Grafting of 2-Oxazolines onto Cellulose and Cellulose Diacetate

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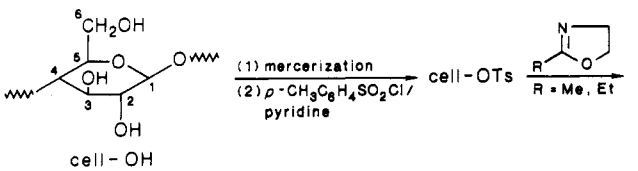
ABSTRACT: Cellulose and cellulose diacetate were sulfonylated and used to induce the polymerization of 2-methyl-2-oxazoline and 2-ethyl-2-oxazoline, giving rise to cellulose-*graft*-poly(*N*-acylethylenimine) (1) and cellulose diacetate-*graft*-poly(*N*-acylethylenimine) (2), respectively. Graft copolymers 1 and 2 were isolated by fractionation and characterized. By an oxidation method using $NaIO_4$, it was shown that one *N*-acetylethylenimine graft chain having an average chain length of 22 is contained per approximately 33 cellulose units.

Introduction

Cellulose is a typical natural polymer and has been widely used for a long time. Cellulose diacetates are useful derivatives as well. These polymers, however, are limited in terms of miscibility (compatibility). Blending of polymers, on the other hand, is a good approach to create new polymer materials such as polymer composites. If an effective way of blending them with a variety of synthetic polymers was found, their applications would be broadened.[1] We have shown that homopolymers of 2-oxazolines such as 2-methyl-2-oxazoline (MeOZO) and 2-*n*-propyl-2-oxazoline are miscible with a synthetic polymer such as poly(vinyl chloride), polystyrene, or poly(vinylidene fluoride).[2,3] Therefore, it is expected that introduction of the poly(2-oxazoline) chain into cellulose and cellulose diacetate is able to make these natural polymers compatible with a synthetic polymer, in which the poly(2-oxazoline) chain acts as a "compatibilizer". The present paper deals with grafting of MeOZO and of 2-ethyl-2-oxazoline (EtOZO) via ring-opening polymerization onto cellulose and cellulose diacetate and with characterization of the product copolymers. Compatibility studies will be reported later. Relevant to the graft copolymerization of cellulose via ring-opening polymerization, the following studies are to be cited: ethylene oxide,[4] β-propiolactone,[5] and ethylenimine[6] were polymerized onto cellulose, and the polymerization of ε-caprolactam[7] was induced by (chlorocarbonylmethyl)cellulose.

Results and Discussion

Grafting onto Cellulose. The degree of polymerization ($\overline{DP}$) of the sample of cellulose used is approximately 200. It is known that the ring-opening polymerization of 2-oxazolines is induced by alkyl sulfonates or halides.[8] For the graft polymerization of 2-oxazolines, cellulose was first mercerized and then tosylated[9] (see eq 1).



cell—(NCH$_2$CH$_2$)$_n$— (1)
RC=O

1 (graft copolymer; R = Me, Et)

Table I gives the result of these procedures. More tosyl groups are introduced under mercerization and tosylation conditions I-B than under those of I-A, and, at the same time, chlorination takes place to a small extent in I-B (DS, degree of substitution = 0.14). The tosylation probably occurs preferentially at the C-6 position as reported before.[10,11] In the case of I-B, the tosylation takes place also at the C-2 and/or C-3 positions in addition to the C-6 position.

Table I
Mercerization and Tosylation of Cellulose

	mercerization		tosylation[a]			
					DS[b]	
code	concn of NaOH, %	days at room temp	days	yield, %	tosyl	Cl
I-A	36	1	1	84	0.48	0.00
I-B	30	7	3	100	1.28	0.14

[a] Tosylation conditions: cellulose:tosyl chloride:pyridine = 1:10:50 at room temperature. [b] The value of degree of substitution (DS) was determined by elemental analysis.

