Studies in the Friedel and Crafts Reaction

Preparation of 2-Aminoanthraquinone from Phthalic Anhydride and Bromobenzene[1,2]

P. H. Groggins, A. J. Stirton, and H. P. Newton

Color and Farm Waste Division, Bureau of Chemistry and Soils, Washington, D. C.

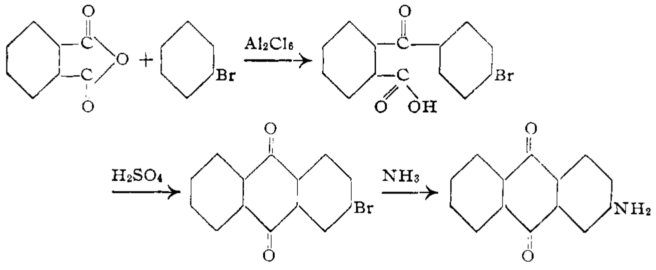
2-Aminoanthraquinone has been prepared according to the Friedel and Crafts reaction from phthalic anhydride and bromobenzene. The synthesis may be divided into three steps as follows: (1) preparation of 4′-bromo-2-benzoylbenzoic acid; (2) formation of 2-bromoanthraquinone by ring closure with concentrated sulfuric acid; and (3) ammonolysis of the halogen compound to obtain 2-aminoanthraquinone.

The first step presented the greatest practical problems for, although the product obtained by the Friedel and Crafts reaction was quite pure, the yields were only 80 to 85 per cent of theory. The recovery of the excess of bromobenzene used in the liquid-phase reactions was, furthermore, only 90 to 93 per cent of the calculated amount. This loss, along with the comparatively low yields, must be attributed to a decomposition of bromobenzene in the presence of anhydrous aluminum chloride.

On ring closure with 95 per cent sulfuric acid, the yields of 2-bromoanthraquinone were as high as 95 per cent of theory. The purity of the product varied with the concentration of the sulfuric acid from which it was precipitated, whereas the yields varied inversely. The 2-aminoanthraquinone resulting from ammonolysis of the halogen compound was in many cases more than 98 per cent pure. The products prepared under optimum conditions required no purification, since microscopic inspection and use in the preparation of vat colors showed that they were comparatively free from deleterious impurities.

THIS laboratory has previously reported the preparation of 2-aminoanthraquinone from phthalic anhydride and chlorobenzene according to the Friedel and Crafts synthesis (*7*). The most stubborn problem in the prior investigations resided in the ammonolysis of 2-chloroanthraquinone, great difficulty being experienced in producing an amine of high purity. A temperature of 200° C. or above was used, and under the best conditions of ammonia ratio and ammonia concentration 2-aminoanthraquinone of only 93 to 95 per cent purity was obtained.

The present investigation relates to the preparation of this valuable vat dye intermediate from bromobenzene and phthalic anhydride. The first step consists in the preparation of 4-bromo-2-benzoylbenzoic acid according to the Friedel and Crafts reaction. When dehydrated with sulfuric acid, the halogen keto acid thus obtained yields 2-bromoanthraquinone. When the bromoanthraquinone is treated with ammonia under pressure, 2-aminoanthraquinone is obtained. The several reactions that occur in the synthesis may be represented by the following structural formulas:



This synthesis of 2-bromoanthraquinone was first accomplished by Ullmann and Sone (*17*), but their report on this work is meager, and their yield of 2-bromoanthraquinone was comparatively low. Isomeric bromobenzoylbenzoic acids have also been prepared by Pechmann (*12*), who heated a mixture of bromophthalic anhydrides with benzene and aluminum chloride, and obtained a product which he called *o*-bromobenzoylbenzoic acid (m. p. 219–221° C.). Stevens (*16*) has made an intensive study of these compounds containing bromine attached to the benzoic acid nucleus, established their physical constants, and proved their structure. Although these bromo-keto acids would yield alpha and beta bromoanthraquinone on ring closure, they are unlike the 4′-bromo-2-benzoylbenzoic acid described in this paper, which contains the halogen substituent attached to the benzoyl nucleus.

As was expected, it was found that the bromine atom is more readily replaced than the chlorine atom from halogenoanthraquinones. This information is of considerable practical importance in the preparation of vat colors. It makes possible the preparation of anthraquinone-imide derivatives with higher yields and purity, on account of the comparative ease in condensing 2-bromoanthraquinone with various amino compounds (*17*).

Preparation of 4′-Bromo-2-Benzoylbenzoic Acid

In order to determine the optimum conditions for the preparation of 4′-bromo-2-benzoylbenzoic acid, a study was made of the following factors involved in the Friedel and Crafts reaction: (1) ratio of bromobenzene to phthalic anhydride, (2) effect of time and temperature of reaction, and (3) effect of using a technical aluminum chloride as the condensing agent. Consideration was also given to the recovery of the excess of bromobenzene used in carrying out certain of these experiments.

Experiments Using Molecular Proportions of Phthalic Anhydride and Bromobenzene—Owing to the comparatively high cost of bromobenzene, it appeared necessary to investigate the feasibility of carrying out the Friedel and Crafts reaction with approximately the molecular combining proportions of phthalic anhydride and bromobenzene. These experiments were made in duplicate, with a technical aluminum chloride obtained from bauxite in one set and a screened, c. p. material made by chlorinating scrap aluminum in the other. The reactions were carried out in an iron mill ap-

---

[1] Received April 22, 1931. Presented before the Division of Dye Chemistry at the 80th Meeting of the American Chemical Society, Cincinnati, Ohio, September 8 to 12, 1930.

[2] Contribution No. 197 from the Color and Farm Waste Division, Bureau of Chemistry and Soils.

paratus which previously gave good results in the similar preparation of 4′-phenyl-2-benzoylbenzoic acid (*5*).

A homogenous suspension of phthalic anhydride and bromobenzene was introduced into the mill, and the anhydrous aluminum chloride was then added. The mill was set in motion and run for 1 hour before heat was applied. The reaction mass was maintained at the operating temperature by means of the heat furnished by gas burners. The charge became spongy as the reaction proceeded from the liquid phase to the aluminum complex of the keto acid, the material showing a distinct tendency to ooze out at the vent. As the reaction progressed, the formation of the anhydrous aluminum compound became evident by the appearance of an orange-brown powder at the hydrogen chloride vent. At the conclusion of each run the reaction mass was hydrolyzed with dilute cold sulfuric acid, boiled with live steam to remove volatile material, cooled, and filtered. The crude keto acid remaining on the filter was then put into solution as the ammonium salt by heating with live steam in 10 liters of very dilute ammonia. After filtering, the 4′-bromo-2-benzoylbenzoic acid was slowly reprecipitated at 90° C. with dilute sulfuric acid. The product separated out as glistening colorless plates which were slightly soluble in boiling water. Owing to this appreciable solubility (1 gram per liter at 100° C., 0.3 gram per liter at 30° C.), the suspension was cooled before filtering.

