Substituent Effects on the Ratio of Proton Capture to Bromide Ion Loss by *o*-Bromophenyl Anions in Methanol[1,2]

J. F. BUNNETT AND D. A. R. HAPPER

Chemistry Department, Brown University, Providence, Rhode Island 02912

Received March 14, 1966

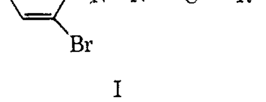
The relative rates of proton capture and bromide ion loss by substituted *o*-bromophenyl anions in methanol are given by the relative yields of aryl bromide VII and bromide ion from the $NaOCH_3$-induced cleavage of substituted 1-(*o*-bromophenyl)-2-sulfonhydrazides of type IIa or IV. Reaction is believed to occur by the mechanism of Scheme I. All the substituents investigated (OCH_3, CH_3, Cl, CF_3) increased the proton capture/bromide loss ratio (Table I). That *o*-haloaryl anions are reaction intermediates is indicated by the obtaining of chlorobenzene-2-*d* from cleavage of chlorohydrazide IIb in CH_3OD.

Two prominent modes of reaction of *o*-halophenyl anions in protic solvents are loss of halide ion, to form arynes, and proton capture from the solvent to form aryl halides.[3] The relative rates of these reactions depend on the halogen,[3] on the solvent, and on other substituents present on the aromatic ring.[4] The effects of substituents are our present interest.

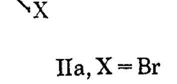
Roberts, *et al.*,[3] showed that the relative rates of proton capture and chloride ion loss by the *o*-chlorophenyl anion in liquid ammonia can be estimated by exposing *o*-deuteriochlorobenzene to potassium amide in ammonia, interrupting the reaction, and determining the change of deuterium content of the unreacted chlorobenzene as a function of the amount of chloride ion liberated. This method was employed by Zoltewicz and Bunnett[4] to determine the effects of several substituents on the proton capture/chloride loss rate ratio. The somewhat surprising result was that all the substituents investigated increased this ratio. Both electron-attracting (Cl, CF_3) and electron-releasing substituents (CH_3, OCH_3) had the same qualitative effect.

A difficulty with the foregoing method is that it requires knowledge of the kinetic isotope effect, $k_{\rm H}/k_{\rm D}$, for abstraction of protons *vs.* deuterons by the base. There is multiple evidence[3] that this isotope effect is about 5.7, and this value was used in the calculations of Zoltewicz and Bunnett. However, it is possible that the isotope effect depends on the substituents present. To the extent that it does, the values of $k_{+\rm H}/k_{-\rm Cl}$ reckoned by Zoltewicz and Bunnett are in error, though probably not enough to change the qualitative order of the substituent effects.

Nevertheless, a determination of substituent effects which did not involve an assumption about isotope effects was desirable. A reaction reported by Hoffmann[5] seemed promising for this purpose. He found that ethanolic sodium ethoxide cleaves N-(*o*-bromophenyl)-N′-acyldiimides (I) with formation of bromobenzene, bromide ion, and phenetole, plus an ester ($RCOOC_2H_5$), and nitrogen gas. He postulated that cleavage of I, initiated by attack of ethoxide ion on carbonyl carbon, formed the ester, nitrogen and *o*-bromophenyl anion. Proton capture by this anion afforded bromobenzene, while bromide ion in loss gave benzyne which added ethanol to form phenetole.



I



IIa, X = Br
b, X = Cl

In preliminary experiments, we found compounds of type I inconvenient to prepare and purify. We then learned that Bradshaw and Lambert[6] had observed a similar fragmentation on treatment of 1-(*o*-bromophenyl)-2-*p*-toluenesulfonhydrazide (IIa) with sodium methoxide in methanol.[7] Inasmuch as compounds of type II are easily synthesized, we undertook a quantitative study of the products of their decomposition induced by methanolic methoxide. When these experiments were nearly completed, Hoffmann[8] published an independent investigation of the action of ethanolic ethoxide on IIa. He did not probe substituent effects.

