Mechanism of Benzidine and Semidine Rearrangements. Part XIX.† Kinetics and Products of the Acid Conversion of 2,2′-Difluorohydrazobenzene

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The acid conversion of 2,2′-difluorohydrazobenzene in ' 60% ' aqueous dioxan at 25° is of first order in the hydrazo-compound and second order in hydrogen ions. The reaction is slower by a factor of 640 than the acid conversion in like conditions of hydrazobenzene, which has the same kinetic form. The sole rearrangement product from 2,2′-difluorohydrazobenzene is 3,3′-difluorobenzidine, 86 mol.% of which is formed in the conditions. The products of disproportionation accounted for the balance of the material, and, as analytically determined, they comprised 7 mol.% 2,2′-difluoroazobenzene and 2 × 6 mol. of 2-fluoroaniline. It is suggested that the thermodynamic effects of halogen substituents on aniline bases may be taken as a guide to the interpretation of their kinetic effects in benzidine rearrangements.

Introductory Remarks on Halogen Substituents.—This phase of our work on benzidine rearrangements, which starts with the work of Part XVI [1] and is continued in the present papers, is concerned with the effects of what have been called (originally in connexion with electrophilic aromatic substitution) ' Type **3** ' *o*- and *p*-aromatic substituents, that is, those substituents which inductively attract but conjugatively release electrons in an electron-demanding reaction (symbolically $-I + K$ substituents). Our work with the substituents NHAc and OMe is here continued with F. And with F we start another series which will run through Cl and Br to I.

These two series seem to establish the operation of the two factors by which, as suggested in 1962,[2] the polar-transition-state theory would interpret Carlin and Odioso's observation of anomalous kinetics in the rearrangement of *o*-hydrazotoluene.

It will assist the picking out of the trends shown in the papers on halogen substituents (in which a number of specialised matters have to be discussed) if we here outline the way in which halogens can exert that combination of polar and steric effects which the polar-transition-state theory invokes as its determinants of catalytic mechanism in benzidine rearrangements.

We set out in Table 1 the base strengths of aniline and its *o*- and *p*-halogen substitution products, as determined all in the same conditions.[3] A brief discussion of them exists,[4] which is the basis of the remarks now to be made.

TABLE 1

Basicity of aniline and *o*- and *p*-halogeno-anilines in 30% aqueous ethanol at 25°: values of $10^{12}K_b$

Aniline 126

2-Fluoroaniline	2·9	4-Fluoroaniline	120
2-Chloroaniline	1·35	4-Chloroaniline	28·5
2-Bromoaniline	1·00	4-Bromoaniline	7·9
2-Iodoaniline	0·36	4-Iodoaniline	7·6

In the 4-derivatives, the halogens exert, first, an electronegative inductive effect $(-I)$, which should fall from fluorine to iodine, and should weaken the halogeno-anilines in that descending order. Secondly, they exert an electropositive conjugative effect $(+K)$, which again falls from fluorine to iodine, and should, if acting alone, strengthen the aniline bases in that descending order. In 4-fluoroaniline the two factors nearly compensate; but the conjugative factor, which requires atomic *p* orbitals of similar sizes, falls off more steeply in the first step of the halogen progression than in the later steps, with the result that the fall in base strength towards 4-iodoaniline is nearly asymptotic.

The 2-halogeno-derivatives are generally more strongly weakened as bases. Much of this will be due to a field effect, associated with the inductive effect, and like it diminishing from fluorine to iodine. But this alone does not take into account the relatively strong base-weakening effect of the 2-iodine atom; nor does it take in Flurscheim's point that all 2-substituents in aniline bases, electropositive as well as electronegative, are base-weakening.[5] His interpretation of this as a steric effect has been restated as an impairment of the solvation shell stabilising the ammonium ionic centre in the conjugate acid of the base.[4] This factor must be generally important in reducing the base strength of 2-substituted anilines. It might not amount to much with fluorine as the substituent, but it should increase substantially with larger halogens as *o*-substituents.

