and allylic monoadducts. The other fraction, b.p. 180–183°, had the same isomers in a 3:7 ratio. (For physical and analytical data see Tables II–IV.)

Addition of benzenethiol to diallyl fumarate with ultraviolet irradiation under the conditions of the above experiment occurred selectively at the allylic bonds. N.m.r. and g.l.p.c. analyses of the reaction mixture before irradiation showed about 50% reaction (45% allylic monoadduct). Irradiation resulted in a somewhat increased conversion but no great change of product distribution (Table I). Fractional distillation of the reaction mixture yielded 15 g. (20%) of the allylic monoadduct as a slightly yellow liquid (Figure 1, Tables II and III) and 10 g. (11%) of a distillation residue consisting of about a 1:1 mixture of mono- and diadducts.

Addition of thiolacetic acid to diallyl maleate occurred on mixing without irradiation. On fractional distillation of the reaction mixture from 0.2 mole of each reactant, 22 g. (40%) of allylic monoadduct was obtained as a colorless liquid distillate. The distillation residue (20 g.) contained a major amount (66%) of the diadduct together with some of the above monoadduct (34%).

Addition of thiolacetic acid to diallyl fumarate took place in the manner described in the above experiment to give the results shown in Tables I and II.

Addition of Diethyldithiophosphoric Acid to Diallyl Maleate.—To 19.6 g. (0.1 mole) of stirred and nitrogenated diallyl maleate, 37.2 g. (0.2 mole) of the acid was added with ice cooling in 20 min. Subsequent n.m.r. analysis indicated that all the maleate disappeared to form 96% of the expected maleic monoadduct. The crude product was dissolved in 150 ml. of ether, washed twice with 200 ml. of 5% aqueous sodium hydrogen carbonate to remove the excess acid, dried over anhydrous sodium sulfate, concentrated to remove the ether, and heated at 80° at 0.1 mm. to distil off the fumarate to yield the purified monoadduct (Tables I and II). A similar addition to diallyl maleate containing 5 mole % dissolved methylhydroquinone yielded the same product.

Anionic Additions.—The catalyst, usually 5 mole % triethylenediamine, was dissolved in the diallyl maleate or fumarate, and the thiol compound was slowly added to the solution under nitrogen with stirring and ice–water cooling. Maleic or fumaric addition was usually complete within 1 hr. The reaction mixtures were worked up by distillation, which produced recovered triethylenediamine in the forerun.

Acknowledgment.—The authors wish to thank T. G. Jermansen for excellent technical assistance.

Electrophilic Substitution of the Benzenethiols.
III. New Thiol Protective Groups and Cleavage Reagents[1]

DEREK WALKER[2]

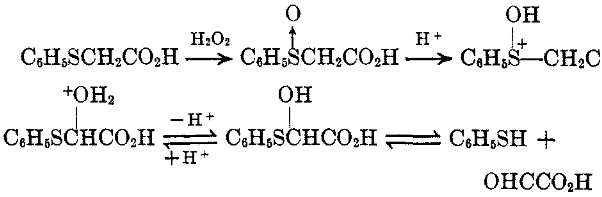
Research Laboratory, Domtar Ltd., Senneville, Quebec, Canada

Received September 14, 1965

The sulfur atom of benzenethiols must be protected prior to carrying out electrophilic substitution reactions in the benzene ring. The general requirements of a protective group in this series are that the group be unaffected by electrophilic reagents and that it may be easily cleaved. The present paper indicates that further general requirements of a sulfur-protective group for benzenethiols are that the group should contain hydrogen on the carbon atom adjacent to sulfur, and that this carbon should be "activated" by an electron-withdrawing group. Such groups are then readily removed by acidic oxidizing agents. It is shown that the acetonyl group and the cyanomethyl group have only limited usefulness as sulfur-protective groups in electrophilic substitution reactions in the benzenethiol series. Finally, the present paper points out the utility of nitric acid and acid permanganate as cleavage reagents.

