-chlorine atom should retard the SN2 reaction.[7]



The aryl-substituted dibenzyl sulfides (**1**) could be dichlorinated and oxidized to the α,α-dichlorobenzyl benzyl sulfoxide (**2**) in good yields (eq 1). Little carbon–sulfur bond cleavage was observed in this system in contrast to benzyl phenyl sulfide (*vide supra*). This in part may be due to the instability of benzylsulfenyl chloride (which would be formed on cleavage) compared to benzenesulfenyl chloride.[8] Although the basis for this instability of alkylsulfenyl chlorides (*cf.* arylsulfenyl chlorides) is kinetic in nature, their thermodynamic stabilities may well parallel the kinetic stabilities.[8] Attempted chlorination (with SO_2Cl_2) of α-chlorobenzyl benzyl sulfoxide to give the known[9] dichloro sulfoxide **2a** instead gave a mixture of at least five different products (benzal chloride was a major constituent), none of which was **2a**. Such behavior is not surprising in view of the ease with which chlorination of sulfoxides can lead to carbon–sulfur bond cleavage in the cases where relatively stable carbonium ions ($PhCHCl^+$ in this case) can be formed.[10]



$$(ArCH_2)_2S \xrightarrow[2.\ MCPBA]{1.\ 2SO_2Cl_2} ArCCl_2\overset{\overset{\displaystyle O}{\|}}{S}CH_2Ar \qquad (1)$$

1a, Ar = C_6H_5	**2a**, Ar = C_6H_5
b, Ar = p-$CH_3C_6H_4$	**b**, Ar = p-$CH_3C_6H_4$
c, Ar = p-ClC_6H_4	**c**, Ar = p-ClC_6H_4
d, Ar = p-$NO_2C_6H_4$	**d**, Ar = p-$NO_2C_6H_4$

A study was made of the reduction of the dichloro sulfoxide **2a** to the monochloro sulfoxides **3a** and **3b** with several reducing agents: hexamethylphosphorous triamide [$(Me_2N)_3P$], chromous chloride, and tri-*n*-butyltin hydride. Tri-*n*-butyltin hydride was used only in one experiment. Owing to the thermal instability of **2a**, the reaction was carried out below room temperature under uv irradiation. The reaction proved to be slow even with 1 *M* tri-*n*-butyltin hydride in tetrahydrofuran (THF), and work-up

Table I
Reduction of Benzyl α,α-Dichlorobenzyl Sulfoxide (2a) with Hexamethylphosphorous Triamide [$(Me_2N)_3P$] at 25° [a]

Aqueous solvent	[3a/3b] ± 5%	Aqueous solvent	[3a/3b] ± 5%
100% EtOH	1.00	70% Dioxane	0.83
100% *t*-BuOH	0.71	46% Dioxane	0.67
90% DMF	0.48	90% EtOH	0.69
90% HMPT	0.65	80% EtOH	0.77
90% THF	1.00	100% EtOH[b]	1.00
90% Dioxane	0.77	90% THF[b]	0.91
80% DMF	0.59	90% HMPT[b]	1.40
70% DMF	0.67	90% DMF[b]	1.11
80% Dioxane	0.77		

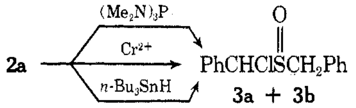
[a] Within experimental error these ratios showed no changes over the temperature range of 25–65°. [b] 1.0 *M* in $LiClO_4$.

Table II
Reduction of Benzyl α,α-Dichlorobenzyl Sulfoxide (2a) with $CrCl_2$ at 25°

Aqueous solvent	[3a/3b] ± 5% [a]	Aqueous solvent	[3a/3b] 5% [a]
90% EtOH	38	90% DMSO	1.0
80% EtOH	66	90% HMPT	5.4
90% MeOH	32	90% DMF	2.5
90% THF	30	80% DMF	6.3
90% Dioxane	30	70% DMF	12
80% Dioxane	48		

[a] Within experimental error, these ratios showed no change over the temperature range of 25–65°. Added lithium perchlorate (up to 2 *M*) also had no apparent effect on these ratios in 90% DMF, 90% dioxane, and 90% ethanol solutions.

