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# $\alpha$-Chlorination of Long-chain Aliphatic Acids[1)]

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**Synopsis.** Chlorination of long-chain aliphatic acids with a $Cl_2$–$O_2$ mixture in the presence of chlorosulfuric acid at 85 °C gave the corresponding $\alpha$-chloro acids in good yields (*ca.* 90%) along with a little amount of aliphatic $\alpha$-sulfo acids, but no $\alpha,\alpha$-dichloro acids.

Halogenation of aliphatic acids can occur *via* either a free-radical[2)] or a acid-catalyzed mechanism.[3,4)] The radical halogenation occurs at random positions, while the acid-catalyzed halogenation tends to give $\alpha$-halo acid. Hell-Volhard-Zelinsky (H-V-Z) procedure using phosphorus tribromide gives exclusively $\alpha$-bromo acid. However, the application of H-V-Z reaction to chlorination of long-chain aliphatic acids often gives $\alpha,\alpha$-dichloro acids along with $\alpha$-chloro acids; the extent of $\alpha,\alpha$-dichlorination increases with the progress of reaction.[5,6)]

We have reported that aliphatic acids can be $\alpha$-chlorinated by molecular chlorine in the presence of strong protic acids such as chlorosulfuric[7–9)] or fuming sulfuric acid[7)] and a radical trapper such as molecular oxygen. Here we wish to report the application of this chlorination method to higher fatty acids, *e.g.*, dodecanoic acid.

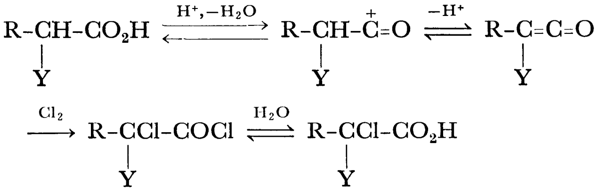
## Results and Discussion

Dodecanoic acid was chlorinated in the presence of chlorosulfuric acid with a gaseous mixture of molecular chlorine and oxygen which acts as a radical trapper.[10)] The effect of reaction time on the yield is shown in Fig. 1. Within initial one hour, the yield of $\alpha$-chlorododecanoic acid increased with progress of the reaction, but after one hour the yield was no more increased, but kept constant (*ca.* 90%). The substrate acid disappeared gradually until only a trace remained after 1 h.

The resulting mixture was extracted with ether and washed with water containing sodium chloride. The washing, after standing for a few days, afforded colorless crystals (0.1—0.6 g) of sodium 1-carboxy-1-undecanesulfonate, $[CH_3(CH_2)_9CH(SO_3Na)CO_2H]$, which is an expected product in view of the known formation of $\alpha$-sulfo acid in the reaction of aliphatic acid with sulfur trioxide,[11–13)] fuming sulfuric acid,[11)] or chlorosulfuric acid.[11)]

Even the chlorination of dodecanoic acid for more than one hour gave $\alpha$-monochlorododecanoic acid with no $\alpha,\alpha$-dichloro acid; further, no $\alpha,\alpha$-dichloro acid was detected in the attempted chlorination of $\alpha$-chlorododecanoic acid as a substrate. Whereas, $\alpha,\alpha$-dichlorination occurs as easy as $\alpha$-chlorination by H-V-Z procedure.[5,6)] Thus our procedure has the advantage that there is no contamination by dichloro acid, which is due to the low reactivity of $\alpha$-chloro acid as well as gradual consumption of $ClSO_3H$ with the progress of reaction.

The mechanism may involve the addition of molecular chlorine to a ketene intermediate.[14)]



$$\mathrm{R\text{-}\underset{Y}{CH}\text{-}CO_2H} \overset{H^+,-H_2O}{\rightleftarrows} \mathrm{R\text{-}\underset{Y}{CH}\text{-}\overset{+}{C}{=}O} \overset{-H^+}{\rightleftharpoons} \mathrm{R\text{-}\underset{Y}{C}{=}C{=}O}$$

$$\xrightarrow{Cl_2} \mathrm{R\text{-}\underset{Y}{CCl}\text{-}COCl} \overset{H_2O}{\rightleftharpoons} \mathrm{R\text{-}\underset{Y}{CCl}\text{-}CO_2H}$$

When $Y=H$ and $R=C_{10}H_{21}$, alkyl substituted ketene is formed, while $\alpha$-chloro acid ($Y=Cl$) gives chloro substituted ketene, which is less reactive to electrophilic chlorine addition; hence the reaction gives only $\alpha$-monochlorination.

Figure 2 shows that the $\alpha$-chlorination increases with increasing amount of catalyst acid, while the total yield of $\alpha$-chlorinated product decreases, since there is a considerable amount of loss as $\alpha$-sulfonated compound. In short, the optimum conditions for the highest yield and the lowest loss of the substrate are obtained with *ca.* 10 mmol of chlorosulfuric acid (1/5 equivalent of substrate).

