

Enantioseparation of some Racemic Compounds on Cellulose Tris (3,5-dimethylphenylcarbamate) Chiral Stationary Phase

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Abstract: Seven chiral compounds were resolved on cellulose tris (3,5-dimethylphenylcarbamate) chiral stationary phase (CDMPC-CSP) using n-hexane/alcohol as mobile phase. Solvent strength and structural characteristics of the compounds effecting on the retention and resolution were discussed. Satisfactory separation was obtained.

Keywords: Enantioseparation, cellulose-based chiral stationary phase, racemic compounds, HPLC.

During the last two decades, polysaccharide derivatives have been widely used in the resolution of racemic compounds by HPLC^{1,2}. In this paper, CDMPC, coated on APS gel prepared according to reference³, was used to resolve racemic compounds in different mobile phase systems. The separation was performed on LC-6A HPLC (Shimadzu, Japan) system with an SPD-6AV ultraviolet-visible detector and a C-R3A chromatographic data recorder. All solvents were of analytical grade (Tianjin Second Chemical Factory). These compounds possess different structures. Their structures are shown in **Figure 1**. The solvent strength of mobile phase and the structural features of the compounds effecting chiral discrimination were investigated. The results are summarized in **Table 1**.

Figure 1

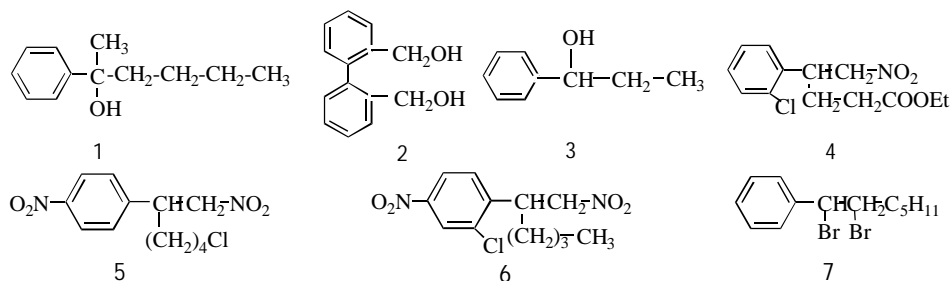


Table 1. Chromatographic separation results of racemates

Compound	Eluent	k_{av}	α	R_s	P^*	dP^*
1	A	11.94	1.24	1.5	0.138	----
	B	4.68	1.17	0.81	0.214	----
	C	3.59	1.12	0.75	0.29	----
	D	2.91	1.17	0.52	0.31	----
	E	4.09	1.39	1.76	0.3	---- 0.024
	F	2.79	1.21	0.8	0.314	0.004
	G	3.14	1.14	0.48	0.294	
3	A	8.15	1.34	2.3	0.138	----
	B	5.21	1.14	0.917	0.214	----
	C	3.53	1.13	0.76	0.29	----
	D	3.03	1.00	----	0.31	----
	E	5.47	1.25	1.04	0.3	---- 0.024
	F	6.86	1.00	----	0.314	0.004
	G	3.43	1.42	0.6	0.294	
4	A	36.4	1.19	0.60	0.138	----
	B	17.2	1.09	0.54	0.214	----
	C	15.7	1.12	0.50	0.29	----
	D	9.62	1.00	----	0.31	----
	E	13.81	1.24	0.72	0.3	---- 0.024
	F	11.04	1.05	0.11	0.314	0.004
	G	9.36	1.00	----	0.294	
5	A	25.01	1.16	0.66	0.138	----
	B	22.98	1.10	0.39	0.214	----
	C	5.53	1.59	0.343	0.29	----
	D	5.14	1.28	0.32	0.31	----
	E	10.60	1.74	0.86	0.3	---- 0.024
	F	7.51	1.00	----	0.314	0.004
	G	10.25	1.25	0.40	0.294	
6	A	12.44	1.36	1.66	0.138	----
	B	8.04	1.35	1.64	0.214	----
	C	7.84	1.32	1.60	0.29	----
	D	5.42	1.47	1.07	0.31	----
	E	6.24	1.22	0.92	0.3	---- 0.024
	F	6.0	1.22	0.74	0.314	0.004
	G	5.36	1.23	0.59	0.294	

Mobile phase: n-hexane: 2-propanol (v/v) A=99:1; B=97:3; C=95:5; F=95:5+0.5% methanol; G=95:5+0.5% 1,2-diethiol; n-hexane: ethanol (v/v) D=95:5; n-hexane: t-butanol (v/v) E=95:5.

