

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Reaction of Bromine with the Silver Salts of Aromatic Acids

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Recently, various types of alkyl bromides have been prepared by the reaction of equal molar amounts of bromine with the silver salts of carboxylic acids.¹ The preparation of aryl bromides by this brominative decarboxylation, however, has not been widely investigated. Bockmüller and Hoffman² have reported that bromine reacts with silver benzoate in boiling carbon tetrachloride to give an 80% yield of bromobenzene while Luttringhaus and Schaede³ claim a yield of only 14%. These latter workers also state that with aromatic acids, in general, this degradation is unsatisfactory but no results are given to justify their claim.

In view of this discrepancy, the reaction of bromine with the silver salts of various aromatic acids has been investigated and the results are summarized in Table I. From these results, it is

TABLE I

Silver salt of	% yield of bromide
<i>m</i> -Nitrobenzoic acid	68
<i>o</i> -Chlorobenzoic acid	46
Benzoic acid	53
<i>m</i> -Toluic acid	27 ^a
<i>m</i> -Methoxybenzoic acid	0 ^b

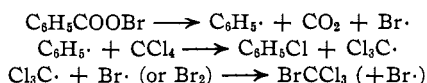
^a A 13% yield of 3,4-dibromotoluene was also obtained.

^b Only acidic compounds could be isolated.

apparent that the usefulness of this reaction is conditioned by the structure of the aromatic acid. The preparation of bromides from benzoic acid and from acids possessing electron-attracting groups (-I), such as nitro and chloro, is quite satisfactory (45-70%). In those cases where the aromatic acid is substituted with electron-donating (+I) groups, such as methyl and methoxyl, the course of the reaction is dependent upon the relative activation of the ring. For example, with *m*-methoxybenzoic acid, the reaction product consisted mainly of 2-bromo-5-methoxybenzoic acid, whereas with *m*-toluic acid, *m*-bromotoluene was obtained in 27% yield, 3,4-dibromotoluene in 13% and starting acid was recovered.

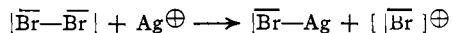
In order to isolate pure aryl bromides, it was found necessary to distil the reaction product through an efficient column. In the case of bromobenzene, which was studied in most detail, a small yield of bromotrichloromethane (6.7%)

and chlorobenzene (5.3%) was obtained. These latter products might arise by the following sequence of reactions.



The formation of an intermediate acyl hypohalite in the reaction of bromine with the silver salt of a carboxylic acid is seemingly well established.^{2,4} In view of the work of Kharasch and collaborators⁵ on the decomposition of diacetyl peroxide in carbon tetrachloride, the nature of the products isolated above tends to suggest a free radical path of formation. To exclude the possibility that moieties present in the reaction might catalyze such a bromine-chlorine exchange, silver acetate was allowed to react with bromine in boiling carbon tetrachloride in the presence of bromobenzene but no exchange was noted. The relationship of this type of free radical reaction, however, to the mechanism of the brominative decarboxylation is open to question.¹

The complete failure of *m*-methoxybenzoic acid to undergo the desired reaction in refluxing carbon tetrachloride and the isolation of a brominated acid prompted us to investigate the nature of the brominating reagent. It was found that identical results were obtained when the reaction was conducted at -20°. Since in carbon tetrachloride neither the free acid or its sodium salt underwent reaction with bromine at -20° to any appreciable extent, one of two possible explanations seemed reasonable for these results. Firstly, bromine could coordinate with the silver salt and give rise to a bromonium ion which in turn could brominate the aromatic nucleus. Birckenbach and Goubeau⁶ have shown that the bromination of benzene can be induced by the action, under anhydrous conditions, of silver perchlorate and postulated that such a catalysis was presumably due to the reaction