Table I, giving experiments in which technical bromobenzene was used (see Distillation Data), shows that in yields or purity of product there was no appreciable difference between the two types of anhydrous aluminum chloride. With increasing quantities of bromobenzene the best results were obtained with the C. P. screened aluminum chloride. This fact is at present ascribed to the presence of ferric chloride in the technical aluminum chloride, which under certain conditions forms stable, alkali-insoluble iron complexes. Such iron compounds are known to form readily when an aromatic compound containing a carboxylic group ortho to another substituent is treated with iron salts (*9*). This phenomenon was also observed when ferric chloride was used as a ring closing agent in the preparation of 2-phenylanthraquinone from 4′-phenyl-2-benzoylbenzoic acid. The formation of such aromatic iron complexes undoubtedly accounts for the abnormally high recovery of hydrogen chloride when it is employed as a condensing agent in Friedel and Crafts reactions. This subject is on the laboratory program for comprehensive study and will be reported later.

Table I—Effect of Type of Aluminum Chloride in Preparation of 4′-Bromo-2-Benzoylbenzoic Acid

(Iron mill apparatus)

Aluminum chloride used, 1 mole + 10%
Mol. wt. bromobenzene, 157. Technical material used in experiments shown below
Mol. wt. phthalic anhydride, 148
Melting point pure 4′-bromo-2-benzoylbenzoic acid, 173.0° C. (cor.)

EXPT.	TYPE Al_2Cl_6 USED	PHTHALIC ANHYDRIDE	BROMOBENZENE	TEMP.	TIME	YIELD KETO ACID	MELTING POINT
		Grams	*Grams*	*° C.*	*Hours*	%	*° C.*
1	Technical	150	157	70–75	12	68.9	170.3–170.8
	C. P. screened	150	157	70–75	12	67.5	170.3–170.8
2	Technical	150	157	75–80	12	78.4	170.5–170.8
	C. P. screened	150	157	75–80	12	76.4	170.2–170.6
3	Technical	148	173	75–80	12	73.8	169.8–170.6
	C. P. screened	148	173	75–80	12	73.8	170.0–170.5
4	Technical	148	173	70–75	14	79.4	170.0–170.5
	C. P. screened	148	173	70–75	14	82.0	169.8–171.0
5	Technical	148	196	70–75	14	80.5	170.0–170.5
	C. P. screened	148	196	70–75	14	82.0	169.8–170.6

The lower yields of the keto acid, as compared with those obtained in the similar condensation of chlorobenzene, may be due to a partial decomposition of bromobenzene by aluminum chloride, which is discussed later in this paper.

As judged by the melting points, the products were of high purity. Titration with standard sodium hydroxide in alcoholic solution showed that a composite sample of the crude material was 99.35 per cent pure, whereas the purified product was 99.70 per cent pure. When recrystallized from toluene and glacial acetic acid, 4′-bromo-2-benzoylbenzoic acid is obtained as glistening plates which melt sharply at 173.0° C. (cor.). Ullmann and Sone (*17*) reported the same constant.

Substance: *0.2207, 0.2004*; AgBr: *0.1357, 0.1232*
Calculated for $C_{14}H_9O_3Br$ (mol. wt. 304.988): Br, 26.23 per cent; found, 26.18, 26.16 per cent

EXPERIMENTS USING EXCESS OF BROMOBENZENE—Experiments were then run to determine whether an improvement in yield could be obtained by employing an excess of bromobenzene. These tests were conducted in large three-neck flasks provided with a mercury-sealed agitator and a reflux condenser. The charges were heated in an electrically controlled hot-water bath. At the end of each run the excess of bromobenzene was recovered by distillation with steam. The crude keto acid was then worked up in the manner previously described. These results are recorded in Table II.

Table II—Preparation of 4′-Bromo-2-Benzoylbenzoic Acid, Liquid Reactions

Phthalic anhydride used, 74 grams = 0.5 mole
Aluminum chloride used, 147 grams = 0.5 mole + 10% excess
Bromobenzene used, 0.5 mole × ratio

EXPT.	TYPE OF Al_2Cl_6	TIME	TEMP.	MOLAR RATIO BROMOBENZENE	YIELD BROMOBENZOYLBENZOIC ACID	SOLVENT RECOVERY
		Hours	*° C.*		%	%
1	C. P. screened	$5^1/_2$	60	6:1	82.7	92
2[a]	C. P. screened	6	60	4:1	79.7	89.2
3	C. P. screened	6	75–80	6:1	81.3	91.1
4	C. P. screened	6	75–80	4:1	78.1	..
5	C. P. screened	15	75–80	4:1	83.9	75.0
6[a]	C. P. screened	15	75–80	4:1	83.0	..
7	Technical	15	75–80	4:1	80.0	78.7
8[a]	Technical	15	75–80	4:1	77.4	..
9	C. P. screened	6	85–90	6:1	83.9	93.0
10	C. P. screened	11	85–90	6:1	82.5	90.0
11	Technical	11	85–90	6:1	72.4	91.8
12[a]	C. P. screened	11	85–90	6:1	78.1	..
13[b]	C. P. screened	11	85–90	6:1	84.6	..

[a] Bromobenzene of b. p. 155–160° C. was used.
[b] Run under slightly reduced pressure.

The data in experiments 1 to 4, inclusive, indicate that slightly better yields are obtainable with a 6:1 ratio than with a 4:1 ratio of bromobenzene to phthalic anhydride. Experiments 4 and 5 show that a longer reaction time with a 4:1 ratio improves the yield, whereas experiments 9 and 10 with a 6:1 ratio show no such increase in yield. As the temperature was raised (experiments 1, 3, and 9), the yields were not markedly altered, but phthalides insoluble in the ammoniacal solution were present. There is evidence in experiments 6 and 8, and 10 and 11 that the use of a C. P. screened aluminum chloride has an advantage over the technical product when the condensation takes place in the presence of an excess of bromobenzene.

