Preparation of Tri-*O*-benzylcellulose by the Use of Nonaqueous Cellulose Solvents

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Synopsis

A procedure has been developed for preparing tri-*O*-benzylcellulose with higher yields than 90%. In this procedure, cellulose was dissolved in a nonaqueous cellulose solvent, SO_2–diethylamine (DEA)–dimethyl sulfoxide (DMSO), and then powdered sodium hydroxide was added. To the suspension thus prepared, benzyl chloride was added in four portions under heating. Chemical and physical properties of tri-*O*-benzylcellulose were studied, and tri-*O*-benzylcellulose prepared from microcrystalline cellulose powder shows the characteristic of thermotropic liquid crystal.

INTRODUCTION

Recently, cellulose has attracted attention as a renewable natural resource, unlike petroleum. Chemical and physical modifications of cellulose have been studied extensively with the aim of adding various valuable properties to cellulose. Thus, it has been utilized as chemicals such as ion exchangers, immobilized supports, metal complexes, gel beads for chromatography, and so on.

As cellulose ethers are more stable to chemical conditions than the other derivatives, such as esters, they have been much utilized as celluloses for various functions. Cellulose ethers are usually prepared by reactions of alkalicellulose with alkyl halides or epoxides, but in general the preparation of highly substituted cellulose ethers, which are soluble in many organic solvents, is rarely attained. Namely, because cellulose cannot be modified as easily and variously as synthetic polymers.

Recently, many kinds of nonaqueous cellulose solvents have been found, and many fundamental and practical works about these solvents have been reported.[1] The appearance of these solvents made it possible to modify cellulose homogeneously. The authors have reported the success of homogeneous chlorination[2] and acetylation[3,4] of cellulose in which nonaqueous cellulose solvents were used as reaction media.

This paper deals with the preparation of tri-*O*-benzylcellulose by the use of nonaqueous cellulose solvents under various conditions, namely, kinds of bases used, kinds of nonaqueous solvents, amounts of reagents added, and so on. Tri-*O*-benzylcellulose was characterized by chemical or physical methods. Thus, tri-*O*-benzylcellulose with a $\overline{\mathrm{DP}}_w$ of 129 was found to have the characteristic of thermotropic liquid crystal.

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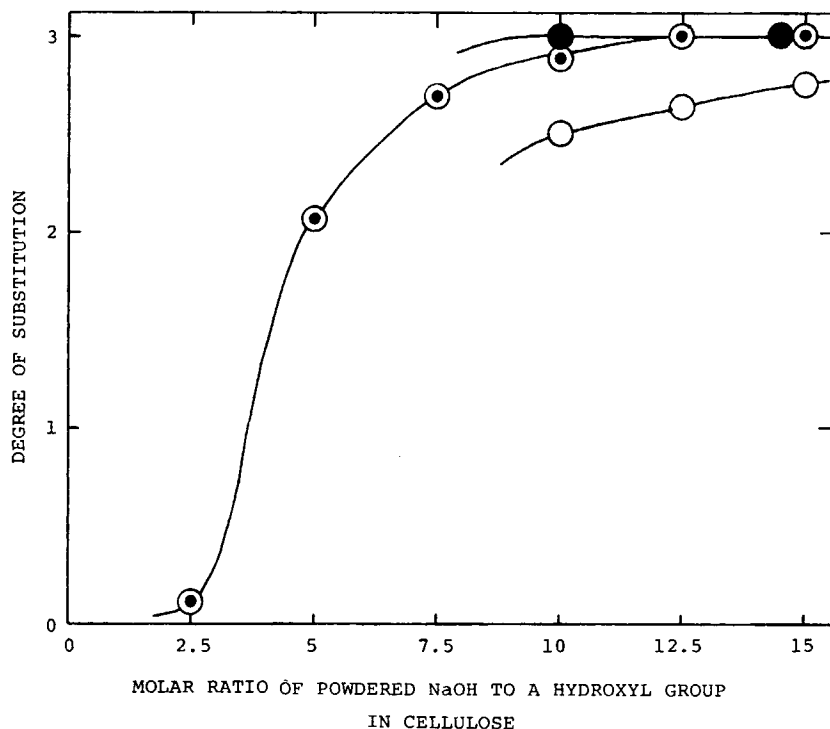
Fig. 1. Degree of substitution of benzylcellulose vs. amounts of reagents: (⊙) SO₂–DEA–DMSO system used as a cellulose solvent; (●) N₂O₄–DMSO system; (○) LiCl–DMAc system.

EXPERIMENTAL

Materials

Cellulose samples were cotton linter ($\overline{DP}_v$ = 1360), its hydrocellulose ($\overline{DP}_v$ = 260), and Avicel (commercial cellulose powder manufactured by Asahi Chemical Ind. Co., Ltd., $\overline{DP}_v$ = 250). These samples were used after drying at 105°C for 3 h.

