[CONTRIBUTION FROM THE INSTITUTE OF PAPER CHEMISTRY]

The Esterification of Cellulose with Methanesulfonyl (Mesyl) Chloride[1]

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A method was developed for preparing a trisubstituted mesylcellulose from cotton linters, a small portion of the total substitution being due to chlorine. Activation of the cellulose by mercerization was most effective when the excess alkali was removed by washing with methanol rather than with water, although the amount of alkali retained by the cellulose did not affect the mesylation reaction. An optimum temperature of about 28° was found for mesylation, and demesylation occurred at higher temperatures. Comparative studies on mesylation and tosylation produced results supporting the hypothesis that tosylation is impeded by steric hindrance effects. One of the side reaction products was identified as pyridinium methanesulfonate; this compound was ineffectual in the mesylation reaction.

Esterification of cellulose with *p*-toluenesulfonyl chloride, or tosyl chloride, has been used in rate and reaction mechanism studies,[3,4] but complete substitution of the hydroxyl groups in cellulose has not been reported. A degree of substitution (D.S.) of 1.5 to 2.0 can be obtained without difficulty and a D.S. of 2.4 has been reported.[5] Spurlin[6] has pointed out that substitution of cellulose in either of the secondary hydroxyl positions may make the remaining secondary hydroxyl less accessible. Timell[7] found that the free hydroxyls in a propylcellulose, whose D.S. was 1.67, could be completely esterified with ethanesulfonyl chloride but not with α-naphthalenesulfonyl chloride, suggesting that steric hindrance effects may be a limiting factor. If steric hindrance also inhibits the tosylation reaction, the use of methanesulfonyl chloride, or mesyl chloride, might be expected to overcome some of the difficulties since it is chemically similar to tosyl chloride but of smaller molecular size. In the only reported work on the mesylation of cellulose, Wolfrom[8] was able to introduce 1.6 mesyl groups per glucose unit into mercerized cotton linters and 1.7 groups into cellulose regenerated from cellulose acetate.

In the present work experimental conditions were evaluated to develop a method of mesylation which would give a high D.S. Due to the introduction of chlorine into the cellulose during the mesylation reaction, a trimesylcellulose was not produced, but the combined effects of mesylation and chlorination accounted for complete substitution of the cellulose hydroxyls. A maximum total D.S. of 2.97 was obtained, of which 2.70 was due to mesyl groups. Comparative studies of mesylation and tosylation showed that mesyl chloride was the more effective esterification agent and gave support to the hypothesis that mesylation would not be impeded by steric hindrance as in the case of tosylation. Numerous side reactions occurred during mesylation and the product of one of these was identified as *pyridinium methanesulfonate*, a compound not previously reported in the literature.

Experimental

Cellulose.—Bleached commercial cotton linters from the Buckeye Cotton Oil Co., Memphis, Tenn.—α-cellulose 98.5%, ash 0.07%, degree of polymerization about 1200. The linters were ground in an Abbé mill and screened; the portion which passed through a 100-mesh screen but was retained by a 300-mesh screen was used in the esterification studies.

Methanesulfonyl Chloride.—To four moles (405 g.) of methanesulfonic acid (Indoil Chemical Co., Chicago) was added five moles (405 ml.) of thionyl chloride over a 1 hr. period while maintaining a liquid temperature between 10 and 25°. The temperature was then raised slowly to 150° in 4 to 6 hr. and the mesyl chloride recovered by distillation. The fraction collected between 161 and 164° during redistillation was retained for use. Analysis of the mesyl chloride by titration with alkali and by gravimetric chlorine analysis showed it to be 98.8% pure.

***p*-Toluenesulfonyl chloride**: Eastman Kodak Co. (m.p. 66–68°), recrystallized from benzene to give a product melting at 67–70°. **Pyridine**: C.P. pyridine was stored over barium oxide and distilled just prior to using. **Formamide**: Eastman Kodak Co. practical grade distilled *in vacuo* before using. **Methanol**: absolute, used as received.

