Electrophilic Substitution of the Benzenethiols. I. Halobenzene- and Halotoluenethiols[1]

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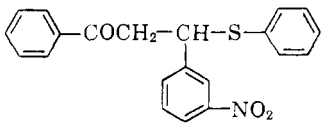
Electrophilic reagents generally attack the sulfur atom of benzenethiols and ring substitution is rarely observed. This paper discloses a new and general procedure for preparing halobenzenethiols from benzenethiols. The benzenethiol is first converted to the corresponding phenylmercaptoacetic acid which is then halogenated in the aromatic ring. The resulting halophenylmercaptoacetic acid is finally cleaved to the halobenzenethiol by hydrogen peroxide in the presence of mineral acid. The chlorination and bromination of phenylmercaptoacetic acid and all three tolylmercaptoacetic acids were studied in some detail. Possible mechanisms for the various substitution reactions are discussed.

As a general rule electrophilic reagents attack the sulfur atom of the benzenethiols and ring substitution is rarely observed. Tarbell and Herz[3] have summarized the literature in this field up to 1953. Since 1953 the chief references of interest concern the direct alkylation of the benzenethiols.[4,5] Alkylation is only apparently direct since complexes formed by the various benzenethiols with alkylation catalysts are postulated as intermediates. Formation of these complexes evidently changes the nature of the thiol group so that the sulfur atom is not susceptible to attack by electrophilic reagents.

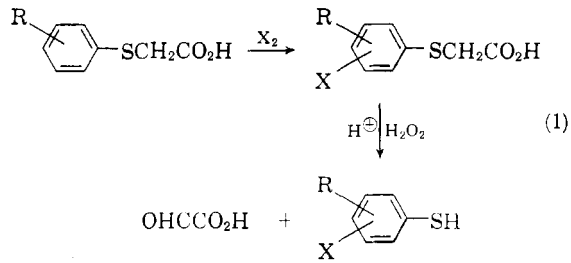
Tarbell and Herz pointed out that the only derivatives of the benzenethiols which have seemed consistently amenable to ring substitution by electrophilic reagents are the simple sulfides, as exemplified by thioanisole. Complex aryl alkyl sulfides such as I, obtained by the addition of



I

benzenethiol to α,β-unsaturated ketones, are cleaved by the action of basic lead acetate,[3,6] to benzenethiol lead mercaptide and the starting ketone. Tarbell and Herz showed that the complex sulfide, β - (3 - nitrophenyl) - β - (phenylmercapto)propiophenone (I), could be substituted in the phenylmercapto ring by electrophilic reagents, and that the resulting compounds could be cleaved to the lead mercaptide of the substituted benzenethiol by the action of basic lead acetate. This work provided the first general method for preparing a variety of substituted benzenethiols from benzenethiol precursors.

In an earlier paper[7] we described the preparation of benzenethiol by the addition of hydrogen peroxide to a boiling suspension of phenylmercaptoacetic acid in aqueous mineral acid. Benzenethiol was removed as it was formed by passing steam into the reaction mixture. In this way a high yield of benzenethiol was obtained. This discovery led us to evaluate the utility of phenylmercaptoacetic acid and all three tolylmercaptoacetic acids as intermediates to halobenzene- and halotoluenethiols. Our aim is summarized by equation 1.

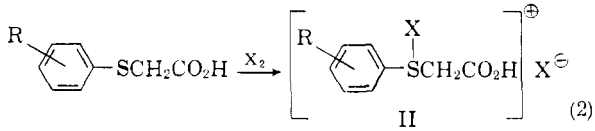


(1)

R = H or CH_3; X = Cl or Br

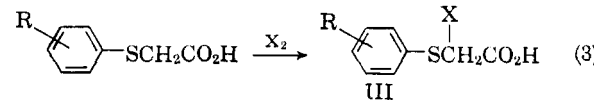
In order to test the utility of equation 1 we required halophenyl and halotolylmercaptoacetic acids. The literature reveals that halogens attack phenyl- and tolylmercaptoacetic acids to give three types of product. These will be referred to by reference to the following equations:

(A) Sulfur halogenation[8]



II (2)

(B) Side chain halogenation[8,9]



III (3)

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

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(3) D. S. Tarbell and A. H. Herz, *J. Am. Chem. Soc.*, **75**, 4657 (1953).

(4) E. A. Bartkus, E. B. Hotelling, and M. B. Neuworth, *J. Org. Chem.*, **25**, 232 (1960).

(5) R. J. Laufer, Abstracts of Papers, 137th National Meeting of the American Chemical, Society Cleveland, Ohio, April, 1960, p. 61-O.

(6) B. H. Nicolet, *J. Am. Chem. Soc.*, **53**, 3066 (1931).

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

(8) R. Pummerer, *Ber.*, **42**, 2275 (1909).

