Copper(I) Catalysed Replacement of Bromine by Chloride Ion in Halonitrobenzenes. Part II*

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The copper(I) catalysed exchange of bromine for chlorine in 2-bromo-3-iodonitrobenzene was studied in order to complete the *ortho*-halogen series described in Part I[1] and to more closely investigate the enhancing effect of the *ortho*-halogens on the exchange rate.

It is concluded that polar effects alone cannot be responsible for this enhancing effect, but that proximity effects of the *ortho*-halogens may also intervene.

In Part I,[1] the copper(I) catalysed exchange of bromine for chlorine with copper(I) chloride in an aqueous hydrochloric acid-acetic acid medium ([Cl⁻] = 5.26 M) was kinetically studied in 2-bromo-3-chloronitrobenzene, 2,3-dibromonitrobenzene, and various other halonitrobenzenes. $CuCl_2^-$ was found to be the catalysing copper(I) complex. The second-order rate of substitution was remarkably insensitive to the nature of the *para*-substituents; 2-bromonitrobenzene and 2-bromo-5-chloronitrobenzene were found to undergo bromine-chlorine exchange at the 2-position at the same rate. This observation was in full accord with the results of Bacon and Hill,[2] who studied substitution reactions between substituted bromobenzenes and copper(I) chloride in pyridine, and found that the *para*-methoxy and *para*-methyl derivatives reacted at about the same rate as the unsubstituted bromobenzene.

Castro *et al.*[3] have also observed a mild pattern of substituent influence from the *meta*- and *para*-positions in the reactions of substituted iodobenzenes with copper(I) phenylacetylide in pyridine

$$ArI + CuC\equiv CPh \longrightarrow ArC\equiv CPh + CuI$$

A comparatively strong activating effect was observed in Part I for an *ortho*-nitro group, which caused the exchange rate to be 100 times greater than that of the isomer carrying the nitro group in the *para*-position.[1] This

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* Ref. 1 considered as Part I.

result is in agreement with the work of Bacon and Hill [2] and Castro et al.[3] In addition, in Part I a bromine or chlorine in the other ortho-position to the bromine to be replaced was found to enhance the rate 10-fold and 7-fold, respectively.[1]

All of these related substituent effects on the rate of halogen exchange with copper(I) salts differ very greatly from the corresponding effects on the rate of reaction of the halides with common nucleophiles, in which case the presence of para-substituents usually alters the second-order rate constant considerably. In the replacement of bromine by chlorine in 2-bromo-3-nitro-benzene diazonium ion Lamm and Liedholm [4] found that a methyl group in the 5-position decreased the exchange rate by a factor 10. (The medium was the same as in the present work.)

The negative entropies of activation ($\Delta S^{\ddagger}$) found for the bromine-chlorine exchange in 2-bromo-3-chloronitrobenzene and in 2,3-dibromonitrobenzene, -41 and -37 cal deg.$^{-1}$ mol^{-1}, respectively, indicate a high degree of order in the transition state. These data together with the enthalpies of activation ($\Delta H^{\ddagger}$), 11 and 12 kcal mol^{-1}, respectively, and the observed substituent effects led to the suggestion of the transition state outlined in Part I,[1] in which the ortho-nitro group participates with CuCl$_2^-$ and the bromine to be replaced in the formation of a tetrahedral copper(I) complex. Such a transition state with the C−Br carbon more or less tetrahedral will allow the ortho-nitro group to be nearly coplanar with the ring with maximum resonance interaction, and consequently a minimum of enthalpy. Such a tetrahedral transition state may also explain the ortho-halogen effects.

A similar transition state is suggested independently by Castro et al.[3] in the substitution of ortho-nitroiodobenzene with copper(I) phenylacetylide.

In order to investigate the proximity effects of the ortho-halogen more closely, this series has now been completed with iodine in the present work.

RESULTS AND CALCULATIONS

The copper(I) catalysed exchange of bromine for chlorine in 2-bromo-3-iodonitrobenzene has been studied kinetically at 80, 90, and 98°C in the same medium as that previously used [1] and in the presence of copper(I) chloride. This halonitrobenzene together with 2-chloro-3-iodonitrobenzene, which was necessary for calibration purpose, were synthesized from 2,6-dinitroaniline, as depicted in Fig. 1.

