Selective Aminolysis of Mixed Esters of Cellulose

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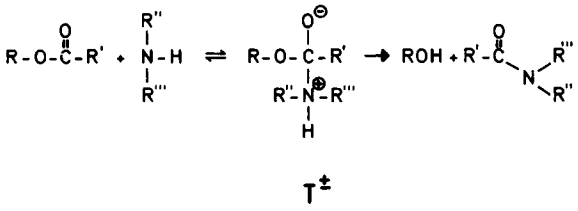
Synopsis

Aminolysis of cellulose esters was investigated. Of the amines tested (pyrrolidine, *n*-butylamine, *sec*-butylamine, 2,2-dimethylpropylamine, piperidine, cyclohexylamine, morpholine), pyrrolidine was the most reactive. The rate of aminolysis by pyrrolidine was approximately the same in dioxane as in dimethyl sulfoxide (DMSO). Using pyrrolidine in DMSO, the relative order of reactivity of the cellulose esters studied was acetate > butyrate ≫ phenylpropionate. With two mixed esters, cellulose acetate 2-phenylpropionate and cellulose acetate polystyrene carboxylate, deacetylation could be achieved with high specificity. Pyrrolidine in DMSO may also be used to perform a controlled deacetylation of cellulose triacetate in a homogeneous solution down to a degree of substitution of about 0.05. The aminolysis conditions did not cause any degradation of the cellulose chains.

INTRODUCTION

A method for grafting well-defined polystyrene chains of relatively low molecular weight onto cellulose acetate has been developed in this laboratory.[1] In this method the anionic end group of living polystyrene was transformed into a carboxylic acid chloride group, which was then allowed to react with the hydroxyl groups of a partially acetylated cellulose. In this way, a series of graft copolymers of varying polystyrene content and chain length was prepared. We were interested also in obtaining the corresponding polystyrene-grafted celluloses, free of acetate groups, for studies of their properties compared to conventional cellulose graft copolymers. For this purpose it was necessary to remove the acetyl groups from the polystyrene-grafted cellulose acetate without appreciably affecting the ester links between the polystyrene grafts and the cellulose backbone.

In the mechanism suggested for aminolysis of esters, a zwitter ionic intermediate $T^{\pm}$ is formed followed by C–O bond cleavage and proton transfer.[2] It is reasonable to assume that the rate of formation and breakdown of such a tetrahedral intermediate is sensitive to steric effects. Thus, the aminolysis of bulky esters should be comparatively slow. This led us to investigate the scope of aminolysis as a method for specific deacetylation of mixed cellulose esters and



$T^{\pm}$

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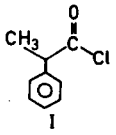
for the removal of acetate groups from specific positions (C-2, C-3, or C-6) of the anhydroglucose units of cellulose triacetate. The steric crowding around both the ester group and the amino group has been varied, and the reactions were performed in different solvents.

EXPERIMENTAL

Ultraviolet spectra were recorded in DMSO on a Varian Cary model 118 spectrophotometer, and IR spectra, on a Perkin–Elmer model 237 infrared spectrophotometer. ^{1}H-NMR spectra were obtained on a Perkin–Elmer R-12 instrument (60 MHz, solvent $CDCl_3$), and ^{13}C-NMR spectra, on a Varian CFT-20 (80 MHz, solvent DMSO-d_6, temp. 100°C).

Synthesis

2-Phenylpropionic Acid Chloride (I). 2-Phenylpropionitrile was prepared from benzyl cyanide and methyl iodide, but substituting sodium hydride in tetrahydrofuran (THF) for sodium in ammonia.[3] The reported purification procedure[4] removed unchanged benzyl cyanide but not the dimethylated product, 2-methyl-2-phenylpropionitrile. Thus, to minimize dimethylation, only about 75% of the theoretical amount of sodium hydride was used. The purified[4] nitrile was hydrolyzed to the corresponding carboxylic acid by treatment with a boiling mixture of water, sulfuric acid, and acetic acid (1:1:1) for 1 hr. The reaction mixture was diluted with water and extracted with chloroform.



