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

BRITA LIEDHOLM

Department of Organic Chemistry, University of Göteborg and Chalmers Institute of Technology, Fack, S-402 20 Göteborg 5, Sweden

The copper(I) catalysed exchange of bromine for chlorine in an aqueous hydrochloric acid-acetic acid medium was kinetically studied under homogeneous conditions in 2-bromo-3-chloronitrobenzene, 2,3-dibromonitrobenzene, and some other halonitrobenzenes at 80, 90, and 98°C. The concentration of the catalysing copper(I) complex, which was found to be $CuCl_2^-$, was estimated from the dependence of the first-order rate on the chloride ion concentration.

A strong accelerating effect of an *ortho* nitro group was observed. The possibility of a transition state 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 is discussed and the activation parameters are presented.

In previous work,[1] the replacement of bromine by chlorine in 2-bromo-3-nitrobenzenediazonium ions in a hydrochloric acid-acetic acid-water medium at 20 and 25°C was kinetically studied. The exchange reaction was quenched by means of a Sandmeyer reaction with copper(I) chloride in hydrochloric acid. However, when the resulting compounds, 2-bromo-3-chloronitrobenzene and 2,3-dichloronitrobenzene, were subjected to the conditions of steam distillation in the presence of univalent copper salts, 2-bromo-3-chloronitrobenzene was found to undergo bromine-chlorine exchange at the 2-position. This exchange reaction has now been investigated along with some other exchanges of bromine by chlorine in halonitrobenzenes. The kinetic runs were performed at 80, 90, and 98°C in an argon atmosphere to preserve the copper(I) chloride from oxidation and in the same medium ($[Cl^-]$=5.26 M) as previously used.[1] The ratio between the concentration of halonitrobenzene and $[Cl^-]$ was about 0.01. Exchange reactions under similar conditions did not occur when copper(I) chloride was absent, nor in the presence of copper(II) chloride.

Exchange between aryl halides and halide ions does not occur as readily as many other typical nucleophilic substitutions. Activation by two nitro groups is generally necessary. However, when the aryl halides are activated by a diazonium group together with one nitro group,[1] the exchange occurs

much more rapidly. Miller *et al.*[2] have investigated exchange between 1-halo-2,4-dinitrobenzenes and lithium halide ions in methanol at 100—138°C. It was soon recognized that copper catalysis facilitates the exchange reactions of slightly activated aryl halides with halide ions, but not much attention has been devoted to this problem. In a comprehensive review of aromatic nucleophilic substitutions Bunnett and Zahler[3] refer to the uncertain mechanism of reactions promoted by transition metals and their salts. Bacon and Hill[4] have studied exchange reactions between aryl halides and copper(I) salts in organic solvents. When applied to substituted bromobenzenes in pyridine at 110.5°C, the reaction with copper(I) chloride was remarkably insensitive to the nature and position of the substituent. The *para* methoxy and *ortho* or *para* methyl substituted compounds reacted at about the same rate as the unsubstituted bromobenzene, the rates of the *meta* and *para* nitro derivatives were 3 and 5 times as great, respectively, but a strong accelerating effect was observed for an *ortho* nitro group: the rate was increased about 400-fold. These results are in marked contrast to those substitutions in polar solvents not involving copper catalysis, which often show only slightly more enhancement of activity by an *ortho* nitro group as compared with a *para* nitro group. Hardy and Fortenbaugh[5] have heated aromatic bromo compounds with copper(I) chloride in α-picoline and other nitrogenous complexing solvents and obtained the corresponding chloro compounds. Nilsson[6] has reported 5 % *o*-dichlorobenzene as by-product in the Ullmann reaction of *o*-chloroiodobenzene with copper at 250°C.
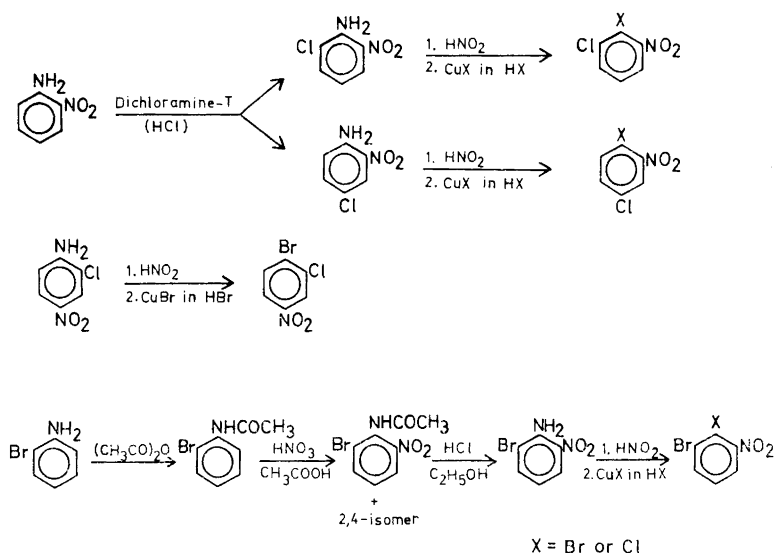

Fig. 1. Routes to the compounds. The X = Cl compounds were synthesized for calibration purposes.

