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Preparation of 6-deoxy-6-fluorocellulose

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Abstract

6-Deoxy-6-fluorocellulose was prepared from cellulose 2,3-diacetate (**1**) or cellulose 2,3-dibenzoate (**2**) in various solvents, and was characterized by ^{19}F and ^{13}C NMR measurements. The best product, having ds of 0.95 at C-6 and 0.04 at C-3, was prepared from cellulose 2,3-dibenzoate in nitrobenzene. Other combinations of starting material and solvent gave a lower (~0.8) ds of fluorine at C-6 and higher (~0.12) at C-2 or C-3. Substitution at C-2 was observed when the combination of **1** and 1,4-dioxane, or **2** and chloroform was used. The products substituted at C-2 by fluorine were relatively resistant to acid hydrolysis.

1. Introduction

Deoxyfluorocelluloses, which are expected to have useful properties as water and oil repellents, to allow permeability of gases, and have novel electrical properties, have been the subject of several synthetic attempts [1–7]. We recently reported an efficient method to introduce fluoro functions into cellulose, replacing the hydroxyl groups without cleavage of the glycosidic linkage [7] by using diethylaminosulfur trifluoride (DAST) as a fluorinating reagent with cellulose acetates having degree of substitution (ds) of 1.7 and 2.2 as starting materials. The maximum ds of fluorine was 0.60, mainly at C-6 and partly at C-3. When all unsubstituted hydroxyl groups at C-6 had been displaced by fluoro substituents, the rate of fluorination became extremely low. Acetyl groups were retained after the fluorination. Complete fluorination at C-6 thus seems difficult to accomplish with these starting materials, and the substitution mode of the resultant cellulose derivative is very heterogeneous.

Preparation of selectively substituted cellulose derivatives, such as those substituted at C-6 or those at C-2 and C-3, is important in clarifying the relationships between their chemical structures and their physical properties. Kondo [8,9]

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discussed intra- and inter-molecular hydrogen bonds involved in cellulose derivatives by the comparison of FT-IR and solid-state CP/MAS ^{13}C NMR spectra of 6-*O*-alkylcelluloses with those of 2,3-di-*O*-alkylcelluloses. 6-Deoxy-6-fluorocellulose would also afford information about the hydrogen bonds involved in cellulose, because a fluoro substituent at C-6 might form an intra- or inter-molecular hydrogen bond with a hydroxyl group, mimicking that of O-6–HO-C of cellulose, and restricting the direction of hydrogen bonds to one mode.

The objective of this paper, was the synthesis of 6-deoxy-6-fluorocellulose completely fluorinated at C-6 and not having fluorine at C-2 and C-3. Analysis of its crystalline structure will be presented separately.

2. Results and discussion

6-Deoxy-6-fluorocellulose was prepared as shown in Fig. 1. *O*-Tritylcellulose was obtained from microcrystalline cellulose by homogeneous reaction in lithium chloride–*N*,*N*-dimethylacetamide, a new method developed in this research that decreases the number of steps for the preparation. The ds of the *O*-tritylcellulose was 1.04 by ^{1}H NMR measurement. This product was esterified (acetylated or benzoylated) and subsequently detritylated. The resulting cellulose 2,3-diacetate (**1**, ds by acetyl 1.84) or dibenzoate (**2**, ds by benzoyl 1.95) was used as the precursor for the 6-deoxy-6-fluorocellulose ester (**3**), because protection of C-2 and C-3 hydroxyl groups was necessary for the selective fluorination, and because excellent solubility of the precursor in the reaction medium was also important for successful displacement by fluoride at C-6. Four different combinations of precursors and reaction media were examined in this study, namely (A) **2** and nitrobenzene, (B) **1** and chloroform, (C) **1** and diethylene glycol dimethyl ether (diglyme), and (D) **1** and 1,4-dioxane. Among these combinations, however, only nitroben-

