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Determination and Use of Rohrschneider–McReynolds Constants for Chiral Stationary Phases Used in Capillary Gas Chromatography

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The overall polarity of 22 chiral stationary phases (CSPs) used in capillary open tubular gas chromatography columns was estimated using the first five Rohrschneider–McReynolds constants. Most of the columns (i.e., 18) were wall-coated, and four were of the wall-immobilized or of the so-called "bonded" type. A wall-coated capillary squalane column was specially prepared as a polarity reference column. All but two of the CSPs were based on derivatized cyclodextrins (CDs) of different sizes. The overall properties of the CSPs are discussed in terms of the five Rohrschneider–McReynolds constants and their average values. It was found that the derivatized cyclodextrin CSP polarity increased with the CD ring size. The bonded CSPs were significantly less polar than their coated homologues due to the apolar polymer used to immobilize the CD rings. The retention behavior of 14 compounds was studied at 100 °C on the capillary columns. Retention parameters are clearly related to the McReynolds constants. Conversely, the enantiomeric resolution capability of a given stationary phase is not related to the constants. The enantioselective resolution mechanism critically depends on the solute structure and on the nature of the CSP.

The efficient separation of racemic mixtures has been one of the most important challenges for analytical chemistry at the end of this century. Tremendous advances have been made in this area in the last 10 years. Chromatographic techniques seem to be the most promising for accurate determination of enantiomer impurities of low levels.[1] All chromatographic techniques, HPLC,[2] TLC,[3–5] SFC,[6–8] and GC,[9–19] can be used for the separation of chiral compounds. The high efficiency of capillary gas chromatography (GC) is particularly advantageous, as it allows the baseline resolution of two enantiomers separated with a relatively low selectivity factor.[15–19] The first commercial chiral stationary phase (CSP) for GC was a poly(siloxane-L-valine-*tert*-butylamide) copolymer that was coated on glass capillaries. These columns are sold under the Chirasil-Val trade name.[9] Cyclodextrins (CDs) were first used as CSPs for HPLC.[20] More recently, derivatized CDs were used as CSPs in coated capillary columns for GC.[14–19] The enantioselective separation abilities of these stationary phases are abundantly documented in the literature.[13–19] However, at the present time, the polarity properties, e.g., Kováts indexes and Rohrschneider–McReynolds constants, of the CSPs for GC are not well documented. In 1990, Wenz et al.[21] measured the overall McReynolds indexes of seven CD derivatives. This lack of data may be due to the fact that these phases are relatively recent and that these constants are less commonly used with capillary columns. Also, several of these stationary phases are not pure compounds. They are often mixtures of a derivatized CD, the enantioselective agent, and a classical GC phase such as a poly(dimethylsiloxane) or a poly(ethylene glycol) phase used as a combination solvent, binding diluent, coating enhancer, etc.

The aim of this work is to determine the Kováts indexes and Rohrschneider–McReynolds constants of several commercially available capillary column CSPs for GC. For the purpose of this study, these CSPs were considered as a single "phase", even

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though they can be a mixture of a chiral selector and one or several diluents. This should allow the classification of the CSPs from a polarity point of view rather than from an enantioselectivity point of view. These polarity data should further help in phase selection, giving more information on the analysis duration, selectivity, and other retention predictions. Also, it should help indicate which CSPs are essentially identical.

THEORETICAL BACKGROUND

Kováts Indexes. The Kováts indexes are measured at a constant temperature. By definition, the index of a linear alkane on any GC stationary phase is 100 times its number of carbon atoms: 600 for *n*-hexane, 1200 for *n*-dodecane, etc.[22] The adjusted retention volumes of linear *n*-alkanes, V_n', increase exponentially at a constant temperature with the number, n, of carbon atoms in the molecule:

$$\log V_n' = An + B \tag{1}$$

A and B are temperature- and phase-dependent constants. The Kováts retention index, $I(x)$, of a given molecule, x, on a given phase is 100 times the number of carbon atoms of a hypothetical *n*-alkane that would have exactly the same retention volume as x under the given experimental conditions. Using eq 1, $I(x)$ is computed as

$$I(x) = 100n + 100\frac{\log V_x' - \log V_n'}{\log V_{n+1}' - \log V_n'} \tag{2}$$

in which V_x' is the adjusted retention volume of compound x and n is the number of carbon atoms of the *n*-alkane that elutes just before compound x. V_n' and V_{n+1}' are the adjusted retention volumes of the two *n*-alkanes that flank the x peak.[23]

Rohrschneider–McReynolds Constants. Slope A of eq 1 is related to the molar free energy of dissolution of a methylene group in the studied liquid stationary phase.[24] Rohrschneider has shown that it is possible to predict the retention increment, ΔI, for a compound eluted first on an apolar column and next on a polar one:[25]

$$\Delta I = aX + bY + cZ + dU + eS \tag{3}$$

The lowercase letters a, b, c, d, and e characterize the compound, and the uppercase letters X, Y, Z, U, and S characterize the polar stationary phase versus a reference nonpolar stationary phase. Squalane was selected by Rohrschneider along with five reference solutes, i.e., solutes for which all $a-e$ parameters are nil but one. The five solutes were benzene with $a = 1$, ethanol with $b = 1$, methyl ethyl ketone ($c = 1$), nitromethane ($d = 1$), and pyridine ($e = 1$). It was then possible to determine the X–S set of Rohrschneider constants of any stationary phase by just comparing the Kováts indexes of the five reference solutes on the squalane reference column and on the studied phase. Later, McReynolds proposed use of 10 reference compounds.[26] The five first compounds, benzene ($a = 1$), *n*-butanol ($b = 1$), 2-pentanone ($c = 1$), nitropropane ($d = 1$), and pyridine ($e = 1$), were analogous to those proposed by Rohrschneider. They were widely accepted to obtain the five X, Y, Z, U, and S Rohrschneider–McReynolds constants for GC stationary phase polarity comparison.[16]

The whole set of constants should be considered in order to have a complete idea as to a stationary phase's retention characteristics. However, many individuals prefer to have a single number to represent the parameter of phase polarity. Consequently, the average value of the five constants is sometimes used for this purpose, even though each Rohrschneider–McReynolds constant is an overall representation of certain molecular interactions. In the text, we shall refer to the average value of the five constants using the word "polarity". This average value is not really indicative of the phase polarity. The interactions related to the five selected solutes can be described as follows:[27–28] X is for benzene, which is a weak, soft base in the gas state and can interact via $\pi-\pi$ interactions. It is related to weak dispersion forces and polarizability character of the phase. Y represents *n*-butanol, which has some acidic properties in the gas state. It also indicates the hydrogen-bonding ability of the phase. Z represent 2-pentanone, a somewhat intermediate polarity compound. Its behavior relates to the polarizability and part of the dipolar character of the stationary phase. U is obtained using nitropropane, a rather strongly polar compound with no proton donor capability. Its retention behavior is related to the electron donor, electron acceptor, and dipolar character of the phase. The S term, from pyridine, a strong proton acceptor and polar molecule, indicates the acidic character of the phase. Some physicochemical parameters of the test solutes are listed in the second table of the Experimental Section.

