Facile Method for the Preparation of Tri-O-(Alkyl)Cellulose

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SYNOPSIS

A simple way to prepare tri-O-(alkyl)cellulose from cellulose acetate (CA) in dimethyl-sulfoxide (DMSO) using the appropriate alkyl iodide and NaOH has been developed. In this procedure, the addition of a small amount of water to the DMSO solution improved the efficiency of etherification. The substitution pattern of (methyl)cellulose (MC) was investigated to determine the effect of added water on the relative reactivities of the glucose ring substituents. This etherification method can be applied to alkylate other polymers with acetate-functional groups that are soluble in DMSO.

INTRODUCTION

(Alkyl)cellulose ethers are an important class of industrial polymers. They are prepared commercially by heterogeneous reaction of aqueous alkalicellulose with alkyl halides or epoxides. Under these reaction conditions, it is difficult to prepare (alkyl)cellulose ethers with high degrees of alkyl group substitution (DS) for the following reasons:

1. Water can participate in undesired side reactions.
2. Heterogeneous reaction conditions may prevent the reagents from penetrating the starting material.
3. The alkylating reagents have limited solubility in water.

Isogai et al.[1,2] proposed a method for the complete alkylation of cellulose in the nonaqueous cellulose solvent SO₂–diethylamine(DEA)–dimethylsulfoxide (DMSO). Modifications of the Hakomori method[3] have been reported[4-6] for the preparation of (methyl)cellulose (MC), but some chain degradation and side reactions occurred. Permethylation of sugars using solid NaOH in DMSO was reported by Ciucanu and Kerek.[7] Recently, Kondo and coworkers[8] succeeded in the quantitative prepara-

tion method of tri-O-(allyl)cellulose from cellulose acetate (CA) in DMSO. In this article, we report an improved procedure that results in the facile preparation of tri-O-(alkyl)cellulose. Interestingly, water, which normally reduces the efficiency of etherification reactions, has been observed to play an important role in this process.

EXPERIMENTAL

Materials

Commercial cellulose acetate samples from cotton linters were provided by Daicel Chemical Ind. Co., Ltd. (DS 1.75, 2.24, and 2.39). The samples were dried at 105°C for 3 h. The DMSO was dehydrated over type 3A molecular sieves. Reagent-grade solvents and alkylating agents (Aldrich Gold Label) were used without further purification. Powdered sodium hydroxide was pulverized by grinding NaOH pellets in a domestic coffee mill.

Preparation Methods

All starting solutions were prepared as follows: 1 g cellulose acetate was completely dissolved in 60 mL DMSO at 60°C for 1 h with constant stirring. The amounts of powdered NaOH and alkylating agents were adjusted according to the number of anhydroglucose units present in 1 g of the cellulose acetate (Table I).

Table I Preparative Conditions for MC Starting from CA with *DS* 2.24

Sample [MC-$X(N,M)$][a]	NaOH Added (g/g CA)	CH$_3$I Added (mL/g CA)
MC-X(5.0,5.0)	2.3	3.7
MC-X(7.5,7.5)	3.5	5.6
MC-X(10.0,10.0)	4.7	7.4
MC-X(12.5,12.5)	5.9	9.3
MC-X(15.0,15.0)	7.0	11.2

[a] X indicates the preparative method, either A,B,C, or D depending on sample series. N and M are the number of moles of NaOH and alkyl iodide, respectively, per three hydroxyl groups (substituted and unsubstituted) in each anhydroglucose unit in the CA sample. For example, the amount of NaOH per g CA is $(1.0/M_w) \times 3 \times N \times 40$ (g), where M_w (molecular weight of 1 acetylglucose unit) = $162 + 42 \times DS$. The amount of CH$_3$I per gram CA is $(1.0/M_w) \times 3 \times N \times 141.94/2.28$ (mL).

The methylation step was investigated using four different reaction conditions to determine the optimum conditions for the preparation of tri-O-(alkyl)cellulose from CA.

