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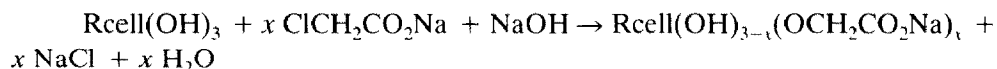
Preparation of *O*-(carboxymethyl)cellulose (CMC) of high degree of substitution

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O-(Carboxymethyl)cellulose (CMC) of various degrees of substitution (d.s.) is now commercially available for use in food additives, cosmetics, detergents, and basic pharmaceutical materials. CMC has generally been prepared by the reaction of sodium monochloroacetate with alkali-cellulose in aqueous medium, formulated as follows,



where Rcell(OH)_3 is a D-glucosyl residue in a cellulose molecule, and x is the degree of substitution (d.s.).

A d.s. of ~ 3 would mean that all of the hydroxyl groups in each D-glucosyl residue in the cellulose molecule had been substituted by carboxymethyl groups.

Chowdhury¹, Sakurada², McLaughlin and Herbst³, and Hayakawa and Morita⁴ earlier tried to prepare CMC of high d.s. values, and, in 1965, Watanabe and Nakamura⁵ proposed a method of CMC preparation using 1 part (by weight) of cellulose suspended in 30 parts (by volume) of 88:12 (v/v) 2-propanol–water and then adding an excess of 50% aq. NaOH and monochloroacetic acid, or of sodium monochloroacetate, under continuous stirring. A long reaction-time was required in this and earlier methods, and substitution could hardly exceed d.s. 1 in a single stage of operation.

In order to obtain CMC of a higher d.s. in a shorter reaction-time, we examined the use of 1,1,3,3-tetramethylurea (Me_4U) plus dimethyl sulfoxide (Me_2SO) as a promotor of *O*-(carboxymethylation) of cellulose, based on our earlier finding that Me_4U efficiently stimulates the Hakomori permethylation of polysaccharides, including cellulose⁶.

EXPERIMENTAL

Earlier procedure (Watanabe's method). — In a 200-mL homogenizer

(Biomixer, Nihon Seikiseisakusho Co., Ltd.) were stirred 1 part (by wt.) of cellulose powder [Cellulose native (Merck)] and 30 parts (by vol.) of 88:12 (v/v) 2-propanol–water for 10 min. Then, a definite volume of 50% aq. NaOH solution was added, corresponding to a molar ratio of 2, 4, 6 and 8 mol, respectively, per mol of D-glucosyl residue of cellulose. After being stirred for 1 min, the mixture was cooled in ice, to maintain the temperature at 10°, the equivalent amount of 50% aq. sodium monochloroacetate solution was added; the mixture was stirred for 1 min, transferred to a 200-mL, round-bottomed flask fitted with a reflux condenser, kept for 90 min at 5°, and then heated on a hot-water bath at 80°, under continuous stirring, for 2.5 h (to complete the reaction). The mixture was now treated as described next (see the present procedure).

Present procedure. — One part (by wt.) of cellulose powder [Cellulose native (Merck)] and 30 parts (by vol.) of $\text{Me}_2\text{SO}-\text{Me}_4\text{U}$ (4:1, 1:1, and 1:4), or Me_2SO or Me_4U only, were stirred in a homogenizer for 10 min at 60°. First, 1/3rd of the total volume of 50% aq. NaOH was added to the homogenized, cellulose suspension, under vigorous stirring during 5 min, and then 1/3rd of the total amount of 50% aq. sodium monochloroacetate solution was added. After stirring for 10 min, the process was repeated twice (to consume all of the reagents). The molar ratio of the reagents per mol of D-glucosyl residue of cellulose was varied (2, 4, 6, and 8 mol per mol) to ascertain the optimal conditions. The mixture was transferred to a 200-mL, round-bottomed flask fitted with a reflux condenser, and then heated, under stirring, for 2.5 h at 90° on a hot-water bath (to complete the reaction). After completion thereof, the mixture was dialyzed against running water for 24 h, and the inner solution was concentrated to 100 mL under diminished pressure below 60°. Finally, the product, CMC, was isolated by lyophilization; yield, 91–95%. The d.s. values of the CMC samples produced were determined by the method of Francis⁷ using the uranyl nitrate reagent.

