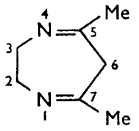
406. *Kinetics of the Halogenation of 2,3-Dihydro-5,7-dimethyl-1,4-diazepine.*

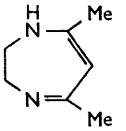
By R. P. Bell and D. R. Marshall.

The bromination of 2,3-dihydro-4,7-dimethyl-1,4-diazepinium perchlorate in the 6-position in aqueous perchloric acid is a simple bimolecular reaction between the cation and bromine, molecular bromine and tribromide ion having similar reactivities. The iodination of the same substance in acetate buffer solutions also involves the cation and is kinetically similar to the iodination of several aromatic species, in that the rate is proportional to $[AcO^-]$ and inversely proportional to $[I^-]\{1 + 714[I^-]\}$, and there is a considerable isotope effect, $k_H/k_D > 2$. It is concluded that the transition state contains the diazepinium cation, an iodine cation, and an acetate ion (or some equivalent combination of species), and that the acetate ion probably acts as a base to remove the proton in the 6-position. The bromination of 6-bromo-2,3-dihydro-5,7-dimethyl-1,4-diazepinium perchlorate in aqueous perchloric acid (to give the 6,6-dibromo-derivative) can occur either through the cation or through the uncharged base, the latter being more reactive by a factor of 10^9. The dependence of rate upon bromide ion concentration indicates that the transition state contains a bromine cation, but the magnitude of the observed velocity constants makes it improbable that this cation is formed prior to the interaction between bromine and the organic species. The last reaction shows a positive salt effect in quantitative agreement with theory.

Several recent Papers on the 1,4-diazepines (diazacycloheptatrienes) have discussed the aromatic character of the ring system, as shown by its reactions, absorption spectra, and acid–base properties.[1-3] The present Paper deals with the kinetics of the halogenation of 2,3-dihydro-5,7-dimethyl-1,4-diazepine [(Ia) or (Ib)]. This substance will be referred to as "the diazepine" for the sake of brevity, and the numbering used is shown. The diazepinium cation can be written in a number of ways, and its high stability is reflected in the high value of pK (13·4) obtained by Schwarzenbach and Lütz.[1] The most reasonable formulation of the cation is (II).



(Ia)



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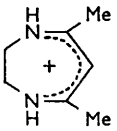
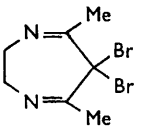


(II)



(III)

Experimental

The diazepinium perchlorate was prepared by condensing ethylenediamine and acetylacetone, as described by Schwarzenbach and Lütz,[1] and, when recrystallized twice from water, had m. p. 139—141° (lit., 140°,[1] 138—141·5° [3]). More than one one recrystallization had no effect on its kinetic or other properties.

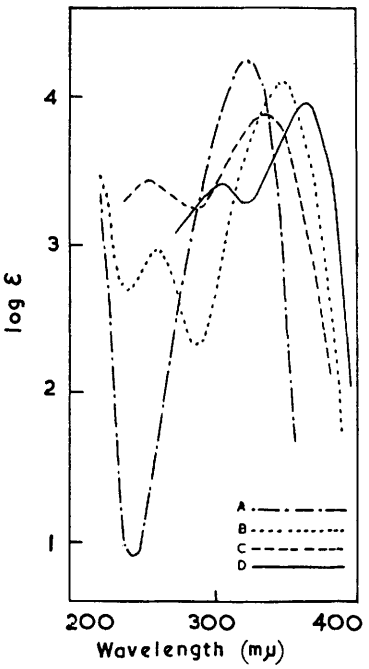
The 6-bromodiazepinium perchlorate was prepared by direct bromination of diazepinium perchlorate with bromine (1 mole).[2] The crude product (mainly the bromide) was dissolved in water and an excess of 2N-sodium hydroxide added. The precipitated base was washed with a little water and dissolved in the minimum quantity of alcohol. Cautious addition of concentrated perchloric acid and cooling gave crystals of the perchlorate which, recrystallized twice from water, had m. p. 160—162° (lit.,[2] 207—208°).

