A STUDY OF THE MESYLATION OF CELLULOSE

A thesis submitted by

Richard Roberts

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Richard Roberts

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INTRODUCTION AND HISTORICAL REVIEW

Except for the esterification of cellulose and cellulose acetate with p-toluenesulfonyl chloride (tosyl chloride), the reaction of cellulose and its derivatives with sulfonic acids and sulfonyl chlorides has not been investigated to any great extent. Tosylation studies of cellulose acetates have aroused considerable interest since selective replacement of primary tosyl groups by iodine permits an analysis of the rate and relative extent of esterification of primary and secondary hydroxyl groups (1-8).

An examination of the data of tosylation of cellulose acetates as reported in the literature shows that complete tosylation of all the remaining free hydroxyl groups has not generally been attained, although in some cases the discrepancies were small enough to be ascribed, in part, to accumulated analytical errors (1-3, 7-8).

Malm, et al. (5) found that a cellulose acetate containing 0.57 free hydroxyl per glucose unit before tosylation still had 0.1 to 0.3 free hydroxyl per glucose unit after tosylation. In another sample which originally possessed 1.22 free hydroxyls, 0.50 remained unesterified after 48 hours of tosylation and 0.25 was unesterified after five days' reaction time. Redfarn and Boyle (7) were only able to esterify a maximum of 0.14 hydroxyl after three hours' tosylation of an acetate containing 0.7 free hydroxyl prior to tosylation. Similar values were obtained by Ward (8).

Incomplete esterification of the free hydroxyls by tosylation

might be of little consequence in these esterification studies if all of the primary hydroxyls were covered. It is not known with absolute certainty if only secondary hydroxyls remain unesterified, and this has not been clarified by iodination studies, since there is considerable doubt as to whether only primary tosyl groups are replaced by iodine (5). Although data and conclusions obtained in such work are presumably quite valid as close approximations, the accuracy obtained is subject to question because of the limitations of both the tosylation and iodination reactions.

It has been suggested that incomplete esterification may be due to steric hindrance effects introduced by the relatively large tosyl groups (8-9). It is interesting to note that in tosylation studies of cellulose itself reported in the literature, the maximum degree of substitution (D.S.) generally attained is in the range of 1.5 to 2.0 (4,6, 10-12). A D.S. of 2.0 can be obtained without much difficulty, but higher values appear to be less reproducible, although Hess and Ljubitsch (11) prepared a tosylcellulose having a D.S. of 2.4. In another instance (12) various samples of hydrocellulose were tosylated to give derivatives containing 15.9 and 16.5% sulfur. Since these sulfur contents correspond to D.S. levels of 3.4 and 4.0, respectively, and since the data do not suggest that complete hydrolysis of the cellulose was attained, the reported results are subject to question.

Under certain conditions chlorine is introduced into tosylcellulose. Normally the amount is quite low, but Hess and Ljubitsch (11) prepared a derivative containing 11.93% chlorine and 10.91% sulfur.

By analogy with the tosylation of starch and simple sugars it has been concluded that the chlorine is present in place of a hydroxyl group (30). The presence of nitrogen in some tosylcellulose samples may be due to a combination of pyridine with the chloroester (30). Even with the additional presence of chlorine, complete esterification is not normally obtained.

Because of the lack of complete tosylation of cellulose and its derivatives, the hypothesis of steric hindrance effects as a limiting factor may be valid. Chippindale (13) has suggested that the incomplete tosylation is due to the formation of an outer layer of tosylcellulose which prevents penetration by the tosyl chloride into unreacted portions of the cellulose. When the tosylation reaction involves a heterogeneous system, this might be true, but since complete tosylation is not produced even in homogeneous systems, this explanation appears less plausible than that of steric hindrance.

If steric hindrance is a factor, a reagent chemically similar to tosyl chloride but smaller in molecular size might permit the attainment of complete esterification. Methanesulfonyl chloride (mesyl chloride) might be satisfactory since it has the desired chemical properties and is smaller than tosyl chloride to the extent of one benzene ring in the molecule.

Very little application of mesyl chloride has been made in the field of cellulose chemistry, although it has been used in work with sugars. Helferich and his coworkers (14-15) have prepared numerous

mesyl derivatives of glucose and glucose acetates, and several English workers (16-17) have made mesyl derivatives of arabinose and galactose.

Apparently only one study has been reported on the mesylation of cellulose (18). In this work Wolfrom and his associates were able to introduce 1.6 mesyl groups per glucose unit into cotton linters which had been activated by mercerization with 18% sodium hydroxide; 1.7 mesyl groups were introduced into regenerated cellulose obtained by saponification of a cellulose acetate. Mesylation of a cellulose acetate containing 1.72 acetyl groups per glucose unit resulted in the introduction of 1.03 mesyl groups.

Timell (19) has reported the esterification of propylcellulose with ethanesulfonyl chloride and with α-naphthalenesulfonyl chloride. By the use of a propylcellulose which had a D.S. of 1.67, he was able to esterify all of the remaining hydroxyl groups with ethanesulfonyl chloride within three days. Esterification with the aromatic sulfonyl chloride proceeded more slowly and reached a maximum of only 0.5 α-naphthalenesulfonyl group per glucose unit. These results led Timell to agree that Spurlin's (9) observation (substitution of cellulose in either of the secondary hydroxyl positions may make the remaining secondary hydroxyl less accessible) is reasonable when applied to bulky substituent molecules.

It has been stated that work on monosaccharides shows that the mesyl group is introduced into the molecule more readily than the tosyl group, which suggests that similar results might be expected in the case of cellulose mesylation in spite of previously reported results to the contrary.

PRESENTATION OF THE PROBLEM

One of the primary objectives of the problem was to make a comparative study of the mesylation and tosylation of cellulose. This was done to determine whether use of the mesyl group would contribute evidence in support of the hypothesis stating that steric hindrance effects limit the extent of tosylation and to establish whether similar difficulties occurred in mesylation.

Since mesylation might be expected to proceed to a greater extent than tosylation, another objective was to prepare a mesylcellulose having the highest obtainable D.S. Because the mesylation reaction as applied to cellulose has received such little attention, not much has been known about it, and therefore it was deemed necessary to establish the effect of various experimental variables on the reaction. Variables to be included for study were the type of reaction used to effect esterification, ratios of reactants used, reaction temperature, and activation of the cellulose prior to esterification.

Other objectives arising from the mesylation study were the development of a method for the purification of mesylcellulose and the investigation of side reactions.

The application of tosylation to studies on the mechanism and rate of cellulose acetylation is subject to criticism on the grounds that the validity of the method has not been thoroughly established. Although mesylation might be expected to have possible advantages over the tosylation technique, and perhaps disadvantages as well, an under-

standing of the nature of the reaction should be considered a necessary prerequisite to further studies on the application of the reaction. Since the apparent steric hindrance difficulties encountered in tosylation work have been more evident in work with cellulose rather than with cellulose acetate, it appeared that the possible occurrence of this factor in mesylation studies would be more readily determined by the use of cellulose as the subject material for study.

EXPERIMENTAL PROCEDURES

PREPARATION OF CELLULOSE MATERIALS

Most of the esterification studies were made on a commercial grade of cotton linters obtained from the Buckeye Cotton Oil Company, Memphis, Tenn. The commercial treatment of these linters consisted of a cook with dilute caustic, a chlorine bleach under acid conditions and also under alkaline conditions, and a thorough water wash. An analysis of the treated linters revealed 98.5% alpha-cellulose, 0.067% ash, and 4.1% extractable by hot, 5% caustic solution (20). The degree of polymerization (D.P.) was about 1200 (21).

These linters were passed through a laboratory Abbè mill and then screened through a shaker sieve. Those which passed through a 100-mesh screen but were retained by a 325-mesh screen were reserved for use in the experimental program.

In a few experiments a regenerated cellulose prepared according to the method described by Heuser, et al. (6) was used. Another type of cellulose preparation was made for several experiments by grinding airdry linters in a laboratory pebble mill with rubber-covered steel balls for a 10-day period. Both preparations were intended to possess improved accessibility characteristics in comparison with the original screened linters.

PREPARATION OF MESYL CHLORIDE

Several methods for preparing the acid chloride from alkane-

sulfonic acids and thionyl chloride have been described (22-24) and a procedure based upon these methods was adopted. The methanesulfonic acid was obtained from the Indoil Chemical Company, Chicago, Illinois, and analyzed 95.7% methanesulfonic acid, 1.14% sulfuric acid, 2.42% water, and 0.17% ash (25).

Practical-grade thionyl chloride (Eastman Kodak Company, Rochester, New York) was used to convert the acid to the sulfonyl chloride in the following manner: About 405 grams (four moles) of the acid were placed in a three-neck, round-bottom, one-liter flask which was equipped with a dropping funnel, thermometer, reflux condenser, and mercury-sealed stirrer. Then 450 ml. (five moles) of thionyl chloride were added slowly through the dropping funnel over a minimum period of about one hour. During this period the temperature in the flask was maintained at 10 to 25°C. After addition of the thionyl chloride was completed, the temperature was raised slowly to 150°C.; this required about four to six hours. The crude product was distilled at atmospheric pressure to remove the acid chloride from the charred materials. The distillate was then redistilled, and the fraction collected at 161 to 164°C. was saved for use.

ANALYSIS OF MESYL CHLORIDE

Two methods were combined for the analysis of the mesyl chloride, a gravimetric and a volumetric method. A sample of about 0.5 gram (accurately weighed) of mesyl chloride was mixed with 100 ml. of distilled water in a 250-ml. Erlenmeyer flask, which was then

stoppered and allowed to stand until all of the mesyl chloride had been hydrolyzed. Complete hydrolysis was indicated by the presence of a homogeneous solution, and this was conveniently attained by allowing the mixture to stand overnight.

The solution was then titrated with carbonate-free sodium hydroxide solution, using phenolphthalein as an indicator. The solution was then acidified with 6 N nitric acid, and an excess of 0.1 N silver nitrate was added to precipitate silver chloride, which was determined gravimetrically.

The hydrolysis of mesyl chloride proceeds according to the equation:

$$CH_3SO_2Cl + H_2O = CH_3SO_3H + HCl$$

Since two moles of acid are produced from each mole of acid chloride, one half of the alkali used in the titration is a measure of the sulfonyl chloride content. This is calculated from the relationship:

$$\text{Purity, } \% = \frac{(\text{ml. of NaOH})(\underline{N} \text{ of NaOH})(0.1146)(100)}{(2)(\text{grams of sample})}$$

Since mesyl chloride theoretically contains 30.96% chlorine, the purity of the sample is calculated from a simple ratio after the actual chlorine content of the sample has been determined.

The mesyl chloride used in most of the experimental work was found to be 98.8% pure by the volumetric method and 98.7% pure by the gravimetric method.

MESYLATION OF CELLULOSE

The method of mesylation used varied somewhat as the technique was developed and improved throughout the work. The procedure finally adopted as a standard is as follows: Enough airdry linters to contain 2.0 grams (0.0123 mole calculated as anhydroglucose) of oven-dry cellulose were mercerized in a stoppered bottle with 50 ml. of 18% sodium hydroxide for at least two hours.

The linters were then collected on a coarse fritted-glass crucible and washed repeatedly with absolute methanol until the washings were no longer alkaline to phenolphthalein. The alcohol was displaced by washing five times with anhydrous pyridine which had been prepared for use by storing high-purity pyridine over barium oxide and distilling just before using. In all washing steps the liquid was removed by suction filtration, but care was taken to prevent drying of the cellulose.

