August, 1980] © 1980 The Chemical Society of Japan NOTES Bull. Chem. Soc. Jpn., 53, 2417—2418 (1980) 2417

The Stoichiometry and Promoter Role of Chlorosulfuric and Fuming Sulfuric Acids for α-Halogenation of Aliphatic Acid[1]

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(Received December 27, 1979)

Synopsis. The stoichiometry for the chlorosulfuric acid promoted α-halogenation and the role of fuming sulfuric acid instead of chlorosulfuric acid have been studied. In the α-bromination with molecular bromine, 1 mol of halogen afforded 2 mol of aliphatic α-bromo acid just as the α-iodination, but it is different from α-chlorination which affords only 1 mol of α-chloro acid. Fuming sulfuric acid instead of chlorosulfuric acid was found to be effective for α-bromination, but the yield was lower, while no α-iodination was observed with fuming sulfuric acid.

We have reported a novel method for the preparation of aliphatic α-halo acids by the reaction of molecular halogen in the presence of strong acid, *e.g.*, $ClSO_3H$,[2] through probable intermediary formation of ketenes.[3]

$$RR'CHCO_2H + ClSO_3H \overset{fast}{\rightleftarrows} RR'C{=}C{=}O + HCl + H_2SO_4 \quad (1)$$

$$RR'C{=}C{=}O + X_2 \xrightarrow{slow} \underset{\mathbf{1}}{RR'CXCOX} \quad (2)$$

The product in iodination (**1**, X=I) was found to regenerate iodine.[2g]

$$RR'CXCOX + H_2SO_4 \longrightarrow RR'CXCO_2H + HX + SO_3 \quad (3a)$$

$$2HX + SO_3 \text{ (or } ClSO_3H) \longrightarrow X_2 + H_2O + SO_2 \text{ (+}HCl) \quad (3b)$$

Hence 1 mol of iodine can give 2 mol of α-iodo acid (Eq. 4), but the stoichiometry is unknown for bromination and chlorination.

$$RR'CHCO_2H + 0.5I_2 + ClSO_3H \longrightarrow RR'CICO_2H + HCl + 0.5SO_2 + 0.5H_2SO_4 \quad (4)$$

Also we found that fuming H_2SO_4 could be used as an acidic promoter for the α-chlorination, but nothing is known about the yield of α-bromination and α-iodination, when fuming H_2SO_4 is used instead of $ClSO_3H$. The present note discloses these obscurities in the halogenation.

Stoichiometry of Bromination. It is known that HBr is oxidized by $ClSO_3H$ to form Br_2,[4] so that Br_2 formed may be used again for the bromination. In fact, we confirmed that 1 mol of Br_2 can give *ca.* 2 mol of aliphatic α-bromo acid as shown in Table 1 (Runs 1, 4, and 5). Hence the stoichiometry of bromination is analogous to that of iodination (Eq. 4).

$$RR'CHCO_2H + ClSO_3H + 0.5Br_2 \longrightarrow RR'CBrCO_2H + HCl + 0.5H_2SO_4 + 0.5SO_2 \quad (5)$$

Runs 4 and 5 imply that an additional amount of aliphatic acids is consumed by the side reaction with $ClSO_3H$[5] (*e.g.*, α-sulfonation), but since there is little difference between the yields in Runs 4 and 5, the rate of α-bromination should be faster than the side reaction.

On the other hand, unless excess aliphatic acid and $ClSO_3H$ based on Eqs. 4 and 5 are used, the yield of iodination is rather low; *e.g.*, Run 8 gives 43% and Run 9 gives 55% of iodo acid, probably because the rate of iodination is lower than that of bromination and comparable to that of the side reaction.[2h] But when excess aliphatic acid and excess $ClSO_3H$ to iodine are used (Run 7), the yield of α-iodination based on the used iodine increases in spite of the increased side reaction.

When a mixture of halogen and aliphatic acid in a stoichiometric ratio according to Eqs. 4 and 5 was used,

Table 1. Yields of α-halogenation of aliphatic acids[a)]

Run	Substrate (mol·dm^{-3})	Halogen (mol·dm^{-3})		Promoter (mol·dm^{-3})		Yield (%)	Unreacted Substrate (mol·dm^{-3})
	$CH_3(CH_2)_6CO_2H$	Br_2	I_2	$ClSO_3H$	fuming H_2SO_4		
1	1.0	0.5	—	1.0	—	88.9	
2	1.0	0.5	—	0.25	—	29.2	0.76
3	1.0	0.5	—	0.1	—	9.7	0.85
4	1.0	0.25	—	1.0	—	97.8	0.11
5	1.0	0.25	—	0.5	—	93.3	0.49
6	1.0	0.25	—	0.3	—	56.5	0.66
7	1.0	—	0.25	1.0	—	100.0[b)]	
8	1.0	—	0.25	0.5	—	43.0[b)]	
9	0.5	—	0.25	0.5	—	54.5[b)]	
10	1.0	0.25	—	—	1.0	71.6	0.50
11	1.0	0.25	—	—	0.5	53.1	0.75
	$CH_3(CH_2)_2CO_2H$						
12	1.7	0.13	—	—	1.0	73.4[c)]	
13	1.0	0.25	—	—	1.0	27.0[c)]	
14	0.2	—	0.2	—	0.13	0.0[b)]	
15	1.7	—	0.15	—	0.6	0.0	

a) The yields were calculated on the basis of molecular halogen according to the stoichiometry of Eqs. 4 and 5.
b) Ref. 2b. c) Ref. 2f.

the yield of bromination (Run 1) was higher (88.9%) than the yield of iodination (54.5%) under analogous conditions. This is ascribed to the higher electrophilic reactivity of bromine than iodine toward C=C bond of ketene as apparent from our previous kinetic data.[2h)]