was complicated by the presence of unreacted tri-*n*-butyltin hydride and tri-*n*-butyltin chloride. However, the reduction of **2a** under these conditions did proceed to give *ca.* a 70% yield of **3a** and **3b** in a ratio of 3:1, respectively.



$$\mathbf{2a} \xrightarrow{(Me_2N)_3P;\ Cr^{2+};\ n\text{-}Bu_3SnH} PhCHCl\overset{O}{\overset{\|}{S}}CH_2Ph \quad \mathbf{3a} + \mathbf{3b} \qquad (2)$$

The chloro sulfoxides **3a** and **3b** have been reported previously (although their configurations have not been assigned) and have the following physical properties: **3a**, mp 113–113.5°, nmr ($CDCl_3$) signal at δ 5.22 for the methine proton,[2m] **3b**, mp 117–118.5°, nmr ($CDCl_3$) signal at δ 5.45 for the methine proton.[2j]

The reaction of **1a** with $(Me_2N)_3P$ was run under a variety of conditions in hopes of realizing a large variation in the product ratio, **3a**:**3b**. However, employing a large number of different solvent and reaction temperature conditions had little marked effect on the product ratios. Under the conditions employed (see Table I), the ratios of **3a**:**3b** varied from *ca.* 0.5 to 1.4.

The effect of added lithium perchlorate was negligible in 90% ethanol and 90% THF solvents, but the salt appeared to cause a significant change in the product ratios in the dipolar aprotic solvents dimethylformamide (DMF) and hexamethylphosphoric triamide (HMPT) (Table I).

The pathway for reduction of **2a** by $(Me_2N)_3P$ appears closely related to analogous reductions observed in the reactions of δ-halo sulfones with triphenylphosphine[4,11] and in the debromination of bis(α-bromobenzyl) sulfoxide with $(Me_2N)_3P$ to give diphenylthiirane 1-oxide and $(Me_2N)_3PBr_2$.[13] These reactions involve intermediate carbanions which can undergo portonation (leading to reduction products[4,12]) or lose halide ion.[13]

The α-sulfinyl carbanion has been of keen interest lately both from a theoretical[14] and experimental[15] standpoint. At the initiation of this work, we felt that a solvent study such as that described above would lead to more insight into the nature of the α-sulfinyl carbanion. However, it is now clear that the stereochemical fate of the α-sulfinyl carbanion is solvent dependent[16] and that the small variation we observe (Table I) in the product ratios can easily be accounted for in terms of asymmetric solvation of the intermediate carbanions.[17]

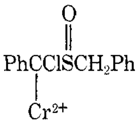
A more interesting result was obtained in the chromous ion (Cr^{2+}) reductions of **2a** to give **3a** and **3b** (Table II). The reaction of Cr^{2+} with **2a** in aqueous solvents appeared to take place instantly. The monochloro sulfoxides **3a** and **3b** could be further reduced to dibenzyl sulfoxide, although at a rate significantly slower than that observed for the reduction of **2a**. The monochloro sulfoxides **3a** and **3b** did not undergo reduction by Cr^{2+} at the same rates; so care was taken to ensure that reduction of **2a** proceeded only as far as to give the monochloro sulfoxides **3a** and **3b**.

It is clear from Table II that the **3a**/**3b** ratio varies significantly with solvent conditions. In particular, use of 90% aqueous dipolar aprotic solvents (DMSO, DMF, and HMPT) gave **3a**/**3b** ratios of *ca.* 1–5 whereas 90% aqueous ether and alcohol solvents gave **3a**/**3b** ratios of *ca.* 30. Furthermore, increasing the per cent of water in all solutions led to a marked increase in the **3a**/**3b** ratio. Again the product ratios showed essentially no change over a 40° temperature range or any change upon added lithium perchlorate.

