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Efficient Optical Resolution of 4-Hydroxy-2-cyclopentenone Derivatives by HPLC on 1-Phenylethylcarbamates of Cellulose and Amylose

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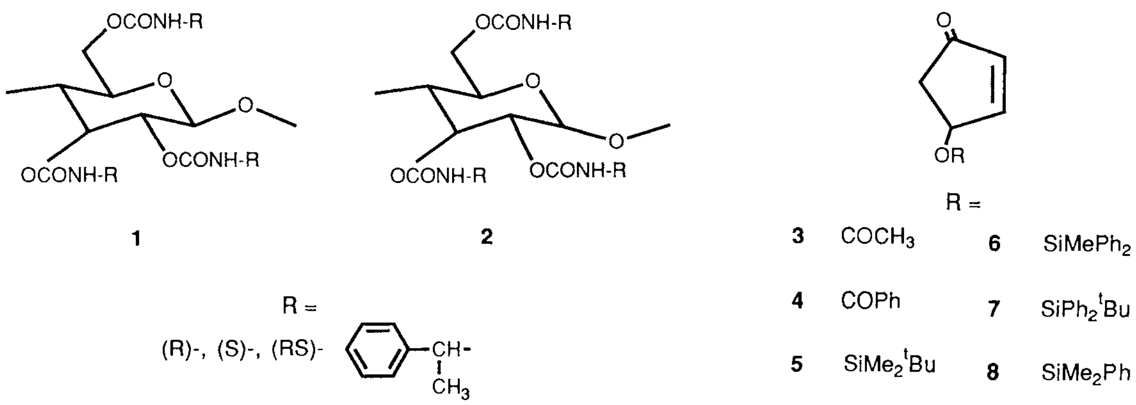
Esters and silyl ethers of 4-hydroxy-2-cyclopentenone which are important building blocks for the synthesis of prostagrangins have been efficiently resolved into optically active isomers by HPLC on amylose tris(1-phenylethyl-carbamate)s.

Optically active 4-hydroxy-2-cyclopentenone derivatives are useful chiral building blocks for the synthesis of prostagrangins, and several synthetic methods have been reported.[1] We previously reported the optical resolution of 4-hydroxy-2-cyclopentenone derivatives on various cellulose phenylcarbamates.[2]

Recently we found that 1-phenylethylcarbamates of cellulose (1) and amylose (2) showed characteristic optical resolving abilities for many racemates.[3] In this paper, we wish to report the optical resolution



of six 4-hydroxy-2-cyclopentenone derivatives (**3**-**8**) by HPLC using (R)-, (RS)-, and (S)-1-phenylethylcarbamates of cellulose and amylose as chiralstationary phases. Amylose (RS)- and (S)-1-phenylethylcarbamates showed high chiral recognition abilities and most compounds were more efficiently separated into optical isomers by the two than by the cellulose phenylcarbamates.[2)]

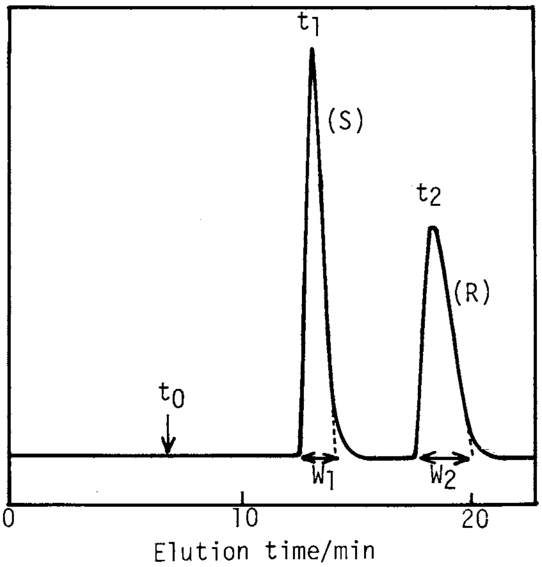


Fig. 1. Optical resolution of **8** on 2-(S). (Eluent: hexane-2-propanol (98:2), 0.5 ml/min, 25 °C)

The preparations of tris(1-phenylethylcarbamate)s of cellulose and amylose and the packing materialswere reported previously.[3)] Packing materials were packed in a stainless-steel tube (25 cm x 0.46 (i.d.) cm) by a slurry method. Chromatographic resolution was accomplished with a JASCO TRIROTAR-II chromatograph equipped with UV (UVIDEC 100-V) and polarimetric (DIP-181C) detectors using a hexane-2-propanol (98:2) mixture as an eluent at 25 °C. Dead time (t_0) was estimated with 1,3,5-tri-tert-butylbenzene.[4)]

Figure 1 shows the chromatogram of resolution of **8** on 2-(S). Sufficient resolution into enantiomers is attained. Capacity factors, k'_1 $(=(t_1-t_0)/t_0)$ and k'_2 $(=(t_2-t_0)/t_0)$ were 1.12 and 2.14, respectively. Separation factor α $(=k'_2/k'_1)$ and resolution factor Rs $(=2(t_2-t_1)/(W_1+W_2))$ were 1.91 and 2.49, respectively.

Figure 2 shows the chromatograms of resolution of 5 on 2-(R), (RS), and (S). All the three columns resolved 5 and 2-(S) column showed the highest chiral recognition ability.

