

when k is expressed in (kilograms of solution)^{1/2} (moles)^{-1/2} (minutes)⁻¹.

Light absorbed by the alkaloids initiates a

different reaction which is affected very little by thermal energy.

CAMBRIDGE, MASS.

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The Unesterified Primary Hydroxyls in Acetone Soluble Cellulose Acetate¹

BY F. B. CRAMER AND C. B. PURVES

It is well known that cellulose triacetate, subjected to a mild hydrolysis, loses some of its original solubilities in organic solvents and acquires new ones, among which a capacity to dissolve in acetone is of great technical importance.² Although there have been various opinions as to the cause of this change,³ it now seems certain that an alteration in the average chain length of the cellulose macromolecule is not necessarily involved.⁴ On the other hand, only those acetates which average 2.1 to 2.6 acetyl groups per anhydroglucose unit are soluble in acetone and they must be prepared by the partial hydrolysis of the triacetate rather than by the partial esterification of cellulose.^{3,5} These observations suggest that true acetone solubility depends not only upon the numerical ratio of acetyl to hydroxyl groups⁶ but also on their relative distribution. Whatever this may be, unesterified hydroxyl is confined to the second, third and sixth positions of the glucose residues and is accordingly of a secondary or a primary alcoholic nature. We have found only one attempt to discriminate chemically between the two possible types of hydroxyl, and this was by determining the molar amount of triphenylmethyl chloride which would condense with commercial acetone-soluble acetate dissolved in pyridine.⁷ By assuming that only unesterified primary as opposed to secondary hydroxyls would re-

act under these conditions, approximately one-third of the free hydroxyls were assigned to the primary or sixth position of the glucose units. This assumption was subsequently shown to be unfounded in the case of simple glycosides⁸ and the result required confirmation by an independent method.

In the present work, two commercial acetone-soluble cellulose acetates averaging 0.56 and 0.67 mole of free hydroxyl per glucose unit were condensed, in dilute pyridine solution at 20°, with a large excess of *p*-toluenesulfonyl chloride (tosyl chloride). Samples were isolated at intervals and their sulfur content plotted against time (Fig. 1). About one-third of the hydroxyls were rapidly esterified in the first three hours, then the rate decreased markedly and the tosylation reached a maximum between the third and tenth days, when the reaction was about three-quarters complete. An extremely slow replacement of tosyl groups by chlorine progressed during the subsequent months. The tosylation removed no acetyl groups because the products analyzed for acetyl retained the original quota. It was also improbable that acetyl had wandered from one hydroxyl to another during the reaction, the reagents used not having caused this even with partly acetylated glucoses where such wandering was known to occur readily.⁹ The tosyl groups were therefore considered to be faithful reproductions of the positions of the hydroxyls in the original cellulose acetate. In order to determine these positions, it was hoped that the tosylated acetate could be degraded to partly tosylated glucoses, the examination of which would give the desired information. Attempts to accomplish this degradation with hydrogen bromide in glacial acetic acid,¹⁰ with cold

(1) Delivered at the Boston meeting of the American Chemical Society, September, 1939.

(2) Berl and Koerber, *THIS JOURNAL*, **61**, 154 (1939), studied the effect of low temperatures on such solubility relationships.

(3) The earlier work has been reviewed adequately by Krüger in "Zelluloseacetate," Theodor Steinkopff, Dresden-Blasewitz, 1933, pp. 173-178. See also Marsh and Wood, "An Introduction to the Chemistry of Cellulose," Chapman and Hall, Ltd., London, 1938, pp. 200-210.

(4) Staudinger and Daumiller, *Ann.*, **529**, 219 (1937). This paper has many literature references.

(5) Direct partial acetylation may give products of limited or temporary solubility or which are too degraded to be of technical value. They are omitted from consideration throughout the present article.

(6) Highfield, *Trans. Faraday Soc.*, **22**, 57 (1926).

(7) Sakurada and Kitabatake, *J. Soc. Chem. Ind. Japan*, **37**, (supplementary binding) 604 (1934).

(8) Hockett and Hudson, *THIS JOURNAL*, **56**, 945 (1934).

(9) Helferich, Bredereck and Schneidmüller, *Ann.*, **458**, 111 (1927).