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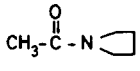
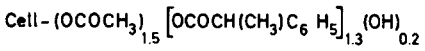
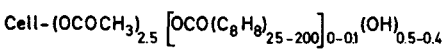


II



III



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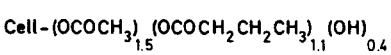


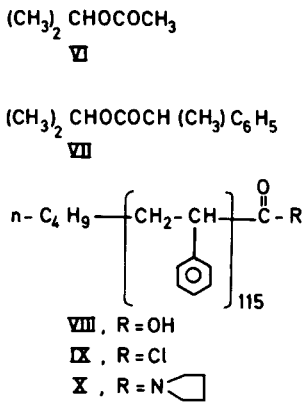
V

The chloroform phase was extracted with saturated aqueous sodium bicarbonate. The aqueous extract was acidified using concentrated HCl and extracted with chloroform. Drying (sodium sulfate) and evaporation of the solvent gave crude 2-phenylpropionic acid. It was converted to the acid chloride by heating with excess thionyl chloride in toluene. The product was distilled at reduced pressure (temp. 85°C, 2 kPa). The overall yield was ~35% based on benzyl cyanide. According to NMR, the product consisted of a mixture of 2-phenylpropionic acid chloride (I), δ 1.6 (*d*, 3 H), δ 4.1 (*q*, 1 H), δ 7.3 (broad *m*, 5 H), and 2-methyl 2-phenylpropionic acid chloride, δ 1.7 (*s*, 6 H), δ 7.3 (broad *m*, 5 H); ratio > 15:1.

1-Acetylpyrrolidine (II). Acetyl chloride, diluted with dichloromethane, was added to an excess of pyrrolidine in dichloromethane. The mixture was washed with saturated potassium carbonate solution and the solvent was evaporated. The product was purified by chromatography on silica gel using acetone as eluent. The amide obtained was pure according to NMR and gas–liquid chromatography (GLC). NMR: δ 1.5–2.2 (*m*, 4 H; CH_2-CH_2-N), δ 2.0 (*s*, 3 H, CH_3), δ 3.2–3.8 (*m*, 4 H).

1-(2-Phenylpropionyl)pyrrolidine, 1-Butyrylpyrrolidine, 1-Propionylpyrrolidine, and 1-Hexanoylpyrrolidine. These were prepared in the same way as 1-acetylpyrrolidine using the appropriate acid chlorides. NMR signals of 1-(2-phenylpropionyl)pyrrolidine at δ 1–2 (*m*, 7 H), δ 3–4 (*m*, 5 H), δ 7.1–7.5 (broad *m*, 5 H).

1-(Polystyrenecarbonyl)pyrrolidine (X). Polystyrene carboxylic acid (VIII, $\overline{M}_n$ = 12,100, 50 mg)[1] was converted to the acid chloride IX by heating with excess thionyl chloride in toluene. The toluene and thionyl chloride were evaporated *in vacuo*. Pyrrolidine (1 ml) and pyridine (50 mg) were added. After



heating at 65°C for 10 min the solvents were evaporated *in vacuo*. According to IR spectroscopy and thin-layer chromatography (TLC) the conversion was complete.

Isopropyl 2-Phenylpropionate (VII). 2-Phenylpropionic acid chloride (200 mg) in THF (1 ml) was treated with isopropyl alcohol (1 ml) and pyridine (0.5 ml) at room temperature. After stirring for about 2 hr dichloromethane was added. The mixture was washed with saturated sodium bicarbonate solution and dried, and the solvent was evaporated *in vacuo*. NMR: δ 1.1 (*d*, 3 H), δ 1.2 (*d*, 3 H), δ 1.5 (*d*, 3 H), δ 3.6 (*q*, 1 H), δ 5.0 (septet, 1 H), δ 7.2 (broad *m*, 5 H).

Cellulose Acetate 2-Phenylpropionate (III). 2-Phenylpropionic acid chloride (I), (5 g) was added to cellulose acetate [2.5 g, degree of substitution (DS) 1.5] dissolved in dry pyridine (50 ml). After heating at 85°C for 45 min, the product was isolated by precipitation in methanol and filtration. It was dissolved in dichloromethane, precipitated in diethyl ether, filtered off, and dried (yield 3.2 g). The molar ratio of acetyl groups to 2-phenylpropionyl groups was found to be about 1.2:1 according to NMR (ratio of acetyl protons to aromatic protons 0.72:1).

Alcoholysis of Cellulose Acetate 2-Phenylpropionate (III). The mixed cellulose ester III (0.125 g) was dissolved in DMSO (2 ml). Anisole (0.0179 g)

was added as an internal standard for GLC quantification. A mixture of DMSO (1 ml) and isopropyl alcohol (1 ml) containing sodium isopropylate (2 mg) was added. After 10 sec at room temperature, a sample was taken from the reaction mixture and the polymer precipitated in diethyl ether. The ether solution was analyzed by GLC for content of the two esters isopropyl acetate (VI) and isopropyl 2-phenylpropionate (VII). (Determination of isopropyl acetate: 20% Carbowax TPA, 50–130°C, 8°C/min; isopropyl 2-phenylpropionate: 10% Carbowax 20 M, 50–180°C, 8°C/min).

