942. *The Kinetics and Mechanisms of Aromatic Halogen Substitution. Part XV.*[1] *Reagents involved in Bromination by Hypobromous Acid in Aqueous Acetic Acid.*

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The ½*o* : *p*-ratio for the bromination of biphenyl by hypobromous acid in 75% acetic acid has been found to depend markedly on the concentration of mineral acid, being 0·17 without acid, and reaching a limiting value, 0·59, in the presence of 0·2M-perchloric acid. These results and those of kinetic measurements suggest that the effective electrophile is a form of positive bromine when mineral acid is added, but that in the absence of mineral acid the neutral species, bromine acetate, is concerned. The partial rate factors for *para*-substitution in biphenyl at 1° are estimated to be about 38 for the cation and about 3000 for the neutral molecule.

THE acid-catalysed reaction of hypobromous acid with aromatic compounds has been studied under a variety of conditions. Shilov and Kaniaev[2] established that an ion Br^+ or H_2OBr^+ was the electrophile responsible for substitution in water, and that added ions (*e.g.*, Cl^-) could divert the reaction by producing a less effective electrophile (*e.g.*, BrCl) in greater concentration. Derbyshire and Waters[3] confirmed this, and de la Mare and Harvey[4] extended the measurements to mixtures of dioxan and water.

Very convenient solvents for preparative bromination are formed by mixtures of hypobromous and acetic acid. In such solvents, equilibria of the type shown in equations (1) and (2) multiply the number of possible electrophilic species that need to be considered.

$$\mathrm{BrOH + HOAc \rightleftharpoons BrOAc + H_2O} \quad \text{. . . . . (1)}$$

$$\mathrm{BrOAc + H^+ \rightleftharpoons BrOHAc^+} \quad \text{. . . . . (2)}$$

Branch and Jones[5] examined such brominations kinetically. They favoured Br^+ or $BrOH_2^+$ as the effective electrophile and considered that $BrOHAc^+$ was improbable on the basis of the dependence of rate on solvent composition.

Examination of the corresponding system involving hypochlorous acid, however, led Stanley and Shorter[6] and de la Mare *et al.*[7,8] to the conclusion that chlorine acetate is a

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[1] Part XIV, de la Mare, Hall, Harris, Hassan, Johnson, and Klassen, *J.*, 1962, 3784.
[2] Shilov and Kaniaev, *Compt. rend. Acad. Sci. U.S.S.R.*, 1939, **24**, 890.
[3] Derbyshire and Waters, *J.*, 1950, 564.
[4] de la Mare and Harvey, 1956, 36.
[5] Branch and Jones, *J.*, 1954, 2317; 1955, 2921.
[6] Stanley and Shorter, *J.*, 1958, 246, 256.
[7] de la Mare, Hilton, and Vernon, *J.*, 1960, 4039.
[8] de la Mare, Hilton, and Varma, *J.*, 1960, 4044.

remarkably effective chlorinating species. The latter authors[8] also produced evidence that $ClOHAc^+$ can be the dominant electrophile in solutions of hypochlorous acid in aqueous acetic acid containing perchloric acid. Comparison of the dependence of rate on the proportion of water and on the acidity of the medium showed similarities between the hypochlorous and the hypobromous systems that led us to re-examine bromination by hypobromous acid in aqueous acetic acid. A preliminary account of this work has been given elsewhere.[9]

EXPERIMENTAL

Kinetic Measurements.—Some of the materials and methods have been described in earlier papers.[4, 10, 11] The solvent is specified as a percentage by weight. For most of the kinetic measurements, samples for analysis were withdrawn by a 5 ml. pipette which delivered a calibrated volume of the solution in two seconds, but for the fastest measurements it was necessary to quench the whole of the reaction mixture by adding potassium iodide solution; the mixture was then titrated in the usual way.

The following is an example of a typical kinetic run; it involved 0·002763M-biphenyl and 0·00131M-hypobromous acid in 75% acetic acid at 1·48°; aliquot parts were removed and titrated with 0·00400N-sodium thiosulphate.

Time (sec.)	37	58	79	101	136
Titre (ml.)	2·048	1·648	1·333	1·128	0·838
k_2 (l. mole^{-1} sec.$^{-1}$)	4·61	4·63	4·70	4·51	4·52

The mean value of k_2 from this plus several other measurements is 4·7 l. mole^{-1} sec.$^{-1}$.