Forty to fifty milliliters of pyridine (40 to 50 moles per mole of cellulose) and 10.1 ml. of mesyl chloride (10 moles per mole of cellulose) were added to the sample from the funnel after the liquids had been cooled to about 4°C. A thin sheet of Pliofilm was placed over the mouth of the reaction bottle before the cap was screwed on. The reactants were thoroughly mixed by vigorously shaking the bottle, which was then placed in surroundings maintained at the desired reaction temperature, usually 28°C.

At the end of the reaction period the reaction mixture was

washed into a beaker containing about 600 ml. of cold distilled water; after standing for about an hour, the insoluble product was filtered on a fritted-glass crucible. It was then placed in about 500 ml. of distilled water and allowed to stand overnight.

On the following day the sample was collected on a filter and transferred to a paper extraction thimble; it was then extracted for 12 hours with absolute methanol in a Soxhlet extraction apparatus. The sample was air dried and placed in a small beaker with 25 ml. of formamide (prepared by vacuum distillation of Eastman Kodak Company practical-grade formamide) and then placed in an oven maintained at 65°C. After 30 to 60 minutes the beaker was removed from the oven, and a small portion of the liquid was decanted off and diluted with water. If a precipitate formed, the mixture of mesylcellulose and formamide was diluted with water and filtered; if no precipitate formed, the mixture was filtered directly. The solid material on the filter was washed well with water, rinsed with methanol, and air dried. The extraction procedure with formamide was repeated until the extracting liquid remained colorless or was only slightly colored. This usually required four to five treatments. After extraction, the product was washed thoroughly with water, rinsed with methanol, air dried, and finally dried for at least 12 hours <u>in vacuo</u> at 65°C. It was then placed in a desiccator over phosphorus pentoxide.

When a series of mesylations was to be made to study the effect of some variable, a single batch of activated cellulose was pre-

pared, so that all individual members of the series were run with linters of uniform reactivity.

TOSYLATION OF CELLULOSE

The tosylation method described by Heuser, Heath, and Shockley (6) was adopted with some modification. Activated cellulose samples were prepared as described in the previous section on mesylation. Tosyl chloride (Eastman Kodak Company) was purified by recrystallization from benzene to give a material melting at 67 to 68°C. A solution of this in dry pyridine was prepared so that an aliquot added to 2.0 grams of cellulose contained 23.5 grams of tosyl chloride (10 moles per mole of cellulose) and 50 ml. of pyridine (50 moles per mole of cellulose). The actual tosylation was then carried out in the same manner as the mesylations.

At the end of the reaction period the contents of the reaction bottle were cooled and poured into a cold solution of 100 ml. of acetone and 10 ml. of water. After about 15 to 30 minutes, the mixture was diluted to 500 ml. with distilled water, filtered on a fritted-glass crucible, and washed well with water. The derivative was then allowed to stand overnight in 500 ml. of water; it was then filtered off, washed with water, rinsed with alcohol, and extracted with methanol for 12 hours in a Soxhlet extraction apparatus. Subsequent drying procedures were the same as already described for the mesylated derivatives. Series of tosylations were carried out in a manner analogous to the mesylation series.

MESYLATION AND TOSYLATION OF CELLULOSE DERIVATIVES

A number of experiments were carried out in which mesylcellulose samples were remesylated and tosylated concurrently and tosylcellulose samples were mesylated and retosylated. This type of experiment was run in the following manner: Two one-gram samples of a derivative were placed in a vial with 25 ml. of dry pyridine and placed on a rotator overnight. Five milliliters of mesyl chloride were added to one sample, after cooling, and 11.8 grams of tosyl chloride to the other. The mesylation reaction was allowed to run for 19 hours and the tosylation for 72 hours, both at 28°C. The reaction products were recovered and treated as previously described for mesyl and tosyl derivatives.

SULFUR ANALYSIS

The extent of mesylation and tosylation was followed by analyzing the samples for sulfur by the Parr peroxide bomb method (6, 8, 26). About 0.2 to 0.4 gram (accurately weighed) of the sulfur-containing sample was mixed well with 0.2 gram of benzoic acid, 0.2 gram of sucrose, 1.0 gram of potassium nitrate, and 15 grams of sodium peroxide.

After ignition of the mixture, the bomb was cooled and the melt dissolved in about 200 ml. of hot water. Concentrated hydrochloric acid was added until the solution was just acid to methyl orange indicator. After filtration to remove carbon particles, the solution was heated to boiling, and 20 ml. of 10% barium chloride

solution were added. The mixture was kept warm for several hours and allowed to stand overnight. The barium sulfate was then filtered into a tared Gooch crucible and treated in the conventional manner.

Because this method tends to give somewhat high values due to contamination of the barium sulfate with nitrate ion (the error involved amounts to about 0.05 mesyl or tosyl group per glucose unit), potassium perchlorate was used in place of the potassium nitrate in the later phases of the experimental program.

Sulfur contents were calculated as follows:

$$\text{Sulfur, \%} = \frac{(13.73)(\text{grams of } BaSO_4)}{(\text{grams of ovendry sample})}$$

CHLORINE ANALYSIS

The Parr peroxide bomb (26) was used for chlorine determinations. The fusion was carried out using a mixture of benzoic acid, sucrose, potassium nitrate, sodium peroxide, and the sample being analyzed. After dissolving the melt and acidifying the solution with nitric acid, chloride ion was precipitated as silver chloride and determined gravimetrically. Chlorine contents were calculated as follows:

$$\text{Chlorine, \%} = \frac{(24.74)(\text{grams of AgCl})}{(\text{grams of ovendry sample})}$$

CARBON, HYDROGEN, AND NITROGEN ANALYSIS

Carbon and hydrogen were determined according to Institute

Method 706. Nitrogen was determined by the Dumas procedure described in Institute Method 708. These determinations were made by Mr. Donald Macdonnell of the Analytical Department.

FREE HYDROXYL DETERMINATION

Direct application of the method of Malm, et al. (27) and modifications of it were applied to the measurement of the free hydroxyl content of mesyl- and tosylcellulose. According to the original method, one-gram samples of the cellulose derivative were heated under reflux for 24 hours at 75 to 80°C., using a 5% solution (by volume) of acetic anhydride in pyridine. A sufficient quantity of reagent was added to provide at least three times the theoretical requirement of the anhydride.

After the reaction period, the reactants were diluted with distilled water and titrated potentiometrically to a pH of 9.0 with standard alkali. The differences in titer of the sample and blanks gave a measure of the acetic anhydride consumed by the cellulose derivative.

Variations of the method were used in which the reflux step was abandoned and acetylations were carried out in stoppered vials. One modification involved acetylation for 30 hours at 28°C., using a solution containing four parts by volume of acetic anhydride, one of pyridine, and 1.5 parts of dioxane which served as a diluent. An accurately weighed sample of about 0.2 gram of the cellulose derivative was treated with 2.0 grams (accurately weighed) of the acetylating mix-

ture, and the consumption of anhydride measured as before. This modification was also tried at higher temperatures, 65 to 75°C.

Another modification was made by using the conditions of the original method except that the acetylations were run at 28°C. in stoppered vials and only one-fifth quantities were used. Because of the smaller quantities used, all reagents were measured gravimetrically rather than volumetrically.

The free hydroxyl content of the original derivatives was calculated as follows:

$$\text{Hydroxyl, \%} = \frac{\left[\begin{matrix}\text{ml. of NaOH} \\ \text{for blank}\end{matrix} - \begin{matrix}\text{ml. of NaOH} \\ \text{for sample}\end{matrix}\right] (\underline{N} \text{ of NaOH})(1.70)}{(\text{grams of ovendry sample})}$$

CALCULATION OF THE DEGREE OF SUBSTITUTION

After analysis of the cellulose derivatives for various substituents, calculations of the degree of substitution of these substituents were calculated by means of simultaneous equations in which the following nomenclature is used:

$\underline{W}$ = Degree of substitution of tosyl groups

$\underline{X}$ = Degree of substitution of mesyl groups

$\underline{Y}$ = Degree of substitution of chlorine

$\underline{Z}$ = Degree of substitution of acetyl groups

For Mesylcellulose

$$\text{Sulfur, \%} = 3206\,\underline{X}/(162 + 78.1\,\underline{X} + 18.46\,\underline{Y})$$

$$\text{Chlorine, \%} = 3546\,Y/(162 + 78.1\,X + 18.46\,Y)$$

For Tosylcellulose

$$\text{Sulfur, \%} = 3206\,W/(162 + 154.2\,W + 18.46\,Y)$$

$$\text{Chlorine, \%} = 3546\,Y/(162 + 154.2\,W + 18.46\,Y)$$

For Mesylated Tosylcellulose and Tosylated Mesylcellulose

$$\text{Sulfur, \%} = 3206\,(W + X)/(162 + 78.1\,X + 154.2\,W + 18.46\,Y)$$

$$\text{Chlorine, \%} = 3546\,Y/(162 + 78.1\,X + 154.2\,W + 18.46\,Y)$$

For Acetylated Mesylcellulose

$$\text{Sulfur, \%} = 3206\,X/(162 + 78.1\,X + 18.46\,Y + 42.0\,Z)$$

$$\text{Chlorine, \%} = 3546\,Y/(162 + 78.1\,X + 18.46\,Y + 42.0\,Z)$$

The value of acetyl group substitution was obtained from the experimentally determined hydroxyl content:

$$\text{Hydroxyl, \%} = 1700\,Z/(162 + 78.1\,X + 18.46\,Y)$$

PRESENTATION AND DISCUSSION OF RESULTS

PRELIMINARY MESYLATION STUDIES

In the only reported work on the mesylation of cellulose (18) the reaction was carried out in pyridine. Since esterification of cellulose is frequently carried out successfully under other conditions, a number of orientation experiments were run to determine if some conditions other than those already reported might be more suitable. In this preliminary work the reaction medium used and the activation method applied to the cellulose were the principal factors considered.

Activation methods used included swelling of the linters in anhydrous pyridine, in 18% sodium hydroxide, in 9.5% lithium hydroxide, and dissolving the linters in 86% or 100% phosphoric acid. A variation which was introduced when the swelling was accomplished through the use of inorganic alkalies was the removal of the alkali by a thorough water wash or by washing with absolute methanol.

The various reaction media considered for study included anhydrous pyridine, anhydrous dioxane, a 1:1 solution of pyridine and dioxane, aqueous sodium hydroxide, powdered sodium hydroxide suspended in diethyl ether, quinoline, and triethylamine. Special catalytic effects were sought through mesylations carried out in pyridine containing boron trifluoride, in benzene containing boron trifluoride, and in benzene containing sulfuric acid.

The procedures followed in this phase varied somewhat and

may be summarized as follows. Cellulose samples which were activated by swelling in pyridine (the swelling period being at least 24 hours) were mesylated directly after the pretreatment by the addition of the desired amounts of pyridine and mesyl chloride. In experiments in which the cellulose was activated by swelling in alkali solution, the alkali was removed, after a minimum swelling period of two hours, by washing thoroughly with water or by washing with absolute methanol until the washings were neutral to phenolphthalein. When the water wash was used, the water was subsequently displaced by washing the sample three to five times with absolute methanol. In all cases the alcohol was displaced by washing four to five times with dry pyridine or with the fluid in which the mesylation was to be conducted. The mesylating reagents were then added, and after completion of the reaction, the product was washed well with water, dried, and analyzed for sulfur only.

The results of these orientation studies are summarized in Table I.

