210. *Quantitative Aspects of the Base-catalysed Reaction of Aliphatic Aldehydes with Iodine. Part III.*[1, 2] *Isobutyraldehyde and Trimethylacetaldehyde.*

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Kinetic measurements and analysis of the products of the reaction of isobutyraldehyde with alkaline iodine show that this compound closely resembles its lower homologues inasmuch as it may either suffer oxidation to the corresponding carboxylic acid or undergo halogen-substitution followed by hydrolysis. The former process predominates at low pH values and the latter becomes important under more alkaline conditions.

Qualitatively similar results are obtained with trimethylacetaldehyde, the behaviour of which is however characterised by a very low overall uptake of iodine; this is probably due to extensive polymerisation or condensation in aqueous alkali.

EARLIER studies [1,2] of the base-catalysed iodination of simple aliphatic aldehydes have now been extended to two branched-chain compounds.

EXPERIMENTAL

Materials.—The purest available commercial sample of isobutyraldehyde was carefully fractionated in a current of nitrogen before use. Trimethylacetaldehyde (pivalaldehyde) was prepared [3] by cautious addition of ethereal t-butylmagnesium chloride to methyl formate at −40°. The Grignard complex was hydrolysed with 2N-hydrochloric acid, the temperature being kept below 10°. The resulting ethereal layer was separated, dried (K_2CO_3), and evaporated. The residue was fractionated and the fraction boiling at 74—75° was collected (lit., b. p. 75°). Trimethylacetaldehyde was not very soluble in water and if attempts were made to prepare solutions more concentrated than 0·02M, a whitish wax-like solid (m. p. *ca.* 21°) separated and did not dissolve on further addition of water. Dilute solutions of this aldehyde foamed, in a manner similar to a dilute soap solution, when vigorously shaken.

All other reagents were of " AnalaR " quality and were further purified where necessary by conventional methods.

General Procedure.—The preparation of buffer solutions, the measurement of pH, and the method of making kinetic measurements have already been described.[1,2]

Qualitative Analysis of Products.—Organic acids were identified by paper chromatography.[4] Formic acid, for which the above method does not give unambiguous results, was reduced with magnesium and hydrochloric acid,[5] and the resulting formaldehyde was detected by its colour reaction with chromotropic acid.[6] The presence of isopropyl alcohol was tested with *p*-dimethylaminobenzaldehyde.[7] No appreciable amount of iodoform could be found under any conditions.

Quantitative Analysis of Products.—Organic acids were estimated approximately by extraction into ether, treatment of the combined ethereal extracts with standard borax solution, and determination of the amount of unchanged borax by acid–base titration. Corrections were applied for the incomplete extraction of isobutyric acid and trimethylacetic acid in ether under the conditions used. Total organically bound iodine was determined by the procedure described previously.[1]

RESULTS

Kinetic Measurements.—With isobutyraldehyde the initial rate of reaction varies linearly with the aldehyde and iodine concentrations (Fig. 1). Owing to the very low overall consumption of iodine by trimethylacetaldehyde, initial rates are more difficult to measure

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[1] Part I, Cullis and Swain, *J.*, 1962, 2228.
[2] Part II, Cullis and Swain, *J.*, 1962, 3348.
[3] Campbell, *J. Amer. Chem. Soc.*, 1937, **59**, 1980.
[4] Hashmi and Cullis, *Analyt. Chim. Acta*, 1956, **14**, 336.
[5] Grant, *Analyt. Chem.*, 1948, **20**, 267.
[6] Bricker and Vail, *Analyt. Chem.*, 1950, **22**, 720.
[7] Auterhoff, *Pharm. Zentralhalle*, 1950, **89**, 293.

accurately with this compound, but the broad kinetic features of the reaction appear to be similar, although at low pH values (<11), the rate becomes almost independent of iodine concentration. The variation of rate with pH (Fig. 2) is qualitatively the same as for the lower aldehydes,[2] the rate reaching a maximum at a pH of *ca.* 12, then falling to a minimum at a pH of *ca.* 13 and thereafter rising again as the alkalinity is further increased.