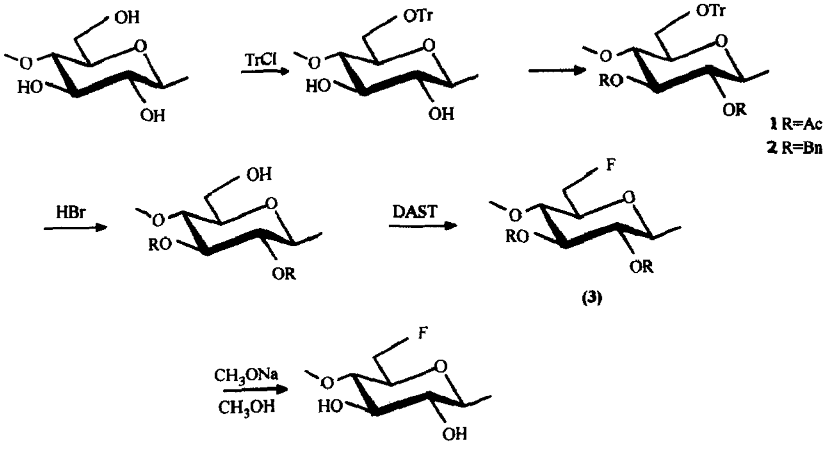

Fig. 1. Scheme for the preparation of 6-deoxy-6-fluorocellulose.

Table 1
The ds and the distributions of fluoro substituents in deoxyfluorocelluloses

Sample	Starting material	Reaction medium	ds			
			C-2	C-3	C-6	Total[a]
A	**2**[b]	nitrobenzene		0.04	0.95	0.99
B	**1**[c]	chloroform	0.14		0.69	0.83
C	**1**[c]	diglyme		0.13	0.70	0.83
D	**1**[c]	1,4-dioxane	0.12	0.13	0.77	1.02

[a] 3 Fluorine contents determined by the alizarin complexation method. [b] **1** Cellulose 2,3-dibenzoate. [c] **2** Cellulose 2,3-diacetate.

zene (A) showed excellent solubility for the precursor. After the fluorination saponification was performed and fluorine contents of the products were determined by the alizarin complexation method (Table 1) [10].

The resulting deoxyfluorocelluloses were then characterized by NMR. The ^{13}C NMR spectra of their hydrolyzates were first recorded (Fig. 2), using hydrolysis as described by Katsura et al. [11]. In the cases of (B) and (D), the hydrolysis was

