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EFFECTS OF CATALYSTS ON CHLORINATION OF PROPIONIC ACID[1]

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Abstract—Chlorination of propionic acid with molecular chlorine at 100–130° in the dark giving various chlorinated propionic acids has been studied. Information concerning the product distribution and the effect of some addenda on the distribution has been obtained. There seems to be a competition between the H atom abstraction by radicals and the addition to the enol of carboxylic acid; the ratio of α-chlorination, α/(α + β), increases in the presence of enolising catalyst such as H_2SO_4, HCl and $FeCl_3$. The radical scavengers such as *m*-dinitrobenzene increase the ratio of α-chlorination and no chloro acid is formed on addition of more than 1 mol % *m*-dinitrobenzene in the absence of enolising catalyst. The addition of 3 mol % *m*-dinitrobenzene in the presence of 95% H_2SO_4, yields only α-chloro acid. The reaction at 120° in the presence of a radical scavenger gives mainly α-chloro acid at an early stage and then α,α-dichloro acid, the latter yield being 7·7% after 7 hr and 33·6% after 12 hr The reaction mechanism is discussed.

HALOGENATION of aliphatic acids proceeds via two mechanisms, i.e., the H atom abstraction by radicals and the addition to the enol of acid halides as a reaction carrier.[2] The H atom abstraction,[3, 4] which gives halo acids substituted at various positions, is accelerated by heat, light and/or radical initiators, and the addition to enol,[5] which is generally feasible in the presence of phosphorus halides, acid halides, acid anhydrides and thionyl chloride—the so-called Hell–Volhard–Zelinsky method (HVZ method) or a modification—yields only α-halo acid.

Lapoworth[6] was the first to suggest that the α-halogenation according to the HVZ method proceeds via the intermediary formation of acid enol analogous to the acid-catalysed halogenation of ketones and related carbonyl compounds. It has been considered that acid halide is the reaction carrier which is formed by the reaction of acid with the catalysts at the initial stage and that either enol[7] or cationic π-complex[8] of acid halide is attacked by halogen to give α-halo acid.

Most previous studies on α-halogenation of aliphatic acids have been on α-bromination. Since α-chlorination has been less successful than α-bromination,[7] the chlorination of propionic acid was investigated to obtain information concerning the product distribution and the effect of some addenda.

RESULTS

Chlorine gas was bubbled into a mixture of propionic acid and an acid catalyst. The oxygen in the reaction system was preliminarily expelled by bubbling nitrogen gas. The product was distilled directly or after extraction with chloroform in vacuum to analyse the distillate with GLC after HCl-catalysed esterification with methanol. A typical gas chromatograph of the chlorination mixture catalysed by benzoyl peroxide at 100° for 5 hr is illustrated in Fig 1. Methyl propionate, methyl α- and β-chloropropionates were identified and estimated by GLC in comparison with

