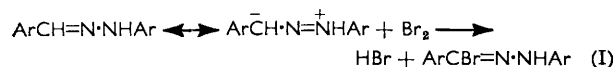


## The Kinetics of Bromination of Hydrazones

By A. F. Hegarty and F. L. Scott

Kinetic measurements on the rate of bromination of a series of arylidene arylhydrazines have been made in 70% aqueous acetic acid at 20°, by following the diffusion current of bromine (initially *ca.* 10<sup>-5</sup>M) at a rotating platinum electrode. Substituents in the benzylidene ring have a smaller effect ( $\rho = -0.62$ ) than those in the other ring ( $\rho = -2.2$ ). This has been rationalised in terms of an intermediate stabilised by considerable charge delocalisation.

HYDRAZONES, which may be considered the formal analogues of enamines, are attacked by electrophilic agents; bromination, for example, leads to the replacement of the methine hydrogen and the formation of the hydrazidic bromides (I), which, unlike the compounds



formed from aliphatic enamines,<sup>1</sup> are relatively stable to hydrolysis. Hydrazidic halides have recently attracted considerable attention in synthetic studies,<sup>2</sup> and particularly as sources of azocarbonium ions<sup>3</sup> and 1,3-dipolar ions.<sup>4</sup> But the bromination reactions by which they can be prepared, although first described<sup>5</sup> forty years ago, have not been previously studied kinetically. These are rapid reactions, and we have followed their rates in 70% aqueous acetic acid containing an excess of bromide ion, using low concentrations of reactants, by measuring the bromine concentration by an electro-metric method.<sup>6</sup>

### EXPERIMENTAL

**Materials.**—Acetic acid (AnalaR) was refluxed over chromium trioxide<sup>7</sup> and distilled; the main fraction was redistilled, and the portion with b. p. 117–118° was used to prepare the reaction solvents. Deionised water was twice distilled from alkaline potassium permanganate in a glass still to remove small amounts of impurity capable of reacting with bromine. All inorganic chemicals were AnalaR grade; potassium bromide was dried at 120° before use. *m*-Nitrophenol, crystallised twice from chloroform, had m. p. 97–98°. Substituted benzylidene-*p*-nitrophenylhydrazines, used as substrates, were prepared by refluxing equimolar quantities of *p*-nitrophenylhydrazine and the substituted benzaldehyde in glacial acetic acid for 15 min. The following hydrazones were prepared and crystallised to constant m. p. from aqueous ethanol mixtures (the prefix and substituent refer to the benzylidene ring of a substituted benzylidene-*p*-nitrophenylhydrazine): 4-nitro, m. p. 254–255° (lit.,<sup>8</sup> 249°); 4-bromo, 207° (207–208°); 4-chloro, 219° (239°); 4-fluoro, 220° (212°); hydro-gen, 194° (192°); 4-isopropyl, 192° (190°); 4-methyl,

203° (200°); 4-methoxy, 161° (161°); 4-dimethylamino, 185° (182°); 3-nitro, 252–253° (247°); 3-bromo, 226–227° (220°); 3-chloro, 216° (216°); 3-methyl, 160° (157°). Immediately before a kinetic run they were finally crystallised from 95% aqueous ethanol in a rigorously similar manner. This minimised the presence of oxidation products.<sup>9</sup> Their sharp melting points favour the presence of single (*syn*) isomers.<sup>10</sup> 4-Cyanobenzylidene-*p*-nitrophenylhydrazine was partly hydrolysed under the conditions used for the preparation of the other hydrazones. This hydrazone, m. p. 230°, was therefore prepared in, and crystallised from, absolute ethanol (Found: C, 62.7; H, 4.0; N, 20.8. C<sub>14</sub>H<sub>10</sub>N<sub>4</sub>O<sub>4</sub> requires C, 63.1; H, 3.8; N, 21.0%).