Distillation Data

(Boiling point C. P. bromobenzene, 158° C.)

BROMOBENZENE TAKEN	DISTILLATION RANGE	LIQUID COLLECTED	
Grams	*° C.*	*Grams*	%
BROMOBENZENE USED IN CONDENSATION EXPERIMENTS OF TABLE I			
1500	52–125	38	2.5
	115–155	37	2.5
	155–160	1201	80.0
	161–165	88	5.9
	165–170	28	1.9
	170–175	30	2.0
	Crude solid[a]	66	4.1
		1488	98.9
BROMOBENZENE USED IN CONDENSATION EXPERIMENTS OF TABLE II			
1000	75–125	9	0.9
	125–155	67	6.7
	155–160	689	68.9
	160–165	126	12.6
	165–175	76	7.6
	Crude solid[a]	30	3.0
		997	**99.7**

[a] Recrystallization from alcohol gave a melting point of 87.8–88.5° C.

REASONS FOR LOW YIELDS—Two reasonable explanations are suggested for the failure to attain yields greater than 80–85 per cent in either the condensations in which the combining proportion of the reactants, or in the liquid reactions wherein an excess of bromobenzene was used: (1) use of an impure bromobenzene, and (2) destructive interaction between aluminum chloride and bromobenzene, with resultant deleterious effects on the yield of keto acid.

Upon ordinary distillation the crude bromobenzene gave the fractions which are shown in the distillation data for two lots of the material.

Both samples contained impurities which remained undistilled at 175° C. On cooling, this residue crystallized out almost entirely as flat white plates. When these crystals were recrystallized from alcohol, a yield of approximately 75 per cent white plates (m. p. 87.8–88.5° C.) was obtained. Bromine determinations according to Parr's method gave results which were in agreement with the formula for dibromobenzene. The crystal structure, melting point, and halogen content indicated, therefore, that the residue remaining in the distillation flask was principally *p*-dibromobenzene.

In this investigation an appreciable quantity of *p*-dibromobenzene was also found to be present in the Friedel and Crafts reaction mass. Its presence became manifest during the removal of the excess bromobenzene by distillation with steam, as some of it separated out as white plates in the condenser column. When the recovered solvent was redistilled it was found that the dark residue remaining after 175° C. had been reached contained *p*-dibromobenzene. The residues from the recovered solvent did not give such high yields of *p*-dibromobenzene (m. p. 87.8–88.5° C.) upon recrystallization as did the original crude liquid. The preceding facts indicate that *p*-dibromobenzene, like *p*-dichlorobenzene, does not react readily according to the Friedel and Crafts reaction and emerges practically unaltered. Its presence alone could not, therefore, account for the low yields when a large excess of bromobenzene was used. When combining proportions of the reactants were employed, however, the presence of the lighter boiling fractions, as well as that of higher brominated constituents, undoubtedly adversely affected the yields of 4′-bromo-2-benzoylbenzoic acid.

In the experimental work, runs 2, 6, 8, and 12 of Table II, in which the 155–160° C. fraction of bromobenzene was employed, the results showed that no benefits were derived from its use when a large excess of bromobenzene was present in the condensations. When monomolecular proportions of the reactants were employed, experiments 1 and 2 of Table III showed definitely that the results with crude bromobenzene were not so good as those obtained by the use of the 155–160° C. fraction.

Table III—Effect of Redistilling Bromobenzene in Preparation of 4′-Bromo-2-Benzoylbenzoic Acid

(Iron mill apparatus)

Phthalic anhydride used, 1 mole = 148 grams
Bromobenzene used, 1 mole + 5% = 165 grams

EXPT.	TIME	TEMP.	BROMOBENZENE USED	YIELD KETO ACID	
	Hours	*° C.*		*Grams*	*%*
1	6	30	Crude (see Distillation Data)	228	74.7
	42	50			
2	6	30	155–160° C. fraction	248	81.3
	42	50			

Since the quality of the bromobenzene used could not satisfactorily explain the failure to secure higher yields in the experiments containing it in large excess, the possibility of a reaction between the aluminum chloride and bromobenzene was considered. Dumreicher (*3*), in investigating the action of anhydrous aluminum chloride on halogenobenzenes, concluded that at 100° C., when the aluminum chloride was less than 50 per cent of the bromobenzene taken, up to 10 per cent of bromobenzene was decomposed according to the following reactions:

$$C_6H_5Br + Al_2Cl_6 = C_6H_5.Al_2Cl_5 + BrCl$$
$$C_6H_5Br + BrCl = C_6H_4Br_2 + HCl$$
$$C_6H_5.Al_2Cl_5 + HCl = C_6H_6 + Al_2Cl_6$$

Although benzene and dibromobenzene are unquestionably formed by the interaction of these substances, it is believed from the behavior of many compounds in the Friedel and Crafts synthesis that the essential feature of the reaction is the presence of halogens in an ionized state.

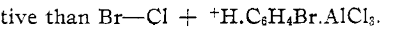
Copisarow (*2*) found the reaction between aluminum chloride and bromobenzene to be complex—"condensation, migration, and pyrogenic fission taking place"—the last being favored by extreme conditions of temperature and concentration of aluminum chloride. As a result of his observations, he concluded, "It is clear that in order to avoid side reactions in the Friedel-Crafts condensations, in which halogen derivatives of benzene are to be employed, chloro derivatives of benzene must be used with aluminum chloride."

EXPERIMENTS WITH 155–160° C. FRACTION OF BROMOBENZENE—With a view to ascertaining the magnitude of such adverse effects in the synthesis of 4′-bromo-2-benzoylbenzoic acid, a control experiment was performed in which the 155–160° C. fraction of bromobenzene was used. No phthalic anhydride was used, but otherwise it was identical with experiment 11 of Table II. The resulting reaction mass was red and viscous, a characteristic of all the condensation experiments under these conditions. It was hydrolyzed with cold dilute sulfuric acid, and the excess solvent was recovered by distillation with steam. The residue in the flask was cooled, filtered, and washed. A reddish black and practically odorless material, 66 grams, was left on the filter. On ignition, 3.2174 grams gave only 0.0879 gram of ash, or 2.73 per cent, showing it to be comparatively free of inorganic matter. The solvent recovered was only 315 grams of the 471 grams of bromobenzene initially used. When subjected to distillation, the recovered solvent, which originally distilled at 155–160° C., now gave the following fractions:

TEMPERATURE	DISTILLATE	DISTILLATE
° C.	*Grams*	*% of total*
90–100	43.5	13.8
100–150	70.5	22.4
155–160	41.0	13.0
160–175	145.0	46.0
Crude solid	5.5	1.7

The distillation data show that only 13 per cent of the recovered bromobenzene distilled over between 155° and 160° C. The quantity of higher boiling material was greater than that of the more volatile constituents. These data undoubtedly confirm Copisarow's observations regarding the interaction between aluminum chloride and bromobenzene in the Friedel and Crafts condensation.

