Journal of Chromatography, 104 (1975) 91–97

CHROM. 7788

GEL PERMEATION CHROMATOGRAPHIC SEPARATION OF STEREOISOMERS OF CYCLO- AND POLYCYCLOALKANES

K. PECKA, S. HÁLA, J. CHLEBEK, M. KURAŠ and B. KREMANOVÁ

Department of Petroleum Technology and Petrochemistry, Institute of Chemical Technology, 166 28 Prague (Czechoslovakia)

(Received July 25th, 1974)

SUMMARY

Methyl derivatives of cyclohexane and several bicyclic and tricyclic saturated hydrocarbons of different stereoisomeric forms were used as model compounds for studying the behaviour of stereoisomers in gel permeation chromatography on a polystyrene gel with a low exclusion limit using tetrahydrofuran as solvent. Differences in elution volumes permit the separation of a number of stereoisomers, the purity of which is greater than 90%. In all of the cases studied, a stereoisomer showing a higher thermodynamic stability and a lower retention index in gas chromatography is eluted from a gel column before a stereoisomer with a higher heat content. In gel permeation chromatography, hydrocarbons with a higher number of stereoisomers were found to have a nearly linear dependence of the elution volume on the relative enthalpy content of stereoisomers calculated by conformational analysis.

INTRODUCTION

The separation efficiency of gel permeation chromatography (GPC) for mixtures of hydrocarbons with small molecules has been demonstrated both on model hydrocarbons of different structures[1–8] and on petroleum fractions[9–12]. In a previous study[13] on the GPC elution behaviour of saturated polycyclic hydrocarbons, we proved that even with this very complicated structural class of hydrocarbons, GPC has an outstanding separation effect; on polystyrene gel with tetrahydrofuran as solvent, model homologous polycycloalkanes, as well as unsubstituted polycycloalkanes with the same carbon number and different numbers of rings in the molecule, were separated. The efficiency of GPC was found to be greatest with several groups of polycycloalkanes of the same molecular weight in which a separation of individual constitutional isomers was attained.

It is characteristic of the high-boiling fractions of polycycloalkanes that in addition to constitutional isomers they also contain a large number of stereoisomeric hydrocarbons differing only in the steric configuration of the rings and in an axial or equatorial orientation of the substituents. Methods for distinguishing these slight

structural differences of individual isomeric hydrocarbons are of great importance in the analysis of these fractions. With regard to the gel column separation effect, ascertained by separating constitutional isomers of polycyclic hydrocarbons, this work was aimed at establishing the efficiency of GPC for separating the stereoisomers of some selected cyclic and polycyclic hydrocarbons whose structures are typical of petroleum naphthenes.

EXPERIMENTAL

Apparatus and procedure

The elution volumes of model hydrocarbons were measured on a system of five 1200 mm × 8 mm I.D. stainless-steel columns arranged in series and packed with the styrene–divinylbenzene copolymer S-GEL-832 (Institute of Macromolecular Chemistry, Czechoslovak Academy of Sciences, Prague, Czechoslovakia). The dry gel particle size was 32–48 μm and the exclusion limit of molecular weight 1000. The samples were injected into the column as 2–10% solutions in tetrahydrofuran and eluted at laboratory temperature with tetrahydrofuran, the flow-rate of which was 16–17 ml/h. A differential refractometer whose cells attained a temperature of 30° was used as a detector. The column system efficiency, measured with cyclohexane, was HETP = 0.25 mm.

Before measuring the elution volumes in GPC, each hydrocarbon was subjected to a determination of the content of individual stereoisomers by means of gas–liquid chromatography (GLC) on a CHROM-3 apparatus (Laboratorní Přístroje, Prague, Czechoslovakia) using 50 m × 0.2 mm I.D. stainless-steel capillary columns coated with squalane or OV-225 as stationary phase. The separation of the stereoisomers on the GPC columns was also checked by the GLC analysis of the collected effluent fractions.

