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CYCLODEXTRINS AND METHYLATED CYCLODEXTRINS AS STATIONARY PHASES IN GAS–SOLID CHROMATOGRAPHY

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SUMMARY

Cyclodextrins and their methylated derivatives were used as stationary phases in gas–solid chromatography and the effect of inclusion on the retention of compounds with various structures and geometries (alkanes, aromatic hydrocarbons, alcohols) was followed. It has been found that inclusion predominates in the gas–solid interaction of compounds with suitable geometric dimensions, while the retention of polar substances is primarily determined by the interactions with the cyclodextrin hydroxyl groups. On decreasing the cyclodextrin polarity by means of methylation, stereoselectivity was evident even in the separation of alcohols. On the other hand, the presence of methyl groups causes steric hindrance to penetration of the guest molecule into the cyclodextrin cavity. The selectivity of the inclusion process is especially important for separations of positional isomers.

INTRODUCTION

Inclusion is a spatial interaction permitted by certain molecular structures. In chromatography separations based on inclusion in the stationary phase are selective with respect to molecular size and shape.

An interesting group of substances are cyclodextrins, which are capable of forming inclusion compounds with various substances[1,2]. This property has been exploited in liquid phase fractionations, but only recently has attention been paid to the formation of inclusion compounds under chromatographic conditions and to their analytical use[3–8].

In our previous work[6] the inclusion properties of α- and β-cyclodextrins (CDs) were studied chromatographically and conclusions were drawn concerning the nature of the interactions. It was confirmed that cyclodextrins are selective stationary phases even in gas–solid chromatography (GSC), *i.e.*, inclusion compounds are formed even when the sorbates are in the gaseous phase. However, with polar substances additional effects are operative, especially the polarity of the cyclodextrin OH groups. Therefore, methylated derivatives of α- and β-CD have now been prepared and their chromatographic properties were compared with those of the parent compounds.

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EXPERIMENTAL

α- and β-CD were obtained from Chinoin (Budapest, Hungary). The preparation of methylated cyclodextrins was based on the work of Casu *et al.*[9]. 4 g of cyclodextrin was dissolved in 20 ml of dimethylsulphoxide, 60 ml of methyl iodide and 40 g of solid barium oxide were added and the reaction mixture was allowed to stand for 7 days at 30–40°C. The pulp product was then extracted with boiling chloroform, the solvent was evaporated and the substance was dried over P_2O_5.

The IR spectrum and the content of active hydrogen (0.42% H* for Me-β-CD) indicated that the product was partially (about two thirds) methylated. On the basis of published data[10], it is assumed that the hydroxyl groups in positions 2 and 6 are methylated, as those in position 3 are less reactive.

The cyclodextrins and their methylated derivatives were deposited (10%, w/w) on Chromosorb W (60–80 mesh) from a dimethylformamide solution, covering the support completely. The specific surface areas of the resulting stationary phases, measured by the thermal desorption method, were 1.4–2.0 m^2/g; hence the effect of the surface area need not be considered in the treatment of the retention data. *n*-Alkanes, branched alkanes, aromatic hydrocarbons and alcohols were used as sorbates.

The measurements were performed on a Chrom 41 instrument (Laboratorní Přístroje, Prague, Czechoslovakia) equipped with a flame ionization detector. Glass columns (120 cm × 2 mm I.D.) and nitrogen as the carrier gas were employed. Saturated sample vapours were injected in small amounts with Hamilton microsyringes.

RESULTS AND DISCUSSION

The retention data were obtained for compounds with various structures and geometries on columns containing α- and β-cyclodextrin (α-CD, β-CD) and their methylated derivatives at 90°C and are summarized as relative retentions in Tables I–III.

Interaction of CD and Me-CD with alkanes

The large differences found for α- and β-CD (see Table I) are in agreement with the differences in the host cavity sizes, and in the guest dimensions. While on β-CD no great difference was found in the retention of linear and branched alkanes, a side group on the main chain is a great obstacle to inclusion into the α-CD cavity; *e.g.*, the retention of heptane is substantially higher than that of isomeric nonanes, even when the latter have higher boiling points; 2,2,4-trimethylhexane is less strongly retained than pentane. As these are non-polar substances, the much greater retention of *n*-alkanes compared with that of branched alkanes can only be explained by the inclusion process.

