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Short communication

Hemispherodextrins, a new class of cyclodextrin derivatives, in capillary electrophoresis

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Abstract

A capped cyclodextrin derivative (THCMH), called hemispherodextrin, was observed to behave as a very efficient chiral selector for a variety of phenoxyacid enantiomeric pairs, both at pH 6 and pH 9. The very low concentration necessary to obtain separation was particularly impressive. The behaviour of THCMH was compared with that of other hemispherodextrins and cyclodextrin derivatives and the conclusions are reported. Some interesting conclusions are drawn by comparing the behaviour of THCMH with that of other hemispherodextrins reported elsewhere.

Keywords: Chiral selectors; Enantiomer separation; Buffer composition; Hemispherodextrins; Cyclodextrins; Phenoxypropionic acids; Organic acids

1. Introduction

Hemispherodextrins are a new class of receptors synthesised in our laboratory. They are obtained by using suitable bridges to bond an α,α′-trehalose moiety with the A and D glucopyranosinic rings of β-cyclodextrin. This results in the formation of a saccharide system that extends over a hemispherical surface, as is suggested by the name. In comparison with the parent cyclodextrin, hemispherodextrins appear to separate the included guest from water more efficiently, thus ensuring higher host–guest complex stability. Three different molecules of this class have been synthesised to date in our laboratories, by varying the kind of bridge used in the bonding process, i.e. either cysteamine (THCMH) [1], ammonia (THAMH) [2], or β-alanineamide (THALAH) [3]. A further member of this class has been synthesised elsewhere [4].

Early in the initial development of capillary electrophoresis, some authors realised the great potential of this technique in chiral separations [5–14]. This paper reports the chiral discrimination properties of THCMH (shown schematically in Fig. 1). Three different enantiomeric pairs of phenoxy-acids with herbicide properties, reported in Fig. 2, were used as analytes in capillary electrophoresis. These were chosen as being appropriate for testing our host since CE results for the same analytes are available in the literature [15–18], thus making it

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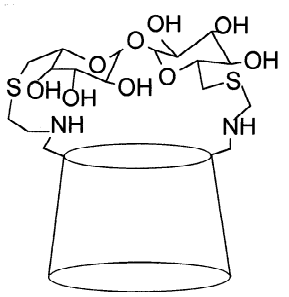

Fig. 1. Schematic representation of the THCMH molecule.

possible to compare the chiral discrimination ability of THCMH with that of other selectors.

2. Experimental

2.1. Materials

Phenoxypropionic acid [2-phenoxypropionic acid (2-PPA), 2-(4-chlorophenoxy)propionic acid (2,4-CPPA) and 2-(3-chlorophenoxy)propionic acid (2,3-CPPA)] racemic mixtures were purchased from Aldrich. Hydrochloric acid, sodium hydroxide, acetone, sodium dihydrogenphosphate and boric acid were obtained from Merck. THCMH was synthesised in our laboratory as previously described [1]. Double-distilled water was used for solution preparation.

2.2. CE measurements

CZE measurements were carried out on a Beckman P\ACE MDQ equipped with a diode-array detector. An uncoated fused-silica capillary [Beckman; 67 cm (effective length 50 cm)×75 μm I.D.) was held at a constant temperature of 20°C. The system operated at a constant voltage of 25 kV.

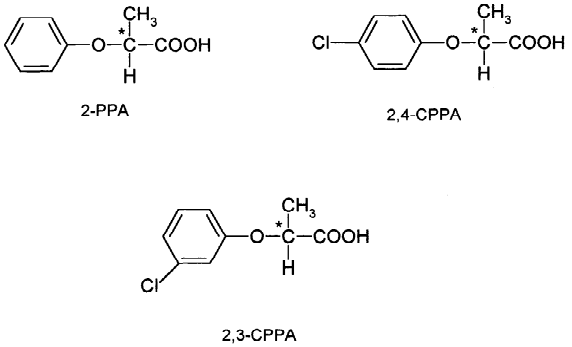

Fig. 2. Structures of the investigated phenoxyacids.

Buffers for the chiral separation experiments were prepared by dissolving THCMH ($1\cdot10^{-4}$–$5\cdot10^{-3}$ mol dm^{-3}) in 0.022 mol dm^{-3} sodium phosphate buffer (pH 6), or in 0.1 mol dm^{-3} borate buffer (pH 9). Phenoxypropionic derivative racemate ($1.0\cdot10^{-4}$ mol dm^{-3}) was dissolved in water. The sample solution was injected at a pressure of 5 p.s.i. after adding acetone as a neutral marker to estimate electroosmotic flow (1 p.s.i.=6894.76 Pa). The capillary was rinsed between runs at 20 p.s.i., first with 0.1 mol dm^{-3} NaOH and then with the phosphate buffer used in separation. The capillary was rinsed daily with 0.1 mol dm^{-3} HCl, water, and 0.1 mol dm^{-3} NaOH, followed by an appropriate buffer.

The enantiomeric resolution (R_s) and the selectivity coefficient (α) were calculated using Eqs. (1) and (2), respectively:

$$R_s = \frac{2(t_2 - t_1)}{w_1 + w_2} \quad (1)$$

$$\alpha = t_2/t_1 \quad (2)$$

where t and w are, respectively, the migration time and the width at the baseline of the two enantiomers.

