p-TOLUENESULFONYL AND IODO DERIVATIVES OF SOME HYDROXYETHYL ETHERS

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by

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A thesis presented to the Faculty
of Graduate Studies and Research
of McGill University in partial
fulfilment of the requirements for
the Degree of Doctor of Philosophy

McGill University June, 1947
Montreal, Canada.

ACKNOWLEDGEMENTS

The investigator expresses his sincere appreciation to Professor Clifford B. Purves, under whose guidance the work was accomplished, to the Sylvania Division, American Viscose Corporation for two Fellowships and to the Canadian Pulp and Paper Association for summer stipends.

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GENERAL INTRODUCTION

The ultimate objective in this research was to determine quantitatively the individual amounts of primary and secondary alcohol groups in an alkali soluble, commercial hydroxyethyl ether of cellulose. The methods proposed for this study had previously been perfected on various other derivatives of cellulose, starch and sugars (1, 2, 3, 4). These methods depended on the fact that the p-toluene sulfonyl (tosyl) esters of primary, as opposed to secondary, alcohols gave quantitative yields of alkyl iodide when treated with sodium iodide in a ketone solvent. However, it was considered advisable first to apply the same techniques to simpler compounds which possessed a structural similarity to the hydroxyethyl ethers of cellulose. Part I is accordingly concerned with the monoethyl ethers of the first three members of the polyethylene glycol series. These compounds may be represented by the general molecular formula $C_2H_5(OCH_2CH_2)_xOH$ in which x is equal to one, two and three respectively. The analogy to the hydroxyethyl ethers of cellulose is established by replacing the ethyl group by the glucose unit of the cellulose macromolecule.

In the course of the investigation, tosyl esters were prepared from ethanol, β-ethoxyethanol (Cellosolve), 2-(β-ethoxyethoxy) ethanol-1 (Carbitol) and from the trimer, 2-(β-ethoxyethoxyethoxy) ethanol-1, $C_2H_5(OCH_2CH_2)_3OH$. Physical properties and analyses were noted for the individuals which had not previously been characterized in a pure state. The p-toluene sulfonate esters were then converted into the corresponding iodine derivatives and these iodo- compounds were also purified and characterized in cases where this had not been previously done. A study was made of the relative ease of hydrolysis in aqueous methanol, and of iodination with sodium iodide in acetonyl acetone, shown by the four tosyl derivatives. The anomalous results they gave in the standard alkoxyl determination was investigated but the investigation was stopped when the question was settled in a recent publication (5).

The great tendency of the purified monoethyl ethers of ethylene and diethylene glycol to form peroxides was noted, and the inherent thermal instability of the two higher tosyl esters was carefully studied. This unexpected reaction liberated high yields of 1,4-dioxane from the p-toluene sulfonate esters of the monoethyl ethers of diethylene and triethylene glycol. Such new experimental evidence, together with indications already present in the literature, justified a new conception of some of the reactions of the polyethylene glycols.

The work on hydroxyethyl celluloses described in Part II of this thesis proceeded with the knowledge that special care had to be taken to guard against errors caused by peroxide formation, by the thermal instability of the tosylated derivatives, and by dependence on the standard alkoxyl estimation. The tosylation-iodination and tosylation-chlorination reactions were used to determine the apparent ratio of primary to secondary alcohol groups in an alkali-soluble hydroxyethyl cellulose. Complications, however, arose owing to the formation of chlorinated by-products and the unexpected elimination of a part of the hydroxyethyl units during tosylation with p-toluenesulfonyl chloride dissolved in pyridine. These complications made the interpretation of the data indecisive.

PART I

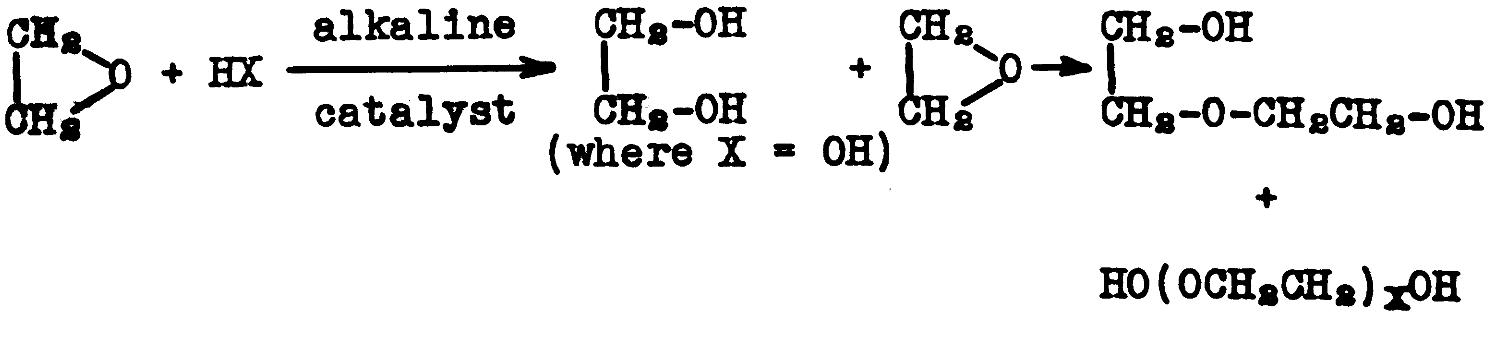
SYNETHETICAL STUDIES IN THE POLYETHYLENE GLYCOL MONOETHYL ETHER SERIES

HISTORICAL INTRODUCTION

The three members of the polyethylene glycol series and their derivatives investigated in this research all contain the repeating unit ($-CH_2CH_2O-$), and in this respect may be considered to be derivatives of ethylene oxide. In fact, the polyethylene glycols have been prepared starting with ethylene oxide as a raw material (6, 7, 8); a method of synthesis was discovered as early as 1859, by Wurtz (9), who heated ethylene oxide with ethylene glycol or water for several weeks. The hydroxyethyl ethers of cellulose are produced commerically by the action of ethylene oxide on alkali cellulose and, at least in certain cases, these derivatives must contain polyethylene glycol chains (5). In order to understand the chemistry of the simple compounds and the cellulose derivatives, it is necessary first to consider the mechanism of the polymerization or condensation of ethylene oxide, secondly to review what was known concerning the physical state of the polymer molecules, and finally to survey their chemistry.

Two general theories are available for the formation of long chain polymer molecules, the Free Radical Theory, the chief proponent of which was H. Staudinger (10), and the Stepwise Addition Theory, due to Whitby (11). Staudinger's mechanism consisted of three steps: one, the activation of the monomer unit to give free radicals (this being the slow rate-determining step); two, propagation by the addition of free radicals to one another in a series of chain reactions; three, termination by the addition of some HX type of molecule to the free radical intermediate, thereby causing its inactivation-saturation. Whitby's Stepwise Addition Theory consisted simply of the activation of a polymer monomer in the presence of a catalyst; the activated molecule rapidly added another monomer molecule with the migration of a hydrogen atom. This dimer then was capable of becoming activated and reactive and the process could be continually repeated. Staudinger proposed two polymerization mechanisms for ethylene oxide; on the one hand, all the short chains up to ten or twelve units were formed by the Stepwise Addition Theory, while, on the other hand, all the long chain polymer molecules were supposed to have been formed by his Free Radical Theory.

In 1933, Hibbert and Perry (12) proposed the Stepwise Addition Theory mechanism to account for the formation of both high and low polymers of ethylene oxide. This mechanism was as follows:



Perry and Hibbert (13, 14) using synthetic methods whereby individual members of the polyethylene glycol series could be obtained in a pure state, prepared analytical samples of the series containing two, three, four, five, six and eighteen ethylene oxide units. Having these derivatives, they conclusively proved that their particular stepwise addition mechanism for the polymerization was valid and that each new member of the series was capable of acting as an intermediate for further chain growth.

The investigators of the Hibbert school, having developed the means for preparing and purifying the polyethylene glycols (13, 15, 16, 17), found themselves in possession of a series of known compounds $HO(CH_2CH_2O)_xH$ in which x was varied from one to one hundred and eighty-six. Another group of workers then proceeded to study the molecular weights, freezing points, molar refractions (16, 17, 18), surface tension constants (19, 23), vapor pressure (20), and viscosity characteristics (21, 22) of these polymers. Various anomalies were encountered in these studies and attempts were made to account for them. In general, the conclusion reached was that the polyethylene glycols existed as zig-zag molecules which apparently were highly convoluted in solution. There also appeared to be quite noticeable intermolecular forces operating between the molecules in the undiluted state. The second member of the series, diethylene glycol, was in several cases distinguished from the other homologs by an apparent ability to assume a structure similar to that of 1,4 dioxane, perhaps because of some sort of intramolecular force.

In keeping with their dual nature as ethers and alcohols, the polyethylene glycols and some of their derivatives are excellent solvents and plasticizers (24, 25). It is a well known fact that the ether oxygen-carbon bond is very stable and unreactive under normal conditions and that the ethers as a group undergo relatively few reactions. One common reaction that they do undergo, with which this research is concerned, is with constant boiling hydriodic acid. Normally this reaction could be expressed as follows:

$$R - O - R + HI \xrightarrow{126^\circ} R - O - H + RI,$$

$$R - O - H + HI \xrightarrow{\qquad} RI + HOH,$$

and it has long been the basis for the quantitative estimation of those alkoxyl groups which yield alkyl halides of b.p. less than 126° (26, 27). However, in the case of the polyethylene glycol type this reaction was shown not to be quantitative (28, 29, 30). Although Lawrie and others (31) obtained ethyl iodide by a Zeisel analysis of hydroxethyl cellulose, they did not report data to indicate what reproducibility was obtained. Morgan (5) in a very recent publication clarified the earlier anomalous results by showing that the following reactions occur.

$$\begin{aligned}
&ROCH_2CH_2OH + 3\,HI && \longrightarrow RI + ICH_2CH_2I + 2\,H_2O \\
&ICH_2CH_2I && \longrightarrow CH_2 = CH_2 + I_2 \\
&ICH_2CH_2I + HI && \longrightarrow CH_3CH_2I + I_2 \\
&CH_2 = CH_2 + HI && \longrightarrow CH_3CH_2I
\end{aligned}$$

or, in total,

$$ROCH_2CH_2OH + (3+x)\,HI \longrightarrow RI + (x)\,CH_3CH_2I + (1-x)\,CH_2{=}CH_2 + I_2 + 2H_2O$$

The total ethyl iodide and ethylene collected and measured in the case of the polyethylene glycols and their derivatives accounted quantitatively for every alkoxyl and every $(-CH_2CH_2O-)$ group in the molecule. This new quantitative method by Morgan enabled him to report the average degree of substitution in hydroxyethyl ethers of cellulose for the first time with some degree of reliability (5).

The reactions of the primary hydroxyl groups in the polyethylene glycol series appeared to be normal. Palomma (32) prepared various monoalkyl ethers of ethylene glycol by the action of sodium on ethylene glycol followed by a coupling reaction with an appropriate alkyl halide.