**Benzylidene-2-bromo-4-nitrophenylhydrazine.**<sup>3c</sup>—Benzylidene-*p*-nitrophenylhydrazine (5 g.), suspended in acetic acid (20 ml.), was stirred while bromine (4.2 ml.) was added during 1 hr. Crystallisation of the solid that separated from acetic acid gave *N*-(2-bromo-4-nitrophenyl)benzhydrazidic bromide, m. p. 172° (lit.,<sup>2a</sup> 171–172°). The hydrazidic bromide was refluxed for 4 hr. in 50% dioxan-water (200 ml.), to give, on cooling, *N*-(2-bromo-4-nitrophenyl)benzhydrazide, m. p. 201–202° (Found: C, 46.2; H, 3.2; N, 12.7. C<sub>13</sub>H<sub>10</sub>BrN<sub>3</sub>O<sub>3</sub> requires C, 46.4; H, 2.9; N, 12.5%). Hydrolysis for 4 hr. at reflux of the benzhydrazide in 50% concentrated hydrochloric acid–ethanol (40 ml.) gave, on cooling, 2-bromo-4-nitrophenylhydrazine hydrochloride, m. p. 195°, which was condensed with benzaldehyde (3 g.) in ethanol (20 ml.), to yield *benzylidene-2-bromo-4-nitrophenylhydrazine* (3.8 g.), m. p. 155–156° (Found: C, 49.1; H, 3.15; Br, 25.0; N, 13.2. C<sub>13</sub>H<sub>10</sub>BrN<sub>3</sub>O<sub>2</sub> requires C, 48.8; H, 3.2; Br, 25.0; N, 13.1%). Benzylidene-2,4-dibromophenylhydrazine, m. p. 97–98° (lit.,<sup>11</sup> 99°), and *benzylidene-2-bromo-4-chlorophenylhydrazine*, m. p. 112° (Found: C, 50.5; H, 3.3; N, 9.0. C<sub>13</sub>H<sub>10</sub>BrClN<sub>2</sub> requires C, 50.4; H, 3.3; N, 9.1%), were prepared in an analogous manner.

**Kinetic Method.**—The bromination reactions were studied by an amperometric method. The reaction vessel was a water-jacketed cell of volume 25 ml., and all kinetic experiments were at 20° ± 0.02°, except where otherwise stated. The indicator system consisted of a platinum electrode, 3 mm. long and 0.5 mm. in diameter, rotated at 750 rev. per min. by a synchronous motor, and a saturated silver-silver chloride reference electrode, separated from the reaction cell by a fine sintered glass disc and an agar plug.

<sup>1</sup> R. Tiollais, H. Bouget, J. Huet, and A. Le Pennec, *Bull. Soc. chim. France*, 1964, 1205.

<sup>2</sup> (a) J. M. Burgess and M. S. Gibson, *Tetrahedron*, 1962, **18**, 1001; (b) I. T. Barnish and M. S. Gibson, *J. Chem. Soc.*, 1965, 2999; R. Fusco, S. Rossi, and E. Merani, *Gazzetta*, 1959, **89**, 2190.

<sup>3</sup> (a) F. L. Scott and J. B. Aylward, *Tetrahedron Letters*, 1965, 841; (b) F. L. Scott and D. A. Cronin, *ibid.*, p. 715; (c) We are grateful for this method to Dr. J. B. Aylward.

<sup>4</sup> R. Huisgen and E. Aufderhaar, *Ber.*, 1965, **98**, 2185, and previous Papers.

<sup>5</sup> F. D. Chattaway and A. J. Walker, *J. Chem. Soc.*, 1925, 975.

<sup>6</sup> A. F. Hegarty and F. L. Scott, *Tetrahedron Letters*, 1965, 3801.

<sup>7</sup> K. J. P. Orton and A. E. Bradfield, *J. Chem. Soc.*, 1927, 986.

<sup>8</sup> C. D. Hodgman *et al.*, "Tables for Identification of Organic Compounds," Chemical Rubber Publishing Co., Ohio, 1960, pp. 68–80.

<sup>9</sup> A. J. Bellamy and R. D. Guthrie, *J. Chem. Soc.*, 1965, 2788, 3528; H. C. Yao and P. Resnick, *J. Org. Chem.*, 1965, **30**, 1832.