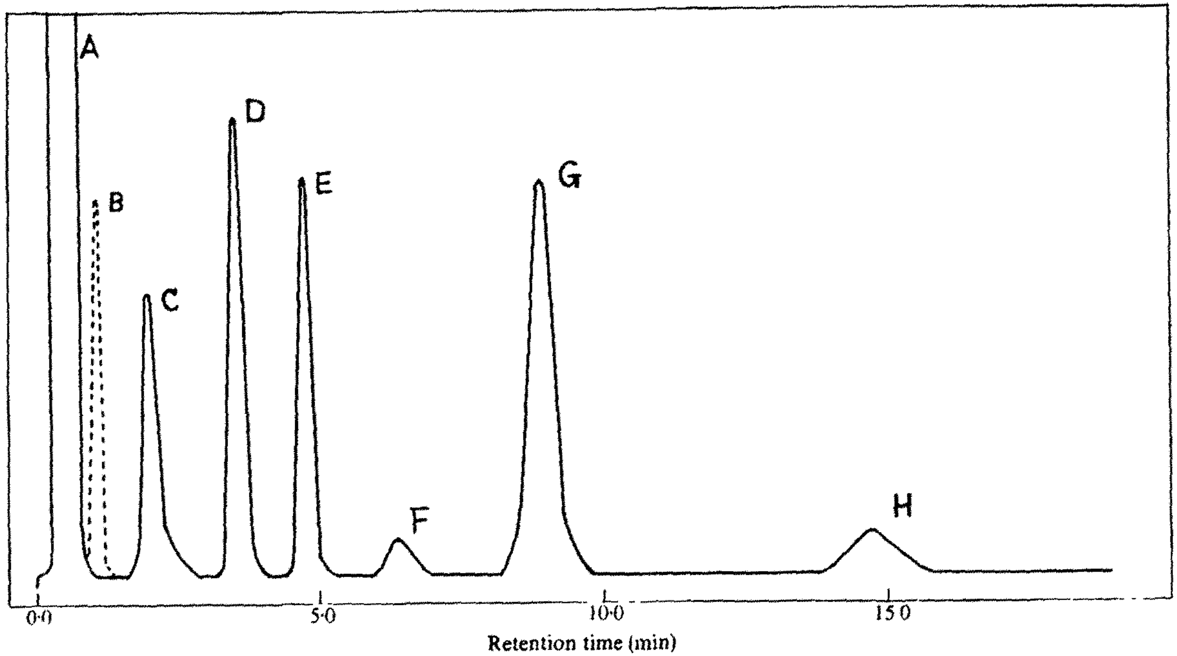


FIG. 1. Gaschromatogram of products obtained by the peroxide-catalysed chlorination of propionic acid at 100°. A, diethyl ether; B, methyl propionate; C, water; D, ethylbenzene; E, methyl α-chloropropionate; F, methyl α,α-dichloropropionate; G, methyl β-chloropropionate; H, methyl β,β-dichloropropionate.

authentic samples, using ethylbenzene as an internal standard. Methyl α,α-dichloropropionate and β,β-dichloropropionate which were isolated by preparative GLC were identified by GLC, IR and NMR spectra, and also elemental analysis, the result being shown in Table 1. Methyl α,β-dichloropropionate was not detected by GLC.

TABLE 1. ANALYSIS OF METHYL DICHLOROPROPIONATE

Compounds	Chlorine content (%)[a]	IR $\nu_{C=O}$ (cm^{-1})	NMR Chemical shift (τ)	
$CH_3CCl_2CO_2CH_3$	44·8	1745	CH_2 H	6·04 (s)
			β-H	7·66 (s)
$CHCl_2CH_2CO_2CH_3$	41·6	1738	CH_2 -H	6·35 (s)
			α-H	6·86 (d)
			β-H	4·05 (t)

[a] Calculated value 45·2%.

Thus chlorination without additives gave two monochloro acids. Then the chlorination at 110° for 3 hr was similarly carried out to study the effect of various enolising catalysts at an early stage. The ratio of yields of α-chloro acid *vs* all monochloro acids, α/(α + β), is listed in Table 2. From the Table it is apparent that an enolising catalysts such as 95% H_2SO_4, anhydrous HCl and $FeCl_3$ increase the ratio from 0·34 to 0·51–0·63. Titainium tetrachloride also showed a slight increase in α-chlorination. Increased amounts of H_2SO_4 has little influence on the ratio. The addition of water decreased the total yield. Virtually no acceleration was observed on addition of a small quantity of propionyl chloride or propionic anhydride, but the acceleration was enhanced on addition of a large quantity of this acid halide or anhydride.

TABLE 2. EFFECT OF ADDITIVES ON α-CHLORINATION[a]

Additives	(mol %)	Yield of reaction mixture (%) Unreacted acid	α-Chloro acid (α)	β-Chloro acid (β)	$\frac{\alpha}{\alpha+\beta}$
None	--	51·5	6·0	11·5	0·34
95% H_2SO_4	(4)	58·5	8·0	6·0	0·57
95% H_2SO_4	(9)	51·0	8·0	5·5	0·59
95% H_2SO_4	(20)	30·0	9·5	9·0	0·51
50% H_2SO_4	(20)	61·0	2·5	1·5	0·63
HCl	(satd.)	62·0	7·0	4·5	0·61
CH_3CH_2COCl	(4)	45·7	7·7	13·0	0·37
CH_3CH_2COCl	(17)	26·7	37·1	1·7	0·96
$(CH_3CH_2CO)_2O$	(4)	42·1	11·1	18·5	0·38
$(CH_3CH_2CO)_2O$	(17)	37·5	12·5	5·0	0·71
$FeCl_3$	(4)	66·5	13·0	8·5	0·60
$TiCl_4$	(2)	35·5	11·9	19·4	0·38

[a] Reaction at 110° for 3 hr, using initially 0·2 mole of propionic acid.

