

CCCCLX.—*Constitutional Factors controlling Prototropic Changes in Carbonyl Compounds. Part I. The Relative Speeds of Enolisation of Acetone and Bromoacetone and the Effect of the Acid Catalyst.*

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It was first shown by Lapworth (J., 1904, **85**, 30) that the reaction of bromine with acetone in dilute aqueous solution occurs in two stages, that in which the halogen takes part being too rapid for measurement, and he suggested that the ketone changes at a relatively slow speed to its enolic form, which is brominated instantaneously :

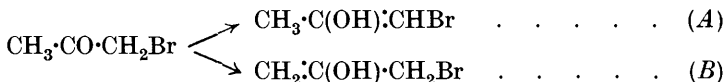


This interpretation is equally applicable to the bromination of acetone in anhydrous solvents (Watson, J., 1927, 3065; Hughes and Watson, *ibid.*, 1929, 1945),* where a variable latent period is followed by rapid disappearance of bromine, the latent period being removed and the reaction rendered much slower by the presence of a little water. Lapworth's view being adopted, these observations are easy to understand, since prototropic changes are not spontaneous (Lowry, J., 1899, **75**, 221; 1925, **127**, 1382), and are catalysed to an extraordinary degree by covalent acids (Meyer,

* Similar results have been recorded more recently by Cohen (*J. Amer. Chem. Soc.*, 1930, **52**, 2827), who, however, overlooked the initial latent period, even in presence of a little quinoline (compare Watson, *loc. cit.*).

Annalen, 1911, **380**, 238). Since Lapworth's original observation the results of various workers have led to the conclusion that the reactions of halogens with carbonyl compounds in general (excluding the majority of carboxylic acids) are preceded by a change of the carbonyl compound to its enolide (for summary, see Watson, *Chem. Reviews*, 1930, **7**, 173). The latter reacts instantaneously with halogen, and the speed of the keto-enol change may therefore be determined conveniently by measurement of the velocity of bromination. This method is now being employed at these laboratories in an investigation of the enolisation of various ketones and allied compounds, the aim being to throw further light on the factors which influence prototropic changes.

According to Sokolowsky (*Ber.*, 1876, **9**, 1687), the reaction of bromoacetone with one mol. of bromine leads to *as.*-dibromoacetone. We find, however, that in aqueous hydrochloric acid both dibromoacetones are obtained in approximately equal amounts, together with small quantities of higher brominated products. Kinetic measurements have shown that the velocity of bromination of bromoacetone in aqueous solution is independent of the concentration of the halogen, and it may be concluded that the ketone first passes into an enolic form (*A* or *B*)



each of these changes being followed by very rapid reaction with bromine.

The mechanism of bromination of bromoacetone is thus completely similar to that established by Lapworth for acetone. When, however, the actual *speeds* are compared, an interesting position is revealed. It is to be anticipated that the strong electron-affinity of the halogen atom ($-I^*$) will facilitate the ionising of the α -proton, and thus accelerate enolisation :



* The terms "inductive effect" (*I*) and "tautomeric effect" (*T*), as used in this series of communications, are intended to convey the meaning assigned to them by Ingold and his collaborators in numerous writings (*e.g.*, *Ann. Reports*, 1926, 140).

† The electron repulsion of methyl ($+I$) is decreased by the substitution of halogen; compare the percentages of *m*-derivative formed in the nitration of benzyl bromide (6.6%, Flürscheim and Holmes, *J.*, 1928, 1607) and toluene (4.4%).

This is actually the case, for in aqueous solution and *in absence of catalyst* bromoacetone reacts with bromine more quickly than does acetone. The autocatalytic influence of the hydrogen bromide is vastly different in the two cases, however; the bromination of acetone is accelerated very markedly as halogen acid accumulates in the system, but there is no appreciable autocatalysis in the case of bromoacetone. The same contrast is observed when hydrochloric acid is present initially; its effect on the speed of bromination of bromoacetone is relatively slight, while acetone now reacts at a much greater speed. This will be made clear by the figures below, where v represents the fall in $N/50$ -thiosulphate titre per hour.

Bromination in aqueous solution at 25°. [Ketone] = 0.25*M*.

Mols. ketone/mols. bromine = 20.

	Acetone.				Bromoacetone.		
HCl, <i>M</i>	0	0.5	1.0	HCl, <i>M</i>	0	0.5	1.0
v	0.10	12.88	27.75	v	0.50	2.22	3.85

These results are in harmony with the proportions of the products obtained when acetone reacts with one mol. of bromine. Even in absence of *added* catalyst, the halogen acid produced during the course of the reaction will accelerate the bromination of the acetone so powerfully that but little of the halogen will react with the bromoacetone. Thus, Sokolowsky (*loc. cit.*), Emmerling and Wagner (*Annalen*, 1880, **204**, 27), Brendler and Tafel (*Ber.*, 1898, **31**, 2683), Nef (*Annalen*, 1904, **335**, 259), and Lapworth (*loc. cit.*) obtained monobromoacetone almost entirely, and the product isolated by us contained some 88 mols. % of monobrominated derivative. A study (Hughes and Watson, *loc. cit.*) of the bromination of pyruvic and lævulic acids revealed a similar contrast in the effect of the acid catalyst :

Pyruvic acid = 1.0*M*.

