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Studies in Nucleophilic Aromatic Substitution Reactions

V.* The Reactions of 2,4-Dichloro-6-iodo- and 2,6-Dichloro-4-iodobenzenediazonium Ions in Aqueous Hydrochloric Acid

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It has been demonstrated that an exchange of iodine for chlorine occurs in 2,4-dichloro-6-iodo- and 2,6-dichloro-4-iodobenzenediazonium ions in 5 M aqueous hydrochloric acid. Only initial rate data could be determined since the iodide ion liberated in the exchange reaction rapidly consumes diazonium ions.

In a previous paper,[1] the specific rates of bromine-chlorine exchange between 4-bromo-2,6-dichloro- and 2-bromo-4,6-dichlorobenzenediazonium ion, respectively, and chloride ion have been determined in 5 M aqueous hydrochloric acid. In the same medium, the chlorine-chlorine exchange between 2,4,6-trichlorobenzenediazonium ion and chloride ion has also been studied, both in the *para* and *ortho* position, by labelling either position with ^{36}Cl. In a later paper,[2] the work was extended to include the nucleophilic exchange of the nitro group for chlorine.

In the search for other, suitable leaving groups in the nucleophilic exchange reaction, iodine was tried in the present work. *A priori*, a major complication in the kinetic behaviour was expected; iodide ion liberated during the exchange reaction would instantaneously react with any diazonium ions present in the system. Experimentally, this has been shown to occur. Therefore, no clear-cut kinetic experiments could be performed. The initial exchange rates could be roughly determined, however, and will be reported below.

Some of the compounds formed in the reactions appear to be new. Their identity has been verified by independent syntheses.

* Part IV: Andersson, B. and Lamm, B. *Acta Chem. Scand.* **23** (1969) 2983.

EXPERIMENTAL

I. Preparation of compounds

Melting points were determined on a Kofler Hot-Stage Microscope or a Kofler Heizbank. The melting points of known compounds are in agreement with those reported in the literature. The purity was further controlled with GLC and NMR.

2,6-Dichloro-4-iodoaniline and *2,4-dichloro-6-iodoaniline* were prepared from 2,6-dichloro- and 2,4-dichloroaniline, respectively, by iodination with iodine monochloride in glacial acetic acid, according to a method used by Kutepov *et al.*[3]

2,6-Dichloro-4-iodo- and *2,4-dichloro-6-iodobenzenediazonium tetrafluoborate* were obtained from the corresponding anilines by a method developed for other trihalobenzenediazonium tetrafluoborates.[1] The crystals were pale green in both cases. The yield of the first isomer was 93 %. The salt was found to decompose at 242°C. The other isomer was formed in a 91 % yield and the decomposition temperature was 224°C.

These compounds have not been found in the literature.

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

1,3-Dichloro-5-iodobenzene. 2,6-Dichloro-4-iodobenzenediazonium tetrafluoborate was reduced with hypophosphorous acid in accordance with a method for the preparation of other trihalobenzenes.[1]

1,2,3,5-Tetrachlorobenzene. A Sandmeyer reaction with cuprous chloride in hydrochloric acid was carried out on 2,4,6-trichlorobenzenediazonium tetrafluoborate in hydrochloric acid.[4]

1,3-Dichloro-4,5-diiodobenzene. To a solution of 3.85 g of 2,4-dichloro-6-iodobenzenediazonium tetrafluoborate (0.01 mole) in 50 ml of cold 5 M hydrochloric acid, 1.7 g of potassium iodide (0.01 mole) in 20 ml of water was added. The mixture was then warmed on a steam bath, and when the evolution of nitrogen had ceased, it was neutralized with sodium carbonate and steam distilled. The crude yield was 2.5 g (63 %). The melting point after recrystallization from ethanol, including treatment with activated charcoal, was 84.0—84.5°C.

1,3-Dichloro-2,5-diiodobenzene was prepared from 2,6-dichloro-4-iodobenzenediazonium tetrafluoborate by the same procedure as the preceding compound. Yield 2.9 g (73 %). M.p. 82.0°C.

The two latter compounds have not been found in the literature. Their identity has been ascertained by NMR and mass spectrometry.

1,3,5-Trichloro-2-iodobenzene was obtained from 2,4,6-trichlorobenzenediazonium tetrafluoborate by the method described above.

II. Decomposition and analyses

2,6-Dichloro-4-iodobenzenediazonium tetrafluoborate (3.86 g, 0.01 mole) was dissolved in 100 ml of 5 M hydrochloric acid. The solution was divided into four test tubes with stoppers and placed in a thermostat at 30.0 ± 0.1°C. There they were kept for 16 days until one of the samples showed no colour reaction with an acetate-buffered solution of 2-naphthol, indicating that all diazonium ions had disappeared.