Total Iodine Consumption.—The number of moles of iodine consumed per mole of aldehyde depends on several factors, one of the most important of which is pH. With isobutyraldehyde, the maximum uptake of halogen attained when a premixed iodine–aldehyde solution is added to the alkali solution at first increases, reaching an apparently steady value at pH *ca.* 10·5 (Fig. 3). Above pH 12·5, however, a further sudden increase occurs. The most remarkable feature of the behaviour of trimethylacetaldehyde (Fig. 3) is the very low overall consumption of iodine even under optimum conditions.

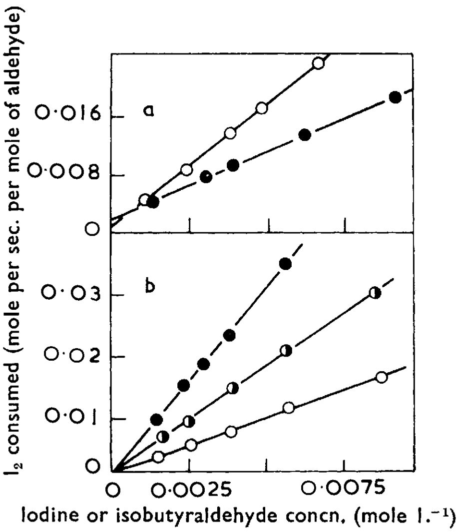

FIG. 1. The influence of iodine and isobutyraldehyde concentrations on the rate of iodine consumption at 0°.

(a) [Isobutyraldehyde] = 0·0025M; [Iodine] varied. ○ pH = 11·44; ● pH = 13·43. (b) [Iodine] = 0·0051M; [Isobutyraldehyde] varied. ○ pH = 10·93; ● pH = 12·67; ◑ pH = 13·18.

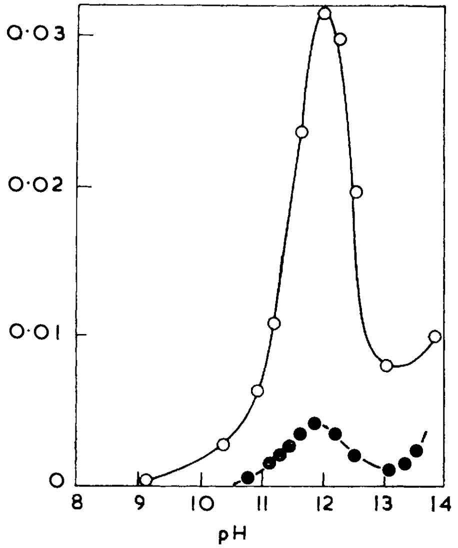

FIG. 2. The influence of pH on the rate of iodine consumption at 0°.

[Iodine] = 0·0051M; ○ [Isobutyraldehyde] = 0·0025M; ● [Trimethylacetaldehyde] = 0·0025M.

Qualitative Analysis of Products.—The results for isobutyraldehyde are shown in Table 1. Isobutyric acid is always a product except under the most strongly alkaline conditions, and acetic (or formic) acid is formed at higher pH values. No iodo-acids can be detected by the normal paper-chromatographic procedure, although dark blue spots of low R_F value are observed on many of the chromatograms when these are sprayed with B.D.H. Universal Indicator;[8] these may indicate the presence of an amino-acid formed from an iodo-acid during the evaporation of the ammoniacal solution. Formic acid is formed in solutions of pH greater than 12·5 and isopropyl alcohol is also detectable under the most strongly alkaline conditions (pH >13).

With trimethylacetaldehyde (Table 1), the main acid product is trimethylacetic acid, although small amounts of propionic and iodopropionic acid are also formed in strongly alkaline solution.

Quantitative Analysis of Products.—Fig. 4 shows the total amounts of iodine consumed and

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[8] Long, Quayle, and Stedman, *J.*, 1951, 2197.

TABLE 1.

Specific products detected in the base-catalysed iodination of isobutyraldehyde and trimethylacetaldehyde.

Temp. = 25°; [Aldehyde] = 0·0025M; [Iodine] = 0·0051M.