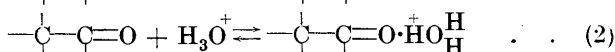
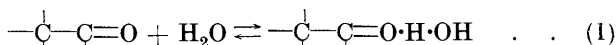
Catalyst.	Fall in titre in 2 hrs.
None	1.70
HCl = 1.15 <i>M</i>	1.85
HBr = 1.7 <i>M</i>	2.00

Lævulic acid = 0.7*M*.

Catalyst.	Fall of titre in 2 hrs.
None	0.15
HCl = 0.46 <i>M</i>	6.30
HBr = 0.69 <i>M</i>	7.90

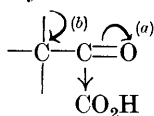
The results outlined above may be summarised as follows. The enolisation of acetone and of lævulic acid in aqueous solution proceeds very slowly in absence of catalyst, but is accelerated very powerfully by acids, whilst that of bromoacetone and of pyruvic acid proceeds relatively quickly in absence of the catalyst and is influenced but little by the presence of acid. The relative effects of acids in non-ionising media (Hughes and Watson, *loc. cit.*) are similar, for while pyruvic acid, after the latent period, is brominated only slowly, acetone and lævulic acid react at great speed.

These facts necessitate the recognition of at least *two* factors which govern the speed of catalysed enolisation. The first step in the keto-enol change in aqueous solution may be regarded (Hughes and Watson, *loc. cit.*) as the co-ordination of the carbonyl oxygen with a molecule of water (in absence of catalyst) or with the oxonium ion (in presence of acid), leading to one or both of the equilibria

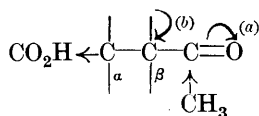


The complex (2) will enolise at a relatively fast rate owing to the effect of the positive pole in augmenting the electronic drift which precedes the ionisation of the α -proton. The co-ordinated water molecule in (1) will, on the other hand, have an insignificant influence. In absence of acid, therefore, the speed of enolisation will depend upon the extent to which the ionisation of the α -proton is favoured by groups inside the molecule. Bromoacetone and pyruvic acid, owing to the electron affinity ($-I$) of the bromine atom and the carboxyl group respectively, will enolise relatively quickly; lævulic acid is less prone to enolisation than is pyruvic, since the methyl group ($+I$ effect) opposes the ionisation of the proton :

Pyruvic acid.



Lævulic acid.



The very influences which facilitate the ionisation of the proton will, however, *oppose* the appropriation of electrons by the carbonyl oxygen (process *a*), and will thus reduce its capacity for co-ordination, particularly with a strongly negative-centre-seeking reagent such as the oxonium ion. In bromoacetone and pyruvic acid, therefore, equilibrium (2) will strongly favour the left-hand side (although very considerable co-ordination with neutral water, as in equilibrium 1, is doubtless possible), and the concentration of the reactive complex will be far smaller than that of the corresponding complex formed by acetone or by lævulic acid. In the last-named, the methyl group will favour co-ordination, and the opposing effect of carboxyl is screened by the α - and the β -carbon atom. It is perhaps worthy of note that addition compounds of acetone with halogen acids have been isolated (*e.g.*, Archibald and McIntosh, *J.*, 1904, **85**, 924). On our view of the reaction, the effect of the acid catalyst is determined

by the extent to which co-ordination of ketone and oxonium ion can occur; hence it is to be anticipated that the enolisation of acetone and of lævulic acid will be accelerated powerfully, whilst that of bromoacetone and of pyruvic acid will be affected to a relatively small degree. This is in harmony with experimental results.

It appears, therefore, that the velocity of a catalysed keto-enol change is dependent in a dual manner upon the influence of substituent groups, and due consideration must be given to the effect of the group (i) in facilitating the ionisation of the proton, and (ii) in promoting co-ordination with the catalyst. The catalysts referred to are, of course, only those of the acid type. Catalysis by a base (*e.g.*, anion of a weak acid) doubtless proceeds through a different mechanism, involving probably the direct attack of the α -proton by the catalyst.

An explanation of another peculiarity of certain carbonyl compounds is now rendered possible. Lævulic acid reacts with one mol. of bromine in aqueous solution to give, mainly at least, the β -mono-brominated acid, whereas in chloroform the $\beta\delta$ -dibrominated derivative is obtained together with unchanged lævulic acid (Hughes and Watson, *loc. cit.*). In β -bromolævulic acid, co-ordination with the oxonium ion will occur only to a limited extent, owing to the influence of the halogen atom (compare bromoacetone); considerable co-ordination with covalent hydrogen bromide may be possible, however, and thus the acid is further brominated in chloroform but not in water. The different products obtained in the two media are thus accounted for.

