

Substituent Effects on the Ratio of Proton Capture to Chloride Ion Loss by *o*-Chlorophenyl Anions in Liquid Ammonia^{1,2}

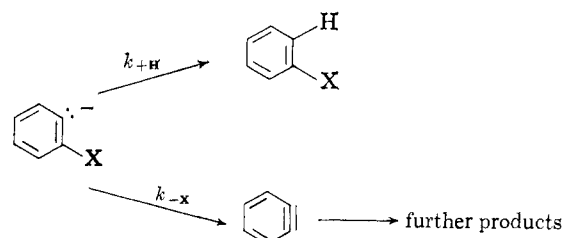
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Contribution from the Metcalf Chemical Laboratory, Brown University, Providence, Rhode Island. Received February 23, 1965

Seven substituted *o*-deuteriochlorobenzenes, admixed in known proportions with the corresponding undeuterated chlorobenzenes, have been submitted to interrupted reaction with potassium amide in 60% liquid ammonia-40% diethyl ether solution. The yield of chloride ion liberated and the deuterium content of the recovered chlorobenzene derivative have been measured. On the basis that amide ion removes hydrogen ortho to chlorine to form an *o*-chlorophenyl anion which may either lose chloride ion to form an aryne or capture a proton from the solvent to regenerate chlorobenzene derivative, the relative rates of proton capture and chloride ion loss have been reckoned as a function of the substituent present. All the substituents studied increased the proton capture/chloride loss rate ratio. A reasonable interpretation takes account of the probable influences of the substituents on phenyl anion and aryne energy levels, and of the likelihood that the transition states for proton capture and chloride ion loss are anion-like and aryne-like, respectively. Reaction of *m*-dichlorobenzene with potassium amide is shown by product analysis experiments to occur 97% via 3-chlorobenzene and 3% via 4-chlorobenzene.

o-Halophenyl anions are recognized to be intermediates in aryne formation³ and in hydrogen isotope exchange^{4,5} by the action of strong bases on aryl halides. They are also implicated as intermediates in the cleavage of 2,6-dihalobenzaldehydes,⁶ *o*-halobenzophenones,⁷ *o*-halophenylacyldiimides,⁸ and *N*-arylsulfonyl-*N'*-(*o*-halophenyl)hydrazines^{8,9} by bases, and in the base-catalyzed isomerization and disproportionation of trihalobenzenes.¹⁰

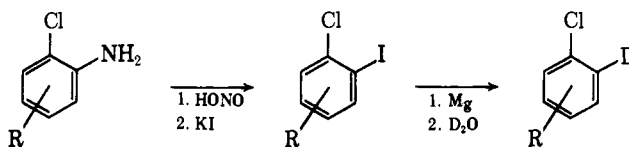
Usually, the life of an *o*-halophenyl anion is terminated either by capture of a proton from the medium to form a halobenzene or by loss of halide ion to generate an aryne (which then quickly undergoes further reactions).¹¹



Two methods for estimating the relative rates of proton capture and halide ion loss have been developed. Roberts, *et al.*,³ showed, in the case of *o*-chlorophenyl anion itself, that this ratio could be reckoned from the yield of chloride ion and the change in deuterium content during an interrupted reaction of partially *ortho*-deuterated chlorobenzene with potassium amide in liquid ammonia. Hoffmann⁸ has shown that if *o*-bromophenyl anions are generated in an alcoholic solvent, the relative rates of proton capture and bromide ion loss are given directly by the yields of bromobenzene and bromide ion. However, the latter method is not applicable to *o*-chlorophenyl anions because chloride ion loss from them is undetectably small in alcohol solvents.⁸

We now report determination of substituent effects on the ratio, k_{+H}/k_{-Cl} , of proton capture to chloride ion loss from *o*-chlorophenyl anions in 60% ammonia-40% diethyl ether medium. We used the general method of Roberts, *et al.*,³ for our measurements. Seven structures, representing different substituents or orientations, were investigated.

*Synthesis of *o*-Deuteriochlorobenzene Derivatives.* All but one of the required deuterated compounds were made by treatment of the corresponding arylmagnesium iodide with D₂O. The iodo precursors of the Grignard reagents were prepared by conventional



diazonium synthesis from the corresponding amines. Though simple in principle, this synthesis is not ideal. By-product formation was considerable both in treatment of the diazonium salts with potassium iodide and in formation of Grignard reagents from the *o*-iodochlorobenzenes. In the latter case, some benzyne formation may have occurred.¹²

Although deuterium oxide containing >99.5% deuterium was used, the extent of deuteration of the chloro-

(1) Presented in part at the 142nd National Meeting of the American Chemical Society, Atlantic City, N. J., Sept. 1962, Abstracts, p. 82Q.

(2) Supported in part by a grant from the Shell Companies Foundation.

(3) J. D. Roberts, D. A. Semenow, H. E. Simmons, Jr., and L. A. Carlsmith, *J. Am. Chem. Soc.*, **78**, 601 (1956).

(4) G. E. Hall, R. Piccolini, and J. D. Roberts, *ibid.*, **77**, 4540 (1955).

(5) J. Hine and P. B. Langford, *J. Org. Chem.*, **27**, 4149 (1962).

(6) J. F. Bunnett, J. H. Miles, and K. V. Nahabedian, *J. Am. Chem. Soc.*, **83**, 2512 (1961).

(7) J. F. Bunnett and B. F. Hrutford, *J. Org. Chem.*, **27**, 4152 (1962).

(8) R. W. Hoffmann, *Chem. Ber.*, **97**, 2763, 2772 (1964); **98**, 222 (1965).

(9) J. S. Bradshaw and W. E. Lambert, III, personal communication.

(10) C. E. Moyer, Jr., and J. F. Bunnett, *J. Am. Chem. Soc.*, **85**, 1891 (1963).