The following are similar data for 0·0325M-benzene with 0·00387M-hypobromous acid at 0·83°.

Time (sec.)	110	335	700	908	1239
Titre (ml.)	8·35	7·09	5·52	4·74	3·78
k_2 (l. mole^{-1} sec.$^{-1}$)	0·0238	0·0255	0·0237	0·0237	0·0234

In Table 1 are summarised the results obtained at 0·86° in 75% acetic acid with and without the addition of electrolytes.

The following results show the effect of temperature on the rate of reaction of biphenyl (0·002—0·003M) with hypobromous acid (0·001—0·002M) in 75% acetic acid:

Temp.	−3·78°	0·86°	1·48°	7·58°	12·65°	20·1°
k_2 (l. mole^{-1} sec.$^{-1}$)	3·5	4·5	4·6	6·4	7·8	12·2

A plot of $\log_{10}k_2$ against $1/T$ is linear, and the Arrhenius parameters, calculated by using the equation $k_2 = B \exp(-E_A/\boldsymbol{R}T)$, are $E_A = 7{\cdot}9$ kcal. mole^{-1} and $B = 9{\cdot}6 \times 10^6$ l. mole^{-1} sec.$^{-1}$.

Measurements of Acidity.—The interpretation of acidity in mixed solvents involving acetic acid, water, and added electrolytes has some theoretical difficulties. It seemed to us, however, that the best measure of this property for the purpose of this work is the Hammett acidity function, h_0,[12] since, for compounds less reactive than those here examined, it has been shown[13] that the rates of bromination by acidified solutions of hypobromous acid follow this function, though effects specific to the added electrolyte and to the aromatic compound were noted.

Accordingly, measurements of the degree of ionisation of indicators in solutions of perchloric acid, of sodium perchlorate, and of sodium acetate in 75% acetic acid at 25° were made with *m*-nitroaniline (m. p. 113·5—114°) and *p*-nitroaniline (m. p. 150—150·5°). Aliquot portions of the indicator in 75% acetic acid were added to solutions of electrolytes and made up to volume. The optical densities were measured with a Unicam S.P. 500 spectrophotometer in 1-cm. cells against the solvent in the regions of maximum absorption, 360 mμ for *m*-nitroaniline and 377 mμ for *p*-nitroaniline. The optical density of the same amount of indicator in water (where it is not protonated) and in 6M-perchloric acid (where it is completely protonated) were

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[9] de la Mare and Maxwell, *Chem. and Ind.*, 1961, 553.
[10] de la Mare and Hassan, *J.*, 1957, 3004.
[11] de la Mare and Robertson, *J.*, 1943, 276, 279.
[12] Paul and Long, *Chem. Rev.*, 1957, **57**, 1.
[13] de la Mare and Hilton, *J.*, 1962, 997.

also measured. Values of H_0 were calculated from the formula $H_0 = \mathrm{p}K_{\mathrm{BH}^+} - \log_{10} [\mathrm{BH}^+]/[\mathrm{B}]$ and values[12] of $\mathrm{p}K_a$ for *m*-nitroaniline of 2·50 and for *p*-nitroaniline of 0·99. The results are recorded in Table 2.

TABLE 1.

Effects of added electrolytes on the rates of bromination of biphenyl and of benzene in 75% acetic acid at 0·86°.

(*a*) Biphenyl, 0·00245M; BrOH, *ca.* 0·0012M.

$HClO_4$ (M)	0·00	0·0053	0·0106	0·0212	0·0267
k_2 (l. mole^{-1} sec.$^{-1}$)	4·7	5·8	7·4	9·7	12·2
10^3h_0	5·1	8·0	12·3	23	29·5

$NaClO_4$ (M)	0·0101	0·0202	NaOAc (M)	0·0096	0·0239	0·0428
k_2 (l. mole^{-1} sec.$^{-1}$)	5·4	5·6		4·7	4·4	4·2
10^3h_0	5·9	5·5		2·4	1·66	1·20

(*b*) Benzene, 0·0238M; BrOH, 0·002—0·004M.