Sodium iodide was "pure" grade, dried at 100°. Its purity was checked by titration

[1] Schwarzenbach and Lütz, *Helv. Chim. Acta*, 1940, **23**, 1147.
[2] Lloyd and Marshall, *J.*, 1956, 2597; 1958, 118.
[3] Barltrop, Richards, Russell, and Ryback, *J.*, 1959, 1132.

against silver nitrate and against potassium iodate. Water was redistilled from alkaline permanganate in an all-glass still. Other inorganic reagents were of AnalaR grade.

The absorption spectra of aqueous solutions of the diazepinium and 6-bromodiazepinium perchlorates are shown as curves A and B of the Figure, the latter being very similar to that of the 6-methoxydiazepinium perchlorate.[4] These spectra were measured with a Unicam S.P. 500 spectrophotometer. When alkali is added to solutions of the 6-bromodiazepinium perchlorate the optical density falls with time, the rate increasing with increasing concentration of alkali; this is probably due to cleavage into ethylenediamine and bromoacetylacetone. Spectra were recorded at one minute intervals with a Perkin-Elmer 4000A Spectrachord instrument, and could be extrapolated back to zero time with little uncertainty. The initial spectrum was the same for alkali concentrations of 0·9, 0·5, and 0·2N; this spectrum was assumed to be that of the 6-bromodiazepine base, and is shown in curve C of the Figure. The close similarity between the spectra of the base and its cation suggest that the



Ultraviolet spectra. A, The diazepinium perchlorate in aqueous solution. B, The 6-bromodiazepinium perchlorate in aqueous solution. C, Spectrum attributed to the 6-bromodiazepine base in alkaline aqueous solution (see text). D, Spectrum attributed to the 6-iodiazepinium cation (see text).

former should be formulated as (Ib) rather than (Ia). At alkali concentrations between 0·01 and 0·001N, initial spectra intermediate between curves B and C were observed, and the optical densities at 347 mμ were used to calculate the ratio [cation] : [base], and hence the dissociation constant of the 6-bromodiazepinium cation. At $[OH^-] = 0{\cdot}01$, 0·005, 0·002, and 0·001, the values obtained were $10^{12}K = 1{\cdot}6$, 1·5, 1·7, and 1·4 (mean $K = 1{\cdot}6 \times 10^{-12}$; $pK = 11{\cdot}8$). This compares with $pK = 13{\cdot}4$ for the diazepinium cation itself,[1] so that the introduction of a bromine atom at the 6-position lowers the basic strength of the diazepine by a factor of about 40.

It was not found possible to prepare the 6-iododiazepine, but the spectrum of its cation was deduced by examining iodinated solutions. Solutions 5×10^{-4}M in the diazepinium perchlorate were allowed to react with varying quantities of iodine in a phosphate buffer of pH 7. At intervals the excess of iodine was removed by titration with sodium thiosulphate and the spectrum of the resulting solution was recorded. The spectrum of the iodinated cation was deduced by subtracting the known contribution due to the unreacted diazepinium cation, a small correction being made for di-substitution. A consistent spectrum was obtained from different experiments, and is shown as D in the Figure.

Bromination Experiments.—Although only the monobromodiazepine has been isolated in bromination experiments, quantitative solution experiments showed that a second stage of

[4] Marshall, Ph.D. Thesis, St. Andrews University, 1958.

bromination also occurred rapidly. The spectra of the solutions always consisted of a superposition of curves A and B of the Figure, referring to the diazepinium and 6-bromodiazepinium cations. The concentrations of these two species could be deduced from the optical density of the solution at 322 and 347 mμ, respectively, and their sum was found to decrease as the amount of bromine added increased: moreover, the amount of bromine consumed was always greater than the amount of the 6-bromodiazepine formed. If the 6-bromodiazepine reacts with one more molecule of bromine, the total amount of bromine consumed should be given by $2[DH]_0 - 2[DH] - [DBr]$, where DH and DBr are the concentrations of the diazepine and the bromodiazepine, and $[DH]_0$ is the initial concentration. Table 1 shows the results of experiments with varying amounts of bromine, all of which was consumed in every experiment. The agreement between the last two columns supports the view that the 6-bromodiazepine reacts with a second molecule of bromine.

TABLE 1.

