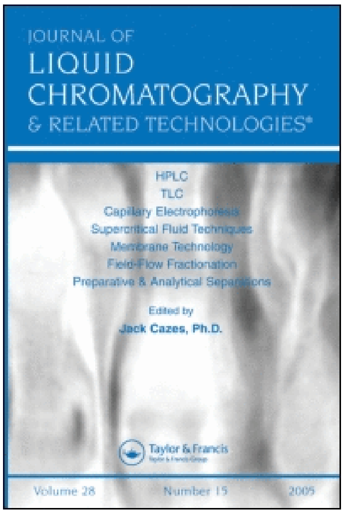
This article was downloaded by:
On: *24 January 2011*
Access details: *Access Details: Free Access*
Publisher *Taylor & Francis*
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

Resolution of Enantiomers by HPLC on Optically Active Poly(triphenylmethyl Methacrylate)

Yoshio Okamoto[a]; Koichi Hatada[a]
[a] Department of Chemistry Faculty of Engineering Science, Osaka University, Toyonaka, Osaka, Japan

To cite this Article Okamoto, Yoshio and Hatada, Koichi(1986) 'Resolution of Enantiomers by HPLC on Optically Active Poly(triphenylmethyl Methacrylate)', Journal of Liquid Chromatography & Related Technologies, 9: 2, 369 — 384
To link to this Article: DOI: 10.1080/01483918608076642
URL: http://dx.doi.org/10.1080/01483918608076642

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: http://www.informaworld.com/terms-and-conditions-of-access.pdf

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

JOURNAL OF LIQUID CHROMATOGRAPHY, 9(2&3), 369-384 (1986)

RESOLUTION OF ENANTIOMERS BY HPLC ON OPTICALLY ACTIVE POLY(TRIPHENYLMETHYL METHACRYLATE)

Yoshio Okamoto and Koichi Hatada
Department of Chemistry
Faculty of Engineering Science
Osaka University
Toyonaka, Osaka 560, Japan

Downloaded At: 16:09 24 January 2011

ABSTRACT

Optically active (+)-poly(triphenylmethyl methacrylate) (PTrMA) which has the chirality due to only helicity has been used as two different types of chiral stationary phases for resolving enantiomers by HPLC. One was prepared with the insoluble (+)-PTrMA ground to small particles and the other by adsorbing the soluble polymer on macroporous silica gel. These stationary phases, particulary the latter, resolved a wide variety of enantiomers including hydrocarbons, esters, amides, halides, phosphoric compounds and so on by using a polar eluent like methanol.

OPTICALLY ACTIVE PTrMA

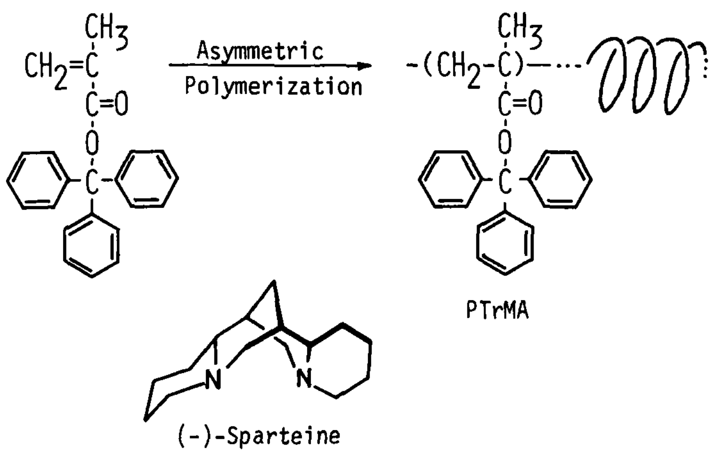
Optically active poly(triphenylmethyl methacrylate) (PTrMA) is the first example of the optically active vinyl polymer whose chirality is caused only by helicity.[1,2] The optically active (+)-polymer can be prepared by asymmetric polymerization of triphenylmethyl methacrylate with chiral anionic initiators such

Copyright © 1986 by Marcel Dekker, Inc.

0148-3919/86/0902-0369$3.50/0

as (-)-sparteine-butyllithium[1] and (+)-(2S,3S)-dimethoxy-1,4-bis(dimethylamino)butane-lithium amide complexes[3] in toluene at low temperature. The polymer shows high crystallinity and the one that has a degree of polymerization greater than about 70 is insoluble in common organic solvents. The rather low-molecular-weight soluble polymer that has almost pure one-handed helicity shows a specific rotation ($[\alpha]_D^{25}$) about +360° (THF).[4] Triphenylmethyl groups in the polymer likely take either right- or left-handed propeller structure.