The surprising circumstance in view of the comparatively small fraction of solvent, b. p. 155–160° C., recovered from the control, is the fact that yields of 4′-bromo-2-benzoylbenzoic acid in excess of 80 per cent of theory were actually obtained by means of the Friedel and Crafts reaction. It must be concluded, therefore, that under the conditions provided in these experiments the tendency to condensation with the formation of the aluminum complex of the keto acid is greater than the tendency towards destructive interaction. In other words, in the competition to combine with the aluminum chloride addition compound of bromobenzene, the aluminum chloride derivative of phthalic anhydride reacts more readily to form the keto acid complex than does the nascent halogen to form fission or condensation products. Thus,



$$C_6H_4\begin{cases}CO.Cl^- \\ COOAlCl_2\end{cases} + {}^+H.C_6H_4Br.AlCl_3$$

is more reactive than Br—Cl + $^+H.C_6H_4Br.AlCl_3$.

Table IV—Effect of Time and Temperature in Preparation of 4′-Bromo-2-Benzoylbenzoic Acid

Aluminum chloride used: C. P., 1 mole + 10% excess; technical, 1 mole + 15% excess

Phthalic anhydride used, 1 mole = 148 grams; bromobenzene used, 1 mole + 5% = 165 grams, b. p. 155° to 160° C.

EXPT.	Al_2Cl_6	TIME	TEMP.	YIELD OF KETO ACID		REMARKS
		Hours	*° C.*	*Grams*	*%*	
1	C. P.	48	40	226	74.1	Al_2Cl_6 added in three 100-gram portions at 3-hour intervals
2	C. P.	30	40	231	75.7	
3	Tech.	6 42	30 50	248	81.3[a]	Ratio agitating material (lbs.) to H_2O capacity (lbs.), 0.4919 (3 bars Fe)
4	Tech.	6 24	30 50	247.5	81.2[a]	
5	Tech.	6 18 6	25 40 70	212	69.5	Insoluble phthalides formed
6	Tech.	6 18 6	25 40 50	253	82.5	Average of two results

[a] Yield corrected for exudation.

Table V—Effect of Agitation in Preparation of 4′-Bromo-2-Benzoylbenzoic Acid

Aluminum chloride used, 1 mole + 15% excess

Phthalic anhydride used, 1 mole = 148 grams; bromobenzene used, 1 mole + 5% = 165 grams, b. p. 155° to 160° C.

EXPT.	Al_2Cl_6	TIME	TEMP.	EXUDATION	RATIO AGITATING MATERIAL TO H_2O CAPACITY	YIELD OF KETO ACID	
		Hours	*° C.*	*Grams*		*Grams*	*%*
1	Tech.	6 18 6	25 40 50	34	0.674[a]	245	80.3[c]
2	Tech.	6 24	30 50	None	0.5525[a]	251	82.3
3	Tech.	6 24	30 50	26	0.4919[b]	247.5	81.2[c]
4	C. P.	6 24	25 50	None	0.5718[a]	258	84.6
5	C. P.	6 24	30 50	23	0.4919[b]	248	81.3[c]

[a] Fe blocks.
[b] Three bars.
[c] Yield corrected for exudation.

Table VI—Effect of Quantity of Aluminum Chloride in Preparation of 4′-Bromo-2-Benzoylbenzoic Acid

Phthalic anhydride used, 1 mole = 148 grams; bromobenzene used, 1 mole + 5% = 165 grams, b. p. 155° to 160° C.

EXPT.	Al_2Cl_6 (C. P.)	TIME	TEMP.	YIELD OF KETO ACID	
		Hours	*° C.*	*Grams*	*%*
1	1 mole + 10% excess	6 18 6	25 40 50	244	80.0
2	1 mole + 15% excess	6 24	25 50	258	84.6
3	1 mole + 10% excess	6 18 6	35 40 65	256.5	84.1[a]
4	1 mole + 15% excess	6 18 6	25 40 50	258	84.6

[a] Yield corrected for exudation.

Table VII—Effect of Portioning Aluminum Chloride in Preparation of 4′-Bromo-2-Benzoylbenzoic Acid

Aluminum chloride used, 1 mole + 10% excess C. P.
Phthalic anhydride used, 1 mole = 148 grams; bromobenzene used, 1 mole + 5% = 165 grams, b. p. 155° to 160° C.

EXPT.	TIME	TEMP.	YIELD OF KETO ACID	
	Hours	*° C.*	*Grams*	*%*
1	48	40	245	80.3
2[a]	48	40	226	74.1

[a] Al_2Cl_6 added in three portions, 3-hour intervals.

STUDY OF VARIOUS FACTORS INVOLVED IN PREPARATION OF 4′-BROMO-2-BENZOYLBENZOIC ACID—A final series of experiments was made in an attempt further to inhibit the deleterious side reaction between aluminum chloride and bromobenzene. A study was made of the various factors involved in the keto acid synthesis, employing molecular proportions of the reactants (1) effect of using technical bromobenzene instead of the 155–160° C. fraction; (2) effect of time and temperature of reaction; (3) effect of varying the grinding mechanism; (4) effect of varying the quantity of aluminum chloride; and (5) effect of adding the aluminum chloride in portions. The resulting data are given in Tables III to VII.

Mention has previously been made of the fact that technical bromobenzene gave inferior yields when approximately the combining proportions of the reactants were used, as shown by data in experiments 1 and 2 of Table III.

By comparing experiment 1 with 2, and 3 with 4 in Table IV, it can be seen that no increase in yield is obtained by prolonging the reaction time beyond 30 hours. Experiments 5 and 6 disclose the deleterious effect of a sudden increase to a relatively high final temperature. The yield dropped off and insoluble phthalides were found in the ammoniacal solution of the keto acid.

The experiments in Table V show no very marked differences in yield on account of the changes in the grinding mechanism; the best results were obtained in those runs in which none of the reaction mass exuded through the hydrogen chloride vent.