From isobutyraldehyde			From trimethylacetaldehyde	
pH	Paper chromatography *	Chemical tests	pH	Paper chromatography *
12·5	$\mathrm{Pr^i{\cdot}CO_2H}$ 0·57 (0·57)	—	11·5	$\mathrm{Bu^t{\cdot}CO_2H}$ 0·71 (0·70)
13·0	$\mathrm{Pr^i{\cdot}CO_2H}$ 0·57 (0·57) AcOH ($\mathrm{H{\cdot}CO_2H}$) 0·38 (0·39)	$\mathrm{H{\cdot}CO_2H}$	12·5	$\mathrm{Bu^t{\cdot}CO_2H}$ 0·70 (0·70), $\mathrm{Et{\cdot}CO_2H}$ 0·50 (0·48)
13·9	AcOH ($\mathrm{H{\cdot}CO_2H}$) 0·38 (0·39)	$\mathrm{H{\cdot}CO_2H}$, $\mathrm{Pr^iOH}$	13·5	$\mathrm{Bu^t{\cdot}CO_2H}$ 0·70 (0·70), $\mathrm{Et{\cdot}CO_2H}$ 0·59 (0·48), $\mathrm{C_2H_4I{\cdot}CO_2H}$ 0·58 (0·56)

* R_F values of acids present in products are given together with the corresponding values determined for the known acids in parentheses.

of organic acids formed during the reaction of isobutyraldehyde at different pH values. Since only a small proportion of any acetic and formic acid present is determined by the analytical procedure used,[2] all the acid found may, to a first approximation, be assumed to be isobutyric acid or its α-iodo-derivative. In the pH range 9—12, the major part of the consumed iodine is clearly used in the oxidation of the aldehyde to carboxylic acids with the same carbon skeleton. In more strongly alkaline conditions, the amounts of such acids decrease and there is a corresponding sharp increase in iodine uptake. At the same time the results in Fig. 4 show

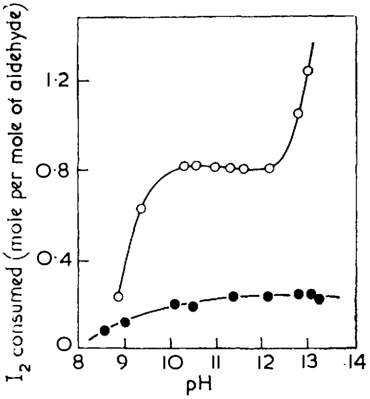

FIG. 3. The influence of pH on maximum iodine consumption at 25°.

○ [Isobutyraldehyde] = 0·0025M; [Iodine] = 0·0031M.

● [Trimethylacetaldehyde] = 0·0025M; [Iodine] = 0·0051M.

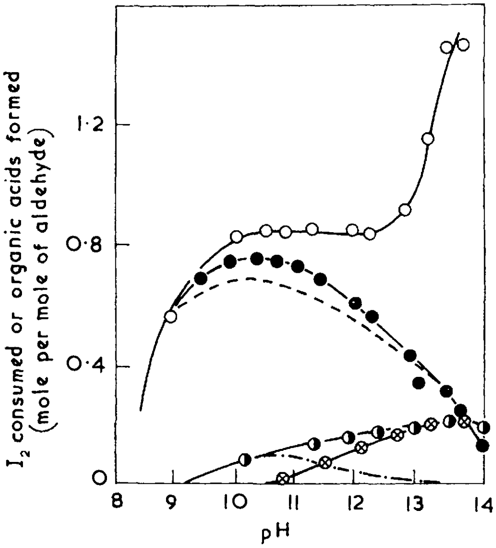

FIG. 4. The influence of pH on the products formed from isobutyraldehyde.

Temp. = 25°; [Isobutyraldehyde] = 0·0025M; [Iodine] = 0·0051M.

