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USEFUL CHIRAL PACKING MATERIALS FOR HIGH-PERFORMANCE LIQUID CHROMATOGRAPHIC RESOLUTION. CELLULOSE TRIACETATE AND TRIBENZOATE COATED ON MACROPOROUS SILICA GEL[1]

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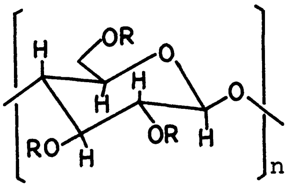
Cellulose triacetate and tribenzoate coated on macroporous silica gel showed excellent capabilities of chiral recognition as packing materials for high-performance liquid chromatographic resolution of various enantiomers. Chiral recognition by the cellulose triacetate was different from that by the microcrystalline cellulose triacetate.

Direct optical resolution of enantiomers by liquid chromatography has been greatly developed in past ten years and several practically useful chiral stationary phases have been reported.[2-6] Since Hesse and Hagel[7] found that microcrystalline cellulose triacetate prepared by heterogeneous acetylation has a capability of resolution superior to cellulose triacetate recovered from a solution, the former triacetate has often been used in liquid chromatographic resolution of aromatic compounds.[8-10] In this communication we report the resolution of enantiomers by means of high-performance liquid chromatography (HPLC) using cellulose triacetate (1) and tribenzoate (2) coated on silica gel. These chiral stationary phases showed a high ability of resolution completely different from that of the microcrystalline cellulose triacetate.



1 (R = CH_3CO)
2 (R = C_6H_5CO)

Cellulose triacetate was prepared from microcrystalline cellulose (Merck) according to the procedure reported in literature,[7] and 2 was synthesized by the reaction of benzoyl chloride with the same cellulose dissolved in N,N-dimethylacetamide-LiCl-pyridine (15 : 1.5 : 7) mixture. Elemental analysis, IR, and ^1H NMR spectra indicated that hydroxy groups of cellulose were nearly completely converted to ester groups. The degree of polymerization of 2 was determined to be 200 from the GPC chromatogram calibrated with polystyrene standard. Macroporous silica gel

(LiChrospher SI 4000, Merck) was treated with a large excess of 3-aminopropyltriethoxysilane, and coated with about 20 wt% of the cellulose triesters. In the process of coating, 1 was dissolved in dichloromethane-ethanol (90 : 10) and 2 in dichloromethane, and the solvents were evaporated under reduced pressure. The packing materials were packed in a stainless steel column (25 cm × 0.46 cm (id)) by slurry method. Theoretical plate numbers of the packed columns for a weakly retained compound were 4000 - 7000. Chromatography was accomplished on a JASCO TRIROTAR II equipped with a JASCO UVIDEC-100-III UV and a DIP-181C polarimeter (cell 5 × 0.30 (id) cm) detectors at 25°C, flow rates of eluents being 0.5 ml min^{-1}.

The results of resolution of various enantiomers are summarized in Table 1 and typical chromatograms are illustrated in Fig. 1. Most racemic compounds except for a pentahelicene derivative 10 were resolved on either 1 or 2. Better separation was attained with eluents of high water contents, suggesting that hydrophobic interaction between the chiral stationary phases and enantiomers plays an important role in chiral recognition.[11)]

In the resolution of Tröger base 3, (+) isomer was eluted first, followed by (-) isomer. This elution order is opposite to that observed in the resolution by microcrystalline cellulose triacetate.[7)] Hesse and Hagel pointed out that microcrystalline cellulose triacetate loses the original ability of chiral recognition when recovered from a solution. Microcrystalline cellulose triacetate prepared by heterogeneous acetylation of native cellulose has a crystalline structure different from the triacetate recovered from a solution.[12)] These unlike crystal structures of the triacetates seem responsible for the reversed elution order against Tröger base. Microcrystalline cellulose triacetate has often been used in low or medium pressure chromatography because of lack of compressive strength. The present chiral packing materials possessed high compressive strength and durability which are important characters for making an efficient column for HPLC.

All compounds listed in Table 1 were resolved on optically active (+)-poly(triphenylmethyl methacrylate) coated on silica gel.[5,13)] This chiral polymer showed higher separation against 3, 4, 6, 7, 9, 10, and 11 than both the cellulose triesters, whereas