EXPERIMENTAL SECTION

Reference Column. The squalane reference column is critical to obtain significant Rohrschneider–McReynolds constants.[29–31] The set of columns we chose to evaluate was of the open tubular capillary type. Indeed, most of the chiral stationary phase GC columns can only be obtained in this format. Since it was not appropriate to use a macrobore squalane reference column, it was necessary to prepare a capillary squalane reference column.

First, 10 m of fused silica capillary tubing (0.25 mm i.d.) from Supelco (Rohm and Haas, Bellefonte, PA) was deactivated by silylation with *n*-octyldimethylchlorosilane (MW 206.8, bp 223 °C, Petrarch Systems 09819, Bristol, PA). The capillary tubing was first etched by filling with gaseous HCl and heating at 300 °C for 2 h. After being flushed with two column volumes of liquid hydrochloric acid (pH ~2), two column volumes of water, and finally nitrogen gas, the capillary tubing was filled with a 5% w/v NaOH solution, sealed by Teflon tubing, and heated at 125 °C for 30 min. Next, the capillary was flushed with water, acetone, and nitrogen gas. It was dried overnight at 250 °C under a slow N_2 gas flow. A 10% v/v *n*-octyldimethylchlorosilane solution in dry

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Table 1. Characteristics of the Capillary Chiral GC Columns

trade name	chiral phase description[a]	company[b]	length (m)	film thickness (μm)	code
ChiraldexPH-A	permethylated *S*-hydroxypropyl-α-CD	Astec	10	0.125	PH-A
PH-B	permethylated *S*-hydroxypropyl-β-CD		10	0.125	PH-B
PH-G	permethylated *S*-hydroxypropyl-γ-CD		10	0.125	PH-G
ChiraldexDA-A	2,6-*O*-dipentylated 3-*O*-acetylated α-CD	Astec	10	0.125	DA-A
DA-B	2,6-*O*-dipentylated 3-*O*-acetylated β-CD		10	0.125	DA-B
DA-G	2,6-*O*-dipentylated 3-*O*-acetylated γ-CD		10	0.125	DA-G
ChiraldexTA-A	2,6-*O*-dipentylated 3-*O*-trifluoroacetylated α-CD	Astec	10	0.125	TA-A
TA-B	2,6-*O*-dipentylated 3-*O*-trifluoroacetylated β-CD		10	0.125	TA-B
TA-G	2,6-*O*-dipentylated 3-*O*-trifluoroacetylated γ-CD		5	0.125	TA-G
Hydrodex B	permethylated β-CD + polysiloxane	M. N.	10	0.25	Hydrodex
Chiraldex B	permethylated β-CD + poly(dimethylsiloxane)	Astec	10	0.125	PM (Astec)
Cyclodex B	permethylated β-CD + DB1701[c]	Chrompack or J&W	25	0.25	Cyclodex
Chirasil Val	L-valine *tert*-butylamide coated	MN	25		CT.C.Sil-Val
Permabond L-Chirasil Val	L-valine *tert*-butylamide bonded	MN	25	bonded	PB.C.Sil-Val
LipodexA	2,3,6-tri-*O*-pentyl-α-CD	MN	10		Lipodex A
B	2,6-di-*O*-pentyl-3-*O*-acetyl-α-CD	MN	10		Lipodex B
C	2,3,6-tri-*O*-pentyl-β-CD	MN	10		Lipodex C
D	2,6-di-*O*-pentyl-3-*O*-acetyl-β-CD	MN	10		Lipodex D
E	2,6-di-*O*-pentyl-3-*O*-butyryl-γ-CD	MN	10		Lipodex E
α-Dex 120	permethylated α-CD (20%) − SPB 35[c] (80%)	Supelco	30		α-Dex 120
β-Dex 110	permethylated β-CD (10%) − SPB 35[c] (90%)	Supelco	30		β-Dex 110
β-Dex 120	permethylated β-CD (20%) − SPB 35[c] (80%)	Supelco	30		β-Dex 120
laboratory prepared	allylpermethylated β-CD + PS537[c] ratio 1:4 w/w		10	bonded	bonded 1:4
laboratory prepared	allylpermethylated β-CD + PS537[c] ratio 1:6 w/w		10	bonded	bonded 1:6
laboratory prepared	pentylpermethylated β-CD + PS537[c] ratio 1:6 w/w		10	bonded	bd pentyl 1:6

[a] The listed CD substitution corresponds to one glucose unit in the CD ring. For example, permethylated β-CD means heptakis(2,3,6-tri-*O*-methyl)-β-CD. [b] Astec, Advanced Separation Technologies, Whippany, NJ; MN, Macherey Nagel GmbH, Düren, Germany; Chrompack, Chrompack International BV, Middleburg, The Netherlands; J&W, J&W Scientific—Fisons, Folsom, CA; Supelco, Supelco Inc., Bellefonte, PA. [c] DB1701, poly(methylsiloxane) with 7% cyanopropyl and 7% phenyl substitution; SPB 35, poly(dimethylsiloxane) with 35% phenyl substitution (OV 11). PS537, poly(methylsiloxane) hydrogen terminated, MW 400 with about 5 dimethylsiloxane units.

toluene was then introduced into the capillary. The reaction took place for 4 h at 125 °C. The deactivated tubing was dried with N_2 and coated with squalane (Aldrich, Milwaukee, WI) using the static method[32] at room temperature with a diethyl ether squalane solution whose concentration (1.66 g/L) gave a 0.125 μm film thickness.