Reaction of the diazepine with bromine {$[DH]_0 = 5 \times 10^{-5}$M throughout}.

$10^5[DH]$	$10^5[DBr]$	$10^5[Br_2]$	$10^5\{2[DH]_0 - 2[DH] - [DBr]\}$
3·98	0·84	1·13	1·20
2·82	1·96	2·26	2·40
2·00	2·48	3·39	3·52
1·22	2·85	4·52	4·71
0·36	3·47	5·65	5·81
0·00	3·21	6·78	6·79

The most probable product of further bromination is the 6,6-dibromodiazepine (III), which contains no conjugated double bonds and should not absorb in the near-ultraviolet region. This structure was confirmed by an experiment in which bromine (0·52 ml., 0·01 mole) in 1M-potassium bromide (25 ml.) was added to the 6-bromodiazepinium bromide (3 g., 0·01 mole) in water (30 ml.) at 35°. A yellow oil separated, and was washed with water and with sodium thiosulphate solution and dried (Na_2SO_4). This oil (yield 2 g.) contained bromine but not nitrogen (Lassaigne test), gave a 2,4-dinitrophenylhydrazine derivative of m. p. 140° (from ethanol), and was not enolic, since it did not dissolve in sodium hydroxide solution and gave no colour with ferric chloride. Its infrared spectrum showed a carbonyl peak at 1720 cm.$^{-1}$. These properties suggest dibromoacetylacetone, $MeCO{\cdot}CBr_2{\cdot}CO{\cdot}Me$, formed by the hydrolysis of (III). The bromine content was determined by alkaline hydrolysis and titration of bromide ion against silver nitrate (Br, 56·6%), and also by reaction with potassium iodide and titration of the liberated iodine against sodium thiosulphate (Br, 57·0%). These figures are lower than required for $C_5H_6O_2Br_2$ (Br, 62·0%), and it is likely that our product was contaminated with monobromoacetylacetone; weak infrared absorption at 1610 cm.$^{-1}$ was consistent with this. The hydrolysis of the dibromodiazepine to dibromoacetylacetone may have taken place in the experiments on bromination in dilute solution, recorded in Table 1, since neither substance absorbs strongly in the near-ultraviolet region.

Both stages of bromination take place very rapidly, and were investigated kinetically by the method in which bromine concentrations in the range 10^{-6}—10^{-9}M are followed by means of a platinum redox electrode, a glass electrode being used as a standard.[5] The bromination of the diazepinium perchlorate was studied at 0°, with initial concentrations of both reactants of *ca.* 10^{-7}M. Seven experiments were carried out with $[Br^-] = 0{\cdot}1$M, in 10^{-2}M-; 10^{-3}M-, and 10^{-4}M-perchloric acid solutions, the ionic strength being made up to $I = 0{\cdot}21$ with sodium perchlorate. Four experiments at $[H^+] = 0{\cdot}01$M had $[Br^-] = 0{\cdot}10$ and 0·20M. Since the rate of reaction of the 6-bromodiazepinium perchlorate with bromine is less than one hundredth that of the diazepinium perchlorate (see next paragraph), the results followed simple second-order kinetics. The second-order velocity constant was found to be independent of both pH and bromide ion concentration [mean $k = (1{\cdot}07 \pm 0{\cdot}04) \times 10^6$ l. mole^{-1} sec.$^{-1}$]. Four experiments were carried out at 25° with $[H^+] = 0{\cdot}01$M, $[Br^-] = 0{\cdot}05$, 0·10, and 0·20M, and $I = 0{\cdot}21$, the initial concentrations of both reactants being in this case *ca.* 10^{-8}M. The velocity constant was again independent of bromine ion concentration [$k = (4{\cdot}4 \pm 0{\cdot}2) \times 10^6$ l. mole^{-1} sec.$^{-1}$].*

The much slower bromination of the 6-bromodiazepinium perchlorate was studied at 0°

* The measurements described in this paragraph were carried out in this laboratory by Mr. G. G. Davis, to whom we express our thanks.