Reactions in CH_3OD.—If *o*-halophenyl anions are formed by the action of methoxide on IIa or b, reaction in methyl alcohol-O-*d* should afford a halobenzene deuterated in one *ortho* position. Cleavage of IIb by 2 *M* sodium methoxide in CH_3OD furnished, in the event, chlorobenzene-2-*d*. Its infrared spectrum matched in full detail that of the best sample of chlorobenzene-2-*d* prepared by Zoltewicz and Bunnett.[4]

The corresponding bromo compound, IIa, was also cleaved by 2 *M* $NaOCH_3$ in CH_3OD. The infrared spectrum of the bromobenzene obtained differed from that of ordinary bromobenzene in the same way that the spectra of chlorobenzene-2-*d* and ordinary chlorobenzene differ.

This cleavage has promise as a method for the preparation of *o*-deuteriohalobenzenes. It is much more convenient than the Grignard route commonly used in the past.[3,4]

Substituent Effects.—Six derivatives of 1-(*o*-bromophenyl)-2-benzenesulfonhydrazide, containing various substituents in the phenylhydrazine moiety, were prepared. Their synthesis was straightforward. The appropriate aniline derivative was diazotized and coupled with the benzenesulfinate ion to form a diazo-

---

[1] Presented in part at the 19th National Organic Chemistry Symposium of the American Chemical Society, Tempe, Ariz., June 16, 1965, Abstracts, p 50.

[2] Supported in part by the National Science Foundation.

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

[4] J. A. Zoltewicz and J. F. Bunnett, *ibid.*, **87**, 2640 (1965).

[5] R. W. Hoffmann, *Chem. Ber.*, **97**, 2763, 2772 (1964).

[6] J. S. Bradshaw and W. E. Lambert, III, unpublished report concerning research performed at the California Institute of Technology. We thank Dr. Bradshaw for furnishing us a copy of this report.

[7] The cleavage of 1-phenyl-2-sulfonhydrazides by base, yielding benzene, nitrogen, and sulfinate ion, was reported many years ago: R. Escales, *Ber.*, **18**, 893 (1885); A. Hälssig, *J. Prakt. Chem.*, [2] **56**, 213 (1897).

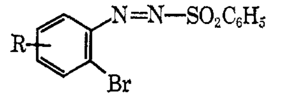
[8] R. W. Hoffmann, *Chem. Ber.*, **98**, 222 (1965).

TABLE I

REACTIONS OF SUBSTITUTED 1-(*o*-BROMOPHENYL)-2-SULFONHYDRAZIDES WITH 2 *M* SODIUM METHOXIDE IN METHYL ALCOHOL AT 61°

Substrate	Substituent	Aryl bromide VII, %	Anisoles X + IX, %	Br^-, %	Anisoles, *p*/*m* ratio	% VII/% Br^- or k_{+H}/k_{-Br}	Notes
IIa	H	86.8 ± 0.6	9.0 ± 0.4	11.2 ± 0.3	...	7.8	*a*
IVa	4-CH_3	89.8 ± 1.4	5.8 ± 0.3	8.7 ± 0.2	0.74 ± 0.10	10.3	*a*
IVb	5-CH_3	89.7 ± 1.7	6.5 ± 0.3	7.9 ± 0.1	0.83 ± 0.11	11.3	*a*
IVc	5-OCH_3	95.9 ± 1.0	*Ca.* 4	3.74 ± 0.04	Ca. 1	26	*a*
IVd	4-Cl	91.7	3.1	4.3	1.9	21	*b*
IVe	5-Cl	89.3	1.3	2.1	2.5	43	*b*
IVf	5-CF_3	96.6 ± 0.4	Trace	2.1	1.9 ± 0.1	46	*a*

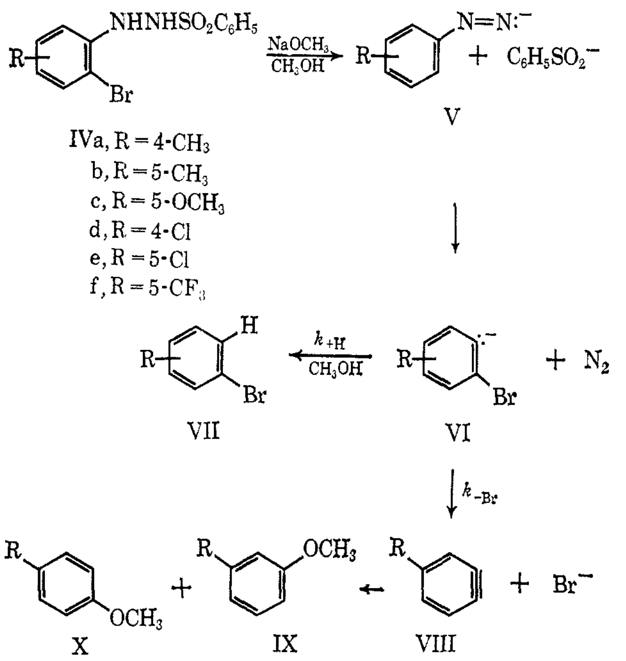
[a] Yields listed are averages of three or four runs; average deviations are listed. [b] Yields listed are derived from best runs; other runs gave similar results.



