TABLE I

ORGANIC PRODUCTS ISOLATED FROM THE REACTION OF HYDRAZINE WITH BENZYL NITRATE

Compound	M.p., °C. Lit.[a]	M.p., °C. Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
$C_6H_5CH_2N_2H_3 \cdot HNO_3$	..	172.5–173.5	45.40	56.24[b]	5.99	6.46[b]	22.69	17.76[b]
$(C_6H_5CH_2)_2N_2H_2 \cdot HNO_3$	..		61.07		6.23		15.26	
$(C_6H_5CH_2)_3N_2H \cdot HNO_3$	..	188–188.5	69.02	69.42	6.34	6.49	11.50	11.04
$(C_6H_5CH_2)_4N_2$	139	139–140	85.67	85.83	7.19	7.05	7.14	7.12
$(C_6H_5CH_2)_2N{-}N{=}CHC_6H_5$[c]	87	83–84	83.96	84.39	6.71	6.96	9.33	8.57

[a] Ref. 17. [b] This analysis indicated a mixture of mono- and higher benzylated hydrazine mononitrates. A hydrochloride was obtained from this product, m.p. 213–215° dec. 1,2-Dibenzylhydrazine monohydrochloride has m.p. 215–217° dec. (A. F. Bickel and W. A. Waters, *Rec. trav. chim.*, 69, 312 (1950)). [c] It was not possible to improve either the m.p. or the analysis of this product. Hydrolysis with HCl gave benzaldehyde and a hydrochloride, m.p. 198.5-199.5°; N, 11.34; reported (ref. 17) for 1,1-dibenzylhydrazine monohydrochloride, m.p. 202°; N (calcd.), 11.26.

mixture after completion of a reaction, immediate extraction with ether, and distillation of the ethanol–ethyl nitrate azeotrope from the ether-soluble fraction. The α-naphthylurethan was prepared directly from the azeotropic mixture. Butanol was characterized by boiling point, refractive index, and by derivatization as the α-naphthylurethan.

Attempts were made to detect aldehyde by refluxing the ether-soluble fractions with dilute HCl (to hydrolyze any hydrazones or azines) and adding 2,4-dinitrophenylhydrazine (DNP). A DNP derivative was obtained from one experiment with isoamyl nitrate and was shown to be that of isovaleraldehyde, m.p. and mixed m.p. 122–123°. No evidence of aldehyde formation was obtained from any experiments using *n*-butyl or ethyl nitrate.

Acknowledgment.—The authors are indebted to Dr. C. A. VanderWerf and Dr. Howard W. Kruse for some of the starting materials; to Dr. S. R. Smith for the mass spectra; and to R. H. Pierson for some of the infrared spectra. Thanks are also due to Kathryne B. Clifton and Mario J. Falbo for assistance in various phases of this investigation.

CHINA LAKE, CALIF.

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Orientation in Aromatic Nitration Reactions[1]

BY JOHN D. ROBERTS,[2,3] JANET K. SANFORD,[2,4] F. L. J. SIXMA,[5] H. CERFONTAIN[5] AND R. ZAGT[5]

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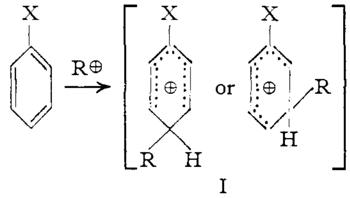
The isotope dilution method has been employed to determine isomer distributions in the nitration of chloro-, bromo- and iodobenzenes and the relative reactivity of iodobenzene with respect to benzene. For nitration at 25°, the following isomer distributions were found: chlorobenzene, *ortho* 29.6 ± 1.7%, *meta* 0.9 ± 0.0%, and *para* 69.5 ± 1.7%; bromobenzene, *ortho* 36.5 ± 1.7%, *meta* 1.2 ± 0.1%, and *para* 62.4 ± 2.8%; iodobenzene, *ortho* 38.3 ± 2.0%, *meta* 1.8 ± 0.3%, and *para* 59.7 ± 2.0%. The reactivity of iodobenzene relative to benzene at 25° was 0.13 in acetic anhydride and 0.22 in nitromethane. The degree of correlation of the nitration reactivities of benzene derivatives with Hammett σ-constants is discussed. Deviations from the Hammett relationship are interpreted in terms of important contributions of transition-state resonance.

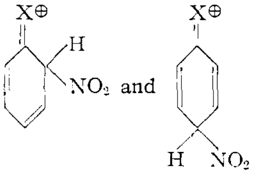
Introduction

Considerable disagreement exists as to the importance, in electrophilic aromatic substitution, of transition-state resonance interactions involving the orienting substituent groups and most easily discussed in terms of the customary pentadienate cation model (I) of the transition state.



I

Although Hammett's statement[6] that relative reactivities in the nitration of substituted benzenes parallel the σ-constants of the substituents would seem to exclude important contributions of the following type for *o*- and *p*-substitutions



II

evidence for significant contributions of such resonance has long been accumulating. Kenner[7] found substantial differences in the charge at the *p*-position of a halobenzene when calculated from nitration rate data and from dipole moment data, respectively, attributed by him to transition state resonance during nitration. Transition state resonance involving the *p*-position also has been postu-

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[6] L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, pp. 198–199.

[7] G. W. Kenner, *Proc. Roy. Soc.*, **A185**, 119 (1946).

lated by Swain and Langsdorf[8] to account for the two curves correlating rates of bimolecular reactions of substituted benzyl bromides with trimethylamine. One curve accommodates unsubstituted and *m*-substituted benzyl bromides, the other accommodates *p*-substituted benzyl bromides.

Prominent resonance contributions would be anticipated in *o*- and *p*-substitution when the substituent can accommodate a positive charge as in the halobenzenes, cinnamic acid and certain related compounds. These compounds have been least satisfactorily described by quantum mechanical[9] and other[7,10] calculations. As not enough experimental data were available for an adequate test of the Hammett relation in this critical area, measurements of the small degree of *m*-isomer formation in the nitration of chloro-, bromo- and iodobenzene were made.

Method of Analysis

The isotope dilution procedure[11] was used for the determination of isomer distribution and the reactivity of iodobenzene relative to benzene for which only an approximate value has been reported.[12] For the isotope dilution analysis of isomer distribution, halobenzenes containing radioactive Cl^{36}, Br^{82} and I^{131} were synthesized and nitrated. The percentages of each of the isomeric nitration products were determined, as shown schematically in Fig. 1, by (1) adding known quantities of the inactive forms of each isomer to fractional parts of the reaction mixture, (2) separating and purifying the diluted isomers to radiochemical and chemical purity, and (3) comparing the activities of the diluted forms with those of the starting materials. To eliminate highly active impurities, each diluted isomer was scavenged repeatedly with inactive forms of all suspected impurities (other nitrohalobenzene isomers, halide ion, halogen and halobenzene). Purification was deemed complete when the activities of the recovered scavenging species were less than that of the scavenged material or until the activity of the scavenged material remained substantially constant on successive treatments. The scavenged diluted isomers were recrystallized, distilled or chromatographed until samples of high chemical purity were obtained. These either were counted as such or converted to silver halides for counting. In the determination of the (small) extent of formation of the *m*-isomers by isotope dilution, especial care was necessary to ensure complete removal of the relatively highly radioactive *o*- and *p*-nitrohalobenzenes. The most satisfactory procedure for this purification took advantage of the very large reactivity of the *o,p*-nitrohalobenzenes toward piperidine as compared to the corresponding *m*-isomers. Generally, three or four piperidine treatments, using added inactive *o,p*-nitrohalobenzenes as scavengers, reduced contamination by the radioactive *o,p*-isomers to negligible proportions.

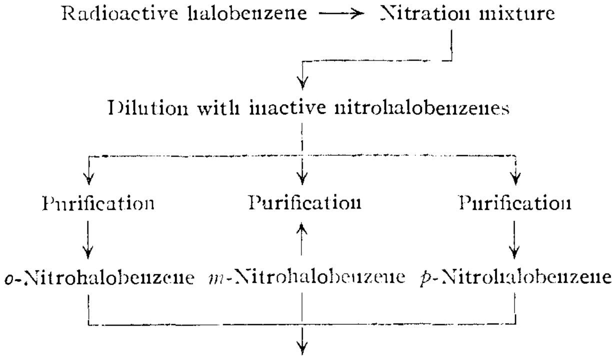

Fig. 1.—Isomer distribution analysis.

The general scheme for determination of the relative reactivities of iodobenzene and benzene, based on the radiochemical determination of *p*-nitroiodobenzene in the products from a competitive nitration, is shown in Fig. 2. From the amount of *p*-nitroiodobenzene formed and the isomer distribution determined above, the amount of iodobenzene nitrated was calculated. Chemical analysis for the total amount of aromatic nitration gave, by difference, the amount of benzene nitrated.