<sup>10</sup> G. J. Karabatsos and R. A. Taller, *J. Amer. Chem. Soc.*, 1963, **85**, 3624.

<sup>11</sup> J. E. Humphries, E. Bloom, and R. Evans, *J. Chem. Soc.*, 1923, 1766.

The electrodes were connected to a Metrohm Polarecord E 261R, which supplied the polarising voltage (200 mv) and recorded the diffusion current as a function of time. The solvent used was 70% aqueous acetic acid, prepared by mixing 70 volumes of acetic acid and 30 volumes of

and the  $k$  values were obtained from these. The kinetics were studied with the reaction solutions kept under nitrogen to minimise the formation of the hydroperoxide.<sup>9</sup> But, since the reaction time was so short (usually 20–300 sec.), the same results were obtained in air-saturated solutions.

In a preliminary test, the bromination of *m*-nitrophenol was studied under conditions used by other workers. With 0.056M-perchloric acid containing 0.12M-sodium bromide as solvent at 25°, and using various initial concentrations of the phenol (*ca.*  $5 \times 10^{-4}$ M) and bromine (*ca.*  $5 \times 10^{-6}$ M), a  $k$  of 98 l. mole<sup>-1</sup> sec.<sup>-1</sup> was obtained. This is the same, within experimental error, as that of Bell *et al.*,<sup>13</sup> but smaller than that of O'Dom and Fernando<sup>14</sup> (115 l. mole<sup>-1</sup> sec.<sup>-1</sup>), probably because dibromination was important at the higher bromine concentrations used. Thus, the three electrometric methods give essentially the same results.

**Product Analysis.**—*N*-(Aryl)arylhydrazidic bromides were prepared by adding bromine (0.55 ml.) during 3 hr. to a stirred suspension of the hydrazone ( $10^{-2}$  mole) in acetic acid (40 ml.). The hydrazidic bromides were washed with water and ether and crystallised several times from glacial acetic acid (Table 2). Satisfactory analytical data and

TABLE 1  
Relationship of diffusion current to  $[\text{Br}_2 + \text{Br}_3^-]$

$[\text{Br}]$ ( $\mu\text{mole l.}^{-1}$ )	Diffusion current (i) $\mu\text{A}$	$\Delta\text{Br}/\Delta i$
2.11	2.0 (0.0)	—
8.29	23.4 (21.4)	9.85
16.18	166.0 (164.0)	9.86
23.70	243.0 (241.0)	9.77
30.90	319.0 (317.0)	9.86
37.77	389.0 (387.0)	9.81

water, containing 0.1M-potassium bromide, and the kinetic data were reproducible with each batch of solvent prepared. Under the kinetic conditions in this solvent, the recorder deflection, less a small correction due to residual current, was proportional to the concentration of the diffusible species,  $\text{Br}_2 + \text{Br}_3^-$ . Table 1 shows a typical current

TABLE 2  
The hydrazidic bromides  $\text{ArCBr}=\text{N}\cdot\text{NHAr}'$

Ar	Ar'	M. p.	Found (%)				Formula	Requires (%)			
			C	H	Br	N		C	H	Br	N
4-F-C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	200–202°	46.6	2.6	23.1	12.4	C <sub>13</sub> H <sub>9</sub> BrFN <sub>3</sub> O <sub>2</sub>	46.1	2.7	23.1	12.4
3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	229	42.8	2.4	21.9	15.3	C <sub>13</sub> H <sub>9</sub> BrN <sub>3</sub> O <sub>4</sub>	42.8	2.5	21.9	15.3
3-Br-C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	178	39.2	2.2	40.1	10.3	C <sub>13</sub> H <sub>9</sub> Br <sub>2</sub> N <sub>3</sub> O <sub>2</sub>	39.1	2.3	40.05	10.5
3-Cl-C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	195	44.2	2.5	22.0	11.7	C <sub>13</sub> H <sub>9</sub> BrClN <sub>3</sub> O <sub>2</sub>	44.0	2.6	22.5	11.8
3-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	136–137	50.4	3.8	24.1	12.4	C <sub>14</sub> H <sub>12</sub> BrN <sub>3</sub> O <sub>2</sub>	50.3	3.6	23.9	12.6
C <sub>6</sub> H <sub>5</sub>	2,4-Br <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	114 *									
C <sub>6</sub> H <sub>5</sub>	2-Br-4-ClC <sub>6</sub> H <sub>3</sub>	112	40.4	2.1	41.2	7.2	C <sub>13</sub> H <sub>9</sub> Br <sub>2</sub> ClN <sub>2</sub>	40.2	2.3	41.1	7.2
C <sub>6</sub> H <sub>5</sub>	2,4-(NO <sub>2</sub> ) <sub>2</sub> C <sub>6</sub> H <sub>3</sub>	227 †									

