

Solvent.	Wt. of solvent. G.	Wt. of free radical. G.	Concentration. %.	Depression of f. p.	Mol. wt.
Benzene	17.42	0.1733	0.98	0.106	469.3
	...	0.3335	1.88	0.194	493.4
	...	0.5120	2.85	0.279	526.7
	17.14	0.1900	1.10	0.126	450.1
	...	0.3446	1.97	0.212	474.2
	...	0.5231	2.96	0.305	500.3
	17.20	0.2140	1.23	0.130	478.5
	...	0.3210	1.83	0.188	496.3
	...	0.4242	2.41	0.247	520.3
	<i>p</i> -Bromotoluene	19.61	0.2612	1.31	0.257
...		0.4563	2.27	0.388	491.8
...		0.6309	3.12	0.528	499.6
19.82		0.1800	0.90	0.167	446.0
...		0.3427	1.70	0.292	485.6
...		0.4453	2.20	0.366	503.3

is a remarkable change with increasing concentrations, the latter change however being somewhat irregular, and the results are possibly not so accurate as might be wished. The free radical, in solution, is evidently monomolecular to the extent of 30 to 38%, and dimolecular to 62 to 70%.

Summary.

1. 2,2'-Sulfonido-triphenyl carbinol and the corresponding chloride were prepared. It was found that this chloride, unlike the chlorides of aryl thio-xanthenols, does not make additive colored compounds with hydrogen chloride.

2. The free radical, 2,2'-sulfonido-triphenylmethyl, was prepared. Its oxygen absorption, the degree of combination with iodine, and extent to which it exists as monomolecular have been determined.

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[CONTRIBUTION FROM THE UNIVERSITY OF TORONTO.]

THE FRIEDEL AND CRAFTS' REACTION. BROMOPHTHALIC ANHYDRIDES, BENZENE AND ALUMINUM CHLORIDE.

By H. N. STEPHENS.

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Rubidge and Qua¹ have studied the reaction between phthalic anhydride, benzene and aluminum chloride and have shown the conditions which will give a good yield of *o*-benzoyl-benzoic acid, and also the conditions which will give no acid and a 35% yield of diphenylphthalide. Lawrance,² who used the nitrophthalic anhydrides and the acetylamino-phthalic anhydrides in this reaction, points out that from each substituted phthalic anhydride there are possible two acid products and two derivatives of diphenyl-phthalide.

¹ Rubidge and Qua, *THIS JOURNAL*, **36**, 732 (1914).

² Lawrance, *ibid.*, **42**, 1871 (1920).

Two investigators have previously prepared *o*-benzoyl-bromobenzoic acid by this method. In 1879, nine years before Friedel and Crafts published their paper on the preparation of *o*-benzoyl-benzoic acid, Pechman³ heated a mixture of bromophthalic anhydrides with benzene and aluminum chloride and obtained a product which he called *o*-bromobenzoyl-benzoic acid, m. p. 219° to 221°. This product was probably an impure specimen of 6-benzoyl-2-bromobenzoic acid, m. p. 231.5°. It will be noticed that, as Pechman used a mixture of the two bromophthalic anhydrides, there would be four possible products while he only described one. The results of the other investigator are given in a German patent.⁴ He obtained two *o*-benzoyl-bromobenzoic acids, one from bromophthalic acid, an excess of aluminum chloride being used to dehydrate the acid, and the other from bromophthalic anhydride. The product from the latter melted at 174° and corresponds to that obtained by Kohler, Heritage and Burnley⁵ by the oxidation of 2,6-dibromo-3-keto-1-phenyl-2,3-dihydrindene. As this product has been obtained in the present investigation from 4-bromophthalic anhydride and as the other product (m. p. 216° to 219°) more closely resembles the product from the 3-bromophthalic anhydride it might be inferred that a mixture of the bromophthalic acids was used in this case also. The present investigation was for the purpose of preparing and identifying the various *o*-benzoyl-bromobenzoic acids and the diphenyl-bromophthalides.

3-Bromophthalic Acid.—This acid has been prepared by Faust,⁶ Pechman,³ and Smith⁷ but in each case the melting point is much too low and the product is evidently a mixture. Guareschi⁸ oxidized 5-bromo-1-nitronaphthalene with potassium permanganate and obtained an acid melting at 174° to 176° but this method gave the writer only a 4% yield and the reduction of the 5-bromo-1-nitronaphthalene to 5-bromo-1-aminonaphthalene before oxidation did not improve the yield. The method finally adopted was the conversion of 3-aminophthalic acid into 3-bromophthalic acid by the Sandmeyer method. The aminophthalic acid was prepared as described by Lawrance.

