

SEPARATION OF MALONIC ACID ESTERS BY GAS CHROMATOGRAPHY

V. PROCHÁZKOVÁ, J. BENEŠ AND K. VEREŠ

Isotope Laboratory of the Institutes for Biological Research, Czechoslovak Academy of Sciences, Prague (Czechoslovakia)

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During preparative alkylation of malonic acid esters both mono- and dialkyl-derivatives are formed. Some of these, in particular, the lower homologues, are only separated with some difficulty in view of their similar boiling points. A relatively rapid separation of the individual derivatives in the series of methyl to hexyl alkyls of diethyl esters of malonic acid was achieved by means of gas chromatography. At the same time, certain graphical relationships between the elution data obtained from chromatographic separation and the various derivatives were investigated as they might be suitable for quick orientation and identification.

The separation of some malonic acid esters by gas chromatography has been studied by several authors, *e.g.*, TEPE AND WESSELMAN¹ and DORFNER² who used a silicone oil as stationary phase. Separation of dimethyl, diethyl and mixed esters of alkylarylmalonic acid is described in a paper by JANÁK, NOVÁK AND SULOVSÝ³. Separation of mono- and dimethyl-alkylated esters on Reoplex 400 using gas chromatography was mentioned in a paper by BENEŠ, VEREŠ AND DOBIÁŠOVÁ⁴.

EXPERIMENTAL

The substances studied here can be divided into three groups:

(1) Dimethyl, methyl ethyl and diethyl esters of malonic acid, methyl malonic and dimethyl malonic acids.

(2) Diethyl esters of higher homologues of methyl malonic acid (ethyl, propyl etc.).

(3) Diethyl esters of dialkylated malonic acid.

The substances were prepared by the usual methods, *i.e.* the alkylation of malonic esters with the corresponding alkyl halides in the presence of sodium alcoholate^{5,6}.

Chromatographic separation was carried out on an Argon Pye ionization chromatograph (W. G. Pye and Co., Ltd, Cambridge, England). A straight column 120 cm in length with an inner diameter of 4 mm was used. The liquid phases used were Reoplex 400 fixed as a polar phase on 80-120 mesh Celite 545 (Johns-Manville, London) and Apiezon M on the same support as nonpolar phase. The amounts used were 2 g Reoplex on 8 g Celite 545 and 1 g Apiezon on 9 g Celite 545. The rate of flow of argon was 20 ml per min. The alkyl derivatives were separated at column temperatures of 108° and 135°.

RESULTS AND DISCUSSION

The fact that during alkylation of malonic esters by the above procedures^{5,6} a mixture of mono- and dialkylated compounds is always formed in addition to a minute amount of the starting non-alkylated ester, was verified by gas chromatography. For separating the mono- as well as the dialkyl-derivatives one can use either the polar Reoplex or the nonpolar Apiezon phase. Differences were found only in the elution values and in graphical relationships. The relative elution values of the compounds investigated, referred to the ethyl-alkylated ethyl ester of malonic acid at two different temperatures on polar and nonpolar columns, are shown in Table I. For

TABLE I

RETENTION VALUES REFERRED TO ETHYL-ALKYLATED DIETHYL ESTER OF MALONIC ACID

<i>Ester of malonic acid</i>	<i>Reoplex 20%</i>		<i>Apiezon 10%</i>	
	<i>108°</i>	<i>135°</i>	<i>108°</i>	<i>135°</i>
DiMe	0.72			
MeEt	0.88			
DiEt	1.02			
Me-alkylated diMe	0.62			
Me-alkylated MeEt	0.66			
Me-alkylated diEt	0.73	0.78	0.51	0.39
DiMe-alkylated diMe	0.54			
DiMe-alkylated MeEt	0.60			
DiMe-alkylated diEt	0.64	0.57	0.51	0.39
Et-alkylated diEt	1.0 ^a	1.0 ^b	1.0 ^c	1.0 ^d
Pro-alkylated diEt	1.45	1.4	1.79	1.58
Bu-alkylated diEt	2.27	1.98	3.13	2.66
Am-alkylated diEt	3.36	3.48	4.81	4.26
Hex-alkylated diEt	6.21	4.66	7.33	7.6
MeEt-alkylated diEt	0.91	0.82		0.75
DiEt-alkylated diEt	1.23	1.22	2.03	1.91
EtPro-alkylated diEt	1.52	1.52	3.25	3.02
DiPro alkylated diEt	2.2	1.99	5.18	4.46
EtBu-alkylated diEt	2.44	2.07	5.25	4.94
ProBu-alkylated diEt	3.22	2.74	8.51	7.5

^a $V_g = 368$ ml.^b $V_g = 147.2$ ml.^c $V_g = 432$ ml.^d $V_g = 166.4$ ml.

better comparison Fig. 1 shows the dependence of the boiling points of the individual substances on the number of carbon atoms. For identification of the individual malonic acid esters we used the graphical dependence of $\log_{10} V_g$, with reference to the ethyl-alkylated ethyl ester of malonic acid, on the number of carbon atoms (Figs. 2, 3 and 4); and the effect of the liquid phases, Reoplex and Apiezon, on $\log_{10} V_g$ is shown in Fig. 5. Both types of graphs have been used frequently by several authors⁷⁻⁹ for analytical differentiation between some types of compounds.