○ Total iodine consumed; ● total organic acids formed; ◑ total organically bound iodine; × iodine present in neutral organic form. —·—·— Iodine present in organic acids ($\mathrm{CMe_2I{\cdot}CO_2H}$) (calc.). ---- Unsubstituted organic acids (isobutyric acid) formed (calc.).

that in no circumstances does more than a small fraction of the consumed iodine become organically bound. The difference between the total iodine converted into an organic form and that found in neutral compounds is presumably present as iodo-acids (probably α-iodo-α-methylpropionic acid); subtraction of the amounts of these compounds from the total amounts of organic acids present provides a measure of the quantity of unsubstituted fatty acids (mainly isobutyric acid, since formic and acetic acid are scarcely determined by the analytical procedure used [2]).

Direct determination of the organic acids formed from trimethylacetaldehyde shows that over the whole of the pH range 9—14, about 15% of the initial aldehyde is converted into the corresponding carboxylic acid. No organically bound iodine can be detected at low pH values but in strongly alkaline solution (pH $>12{\cdot}8$), up to 0·04 mole of iodine is found in an organic form per initial mole of aldehyde.

DISCUSSION

Reactions of Isobutyraldehyde.—The kinetic relations shown in Figs. 1 and 2 are formally similar to those found with acetaldehyde and propionaldehyde [2] and suggest that isobutyraldehyde may undergo either direct oxidation or substitution. By analogy with the behaviour of its lower homologues the total rate of iodine consumption may be represented by an expression of the form:

$$-\mathrm{d}[\mathrm{I}_2]/\mathrm{d}t = k_1[\mathrm{HIO}][\mathrm{Pr}^{\mathrm{i}}\cdot\mathrm{CHO}] + k_2[\mathrm{OH}^-][\mathrm{Pr}^{\mathrm{i}}\cdot\mathrm{CHO}]$$

where k_1 and k_2 are the velocity constants for oxidation and iodination, respectively. From measurements of the slopes and intercepts of plots of initial rate against iodine and aldehyde concentrations (Fig. 1), it may readily be calculated that at 0° $k_1 = 6$ and $k_2 = 10^{-2}$ l. mole^{-1} sec.$^{-1}$.

The occurrence of two distinct reactions is borne out by the analytical results (Fig. 4). Thus at low pH values (<10), oxidation is predominant; isobutyric acid, possibly together with its α-iodo-derivative in much smaller amounts, are the only organic products detected (Table 1), being formed by the overall reactions:

$$\mathrm{Pr}^{\mathrm{i}}\cdot\mathrm{CHO} + \mathrm{I}_2 + 2\mathrm{NaOH} = \mathrm{Pr}^{\mathrm{i}}\cdot\mathrm{CO}_2\mathrm{H} + 2\mathrm{NaI} + \mathrm{H}_2\mathrm{O} \quad \ldots\ldots\ldots \quad (1)$$

$$\mathrm{Pr}^{\mathrm{i}}\cdot\mathrm{CHO} + 2\mathrm{I}_2 + 3\mathrm{NaOH} = \mathrm{Me}_2\mathrm{CI}\cdot\mathrm{CO}_2\mathrm{H} + 3\mathrm{NaI} + 2\mathrm{H}_2\mathrm{O} \quad \ldots\ldots \quad (2)$$

Since isobutyric acid does not react with iodine under the conditions used,[9] the iodo-acid must be formed by oxidation of the corresponding aldehyde.

At somewhat higher pH values (10—12), the amounts of acids decrease but, since there is a simultaneous increase in the quantities of neutral iodine-containing products, the total iodine consumption remains effectively constant. Presumably at high pH values, substitution tends to take place at the α-carbon atom and this is followed by hydrolysis. Thus, for example, the reaction:

$$\mathrm{Pr}^{\mathrm{i}}\cdot\mathrm{CHO} + \mathrm{I}_2 + \mathrm{NaOH} = \mathrm{Pr}^{\mathrm{i}}\mathrm{I} + \mathrm{H}\cdot\mathrm{CO}_2\mathrm{H} + \mathrm{NaI} \quad \ldots\ldots\ldots \quad (3)$$

would result in the same overall consumption of iodine as reaction (1), so that the progressive replacement of one by the other would lead to the observed approximate constancy of total halogen uptake.

