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2,3-Di-*O*-methoxymethyl-6-*O*-*tert*-butyldimethylsilyl-β-cyclodextrin, a useful stationary phase for gas chromatographic separation of enantiomers

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Abstract

Heptakis(2,3-*di*-*O*-methoxymethyl-6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (2,3-MOM-6-TBDMS-β-CD), synthesized by using methoxymethylchloride (MOM-Cl) as derivatization reagent, was used for capillary gas chromatographic separation of enantiomers. The new chiral stationary phase proved to be suitable for the enantiodifferentiation of volatiles from various chemical classes. Compared to the corresponding γ-CD derivative (2,3-MOM-6-TBDMS-γ-CD), the spectrum of compounds for which enantiomers could be separated was more limited and the enantioseparation achieved was generally less pronounced. Unusually high separation factors were observed for 2-alkyl esters of short chain acids (C_2–C_6). Phenomena underlying the enantioseparation of 2-pentyl acetate (α: 4.31; 35 °C) were investigated by determining thermodynamic parameters. Data show that only one enantiomer is retained significantly on the chiral stationary phase whereas the other one behaves like the hydrocarbons used as references.

Keywords: Cyclodextrin; Chiral stationary phase; Methoxymethyl; Side-chain; Enantioseparation

1. Introduction

Cyclodextrins (CD) are the most popular chiral stationary phases (CSP) presently used in gas chromatographic analysis [1–3]. They have found wide application especially for enantiodifferentiations of chiral flavor and fragrance compounds [4,5]. To make cyclodextrins suitable as stationary phases, the free hydroxy groups have been subjected to various types of derivatizations [3]. Blocking the 6-hydroxy position of the glucose unit with a bulky silyl group and subsequent modification of the 2,3-hydroxy groups by acylation or alkylation resulted in useful CSP [6,7]. Recently, a new class of cyclodextrin derivatives bearing acetal functions at positions 2 and 3 of the glucose units has been introduced as chiral stationary phase [8]. Octakis(2,3-di-*O*-methoxymethyl-6-*O*-*tert*-butyldimethylsilyl)-γ-cyclodextrin (2,3-MOM-6-TBDMS-γ-CD) has been shown to be suitable for the separation of enantiomers of a broad spectrum of volatiles from various chemical classes. High α values were determined for α-hydroxy ketones (e.g., 1.8 for acetoin) and some methyl branched ketones. The enantiomers of cyclic pentenolone and furanone derivatives were also well separated.

To investigate the influence of the size of the cyclodextrin torus on the enantiodifferentiations achieved after introducing acetal groups as side chains, the corresponding β-cyclodextrin derivative was synthesized. This paper presents separation characteristics of heptakis(2,3-di-*O*-methoxymethyl-6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (2,3-MOM6-TBDMS-β-CD).

2. Experimental

2.1. Materials

β-Cyclodextrin was obtained from Tokyo Kasei Kōgyō (Tokyo, Japan). Purification of the crude material was

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accomplished by column chromatography using silica gel 60 from Merck (Darmstadt, Germany) with toluene and ethanol (95%) as eluting solvent. The effluent was monitored by thin-layer chromatography (TLC) on silica gel plates Polygram Sil G/UV$_{254}$ from Macherey–Nagel (Düren, Germany) and the spots were detected by dipping the TLC sheets into acidic phosphomolybdic acid and subsequent heating to 105 °C for 5 min. *tert*-Butyldimethylchlorosilane was obtained from Merck-Schuchardt (Hohenbrunn, Germany) and diisopropylethylamine and methoxymethylchloride from Aldrich (Steinheim, Germany). Polysiloxane OV-1701vi was purchased from Supelco (Bellefonte PA, USA) and raw fused-silica capillary column was obtained from Microquartz (Munich, Germany). Other commonly used reagents and solvents were obtained from Aldrich and Fluka (Buchs, Switzerland), respectively.

2.2. Instruments

NMR spectra were recorded with a Bruker AC 250 spectrometer (^{1}H 250.133 MHz, ^{13}C 62.896 MHz) with ASPECT 3000 workstation running DISR94 program. The chemical shift values for both ^{1}H and ^{13}C spectra were recorded in part per million and acetone-d_6 was used as solvent and internal chemical shift standard (2.05 ppm and 30.8 ppm, respectively).