Capillary Columns with a Chiral Stationary Phase. Table 1 lists the 22 capillary columns with CSPs tested. Most columns were 10 m long capillary columns coated with a CSP. The Permabond column from Macherey Nagel is a commercial column whose CSP is bonded, i.e., thermally immobilized, inside the capillary tubing. Three laboratory-prepared columns recently examined from the enantioselectivity point of view were added as wall-immobilized CD−CSP capillary columns.[33] All CSPs are based on CD derivatives, except the Permabond and Chirasil-Val columns, which are based on the same amino acid derivative. The values not listed in Table 1 were not provided by the manufacturers. The Chiraldex B column, referred as PM (Astec), is not currently marketed. It was specially prepared for us by Astec with the widely used "permethylated CD" phase, i.e., heptakis-(2,3,6-tri-*O*-methyl)-β-CD−CSP, in order to compare its polarity with those of the other columns said to contain the same CSP. This CSP is often mixed with a silicon−oil solvent phase that can modify the overall polarity. During the processing time of this work, three capillary columns with a CSP based on such a "permethylated" phase were introduced by Supelco, who kindly communicated the corresponding Rohrschneider−McReynolds constants. This information was included in the tables.

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Table 2. Polarity Properties of the Five First McReynolds Test Solutes[a]

solute	bp (°C)	ΔI		ε	μ (10^3 C·m)	n	α (10^{24} cm^3)
benzene	80.1	*X*		2.27	0	1.501	10.4
butanol	117.7	*Y*		17.5	5.8	1.398	8.8
2-pentanone	102.3	*Z*		15.4	9.0	1.391	10.0
nitropropane	130	*U*		35.8	13	1.402	8.6
pyridine	115.3	*S*		12.9	7.9	1.510	9.5

[a] bp, boiling point; Δ*I*, increment of the Kováts retention index (eq 3); ε, dielectric constant (dimensionless); μ, dipolar moment; *n*, refractive index; α, polarizability (eqs 4 and 5).

Chemicals. The C6−C12 *n*-alkane reference solutes were obtained from Sigma (St. Louis, MO). Table 2 lists some physicochemical constants of the five McReynolds test solutes. The Δ*I* column indicates which constant is obtained with the Kováts index difference, Δ*I*, of the solute between the studied phase and the reference squalane phase. The polarizability, α, was computed using

$$\alpha = 3R_m/(4\pi N_A) \quad (4)$$

in which N_A is the Avogadro number and R_m is the molar refraction defined by the Lorentz equation:

$$R_m = [(n^2 - 1)/(n^2 + 2)]M/d \quad (5)$$

M, *n*, and *d* are the molar mass, the refractive index, and the solute density, respectively. The dielectric constant, the dipolar moment,

Table 3. Kovats Indexes of the Five First Test Solutes at 100 °C

column	benzene	butanol	2-pentanone	nitropropane	pyridine	t_m (s)	u (cm/s)	d (mL/min N_2)
squalane	649.9	600.0	620.3	649.6	708.5	51.2	19.5	0.575
PH-A	799.0	933.0	799.0	946.6	1085.7	94.8	10.5	0.311
PH-B	854.8	1000.2	899.3	1036.7	1065.7	74.8	13.4	0.394
PH-G	856.0	1015.4	902.1	1051.0	1077.1	70.5	14.2	0.418
DA-A	662.3	787.0	691.4	794.3	842.7	87.5	11.4	0.337
DA-B	742.8	778.5	713.5	800.0	859.9	74.3	13.5	0.397
DA-G	739.9	800.0	739.9	815.3	877.3	87.0	11.5	0.339
TA-A	730.3	812.7	812.7	1119.6	929.3	74.0	13.5	0.398
TA-B	755.7	836.0	836.0	1023.1	1069.5	76.5	13.1	0.385
TA-G	766.4	949.1	847.4	873.6	1154.1	43.0	11.6	0.343
Hydrodex B	754.0	825.8	789.7	900.1	884.1	114.0	8.8	0.258
PM (Astec)	756.7	826.9	792.5	901.4	919.7	60.0	16.7	0.491
Cyclodex B	753.7	821.4	790.3	900.0	877.4	253.6	9.9	0.290
CT.C.Sil-Val	750.4	841.3	781.1	872.9	887.1	250.0	10.0	0.295
PB.C.Sil-Val	736.6	820.4	773.5	861.5	885.1	193.0	13.0	0.382
Lipodex A	735.4	800.0	735.4	838.0	851.8	104.4	9.6	0.282
Lipodex B	772.1	852.2	772.1	900.5	907.4	170.6	5.9	0.173
Lipodex C	726.1	786.6	726.1	800.0	839.6	108.2	9.2	0.272
Lipodex D	785.3	883.8	860.3	1135.5	1007.6	78.8	12.7	0.374
Lipodex E	764.2	844.9	861.1	1033.7	917.9	137.3	7.3	0.215
bonded 1:4	725.3	763.2	720.9	804.1	835.2	61.0	16.4	0.483
bonded 1:6	716.0	757.9	716.0	800.0	865.1	59.8	16.7	0.493
Bd pentyl 1:6	732.0	754.4	713.8	800.0	837.3	67.4	14.8	0.437

the refractive index, and the polarizability are listed for polarity comparison. The test solutes and the chiral solutes were obtained from Sigma, Aldrich, and Fluka (Ronkonkoma, NY), A fresh mixture was prepared daily in ethyl ether in the concentration range 0.15–0.25 mg/mL. The chiral solutes cover a wide variety of functionalities: alcohols, amines, aromatics, esters, ethers, bromoalkanes, and terpenes. However, the polar alcohol and amino groups, except the hydroxy group of pantolactone, were all trifluoroacetylated to increase solute volatility.

Apparatus. All chromatographic measurements were performed at 100 °C on a Varian Model 3700 gas chromatograph (San Fernando, CA) with a flame ionization detector. The injector and the detector temperature were both set at 250 °C. The split ratio was 100/1. The carrier gas was nitrogen with an inlet pressure close to 0.3 kg/cm^3 (~4–5 psi), which gave an average linear velocity of ca. 10 cm/s. With such experimental conditions, the actual dead time was roughly proportional to the column length.

RESULTS AND DISCUSSION

Kováts Indexes. Table 3 lists the Kováts retention indexes of the first five McReynolds solutes (Table 2) on the 22 capillary columns with CSPs and on the squalane reference column. The listed indexes are the average values of triplicate measurements, with a relative standard deviation lower than 2%. The dead time, t_m, was computed according to the Guardino method.[34] Using three successive linear alkanes, t_m is obtained by

$$t_m = [t_n^2 - (t_{n-1})(t_{n+1})]/[2t_n - t_{n-1} - t_{n+1}] \quad (6)$$

The subscript n corresponds to the number of carbons of the linear alkane whose uncorrected retention time, t_n, was considered. The dead time, t_m, was used to correct all retention times and to estimate the linear gas velocity and the average gas flow rate at column exit (Table 3).