Mesylation.—Enough air-dry cotton linters to contain 2.0 g. (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 2 hr. The linters were then collected on a coarse fritted glass crucible and washed with absolute methanol until the washings were neutral to phenolphthalein. Pyridine was used to displace the alcohol and a sufficient amount was added to give 40 to 50 moles of pyridine per mole of anhydroglucose. Then 10.1 ml. (10 moles per mole of anhydroglucose) of mesyl chloride were added after cooling all reagents to about 4°. The reactants were thoroughly mixed by shaking in a closed bottle which was then placed in a constant temperature bath. A temperature of 28° was used except in some special cases. After the reaction period the reactants were poured into cold water and filtered off, washed well with water, and suspended overnight in water. On the following day the product was collected on a filter, transferred to a paper extraction thimble and extracted for 12 hr. with methanol in a Soxhlet extraction apparatus. It was then mixed with 25 ml. of formamide in a small beaker and placed in an oven at 65° for 30 to 60 minutes. A small portion of the liquid was then decanted and diluted with water. If a precipitate formed, the formamide and mesylcellulose mixture in the beaker was diluted with water and filtered; if no precipitate formed, the mixture was filtered directly. The formamide treatment was repeated until the decanted liquid was colorless or only slightly colored; this usually required four or five treatments. After extraction the product was washed thoroughly with water, air-dried, dried *in vacuo* at 65° for at least 12 hr. and stored over phosphorus pentoxide in a desiccator.

Tosylation.—The procedure described by Heuser[3] was followed with a few modifications. The activated cellulose was prepared in the same manner described for the mesylation studies. The molar ratio of reactants used in tosylation

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[1] A portion of a thesis submitted in partial fulfillment of the requirements of The Institute of Paper Chemistry for the degree of Doctor of Philosophy from Lawrence College, Appleton, Wis., June, 1951. This work was carried out under the direction of John W. Green.

[2] Marathon Corp., Rothschild, Wisc.

[3] E. Heuser, M. Heath and W. H. Shockley, THIS JOURNAL, **72**, 670 (1950).

[4] F. Honeyman, *J. Chem. Soc.*, 168 (1947).

[5] K. Hess and N. Ljubitsch, *Ann.*, **507**, 62 (1933).

[6] H. M. Spurlin, in Ott, "Cellulose and Cellulose Derivatives," Interscience Publishers, Inc., New York, N. Y., 1946, p. 608–609.

[7] Timell, "Studies on Cellulose Reactions," Kungl. Tekniska Hogskolan, Stockholm, 1950, p. 113–114.

[8] M. L. Wolfrom, J. C. Sowden and E. A. Metcalf, THIS JOURNAL, **63**, 1688 (1941).

was 50:10:1 for pyridine:tosyl chloride:cellulose and the final product was extracted with methanol only.

Re-esterification of Tosyl- and Mesylcellulose Derivatives.—Both tosyl- and mesylcellulose samples were subjected to re-esterification with mesyl chloride or tosyl chloride. For example, two 1-g. samples of tosylcellulose were each placed in a vial with 25 ml. of pyridine and shaken slowly overnight. After cooling all reagents to about 4°, 5 ml. of mesyl chloride was added to one sample and 11.8 g. of tosyl chloride to the other. The mesylation was carried out for 19 hr. and the tosylation for 72 hr., both reactions being run at 28°. The products were recovered and treated as previously described for mesyl- and tosylcellulose.