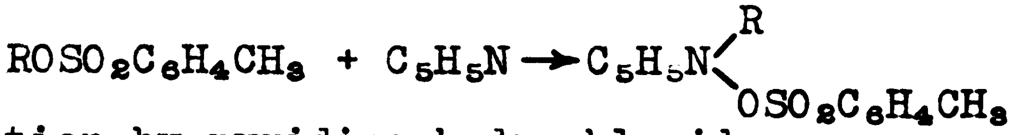
The products obtained in a pure state by fractional distillation could be esterified by an acid anhydride in pyridine solution. Cretcher and Pittenger (33) made the monoalkyl derivatives of ethylene glycol by the action of ethylene oxide on an alcohol in the presence of dissolved sodium and by the condensation of alcoholates with ethylene chlorohydrin. The yields by the first method ranged from 26 to 50 percent, and in the latter case from 25 to 60 percent. Other investigators (34, 35, 36) have since used the general reaction of an alcohol and ethylene oxide in the presence of metallic catalysts to prepare the monoalkyl ethers of the polyethylene glycol series. A summary of the physical constants for some of the monoethyl ethers of the polyethylene glycols has been recorded (25). Diethers of the type $R(OCH_2CH_2)_xOR'$ were obtained, not in very good yields however, by first making the sodium salt of the monoether $R(OCH_2CH_2)_xOH$ and then condensing it with an appropriate alkyl halide (37). Other investigators also employed similar Williamson ether syntheses for the preparation of the mono- and dialkyl ethers of ethylene and diethylene glycol (38, 39).

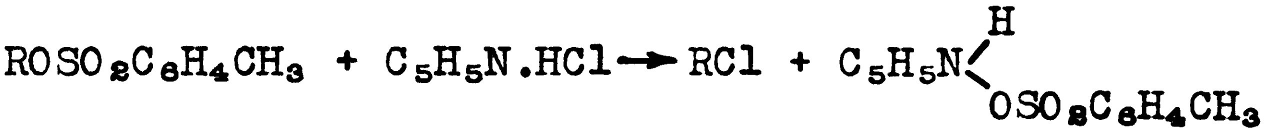
A very interesting fact in connection with the polyethylene glycols and their monoalkyl ethers was noted by Davidson (25) who observed that the boiling points of the monoethyl ethers were very close to those of the next lower, unsubstituted polyethylene glycol. Unfortunately, this fact was overlooked or disregarded up to 1941, when Seikel (40) found that the commercial monoethyl ether of diethylene glycol (Carbitol) could not be satisfactorily freed from ethylene glycol by fractional distillation. This investigator showed that commercial samples of Carbitol contained up to 28 percent ethylene glycol, and that up to 8.5 percent of the latter was present in commercial methyl Carbitol. The observation explains why the physical constants quoted for Carbitol and its various derivatives vary from source to source in the literature.

Further evidence of the normal reactivity of the primary hydroxyl groups in the polyethylene glycol series is to be found in the fact that the diesters can be readily prepared. Holt (41) obtained the dipropionates by treating glycol in toluene solution with propionic acid, using sulfuric acid as catalyst. Rinkenbach (42), likewise, formed the dinitrate of ethylene glycol by subjecting glycol to the action of a commercial nitrating acid mixture. The ditrityl esters of the first three members of the polyethylene glycol series were easy to prepare (43).

The monoalkyl ethers of ethylene and diethylene glycol, the Cellosolves and Carbitols respectively, were not commercially available before the late 1920's, even though some of them were synthesized years earlier by Palomma (32). They were studied but little prior to 1932, when Conn and his coworkers (44) started what became a long series of investigations. These workers prepared the benzoate and p-nitrobenzoate esters of a number of the Cellosolves and Carbitols using Palomma's original method (32). They found that in general the derivatives were high boiling liquids which were insoluble in water, but which were soluble in the common organic solvents. Difficulty was experienced in obtaining pure derivatives in the case of diethylene glycol monoethyl ether.

Whitmore and Lieber (45), noting the fact that up to 1935 no fundamental data existed in the literature for the qualitative determination of the Cellosolves and Carbitols, undertook to prepare some crystalline derivatives. They were able to obtain crystalline xanthates in a pure state for methyl-, ethyl- and butyl Cellosolves, but failed to obtain a good derivative for ethyl Carbitol. Other investigators, Veraguth and Diehl (46) made the 3-nitrophthalates of a series of the monoalkyl ethers of ethylene and diethylene glycol; good crystalline esters being obtained for all the ethylene glycol derivatives investigated, but only one being found in the diethylene glycol series. An excellent review of all attempts to prepare crystalline derivatives of the Cellosolves and Carbitols up to 1940 is to be found in two papers by Mason and Manning (47, 48). These authors, also after numerous failures, managed to prepare some new solid derivatives which included the p-nitrophenyl urethane, the picramides of the Cellosolve and Carbitol esters of anthranilic acid, the 2-amino-4-nitrophenylethers, the azo compounds obtained by the diazotization of the p-aminobenzoates of the Cellosolves and Carbitols and coupling with dimethyl aniline, and finally the picrates and hydrochlorides of the β-4-morpholinoethyl ethers. Seikel's article then appeared concerning the presence of ethylene glycol in ethyl Carbitol purified by fractional distillation (40). Since all the above work was done on commercial Cellosolves and Carbitols which were purified by fractional distillation, doubt now surrounds the validity of most of it and the difficulties encountered in obtaining crystalline derivatives are explicable to some degree. Once the glycol impurity was eliminated (40) the monotrityl derivatives for a number of Carbitols and Cellosolves were easily prepared in good crystalline form (43). However, the trityl derivative of Carbitol itself was not isolated although Shupe (49) found that the crystalline xanthate could be prepared provided ethylene glycol was completely eliminated. He made this derivative the basis for a quantitative method of estimating ethyl Carbitol, thereby succeeding where Whitmore (45) had failed. Very recently, other investigators (50) prepared crystalline triiodobenzoic acid esters from the Cellosolves and Carbitols with no particular trouble.

Tipson (51) in an investigation of the tosylation of Cellosolves, discussed in considerable detail the side reactions which may take place during the esterification. Considering any tosyl ester $ROSO_2C_6H_4CH_3$, ether formation, $ROSO_2C_6H_4CH_3 + ROH \rightarrow ROR + HOSO_2C_6H_4CH_3$, the formation of quaternary salts with the pyridine reaction medium,  $ROSO_2C_6H_4CH_3 + C_5H_5N \rightarrow C_5H_5N{<}^{R}_{OSO_2C_6H_4CH_3}$ and chlorination by pyridine hydrochloride,



$$ROSO_2C_6H_4CH_3 + C_5H_5N.HCl \rightarrow RCl + C_5H_5N{<}^{H}_{OSO_2C_6H_4CH_3}$$

were all possibilities. He described a procedure which gave good results by keeping these side reactions down to a negligible amount. The esters of p-toluenesulfonic acid are interesting in that they show a great deal of similarity to the alkyl halides. They may, for example, be used in place of the latter in the malonic acid synthesis (52) where, although slower to react, they are just as efficient. Similarly, they may be employed in the alkylation of acetoacetic esters (53) with complete success. The tosyl esters are important alkylating agents (51), especially for the alkylation of phenolic substances containing one or more tertiary amine nitrogen atoms, since the phenolic hydroxyl groups can be preferentially alkylated without affecting the tertiary amino units. These esters have been employed in many cases to substitute the $R(OCH_2CH_2)_xO-$ group into other molecules (51, 54, 55, 56).

Ethyl p-toluenesulfonate is the first member of the homologous series of tosylated monoalkyl ethers of the polyethylene glycols and has the proper formula ($C_2H_5(OCH_2CH_2)_xOH$) when x is zero. It was first prepared and characterized by Freiman and Sugden (57), whose results were later confirmed in other work (51). The tosyl esters of a large number of the monoalkyl ethers of ethylene glycol, the second member of the homologous series, have been prepared and characterized (54, 55), including that of the ethyl ether, Cellosolve (51, 54). In some cases where these derivatives were oils which decomposed on distillation (55), thorough washing of the crude products with water and thorough drying yielded samples which gave excellent elementary analyses. This observation suggests that these esters were not readily hydrolyzed by cold water. Adams (56) in a patent made reference in general terms to tosyl esters of the class $RO(CH_2CH_2O)_xTs$. They were prepared with tosyl chloride and the ether-alcohol $RO(CH_2CH_2O)_xH$ in the presence of an alkaline solvent. He characterized the compounds as heavy, viscous, oily substances which were insoluble in water, but which were soluble in the usual organic solvents. Presumably, the tosyl esters of the monoethyl ethers of diethylene and triethylene glycol would come under this patent, but no characterizations of pure substances were made.

That the tosyl ester group may be quantitatively replaced from a primary alcohol unit such as ($-CH_2-OTs$) by iodine, employing an inorganic halide salt, such as sodium iodide in acetone or acetonyl acetone solution, has been well established by workers in carbohydrate chemistry (1, 2, 3, 4). In the case of the tosyl esters discussed above, such a replacement would result in a homologous series of β-iodoethyl ethers of the general type, $C_2H_5(OCH_2CH_2)_xI$. Ethyl iodide would be the first member of this series ($x = 0$) and is also the only one which is not a β-iodoethyl ether. The second member of this series is β-iodo-diethyl ether which was first encountered by Baumstark (58) as a by-product in the preparation of ethylene di-iodide from ethylene and an alcoholic solution of iodine. He noted some of its physical properties, but failed to establish its molecular structure correctly. The correction was made by Demole (59) who prepared the substance by using the well known reaction between phosphorus triiodide and β-hydroxy diethyl ether. This work was later repeated (60). More recently the iodo derivative was prepared by the action of sodium iodide in ethanol solution on β-chloro-diethyl ether (61).

No reference has been found for the preparation or characterization of β-iodo-β'-ethoxy-diethyl ether or of β-iodo(β-ethoxy) β'-ethoxy-diethyl ether. These substances would result from the replacement of the ester group in the tosyl esters of the monoethyl ethers of diethylene glycol (Carbitol) and triethylene glycol respectively. However, other derivatives analogous to the β-iodo-β'-ethoxy diethyl ether have been investigated (62, 63).