Twenty-five g. of 3-nitrophthalic acid was reduced and the hydrochloride of the amino acid mixed with 200 cc. of 18% hydrochloric acid, diazotized, and poured into 150 cc. of a warm 10% solution of cuprous bromide. After warming gently on the water-bath to drive off oxides of nitrogen the solution was allowed to stand for several hours and a precipitate of *o*- and *m*-bromobenzoic acids was then filtered off and the filtrate extracted with ether, affording a yield of 28%. In this reaction a reddish oil is fre-

³ Pechman, *Ber.*, **12**, 2126 (1879).

⁴ Gesellschaft für Anilin Fabrikation.

⁵ Kohler, Heritage and Burnley, *Am. Chem. J.*, **44**, 60 (1910).

⁶ Faust, *Ann.*, **160**, 62 (1871).

⁷ Smith, *J. Chem. Soc.*, **35**, 792 (1879).

⁸ Guareschi, *Ann.*, **222**, 292 (1884).

quently obtained which may be removed by dissolving the acid in potassium hydroxide and oxidizing with potassium permanganate. The acid, recrystallized from water, melts at 177° to 8°.

Analysis. Calc. for $C_8H_5O_4Br$: Br. 32.6. Found: 32.4.

The anhydride was prepared from the acid by distillation and recrystallization from glacial acetic acid, m. p. 130–1°.

4-Bromophthalic Acid.—Nourrisson⁹ prepared this acid from bromo-*o*-toluidine by converting it into the nitrile, hydrolyzing the nitrile and oxidizing the resulting bromo-*o*-toluic acid. Miersch¹⁰ obtained the acid by oxidizing *p*-bromohydrindene with 25% nitric acid, and Perkin and Revay¹¹ oxidized bromo-indene with dil. nitric acid. The method finally adopted was that described by Armstrong and Rossiter¹² who oxidized 1,6-dibromo-2-naphthol and obtained a small quantity of 4-bromophthalic acid but give no quantitative details.

One hundred g. of β -naphthol was dissolved in 500 cc. of glacial acetic acid and a mixture of 223 g. of bromine and 100 cc. of acetic acid added. After standing overnight the crystals were filtered off, washed with water and dried in a vacuum oven at 70° for one hour. Evaporation of the mother liquor yielded more of the product. Recrystallized from 80% acetic acid the dibromo-naphthol melts at 106°; yield 90%.

Sixty g. of dibromonaphthol was dissolved in 1200 cc. of water containing 20 g. of potassium hydroxide, and 160 g. of potassium permanganate was added gradually with constant stirring, the temperature being kept low. After standing for 3 or 4 hours the solution was heated on the water-bath and potassium permanganate added gradually until a permanent pink color was obtained. The solution was then decolorized with ferrous sulfate, filtered, evaporated to 400 cc., acidified and extracted with ether. The product when recrystallized from water containing a few drops of sulfuric acid, melted at 170.5° and the yield of crude acid was 47% calculated on the dibromo-naphthol. The anhydride was prepared by distilling the acid; yield, 80%. The distillate was a white, crystalline mass, m. p. 104° to 106°. No solvent was found from which it could be recrystallized. On standing it changed slowly back to the acid.

Reaction of 3-Bromophthalic Anhydride with Benzene and Aluminum Chloride.

Four and three-tenths g. of powdered 3-bromophthalic anhydride, 12 cc. of benzene and 5 g. of aluminum chloride were boiled for 4 hours on the water-bath under a return condenser. After the addition of 100 cc. of 10% hydrochloric acid the benzene was distilled with steam and the precipitate digested with a hot solution of sodium carbonate which left a slight residue of phthalide. The solution was diluted to about 250 cc. and very slowly acidified with 5% hydrochloric acid. If the acid is precipitated rapidly it separates as a gum which becomes crystalline only on long standing. The dry product was dissolved in 75 cc. acetone, 60 cc.

⁹ Nourrisson, *Ber.*, **20**, 1016 (1887).

¹⁰ Miersch, *ibid.*, **25**, 2115 (1892).

¹¹ Perkin and Revay, *J. Chem. Soc.*, **65**, 253 (1894).

¹² Armstrong and Rossiter, *Ber.*, **24**, ref. 705 (1891).

water added and the solution left overnight to crystallize. After several recrystallizations a constant melting point, 231.5° , was obtained. This substance is the only acid product of the reaction and is probably identical with the substance described by Pechman, m. p. $219-21^{\circ}$; yield, 89%, calculated on the bromophthalic anhydride.

Identification of the Substance Melting at 231.5° .—Eight g. of potassium hydroxide was dissolved in a little water in a nickel crucible and 1 g. of the substance added. The mixture was slowly heated on a sand-bath, with constant stirring, and held at $220-5^{\circ}$ for 25 minutes. After dissolving in water and acidifying, the precipitate contained benzoic acid and *o*-bromobenzoic acid. The substance is therefore, 6-benzoyl-2-bromobenzoic acid.

