

The Orientation and Reactivity in Nucleophilic Addition to Arynes Possessing Charged Substituents. I. Orientation and Reactivity in Nucleophilic Addition to Benzyne-3- and -4-carboxylate^{1a}

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Received July 15, 1968

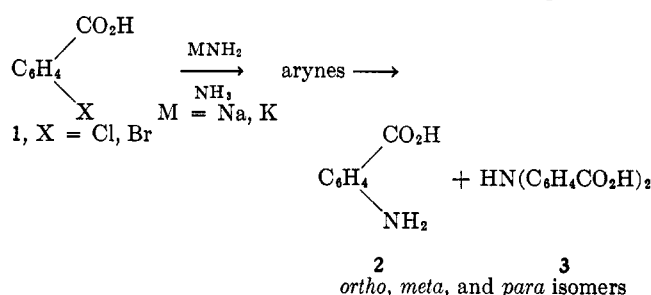
The aminobenzoic acid *ortho:meta* and *meta:para* ratios have been obtained from the amination of halobenzoic acids in liquid ammonia. The aminobenzoic acid *ortho:meta* ratio changed from 36:64 to 17:83 whereas the *meta:para* ratio changed from 85:15 to 75:25 as the amide ion concentration was varied from 1.5×10^{-3} (sodamide) to 1.7 M (potassium amide). Also, certain anions of active hydrogen compounds have been found to add indiscriminantly to benzyne-4-carboxylate in contrast to that found previously for anion addition to benzyne-3-carboxylate.⁶ An explanation in terms of the relative reactivities of the various nucleophiles and the relative contribution of the field, resonance, and inductive effects of the carboxylate group is presented.

Since the inception of the aryne postulate, there have been many investigations concerning the orienting effect of neutral substituents on nucleophilic additions to monosubstituted arynes.² On the other hand, only one investigation concerning the orienting effect of arynes containing charged substituents (O^- and NH^- directly attached to the ring) has been reported.³ In that study the arynes were generated from the reaction of the corresponding halophenols or haloanilines with potassium amide in liquid ammonia. However, the low yields (20%) of the aminated products precluded careful evaluation of orientation effects.

Arynes with substituents containing a charged atom γ (or higher) to the aromatic ring have been readily generated by Huisgen⁴ and Bunnett.⁵ However, the facile intramolecular addition of the side chain substituent to the "triple bond" precluded any orienting study in these systems.

In the course of our investigation of the extension of the general benzyne-carbanion phenylation reaction, we observed that the reaction of *o*-chlorobenzoic acid with sodamide and several anions of active hydrogen compounds in liquid ammonia produced the corresponding *m*-carboxyphenylated products in 49–71% yields (no *ortho* isomer) plus mixtures of *o*- and *m*-aminobenzoic acids in 10–20% yields.⁶ These results indicated that (1) an aryne possessing a substituent containing a negatively charged atom β to the ring could be readily generated; (2) only products resulting from external nucleophilic addition (no intramolecular cyclization products) were obtained; and (3) the carboxylate group was exhibiting an unusual orienting effect. Therefore, an investigation of the orienting effect of arynes possessing substituents with charged atoms β to the ring was undertaken.

This paper reports the results of a study of the action of sodamide and potassium amide on *o*-, *m*-, and *p*-chloro- and -bromobenzoic acids (1). The products



were found to be a mixture of the isomeric aminobenzoic acids (2) and new compounds whose structures were shown to be certain isomeric dicarboxydiphenylamines 3 (iminodibenzoic acids). The isomer distribution of both the aminobenzoic acids and the specific iminodibenzoic acids were determined in order to evaluate the orienting effect of the carboxylate group on the mode of amide ion and ammonia addition to the benzyne ring.

Similarly, the reaction of *p*-chlorobenzoic acid with certain active hydrogen compounds was studied in order to determine the orientation of anion addition to benzyne-4-carboxylate.

Experimental Section⁷

Materials.—The halobenzoic acids were obtained as commercial samples from Matheson Coleman and Bell and subsequently purified by crystallization from methanol-water. The melting points of the purified acids were *o*-chloro, 142°; *m*-chloro, 158°; *p*-chloro, 242°; *o*-bromo, 148–150°; *m*-bromo, 155°; *p*-bromo, 252°. Anhydrous liquid ammonia was obtained from Van Waters Co., Dallas, Texas, and used as received. Reagent grade sodium and potassium metals were obtained from J. T. Baker. All other chemicals employed were either reagent grade or the best research grade obtainable from commercial sources and were distilled or recrystallized at least once before using.

