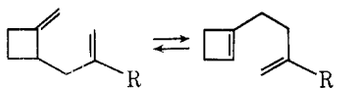
Methylenecyclobutanes 1 and 2 differ only with respect to the substituents at the 2 position of the 1,5-hexadiene chain (eq 2). The >90-fold rate enhancement resulting from sub-



(2)

1, R = CH_3
2, R = CH_2=CH

stitution of a vinyl for a methyl group ($\Delta\Delta G^{\ddagger}_{443.6}$ = 3.9 kcal/mol) implies that the Cope rearrangement of methylenecyclobutanes is quite sensitive to electron-delocalizing groups at the 2(5) position of the 1,5-hexadiene chain. The rate difference, however, is smaller than what one would expect on the basis of the relative radical stabilizing abilities of methyl and vinyl groups.

This finding is in qualitative agreement with the earlier results of Dewar and Wade,[9] who report a 69-fold rate increase at 189.8 °C when phenyl is substituted for hydrogen at the 2 position of 1,5-hexadiene. The similar response to phenyl and vinyl substituents in two disparate [3,3] sigmatropic rearrangements suggests the rate enhancement is a general phenomenon. These results are entirely consistent with, and have been interpreted in terms of,[9,10] a biradicaloid transition state that leads to a 1,4-diradical intermediate (eq 1). Electron-delocalizing groups are expected to stabilize transition states with developing unpaired electron density at the site of substitution. Implicit in this analysis, however, is the expectation that phenyl and vinyl groups will have little influence on the hypothetical pericyclic transition state.[11] This has indeed been proposed by Dewar and Wade[9] although it must be recognized that alternative explanations have been offered.[12]

Experimental Section

Infrared spectra were measured on a Perkin-Elmer 287 spectrophotometer. Only major infrared bands are given. Proton NMR spectra were recorded on either Varian A 56-60 or Bruker WH 90 spectrometers. Preparative VPC analyses were performed on a Varian Aerograph 920 gas chromatograph using a 15 ft, 30% SE-30 on 60/80 Chrom W (AW-DCMS) column at 100 °C. Analytical VPC were obtained on either a Hewlett Packard 700 laboratory chromatograph using a 10 ft, 10% Hi Eff on 60/80 Gas Chrom R column or a Hewlett Packard 5710A chromatograph equipped with a 15 ft, 8% SE-30 on 80/100 Gas Chrom Q column.

2-(2-Methyl-2-propenyl)methylenecyclobutane (1). Methylenecyclobutane[13] (9.8 mL, 100 mmol) was added over 5 min to a stirred solution of TMEDA (33 mmol), hexane (20 mL), and *n*-butyllithium (15 mL, 2.22 M, 33 mmol) at −78 °C under nitrogen. Stirring was continued at −78 °C for 15 min and then the reaction mixture was allowed to warm to room temperature. After stirring for 6 h the reaction mixture consisted of two yellow liquid phases. The mixture was cooled again to −78 °C, and 3-chloro-2-methylpropene (1.49 g, 16.5 mmol) in hexane (5 mL) was added over a 30-min period with stirring. The cold bath was removed, and the reaction mixture was stirred at room temperature for 3.5 h before it was quenched with saturated NH_4Cl (10 mL). The organic layer was washed (5% HCl, 3 × 10 mL), dried (Na_2SO_4), and then concentrated by distillation. Analysis and product isolation was performed by VPC. Two isomers were obtained in 93% yield; in order of elution, 2-(2-methyl-2-propenyl)methylenecyclobutane (1) [IR ($CDCl_3$) 3088, 2985, 2940, 2925, 1673, 1651, 1449, 1429, 1377, 872 cm^{-1}; NMR ($CDCl_3$) δ 1.7 (s, 3 H), 1.8–2.8 (m, 6 H), 3.0 (m, 1 H), 4.67 (br s, 4 H)] and 1-(3-methyl-3-butenyl)cyclobutene (3) [IR ($CDCl_3$) 3075, 3040, 2925, 2845, 1648, 1628, 1445, 1372, 874, 850 cm^{-1}; NMR ($CDCl_3$) δ 1.70 (s, 3 H), 2.12 (s, 4 H), 2.40 (s, 4 H), 4.65 (br s, 2 H), 5.65 (s, 1 H)]. The ratio of products 1/3 was 85:15.

