Journal of Chromatography, 241 (1982) 3–8
Elsevier Scientific Publishing Company, Amsterdam — Printed in The Netherlands

CHROM. 14,356

STUDY OF THE PROPERTIES OF CYCLODEXTRINS AS STATIONARY PHASES IN GAS CHROMATOGRAPHY

E. SMOLKOVÁ*, H. KRÁLOVÁ, S. KRÝSL and L. FELTL
Department of Analytical Chemistry, Charles University, Prague (Czechoslovakia)

SUMMARY

The formation and properties of inclusion compounds of α- and β-cyclodextrin were studied in a gas–solid chromatographic system. Substances of various structural types and geometries (hydrocarbons, hydrocarbon halogeno derivatives, alcohols, aromatic compounds) were used as sorbates. The results of chromatographic measurements are correlated with polarizability and polarity data for the sorbate molecules, and interpreted in terms of the possible interactions involved.

INTRODUCTION

Much attention has recently been paid to the specific properties of cyclodextrins, both from the point of view of theory and from that of practical application[1–6]. It has been found that chromatographic methods can also yield interesting information on their properties[7].

Cyclodextrins (CDs) are cyclic oligosaccharides which can be obtained on a laboratory scale by enzymatic degradation of starch. The most abundant products are α-, β- and γ-cyclodextrins, formed by six, seven and eight glucose units, respectively. The cyclodextrin structure has a special arrangement of the functional groups, which has a marked effect on the differences in the properties of α-, β- and γ-cyclodextrin. The secondary hydroxyl groups are localized on one side of the ring, whereas the primary ones are on the opposite side. The inside of the ring contains only circular configurations of hydrogen atoms and glycoside oxygen atoms and is therefore apolar compared with water. The holes in the CD molecules are somewhat conical and are wider at the side of the secondary hydroxyl groups than on the side of the primary groups. The primary hydroxyl groups can rotate and thus partially block the cavities, while the secondary hydroxyl groups cannot rotate[8]. The glucose units assume the chair conformation. Intramolecular hydrogen bonding occurs between the secondary hydroxyl groups of the glucose units and makes the cyclodextrin ring more rigid. α-, β- and γ-cyclodextrins form cavities with a size of 5–8 Å, enabling inclusion of molecules with appropriate dimensions. In contrast to classical clathrates, the inclusion compounds formed are capable of existence even in aqueous solutions.

In view of the interesting properties of these substances, we studied the behaviour of α- and β-cyclodextrins as stationary phases in gas–solid chromatography

0021-9673/82/0000–0000/$02.75

TABLE I

RETENTION DATA OF VARIOUS SORBATES ON α- AND β-CYCLODEXTRIN

D = Dielectric constant; α = polarizability.

Sorbate	*B.p.* (°C)	*D*	α (Å^3)	α-*Cyclodextrin*				β-*Cyclodextrin*					
				60°C		*80°C*		*50°C*		*60°C*		*80°C*	
				t'_r (*sec*)	*log k'*	t'_r (*sec*)	*log k'*	t'_R (*sec*)	*log k'*	t'_R (*sec*)	*log k'*	t'_R (*sec*)	*log k'*
n-Pentane	36.07	1.844	9.95	922	1.603	496	1.354	25	0	18	−0.125	5	−0.662
n-Hexane	68.7	1.890	11.78	–	–	*	–	80	0.505	40	0.222	25	0.115
n-Heptane	98.42	1.926	13.61	–	–	*	–	236	0.975	192	0.903	75	0.513
Isopentane	28.0	1.843	10.1	–	–	–	–	–	–	–	–	–	–
Cyclohexane	80.7	2.055	10.9	–	–	1588	1.854	301	1.081	244	0.785	81	0.573
Benzene	80.1	2.28	10.32	–	–	1628	1.869	557	1.348	352	1.166	133	0.762
Toluene	110.8	2.34	12.15	–	–	1379	1.797	712	1.455	444	1.267	191	0.919
Chloroform	61.2	4.79	11.19	432	1.274	322	1.342	375	1.176	296	1.091	112	0.687
Tetrachloromethane	76.8	2.205	10.5	324	1.587	254	1.062	304	1.085	227	0.976	105	0.659
1,2-Dichloroethane	83.7	10.5	11.31	–	–	1429	1.813	624	1.397	389	1.210	154	0.826
1,1,2,2-Tetrachloroethane	146.2	8.20	12.25	–	–	850	1.587	–	–	572	1.377	228	0.996
Trichloroethylene	87.0	3.27	10.2	–	–	1730	1.342	639	1.408	268	1.048	111	0.684
Tetrachloroethylene	121.2	2.29	12.13	–	–	550	1.398	561	1.351	766	1.504	217	0.975
Chlorobenzene	132.1	5.59	12.25	–	–	3328	2.180	2840	2.055	1568	1.815	501	1.338
Bromobenzene	156.2	5.53	13.58	–	–	*	–	–	–	2502	2.018	1008	1.642
Methanol	64.7	32.35	3.23	888	1.149	437	1.298	1929	1.887	1170	1.608	686	1.475
Ethanol	78.4	25.0	5.06	–	–	790	1.555	1715	1.836	921	1.584	348	1.180
n-Propanol	97.8	20.10	6.89	–	–	2169	1.994	3645	2.164	3286	2.136	1119	1.687
Isopropanol	82.4	18.62	7.05	–	–	1577	1.855	2538	2.007	1556	1.812	487	1.326
Isobutanol	107.7	15.5	8.81	–	–	3882	2.247	-	–	3668	2.184	1652	1.856
Benzyl alcohol	204.7	13.5	13.02	–	–	2688	2.085	–	–	–	–	*	–
Diethyl ether	34.51	4.24	9.02	–	–	723	1.517	2072	1.918	1434	1.776	914	1.599
Diisopropyl ether	67.8	3.95	12.67	–	–	232	1.023	365	1.164	233	0.987	107	0.668