The results in Table VI and elsewhere indicate that technical aluminum chloride served as well as the C. P. screened material when the combining proportions of the reactants were used. The experiments in Table VII reveal that the best results were obtained by adding all the aluminum chloride at the start of the reaction.

Considerable previous experience in the preparation of keto acids had demonstrated the advantages of operating at the lowest practical temperature range. Copisarow (*2*) had further shown that the decomposition of bromobenzene was favored by an elevation of temperature. In this investigation the results in general show that operations conducted at a lower temperature over longer periods of time were not altogether successful in inhibiting deleterious side reactions.

Conversion of 4′-Bromo-2-Benzoylbenzoic Acid into 2-Bromoanthraquinone

A large quantity of 4′-bromo-2-benzoylbenzoic acid, m. p. 170.0° to 170.5° C., was accumulated as a result of the experiments in the preparation of the keto acid. This material was thoroughly mixed and the composite used for the experiments on ring closure.

EFFECT OF TIME AND TEMPERATURE—Some preliminary experiments were first made to determine the time and temperature factors for complete conversion with various proportions of sulfuric acid. The 2-bromoanthraquinone was precipitated in a crude state by diluting the reaction mass with a large quantity of water. The dilute acid was removed by filtration, and the grayish product was washed with hot water and dilute alkali. The absence of keto acid in the boiling alkaline wash waters was taken to be indicative of complete conversion of the keto acid to anthraquinone. The melting point of the crude 2-bromoanthraquinone thus obtained was 204–205° C., which was identical with the constant obtained by Ullmann and Sone (*17*) on their recrystallized product.

EFFECT OF RESIDUAL ACIDITY—The information thus obtained regarding the factors insuring complete ring closure was utilized in making the following series of experiments to ascertain the most desirable conditions for separating the 2-bromoanthraquinone from the sulfuric acid used for dehydration. The procedure involved the fractional crystallization of the product by reducing the acidity of the reaction mass from 95 per cent sulfuric acid to the desired residual acidity with diluted sulfuric acid. This method was found to give eminently satisfactory results in the preparation of 2-chloroanthraquinone (*7*) and 4′-chloro-2-phenylanthraquinone (*5*). The main product was thus precipitated, while most of the more soluble impurities remained in solution. From Table VIII it can be seen that increased purity of the 2-bromoanthraquinone is secured by sacrifices in the yield of product.

The charges were heated in agitated vessels on an electrically heated apparatus. The temperature was controlled to ±2° C. of the desired point by means of external resistance coils. At the end of each run the contents were cooled to about 70° C., and the calculated quantity of diluting acid added with constant stirring. The 2-bromoanthraquinone was precipitated as yellow needles, the intensity of the yellow color decreasing with the addition of more dilute acid. The charge was put on a filtros filter and the sulfuric acid removed by suction. The product was washed first with 100 cc. of 50 per cent sulfuric acid to displace the mother liquor, and then with hot water until only faintly acid. The material was then boiled in a 2 per cent sodium hydroxide solution and after filtering was washed with hot water.

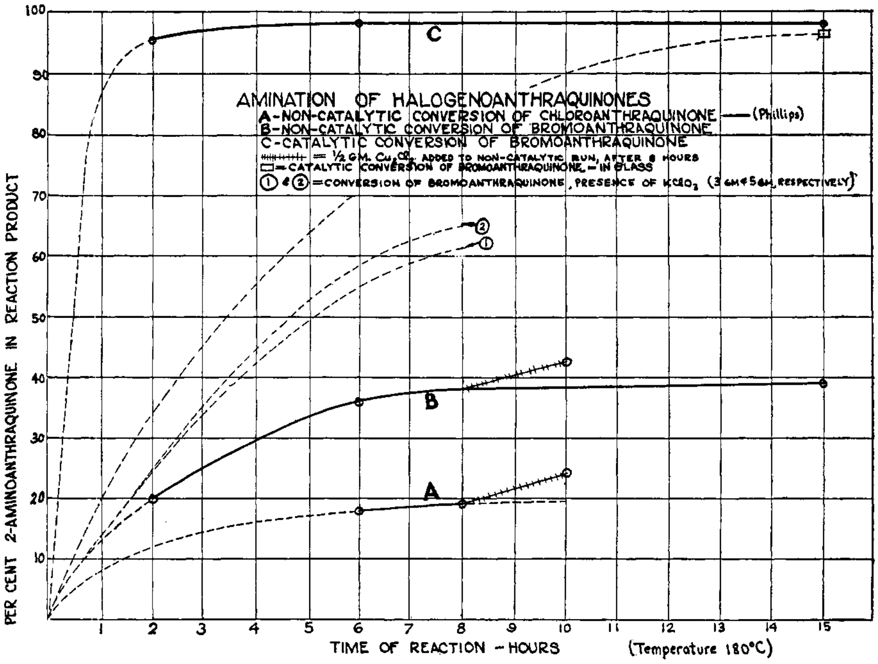
Table VIII—Effect of Residual Acidity in Preparation of 2-Bromoanthraquinone from 4′-Bromo-2-Benzoylbenzoic Acid

4′-Bromo-2-benzoylbenzoic acid taken, 100 grams; m. p. 170–170.5° C.
Sulfuric acid, 95% H_2SO_4
100 cc. of 50% H_2SO_4 used for washing precipitates; 25% H_2SO_4 used for making 50 % residual acidities; 50% H_2SO_4 used for making higher residual acidities

Expt.	H_2SO_4 Ratio	Time	Temp.	Residual Acidity	Yield	M. P.[a]
		Hours	*° C.*	% H_2SO_4	%	*° C.*
A-1	4:1	5	150	80	92.3	206.5–206.9
A-2	4:1	5	150	70	93.6	206.0–206.3
A-3	4:1	5	150	50	94.3	205.5–205.8
B-1	6:1	4	140	80	94.0	208.8–209.1
B-2	6:1	4	140	70	94.3	208.3–208.8
B-3	6:1	4	140	50	95.5	208.0–208.5
C-1	10:1	4	135	86	86.0	209.3–209.5
C-2	10:1	4	135	80	89.3	209.1–209.3
C-3	10:1	4	135	70	92.4	208.8–209.0
C-4	10:1	4	135	60	93.5	208.5–208.8
C-5	10:1	4	135	50	95.1	208.2–208.6

[a] Melting point pure 2-bromoanthraquinone, 209.5° C. (cor.).

