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# Optical resolution by high-performance liquid chromatography on benzylcarbamates of cellulose and amylose

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ABSTRACT

Nine benzylcarbamate derivatives of cellulose and amylose were prepared and their optical resolving abilities as chiral stationary phases for high-performance liquid chromatography were evaluated. Among the derivatives, 1-phenylethylcarbamates and 1-phenylpropylcarbamates showed characteristic high optical resolution, and the amylose derivatives resolved many racemates. The influence of the chirality of the 1-phenylethylcarbamate group was also studied. Of the cellulose derivatives, the (*R*)- and (*RS*)-derivatives showed higher optical resolving ability than the (*S*)-derivative. Of the amylose derivatives, the (*RS*)- and (*S*)-derivatives showed higher chiral recognition than the (*R*)-derivative. The optical resolving abilities of 1-phenylethylcarbamate derivatives bearing a methyl or chloro substituent on their phenyl groups were also evaluated. The chiral recognition varied depending on the nature and position of the substituents.

## INTRODUCTION

Since we reported that trisphenylcarbamate derivatives of cellulose [1,2] and amylose [3] supported on silica gel show high chiral recognition, many racemates have been resolved by HPLC on the derivatives [4,5]. The optical resolution on the carbamates depends greatly on the substituents on the phenyl group [2]. Tris(1-phenylethylcarbamate)s of cellulose and amylose also show characteristic high optical resolution [6], although cellulose trimethylcarbamate and tribenzylcarbamate [6] possess poor optical resolving power. However, no systematic study has been made on the optical resolution with other benzylcarbamate derivatives of cellulose and amylose.

In this work, the optical resolving abilities of nine benzylcarbamate derivatives, benzylcarbamate (**1a**, **2a**), 1-phenylethylcarbamate (**1b**, **2b**),

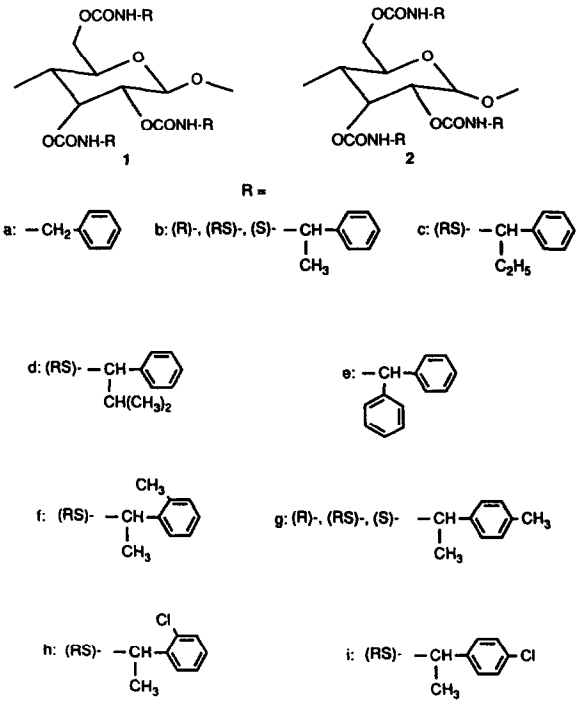


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TABLE I

ELEMENTAL ANALYSES DATA FOR BENZYLCARBAMATE DERIVATIVES OF CELLULOSE (**1a–i**) AND AMYLOSE (**2a–i**)

Calculated values are shown in parentheses; *DS* values were calculated from the N(%) values.

| Compound | C(%) | H(%) | N(%) | Cl(%) | *DS* | Compound | C(%) | H(%) | N(%) | C(%) | *DS* |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **1a** | 64.11 | 5.34 | 7.22 | | 2.89 | **2a** | 63.94 | 5.05 | 7.13 | | 2.85 |
| | (64.17 | 5.53 | 7.49) | | 2.92 | | (64.17 | 5.53 | 7.49) | | |
| **1b**-(*S*) | 64.42 | 6.08 | 6.78 | | 2.99 | **2b**-(*S*) | 63.93 | 6.05 | 6.72 | | 2.90 |
| **1b**-(*RS*) | 65.02 | 6.15 | 6.94 | | 2.99 | **2b**-(*RS*) | 64.52 | 6.08 | 6.83 | | 2.94 |
| **1b**-(*R*) | 65.47 | 6.19 | 6.96 | | | **2b**-(*S*) | 64.85 | 6.11 | 6.87 | | 2.96 |
| | (65.67 | 6.14 | 6.97) | | | | (65.67 | 6.14 | 6.97) | | |
| **1c** | 65.25 | 6.60 | 6.33 | | 2.92 | **2c** | 66.06 | 6.60 | 6.44 | | 2.97 |
| | (66.96 | 6.72 | 6.51) | | | | (66.96 | 6.72 | 6.51) | | |
| **1d** | 67.83 | 6.89 | 5.96 | | 2.92 | **2d** | 67.54 | 6.78 | 5.97 | | 2.93 |
| | (68.12 | 7.13 | 6.11) | | | | (68.12 | 7.13 | 6.11) | | |
| **1e** | 67.12 | 5.44 | 4.56 | | 2.70 | **2e** | 72.76 | 5.34 | 5.21 | | 2.94 |
| | (73.00 | 5.45 | 5.32) | | | | (73.00 | 5.45 | 5.32) | | |
| **1f** | 66.33 | 6.62 | 6.50 | | *ca.*3 | **2f** | 65.61 | 6.61 | 6.31 | | 2.91 |
| | (66.96 | 6.71 | 6.51) | | | | (66.96 | 6.71 | 6.51) | | |
| **1g**-(*S*) | 65.26 | 6.63 | 6.39 | | 2.94 | **2g**-(*S*) | 66.16 | 6.65 | 6.46 | | 2.97 |
| **1g**-(*RS*) | 66.32 | 6.64 | 6.45 | | 2.97 | **2g**-(*RS*) | 66.43 | 6.52 | 6.31 | | 2.91 |
| **1g**-(*R*) | 66.44 | 6.68 | 6.14 | | 2.83 | **2g**-(*R*) | 66.85 | 6.64 | 6.47 | | 2.97 |
| | (66.96 | 6.71 | 6.51) | | | | (66.96 | 6.71 | 6.51) | | |
| **1h** | 55.67 | 4.83 | 6.04 | 15.04 | *ca.*3 | **2h** | 55.96 | 4.87 | 6.05 | 15.08 | *ca.*3 |
| | (55.82 | 4.83 | 5.92 | 14.98) | | | (55.82 | 4.83 | 5.92 | 14.98) | |
| **1i** | 55.73 | 4.83 | 6.01 | 14.87 | *ca.*3 | **2i** | 56.09 | 4.81 | 6.00 | 14.86 | *ca.*3 |
| | (55.82 | 4.83 | 5.92 | 14.98) | | | (55.82 | 4.83 | 5.92 | 14.98) | |

