

Studies in Nucleophilic Aromatic Substitution Reactions

IV.* Replacement of the Nitro Group in 2,6-Dichloro-4-nitro- and 2,4-Dichloro-6-nitrobenzenediazonium Ions by Chloride Ion

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The nucleophilic replacement of the nitro group by chlorine has been studied kinetically in 2,6-dichloro-4-nitro- and 2,4-dichloro-6-nitrobenzenediazonium ions in 5 M aqueous hydrochloric acid in the temperature range 15–25°C, and the activation parameters have been calculated. The results are in agreement with a two-step mechanism in which the first step is rate-determining. The rate constants for the 2,4-dichloro-6-nitro isomer is higher than that for the 2,6-dichloro-4-nitro isomer, which is ascribed to steric factors.

In Part II of this series,¹ the exchange rates of bromine in 4-bromo-2,6-dichlorobenzenediazonium ion and 2-bromo-4,6-dichlorobenzenediazonium ion for chloride ion in hydrochloric acid were determined. The exchange rates of radioactive chlorine for chloride ion in 2,4,6-trichloro-4-³⁶Cl-benzenediazonium ion and 2,4,6-trichloro-2-³⁶Cl-benzenediazonium ion were also determined. The activation parameters were calculated for the *para* Br/Cl, *para* Cl/Cl, and *ortho* Br/Cl exchange reactions. The activation enthalpies and entropies were found to be similar for *para* Br/Cl and *para* Cl/Cl exchange, the entropy of the Cl/Cl exchange having been corrected for the symmetry of the reaction. The situation is thus similar to that found by Bunnett *et al.*² in their work on the "absence of element effect".

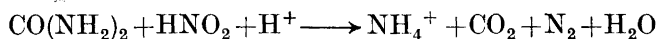
It was thought to be of interest to expand the present study to other leaving groups in order to see if the activation parameters would remain constant. Clearly, one is more restricted in the present case than were Bunnett *et al.*, who worked with different 2,4-dinitro-substituted benzene derivatives. Iodine, for example, proved useless for quantitative work,** since when iodide ion is liberated in a diazonium solution, it immediately reacts with the diazo-

* Part III: Lamm, B. and Liedholm, B. *Acta Chem. Scand.* 21 (1967) 2679.

** See, however, Paper V of this series.⁴

nium ions. In the present paper, a nitro group has been used as the leaving group. The reaction is not new; it was discovered by Sihlbom³ in his work on the "self-diazotization" of dinitroanilines.

Both exchange from the *ortho* position (2,4-dichloro-6-nitrobenzenediazonium ion as the reactant) and from the *para* position (2,6-dichloro-4-nitrobenzenediazonium ion) were studied. The entering group was the chloride ion, and the kinetic experiments were carried out exactly as in Part II of this series¹ in 5 M hydrochloric acid. At suitable intervals, aliquots of a reacting solution were withdrawn and quenched with hypophosphorous acid, which causes replacement of the diazonium group by hydrogen. Trouble was initially experienced since the liberated nitrous acid (from the nitro group) accelerated the decomposition of the diazonium ions. It proved necessary, therefore, to add urea to the solutions. Urea consumes nitrous acid in the well-known Knop reaction:₄



The addition of urea was found to have no influence on the exchange rates under study, as was verified in a check experiment with twice the amount of urea present in the solution.

EXPERIMENTAL

a. Preparation of compounds

All melting points were recorded on a Kofler Heizbank. The purity of the compounds was further ascertained by NMR and GLC analyses.

2,4-Dichloro-6-nitroaniline was prepared from 2,4-dichloroaniline (Fluka, practical grade, purified by steam distillation and then recrystallized from ethanol-water) in accordance with a method by Hodgson and Kershaw,⁵ *via* 2,4-dichloro-6-nitroacetanilide. Purification of the compound was effected by recrystallization from ethanol including treatment with activated charcoal. The over-all yield was 39 %. M.p. 102°C, lit.⁵ 102°C.

2,6-Dichloro-4-nitroaniline. A commercial product (Fluka, practical grade, m.p. 190–193°C) was purified by recrystallization twice from acetic acid and once from ethanol including treatment with activated charcoal. M.p. 195°C, lit.⁶ 195°C.

2,4-Dichloro-6-nitrobenzenediazonium tetrafluoborate. A solution of nitrosylsulphuric acid (6.5 g, 0.05 mole) in 25 ml of concentrated sulphuric acid was refrigerated to about –5°C. 2,4-Dichloro-6-nitroaniline (10.3 g, 0.05 mole) was carefully added to this solution with stirring. The diazotization was completed by keeping the solution at 0°C for 2 h and at 10°C for 1 h. It was then poured onto 200 g of crushed ice, and a small amount of a yellow precipitate was filtered off. The yellow filtrate was refrigerated once more, and a concentrated aqueous solution of 30 g (0.27 mole) of sodium tetrafluoborate was added with stirring. A precipitate formed immediately, and after one hour in an ice-bath the crystals were filtered off and washed with aqueous sodium tetrafluoborate solution, cold methanol and finally ether. The yield of pale green crystals, which decomposed at 160°C, was 12.3 g (80 %, 0.04 mole). This compound has not been found in the literature.