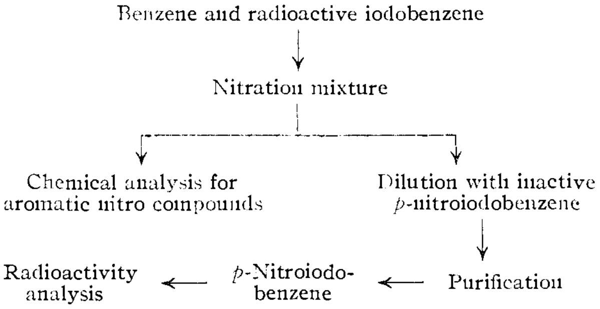

Fig. 2.—Relative reactivity determination.

Preparation of Radioactive Halobenzenes

Radioactive chloro- and iodobenzenes were prepared by decomposition of benzenediazonium compounds in the presence of the respective radioactive halide ions. The iodobenzene synthesis could be achieved readily by standard procedures,[13] but the published procedures for the synthesis of chlorobenzenes from the diazonium salts required large excesses of chloride ion (four[14] to sixty[15] moles)

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(8) C. G. Swain and W. P. Langsdorf, Jr., THIS JOURNAL, **73**, 2813 (1951).

(9) (a) G. W. Wheland, *ibid.*, **64**, 900 (1942); (b) J. D. Roberts and A. Streitwieser, Jr., *ibid.*, **74**, 4723 (1952).

(10) The high accuracy reported by T. Ri and H. Eyring, *J. Chem. Phys.*, **8**, 433 (1940), for calculations of isomer distributions from dipole moment data is probably illusory since it depends on assumption of an arbitrary and physically unrealistic electrostatic model for the nitration transition state as well as "semi-empirical" adjustment of *o*-*p* ratios. For the halobenzenes, the Ri and Eyring procedure leads to proportions of *m*-isomers which are shown later in this paper to be substantially incorrect.

In our opinion, the quantitative significance of the Ri and Eyring calculations has been overestimated by L. N. Ferguson, *Chem. Revs.*, **50**, 47 (1952), and A. E. Remick, "Electronic Interpretations of Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 2nd Ed., 1949, pp. 218–220.

(11) F. C. Henriques, Jr. and C. Margnetti, *Ind. Eng. Chem., Anal. Ed.*, **18**, 476 (1948).

(12) M. L. Bird and C. K. Ingold, *J. Chem. Soc.*, 918 (1938).

(13) L. Gattermann and H. Wieland, "Laboratory Methods of Organic Chemistry," translated from the 24th German Edition by W. McCartney, The Macmillan Co., New York, N. Y., 1938, p. 81; H. J. Lucas and E. R. Kennedy, *Org. Syntheses*, **19**, 55 (1939).

(14) A. Angeli, *Gazz. chim. ital.*, **21**, II, 258 (1891).

(15) L. H. Welsh, THIS JOURNAL, **63**, 3276 (1941).

TABLE I

DILUTION AND ACTIVITY DATA FOR THE NITRATION OF HALOBENZENES

Experiment	I		II	III	IV		V		VI		VII	VIII	IX	
Halobenzene	C_6H_5Cl		C_6H_5Br	C_6H_5Br	C_6H_5I		C_6H_5I		C_6H_5I		C_6H_5I	C_6H_5I	C_6H_5I	
Amount nitrated, g.	2.867		11.4	12.9	6.0		9.02		8.4089		5.7646	2.0988	10.186	
Reaction time, hr., 25°	54		10	11	36		52		52		52	54	20	
Solvent	CH_3NO_2		CH_3NO_2	CH_3NO_2	CH_3NO_2		CH_3NO_2		CH_3NO_2		CH_3NO_2	CH_3NO_2	CH_3NO_2	
Activity of halobenzene														
Active halobenzene, g.	0.1594		0.749	0.6227	0.0299		...[c]		...[c]		1.5224	1.5224	0.1006	0.1006
Diluted with inactive halobenzene, g.	0.8134		2.247	2.6791	1.519		...[c]		...[c]		2.0125	2.0125	32.0894	32.0894
Activity, c./min.	21,942[a]		7202[b]	6382[b]	2076[a]		1383[a,d]	301[a,e]	1383[a,d]	301[a,e]	4067[f]	3985[f]	1409[b,d]	1765[b,e]
o-Halonitrobenzene														
Aliquot taken, wt. %	10.0	....	6.42	6.18	1.274	0.958	....	10.0	....	10.0			3.76	3.62
Added inactive *o*-isomer	10.0329	....	9.9280	10.0531	10.208	7.244	....	20.0224	....	19.7386	10.0156	10.0276	17.1098	13.3605
Activity, c./min.	1638[a]	....	883[b]	1204[b]	305[a]	349[a]	....	66[a,e]	....	65[a,e]	841[f]	763[f]	1160[b,d]	1800[b,e]
m-Halonitrobenzene														
Aliquot taken, wt. %	....	80.0	87.2	87.7	45.094	44.624	80.0	....	80.0	....	....	....	39.15	46.20
Added inactive *m*-isomer, g.	....	10.0625	8.6614	9.1505	10.005	7.095	9.7683	....	9.8106	....	....	....	22.4140	18.7212
Activity, c./min.	....	426[a]	445[b]	635[b]	429[a]	557[a]	216[a,d]	....	266[a,d]	....	....	....	359[b,d]	506[b,e]
p-Halonitrobenzene														
Aliquot taken, wt. %	10.0	80.0	6.38	6.15	0.948	0.935	80.0	10.0	80.0	10.0			3.68	3.60
Added inactive *p*-isomer, g.	10.0130	10.0056	5.0029	4.9918	10.510	7.088	7.4627	9.5592	10.3014	9.9295	7.0586	7.1210	19.7750	16.3813
Activity, c./min.	3499[a]	26,719[a]	2733[b]	3846[b]	406[a]	457[a]	6409[a,d]	228[a,e]	5856[a,d]	201[a,e]	1596[f]	1354[f]	1324[b,d]	1957[b,e]
Isomer distribution, g. of each isomer														
ortho-	1.24	....	5.100	5.996	2.27	2.46	....	2.11	....	2.05	0.98	0.90	1.13	1.14
meta-	....	0.040	0.163	0.199	0.089	0.083	0.091	....	0.113	....	....	....	0.045	0.036
para-	2.69	3.12	8.592	10.400	4.20	3.23	2.64	3.57	3.25	3.26	1.47	1.38	1.55	1.54
Isomer ratios,														
ortho/para	....		....	....	....	....	....	....	....	....	0.665	0.652	....	
Isomer distribution, wt. %														
ortho-	29.6 ± 1.7		36.80	36.14	38.4 ± 3.0		39.8 ± 3.5		37.9 ± 0.1		....	....	41.8 ± 0.3	
meta-	0.9 ± 0.0		1.17	1.19	1.4 ± 0.1		1.8 ± 0.2		2.1 ± 0.0		....	....	1.5 ± 0.2	
para-	69.5 ± 1.7		62.01	62.67	60.2 ± 4.0		58.4 ± 3.5		60.0 ± 0.1		....	....	56.7 ± 0.1	

[a] Determined as silver halide, after correction for background and decay. In each column, samples of the same size were used. [b] Determined as halonitrobenzenes, after correction for background and decay. Samples of 1.000 g. were used for counting. [c] Dilution 1:20 by volume. [d,e] The decay reference times in these radioactive determinations for all values marked *d* are the same and for all values marked *e* are the same. [f] Determined in solution with a platinum-screen-γ-counter, corrected for background and decay.