(9) G. M. Oksengendler and Yu. E. Gerasimenko, *Zh. Obsch. Khim.* **29**, 919 (1959).

(10) Soc. pour L'ind. Chim. a Bale, Swiss Patent 168,619 (1934).

(11) C. W. Schimelpfenig and J. J. Spurlock, *J. Org. Chem.*, **25**, 1251 (1960).

TABLE I

BROMINATION OF ARYLMERCAPTOACETIC ACIDS

Starting material	Solvent	Yield, %	Product	M.p., °C.	Calcd. C	Calcd. H	Calcd. S	Calcd. Br	Found C	Found H	Found S	Found Br
$C_6H_5SCH_2CO_2H$	CH_3CO_2H	65	4-$BrC_6H_4SCH_2CO_2H$	117–118								
	CCl_4	81										
2-$CH_3C_6H_4SCH_2CO_2H$	CH_3CO_2H	90	4-Br-2-$CH_3C_6H_3SCH_2CO_2H$[a]	130–131	41.4	3.47	12.29	30.55	41.15	3.38	12.29	30.95
	CCl_4	50										
3-$CH_3C_6H_4SCH_2CO_2H$	CH_3CO_2H	94	4-Br-3-$CH_3C_6H_3SCH_2CO_2H$[a]	107–108	41.4	3.47	12.29	30.55	42.18	3.47	12.33	30.80
	CCl_4	80										
4-$CH_3C_6H_4SCH_2CO_2H$	CH_3CO_2H	40	4-CH_3-2-$BrC_6H_3SCH_2CO_2H$[a]	120–121	41.4	3.47	12.29	30.55	41.64	3.58	12.57	30.23
	CCl_4	70	4-$CH_3C_6H_3SCH(Br)CO_2H$[b]	103–105	41.4	3.47	12.29	30.55	41.64	3.39	12.58	30.60
4-$BrC_6H_4SCH_2CO_2H$	CCl_4	65	4-$BrC_6H_4SCH(Br)CO_2H$[c]	140–142	29.46	1.85	9.83	49.04	29.49	1.83	10.08	48.70

[a] Authentic specimens, for positive identification, prepared from the bromotoluidines by Mr. Alfred Bleichert. [b] Melting point deteriorates on standing. Analytical sample, m.p. 105–106°, prepared by crystallizing the crude material from carbon tetrachloride. [c] Melting point deteriorates on standing. Analytical sample, m.p. 146–147°, prepared by crystallizing the crude material from carbon tetrachloride.

(C) Ring halogenation[8-11]

$$\text{R-C}_6\text{H}_4\text{-SCH}_2\text{CO}_2\text{H} \xrightarrow{X_2} \text{R(X)-C}_6\text{H}_3\text{-SCH}_2\text{CO}_2\text{H} \quad (4)$$

IV

R = H or CH_3; X = Cl or Br

We were able to prepare all of the ring-halogenated products (IV) required to test equation 1 except a ring-chlorinated *p*-tolylmercaptoacetic acid (see Tables I and II).

The halophenyl- and halotolylmercaptoacetic acids are readily cleaved, by the action of hydrogen peroxide in the presence of mineral acid, to give halobenzene- and halotoluenethiols in high yield (see Table IV).

In addition to realizing the objective of this paper as set down in equation 1 we studied the routes by which the various halogen-substituted products (II–IV) are formed. Mechanisms are suggested to explain the halogenation reactions.

Results and Discussion

(I) **Preparation of Bromoarylthiols. (A) Bromination of Arylmercaptoacetic Acids.**—The bromination of phenylmercaptoacetic acid and the three tolylmercaptoacetic acids was studied in acetic acid and in carbon tetrachloride as solvent (Table I). As would be expected brominations in acetic acid were faster than brominations in carbon tetrachloride. Ring-brominated products were obtained in good yield from all the reactions except the bromination of *p*-tolylmercaptoacetic acid in carbon tetrachloride (see below). Bromine preferentially substituted the ring *para* to the sulfur atom when this position was open. When the *para* position was blocked, as in the case of *p*-tolylmercaptoacetic acid, bromine entered the *ortho* position.

Qualitative observations indicated that the rates of ring bromination of phenyl- and tolylmercaptoacetic acids followed the order *m*-tolyl > *o*-tolyl > phenyl > *p*-tolyl.

We were unable to substitute more than one bromine atom in the ring of phenyl- and tolylmercaptoacetic acids.