with initial concentrations of *ca.* 10^{-4}M for the diazepinium salt and *ca.* 10^{-6}M for bromine. Under these conditions, the reaction is of the first-order with respect to bromine, and the velocity constant can be derived from the slope of the linear plot of e.m.f. against time, as previously described.[5] The velocity constants are dependent both on hydrogen ion concentration and on bromide ion concentration, as shown in Table 2. Velocity constants were calculated from eqns. (1) and (2):

$$k[Br^-](1 + 20[Br^-]) = 59 + 0{\cdot}090/[H^+] \quad (1)$$

$$k[Br^-](1 + 20[Br^-]) = 109 + 0{\cdot}135/[H^+] \quad (2)$$

relating, respectively, to $I = 0{\cdot}1$ and $I = 0{\cdot}4$.

Iodination Experiments.—Although it was not found possible to isolate the 6-iododiazepine, the similarity of spectrum D in the Figure to those of the other 6-substituted diazepinium cations is strong evidence for its formation. For long reaction times, this spectrum decreases in intensity and more than one molecule of iodine is eventually consumed per molecule of the diazepine; some evidence was obtained that this is due to di-substitution, perhaps with subse-

TABLE 2.

Bromination of the 6-bromodiazepinium perchlorate in perchloric acid solutions at 0°.

I = Ionic strength. k = Second-order velocity constant (in l. mole^{-1} sec.$^{-1}$).

$[H^+]$ (M)	$[Br^-]$ (M)	I	$k_{obs.}$	$k_{calc.}$	$[H^+]$ (M)	$[Br^-]$ (M)	I	$k_{obs.}$	$k_{calc.}$
2×10^{-4}	0·1	0·1	1710	1697	3×10^{-4}	0·1	0·4	1825	1863
3×10^{-4}	0·1	0·1	1100	1197	3×10^{-4}	0·2	0·4	574	559
1×10^{-3}	0·1	0·1	494	497	1×10^{-2}	0·05	0·4	1185	1225
1×10^{-2}	0·1	0·1	225	227	1×10^{-2}	0·1	0·4	400	410
3×10^{-4}	0·07	0·4	3240	3330	1×10^{-2}	0·2	0·4	135	123

quent cleavage, as in the bromination reaction, but no kinetic measurements were made on the second stage of iodination. Before the second iodination becomes appreciable, the iodine concentration reaches a steady value which is greater than that corresponding to complete mono-iodination, and experiments at different concentrations of iodide and hydrogen ions gave an approximate equilibrium constant, $K_I = [DI][H^+][I^-]f_\pm^2/[DH][I_2] = 4 \times 10^{-5}$, where DH and DI denote the cations of the diazepine and the 6-iododiazepine. In this expression, $[I_2]$ represents the concentration of free molecular iodine, excluding that of I_3^-.

The rate of iodination of the diazepinium perchlorate was measured at 25° in acetate buffer solutions by titration of samples with sodium thiosulphate solution. Typical initial concentrations were 0·05M-diazepine, 0·01M-sodium iodide, and 2×10^{-4}M-iodine; the ionic strength was made up to $I = 0{\cdot}2$ by adding sodium nitrate when necessary. Identical rates were observed in blackened and unblackened vessels. The iodide concentration was kept low so as to minimize the reversibility of the iodination reaction; 20 ml. samples were titrated with 0·002N-thiosulphate solution and the reactions were followed to the extent of 50—80%. For each reaction mixture, the equilibrium concentration of titratable iodine, $[I_2]_e^*$, was calculated from the equilibrium constant given in the last paragraph and from $[I_3^-]/[I_2][I^-] = 714$.[6] A first-order velocity constant, k_1, was obtained from the linear plot of $\log_{10}\{[I_2]^* - [I_2]_e^*\}$ against time, and the second-order velocity constant for the forward reaction, k, was then calculated from the expression

$$k([DH] + [H^+][I^-]f_\pm^2/K_I) = k_1 \quad (3)$$

since the concentration of the diazepine, [DH], is effectively constant in each experiment. (The value assigned to $f_\pm^2$ is not important, since it cancels out with the same factor used in calculating $[H^+]$ in the buffer solution.) The correction for the reverse reaction is never more than a few per cent, and essentially the same values of k, though somewhat less accurate, are obtained if the expression $k[DH] = -\mathrm{d}\ln[I_2]^*/\mathrm{d}t$ is applied to the first 30% of the reaction.