Identification of Pyridine Methanesulfonate.—Upon mixing pyridine and mesyl chloride in a stoppered bottle, the solution became dark brown and quite opaque in about 4 hr. A dark solid gradually formed from which light tan crystals were obtained after dissolving in ethanol and decolorizing with carbon black. These crystals melted at 177 to 178°, produced the odor of pyridine when treated with strong caustic, and had an equivalent weight of 177. A white compound of similar properties was formed by the reaction between pyridine and methanesulfonic acid; this material melted at 180° and had an equivalent weight of 175. The mixed melting point of the two materials was 178°. Because of these similarities it was concluded that each was a complex of pyridine and methanesulfonic acid, pyridinium methanesulfonate, $C_5H_5N \cdot CH_3SO_3H$. *Anal.* Calcd.: C, 41.13; H, 5.18; S, 18.30; N, 8.00. Found for the crystals prepared from methanesulfonic acid: C, 41.13; H, 5.13; S, 18.35; N, 7.65.

Analytical Methods

Sulfur.—The modified Parr peroxide procedure described by Heuser[8] was used. **Chlorine:** The Parr peroxide bomb method[9] was used.

Calculations of D.S.—After analysis of the derivatives for sulfur and chlorine, D.S. values were calculated by means of simultaneous equations in which W = D.S. of tosyl groups, X = the D.S. of mesyl groups and Y = the D.S. of chlorine.

For mesylcellulose

$$\text{sulfur, } \% = 3206X/(162 - 78.1X - 18.46Y)$$
$$\text{chlorine, } \% = 3546Y/(162 - 78.1X - 18.46Y)$$

For tosylcellulose

$$\text{sulfur, } \% = 3206W/(162 - 154W - 18.46Y)$$
$$\text{chlorine, } \% = 3546Y/(162 - 154W - 18.46Y)$$

For mesylated tosylcellulose and tosylated mesylcellulose

$$\text{sulfur, } \% = 3206(W - X)/(162 - 78.1X - 154W - 18.46Y)$$
$$\text{chlorine, } \% = 3546Y/(162 - 78.1X - 154W - 18.46Y)$$

Results and Discussion

In the only reported work on the mesylation of cellulose[8] the reaction was conducted in pyridine after activating the cellulose by mercerizing it in 18% sodium hydroxide solution. Since esterification of cellulose is frequently run successfully under other conditions, preliminary studies were made to determine the most suitable reaction medium and method of cellulose activation. Results of these preliminary studies are shown in Table I.

Since alkali cellulose formed by mercerization decomposes easily in the presence of water, trials were also made in which this was avoided by using methanol to remove the mercerizing alkali. As can be seen from Table I, this treatment resulted in the most successful mesylation reaction. Activation in the absence of alkali was attempted with pyridine but this gave a product which responded only slightly to mesylation. Activation with 9.5% lithium hydroxide solution, which is a more effective swelling agent than sodium hydroxide, gave a somewhat less reactive cellulose than obtained with sodium hydroxide solution under analogous conditions. Other reaction media, such as quinoline, 1:1 pyridine:dioxane and aqueous sodium hydroxide, which have been used in other esterification studies,[10,11] were ineffective.

TABLE I

METHODS OF CELLULOSE MESYLATION[a]

Swelling agent	Wash liquid[b]	Reaction medium	Molar ratio[c]	Reaction time, days	Sulfur content, %	Mesyl groups per glucose unit
Pyridine	..	Pyridine	10:1	1	2.2	0.1
				2	2.4	0.1
NaOH	H_2O	1:1 Dioxane pyridine	10:1	1	13.9	1.1
				2	15.3	1.2
NaOH	..	18% NaOH	20:1	0.25	0.9	0.04
NaOH	H_2O	Quinoline	10:1	1	3.9	0.2
				2	7.2	0.4
LiOH	H_2O	Pyridine	10:1	1	6.5	0.4
				2	12.5	0.9
NaOH	CH_3OH	Pyridine	10:1	2	22.5	2.5

[a] All mesylations run at 28°. [b] Liquid used to displace the swelling agent. The wash liquid was then displaced by CH_3OH which in turn was displaced by the reaction medium. [c] Moles of mesyl chloride per mole of anhydroglucose.