Preparation of Cellulose Solutions

Cellulose–N₂O₆–DMSO Solution. Beforehand, an N₂O₄–DMSO mixture was prepared by pouring liquid N₂O₄ into DMSO in a volumetric flask, and the content of N₂O₄ was determined by the weight increase. One gram of cellulose was well dispersed in 40 mL of DMSO at room temperature and then the N₂O₄–DMSO mixture containing 1.71 g of N₂O₄ (N₂O₄/Cell–OH = 1/1, molar ratio) was poured into the cellulose suspension under stirring. The cellulose concentration was adjusted to 1.5% (w/w).

Cellulose–SO₂–Diethylamine (DEA)–DMSO Solution. Beforehand, a SO₂–DMSO mixture was prepared by bubbling SO₂ into DMSO, and the content of SO₂ was determined by the weight increase and by titration. 1 g of cellulose was well dispersed in 18.2 mL of DMSO ultrasonically at room temperature for
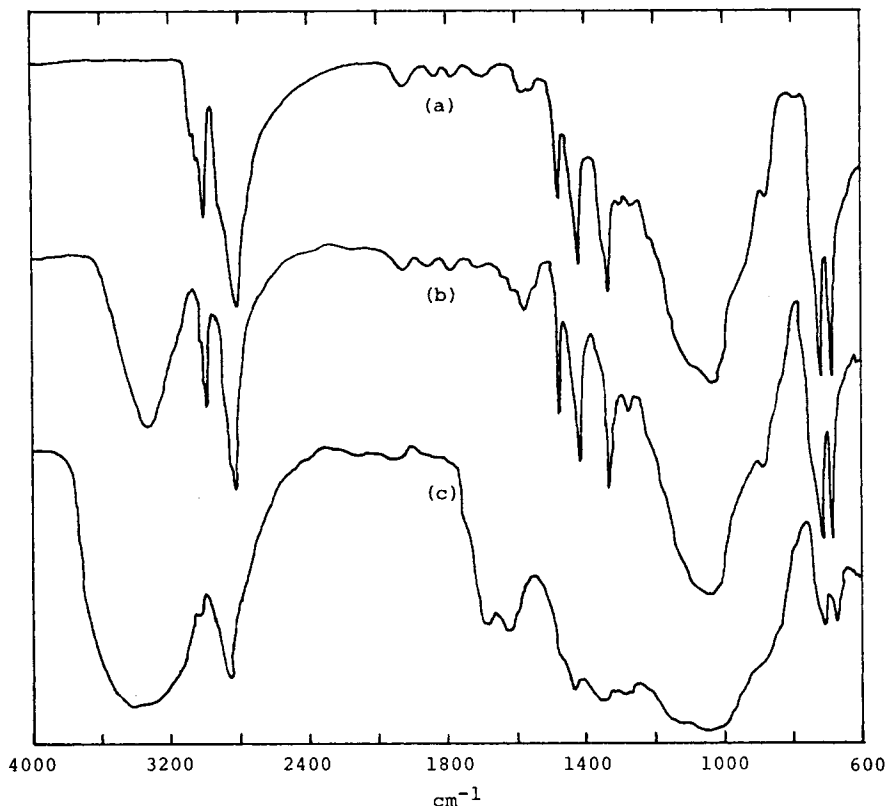
Fig. 2. IR spectra of products obtained by benzylation in nonaqueous solvents: (a) tri-*O*-benzylcellulose, chloroform-extractable product by benzylation both in N_2O_4–DMSO and SO_2–DEA–DMSO; (b) chloroform-insoluble benzylcellulose prepared by addition of insufficient amounts of reagents in both SO_2–DEA–DMSO and LiCl–DMAc; (c) chloroform-insoluble byproduct obtained by benzylation in N_2O_4–DMSO.

10 min, and then the SO_2–DMSO mixture containing 1.19 g of SO_2 and 1.36 g of DEA were poured successively into the cellulose suspension under stirring (SO_2/DEA/Cell–OH = 1/1/1, molar ratios).   Cellulose was dissolved within 3 min after the addition of DEA.   The cellulose concentration was adjusted to 2.7% (w/w).

Cellulose–LiCl–Dimethylacetamide (DMAc) Solution.   The preparation method by Turbak et al.[5] was adopted.   One gram of cellulose and 28 mL of DMAc were heated at 165°C for 30 min under stirring.   The slurry was then allowed to cool to 100°C at which point 2.63 g of anhydrous LiCl was added.   After 3 days stirring of the slurry at room temperature, trace amounts of undissolved cellulose was removed by centrifugation.   The cellulose concentration was adjusted to 3.05% (w/w).

Preparation of Benzylcellulose

Preparation of Tri-*O*-benzylcellulose.   Cellulose was benzylated soon after dissolution of cellulose in a nonaqueous solvent in order to avoid the changes of

TABLE I
Effects of Kinds of Nonaqueous Cellulose Solvent Systems on Benzylation of Cellulose

Solvents	N_2O_4–DMSO	LiCl–DMAc	SO_2–DEA–DMSO
Time required for preparation of cellulose solution	30 min	3 days	10 min
DS of benzylcellulose[a]	3.0	2.8	3.0
Yields of benzylcellulose	58%	75%	95%
Ratio of $\overline{DP}_w$ of benzylcellulose to $\overline{DP}_v$ of original cellulose[b]	—	$\frac{1}{4}$	$\frac{1}{2}$