Materials

1,2-Dimethylcyclohexane, 1,3,5-trimethylcyclohexane and 1,2,4,5-tetramethylcyclohexane were prepared from the corresponding methylbenzenes by hydrogenation under pressure over Raney nickel in a rotary steel autoclave. Decahydronaphthalene was a commercial-grade product (Lachema, Brno, Czechoslovakia) purified by rectification. Trimethylenenorbornane (tetrahydrodicyclopentadiene) was prepared by hydrogenation under pressure of dicyclopentadiene (Koch-Light, Colnbrook, Great Britain) over Raney nickel; mild isomerization of the product enabled the *exo*-isomer content to be increased to *ca.* 40%. Perhydroacenaphthene, perhydrofluorene, perhydroanthracene and perhydrophenanthrene were prepared by means of repeated hydrogenation under pressure of the corresponding tricyclic aromatics over Raney nickel at 180°. All of the hydrocarbons prepared by hydrogenation were purified by shaking with sulphuric acid and, after washing and drying, they were distilled and filtered through a column packed with activated silica gel; the purity of the hydrocarbons obtained was 98–99%. All of the hydrocarbons were checked by gas chromatography and mass spectrometry (LKB-9000 combined gas chromatograph–mass spectrometer, LKB, Stockholm, Sweden).

RESULTS AND DISCUSSION

The results of the elution volume measurements carried out on the GPC column are summarized in Table I. Comparison of the elution volumes of hydrocarbons of various structures indicates that in addition to the molecular weight, structural factors such as the number of methyl groups on the ring and the number of rings in a molecule also influence the elution behaviour. Methyl groups on a cyclohexane ring increase the effective dimensions of a molecule much more than the same number of carbon atoms bonded in a further ring. Thus, 1,4-dimethylcyclohexane is eluted from the gel column prior to decahydronaphthalene (two carbon atoms more) and its elution volume is approximately the same as that of tricyclic perhydroanthracene, which has six more carbon atoms in the molecule. Three C_{10} hydrocarbons eluted in the order tetramethylcyclohexane, decahydronaphthalene, trimethylenenorbornane, *i.e.*, in the order monocyclic, dicyclic, tricyclic hydrocarbon. Both of the above structural factors have an analogous effect on the elution sequence of the hydrocarbons measured, which was observed previously in the GPC of polycycloalkanes with an adamantane structure[13].

As shown in Table I, the stereoisomers of all of the nine hydrocarbons measured are separated by GPC. Elution volumes are given only for stereoisomers present in the original hydrocarbon sample in significant concentrations (the total number of stereoisomers is indicated in parentheses for each hydrocarbon). Configurations of stereoisomers were determined on the basis of published retention indices[15], of the GLC retention order[16–18] and of the relative content of stereoisomers in the original and equilibrium mixtures[18,19].

From the data given in Table I, it is evident that the GPC elution of the stereoisomers is dependent on their configurations. In the case of hydrocarbons with two stereoisomeric forms, the stereoisomer displaying the higher thermodynamic stability is eluted first, followed by the stereoisomer with the higher heat content. This fact is in accordance with the concept of GPC separations based on molecular volumes, as the stereoisomer eluted first has a larger molecular volume and thus lower intramolecular steric interactions, which, of course, is reflected in a lower enthalpy. Within the series of methyl derivatives of cyclohexane studied, the stereoisomers with all methyl groups equatorial, such as *trans*-1,4-dimethylcyclohexane and *cis,cis*-1,3,5-trimethylcyclohexane, have a lower enthalpy and are also found to have lower GPC elution volumes. Similarly, the *trans*- and *exo*-isomers of decahydronaphthalene and trimethylenenorbornane, respectively, whose configuration of rings with minimum non-bonding interactions is more advantageous from the standpoint of energy, are eluted first. This relationship between GPC elution volumes and enthalpy is, in fact, another illustration of the well-known rules[20] (Auwers rule; conformational rule[21]) concerning the relationship between the heat content of cycloalkane stereoisomers and their densities, refractive indices and other properties directly connected with the molecular volume.