(10) Hess, Littmann and Pfleger, *ibid.*, **507**, 55 (1933), obtained 2,3,6-tritosylacetobromoglucose in 70% yield from tritosyl starch by using this reagent.

72% sulfuric acid,¹¹ or with cold 43% hydrochloric acid¹² produced dark decomposition products. The use of alcoholic hydrogen chloride in a sealed tube¹³ removed the tosyl residues. In these circumstances recourse was had to less drastic methods.

When *p*-toluenesulfonyl esters of glucose were heated with an excess of sodium iodide in acetone, the residues in the primary or sixth position were exclusively and quantitatively replaced by iodine.¹⁴ This method of estimating primary in the presence of secondary hydroxyl proceeded very smoothly in the present case and showed that 0.197 tosyl group was in the sixth position of the anhydroglucose units. Of the available 0.56 hydroxyls in the original acetone soluble acetate, 0.197 or 35% was accordingly of a primary nature. The acetyl and sulfur analyses of the fully tosylated material failed to account for 0.13 mole of original hydroxyl. Failure to reacetylate this completely, together with the presence of traces of chlorine and nitrogen, suggested that the discrepancy was partly due to the accumulation of small analytical errors. The above estimate of 35% primary hydroxyl was therefore a minimum value and the true figure may have been close to 50%.

Pyridinium hydrochloride, in pyridine solution at 100°, rapidly replaced a tosyl group on the primary hydroxyl of methyl glucoside by chlorine.¹⁵ When the fully tosylated cellulose acetate was submitted to this reaction, 0.24 mole of chlorine was introduced and 0.24 or 43% of the original hydroxyls were by inference primary. Thus both estimations went to show that one-third to one-half of the exposed hydroxyls in acetone-soluble acetate were in the sixth position of the anhydroglucose units. It followed that the partial deacetylation of cellulose triacetate to the acetone soluble condition involved the removal of acetyl from primary and secondary positions at approximately the same rate.

The amount of primary hydroxyl corresponded quite closely with the number of tosyl groups entering the cellulose acetate molecule in the initial, rapid reaction. This fact, in conjunction with the occasional preferential reaction of the same group

(11) Monier-Williams, *J. Chem. Soc.*, 803 (1921).

(12) Willstätter and Zechmeister, *Ber.*, **62**, 722 (1929).

(13) Irvine and Hirst, *J. Chem. Soc.*, 1585 (1922).

(14) Oldham and Rutherford, *THIS JOURNAL*, **54**, 366 (1932).

(15) Hess and Stenzel, *Ber.*, **68**, 981 (1935). The fourth position in tosylated methyl glucoside also was chlorinated but in cellulose this is blocked by the glycosidic linking.

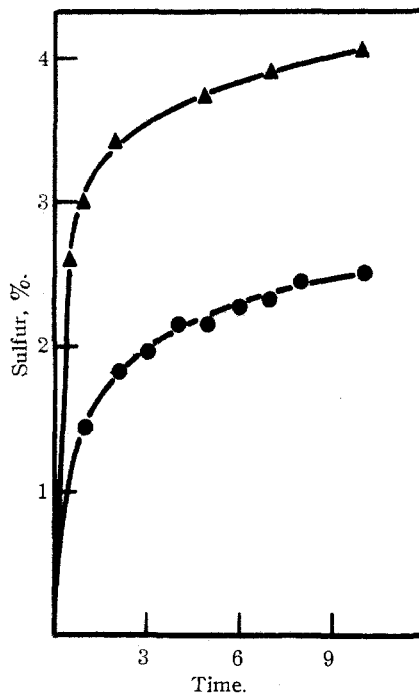


Fig. 1.—Tosylation rate curve of acetone soluble cellulose acetate I. Initial portion, ●; time in hours. Later portion of same curve ▲; time in days.

in methylglycosides,¹⁶ suggested that the product be isolated and examined at the break in the tosylation-rate curve (Fig. 1). Specimens from two different cellulose acetates both contained 0.19 tosyl group per glucose unit, of which no less than 84 and 90% was in the primary position and replaceable by iodine. The form of the tosylation rate curve was thus definitely shown to be determined by the eleven- or twelvefold superiority in reaction velocity of the primary in contrast to the combined rates of the two secondary hydroxyls. There is no reason to believe that this superiority is displayed only toward *p*-toluenesulfonyl chloride. It is therefore probable that other acid chlorides in pyridine solution will acylate up to 0.2 mole of primary hydroxyl in acetone soluble cellulose acetates with rapidity and without causing acetyl wandering. Mixed acylated celluloses of approximately known constitution probably can be prepared in this way.