TABLE II

ISOMER DISTRIBUTION IN THE NITRATION OF HALOBENZENES

Substance nitrated	Conditions, 25°	Method of analysis	Distribution, % *ortho*	*meta*	*para*	Investigators
C_6H_5Cl	$AcNO_3$ in CH_3NO_2	Isotope diln.	29.6	0.9	69.5	This research (I)
C_6H_5Cl	$AcNO_3$ in CH_3NO_2	Cryoscopic	30.2	0.0	69.8	Ref. 12
C_6H_5Cl	$AcNO_3$ in CH_3CN	Cryoscopic	30.2	0.0	69.8	Ref. 12
C_6H_5Cl	HNO_3 (heterogeneous)[a]	Cryoscopic	33.1	0.0	66.9	Ref. *b*
C_6H_5Br	HNO_3 in CH_3NO_2	Isotope diln.	36.5	1.2	62.3	This research (II and III)
C_6H_5Br	$AcNO_3$ in Ac_2O	Cryoscopic	42.0	0.0	58.0	Ref. 12
C_6H_5Br	HNO_3 (heterogeneous)[a]	Cryoscopic	40.4	0.0	59.6	Ref. *c*
C_6H_5I	$AcNO_3$ in CH_3NO_2	Isotope diln.	38.3	1.8	59.7	This research (IV–VIII)
C_6H_5I	HNO_3 in CH_3NO_2	Isotope diln.	41.8	1.5	56.7	This research (IX)
C_6H_5I	HNO_3 (heterogeneous)[a]	Cryoscopic	43.2	0.0	56.8	Ref. *d*

[a] Extrapolated from experiments at 0° and −30°. [b] A. F. Holleman and B. R. de Bruyn, *Rec. trav. chim.*, **19**, 188 (1900). [c] A. F. Holleman and B. R. de Bruyn, *ibid.*, **19**, 364 (1900). [d] A. F. Holleman, *ibid.*, **32**, 134 (1913).

and, hence, were not well suited to the preparation of radioactive chlorobenzene. After a number of trials, radioactive chlorobenzene was found to be prepared best by decomposition of anhydrous benzenediazonium chloride in the presence of radioactive hydrochloric acid in anhydrous dioxane with copper powder as a catalyst. The yield was 23–44% based on total chloride ion. The reaction is similar to those carried out by Hantzsch and Semple,[16] except for the use of the copper catalyst which permitted a more reasonable reaction rate. Radioactive iodobenzene also was prepared by oxidative, direct iodination.[17] Since, in this synthesis, nitric acid is used as oxidant, the purity of the iodobenzene was checked for small amounts of radioactive nitroiodobenzenes which might have been formed during the reaction.

Radioactive bromobenzene was prepared in 64–67% yields (based on total bromine) by bromination of benzene with a mixture of potassium bromate, radioactive bromine and sulfuric acid at 30°.[18]

Experimental Results

The radioactive halobenzenes were nitrated by the method of Bird and Ingold.[12] Data obtained in a single determination of the isomer distribution in the nitration of chlorobenzene, two determinations for bromobenzene and five determinations for iodobenzene are summarized in Table I which also includes the reaction times and conditions. In Table II, the average results are compared with those from earlier investigations where the *meta*-isomer content was assumed negligible. Aside from the *meta*-isomer contents, agreement is good.

Reactivity calculations were made as described by Ingold, Lapworth, Rothstein and Ward[19] except in those experiments where *o*–*p* and *m*–*p* ratios were determined for separate fractions of the reaction mixture.

In Table III are listed the isomer distributions and relative reactivity data for the halobenzenes and some other benzene derivatives[20] studied by other investigators along with the σ-constants of the substituents. A semi-logarithmic plot of relative reactivities against σ-constants is shown in Fig. 3.

TABLE III

REACTIVITIES IN NITRATION OF MONOSUBSTITUTED BENZENES IN ACETIC ANHYDRIDE AT 25°

	Isomer distribution, %		Reactivity,[a] log k/k^0	σ	r[b]
CH_3[c,d]	*meta*	4.3 ± 0.2	0.491	−0.069	0.045
	para	37.4 ± 0.1	1.731	− .170	.080
$-CO_2C_2H_5$[e,f]	*meta*	72.0	−2.098	+ .334[g]	.014
	para	4.0	−3.051	+ .402[g]	.038
H	..	....	(0.000)	.000	.043
F[h]	*meta*	....	......	.....	...
	para	85.4[i]	−0.073	+ .062	.065
Cl[h,j]	*meta*	0.9 ± 0.0	−2.975	+ .373	.053
	para	69.5 ± 1.7	−0.832	+ .227	.054
Br[h,j]	*meta*	1.2 ± 0.1	−2.967	+ .391	.051
	para	62.3 ± 2.9	−0.950	+ .232	.043
I[j]	*meta*	1.8 ± 0.3	−2.154	+ .352	.056
	para	59.7 ± 2.0	−0.339	+ .276	.067

[a] Ratio of rate of nitration at the single *m*- or *p*-position to rate at a single benzene position. [b] Median deviation of σ, see ref. 6. [c] Ref. 19. [d] Calculated from data at 0° and 30°. [e] C. K. Ingold and M. S. Smith, *J. Chem. Soc.*, 905 (1938). [f] Data for 18°. [g] J. D. Roberts and W. T. Moreland, Jr., THIS JOURNAL, **75**, 2267 (1953). [h] Ref. 12. [i] Orientation in acetic anhydride or nitromethane has not been determined; listed values for nitration in nitric acid taken from A. F. Holleman, *Chem. Revs.*, **1**, 187 (1924). See ref. 12 for a comparison of orientation in nitric acid and acetic anhydride solution with chloro- and bromobenzenes. [j] See Tables I and II.

Discussion

Although the Hammett relation has been singularly useful in correlating equilibrium and rate data for many reactions of *m*- and *p*-substituted benzene derivatives where the seat of reaction is not in the benzene ring, it appears from the scatter of many of the points in Fig. 3 that it applies rather less accurately to aromatic nitration.

From theoretical considerations,[21] one would expect that the Hammett relation should hold for electrophilic substitution reactions in the benzene ring only in those cases where there are no important differences in resonance interaction involving the substituent and aromatic ring between

[16] A. Hantzsch and W. Semple, *Ber.*, **33**, 2533 (1900).

[17] F. B. Dains and R. Q. Brewster, *Org. Syntheses*, **9**, 46 (1929).

[18] F. Krafft, *Ber.*, **8**, 1044 (1875).

[19] C. K. Ingold, A. Lapworth, E. Rothstein and D. Ward, *J. Chem. Soc.*, 1959 (1931).

[20] The relative reactivity data for *particular* positions in Table III were computed from the over-all nitration reactivities in acetic anhydride and isomer distributions obtained in acetic anhydride or nitromethane. All available evidence indicates that, although over-all nitration reactivities are different in nitromethane and acetic anhydride, the isomer distributions are insensitive to this degree of solvent variation.

[21] F. L. J. Sixma, *Rec. trav. chim.*, **73**, 243 (1954).

the ground and the transition states. The data of Fig. 3 indicate that the reactivities of the *m*-positions of the compounds so far studied show a quite satisfactory linear relationship with the σ-values. The point for the reactivity of the *p*-position of ethyl benzoate falls close to the line as would be expected for a substituent where important contributions of resonance forms of type II are unlikely. The following equation (least-squares fit) was obtained from the points for the *m*-positions and *p*-$CO_2C_2H_5$.

$$\log k/k^0 = -7.223\sigma + 0.031$$

The value of ρ for aromatic nitration is thus -7.22 at 25° in acetic anhydride. It is particularly satisfactory that the equation indicates that σ for hydrogen, as the unsubstituted aromatic ring, is essentially zero, as would be expected if ground-state inductive and resonance substituent effects alone were important.

Substantial *positive* deviations clearly are evident for the available reactivities *para* to *ortho-para* directing groups and it may be inferred that these are able to stabilize the transition state (I) for *p*-substitution more than might be expected from their σ-constants alone. The effects might be ascribed to resonance structures of type II which could contribute relatively more to the stability of the transition state for *p*-substitution than to the transition state for *m*-substitution or the ground state. While the deviations are rather small for *p*-CH_3– and *p*-F, *p*-I shows much higher reactivity than expected from its σ-constant. The deviations for *p*-Cl and *p*-Br are of intermediate magnitude. If the enhanced reactivities are interpreted in terms of the magnitude of the resonance interaction of the substituent in the transition state, it follows that this interaction decreases in the order, $I > Br \sim Cl > CH_3 \geq F$.

There has been substantial disagreement in the literature as to the order in which the electromeric and inductomeric polarizabilities of the halogen atoms should decrease. Ingold[12] once suggested that electromeric polarizability probably would decrease in the order, $I > Br > Cl > F$. However, Baddeley, Bennett, Glasstone and Jones[22] have reasoned that the resonance effect for halogens decreases in the reverse order and that the similarity in the effects ascribed to resonance and electromerism suggests that these influences have a common origin. In their opinion, therefore, electromeric polarizability should decrease in the order $F > Cl > Br > I$; for this reason, concomitant operation of an inductomeric effect with the order $I > Br > Cl > F$ was postulated to account for experimental orders in the reverse direction. Regardless of the designations for the origin of the transition-state stabilizing influence of *p*-halogen substituents, our results permit little doubt as to the relative order of the halogens for nitration. If one allows that the conjugating effectiveness of the halogens is $F > Cl > Br > I$ in interaction symbolized by resonance structures of type II (*i.e.*, involving *electron exchange in overlapping orbitals*) then the extra rate-enhancing influences of the halogens of higher atomic number must be ascribed to their electrostatic *polarizability* under the influence of the strong electrical field in the nitration transition state (I). Clearly, influences of this sort will only be operative in reactions where the carbon adjacent to the halogen is very substantially charged in the transition state and may not be confined to electrophilic processes.