General Procedure for the Reaction of Halobenzoic Acids and Alkali Amides in Liquid Ammonia.—The alkali amide was prepared *in situ* by the addition of 0.6 g-atom of the corresponding alkali metal and 0.1 g of ferric nitrate to 200 ml of liquid ammonia. Then the appropriate halobenzoic acid (0.1 mol) was added in portions over a period of 5–7 min to a stirred suspension (in the case of sodamide) or solution (in the case of potassium amide) of amide. After the mixture was stirred and refluxed for 1 hr, 0.4 mol of ammonium chloride was added and the ammonia was removed by heating with a steam bath. Ether

(1) (a) Supported in part by Grant No. N-118 from the Robert A. Welch Foundation, Houston, Texas; (b) Robert A. Welch Predoctoral Fellows.

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(4) R. Huisgen and H. König, *Angew. Chem.*, **69**, 268 (1957); *Chem. Ber.*, **92**, 203, 429 (1959); R. Huisgen, H. König, and N. Blecker, *ibid.*, **92**, 424 (1959); R. Huisgen, H. König, and A. R. Lepley, *ibid.*, **93**, 1496 (1960).

(5) B. F. Hrtutford and J. F. Bunnett, *J. Amer. Chem. Soc.*, **80**, 2021, 4745 (1958); **83**, 1691 (1961).

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(7) All melting points are uncorrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

TABLE I
R_f VALUES FOR THE ISOMERIC IMINODIBENZOIC ACIDS

| Isomer | R _f |
|--------|----------------|
| 2,2' | 0.27 |
| 2,3' | 0.52 |
| 3,3' | 0.37 |
| 2,4' | 0.58 |
| 3,4' | 0.35 |
| 4,4' | 0.15 |

was added to the residue and the stirred suspension was refluxed for 1 hr to ensure the removal of most of the ammonia. (Failure to remove most of the ammonia resulted in gumlike precipitates produced further along in the work-up procedure.) After decanting most of the ether solution, the residue was dissolved in ca. 250 ml of water, and the resulting solution was filtered. On acidification of this solution to pH 1 with cold (0°) 6 *N* hydrochloric acid, the iminodibenzoic acids and starting halobenzoic acid precipitated. The precipitate was collected by filtration, air dried, and analyzed by tlc techniques described below. The acidic filtrate, containing the isomeric aminobenzoic acids, was analyzed directly by the procedure of Biehl and Li.⁸ No attempt was made to isolate the aminobenzoic acids.

General Procedure for the Reaction of *p*-Chlorobenzoic Acid with Active Hydrogen Compounds.—The aryne reactions using 0.1 mol of *p*-chlorobenzoic acid, 0.3 mol of active hydrogen compound and 0.6 mol of sodamide in 500 ml of liquid ammonia were carried out in a similar manner described above for the reaction of halobenzoic acids and alkali amides.

The quantitative determination of most of the *m*- and *p*-carboxyphenylated compounds obtained upon acidification of the basic reaction aqueous solution was accomplished by glpc analysis of the corresponding methyl esters. However, the mixture containing *m*- and *p*-carboxyphenylacetoneitriles was analyzed by infrared spectrophotometry. Details of the analytical methods are described below.

Analysis of the Iminodibenzoic Acids Mixtures.—Individual spots of the mixture and known iminodibenzoic acids (dissolved in a minimum amount of DMF) were placed on a silica thin layer chromatogram plate (Distillation Products, Inc.) and the chromatogram was developed with a benzene/dioxane/acetic acid (90/24/4) solvent system. The components in the mixture were identified by comparing their R_f values with those of the known compounds (Table I). Estimation of the amount of each component in the mixture was accomplished by utilizing the graphical method of Purdy and Truter.⁹

Analysis of the Carboxyphenylated Active Hydrogen Compound Mixtures. A. Gas-Liquid Chromatographic Analysis.—The acids in the solid mixtures were converted into their methyl esters by treatment with an excess of boron trifluoride-methanol solution¹⁰ (Applied Scientific Lab). The methyl esters were analyzed using a MicroTek Model GC-1600 gas chromatograph equipped with a hydrogen flame detector and a 5-ft column containing 3% SE-30 on Chromoport 80-100. The analyses were conducted at a column temperature of 110° using a helium gas flow rate of 120 ml/min and inlet temperature of 250°. The chromatographic bands were identified by comparing their retention times with those of authentic samples. Percentages of each compound were calculated from the areas of the bands. These areas were assumed to be equal to the peak height times the width at one-half peak height. Molar response ratios were determined and the observed areas were corrected as necessary.

B. Infrared Spectrophotometric Analysis.—A Beckman IR5 spectrophotometer was employed for the analysis of the reaction mixture containing α -cyano-*m*- and α -cyano-*p*-toluic acids. Potassium bromide pellets of the mixture were prepared and the infrared spectra were recorded. The percentages of each isomer were obtained by comparing the peak heights at 820 (*meta* isomer) and 833 cm⁻¹ (*para* isomer) with those obtained using known mixtures of authentic samples.¹¹

Preparation of Authentic Samples of the Isomeric Iminodibenzoic Acids.—The 2,2', 2,3', and 2,4'-iminodibenzoic acids

were prepared by the Ullmann reaction¹² whereas the 4,4' acid was prepared according to the procedure of Kizber.¹³ The 3,3' and 3,4' acids could not be prepared by the above procedures. However, the acids could be prepared using a modified Ullmann reaction which is described below.

