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Tris(1-phenylethylcarbamate)s of Cellulose and Amylose as Useful Chiral Stationary Phases for Chromatographic Optical Resolution

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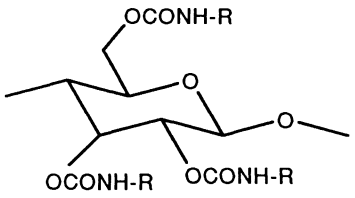
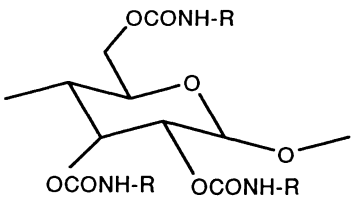
(R)-, (S)-, and (RS)-1-phenylethylcarbamates of cellulose and amylose were synthesized and used as chiral stationary phases for high-performance liquid chromatography. The chiral recognition abilities of the 1-phenylethyl derivatives depended greatly on the chirality of 1-phenylethyl groups. Among six derivatives, amylose tris((S)-1-phenylethylcarbamate) showed high optical resolving ability for many compounds.

We reported that phenylcarbamate derivatives of polysaccharides such as cellulose and amylose showed high optical resolving abilities for many racemic compounds as chiral stationary phases (CSP) for high-performance liquid chromatography (HPLC).[1-5] Their chiral recognition abilities depended on the substituents on the phenyl groups. On the other hand, cellulose tris(methylcarbamate) showed very low optical resolving ability.[2]

In the present study, we synthesized cellulose triscarbamates (1-(R), -(S), -(RS)) and amylose triscarbamates (2-(R), -(S), -(RS)) having chiral side groups, (R)-, (S)-, or (RS)-1-phenylethyl, and used them as CSP for HPLC.

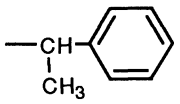


1 -(R), -(S), -(RS)



2 -(R), -(S), -(RS)

R = -(R), -(S), -(RS)



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Cellulose (Merck, Avicel) and amylose (Nacalai Tesque, MW= 16000) were dissolved in N,N-dimethylacetamide-LiCl, and then allowed to react with excess of (R)-, (S)-, and (RS)-1-phenylethyl isocyanates in the presence of pyridine at 100 °C. The reaction products were precipitated in methanol. Elemental analyses and IR and NMR spectra of the polysaccharide carbamates indicated that almost all hydroxy groups of cellulose and amylose were converted into urethane moieties. In the preparation of (RS)-derivatives, the enantiomer-selective reaction did not seem to proceed because the unreacted isocyanate was almost optically inactive. The obtained carbamates (0.75 g) were dissolved in $CHCl_3$ and adsorbed on macroporous silica gel (Nucleosil 4000-7, 3 g) which was treated with 3-aminopropyltriethoxysilane.[2] The packing materials thus obtained were dispersed in hexane-paraffin oil (2:1, 30 ml) and packed in a stainless steel tube (25 cm x 0.46 (I.D.) cm) at a pressure of 350 kg cm^{-2}. Chromatographic analysis was accomplished using a hexane-2-propanol (90:10) mixture as an eluent on a JASCO-TRIROTAR-II chromatograph equipped with UV (JASCO UVIDEC-100-III) and polarimetric (JASCO DIP-181C) detectors at 25 °C. Dead times (t_0) of the columns were estimated with 1,3,5-tri-t-butylbenzene.[6]

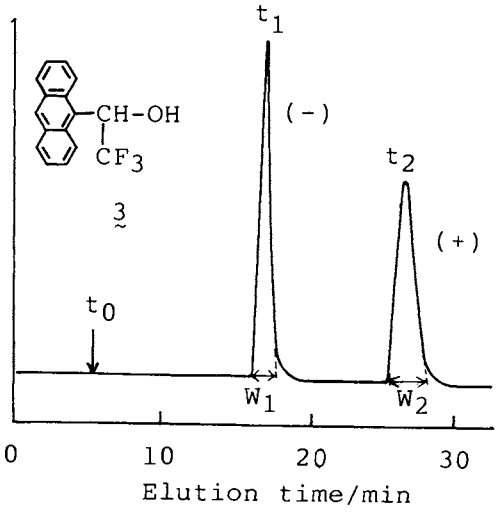
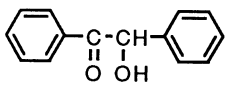


Fig. 1. Optical resolution of 1-(9-anthryl)-2,2,2-trifluoroethanol (3) on amylose tris((S)-1-phenylethylcarbamate) (2-(S)).

Figure 1 shows the chromatogram of the resolution of 1-(9-anthryl)-2,2,2-trifluoroethanol (3) on 2-(S) column. The (-)-isomer eluted at t_1 and the (+)-isomer at t_2, and capacity factors, $k'_1(=(t_1-t_0)/t_0)$ and $k'_2(=(t_2-t_0)/t_0)$, were obtained as 1.95 and 3.67, respectively. Separation factor ($\alpha=k'_2/k'_1$) and resolution factor ($Rs=2(t_2-t_1)/(W_1+W_2)$) were 1.88 and 5.67, respectively.

The results of optical resolution of ten racemates (3-12) on 1-(R), 1-(S), and 1-(RS) are summarized in Table 1, and those on 2-(R), 2-(S), and 2-(RS) columns in Table 2. In both cellulose and amylose carbamates, optical resolving abilities depended greatly on the chirality of side groups. In case of cellulose, 1-(R) and 1-(RS) showed higher optical resolving ability than 1-(S).