1-phenylpropylcarbamate (**1c**, **2c**), 2-methyl-1-phenylpropylcarbamate (**1d**, **2d**), 1,1-diphenylmethylcarbamate (**1e**, **2e**) and four 1-phenylethylcarbamates bearing a methyl or chloro substituent on the phenyl group (**1f–i**, **2f–i**), were evaluated. The influence of the chirality of the 1-phenylethyl group and 1-(4-tolyl)ethyl groups on optical resolution was also investigated.

## EXPERIMENTAL

Benzyl isocyanate derivatives were synthesized by the reaction of the corresponding benzylamines and phosgene in toluene under reflux. 1-Phenylpropylamine was prepared from propiophenone and ammonium formate according to a convenient method [7]. 2-Methyl-1-phenylpropylamine and four 1-phenylethylamine derivatives having a methyl or chloro group on their phenyl groups were synthesized in the same way. (*R*)- and (*S*)-1-(4-tolyl)ethylamines were kindly supplied by Yamakawa Chemical.

Cellulose (Avicel, Merck, 1 g) or amylose (Nacalai Tesque, $M_r$ 16 000, 1 g) was dissolved in an N,N-dimethylacetamide (15 ml)–LiCl (1.5 g) mixture with stirring at about 80°C for 24 h, and an excess of benzyl isocyanate derivatives and dry pyridine (7 ml) were added to the polysaccharide solutions. The reaction was continued for about 24 h at 100°C. Benzylcarbamates of polysaccharides were precipitated in methanol, filtered and dried *in vacuo* at 60°C; the yields were 80–98%. When racemic isocyanates were used, the enantioselective reaction did not seem to proceed, because unreacted isocyanates were almost racemic. Elemental analysis (Table I) and IR and $^1$H NMR spectra indicated that almost all hydroxy groups of cellulose and amylose were converted into carbamate moieties [degree of substitution (DS) $\approx$ 2.7–3.0].

Packing materials were prepared as reported previously [8] and were packed in a stainless-steel tube (25 cm × 0.46 cm I.D.) by a slurry method. The theoretical plate numbers of these columns were calculated to be 3200–6400, using benzene.

Chromatographic resolution was accomplished on a JASCO BIP-I chromatograph equipped with a JASCO 875-UV (254 nm) and a JASCO DIP-181C polarimetric detector (Hg, without filters). Separation was carried out with a hexane–2-propanol (90:10) at 25°C. The dead time ($t_0$) was determined with 1,3,5-tri-*tert.*-butylbenzene [9]. $^1$H NMR spectra were measured with JEOL GXW-270 (270 MHz) and Varian VXR500 (500 MHz) spectrometers using TMS as an internal standard. The IR spectra were taken on a JASCO IR-810 spectrophotometer in Nujol. Circular dichroism (CD) and UV spectra were measured on JASCO J-500 and J-720 spectrometers and a JASCO Ubest-55 with a 1-mm cell in tetrahydrofuran (THF) (concentration $c \approx 1$ mg ml$^{-1}$) or a film prepared by casting their solutions [$c \approx 1$ mg ml$^{-1}$ in tetrahydrofuran (THF)] on the surface of a quartz plate. The CD intensity was calibrated on the basis of UV intensity.

## RESULTS AND DISCUSSION

Fig. 1 shows the chromatogram for the resolution of Tröger base (**3**) on a column of amylose tris [(*RS*)-1-phenylethylcarbamate) (**2b**-(*RS*)]. Compound **3** has been resolved on phenylcarbamates of cellulose and amylose and benzoates of cellulose [4,5]. The enantiomers eluted at retention times $t_1$ and $t_2$. The capacity factors [$k'_1 = (t_1 - t_0)/t_0$ and $k'_2 = (t_2 - t_0)/t_0$] were 0.72 and 1.87, respectively. The separation

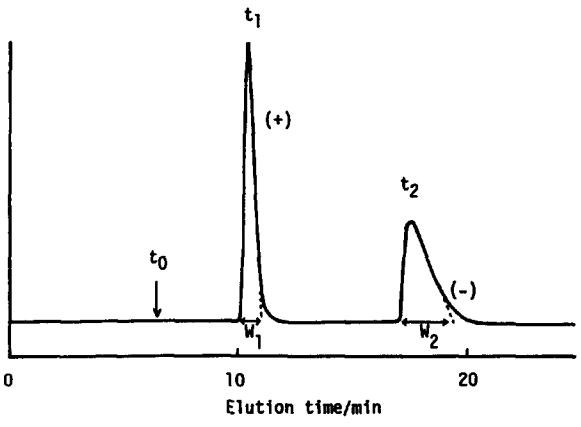



Fig. 1. Optical resolution of Tröger base (**3**) on amylose tris[(*RS*)-1-phenylethylcarbamate) (**2b**-(*RS*)]. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