A. 3,3'-Iminodibenzoic Acid.—A mixture consisting of 10 g (0.05 mol) of *m*-bromobenzoic acid, 6.9 g (0.05 mol) of *m*-aminobenzoic acid, 1 g of copper, 17.3 g (0.13 mol) of anhydrous potassium carbonate and 200 ml of dimethyl sulfoxide was heated at 100–120° with stirring for 3 days. The mixture was then cooled to room temperature, treated with charcoal, and filtered. On acidification of the mother liquor with 200 ml of 6 *N* hydrochloric acid, the impure product precipitated. The crude 3,3' acid was collected by filtration, dried, and recrystallized from DMF-water to yield 4.5 g (35%) of reddish brown crystals, mp 258–62° (lit.¹⁴ mp 300°). Repeated recrystallizations gave an analytical sample, mp 260–262°.

Anal. Calcd for C₁₄H₁₁NO₄: C, 65.36; H, 4.31; N, 5.45. Found: C, 65.18; H, 4.20; N, 5.20.

B. 3,4'-Iminodibenzoic Acid.—Using a procedure similar to that described for the preparation of the 3,3' acid, 20.1 g (0.1 mol) of *m*-bromobenzoic acid, 13.7 g of *p*-aminobenzoic acid, 20 g of potassium carbonate, 1 g of copper, and 300 ml of dimethyl sulfoxide were allowed to react to yield 12.6 g (40%) of brown crystals, mp 270°, after three recrystallizations from DMF-water.

Anal. Calcd for C₁₄H₁₁NO₄: C, 65.36; H, 4.31; N, 5.45. Found: C, 65.60; H, 4.22; N, 5.22.

Preparation of Authentic Carboxyphenylated Active Hydrogen Compounds.—*m*-Phenylthiobenzoic acid,⁶ *m*-methylthiobenzoic acid,⁶ α -cyano-*p*-toluic acid,¹⁵ and *m*-(1-cyanoethyl)benzoate⁶ were prepared according to published procedures. The other carboxyphenylated compounds were synthesized as follows.

α -Cyano-*m*-toluic Acid.—To a refluxing solution containing 65 g (1 mol) of potassium cyanide dissolved in 300 ml of 1:1 water-acetone mixture was added 110 g (0.5 mol) of α -bromo-*m*-toluic acid dissolved in 450 ml of acetone. After refluxing for 4 hr, the acetone was removed by distillation and the remaining slurry was dissolved in 200 ml of 1 *N* NaOH solution. The basic solution was treated with charcoal (Norit), filtered, and acidified with 6 *N* hydrochloric acid. The crude product, formed on acidification, was collected by filtration and recrystallized three times from ethanol-water to yield 40 g (50%) of white needles melting at 176–177°.

Anal. Calcd for C₈H₇NO₂: C, 67.07; H, 4.38; N, 8.69. Found: C, 66.70; H, 4.34; N, 8.47.

***p*-Phenylthiobenzoic Acid.**—To a stirred mixture consisting of 0.3 mol of sodamide and 500 ml of liquid ammonia was added 7.2 g (0.05 mol) of *p*-mercaptobenzoic acid (prepared by the procedure of Hydock and Price⁶). After 1 hr, 47.1 g (0.3 mol) of bromobenzene was added dropwise over a period of 5 min and the mixture was stirred for 1 additional hr. After this time, 17 g of ammonium chloride was added, the ammonia was removed by heating with a steam bath and the residue was dissolved in ca. 400 ml of 5% sodium hydroxide solution. The basic solution was washed with ether and *p*-phenylthiobenzoic acid was precipitated by acidifying with 12 *N* hydrochloric acid. The crude product was filtered, air dried and recrystallized from methanol-water to give 8.0 g (70%) of white needles melting at 174° (lit.¹⁷ mp 176–177°).

α -Cyano- α -phenyl-*m*-toluic Acid.—Using the procedure of Biehl and Li,⁸ 15.7 g (0.1 mol) of *o*-chlorobenzoic acid (Matheson Coleman and Bell), 35.2 g (0.3 mol) of phenylacetoneitrile (Matheson Coleman and Bell), and 23.4 g (0.6 mol) of sodamide were allowed to react to give 18.7 g (79%) of crude material. Recrystallization from water-methanol afforded white crystals, mp 172–172.5°. Tlc analyses using silica plates and a solvent system of benzene-dioxane-acetic acid (90:25:4) indicated that only one compound was present.