It follows from the data given in Table I that methylation of the hydroxyl groups causes a decrease in the selectivity. The differences in the retention of *n*-alkanes and branched alkanes are less pronounced. Heptane is eluted at a time similar to that of isomeric nonanes. The retention of *n*-alkanes is also substantially decreased and thus even the retention of higher *n*-alkanes (decane) can be followed within a

TABLE I

RELATIVE RETENTIONS ($r_{1,2}$) OF ALKANES ON CD AND Me-CD

Alkane	*b.p. (°C)*	$r_{1,2}$			
		α-CD	*β-CD*	*Me-α-CD*	*Me-β-CD*
Butane	−0.5	0.144	–	–	–
Pentane	36.0	1.00	1.00	1.00	1.00
Hexane	69.0	6.23	2.58	2.33	1.83
Heptane	98.4	23.9	6.83	5.75	2.90
Octane	125.7	–	19.6	13.1	5.26
Nonane	150.8	–	54.8	27.9	10.2
Decane	174.1	–	142	57.5	18.0
3,3-Dimethylpentane	86.1	0.056	5.75	1.00	1.34
3-Ethylpentane	93.5	0.058	4.33	1.67	1.10
3,3-Dimethylpentane	112	0.127	9.08	2.75	2.05
3,4-Dimethylhexane	117.7	9.75	12.5	3.33	1.90
2-Methylheptane	117.7	8.01	16.7	4.75	2.11
3-Methylheptane	119	17.0	–	–	2.09
2,2,4-Trimethylhexane	126.5	0.261	29.5	3.00	2.18
2,4-Dimethylheptane	133.5	1.96	20.8	6.67	2.20

measurable time, while on α-CD even octane was very strongly retained. As only dispersion forces are operative, these changes can only be explained by steric effects. The voluminous methyl groups that replaced the hydrogen atoms originally present decrease the accessibility of the CD cavity. Therefore, only α-CD has practical importance for selective separations of this group of compounds.

Interaction of CD and Me-CD with alcohols

In contrast to alkanes, pronounced stereoselectivity has not been found for the

TABLE II

RELATIVE RETENTIONS OF ALCOHOLS ON CD AND Me-CD

Alcohol	*b.p. (°C)*	$r_{1,2}$			
		α-CD	*β-CD*	*Me-α-CD*	*Me-β-CD*
Methanol	65.0	2.50	2.25	1.16	0.59
Ethanol	78.5	1.00	1.00	1.00	1.00
n-Propanol	97.4	2.57	2.41	2.58	3.18
n-Butanol	117.3	13.45	6.61	6.21	8.52
n-Pentanol	137.3	–	11.3	–	18.3
tert.-Butanol	82.2	2.91	1.74	0.108	0.34
Isopropanol	82.4	1.28	1.22	0.488	1.13
sec.-Butanol	99.5	6.11	2.78	1.00	–
tert.-Pentanol	102	14.4	2.79	0.17	0.61
Isobutanol	108	7.48	4.94	1.31	3.18
3-Methyl-2-butanol	112.9	18.5	4.60	0.377	1.88
3-Pentanol	116.1	28.6	–	0.955	3.70
2-Pentanol	118.9	23.9	–	2.12	4.05
Isopentanol	128.5	–	10.2	2.96	6.92

TABLE III

RELATIVE RETENTIONS OF AROMATIC HYDROCARBONS

Hydrocarbon	*b.p. (°C)*	$r_{1,2}$			
		α-CD	*β-CD*	*Me-α-CD*	*Me-β-CD*
Benzene	80.1	1.00	1.00	1.00	1.00
Toluene	110.6	2.25	0.963	1.82	1.07
Ethylbenzene	136.2	8.64	1.50	2.01	1.80
n-Propylbenzene	159.2	18.5	3.11	5.15	2.79
n-Butylbenzene	183	–	6.11	9.92	4.72
p-Xylene	138.4	13.5	1.16	3.17	1.71
m-Xylene	139.1	1.52	0.935	2.55	0.71
o-Xylene	144.4	0.882	1.47	1.86	0.71
Isopropylbenzene	152.4	1.03	2.54	1.64	0.76
1,3,5-Trimethylbenzene	164.7	0.120	0.778	3.02	0.22
1,2,4-Trimethylbenzene	169.4	1.37	2.63	3.25	1.26
1,2,3-Trimethylbenzene	176.1	0.211	1.60	2.73	0.69
tert.-Butylbenzene	169	0.122	5.56	1.74	0.82
sec.-Butylbenzene	173	0.942	4.00	2.70	0.76
1-Methyl-4-ethylbenzene	162	–	2.56	–	–
1-Methyl-3-ethylbenzene	161.3	–	1.72	–	–
1-Methyl-2-ethylbenzene	165.2	–	1.58	–	–

interaction of alcohols with α- and β-CD, even when the retention on α-CD is higher than that on β-CD (see Table II). In addition to the effect of cavity size, hydrogen bonding between the alcohols and the cyclodextrin OH groups plays a major rôle in the interaction.

Methylation of the hydroxyl groups weakens the polar interaction between alcohols and cyclodextrins and the steric selectivity is again enhanced (Table II). Branched alcohols with more voluminous molecules are always retained less strongly than the corresponding linear alcohols; tertiary alcohols have the weakest retention. This effect is especially marked with Me-α-CD, but it is strong even with Me-β-CD. It follows from Table II that methylated α-CD is suitable for separations of alcohols with similar boiling points, *e.g.*, *tert.*-butanol, isopropanol and ethanol, or *tert.*-pentanol, *sec.*-butanol and propanol.