Downloaded At: 16:09 24 January 2011



CHIRAL STATIONARY PHASE

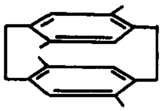
Insoluble (+)-PTrMA of high-molecular-weight was ground and the particles of 20-44 μm were used as a chiral stationary phase.[5] The material (1.3g) was packed carefully in an HPLC column (25x0.46 (id)cm) by slurry method. The column showed a plate number about 2200 for acetone when methanol was used as eluent. The preparation of an effective HPLC column by this method was not easy with a small quantity of the polymer and the durability of the column was not satisfactory.

In order to overcome these defects, lower-molecular-weight soluble (+)-PTrMA (0.6g) was adsorbed on macroporous silica gel (10 μm, pore size 1000 or 4000 Å, 3g) which had been treated with a silanizing agent such as dichlorodiphenylsilane.[6] By this procedure, we could get easily a more effective stationary phase with higher durability. The column (25x0.46 (id)cm) packed with the (+)-PTrMA-coated silica gel (about 2.5 g) showed a plate number 4000 - 7000 for acetone. Almost no polymer was eluted from the column when non-solvents to the polymer (for instance, hexane, acetonitrile, and methanol) were employed as eluents. The use of macroporous silica gel as a support of chiral polymers has also been successfully applied to the preparation of other chiral stationary phases comprising cellulose esters[7] and polysaccharide carbamate derivatives.[8] This coating method is very convenient and useful to prepare stationary phases for HPLC with polymers and must be applicable to many polymer systems.

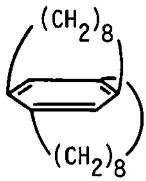
RESOLUTION ON GROUND (+)-PTrMA

Several years ago, we demonstrated that optically active PTrMA had remarkable chiral recognition ability to several hydrocarbons like **1** - **3**.[9]

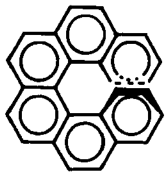
Downloaded At: 16:09 24 January 2011



1



2



3

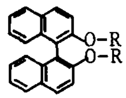
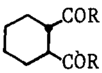
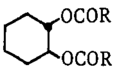
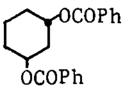
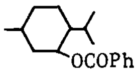
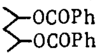
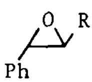
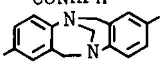
Then, the polymer was employed to prepare an HPLC column. The HPLC column of finely ground (+)-PTrMA resolved various racemic compounds having aromatic group by using methanol as eluent (Table 1).[5] Although the ground polymer is particularly useful for resolving helicenes,[9,10] the HPLC column was not enough for practical use because of lack of durability.

Downloaded At: 16:09 24 January 2011

RESOLUTION ON (+)-PTrMA-COATED SILICA GEL[11]

(+)-PTrMA-coated silica gel more easily gave us a column of a higher plate number than the ground (+)-PTrMA, and made it possible to perform more efficient resolution (Fig. 1). Interestingly, these two stationary phases showed different chiral recognitions, as observed in the resolution of 1,1'-binaphthyl derivatives (Table 2). Generally, more expeditious chromatography was attained with the (+)-PTrMA-coated packing; that is, capacity factors (k') of enantiomers are smaller for the (+)-PTrMA-coated packing than for the ground (+)-PTrMA packing. Most compounds listed in Table 1 were resolved on the coated packing. Besides these, many enantiomers were also separated on the column (Fig. 2). 2-Butanol and 1-phenylethanol were not resolved, but

TABLE 1
Resolution on the Finely Ground (+)-PTrMA[a]