The effect of reaction temperature on the yield is

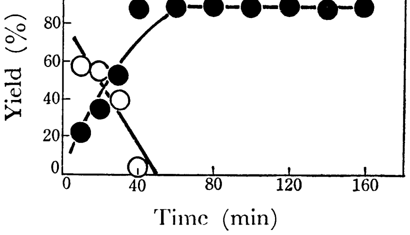


Fig. 1. Effect of reaction time on $\alpha$-chlorination of dodecanoic acid (50 mmol) in the presence of chlorosulfuric acid (12.5 mmol) at 85 °C. ●: $\alpha$-Chlorododecanoic acid, ○: dodecanoic acid.

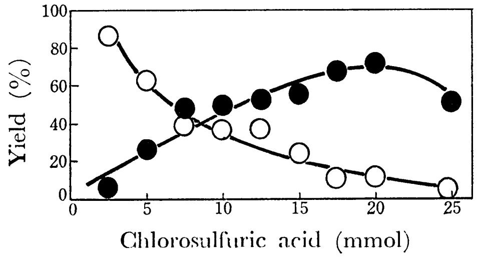


Fig. 2. Effect of amount of chlorosulfuric acid on $\alpha$-chlorination of dodecanoic acid (50 mmol) at 85 °C for 30 min. ●: $\alpha$-Chlorododecanoic acid, ○: dodecanoic acid.

TABLE 1. YIELDS AND PHYSICAL PROPERTIES FOR α-CHLORO ACIDS

| α-Chloro acid | Yield % | Mp (°C) | IR $\nu_{C=O}$ (cm$^{-1}$) | NMR[c] α-H (δ ppm) |
|---|---|---|---|---|
| $CH_3(CH_2)_5\underset{\substack{\mid \\ Cl}}{C}HCO_2H$ | 90 | liquid | 1720[a] | 4.17 |
| $CH_3(CH_2)_7\underset{\substack{\mid \\ Cl}}{C}HCO_2H$ | 89 | liquid | 1720[a] | 4.15 |
| $CH_3(CH_2)_9\underset{\substack{\mid \\ Cl}}{C}HCO_2H$ | 90 | 36—37 | 1720[b] | 4.17 |
| $CH_3(CH_2)_{11}\underset{\substack{\mid \\ Cl}}{C}HCO_2H$ | 91 | 41—42 | 1715[b] | 4.15 |
| $CH_3(CH_2)_{13}\underset{\substack{\mid \\ Cl}}{C}HCO_2H$ | 92 | 52—53 | 1720[b] | 4.15 |

a) Neat. b) KBr. c) $CCl_4$.

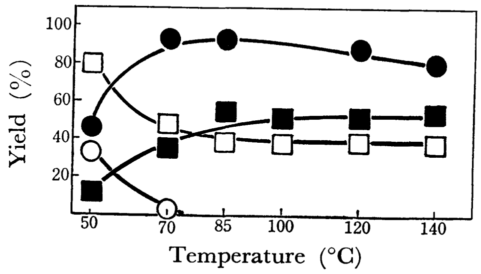


Fig. 3. Effect of temperature on α-chlorination of dodecanoic acid (50 mmol) in the presence of chlorosulfuric acid (12.5 mmol) for 30 or 120 min. ■: α-Chlorododecanoic acid (30), □: dodecanoic acid (30), ●: α-chlorododecanoic acid (120), and ○: dodecanoic acid (120 min).

less important (Fig. 3), probably because the favorable effect of increasing rate is compensated with the reverse effects of a decrease of chlorine solubility and an acceleration of α-sulfonation with increasing temperature.

This method can generally be applied to α-chlorination of other long-chain aliphatic acids with satisfactory yields. The optimum conditions for α-chlorination are as follows: A mixture of 50 mmol of substrate acid and 12.5 mmol of chlorosulfuric acid is heated at 85 °C for 60 min. The yields and physical properties for identification of α-chloro acids are listed in Table 1. Little effect of structure, *i.e.*, length of the chain, on the yield was observed.

The mechanism may involve the addition of molecular chlorine to a ketene intermediate.[14]

## Experimental

Chlorosulfuric acid (1.45 g 12.5 mmol) was added gradually with stirring to substrate acid (50 mmol) and the mixture was heated slowly to 85 °C. The mixture of chlorine and oxygen in a molar ratio of 2:1 was bubbled into it for 60 min. After completion of the reaction chlorine was removed by introducing nitrogen, the mixture was cooled to room temperature, and extracted with ether (60 ml). The extract was washed with aqueous sodium chloride (20 ml) for three times. Ether was removed at 60 °C under reduced pressure. The residual material was cooled to freeze and dried *in vacuo*. The product was esterified with diazomethane[15] in ether and analyzed on a Yanagimoto G 180 gas chromatograph using a copper column packed with PEG 20 M 10% on Chromosorb WAW or Apiezon Grease L 15% on Celite 545.

The isolated α-chloro fatty acids ($C_8$—$C_{16}$) were identified by comparing the $^1H$ NMR and IR spectra with those of authentic samples. NMR and IR spectra were measured by means of a Hitachi R-24B NMR spectrometer and Perkin-Elmer Model 337 IR spectrophotometer, respectively.

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