* Not eluted even after 90 min.

(GSC), and compared the results with those of previous work on inclusion compounds[9-13].

EXPERIMENTAL

Stationary phases consisting of 10% (w/w) α-CD or β-CD deposited on Chromosorb W (60–80 mesh) were prepared. The cyclodextrin was deposited from a dimethylformamide solution and the phases were packed into glass columns (120 cm × 3 mm I.D.).

The sorbates were selected so that organic molecules of various structural types and geometries were included (hydrocarbons, hydrocarbon halogeno derivatives, alcohols, ethers and aromatic hydrocarbons). All measurements were carried out on a Hewlett-Packard 5700A gas chromatograph equipped with a flame ionization detector.

The samples were injected with Hamilton microsyringes.

RESULTS AND DISCUSSION

Measurements with a wide range of sorbates were performed at temperatures from 50 to 80°C. The retention data obtained (adjusted retention times, t'_R, and capacity factors, k') are summarized in Table I, together with the physical characteristics with which the data were correlated.

To evaluate the interactions occurring, the dependence of the retention data on the sorbate polarizability was studied, as a measure of the effect of dispersion forces operating inside the cyclodextrin ring. However, the effect of surface forces during inclusion cannot be completely excluded, as the sorbate molecules are in equilibrium not only with respect to the interior of the cyclodextrin ring, but also with respect to its surface. The inclusion process proceeds through the outer surface of the CD into its cavity; therefore, the retention time can also be determined by the time required for deposition on the surface before the interaction in the CD cavity. Hence the retention times can be characterized as the ratio of the effects of dispersion and surface forces.

Inclusion can sometimes be related to the boiling points. However, the guest structure can be considered as the chief criterion, together with the relative sizes of the guest molecule and of the CD cavity; the stability of the inclusion compounds often changes with increasing size of the sorbate molecule.

n-Alkane–CD interaction

The dependence of the logarithm of the adjusted retention times of aliphatic hydrocarbons on their polarizability is linear both for α- and β-CD (Fig. 1). The slope of the straight lines does not change with changing temperature, indicating a constant interaction mechanism.

Only dispersion forces are operative with aliphatic hydrocarbons and thus the large differences in retention on α- and β-CD can only be explained by the inclusion process. In view of the smaller cavity of α-CD, this process is even more marked than with β-CD, as demonstrated by the retention data: the difference in retention for *n*-pentane between α- and β-CD is 490 sec and the interaction of higher hydrocarbons is so strong that they are completely retained in the α-CD cavity.

