Research Article

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Homogeneous synthesis of partially substituted cellulose phenylcarbamates aiming at chiral recognition

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Abstract

Homogeneous carbanilation of cellulose with nine kinds of substituted phenyl isocyanates, in which the substituents were varied from electron-donating to electron-withdrawing groups, was carried out in 1-allyl-3-methylimidazolium chloride (AmimCl) without any catalyst. The degree of substitution (DS) of cellulose phenylcarbamates in a range from 0 to 3 was readily controlled by altering reaction temperature, reaction time and molar ratio of phenyl isocyanate/anhydroglucose unit. Furthermore, the electronic effect of the substituents on the aromatic ring had a prominent impact on the reactivity of phenyl isocyanates. The phenyl isocyanates with stronger electron-withdrawing substituents exhibited a higher reactivity. A plot of DS and Hammett substituent constants exhibited linearity with a positive slope. Subsequently, four kinds of partially substituted cellulose phenylcarbamates with DS of 2.0 were synthesized successfully in AmimCl, and then employed as coated-type chiral stationary phases (CSPs) for high-performance liquid chromatography. The enantioseparation results demonstrated that these CSPs exhibited high chiral recognition abilities for some racemates. The substituents on the phenyl moieties had a considerable effect on the chiral recognition ability of cellulose phenylcarbamate-based CSPs.

Keywords: cellulose phenylcarbamate; ionic liquid; partial substitution; chiral recognition

INTRODUCTION

Many biologically interesting compounds, such as DNA, enzymes, pharmaceuticals, pesticides and even fragrances, are chiral, and a pair of enantiomers often exhibits quite different biological and pharmacological activities. Therefore, the preparation of enantiomers with high optical purity is demanded strongly in the biological, pharmaceutical and pesticide industries. Chromatographic enantioseparations, especially chiral recognition by HPLC, are recognized as the most reliable tool not only for determining the enantiomeric excess (ee) but also for obtaining optically pure enantiomers on analytical and industrial scales. The key to chromatographic chiral separation is the preparation of effective chiral stationary phases (CSPs) with high chiral recognition abilities. Currently, many commercial CSPs for HPLC are available. Among them, polysaccharide-based derivatives, especially phenylcarbamate and benzoate esters of cellulose and amylose, are some of the most efficient CSPs for HPLC, and nearly 90% of chiral compounds can be successfully resolved.[1,2]

However, unmodified cellulose is neither meltable nor soluble in conventional solvents, due to its developed hydrogen-bonding network and partially crystalline structure. Thus, the traditional preparation method for cellulose-based CSPs begins with a heterogeneous reaction between cellulose and a large excess of reagent, which leads to some undesirable problems, such as non-uniform distribution of substituents, side reactions and being time-consuming.[3–5] More importantly, under heterogeneous conditions, it is difficult to control the synthesis process and chemical structure of the resultant cellulose derivatives. As a consequence, only fully substituted cellulose derivatives are obtained, and it is impossible to get partially substituted products and to control the distribution of substituents directly, which limits the study of structure–property relationships and the recognition of chiral separation mechanism. Actually, the type, quantity and distribution of substituents on cellulose derivatives have a significant impact on the helical structure and local polarity, and accordingly on the recognition abilities. Toga *et al.* studied the chiral recognition ability of partially substituted cellulose benzoates with a degree of substitution (DS) from 2.1 to 2.8, which were prepared by aminolysis of cellulose tribenzoate with hydrazine in 1-methyl-2-pyrrolidone, and indicated that some enantiomeric pairs were resolved only by partially substituted cellulose benzoates.[6] Yuan and co-workers also found

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that partially substituted cellulose derivatives, compared with fully substituted ones, showed good separation factors for some racemates, namely the chiral discrimination ability was not proportional to DS.[7] And even some racemates could be separated using unmodified cellulose directly.[8] In addition, Kaida and Okamoto[9] and Kasuya *et al.*[10] demonstrated that the distribution of the substituents in cellulose mixed esters dramatically influenced their chiral discrimination. Therefore, the development of an effective method for the synthesis of cellulose-based CSPs with controllable DS and distribution of substituents is extremely attractive. Moreover, partially substituted cellulose derivatives can be made conveniently into new covalently bonded-type CSPs with high solvent stability and versatility by adding bifunctional reagents as crosslinker.[2,11–14]