Reaction of 1-Cyclobutenylmethyllithium with 2-Bromomethylenecyclobutane. In a similar manner 2-bromomethylenecyclobutane (0.95 g, 6.5 mmol)[14] was added to 1-cyclobutenylmethyllithium (one-half scale). After workup and distillation, the residue was vacuum transferred. Analysis and isolation were performed as before by preparative VPC. Three isomeric $C_{10}H_4$ hydrocarbons were formed in 85% overall yield; their relative yields, in order of increasing retention time, are 4 (22.5%), 6 (45.5%), and 5 (32%). 2-(2-Methylenecyclobutane)methylenecyclobutane (4): IR ($CDCl_3$) 3072, 2980, 2940, 2920, 2882, 1670, 1450, 1425, 1405, 874 cm^{-1}; NMR ($CDCl_3$) δ 1.4–2.5 (m, 8 H), 3.1 (m, 2 H), 4.7 (br s, 4 H). 2-(1-Cyclobutenylmethyl)methylenecyclobutane (6): IR ($CDCl_3$) 3075, 3050, 2925, 2850, 1675, 1630, 1430, 1300, 1075, 874, 855 cm^{-1}; NMR ($CDCl_3$) δ 1.3–2.0 (m, 2 H), 2.0–2.9 (m, 8 H), 3.0 (m, 1 H), 4.7 (br s, 2 H), 5.7 (s, 1 H). 1,2-Bis(1-cyclobutenyl)ethane (5): IR ($CDCl_3$) 3040, 2920, 2840, 1630, 1062, 853 cm^{-1}; NMR ($CDCl_3$) δ 2.13 (br s, 4 H), 2.35 (br s, 8 H), 5.65 (br s, 2 H).

2-(2-Methylidene-3-butenyl)methylenecyclobutane (2). 2-(1-Cyclobutenylmethyl)methylenecyclobutane (6) (11.7 mg, 0.087 mmol) was diluted with 0.7 mL of cyclohexane, degassed by several freeze–thaw cycles, and then sealed. After heating at 168 °C for 2 h, the tube was cooled, opened, and analyzed by VPC. Triene product 2 was found (81%) in addition to minor amounts of starting material (6, 3%), 5-(1-cyclobutenyl)-3-methylidene-1-pentene (8, 5%), and 3,6-dimethylidene-1,7-octadiene (9, 11%). Compound 2: IR (CS_2) 3085, 3070, 2970, 2930, 2910, 1672, 1595, 988, 900, 891, 871 cm^{-1}; NMR ($CDCl_3$) δ 1.5–2.7 (m, 6 H), 3.18 (m, 1 H), 4.75 (m, 2 H), 4.98–5.32 (m, 4 H), 6.39 (dd, *J* = 17.4 and 10.2 Hz, 1 H). Compound 8 showed the following: IR (CS_2) 3085, 3040, 2940, 2915, 1631, 1595, 988, 901, 891, 851 cm^{-1}; NMR ($CDCl_3$) δ 2.29–2.46 (m, 8 H), 5.01–5.33 (m, 4 H), 5.71 (s, 1 H), 6.39 (dd, *J* = 17.8 and 11.0 Hz, 1 H). Spectral properties of tetraene 9 are consistent with those reported.[15]

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Registry No.—1, 66290-31-1; 2, 66290-32-2; 3, 66290-33-3; 4, 66290-34-4; 5, 66290-35-5; 6, 66290-36-6; 8, 66290-37-7; 9, 3382-59-0; methylenecyclobutane, 1120-56-5; 3-chloro-2-methylpropene, 563-47-3; 2-bromomethylenecyclobutane, 32442-49-2; 1-cyclobutenylmethyllithium, 66290-38-8.