Anal. Calcd for C₁₅H₁₁NO₂: C, 75.93; H, 4.67; N, 5.91. Found: C, 75.72; H, 4.54; N, 5.71.

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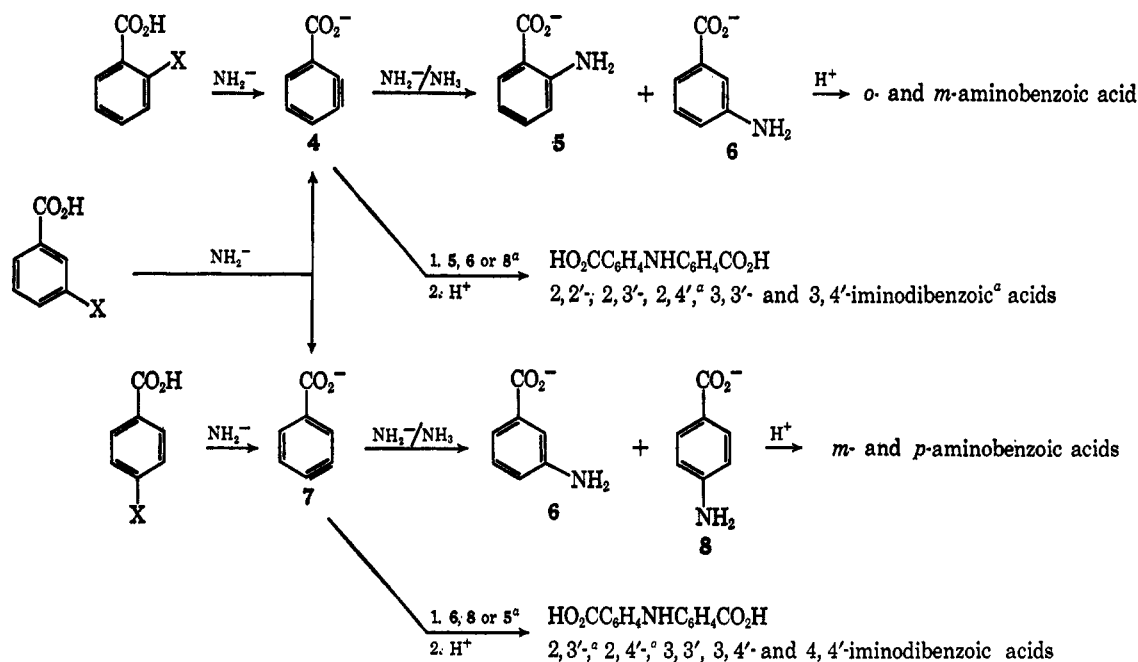
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SCHEME I



^aIn the case of *m*-halobenzoic

X = Cl or Br

α -Cyano- α -phenyl-*p*-toluic Acid.—Using a similar procedure that was described for the preparation of *p*-phenylthiobenzoic acid, 16.1 g (0.1 mol) of α -cyano-*p*-toluic acid was allowed to react with 94.2 g (0.6 mol) of bromobenzene and 0.6 mol of sodamide to yield 4.7 g (20%) of product, mp 201°, after recrystallization from methanol.

Anal. Calcd for $\text{C}_{15}\text{H}_{11}\text{NO}_2$: C, 75.93; H, 4.67; N, 5.91. Found: C, 75.72; H, 4.75; N, 5.70.

***m*-(1-Cyano-*n*-butyl)benzoic Acid.**—To a stirred mixture of 0.1 mol of sodamide and 200 ml of liquid ammonia was added 7.9 g (0.05 mol) of α -cyano-*m*-toluic acid in small portions over a period of 5 min. After stirring the mixture for 1 hr, 23.4 g (0.3 mol) of *n*-propyl chloride (Distillation Products, Inc.) was added dropwise and the stirring was continued for an additional 3 hr. After this time, the reaction was quenched by the addition of 21.4 g (0.4 mol) of ammonium chloride and the solvent removed by heating on a steam bath. The residue was dissolved in ca. 200 ml of water and the basic solution was washed with ether, filtered and acidified to pH 1 by the addition of 6 *N* hydrochloric acid. The crude product was collected by filtration, dried and recrystallized four times from water-methanol to yield 3.9 g (45%) of white crystals which melted at 130–131°.

Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_2$: C, 70.91; H, 6.44; N, 6.89. Found: C, 70.77; H, 6.42; N, 6.87.

***p*-(1-Cyano-*n*-butyl)benzoic Acid.**— α -Cyano-*p*-toluic acid (8.1 g, 0.05 mol) was propylated with 23.4 g (0.3 mol) of *n*-propyl chloride and 0.1 mol of sodamide in liquid ammonia in the same manner described above. Work-up of the reaction mixture yielded 4.2 g (48%) of product, mp 185°, after three recrystallizations from methanol.