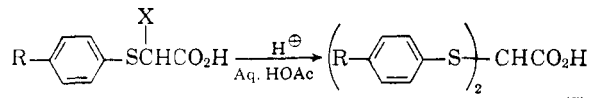
Ring bromination of phenylmercaptoacetic acid and the tolylmercaptoacetic acids can be complicated by the formation of sulfur and side chain brominated products (II and III, respectively, X = Br). Sulfur bromination is a facile, well characterized reaction[8] and undoubtedly preceeds the slower side chain bromination reaction (equation 3) and competes with ring bromination (equation 4). However, sulfur bromination may pass unnoticed in those cases where compounds of type II undergo conversion to ring-brominated products.[8] In some instances compounds of type II do not undergo such conversion; instead side chain brominated products III are formed. Thus II

TABLE II
CHLORINATION OF ARYLMERCAPTOACETIC ACIDS

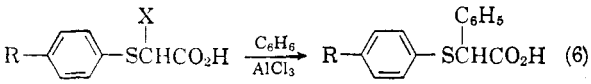
Starting material	Chlorinating agent	Solvent	Yield, %	Product	M.p., °C.
$C_6H_5SCH_2CO_2H$	SO_2Cl_2:$SbCl_5$	Chlorobenzene	80	$4\text{-}ClC_6H_4SCH_2CO_2H$	104–105
$2\text{-}CH_3C_6H_4SCH_2CO_2H$	SO_2Cl_2:$SbCl_5$	Chlorobenzene	70–75	$4\text{-}Cl\text{-}2\text{-}CH_3C_6H_3SCH_2CO_2H$	126–127
$3\text{-}CH_3C_6H_4SCH_2CO_2H$	SO_2Cl_2:$SbCl_5$	Chlorobenzene	75	$4\text{-}Cl\text{-}3\text{-}CH_3C_6H_3SCH_2CO_2H$	103–104
$4\text{-}CH_3C_6H_4SCH_2CO_2H$	SO_2Cl_2	Carbon tetrachloride	100	$4\text{-}CH_3C_6H_4SCH(Cl)CO_2H$	77–80[a]

[a] Melting point deteriorates on standing. Several crystallizations from petroleum ether (b.p. 88–98°) were necessary to obtain an analytically pure sample, m.p. 88–89°. *Anal.* Calcd. for $C_9H_9ClO_2S$: C, 49.88; H, 4.19; Cl, 16.36; S, 14.80. Found: C, 50.19; H, 4.37; Cl, 15.92; S, 14.80

(R = *p*-CH_3 or *p*-Br, X = Br) when warmed for several days in carbon tetrachloride, gave III (R = *p*-CH_3 or *p*-Br, X = Br) in good yield (see Table I). Further support for structures of type III was obtained in the manner summarized by equations 5 and 6 (R = CH_3 or Br, X = Br).



(5)



(6)

The preparations of bis(arylmercapto)acetic acids carried out according to equation 5 are listed in Table III. We were led to the structure proof provided by equation 6 as a result of abortive attempts to rearrange compounds III (R = *p*-CH_3 or *p*-Br, X = Br) to ring-brominated products IV (R = *p*-CH_3 or *p*-Br, X = Br) with aluminum chloride.

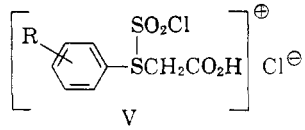
Side chain bromination proceeds at a very slow rate and is probably the result of an intramolecular rearrangement of the corresponding bromosulfonium bromide (II, X = Br), a process evidently aided by ultraviolet light.[9] We regard the mechanism of this rearrangement as similar to that suggested by Bordwell and Pitt[12a] to explain the formation of phenyl chloromethyl sulfide by the chlorination of thioanisole. The relationship between this mechanism and that recently proposed[7] to explain the rearrangement of the conjugate acid of phenylsulfinylacetic acid to phenylmercaptohydroxyacetic acid should be noted.

Arylmercaptobromoacetic acids (III, X = Br) like bromosulfonium bromides (II, X = Br) are rapidly hydrolyzed by water to give arylthiols.

(B) Cleavage of Bromoarylmercaptoacetic Acids.—The acid-catalyzed oxidative cleavage of phenylmercaptoacetic acid to benzenethiol, previously described by us,[7] was successfully applied to the cleavage of bromophenyl- and bromotolylmercaptoacetic acids (equation 1). The bromobenzene- and bromotoluenethiols produced by the cleavage were removed as they were formed by passing steam into the reaction mixture. Disulfide formed in the process was reduced to thiol by adding zinc dust to the reaction mixture. Table IV lists the bromoarylthiols prepared using this technique. Table V summarizes some properties of the corresponding disulfides.

(II) Preparation of Chloroarylthiols. (A) Chlorination of Arylmercaptoacetic Acids.—According to a Swiss Patent[10] *m*-tolylmercaptoacetic acid can be chlorinated in the aromatic ring by sulfuryl chloride in chlorobenzene under catalysis by antimony pentachloride. When we applied this procedure to the chlorination of phenylmercaptoacetic acid and all three tolylmercaptoacetic acids, all but *p*-tolylmercaptoacetic acid (see below) gave good yields of ring-chlorinated products (IV, X = Cl).