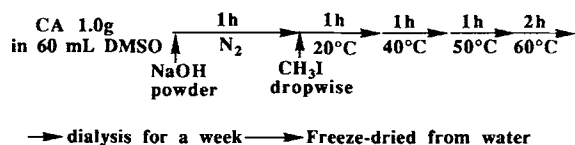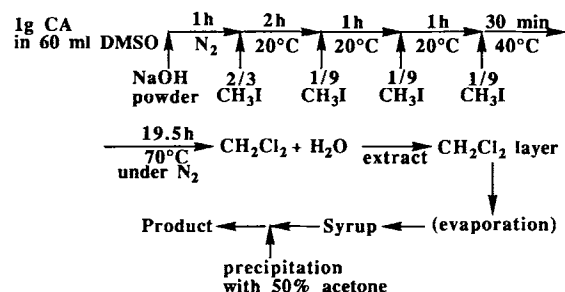Series A (methyl)cellulose samples (MC-A) were prepared according to Scheme 1, as reported previously.[1]

Series B samples were prepared as for series A, but with reaction times at 60°C increased from 2–21 h.

To prepare series C samples, iodomethane (CH$_3$I) was added dropwise at four different times during the reaction. The first portion comprised two thirds of the total amount of CH$_3$I. The three remaining portions comprised one ninth of the total, as shown in Scheme 2.

Series D samples were prepared as for series C, but 1 mL distilled water was added to the starting CA–DMSO solution.

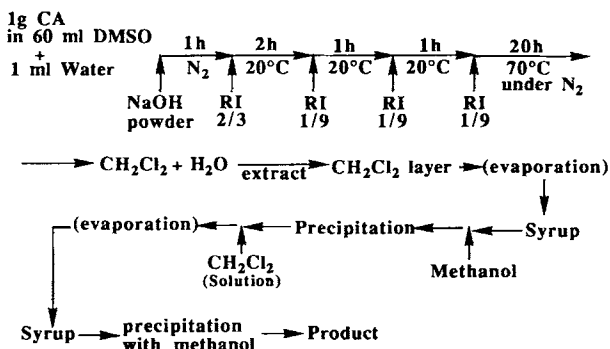## Complete Alkylation of Cellulose

The series D method (Scheme 3) was applied to the preparation of other cellulose ethers. Typically, 5.86 g powdered NaOH was dispersed in a CA–DMSO solution containing 1 mL water. Following 1-h stir-

Scheme 2 Procedure for preparation of series C MC samples.

ring under a nitrogen atmosphere, two thirds of the total amount of the alkyl iodide (RI) was added dropwise to the solution. At 2, 3, and 4 h after the first addition of RI, one third of the remaining RI was added dropwise, respectively. Following the last addition of RI to the solution, the temperature was raised to 70°C and kept at this temperature for 20 h under a nitrogen atmosphere. The reaction mixture was cooled to room temperature, and 100 mL of both water and methylene chloride was added. The methylene chloride layer was separated, washed with water, and evaporated under reduced pressure at 40°C until a syrup remained. The tri-O-(alkyl)cellulose was precipitated from the syrup by the addition of 100 mL methanol (50% acetone for the methylation product). Following filtration, the precipitate was dissolved in 100 mL methylene chloride and reprecipitated according to the same procedure. The filtered product was air-dried followed by drying under vacuum at 60°C.

Analyses

The distribution of methyl groups in the MC samples was determined by acid hydrolysis and analysis

Scheme 1 Procedure for preparation of series A MC samples.

Scheme 3 Procedure for complete alkylation of cellulose with alkyl iodide (RI).

of the components as partially methylated alditol acetates by gas–liquid chromatography (GLC).[9] MC (50 mg) was dissolved in 15 mL 3% sulfuric acid and was hydrolyzed at 120°C for 1 h. The hydrolyzates were neutralized at pH 5.5 with barium hydroxide, and the precipitated barium sulfate was removed by centrifugation. The partially methylated glucoses thus obtained were reduced with $NaBH_4$ and then acetylated. The partially methylated alditol acetates were analyzed in triplicate by a Hewlett-Packard Model 5890A gas–liquid chromatograph equipped with a Hewlett-Packard Model 3392A integrator, a flame-ionization detector, and a J. & W. Scientific DB-1 fused-silica capillary column (0.25 mm × 30 m; film thickness 0.25 μm). The temperature was increased from 190 to 215°C at 1°C/min.

IR spectra were obtained with a Mattson Cygnus Fourier transform infrared (FTIR) spectrophotometer with photoacoustic detection. ^1H and ^{13}C nuclear magnetic resonance (NMR) spectra were obtained from a Varian XL 200 spectrometer at frequencies of 200 and 50.4 MHz, respectively. Deuterated chloroform ($CDCl_3$) was used as the solvent at 30°C. Spectra were referenced relative to $CHCl_3$ for ^1H NMR and $CDCl_3$ for ^{13}C NMR measurements.