A number of studies have been made on the reduction of alkyl halides with chromous ion.[18] These reactions are believed to involve several steps: a slow abstraction of a chlorine atom (in RCl) by Cr^{2+} to give $[CrCl]^{2+}$ + R·, followed by a rapid coupling of R· with another Cr^{2+} to give $[RCr]^{2+}$, and finally a slow protonolysis of the C–Cr bond to give RH + Cr^{3+}. This last step occurs with retention of configuration[19] and can be followed spectrophotometrically.[20]

We briefly examined the question of whether we observed the intermediate 4 in the reaction of **2a** with Cr^{2+} and found that on mixing of a solution of **2a** with Cr^{2+}, an appreciable absorbance was observed at 365 nm. The absorbance decreased with time, and a plot of log ($A - A_\infty$) *vs.* time gave a linear plot, indicating that first-order kinetics was being observed. This observation is consistent with results from kinetic studies of similar reactions.[23]

The product-determining step in the reaction of **2a** with Cr^{2+} would appear to be the coupling of the benzylic radical $Ph\dot{C}ClS(O)CH_2Ph$ with a chromous ion[18,21] to give 4 (actually a set of diastereomers). It seems unlikely that the change in solvent has an appreciable effect on the conformation of the intermediate radical. However, the chemical nature of chromous ion probably is sensitive to solvation effects,[21,22] and therefore a change in solvent is likely to lead to a significant change in reactivity.



$$Ph\underset{Cr^{2+}}{\underset{|}{C}}Cl\overset{O}{\overset{\|}{S}}CH_2Ph$$

4

Experimental Section

Melting points were taken on a Mel-Temp apparatus and are uncorrected. The nmr spectra were recorded on a Varian Associates A-60D nmr spectrometer at ambient temperatures. The spectra were taken in deuteriochloroform with tetramethylsilane (δ 0.00) as an internal standard. The ir spectra of the isolated compounds were taken in KBr pellets; those spectra of solutions were taken in carbon tetrachloride solutions. Elemental analyses were performed by Dr. Franz Kasler and Mrs. Shelesa Brew at the Department of Chemistry, University of Maryland.

Attempted Syntheses of α,α-Dichlorobenzyl Phenyl Sulfoxide. To a solution of 1 g (5.0 mmol) of benzyl phenyl sulfide in 10 ml of carbon tetrachloride was added dropwise (at room temperature) 1.5 g (11 mmol) of sulfuryl chloride in 2 ml of carbon tetrachloride. The course of the reaction was monitored by nmr spectroscopy, which showed that the benzyl phenyl sulfide was smoothly converted by the first equivalent of sulfuryl chloride to α-chlorobenzyl phenyl sulfide. An nmr spectrum of the reaction mixture taken after all the sulfuryl chloride solution had been added showed that a significant amount of benzal chloride (benzylic proton located at δ 6.6) and a smaller amount of benzyl chloride (benzylic proton located at δ 4.5) had been formed. The carbon tetrachloride was removed by rotary evaporation and the oil was dissolved in 10 ml of dry methylene chloride. To this mixture was added 1.0 g (5.0 mmol) of *m*-chloroperoxybenzoic acid (MCPBA). The reaction mixture was stirred for 10 min and then washed with dilute sodium bicarbonate. The solution was dried ($MgSO_4$) and the solvent was removed by rotary evaporation. An ir spectrum showed the absence of any appreciable absorption in the region of 1050–1100 cm^{-1}, where the S–O stretching frequency for sulfoxides is found.[23] Variations in reaction times and temperatures as well as solvents (DMF, methylene chloride, and sulfolane were used) still led to no observable amount of α,α-dichlorobenzyl phenyl sulfoxide.

Attempts to chlorinate α-chlorobenzyl phenyl sulfoxide[2f] (which can be made in nearly quantitative yield by the monochlorination of benzyl phenyl sulfoxide) with sulfuryl chloride and pyridine[2g] in several solvents (DMF, methylene chloride, and sulfolane) gave only cleavage products[24] and recovered starting material.