Attempts to prepare ring-chlorinated arylmercaptoacetic acids using sulfuryl chloride in the absence of antimony pentachloride led only to sulfur and side chain chlorinated products. Formation of chlorosulfonium chlorides from arylmercaptoacetic acids and sulfuryl chloride apparently proceeds by way of a complex such as V.



V

Compounds of type V were not isolated; their presence was suggested by the slow evolution of sulfur dioxide from solutions obtained by adding sulfuryl chloride to arylmercaptoacetic acids in inert solvents.[12b]

It is important to point out that chlorosulfonium chlorides (II, X = Cl), unlike the corresponding bromosulfonium bromides, show little or no tendency to rearrange to give ring-substituted products. Rearrangement to give side chain chlorinated products (III) was demonstrated by the isolation of *p*-tolylmercaptochloroacetic acid from the chlorination of *p*-tolylmercaptoacetic acid with sulfuryl chloride alone or with sulfuryl chloride in the presence of antimony pentachloride. Support for the structure of *p*-tolylmercaptochloroacetic acid was gained from reactions summarized by equations 5 and 6 (R = CH_3, X = Cl).

(12) (a) F. G. Bordwell and B. M. Pitt, *J. Am. Chem. Soc.*, **77**, 572 (1955); (b) F. G. Bordwell and B. M. Pitt, *ibid.*, proposed a somewhat similar intermediate to V in interpreting the reaction between thionyl chloride and phenyl methyl sulfoxide.

TABLE III

BIS(ARYLMERCAPTO)ACETIC ACIDS

Starting material	Yield, %	Product	M.p., °C.	Calcd. C	Calcd. H	Calcd. S	Calcd. Br	Found C	Found H	Found S	Found Br
4-$BrC_6H_4SCH(Br)CO_2H$	75	(4-$BrC_6H_4S)_2CHCO_2H$	189[a]	38.75	2.32	14.78	36.8	38.59	2.30	15.10	37.15
4-Br-2-$CH_3C_6H_3SCH(Br)CO_2H$	60	(4-Br-2-$CH_3C_6H_3S)_2CHCO_2H$	171–172[b]	41.54	3.05	13.85	34.61	41.39	3.11	14.14	35.30
4-$CH_3C_6H_4SCH(Br)CO_2H$	90	(4-$CH_3C_6H_4S)_2CHCO_2H$	127–128[b]	63.14	5.27	21.07	...	63.15	5.78	20.99	...
4-$CH_3C_6H_4SCH(Cl)CO_2H$	95										

[a] Crystallized from carbon tetrachloride containing a little methanol. [b] Crystallized from a mixture of carbon tetrachloride and petroleum ether (b.p. 88–98°).

The difference between chlorosulfonium chlorides (II, X = Cl) and the corresponding bromosulfonium bromides probably reflects the different electronegativities of chlorine and bromine.

The above results suggested that the ring-chlorinating species was actually antimony pentachloride. Support for this view was gained by the ring chlorination of *m*-tolylmercaptoacetic acid with antimony pentachloride alone and with antimony trichloride and sulfuryl chloride. Antimony pentachloride probably acts as a chlorinating agent in the form $[SbCl_4]^{\oplus}$ $[SbCl_6]^{\ominus}$. If $[SbCl_4]^{\oplus}$ is the ring chlorinating species this cation might form and react, in inert media, by the following scheme:

Regeneration of antimony pentachloride will result from the interaction of the trichloride with either sulfuryl chloride or a complex such as V, or by both routes.

The weak nucleophilic character of $SbCl_6^{\ominus}$ could play, indirectly, a vital part in the process of ring chlorination. Thus $[SbCl_6]^{\ominus}$ may be too weak a nucleophile to aid in the removal of proton from the methylene group of complex VI, and hence be too weak to assist in a rearrangement of VI to III (contrast Bordwell and Pitt[12a]).

In order to check that arylmercaptochloroacetic acids did not rearrange to chloroarylmercaptoacetic acids, we prepared a solution of phenylmercaptochloroacetic acid and treated it with a catalytic amount of antimony pentachloride. Hydrolysis of the reaction mixture gave benzenethiol which did not contain detectable amounts of *p*-chlorobenzenethiol.

Table II summarizes the results of the chlorination experiments.

(B) Cleavage of Chloroarylmercaptoacetic Acids.—The acid-catalyzed oxidative cleavage of the chloroarylmercaptoacetic acids proceeded smoothly (compare section IB) and high yields of the chloroarylthiols were obtained (Table IV).