Mass spectrometry data were obtained after direct introduction of the derivatized CD (methanol solution) into an Esquire 3000+ (Bruker) instrument. Electron spray ionization was used to ionize the cyclodextrin molecule in positive mode, with source voltage of 4.0 kV, nebulizer gas flow of 5.0 L/min (operating at 69 kPa) and drying temperature of 300 °C.

Gas chromatograms were recorded on Carlo Erba Strumentazione models 4130 and 4160 equipped with flame ionization detectors. The chromatograms were processed by the Chromcard system from Thermoquest (Milan, Italy). Hydrogen was used as carrier gas at an inlet pressure of 100 kPa, and the analytes were introduced via split injection (split ratio, 30:1) of solutions (1 μL) of the samples in diethyl ether (0.2 μg/mL). Injector and detector temperatures were 220 °C and 230 °C, respectively.

A glass drying oven (bulb-to-bulb distillation apparatus) B-580 GKR from Büchi (Flawil, Switzerland) was used to dry the intermediate cyclodextrin derivative.

2.3. Synthesis of heptakis(2,3-di-O-methoxymethyl-6-O-tert-butyldimethylsilyl)-β-cyclodextrin

Heptakis(6-*O*-TBDMS)-β-cyclodextrin was synthesized according to a procedure described by Fuegedi [9]. This intermediate was heated at 100 °C under high vacuum (0.001 mmHg) overnight using a bulb-to-bulb distillation apparatus. The obtained dry heptakis(6-*O*-TBDMS)-β-cyclodextrin (206 mg) was dissolved in dry dichloromethane (10 mL). Diisopropylethylamine (3.5 g) was added at room temperature and stirred. The clear solution was cooled to 0 °C with an ice-water bath and methoxymethylchloride (1.59 g) was added drop-wise. After stirring at 0 °C for 15 min, the solution was allowed to warm up to room temperature and then stirred overnight at 40 °C. After TLC analysis showed completion of the reaction, the reaction mixture was poured into a water/MTBE mixture and extracted with MTBE. The organic phase was washed with 1N HCl aq., water, sodium bicarbonate solution, saturated sodium chloride solution and dried over anhydrous magnesium sulfate, concentrated and purified by column chromatography (Silica gel 60, toluene:ethanol = 93:7, v/v) to yield 174 mg of the titled compound as fine white powder (isolated yield, 64%). The structure was checked by means of NMR (^{1}H, ^{13}C and DEPT 135) and MS.

2.3.1. ^{1}H NMR

0.02 [*s*; 42H; Si(C**H**$_3$)$_2$]; 0.95 (*s*; 63H; Si(C**H**$_3$)$_3$); 3.38–3.42 (*m*; 7H; H$_2$); 3.39 (s; 21H; –OCH$_2$OC**H**$_3$); 3.44 (s; 21H; –OCH$_2$OC**H**$_3$); 3.62–3.80 (*m*; 14H; H$_6$); 3.88–4.02 (*m*; 14H; H$_3$ + H$_4$); 4.33 (*d*; *J* = 11.8 Hz; 7H; H$_5$); 4.75 (*d*; *J* = 7.0 Hz; 7H; –OC**H**$_2$OCH$_3$); 4.79 (*d*; *J* = 7.0 Hz; 7H; –OC**H**$_2$OCH$_3$); 4.83 (*d*; *J* = 6.3 Hz; 7H; –OC**H**$_2$OCH$_3$); 5.02 (*d*; *J* = 6.3 Hz; 7H; –OC**H**$_2$OCH$_3$); 5.30 (*d*; *J* = 3.0 Hz; 7H; H$_1$).

2.3.2. ^{13}C NMR

−3.6 [Si(***C***H$_3$)$_2$C(CH$_3$)$_3$], −3.3 [Si(***C***H$_3$)$_2$C(CH$_3$)$_3$], 20.0 [Si(CH$_3$)$_2$***C***(CH$_3$)$_3$], 27.5 [Si(CH$_3$)$_2$C(***C***H$_3$)$_3$], 57.12 [–OCH$_2$O***C***H$_3$], 57.14 [–OCH$_2$O***C***H$_3$], 64.3 (C6), 74.0, 78.7, 79.6, 80.0 (C2, C3, C4, C5), 99.5 (–O***C***H$_2$OCH$_3$), 100.6 (–O***C***H$_2$OCH$_3$), 101.0 (C1).