Racemate	R	No.	k_1'[b] (rotation)	α[c]	Rs[d]
	H	4	1.50 (+)	2.13	2.39
	H, CH_3	5	3.78 (+)	1.76	1.86
	CH_3	6	9.67	1.65	1.39
	OPh	7	4.39 (+)	1.29	1.05
	NHPh	8	1.47 (-)	3.54	1.48
	Ph	9	4.88 (+)	1.45	1.68
	$(CH_2)_6CH_3$	10	0.86	1.12	0.6
		11	4.07 (+)	1.66	2.07
		12	2.06 (-)	1.19	0.7
		13	1.94 (+)	1.32	0.93
$(CH_3\text{-}CH(Ph)\text{-})_2S$		14	1.83 (+)	1.63	1.72
	Ph	15	2.27 (-)	2.17	2.39
	H	16	1.21	~1	~0
		17	0.71 (-)	1.46	0.98
		18	1.74 (+)	1.77	2.15
Hexahelicene		3	5.12 (-)	>13	>1
9-Anth-CH(CF_3)-OH		19	0.61 (+)	1.57	1.10

[a] Operating condition: column 25 × 0.46 cm (i.d.), flow rate of methanol 0.72 ml/min.
[b] Capacity factor to the first-eluted isomer = (retention volume of the isomer - void volume of column)/(void volume of column).
[c] Separation factor = k_2'/k_1'.
[d] Resolution factor = 2 × (distance between the peaks of more and less retained isomers)/(sum of bandwidth of two peaks).

Downloaded At: 16:09 24 January 2011

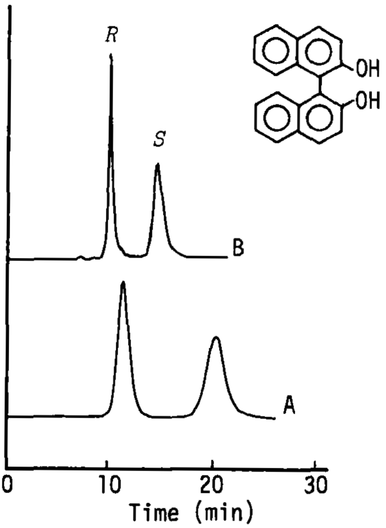


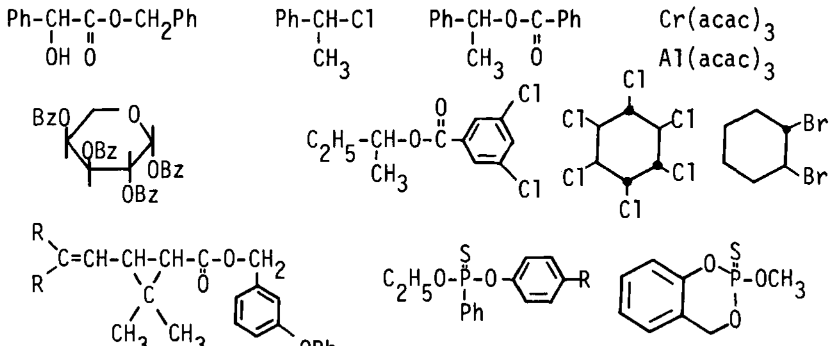
FIGURE 1. Resolution of binaphthol on ground (+)-PTrMA (A) and (+)-PTrMA-coated silica gel (B) columns (column: 25 x 0.46 (id) cm, eluent: methanol, 0.72 ml/min for A and 0.50 ml/min for B)

Downloaded At: 16:09 24 January 2011

TABLE 2
Resolution of 2,2'-Disubstituted 1,1'-Binaphthyls on (+)-PTrMA Columns

Substituents	(+)-PTrMA-coated silica gel column[a]				Ground (+)-PTrMA column[b]			
	k'_1	k'_2	α	Rs	k'_1	k'_2	α	Rs
HO-	0.50	1.16	2.32	3.83	1.50	3.20	2.13	2.39
CH_3O-	4.76	8.23	1.73	0.93	9.67	15.9	1.65	1.39
NH_2-	1.67	2.32	1.39	1.08	5.62	15.9	2.80	2.52
Br-	3.77	5.32	1.41	1.06	9.0	9.0	~1	~0
CH_3-	3.01	4.30	1.43	1.63	6.1	6.1	~1	~0

[a] See Fig. 1. [b] See Table 1.