References and Notes

(1) For recent reviews, see (a) S. J. Rhoads and N. R. Raulins, *Org. React.*, **22**, 1 (1975); (b) F. E. Ziegler, *Acc. Chem. Res.*, **10**, 227 (1977).
(2) G. B. Bennett, *Synthesis*, 91 (1977).
(3) (a) R. Willcott, R. L. Cargill, and A. B. Sears, *Prog. Phys. Org. Chem.*, **9**, 25 (1972); P. J. Robinson and K. A. Holbrook, "Unimolecular Reactions", Wiley-Interscience, New York, N.Y., 1972, p 196; (c) S. W. Benson and H. E. O'Neal, *Natl. Stand. Ref. Data Ser., Natl. Bur. Stand.*, **21** (1970).
(4) W. E. Doering, V. G. Toscano, and G. H. Beasley, *Tetrahedron*, **27**, 5299 (1971).
(5) S. R. Wilson and L. R. Phillips, *Tetrahedron Lett.*, 3047 (1975).
(6) Interestingly, the reaction of 1-cyclobutenylmethyllithium with 2-bromomethyl-1,3-butadiene results in a virtually identical product distribution as that obtained from coupling with 2-bromomethylmethylenecyclobutane.
(7) Compare, for example, the rate of ring opening of 1-(2-propenylcyclobutene, k(170.6 °C) = 5.04 × 10^{-4} s^{-1}: D. Dickens, H. M. Frey, and R. F. Skinner, *J. Chem. Soc., Faraday Trans. 1*, **65**, 453 (1969).
(8) D. L. Bunker and F. Houle, Quantum Chemistry Program Exchange (Program No. 293).
(9) M. J. S. Dewar and L. E. Wade, Jr., *J. Am. Chem. Soc.*, **99**, 4417 (1977).
(10) M. J. S. Dewar, G. P. Ford, M. L. McKee, H. S. Rzepa, and L. E. Wade, *J. Am. Chem. Soc.*, **99**, 5069 (1977).
(11) A vinyl substituent has recently been shown to produce a thirtyfold rate enhancement in an electrocyclic ring closure: C. W. Spangler, *Tetrahedron*, **32**, 2681 (1976).
(12) W. T. Bordon, "Modern Molecular Orbital Theory for Organic Chemists", Prentice-Hall, Englewood Cliffs, N.J., 1975, p 130.
(13) J. D. Roberts and C. W. Sauer, *J. Am. Chem. Soc.*, **71**, 3925 (1949).
(14) E. R. Buchman and D. R. Howton, *J. Am. Chem. Soc.*, **70**, 2517 (1948).
(15) G. B. Butler and M. A. Raymond, *J. Org. Chem.*, **30**, 2410 (1965).

Synthesis of Biphenyl 2,3-Oxide

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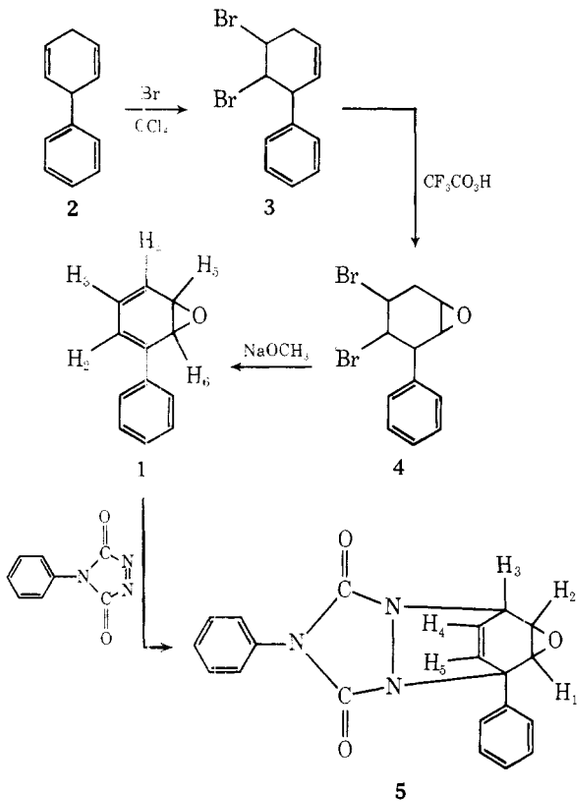
A recent study reported that the polynuclear aromatic hydrocarbons (PAH), including biphenyl, are ubiquitous pollutants which frequently reach concentrations of 0.1 ng/m^3.[1a]