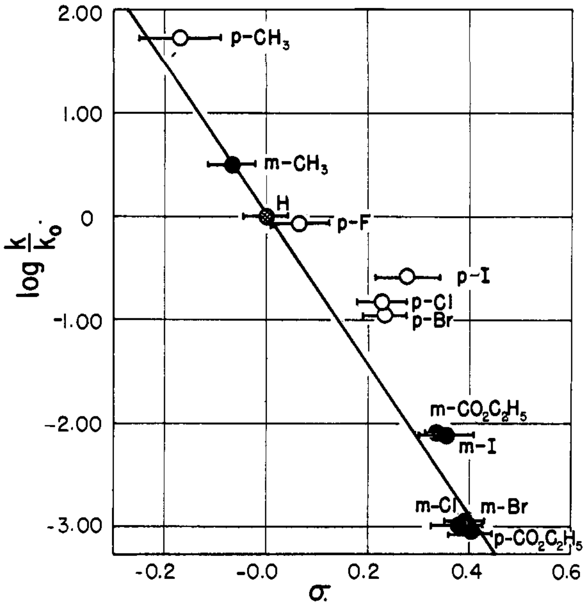

Fig. 3.—Comparison of relative reactivity in nuclear nitration reactions ($\log k/k^\circ$) with σ-constants. Substituents which are not expected to show significant transition state resonance effects are shown as ●, other substituents as ○. The straight line was determined by the method of least-squares for the substituents of the first category not including hydrogen. The horizontal lines through the points represent the median deviations (r) of σ.

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Experimental Part

Reagents used in nitration and for dilution were the best available grades further purified as follows. Chlorobenzene, dried with Drierite, and benzene were fractionated in a 12-mm. × 100-cm. column packed with glass helices; chlorobenzene, b.p. 130.9°; benzene, b.p. 79.8–80.2°, $n^{25}\text{D}$ 1.4972. Iodobenzene was shaken with Drierite, decolorized with activated carbon, and distilled through a 20-cm. Vigreux column; b.p. 185.6°, $n^{25}\text{D}$ 1.6168–1.6170.

The nitrochlorobenzenes were decolorized with activated carbon and fractionally crystallized from the solvents indicated: *ortho*, m.p. 32.8–33.2° (pentane); *meta*, m.p. 45.3–

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[22] (a) G. Baddeley, G. M. Bennett, S. Glasstone and B. Jones, *J. Chem. Soc.*, 1827 (1935); (b) see also C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, Chap. III, Secs. 7c and 7e; (c) J. C. D. Brand and R. P. Paton, *J. Chem. Soc.*, 281 (1952).

45.8° (pentane or successively from 95% alcohol and pentane); *para*, m.p. 83.5–84.2° (95% alcohol).

Anhydrous nitric acid was distilled in diffuse light from a mixture of equal volumes of concentrated sulfuric acid and colorless fuming nitric acid which were chilled before mixing; b.p. 18° (13 mm.), pale straw color. An all-glass Vigreux column with a Claisen still-head was used. The acid was stored in glass-stoppered bottles in a refrigerator.

Acetic anhydride was fractionated in a 12-mm. × 100-cm. column packed with glass helices; b.p. 139.4°. Nitromethane was fractionated through a 14-cm. Vigreux column with a Claisen head; b.p. 100.5–101.2°. Acetonitrile was distilled from phosphorus pentoxide through a Vigreux column with a Claisen head.

Radioactive Isotopes.—A 40-μc. sample of 1.03 *N* radioactive hydrochloric acid (Cl^{36}, half-life 10^6 years) and a 20-mc. sample of carrier-free radioactive potassium iodide (I^{131}, half-life 8.1 days) were obtained on allocation from the U. S. Atomic Energy Commission from the Carbide and Carbon Chemicals Corp., Oak Ridge, Tenn. A 3-mc. sample of I^{131} was obtained from A.E.R.E., Harwell, Berks., England. Small samples of radioactive bromine were prepared by irradiation of sodium selenite with deuterons in the cyclotron of the Instituut voor Kernphysisch Onderzoek (Institute for Nuclear Research) at Amsterdam through the courtesy of Prof. Dr. A. H. W. Aten, Jr.

Apparatus.—Radioactivity measurements were made with (1) a platinum-screen γ-ray counter, (2) an end-window Geiger–Mueller counter, and (3) a windowless, methane-filled proportional flow counter (Nucleometer). Samples for γ-ray measurements were dissolved in 100 ml. of water or acetone and placed in cylindrical glass-stoppered cells of 100-ml. capacity which fitted snugly around the γ-ray counter tubes. The cells and counter were shielded with 5 cm. of lead. The end-window Geiger–Mueller counter was mounted vertically above a conventional shelf arrangement in a 5-cm. lead shield. Samples were placed in 2.5-cm. shallow aluminum or copper dishes. The proportional counter was shielded with about 5 cm. of lead. Conventional amplifying and scaling equipment was used.

Chlorobenzene-Cl^{36}.—Anhydrous benzenediazonium chloride was prepared by the method of Smith and Waring[23] in nearly quantitative yield.[24] Conversion of 0.30 mole of the diazonium salt to chlorobenzene was carried out in a 1-l. indented three-necked flask equipped with a thermometer well, solid-addition tube, gas outlet, and a high-speed stirrer. The gas-outlet was connected through two Dry Ice traps to a wet-test gas meter. The reaction flask was cooled in a calcium chloride–ice-bath.

To a thick slurry of the diazonium salt in 250 ml. of anhydrous dioxane was added 4.7 ml. of 1.03 *N* hydrochloric acid containing 40 μc. of Cl^{36} followed by 115 ml. of anhydrous dioxane used in part to rinse the Cl^{36} container. Thirty minutes was allowed for equilibration of the various species of chloride ion and then 3 g. of dry copper powder was gradually added over a period of 10 minutes. Following a brief induction period, nitrogen evolution became rapid, and, within 15 minutes, 6 l. (91%) of gas was evolved. The rate of reaction was controlled by slow addition of the catalyst, rapid and efficient stirring, and external cooling, so that the internal temperature did not exceed 29°.

The light-amber liquid, in which all of the copper appeared to be dissolved, was made alkaline and steam distilled. Dioxane, salted out of the first part of the steam distillate with calcium chloride, was combined with ether used to extract continuously the aqueous distillate. To 1% of the extracts, dried over calcium chloride, was added 5.4783 g. of inactive chlorobenzene. The activity of the chlorobenzene recovered from this portion indicated a yield of 44.8%.

Ether and most of the dioxane were removed from the major fraction of active chlorobenzene through a 100-cm. glass helix-packed column. After extensive purification by distillation through a Podbielniak vacuum-jacketed concentric-tube column, 3.10 g. (9.5%) of active chlorobenzene was obtained; $n^{25}D$ 1.5163–1.5171. In prior inactive runs, yields of 24 and 34% of chlorobenzene were achieved. The product appeared to be spectroscopically pure except for two quite small unidentified infrared absorption bands at 769 and 795 cm.$^{-1}$.

Nitration of Radioactive Chlorobenzene.—The procedure of Bird and Ingold[12] was followed. Active chlorobenzene (2.867 g., 0.0255 mole) in nitromethane (11.5 ml.) was nitrated at 25° with acetyl nitrate (0.038 mole) prepared from equivalent amounts of anhydrous nitric acid and acetic anhydride at 0°. After 54 hours, the reaction mixture was diluted to 50.00 ml. with ether.

The ether solution was divided into three fractions: A, 3.00 ml. (6%), was used to determine the total activity of the reaction mixture; B, 40.0 ml. (80%), was added to a mixture of *m*-nitrochlorobenzene (10.0625 g.), *p*-nitrochlorobenzene (10.0056 g.), chlorobenzene (10.0440 g.) and sodium chloride and chlorine (11.85 meq.) in water (25 ml.); C, 5.00 ml. (10%), was added to a mixture of *o*- (10.0329 g.) and *p*-nitrochlorobenzenes (10.0130 g.). Ice was added to each fraction to hydrolyze the acetyl nitrate.

A. **Determination of Total Activity.**—Mixture A was diluted with ether, washed with 5% sodium hydroxide solution and water and dried over Drierite. Sodium chloride (0.5137 g.) was added to the combined aqueous layers. After decolorization by boiling with charcoal, the chloride ion was precipitated as silver chloride and its activity determined.

The solvent was removed from the dried ethereal extracts and the residue dissolved in 35 ml. of absolute ethanol. The solution was heated under reflux and 3.5 g. of sodium metal gradually added. After disappearance of the sodium, the reaction mixture was chilled, diluted with water, acidified with 6 *N* sulfuric acid (25 ml.) and made up to 250.0 ml. with water and acetone. A 100.0-ml. portion was added to 1.0028 g. of sodium chloride and a 125.0-ml. portion to 1.0047 g. of sodium chloride. After decolorization with charcoal and evaporation of alcohol and acetone, the chloride ion was precipitated and its activity determined.