In an earlier paper Walker and Leib[3] demonstrated that phenylmercaptoacetic acid could be cleaved in high yield to benzenethiol and glyoxylic acid by adding hydrogen peroxide to a boiling mineral acid suspension of phenylmercaptoacetic acid, and removing the benzenethiol as it was formed, by passing steam into the reaction mixture. This reaction was shown to proceed through phenylsulfinylacetic acid, which compound underwent rearrangement to phenylmercaptohydroxyacetic acid in the presence of mineral acid. This hemimercaptal then disproportionated to give benzenethiol and glyoxylic acid. Equation 1[4] describes the reaction.

The rapid oxidative cleavage of the carboxymethyl group suggested the utility of this group as a readily removable sulfur-protective species which would enable electrophilic substitution of the aromatic ring of benzenethiols to be carried out. A number of halo- and acylarylthiols were subsequently prepared using this scheme.



$$C_6H_5SCH_2CO_2H \xrightarrow{H_2O_2} C_6H_5\overset{O\uparrow}{S}CH_2CO_2H \xrightarrow{H^+} C_6H_5\overset{OH}{\overset{|}{S^+}}{-}CH_2CO_2H$$

$$C_6H_5S\overset{^+OH_2}{\overset{|}{C}}HCO_2H \underset{+H^+}{\overset{-H^+}{\rightleftharpoons}} C_6H_5S\overset{OH}{\overset{|}{C}}HCO_2H \rightleftharpoons C_6H_5SH + OHCCO_2H \quad (1)$$

The present paper describes experiments with other sulfur-protective groups and with oxidizing agents other than hydrogen peroxide.

Since the carboxymethyl group of phenylmercaptoacetic acid is readily cleaved with hydrogen peroxide and mineral acid, and since simple aryl alkyl sulfides do not undergo this reaction, it seemed reasonable to expect that compounds of type I, wherein X is an electron-withdrawing group, would undergo cleavage,

$C_6H_5SCH_2X$
Ia, $X = CN$
b, $X = COCH_3$

$RC_6H_4SCR_1R_2CO_2H$
IIa, $R = 4\text{-}CH_3$; $R_1 = C_6H_5$; $R_2 = H$
b, $R = H$; $R_1 = R_2 = CH_3$

$C_6H_5S(CH_2)_2CO_2H$
III

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(1) The work described in this paper is the subject of Canadian, United States, and other patent applications.

(2) Arapahoe Chemicals, Inc., Boulder, Colo. 80301.

(3) D. Walker and J. Leib, *Can. J. Chem.*, **40**, 1242 (1962).

(4) The rearrangement of sulfoxides described by eq 1 has been the subject of considerable work in recent times. It is now not certain that the hydroxyl group attached to positive sulfur migrates to the adjacent carbon atom as implied in eq 1. For further mechanistic considerations, the interested reader is referred to the following papers: H.-D. Becker, *J. Org. Chem.*, **29**, 1358 (1964); W. E. Parham and M. D. Bhavsar, *ibid.*, **28**, 2686 (1963); H.-D. Becker, G. J. Mikol, and G. A. Russell, *J. Am. Chem. Soc.*, **85**, 3410 (1963).

(5) D. Walker and J. Leib, *J. Org. Chem.*, **27**, 4455 (1962).

(6) D. Walker and J. Leib, *ibid.*, **28**, 3077 (1963).

whereas compounds such as III would give only a low yield of cleavage product or none at all.

Further, if the mechanism of the acid-catalyzed cleavage of phenylsulfinylacetic acid involves a hydrogen atom of the methylene group, as all mechanisms proposed so far demand,[3,4] it might be expected that compounds of type IIa would undergo cleavage, while those of type IIb would fail to cleave.

Sulfides I–III were prepared and subjected to the action of hydrogen peroxide and mineral acid under conditions which caused cleavage of phenylmercaptoacetic. The results are summarized in Table I.