Interaction of CD and Me-CD with aromatic hydrocarbons

The retention data of aromatic hydrocarbons on α- and β-CD (see Table III) again indicate an effect of the cavity size. Simple spatial assumptions permit prediction of the extent of interaction between CD and a guest. The effect of inclusion on the retention is most marked with positional isomers, *e.g.*, *o*-, *m*-, *p*-xylenes and trimethylbenzenes. Isomers of xylene exhibit not only different retentions, but even different retention orders on the two cyclodextrins. Greater differences are again found on α-CD, where the elution order is *o*-, *m*- and *p*-isomer, while the *o*-isomer is most strongly retained on β-CD. With trimethylbenzenes, the elution order is 1,3,5-trimethylbenzene, 1,2,3-trimethylbenzene and 1,2,4-trimethylbenzene, on both α- and β-CD. The most voluminous symmetrical isomer is least strongly retained by the two phases and its elution time is less than that of benzene. A similar order was

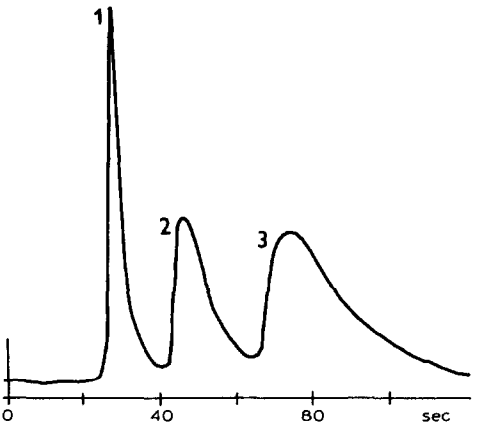

Fig. 1. Separation of trimethylbenzenes on β-CD. Carrier gas flow-rate: 25 ml/min. Column temperature: 90°C. Peaks: 1 = 1,3,5-trimethylbenzene; 2 = 1,2,3-trimethylbenzene; 3 = 1,2,4-trimethylbenzene.

also found for methylethylbenzenes. It can be concluded from these measurements that the inclusion of the benzene ring into the CD cavity is decisive for the retention of aromatic hydrocarbon isomers. An increase in the molecular volume and voluminous substituents prevent inclusion of the benzene ring.

Methylation of the two cyclodextrins leads again to changes in the retention of the test substances. With β-CD the selectivity of the separation of positional isomers increases and *p*-xylene is the most strongly retained of the xylene isomers. The situation with α-CD is similar. 1,3,5-Trimethylbenzene has a substantially shorter retention time than benzene. On the other hand, the selectivity decreases on methylated α-CD, due to steric hindrance; the differences in the retention of trimethylbenzene isomers are negligible. All these results indicate that the spatial arrangement is the predominating factor, and the contribution from specific interactions of the CD hydroxyl groups with the π-electrons of aromatic compounds is of secondary importance.

Chromatographic use of the inclusion selectivity

The results permitted an evaluation of the use of various types of interactions

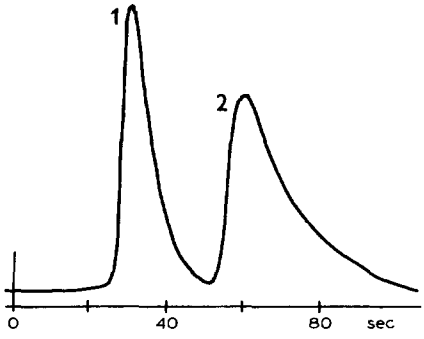

Fig. 2. Separation of 3-methyl-*cis*-2-pentene (1) and 3-methyl-*trans*-2-pentene (2) on α-CD. Carrier gas flow-rate: 60 ml/min.

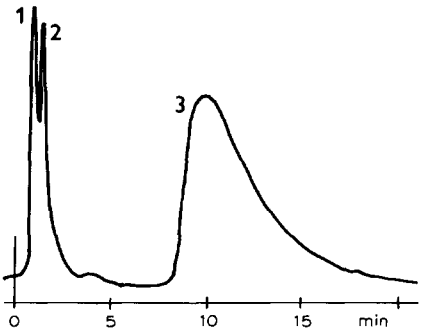

Fig. 3. Separation of xylenes on α-CD. Carrier gas flow-rate: 60 ml/min. Column temperature: 90°C. Peaks: 1 = *o*-xylene; 2 = *m*-xylene; 3 = *p*-xylene.

in which the steroselectivity of cyclodextrins is important, when these substances are used as stationary phases. It has been confirmed that the cyclodextrin–guest inclusion interaction occurs even in the gas–solid system and can be utilized for some specific analytical applications. Examples of chromatograms are given in Figs. 1–3. Analytically, it is necessary to evaluate critically the possibilities provided by GSC, *i.e.*, the necessity of working with very small amounts of test substances in order to operate in the linear part of the separation isotherm, and some problems connected with the kinetics of the inclusion process.

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