20 21

FIGURE 2. Compounds resolved on a (+)-PTrMA-coated column

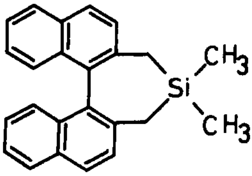
Downloaded At: 16:09 24 January 2011

were resolved completely as their 3,5-dichlorobenzoate and benzoate, respectively.[12)]

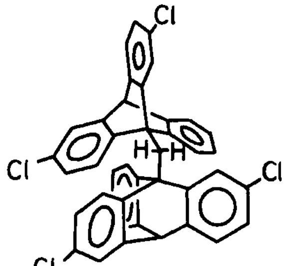
Trisacetylacetonates, $Co(acac)_3$ and $Cr(acac)_3$, were resolved,[13)] and $Al(acac)_3$ was for the first time separated into optically active forms.[14)] It was possible to resolve racemic compounds having a phosphorous as a chiral center.[15)] Insecticides, EPN (20) and salithion (21), were resolved. Some halides were also suitable compounds for the resolution on (+)-PTrMA.

The (+)-PTrMA column is particularly useful for the resolution of stereochemically interesting compounds (22 - 32)[16-27)] that are difficult to be resolved by other methods because of lack of functionalities.

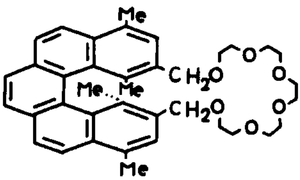
Biochemically interesting compounds, 33, 34, and 35 were also separated. An intermediate 33 for the synthesis of an antibiotics was completely resolved.[28)] Three peaks were observed in the resolution of 34 which consisted of four isomers.[29)] The column was useful for distinguishing three types of α-tocopherol 35 as acetate.[30)]



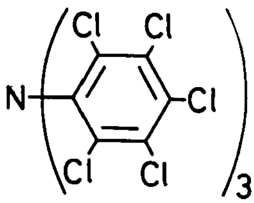
22[16]



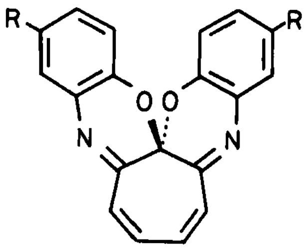
23[17,18]



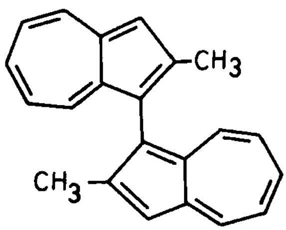
24[19]



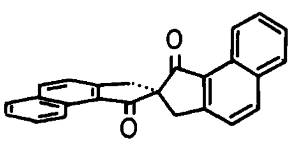
25[20]



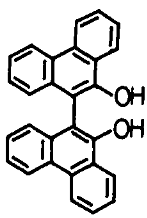
26[21]



27[22]

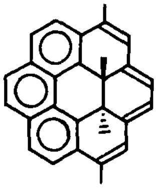


28[23]

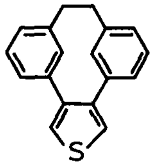


29[24]

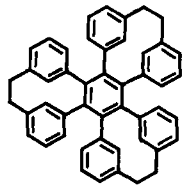
Downloaded At: 16:09 24 January 2011



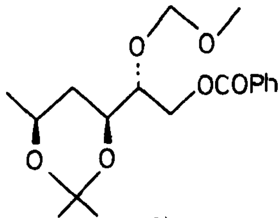
30[25)]



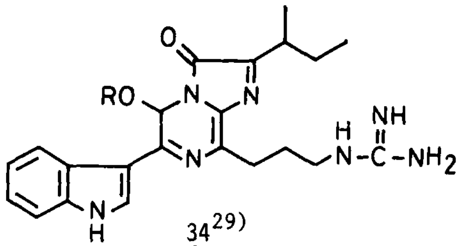
31[26)]



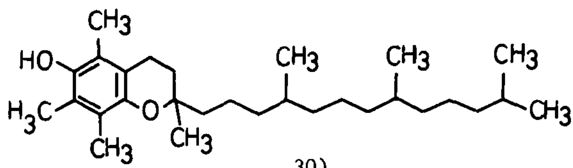
32[27)]



33[28)]



34[29)]



35[30)]

Downloaded At: 16:09 24 January 2011

INFLUENCE OF ELUENT

The eluents that one can use to the (+)-PTrMA-coated packing are limited. Aromatic hydrocarbon, chloroform, and THF must be avoided because of the solubility of the polymer. For many compounds, methanol is the most suitable eluent, although hexane-2-propanol mixture is sametimes preferable (Table 3). This suggests that the nonpolar interaction between nonpolar groups, probably, triphenylmethyl propellers and nonpolar groups of

TABLE 3
Effect of Eluent on Resolution of Racemic Compounds

Eluent	4	18	15	Benzoin	$Cr(acac)_3$
Hexane	N	P	C	N	P
CH_3CN	N	P	C	N	N
C_2H_5OH	C	C	C	P	P
CH_3OH	C	C	C	C	P
CH_3OH/H_2O				C	C

C: Complete (base line) separation.