III

sulfone of type III. Reduction with zinc and acetic acid in ethanol afforded the hydrazide of type IV (see Scheme I).

SCHEME I



Hydrazide IIa and the six hydrazides of type IV were exposed to 2 *M* sodium methoxide in methyl alcohol. Reactions were run in a constant temperature bath at 61° for 1 hr. Organic products were determined by gas–liquid partition chromatography, and bromide ion by argentimetric titration. More than 96% of the bromine introduced was accounted for as aryl bromide or bromide ion, except in one case (91.4%). Results are summarized in Table I.

Hydrazide IIa was also submitted to the action of other sodium alkoxides, in the corresponding alcohols as solvents, under conditions similar to those employed with sodium methoxide–methyl alcohol. The yields of bromobenzene, bromide ion, and phenyl alkyl ether with ethoxide–ethyl alcohol and isopropoxide–*sec*-propyl alcohol were not significantly different for those with methoxide–methanol as listed in Table I. With *t*-butoxide–*t*-butyl alcohol, 14.6% of bromide ion was obtained plus 65% of bromobenzene, but only about 2% of phenyl *t*-butyl ether was detected.

Discussion

The reactions of methanolic sodium methoxide with IIa and the several compounds of type IV are believed to occur by the mechanism of Scheme I. Hoffmann[8] has shown that the ethoxide–ethyl alcohol cleavage of IIa, of several compounds of type I, and of other substances of diverse types affords bromobenzene and bromide ion in essentially constant ratio. This testifies to there being a common intermediate in all the reactions, and it is plausibly *o*-bromophenyl anion as inferred by Hoffmann.

All the substances utilized by Hoffmann as sources of *o*-bromophenyl anion are possible precursors of *o*-bromophenyldiimide or its anion V (R = H). His experiments do not exclude the possibility that the common intermediate is the aryldiimide or its anion. Conceivably V undergoes concerted protonation and loss of nitrogen to yield VII, or concerted loss of nitrogen and bromide ion to form VIII, without the intermediacy of the aryl anion VI.

Cram and Bradshaw[9] have used the base-induced decomposition of optically active 1-(2-phenyl-2-butyl)-2-*p*-toluenesulfonhydrazide as a means of generating the 2-phenyl-2-butyl anion. They have presented arguments that if the 2-phenyl-2-butyldiimide anion is an intermediate, its lifetime is very short. They judged that no important fraction of the 2-phenylbutane formed resulted from direct protodenitrogenation of the diimide ion. In view of the greater acidity of the 2-hydrogen of bromobenzene than of the α hydrogen of 2-phenylbutane,[10] an *o*-haloaryldiimide ion of type V should have an even greater tendency to lose nitrogen and form a carbanion.

In the ensuing discussion, we consider that the cleavage reactions studied do occur *via* *o*-bromoaryl anions of Type VI. As will be shown, the results of this

---

(9) D. J. Cram and J. S. Bradshaw, *J. Am. Chem. Soc.*, **85**, 1108 (1963).

(10) The rate of exchange of 2-phenylbutane-α-*t* with cyclohexylamine, catalyzed by cesium cyclohexylamide, is about one-third that of benzene-*t*.[11] An *o*-halogen substituent accelerates abstraction of aryl hydrogen by bases by several powers of 10.[12] Taking exchange rates as indicative of the acidities of hydrogen atoms, we therefore judge the pK_a of bromobenzene to be perhaps 10 p*K* units lower than that of 2-phenylbutane.

(11) A. Streitwieser, Jr., and R. A. Caldwell, *J. Am. Chem. Soc.*, **87**, 5394 (1965).

(12) (a) G. E. Hall, R. Piccolini, and J. D. Roberts, *ibid.*, **77**, 4540 (1955); (b) R. Huisgen, W. Mack, K. Herbig, N. Ott, and E. Anneser, *Chem. Ber.*, **93**, 412 (1960).

investigation offer some independent support for this view.