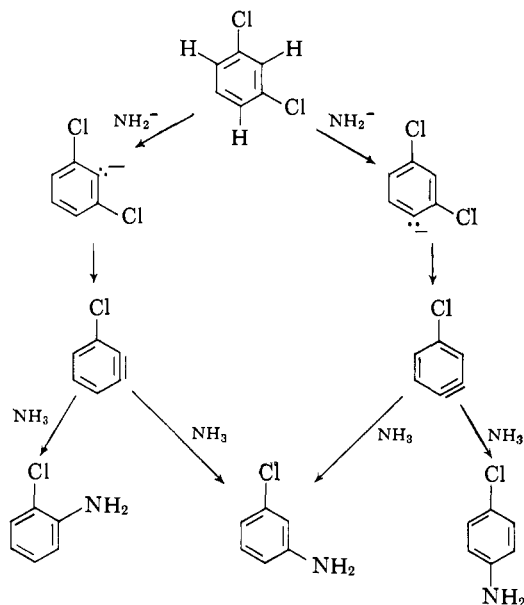
(11) R. Huisgen and J. Sauer, *Angew. Chem.*, **72**, 91 (1960); J. F. Bunnett, *J. Chem. Educ.*, **38**, 278 (1961).

(12) H. Heaney, F. G. Mann, and I. T. Millar, *J. Chem. Soc.*, 3930 (1957).

benzene derivatives obtained was only 77 to 93%. Similar observations have been reported by Dunn, Krueger, and Rodewald.¹³ It is thought that decomposition of the Grignard reagent may occur in part *via* radical intermediates which can abstract hydrogen from the ether solvent.¹⁴

1,3-Dichlorobenzene-2-*d* was obtained by alkali cleavage of 2,6-dichlorobenzaldehyde in deuterium oxide medium.⁶

The Sense of Aryne Formation from m-Dichlorobenzene. *A priori*, we judged that aryne formation from 1,3-dichlorobenzene should occur mainly by abstraction of the 2-proton, which is the most acidic,⁵ to form 2,6-dichlorophenyl anion which would then lose chloride ion to form 3-chlorobenzene. An alternative possibility is that one of the (equivalent) 4- or 6-protons might be removed; chloride ion loss from the resulting 2,4-dichlorophenyl anion would form 4-chlorobenzene.



Inasmuch as ammonia addition to the isomeric chlorobenzynes leads to different chloroaniline product mixtures, this question can be settled by experiment. Only 4-chlorobenzene can be formed by the action of potassium amide on *p*-dichlorobenzene; the proportions of *m*- and *p*-chloroaniline obtained therefore testify to the orientation of addition to this aryne. From the percentage of *p*-chloroaniline formed in the reaction of potassium amide with *m*-dichlorobenzene, the fraction of reaction *via* 4-chlorobenzene can then be judged.

By gas-liquid chromatography of chloroaniline isomer mixtures, we were able to detect the *ortho* isomer as a discrete peak but the *meta* and *para* isomers were not separated. The content of *m*-chloroaniline was determined by oxidizing the mixture of isomers to the corresponding chloronitrobenzenes with peracetic acid, allowing the chloronitrobenzenes to react with excess piperidine, and measuring the amount of chloride ion liberated. This procedure was patterned after one employed by Klapproth and Westheimer.¹⁵ *m*-Chloro-

nitrobenzene is unreactive with piperidine under conditions in which its *ortho* and *para* isomers react quantitatively.¹⁶

By this means, we found that reaction of *p*-dichlorobenzene with potassium amide affords *m*- and *p*-chloroaniline in the ratio 19:81. From preparative experiments, it was reported that the product is *p*-chloroaniline.¹⁷ Our analysis indicates that *m*-dichlorobenzene forms *o*-, *m*-, and *p*-chloroaniline in the ratio 0.7:97:2.3. Preparatively, the product was described as *m*-chloroaniline.¹⁷ From these data, we reckon that 3% of the aminodechlorination of *m*-dichlorobenzene occurred *via* 4-chlorobenzene, and 97% *via* 3-chlorobenzene.¹⁸

Experiments with Potassium Anilide Base. In an ammonia-ether medium containing excess aniline, potassium anilide did not affect 1,2-dichlorobenzene-3-*d* during 2 hr. at reflux temperature. Neither chloride ion liberation nor hydrogen isotope exchange occurred. However, under the same conditions 1,3-dichlorobenzene-2-*d* suffered complete loss of its deuterium label although no chloride ion was produced. Hine and Langford⁶ have reported 1,3-dichlorobenzene-2-*d* to exchange hydrogen without chloride ion loss on treatment with sodium methoxide in methanol at 100°.

Quantitative Methods. The deuterium content of each deuteriochlorobenzene derivative prepared was determined mass spectrometrically. Mixtures of known deuterium content were then prepared by admixture with the corresponding undeuterated compound. From the infrared spectra of these, calibration plots were constructed. The deuterium content of samples recovered from exposure to potassium amide was determined by infrared measurements, with reference to the calibration plots.

Roberts, *et al.*,³ derived an equation whereby the ratio, k_{+H}/k_{-Cl} , could be computed from knowledge of the initial and final deuterium contents and the percent chloride ion formed on interrupted exposure of *o*-deuteriochlorobenzene-chlorobenzene mixtures to potassium amide. A similar derivation has been given by Dunn, *et al.*¹³ Essentially the same equation can be and was used to compute results for many of the compounds we studied. However, new expressions had to be developed for the *p*- and *m*-dichlorobenzene systems. A deuterium atom in *p*-dichlorobenzene occupies one of *four* equivalent positions while there is no other position equivalent to the 2-position in *m*-dichlorobenzene. Also, whereas the *o*-chlorophenyl anions derived from all the other systems of present interest

(15) W. J. Klapproth and F. H. Westheimer, *J. Am. Chem. Soc.*, **72**, 4461 (1950).

(16) R. J. W. LeFevre and E. E. Turner, *J. Chem. Soc.*, 1113 (1927).

(17) J. H. Wotiz and F. Huba, *J. Org. Chem.*, **24**, 595 (1959).

(18) This method for judging the orientation of aryne formation and addition to arynes is subject to some uncertainty because the anilines initially generated are in part consumed by further addition to arynes, forming di- and triarylamines.¹⁹ The more the isomeric chloroanilide ions differ in their reactivity with arynes, or the more the isomeric arynes differ in reactivity toward anilide ions, the less valid will be the conclusions we have drawn. In the present case, it would be necessary that 4-chlorobenzene be highly selective in favor of chloroanilide ions, or for *p*-chloroanilide to be much more reactive than *m*-chloroanilide ions toward arynes, in order seriously to disturb our conclusion that the amount of reaction *via* 4-chlorobenzene is small enough to be neglected in first-approximation calculations. Differences in the efficiency of oxidation of isomeric chloroanilines to chloronitrobenzenes would also affect the accuracy of our estimates.