$HClO_4$ (M)	0·00	0·0025	0·0050	0·0126	0·0412	0·0759	0·101
k_2 (l. mole^{-1} sec.$^{-1}$)	0·0238	0·0340	0·0487	0·102	0·371	0·724	1·01
10^3h_0	5·1	6·5	8·0	13·5	41	76	112

$NaClO_4$ (M)	0·0052	0·0130	0·0438	NaOAc (M)	0·0191	0·0382	0·0682
k_2 (l. mole^{-1} sec.$^{-1}$)	0·0270	0·0327	0·0410		0·0100	0·0076	0·0061
10^3h_0	5·5	6·2	6·8		1·82	1·32	1·05

TABLE 2.

Optical densities of solutions of bases.

(*a*) *m*-Nitroaniline at 360 mμ; optical density in water, 0·680; in 6M-$HClO_4$, 0·050.

$HClO_4$ (M)	0·00	0·0056	0·011	0·028
Optical density	0·292	0·233	0·182	0·110
H_0	2·29	2·11	1·92	1·52

(*b*) *m*-Nitroaniline at 360 mμ; optical density in water, 0·457; in 6M-$HClO_4$, 0·025.

$NaClO_4$ (M)	0·00	0·0050	0·0100	0·0200
Optical density	0·189	0·179	0·175	0·167
H_0	2·29	2·24	2·23	2·19

(*c*) *m*-Nitroaniline at 360 mμ; optical density in water, 0·569; in 6M-$HClO_4$, 0·056.

NaOAc (M)	0·00	0·010	0·020	0·048
Optical density	0·252	0·350	0·385	0·427
H_0	2·29	2·63	2·75	2·92

(*d*) *p*-Nitroaniline at 377 mμ; optical density in water, 0·498; in 6M-$HClO_4$, 0·010.

$HClO_4$ (M)	0·056	0·113	0·225
Optical density	0·330	0·226	0·116
H	1·27	0·89	0·44

These values are consistent with those previously reported for acetic acid[14] and for perchloric acid in acetic acid containing 0·3M-sodium perchlorate.[15]

Interpolation from plots of H_0 against concentration of electrolyte gave the values of h_0 which are included in Table 1 and plotted against the rate coefficients, k_2, in the Figure, where the data given by Branch and Jones[5] for *p*-nitroanisole are treated similarly.

Products of Bromination of Biphenyl.—The $\frac{1}{2}o : p$-ratio for bromination of biphenyl under various conditions was determined by vapour-phase chromatographic analysis. The reactions were carried out at concentrations (biphenyl, *ca.* 0·005M; hypobromous acid, *ca.* 0·0025M) approximating to those used for the kinetic measurements. The reaction was allowed to proceed for more than ten half-lives, the concentration of hypobromous acid being then reduced nearly to zero. The reaction mixture was then poured on to a mixture of ice and aqueous sodium hydroxide in amount sufficient to neutralise the acetic acid. The mixture was extracted four times with benzene: the extract was washed with water and almost all the benzene was distilled

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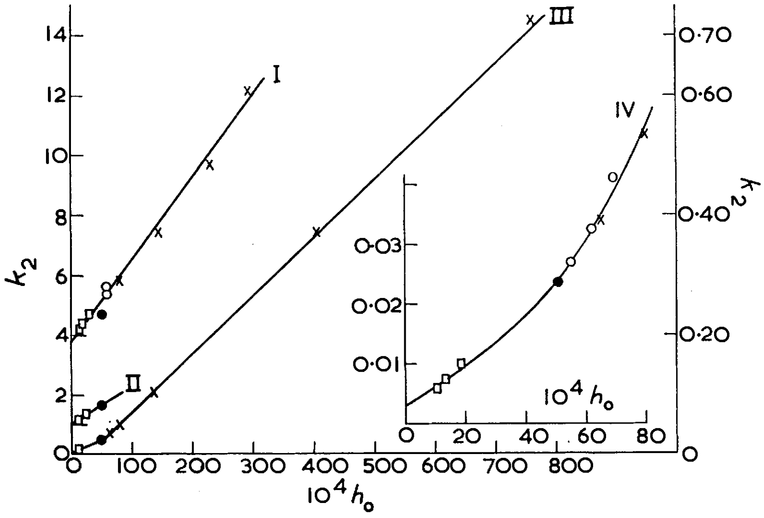
[14] Bascombe and Bell, *J.*, 1959, 1096.