The insolubility of tosylated sample I-A is almost the same as that of cellulose itself, which is insolubile in all organic solvents. However, higher DS of tosylation improves the solubility, i.e., sample I-B is insoluble in CH_3CN and $CHCl_3$, swells in CH_2Cl_2, DMF, and DMSO, but is soluble in PhCN. The enhanced solubility of sample I-B is probably due to the higher DS of tosylation, which prevents the intermolecular hydrogen bonding of cellulose molecules and thus decreases the crystallinity of cellulose.

Grafting of MeOZO and EtOZO onto cellulose was carried out in PhCN or CH_3CN by using tosylated samples I-A and I-B as initiator. The graft copolymerization of I-A was heterogeneous in both PhCN and CH_3CN. On the other hand, all reactions of I-B in PhCN proceeded in a homogeneous system. These graft copolymerization conditions and results are given in Table II. Yields are based on the total polymeric materials obtained after workup procedures.

The fractionation of the polymers was then performed in $CHCl_3$ and MeOH (Table III). Cellulose is insoluble in both solvents, whereas homopolymers of MeOZO and EtOZO are soluble in both. With samples 1 and 2, a large fraction of polymer insoluble in $CHCl_3$ was produced. This $CHCl_3$-insoluble fraction is considered to be made of graft copolymers, since it contains nitrogen (elemental analysis) and since the IR spectrum clearly shows the presence of the poly(*N*-acetylethylenimine) moiety. The elemental analysis of the $CHCl_3$-insoluble fraction of polymer sample 2 was as follows: C, 54.54; H, 7.94; N, 14.41. These results lead to a ratio of the *N*-acetylethylenimine unit of the graft chain to the glucopyranosidic unit of cellulose ([ROZO]/[cellulose]) of 20.4. On the other hand, this unit ratio can be calculated from the material balance as follows. In experiment 2, the mass of the charged initiator I-A (0.070 g) and MeOZO (0.70 g) is 0.77 g, and the mass of the polymer obtained was 0.750 g. This is a nearly quantitative yield. The $CHCl_3$-insoluble fraction weighs 0.600 g, which is the graft copolymer, and the $CHCl_3$- as

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Table II
Graft Copolymerization onto Cellulose

code	amt of initiator, g	R of ROZO (amt, g)	[ROZO]/[TsO]	solvent (amt, mL)	reaction temp, °C	reaction time, h	polymer yield, %
			Initiator I-A				
1	0.137	Me (1.32)	56	CH_3CN (2.5)	80	110	95
2	0.070	Me (0.70)	58	PhCN (2.7)	90	50	98
			Initiator I-B				
3	0.089	Me (0.866)	36	PhCN (8.0)	90	50	96
4	0.041	Me (0.198)	18	PhCN (3.7)	90	50	88
5	0.089	Me (0.278)	12	PhCN (8.0)	90	50	87
6	0.145	Me (0.199)	5	PhCN (13.0)	90	50	83
7	0.102	Et (0.170)	6	PhCN (9.2)	90	50	72

[a] Weight of total polymeric materials obtained/weight of initiator + ROZO.

Table III
Fractionation of Polymers

code	amt of polymer sample, g	$CHCl_3$-insol fraction, g	$CHCl_3$-sol fraction MeOH-insol, g	$CHCl_3$-sol fraction MeOH-sol, g
1	1.390	0.742	0.0	0.630
2	0.750	0.600	0.0	0.150
3	0.920	0.0	0.0	0.920
4	0.263	0.010	0.002	0.251
5	0.305	0.025	0.077	0.203
6	0.292	0.022	0.122	0.148
7	0.196	0.013	0.090	0.093

well as MeOH-soluble fraction weighs 0.150 g, which is the homopolymer of MeOZO. In the graft copolymer, the weight of cellulose moiety is 0.046 g from 0.070 g of initiator I-A, and that of poly(*N*-acylethylenimine) must be 0.55 g (0.70 g − 0.150 g). Therefore, the unit ratio of 21.8 is derived, which is very close to that obtained by the elemental analysis. It is striking that the graft copolymer is insoluble in $CHCl_3$ in spite of the fact that the copolymer contains such a large quantity of poly(*N*-acetylethylenimine) graft chain. Homopolymers of MeOZO were probably formed by a chain-transfer reaction during grafting.[12]