There appeared to be competition between the H atom abstraction by radicals and the addition to enol; the ratio of α-chlorination increasing in the presence of enolising catalyst. Radical scavengers such as *m*-dinitrobenzene and 1,3,5-trinitrobenzene increased the ratio of α-chlorination as shown in Table 3. No chloro acid was formed at all on addition of more than 1 mol % m-dinitrobenzene in the absence of enolising catalyst. Addition of 3 mol% m-dinitrobenzene in the presence of 95% H_2SO_4, produced α-chloro acid alone, but the yield dropped from 6·0% with 1 mol % m-dinitrobenzene to 3·5%. Similarly, the addition of 17 mol % propionyl chloride decreased the yields of α-chloro acid from 37·1% to 9·2%.

TABLE 3. EFFECT OF RADICAL SCAVENGERS ON CHLORINATION[a]

Additives	(mol %)	Yield of reaction mixture (%)			$\frac{\alpha}{\alpha + \beta}$
		Unreacted acid	α-Chloro acid (α)	β-Chloro acid (β)	
m-$C_6H_4(NO_2)_2$	(1)	87·2	None	None	—
1,3,5-$C_6H_3(NO_2)_3$	(1)	70·2	0·5	1·0	0·33
I_2	(4)	85·0	0·5	1·5	0·25
95% H_2SO_4 m-$C_6H_4(NO_2)_2$	(9) (1)	73·5	6·0	1·0	0·86
95% H_2SO_4 m-$C_6H_4(NO_2)_2$	(9) (2)	71·5	7·5	0·5	0·94
95% H_2SO_4 m-$C_6H_4(NO_2)_2$	(9) (3)	66·5	3·5	None	1·00
CH_3CH_2COCl m-$C_6H_4(NO_2)_2$	(16) (3)	62·5	9·2	None	1·00
$FeCl_3$ m-$C_6H_4(NO_2)_2$	(4) (2)	50·2	9·0	10·0	0·47

[a] Reaction at 110° for 3 hr, using initially 0·2 mole of propionic acid.

The effects of temperature and time on α-chlorination in the presence of m-dinitrobenzene and 95% H_2SO_4 are summarized in Table 4. α-Chloro acid together with a small amount of β-chloro isomer, but no α,β-dichloro acid were obtained. The reaction at 120° in the presence of a radical scavenger gave mainly α-chloro acid at an early stage and then α,α-dichloro acid, the latter yield being 7·7 % at 7 hr and 33·6% at 12 hr. No α,β-dichloro acid was obtained under these conditions. The ratio, α/(α + β),

TABLE 4. EFFECT OF TEMPERATURE AND TIME OF REACTION[a]

Temp (°C)	Time (hr)	Yield of reaction mixture (%)			
		Unreacted acid	α-Chloro acid	β-Chloro acid	α,α-Dichloro acid
110	3	66·5	3·5	None	None
120	3	60·0	10·0	1·0	None
130	3	46·0	21·5	4·0	None
120	7	39·0	23·5	4·5	7·7
120	12	None	23·0	1·0	33·6

[a] Initial moles of the starting materials: propionic acid, 0·2 mole; 95% H_2SO_4, 9 mol %; m-dinitrobenzene, 3 mole %.

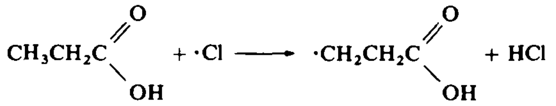
increased from 0·34 without additives to 0·60 on additon of $FeCl_3$, but decreased to 0·47 with the coexistence of $FeCl_3$ and *m*-dinitrobenzene.