Gel permeation chromatograms in chloroform and tetrahydrofuran were obtained with a Waters ALC/GPC system and 10^5, 10^4, 10^3, 500, and 100 Å μ-Styragel columns in series. The column set was calibrated with poly(styrene) standards.

RESULTS AND DISCUSSION

Preparation of MC

Table II shows the results of GLC analyses of the substituent distribution [X_n (n = 2, 3, and 6)] for the MC samples. X_2, X_3, and X_6 were calculated from molar ratios of glucitol (S_0) and its mono-, di-, and triderivatives (S_2–S_{236}) (Fig. 1), which were derived from the hydrolysates of the polymers as determined by GLC:

$$X_2 = S_2 + S_{23} + S_{26} + S_{236}$$

$$X_3 = S_3 + S_{23} + S_{36} + S_{236}$$

$$X_6 = S_6 + S_{26} + S_{36} + S_{236}$$

$$DS = X_2 + X_3 + X_6.$$

These values (X_n) indicate the reactivities of each hydroxy group, as well as the distribution of sub-

Table II Distribution of Methyl Groups in MC Samples[a]

Samples	DS^b	Molar Ratios (%)[c]								DS in Each Position		
		S_0	S_2	S_3	S_6	S_{23}	S_{36}	S_{26}	S_{236}	X_2^d	X_3	X_6
From DS 2.24												
MC-A(5.0,5.0)	1.85	10.6	16.3	8.5	2.6	13.7	3.7	11.2	33.5	0.75	0.59	0.51
MC-A(7.5,7.5)	2.80	0	0.6	0	0	7.4	2.0	9.6	80.4	0.98	0.90	0.92
MC-A(10.0,10.0)	2.73	0	1.0	0.2	0.2	8.6	2.2	12.5	75.3	0.97	0.86	0.90
MC-A(12.5,12.5)	2.70	0.4	1.3	0	0.4	7.1	1.7	16.9	72.3	0.98	0.81	0.91
From DS 2.39												
MC-A(5.0,5.0)	2.64	0.7	3.1	0.9	0.5	9.4	1.7	11.5	72.2	0.96	0.84	0.84
MC-A(7.5,7.5)	2.81	0	0.4	0	0	6.4	2.1	9.3	81.8	0.98	0.90	0.93
MC-A(10.0,10.0)	2.77	0	1.2	0.2	0	9.8	1.2	9.6	78.0	0.99	0.89	0.89
MC-A(15.0,15.0)	2.77	0	0	0.7	0	5.3	1.1	15.2	77.7	0.98	0.85	0.94
From DS 2.24												
MC-B(10.0,10.0)	2.71	0	1.5	0.3	0.2	9.2	2.6	13.7	72.4	0.97	0.85	0.89
MC-C(12.5,10.0)	2.92	0	0	0	0	3.6	0.8	2.6	93.0	0.99	0.97	0.96
MC-D(10.0,10.0)	2.89	0	0.2	0.2	0.1	4.8	1.4	3.5	89.9	0.98	0.96	0.95
MC-D(12.5,10.0)	3.00	0	0	0	0	0	0	0	100.0	1.00	1.00	1.00

[a] Nomenclature of samples is given in Table I.
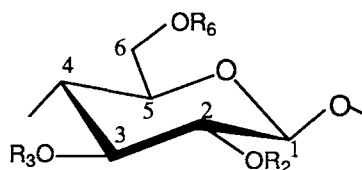
[b] $DS = X_2 + X_3 + X_6$.

[c] Calculated from yields of glucitol (S_0) and its partially methylated derivatives (S_2–S_{236}) determined by GLC. For example, S_2 means the molar ratio of 2-methylglucitol acetate.

[d] X_n is the ratio of glucitol derivatives substituted at the OH of carbon n (n = 2, 3, and 6) position. For example, $X_2 = (S_2 + S_{23} + S_{26} + S_{236})/100$.

stituents at OH in each position (C-2, C-3, and C-6) of the ring carbons. The DS represents the sum of X_2, X_3, and X_6.