Anal. Calcd for $\text{C}_{12}\text{H}_{13}\text{NO}_2$: C, 70.91; H, 6.44; N, 6.89. Found: C, 70.75; H, 6.55; N, 6.80.

***p*-(1-Cyanoethyl)benzoic Acid.**— α -Cyano-*p*-toluic acid (8.1 g, 0.05 mol) was methylated with 37.8 g (0.3 mol) of methyl sulfate and 0.1 mol of sodamide in the manner described above. Work-up of the reaction mixture yielded 4.0 g (46%) of product, mp 150°, after three recrystallizations from methanol-water.

Anal. Calcd for $\text{C}_{10}\text{H}_9\text{NO}_2$: C, 68.54; H, 5.18; N, 8.00. Found: C, 68.75; H, 5.01; N, 7.87.

Results and Discussion

Scheme I diagrams the manner in which the isomer mixtures consisting of aminobenzoic acids 2 and iminodibenzoic acids 3 were formed from the reaction of halobenzoic acids 1 with sodamide or potassium amide

in liquid ammonia. From the product distributions that are listed in Table II, it is evident that the products were formed *via* benzyne-3- and/or -4-carboxylate intermediates (4 and 7, respectively). The isomer ratios obtained from the reaction of *o*- and *p*-halobenzoic acids (runs 1, 2, 6, and 7) are essentially independent of the halogen atom and indicate that a possible $\text{S}_{\text{N}}2$ displacement mechanism¹⁸ was inoperative under our conditions. Thus, the *m*- and *p*-aminobenzoic acids (runs 6 and 7) were formed by the addition of ammonia and/or amide ion to the *meta* and *para* positions of 7 and the iminodibenzoic acids were formed by the addition of *m*- and *p*-aminobenzoate ions (6 and 8) to 7. The formation of the products in runs 1 and 2 can be rationalized in terms of addition of ammonia, amide ion, and *o*- and *m*-aminobenzoate ions (5 and 6) to 4. Also, the product distributions obtained in runs 4 and 5 (all possible mono- and diisomers) demonstrate that both arynes 4 and 7 were generated from *m*-halobenzoic acids.

The determination of the isomer ratios in runs 1, 2, 6, and 7 presented some difficulties because the initially formed aminobenzoate ions were in part consumed by further addition to arynes 4 and 7, forming iminodibenzoic acids. Since the *ortho:meta* aminobenzoic acid ratios (runs 1 and 2) were in the opposite direction to that of the *meta:para* aminobenzoic acid ratios (runs 6 and 7), it was necessary that the amounts of the iminodibenzoic acids be taken into account. Clearly, the symmetrical 2,2'-, 3,3'- and 4,4'-iminodibenzoic acids are formed by the addition of *o*-, *m*- and *p*-aminobenzoate ions to the *ortho*, *meta*, and *para* positions of 4 or 7, respectively. The formation of the nonsymmetrical 2,3'-, 2,4'-, 3,4'-iminodibenzoic acids from the respective aminobenzoate ions is less clear. For example, 2,3'-iminodibenzoic acid could result from

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TABLE II
THE REACTION OF CERTAIN HALOBENZOIC ACIDS WITH SODAMIDE AND POTASSIUM AMIDE IN LIQUID AMMONIA^a

| Run | Halo- benzoic acid | MNH ₂ ^b M | Yield, % | | | | | | | | Isomer ratio ^c | | |
|-----|--------------------------|------------------------------------|-----------------------|----------|----------|----------------------|-------|-------|-------|-------|----------------------------|---------------------------|--|
| | | | Aminobenzoic acids | | | Iminodibenzoic acids | | | | | <i>ortho</i> : <i>meta</i> | <i>meta</i> : <i>para</i> | |
| | | | <i>o</i> | <i>m</i> | <i>p</i> | 2, 2' | 2, 3' | 3, 3' | 3, 4' | 4, 4' | 2, 4' | | |
| 1 | <i>o</i> -Br | Na | 18 | 30 | | 12 | 15 | 18 | | | | 38:62 | |
| 2 | <i>o</i> -Cl | Na | 16 | 32 | | 12 | 12 | 18 | | | | 36:64 | |
| 3 | <i>o</i> -Cl | K | 14 | 68 | | 1 | 1 | 4 | | | | 17:83 | |
| 4 | <i>m</i> -Cl | Na | 9 | 36 | 4 | 6 | 5 | 24 | 3 | 3 | 1 | | |
| 5 | <i>m</i> -Br | Na | 9 | 41 | 7 | 5 | 3 | 32 | 2 | 2 | 1 | | |
| 6 | <i>p</i> -Br | Na | 46 | 16 | | | | 29 | 1 | 1 | | 83:17 | |
| 7 | <i>p</i> -Cl | Na | 52 | 13 | | | | 24 | 1 | 1 | | 85:15 | |
| 8 | <i>p</i> -Cl | K | 66 | 22 | | | | 3 | 1 | 1 | | 75:25 | |

^a Using 0.3 mol of base per 0.1 mol of halobenzoic acid. ^b Sodamide concentration = $1.5 \times 10^{-3} M$; potassium amide concentration = 1.7 M. ^c For aminobenzoic acids formed initially.