RESULTS AND CALCULATIONS

The halonitrobenzenes kinetically studied in the present work under homogeneous conditions in an aqueous hydrochloric acid-acetic acid medium in the presence of copper(I) chloride were 2-bromo-3-chloronitrobenzene, 2,3-dibromonitrobenzene and, to a limited extent because of the reasons mentioned below, 4-bromo-3-chloronitrobenzene, 4-bromonitrobenzene, 2-bromonitrobenzene, and 2-bromo-5-chloronitrobenzene. The compounds were synthesized by the procedures depicted in Fig. 1.

In most runs, the reactions were followed for at least one half-life.

From the GLC data two small impurities (about 2 % together) besides the two main compounds were detected in the exchange-reaction solutions. The by-products were separated from the main compounds by preparative thin-layer chromatography on silica using benzene as solvent. In the case of the exchange mixture of 2-bromo-3-chloro- and 2,3-dichloro-nitrobenzene, the mass spectra * of the by-products showed a triplet structure centered at m/e 207, the molecular weight of 2-bromo-3-chloroaniline, and a triplet centered at m/e 162, the molecular weight of 2,3-dichloroaniline. The mass spectra of the by-products from the halogen exchange in 2,3-dibromonitrobenzene showed a triplet at m/e 251 and a triplet at m/e 207, the molecular weights of 2,3-dibromoaniline and 3-bromo-2-chloroaniline, respectively. Evidently the copper(I) ion had reduced the nitro groups to a small extent. Owing to the stoichiometric proportion between the copper compound and the organic material the loss of catalyst by this side reaction is negligible.

To investigate the reversibility of the bromine-chlorine exchange step 2,3-dichloronitrobenzene was subjected to similar conditions to those used for 2-bromo-3-chloronitrobenzene and an equimolar quantity of bromide ion was added. No chlorine-bromine exchange was detected at 90°C.

For 4-bromo- and 4-bromo-3-chloro-nitrobenzene, both with a nitro group *para* to the reaction site, the exchange reactions were too slow to be determined accurately under the prevailing experimental conditions.

Unfortunately, 2-bromo- and 2-bromo-5-chloro-nitrobenzene gave a higher percentage of impurities, and the rate constants will in consequence of this only be given as approximate values.

The reactions display pseudo first-order kinetics as illustrated in Fig. 2 for the reaction of 2-bromo-3-chloronitrobenzene. The pseudo first-order rate constant k_{obs} was calculated from the slope of the lines by the method of least squares. All calculations were carried out on an Olivetti Programma 101 electronic desk-top computer.

The investigation of the catalytic enhancement of the exchange rate due to copper(I) chloride is complicated because copper(I) chloride in a hydrochloric acid-water-acetic acid solution may exist in several copper(I) ion complexes and furthermore one must determine which of these species has catalytic effect on the halogen exchange reactions.

In order to cast some light on this problem a series of runs with 2-bromo-3-chloronitrobenzene was carried out at 90°C. The copper(I) chloride concentra-

---

* Performed on an LKB A 9000 instrument at the Department of Organic Chemistry, University of Lund.
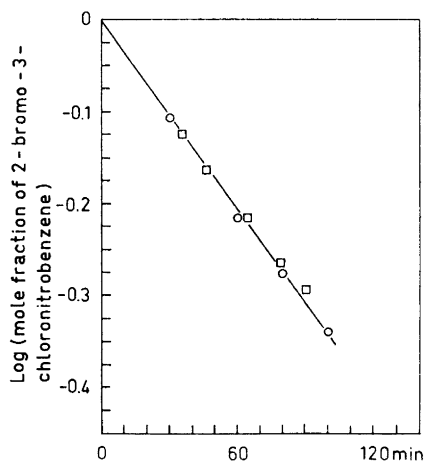
Fig. 2. Two representative runs (○ and □, respectively) of Br/Cl exchange in 2-bromo-3-chloronitrobenzene at 90°C.
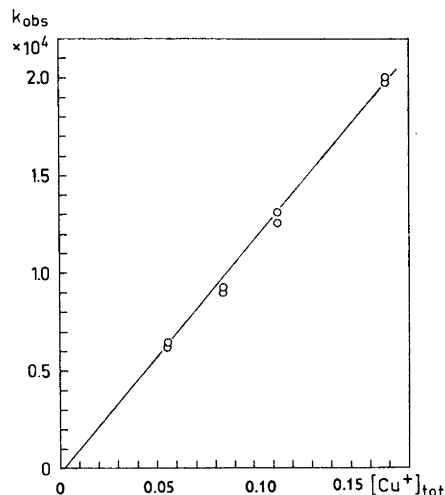
Fig. 3. k_{obs} for 2-bromo-3-chloronitrobenzene at 90°C plotted *versus* the total concentration of copper(I) ion at constant chloride ion concentration (5.26 M).

