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Short communication

Plots of relative retention against solute boiling points may indicate host–guest interactions with modified cyclodextrin gas chromatographic phases

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Abstract

Relative retention times with respect to *n*-undecane, obtained on six different modified α -, β - and γ -cyclodextrin capillary gas chromatographic stationary phases, were plotted against the literature boiling points for nine low-polarity solutes which occur in various volatile oils. Linear relationships (with correlation coefficients of at least 0.994) could be calculated by selecting seven to four solute data points, and it is presumed that those solutes which showed extra retention away from the lines (particularly bicyclic molecules) exhibit host–guest molecular interactions with the cyclodextrins. On four of these phases, the bicyclic camphene, for example, with a boiling point of 158°C, is retained behind myrcene, which boils at 167°C. Only α -terpinene and myrcene failed to show extra retention on any of the cyclodextrins.

Keywords: Relative retention times; Host–guest interaction; Stationary phases, GC; Cyclodextrin phases

1. Introduction

Referees of the author's previous papers have objected to any assumption that various modified cyclodextrin (CD) phases for gas chromatography can retard some volatile oil solutes by trapping them temporarily in their ring cavities in a host–guest molecular interaction. As a method to indicate that such interaction possibly does occur with some solutes, the work of Saura-Calixto et al. [1] appeared relevant. They deduced that the following linear expression applies to the retention index (I_R):

$$I_R = at + b \quad (1)$$

where t (°C) is the boiling point of a given solute from a series, a is a constant related to a standard functional group of the series and b is another constant related to the stationary phase, as well as the functional group of the solute series again. They obtained experimental linear plots of I_R as a function of t for the families of compounds of similar polarity such as alcohols, ketones and esters, using conventional stationary phases such as a high-polarity Carbowax and the low-polarity polysiloxane SE-52 (5% phenyl, 95% methyl).

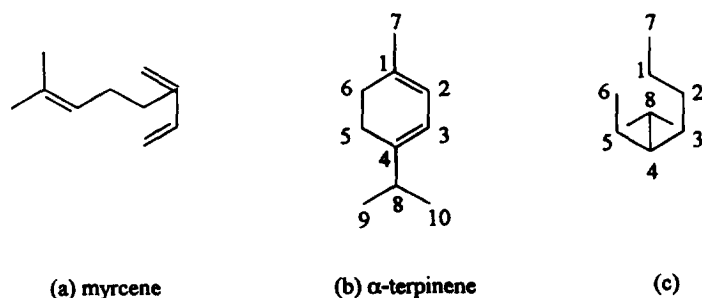


Fig. 1. (a) Myrcene, acyclic monoterpene. (b) α -Terpinene, monocyclic monoterpene. Without the unsaturated 3-4-ene bond, this is then γ -terpinene with 4-5-ene, limonene with 8-9-ene, 3-carene with a 5-8 bond, α -pinene with a 6-8 bond and *p*-cymene with an aromatic ring. (c) Base structure for bicyclic monoterpenes. This is α -pinene with an unsaturated 1-2-ene bond plus 1-6 and 6-8 bonds; camphene with 1-7-ene plus 1-8 and 2-6 bonds; and cineole with 1-6 and 1-oxy-8 bonds.

As volatile oil constituents have diverse chemistry, the group of low-polarity substances was selected as likely to provide suitable solutes which avoid polar interactions, to test a relationship similar to Eq. 1 on CD phases. This group consists of diverse monoterpene hydrocarbons, the aromatic *p*-cymene and the ether cineole (see Fig. 1). To utilize previous results, relative retention times with respect to *n*-undecane were taken instead of I_R . This C_{11} alkane is actually used for I_R determinations of any solutes with retention times close to it. If a linear relationship could be found for some of these solutes, deviations from this expression should be indicative of CD host-guest interactions by other low-polarity substances.

capillaries at less than $10^\circ\text{C min}^{-1}$ to avoid possible damage.

Chiraldex-modified CD capillaries ($10\text{ m} \times 0.25\text{ mm I.D.}$, film thickness $0.125\ \mu\text{m} \pm 10\%$) were obtained from ASTEC (Whippany, NJ, USA). Chiraldex A-PH is hexakis-2-hydroxypropyl-3,6-dimethyl- α -CD, with G-PH being the γ -CD analogue. A-DA is hexakis-2,6-dipentyl- α -CD, with G-DA the γ -CD analogue, the latter being kindly donated by ASTEC. G-PN is octakis-3-propionyl-2,6-dipentyl- γ -CD. The Cyclodex-B capillary was purchased from J & W Scientific (Folsom, CA, USA) and a 10-m length of the initial $30\text{ m} \times 0.25\text{ mm I.D.}$ capillary was used; the film thickness of the heptakis-trimethyl- β -CD was given as $0.25\ \mu\text{m}$.