TABLE I

INVESTIGATION OF METHODS OF CELLULOSE MESYLATION

Run	Swelling Agent	Wash Liquid	Reaction Medium	Molar[1] Ratio	Reaction Time, days	Sulfur Content, %	Mesyl D.S.
1	Pyridine	--	Pyridine	20:1	1	2.5	0.1
					2	3.6	0.2
					3	3.3	0.2
					7	4.7	0.3
2	Pyridine	--	Pyridine	10:1	1	2.2	0.1
					2	2.4	0.1
					3	3.2	0.2
					7	3.9	0.2
3	NaOH	H_2O	Pyridine	10:1	1	13.9	1.1
					2	15.3	1.2
4	NaOH	H_2O	Dioxane	10:1	1	0.0	0.0
					2	1.4	0.1
5	NaOH	H_2O	1:1 Pyridine-dioxane	10:1	1	0.0	0.0
					2	0.6	0.03
6	NaOH	H_2O	Pyridine	100:1	1	9.4	0.6
7	NaOH	--	18% NaOH	20:1	0.25	0.9	0.04
8	NaOH	H_2O	NaOH in ether	10:1	1	0.0	0.0
9	NaOH	H_2O	H_2SO_4 in benzene	10:1	1	0.3	0.02
					2	0.4	0.02
10	NaOH	H_2O	BF_3 in pyridine	10:1	1	17.8	1.6
					2	11.6	0.8
11	NaOH	H_2O	BF_3 in benzene	10:1	1	0.2	0.02
					2	0.4	0.02
12	NaOH	H_2O	Quinoline	10:1	1	3.9	0.2
					2	7.2	0.4

TABLE I (continued)

INVESTIGATION OF METHODS OF CELLULOSE MESYLATION

Run	Swelling Agent	Wash Liquid	Reaction Medium	Molar[1] Ratio	Reaction Time, days	Sulfur Content, %	Mesyl D.S.
13	LiOH	H_2O	Pyridine	10:1	1 2	6.5 12.5	0.4 0.9
14	NaOH	CH_3OH	Pyridine	10:1	2	22.5	2.5
15	NaOH	CH_3OH	Pyridine	10:1	1 2	22.0 21.6	2.4 2.3
16	NaOH	CH_3OH	Dioxane	10:1	6	1.9	0.1
17	NaOH[2]	H_2O	Triethyl-amine	10:1	1 2	0.4 0.4	0.02 0.02
18	NaOH[2]	H_2O	Pyridine	10:1	1 2	22.7 22.6	2.5 2.5
19	LiOH[2]	H_2O	Pyridine	10:1	0.75 1.67	19.4 20.7	1.9 2.1
20	NaOH[3]	H_2O	Pyridine	10:1	1 2	17.2 20.2	1.5 2.0
21	(Sample dissolved in 86% H_3PO_4, dioxane, ether)			20:1	0.5	2.7	0.1
22	(Sample dissolved in 100% H_3PO_4, dioxane, acetone)			20:1	0.3	0.0	0.0

All reactions run at about 23°C. with cotton linters

[1]Moles of mesyl chloride per mole of cellulose
[2]Regenerated cellulose used for mesylation
[3]Ball-milled linters used for mesylation

An examination of the data in Table I reveals that most of the attempted methods were quite unsatisfactory. It should be pointed out that some of the methods might prove to be quite satisfactory after a more intensive investigation, but for the purposes of the present problem, those which gave derivatives having a low sulfur content were deemed unsuitable for further study.

Activation of the cotton linters by swelling in pyridine resulted in a low degree of mesylation, whereas swelling in 18% sodium hydroxide followed by a water wash to remove the alkali gave greatly increased reactivity. This can be seen by a comparison of Run 3 with Runs 1 and 2. But when the alkali was removed by washing the mercerized linters with absolute methanol (Runs 14 and 15), a considerable improvement was obtained over the results of Run 3. Mercerization, of course, causes a pronounced swelling of the fibers, and since 18% sodium hydroxide was found to be an effective reagent for the activation, it was thought that 9.5% lithium hydroxide, which is a more effective swelling agent than sodium hydroxide (30), might be even more suitable for the activation step. Several experiments (Runs 13 and 19) were carried out using 9.5% lithium hydroxide. All other conditions were the same as those in the experiments in which sodium hydroxide was used, but the extent of mesylation following lithium hydroxide treatment was somewhat less than in the experiments involving the use of sodium hydroxide (Runs 3 and 18). This might be interpreted to mean that some factor other than swelling might be involved in the activation of cellulose.

A recent paper (28) presents evidence to show that the

acylation of cellulose with propionyl chloride in a pyridine medium is more effective when the reaction system is diluted with 1,4-dioxane rather than when an amount of pyridine is used which is greatly in excess of the amount theoretically equivalent to the acid chloride present. Application of this idea was made in Runs 4, 5, and 16, in which a 1:1 pyridine-dioxane solution or dioxane alone was used as the reaction medium. In all cases the amount of mesylation was negligible.

It has also been shown (28) in acylation work that a large excess of the acid chloride or pyridine gives unsatisfactory esterification. Results in accord with this were obtained in a run (Run 6) in which 100 moles of mesyl chloride per mole of cellulose and 50 moles of pyridine per mole of cellulose were used.

A Schotten-Baumann reaction (Run 7) and a modification in which powdered sodium hydroxide suspended in dry ether served as the reaction medium (Run 8) were both very poor. Rigby (10), however, has patented a method in which aqueous sodium hydroxide is used as an esterification medium but large quantities of acid chloride are required. This indicates that more successful mesylation results than those obtained here might be produced by this technique.

Special catalytic effects were sought through the use of sulfuric acid in benzene (Run 8) and boron trifluoride in benzene (Run 9) or in pyridine (Run 10). The amount of sulfuric acid used was 15% of the weight of cellulose, but esterification was not promoted. Boron trifluoride has been recommended as an esterification catalyst (29), and when used

in a pyridine-medium (Run 10), it appeared to be helpful, but when used in a benzene medium (Run 11), the esterification was again negligible. The boron trifluoride was used in the form of the etherate complex (General Chemical Company, New York City) whose catalyst content was 7.6% expressed as boron. The amount of catalyst used, calculated as the trifluoride, was 5% of the weight of cellulose. When run in a pyridine medium, the esterification apparently reached a maximum and then fell off with continuing reaction time. As more effective mesylation methods were developed later, further examination of the use of boron trifluoride was not undertaken.

Malm, et al. (28) have shown that tertiary amines other than pyridine are not very effective in promoting esterification, although β-picoline is an exception to this, since it was as suitable as pyridine. In esterifications made with propionyl chloride they found that quinoline and dimethylaniline were less satisfactory than pyridine whereas α-picoline and γ-picoline were very poor. Similar results were obtained in the present work when it was found that quinoline (Run 12) and triethylamine (Run 17) were unsuitable for mesylation media.

Attempted mesylations of cellulose dissolved in phosphoric acid (Runs 21 and 22) were unsuccessful. Several experiments (Runs 17 to 19) were carried out with regenerated cellulose, and the extent of mesylation was better than that produced when the original linters were treated in an identical manner. In another trial (Run 20) in which linters were used which had been mechanically disintegrated in a

pebble mill, the mesylation results were quite favorable. It appears likely that the improved accessibility of these samples (32) over that of the original linters was a factor involved in the increased esterification obtained. But as later work showed that very satisfactory results could be obtained with the original linters under suitable conditions, little additional use was made of the special cellulose samples.

The preliminary studies showed that pyridine was the most effective medium in which to conduct mesylation and that the best activation of the linters was produced by mercerizing with 18% sodium hydroxide and washing out the alkali with absolute methanol.

PURIFICATION STUDIES

A problem which arose early in the work was the purification of the mesylcellulose derivatives which were generally light to dark brown as a result of the presence of contaminants produced in side reactions which take place between pyridine and mesyl chloride. Similar results have been reported in some tosylation work (3), but the development of color occurred very slowly and to a vastly lesser extent. In this tosylation work it was intimated that the color was associated with the introduction of chlorine into the tosylcellulose but colorless, high-chlorine content tosylcellulose has been reported (11).

In tosylation work the customary method of purification has been to extract the derivatives with methanol (11-12) and also with diethyl ether (6). Washing of the mesylcellulose samples with water, followed by a 12-hour extraction period with methanol, removed a considerable amount of color, but the extracted samples were still brown.

A more ideal purification method, of course, would have involved dissolving the mesyl derivative in an inert solvent and then recovering the sample by precipitation. Numerous organic liquids were examined for their dissolving effect, but no good solvent was found. Solubility tests were made by placing about 0.05 gram of airdry mesylcellulose in about 10 ml. of solvent and then placing the test sample on a rotator for about 12 hours. Solvents tested included pyridine, acetone, chloroform, carbon tetrachloride, dichloromethane, ethyl

acetate, diethyl ether, benzene, dioxane, diacetone alcohol, m-cresol, formamide, dimethylformamide, methyl p-toluenesulfonate, and acetonylacetone.

With the exception of the case involving acetonylacetone, the heating of the solvent and mesylcellulose mixture did not appear to facilitate solution. Wolfrom, et al. (18) heated mesylcellulose in acetonylacetone (b.p. 194°C.) to effect solution. This method was applied in the present work, but it was found that the treatment had to be carried out for several hours to obtain even partial solution. The dissolved portion was readily recovered in a very finely divided form by precipitating the solution into either water or methanol. Because of its finely divided state, the precipitate could not be filtered easily, so it was recovered by centrifuging and decanting the brown supernatant liquid. By repeated washing of the residue with water or alcohol, a creamy white product was ultimately obtained.

A single purification by means of acetonylacetone resulted in a decrease in the sulfur content, but a second purification caused a negligible decrease. Thus, in one instance the original mesylcellulose contained 22.11% sulfur, and after the first purification, the value was 19.70%. After a second purification, there was 19.67% present.

While the solubility tests were being made, it was noted that formamide was quite effective in extracting colored products, although it did not dissolve the mesylcellulose. By carrying out successive extractions with formamide at 65°C., a point was soon

reached at which the separated liquid was colorless or nearly so. The mesylcellulose treated in this manner had a final color ranging from white to dark brown. Samples which had been mesylated for several days or at relatively high temperatures, i.e., 50 to 60°C., were decolorized the least by this method. The majority of the products, however, were finally obtained as light tan solids. Subsequent extraction in a Soxhlet apparatus with acetone or methyl alcohol after the formamide treatment did not bring about further color removal.

Both the sulfur and chlorine contents of the mesylcellulose derivatives were decreased by the formamide treatment. One sample which had 22.49% sulfur and 3.81% chlorine before the extraction contained 21.40% sulfur and 1.98% chlorine after four extractions, and 21.10% sulfur and 1.85% chlorine after six treatments. A comparison of the changes in D.S. for this sample shows that both the calculated mesyl and chlorine content decreased; there were 2.63 mesyl groups and 0.38 chlorine per glucose unit before extraction, and 2.24 mesyl groups and 0.19 chlorine after six extractions. On another sample the sulfur contents after two, four, and eight formamide extractions were 20.08, 19.48, and 19.53% respectively. Both the amount of color removed and changes in sulfur and chlorine content were small after four extractions.

Quantitative runs were made on two samples to determine the loss of material as the result of formamide extraction. One sample, which contained 21.56% sulfur and 1.40% chlorine after the treatments, suffered a loss of 8.7% of the material present before extraction. A second sample, whose analysis after extraction was 21.40% sulfur and

1.98% chlorine, underwent a loss of 6.6%. Four extractions were used on each sample.

In contrast to these tests, a quantitative run was made on a sample treated by heating in acetonylacetone under reflux. After a two-gram sample of mesylcellulose had been treated for 18 hours, 20.5% of the sample (0.42 gram) remained insoluble, 63.7% (1.29 grams) was recovered from solution, and 15.8% (0.32 gram) was unaccounted for.

