

# The Stoichiometry and Promoter Role of Chlorosulfuric and Fuming Sulfuric Acids for $\alpha$ -Halogenation of Aliphatic Acid<sup>1)</sup>

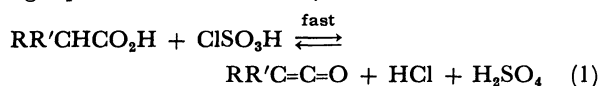
Yoshiro OGATA\* and Shinya WATANABE

Department of Applied Chemistry, Faculty of Engineering, Nagoya University, Chikusa-ku, Nagoya 464

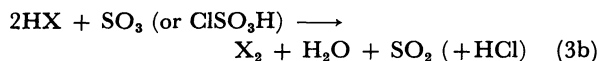
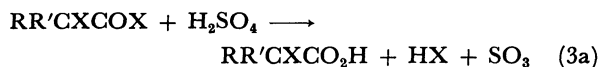
(Received December 27, 1979)

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

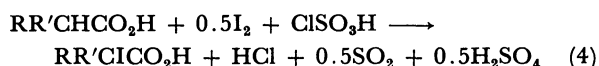
We have reported a novel method for the preparation of aliphatic  $\alpha$ -halo acids by the reaction of molecular halogen in the presence of strong acid, *e.g.*,  $\text{ClSO}_3\text{H}$ ,<sup>2)</sup> through probable intermediary formation of ketenes.<sup>3)</sup>



The product in iodination (**1**,  $\text{X}=\text{I}$ ) was found to regenerate iodine.<sup>2g)</sup>

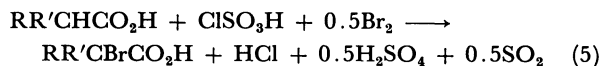


Hence 1 mol of iodine can give 2 mol of  $\alpha$ -iodo acid (Eq. 4), but the stoichiometry is unknown for bromination and chlorination.



Also we found that fuming  $\text{H}_2\text{SO}_4$  could be used as an acidic promoter for the  $\alpha$ -chlorination, but nothing is known about the yield of  $\alpha$ -bromination and  $\alpha$ -iodination, when fuming  $\text{H}_2\text{SO}_4$  is used instead of  $\text{ClSO}_3\text{H}$ . The present note discloses these obscurities in the halogenation.

**Stoichiometry of Bromination.** It is known that  $\text{HBr}$  is oxidized by  $\text{ClSO}_3\text{H}$  to form  $\text{Br}_2$ ,<sup>4)</sup> so that  $\text{Br}_2$  formed may be used again for the bromination. In fact, we confirmed that 1 mol of  $\text{Br}_2$  can give *ca.* 2 mol of aliphatic  $\alpha$ -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).



Runs 4 and 5 imply that an additional amount of aliphatic acids is consumed by the side reaction with  $\text{ClSO}_3\text{H}$ <sup>5)</sup> (*e.g.*,  $\alpha$ -sulfonation), but since there is little difference between the yields in Runs 4 and 5, the rate of  $\alpha$ -bromination should be faster than the side reaction.

On the other hand, unless excess aliphatic acid and  $\text{ClSO}_3\text{H}$  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.<sup>2h)</sup> But when excess aliphatic acid and excess  $\text{ClSO}_3\text{H}$  to iodine are used (Run 7), the yield of  $\alpha$ -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  $\alpha$ -HALOGENATION OF ALIPHATIC ACIDS<sup>a)</sup>

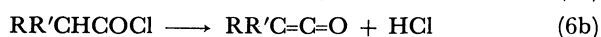
Run	Substrate (mol·dm <sup>-3</sup> ) $\text{CH}_3(\text{CH}_2)_6\text{CO}_2\text{H}$	Halogen (mol·dm <sup>-3</sup> )		Promoter (mol·dm <sup>-3</sup> )		Yield (%)	Unreacted Substrate (mol·dm <sup>-3</sup> )
		$\text{Br}_2$	$\text{I}_2$	$\text{ClSO}_3\text{H}$	fuming $\text{H}_2\text{SO}_4$		
1	1.0	0.5	—	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 <sup>b)</sup>	
8	1.0	—	0.25	0.5	—	43.0 <sup>b)</sup>	
9	0.5	—	0.25	0.5	—	54.5 <sup>b)</sup>	
10	1.0	0.25	—	—	1.0	71.6	0.50
11	1.0	0.25	—	—	0.5	53.1	0.75
	$\text{CH}_3(\text{CH}_2)_2\text{CO}_2\text{H}$						
12	1.7	0.13	—	—	1.0	73.4 <sup>c)</sup>	
13	1.0	0.25	—	—	1.0	27.0 <sup>c)</sup>	
14	0.2	—	0.2	—	0.13	0.0 <sup>b)</sup>	
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.