[a] Reagents (powdered NaOH and benzyl chloride)/Cell–OH = 15 (mol/mol).
[b] These benzylcelluloses were prepared under air atmosphere.

cellulose quality. This procedure is essentially the same as that for the preparation of tri-O-benzylamylose.[6]

Powdered sodium hydroxide (9.3 g, 12.5 mol/mol hydroxyl groups in cellulose) was added to a cellulose solution containing 1 g of cellulose. After the addition of benzyl chloride, the temperature was raised to 70°C. At 1, 2, and 12 h after the raising to 70°C, 3-mL portions of benzyl chloride were added dropwise. After the last drop of benzyl chloride, the temperature was raised to 85°C and kept at this temperature for 2 h. The reaction mixture was cooled to room temperature, and 100 mL of water and 100 mL of chloroform was added. The chloroform layer was separated, and the aqueous layer was extracted with three 40-mL portions of chloroform. The chloroform extracts were combined, washed with 300 mL × 3 of water, and evaporated under diminished pressure at 60°C to a syrup. Tri-O-benzylcellulose was precipitated from the syrup by the addition of 100 mL of 95% ethanol under stirring. After immersion in 100 mL of 95% ethanol for 24 h, the precipitate was filtered and then washed several times with water, with 95% ethanol, and finally with hexane. The product was filtered off, air-dried, and then dried under vacuum at 50°C. Tri-O-benzylcellulose obtained by this method was white fine powder, with a yield of 2.53 g (95% of theoretical yield), no hydroxyl absorption at 3500–3300 cm^{-1}, $[\alpha]_D^{20} = +17°$ (C 1.0, chloroform).

ANAL. Calcd for $C_{27}H_{28}O_5$: C, 75.00%; H, 6.48%. Found: C, 74.55%; H, 6.59%.

Benzylation of Cellulose under Various Conditions. Benzylcellulose was prepared also under various conditions, namely, kinds of bases used, kinds of cellulose solvents, amounts of reagents, and so on. On benzylation, benzyl chloride was added in four portions to cellulose solution–base suspension as described above, and total amounts of benzyl chloride were adjusted to the equimolar amounts of bases added. Benzylcellulose prepared under various condition was isolated by addition of methanol–water (1/1; v/v) into a reaction mixture and filtration, and purified by washing several times with methanol and water and finally with hexane. Purified and dried benzylcellulose was analyzed by elementary analysis and IR spectrometries.

General Analyses

IR spectra were measured using a Shimazu IR-400 spectrophotometer by the KBr disk technique and the deposited film technique from chloroform solutions. ^{13}C-NMR spectra were measured in chloroform-d_1 with tetramethylsilane as

TABLE II
Effects of Kinds of Bases on the DS and Yields of Benzylcellulose Prepared in LiCl–DMAc[a]

Base	NaH–oil, room temp	NaH–oil 70–85°C	t-BuOK	Powdered NaOH
DS	0.3	2.5	0.3	2.6
Yields (%)	98	65	20	70

[a] Reagents (based on benzyl chloride)/Cell–OH = 10 (mol/mol).

an internal reference, using an FX 100 type spectrometer (Japan Electro Optics Laboratory, JEOL). Samples were examined as 8% solutions in NMR. Optical rotations were measured using a Jasco SIP-4 Digital Polarimeter.

Gel permeation chromatograms were obtained using a Waters ALC/GPC 244 system with Styragel columns 10, 10, 10, 500, and 100 Å in series and chloroform as an eluant. Polystyrene standards were used to obtain a calibration curve.

T_g and DSC curves were measured using Rigaku-denki standard model T_g and DSC. 10 mg of a sample was set on an alminum pan, and T_g and DSC curves were measured from room temperature to 500°C at the rate of 5°C/min in He atmosphere. Dynamic viscoelasticities were measured using a $\overline{O}$yodenki Laboratory RB-1 by tortional braid analyses. The glass–wool braid impregnated with chloroform solution containing 60 mg of a sample was heated from room temperature to 200°C at the rate of 1°C/min in vacuum. Melting points were determined using a Yanako melting points apparatus with a polarizing microscope (× 60).

X-ray diffractograms were obtained by the use of a disk of 30 mg of a sample prepared by compressing at the pressure of 100 kg/cm². The equational diffraction pattern was measured from 5° to 35° values of 2θ using CuKα radiation at 35 kv and 35 mA. Scanning rate and slit width were set at 1°/min and 2–2 mm, respectively.

RESULTS AND DISCUSSION

Preparation of Tri-O-Benzylcellulose

Ethers of usual alcohols can be prepared easily by the reaction of alcoholates with alkylating reagents. On the other hand, cellulose ethers have been prepared by the reaction of alkalicellulose with alkylating reagents (alkyl halides or epoxides). The preparation of highly substituted cellulose ethers by this method, however, is difficult for the following reasons: (1) all hydroxyl groups in cellulose are rarely converted to alcoholates with aqueous alkaline media, (2) side reactions involving water occur necessarily and thus waste reagents, and (3) alkylating reagents cannot penetrate easily into cellulose crystallites owing to their low solubilities in aqueous media.