2.3.3. MS

m/*z* = 2573.6 [M + Na + H].

2.4. Synthesis of octakis(2,3-di-O-methoxymethyl-6-O-tert-butyldimethylsilyl)-γ-cyclodextrin

Octakis(2,3-di-*O*-methoxymethyl-6-*O*-TBDMS)-γ-cyclodextrin was synthesized as previously described [8].

2.5. Preparation of the capillary columns

The cyclodextrin derivative synthesized was diluted in polysiloxane OV-1701vi (0.11 mol/kg) for use as GC stationary phase. Untreated fused-silica capillary column (i.d., 0.25 mm; length, 30 m) was deactivated using phenyldimethylsilane at 380 °C (reaction time: 10 h). The deactivated fused-silica column thus prepared was coated with the above-described phase by means of the static coating method according to Grob [10]. A mixture of *n*-pentane and dichloromethane (1:1, v/v) was used as solvent in the coating procedure. The column was coated in stationary phase thickness of 0.25 μm. After coating

was completed, the column was mounted on a GC oven and conditioned as follows: 40 °C (initial temperature, 15 min hold), then ramp at rate of 2 °C/min to 210 °C (final temperature, held for 4 h). The column thus prepared was tested by injecting 1 μL of Grob-I test mixture [10].

2.6. Equations used for calculation of thermodynamic parameters

Thermodynamic data were acquired and processed according to the approach introduced by Schurig and Jung [11] using the following equations.

$$R'_{(E1)} = \frac{r_{(E1)} - r_0}{r_0} \quad (1a)$$

$$R'_{(E2)} = \frac{r_{(E2)} - r_0}{r_0} \quad (1b)$$

$$R \ln \left(\frac{R'_{(E2)}}{R'_{(E1)}} \right) = - \left(\frac{\Delta_{E1,E2}(\Delta H^0)}{T} \right) + \Delta_{E1,E2}(\Delta S^0) \quad (2)$$

where r_0: ratio of net retentions of the analyte and a reference hydrocarbon on the achiral phase; $r_{(E1)}$, $r_{(E2)}$: ratios of net retentions of the analyte and a reference hydrocarbon on the chiral phase for the first and second eluted enantiomer; $R'_{(E1)}$, $R'_{(E2)}$: retention increases for the first and second eluted enantiomer; R: gas constant; T: absolute temperature (K); $\Delta_{E1,E2}(\Delta H^0)$: association enthalpy (J/mol); $\Delta_{E1,E2}(\Delta S^0)$: association entropy (J mol^{-1} K^{-1}).

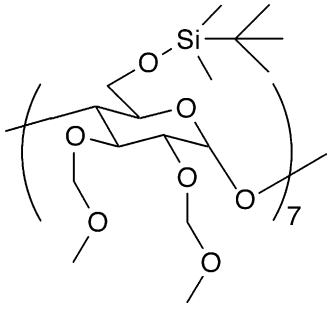

Fig. 1. Structure of 2,3-MOM-6-TBDMS-β-CD.

3. Results and discussion

Heptakis(2,3-di-*O*-methoxymethyl-6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin (2,3-MOM-6-TBDMS-β-CD; Fig. 1) was obtained by reaction of heptakis(6-*O*-*tert*-butyldimethylsilyl)-β-cyclodextrin with methoxymethylchloride (MOM-Cl). In analogy to the synthesis of 2,3-MOM-6-TBDMS-γ-CD [8], the reaction proceeded efficiently and resulted in sufficient and reproducible yield.

The column was prepared by statically coating a fused-silica capillary with 28% (w/w) 2,3-MOM-6-TBDMS-β-CD in OV-1701vi (film thickness: 0.25 μm). Its general performance was tested using the Grob test mixture I. Except for a tailing observed for the acid, the column exhibited excellent performance for all compound classes contained in the mixture (Fig. 2).