[15] Wiberg and Evans, *J. Amer. Chem. Soc.*, 1958, **80**, 3019.

off. The relative quantities of 2- and 4-bromobiphenyl in the residue were determined by vapour-phase chromatography at 200° on a column of 20% Apiezon-M on Celite (60—80 mesh).[16] The only compounds detected were biphenyl, 4-bromobiphenyl, and 2-bromobiphenyl; neither 3-bromobiphenyl nor any dibrominated product was noted, and the method was shown by examination of suitable mixtures to be sensitive enough to detect 1% of either of these had either bee present.



Bromination in 75% acetic acid.

I, Biphenyl, 0·9° (left-hand scale). II, *p*-Nitroanisole, 19·8° (ref. 5; $10k_2$ plotted; left-hand scale). III, Benzene, 0·9° (right-hand scale). IV, Benzene, 0·9°.

● No added electrolyte. × HClO_4. □ NaOAc. ○ NaClO_4.

Table 3 gives the results of these analyses.

TABLE 3.

Percentages of 4-bromobiphenyl in the monobromobiphenyls obtained by bromination of biphenyl in 75% acetic acid.

At 1·0°: (*a*) HClO_4 (M)	0·0	0·008	0·016	0·034	0·11	0·16	0·20
4-Bromobiphenyl (%)......	75	68	65	53	47	46	46 (44,* 46 †)
(*b*) NaOAc (M)	0·005	0·01					
4-Bromobiphenyl (%)......	79	79	(78,* 78†)				

* At 25·0°. † At 50·0°.

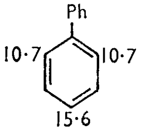
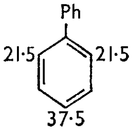
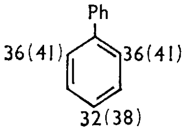
DISCUSSION

(i) *The Positive Brominating Species.*—(*a*) *Kinetic form.* The reactions uniformly followed second-order kinetics, $-\text{d}[\text{BrOH}]/\text{d}t = k_2[\text{ArH}][\text{BrOH}]$, within experimental error. Branch and Jones,[5] who earlier studied the bromination of *p*-nitroanisole in 75% acetic acid with and without added electrolytes, concluded, from the form of the catalysis by acid and anticatalysis by base, that the effective brominating species was positively charged. For biphenyl, as for *p*-nitroanisole, there is no doubt that a positively charged species makes a contribution to the reactivity. The rate increases with molar concentration of perchloric acid, and is very nearly linear with h_0 (as measured by the extent of protonation of *m*-nitroaniline). In the presence of sodium perchlorate or of sodium

[16] Johnson, in " Steric Effects in Conjugated Systems," ed. Gray, Butterworths Scientific Publns. London, 1958, p. 174.

acetate the rate is still well predicted by the value of h_0, and there is no definite indication of any environmental effect on the rate caused by the presence of electrolytes, though the reaction is very fast, and a small effect of this sort cannot be excluded in view of the experimental uncertainty.

The bromination of benzene in the presence of perchloric acid has the same characteristics. Its rate of reaction is slower than that of biphenyl, and satisfactory measurements were made with perchloric acid in concentration up to 0·1M. There is a considerable range over which the rate of reaction is linear with h_0, as measured by the extent of protonation of *m*-nitroaniline and of *p*-nitroaniline.

Partial rate factors:			
	(I)	(II)	(III)
Reagent and conditions:	Positive bromine 50% dioxan 25°	Positive bromine AcOH 0·9°	NO_2^+ Ac_2O 0°
Rel. rate (PhH = 1) …………	12·5	26·9	35

(*b*) *Products of bromination of biphenyl.* Previously it had been shown that, whereas bromination of biphenyl by molecular bromine gives very little *ortho*-substitution,[17 cf. 18] bromination by positive bromine gives more *ortho*- than *para*-substituted product,[10] there being formed 42·5% of *p*-bromobiphenyl ($\frac{1}{2}o : p = 0{\cdot}68$) in 50% dioxan at 25° under catalysis by perchloric acid. The limiting amount of *p*-bromobiphenyl which we now find to be formed by bromination in 75% acetic acid is 46% ($\frac{1}{2}o : p = 0{\cdot}59$), a result which confirms that *ortho*- predominates over *para*-substitution in bromination by a positive reagent. Since only 1·5% of *meta*-substitution was revealed by our previous investigation, very little *meta*-substituted product would have been expected in the present experiments; and with the less sensitive method of determination used in the present study, none was found, nor was there any sign of disubstitution.