With initiator I-B, soluble graft copolymers were mainly obtained. In experiments 3 and 4, most of the products were also soluble in MeOH. The $CHCl_3$-insoluble fraction is absent or very small. It does not contain poly(*N*-acetylethylenimine) but contains some unreacted initiator. The MeOH-soluble fractions are a mixture of graft copolymer and homopolymer of MeOZO. This was confirmed by ^1H NMR and gel permeation chromatography (GPC). The ^1H NMR spectrum of the fractions shows the presence of both cellulose and poly(*N*-acetylethylenimine) moieties. The GPC chart indicates two peaks, which are reasonably assigned to the graft copolymer and homopolymer of MeOZO, respectively, because a separate experiment showed that the copolymer and the homopolymer appeared as two peaks by similar GPC analysis. The solubility difference in graft copolymers 1 prepared from initiators I-A and I-B is mainly due to the difference of the initiators. They may have a different crystalline structure caused by different mercerization and tosylation conditions. The length and number of the graft chain may also influence the solubility. The reason for that is not well understood at present. Similarly in experiments 5–7, the $CHCl_3$-insoluble fraction is low. From the $CHCl_3$-soluble fraction, the MeOH-soluble polymer was removed, and it was confirmed again as a mixture of graft copolymer and homopolymer of MeOZO or EtOZO. The residual MeOH-insoluble part consists exclusively of graft copolymer 1.

Characterization data for the graft copolymers are given in Table IV. The IR spectrum of the copolymer clearly

Table IV
Characterization of Graft Copolymer 1

code	elem anal. found, % C	H	N	S	[ROZO]/[cellulose][a] unit ratio in 1 from elem anal.[b]	from ^1H NMR[c]
5	51.36	5.88	4.85	8.95	2.28	2.9
6	51.32	5.38	3.56	10.43	1.49	1.6
7	49.63	5.26	1.46	9.98	0.55	0.8

[a] *N*-Acylethylenimine unit of the graft chain/glucopyranosidic unit of cellulose. [b] Calculated from C and N values as well as DS of tosyl group = 1.28. [c] Calculated from the ratio of integration of the signal of CH_3CO or that of CH_3 of CH_3CH_2CO versus all other signals.

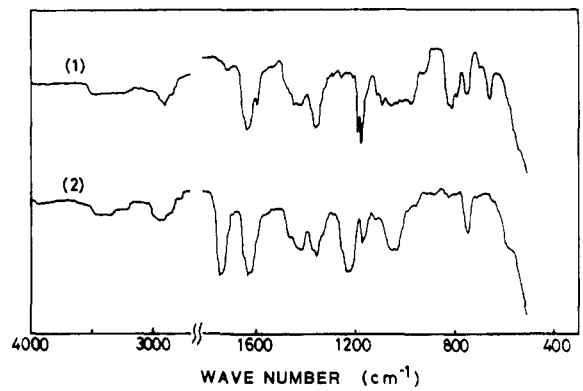

Figure 1. IR spectra (KBr) of (1) graft copolymer 1 (sample code 6) and (2) graft copolymer 2 (sample code 12).

shows the presence of the amide group ($\nu_{C=O}$ = 1630 cm^{-1}) due to poly(*N*-acetylethylenimine) (Figure 1(1)). The unit ratio of the graft chain [ROZO]/[cellulose] was determined by elemental analysis and by ^1H NMR. Both values roughly agreed. The ratio is higher for MeOZO (experiments 5 and 6) than for EtOZO (experiment 7).

The average value of the unit ratio is very low (<3) for graft copolymers. This does not necessarily mean that the average length of the graft chain is lower than 3. A graft copolymer was subjected to further reactions to shed light on this problem. A copolymer was prepared separately by grafting MeOZO on cellulose tosylate: DS of tosylation = 0.95 and [MeOZO]/[cellulose] unit ratio = 0.67. This sample was oxidized by aqueous $NaIO_4$ solution followed by reduction as well as hydrolysis (Smith's decomposition method).[13,14] Under these reaction conditions, the cellulose main chain was decomposed, and the branch chain of poly(*N*-acetylethylenimine) was converted to poly(ethylenimine) chain. The GPC analysis of the products revealed the formation of polymers of average molecular weight of 950 by using a polystyrene standard. This corresponds to a $\overline{DP}$ value of 22 for the ethylenimine unit.