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Table 4. Rohrschneider–McReynolds Constants of the Five First Test Solutes at 100 °C

column	X	Y	Z	U	S	av	A^a
squalane	0.0	0.0	0.0	0.0	0.0	0.0	0.299
PH-A	149.1	333.0	178.7	297.0	377.2	267.0	0.286
PH-B	204.9	400.2	279.0	387.1	357.2	325.7	0.268
PH-G	206.1	415.4	281.8	401.4	368.6	334.7	0.254
DA-A	12.4	187.0	71.1	144.7	134.2	109.9	0.291
DA-B	92.9	178.5	93.2	150.4	151.4	133.3	0.344
DA-G	90.0	200.0	119.6	165.7	168.8	148.8	0.262
TA-A	80.4	212.7	192.4	470.0	220.8	235.3	0.284
TA-B	105.8	236.0	215.7	373.5	361.0	258.4	0.297
TA-G	116.5	349.1	227.1	224.0	445.6	272.5	0.294
Hydrodex B	104.1	225.8	169.4	250.5	175.6	185.1	0.274
PM (Astec)	106.8	226.9	172.2	251.8	211.2	193.8	0.286
Cyclodex B	103.8	221.4	170.0	250.4	168.9	182.9	0.281
CT.C.Sil.Val	100.5	241.3	160.8	223.3	178.6	180.9	0.250
PB.C.Sil-Val	86.7	220.4	153.2	211.9	176.6	169.8	0.291
Lipodex A	85.5	200.0	115.1	188.4	143.3	146.5	0.294
Lipodex B	122.2	252.2	151.8	250.9	198.9	195.2	0.237
Lipodex C	76.2	186.6	105.8	150.4	131.1	130.0	0.284
Lipodex D	135.4	283.8	240.0	485.9	299.1	288.8	0.284
Lipodex E	114.3	244.9	240.8	384.1	209.4	238.7	0.291
α-DEX 120	102	243	142	221	170	175.6	
β-DEX 110	112	236	153	130	184	163.0	
β-DEX 120	119	264	154	134	187	171.6	
bonded 1:4	75.4	163.2	100.6	154.5	126.7	124.1	0.322
bonded 1:6	66.1	157.9	95.7	150.4	156.6	125.3	0.281
Bd pentyl 1:6	82.1	154.4	93.5	150.4	128.8	121.8	0.315

[a] A is the slope of eq 1 ($\log(t_{n+1}/t_n)$).

The Kováts indexes of the McReynolds standards on the squalane reference column are in agreement with values found in the literature. The sequence 647, 588, 624, 647, and 707 was measured on a classical squalane column at 100 °C by Castello and D'Amato[35] for the five standards. Rohrschneider[27] recommended the values 649 and 695 for benzene and pyridine, respectively, at 100 °C. The capillary squalane column can be considered as a correct reference column for Rohrschneider–McReynolds constant determination.

The highest Kováts indexes were 1154 and 1136, obtained for pyridine and nitropropane on the TA-G and Lipodex D columns,

(35) Castello, G.; D'Amato, G. *J. Chromatogr.* **1977**, *131*, 41–45.

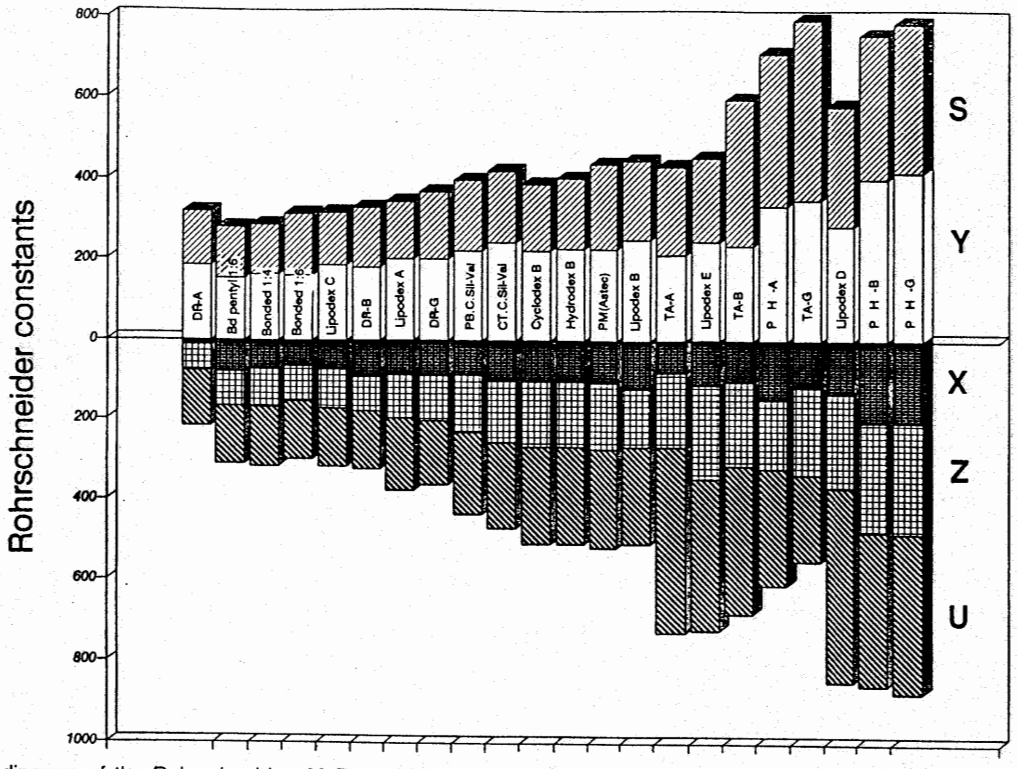


Figure 1. Bar diagram of the Rohrschneider–McReynolds constants of the capillary GC columns studied arranged in increasing polarity order. The *Y* and *S* constants have a positive coefficient. The *X*, *Z*, and *U* constants have a negative coefficient.

