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Optical Resolution of Helical and Planarchiral Metacyclophanes by High Performance Liquid Chromatography on (+)-Poly(triphenylmethyl-methacrylate)

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Abstract. Racemic helical and planarchiral ten-membered metacyclophanes **1** to **7** are efficiently resolved into the enantiomers using high performance liquid chromatography on (+)-poly(triphenylmethyl-methacrylate).

Key words: Chiral recognition, enantiomer separation, helical and planarchiral molecules, HPLC, inclusion chromatography, (+)-poly(triphenylmethyl-methacrylate).

Planarchiral [1] heterocyclic and helical [2–4] [2.2]metacyclophanes like **1**,**2** and **3**–**7** are valuable models for systematic investigations of chiral molecular recognition and inclusion phenomena [5]. Optical resolutions of (±)-**1** and (±)-**3** to (±)-**7** had been achieved by semi-preparative liquid chromatography on microcrystalline cellulose triacetate [1–4]. However, this method only provided partially resolved enantiomers and optical resolution by other methods proved fruitless. The chiroptical properties of the pure enantiomers of some representatives of these compound families therefore remained unknown.

We expected the enantiomers of these small and rigid chiral molecules to be recognized inside the helical tube-like niches and cavities of (+)-poly(triphenylmethyl-methacrylate) [6–9].

In fact, efficient resolutions of (±)-**1** to (±)-**7** are easily achieved by high performance liquid chromatography (HPLC) on optically active (+)-poly(triphenylmethyl-methacrylate) [10] {(+)-PTrMa} coated on microporous silica gel.

The chromatograms of (±)-**1** to (±)-**7** obtained with the (+)-PTrMa column used (see Experimental Section) are shown in Figure 1. The helical compounds **5**–**7** show complete resolutions especially when absolute methanol is used as solvent and eluent. The (−)-enantiomer of **5** and the (+)-enantiomer of **7** were first eluted. **2**, **3** and **4** exhibit satisfactory resolutions; (+)-**3** is first eluted. The separation into the enantiomers of **1** and **4** has not been satisfactory to date, but most likely a change of solvent would improve the enantiomeric enrichment.

The identification of (+)-**5**, (−)-**7** and (+)-**3** was achieved by injecting the authentic enantiomers [1–4] of **5**, **7** and **3** on the column and comparing them with the retention volumes of the racemic samples.

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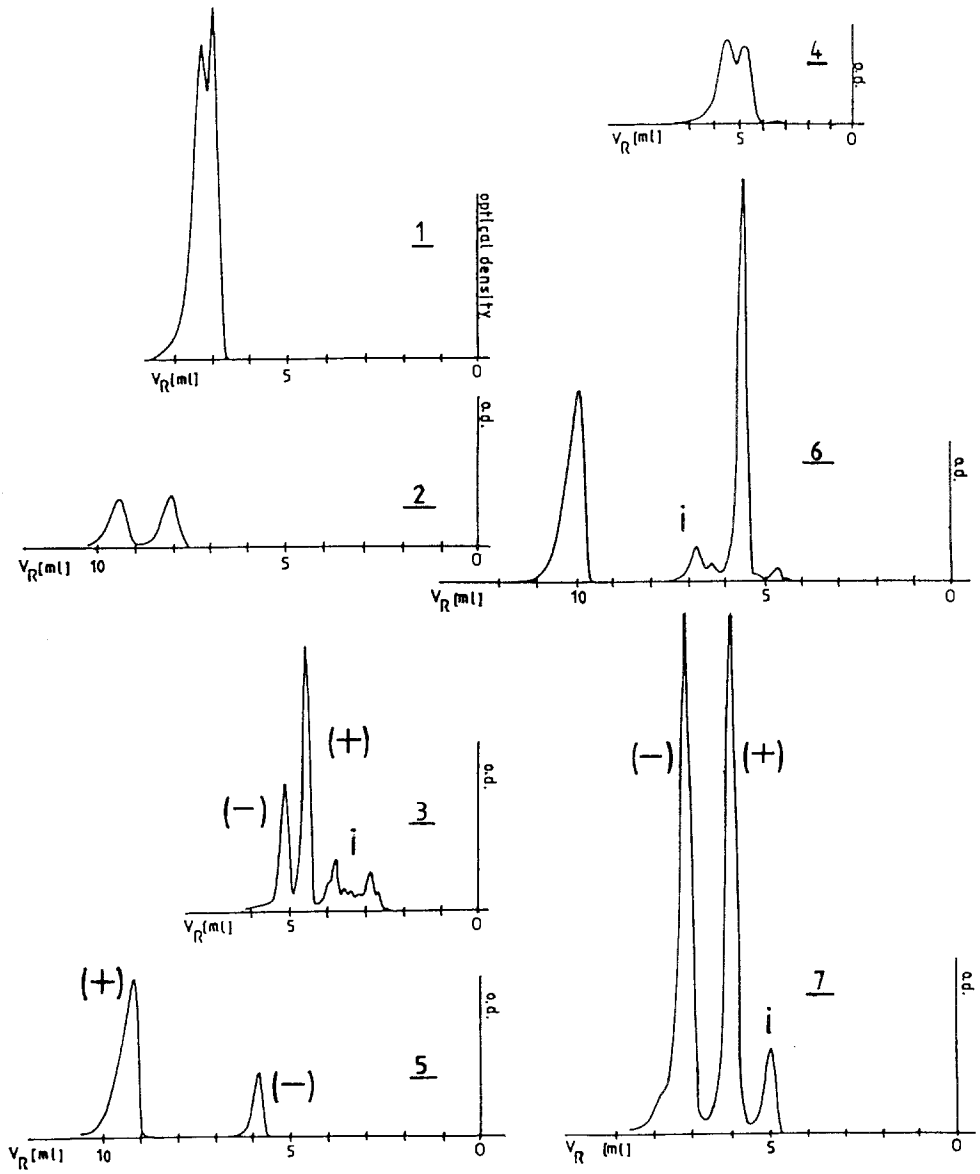
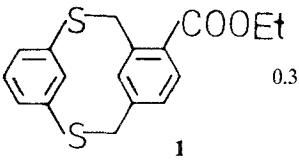
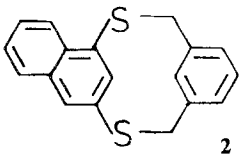
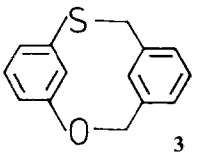
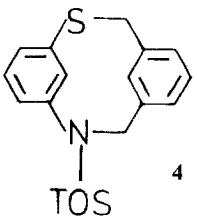
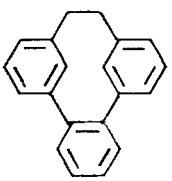
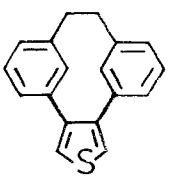
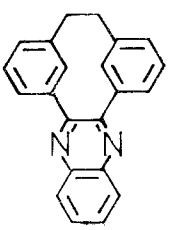


