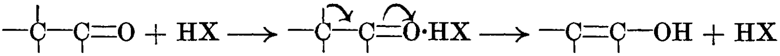
160. *Constitutional Factors controlling Prototropic Changes in Carbonyl Compounds. Part II. Acid and Base Catalysis in the Bromination of Halogenated Acetones.*

By Herbert Ben Watson and Edmund Denys Yates.

It has long been known that prototropic changes are accelerated by both hydrogen and hydroxyl ions, and the work of Dawson, Brönsted, and others (for full references, see Ingold, J., 1930, 1033) has shown that undissociated molecules and the anions of weak acids must also be included in the list of catalysts. As Dawson and Key (J., 1928, 543) point out, however, "it seems probable that the activity of all such ions and molecules depends on their acid or basic character, that is to say, on their ability to act as proton donators or proton acceptors," this being, in reality, a re-statement of Lowry's view (J., 1925, 1383). There can be no doubt, indeed, that a prototropic change may proceed by two different mechanisms, as originally suggested by Lapworth and Hann (J., 1902, **81**, 1513) in the following words: "it is possible that a desmotropic or tautomeric change may be the result of one or both of two superposed reactions, one due to ionisation of the compound itself, accelerated by bases and retarded by acids, and the other due to an additive phenomenon, accelerated by acids and retarded by bases." Later, Lapworth (*Mem. Manchester Phil. Soc.*, 1920, **64**, 13) put forward the conception of direct removal of the proton by a basic catalyst. Similar views are expressed by Ingold (*loc. cit.*) in the suggestion that in basic catalysis the reactant confers on the catalyst a positive charge, while in acid catalysis the reactant receives from the catalyst a positive charge, and the two mechanisms are implied in Baker's classification of catalysts (J., 1928, 1584) as those which attack the ionising proton directly (bases) and those which facilitate indirectly its liberation (acids).

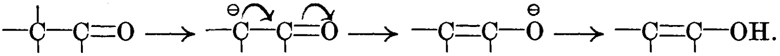
In the special case of a keto-enol change, an " acid mechanism " suggested by Hughes and Watson (J., 1929, 1949) is as follows :



$$-\overset{|}{\underset{|}{C}}-\underset{|}{C}=O + HX \longrightarrow -\overset{|}{\underset{|}{C}}-\underset{|}{C}=O\cdot HX \longrightarrow -\underset{|}{C}=\underset{|}{C}-OH + HX$$

Ketone. Complex. Enol.

where $X = H_2O$ (for catalysis by the oxonium ion), an anion (for undissociated acid), or OH (for water); for the " basic mechanism " a sequence of the following type is probable, the scheme being not fundamentally different from that suggested by Lowry (J., 1927, 2559; compare also Lapworth, *loc. cit.*):



$$-\overset{|}{\underset{|}{C}}-\underset{|}{C}=O \longrightarrow -\overset{\ominus}{\underset{|}{C}}-\underset{|}{C}=O \longrightarrow -\underset{|}{C}=\underset{|}{C}-\overset{\ominus}{O} \longrightarrow -\underset{|}{C}=\underset{|}{C}-OH.$$

Ketone. Ketonic ion. Enolic ion. Enol.

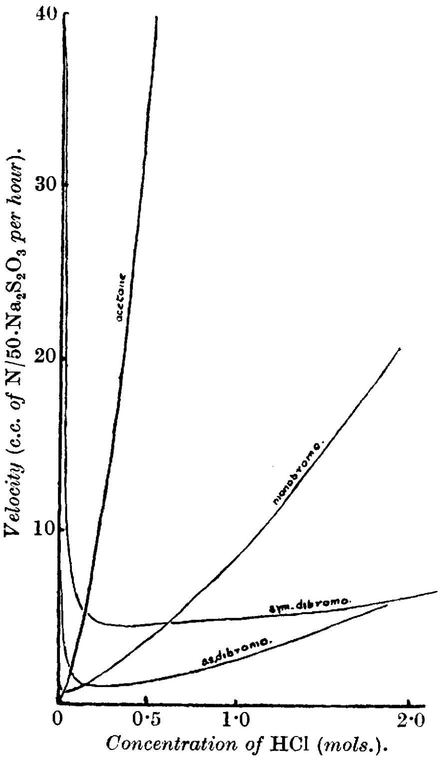
Chief among the basic catalysts which will promote such a series of changes are the anions of weak acids (of which hydroxyl is a special example), and the increasing activity of these ions as the strength of the corresponding acid diminishes is obviously due to increasing ability to act as proton acceptor.