Table 2 shows the calculated amounts of iodine used in reactions (1), (2), and (3), respectively. Below a pH of 12·5, the sum of these is in good agreement with the measured overall iodine consumption, but in more strongly alkaline conditions an increasing amount of the iodine used cannot be accounted for in terms of the simple organic products shown. On the other hand, the theoretical quantity of isobutyraldehyde consumed in these three reactions is always considerably smaller than the amount initially present. The difference is presumably ascribable to polymerisation of the aldehyde, which would also account for the fact that over the pH range 10—12 the observed molar iodine consumption is somewhat lower than would be expected from the stoicheiometry of reactions (1)—(3).

The difference, found at high pH values, between the total iodine consumed and that used in forming the simple organic products shown in Table 2 suggests that certain of these compounds can react further with iodine in strongly alkaline solution. Fatty acids and their iodo-derivatives have been shown experimentally to be stable under the experimental conditions used,[9] but isopropyl iodide is readily hydrolysed to isopropyl alcohol which can be detected in the system above pH 13·5. The sharp increase in iodine consumption at the highest pH values investigated is probably due to the tendency of this alcohol to undergo oxidative fission, *e.g.*:

$$Me_2CH{\cdot}OH + 4I_2 + 8NaOH = AcOH + H{\cdot}CO_2H + 8NaI + 5H_2O \quad . \; . \; . \; . \; . \; (4)$$

An increasing contribution from reactions of this type would explain why the average molar iodine consumption rises well above unity under the most strongly alkaline conditions.

Reactions of Trimethylacetaldehyde.—One of the most striking features of the reaction of trimethylacetaldehyde with alkaline iodine is the very low halogen uptake, only about one molecule of iodine being consumed, even under optimum conditions, for every four molecules of the aldehyde initially present. The present observations (p. 1139), together with other evidence,[10] suggest that trimethylacetaldehyde undergoes extensive polymerisation or condensation on addition to water or aqueous alkali and that consequently only a small proportion of the compound exists as the monomer in dilute solution.

TABLE 2.

Influence of pH on the products formed from isobutyraldehyde.

Temp. = 25°; [Isobutyraldehyde] = 0·0025M; [Iodine] = 0·005M.

pH	Iodine (10^{-5} mole) consumed in forming: $Me_2CH{\cdot}CO_2H$	$Me_2CI{\cdot}CO_2H$	Neutral org. cpd.	Total iodine consumed (calc.) (10^{-5} mole)	Total iodine consumed (expt.) (10^{-5} mole)	Total aldehyde consumed (calc.) (10^{-5} mole)	Total aldehyde present (10^{-5} mole)
10·0	3·41	0·63	nil	4·04	4·05	3·72	5·00
10·5	3·45	0·90	0·02	4·37	4·20	3·92	5·00
11·0	3·18	0·82	0·31	4·31	4·25	3·80	5·00
11·5	2·90	0·70	0·71	4·31	4·20	3·96	5·00
12·0	2·65	0·49	0·98	4·12	4·15	3·88	5·00
12·5	2·30	0·32	1·32	3·94	4·20	3·78	5·00
13·0	1·90	0·10	1·74	3·74	4·90	3·74	5·00
13·5	1·40	nil	1·90	3·30	6·90	3·30	5·00
14·0	0·80	nil	1·72	2·52	—	2·52	5·00

The principal reaction which the monomer undergoes is undoubtedly straight oxidation to trimethylacetic acid and this acccounts for the major part of the halogen taken up. At high pH values, however, a small amount of the iodine consumed is organically bound. This fact and the appearance, under strongly alkaline conditions, of propionic acid and its iodo-derivative (Table 1) suggest that substitution followed by fission of C–C bonds can also occur.

The kinetic results and in particular the variation of rate with pH (Fig. 2) suggest that despite the low iodine uptake there is competition between oxidation and substitution, analogous to that found with the lower homologous aldehydes.

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[9] Cullis and Hashmi, *J.*, 1956, 2512.

[10] Cf. Conant, Webb, and Mendum, *J. Amer. Chem. Soc.*, 1929, **51**, 1246.