B. **Determination of *m*- and *p*-Nitrochlorobenzene, Chlorobenzene and Chlorine.**—The aqueous layer of mixture B was separated and the ether solution extracted with 5% sodium bisulfite solution (20 ml.). The combined aqueous layers were washed, acidified, boiled with charcoal, filtered and used for the determination of the chlorine activity.

The ether solution was dried over calcium chloride, concentrated and cooled in a Dry Ice–trichloroethylene-bath. The crystals (6.2 g.) which separated from the solution were dissolved in a little benzene and chromatographed on a 40-mm. × 100-cm. column of alumina. The absorbed material, visible as a purple band under ultraviolet light was eluted with pentane in two portions. The mother liquor was similarly chromatographed.

From the chromatographic separations, a fraction was isolated which was shown by its infrared spectrum to be predominantly *p*-nitrochlorobenzene. This portion was combined with inactive *o*-nitrochlorobenzene (1 g.) and again chromatographed. The first fraction yielded *p*-nitrochlorobenzene (m.p. 83.1–83.6°) with the activity of 2704 c./min. (activity before scavenging, 2708 c./min.). After one further scavenging with inactive *o*-nitrochlorobenzene (1 g.) and chlorobenzene (2 ml.), 1.14 g. of *p*-isomer was recovered (m.p. 83.4–84.2°), converted to silver chloride and the activity determined.

The second fractions of the original chromatographic separations contained the major amount of chlorobenzene and *m*-isomer as shown by infrared analyses. These portions were refluxed for 2 hours with inactive *o*- (2 g.) and *p*-nitrochlorobenzene (2 g.) and piperidine (50 ml.). The piperidine hydrochloride was removed by filtration and the treatment with piperidine and inactive *o*- and *p*-isomers repeated four times. The final reaction mixture was acidified and steam distilled, the distillate extracted with ether and the extracts washed with sulfuric acid, sodium hydroxide and water and dried over calcium chloride. After removal of the ether, the mixture, shown by infrared analysis to contain some unidentified material and about equal amounts of chlorobenzene and the *m*-isomer, was chromatographed on alumina with pentane. The first fraction was shown by infrared analysis to be a mixture of benzene and chlorobenzene. The chlorobenzene activity was obtained from this fraction. The other fractions yielded 1.9 g. of *m*-isomer, m.p. 45.3–45.8°, after recrystallization from pentane.

C. **Determination of the *o,p*-Ratio.**—Mixture C was extracted with ether. The extracts were washed with aqueous calcium chloride solution, dried over calcium chlo-

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[23] W. Smith and C. E. Waring, THIS JOURNAL, **64**, 469 (1942).

[24] The product was assayed by decomposing a weighed sample with water and measuring the gas evolved by heating at 90°.

ride, combined with inactive chlorobenzene (1 ml.) and distilled to remove the ether. A portion of the *p*-isomer separated by fractional crystallization was recrystallized from alcohol and counted (m.p. 83.2–84.2°, activity 416 c./min.). The remainder of the material was chromatographed on alumina. The recovered *p*-isomer was mixed with inactive *m*-isomer (0.25 g.) and inactive chlorobenzene (2 ml.) and again chromatographed. After recrystallization from 95% ethanol, it had m.p. 84.6–85.2° and was used for the activity determination.

The crude *o*-isomer recovered from the chromatographic separation was mixed with inactive *p*- (2 g.) and *m*-isomers (0.3 g.) and chlorobenzene (2 ml.). After chromatographic separation, the recovered *p*-isomer had an activity of 1014 c./min. The *o*-isomer (m.p. 32.5–33.2°) had an activity of 1074 c./min. and was, therefore, adequately scavenged. It was converted to silver chloride for the final radioactivity determination.

Radioactivity Analysis.—Approximately 1-g. samples of each of the recovered nitrochlorobenzenes, and of the recovered and original chlorobenzene (the latter after dilution to 16.39% of its original activity with inactive chlorobenzene) was decomposed with sodium in absolute ethanol.[25] When the sodium had dissolved completely, the solutions were cooled, diluted with water (200 ml.), acidified with sulfuric acid and boiled to remove the alcohol. Activated carbon was added prior to the last operation to remove colloidal organic matter. The chloride was precipitated with silver nitrate, redissolved in 5% sodium or potassium cyanide solution and reprecipitated with acid. The precipitates were washed with water and acetone, dried at 120°, weighed into copper counting dishes, covered with an aluminum foil and pelleted with a hammer and brass plunger. The aluminum foil was removed and the resulting smooth-surfaced pellet trimmed to the desired sample weight (0.7500 g.).

The activity was measured in a Nucleometer; for each sample three to six measurements of more than 5000 counts each were averaged. A total of 101.2 ± 1.0% of the Cl^{36} was accounted for; the other results are given in Table I.

The isotope dilution analysis for *m*-chloronitrobenzene was approximately checked by infrared analysis of the products from the nitration reaction in the following way. Two samples of chlorobenzene (0.0111 mole) were nitrated for 53 hours, one in acetic anhydride (5 ml.) and the other in nitromethane (5 ml.). Carbon disulfide extracts of the reaction products were neutralized with potassium hydroxide solution, washed with water and dried over Drierite. After concentration, the infrared spectrum of the mixture of reaction products was compared with spectra of synthetic mixtures dissolved in carbon disulfide. It was estimated that about 1% of the *m*-isomer was formed in each case.

Radioactive Bromobenzene.—Sodium selenite was irradiated for 20 minutes with deuterons (5 μ amp.) in a cyclotron. The target material was dissolved in water (75 ml.) and inactive bromine (2 g.) was added. The bromine was distilled into benzene (50 ml.) cooled at 7°. Sulfuric acid (30%, 240 ml.) was added to this solution. The mixture was emulsified by high-speed stirring and potassium bromate (30 g.) and water (50 ml.) were added in the course of one hour. The stirring was continued for 1.5 hours. During the reaction the temperature was kept at 30°. The reaction mixture was extracted with ether, washed with sodium hydroxide and water, dried and distilled. The yield of bromobenzene, b.p. 152–154°, was 64–67% in six experiments.

Nitration of Bromobenzene.—In a typical experiment (III, Table I), radioactive bromobenzene (12.9 g.) in nitromethane (50 ml.) was nitrated at 25° for 11 hours with a mixture of anhydrous nitric acid (43 ml.) in nitromethane (56 ml.). The reaction mixture was divided into three portions (A–C).

A. Determination of *o*-Nitrobromobenzene—Part of the nitration mixture (12.568 g.) was added to inactive *p*- (9.862 g.) and *o*-nitrobromobenzene (10.053 g.). The resulting mixture was dissolved in ether, washed with sodium hydroxide and water, dried and, after evaporation of the ether, dissolved in hot ethanol (50 ml.). On cooling the greater part of the *p*-isomer crystallized and was separated. Inactive *p*-isomer was added to the mother liquor and the crystallization from hot ethanol repeated. After another repetition, the activity of the recovered *p*-isomer was negligible (76 c./min./g.). The *o*-isomer was isolated from the mother liquor by fractional crystallization and, after repeated recrystallizations from petroleum ether, it melted at 35.4–36.4°. The *o*-nitrobromobenzene obtained in this way still contained some of the (nearly inactive) *p*-isomer. Owing to the short half-life of the radioactive bromine, and the low level of activity, no attempt was made to purify the *o*-isomer further but instead the amount of the impurities was determined by thermal analysis. The activity was then corrected for the presence of these non-radioactive impurities.

B. Determination of *m*-Nitrobromobenzene.—Another part of the nitration mixture (178.22 g.) was added to inactive *m*- (9.151 g.) and *o*-nitrobromobenzene (6.044 g.), dissolved in ether, neutralized with sodium hydroxide, washed with water and dried. Ether and nitromethane were removed *in vacuo* and the residue was dissolved in 50 ml. of hot ethanol. The radioactive *p*-nitrobromobenzene was removed by repeated crystallization from ethanol, each time with addition of 9 g. of inactive *p*-isomer (as described under A) until the activity of the recorded *p*-isomer was essentially negligible.

After removal of ethanol from the mother liquor, the residue was treated with boiling piperidine (40 ml.) for 15 minutes. The reaction mixture was cooled, diluted with water, extracted with ether, and the extract washed with dilute hydrochloric acid. The ethereal solution was dried and the ether removed. The piperidine treatment was repeated three times, each time adding a few grams of inactive *o*-isomer. The piperidine hydrobromide from the last treatment was converted to silver bromide and counted. The low activity (15 c./min./g.) proved that the scavenging was satisfactory. The resulting *m*-isomer was recrystallized from petroleum ether, m.p. 52.0–53.0°.