Scheme I



Furthermore, biphenyl is also the parent hydrocarbon from which the polychlorinated biphenyls, widespread and persistent environmental contaminants,[1b] are derived. Since PAHs are metabolized by hepatic monooxygenases via arene oxides, some of which are mutagenic and carcinogenic,[2] we have attempted to prepare biphenyl oxides in order to study their properties. The present report describes the first synthesis of a biphenyl oxide [5,6-epoxy-1-phenyl-1,3-cyclohexadiene (**1**), hereafter called biphenyl 2,3-oxide].

Scheme I outlines the synthetic procedure utilized for the formation of **1**. The addition of bromine to **2** resulted in an oil which analyzed for 3-phenyl-4,5-dibromocyclohexene (**3**). The NMR of **3** was quite complex indicating a mixture of diastereoisomers. No attempt was made to separate the diastereoisomers since the ratio of aliphatic hydrogens to aromatic hydrogens was as expected. The synthesis of **4** was accomplished using the procedure of Emmons and Pagano.[3] The NMR of **4** again showed the presence of diastereoisomers. The diastereoisomeric mixture of **4** gave the correct elemental analysis. The dehydrohalogenation of the diastereoisomeric mixture of **4** was accomplished using sodium methoxide at 0 °C. Analysis of **1** by TLC indicated the presence of a single product. Since **1** was unstable at room temperature, a Diels–Alder adduct (**5**) of **1** and the dienophile 4-phenyl-1,2,4-triazoline-3,5-dione was prepared and was found to have the expected elemental analysis. Compound **5** was stable indefinitely at room temperature.

The NMR spectrum of **1** (Scheme I) was obtained in tetrahydrofuran. The signal for the vinyl hydrogen H_2 appeared within the envelope of aromatic hydrogens due to the benzene ring. Multiplets at 4.27 and 4.53 ppm were assigned to the oxirane hydrogens H_5 and H_6, respectively, based on their chemical shifts[4] and on the fact that H_6 appears as a doublet of doublets while H_5 is a complex multiplet at 100 MHz. Coupling constants of 2.4 and 3.4 Hz at H_6 are due to coupling to H_2 and H_5 but are too close in magnitude to be individually assigned. Complex multiplets at 6.42 and 6.63 ppm were assigned as hydrogens H_3 and H_4. If analogy can be drawn to the spectrum of benzene oxide,[5] the signal at lower field is due to hydrogen H_3.

The instability of **1** prompted us to examine the breakdown products of **1** both in the presence and absence of water. Solutions of **1** in dry tetrahydrofuran and water were sealed and stirred for 4 h. GLPC analysis indicated that in both cases only two products were found, 2-phenylphenol and 3-phenylphenol in the ratio of 49:1.

Previously, studies of the isomerization of 3- and 4-chlorobenzene oxides established that neither arene oxide produced much 3-chlorophenol upon isomerization.[7] Since 3-chlorophenol is a metabolite of chlorobenzene in mammals, a non-arene oxide pathway was suggested to account for its formation.[8] Recent studies on the metabolism of biphenyl have shown that the ratio of 2- to 3-phenylphenol formed by liver microsomes varies from 1:1 to 2:1 depending on the species of animal studied.[9] In light of the present results which indicate that 3-phenylphenol is only a trace isomerization product from biphenyl 2,3-oxide under a variety of conditions, Billings and McMahon[9] suggested that a non-arene oxide pathway was responsible for the formation of 3-phenylphenol.