According to the polar-transition-state theory, the main problem of activation in a benzidine rearrangement is to create the first electrostatic bond (whose electrostatic character can then pass into other bonds) out of the original NN'-covalency. In the acid-catalysed reactions, this is done after protonation, and often with the assistance of one or both of two constitutional effects that can make a difference to the degree of protonation needed to enable thermal energy to complete the activation. One such constitutional factor is that which enhances the supply of electrons from an aryl ring to one nitrogen atom, so aiding its release of electrons towards the other nitrogen atom in the initiating

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† Part XVIII, D. V. Banthorpe, A. Cooper, and C. K. Ingold, preceding paper.

[1] D. V. Banthorpe, C. K. Ingold, and J. Roy, *J. Chem. Soc.* (*B*), 1968, 64.

[2] C. K. Ingold, ' The Transition State,' *Chem. Soc. Special Publ.*, No. 16, 1962, p. 118.

[3] G. M. Bennett, G. L. Brooks, and S. Glasstone, *J. Chem. Soc.*, 1935, 1821.

[4] C. K. Ingold, ' Structure and Mechanism in Organic Chemistry,' Cornell University Press, Ithaca, N.Y., 1953, pp. 740—744.

[5] B. Flurscheim, *J. Chem. Soc.*, 1909, **95**, 718.

polarisation. The other factor is that of so reducing the basic strength at nitrogen that its protonation produces a local electron affinity, which is beyond the capacity of the solvation shell to satisfy, and therefore has to be satisfied by electrons shared with the other nitrogen atom, *i.e.* by extensive *NN'*-polarisation. Either or both of these factors may allow activation to proceed without a second added proton. If the main factor which does this is electron release from a substituted aryl group, then the change from a two-proton to a one-proton mechanism should be associated with a large increase in absolute rate. This has been illustrated in the two preceding papers on the acid conversions of the methoxy- and acetamido-substituted hydrazobenzenes. If the constitutional factor leading to the change of mechanism is base-weakening, *i.e.* a thermodynamic restriction to protonation, then the change of mechanism should be associated with a large decrease in absolute rate. This has not yet been illustrated, and to realise it is the main object of the investigation, which this paper initiates, of the effects of halogen substituents. If the two factors of electron release and base weakening should contribute comparably to the inducing of a change of mechanism, the associated changes in absolute rate, being a difference of comparable opposing effects, will be generally smaller. This is believed to be the case [2] in Carlin and Odioso's example, as reinvestigated in our Part VII,[6] in which the substituents were *o*-methyl groups.

Kinetics of the Acid Conversion of 2,2'*Difluorohydrazobenzene*.—This conversion proceeds very much more slowly than do those of the acetamido- and methoxy-substituted hydrazobenzenes dealt with in the two preceding papers: and, as we shall see, it goes with two-proton, not with one-proton, kinetics. The kinetics were studied in ' 60% ' aqueous dioxan at 25°. Hydrogen ion was supplied as perchloric acid over the concentration range 0·1—0·8N. It was necessary to eliminate variable ionic-strength effects, and hence, for all acidities in this range, the total concentration of univalent electrolyte was made up to 1·0M by additions of lithium perchlorate.

All runs accurately obeyed the first-order rate law. This establishes that the conversions are of order unity in the hydrazo-compound at all acidities within the range.

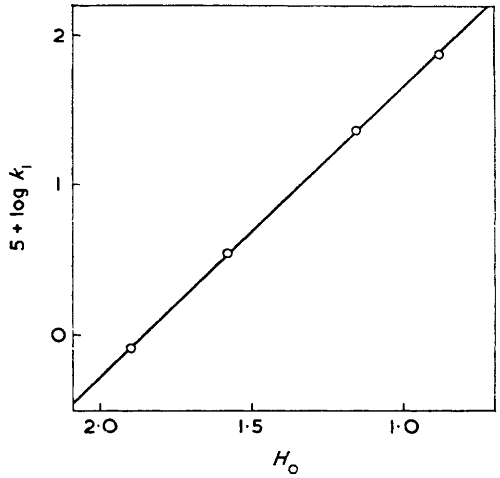
The acid range runs up to far beyond the limit to which the Hammett function H_0 parallels pH in the medium, and we therefore have to use h_0 rather than $[H^+]$ in order to check the dependence of the first-order rate constants on the acidity. The acidity scale from which the values of h_0 are taken must be appropriate to the acid, the solvent, and its salt content. An acidity scale for perchloric acid in ' 60% ' aqueous dioxan with the formal ionic strength made up to 1·0 by additions of lithium perchlorate was provided in Part VIII;[7] and was the scale here employed. Some first-order rate constants are correlated with the concentrations of perchloric acid, and with H_0 values on this scale, in Table 2.