The influence of the substituent upon the prototropy of a monohalogenated acetone has been discussed in Part I of this series (Hughes, Watson, and Yates, J., 1931, 3318). It was there shown that while, in absence of acid, bromoacetone passes into its enolic form more quickly than acetone, the prototropic change is accelerated by acids to a much smaller extent, and the interpretation suggested was that the electron affinity of the halogen atom (— *I*) causes (*a*) a diminution in the capacity of the ketone for co-ordination with an acid, the change through the " acid mechanism " being thus rendered far less rapid, and (*b*) an increased readiness of the proton to ionise. If these effects are operative in monobromoacetone, they should also be observed, but in an enhanced degree, in the higher halogenated acetones, and this expectation has been fully realised in the investigation now described.

We have examined the kinetics of bromination of a number of halogen-substituted acetones, and in every case the speed of disappearance of the halogen is independent of its concentration; the velocity measured is therefore, as in the case of acetone itself, that of the tautomeric change, which is followed by relatively instantaneous reaction with the halogen. No detectable quantity of enolide is present in any of the ketones, since the measurable reaction is never preceded by an instantaneous disappearance of any of the bromine. The medium used in our experiments was 50% acetic acid, owing to the low solubility in water of the majority of the ketones; the work differs therefore from that described in

Part I (aqueous solution) in that acetate ions and un-ionised acetic acid molecules are always present. The speeds of bromination of $0{\cdot}1M$-solutions of the ketones in presence of various concentrations of added hydrochloric acid (0 to $2M$) were measured, and the very marked effect of the halogen substituents in decreasing the activity of acid catalysts is seen by an inspection of the slopes of the curves in Fig. 1, where velocity is plotted against concentration of added hydrochloric acid. An accompanying increase in the facility with which a proton is removed is suggested by our observation that very dilute aqueous solutions of all the bromoacetones have a definite hydrogen-ion concentration; the ketones are therefore strong enough acids to yield up their proton to the weak acceptor, water, and this characteristic becomes stronger as the number of bromine atoms increases.

FIG. 1.

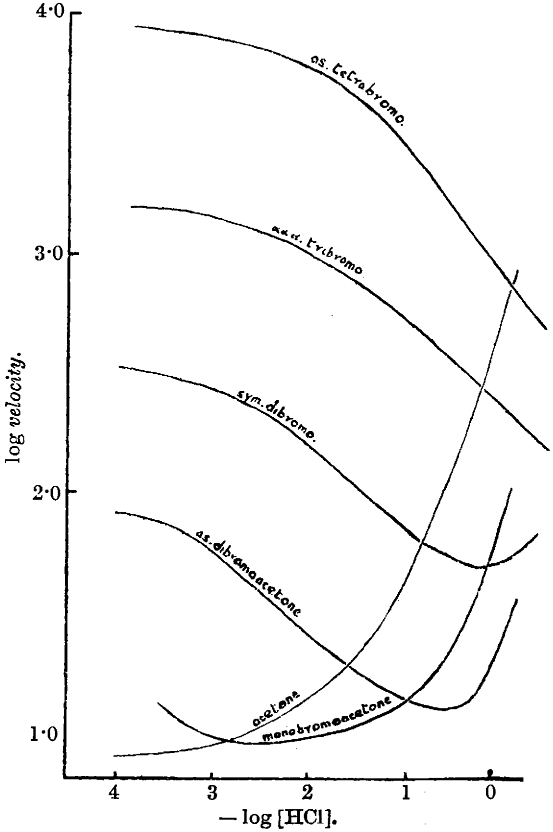


The influence of substituent halogen atoms is shown most clearly, however, when the relative efficiencies of acid and basic catalysts (*i.e.*, the ratio $k_{\text{acid}}/k_{\text{base}}$) are considered. On our view, the effect of the halogen will be a decrease in this ratio, for not only will acid catalysts be rendered less active (k_{acid} smaller), but the increased ease with which the proton ionises will give a greater activity to basic catalysts (k_{base} greater). This is in harmony with Dawson and Carter's observation (J., 1926, 2294) that the influence of acid catalysts on the reaction of chloroacetone with iodine is smaller in comparison with that of basic catalysts than is the case in the acetone–iodine reaction. Moreover, Ingold (*loc. cit.*, pp. 1036, 1038) has pointed out that, for catalysis by hydrogen and hydroxyl ions in ester hydrolysis, the ratio $k_{\text{H}}/k_{\text{OH}}$ is a measure of the polarity of the groups R and R′ in the ester R·CO$_2$R′; he finds, for example, that the ratio has a lower value for chloroacetic than for acetic esters.

