the formation of the N-(5-nitro-2-thenyl)-piperidine picrate.

The 5-nitro-2-thenyl bromide was transformed to its hexamethylenetetramine salt and this salt in turn, hydrolyzed to the aldehyde both by steam distillation and also by refluxing it in 50% ethanol. Since neither method of hydrolysis gave an appreciable yield of the aldehyde, an alternative method of preparation was investigated. 5-Nitro-2-thenyl bromide was then oxidized to 5-nitro-2-thenaldehyde with selenium dioxide.[4] The product from the selenium dioxide oxidation was an oil which, after washing with water, gave a negative halogen test with alcoholic silver nitrate. Since attempted crystallization from such solvents as water and a variety of organic solvents were of no avail, the aldehyde was isolated in the form of its semicarbazone in a yield of 50%.

Experimental[5]

5-Nitro-2-thenyl Bromide.—2-Methyl-5-nitrothiophene (33 g., 0.23 mole), dissolved in 100 ml. of carbon tetrachloride, was treated with 27.38 g. of N-bromosuccinimide and 0.25 g. of benzoyl peroxide. There was no reaction on mixing and only after two to three hours of reflux did the reaction take on a reddish tinge. The mixture was then refluxed for 24 hours to ensure completion of the reaction. It was now cooled, filtered to remove the succinimide and distilled. It was then cooled, filtered to remove the succinimide and distilled. Unreacted 5-nitro-2-methylthiophene was removed at reduced pressure, b.p. 106° (6 mm.). Because of decomposition the 5-nitro-2-thenyl bromide was not distilled. Instead a portion was characterized as its piperidine picrate and the remainder converted to its hexamethylentetramine salt with a yield of 60%.

N-(5-Nitro-2-thenyl)-piperidine Picrate.—A portion of the above after re-solution in carbon tetrachloride was treated with an excess of piperidine dissolved in carbon tetrachloride. There was an immediate precipitation of piperidine hydrobromide. The solution was filtered and added to a saturated solution of picric acid in carbon tetrachloride. The picrate separated in yellow crystals, m.p. 193–194°.

Anal. Calcd. for $C_{16}H_{17}O_9N_5S$: N, 15.38. Found: N, 15.40.

Hydrolysis of Hexamethylenetetramine Salt.—(a).—The salt prepared as above was suspended in water and steam distilled. The distillate (2 liters) was extracted with ether, the ether removed and a small amount of a dark brown oil remained. This was converted to its 2,4-dinitrophenylhydrazone, m.p. 250° (dec.).

Anal. Calcd. for $C_{11}H_7O_6N_5S$: N, 20.77. Found: N, 20.70.

(b).—The hexamethylenetetramine salt was suspended in a solution of 50% ethanol and refluxed for two hours. The ethanol was removed and the residue chilled to induce crystallization. Since there was no separation of solid, the alcohol was removed and the residue extracted with ether. After drying and removal of the ether, a very small amount of brown solid remained. This was not further identifiable as the aldehyde.

Selenium Dioxide Oxidation.—5-Nitro-2-thenyl bromide (11.1 g., 0.05 mole) was dissolved in ethanol. Freshly prepared selenium dioxide (5.55 g., 0.05 mole) was added and the mixture kept at 140–150° (oil-bath) for two hours, during which time most of the solvent was allowed to distil off. After the reaction was completed, the residue was washed with water. Attempted crystallization from the usual organic solvents was unsuccessful and, consequently, the aldehyde was isolated as its semicarbazone, m.p. 223°, yield 50%.

Anal. Calcd. for $C_6H_6N_4O_3S \cdot H_2O$: N, 24.13. Found: N, 24.41.

Acknowledgments.—This work was carried out under the aegis of the Office of Naval Research. The analyses were performed by A. A. Sirotenko of this Department.

CONTRIBUTION NO. 251 FROM THE DEPARTMENT
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[4] C. H. Fisher, THIS JOURNAL, **56**, 2056 (1934).

[5] Shortly before receipt of our proofs there appeared a Note by Emerson and Patrick (*ibid.*, **74**, 1356 (1952)) describing a different synthesis. The final data are in agreement with ours.