For 2,3-MOM-6-TBDMS-γ-CD, the stability of the acetal groups present as side chains has been demonstrated by repeated injection of water-containing samples [8]. 2,3-

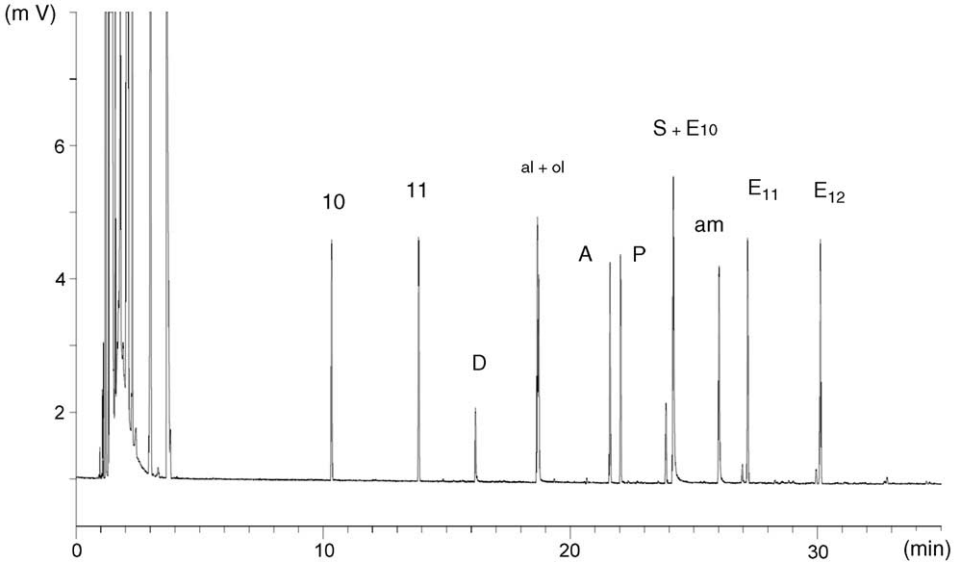

Fig. 2. Grob test chromatogram of a 2,3-MOM-6-TBDMS-β-CD (0.11 M OV-1701vi) column. Temperature programming: 40 °C initial (2 min hold) then ramp at 4.0 °C/min rate. 10: *n*-decane; 11: *n*-undecane; D: (−)-2,3-butanediol; al: 1-nonanal; ol: 1-octanol; A: 2,6-dimethylaniline; P: 2,6-dimethylphenol; E10: methyl *n*-decanoate; S: 2-ethylhexanoic acid; am: dicyclohexylamine; E11: methyl *n*-undecanoate; E12: methyl *n*-dodecanoate.

MOM-6-TBDMS-β-CD also proved to be stable under harsh conditions (e.g., heating at 220 °C for 12 h, injection of free alkanoic acids or temperature programming up to 230 °C); a column used daily for 10 months showed no decrease in performance.

The properties of the new stationary phase were assessed by testing enantioseparations of various flavor compounds representing different chemical classes. Table 1 shows data for compounds the enantiomers of which had been separated on 2,3-MOM-6-TBDMS-γ-CD [8] and which could also be enantiodifferentiated on the β-CD analog.

As shown in Table 1, among the methyl branched compounds representatives of alcohols, ketones and esters could be separated into their enantiomers. However, neither methyl branched aldehydes and their acetals nor 2-methyl branched acids could be resolved satisfactorily. The ketones 3-methyl-2-pentanone, 5-methyl-2-hepten-4-one (Filbertone®) and 3,3,5-trimethylcyclohexanone which exhibited good resolutions on 2,3-MOM-6-TBDMS-γ-CD (α: 1.65, 1.69 and 1.60, respectively) were also well separated on 2,3-MOM-6-TBDMS-β-CD, but with slightly lower separation factors.

2,3-MOM-6-TBDMS-β-CD turned out to be not very suitable for the separation of enantiomers of secondary alcohols. Investigations of saturated and unsaturated representatives showed that 2-methyl-3-hexanol, 2-heptanol, 3-buten-2-ol and 3-octen-2-ol could be moderately resolved into their enantiomers; however, 2-butanol, 2-pentanol, 2-hexanol, 5-methylhexanol, 1-penten-3-ol and 1-octen-3-ol could not be separated.

Except for δ-heptalactone, the enantiomers of δ-lactones could not be separated on 2,3-MOM-6-TBDMS-β-CD. The separation factors determined for γ-lactones are in the same range as those observed on 2,3-MOM-6-TBDMS-γ-CD. For sotolone, a γ-lactone possessing an enol-structure in the ring, the separation (α: 1.49) was significantly better on 2,3-MOM-6-TBDMS-β-CD than on the corresponding γ-CD analog (α: 1.15).