Homogeneous derivatization of cellulose in appropriate media, the alternative procedure to the heterogeneous process, has drawn much attention, because it has opened a new avenue for achieving excellent control of the DS value and distribution and uniformity of functional groups along the cellulose chain, and avoiding many problems associated with heterogeneous reactions. Over the last decade, as new kinds of aprotic polar solvents, room temperature ionic liquids (ILs) with excellent abilities for dissolving cellulose have provided a new and versatile platform for the efficient and homogeneous derivatization of cellulose.[15,16] A variety of traditional and novel cellulose derivatives, especially partially and regioselectively substituted cellulose esters, have been successfully prepared using ILs as reaction media.[17–22] The homogeneous derivatization of cellulose in ILs not only provides opportunities to control the DS and chemical structure of the cellulose derivatives, but also gives high efficiency and yield protection. In particular, the homogeneous syntheses of cellulose phenylcarbamates and cellulose benzoates in ILs have been reported by Barthel and Heinze[19] and Zhang *et al.*[20] It has been demonstrated that DS (0.26–3.0) and distribution of substituents can be controlled effectively by adjusting the reaction conditions, with the products expected to be used for chiral separation. Recently, Liu *et al.* prepared fully and regioselectively substituted cellulose 3,5-dimethylphenylcarbamate CSPs in 1-allyl-3-methylimidazolium chloride (AmimCl), and subsequently separated some racemic pesticides successfully.[23,24]

In the work reported here, homogeneous cellulose carbanilation with nine kinds of substituted phenyl isocyanates in AmimCl was investigated. The effect of reaction conditions and substituents on the phenyl moieties on the reaction rate was studied in detail. Then, partially substituted cellulose phenylcarbamates were synthesized and made into coated CSPs, and their chiral recognition abilities for eight pairs of enantiomers were evaluated in HPLC.

EXPERIMENTAL

Materials

Microcrystalline cellulose with degree of polymerization of 220 was dried in vacuum at 80 °C for 24 h prior to use. The IL AmimCl was synthesized according to our previous work.[25] 4-Nitrophenyl isocyanate and 4-methoxyphenyl isocyanate were purchased from Sigma Aldrich. 2-Fluorophenyl isocyanate, 4-fluorophenyl isocyanate, 4-chlorophenyl isocyanate, 2-tolyl isocyanate and 4-tolyl isocyanate were obtained from Alfa-Aesar. Phenyl isocyanate, 3,5-dimethylphenyl isocyanate and 3-aminopropyltriethoxysilane were received from Aikeda Reagent Company, Maya Reagent Company and TCI, respectively. All other chemicals were supplied by Beijing Chemical Reagent Company, China. All reagents were of analytical grade and used as received without further purification.

Porous sphere silica gel with a mean particle size of 5.8 μm and a mean pore diameter of 26 nm was obtained from Beijing Greenherbs Science and Technology Development Company. It was treated with a large excess of 3-aminopropyltriethoxysilane in toluene in the presence of a catalytic amount of pyridine to obtain 3-aminopropyl silica before use.

Measurements and characterization

NMR spectra were acquired using Bruker NMR spectrometers with 16 scans for ^{1}H NMR (Bruker AV400) and 10 000–18 000 scans for ^{13}C NMR (Bruker AV600 or AV400) at room temperature in deuterated dimethylsulfoxide (DMSO-d_6). A few drops of trifluoroacetic acid-d_1 were added to shift active hydrogens to low-field area for ^{1}H NMR spectra.

Fourier transform infrared (FTIR) spectra were recorded with a Bruker Tensor 27 FTIR spectrometer from 400 to 4000 cm^{-1}.

The DS of cellulose derivatives was calculated from ^{1}H NMR spectra using the following equation:[26]

$$\mathrm{DS} = \frac{7I_{\mathrm{phenyl}}}{nI_{\mathrm{AGU}}} \quad (1)$$

where I_{phenyl} is the peak integral of phenyl protons; I_{AGU} the peak integral of protons of anhydroglucose unit (AGU); and n the number of protons on the benzene ring of phenyl isocyanates.

Synthesis of cellulose phenylcarbamates

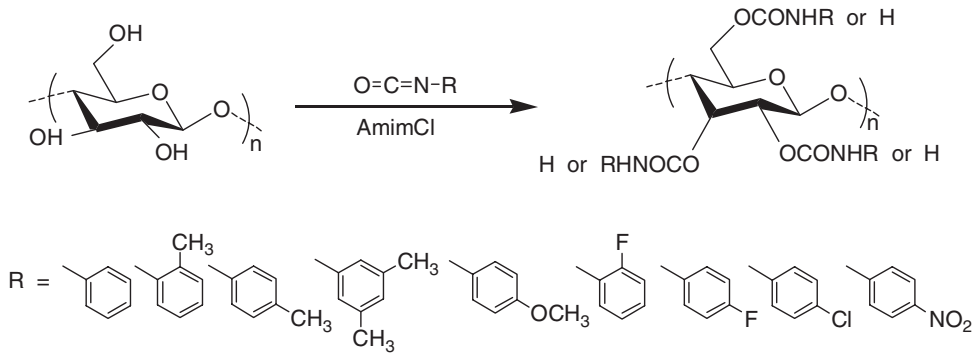
For a typical preparation of cellulose solution in AmimCl, 0.4 g of dried microcrystalline cellulose was added to 9.6 g of AmimCl in a three-necked flask. Then, the mixture of cellulose and AmimCl was mechanically stirred at 80 °C for 2 h to yield a clear and viscous solution with a cellulose concentration of 4.0 wt%.

