Journal of Chromatography, 240 (1982) 377–385
Elsevier Scientific Publishing Company, Amsterdam — Printed in The Netherlands

CHROM. 14,710

GAS–LIQUID CHROMATOGRAPHIC ANALYSES

IV. GLASS CAPILLARY GAS CHROMATOGRAPHY OF METHYL AND CHLOROMETHYL MONOCHLORO ESTERS OF ALIPHATIC C_5-CARBOXYLIC ACIDS

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(Received December 4th, 1981)

SUMMARY

The gas chromatography of methyl and chloromethyl esters of pivalic, 2-methylbutyric, isovaleric and valeric acid and certain of their monochloro derivatives was studied. Separation of the combined mixtures of methyl and chloromethyl esters was better on Carbowax 20M than on SE-30. The retention times of esters with substituents adjacent (*i.e.* at C-2) to the carboxyl group appear to be sensitive to column polarity, particularly in the case of the chloromethyl esters. The retention order and relative retention times of compounds are discussed.

INTRODUCTION

Earlier studies have reported the gas chromatographic (GC) separations of mixtures with a wide range of chain lengths of methyl and chloromethyl monochloro esters of aliphatic *n*-carboxylic acids on Carbowax 20M glass capillary columns[1–5]. Also the GC of higher chlorinated methyl propionates[6,7] and methyl butyrates[7,8] has been studied.

Although numerous papers have been published on the GC of aliphatic carboxylic acids and their derivatives, few published chromatographic data are available for lower branched-chain methyl esters[9–14] and studies on their chlorinated derivatives have not yet been reported.

This paper describes a GC study of methyl, chloromethyl and the corresponding monochloro esters of pivalic, 2-methylbutyric, isovaleric and valeric acid. The separations of combined mixtures of both esters were studied on a Carbowax 20M glass capillary column and on a vitreous-silica SE-30 wall-coated open tubular (WCOT) column. Retention times of derivatives were compared by separating the mixtures of methyl and chloromethyl esters of each acid under the same operating conditions.

0021-9673/82/0000–0000/$02.75

EXPERIMENTAL

Apparatus

GC analyses were carried out on a Varian Model 2400 gas chromatograph, adapted for glass capillary work, and on a Perkin-Elmer Model Sigma 3 instrument. The former was equipped with a glass capillary column (50 m × 0.30 mm I.D.) prepared in our laboratory (drawn from soda-glass, etched with hydrogen chloride gas and coated with a 3% Carbowax 20M stationary phase). The latter chromatograph was equipped with a vitreous-silica SE-30 WCOT column (25 m × 0.22 mm I.D.) supplied by Scientific Glass (North Melbourne, Australia). The operating conditions for both columns were as follows: injector and flame-ionization detector temperatures 230 and 250°C, respectively; nitrogen carrier gas flow-rates 1 ml/min; splitting ratios *ca.* 1:20. The column temperatures for the analyses are shown in Figs. 1–3.

The samples were purified using a Perkin-Elmer Model 800 instrument, adapted for preparative work, on a 6 m × 9.5 mm O.D. aluminium tube packed with 10% Carbowax 20M on Chromosorb W (60–80 mesh). Appropriate temperatures were used, with a nitrogen flow-rate of 120 ml/min.

Samples

Methyl pivalate (1), methyl 2-methylbutyrate (3), methyl isovalerate (9) and methyl valerate (13) were obtained via treatment of the corresponding acids with thionyl chloride and methanol. Valeric acid and isovaleric acid were commercial products (Fluka, Buchs, Switzerland); 2-methylbutyric acid and pivalic acid were prepared by a general method[15] employing the carboxylation of the corresponding Grignard reagent.

