166. *The Catalytic Reduction of Organic Halogen Compounds: 5-Bromo-5-alkylbarbituric Acids.*

By G. K. Hughes, A. Killen Macbeth, and S. W. Pennycuick.

The behaviour of the halogen atom in organic compounds in the presence of reducing agents has already been discussed (J., 1922, **121**, 892; *et seq.*). As a particular case, it was observed (J., 1926, 1248) that one of the halogen atoms is removed from 5:5-dichloro- and 5:5-dibromo-barbituric acids on treatment with hydrazine hydrate. Baeyer (*Annalen*, 1864, **130**, 133) recorded the difference in reactivity of two such atoms (see also Backes, West, and Whiteley, J., 1921, **119**, 377) and Nightingale and Schaefer (*J. Amer. Chem. Soc.*, 1932, **54**, 236) submitted additional evidence in support of such behaviour by showing that 5:5-dibromobarbituric acid is converted into 5-bromo-7-alkyluracils by the action of alkylamines.

The absorption spectra of a series of barbituric acids and their halogen derivatives (J., 1927, 740) showed that the parent acids and the 5-halogeno-acids exist in the enolic form, whereas the 5:5-dialkyl- and the 5:5-dihalogeno-acids have a ketonic structure. The enolic modification is excluded in the 5-bromo-5-alkyl acids, and easy removal of the halogen atom is therefore to be expected in such cases. Preliminary observations showed that there was a considerable increase in the conductivities of alcoholic solutions of these acids on standing, and that this increase could be accelerated by the addition of a catalyst. These facts have now been used to examine the reaction and determine the rate of decomposition of the acids.

The solutions examined were made up to $M/400$-concentration of the bromo-acid in water of specific conductivity 3 gemmhos, containing alcohol ranging from 2 to 10% of the total volume. The alcohol present functions as a reducing agent, and Schiff's reagent and other colour tests showed that an aldehyde was always present as a reaction product. The presence of acetaldehyde was further shown by the isolation and identification of its dimedon compound, m.p. 148—150°. The reaction may accordingly be written $R{\cdot}Br + C_2H_5{\cdot}OH = R{\cdot}H + HBr + CH_3{\cdot}CHO$. As the molecular ratio of the alcohol to the bromo-acid was rarely less than 800 : 1 in the experiments, variations in the alcohol concentration may be neglected. The reaction may therefore be regarded as unimolecular, and the corresponding formula applied.

Hydrobromic acid has the greatest conductivity of all the components of the reaction mixture, the other substances being weak electrolytes or non-electrolytes. Wood (J., 1906, **89**, 1831) gives $3{\cdot}83 \times 10^{-5}$ and $3{\cdot}7 \times 10^{-8}$ as the values of the dissociation constants of 5-ethyl- and 5:5-diethyl-barbituric acid respectively; and the values for the series 5-bromo-5-alkylbarbituric acids were found to be 1·08, 2·25, 2·51, 1·96, 2·76, and $2{\cdot}98 \times 10^{-7}$ for alkyl = Me, Et, Pr^{α}, Pr^{β}, Bu, and *iso*C_5H_{11} respectively (Cox, Macbeth, and Pennycuick, J., 1931, 1871).

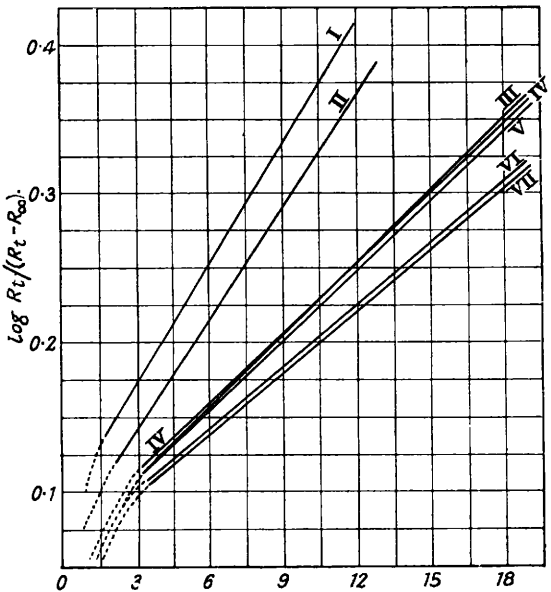
At any time t, however, the concentration of the bromo-acid is proportional to $L_{\infty} - L_t$, where L represents equivalent conductivity; and the expression is independent of the substances contributing to the conductivity provided that there are no abnormal developments in the common-ion effect. Integrating the unimolecular relation $dx/dt = k(a - x)$ between two time limits, and writing the relationship of $L_{\infty} - L_t$ to $(a - x)$ referred to above, we obtain