A variety of cellulose phenylcarbamates were synthesized homogeneously in AmimCl according to Scheme 1. At a given temperature, phenyl isocyanates were added into cellulose–AmimCl solutions under vigorous stirring. After the required time, the resultant products were isolated as methanol-insoluble fractions, filtered and washed three times with methanol. They were redissolved in DMSO, precipitated again and thoroughly washed with methanol. Finally, the products were dried under vacuum at 80 °C.

Preparation of cellulose phenylcarbamate-coated CSPs and chromatographic conditions

First, cellulose bis(phenylcarbamate) (CBI2.0), cellulose bis(4-methylphenylcarbamate) (CPMI2.0), cellulose bis(3,5-dimethylphenylcarbamate) (CDMI2.0) and cellulose bis(4-chlorophenylcarbamate) (CPCI2.0) were synthesized homogeneously in AmimCl. Then, the CSPs were prepared as follows. An amount of 3.0 g of 3-aminopropyl silica gel (APS) was suspended in 20 mL of tetrahydrofuran (THF). An appropriate amount of cellulose phenylcarbamate was dissolved in 30 mL of THF and added dropwise to the APS/THF slurry at a rate of 0.03 mL min^{-1}. The suspension was stirred overnight, and then the solvent was slowly removed in a rotary evaporator at room temperature. Finally, the four CSPs, CSP-CBI2.0, CSP-CPMI2.0, CSP-CDMI2.0 and CSP-CPCI2.0, were dried under vacuum at 50 °C.

Packing CSPs were suspended in a hexane–2-propanol mixture (70:30, v/v) and packed into 250 × 4.6 mm (inner diameter) columns using the stirred slurry method. Packing pressure was



Scheme 1. Synthetic route to cellulose phenylcarbamates.

5800 psi (40 MPa). Hexane–2-propanol (90:10, v/v) was employed as the displacing solvent.

Chromatography was performed at 25 °C using a Waters e2695 liquid chromatograph equipped with an ultraviolet detector (Waters UV-2489) and Empower workstation. The mobile phase was a hexane–2-propanol mixture (98:2, v/v), at a flow rate of 1 mL min^{-1}. The dead time (t_0) was determined using 1,3,5-tri-*tert*-butylbenzene as unretained compound. UV detection was carried out at 254 nm.

RESULTS AND DISCUSSION

Homogeneous synthesis of cellulose phenylcarbamates in AmimCl

Homogeneous carbanilation of cellulose dissolved in AmimCl with nine kinds of substituted phenyl isocyanates was achieved in one facile step without any catalyst. The DS values of all the cellulose phenylcarbamates in a wide range (from 0 to 3) could be regulated by employing appropriate reaction conditions, such as temperature, reaction time and molar ratio of phenyl isocyanate/AGU. The detailed experimental conditions and results are presented in Table 1. It is clear that, with an increase of reaction temperature, the reaction is accelerated. For example, during the carbanilation of cellulose with 4-tolyl isocyanate, under the same conditions of a molar ratio of 3:1 and reaction time of 1 h, an increase of reaction temperature from 60 to 80 and 100 °C leads to an increase in DS from 0.77 to 1.11 and 1.46, respectively (from CpTI1 to CpTI2 and CpTI3). In addition, the DS of products increases as reaction time increases. During the reaction between cellulose and phenyl isocyanate with a molar ratio of 3:1 at 80 °C, an increase of reaction time from 0.5 to 1 and 2 h leads to an increase in DS from 1.22 to 1.37 and 1.62, respectively (CPI2). Furthermore, an increase of molar ratio of phenyl isocyanate/AGU generates a dramatic increase of DS. For instance, during the reaction of cellulose with 4-tolyl isocyanate, an increase of the molar ratio of 4-tolyl isocyanate/AGU from 3:1 to 5:1 results in an increase of DS from 1.52 to 2.07 for 2 h at 100 °C (CpTI3 to CpTI4).