Distribution of Hydroxyl Groups in Carboxymethyl Cellulose[1]

BY ELIZABETH DYER AND HARRY E. ARNOLD

RECEIVED DECEMBER 1, 1951

Prior to the completion of this work, there was only one report of the distribution of the free and substituted hydroxyl groups in carboxymethyl cellulose. Timell[2] determined glycol groups by periodate oxidation and stated that the tosylation–iodination method, used for other cellulose ethers,[3] was not applicable to this substance. In a recent extensive study of carboxymethyl cellulose, Rydholm[4] also used the periodate oxidation and stated that tosylation was tried without success.

In the present work both the tosylation–iodination procedure and the periodate method were used on two samples of carboxymethyl cellulose,[5] of a degree of substitution of 0.75 and 0.77. CMC 1 had been prepared by a slurry technique, and CMC 2 by dry mixing. The viscosity of a 2% aqueous solution was 4000 cps. and 500 cps. for CMC 1 and 2, respectively.

TABLE I

TOSYLATION OF CARBOXYMETHYL CELLULOSE AT 20°

CMC	Time, days	S,[a] %	Tosyloxy,[b] moles/g.u.[e]	Cl,[a] %	$-OCH_2-COOH$,[c] mole/g.u.	$\eta_{rel.}$[d]
1	0	0	0	0.06	0.75	1.39
	0.25	7.01	0.68			
	0.50	7.95	.83			
	1.00	8.40	.91			
	2.00	8.70	.96	0.16	0.76	1.11
	3.00	9.01	1.02	.18	.78	1.04
	8.00	9.33	1.08	.33	.77	1.02
2	0	0	0	.07	.77	1.43
	0.25	6.99	0.68			
	0.50	7.66	.78			
	1.00	8.16	.87			
	2.00	8.62	.94	0.15	0.81	1.08
	3.00	8.90	1.01	.15	.77	1.06
	8.00	9.28	1.08	.33	.76	1.04

[a] Average value of at least two determinations done gravimetrically with the Parr bomb. [b] Calculations based on values of 0.75 and 0.77 for $-OCH_2COOH$ in tosylates of CMC 1 and 2, respectively. [c] Except for zero time, only small samples were available for analysis; hence the value at zero time, known with greater precision, was used in calculations. [d] Ratio of time of flow of solution and solvent in a Bingham viscometer at 25°, using a 0.2% solution of the compound in 0.25% aqueous sodium hydroxide. [e] G. u. means anhydroglucose unit.

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[1] From the M.S. Thesis of Harry E. Arnold, September, 1950.

[2] T. Timell, *Svensk Papperstidn.*, **52**, 61 (1949).

[3] (a) J. F. Mahoney and C. B. Purves, THIS JOURNAL, **64**, 9, 15 (1942); (b) C. W. Tasker and C. B. Purves, *ibid.*, **71**, 1017, 1023 (1949); (c) T. Timell, *Svensk Papperstidn.*, **51**, 52 (1948).

[4] S. Rydholm, *ibid.*, **53**, 561 (1950).

[5] du Pont Sodium CMC, supplied through the courtesy of the Explosives Department of E. I. du Pont de Nemours and Company.

The tosylation reaction was carried on in pyridine, with the cellulose derivative in a highly swollen, but not dissolved condition. Purification of the product was done by repeated steeping and washing, since its insolubility prevented reprecipitation. Table I shows that the initial rapid reaction had slowed almost to a stop within three days, when tosyl substitution equivalent to a monoester was found. However, complete tosylation did not occur even under the prolonged reaction period of eight days. No explanation is available for this phenomenon as a sufficient excess of tosyl chloride was used.

The chlorine content increased slightly as the reaction progressed, but the amount was so small it was assumed to be negligible in subsequent calculations (done with 2- and 3-day tosylates). Partial justification of this procedure is the fact that chlorine which replaced tosyloxy groups would be quantitatively exchanged for iodine,[6] and no increase in iodine unaccounted for by loss in tosyloxy was observed.