\* Lit.,<sup>5</sup> 114°. † Lit.,<sup>2a</sup> 224–225°.

response for the addition of successive aliquots of a standard bromine solution in 70% acetic acid containing 0.1M-potassium bromide to 20 ml. of the same solvent in the cell. The ratio  $\Delta\text{Br}/\Delta i$  was constant within experimental error over the range  $10^{-4}$ – $10^{-6}$ M. However, the diffusion current for a given bromine concentration is very sensitive to both cell geometry and the pretreatment of the electrodes, and values can only be reproduced within 10% when the cell is reassembled.<sup>12</sup> Thus, the absolute bromine concentration could not be obtained directly from the diffusion current. This is not an important limitation, since the kinetics were studied under pseudo-first-order conditions, with the hydrazone in excess, and only relative bromine concentrations were required.

The bromine concentration–time curves were obtained as follows. Approximately 1 ml. of a solution of bromine ( $10^{-3}$ – $10^{-5}$ M) in 70% acetic acid containing 0.1M-potassium bromide was introduced into 20 ml. of the same solvent in the reaction cell, and, on attainment of a steady diffusion current (several sec.), 1 ml. of the hydrazone dissolved in glacial acetic acid (*ca.*  $10^{-2}$ M) was added rapidly from a calibrated syringe through a self-sealing cap. Sufficient water had been added to the solution in the cell to make the final solvent composition 70 : 30 (v/v) acetic acid–water. The bromine concentration–time curves were then recorded,

<sup>12</sup> J. E. Dubois, P. Alcais, and G. Barbier, *J. Electroanal. Chem.*, 1964, **8**, 359.

melting points were obtained for the reported hydrazidic bromides.<sup>3a</sup> The hydrazidic bromides were recovered in quantitative yields under kinetic conditions when the initial hydrazone and bromine concentrations were similar. At higher hydrazone-to-bromine concentrations separation of the small amount of hydrazidic bromide formed was difficult by fractional crystallisation from acetic acid, but this could readily be achieved by thin-layer chromatography on silica gel G (Merck) with benzene–light petroleum (1 : 1) as the mobile phase. Under these conditions, *N*-(*p*-nitrophenyl)benzhydrazidic bromide ( $R_F$  0.45) was detected in the bromination of benzylidene-*p*-nitro-phenyl-hydrazine ( $R_F$  0.10) when the latter was initially in fifty-fold excess.

## RESULTS AND DISCUSSION

The bromination reactions were studied in aqueous acetic acid containing an excess of bromide ion. Under these conditions, the active brominating species are molecular bromine and, possibly, tribromide ion.<sup>15</sup>

<sup>13</sup> R. P. Bell and D. J. Rawlinson, *J. Chem. Soc.*, 1961, 63; R. P. Bell and T. Spencer, *ibid.*, 1959, 1157.

<sup>14</sup> G. O' Dom and Q. Fernando, *Analyt. Chem.*, 1965, **37**, 893.

<sup>15</sup> P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworths, London, 1959, ch. 9.