The IR spectrum of a mixture of carboxylic acid with $FeCl_3$ is little known.[9, 10] The IR spectra of propionic acid shows lowering of carbonyl frequency on addition of $FeCl_3$; this fact implies that the acceptor atom is coordinated with the carbonyl O atom as a donor.[10, 11] Similarly, a mixture of *m*-dinitrobenzene-$FeCl_3$ (1:1 or 1:2) gave IR spectra slightly different from pure *m*-dinitrobenzene. Both spectra show some interaction of nitro group with Lewis acids, although this interaction is less than that of nitrobenzene.[12] Furthermore, a mixture of $FeCl_3$, propionic acid and *m*-dinitrobenzene in a molar ratio of 2:2:1 shows both absorption spectra of propionic acid-$FeCl_3$ and *m*-dinitrobenzene-$FeCl_3$ mixtures.

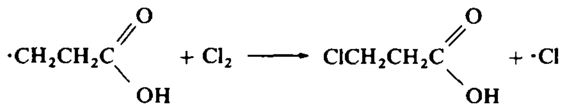
DISCUSSION

The vapor phase chlorination of paraffins requires a temperature above 200°[13] because of the low degree of dissociation of molecular chlorine, e.g., 0·035% even at 1000° K. β-Chloro acid was obtained in the dark at 110°, but not at all in the presence of a radical scavenger. This suggests that atomic chlorine participates in β-chlorination. For example, products of radical reactions are obtained by molecule-induced homolysis of molecular chlorine with cyclohexene in the dark at 25°[14] and there is competition between the random and selective α-chlorination with cyclohexanecarboxylic acid in the dark at 77–195°.[15] Our observation that no chlorination occurred on addition of a radical scavenger in the absence of an enolising catalyst suggests that the enolisation hardly occurs in the absence of the catalyst. Therefore, the formation of β-chloro acid may be ascribed not to molecule-induced homolysis, but to atomic chlorine produced by the dissociation of molecular chlorine catalysed by molecular oxygen, peroxides or other impurities. Hence, the chlorination mechanism in the absence of acid catalysts would involve the following H atom (predominantly β-H) abstraction.

$$Cl_2 \rightleftharpoons 2\cdot Cl \qquad (1)$$



$$CH_3CH_2C(=O)OH + \cdot Cl \longrightarrow \cdot CH_2CH_2C(=O)OH + HCl \qquad (2)$$

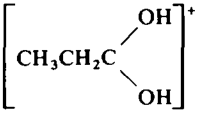


$$\cdot CH_2CH_2C(=O)OH + Cl_2 \longrightarrow ClCH_2CH_2C(=O)OH + \cdot Cl \qquad (3)$$

This mechanism explains the small ratio of $\alpha/(\alpha + \beta)$ without additives in view of the inductive and steric effects of carboxyl group.

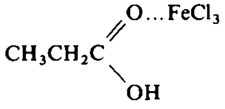
The effect of substituents on the rate of the acid-catalysed enolisation of ketones is influenced mainly by the hyperconjugative stabilization and also by the combination of resonance, inductive and steric effects.[16] Hammett's ρ value for the acid-catalysed bromination of substituted phenyl methyl ketones is negative[17] and the acid-catalysed enolisation of acetone is faster than that of bromoacetone.[18] Hence, it is probable that the basicity of ketones parallels the rate of the acid-catalysed enolisation. Generally, halogenation of ketones is faster than the corresponding carboxylic acid, e.g., the rate constant for bromination of benzyl phenyl ketone is $7{\cdot}7 \times 10^{-4}$ M^{-1} sec^{-1} at 55°,[19] while the apparent rate constant for the present chlorination of propionic acid is $3{\cdot}24 \times 10^{-6}$ sec^{-1} at 110°. Bromination of acetyl bromide is similarly fast, e.g., the rate constant for bromination of acetyl bromide is $1{\cdot}21 \times 10^{-4}$ M^{-1} sec^{-1} at 51°, where the enolisation step is fast because of the rate dependence on bromine concentration and no influence of $FeCl_3$ or H_2SO_4 on the rate.[20, 21] Carbonyl compounds of a general formula RCOX, where X is CH_3, C_6H_5, Br or Cl, are easily halogenated as described above, but for carboxylic acid (X = OH) the halogenation is comparatively slow in spite of the electron-releasing order due to the inductive effect of $Cl < Br < OH < C_6H_5 < CH_3$. It may be supposed that the equilibrium concentration of the monomeric carboxylic acid is low and its keto form is more stable than the enol because of the stabilization of dimer by H-bonding and also the electron-releasing property of OH group due to resonance effect.