Under conditions of $2[\mathrm{Br_2}]_0 > [\mathrm{ClSO_3H}]_0$ (Runs 2, 3 and 6), the molar yield of α-bromo acid is approximately equal to the moles of $ClSO_3H$ used, whereas the molar yield of α-chloro acid is *ca.* four fold of the moles of $ClSO_3H$ used in spite of the otherwise analogous reaction conditions.[2e)] This phenomenon is tentatively explained by the following mechanism for chlorination.

$$\mathrm{RR'CClCOCl + RR'CHCO_2H \rightleftarrows RR'CClCO_2H + RR'CHCOCl} \qquad (6a)$$

$$\mathrm{RR'CHCOCl \longrightarrow RR'C{=}C{=}O + HCl} \qquad (6b)$$

Here, α-chloroacyl chloride, which has been formed through addition of Cl_2 to ketene (Eqs. 1 and 2), can convert unreacted aliphatic acid into acyl chloride (Eq. 6a);[6)] the acyl chloride thus formed is known to give again ketene (Eq. 6b),[7)] which should react with Cl_2, giving again α-chloroacyl chloride.[2f)] Thus only catalytic amount of $ClSO_3H$ can give a high yield of α-chloro acid because of the easier elimination of HCl from acyl chloride (Eq. 6b). On the other hand, the oxidation of α-bromoacyl bromide with chlorosulfuric acid affording Br_2 occurs at 80 °C (Eq. 3) because of the lower oxidation potential of Br^- (+1.066 V for $Br^- \rightarrow 1/2\ Br_2$; +1.358 V for $Cl^- \rightarrow 1/2\ Cl_2$); hence the bromination obeys the stoichiometry of Eq. 5, regenerating Br_2.

Bromination and Iodination with Fuming Sulfuric Acid as a Promoter. As has been observed with α-chlorination,[2a,d)] the α-bromination could be carried out with fuming H_2SO_4 (Runs 10 and 11) *via* a ketene formed as shown in Eq. 7.

$$\mathrm{RR'CHCO_2H + SO_3 \rightleftarrows RR'C{=}C{=}O + H_2SO_4} \qquad (7)$$

Since 30% fuming H_2SO_4 is expressed as H_2SO_4–$0.5SO_3$, the yield 53% of α-bromo acid in Run 11 corresponds to the moles of SO_3 contained in fuming H_2SO_4 used.

On the other hand, no iodination occurred with fuming H_2SO_4; this is ascribed to the easy decomposition of α-iodo acid with fuming H_2SO_4. In fact, when 15 mmol of fuming H_2SO_4 was introduced into the 1,2-dichloroethane solution of 4.2 mmol of α-iodobutyric acid, 0.63 mmol of iodine were easily liberated at room temperature after 5 min, but only 0.016 mmol of iodine were liberated with $ClSO_3H$. Similar decomposition giving I_2 was observed with α-iodobutyryl chloride and fuming H_2SO_4.

Also the lower yield of bromination with fuming H_2SO_4 than that with $ClSO_3H$ may be due to the slower yet noticeable decomposition of α-bromoacyl bromide by fuming H_2SO_4. Indeed, 1.8 mmol of α-bromopropionyl bromide mixed with 5 mmol of fuming H_2SO_4 gave 0.42 mmol of bromine and 0.23 mmol of α-bromopropionyl bromide at 80 C° after 30 min. But 1.4 mmol of α-bromopropionyl bromide mixed with 5 mmol of $ClSO_3H$ gave only 0.05 mmol of bromine and 0.78 mmol of α-bromopropionyl bromide at 80 °C after 30 min.

On the other hand, no molecular chlorine was detected in the reaction of chloroacetyl chloride ($CH_2ClCOCl$) with fuming H_2SO_4 or $ClSO_3H$, hence chlorine as acyl chloride produced during chlorination cannot be recycled by oxidation with $ClSO_3H$.

Experimental

Materials. Commercial first grade octanoic acid (bp 147—148 °C/35 mmHg), butyric acid (bp 73—74 °C/20 mmHg) and chlorosulfuric acid (bp 86—88 °C/33 mmHg) were distilled before use. Commerical first grade bromine, iodine, chloroacetyl chloride, and fuming H_2SO_4 were used without futher purification. α-Iodobutyric acid (mp 39—40 °C) and α-iodobutyryl chloride (bp 36—38 °C/0.38 mmHg) were prepared in thionyl chloride by the literature method.[8)] α-Bromopropionyl bromide (bp 154—155 °C) was prepared by the literature method.[9)] Methyl esters of those aliphatic acids had single GLC peaks. The physical properties of methyl α-bromooctanoate were: bp 136—138 °C/24 mmHg; NMR (CCl_4): δ 3.71 (s, 3H, OCH_3), 4.09 (t, J=7.8 Hz, 1H, α-H). The physical properties of other products were reported previously.[2f,h)]

Products. A 1,2-dichloroethane solution (50 ml) containing aliphatic acid and halogen was thermostated at 80 °C and $ClSO_3H$ (or fuming H_2SO_4) was introduced and heated at 80 °C for 2 h. After an appropriate time, 2 ml of the solution was treated with $Na_2S_2O_3$ to remove halogen, and esterified by an ethereal solution of diazomethane.

The yield was measured by means of GLC using a Yanagimoto GCG-550 gas chromatograph equipped with a H-flame ionization detector employing a copper column 3 mm × 100 cm packed with PEG 20 M (10%) on Chromosorb WAW (60—80 mesh) with methyl caprate as an internal standard. The isolated methyl α-bromooctanoate was identified by GLC and NMR (a 60 MHz Hitachi R-24 B NMR spectrometer).

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