

# Chlorination of Esters. IV. Chlorination of Chloromethyl Esters of Aliphatic C<sub>3</sub>–C<sub>12</sub> n-Carboxylic Acids. Determination of Monochloro Products by Gas-Liquid Chromatography and Gas-Liquid Chromatography–Mass Spectrometry

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The chlorinations with chlorine in the liquid phase at room temperature have been studied, in the absence and in the presence of benzene. The products of ten substrates, 65 compounds altogether, were identified and estimated by gas-liquid chromatography (GLC) and gas-liquid chromatography–mass spectrometry (GLC–MS). The chlorinations yield all possible monochloro isomers, the ( $\omega$ -1)-chloro isomers being in general the main products in the absence of benzene. The solvent alters the selectivity of the reagent, the main product varying from ( $\omega$ -1)- to ( $\omega$ -4)-chloro isomer with an increase in chain length. The amounts of  $\omega$ -chloro isomers were 1.1–4.3 times greater in the absence of benzene. The isomeric monochloro chloromethyl esters are eluted in direct order from 2- to  $\omega$ -chloro isomer on a Carbowax 20M glass capillary column. The 2-, 3-, 4-, 5- and  $\omega$ -chloro isomers can be distinguished by mass spectrometry from the other isomers on the basis of characteristic fragment ions. The mass spectra of the mid-chain isomers were nearly similar to each other.

Numerous papers have appeared on the chlorination of aliphatic methyl esters by various methods, but none on the chlorination of chloromethyl esters.

Recently, the chlorination of straight-chain methyl esters from propanoic to octadecanoic acid has been reported to produce chloromethyl esters as a side product.<sup>1–3</sup>

The present paper describes the chlorination of aliphatic chloromethyl esters from propanoic to dodecanoic acid with chlorine in the liquid phase, in

the absence and in the presence of benzene. The monochlorinated isomers formed were determined by gas-liquid chromatography (GLC) and gas-liquid chromatography–mass spectrometry (GLC–MS). The gas-liquid chromatography of combined mixtures of even- and odd-carbon-number chloromethyl monochloro esters has been reported earlier.<sup>4</sup> The mass spectra of the compounds will be published later.

## EXPERIMENTAL

*Samples.* Chloromethyl esters, used as starting materials in the chlorinations, were prepared from the corresponding acid chlorides and paraformaldehyde in the presence of a trace amount of zinc chloride.<sup>5</sup> 2-Chloro C<sub>5</sub>–C<sub>12</sub> acid chlorides,<sup>6,7</sup> monochloro propanoyl<sup>8</sup> and butanoyl chlorides<sup>9–11</sup> and the mixtures of monochloro C<sub>5</sub>–C<sub>12</sub> acid chlorides obtained by chlorination of the parent compounds with chlorine were converted<sup>5</sup> to chloromethyl esters.

The structures of the separately prepared authentic chloromethyl esters were confirmed by <sup>1</sup>H NMR and MS.

*Chlorinations.* Chloromethyl esters were chlorinated with chlorine in the liquid phase at room temperature without solvent and in benzene solution (molar ratio substrate–benzene was 1:10) as described earlier.<sup>1</sup> After removal of excess of chlorine and hydrogen chloride liberated with dry nitrogen, the crude chlorination mixtures were analyzed by GLC and GLC–MS. Variable amounts of unreacted substrates were observed as less than an equimolar amount of chlorine was used.

The quantities of higher chlorinated products were at greatest a few per cent.

**Gas-liquid chromatography.** A Varian Model 2400 gas chromatograph with a flame-ionization detector and 3% Carbowax 20M glass capillary column (50 m  $\times$  0.3 mm I.D.) was used for the qualitative and quantitative analyses of the chlorination products. The column temperature was programmed from 50 to 190 °C at 4 °C/min and held at 190 °C until the elution of peaks ceased. Nitrogen was used as the carrier gas at a flow-rate of 1 ml/min. The splitting ratio was 1:20 and the temperatures of injector and detector were 220 and 240 °C, respectively. The chromatographic data were analyzed with a Hewlett-Packard Model 3390A Reporting Integrator using standard programs.