As to benzylcellulose among many kinds of cellulose ethers, tri-O-benzylcellulose has never been prepared in aqueous media. The addition of phase transfer catalysts such as tetraalkylammonium salts to alkalicellulose in aqueous media improved the extent of benzylation, but the maximum DS (degree of substitution) was 2.4.[7] Keilich et al.[8] succeeded in the preparation of tri-O-benzylcellulose by treating acetylcellulose (DS = 1) twice with benzyl chloride and methylsulfinyl anion (DMSO–NaH), but the yields were only 30%.

Base	$CH_3SOCH_2^-Na+$	NaH–oil	$NaNH_2$	t-BuOK	Powdered KOH	Powdered NaOH
DS	—^{b}	0.3	0.7	1.5	0.1	2.1
Yields (%)	—	60	60	50	92	90

^{a} Reagents (base and benzyl chloride)/Cell–OH = 5 (mol/mol).
^{b} Gelation of cellulose solution occurred.

In order to overcome the above-mentioned difficulties, nonaqueous cellulose solvents were applied as reaction media.

Effects of Kinds of Nonaqueous Solvents and Amounts of Reagents on Benzylation. Three kinds of nonaqueous solvents, N_2O_4–DMSO, SO_2–DEA–DMSO, and LiCl–DMAc systems were selected, because DMSO and DMAc were stable to anhydrous basic conditions and the undesired reactions such as the formations of ethers Cell—O—$(CH_2O—)_n$—R found in a cellulose–paraformaldehyde–DMSO system[9] could not be expected in the case of these three systems.

Figure 1 shows the relations between the amounts of reagents and DS of benzylcellulose prepared by the use of three nonaqueous solvent systems.

When N_2O_4–DMSO was used as a solvent, chloroform-extractable tri-O-benzylcellulose having no hydroxyl absorption around 3400 cm^{-1} was obtained by addition of more reagents than 10 mol/mol hydroxyl groups in cellulose, but the yields were only 58%. IR spectra of tri-O-benzylcellulose and a byproduct recovered by dialysis of chloroform-insoluble parts were shown in Figure 2(a) and (c), respectively. The characteristic bands at 3200–2800, 720, and 690 cm^{-1} due to benzyl groups could be detected in their spectra, but, in the spectrum (Fig. 2c), the bands around 1740–1600 cm^{-1} due to carboxyl and/or carbonyl groups were also detected. The reason why the yields of tri-O-benzylcellulose were limited to 58%, was thought to be based on the formations of chloroform-insoluble, oxidized products by heating the reaction mixture containing alkali, N_2O_4, oxygen, and cellulose.

When LiCl–DMAc was used as a cellulose solvent, no side reactions occurred on benzylcellulose as shown in Figure 2(b). But even by the addition of 15 mol reagents/mol hydroxyl groups in cellulose, benzylcellulose with a DS higher than 2.8 was not obtained (Fig. 1). Namely, this cellulose solvent was inferior to the other two solvents in efficiency on benzylation. The $\overline{DP}_w$ of benzylcellulose with the DS of 2.8 prepared under air atmosphere was found by GPC analysis to be ¼ of the $\overline{DP}_v$ of original cellulose. Furthermore, the preparation of this cellulose solution required much more time than those of the other two.

When SO_2–DEA–DMSO was used as a cellulose solvent, tri-O-benzylcellulose was obtained by the addition of more reagents than 12.5 mol/mol hydroxyl groups in cellulose, as shown in Figure 1. It should be noted that the yields of tri-O-benzylcellulose obtained by benzylation in this solvent were almost quantitative, differing from those in the other solvent systems. As shown in Figure 2(b), no other reactions than benzylation occurred to cellulose in this solvent. Gel permeation chromatography revealed that cellulose with the $\overline{DP}_v$ of 1360, 260,
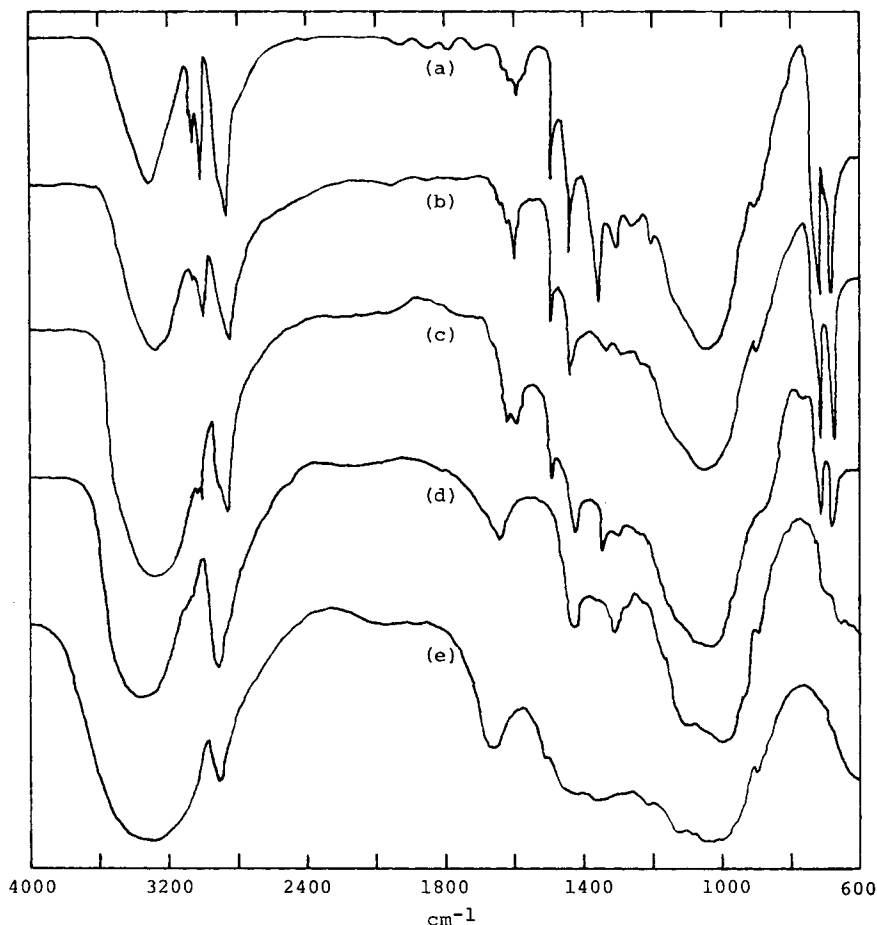
Fig. 3. IR spectra of benzylcellulose prepared in SO_2–DEA–DMSO by the use of the following bases: (a) powdered NaOH; (b) *t*-BuOK; (c) $NaNH_2$; (d) NaH–oil; (e) powdered KOH. Reagents/Cell–OH = 5 (mol/mol).