Calc. for $C_{14}H_9O_3Br$: Br, 26.2. Found: 26.1.

Reaction of 4-Bromophthalic Anhydride with Benzene and Aluminum Chloride.

Four and three tenths g. of 4-bromophthalic anhydride, 12 cc. of benzene and 5 g. of aluminum chloride were boiled for 6 hours. The product of the reaction was obtained as in the previous experiment. The greenish gum given by the slow acidification of the sodium carbonate solution became crystalline on standing for a few hours; yield, 97%. The precipitate was washed, dried, dissolved in 40 cc. of alcohol, and water added just to turbidity. After standing for 12 hours in a covered dish the precipitate was filtered off and a second precipitate obtained by allowing the filtrate to stand for a day in an open dish.

After several recrystallizations the first fraction gave flat needles, soluble in ether and acetone, moderately soluble in alcohol, slightly soluble in hot benzene and insoluble in ligroin; m. p. 193° . This fraction was about 55% of the total yield of acids. The second fraction, after several recrystallizations, gave small rhombohedrons, m. p. 172.5° , very soluble in alcohol, ether and acetone, slightly soluble in hot benzene and insoluble in ligroin. This substance is, no doubt, identical with that described by Kohler, Heritage and Burnley⁵ (m. p. 174°) and with that described in the German patent.⁴ This fraction represents about 45% of the total yield of acids.

Identification of the Substance Melting at 193° .—The substance was hydrolyzed by fusing with potassium hydroxide for 10 minutes at $185-90^{\circ}$. The fusion products were benzoic acid and *p*-bromobenzoic acid, and the substance is therefore 2-benzoyl-4-bromobenzoic acid.

Calc. for $C_{14}H_9O_3Br$: Br, 26.2. Found: 26.3.

Identification of the Substance Melting at 172.5° .—In the fusion of this substance the temperature was kept at $170-5^{\circ}$ for 20 minutes. The fusion products were benzoic acid and *m*-hydroxybenzoic acid. As

m-bromobenzoic acid is changed to *m*-hydroxybenzoic acid by fusion with potassium hydroxide this identifies the substance as 6-benzoyl-3-bromobenzoic acid although Kohler, Heritage and Burnley described it as *p*-bromo-*o*-benzoylbenzoic acid.

Reaction of 3-Bromophthalic Anhydride with Benzene, Aluminum Chloride and Acetic Anhydride.

Four and three tenths g. of 3-bromophthalic anhydride, 12 cc. of benzene and 5 g. of aluminum chloride were boiled for 4 hours and then 3 cc. of acetic anhydride and an additional 12 cc. of benzene were added, and boiling was continued for 3 hours. After treatment with sodium carbonate only a small quantity of insoluble material remained which on recrystallization from benzene melted at 148–50°.

As 3-bromophthalic anhydride gave only 6-benzoyl-2-bromobenzoic acid, only the diphenyl-bromophthalide corresponding to this acid is to be expected in the above reaction.

Diphenyl-3-Bromophthalide.

Pechman¹³ prepared diphenyl-phthalide from the mixed anhydride of *o*-benzoyl-benzoic acid and acetic anhydride with benzene and aluminum chloride. Following Pechman's method the anhydride of 6-benzoyl-2-bromobenzoic acid and acetic acid was prepared and then from it the corresponding diphenyl-bromophthalide.

Two g. of 6-benzoyl-2-bromobenzoic acid was heated on a water-bath with 4 cc. of acetic anhydride for 12 hours, and the liquid then poured into an equal volume of 95% alcohol. On standing for several hours a white crystalline substance separated which on recrystallization from alcohol gave fine colorless needles; m. p. 168.5°.

Analysis. Calc. for C₁₆H₁₁O₄Br: Br, 23.05. Found: 22.9.

One g. of this anhydride was heated with 5 cc. of benzene and 0.8 g. of aluminum chloride for 6 hours. After acidification the benzene was distilled with steam and the solid heated with sodium carbonate solution to remove acids. The insoluble residue was recrystallized from benzene and then from alcohol; m. p. 131°; yield, 71%.

Analysis. Calc. for C₂₀H₁₃O₂Br: Br, 21.9. Found: 20.4.

The very small quantity of the product, m. p. 148–50°, obtained from the 3-bromophthalic anhydride with benzene, aluminum chloride and acetic anhydride is not, therefore, diphenyl-3-bromophthalide.

Reaction of 4-Bromophthalic Anhydride with Benzene, Aluminum Chloride and Acetic Anhydride.