In our experiments on the halogen-substituted acetones, we find that the simplest method of demonstrating a change in the value of the ratio $k_{\text{acid}}/k_{\text{base}}$ consists in the determination of the conditions under which the velocity of the prototropic change has its minimum value. Dawson and Carter (*loc. cit.*, p. 2287) have shown that, as the concentration of hydrogen ion falls, the speed of iodination of acetone in aqueous solutions containing acetic acid (constant) and sodium acetate (variable) decreases, passes through a minimum, and again increases, and this phenomenon has been observed in other reactions which are susceptible to catalysis by both acids and bases (*e.g.*, ester hydrolysis, Dawson and Lowson, J., 1927, 2107; Ingold, *loc. cit.*). It is evident that on one side of the minimum point the prototropic change proceeds mainly through the "acid mechanism," and on the other side mainly through the "basic mechanism." Throughout our experiments (in 50% acetic acid) the concentration of un-ionised acetic acid does not change appreciably, while hydrogen and acetate ions are present in variable concentration, and the point of minimum velocity is characterised, as in the work of Dawson and Dean (J., 1926, 2873) by the equality of the effects of these ions, *i.e.*, $(v_{\text{H}})_i = (v_{\text{A}})_i$, or $k_{\text{H}}[\text{H}^{\bullet}]_i = k_{\text{A}}[\text{A}']$. It is evident that if, in a halogenated acetone, the *efficiency* of acid catalysts relative to that of basic catalysts is smaller than in acetone ($k_{\text{H}}/k_{\text{A}}$ smaller), a higher concentration of hydrogen ion will be required to produce equality of the catalytic *effects*. The anticipated fall in the ratio $k_{\text{acid}}/k_{\text{base}}$ should therefore be expressed as a displacement of the minimum point in the direction of higher acid concentration. Dawson and Dean (*loc. cit.*) have, in fact, deduced the quantitative relationship $[\text{H}^{\bullet}]_i = \sqrt{KCk_{\text{A}}/(k_{\text{H}} - k_{\text{M}})}$, which for a weak acid reduces to $[\text{H}^{\bullet}]_i = \sqrt{KCk_{\text{A}}/k_{\text{H}}}$, where K and C are respectively the dissociation constant and the concentration of the acid. Solutions of hydrogen chloride in 50% acetic acid are obviously unsuitable for quantitative treatment, but Dawson and Dean's expression nevertheless supports our argument that a decrease in the value of $k_{\text{H}}/k_{\text{A}}$ should lead to an increase in $[\text{H}^{\bullet}]_i$.

Our results, which will be made clear by reference to Fig. 2, have demonstrated that displacement of the minimum point occurs to a very marked extent, the acid concentration at this point increasing steadily as halogen atoms are successively introduced into the acetone molecule. In 50% acetic acid the minimum point for acetone itself ($p_{\text{H}} = 4$ in Dawson and Dean's experiments) is not detected, but the velocity of the autocatalysed bromination of monobromo- and of monochloro-acetone reaches its minimum value when the concentration of hydrogen bromide formed is 0·002*M* (± 0·0005); *i.e.*, $[H^{\cdot}]_i$ is greater than for the unsubstituted ketone. A careful inspection of the figures recorded in Part I (p. 3324) reveals a minimum in the velocity of bromination of bromoacetone (but not of acetone) in aqueous solution, and the earliest stages of the autocatalysed reaction must here proceed mainly through the "basic mechanism" with water as proton acceptor. The "short initial period of greater speed" observed by Hughes and Watson (*loc. cit.*, p. 1948) in the bromination of pyruvic acid, and attributed to "the formation of a small amount of unsaturated impurity," may also be due to a reaction through the "basic mechanism."

Fig. 2.



