Hydrolysis of α-Bromo-t-Butylmalonic Acid

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In connection with an investigation of the kinetics of the hydrolysis of some organic bromides, a short account of which has already been given [1], the hydrolysis of α-bromo-t-butylmalonic acid in alkaline solution was also studied. The hydrolyses were usually followed by titration of the alkali consumed in the reaction. With the above mentioned acid this method, however, gave unsatisfactory results. The titration showed an initial comparatively rapid consumption of alkali, which soon became much slower and no useful kinetics could be obtained from these results. Titration of the liberated bromide ions gave however good first order kinetics. The initial rapid decrease in alkalinity corresponded approximately in speed to the liberation of bromide ions, whereas the later, slower part of the consumption of alkali proceeded long after all the organically bound bromine had been converted into bromide ion. However the total consumption of alkali in the hydrolysis was one equivalent. It is thus evident that there must be formed some bromine-free intermediate, which slowly reacts further with consumption of alkali.

In order to get some idea of the nature of this slower reaction a calculation of the rate constant was made taking as zero time a time when the first rapid reaction is completed, as judged by the complete conversion of bound bromine into bromide ion. Although a rather good first order constant could be obtained from each run, a comparison of the rate constants from runs with increasing concentration of alkali showed a definite increase in the rate. It is thus evident that this second reaction is at least partly bimolecular, although no agreement between second order rate constants from different runs could be obtained. As will be shown later carbon dioxide is liberated in the reaction, which makes the determination of the hydroxyl ion concentration by titration, using phenolphtalein as indicator, unreliable, and this is supposed to be the cause to these differences.

A search for the products of hydrolysis gave then further information about this rather complex reaction. As reaction products were found trimethylacrylic acid, methylmalonic acid and acetone. It was further found that the proportion of these products varied with the concentration of alkali, as is seen from Table 1.
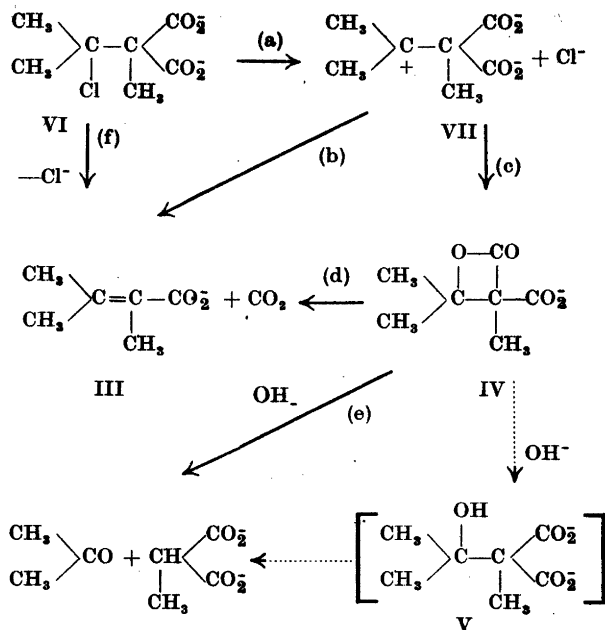
Table 1.

Molar proportion alkali : acid	[OH⁻]	Acetone mole %	Methyl-malonic acid mole %	Trimethyl-acrylic acid mole %
3 : 1	0.1 N	11	11	76
4 : 1	0.1 N	28	27	68
4 : 1	0.2 N	33	32	62
4 : 1	0.3 N	43	43	54
4 : 1	0.5 N	49	40	53
6 : 1	0.2 N	41	35	55
8 : 1	0.2 N	43	41	60

