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Synthesis and characterization of highly substituted deoxyfluorocellulose acetate

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ABSTRACT

Deoxyfluorocellulose acetates were prepared from cellulose acetate (CA, degree of substitution by acetyl groups: 2.2 and 1.7) by using diethylaminosulfur trifluoride (DAST) in 1,4-dioxane or diglyme. The maximum degree of substitution of fluorine of the products was ~ 0.60, and depolymerization was not significant during fluorination. The replacement of hydroxyl groups by fluorine atoms occurred exclusively at C-6, as confirmed by carbon-13 NMR spectroscopy. In the presence of pyridine, an *N*-pyridinium derivative of CA was obtained instead of a deoxyfluoro derivative of cellulose.

INTRODUCTION

Many investigations have been carried out concerning the introduction of fluorine atoms into cellulose and its derivatives to improve such properties as water and oil repellencies, permeability of gases, and dielectric loss. However, only a few of them[1–8] have dealt with the preparation of deoxyfluorocellulose.

Replacement of mesyl and/or tosyl groups by fluorine atoms has been developed as one of the methods to produce deoxyfluorocellulose[1–3]. Pacsu et al.[1] and Titcombe et al.[3] have treated *O*-mesylcellulose with an aqueous solution of sodium fluoride and with tetrabutylammonium fluoride in acetonitrile, respectively. However, the fluorine contents of the products were no more than 1%. Sletkina and Rogovin[2] prepared deoxyfluorocellulose by the reaction of *O*-tosylcellulose with potassium fluoride. The maximum ds of fluorine of the products was 0.28.

Gorvunov et al.[4] adopted more severe conditions for deoxyfluorination. They used sulfur tetrafluoride as a fluorinating reagent at elevated temperature ($< 140°$), and obtained products that had high fluorine contents ($< 15\%$), but they were severely depolymerized and some of them became powders.

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Diethylaminosulfur trifluoride (DAST) has been often used in the fluorination of mono- and oligo-saccharides[5–8]. In contrast to other reagents such as SF_4, $SeF_4 \cdot$ pyridine $\cdot$ HF, HF $\cdot$ pyridine and $(C_2H_5)_2NCF_2CFHCl$, DAST is known to replace hydroxyl groups with fluorine without causing extensive rearrangement or dehydration[7].

Middleton[8] reported that a fluorinated cellulose thimble was obtained from a Soxhlet thimble by treating with DAST in dichloromethane for 24 h at 25°. However, the ds calculated from his data was less than 0.06.

The present paper describes the homogeneous deoxyfluorination of partially acetylated cellulose under various conditions. This affords highly substituted deoxyfluorocellulose acetate without severe depolymerization. The position of substitution and the mechanism of the substitution reaction are also discussed.

EXPERIMENTAL

Materials.—Commercial cellulose acetates (ds; 2.2 and 1.7: Daicel Chemical Industries, Ltd.) were employed for the preparation of deoxyfluorocellulose. The cellulose acetates were dried in a vacuum oven for 3 h at 60°. Reagent-grade diethylaminosulfur trifluoride (DAST: Aldrich Chemical Company, Inc.), diethylene glycol dimethyl ether (diglyme: Wako Pure Chemical Industries, Ltd), and 1,4-dioxane (Wako Pure Chemical Industries, Ltd.) were used without further purification.

Fluorination of cellulose acetate.—The cellulose acetates (1 g) having ds of 2.2 and 1.7 were dissolved in 50 mL of diglyme and 1,4-dioxane, respectively. The solution was added dropwise into DAST (2.5 mL) which was previously cooled to $-30°$ under N_2. In some cases, pyridine (1.6 mL) was used together with DAST. After addition of the solution, the mixture was kept for a prescribed period (2, 12, 24 and 42 h) at room temperature. Then it was cooled again to $-30°$ and 10 mL of MeOH was slowly dropped in it to arrest the reaction. The mixture was kept for 10 min at $-30°$, and then dialyzed against running tap-water for 24 h. The product recovered was dissolved in Me_2SO, dialyzed again for 24 h, and freeze-dried.