The velocity constants thus obtained are given in Table 3, in which the values of $[H^+]$ were calculated by assuming that $[H^+][AcO^-]/[AcOH] = 2{\cdot}92 \times 10^{-5}$ at $I = 0{\cdot}2$.[7] The observed

[5] Atkinson and Bell, *J.*, 1963, 3260.
[6] Jones and Kaplan, *J. Amer. Chem. Soc.*, 1928, **50**, 1845.
[7] Larsson and Adell, *Z. phys. Chem.*, 1931, **156**, 352.

velocity shows no dependence upon $[H^+]$, but depends both on $[AcO^-]$ and $[I^-]$, and the velocity constants were calculated from the expression

$$10^5k = 8{\cdot}0 + 111[AcO^-]/[I^-](1 + 714[I^-]) \quad (4)$$

A few kinetic measurements were made by following the decrease of the tri-iodide absorption at 390 mμ, in a Unicam S.P. 500 spectrophotometer. This method gave results in good agreement with those obtained by titration, and was used in the study of the deuterium isotope effect (see below).

The results in Table 3 refer to a constant concentration of the diazepine (0·051M). The second-order velocity constant is somewhat dependent on the diazepine concentration, decreasing by about 30% as the latter increases from 0·008 to 0·06M. This decrease is believed to be due to a reduction in the amount of free iodine by complexing with the diazepinium cation, which is a common phenomenon with aromatic amines. The addition of diazepinium perchlorate to an iodine–iodide solution in an acetate buffer solution causes an immediate drop of 1—3mv in the redox potential, and if concentrated solutions are used a brown oil of variable

TABLE 3.

Iodination of the diazepinium perchlorate in acetate buffers at 25°.

k = Second-order velocity constant (in l. mole^{-1} sec.$^{-1}$). I = 0·2. [The diazepine] = 0·051M throughout.

(*a*) $[I^-]$ = 0·0110M.

$10^4[AcO^-]$ (M)	$10^4[AcOH]$ (M)	$10^8[H^+]$ (M)	$10^5k_{obs.}$	$10^5k_{calc.}$	$10^4[AcO^-]$ (M)	$10^4[AcOH]$ (M)	$10^8[H^+]$ (M)	$10^5k_{obs.}$	$10^5k_{calc.}$
206	19	263	33	32	413	98	692	56	55
413	37	263	57	55	825	196	692	102	102
825	74	263	106	102	1238	293	692	150	149
1033	93	263	126	126	166	50	884	24	29
186	31	482	29	29	414	125	884	55	55
372	62	482	51	50	828	250	884	105	103
744	123	482	90	94	1380	420	884	169	166
1116	185	482	136	135					

(*b*) $[AcO^-]$ = 0·1033M; $[AcOH]$ = 0·0093M; $[H^+] = 2{\cdot}63 \times 10^{-6}$M.

$10^4[I^-]$ (M)	$10^5k_{obs.}$	$10^5k_{calc.}$	$10^4[I^-]$ (M)	$10^5k_{obs.}$	$10^5k_{calc.}$
24	1560	1660	88	184	182
45	566	590	110	126	126
64	298	323	130	92	93

composition separates out which contains the diazepine, iodide, and free iodine, but no perchlorate. The absolute velocity constants obtained may therefore be somewhat in error, but it is not thought that the interpretation of the results in Table 3 is affected, since the diazepine concentration was constant throughout and much greater than that of iodine.