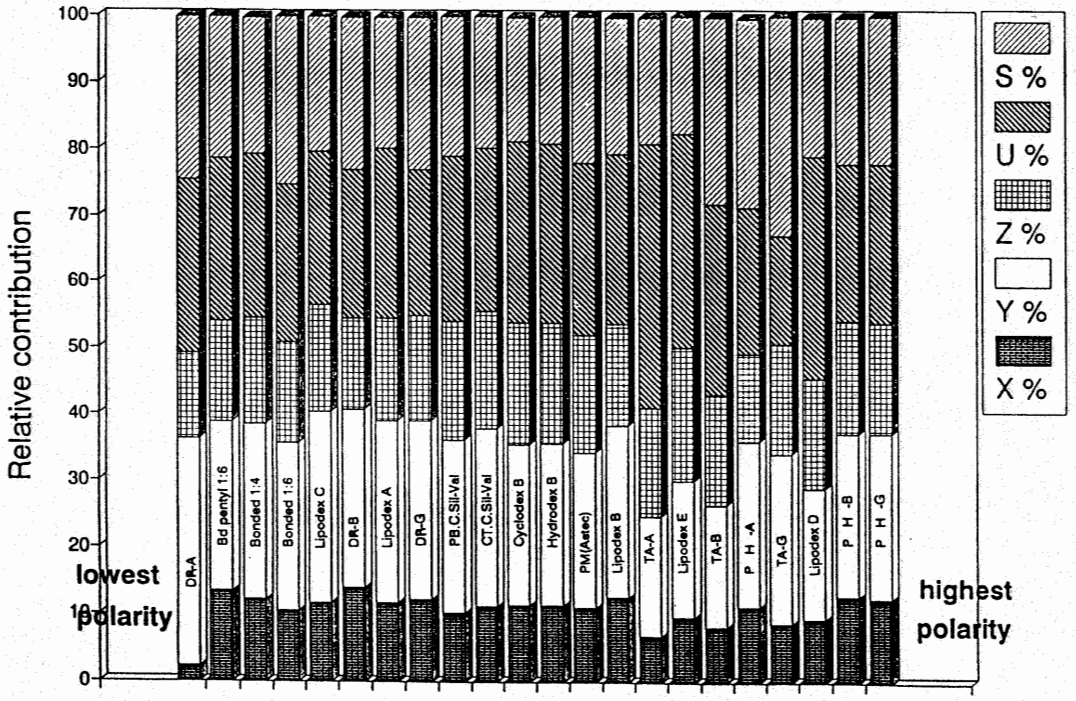


Figure 2. Relative contribution of the individual *X*...*S* Rohrschneider–McReynolds constants to the overall polarity normalized to 100. The increasing polarity order of Figure 1 was retained.

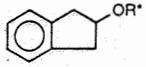
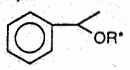
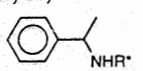
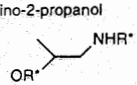
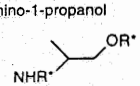
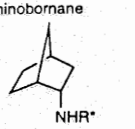
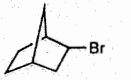
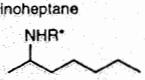
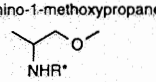
respectively. The corresponding retention times were 98 and 208 s at 100 °C, respectively. The lowest retention indexes, besides the squalane reference indexes, were obtained on the DA-A column, with the lowest value, 662, for benzene (Table 3). It corresponded to a retention time of 104 s.

Rohrschneider–McReynolds Constants. Table 4 lists the Rohrschneider–McReynolds constants of the five reference solutes on the 25 capillary columns with CSP. The average value of the five constants, the polarity of the phase, and the *A* parameter,

$$A = \log(t_{n+1}/t_n) \qquad (7)$$

are also listed. *A* is the slope of the Kováts standardization line (eq 1). Figure 1 shows the Rohrschneider–McReynolds constants arranged in increasing polarity order, from the less polar column, DA-A with an overall polarity value of 110, to the most polar one, PH-G with an average polarity value of 335 (Table 4).

Table 5. Enantioselectivity Parameter (α), Capacity Factor (*k'*), and Kováts Index (*I*) of Some Solutes[a]