The results of optical resolution of **3**-**8** on each three columns of 1 and 2 are summarized in Table 1. The results on tris(phenylcarbamte)s (R=Ph) of cellulose[5)] (CTPC) and amylose[6)] (ATPC) are also showen in Table 1 for comparison. Though the cellulose derivatives (1-(R), (RS), and (S)) showed

(R), (RS), and (S)) showed quite high optical resolving powers and all compounds (**3**-**8**) were resolved with higher α values at least on one of the derivatives than on CTPC. Complete separation of **3** and **4** could not be

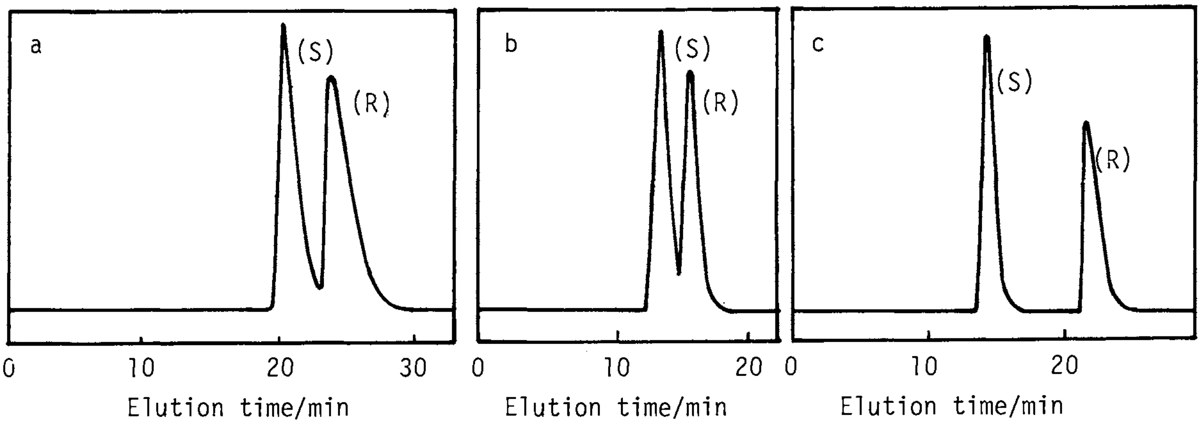


Fig. 2 Optical resolution of **5** on **2**-(R) (a), **2**-(RS) (b), and **2**-(S) (c). (Eluent: hexane-2-propanol (98:2), 0.5 ml/min, 25 °C)

Table 1. Optical resolution of 4-hydroxy-2-cyclopentenone derivatives (**3**-**8**) on (R)-, (RS)-, and (S)-1-phenylethylcarbamates of cellulose (**1**) and amylose (**2**)[a)]

	3			**4**			**5**		
	k'_1	α	Rs	k'_1	α	Rs	k'_1	α	Rs
1-[R]	2.81	1.00		2.71(R)	1.21	1.20	0.40(R)	≈1	
1-[RS]	8.77(S)	≈1		6.57(R)	1.09		0.17(R)	≈1	
1-[S]	5.23(S)	≈1		4.59	1.00		0.23(R)	≈1	
CTPC	4.13(R)	1.04		5.03(R)	1.04		1.03(R)	1.32	1.38
	6			**7**			**8**		
	k'_1	α	Rs	k'_1	α	Rs	k'_1	α	Rs
1-[R]	2.17	1.00		0.60(R)	≈1		0.53	1.00	
1-[RS]	1.63	1.00		1.29(R)	≈1		1.00(S)	≈1	
1-[S]	2.64	1.00		0.60	1.00		0.67	1.00	
CTPC	2.03(R)	1.14	1.14	0.95(R)	1.14	0.68	1.43(R)	1.17	1.30
	3			**4**			**5**		
	k'_1	α	Rs	k'_1	α	Rs	k'_1	α	Rs
2-[R]	7.80(S)	1.48	1.12	7.03(S)	1.30	1.14	0.55(S)	1.45	2.53
2-[RS]	6.14(S)	1.56	2.21	6.55(S)	1.18	1.34	0.65(S)	1.52	2.52
2-[S]	5.17(S)	1.78	4.01	4.52(S)	≈1		1.03(S)	1.47	2.00
ATPC	5.12(R)	≈1		9.10(S)	1.43	1.68	0.16(R)	≈1	
	6			**7**			**8**		
	k'_1	α	Rs	k'_1	α	Rs	k'_1	α	Rs
2-[R]	4.77(S)	≈1		2.17(S)	1.14		3.13(S)	1.21	0.99
2-[RS]	2.59(S)	1.42	3.20	1.80(S)	1.38	1.99	1.33(S)	≈1	
2-[S]	2.31(S)	1.46	2.19	1.88(S)	1.23	1.03	1.12(S)	1.91	2.49
ATPC	1.49(R)	≈1		1.23(S)	≈1		2.14(R)	≈1	

a) Eluent: hexane-2-propanol (98:2), 0.5 ml/min, 25 °C.

attained on cellulose phenylcarbamates.[3] However, 3 was completely resolved on 2-(R), (RS), and (S) columns, and **4** was resolved on **2**-(R). Particularly, 2-(RS) and (S) showed high optical resolving abilities and resolved five racemic compounds except **4** more efficiently than other polysaccharide derivatives.

The (R) isomers of **3**-**8** always eluted first on cellulose phenylcarbamates,[3] whereas their (S) isomers always eluted first on the three **2** columns. This suggests that chirality of 1-phenylethyl groups is not the main factor for chiral discrimination. The solutes may interact the carbamate groups of chiral stationary phases through the hydrogen bond, and the glucose units of the polysaccharides may mainly contribute to the chiral recognition.

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