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Liquid chromatographic resolution of enantiomers of deltahedral carborane and metallaborane derivatives

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ABSTRACT

A successful liquid chromatographic separation of twelve enantiomeric pairs of zwitterionic eleven-vertex *nido*-carboranes of the type L-R-7,8-$C_2B_9H_{10}$ (L = Me_2S, Me_2SCH_2, C_6H_5N, $C_6H_5NCH_2$; R = H, CH_3, C_6H_5; Me = methyl) and of the 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ mixed sandwich complex on β-cyclodextrin (CD) chiral stationary phases (CSP) in aqueous–organic mobile phases is described. A comparison of two β-CD CSP columns. Tessek β-CD and Astec Cyclobond I, differing in enantioselectivity and resolution of individual compounds (to some extent), is presented together with a study of the factors controlling retention and enantiomeric resolution.

INTRODUCTION

Because of its efficiency, speed, wide applicability and reproducibility, liguid chromatography (LC) on chiral stationary phases (CSPs) has received considerable attention in organic chemistry in last decade [1–3]. However, it seems that no attempt at extending the chromatographic resolution of enantiomers (CRE) to protochiral deltahedral borane derivatives has been reported. Bearing in mind that only about twenty chiral compounds with deltahedral boron cages have so far been reported [4], it is difficult to overestimate the impact of LC separations with the use of CSPs in this area of research. It could open up a new vast realm of stereochemically unique systems for subtle mechanistic studies, for chiral catalysis and eventually for biochemical applications. This is why we decided to modify the current CRE techniques for protochiral deltahedral boron cage species. The task is not trivial because the deltahedral boron derivatives are different from organic species both in molecular architecture and in general properties [5–7].

In our first attempts we tried to solve this problem by applying commercially available CSPs and columns for chiral separations. The columns used were the *d*-phenylglycine column [2,8] and columns with various types of cyclodextrin (CD)-bonded CSPs [9–17].

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EXPERIMENTAL

Columns

A Pirkle concept covalently bonded 3,5-dinitrobenzoyl-*d*-phenylglycine (5 μm) column (250 × 4 mm I.D.) was purchased from Regis (Norton

0021-9673/92/$05.00

Grove, IL, USA). A silica material Separon SGX (7 μm) column (250 × 4 I.D. mm) from Tessek (Prague, Czechoslovakia) was used for purity monitoring of the solutes.

β-Cyclodextrin high-performance liquid chromatographic (HPLC) columns were purchased as follows: column A, from Tessek, 7 μm (250 × 4 mm I.D.), β-CD directly bonded to the silica support; column B, from Astec (Whippany, NY, USA) Cyclobond I, 5 μm (250 × 4.6 mm I.D.), β-CD covalently bonded to silica via a 6–8-atom spacer (not containing nitrogen atoms). The void volumes of the β-CD columns were determined according to the reported method [11].

α-Cyclodextrin (4 μm) (250 mm × 4 mm I.D.) and γ-cyclodextrin (glass cartridge, 150 × 3 mm I.D.) columns were packed with Daltosin 100 (Serva, Heidelberg, Germany) α-CD and γ-CD CSPs by a slurry packing method in the Tessek Service Department.

Eluents

HPLC-grade acetonitrile and dichloromethane were obtained from Merck (Darmstadt, Germany) and were used as purchased. Deionized water was used for the preparation of aqueous–organic mobile phases. All other chemicals were of analytical-reagent grade (Lachema, Brno, Czechoslovakia and Laborchemie, Apolda, Germany). Methanol, 2-propanol, *tert.*-butanol and *n*-hexane were distilled before use. *n*-Hexane was dried over a 4 Å molecular sieve prior to distillation. The eluents were filtered through a 0.45-μm filter and briefly degassed under vacuum.

Apparatus

The chromatographic equipment consisted of a VCR 40 pulseless dual-piston, high-pressure pump (Development Workshops, Czechoslovak Academy of Sciences, Prague, Czechoslovakia), a Rheodyne (Cotati, CA, USA) Model 7125 sampling valve with 10- or 20-μl loops, an LCD 2040 variable-wavelength (190–360 nm) UV spectrophotometric detector (Laboratory Instruments, Prague, Czechoslovakia), a PKS-1 column holder (Tessek), a glass column-cooling jacket with circulating water from an MK 70 cryostat (MLW, Germany), a Servogor 2s line recorder (Brown Boveri, Germany) and a CI 100 integrator (Laboratory Instruments).

Sample preparation and detection

All deltahedral borane compounds (**1–18**, Tables I–III) were prepared in the Boron Chemistry Group of the Institute of Inorganic Chemistry, Czechoslovak Academy of Sciences. The syntheses and properties of the still unknown zwitterionic isomeric compounds 9-L, 7-R-$C_2B_9H_{10}$ and 11-L, 7-R-$C_2B_9H_{10}$ (R = Me, Ph, L = Me_2S, py; **2–11**, Tables I and II) and 9-Me-11-py-$C_2B_9H_{10}$ (**14**) (Me = methyl, Ph = phenyl; py = pyridine) will be the subject of a separate paper [18]. The syntheses of 3-Me-9-Me_2S-$C_2B_9H_{10}$ (**12**), 4-Me-9-Me_2S-$C_2B_9H_{10}$ (**13**), 4-Me_2S-4′-MeS-(1,2,-$C_2B_9H_{10})_2$-3-Co (**18**) and 4-C_5H_5-Co-1,7-$C_2B_9H_{11}$ (**16**) have not yet been published [19].