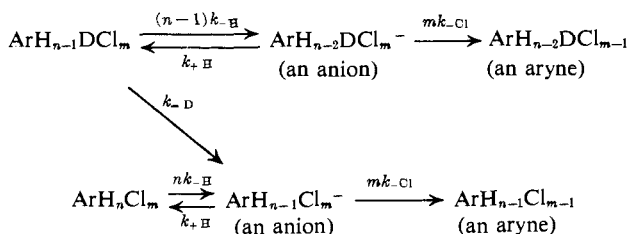
(19) J. D. Roberts, C. W. Vaughan, L. A. Carlsmith, and D. A. Semenov, *J. Am. Chem. Soc.*, **78**, 611 (1956).

(13) G. E. Dunn, P. J. Krueger, and W. Rodewald, *Can. J. Chem.*, **39**, 180 (1961).

(14) L. H. P. Weldon and C. L. Wilson, *J. Chem. Soc.*, 235 (1946); see also D. V. Banthorpe and E. D. Hughes, *ibid.*, 3314 (1962).

can expel chloride ion in but one way, the 2,6-dichlorophenyl anion from *m*-dichlorobenzene can expel either of two equivalent chlorines.

Consider a chlorobenzene derivative having *ortho* to chlorine *n* equivalent hydrogens, one of which is deuterium in some molecules, and *m* equivalent chlorine atoms *ortho* to each of said hydrogens. Following Roberts, *et al.*,³ and Dunn, *et al.*,¹³ we may visualize the following reaction scheme.²⁰



Let us employ the following symbolism: *i* is the kinetic isotope effect, k_{-H}/k_{-D} ; *G* is the fraction of aryl anions which lose chloride to yield aryne, $mk_{-Cl}/(k_{+H} + mk_{-Cl})$; *P* is the fractional yield of chloride ion; and *d*₀ and *d* are the mole fractional deuterium content of the chlorobenzene derivative before and after reaction, respectively.

By methods previously described,^{3,13} the appropriate differential equation may be set up and integrated. The integrated equation²² is perhaps most conveniently used in the form

$$\log \left[\frac{d}{d_0} (1 - P) \right] = \frac{(n-1)Gi + 1}{Gi - 1} \times \log \frac{1/d - 1 + \frac{G-1}{Gi-1}}{1/d_0 - 1 + \frac{G-1}{Gi-1}}$$

Since *d*₀, *d*, and *P* are experimental quantities and *n* follows from the structure of the compound being studied, this amounts to an equation in two unknowns, *G* and *i*. In practice, one assumes values for the isotope effect and then calculates *G*.

Results

Our principal observations are summarized in Table I. This table gives the main experimental data for each run, values of *G* and of k_{+H}/k_{-Cl} calculated therefrom, and the average value of the latter for each substrate.








All values of *G* and of k_{+H}/k_{-Cl} listed in Table I were reckoned on the basis that *i*, the kinetic isotope effect, is 5.7. This magnitude of *i* was indicated by experiments of Roberts, *et al.*,³ in analogous systems, and was used in the calculations of Dunn, Krueger, and Rodewald.¹³ Computations based on different *i* values provide different solutions for *G* and for k_{+H}/k_{-Cl} in the sense that a lower *i* generates a higher *G* and a lower proton capture/chloride loss ratio. For example, for the second *p*-dichlorobenzene run in Table I the solutions are 0.00560 for *G* and 180 for k_{+H}/k_{-Cl} if *i* is 4.0, in contrast to 0.00393 and 250, respectively, if *i* is 5.7.

(20) Chloride ion recapture by the arynes^{8,21} is most unlikely because of the strong competing nucleophiles (amide and anilide ions) present in this system.

(21) G. Wittig and R. W. Hoffmann, *Chem. Ber.*, **95**, 2729 (1962).

(22) Although potassium amide concentration appears in the initial differential equations, it cancels out during the derivation.

Table I. Interrupted Reactions of Chlorobenzene Derivatives with KNH₂ in 60% Ammonia:40% Diethyl Ether

Substrate	Wave length for D anal., μ	Deuterium content ^a Initial	Deuterium content ^a Final	Yield of chloride ion	<i>G</i> ^b	k_{+H}/k_{-Cl}
	10.10	0.280	0.188	0.662	0.119	7.4
		0.234	0.181	0.458	0.110	8.1
		0.372	0.268	0.541	0.119	7.4
Average of three runs						7.6
	10.22	0.331	0.291	0.0300	0.0219	45
		0.198	0.160	0.0633	0.0256	38
Average of two runs						41
	10.11	0.139	0.0325	0.0619	0.00780 ^c	250
		0.252	0.0672	0.0587	0.00853 ^c	230
Average of two runs						240
	8.75, 11.08	0.130	0.0748	0.0548	0.00450	220
		0.188	0.0812	0.0720	0.00393	250
Average of two runs						240
	11.36	0.123	0.0765	0.553	0.0857	10.7
		0.240	0.128	0.558	0.0772	12.0
Average of two runs						11.4
	10.51, 10.87	0.0987	0.0222	0.0680	0.00413	240
		0.556	0.0375	0.1210	0.00450	220
Average of two runs						230
	13.90	0.0943	0.0765	0.0218	0.00915	108
		0.0989	0.0392	0.0941	0.00914	109
		0.251	0.218	0.0191	0.0125	79
Average of three runs						99

^a Mole fraction. ^b *G* symbolizes the fraction of aryl anions which lose chloride ion to form aryne, and is reckoned on the assumption that k_{-H}/k_{-D} is 5.7. ^c Corrected for 4-chlorobenzene formation; *G* values before correction were 0.00785 and 0.00862.

When a different *i* value is employed, the solutions for the proton capture/chloride loss ratio for all runs in Table I change in the same direction. The order of substituent effects is not disturbed.

It is probable that the kinetic isotope effect is itself a function of substrate structure. We do not have experimental information on this point. It is apparent, however, that the substrate-dependence of *i* would have to be very great if it were to disturb the qualitative order of substituent effects as indicated in Table I. A great variation of *i* within the series studied is unlikely.

It is remarkable that all the substituents investigated increased the rate of proton capture relative to that of chloride ion loss. The substituents investigated include two (Cl and CF₃) which are normally electron attracting and two (CH₃ and OCH₃) which are normally electron releasing. With one exception, substituents in the former class increase k_{+H}/k_{-Cl} more strongly.