Although it was found important to use alcohol to displace the mercerizing alkali, the amount of alkali retained by the activated cellulose was unimportant. This is shown by the data in Table II in which decreasing amounts of alkali in the cellulose were produced by successive washings with methanol.

TABLE II

EFFECT OF ALKALI CONTENT OF CELLULOSE ON MESYLATION

Moles cellulose per mole NaOH	D.S. of sulfur	D.S. of chlorine	Total D.S.
3.4	2.55	0.17	2.72
4.4	2.48	.17	2.65
6.1	2.52	.24	2.76
8.3	2.38	.34	2.72
11.3	2.51	.18	2.69
17.4	2.49	.24	2.73

The mesylcellulose obtained by esterification in a pyridine medium was invariably dark brown unless a very short reaction time or a low temperature was used. Conditions which minimized the formation of dark color also inhibited the reaction. The derivative could not be purified readily by precipitation from solution as no satisfactory inert solvent was found. Heating the mesylcellulose in various solvents did not improve the solubility greatly except in the case of acetonylacetone; with this solvent an appreciable portion of the solid dissolved when heated under reflux at 150°. Precipitation of this solution into water produced a finely divided solid which, after washing with water or methanol, was a creamy white.

No attempts were made in this work to study the reasons for the insolubility of the various esters in solvents, or the possibility of cross-linking. It is interesting to note that Wolfrom, Sowden and

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(9) Parr Instrument Co., "Peroxide Bomb Apparatus and Methods," Parr Manual 131, Moline, Ill., 1950.

(10) G. W. Rigby, U. S. Patent 2,123,806, July 12, 1938.

(11) C. J. Malm, L. B. Genung and R. F. Williams, Jr., *Ind. Eng. Chem.*, **43**, 684 (1951).

Metcalf[8] prepared a mesylated product with a D.S. of 1.6 from cotton linters; it was insoluble in solvents, a behavior similar to that of the products of higher D.S. prepared in the present work. A mesyl ester (D.S. 1.7) prepared from a regenerated cellulose (derived from cellulose acetate and hence of lower D.P. than the cotton linters) was soluble in boiling acetonylacetone. They also prepared a mesylcellulose acetate (D.S. 1.72 acetyl and 1.03 mesyl) from cellulose acetate which was readily soluble in acetone and pyridine. Hence, it can be said that (a) the mesyl groups do not promote solubility whereas the acetyl groups do and (b) mesyl celluloses of lower D.P. seem to be more soluble than those of higher D.P.

Formamide was found to be very effective in extracting the brown color from the derivatives. Both sulfur and chlorine contents were decreased somewhat by the formamide extraction or by dissolving in acetonylacetone, but constant values were attained after two to four treatments. Substantially better yields were obtained with the formamide treatment and for this reason and because of its greater simplicity, this treatment was preferred over that using acetonylacetone.

Temperature was found to be very influential on the extent of mesylation and, as shown in Fig. 1, an optimum was found at about 28°. At higher temperatures the introduction of chlorine into the product became more pronounced and a decrease occurred in the extent of mesylation. Demesylation was found to occur when a reaction which had produced a fairly high D.S. at one temperature was allowed to proceed at a considerably higher temperature. Samples I and II, in Table III, illustrate this effect. Raising the temperature for sample I, after the initial four hours, caused a decrease in mesyl content, but allowing sample II to proceed at the same initial temperature resulted in an increase in mesyl content. Sample III showed the effect of high temperature in limiting the extent of mesylation even though the reaction time allowed was adequate for the lower temperatures.

