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Chlorination of Esters. I. Chlorination of Methyl Esters of Propanoic, Butanoic, Pentanoic and Hexanoic Acids. The Isomer Distribution of Monochloro Esters Formed

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The chlorination of methyl esters with chlorine in the liquid and vapor phase and with sulfuryl chloride in the liquid phase has been investigated. The chlorination yields all possible monochloro ester isomers with the 2-chloro isomer in the smallest amount. The products were identified by NMR and mass spectrometry. The isomer distribution and mass spectra of products were studied in detail.

The chlorination of carboxylic acids and their derivatives with chlorine and sulfuryl chloride has lately received little interest and most of the publications dealing with the chlorination products come from the nineteen fifties. Now when analysis methods, especially gas chromatography, have developed and the general interest in chlorine containing compound has strongly increased we have started to reinvestigate this subject. Firstly, we try to find out the structures and isomer proportions formed in the chlorination of carboxylic acid methyl esters and, secondly, to study the mass, ^{1}H and ^{13}C NMR spectra. This paper gives the results of chlorination of propanoic, butanoic, pentanoic and hexanoic acid methyl esters.

The first paper dealing with chlorination of short-chain acids and their derivatives was published by Michael and Garner.[1] Later Kharash,[2] Bruylants,[3,4] den Hertog,[5] Smit,[6–8] Brown[9] and Magritte[10] and their co-workers have published results from analogous investigations. There are, however, remarkable differences in the isomer ratios of formed compounds due to the difficulties in the analysis which were, for the most part, based on fractional distillations.

RESULTS

Esters were chosen as starting materials because the chlorination process could be continuously checked by gas chromatography. Methyl esters are also preferable due to their lower boiling points and better reactivity compared with other alkyl esters. In addition, the chlorination of esters of higher alcohols leads to a noticeable reaction in the alkoxy group. In the cases studied, only methyl propanoate gave a substantial amount of chloromethyl ester (14 – 25 %).

To find out the influence of reaction conditions we made a series of chlorination experiments under various conditions: Chlorination with chlorine or sulfuryl chloride at different temperatures (20, 60 °C and the boiling point of the ester) with or without catalyst (UV-light, benzoyl peroxide). The results are presented in Table 1.

The chlorination with chlorine and sulfuryl chloride gave approximately the same results, independent of catalyst and reaction conditions. Undoubtedly all possible monochloromethylester isomers were formed with 2-chloro compounds in smallest amount indicating the strong deactivating effect of the ester group on the α-carbon atom. The deactivating effect is quite strong on the β-position too, as can be seen from the results of methyl pentanoate and hexanoate. Fig. 1 shows the chromatogram of a mixture of chlorination products indicating the retention order of compounds.

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Table 1. The isomer distribution for the chlorinations of methyl esters. Values are the averages of two experiments analyzed by GLC.

Substrate	Method[a]	Monochloro esters formed/% Chloro-methyl	2-Cl	3-Cl	4-Cl	Substrate	Monochloro esters formed/% Chloro-methyl	2-Cl	3-Cl	4-Cl	5-Cl	6-Cl
Methyl propanoate	1	14	35	51		Methyl pentanoate	1	4	28	41	26	
	2	18	27	55			2	3	25	45	25	
	3	19	22	59			1	8	25	46	20	
	4	19	25	56			2	3	26	45	24	
	5	25	28	47			3	4	31	44	18	
	6	20	39	41			2	5	31	46	16	
	7	18	34	48			2	5	30	44	19	
Methyl butanoate	1	2	8	52	38	Methyl hexanoate	<1	3	17	25	30	24
	2	2	7	50	41		<1	3	16	29	33	18
	3	3	16	45	36		<1	2	17	30	33	17
	4	3	7	51	39		<1	2	15	31	35	16
	5	4	8	51	37		<1	3	21	29	31	15
	6	4	10	58	28		<1	3	20	35	31	10
	7	3	8	55	34		<1	2	18	33	33	13

[a] Chlorination at (1) b.p. of ester, Cl_2, UV-light (2) 20 °C, Cl_2, UV (3) 20 °C, Cl_2, Bz_2O_2, dark (4) 20 °C, Cl_2, Bz_2O_2, UV (5) 20 °C, SO_2Cl_2, UV (6) 60 °C, SO_2Cl_2, Bz_2O_2, dark (7) 20 °C, SO_2Cl_2, Bz_2O_2, UV.

