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SEPARATION AND IDENTIFICATION OF HALOCYCLOALKANES BY GAS CHROMATOGRAPHY. PART II

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SUMMARY

Mixtures of isomeric dihalo- and halomethylcyclopentanes and of dihalo-,halomethyl- and halocyanocyclobutanes have been separated by gas chromatography on a tritolylphosphate column. The order of elution is the same for each set of isomeric disubstituted cycloalkanes. The relative retention volumes can be used to determine rapidly the structure of a given isomer and distinguish it from other stereoisomers. An attempt is made to rationalise the retention volume data in terms of the structural properties of the cycloalkanes.

INTRODUCTION

Chlorination or bromination of a substituted cyclopentane or cyclobutane produces a set of five isomeric disubstituted cycloalkanes. These isomers must be separated and identified in order to obtain a fuller understanding of the halogenation process[1]. The isomer configurations can be established by the usual physico-chemical methods, once pure samples can be obtained.

In this paper we report a method of separation which is appropriate for a wide variety of disubstituted cycloalkanes, and show that an isomer's configuration can be established from its relative retention volume.

EXPERIMENTAL

Materials

Methylchlorocyclobutane isomers were prepared by gas-phase chlorination of methylcyclobutane at 80°, using ten parts methylcyclobutane to one part chlorine. The products were distilled through Carbosorb to remove HCl and unreacted chlorine, giving a mixture of the five methylchlorocyclobutanes, with the chloromethyl isomer, in a solution of unreacted methylcyclobutane[2]. Chlorocyanocyclobutane isomers were prepared by gas-phase chlorination of cyanocyclobutane[2]. Bromochloro- and dibromocyclobutane isomers were prepared by gas-phase bromination of chlorocyclobutane and bromocyclobutane, respectively.

Methylchloro- and chlorofluorocyclopentane isomers were prepared by gas-phase chlorination of methylcyclopentane and fluorocyclopentane, respectively. Methylbromo-, bromofluoro-, bromochloro-, and dibromocyclopentane isomers were prepared by gas-phase bromination of methylcyclopentane, fluorocyclopentane, chlorocyclopentane, and bromocyclopentane, respectively.

Product isomers were identified by injecting a sample of each mixture into a 15% w/w tritolylphosphate (TTP) column, housed in a Perkin-Elmer F11 gas chromatograph, maintained at a suitable temperature. The effluent from the column was led via a single stage Bieman separator into the source of an A.E.I. MS12 mass spectrometer. Mass spectra were thus obtained for the separated isomers, which could then be identified.

Method

The analytical data were obtained by a method similar to that described previously[3]. A 15% w/w tritolylphosphate column, having a resolution of about 1100 theoretical plates, was employed. The retention volumes were measured relative to that of *trans*-1,2-dichlorocyclohexane, whose suitability as a standard has already been established for a variety of chromatographic conditions.

The isomers were separated using one of the following sets of conditions. The particular conditions for a given set of isomers are indicated in the appropriate table in the RESULTS section. (a) Column temperature, 70°; nitrogen flow rate, 60 ml/min; inlet pressure, 8.5 lbs./in.^{2}; (b) column temperature, 75°; nitrogen flow rate, 55 ml/min; inlet pressure, 7.9 lbs./in.^{2}; (c) column temperature, 115°; nitrogen flow rate, 75 ml/min; inlet pressure, 12 lbs./in.^{2}; (d) column temperature, 115°; nitrogen flow rate, 71 ml/min; inlet pressure, 10.2 lbs./in.^{2}; (e) column temperature, 100°; nitrogen flow rate, 50 ml/min; inlet pressure, 7.2 lbs./in.^{2}; (f) column temperature, 100°; nitrogen flow rate, 71 ml/min; inlet pressure, 10.2 lbs./in.^{2}.