A comparison of the two methods of purification, i.e., recovery from acetonylacetone solution and extraction with formamide, was undertaken to determine whether there was any marked difference between them. It was sought to establish this through an elemental analysis of the purified products obtained by each method.

Since the mesylcellulose samples are not necessarily composed of uniformly substituted anhydroglucose chains whose elemental analysis could be interpreted with absolute certainty, and because two different samples were used in the study, a comparison of the percentage composition of the purified samples is not informative. Consequently, the comparison was made in the following manner: The percentage values for each element (carbon, hydrogen, oxygen, sulfur, chlorine, and nitrogen) were converted to the relative number of atoms of each; the percentage of oxygen was obtained by difference. All the atoms associated with the mesyl groups (CH_3SO_2-) were deducted from the totals for carbon, hydrogen, and oxygen.

In one calculation, all of the sulfur was assumed to be

contained in the mesyl groups, and the presence of nitrogen, which was present in small amounts, was neglected. In a second calculation a correction was made for the nitrogen content by the assumption that it was present as a complex of pyridine and mesyl chloride. This, of course, is not necessarily the case, but since the purification methods were shown to decrease both the sulfur and chlorine content of mesyl-cellulose, the assumption may be regarded as a reasonable approximation. The correction was then made by the deduction of all the atoms associated with the nitrogen (assumed to be present in the form $C_5H_5N \cdot CH_3SO_2Cl$) from the gross numbers of atoms. This was followed by deducting the atoms associated with the mesyl groups.

After these calculations the remaining atoms constituted the skeletal carbohydrate structure depleted by the oxygen and hydrogen atoms which had been replaced by mesyl and chlorine substitution. Corrections for this, based on the degree of substitution of mesyl groups and chlorine, were made, and the resulting figures were expressed as percentage compositions of the carbohydrate structure. This could then be compared to the theoretical composition of cellulose. The original analytical data are presented in Table II and the results of the calculations in Table III.

TABLE II

ELEMENTAL ANALYSIS OF MESYLCELLULOSE

	Mesylcellulose Purified by Treatment with	
	Acetonylacetone	Formamide
Carbon, %	29.68	28.53
Hydrogen, %	4.22	4.01
Sulfur, %	20.62	22.33
Chlorine, %	2.40	1.53
Nitrogen, %	0.15	0.27
Oxygen, %[1]	42.93	43.33

[1]Determined by difference

TABLE III

COMPOSITION OF THE CARBOHYDRATE SKELETON OF MESYLCELLULOSE

	Mesylcellulose Purified by				Theoretical Composition of Cellulose
	Formamide		Acetonylacetone		
	A[1]	B[2]	A[1]	B[2]	
Carbon, %	45.3	44.4	45.4	44.9	44.4
Hydrogen, %	5.9	5.9	6.2	6.1	6.2
Oxygen, %	48.7	49.8	48.4	49.0	49.3

[1]Effect of nitrogen content neglected
[2]Correction made for nitrogen content

The main conclusion to be drawn from this work is that the two purification methods are comparable in their effect on the mesylcellulose and that neither method appears to cause marked constitutional changes.

On a practical basis, the formamide method is to be preferred over the acetonylacetone treatment, since the former can be carried out more simply and rapidly and a better yield of product is obtained.

The presence of free sulfur in mesylcellulose as the result of the possible decomposition of the various sulfur compounds present during the reaction does not appear likely, since extraction of the formamide-treated samples with carbon disulfide failed to produce a significant change in sulfur content.

EFFECT OF REACTANT RATIOS ON MESYLATION

In previous tosylation and mesylation work reported in the literature, it has been customary to use about 10 moles of the acid chloride and 50 to 75 moles of pyridine per mole of cellulose, but apparently no investigation has been made to determine the most suitable reactant ratios.

Apparently, 10 moles of acid chloride per mole of cellulose has been selected rather arbitrarily in much of the reported work, as have the various other ratios used in work with cellulose derivatives. In all cases an obvious reason for the selected ratio has been to insure

that an adequate excess of acid chloride over the theoretical requirement has been provided. In one instance (6), at least, the use of a large excess of tosyl chloride has eliminated it as a factor to be considered in subsequent esterification-rate studies. As already shown in Table I, there was not a significant difference in the results obtained when 10:1 or 20:1 molar ratios of mesyl chloride to cellulose were used. Although the latter was slightly better, the former was found to be adequate. A 100:1 ratio was unsatisfactory, as has already been discussed.

Experiments were run in which the mesylation was carried out according to the standardized procedure, except that the amount of pyridine used was varied. One to six moles of pyridine per mole of mesyl chloride (10 to 60 moles per mole of cellulose) were used and the results obtained are presented in Table IV.

The introduction of chlorine into mesylcellulose appears to be quite independent of the relative amounts of pyridine and mesyl chloride. The actual mesylation was not affected strongly by the reagent ratio within the range considered. Malm, et al., (28) in describing the esterification of cellulose with propionyl chloride, state that, as a general rule, the amount of pyridine used should be limited to a slight excess over the theoretical amount required to combine with the acid chloride. In the present work this was not found to be the case. The reaction between mesyl chloride and pyridine occurs exothermally, and at low molar ratios the dissipation of this

TABLE IV

EFFECT OF PYRIDINE TO MESYL CHLORIDE RATIO ON MESYLATION

Molar Ratio[1]	% Sulfur		Mesyl D.S.		Chlorine Content			
	Run 38	Run 40	Run 38	Run 40	Run 38 %	Run 38 D.S.	Run 40 %	Run 40 D.S.
1.0	20.6	--	2.12	--	2.05	0.18	--	--
1.2	21.4	21.4	2.28	2.28	1.66	0.13	1.10	0.11
1.4	21.4	20.9	2.31	2.32	1.98	0.16	1.99	0.11
1.6	18.8	20.7	1.84	2.16	4.72	0.22	1.88	0.16
1.8	22.5	21.0	2.46	2.22	1.61	0.16	1.82	0.17
2.0	22.1	21.5	2.48	2.32	2.02	0.19	1.68	0.17
2.2	--	21.4	--	2.32	--	--	1.59	0.17
3.0	--	21.6	--	2.33	--	--	1.40	0.14
4.0	22.0	21.5	2.43	2.38	1.46	0.14	1.95	0.17
6.0	20.9	20.1	2.19	2.02	1.58	0.16	0.72	0.08

[1]Moles of pyridine per mole of mesyl chloride; 10 moles of mesyl chloride per mole of cellulose used in all runs

heat is not very satisfactory. The heat effect can, of course, be minimized by external cooling and by using a slow rate of addition of the mesyl chloride to pyridine. It was, however, difficult to control the liberation of heat when the ratio used was about 1.2:1 or lower; the mesyl chloride was added from a 10-ml. Mohr pipet at a natural flow rate. In some instances the heat generated was sufficient to cause the charring of the linters.

As can be seen from the data, there is no clearly defined trend in the extent of mesylation obtained at various ratios, although

there are indications that the esterification may fall off somewhat at higher ratios. A more practical factor governing the selection of a ratio to be used is the fluidity of the reaction mixture. When the ratio was about 2:1 or lower, the fluidity was low, and it was difficult to insure a thorough mixing of the reagents by shaking the reaction vessel. Consequently, a ratio of 4:1 or 5:1 was used in most of the experimental work.

EFFECT OF TEMPERATURE ON MESYLATION

Previous workers (18) have intimated that the extent of mesylation decreases as the reaction temperature is increased above room temperature. In general this was found to be true, but it was learned further that an optimum temperature (about 30°C.) exists. Duplicate series of mesylations run at various temperatures for 14 hours were conducted to examine this variable, and the results obtained are presented in Table V and Figure 1.

As can be seen from the curves and data, temperature has a very strong influence on the extent of mesylation; both low and high temperatures cause limited amounts of substitution. Chlorine substitution, however, continues to rise with increasing temperature, and the effect becomes quite pronounced as the temperature rises beyond 30°C.

Further studies of the temperature effect were made by mesylating two samples simultaneously, one at 28°C. for 17 hours, the other at 28°C. for the initial four hours of the run and at 59°C. for

TABLE V

EFFECT OF TEMPERATURE ON MESYLATION

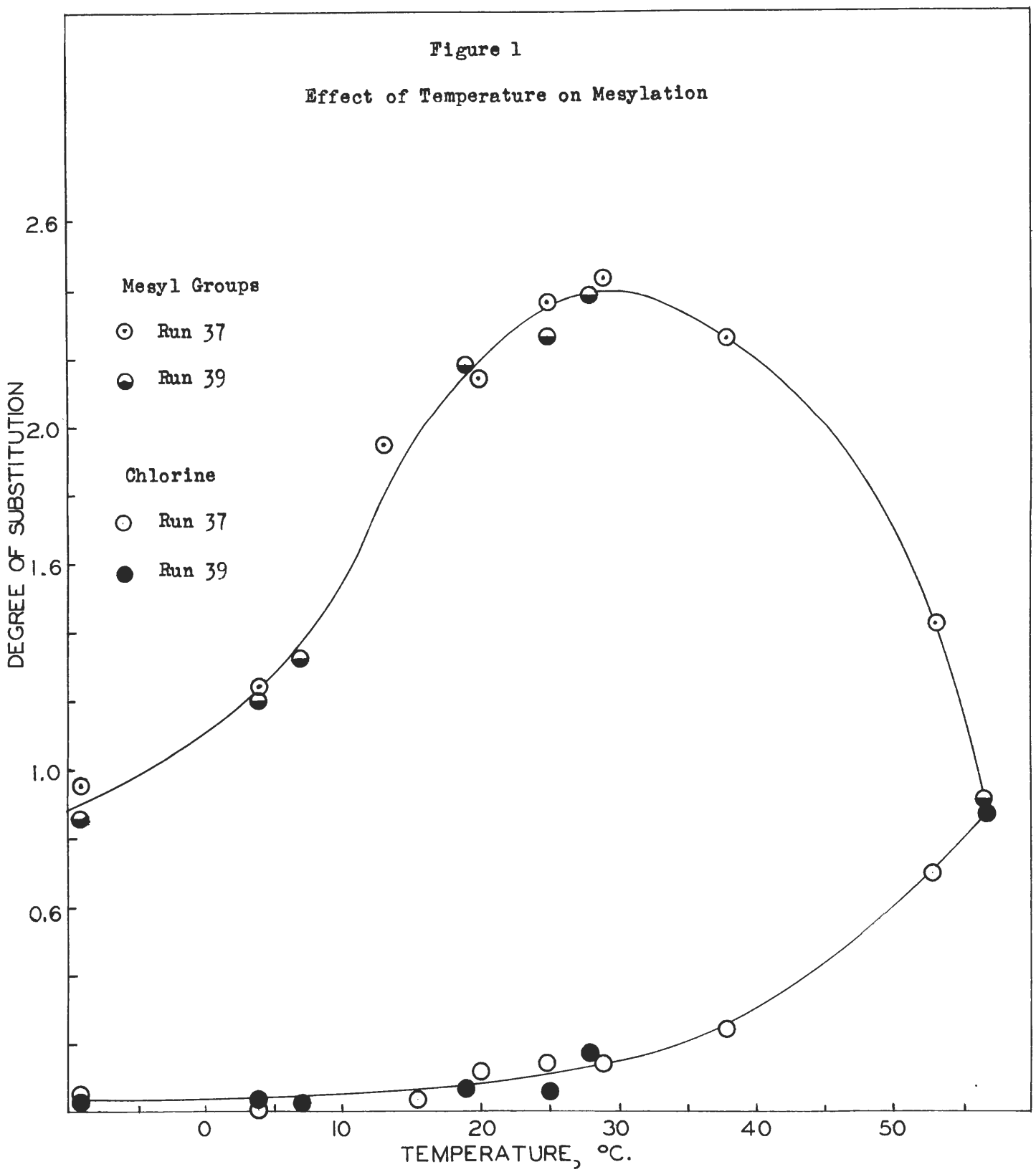
Temp., °C.	Sulfur, %		Mesyl D.S.		Chlorine Content			
	Run 37	Run 39	Run 37	Run 39	Run 37 %	37 D.S.	Run 39 %	39 D.S.
-9	12.8	12.0	0.95	0.86	0.11	0.05	0.58	0.03
4	15.1	15.0	1.22	1.20	0.06	0.01	0.57	0.04
7	--	15.9	--	1.32	--	--	0.47	0.03
13	19.8	--	1.94	--	0.51	0.04	--	--
19	--	20.9	--	2.18	--	--	0.58	0.07
20	20.7	--	2.14	--	1.04	0.12	--	--
25	21.7	21.3	2.36	2.26	1.26	0.14	0.78	0.06
28	--	21.5	--	2.38	--	--	1.95	0.17
29	22.0	--	2.43	--	1.46	0.14	--	--
38	21.1	17.6[2]	2.26	1.64[2]	2.82	0.24	5.83[2]	0.31[2]
53	15.9	--	1.42	--	8.79	0.70	--	--
57	--	11.7	--	0.91	--	--	11.32	0.87