tion was varied in the interval 0.056—0.168 M, but [Cl⁻] in the medium was held constant at 5.26 M. Under these conditions, the ratio between k_{obs} and the total concentration of copper(I) ion was found to be constant (Fig. 3).

According to Noyes and Ming Chow,[7] copper(I) is present in chloride solutions primarily in the form of the complex anion $CuCl_2^-$ as long as the chloride concentration is moderate. In more concentrated solutions a large portion of the copper is bound as the anion $CuCl_3^{2-}$. However, it is not excluded that complexes of a higher chloride content may occur.

To obtain some indication of the chloride content of the catalysing copper(I) complex, the [Cl⁻] concentration of the medium was varied in the interval 2.01—5.26 M in a series of experiments while the total copper(I) concentration was held constant at 0.1124 M. In order to maintain as nearly as possible the same ionic strength a mixture of hydrochloric acid and perchloric acid was used.[8] The acid concentration was held constant at 5.26 M. Perchloric acid is thought to be indifferent toward the formation of copper(I) complexes.

The results of the bromine-chlorine exchange in 2-bromo-3-chloronitrobenzene at 80, 90, and 98°C when [Cl⁻] was varied but the total copper(I) concentration was constant are presented in Table 1. k_{obs} is seen to increase with decreasing [Cl⁻] concentration, which according to Noyes and Ming Chow [7] may be taken to imply that $CuCl_2^-$ is the catalysing species in the halogen exchange reaction.

Vestin *et al.*[8] have investigated the solubility of copper(I) chloride in a 4 molal mixture of hydrochloric acid and perchloric acid at 25°C. They have

Table 1. Bromine-chlorine exchange in 2-bromo-3-chloronitrobenzene (0.0562 M). $[Cu^+]_{tot} = 0.1124$ M, $[Cl^-] + [ClO_4^-] = 5.26$ M.

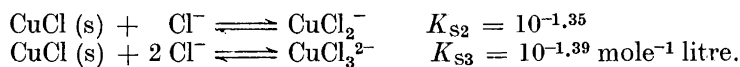| $[Cl^-]^a$	Temp.°C^b	$k_{obs} \times 10^{4c}$	S.E. $\times 10^{4d}$
2.01	79.95	1.076	0.029
3.02	79.95	1.017	0.010
5.26	79.95	0.720	0.014
5.26	79.95	0.766	0.016
2.01	89.98	1.962	0.069
3.02	89.98	1.892	0.027
4.02	89.98	1.742	0.029
4.43	89.98	1.624	0.023
5.26	89.98	1.306	0.026
5.26	89.98	1.249	0.032
2.01	98.05	2.78	0.25
3.02	98.05	2.59	0.12
5.26	98.05	2.315	0.045
5.26	98.05	2.196	0.055

^{a} Determined by Mohr titration, accuracy ± 1 %.
^{b} Accuracy ± 0.05.
^{c} Pseudo first-order rate constant in sec^{-1}. Calculated by the method of least squares.
^{d} Standard error in k_{obs}.

found that if the activity coefficients are assumed to be constant, the solubilities can be referred to the two equilibria:

$$CuCl \text{ (s)} + Cl^- \rightleftharpoons CuCl_2^- \qquad K_{S2} = 10^{-1.35}$$
$$CuCl \text{ (s)} + 2 Cl^- \rightleftharpoons CuCl_3^{2-} \qquad K_{S3} = 10^{-1.39} \text{ mole}^{-1} \text{ litre.}$$

Noyes and Ming Chow [7] have found K_{S2} at 25°C to be $10^{-1.18}$ and at 75°C $10^{-0.5}$. They have made their investigations in hydrochloric acid at concentrations in the interval 0.1—0.3 M, where only $CuCl_2^-$ is presumed to be present. If the solubility constants K_{S2} and K_{S3}, determined by Vestin *et al.*,* are used together with the solubility product of CuCl, $K_{S0} = 10^{-6.73}$,[9] one obtains the complex constants β_2 and β_3 at 25°C.