TABLE III

EFFECT OF TEMPERATURE ON MESYLATION

Sample	Reaction time, hr.	Reaction temp., °C.	Sulfur content, %	Sulfur content, D.S.	Chlorine, content, %	Chlorine, content, D.S.
I	4	28	20.4	2.10	1.72	0.16
	13	59	18.3	1.73	6.51	.31
II	4	28	20.0	2.00	1.42	.11
	17	28	23.0	2.74	2.91	.29
III	2	57	12.0	0.93	10.73	.72
	5	57	12.2	.93	10.52	.75
	11	57	12.0	.95	10.58	.72
	20	57	12.5	1.00	12.93	.86

Comparative mesylation and tosylation studies were carried out at 28° and the results shown in Fig. 2 obtained. Mesylation proceeded much more rapidly than tosylation and reached a higher D.S. level. Somewhat more chlorine was introduced into the derivatives by mesylation and, after an initial reaction period of 10 hr. or less, chlorination proceeded at an approximately linear rate in both reactions. In the mesylation work a maximum of 0.5 chlorine atom per glucose unit was introduced; the amount was less than 0.1 during the first four hours of reaction time and less than 0.3 up to 72 hr. Chlorine substitution was at a lower level in the tosylation work, and its D.S. did not exceed 0.1 until after 28 hr.; a maximum of 0.3 was reached.

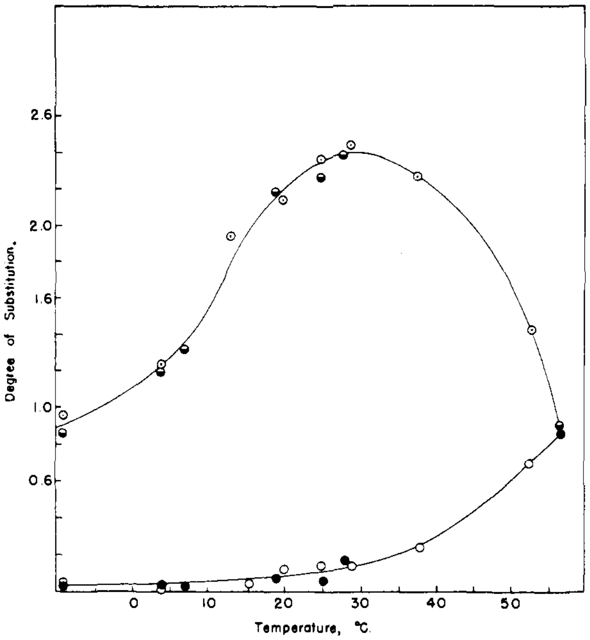

Fig. 1.—Effect of temperature on mesylation; time of reaction 14 hours: mesyl groups, ⊙ run 37, ◒ run 39; chlorine, ○ run 37, ● run 39.

The results clearly indicate that a more complete esterification is obtainable by mesylation than tosylation when both are conducted under similar conditions. This supports the hypothesis that tosylation may be inhibited by steric hindrance effects.

Re-esterification of tosylcellulose with mesyl chloride and with tosyl chloride furnishes further supporting evidence. The data of Table IV show that when tosylcellulose, containing from 0.88 to 2.14 tosyl groups per anhydroglucose unit, was treated with mesyl chloride, complete substitution by a combination of mesyl, tosyl and chlorine groups was attained. Treatment of the original tosylcellulose with tosyl chloride did not produce complete esterification. The presence of tosyl groups in the original sample definitely limited further entry of tosyl groups but apparently did not impede the introduction of mesyl groups. It should be pointed out that an element of uncertainty is present in the calculations because of the increase in chlorine content upon re-esterification. During this step either tosyl or mesyl groups, or both, may be replaced by chlorine. Since the course of this possible replacement is not known, the calculations were based on the assumption that all of the original tosyl groups were present in the final product. Since the total D.S. of the mesylated tosylcellulose 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