Hydrocarbons consisting only of six-membered unstrained rings permit the quantitative observation of the relationships between the GPC volumes and enthalpy. Differences in the enthalpies of stereoisomers of these hydrocarbons were calculated on the basis of conformational analysis[19,22] and correlated with the most stable stereoisomer of the particular hydrocarbon. In calculations, the value of 9.0 kcal/

TABLE I

GPC ELUTION VOLUMES AND DIFFERENCES IN ENTHALPIES OF STEREOISOMERS

Compound (No. of stereoisomers in parentheses)	*Original mixture composition (%)*	*GPC elution volume (ml)*	*Purity of the isomer separated (%)*	*GLC retention index*	*Calculated* difference in enthalpy, $-\Delta H$ (kcal/mole)*
1,4-Dimethylcyclohexane (2)					
trans	41.1	197.1	99.0	789**	0.0
cis	58.9	198.9	—	810**	1.8
1,3,5-Trimethylcyclohexane (2)					
cis,cis	65.3	188.5	96.4	859***	0.0
trans,cis	32.7	192.9	66.0	875***	1.8
1,2,4,5-Tetramethylcyclohexane (5)					
trans,cis,cis	38.5	189.0	80.7	969***	1.8§
cis,trans,cis	4.8	191.1	—	996***	3.6§
cis,cis,cis	49.3	194.0	92.7	1015***	5.5§
Decahydronaphthalene (2)					
trans	54.2	203.1	98.9	1089§§	0.0
cis	45.8	207.7	95.5	1132§§	2.7
Trimethylenenorbornane (2)					
exo	39.6	208.8	95.5	1071***	Stable
endo	60.4	213.2	94.9	1100***	Unstable
Perhydroacenaphthene (6)					
trans,trans,trans	16.9	200.7	95.5	1274§§	Stable
cis,cis,trans	24.9	204.9	70.3	1317§§	Stable
cis,trans,cis				1323§§	Stable
cis,cis,cis	53.1	208.3	93.6	1352§§	Unstable
Perhydrofluorene (6)					
cis,anti,trans	43.7	197.1	63.1	1388§§§	Most stable
cis,anti,cis	17.3	198.6	56.5	1425§§§	Stable
cis,syn,cis	16.2	202.3	91.0	1452§§§	Unstable
Perhydroanthracene (5)					
trans,syn,trans	16.3	192.4	99.0	1481§§	0.0
cis,syn,trans	45.7	195.8	88.3	1513§§	2.7
cis,syn,cis	32.6	199.9	86.8	1549§§	6.6
Perhydrophenanthrene (6)					
trans,anti,trans	51.5	194.5	99.0	1493§§	0.9†
cis,syn,trans	31.7	197.9	65.9	1537§§	3.6†

* For hydrocarbons with five-membered rings only the relative stability is given.
** Retention indices on squalane at 70°, see ref. 14.
*** On squalane at 110°.
§ Relative to the *trans,cis,trans*-isomer.
§§ On SE-30 at 150°, see ref. 15.
§§§ On squalane at 140°.
† Relative to *trans,syn,trans*-perhydroanthracene.

mole (ref. 23) was used for the potential energy of each *gauche*-butane conformation in a molecule. For the 1,3-diaxial interaction of methyl groups in *cis,cis,cis*-1,2,4,5-tetramethylcyclohexane, the value of 3.7 kcal/mole found experimentally by Allinger and Miller[24] was used, which, including the two *gauche*-butane interactions, gives a total difference of 5.5 kcal/mole compared with the most stable *trans,cis,trans*-

configuration. The interaction of the two methylene groups, diaxially bonded to the central ring in *cis,syn,cis*-perhydroanthracene, were evaluated according to Johnson's estimation[25] by a contribution of 4.8 kcal/mole. The calculated values of $-\Delta H$ are given in Table I. For tricycloalkanes with five-membered strained rings, only the relative stabilities of stereoisomers are given, as determined on the basis of the equilibrium mixture compositions and qualitative strain comparisons for individual configurations[19].

The calculations show that with increasing enthalpy of stereoisomers, the GPC volumes increase on average by 1.4 ml per 1 kcal. A plot of the elution volumes of $C_{14}H_{24}$ perhydro-aromatic stereoisomers and of 1,2,4,5-tetramethylcyclohexane stereoisomers against enthalpy differences (Fig. 1) suggests that the dependence is almost linear. The same correlations for constitutional isomers of polycycloalkanes of various structures were found in our previous work[13]. These results show that in the case of cyclic and polycyclic non-polar molecules, the conformational parameters influencing the total enthalpy of the compound bear a simple relationship to the GPC elution volumes, as described by Schulz[8] for a class of branched alkanes where the elution volumes of isomers are a logarithmic function of an average number of *gauche*-conformations (Zg) in the molecule.