TABLE 2

Dependence of the first-order rate constants (k_1 in sec.$^{-1}$) of the acid conversion of 2,2'-difluorohydrazobenzene on the concentration and acidity function of perchloric acid in ' 60% ' aqueous perchloric acid at the formal ionic strength 1·0 made up with lithium perchlorate and at 25° (Initial concentration of hydrazo-compound about 0·004M)

$[HClO_4]$	H_0	10^5k_1	10^3k_3
0·0945	1·90	0·835	52
0·184	1·57	3·21	44
0·474	1·15	23·0	46
0·775	0·89	69·2	44

The first-order rate constants bear no simple relation to the concentration of perchloric acid. However, the plot of the logarithms of the rate constants against the H_0 values is essentially linear, as shown in the Figure.



Plot of the logarithm of the first-order rate constant of acid conversion of 2,2'-difluorohydrazobenzene against Hammett's H_0, in ' 60% ' aqueous dioxan at 25° and with μ = 1·0. The line shown has slope 1·95

The slope of the line there drawn is 1·95. Having regard to the experimental errors, this slope is not significantly different from 2, and the conclusion is therefore drawn that the acid conversion of 2,2'-difluorohydrazobenzene is of second order in hydrogen ions. The mean third-order rate constant, defined for this two-proton reaction in terms of h_0 rather than $[H^+]$, is 47×10^{-3} sec.$^{-1}$ mole^{-2} l.^{2} (Table 2).

The kinetic form of this reaction is therefore the same as that of the acid conversion of hydrazobenzene; but the reaction of the fluorine derivative is much slower The data in Part VIII [7] for the rates of conversion of hydrazobenzene with perchloric acid in ' 60% ' aqueous dioxan, at an ionic strength of 1·0 made up with lithium

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[6] D. V. Banthorpe, C. K. Ingold, J. Roy, and S. M. Somerville, *J. Chem. Soc.*, 1962, 2436.

[7] D. V. Banthorpe, E. D. Hughes, C. K. Ingold, and J. Roy, *J. Chem. Soc.*, 1962, 3294.

perchlorate, but at 0°, lead to a third-order rate constant, calculated in the same way, of 1·58 sec.^{-1} mole^{-2} l.^{2}. We have not an activation energy for the reaction in this solvent, but, if we use Croce and Gettler's value of 19 kcal./mole for the reaction in '90%' aqueous ethanol,[8] the rate at 25° is calculated to be 19 times larger, so that the third-order constant would be 30 sec.^{-1} mole^{-2} l.^{2}. It thus appears that the introduction of the 2,2′-difluoro-substituents reduced the rate of the two-proton conversion by a factor of 640.

Products of the Acid Conversion of 2,2′-*Difluorohydrazobenzene.*—Only three products could be detected by paper or thin-layer chromatography. The principal product was a crystalline basic substance with the spectral and chromatographic properties of a benzidine: in view of its composition and origin, we take it to be 3,3′-difluorobenzidine. One of the other products was the only non-basic material formed, and thus was readily separated: it was identified by direct comparison as 2,2′-difluoroazobenzene. The third product was identified by its chromatographic and spectral properties, monitored by comparison with an authentic sample, as *o*-fluoroaniline.