2.2. Methods

Nine low-polarity monoterpene solutes found in diverse volatile oils were obtained from various commercial sources. They are given in the tables, and their chemical relationships are shown in Fig. 1. Some solutes showed minor impurities, but the main peaks were employed, using trace residues from an "emptied" microsyringe. Hold-up times, obtained by extrapolating to methane the retention times for *n*-heptane and *n*-hexane on semi-logarithmic graph paper, were deducted from the observed retention times. Relative retention times with respect to *n*-undecane were used.

2. Experimental

2.1. Apparatus

A Hewlett-Packard Model 5790A gas chromatograph was used, fitted with a capillary control unit and a splitter injection port. This latter, and the flame ionization detector, were maintained at 215°C . Helium was used as the mobile phase at a flow-rate of $0.6\text{--}1.1\text{ ml min}^{-1}$ and as the make-up gas to the detector. Oven temperatures of 100 and 125°C were used, heating and cooling the various stationary phase

3. Results and discussion

Relative retention times with respect to *n*-undecane for nine solutes determined at 100°C, with values previously found at 125°C [2,3], are presented in Table 1 for two selected CD phases. Here, the low-polarity solutes are arranged in decreasing sequence of literature boiling points. Three solutes present potential resolution problems, in that they all have boiling points around 177°C. In Fig. 2, the data are plotted for 100°C results, together with the lines of best fit for seven out of nine results on ChiralDEX A-PH, but for only four values from G-DA. The lines have correlation coefficients of 0.995 or more, but these are reduced if extra data points are included. γ -Terpinene and *p*-cymene on A-PH exhibit longer retentions than their boiling points imply; however, these two solutes, with α -terpinene and myrcene, behave linearly according to their boiling points on G-DA. With this latter phase all the bicyclics are considerably retained, and cineole and camphene values fall off the right side of the figure. These observations can be interpreted as evidence of selective CD host-guest solute interaction, in this case with the rigid box-like bicyclic molecules.

Berthod et al. [4], considering only the CD-

ester phase mechanism of resolving moderate polarity enantiomeric pairs, concluded that some solutes “form enantioselective inclusion complexes” whilst others “resolve as a result of ‘looser’ possible external... association”. They speculated that the “mechanism... may be temperature dependent (i.e., more... at low temperature)”. The considerably higher relative retention times at 100°C than 125°C in Table 1 for the bicyclics cineole and camphene on ChiralDEX G-DA agree with this.

At the higher temperature of 125°C on A-PH (Fig. 3), the same seven solutes give a different line of best fit. These lines for this phase can be defined by the following expressions for each contributing solute:

$$t_{R \text{ rel. } C_{11}} (125^\circ\text{C}) = 0.02606t - 3.61 \quad (2)$$

$$t_{R \text{ rel. } C_{11}} (100^\circ\text{C}) = 0.02389t - 3.37 \quad (3)$$

where *t* is solute boiling point in °C.

At 125°C, another α -CD phase, ChiralDEX A-DA (Fig. 3), has only five solutes exhibiting a linear relationship [3], but these include γ -terpinene and *p*-cymene as on G-DA. It is the bicyclics which again, on another smaller ring dipentyl-CD, exhibit extra retention, probably by molecular inclusion. As an example of a β -CD,

Table 1

Relative retention times (*n*-undecane = 1.00) on two modified cyclodextrin phases at 100°C (new observations) and at 125°C (from Refs. [2] and [3])