Determination of fluorine.—Determination of fluorine was performed according to the alizarin complexation method of Hashitani et al.[9].

Determination of acetyl group content.—Acetyl groups were determined as follows: The sample (20 mg) was soaked in 72% D_2SO_4 (120 μL) for 45 min in an ultrasonic bath and D_2O (2.5 mL) was added so that the percentage of D_2SO_4 was 5%. After being kept for 3 h at 90°, EtOH (8.0 μL) was added as an internal standard.

^{1}H-NMR spectra were recorded on a Bruker AC300 NMR spectrometer (300 MHz). The contents of acetyl groups were calculated based on the ratio of the peak area of the methyl protons of AcOH (2.1 ppm) to that of EtOH (1.1 ppm).

^{13}C-NMR spectroscopy.—Samples (100 mg) were soaked in 72% D_2SO_4 (120 μL) for 45 min in an ultrasonic bath and D_2O (2.5 mL) was added. After being

kept for 3 h at 90°, the hydrolyzates were filtered. ^{13}C-NMR spectra of the samples were recorded on a Bruker AC300 NMR spectrometer (75 MHz) in the power gated-decoupling mode. In addition, ^{13}C-NMR spectra of 7% (w/w) solutions of the polymer samples in Me_2SO-d_6 were also measured using the same decoupling mode at 70° with 16000 scans.

High-performance size-exclusion chromatography.—A 0.05 M lithium chloride–*N*,*N*-dimethylformamide (DMF) solution of the sample [0.5% (w/w)] was injected into a serial two-column system, TSKgel G2500Hxl-G4000Hxl (Tosoh, Tokyo, Japan), on an LC4A liquid chromatograph (Shimadzu, Kyoto, Japan). The signals were detected by an RI detector, Erma Optical Work · ERC-7520 (Tokyo, Japan), and also a UV detector (260 nm). The measuring conditions were as follows solvent: 0.05 M LiCl in DMF; flow rate: 1.0 mL/min; temperature: 20°.

RESULTS AND DISCUSSION

Deoxyfluorination in the absence of pyridine.—Although Middleton[8] fluorinated cellulose with DAST, the ds of deoxyfluoro groups in the products was quite low, because of the heterogeneous nature of his reaction. Therefore, partially acetylated celluloses soluble in diglyme or 1,4-dioxane were used as starting materials in this paper.

Fig. 1 shows the relationship between the fluorine content (w/w) of the product and the time of reaction. The fluorine content increased rapidly in the beginning and finally levelled off. In the uppermost curve, obtained for the samples prepared in 1,4-dioxane from cellulose acetate (CA) having ds of 1.7, the fluorine content reached 5.2% after 24 h.

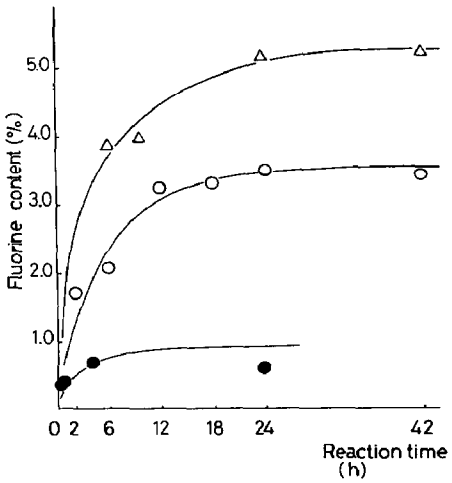

Fig. 1. Fluorine contents of fluorinated CA: (△) prepared from CA (ds 1.7) at room temperature in 1,4-dioxane; (○) prepared from CA (ds 2.2) at room temperature in diglyme; and (●) prepared from CA (ds 2.2) at −30° in diglyme.