Series A did not yield tri-O-(methyl)cellulose. Complete methylation was not achieved despite varying the amount of reagents, the DS of starting materials, and the reaction time in the procedure of Scheme 1 (samples MC-A and MC-B in Table II). The methyl group DS reached a limit after addition of 7.5 mol reagent per mol of substituted and unsubstituted hydroxy group for two samples. From values of X_n, it was determined that the relative reactivity of hydroxy groups (OH-2, OH-3, and OH-6, respectively) at the two (C-2), three (C-3), and six (C-6) positions of the anhydroglucose unit was in general OH-2 > OH-6 > OH-3 in this system. This order of reactivities is the same as that reported for MC prepared from alkalicellulose in an aqueous solvent system,[10,11] but differs from the order (OH-6 > OH-2 $\simeq$ OH-3) observed in a nonaqueous system.[12]

Figure 2 shows IR spectra of MC prepared by stepwise addition of reagents (series C and D). MC-C (10.0, 10.0) (curve 2 in Fig. 2) shows complete methylation of the free hydroxy groups in CA. Following methylation, the number of acetyl groups remaining from the original CA (curve 1 in Fig. 2) is very small. The addition of an excess amount of powdered NaOH to the amount of CH_3I resulted in a reduction in the number of acetyl groups (curve 3 in Fig. 2). This MC-C (12.5, 10.0) sample did not have hydroxy groups and the remaining acetyl groups were mainly in the C-6 and C-3 position
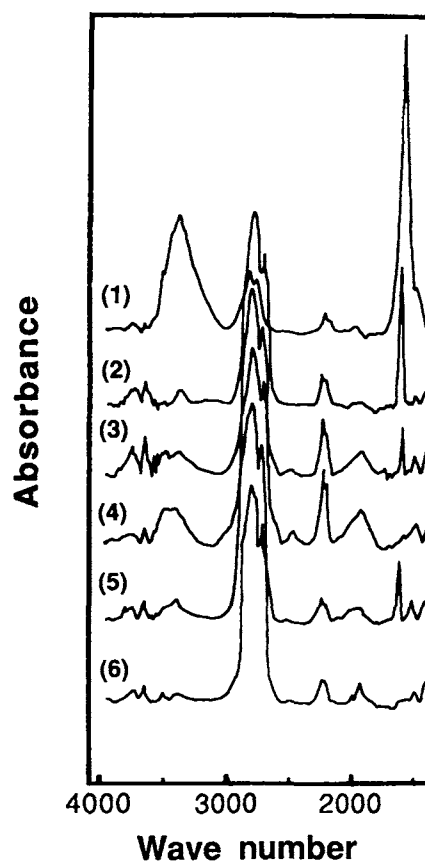

Figure 2   IR spectra for (methyl)celluloses (series C and D). (1), CA (DS, 2.24) starting material; (2), MC-C (10.0, 10.0); (3), MC-C (12.5, 10.0); (4), MC-D (10.0, 7.5); (5), MC-D (10.0, 10.0); (6), MC-D (12.5, 10.0) (tri-O-(methyl)cellulose). For sample nomenclature, see Table I.

	R_2	R_3	R_6
(1)	H	H	H
(2)	Alkyl	H	H
(3)	H	Alkyl	H
(4)	H	H	Alkyl
(5)	Alkyl	Alkyl	H
(6)	Alkyl	H	Alkyl
(7)	H	Alkyl	Alkyl
(8)	Alkyl	Alkyl	Alkyl

Figure 1   Structure of the eight possible glucoside residues of the products.

[MC-C (12.5, 10.0) in Table II)]. Thus, acetyl groups in C-6 and C-3 positions are most resistant to saponification in this system.

These etherification reaction conditions can be considered heterogeneous. This is due to the solid state of the powdered NaOH used as a base in the CA–DMSO solutions. The addition of a small amount of water in series D may solubilize the solid NaOH. Following the addition of 1 mL water to the CA–DMSO solution, the solution remained homogeneous. Varying the quantities of reagents led to the optimum conditions for the preparation of tri-O-(methyl)cellulose shown in the last entry of Table II, with 1 mL distilled water and 12.5 mol/mol and 10 mol/mol of powdered NaOH and iodomethane, respectively. (In fact, methylation does not require heating at 70°C for prolonged periods as was the case for the other alkylations.) The ^{13}C NMR

chemical shifts for these samples were identical to those reported previously.[1] The other CA samples with DS of 2.39 and 1.75 also yielded tri-O-(methyl)cellulose when subjected to these conditions. Thus, NMR and IR evidence confirms the formation of completely substituted MC, independent of the DS of the cellulose acetate starting material.