From the data recorded in Table VIII it can be seen that the purity of the 2-bromoanthraquinone, as indicated by the higher melting point, varies directly with the residual acidity of the sulfuric acid. The yields, however, vary inversely with the final concentration of acid, the best yields being obtained with more dilute acids. The choice of operating conditions will, of course, finally rest with the producer. It is also evident from the foregoing data that the employment of a 4:1 ratio of sulfuric acid is productive of 2-bromoanthraquinone of inferior quality, with generally lower yields. With the same final acid concentration the best product is obtained when a 10:1 acid ratio is used. Subsequent experiments for stock purposes, in which conditions were the same as those in experiments B-1 and C-1 of Table VIII, except that 300- to 500-gram charges were used, gave an increase in yield of 2 to 5 per cent.



Properties of 2-Bromoanthraquinone—When recrystallized from toluene, 2-bromoanthraquinone was obtained as fine yellow needles which gave a constant melting point of 209.6° C. (cor.). The material separated by fractional crystallization in experiment C-1 gave practically the same constant. 2-Bromoanthraquinone is readily soluble in toluene and chlorobenzene. It produces a red vat with alkaline hydrosulfite. Bromine determinations according to Parr's method gave results which were in agreement with the formula for bromoanthraquinone.

Substance: 0.2534, 0.3322. AgBr: 0.1653, 0.2165
Calculated for $C_{14}H_7O_2Br$: 27.85 per cent Br; found, 27.77, 27.74 per cent

Preparation of 2-Aminoanthraquinone

A considerable quantity of 2-bromoanthraquinone, prepared according to experiments B-1 and C-1, Table VIII, was blended as stock material for carrying out the work on its conversion to the amino derivative. This composite was a fluffy, matted, yellow product, which melted at 208.8–209.3° C. The equipment used was essentially similar to that described previously (*7, 13*), but contained a number of added devices to insure automatic control for time and temperature. A somewhat detailed description of the present apparatus has been published elsewhere (*6*).

Preliminary experiments at 180° C. showed conclusively that bromine could be replaced from halogen anthraquinone much more readily than chloride (see illustration). Furthermore, analytical and microscopic examination of the amino compound showed that it was quite pure and essentially free of the hydroxy and imino impurities which characterized the material obtained under similar conditions from the chloro derivative.

The fact that 2-bromoanthraquinone reacts readily with ammonia to form the amine, whereas the chloro compound is not so easily converted, appears not to be in accord with any general rule. Sprung (*15*), who has investigated the reactivities of chloro and bromo aromatic compounds, particularly the halogen nitrobenzenes and halogen benzoyl chlorides, states that "about as many pairs of compounds have been investigated in which the bromine compound has shown a greater reactivity than the chlorine compound as of those in which the reverse relationship has been found to hold."

Copper salts were found to be of unquestionable value in promoting the formation of 2-aminoanthraquinone from the bromine derivative. Copper salts made possible the use of an operating temperature as low as 150° C. as compared with 215° C. which was required for the treatment of the chloro-2-phenylanthraquinones (*5*). The employment of copper compounds was furthermore found to be instrumental in the production of a light brown 2-aminoanthraquinone of high purity.

The ammonolysis of the bromine compound was given detailed consideration, since it brought out two factors of practical importance—namely, the feasibility of producing a high-grade 2-aminoanthraquinone; and the behavior of metal catalysts in the amination process.

In the following experiments the autoclave charge was first cooled and then put on a filter. The material was thoroughly washed with hot water and then dried to constant weight. No purification or other treatment was necessary, since titration with sodium nitrite, and use in the preparation of vat colors showed that the product made under optimum conditions was essentially free of deleterious impurities.

EFFECT OF CATALYSTS—The first series of experiments was run to determine the reactivity of 2-bromoanthraquinone in the presence of copper salts or nitrobenzene as catalysts. From these data, which are set out in Table IX, it can be seen that the presence of a catalyst is essential for complete conversion. It is interesting to observe that increased quantities of copper catalyst within the limits noted had practically no effect on the purity of the 2-aminoanthraquinone but appeared to increase the yields. Subsequent experiments showed that an increase in the quantity of catalyst up to certain limits was distinctly beneficial when the size of the bromoanthraquinone charge was increased.

Table IX—Effect of Catalyst in Preparation of 2-Aminoanthraquinone

2-Bromoanthraquinone taken, 0.05 mole = 14.35 grams
28.3% NH_4OH, 250 grams
Temperature, 180° C.
Time, 15 hours
Yield theory, 11.15 grams

EXPT.	CATALYST		YIELD	PURITY	REMARKS
		Grams	*%*	*%*	
1	None	None	87.4	38.7	Dark product
2	Nitrobenzene	14.4	80.2	88.8[a]	Dark product
3	Cu_2Cl_2	0.5	91.8	98.0	
4	Cu_2Cl_2	1.0	94.0	98.2	
5	Cu_2Cl_2	2.0	94.2	98.2	
6	Cu_2O	0.36	91.8	98.4	
7	Cu_2O	0.72	92.3	98.5	
8	Cu_2O	1.0	93.4	98.4	

[a] Much better results are obtained when 28.7 grams nitrobenzene are used. See Table II.

EFFECT OF TEMPERATURE—The feasibility of aminating at comparatively low temperature is shown by the data in Table X. This is a matter of considerable industrial importance, since it is more desirable to operate at pressures from 300 to 400 pounds than at 1000 pounds per square inch. A longer operating cycle is manifestly required when aminating at 150° C., because the bright orange-brown product contained some unconverted bromoanthraquinone.

Table X—Effect of Temperature of Amination in Preparation of 2-Aminoanthraquinone

2-Bromoanthraquinone taken, 14.35 grams
28.3% NH_4OH, 250 grams
Yield theory, 11.15 grams

EXPT.	TIME	TEMP.	CATALYST		YIELD	PURITY
	Hours	*° C.*		*Grams*	*%*	*%*
1-A	6	180	None	None	92.1	35.9
1-B	6	150	None	None	100+	1.97
2-A	6	180	Cu_2Cl_2	0.5	93.2	98.0
2-B	6	150	Cu_2Cl_2	0.5	100+	67.2
3-A	15	180	Cu_2Cl_2	0.5	91.8	98.0
3-B	15	150	Cu_2Cl_2	0.5	96.9	94.1
4-A	15	180	Cu_2Cl_2	1.0	94.0	98.2
4-B	15	165	Cu_2Cl_2	1.0	94.6	97.8
4-C	15	150	Cu_2Cl_2	1.0	96.0	94.0
5-A	15	180	Cu_2O	0.36	91.8	98.4
5-B	15	150	Cu_2O	0.36	96.5	95.0
6-A	15	180	Cu_2O	0.72	92.3	98.5
6-B	15	165	Cu_2O	0.72	93.3	96.8
6-C	15	150	Cu_2O	0.72	95.6	95.6

From the foregoing data it is definitely established that the reaction proceeds much more rapidly at 180° C. than at 150° C. It appears also that equivalent weights of cuprous oxide are very slightly more potent catalytically than cuprous chloride.

