

## Copper(I) Catalysed Replacement of Iodine by Chloride Ion in Halonitrobenzenes

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In the present work the copper(I) catalysed exchange of iodine for chlorine in 3-bromo-2-iodonitrobenzene, 3-chloro-2-iodonitrobenzene, and 5-chloro-2-iodonitrobenzene is investigated. On comparison with the previously investigated compounds<sup>1,2</sup> with bromine as the leaving group, the iodine-chlorine exchange is found to be slower than the bromine-chlorine exchange.

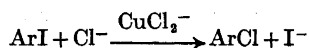
The conclusion from these results is that the rate-determining step in these copper(I) catalysed exchange reactions can hardly involve some breaking of the C-I and C-Br bonds, respectively.

In the previous studies<sup>1,2</sup> the copper(I) catalysed replacement of bromine by chlorine was studied in 2-halo-6-nitrobromobenzenes.

A large accelerating effect of an *ortho*-nitro group on the exchange rate was observed, and it was also found that *ortho*-halogen accelerates the reaction. The possibility of a tetrahedral transition state involving the copper(I) complex, the *ortho*-nitro group and the bromine to be replaced was suggested.<sup>1</sup>

In order to obtain information about the rate-determining step, it was necessary to vary the leaving group. In ordinary non-catalysed nucleophilic substitution a two-step mechanism is assumed to operate, with the first step rate-determining. This assumption is based on the absence of an "element effect" on the reaction rates, observed by Bunnett *et al.*,<sup>3</sup> when 2,4-dinitro-1-X-benzenes react with piperidine, and X is varied. This is taken as evidence that the C-X bond is not broken in the rate-determining step. Similar results in non-catalysed halogen exchange have been found by Lamm and co-workers. (See for instance Ref. 4.)

In the present work, iodine has been studied as leaving group in the same aqueous hydrochloric acid-acetic acid medium as previously used, where  $[Cl^-] = 5.26 \text{ M}$ .<sup>1</sup>



## RESULTS AND CALCULATIONS

The copper(I) catalysed exchange of iodine for chlorine in 3-bromo-2-iodonitrobenzene, 3-chloro-2-iodonitrobenzene, and 5-chloro-2-iodonitrobenzene, synthesized together with the calibration substances according to Fig. 1, has been investigated at 98°C. The study was limited to this tempera-

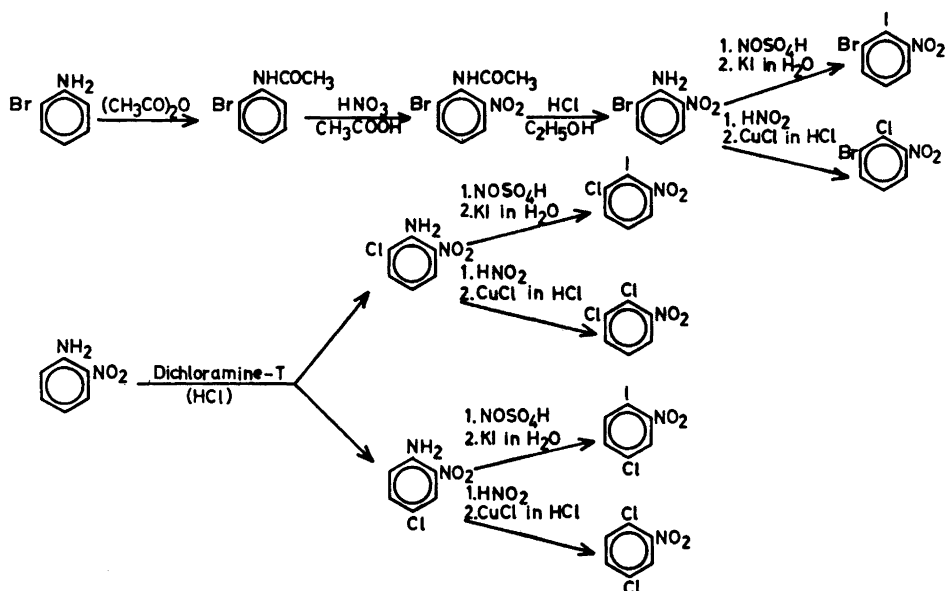


Fig. 1. Routes to the compounds.

ture because these substances were unsatisfactorily soluble in the present solution (hydrochloric acid-acetic acid-water) at lower temperatures.

As in the series with bromine as leaving group<sup>1,2</sup> a small amount of the exchange products had the *ortho*-nitro group reduced, probably by the copper(I) chloride. However, the present exchange reactions with iodine as leaving group were further complicated by another side-reaction, namely reductive dehalogenation (ArI → ArH).