and 250 were depolymerized to tri-*O*-benzylcellulose with the $\overline{DP}_w$ of 560, 190, and 130, respectively, by the procedure described under Experimental. Benzylation under nitrogen atmosphere could protect cellulose from the depolymerization. Therefore, this depolymerization is due to the contact with air in the presence of alkali.

TABLE IV

Degree of Substitution of Benzylcellulose Prepared in Various Reaction Media[a]

Reaction media	H_2O	DMSO	$DMSO + SO_2 + DEA$[b]	SO_2–DEA–DMSO
DS	1.4	2.5	2.3	3.0

[a] The first three reaction media could not dissolve cellulose whereas the last one dissolved it. The procedure described under Experimental for benzylation in the last medium was applied to the benzylation in the first three media.

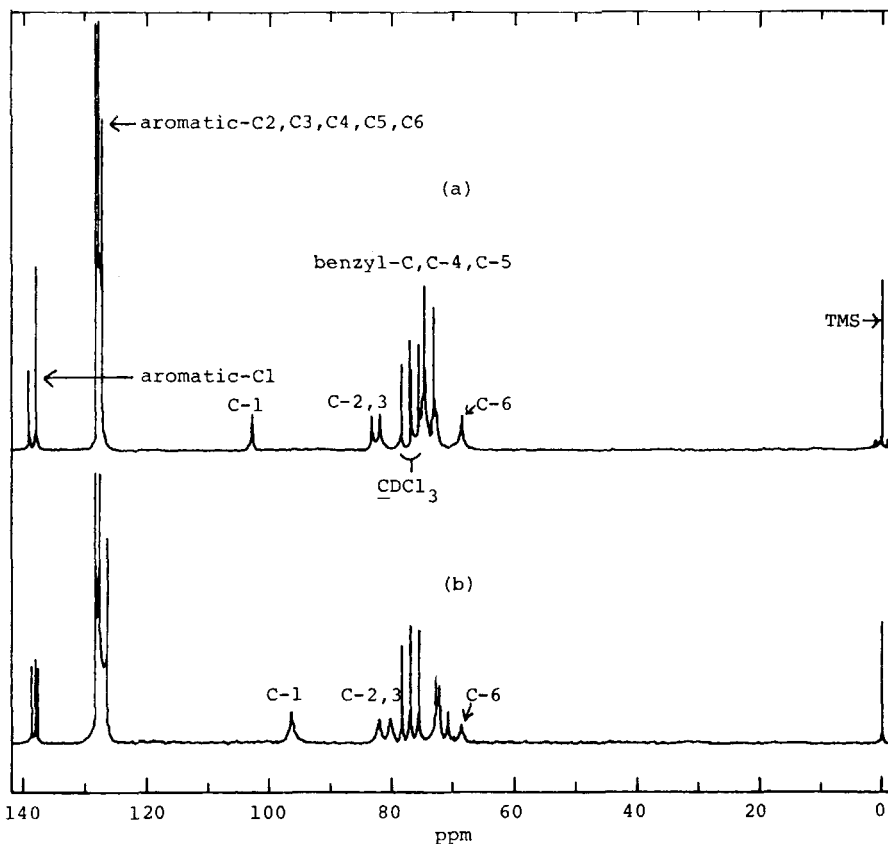[b] Cellulose was dispersed in DMSO, and then powdered NaOH, SO_2–DMSO mixture, and DEA were added in this order.

Fig. 4. ^{13}C-NMR spectra of (a) tri-O-benzylcellulose and (b) tri-O-benzylamylose.