It is interesting to note that the tosylation rate curve (Fig. 1) is similar in shape to that observed in the heterogeneous acetylation of fibrous cellulose.¹⁷ The break in the latter was considered to

(16) Compton, *THIS JOURNAL*, **60**, 395 (1938); Lieser and Schweitzer, *Ann.*, **519**, 271 (1935).

(17) Hess and Trogus, *Z. physik. Chem.*, **B15**, 157 (1931).

mark the end of a rapid, superficial, intramicellar reaction, involving one-third to one-half of the hydroxyls, and the beginning of a slower reaction governed by the rate of diffusion into the interior of the micelles. As these were undoubtedly penetrated, it is possible that the entire reaction was permutoid in character and conditioned by the greater esterification rate of that third of the hydroxyls which were primary. Such a directly acetylated product might have the same acetyl content and the same average molecular weight as an acetone soluble acetate produced by the partial saponification of the triacetate. The distribution of acetyl and hydroxyl would nonetheless be sharply different, as primary hydroxyl would be present in the latter case and none in the former.¹⁸ Free primary hydroxyl may prove to be necessary for true solubility in acetone.¹⁹

Attempts were made to confirm the presence of iodine in the primary position of the iodo-cellulose acetate by degrading it to 6-iodoglucose. The iodine atom was as unstable toward the usual reagents as the tosyl group was found to be in the earlier experiments. A highly degraded desoxy-cellulose acetate was finally prepared in almost quantitative yield by reducing the iodo acetate with a zinc-copper couple. The fact that glucomethylose (isorhamnose) units were present in the desoxy acetate was supported by the formation of methyl furfural on distillation with aqueous acid, and also by the isolation of isorhamnose as the crystalline, well-defined tetraacetate after the degradation had been completed by standard methods. With the exception of these degradations, all the reactions described proceeded practically quantitatively and without significant alteration in the average chain length as measured by Staudinger's viscosity method.²⁰ The derivatives had a wide range of complete solubility in organic solvents and, chlorinated and degraded products excepted, were fibrous.

Experimental

The Roman numerals refer to the table of viscosities at the end of the article.

(18) Spurlin, *THIS JOURNAL*, **61**, 2222 (1939), dealt mathematically with the arrangement of substituents in cellulose derivatives and reviewed the literature.

(19) The acetone soluble acetate loses this property when heated with glacial acetic acid (U. S. Patent 1,608,946), which probably re-esterifies the primary hydroxyls preferentially. A direct acetylation of cellulose with acid catalysts in presence of sufficient aldehyde may produce acetone soluble products of technical value (U. S. Patent 1,930,145). Here some primary hydroxyls may be protected from acetylation by a prior and selective reaction with the aldehyde.

(20) Staudinger, "Die hochmolekularen organischen Verbindungen," Verlag J. Springer, Berlin, 1932.

Materials.—Two commercial acetone soluble acetates were studied, sample I being an Eastman Kodak Co. and sample II a du Pont Co. product.²¹ The acetyl analyses were 39.7 and 38.6%, respectively, corresponding to averages of 2.44 and 2.33 moles per glucose unit. The ash was 0.063 and 0.044%, the sulfur contents were negligible and both specimens dissolved completely in acetone to almost colorless solutions free of opalescence. They were dried over phosphorus pentoxide *in vacuo* at 55–65°.

High grade pyridine was redistilled from barium oxide shortly before use and the *p*-toluenesulfonyl chloride was recrystallized from ether.