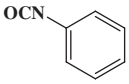
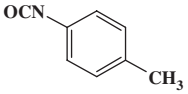
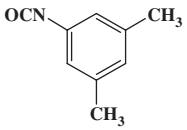
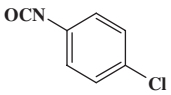
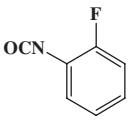
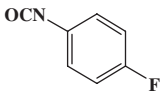
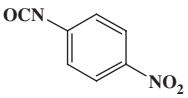
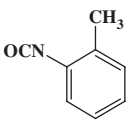
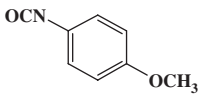
From Table 1, it also can be seen distinctly that the substituents on the phenyl moieties have a significant impact on the reaction rate of cellulose carbanilation. The electron-withdrawing substituents of phenyl isocyanates accelerate the carbanilation reaction, while the electron-donating groups reduce the reaction rate. For example, the reactivity of 4-nitrophenyl isocyanate and 4-chlorophenyl isocyanate is much higher than that of phenyl isocyanate, while the reactivity of 3,5-dimethylphenyl isocyanate is lower than that of phenyl isocyanate. Under the same reaction parameters (molar ratio of carbanilation reagent/AGU = 3:1, temperature = 80 °C, time = 1 h), when phenyl isocyanate is used as the carbanilation reagent, DS is 1.37 (CPI2); while DS increases to 2.18 when 4-nitrophenyl isocyanate is used as the carbanilation reagent (CpNI); and DS decreases to 0.83 when 3,5-dimethylphenyl isocyanate is used as the carbanilation reagent (CdMI2).

The Hammett correlation, which is of widespread importance in physical organic chemistry, is a visualizing hallmark for elucidating structure–reactivity relationships of reagents and predicting reaction rate.[27,28] Combining Hammett constants (σ) with the effect of substituents on the reactivity of substituted phenyl isocyanates, a plot of σ *versus* DS is obtained, as shown in Fig. 1. The Hammett plot is linear with a positive slope. Therefore, the higher the value of Hammett parameter, the higher is the reactivity of the corresponding substituted phenyl isocyanate. In other words, the reactivity of the substituted phenyl isocyanates is enhanced by electron-withdrawing substituents (NO_2, Cl) and weakened by electron-donating substituents (CH_3, OCH_3) on the aromatic ring. It is well known that carbanilation is a nucleophilic addition reaction, and the introduction of electron-withdrawing substituents into the phenyl moieties increases the polarity of the isocyanate group, and thus phenyl isocyanates with stronger electron-withdrawing substituents exhibit higher reactivity. Based on the linear Hammett correlation, it is possible to anticipate the reaction rate of future reactions from Hammett constants of substituents, which can be obtained by consulting tables in physical organic chemistry handbooks.

Structural characterization and solubility of cellulose phenylcarbamates

Synthesized cellulose phenylcarbamates were first analyzed using FTIR spectroscopy. Figure 2 shows the FTIR spectra of unmodified cellulose, cellulose phenylcarbamate with DS of 2.00, cellulose 4-methylphenylcarbamate with DS of 2.07 and cellulose 4-chlorophenylcarbamate with DS of 2.11. These spectra provide a clear evidence of successful carbanilation by exhibiting the presence of some characteristic peaks at 1728, 1724 and 1725 cm^{-1} for C═O stretching in ester, 1542, 1533 and 1539 cm^{-1} for aromatic C═C stretching, and 1222, 1224 and 1221 cm^{-1} for stretching of (O)C—O. Of note, in Figs 2(c) and (d), the peaks appearing at 818 and 827 cm^{-1}, which correspond to C—H out-of-plane bending, further confirm these products are *para*-substituted benzenoid compounds. Moreover, due to the partial modification of hydroxyls partly breaking hydrogen bonds, the O—H peak at 3361 cm^{-1}, which corresponds to hydroxyl group of unmodified cellulose, shifts to around 3394 cm^{-1}, and the intensity of peaks at

Table 1. Conditions and results of homogeneous carbanilation of cellulose with various phenyl isocyanates in AmimCl

Sample	Phenyl isocyanate	Molar ratio of phenyl isocyanate/AGU	Temperature (°C)	DS		
				Reaction time		
				0.5 h	1.0 h	2.0 h
CPI1		3:1	60	–	1.15	1.34
CPI2		3:1	80	1.22	1.37	1.62
CPI3		3:1	100	1.46	1.54	1.81
CPI4		5:1	100	2.00	2.19	2.38
CpTI1		3:1	60	–	0.77	1.03
CpTI2		3:1	80	0.81	1.11	1.42
CpTI3		3:1	100	1.23	1.46	1.52
CpTI4		5:1	100	1.66	1.73	2.07
CdMI1		3:1	60	–	0.27	0.52
CdMI2		3:1	80	0.47	0.83	1.17
CdMI3		5:1	100	1.16	1.74	2.14
CpCl1		3:1	80	1.78	1.88	1.95
CpCl2		5:1	80	2.11	2.32	2.56
CoFI		3:1	80	1.70	1.87	2.08
CpFI		3:1	80	1.61	1.82	1.99
CpNI		3:1	80	1.86	2.18	2.28
CoTI		3:1	80	0.60	0.93	1.16
CpMI		3:1	80	0.87	1.15	1.39

3361 (O—H stretching) and 1372 cm^{-1} (O—H bending) obviously decreases.