P: Partial separation (two peaks).

N: No separation.

Downloaded At: 16:09 24 January 2011

chiral compounds plays an important role for effective chiral recognition in the chromatography.

INFLUENCE OF (+)-PTrMA/SILICA GEL RATIO ON RESOLUTION

As discussed earlier, two different types of the stationary phases showed different chiral discrimination. More detailed data on this were obtained from the experiment shown in Fig. 3,[31] where the differences of retention volumes between each enantiomers of 4 and trans-1,2-cyclobutanedicarboxylic acid dianilide 36 are plotted against the weight ratio of (+)-PTrMA to silica gel on the (+)-PTrMA-coated stationary phase. The difference of retention volume for the enantiomers of 4 increased linearly with an increase of the concentration of (+)-PTrMA on silica gel, whereas that for 36 was maximum at the ratio about 0.2.

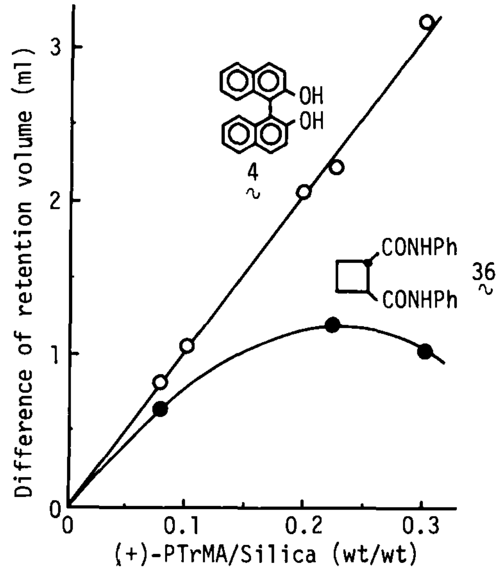


FIGURE 3. Infuence of (+)-PTrMA/silica gel ratio on the difference of retention volumes of enantiomers, 4 and 36

These results may be interpretated in the following way. When the concentration of the polymer is low, each polymer chain exists isolatedly (Fig. 4(a)). Then, the resolution must be governed on the chiral sites on a single polymer chain. At high concentrations of the polymer, (+)-PTrMA will associate in an ordered form because of high crystallinity of the polymer (Fig. 4 (b)). Then, new chiral spaces must be formed between the polymer chains. These spaces probably show chiral recognition different from that of the isolated polymer chain. Therefore, one compound will be resolved better on the poorly (+)-PTrMA-coated silica gel and another compound on the ground (+)-PTrMA as well as on the heavily (+)-PTrMA-coated silica gel (Table 2).