The observed rate constant for the bromination of the hydrazone may then be represented as

$$k_2 = (k + k'K[\text{Br}^-]) / (1 + K[\text{Br}^-]),$$

where  $k$  and  $k'$  are the second-order rate constants for the reaction of the hydrazone with bromine and tribromide ion, respectively, and  $K$  is the equilibrium constant for the reaction  $\text{Br}_2 + \text{Br}^- \rightleftharpoons \text{Br}_3^-$ . To simplify the kinetics, the reactions were studied under pseudo-first-order conditions, with the hydrazone initially in at least a twenty-fold excess. The rate of disappearance of bromine then simplifies to

$$-d\text{Br}_2/dt = k_1[\text{Br}_2 + \text{Br}_3^-]$$

where  $k_1 = k_2[\text{Hydrazone}]$ . That the bromination reaction was truly first-order in each reactant was shown by the constancy of the  $k_2$  values for various initial concentrations of both hydrazone and bromine (Table 3).

TABLE 3

Bromination of benzylidene-*p*-nitrophenylhydrazine

$10^4[\text{Br}_2]$ (moles l. <sup>-1</sup> )	$10^4[\text{Hydrazone}]$ (moles l. <sup>-1</sup> )	$10^3k_1$ (sec. <sup>-1</sup> )	$k_2$ (l. mole <sup>-1</sup> sec. <sup>-1</sup> )
5.0	4.07	6.4	157
5.0	2.26	3.5	155
5.0	1.13	1.8	161
8.3	4.07	6.5	160
2.6	4.07	6.4	157

Tribromide ion was shown to be an ineffective brominating agent in the present instance, since a plot of  $k_2(1 + K[\text{Br}^-])$  against  $[\text{Br}^-]$ , which was varied from 0.2 to 0.002M at constant ionic strength, gave a straight line with zero slope.

For the nine 4- and four 3-substituted benzylidene-*p*-nitrophenylhydrazines studied (Table 4), a plot of

TABLE 4

Bromination of arylidene-*p*-nitrophenylhydrazines  
( $\text{X} \cdot \text{C}_6\text{H}_4 \cdot \text{CH}=\text{N} \cdot \text{NH} \cdot \text{C}_6\text{H}_4 \cdot \text{NO}_2$ ) ( $k_2$  in l. mole<sup>-1</sup> sec.<sup>-1</sup>)

X	$k_2$	X	$k_2$	X	$k_2$
4-NO <sub>2</sub> ...	50	H .....	158	3-NO <sub>2</sub> ...	65
4-CN .....	63	4-CHMe <sub>2</sub> ..	179	3-Br .....	97
4-Br .....	115	4-Me .....	211	3-Cl .....	98
4-Cl .....	116	4-OMe ...	338	3-Me .....	187
4-F .....	148	4-NMe <sub>2</sub> ...	565		

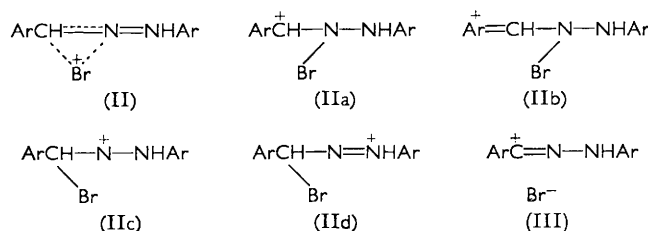
$\log k_2$  against  $\sigma$  gave <sup>16</sup> a  $\rho$  of  $-0.62$ , with a correlation coefficient ( $r$ ) = 0.998 and standard deviation ( $s$ ) = 0.035; the intercept of the regression line with the ordinate ( $\log k_0$ ) = 2.201. The rate data for the 4-methoxy-compound were not included in this correlation, since its  $k_2$  value fell far off the line using either  $\sigma$  or  $\sigma^+$  values.

These rate data are consistent with an azabromonium ion type of intermediate (II) which is resonance-stabilised by the contributing structures (IIa)—(IId).

<sup>16</sup> D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.

<sup>17</sup> J. Hine, "Physical Organic Chemistry," McGraw-Hill, New York, 1962, p. 163.