From the time of the first preparation of the β halogen ethers, various investigators have noted that these substances are often extremely unreactive and yet on occasion give unorthodox reactions. Baumstark (58) and Demole (59) found that β-iodo-diethyl ether was stable to the action of sodium amalgam and that strong potassium hydroxide solution or even the solid base failed to displace the halogen even at a temperature of 150°. Reaction occurred, however, with sodium ethylate in a sealed tube at 150°. Henry (60) found that the iodo-ether was not decomposed when it was redistilled (b.p. 154-155°) from pulverized silver, and Karvonen (64)indeed claimed that the best way to purify the substance was to redistil it many times over solid sodium hydroxide. Karvonen also noted that β-iodo diethyl ether did not react with tertiary propyl amine even after heating at 100° for a period of one hour. Swallen and Boord (61) found that the β-bromoethyl alkyl ethers could be distilled from solid sodium hydroxide without apparent decomposition. A general observation was made (64) to the effect that metallic sodium reacts only slowly on the β-iodoethyl alkyl ethers in the cold, although more rapidly at high temperatures. With aqueous or aqueous-alcoholic solutions of silver nitrate (64) all of the ethers investigated caused the deposition of silver iodide. The β-halogen ethers, water-insoluble and extremely resistant to hydrolysis, stand in sharp contrast to the more water soluble and much more readily hydrolyzed α isomers.

β, β'-Dichloroethyl ether was found to be exceptionally stable to the action of sodium ethylate. Although this conclusion has been questioned (18), it seems that reaction does not take place at room temperature but that heating for eight to fifteen hours is required (42). In similar fashion β,β'-dichloroethyl ether only reacted with sodium acetate to form the mono- and diacetates when a catalyst such as diethylamine and heat at 190° were employed for a number of hours. Later it was found that the β-halogen ethyl alkyl ethers did not form stable Grignard reagents with metallic magnesium, the products of the reaction being always ethylene and the alkoxyl magnesium halide Mg(OR)X (65). The nature of the alkyl group present in the ether did not appear to effect the course of the reaction.

Although the polyethylene glycols themselves, their mono- and dialkyl ethers, and other derivatives, all contain ether oxygen linkages, no mention has been observed in the literature that they form peroxides on standing. The only hint that they might possess this capacity is in some work by Liston and Dehn (37), who reported that the dialkyl ethers of ethylene and diethylene glycol underwent certain decompositions during their formation, distillation and storage. Upon distillation after storage some derivatives decomposed with explosive violence.

EXPERIMENTAL

Note: Unless definitely specified all boiling points and melting points determined in this work are uncorrected

I. The Purification of Reagents Employed

2-Ethoxyethanol-1 (Cellosolve) ($C_2H_5OCH_2CH_2OH$)

The technical material (Carbide and Carbon Chemical Corporation) was dried for at least twelve hours over anhydrous calcium sulfate, with frequent shaking, and was fractionally distilled through a 20 inch Vigreux type column containing 20 sets of indentations per inch. The fraction with a constant b.p. of 134.5°, and with n_D^{20}, 1.4073, was collected. These values agree well with those, b.p. 134-134.6° and n_D^{20}, 1.40737, quoted by Tallman (65).

2-(β-Ethoxyethoxy)ethanol-1 (Carbitol) ($C_2H_5(OCH_2CH_2)_2OH$)

The technical Carbitol obtained from Canadian Industries Limited was purified according to the method of Seikel (40). A solution of 250 grams in 750 cc. of benzene was extracted repeatedly with 5 cc. portions of water, allowing ten minutes for the water and benzene layers to separate each time. The increase in volume of the aqueous layer caused by the selective extraction of ethylene glycol was noted after each extraction. The extractions were continued until this increase in volume became constant. The benzene solution was then dried over anhydrous sodium sulfate. Finally, the benzene was removed and the residue distilled through the column used for the Cellosolve. The fraction of b.p. 201.2° (uncor.) and n_D^{20}, 1.4273 was collected. These constants checked well with those, b.p. 196°/762 mm. and n_D^{20}, 1.4273, given by Seikel (40). Before the benzene solvent was removed, some samples of Carbitol were also purified further by treating with 12 g. of lead tetraacetate prepared according to Hockett and McClenahan (66). After the consumption of lead tetraacetate became very slow, the excess was decomposed by the addition of 100 cc. of water. The acetic acid formed by this decomposition was neutralized by vigorous shaking with powdered caustic soda. The aqueous layer resulting from the decomposition of the lead tetraacetate was removed and the benzene solution was washed with water until neutral, then dried and concentrated. The Carbitol residue, on fractionation as described, gave the same physical constants as those obtained without the lead tetraacetate treatment. Anal. Calc. for $C_6H_{14}O_3$: C, 53.7; H, 10.8. Found: C, 53.7, 53.7; H, 10.8, 10.7%.

p-Toluene Sulfonyl Chloride

Approximately 300 grams of crude tosyl chloride (Monsanto Chemical Corporation) was dissolved in 600 cc.

of benzene and the solution was washed with cold water until the wash water remained neutral. The benzene solution was then dried over anhydrous calcium chloride for twelve hours. After drying, the solution was decolorized with bone black and the benzene was removed under diminished pressure on a steam bath. The tosyl chloride was then recrystallized from a minimum amount of boiling ether and the product was dried in a vacuum desiccator over phosphorus pentoxide. Further similar recrystallizations were made from ether, if necessary, until the m.p. was sharp at 68.6°. Anal. Calcd. for $C_7H_7SO_2Cl$: C, 44.15; H, 3.71; S, 16.82. Found: C, 44.15; H, 3.64; S, 16.88, 16.79%.

Pyridine

High grade 2-A reagent pyridine was dried by heating under reflux with anhydrous calcium or barium oxide. The drying agent was removed by filtration before use and the dry filtrate was redistilled. B.p. 115°/760 mm.

Acetonylacetone

The acetonylacetone (employed as an iodination medium) was stored over anhydrous calcium chloride and was freshly distilled under reduced pressure immediately before use. B.p. 194°/760 mm.

Acetone

Werner's method of purification (67) was employed. Three grams of silver nitrate in 20 cc. of water and 20 cc. of a 1N sodium hydroxide solution was added to 700 cc. of stock acetone contained in a one-liter bottle. The mixture was shaken for ten minutes after which it was filtered. The filtrate was dried over anhydrous calcium chloride and was redistilled as required. The portion having a constant boiling point 56.5°/760 mm. was used.

Glacial Acetic Acid

Stock acetic acid was heated under reflux with chromium trioxide (68), 20 grams per liter, for twelve hours and was fractionated through a Vigreux type column until a constant boiling fraction was obtained. B.p. 118°/760 mm.

Absolute Methanol and Ethanol

Two liters of the stock alcohol was treated with magnesium methoxide, prepared from 20 grams of magnesium turnings and 500 cc. of the absolute alcohol (69). The mixture was heated under reflux for twelve hours and then distilled. The portion with the proper b.p. was collected and stored in an air-tight container.

Ethylene Chlorohydrin

Technical ethylene chlorohydrin (Carbide and Carbon Chemical Corporation) was dried over anhydrous sodium sulfate for three days before being vacuum distilled in the presence of a stream of dry carbon dioxide bubbles to prevent bumping. Vacuum distillation was employed to avoid thermal decomposition (70). The fraction having a constant boiling point at 38.5-39.0°/10 mm. was collected and was found to have b.p. 128.7°/760 mm. and n_D^{15}, 1.4438. These values check those in the literature (71).

Benzene

Commercial benzene was shaken with frequently renewed amounts of concentrated sulfuric acid until the reaction for thiophene was negative (72). After washing with water, drying, and fractionating, the portion having a constant b.p. of 80° was collected and stored over sodium wire. The benzene was redistilled from the metal as required.

II. Methods of Analysis

Carbon and Hydrogen Analyses

All those reported were determined on a semimicro scale using the general procedure and technique outlined in such standard texts as Niederl and Niederl (73a).

Sulfur Analysis

In the first part of the research, attempts were made to employ the method described by Mahoney and Michell (74), which involved the use of a sodium peroxide-carbon fusion followed by a barium chloride titration with tetrahydroquinone as an indicator. This method had to be discarded owing to the difficulty of determining the end point. All sulfur analyses reported were obtained by the standard Carius method employing barium chloride in the bomb tube instead of silver nitrate (73b).

Iodine Analysis

Some of the analyses were carried out employing the method outlined by Mahoney and Purves (3a). The weighed sample was placed in 25 cc. of absolute ethanol in which 1 g. of solid potassium hydroxide had been dissolved. The mixture was boiled under reflux for one hour. After dilution to 100 cc. with water and acidification with dilute (or conc.) sulfuric acid, the estimation was completed by Doering's method (75) with the use of 0.01 N sodium thiosulfate in the final titration.

With the exception of one case, consistently low and variable results were obtained, so the standard gravimetric Carius method (73c) was adopted and good results were obtained with no difficulty.

Alkoxyl Estimations

The standard alkoxyl estimation, as developed by Zeisel (26) and Viebock (27), and modified by Clark (76), was employed, 2.5 g. of phenol per 5 cc. of constant boiling hydriodic acid (b.p. 126°) being used in all cases. Morgan's new method (5) did not appear until most of this work was completed.

Determination of Peroxide Oxygen

The method used was developed by Liebhafsky and Sharky (77). One cc. of potassium iodide solution (0.4 g./cc.) was added to 25 cc. of glacial acetic acid and approximately 1.5 g. of sodium bicarbonate contained in a glass stoppered iodine flask. The mixture usually became slightly yellow, and 0.01 N sodium thiosulfate was then added, 2 drops at a time, with gentle swirling, until the color was that of the end point. It was safer to take the end point as the faintest yellow perceptible to the eye, since starch was an unsatisfactory indicator in the acetic acid system. Because the reaction between the sodium thiosulfate and iodine in these conditions was not instantaneous, about ten seconds was allowed to elapse between successive additions of thiosulfate. When no further deepening of the iodine color occurred on standing, the sample for analysis was added, the flask was stoppered and placed in a dark cupboard for five minutes. The liberated iodine was then titrated with standard 0.01 N thiosulfate and the flask was replaced in the cupboard for another five minute period. If no further iodine was liberated the end point of the estimation had been attained.

With 5 cc. samples of the unknown, the limit of error was about 0.1 cc. of 0.01 N thiosulfate, corresponding to 2 x 10^{-4} N peroxide. A blank of 0.1 cc. was usually found and all the data were corrected correspondingly. The volume in cc. of peroxide oxygen per liter of unknown was 11.2 times the consumption of 0.01 N thiosulfate per 5 cc. sample (78).

A qualitative test for peroxides, based on the above method, was also used. One cc. of the compound to be examined was placed in a small test tube, 1 cc. of a 50 percent solution (by volume) of aldehyde-free acetic acid was added and the tube was shaken. A few mg. of potassium iodide was added and completely dissolved. The tube was kept in the dark for five minutes together with a blank. No difficulty was encountered in detecting small traces of peroxide oxygen, which were usually sufficient to develop a deep iodine color immediately.

Detection of Carbonyl Compounds

Both Schiff's and Brady's reagents were employed. Brady's reagent (79) was prepared by dissolving 5 g. of 2,4-dinitrophenylhydrazine in 10 cc. of concentrated sulfuric acid followed by the addition of 75 cc. of dry ethanol.