The three remaining samples were then neutralized with sodium carbonate and extracted with ether (3×25 ml). The ether solution was dried over calcium chloride and the ether was allowed to evaporate in the air to dryness. The residue was dissolved in carbon tetrachloride and analysed with GLC and NMR.

The complete decomposition of 2,4-dichloro-6-iodobenzenediazonium tetrafluoborate took 24 days under the same conditions as above.

Analyses were carried out on a Perkin-Elmer Model 116E gas chromatograph equipped with a Model D2 digital integrator. A 4 mm i.d., 2 m Perkin-Elmer "O"-column was used (silicon grease on Chromosorb), temp. 195°C, flow rate 80 ml/min, carrier gas helium. The peaks in the chromatograms were identified with the aid of pure reference compounds. A quantitative calibration of the GLC detector sensitivity for the various compounds was not performed. On the basis of previous work,[1,2,5] it may be assumed, however, that the peak areas, determined with the integrator, are proportional to the

molar amounts in the sample since the compounds are closely related. The GLC detector used was of the thermal conductivity type, employing a thermistor bridge. With a FID detector, calibrations would have been necessary.

III. Rate determination

2,6-Dichloro-4-iodobenzenediazonium tetrafluoborate (1.93 g, 0.005 mole) was dissolved in 50 ml of pre-thermostated 5 M hydrochloric acid. Zero time was recorded at the time of dissolution. This solution was divided into four pre-thermostated test tubes with stoppers, which were placed in a thermostat at 25.0±0.1°C. At different times the reaction in each one of the test tubes was quenched by rapid cooling and then the contents were quantitatively poured onto chilled 50 % hypophosphorous acid, thus causing replacement of the diazonium group by hydrogen. This procedure was developed and used in Part II of this series.[1] When the reaction was complete (30 min) the pH value of the solution was adjusted to about 8 with sodium carbonate and the solution was extracted with carbon tetrachloride. The carbon tetrachloride solution was dried with calcium chloride, filtered and evaporated to a volume of about 2 ml. This concentrated solution was analysed by gas chromatography as described above. The 2,4-dichloro-6-iodo isomer was treated in exactly the same way. The analytical results are collected in Table 1.

Table 1. Analytical data from the kinetic exchange experiments with 2,6-dichloro-4-iodo- and 2,4-dichloro-6-iodobenzenediazonium ions in 5 M hydrochloric acid at 25.0°C.

Substituents	Time [a]	Mole % [b]				
		E	F	G	H	(G+H)
2,6-Dichloro-4-iodo-	2	2.1	1.9	94.3	1.7	96.0
	4	3.8	3.4	90.3	2.5	92.8
	4	4.2	3.4	90.0	2.3	92.3
	6	5.4	3.9	87.9	2.7	90.6
2,4-Dichloro-6-iodo-	3	1.1	2.0	96.9	[c]	
	3	1.2	2.2	96.6	[c]	
	5	1.9	2.3	95.8	[c]	
	7	3.4	2.4	94.2	[c]	

[a] In hours. [b] Percent peak area of the sum of peak areas in the chromatograms. See the text. [c] Compound I (Fig. 2) was expected to be formed, but none of it was detected.

CALCULATIONS AND RESULTS

The decompositions were found to follow the reaction schemes in Figs. 1 and 2.

When the three samples originating from the complete decomposition of 2,6-dichloro-4-iodobenzenediazonium ion, compound A in Fig. 1, were analyzed, the average distribution of peak areas of the resulting compounds was the following: D: 3 %, E: 63 %, H: 34 %, F: <1 %, G: <1 %.

2,4-Dichloro-6-iodobenzenediazonium ion, compound B in Fig. 2, similarly gave: D: 2 %, E: 83 %, I: 15 %, F: <1 %, G: <1 %.

Compounds F and G, obtained by reductive displacement of the diazonium group, were formed in trace amounts only. The replacement of the diazonium group by hydrogen has been observed in a related system.[5]

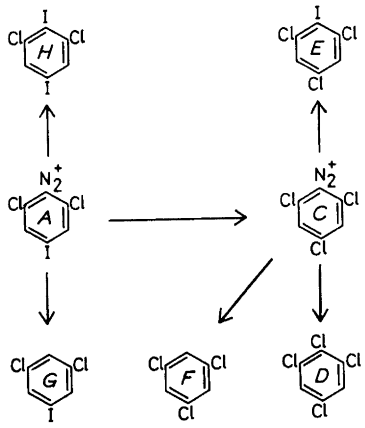

Fig. 1. Reaction chart of 2,6-dichloro-4-iodobenzenediazonium ion in 5 M hydrochloric acid.