Fig. 1. Chromatograms of the resolutions of (±)-**1** to (±)-**7** on a (+)-PTrMa column (i: impurity); *x*-scale: retention time in ml, *y*-scale: optical density at 254 nm.

The successful separations of all chiral substances studied in this work demonstrate that (+)-PTrMa is a very promising material for optical resolutions of similar aromatic ring assemblies. This material is even more attractive as earlier attempts of separation applying cellulose triacetate ring assemblies. Our interest in using this material increases because the earlier attempts of separation applying cellulose triacetate columns in some cases failed because of solvent problems or insufficient optical resolutions.

Table I. Experimental conditions for the resolution of (±)-**1** to (±)-**7**.

	Flow rate (ml/min)	Pressure (bar)	Retention volume (ml)		Solvent	(vol %)
 **1**	0.3	38.5	7.0	7.4	methanol	100
 **2**	0.3	38.5	8.1	9.5	methanol	100
 **3**	0.3	38.5	4.5 (+)	5.1 (−)	methanol	100
 **4**	0.5	28	5.6	4.8	*n*-hexane propanol-2	92 8
 **5**	0.3	38.5	5.8 (−)	9.1 (+)	methanol	100
 **6**	0.3	38.5	5.6	9.9	methanol	100
 **7**	0.3	98	5.9 (+)	7.1 (−)	methanol *n*-hexane	80 20

Experimental Section

The preparations of (±)-**1** to (±)-**7** [1–4], (+)-poly(triphenylmethyl-methacrylate) [6–10] and the packing material have been reported (see Table I). The chiral phase, coated on 5 μ silica gel, was packed in a column (250 mm long and 4 mm in diameter) by *n*-heptane as eluent, the flow rate was 0.5 ml/min, and pressure 20 bar. The column was tested with 20 μl samples of benzene (1.0 mg/ml) and nitrobenzene (0.01 mg/ml).

Absolute methanol (p.a., Merck, Art. 6009), methanol/isopropanol (p.a., Riedel-de-Haen, 33539) and *n*-hexane (p.a., Riedel-de-Haen, 32293) were used as eluents for the resolution of **1–7**. The chromatography was accomplished on a Waters Associate chromatograph equipped with a UV-detector (Waters Associate, Model 440) and a plotter (Servogor Z 10).

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10. We thank Prof. Dr Y. Okamoto, Osaka University, for a sample of (+)-PTrMa [Chiralpak OT(+)].