The synthesis and properties of the 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ (**15**) racemic compound and of its partially chemically resolved *d*-enantiomer will be published elsewhere [20]. Further enhancement of the enantiomeric purity of *d*-4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ was achieved by the following procedure. A hot saturated solution of 0.10 g of the partially resolved *d*-4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ (66% of *d*-**15**) in ethanol (m.p. 208°C) was left to crystallize for 24 h; the first crop of crystals was recovered and evaporation under vacuum of an aliquot of the mother liquors afforded the first fraction of the enriched *d*-**15**; the remaining mother liquors were concentrated to two thirds of the original volume to yield a second crop of crystals and the second fraction of enriched *d*-**15**. The second concentration of the mother liquors to the one third of the original volume furnished the third crop of crystals and the final mother liquors (third fraction, *d*-**15**-III) containing 0.04 g of the sandwich complex with 80% of the dextrorotatory enantiomer. All fractions were characterized by m.p. determination and the HPLC method under discussion.

The other compounds, 9-Me_2S-7,8-$C_2B_9H_{11}$ (**1**) [21] and 4-Me_2S-1,2-$C_2B_9H_{10}$-3-Co-1,2-$C_2B_9H_{11}$ (**17**) [22], were prepared according to previously published methods.

Precautions were taken to ensure that the chromatographic peaks attributed to the solute enantiomers were actually those of the enantiomers. Special care was taken to ensure the purity of the individual protochiral compounds and positional isomers used in this study. The purity of all species

was checked by ^{1}H and ^{11}B NMR spectrometry, mass spectrometry and normal-phase chromatography on a Separon SGX silica column with hexane–dichloromethane as mobile phase.

The samples for normal-phase separation were dissolved in the mobile phases. The samples for separation on cyclodextrin CSPs were prepared as methanolic solutions of concentrations 0.5 mg/ml (compounds **1–14**) or 0.25 mg/ml (cobaltaborane sandwich species **15–18**). All samples were filtered before injection through a 0.45-μm PTFE microfilter (Tessek).

The compounds bearing phenyl or pyridyl groups (**3–7, 10, 11, 14**) were detected at 254 nm, **15** at 280 nm, **16–18** (Table III) at 290 nm and other compounds at 205 nm.

Methods for purity checking

NMR spectra were measured on a Varian XL-200 spectrometer at 200 MHz (^{1}H) and 64.18 MHz (^{11}B) in hexadeuteroacetone and mass spectra were recorded using a Jeol HP-5985 instrument with electron impact ionization at 70 eV circular dichroism (CD) spectra were recorded on an Auto Dichrographe Mark V instrument (Jobin Yvon, France). The instrument is driven by a microcomputer (Silex, France) loaded with our own software. The measurements were performed in acetonitrile (Uvasol, Merck) (concentration $1{,}5 \cdot 10^{-3}$–$3.0 \cdot 10^{-3}$ *M*) in quartz cells with optical path length 0.02–0.1 cm. The spectra are computer averages over 2–3 instrument scans and the data are presented as $\Delta\varepsilon$ values. Specific rotations were measured on a Perkin-Elmer 241 polarimeter in a 5-cm tube in acetonitrile.

RESULTS AND DISCUSSION

After preliminary experiments with a variety of protochiral deltahedral borane derivatives, we chose the zwitterionic substituted eleven-vertex *nido* species of the L-R-7,8-$C_2B_9H_{10}$ type (R = H, methyl, phenyl; L = Me_2S-, pyridine) (Fig. 1) (**1–14**, Tables I and II) along with several substituted cobaltacarborane sandwich compounds (Fig. 2) (**15–18**, Table III). These compounds are sufficiently stable not only in hexane–dichloromethane or hexane–alcoholic mobile phases used in normal-phase separations, but also in aqueous methanolic or aqueous acetonitrile mobile phases frequently applied in reversed-phase separations with cyclodextrin CSPs.

Preliminary attempts on the π-acceptor *d*-phenylglycine column to effect normal-phase separations with hexane–dichloromethane, hexane–2-propanol or hexane–*tert.*-butanol mobile phases (adjusting mobile phase strength to set k' values in the range 4–6) showed no resolution of enantiomers of the compounds under discussion. Similarly, compounds **1–18** were not distinctly resolved (except for peak broadening) on both α- and γ-cyclodextrin CSPs in aqueous methanolic mobile phases, although the k' values gave evidence for some type of interaction. These results are not shown or discussed here.