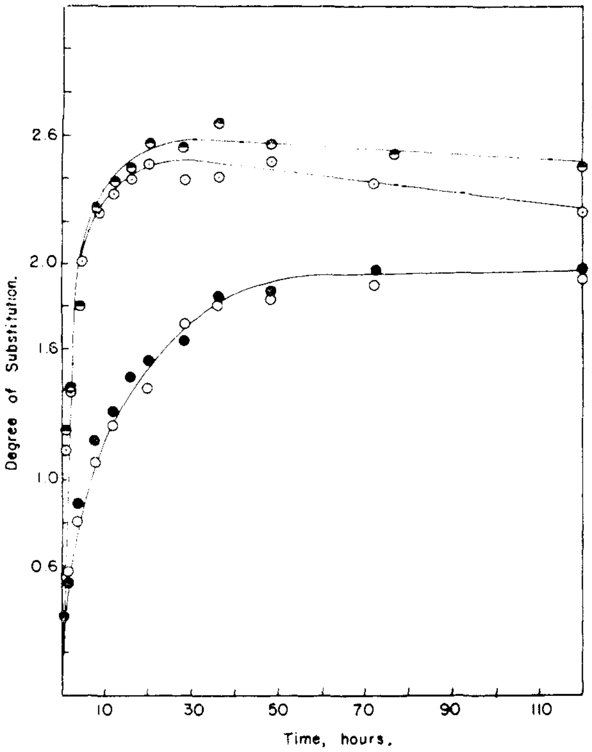

Fig. 2.—Comparative mesylation and tosylation of cellulose, temperature of reaction 28°: mesylation series, ◓ run 46, ◎ run 41; tosylation series, ● run 35, O run 41.

Table IV

Re-esterification of Tosylcellulose

	Original tosylcellulose	Retosylated tosylcellulose	Mesylated tosylcellulose
		Run A	
Sulfur, %	10.72	14.12	19.00
Chlorine, %	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, %	9.46	14.06	20.21
Chlorine, %	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, %	13.93	14.17	16.06
Chlorine, %	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

agreement regardless of whether the original sample had as little as 0.88 or as much as 2.14 tosyl groups per glucose unit.

Trisubstituted mesylcellulose was prepared in a single step by using a 20:1 molar ratio of mesyl chloride to cellulose; total D.S. values of 2.95, or more, were obtained. When a 10:1 ratio was used, the total D.S. rarely exceeded 2.85. Typical analytical values produced by the 20:1 ratio were 22.9% sulfur and 2.15% chlorine, 22.5% sulfur and 3.18% chlorine. Remesylation of a mesylcellulose having a total D.S. of 2.0 also resulted in the formation of products having a total D.S. of approximately 3.0.

The side reaction product, pyridinium methanesulfonate, was ineffectual in causing esterification of the cellulose as was shown by unsuccessful attempts to cause these two materials to react together. The formation of this material simply resulted in a depletion of the active mesylating agent. The active agent was present in the dark brown liquid separated from the solid by-product. Three days after the original mixing of mesyl chloride and pyridine, the liquid portion was still able to introduce about 11% sulfur into a sample of activated cellulose.

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[Contribution from the Northern Utilization Research Branch[1]]

Characterization of Dextrans by the Optical Rotation of their Cuprammonium Complexes

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Optical rotations at 4358 Å. in water and cuprammonium solutions have been measured for several dextrans differing widely in their content of 1,6-, 1,4- and 1,3-like linked anhydroglucopyranoside units as determined by periodate oxidation analyses. Based on previous results for the optical rotational shifts of simple glucopyranosides, it is shown how the optical rotational shift data for dextrans can be used to resolve the percentage of 1,4-like linked units derived from periodate oxidation analyses into the proportions of 1,4- and 1,2-linked units. By this method a large proportion of the 1,4-like linked units in NRRL B-1299 and NRRL B-1399 dextrans were found to be linked through position 2. These are the first dextrans to be reported to contain the 1 → 2-linkage. Optical rotation shift data also indicate that NRRL B-1149 and NRRL B-1355 fraction S dextrans have non-1,6-linked units which occur in linear portions of the polysaccharide chain rather than as branch points in the molecule.

Periodate oxidation reaction analyses of a large number of dextrans have shown that the majority of the anhydroglucose units in these polysaccharides are joined through 1→6-glucosidic linkages,

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