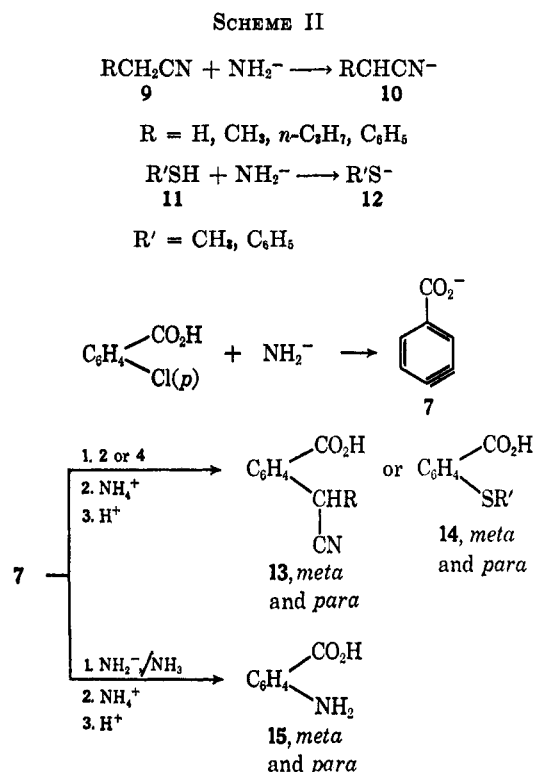
TABLE III
REACTION OF *p*-CHLOROBENZOIC ACID WITH CERTAIN ACTIVE HYDROGEN COMPOUNDS

| Active hydrogen compound | Carboxyphenylated products | | | Isomer ratio <i>meta</i> : <i>para</i> | Aminated products | | | Isomer ratio <i>meta</i> : <i>para</i> |
|--|----------------------------|-------------|-------------|---|-------------------|-------------|-------------|---|
| | Total | <i>meta</i> | <i>para</i> | | Total | <i>meta</i> | <i>para</i> | |
| CH ₃ CN | 74 | 37 | 37 | 50:50 | 15.7 | 13.0 | 2.7 | 83:17 |
| CH ₂ CH ₂ CN | 70 | 35 | 35 | 50:50 | 11.0 | 9.1 | 1.9 | 83:17 |
| CH ₂ (CH ₂) ₃ CN | 68 | 33 | 35 | 48:52 | 14.5 | 12.0 | 2.5 | 82:18 |
| C ₆ H ₅ CH ₂ CN | 79 | 38 | 41 | 48:52 | 15.7 | 13.0 | 2.7 | 83:17 |
| CH ₃ SH | 71 | 36 | 35 | 51:49 | 22.5 | 18.7 | 3.8 | 83:17 |
| C ₆ H ₅ SH | 73 | 36 | 37 | 49:51 | 16.5 | 13.9 | 2.6 | 84:16 |

either the addition of *o*-aminobenzoate ion to the *meta* position of 4 or the addition of *m*-aminobenzoate ion to the *ortho* position of 4. Since the yields of the non-symmetrical acids are small and one is concerned with the ratio of the isomers, no serious error would be introduced by neglecting the amounts of the nonsymmetrical acids in the calculation of the isomer ratios. Hence the initial amount of each aminobenzoic acid isomer was calculated from the sum of the yield of the corresponding mono- and symmetrical diproducts. No attempt was made to calculate the isomer ratios from *m*-halobenzoic acids due to the myriad of diproducts formed.

Interestingly, the aminobenzoic acid *ortho*:*meta* ratio changed from 36:64 (run 2) to 17:83 (run 3) whereas the *meta*:*para* ratio changed from 85:15 (run 7) to 75:25 (run 8) as the base was varied from sodamide to potassium amide. It is important to note that the concentration of amide ion was much higher in the potassium amide reactions than in the sodamide reactions since the solubility of potassium amide (1.7 mol/l.)¹⁹ is much higher than that of sodamide (1.5×10^{-3} mol/l.)²⁰ in liquid ammonia. Therefore, these variations of the isomer ratios reflect their dependency on the amide ion concentration.