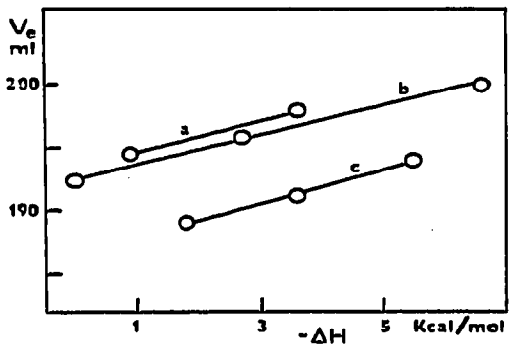

Fig. 1. Correlation of GPC elution volume (V_e) with enthalpy differences ($-\Delta H$) for stereoisomers of perhydrophenanthrene (a), perhydroanthracene (b) and 1,2,4,5-tetramethylcyclohexane (c).

In most of the cases under investigation, differences between the elution volumes permit individual stereoisomers to be isolated from the original mixture. Even if the purity of the isolated stereoisomers is dependent on their original content and on differences in the elution volumes, the purity of more than half of the individual stereoisomers obtained from the gel columns was 91–99%. In most other cases, the stereoisomers were at least considerably concentrated.

The GPC elution behaviour of stereoisomers is illustrated in Fig. 2 with a chromatogram of perhydroanthracene on which the separated fractions are also indicated. The purity of the isolated stereoisomers (87–99%) was determined by means of the direct GLC analysis of tetrahydrofuran fractions collected at the RI-detector outlet. For comparison, Fig. 2 shows a GLC check of the initial hydrocarbon. The order of elution of stereoisomers from the gel columns is the same as that in GLC on a non-polar stationary phase. The gel chromatogram indicates that for these com-

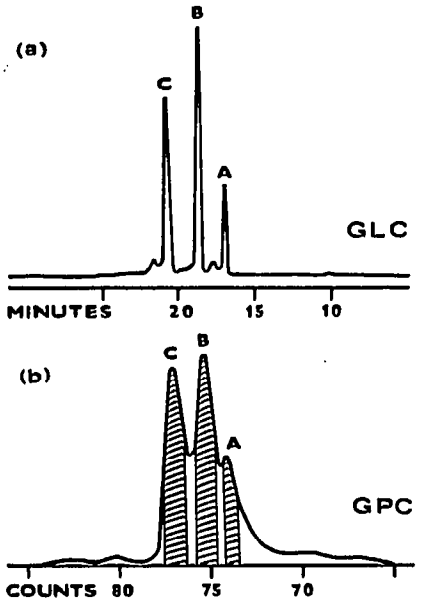

Fig. 2. (a) Gas chromatogram of perhydroanthracene on a 50-m long capillary column coated with OV-225; column temperature 180°. (b) Gel chromatogram of perhydroanthracene. Operating conditions are described in the text. A = *trans,syn,trans*-isomer; B = *cis,syn,trans*-isomer; C = *cis,syn*, *cis*-isomer. The shaded regions show the fractions collected. For purity of stereoisomers isolated, see Table I.

pounds GPC shows a separation efficiency similar to that of preparative gas chromatography.

The influence of the size of the hydrocarbon sample injected into the gel column on the separation of the *cis*- and *trans*-isomers of decahydronaphthalene is shown in Fig. 3. The separation of both isomers is still satisfactory on injecting

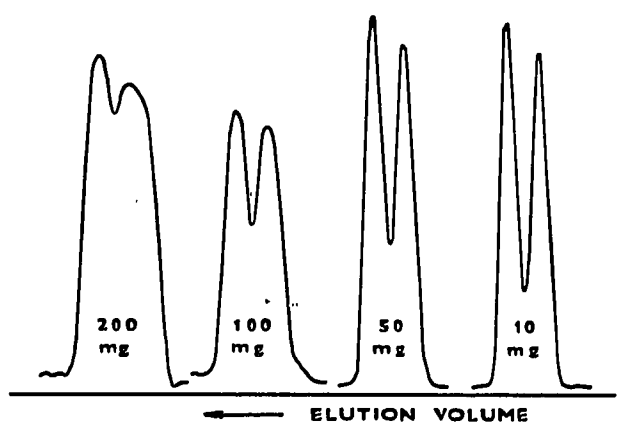

Fig. 3. Effect of sample weight (10–200 mg) on the GPC peak resolution of *cis,trans*-isomers of decahydronaphthalene. Operating conditions are described in the text.

