

BASE CATALYSED HALOGENATION OF ALIPHATIC ALDEHYDES

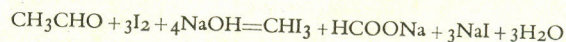
Part I.—Iodination of Acetaldehyde

NAZIR RAMZAN AND RIAZ-UR-RAHMAN

University Institute of Chemistry, Lahore

(Received November 29, 1962)

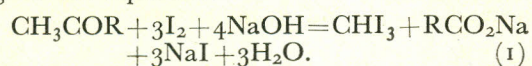
Iodination of acetaldehyde has been carried out in the presence of large excess of alkali. The reaction does not take place strictly according to the equation:



In addition to the normal products predicted by this equation, acetic acid and monoiodoacetic acid were also found showing thereby that the halogenation is followed by the oxidation of acetaldehyde. The low consumption of iodine per mole of acetaldehyde was probably due to some aldol condensation in the presence of alkali. The rate of halogenation was found to be controlled by the order of mixing the reactants and alkali concentration but independent of the iodine concentration.

The haloform reaction has been extensively studied and a large literature, too bulky to be discussed here has accumulated. Lieben's¹ work on iodination of alcohols and ketones led him to believe that the "iodoform test" is given by the compounds containing the CH_3CO -group linked either to carbon or hydrogen. His findings have proved very useful for the detection of water soluble alcohols and methyl ketones. In 1880, Kramer² attempted this reaction for the quantitative estimation of the principal product i.e. iodoform by using a gravimetric procedure which is still occasionally used.³ Messinger⁴ adopted a volumetric method to study the kinetics of the reaction, which was later on, improved by Hatcher and Mueller⁵ in order to obtain maximum accuracy. However, they found that the reaction never gave the theoretical yield of iodoform.

Cullis and Hashmi^{6,7} made a detailed study of the base-catalysed iodination of methyl ketones and related compounds. They observed that the reaction does not occur quantitatively according to the equation:



The present paper deals with the iodination of acetaldehyde which has hitherto remained unexplored. It is found that the overall reaction does not proceed strictly according to the equation (1) under the conditions used by Messinger.⁴

Experimental

Materials.—Commercial sample of acetaldehyde was freshly distilled in a current of nitrogen. The middle fraction was collected and stored in a black-lacquered bottle to prevent photo-decomposition. Acetaldehyde solution was prepared by weight according to Goodwin's procedure⁸ and diluted

to the desired strength. The concentration was confirmed by bisulphite method.⁹ All other reagents were "AnalaR" materials.

Kinetic Measurements.—Since this reaction is fairly rapid at 0°C ., the rate measurements were carried out in Y-tubes as described by Cullis and Hashmi.⁶ Acetaldehyde and sodium hydroxide were placed in one limb and iodine solution was run into the other. The tubes were closed with rubber bungs covered with tin-foil and then suspended in the thermostat to attain the requisite temperature. The reaction was started by quickly tilting the Y-tube to mix the reagents and stopped at desired times by pouring the reaction mixture in slight excess of sulphuric acid. The liberated iodine was immediately titrated against a standard sodium thiosulphate solution.

The velocity constants were calculated from the initial slopes of $\text{Log}_{10} (V_t - V_\infty)$ —times curves, where V_t and V_∞ are the volumes of thiosulphate consumed at times t and infinity, respectively.

Measurement of Total I_2 Consumption.—During this investigation, it has been observed that the order of mixing the reactants does affect the overall consumption of iodine. If the reactants are mixed in the order acetaldehyde-sodium hydroxide iodine, the uptake of iodine was found to be maximum and constant (Fig. 1).

Acetaldehyde (25 ml.) and varying volumes of sodium hydroxide solution were placed in a well cleaned stoppered conical flask and total volume made to 75 ml. with water. Iodine solution (25 ml.) was added with constant stirring. After a measured period the mixture was acidified with a calculated amount of sulphuric acid, and the liberated iodine was titrated against thiosulphate.

Analysis of Reaction Products.—In alkaline solution iodine reacts with acetaldehyde giving fatty acids and iodinated species.