The rate of replacement of tosyloxy groups by iodine is shown in Table II. Since the iodine and tosyloxy contents became almost constant after four hours at 120°, it can be concluded that this procedure does differentiate primary from secondary hydroxyl in carboxymethyl cellulose. Taking the averages of the data in the last five lines of Table II gives 0.65 and 0.64 mole of free primary hydroxyl in CMC 1 and 2.

A small but consistent loss of tosyloxy took place during the iodination. This loss cannot be explained on the basis of analytical errors. A similar effect was observed by Malm, Tanghe and Laird[6] on prolonged iodination of cellulose tosylate.

The rate of oxidation of adjacent hydroxyl groups by periodate is shown in Fig. 1. The consumption of oxidant reached a zero slope in five days, which corresponds to 0.71 and 0.69 mole glycol per glucose unit for CMC 1 and 2, respectively. This is slightly higher than the 0.62 mole glycol reported by Rydholm[4] for carboxymethyl cellulose of the same initial degree of substitution. Dürig and Banderet[7] found 0.63 and 0.65 mole glycol in carboxymethyl cellulose containing 0.65 and 0.67 ether group.

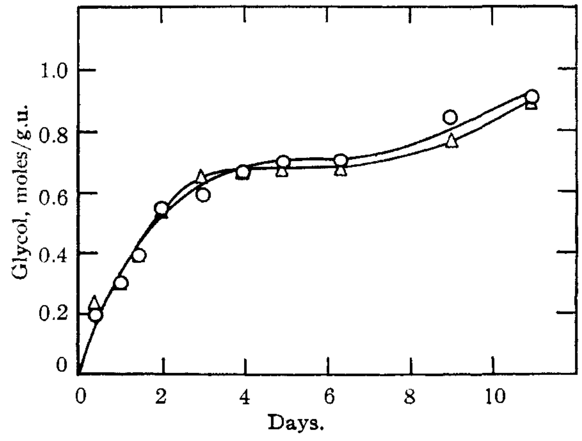

Fig. 1.—Periodate oxidation of CMC 1, O; CMC 2, Δ.

TABLE II

IODINATION OF TOSYLATED CARBOXYMETHYL CELLULOSE

Sample CM-C No.	Sample Tosyloxy, moles/g.u.	Iodin. temp., °C.	Time, hr.	S, %	Tosyloxy,[a] moles/g.u.	Iodine %	Iodine mole/g.u.	Loss[b] of tosyloxy, moles/g.u.
1	0.98[d]	100	1	4.53	0.46	17.79	0.46	0.06
			2	3.67	.37	20.52	.51	.10
			4	3.61	.36	22.66	.59	.03
1	0.98[d]	120	1	3.38	.33	19.96	.49	.16
			2	2.72	.27	24.40	.60	.12
			4	2.37	.23	25.93	.63	.13
1	0.96[c]	120	4	1.98	.19	26.28	.66[e]	.11
	1.02[d]		4	2.61	.26	25.60	.64[f]	.12
2	0.94[c]	120	4	2.03	.18	26.21	.63[f]	.13
	1.01[d]		4	2.22	.22	26.52	.65[f]	.14

[a] Based on 0.75 and 0.77 mole $-OCH_2COOH$ for iodinated tosylates of CMC 1 and 2. Analysis of selected samples indicated no change in carboxymethyl content during iodination. [b] Difference between moles tosyloxy lost and moles iodine gained during iodination. [c] Tosylated for 2 days. [d] Tosylated for 3 days. [e] Relative viscosity after iodination 1.04. [f] Relative viscosity 1.03.

A summary of the data on the distribution of hydroxyl groups in CMC 1 and 2 is given in Table III. The similarity in the results from the two samples shows that the differences in the methods of preparation had no appreciable effect on the location of the ether groups. The application of the test for homogeneity devised by Mahoney and Purves[3a] shows that there is not a completely uniform distribution of the ether groups on the secondary hydroxyls. (The values of G are intermediate between $H^2/4$ and $H/2$.) This is not in accord with the findings of Rydholm.[4]

TABLE III

DISTRIBUTION OF HYDROXYL GROUPS[a] IN CARBOXYMETHYL CELLULOSE

		Primary		Secondary					
CMC	D.S.	Free	Subst.	Free adj.	Subst.	G[b]	H[c]	$H^2/4$	H/2
1	0.75	0.65	0.35	1.42	0.40	0.71	1.60	0.64	0.80
2	.77	.64	.36	1.38	.41	.69	1.59	.63	.79

[a] Moles per glucose unit. [b] Glycol. [c] Total free secondary -OH.