Table I shows the effects of kinds of nonaqueous solvents on benzylation of cellulose. In these three nonaqueous cellulose solvent systems, the SO_2–DEA–DMSO system was the best for preparation of tri-O-benzylcellulose, and the result of Figure 1 indicates that it is possible to control DS of benzylcellulose in this cellulose solvent system by changing the amounts of reagents.

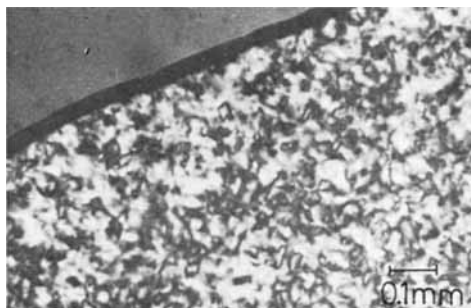**Effects of Kinds of Bases on Benzylation.** As shown in Table II, when

Fig. 5. Photomicrograph of tri-O-benzylcellulose prepared from Avicel taken with crossed polarizers at 200°C.
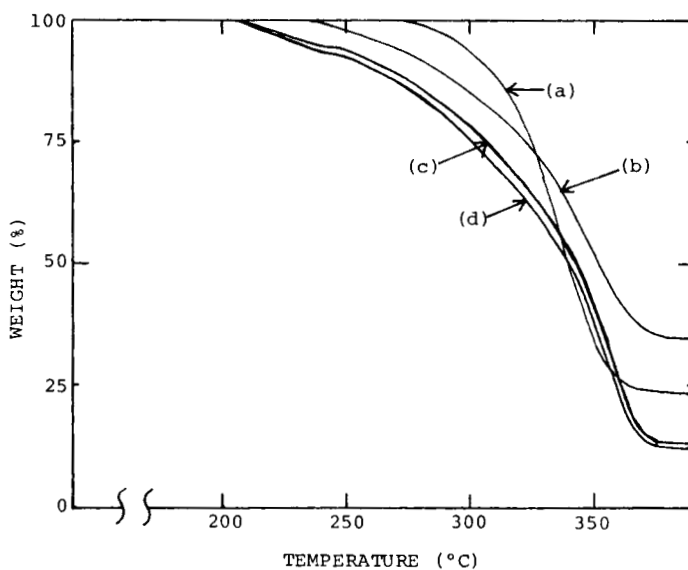
Fig. 6. T_g curves of benzylcellulose: (a) cellulose; (b) benzylcellulose, DS = 1.5; (c) tri-*O*-benzylcellulose, $\overline{DP}_w$ = 564; (d) tri-*O*-benzylcellulose $\overline{DP}_w$ = 130.
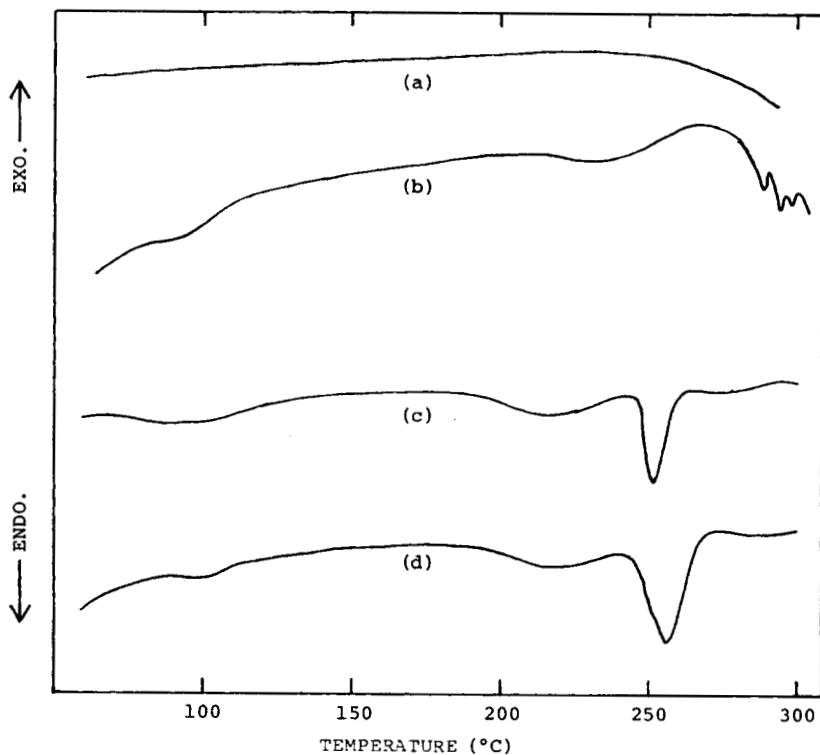