Rate of Tosylation.—Twenty grams (1 mole hydroxyl) and 106 g. of pure tosyl chloride (18.3 moles) were separately dissolved in 115 and 240 cc., respectively, of pyridine. The solutions were separately brought to 20°, quickly mixed by shaking and the mixture kept at 20°. At intervals, 30-cc. samples were withdrawn, quickly cooled to 0° and mixed with equal volumes of ice-cold acetone containing more than sufficient water to decompose the excess tosyl chloride. After five minutes of shaking in a bath at 0°, the mixture was stirred into 600 cc. of distilled water and twenty minutes later the precipitate was filtered, washed well with water and dried over anhydrous calcium chloride. Solution in 40 cc. of acetone, filtration to remove impurities, reprecipitation from water, washing and drying followed. The above procedure diminished local heating of the viscid samples during isolation and thus avoided a replacement of tosyl by chlorine. A white, fibrous, acid-free product was obtained in nearly quantitative yield. After a final drying over phosphorus pentoxide *in vacuo*, analyses for sulfur were made by Waters' method,²² since Carius estimations were erratic and frequently low. The data were plotted in Fig. 1.

The cellulose acetate II gave very similar results, with a sulfur maximum of 4.43% (fourth and eleventh days). This corresponded to a substitution of 2.33 acetyl and 0.46 mole tosyl per glucose unit, *i. e.*, to a substitution of 73% of the original 0.67 mole of hydroxyl. The very slow and partial replacement of primary tosyl by chlorine at 20° was followed on this sample for another four months.

Anal. Calcd. for 2.33 acetyl, 0.39 tosyl and 0.22 chlorine: S, 3.80; Cl, 2.41. Found (III): S, 3.81, 3.79; Cl, 2.40, 2.37.

Maximum Degree of Tosylation.—A 20-g. batch of the acetate, sample I, was withdrawn from the above reaction mixture after ten days, or when the sulfur content was near the maximum. The white, fibrous material was completely soluble in acetone, glacial acetic acid, dioxane, pyridine and chloroform to clear, nearly colorless, viscid solutions. It was insoluble in alcohols, ether and hydrocarbons.

Anal. Calcd. for 2.44 acetyl and 0.43 tosyl groups: acetyl, 31.7; S, 4.16. Found (IV): acetyl, 31.3, 31.5; S, 4.04, 4.08. Nitrogen and chlorine were present in traces.

(21) We wish to thank Drs. J. W. Hill and F. Schulze of the du Pont Co., for the gift of this acetate. It was part of an individually manufactured lot representing the most uniform type of high grade commercial product. The acetyl quoted was 39.3% and a 24% solution in anhydrous acetone had a viscosity of 375 poises.

(22) Waters, *Ind. Eng. Chem.*, **13**, 482 (1920).

A second preparation (acetyl, 31.4; S, 3.9%) was reacylated with pyridine and acetic anhydride. *Anal.* Calcd. for complete substitution with 2.57 moles acetyl and 0.43 moles tosyl: acetyl, 33.0. Found (V): acetyl, 31.6, 31.9.

A 6-Chloro-tosyl Cellulose Acetate.—The dry, tosylated acetate (IV), 2 g., dissolved in 20 cc. of pyridine, was added to the suspension made by passing 1.5 g. of dry hydrogen chloride into 30 g. of pyridine. The pyridine hydrochloride dissolved while the mixture was kept at 80–85° in a glass-stoppered flask. After four hours the dark solution was cooled and stirred into 600 cc. of water and the white precipitate, which filtered normally, was well washed and dried. Solution of this precipitate in acetone, filtration and addition of water to the filtrate gave a colloidal suspension which was separated with difficulty. The material dried to a horny mass which behaved in the same way when reprecipitated from acetone by water. Among the cellulose derivatives studied, the 6-chloro-tosyl acetate was the only one with a marked tendency to disperse in this fashion.

Anal. Calcd. for 2.44 acetyl, 0.19 tosyl and 0.24 moles chlorine: S, 2.04; Cl, 2.86. Found (VI): S, 1.89, 1.92; Cl, 2.80.

A 6-Iodo-tosyl Cellulose Acetate.—Ten grams of the tosylated acetate (IV) and 20 g. of sodium iodide were dissolved in 150 cc. of pure dry acetone. The glass-stoppered bottle containing the solution was kept at 100° for two hours in an autoclave containing additional acetone to compensate the pressure within and without the bottle. After cooling and diluting with acetone, the viscous solution was filtered from the insoluble sodium *p*-toluenesulfonate. The acetone filtrate was poured into much distilled water and the precipitate purified by reprecipitation in the usual way. Tests with silver nitrate and starch solutions showed that iodine, either free or combined, was absent from the final supernatant liquors. The iodo-tosyl acetate was fibrous, had a slight yellow tinge and the same solubilities as the parent tosyl derivative.