α-Chlorination of Benzyl Phenyl Sulfides Containing Electron-Withdrawing Groups. To a solution of 1.0 g (4.1 mmol) of 4-nitrobenzyl phenyl sulfide[25] dissolved in 20 ml of dry carbon tetrachloride was added dropwise 1.34 g (9.9 mmol) of sulfuryl chloride in 5 ml of carbon tetrachloride. After 30 min, the carbon tetrachloride was removed by rotary evaporation and the oil was taken up in 20 ml of dry methylene chloride. To this solution was added, in increments of *ca.* 0.2 g, 0.81 g (4.0 mmol) of 85% MCPBA. After 5 min, the reaction mixture was washed with water and 10% sodium bicarbonate solution. The organic layer was dried ($MgSO_4$) and the solvent was removed by rotary evaporation. On standing, the oil (1 g) solidified, mp 82–91°. An ir spectrum of this material showed a sulfoxide band at 1105 cm^{-1} and no carbonyl band; tlc on alumina showed one major and several minor spots. Attempts to recrystallize this material from Skellysolve B–methylene chloride led to considerable decomposition of the material. When this material was heated in absolute methanol for a few minutes, methyl 4-nitrobenzoate, mp 94.0–94.5 (lit.[26] mp 96°), was isolated when the solution was cooled. Similar results were obtained when these procedures were attempted with 4-cyanobenzyl phenyl sulfide.

Benzyl α,α-Dichlorobenzyl Sulfoxide (2a). Dibenzyl sulfide (5.0 g, 23 mmol) was dissolved in 20 ml of dry carbon tetrachloride. To this solution was added, dropwise, over a 1-hr period, 6.5 g (48 mmol) of sulfuryl chloride in 15 ml of dry carbon tetrachloride. After the reaction mixture had stirred for an additional 1 hr, the solvent was removed by rotary evaporation. To the resulting oil were added 40 ml of dry methylene chloride and, in increments, 4.7 g (23 mmol) of 85% MCPBA. Five minutes later, the reaction mixture was washed with two portions of a saturated sodium carbonate solution and dried ($MgSO_4$). Rotary evaporation of the solvent yielded an oil which solidified upon cooling to 0°. This solid was collected, washed with pentane, and recrystallized from methylene chloride–Skellysolve B to give 5.0 g (72%) of **2a**, mp 87.0–88.0° (lit.[9] mp 86.6–89.5°).

α,α-Dichloro-4-Methylbenzyl 4-Methylbenzyl Sulfoxide (2b). In a fashion similar to the procedure given for the preparation of **2a**, 2.0 g (8.2 mmol) of bis(4-methylbenzyl) sulfide[27] was treated first with 2.3 g (17.0 mmol) of sulfuryl chloride and then with 1.65 g (8.1 mmol) of 85% MCPBA. The crude product was recrystallized from methylene chloride–Skellysolve B to give 1.5 g (56%) of the product **2b**: mp 106.0–107.0°; nmr δ 2.32 (s, 3 H), 2.42 (s, 3 H), 3.42 (d, 1 H), 4.10 (d, 1 H, *J* = 13 Hz), 7.0–7.7 (m, 8 H); ir 1086 cm^{-1} (SO).

Anal. Calcd for $C_{16}H_{16}Cl_2OS$: C, 58.71; H, 4.95. Found: C, 58.52; H, 4.98.

4-Chlorobenzyl α,α-4-Trichlorobenzyl Sulfoxide (2c). In a fashion similar to the procedure given for the preparation of **2a**, 5.0 g (18 mmol) of bis(4-chlorobenzyl) sulfide[27] was treated first with 4.9 g (36 mmol) of sulfuryl chloride and then with 3.6 g (18 mmol) of 85% MCPBA. The crude product was recrystallized from methylene chloride–Skellysolve B to give 4.1 g (63%) of **2c**: mp 106.5–107.0°; nmr δ 3.42 (d, 1 H), 4.16 (d, 1 H, *J* = 13 Hz), 7.1–7.9 (m, 8 H); ir 1087 cm^{-1} (SO).

Anal. Calcd for $C_{14}H_{10}Cl_4OS$: C, 45.68; H, 2.74. Found: C, 45.41; H, 2.70.

α,α-Dichloro-4-nitrobenzyl 4-Nitrobenzyl Sulfoxide (2d). Bis(4-nitrobenzyl) sulfide[27] (2.00 g, 6.6 mmol) was dissolved in 50 ml of dry methylene chloride. To this solution was added, dropwise, over a 30-min period, 1.84 g (13.6 mmol) of sulfuryl chloride in 8 ml of dry methylene chloride. Four hours later, the solvent was removed by rotary evaporation. To the resulting oil were added 20 ml of dry methylene chloride and, in increments, 1.34 g (6.6 mmol) of 85% MCPBA. Five minutes later, the reaction mixture was washed with two portions of a saturated sodium carbonate solution and dried ($MgSO_4$). Rotary evaporation of the solvent yielded an oil which solidified upon cooling to 0°. This solid was collected, washed with pentene, and recrystallized from methylene chloride–Skellysolve B. The yield of **2d** was 1.75 g (68%): mp 123.0–124.0; nmr δ 3.33 (d, 1 H), 4.07 (d, 1 H, *J* = 13 Hz), 6.9–8.0 (m, 8 H); ir 1510 (NO_2) and 1100 cm^{-1} (SO).