TABLE II

OPTICAL RESOLUTION OF RACEMATES (3–11) ON BENZYLCARBAMATES (1a–e) OF CELLULOSE

Optical rotation of the first-eluted isomers is shown in parentheses. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

| Racemate | 1a | | | 1b | | | 1c | | | 1d | | | 1e | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ |
| **3** | 0.39(+) | *ca.*1 | | 0.62(+) | *ca.*1 | | 0.78(+) | *ca.*1 | | 0.42(+) | *ca.*1 | | 0.97(+) | *ca.*1 | |
| **4** | 0.27 | 1.00 | | 0.52(−) | 1.12 | | 0.58(−) | 1.09 | | 0.30(−) | *ca.*1 | | 0.50(+) | *ca.*1 | |
| **5** | 2.03 | 1.00 | | 3.67(+) | 1.18 | 2.38 | 4.73(+) | 1.22 | 3.32 | 0.88(+) | *ca.*1 | | 3.58 | 1.00 | |
| **6** | 1.28 | 1.00 | | 4.30(−) | 1.93 | 6.98 | 0.89(−) | 1.97 | 8.00 | 1.02 | 1.00 | | 1.22 | 1.00 | |
| **7** | 0.61(−) | *ca.*1 | | 1.19(−) | 1.09 | 0.68 | 1.43(−) | 1.02 | | 0.54(−) | *ca.*1 | | 0.99(−) | *ca.*1 | |
| **8** | 0.64 | 1.00 | | 1.76 | 1.00 | | 2.15(+) | 1.03 | | 0.66(+) | *ca.*1 | | 0.86 | 1.00 | |
| **9** | 1.47 | 1.00 | | 3.17(−) | 1.06 | | 5.83 | 1.00 | | 1.08 | 1.00 | | 1.70 | 1.00 | |
| **10** | 0.57(−) | *ca.*1 | | 0.61(+) | 1.37 | 1.25 | 0.95(+) | 1.56 | | 0.32(+) | *ca.*1 | | 1.20(+) | *ca.*1 | |
| **11** | 2.57(−) | *ca.*1 | | 3.18(−) | 1.20 | 1.57 | 5.74(−) | 1.20 | 2.00 | 0.86(−) | 1.04 | | 1.54(−) | 1.08 | |

TABLE III

OPTICAL RESOLUTION OF RACEMATES (3–11) ON BENZYLCARBAMATES (2a–e) OF AMYLOSE

Optical rotation of the first-eluted isomers is shown in parentheses. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

| Racemate | 2a | | | 2b | | | 2c | | | 2d | | | 2e | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ |
| **3** | 1.01(+) | *ca.*1 | | 0.72(+) | 2.60 | 4.20 | 0.86(+) | 2.19 | 3.47 | 0.27 | 1.00 | | 0.63(+) | *ca.*1 | |
| **4** | 0.67(+) | 1.13 | | 1.68(+) | 1.15 | 0.83 | 0.61(+) | 1.15 | 0.55 | 0.20(+) | *ca.*1 | | 0.72(+) | *ca.*1 | |
| **5** | 4.11(+) | 1.21 | 1.05 | 3.51(+) | 1.41 | 4.02 | 3.32(+) | 1.36 | 4.47 | 0.67(+) | 1.10 | | 5.11(−) | 1.11 | |
| **6** | 1.43(+) | *ca.*1 | | 4.30(+) | 1.24 | 1.91 | 4.08(+) | 1.39 | 2.98 | 0.48(+) | 1.04 | | 0.80(+) | *ca.*1 | |
| **7** | 1.14(+) | 1.05 | | 1.18(+) | *ca.*1 | | 1.37(+) | *ca.*1 | | 0.24(+) | *ca.*1 | | 0.98(−) | *ca.*1 | |
| **8** | 3.02(−) | *ca.*1 | | 2.13(+) | 1.11 | 0.83 | 2.15(−) | *ca.*1 | | 0.37(−) | *ca.*1 | | 1.32(−) | *ca.*1 | |
| **9** | 2.01(+) | 1.12 | | 1.80(−) | 1.14 | 0.86 | 2.09(−) | 1.16 | 1.69 | 0.40(−) | *ca.*1 | | 4.01(−) | *ca.*1 | |
| **10** | 1.92(+) | *ca.*1 | | 0.75(+) | *ca.*1 | | 0.68(+) | 1.09 | | 0.27(+) | 1.20 | 1.45 | 1.25(+) | *ca.*1 | |
| **11** | 1.01(+) | *ca.*1 | | 1.69(−) | 1.24 | 1.37 | 1.88(−) | 1.14 | 0.93 | 0.91(−) | *ca.*1 | | 1.10(−) | 1.08 | |

factor ($\alpha = k_2'/k_1'$) and the resolution factor [$R_s = 2(t_2 - t_1)/(W_1 + W_2)$] were determined to be 2.60 and 4.20, respectively.

*Optical resolution on various aralkylcarbamates of cellulose and amylose*

Table II shows the results for the optical resolution of racemates (**3–11**) on five cellulose tris(benzylcarbamate)s (**1a–e**). Among the five derivatives, 1-phenylethyl- (**1b**) and 1-phenylpropylcarbamate (**1c**) showed characteristic high optical resolution. The other derivatives, benzyl-, (**1a**), 2-methyl-1-phenylpropyl- (**1d**) and 1,1-diphenylmethylcarbamates (**1e**), showed low optical resolution in spite of the similarity of their structures to those of **1b** and **1c**. Fig. 2 shows the chromatograms for the resolution of **3** on **1a–e**. Although **3** was not resolved on any column, a clear difference was observed between the chromatograms on **1b** and **1c** and the others. The peaks observed on **1b** and **1c** are sharp, whereas on the others they are very broad. These results suggest that **1b** and **1c** may have a limited number of adsorbing sites owing to the regular structure of the cellulose derivatives, but the other derivatives may have many kinds of absorbing sites owing to irregular structures.

The CD spectra of the films of **1a–e** are shown in Fig. 3. Intense peaks are observed for only **1b** and **1c**; the other derivatives show much weaker