Fig. 7. DSC curves of benzylcellulose: (a) cellulose; (b) benzylcellulose DS = 1.5; (c) tri-*O*-benzylcellulose $\overline{DP}_w$ = 564; (d) tri-*O*-benzylcellulose $\overline{DP}_w$ = 130.
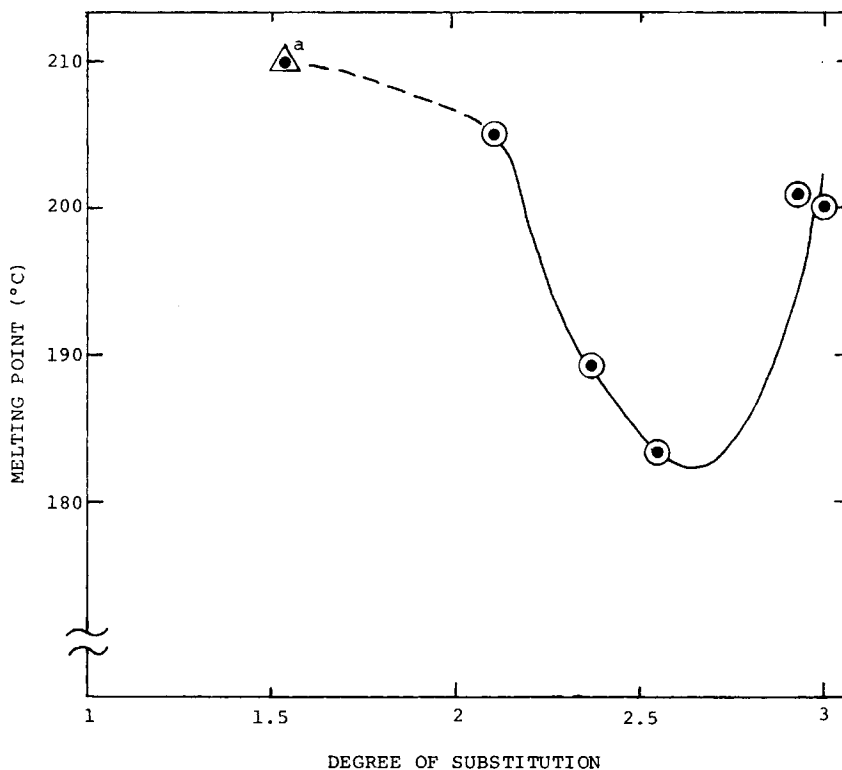
Fig. 8. Relation between melting points and DS of benzylcellulose prepared from Avicel. (a) This sample has a decomposition point instead of a melting point.

LiCl–DMAc was used as a cellulose solvent, powdered sodium hydroxide was found to be the best base for benzylation on the standpoints of DS and yields.

Table III shows the effects of kinds of bases on benzylation in the SO_2–DEA–DMSO system. In the case of this cellulose solvent, powdered sodium hydroxide was also found to be the most effective base in the six bases tested. Variation in DS of benzylcellulose prepared by the use of the various kinds of bases could also be detected in IR spectra as shown in Figure 3. Namely, the absorption of hydroxyl groups around 3400 cm^{-1} decreased with the increase of DS. Figure 3 shows also that any other reactions than benzylation didn't occur on cellulose.

Effects of Decrystallization of Cellulose on Benzylation. To clarify the effects of reaction medium, Avicel was benzylated in various media under the same condition as used in the preparation of tri-O-benzylcellulose described under Experimental. The first three media in Table IV could not dissolve cellulose, whereas the fourth medium dissolved it. Although the DMSO + SO_2 + DEA system has the same composition as the SO_2–DEA–DMSO system, the former can not dissolve cellulose, differing from the latter (see the footnote to Table IV). The DS of the product prepared in the aqueous medium was much lower than those prepared by the use of the last three nonaqueous media. Clearly the presence of water disturbs the formation of benzyl ethers. The DS of the
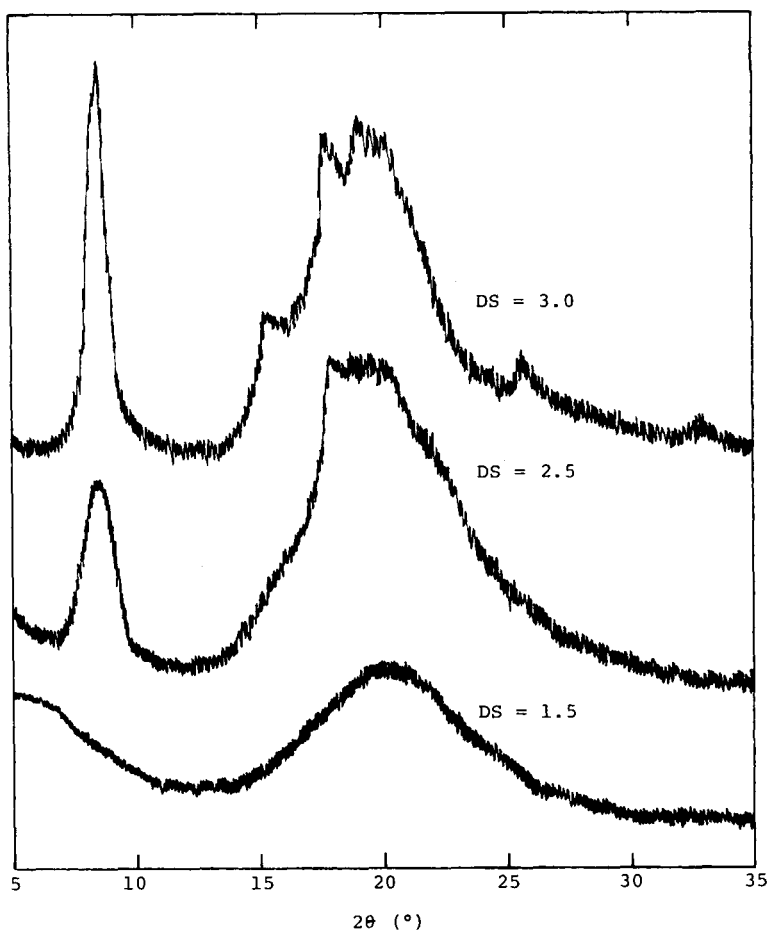
Fig. 9. Equational X-ray diffractometries of benzylcellulose.