(*c*) *Partial rate factors; the* $\frac{1}{2}$o : p-*ratio.* From the plots of rate against h_0, the third-order velocity-coefficient ($k_3 = k_2/h_0$, based on the rate equation $-d[BrOH]/dt = k_3[BrOH][ArH]h_0$) can be calculated to have the values 275 l.^{2} mole^{-2} sec.$^{-1}$ for biphenyl and 10·2 l.^{2} mole^{-2} sec.$^{-1}$ for benzene at 0·9°. From these values, and the isomeric proportions, partial rate factors can be calculated as shown. The values for nitration, given for comparison, are from two reasonably concordant investigations.[19, 20]

The extent of activation of the *ortho*- and *para*-positions is similar for bromination and nitration, though there are significant differences between the two brominating species, a fact which will be discussed below. The $\frac{1}{2}o : p$-ratio is very nearly the same for the two conditions of bromination, and is significantly less than that for nitration. This is a point of difference on which we commented in earlier papers.[10, 21; cf. 20] It now seems most unlikely that there is any considerable difference in entropy of activation for substitution at the *ortho*- and the *para*-position, since in the present experiments the $\frac{1}{2}o : p$-ratio was not far from unity and was unchanged within experimental error over the range 0—50°. So it seems quite unlikely that entropic steric effects are significant in determining the $\frac{1}{2}o : p$-ratios.

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[17] Berliner and Powers, *J. Amer. Chem. Soc.*, 1961, **83**, 905.
[18] Buckles, Hausman, and Wheeler, *J. Amer. Chem. Soc.*, 1950, **72**, 2494.
[19] Simamura and Mizumo, *Bull. Chem. Soc. Japan*, 1957, **30**, 196.
[20] Billing and Norman, *J.*, 1961, 3885.
[21] de la Mare and Hassan, *J.*, 1958, 1519.

(*d*) *Nature of the positive species.* The positive brominating species to which we have been referring could be Br^+, $BrOH_2^+$, or $BrOHAc^+$. The relative rates of reaction in various solvents throw some light on this problem. Table 4 gives estimated values for benzene at 25°.

A good deal of the difference in rate between the different solvents can be attributed to the differing protonating power of perchloric acid. There is no definite evidence from the present data that the positively charged brominating species in aqueous acetic acid is fundamentally different from that in water or aqueous dioxan, for which solvent it has been argued [13] (though not made certain) that the active species is probably $BrOH_2^+$.

(ii) *The Neutral Brominating Species.*—The kinetics of the reaction show clearly that there is a component of reactivity which is not dependent on the acidity of the medium. If the rate is plotted against either the concentration of acid (the acidity of 75% acetic acid [6, 23] is taken as 0·01M) or against the value of h_0 (Figure), the rate of reaction when extrapolated to zero acidity is finite. This is so even for benzene, though here to obtain a satisfactory extrapolation it is essential to use measurements made in the presence of sodium acetate; but the neutral component of the rate is very large and obvious both for biphenyl and for *p*-nitroanisole.[5]

TABLE 4.

Solvent-effect in bromination of benzene by positive bromine.

Solvent	k_2/h_0 (l. mole^{-1} sec.$^{-1}$)	$k_2/[HClO_4]$ (l. mole^{-1} sec.$^{-1}$)	Ref.
Water	20	20	13
50% Dioxan	(6) *	0·6	4
75% Acetic acid	40 †	40	This paper

* It is assumed that $h_0 = 0{\cdot}02$ for 0·2M-$HClO_4$ by interpolation between 40% dioxan and 60% dioxan.[22] † Extrapolated from results at lower temperatures.

Such a result means that there is a component of the rate which follows the kinetic form: $-d[BrOH]/dt = k[ArH][BrOAc]$. Bearing in mind the analogy with the results for chlorination, in which we consider that we have shown [7, 8] that chlorine acetate is the effective electrophile concerned in chlorinations by hypochlorous acid in aqueous acetic acid, we now propose that bromine acetate is the electrophile concerned in the related neutral brominations.