The exchange mixture was analysed by GLC which revealed the presence of two small impurities (about 2 % together) besides the two main compounds, 2-bromo-3-iodonitrobenzene   and   2-chloro-3-iodonitrobenzene.   The mass
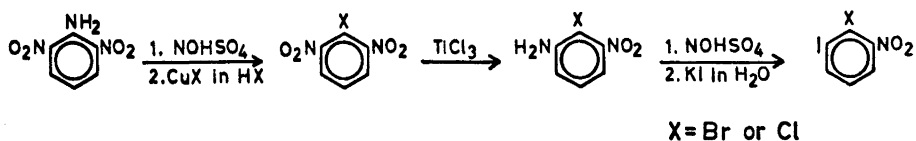

Fig. 1. Preparation of 2-bromo-3-iodonitrobenzene and 2-chloro-3-iodonitrobenzene.

spectra * of the by-products showed molecular ions at m/e 253 and 255 of relative abundances 3/1, due to 2-chloro-3-iodoaniline, and at m/e 297 and 299 of 1/1 isotopic ratio, which indicates 2-bromo-3-iodoaniline. Both of the impurities thus arise from reduction of the nitro group, evidently caused by the Cu^+ ion, which was also observed in Part I.[1]
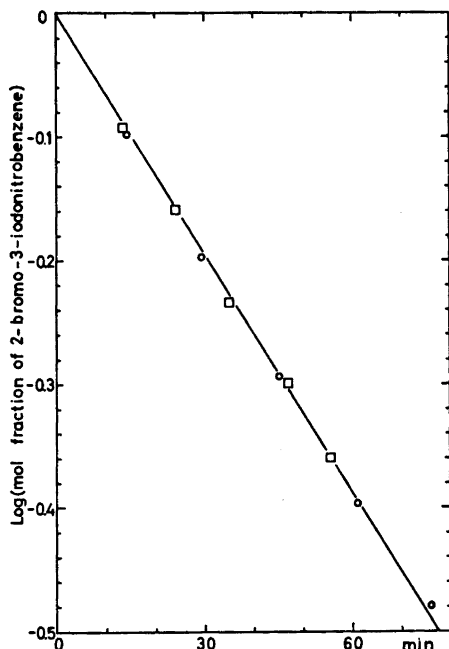

Fig. 2. Two representative runs (O and ☐) of bromine-chlorine exchange at 90°C.

The exchange reaction displayed pseudo first-order kinetics, as illustrated in Fig. 2. The pseudo first-order rate constant k_{obs} was calculated from the slope of the line by the method of least squares. The second-order rate constant k_2 was calculated from the concentration of $CuCl_2^-$, which was assumed to be the catalysing species. Because complex constants were not available for the medium used at the temperatures of interest, an estimate of the $CuCl_2^-$ concentration has been made from the dependence of the first-order rate on the chloride ion concentration, as described in Part I.[1] In the present investigation three different chloride ion concentrations were used at 90°C. When the value of k_{obs} $(1 + \alpha[Cl^-])$ was computed by means of the constant α_{90} found in Part I, the constancy was as good as in that case. The chloride ion concentration was not varied at 80 and 98°C, and the previously found α_{80} and α_{98} were used.

The exchange reaction did not occur at 90°C in the absence of copper(I) chloride.

The reaction should not be complicated to any marked extent by reversibility, for when 2-chloro-3-iodonitrobenzene, in the presence of an equimolar quantity of bromide ion, was submitted to the same conditions as 2-bromo-3-iodonitrobenzene at 90°C, no exchange reaction was detected.

The results for k_{obs} and k_2 for 2-bromo-3-iodonitrobenzene are summarized together with some results from Part I [1] in Table 1. The activation parameters were calculated from k_2 in Table 1 and the Eyring equation:

Table 1. Kinetic runs involving halonitrobenzenes and chloride ion.
[Cl⁻] = 5.26 M, [Cu⁺]$_{tot}$ = 0.1124 M.