Anal. Calcd for $C_{14}H_{10}Cl_2N_2O_5S$: C, 43.20; H, 2.59. Found: C, 43.12; H, 2.64.

Treatment of Dibenzyl Sulfoxide with 2 Equiv of Sulfuryl Chloride in the Presence of Pyridine. In 20 ml of dry methylene chloride was dissolved 3.0 g (13.0 mmol) of dibenzyl sulfoxide, and the solution was cooled to 0°. To this solution were added 4.05 g (51.2 mmol) of pyridine and, over a period of 1 hr, 3.46 g (25.6 mmol) of sulfuryl chloride in 8 ml of dry methylene chloride. Thirty minutes later, the solution was washed with a dilute hydrochloric acid solution and a dilute sodium thiosulfate solution and dried ($MgSO_4$). The solvent was removed by rotary evaporation. The nmr spectrum of the resulting oil contained, in addition to the aromatic region (δ 7.1–8.2), a singlet at δ 6.6, corresponding to benzal chloride, and a multiplet between δ 3.6 and 4.7. The range of the latter multiplet ruled out the possibility of the presence of the α,α-dichloro sulfoxide **2a** and both of the diastereomers of the α-chloro sulfoxide **3a** and **3b**. Tlc (50% ether–50% Skelly B) showed that five compounds were present. Nothing further was done with this mixture.

Dibenzyl sulfide (5 g, 23.3 mmol) was dissolved in 20 ml of dry carbon tetrachloride. To this solution was added, dropwise, 3.14 g (23.3 mmol) of sulfuryl chloride in 8 ml of dry carbon tetrachloride. After 30 min, the carbon tetrachloride was removed by rotary evaporation. To the resulting oil were added 25 ml of dry methylene chloride and then, in increments, 4.73 g (23.3 mmol) of 85% MCPBA. Ten minutes later the reaction mixture was washed with a saturated sodium carbonate solution and dried ($MgSO_4$). A solid remained after rotary evaporation of the solvent. This was shown by its nmr spectrum to be benzyl α-chlorobenzyl sulfoxide (5.3 g, 86%); the two diastereomers **3a** and **3b** were formed in a 1:1 ratio. Repeated recrystallization of this mixture from carbon tetrachloride–Skellysolve B led to the isolation of the pure diastereomer **3a**, mp 113.0–113.5° (lit.[2m] mp 112–113°).

The supernatants from the recrystallizations described above were combined, and out of the resulting solution was isolated the other diastereomer **3b**, which had mp 117.0–118.5° (lit.[2j] mp 118.0–118.5°).

Reduction of Benzyl α,α-Dichlorobenzyl Sulfoxide (2a) with Hexamethylphosphorous Triamide. General Procedure. The sulfoxide **2a** (0.25 g, 0.84 mmol) was dissolved in 4.0 ml of the chosen solvent. Reagent-grade solvents were used in every case. The following solvents were further purified: dioxane (distillation from sodium), THF (distillation from lithium aluminum hydride), DMSO (vacuum distillation from calcium hydride), and HMPT (vacuum distillation from calcium hydride). To the solution were added 0.1 g (1.0 mmol) of triethylamine and 0.14 g (0.84 mmol) of hexamethylphosphorous triamide. After the reaction mixture had stirred for 15 min, it was poured into 20 ml of water, and the products were extracted with three 15-ml portions of ether. The combined ethereal extracts were washed with four 15-ml portions of water and were dried ($MgSO_4$); the solvent was removed by rotary evaporation. An nmr spectrum was taken of the mixture, and the ratio of the area of the peaks caused by the methine protons of **3a** and **3b** was determined. The monochloro sulfoxides **3a** and **3b** were isolated either by crystallization or chromatography and identified by melting point, mixture melting point, and spectroscopy (ir and nmr).