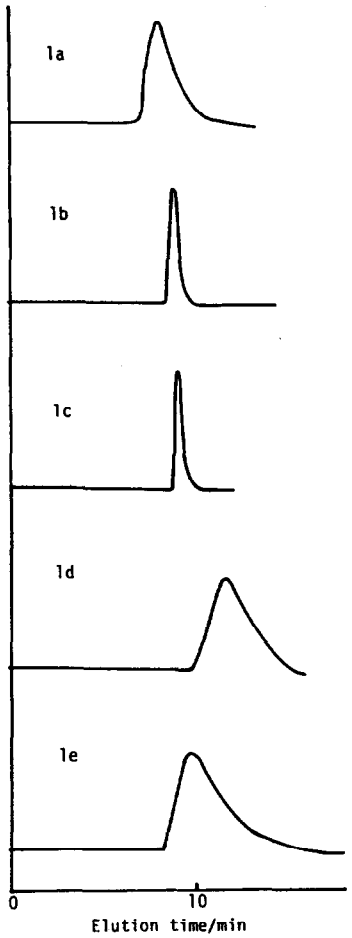
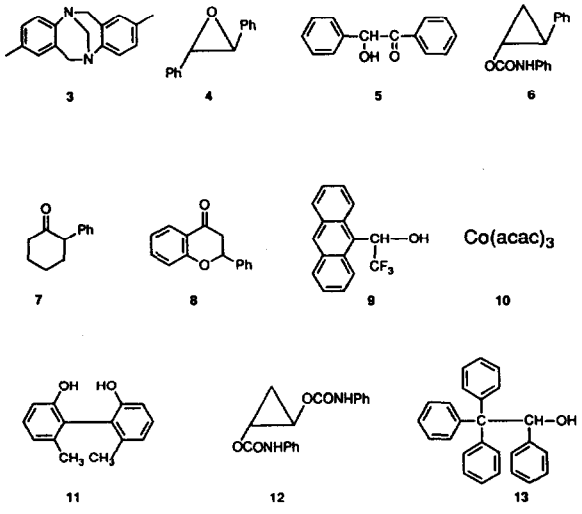



Fig. 2. Chromatograms for resolution of **3** on cellulose benzylcarbamates (**1a–e**). Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.




peaks. These results support the above speculation that the higher order structure of **1b** and **1c** may be more regular than those of the other derivatives. Hence a too small group such as benzyl and too bulky groups such as 2-methyl-1-phenylpropyl and 1,1-diphenylmethyl seem to disturb the higher order structure of the carbamate derivatives.

The results for the optical resolution of **3–11** on the amylose derivatives (**2a–e**) are summarized in Table III. Similar results to those on the cellulose derivatives were obtained. 1-Phenylethyl and 1-phenylpropyl groups again appear to

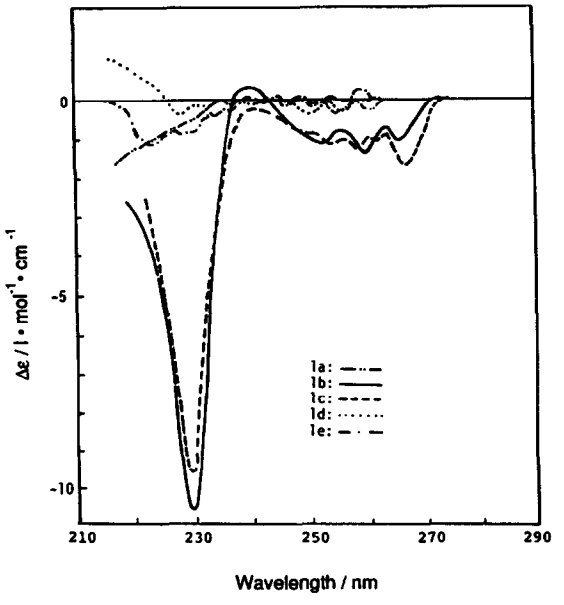



Fig. 3. CD spectra of cellulose benzylcarbamates (**1a–e**) cast from THF solutions.

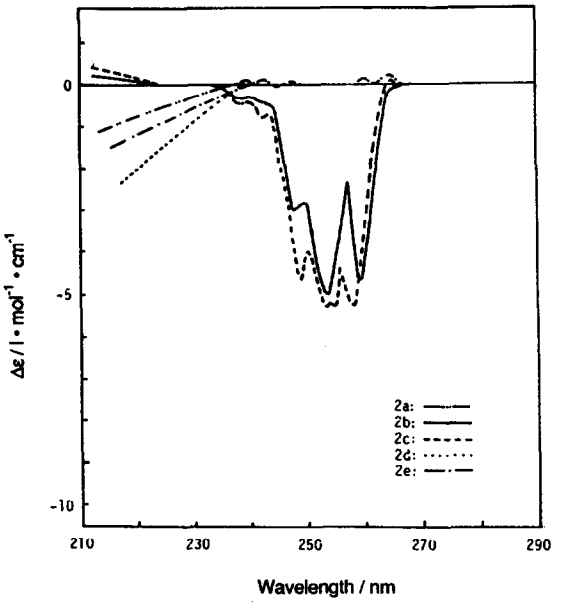



Fig. 4. CD spectra of amylose benzylcarbamates (**2a–e**) cast from THF solutions.

be suitable for keeping the regular higher order structure. The derivatives of **2b** and **2c** showed higher optical resolving abilities than the corresponding cellulose derivatives **1b** and **1c** and could resolve several racemates that were not sufficiently resolved on phenylcarbamates of cellulose and amylose. For example, **3** was resolved on **2b** and **2c** with higher $\alpha$ values than on other phenylcarbamates of amylose [3].

The difference in chiral recognition abilities between cellulose derivatives and amylose derivatives may be due to the differences in their higher order structures. Fig. 4 shows the CD spectra of films of **2a–e**. Intense peaks are again observed only for **2b** and **2c**, although the spectral pattern of **2b** is different from that of **1b**. This may be ascribed to the difference in the conformations between **1b** and **2b**. The chiral recognition abilities of these polysaccharide derivatives depend greatly on their conformation. For example, both phenylcarbamates of cellulose (CTPC) and amylose (ATPC) show high chiral recognition abilities, and the elution order of enantiomers on ATPC is often the reverse of that on CTPC [4]. The higher order structure of CTPC reported by Vogt and Zugenmaier on the basis of the X-ray analysis is a left-handed threefold (3/2) helix [10] and that of ATPC is a left-handed fourfold (4/1) helix [11]. This difference in conformations between CTPC and ATPC may be responsible for the difference in chiral recognition abilities.