$$k = 1/(t_2 - t_1) \,.\, \log_e (L_{\infty} - L_{t_1})/(L_{\infty} - L_{t_2})$$

and since zero time values are unreliable, the expression is in its most convenient form. To simplify calculations we may reduce the expression to a modified form in which resistances are introduced instead of equivalent conductivities :

$$k = 1/(t_2 - t_1) \,.\, \log_e (R_{t_1} - R_{\infty})R_{t_2}/(R_{t_2} - R_{\infty})\, R_{t_1}.$$

The constancy of k may be examined by plotting $\log R_t/(R_t - R_{\infty})$ against time and measuring the slope of the graph between the limits t_1 and t_2.



I. 5 : 5-*Dibromobarbituric acid.*
II. 5-*Bromo*-5-iso*propylbarbituric acid.*
III. 5-*Bromo*-5-iso*amylbarbituric acid.*
IV. 5-*Bromo*-5-*propylbarbituric acid.*
V. 5-*Bromo*-5-*ethylbarbituric acid.*
VI. 5-*Bromo*-5-*methylbarbituric acid.*
VII. 5-*Bromo*-5-*butylbarbituric acid.*

The first observations were made with platinised electrodes (the platinum-black acting as the catalyst). Under these conditions, there was a steady fall in resistance which extended over several days, but reproducible results could not be obtained even when the cell was gently agitated mechanically throughout the experiment. Wood (*loc. cit.*) observed that solutions of 5-ethylbarbituric acid showed a considerable change in conductivity on standing, and we found that the other 5-alkyl acids we examined behaved similarly. Side reactions are therefore to be expected during the slow reduction of the bromo-alkyl acids, and since trustworthy results cannot therefore be looked for, the use of platinised electrodes was abandoned.

Reproducible results are obtained when the catalyst is distributed throughout the solution of the bromo-acid in the form of colloidal platinum. This was prepared as described by one of us (J., 1927, 2600) and several preparations of various activities were used. In order to maintain a check on any particular sample of the colloidal solution in use in a series of experiments, the values recorded in the first experiment were compared with a set of control determinations carried out on the same substance on completion of the series. The agreement between the constants thus obtained was within the margin of experimental error when the age of the colloidal preparation did not exceed eight days.