C. Determination of *p*-Nitrobromobenzene.—Another part of the nitration mixture (12.517 g.) was added to inactive *p*- (4.992 g.) and *o*-nitrobromobenzene (3.088 g.). After neutralization with sodium hydroxide, the mixture was homogenized with boiling acetic acid. On cooling the *p*-isomer separated; it was recrystallized twice.

To 1.8 g. of the crystallized *p*-isomer were added inactive *o*- (0.3 g.) and *m*-nitrobromobenzene (0.1 g.) and bromobenzene (0.3 ml.). After another recrystallization, the recovered *p*-isomer melted at 124.5–125.5°. The activity before and after this last scavenging procedure did not differ significantly.

Radioactivity Analysis.—Samples of 1.000 g. of the dry powdered nitrobromobenzenes were weighed into aluminum counting dishes of identical size and counted with a mica end-window counter. The reproducibility of this method of counting was proved by independent experiments to be satisfactory. For each sample, at least three measurements of more than 10,000 counts were averaged.

For the determination of the original activity of the bromobenzene, 0.6227 g. of it was diluted with inactive bromobenzene (2.6791 g.) and converted to nitrobromobenzenes by nitration at 0°. The *p*-isomer isolated from the nitration product by recrystallization from acetic acid and ethanol was counted.

By using the above procedures and a 15-fold excess of nitric acid for the nitration reaction it was possible to finish a complete determination including the preparation of the radioactive bromine and the final activity determinations within 48 hours. The principal experimental results are summarized in Table I. In two runs, it was estimated from the recovery of nitrobromobenzenes that nitration took place to the extent of 97–100%.

Iodobenzene-I^{131}. I.—Radioactive iodobenzene was prepared in 51% yield from 20 mc. of carrier-free I^{131} (as sodium iodide) diluted with inactive potassium iodide (15 g.) by the method of Gattermann and Wieland.[13] The product was repeatedly fractionated; b.p. 126.2–126.7° (138 mm.), $n^{17.9}\text{D}$ 1.6200.

II.—Iodobenzene was also prepared by the method of Lucas and Kennedy[18] in 57 and 71% yields; $n^{25}\text{D}$ 1.6162–1.6168 and 1.6154–1.6169.

III.—In one experiment, the radioactive iodobenzene was prepared by the method of Dains and Brewster[17] from 14.6 g. of potassium iodide containing 2 mc. of I^{131} in 66% yield. In this procedure nitric acid is used, and, therefore, it was possible that the iodobenzene was contaminated by

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[25] O. Kamm, "Qualitative Organic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1932, p. 200.

small amounts of nitroiodobenzenes. To check the purity of the active iodobenzene, 0.0985 g. was diluted with inactive iodobenzene (1.8 g.) and inactive *m*-nitroiodobenzene (9.803 g.). After two recrystallizations from petroleum ether, 8.1 g. of *m*-nitroiodobenzene was recovered. Again this was scavenged with inactive iodobenzene and recrystallized. At this stage, the *m*-nitroiodobenzene activity amounted to 2.5 ± 3 c./min./g. To 4.4 g. of the *m*-material was added 1.8 g. of inactive iodobenzene and, after two recrystallizations, the activity was again determined (0.5 ± 3 c./min./g.). From the final activity and the activity of the original iodobenzene it was calculated that the iodobenzene contained less than $10^{-3}\%$ of *m*-nitroiodobenzene. This amount was considered unlikely to interfere seriously with the determination of the isomer ratios in the nitration product.

Nitration of Radioactive Iodobenzene.—In expt. IV, VII and VIII, the nitrations were carried out by the procedure of Bird and Ingold,[12] with a 50:50 nitric acid–acetic anhydride mixture in acetic anhydride at 25.0°. In expt. V and VI a 60:40 mixture was used and in expt. IX, the nitration was carried out with 10.186 g. of iodobenzene and absolute nitric acid (8.3 ml.) in nitromethane (100 ml.).

Details of typical run (expt. VI) follow. To a mixture of active iodobenzene (8.409 g., 0.412 mole) and nitromethane (20 ml.) in a 250-ml. glass-stoppered flask was added gradually with stirring at 25° a mixture of anhydrous nitric acid (2.60 ml., 0.062 mole) and acetic anhydride (3.72 ml., 0.039 mole) combined at 0°. After 52 hours at 25.0°, the flask was filled with ice, shaken and allowed to stand overnight. The reaction products were isolated by continuous extraction with carbon disulfide. The carbon disulfide extract was then diluted to 250.0 ml. and divided into three fractions[26]: A, 5.00 ml. (2%), used for the determination of the total activity of the reaction mixture; B, 200.0 ml. (80%), used for the determination of *m*- and *p*-nitroiodobenzene, iodobenzene and iodine and mixed with inactive *m*- (9.8106 g.) and *p*-nitroiodobenzene (10.3014 g.) and iodobenzene (9.9512 g.); C, 25.0 ml. (10%), used for the determination of the *o,p*-isomer ratio and mixed with inactive *o*- (19.7386 g.) and *p*-nitroiodobenzene (9.9295 g.). Fractions B and C were made homogeneous by adding additional solvent and refluxing until solution was complete.

A. **Determination of Total Activity.**—After evaporation of most of the solvent, A was diluted with absolute ethanol (35 ml.), boiled to eliminate the rest of the original solvent and the halide decomposed by the gradual addition of 3.5 g. of sodium. The reaction mixture was cooled and made up to 100 ml. with water. Of this solution, 40.0- and 45.0-ml. portions were added to potassium iodide (1.0663 and 1.0622 g., respectively) and made up to 100 ml. for γ-ray counting with a platinum-screen counter.

B. **Determination of *m*- and *p*-Nitroiodobenzene, Iodobenzene and Iodine.**—Fraction B was shaken with 5 ml. of 0.3463 *N* iodine in carbon disulfide, allowed to stand for half an hour, and extracted with sodium thiosulfate solution. The thiosulfate extracts, washed with ether, were used for the determination of iodide and iodine formed during nitration.

On concentration of the carbon disulfide solution, most of the *p*-nitroiodobenzene crystallized. It was scavenged twice by recrystallization from acetone–alcohol solution containing the inactive *o*- (1.0 g.) and *m*-isomers (0.5 g.) and inactive iodobenzene (1 ml.). The *p*-nitroiodobenzene had m.p. 174.6–175.4°. Since the activity did not change significantly in the last scavenging treatment, radiochemical purity was adequate.

The *m*-nitroiodobenzene and iodobenzene remaining in the original carbon disulfide solution were separated by distillation of the iodobenzene. The latter was mixed with 1-g. portions of inactive *o*- and *p*-nitroiodobenzenes and heated in 35 ml. of refluxing piperidine for 30 hours. Two additional 1-g. portions of each isomer were added during this period. The iodobenzene, separated by steam distillation of the acidified piperidine solution, was dissolved in ether, washed with sodium hydroxide, hydrochloric acid, and water, dried and distilled from 0.5 g. of inactive *m*-nitroiodobenzene. The distillate had $n^{25}\text{D}$ 1.6158. After a second scavenging with inactive *o*- (0.25 g.), *m*- (0.1 g.) and *p*-isomers (0.25 g.) the activity was essentially unchanged.

The crude, radioactive *m*-isomer was treated with boiling piperidine (50 ml.) for 10 hours. The reaction mixture was acidified and steam distilled. The crude product was sublimed, then mixed with 1-g. portions of *o*- and *p*-nitroiodobenzenes and again boiled with piperidine for two days. Two additional 1-g. portions of each isomer were added during this period. The isolated *m*-isomer was then dissolved in ether, washed with sodium hydroxide and hydrochloric acid, recovered and recrystallized from pentane containing inactive iodobenzene (1 ml.). The final material had m.p. 37.8–38.5°. Additional scavenging with 0.3-g. portions of inactive *o*- and *p*-isomers did not change the activity significantly.

C. **Determination of the *o,p*-Ratio.**—Fraction C was neutralized and concentrated. The *p*-isomer was separated by recrystallization and recrystallized three times from acetone and alcohol containing inactive *o*- (1 g.) and *m*-isomers (0.5 g.). The recovered *p*-isomer had m.p. 174.6–175.2°. The activities before and after the last crystallization were essentially the same.

The carbon disulfide solution containing the active *o*-isomer was scavenged twice with *p*- (5 g.) and *m*-nitroiodobenzenes (1 g.). This process was found to reduce the radioactivities of the residual *m*- and *p*-isomers to less than the activity of the *o*-isomer. Unreacted iodobenzene was eliminated by distilling successively three 2-ml. portions of inactive iodobenzene from the *o*-isomer before the latter was fractionally crystallized from pentane. The fractions combined for analysis had separate m.p.'s of 50.4–51.0°, 50.7–51.7° and 50.9–51.6°.