*Optical resolution on (R)-, (RS)- and (S)-1-phenylethylcarbamates of cellulose and amylose*

(*R*)- and (*S*)-1-phenylethylcarbamates of cellulose [**1b**-(*R*), -(*S*)] and amylose [**2b**-(*R*), -(*S*)] were prepared to evaluate the influence of the chirality of the side-chain on chiral recognition [6]. Tables IV and V show the optical resolution of **3–13** on (*R*)-, (*S*)- and (*RS*)-1-phenylethylcarbamates of cellulose [**1b**-(*R*), -(*S*), -(*RS*)] and amylose [**2b**-(*R*), -(*S*), -(*RS*)], respectively. For both the cellulose and amylose carbamates, the optical resolution depends on the chirality of the side-groups. In the cellulose derivatives, **1b**-(*R*) and -(*RS*) showed a higher optical resolving ability than **1b**-(*S*). The amylose derivatives showed a higher optical resolving ability than the cellulose derivatives for most racemic compounds. Especially **2b**-(*RS*) and -(*S*) can resolve many racemates effectively. The elution order of

TABLE IV

OPTICAL RESOLUTION OF RACEMATES (3–13) ON **1b**-(*R*), -(*S*) AND -(*RS*)

Optical rotation of the first-eluted isomers is shown in parentheses. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

| Racemate | **1b**-(*R*) | | | **1b**-(*S*) | | | **1b**-(*RS*) | | |
|---|---|---|---|---|---|---|---|---|---|
| | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ |
| **3** | 0.62(−) | 1.22 | | 0.45(−) | *ca.*1 | | 0.62(+) | *ca.*1 | |
| **4** | 0.50(−) | 1.21 | 0.84 | 0.37(−) | *ca.*1 | | 0.52(−) | 1.12 | |
| **5** | 4.62(−) | *ca.*1 | | 2.24(+) | 1.16 | 1.20 | 3.67(−) | 1.18 | 2.38 |
| **6** | 4.08(−) | 1.84 | 2.31 | 4.35(−) | *ca.*1 | | 4.30(−) | 1.93 | 6.98 |
| **7** | 1.19(−) | 1.12 | 0.71 | 0.73(−) | *ca.*1 | | 1.19(−) | 1.09 | 0.68 |
| **8** | 1.87(+) | *ca.*1 | | 1.11 | 1.00 | | 1.76 | 1.00 | |
| **9** | 3.15(+) | 1.13 | | 2.03(−) | 1.28 | 1.34 | 3.17(−) | 1.06 | |
| **10** | 0.62(+) | *ca.*1 | | 0.50(+) | 1.19 | | 0.61(+) | 1.37 | 1.25 |
| **11** | 4.55(−) | 1.32 | 1.22 | 2.55(+) | *ca.*1 | | 3.18(−) | 1.20 | 1.57 |
| **12** | 4.08(−) | 1.84 | 2.31 | 3.58(−) | *ca.*1 | | 4.30(−) | 1.93 | 6.98 |
| **13** | 2.14(−) | *ca.*1 | | 2.26(−) | *ca.*1 | | 2.00(−) | 1.09 | |

enantiomers was sometimes influenced by the chirality of the side-group. For instance, a reversed elution order of **9** was observed between **1b**-(*R*) and **1b**-(*S*). The amylose derivatives also exhibited a reversed elution order of enantiomers of **9**. These results indicate that not only the chirality of the glucose unit but also the chirality of the 1-phenylethyl group directly influence the chiral recognition, although the former may be more important because such a reversal of elution order cannot be observed for other racemates except for **5** and **11** on **1b** and **7**, **8** and **10** on **2b**.

Fig. 5 shows the $^1$H NMR spectra of **1b**-(*R*), -(*RS*) and -(*S*) in perdeuterated dimethyl sulphoxide (DMSO-$d_6$) at 130°C. Changes in the spec-

TABLE V

OPTICAL RESOLUTION OF RACEMATES (3–13) ON **2b**-(*R*), -(*S*) AND -(*RS*)

Optical rotation of the first-eluted isomers is shown in parentheses. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

| Racemate | **2b**-(*R*) | | | **2b**-(*S*) | | | **2b**-(*RS*) | | |
|---|---|---|---|---|---|---|---|---|---|
| | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ |
| **3** | 0.74(+) | 1.86 | 2.41 | 0.90(+) | 2.38 | 4.43 | 0.72(+) | 2.60 | 4.20 |
| **4** | 0.61(+) | 1.19 | 0.83 | 0.61(+) | 1.28 | 1.52 | 1.68(+) | 1.15 | 0.83 |
| **5** | 3.37(+) | 1.14 | 1.29 | 4.29(+) | 1.98 | 9.10 | 3.51(+) | 1.41 | 4.20 |
| **6** | 4.46(+) | 1.18 | 1.01 | 4.79(+) | 1.19 | 1.67 | 4.30(+) | 1.24 | 1.91 |
| **7** | 1.10(−) | *ca.*1 | | 1.50(+) | 1.21 | 1.68 | 1.18(+) | *ca.*1 | |
| **8** | 2.07(+) | 1.07 | | 3.02(−) | *ca.*1 | | 2.13(+) | 1.11 | 0.83 |
| **9** | 1.97(+) | 1.05 | | 1.95(−) | 1.88 | 5.67 | 1.80(−) | 1.14 | 0.86 |
| **10** | 0.92(+) | *ca.*1 | | 0.46(−) | *ca.*1 | | 0.75(−) | *ca.*1 | |
| **11** | 1.93(−) | 1.18 | 1.10 | 1.75(−) | 1.31 | 1.69 | 1.69(−) | 1.24 | 1.37 |
| **12** | 1.02(+) | 1.54 | 1.33 | 1.36(+) | 1.33 | 0.55 | 1.21(+) | 1.40 | 0.79 |
| **13** | 4.11(−) | 1.04 | | 1.42(+) | 1.26 | 0.84 | 1.43(−) | 1.06 | |

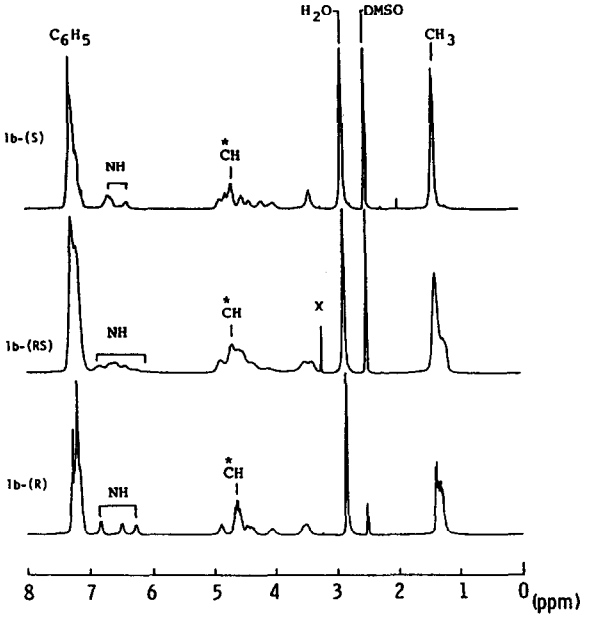



Fig. 5. $^1$H NMR spectra of **1b**-(*R*), -(*RS*) and -(*S*). DMSO-$d_6$, 130°C, 270 MHz.