Determination of Acidity

Five cc. of the samples were pipetted accurately into 25 cc. of water contained in a 100 cc. ground glass jointed flask, a reflux condenser was fixed in position and the solution was heated under reflux for one hour to decompose any peroxides which might have been present. At the end of the reflux period, the condenser and ground joints were all washed well with water, the washings being collected directly in the flask. After cooling to room temperature, 25 cc. of a 0.1 N sodium hydroxide solution was added and allowed to stand for five minutes, then the excess alkali was back-titrated with standard 0.1 N hydrochloric acid. The acidity found was arbitrarily calculated as normality. This method was devised on the basis of work done by Wieland and Wingler (80).

III. Preparations

2-(β-Ethoxyethoxyethoxy)-ethanol-1 ($C_2H_5(OCH_2CH_2)_3OH$)

A three-neck, round bottom 500 cc. flask equipped with standard ground glass fittings was provided with a capillary bubbling tube, a mechanical stirrer with mercury seal and a reflux condenser closed by a calcium chloride drying tube. Anhydrous methanol, 175 cc. was placed in the flask and the entire system was swept out by a stream of dry, oxygen-free nitrogen admitted below the surface of the methanol through the capillary bubbler. The nitrogen was first passed through alkaline pyrogallol, concentrated sulfuric acid, pellets of solid sodium hydroxide and finally through a calcium chloride tube to ensure the removal of any oxygen and moisture. When the atmosphere in the flask had been completely changed many times, 16.2 g. (0.704 moles) of freshly cut, clean metallic sodium was added through the condenser slowly, so that the reaction mixture refluxed only gently. After all the sodium had completely dissolved, 105 g. (0.784 moles or 110 percent of theory) of pure Carbitol was added. Keeping a large flow of nitrogen going through the system at all times, the mercury seal stirrer was replaced by a plug and the reflux condenser was turned downward for distillation. The methanol was gradually removed by increasing the water bath temperature gradually to 100° and simultaneously decreasing the pressure to 20 mm. This removal displaced the equilibrium,

$$CH_3ONa + C_2H_5(OCH_2CH_2)_2OH \rightleftarrows C_2H_5(OCH_2CH_2)_2ONa + CH_3OH$$

to the right and the product, sodium Carbitolate, was very viscous and deep red-brown in color. To assist in the complete removal of the methanol, 32.3 g. more of pure Carbitol was added, thereby bringing the total excess of this constituent to 45 percent. Further evacuation, always in the presence of a continuous stream of pure nitrogen, was carried out for fourteen hours at 20-25°/30 mm., ten hours at 100°/20 mm. and finally for two days at 100°/15 mm.. After replacing the plug with a dropping funnel, 63 g., (0.774 moles or 10.6 percent excess) of ethylene chlorohydrin was added slowly. The reaction mixture was then stirred vigorously and heated under a reflux condenser at 70-80° for a period of twelve hours. No volatile material passed through the reflux condenser, which was cooled to 20°. The contents of the reaction flask were diluted with dry ether and the mixture was filtered, the filter cake was washed repeatedly with ether and the washings were added to the original filtrate. The residue of sodium chloride, 39.7 g. after drying, corresponded to a 95.6 percent yield. The ether was removed from the filtrate on a steam bath and the residue was fractionally distilled at 15 mm. from a Claisen flask into two portions, one boiling up to 95°/15 mm., and the other of b.p. 95-150°/15 mm..

Refractionation of the first portion at 15 mm., yielded unreacted ethylene chlorohydrin and 33.3 g. of Carbitol. The second portion, fractionated at 0.5 mm., yielded 48 g. of unreacted Carbitol and 38 g. of a substance having a constant boiling point of 85-90°/0.5 mm., and n_D^{20}, 1.4382. The portion was further fractionated very slowly, during eleven hours, from a Widmer flask of 50 cc. capacity with the results listed in Table I.

TABLE I

FRACTIONATION OF CRUDE 2-(β-ethoxyethoxyethoxy)-ethanol-1[(a)]

Fraction No	Bath Temp. °C	Distillation Temp. °C	n_D^{20}
1	up to 110	up to 86	1.4370
2	111	86-87	1.4380
3	113	87-89	1.4380
4	115	89-90	1.4380
5	115-116	90-91	1.4380

(a) At 0.5 mm. pressure throughout.

The fractions having n_D^{20}, 1.4380 weighed 36 g., being a 28.69 percent yield based on the sodium and 48.44 percent on the Carbitol used. The product was thoroughly dried in a vacuum desiccator over phosphorus pentoxide for two days at 25°/20 mm. and was stored in the same conditions. Anal. Calcd. for $C_8H_{18}O_4$: C, 53.9; H, 10.2. Found: C, 53.7

53.7; H, 10.8, 10.3%.

Davidson (25) quoted n_D^{26}, 1.4389 for pure 2-(β-ethoxyethoxyethoxy)-ethanol-1 and this value is probably high.

An earlier preparation gave a 14.92 percent yield on the basis of the sodium employed and another, using a larger excess of ethylene chlorohydrin, resulted in no product at all.

Ethyl p-toluenesulfonate ($C_2H_5OSO_2C_6H_4CH_3$)

Using a published method (51), 22 g. of p-toluene sulfonyl chloride was dissolved in 88 cc. of dry pyridine at 22-24°. The solution was cooled to -10°, and 6.1 cc. (approx. 0.102 moles) of absolute ethanol was added. The temperature was held at -10° for fifteen minutes after the crystallization of pyridine hydrochloride started, then 250 cc. of 5 N sulfuric acid was rapidly added with swirling and cooling. Upon re-cooling to 4° crystallization again occurred; the crystals were filtered, washed free of pyridine, and dried in a vacuum desiccator. The yield was 15 g. or 73.4 percent, reduced to 49 percent upon recrystallization from petroleum ether. The melting point was correct at 33-34°.

2-(Ethoxy)-ethyl p-toluenesulfonate-1 ($C_2H_5OCH_2CH_2OSO_2C_6H_4CH_3$)

This compound was prepared according to Tipson's procedure (51). Pure Cellosolve, 0.167 moles, was dissolved in 100 cc. of pure dry pyridine; the solution was cooled to -5° in an ice-salt bath and 0.183 moles of p-toluene sulfonyl chloride (1.1 equivalents based on the Cellosolve) was added in one portion. The reaction flask was closed by a rubber stopper through which a thermometer was inserted and the flask was swirled with cooling to 0° until all the p-toluene sulfonyl chloride had dissolved, then maintained at 0° for two hours. With swirling and cooling so that the temperature never exceeded 5°, 10 cc. of water was added in portions of 1, 1, 1, 2, and 5 cc. to decompose any remaining tosyl chloride, then the reaction mixture was flooded with 100 cc. of ice water. The aqueous pyridine solution was extracted three times with 100 cc. portions of chloroform; the united extracts were washed successively with ice cold dilute sulfuric acid, until all the pyridine was removed; then with ice water, sodium bicarbonate and water until the latter remained neutral. The chloroform solution was dried over anhydrous sodium sulfate, filtered and the chloroform removed under diminished pressure, using a capillary bubbler and pure nitrogen gas, finally at 100°/20 mm.. A yield of 36.9 g. of a yellow viscous oil was obtained having m.p. 15-18° and n_D^{25}, 1.5025. Upon high vacuum distillation from an oil bath at 165-170°, a clear colorless oil, b.p. 135°/0.14 mm., n_D^{25}, 1.5032 and m.p. 18.5° was obtained in 83 percent yield.

Anal. Calcd. for $C_{11}H_{16}O_4S_1$: C, 54.1; H, 6.6; S, 13.1: Found: C, 53.9, 54.1; H, 6.5, 6.8; S, 13.3, 13.1%.

2-(β-Ethoxyethoxy)-ethyl p-toluenesulfonate-1 ($C_2H_5(OCH_2CH_2)_2OSO_2C_6H_4CH_3$)

Carbitol freshly purified by Seikel's method (40) was very carefully fractionated until all traces of peroxides and aldehydes disappeared, then 30 g. (0.224 moles) were tosylated according to Tipson's method as described in the previous preparation. The aqueous pyridine solution was extracted four times with 100 cc. volumes of chloroform. The chloroform solution, washed free from pyridine by dilute sulfuric acid, was washed with water, sodium bicarbonate and water until neutral, and was then dried over anhydrous sodium sulfate. The solution was filtered and the chloroform was removed under diminished pressure, using a capillary bubbler and pure nitrogen gas, for ten hours at 42°/23 mm., and finally for seven hours at 42-45°/0.1 mm. A yield of 51.1 g. or 79.2 percent of a light yellow viscous oil, n_D^{25}, 1.4976, was obtained.

Anal. Calcd. for $C_{13}H_{20}O_5S_1$: C, 54.2; H, 7.0; S, 11.1: Found: C, 53.8, 53.8; H, 7.1, 7.0; S, 11.1, 11.0%.

Further preparations gave yields of 83.8, 83.7 and 74.2 percent of this product. The differences found between the calculated and observed carbon analysis are not considered excessive since this tosyl ester could not be crystallized and decomposed on distillation, even under highly diminished pressure.

2-(β-Ethoxyethoxyethoxy)-ethyl p-toluenesulfonate-1

$(C_2H_5(OCH_2CH_2)_3OSO_2C_6H_4CH_3$

Ten grams (0.0561 moles) of pure triethylene glycol monoethyl ether was esterified with 12.82 g. (0.0673 moles) of p-toluene sulfonyl chloride in 100 cc. of dry pyridine as previously described for the lower homolog. A yield of 13.1 g. (71.1 percent of theory) of a light yellow viscous oil was obtained that would not crystallize. The oil was extracted twice with 10 cc. portions of pure 30-60° petroleum ether, then was dissolved in 200 cc. of benzene and was decolorized with charcoal by heating under reflux for two hours. The solution was filtered and the benzene was removed under diminished pressure, finally using a water bath at 60-70°/20 mm. Upon cooling the resulting colorless oil no crystallization occurred, but an immiscible oil appeared to separate from the bulk of the liquid. The two phase system was again dissolved in 100 cc. of dry benzene and the solution was washed with 10 cc. of a 10 percent sodium bicarbonate solution, then with water until neutral and was dried over anhydrous sodium sulfate. The benzene was removed under diminished pressure and upon cooling the two immiscible layers reappeared. Analyses of the homogeneous system (obtained by warming slightly) showed no halogen present, but the sulfur content was lower than theory. Since the oil had again become slightly yellow, it was decolorized as before and, after the benzene was removed, was dissolved in the minimum amount of boiling (30-60°) petroleum ether. The oil which separated on cooling was evacuated at 30-40°/0.5 mm. for three hours. Although this oil remained homogeneous when chilled it could not be crystallized or purified by high vacuum distillation. The refractive index was n_D^{25}, 1.4959.

Anal. Calcd. for $C_{15}H_{24}O_6S_1$: C, 54.2; H, 7.3; S, 9.6: Found: C, 53.8, 53.8; H, 7.3, 7.5; S, 9.5, 9.7%.