However, β-cyclodextrin columns were found to give very good enantioselectivity and resolution of enantiomers for most of the protochiral compounds studied. Also, most of the 9- and 11-base-substituted positional isomers of the L-7-R-7,8-$C_2B_9H_{10}$ series were excellently resolved on this type of CSP. Use of a β-CD CSP and aqueous methanolic or aqueous acetonitrile mobile phases permitted the resolution of the first deltahedral borane derivative enantiomers by the CRE technique. Values of the capacity factors (k'), selectivities (α) and resolutions (R_s) of R-L-7,8-$C_2B_9H_{10}$ derivatives (**1–14**) on a β-CD CSP in aqueous–organic mobile phases are summarized in Tables I and II.

Similar retention behaviour of all mono- and disubstituted zwitterionic species R-L-7,8-$C_2B_9H_{10}$ was observed under various chromatographic conditions. The monosubstituted species (compounds **1–3** in Tables I and II) usually exhibited higher k' values than did disubstituted species. The pyridine-

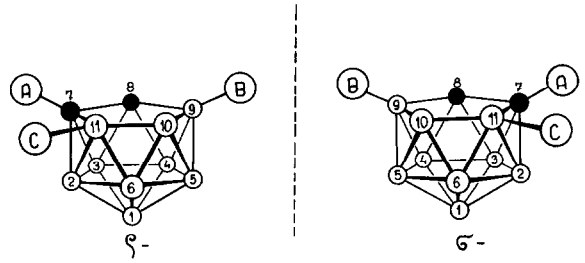

Fig. 1. Enantiomers of 7-A-9-B-11-C-7,8-$C_2B_9H_9$ species. The pictograms indicate the deployment of the numbering spiral [25]. For simplicity the terminal hydrogens and hydrogen bridge are omitted. ○ = Boron; ● = carbon.

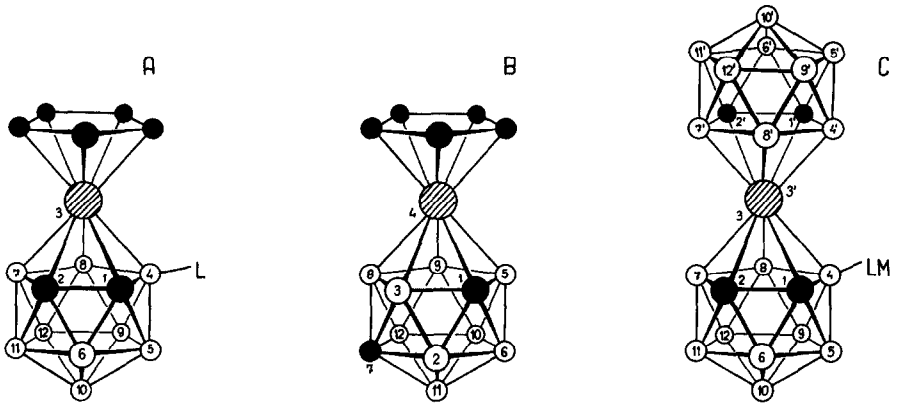

Fig. 2. Structures of (A) 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ (**15**), (B) 4-C_5H_5-1,7,4-$C_2CoB_9H_{11}$ (**16**) and (C) 4-Me_2S-1,2-$C_2B_9H_{10}$-3-Co-$C_2B_9H_{11}$ (**17**). The terminal hydrogen atoms are omitted. ○ = Boron, ● = carbon; ⊘ = cobalt; L = MeS; LM = Me_2S.

substituted compounds eluted before the corresponding dimethylsulphido derivatives.

An inclusion process along with some type of hydrogen bonding or steric interaction is considered to be responsible for chiral recognition on CD CSPs [11,16,17]. Comparing the retention behaviour of the monosubstituted compounds (**1–3**) with disubstituted compounds (**4-14**) and likewise the retention behaviours of disubstituted species bearing 7-methyl (**8-10**) and 7-phenyl (**4–7**) substituents, it can be seen that in all instances the compounds enter the β-CD cavity by their more hydrophobic carborane part. Substituents (including phenyl) probably interact with the hydroxyl groups at the rim of the cyclodextrin cone.

TABLE I

CAPACITY FACTORS k' SELECTIVITIES (α) AND RESOLUTION R_s OF ENANTIOMERS OF ISOMERIC COMPOUNDS OF THE R-L-$C_2B_9H_{10}$ TYPE ON A TESSEK β-CYCLODEXTRIN COLUMN (7 μm) (250 × 4 mm I.D.) WITH AQUEOUS–ORGANIC MOBILE PHASES

Flow-rate, 0.8 ml/min.