Solute	Boiling point (°C) at 760 mmHg	ChiralDEX A-PH		ChiralDEX G-DA		Increase (G-DA – A-PH) (%) at 100°C
		125°C	100°C	100°C	125°C	
γ -Terpinene	183 ^a	<i>1.29</i>	<i>1.18</i>	1.28	1.27	8
(+)-Limonene	177.7 ^b	1.03	0.88	<i>1.18</i>	<i>1.22</i>	34
<i>p</i> -Cymene	177.1 ^a	<i>1.22</i>	<i>1.08</i>	1.07	1.10	–1
Cineole	176.4 ^b	0.99	0.83	<i>3.88</i>	<i>2.95</i>	367
α -Terpinene	174.2 ^a (av.)	0.93	0.80	0.95	0.97	19
(+)-3-Carene	170.5 ^{a,b} (est.)	0.81	0.70	<i>1.30</i>	<i>1.27</i>	86
Myrcene	167 ^b	0.71	0.59	0.73	0.74	24
(+)-Camphene	158 ^b	<i>0.54</i>	0.43	<i>2.14</i>	<i>1.75</i>	398
α -Pinene	156.2 ^b	0.44	0.34	<i>1.24</i>	<i>1.12</i>	265

Italicized values do not conform to a linear relationship with the other solutes.

^a From the Merck Index, Merck, Rahway, NJ.

^b From *Handbook of Chemistry and Physics*, Chemical Rubber Co., Cleveland, OH.

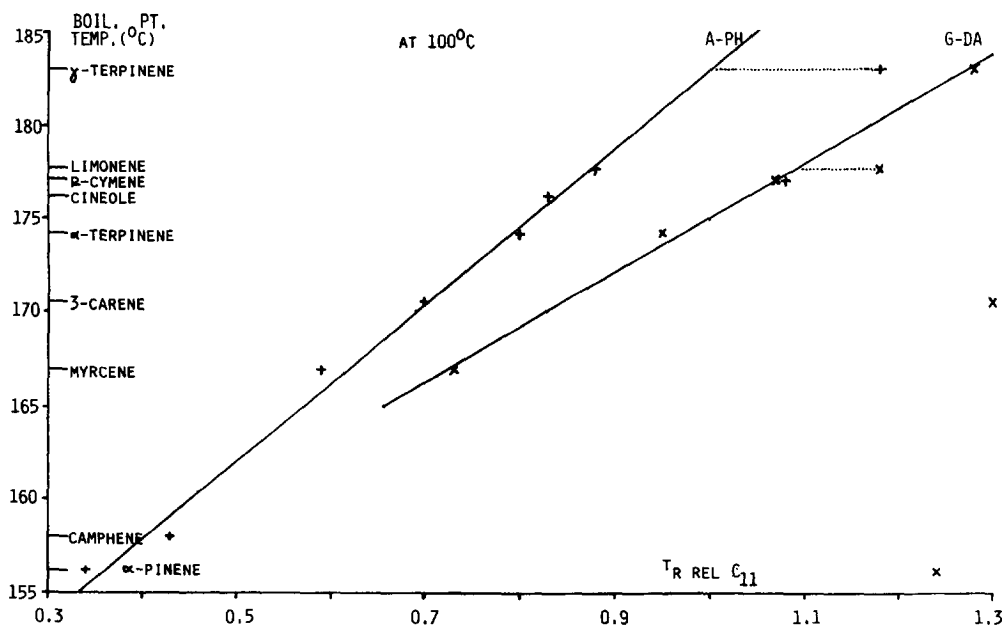


Fig. 2. Plots of nine solute relative retention times (*n*-undecane = 1.00) at 100°C against their boiling points (°C, 760 mmHg), with lines of best fit for some selected data points. (+) A-PH is hydroxypropyldimethyl- α -CD and (x) G-DA is dipentyl- γ -CD.