Other preparations gave oils in 77 percent yield with n_D^{25}, 1.4960, and the phenomenon of two immiscible layers forming when the crude products were chilled was also encountered. The carbon analyses again tended to be low but are as close as might be expected from the means of purification available. As will be explained later, this compound, together with the tosyl ester of Carbitol, gave difficulty during the semi-micro combustion.

β-Iodoethyl ethyl ether ($C_2H_5OCH_2CH_2I$)

The pure Cellosolve tosylate (0.0205 moles) and C.P. dry sodium iodide (0.0501 moles) were dissolved in 75 cc. of pure, dry acetone contained in a small stainless steel bomb (1). The bomb was sealed and immersed in an oil bath which was then warmed for two hours at 115°. The bomb was cooled and its contents were filtered to remove the insoluble sodium p-toluene sulfonate that had formed, the filter cake was washed with a few cc. of dry acetone, the washings being added to the original filtrate, now contained in a distillation flask. The acetone was evaporated at ordinary pressure, and the distillate that started coming over at a temperature above 100° was collected separately. This crude, light yellow oil was purified according to Karvonen (64) by repeated redistillation over solid sodium hydroxide. The pure derivative was obtained in an 81 percent yield and had b.p., 154°/754 mm. and n_D^{20}, 1.4965.

Anal. Calcd. for C_4H_9OI: I, 63.5; Found: I, 63.5, 63.5%.

The iodine analysis was carried out by the method outlined by Mahoney and Purves (3a).

The compound was also prepared by allowing the same reaction mixture to stand for forty hours at 25°. As the filtered acetone solution was warmed to remove the acetone, a further reaction was signalized by the formation of more insoluble sodium p-toluene sulfonate. This additional precipitate was isolated, washed free from impurities by acetone, dried, and weighed. The weight indicated that roughly 40 percent of the reaction had taken place after the removal of acetone (or after heating) had started.

β-Iodo-β'-ethoxydiethyl ether ($C_2H_5(OCH_2CH_2)_2I$)

This synthesis was started employing 0.0745 moles of pure Carbitol. After tosylation according to the previously described method, the product, obtained in 84 percent yield, was iodinated with 28 g. of C.P. sodium iodide in 625 cc. of acetone. The mixture was allowed to react for sixty hours at 22-23°; then it was filtered and the filtrate was concentrated to approximately 100 cc. at 30° under diminished pressure. To the acetone solution, 200 cc. of dry ethyl ether was added in order to precipitate any residual sodium iodide. The ethereal solution, together with 100 cc. of ether washings, was shaken with 100 cc. of 10 percent sodium thiosulfate to extract the free iodine which was present in the mixture, was then washed with two volumes (100 cc. each) of ice water and was dried over anhydrous potassium carbonate for eighteen hours. The ether was removed from the dried solution under diminished pressure, finally at 30°/0.06 mm. until no further loss in weight occurred. A yield of 12.9 g. of a light yellow oil was obtained; corresponding to 80.5 percent of theory based on the starting Carbitol, or to 95.8 percent based on the Carbitol ester. Redistillation gave an 88 percent yield, based on the Carbitol ester, of a colorless oil, b.p., 42°/0.4 mm. and n_D^{20}, 1.4908 or n_D^{25}, 1.4881. This product was stored in an ice box for five months, after which time it had become slightly yellow again. A solution in 10 cc. of benzene was extracted with 5 cc. of 5 percent sodium bisulfite solution, washed with 3 portions of water (10 cc. each) and then dried over anhydrous sodium sulfate. After filtration, the benzene was removed by distillation and the residue was fractionated from a Widmer flask (see Table II).

TABLE II

FRACTIONATION OF β-IODO-β'-ETHOXYDIETHYL ETHER AT 15 mm. PRESSURE

Fraction No	Bath Temp. °C	Distillate Temp. °C	n_D^{25}
1	58-59	40-41	1.4881
2	59-60	41-42	1.4881
3	60-61	42-43	1.4881
4	61	43	1.4885

Fractions 1, 2 and 3 were considered pure. The iodine analysis was made according to the regular Carius method.

Anal. Calcd. for $C_6H_{13}O_2I$: C, 29.5; H, 5.4; I, 52.0; Found: C, 29.9, 29.7; H, 5.5, 5.7; I, 51.5, 51.4%.

β-Iodo-β'-ethoxyethoxydiethyl ether ($C_2H_5(OCH_2CH_2)_3I$)

Pure triethylene glycol monoethyl ether (0.0561 moles) was tosylated in 77 percent yield as previously described and the ester was dissolved in 625 cc. of acetone containing 21.1 g. of C.P. dry sodium iodide. The reaction was allowed to proceed at room temperature (20-25°) for a total time of five days. Sodium p-toluene sulfonate was recovered from the reaction mixture, after thorough washing with acetone, in 96.7 percent of the theoretical yield. The acetone was removed from the filtrate under vacuum at 48° and the residue was thoroughly extracted with 200 cc. of dry ethyl ether and filtered. The ether was distilled and the red oil obtained was taken up again in ether and extracted with 50 cc. of a 10 percent sodium bisulfite solution, then with water, and dried over anhydrous sodium sulfate. The ether was distilled under a vacuum of 20 mm., and the product was evacuated for one and one-half hours at 40-50°/0.15 mm. A very light yellow, clear oil was obtained in a 73.1 percent yield based on the tosyl ester, or in a 61.3 percent yield based on the triethylene glycol monoethyl ether used. Distillation gave a clear liquid, b.p. 97-98°/0.15 mm. from a bath at 112-113° having n_D^{25}, 1.4870. Iodine analyses were by the regular Carius method.

Anal. Calcd. for $C_8H_{17}O_3I$: C, 33.3; H, 6.0; I, 44.1; Found: C, 33.4, 33.5; H, 5.8, 6.1; I, 43.9, 44.0%.

IV. The Determination of Physical Properties

Density Determinations

These determinations were carried out according to accepted procedure (81a). Two small pycnometers were employed; one had a capacity of approximately one cc. and was fitted with ground glass caps for closing the ends; the other had a capacity of approximately 0.1 cc. and was fitted with rubber and glass rod caps for end closures. The pycnometer volume was determined by weighing the apparatus empty and then filled with water (whose density was known) at the temperature under consideration. The density values were calculated by dividing the weight of the unknown held by the pycnometer by the volume of the pycnometer at the same temperature.

Refractive Index Determination

All the refractive indices tabulated in Table III were determined with a water jacketed Abbé Refractometer, the temperature of which could be controlled to within ±0.1°. The procedure followed was standard (81b). Periodically the instrument was calibrated against liquids of known purity and refractivity.

Molecular Refractions

The observed molar refractions were all calculated by the Lorenz and Lorentz equation,

$$\text{Molar Refraction} = \frac{M}{d}\,\frac{(n^2 - 1)}{(n^2 + 2)}$$

where M, d and n are the molecular weight, the density and refractive index at some particular temperature. The calculated molar refraction values were determined from a table of atomic refractivities given by Gilman (82). The results are listed in Table III, page 42.

From the observed molar refractions of the four pure p-toluenesulfonate esters, the group refraction for the sulfonate group ($-O-SO_2-$) was determined by subtracting the calculated contribution of the remainder of the molecule from the observed values.

V. The Action of Metallic Sodium on the Monoethylether of Diethylene Glycol

The pure monoethyl ether, 0.298 moles, was placed in a tightly stoppered Claisen flask. Very slowly 0.298 moles of clean, freshly cut metallic sodium was added, the evolved hydrogen being allowed to escape continuously through a capillary tube attached to the side arm of the flask. At first the reaction was rather rapid, then it slowed to the point where it was hardly perceptible after four hours had elapsed. The mixture became very dark red-brown and viscous. After a period of one week at room

TABLE III

PHYSICAL CONSTANTS OF THE POLYETHYLENE GLYCOL DERIVATIVES

Compound	n_D(°C)	D^{25}_{25}	Molar Refraction Observed	Molar Refraction Calc. minus the $-O-SO_2-$ group	Contribution of the $-O-SO_2-$ group
$C_2H_5(OCH_2CH_2)_3OH$	1.4380 (20°)	1.0211^{20}_{20}	45.78	-	-
$C_2H_5OSO_2C_6H_4CH_3$	1.5067 (35°) 1.5050 (40°)	1.1637^{40}_{40}	51.04	40.16	10.88
$C_2H_5OCH_2CH_2OSO_2C_6H_4CH_3$	1.5032 (25°) 1.5000 (35°) 1.4981 (40°)	1.1677	61.79	51.04	10.75
$C_2H_5(OCH_2CH_2)_2OSO_2C_6H_4CH_3$	1.4976 (25°)	1.1599	72.80	61.92	10.88
$C_2H_5(OCH_2CH_2)_3OSO_2C_6H_4CH_3$	1.4959 (25°)	1.1698	82.97	72.80	10.17
$C_2H_5OCH_2CH_2I$	1.4996 (15°) 1.4965 (20°)	$^{*}1.6698^{15}_{4}$	35.21	-	-
$C_2H_5(OCH_2CH_2)_2I$	1.4908 (20°) 1.4881 (25°)	1.5210	46.24	-	-
$C_2H_5(OCH_2CH_2)_3I$	1.4889 (20°) 1.4870 (25°)	1.4557	56.93	-	-

*Density value quoted by Karvonen (64).

From the observed molar refractions of the four pure p-toluenesulfonate esters, the group refraction for the sulfonate group ($-O-SO_2-$) was determined by subtracting the calculated contribution of the remainder of the molecule from the observed values. 10.53±0.35

temperature, although the sodium had not completely reacted, the flask was arranged for a distillation. The water-cooled receiver was connected to a chloroform-solid carbon dioxide trap and the distillation was started on a steam bath at ordinary pressure. Heating for twenty-five hours at 100° failed to produce a distillate or to complete the reaction. The distillation was then carried out at a bath temperature up to 170°/0.15 mm. The sodium slowly but completely dissolved but no volatile material was collected in either of the receivers. The mixture was fluid at 170° and possessed a deep red color, but on cooling to room temperature it became dirty brown in appearance and set into a jelly-like mass. The experiment showed that the direct formation of the sodium derivative of Carbitol was probably not feasible.

VI. Ordinary Alkoxyl Estimations in the Polyethylene Glycol Series

The results tabulated in Table IV were obtained employing the regular alkoxyl estimation (76) with 10 to 20 mg. samples.