Table V
Sulfonylation of Cellulose Diacetate[a]

code	$R'SO_2Cl$	days	yield, %	DS[b] AcO	$R'SO_3$	Cl	OH
II-A	$R' = p\text{-}CH_3C_6H_4$	4	87	2.41	0.42	0.07	0.10
II-B	$R' = CH_3$	1	100	2.41	0.54	0.07	0.00

[a] Sulfonylation conditions: cellulose diacetate:RSO_2Cl:pyridine = 1:10:50 at room temperature. [b] Determined by elemental analysis.

These results can be explained as follows. The initiation of MeOZO by cellulose tosylate is very slow in comparison with the propagation of MeOZO. So, roughly speaking, a graft polymer sample contains poly(*N*-acylethylenimine) graft chain of $\overline{DP} \sim 22$ per approximately 33 cellulose units; tosylate groups reacted being roughly 3%.

Grafting onto Cellulose Diacetate. The starting sample had $\overline{DP} \simeq 200$ and DS of acetylation = 2.41. In a similar manner as for cellulose itself, cellulose diacetate was tosylated or mesylated. Under the sulfonylation conditions (eq 2) chlorination also took place (Table V).

$$C_6H_7O_2(OAc)_{2.41}(OH)_{0.59} \xrightarrow[\text{pyridine}]{R'SO_2Cl} \underset{(cell(OAc)_2OH)}{}$$

$$C_6H_7O_2(OAc)_{2.41}(O_3SR')_x Cl_y(OH)_z \xrightarrow{\text{R = Me, Et}}$$

$$R' = CH_3,\ p\text{-}CH_3C_6H_4\text{-}$$
$$(cell(OAc)_2(O_3SR'))$$

$$cell(OAc)_2\text{—}\{NCH_2CH_2\}_n \quad (2)$$
$$\qquad\qquad RC{=}O$$

2 (graft copolymer; R = Me, Et)

The sulfonylated products are similar in solubility to cellulose diacetate, which is soluble in PhCN, CH_3CN, acetone, etc.

Table VI shows results of graft copolymerizations of MeOZO and EtOZO onto cellulose diacetate by using polymers II-A and II-B as initiator. CH_3CN and PhCN were used as solvent for II-A and a mixed solvent of PhCN–1,4-dioxane for II-B. All graft copolymerizations proceeded in a homogeneous system.

Initiators II-A and II-B are insoluble in MeOH, whereas homopolymers of MeOZO and EtOZO are soluble in this solvent. So, fractionation was carried out using MeOH (Table VII). It was confirmed by IR spectroscopy that all the MeOH-soluble fractions contain only the homopolymer MeOZO or EtOZO and no graft copolymer at all. The MeOH-insoluble fractions are graft copolymers (**2**) in all runs, which was established by IR (Figure 1(2)) and GPC analysis (Figure 2). The IR spectrum (KBr disk) indicates the presence of both the amide (1630 cm^{-1}) and ester (1750 cm^{-1}) groups. The GPC charts of the copolymers show only one peak, indicating one polymer component of the copolymers.

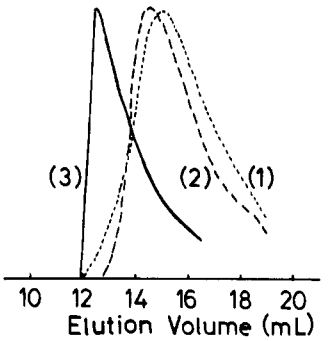

Figure 2. GPC charts of graft copolymers **2**: (1) code 11, (2) code 12, and (3) code 13; eluent, $CHCl_3$ at a rate of 1 mL/min.