Identification of Fatty Acids.—After titrating the excess of iodine, the mixture was shaken with ether (4×5 ml.). Iodoform and organic acids went into the ethereal layer. The combined ethereal extracts were removed and washed with aqueous ammonia (4×5 ml.). The aqueous layer containing the ammonium salts of the fatty acids and iodinated organic acids was separated and analysed for its anions by a circular paper chromatographic method.¹⁰ The filter paper (Whatman No. 1) used was thoroughly acid washed.¹¹

Estimation of Iodinated Products.—The iodinated neutral and acid products were separated and estimated as follows:

Excess of halogen was removed by titrating against sodium thiosulphate. The reaction mixture was then shaken with ether (8×5 ml.) The combined ethereal extracts were further treated with 0.1N NaOH (3×5 ml.). The alkaline layer containing sodium salt of iodo-acids was separated from ethereal layer and treated with halogen-free nitric acid to release the acids. The acids were then extracted with ether. Both the ethereal extracts were estimated for their iodine contents by Dragin and Rasanoff's sodium alcohol method.

Estimation of Iodoform.—The reaction mixture was treated with acid and the liberated iodine was titrated against sodium thiosulphate. The organic contents were extracted with chloroform, and shaken with 0.20% aqueous hydroxylamine hydrochloride¹³ to destroy any carbonyl compounds. The optical densities for iodoform were then measured at 3470 Å with a unicam sp. 500 spectrophotometer fitted with a 2-cm. quartz cell for each sample. The amount of iodoform was calculated from the plot for optical density-concentration curves.

Results

Kinetic Measurements.—Measurements of the rates of iodination of acetaldehyde have been carried out in very dilute solutions of the reagents. Since the reaction takes place spontaneously even at 0°C., the conditions used for the limiting uptake of iodine could not be strictly followed. It is observed that the iodine disappears according to a first order kinetic law in a large excess of alkali.

Plots of $\log_{10} (V_t - V_\infty)$ against time (t) are found to be linear over at least first half of the reaction after which the rates tend to fall off less rapidly. The results show that the initial rates of iodination are independent of the iodine concentration (Table 1) and directly proportional to the concentration of free alkali (Table 2).

TABLE 1.—INFLUENCE OF IODINE CONCENTRATION ON THE IODINATION OF ACETALDEHYDE.

[Iodine] (M)	Velocity constant $k(\text{Sec}^{-1} \times 10^3)$
0.01	17.40
0.02	17.38
0.03	17.41

Note: Temp.=25°C. $[\text{CH}_3\text{CHO}] = 0.0025 \text{ M}$ $[\text{NaOH}] = 0.1 \text{ M}$.

TABLE 2.—INFLUENCE OF ALKALI CONCENTRATION ON THE IODINATION OF ACETALDEHYDE.

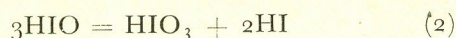
[NaOH] (M)	Velocity constant $K(\text{Sec}^{-1} \times 10^3)$	$K/(\text{OH})$
0.1	17.4	174
0.2	34.6	173
0.3	52.2	174

Note: Temp.=25°C. $[\text{CH}_3\text{CHO}] = 0.0025 \text{ M}$ $[\text{Iodine}] = 0.01 \text{ M}$.

The consumption of iodine by acetaldehyde is controlled by the following factors:

(a) *Order of Mixing the Reactants.*—Two reagent solutions were mixed in a stoppered conical flask suspended in the thermostat maintained at 25°C. for varying periods before the third solution was added. Fig. 1 shows that when acetaldehyde and sodium hydroxide or acetaldehyde and iodine are mixed and set aside, the extent of iodine consumption is independent of the time which elapses before the addition of the third component, but gradually decreases when iodine and sodium hydroxide are premixed.

The principal iodinating species is thought to be hypiodous acid¹⁴ which is being converted into iodate in reaction:



Thus the low uptake of iodine, when iodine and alkali are mixed, is evidently due to the wastage of iodine as a result of disproportionation of hypoiodite to iodate. To retard this process i.e. hypoiodite to iodate, the iodine was added with constant agitation and alkali used was 10 to 20 times more than that required according to stoichiometric ratio.