VII. The Thermal Decomposition of the Tosylates of the Monoethyl Ethers of the two higher Polyethylene Glycols

2-(β-Ethoxyethoxy)-ethyl p-toluenesulfonate-1

($C_2H_5(OCH_2CH_2)_2OSO_2C_7H_7$)

Tosylated Carbitol (0.786 moles), having the

TABLE IV

ALKOXYL DETERMINATIONS IN THE POLYETHYLENE GLYCOL SERIES

Compound	% C_2H_5O Found	% C_2H_5O Calcd.	Range of Differences between % Found and % Calcd. values
$C_2H_5OCH_2CH_2OH$	49.85 49.38 49.29	50.00	-0.71 to -0.15
$C_2H_5(OCH_2CH_2)_2OH$	36.30 33.62 33.35 33.55 33.65	33.58	-0.23 to 2.72
$C_2H_5(OCH_2CH_2)_3$ OH	29.75 28.50	25.28	3.22 to 4.47
$C_2H_5OSO_2C_7H_7$	22.63 22.75 22.28 22.28	22.50	-0.22 to +0.25
$C_2H_5OCH_2CH_2OSO_2C_7H_7$	16.97 18.54 17.30 18.42 17.91	18.45	-1.48 to +0.09
$C_2H_5(OCH_2CH_2)_2OSO_2C_7H_7$	23.75 21.30	15.63	5.67 to 8.12
$C_2H_5(OCH_2CH_2)_3OSO_2C_7H_7$	20.42 21.85	13.56	6.86 to 8.29
$C_2H_5(OCH_2CH_2)_2I$	33.91 33.06	18.45	14.61 to 15.46
Polyethylene glycol polymer, D.P. = 186 Prepared by Hibbert and Fordyce (17)	2.14 1.63 0.00 2.92	0.00	0.00 to +2.92
$C_7H_7SO_2OCH_2CH_2OSO_2C_7H_7$	1.29 0.97	0.00	0.97 to 1.29

correct elemental analysis, was placed in a 50 cc. distilling flask which was then packed with glass wool. An ordinary air-cooled 50 cc. distilling flask was employed as the first receiver and a cold finger immersed in a solid carbon dioxide-chloroform mixture was the second receiver. The system was evacuated to 0.13 mm. and was then slowly heated in an oil bath up to 160°. Slow, even distillation took place at 125°/0.13 mm., no increase in pressure being observed. Periodically the distillation had to be stopped and the delivery tube allowed to warm in order to melt the distillate that had solidified at the entrance to the cold finger. In the first, air-cooled receiver, 15.33 g. of a slightly yellow, slightly acid oil was obtained, with m.p. 30-33° and n_D^{40}, 1.5035, changed to m.p. 34-35° and n_D^{40}, 1.5050 upon recrystallization from (30-50°) petroleum ether. A mixed m.p., 34-35°, was observed with a pure sample of ethyl p-toluenesulfonate which also had m.p. 34-35° and n_D^{40}, 1.5050. The yield was 97.4 percent of theory.

In the dry ice - chloroform cold finger, 6.65 g. of a clear colorless liquid had collected which had n_D^{25}, 1.4190, m.p. range 6-9°, b.p. 100°, and which formed an orange-yellow crystalline derivative, m.p. 65-66° with bromine. The physical constants quoted for pure 1,4 dioxane by Huntress and Mulliken (83a) were n_D^{25}, 1.4198, m.p. 11.8°, and b.p., 101.3-101.4°, and the melting point of the bromine derivative was given as 65-66°. A mixed melting point was made using an authentic sample of the bromine-1,4-dioxane compound and no depression was noted. It was concluded that the compound under investigation was slightly impure 1,4 dioxane obtained in 97.0 percent of the calculated yield.

In various other attempts to prepare the pure p-toluenesulfonate ester of Carbitol by high vacuum distillation of the crude oil, the ethyl ester of p-toluenesulfonic acid was isolated in a slightly acidic condition in yields of 100.5, 103.8 and 54.2 percent of those calculated. The melting points of these specimens were 10-22°, 18-25° and 34-35° respectively, and all upon one recrystallization from petroleum ether had the correct melting point of 34-35°. The analyses obtained were as follows:
Anal. Calcd. for $C_9H_{12}O_3S_1$: C, 54.0; H, 6.0; S, 16.0; EtO, 22.5: Found: C, 53.7, 53.7; H, 6.0, 5.8; S, 16.1, 16.2; EtO, 22.6, 22.8%

2-(β-Ethoxyethoxyethoxy)-ethyl p-toluenesulfonate-1 $(C_2H_5(OCH_2CH_2)_3OSO_2C_7H_7)$

In this case 0.01085 moles (3.6 g.) of the purified ester was placed in a 10 cc. Claisen flask and the flask was inserted into the same system as previously described, using correspondingly smaller vessels for receivers.

The system was evacuated to 0.03 mm. and the flask was heated slowly on an oil bath up to 160-170°, when even, smooth distillation occurred. No increase in the pressure was noted as distillation proceeded at b.p. 133-135°/ 0.03 mm. In the air-cooled receiver 2.03 g. of a light yellow, slightly acidic oil having n_D^{25}, 1.5010, collected which upon recrystallization to a constant melting point of 18-19° had n_D^{25}, 1.5030. A mixed melting point with pure tosyl Cellosolve, m.p. 18-19°, n_D^{25}, 1.5030 showed no depression. The yield was 76.6 pércent of the theoretical. In the cold receiver there was 0.94 g. of a colorless liquid n_D^{25}, 1.4160, that showed some traces of unsaturation. Upon fractionation this substance yielded 0.6 g. of a clear liquid, b.p. 100°, n_D^{25}, 1.4190, m.p. 8-10°.

These physical constants agree well with those quoted for 1,4-dioxane (83a) and the yield was 62.8 percent of the theoretical. Like dioxane, the distillate gave a white crystalline derivative with concentrated sulfuric acid and orange-yellow crystals, m.p. 65-66°, with bromine. Admixture of the latter crystals with a similar product prepared from authentic 1,4-dioxane did not depress the melting point.

VIII. The Relative Rates of Solvolysis of the Four p-Toluenesulfonates in Aqueous-Methanol at 65±1°

The procedure employed in all cases consisted of transferring exactly 0.0015 moles of ester from a small glass-stoppered weighing bottle to a 250 cc. volumetric flask with anhydrous methanol. Twenty-five cc. of water was added and the solution was made up to the mark at 25° with more anhydrous methanol. After thorough mixing the solution was transferred to a 500 cc. flask, attached to a water cooled condenser fitted with a calcium chloride drying tube, and immersed in a water bath at $65 \pm 1°$. After one and one-half hours the system was at thermal equilibrium and a sample was removed by pipet, cooled rapidly to 25° and exactly 10 cc. was titrated with standard sodium hydroxide from a microburet. The total amount of water employed was 1.5569 moles in comparison with the 0.0015 moles of ester; therefore, it was assumed that the reaction would follow a pseudo-monomolecular or first order rate course given by, $k_1T = 2.303 (\log a - \log c)$ where c is the concentration of unchanged ester at any time T. The assumption was justified from evidence given in the literature (84). The percent solvolysis was given by

$$\frac{\text{cc. standard alkali consumed/10 cc. sample} \times 2.5 \times \text{N. of alkali}}{1.5 \times 10^{-3}}$$

and the results are in Tables V, VI, VII and VIII.

TABLE V

(see Fig. 5)

THE SOLVOLYSIS OF ETHYL p-TOLUENESULFONATE AT 65±1°

Time in hours	cc. of 0.0098 N NaOH consumed per 10 cc. sample	% Solvolysis	Conc. ($c.10^4$) moles/250 cc.	log c
0.0	0.00	0.00	15.0	$\bar{2}.8238$
1.5	1.10	18.03	12.3	$\bar{2}.9101$
3.5	2.06	33.75	9.9	$\bar{3}.0044$
6.0	3.10	50.90	7.4	$\bar{3}.1308$
8.0	3.68	60.30	6.0	$\bar{3}.2218$
10.0	4.15	68.10	4.0	$\bar{3}.3979$
12.0	4.52	74.15	3.9	$\bar{3}.4589$

TABLE VI

(see Fig. 5)

THE SOLVOLYSIS OF 2-(ETHOXY)-ETHYL p-TOLUENESULFONATE-1 AT 65±1°

Time in hours	cc. of 0.0098 N NaOH consumed per 10 cc. sample	% Solvolysis	Conc. (c.10^4) moles/250 cc.	log c
0.0	0.00	0.00	15.00	$\bar{2}.8238$
1.5	0.40	6.68	14.00	$\bar{2}.8539$
3.5	0.42	6.88	13.97	$\bar{2}.8548$
6.0	0.65	10.67	13.40	$\bar{2}.8729$
8.0	0.74	12.13	13.18	$\bar{2}.8801$
10.0	0.97	15.91	12.61	$\bar{2}.8993$
12.0	1.02	16.72	12.49	$\bar{2}.9034$

TABLE VII

(see Fig. 5)

THE SOLVOLYSIS OF 2-(β-ETHOXYETHOXY)-ETHYL p-TOLUENESULFONATE-1 AT 65±1°

Time in hours	cc. of 0.0098 N NaOH consumed per 10 cc. sample	% Solvolysis	Conc. ($c.10^4$) moles/250 cc.	log c
0.0	0.00	0.00	15.00	$\bar{2}.8238$
2.0	0.35	5.77	14.13	$\bar{2}.8499$
4.0	0.60	9.90	13.51	$\bar{2}.8693$
6.0	0.87	14.34	12.85	$\bar{2}.8911$
8.0	1.05	17.35	12.40	$\bar{2}.9066$
10.0	1.25	20.62	11.91	$\bar{2}.9241$
12.0	1.47	24.25	11.36	$\bar{2}.9446$
14.0	1.63	26.94	10.96	$\bar{2}.9602$

TABLE VIII

(see Fig.5)

THE SOLVOLYSIS OF 2-(β-ETHOXYETHOXYETHOXY)-ETHYL p-TOLUENESULFONATE-1 AT 65±1°

Time in hours	cc. of 0.0098 N NaOH consumed per 10 cc. sample	% Solvolysis	Conc. ($c.10^4$) moles/250 cc.	log c
0.0	0.00	0.00	15.00	$\bar{2}.8238$
1.5	0.50	8.19	13.77	$\bar{2}.8611$
3.5	0.57	9.35	13.60	$\bar{2}.8665$
6.0	0.68	11.15	13.33	$\bar{2}.8752$
8.0	0.85	13.94	12.91	$\bar{2}.8891$
10.0	1.09	17.86	12.32	$\bar{2}.9094$
12.0	1.22	20.00	12.00	$\bar{2}.9208$

The specific reaction rate constants (k_1) for the overall solvolysis reactions were obtained by multiplying the slope of the log c - time plots by 2.303.