Radioactivity Analysis.—Iodobenzene and the nitroiodobenzenes were converted to silver iodide by the same procedure as used for the chlorocompounds.[27] Pellets of silver iodide were prepared as described for silver chloride; the sample weight was arbitrarily chosen for each series of precipitates as the weight of the smallest sample of the group.

Activities of silver iodide samples were measured in a Nucleometer within a short period of time to minimize instrumental variations.

In expt. IX, the nitroiodobenzenes were counted directly as described for the nitrobromobenzenes.

Infrared Analysis of Iodobenzene Nitration Products.—As an independent check on the isomer distribution, carbon disulfide solutions were made up to contain 50.0, 35.5 and 24.0 mg. of *o*-, *p*-nitroiodobenzene and iodobenzene, respectively, and increasing amounts of *m*-nitroiodobenzene (0.0, 0.5, 1.0, 2.0, 3.0, 5.0 and 10.0% based on the total nitroiodobenzene content) in 3 ml. of solution. Infrared spectra of these reference solutions were compared with the infrared spectrum of a sample of inactive iodobenzene nitrated in nitromethane (Fig. 4). The nitrated iodobenzene sample was prepared for infrared analysis by extracting the ice-treated reaction mixture three times with carbon disulfide. The extracts were washed successively with water, three portions of potassium hydroxide solution, and water, and dried over Drierite. A one-quarter aliquot of the extracts was concentrated until nearly saturated by careful distillation of part of the solvent through a small Vigreux column.

Infrared spectra from 11 to 15 μ were recorded on a Baird double-beam infrared spectrophotometer and are reproduced in Fig. 4. A 1.0-cm. sodium chloride cell, balanced by a sodium chloride reference block, was used.

In Fig. 4, the lowest curve, that of the reaction mixture, most closely resembles curve 4 of the reference spectra which corresponds to 2.0% *m*-nitroiodobenzene, 40.7% *o*-nitroiodobenzene and 57.3% *p*-nitroiodobenzene.

Similar spectra were recorded for nitrations in acetic anhydride, acetonitrile and nitromethane using matched 0.1-mm. cells. No differences in isomer distribution could be detected.

Competitive Nitration of Benzene and Iodobenzene.—The method of Bird and Ingold[12] was followed for the competitive nitration of benzene and radioactive iodobenzene.

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[26] In Expt. IX, the (homogeneous) reaction mixture was divided as such into two series of three portions, which were used for the determination of the isomeric nitroiodobenzenes by the same procedure as described above for the nitration of bromobenzene.

[27] The Thompson–Oakdale method for conversion of organic iodide to silver iodide (J. J. Thompson and U. O. Oakdale, THIS JOURNAL, **52**, 1195 (1930)) was found to be less satisfactory for iodobenzene. It is considerably longer and, unless modified, decomposition may not be complete. Furthermore, coprecipitation of both silver sulfite and silver arsenate may occur.

To a mixture of 3.9 g. (0.050 mole) of benzene and 10.2 g. (0.050 mole) of radioactive iodobenzene in 20 ml. of nitromethane was added gradually with stirring at 25° a mixture of 1.58 ml. (0.0375 mole) of anhydrous nitric acid and 3.53 ml. (0.0375 mole) of acetic anhydride combined at 0° and diluted with 6 ml. of nitromethane. After 1 hour at 25.0°, the mixture was poured onto 400 g. of ice. Ether was used to rinse the flasks, the washings being added to the appropriate samples. After standing for three days, the reaction mixture was made alkaline with 40% sodium hydroxide and shaken well. The organic layers and ether extracts of the aqueous layers were shaken with 5% sodium hydroxide solution, washed with water, and dried over anhydrous calcium chloride.

A similar competitive nitration was carried out substituting acetic anhydride for nitromethane and nitrating at 25.0° for 8 hours. The mixture was made alkaline and extracted, and the extracts were washed and dried as in the nitromethane experiment.

The drying agent separated by filtration from the ether solution was thoroughly extracted with ether before being discarded. Ether was distilled from the combined ether solutions and extracts for each run through a Vigreux column with a Claisen still-head. Each solution was made up to 50.0 ml. with glacial acetic acid to give appropriate concentrations.

The method of Butts, Meikle, Shovers, Kouba and Becker[28] was used to determine the aromatic nitro compounds formed in the competitive nitrations. Titanium trichloride solution was prepared and stored under nitrogen, and all titrations were carried out in an atmosphere of nitrogen which had been washed with titanium trichloride solution and water. The titanium solution was standardized directly with ferrous ammonium sulfate[29] and used at once to standardize the ferric alum solution which then served for daily standardization of the titanium solution.

Titrations were carried out as follows. The air in a 300-ml. glass-stoppered erlenmeyer flask was displaced with nitrogen for 5 minutes. A 2-ml. aliquot of the acetic acid solution of the nitration products from nitromethane (4 ml. for the nitration products from acetic anhydride), 30 ml. of 20% sodium acetate solution and 40.00 ml. of titanium trichloride solution were added. The flask was swirled just one minute under nitrogen, 25 ml. of 15% hydrochloric acid was added, and the excess titanium trichloride was titrated with standard ferric alum solution, 5 ml. of 20% potassium thiocyanate solution being added near the endpoint. Suitable blanks were titrated similarly.

A sample of nitrobenzene dissolved in glacial acetic acid assayed 99.3% in duplicate determinations. A sample of *p*-nitroiodobenzene, dissolved in 4 ml. of a blank (iodobenzene and benzene added after pouring onto ice) acetic anhydride nitration mixture and 25 ml. of glacial acetic acid, assayed 94.8% in a single determination.

During the competitive nitration in nitromethane, duplicate determinations of the total extent of nitration showed the apparent formation of 23.1 ± 0.1 millimoles of aromatic nitro compound. During the acetic anhydride nitration, 12.4 ± 0.1 millimoles were formed. If the small corrections are made (using the analysis of nitroiodobenzene given below) and the blank analyses for nitrobenzene and *p*-nitroiodobenzene, the amounts of total nitration in nitromethane and acetic anhydride become 23.5 ± 0.1 and 12.5 ± 0.1 millimoles, respectively.

The amount of nitration of iodobenzene was determined as follows. To 40 ml. (80%) of the glacial acetic acid solution of the products of the competitive nitration carried out in nitromethane were added 4.0384 g. of inactive *p*-nitroiodobenzene and 0.7 and 1.2 g., respectively, of inactive *m*- and *o*-nitroiodobenzenes. The solution was neutralized with 40% sodium hydroxide, benzene being added to replace the acetic acid as solvent for the nitroiodobenzenes. To the 3.5 g. of *p*-nitroiodobenzene, recovered from the neutral benzene solution by fractional crystallization, were added 0.5 g. of inactive *o*-nitroiodobenzene, 2 ml. of inactive iodobenzene, and enough benzene to dissolve the mixture. The solution was chromatographed on a 45-mm. × 100-cm. column of alumina (Merck). Continuous cycling of pen-