The methyl esters of chlorinated acids were obtained as follows: methyl 2-chloro-2-methylbutyrate (4), methyl 2-chloroisovalerate (10) and methyl 2-chlorovalerate (14) by esterification of the corresponding acid chlorides[16] with methanol; methyl *erythro*-3-chloro-2-methylbutyrate (5), methyl 3-chloroisovalerate (11) and methyl 3-chlorovalerate (15) from α,β-unsaturated methyl esters[17] (methyl *trans*-2-methyl-2-butenoate and methyl 3-methyl-2-butenoate were prepared from the corresponding commercial acids (E. Merck, Darmstadt, G.F.R.) with hydrogen chloride[18]; methyl chloropivalate (2), methyl *threo*-3-chloro-2-methylbutyrate (6), methyl 2-chloromethylbutyrate (7), methyl 4-chloro-2-methylbutyrate (8), methyl 4-chloroisovalerate (12) and methyl 4-chlorovalerate (16) by isolation from the reaction mixtures of monochloro esters obtained by chlorinating[1] the parent esters (1, 3, 9 and 13) with chlorine; methyl 5-chlorovalerate (17) from commercial acid (E. Merck) by appropriate esterification method.

Chloromethyl pivalate (18), chloromethyl 2-methylbutyrate (20), chloromethyl isovalerate (26) and chloromethyl valerate (30) were prepared from the corresponding acid chlorides and paraformaldehyde in the presence of a trace amount of zinc chloride[19]. Chloromethyl monochloro isomers (19, 21–25, 27–29 and 31–34) were obtained by chlorination[20] of the corresponding starting materials (18, 20, 26 and 30) in the liquid phase with chlorine.

The purities of the separately prepared esters were checked by GC and when required the products were purified by preparative gas–liquid chromatography. The

structures of compounds were confirmed by ^1H nuclear magnetic resonance and mass spectrometry. The mixtures of the isomeric chloromethyl monochloro esters were analysed by GC and GC–mass spectrometry and products were identified as described earlier[20]. The crude chlorination mixtures of chloromethyl esters were used for the GC analyses.

RESULTS AND DISCUSSION

The retention times of positional isomers of equivalent monochloro esters increase continuously as the chlorine substituent is separated from the carbonyl group, 2-chloro isomers always being eluted first[1–5]. By separating the mixtures of closely related compounds, the order of elution on a non-polar column such as SE-30

TABLE I

ABSOLUTE AND RELATIVE RETENTION TIMES FOR METHYL, CHLOROMETHYL AND METHYL MONOCHLORO ESTERS OF ALIPHATIC C_5-CARBOXYLIC ACIDS

Conditions as shown in Fig. 1.

Peak	*Compound (methyl ester = Me; chloromethyl ester = Cl–Me)*	*Column*				
		Carbowax 20M		*SE-30*		
		*Time**	*RRT***	*Time**	*RRT***	*RRT****
1	Me pivalate	4.18	1.00	3:55	1.00	0.85
18	Cl–Me pivalate	5.73	1.37	8.40	2.37	1.47
2	Me chloropivalate	6.74	1.61	10.45	2.94	1.55
3	Me 2-methylbutyrate	4.34	1.00	4.70	1.00	1.08
4	Me 2-chloro-2-methylbutyrate	6.03	1.39	9.69	2.06	1.61
5	Me 3-chloro-2-methylbutyrate (*erythro*)	6.91	1.59	10.68	2.27	1.55
20	Cl–Me 2-methylbutyrate	7.20	1.66	11.07	2.36	1.54
6	Me 3-chloro-2-methylbutyrate (*threo*)	7.56	1.74	11.60	2.47	1.53
7	Me 2-chloromethylbutyrate	8.51	1.96	12.72	2.71	1.49
8	Me 4-chloro-2-methylbutyrate	9.30	2.14	13.68	2.91	1.47
9	Me isovalerate	4.36	1.00	4.74	1.00	1.09
10	Me 2-chloroisovalerate	6.83	1.57	10.55	2.23	1.54
11	Me 3-chloroisovalerate	6.55	1.50	9.49	2.00	1.45
26	Cl–Me isovalerate	7.70	1.77	11.07	2.34	1.44
12	Me 4-chloroisovalerate	10.20	2.34	14.22	3.00	1.39
13	Me valerate	4.60	1.00	5.91	1.00	1.28
14	Me 2-chlorovalerate	7.70	1.67	12.15	2.06	1.58
15	Me 3-chlorovalerate	9.15	1.99	13.05	2.21	1.43
30	Cl–Me valerate	9.37	2.04	13.63	2.31	1.45
16	Me 4-chlorovalerate	10.13	2.20	14.05	2.38	1.39
17	Me 5-chlorovalerate	15.60	3.39	18.04	3.05	1.16

* Absolute retention times (min) measured from Fig. 1a and b.