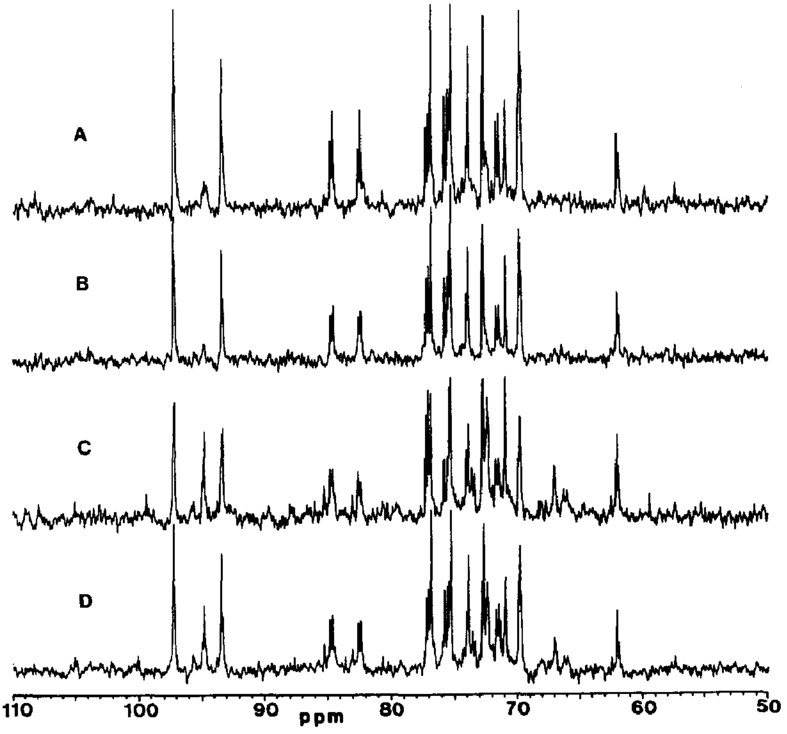

Fig. 2. ^{13}C NMR spectra of hydrolyzates of deoxyfluorocelluloses. The precursors and the media for fluorination were as follows; (A) cellulose 2,3-dibenzoate and nitrobenzene, (B) cellulose 2,3-diacetate and chloroform, (C) cellulose 2,3-diacetate and diglyme, (D) cellulose 2,3-diacetate and 1,4-dioxane.

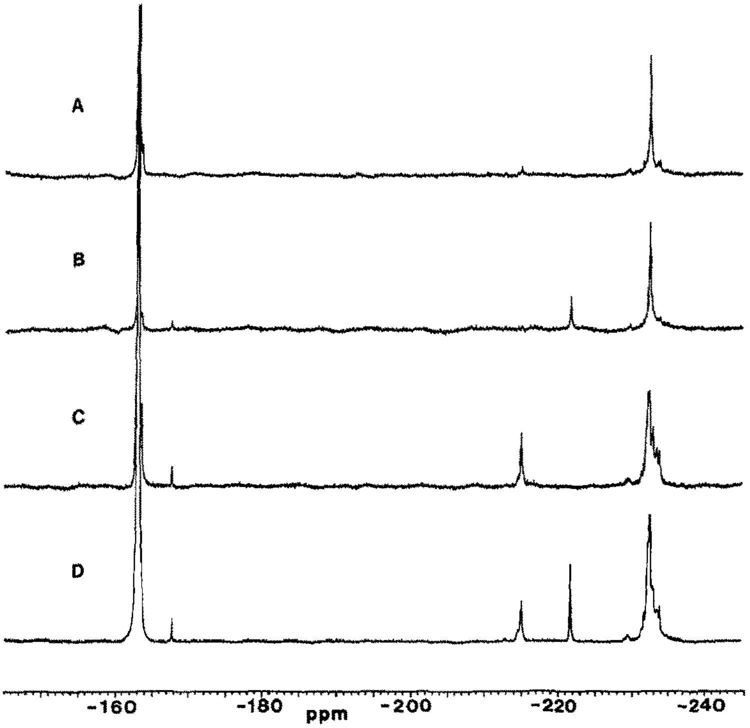

Fig. 3. ^{19}F NMR spectra of deoxyfluorocelluloses. The precursors and the media for fluorination were as follows; (A) cellulose 2,3-dibenzoate and nitrobenzene, (B) cellulose 2,3-diacetate and chloroform, (C) cellulose 2,3-diacetate and diglyme, (D) cellulose 2,3-diacetate and 1,4-dioxane.

incomplete, because some precipitate was observed for those two combinations. It may be noted that the upper two spectra resemble each other closely, and the lower two likewise. For all of the hydrolyzates, two doublets at 82.9 ppm (d, $J_{C\text{-}6,F}$, 168.2 Hz) and 82.7 ppm (d, $J_{C\text{-}6,F}$, 167.3 Hz) attributable to the C-6 carbons of 6-deoxy-6-fluoro-α-and-β-D-glucopyranose [12,13], respectively, may be recognized. With regard to (C) and (D), signals around 67.0 ppm and those around 94.8 ppm may be attributed to the C-2 and C-3 carbons of 3-deoxy-3-fluoro-α-and-β-D-allopyranose [13,14], respectively. No evidence for substitution by fluorine at C-2 is observed in any of these ^{13}C NMR spectra of the hydrolyzates.