$$\frac{K_{S2}}{K_{S0}} = \frac{[CuCl_2^-]}{[Cu^+][Cl^-]^2} = \beta_2 \qquad \beta_2 = 10^{5.38} \text{mole}^{-2} \text{ litre}^2$$

$$\frac{K_{S3}}{K_{S0}} = \frac{[CuCl_3^{2-}]}{[Cu^+][Cl^-]^3} = \beta_3 \qquad \beta_3 = 10^{5.34} \text{mole}^{-3} \text{ litre}^3$$

Because complex constants for the copper(I) complexes are not available for our medium and the temperatures at which our experiments were performed, we have been forced to obtain a rough estimate of the $CuCl_2^-$ concentration. In view of the results in the experiments at 90°C, in which the

---

* Vestin *et al.* have given their values in mole/1000 g of water. However, they have worked with such diluted solutions that the figures can be considered the same in mole/litre.

copper(I) concentration was varied but [Cl$^-$] held constant (Fig. 3), the ratio between k_{obs} and the $CuCl_2^-$ concentration (which varies with [Cl$^-$], see Table 1) is expected to be a constant. Only mononuclear copper(I) complexes are assumed.

The following relations are valid ([Cu$^+$]$_{tot}$=total concentration of copper in the solution):

$$[Cu^+]_{tot} = [Cu^+] + \sum_{n=2}^{N} \beta_n [Cu^+] [Cl^-]^n$$

$$\frac{[CuCl_2^-]}{[Cu^+]_{tot}} = \frac{\beta_2 [Cu^+] [Cl^-]^2}{[Cu^+] + \beta_2 [Cu^+][Cl^-]^2 + \beta_3 [Cu^+][Cl^-]^3}$$

It is obvious that the concentration of $CuCl_2^-$ will be proportional to the total concentration of copper as long as the ionic strength and the chloride ion concentration are held constant. Since the concentration of uncomplexed copper(I) ion can be neglected in comparison with those of the complexes in the concentration range studied, the ratio may be written

$$\frac{[CuCl_2^-]}{[Cu^+]_{tot}} = \frac{1}{1 + \alpha[Cl^-]}$$

where
$$\alpha = \beta_3/\beta_2$$

The α-values were determined from the values of Table 1. The product $k_{obs}(1 + \alpha[Cl^-])$ was nearly constant (small deviations are probably due to variations in ionic strength) for the following α-values at the indicated temperatures:

$$\alpha_{80} = 0.19, \; \alpha_{90} = 0.15, \text{ and } \alpha_{98} = 0.09 \text{ mole}^{-1} \text{ litre.}$$

The second-order rate constant k_2 was calculated from the concentration of $[CuCl_2^-]$, which was computed from the α-values.

The results for k_{obs} and k_2, based on α_{90}, for 2-bromo-3-chloronitrobenzene with the copper(I) chloride concentration in the range 0.056—0.168 M and [Cl$^-$]=5.26 M are presented in Table 2.

All kinetic data for the investigated halonitrobenzenes are summarized in Table 3.

DISCUSSION

The strong accelerating effect of a nitro group *ortho* to the reaction site is apparent (see Table 3). The activating effect of a halogen in the other *ortho* position has also been demonstrated by the present work. The special reactivity in the presence of an *ortho* nitro group may be due to the possibility of a transition state in which this group participates with the anion $CuCl_2^-$ and the bromine to be replaced in the formation of a tetrahedral copper(I) complex (see Fig. 4). Such a transition state with a more or less tetrahedral carbon atom would allow the nitro group to become coplanar with the ring and may also be the explanation for the observed activating effect of *ortho* halogen.

A chlorine substituent *para* to the reaction site does not alter the rate compared to the corresponding unsubstituted 2-bromonitrobenzene. This is

Table 2. Bromine-chlorine exchange in 2-bromo-3-chloronitrobenzene (0.0562 M). [Cl⁻] = 5.26 M. Temp. = 89.98°C.

$[Cu^+]_{tot}$	$[CuCl_2^-]^a$	$k_{obs} \times 10^{4b}$	S.E. $\times 10^{4c}$	$k_2 \times 10^{4d}$
0.0562	0.031	0.641	0.012	20.4
0.0562	0.031	0.619	0.019	19.7
0.0843	0.047	0.926	0.035	19.7
0.0843	0.047	0.893	0.007	18.9
0.1124	0.063	1.306	0.026	20.8
0.1124	0.063	1.249	0.032	19.9
0.1684	0.094	1.999	0.055	21.2
0.1684	0.094	1.966	0.099	20.9

[a] Calculated from the results in Table 1.
[b] Pseudo first-order rate constant in sec⁻¹.
[c] Standard error in k_{obs}.
[d] Second-order rate constant, 1 mole⁻¹sec⁻¹. Calculated on $[CuCl_2^-]$.