Compound	No.	Methanol–water[a]				Acetonitrile–water[a]			
		k'_1	α	R_s	Methanol (%)	k'_1	α	R_s	Acetonitrile (%)
9-Me_2S-7,8-$C_2B_9H_{11}$	**1**	7.4	1.0	NR	60	11.5	1.04	0.55	28
9-Me_2S-CH_2-7,8-$C_2B_9H_{11}$	**2**	10.4	1.08	0.88	60	11.2	1.06	0.7	28
7-Py-CH_2-7,8-$C_2B_9H_{11}$	**3**	7.45	1.09	0.6	57	3.85	1.05	0.55	28
9-Ph-11-Me_2S-7,8-$C_2B_9H_{10}$	**4**	2.46	1.0	NR	58	5.84	1.04	0.5	27
7-Ph-9-Me_2S-7,8-$C_2B_9H_{10}$	**5**	4.50	1.09	1.12	58	7.54	1.08	1.05	27
7-Ph-11-py-7,8-$C_2B_9H_{10}$	**6**	3.88	1.09	0.65	55	5.82	1.07	0.65	27
7-Ph-9-py-7,8-$C_2B_9H_{10}$	**7**	6.86	1.09	1.00	55	7.06	1.09	1.06	27
7-Me-11-Me_2S-7,8-$C_2B_9H_{10}$	**8**	3.89	1.0	NR	60	6.60	1.06	0.60	28
7-Me-9-Me_2S-7,8-$C_2B_9H_{10}$	**9**	3.42	1.08	0.72	60	5.69	1.08	0.75	28
7-Me-11-py-7,8-$C_2B_9H_{10}$	**10**	3.94	1.0	NR	58	4.38	1.0	NR	28
7-Me-9-py-7,8-$C_2B_9H_{10}$	**11**	4.17	1.04	0.6	55	3.28	1.07	0.7	28
3-Me-9-Me_2S-7,8-$C_2B_9H_{10}$	**12**	5.00	1.05	0.6	60	8.09	1.06	0.6	28
4-Me-9-Me_2S-7,8-$C_2B_9H_{10}$	**13**	2.8	1.16	1.5	60	6.26	1.15	1.20	28
9-Me-11-py-7,8-$C_2B_9H_{10}$	**14**	4.08	1.08	1.10	58	9.63	1.08	1.20	27

[a] k'_1 = Capacity factor of the first-eluting enantiomer. NR = Not resolved.

TABLE II

CAPACITY FACTORS (k'), SELECTIVITIES (α) AND RESOLUTION (R_s) VALUES OF ENANTIOMERS OF ISOMERIC COMPOUNDS OF THE R-L-$C_2B_9H_{10}$ TYPE ON AN ASTEC β-CYCLODEXTRIN Cyclobond I (5 μm) COLUMN (250 × 4.6 mm I.D.) WITH AQUEOUS METHANOLIC MOBILE PHASES

Flow-rate, 0.8 ml/min.

Compounds	No.	k'_1	α	R_s	Methanol (%)
9-Me_2S-7,8-$C_2B_9H_{11}$	**1**	3.09	1.0	NR[a]	50
7-Py-CH_2-7,8-$C_2B_9H_{11}$	**3**	3.85	1.13	1.06	45
7-Ph-11-Me_2S-7,8-$C_2B_9H_{10}$	**4**	3.99	1.14	2.21	45
7-Ph-9-Me_2S-7,8-$C_2B_9H_{10}$	**5**	5.45	1.08	1.23	45
7-Ph-11-py-7,8-$C_2B_9H_{10}$	**6**	3.39	1.14	1.80	45
7-Ph-9-py-7,8-$C_2B_9H_{10}$	**7**	3.88	1.11	1.30	45
7-Me-11-Me_2S-7,8-$C_2B_9H_{10}$	**8**	2.74	1.07	0.85	45
7-Me-9-Me_2S-7,8-$C_2B_9H_{10}$	**9**	4.20	1.03	0.5	45
7-Me-11-py-7,8-$C_2B_9H_{10}$	**10**	4.21	1.04	0.6	45
7-Me-9-py-7,8-$C_2B_9H_{10}$	**11**	2.63	1.08	1.0	45
3-Me-9-Me_2S-7,8-$C_2B_9H_{10}$	**12**	3.28	1.10	1.10	45
4-Me-9-Me_2S-7,8-$C_2B_9H_{10}$	**13**	3.61	1.08	0.80	45
9-Me-11-py-7,8-$C_2B_9H_{10}$	**14**	5.18	1.12	2.0	45

[a] NR = Not resolved.

As follows from the R_s values in Tables I and II for compounds **1–3**, one substituent on the $[C_2B_9H_{12}]^-$ skeleton suffices for successful enantiomeric separation. However, it should be noted that the R_s values for monosubstituted compounds are in most instances lower than those for the corresponding disubstituted species. Of the three monosubstituted compounds under study, two (**2** and **3**) were successively resolved; the third compound, 9-Me_2S-$C_2B_9H_{11}$, remained unresolved, except for partial resolution (R_s 0.55) in aqueous acetonitrile or extensive band broadening in aqueous methanolic mobile phases. The improvement in the selectivity and the resolution values on β-CD CSPs by lengthening the side-chain or by varying the substituent size is well known from studies dealing with the optimization of the shape of substituent groups on metallocenes [12] and organic molecules [23,24] for interaction with cyclodextrins. Noteworthy are the unexpectedly small k' values in the series of monosubstituted species (Tables I and II) and the relatively high R_s values for 7-pyridiniomethyl-substituted compound **3** on column B (Cyclobond I) (Fig. 3).