It follows from Scheme I that the ratio of yields of aryl bromide VII and bromide ion is directly expressive of the ratio of first-order rate coefficients, $k_{+\mathrm{H}}/k_{-\mathrm{Br}}$.[13] In Table I, it is evident that all the substituents studied increased this ratio, regardless of whether they are electron releasing or electron attracting as judged by the usual criteria. Qualitatively, this matches the experience of Zoltewicz and Bunnett[4] concerning $k_{+\mathrm{H}}/k_{-\mathrm{Cl}}$ for *o*-chlorophenyl anions in ammonia.

The two sets of results are also quantitatively similar. By sheer coincidence, the value of $k_{+\mathrm{H}}/k_{-\mathrm{Br}}$ for VI, R = H (7.8), is nearly the same as $k_{+\mathrm{H}}/k_{-\mathrm{Cl}}$ for unsubstituted *o*-chlorophenyl anion in ammonia (7.6). Though of no more than passing interest for itself, this near identity of ratios for the unsubstituted anions does facilitate comparison of the two series.

Comparison of substituent effects between the present and the earlier study is possible only for those cases where the substituent is *para* to the halogen and *meta* to the anionic center. When the substituent so located is methyl (reaction of IVb), $k_{+\mathrm{H}}/k_{-\mathrm{X}}$ is 11.3 in the present study whereas it was 11.4 in the ammonia system. When the substituent is methoxy (IVc), the ratio now reported is 26; it was 99 in the ammonia system. When it is chlorine (IVe), $k_{+\mathrm{H}}/k_{-\mathrm{Br}}$ in methanol is 43; $k_{+\mathrm{H}}/k_{-\mathrm{Cl}}$ in ammonia was 240. When the substituent is CF_3 (IVf), the ratio now reported is 46; in ammonia it was 230.

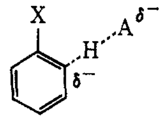
The results from the two studies are closely parallel. The small ratio-enhancing effect of methyl is nearly the same in both series. In both series methoxy has a larger effect. In both series the largest effects observed are due to chlorine and trifluoromethyl, and are nearly the same for these two groups.

We note again that the values of $k_{+\mathrm{H}}/k_{-\mathrm{Cl}}$ in ammonia depend on the value of $k_\mathrm{H}/k_\mathrm{D}$ used in the computations. Had lower values of $k_\mathrm{H}/k_\mathrm{D}$ been used, lower values of $k_{+\mathrm{H}}/k_{-\mathrm{Cl}}$ would have been obtained, more closely resembling the corresponding $k_{+\mathrm{H}}/k_{-\mathrm{Br}}$ in Table I.

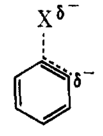
The similarity of substituent effects in the two series implies that both ratios are determined by similar factors. Specifically, since an *o*-halophenyl anion is clearly the intermediate partitioned in the liquid ammonia system (an aryldiimide ion intermediate is inconceivable), an *o*-halophenyl anion rather than an aryldiimide ion is indicated as the intermediate partitioned in cleavage of hydrazides of type IV.

Also, since proton transfer from ammonia to aryl anions does not occur at a rate controlled by diffusion or rearrangement of the ion's solvent shell,[15] it is unlikely that $k_{+\mathrm{H}}$ in the present study is limited only by such physical factors. This conclusion is at variance with Hoffmann's judgment[8] that proton transfer to the *o*-bromophenyl anion from ethyl alcohol is diffusion controlled. Though the pK discrepancy between a halobenzene and an alcohol is indeed large, as he mentions, the aryl anion probably is not solvated *via* hydrogen bonds. In such cases, the rate of proton transfer may lag far behind the physical limit despite a large difference of pK between donating and accepting bases.[16]

Zoltewicz and Bunnett[4] interpreted the effect of electron-attracting substituents on $k_{+\mathrm{H}}/k_{-\mathrm{X}}$ in terms of polar interaction of the substituent with partially anionic carbon in the transition states for proton capture (XI) and halide ion loss (XII). From the fact that the proton capture transition states XI are more favorably affected by such substituents, they were judged to have more negative charge on carbon. Structure XI was considered to lie close to the phenyl anion on the reaction coordinate, and XII close to the aryne.