In the case of the exchange mixture from 3-bromo-2-iodonitrobenzene, the mass spectra\* of the by-products showed a triplet at *m/e* 205, 207, and 209, with relative abundances 3/4/1, and a doublet at *m/e* 297 and 299 in the proportions 1/1, due to 3-bromo-2-chloroaniline and 3-bromo-2-iodoaniline, respectively, (< 1 %) and besides a doublet at *m/e* 171 and 173, and a doublet at *m/e* 201 and 203, due to 3-bromoaniline and 3-bromonitrobenzene, respectively (about 5 % together). For 3-chloro-2-iodonitrobenzene the reductive

\* Performed on an LKB A 9000 instrument at Instrumentstationen, Kemicentrum, University of Lund.

deiodination was also estimated to occur to the extent of about 5 %, but in the case of 5-chloro-2-iodonitrobenzene, which exchanged very slowly, about 8 % of the deiodination product was detected. The mass spectra showed molecular ions at  $m/e$  127 and 129 of relative abundances 3/1, which indicates chloroaniline.

Bacon and Wright<sup>5</sup> have investigated the competition between copper(I) catalysed nucleophilic and reductive replacement of halogen in reactions between sodium methoxide and bromo- or iodobenzene derivatives and have found, in agreement with the present and previous<sup>1,2</sup> results, that the employment of an iodo compound in place of the corresponding bromo compound led to an increase in the amount of reduction relative to that of nucleophilic substitution. No indication of dehalogenation products was observed in the previously reported<sup>1,2</sup> exchange experiments with bromine as leaving group. The reductive dehalogenation was regarded by Bacon and Rennison<sup>6</sup> as either copper assisted displacement of halide by hydride ion or a homolytic process involving an intermediate aryl radical.

No Ullmann-type coupling of the halides was observed in the present exchange experiments.

No exchange was detected at 98°C in the absence of copper(I) chloride, nor was the reaction found to be reversible, as shown by the fact that when an equimolar quantity of iodide ion was added to 3-bromo-2-chloronitrobenzene, under the same conditions as for 3-bromo-2-iodonitrobenzene, no 3-bromo-2-iodonitrobenzene was detected.

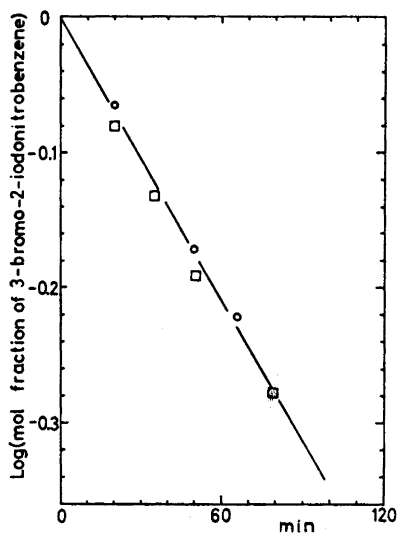


Fig. 2. Two representative runs (O and □) of iodine-chlorine exchange in 3-bromo-2-iodonitrobenzene at 98°C.

The reactions may be seen from Fig. 2 to follow pseudo first-order kinetics.  $k_{\text{obs}}$  was calculated from the slope of the line and the second-order rate constant  $k_2$  from estimation of the catalysing  $\text{CuCl}_2^-$  concentrations as described previously.<sup>1</sup>

The results are summarized in Table 1 together with some values from previous work for comparison.

Table 1. Kinetic runs involving halonitrobenzenes and chloride ion.  $[\text{Cl}^-] = 5.26 \text{ M}$ ,  $[\text{Cu}^+]_{\text{tot}} = 0.1124 \text{ M}$ ,  $[\text{CuCl}_2^-] = 0.076$ .<sup>a</sup> Temp. =  $98.05^\circ\text{C}$ .<sup>b</sup>

Compound 0.0562 M	$k_{\text{obs}} \times 10^{4c}$	S.E. $\times 10^{4d}$	$k_2 \times 10^{4e}$
3-Bromo-2-iodonitro- benzene	1.3	0.02	17.2
	1.3	0.04	17.3
3-Chloro-2-iodonitro- benzene	0.95	0.02	12.5
	1.0	—	13.6
5-Chloro-2-iodonitro- benzene	$\sim 0.13$	—	$\sim 1.7$
2-Bromo-3-iodonitro- benzene <i>f</i>	4.016	0.080	52.6
	4.078	0.078	53.4
2,3-Dibromonitro- benzene <i>g</i>	3.435	0.089	45.0
	3.390	0.073	44.4
2-Bromo-3-chloronitro- benzene <i>g</i>	2.315	0.045	30.3
	2.196	0.055	28.8

<sup>a</sup> Estimated from the data in Ref. 1. <sup>b</sup> Accuracy  $\pm 0.05$ . <sup>c</sup> Pseudo first-order rate constant in  $\text{sec}^{-1}$ . <sup>d</sup> Standard error in  $k_{\text{obs}}$ . <sup>e</sup> Second-order rate constant,  $1 \text{ mol}^{-1}\text{sec}^{-1}$ . Calculated on  $[\text{CuCl}_2^-]$ . <sup>f</sup> Values from Ref. 2. <sup>g</sup> Values from Ref. 1.