This conclusion is supported by the change in $\frac{1}{2}o : p$-ratio observed in the bromination of biphenyl when perchloric acid is added to the reaction mixture. The limiting percentage of *para*-substitution in the nearly non-acidic solutions (when sodium acetate has been added) is 79% ($\frac{1}{2}o : p = 0{\cdot}13$), and as the acidity of the medium is made greater there is a decrease in amount of *para*-substitution, until when from the rate of the reaction it would be judged that substantially all the bromination is by the positive species, the value approaches that for bromination by acidified hypobromous acid in aqueous dioxan, becoming in fact 46% ($\frac{1}{2}o : p = 0{\cdot}59$). A relatively high value for the proportion of *para*-substitution would be expected for a neutral reagent, by analogy with that established by Berliner, Zimmerman, and Pearson [24] for molecular bromination in 50% acetic acid, namely 93·9% ($\frac{1}{2}o : p = 0{\cdot}03$).

Our values enable us to calculate partial rate factors for bromination of biphenyl by our neutral reagent. They must be regarded as approximate; the extrapolation of the results to zero acidity is less satisfactory for benzene (for which we have adopted the value $k_2^{extrap} = 0{\cdot}003$; see Figure) than for biphenyl ($k_2^{extrap} = 3{\cdot}8$) because the neutral rate

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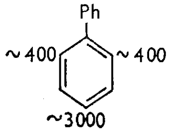
[22] Bunton, Ley, Rhind-Tutt, and Vernon, *J.*, 1957, 2327.
[23] Kipling, *J.*, 1952, 2858.
[24] Berliner, Zimmerman, and Pearson, unpublished results; see ref. 17.

for the former compound is so small. The results are in diagram IV, below; those for molecular bromine [17, 24] (V) and for molecular chlorine [25] (VI) are given for comparison.

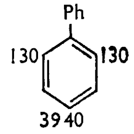
It appears that bromine acetate, like molecular bromine, gives a considerable rate-spread in a reaction such as this, where it can exert its electron-demanding power, and therefore that reaction with this reagent will be found to have a high ρ-value when H. C. Brown's modified Hammett equation [26] is applied to its reaction. The $\frac{1}{2}o : p$-ratio, though low, is not as low as for molecular bromine; for both these reagents it seems probable that there is substantial steric inhibition of attack on the *ortho*-position in biphenyl.

It is noteworthy that the rate of reaction of bromine acetate with biphenyl in 75% acetic acid is very fast (k_2 = 15 l. mole^{-1} sec.$^{-1}$ at 25°, by extrapolation from results at lower temperatures). The corresponding value for reaction with molecular bromine in 50% acetic acid [17] is 0·0006 l. mole^{-1} sec.$^{-1}$. So bromine acetate must be at least 20,000 times more reactive than molecular bromine, even if it is present as the bulk bromine-containing component of the reaction mixture in aqueous acetic acid.

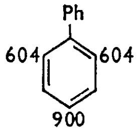
Partial rate factors:



(IV)



(V)



(VI)*

	(IV)	(V)	(VI)*
Reagent and conditions:	BrOAc 75% AcOH 0·9°	Br_2 50% AcOH 25°	Cl_2 AcOH 25°
Rel. rate (PhH = 1)	~1270	1400	422

* These values have been calculated by assuming that the relative rates of attack on the *ortho*- and the *para*-position are given by the proportions of *ortho*- and *para*-substituted monochloro-derivatives found in the products. For a justification of the procedure (necessary for chlorination, since some chlorine is used up in forming adducts [25]), see Part XIV.[1]

Much of the difference in reactivity between bromine and bromine acetate appears to be contained in the energy of activation. Berliner and Powers [17] record a value of 17·1 kcal. mole^{-1} for molecular bromine in 50% acetic acid, and our results for bromine acetate in 75% acetic acid give a value of 7·9 kcal. mole^{-1}. The latter value is, however, composite, since the equilibrium BrOH + HOAc $\rightleftharpoons$ BrOAc + H_2O is also concerned, so further discussion of this point is not justified. It is, however, valid to argue that the $\frac{1}{2}o : p$-ratio for bromination by bromine acetate varies little with a considerable temperature change, and so, as has already been pointed out in regard to acid-catalysed bromination, it is unlikely that entropy factors specified to the *ortho*-position are much concerned in determining the $\frac{1}{2}o : p$-ratio.

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[25] Beaven, de la Mare, Hassan, Johnson, and Klassen, *J.*, 1961, 2749.
[26] Brown and Okomoto, *J. Amer. Chem. Soc.*, 1957, **79**, 1913.