The ^{1}H NMR spectrum of cellulose phenylcarbamate with DS = 1.81 is provided in Fig. 3(A). The peaks in the range 6.5–7.8 and 2.8–5.6 ppm are attributed to the aromatic protons of phenylcarbamate and the protons of cellulose backbone, respectively. The amino protons of cellulose phenylcarbamate appear around 9.5 ppm. These peaks confirm the successful carbanilation of cellulose. Furthermore, the defined structure of cellulose phenylcarbamate with DS = 1.03 is characterized clearly using ^{13}C NMR spectroscopy, as shown in Fig. 3(B). The peak at 153.7 ppm is attributed to the carbonyl carbon (C-7), the peaks at 118.8, 122.9, 129.2 and 139.4 ppm to the phenyl ring in phenylcarbamate group and the peaks at 60–103 ppm to cellulose backbone carbons (C-1, C-2, C-3, C-4, C-5, C-6 and C-6′). Moreover, the chemical shift and peak shape of C-7, C-1, C-4 and C-6, which are affected significantly by the substitution of three hydroxyl groups at C-2, C-3 and C-6 of cellulose, can be used to determine the position and distribution of substituent groups. In Fig. 3(B), the peak of C-6 influenced by esterification of the primary hydroxyl at C-6 position appears at 63.4 ppm (C-6′), exhibiting a downfield shift of about 3 ppm, compared with the C-6 connecting with unmodified hydroxyl. The signals of C-1 and C-4 become broad only, and new peaks indicating a substituted hydroxyl group do not emerge, thus a small amount of the secondary hydroxyls is substituted. These phenomena indicate that the carbanilation reaction is preferred at C-6, and the order of reactivity is C6-OH > C3-OH ≅ C2-OH.

The solubility of cellulose phenylcarbamates in some common organic solvents was investigated (Table 2). It can be seen that almost all of the samples are soluble in DMSO and *N*,*N*-dimethylformamide (DMF), except cellulose 4-chlorophenylcarbamate with DS = 0.27. In other organic solvents, the solubility of samples strongly depends on their DS values. In THF, when the DS is near or above 2.0, the samples dissolve rapidly. In acetone, samples with low DS, i.e. 0.27, cannot be

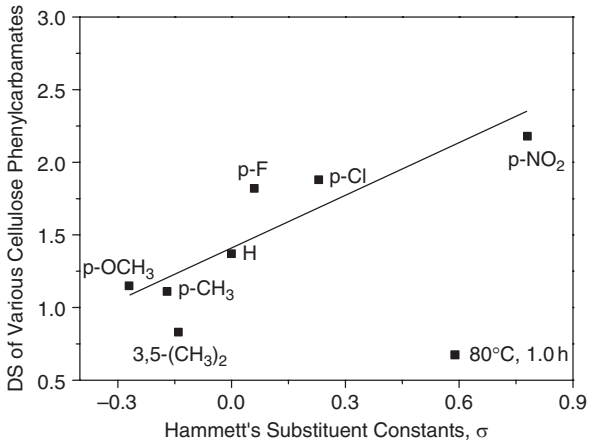


Figure 1. DS of various cellulose phenylcarbamates plotted against the Hammett constants of substituents in phenyl isocyanates.

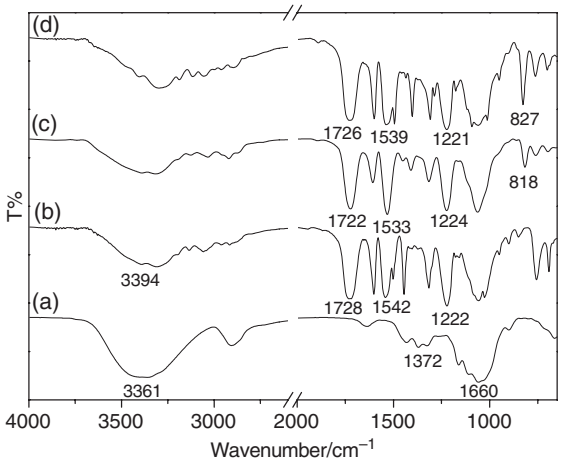


Figure 2. FTIR spectra of (a) unmodified cellulose, (b) cellulose phenylcarbamate with DS = 2.00, (c) cellulose 4-methylphenylcarbamate with DS = 2.07 and (d) cellulose 4-chlorophenylcarbamate with DS = 2.11.

dissolved, while those samples with DS up to 1.0 can be swollen, and others with DS above 2.5 can be dissolved.