compound, structure		squalane	PH-A	PH-B	PH-G	DA-A	DA-B	DA-G	TA-A	TA-B	TA-G	Hydro-dex	Cyclo-dex	C.T.C.-Sil-Val	PB.C.-Sil-Val	Lipodex A	Lipodex B	Lipodex C	Lipodex D	Lipodex E	bonded 1:4
2-indanol 	*k'*	2.35	10.14	9	10.95	7.72	17.34	11.37	6.24	6.01	10.05	18.99	15.02	3.69	4.49	8.36	3.43	3.65	10.28	9.19	6.98
	I	1149	1408	1285	1451	1276	1320	1331	1270	1310	1334	1347	1348	1312	1318	1383	1347	1220	1422	1364	1302
α-phenylethanol 	α	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.04	1.00
	k'	0.4	1.64	1.69	2.16	1.16	2.77	2.25	2.28	1.01	5.73	3.92	3.35	0.91	1.18	1.74	0.77	1.11	2.16	1.93	1.46
	I	901	1126	1031	1198	1015	1069	1088	1119	1057	1254	1105	1114	1094	1099	1148	1087	1045	1181	1124	1065
α-phenylethylamine 	α	1.00	1.00	1.04	1.04	1.01	1.01	1.03	1.01	1.01	1.04	1.00	1.00	1.03	1.03	1.04	1.06	1.05	1.21	1.05	1.01
	k'	2.54	28.43	21.73	39.64	15.13	34.21	24.45	12.79	9.15	18.04	45.42	36.25	9.15	9.31	13.61	6.49	6.25	45.17	29.83	11.72
	I	1160	1568	1419	1652	1368	1413	1446	1378	1369	1418	1481	1486	1454	1438	1455	1457	1300	1651	1545	1380
1-amino-2-propanol 	α	1.00	1.00	1.00	1.00	1.04	1.00	1.00	1.16	1.00	1.03	1.00	1.00	1.00	1.00	1.00	1.00	1.00		1.26	1.00
	k'	0.17	6	4.82	9.87	2.76	23.45	4.69	5.38	1.46	2.83	12.21	10.42	2.17	212	3.21	2.07	1.75		24.5	2.33
	I	786	1327	1190	1435	1134	1361	1198	1248	1109	1153	1279	1291	1230	1195	1240	1259	1112	1464	1515	1136
2-amino-1-propanol 	α	1.00	1.00	1.02	1.01	1.00	1.00	1.00	1.00	1.01	1.02	1.00	1.04	1.12	1.08	1.04	1.00	1.00		1.20	1.00
	k'	0.21	23.39	19.94	37.42	9.31	25.77	18.5	6.41	5.57	9.71	21.3	16.51	7.22	6.75	8.02	6.37	3.65		44.86	7.95
	I	813	1537	1403	1643	1301	1374	1404	1274	1299	1329	1365	1363	1417	1385	1376	1454	1220	1774	1608	1321
2-aminobornane 	α	1.00	1.02	1.01	1.00	1.02	1.00	1.00	1.02	1.03	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.10	1.04	1.06
	k'	1.24	11.29	15	15.41	8.93	24.83	12.36	9.95	9.15	10.06	31.7	24.64	5.41	5.77	9.52	3.45	3.93	30.88	16.52	17.33
	I	1059	1425	1362	1505	1296	1369	1343	1340	1369	1334	1426	1426	1372	1360	1402	1348	1231	1592	1454	1440
2-bromonorbornane 	α	1.00	1.00	1.00	1.00	1.11	1.00	1.11	1.00	1.01	1.01	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.03	1.00
	k'	0.86	2.93	3.36	2.98	3.8	11.16	4.51	2.62	3.78	4.47	8.08	6	1.3	1.71	2.71	1.38	1.96	2.91	3.14	4.96
	I	1009	1215	1135	1248	1178	1260	1192	1140	1243	1218	1216	1204	1150	1159	1214	1188	1129	1228	1199	1250
2-aminoheptane 	α	1.00	1.00	1.05	1.01	1.00	1.00	1.05	1.04	1.00	1.03	1.00	1.01	1.01	1.00	1.00	1.00	1.00	1.17	1.12	1.02
	k'	0.58	5.21	4	6.26	5.23	6.91	4.6	5.12	2.21	3.83	12.65	10.51	2.39	2.61	4.32	1.71	1.75	9.83	6.45	4
	I	955	1305	1162	1364	1222	1194	1195	1241	1167	1196	1285	1292	1244	1229	1284	1226	1112	1415	1310	1218
2-amino-1-methoxypropane 	α	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.10	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.02
	k'	0.49	1.57	2.09	1.91	1.4	2.7	2.07	1.16	4.15	1.68	3.33	2.84	0.74	1.03	1.07	0.76	0.9	1.78	1.8	1.47
	I	931	1119	1063	1179	1041	1066	1075	1018	1257	1078	1079	1088	1061	1076	1075	1084	1014	1151	1141	1072
β-butyrolactone 	α	1.00	1.00	1.00	1.01	1.00	1.00	1.00	1.18	1.00	1.00	1.00	1.32	1.00	1.00	1.00	1.00	1.00	1.34	1.15	1.00
	k'	0.12	0.36	1.27	1.62	0.64	1.22	0.9	5.04	3.78	0.53	1.86	1.6	0.38	0.52	0.74	0.6	0.41	8.85	4.67	0.67
	I	732	889	988	1153	933	957	949	1233	822	914	990	998	957	964	1021	1045	898	1399	1260	946
α-methyl-α-butyrolactone 	α	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.43	1.00	1.00	1.01	1.00	1.00	1.00	1.01	1.00	1.05	1.07	1.00	1.00
	k'	0.4	3.29	4.09	5.08	1.59	4.14	20.84	5.81	1.39	1.89	6.08	5.05	1.3	1.6	2.26	1.11	1.68	31.33	21.29	2.42
	I	901	1233	1165	1331	1059	1124	1422	1260	1101	1095	1172	1178	1150	1148	1187	1150	1106	1594	1493	1142

pantolactone	α	1.00	1.00	1.13	1.00	1.00	1.05	1.02	1.09	1.05	1.03	1.17	1.12	1.06	1.05	1.00	1.03	1.26	–	–	1.09
	k'	0.49	24.43	37.9	37.8	10.6	43.25	21.38	12.1	13.7	14.73	31.5	24.15	8.4	7.58	8.4	4.45	3.65	–	–	20.93
	I	931	1545	1503	1645	1319	1445	1425	1369	1427	1389	1425	1422	1441	1404	1383	1392	1220	–	–	1468
tetrahydro-2-(2-propynyloxy)pyran	α	1.00	1.06	1.05	1.00	1.06	1.00	1.00	1.00	1.00	1.00	1.03	1.02	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	k'	0.68	3.57	4.73	4.15	4.18	3.49	3.69	2.02	2.13	2.87	5.73	4.52	1.18	1.52	2.65	1.23	1.61	261	244	3.04
	I	976	1246	1187	1300	1191	1101	1162	1101	1162	1155	1163	1160	1134	1140	1211	1168	1100	1210	1160	1176
limonene	α	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.01	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	k'	0.96	1.21	1.73	1.36	1.87	3.94	2.43	1.59	1.46	2.17	3.56	2.65	0.75	1.01	2.14	0.83	1.25	1.33	1.42	1.89
	I	1024	1079	1034	1126	1081	1118	1099	1065	1109	1115	1090	1077	1063	1073	1179	1099	1063	1106	1077	1104
no. of compds separated			2	6	4	5	2	4	7	5	6	4	6	4	3	3	2	4	5	8	4

[a] R*, $COCF_3$, trifluoroacetyl derivatizing group.

The bars representing the *Y* and *S* contributions were drawn with a positive value. The bars of the *X*, *Z*, and *U* contributions were drawn with a negative value to enhance the contribution of each parameter to the overall polarity. For example, such representation clearly shows that the TA-G column differs in selectivity from the Lipodex D column, although both columns have a similar average polarity, 273 and 289, respectively. The *U* value, from nitropropane, is 224 for the TA-G column and 486 for the Lipodex D column, a 117% difference. This is compensated by the *Y* (butanol) and *S* (pyridine) values, respectively 349 and 446 for the TA-G CSP and only 284 and 299 for the Lipodex D CSP columns. Dipolar solutes will likely be more retained on the Lipodex D phase than on the TA-G one. Conversely, basic solutes and/or those with hydrogen-bonding capabilities will be more retained on the TA-G column.

Figure 2 shows the relative contribution of each Rohrschneider–McReynolds constant when the overall polarity was normalized to 100. The increasing polarity order of Figure 1 was retained. The average values for the *X*, *Y*, *Z*, *U*, and *S* contribution are 10.6%, 24.9%, 16.4%, 25.9%, and 22.1%, respectively. If we compare again the TA-G and the Lipodex D columns of similar polarity, the relative weight of the *S* term for the TA-G column is 33% of the overall polarity. It is only 21% of the Lipodex D polarity, close to the average 22.1% value. The *U* term makes 33.6% of the Lipodex D polarity and only 16.4% of the TA-G polarity. 33.6% is the second highest relative *U* value, after 40% for the TA-A phase, and 16.4% is the lowest. For most studied CSPs, the increase of the overall polarity is due to a monotonous increase of the five *X*...*S* Rohrschneider–McReynolds constants. The relative percentage weight of the constants remains comparable. The high *U*% values of the TA-A and Lipodex D phases and the high *S*% value of the TA-G phase seem rather to be exceptions.