A few experiments were carried out on the deuterium isotope effect in the iodination of the diazepine. Both the diazepinium perchlorate and the 6-bromodiazepinium perchlorate were deuterated by recrystallization from 96% deuterium oxide; the results were the same if the solution was boiled for an hour before cooling. The infrared spectra of the deuterated and undeuterated substances in potassium bromide discs were recorded with a Perkin-Elmer 21A spectrophotometer. All the spectra are complex in the region 2700—3400 cm.$^{-1}$, giving 8—10 shoulders or maxima. The intensity in the region 3100—3150 cm.$^{-1}$ decreases markedly when the diazepine is converted into the 6-bromodiazepine, so that the stretching frequency of the C–H bond in the 6-position is probably in this region. When the 6-bromodiazepine is deuterated, the peak at 3330 cm.$^{-1}$ decreases in intensity and a new peak appears at 2430 cm.$^{-1}$; these must represent, respectively, N–H and N–D stretching, the former overlapping with C–H stretching frequencies. [3330 cm.$^{-1}$ is a higher frequency than that found by Stone, Craig, and Thompson [8] for the cations of tertiary amines, but it is near the lower limit of the range quoted by Bellamy [9] for N–H stretching at an uncharged nitrogen atom; it is thus compatible

[8] Stone, Craig, and Thompson, *J.*, 1958, 52.
[9] Bellamy, "Infra-red Spectra of Complex Molecules," 2nd edn., Methuen, London, 1958.

with an N–H group carrying a partial positive charge, as indicated by structure (II)]. When the diazepine is deuterated, two new peaks appear at 2450 and 2300 cm.$^{-1}$. The former is clearly the N–D stretching frequency, and the latter can only be the C–D stretching band due to the introduction of deuterium at the 6-position. It may therefore be concluded that in deuterium oxide at 100° the diazepinium perchlorate exchanges rapidly the hydrogen atoms attached to nitrogen, and also that on the 6-carbon atom.

The deuterium isotope effect was determined by comparing the rates of iodination of the diazepinium perchlorate (0·05M) in solutions with [AcO^-] = 0·075M, [AcOH] = 0·0075M, and [I^-] = 0·002M, in water and in 96% deuterium oxide. In the latter case, the solution was allowed to stand for several hours before the addition of iodine, in order to effect exchange. The initial iodine concentration was 10^{-4}M, and the rates were measured spectrophotometrically by following the tri-iodide absorption at 390 mμ. Since the isotope effect on the iodination equilibrium constant is unknown, the kinetic isotope effect was determined by comparing the initial slopes of plots of the logarithm of the optical density against time. Exchange times of 2 and 24 hr. gave k_H/k_D = 1·8 and 2·2, respectively. Exchange must have been effectively complete in the latter case, and since the system contained only 96% of deuterium in the deuterium experiments, the true isotope effect must be rather greater than 2·2.

Discussion

The simplest kinetic behaviour is shown by the bromination of the diazepine, which appears to be a straightforward electrophilic substitution of the diazepinium cation by bromine. The absence of any dependence on bromide ion concentration shows that molecular bromine and tribromide ion must have similar reactivities; this is surprising for a rate constant as low as 10^6 l. mole^{-1} sec.$^{-1}$, since previous work [10–12] on the bromination of aromatic compounds suggests that the reactivity of tribromide becomes comparable with that of bromine only when the rate constant is as high as 10^9 or 10^{10} l. mole^{-1} sec.$^{-1}$. It is possible, however, that the positive charge on the diazepinium cation favours reaction with the negative tribromide ion. Our measurements at 0 and 25° give an activation energy of 9·1 kcal./mole, and a pre-exponential factor of about 10^{13} l. mole^{-1} sec.$^{-1}$. The latter is greater than the collision-theory value of about 10^{11} l. mole^{-1} sec.$^{-1}$, as might be expected for a reaction between two ions of opposite charge.

The bromination of the 6-bromodiazepine shows the more complicated behaviour represented by equations (1) and (2). The observed velocity now contains two terms, one independent of [H^+] and one inversely proportional to it, showing that both the cation and the uncharged base can undergo bromination. Since we have found pK = 11·8 for the 6-bromodiazepine, the values of the coefficients in equations (1) and (2) indicate that the uncharged base is about 10^9 times as reactive as the cation. No reaction with uncharged base was detected with the diazepine itself; this can be related to its greater basic strength (pK = 13·4), and it is also probable that the ratio of the reactivities of the two species will be less than 10^9 for a substance of such high reactivity.