When a suspension of *m*-methoxybenzoic acid and silver perchlorate in carbon tetrachloride was allowed to react with bromine for fifteen minutes at -20°, however, the latter reagent did not appear to react with either constituent and the *m*-methoxybenzoic acid was recovered unchanged. Inasmuch as no reaction was noticed, no evidence for this type of mechanism could be obtained. This non-reactivity perhaps

(1) Arcus, Campbell and Kenyon, *J. Chem. Soc.*, 1510 (1949); Arnold and Morgan, *THIS JOURNAL*, **70**, 4248 (1948); Cason and Way, *J. Org. Chem.*, **14**, 31 (1949); Doering and Farber, *THIS JOURNAL*, **71**, 1514 (1949); Kleinberg, *Chem. Revs.*, **40**, 381 (1947); Allen and Wilson, "Organic Syntheses," Vol. 26, John Wiley and Sons, New York, N. Y., 1946, p. 52.

(2) Bockmüller and Hoffman, *Ann.*, **519**, 165 (1935).

(3) Luttringhaus and Schaede, *Ber.*, **74**, 1565 (1941).

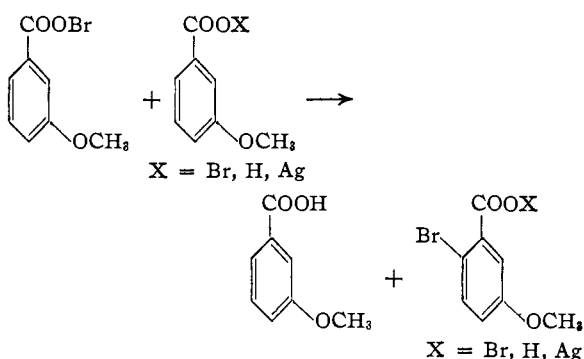
(4) Birckenbach, Goubeau and Berninger, *Ber.*, **65**, 1339 (1932).

(5) Kharasch, Jensen and Urry, *THIS JOURNAL*, **69**, 1100 (1947).

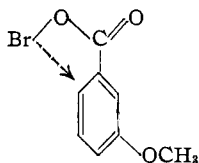
(6) Birckenbach and Goubeau, *Ber.*, **65**, 395 (1932); see also Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, p. 312.

is due to the different nature of the solvents, *i. e.*, benzene and carbon tetrachloride, since Birckenbach and Goubeau⁶ have shown that silver perchlorate does not react with halogens in solvents of the type of chloroform, hexane, etc.⁷

Secondly, it is plausible that the intermediate acyl hypobromite itself could be the active brominating agent and the course followed by this compound would depend upon the other species present in the reaction.⁸



The acyl hypobromite could react either with another similar moiety or with unreacted silver salt. As the reaction proceeded, the hypobromite could react with the starting acid which would then also be present. The ability of an acyl hypobromite to brominate another aromatic nucleus in carbon tetrachloride was demonstrated by allowing a filtered solution of acetyl hypobromite to react with anisole at -20° ; *p*-bromoanisole was obtained.⁹ It is also possible that the bromination, where sterically able, may occur by an intramolecular type of reaction.



Previously, Papa and Schwenk¹⁰ have reported that when bromine was allowed to react with silver β -(*m*-methoxyphenyl)-propionate, the only product obtained was β -(2-bromo-5-methoxyphenyl)-propionic acid. They also found that many aryl aliphatic acids could be halogenated when silver acetate was employed as the silver

(7) This non-reactivity of silver perchlorate with bromine in carbon tetrachloride solution falls in line with the recent observations of Benesi and Hildebrand, (*THIS JOURNAL*, **71**, 2703 (1949)) on the interaction of iodine with aromatic hydrocarbons.

(8) The ionic nature of the positive bromine in an acyl hypobromite would seem to be much less than that of the bromonium ion postulated above.

(9) A similar type of halogenation has been reported by Carlsohn ("Über eine neue Klasse von Verbindungen des positiv einwertigen Iods," Verlag von S. Hirzel, Leipzig, 1932) who showed that the pyridine coordination compound of an acetyl hypiodite would immediately attack an acidic solution of phenol to yield *p*-iodophenol.