Influence of the Cyclodextrin Substituents. As expected, the CD substituents modify significantly the phase overall polarity. The lowest polarity was obtained with the Chiraldex DA columns, which are dipentyl-CD derivatives. Also, the laboratory-bonded peralkylated CD phases showed a low overall polarity. The Lipodex B and D columns contain a derivatized chiral selector close to the DA series's one. However, they are significantly more polar than the DA phases. This shows the effect on polarity of the embedding or diluent phase, whose nature was not given by the manufacturer (Table 1). In the average polarity order, the perpentylated phases of the Lipodex A and C columns come next with very similar polarity. The two non-CD-based CSPs, Chirasil-Val and Permabond, have a medium polarity, with an average value of 175. The three permethylated CSPs studied, Cyclodex, Hydrodex, and PM (Astec), are located around the average polarity value of 185. The permethylated α-DEX and β-DEX capillary columns have an average polarity of the same order of magnitude in the 170 range. The dipentyltrifluoroacetylated CD phases, the TA series, are significantly more polar than their acetylated homologues of the DA series (Table 1). The PH series shows the highest polarity. Although the secondary hydroxyls of the (*S*)-hydroxypropyl groups grafted on the CD rings of the PH phases were methylated, they seem to increase the phase polarity.

When the relative contributions are considered, the effect of the CD substituents is less obvious. The relative polarity contributions of the highly polar PH phases were close to the average values. The methylated alcohol group of their hydrox-

ypropyl substituent does not increase the Y term more than the other terms, as a free hydroxyl group would have done. The polar TA phases have an X relative contribution in the 7–8% range and a Y relative contribution in the 18–21% range, significantly lower than the average values, 10.6% and 24.9%, respectively (Figure 2). But, as already noted, the relative U value of TA-G is the lowest (16.4%), and its relative S value is the highest (33%), while it is the opposite for the TA-A phase: highest relative U value (40%) and very low relative S value (18.7%).

CD Ring Size and Polarity. Increasing the CD ring size from α-CD (six glucose units) to γ-CD (eight glucose units) seems to increase significantly the average CD-CSP polarity. With the Chiraldex DA series, the DA-A, DA-B, and DA-G CSPs increase in average polarity from 110, 133, to 149, respectively (Table 4). The Chiraldex TA series shows a 16% increase in average polarity, from 235, 258, to 273 as the CD ring size increases from α, β, to γ, respectively. Also, the PH series shows a 25% increase with the polarity sequence 267, 326, and 335 as the CD ring increase. The Lipodex B and D phases are α- and β-CD with identical substitution patterns (Table 1). Their respective average polarity values are 195 and 289. However, this is not the case with Lipodex A and C: the α-CD derivative, Lipodex A, is 17 polarity units more polar than the β-CD derivative, Lipodex C (Figure 1).

Studying the relative contributions (Figure 2), it is evident that the CD ring size increase is associated with selectivity changes. The X contribution (benzene) in the Chiraldex DA-A is very low (12 units or 2%). For the β and γ-CD homologues (DA-B and DA-G), the X value is in the 13% range (90 units). A rapid decrease of the relative contribution of the U term (nitropropane) was already noted in the TA CSP series with the CD ring increase. This decrease is compensated by the increase of the S term (Figure 2). However, there is no obvious selectivity change with CD ring increase in the Chiraldex PH and Lipodex series.

Coated versus Bonded. The capillary bonded phases are actually thermally and/or catalytically immobilized phases. Such phases are more rugged and stable than their coated analogues. The benefits regarding column lifetime, temperature stability, and injection procedure have never been fully proved experimentally.[33,36,37] Immobilization is only necessary for SFC applications. From the polarity point of view, the bonded phases are about 50 units less polar than the coated equivalent ones (Table 4). This is due to the large amount (80–86% w/w) of apolar poly(dimethylsiloxane) (PS357) that was used in the phase preparation procedure.[33] The Permabond Chirasil-Val CSP is also 10 units less polar than the coated equivalent. No information on the immobilizing agent was found. As already noted, the embedding polymer has a significant effect on the overall polarity of coated columns. The Rohrschneider–McReynolds constants of SPB-35, also named OV-11, are $X = 101$, $Y = 146$, $Z = 151$, $U = 219$, and $S = 202$.[38] This embedding polymer makes more than 80% of the coated phase of the Supelco α and β-DEX columns (Table 1). The Rohrschneider–McReynolds data corresponding to these columns show that the permethylated CDs do not change the Z term (Table 4). The doubling in permethylated β-CD concentration from 10% w/w (β-DEX 110) to 20% w/w (β-DEX 120) induces an increase of the X and Y terms with no significant changes of the Z, U, and S terms. Recently it was noted that analogous coated and bonded CSPs sometimes had different enantioselectivities for certain compounds.[33] Also, changing the ratio of the "diluent" to the cyclodextrin affected selectivity and retention in many cases.[33] On all CSPs, coated or bonded, the measured Rohrschneider–McReynolds constants quantify the combined polarity of the chiral selector and the embedding polymer, if any.

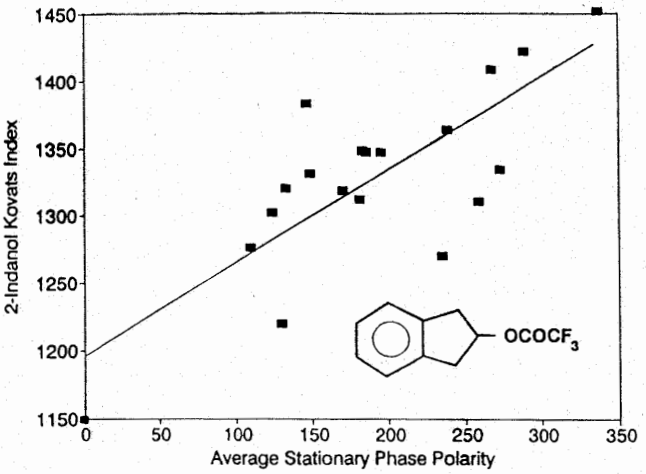


Figure 3. Plot of the Kováts retention index of 2-indanol (trifluoroacetylated) versus the average polarity of the capillary column CSPs. The posted line (eq 8) has a regression coefficient of 0.603.