RESULTS AND DISCUSSION

The retention volumes of the isomers of methylchloro-, chlorocyano-, bromochloro-, and dibromocyclobutane, relative to *trans*-1,2-dichlorocyclohexane, are given in Table I. The relative retention volume data for methylchoro-, chlorofluoro-,

TABLE I

RELATIVE RETENTION VOLUMES (V'_R) OF DISUBSTITUTED CYCLOBUTANES ON 15% TTP

trans-1,2-Dichlorocyclohexane was used as internal standard. Conditions are described in text under *Method*.

Compound	*Isomer*					*Conditions*
	1,1	*trans-1,2*	*trans-1,3*	*cis-1,3*	*cis-1,2*	
C_4H_6MeCl[a]	0.025	0.030	0.033	0.033	0.039	b
C_4H_6CNCl	0.377	1.43	1.56	2.80	4.94	e
C_4H_6ClBr	0.184	0.355	0.395	0.555	0.974	c
$C_4H_6Br_2$	0.395	0.751	1.12	2.60	—	c

[a] $C_2H_7CH_2Cl$, $V'_R = 0.051$.

TABLE II

RELATIVE RETENTION VOLUMES (V'_R) OF DISUBSTITUTED CYCLOPENTANES ON 15% TTP

trans-1,2-Dichlorocyclohexane was used as internal standard. Conditions are described in text under *Method*.

Compound	*Isomer*					*Conditions*
	1,1	*trans-1,2*	*trans-1,3*	*cis-1,3*	*cis-1,2*	
C_5H_8MeCl[a]	0.059	0.072	0.077	0.077	0.089	b
C_5H_8ClF	0.035	0.039	0.039	0.068	0.174	a
C_5H_8MeBr	0.263	0.304	0.333	0.333	0.377	f
C_5H_8BrF	0.112	0.183	0.183	0.395	—	f
C_5H_8ClBr	0.368	0.694	1.91	2.20	—	c
$C_5H_8Br_2$	0.681	0.874	1.39	2.61	—	d
$C_5H_8Cl_2$[b]	0.187	0.214	0.284	0.478	0.946	c
$C_7H_{12}Cl_2$[b]	1.16	2.05	3.18	3.94	6.13	c

[a] $C_5H_9CH_2Cl$, $V'_R = 0.124$.
[b] Corrected values for dichlorocyclopentane and dichlorocycloheptane isomers.

methylbromo-, bromofluoro-, bromochloro-, and dibromocyclopentane isomers are given in Table II.

The order of elution is the same for each set of isomers, *i.e.* 1,1; *trans*-1,2; *trans*-1,3; *cis*-1,3; *cis*-1,2. With several of the series the *trans*-1,3- and *cis*-1,3-isomers were eluted as a single peak. This order of elution is identical with that found previously for dihalocyclohexane and dihalocycloheptane isomers[3].

Two major trends in the results may be noted at once. The spread in the relative retention volumes for a set of chloro- or bromomethyl isomers is much less than the spread for a set of dihaloisomers. For instance in Table I, V_R' changes from 0.025 for 1-methyl-1-chlorocyclobutane to 0.039 for *cis*-1-methyl-2-chlorocyclobutane, whereas a much bigger change from 0.184 to 0.974 is observed for the corresponding bromochloroisomers. Secondly, the long relative retention times of the chlorocyanocyclobutanes, in relation to their molecular weight, are also of interest.

We previously proposed that the retention volume data could be rationalised in terms of the availability of the ring substituents to interact with the tritolylphosphate stationary phase[3]. With the *cis*-isomers both substituents were available on the same side of the molecule so that interaction was strong. For the *trans*-isomers the availability of both substituents becomes less, until for the *trans*-1,2- or 1,1-isomers only one substituent could interact with the stationary phase. The data reported here can also be interpreted in terms of the same proposal. For the methylhalo isomers only one halogen substituent is available for interaction with the stationary phase irrespective of the isomer configuration. The methyl substituent being less polar will interact only weakly. The small spread of values of the methylhalocycloalkane relative retention times is thus readily understood. The cyano substituent being even more polar than halogen, interacts more strongly so that the relative retention volumes of the halocyanocyclobutanes are very long. On going from the 1,1- to the *cis*-1,2-chlorocyanocyclobutane a chlorine substituent also becomes available to interact with the stationary phase. Hence the spread of relative retention volume values from the 1,1-

to the *cis*-1,2-chlorocyano isomers would be expected to be about the same as for a set of dihaloisomers; exactly as is observed.