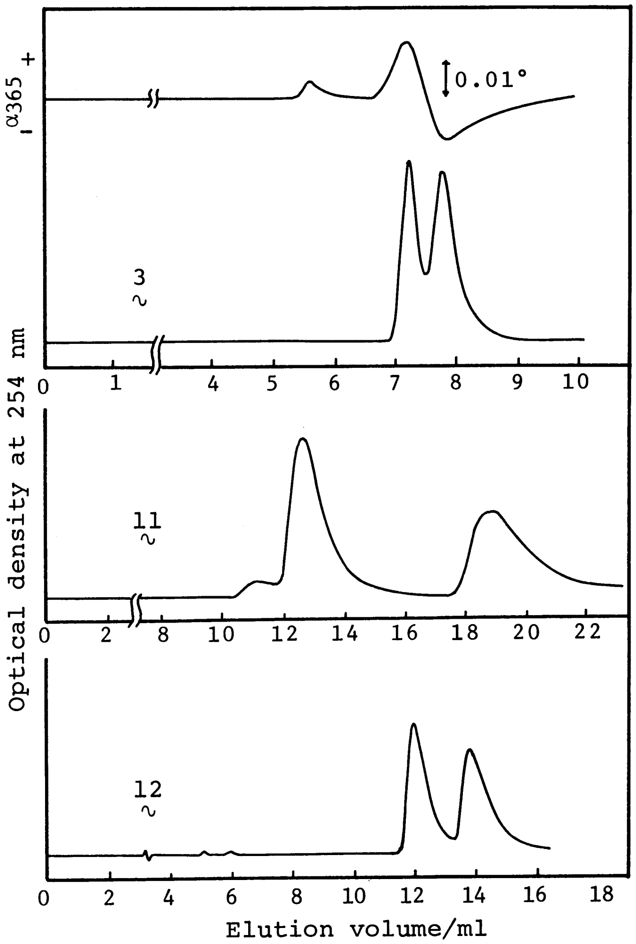
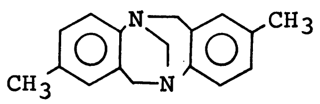
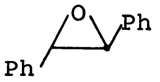
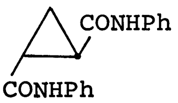
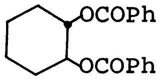
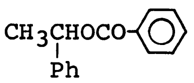
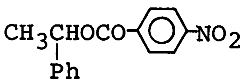
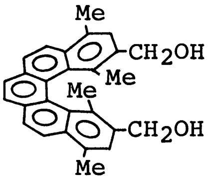
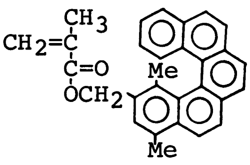
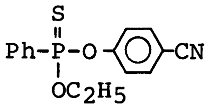


Fig. 1. Resolution of 3, 11, and 12 on cellulose triacetate column. Conditions are shown in Table 1; eluent: 50% EtOH.

Table 1. Resolution of enantiomers on cellulose triacetate and tribenzoate by using ethanol-water mixtures as eluents[a)]

Compound	Entry	Triacetate column				Tribenzoate column			
		H_2O(vol%)	k_1[b)]	α[c)]	Rs[d)]	H_2O(vol%)	k_1[b)]	α[c)]	Rs[d)]
	3	0	0.09(+)	1.36	0.33	0	1.20(+)	1.15	
		15	0.07	≈1					
		30	0.14(+)	1.1		20	1.68(+)	1.18	
		50	1.48(+)	1.14	0.96				
	4	0	0.17(−)	1.27	0.67	0	0.65(+)	1.40	1.72
		50	2.16(−)	1.33	1.78	20	2.66(+)	1.38	1.76
	5	50	1.00(−)	1.28	1.09	0	0.30(−)	1.59	0.48
						20	0.96(−)	1.52	0.63
	6	50	1.28	1.22	0.52	20	3.15(+)	≈1	
	7	50	1.5 (+)	≈1		0	0.63(+)	1.14	0.42
						20	1.92(+)	1.18	0.59
	8	50	5.10(−)	1.11	0.86	0	1.48(+)	1.28	1.23
						20	6.35(+)	1.33	1.62
hexahelicene	9	50	5.93(−)	1.34	1.30	0	1.35(+)	≈1	
	10	50	1.30(−)	≈1		0	0.10	≈1	
	11	50	3.70(−)	1.61	2.14	0	1.64(+)	≈1	
	12	50	2.75(+)	1.20	1.29	20	2.85(+)	≈1	

a) Column (25 cm × 0.46 cm (id)), flow rate 0.5 ml min^{-1}, temp 25 °C. b) Capacity factor of the first eluted isomer = (retention time of the first eluted isomer − dead time)/dead time. The sign in the parentheses is that of the optical rotation at 365 nm of isomer. c) Separation factor = (capacity factor of the second eluted isomer)/k_1. d) Resolution factor = 2 × (difference of retention times of (+) and (−) isomers)/(the sum of times corresponding the base lines of the two peaks).

other compounds, 5, 8, and 12, were better or comparably resolved on either of the cellulose triesters. Durability of the cellulose triester columns was higher than that of the (+)-poly(triphenylmethyl methacrylate) column.

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