(10) Papa and Schwenk, Abstracts, American Chemical Society, Chicago meeting, April, 1948, p. 3L.

salt and acetic acid as the reaction medium.¹¹ It is not definite as to the exact role of the silver acetate, that is, catalytic or formation of acetyl hypobromite. It was found, however, in the present work that *m*-methoxybenzoic acid was rapidly brominated in carbon tetrachloride suspension at -20° in the presence of an equivalent amount of silver acetate. In view of the results discussed previously, it seems likely that acetyl hypobromite is the halogenation agent when carbon tetrachloride is the solvent.

The isolation of 3,4-dibromotoluene in addition to *m*-bromotoluene from the reaction of bromine with silver *m*-toluate was of interest since it showed that with *m*-toluic acid the aromatic system is so substituted that both the bromination and decarboxylation reaction can occur. It is reasonable to expect such a case in view of the graded electronic differences in substituted aromatic rings. It was not possible, however, to determine in the formation of the dibromo product whether an acid derivative or the bromotoluene was brominated. Since no bromotoluic acid was obtained, it suggests that the bromotoluene was the moiety which was attacked.

The reaction of bromine with the silver salts of 1(and 2)-naphthoic acid yields only a complicated mixture. From 1-naphthoic acid, carbon dioxide amounting to 14% of theory was evolved and the neutral fraction consisted of an inseparable mixture of brominated naphthalenes. The acid fraction contained both a bromoacid and starting acid. A similar result was obtained with 2-naphthoic acid except that only 4% of the theoretical amount of carbon dioxide was given off and thus only a very small neutral fraction was obtained.

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Experimental¹²

The bromine was dried for several days over phosphorus pentoxide before use. The carbon tetrachloride was dried over calcium chloride and distilled. The silver salts were prepared following the procedure of Zingaro, Goodrich, Kleinberg and VanderWerf¹³ and were dried in a vacuum oven at 70° for at least twenty-four hours. All products were distilled through a 24-inch column which was packed according to the method of Mitchell and O'Gorman¹⁴ and which under the conditions employed in this work, showed a thirty-plate efficiency.

Bromobenzene.—A solution of 32.0 g. (0.2 mole) of bromine in 50 cc. of carbon tetrachloride was added during the course of twenty minutes to a refluxing mixture of 45.8 g. (0.2 mole) of silver benzoate and 250 cc. of carbon

(11) Birckenbach and Goubeau (*Ber.*, **66**, 1280 (1933)) have also shown that benzene is rapidly halogenated in the presence of silver acetate and Sletzinger and Dawson (*J. Org. Chem.*, **14**, 870 (1949)) have found that Prevost reagent iodinate substituted anisoles.

(12) Analyses by the Microanalytical Laboratory of the Department of Chemistry, University of California. All melting points are corrected.

(13) Zingaro, Goodrich, Kleinberg and VanderWerf, *THIS JOURNAL*, **71**, 575 (1949).

(14) Mitchell and O'Gorman, *Anal. Chem.*, **20**, 315 (1948).

tetrachloride. The heating was continued for an additional fifty minutes, the silver bromide filtered and the solid washed with 100 cc. of warm carbon tetrachloride. The filtrate was extracted twice with 25 cc. of 0.5 *M* sodium carbonate solution and the entire reaction mixture distilled through a column. Three fractions were collected: (1) bromotrichloromethane, b. p. 103°, d_{25}^{28} 1.992, n_D^{19} 1.5066, yield 2.63 g. (6.7%), (reported¹⁵ b. p. 104°, d_{20}^{20} 1.994 and n_D^{19} 1.5060). *Anal.* Calcd. for CCl_3Br : C, 6.06; Cl, 53.64; Br, 40.30. Found: C, 6.20; Cl, 54.2; Br, 40.1. (2) Chlorobenzene, b. p. 129–131°, n_D^{20} 1.5202 (pure sample b. p. 130°, n_D^{20} 1.5200), yield 1.19 g. (5.3%). The distillate was nitrated in the usual manner and then recrystallized from ethanol, m. p. 45.8–46.6°. No depression in melting point was noted upon admixture with an authentic sample. *Anal.* Calcd. for $\text{C}_6\text{H}_5\text{O}_4\text{N}_2\text{Cl}$: C, 35.57; H, 1.49; Cl, 17.50. Found: C, 35.58; H, 1.50; Cl, 17.81. (3) Bromobenzene, b. p. 154°, n_D^{20} 1.5564 (reported¹⁶ n_D^{20} 1.5571, yield 16.8 g. (53%)).