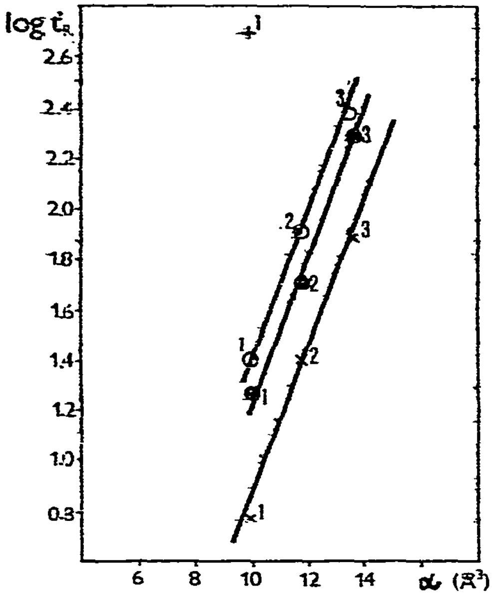


Fig. 1. Dependence of log t'_R on polarizability for *n*-alkanes on β-CD at 50°C (○), 60°C (●) and 80°C (×) and on α-CD at 80°C (+). 1 = *n*-Pentane; 2 = *n*-hexane; 3 = *n*-heptane.

Hydrocarbon halogeno derivative–CD interaction

With halogeno derivatives, the retention times obtained on α-CD are also longer than on β-CD. This indicates that the forces operating inside the cyclodextrin ring predominate during the interaction, since the dispersion forces act over a shorter distance in the α-CD cavity.

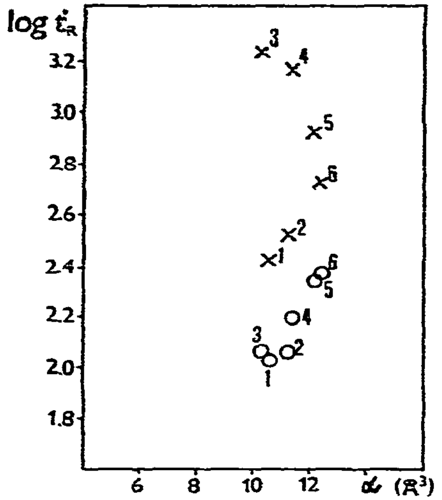
A comparison of the dependences of log t'_R on the polarizability (Fig. 2) shows marked differences, from which it can be assumed that, during inclusion of a halogeno derivative in α-CD, different primary interactions than with β-CD are encountered. The difference in the retention data for trichloroethylene and 1,2-dichloroethane is especially large and is even more marked when it is considered that their boiling points are 40–60°C lower than those for the tetrahalogeno derivatives studied, whose retention is substantially lower.

Cyclic compound–CD interaction

The log t'_R *vs.* polarizability dependence for cyclic compounds (Fig. 3) again indicates a stronger interaction with α-CD. This difference is greatest for cyclohexane, but comparison of the data for benzene and toluene is more interesting, as the retention order changes, demonstrating again the presence of inclusion interactions.

Ether–CD interaction

The effect of the geometry of the sorbate is marked for diethyl ether and diisopropyl ether. As follows from Table I, the retention of the more volatile diethyl ether is more than three-fold greater on α-CD and almost nine-fold greater on β-CD compared with diisopropyl ether. The polarizability values of the two sorbates also



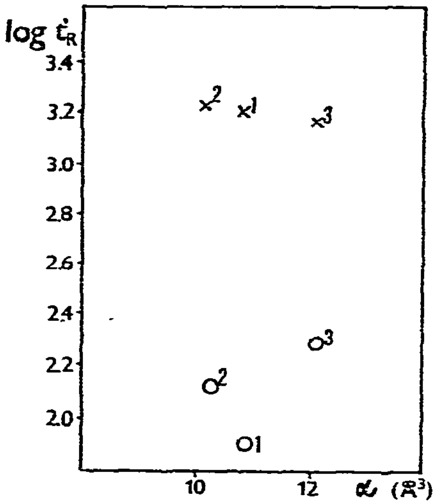


Fig. 2. Dependence of log t'_R on polarizability for the halogeno derivatives on β-CD (O) and α-CD (×) at 80°C. 1 = Tetrachloromethane; 2 = chloroform; 3 = trichlorethylene; 4 = 1,2-dichloroethane; 5 = 1,1,2,2-tetrachloroethane; 6 = tetrachloroethylene.