RESULTS AND DISCUSSION

The experimental results showed that the present method for the preparation of CMC, namely, by the addition of Me_2SO or Me_4U , and especially, the combination $\text{Me}_2\text{SO}-\text{Me}_4\text{U}$, gave, in a single stage of operation, CMC of higher d.s. values than any of the earlier methods (see Table I).

The 1:1 and 1:4 ratios of $\text{Me}_2\text{SO}-\text{Me}_4\text{U}$ gave no significant difference in the d.s. of the CMC formed. Using 1:1 $\text{Me}_2\text{SO}-\text{Me}_4\text{U}$, CMC of higher d.s. was obtained by increasing the molar equivalents of the reagents (NaOH and sodium monochloroacetate), whereas this had no significant effect on the d.s. in the Watanabe procedure⁵. By the earlier methods, CMC of higher d.s. values could only be attained by repeated, multiple stages of the process. Our present method, using 1:1 $\text{Me}_2\text{SO}-\text{Me}_4\text{U}$ as the solvent and 4 moles each of aq. NaOH and sodium monochloroacetate as the reagents, yielded, within a short reaction time, CMC of d.s. 2.36 by only two repetitions of the process (see Table II).

TABLE I

THE EFFECTS OF THE $\text{Me}_2\text{SO}-\text{Me}_4\text{U}$ RATIO ON THE D.S. VALUES OF CMC PRODUCED BY A SINGLE-STAGE REACTION USING 4 MOL EACH OF NaOH AND $\text{ClCH}_2\text{CO}_2\text{Na}$ PER MOL OF D-GLUCOSYL RESIDUE OF CELLULOSE

Solvent	Ratio	D.s. of CMC
Me_2SO		1.44–1.46
$\text{Me}_2\text{SO}/\text{Me}_4\text{U}$	4:1	1.53–1.54
$\text{Me}_2\text{SO}/\text{Me}_4\text{U}$	1:1	1.61–1.64
$\text{Me}_2\text{SO}/\text{Me}_4\text{U}$	1:4	1.64–1.71
Me_4U		1.56–1.57

TABLE II

THE EFFECTS OF THE MOLAR RATIO OF THE REAGENTS TO THE D-GLUCOSYL RESIDUES OF CELLULOSE ON THE D.S. VALUE OF THE CMC PRODUCED

Solvent	NaOH (mol)	$\text{ClCH}_2\text{CO}_2\text{Na}$ (mol)	D.s. of CMC	Mode of reaction ^a
$\text{Me}_2\text{SO}/\text{Me}_4\text{U}$ (1:1)	2	2	1.24	s
	4	4	1.61–1.64	s
	4	4	2.23–2.36	d
	6	6	1.83–1.84	s
	8	8	1.98–2.02	s
Aq. 2 PrOH (88%)	2	2	0.81–0.85	s
	8	8	1.19–1.22	s

^as, one stage; d, two stages.

As in our modified-Hakomori permethylation of polysaccharides⁶, Me_4U promoted the *O*-(carboxymethylation) of cellulose, to produce CMC of higher d.s. values, probably by the same mechanism, namely, by inducing relaxation of the higher molecular structure of cellulose by virtue of the hydrogen-bond-accepting activity of Me_4U . Some solvent effects might also participate in this case, as the promoting activity of Me_4U was enhanced by its combination with Me_2SO .

The CMC having d.s. 2.36, obtained in the present study, is less soluble in water than those of lower d.s., and it is readily soluble in slightly acidic (pH 2.0), 4:1 methanol–water, in which samples of CMC having lower d.s. values are insoluble.

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