TABLE I

Acetyl and fluorine contents of the fluorinated samples and the ds values calculated on the basis of these contents

Sample	Reaction time (h)	Acetyl group (wt%)	Ds [a]	Fluorine (wt%)	Ds [b]
CA (ds 2.2)	–	37.13	2.19	–	–
Diglyme-2 [c]	2	35.81	2.08	1.73	0.20
-12	12	33.99	1.93	3.24	0.41
-24	24	33.28	1.87	3.51	0.45
-42	42	32.78	1.82	3.43	0.44
CA (ds 1.7)	–	32.14	1.76	–	–
Dioxane-6 [d]	6	31.62	1.66	3.89	0.48
-9.5	9.5	29.75	1.59	3.98	0.48
-24	24	26.81	1.36	5.19	0.59
-42	42	25.94	1.32	5.22	0.60

[a] Ds of acetyl group calculated from acetyl and fluorine contents. [b] Ds of fluorine calculated from acetyl and fluorine contents. [c] Samples prepared in diglyme at room temperature from CA having ds of 2.2. [d] Samples prepared in 1,4-dioxane at room temperature from CA having ds of 1.7.

The acetyl contents of the deoxyfluorinated products were also determined by ^{1}H-NMR, and then the ds values of acetyl and deoxyfluoro groups were calculated on the basis of acetyl and fluorine contents (Table I). Although the acetyl content decreased gradually as the reaction period increased, it remained high, even after 42 h.

In order to establish the substitution position, a ^{13}C-NMR spectrum of a hydrolyzate of the product was recorded (Fig. 2B). Two doublets at 82.91 ppm (d, $J_{C\text{-}6,F}$ 168.2 Hz) and at 82.70 ppm (d, $J_{C\text{-}6,F}$ 167.3 Hz) coincide well with the data[10] for C-6 carbon atoms of 6-deoxy-6-fluoro-α-D-glucopyranose (83.65 ppm, d, $J_{C\text{-}6,F}$ 167.2 Hz) and of 6-deoxy-6-fluoro-β-D-glucopyranose (83.47 ppm, d, $J_{C\text{-}6,F}$ 167.6 Hz), respectively.

Card et al.[11] synthesized methyl 3,6-dideoxy-3,6-difluoro-β-D-allopyranoside from methyl β-D-glucopyranoside in good yield (51%), indicating that the ring fluorination at C-3, accompanied by Walden inversion, occurred. Therefore, 3,6-dideoxy-3,6-difluoroallose possibly exists in the hydrolyzate of our fluorinated product. As the signal arising from the C-3 carbon of methyl 3,6-dideoxy-3,6-difluoro-β-D-allopyranoside appears at 93.6 ppm (d, $J_{C\text{-}3,F}$ 177.9 Hz)[11], the two doublets arising from C-3 carbons of the α- and β-anomers of 3,6-dideoxy-3,6-difluoroallose may be expected to appear around 93.6 ppm.

Actually, a signal could be detected at 93.5 ppm (Fig. 2B). However, it cannot be attributable to the C-3 carbon atom substituted by a fluorine atom, although it remains to be assigned, because the signal is not doublet but a singlet. The possibility that the other line of a doublet overlaps completely with the signal at 92.1 ppm derived from the C-1 carbon of α-D-glucopyranose, can be excluded, because the $J_{C\text{-}3,F}$ value of the assumed doublet is too small for 3,6-dideoxy-3,6-difluoroallose.