100 mg of decahydronaphthalene into the column. The peak resolution (R) on the gel column calculated from the relationship used in GLC[26] is within the range 0.90–0.91 for samples of 5–10 mg and 0.70–0.77 for samples of 50–100 mg of decahydronaphthalene. When injecting a 200-mg sample, the peak resolution decreases to $R = 0.43$. In the case of hydrocarbons with boiling points lower than 200°, the recovery of a substance from a tetrahydrofuran GPC fraction shows losses of several tens per cent; nevertheless, for high-boiling hydrocarbons, the recovery of which is nearly quantitative, GPC is a mild (low-temperature) separation method which in many respects is more advantageous than preparative gas chromatography for analyses of mineral oils and other heavy hydrocarbon fractions.

REFERENCES

1 W. B. Smith and A. Kollmansberger, *J. Phys. Chem.*, 69 (1965) 4157.
2 J. G. Hendrickson and J. C. Moore, *J. Polym. Sci., Part A-1*, 4 (1966) 167.
3 J. Cazes and D. R. Gaskill, *Separ. Sci.*, 2 (1967) 421.
4 J. G. Hendrickson, *J. Chromatogr.*, 32 (1968) 543.
5 T. Edstrom and B. A. Petro, *J. Polym. Sci., Part C*, 21 (1968) 171.
6 R. E. Thompson, E. G. Sweeney and D. C. Ford, *J. Polym. Sci., Part A-1*, 8 (1970) 1165.
7 H. H. Oelert and J. H. Weber, *Erdöl Kohle*, 23 (1970) 484.
8 W. W. Schulz, *J. Chromatogr.*, 55 (1971) 73.
9 H. J. Coleman, D. E. Hirsch and J. E. Dooley, *Anal. Chem.*, 41 (1969) 800.
10 H. H. Oelert, *Erdöl Kohle*, 22 (1969) 19 and 536.
11 H. H. Oelert, *J. Chromatogr.*, 53 (1970) 241.
12 J. F. McKay and D. R. Latham, *Anal. Chem.*, 45 (1973) 1050.
13 S. Hála, K. Pecka and B. Kremanová, *Collect. Czech. Chem. Commun.*, 39 (1974) 3649.
14 G. Schomburg, *J. Chromatogr.*, 23 (1966) 18.
15 J. Vaněk, B. Podroužková and S. Landa, *Collect. Czech. Chem. Commun.*, 52 (1970) 77.
16 R. L. Clarke, *J. Amer. Chem. Soc.*, 83 (1961) 965.
17 V. A. Zacharenko, I. O. Delone, S. S. Berman and A. A. Petrov, *Neftekhimiya*, 9 (1969) 656.
18 D. Kogan and Y. Mazur, *Tetrahedron Lett.*, (1971) 2401.
19 A. A. Petrov, *Chimiya Naftenov*, Izdatelstvo Nauka, Moscow, 1971.
20 H. van Bekkum, A. van Veen, P. E. Verkade and B. M. Wepster, *Rec. Trav. Chim. Pays-Bas*, 80 (1961) 1310.
21 N. L. Allinger, *J. Amer. Chem. Soc.*, 79 (1957) 3443.
22 A. Schneider, R. W. Warren and E. J. Janoski, *J. Org. Chem.*, 31 (1966) 1617.
23 C. W. Beckett, K. S. Pitzer and R. Spitzer, *J. Amer. Chem. Soc.*, 69 (1947) 2488.
24 N. L. Allinger and M. A. Miller, *J. Amer. Chem. Soc.*, 83 (1961) 2145.
25 W. S. Johnson, *J. Amer. Chem. Soc.*, 75 (1953) 1498.
26 Anonymous, *J. Gas Chromatogr.*, 6 (1968) 1.