The contribution of forms (IIa) and (IIb) imposes a positive charge on the arylidene ring and produce the negative  $\rho$ . The numerical value of  $\rho$  is small when



compared with typical values <sup>17</sup> for solvolysis reactions involving carbonium ion intermediates, which are usually in the region  $-4$  to  $-5$ . This may be substantially reduced, however, if the charge in the transition state towards the formation of the intermediate could be successfully delocalised away from the ring. Thus Yates and Wright <sup>18</sup> interpreted the  $\rho$  ( $-2.23$ ) for the bromination of substituted styrenes in acetic acid in terms of the formation of a cyclic bromonium ion. The thermodynamic data for this reaction are similar to those obtained in the bromination of hydrazones (Table 5). However, the large difference

TABLE 5

Thermodynamic data for the bromination of substituted benzylidene-4-nitrophenylhydrazines

Subst.	$k_2$ (at 10°) (l. mole <sup>-1</sup> sec. <sup>-1</sup> )	$\Delta H^\ddagger$ (kcal.)	$\Delta S^\ddagger$ (e.u.)
4-NO <sub>2</sub> .....	28.4	9.6	-33.1
4-Cl .....	61.8	9.8	-30.8
4-F .....	78.5	9.7	-30.7
H .....	80.6	9.7	-30.5
4-Me .....	113	9.7	-30.0
4-OMe .....	164	11.2	-24.0

in the  $\rho$  values suggests that this is not the only mode of delocalisation in the present case. This is confirmed by the large response of the bromination reaction to substituents in the hydrazone ring. For the five compounds (Table 6) variously substituted in the hydrazone

TABLE 6

Bromination of benzylidene arylhydrazines  
( $\text{C}_6\text{H}_5 \cdot \text{CH}=\text{N} \cdot \text{NHAr}'$ )

Ar'	$k_2$ (l. mole <sup>-1</sup> sec. <sup>-1</sup> )
2,4-Dinitrophenyl .....	3.9
2-Bromo-4-nitrophenyl .....	32
4-Nitrophenyl .....	158
2,4-Dibromophenyl .....	890
2-Bromo-4-chlorophenyl .....	980

ring, a Hammett plot gave a  $\rho$  of  $-2.17$  ( $r = 0.992$ ,  $s = 0.057$ , and  $\log k_0 = 3.876$ ). This  $\rho$  value is relatively close to that reported <sup>19</sup> for the protonation of aniline ( $-2.77$ ), indicating that forms (IIc) and (IIId) are the major contributors to the stabilisation of the intermediate. For the formation of the azocarbonium ion

<sup>18</sup> K. Yates and W. V. Wright, *Tetrahedron Letters*, 1965, 1927.

<sup>19</sup> H. H. Jaffe, *Chem. Rev.*, 1953, **53**, 191.

(III), where such extensive delocalisation can only be gained by tautomerism, the  $\rho$  of  $-0.93$  obtained for the benzylidene ring<sup>3a</sup> is consistent with our present data.

The possibility exists that the formation of hydrazidic bromides (or indeed any other<sup>20</sup> electrophilic attack at an arylidene hydrazine) involves attack at nitrogen first, *i.e.*, in this case the formation of an *N*-bromo-compound such as  $\text{ArCH}=\text{N}\cdot\text{NBrAr}'$ . Bell<sup>21</sup> demonstrated that *N*-bromo-compounds in protic solvents and in the presence of an excess of bromide ion are readily cleaved to regenerate bromine and the appropriate NH compounds. Therefore, even if *N*-bromo-hydrazones

are formed readily, under our reaction conditions they should be equally rapidly dehalogenated. The process of irreversible C-bromination can therefore be visualised in terms of the intermediate proposed.

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<sup>20</sup> A. W. Nineham, *Chem. Rev.*, 1955, **55**, 355; F. L. Scott, D. A. Sullivan, and J. O'Reilly, *J. Amer. Chem. Soc.*, 1953, **75**, 5301.

<sup>21</sup> R. P. Bell, *J. Chem. Soc.*, 1936, 1154.