** Relative retention times for unchlorinated methyl esters taken as 1.00.

*** Relative retention times for compounds on Carbowax 20M taken as 1.00.

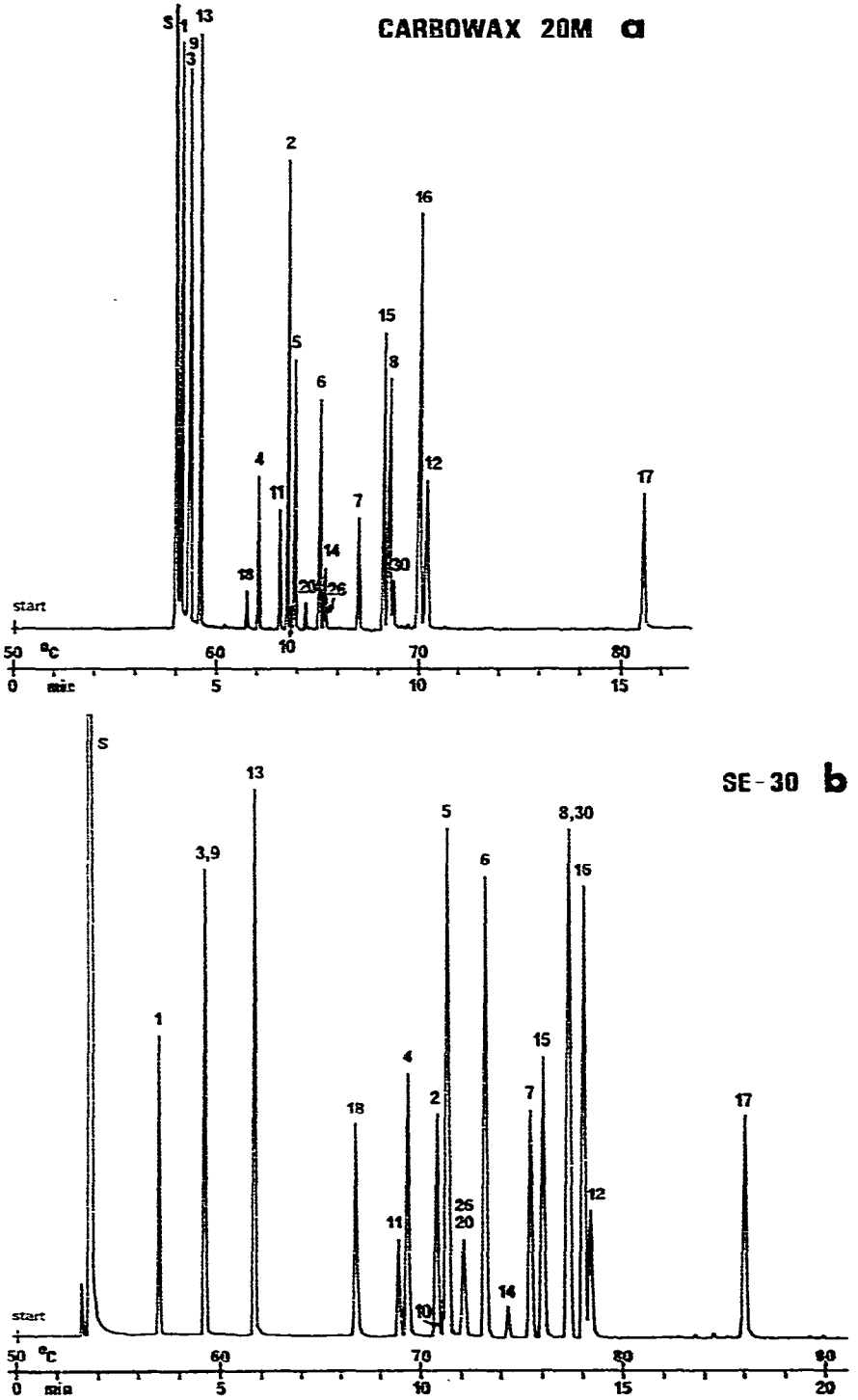

Fig. 1. Chromatogram of the mixture of methyl, chloromethyl and methyl monochloro esters of aliphatic C_5-carboxylic acids analysed on Carbowax 20M (a) and on SE-30 (b). Temperature programme: 50°C at 2°C/min. S = solvent; peaks identified in Table I.