t.	R_t.	$R_t - R_\infty$.	log $R_t/(R - R_\infty)$.	t.	R_t.	$R_t - R_\infty$.	log $R_t/(R_t - R_\infty)$.
Bromomethylbarbituric acid (I).				Bromoethylbarbituric acid (I).			
2	1690	1404	0·0806	2	1760	1452	0·0835
3	1380	1094	0·1048	3	1440	1132	0·1045
4	1200	914	0·1183	4	1240	932	0·1240
5	1080	794	0·1336	5	1090	782	0·1442
6	980	694	0·1498	6	994	686	0·1611
7	911	625	0·1636	7	918	610	0·1775
8	854	568	0·1772	8	855	547	0·1940
9	808	522	0·1897	9	802	494	0·2105
10	765	479	0·2034	10	760	452	0·2257
12	695	409	0·2303	12	690	382	0·2567
15	617	331	0·2705	15	615	307	0·3018
18	558	272	0·3120	18	562	244	0·3625
21	510	224	0·3574	21	520	212	0·3897
25	460	174	0·4223	25	476	168	0·4523
30	415	129	0·5074	30	433	125	0·5394
∞	286			∞	308		
Bromo-*n*-propylbarbituric acid (I).				Bromo*iso*propylbarbituric acid (II).			
2	1620	1320	0·0889	2	860	653	0·1196
3	1320	1020	0·1120	3	730	523	0·1448
4	1150	850	0·1313	4	640	433	0·1697
5	1030	730	0·1495	5	574	367	0·1943
6	948	642	0·1666	6	523	316	0·2188
7	875	575	0·1823	7	484	277	0·2269
8	818	518	0·1985	8	449	242	0·2884
9	774	474	0·2129	9	424	217	0·2909
10	703	403	0·2427	10	401	194	0·3153
15	606	306	0·2968	15	324	117	0·4423
18	552	252	0·3405	18	294	87	0·5288
21	511	211	0·3841	22	266	59	0·6256
25	467	167	0·4456	25	249	42	0·7730
30	423	123	0·5364	30	227	20	1·0550
∞	300			∞	207		
Bromobutylbarbituric acid (II).				Bromo*iso*amylbarbituric acid (I).			
2	910	757	0·0799	2	2000	1695	0·0718
3	750	597	0·0991	3	1600	1295	0·0918
4	652	499	0·1161	4	1340	1035	0·1122
5	581	428	0·1328	5	1180	875	0·1299
6	534	377	0·1480	6	1070	765	0·1457
7	492	339	0·1618	7	980	675	0·1619
8	459	306	0·1761	8	917	608	0·1785
9	433	280	0·1893	9	860	555	0·1902
10	412	259	0·2016	10	815	510	0·2036
12	376	223	0·2269	12	744	439	0·2291
15	335	182	0·2654	15	663	358	0·2676
18	303	150	0·3053	18	602	294	0·2968
21	278	125	0·3571	21	553	248	0·3482
25	253	100	0·4031	25	503	198	0·4049
30	228	75	0·4828	30	454	149	0·4839
∞	153			∞	305		
Dibromobarbituric acid (I).							
2	564	407	0·1417	9	288	131	0·3421
3	475	318	0·1743	10	275	118	0·3674
4	416	259	0·2058	12	253	96	0·4208
5	376	219	0·2348	15	230	73	0·4984
6	346	189	0·2626	21	202	45	0·6522
7	324	167	0·2878	26	180	23	0·8836
8	304	147	0·3156	∞	157		

The numbers in parentheses after the name of the bromo-acid indicate the cell used in that experiment, the constant of cell I being 0·310 and that of cell II 0·152. The experimental solutions were prepared by running equal volumes of the colloidal platinum sol and an $M/200$-solution of the bromo-acid of appropriate alcoholic content into the conductivity cell, all solutions and vessels having previously attained temperature equilibrium in a thermostat at 30°. Resistances were measured on a Pye dial-type bridge, the null point being determined by means of an oscillator combination.

An alkylbarbituric acid is produced as a reaction product in the reduction, so it was thought desirable to examine the stability of solutions of such substances in the presence of colloidal platinum, but very slight change in resistance was found on standing; *e.g.*, the resistance of an $M/400$-solution of 5-methylbarbituric acid only varied from 299 to 302 ohms in 3 days, whilst an $M/400$-solution of *iso*amylbarbituric acid showed a change from 1034 to 1057 ohms during 15 days.

The results obtained in a typical series of reduction experiments are set out in the table on p. 771, and plotted in the fig. In all these cases the solutions contained 10% of alcohol, and the same sample of colloidal platinum (Pt IV) was used throughout. The infinity readings were taken at the end of an hour and were found to be practically unchanged after 12 hours.

The graphs shown in the fig. are straight lines over the major part of the observations, and indicate the unimolecular nature of the reaction. On account of the difficulty of obtaining reliable values in the early stages of the reduction (when the resistance is changing considerably), the initial portions of the graphs are somewhat curved; the initial time t_1 was therefore taken as 4 minutes in deriving the average values of k set out below.