**Gas-liquid chromatography – mass spectrometry.** A Varian MAT-212 mass spectrometer connected with a Varian Model 3700 gas-liquid chromatograph was used. It was equipped with the same column as above with a helium flow-rate of 1 ml/min. Appropriate temperatures were used to

separate the isomeric monochloro esters. Electron ionizing energy was 70 eV and ion source temperature 240 °C. Data were acquired and processed on a Spectro System MAT-188.

## RESULTS AND DISCUSSION

The chlorination rate of chloromethyl esters seems to be slightly greater than that of the corresponding methyl esters. Thus, the monochlorinated isomers formed react further easily to di- and polychloro compounds. To avoid this and to control the reaction, the use of a diluent is recommended. Benzene was chosen as a solvent, because it has been found to alter the selectivity of the reagent. This leads to a different isomer distribution.<sup>12-14</sup>

**Identification.** The products were identified by GLC and GLC-MS, through comparison with authentic samples. On a Carbowax 20M glass

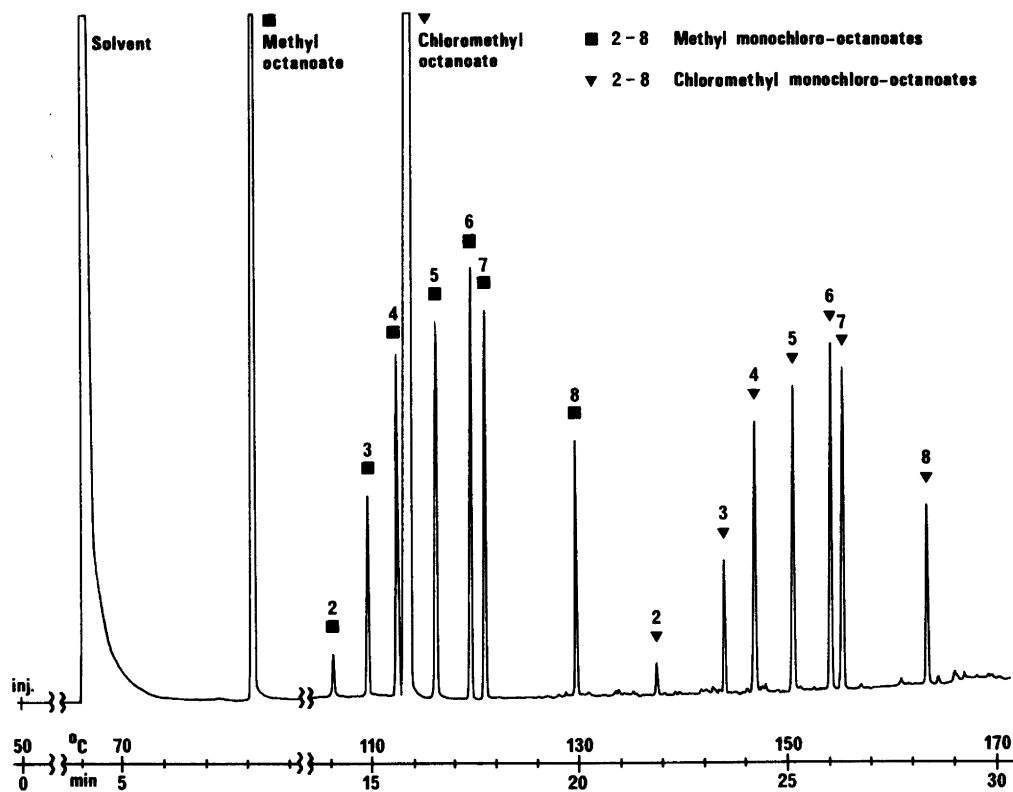


Fig. 1. Chromatogram of a mixture of methyl and chloromethyl monochloro-octanoates. S = solvent; peak number = position of Cl-substituent.

capillary column, which separated the chlorination mixtures better than a non-polar SE-30 column, all of the isomeric monochloro chloromethyl esters were

resolvable except for chloromethyl 6-chloro- and 7-chlorododecanoates.<sup>4</sup> The amounts of isomers had to be estimated through comparison with corresponding isomers formed in the chlorination of methyl dodecanoate.<sup>3</sup>