is largely determined by the boiling point of the esters. However, on a polar column such as Carbowax 20M the order in which the compounds appear is greatly influenced by their structure.

Fig. 1 illustrates the separation of methyl, chloromethyl and methyl monochloro esters of aliphatic C_5-carboxylic acids analysed on Carbowax 20M and SE-30. Table I gives the identification of peaks and the absolute and relative retention times for the compounds. All retention times were measured from sample injection and are tabulated relative to unchlorinated methyl esters = 1.00. The retention is also expressed as the ratios of the retention times of the compounds on SE-30 divided by the times on Carbowax 20M.

Silica WCOT columns are more efficient than glass capillary columns. The analysis time of the mixture on SE-30 was longer than on Carbowax 20M under the same operating conditions used, in spite of the double length of the latter. However, separation of the compounds was better on a polar column, only methyl 2-chlorovalerate (14) and chloromethyl isovalerate (26) and also partly methyl 2-methylbutyrate (3) and methyl isovalerate (9) overlapping. The latter compounds 3 and 9 were coincident on SE-30 owing to their similar boiling points, 116 and 117°C, respectively. Obviously the methyl substituent adjacent to the carboxyl group (*i.e.* at C-2) has the stronger effect on the polarity of the compound than the substituent farther away causing the separation of compounds 3 and 9 on Carbowax 20M. Methyl 2-chloroisovalerate (10) was eluted as a shoulder with methyl *erythro*-3-chloro-2-methylbutyrate (5), and methyl 4-chloro-2-methylbutyrate (8) and chloromethyl valerate (30) fully overlapped giving a broadened peak on SE-30.

The elution order of the compounds on the polar and non-polar column was with one exception the same: methyl 3-chloroisovalerate (11) was eluted from the SE-30 column before methyl 2-chloro-2-methylbutyrate (4), the samples being eluted on the Carbowax 20M column in the opposite order.

The polar column also provided a more efficient separation of chloromethyl esters as may be seen from Fig. 2. The identification and absolute and relative retention times of various peaks are given in Table II. Like the corresponding methyl esters, chloromethyl 2-methylbutyrate (20) and chloromethyl isovalerate (26) were coincident on SE-30, whereas the compounds were fully separated on Carbowax 20M. Chloromethyl pivalate (19) and chloromethyl 2-chloroisovalerate (27) overlapped on both columns, 27 being eluted as a shoulder with 19 on SE-30. In addition, chloromethyl 4-chloro-2-methylbutyrate (25) and chloromethyl 3-chlorovalerate (32) were coincident on Carbowax 20M and chloromethyl *threo*-3-chloro-2-methylbutyrate (23) and chloromethyl 2-chlorovalerate (31) on SE-30, 32 and 31 being eluted as shoulders.

The elution order of isomeric monochloro esters studied in previous papers[3–5] has always been the same, independent of the polarity of the column. In this work, however, as may be seen from Fig. 2a, chloromethyl 2-chloroisovalerate (27) left the Carbowax 20M column before chloromethyl 3-chloroisovalerate (28). Chloromethyl 2-chloro esters (21, 27 and 31) are less polar than the other isomers having relatively short retention times on the polar column (Table II). The same effect has been reported earlier with chloromethyl monochloro esters of aliphatic *n*-carboxylic acids[5].

Like the corresponding methyl isomer, chloromethyl 3-chloroisovalerate (28) has a shorter retention time on SE-30, being eluted before chloromethyl chloropi-

TABLE II

ABSOLUTE AND RELATIVE RETENTION TIMES FOR CHLOROMETHYL AND CHLOROMETHYL MONOCHLORO ESTERS OF ALIPHATIC C_5-CARBOXYLIC ACIDS

Conditions as in Fig. 2.