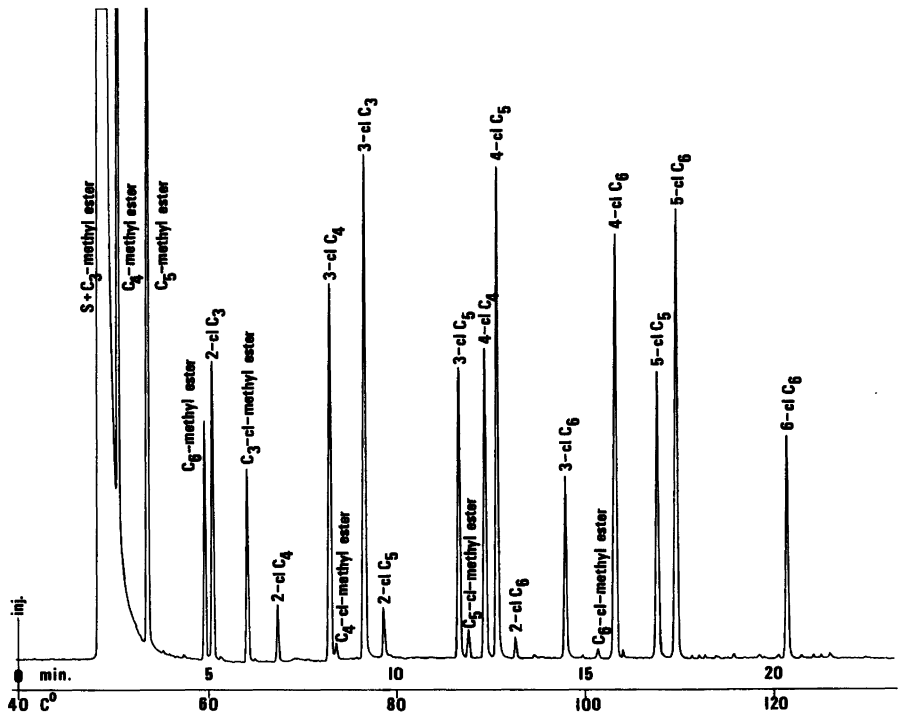

Fig. 1. The gas chromatogram of combined chlorination products of methyl propanoate, butanoate, pentanoate and hexanoate. For operating and other details see the experimental section.

MASS SPECTRA

The 70 eV mass spectra of compounds *(1 – 14)* are presented in the experimental section. The spectra of chloroesters are quite different from those of parent compounds although some characteristic fragmentations are retained.

As expected, the molecular ions of chloroesters are unstable and the molecular peak $M^{\cdot +}$ can be seen only in *2*. α-Cleavage gives a very intense peak at *m/e* 59 $(COOCH_3)^+$ in all spectra. The other α-chleavage gives the chlorine containing ions $(M - OCH_3)^+$. These peaks are small in *1* and *3* and are not present in *6* and *10* indicating the strong electron withdrawing effect of a chlorine atom in 2-position.

β-Cleavage with hydrogen rearrangement gives a very intense peak at *m/e* 74 (base peak in *5*, *12* and *14*) and at *m/e* 108/110 (base peak in 2-chloroesters *3*, *6* and *10*). This fragment is very small in 3-chloroesters *4* and *7* because the loss of chlorine atom from the molecular ion is intense (base peak in *4*).

The γ-cleavage gives the peak at *m/e* 87 $(CH_2CH_2COOCH_3)^+$. However, the corresponding fragment *m/e* 121/123 is missing when there is chlorine in position 2 or 3 (compounds *6*, *7*, *10* and *11*).

Loss of a chlorine atom from the molecular ion is shown in nearly all spectra and it is in *4* and *7* even more intense than the peak from McLafferty rearrangement. This fragment is the base peak in *2* and *4*.

Finally, loss of hydrogen chloride from molecular ion gives the unsaturated methyl ester, from which the loss of CH_3OH is important (*m/e* 82 in *7*, *8* and *9* and *m/e* 96 in *11*, *12* and *13*).

EXPERIMENTAL

Materials and Methods. The starting materials, methyl propanoate, butanoate, pentanoate and hexanoate, were obtained by esterification of corresponding acids with methanol. The preparation and purification of isomeric monochloro esters used as reference compounds, is described in a previous paper[11] as well as the ^1H and ^{13}C NMR spectra. Chloromethyl esters which also are formed in the chlorination of esters were synthesized for identification purposes in pure form from corresponding acid chloride and paraformaldehyde with zinc chloride.[12]

Chlorinations. The esters were reacted by UV-irradiating in the liquid phase at room temperature and in the vapor phase at esters boiling point as described by den Hertog.[5] Before reaction, oxygen was eliminated by bubbling dry nitrogen through the substrate. In order to prevent the formation of higher chlorinated products, less than an equimolar quantity of chlorine was introduced. The chlorination progress was investigated by GLC. Unreacted chlorine and formed hydrogen chloride remaining in the solution were removed by bubbling dry nitrogen through the reaction mixture after which the products were analyzed by GLC.