Chiral separation of racemates on cellulose phenylcarbamate-coated CSPs

Based on the above synthesis results, four kinds of partially substituted cellulose phenylcarbamtes with DS ≈ 2.0 were synthesized readily in AmimCl, and then coated on APS to obtain coated-type CSPs. Subsequently, the chiral recognition abilities of the obtained cellulose phenylcarbamate-coated CSPs were evaluated using HPLC with eight racemates: (1) 2-phenylcyclohexanone, (2) 1-(2-naphthyl)ethanol, (3) Tröger's base, (4) D,L-*sec*-phenethyl alcohol, (5) flavanone, (6) benzoin, (7) cobalt(III) acetylacetonate and (8) *trans*-stilbene oxide.

The chromatograms of optical resolution for racemates 2, 3 and 7 eluted with *n*-hexane–2-propanol mixture (98:2, v/v) on CSP-CBI2.0, CSP-CPMI2.0, CSP-CDMI2.0 and CSP-CPCI2.0 are shown in Fig. 4. Obviously, these CSPs exhibit high recognition abilities. Complete or near-baseline separation is achieved. And the substituents on the phenyl moieties have a considerable effect on the recognition ability of cellulose phenylcarbamate-based CSPs. For the enantioseparation of 1-(2-naphthyl)ethanol and Tröger's

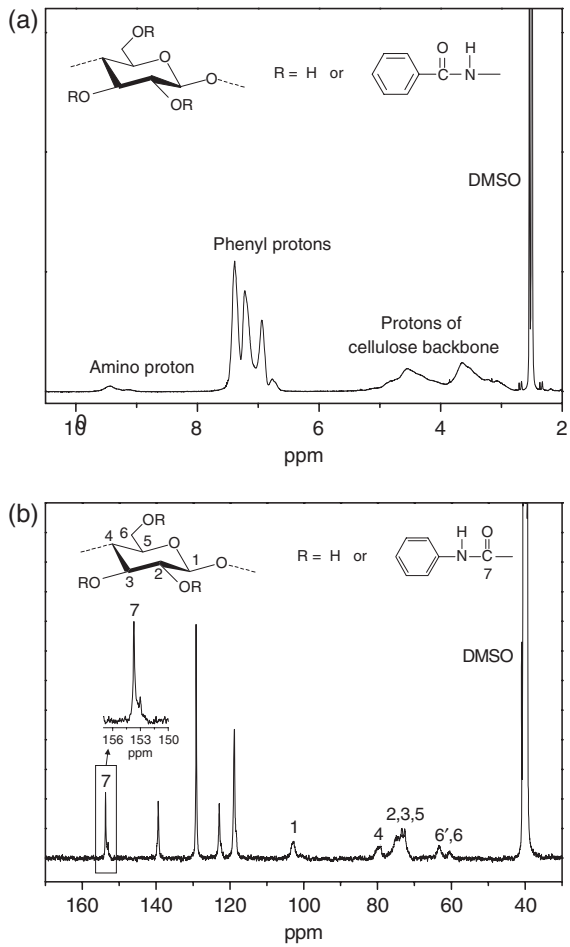


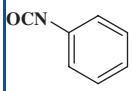
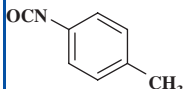
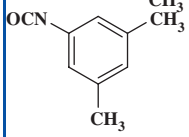
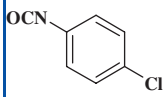
Figure 3. (A) ^{1}H NMR spectrum of cellulose phenylcarbamate with DS = 1.81. (B) ^{13}C NMR spectrum of cellulose phenylcarbamate with DS = 1.03.

base, the methyl-substituted cellulose bisphenylcarbamates (CPMI2.0 and CDMI2.0) exhibit better chiral recognition abilities than chloro-substituted one (CSP-CPCI2.0) and CSP-CBI2.0. For the enantioseparation of cobalt(III) acetylacetonate, CSP-CBI2.0 and CSP-CPCI2.0 show better chiral recognition abilities than CPMI2.0 and CDMI2.0.

Furthermore, compared with traditional cellulose tris(3,5-dimethylphenylcarbamate) stationary phase,[29] partially substituted cellulose CSP-CDMI2.0 shows higher chiral recognition ability for cobalt(III) acetylacetonate ($\alpha = 1.19$, Fig. 4(C)). Thus, partially substituted cellulose derivatives are shown to have a good chiral recognition ability for some racemates, and the chiral discrimination ability of cellulose derivatives is not proportional to DS.