IX. The Relative Rates of Iodination of the Four p-Toluenesulfonates with Sodium Iodide in Acetonylacetone at 22±0.5°

The rates at which the iodine atom replaced the p-toluenesulfonate ester group in the various esters were followed by the changes in the refractive index of the reaction mixture. The reactants, in each case 0.0075 moles of C.P. dry sodium iodide and 0.0025 moles of the p-toluenesulfonate ester, were placed in a 50 cc. glass stoppered flask and were dissolved in exactly 25 cc. of pure acetonylacetone by shaking. As soon as solution was complete (five minutes), its refractive index was recorded on an Abbé refractometer and the mixture was kept in the dark at 22±0.5°. At the end of two hour periods samples were removed by a capillary pipet and transferred directly into the refractometer for measurement. Since the sodium p-toluenesulfonate precipitated in rather large crystals which settled readily, it was easy to exclude this salt from the samples provided care was taken. When the change in refractive index became slow, the flask and contents were warmed to 100° for two hours in an oil bath under a reflux condenser before being cooled to room temperature. The refractive index corresponding to complete reaction was then noted. To check the possibility of incomplete reaction the sodium p-toluenesulfonate was recovered and weighed after thorough washing and drying. In Tables IX, X, XI and XII (a) is equal to the initial concentration of the ester, 0.10 moles per liter, (b) to that of the sodium iodide, 0.30 moles per liter, and (x) is the moles of ester reacted in time (T). The usual second order equation $k_2T = \frac{1}{a-b} \ln\frac{b}{a}\frac{(a-x)}{(b-x)}$ was assumed. The values of (x) were determined by dividing the observed $(-\Delta n_D^{22})$ by the total change in refractive index, assuming that the change was directly proportional to the amount of ester present at any time.

TABLE IX

(see Fig. 6)

THE IODINATION OF ETHYL p-TOLUENESULFONATE AT 22±0.5°

Time in hours (T)	$-\Delta n_D^{22} . 10^3$	$x.10^2$	$\log \frac{b}{a}\frac{(a-x)}{(b-x)}$
2.17	1.2	3.077	0.1127
4.09	1.9	4.872	.2131
6.17	2.2	5.641	.2702
8.84	2.8	7.177	.4305
11.09	3.4	8.718	.7430
13.09	3.6	9.231	.9544
23.50	3.9	10.000	-

After heating and cooling total $-\Delta n_D^{22}.10^3 = 3.9$

Recovery of sodium p-toluenesulfonate = 99.4 percent of theory.

TABLE X

(see Fig. 6)

THE IODINATION OF 2-(ETHOXY)-ETHYL p-TOLUENESULFONATE-1 AT 22±0.5°

Time in hours (T)	$-\Delta n_D^{22}.10^3$	$x.10^2$	$\log \frac{b}{a} \frac{(a-x)}{(b-x)}$
2.17	0.2	0.50	$\bar{0}.0149$
4.09	0.3	0.75	.0229
6.17	0.5	1.25	.0395
8.84	0.9	2.25	.0768
11.00	1.2	3.00	.1091
13.17	1.5	3.75	.1461
23.50	2.2	5.50	.2588
29.92	2.3	5.75	.2792
49.92	3.1	7.75	.5180

After heating and cooling total $-\Delta n_D^{22}.10^3 = 4.0$

Recovery of sodium p-toluenesulfonate = 99.2 percent of theory.

TABLE XI

(see Fig.6)

THE IODINATION OF 2-(β-ETHOXYETHOXY)-ETHYL p-TOLUENE SULFONATE-1 AT 22±0.5°

Time in hours (T)	$-\Delta n_D^{22} \cdot 10^3$	$x \cdot 10^2$	$\log \frac{b}{a} \frac{(a-x)}{(b-x)}$
1.00	0.1	0.294	$\bar{0}.00869$
2.00	0.3	0.882	.0271
3.00	0.5	1.471	.0424
4.00	0.6	1.765	.0580
5.00	0.7	2.059	.0693
6.00	0.8	2.353	.0809
7.00	0.9	2.647	.0934
8.00	1.0	2.941	.1065
9.00	1.1	3.235	.1202
10.00	1.2	3.529	.1344
11.00	1.3	3.823	.1500
12.00	1.4	4.117	.1663
13.00	1.5	4.411	.1888
14.00	1.6	4.705	.2021
24.25	2.1	6.175	.2904
29.50	2.3	6.763	.3789
49.00	2.7	7.939	.5524

After heating and cooling total $-\Delta n_D^{22} \cdot 10^3 = 3.4$

Recovery of sodium p-toluene sulfonate = 95.4 percent of theory.

TABLE XII

(see Fig.6)

THE IODINATION OF 2-(β-ETHOXYETHOXYETHOXY)-ETHYL p-TOLUENESULFONATE-1 AT 22±0.5°

Time in hours (T)	$-\Delta n_D^{22}.10^3$	$x.10^2$	$\log \frac{b}{a}\frac{(a-x)}{(b-x)}$
1.92	0.6	1.818	$\bar{0}.0600$
3.92	1.0	3.030	.1105
5.92	1.7	5.151	.2326
7.92	2.0	6.030	.3038
10.92	2.3	6.969	.4037
20.60	2.7	8.181	.6017
26.08	3.0	9.090	.8842
31.08	3.0	9.090	.8842
44.60	3.2	9.697	$\bar{1}.3489$
47.92	3.3	10.00	-

After heating and cooling total $-\Delta n_D^{22}.10^3$ = 3.3

Recovery of sodium p-toluenesulfonate = 98.0% of theory

The specific reaction rate constants (k_2) for the overall iodination reaction were obtained by multiplying the slope of the log $\frac{b}{a}\frac{(a-x)}{(b-x)}$ - time plot by 2.303/(a-b)

Two further experiments were conducted, one on ethyl p-toluenesulfonate and the other on β-ethoxyethyl p-toluenesulfonate, as previously described except that equimolar amounts of sodium iodide and the p-toluenesulfonate were employed. In this case, where $a = b = 0.150$ moles per liter the second order equation reduces to $k_2T = \frac{x}{a(a-x)}$, and the plot of (T) against $\frac{x}{a-x}$ should be linear (Tables XIII and XIV, Fig. 6).

TABLE XIII

(see Fig.7)

THE IODINATION OF ETHYL p-TOLUENESULFONATE WITH AN EQUIMOLAR QUANTITY OF SODIUM IODIDE AT 22±0.5°

Time in hours (T)	$-\Delta n_D^{22}.10^3$	% of Ester reacted in time (T)	$x.10^2$	$\frac{x}{a-x}$
0.92	0.6	11.53	1.73	0.1304
1.92	1.2	23.08	3.46	0.2998
2.92	1.2	23.08	3.46	0.2998
5.17	1.7	32.70	4.91	0.4856
21.67	3.5	67.30	10.10	2.061
26.17	3.7	71.15	10.67	2.487
36.00	4.1	78.85	11.83	3.732
47.42	4.3	82.70	12.41	4.791
57.42	4.4	84.60	12.69	5.493

After heating and cooling total $-\Delta n_D^{22}.10^3 = 5.2$

TABLE XIV

(see Fig.7)

THE IODINATION OF 2-(ETHOXY)-ETHYL p-TOLUENESULFONATE-1 WITH AN EQUIMOLAR QUANTITY OF SODIUM IODIDE AT 22±0.5°

Time in hours (T)	$-\Delta n_D^{22} . 10^3$	% of Ester reacted in time (T)	$x . 10^2$	$\frac{x}{a-x} . 10^1$
0.92	0.0	0.00	0.00	0.000
1.92	0.1	2.00	0.30	0.204
2.92	0.1	2.00	0.30	0.204
5.17	0.1	2.00	0.30	0.204
21.67	0.8	16.00	0.40	1.905
26.17	1.0	20.00	3.00	2.500
36.00	1.4	28.00	4.20	3.888
47.42	1.6	32.00	4.80	4.705
57.42	1.7	34.00	5.10	5.150

After heating and cooling total $-\Delta n_D^{22} . 10^3 = 5.0$

The specific reaction rate constants at 22° were obtained by multiplying the slope of the $\frac{x}{a-x}$ vs. time plot by $\frac{1}{a}$.

X. Peroxide Formation in the Alkyl Ethers of Ethylene and Diethylene Glycol

In every case the samples examined contained peroxides and aldehydes, as shown by the tests outlined in the analytical section. They were examined quantitatively with the following results.

A. A sample of commercial Cellosolve was taken directly from the tin shipping container where it had been stored for an indefinite period.
Anal. 0.00060 N in peroxides; 3.4 cc. peroxide oxygen/Liter; 0.0172 N in acids.

B. A sample of commercial Cellosolve was purified by careful fractionation. A fraction was stored in a dark colored, glass stoppered bottle for a period of one year, during which time the stopper was periodically removed.
Anal. 0.0434 N in peroxides; 243.0 cc. peroxide oxygen/Liter. The refractive index remained unchanged at n_D^{20}, 1.4080.

C. A sample of commercial Cellosolve was purified by repeated fractionation until the qualitative tests for peroxides and aldehydes were negligible. At this state of purity it was noted that the characteristic fruity odor described for Cellosolve had substantially disappeared and the refractive index was n_D^{20}, 1.4080. The sample was stored in a dark, glass stoppered bottle for two days and then the atmosphere in the bottle was replaced by nitrogen. After a further six days of storage, the sample was analyzed.

Found: 0.00171 N in peroxides; 9.6 cc. of peroxide oxygen/liter. The refractive index remained unchanged.

D. An unpurified sample of commercial Cellosolve was stored in a white glass Erlenmeyer flask over anhydrous calcium sulfate for one year, being exposed to diffuse daylight.

Anal. 0.2462 N in peroxides; 1380 cc. peroxide oxygen/liter; n_D^{20}, 1.4090. After further storage under the same conditions for two more months, the results were 0.0012 N in peroxides; 6.8 cc. peroxide oxygen/liter; 0.261 N in acids. This sample was the same age as that described in A.

E. An unpurified sample of commercial Methylcellosolve, ($CH_3OCH_2.CH_2OH$) which had been in a brown colored reagent bottle for an indefinite period of time was examined.

Anal. 0.0706 N in peroxides; 395.5 cc. of peroxide oxygen/liter.

F. An unpurified sample of the dimethyl ether of ethylene glycol which had been stored for an indefinite period in a brown glass reagent bottle was 0.2788 N in peroxides or had 1560 cc. peroxide oxygen/liter.

G. A commercial sample of Carbitol was purified both by Seikel's method (40) and by treatment with lead tetraacetate followed by fractionation. The sample was then stored in a dark, glass stoppered bottle in a cupboard for four months and after this time peroxides were detected. Then the sample, contained in an Erlenmeyer flask fitted with a cork stopper, was oxygenated for a period of six hours by bubbling a stream of oxygen through it. Then it was stored in diffuse daylight for two weeks. Anal. 0.0469 N in peroxides; 263 cc. of peroxide oxygen/liter. The sample was stored two months longer under the same conditions. Anal. 0.0692 N in peroxides; 387 cc. of peroxide oxygen/liter; 0.305 N in acids.

H. A commercial sample of Carbitol was stored over anhydrous calcium sulfate in a tightly stoppered white glass bottle for a period of one year. Anal. 0.00908 N in peroxides; 50.7 cc. of peroxide oxygen/liter. After a further two months' storage under the same conditions the values had changed to 0.0033 N in peroxides; 18.6 cc. peroxide oxygen/liter.

I. A commercial sample of Carbitol was purified both by Seikel's method, then by treatment with lead tetraacetate followed by fractionation. After standing for a period of four days in a cork stoppered Erlenmeyer flask exposed to diffuse daylight peroxides were present.
Anal. 0.0322 N in peroxides; 180 cc. of peroxide oxygen/liter.