In addition, the reaction of 1 equiv of *p*-chlorobenzoic acid with 3 equiv of the appropriate nitrile 9 or mercaptan 11 and 6 equiv of sodamide yielded predominantly the corresponding *m*- and *p*-carboxyphenylated nitriles 13 or sulfides 14 in a ratio of *ca.* 50:50 *meta*:*para*. The formation of 13 and 14 *via* the addition of the respective anions of 9 and 11 to benzyne-4-carboxylate, 7, is shown in Scheme II. A small amount of a mixture



of *m*- and *p*-aminobenzoic acids 15 was also formed in a ratio of *ca.* 83:17 *meta*:*para*, which is similar to those calculated in the amination reaction of *p*-halobenzoic acids. Table III summarizes the results of the foregoing experiments.

Additions to Benzyne-4-carboxylate.—Bunnett²¹ has

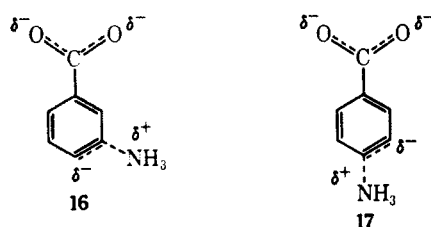
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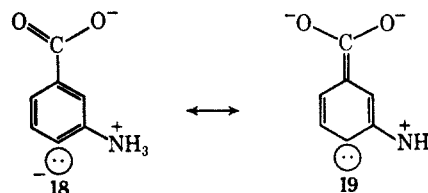
shown that a stronger orienting effect prevails in methanol than in methoxide ion addition to 4-chlorobenzene indicating that neutral addition is more selective (less reactive) than anion addition toward 4-chlorobenzene. The order of selectivities observed in this study, namely, aminations in low amide ion concentration > aminations in high amide ion concentration > carboxyphenylations, are also consistent with Bunnett's observations. Experimentally we cannot determine the relative amounts of amide ion and ammonia additions to benzyne-4-carboxylate. However, the higher selectivity observed in sodamide reactions than in potassium amide reactions indicates that ammonia addition is greater in sodamide reactions than in potassium amide reactions whereas amide ion addition is greater in potassium amide reactions.

The predominance of *m*- over *p*-aminobenzoic acid may be comprehended with reference to the transition states for ammonia addition to benzyne-4-carboxylate represented by 16 and 17. Each transition state has a



partial negative charge on the carboxylate oxygens and a carbon atom plus a partial positive charge on a nitrogen atom. The genesis of the orienting effect for noncharged substituents is generally assumed to be stabilization of the partial negative charge on carbon primarily by induction. However, the electron withdrawing ($-I$) nature of the carboxylate group ($\sigma_m = +0.10$)²² does not account for the direction of the orienting effect. Since the carboxylate group is a remote charged substituent, its electrostatic effect is almost certainly field rather than σ inductive in nature. Wells²³ cites the value $\sigma_1 = 0.00$ in aqueous solution, indicating that the purely polar effect of this substituent is negligibly small at the conditions under which this value was observed. However, due to the lower dielectric constant of ammonia *vs.* water, field interactions should be greater in ammonia than in water. Accordingly, the observed orientation can be explained in part by more favorable field interaction between the carboxylate group and the partial charges on nitrogen and ring carbon atom in 16 than in 17. Also, Roberts²⁴ has suggested that in the case of a 4 substituent, conjugative effects may also influence the nucleophilic orientation. The similarity of the magnitude of σ_m ($+0.10$) and σ_p ($+0.18$) suggests that the carboxylate group does not interact strongly with a phenyl ring by resonance. However, to the extent that it does, one might explain also in part the observed preference for the transition state represented by 16 in terms of carbene-carbanion resonance structures²⁴ 18 and 19,²⁵

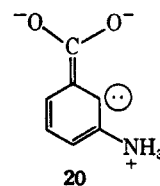
The orienting effect of the carboxylate group would be expected to be less pronounced in anion addition



since there is presumably less negative charge on carbon in the transition states for anion addition than for neutral addition²¹ and the field effect would favor *para* addition. The lower *meta*:*para* ratio obtained in the potassium amide reaction is consonant with increased addition at the *para* position of the more reactive amide ion over that of the less reactive ammonia molecule.

Additions to Benzyne-3-carboxylate.—It has been previously established that carbanions add exclusively to the *meta* position of benzyne-3-carboxylate.⁶ The direction of the *ortho*:*meta* ratio change (33:67–18:82) toward greater *meta* addition with increased amide ion concentrations is also that expected for increased amide ion addition. The values of these *ortho*:*meta* isomer ratios show that addition to the *meta* position of benzyne-3-carboxylate is more favored than that to the *ortho* position with the order of selectivity appearing to be in the opposite direction to that observed for additions to benzyne-4-carboxylate. These results, however, are intelligible if the relative reactivities of the nucleophiles and the field, resonance and inductive effects of the carboxylate group are considered.