The calculated results of optical resolution for the eight racemates on the CSP-CBI2.0, CSP-CPMI2.0, CSP-CDMI2.0 and CSP-CPCI2.0 columns are summarized in Table 3. All the racemates were eluted with *n*-hexane–2-propanol mixture (98:2, v/v) using HPLC. These CSPs exhibit different recognition abilities, which depend markedly on the substituents on the phenyl ring in phenylcarbamate group, although a simple correlation is not observed between the separation factors (α) and the nature of substituent. CSP-CBI2.0 shows chiral recognition for racemates 2 and 3, and especially racemate 7. Compared with CSP-CBI2.0, cellulose phenylcarbamates with electron-donating substituents

Table 2. Solubility of cellulose phenylcarbamates with various DS in common organic solvents

Carbanilation reagent	DS	Solubility[a]			
		DMSO	DMF	THF	Acetone
	1.15	+	+	±	±
	1.96	+	+	+	±
	2.54	+	+	+	+
	0.81	+	+	±	±
	1.73	+	+	+	±
	2.23	+	+	+	±
	1.08	+	+	±	±
	2.14	+	+	+	±
	3.0	+	+	+	+
	0.27	+	±	±	−
	1.78	+	+	+	+
	2.68	+	+	+	+

[a] +, Soluble; ±, swollen; −, insoluble.

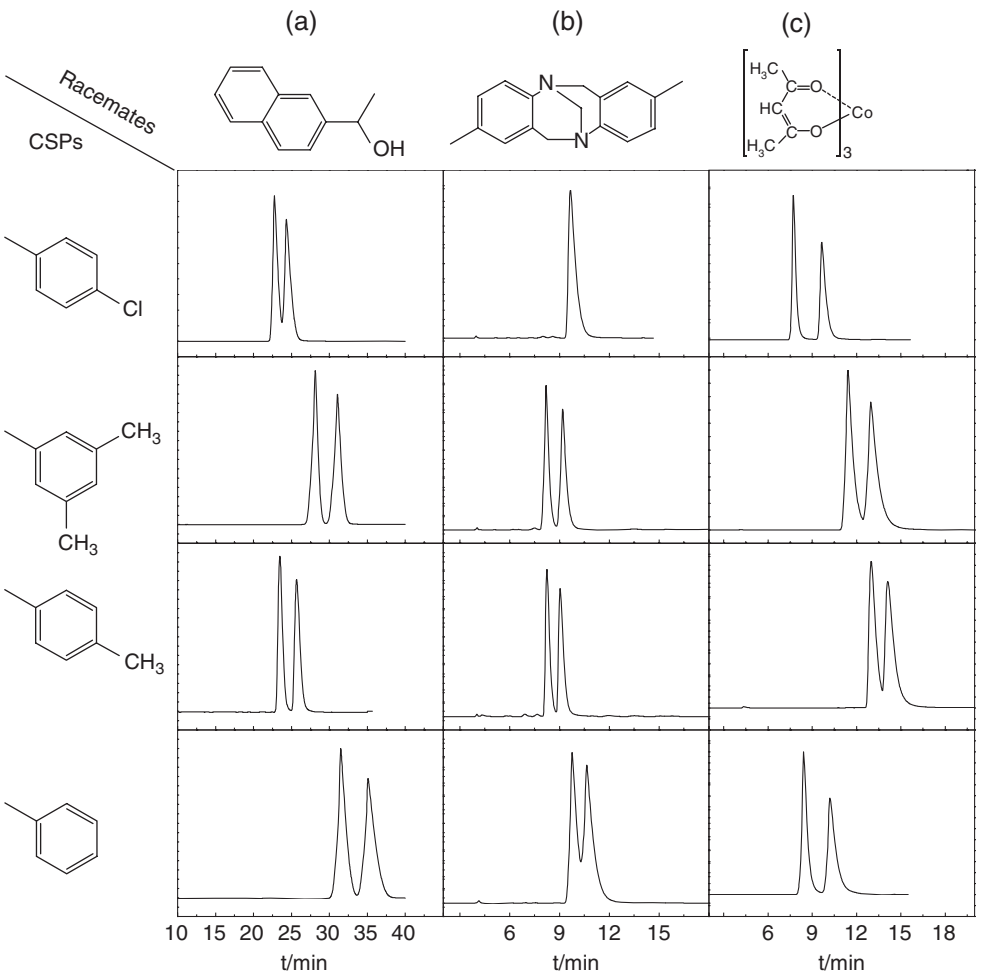
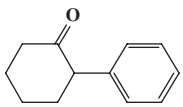
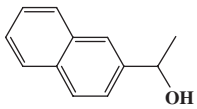
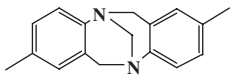
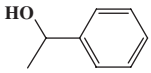
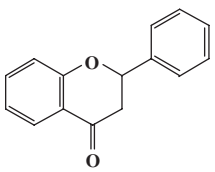
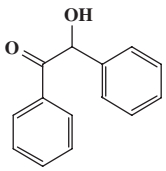
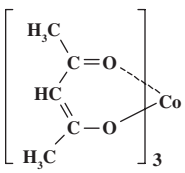
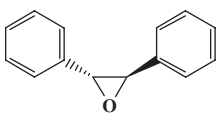