^{19}F NMR spectra were next recorded for the polymeric deoxyfluorocelluloses (Fig. 3). The four samples seem to show different distributions of fluoro substituent. A signal at 232.4 ppm attributable to the fluoro substituent at C-6 is recognized for all of the samples, and signals at 215.0 and 221.7 ppm are attributable to fluoro substituents at C-3 and C-2, respectively, suggesting the occurrence of Walden inversion at the respective sites [13,15]. It may be observed that fluoro substituents were incorporated at C-2 for (B) and (D), which is different from the results from the ^{13}C NMR spectra of the hydrolyzates. The difference is presumably attributable to the incomplete hydrolysis of deoxyfluoro-

Table 2
Relative ds at each carbon position to that at C-6

Sample	C-2	C-3	C-6
A		4.21	100
	(	9.37	100) [a]
B	20.29		100
	(1.81	3.65	100) [a]
C		18.57	100
	(	18.46	100) [a]
D	15.58	16.88	100
	(4.01	15.85	100) [a]

[a] Data in parentheses were calculated from the results of the hydrolyzates.

celluloses having fluoro substituents at C-2 (to be discussed later). Incorporation of halo substituents at C-2 has not yet been reported for deoxyhalocelluloses.

From the fluorine contents just mentioned and relative peak areas in the ^{19}F NMR spectra, the distributions of fluoro substituents were calculated (Table 1). With regard to sample A, almost all hydroxyl groups at C-6 (0.95/1.00) had been displaced with fluorine atoms, and there was only slight incorporation of fluorine at C-3. This is the first demonstration of a deoxyfluorocellulose having ds ~ 1.0 that is selectively and almost completely substituted at C-6. Other samples had a lower ds at C-6, and higher ds at C-2 and C-3 than those of sample A. The lower ds at C-6 may be explained by the low solubility of **1** to the medium, and the higher ds at C-2 and C-3 may be attributable to the lower stability of the acetyl groups in comparison with the benzoyl groups, as well as by the larger proportion of unsubstituted hydroxyl groups in **1** (1.16 per glucose residue) than in **2** (1.05).

The relative ds by fluorine at each carbon position, in relation to that at C-6, was calculated from the distributions already mentioned (Table 2). The numbers in parentheses were also the relative ds by fluorine as determined by ^{19}F NMR for the hydrolyzates. There is only a small difference between the values at C-3 for the polymer and for the hydrolyzates. In contrast, significant differences are found between the values at C-2 (B and D). These results indicate that the distribution of fluoro substituents in the cellulose derivatives may be quite heterogeneous and a cellulose fraction substituted at C-2 is preferentially retained in the residual fraction after acid hydrolysis. These phenomena may be explained by the difficulty of producing a resonance-stabilized cation on acid hydrolysis because of the incorporation of a strongly electron-withdrawing substituent [16]. Therefore, the relative values by ^{19}F NMR measurements for the polymer state are more trustworthy than those for the hydrolyzates.

3. Experimental

Materials.—Microcrystalline cellulose (Whatman cellulose, CF-11) was used as the starting material. Reagent-grade Ac_2O (Wako Pure Chemical Industries, Ltd.), BzCl (Wako Pure Chemical Industries, Ltd.), and diethylaminosulfur trifluoride (DAST: Aldrich Chemical Company, Inc.) were used without further purification. Solvents (Wako Pure Chemical Industries, Ltd.) were also used without further purification.

Hydrolysis [11].—The sample (1.0 g) was immersed in 72% aq H_2SO_4 (1.0 mL) for 5 h. Water was added to the solution to dilute the solute down to 5%, and the mixture was kept for 1 h at 120°, and then neutralized ($BaCO_3$). The filtrate was concentrated, dissolved in Me_2SO-d_6 (1.0 mL), and subjected to NMR measurements.

NMR measurements.—A Bruker AC300 spectrometer operating at 300.1 MHz for ^{1}H, 75.5 MHz for ^{13}C, and 282.4 MHz for ^{19}F, respectively was used. ^{13}C NMR measurements were performed in the power gated-decoupling sequence, and ^{19}F NMR measurements in the decoupled mode. Samples were dissolved in Me_2SO-d_6 for measurement. Tetramethylsilane was used as the reference for measurements of ^{1}H and ^{13}C, and hexafluorobenzene for ^{19}F. The concentrations of polymer samples were ~ 2% (w/w).