Since negligible negative charge on carbon has presumably developed in the transition state for anion addition, one might expect anion addition to be indiscriminate. However, the high energy electrostatic interaction between the anion and the carboxylate group apparently blocks *ortho* addition. On the other hand, in neutral addition considerable negative charge on ring carbon has developed. Since the carboxylate group no longer is a remote substituent, its electron-withdrawing inductive effect favoring *meta* addition should be important. Also, the resonance interaction between the negative charge on ring carbon and the carboxylate group represented by 20 would also favor



meta addition. That exclusive *meta* addition by the less reactive ammonia molecule is not observed in most likely due to the unfavorable field interaction between the carboxylate group and the partial negative charge on the *ortho* carbon atom. In fact, addition to the

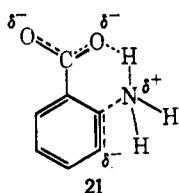
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(25) We wish to thank the referee for pointing out this very important resonance effect.

ortho position may be aided by means of an intramolecular hydrogen bonded transition state represented by **21**. Nevertheless, that more *meta* than *ortho* addition occurs even in low amide concentration



indicates that induction and resonance effects of the carboxylate group predominate over the field effect in neutral additions.

Registry No.—3,4'-Iminodibenzoic acid, 18908-52-6; 3,3'-iminodibenzoic acid, 19,039-48-6; α -cyano-*m*-toluic acid, 5689-33-8; α -cyano- α -phenyl-*m*-toluic acid, 18908-55-9; α -cyano- α -phenyl-*p*-toluic acid, 18908-56-0; *m*-(1-cyano-*n*-butyl)benzoic acid, 5485-72-3; *p*-(1-cyano-*n*-butyl)benzoic acid, 18908-58-2; *p*-(1-cyanoethyl)benzoic acid, 18908-59-3; *p*-chlorobenzoic acid, 74-11-3.

Synthesis and Ionization Constants of *meta*- and *para*-Substituted 1-Phenyl-2-methylcyclopropene-3-carboxylic Acids

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Received July 3, 1968

1-Phenyl-2-methylcyclopropene-3-carboxylic acid and the *p*-OCH₃, *m*-CH₃, *p*-F, *p*-Cl, and *m*-Cl derivatives were prepared by the addition of ethyl diazoacetate to the appropriately substituted 1-phenylpropyne with subsequent hydrolysis. The ionization constants in 50% ethanol at 25° give $\rho = 0.57$ ($-\log K_0 = 6.45$) using σ^0 values. The cyclopropene ring appears to transmit resonance effects about as well as does the cyclopropane ring.

A number of investigators have attempted to evaluate the factors involved in the transmission of substituent effects to a functional group.² The relative transmission by various groups interposed between an aromatic ring and a functional group have been assessed by a comparison of Hammett ρ values for a given reaction of the several series. On this basis, the cyclopropyl group exhibits enhanced transmission relative to the dimethylene group (but less than an ethylenic linkage^{3,4}), which is consistent with the proposed conjugative ability of the three-membered ring.⁵

Another point of view expressed by Bowden⁴ is that the relative abilities to transmit electronic influences within similar series may not necessarily be a function of conjugative or inductive effects but rather of an electrostatic interaction between the reaction site and the substituent. This electrostatic effect is a function of the distance and the direction of the substituent dipole relative to the reaction center.

The conjugative effect attributed to cyclopropane may be the result of *p*-orbital overlap with the C-C

bond orbitals of cyclopropane,⁶ which also have a large fraction of *p*-orbital character.⁵ This introduces the possibility that other highly strained systems might also exhibit an enhancement in the transmission of electronic effects relative to an ordinary C-C σ bond.

The C-C single bond in cyclopropene may provide another such model. The structure of cyclopropene has been considered by several investigators, and the results have been reviewed.⁷ The external methylene bonds in cyclopropene are considered to be $sp^{2.5}$ hybridized indicating that the C-C single bonds have increased *p*-orbital character. The strain energy of cyclopropene is about 27 kcal/mol greater than that of cyclopropane, based on the heats of formation.⁸

The cyclopropene group will also serve for an additional examination of the electrostatic theory of substituent effects as discussed by Bowden.⁴ Since this theory considers the distance and direction of the substituent dipole, conformational factors are important. In this regard, the rigidity of the cyclopropene system removes conformational factors as a variable.

This study is concerned with the ease with which electronic effects are transmitted from a substituent to a reaction site joined by means of the C-C single bond in cyclopropene. The compounds used in this study were a series of *meta*- and *para*-substituted 1-phenyl-2-methylcyclopropene-3-carboxylic acids.

(1) Author to whom correspondence should be directed. Support of this work by The Robert A. Welch Foundation Grant E-136 is gratefully acknowledged. Based on the Ph.D. Dissertation of A. B. T., University of Houston, June 1968. Presented in part at the 2nd Conference on Linear Free Energy Relationships, University of California at Irvine, Irvine, Calif., March 29, 1968.

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