Anal. Calcd. for 2.44 acetyl, 0.233 tosyl and 0.197 moles iodine: S, 2.31; I, 7.77. Found (VII): S, 2.33, 2.36; I, 7.94, 7.88.

A duplicate iodination on a smaller scale was heated for sixteen hours at 100° without increasing the iodine content of the product, which was therefore the maximum obtainable. Found: I, 7.7.

Partial Tosylation of Cellulose Acetate I.—The mixture already described was used and the tosylation was interrupted after three hours at 20°. The initial, rapid reaction was then almost over (Fig. 1).

Anal. Calcd. for 2.44 acetyl and 0.19 tosyl groups: acetyl, 35.7; S, 2.07. Found (VIII): acetyl, 35.0; S, 2.00.

A 6-Iodo-cellulose Acetate.—The above partially tosylated derivative (VIII) was heated in 10% acetone solution with twice its weight of sodium iodide at 100° for two hours before isolation of the product.

Anal. Calcd. for 2.44 acetyl, 0.031 tosyl and 0.159 iodine: S, 0.35; I, 7.04. Found (IX): S, 0.32; I, 6.55, 6.51.

Of the original tosyl groups, 0.159 or 84% had been replaced by iodine.

A Desoxy-cellulose Acetate.—The partial tosylation of the acetone soluble acetate (II), 162 g., was carried out as before save that only one-tenth of the previous amount of tosyl chloride was used. This economy was compensated by a reaction time of twenty-four hours instead of three. The mixture was then diluted with 1500 cc. of acetone containing 30 cc. of water and after ten minutes was worked up in the ordinary way; yield, 175 g. or 97%.

Anal. Calcd. for 2.33 acetyl and 0.19 tosyl: S, 2.10. Found (X): S, 2.10.

The iodination of 170 g. of this derivative was with 1400 cc. of acetone and 170 g. of sodium iodide: yield of 6-iodo-cellulose acetate, 165 g. or quantitative. *Anal.* Calcd. for 2.33 acetyl, 0.02 tosyl and 0.17 iodine: S, 0.23; I, 7.67. Found (XI): S, 0.17; I, 7.56, 7.53. Here 89.5% of the original tosyl groups had been replaced by iodine.

The iodo acetate, 20-g. lots, dissolved in 300 cc. of glacial acetic acid on the steam-bath, was stirred vigorously while 100 g. of a zinc-copper couple was added during forty-five minutes. Heating and stirring were continued for a total of five hours. The pasty mass, containing zinc acetate, was then poured into 3000 cc. of water and the precipitate was filtered, washed, dried and extracted with acetone. This extract was centrifuged to remove small particles of zinc and the desoxy acetate precipitated by pouring the concentrated solution into cold, dilute hydrochloric acid. As soon as traces of gray, colloidal zinc had dissolved and the powdery product was perfectly white, it was recovered by filtration, washed well with water and dried. An almost quantitative yield (149 g. from 160 g. of the iodo acetate) of iodine free material was obtained.

Anal. Calcd. for 2.33 acetyl, 0.02 tosyl: acetyl 38.6; S, 0.25. Found (XII): acetyl, 38.6; S, 0.14, 0.25. The reduction had not altered the number of acetyl or tosyl groups.²³

Examination of the Desoxy Cellulose Acetate.—(a) The customary procedure for furfural analysis²⁴ gave 0.0338 g. of phloroglucide from 0.7377 g. of material. This phloroglucide resembled that of methylfurfural in being completely soluble in alcohol and in having a red-brown color. In the same circumstances pure α -methylisorhamnoside, 0.0496 g., gave 0.0274 g. of a similar phloroglucide. Calculation from this preliminary calibration experiment showed the presence of 8.3% of methylisorhamnoside residues in the desoxy cellulose acetate. Calcd. from the 6-iodo acetate, 11.6%.