In the class of aromatic compounds it is interesting to note that the separation factor for 1-phenylethanol on 2,3-MOM-6-TBDMS-β-CD is lower than on 2,3-MOM-6-TBDMS-γ-CD (α: 1.05 versus 1.14), whereas the corresponding acetate is resolved much better on the β-CD derivative (α: 1.22 versus 1.06).

For acetoin, the hydroxy ketone for which a high α-value of 1.81 has been determined on 2,3-MOM-6-TBDMS-γ-CD, the separation factor observed on the β-CD derivative was also in the upper range (α: 1.46). On the other hand, the pronounced enantioseparations observed for cyclic pentenolones on 2,3-MOM-6-TBDMS-γ-CD could not be confirmed on 2,3-MOM-6-TBDMS-β-CD; for example, 3,5-dimethyl-2-hydroxy-2-cyclopentenone (Coronol®) was not separated at all into its enantiomers. The tertiary monoterpene alcohol linalool which had not been separated on 2,3-MOM-6-TBDMS-γ-CD showed a sufficiently high separation factor on 2,3-MOM-6-TBDMS-β-CD.

Apart from a few exceptions, the overall conclusion to be drawn from the comparison of separation characteristics as summarized in Table 1 is that 2,3-MOM-6-TBDMS-β-CD is a useful stationary phase for gas chromatographic separation of enantiomers of compounds from various chemical classes. However, compared to 2,3-MOM-6-TBDMS-γ-CD the spectrum of compounds for which enantiomers can be separated is more limited and the enantioseparations achieved are generally less pronounced.

An additional class of flavoring compounds which in the course of the present study was included in the set of substances screened to test the potential of 2,3-MOM-6-TBDMS-β-CD and which had not been tested previously on 2,3-MOM-6-TBDMS-γ-CD are esters of secondary alcohols. For 2-pentyl acetate a high separation factor α of 4.31 ($K_1 = 20.61$ at 35 °C isothermal) was found. So far, α-values in that order of magnitude have been mainly reported for compounds containing halo atoms [12–15], among them 2-(fluoromethoxy)-3-methoxy-1,1,1,3,3-pentafluoropropane, for which a separation factor of 10 has been observed on Lipodex E [16].

Based on this result obtained for 2-pentyl acetate (Fig. 3), a homologous series of esters of secondary alcohols varying in chain lengths were investigated. A comparison of the separation data determined on 2,3-MOM-6-TBDMS-β-CD and 2,3-MOM-6-TBDMS-γ-CD is given in Table 2. On both stationary phases the separation factors decreased with increasing chain lengths of the acyl moieties (from acetate to hexanoate) and of the alcohol moieties (from 2-pentanol to 2-nonanol). The suitability for enantiodifferentiation of the acetates of secondary alcohols was especially pronounced for 2,3-MOM-6-TBDMS-β-CD. On 2,3-MOM-6-TBDMS-γ-CD the decreases in separation factors upon elongation of the acid chain length were not so drastic; consequentially, α-values determined for the butanoates and hexanoates are higher on the 2,3-MOM-6-TBDMS-γ-CD than on the β-CD derivative.

It is interesting to note that in contrast to the good enantioseparations observed for the esters of secondary alcohols on 2,3-MOM-6-TBDMS-β-CD the corresponding free alcohols 2-pentanol and 2-nonanol could not be separated and the α-value observed for 2-heptanol was rather low. The above-described differences in separation factors for 1-phenylethanol and 1-phenylethyl acetate on 2,3-MOM-6-TBDMS-β-CD are in agreement with these observations.

To get some understanding of the phenomena underlying the enantioseparation of 2-pentyl acetate on 2,3-MOM-6-TBDMS-β-CD, thermodynamic parameters were determined. Since the cyclodextrin derivative is used as stationary phase after dilution in OV-1701vi silicone, a method introduced by Schurig and Jung [11] is applicable. According to this procedure, thermodynamic data of chiral recognition ($\Delta_{R,S}(\Delta G)$, $\Delta_{R,S}(\Delta H)$ and $\Delta_{R,S}(\Delta S)$) can be determined by measuring the retention increments R' of the enantiomers on the cyclodextrin dissolved in the solvent (i.e., OV-1701vi) in comparison to a reference column