Peak	*Chloromethyl ester of*	*Column*						
		Carbowax 20M			*SE-30*			
		*Time**	*RRT***	*RRT*[‡]	*Time**	*RRT***	*RRT****	*RRT*[‡]
18	Pivalic acid	5.19	1.00	1.23	7.01	1.00	1.35	2.01
19	Chloropivalic acid	11.97	2.31	2.05	14.31	2.04	1.20	1.70
20	2-Methylbutyric acid	6.03	1.00	1.47	8.85	1.00	1.47	2.04
21	2-Chloro-2-methylbutyric acid	10.35	1.72	1.89	13.58	1.53	1.31	1.70
22	3-Chloro-2-methylbutyric acid (*erythro*)	12.45	2.06	2.04	14.70	1.66	1.18	1.71
23	3-Chloro-2-methylbutyric acid (*threo*)	13.05	2.16	2.02	15.28	1.73	1.17	1.66
24	2-Chloromethylbutyric acid	14.30	2.37	2.03	16.17	1.83	1.13	1.64
25	4-Chloro-2-methylbutyric acid	15.06	2.50	2.02	16.88	1.91	1.12	1.63
26	Isovaleric acid	6.29	1.00	1.35	8.88	1.00	1.41	2.07
27	2-Chloroisovaleric acid	11.98	1.90	1.91	14.40	1.62	1.20	1.67
28	3-Chloroisovaleric acid	12.19	1.94	2.01	13.90	1.57	1.14	1.78
29	4-Chloroisovaleric acid	16.05	2.55	2.19	17.38	1.96	1.08	1.62
30	Valeric acid	7.32	1.00	1.57	10.39	1.00	1.42	1.98
31	2-Chlorovaleric acid	12.78	1.75	1.98	15.21	1.46	1.19	1.60
32	3-Chlorovaleric acid	15.08	2.06	2.08	16.39	1.58	1.09	1.62
33	4-Chlorovaleric acid	15.90	2.17	2.08	17.21	1.66	1.08	1.59
34	5-Chlorovaleric acid	19.21	2.62	1.94	19.72	1.90	1.03	1.51

* Absolute retention times (min) measured from Fig. 2a and b.

** Relative retention times for unchlorinated chloromethyl esters taken as 1.00.

*** Relative retention times for compounds on Carbowax 20M taken as 1.00.

‡ Relative retention times for the corresponding methyl esters taken as 1.00, determined from the mixtures of methyl and chloromethyl esters of the same acids (*e.g.* Fig. 3a and b).