Table 3. Kinetic runs involving halonitrobenzenes and chloride ion. [Cl⁻] = 5.26 M, $[Cu^+]_{tot} = 0.1124$ M.

Compound 0.0562 M	Temp.°C[a]	$[CuCl_2^-]^b$	$k_{obs} \times 10^{4c}$	S.E. $\times 10^{4d}$	$k_2 \times 10^{4e}$
2-Bromo-3-chloro-nitrobenzene	79.95	0.056	0.720	0.014	12.8
»	79.95	0.056	0.766	0.016	13.6
»	89.98	0.063	1.306	0.026	20.8
»	89.98	0.063	1.249	0.032	19.9
»	98.05	0.076	2.315	0.045	30.3
»	98.05	0.076	2.196	0.055	28.8
2,3-Dibromonitro-benzene	79.95	0.056	1.023	0.019	18.2
»	79.95	0.056	1.028	0.018	18.3
»	89.98	0.063	1.833	0.028	29.2
»	89.98	0.063	1.829	0.063	29.1
»	98.05	0.076	3.435	0.089	45.0
»	98.05	0.076	3.390	0.073	44.4
2-Bromo-5-chloro-nitrobenzene	89.98	0.063	~0.2		~3
2-Bromonitrobenzene	89.98	0.063	~0.2		~3
4-Bromonitrobenzene	98.05	0.076	<0.005		<0.05
4-Bromo-3-chloro-nitrobenzene	98.05	0.076	<0.01		<0.1

[a] Accuracy ± 0.05.
[b] Calculated from the results in Table 1.
[c] Pseudo first-order rate constant in sec⁻¹.
[d] Standard error in k_{obs}.
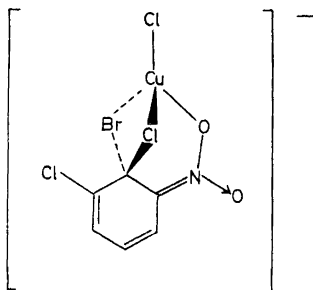[e] Second-order rate constant, 1 mole⁻¹sec⁻¹. Calculated on $[CuCl_2^-]$.

Fig. 4.

in complete agreement with the observations of Bacon and Hill.[4] On the other hand a bromine or chlorine in the *ortho* position enhances the rate 10-fold and 7-fold, respectively. The polar effects for a bromine or chlorine atom are almost the same in the *ortho* as in the *para* position according to Taft,[10] although this conclusion has been strongly criticized. In any event there is evidence that proximity effects in the *ortho* position may cause changes in the exchange rates. Electron diffraction data on *o*-dibromo- and *o*-dichloro-benzene, reported by Allen and Sutton,[11] indicate that the halogens are bent out of the ring plane by 18°. Bondi [12] has calculated the van der Waals volume for bromine to be 15.1 cm^3/mole and that for chlorine 12 cm^3/mole. For hydrogen the corresponding value is 3.4. The presence of *ortho* halogen substituents leads to acceleration presumably because there is relief of strain, compared to the initial state, as the configuration at the attacked carbon atom changes to tetrahedral in the transition state.

The activation parameters for 2-bromo-3-chloronitrobenzene and 2,3-dibromonitrobenzene were calculated from k_2 in Table 3 and the Eyring equation:

$$k_2 = \frac{kT}{h} \left(e^{-\Delta H^{\ddagger}/RT} \, e^{\Delta S^{\ddagger}/R} \right)$$

$$\ln\left(\frac{k_2}{T}\right) = -\frac{\Delta H^{\ddagger}}{R} \frac{1}{T} + \frac{\Delta S^{\ddagger}}{R} + \ln\left(\frac{k}{h}\right)$$

where $\Delta H^{\ddagger}$ is the enthalpy of activation and $\Delta S^{\ddagger}$ is the entropy of activation and the other symbols have their usual meaning.

If $\ln(k_2/T)$ is plotted against $1/T$, $-\Delta H^{\ddagger}/R$ gives the slope of the line and $(\Delta S^{\ddagger}/R) + \ln(k/h)$ the intercept. The calculations were all carried out on a computer by the method of least squares. For 2-bromo-3-chloronitrobenzene $\Delta S^{\ddagger} = -41 \pm 4$ cal. deg.$^{-1}$ mole^{-1} and $\Delta H^{\ddagger} = 11 \pm 2$ kcal. mole^{-1} and for 2,3-dibromonitrobenzene $\Delta S^{\ddagger} = -37 \pm 3$ cal. deg.$^{-1}$ mole^{-1} and $\Delta H^{\ddagger} = 12 \pm 1$ kcal. mole^{-1}.* They are to be considered as relative values due to the uncertainty in the estimation of k_2 (*vide supra*).