Salt Effect Study. In these experiments 0.42 g of anhydrous lithium perchlorate was added to the reaction mixture, making the solution 1 *M* with respect to the salt.

Temperature Study. The above procedure was followed except that the reaction mixture was held at the specified temperature (45 or 65°) for the 15-min reaction period.

Test for Epimerization of Benzyl α-Chlorobenzyl Sulfoxide under Conditions of the Reduction. In 10% Water-90% THF. To approximate the reaction conditions as closely as possible, it was assumed that a reduction had proceeded to 50% completion and that the phosphine and the monochloro sulfoxide were, therefore, present in equal concentration. To 13.5 ml of THF were added 0.40 g of benzyl α-chlorobenzyl sulfoxide (**3a**), **3b** (1.5 mmol), 0.3 g (3.0 mmol of triethylamine, 1.5 ml (1.5 mmol) of a 1.0 *M* hydrochloric acid solution, and 0.24 g (15 mmol) of hexamethylphosphorous triamide. Portions of 4.5 ml of this solution were withdrawn after 15 min, 1 hr, and 3 hr; each aliquot was worked up as outlined in the General Procedure above. Initially the ratio was 1:>99; *i.e.*, diastereomer **3b** was not detectable. This ratio was not observed to change during the 3-hr period.

In 10% Water-90% DMF. The above procedure was repeated with DMF substituted for THF. After 15 min, the ratio of **3b** to **3a** was 1:94; after 1 hr, the ratio was 1:81; after 3 hr, it was 1:38.

Under these conditions, no reduction of benzyl α-chlorobenzyl sulfoxide occurred.

Test for Mass Loss during the Reduction. In 10% Water-90% THF. The sulfoxide **2a** (0.50 g, 1.68 mmol) was dissolved in 8.0 ml of a 10% water-90% THF solution. To this solution was added 0.1 g of acetophenone as an internal standard. Four milliliters of the solution was withdrawn and worked up as described in the General Procedure. A pmr spectrum showed the ratio of the area of the peaks caused by the methylene protons of sulfoxide **2a** to the area of the methyl singlet of acetophenone to be 1.7:1.0. To the remaining solution were added 0.1 g (1.0 mmol) of triethylamine and 0.14 g (0.84 mmol) of hexamethylphosphorous triamide. One hour later, this solution was worked up as usual. The ratio of the total area of the peaks caused by the methylene protons of **2a**, **3a**, and **3b** to the area of the methyl singlet of acetophenone was 1.5:1.0.

Reduction of Benzyl α,α-Dichlorobenzyl Sulfoxide (2a) with Triphenylphosphine. To a solution of 0.5 g (1.68 mmol) of sulfoxide **2a** in 25 ml of methanol was added 0.2 g (2.0 mmol) of triethylamine and 0.52 g (2.0 mmol) of triphenylphosphine. The reaction mixture was held at reflux (65°) for 24 hr; at that time tlc (70% ether-30% Skellysolve B) indicated that all of the starting material had been reduced. The reaction mixture was poured into 20 ml of water, and the products were extracted with two 20-ml portions of methylene chloride; the organic portions were dried ($MgSO_4$), and the solvent was removed by rotary evaporation. An nmr spectrum of the resulting oil indicated that the two α-chloro sulfoxides **3a** and **3b** were formed in equal amounts in a clean reaction. Under these same conditions, hexamethylphosphorous triamide reacted with **2a** in less than 1 min to give **3a** and **3b** in the same ratio.

Reduction of 2a with Tri-*n*-butyltin Hydride. To 0.25 g (0.84 mmol) of the sulfoxide **2a** dissolved in 1.5 ml of THF was added 0.50 g (1.74 mmol) of tri-*n*-butyltin hydride. Nitrogen was flushed through the system, and the temperature of the solution was kept between 0 and 25° as the reaction flask was irradiated with uv light for 4 hr. Tlc (70% ether-30% Skellysolve B) at that time indicated that nearly all of the starting material had been reduced. The THF was removed by rotary evaporation. An nmr spectrum of the resulting solution showed that the diastereomers **3a** and **3b** had been formed in the ratio 3:1. The sulfoxides **3a** and **3b** were isolated by chromatography (silica gel, 10% ether-Skellysolve B eluent) in 70% yield.