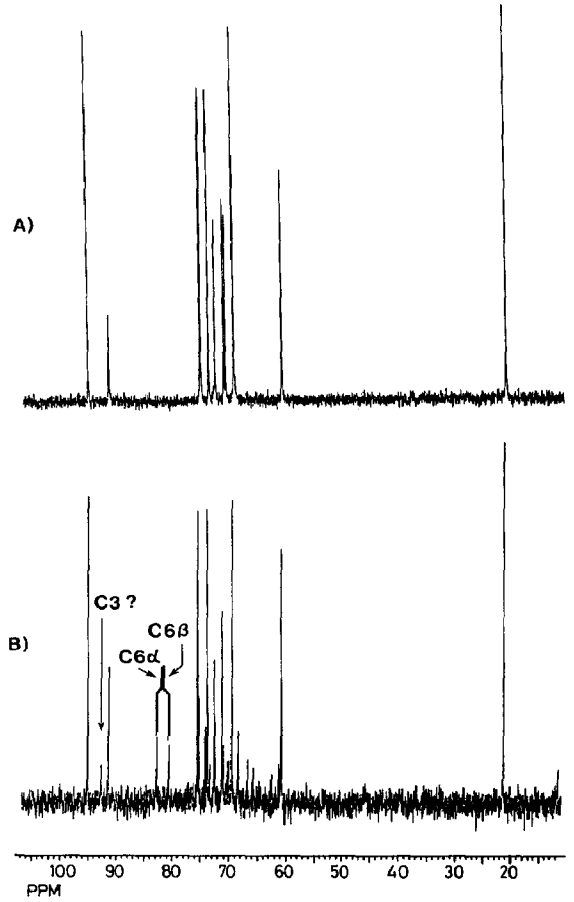

Fig. 2. ^{13}C-NMR spectra of hydrolyzates of (A) CA (ds 1.7), and (B) its deoxyfluoro derivative prepared at room temperature for 24 h. The signal of the methyl carbon (20.6 ppm) provided the standard.

From these results, it may be concluded that the fluorination occurred almost exclusively at C-6 under the conditions used here.

The ^{13}C-NMR spectra of nonhydrolyzed samples are shown in Fig. 3A. Miyamoto et al.[12] reported that the peaks at 60.3 and 102.5 ppm in CA samples may be assigned to the C-6 carbon bearing an unsubstituted 6-hydroxyl group, and the C-1 carbon adjacent to the C-2 carbon bearing an unsubstituted hydroxyl group, respectively. The C-6 peaks at 62.8 ppm may be assigned to the C-6 carbon bearing an acetyl group, and the peak designated as C-1′ (99.1 ppm) may be assigned to the C-1 carbon adjacent to the C-2 carbon bearing an acetyl group.

No C-6 carbons having an unsubstituted hydroxyl group were detected in the spectrum of the nonhydrolyzed deoxyfluorinated CA from CA having ds 1.7 by acetyl groups (Fig. 3B). Instead, several peaks around 83 ppm were observed. This fact also indicates that these peaks are attributable to C-6 carbon atoms bearing a fluorine atom.

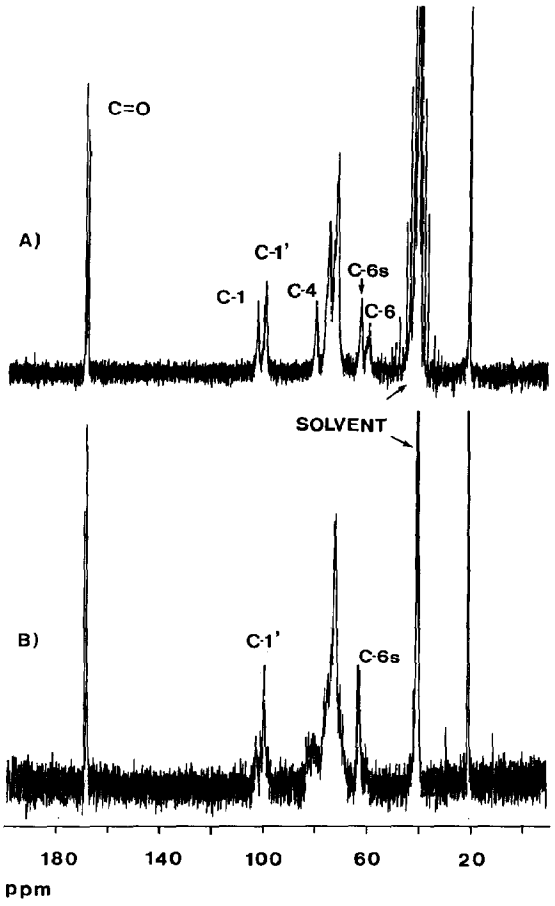

Fig. 3. ^{13}C-NMR spectra of (A) CA (ds 1.7) and (B) its deoxyfluoro derivative prepared at room temperature for 24 h. The signal of the methyl carbon (20.6 ppm) provided the standard.