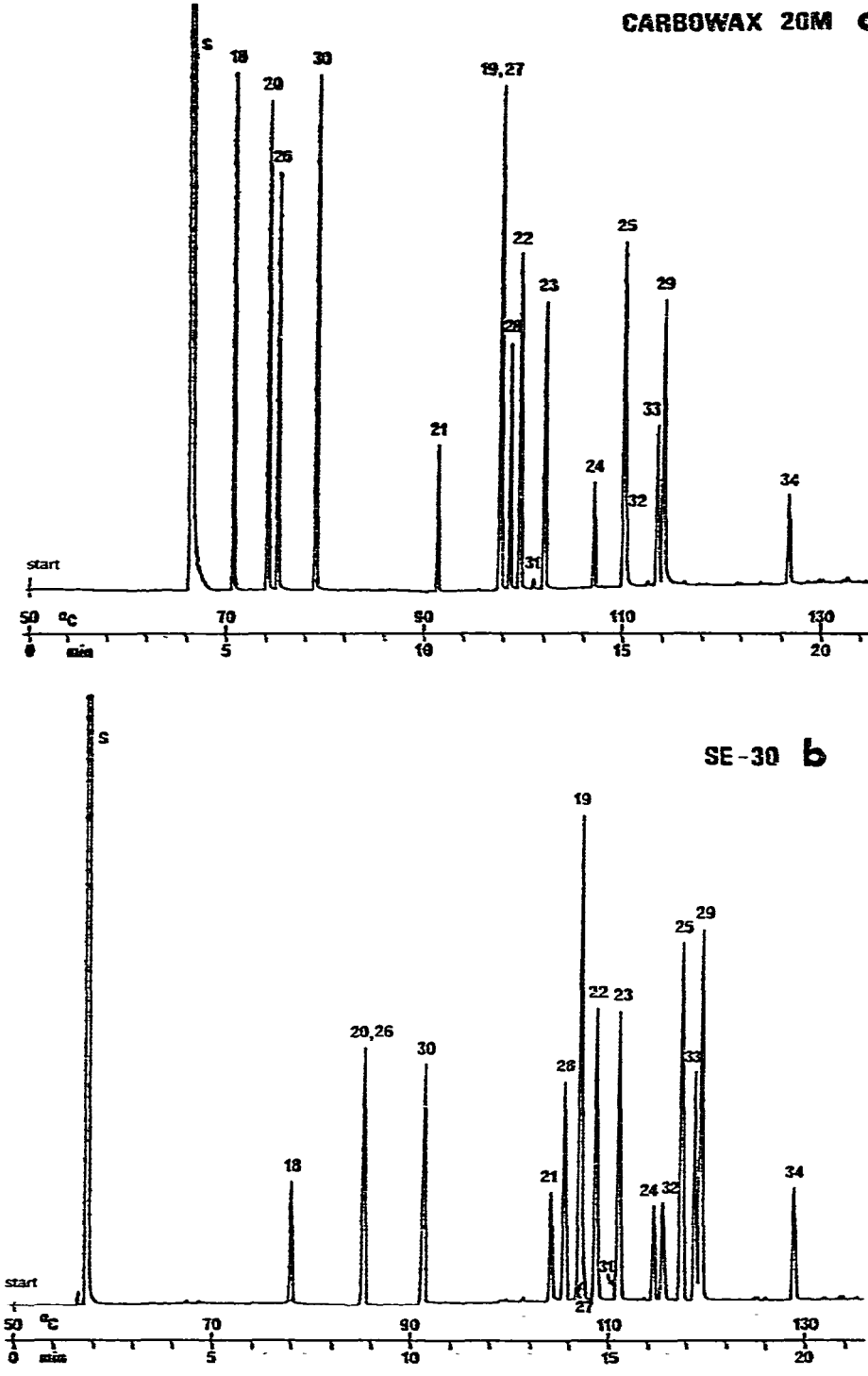

Fig. 2. Chromatogram of the mixture of chloromethyl and chloromethyl monochloro esters of aliphatic C_5-carboxylic acids analysed on Carbowax 20M (a) and on SE-30 (b). Temperature programme: 50°C at 4°C/min. S = solvent; peaks identified in Table II.