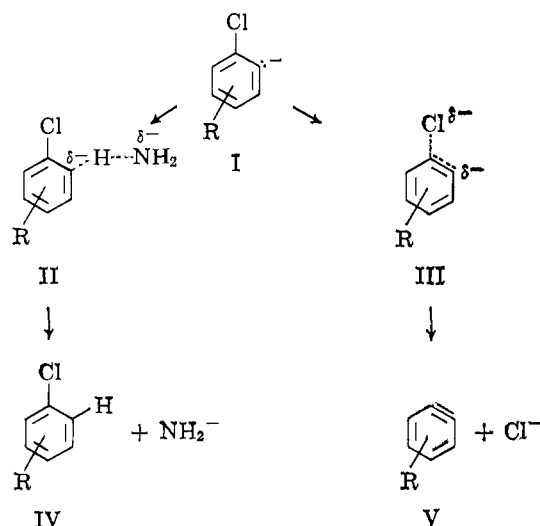
Our value for the proton capture/chloride loss ratio for *o*-chlorophenyl anion itself, namely 7.6, compares with 6.4 as reported by Dunn, Krueger, and Rodewald.¹³ It should be noted that their solvent was neat liquid ammonia, whereas ours contained 40% diethyl ether.

We expect k_{+H} , and therefore k_{+H}/k_{-Cl} , to increase if any acid stronger than ammonia is added to the system. The values reported are valid only for the medium employed in our experiments.

Discussion

Our observation that substituents increase the rate of proton capture relative to that of chloride ion loss does not necessarily mean that they accelerate proton capture. This is possible, but it could be that both modes of reaction are retarded, aryne formation more than proton capture.

Let us consider substituent effects on the free energies of the anion (I) and of the transition states for proton capture (II) and chloride ion loss (III). For unsubstituted *o*-chlorophenyl anion, the energy profile for the system is probably as represented by the solid line in Figure 1. This shows proton capture by the anion as exoenergetic and aryne formation as endoenergetic.



The effects of the trifluoromethyl and chlorine substituents are rather easily rationalized in terms of inductive or electrostatic stabilization of negative charge on ring carbon by electron-attracting substituents. These substituents are known to accelerate abstraction of protons from ring positions by bases.^{4,23} This shows that they reduce the free energy of proton-transfer transition states of type II relative to chlorobenzene derivatives IV. Also it implies, though it does not require, that they stabilize the phenyl anions which are formed.²⁴

If this stabilization is largely inductive or electrostatic in character, as is probable when the substituent is *meta* to the anionic center and possible when it is *ortho*,²⁵ the free energies of transition states of types II and III should also be reduced by these substituents, and the reduction should be greater the larger the negative charge in the transition state on the erstwhile phenyl anion center. (It is to be noted that I, II, and III all carry a full or partial negative charge on the same carbon atom.)

(23) R. Huisgen, W. Mack, K. Herbig, N. Ott, and E. Anneser, *Chem. Ber.*, **93**, 412 (1960).

(24) The effect of CF_3 and Cl substituents on hydrogen isotope exchange rates is strongest when they are *ortho* but appreciable when they are *meta* to the proton being removed. In the present work, the substituent under study is *ortho* to the anionic carbon only in the case of *m*-dichlorobenzene; it is *meta* in all the other examples.

(25) Cf. M. Charton, *J. Am. Chem. Soc.*, **86**, 2033 (1964).

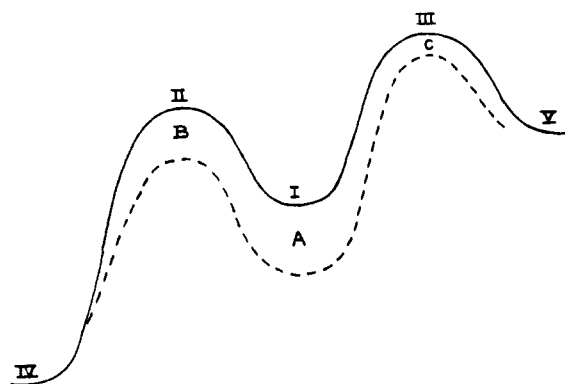


Figure 1. Probable energy profile for reactions of an *o*-chlorophenyl anion (I) to form aryne (V) or chlorobenzene derivative (I): solid line, unsubstituted *o*-chlorophenyl anion; dashed line, *o*-chlorophenyl anion with electron-attracting substituent.

From the fact that CF_3 and Cl favor proton capture over chloride ion loss, one deduces that the energy of transition state II is lowered more than that of III, and therefore that II has more negative charge on carbon.

The energy profile for a trifluoromethyl- or chlorine-substituted *o*-chlorophenyl anion is represented by the dashed line in Figure 1. The reduction of the free energies of I, II, and III is represented by gaps A, B, and C, respectively. Gap B is shown greater than C but less than A.

If transition state II has more negative charge on carbon than does III, II is more "phenyl anion-like" than III, which is "aryne-like." The same judgment, that II should resemble the phenyl anion reactant and III the aryne product, could have been made *a priori* with reference to the postulate²⁶ that transition states for exothermic reactions are attained earlier on the reaction coordinate than those for endothermic reactions.

The implication that the carbon-chlorine bond is largely sundered in transition state III is in harmony with observations of Huisgen and Zirngibl.²⁷ By the principle of microscopic reversibility, III would also be the transition state for addition of chloride ion to aryne.²¹ Our deduction is equivalent to saying that the transition state for chloride addition is attained very early on the reaction coordinate. Huisgen and Zirngibl found that steric effects on the addition of nucleophiles to 1,2-naphthalene are small. They concluded that the transition state was attained very early on the reaction coordinate for addition, at a point where the slightly formed carbon-to-nucleophile bond was very long.

In Table I, the effect of the second chlorine in *o*-dichlorobenzene on the proton capture/chloride loss ratio is seen to be less than in *m*- or *p*-dichlorobenzene. A possible explanation is that its polar effect on transition state energy levels is partially offset by a steric effect in favor of chloride ion expulsion. Repulsive interactions inherent in having two chlorines *ortho* to each other²⁸ would be largely relieved in a transition state of type III, but not of type II.

(26) G. S. Hammond, *ibid.*, **77**, 334 (1955).

(27) R. Huisgen and L. Zirngibl, *Chem. Ber.*, **91**, 1438, 2375 (1958).

(28) G. Ferguson and J. M. Robertson in "Advances in Physical Organic Chemistry," Vol. 1, V. Gold, Ed., Academic Press Inc., New York, N. Y., 1963, p. 233.

