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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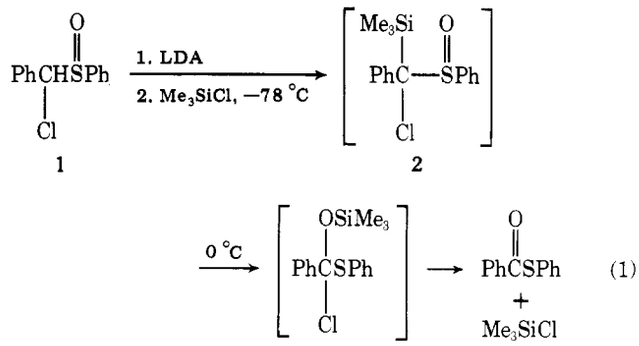
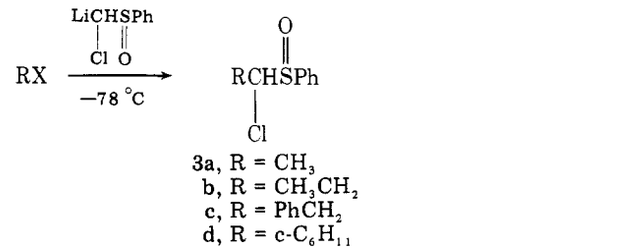
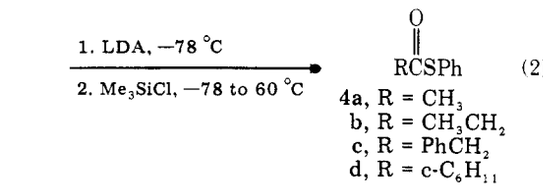
In recent years considerable attention has been given to the development of acyl anion equivalents for aldehydes, ketones, esters, and other carbonyl functions.[1] As part of a program to develop new methods for the synthesis of thiol esters, we have been interested in finding procedures for the nucleophilic 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.

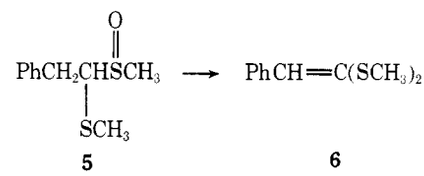
The key step in this transformation is silicon Pummerer rearrangement[3,4] of an α-chloro sulfoxide, leading to the thiol ester involving facile elimination of chlorotrimethylsilane in the final step. This process is illustrated in eq 1, where α-chlorobenzyl phenyl sulfoxide (**1**) has been silyated 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-

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ceptable yields of the corresponding thiol esters (**4**). The conversion of alkylated chloromethyl phenyl sulfoxide to thiol ester can be carried out in one pot without isolation of the intermediate α-chloro α-trimethylsilyl sulfoxide (e.g., **2**). In the reaction of **1**, following silylation at −78 °C, warming to 0 °C was sufficient to obtain rearrangement (eq 1). However, with the alkylated chloromethyl phenyl sulfoxides (**3**) obtained from methyl iodide, benzyl bromide, ethyl bromide, and cyclohexyl iodide, refluxing at 60 °C for 2 h was required in order to obtain a satisfactory yield of thiol ester (**4**) (eq 2). In these reactions minor amounts of other products were produced, including some that according to NMR retained the trimethylsilyl substituent; however, attempts to isolate these compounds were unsuccessful due to their low relative stability.

Experimental Section[8]

***S*-Phenyl Thiolbenzoate.** α-Chlorobenzyl phenyl sulfoxide (**1**;[9b] 1.25 g, 5.0 mmol) in THF (2 mL) was added dropwise with stirring over a 3-min period to lithium diisopropylamide (5.0 mmol, prepared from 0.50 g of diisopropylamine and 3.2 mL of 1.58 M *n*-BuLi in hexane at 0 °C) in THF (10 mL) under a nitrogen atmosphere at −78 °C. It was stirred at −78 °C for 30 min and then the anion solution was transferred to excess chlorotrimethylsilane (1.62 g, 15 mmol) in THF (10 mL) at −78 °C dropwise with stirring over a 5-min period. The reaction mixture was allowed to warm to 0 °C. After stirring for 1 h at 0 °C, 2% hydrochloric acid (5 mL) was added dropwise and the mixture was extracted with dichloromethane (3 × 40 mL), dried (Na_2SO_4), and concentrated under reduced pressure to give the product as a yellow solid. This was crystallized from hexane–ether to give white crystals (0.790 g, 74%): mp 54–55 °C (lit.[10] 55–56 °C); NMR ($CDCl_3$) δ 8.50–7.85 (m, 2 H), 7.60–7.20 (m, 8 H); IR (KBr) 1685 cm^{-1}.