TABLE I

Compd	Moles of H_2O_2/mole of sulfide	Yield of disulfide (D) or thiol (T), %
Phenylmercaptoacetonitrile (Ia)	1.9	51 (D)
Phenylmercaptoacetone (Ib)	1.9	62.5 (D)
4-Methylphenylmercaptophenylacetic acid (IIa)	1.9	81 (T)
Phenylmercaptoisobutyric acid (IIb)	1.65	9 (D)
3-Phenylmercaptopropionic acid (III)	1.65	9 (D)

Phenylmercaptoacetonitrile (Ia), phenylmercaptoacetone (Ib), 4-methylphenylmercaptophenylacetic acid (IIa), and β-phenylmercaptopropionic acid (III) behaved in the expected manner, III giving a low yield of diphenyl disulfide, probably owing to the diminished effect of the carboxyl group. Unexpectedly, however, phenylmercaptoisobutyric acid (IIb) did cleave to a small extent. The mechanism of this process is unknown but the low yield of diphenyl disulfide and the slowness of its formation were such as to lend support to the view that hydrogen atoms on the carbon adjacent to sulfur are necessary for a *facile* rearrangement and cleavage such as outlined in eq 1.

Since both the cyanomethyl and the acetonyl group are readily cleaved by hydrogen peroxide and mineral acid, it was of interest to determine whether these groups could be used as sulfur-protective species in electrophilic substitution reactions. Phenylmercaptoacetonitrile was acetylated to give, after hydrolysis, a moderate yield of 4-acetylphenylmercaptoacetic acid which compound is known to cleave to bis(4-acetylphenyl) disulfide with hydrogen peroxide and mineral acid.[5] Acetylation of phenylmercaptoacetone gave a moderate yield of 4-acetylphenylmercaptoacetone; this compound, when treated with hydrogen peroxide and mineral acid, gave a fair yield of bis(4-acetylphenyl) disulfide. Bromination of phenylmercaptoacetonitrile gave an oily bromo compound which did not give detectable amounts of 4-bromobenzenethiol when treated with hydrogen peroxide and mineral acid, but which did give a small amount of 4-bromobenzenethiol when boiled with zinc and dilute sulfuric acid. Bromination of phenylmercaptoacetone led only to side-chain brominated products.

The utility of oxidizing agents other than hydrogen peroxide was illustrated using 4-bromophenylmercaptoacetic acid as a model compound. This acid cleaved to give moderate yields of bis(4-bromophenyl) disulfide when either potassium permanganate or nitric acid was used as the oxidant. In the case of the nitric acid oxidation, a small amount of 4-bromophenyl-4-bromobenzenethiol sulfonate was separated from the bis(4-bromophenyl) disulfide. It was also noticed, in contrast with cleavage experiments carried out using hydrogen peroxide, that 4-bromobenzenethiol could not be distilled with steam as it was formed during addition of either potassium permanganate or nitric acid.

Experimental Section[7]

Preparations.—Literature methods were used to prepare phenylmercaptoacetonitrile,[8] phenylmercaptoacetone,[9] 4-methylphenylmercatophenylacetic acid,[5] phenylmercaptoisobutyric acid,[10] and 3-phenylmercaptopropionic acid.[11]

Oxidative Cleavage Reactions. Phenylmercaptoacetonitrile (Ia).—A mixture of phenylmercaptoacetonitrile (3.75 g, 0.025 mole), water (25 g), and sulfuric acid (2.3 g) was heated to reflux and 30% hydrogen peroxide (2.85 ml, 0.028 mole) was added over 10 min. After 10 min a further 1.4 ml of hydrogen peroxide was added over 5 min. Finally, 5 min later, an additional 0.7 ml of hydrogen peroxide was added and the mixture was refluxed for 1 hr and cooled. The mixture was filtered and the solid was extracted with aqueous sodium hydroxide to leave diphenyl disulfide (1.4 g, 51%), mp 58–60°. Acidification of the aqueous sodium hydroxide filtrate gave 0.36 g (8%) of crude phenylsulfonylacetonitrile which was crystallized from methanol–carbon tetrachloride to give pure sulfone, mp 112–113°, identical with an authentic specimen.