In the separation of disubstituted species (compounds **4–14**, Tables I and II) some differences in the selectivity and resolution of enantiomers of individual positional isomers can be seen for the two β-CD CSPs tested. A comparison of R_s values of compounds **4, 6, 8** and **10** for column A (Tessek) (Table I) with those obtained on column B (Cyclobond I, Astec) shows dramatic differences in selectivity and R_s values for the 11-L-7-R-$C_2B_9H_{10}$ positional isomer series [*e.g.*, those with substituents in vicinal ("*ortho*") positions]. Whereas on column A these species remained unresolved or were only partially resolved, on column B they could be separated with high enantioselectivity and R_s values. Surprisingly, the resolution of enantiomers of the above-mentioned *ortho*-isomers on column B is often better (**4, 6** and **8**) than that for corresponding compounds with "*meta*-"positioned substituents (**5, 7** and **9**) (see Fig. 4, for example). Exceptional is behaviour of the *ortho*-7-Me-11-py-$C_2B_9H_{10}$ (**10**), which eluted after the "*meta*-"substituted isomer 7-Me-9-py-$C_2B_9H_{10}$ (*i.e.*, reversed elution behaviour in comparison with two related isomers of other compounds) and gave a poor resolution on both materials used.

"*Meta*-"substituted compounds **5, 7, 9, 11,** and **14** are separated on both types of CSP using aqueous methanolic mobile phases (Tables I and II, Fig. 4) with comparatively good R_s values, taking into account that column B (Table II) exhibited a higher

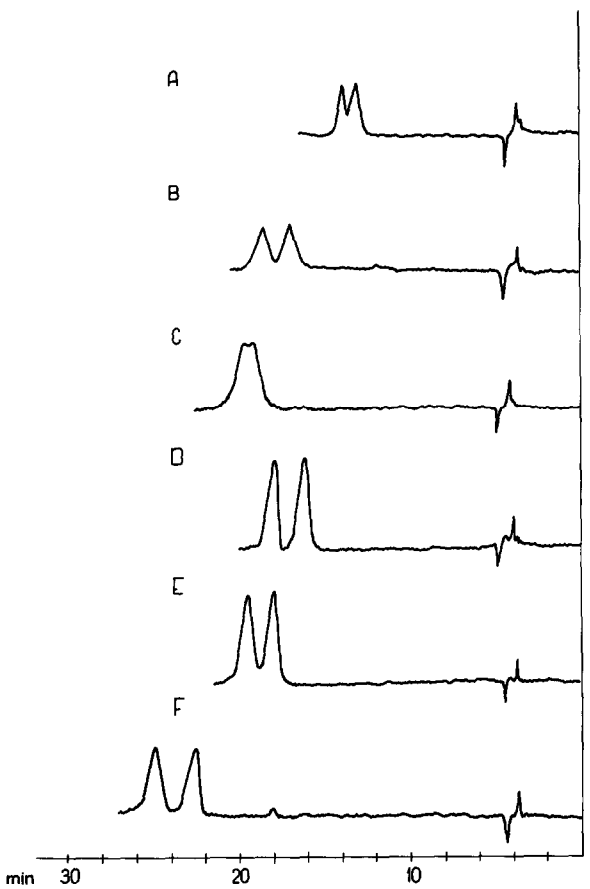

Fig. 3. Separation of the enantiomers of pyridine-substituted zwitterioninic species of the R-py-$C_2B_9H_{10}$ type. Column, Cyclobond I β-CD (250 × 4.6 mm I.D.); mobile phase, 45% aqueous methanol; flow-rate, 0.8 ml/min; detection, UV at 254 nm; sensitivity, 0.02 a.u.f.s. Chromatograms: A = 7-py-CH_2-$C_2B_9H_{11}$; B = 7-Me-9-py-$C_2B_9H_{10}$; C = 7-Me-11-py-$C_2B_9H_{10}$; D = 7-Ph-11-py-$C_2B_9H_{10}$; E = 7-Ph-9-py-$C_2B_9H_{10}$; F = 9-Me-11-py-$C_2B_9H_{10}$.