EFFECT OF REACTION TIME—The effect of variations in the reaction time is shown in Table XI. In the absence of a catalyst a maximum conversion of about 38.7 per cent is obtained, the product being black and more or less carbonized. In the presence of a cuprous catalyst the reaction proceeds rapidly to completion. Experiment 2-C at 180° C. for 2 hours shows a conversion equivalent to experiment 3-A, which was run 15 hours at 150° C. It was found, however, that a lighter colored product was invariably obtained when the operation was conducted at 150° or 165° C.

Table XI—Effect of Reaction Time on Preparation of 2-Aminoanthraquinone

2-Bromoanthraquinone taken, 14.35 grams
28.3% NH_4OH, 250 grams
Yield theory, 11.15 grams

EXPT.	TIME	TEMP.	CATALYST		YIELD	PURITY
	Hours	*° C.*		*Gram*	*%*	*%*
1-A	15	180	None	None	87.4	38.7
1-B	6	180	None	None	92.1	35.9
1-C	2	180	None	None	100+	19.7
2-A	15	180	Cu_2Cl_2	0.5	91.8	98.0
2-B	6	180	Cu_2Cl_2	0.5	93.2	98.0
2-C	2	180	Cu_2Cl_2	0.5	94.4	95.4
3-A	15	150	Cu_2Cl_2	0.5	96.9	94.1
3-B	6	150	Cu_2Cl_2	0.5	100+	67.2
4-A	15	150	Cu_2O	0.36	96.5	95.0
4-B	6	150	Cu_2O	0.36	100+	70.8

EFFECT OF RATIO OF 2-BROMOANTHRAQUINONE TO AMMONIA—Practical considerations made it desirable to increase the quantity of 2-bromoanthraquinone in the charges with respect to the ammonia used. A series of experiments was run with this end in view. The data in Table XII show clearly that the purity of the 2-aminoanthraquinone decreases as the quantity of halogen derivative is increased. It appears also that an increase in the amount of catalyst used under such conditions (experiments 3-B and 4) is helpful in accelerating the reaction.

Table XII—Effect of Ammonia Ratio in Preparation of 2-Aminoanthraquinone

Temperature, 180° C.
Time, 15 hours
28.3% NH_4OH, 250 grams

EXPT.	BROMOANTHRAQUINONE	CATALYST	YIELD	PURITY
	Grams	*Grams*	*%*	*%*
		Cu_2O		
1-A	14.35	0.36	91.9	98.5
1-B	28.70	0.36	95.3	95.0
2-A	35.87	1.44	95.4	93.0
2-B	43.05	1.44	97.1	90.6
		Cu_2Cl_2		
3-A	14.35	0.5	92.0	98.0
3-B	28.70	0.5	95.1	92.2
4	28.70	1.0	95.5	95.0
5	35.87	2.0	96.3	92.5

From theoretical considerations it would appear that the use of a stronger ammonia liquor—i. e., a higher ammonia concentration—would lead to better results during ammonolysis. Under such conditions the partial pressure, and hence activity, of the dissolved ammonia would be proportionately greater than the partial pressure of water. It is obvious from a consideration of the law of mass action that bromoanthraquinone will undergo ammonolysis or hydrolysis in proportion to the relative partial pressures of ammonia and water. One must therefore expect to find evidence of the influence of dissociated water in the products of the reaction. Thus, when aqueous ammonia is employed in the manufacture of aniline from chlorobenzene, phenol is always found as one of the associated products of ammonolysis.

EFFECT OF AMMONIA CONCENTRATION—In experiments 3, 4, 5, and 6 (Table XIII), practically the same quantity of ammonia is employed, yet there is a distinct retrogression in the purity of the amine. From an examination of the data it becomes apparent that the employment of a more concentrated ammonia solution leads to the formation of a purer amino compound. The application of the law of mass action in this process has been found in other similar reactions to be the only satisfactory way of increasing the purity of the product.

Table XIII—Effect of Ammonia Concentration in Preparation of 2-Aminoanthraquinone

2-Bromoanthraquinone taken, 28.7 grams
Temperature of amination, 165° C.
Time, 20 hours
Cu_2Cl_2 as catalyst, 1 gram

Expt.	Ammonium Hydroxide	Ammonia		Yield	Purity
	Grams	%	*Grams*	%	%
1	250	35.0	87.5	96.5	97.2
2	225	35.0	78.7	96.2	97.0
3	200	35.0	70.0	96.7	96.9
4	250	28.3	70.8	96.3	96.0
5	328	22.0	72.2	96.0	94.2
6	450	16.0	72.0	94.8	91.8

CATALYTIC ACTIVITY OF METAL AMMONIUM COMPOUNDS—Considerable discussion has taken place regarding the efficacy of various copper salts in the ammonolysis of halogen compounds requiring the presence of a catalyst (*4, 8, 11, 13, 14*). There appears to be substantial evidence to show that copper compounds initiate an electrolytic activity which promotes amination. An iron autoclave containing ammonia liquor and a copper electrode is indeed a voltaic cell. When the copper electrode is attached to the negative pole and the iron autoclave to the positive pole of a voltmeter, an electric current is set up. The e. m. f. of the cell will increase with the temperature, and with the cuprammonium $[Cu(NH_3)_2^+]$ ions in solution. These complex ions are more reactive than ordinary copper ions, for their hydroxide and chloride salts are very soluble.