The bromination of dibromoacetone has its minimum velocity at a much higher concentration of acid than in the case of monobromoacetone, the concentration of added hydrogen chloride being 0·2M for the asymmetrical and 0·45—0·5M for the symmetrical derivative, and experiment thus confirms expectation. The most striking confirmation of our view regarding the influence of halogen substituents was obtained, however, by the extension of the investigation to include more highly substituted acetones, when a remarkable fact was revealed. The bromination of $\alpha\alpha\alpha$-tribromoacetone and of *as*.-tetrabromoacetone becomes continuously slower as hydrochloric acid is added, even up to 2M concentration, *i.e.*, the concentration of acid necessary to give the minimum velocity is greater than this value. This appears to be the first recorded example of a definite retardation of enolisation by the addition of considerable quantities of a strong acid, but it obviously differs from the well-known cases only in the fact that the minimum point occurs at a high concentration of hydrogen ion. Comparable results were obtained in another series of experiments where 0·5M solutions of the ketones in 75% acetic acid were examined.

The continuous and very considerable displacement of the minimum point which accompanies the substitution of hydrogen by halogen indicates, as pointed out above, a progressive diminution in the activity of acid catalysts relative to basic catalysts; in other words, the sequence of changes constituting the " acid mechanism " is rendered continuously less facile than that constituting the " basic mechanism." In the case of tri- and tetra-bromoacetones, indeed, reaction occurs through the latter mechanism even in presence of high concentrations of acid. The observations recorded in this communication thus provide strong evidence in support of our views regarding the influence of electron-attracting substituents ($-I$ effect) upon the prototropy of carbonyl compounds. The work is now being extended to include a study of substituents other than halogens.

EXPERIMENTAL.

Preparation of Materials.—Mono- and di-brominated acetones were prepared from acetone as described in Part I; $\alpha\alpha\alpha$-tribromoacetone (which has now been obtained as a solid, m. p. 26°) and *as*.-tetrabromoacetone from *iso*propyl alcohol (Dippy, Watson, and Yates, J., 1931, 2508), or, equally easily, from acetone. The chloroacetones were purchased from Messrs. British Drug Houses and purified by distillation under low pressure (monochloro-) and crystallisation from light petroleum (dichloro-). The acetic acid was purified by the method of Orton and Bradfield (J., 1927, 983).

Products of Bromination of as.-*Dibromoacetone.*—47 G. of the ketone were dissolved in 200 c.c. of 75% acetic acid, 11·7 c.c. of bromine (1 mol.) added, and the mixture kept till colourless. On addition of sodium carbonate, an oil separated; this was removed, the aqueous layer extracted with ether, and oil and extract dried over anhydrous sodium sulphate. Repeated fractionation gave the following: unchanged dibromoacetone (8 g.), $\alpha\alpha\alpha$-tribromoacetone (31 g.; b. p. 106—107°/9 mm., m. p. 26°. Found: Br, 81·2. Calc.: Br, 81·3%), $\alpha\alpha\alpha'$-tribromoacetone (6 g.; b. p. 85—88°/9 mm. Found: Br, 80·6%. Gave no carbylamine with aniline and potash), higher brominated products (7 g. Found: Br, 87·4. Calc. for tetrabromoacetone: Br, 85·5%). The very large proportion of the $\alpha\alpha\alpha$-tribrominated derivative is doubtless to be ascribed to the fact that the reaction occurs almost entirely by the basic mechanism, which will result in the removal of the proton most influenced by, and therefore nearest to, the bromine atoms. Co-ordination with an acid catalyst, on the other hand, causes activation of both alkyl groups.

Kinetic Measurements.—It was impossible to eliminate the reaction of hydrogen iodide with the higher brominated acetones by the use of a buffer solution as described in Part I, and attempts to determine the bromine by arsenious acid, a sulphite, or a ferrous salt were unsuccessful. The velocity measurements (all at 25°) were therefore carried out as follows. To the desired quantities of ketone and catalyst in 50% or 75% acetic acid, different volumes of a solution of bromine in the same medium were added to give 25 c.c. of reaction mixture, and the time required for the complete disappearance of the colour of the halogen was observed (compare Meyer, *Annalen*, 1911, **380**, 235; Dawson and Key, J., 1928, 2154). This point could be detected with considerable accuracy. The amount of bromine added was determined by addition of an equal portion to potassium iodide and titration with thiosulphate. The accuracy of the method was checked by comparison with the usual titration process; the following figures for 0·5*M*-ketone and 0·5*M*-hydrochloric acid in 75% acetic acid are typical; they refer to fall in bromine concentration (*M*) per hour:

	Acetone.
Titration	

In presence of excess of ketone and of hydrochloric acid, the velocity of bromination is independent of the concentration of bromine, and the straight line connecting this concentration with time passes through the origin (absence of enol). The figures in the following table refer to bromination in 75% acetic acid, concentrations of ketone and hydrochloric acid being 0·5*M*. The three columns give initial *N*/10-titre (*c*), time in minutes (*t*), and fall in titre per hour (*k*).