Experimental Section

NMR spectra were recorded on Varian HA-100 and Varian HR 220-MHz instruments. Mass spectra were obtained on a Finnegan 1015-D. 3-Phenyl-1,4-cyclohexadiene was obtained from the Aldrich Chemical Co. Since heating promoted decomposition of the diene, it was used without purification even though 5–10% biphenyl was present.

3-Phenyl-4,5-dibromocyclohexene (3). A solution of 3-phenyl-1,4-cyclohexadiene (3 g of crude material) dissolved in 20 mL of carbon tetrachloride was cooled to 0–5 °C. A solution of 10% bromine in carbon tetrachloride was added dropwise with stirring until the reaction mixture remained red for 30 s. A solution of sodium thiosulfate was added to decompose excess bromine. The carbon tetrachloride solution was dried and concentrated to an oil which was distilled to provide 3-phenyl-4,5-dibromocyclohexene (2.8 g, 0.009 mol) bp 150–2 °C (1.8 mm). The mass spectrum of **3** showed a parent peak at 314 and a parent +2 peak at 316. The NMR spectrum (CCl_4) was complex owing to the presence of stereoisomers. However, the ratio of aliphatic hydrogens to aromatic hydrogens was 7:5 as required. The analysis follows for the mixture of stereoisomers. Anal. Calcd for $C_{12}H_{12}Br_2$: C, 45.60; H, 3.83; Br, 50.57. Found: C, 45.83; H, 3.61; Br, 50.18.

3-Phenyl-4,5-dibromo-1,2-epoxycyclohexane (4). Peroxytrifluoroacetic acid, prepared from 15 mL of trifluoroacetic anhydride and 3 mL of 90% hydrogen peroxide, in 25 mL of methylene chloride was added dropwise with stirring to a slurry of **3** (1 g, 0.003 mol) and sodium carbonate (5 g) in 50 mL of methylene chloride. The diminution of **3** was monitored by GLPC (3% SE-30 on Gas Chrom Q at a flow rate of 80 cm^3/min, programmed from 100 to 200 °C at a rate of change of 10 °C/min). The GLPC chromatogram showed the appearance of four new peaks. The four new products were isolated by centrifuging the methylene chloride solution away from the sodium carbonate. Removal of the solvent under reduced pressure yielded a mixture of the four stereoisomers of **4** (0.63 g, 0.0018 mol, 61%). The NMR spectrum (CCl_4) of the isomer mixture was complex, but integrated for an aliphatic hydrogen to aromatic hydrogen ratio of 7:5. Anal. Calcd for $C_{12}H_{12}Br_2O$: C, 43.40; H, 3.64; Br, 48.13. Found: C, 43.21; H, 3.72; Br, 48.33.

Biphenyl 2,3-Oxide (1). In a 50 mL Erlenmeyer flask equipped with a stirrer and an addition funnel **4** (0.5 g, 0.0015 mol) was dissolved in 25 mL of dry tetrahydrofuran. The solution was cooled to 0 °C and sodium methoxide (2 g) was added slowly with stirring. Stirring was continued for 2 h, after which the reaction mixture was poured onto a column of neutral alumina. Compound **1** was eluted with tetrahydrofuran. Removal of the solvent under reduced pressure yielded **1** (0.08 g, 0.00046 mol, 31%). The 100 MHz NMR spectrum [tetrahydrofuran (D_8) at −20 °C]: 4.27 ppm (m, 1 H, H_5), 4.53 ppm (dd, 1 H, H_6), 6.42 ppm (m, 1 H, H_4), 6.63 ppm (m, 1 H, H_3), 7.40 ppm (m, 6 H, H_2 + aromatic H). The coupling constants of J = 2.4 and 3.4 Hz were observed at H_6.

On thin layer chromatography (silica gel, benzene/chloroform/ethyl acetate (1:1:1) containing 5% triethylamine) the arene oxide gave a single spot at R_f 0.4 provided the spotting area of the plate had been

pretreated with triethylamine while 2-phenylphenol chromatographed at R_f 0.2.