Experimental Section

Materials. Cellulose ($\overline{DP}$ = 200) and cellulose diacetate ($\overline{DP}$ = 200, DS = 2.41) were supplied from Daicel Chemical Ind., Tokyo. PVC ($\overline{DP}$ = 450) was given by Sumitomo Chemical Co., Osaka. MeOZO and EtOZO were prepared by the reaction of 2-aminoethanol with acetonitrile and propionitrile, respectively, in the presence of $Zn(OAc)_2$.[15] All solvents were purified in the usual manner.

Tosylation of Cellulose. Tosylation of sample I-A was carried out as follows.[8] Cellulose (5.0 g) was placed in 125 mL of 36% NaOH aqueous solution and stirred for 1 day at room temperature. The cellulose was separated by filtration, washed with methanol until the washings became neutral to phenolphthalein, and dried in a vacuum for 10 h at room temperature. The cellulose thus mercerized, and 125 mL of pyridine was placed in a 300-mL flask. To the mixture, 59.1 g of *p*-toluenesulfonyl chloride was slowly added below 10 °C. Then, the mixture was stirred for 1 day at room temperature, poured into 300 mL of cold water, and separated by filtration. The washing of the tosylated cellulose with cold water was repeated three times. Then, the tosylated cellulose was futher purified by extracting with anhydrous methanol in a Soxhlet extraction apparatus for 20 h and dried in a vacuum for 20 h at 50 °C to give 4.78 g of the tosylated cellulose (sample I-A, 84% yield). Anal. Found: C, 46.15; H, 5.37; S, 6.49; Cl, 0.00. These analytical data led to a degree of tosylation (DS) = 0.48.

The tosylated cellulose sample I-B was prepared similarly except that mercerization was carried out in a 30% NaOH aqueous solution for a week and that tosylation was allowed to proceed for 3 days. Anal. Found: C, 49.24; H, 4.87; S, 11.36; Cl, 1.39. These data indicate DS = 1.28.

Grafting onto Cellulose. Graft copolymerization of MeOZO onto cellulose of code 6 in Table II is taken as an example. In a 20-mL reaction tube containing 13 mL of benzonitrile under nitrogen, the tosylated cellulose, sample I-B (DS = 1.28, 0.145 g = 0.457 mmol equivalent to tosyl group) and MeOZO (0.199 g = 2.34 mmol) were placed. The tube was sealed at −78 °C and kept at 90 °C for 50 h. The tube was opened, and the reaction mixture was poured into 200 mL of diethyl ether to precipitate

Table VI
Graft Copolymerization onto Cellulose Diacetate

code	amt of initiator, g	R of ROZO (amt, g)	[ROZO]/[$R'SO_3$]	solvent (amt, mL)	time of rctn at 90 °C, h	polymer yield, g
			Initiator II-A			
8	0.082	Me (0.143)	16	CH_3CN (4.6)	50	0.225
9	0.129	Me (0.643)	46	PhCN (5.7)	50	0.680
10	0.097	Me (0.947)	90	CH_3CN (5.5)	50	1.044
			Initiator II-B			
11	0.348	Me (0.706)	14	*b* (20.4)	144	1.050
12	0.217	Me (1.009)	31	*b* (12.7)	105	1.197
13	0.216	Me (2.198)	68	*b* (12.7)	87	2.300
14	0.250	Et (1.212)	28	*b* (14.7)	118	1.418

[a] Weight of total polymeric materials obtained. [b] PhCN–1,4-dioxane (2.3:1) mixed solvent.

Table VII
Fractionation of Polymers

code	amt of MeOH-insol graft copolymer 2, g	amt of MeOH-sol homopolymer ROZO, g	graft efficiency,[a] %	[ROZO]/[cellulose] unit ratio of 2	
				b	*c*
8	0.091	0.134	7		0.42
9	0.237	0.443	20		3.24
10	0.354	0.617	27		10.25
11	0.409	0.641	9	1.20	0.63
12	0.365	0.832	15	1.75	2.46
13	0.568	1.738	17	7.08	5.88
14	0.396	1.044	13	1.67	1.81