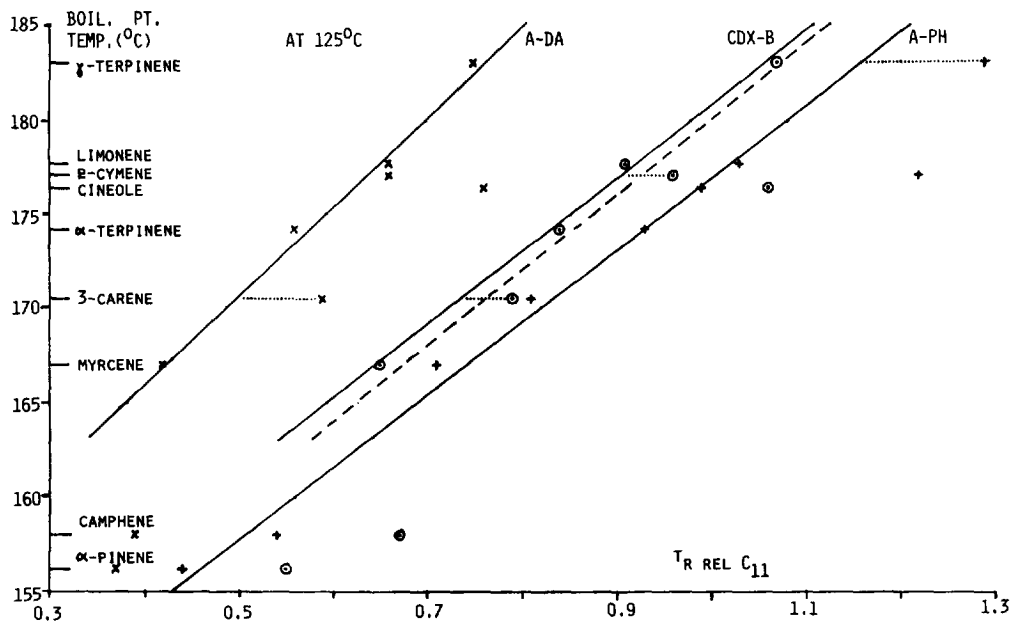


Fig. 3. Plots of nine solute relative retention times (*n*-undecane = 1.00) at 125°C against their boiling points (°C, 760 mmHg), with lines of best fit for some selected data points. (x) A-DA is dipentyl- α -CD, (+) A-PH is hydroxypropyldimethyl- α -CD and (⊙) CDX-B is trimethyl- β -CD. The dashed line of best fit for CDX-B uses six instead of four data points.

Cyclodex-B [5] behaves like A-DA (Fig. 3). It gives a correlation coefficient of 0.994 for four solutes [γ -terpinene, limonene, α -terpinene (all monocyclics) and myrcene] which falls to 0.976 if 3-carene and *p*-cymene are included (dashed line, Fig. 3). Fig. 4 displays G-DA results at 125°C [3], with a linear relationship again only apparent for the same four solutes, and the other five presumed to undergo special CD-phase interactions. The linear expressions for the G-DA phase are

$$t_{R \text{ rel. } C_{11}}(125^\circ\text{C}) = 0.03351t - 4.85 \quad (4)$$

$$t_{R \text{ rel. } C_{11}}(100^\circ\text{C}) = 0.03446t - 5.03 \quad (5)$$

Comparison with two other γ -CD phases, Chiraldexes G-PH and the ester G-PN [3], also revealed four-solute linearity, but with limonene replacing *p*-cymene as one of the set (Fig. 4). The only two solutes which always form part of the above linear plots on various CDs are the monocyclic α -terpinene and the acyclic myrcene. These are the only two molecules with conju-

gated sets of double bonds. The bicyclics rarely behave linearly, although it is seen on Chiraldex A-PH. The pair of CD phases in Fig. 2 represents the best combination to show selective retention of seven of the nine low-polarity solutes on one phase or the other, a likely result of host-guest molecular inclusions. The expressions derived for them (Eqs. 2–5) provide a means of noting abnormal retention of solutes by the CD phases. Table 1 includes the percentage increases in the relative retention times of solutes on changing from Chiraldex A-PH to G-DA at 100°C. The group of four bicyclic solutes shows the largest increase, of at least 86%, with two increasing by over 365%. The only aromatic solute is virtually unchanged in relative retention, leaving three monocyclics, with the acyclic monoterpene, showing a low 8–34% increase.

Table 2 presents the numbered elution sequence of the nine solutes (the top one usually emerging last) on the CD phases considered here at 125°C. This is not the simple sequence corresponding to increasing boiling points, as is given