(III) Summary.—The process described by equation 1 provides a new, simple, and cheap method of converting benzene- and toluenethiols to their monochloro and monobromo derivatives. Previously these haloarylthiols could only be obtained

TABLE IV
HALOARYLTHIOLS

Haloarylthiol	Yield, %	M.p. or b.p., °C.	Calcd. C	Calcd. H	Calcd. Hal.	Calcd. S	Found C	Found H	Found Hal.	Found S
4-BrC_6H_4SH	66	76	...	...	...	...	...	...	...	...
4-Br-2-$CH_3C_6H_3SH$	55	122/12 mm.	41.39	3.47	39.30	15.78	41.82	3.54	39.80	15.50
4-Br-3-$CH_3C_6H_3SH$	73	126–127/14 mm.	41.39	3.47	39.30	15.78	42.37	3.32	39.00	15.40
2-Br-4-$CH_3C_6H_3SH$	77	61–62/0.5 mm.	...	...	...	..	...	...	...	...
4-ClC_6H_4SH	77	50–52	...	...	...	...	...	...	...	...
4-Cl-2-$CH_3C_6H_3SH$	86	102.5–104/8 mm.	52.99	4.48	22.35	20.21	52.80	4.39	22.75	20.30
4-Cl-3-$CH_3C_6H_3SH$	76	106–107/11 mm.	52.99	4.48	22.35	20.21	53.26	4.54	22.30	20.15

TABLE V
HALOARYL DISULFIDES

Haloaryl disulfide	Crystallizing solvent	M.p., °C.	Calcd. C	Calcd. H	Calcd. Hal.	Calcd. S	Found C	Found H	Found Hal.	Found S
$(4\text{-}BrC_6H_4S)_2$	Methanol	95–96	...	...	...	...	...	...	...	...
$(4\text{-Br-2-}CH_3C_6H_3S)_2$	Methanol	90–91	41.60	2.99	39.54	15.86	41.82	2.98	39.80	16.10
$(4\text{-Br-3-}CH_3C_6H_3S)_2$	Aqueous methanol	83–84	41.60	2.99	39.54	15.86	41.73	2.84	39.95	15.50
$(2\text{-Br-4-}CH_3C_6H_3S)_2$	Methanol	99–100	41.60	2.99	39.54	15.86	41.47	2.84	39.81	16.10
$(4\text{-}ClC_6H_4S)_2$	Aqueous methanol	71–72	50.18	2.81	24.69	22.32	50.20	2.78	24.65	22.60
$(4\text{-Cl-2-}CH_3C_6H_3S)_2$	Methanol	51–52	53.33	3.83	22.49	20.34	53.57	3.48	22.75	20.50
$(4\text{-Cl-3-}CH_3C_6H_3S)_2$	Methanol	66–67	53.33	3.83	22.49	20.34	53.20	3.43	22.65	20.00

by applying classical procedures to such comparatively inaccessible starting materials as haloarylsulfonyl chlorides and haloarylamines, or by the rather more complex method described by Tarbell and Herz.[3]

There is every indication that the present method could be extended to compounds of general formula $RSCH_2CO_2H$ in which R may be a heterocyclic ring, or a condensed homocyclic aromatic ring. The method is limited inasmuch as the position taken up by the entering halogen atom depends on the substituents already in the ring. Further limitations are suggested by our inability to substitute more than one halogen atom in the ring of phenyl and tolylmercaptoacetic acids.

Experimental[13]

Phenylmercaptoacetic acid and all three tolylmercaptoacetic acids were prepared from benzenethiol and the toluenethiols by condensation with chloroacetic acid in the presence of base.

Brominations. (1) **In Acetic Acid.**—The arylmercaptoacetic acid (0.05 mole) was dissolved in three to four times its weight of acetic acid and the theoretical quantity of bromine added dropwise over about 15 min. A cold water bath was used to maintain the temperature at 20–35° during the addition. After all the bromine had been added the mixture was allowed to stand until the reaction was judged complete. The reaction with *m*-tolylmercaptoacetic acid was essentially over in less than 1 hr.; *p*-tolylmercaptoacetic acid, on the other hand, brominated fairly slowly and the reaction mixture was usually allowed to stand for several days. The crystals which deposited were filtered and dried. Dilution of the acetic acid filtrate with water usually yielded further impure product which was purified by crystallization from aqueous acetic acid or carbon tetrachloride.

Sulfur bromination and/or side chain bromination were detected by the presence of thiols in the drowned reaction mixture. In the case of the bromination of *p*-tolylmercaptoacetic acid dilution of the acetic acid filtrate produced considerable quantities of *p*-toluenethiol.