(b) *Influence of Alkali Concentration.*—A fixed volume of iodine solution was added to acetaldehyde and alkali mixtures, containing different concentrations of alkali, and set aside for one hour at 25°C. It will be seen from Fig. 2 that the uptake of iodine increases with alkali concentra-

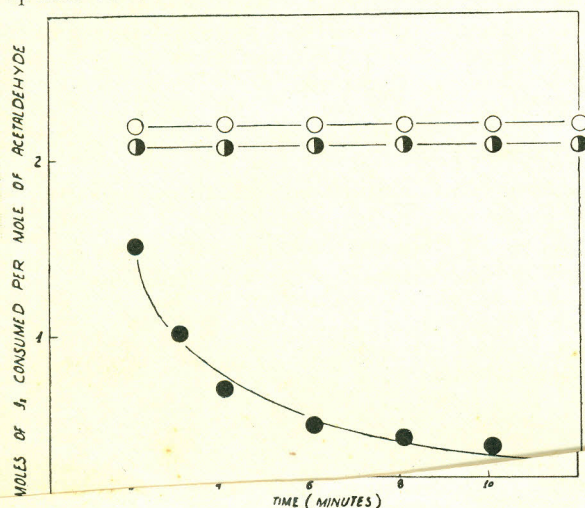


Fig. 1.—The influence of order of mixing of the reactants on consumption of iodine. Temp. = 25°C; [Acetaldehyde] = 0.01 M. [Iodine] = 0.04 M [NaOH] = 0.1 M. ○ Acetaldehyde and sodium hydroxide mixed; iodine added after time t. ● Acetaldehyde and iodine mixed; sodium hydroxide added after time t. ● Iodine and sodium hydroxide mixed; Acetaldehyde added after time t.

tion reaching a limiting value of 2.3 moles per mole of acetaldehyde. Several sets were taken and in no case was the consumption of iodine observed as required by the equation (1). This behaviour is in direct contrast to that found in the case of simple ketones by earlier workers under similar conditions.⁶ The reason cannot be ascribed to the disproportion of the halogenating species. It is believed to be due to some acetaldehyde undergoing aldol condensation in the presence of alkali. The limiting value remains constant over wide range of alkali concentrations in spite of the fact that the rate of aldol condensation should increase in large excess of alkali present.

(c) *Influence of Iodine Concentration.*—Equal volumes of different iodine solutions were added to a standard acetaldehyde-alkali mixture. Figure 3 shows that at high alkali concentration, the uptake of iodine increases reaching a limiting value with the increase of iodine concentration but at low alkali concentration, the consumption of iodine is found to fall off rapidly. This is believed to be the depletion of hydroxyl ions as a result of the reaction.

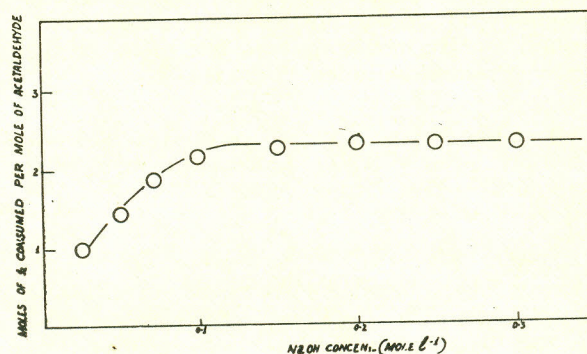
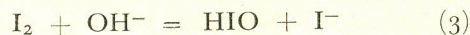


Fig. 2.—The influence of alkali concentration on iodine consumption by Acetaldehyde. Temp. = 25°C; [Acetaldehyde] = 0.01 M. [Iodine] = 0.04 M.

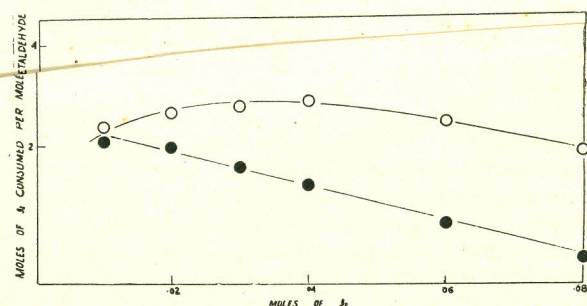


Fig. 3.—The influence of iodine concentration on consumption of iodine by acetaldehyde. Temp = 25°C; [Acetaldehyde] = 0.0025 M; ○ [NaOH] = 0.4 M. ● [NaOH] = 0.05 M.