Direct GLPC analysis of **1** under the conditions described in the synthesis of **4** indicated that thermal isomerization occurred to a 49:1 mixture of 2-phenylphenol (2.5 min) and 3-phenylphenol (3.5 min). The same ratio of phenols was observed after **1** had completely isomerized in water (4 h) or tetrahydrofuran (4 days) at room temperature.

A Diels–Alder adduct (**5**) of **1** was prepared by adding 4-phenyl-1,2,4-triazoline-3,5-dione[6] to a solution of **1** in tetrahydrofuran. The adduct **5** was collected and recrystallized from benzene, mp 125–126 °C. The mass spectrum of **5** showed a parent peak at 345. The 220 MHz NMR spectrum ($CDCl_3$) of **5** showed H_1 3.68, H_2 3.84, H_3 5.43. H_4 6.30, H_5 6.80, and ten aromatic hydrogens at 7.3–8.2 ppm with $J_{1,2}$ = 4.2, $J_{1,5}$ = 1.4, $J_{2,3}$ = 4.4, $J_{2,4}$ = 1.1, $J_{3,4}$ = 6.0, $J_{3,5}$ = 1.4, and $J_{4,5}$ = 8.5 Hz. Anal. Calcd for $C_{20}H_{15}N_3O_3$: C, 69.55; H, 4.38; N, 12.17. Found: C, 69.71; H, 4.22; N, 12.21.

Registry No.—**1**, 65916-08-7; **2**, 4794-05-2; **3**, 65916-09-8; **4**, 65916-10-1; **5**, 65916-11-2; 4-phenyl-1,2,4-triazoline-3,5-dione, 4233-33-4.

References and Notes

(1) (a) A. M. Krstulovic, D. M. Rosie, and P. R. Brown, *Am. Lab.*, 11 (July 1977); (b) O. Hutzinger, S. Safe, and V. Zitko, "The Chemistry of PCB's", Chemical Rubber Publishing Co., Cleveland, Ohio, 1974; R. W. Risebrough, P. Reiche, D. B. Peakall, S. G. Herman, and M. N. Kirven, *Nature (London)*, **220**, 1098 (1968).
(2) D. M. Jerina and J. W. Daly, *Science*, **185**, 573 (1974); P. Sims and P. L. Grover, *Adv. Cancer Res.*, **20**, 165 (1974).
(3) W. D. Emmons and A. S. Pagano, *J. Am. Chem. Soc.*, **76**, 3742 (1954).
(4) E. Vogel and H. Gunther, *Angew. Chem., Int., Ed. Engl.*, **6**, 385 (1967).
(5) E. Vogel, W. A. Boll, and H. Gunther, *Tetrahedron Lett.*, 609 (1965).
(6) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. I, Wiley, New York, N.Y., p 849. 4-Phenylurazole was purchased from the Aldrich Chemical Co.
(7) H. G. Selander, D. M. Jerina, D. E. Piccolo, and G. A. Berchtold, *J. Am. Chem. Soc.*, **97**, 4428 (1975).
(8) J. E. Tomaszewski, D. M. Jerina, and J. W. Daly, *Biochemistry*, **14**, 2024 (1975).
(9) R. E. Billings and R. E. McMahon, *Mol. Pharmacol.*, **14**, 145 (1978).

Alkylation and Silicon Pummerer Rearrangement of Chloromethyl Phenyl Sulfoxide. A Thiol Ester Acyl Anion Equivalent