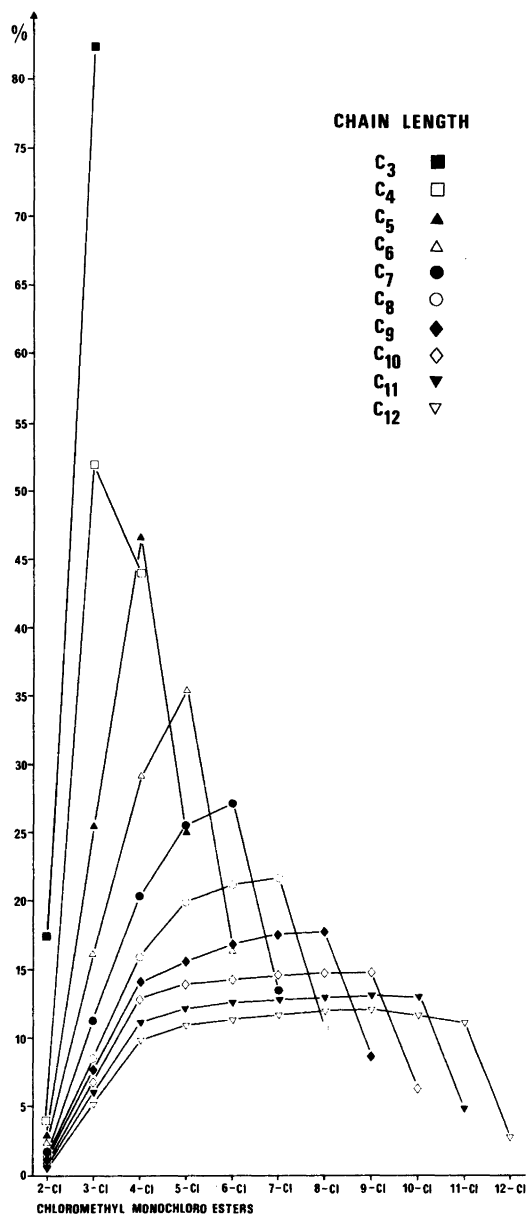


Fig. 2. Isomer distribution of chloromethyl monochloro esters of aliphatic C<sub>3</sub>-C<sub>12</sub> n-carboxylic acids based on GLC analyses. Chlorinations were carried out without solvent with chlorine at room temperature.