(b) The degradation of 100 g. of the desoxy acetate was accomplished by alternately heating under reflux with 2% methyl alcoholic hydrogen chloride and reacylating the undissolved residue. When all had been dissolved, the combined, neutralized, alcoholic solutions were concentrated and about 50 g. of crystalline methylglucosides were removed. The residual sirup was hydrolyzed to constant rotation with 5% sulfuric acid on the steam-bath (225 min.), the solution was neutralized, fermented to remove glucose and evaporated to dryness. Acetylation of the residue with acetic anhydride and anhydrous sodium

(23) Our thanks are due to Dr. G. E. Murray for these analyses.

(24) *Ind. Eng. Chem.*, **15**, 748 (1923).

acetate gave 2.7 g. of pure glucomethylose (isorhamnose) tetraacetate with a specific dextrorotation of 21.6° in chloroform (sodium light) and m. p. $145\text{--}146^\circ$ (corr.), not depressed by admixture with an authentic specimen. *Anal.* Calcd. for $C_{16}H_{26}O_{10}(\text{COCH}_3)_4$: acetyl, 51.8. Found: acetyl, 52.3, 52.5.

This authentic specimen was prepared from α -methylglucomethyloside by hydrolysis and acetylation exactly similar to that employed above. As the yield was only 52%, 100 g. of the desoxy cellulose acetate contained the equivalent of $2.7 \times 100/52$ or 5.4 g. of the glucomethylose tetraacetate, *i. e.*, about 25% of the calculated amount.

Viscosities of the above Derivatives.—Staudinger's methods²⁰ were followed, the solvent being glacial acetic acid at $25 \pm 0.1^\circ$ in every case. An Ostwald type viscometer was used and η_{sp}/c became approximately constant in the range c 0.006 to 0.001 molar glucose residues per liter. The Roman numerals in Table I refer to derivatives and analyses already recorded.

TABLE I
VISCOSITIES OF ACETONE SOLUBLE CELLULOSE ACETATES
AND VARIOUS DERIVATIVES

	Calcd. mol. wt.	η_{sp}/c
Derivatives of Acetate I		
Acetate I	264	44.1
Fully tosylated IV	331	39.4
IV, reacetylated V	337	42.9
6-Chlorotosyl VI	298	41.2
6-Iodotosyl VII	322	39.6
Partly tosylated VIII	294	49.1
6-Iodo acetate IX	292	46.6
Derivatives of Acetate II		
Acetate II	260	52.5
6-Chlorotosyl III	324	53.3
Partly tosylated X	289	54.3
6-Iodo acetate XI	282	50.5
6-Desoxy acetate XII	260	6.8 ^a

^a c was 0.03 to 0.01 mole per liter.

Summary

1. *p*-Toluenesulfonyl chloride in pyridine at 20° rapidly esterified about one-third of the free hydroxyl groups in commercial, acetone soluble cellulose acetates. The remainder reacted much more slowly. No removal, and probably no wandering, of acetyl groups occurred.

2. Sodium iodide in acetone at 100° , or hydrogen chloride in pyridine at 85° , smoothly substituted iodine or chlorine atoms for *p*-toluenesulfonyl residues derived from primary, as opposed to secondary, hydroxyls. Analyses of the halogenated mixed cellulose esters indicated that at least one-third of the free hydroxyls in acetone soluble cellulose acetate were in the primary (sixth) positions of the anhydroglucose units.

3. The esterification (1) was interrupted at the end of the initial, rapid reaction and the groups introduced were replaceable to the extent of 85 to 90% by iodine. *p*-Toluenesulfonyl chloride had therefore reacted ten or twelve times as rapidly with the free primary as with the free secondary hydroxyl groups (second and third positions).

4. All the above reactions proceeded almost quantitatively and without appreciable degradation of the cellulose as measured by viscosity methods.

5. The position of iodine in a 6-iodocellulose acetate was confirmed by reduction to a degraded iodine-free desoxy acetate. This gave methylfurfural on distillation with mineral acid and glucomethylose (isorhamnose) after complete hydrolysis. Glucomethylose was identified as the crystalline tetraacetate, m. p. $145\text{--}146^\circ$, with a specific dextrorotation of 21.6° in chloroform.

CAMBRIDGE, MASS.

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