It is unlikely that the effects of the methyl and methoxy substituents on k_{+H}/k_{-Cl} are due to selective reduction of the energies of proton capture as compared to chloride loss transition states. Methyl depresses the rate of abstraction of ring-bound protons by bases²⁹ and methoxy, as a *meta* substituent, has little effect.^{4,23} This indicates that these substituents do not significantly stabilize phenyl anion centers.

It is possible that CH_3 and OCH_3 exert their effects through increasing the energy levels of the aryne-forming transition states. Since these transition states appear to resemble the aryne products, this would imply that these substituents raise the free energies of arynes.

There are other indications that electron-releasing substituents destabilize arynes. Huisgen and co-workers³⁰ have shown that 3-methoxy- and 3-dimethylaminobenzynes are less selective toward nucleophiles than is benzyne itself.³¹ If lesser selectivity is a consequence of greater reactivity, this implies that these electron-releasing substituents raise the free energy associated with the aryne "triple bond."

Huisgen, *et al.*,³⁰ also found 3-trifluoromethylbenzyne to be less selective than benzyne, though more selective than the two arynes mentioned above.³¹ Perhaps part of the effect of CF_3 on k_{+H}/k_{-Cl} may be traced to unfavorable interaction with the partially formed aryne structure in a transition state of type III.

These interpretations of substituent effects are of course preliminary in character. Experimental evidence in this whole area is still rather sparse.

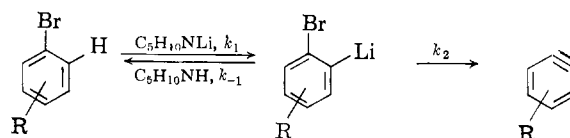
The substituent effects we have observed have certain practical consequences. First, they make it possible to realize a virtual equilibrium between base and halobenzene, on the one hand, and halophenyl anion and conjugate acid of the base, on the other. This effect can be further magnified if the substituent accelerates proton abstraction, for then the anion may be generated at an appreciable rate with use of a weaker base; the base's conjugate acid will be a stronger acid and proton capture will be accelerated, further increasing the disparity between proton capture and halide ion loss rates. In the extreme it becomes possible to realize complete exchange of hydrogen without detectable halide ion loss, as reported above for 1,3-dichlorobenzene-2-*d* with potassium anilide in ammonia-ether medium and by Hine and Langford⁵ for the same substrate with sodium methoxide in methanol.

Second, if substituents increase the proton capture/chloride loss ratio, they probably also increase the rate of reaction of *o*-halophenyl anions with other electrophiles relative to the rate of halide ion expulsion. *o*-Halophenyl anions are thus enabled to take part in a variety of reactions without excessive jeopardy of decomposing to halide ion and aryne. A probable example is the anilide ion catalyzed isomerization and disproportionation of trihalobenzenes in liquid ammonia.¹⁰

The substituent effects we have observed aid understanding of some observations of Huisgen, *et al.*,²³ concerning rates of aryne formation by action of

lithium piperidide on substituted bromobenzenes in ether solution, as affected by piperidine concentration. Aryne formation from bromobenzene itself, 1-bromonaphthalene, 9-bromophenanthrene, and from the *o*-methyl, *p*-dimethylamino, and *p*-methoxy derivatives of bromobenzene was accelerated by addition of piperidine. Piperidine had little effect on the reactions of *o*-dibromobenzene and *m*-bromoanisole, and it decelerated aryne formation from *m*-bromobenzotrifluoride, *m*- and *p*-bromofluorobenzene, and *m*-dibromobenzene.

Huisgen's system can be represented²³ as



The rate of aryne formation should then be

$$\text{rate} = \frac{k_1 k_2 [\text{ArBr}] [\text{C}_5\text{H}_{10}\text{NLi}]}{k_{-1} [\text{C}_5\text{H}_{10}\text{NH}] + k_2}$$

With bromobenzene itself, $k_2/k_{-1}[\text{C}_5\text{H}_{10}\text{NH}]$ is doubtless so large that increases in piperidine concentration do not sensibly affect the denominator. The accelerating effect on piperidine on k_1 , which has been discussed,³² predominates. However, when a substituent such as Br, F, or CF_3 is present, $k_2/k_{-1}[\text{C}_5\text{H}_{10}\text{NH}]$ is much reduced, possibly to less than unity, and over-all rate is depressed by added piperidine owing to the $[\text{C}_5\text{H}_{10}\text{NH}]$ factor in the denominator. This effect overshadows the accelerating influence of piperidine on the proton abstraction step.³³

Experimental

Chlorobenzene-2-d, n^{25D} 1.5209 (lit.¹³ $n^{21.8D}$ 1.5261), was prepared in 52% yield by the method of Dunn, Krueger, and Rodewald.¹³ Mass spectrometric analysis indicated 79.8 mole % deuteration.

1,2-Dichloro-3-iodobenzene was prepared by diazotization of 2,3-dichloroaniline in concentrated sulfuric acid solution, dilution of the diazonium solution with 0.75 of its volume of glacial acetic acid, and addition of powdered potassium iodide to the diluted solution. After it had stood overnight, the reaction mixture was steam distilled. Neutral products were recovered from the distillate by standard extraction procedures and distilled under vacuum. The combined fractions of b.p. 110–127° (23 mm.) represented a 46% yield. Upon redistillation, a light yellow oil of b.p. 123–126° (20 mm.) was obtained; it solidified to a light yellow solid, m.p. 35–36°.

Anal. Calcd. for $C_6H_3Cl_2I$: C, 26.40; H, 1.11. Found³⁴: C, 26.43; H, 1.39.

4-Chloro-3-iodotoluene,³⁵ b.p. 125–126° (16 mm.), n^{25D} 1.6182, was prepared in 54% yield by a similar procedure.

4-Chloro-3-iodobenzotrifluoride was similarly obtained from 3-amino-4-chlorobenzotrifluoride (from stannous

(29) A. I. Shatenshtein, *Tetrahedron*, **18**, 95 (1962); G. E. Hall, E. M. Libby, and E. L. James, *J. Org. Chem.* **28**, 311 (1963); A. Streitwieser, Jr., and R. G. Lawler, *J. Am. Chem. Soc.*, **85**, 2854 (1963).

(30) R. Huisgen, "Organometallic Chemistry," H. Zeiss, Ed., Reinhold Publishing Co., New York, N. Y., 1960, p. 75.