$CH_2Br\cdot CO\cdot CH_3$.			$CHBr_2\cdot CO\cdot CH_3$.			$CH_2Br\cdot CO\cdot CH_2Br$.		
c.	*t.*	*k.*	*c.*	*t.*	*k.*	*c.*	*t.*	*k.*
3·82	32	7·15	2·78	71·5	2·38	3·90	117	1·95
9·30	80	7·00	9·68	240	2·42	7·85	416	1·90
13·28	116	6·88	16·80	455	2·40			

$CBr_3\cdot CO\cdot CH_3$.			$CBr_3\cdot CO\cdot CH_2Br$.		
c.	*t.*	*k.*	*c.*	*t.*	*k.*
9·35	62·5	8·98	3·92	8·9	26·5
13·30	137	8·98	7·78	17·3	26·8
			15·32	34·3	26·8

The next table indicates the speed of bromination in presence of various amounts of added hydrochloric acid. The curves in Figs. 1 and 2 are constructed from these data, together with the values for lower concentrations of halogen acid, obtained in some cases by similar measurements, and in others from the slope of the appropriate portion of the curve for the reaction when no halogen acid is present initially. The figures represent fall in *N*/10-thiosulphate titre per hour, for 0·1*M*-solutions of the ketones in 50% acetic acid.

HCl added (*M*).	0·5*M*.	1·0*M*.	2·0*M*.
$CH_3\cdot CO\cdot CH_3$	4·85	11·95	—
$CH_2Br\cdot CO\cdot CH_3$	0·75	1·70	—
$CH_2Cl\cdot CO\cdot CH_3$	0·68	1·55	—
$CH_2Br\cdot CO\cdot CH_2Br$	0·95	1·00	1·28
$CH_2Cl\cdot CO\cdot CH_2Cl$	0·56	0·64	0·86
$CHBr_2\cdot CO\cdot CH_3$	0·28	0·55	—
$CBr_3\cdot CO\cdot CH_3$	—	4·50	3·50
$CBr_3\cdot CO\cdot CH_2Br$	—	15·80	11·00

The following figures give the speed of bromination when no hydrochloric acid is added initially (" autocatalysed reaction "). They refer to 0·1*M*-solutions of the ketones in 50% acetic acid, and represent the time in minutes required for the fall of *x* c.c. in *N*/10-thiosulphate titre.

x =	1.	2.	5.	10.
$CH_3\cdot CO\cdot CH_3$	72	138	330	—
$CH_2Br\cdot CO\cdot CH_3$	49	106	315	575
$CH_2Cl\cdot CO\cdot CH_3$	14	72	290	585
$CH_2Br\cdot CO\cdot CH_2Br$	2·05	4·1	11·1	24·5
$CHBr_2\cdot CO\cdot CH_3$	8·1	17·5	54	137
$CBr_3\cdot CO\cdot CH_3$	0·4	0·8	2·05	4·15
$CBr_3\cdot CO\cdot CH_2Br$	—	0·15	0·40	0·85

Ionisation of Brominated Acetones.—The p_H values of *M*/400-solutions of the ketones in pure water were determined by the indicator method, standards for comparison being prepared from mixtures of 0·2*N*-acetic acid and -sodium acetate (Walpole, J., 1914, **105**, 2509). The solutions were free from bromide ion, and the hydrogen ions are therefore not produced by hydrolysis. The ionisation occurs at a slow rate, and a constant p_H value was reached only after several hours; it is hoped shortly to carry out a more detailed investigation of this point.

Ketone.	Indicator.	p_H by using 0·05 c.c. of indicator.	p_H by using 0·1 c.c. of indicator.
$CH_3{\cdot}CO{\cdot}CH_3$	Rosolic acid	6·5	7
$CH_2Br{\cdot}CO{\cdot}CH_3$	Methyl-red	5·5	5·4
$CHBr_2{\cdot}CO{\cdot}CH_3$	Methyl-red	4·5	4·7
$CH_2Br{\cdot}CO{\cdot}CH_2Br$	Methyl-orange	4·3	4·3
$CBr_3{\cdot}CO{\cdot}CH_3$	Methyl-orange	3·8	3·8
$CBr_3{\cdot}CO{\cdot}CH_2Br$	Thymol-blue	2·8	2·8

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