product prepared in DMSO + SO_2 + DEA is lower than that in SO_2–DEA–DMSO. This result indicates that the SO_2 + DEA complex does not act as a phase transfer catalyst. Therefore, the difference among the DS of the products prepared in the last three kinds of nonaqueous media indicates that the dissolution of cellulose or the destruction of cellulose crystallite is prerequisite for synthesis of tri-*O*-benzylcellulose. In other words, some intermolecular restrictions may remain even in swelled alkalicellulose and decrease the efficiency of benzylation.

Chemical and Physical Properties of Tri-*O*-Benzylcellulose

Tri-*O*-benzylcellulose obtained by the above-described method was white powder and soluble in chloroform, dichloromethane, benzene, dioxane, tetrahydrofuran, pyridine, dimethylformamide, and so on.

Tri-*O*-benzylcellulose together with tri-*O*-benzylamylose were characterized by ^{13}C-NMR (Fig. 4). Three peaks at 68.0, 82.0, and 83.2 ppm in the spectrum

of tri-O-benzylcellulose can be ascribed to the benzylated C-6, C-2 (or C-3), and C-3 (or C-2) of glucose residues, respectively. The peaks in the region of 70–80 ppm are due to benzyl carbon, C-4, C-5, and chloroform carbon. The chemical shift due to C-1 in tri-O-benzylcellulose appeared at 102.6 ppm, whereas in the case of tri-O-benzylamylose it appeared at 96.2 ppm. Two peaks at 139.4 and 138.4 ppm are due to aromatic Cl carbons. The peaks in the region of 127–129 ppm were due to aromatic C2, C3, C4, C5, and C6 carbons. The peaks of tri-O-benzylamylose corresponds roughly to those of tri-O-benzylcellulose except that of C-1 carbon.

Benzylcellulose is well known to have unique electrical and thermal properties. It has been reported that benzylcellulose with a DS of 2.0 has a melting or softening point between 100–130°C, and softening points depend on DS of benzylcellulose.[10] In our experiments, tri-O-benzylcellulose with the $\overline{DP}_w$ of 564 and 185, and benzylcellulose with the DS of 1.5 prepared from linter showed neither softening nor melting points. However, tri-O-benzylcellulose with the $\overline{DP}_w$ of 130 ($\overline{DP}_n$ = 30) prepared from Avicel showed the melting point, and the characteristic of thermotropic liquid crystal was observed on this sample during the course of cooling after melting (Fig. 5). This phenomenon will be discussed in another paper. T_g and DSC curves of benzylcellulose with the different $\overline{DP}_w$ and DS are shown together with those of cellulose in Figures 6 and 7, respectively. As shown in Figure 6, the thermal decomposition points depend on the DS of the samples. The clear exo- or endothermic peaks were not detected below the thermal decomposition points in the DSC curves (Fig. 7). These results indicate that the melting points of benzylcellulose are closely related to their degradation points. Small endothermic peaks of benzylcellulose are detected around 100°C in Figure 7, but they were not found to be due to glass transition points by tortional braid analyses. It is not clarified why these peaks occurred.

The relation between melting points and DS of benzylcellulose prepared from Avicel was shown in Figure 8. The decrease in melting points accompanied by the increase in DS seemed reasonable, because the introduction of benzyl groups can decrease the numbers of hydrogen bonds. The increase in melting point caused by complete substitution may be explained by the increase in the new crystallinity owing to the increase in its regularity. The increases in the crystallinity caused by complete substitution were proved by X-ray analyses (Fig. 9).

Tri-O-benzylcellulose could not be hydrolyzed completely by HCl–MeOH in chloroform, whereas tri-O-benzylamylose was depolymerized completely under the same condition to produce methyl 2,3,6-tri-O-benzylglucoside.[6] This result indicates that β-glucosidic bonds in tri-O-benzylcellulose are more stable to acid hydrolysis than α-glucosidic bonds.

CONCLUSION

Tri-O-benzylcellulose could be prepared in high yields by the use of powdered sodium hydroxide, benzyl chloride, and SO_2–DEA–DMSO as a cellulose solvent system. Tri-O-benzylcellulose has no softening points, but has melting points when its $\overline{DP}_w$ is less than 140. Tri-O-benzylcellulose with the $\overline{DP}_w$ of 130 shows the characteristic of thermotropic liquid crystal.

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