The total number of hydroxyl groups (free and substituted) accounted for by the data given in Table III is 2.82 and 2.79 per glucose unit. The difference of this total from 3.00 could be due to the free, non-adjacent secondary hydroxyls, which were not determined.

Experimental

Carboxymethyl Cellulose.—The free acid was prepared from the salt[8] by treatment with a mixture of water, sulfuric acid and ethanol. After thorough washing and drying at 55° *in vacuo*, the products had ash contents of 0.02 and 0.08% for CMC 1 and 2, respectively. The average degrees of etherification, based on five determinations[8] for each, were 0.75 and 0.77.

Tosylation.—To 23 g. of carboxymethyl cellulose (0.25 mole unsubstituted hydroxyl) activated by treatment with water followed by distillation of pyridine was added a cold (20°) solution of 2.5 moles (475 g.) of tosyl chloride in 9 moles (600 ml.) of dry pyridine. The reaction mixture was tumbled at 20 ± 1°. At appropriate intervals a 150-ml. sample was removed and added to 1000 ml. of ice-cold 10% aqueous acetone. After stirring for five minutes the entire slurry was poured into 1500 ml. of distilled water. The

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[6] C. J. Malm, L. J. Tanghe and B. C. Laird, THIS JOURNAL, **70**, 2740 (1948).

[7] G. Dürig and A. Banderet, *Helv. Chim. Acta*, **33**, 1106 (1950).

[8] R. W. Eyler, E. D. Klug and F. Diephuis, *Anal. Chem.*, **19**, 24 (1947).

product was filtered, then steeped ten times with 1-liter portions of water. Halide ions were absent in the filtrate after the third washing. After a week of steeping in acetone, the dried product was a fine white powder.

Iodination.—Samples of 1.5–2.5 g. of the tosylated product were treated with 75–125 g. of a 15% solution of sodium iodide in freshly distilled acetonylacetone under the conditions shown in Table II. Purification and analysis for iodine were done by the methods of Mahoney and Purves.[9]

Periodate Oxidation.—Reactions were carried out in the dark[10] at a *p*H of 5.4[11] in the presence of bicarbonate with the temperature at 20 ± 1°. Separate 25-ml. portions of a 0.4% aqueous solution of CMC were treated with 50 ml. of oxidant solution (0.0796 *N* in $NaIO_4$) prepared from sodium paraperiodate. The amount of oxidant consumed after a given period was determined by the method of Davidson.[12]

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[9] Reference 3a, page 10.

[10] F. S. H. Head, *J. Textile Inst.*, **20**, A23 (1950).

[11] C. C. Price and H. Kroll, THIS JOURNAL, **60**, 2726 (1938).

[12] G. F. Davidson, *J. Textile Inst.*, **31**, T81 (1940); *ibid.*, **32**, T109, 132 (1941).

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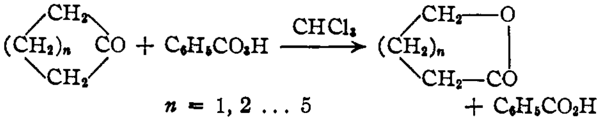
Further Observations on the Reaction of Cyclanones with Perbenzoic Acid

BY S. L. FRIESS[1] AND P. E. FRANKENBURG

RECEIVED DECEMBER 7, 1951

In a previous communication[2] dealing with kinetic and stoichiometric studies of the reaction of cyclanones with perbenzoic acid, limited data were ob-



tained for those members of the ketone sequence with n = 2, 3 and 4. These data have now been extended to include the reactions of the four and eight-membered ring ketones (n = 1, 5). In addition, temperature coefficients and thermodynamic quantities of activation have been determined for the peracid reaction of the entire ketone series, as well as comparative values of rate constants for all members of the series, referred to a single peracid solution. The latter data furnish a completed picture of the reactivity of the carbonyl group toward peracid addition,[2] in the range n = 1 to 5, as a function of ring size of the cyclic ketone.