Influence of Water and Reagent Quantity on Reaction Efficiency

The addition of a small amount of water improves the efficiency of the methylation reaction. According to the results presented in Table III, an increase in the amount of water results in a decrease in the DS. The addition of water may result in the dissolution of NaOH in the DMSO solvent. The addition of powdered NaOH to a CA–DMSO solution without water resulted in the precipitation of polymer. However, no precipitate formed on addition of powdered NaOH when 1 mL water was added to the CA–DMSO solution. The more homogeneous solution observed in the presence of water may facilitate saponification of the acetyl groups in the C-6 position.

Interestingly, in the cases where 5 and 10 mL water were added, there were high molar ratios of S_0 and S_{236} corresponding to unsubstituted and completely substituted glucose units, respectively (nos. 1 and 2 in Table III). This suggests that these (methyl)celluloses are blocky in nature.

The quantity of reagents had little effect on the methylation efficiency. The addition of 2.5 mol CH_3I/mol yielded the almost totally methylated cellulose and 10.0 mol CH_3I/mol addition was suf-

ficient to give tri-O-(methyl)cellulose (nos. 4, 5, and 6 in Table III).

The reactivity order of hydroxy groups in series D was OH-6 $\geq$ OH-2 $\geq$ OH-3, very similar to that proposed for the SO_2–DEA–DMSO,[12] even though a trace of water was present in the solution.

Application to the Complete Alkylation of Cellulose

As shown in Table IV, tri-O-(alkyl)cellulose from methyl to n-decyl were obtained in high yields without significant depolymerization. The derivatives with alkyl substituents from methyl to n-pentyl were isolated as white solids; tri-O-(n-hexyl), tri-O-(n-heptyl), tri-O-(n-octyl), tri-O-(n-nonyl), and tri-O-(n-decyl)celluloses were isolated as sticky solids.

The IR spectra for tri-O-(methyl), tri-O-(propyl), tri-O-(n-pentyl), and tri-O-(n-octyl)celluloses are shown in Figure 3. These show no hydroxyl absorption band around 3400 cm^{-1}. The absorptions around 2800–3000 cm^{-1} due to C—H stretching vibrations and 1460 and 1370 cm^{-1} due to C—H bending vibrations increased with an increase in the chain length of the n-alkyl substituents. ^{13}C NMR chemical shifts of these derivatives were in agreement with published data.[1] The observed absence of splitting for each of the ring carbons indicates complete substitution of the neighboring carbons.[13] No evidence of side reactions such as oxidation was detected by IR or NMR.

Preliminary results show that this method is also effective for the complete methylation and ethylation of poly(vinyl alcohol) (M_w 78,000, Polyscience Inc.) and poly(vinyl acetate) (M_w 500,000, Poly-

Table III   Distribution of Methyl Groups in MC Prepared by Changing the Amount of Water and CH_3I

| Sample | DS | \multicolumn{8}{c|}{Molar Ratios (%)} | \multicolumn{3}{c}{DS in Each Position} |
		S_0	S_2	S_3	S_6	S_{23}	S_{36}	S_{26}	S_{236}	X_2	X_3	X_6
MC-D(12.5,10.0)[a]												
1. +10 mL H_2O	0.91	55.7	6.1	2.0	8.6	3.9	1.3	3.3	19.2	0.33	0.26	0.32
2. +5 mL H_2O	1.28	35.8	5.9	1.7	18.2	5.1	3.1	5.1	25.1	0.41	0.35	0.52
3. +2 mL H_2O	2.99	0	0	0	0	0.5	0.4	1.3	97.8	1.00	0.99	1.00
4. +1 mL H_2O	3.00	0	0	0	0	0	0	0	100.0	1.00	1.00	1.00
With 1 mL water addition												
5. MC-D(12.5,5.0)	2.97	0	0	0	0	0.9	0.7	1.0	97.5	0.99	0.99	0.99
6. MC-D(12.5,2.5)	2.98	0	0	0	0	1.2	0.5	1.1	97.2	1.00	0.99	0.99
7. MC-D(12.5,1.0)	2.86	0.6	0	0	4.0	1.4	1.4	1.9	90.7	0.94	0.94	0.98

[a] Nomenclature of samples is given in Table I.

