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CHROMATOGRAPHIC RESOLUTION OF ENANTIOMERS HAVING AROMATIC GROUP BY OPTICALLY ACTIVE POLY(TRIPHENYLMETHYL METHACRYLATE)[1)]

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Various racemic compounds containing aromatic groups were completely resolved by high-performance liquid chromatography on optically active (+)-poly(triphenylmethyl methacrylate) using methanol as eluent.

Previously we have reported that the polymerization of triphenylmethyl methacrylate by chiral anionic catalysts forms an isotactic, optically active polymer (PTrMA) which has the chirality caused only by helicity.[2)] The high-molecular-weight polymer is insoluble in common organic solvents and many racemic compounds such as alcohol, ester, amine, and hydrocarbon were partly resolved by liquid chromatography on this new type of chiral adsorbent, using hexane as solvent.[3)] However, we have found that better resolution can be achieved when methanol is used as eluent, and various enantiomers with aromatic groups were completely resolved for the first time by high-performance liquid chromatography. This letter describes the new useful results of the resolution. Liquid chromatography seems to be a promising method for resolving racemic compounds.[4,5)]

The optically active polymer, (+)-PTrMA, was prepared as described previously.[3)] The specific rotation of this polymer was considered to be greater than +250° and the degree of polymerization was estimated to be about 220. The polymer was ground and the particles of 20-44 μm were used as packing. A stainless-steel column (25 × 0.46 cm (i.d.)) was packed with (+)-PTrMA (1.3 g) by slurry technique. The packed column gave 2200 and 1800 theoretical plates for acetone and benzene, respectively. The void volume of the column was estimated to be 3.4 ml with water. The high-performance liquid chromatography was accomplished on a JASCO Twincle chromatograph equipped with a JASCO UV-254-II or UV-100-III detector at 20 ± 1°C. The flow rate of eluent (methanol) was 0.72 ml/min and 4×10^{-4} - 4×10^{-1} mg of racemic compounds were used. Most of racemic compounds are either trivial derivatives of, or are themselves, well known compounds. They were identified by IR and ^1H NMR spectroscopies.

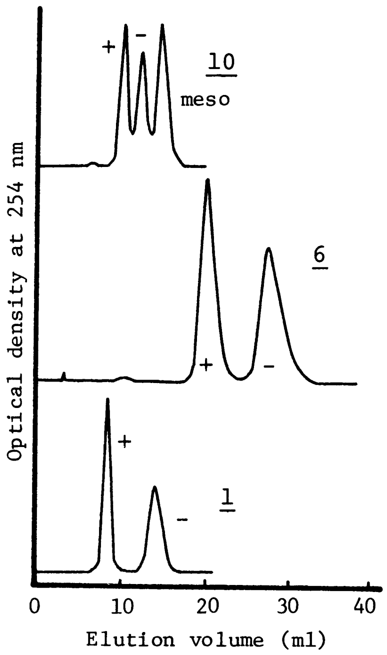
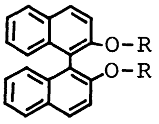
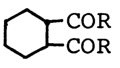
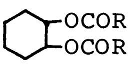
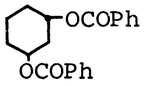
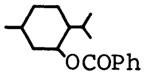
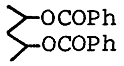
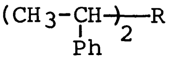
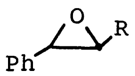
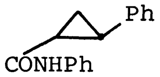
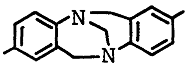
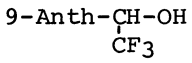
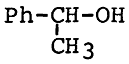
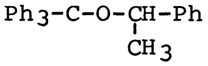


Fig. 1. Resolution of 1, 6, and 10.

Table 1 shows the results of the resolution of various racemic compounds. Many compounds were almost completely resolved under the conditions employed; that is, the resolution factors R_S were greater than one. Fig. 1 is the chromatogram of 1, 6, and 10. 1,1'-Binaphthyl derivatives 1, 2, and 3 were completely separated and the retention volume of each compound increased with a decrease of polarity. Chiral 1 is the key compound for the preparation of chiral crown ethers which show excellent ability of resolving racemic amino acids[6,7] and for the effective asymmetric reduction of ketones by $LiAlH_4$.[8] trans-1,2- And 1,3-disubstituted cyclohexanes, 4, 5, 6, and 8, containing phenyl groups were also resolved. Octanoic acid ester 7 was not resolved to a measurable extent at a flow rate of 0.72 ml/min, but was resolved to give $\alpha = 1.12$ at 0.20 ml/min. Successful resolution of 6 and 8 suggests that (+)-PTrMA may be useful for the resolution of some sugar derivatives. (±)-Menthyl benzoate 9 gave a diagram with two peaks which were not observed in the previous chromatography with hexane as eluent.[3] Three isomers, (±) and meso, of each 10 and 11 were separated. In 10, meso isomer was eluted last of all, but in 11 it appeared between (+) and (-) isomers. Three isomers of the ether 12 did not show clearly separated peaks. trans-Stilbene oxide 13 was finely resolved, but styrene oxide 14 was not. trans-1,2-Disubstituted cyclopropane 15 was almost completely resolved. Tröger base 16 was better resolved than the chromatography using hexane as eluent which gave the separation factor $\alpha = 1.36$.[3] (-)-Hexahelicene came out completely at 14-33 ml elution volume but (+) isomer was not eluted even at 240 ml. A fluoro alcohol 18, whose chiral derivative is known to show chiral recognition of enantiomers,[9] was sufficiently separated on (+)-PTrMA. 1-Phenylethyl alcohol 19 was not resolved but its triphenylmethyl ether was partially resolved. Methanol was the best eluent for the resolution of 13. The reason for this result is now under investigation.