[1]Molar ratio of pyridine:mesyl chloride:cellulose was 40:10:1

[2]The temperature of this sample went out of control during the reaction and rose to an unknown value

Figure 1

Effect of Temperature on Mesylation



the final 13 hours. Later a sample was run at 57°C. for 20 hours; portions were withdrawn for analysis after 2, 5, 11, and 20 hours. The data of this study are shown in Table VI.

TABLE VI

EFFECT OF TEMPERATURE ON MESYLATION

Reaction Time, hr.	Reaction Temp., °C.	Sulfur Content %	Sulfur Content D.S.	Chlorine Content %	Chlorine Content D.S.
4	28	20.4	2.10	1.72	0.16
13	59	18.3	1.73	6.51	0.31
4	28	20.0	2.00	1.42	0.11
17	28	23.0	2.74	2.91	0.29
2	57	12.0	0.93	10.73	0.72
5	57	12.2	0.93	10.52	0.75
11	57	12.0	0.95	10.58	0.72
20	57	12.5	1.00	12.93	0.86

The data of Table VI indicate that some demesylation may occur if a reaction which has produced a fairly high level of substitution at one temperature is allowed to continue at a considerably higher temperature. However, if the reaction is carried out entirely at the higher temperature, the amount of mesylation is limited to a relatively low level which probably is not greatly exceeded at any time during the reaction.

A possible explanation for this behavior may be as follows. As will be shown later, a number of side reactions take place between

pyridine and mesyl chloride and, as a result of at least some of these reactions, the mesyl chloride is altered in such a manner that it will no longer esterify cellulose. At higher temperatures, then, the rates of competing side reactions may have increased more than the rate of cellulose esterification, so that the extent of mesylation becomes limited to a fairly low level.

EFFECT OF CELLULOSE ACTIVATION ON MESYLATION

It was determined early in the experimental work that the activation of the cellulose played an important role in subsequent mesylation, and that best results were obtained when the linters were mercerized in 18% sodium hydroxide and then washed with absolute methanol and pyridine. In some of the runs there seemed to be a slight variation in reactivity of various batches of activated linters. One factor which had not been held constant in all runs was the mercerization time; this varied from two to six hours, but the amount of swelling of the fibers should not have been affected (30). However, as has been previously discussed, a comparison of activation with 18% sodium hydroxide and 9.5% lithium hydroxide indicated that swelling might not be the sole factor involved in reactivity. Consequently, a series of mesylations was carried out to examine the effect of mercerization time, using 18% sodium hydroxide, on the reactivity of the linters; the results are shown in Table VII.

All the samples used in this work were mercerized and washed with methanol and pyridine in the same manner. They were then

mesylated simultaneously for four hours at 20°C. The results obtained from an analysis of the purified samples obviously do not support the idea that mercerization time may be influential in mesylation.

TABLE VII

EFFECT OF MERCERIZATION TIME ON MESYLATION

Time, hr.	Sulfur Content %	D.S.	Chlorine Content %	D.S.	Total D.S.
2	17.56	1.55	0.52	0.04	1.59
4	16.90	1.46	0.73	0.06	1.52
8	17.58	1.56	0.65	0.04	1.60
16	17.56	1.55	0.71	0.04	1.59
32	17.23	1.51	0.74	0.04	1.55

Another possible explanation for differences in reactivity appeared to be found in the fact that the removal of mercerizing alkali with absolute methanol resulted in variations in the amount of alkali remaining in the different batches of linters. This possibility was examined in the following manner. A large batch of linters was mercerized for three hours and filtered on a large fritted-glass filter funnel. After several washings with methanol, the linters were thoroughly mixed, and a sample containing about two grams of linters was removed. This sample was transferred to a small filter crucible and washed with dry pyridine to remove the alcohol. It was then thoroughly mixed and divided into two portions, one for mesylation and one for alkali content analysis. The main body of linters on the large funnel was given further alcohol washes and withdrawn samples

were treated as just described.

Sufficient amounts of reagents were added to each sample used for mesylation to give a molar reactant ratio of 50:10:1 for pyridine:mesyl chloride:cellulose. The reaction was carried out for 16 hours at 28°C., and the products were purified according to the standardized procedure. The samples set aside for alkali analysis were titrated with standard hydrochloric acid to a phenolphthalein end point and the weight of linters present in each sample was determined after washing and drying. The results obtained are shown in Table VIII.

It is readily apparent from the data that the alkali content of the linters in the range considered does not exert a strong influence on the mesylation.

Because of the differences in reactivity obtained when the mercerized linters were washed with water or with methanol prior to mesylation, it seems likely that the linters were collapsed more by the water wash than by the alcohol wash. Experimentally, it was noted that when this wash liquid was later displaced by pyridine, the linters appeared to be considerably more fluffy and gelatinous when alcohol had served as the wash liquid than when water was used.

The reasons for the slight differences in reactivity noted for various batches of linters which were prepared using the alcohol wash method remain undetermined.

TABLE VIII

EFFECT OF NaOH CONTENT OF MERCERIZED LINTERS ON MESYLATION

Sample	Cellulose, moles	NaOH, moles	Moles of Cellulose per Mole of NaOH	Sulfur Content %	Sulfur Content D.S.	Chlorine Content %	Chlorine Content D.S.	Total D.S.
1	0.0158	0.00462	3.4	22.5	2.55	1.75	0.17	2.72
2	0.0127	0.00288	4.4	22.2	2.48	1.69	0.17	2.65
3	0.0120	0.00198	6.1	22.3	2.52	2.25	0.24	2.76
4	0.0149	0.00181	8.3	21.6	2.38	3.73	0.34	2.72
5	0.0086	0.00076	11.3	22.3	2.51	1.93	0.18	2.69
6	0.0065	0.00037	17.4	22.1	2.49	2.24	0.24	2.73

COMPARISON OF MESYLATION AND TOSYLATION OF CELLULOSE

Comparative mesylations and tosylations were run simultaneously as a portion of the investigation of the hypothesis that tosylation is inhibited by steric hindrance effects. If steric hindrance is a factor, it might be expected that a more complete esterification would be attained through the use of the mesyl group than with the bulky tosyl group.

In setting up the experiment, a large batch of linters was activated and treated with methanol and pyridine according to the standardized procedure. Enough two-gram samples were prepared to carry out one mesylation series and one tosylation series. This procedure was chosen so that all of the samples possessed a common history, and thus the introduction of unknown variables in the pretreatment steps was minimized. The reactions were carried out under identical conditions, using a 50:10:1 ratio of pyridine:sulfonyl chloride:cellulose. The reagents were mixed at room temperature, and the reactions were conducted at 28°C.

A second experiment was run in an identical manner, except that the reagents were cooled before mixing, in an attempt to reproduce the results of the first. The tosylation data was fairly reproducible, but large variations were found in the mesylation results. Therefore, another run was made of the mesylation series only, and a better level of reproducibility was obtained. The most reproducible data are presented in Table IX and Figures 2 and 3; the anomalous data are considered in Appendix I.

TABLE IX

COMPARATIVE MESYLATION AND TOSYLATION OF CELLULOSE

Reaction Time, hr.	Sulfur Content				Chlorine Content				Total D.S.	
	Run 41		Run 46[1]		Run 41		Run 46[1]		Run 41	Run 46[1]
	%	D.S.	%	D.S.	%	D.S.	%	D.S.		
Mesylation Series										
1	14.5	1.14	14.9	1.23	0.15	0.03	0.80	0.06	1.17	1.29
2	16.5	1.41	17.0	1.42	0.14	0.02	0.29	0.02	1.43	1.44
4	20.0	2.01	19.0	1.80	1.71	0.13	1.41	0.12	2.14	1.92
8	21.2	2.24	21.2	2.26	1.32	0.13	1.69	0.15	2.37	2.41
12	21.6	2.32	21.7	2.38	1.10	0.11	1.86	0.18	2.43	2.56
16	21.8	2.39	21.9	2.44	1.44	0.16	2.15	0.22	2.55	2.66
20	22.1	2.46	22.5	2.56	1.92	0.19	2.27	0.22	2.65	2.78
28	21.8	2.39	22.4	2.54	1.64	0.16	2.44	0.25	2.55	2.79
36	21.7	2.40	22.7	2.65	2.71	0.25	2.78	0.28	2.65	2.93
48	22.0	2.47	22.4	2.55	2.88	0.29	2.81	0.29	2.76	2.84
72	21.5	2.36	--	--	3.19	0.30	--	--	2.96	--
77	--	--	22.0	2.50	--	--	3.63	0.33	--	2.83
120	20.8	2.23	21.7	2.44	4.23	0.42	4.21	0.49	2.65	2.93
Tosylation Series										
1	5.4	0.37	5.4	0.37	0.50	0.02	0.22	0.01	0.39	0.38
2	7.0	0.53	7.4	0.57	0.60	0.06	0.19	0.01	0.59	0.58
4	9.6	0.89	9.0	0.81	0.30	0.04	0.29	0.02	0.93	0.83
8	11.0	1.18	10.5	1.08	0.28	0.03	0.49	0.05	1.21	1.13
12	11.5	1.32	11.3	1.25	0.64	0.08	0.43	0.04	1.40	1.29
16	12.1	1.47	--	--	0.93	0.10	--	--	1.57	--
20	12.4	1.55	12.2	1.42	0.65	0.09	0.63	0.07	1.64	1.49
28	12.6	1.64	12.9	1.72	0.77	0.08	0.93	0.11	1.72	1.83
36	13.2	1.84	12.9	1.80	1.08	0.14	1.15	0.14	1.98	1.94
48	13.3	1.87	13.1	1.83	0.86	0.11	1.22	0.14	1.98	1.97
72	13.5	1.96	13.3	1.89	1.44	0.17	1.67	0.22	2.13	2.11
120	13.5	1.97	13.3	1.92	1.84	0.25	2.57	0.34	2.22	2.26

[1]Mesylations and tosylations reported under this column were not run simultaneously; the mesylation was run separately at a later time. The tosylation data is from Run 35; see Appendix I for the mesylation data of Run 35.