A plot of log V_R' against boiling point is shown in Fig. 1 for all the isomers having known boiling points (refs. 4–6; other boiling points were determined in our laboratories), including those studied previously such as the dichlorocyclobutanes whose boiling points we have recently obtained. A general linear tendency can be observed, but the graph shows two kinds of structures as illustrated in Figs. 1a and 1b, respectively. The graph can be resolved into three straight lines: one line passing close to all the disubstituted cyclobutanes, one line representing the disubstituted cyclopentanes, and a third line correlating the cyclohexane isomers. The graph may also be resolved into a series of curves, each curve representing one set of isomers. The curvature is most marked for the *cis*-isomers, particularly the *cis*-1,2-isomers, indicating the increased interaction with the stationary phase shown by these isomers having two substituents available on the same side of the molecule.

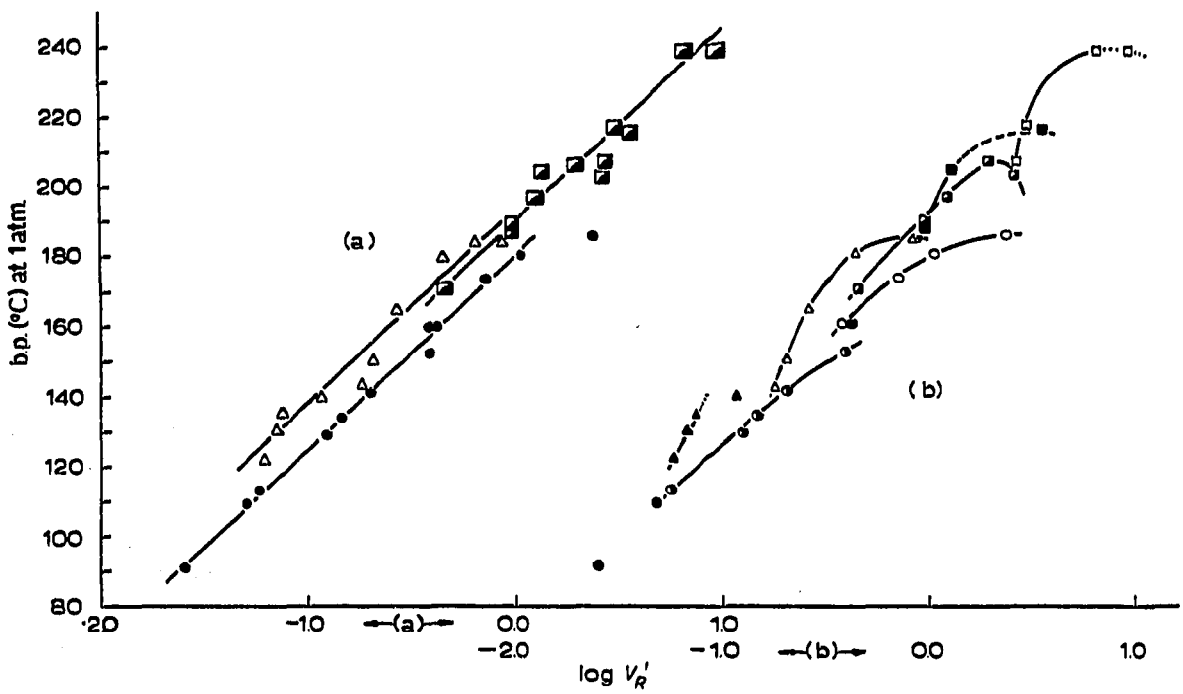

Fig. 1. Correlation of boiling point with log V'_R. (a) ●, Disubstituted cyclobutanes; △, disubstituted cyclopentanes; ◪, disubstituted cyclohexanes. (b) ●, Methylchlorocyclobutane isomers and *trans*-1-bromo-3-chlorocyclobutane; ◑, dichlorocyclobutane isomers; ○, dibromocyclobutane isomers; △, methylchlorocyclopentane isomers and $C_5H_9CH_2Cl$; ▲, dichlorocyclopentane isomers; ◪, dichlorocyclohexane isomers; ■, chlorobromocyclohexane isomers; □, dibromocyclohexane isomers.