2,6-Dichloro-4-nitrobenzenediazonium tetrafluoborate was obtained from 2,6-dichloro-4-nitroaniline in the same way as the preceding isomer from its precursor. Yield 63 %. Decomposition temperature 181°C, lit.⁷ 181°C.

It was not possible to recrystallize these diazonium tetrafluoborates by dissolving them in ethanol at room temperature and reprecipitating with ether, as was possible with the 2,4,6-trihalobenzenediazonium tetrafluoborates in Part II.¹ The ethanol solution became yellow and nothing reprecipitated with ether. It was found that a replacement

of the diazonium group by hydrogen had taken place.⁸ In both cases this led to the formation of 1,3-dichloro-5-nitrobenzene.

1,3-Dichloro-5-nitrobenzene. 2,4-Dichloro-6-nitrobenzenediazonium tetrafluoroborate was reduced with 50 % hypophosphorous acid in accordance with a method developed for 1,3,5-trihalobenzenes in Part II.¹ Yield 64 %. M.p. (after recrystallization from ethanol) 64°C, lit.⁹ 65°C.

2,4,6-Trichlorobenzenediazonium tetrafluoroborate and *1,3,5-trichlorobenzene* were available from earlier work.¹

b. Kinetic procedure

The diazonium tetrafluoroborate under study (3.06 g, 0.01 mole) was dissolved in a solution of 0.6 g (0.01 mole) of urea in 100 ml of 5 M hydrochloric acid, which was prethermostated to the desired temperature. At the moment of dissolution, zero time was recorded. Aliquots of 10 ml were withdrawn at suitable intervals, filtered if necessary and rapidly cooled to -20°C . They were then allowed to react with a tenfold excess of 50 % hypophosphorous acid at 0°C , with a trace of cuprous oxide present. After the reaction was complete (30 min), the pH value was adjusted with sodium carbonate to about 8, and the mixture was extracted with carbon tetrachloride (3×25 ml). After the solution had been dried with calcium chloride, the carbon tetrachloride was distilled off until only a few ml remained. The solution was then analyzed as described below.

The temperature in the thermostat varied $\pm 0.05^{\circ}\text{C}$ around the preset values, which were controlled with a certified thermometer.

c. Analytic procedure

The mixtures of 1,3-dichloro-5-nitrobenzene and 1,3,5-trichlorobenzene were analyzed as described previously¹ on a Perkin-Elmer Model 116E fractometer equipped with a Model D2 digital integrator. A 4 mm i.d., 2 m Perkin-Elmer "O"-column (silicone grease on Chromosorb) was used, temperature 195°C , flow rate 80 ml/min, carrier gas helium.

To insure that the analyzed ratio of 1,3-dichloro-5-nitrobenzene and 1,3,5-trichlorobenzene was the real ratio between the corresponding diazonium ion concentrations in the kinetic solution at the time of withdrawal, calibrations of the analytical procedure were made in the following manner.

The whole sequence of quenching, isolation of the compounds, and GLC analysis was carried out with weighed mixtures of the two diazonium tetrafluoroborates. It was found that the peak areas in the gas chromatograms had the same ratio as the known molar amounts of the compounds within the error limits. This is valid for both the *ortho*-nitro and *para*-nitro exchange reactions. Hence the analyses give the correct ratios of the compounds in the kinetic solution.

In a separate calibration, known mixtures of 1,3-dichloro-5-nitrobenzene and 1,3,5-trichlorobenzene were analyzed on the gas chromatograph. It was found that the sensitivity of the thermal conductivity detector was the same for both compounds, since the peak areas corresponded to the molar amounts.

CALCULATIONS AND RESULTS

In the kinetics runs, a large excess (50-fold) of hydrochloric acid was present and the reaction was studied far from equilibrium, so that the reversibility could be disregarded. Under these conditions the following first-order rate law is obeyed:

$$a/a_0 = e^{-kt} \quad (1)$$

In this case a/a_0 will be equal to the mole fraction of the nitro substituted diazonium ion in the mixture of both diazonium ions. The different values of a/a_0 were obtained from the analyses described above. When $\ln(a/a_0)$ vs. t was plotted, straight lines were obtained with slopes $-k$.

The k value evaluated in this fashion is a pseudomonomolecular rate constant and consequently a function of the medium. Formally, k may be divided by the stoichiometric chloride ion concentration to obtain the bimolecular rate constant k_2 :

$$k_2 = k/[\text{Cl}^-] \quad (2)$$

The stoichiometric chloride ion concentration in the medium was determined by titration with standard sodium hydroxide solution.

The data from the kinetic runs were treated by the method of least squares. All calculations were carried out on an Olivetti Programma 101 electronic desk-top computer, with a program recording the slope of the line, the standard error in the slope, the intercept and the standard error in the intercept. The values of k_2 for each run obtained in this way are listed in Table 1, together with standard errors, the mean value of k_2 for each temperature and, for each run, the final extent of reaction, defined as $1 - a/a_0$.