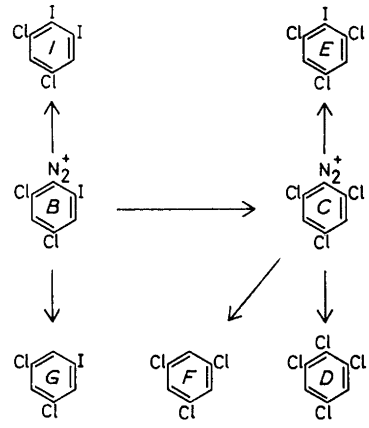

Fig. 2. Reaction chart of 2,4-dichloro-6-iodobenzenediazonium ion in 5 M hydrochloric acid.

In Table 1 it can be seen that in the case of 2,6-dichloro-4-iodobenzenediazonium ion, the kinetic experiments gave compounds E, F, G, and H (Fig. 1). Of these, E and F were formed from the diazonium ion after the exchange reaction had taken place, and G and H before the exchange reaction. On the basis of earlier results,[1,2] the reaction ought to be a pseudo-monomolecular reaction obeying the first order rate law $a/a_0 = e^{-kt}$. At the beginning of the reaction a rather good approximation of the disappearance rate and thus of the exchange rate of compound A is obtained if ln mole% (G+H) is plotted *vs.* time. That this treatment is justified is apparent from Fig. 3, which shows the actual plot. The final extent of the reaction was 10 %.

A completely analogous treatment can be applied to the *ortho* iodo isomer. In this case, however, the concentration of I (Fig. 2) in the samples obtained after quenching was negligible, so that a plot of ln mole% G *vs.* time gave

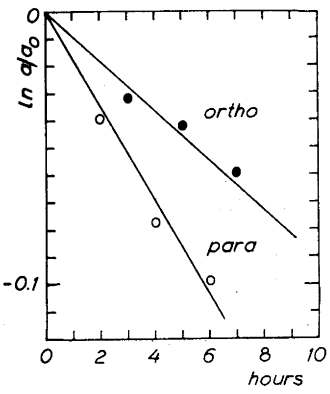

Fig. 3. Kinetic plots for the iodine-chlorine exchange reactions in 2,6-dichloro-4-iodo- and 2,4-dichloro-6-iodobenzenediazonium ions in 5 M hydrochloric acid, *cf.* the text.

a straight line (Fig. 3). The GLC analysis method used, however, is less sensitive to very small amounts of compound I than to the others in the mixture since it has a much longer retention time. The final extent of the reaction was 6 % in this case.

DISCUSSION

The initial exchange rate experiments show that iodine *para* to the diazonium group is exchanged for chlorine faster than is iodine in the *ortho* position. This agrees with our earlier results for bromine-chlorine and chlorine-chlorine exchange.[1] Compared with *para* bromine, *para* iodine is exchanged about 1.6 times as fast at 25°C, and in the *ortho* case, iodine is about 4.6 times as fast as bromine. The *para* I/Cl exchange rate is thus rather similar to that of *para* Br/Cl. The *ortho* I/Cl exchange rate deviates somewhat more from the *ortho* Br/Cl rate, but steric factors influence the rate in the *ortho* case.[1,2]

In spite of these small deviations, the data lend additional support to the two-step mechanism suggested earlier[1,2] for the exchange reactions in diazonium compounds.

In Table 1 it can be seen that compounds E and H (Fig. 1) were formed in comparable amounts until 5 % of the exchange reaction had occurred. This is a very surprising result considering that at the beginning of the reaction compound A (Fig. 1) is present in very large excess. Iodide ion, in this case liberated during the reaction, cannot be expected to be particularly selective in its reactions with diazonium ions differing by the kind of halogen atom present as a substituent. A reasonable explanation for the formation of compound E at a much higher rate than H is that E is formed before the iodide ion has completely left the diazonium ion. The two ions possibly form some kind of ion pair. This makes an attack of the iodide ion on its parent molecule more favourable than an attack on some other molecule. Those iodide ions which have left their parent molecule before reacting may choose between A and C in the usual way.

In the *ortho* case very little of compound I is formed (Table 1 and Fig. 2), E being the exclusive iodination product. If the compounds B and C were present in comparable amounts steric hindrance for attack *ortho* to the iodine in B could explain that formation of E was favoured at the expense of I. This argument can hardly explain the very great difference in this case, however, since at the beginning of the reaction (which is studied quantitatively) B, which is forming I, is present in a large excess over C.

An additional and more satisfying explanation, which seems probable even in the *ortho* case, is the one made for the *para* case above. An alternative explanation is that the intermediate in the nucleophilic substitution reaction decomposes intramolecularly to the products. When the leaving group, iodide ion in this reaction, is in an *ortho* position to the diazonium group, this intramolecular type of reaction ought to be particularly favourable. Since this step occurs *after* the rate-determining addition of chloride ion to the diazonium ion, it is in principle hidden kinetically.

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