Reaction Products.—Iodoform separates out as a yellow insoluble substance during the iodination of acetaldehyde. Fatty acids and iodinated organic acid have been identified by circular paper chromatography.

Fatty Acids.—Ammonium salts of the acids were applied to the chromatograms. The developing solvent contained 30% V/V of aqueous ammonia (sp. gr. 0.88) and 70% V/V n-propyl alcohol. The chromatograms after drying were

sprayed with a slightly alkaline solution of B.D.H. universal indicator (pH adjusted to 9.5). Formic acid and acetic acid were identified from the reaction products. They appear as red bands on a blue background.

Iodinated Organic Acid.—The procedure involved in this case was different from that for fatty acids. The developed chromatograms were allowed to hang for 10 seconds in a glass tank filled with dilute gaseous chlorine (produced by the action of HCl on solid KMnO_4). Chlorine liberated iodine from the iodo-acid which reacted with ammonia (present in the paper from developing solvents) and left a yellow stain on a white background. Only moniodo acid has been detected in the reaction products.

R_f values for acids present in the reaction products are given in Table 3 along with the value determined from the known acids.

TABLE 3.— R_f VALUES OF ACIDS DETECTED IN THE REACTION PRODUCTS.

Acid	R_f
HCOOH	0.375 (0.38)
CH_3COOH	0.384 (0.39)
CH_2ICOOH	0.50 (0.50)

Quantitative Estimation of Iodinated Products.—The amount of iodine present in the iodinated products in the case of a typical set are given in Table 4. It will be seen that almost all the iodine is converted to organic form. The major portion of iodine form iodoform and very small quantity of it is found in moniodo acid. This is in good agreement between the total amount of iodine found in iodoform and moniodo acid, and consumed by the reaction. The amount of iodine

TABLE 4.—INFLUENCE OF NaOH ON THE IODINATED PRODUCTS FORMED FROM ACETALDEHYDE.

NaOH (Mole l^{-1})	Iodinated products found experimentally			I_2 Consumed
	Neutral	Acid	Total	
0.05	1.40	—	1.40	1.45
0.10	2.05	0.05	2.10	2.15
0.15	2.14	0.06	2.20	2.25
0.20	2.19	0.06	2.25	2.30
0.25	2.18	0.06	2.24	2.30
0.30	2.18	0.07	2.25	2.30

Note: Temp. = 25°C. $[\text{CH}_3\text{CHO}] = 0.01\text{M}$ [Iodine] = 0.04M.

TABLE 5.—IODOFORM PRESENT IN THE NEUTRAL PRODUCT.

NaOH (Mole l^{-1})	Mole of I_2 per mole of acetaldehyde	
	Neutral	Iodoform
0.05	1.40	1.41
0.10	2.05	2.03
0.15	2.14	2.12
0.20	2.19	2.20
0.25	2.18	2.20
0.30	2.18	2.20

Note: Temp. = 25°C. $[\text{CH}_3\text{CHO}] = 0.01$ [Iodine] = 0.04M.

found in iodoform by spectroscopic method present in the reaction mixture closely resembles the iodine present in the neutral products. It is quite obvious that no neutral product containing iodine except iodoform is formed.

Discussion

The analytical results show that in an alkaline solution, iodination of acetaldehyde leads to the formation of iodoform, formic acid, moniodoacetic and acetic acid. However, the uptake of iodine (Fig. 2) is not found to be that required by the stoichiometric equation. The iodinating species initially present in the solutions are I'_3 , HIO , I'_0 and I_2 . Of these hypiodous acid has been suggested by the earlier workers¹⁴ as the principal active entity responsible for iodinating and to some extent for the oxidation of acetaldehyde. The reaction $3\text{HIO} = \text{HIO}_3 + 2\text{HI}$ which causes the disproportion of hypiodite to iodate takes place at the same time and is responsible for the low uptake of iodine in the presence of small alkali concentration (Fig. 1). High alkali concentration and the addition of iodine with constant agitation does minimize the occurrence of this reaction.