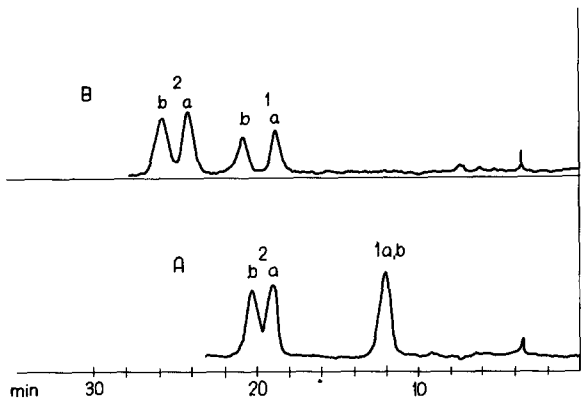

Fig. 4. Comparison of the separation of the "*ortho-*" and "*meta-*" substituted species 7-Ph-11-Me_2S-$C_2B_9H_{10}$ (**4**) and 7-Ph-9-Me_2S-$C_2B_9H_{10}$ (**5**) and resolution of their enantiomers on the two β-CD CSPs used. (A) column, Tessek β-CD (7 μm) (250 × 4 mm I.D.); mobile phase, 58% aqueous methanol; flow-rate, 0.8 ml/min; detection, UV at 254 nm. (B) Column, Cyclobond I β-CD (250 × 4.6 mm I.D.); conditions as in Fig. 3. Peaks: 1a and b = enantiomers of **4**, 2a and b = enantiomers of **5**.

efficiency and gave slightly better selectivity values.

Inspection of the results summarized in Tables I and II for aqueous methanolic mobile phases reveals no significant differences in R_s values between Me_2S- and the corresponding pyridine-substituted compounds having the second identical substituent groups in position 7. A more important effect was the replacement of the phenyl substituent in position 7 with a methyl group. Whereas the former series of compounds (**5** and **7** on column A and **4**–**8** on column B) gave the R_s values above 1.0 (baseline or nearly baseline resolution on column B), the worst values of α and R_s were obtained for the corresponding 7-methyl-substituted isomers (**8**–**11**). In contrast, the highest values of selectivity and resolution were achieved on column A for the 9-Me-11-py-7,8-$C_2B_9H_{10}$ (**14**) and 4-Me-9-Me_2S-$C_2B_9H_{10}$ (**13**) (methyl group in bottom pentagon of the boron skeleton) species.

The influence of several factors on the retention behaviour and resolution of the enantiomers of the R-L-$C_2B_9H_{10}$ species was studied on both β-CD CSPs, including variation of the mobile phase composition (type and percentage of organic solvent) and the effect of the separation temperature. The compounds exhibit a gradual increase in k' and R_s values with decreasing methanol content in the mobile phase from 75 to 55% (35–27% of acetonitrile) on column A. The respective values for column B giving a weaker hydrophobic interaction were from 60 to 40% methanol and from 30 to 20% acetonitrile. No resolution was observed approximately above the upper values. The peak broadening was usually seen on the lower borderline of the above regions. The values in Tables I and II usually correspond to the mobile phase composition giving the optimum k' values with the highest R_s value.

An example of the influence of the methanol concentration on enantiomer resolution is shown in Fig. 5. The replacement of methanol with acetonitrile has only a slightly decreasing or in some instances increasing effect on the resolution of some enantiomers on column A (Table I). In contrast, on column B the use of aqueous acetonitrile mobile phases provided a better resolution only for compound **1** (R_s = 0.55, α = 1.03, k'_1 = 5.1 with 23% acetonitrile), had no effect on the resolution of compound **9** and led to a marked decrease in the R_s values the other compounds, owing to peak broadening. The last effect can be attributed to the slower mass transfer, probably owing to limited solubility of the solutes in mobile phases with low concentrations of the organic modifier (20–23%). No resolution was observed in aqueous 2-propanol mobile phases.

In accordance with the literature [11], a decrease in separation temperature on column A led to an increase in the k' values of individual compounds. The effect on R_s value was small, probably owing to a slower mass transfer [11], but in some instances a slight increase in α and consequently in R_s values was observed. For example, α values of 1.10 and 1.12 with respective R_s values 1.10 and 1.13 were obtained for compound **14** in 70% aqueous methanol at 10 and 0°C, respectively.

In addition to the above-discussed species, the resolving power of the β-CD-bonded CSPs for several cobaltaborane compounds was also examined. The results are summarized in Table III.

It was found that the β-CD CSP on column A is well suited for the successful resolution of the enantiomers of the 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ complex (**15**) in aqueous methanolic mobile phases. Our intention to apply the method to quantitative analysis (see below) led us to raise the R_s value (originally about 0.8 in a 58% methanolic eluent at a flow-rate of 0.8 ml/min). The study of the factors mentioned in the preceding section was also performed in the case of the cobaltaborane compounds. The only, but very important, difference in chromatographic behaviour was in the lack of enantioselectivity on replacing methanol with acetonitrile. The most effective factor in increasing the resolution was found to be a decrease in flow-rate. The enhancing effect on resolution of decreasing the flow-rate from 1 to 0.2 ml/min is shown in Table IV. The best R_s value of 0.94 obtained at 0.4 ml/min remained small enough for quantitative analysis, but allowed at least an approximate evaluation of the enantiomer contents in the samples.