Table 1. Rate constants for the exchange reactions of the nitro group for chlorine in 2,4-dichloro-6-nitro- and 2,6-dichloro-4-nitrobenzenediazonium ions.

Substituents	Temp. ^a	Cl ⁻ ^b	Extent of reaction ^c	$k_2 \times 10^6$ ^d	S.E. ^e	k_2 average $\times 10^6$ ^f
2,4-Dichloro-6-nitro-	14.98	4.95	0.48	11.97	0.23	12.0
			0.49	11.95	0.18	
	20.04	4.95	0.58	24.22	0.27	24.0
			0.59	23.86	0.31	
	25.05	4.95	0.65	46.87	0.59	46.0
			0.51	45.16	0.63	
2,6-Dichloro-4-nitro-	14.98	4.95	0.35	0.4705	0.0056	0.475
			0.35	0.4802	0.0076	
	20.04	4.95	0.70	0.9323	0.0027	0.932
			0.69	0.9323	0.0140	
	25.05	4.95	0.60	1.808	0.034	1.79
			0.61	1.774	0.012	

^a Degrees centigrade, accuracy $\pm 0.05^\circ\text{C}$. ^b Stoichiometric value, mole l⁻¹, accuracy ± 0.02 . ^c Defined as $1 - (a/a_0)$. ^d In l mole⁻¹sec⁻¹. Calculated by the least-squares method. ^e Standard error in k_2 , from the least-squares calculation. (See the text.) ^f Mean value. The last figure is uncertain.

The activation enthalpy (ΔH^\ddagger) and entropy (ΔS^\ddagger) were calculated from the expression

$$\ln(k_2/T) = -\Delta H^\ddagger/RT + \Delta S^\ddagger/R + \ln(k/h) \text{ Ref. 10} \quad (3)$$

The method of least squares was used, and all calculations were made with the computer.* This procedure gives the average ΔH^\ddagger and ΔS^\ddagger values in the temperature range. The results are presented in Table 2.

* The program was written and kindly lent by fil.lic. P. Berntsson.

Table 2. Activation enthalpies and entropies and relative rates of the exchange reactions of various benzenediazonium ions with chloride ion.

Substituents	ΔH^\ddagger ^a	ΔS^\ddagger ^b	k_{relative} ^c
2,6-Dichloro-4-nitro-	21.9 ± 0.5^d	-11.4 ± 1.8^d	3.30
2,4-Dichloro-6-nitro-	22.3 ± 0.8^d	-3.7 ± 2.7^d	84.50
4-Bromo-2,6-dichloro- ^e	23.0 ± 1.0	-9.9 ± 3.4	1.00
2-Bromo-4,6-dichloro- ^e	24.1 ± 1.2	-10.0 ± 4.0	0.16
2,4,6-Trichloro-4- ³⁶ Cl- ^e	23.4 ± 2.0	-10.0 ± 6.8^f	0.51 ^f
2,4,6-Trichloro-2- ³⁶ Cl- ^e	—	—	0.16 ^f

^a In kcal mole⁻¹. ^b In cal mole⁻¹ degree⁻¹. ^c Relative values at 25°C. ^d The errors are 3 S.E., from the least-squares calculations. ^e Results from Part II.¹ ^f Corrected for the symmetry of the reaction.

DISCUSSION

Nitro-chlorine versus *chlorine-chlorine* and *bromine-chlorine* exchange. In Parts I¹¹ and II¹ it was pointed out that a two-step mechanism, in which the addition of the chloride ion is rate determining, is very likely for the two latter exchange reactions. Since a carbon-nitrogen bond is more easily broken than a carbon-chlorine bond, it is probable that in the NO₂/Cl exchange also the first step should be rate determining (see the introduction). This means that the activation parameters observed are those of the first step.

A comparison of the specific rates for the three reactions (see Table 2) shows that the *para* NO₂/Cl exchange is 3.3 times as fast as the *para* Br/Cl and 6.5 times as fast as the *para* Cl/Cl exchange, the latter having been corrected for symmetry. This is a reasonably good agreement. In fact, it was found that activation entropies, ΔS^\ddagger , as well as activation enthalpies, ΔH^\ddagger , are similar for the *para* NO₂/Cl, Br/Cl, and Cl/Cl exchange reactions.

The present study thus provides further support for the two-step mechanism of nucleophilic substitution in aromatic compounds activated by a diazonium group, since the "absence of element effect" criterion seems to be fulfilled.

The ortho/para ratio. For the NO₂/Cl-exchange, the rate constant for the *ortho* isomer is much higher than that for the *para* isomer. This is the reverse of the results obtained for the Br/Cl and Cl/Cl exchange reactions in Part II¹ where the *para* isomer reacted faster. Several factors can influence the *ortho/para* ratio in nucleophilic aromatic substitution.

A possible explanation of the *ortho/para* ratio is that in the *ortho* case, the solvated diazonium group sterically interacts with the nitro group. This destabilizes the molecule with respect to the *para* isomer. In the transition state of the rate-determining first step of the reaction, the bond between the carbon atom and the nitro group has been bent out of the plane of the benzene ring which relieves the strain. This effect should thus favour a higher reaction rate in the *ortho* case.

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