XI



XII

In the present system, transition state XI would be expected to lie even closer to aryl anion because methanol is more acidic than ammonia. But XII would also be expected to lie closer to the anion, because bromine is a better leaving group than chlorine and because methyl alcohol provides better solvation for anions. Inasmuch as substituent effects are somewhat lower in the present system, the degrees of carbanionic character in the two transition states are judged to be now more nearly equal. Thus it appears that the change of system has affected the character of XII more than of XI.

The substituent effect of chlorine *meta* to bromine and *para* to the anionic center of VI is consistent with this interpretation. In the reaction of IVd, $k_{+\mathrm{H}}/k_{-\mathrm{Br}}$ is much lower than for IVe. The stabilizing effect of halogen on a phenyl anion is known to diminish in the order, *ortho* >> *meta* > *para*.[12a] The effect of chlorine *para* to the anionic center therefore should be smaller.

The effect of electron-releasing substituents on $k_{+\mathrm{H}}/k_{-\mathrm{X}}$ was tentatively ascribed by Zoltewicz and Bunnett to destablilization of the arynes formed, and consequently of transition states XII with their partial aryne character. The apparently smaller effect of methoxy (reaction of IVc) in the present than in the former system is intelligible if XII now has less aryne character, as already proposed from other considerations.

Again we caution that these interpretations of substituent effects are hypothetical. It is satisfying, however, that the hypotheses of Zoltewicz and Bunnett, with but straightforward modification to take account of the changes in solvent and leaving group, give an agreeable account of the present observations.

---

[13] Nucleophilic addition of bromide ion to benzyne in alcoholic solvents has been observed.[14] However, as Hoffmann has commented,[8] it is quantitatively negligible at very low bromide ion concentrations such as prevailed in the present experiments.

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

[15] 1,3-Dichlorobenzene-2-*d*, on interrupted reaction with KNH_2 in ammonia, experiences considerable hydrogen exchange and some loss of chloride ion.[4] On extended treatment with potassium anilide–aniline in ammonia, complete hydrogen exchange occurs without loss of chloride ion. Were protonation of the anion occurring at a solvent reorientation-controlled rate, the anion would be partitioned between proton capture and chloride loss in constant ratio unaffected by addition of aniline to the system.

[16] M. Eigen, *Angew. Chem.*, **75**, 498 (1963); *Angew. Chem. Intern. Ed. Engl.*, **3**, 1 (1964).

TABLE II

SUBSTITUTED 1-(2-BROMOPHENYL)-2-BENZENESULFONHYDRAZIDES (IV)

Substituent	Structure	Recrystn solvent	Mp, °C	Calcd, % C	Calcd, % H	Calcd, % X	Found, % C	Found, % H	Found, % X
4-CH_3	IVa	Ethyl alcohol–water	122–122.5	45.75	3.81	23.46[a]	45.78	3.91	23.65
5-CH_3	IVb	Methyl alcohol	146.6–146.8	45.75	3.81	23.46[a]	45.75	4.00	23.26
5-OCH_3	IVc	Benzene	138.5	43.70	3.64	22.41[a]	43.54	3.77	22.03
4-Cl	IVd	Benzene–methyl alcohol	154–154.5	39.83	2.77	31.95[b]	39.84	2.90	31.75
5-Cl	IVe	Methyl alcohol	155	39.83	2.77	31.95[b]	40.09	3.07	31.91
5-CF_3	IVf	Methyl alcohol–water	166	39.49	2.53	20.25[a]	39.59	2.66	20.48

[a] Bromine. [b] Bromine plus chlorine.

Experimental Section

1-(*o*-Bromophenyl)-2-*p*-toluenesulfonhydrazide (IIa), mp 141° (lit.[8] 147.5–148°), was prepared by reaction of *o*-bromophenylhydrazine, in pyridine solution at −10°, with *p*-toluenesulfonyl chloride.[6]

1-(*o*-Chlorophenyl)-2-*p*-toluenesulfonhydrazide (IIb), mp 144–145°, was similarly prepared from *o*-chlorophenylhydrazine.

Anal. Calcd for $C_{13}H_{13}ClN_2O_2S$: C, 52.61; H, 4.42. Found: C, 52.77; H, 4.58.