(2) **In Carbon Tetrachloride.**—The arylmercaptoacetic acid was dissolved in sufficient carbon tetrachloride to make a fairly saturated solution at 24–35°. The theoretical quantity of bromine was added all at once except in the case of *m*-tolylmercaptoacetic acid where a dropwise addition was necessary because of the vigor of the reaction. In this last case the reaction was essentially complete in less than 1 hr. In all other cases the reaction mixture was usually warmed to 50–60° from time to time to dissolve the crystals which deposited. This process was repeated two or three times a day for several days (9 days or more in the case of *p*-tolylmercaptoacetic acid). At the end of the reaction period the crystals were filtered and dried (vacuum drying for the product from *p*-tolylmercaptoacetic acid).

A summary of the results is given in Table I. Where yields of ring brominated compounds are low, qualitative observations frequently indicated considerable side chain bromination. The ring brominated products were generally difficult to purify to a sharp melting point suggesting the possible presence of small quantities of other isomers. This suggestion is not without precedent.[11]

Chlorinations. (1) **With Catalyst.**—The method employed was essentially that described in the Swiss patent.[10] Chlorobenzene was used as the solvent. The following solution strengths were found convenient (g./100 ml.): phenylmercaptoacetic acid (10.5), *o*-tolylmercaptoacetic acid (16.5), *m*-tolylmercaptoacetic acid (25). About 3-5 g. of antimony pentachloride per mole of arylmercaptoacetic acid was introduced to the solution and a theoretical amount of sulfuryl chloride added at a brisk rate, keeping the temperature preferably below 10° by means of an ice water bath. After all the sulfuryl chloride had been added the mixture was stirred and allowed to warm to room temperature. After about 6–8 hr. the mixture was poured into 10% aqueous sodium carbonate, the chlorobenzene distilled with steam, and the chloroarylmercaptoacetic acid obtained by acidification. The crude product was purified by crystallization from aqueous acetic acid, or toluene–petroleum ether (b.p. 88–98°), or carbon tetrachloride.

Antimony trichloride was substituted for antimony pentachloride in the case of *m*-tolylmercaptoacetic acid without affecting the chlorination result.

Sulfur chlorinated and side chain chlorinated products were frequently detected during work-up on account of the

(13) Temperatures are uncorrected. Microanalyses are by Drs. G. Weiler and F. B. Strauss, Oxford, England.

(14) J. J. Ritter and E. D. Sharpe, *J. Am. Chem. Soc.*, **59**, 2351 (1937).

ready hydrolysis of these materials to the corresponding benzenethiols. Isolation or detection of bis(arylmercapto)-acetic acids constituted further evidence for side chain chlorination. As a general rule low yields of ring chlorinated compounds were accompanied by high yields of sulfur chlorinated and side chain chlorinated products and vice versa. In the case of *p*-tolylmercaptoacetic acid no ring chlorinated acid was obtained using the above technique; instead, bis-(*p*-tolylmercapto)acetic acid (28%) and *p*-toluenethiol were the major products.

A convenient method for working up the product from the chlorination of phenylmercaptoacetic acid was to destroy the bis(phenylmercapto)acetic acid present in the final product by heating the dry acid mixture at 160° for several hours. In the chlorination of phenylmercaptoacetic acid evidence for the presence of a small amount of *o*-chlorophenylmercaptoacetic acid was obtained from the infrared spectrum of the product. *Ortho* chlorinated products are probably formed, to a small extent, in the chlorination of *o*-tolyl- and *m*-tolylmercaptoacetic acids, a statement supported by the necessity of several crystallizations for obtaining highly pure products. (Compare bromination.)

(2) Without Catalyst.—Carbon tetrachloride and chlorobenzene were used as solvents. The reaction was conducted in the same manner as for chlorinations with a catalyst. The only side chain chlorinated product isolated was *p*-tolylmercaptochloroacetic acid. This was obtained from a carbon tetrachloride solution which had been allowed to stand for 10 days. The carbon tetrachloride was evaporated *in vacuo* at 50°. The product was an oil which solidified on standing. Sulfur chlorination and side chain chlorination were established in the other cases by the presence of thiol in the hydrolyzed reaction mixture, by the isolation of bis-(phenylmercapto)acetic acid in the case of the chlorination of phenylmercaptoacetic acid, and by our inability to isolate any ring chlorinated products.

(3) With Antimony Pentachloride Alone.—A solution of *m*-tolylmercaptoacetic acid (3.64 g., 0.02 mole) in chlorobenzene (25 ml.) was treated with antimony pentachloride (6 g., 0.02 mole) over 5 min. keeping the temperature at 30–40°. After all the antimony pentachloride had been added the mixture was warmed at 50–70° for 3 hr. and worked up as previously described for the sulfuryl chloride–antimony pentachloride chlorinations. The yield of crude product, m.p. 92–95°, was 3 g. Further purification yielded 4-chloro-3-methylphenylmercaptoacetic acid identical with an authentic specimen.

The results of the chlorination experiments are summarized in Table II.