The dimeric form of carboxylic acid is more stable by several kcal/mol than the monomeric one in the liquid state owing to the H bonding.[22] Probably, the rate of enolisation is not increased by the H-bonding, since an increase of positive charge at carbonyl C atom is suppressed by the π-electron-delocalisation in the plane of H-bonding which is effective for stabilization. The spectroscopic study[23] supports the protonation of carboxylic acid in conc H_2SO_4 as shown in I. The IR spectrum in this experiment shows the coordination II of $FeCl_3$ to carbonyl O atom. Likewise carbonyl C atom may be charged positively by the enolising catalyst; then the protonated species would readily eliminate an α-proton to give the enol.



$[CH_3CH_2C(OH)_2]^+$

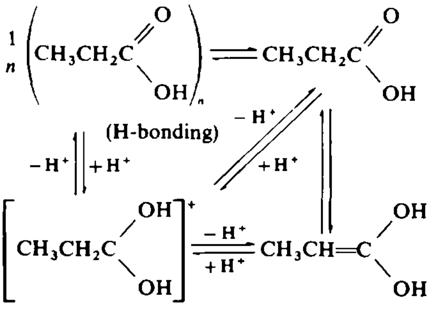
I



$CH_3CH_2C(=O\cdots FeCl_3)OH$

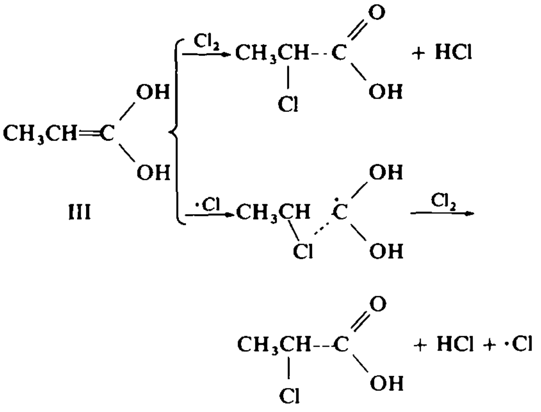
II

The acid-catalysed α-halogenation of carboxylic acid may proceed by way of either (i) enolisation of acid itself or (ii) intermediary formation of acid halide. The reaction is not accelerated on addition of a small amount of propionyl chloride or propionic anhydride. Propionyl chloride may be formed, but it would be expelled from the system because of its low boiling point (80°). In view of these facts a probable mechanism could be through (ii), i.e., the following enolisation step.



III

(4)



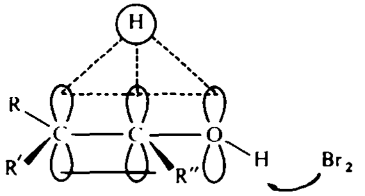
III

(5)

(6)

In the absence of enolising catalyst, α-chlorination is difficult because of the very small equilibrium concentration of the enol III owing to H-bonding and resonance as stated above. But in the presence of enolising catalyst, the rate of enol formation becomes fast, which enables α-chlorination by both molecular and atomic chlorine (Eqs. 5 and 6). α-Chloro acid which is formed at an early stage, cannot be chlorinated faster than the original acid to give α,α-dichloro acid, since α-chloro acid is a much weaker base than the original acid, i.e., the proton affinity is lower.

Recently, Kwart and Scalizi[8] proposed that a π-complex IV could be an intermediate in bromination and formed via acid-catalysed bridging of the α-proton to the carbonyl center. But this intermediate is not appropriate for the present reaction, because it is difficult for electrophilic chlorine to react with the cation and further, no acceleration of α-chlorination was observed on addition of a comparatively large amount of H_2SO_4.



IV

(7)

A radical scavenger such as nitro aromatics seems to trap radicals with its nitro group.[24] The perfect inhibition for β-chlorination requires only 1 mol % of *m*-dinitrobenzene without enolising catalyst, but 3 mol % in the presence of 95% H_2SO_4. This is probably due to the formation of an association compound of *m*-dinitrobenzene with H_2SO_4 which renders it difficult for an electrophilic Cl atom to attack the nitro group.[25] The fact that β-chloro acid was obtained in the presence of $FeCl_3$ even on addition of *m*-dinitrobenzene suggests that the scavenging function of nitro group is lost by the interaction of nitro group with $FeCl_3$ as supposed from the IR data.