Downloaded At: 16:09 24 January 2011

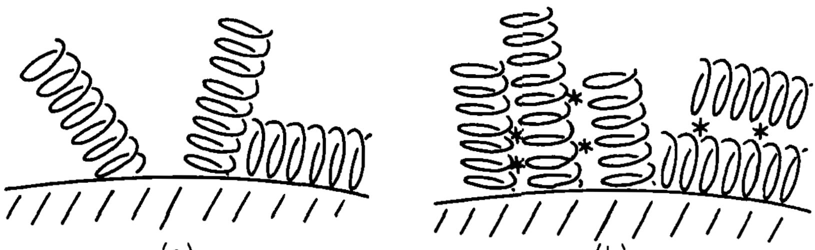


FIGURE 4. Schematic representation of (+)-PTrMA-coated silica gel

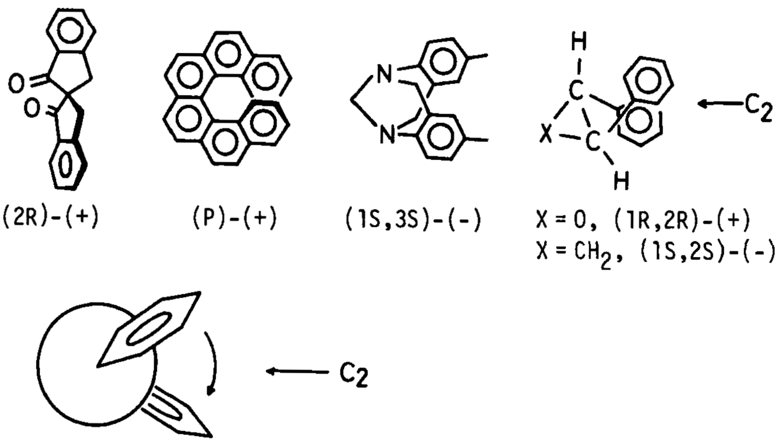


FIGURE 5. Enantiomers adsorbed more strongly on (+)-PTrMA

Downloaded At: 16:09 24 January 2011

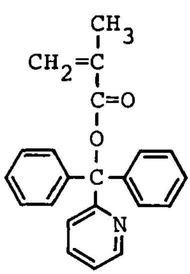
STEREOCHEMISTRY OF RESOLUTION

The (+)-PTrMA columns showed a tendency in the resolution of the compounds which possess a C_2 axis and two aromatic groups (Fig. 5);[5] that is, more retained enantiomers have P-helicity with respect of their aromatic groups if one looks at the molecule from the direction perpendicular to a C_2 axis. This is also true to **24** and **26**. Therefore, absolute configuration of compounds is predictable from the results of resolution if the compounds are similar in their structure to those in Fig. 5.

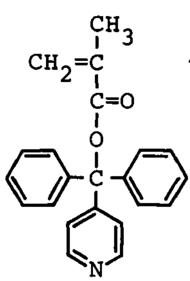
RESOLUTION ON OTHER CHIRAL POLYMETHACRYLATES

A defect of the (+)-PTrMA stationary phases is the fact that triphenylmethyl ester is solvolyzed in methanol to afford methyl triphenylmethyl ether. Therefore, it is preferable to use the chiral columns at low temperature when an alcoholic eluent is used and the solvent for reserving the column must be non-alcoholic.

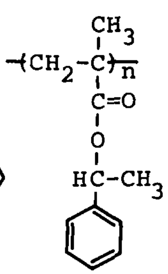
Optically active polymers similar to (+)-PTrMA are obtainable by the asymmetric anionic polymerizations of diphenyl-2-pyridylmethyl methacrylate (**37**) and diphenyl-4-pyridylmethyl methacrylate (**38**).[32] Although optical resolution abilities of these polymers were low compared with that of (+)-PTrMA when polar eluents were used, they showed interesting chiral recogni-



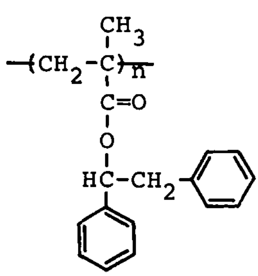
37



38



39



40

Downloaded At: 16:09 24 January 2011

tion toward polar compounds by using a hexane-2-propanol mixture as eluent. Hydrogen bond between the pyridyl groups of the polymer and enantiomers may contribute to the resolution.

The chiral recognition abilities of these polymethacrylates seem to be special because optically active isotactic polymethacrylates (39, 40) having chiral ester groups showed no chiral recognition to many compounds.[33)] The rigid helical structure which arises from the bulky triarylmethyl groups may be a key point for the high chiral recognition abilities of PTrMA and its analogues.

Downloaded At: 16:09 24 January 2011

CONCLUSION

(+)-PTrMA is a unique polymer having a rigid helical conformation. The polymer showed interesting chiral recognition, particularly when it was coated on macroporous silica gel. The (+)-PTrMA-coated silica gel resolved a wide variety of racemic compounds as a stationary phase for HPLC.

ACKNOWLEDGEMENT

The authors acknowledge Professor Emeritus H. Yuki for his advice and encouragement. We also thank many co-workers and those who kindly afforded their variable samples. The work was supported by a Grant-in-Aid for Scientific Research by the Ministry of Education.