Solute Retention and Polarity. Table 5 lists the chromatographic parameters of 14 solutes that were injected on the studied capillary columns. For the 13 chiral compounds, α is the enantioselectivity parameter computed from the ratio of the retention times of the most retained enantiomer to the first eluted one, k' is the capacity factor, and I is the Kováts index of the first eluted enantiomer. For the whole set of solutes, the trend is for the solute retention times to increase with the phase average polarity. Figure 3 shows the plot of the Kováts index, I, versus the average phase polarity, P, for 2-indanol, a nonchiral compound. The regression coefficient of the posted line,

$$I = \underset{(\pm 0.13)}{0.69P} + \underset{(\pm 45)}{1200} \qquad (8)$$

$$n = 20 \qquad r^2 = 0.603$$

is too low to establish a direct relationship between retention and polarity. However, the trend is clear. For the chiral compounds, the data point dispersion of such I versus P plots may be higher because the first eluting enantiomer (or the last eluting enantiomer) may be the R form of the solute on some CSPs and the S form on other CSPs. The k' and I values are definitively linked to analysis duration. Table 5 and Figure 3 show that the higher the Rohrschneider–McReynolds constants, the higher the retention times.

The five constants of the Hydrodex and Cyclodex phases are very close. The retention data obtained on these two phases for the whole set of compounds are similar (Table 5), which is not surprising for two similar (if not identical) phases.

Rohrschneider–McReynolds Constants and Enantioselectivity. The last line of Table 5 lists the number of compounds resolved ($\alpha \neq 1$) by the corresponding capillary column. The most successful phases for the set of solutes studied were the Lipodex E and the Chiraldex TA-A phases, which were able to resolve eight and seven of the 13 chiral compounds, respectively.

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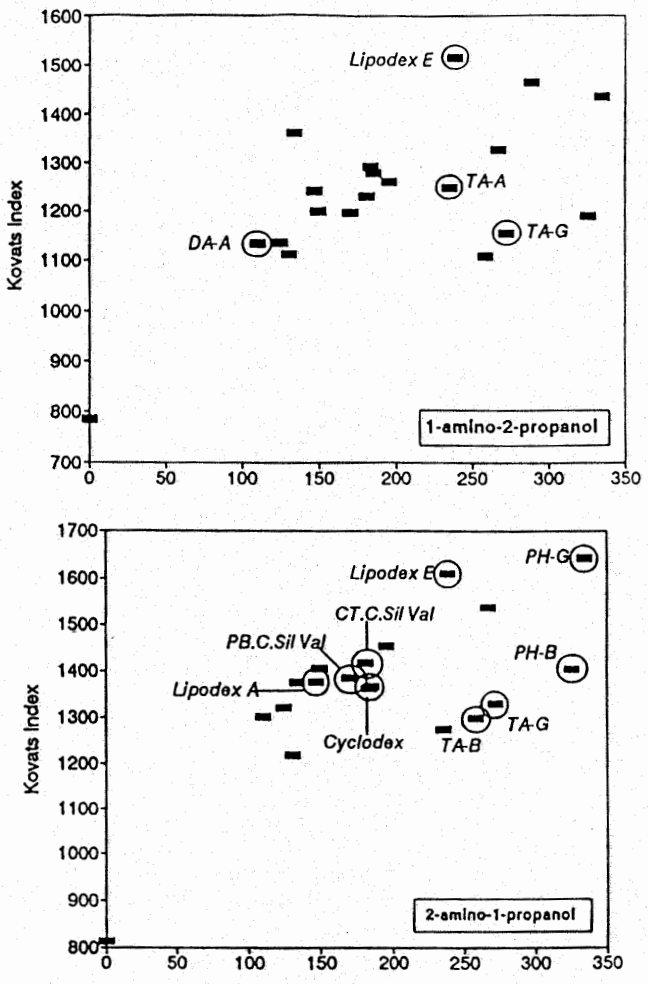

Figure 4. Plot of the Kováts retention index of 1-amino-2-propanol (top) and 2-amino-1-propanol (bottom), both trifluoroacetylated, versus the average polarity of the capillary column CSPs. Circled points, indicate that the enantiomers were resolved.

By chance, these two phases have very similar average polarity. They do not resolve the same compounds because they do not contain the same chiral selector (Table 1). Three CSPs, the Chiraldex DA-B, Chiraldex PH-A, and Lipodex B phases, can resolve only two compounds. These three phases have very different polarities. The least polar phase, Chiraldex DA-A, can resolve five compounds. The most polar phases, Chiraldex PH-B and PH-G, can resolve six and four compounds, respectively. Polarity and enantioselective ability of a phase seem to be completely independent.

Enantioselective retention mechanisms in gas chromatography were recently studied in detail.[39] The data obtained in this work can give some information on chiral recognition mechanisms. α-Phenylethanol and α-phenylethylamine are closely related compounds (MW 122 and 121, bp 203 and 187 °C, respectively). The trifluoroacetyl derivatives of the α-phenylethylamine enantiomers were separated by all CSPs, except for the permethylated CD-CSPs: Chiraldex PH-A, Hydrodex, and Cyclodex phases. The trifluoroacetyl derivatives of the α-phenylethanol enantiomers were separated by the Lipodex E phase only. The retention of the α-phenylethylamine derivative is higher than the retention of the alcohol derivative on all phases, but the relative retention variations are similar: lowest retention on the Chiraldex DA-A phase, highest retention on the Chiraldex PH-G phase. This shows that the hydrogen-bonding capability of the amido group on the chiral center is the main cause of the chiral recognition of the molecule by a variety of phases. Also, the change of one atom in a molecule slightly modifies its retention behavior and completely changes its chiral recognition mechanism.

1-Amino-2-propanol and 2-amino-1-propanol are structural isomers of similar polarity. Figure 4 compares their *I* versus *P* plots. The circled points correspond to successful chiral recognitions. On all phases, the 2-amino-1-propanol is 2–3 times more retained than the other isomer (Table 5). The retention trend shown in Figure 4 is comparable for both isomers. However, 2-amino-1-propanol is the isomer that bears the amido group on the stereogenic center. Its enantioresolution is much better than that of the other isomer (circled points in Figure 4).

In conclusion, the knowledge of the Rohrschneider–McReynolds constants of a chiral stationary phase allows the estimation of solute retention parameters, especially the analysis duration. It gives also an idea of the selectivity of the phase. There is no direct connection between chiral recognition mechanism and polarity. The Rohrschneider–McReynolds constants do not give any information on the optical resolving power of the phase.

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