EXPERIMENTAL

Materials. Propionic acid (b.p. 142°) was purified by fractional distillation after being dried over P_2O_5. Propionyl chloride (b.p. 80°) was obtained by the reaction of benzoyl chloride (200 g) with propionic acid (53 g) and distilled.[26] Propionic anhydride (b.p. 72–74/23 mm) was synthesized by adding propionic acid to a complex of propionyl chloride (31 g) and pyridine (53 g) in benzene.[27] Methyl propionate (b.p. 79–80°) was obtained by the H_2SO_4-catalysed esterification of propionic acid with methanol. Methyl α-chloropropionate (b.p. 132°), which on hydrolysis gives α-chloropropionic acid (b.p. 85°/12 mm), was synthesized by the reaction of methyl lactate with thionyl chloride.[28] β-Chloropropionic acid (b.p. 108°/12 mm) was distilled and esterified with MeOH in ethylene chloride to methyl ester (b.p. 61°/30 mm).[29] Ferric chloride was obtained from the hexahydrate by dehydration with thionyl chloride.[30] *m*-Dinitrobenzene (m.p. 90°) was purified by recrystallisation from EtOH.

Chlorination of propionic acid. In a 100 ml 4-necked flask, fitted with a Dimroth reflux condenser and a thermometer, were placed propionic acid (0·2 mole) and additives. The mixture was reacted at a given temp for a given time by bubbling Cl gas dried with conc H_2SO_4, after being passed with N_2 for *ca* 30 min to eliminate oxygen. After the reaction was complete, Cl remaining in the soln was removed by bubbling N_2 gas into it for *ca* 30 min. In general, the reaction mixture after the expulsion of Cl was immediately distilled except for the reaction with iodine in the absence of 95% H_2SO_4. In other runs, the mixture was added with water (10 ml), extracted 3 times with chloroform (each 20–10 ml), because decomposition occurred in the presence of 95% H_2SO_4 during distillation. The chloroform extract was dried over Na_2SO_4 and distilled under vacuum. The losses during the distillation were 0·002 mole of propionic acid, 0·003 mole of α-chloropropionic acid and 0·006 mole of β-chloropropionic acid, and this corresponds to about 6 mol % of propionic acid used initially. The water extract was neutralised with $Ba(OH)_2$ to eliminate H_2SO_4. The filtrate was evaporated to dryness; the residue corresponded to 0·8 wt %, and contained no chlorine and showed the absorption of a carboxylate group in the IR spectra. In this procedure, little by-product was formed. The distillate (3 g) was esterified with 0·1N HCl–MeOH at 50° for 3 hr. Ice water (30 ml) was added into the esterification mixture and extracted 3 times with ether (each 20–10 ml). The ether extract was washed 3 times with ice water (each 5 ml), dried over Na_2SO_4, and analysed by GLC.

GLC analysis. A Yanagimoto Model-220 gas chromatograph employing a thermister detector and a 2-meter copper column packed with 30% PEG 6000 on Celite 545 was used at 120° with a flow rate of H_2 of 60 ml/min to separate the methyl esters of carboxylic acids. Propionic acid, α- and β-chloropropionic acids and/or their mixtures were esterified to determine by the GLC analysis the extent of esterification. It was found that esterification was *ca* 0·82 which was not affected by mixing the other acids. Because of the difficult esterification of α,α-dichloropropionic acid under these conditions, the yield was determined from the chlorine content of the reaction mixture by subtracting from the total amount of acids, the amount of the other acids which could be determined by GLC analysis.

IR absorption spectra. Ferric chloride (1·6 g), *m*-dinitrobenzene (0·8 g) and nujol (2 g) were mixed in a test tube at 100° with careful shut-out of atmospheric moisture and the IR spectra measured using a Perkin–Elmer Model 337 spectrophotometer. In the same way, a mixture of $FeCl_3$-propionic acid (1:1), and a mixture of $FeCl_3$-*m*-dinitrobenzene were prepared for the IR spectra (1:1 and 2:1).

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