(31) Unfortunately, data are not available concerning effects of 4-substituents on aryne selectivity.

(32) R. Huisgen and J. Sauer, *Chem. Ber.*, **92**, 192 (1959).

(33) Huisgen, *et al.*,²³ judged in 1960 that "Entmetallierung der *o*-Lithiumverbindung" was kinetically significant in reactions of the more acidic aryl bromides.

(34) Analysis by Micro-Tech Laboratories, Skokie, Ill.

(35) Cf. F. Ullmann and O. v. Glenck, *Ber.*, **49**, 2487 (1916).

chloride-hydrochloric acid reduction of 4-chloro-3-nitrobenzotrifluoride), in 30% yield. The product was an oil, b.p. 97–98° (18 mm.), n^{25}_D 1.5380.

Anal. Calcd. for $C_7H_3ClF_3I$: C, 27.25; H, 0.98. Found³⁴: C, 27.51; H, 1.20.

4-Chlorobenzotrifluoride. A sample free of isomeric impurities was obtained by hypophosphorous acid deamination³⁶ of 3-amino-4-chlorobenzotrifluoride. The purified product had b.p. 135–136°, n^{25}_D 1.4440.

3-Amino-4-chloroanisole was obtained by stannous chloride-hydrochloric acid reduction of 4-chloro-3-nitroanisole³⁷ in 61% yield. It was obtained as a colorless oil, b.p. 119–120° (3–4 mm.), n^{25}_D 1.5850.

Anal. Calcd. for C_7H_8ClNO : C, 53.34; H, 5.12. Found³⁴: C, 53.52; H, 4.95.

4-Chloro-3-iodoanisole was obtained in 17% yield by diazotization of the above amino compound in concentrated sulfuric acid, dilution with an equal volume of glacial acetic acid, and addition of potassium iodide. The product, isolated by standard procedures, was an oil, b.p. 144–146° (16 mm.).

Anal. Calcd. for C_7H_6ClIO : C, 31.31; H, 2.25. Found³⁴: C, 31.28; H, 2.24.

Preparations of this and other iodo compounds often had a reddish color, doubtless due to traces of elemental iodine.

Procedure for the Preparation of Deuterioaryl Chlorides. The procedure used to prepare 1,2-dichlorobenzene-3-*d* is representative. The reaction was conducted in flame-dried glassware under a dry nitrogen atmosphere.

To the Grignard reagent formed from 140.4 g. of 1,2-dichloro-3-iodobenzene and 12.3 g. of magnesium turnings in 500 ml. of absolute ether, 12 ml. of >99.5% deuterium oxide was added. After the reaction mixture had stirred overnight, dilute hydrochloric acid was added to dissolve salts. The ether layer was washed with water, dried over anhydrous magnesium sulfate, and concentrated. After two distillations, 40 g. (53%) of 1,2-dichlorobenzene-3-*d* of b.p. 57.5–58° (10 mm.), n^{26}_D 1.5489, was obtained. Mass spectrometry indicated 90.0 mole % deuteration.

1,4-Dichlorobenzene-2-*d* was similarly obtained from 1,4-dichloro-2-iodobenzene.³⁸ The crude product was recrystallized from ethanol; chromatography on Merck aluminum oxide with petroleum ether (b.p. 30–60°) eluent then removed colored impurities and afforded a white product, m.p. 54–55°, which did not depress the melting point of an authentic sample of *p*-dichlorobenzene. Mass spectrometry indicated 76.8 mole % deuteration.

4-Chlorotoluene-3-*d* was obtained in 52% yield by the standard procedure. It had b.p. 160–162°, $n^{25.5}_D$ 1.5180, and was shown by mass spectrometry to contain 89.6 mole % of the deuterio compound.

4-Chlorobenzotrifluoride-*d* was obtained in 46% yield by the standard procedure. It had b.p. 135–136°, n^{25}_D 1.4440, and was shown by mass spectrometry to contain 90.0 mole % of the deuterio compound.

(36) N. Kornblum, *Org. Reactions*, 2, 262 (1944).

(37) H. Van Erp, *J. prakt. Chem.*, 127, 20 (1930); H. H. Hodgson and J. H. Crook, *J. Chem. Soc.*, 1812 (1932).

(38) C. Willgerodt and A. Landenberger, *J. prakt. Chem.*, [2] 71, 540 (1905).

4-Chloroanisole-3-*d* was similarly obtained in 63% yield. It had b.p. 83–84° (17 mm.), $n^{25.5}_D$ 1.5326, and was shown by mass spectrometry to contain 93.0 mole % of the deuterio compound.

1,3-Dichlorobenzene-2-*d*. To 60 ml. of >99.5% deuterium oxide was added 16 g. of potassium metal during a period of 3 hr. with a good flow of dry nitrogen at all times. Thirty grams of 2,6-dichlorobenzaldehyde was added, and the mixture was heated for 17 hr. at 100–120°. The resulting 1,3-dichlorobenzene-2-*d*, isolated by conventional procedures in 74% yield, had b.p. 62–63° (15 mm.), n^{25}_D 1.5438, and was shown by mass spectrometry to contain 93.9 mole % of the deuterio compound.

Purity of Reactants and Products. All reactants for and products from the interrupted reactions with potassium amide were examined by gas-liquid chromatography at temperatures in the range 125–175°. An FM Model 500 instrument was used, with either a 2- or 4-ft. silicone rubber column. The impurity level in all samples was indicated to be 1% or less. Deuterated compounds had retention times identical with those of the corresponding undeuterated compounds.

Mass Spectrometric Determination of Deuterium Content. A Consolidated Engineering Corp. Model 21-103C mass spectrometer at Harvard University was used.³⁹ Intensities of peaks due to species containing only Cl^{35} were measured. Since the peak which reports the abundance of the deuterium compound, at one mass unit greater than the “normal” species, also represents small contributions due to the natural abundance of C^{13} , a correction was applied as follows. From the measured intensity of said peak, there was subtracted $0.011cI_H$, where c is the number of carbon atoms in the molecule and I_H is the intensity of the peak due to the “normal” species.⁴⁰ This gave the corrected intensity of the “deuterio” peak, symbolized I_{cor} . The mole per cent of deuteration is then given by

$$\text{mole per cent deuteration} = \frac{I_{cor}}{I_{cor} + I_H} \times 100$$

In the case of *p*-chlorotoluene, an intense peak was observed one mass unit less than the molecular ion peak. This peak probably represents a chlorotropylium ion⁴² and was used to determine the deuterium content of *p*-chlorotoluene samples in a manner similar to that used with other compounds in respect to the molecular ion peaks.