[a] ROZO in graft copolymer/ROZO charged. [b] Determined by elemental analysis values of C and N as well as DS value = 0.54. [c] Calculated by the relationship [(graft copolymer 2 − initiator used)/mol wt of ROZO]/[initiator used/unit mol wt of esterified cellulose diacetate].

polymeric materials (0.292 g after drying in a vacuum). All the materials were poured in 20 mL of $CHCl_3$, and 0.022 g of an insoluble fraction was obtained after separation and drying in a vacuum. The $CHCl_3$ solution of the polymer was poured into 100 mL of methanol and stirred for 2 days at room temperature. The methanol-insoluble fraction was separated and subjected to GPC analysis. The insoluble fraction was further washed with methanol two more times, and it was confirmed by GPC analysis that the fraction showed a single peak. After separation and drying, 0.122 g of the methanol-insoluble fraction and 0.148 g of the methanol-soluble fraction were obtained. The methanol-insoluble fraction is a graft copolymer (1) as described above.

Tosylation of Cellulose Diacetate. Cellulose diacetate (5.12 g) and pyridine (93 mL) were mixed to give a homogeneous solution. To the solution 21.9 g of *p*-toluenesulfonyl chloride was added below 10 °C with stirring. The mixture was stirred at room temperature for 4 days. The mixture solution was diluted with acetonitrile and then poured into a large amount of cold water. The reprecipitation was repeated once more, and, finally, the polymer solution was poured into a large amount of diethyl ether for precipitation. The polymer thus tosylated was separated by filtration and dried in a vacuum at room temperature for 10 h. Further washing was carried out with methanol in a Soxhlet extraction apparatus for 20 h to remove unreacted *p*-toluenesulfonyl chloride and pyridinium hydrochloride. The polymer was dried in a vacuum at room temperature for 20 h to give 5.65 g of sample code II-A.

Mesylation of Cellulose Diacetate. Into a homogeneous solution of 5.0 g of cellulose diacetate in 90.2 mL of pyridine, 8.67 mL of methanesulfonyl chloride was added slowly. During the addition the temperature was kept below 10 °C. The reaction was then allowed to proceed with stirring at room temperature for 24 h and followed with the purification and separation procedures similar to those used above for the tosylation. Thus, sample II-B (6.73 g) was obtained.

Grafting onto Cellulose Diacetate. Graft copolymerization of MeOZO onto cellulose diacetate in experiment code 12 in Table VI is taken as a typical example. In a 20-mL test tube, 0.217 g of mesylated cellulose diacetate (initiator II-B), 8.9 mL of benzonitrile, and 3.8 mL of 1,4-dioxane were placed under nitrogen. The mixture gave a homogeneous solution after stirring at room temperature. At −78 °C, 1.009 g of MeOZO, which corresponds to 31 mol equiv of mesylated group, was added to the mixture. The tube was sealed and kept at 90 °C for 105 h. Then, the tube was opened while being maintained at −78 °C, and the reaction mixture was poured into 300 mL of diethyl ether to precipitate polymeric materials: 1.197 g after drying in vacuo (98% yield). All of the materials obtained were fractionated by using 100 mL of methanol. After vigorous stirring of the polymeric materials in methanol at room temperature for 24 h, the methanol-insoluble fraction was separated and dried in vacuo to give 0.365 g. From the methanol solution, 0.832 g of a methanol-soluble fraction was obtained after evaporation of methanol and drying in vacuo. The GPC analysis of the methanol-insoluble fraction showed only a single peak (Figure 2). The IR spectrum of the fraction showed characteristic bands at 1630 cm^{-1} due to the *N*-acetyl group and 1750 cm^{-1} due to the acetate group respectively (Figure 1(2)). The ^1H NMR spectrum (CD_2Cl_2) of the fraction showed broad peaks at δ 1.5–2.2 (CH_3CO_2 and $CH_3C(O)N$), 3.5 (CH_2N), a sharp peak at 2.7 (CH_3SO_3), and very broad signals at 3–5 (protons of cellulose main chain). From these data it was concluded that the methanol-insoluble fraction was a graft copolymer (2). Anal. Found: C, 47.95; H, 6.37; N, 5.34; S, 3.23. From these analytical data of C and N values, the average graft chain length per cellulose diacetate unit (*n* value in 2) was calculated as 1.75. The average absolute length of the graft chain is 3.24 (1.75/0.54). A ^1H NMR spectrum of the methanol-soluble fraction confirmed the presence of the homopolymer of MeOZO.