The amylose derivatives generally showed higher optical resolving abilities than the cellulose derivatives. Especially, 2-(RS) and 2-(S) resolved many racemates effectively. Separation factor (α=1.98) for



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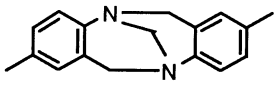

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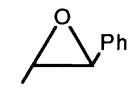

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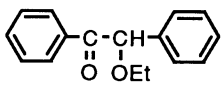

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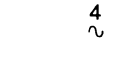

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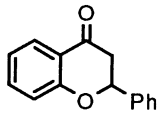

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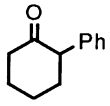

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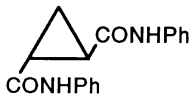

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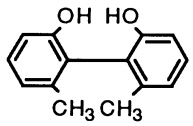

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Table 1. Optical resolution of racemates (3-12) on 1-(R), -(S), and -(RS)[a)]

Racemate	1-(R)			1-(S)			1-(RS)		
	k_1'	α	Rs	k_1'	α	Rs	k_1'	α	Rs
3	3.15(+)	1.13		2.03(-)	1.28	1.34	3.17(-)	1.06	
4	4.62(-)	1.0		2.24(+)	1.16	1.20	3.67(-)	1.18	2.38
5	0.62(-)	1.22		0.45(-)	1.0		0.62(+)	1.0	
6	0.50(-)	1.21	0.84	0.37(-)	1.0		0.52(-)	1.12	
7	0.58(-)	1.0		0.33(-)	1.0		0.61(-)	1.0	
8	0.62(+)	1.0		0.50(+)	1.19		0.61(+)	1.37	1.25
9	1.87(+)	1.0		1.11	1.0		1.76	1.00	
10	1.19(-)	1.12	0.71	0.73(-)	1.0		1.19(-)	1.09	0.68
11	4.08(-)	1.84	2.31	3.58(-)	1.0		4.30(-)	1.93	6.98
12	4.55(-)	1.32	1.22	2.55(+)	1.0		3.18(-)	1.20	1.57

a) Eluent : hexane-2-propanol (90:10).

Table 2. Optical resolution of racemates (3-12) on 2-(R), -(S), and -(RS)[a)]

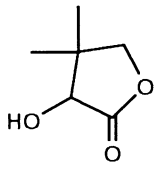
Racemate	2-(R)			2-(S)			2-(RS)		
	k_1'	α	Rs	k_1'	α	Rs	k_1'	α	Rs
3	1.97(+)	1.05		1.95(-)	1.88	5.67	1.80(-)	1.14	0.86
4	3.37(+)	1.14	1.29	4.29(+)	1.98	9.10	3.51(+)	1.41	4.02
5	0.74(+)	1.86	2.41	0.90(+)	2.38	4.43	0.72(+)	2.60	4.20
6	0.61(+)	1.19	0.83	0.61(+)	1.28	1.52	1.68(+)	1.15	0.83
7	0.78(-)	1.49	2.16	0.72(-)	1.48	2.37	0.75(-)	1.65	2.75
8	0.92(+)	1.0		0.46(-)	1.0		0.75(-)	1.0	
9	2.07(+)	1.07		3.02(-)	1.0		2.13(+)	1.11	0.83
10	1.10(-)	1.0		1.50(+)	1.21	1.68	1.18(+)	1.0	
11	4.46(+)	1.18	1.01	4.79(+)	1.19	1.67	4.30(+)	1.24	1.91
12	1.93(-)	1.18	1.10	1.75(-)	1.31	1.69	1.69(-)	1.24	1.37

a) Eluent : hexane-2-propanol (90:10).

benzoin (4) on 2-(S) is the highest among the values observed on phenylcarbamates of polysaccharides. Eluent order of enantiomers was sometimes influenced by the chirality of side groups. For instance, reversed elution order of 3 was observed between 1-(R) and 1-(S). The amylose derivatives also exhibited the reversed elution order of enantiomers for 3. These results indicate that not only the chirality of glucose unit but the chirality of 1-phenylethyl group influences the chiral recognition, although the former may be more important.

1-phenylethyl group may be a special group because benzylcarbamates and diphenylcarbamates of cellulose and amylose showed very low optical resolving abilities compared with those of 1-phenylethylcarbamates. For instance, cellulose tris(benzylcarbamate) showed no separation for the compounds 3-12. Restricted selection of side groups appears to be important to obtain effective CSPs. Too small or too bulky groups may disturb the higher-order structure of carbamate derivatives.

As mentioned above, 2-(S) column showed interesting optical resolving ability. Especially, this was useful for the resolution of carbonyl compounds. Some racemic compounds which were not sufficiently resolved on the phenylcarbamate derivatives of polysaccharides were effectively resolved on 2-(S). For example, pantoyl lactone (13) (α=1.42), 3-chloro-2-butanone (14) (α=1.13), and muscon (15) (α=1.51) were almost completely resolved into enantiomers. These CSPs were quite stable in eluting system consisting of hexane with 0-20% of 2-propanol.



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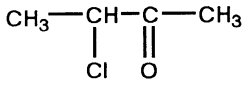

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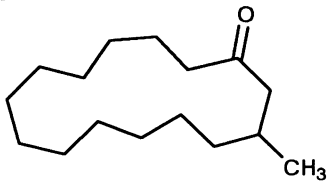

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