Structure of Arylmercaptohaloacetic Acids.—The simplest evidence for this class of compound was obtained by warming the suspected side chain chlorinated product in water when the corresponding benzenethiol was liberated. Further evidence was provided by the following experiments.

(1) Preparation of Bis(arylmercapto)acetic Acids.—The arylmercaptohaloacetic acid (1 g.) was dissolved in acetic acid (3–5 ml.), the mixture treated with water (0.5 ml.) and concentrated sulfuric acid (1 drop) and then refluxed for 4–5 hr. The solution turned from colorless to yellow during this period. The reaction mixture was cooled and the product filtered. Dilution of the mother liquors gave further crude product.

Isolation and purification of the arylmercaptohaloacetic acid was not necessary. Bis(4-bromo-2-methylphenylmercapto)acetic acid was prepared by brominating 4-bromo-2-methylphenylmercaptoacetic acid in chloroform (reaction mixture stood for 2 weeks), evaporating the chloroform (rotary evaporator) and applying the above technique. A useful alternative is illustrated by the one-step conversion of *p*-tolylmercaptoacetic acid to bis(*p*-tolylmercapto)acetic acid:

A solution of *p*-tolylmercaptoacetic acid (3.1 g., 0.017 mole) in acetic acid (5 ml.) was treated with sulfuryl chloride (2.3 g., 0.017 mole) over 5 min. The temperature of the reaction mixture was maintained below 40° with a cold water bath. When all the sulfuryl chloride had been added the mixture was allowed to stand for several days (no attempt was made to establish a shorter reaction time). After this time water (0.5 ml.) and concentrated sulfuric acid (2 drops) were added and the mixture refluxed for 4 hr. The yellow solution on cooling gave bis(*p*-tolylmercapto)acetic acid (2.4 g., 93%, m.p. 127–128°).

Table III lists the bis(arylmercapto)acetic acids prepared using these techniques.

(2) Preparation of α-(Arylmercapto)phenylacetic Acids. (a) **α-(*p*-Bromophenylmercapto)phenylacetic Acid.**—*p*-Bromophenylmercaptobromoacetic acid (19 g., 0.058 mole) was stirred into benzene (380 ml.) at 40°. Aluminum chloride (6.5 g., 0.049 mole) was added over 10 min., the temperature being held at 40–50°. After all the aluminum chloride had been added the reaction mixture was stirred at 40–50° for 1.5 hr. After this period the mixture was decomposed by pouring into ice and hydrochloric acid. The benzene layer was separated, washed well with water and the acid product extracted from it with saturated aqueous sodium bicarbonate. Acidification of the latter gave α-(*p*-bromophenylmercapto)phenylacetic acid (16 g., 85%, m.p. 168–170°). An analytically pure sample, m.p. 172°, was obtained by crystallization from a toluene–petroleum ether (b.p 88–98°) mixture.

Anal. Calcd. for $C_{14}H_{11}BrO_2S$: C, 52.02; H, 3.43; Br, 24.73; S, 9.91. Found: C, 52.39; H, 3.63; Br, 25.0; S, 9.89.

(b) **α-(*p*-Tolylmercapto)phenylacetic Acid.**—*p*-Tolylmercaptobromoacetic acid (4.5 g., 0.017 mole), benzene (50 ml. and aluminum chloride (1.3 g., 0.01 mole) subjected to the above process gave, after crystallization from a mixture of toluene and petroleum ether (b.p 88–98°) about 70% of pure α-(*p*-tolylmercapto)phenylacetic acid, m.p. 129.5–130.5°.

Anal. Calcd. for $C_{15}H_{14}O_2S$: C, 69.64; H, 5.46; S, 12.41. Found: C, 69.66; 5.31; S, 12.65.

α-(*p*-Tolylmercapto)phenylacetic acid was also obtained, in about 70% yield, from *p*-tolylmercaptochloroacetic acid (7 g., 0.032 mole), benzene (90 ml.), and aluminum chloride (1.9 g., 0.014 mole).

(3) Diphenylacetic Acid from α-(Arylmercapto)phenylacetic Acids. (a) **From α-(*p*-Bromophenylmercapto)phenylacetic Acid.**—This acid (5 g., 0.015 mole) in benzene (150 ml.) was treated with aluminum chloride (4 g., 0.03 mole) and the mixture stirred at 60–70° for 3 hr. At the end of the reaction the mixture was decomposed by pouring onto ice and hydrochloric acid. The benzene layer was separated, washed with water, and then extracted with aqueous sodium bicarbonate. Acidification of the latter gave crude diphenylacetic acid (1.4 g., 42%, m.p. 95–105°). The crude material was purified by two crystallizations from water. The material obtained, m.p. 143–145°, did not depress the melting point of authentic diphenylacetic acid.