## DISCUSSION

The copper(I) catalysed exchange rates of the bromo compounds are roughly 2–3 times as great as those of the iodo compounds, as seen from Table 1. From a consideration of these results together with the facts that iodine is a better leaving group than bromine and that the stability of copper(I) halide complexes increases with increasing atomic number of the halogens, it appears unlikely that the rate-determining step involves breaking of the C–I and C–Br bonds, respectively.

A possible reason why the iodo compounds react at a lower rate than the bromo ones may be found in the less favourable geometry of the intermediate Cu(I) complex due to the large size of the iodine atom.

The accelerating effect of an *ortho*-halogen is further demonstrated in the present work. The exchange rate of 3-chloro-2-iodonitrobenzene was about 7 times as great as the rate of 5-chloro-2-iodonitrobenzene, in good agreement with previous results.<sup>1</sup> In addition, the accelerating effect on the exchange rate is greater for an *ortho*-bromine than for an *ortho*-chlorine, which also agrees with previous experiments.<sup>1,2</sup>

## 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-Bromo-6-nitroaniline* was synthesized from 2-bromoaniline (Fluka AG, *purum*) as described in previous work.<sup>1</sup> M.p. 73.5–75.0°, lit.<sup>7</sup> 74–75°.

*3-Bromo-2-iodonitrobenzene*. 3.3 g (0.015 mol) of 2-bromo-6-nitroaniline was dissolved in 25 ml of conc. sulfuric acid and diazotized with 1.26 g (0.018 mol) of sodium nitrite in 15 ml of conc. sulfuric acid at 5°C. The diazonium solution was stirred for 1 h at 35–40°C and then added to 3.72 g (0.0225 mol) of potassium iodide in ice and water, and left for 24 h at 10°C. The solution was made alkaline with 10 % aqueous sodium hydroxide and extracted with ether, whereupon the crude 3-bromo-2-iodonitrobenzene was chromatographed on alumina with benzene as eluent. The yield was 3.5 g (71 %), m.p. 120.5–121.5°, lit.<sup>8</sup> 119–120°.

*3-Bromo-2-chloronitrobenzene* was synthesized from 2-bromo-6-nitroaniline as described by Liedholm.<sup>1</sup> M.p. 57.5–58.5° after two recrystallizations from methanol, lit.<sup>1</sup> 57.5–58.5°.

*2-Chloro-6-nitroaniline* and *4-chloro-2-nitroaniline* were prepared from *ortho*-nitroaniline (Fluka AG, *puriss.*), according to Liedholm.<sup>1</sup> M.p. 75.5–76.0°<sup>1</sup> and 116–117°<sup>1</sup> respectively.

*3-Chloro-2-iodonitrobenzene* was synthesized from 2.6 g (0.015 mol) of 2-chloro-6-nitroaniline in 25 ml of conc. sulfuric acid by the procedure described for 3-bromo-2-iodonitrobenzene. Yield 3.0 g (71 %), m.p. 102.0–103.0°, lit.<sup>9</sup> 100–101°.

*2,3-Dichloronitrobenzene* was also synthesized from 2-chloro-6-nitroaniline according to Lamm and Liedholm,<sup>10</sup> m.p. 61.5–62.0°, lit.<sup>10</sup> 61.5–62.0°.

*5-Chloro-2-iodonitrobenzene* was prepared from 2.6 g (0.015 mol) of 4-chloro-2-nitroaniline in 25 ml of conc. sulfuric acid by the procedure described for 3-bromo-2-iodonitrobenzene. Yield 2.3 g (54 %), m.p. 61.5–62.5°, lit.<sup>11</sup> 63.3°.

*2,5-Dichloronitrobenzene* was synthesized according to Liedholm<sup>1</sup> from 4-chloro-2-nitroaniline. M.p. 53.5–54.0°, lit.<sup>1</sup> 53.5–54.0°.

The copper(I) catalysed replacement of iodine by chloride ion was carried out as described for replacement of bromine by chloride ion in previous work.<sup>1</sup> The composition of the reaction mixture was determined 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. 130°C, carrier gas He. A calibration curve was made by means of the pure compounds, 3-bromo-2-iodonitrobenzene and 3-bromo-2-chloronitrobenzene. It was found to be linear with unit slope. NMR and IR spectra were also used for identification purposes.

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

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