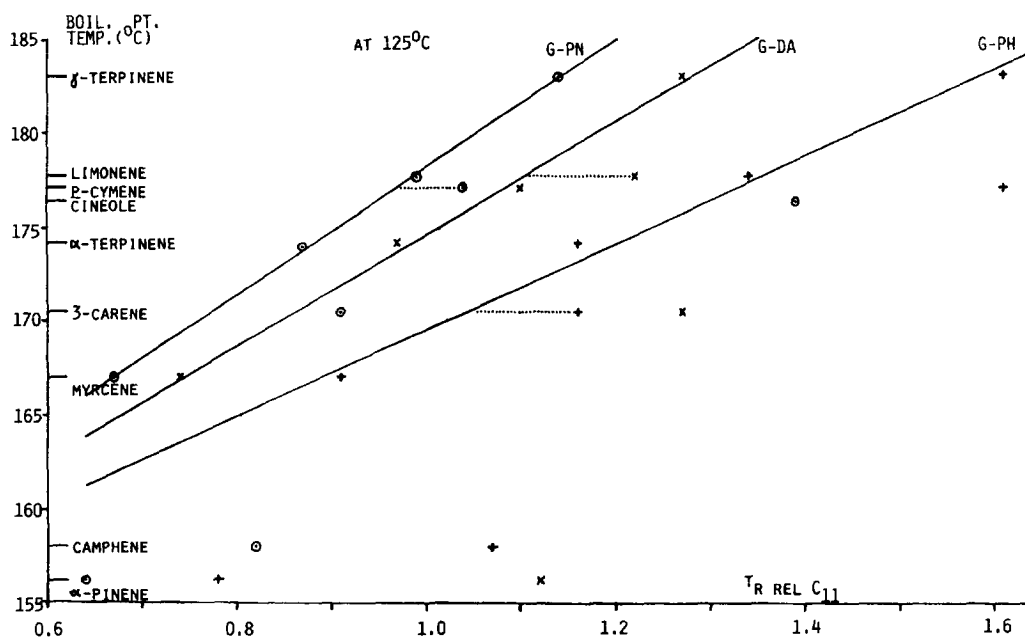


Fig. 4. Plots of nine solute relative retention times (*n*-undecane = 1.00) at 125°C against their boiling points (°C, 760 mmHg), with lines of best fit for some selected data points. (○) G-PN is propionyl-dipentyl- γ -CD, (×) G-DA is dipentyl- γ -CD and (+) G-PH is hydroxypropyl-dimethyl- γ -CD.

Table 2

Elution sequences at 125°C of nine low-polarity solutes (1 being first and 9 last) from six modified CD phases [2,3] and from methyl polysiloxane [3]

Solute	Chiraldex G-PN ^a	Chiraldex G-PH ^b	Chiraldex A-DA	Cyclodex-B	Methyl polysiloxane	Chiraldex A-PH	Chiraldex G-DA
Cineole	<i>9^c</i>	<i>9^c</i>	<i>9^d</i>	<i>8^d</i>	7	6	<i>9^c</i>
γ -Terpinene	8	7=	8	9	9	<i>9^d</i>	6
<i>p</i> -Cymene	7	<i>7=</i> ^d	6=	7	6	<i>8^d</i>	3
Limonene	6	6	6=	6	8	7	<i>5^d</i>
3-Carene	<i>5^d</i>	<i>4=</i>	<i>5</i>	<i>4</i>	4	4	<i>7^c</i>
α -Terpinene	4	4=	4	5	5	5	2
Camphene	<i>3^d</i>	<i>3^d</i>	2	3	2	2	<i>8^c</i>
Myrcene	2	2	3	2	3	3	1
α -Pinene	<i>1^d</i>	<i>1^d</i>	1	<i>1^d</i>	1	1	<i>4^c</i>

Solutes numbered in italics do not show a linear relationship with the other solutes and exhibit greater retention than is expected from their boiling points.

^a Chiraldex suffixes are explained in Section 2.1.

^b Using previously unpublished relative retention times with respect to *n*-undecane of cineole 1.90, γ -terpinene and *p*-cymene 1.58, limonene 1.34, 3-carene and α -terpinene 1.16, camphene 1.07, myrcene 0.91 and α -pinene 0.77.

^c Very strong extra retention.

^d Strong extra retention.

by low-polarity methyl polysiloxane phase [3]. Those solutes retained beyond the linear relationship are indicated in italics. In Table 2, G-DA is clearly the most aberrant CD phase, whilst A-PH comes closest to the boiling point sequence, except for the usual CD inversion of *p*-cymene (b.p. 177°C) after limonene (178°C). The largest boiling point sequence discrepancy is shown by bicyclic camphene (158°C) being delayed after myrcene (167°C), except on the two α -CDs. Bicyclic 3-carene (170°C) is also retained behind α -terpinene (174°C), except on A-PH and Cyclodex-B. Apart from these two CDs, another bicyclic, cineole (b.p. 176°C), is also delayed behind several other solutes, including γ -terpinene (183°C). The lowest boiling point (156°C) fourth bicyclic, α -pinene, although re-

tained on five of the six CDs, only emerges after some other solutes on G-DA, these including *p*-cymene. This latter aromatic substance exhibits extra retention on four CD phases. The solute sequences, and their changes, do not necessarily reveal possible solute-CD interactions.

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