However, the values are of comparable magnitude to those found by Greizerstein and Brieux [13] for the reaction of dihalonitrobenzenes with piper-

---

* The errors are 3 S.E. from the least square method calculations.

idine. It is assumed by Hawthorne [14] that in amine reactions the transition state configurations are close to the hypothetical tetrahedral intermediate, and thus the nitro group of the *ortho* substituted compound may be allowed to become more nearly coplanar with the ring. It is well known [15] that under these conditions the resonance energy for the interaction of the nitro group with the ring is at a maximum and the enthalpy is at a minimum for the compound in the coplanar structure as far as the contribution from resonance energy is concerned.

EXPERIMENTAL

Melting points were determined with 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-6-nitroaniline. Attempts to prepare this substance according to Wolf and Pfister [16] from *o*-nitroaniline (Fluka AG, *puriss.*) by blocking the *para* position by sulfonation with subsequent chlorination gave 2-chloro-6-nitroaniline contaminated with about 10 % 2,4-dichloro-6-nitroaniline, as shown by an NMR spectrum. However, we were unsuccessful in purifying the substance (distillation *in vacuo* and column chromatography), and the following method was used instead.

A solution of 6.15 g (0.025 mole) 98 % *N,N*-dichloro-*p*-toluenesulphonamide (Dichloramine-T) in 25 ml of chloroform (Fischer reagent) was added to a solution of 6.9 g (0.05 mole) of *o*-nitroaniline in 35 ml of chloroform, containing a trace of hydrochloric acid as catalyst. After 24 h at room temp. the chloroform was removed in a rotary evaporator *in vacuo* and the remainder steam distilled until 1 l of distillate was collected. 2.5 g of the crude substance was obtained and isolated, dried and chromatographed on alumina with benzene (*pro analysi*) as eluent to yield 1.25 g (14.5 %) of 2-chloro-6-nitroaniline, m.p. 75.5−76.0°, lit.[17] 76°, lit.[16] 72−73°. The remainder on the alumina column was mainly 4-chloro-2-nitroaniline.

4-Chloro-2-nitroaniline. The steam distillation from the preceding experiment was continued until the material ceased to come over (2 l). 3.0 g of crude material was isolated. The substance was dissolved in ether and HCl gas introduced. The hydrochloride of 4-chloro-2-nitroaniline was isolated by filtration, made alkaline with aqueous sodium carbonate and afterwards extracted with ether. The ether solution was dried with anhydrous potassium carbonate and evaporated to dryness *in vacuo* to yield 2.3 g (27 %) of 4-chloro-2-nitroaniline, m.p. 116−117°, lit.[18] 116−117°.

2-Bromo-3-chloronitrobenzene was prepared from 2-chloro-6-nitroaniline according to a procedure reported previously.[1] M.p. 83−84°, lit.[1] 83−84°.

2,3-Dichloronitrobenzene was also synthesized from 2-chloro-6-nitroaniline according to Lamm and Liedholm.[1] M.p. 61.5−62.0°, lit.[1] 61.5−62.0°.

2-Bromo-5-chloronitrobenzene was prepared from 4-chloro-2-nitroaniline with the procedure reported for 2-bromo-3-chloronitrobenzene.[1] 2.6 g (0.015 mole) of 4-chloro-2-nitroaniline was dissolved in 140 ml of 52 % hydrobromic acid (Riedel de Haën AG, *pro analysi*). The crude yield was 3.0 g (85 %). Two recrystallizations from methanol (*pro analysi*) gave m.p. 69.5−70.5°, lit.[19] 70°.

2,5-Dichloronitrobenzene was synthesized from 4-chloro-2-nitroaniline according to the same procedure as reported for 2,3-dichloronitrobenzene.[1] 2.6 g (0.015 mole) of 4-chloro-2-nitroaniline was dissolved in 75 ml of conc. hydrochloric acid (Riedel de Haën AG, *pro analysi*). The crude yield was 2.1 g (73 %). M.p. 50−53°. After two recrystallizations from methanol the m.p. was 53.5−54.0°, lit.[20] 53°.

4-Bromo-3-chloronitrobenzene. 2-Chloro-4-nitroaniline (Fluka AG, pract. grade) was purified *via* the hydrochloride. The pure amine (8.6 g, 0.05 mole), m.p. 107.0−107.5°, lit.[18] 104−105°, was dissolved in 280 ml of 52 % hydrobromic acid and diazotized with 5 g (0.07 mole) of sodium nitrite (*pro analysi*) in the minimum amount of water at 20−25°C. After 1 h at room temp. the solution was added to 14.5 g (0.1 mole) of copper(I) bromide (Riedel de Haën AG, *pro analysi*) dissolved in 25 ml of 52 % hydrobromic acid. 4-Bromo-3-chloronitrobenzene was isolated by steam distillation followed by filtration

of the distillate (1 l). The yield was 7.6 g (65 %). After two recrystallizations from methanol, the m.p. was 60.5 — 62.0°, lit.[21] 62°.