Figure 4. Chromatographic resolution of (A) 1-(2-naphthyl)ethanol, (B) Tröger's base and (C) cobalt(III) acetylacetonate on cellulose bis(phenylcarbamate) column, cellulose bis(4-methylphenylcarbamate) column, cellulose bis(3,5-dimethylphenylcarbamate) column and cellulose bis(4-chlorophenylcarbamate) column.

Table 3. Chromatographic results of eight racemates on cellulose phenylcarbamate-coated CSPs

	CSP-CBI2.0			CSP-CPMI 2.0			CSP-CDMI 2.0			CSP-CPCI 2.0		
Racemate	k'_1[a]	α[b]	R_s[c]	k'_1	α	R_s	k'_1	α	R_s	k'_1	α	R_s
1. 	3.05	1.03	0.65	1.75	1.08	0.97	1.89	1.08	1.29	2.52	*ca* 1	-
2. 	8.78	1.13	3.44	6.10	1.11	1.83	7.74	1.12	3.47	5.83	1.08	1.84
3. 	2.03	1.13	1.95	1.49	1.16	1.76	1.55	1.20	3.05	1.90	*ca* 1	–
4. 	3.74	1.05	1.23	3.04	1.05	0.77	3.76	1.07	1.14	2.96	1.04	0.89
5. 	3.31	*ca* 1	–	1.82	*ca* 1	–	2.32	*ca* 1	–	2.34	1.05	0.95
6. 	3.07	1.03	0.77	4.96	*ca* 1	–	6.73	*ca* 1	–	8.11	*ca* 1	–
7. 	1.62	1.34	3.47	2.93	1.12	1.41	2.55	1.19	2.79	1.32	1.44	4.84
8. 	0.44	*ca* 1	–	0.42	*ca* 1	–	0.57	1.07	0.7	0.50	1.17	1.18

[a] Capacity factor of the first eluted enantiomer, which is estimated as $(t_1 - t_0)/t_0$.
[b] Separation factor estimated as k'_2/k'_1.
[c] Resolution estimated as $1.18(t_2 - t_1)/(w_1 + w_2)$, where t_1 and w_1 are the retention time and half-height peak width, respectively.

(CSP-CPMI2.0 and CSP-CDMI2.0) present better chiral resolution ability for racemates 1, 3, 4 and 8. A cellulose phenylcarbamate with electro-withdrawing substituent (CSP-CPCI2.0) exhibits low chiral recognition for racemates 1–4, but high chiral recognition ability for racemates 5, 7 and 8. As shown above, partially substituted cellulose derivatives can be considered as efficient polysaccharide-based CSPs for some racemates.

CONCLUSIONS

Under mild conditions, the homogeneous carbanilation of cellulose with nine kinds of substituted phenyl isocyanates was successfully carried out in AmimCl without any catalyst. In particular, the DS of the products could be easily controlled by altering reaction temperature, reaction time and molar ratio of carbanilation reagent/AGU. In addition, substituents on the benzene ring of phenyl isocyanates also had an obvious impact on the carbanilation reaction. Electron-withdrawing substituents accelerated the carbanilation reaction, while electron-donating substituents reduced the reaction rate. Subsequently, by taking advantage of the synthesis result, four kinds of partially substituted cellulose phenylcarbamates with different substituents on the phenyl moiety were successfully prepared and adsorbed on silica gel. The obtained CSPs were employed in

chiral separation of eight racemates for HPLC and exhibited good chiral recognition abilities for most of the racemates. In addition, the chiral recognition ability depended markedly on the substituents on the aromatic ring. On CSP-CPMI2.0 and CSP-CDMI2.0, racemates 1-(2-naphthyl)ethanol, Tröger's base and cobalt(III) acetylacetonate achieved baseline separation. CSP-CPCI2.0 showed the best chiral recognition for cobalt(III) acetylacetonate and *trans*-stilbene oxide. Regarding the potential of partially substituted cellulose-based CSPs as promising chiral separation materials, studies of bonded-type CSPs utilizing free hydroxyl groups on the partially substituted cellulose derivatives are expected to be conducted in the future.

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