In addition to the analytical separation we thought it might be of interest to see whether the elution data could be correlated with values characterizing the changes in the structure of the given compounds. Structural changes which can be

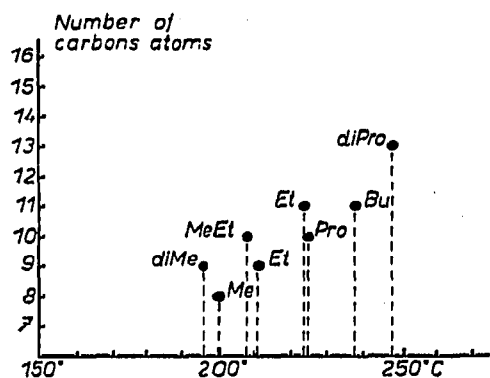


Fig. 1. Dependence of the boiling points of the individual substances on the number of carbon atoms.

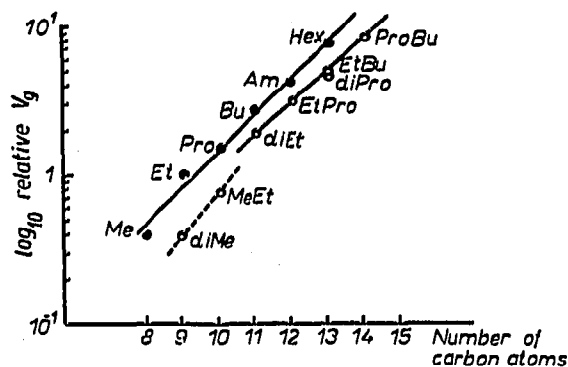


Fig. 2. Dependence of $\log_{10} V_g$ relative to the ethyl-alkylated ethyl ester of malonic acid on the number of carbon atoms (Apiezon, 135°).

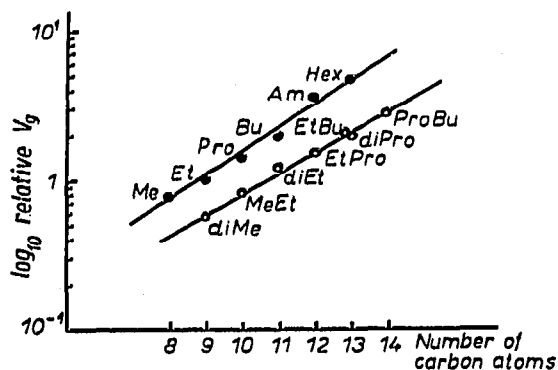


Fig. 3. Dependence of $\log_{10} V_g$ relative to the ethyl-alkylated ethyl ester of malonic acid on the number of carbon atoms (Reoplex, 135°).

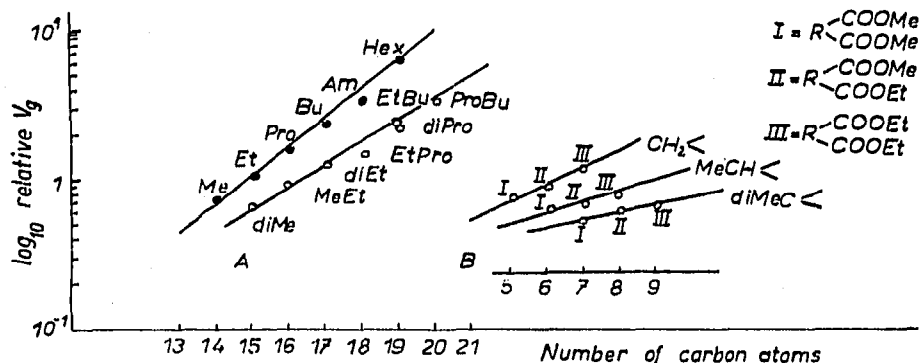


Fig. 4. Effect of the increasing number of α -C-substituents on $\log_{10} V_g$ (Reoplex, 108°).

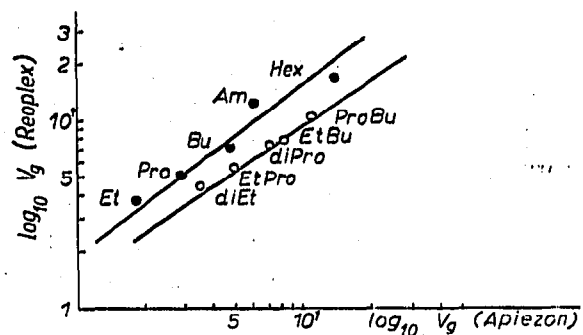


Fig. 5. Effect of the liquid phases, Reoplex and Apiezon on $\log_{10} V_g$.