The yield of acetone and methylmalonic acid thus increases not only with an increase in the molar proportion total alkali: free acid, but also with an increase in the concentration of free alkali, whereas the yield of trimethylacrylic acid correspondingly decreases. When the hydrolysis was carried out with the free acid without any addition of alkali no acetone was formed and the only isolable acid was trimethylacrylic acid. The sum of acetone or methylmalonic acid and trimethylacrylic acid accounts for about 90—100 % of the reaction. On the basis of the above mentioned facts the following mechanism is proposed for the hydrolysis of a-bromo-t-butylmalonic acid in alkaline solution.
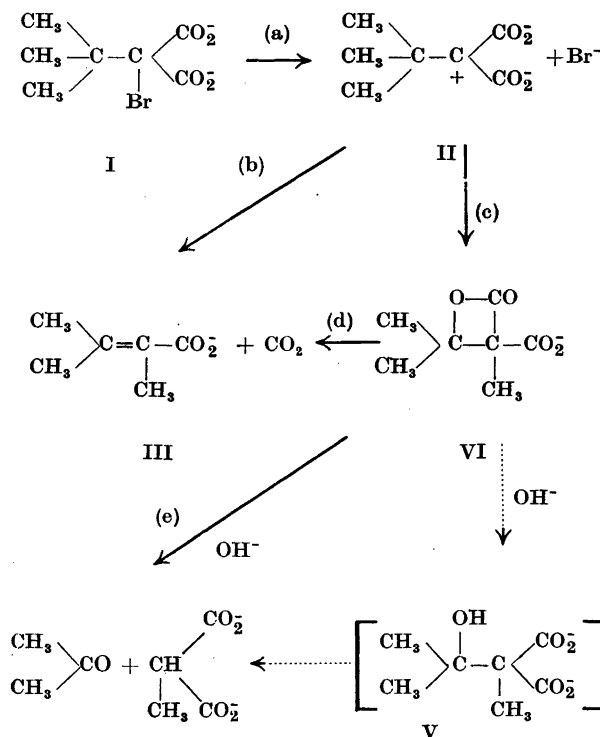
The reaction (a) is the first order reaction measured by the release of bromide ion. The formed carbonium ion (II) then reacts in two different ways, (b) and (c), both reactions being faster than (a) but of about equal speed. The reaction (b) accounts for the initial faster consumption of alkali because the carbon dioxide formed acts as an acid towards phenolphtalein, that was used as indicator in the titration. The reaction (c) gives a β-lactone (IV) which then reacts according to (d) and (e), which reactions correspond to the later slower consumption of alkali. The formation of β-lactones in the hydrolysis of β-halogensubstituted acids has been noted before and Johansson [2] succeeded in isolating such a lactone from the hydrolysis of β-bromobutyric acid. That (III) cannot be formed exclusively by path (b), but must be formed partly also by path (d) follows from the greater amount of acetone and methylmalonic acid formed when the hydroxyl ion concentration is increased. If only (b) were prevailing no such change should be expected, since the proportion of trimethylacrylic acid to methylmalonic acid and acetone would depend solely on the relative rates of (b) and (c), which must be assumed to be independent of the concentration of alkali. On the other hand the bimolecular reaction (e) certainly increases its speed with increasing hydroxyl ion concentration, whereas (d) can be assumed to be unimolecular and thus independent of the hydroxyl ion concentration, which leads to the observed increase in yield of the products from (e). Although decarboxylation of β-lactones is well known, it has been stated [3,4] that this does not occur in the presence of water. In this case we are, however, forced to assume that loss of carbon dioxide can occur also in the presence of water. Whether the formation of acetone and methylmalonic acid from lactone (IV) goes directly or whether the corresponding β-hydroxyacid (V) is an intermediate can not be said with certainty. Usually alkylsubstituted β-hydroxy acids [5], even β-hydroxymalonic acids [6,7] are stable towards alkali, whereas β-hydroxy acids with aryl and aralkyl groups sometimes are split in the same way as that pictured above [5,8].

In order to find some further support for the mechanism described above the hydrolysis of methyl-1-chloro*iso*propylmalonic acid (VI) was studied. This acid, which has not been described before, was prepared by chlorination of methyl*iso*propylmalonic acid with sulphurylchloride in the presence of catalytic amounts of benzoyl peroxide [9]. Although the structure of the chlorination product obtained has not been determined by any independent means, analysis and the products of hydrolysis clearly show that it must be the desired acid (VI), Hydrolysis of this acid gave the same three products as were obtained in the hydrolysis of α-bromo-*t*-butylmalonic acid *viz.* acetone, methylmalonic acid and trimethylacrylic acid in 21, 18 and 62 % yield, respectively. The yield of acetone and methylmalonic acid is lower and that of trimethylacrylic acid higher than from α-bromo-*t*-butylmalonic acid under comparable conditions. This reaction can be assumed to take the following course:

$$\begin{array}{ccc}
\mathrm{CH_3}\!\!\diagdown & & \mathrm{CO_2^-} \\
& \mathrm{C-C} & \\
\mathrm{CH_3}\!\!\diagup & \;|\;\;\;| & \mathrm{CO_2^-} \\
& \mathrm{Cl\;\;CH_3} &
\end{array}
\quad\xrightarrow{\text{(a)}}\quad
\begin{array}{ccc}
\mathrm{CH_3}\!\!\diagdown & & \mathrm{CO_2^-} \\
& \mathrm{C-C} & \\
\mathrm{CH_3}\!\!\diagup + & |\;\; & \mathrm{CO_2^-} \\
& \mathrm{CH_3} &
\end{array}
+\;\mathrm{Cl^-}$$

VI $\Big|$(f)   VII $\Big|$(c)

$-\mathrm{Cl^-}\downarrow$ (b) $\downarrow$(c)

$$\begin{array}{c}
\mathrm{CH_3}\!\!\diagdown \\
\quad\quad \mathrm{C{=}C-CO_2^-} + \mathrm{CO_2} \\
\mathrm{CH_3}\!\!\diagup \quad |\\
\quad\quad\;\; \mathrm{CH_3}
\end{array}
\quad\xleftarrow{\text{(d)}}\quad
\begin{array}{c}
\mathrm{O{-}CO} \\
|\quad | \\
\mathrm{CH_3}\!\!\diagdown\;\mathrm{C-C-CO_2^-} \\
\mathrm{CH_3}\!\!\diagup\quad\; | \\
\mathrm{CH_3}
\end{array}$$

III   OH_   IV
          (e)
                            $\downarrow$ OH⁻

$$\begin{array}{c}
\mathrm{CH_3}\!\!\diagdown \\
\quad\quad \mathrm{CO} + \mathrm{CH}\diagdown \quad \mathrm{CO_2^-} \\
\mathrm{CH_3}\!\!\diagup \quad\quad\quad \mathrm{CO_2^-} \\
\quad\quad\quad | \\
\quad\quad\quad \mathrm{CH_3}
\end{array}
\quad\xleftarrow{\hspace{1cm}}\quad
\left[
\begin{array}{c}
\mathrm{OH} \\
| \\
\mathrm{CH_3}\!\!\diagdown\;\mathrm{C-C}\diagdown\;\mathrm{CO_2^-} \\
\mathrm{CH_3}\!\!\diagup\quad\; |\quad \mathrm{CO_2^-} \\
\mathrm{CH_3}
\end{array}
\right]$$

V

The higher yield of trimethylacrylic acid can be explained as the result of a direct decarboxylative elimination [10] (f). Although there is no kinetic evidence for the unimolecular nature of reaction (a), this can be inferred from analogy, (VI) being a tertiary halogenide. There is further no direct evidence for the formation of the β-lactone (IV) but as the rearrangement of (II) into (IV) evidently must go through (VII) its inclusion in the scheme seems inevitable. This scheme is thus very closely related to the earlier one, the main difference being the lack of any rearrangement in the latter case.

This rearrangement is of course a typical Wagner-rearrangement, but the interesting point here is that in the series $(CH_3)_3CCH_2Br$, $(CH_3)_3CCHBrCO_2^-$ and $(CH_3)_3CCBr(CO_2^-)_2$, the first [11] and the third undergo hydrolysis with rearrangement, whereas the second gives a high yield of trimethyllactic acid, thus hydrolysing without rearrangement. The mechanism is in all three cases definitely S_N1^1 and it appears thus probable that there must be two different factors which decide whether a rearrangement of the primarily formed cation takes place or not.

EXPERIMENTAL

a-Bromo-t-butylmalonic acid. *t*-Butylmalonic acid was prepared according to Widequist [12]. Its conversion into *a*-bromo-*t*-butylmalonic acid was carried out according to Abderhalden and Rossner [13]. After recrystallisation from ether-light petroleum it had m.p. 188°. (Lit. 183° [13], 180−183° [14]) (Found: Br 32.5; $C_7H_{11}O_4Br$ requires Br 33.4).