Compound 0.0562 M	Temp.°C [a]	[CuCl₂⁻] [b]	$k_{obs} \times 10^4$ [c]	S.E. $\times 10^4$ [d]	$k_2 \times 10^4$ [e]
2-Bromo-3-iodo-nitrobenzene	79.95	0.056	1.333	0.027	23.7
	79.95	0.056	1.340	0.013	23.8
	89.98	0.063	2.427	0.033	38.6
	89.98	0.063	2.432	0.039	38.7
	98.05	0.076	4.016	0.080	52.6
	98.05	0.076	4.078	0.078	53.4
2-Bromo-3-chloro-nitrobenzene [f]	89.98	0.063	1.306	0.026	20.8
	89.98	0.063	1.249	0.032	19.9
2,3-Dibromo-nitrobenzene [f]	89.98	0.063	1.833	0.028	29.2
	89.98	0.063	1.829	0.063	29.1
2-Bromo-5-chloro-nitrobenzene [f]	89.98	0.063	∼ 0.2		∼ 3
2-Bromonitro-benzene [f]	89.98	0.063	∼ 0.2		∼ 3

[a] Accuracy ± 0.05.
[b] Estimated from the data in Part I.[1]
[c] Pseudo first-order rate constant in sec⁻¹.
[d] Standard error in k_{obs}.
[e] Second-order rate constant, 1 mol⁻¹sec⁻¹. Calculated on [CuCl₂⁻].
[f] Values from Part I.[1]

$$k_2 = \frac{kT}{h} \exp(-\Delta H^{\neq}/RT) \exp(\Delta S^{\neq}/R)$$

All calculations were carried out on an Olivetti Programma 101 electronic desk-top computer by the method of least squares. The enthalpy of activation ($\Delta H^{\neq}$) and the entropy of activation ($\Delta S^{\neq}$) for 2-bromo-3-iodonitrobenzene together with the values for the activation parameters of the compounds investigated in Part I [1] are presented in Table 2.

DISCUSSION

It may be seen from Table 1 that the ease of bromine-chlorine exchange in 2-bromo-3-halonitrobenzenes follows the order:
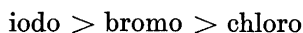
iodo > bromo > chloro

Table 2. Activation enthalpies and entropies. The errors are 3 S.E. from the least squares method calculations.

Compound	$\Delta H^{\ddagger\,a}$	$\Delta S^{\ddagger\,b}$
2-Bromo-3-iodonitrobenzene	11 ± 1	-40 ± 3
2-Bromo-3-chloronitrobenzene *c*	11 ± 2	-41 ± 4
2,3-Dibromonitrobenzene *c*	12 ± 1	-37 ± 3

[a] In kcal. mol^{-1}.
[b] In cal. deg.$^{-1}$ mol^{-1}.
[c] Values from Part I.[1]

According to Buckley *et al.*[5] the polar effect of an *ortho*-halogen is greater than that of one in the *para*-position. The polar substituent constants, σ_o, for *ortho*-halogen, based on pK_a values of *ortho*-halobenzoic acids, were calculated [5] to be as follows:

	Cl	Br	I
σ_o	$+0.83$	$+0.91$	$+0.84$

However, the polar effect alone cannot be responsible for the entire accelerating effect of an *ortho*-halogen. Proximity effects may also intervene. Bondi [6] has reported the van der Waals volume for iodine to be 19.6 cm^3/mol as compared to 15.1, 12, and 3.4 for bromine, chlorine, and hydrogen, respectively. There are also indications from electron diffraction data that in *ortho*-dihalobenzenes [7] the halogens are bent out of the ring plane. The *ortho*-halogen substituents cause an enhancement of the exchange rate, probably because there is relief of strain as the configuration at the attacked carbon changes to tetrahedral in the suggested transition state.[1]

The activation parameters found in the present work are of comparable magnitude to those determined by Castro *et al.*[3] for substitution of iodobenzenes with copper(I) phenylacetylide.

EXPERIMENTAL

Melting points were determined on a Kofler Hot-stage Microscope. NMR spectra were obtained with a Varian A-60 instrument, and IR spectra with a Beckman IR-9 spectrophotometer.