2-Bromonitrobenzene, 2-chloronitrobenzene, and *4-bromonitrobenzene* were commercial products (Fluka AG, *purum*) which were purified by recrystallization from ethanol when necessary.

2-Bromoacetanilide. 17.2 g (0.1 mole) of 2-bromoaniline (Fluka AG, *purum*) was dissolved in 30 ml of benzene and 10.7 g (0.105 mole) of acetic anhydride (Fischer reagent, min. 99.1 %) was added. After 24 h the acetanilide was isolated by filtration. Yield 20.35 g (95 %), m.p. 100 — 101°, lit.[22] 99°.

2-Bromo-6-nitroaniline. 15.0 g (0.07 mole) of 2-bromoacetanilide was nitrated according to the method of Franzen and Engel.[17] Yield 13.35 g (74 %) of *ortho* and *para* mononitration products which were separated with "Witt-Utermann solution" (75 g of potassium hydroxide, 475 ml of water and 100 ml of ethanol) according to Gibson and Johnson.[23] The *ortho* isomer, 2-bromo-6-nitroacetanilide, was hydrolysed with hydrochloric acid following the description of Gibson and Johnson,[23] and 2-bromo-6-nitroaniline was isolated by steam distillation which gave a yield of 3.65 g (24 % calculated on 2-bromoacetanilide), m.p. 73.0 — 74.5°, lit.[23] 74 — 75°.

2,3-Dibromonitrobenzene. 3.3 g (0.015 mole) of 2-bromo-6-nitroaniline was dissolved in 90 ml of 52 % hydrobromic acid and diazotized with 1.7 g (0.025 mole) of sodium nitrite in the minimum amount of water at 0 — 5°C and was then left for 1 h at room temp. This solution was added to a hot solution of 4.5 g (0.03 mole) of copper(I) bromide in 20 ml of 52 % hydrobromic acid. The product was recovered by steam distillation. The crude yield was 3.6 g (85 %). After three recrystallizations from methanol the m.p. was 84.5 — 85.0°, lit.[24] 85°.

3-Bromo-2-chloronitrobenzene. 2.17 g (0.01 mole) of 2-bromo-6-nitroaniline was dissolved in 50 ml of conc. hydrochloric acid and diazotized at 0 — 5°C with 0.8 g (0.0115 mole) of sodium nitrite, dissolved in the minimum amount of water. The solution was left for 1 h at room temperature and then added to a hot solution of 2.0 g (0.02 mole) of copper(I) chloride in 10 ml of conc. hydrochloric acid. The mixture was steam distilled and yielded 2.1 g (89 %) of the crude product, m.p. 54 — 58°. A sample purified by preparative GLC on an Aerograph Autoprep A 700 (carrier gas N_2, Silicone SI 30, 6 m column, i.d. 3/8″, column temperature 215°C) gave m.p. 57.5 — 58.5°, lit.[25] 65°. Two recrystallizations of the crude product from methanol gave m.p. 57 — 58°. It was also verified by NMR and IR spectra that the substance obtained was actually 3-bromo-2-chloronitrobenzene.

Copper(I) chloride (Fischer reagent), purified according to Keller and Wycoff,[26] was a perfectly white substance.

Copper(I) catalysed replacement of bromide ion by chloride ion. All reactions with copper(I) chloride were carried out in an atmosphere of argon. To a two-necked round-bottomed flask (100 ml), fitted with a gas inlet tube and a reflux condenser equipped with a fermentation-tube on the top half-filled with acetic acid to control the gas rate, was added 0.0025 mole of halonitrobenzene in a medium containing 20 ml of acetic acid (Fischer reagent, min. 99.7 %) and 25 ml of 9 M hydrochloric acid. The reaction mixture was swept with argon for half an hour and then the flask was entirely immersed in a thermostated glycerol-water bath and the argon stream was continued another half-hour. The copper(I) chloride in a little glass bulb was thrown into the reaction mixture through the reflux condenser and the substitution reaction started immediately. A slow current of argon was passed over the solution during the experiment. At different times aliquots of the thermostated reacting solution were withdrawn through the reflux condenser and added to ice. The pH-value was adjusted to about 8 and extraction with ether was performed. The mixtures of compounds were analyzed on a Perkin-Elmer Model 116 E Fractometer equipped with a Model D 2 printing integrator. A 4 mm i.d., 2 m O-column (silicon grease on Chromosorb) was used, temp. 185°C, carrier gas He. Calibration curves were made from pure compounds which were subjected to the same procedure with ether extraction as described above. The composition of the exchange mixture was also verified by NMR and IR spectra. The calibration curves obtained were all straight lines with unit slope as illustrated in Fig. 5.