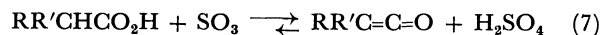
the yield of bromination (Run 1) was higher (88.9%) than the yield of iodination (54.5%) under analogous conditions. This is ascribed to the higher electrophilic reactivity of bromine than iodine toward C=C bond of ketene as apparent from our previous kinetic data.<sup>2h)</sup>

Under conditions of  $2[\text{Br}_2]_0 > [\text{ClSO}_3\text{H}]_0$  (Runs 2, 3 and 6), the molar yield of  $\alpha$ -bromo acid is approximately equal to the moles of  $\text{ClSO}_3\text{H}$  used, whereas the molar yield of  $\alpha$ -chloro acid is *ca.* four fold of the moles of  $\text{ClSO}_3\text{H}$  used in spite of the otherwise analogous reaction conditions.<sup>2e)</sup> This phenomenon is tentatively explained by the following mechanism for chlorination.



Here,  $\alpha$ -chloroacyl chloride, which has been formed through addition of  $\text{Cl}_2$  to ketene (Eqs. 1 and 2), can convert unreacted aliphatic acid into acyl chloride (Eq. 6a);<sup>6)</sup> the acyl chloride thus formed is known to give again ketene (Eq. 6b),<sup>7)</sup> which should react with  $\text{Cl}_2$ , giving again  $\alpha$ -chloroacyl chloride.<sup>2f)</sup> Thus only catalytic amount of  $\text{ClSO}_3\text{H}$  can give a high yield of  $\alpha$ -chloro acid because of the easier elimination of HCl from acyl chloride (Eq. 6b). On the other hand, the oxidation of  $\alpha$ -bromoacyl bromide with chlorosulfuric acid affording  $\text{Br}_2$  occurs at 80 °C (Eq. 3) because of the lower oxidation potential of  $\text{Br}^-$  (+1.066 V for  $\text{Br}^- \rightarrow 1/2 \text{Br}_2$ ; +1.358 V for  $\text{Cl}^- \rightarrow 1/2 \text{Cl}_2$ ); hence the bromination obeys the stoichiometry of Eq. 5, regenerating  $\text{Br}_2$ .

**Bromination and Iodination with Fuming Sulfuric Acid as a Promoter.** As has been observed with  $\alpha$ -chlorination,<sup>2a,d)</sup> the  $\alpha$ -bromination could be carried out with fuming  $\text{H}_2\text{SO}_4$  (Runs 10 and 11) *via* a ketene formed as shown in Eq. 7.



Since 30% fuming  $\text{H}_2\text{SO}_4$  is expressed as  $\text{H}_2\text{SO}_4 \cdot 0.5\text{SO}_3$ , the yield 53% of  $\alpha$ -bromo acid in Run 11 corresponds to the moles of  $\text{SO}_3$  contained in fuming  $\text{H}_2\text{SO}_4$  used.

On the other hand, no iodination occurred with fuming  $\text{H}_2\text{SO}_4$ ; this is ascribed to the easy decomposition of  $\alpha$ -iodo acid with fuming  $\text{H}_2\text{SO}_4$ . In fact, when 15 mmol of fuming  $\text{H}_2\text{SO}_4$  was introduced into the 1,2-dichloroethane solution of 4.2 mmol of  $\alpha$ -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  $\text{ClSO}_3\text{H}$ . Similar decomposition giving  $\text{I}_2$  was observed with  $\alpha$ -iodobutyryl chloride and fuming  $\text{H}_2\text{SO}_4$ .

Also the lower yield of bromination with fuming  $\text{H}_2\text{SO}_4$  than that with  $\text{ClSO}_3\text{H}$  may be due to the slower yet noticeable decomposition of  $\alpha$ -bromoacyl bromide by fuming  $\text{H}_2\text{SO}_4$ . Indeed, 1.8 mmol of  $\alpha$ -bromopropionyl bromide mixed with 5 mmol of fuming  $\text{H}_2\text{SO}_4$  gave 0.42 mmol of bromine and 0.23 mmol of  $\alpha$ -bromopropionyl bromide at 80 °C after 30 min. But 1.4 mmol of  $\alpha$ -bromopropionyl bromide mixed with 5 mmol of  $\text{ClSO}_3\text{H}$  gave only 0.05 mmol of bromine and 0.78 mmol of  $\alpha$ -bromopropionyl bromide at 80 °C after 30 min.