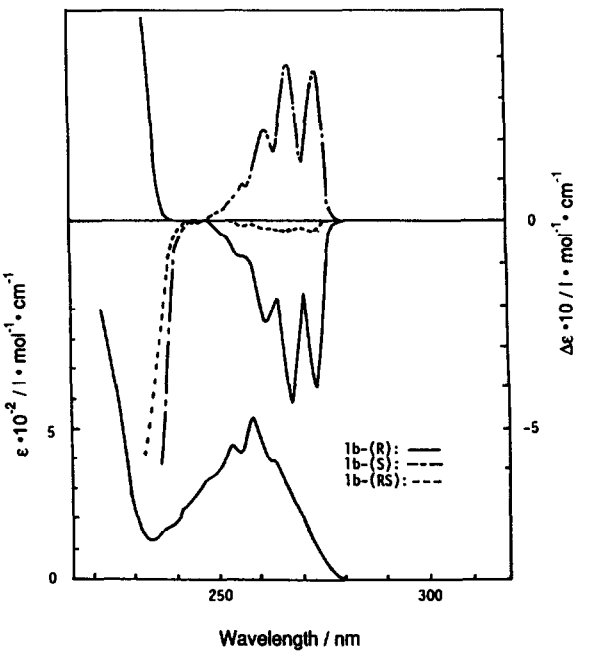



Fig. 6. CD spectra of **1b**-(*R*), -(*RS*) and -(*S*) in THF solutions.

tral patterns were observed for the NH and main chain protons of cellulose and the methyl and methine protons of the 1-phenylethyl group. This suggests that the chirality of the 1-phenylethyl group may influence the conformation of the glucose units.

UV and CD spectra of **1b**-(*R*), -(*RS*) and -(*S*) derivatives in THF are shown in Fig. 6. The spectral pattern of **1b**-(*R*) is almost symmetrical with that of **1b**-(*S*). This implies that the arrangement of side-chains of **1b** may not be much influenced by the chirality of glucose units in the solution. Fig. 7 shows the CD spectra of the films of these derivatives cast from THF solutions. Although the three spectra show similar patterns, differences are observed in the wavelengths of the peak tops and the intensities of the peaks. The chirality of 1-phenylethyl groups may influence not only the conformation of the side-chains but also that of the glucose units in the solid film. These differences in the conformation of chiral stationary phases (CSPs) probably affect their chiral separation because the cellulose derivatives on the silica gel surface are presumed to exist in a similar state to the above film.

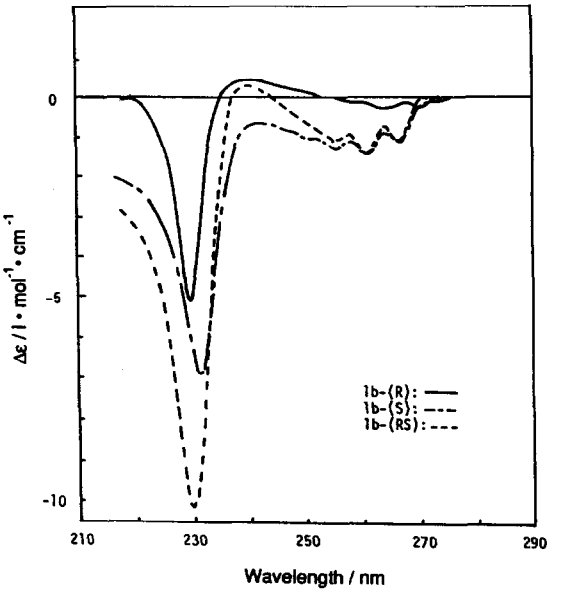



Fig. 7. CD spectra of films of **1b**-(*R*), -(*RS*) and -(*S*) cast from THF solutions.

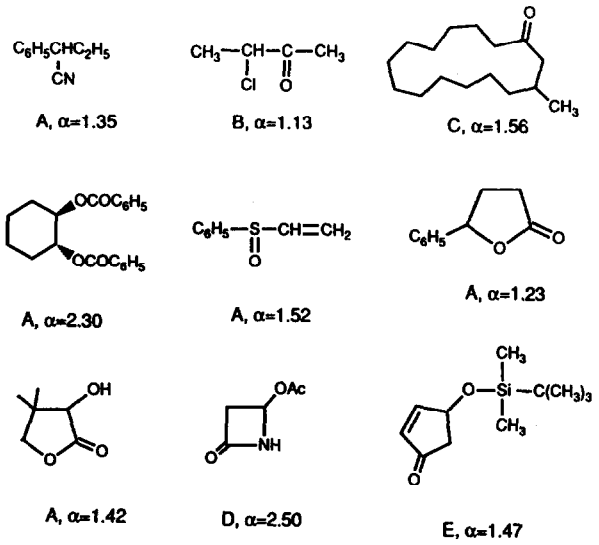



Fig. 8. Compounds resolved on **2b**-(*S*). Eluent: (A) hexane–2-propanol (90:10); (B) hexane–2-propanol (99:1); (C) hexane; (D) hexane–ethanol (80:20); (E) hexane–2-propanol (98:2).

Hence the difference in the higher order structures between the cellulose and amylose derivatives caused by the chirality of the 1-phenylethyl group may be partly responsible for the difference in the optical resolution between the cellulose and amylose derivatives. The fact that **1b**-(*R*) and -(*RS*) form lyotropic liquid crystalline phases in THF but **1b**-(*S*) does not also suggest that the higher order structures of these derivatives may differ depending on the chirality.