Determination of Deuterium Content by Infrared Analysis. For each structure investigated, a series of at least five samples of different deuterium content was prepared by mixing weighed quantities of the unlabeled compound and the deuterium compound (of deuterium content known by mass spectrometry). With use of infrared absorption intensities of C–D deformation peaks and a base-line technique, calibration plots were

(39) We thank the Harvard Chemistry Department, and especially Dr. Gerald O. Dudek, for their courtesy in making this instrument available to us.

(40) The natural abundance of C^{13} was taken as 1.1 atom %.⁴¹ This abundance was also indicated by the mass spectra of unlabeled samples of the several compounds.

(41) D. W. Stewart, “Physical Methods of Organic Chemistry,” Part II, A. Weissberger, Ed., 2nd Ed., Interscience Publishers, Inc., New York, N. Y., 1949, p. 2026.

(42) P. N. Rylander, S. Meyerson, and H. M. Grubb, *J. Am. Chem. Soc.*, 79, 842 (1957).

Table II. Interrupted Reactions of Chlorobenzene Derivatives with KNH_2 . Reaction Times and Quantities Employed^a

Substrate	K, g.	KNH ₂ flask		Reaction flask		Reaction time, min.
		Ether, ml.	NH ₃ , ml.	Ether, ml.	NH ₃ , ml.	
$\text{C}_6\text{H}_5\text{Cl}-d$	4.4-4.7	200	300	440	660	20-30
$\text{C}_6\text{H}_4\text{Cl}_2-d$ (3 isomers)	0.6-0.8	160	245	325	500	4-8
$\text{CH}_3\text{C}_6\text{H}_4\text{Cl}-d$	ca. 4	160	250	400	610	ca. 15
$\text{CF}_3\text{C}_6\text{H}_4\text{Cl}-d$	0.6-0.7	150	250	190	265	ca. 2
$\text{CH}_3\text{OC}_6\text{H}_4\text{Cl}-d$	0.5-0.7	180	250	250	400	2.5-4

^a Ten grams of chlorobenzene derivative used in each run, except 8 g. with $\text{CF}_3\text{C}_6\text{H}_4\text{Cl}-d$ and $\text{CH}_3\text{OC}_6\text{H}_4\text{Cl}-d$.

constructed. The deuterium contents of unknown samples were estimated with reference to the calibration plots. Measurements were made with a 0.1-mm., fixed thickness cell and either a Perkin-Elmer Model 21 spectrometer or a Perkin-Elmer Model 112-G, single-beam, double-pass, grating spectrometer with fore prism. A thermocouple detector and strip chart recorder were used with the latter. First-order instrument settings were used with the 112-G in all cases. Liquids were examined neat, and 1,4-dichlorobenzene in carbon tetrachloride solution. The absorption intensity of 1,4-dichloro-2-deuteriobenzene was shown to be independent of added 1,4-dichlorobenzene.

The wave lengths used for analytical purposes are recorded in Table I.

Procedure for Interrupted Reactions with Potassium Amide. A flame-dried apparatus similar to that described by Bunnett and Hrutford⁴³ was used, except that each Dry Ice condenser was fitted to its round-bottom flask through a connecting tube with parallel side arm. Into the inner arm of the connecting tube was inserted a calibrated dropping funnel with pressure-equalizing side arm. In each flask was placed a measured volume of anhydrous diethyl ether and in one a weighed amount of chlorobenzene derivative of known deuterium content. Ammonia gas from a commercial cylinder was condensed in a third flask by means of a Dry Ice condenser, and portions were then forced by dry nitrogen pressure into the two dropping funnels. The volumes of liquid ammonia were recorded, and the ammonia was released into the flasks. The dropping funnels were removed and replaced by stoppers.

Quantities of reactants and solvents used in the various experiments, as well as reaction times, are listed in Table II.

To the flask not containing the chlorobenzene derivative, a weighed amount of potassium metal was added and then a little crushed ferric nitrate. After the blue color had disappeared, the resulting grey solution was forced by dry nitrogen pressure into the solution of the chlorobenzene derivative. Addition required a minute or two; the reaction times listed in Table II include the time for addition. There was often gentle refluxing of the solvent as reaction occurred. The reaction was quenched by addition of excess powdered ammonium nitrate. After the solvent had evaporated to a small volume, the residue was treated with water and the entire mixture was quantitatively transferred to a separatory funnel where the aqueous phase was removed. The ether layer was washed several times with

water. The combined aqueous layers were heated on a steam bath to drive off ammonia and ether and then diluted quantitatively to 250 ml. Chloride ion was determined in triplicate by potentiometric titration of aliquots with silver nitrate.

Amines were removed from the ether layer by extraction with 3 to 5 *M* hydrochloric acid. The ether layer was washed with water, dried over anhydrous magnesium sulfate, and concentrated. The recovered chlorobenzene derivative was distilled twice through either a 10- or a 20-cm. Vigreux column at reduced pressure and then analyzed for purity by gas-liquid chromatography. The deuterium content of this recovered material was determined by infrared measurements as described above.

Procedure for Interrupted Reactions with Potassium Anilide. The procedure was the same as with potassium amide except that about 1.5 moles of aniline/mole of potassium amide was added to the potassium amide flask before addition to the solution of the chlorobenzene derivative. The reaction solution thus contained some free aniline. The total reaction time was 2 hr.

*Reaction of *p*-Dichlorobenzene with Potassium Amide.* To a suspension of potassium amide made from reaction of 4.5 g. of potassium metal with 1 l. of liquid ammonia and addition of 500 ml. of absolute ether, a solution of 24 g. of *p*-dichlorobenzene in 50 ml. of absolute ether was added. After 1 hr. at reflux, the highly colored reaction mixture was quenched by addition of excess ammonium nitrate. After the ammonia had evaporated, the remaining ether layer was washed successively with water and with three portions of 9.5 *M* hydrochloric acid. The combined aqueous layers were made basic by addition of sodium hydroxide and thrice extracted with ether. The combined ether extracts were dried over anhydrous magnesium sulfate, concentrated, and distilled; 5.0 g. of a partially solid product, b.p. 97-99° (15-18 mm.), was obtained. Gas-liquid chromatography on a 4-ft. Carbowax 6000 column at 165° revealed a single peak with retention time identical with that for an authentic mixture of *m*- and *p*-chloroaniline.