Our analysis was subsequently repeated more quantitatively by Dr. A. Cooper whose figures we quote. The products comprised 86 mol.% of 3,3′-difluorobenzidine, 7 mol.% of 2,2′-difluoroazobenzene, and 2 × 6 mol.% of 2-fluoroaniline. The summary is that 86% of the 2,2′-difluorohydrazobenzene suffers rearrangement, and 13—14% becomes converted to products of disproportionation.

EXPERIMENTAL

Materials.—The starting point was *o*-fluoroaniline, which was first oxidised by manganese dioxide to 2,2′-difluoroazobenzene.[9] A solution of the fluoroaniline (5 g.) in benzene (250 ml.) was boiled under reflux with precipitated manganese dioxide (16 g., dried at 110°), in an apparatus arranged for the continuous draining-off of separated water. The azo-compound, obtained by concentration of the benzene solution, and crystallised from ethanol, had m.p. 102°. It was reduced to the hydrazo-derivative by the following adaptation of the zinc-dust method. The azo-compound (1 g.) was dissolved in a mixture of acetone (50 ml.) and methanol (50 ml.), and, after addition of ammonium chloride (2 g.) in saturated aqueous solution, was shaken with zinc dust (5 g.). After the colour of the azo-compound had been discharged, the mixture was poured into ice-water and filtered. The hydrazo-compound was extracted from the solid residue with benzene. It was crystallised from that solvent and then from ethanol to give colourless crystals, m.p. 66—67° (Found: C, 65·2; H, 4·6. Calc. for $C_{12}H_{10}N_2F_2$: C, 65·5; H, 4·9%). The reduction of 2-fluoronitrobenzene to 2,2′-difluoroazobenzene, m.p. 71°, and thence to 2,2′-difluorohydrazobenzene, m.p. 52·5°, has been described,[10] but it is not understood why these m.p.s (and the m.p. of the finally resulting 3,3′-difluorobenzidine) do not agree better with our m.p.s. The only other record from the literature is one of the azo-compound [9] having m.p. 98° in much better agreement with our value.

Bindschedler's Green was prepared and solvents were purified and degassed as indicated in the two preceding papers.

Kinetic Methods.—They were essentially as described in Part I.[11] In general, we have two methods of starting runs and securing timed samples, but in this case used the flask rather than the Y-tube method as allowed by the low rate of reaction. The temperature being 25°, we had no need to use jacketted pipettes for sampling. In general, we have two methods of quenching reaction, but in this case quenched with Bindschedler's Green, the excess of which was titrated with titanous chloride.[12] This was allowable, because no semidines are produced or any other products which reduce Bindschedler's Green.

Product Analysis.—The products were searched by paper and thin-layer chromatography, but only the three already mentioned products could be detected. Quantitative estimations were generally as described in Part I [11] and in the two preceding papers. The 3,3′-difluorobenzidine was separated gravimetrically. It has an R_F value of 0·12 on formamide–ethanol paper (Whatman No. 4), and 0·09 on a thin-layer plate (Merck G-alumina, activated at 110° for 10 min.), the development in both cases being with cyclohexane. These are chromatographic systems known for their efficiency in separating typical mixtures formed by benzidine rearrangements. The u.v. spectrum in ethanol had its main band at $\lambda_{\text{max.}}$ 278 mμ ($\varepsilon_{\text{max.}}$ 19,700). These properties agree with the identification. Crystallised from ethanol, it had m.p. 111° (lit.,[10] 105°) (Found: C, 65·3; H, 4·0; N, 12·3; F, 16·8. $C_{12}H_{10}N_2F_2$ requires C, 65·5; H, 4·5; N, 12·7; F, 17·3%).

2,2′-Difluoroazobenzene was separated by extraction as the only non-basic product, and was estimated spectrophotometrically, with calibration by means of an authentic sample. *o*-Fluoroaniline was identified chromatographically and spectrophotometrically, again using an authentic specimen for comparison. We are most grateful to Dr. A. Copper for running these analyses.

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[10] G. Olah, A. Pavlath, and I. Kuhn, *Acta Chim. Acad. Sci. Hung.*, 1955, **7**, 71.

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[12] M. J. S. Dewar, *J. Chem. Soc.*, 1946, 777.