Table 1
Separation characteristics of 2,3-MOM-6-TBDMS-β-CD

Compound	T (°C)	k_1	α	R_S
Methyl branched compounds				
Alcohols				
2-Methylbutanol	40	28.90	1.04	2.03
2-Methylpentanol	55	18.01	1.02	1.43
Ketones				
3-Methyl-2-pentanone	40	17.80	1.50	22.07
5-Methyl-2-hepten-4-one	65	16.48	1.55	28.93
2-Methylcyclohexanone	70	15.62	1.03	1.90
3-Methylcyclohexanone	75	15.08	1.02	1.18
3,3,5-Trimethylcyclohexanone	80	16.54	1.43	25.55
2-Methylcyclopentanone	60	13.50	1.08	3.48
Esters				
Methyl 2-methylbutanoate	40	10.73	1.09	4.68
Ethyl 2-methylbutanoate	40	15.16	1.10	5.78
Propyl 2-methylbutanoate	60	16.90	1.04	2.34
Butyl 2-methylbutanoate	60	21.90	1.02	1.56
Secondary alcohols				
2-Methyl-3-hexanol	60	15.07	1.07	4.13
2-Heptanol	60	22.72	1.03	1.63
3-Buten-2-ol	30	12.21	1.04	1.67
3-Octen-2-ol	65	35.34	1.02	1.31
Lactones				
γ-Pentalactone	100	9.65	1.28	15.19
γ-Hexalactone	110	8.98	1.15	10.20
γ-Heptalactone	120	9.09	1.10	6.79
γ-Octalactone	130	9.83	1.05	3.61
γ-Nonalactone	140	10.60	1.04	2.82
γ-Decalactone	150	11.24	1.03	1.99
γ-Undecalactone	160	11.74	1.02	1.40
γ-Dodecalactone	170	12.40	1.01	1.10
trans-Whiskey lactone	120	16.42	1.08	5.99
cis-Whiskey lactone	120	21.10	1.01	1.07
Sotolone	125	11.19	1.49	29.58
δ-Heptalactone	120	11.82	1.02	1.38
ε-Decalactone	140	13.98	1.03	2.37
Aromatics				
1-Phenylethanol	100	11.85	1.05	3.30
Hydratropalcohol	110	11.53	1.03	2.28
1-Phenylethyl acetate	90	19.48	1.22	15.48
1-Phenylethyl propanoate	100	19.79	1.02	1.26
(*E*)-Ethyl methylphenylglycidate	140	16.23	1.02	1.54
Sulfur-containing compounds				
2-Pentanethiol	40	9.79	1.06	3.12
threo-2-Mercapto-3-butanol	70	24.73	1.02	1.11
cis-2-Methyl-4-propyl-1,3-oxathiane	85	16.55	1.03	2.13
trans-2-Methyl-4-propyl-1,3-oxathiane	85	21.74	1.05	3.95
Miscellaneous				
Limonene	50	25.10	1.03	2.05
Linalool	80	13.70	1.02	1.42
Acetoin	70	12.38	1.46	19.65
Acetoin *n*-butanoate	80	20.08	1.11	7.33
3,4-Dimethyl-2-hydroxy-2-cyclopentenone (methyl corylone)	90	23.68	1.27	19.85
2-Methyltetrahydrofuran-3-one	60	12.10	1.04	2.84
Ethyl 3-hydroxyhexanoate	80	11.83	1.06	4.33
1-Octen-3-yl acetate	80	13.47	1.32	19.62

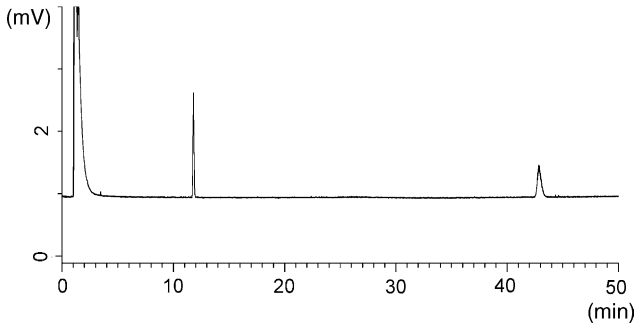

Fig. 3. Separation of the enantiomers of 2-pentyl acetate on 2,3-MOM-6-TBDMS-β-CD (40 °C, isothermal).

coated only with the dissolving achiral phase. In addition to 2-pentyl acetate, the procedure was also performed for γ-pentalactone. This compound was selected as comparator because it exhibits a moderately high α-value on 2,3-MOM-6-TBDMS-β-CD and its thermodynamic parameters have been determined on another CD derivative [17].