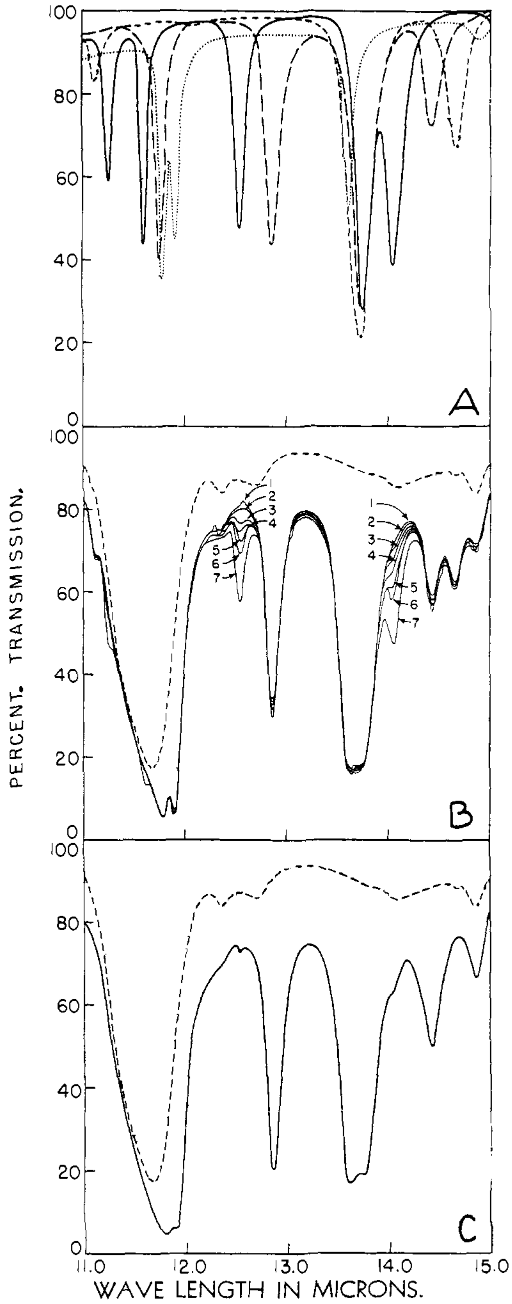

Fig. 4.—(a) Infrared spectra of iodobenzene and nitroiodobenzenes: iodobenzene, - - - -; *o*-nitroiodobenzene, — —; *m*-nitroiodobenzene, ——; *p*-nitroiodobenzene, ... Solutions contain 50 mg. of solute in 0.50 ml. of carbon disulfide; cell thickness, 0.1 mm. (b) Infrared spectra of synthetic mixtures containing 41.5% of *o*-nitroiodobenzene, 58.5% of *p*-nitroiodobenzene and 28.1% of iodobenzene (based on total weight of *o*- and *p*-isomers) and varying percentages of *m*-nitroiodobenzene (based on total weight of three isomers): 1, 0% *m*-isomer; 2, 0.5% *m*-isomer, 3, 1.0% *m*-isomer; 4, 2.0% *m*-isomer; 5, 3.0% *m*-isomer; 6, 5.0% *m*-isomer; 7, 10.0% *m*-isomer. Carbon disulfide solutions (3.0 ml.) contain 0.110 g. of *o*- and *p*-nitroiodobenzenes and iodobenzene; cell thickness, 10 mm.; transmission of empty cell, - - - - -. (c) Infrared spectrum of reaction products from the nitration of iodobenzene in nitromethane. Nearly satd. soln. in carbon disulfide; cell thickness, 1.0 mm.; transmission of empty cell, – – –.

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[28] P. G. Butts, W. J. Meikle, J. Shovers, D. L. Kouba and W. W. Becker, *Anal. Chem.*, **20**, 947 (1948).

[29] W. F. Hillebrand and G. E. F. Lundell, "Applied Inorganic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1929, p. 309.

tane was used to develop the chromatogram and elute the *p*-nitroiodobenzene.

The positions of the iodobenzene and nitrated isomers could be observed under ultraviolet light. Iodobenzene (bluish-white fluorescence) was eluted first and was followed by *p*-, *m*- and *o*-iodobenzenes (purple fluorescence) in order. Although these were not developed into separate bands, the head of the band was a deeper purple than the latter portions of the band and was found to be nearly pure *p*-isomer.

Material recovered from the head of the purple band melted at 174.8–175.6° and was decomposed without further purification. The activity of the silver iodide counted (0.4999 g.) was 3650 c./min., after correction for decay, compared to an activity of 29,774 c./min. given by silver iodide from the original iodobenzene. From these data and the percentage of *p*-isomer determined above, it was found that the number of millimoles of iodobenzene nitrated was 4.8 ± 0.1.

A similar analysis was carried out on the products of nitration in acetic anhydride. To 35.0 ml. (70%) of the glacial acetic acid solution of the products were added 3.1919 g. of inactive *p*-nitroiodobenzene and 0.07 g. and 1.4 g., respectively, of inactive *m*- and *o*-nitroiodobenzenes. From the acetic acid solution when chilled was recovered 3 g. of crystalline *p*-nitroiodobenzene. This material, 0.5 g. of inactive *o*-nitroiodobenzene and 5 ml. of inactive iodobenzene were dissolved in benzene and chromatographed on a 45-mm. × 70-cm. column of alumina. The *p*-nitroiodobenzene recovered (m.p. 174.8–175.6°) was converted to silver iodide which had an activity of 1076 c./min. The amount of iodobenzene nitrated in acetic anhydride was, therefore, 1.51 ± 0.01 millimoles. When used to calculate the reactivity toward acetyl nitrate of iodobenzene with respect to benzene this gave the values 0.22 ± 0.01 and 0.13 ± 0.01 for nitration in nitromethane and acetic anhydride, respectively.

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[CONTRIBUTION FROM THE MCPHERSON CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Acid Catalysis in the Decomposition of Benzazide[1]

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The rates of Lewis acid catalyzed decomposition of benzazide into phenyl isocyanate and nitrogen have been determined in benzene and nitrobenzene. When the acids were gallium chloride, aluminum bromide, aluminum chloride and ferric chloride, the kinetics of the nitrogen evolution indicates that an acid–benzazide complex formed rapidly, then decomposed slowly by first-order kinetics. Furthermore, the released catalyst does not complex with phenyl isocyanate but immediately recombines with unreacted azide. The decomposition in the presence of antimony pentachloride, titanium tetrachloride, stannic chloride and tellurium tetrachloride were first order with respect to azide and to halide. The rate measurements suggest that the order of decreasing acid strength is as follows: gallium chloride, aluminum bromide, aluminum chloride, ferric chloride, antimony pentachloride, titanium tetrachloride, stannic chloride, tellurium tetrachloride and antimony tetrachloride. Arsenic trichloride, arsenic tribromide, phosphorus trichloride and phosphorus pentachloride were without effect on the decomposition rate.

The decomposition of benzazide into nitrogen and phenyl isocyanate in non-aqueous solvents was found to be catalyzed by protonic acids and by boron fluoride in dioxane.[2] This suggested that the relative strengths of Lewis acids might be determined by measuring their catalytic effect on the rate of benzazide decomposition. In order that complicating factors such as the formation of carbon dioxide gas[3] and products other than phenyl isocyanate be excluded, this study was confined to non-protonic acids in aprotic solvents. In benzene and nitrobenzene solutions, the rate of decomposition of benzazide is increased to varying degrees by soluble metallic halides and could be followed by measurements of the evolved nitrogen.

Experimental

Reagents.—The benzazide, prepared from recrystallized benzhydrazide and nitrous acid, was recrystallized from petroleum ether to a melting point of 27.1–27.2°. The melting point remained unchanged over a period of four months when stored near 0°.

The following C.P. or reagent quality chemicals were distilled in all-glass apparatus at atmospheric pressure (b.p.'s uncorrected): antimony tribromide, 279–281°; antimony trichloride, 217–218°; arsenic tribromide, 215–216°; stannic chloride, 110.5–111°; titanium tetrachloride, 131.5–132.5°; tellurium dichloride, 321.4°; antimony pentachloride 89° at 30 mm. Anhydrous aluminum chloride was twice sublimed in a stream of dry nitrogen. Gallium trichloride, b.p. 195–196°, was prepared by chlorinating hot metallic gallium. Ferric chloride was prepared from the elements.[4] Tellurium tetrachloride, formed by chlorinating tellurium dichloride, was distilled. Aluminum bromide (Westvaco) was redistilled, b.p. 349–351°. Boron tribromide, distilled from a mixture of aluminum bromide and sodium fluoroborate,[5] was redistilled, b.p. 96–97°. Arsenic trichloride, mercuric bromide, phosphorus trichloride and phosphorus pentachloride (all C.P. grade) were used without further purification.

The benzene was C.P. "thiophene free," distilled over sodium. "Pure" grade nitrobenzene was partially crystallized and centrifuged; the crystals were then melted, the liquid dried over phosphorus pentoxide and distilled, b.p. 82–83° at 8 mm.

Apparatus.—A 125-ml. round-bottom reaction flask with a sealed-on water cooled condenser was immersed in a constant temperature bath. The top of the condenser was connected by Tygon tubing to a Hempel gas buret. Changes in atmospheric pressure and temperature were automatically corrected for by balancing a reference reaction flask containing only solvent against the reacting system through a glycol manometer. By doing this, the volume of gas collected was converted to standard conditions with but one conversion factor. During runs, the flask was subjected to pendulum-type agitation.

Procedure.—Twenty-five ml. of solvent was pipetted into a dried reaction flask, then one to three millimoles of the metallic halide was added. After allowing the solution to reach equilibrium temperature, a small tube containing approximately three millimoles of benzazide was placed in the top of the condenser on a movable iron support. The entire gas system was then closed off and balanced against the reference system; the azide was then allowed to drop into the solvent by moving the iron support with a magnet.

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[1] Taken from the Ph.D. thesis of R. A. C., The Ohio State University, 1951.

[2] M. S. Newman and H. L. Gildenhorn, THIS JOURNAL, **70**, 317 (1948).

[3] See M. S. Newman, S. H. Lee and A. B. Garrett, *ibid.*, **69**, 113 (1947), for references.

[4] L. F. Audrieth, *et al.*, "Inorganic Syntheses," McGraw-Hill Book Co., Inc., New York, N. Y., 1950, Vol. III, p. 29.

[5] Reference 4, p. 191.