Figure 2

Comparative Mesylation and Tosylation of Cellulose

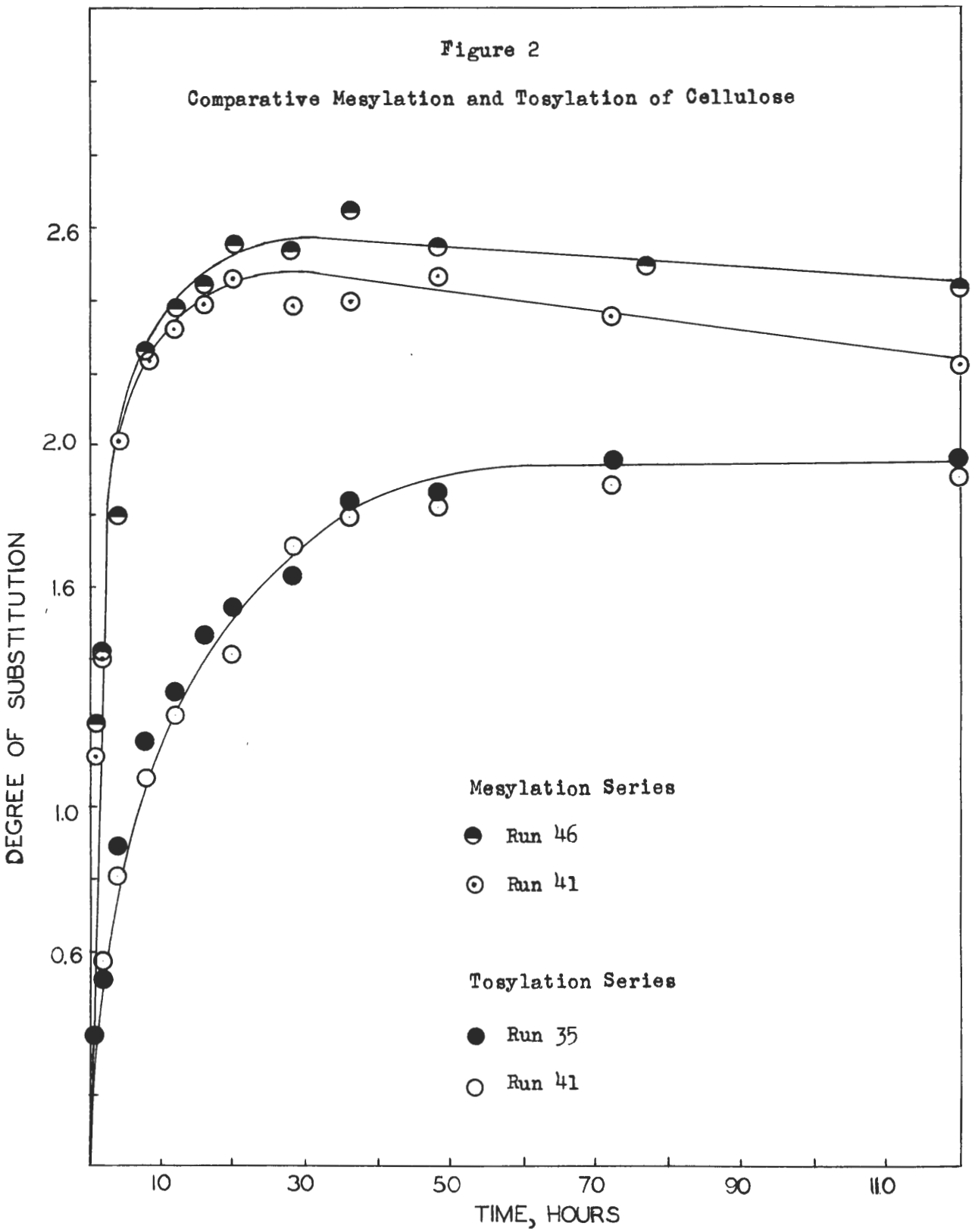
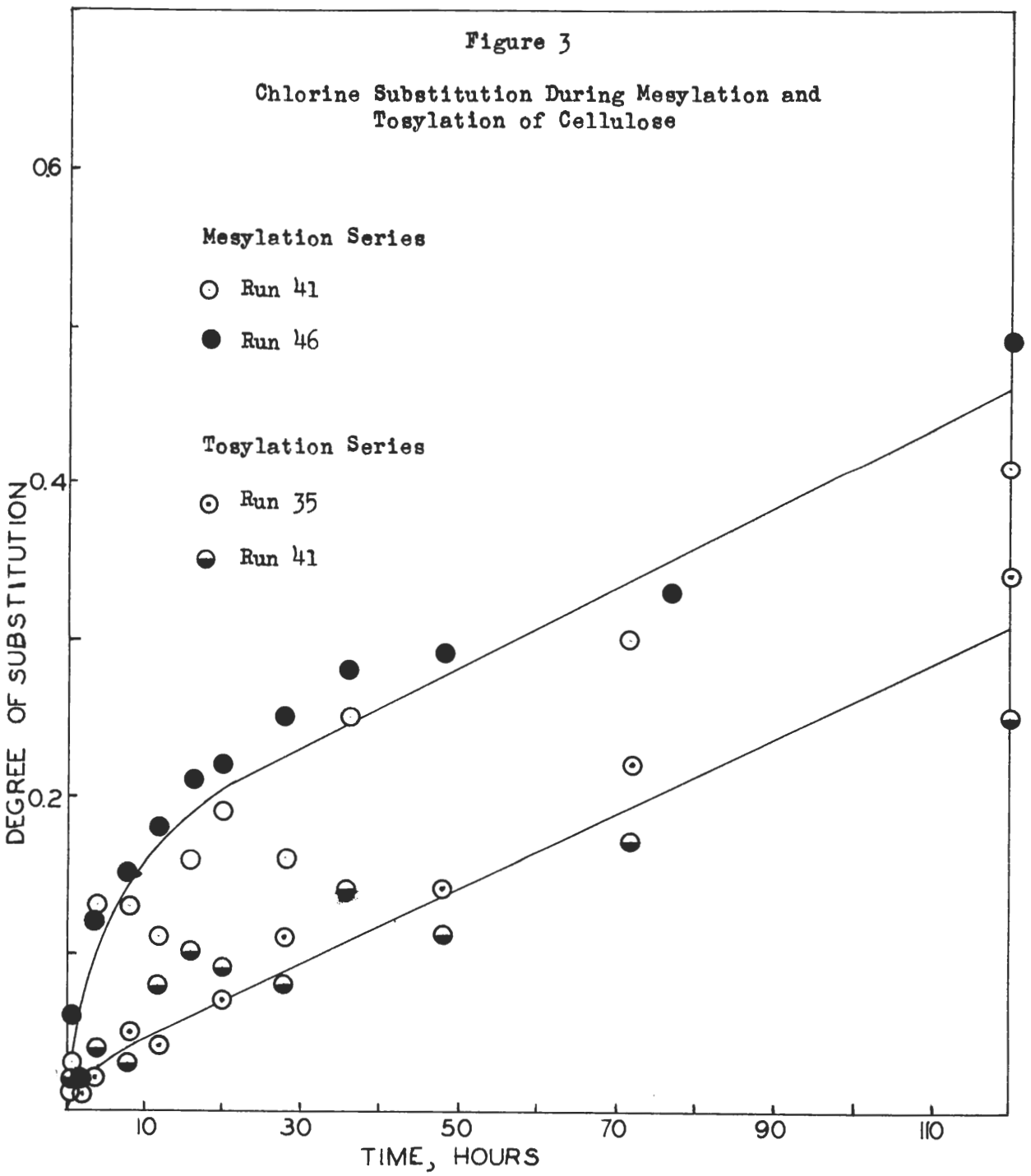


Figure 3

Chlorine Substitution During Mesylation and Tosylation of Cellulose



A number of facts are immediately apparent upon examination of the data and graphs:

1. Mesylation proceeded much more rapidly than tosylation and also reached a higher level of substitution. The maximum introduction of mesyl groups occurred in about 24 to 36 hours, whereas at least three days are required to closely approach an apparent limiting value of tosylation.

2. A point was reached in the mesylation reaction where a slight decrease in mesyl content occurred. However, since the total D.S. remains approximately constant in the latter phases of the reaction, the change may be due to replacement of mesyl groups by chlorine. Similar changes were not found for the tosylation reaction within the time interval considered.

3. Somewhat more chlorine was introduced by mesylation than by tosylation. Although the differences are not great, slightly higher chlorine contents were found quite consistently in the mesylation series. After an initial reaction period of 10 to 20 hours, the introduction of chlorine proceeded as a linear function of time and at about the same rate for both mesylation and tosylation.

4. The reproducibility of the tosylation work was considerably better than that of the mesylation, which may indicate that the latter is more sensitive to experimental variables.

The results of these experiments clearly indicate that a

more complete esterification is obtainable by mesylation than by tosylation carried out under similar experimental conditions. This difference in extent of esterification tends to support the hypothesis that tosylation may be inhibited by steric hindrance effects.

RE-ESTERIFICATION OF MESYL AND TOSYL DERIVATIVES

Further evidence in support of the steric hindrance hypothesis was sought through re-esterification studies on mesyl- and tosylcellulose. In a typical experiment, two one-gram samples of tosylcellulose were each dispersed, or dissolved, by mixing overnight with 25 ml. of dry pyridine. Then 5 ml. of mesyl chloride were added to one sample and 11.8 grams of tosyl chloride to the other. Both were allowed to react at 28°C. for periods which would allow maximum esterification to be approached; 19 hours was used for mesylation and 72 hours for tosylation. The products were then recovered and purified according to the standardized procedures adopted for mesylation and tosylation. Similar experiments were run with mesylcellulose.

The results of these experiments are presented in Table X.

TABLE X

RE-ESTERIFICATION OF TOSYLCELLULOSE

	Original Tosyl-cellulose	Retosylated Tosyl-cellulose	Mesylated Tosyl-cellulose
Run A			
Sulfur content, %	10.72	14.12	19.00
Chlorine content, %	0.28	0.46	1.72
D.S. of tosyl	1.13	2.15	1.13
D.S. of mesyl	--	--	1.65
D.S. of chlorine	0.02	0.06	0.23
Total D.S.	1.15	2.21	3.01
Run B			
Sulfur content, %	9.46	14.06	20.21
Chlorine content, %	0.16	0.60	1.62
D.S. of tosyl	0.88	2.18	0.88
D.S. of mesyl	--	--	2.02
D.S. of chlorine	0.08	0.07	0.21
Total D.S.	0.96	2.25	3.11
Run C			
Sulfur content, %	13.93	14.17	16.06
Chlorine content, %	0.47	1.50	2.25
D.S. of tosyl	2.14	2.26	2.14
D.S. of mesyl	--	--	0.58
D.S. of chlorine	0.02	0.12	0.34
Total D.S.	2.16	2.38	3.06

It is evident from the data that when only tosyl groups and chlorine were present in the re-esterified samples, the total D.S. never exceeded 2.4, but when mixed esters were prepared, the total substitution closely approximated the theoretical maximum in all cases.

These results provide additional evidence in support of the hypothesis postulating the presence of steric hindrance effects in tosylation work. The presence of tosyl groups in the original sample definitely limited further entry of tosyl groups. However, the unesterified hydroxyls in the original samples were all accessible to further esterification, as is shown by the fact that they were all covered by the mesylation procedure.