In order to put its structure beyond any doubts it was converted, by heating to 200°, into *a*-bromo-*t*-butylacetic acid, m.p. 72°, undepressed when mixed with an authentic sample [15]. It was further reduced with zinc and acetic acid to *t*-butylmalonic acid of m.p. 152° (alone or in mixture test).

Hydrolysis of *α*-bromo-t-butylmalonic acid

a) *Kinetics.* The solutions in water were made up at 0° and samples of 5 ml were sealed into bulbs. These were placed in a termostat heated to the appropriate temperature and shaken for one minute. One bulb was taken out and broken, either under 100 ml of ice cold water and titrated with hydrochloric acid using phenolphtalein as indicator, or under 100 ml 6 N nitric acid, a known excess of silver nitrate solution added and the excess titrated with ammonium rhodanide. The time when this bulb was taken out was taken as zero time, unless stated otherwise. The other bulbs were then treated in the same manner after appropriate time intervals.

Table 2. Temp. 59.8°. (a−x) = [(CH₃)₃CCBr(CO₂⁻)₂] and (b−x) = [OH⁻] expressed in ml 0.0264 N HCl per 5 ml sample.

Time (min)	0	3	6	9	12	16	20	30
$(a-x)$	10.50	5.83	4.23	3.33	2.54	1.74	1.32	0.79
$(b-x)$	19.82	15.05	13.45	12.55	11.76	10.96	10.54	10.01
$k_1 \cdot 10^3$ (sec⁻¹)		3.27	2.53	2.13	1.97	1.71	1.15	0.75
$k_2 \cdot 10^2$ (sec⁻¹ gmol⁻¹ l)		4.50	2.97	2.63	2.56	2.58	2.47	2.17

Table 3. Temp. 48.2°. [(CH₃)₃CCBr(CO₂⁻)₂] expressed in ml 0.0244 N NH₄CNS per 5 ml sample.

Time (min)	0	2	4	5	6	8	10
[(CH₃)₃CCBr(CO₂⁻)₂]	9.63	5.45	3.24	2.50	2.13	1.09	0.53
$k_1 \cdot 10^3$ (sec⁻¹)		4.73	4.54	4.42	4.19	4.54	4.83
					Mean 4.59		

By extrapolation from the figures of Table 3 a time of 13 min. can be derived at as the time all the (CH₃)₃CCBr(CO₂⁻)₂ has disappeared. This time is in the following three runs taken as zero time.

Table 4. Temp 48.2°. (a−x) and (b−x) expressed in ml 0.0268 N HCl per 5 ml sample. Initial [NaOH] = 0.075 N.

Time (min)	0	7	15	25	35	45
$(a-x)$	5.11	4.19	3.68	2.90	2.48	2.04
$(b-x)$	8.61	7.69	7.18	6.40	5.98	5.54
$k_1 \cdot 10^4$ (sec⁻¹)		4.73	3.64	3.78	3.44	3.40
						Mean 3.80
$k_2 \cdot 10^3$ (sec⁻¹gmol⁻¹ l)		10.85	8.69	9.60	9.11	9.43
						Mean 9.54

Table 5. The same, but initial [NaOH] = 0.11 N.

Time (min)	0	6	12	18	24	30	38	46	54
$(a-x)$	5.01	4.17	3.35	2.78	2.43	2.01	1.60	1.39	1.09
$(b-x)$	15.55	14.71	13.89	13.32	12.97	12.55	12.14	11.93	11.63
$k_1 \cdot 10^4$ (sec⁻¹)		5.10	5.59	5.45	5.02	5.07	5.01	4.65	4.70
							Mean 5.07		
$k_2 \cdot 10^3$ (sec⁻¹gmol⁻¹ l)		6.30	7.13	7.12	6.67	6.87	6.91	6.52	6.76
							Mean 6.79		

Table 6. *The same, but initial* [NaOH] = 0.19 N.