The stoichiometric chloride ion concentration in the medium was determined by Mohr titration according to the standard procedure.[27]
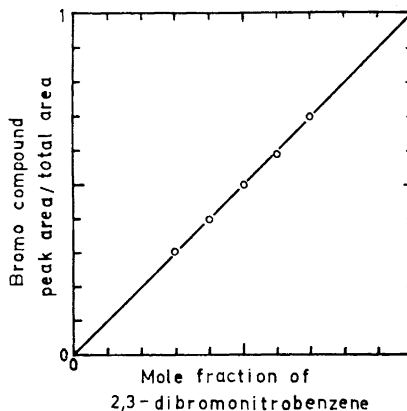
Fig. 5. Calibration curve for Br/Cl exchange in 2,3-dibromonitrobenzene.

REFERENCES

1. Lamm, B. and Liedholm, B. *Acta Chem. Scand.* **21** (1967) 2679.
2. (a) Kendall, F. H. and Miller, J. *J. Chem. Soc.* **B 2 1967** 119;
   (b) Miller, J. and Parker, A. J. *J. Am. Chem. Soc.* **83** (1961) 117.
3. Bunnett, J. F. and Zahler, R. F. *Chem. Revs.* **49** (1951) 273.
4. Bacon, R. G. R. and Hill, H. A. O. *J. Chem. Soc.* **1964** 1097.
5. Hardy, W. B. and Fortenbaugh, R. B., U.S. 2,769,815 (1956); *Cf. Idem. J. Am. Chem. Soc.* **80** (1958) 1716.
6. Nilsson, M. *Acta Chem. Scand.* **12** (1958) 537.
7. Noyes, A. A. and Ming Chow *J. Am. Chem. Soc.* **40** (1918) 739.
8. Vestin, R., Somersalo, A. and Mueller, B. *Acta Chem. Scand.* **7** (1953) 745.
9. Sillén, L. G. and Martell, A. E. *Stability constants of metal-ion complexes*, The Chemical Society, Special Publication No. 17, London 1964.
10. Taft, R. W. In Newman, (Ed.), *Steric Effects in Organic Chemistry*, Wiley, New York 1956, p. 593.
11. Allen, P. W. and Sutton, L. E. *Acta Cryst.* **3** (1950) 46.
12. Bondi, A. *Physical Properties of Molecular Crystals, Liquids and Glasses*, Wiley, New York 1968.
13. Greizerstein, W. and Brieux, J. A. *J. Am. Chem. Soc.* **84** (1962) 1032.
14. Hawthorne, M. F. *J. Am. Chem. Soc.* **76** (1954) 6358.
15. Leffler, J. E. and Grunwald, E. *Rates and Equilibria of Organic Reactions*, Wiley, New York and London 1963, p. 50.
16. Wolf, F. J. and Pfister, K., 3rd, Wilson, R. M., Jr. and Robinson, C. A. *J. Am. Chem. Soc.* **76** (1954) 3551.
17. Franzen, H. and Engel, E. *J. prakt. Chem.* [2] **102** (1921) 178.
18. *Handbook of Chemistry and Physics*, 47th Ed., The Chemical Rubber Co. (1966—1967), p. C—117.
19. Holleman, A. F. *Rec. Trav. Chim.* **34** (1915) 208.
20. Booy, J. and Dienske, J. W. *Rec. Trav. Chim.* **45** (1926) 449.
21. Körner, G. and Contardi, A. *Atti Accad. Lincei* [5] **22 I** (1913) 824.

22. *Handbook of Chemistry and Physics*, 47th Ed., The Chemical Rubber Co, (1966 – 1967), p. C – 77.
23. Gibson, C. S. and Johnson, J. D. A. *J. Chem. Soc.* **1928** 3092.
24. Holleman, A. F. *Rec. Trav. Chim.* **27** (1908) 151.
25. Körner, G. and Contardi, A. *Atti Accad. Lincei* [5] **15 I** (1906) 528.
26. Keller, R. N. and Wycoff, H. D. *Inorg. Syn.*, Vol. II, McGraw, New York and London 1946, p. 1.
27. Kolthoff, I. M. and Sandell, E. B. *Textbook of Quantitative Inorganic Analysis*, 1st revised Ed., Macmillan, New York 1943, p. 570.