Among these derivatives, **2b**-(*S*) seems to show the highest optical resolving abilities for a variety of compounds, and resolves many racemic carbonyl compounds that are not sufficiently resolved on the phenylcarbamate derivatives of polysaccharides. Some examples of the compounds are shown in Fig. 8. They include β-lactams [12] and 4-hydroxy-2-cyclopentenone derivatives [13].

### *Optical resolution on 1-phenylethylcarbamate derivatives having a methyl or chloro substituent on their phenyl groups*

The optical resolving abilities of the derivatives of 1-phenylethylcarbamates of cellulose (**1f–i**) and amylose (**2f–i**) having a methyl or chloro group on their phenyl groups were also evaluated (Tables VI and VII). The chiral recognition for **3–11** depended greatly on the nature and position of the substituents on the phenyl groups. For example, although **2b**, **2f**, **2g** and **2i** can not resolve **10**, only **2h** can completely resolve it. CD spectra of **1b**, **1f** and **1g** are shown in Fig. 9. Different patterns are observed, although the UV spectra of these derivatives are similar, showing $\lambda_{max}$ at 208 nm (**1b**), 212 nm (**1f**) and 209 nm (**1g**). The structures of these derivatives may be affected by polarization of the charge on the phenyl groups and steric effects of the substituents. Therefore, the conformations of these derivatives may be different in the film states.

The influence of the chirality of the side-groups of **1g** and **2g** was also evaluated (Table VIII). The optical resolving abilities of these derivatives also depended on the chirality of the side-chains. Although **1b**-(*R*) and -(*RS*) showed a higher optical resolving ability than **1b**-(*S*), **1g**-(*R*) did not show a significantly higher optical resolving ability than **1g**-(*S*) and -(*RS*). The methyl group on the phenyl group appears to influence the conformation of **1g**.

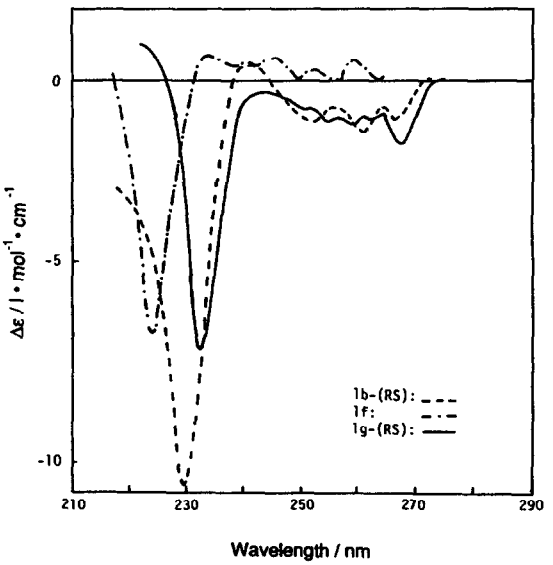



Fig. 9. CD spectra of films of **1b**-(*RS*), **1f** and **1g**-(*RS*) cast from THF solutions.

TABLE VI

OPTICAL RESOLUTION OF RACEMATES (3–11) ON 1-PHENYLETHYLCARBAMATE DERIVATIVES [1b-(*RS*), 1f–i] OF CELLULOSE

Optical rotation of the first-eluted isomers is shown in parentheses. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

| Racemate | 1b-(*RS*) | | | 1f | | | 1g | | | 1h | | | 1i | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ |
| **3** | 0.62(+) | *ca.*1 | | 0.46(+) | *ca.*1 | | 0.71(+) | 1.15 | 0.64 | 0.63(+) | *ca.*1 | | 0.83(+) | *ca.*1 | |
| **4** | 0.52(−) | 1.12 | | 0.31(−) | 1.23 | 0.58 | 0.52(−) | *ca.*1 | | 0.52(−) | 1.12 | | 0.56(−) | *ca.*1 | |
| **5** | 3.67(+) | 1.18 | 2.38 | 2.71(+) | 1.25 | 0.72 | 3.79(+) | 1.08 | | 3.72(+) | 1.34 | 3.58 | 3.56(+) | 1.11 | 1.07 |
| **6** | 4.30(−) | 1.93 | 6.98 | 2.98(−) | 1.85 | 4.44 | 6.83(−) | 1.97 | 8.00 | 3.51(−) | 2.24 | 7.09 | 3.33(−) | 1.77 | 4.68 |
| **7** | 1.19(−) | 1.09 | 0.68 | 0.82(−) | 1.07 | 0.44 | 1.25(−) | *ca.*1 | | 1.63(−) | *ca.*1 | | 1.39(−) | 1.10 | 0.53 |
| **8** | 1.76 | 1.00 | | 1.44(+) | *ca.*1 | | 2.02 | 1.00 | | 1.73(+) | *ca.*1 | | 1.80(+) | *ca.*1 | |
| **9** | 3.17(−) | 1.06 | | 3.26(−) | 1.13 | 0.61 | 5.88 | 1.00 | | 2.03(+) | 1.10 | 0.81 | 2.17 | 1.00 | |
| **10** | 0.61(−) | 1.37 | 1.25 | 0.48(+) | 1.25 | 0.72 | 0.55(+) | 1.51 | 2.21 | 0.69(+) | 1.29 | 0.88 | 0.87(+) | 1.38 | 1.24 |
| **11** | 3.18(−) | 1.20 | 1.57 | 3.48(−) | 1.13 | 0.97 | 5.84(−) | 1.12 | 1.27 | 3.55(−) | 2.18 | 4.16 | 2.99(−) | *ca.*1 | |