It should be pointed out that an element of uncertainty is present in the calculations which is due, primarily, to the increase in chlorine content upon re-esterification. During the second esterifications, either tosyl or mesyl groups, or both, may have been replaced by chlorine. Since the nature of such replacement was not known, calculations were based on the assumption that all the original tosyl groups were present in the final products. Since the total D.S. of the final products was very close to the theoretical value of 3.00, the error involved may be negligible. It should be noted that the final results were in good agreement, regardless of whether the original sample had 0.88 or 2.14 tosyl groups per glucose unit.

Another possible error may have been introduced by the

replacement of tosyl groups by mesyl groups, which would cause an increase in sulfur content without a corresponding increase in D.S. Such a possibility was found to be particularly likely in experiments in which samples of mesylcellulose were tosylated. In these cases the sulfur content of the tosylated products was lower than that of the original sample, which is to be expected when the larger tosyl groups are introduced into mesylcellulose. However, attempts to solve the simultaneous equations used for D.S. calculations were unsuccessful which suggests that changes in sulfur content may have been due, in part, to replacement of mesyl groups by tosyl groups. In one case the original sample had 19.80% sulfur and 1.71% chlorine (1.95 mesyl groups and 0.07 chlorine per glucose unit), and after tosylation the analyses were 19.41% sulfur and 0.92% chlorine. In another case the original values were 20.83% sulfur and 1.32% chlorine (2.17 mesyl groups and 0.11 chlorine per glucose unit), and the final values were 20.10% sulfur and 1.32% chlorine.

The greater susceptibility of mesyl groups over tosyl groups to replacement by other groups has been demonstrated in work with mesyl derivatives of monosaccharides (14), and the results noted in the present work might be accounted for in this manner.

PREPARATION OF TRISUBSTITUTED MESYLCHLOROCELLULOSE

In all of the experimental work carried out, a trimesylcellulose was never prepared, since the method used always resulted in the introduction of chlorine into the derivative if a high total D.S.

was obtained. A completely substituted product was not normally attained in a one-stage mesylation treatment. A few instances occurred in which the total D.S. closely approximated the theoretical maximum but such results could not be reproduced consistently with other cellulose samples and using the standardized procedure.

When this procedure, using molar ratios of 50:10:1 for pyridine:mesyl chloride:cellulose was employed, the results obtained were fairly reproducible. Thus, four samples treated separately for 26 hours at 28°C. all had a total D.S. in the range of 2.85 to 2.89; the mesyl contents of these samples were 2.54 to 2.66. Carrying out similar reactions using twice as much mesyl chloride gave somewhat higher values; the two samples run had total D.S. values of 2.95 and 2.97, of which the respective mesyl contents were 2.68 and 2.70.

Remesylation of mesylcellulose appeared, under certain conditions, to be fairly effective in producing completely substituted derivatives. When linters were mesylated to a total D.S. of about 2.3 or higher, repeated mesylations did not raise the D.S. above 2.9. This seemed to be the case regardless of whether the remesylation was carried out by immediate replacement of the mesylating solution with fresh solution after the first-stage mesylation step or by remesylation of airdry mesylcellulose after activation of the derivative in pyridine.

Several samples of airdry mesylcellulose which had a total D.S. of 2.0 or less were given a single remesylation after being treated overnight in pyridine. Total D.S. values of the purified products

were 3.05 (2.75 mesyl groups and 0.30 chlorine), 2.91 (2.58 mesyl groups and 0.33 chlorine), and 2.97 (2.76 mesyl groups and 0.21 chlorine); the respective values before the remesylation were 1.17 (1.14 mesyl groups and 0.03 chlorine), 1.92 (1.80 mesyl groups and 0.12 chlorine), and 2.02 (1.95 mesyl groups and 0.07 chlorine). One sample which had an initial D.S. of 2.28 (2.17 mesyl groups and 0.11 chlorine) was only raised to a total of 2.81 (2.67 mesyl groups and 0.14 chlorine) by remesylation. In another case where four remesylation steps were tried, the initial step gave a total D.S. of about 2.5, but the values after the third and fourth remesylations were 2.85 and 2.89 respectively; 0.17 chlorine was present in each of the remesylated samples.

Attempts to limit the entry of chlorine by conducting all reactions under 20°C. were not successful, since at least 0.1 chlorine per glucose unit was present in the final product, and the use of the lower temperatures inhibited the desired mesylation reaction.

INVESTIGATION OF SIDE REACTIONS OCCURRING DURING MESYLATION

Side reactions present during the mesylation of cellulose in a pyridine medium appear to exert a rather strong influence on the main reaction, and for this reason were subjected to a partial examination. Indications of side reactions were obtained early in the work when attempts were made to develop a rapid analytical method for following the course of mesylation by measuring the decrease in acidity of the mesylating solution. This was abandoned when it was found that there was a decrease in acidity of a blank containing mesyl chloride and

pyridine only. After such a mixture had been allowed to stand for about five days, only 85% of the original amount of mesyl chloride could be accounted for by titration.

When mesyl chloride was added to pyridine, an exothermic reaction took place, and the solution gradually darkened and became opaque in a matter of four to six hours. The colored material, whose composition is unknown, appears to be responsible for the presence of a brown color in mesylcellulose. Allowing the dark solution to stand overnight results in the formation of a dark-colored solid material on the walls of the vessel, and further periods of standing causes the amount of solid to increase. Prolonged periods of standing, several weeks or more, result in a fairly complete solidification of the mixture, at least in cases where the molar ratio of pyridine to mesyl chloride was about 3:1 or less. A gaseous product is also formed in the initial stages of the standing period.

Only partial success was obtained in identifying some of the various products. When the gas generated in the reaction mixture was passed into limewater, a white precipitate was formed, and acidification of this mixture with dilute hydrochloric acid caused hydrogen sulfide to be evolved. The hydrogen sulfide was definitely identified on the basis of its odor and through the formation of black lead sulfide, yellow cadmium sulfide, and black mercuric sulfide under suitable conditions.

Similar results were obtained when the gas was absorbed in

sodium hydroxide solution, except that a precipitate was not formed in the alkali. The original gas, however, responded negatively to all attempts made to identify it as hydrogen sulfide. The possibility that the gas may have been a mercaptan was considered, but attempts to produce a thioether derivative with 2,4-dinitrochlorobenzene were unsuccessful.

The dark solid product obtained from the pyridine and mesyl chloride mixture dissolved fairly readily in absolute ethanol. When the solution was filtered, a dark residue remained which was insoluble in water, acetone, benzene, and diethyl ether. The portion present in the alcohol was recovered by concentrating the solution and then cooling to effect crystallization. During the concentration step a strong garlic odor, which suggests the presence of a mercaptan, was evolved.

The recovered crystalline product was subjected to numerous recrystallizations from alcohol and treatments with decolorizing carbon. A light tan product which had a melting point of 177 to 178°C. was ultimately obtained. No clues to the identity of this compound were found in the literature, and final identification was obtained through experiments with pyridine and methanesulfonic acid. These two compounds reacted quite violently to form a white to light tan crystalline product. A final melting point of 180°C. was obtained for this material after several decolorizing treatments and recrystallizations from ethanol.

Several similarities were noted between the compound obtained from mesyl chloride and that prepared from methanesulfonic acid. The

odor of pyridine was obtained from each when treated with strong sodium hydroxide solution, which indicated that the compounds were probably pyridine complexes. When dissolved in water, each gave an acidic reaction to methyl orange indicator, and the equivalent weight of each was readily determined. A comparative summary of the properties of each is as follows:

	Product prepared from pyridine and	
	mesyl chloride	methanesulfonic acid
Color	light tan	white
Melting point	177-178°C.	180°C.
Equivalent weight	177	175

The mixed melting point of the two samples was 178°C.

As the evidence indicated that the product was a complex of pyridine and methanesulfonic acid in both cases, a thorough literature search was made, but this failed to uncover any reports of such a compound. Consequently, an elemental analysis was made of the product obtained from methanesulfonic acid and gave the results of Table XI.

TABLE XI

ANALYSIS OF THE PYRIDINE-METHANESULFONIC ACID COMPLEX

	Theoretical Composition	Determined Composition
Carbon, %	41.13	41.13
Hydrogen, %	5.18	5.13
Sulfur, %	18.30	18.35
Nitrogen, %	8.00	7.65

On the basis of the experimental results it is concluded that the compound is pyridinium methanesulfonate, $C_5H_5N \cdot CH_3SO_3H$.

Attempts to isolate a mercaptan from the alcoholic solution which had evolved the garlic odor were unsuccessful. A derivative was obtained with 2,4-dinitrochlorobenzene which, after purification, had a melting point of 84°C. It was subsequently found, however, that this derivative resulted from a reaction between the 2,4-dinitrochlorobenzene and pyridine present in the alcoholic solution.

MISCELLANEOUS MESYLATION STUDIES

A number of short studies were undertaken to elucidate various points of interest not included in the primary investigations.

PROSYLATION

Tosylcellulose derivatives having a D.S. of about 2.0 were dissolved by pyridine without difficulty, but mesylcellulose samples were insoluble, regardless of the level of substitution. A possible explanation might be found in the relative sizes of the two types of substituent groups. In comparison with mesyl groups, the larger tosyl groups might be expected to cause a greater decrease in hydrogen bonding between the remaining free hydroxyl groups and force the cellulose chains further apart to give a decreased packing effect of the polymer. Both of these factors would tend to improve solubility (31).

A group intermediate in size to the tosyl and mesyl groups

might be expected to produce derivatives of intermediate solubility characteristics. The prosyl group, i.e., the group obtained from propanesulfonyl chloride, was chosen for this purpose. Prosyl chloride was prepared from a mixture of methane-, ethane-, and propanesulfonic acids by treatment with thionyl chloride. The mixture of acid chlorides was subjected to vacuum distillation, but because there was no clear-cut separation of fractions, the fraction at the high end of the boiling point range was presumed to be rich in prosyl chloride since mesyl chloride was known to distill at the lower end of the temperature range used.

Two samples of linters were activated and prosylated, one at 9°C. and one at 20°C., in a manner analogous to the standardized mesylation procedure. The approximate D.S. values were 1.55 prosyl groups and 0.67 chlorine for the sample run at 9°C., and 1.44 prosyl groups and 0.64 chlorine for the sample prepared at 20°C. About 0.05 gram of each of the purified derivatives and of a mesylcellulose having a similar level of substitution (1.42 mesyl groups and 0.70 chlorine per glucose unit) was dispersed separately in 10 ml. of dry pyridine and placed on a rotator. None of the samples showed any solubility even after a week's treatment with the solvent. Microscopic examination of particles removed from the pyridine did not disclose any physical differences.

Therefore, it is to be concluded from this work that if the size of the substituent groups is a factor in determining solubility characteristics as previously described, the prosyl group apparently

does not exert any more noticeable influence than the mesyl group on these factors.

NATURE OF THE MESYLATING AGENT

As previously pointed out, a dark solution and a dark solid form when mesyl chloride and pyridine are mixed. To determine which of these contains the active mesylating agent, a solution of 50 ml. of pyridine and 10 ml. of mesyl chloride was allowed to stand for three days, after which the solid and liquid components were separated. The liquid was used as recovered but the solid was rinsed several times with pyridine and dispersed in fresh pyridine.

One gram of activated linters was added to each component and allowed to react for 24 hours at 28°C. The derivative which had been prepared in the dark solution contained 11.0% sulfur and 0.9% chlorine; that treated with the solid dispersed in pyridine contained only 0.4% sulfur and 0.2% chlorine.

It is evident that the actual mesylating agent is present in the dark solution and that the formation of the solid material as a result of side reactions in the mesylating mixture causes a reduction in the amount of mesyl chloride available for esterification.