3. Results and discussion

The CE chiral separation of enantiomeric pairs of phenoxyacids in the presence of THCMH was carried out at two different pH values. As observed in previous experiments, in borate buffer THCMH is unprotonated, while in phosphate buffer (pH 6) it exists as a diprotonated species.

The results are summarized in Table 1, while electropherograms for the 2,4-CPPA enantiomer separation at two different concentrations of THCMH are reported in Fig. 3. As can be seen, the resolution R_s and the selectivity factor α were calculated for the experiments.

It is readily apparent from these data that THCMH is a very efficient chiral selector for all three pairs of enantiomers. Selection occurs at both pH values. However, higher selectivity factor and resolution

Table 1
Resolution (R_s) and selectivity coefficients (α) in the CE separation of the phenoxyacid enantiomeric pairs at two different pH values and in the presence of different concentrations of THCMH

pH	$C_{selector}$ ($\cdot 10^3$ mol dm^{-3})	2-PPA		2,4-CPPA		2,3-CPPA	
		R_s	α	R_s	α	R_s	α
6	0.10	0.88	1.02	0.94	1.03	1.46	1.04
	0.80	1.38	1.09	3.54	1.13	1.46	1.04
	1.00	2.82	1.11	4.14	1.12	5.75	1.24
	1.50	4.03	1.14	3.82	1.11	6.96	1.20
	2.50	5.00	1.16	3.06	1.09	6.96	1.20
	5.00	6.52	1.16				
9	0.80	0.44	1.01	0.83	1.02	1.15	1.02
	1.00	0.73	1.01	0.86	1.02	1.30	1.03
	1.50	0.86	1.01	1.00	1.02	1.37	1.03
	2.50	1.06	1.02	0.93	1.02	1.70	1.03
	5.00			1.03	1.02	2.00	1.03

values are obtained at acidic pH. This is to be expected since, at lower pH, the host and guest charges are opposite and the resulting electrostatic interaction contributes to complex stabilisation.

A very low concentration of THCMH was required in order to achieve separation. This is all the more impressive if compared with the much higher concentrations used in other studies on the same guests [15–18]. It should also be borne in mind that concentrations might be lowered even further in phosphate buffer. The limit appears to be related to the minimum local host–guest concentration ratio. For the optical detection of a guest it is not possible to reduce the guest concentration beyond $1 \cdot 10^{-4}$ mol dm^{-3}. As a consequence, it is not possible to reduce the selector concentration either. In THALAH, another hemispherodextrin, β-alanineamide bridges were used to replace cysteamine bridges. THALAH was used at acidic pH only and was seen to behave with a resolution which can be considered comparable to that of THCMH. In particular, THALAH shows a slightly greater selectivity for 2-PPA (e.g., for $5.00 \cdot 10^3$ mol dm^{-3} concentration at pH 6: R_s = 5.38, $\alpha = 1.19$), but is less efficient for 2,3-CPPA [19]. The behaviour of THAMH, in which simple ammonia bridges are present, differs by completely separating the 2-PPA enantiomeric pair at acidic pH at the two highest concentrations only (for 2.5 and $5.00 \cdot 10^3$ mol dm^{-3} concentration at pH 6: $R_s = 0.74$, $\alpha = 1.03$; $R_s = 1.62$, $\alpha = 1.05$, respectively) [19]. Partial overlapping is observed at basic pH for 2,3-CPPA separation. In all other systems investigated, THAMH was not seen to separate under the experimental conditions employed. The structural feature that sets THAMH apart from THALAH and THCMH is the length of its capping unit, which is significantly shorter than that of the other two hemispherodextrins. Consequently, there is less space available for the guest molecule. The complex

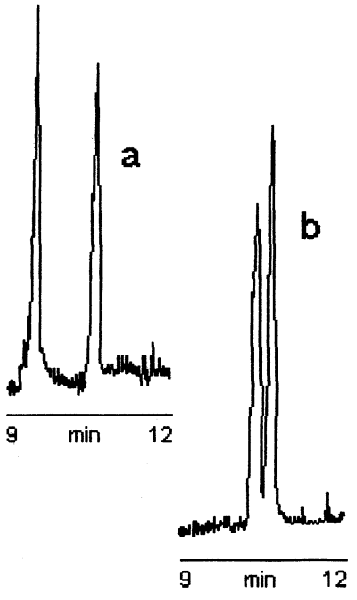

Fig. 3. Separation of enantiomers of 2,4-CPPA in the presence of two different THCMH concentrations: (a) $8.0 \cdot 10^{-4}$ mol dm^{-3}; (b) $1.0 \cdot 10^{-4}$ mol dm^{-3}.

is thus destabilised, as can also be seen in that the guest retention time differs slightly upon addition of THAMH.

In conclusion, the investigated hemispherodextrin THCMH appears to be a very promising chiral selector in capillary electrophoresis. Comparison with other hemispherodextrins points to the importance of the length of the capping chain in determining the affinity for specific guests. The addition of a disaccharide in order to surround the guest molecule more efficiently also appears to have promising applications.

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