Four and three tenths g. of 4-bromophthalic anhydride, 12 cc. of benzene and 5 g. of aluminum chloride were boiled for 6 hours, and then 3 cc. of

¹³ Pechman, *Ber.*, **14**, 1865 (1881).

acetic anhydride and 12 cc. of benzene were added and the boiling continued for 3.5 hours. After treatment with sodium carbonate the insoluble residues (diphenyl-bromophthalides) represented a total yield of 60%. This product was dissolved in a small amount of benzene and after standing for 24 hours gave a thick reddish liquid and a crystalline mass. The crystals after several recrystallizations from benzene melted at 186°. The reddish liquid was heated in a vacuum oven to remove benzene and the hard gummy residue was dissolved in a small quantity of hot alcohol, which on cooling deposited a reddish gum, but the remaining liquid after several hours gave a white crystalline substance which after several recrystallizations from methyl alcohol melted at 115–6°.

Identification of the Diphenyl-bromophthalide, m. p. 186°.—Two g. of 2-benzoyl-4-bromobenzoic acid was heated with 4 cc. of acetic anhydride for 4 hours on the water-bath. The solution was then poured into an equal volume of 80% alcohol and allowed to stand for several hours, when a gummy substance separated which on solution in hot alcohol, and cooling, gave a white amorphous powder; m. p. 83–7°. This powder with benzene and aluminum chloride gave a product, m. p. 186°, identical with one of those obtained from the 4-bromophthalic anhydride. It is, therefore, diphenyl-5-bromophthalide. Yield, 56%.

Calc. for $C_{20}H_{13}O_2Br$: Br, 21.9. Found: 21.8.

Identification of the Diphenyl-bromophthalide, m. p. 115.6°.—Two g. of 6-benzoyl-3-bromobenzoic acid was heated on the water-bath for 6 hours with 4 cc. of acetic anhydride. The product was then poured into double its volume of hot 50% alcohol and an oil separated on cooling. This oil did not crystallize after several precipitations from hot methyl alcohol but hardened to a gum with no definite melting point when dried *in vacuo*. This gum with benzene and aluminum chloride gave a product, m. p. 115–6°, identical with the product from 4-bromophthalic anhydride, benzene and aluminum chloride. It is, therefore, diphenyl-4-bromophthalide. Yield of crude material, 69%.

Calc. for $C_{20}H_{13}O_2Br$: Br, 21.9. Found: 22.1.

When 3-bromophthalic anhydride reacts with benzene and aluminum chloride only 6-benzoyl-2-bromobenzoic acid is obtained but when 4-bromophthalic anhydride is used approximately equal quantities of 2-benzoyl-4-bromobenzoic acid and 6-benzoyl-3-bromobenzoic acid are formed. The total yield in each case is good. The fact that only one product is obtained from 3-bromophthalic anhydride might be due to steric hindrance but Mr. Lawrance, in this laboratory, has found that the tetrahalogen-phthalic anhydrides with benzene and aluminum chloride give good yields of the benzoyl-tetrahalogen-benzoic acids.

Using benzene, aluminum chloride and acetic anhydride, 3-bromophthalic anhydride gave no diphenyl-bromophthalide, while a good yield

of both the possible diphenyl-bromophthalides was obtained from 4-bromophthalic anhydride. Oddy, working at McMaster University, has obtained good yields of the diphenyl-tetrahalogen-phthalides from the tetrahalogen-phthalic anhydrides.

Summary.

1. Each of the two bromophthalic anhydrides has been found to react with benzene and aluminum chloride forming benzoyl-bromobenzoic acids. The 3-anhydride yielded only one acid while the 4-anhydride gave two in approximately equal quantities.

2. Under the conditions favorable to the production of diphenyl-bromophthalides, the 3-anhydride gave no diphenyl-bromophthalide while the 4-anhydride gave two.

3. A new method is described for the preparation of 3-bromophthalic acid and detailed directions given for the preparation of 1,6-dibromo-2-naphthol and 4-bromophthalic acid.

4. Seven new compounds have been prepared: 2-benzoyl-4-bromobenzoic acid, m. p. 193°; diphenyl-3-bromophthalide, m. p. 131°; diphenyl-4-bromophthalide, m. p. 115-6°; diphenyl-5-bromophthalide, m. p. 186°; mixed anhydride of 6-benzoyl-2-bromobenzoic acid and acetic acid, m. p. 168.5°; mixed anhydride of 2-benzoyl-4-bromobenzoic acid and acetic acid, m. p. 83-7°; and mixed anhydride of 6-benzoyl-3-bromobenzoic acid and acetic acid.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY,
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THE ACTIVITY OF ADSORBED INVERTASE.

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The action on sucrose solutions of invertase adsorbed on charcoal and on gelatinous aluminum hydroxide was studied by Nelson and Griffin¹. They reported that in their experiments a given quantity of enzyme exhibited the same activity when adsorbed on a solid in the bottom of the reaction vessel as when uniformly distributed throughout the solution. The importance of this observation and its bearing on the true nature of

¹ Nelson and Griffin, *THIS JOURNAL*, **38**, 722, 1109(1916).