The dependence of reaction velocity on bromide ion concentration is shown by the left-hand side of equations (1) and (2). If $[Br_3^-]/[Br_2][Br^-] = K$, then the fraction of total bromine present as Br_2 is $(1 + K[Br^-])^{-1}$. At 25° K = 16,[13] and it is probably somewhat greater at 0°; hence the term $1 + 20[Br^-]$ suggests that bromination is effected by Br_2 but not by Br_3^-. There is, however, an additional inverse dependence on bromide ion concentration, showing that a bromide ion is lost when the transition state is formed from the 6-bromodiazepine (or its cation) and a bromine molecule. A kinetically equivalent hypothesis is that halogenation is effected by a small quantity of bromine cations in equilibrium with bromine molecules and bromide ions. However, even if we suppose that Br^+

[10] Bell and Ramsden, *J.*, 1958, 161.
[11] Bell and Spencer, *J.*, 1959, 1156.
[12] Bell and Rawlinson, *J.*, 1961, 63.
[13] Griffith, McKeown, and Winn, *Trans. Faraday Soc.*, 1932, **28**, 101; Jones and Baeckström, *J. Amer. Chem. Soc.*, 1934, **56**, 1517.

and the 6-bromodiazepine (or its cation) react with a velocity constant as large as 10^{11} l. mole^{-1} sec.$^{-1}$, then in order to account for the numerical coefficients in equations (1) and (2), the equilibrium constant $[Br^+][Br^-]/[Br_2]$ would have to be at least 10^{-9} to account for the reaction with the cation, and approximately unity for the reaction with the uncharged base. It therefore seems preferable to suppose that the bromine molecule loses a bromide ion only when it reacts with the organic species, though of course the bromide ion must have separated completely by the time the transition state is reached.

There is a considerable difference between the numerical coeffients of equations (1) and (2), relating, respectively, to $I = 0{\cdot}1$ and $I = 0{\cdot}4$, thus suggesting a large positive salt effect. This is in fact what would be expected on the basis of the above mechanism. Since almost all the 6-bromodiazepine is present as its cation (DH_2^+), the formation of the two transition states can be written as

$$DH_2^+ + Br_2 \rightleftharpoons [DH_2Br]^{2+} + Br^- \quad (A)$$

$$DH_2^+ + Br_2 \rightleftharpoons DH + H^+ + Br_2 \rightleftharpoons [DHBr]^+ + H^+ + Br^- \quad (B)$$

If the activity coefficients of ions of the same numerical valency can be cancelled out, then the usual treatment predicts that (A) and (B) should show primary salt effects of $1/f_2$ and $1/f_1^2$, respectively, *i.e.*, both terms in equations (1) and (2) should exhibit a positive salt effect, which should be greater for the term independent of $[H^+]$. This is in fact what is observed; moreover, the observed salt effects are close to those predicted theoretically. The expression $-\log_{10} f_z = 0{\cdot}5\, z^2 I^{\frac{1}{2}}/(1 + I^{\frac{1}{2}})$ predicts that on going from $I = 0{\cdot}1$ to $I = 0{\cdot}4$, reaction (A) should be accelerated by a factor of 1·85 and reaction (B) by a factor of 1·42; the observed accelerations are 2·01 and 1·50.

In the iodination of the diazepine (eqn. 4) the reaction velocity is independent of $[H^+]$, and (apart from the small constant term) is proportional to $[AcO^-]$ and inversely proportional to $[I^-](1 + 714[I^-])$. Since $[I_3^-]/[I_2][I^-] = 714$ at 25°,[6] the interpretation is analogous to that given above, and we must suppose that the transition state contains the diazepinium cation, an iodine cation, and an acetate ion, or some equivalent combination of species. However, it is again impossible to distinguish between different paths by which the transition state can be formed, and the suggestion that the halogenating agent is the iodine cation or iodine acetate, proposed to explain similar experimental findings in the iodination of various aromatic compounds,[14-22] is only one way of viewing the situation. In common with most (but not all) of these last reactions, the iodination of the diazepine shows an isotope effect, $k_H/k_D > 2$, showing that the hydrogen atom in the 6-position is considerably loosened in the transition state. It is probable, therefore, that the acetate ion is acting as a base to remove this proton. The small term independent of $[AcO^-]$ in equation 4 may represent removal of a proton by water molecules; it should, of course, be dependent upon iodide concentration, but there are insufficient experimental results to reveal this.

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