Alkylation of Chloromethyl Phenyl Sulfoxide. A solution of lithium diisopropylamide (15 mmol) in THF was prepared under nitrogen by addition of 6.8 mL of 2.2 M *n*-butyllithium in hexane to a solution of 1.52 g of diisopropylamine in THF (15 mL) at −78 °C followed by stirring at −78° for 15 min. To this was added dropwise (5 min) with stirring a solution of chloromethyl phenyl sulfoxide[9] (2.61 g, 15 mmol) in THF (3 mL). The resulting light yellow solution was then allowed to stir at −78 °C for 30 min. At this point a solution of the alkyl halide (1 equiv of benzyl bromide or cyclohexyl iodide was used while 2 equiv of the more volatile methyl iodide or ethyl bromide were used) in THF (3 mL) was added and stirring was continued for 30 min at −78 °C before the ice bath was removed and the reaction was allowed to warm to room temperature. Stirring was continued for 45 min at room temperature before the reaction was stopped by pouring into a 2% HCl–ice mixture. The product was extracted with methylene chloride (3 × 50 mL) which was dried (Na_2SO_4) and concentrated to give the product as an oil. 1-Chloroethyl phenyl sulfoxide (**3a**; 95% yield) as well as 1-chloropropyl phenyl sulfoxide (**3b**; 95% yield) were further dried by short-path distillation under reduced pressure. 1-Chloro-2-phenylethyl phenyl sulfoxide (**3c**; 87% yield) and α-chlorocyclohexylmethyl phenyl sulfoxide (**3d**; 90% yield) were dried by allowing them to stand overnight under reduced pressure (1 mm) at room temperature. In all cases a mixture of both diastereomers was obtained. After drying, this mixture was used directly without further purification in the silicon Pummerer rearrangement to form the corresponding thiol esters.

The diastereomeric mixture (6:4) of 1-chloroethyl phenyl sulfoxides (**3a**) obtained using methyl iodide as the alkylating agent was separated by column chromatography on silica gel, eluting with benzene–ethyl acetate (9:1). The first isomer obtained from the column gave the following NMR data ($CDCl_3$): δ 7.85–7.30 (m, 5 H), 4.50 (q, 1 H, J = 7 Hz), 1.82 (d, 3 H, J = 7 Hz). The second isomer eluted from the column was the major isomer: NMR ($CDCl_3$) δ 7.80–7.30 (m 5 H), 4.70 (q, 1 H, J = 7 Hz), 1.58 (d, 3 H, J = 7 Hz). This second isomer gives the same NMR data as that isolated in the reaction of ethyl phenyl sulfoxide with sulfuryl chloride.[9b]

Conversion of Alkylated Chloromethyl Phenyl Sulfoxides to Thiol Esters. To a solution of lithium diisopropylamide (5 mmol) in THF (10 mL) under nitrogen at −78 °C was added a solution of the alkylated chloromethyl phenyl sulfoxide (**3**; 5 mmol) in THF (2 mL) dropwise over a period of 2 min. This was allowed to stir at −78 °C for 30 min. The resulting anion solution was then added dropwise (5 min) to chlorotrimethylsilane (2.7 g, 2.5 mmol) in THF (10 mL) at −78 °C. The reaction was allowed to warm to room temperature (30 min) and then warmed slowly (1 h) to reflux (60 °C). Refluxing was continued for 2 h before the reaction was stopped by cooling to room temperature, followed by addition to a mixture of 2% HCl and ice. The product was extracted with ether (3 × 50 mL) and dried (Na_2SO_4) and the ether concentrated to give an oil which was immediately subjected to column chromatography on silica gel eluting with benzene–hexane (1:1). In this manner the following thiol esters (**4**) were prepared.

S-Phenyl thiolacetate (**4a**) was obtained from 1-chloroethyl phenyl sulfoxide (**3a**) in 63% yield following short-path distillation [bp 65 °C (1 mm); lit.[10] bp 95 °C (7 mm)]: NMR ($CDCl_3$) δ 7.33 (s, 5 H), 2.31 (s, 3 H); IR (film) 1700 cm^{-1}.

S-Phenyl thiolpropionate (**4b**) was obtained from 1-chloropropyl phenyl sulfoxide (**3b**) in 62% yield following short-path distillation [bp 90–95 °C (bath temp) (1 mm); lit.[11] bp 170–180 °C (10 mm)]: NMR ($CDCl_3$) δ 7.22 (s, 5 H), 2.62 (q, 2 H, J = 8 Hz), 1.15 (t, 3 H, J = 8 Hz); IR (film) 1705 cm^{-1}.