The facts described in the preceding paragraph indicate that the levelling off of the curves in Fig. 1 is due to the almost complete replacement of free hydroxyl groups at C-6 by fluorine atoms. With all of the C-6 positions either acetylated or fluorinated, the ds by the deoxyfluoro group was calculated to be 0.59 (Table I).

The ds by acetyl group at C-6 position is thus 0.41. This value, together with the fact that the ds of acetyl group after deoxyfluorination for 24 h of CA having ds 1.7 is 1.36 suggests, that almost half (0.95/2.0) of the hydroxyl groups at C-2 and C-3 positions are not substituted.

Fig. 4 shows a HPSEC of CA and the fluorinated products. On the basis of these chromatograms, we can conclude that the number-average degree of polymerization did not decrease severely.

Fluorination in the presence of pyridine.—In the fluorination of monosaccharides, some authors[13,14] have reported that the yields of fluorinated products is increased by the addition of pyridine to the reaction medium. Pyridine was thus

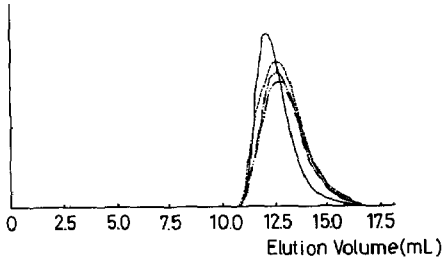

Fig. 4. High-performance size-exclusion chromatograms of CA (ds 2.2) and its derivative prepared by fluorination: (———) CA; (- - - - - -) in diglyme at room temperature for 6 h; (- - - - -) for 12 h; and (- · - · - · -) for 24 h.

tested as a catalyst in our system, but reproducible results with respect to fluorine contents could not be obtained.

The ^{13}C-NMR spectrum of a hydrolyzate of a product prepared in the presence of pyridine is shown in Fig. 5B. The two doublets around 83 ppm, which indicate deoxyfluorination at the C-6 position, are not observed here. Instead, several

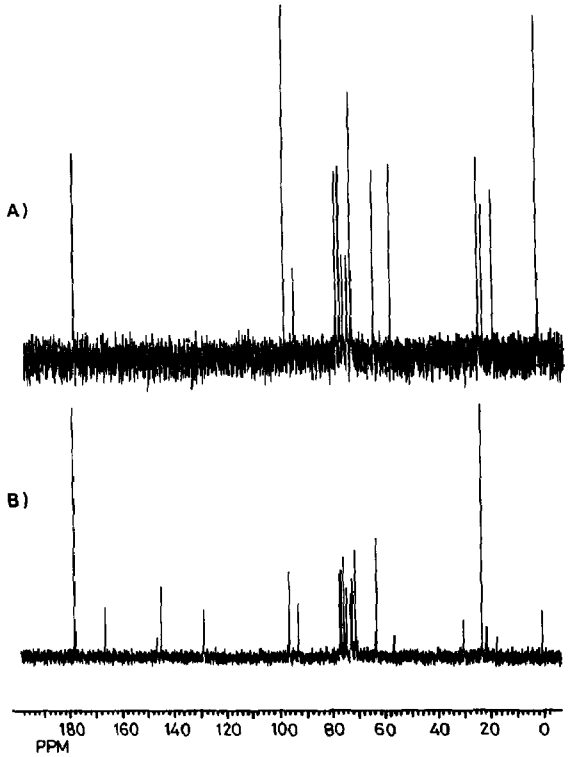

Fig. 5. ^{13}C-NMR spectra of hydrolyzates of (A) CA (ds 2.2), and (B) its derivative prepared by fluorination at room temperature in the presence of pyridine. Sodium 4,4-dimethyl-4-silapentane-sulfonate was added as the standard.