Fig. 3. Dependence of log t'_R on polarizability for cyclic compounds on β-CD (O) and α-CD (×) at 80°C. 1 = Cyclohexane; 2 = benzene; 3 = toluene.

are not in accord with the retentions measured. This phenomenon can be explained on the basis of the steric arrangement, where, in analogy with urea, the branched ether is less strongly retained.

Alcohol–CD interaction

The dependence of log t'_R *vs.* polarizability for six alcohols interacting with α- and β-CD is given in Fig. 4. In contrast to the previous sorbates, the retention data on

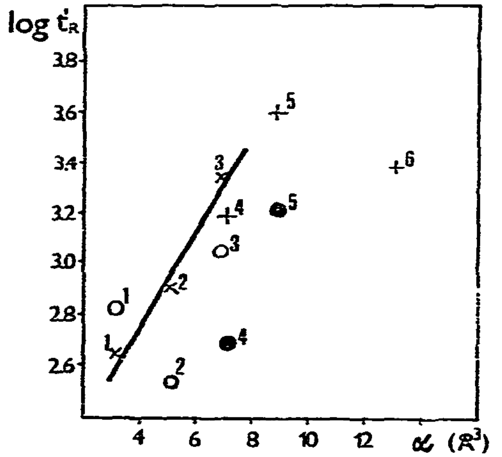


Fig. 4. Dependence of log t'_R on polarizability for unbranched (×, O) and branched (+, ●) aliphatic alcohols on α-CD (×, +) and on β-CD (O, ●) at 80°C. 1 = Methanol; 2 = ethanol; 3 = *n*-propanol; 4 = isopropanol; 5 = isobutanol; 6 = benzyl alcohol.

the two cyclodextrins are not very different. This can be explained by the effect of surface hydroxyl groups, which markedly contribute to the retention of polar substances on the two cyclodextrins. In addition, the inclusion process is also operative, especially with α-CD, where the small cavity leads to the formation of stronger complexes due to closer contact of alcohols with the cavity.

Matsui and Mochida[14] arrived at the same conclusion and demonstrated a greater stability for the α-CD inclusion compound with an unbranched aliphatic alcohol by calculating the association constants for inclusion compounds of α- and β-CD with various alcohols in aqueous solution. The difference found between the association constants again confirms the large effect of the volume of the guest molecule on the stability of the CD–alcohol inclusion compound.

A significant contribution from surface forces to the total alcohol retention is evident from the dependence of the alcohol retention data on permittivity; the retention data of alkanes and cyclic compounds are unaffected by permittivity.

It follows from the results obtained that all the cases involve forces operative inside the cyclodextrin ring, *i.e.*, inclusion compounds are formed even if the cyclodextrin host substance is in contact with the sorbates in the gaseous state.

REFERENCES

1 M. L. Bender and M. Komiyama, *Cyclodextrin Chemistry*, Springer, Berlin, Heidelberg, New York, 1978.
2 W. Saenger, *Angew. Chem.*, 92 (1980) 343.
3 R. L. van Etten, J. F. Sebastian, G. A. Clowes and M. L. Bender, *J. Amer. Chem. Soc.*, 89 (1967) 3242.
4 R. S. Bergeron, M. A. Channing, G. J. Gibeily and D. M. Pillor, *J. Amer. Chem. Soc.*, 99 (1977) 5146.
5 M. Komiyama and M. L. Bender, *J. Chem. Phys.*, 100 (1978) 2259.
6 J. Szejtli and Zs. Budai, *Acta Chim. (Budapest)*, 99 (1979) 433.
7 E. Smolková-Keulemansová and S. Krýsl, *J. Chromatogr.*, 184 (1980) 347.
8 A. Hybl, R. E. Rundle and D. E. Williams, *J. Amer. Chem. Soc.*, 87 (1965) 2779.
9 K. Mařík, *Ph.D. Thesis*, Charles University, Prague, 1972.
10 K. Mařík and E. Smolková, *J. Chromatogr.*, 91 (1974) 303.
11 E. Smolková, L. Feltl and J. Všetečka, *J. Chromatogr.*, 148 (1978) 3.
12 E. Smolková, L. Feltl and J. Všetečka, *Chromatographia*, 12 (1979) 147.
13 E. Smolková, *Plenary Lecture Int. Symp. Clathrate Compounds and Molecular Inclusion Phenomena, Jachranka (Warsaw), 1980.*
14 Y. Matsui and K. Mochida, *Bull. Chem. Soc. Jap.*, 52 (1979) 2800.