2-Chloro-1,3-dinitrobenzene was prepared from 36.6 g (0.20 mol) of 2,6-dinitroaniline (Fluka AG, *puriss.*) in 400 ml of hot glacial acetic acid by diazotization, followed by a Sandmeyer reaction with copper(I) chloride according to a procedure described by Gunstone and Tucker,[8] except that the solution was stirred at 40°C for 1 h after the addition of 2,6-dinitroaniline to the nitrosylsulfuric acid solution was completed. The yield of crude product was 32.4 g (80 %), m.p. 80 − 86°. After recrystallization from acetic acid the m.p. was 86.5 − 87.5°, lit.[9] 88°.

2-Chloro-3-nitroaniline was prepared from the preceding compound by reduction with titanium(III) chloride. 12.3 g (0.0608 mol) was dissolved in 450 ml of ethanol, and 230 g of 10 % aqueous titanium(III) chloride (Riedel de Haën AG) was added at 25 − 28°C

during 2.5 h. The solution was stirred for 1.5 h, and the ethanol was then removed under reduced pressure. The mixture was made alkaline with 10 % sodium hydroxide and then extracted with ether. The ether solution was washed with 5 % hydrochloric acid and dried with potassium carbonate, whereupon HCl gas was introduced. The hydrochloride of 2-chloro-3-nitroaniline was filtered off and converted to the free base with aqueous sodium carbonate and extracted with ether. Evaporation of the ether solution gave 3.95 g (38 %) of 2-chloro-3-nitroaniline, m.p. 94.5 − 95.5°, lit.[10] 94.0 − 94.5°.

2-Chloro-3-iodonitrobenzene. 2.59 g (0.015 mol) of 2-chloro-3-nitroaniline was dissolved in 25 ml of conc. sulfuric acid and diazotized at 5°C with 1.26 g (0.018 mol) of sodium nitrite in 15 ml of conc. sulfuric acid. After 1 h at room temperature the solution was added to 3.72 g (0.0225 mol) of potassium iodide in ice and water, and was left for 24 h at 10°C. The mixture was made alkaline with 10 % sodium hydroxide and extracted with ether. After evaporation of the ether the crude yield of 2-chloro-3-iodonitrobenzene was 3.6 g (85 %), m.p. 56 − 58.5°. After recrystallization from methanol the m.p. was 60.5 − 61.0°, lit.[11] 59.8°.

2-Bromo-1,3-dinitrobenzene was synthesized from 36.6 g (0.20 mol) of 2,6-dinitroaniline by the procedure described above for 2-chloro-1,3-dinitrobenzene, except that the diazonium solution was added to a solution of 63 g of copper(I) bromide (0.44 mol) in 400 ml of 48 % hydrobromic acid. The yield of 2-bromo-1,3-dinitrobenzene was 42.1 g (85 %), m.p. 105.0 − 105.5°, lit.[12] 107°.

2-Bromo-3-nitroaniline. 15 g (0.0608 mol) of 2-bromo-1,3-dinitrobenzene, which had been steam distilled to remove all traces of copper salts, was reduced with titanium(III) chloride in 475 ml of ethanol by the procedure described above for 2-chloro-3-nitroaniline. The crude yield of 2-bromo-3-nitroaniline was 5.0 g (38 %), m.p. 96.5 − 97.5°, lit.[13] 97 − 98°.

2-Bromo-3-iodonitrobenzene. 3.3 g (0.015 mol) of 2-bromo-3-nitroaniline was diazotized and added to potassium iodide by the procedure described above for 2-chloro-3-iodonitrobenzene. The crude 2-bromo-3-iodonitrobenzene was chromatographed on alumina with benzene as eluent to yield 5.6 g (86 %), m.p. 99 − 100°. The substance has apparently not been described in the literature.

Copper(I) catalysed replacement of bromine by chloride ion. The reactions with copper(I) chloride were carried out in an atmosphere of argon with the apparatus and the method described in Part I.[1] The reaction mixtures were analysed on a Perkin Elmer F 11 Hot Wire Gas Chromatograph, equipped with a Model D 2 printing integrator. A 1/8″ o.d. 2 m SE 30-column was used, temp. 145°C, carrier gas He. A calibration curve was prepared from known mixtures of pure compounds, subjected to the extraction procedure described for the exchange products.[1] The composition of the exchange mixture was also verified by NMR and IR spectra. A calibration curve was made, and was found to be linear with unit slope.

The stoichiometric chloride ion concentration in the medium was determined by Mohr titration.

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