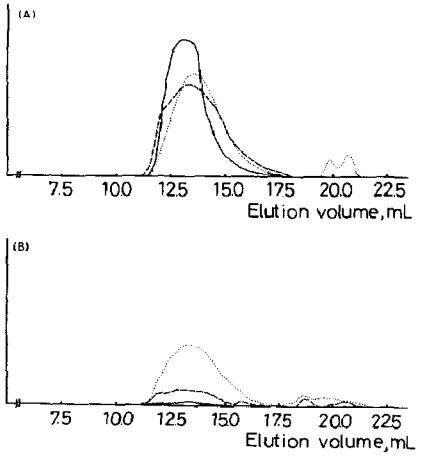

Fig. 6. High-performance size-exclusion chromatograms of CA and its derivatives, detected by (A) RI and (B) by UV (260 nm): (———) CA (ds 2.2); (— — —) product prepared by fluorination at room temperature for 24 h without pyridine; and (· · · · · ·) prepared in the presence of pyridine.

signals at lower field than 120 ppm were detected. These signals do not coincide with those of pyridine, but they may arise from a pyridine derivative.

The HPSEC curves of a DMF/LiCl solution of CA and those of the fluorinated products in the presence of pyridine are shown in Fig. 6. The upper chromatogram (Fig. 6A) was detected by refractive index, and the lower (Fig. 6B) by UV (260 nm). The dotted curve in Fig. 6B shows a larger peak than the others around 13 mL,

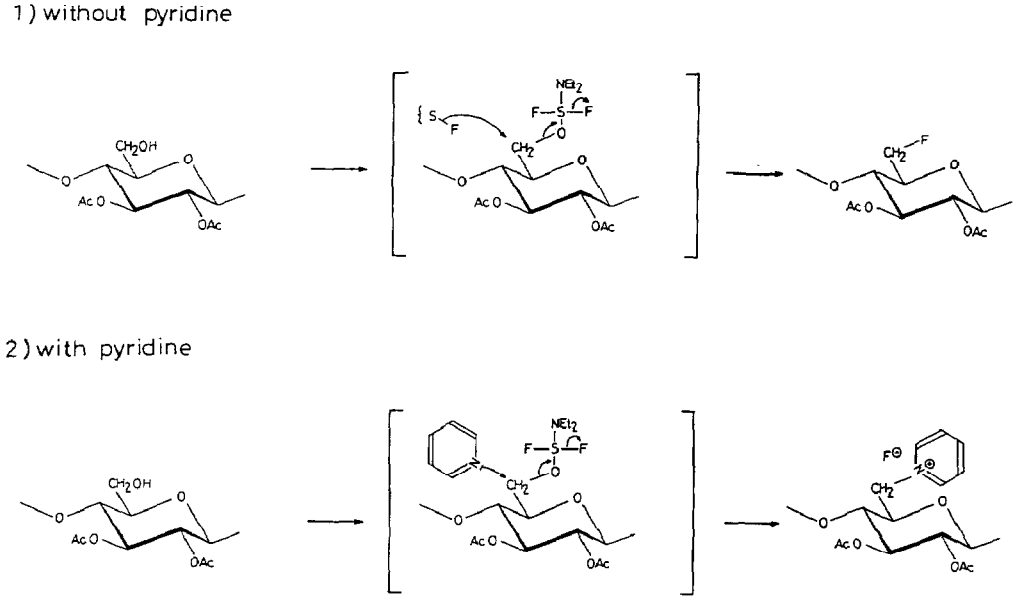

Fig. 7. Proposed reaction mechanisms during fluorination (1) without, and (2) with pyridine.

suggesting that a compound having high UV absorption at 260 nm, probably a pyridine derivative, was bound up with CA. This corresponds with the result revealed by Fig. 5.

Based on the above results, we propose the reaction mechanism shown in Fig. 7. Pyridine was introduced into cellulose instead of a fluorine atom when pyridine was present[15].

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