The possibilities of further applications of the ideas outlined above are being explored.

EXPERIMENTAL.

Products of Bromination of Acetone.—138 G. of bromine were added slowly to 50 g. of acetone in 80 c.c. of water and 20 c.c. of concentrated hydrochloric acid. The oil which separated was removed, the aqueous layer extracted with ether, and the oil and extract dried over anhydrous sodium sulphate. After several fractionations under low pressure, 89 g. of monobromoacetone were isolated (b. p. $39.5^\circ/18$ mm. Found: Br, 58.7. Calc.: Br, 58.4%), together with 14 g. of a liquid containing Br, 78.9% (Calc. for dibromoacetone, 74.1%). All the halogen estimations were done by Robertson's method (*J.*, 1915, 107, 902).

Products of Bromination of Bromoacetone.—118 G. of bromine were added to 100 g. of bromoacetone in 100 c.c. of water and 50 c.c. of concentrated hydrochloric acid. After treatment as above, the products isolated were *s.*-dibromoacetone (49 g.; m. p. 24.1° , b. p.

57—58°/4 mm. Found: Br, 74.3. Calc.: Br, 74.1%), *as*-dibromoacetone (53 g.; b. p. 38—40°/7 mm. Found: Br, 74%. Acetic acid was recognised among the products of oxidation), unchanged monobromoacetone (7 g. Found: Br, 61.1%), a liquid (9 g. Found: Br, 81.7. Calc. for tribromoacetone: Br, 81.4%), and another liquid (6 g. Found: Br, 84.8. Calc. for tetrabromoacetone: Br, 85.6%).

Kinetic Measurements.—Bromoacetone was obtained as above. Acetone was purified by the sodium iodide method, and water by distillation from permanganate and potash. 100 C.c. of solution were made containing the reagents in the desired proportions, the ketone always being in large excess (at least 20 mols. per mol. of bromine). All reactions were carried out at 25°, and were followed by titration at suitable intervals of the iodine liberated from potassium iodide by 10 c.c. of the reaction mixture. The very considerable reduction of bromoacetone by hydriodic acid, however, introduced a difficulty in the estimation. It was found necessary to add portions of the mixture to potassium iodide in presence of a quantity of sodium acetate and acetic acid carefully adjusted to render the reduction of bromo-ketone negligible, and at the same time to give the full bromine titre. The quantities necessary were determined by preliminary experiments; for example, for 10 c.c. of a reaction mixture containing 0.5*M*-bromoacetone and 0.5*M*-hydrochloric acid, correct results were obtained by using from 1.0 to 2.5 g. of crystalline sodium acetate, 0.25 g. of potassium iodide and 10 c.c. of glacial acetic acid (stable to halogens), diluted to 120 c.c. On increasing the hydrochloric acid to 1.0*M*, it was necessary to increase the sodium acetate to 4.7—4.8 g. In measurements of the bromination of acetone itself, the amount of bromo-ketone formed was so small that correct results were obtained either with or without the buffer solution. The figures which follow refer to bromination in aqueous solution. Time is expressed in hours, and titres in c.c. of *N*/50-thio-sulphate.

The velocity is always independent of the concentration of the halogen, as shown in the first table.

$$[\text{Bromoacetone}] = 0.5M. \quad [\text{HCl}] = 0.5M.$$

Initial titre.	Fall in titre after (hrs.)							Fall per hour.
	0.5.	1.	1.5.	2.	3.	4.	6.	
10.90	2.35	4.72	7.08	9.60	Gone			4.75
18.75	2.35	4.75	7.10	9.55	14.38	Gone		4.75
29.20	2.32	4.68	7.10	9.58	14.32	19.15	28.80	4.75

The velocities of bromination of acetone and bromoacetone in presence of acid catalyst are compared in the next table.

Acetone.			Bromoacetone.		
[Ketone], M.	[HCl], M.	Fall per hour.	[Ketone], M.	[HCl], M.	Fall per hour.
0.50	0.50	26.12	0.50	0.50	4.75
0.50	0.63	34.40	0.50	1.00	8.28
0.25	0.22	5.60			
0.25	0.50	12.88	0.25	0.50	2.22
0.25	1.00	27.75	0.25	1.00	3.83

The last table indicates the velocities of bromination of the ketones when no acid is present initially. It will be seen that the

$$[\text{Ketone}] = 0.25M.$$

	Initial titre.	Fall of titre after (hrs.)				
		4.	12.	24.	36.	48.
Acetone	18.82	0.40	1.48	3.25	6.52	11.05
Bromoacetone	20.72	1.98	5.40	10.82	17.15	Gone

hydrogen bromide produced accelerates the bromination of acetone very powerfully, whereas in the case of bromoacetone autocatalysis is hardly perceptible. The acid produced was sufficient to cause considerable reaction of the bromo-ketone with potassium iodide, and hence in the bromoacetone experiments a constant excess of hydrochloric acid was added before titration, and the appropriate buffer solution used.

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