A particularly interesting case is that of the methylchlorocyclopentanes. Since only one halogen substituent is available from all the isomers, little or no curvature would be expected. The 1,1- and *trans*-isomers clearly lie on a straight line, but unfortunately it was not possible to measure the boiling point of the *cis*-1-methyl-2-chlorocyclopentane, nor is a value for the pure material given in the literature.

In Fig. 2a a plot of log V_R' against molecular weight is shown for all the dihalocyclobutane and dihalocyclopentane isomers, excluding the fluorine containing com-

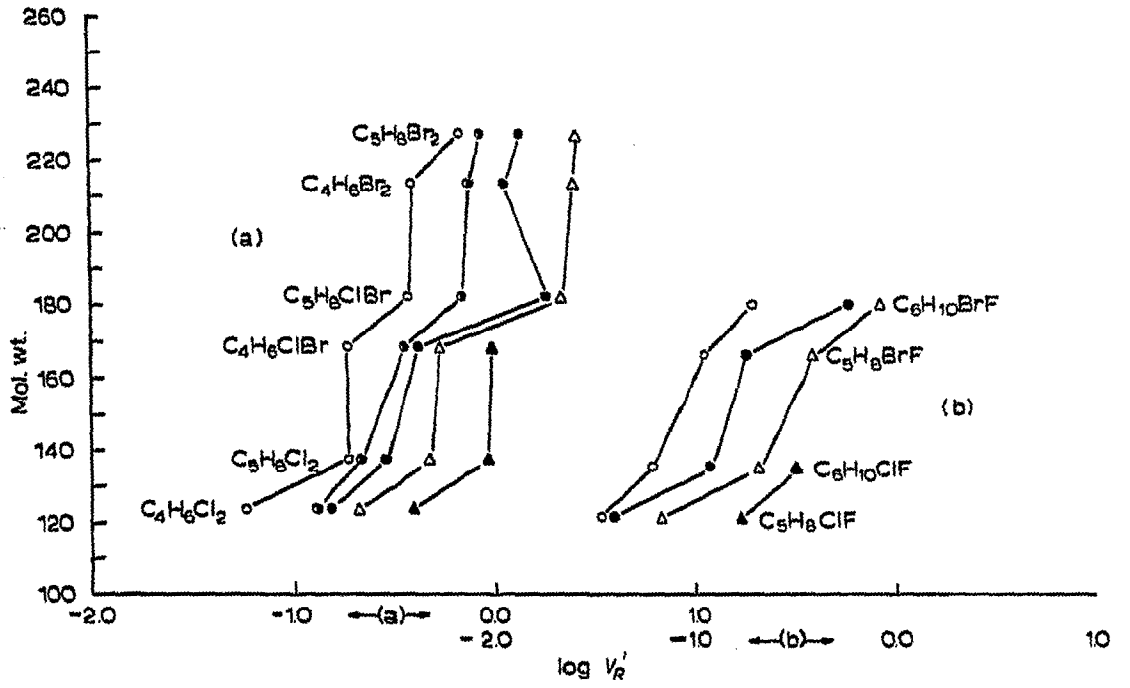

Fig. 2. Plot of log V'_R against molecular weight. (a) ○, 1,1-isomers; ◑, *trans*-1,2-isomers; ●, *trans*-1,3-isomers; △, *cis*-1,3-isomers; ▲, *cis*-1,2-isomers. (b) ○, 1,1-isomers; ●, *trans*-1,2- and *trans*-1,3-isomers; △, *cis*-1,3-isomers; ▲, *cis*-1,2-isomers.

pounds. A fairly regular progression from one set of isomers to another is generated, similar to that obtained previously with disubstituted cyclohexane isomers[3]. The fluorine containing isomers also form a regular progression within themselves (see Fig. 2b) but do not fit in well with the other series. The order of elution of these isomers is the same as for other dihalocycloalkanes, but the magnitude of their relative retention volumes is much less.