On the other hand, no molecular chlorine was detected in the reaction of chloroacetyl chloride ( $\text{CH}_2\text{ClCOCl}$ ) with fuming  $\text{H}_2\text{SO}_4$  or  $\text{ClSO}_3\text{H}$ , hence chlorine as acyl chloride produced during chlorination cannot be recycled by oxidation with  $\text{ClSO}_3\text{H}$ .

## 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. Commercial first grade bromine, iodine, chloroacetyl chloride, and fuming  $\text{H}_2\text{SO}_4$  were used without further purification.  $\alpha$ -Iodobutyric acid (mp 39–40 °C) and  $\alpha$ -iodobutyryl chloride (bp 36–38 °C/0.38 mmHg) were prepared in thionyl chloride by the literature method.<sup>8)</sup>  $\alpha$ -Bromopropionyl bromide (bp 154–155 °C) was prepared by the literature method.<sup>9)</sup> Methyl esters of those aliphatic acids had single GLC peaks. The physical properties of methyl  $\alpha$ -bromooctanoate were: bp 136–138 °C/24 mmHg; NMR ( $\text{CCl}_4$ ):  $\delta$  3.71 (s, 3H,  $\text{OCH}_3$ ), 4.09 (t,  $J=7.8$  Hz, 1H,  $\alpha$ -H). The physical properties of other products were reported previously.<sup>2f,h)</sup>

**Products.** A 1,2-dichloroethane solution (50 ml) containing aliphatic acid and halogen was thermostated at 80 °C and  $\text{ClSO}_3\text{H}$  (or fuming  $\text{H}_2\text{SO}_4$ ) was introduced and heated at 80 °C for 2 h. After an appropriate time, 2 ml of the solution was treated with  $\text{Na}_2\text{S}_2\text{O}_3$  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  $\times$  100 cm packed with PEG 20 M (10%) on Chromosorb WAW (60–80 mesh) with methyl caprate as an internal standard. The isolated methyl  $\alpha$ -bromooctanoate was identified by GLC and NMR (a 60 MHz Hitachi R-24 B NMR spectrometer).

## References

- 1) Contribution No. 270.
- 2) a) Y. Ogata, T. Harada, K. Matsuyama, and T. Ikejiri, *J. Org. Chem.*, **40**, 2960 (1975); b) Y. Ogata and K. Matsuyama, *Tetrahedron*, **26**, 5929 (1970); c) Y. Ogata and T. Sugimoto, *Chem. Ind. (London)*, **1977**, 538; d) Y. Ogata and T. Ikejiri, *Nippon Kagaku Kaishi*, **1975**, 1517; e) Y. Ogata, T. Sugimoto, and M. Inaishi, *Bull. Chem. Soc. Jpn.*, **52**, 255 (1979); f) Y. Ogata and T. Sugimoto, *J. Org. Chem.*, **43**, 3684 (1978); g) Y. Ogata and S. Watanabe, *ibid.*, **44**, 2768 (1979); h) Y. Ogata and S. Watanabe, *ibid.*, **45**, in press (1980).
- 3) Y. Ogata, T. Harada, and T. Sugimoto, *Can. J. Chem.*, **55**, 1268 (1977).
- 4) Gmelins Handbuch, **7**, 212 (1931).
- 5) a) F. Gunther and J. Hetzer, U. S. Patent 1926442 [*Chem. Abstr.*, **27**, 6001 (1933)]; b) J. K. Weil, L. P. Witnauer, and A. J. Stirton, *J. Am. Chem. Soc.*, **75**, 2526 (1953); c) E. E. Gilbert, *Chem. Rev.*, **62**, 549 (1962).
- 6) H. B. Watson, *Chem. Rev.*, **7**, 173 (1930).
- 7) a) M. S. Newman and E. A. Zuech, *J. Org. Chem.*, **27**, 1436 (1962); b) R. C. Fuson, L. J. Armstrong, D. H. Chadwich, J. W. Kneisley, S. P. Rowland, W. J. Shenk, Jr., and Q. F. Soper, *J. Am. Chem. Soc.*, **67**, 386, 1937 (1945).
- 8) D. N. Harpp, L. Q. Bao, C. J. Black, J. G. Gleason, and R. A. Smith, *J. Org. Chem.*, **40**, 3420 (1975).
- 9) C. W. Smith and D. G. Norton, *Org. Synth.*, Coll. Vol. IV, 348 (1963).