Phenylmercaptoacetone (Ib).—A boiling solution of phenylmercaptoacetone (4.15 g, 0.025 mole) in acetic acid (30 ml), concentrated sulfuric acid (3.6 g), and water (30 ml) was treated with 4.95 ml of 30% hydrogen peroxide (added in three portions as in the previous experiment) to give diphenyl disulfide (1.7 g, 62.5%), mp 57–60°.

4-Methylphenylmercaptophenylacetic Acid (IIa).—A suspension of this acid was oxidized as described for Ia, except that in this case the *p*-toluenethiol (81%) was removed as formed by passing steam into the reaction mixture.[3] The thiol was identified as its benzoyl derivative, mp 74–75°, which gave no depression of melting point when mixed with an authentic sample. The steam distillate also contained a small amount (13%) of benzoic acid, mp 121–122°.

Phenylmercaptoisobutyric Acid (IIb).—This acid was oxidized as described for IIa. No odor of benzenethiol could be detected in the steam distillate, though "butyric acid" was present. A small amount (9%) of diphenyl disulfide, mp 51–55°, was collected from the condenser and steam distillate. The contents of the reaction flask were extracted with ether. The ether solution was extracted first with aqueous sodium bicarbonate and then with aqueous sodium hydroxide. The sodium bicarbonate fraction on acidification and evaporation gave a small amount of a solid which was crystallized from carbon tetrachloride–petroleum ether (bp 88–98°) to give needles, mp 142–144°, equiv wt 226. Phenylsulfonylisobutyric acid (equiv wt 228) is reported[10] to melt at 146°.

The ether extract was dried and evaporated to give 4.2 g of an unidentified oil.

It was found, in separate experiment, that phenylmercaptoisobutyric acid when boiled with zinc dust in 9% sulfuric acid gave a 92% yield of benzenethiol. In the absence of zinc dust no benzenethiol was formed.

β-Phenylmercaptopropionic Acid (III).—This acid (9.1 g) was oxidized according to the procedure used for IIa. The steam distillate contained a small amount (3.6%) of diphenyl disulfide, mp 53–56°. Further diphenyl disulfide (5.4%, mp 51–53°) was obtained from the ether extract of the reaction flask after this had been extracted with aqueous sodium bicarbonate. The sodium bicarbonate extract gave 6.5 g of solid, mp 117–120°, probably a mixture of β-phenylsulfinylpropionic acid and β-phenylsulfonylpropionic acid. Further oxidation, with excess hydrogen peroxide, gave a solid which, recrystallized from

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[7] Temperatures are uncorrected. Microanalyses were by Drs. G. Weiler and F. B. Strauss, Oxford, England.

[8] R. Dijkstra and H. J. Backer, *Rec. Trav. Chim.*, **73**, 569 (1954).

[9] W. Autenrieth, *Ber.*, **24**, 159 (1891).

[10] W. Piechulek and J. Suszko, *Roczniki Chem.*, **13**, 520 (1933).

[11] B. Holmberg and E. Schjanberg, *Arkiv Kemi, Mineral. Geol.*, **A15**, No. 20 (1942); *Chem. Abstr.*, **38**, 2943 (1944).

toluene, yielded a material, mp 123–125°, with equiv wt of 211. The literature[12] melting point for β-phenylsulfonylpropionic acid (equiv wt 214) is 125.5–126°.

β-Phenylmercaptopropionic acid was not cleaved by boiling with zinc dust in 9% sulfuric acid.

Acetylations. Phenylmercaptoacetonitrile (Ia).—A slurry of aluminum chloride (27.4 g, 0.205 mole) in carbon disulfide (75 ml) and nitrobenzene (20 ml) was treated dropwise with acetyl chloride (4.32 g, 0.055 mole), the temperature being maintained at 15–20° with an ice–water bath. Phenylmercaptoacetonitrile (7.45 g, 0.05 mole) was then added slowly at 10–15°. Evolution of hydrogen chloride had ceased after 4 hr and the reddish orange mixture was decomposed by pouring into ice and hydrochloric acid. Carbon disulfide, nitrobenzene, and unreacted phenylmercaptoacetonitrile were removed by steam distillation. The sticky solid left in the reaction flask was filtered and boiled with 5% aqueous sodium hydroxide. A small amount of tar was filtered with the aid of Celite, and the sodium hydroxide solution was acidified to give 4-acetylphenylmercaptoacetic acid (3.8 g, 36%).