Table IV   Cellulose Ethers (series D) Prepared with Water,[a] Powdered NaOH,[b] and Alkyl Iodide in the CA[c]–DMSO Solution

No.	Reagent	Amount (mL) (1st portion, others)	DS	Yield (%)	Solvent for Precipitation	M_w[d] $(\times 10^5)$
1.	CH_3I	4.9, 0.8 (3times)$\geq$	3.0	94	50% Acetone	0.92
2.	CH_3CH_2I	6.3, 1.1 (3times)	3.0	99	Methanol	0.89
3.	$CH_3(CH_2)_2I$	7.3, 1.4 (3times)	3.0	88	Methanol	0.85
4.	$CH_3(CH_2)_3I$	9.0, 1.5 (3times)	3.0	80	Methanol	0.85
5.	$CH_3(CH_2)_4I$	10.4, 1.7 (3times)	3.0	89	Methanol	—
6.	$CH_3(CH_2)_5I$	11.8, 1.9 (3times)	3.0	60	Methanol	—
7.	$CH_3(CH_2)_6I$	13.0, 2.2 (3times)	3.0	62	Methanol	—
8.	$CH_3(CH_2)_7I$	14.4, 2.4 (3times)	3.0	60	Methanol	—
9.	$CH_3(CH_2)_8I$	16.5, 2.8 (3times)	3.0	73	Methanol	—
10.	$CH_3(CH_2)_9I$	16.8, 2.8 (3times)	3.0	60	Methanol	—

[a] The amount of water was 1.0 mL.
[b] The amount of powdered NaOH was 5.86 g.
[c] CA; cellulose acetate with DS of 224 and M_w of 1.09×10^5.
[d] Approximate M_w; values are for poly(styrene) chains whose GPC elution curves correspond to the cellulose ethers.

science Inc.) in one step. IR analysis confirmed the absence of hydroxyl and acetyl bands in the products. Thus, the method can be applied to other polymers soluble in DMSO.
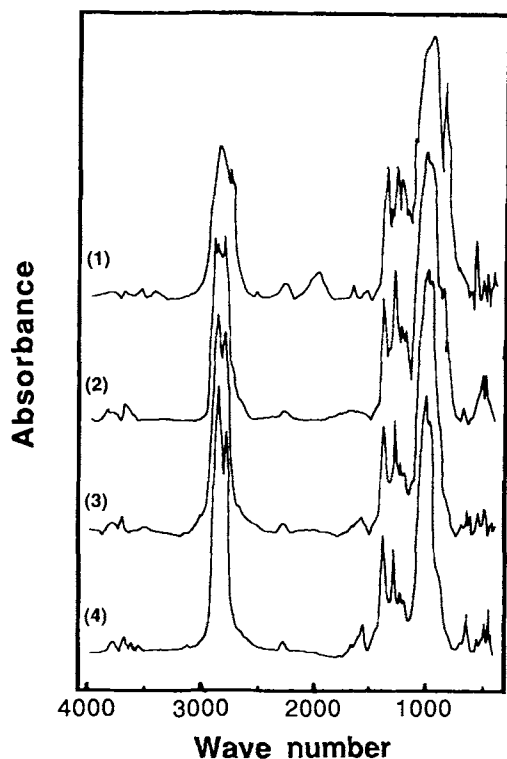

Figure 3   IR spectra of tri-O-(alkyl)cellulose. (1), tri-O-(methyl)cellulose; (2), tri-O-(propyl)cellulose; (3), tri-O-(n-pentyl)cellulose; (4), tri-O-(n-octyl)cellulose.

CONCLUSIONS

1. Tri-O-(alkyl)celluloses were prepared without significant depolymerization by adding powdered NaOH and alkyl iodide to a solution of cellulose acetate in DMSO containing a small amount of water.
2. In this procedure, the addition of a small amount of water improved the efficiency of alkylation of the cellulose acetate, presumably by facilitating hydrolysis. Addition of larger amounts of water resulted in incomplete alkylation.
3. The order of reactivity of the acetylated starting material was C-2 > C-6 > C-3 in the water-free DMSO system (series A) and C-6 $\geq$ C-2 $\geq$ C-3 in the DMSO–water system (series D).
4. This novel method can also be applied to the alkylation of other macromolecules soluble in DMSO.

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