Substituted barbituric acid.	100 k.	Substituted barbituric acid.	100 k.
5-Bromo-5-methyl-	1·41	5-Bromo-5-butyl-	1·40
5-Bromo-5-ethyl-	1·50	5-Bromo-5-*iso*amyl-	1·56
5-Bromo-5-propyl-	1·52	5 : 5-Dibromo-	2·80
5-Bromo-5-*iso*propyl-	2·53		

The rate of reduction of the bromo-acids in general varies but slightly with the mass of the alkyl group, but the *iso*propyl acid is a marked exception to the ordinary behaviour. In all the determinations, its rate of reaction exceeded those of other members of the series, and in this connexion it may be recalled that the value of its dissociation constant is also an exception to the general increase in the values observed for successive members of the series.

It has been pointed out that, on account of the concentrations used, the alcoholic content of the solutions may be considered to remain constant, thus giving a reaction of the unimolecular type. For different alcoholic concentrations, however, the velocity constants may be expected to vary, and this is in fact realised in practice :

Solute : *5-Bromo-5-*iso*amylbarbituric acid.*

Solvent, alcohol, %	2	5	10	10	40
Catalyst	Pt VI	Pt VI	Pt VI	Pt II	Pt II
100 k	1·00	1·53	2·36	1·05	2·06

The values show that although k increases with alcoholic concentration, a simple proportionality is not found. The failure of the mass law is not unusual in cases where reactions occur at catalytic surfaces, particularly when the concentrations used are high. In the extreme case where all the active points of the catalyst are engaged, further increase in the concentration of a reactant would leave the velocity constant unaffected.

In general, it is also to be expected that the velocity constant will increase as the concentration of the catalyst rises. On this account, the relative velocities of reduction of the series of bromo-acids were determined with the catalyst of uniform activity throughout. Definite estimations of the amounts of platinum in the various samples were not made, since it is well known that the actual colloid content of a sol is not directly related to its activity. Colloidal platinum offers no exception to this behaviour, and different samples prepared under the same conditions are often found to be of widely differing activities. Examples of changes in the reaction velocities with various samples of colloidal platinum are given below. The solvent in all cases contained 10% of alcohol.

Barbituric acid.	Catalyst.	100 k	Barbituric acid.	Catalyst.	100 k.
5-Bromo-5-propyl-	Pt I	0·10	5-Bromo-5-*iso*amyl-	Pt II	1·05
,,	Pt III	1·10	,,	Pt IV	1·56
,,	Pt IV	1·52	,,	Pt V	2·01
5-Bromo-5-*iso*propyl-	Pt I	0·13	,,	Pt VI	2·36
,,	Pt III	2·06			
,,	Pt IV	2·53			

These constants may be used to compare the catalytic activity of different sols or even to prepare by dilution two sols of comparable strength. The abnormalities in the activity of different platinum sols are strikingly emphasised by observing the effect of dilution; *e.g.*, Pt I was obtained by diluting Pt IV to four volumes with distilled water; but the effect on the velocity constant was a decrease, not of 1/4, but of 1/15 in the case of 5-bromo-5-propyl-, and of 1/19 in that of 5-bromo-5-*iso*propylbarbituric acid. Such abnormal changes are difficult to explain and are being further examined.

Experiments were also carried out with colloidal catalysts other than platinum, notably colloidal silver and colloidal tungsten. These were prepared by sparking methods, the technique followed being similar to that adopted in the case of colloidal platinum. Colloidal silver, which has silver hydroxide present as an electrolyte, was quite unsuitable on account of the side reactions with hydrobromic acid. The activity of colloidal tungsten was small compared with that of colloidal platinum, and the reaction was not completed even after 14 days.

SUMMARY.

The 5-bromo-5-alkylbarbituric acids are rapidly reduced by alcohol in presence of colloidal platinum, but only slowly in presence of colloidal tungsten. When the concentration of alcohol is sufficiently high to be assumed constant throughout, the reductions are unimolecular.

In general, the velocity constant varies little with the alkyl group, but the *iso*propyl acid shows an exceptional increase.

Changes in the velocity constant due to variations in the concentration of alcohol and in colloid content are also examined.

THE JOHNSON LABORATORIES, UNIVERSITY OF ADELAIDE. [*Received, February 12th,* 1934.]