Table XIV—Catalytic Activity of Metal Ammonium Compounds in Preparation of 2-Aminoanthraquinone

2-Bromoanthraquinone taken, 28.7 grams
28.3% $NH_4 \cdot OH$, 250 grams
Temperature, 165° C.
Time, 20 hours

Expt.	Catalyst		Yield	Purity	Remarks
		Grams	%	%	
1	$Fe(NH_4)_2(SO_4)_2$	10.0			Complete decomposition
2	NiO	0.6	100+	30.5	
3	$Co(CH_3COO)_2$	1.5	100+	31.2	
4	Cu powder, red	15.0	90.8	80.0	Amino compd. boiled with dil. HNO_3 to remove excess of copper
5	Cu gauze	21.3	98.5	85.9	
6	Cu_2Cl_2	1.0	96.3	96.0	
7	Cu_2O	0.72	96.5	96.8	
8	$CuCl_2 \cdot 2H_2O$	3.50	97.9	93.0	
9	Cu_2O	4.35	94.2	97.8	
10	Cu_2O	4.35	95.5	92.6	Contaminated with copper
	Cu tube	35.59			
11	AgCl	8.0	100+	70.0	Contaminated with AgBr

In Table XIV are recorded data relating to the use of various catalysts capable of forming ammonium complexes, such as ammono argentic chloride $[Ag(NH_3)_2^+Cl^-]$ or ammono nickel hydroxide $[Ni(NH_3)_6^{++}(OH)^{--}]$. The efficacy of such metal amines as catalysts is attributed to an increased electrolytic dissociation due to the combination of the solute molecule with molecules of the solvent (*1, 10*). This association keeps more ammonia in solution in contact with the halogeno anthraquinone. Catalysis is believed to take place on the surface of the metal as an adsorption process, and for this reason cuprous compounds have been found to be more effective than cupric compounds. It has been ascertained in this laboratory that the compounds of metals following hydrogen in the electromotive series, such as copper and silver, can be used advantageously as a catalyst in the substitution of aromatic halogen.

The previous work had demonstrated that ammonolysis proceeded very rapidly at 180° C. with the production of a reddish brown amino compound, whereas a golden-brown 2-aminoanthraquinone was obtained by aminating at 150° C. A final series of runs was made at 165° C., with 28.7 grams of bromoanthraquinone, in an attempt to secure results of more practical interest. The ratio of ammonia liquor to halogen anthraquinone was approximately 10:1, which is in line with most industrial operations of this character. The results of these experiments are recorded in Table XV.

Table XV—Effect of Type of Catalyst in Preparation of 2-Aminoanthraquinone

2-Bromoanthraquinone taken, 28.7 grams
28.3% NH_4OH, 275 grams
Temperature, 165° C.
Time, 20 hours

Expt.	Catalyst		Yield	Yield	Purity
		Grams	*Grams*	%	%
1	Nitrobenzene	28.7	20.75	92.8	97.8
2	Cu_2Cl_2	1.0	21.48	96.3	95.0
3	Cu_2Cl_2	1.5	21.49	96.3	95.5
4	Cu_2Cl_2	2.0	21.69	97.2	95.9
5	Cu_2Cl_2	6.0	21.77	97.5	96.1
6	Cu_2O	0.72	21.55	96.7	96.6
7	Cu_2O	1.1	21.34	95.7	97.3
8	Cu_2O	1.45	21.20	95.1	97.6
9	Cu_2O	4.35	21.00	94.2	97.8
10	Cu_2O	4.35	21.13	94.8	92.6
	Cu tube	35.59			

The 2-aminoanthraquinone obtained from all the abovementioned experiments (except 1, 5, 9, and 10) was a golden-brown uniform product. Under the microscope the products showed no evidence of the dark spots or streaks which characterized the amine previously obtained from 2-chloroanthraquinone (*7*). The purity of the 2-aminoanthraquinone was higher in the charges containing cuprous oxide as catalyst. As the quantity of catalyst was increased, there was a gradual increase in the purity of the product and in experiments 6 to 8, inclusive, a compensating diminution in yield. When the best products were dissolved in sulfuric acid, they produced a greenish coloration which was indicative of a high degree of purity. When properly diazotized, a clear yellowish solution was obtained, through which it was possible to read printed matter. Experiment 1, in which nitrobenzene was the oxidant, gave a reddish brown crystalline product of high purity. The products from experiments 9 and 10 were dull, and the last contained traces of copper.

Conclusion

The preparation of 2-aminoanthraquinone from bromobenzene and phthalic anhydride is of considerable practical importance. It offers a procedure for obtaining 2-aminoanthraquinone directly in a high state of purity. On account of the relative ease in replacing the halogen atom from 2-bromoanthraquinone, it also looms up as a vat dye intermediate of industrial importance, for the preparation of anthraquinone-imide derivatives. In spite of the apparent and considerable disadvantage which accrues from the employment of the costly bromobenzene, the procedure provides a method of obtaining 2-bromoanthraquinone and 2-aminoanthraquinone with high yields and in a comparatively pure state. The ultimate success of this synthesis will depend on economic factors which must be worked out by the interested concerns.

Literature Cited

(1) Bodlander, G., and Fittig, R., *Z. physik. Chem.*, **39**, 597 (1902).
(2) Copisarow, M., and Long, C. N. H., *J. Chem. Soc.*, **119**, 442 (1921).
(3) Dumreicher, O. v., *Ber.*, **15**, 1866 (1882).
(4) Groggins, P. H., *Chem. Met. Eng.*, **36**, 273 (1929).
(5) Groggins, P. H., IND. ENG. CHEM., **22**, 620 (1930).
(6) Groggins, P. H., and Hellbach, R., *Chem. Met. Eng.*, **37**, 693 (1930).
(7) Groggins, P. H., and Newton, H. P., IND. ENG. CHEM., **21**, 369 (1929).
(8) Hale, W. J., and Britten, J., U. S. Patent 1,607,824 (Nov., 1926).
(9) Hotz, E., U. S. Patent 1,690,785 (1928).
(10) Kendall, J., and Booge, J. E., *J. Am. Chem. Soc.*, **39**, 2523 (1917).
(11) McMaster, L., and Steiner, A., IND. ENG. CHEM., **22**, 547 (1930).
(12) Pechmann, H. v., *Ber.*, **12**, 2126 (1879).
(13) Phillips, M., IND. ENG. CHEM., **17**, 721 (1925).
(14) Quick, A. J., *J. Am. Chem. Soc.*, **42**, 1033 (1920).
(15) Sprung, M., *Ibid.*, **52**, 1640 (1930).
(16) Stevens, H. N., *Ibid.*, **45**, 1950 (1921).
(17) Ullmann, F., and Sone, M., *Ann.*, **380**, 357 (1911).