Preparation of LiCl–DMAc solution of cellulose.—The solution was prepared according to the method by Turbak et al. [17]. Cellulose (1.0 g) and *N,N*-dimethylacetamide (28.0 mL) were heated for 30 min at 165°C with stirring. After cooling to 100°C, anhyd LiCl (2.6 g) was added to the slurry, which was stirred for 3 days at room temperature. When a precipitate formed in the solution it was centrifuged off and the supernatant was used for the following steps.

Tritylation.—Into a cellulose–LiCl–DMAc solution (28.0 mL), pyridine (4.5 mL) and Ph_3CCl (15.0 g) were added, and the mixture was stirred for 5 h at 85°C. After cooling to room temperature, the solution was poured into MeOH (300 mL). The product was washed repeatedly with MeOH (300 mL), and then dried in a vacuum oven for 1 day at 60°C; yield 86%, ds by trityl groups 1.04 (^{1}H NMR).

Esterification (acetylation or benzoylation).—Esterification was accomplished by the method of Hall et al. [18] with slight modification. 6-*O*-Tritylcellulose (1.0 g) was dissolved in pyridine (30.0 mL) and anhyd Ac_2O (2.5 mL) or BzCl (3.0 mL) was added to the solution. The mixture was kept for 20 h at 60°C, and then poured into MeOH (300 mL). The resultant precipitate was washed several times with hot MeOH (300 mL), and then dried in a vacuum oven for 1 day at 60°C; yield, 82% for the acetylated product and 88% for the benzoylated product.

Detritylation.—The procedure of Horton et al. [19] was used with some modification. 6-*O*-Tritylcellulose 2,3-diacetate (1.0 g) or 6-*O*-tritylcellulose 2,3-dibenzoate (1.1 g) was dissolved in CH_2Cl_2 (30.0 mL), and AcOH (5.0 mL) was added to the solution. Then 25% (w/w) HBr in AcOH (1.0 mL) was added, and the mixture was stirred. Two min after the addition of the HBr solution, the mixture was poured into MeOH (300 mL) and the mixture stirred for another 2 min, and then NaOAc was added to the solution for neutralization. The precipitate was filtered off, washed with MeOH (300 mL) several times, and dried in vacuo for 24 h at 60°C. The yields of the products were 84% for cellulose 2,3-diacetate and 91% for 2,3-dibenzoate, respectively. The ds of acetyl group was 1.84 and that of benzoyl group was 1.95 (^{1}H NMR).

Fluorination.—Fluorination was accomplished following the method previously reported [7]. Cellulose 2,3-diacetate (1.0 g) or cellulose 2,3-dibenzoate (1.5 g) were dissolved in the solvent (30 mL) mentioned in the Results and Discussion section. DAST (2.5 mL) was added to the solution, which was stirred for 24 h at room temperature. Methanol (300 mL) was then added to the solution to quench the reaction. The precipitate was washed repeatedly with MeOH (300 mL) and dried in a vacuum oven at 60°C for 24 h; yields, 90–96%. Anal. Calcd for $C_{20}H_{17}FO_6$: C, 64.51; H, 4.60; F, 5.10. Found: C, 64.20; H, 4.61; F, 5.06.

Saponification.—The sample (1.0 g) was dissolved in CH_2Cl_2 (50.0 mL) and 15% (w/w) CH_3ONa–CH_3OH solution (2.0 mL) was added to the mixture, which was stirred for 1 h. The mixture was then poured into MeOH (300 mL) and the precipitate was washed several times with MeOH (300 mL) and the product was dried in a vacuum oven for 24 h at 60°C. The yields of the products were 92–95%. The fluorine content was determined according to the alizarin complexation method (Table 1) [10]. Anal. Calcd for $C_6H_9FO_4$: C, 43.91; H, 5.53; F, 11.57. Found: C, 43.05; H, 5.50; F, 11.50.

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