Aminolysis of Cellulose Acetate. Cellulose acetate (Eastman 40% acetyl, DS 2.5, 5 g) was swollen in pyrrolidine (50 ml). After heating the gel at 60°C for 15 hr, the IR absorption of 1740 cm^{-1} (ester C=O) had been completely replaced by a band at 1635 cm^{-1} (amide C=O). Diethyl ether was added and the polymer was removed by filtration. Pyrrolidine and diethyl ether were evaporated from the filtrate leaving a high-boiling fraction (4.4 g). This was analyzed by NMR, IR, and GLC and was found to consist of 1-acetylpyrrolidine by comparison with the authentic material (see above). In a separate experiment an internal standard (1-propionylpyrrolidine) was added along with the pyrrolidine and the amount of 1-acetylpyrrolidine formed was determined by GLC (conditions: 5% Castorwax, 170°C). According to this analysis the cellulose acetate contained 39% acetyl (standard acetyl determination by saponification/titration: 39%).

Degradation Study

Cellulose triacetate (Fluka, 3.0 g) was dissolved in dimethylformamide (DMF, 30 ml). Pyrrolidine (20 ml) was added. After heating at 80°C for 80 min, the excess pyrrolidine was distilled off at reduced pressure from the polymer solution. A sample (5 ml) of the polymer solution was withdrawn and added to methanol. The precipitated, partially aminolyzed cellulose acetate sample was redissolved in pyridine and again precipitated in methanol. The sample was dried at 50°C *in vacuo* for several hours. Its acetyl content was found to be about 30% by GLC quantification of the amide formed on complete aminolysis as described above. To the remaining solution of partially aminolyzed cellulose acetate in DMF, acetic anhydride (20 ml) and pyridine (20 ml) were added. The mixture was stirred at room temperature for 18 hr, precipitated in methanol, washed, and dried *in vacuo*.

The molecular weights of the cellulose triacetates were determined by measurement of their solution viscosities using an Ubbelohde viscosimeter. Procedure and calculations were according to ref. 5. The viscosity-average molecular weights of the original cellulose triacetate and that obtained via partial aminolysis and reacetylation were found to be 91,000 and 96,000, respectively. According to the manufacturer, the molecular weight of the original cellulose triacetate ranged 72,000–74,000.

Aminolysis Rate Studies

The general procedure described below was used to determine the rates of aminolysis of cellulose triacetate and the cellulose esters III and V by pyrrolidine.

The cellulose ester (2.0 g) was dissolved in DMSO or dioxane (25 ml). Pyr-

rolidine (15 ml) and an appropriate amount of the internal standard (1-hexanoylpyrrolidine) were added. The solution was heated and samples were taken at suitable intervals. The cellulose polymers in the samples were removed by precipitation in methanol. The solutions were analyzed by GLC for their contents of amides (3% Versamide 900, 110–180 °C, 8°C/min).

Screening tests of the relative reactivities of various amines (pyrrolidine, *n*-butylamine, *sec*-butylamine, 2,2-dimethylpropylamine, piperidine, cyclohexylamine, and morpholine) were performed by dissolving cellulose triacetate (5 wt %) in a solution (2.5*M*) of the amine in DMSO. The mixtures were then heated at 85°C for 45 min. The polymers were precipitated in methanol, washed, and dried. Their residual acetyl content was determined by aminolysis as described above for cellulose triacetate.

Deacetylation of Polystyrene-Grafted Cellulose Acetate (IV) by Aminolysis

A polystyrene-grafted cellulose acetate (composition according to Table I) was prepared.[1] This copolymer (210 mg) was dissolved in pyrrolidine (3 ml). After heating at 60°C for 30 min the copolymer (still in solution) was recovered by precipitation in dichloromethane/diethyl ether (3:2) followed by filtration, washing, and drying *in vacuo*. The acetyl content in the polymer was found to be 4.7% by GLC quantification of the amide formed on complete aminolysis as described above. The solvents from the combined filtrates and washings were evaporated *in vacuo*, leaving a residue which was analyzed by TLC on silica gel using dichloromethane as eluent. A UV-absorbing substance having the same mobility as the amide X (see above) was observed (R_f = 0.8). The material was purified by passing it through a small column of silica gel eluted with dichloromethane. The polystyrene content was found by UV measurements at 260 nm to be less than 5 mg.