Analytical data on which the calculation of Table VII is based: Sample 11: C, 46.15; H, 5.88; N, 3.99; S, 3.88. Sample 13: C, 50.80; H, 7.51; N, 10.42; S, 1.58. Sample 14: C, 50.32; H, 6.81; N, 5.44; S, 3.34.

Hydrolysis of Graft Copolymer of Cellulose.[13,14] A sample copolymer, cellulose-*graft*-poly(*N*-acetylethylenimine), was prepared by inducing the MeOZO polymerization with an initiator of tosylated cellulose. Anal. Found: C, 47.18; H, 4.96; S, 9.47; Cl, 1.42. These data give the DS of tosylation = 0.95. The product graft copolymer gave analytical data: C, 48.16; H, 5.71; N, 2.15; S, 6.54. From these C and N values, the molar ratio of [MeOZO]/[cellulose] was 0.67. The graft copolymer (0.204 g) was dissolved in 200 mL of 0.1 N $NaIO_4$ aqueous solution and stirred in the dark at room temperature for a week. The residue was collected, washed, and dissolved in 50 mL of 28% ammonia to keep the system alkaline. Powdered $NaBH_4$ (300 mg) was added to the solution to reduce $NaIO_4$ with stirring overnight. Then, 2 N acetic acid was added to neutralize the excess $NaBH_4$. The reaction mixture was filtered and washed. Polyalcohols thus obtained were further decomposed by refluxing in a 90% formic acid solution (50 mL) for 24 h. After concentration in vacuo, a 2 N H_2SO_4 aqueous solution (100 mL) was added to the residue and heated at 100 °C for 5 h to achieve thorough decomposition of the polyalcohols. The mixture was concentrated in vacuo and neutralized. Then, the product poly(ethylenimine) was extracted several times with $CHCl_3$. The $CHCl_3$ solutions were combined, dried over Na_2SO_4, and subjected to evaporation to give 0.04 g of waxy materials, which were analyzed by gel permeation chromatography.

Measurements. ^1H NMR spectra were recorded on a Hitachi R-20B (60 MHz) nuclear magnetic resonance spectrometer. A Hitachi 260-50 IR spectrophotometer was used for IR measurements. Gel permeation chromatography (GPC) analysis was carried out with a Jasco Trirotar liquid chromatograph with a Shodex GPC-A-804 column with $CHCl_3$ as an eluent.

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Registry No. (Cell-OH)(MeOZO) (graft copolymer), 114377-68-3; (Cell-OH)(EtOZO) (graft copolymer), 114377-69-4; (Cell($OAc)_2$OH)(MeOZO) (graft copolymer), 114377-70-7; (Cell-($OAc)_2$OH)(EtOZO) (graft copolymer), 114377-71-8.

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Poly(anhydrides). 2. One-Step Polymerization Using Phosgene or Diphosgene as Coupling Agents

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ABSTRACT: Two approaches for one-step solution polymerization of poly(anhydrides) at ambient temperature were developed. In the first approach highly pure polymers (>99.7%) were obtained by the use of sebacoyl chloride, phosgene, or diphosgene as coupling agents and poly(4-vinylpyridine) or K_2CO_3 as insoluble acid acceptors. In this approach, the polymer is exclusively soluble in the reaction solution and the only byproduct formed is the insoluble acid acceptor–hydrochloric acid salt. Polymerization of sebacic acid with phosgene, either as a gas or in solution, or diphosgene as a coupling agent with triethylamine as an acid acceptor yielded a polyanhydride with a weight average molecular weight up to 16300. This poly(anhydride) was contaminated with Et_3N·HCl (up to 80%, mol %). The use of insoluble acid acceptors gave pure polymers (>99.7%) with a weight average molecular weight up to 13950. The second approach for one-step synthesis of pure poly(anhydrides) was the use of an appropriate solvent where the polymer is exclusively soluble but the corresponding polymerization byproduct (e.g., Et_3N·HCl) is insoluble. Under this condition polymerization of sebacic acid gave the best results in *N,N*-dimethylformamide and in toluene.