In preliminary runs on a preparative scale, purified samples of cyclobutanone (I) and cycloöctanone (II) were allowed to react with excess perbenzoic acid in dry chloroform. The lactone products of these reactions were converted into their respective ω-hydroxyhydrazides, for ease of handling and purification, and furnished amounts of crystalline hydrazides corresponding to product yields of 70 and 61% from I and II. The yield cited for II is based on that amount of ketone unrecovered from its sluggish reaction mixture after an extensive reaction interval at room temperature.

Since all members of the ketone series have now been shown to undergo the primary ketone → lactone reaction, it was of considerable interest to obtain values of the rate constants for this process, referred to a single peracid solution of normal oxidative activity,[2,3] for comparison with other chemical indices of reactivity[4] of these cyclanones. Accordingly, the initial rates of reaction were determined for all members of the ketone series at 25.65°, and second order rate constants (k_2) evaluated for each ketone reaction. Since a rate run on a standard ketone (cyclohexanone or cyclopentanone) was made simultaneously with runs on every other member of the series, all k_2 values could be normalized[3] to an average k_2 value for cyclohexanone of 9.58×10^{-4} l./mole sec., or 1.36×10^{-4} l./mole sec. for cyclopentanone, in a process equivalent to standardization of all runs to the activity of a single peracid solution. New data obtained in this portion of the study include k_2 values for I and II at 25.65° of $(7.0 \pm 1.0) \times 10^{-5}$ and $(2.28 \pm 0.15) \times 10^{-5}$ l./mole sec., respectively. Rate constant data for the entire series at this temperature are shown plotted in Fig. 1, as a function of ketone ring size.

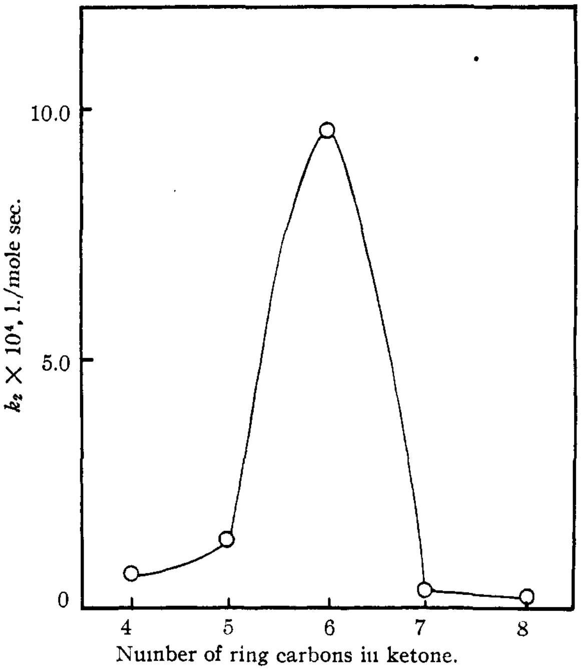


Fig. 1.—Rate constants in dry chloroform at 25.65°.

Significantly, the reaction rate for the six-membered ketone is at a maximum for the series, with a sustained drop in rate as ring size is either increased or decreased from this peak value. This particular result is for the most part in accord with the concept of Brown,[4] relating to I-strain as the determining factor in the rates of addition reactions to carbonyl groups contained in common-sized rings. However, the relatively low reactivity of the four-membered cyclanone I is surprising when viewed on this basis, since a lesser degree of strain should be inherent in the transition state for a rate-determining addition or coördination process than that present in the initial ketone molecule, with a net result of

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[1] Naval Medical Research Institute, Bethesda, Md.

[2] S. L. Friess, THIS JOURNAL, **71**, 2571 (1949).

[3] S. L. Friess and A. H. Soloway, *ibid.*, **73**, 3968 (1951).

[4] See, for example, the compilation and interpretation of reactivity data by H. C. Brown, R. S. Fletcher and R. B. Johannesen, *ibid.*, **73**, 212 (1951).