S-Phenyl phenylthiolacetate (**4c**) was obtained from 1-chloro-2-phenylethyl phenyl sulfoxide (**3c**) as a light yellow solid in 60% yield after column chromatography on silica gel. White crystals were obtained after crystallization from hexane: mp 39 °C (lit.[10] mp 40 °C); NMR ($CDCl_3$) δ 7.31 (s, 5 H), 7.28 (s, 5 H), 3.85 (s, 2 H); IR (KBr) 1700 cm^{-1}.

S-Phenyl cyclohexanecarbothioate (**4d**) was obtained from α-chlorocyclohexylmethyl phenyl sulfoxide (**3d**) in 58% yield following short-path distillation [bp 130–140 °C (bath temperature) (3 mm): NMR ($CDCl_3$) δ 7.12 (s, 5 H), 2.8–2.4 (m, 1 H), 2.1–1.1 (m, 10 H); IR (film) 1705 cm^{-1}].

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Registry No.—**1**, 21128-89-2; **2**, 66102-71-4; **3a** isomer 1, 66102-72-05; **3a** isomer 2, 66102-73-6; **3b** isomer 1, 66102-74-7; **3b** isomer 2, 66102-75-8; **3c** isomer 1, 66102-76-9; **3c** isomer 2, 66102-77-0; **3d** isomer 1, 66102-78-1; **3d** isomer 2, 66102-79-2; **4a**, 934-87-2; **4b**, 18245-72-2; **4c**, 18245-74-4; **4d**, 58587-03-4; *S*-phenyl thiolbenzoate, 884-09-3; chloromethyl phenyl sulfoxide, 7205-94-9; benzyl bromide, 100-39-0; cyclohexyl iodide, 626-62-0; methyl iodide, 74-88-4; ethyl bromide, 74-96-4.

References and Notes

(1) H. O. House, "Modern Synthetic Reactions," 2nd ed, W. A. Benjamin, Menlo Park, Calif., 1972.
(2) D. Seebach, *Angew. Chem., Int. Ed. Engl.*, **8**, 639 (1969); D. Seebach and M. Kolb, *Chem. Ind. (London)*, 687 (1974). Two thiol ester acyl anion equivalents have recently been developed for the conversion of aldehydes and ketones to thiol ester homologues: D. Seebach and R. Burstinghaus, *Synthesis*, 461 (1975); R. E. Damon, T. Luo, and R. H. Schlessinger, *Tetrahedron Lett.*, 2749 (1976).
(3) A. G. Brook and D. G. Anderson, *Can. J. Chem.*, **46**, 2115 (1968); A. G. Brook, *Acc. Chem. Res.*, **7**, 77 (1974).
(4) E. Vedejs and M. Mullins, *Tetrahedron Lett.*, 2017 (1975).
(5) A related but less general transformation has been reported wherein an α-bromo-β-keto sulfoxide is converted to an α-keto thiol ester in 40% yield using sulfuric acid: G. A. Russell and G. J. Mikol, *J. Am. Chem. Soc.*, **88**, 5498 (1966); G. A. Russell and L. A. Ochrymowycz, *J. Org. Chem.*, **34**, 3618 (1969). See also S. Iriuchijima, K. Maniwa, and G. Tsuchihashi, *J. Am. Chem. Soc.*, **97**, 596 (1975).
(6) H. Böhme and W. Stammberger, *Justus Liebigs Ann. Chem.*, **754**, 56 (1971).
(7) Nucleophilic displacement at sulfur occurs in the reaction of *n*-butyllithium or *tert*-butyllithium with sulfoxides and methyllithium or LDA are recommended as superior bases for generation of α-lithio sulfoxides: T. Durst, M. J. LeBelle R. Van den Elzen, and K.-C. Tin, *Can J. Chem.*, **52**, 761 (1974).
(8) Infrared spectra were recorded on a Perkin-Elmer Model 457 spectrometer. Nuclear magnetic resonance spectra were taken on a Varian A-60A spectrometer using tetramethylsilane (Me_4Si) as an internal standard. THF was dried over potassium metal and distilled just prior to use. Silica gel used in column chromatography was Baker reagent grade (60–200 mesh). Melting and boiling points are uncorrected.
(9) (a) K.-C. Tin and T. Durst, *Tetrahedron Lett.*, 4643 (1970); (b) G. I. Tsuchihashi, K. Ogura, S. Iriuchijima, and S. Tomisawa, *Synthesis*, 89 (1971).
(10) K. Miyaki and S. Yamagishi, *J. Pharm. Soc.*, **76**, 436 (1956).
(11) W. Rappe, H. Kooper, H. J. Pistor, and H. Schlenck, *Justus Liebigs Ann. Chem.*, **582**, 38 (1953).