DEGREE OF POLYMERIZATION

Conventional methods of determining the degree of polymerization did not appear very applicable to mesylcellulose because of its very poor solubility characteristics. The dissolving of mesylcellulose

in hot acetonylacetone was very likely accompanied by degradation, and therefore these solutions would be of limited value in degree of polymerization studies. That degradation had been caused by the hot acetonylacetone was evidenced by the fact that mesylcellulose recovered from solution was almost completely soluble in pyridine; the original mesylcellulose, of course, was very insoluble in pyridine.

Qualitative indications that the mesylation reaction may not have caused a high amount of degradation are furnished by the behavior of the derivatives in formamide. In most instances there was no pronounced swelling of the derivatives when treated with this solvent, and a precipitate was not generally formed when the supernatant liquid was poured into water. In a few cases there was a pronounced swelling, and some material could be precipitated from the formamide. In an extreme case where this had been most noticeable, the dissolved portion was recovered and found to amount to only 12.5% of the sum of the soluble and insoluble portions. This particular sample was one which had been mesylated at 57°C., and more degradation would be expected here than in mesylations carried out at 30°C. The difference in solubility between the two fractions could not be attributed to differences in composition since both had similar mesyl group and chlorine contents.

MESYLATION OF COTTON THREAD

A sample of cotton thread was activated by mercerization and subsequently mesylated for 17 hours at 23°C. The purified product had a total D.S. of about 2.0 (19.5% sulfur and 1.29% chlorine) and retained its thread form without having suffered any great decrease in

strength. The thread did not have flame-resistant properties. The light tan color which remained after the formamide extraction could be converted to a light yellow by bleaching with calcium hypochlorite. Bleaching with bromine water or hydrogen peroxide was not as effective as with hypochlorite.

YIELD OF MESYLCELLULOSE

Because of the uncertainty of the purity of mesylcellulose preparations, yield determinations were not generally carried out. In one case, however, special precautions were taken to minimize mechanical losses during the recovery and purification steps. Calculated on the basis of the sulfur and chlorine content of the product, the yield was found to be 99% of the theoretical value. In several other instances where no special precautions against losses were taken, the yields were found to be 85 to 95% of theory.

SUMMARY AND CONCLUSIONS

A number of different types of reactions and conditions which might be expected to be satisfactory for the mesylation of cellulose have been examined briefly and most of them have been found to be unsuitable. Pyridine has been found to be the most suitable reaction medium; other media or catalysts are generally less suitable or completely unsuitable.

Activation of the cellulose is very influential in determining the extent of mesylation attained. Swelling the cotton linters in pyridine prior to esterification gives moderately successful results. Cotton linters mercerized in 18% sodium hydroxide are mesylated almost completely, especially if the alkali is removed before mesylation by elution with absolute methanol rather than water.

Cellulose activation appears to involve more than just a swelling action, since linters mercerized in 9.5% lithium hydroxide, which is a more effective swelling agent than 18% sodium hydroxide, are mesylated to a lesser extent than those mercerized in the caustic soda. Differences found in the reactivity of various samples of activated cellulose are not due to differences in mercerization time used or to the amount of alkali still present in the samples at the time of mesylation.

Temperature conditions are very influential in the mesylation reaction; the optimum is about 30°C. Maximum mesylation occurs at this point and falls off at either higher or lower temperatures. Some

demesylation may take place if the reaction temperature is raised markedly during the course of the esterification. At temperatures of about 60°C. the amount of substitution reaches a limiting value rather rapidly, and this value is relatively low. This low limiting value may be due to the more rapid acceleration of the rates of interfering side reactions with increasing temperature than the rate of esterification.

The introduction of chlorine into the mesyl derivative takes place to a limited extent, in most cases, and with the methods used in this work it is difficult to prevent. The amount introduced is not affected by the ratios of reagents employed but increases markedly as the reaction temperature is increased above the optimum mesylation temperature.

Mesylcellulose prepared from cotton linters is insoluble in the common organic solvents but will dissolve slowly when refluxed in acetonylacetone. The mesylcellulose derivative is normally obtained as a dark brown product, and most of the color can be removed by repeated extraction with formamide at 65°C. The elemental analysis of the derivative purified by formamide extraction compares favorably with that of the material recovered from acetonylacetone solution.

Mesylation of cellulose occurs at a more rapid rate and to a greater extent than tosylation under identical experimental conditions. Introduction of chlorine is somewhat more pronounced in mesylation, but in both types of reaction the rate of chlorination is about the same after the initial phases of the esterification. The mesylation reaction

is not as reproducible as the tosylation reaction.

Comparative studies of mesylation and tosylation support the hypothesis that the inability to attain complete tosylation of cellulose may be due to steric hindrance effects of the relatively large tosyl group. Completely substituted mixed esters of cellulose can apparently be produced by the mesylation of a tosylcellulose, whereas retosylation of the same original samples does not give more than 80% of the hydroxyl esterification required for complete substitution.

D.S. values of 2.9 can be reproduced quite readily by single-step mesylations. Higher values can be attained in a single treatment by using a 20:1 molar ratio of mesyl chloride to cellulose. Remesylation of a mesylcellulose having a total D.S. in the approximate range of 1.0 to 2.0 will also produce derivatives approaching the theoretical maximum of substitution.

A variety of side reactions take place between pyridine and mesyl chloride, and the brown color of mesylcellulose appears to be due to contamination by a dark-colored side-reaction product whose identity is undetermined. A new crystalline compound, pyridinium methanesulfonate, is formed in one of the side reactions, and it has been isolated and identified. The presence of a gaseous side-reaction product, which has acidic properties and from which hydrogen sulfide can be produced, has been established, but its identity is unknown. The presence of a mercaptan as a side-reaction product is suspected, but efforts to isolate and identify it have been unsuccessful.

Pyridine and mesyl chloride react to form a dark-colored solution and a dark solid. The solid is ineffectual as a mesylating agent and represents a loss in the total mesyl chloride available for esterification. The actual mesylating agent is contained in the dark solution.

Cotton thread can be mesylated without destroying the thread-like characteristics. The product is not flame-resistant and can be bleached to a light yellow color with calcium hypochlorite solution.

APPENDIX I

REPRODUCIBILITY OF MESYLATION WORK

In running the two series of comparative mesylation and tosylation studies, poor reproducibility was obtained for the mesylation work. The first series (Run 35) was made by mixing all reagents at room temperature, whereas the second series (Run 41) was initiated after the reactants had been cooled to about 4°C. before mixing. A third mesylation series (Run 46) was run, using the conditions of Run 41, and a fair agreement between these two runs was obtained.

An attempt was made to reproduce the initial results of Run 35 in which the D.S. of both the mesyl groups and chlorine passed through a rather pronounced maximum and then decreased. The conditions of Run 35 were duplicated in Run 61, but the results obtained in the latter were more similar to those of Runs 41 and 46. The reasons for the anomalous behavior of Run 35 are not known. The data for these runs are presented in Table XII.

TABLE XII

REPRODUCIBILITY OF MESYLATION WORK

Time, hr.	Run 35	Run 41	Run 46	Run 61
	D.S. of Mesyl Groups			
1	1.80	1.14	1.23	--
2	1.86	1.41	1.42	1.52
4	2.14	2.01	1.80	1.84
8	2.23	2.24	2.26	2.24
12	2.38	2.32	2.38	2.41
16	--	2.39	2.44	--
20	2.26	2.46	2.56	2.52
28	2.22	2.39	2.54	2.46
36	2.19	2.40	2.65	2.46
48	2.04	2.47	2.55	--
72	1.85	2.36	2.50	--
120	1.71	2.23	2.44	--
	D.S. of Chlorine			
1	0.18	0.03	0.06	--
2	0.27	0.02	0.02	0.21
4	0.30	0.13	0.12	0.17
8	0.37	0.13	0.15	0.24
12	0.36	0.11	0.18	0.27
16	--	0.16	0.22	--
20	0.32	0.19	0.22	0.32
28	0.27	0.16	0.25	0.30
36	0.26	0.25	0.28	0.30
48	0.28	0.29	0.29	--
72	0.31	0.30	0.36	--
120	0.31	0.42	0.55	--

APPENDIX II

DETERMINATION OF FREE HYDROXYL CONTENT OF MESYLCELLULOSE

An attempt was made to check the D.S. values obtained from sulfur and chlorine analysis by determining the remaining free hydroxyl content of the derivatives. The quantitative acetylation method of Malm, et al. (27) was investigated, as were previously described modifications. Calculations of the acetyl content were based on the assumption that the D.S. of mesyl and chlorine was not changed during the acetylation and, to check this assumption, a number of the acetylated samples were re-analyzed for sulfur and chlorine content.

Initial studies using the basic method (27) were made on a number of samples which had been extracted with methanol only, and the results are reported in Table XIII.

As can be seen from the data, the sulfur contents of the acetylated derivatives were considerably lower than the calculated values which were based on the assumption that there was no loss of sulfur or chlorine during the acetylation. Although the analytical values can be considered as only approximate, since the mesyl derivatives had only been extracted with methanol and therefore were probably contaminated, the large decreases in sulfur content appear to indicate the occurrence of demesylation during acetylation. Furthermore, since the total D.S. values of these samples ranged from 2.2 to 3.3, the applicability of the method to mesylcellulose is doubtful.

TABLE XIII

DETERMINATION OF FREE HYDROXYL CONTENT OF MESYLCELLULOSE

Sample	Degree of Substitution of			Sulfur in Acetates, %	
	Mesyl	Chlorine	Acetyl	Calculated	Found
1	1.85	0.22	0.88	17.1	11.5
2	1.95	0.30	0.81	--	--
3	2.26	0.38	0.65	19.5	13.1
4	1.83	0.37	0.72	17.1	14.5
5	2.29	0.38	0.09	20.8	14.9
6	2.26	0.37	0.00	21.0	15.5
7	2.39	0.41	0.15	21.2	14.2
8	2.25	0.37	0.00	21.1	15.2
9	2.34	0.42	0.52	20.0	13.1
10	1.86	0.32	0.71	17.4	13.8
11	2.11	0.35	0.64	18.8	13.9

After extracting with formamide, four of the original mesylcellulose samples in Table XIII (Samples 3, 6, 8, and 10) were acetylated at 28°C. with a 4:1 solution of acetic anhydride and pyridine. In this work the differences between the calculated and determined sulfur contents of the acetylated derivatives were 0.7, 0.8, 0.1, and 0.2%. Thus it appears that the demesylation occurring during acetylations run at 28°C. is less than in the reactions run at 75°C. However, the unreliability of the data obtained at the lower temperature is evident in Table XIV.

TABLE XIV

DETERMINATION OF FREE HYDROXYL CONTENT OF MESYLCELLULOSE

Sample	Degree of Substitution of Mesyl	Chlorine	Acetyl	Total D.S.
2	1.95	0.30	0.56	2.41
3	2.26	0.38	0.52	3.16
5	2.29	0.38	0.09	3.21
6	2.26	0.37	0.19	2.82
8	2.25	0.37	0.58	3.20
9	2.34	0.42	0.29	3.05
10	1.86	0.32	0.31	2.49
12	0.95	0.05	1.11	2.11
	0.95	0.05	1.58	2.58

Because of the inconsistency of results obtained, and since incomplete acetylation took place in many instances, particularly with samples having a low, original D.S., the acetylation methods for the determination of the free hydroxyl content of mesylcellulose derivatives were deemed unsuitable for further consideration. Similar results were obtained in the acetylation of tosylcellulose.

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