Table 1. Liquid Chromatographic Resolution of Racemic Compounds[a]

racemate			k'[b] and (rotation)		α[c]	R_s[d]
	R	No.	less retained	more retained		
	H	1	1.50 (+)	3.20 (-)	2.13	2.39
	H, CH_3	2	3.78 (+)	6.67 (-)	1.76	1.86
	CH_3	3	9.67	15.94	1.65	1.39
	OPh	4	4.39 (+)	5.68 (-)	1.29	1.05
	NHPh	5	1.47 (-)	5.21 (+)	3.54	1.48
	Ph	6	4.88 (+)	7.06 (-)	1.45	1.68
	$(CH_2)_6CH_3$	7	0.86^e	0.96^e	1.12	0.6
		8	4.07 (+)	6.67 (-)	1.66	2.07
		9	2.06 (-)	2.44 (+)	1.19	0.7
		10	1.94 (+)	2.56 (-)[f]	1.32	0.93
 $(CH_3\text{-}\underset{Ph}{CH}\text{-})_2R$	-S-	11	1.83 (+)	2.99 (-)[g]	1.63	1.72
	-O-	12	0.76		∿1	∿0
	Ph	13[h]	2.27 (-)	4.92 (+)	2.17	2.39
	H	14	1.21		∿1	∿0
		15	0.71 (-)	1.04 (+)	1.46	0.98
		16	1.74 (+)	3.08 (-)	1.77	2.15
Hexahelicene		17	5.12 (-)	>69 (+)	>13	>1
 $9\text{-Anth-}\underset{CF_3}{CH}\text{-OH}$		18	0.61 (+)	0.96 (-)	1.57	1.10
 $Ph\text{-}\underset{CH_3}{CH}\text{-OH}$		19	0.53		∿1	∿0
 $Ph_3\text{-C-O-}\underset{CH_3}{CH}\text{-Ph}$		20	6.06	8.10	1.34	0.6

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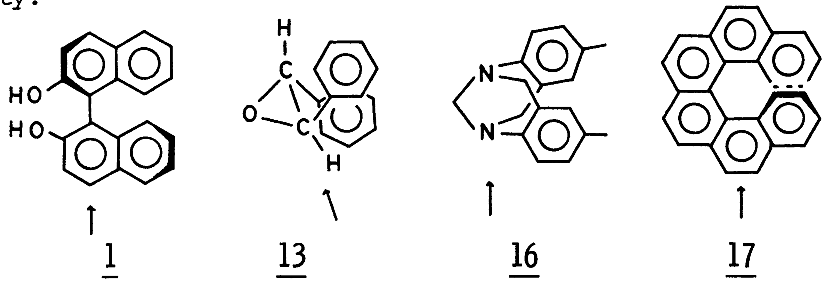
[a] Operating condition: column 25×0.46 cm (i.d.), flow rate of methanol 0.72 ml/min.
[b] Capacity factor = (retention volume of enantiomer - void volume of column)/(void volume of column).
[c] Separation factor = (k' of more retained enantiomer)/(k' of less retained enantiomer).
[d] Resolution factor = 2 × (distance between the peaks of more and less retained enantiomers)/(sum of bandwidth of two peaks).
[e] Flow rate of methanol was 0.20 ml/min.
[f] The k' for meso isomer was 3.26.
[g] The k' for meso isomer was 2.38.
[h] When ethanol, isopropanol, and acetonitrile were used as eluents, 13 was not clearly separated with two peaks.

Fig. 2 shows the structure of (S)-(-)-1,[10] (1R,2R)-(+)-13,[11] (1S,3S)-(-)-16,[12] and (P)-(+)-17,[13] which were more retained to (+)-PTrMA. All compounds have the C_2 axis and right-handed (or P) helicity with respect to their aromatic groups. This indicates that (+)-PTrMA may have P helicity, since (+)-PTrMA has extremely strong interaction with (+)-PTrMA but very weak one with (-)-PTrMA which has opposite helicity.[14]



1 13 16 17

Fig. 2. Structure of (S)-(-)-1, (1R,2R)-(+)-13, (1S,3S)-(-)-16, and (P)-(+)-17, which had stronger interaction with (+)-PTrMA.

The theoretical plates of (+)-PTrMA column used in this work did not change after continuous use for 5days. The column seems to be very useful to resolve th racemic compounds, especially those containing aromatic moiety.

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References and Note

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