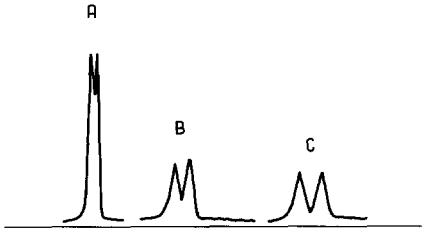

Fig. 5. Enantiomeric separation and resolution of 7-Ph-9-Me_2S-$C_2B_9H_{10}$ as a function of the percentage of methanol in the mobile phase. Column, Tessek β-CD; flow-rate, 0.8 ml/min; detection, UV at 254 nm; mobile phase, aqueous methanol. Methanol content k' and R_s values: (A) 70%, k'_1 = 1.22, k'_2 = 1.31, R_s = 0.7; (B) 60%, k_1 = 3.06, k_2 = 3.31, R_s = 0.95; (C) 58%, k_1 = 4.50, k_2 = 4.89, R_s = 1.12.

In contrast, it should be pointed out that no resolution of the cobaltaborane **15** was observed on column B using methanolic mobile phases, although this column was far more active with the former series of species. In contrast to column A, aqueous acetonitrile gave a partial resolution of **15** on this type of material, but the α and R_s values remained small enough.

With the related protochiral cobaltaborane sandwich compounds **16–18**, no or only a partial resolution (with R_s values ranging from 0.5 to 0.6, Table III) was observed. The higher k' value of the 4-C_5H_5-4-Co-1,7-$C_2B_9H_{11}$ (**16**) sandwich compound and the very extensive broadening of its peaks suggest strong inclusion complex formation and some kind of additional interaction. However, although the capacity factors of compounds **17** and **18** on column A resemble that of **15**, very poor or no enantimeric resolution was observed. On column B the 4-Me_2S-4′-MeS-(1,2-$C_2B_9H_{10}$)$_2$-3-Co (**18**) complex exhibits surprisingly high k' values in comparison with those for the corresponding compounds **15** and **17**. However, its resolution still remains low.

The usefulness of the method described above can be exemplified by its application to monitoring the process of the separation of *d*-**15** from the *dl*-**15** sandwich by crystallization. The synthesis and optical properties of the partially resolved *d*-enantiomer

TABLE III

CAPACITY FACTORS (k'), SELECTIVITIES (α) AND RESOLUTION (R_s) VALUES OF ENANTIOMERS OF COBALTACARBORANE SANDWICH COMPOUNDS ON (A) A TESSEK β-CYCLODEXTRIN COLUMN (7 μm) (250 × 4 mm I.D.) AND (B) AN ASTEC Cyclobond I COLUMN (5 μm) (250 × 4.6 mm I.D.) WITH METHANOLIC OR AQUEOUS ACETONITRILE MOBILE PHASES

Flow-rate, 0.8 ml/min.

Column	Compound	No.	k'_1	α	R_s	Organic modifier[a] (%)
A	4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$	**15**	3.12	1.08	0.82	60 (M)
		15	5.24	1.0	NR[b]	30 (A)
	4-C_5H_5-4-Co-1,7-$C_2B_9H_{11}$	**16**	9.49	–	NR	60 (M)
	4-Me_2S-1,2-$C_2B_9H_{10}$-3-Co-$C_2B_9H_{11}$	**17**	3.23	1.0	NR	60 (M)
		17	5.19	1.0	NR	30 (A)
	4-MeS-4′-Me_2S-(1,2-$C_2B_9H_{10}$)$_2$-3-Co	**18**	3.29	1.08	0.55	60 (M)
B	4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$	**15**	3.56	1.0	NR	45 (M)
		15	3.50	1.04	0.55	23 (A)
	4-C_5H_5-4-Co-1,7-$C_2B_9H_{11}$	**16**	1.87		NR	60 (M)
		16	3.33		NR	28 (A)
	4-Me_2S-1,2-$C_2B_9H_{10}$-3-Co-$C_2B_9H_{11}$	**17**	4.10	1.0	NR	45 (M)
	4-MeS-4-Me_2S-(1,2-$C_2B_9H_{10}$)$_2$-3-Co	**18**	8.08	1.05	0.5	45 (M)
			1.33	1.0	NR	28 (A)

[a] M = methanol; A = acetonitrile.
[b] NR = Not resolved.

have been described elsewhere [20]. Threefold fractional crystallization of the above product (partially optically active, 66% of *d*-enantiomer) from ethanol afforded the sample (*d*-**15**-III) with about 80% of the dextrorotatory enantiomer. The CD spectrum of the last crystallization fraction *d*-**15**-III is depicted in Fig. 6. Comparison of chromatograms of *dl*-**15** with *d*-**15**-III in Fig. 7 clearly shows that the second peak belongs to this dextrorotatory enantiomer. The less soluble racemate crystallized preferentially as coarse prisms (m.p. 218–219°C), whereas the *d*-enantiomer accumulated in the mother liquors and was finally crystallized as long needles (m.p. 211–212°C). It is apparent that this puri-

TABLE IV

EFFECT OF FLOW-RATE ON THE RESOLUTION (R_s) OF THE ENANTIOMERS OF 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ (**15**)

Column, Tessek β-CD (7 μm) (250 × 4 mm I.D.); mobile phase, 60% aqueous methanol; detection, UV at 280 nm; sensitivity, 0.02 a.u.f.s.; injection, 3 μl of a solution of **15** of concentration 0.25 mg/ml.