Irregularities in the correlation of log V_R' with molecular weight can probably be attributed to changes in the inter-halogen distance which occur for a given isomer structure. For instance, the inter-halogen distance in the *cis*-1,3-isomers may vary, not only with the type of halogen present, but also because of changes in ring size, and ring conformation. The number of stable isomer conformations depends on ring size and on the type of substituent present[7]. For the 1,1-isomers the cycloalkane ring might simply be regarded as a hydrocarbon "tail" attached to one active site capable of interaction with the stationary phase. Conformational and other changes in the ring as the substituents are varied, should have a relatively minor effect. A much more regular relationship of log V_R' with molecular weight would then be expected for the 1,1-isomers only.

Fig. 3 shows the plot obtained for all the 1,1-isomers containing chlorine and/or bromine. A very regular array is formed, the only serious deviation being that of 1,1-dibromocyclopentane. The relative retention volumes of this limited range of compounds are a simple function of the numbers of carbon, chlorine and/or bromine atoms present. This function obviously has a very limited range of application. The fluorine containing 1,1-compounds do not fit into the same sequences, although they probably

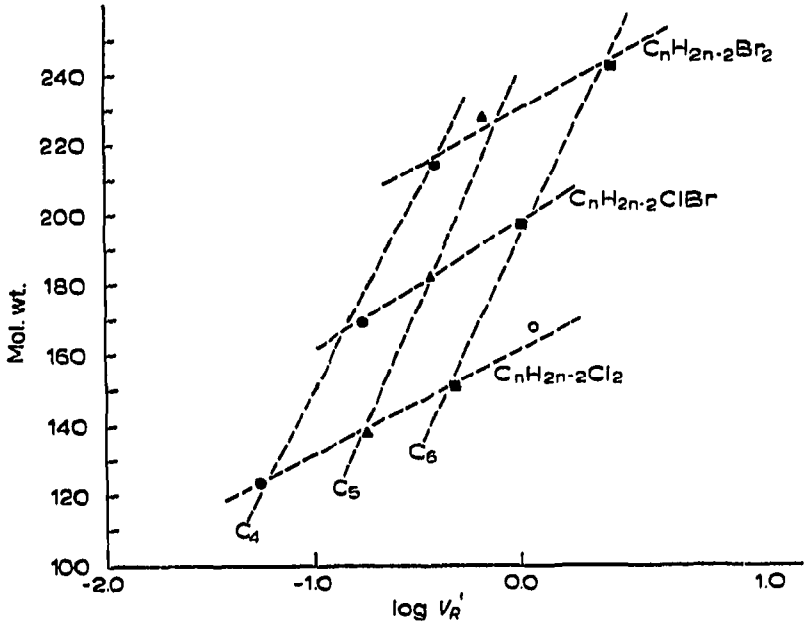

Fig. 3. 1,1-Dihalo isomers: plot of log V'_R against molecular weight. ●, Dihalocyclobutanes; ▲, dihalocyclopentanes; ■, dihalocyclohexanes; ○, 1,1-dichlorocycloheptane.

isomers. However, the data are not extensive enough to check this point. Attempts to prepare chlorofluoro- and bromofluorocyclobutane isomers have so far failed. The regular function may, however, be applicable to the cycloheptane series of chloro/bromo-1,1-isomers. Thus, the predicted relative retention volume for 1,1-dichlorocycloheptane is 1.5, which compares reasonably with the observed value of 1.2 (see Fig. 3).

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