Reduction of 2a with Chromous Ion. General Procedure. All reductions were carried out in a manner analogous to this one example. To 9 ml of THF in a three-necked flask was added 0.3 ml of water. (If a 20% water-80% THF solution were needed, 1.3 ml of water would be added to 8 ml of THF. Similar adjustments were made for other solvent systems.) In another flask was dissolved 0.25 g (0.84 mmol) of the sulfoxide **2a** in 2 ml of a solution of 10% water-90% THF. Nitrogen was bubbled through both solutions for 5 min. Into the first solution were injected through a septum 0.7 ml (1.4 mmol) of a 2 *M* aqueous solution of chromium(II) chloride and then, as rapidly as possible, the sulfoxide solution. The reaction mixture was immediately poured into 20 ml of water, and the products were extracted with three 15-ml portions of ether. The combined ethereal extracts were washed with four 15-ml portions of water and were dried ($MgSO_4$). After the solvent had been removed by rotary evaporation, an nmr spectrum was taken of the crude reaction mixture, and the ratio of the areas of the peaks caused by the methine protons of **3a** and **3b** was determined.

Salt Effect Study. The above procedure was followed with the following addition. To the chromium(II) chloride solution was added 1.06 g of anhydrous lithium perchlorate, and to the sulfoxide solution was added 0.21 g of anhydrous lithium perchlorate, making both solutions 1 *M* with respect to the salt. These amounts of lithium perchlorate were doubled when a 2 *M* solution was used.

Temperature Study. The above procedure was followed except that both solutions were heated to the specified temperature (45 or 65°) before they were mixed together.

Dilution Study. In this case, the volume of the chromium(II) chloride solution was increased to 60 ml. The sulfoxide was dissolved in 2 ml of the solvent as before.

Reduction of Benzyl α-Chlorobenzyl Sulfoxide (3) with Chromium(II) Chloride. As described in the General Procedure above, 0.28 g (1.1 mmol) of a mixture of the diastereomers **3a** and **3b** was treated with 0.4 mmol of chromium(II) chloride. The initial ratio of the two isomers was 0.83:1.0. After the reduction, the α-chloro sulfoxides which remained (**3a** and **3b**) were in the ratio of 1.0:1.0.

Treatment of 2a with Potassium Thiophenoxide. To 0.25 g (0.84 mmol) of sulfoxide **2a** dissolved in 15 ml of absolute ethanol was added 0.25 g (1.68 mmol) of potassium thiophenoxide. The reaction mixture was heated to 60° for 2 hr. It was then poured into 20 ml of water, and the product was extracted with three 15-ml portions of ether. The combined ethereal extracts were washed with water and dried ($MgSO_4$). The solvent was removed by rotary evaporation. A pmr spectrum of the crude product showed that a considerable amount of starting material was present; no peaks occurred between δ 5 and 6, indicating that none of the reduced compound **3** had been formed. (Compounds **3a** and **3b** were stable under these conditions.) Similar results were obtained in 90% aqueous DMF solvent at 25°.

Registry No.—**1a**, 538-74-9; **1b**, 13250-88-9; **1c**, 23566-23-6; **1d**, 1835-71-8; **2a**, 30505-98-7; **2b**, 50323-83-6; **2c**, 50323-84-7; **2d**, 50323-85-8; dibenzyl sulfoxide, 621-08-9.

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Desulfurization of β-Keto Sulfides and Thiocyanates with Tris(dialkylamino)phosphines[1a]

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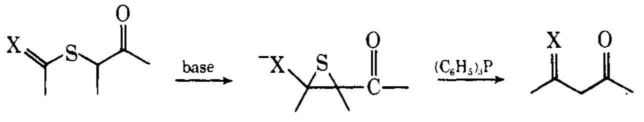
Tris(dimethylamino)phosphine (**4a**) desulfurizes β-keto sulfides to afford a variety of products including ketones and enol ethers. The mechanism probably involves a phosphonium salt. Benzyl thiocyanate was readily desulfurized by **4a** in a complex reaction to afford benzyl cyanide and dibenzyl sulfide as the main products.