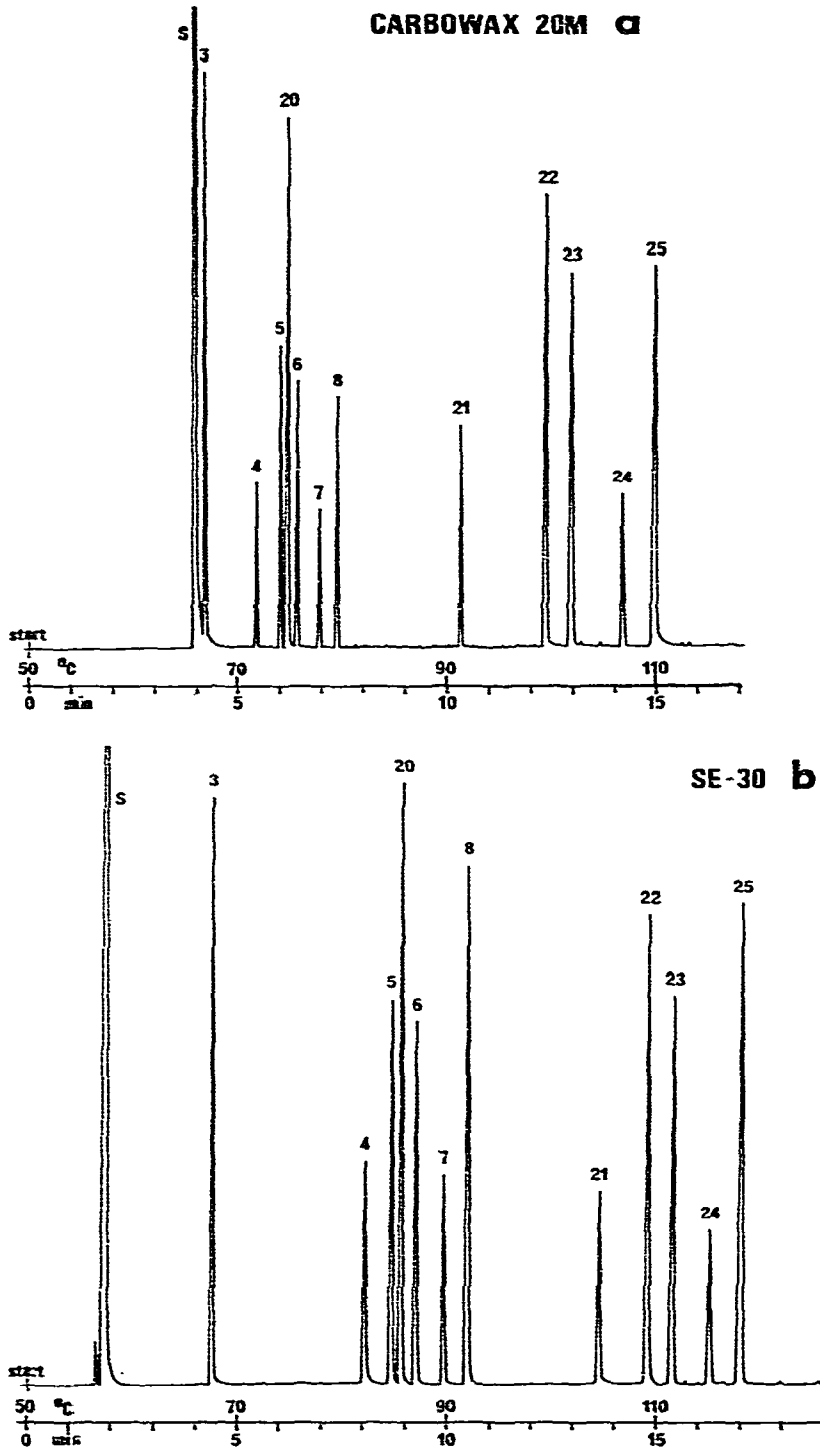

Fig. 3. Chromatogram of the mixture of methyl and chloromethyl 2-methylbutyrates and their monochloro derivatives analysed on Carbowax 20M (a) and on SE-30 (b). Temperature programme: 50°C at 4°C/min. S = solvent; peaks identified in Tables I and II.

valate (19). Also, chloromethyl 3-chlorovalerate (32) left the non-polar column before chloromethyl-4-chloro-2-methylbutyrate (25).

To compare the elution times, GC separations of the mixtures of methyl and chloromethyl esters of the same acids were performed under the same operating conditions. The results are presented in Table II and tabulated relative to the corresponding methyl esters = 1.00. The gas chromatograms of the mixture of methyl and chloromethyl 2-methylbutyrates are illustrated in Fig. 3. It can be seen that the highest values, *ca.* 2.0, for the unchlorinated chloromethyl esters are observed on SE-30, whereas on Carbowax 20M these are the lowest ones, from 1.2 to 1.6. The relative retention times of isomeric monochloro esters vary little on SE-30, while on the other hand, the 2-chloro and ω-chloro isomers give rise to the greatest disparities on Carbowax 20M.

As can be seen from Tables I and II, the relative retention times, relative to the corresponding esters on Carbowax 20M, of compounds on SE-30 are with one exception (methyl pivalate, 1) greater than on Carbowax 20M under the operating conditions used. The values for chlorinated methyl and chloromethyl esters vary from 1.6 to 1.2 and from 1.3 to 1.0, respectively, the 2-chloro isomers giving always the highest and the ω-chloro compounds the lowest values.

ACKNOWLEDGEMENT

This work was financially supported by the Academy of Finland.

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