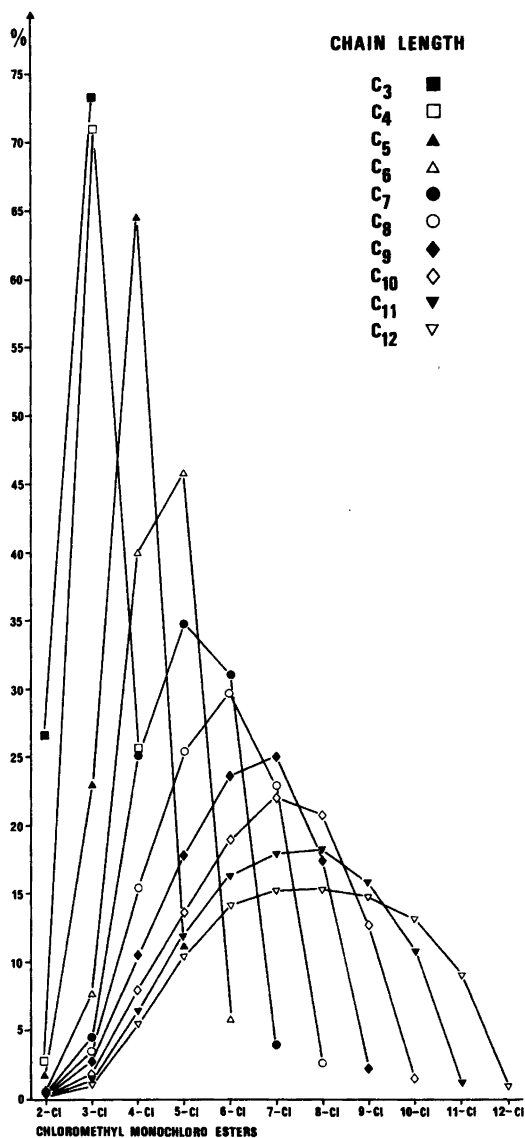


Fig. 3. Isomer distribution of chloromethyl monochloro esters of aliphatic C<sub>3</sub>-C<sub>12</sub> n-carboxylic acids based on GLC analyses. Chlorinations were carried out in benzene with chlorine at room temperature.

As expected, the isomeric monochloro chloromethyl esters are eluted in the direct order from 2-chloro to  $\omega$ -chloro compound<sup>4</sup> like the corresponding methyl derivatives.<sup>15</sup> In order to confirm this,  $C_5$ – $C_{12}$  acid chlorides, which certainly yield all monochlorinated isomers,<sup>1–3</sup> were chlorinated with chlorine in the liquid phase. However, the amounts of 2-chloro isomers formed in the reactions of long-chain ( $>C_8$ ) compounds were negligible, wherefore isomers were prepared separately.<sup>6,7</sup> One part of the chlorination mixtures was esterified with methanol and the other part was converted to chloromethyl esters.<sup>5</sup> The combined mixture of the derivatives was analyzed by GLC. A chromatogram of the mixture of octanoates is illustrated in Fig. 1. The patterns of methyl and chloromethyl isomers show similar isomer distributions. Further, the GLC analyses of the mixtures of chloromethyl monochloro esters, formed by two pathways, indicate the identity of the mixtures. The final identification was made with GLC–MS.

The mass spectra of chloromethyl esters differ somewhat from the spectra of methyl esters. The molecular ion peaks of parent esters are low and as expected,  $M^+$  is not shown by any of the monochloro isomers.  $\alpha$ -Cleavages give intense  $M - ClCH_2O^+$  and  $M - ClCH_2OCO^+$  ions in all parent esters and in short-chain chloro esters. The 2-chloro isomers can easily be identified and distinguished from the other isomers on the basis of the McLafferty rearrangement (fragment ion  $C_3H_4Cl_2O_2^{+}$  at  $m/z$  142). The corresponding ion at  $m/z$  108 is the base peak in  $C_6$ – $C_{11}$  parent esters and nearly in all 4-chloro and  $\omega$ -chloro isomers. On the other hand, this fragment ion is small in all 3-chloro and 5-chloro esters. The loss of a chlorine atom from the molecular ion is characteristic for 3-chloro isomers and small  $M - 101$ ,  $M - Cl - CH_2ClOH$  or  $M - HCl - ClCH_2O^+$ , and  $M - 102$ ,  $M - CH_2ClOH - HCl$ , peaks for  $\omega$ -chloro isomers. The other isomers, however, are indistinguishable by MS on the basis of their very similar mass spectra, as are also the corresponding methyl esters.<sup>16</sup>

*Isomer distribution.* The results of the quantitative analyses of monochloro isomers formed in two different chlorination processes are illustrated in Figs. 2 and 3. The quantities of monochloro esters are given relative to the  $\omega$ -chloro isomers and to the isomers, formed in the chlorinations without benzene (Table 1). The isomer distributions were

estimated by GLC without weight response factors, the determination of which would have required laborious syntheses of model samples. However, owing to the use of a glass capillary column with temperature programming, the differences between factors of monochloro esters were supposed to be negligible.<sup>2</sup>

The chlorinations of chloromethyl esters and methyl esters<sup>1–3</sup> gave nearly the same isomer distributions under the same reaction conditions, without solvent. The amounts of 2-chloro and  $\omega$ -chloro isomers were, however, smaller in the reactions of the chloromethyl esters, particularly, with increase in chain length.