assumed to occur in a series of mono- and dialkylated malonic esters can be due first of all to the presence or absence of an acid hydrogen in the α -position of malonic acid esters. This hydrogen, in view of its mobility, can bring about a number of mesomeric states and thus cause a generally higher reactivity of molecules and changes of their polarity. For this reason it might be possible to compare the individual dipole moments of the above compounds with their retention values. In this case we investigated in some detail the increase of retention volumes in individual homologous series on a polar and nonpolar column at two temperatures and defined the above-mentioned graphical relationships. For defining the rise in the retention volume with increasing number of carbon atoms we used the symbol f (= increment factor in the relative retention volume for a chain extension of a single methylene group).

$$f = \frac{\text{rel.}V_{\theta} \text{ of malonic ester with } X \text{ carbon atoms}}{\text{rel.}V_{\theta} \text{ of malonic ester with } (X-1) \text{ carbon atoms}}$$

A comparison of these factors for the homologous series of monoalkyls and dialkyls is shown in Table II.

It follows from the f values that the retention values rise much more rapidly with increasing number of carbon atoms in the monoalkyl homologous series than in the dialkyl series; this is apparent from the graphical representation of the dependence of the number of carbon atoms on $\log_{10}V_{\theta}$ (Figs. 2, 3 and 4). A difference in the polarity of molecules may also be observed here: on substitution of the acid carbon in the α -position it decreases. The effect on $\log_{10}V_{\theta}$ of increasing the number of substituents on the α -C starting from nonalkylated malonic ester to the dialkylated one is shown in Fig. 4B.

A change in the value of the f factor is also apparent between the two phases. On Apiezon, the values are much higher than those for the same derivatives on Reoplex. The differences follow from the dissimilar character of the separation on the

TABLE IIA

INCREMENT FACTORS IN THE RELATIVE RETENTION VOLUME FOR CHAIN EXTENSION BY A SINGLE METHYLENE GROUP ON REOPLEX

<i>Comparison in the monoalkyl series</i>			<i>Comparison in the dialkyl series</i>		
<i>Ratio of the number of carbon atoms in alkyl groups</i>	<i>f</i>		<i>Ratio of the number of carbon atoms in alkyl groups</i>	<i>f</i>	
	<i>135°</i>	<i>108°</i>		<i>135°</i>	<i>108°</i>
$\frac{2}{1}$ <u>Et</u>	1.28	1.37	$\frac{3}{2}$ <u>MeEt</u>	1.42	1.38
$\frac{3}{2}$ <u>Me</u>			$\frac{4}{3}$ <u>diMe</u>		
$\frac{3}{2}$ <u>Pro</u>	1.40	1.45	$\frac{4}{3}$ <u>diEt</u>	1.49	1.38
$\frac{4}{2}$ <u>Et</u>			$\frac{5}{3}$ <u>MeEt</u>		
$\frac{4}{2}$ <u>Bu</u>	1.41	1.57	$\frac{5}{4}$ <u>EtPro</u>	1.25	1.23
$\frac{5}{3}$ <u>Pro</u>			$\frac{6}{4}$ <u>diEt</u>		
$\frac{5}{4}$ <u>Am</u>	1.76	1.48	$\frac{6}{5}$ <u>diPro</u>	1.31	1.45
$\frac{6}{4}$ <u>Bu</u>			$\frac{7}{5}$ <u>EtPro</u>		
$\frac{6}{5}$ <u>Hex</u>	1.34	1.85	$\frac{7}{6}$ <u>ProBu</u>	1.37	1.45
$\frac{7}{5}$ <u>Am</u>			$\frac{8}{6}$ <u>diPro</u>		
\emptyset	1.43	1.54	\emptyset	1.37	1.38

TABLE IIB

COMPARISON OF INCREMENT FACTORS IN THE RELATIVE RETENTION VOLUME FOR CHAIN EXTENSION BY A SINGLE METHYLENE GROUP ON REOPLEX AND APIEZON

Ratio of carbon atoms in the alkyl	<i>f</i>	
	Reoplex 135°	Apiexon 135°
$\frac{2}{1}$ Et Me	1.28	2.56
$\frac{3}{2}$ Pro Et	1.40	1.58
$\frac{4}{3}$ Bu Pro	1.41	1.68
$\frac{5}{4}$ Am Bu	1.76	1.60
$\frac{6}{5}$ Hex Am	1.34	1.78

two phases. The different polarity of mono- and dialkyls which is well marked on Reoplex as a polar phase is much less pronounced on Apiexon as a nonpolar base.

SUMMARY

A separation of some mono- and dialkyl derivatives of malonic acid was carried out on polar and nonpolar phases by means of gas chromatography. The retention data are given.

The graphical relationship between retention value and the number of carbon atoms of the individual derivatives was investigated. A more detailed examination of the rise of retention values in a homologous series of mono- and dialkyl derivatives consisted of using an increment factor for the retention volume for an extension of the chain by a single methylene group.

The retention volumes for the dialkyl derivatives of malonic acid investigated were found to be generally lower than those of the monoalkyl derivatives.

The differences in retention data are apparently due to changes in polarity of the molecules that occur with increasing number of substituents on the α -C.

The paper gives an example of applying gas chromatography to the separation of related homologues of organic compounds and to the investigation of some changes in the physico-chemical properties of compounds.

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