The mobile phase strength⁶: $P^* = AX_1 + BX_2 + CX_3 + \dots$ (A, B, C...represented polarity strength of pure solvent A, B, C, *etc.*; X_1, X_2, X_3, \dots represented volume fraction of each component respectively). $dP^* = P[\text{TMP}] - P[\text{BMP}]$. P[TMP]: ternary mobile phase strength, P[BMP]: binary mobile phase. $k_{av} = (k_1 + k_2) / 2$.

Flow rate: 1.00ml/min; 254nm; 0.02AUF

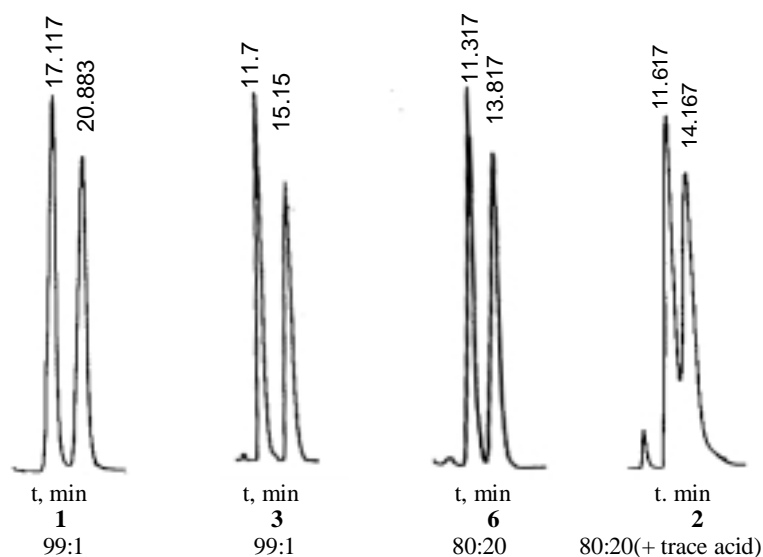
In the binary mobile phase (BMP) systems, the mobile phase strength increased with increase in the concentration of 2-propanol in the mobile phase. The retention factor (k_{av}) of all racemates decreased. The parameters (R_s, α) for the compounds **1, 3** decreased. The compound **2** can be separated well when trace trifluoroacetic acid was added to the mobile phase. The parameters (R_s, α) for the compound **6** remained almost unchanged. The parameters (R_s, α) of compounds **4** and **5** showed different changes. These results showed that the hydrogen bonding predominated in the chiral recognition for compounds **1-3**. Changing steric bulk of alcohol in BMP systems, the solvent strength increased in the following order: 0.29 (C, 2-propanol), 0.30 (E, t-butanol), 0.31 (D,

ethanol). The retention factors (k_{av}') for the compounds **4**, **6** and **7** decreased with increasing the solvent strength. The retention factors (k_{av}') for the compound **1**, **2**, **3** and **5** decreased with decreasing steric bulk of alcohol. These indicated that alcohol can compete with analytes for hydrogen bonding sites on the CSP, and the structure of alcohol had some effect on the chiral discrimination. This result accorded with the result of Wainer⁵ on OB-CSP.

In ternary mobile phase (TMP) systems, it can be seen that a little change of modifier concentration had a tremendous effect on the retention and resolution. These results showed that the effect of the structure of the additional second alcohol was larger than that of its strength on chiral discrimination.

Regarding the structure of the compounds **4-7**, the steric inclusion into chiral groove and π - π interaction between CSP and solute dominated in chiral recognition and resolution. The compound **6** gave better separation when smaller alcohol, ethanol, 2-propanol (BMP) and methanol (TMP) were used as mobile phase modifiers. Because the steric hindrance of carboxyl group in compound **4** was bigger than that of aryl group in compound **6**, steric inclusion interaction decreased for compound **4**. These suggested that the steric inclusion interaction played an important role in chiral discrimination for compounds **4** and **6**. The compound **5** can be separated with larger alcohol, t-butanol(BMP) and 1,2-diethiol (TMP). This explained that π - π interaction gave more effective function on the chiral discrimination than steric inclusion interaction owing to nitrophenyl substituent group on the chiral carbon of the analyte. The compound **7** failed to be separated in all mobile phases used because of weaker interactions between the analyte and the CSP. As example, the chromatograms of compounds **1**, **2**, **3** and **6** are shown in **Figure 2**.

Figure 2 Chromatograms of compounds **1**, **2**, **3** and **6**



Mobile phase: n-hexana: 2-propanol Flow rate: 1ml/min; 254nm; 0.02 AUF

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