Retention increments for the enantiomers of γ-pentalactone obtained using reference standards (*n*-decane to *n*-pentadecane) at 85 °C are listed in Table 3. Additionally, retention increments data using the same hydrocarbon standards were elaborated in a temperature range from 85 °C to 115 °C at 5 °C temperature intervals. Average ratios $R'_{(E2)}/R'_{(E1)}$ were determined and the correlation between $R\ \ln(R'_{(E2)}/R'_{(E1)})$ and $1/T$ is depicted in Fig. 4a. On

Table 2
Comparison of the separations of 2-alkyl esters on 2,3-MOM-6-TBDMS-β-CD and 2,3-MOM-6-TBDMS-γ-CD

	2,3-MOM-6-TBDMS-β-CD			2,3-MOM-6-TBDMS-γ-CD		
	α	k_1	T (°C)	α	k_1	T (°C)
2-Pentyl acetate	3.80	15.1	40	2.44	13.1	35
2-Pentyl butanoate	1.09	12.3	65	1.68	13.0	60
2-Pentyl hexanoate	1.03	14.3	90	1.14	14.6	85
2-Heptyl acetate	1.72	13.4	70	1.30	15.8	60
2-Heptyl butanoate	1.03	13.9	90	1.15	14.1	85
2-Heptyl hexanoate	1.01	16.8	110	1.03	14.2	110
2-Nonyl acetate	1.25	13.8	95	1.10	14.0	90
2-Nonyl butanoate	1.01	13.5	115	1.05	14.1	110
2-Nonyl hexanoate	[a]	14.0	135	1.01	15.9	130

The separation factor (α), the adjusted retention factor for the first eluted enantiomer (k_1) and the oven temperature (°C) are given.
[a] No resolution.

Table 3
Relative retention data of γ-pentalactone and 2-pentyl acetate measured on 2,3-MOM-6-TBDMS-β-CD and a reference column containing OV-1701vi only

Standard	T (°C)	r_0	$r_{(E1)}$	$r_{(E2)}$	$R'_{(E1)}$	$R'_{(E2)}$	$\Delta\Delta G$ (kJ/mol)
γ-Pentalactone							
n-Decane	85	3.07	8.04	11.08	1.62	2.61	−1.42
n-Undecane	85	1.610	4.08	5.62	1.53	2.49	−1.44
n-Dodecane	85	0.834	2.04	2.81	1.45	2.37	−1.47
n-Tridecane	85	0.430	1.02	1.40	1.37	2.26	−1.50
n-Tetradecane	85	0.221	0.504	0.695	1.28	2.14	−1.53
n-Pentadecane	85	0.114	0.251	0.346	1.20	2.04	−1.57
2-Pentyl acetate							
n-Octane	35	2.849	3.20	13.77	0.12	3.83	−8.84
	40	2.728	3.01	11.43	0.10	3.19	−8.93
	45	2.635	2.85	9.84	0.08	2.56	−9.17
	50	2.522	2.68	7.76	0.06	2.08	−9.35
	55	2.440	2.55	6.38	0.04	1.61	−9.85
	60	2.341	2.41	5.38	0.03	1.30	−10.4
	65	2.247	2.27	4.45	0.01	0.98	−12.5
n-Nonane	35	1.154	1.22	5.24	0.05	3.54	−10.7
	40	1.144	1.19	4.51	0.04	2.94	−11.4
	45	1.136	1.16	3.82	−0.04	2.18	–
	50	1.126	1.13	3.28	−0.05	1.36	–
	55	1.120	1.12	2.80	−0.03	1.50	–
	60	1.111	1.10	2.45	−0.01	1.20	–
	65	1.104	1.08	2.12	−0.02	0.92	–