Phenylmercaptoacetone (Ib).—Aluminum chloride (27.4 g, 0.205 mole) in nitrobenzene (25 ml) and carbon disulfide (75 ml) was treated at <15° with acetyl chloride (4.32 g, 0.055 mole). Phenylmercaptoacetone (8.3 g, 0.05 mole) was added over about 20 min at 10–15°, and the mixture was stirred for 1 hr at 15° before being allowed to warm to room temperature. After stirring for 5 hr, during which time the color of the mixture turned through orange-red to bluish red, evolution of hydrogen chloride had ceased. The bluish red solution was poured onto ice and hydrochloric acid, and the carbon disulfide and nitrobenzene were distilled with steam. Further steam distillation removed a solid, 0.65 g, mp 65–70°, which was crystallized from aqueous methanol to give needles, mp 78–79°. This compound appeared to be 2-acetyl-3-methylbenzo[*b*]thiophene (lit.[13] mp 76.5–77.5°), a plausible cyclization product of 2-acetylphenylmercaptoacetone.

Anal. Calcd for $C_{11}H_{10}OS$: C, 69.44; H, 5.30; S, 16.85. Found: C, 69.28; H, 5.30; S, 16.55.

The product remaining in the steam distillation flask (6.1 g, mp 75–77.5°) was dried and Soxhlet extracted with petroleum ether (bp 60–80°) to give 4-acetylphenylmercaptoacetone (5.5 g, 53%), mp 83–84°.

Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.80; S, 15.39. Found: C, 63.80; H, 5.78; S, 15.55.

Oxidative Cleavage of 4-Acetylphenylmercaptoacetone.—A suspension of 4-acetylphenylmercaptoacetone (1.04 g, 0.005 mole) in water (30 ml), concentrated sulfuric acid (2 ml), and acetic acid (5 ml) was boiled and 30% hydrogen peroxide (0.6 ml, 0.006 mole) was added over 5 min. After a 10-min interval, a further quantity (0.25 ml, 0.0025 mole) of 30% hydrogen peroxide was added and the mixture was refluxed for 1 hr. The solid obtained was Soxhlet extracted with petroleum ether (bp 60–80°) to give bis(4-acetylphenyl) disulfide (0.4 g, 53%), mp 91–93°. One crystallization from petroleum ether gave a product, mp 94–95°, identical (mixture melting point) with authentic bis(4-acetylphenyl) disulfide.

Brominations. Phenylmercaptoacetonitrile (Ia).—A solution of phenylmercaptoacetonitrile (7.45 g, 0.05 mole) in acetic acid (12 ml) was treated dropwise with bromine (8.2 g, 0.051 mole) over 10 min, the temperature being maintained between 20 and 25° with a cold-water bath. The mixture was allowed to stand for 4 days, diluted with water, and extracted with ether. The ether extract was washed with water to remove acetic acid and dried over anhydrous magnesium sulfate. Evaporation of the ether gave 10.6 g of a golden brown oil which was slightly lachrymatory.

Attempted oxidative cleavage of this oil by the method used for IIa above gave only a trace of steam-volatile product. No attempt was made to identify the sticky solid remaining in the reaction flask. An attempted oxidative cleavage using the procedure outlined above for phenylmercaptoacetonitrile (Ia) likewise gave only an oil from which no solid bis(4-bromophenyl) disulfide could be obtained.

When the golden brown oil was reduced with zinc and sulfuric acid and steam distilled, a small quantity of 4-bromobenzenethiol (identified as its benzoyl derivative, mp 81–82°, no depression with authentic material) was collected.