From Figs. 2 and 3 it can be seen that benzene strongly affects the selectivity of the reagent. In the chlorination without solvent the reactivities of  $C_2 - H$  up to  $C_{\omega-1} - H$  increase as usual with increasing distance from the deactivating chloromethoxyl group the main reaction product appearing to be in general the ( $\omega$ -1)-chloro isomer. With an increase in chain length, however, the selectivity of the substitution of ( $\omega$ -1)-hydrogen decreases and the amounts of the mid-chain isomers become relatively more abundant.

When the reaction was carried out in benzene, the main product varied with increasing the chain length from the ( $\omega$ -1)-chloro to the ( $\omega$ -4)-chloro isomer. As with the chlorinations of alkane carbochlorides,<sup>12–14</sup> the most striking difference between the chlorination methods given in this work is the small amounts of  $\omega$ -chloro isomers formed in benzene, compared with the 1.1–4.3 times greater amounts without solvent (Table 1). The quantities of 2-chloro and 3-chloro isomers were smaller in benzene and the proportions of the mid-chain isomers, as a consequence, higher.

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Table 1. The relative quantities<sup>a</sup> of monochloro esters formed in the chlorinations of aliphatic n-C<sub>3</sub>–C<sub>12</sub> chloromethyl esters.

Chain length	Method <sup>b</sup>	Isomeric monochloro esters										
		2-Cl	3-Cl	4-Cl	5-Cl	6-Cl	7-Cl	8-Cl	9-Cl	10-Cl	11-Cl	12-Cl
C <sub>3</sub>	A	0.2	1.0									
	B	0.4	1.0									
	B/A	1.5	0.9									
C <sub>4</sub>	A	0.1	1.2	1.0								
	B	0.1	2.7	1.0								
	B/A	0.8	1.4	0.6								
C <sub>5</sub>	A	0.1	1.0	1.9	1.0							
	B	0.1	2.1	5.8	1.0							
	B/A	0.6	0.9	1.4	0.4							
C <sub>6</sub>	A	0.1	0.9	1.7	2.1	1.0						
	B	0.1	1.3	6.9	7.9	1.0						
	B/A	0.2	0.5	1.4	1.3	0.3						
C <sub>7</sub>	A	0.1	0.8	1.5	1.9	2.0	1.0					
	B	0.1	1.1	6.3	8.7	7.8	1.0					
	B/A	0.2	0.4	1.2	1.4	1.1	0.3					
C <sub>8</sub>	A	0.1	0.8	1.4	1.9	2.0	2.0	1.0				
	B	0.1	1.3	6.0	9.8	11.5	8.9	1.0				
	B/A	0.1	0.4	1.0	1.3	1.4	1.1	0.2				
C <sub>9</sub>	A	0.1	0.9	1.6	1.8	1.9	2.0	2.1	1.0			
	B	0.1	1.3	4.8	8.1	10.8	11.5	8.0	1.0			
	B/A	0.1	0.3	0.8	1.1	1.4	1.4	1.0	0.2			
C <sub>10</sub>	A	0.1	1.1	1.9	2.2	2.3	2.3	2.4	2.4	1.0		
	B	0.1	1.1	5.3	8.5	12.7	14.9	13.9	8.5	1.0		
	B/A	0.1	0.2	0.7	1.0	1.3	1.5	1.4	0.8	0.2		
C <sub>11</sub>	A	0.1	1.2	2.2	2.5	2.6	2.6	2.7	2.7	2.7	1.0	
	B	0.1	1.1	4.9	9.2	12.5	13.8	14.1	12.2	8.0	1.0	
	B/A	0.1	0.2	0.6	1.0	1.3	1.4	1.4	1.2	0.8	0.3	
C <sub>12</sub>	A	0.1	1.8	3.3	3.9	3.9	4.0	4.2	4.2	4.1	3.9	1.0
	B	0.1	1.0	5.7	10.6	14.0	15.0	15.4	14.9	13.2	9.1	1.0
	B/A	0.1	0.2	0.6	0.9	1.2	1.3	1.3	1.2	1.1	0.8	0.3

<sup>a</sup>Relative to the ω-chloro isomers (=1.0) and isomers formed in the chlorination of the neat substrates (B/A).<sup>b</sup>Chlorination in the absence (A) and in the presence (B) of benzene.

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