*Analysis of Chloroaniline Mixture from *p*-Dichlorobenzene.* To a stirred mixture of 30 ml. of chloroform, 7 ml. of 98% hydrogen peroxide, and 2 drops of concentrated sulfuric acid, cooled in an ice bath, 30 ml. of acetic anhydride was added over a 0.5-hr. period. After the mixture had warmed to room temperature it was quickly heated to boiling; heat was removed and 4.5 g. of the chloroaniline mixture dissolved in 10 ml. of chloroform was added at a rate sufficient to maintain

(43) J. F. Bunnett and B. F. Hrutford, *J. Am. Chem. Soc.*, **83**, 1691 (1961).

boiling.⁴⁴ After the addition was complete, the mixture was heated at reflux for 3.5 hr. during which time it became light yellow. The cooled mixture was poured into 150 ml. of water and the organic phase was washed repeatedly with 20% aqueous sodium hydroxide, until the washings were no longer colored. The organic phase was washed with 50 ml. of 15% hydrochloric acid, dried over anhydrous magnesium sulfate, concentrated, and distilled. The distillate, b.p. 103–105° (15–17 mm.), weighed 4.5 g. (81%). Gas-liquid chromatography on a 4-ft. di-*n*-decyl phthalate column at 155° revealed a single peak with retention time equal to that of an authentic mixture of *m*- and *p*-chloronitrobenzenes.

Two *ca.* 1-g. samples of this mixture were combined with *ca.* 4 ml. of piperidine in sealed tubes and heated 12 hr. at 50°. Each resulting mixture was transferred to a separatory funnel quantitatively, benzene was added, and the mixture was extracted four times with distilled water. The combined aqueous extracts were heated on the steam bath to drive off traces of benzene, acidified by addition of nitric acid, and diluted quantitatively to 50 ml. Aliquots were titrated potentiometrically with silver nitrate, in duplicate. On the assumption that only *p*-chloronitrobenzene yielded chloride ion under these conditions, the titer from each run indicated that the chloronitrobenzene mixture was 81.3% *para* isomer.

Reaction of m-Dichlorobenzene with Potassium Amide. The procedure was the same as with *p*-dichlorobenzene; 21.5 g. of *m*-dichlorobenzene and 5.4 g. of potassium were used. There was obtained 6.17 g. (33%) of a

(44) This procedure is adapted from W. D. Emmons, *J. Am. Chem. Soc.*, **79**, 5528 (1957).

chloroaniline mixture, b.p. 97–98° (15–17 mm.). No attempt was made to recover unreacted starting material. Gas-liquid chromatography on a 4-ft. Carbowax 6000 column at 165° revealed two peaks, whose retention times were the same as those of *o*-chloroaniline and of a mixture of *m*- and *p*-chloroaniline. The area under the *o*-chloroaniline peak indicated 0.7% of this isomer; the same analysis was obtained on the product of a duplicate run from *m*-dichlorobenzene.

Analysis of Chloroaniline Mixture from m-Dichlorobenzene. The oxidation procedure described above was employed. The product was collected from distillation, b.p. 103–105° (15–17 mm.), in two fractions. The first, 0.6 g., showed several peaks by gas-liquid chromatography. The second, 5.0 g., froze to a solid of m.p. 43–44°. The reported melting point of *m*-chloronitrobenzene is 44°. The total yield was 74% of theory.

Each fraction was allowed to react with excess piperidine for 21 hr. at 40°, much as described above, and chloride ion in the products was determined in substantially the same way. The yield of chloride ion from the first fraction was 3.65% and from the second, 2.3%. Similar determinations on the products from a similar but independent sequence of reactions from *m*-dichlorobenzene gave 3.39 and 3.42% chloride ion. We have taken 3.0% as a basis for yield calculations. If this represents the combined yields of *o*- and *p*-chloronitrobenzene, and there was no change of isomer ratio on oxidation of the chloroanilines, the composition of the mixture of chloroanilines from reaction of *m*-dichlorobenzene with potassium amide was 0.7% *ortho*, 97.0% *meta*, and 2.3% *para*.

(45) V. v. Richter, "The Chemistry of the Carbon Compounds," Vol. III, Elsevier Publishing Co., New York, N. Y., 1946, p. 62.

Cumulative Influence of Methylthio Groups on the π -System Properties of Aromatic Hydrocarbons¹

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Charge-transfer maxima, polarographic oxidation potentials, and n.m.r. spectral data are reported for methylthio-substituted benzenes, anisoles, and N,N-dimethylanilines. Relative energy levels for 25 compounds are found to agree with polarographic oxidation potentials with a standard deviation of as little as 0.03 v. with six Huckel heteroatom parameters. Either the p- or d-orbital model for sulfur may be employed, but the parameters permissible for a good linear correlation fall in a narrow range, as shown by a nonlinear, least-squares estimation study. The parameters show that none of the other 46 planar combinations and permutations of dimethylamino, methylthio, and methoxy groups on a benzene nucleus can approach the low ionization potential of N,N,N',N'-tetramethyl-p-phenylenediamine. Correlation of aromatic proton chemical shifts with Huckel calculated charge densities is found to be less

satisfactory; however, the results decidedly favor use of the p-orbital model for sulfur.

Introduction

In previous papers²⁻⁶ we have shown that some π -electronic properties of benzene derivatives containing

(1) Cumulative Influence of Conjugated Substituents on the π -system Properties of Aromatic Hydrocarbons. Part X. Part IX: A. Zweig and W. G. Hodgson, *Proc. Chem. Soc.*, 417 (1964).

(2) Part VIII: A. Zweig, J. E. Lancaster, M. T. Neglia, and W. H. Jura, *J. Am. Chem. Soc.*, **86**, 4130 (1964).

(3) A. Zweig, W. G. Hodgson, and W. H. Jura, *ibid.*, **86**, 4124 (1964).

(4) A. Zweig, J. E. Lehnsen, J. E. Lancaster, and M. T. Neglia, *ibid.*, **85**, 3940 (1963).

(5) A. Zweig, J. E. Lehnsen, and M. A. Murray, *ibid.*, **85**, 3933 (1963).

(6) A. Zweig, *J. Phys. Chem.*, **67**, 506 (1963).