Time (min)	0	7	15	25	35	45	55
$(a-x)$	4.41	2.77	2.25	1.37	0.96	0.73	0.36
$(b-x)$	29.56	27.92	27.40	26.52	26.11	25.88	25.51
$k_1 \cdot 10^4$ (sec⁻¹)		(11.07)	7.31	7.91	7.26	6.66	7.60
							Mean 7.35
$k_2 \cdot 10^3$ (sec⁻¹gmol⁻¹ l)		(7.21)	4.92	5.25	4.95	4.58	5.30
							Mean 5.00

b) *Hydrolysis products.* The experiments, the results of which are given in Table 1, were made in the following way. An appropriate amount of the acid was dissolved in a potassium hydroxide solution of known concentration. This was heated in a flask provided with a reflux condenser at 50° for three hours. The content of the flask was after cooling neutralised and distilled until no more acetone came over. In the distillate the acetone was determined by titration with iodine [16]. The acetone was further identified as its 2,4-dinitrophenylhydrazone, m.p. 120°. Mixed with authentic acetone 2,4-dinitrophenyl-hydrazone of m.p. 121—123° it had m.p. 120—122°.

The solution from which the acetone had been removed was, when necessary, further evaporated till a volume of about 40 ml. This was then acidified, whereby trimethyl-acrylic acid precipitated. One extraction of the mother liquor with ether gave a further amount. After recrystallisation from dilute alcohol it had m.p. 69—70°. No depression when mixed with an authentic sample. (Found: C 63.25; H 8.8; Eq.wt. 115.1; $C_6H_{10}O_2$ requires C 63.1; H 8.8; Eq.wt. 114.1).

The solution remaining after the separation of trimethylacrylic acid was carefully evaporated to dryness and the residue was extracted with ether. Evaporation of the ether gave methylmalonic acid. After recrystallisation from light petroleum it had m.p. 130—132°, undepressed when mixed with an authentic sample. (Found: C 40.8; H 5.2; Eq. wt. 59.3; $C_4H_6O_4$ requires C 40.7; H 5.1; Eq.wt. 59.0).

Methyl-1-chloroisopropylmalonic acid. Methyl*iso*propylmalonic acid (3.0 g) and sulphuryl chloride (2.55 g) were dissolved in benzene (20 ml). Benzoyl peroxide (23 mg) was added as catalyst, and the mixture heated on a steam bath for 9 hours. The benzene was then evaporated, first on a steam bath and finally in vacuum. The residue (3.5 g) was recrystallised from ether-light petroleum or ether-benzene giving a substance of m.p. 170°. The yield of pure product was very poor, only 0.3 g. (Found: C 43.5; 5.8; $C_7H_{11}O_4Cl$ requires C 43.2; H 5.7).

The hydrolysis of this acid was carried out in the same way as described for *a*-bromo-*t*-butylmalonic acid, using a molar proportion of alkali to acid of 6.5 : 1, the concentration of the free alkali being 0.6 N. The products of hydrolysis were isolated and identified as before.

a-Bromo-t-butylacetic acid. This acid was prepared according to Homeyer, Whitmore and Wallingford [14]. It had m.p. 72°. (Lit. 72—73° [14]). 2.5 g was dissolved in 0.1 N sodium hydroxide solution (250 ml) and heated on a steam bath for 4 hours. The solution was neutralised and evaporated to a small volume (No acetone could be detected in the distillate). It was then acidified with hydrochloric acid and evaporated to dryness in a vacuum desiccator over sodium hydroxide. The residue was extracted with ether and the ether evaporated leaving 1.4 g (82 %) of β,β,β-trimethyllactic acid. After recrystallisation from chloroform it had m.p. 87—88°. (Lit. 87—88° [17], 90—91° [18], 86.5—87.5° [19].) (Found: C 54.5; H 9.2; Eq.wt. 132.4; $C_6H_{12}O_3$ requires C 54.5; H 9.15; Eq.wt. 132.2.) The isomeric, also possible hydrolysis product, a,β-dimethyl-β-hydroxybutyric acid is an oil [20,21].

SUMMARY

Hydrolysis of a-bromo-t-butylmalonic acid in alkaline solution gives trimethylacrylic acid, methylmalonic acid and acetone. The mechanism of this reaction is discussed.

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