o-Chlorobromobenzene.—Following the procedure described above, 52.8 g. (0.2 mole) of silver *o*-chlorobenzoate was allowed to react with 32.0 g. (0.2 mole) of bromine in carbon tetrachloride; yield 17.5 g. (46%), b. p. 79–82° (14 mm.), n_D^{20} 1.5780 (reported¹⁷ n_D^{20} 1.5786).

m-Nitrobromobenzene.—Proceeding as above, 10.9 g. (0.04 mole) of silver *m*-nitrobenzoate was allowed to react on 6.4 g. (0.04 mole) of bromine; yield 5.50 g. (68%), b. p. 138° (38 mm.), m. p. 53–56° (reported¹⁸ 56°).

m-Bromotoluene.—Following the procedure above, 48.6 g. (0.2 mole) of silver *m*-toluate was allowed to react with 32.0 g. (0.2 mole) of bromine. The acid fraction yielded 9.5 g. (34.9%) of *m*-toluic acid, m. p. 107–109°. The lower boiling neutral fraction was *m*-bromotoluene, yield 9.15 g. (26.8%), b. p. 82° (18 mm.), n_D^{20} 1.5474 (pure sample n_D^{20} 1.5480) and the higher boiling neutral fraction was 3,4-dibromotoluene, yield 6.55 g. (13.1%), b. p. 116° (18 mm.), n_D^{20} 1.5822. This latter material was oxidized to 3,4-dibromobenzoic acid, m. p. 230–231° (reported¹⁹ 229–230°).

2-Bromo-5-methoxybenzoic Acid.—A solution of 74.1 g. (0.46 mole) of bromine in 50 cc. of carbon tetrachloride was added over the period of thirty minutes to a boiling suspension of 120 g. (0.46 mole) of silver *m*-methoxybenzoate in carbon tetrachloride. The bromine was decolorized immediately and no carbon dioxide was evolved. The reaction mixture was filtered and the silver bromide washed with two 100-cc. portions of boiling carbon tetrachloride. The precipitate was dried, extracted with aqueous sodium carbonate solution and the acidified extract deposited 58.3 g. of solid acid. The product was recrystallized three times from water, m. p. 159–160° (reported²⁰ 160°), yield 54 g. (50.5%). No depression in melting point was observed upon admixture with 2-bromo-5-methoxybenzoic acid. The *p*-nitrobenzyl ester melts 117–118°.

The combined carbon tetrachloride solutions were extracted with dilute alkali. Acidification of the alkaline extracts yielded a dark oil which solidified. The carbon tetrachloride solution upon concentration yielded only a few drops of neutral material.

The crude acid fraction from the carbon tetrachloride solution was esterified first with methanol and then with