(b) **From α-(*p*-Tolylmercapto)phenylacetic Acid.**—This acid (1.5 g., 0.006 mole), benzene (40 ml.) and aluminum chloride (2 g., 0.015 mole) gave, when subjected to the above process, a similar yield of poor quality diphenylacetic acid.

Haloarylthiols from Haloarylmercaptoacetic Acids.—The general procedure used was as follows: A 500-ml., three-necked flask was fitted as for a steam distillation, the third neck being occupied by a dropping funnel. The flask was charged with haloarylmercaptoacetic acid (0.1 mole), water (200 ml.), and concentrated sulfuric acid (5–10 ml.). The mixture was raised to the boil and steam passed in. Hydrogen peroxide (22.8 ml. of 30% aqueous solution, 0.2 mole) was then added dropwise over a period of about 60–75 min. Steam distillation was continued for 30 min. after the addition of the hydrogen peroxide had been completed. Zinc dust (2 g., 0.03 mole) was then added slowly and the steam distillation continued until no more haloarylthiol passed

over. This latter process reduced the disulfide formed during the oxidation stage. The haloarylthiol was extracted from the steam distillate with ether. The ether layer was dried over anhydrous sodium sulfate and the haloarylthiol recovered by evaporation of the ether and distillation. Table IV lists the haloarylthiols prepared by this method.

Haloaryl Disulfides.—The haloarylthiols obtained in the above process were all converted to their disulfides by the method described by Ritter and Sharpe.[14] When the oxidative acid-catalyzed cleavage of the haloarylmercaptoacetic acids was carried out without using the steam distillation process the haloarylthiols produced were oxidized to their disulfides. Very high yields of haloaryl disulfides were obtained in all cases. Table V summarizes our results.

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Reduction of Mercuric Salts by Dioxenes

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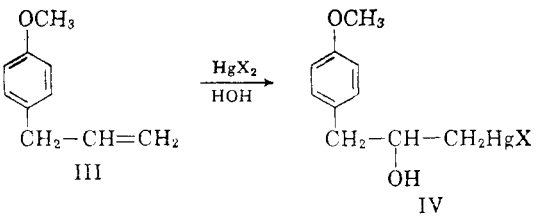
Mercuric salts in aqueous solutions are reduced rapidly and quantitatively by dioxene at room temperature. Isolation of glyoxal as a major product indicates that the double bond of dioxene is a faster reducing agent towards Hg^{+2} than is the aldehyde group of glyoxal. *m*-Propenylanisole does not reduce mercuric salts under conditions that give extensive reduction by its *ortho* or *para* isomer. 2-Methyl-*p*-dioxene is a fast reducing agent; its isomer, *exo*-methylene-*p*-dioxane, is very slow. Easy ionization of the mercury from an intermediate addition compound to form a stable carbonium ion is postulated to account for the fast and strong reducing action towards mercuric salts of dioxene and related compounds.

p-Dioxadiene appears to undergo substitution[2] with mercuric salts, but no other chemical reactions usually associated with aromaticity have been observed.[3] It therefore seemed interesting to determine whether *p*-dioxene, the related compound possessing a single double bond, would also be mercurated, or whether it would form the addition compounds typical of an olefin. When dioxene was treated with aqueous mercuric acetate, neither substitution nor addition products were isolated; but oxidation–reduction took place, nearly quantitative yields of free mercury, glyoxal, and ethylene glycol being obtained. The double bond of the dioxene must be a considerably faster reducing agent toward mercuric salts than the aldehyde groups of glyoxal, since, if the reverse had been true, little glyoxal would have been isolated.

When two moles of mercuric acetate were used, the reduction product was mercurous acetate, rather than free mercury. The same fast reduction takes place in methanol, but substitution of anhydrous benzene or an excess of dry dioxene for water as a solvent slowed the reducing action markedly, and the only isolated product was *p*-dioxane-2,3-diol diacetate.

Although most olefins react with mercuric salts to form addition compounds,[4] reducing action has also been observed and occasionally studied.[5] The previous work most closely related to our own is that of Balbiano and Paolini,[6] who found that aqueous mercuric acetate was reduced to free mercury by anethol (I), the latter undergoing oxidation to a mixture of isomers of 1-*p*-anisyl-1,2-propanediols (II) (see Chart B). In contrast, methylchavicol (III) forms stable mercury addition compounds such as IV. A number of related



compounds were studied. In summary, those compounds containing a double bond adjacent to the ring and *ortho* or *para* to an ether group reduced mercuric salts, whereas the isomeric compounds containing an allyl type of unsaturation formed stable addition compounds. A simple example of a compound with the double bond adjacent to the ring but *meta* to the methoxyl group was not studied. The reducing action, or lack of it, of the double bond of the substituted anisoles has been used by Lauer and Leeckley[7] as evidence of the location of the double bond in this general type of compound; those containing a double bond adjacent to the benzene ring reduced mercuric salts.

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