The reaction of trivalent phosphorus compounds with a wide variety of sulfur-containing molecules has received considerable attention in recent years, particularly as a technique for modifying the substrate by extrusion of the divalent sulfur atom.[2] While simple sulfides are inert to phosphines and phosphites, activated sulfides of type **1** are desulfurized in the presence of triphenylphosphine and base.[3] The reaction is widely applicable to the preparation of secondary vinylogous amides or enolizable β-diketones **3**. It has been suggested that **1** is first converted to an episulfide **2** which is then desulfurized.[4]



1, X = O, N– 2 3

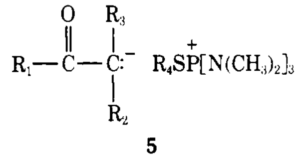
Related work has shown that tris(dialkylamino)phosphines (**4**) are particularly useful reagents for smoothly extruding sulfur from a variety of molecules. These include disulfides,[2] thiosulfonates ($RSSO_2R$),[5] sulfenyl thiosulfonates ($RSSSO_2R$),[5b] thiosulfinate esters [RS(=O)SR],[6] trisulfides,[7] sulfenimides [$RSN(C(=O)R)_2$],[8] and sulfenate esters (RSOR).[9]

$(R_2N)_3P$
4a, R = CH_3
b, R = CH_2CH_3

The desulfurization reactions are in some cases known to be two-step processes[2] as shown below.

$$RSXR' + :P\!< \xrightarrow{\text{slow}} RS\overset{+}{P}\!<\ {}^{-}XR' \xrightarrow{\text{fast}} RXR' + S{=}P\!<$$

Reactions of β-Keto Sulfides. If the above pathway could be used to generate carbanions which fulfilled the dual role of leaving group and nucleophile, a new procedure for carbon–carbon bond formation would be available. Accordingly, a number of β-keto sulfides were prepared and their reaction with tris(dimethylamino)phosphine (**4a**) was examined. Previous work[2,5-9] suggested that the proposed reaction would probably involve a phosphonium salt intermediate **5**.[15a-c]

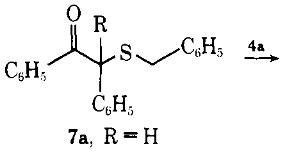


$$R_1{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}\underset{\underset{\displaystyle R_2}{|}}{\overset{\overset{\displaystyle R_3}{|}}{C}}{:}^{-}\quad R_4S\overset{+}{P}[N(CH_3)_2]_3$$

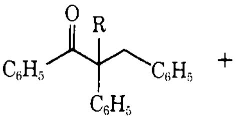
5

To facilitate displacement of the carbanion of **5**, a phenyl group was used at R_2. It appeared that a benzyl moiety at R_4 might encourage easy displacement of tris(dimethylamino)phosphine sulfide (**6**). α-Benzoyl-α-phenylmethyl benzyl sulfide (**7a**)[10] reacts extremely slowly with phosphine **4a** (in a variety of solvents), giving deoxybenzoin ($C_6H_5COCH_2C_6H_5$, **9**) as the principal product.

When the reaction was carried out in the absence of solvent, the starting materials were consumed in less than 1 hr to give three products as analyzed by quantitative vpc: 1-benzoyl-1,2-diphenylethane (**8a**, 69%), deoxybenzoin (**9**, 22%), and tris(dimethylamino)phosphine sulfide (**6**, 86%). **8a** was subsequently isolated in 43% yield.



7a, R = H
b, R = D



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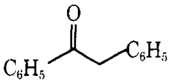

\+ $[(CH_3)_2N]_3P{=}S$

8a, R = H
b, R = D **9** **6**

It appears that **5** ($R_1 = R_2 = C_6H_5$; $R_4 = C_6H_5CH_2$; $R_3 = H$) is formed, but that the anion is partially diverted by proton abstraction to give deoxybenzoin (**9**). The proton attached to the α carbon atom in **7a** is likely to be the one abstracted. This was confirmed by isolation of $PhCOCD_2Ph$ after the reaction of keto sulfide **7b** with aminophosphine.

To determine whether alkylative coupling could occur for a β-keto sulfide that did not have a benzyl group as the second substituent on the sulfur atom, α-benzoyl-α-