diazomethane. The ester was fractionally distilled through a column and three main fractions were collected: (1) methyl *m*-methoxybenzoate, b. p. 104° (4.5 mm.), n_D^{20} 1.5240, yield 5.0 g. (6.7%). *Anal.* Calcd. for $\text{C}_8\text{H}_{10}\text{O}_3$: C, 65.05; H, 6.07. Found: C, 64.73; H, 6.05. The ester was saponified and 4.3 g. of crude acid, m. p. 104–105° (reported, 107°) was obtained. (2) Methyl bromo-5-methoxybenzoate, b. p. 141° (4.2 mm.), n_D^{20} 1.5620, yield 15.0 g. (14%). *Anal.* Calcd. for $\text{C}_8\text{H}_9\text{O}_3\text{Br}$: C, 44.10; H, 3.70. Found: C, 43.95; H, 3.56. The ester was saponified and yielded 12.7 g. of isomeric monobromo acids, m. p. 137–151°. This mixture could not be easily separated by fractional crystallization or fractional acidification. *Anal.* Calcd. for $\text{C}_8\text{H}_7\text{O}_3\text{Br}$: C, 41.58; H, 3.05; Br, 34.59. Found: C, 41.94; H, 3.05; Br, 34.90. (3) Methyl 2,4-dibromo-5-methoxybenzoate, b. p. 171° (4.2 mm.), n_D^{20} 1.5820, yield 11.6 g. (7.7%). The ester was saponified by heating with 10% aqueous sodium hydroxide solution for forty-eight hours. The crude acid was recrystallized from water, m. p. 199–200° (reported, 201–202°²¹).

Bromination of Anisole with Acetyl Hypobromite.—To a suspension of 6.7 g. (0.04 mole) of silver acetate in 50 cc. of carbon tetrachloride which was cooled to –20°, there was added in the course of ten minutes 5.8 g. (0.036 mole) of bromine dissolved in 25 cc. of carbon tetrachloride also cooled to –20°. The bromine color persisted for fifteen minutes longer. The reaction mixture was then filtered by means of a filter-stick into a storage reservoir cooled to –20°. The filtrate which had a light brown color was added over a period of fifteen minutes to 4.3 g. (0.04 mole) of anisole dissolved in 10 cc. of carbon tetrachloride. The reaction mixture was kept at –20°. The colorless anisole solution turned a red color during the addition but this color had lightened to yellow after the addition was complete. A total time of ten minutes elapsed between the beginning of the addition of the acetyl hypobromite and quenching of the reaction with aqueous sodium carbonate solution. The mixture was processed in the usual manner and yielded 2.4 g. (55.8%) of anisole and 1.5 g. (19.5%) of *p*-bromoanisole, b. p. 110–114° (26 mm.), n_D^{20} 1.5606 (reported²² n_D^{20} 1.5605).

Summary

1. The reaction of bromine with the silver salts of benzoic, *o*-chlorobenzoic and *m*-nitrobenzoic acid yields the expected aryl bromides in good yield.

2. The reaction of bromine with silver *m*-toluate yields 3,4-dibromotoluene in addition to the expected *m*-bromotoluene.

3. The reaction of bromine with silver *m*-methoxybenzoate yields mainly 2-bromo-5-methoxybenzoic acid.

4. The isolation of bromotrichloromethane and chlorobenzene from the reaction of silver benzoate with bromine suggests that the intermediate benzoyl hypobromite is capable of a free radical type of decomposition.

5. The bromination of an aromatic nucleus under the condition of the silver salt reaction is apparently due to the halogenation ability of an acyl hypobromite.

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(15) Thorpe, *J. Chem. Soc.*, **37**, 203 (1880); Simons, Sloat and Meunier, *THIS JOURNAL*, **61**, 435 (1939); Kharasch, Freiman and Urry, *J. Org. Chem.*, **13**, 570 (1948).

(16) Williams and Krchma, *THIS JOURNAL*, **48**, 1888 (1926).

(17) Phillip, *J. Chem. Soc.*, **101**, 1866 (1912).

(18) Bruhl, *Z. physik. Chem.*, **22**, 373 (1897).

(19) Huber and Burghard, *Ber.*, **8**, 558 (1875).

(20) Bachman and Picha, *THIS JOURNAL*, **68**, 1599 (1946).

(21) Bauer and Vogel, *J. prakt. Chem.*, [2] **88**, 330 (1913).

(22) Brand and Kranz, *ibid.*, **115**, 160 (1897).