RESULTS AND DISCUSSION

When cellulose triacetate was treated with pyrrolidine, deacetylation occurred. By comparison with authentic material, it was found that 1-acetylpyrrolidine (II) had been formed in high yield. A quantitative determination by GLC of the 1-acetylpyrrolidine formed on complete deacetylation of cellulose acetate showed that the theoretical quantity of this compound had been formed. Typical plots of the conversion versus time for aminolysis of cellulose triacetate with excess pyrrolidine in DMSO and in dioxane are given in Figure 1. The cellulose acetate started to precipitate from the reaction mixtures when the acetyl content

TABLE I
Composition of Polystyrene-Grafted Cellulose Acetate before and after Aminolysis

	Polystyrene,[a] wt %	Degree of substitution (DS)	
		Polystyrene groups	Acetyl groups
Before aminolysis	55[b]	0.027	2.4
After aminolysis	62	0.026	0.5

[a] $\overline{M}_n$ = 12,100, $\overline{M}_w/\overline{M}_n$ = 1.04.
[b] Calculated from UV measurements.

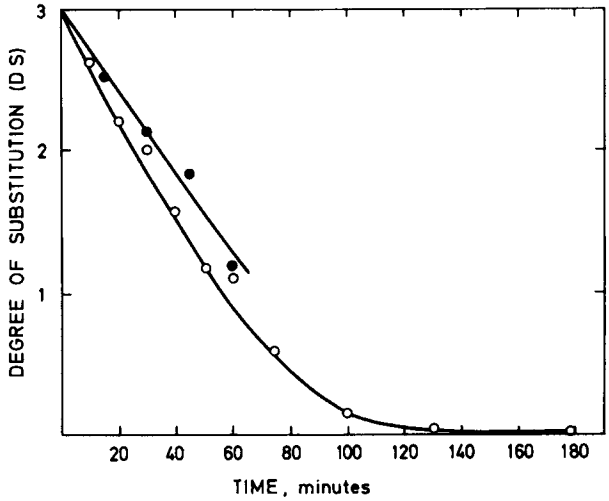


Fig. 1. Aminolysis of cellulose triacetate using pyrrolidine in (○) DMSO and in (●) dioxane. DS vs. time. Temp.: 90 °C; other conditions; see Experimental section.

fell below about 1.4% (DS 0.05) and 28% (DS 1.5), respectively, when DMSO and dioxane were used together with pyrrolidine. In addition to using GLC, the course of the deacetylation could be conveniently followed by infrared spectroscopy.

Approximate rates of aminolysis of several acetate esters other than cellulose acetate were also determined. According to their reactivity against pyrrolidine, we found that the esters investigated could be divided into three groups. Aminolysis of the first group of esters (cellulose acetate, cellobiose octaacetate, and inosityl hexaacetate) was approximately 15 times faster than that of the second group (1,2-diacetoxypropane and 2-methoxyethyl acetate) and several hundred times faster than that of the third group (*n*-butyl acetate, cyclohexyl acetate, and 2,4-diacetoxypentane). It appears that the rate of aminolysis is quite sensitive to the presence of vicinal oxygen-containing substituents.

In the aminolysis of cellulose acetate, degradation of the cellulose chain under the mild basic conditions was considered unlikely. Evidence for this view was obtained as follows. Cellulose triacetate was aminolyzed to a DS of 1.6 using pyrrolidine in DMF. The liberated hydroxyl groups were reacetylated (acetic anhydride/pyridine) before molecular weight determination. Comparison of the viscosity-average molecular weights of the untreated and the pyrrolidine-treated cellulose triacetates showed that no degradation of the cellulose chains had occurred during the aminolysis reaction.

The influence of amine structure on the rate and selectivity of aminolysis of cellulose triacetate in DMSO was briefly studied. The relative rates of the aminolysis using various amines were determined by comparing the acetyl contents in the cellulose acetates obtained after a certain time of treatment. Pyrrolidine was the most reactive amine of those tested and, except for *n*-butylamine, the other amines hardly caused any deacetylation under the conditions chosen (see Table II).