Introduction

Several studies have shown that poly(anhydrides) have unique properties: they are biodegradable, and display surface erosion, and erosion rates can be changed several thousand-fold by simple changes in the choice of monomer.[1-4] However, approaches for synthesizing highly pure poly(anhydrides) have yet to be developed. In a previous report[5] we described an improved melt–polycondensation method in which poly(anhydrides) were synthesized from highly pure prepolymers under optimized conditions. Although high molecular weight pure polymers were obtained,[5] this method could be applied only to heat-stable monomers. On the other hand, solution polymerization is well-suited for heat-sensitive monomers such as poly(anhydrides) of dipeptides and therapeutically active diacids.

A variety of solution polymerizations of poly(anhydrides) at ambient temperature have been reported.[6-9] Partial hydrolysis of diacid chloride in the presence of pyridine as an acid acceptor yielded very low molecular weight polymers (e.g., for poly(terephthalic anhydride), MW was 2100).[8] The use of dehydration agents may also effect poly(anhydride) formation.[9] The use of *N,N*-bis(2-oxo-3-oxazolidinyl)phosphoramido chloride, dicyclohexylcarbodiimide, and chlorosulfonyl isocyanate as coupling agents have been reported.[9] These coupling agents yielded impure polymers of low molecular weight. In all previously reported methods the final products contained polymerization byproducts (e.g., amine–hydrochloride, dehydration agents residues) which had to be removed by washing with protic solvents. This last purification step may cause hydrolysis of the polymer (vide infra). In addition, the need for diacid chloride prepolymers of high purity requires an additional synthetic step.

Dichloroformate (phosgene) is a reactive gas that is commonly used in organic synthesis.[10] Yet, its vapor toxicity limits its applicability. Trichloromethyl chloroformate (diphosgene) is a phosgene dimer and can be viewed as a liquid phosgene substitute.[11] The use of diphosgene has advantages over phosgene:[11] (1) it is a liquid with low vapor pressure at room temperature, (2) reactions are simpler to perform as no elaborate traps are needed, and (3) it can be weighed directly. Diphosgene has been used for various applications in organic synthesis. Alcohols react with diphosgene to give the corresponding carbonate or in the presence of amine base (e.g., pyridine) the chloroformate.[12] Isocyanates and ureas are prepared from the reaction of diphosgene and amine. *N*-Carboxy-α-amino acid anhydrides were prepared by the reaction of α-amino acids with either phosgene or diphosgene.[13] The use of phosgene in poly(anhydride) synthesis has been previously attempted;[14] however, only sebacic acid oligomers were obtained (DP = 7).

In searching for an alternative synthetic method, we sought an approach where sensitive diacids could be converted to the corresponding polymer, at ambient temperature, without subsequent purification steps. We now report on new ways for synthesizing poly(anhydrides) using dicarboxylic acid chloride, phosgene, or diphosgene as coupling agents and a removable acid acceptor to effect a one-step polymerization of dicarboxylic acids. These coupling agents are suitable for one-step polymerizations whereby the only byproduct formed is a hydrochloric acid–acid acceptor salt. This acid acceptor is typically an amine base or potassium carbonate. This salt can be removed from the polymerization mixture by either (1) using an insoluble acid acceptor (e.g., cross-linked polyamides, inorganic bases) (eq 1) or (2) using solvents that dissolve exclusively either the poly(anhydride) or the hydrochloric acid–acid acceptor salts (eq 2). In both cases, the byproduct or the precipitating polymer is isolated by simple filtration.

In this study we investigated two approaches for one-step solution polymerization using phosgene, diphosgene, and sebacoyl chloride as coupling agents. In the first approach the effects of various insoluble bases (e.g.,

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