The benzoyl peroxide catalyzed chlorination of esters with sulfuryl chloride was carried out as described in the paper by Danechrad.[13] Excess sulfuryl chloride was removed *in vacuo* before GLC analysis.

GLC-analyses were achieved on a Varian Model 2400 Gas Chromatograph equipped with a flame ionization detector, a 90 ft × 0.012 in. 5 % Carbowax 20 M glass capillary column with a flow rate of carrier gas (N_2) 1 ml/min. Column programmed from 40 to 130 °C, 4 °C/min, split ratio 1:20 and chart speed 10 mm/min.

Mass-spectra were measured at 70 eV using a Perkin-Elmer 270 B mass spectrometer with GLC.

Mass spectra of compounds (1 – 14). Methyl 2-chloropropanoate (1). 43 (15), 55 (15), 59 (94), 62 (10), 63 (100), 65 (33), 87 (18), 91 (10), 93 (4).

Methyl 3-chloropropanoate (2). 55 (15), 59 (25), 63 (47), 65 (16), 87 (100), 91 (52), 93 (17), 122 (3), 124 (1).

Methyl 2-chlorobutanoate (3). 36 (13), 39 (14), 41 (71), 42 (10), 59 (73), 69 (17), 77 (38), 79 (15), 101 (16), 105 (10), 107 (3), 108 (100), 110 (32).

Methyl 3-chlorobutanoate (4). 39 (17), 41 (53), 42 (20), 59 (77), 69 (14), 77 (30), 79 (12), 101 (100), 105 (27), 107 (9).

Methyl 4-chlorobutanoate (5). 41 (33), 42 (10), 43 (19), 59 (28), 74 (100), 77 (17), 105 (39), 107 (13).

Methyl 2-chloropentanoate (6). 55 (87), 59 (46), 83 (10), 91 (9), 93 (3), 108 (100), 110 (33), 115 (13).

Methyl 3-chloropentanoate (7). 39 (10), 41 (19), 43 (13), 54 (16), 55 (100), 56 (12), 59 (45), 72 (19), 73 (18), 82 (35), 83 (35), 114 (26), 115 (45), 119 (15), 121 (5).

Methyl 4-chloropentanoate (8). 36 (13), 39 (15), 41 (15), 42 (10), 43 (33), 54 (14), 55 (100), 56 (16), 59 (38), 74 (82), 82 (10), 83 (15), 114 (14), 115 (10), 119 (32), 121 (10).

Methyl 5-chloropentanoate (9). 39 (11), 41 (14), 43 (12), 54 (14), 55 (100), 59 (50), 72 (12), 73 (21), 74 (21), 82 (19), 83 (24), 87 (54), 91 (27), 93 (8), 114 (10), 115 (35), 119 (30), 121 (10).

Methyl 2-chlorohexanoate (10). 41 (30), 42 (12), 43 (14), 55 (20), 59 (28), 69 (29), 87 (12), 101 (10), 108 (100), 110 (32), 129 (16).

Methyl 3-chlorohexanoate (11). 36 (10), 39 (36), 41 (100), 42 (23), 43 (36), 53 (13), 55 (55), 59 (46), 67 (12), 68 (89), 69 (94), 71 (10), 74 (70), 87 (27), 96 (18), 97 (36), 129 (24), 133 (11), 135 (19), 137 (6).

Methyl 4-chlorohexanoate (12). 39 (31), 41 (74), 42 (21), 43 (39), 53 (13), 55 (47), 59 (25), 67 (14), 68 (62), 69 (68), 71 (10), 74 (100), 85 (24), 96 (11), 97 (23), 128 (13).
Methyl 5-chlorohexanoate (13). 39 (41), 41 (96), 42 (25), 43 (48), 53 (18), 54 (12), 55 (70), 59 (46), 67 (24), 68 (100), 69 (76), 71 (15), 74 (93), 85 (11), 87 (20), 96 (21), 97 (34), 128 (19).
Methyl 6-chlorohexanoate (14). 39 (15), 41 (40), 42 (11), 43 (37), 55 (21), 59 (26), 68 (11), 69 (34), 74 (100), 87 (20), 133 (12).

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