Phenylmercaptoacetone (Ib).—Bromine reacted vigorously with phenylmercaptoacetone, in either carbon tetrachloride or acetic acid, to give a lachrymatory oil which, when oxidized with hydrogen peroxide according to the procedure used for oxidizing phenylmercaptoacetone, gave 53% crude diphenyl disulfide, mp 57–59°.

Oxidative Cleavage of 4-Bromophenylmercaptoacetic Acid with Nitric Acid.—A slurry of 4-bromophenylmercaptoacetic acid (6.2 g, 0.025 mole) in water (30 ml) was refluxed and treated with a solution of concentrated nitric acid (3.2 ml, 0.05 mole) in water (20 ml) over 75 min. The mixture was refluxed a further 15 min, then cooled and filtered. Extraction of the solid with aqueous sodium bicarbonate and acidification of this extract gave 0.8 g of crude 4-bromophenylmercaptoacetic acid [mp 111–115°, mmp 113–116° with authentic acid (mp 117–118°)].

The sodium bicarbonate insoluble solid was extracted with boiling petroleum ether (bp 60–80°). The fraction soluble in petroleum ether (2.5 g) melted at 86–88° and on crystallization from petroleum ether gave pure bis(4-bromophenyl) disulfide, mp 92–93°. The solid insoluble in petroleum ether (0.6 g, mp 153–155°) was recrystallized from methanol to give plates, mp 160–161°, which gave no depression of melting point when mixed with 4-bromophenyl-4-bromobenzenethiol sulfonate. This ester was prepared unambiguously as follows.

Bis(4-bromophenyl)disulfide (2.7 g, 0.0072 mole) in acetic acid (30 ml) and water (5 ml) was treated with 3 drops of concentrated sulfuric acid and then with 30% hydrogen peroxide (1.6 ml, 0.016 mole), the latter being added over 10 min. The mixture was refluxed for 75 min and cooled, and the solid was filtered. The crude product (2.5 g, 85%), mp 150–154°, was recrystallized twice from methanol to give plates, mp 161–162°.

Anal. Calcd for $C_{12}H_8Br_2O_2S_2$: C, 35.31; H, 1.97; Br, 39.16. Found: C, 35.57; H, 1.75; Br, 39.40.

When the oxidative cleavage of 4-bromophenylmercaptoacetic acid was carried out using half the above nitric acid and a steam distillation procedure, only a small amount of steam-volatile material was obtained.

Oxidative Cleavage of 4-Bromophenylmercaptoacetic Acid with Permanganate.—A suspension of 4-bromophenylmercaptoacetic acid (6.2 g, 0.025 mole) in water (30 ml) containing concentrated sulfuric acid (1 ml) was treated at the boiling point with a solution of potassium permanganate (1.6 g, 0.01 mole) in water (30 ml) over a period of 40 min, steam distillation being carried out throughout the addition. Only a very small amount of steam-volatile product was obtained; so an additional quantity of potassium permanganate (1.2 g, 0.0075 mole) in water (20 ml) was added over 40 min and the steam distillation was continued for a further 30 min. The quantity of permanganate used was sufficient to cause the brown color of manganese dioxide to persist.

The steam distillation product (0.4 g, 8.5%) was crude bis(4-bromophenyl) disulfide, mp 87–90°. The solid remaining in the reaction flask was freed from manganese dioxide by the addition of aqueous sodium bisulfite. This material (1.9 g, mp 68–80°) was washed with aqueous sodium bicarbonate and recrystallized first from methanol and then from petroleum ether (bp 60–80°) to give pure bis(4-bromophenyl)disulfide (1.4 g, 30%), mp 92–93°.

Acknowledgment.—We wish to thank the Directors of Domtar Ltd. for permission to publish this work.

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[12] C. D. Hurd and L. L. Gershbein, *J. Am. Chem. Soc.*, **69**, 2328 (1947).

[13] R. Gaertner, *ibid.*, **74**, 2185 (1952).