In the selectivity investigation, cellulose triacetate was aminolyzed to DS ~1.5 using pyrrolidine, *sec*-butylamine, cyclohexylamine, neopentylamine, or pi-

TABLE II
Acetyl DS of Cellulose Triacetate after Aminolysis using Various Amines in DMSO[a]

Amine	DS
Pyrrolidine	2.2
n-Butylamine	2.5
sec-Butylamine	2.9
2,2-Dimethylpropylamine	2.8
Piperidine	2.8
Cyclohexylamine	2.9
Morpholine	3.0

[a] Conditions: see Experimental section.

peridine in DMSO. The distribution patterns of the acetyl groups in the anhydroglucose units of the partially deacetylated celluloses obtained were then investigated by ^{13}C-NMR. The acetate methyl resonances of cellulose triacetate were not completely resolved. However, resonances owing to the three acetate carbonyl carbons were well resolved.[6,7] The acetyl groups in all products were found to be essentially randomly distributed over the 2-, 3-, and 6-positions of the anhydroglucose rings. Minor differences in the distribution patterns, however, could not be detected by this method. It is possible that, although the aminolysis reaction itself was selective, subsequent base-catalyzed migration of the acetyl groups occurred,[8] leading to a more random distribution of the acetyl groups. In any case, one may conclude that aminolysis of cellulose triacetate cannot be utilized as a method for preparation of cellulose mono- or diacetates having their acetate groups at specific positions in the anhydroglucose units.

The original purpose of this investigation was to find a method for selective removal of the acetyl groups from celluloses esterified[1] both with acetic acid and with polystyrene carboxylic acids (copolymers of type IV). The selectivity was first treated on the model mixed cellulose ester III derived from acetic acid and 2-phenylpropionic acid. The latter acid is used as a model compound for polystyrene carboxylic acid. When the mixed cellulose ester III was treated with sodium isopropylate in isopropyl alcohol/DMSO, considerable amounts of the esters VI and VII were detected after a very short reaction time (10 sec, room temp.). This result discouraged us from further attempts to selectively remove the acetate groups by alcoholysis.

The result from an aminolysis of the mixed ester III using pyrrolidine is recorded in Figure 2. As can be seen, the rate of aminolysis of the acetate ester groups was much higher than that of the 2-phenylpropionate groups. These results indicated that it should be possible to remove the acetyl group from the above-mentioned mixed cellulose ester IV, in which one of the acids is polystyrene carboxylic acid, with a high degree of selectivity. These expectations were fulfilled as shown by the following experiments.

A cellulose acetate esterified[1] with polystyrene carboxylic acid (composition, see Table I) was heated in pyrrolidine to remove most of the acetyl groups. After 30 min at 60°C, the copolymer was still in solution. The copolymer was precipitated in a mixture of dichloromethane and diethyl ether (polystyrene with a molecular weight of 12,000 is soluble in this mixture). Its acetyl content was determined to 4.7%. The liquid obtained after removal of the aminolyzed copolymer was found by UV spectroscopy to contain less than 5% of the polystyrene present in the original copolymer.

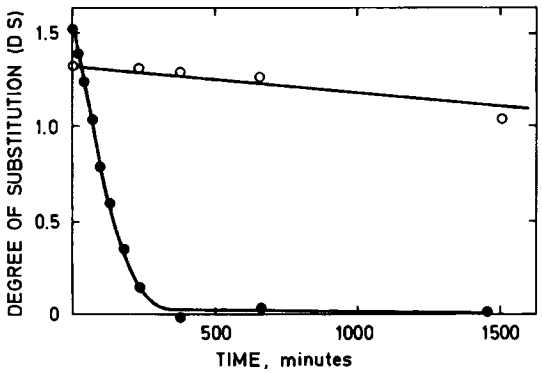


Fig. 2. Aminolysis of cellulose acetate 2-phenylpropionate (III) using pyrrolidine in DMSO. DS vs. time. Temp.: 84 °C; other conditions; see Experimental section; (○) phenylpropionate groups; (●) acetate groups.

The possibility of obtaining selective aminolysis in other mixed cellulose esters was also investigated. Kinetic results from aminolysis of a cellulose acetate butyrate (V) showed that the acetate groups reacted about three times faster than the butyrate groups.

CONCLUSIONS

By using pyrrolidine in DMSO it is possible to deacetylate a cellulose acetate to any desired DS between 3 and about 0.05. Because of the homogeneous conditions, the products have a uniform DS. No cellulose chain degradation occurred.

In the treatment of mixed cellulose ester with pyrrolidine, a selective removal of the various ester groups according to their bulkiness was observed. The rate of aminolysis of acetyl groups was about three times that of butyrate groups. It is likely that cellulose esterified with long-chain fatty acids would react even slower than butyrates. Selective aminolysis may thus have a potential for the preparation of cellulose fatty esters via mixed esters.

By treating a cellulose esterified both with acetic acid and polystyrene carboxylic acid with pyrrolidine, the acetyl groups could be removed with only a negligible loss of polystyrene from the cellulose backbone.

Thus, aminolysis has been shown to be of appreciable utility in the chemistry of cellulose esters.

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