Substituted *o*-Bromoanilines.—2-Bromo-4-methylaniline and 2-bromo-5-trifluoromethylaniline were available as commercial products. 2-Bromo-5-methylaniline was synthesized by diazotization of 4-methyl-2-nitroaniline, treatment with cuprous bromide, and reduction of the resulting bromonitrotoluene with iron and dilute hydrochloric acid. 2-Bromo-5-methoxyaniline was similarly prepared from 4-methoxy-2-nitroaniline; the hydrochloride of the product had mp 184–185° in agreement with the literature.[17] 2-Bromo-4-chloroaniline was prepared after Owen.[18] 2-Bromo-5-chloroaniline, mp 37.5–38° (lit.[19] 38°), was prepared after van de Lande.[19]

Substituted 1-(*o*-Bromophenyl)-2-benzenesulfonhydrazides (IV).—The appropriate substituted *o*-bromoaniline was diazotized, and the diazonium solution was poured into a stirred, chilled solution of sodium benzenesulfinate. The diazosulfone (III) immediately precipitated, often as a gum which solidified on standing. The diazosulfone was reduced,[8,20] in an ethyl alcohol solution containing about 5% of acetic acid, by addition of zinc dust, with stirring, until the yellow color of the diazosulfone had been discharged. The hydrazide IV was isolated by conventional procedures, and recrystallized from methyl alcohol, aqueous ethyl alcohol, or benzene. Properties of the several sulfonhydrazides of type IV are summarized in Table II.

Reactions of Sulfonhydrazides with Sodium Methoxide.—The reaction vessel was a 50-ml round-bottom flask fitted with a water-cooled condenser leading to a gas buret. The flask was immersed in a thermostat at 61° and in the flask was placed 20 ml of 2 *M* sodium methoxide in methyl alcohol. A small glass capsule, open at one end, containing a weighed portion (*ca.* 0.001 mole) of the hydrazide (IIa or type IV) was dropped into the flask, the condenser was connected, and the flask was swirled. The hydrazide quickly dissolved, the solution assumed an intense color (varying from red-orange to violet), and a gas was evolved. Progress of the reaction was noted by means of the gas buret. The reaction was allowed to proceed for 1 hr, at which time gas evolution had ceased and the solution had faded to light pink or orange. The flask was removed from the thermostat, 10 ml of a standard solution of either chlorobenzene or bromobenzene in benzene was added, and the resulting mixture was combined in a separatory funnel with 100 ml of water and 50 ml of 3 *M* nitric acid. The layers were separated and the halide ion content of the aqueous layer was determined by potentiometric titration with silver nitrate. The benzene layer was dried over anhydrous magnesium sulfate and analyzed by gas–liquid partition chromatography. Carbowax 6000 columns were used in the experiments with IVd–f, 5% SE-30 silicon rubber/5% Bentone-34 on Chromosorb P columns were used with IIa and IVb, and Bentone 34 columns were used with IVa and c. The yield of aryl bromide VII was reckoned from the relevant peak area with reference to the area of the chlorobenzene or bromobenzene standard peak, and the areas of the peaks for the substituted anisoles were estimated with reference to the same standard. All peaks were recognized by retention time analysis by comparison with authentic samples. Resolution of peaks was good.

One reaction with IIa was run in the usual way but at room temperature in an electron spin resonance spectrometer. A spectrum was obtained, a complex one which suggested that the odd electron was associated mainly with the nitrogen atoms. The signal decayed with a half-life of perhaps 10 min. It is not known whether the radical species is an intermediate in generation of V or VI (R = H) from IIa, or whether it is a minor by-product.

Reactions in methyl alcohol-O-*d* were performed in the same way, except that 5 ml of 2 *M* sodium methoxide in CH_3OD was used with *ca.* 0.001 mole of hydrazide and that pentane (10 ml) was used instead of benzene as an extraction solvent (and no chlorobenzene or bromobenzene was added). The pentane layer was washed with water, dried, and passed through a short (*ca.* 1 cm) bed of alumina to remove colored impurities. Careful evaporation of the pentane at 0° under reduced pressure gave a substantially pure sample of the halobenzene, the infrared spectrum of which was determined.

Acknowledgment.—We thank Dr. Hiroaki Takayama for his careful repetition of two experiments, to resolve minor anomalies.

---

(17) H. H. Hodgson and R. J. H. Dyson, *J. Chem. Soc.*, 947 (1935).

(18) G. Owen, *ibid.*, 123, 3392 (1923).

(19) L. M. F. van de Lande, *Rec. Trav. Chim.*, **51**, 106 (1932).

(20) W. Königs, *Ber.*, **10**, 1531 (1877).