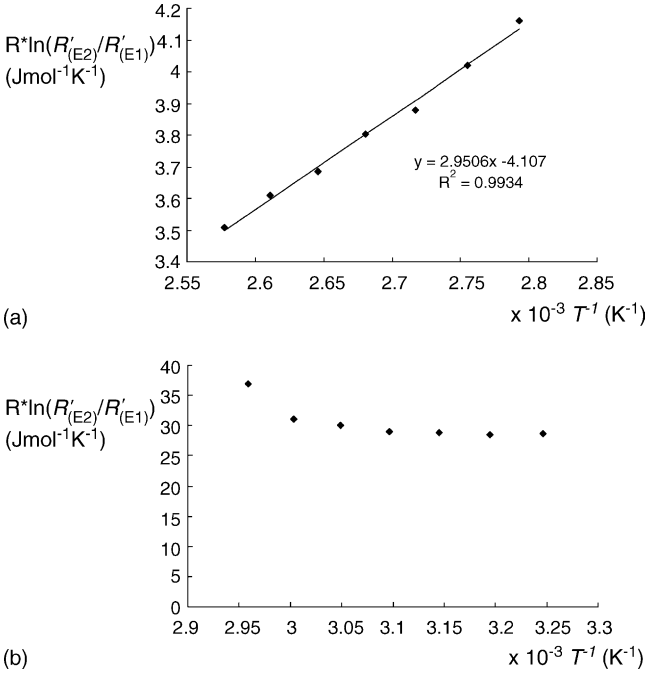

Fig. 4. Plot of $R\ \ln(R'_{(E2)}/R'_{(E1)})$ vs. T^{-1} for: (a) γ-pentalactone: averaged $R\ \ln(R'_{(E2)}/R'_{(E1)})$ from datasets utilizing standards through C_{10}–C_{15} was used to plot the data. Estimated association enthalpy and association entropy was $\Delta_{E2,E1}(\Delta H_0) = -2.95$ kJ/mol, $\Delta_{E2,E1}(\Delta S_0) = -4.11$ J mol^{-1} K^{-1}, respectively, and T_{ISO} was calculated to be 445 °C; (b) 2-pentyl acetate: plot of $R\ \ln(R'_{(E2)}/R'_{(E1)})$ vs. T^{-1}. Datasets shown on Table 3 utilizing *n*-octane as standard were used to plot the data.

the basis of the linear regression ($R^2 > 0.99$), the thermodynamic parameters ($\Delta_{R,S}(\Delta H_0) = -2.95$ kJ/mol, $\Delta_{R,S}(\Delta S_0) = -4.11$ kJ/mol) as well as the isoenantioselective temperature ($T_{iso} = 445$ °C) could be determined.

The attempt to determine thermodynamic parameters for the separation of 2-pentyl acetate on 2,3-MOM-6-TBDMS-β-CD by the same approach is summarized in Table 3. Using *n*-octane as standard it was possible to estimate $\Delta\Delta G$ but the plot of $R\ \ln(R_{(E2)}/R_{(E1)})$ versus $1/T$ did not result in a linear relationship and the calculation of the thermodynamic parameters was not possible (Fig. 4b).

The retention increments R' for the enantiomers of γ-pentalactone range from 1.20 to 1.62 for the first and from 2.04 to 2.61 for the second eluted enantiomer (Table 3). They are lower than those calculated from data reported for the enantioseparation of γ-pentalactone on 2,3-*O*-*n*-propanoyl-6-*O*-TBDMS-γ-CD ($R'_{(E1)}$, 5.26–12.2 and $R'_{(E2)}$, 5.46–13.0) [17]. That means, the interactions of the enantiomers with this CD derivative are stronger than those with 2,3-MOM-6-TBDMS-β-CD. However, the differences between the two enantiomers are more pronounced on 2,3-MOM-6-TBDMS-β-CD.

In contrast, for 2-pentyl acetate, only the retention increments for the second eluted enantiomers are in the order of magnitude as reported for enantiodifferentiations on cyclodextrin stationary phases [11,16,18,19]. For the first eluted enantiomer, however, the R' values are extremely low, indicating that the interactions of this enantiomer with the chiral selector are comparable to the interactions of the hydrocarbons used as references.

Different types of ratios of retention increments resulting in enantiodifferentiations have been reported [11,17–19]. As to the authors' knowledge, the phenomenon shown for the enantioseparation of 2-pentyl acetate on 2,3-MOM-6-TBDMS-β-CD, i.e., only one enantiomer is significantly retained whereas the other one shows a retention behavior comparable to the hydrocarbons used as references, has not yet been described. Analogous studies are in progress to find out whether this principle is of general relevance for enantioseparations on CD derivatives possessing acetal groups as side chains.

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