TABLE VII

OPTICAL RESOLUTION OF RACEMATES (3–11) ON 1-PHENYLETHYLCARBAMATE DERIVATIVES [2b-(*RS*), 2f–i] OF AMYLOSE

Optical rotation of the first-eluted isomers is shown in parentheses. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

| Racemate | 2b-(*RS*) | | | 2f | | | 2g | | | 2h | | | 2i | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ | $k'_1$ | $\alpha$ | $R_s$ |
| **3** | 0.72(+) | 2.60 | 4.20 | 0.91(+) | 1.57 | 1.69 | 0.47(+) | 2.14 | 3.38 | 0.73(+) | 2.31 | 4.57 | 1.16(+) | 1.77 | 3.77 |
| **4** | 1.68(+) | 1.15 | 0.83 | 0.65(+) | *ca.*1 | | 0.55(+) | 1.20 | 0.73 | 0.56(+) | 1.15 | 0.72 | 0.69(−) | *ca.*1 | |
| **5** | 3.51(+) | 1.41 | 4.02 | 3.34(+) | 1.25 | 2.17 | 2.19(+) | 1.45 | 4.50 | 3.54(+) | 1.47 | 5.43 | 4.03(+) | 1.24 | 3.28 |
| **6** | 4.30(+) | 1.24 | 1.91 | 4.84(+) | 1.35 | 1.94 | 3.68(+) | 1.15 | 1.27 | 4.05(+) | 1.23 | 1.91 | 4.41(+) | 1.16 | 1.61 |
| **7** | 1.18(+) | *ca.*1 | | 1.13(+) | 1.07 | | 0.99(+) | *ca.*1 | | 1.47(−) | *ca.*1 | | 1.76(+) | 1.10 | 0.83 |
| **8** | 2.13(+) | 1.11 | 0.83 | 2.22 | 1.00 | | 2.06(+) | 1.04 | | 1.78(+) | *ca.*1 | | 2.21 | 1.00 | |
| **9** | 1.80(−) | 1.14 | 0.86 | 2.39(−) | 1.20 | 1.00 | 1.92(−) | 1.20 | 1.28 | 1.17(−) | 1.09 | 0.60 | 1.57 | 1.00 | |
| **10** | 0.75(+) | *ca.*1 | | 0.80(+) | *ca.*1 | | 0.53(−) | *ca.*1 | | 1.04(−) | 1.39 | 2.49 | 1.00 | 1.00 | |
| **11** | 1.69(−) | 1.24 | 1.37 | 1.95(−) | 1.07 | | 2.01(−) | 1.13 | 0.58 | 1.88(−) | 1.27 | 1.41 | 1.85(−) | 1.15 | 0.74 |

TABLE VIII

OPTICAL RESOLUTION OF RACEMATES (3–5, 7–12) ON 1g- AND 2g-(*R*), -(*S*) AND -(*RS*)

Optical rotation of the first-eluted isomers is shown in parentheses. Eluent: hexane–2-propanol (90:10), 0.5 ml/min, 25°C.

| Racemate | 1g-(*R*) | | | 1g-(*S*) | | | 1g-(*RS*) | | | 2g-(*R*) | | | 2g-(*S*) | | | 2g-(*RS*) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ | $k_1'$ | $\alpha$ | $R_s$ |
| **3** | 0.33(+) | *ca.*1 | | 0.34(+) | *ca.*1 | | 0.52(−) | *ca.*1 | | 0.29(−) | *ca.*1 | | 0.58(+) | 1.24 | | 0.74(+) | 2.14 | |
| **4** | 0.21(−) | *ca.*1 | | 0.26(−) | *ca.*1 | | 0.71(+) | 1.15 | 0.64 | 0.15(+) | *ca.*1 | | 0.40(+) | *ca.*1 | | 0.55(+) | 1.20 | |
| **5** | 1.31(−) | *ca.*1 | | 1.11(+) | 1.24 | | 3.79(+) | 1.08 | | 0.85(+) | 1.25 | 1.30 | 1.51(+) | 1.20 | 0.97 | 2.91(+) | 1.45 | |
| **7** | 0.28(−) | *ca.*1 | | 0.45(−) | *ca.*1 | | 1.25(−) | *ca.*1 | | 0.24(−) | *ca.*1 | | 0.55(+) | 1.09 | | 0.99(+) | *ca.*1 | |
| **8** | 0.63(−) | *ca.*1 | | 0.69(+) | *ca.*1 | | 2.02 | 1.00 | | 0.52(+) | 1.30 | 1.22 | 1.06(−) | 1.20 | 0.74 | 2.06(+) | 1.04 | |
| **9** | 2.01(−) | 1.20 | 1.30 | 1.42(−) | 1.26 | 1.33 | 5.88 | 1.00 | | 0.90(−) | *ca.*1 | | 1.36(−) | 1.30 | 1.48 | 1.92(−) | 1.20 | |
| **10** | 0.25(+) | *ca.*1 | | 0.34(+) | 1.42 | 1.15 | 0.55(+) | 1.51 | 2.21 | 0.20(−) | *ca.*1 | | 0.40(+) | *ca.*1 | | 0.53(−) | *ca.*1 | |
| **11** | 1.50(−) | *ca.*1 | | 1.43(+) | *ca.*1 | | 1.46(+) | *ca.*1 | | 1.19(−) | 1.18 | | 1.27(−) | *ca.*1 | | 2.01(−) | *ca.*1 | |
| **12** | 1.44(−) | 1.38 | 0.96 | 0.88(−) | *ca.*1 | | 1.25(−) | 1.25 | 0.86 | 0.50(+) | 1.76 | 0.94 | 0.75(+) | 1.45 | 0.91 | 0.87(+) | 1.32 | 0.93 |

## CONCLUSIONS

Nine benzylcarbamates of cellulose and amylose were adsorbed on silica gel and used as CSPs for HPLC. Among them, 1-phenylethyl- and 1-phenylpropylcarbamates showed high optical resolution. Too small or too bulky benzyl groups are not suitable for obtaining efficient CSPs. In the case of 1-phenylethylcarbamates, chiral recognition depends on the chirality of the 1-phenylethyl group. In the cellulose derivatives (*R*)- and (*RS*)-1-phenylethylcarbamates showed higher optical resolving ability than the (*S*)-derivative, and with amylose the (*RS*)- and (*S*)-derivatives resolved many racemates more efficiently than the (*R*)-derivative. The $^1$H NMR and CD spectra of the 1-phenylethylcarbamates indicate that the conformation of the glucose units of the polysaccharides may be influenced by the chirality of the 1-phenylethyl group. The chiral recognition abilities of 1-phenylethylcarbamate derivatives of cellulose and amylose bearing a methyl or chloro substituent on the phenyl group were also evaluated. The optical resolution on these derivatives depends on the nature and position of the substituents.

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