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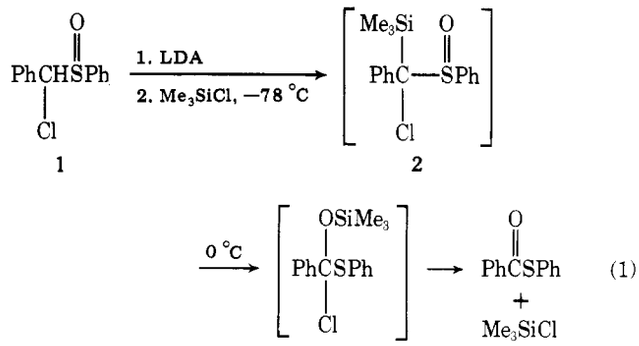
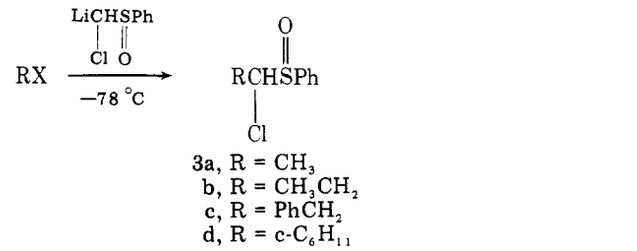
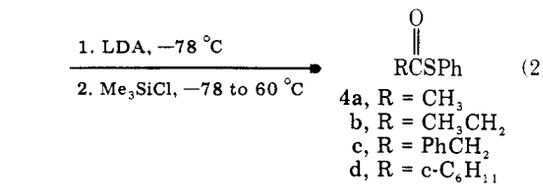
In recent years considerable attention has been given to the development of acyl anion equivalents for aldehydes, ketones, esters, and other carbonyl functions.[1] As part of a program to develop new methods for the synthesis of thiol esters, we have been interested in finding procedures for the nucleophilic introduction of the thiol ester group. We report here the first example of a carbothioate acyl anion equivalent which is capable of homolagation of alkyl halides permitting conversion to thiol ester derivatives.[2] Acyl anion equivalents that permit the introduction of a thiol ester function are of interest in view of the high relative reactivity of the thiol ester group and the potential therein for other synthetic applications.

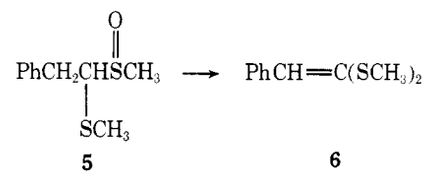
The key step in this transformation is silicon Pummerer rearrangement[3,4] of an α-chloro sulfoxide, leading to the thiol ester involving facile elimination of chlorotrimethylsilane in the final step. This process is illustrated in eq 1, where α-chlorobenzyl phenyl sulfoxide (**1**) has been silyated with chlorotrimethylsilane at −78 °C to give **2**. Upon warming to 0 °C **2** is converted to *S*-phenyl thiolbenzoate in 74% isolated yield.[5]



The overall transformation of alkyl halides to *S*-phenyl thiol ester homologues involves initial alkylation of chloromethyl phenyl sulfoxide followed by silicon Pummerer rearrangement of this derivative to give the thiol ester. Butyllithium induced alkylation of chloromethyl phenyl sulfoxide with chloromethylamines has been reported to occur in 40–45% yield.[6] We have found that high yields may be obtained in the alkylation of chloromethyl phenyl sulfoxide when lithium diisopropylamide (LDA) is employed as the base.[7] Alkylation of the lithiochloromethyl phenyl sulfoxide with 2 equiv of methyl iodide results in a 95% yield of a 6:4 diastereomeric mixture of α-chloroethyl phenyl sulfoxides (**3a**). Less than 4% of the bismethylation byproduct was formed according to NMR analysis of the crude reaction mixture. Primary alkyl bromides as well as secondary alkyl iodides have been employed, including ethyl bromide, benzyl bromide, and cyclohexyl iodide. With the latter two halides 1 equiv of alkyl halide was used and yields in the range of 87–90% of the diastereomeric mixture of alkylated α-chloro sulfoxide products (**3**) were produced.







The presence of an α-halo substituent appears to be necessary in order to obtain silicon Pummerer rearrangement leading to formation of the thiol ester group. For example, it has been reported that α-methylthio sulfoxide **5** undergoes the silicon Pummerer rearrangement to give elimination product **6** in 86% yield. In a parallel reaction carried out under similar conditions on structurally related α-chloro sulfoxide **3c**, thiol ester **4c** was obtained as the major product in 60% yield. Although it is necessary to carefully dry the alkylated α-chloro sulfoxide (**3**) prior to the rearrangement step we found that careful purification of these products by column chromatography was not necessary in order to obtain ac-

0022-3263/78/1943-2713$01.00/0