REFERENCES

1) Y. Okamoto, K. Suzuki, K. Ohta, K. Hatada, H. Yuki, J. Am. Chem. Soc., 101, 4769 (1979).
2) Y. Okamoto, K. Suzuki, H. Yuki, J. Polym. Sci. Polym. Chem. Ed., 18, 3043 (1980).
3) Y. Okamoto, H. Shohi, H. Yuki, J. Polym. Sci. Polym. Lett. Ed., 21, 601 (1983).
4) Y. Okamoto, I. Okamoto, H. Yuki, J. Polym. Sci. Polym. Lett. Ed., 19, 451 (1981).
5) Y. Okamoto, I. Okamoto, H. Yuki, Chem. Lett., 1981, 835.
6) Y. Okamoto, S. Honda, I. Okamoto, H. Yuki, S. Murata, R. Noyori, H. Takaya, J. Am. Chem. Soc., 103, 6971 (1981).
7) Y. Okamoto, M. Kawashima, K. Yamamoto, K. Hatada, Chem. Lett., 1984, 739.
8) Y. Okamoto, M. Kawashima, K. Hatada, J. Am. Chem. Soc., 106, 337 (1984).
9) H. Yuki, Y. Okamoto, I. Okamoto, J. Am. Chem. Soc., 102, 6356 (1980).
10) M. Nakazaki, K. Yamamoto, M. Maeda, Chem. Lett., 1980, 1553; J. Org. Chem., 46, 1985 (1981).
11) This type of packing material and packed columns (Chiralpak-OT-(+)) are commercially available from Daicel Chemical Industries, 8-1, Kasumigaseki 3-Chome, Chiyoda-ku, Tokyo 100, Japan.
12) Y. Okamoto, S. Honda, K. Hatada, H. Yuki, Bull. Chem. Soc. Jpn., to be submitted.
13) Y. Okamoto, S. Honda, E. Yashima, H. Yuki, Chem. Lett., 1981, 1221.
14) Y. Okamoto, E. Yashima, K. Hatada, J. Chem. Soc. Chem. Commun., 1984, 1051.
15) Y. Okamoto, S. Honda, I. Okamoto, Y. Toga, S. Kobayashi, Bull. Chem. Soc. Jpn., 59, 1681 (1984).
16) R. Noyori, N. Sano, S. Murata, Y. Okamoto, H. Yuki, Tetrahedron Lett., 23, 2969 (1982).
17) Y. Kawada, H. Iwamura, Y. Okamoto, H. Yuki, Tetrahedron Lett., 24, 791 (1983).
18) Y. Kawada, Y. Okamoto, H. Iwamura, Tetrahedron Lett., 24, 5359 (1983).
19) M. Nakazaki, K. Yamamoto, T. Ikeda, T. Kitsuki, Y. Okamoto, J. Chem. Soc. Chem. Commun., 1983, 787.
20) Y. Okamoto, E. Yashima, K. Hatada, K. Mislow, J. Org. Chem., 49, 557 (1984).
21) Y. Okamoto, S. Honda, H. Yuki, H. Nakamura, Y. Iitaka, T. Nozoe, Chem. Lett., 1984, 1149.
22) A. Tajiri, M. Fukuda, M. Hatano, T. Morita, K. Takase, Angew. Chem. Int. Ed. Engl., 22, 870 (1983).
23) N. Harada, J. Iwabuchi, Y. Yokota, H. Uda, Y. Okamoto, H. Yuki, Y. Kawada, Proceeding at 15th Symposium on Structural Organic Chemistry, Kyoto, 1982, October, Abst. No. B3-35.
24) K. Yamamoto, H. Fukushima, Y. Okamoto, K. Hatada, M. Nakazaki, J. Chem. Soc. Chem. Commun., 1984, 1111.

Downloaded At: 16:09 24 January 2011

25) K. Yamamoto, T. Ueda, H. Yumioka, Y. Okamoto, T. Yoshida, Chem. Lett., 1984, 1977.

26) K. Meurer, A. Aigner, F. Vogtle, J. Inclusion Phen., 3, 51 (1985).

27) W. Kissener, F. Vogtle, Angew. Chem. Int. Ed. Engl., 97, (1985) in press.

28) Y. Takeuchi, M. Furumura, E. Yoshii, Chem. Pham. Bull., 31, 3967 (1983).

29) Y. Toya, S. Nakatsuka, T. Goto, Tetrahedron Lett., 24, 5753 (1983).

30) H. Yamaguchi, Y. Itakura, K. Kunihiro, Iyakuhin Kenkyu, 15, 536 (1984).

31) Y. Okamoto, S. Honda, K. Hatada, H. Yuki, J. Chromatogr. to be submitted.

32) Y. Okamoto, M. Ishikura, K. Hatada, H. Yuki, Polym. J., 15, 851 (1983).

33) Y. Okamoto et al., unpublished data.

Downloaded At: 16:09 24 January 2011