Flow-rate (ml/min)	k_1	k_2	α	R_s
1.0	2.93	3.18	1.08	0.77
0.8	3.12	3.37	1.08	0.82
0.6	3.14	3.39	1.08	0.85
0.5	3.14	3.43	1.09	0.875
0.4	3.17	3.46	1.09	0.94
0.2	3.16	3.45	1.09	0.90

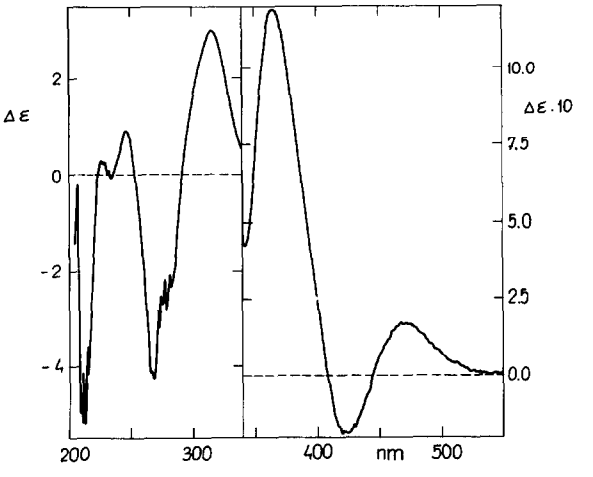

Fig. 6. CD spectrum of the last fraction of *d*-enriched 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ (*d*-**15**-III) (80% of the *d*-enantiomers).

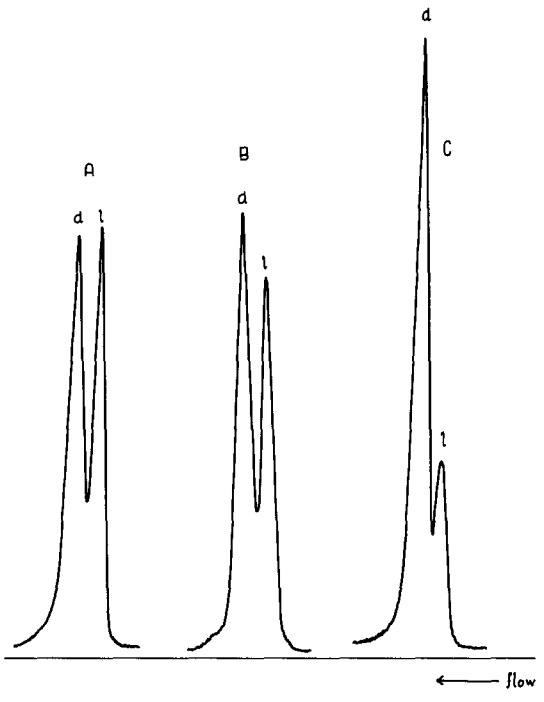

Fig. 7. Chromatographic separation of the enantiomers of 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ (**15**) sandwich on column A. Examples of monitoring the enantiomeric purity of samples after the separation of *d*-**15** from *dl*-**15** by crystallization from ethanol. Samples: (A) racemic *dl*-**15**; (B) last crop of crystals; (C) third fraction of enriched *d*-**15**-III (mother liquours). Column, Tessek β-CD (7 μm) (250 × 4 mm I.D.); mobile phase, 60% aqueous methanol; flow-rate, 0.4 ml/min; detection, UV at 280 nm; sensitivity, 0.02 a.u.f.s.; injection, 3 μl methanolic solution of concentration 0.25 mg/ml.

fication would hardly be possible without this microscale HPLC monitoring.

CONCLUSIONS

Probably the first successful LC separation of enantiomeric pairs in the series of deltahedral carborane and metallaborane compounds has been described. The separation of chiral compounds of the L,R-$C_2B_9H_{10}$ type and 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ was achieved using commercially available β-CD CSP columns and aqueous methanolic or aqueous acetonitrile mobile phases. Of the two β-CD CSPs tested, Astec Cyclobond I and Tessek β-CD, the former proved to be more efficient in the separation of the enantiomers of the isomeric species of the 9-L-R-$C_2B_9H_{10}$ and 11-L-R-$C_2B_9H_{10}$ series. The latter column was unique in the separation of the 4-MeS-3-C_5H_5-1,2,3-$C_2CoB_9H_{10}$ mixed sandwich complex. These differences probably arise from the different types of cyclodextrin molecule attachment in these CSPs. The possibility of additional interaction with sorbent surface groups of the individual materials cannot be eliminated from taking part in the separation mechanism.

The main shortcoming with the use of cyclodextrin-based CSPs in chiral separations is the explicit need for aqueous–organic mobile phases. This disadvantage hinders the extension of this approach to the broad range of protochiral deltahedral borane compounds with low hydrolytic stability. This leads to a challenge to search for other efficient chiral stationary phases.

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