The unexpected low consumption of iodine at high alkali concentration cannot be ascribed to the disproportionating of hypiodite to iodate but it is believed to be due to some of acetaldehyde undergoing aldol-condensation. The results on the consumption of iodine by iodoform and moniodo acid (Tables 4 and 5), of a typical set also support our belief that approximately 0.25 moles of acetaldehyde do not take up iodine.

The base-catalysed iodination of acetaldehyde proceeds according to the following stages:

(i) *Enolisation of the Acetaldehyde.*—Acetaldehyde is converted into enolate ion by the catalytic effect

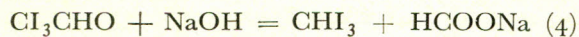
of hydroxyl ions. If B is a basic catalyst i.e. hydroxyl on, the reaction is represented as:



Studies on the kinetics of haloform reaction have shown that the rate determining stage¹⁵ is the formation of enolate ion. Since the measured rate is independent of iodine concentration and directly proportional to the free alkali concentration, it is believed that the rate of iodination is in fact the rate of enolisation.

(ii) *Iodination of the Enolate Ions.*—The enolate ion thus formed may immediately react to give mono-iodo-acetaldehyde CH_2ICHO , which is further rapidly iodinated to yield tri-iodo-derivative. This progressive iodination is effected by hypoiodous acid.

(iii) *Hydrolysis of Tri-iodo-acetaldehyde.*—Tri-iodo-acetaldehyde is hydrolysed to form iodoform and sodium formate.



in a similar fashion as in the formation of chloroform by alkaline hydrolysis of chloral.

Acetic acid and monoiodo-acid are formed in addition to the normal products. The presence of these acids have been confirmed by paper chromatography. The formation of acetic acid is due to the oxidation of acetaldehyde by hypoiodous acid. If the reaction goes normally according to the equation (1) on the basis of iodoform results, 2.25 moles of iodine are required. The excess of iodine (i.e. 1.6%) is therefore taken up by acetaldehyde to form iodo-acid.

It is concluded that the method involving base-catalysed iodination for the quantitative analysis

of acetaldehyde is unsatisfactory as it forms iodo-acid and acetic acid in addition to the normal products. Moreover some of the acetaldehyde is believed to undergo aldol-condensation under these conditions.

Acknowledgement.—One of the authors Nazir Ramzam is very much indebted to Dr. B.A. Khokhar for his valuable suggestions and to Dr. Badar-ud-Din, Director, Institute of Chemistry, for providing facilities.

References

1. Lieben Ann. Spl. Bd., **7**, 218 (1870).
2. Kramer, Ber., **13**, 1000 (1880).
3. Hennion and Pillar, J. Am. Chem. Soc., **72**, 5317 (1950).
4. Messinger, Ber., **21**, 3366 (1888).
5. Hatcher and Mueller, Trans. Roy. Soc., Canada, **23**, 1473 (1951).
6. Cullis and Hashmi, J. Chem., Soc. 2512 (1956).
7. Cullis and Hashmi, J. Chem. Soc., 1548 (1957).
8. Goodwin, J. Am. Chem. Soc., **42**, 39 (1920).
9. Parkinson and Wagner, Industrial and Engineering Chemistry, Analytical Edition, **6**, 433 (1934).
10. Hashmi and Cullis, Anal. Chim. Acta, **14**, 336 (1956).
11. Richard J. Block, Emmett L. Durrum and Gunter Zweig, *Paper Chromatography and Paper Electrophoresis* (Academic Press Inc., Publisher, New York, 1958), p. 260.
12. Drogin and Rosnoff, J. Am. Chem. Soc., **38**, 711 (1916).
13. Dalgogare, Norris and Mitchell, Anal. Chim., **23**, 1473 (1951).
14. Morgan, Bardwell, and Cullis, J. Chem. Soc., 3190 (1950).
15. Bell, "Acid-Base Catalysis" (Oxford University Press, 1941), p. 35.