J. Samples of commercial Cellosolve and Carbitol were purified by methods previously outlined until they contained no peroxides or aldehydes, detectable by the qualitative tests outlined. At this point neither Cellosolve nor Carbitol had any odor. Then these samples were divided into two portions; one was kept in a dark, glass stoppered bottle under an atmosphere of nitrogen and one was allowed to stand exposed to diffuse daylight in an Erlenmeyer flask. Periodically, samples were titrated for peroxides. When a sample was removed from those materials stored under nitrogen a continuous stream of nitrogen was allowed to sweep through the bottle. The results are in Tables XV and XVI.

Employing the method proposed by Allen (85) for the qualitative identification of small amounts of carbonyl compounds, a reddish-orange 2,4-dinitrophenylhydrazone was obtained as small needle-like crystals from both Cellosolve and Carbitol samples which contained peroxides. After recrystallization from either glacial acetic acid or nitrobenzene the substance melted with decomposition at 313° or at 332.40° (corr.). According to Glasstone and Hickling (86) the melting point of the bis-2,4-dinitrophenylhydrazone of glyoxal is 3306 (corr.) and a mixed melting point of the unknowns with a pure sample of this substance showed no depression.

No peroxides or aldehydes could be found in the monoethyl-ether of triethylene glycol, although careful tests were made after exposure to a variety of conditions.

XI. The Action of Lead Tetraacetate on Carbitol Containing Small Amounts of Ethylene Glycol

To 45 cc. of aldehyde-free glacial acetic acid in a 100 cc. glass stoppered volumetric flask, 1.0181 grams of dry Carbitol, purified by Seikel's extraction procedure (40), and 50 cc. of a standard lead tetraacetate solution

TABLE XV

(see Fig.1)

PEROXIDE FORMATION IN PURIFIED CELLOSOLVE STORED UNDER DIFFERENT CONDITIONS

Time in days	Cc. of 0.01009N thiosulfate consumed per 10 cc. sample		Normality in Peroxides x 10^3	
	Stored in dark under nitrogen	Stored in light in presence of atmospheric O_2	Stored in Dark under nitrogen	Stored in light in presence of atmospheric O_2
7	0.85	1.70	0.858	1.72
14	1.40	3.50	1.41	3.53
21	2.30	6.30	2.32	6.36
28	2.00	7.40	2.02	7.47

TABLE XVI

(see Fig. 1)

PEROXIDE FORMATION IN PURIFIED CARBITOL STORED UNDER DIFFERENT CONDITIONS

Time in days	Cc. of 0.01009 N thiosulfate consumed per 10 cc. sample		Normality in Peroxides x 10^3	
	Stored in dark under nitrogen	Stored in light in presence of atmospheric O_2	Stored in dark under nitrogen	Stored in light in presence of atmospheric O_2
13	-	23.00*	-	22.2
19	0.50	-	0.505	-
27	-	95.50*	-	96.36
33	1.10	-	1.11	-
47	1.50	-	1.51	-

* Both samples had n_D^{25}, 1.4256; pure Carbitol n_D^{25}, 1.4254

were added (66b). The solution was made up to volume by more glacial acetic acid, was well mixed and was kept at 25±1°. At noted time intervals 10 cc. samples were removed and titrated for remaining lead tetraacetate, using the potassium iodide - sodium thiosulfate method. The results are reproduced in Table XVII and Fig. 2 after correction for the blank.

TABLE XVII

(see Fig. 2)

LEAD TETRAACETATE OXIDATION OF CARBITOL CONTAINING SMALL AMOUNTS OF ETHYLENE GLYCOL

Time in hours	Cc. of 0.0244 N thiosulfate consumed in:			Moles of Oxidant consumed / gram of unknown
	Blank	Total	Sample	$M.10^4$
0.50	28.00	27.85	0.15	0.151
21.00	26.80	24.60	2.20	2.213
49.75	26.30	22.85	3.45	3.471
70.00	25.10	21.15	3.95	3.974
93.50	25.10	19.90	4.05	4.074
114.50	22.30	17.95	4.35	4.376
137.50	20.80	16.30	4.50	4.527

DISCUSSION OF EXPERIMENTAL RESULTS

I. Peroxide Formation in the Alkyl Ethers of Ethylene and Diethylene Glycol

The formation of peroxides in ethers has been thoroughly studied by various investigators (77, 80, 87, 88, 89, 90, 91), and some of the more important observations may be summed up as follows. Light is not essential for the formation of peroxides, although sunlight favors their accumulation up to a certain point and also catalyzes their decomposition. Oxygen was found to enhance peroxide formation, while water, alcohol or heat caused decomposition; the decomposition products being mainly aldehydes. Among other products, acids, alcohols and possibly carbon dioxide and alkanes are formed.

Fig. 1 (see Tables XV and XVI) shows clearly that peroxide formation in very carefully purified samples of Cellosolve and Carbitol is greater in presence of air and light than in the absence of these agents. It is interesting to note that Carbitol was very much more liable than Cellosolve to peroxide formation and that no peroxides or aldehydes at all were detected in the higher homolog, the monoethyl ether of triethylene glycol. Several other examples detailed in the Experimental Portion, show that the peroxide content varied with the conditions of storage

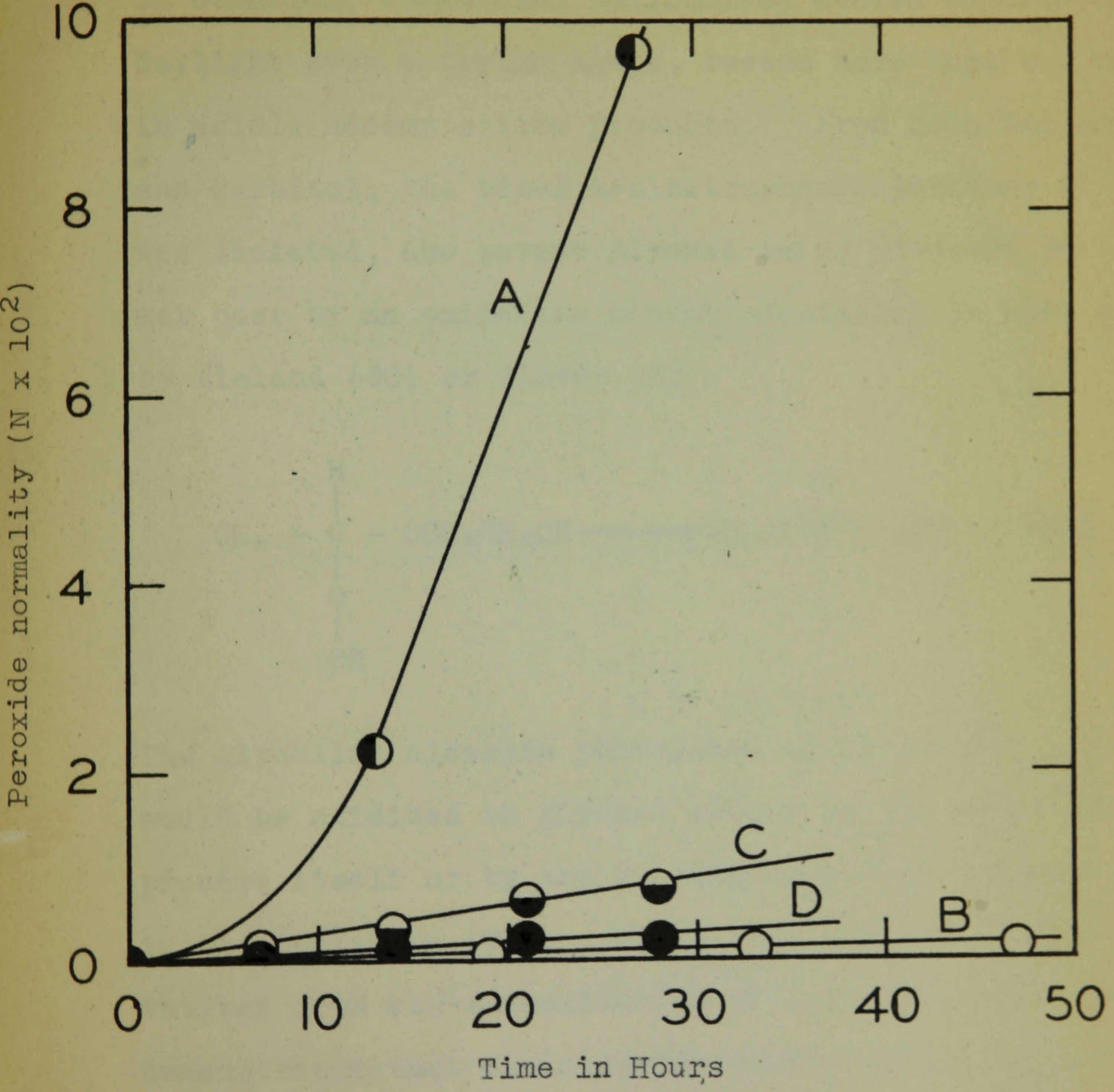
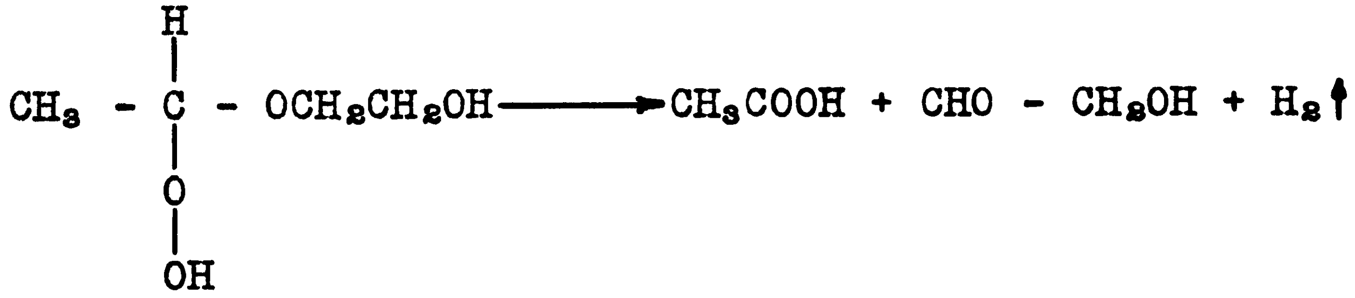


Fig. 1 (See Tables XV and XVI) Peroxide Formation in Purified Carbitol and Cellosolve on Storage

Plot A ◐ Carbitol stored in light and in presence of atmospheric oxygen.
Plot B ○ Carbitol stored in dark and in presence of nitrogen.
Plot C ◒ Cellosolve stored in light and in presence of atmospheric oxygen
Plot D ● Cellosolve stored in dark and in presence of nitrogen.

and sometimes decreased with time. Such variation is to be expected, for the autooxidation process is one of continual formation of peroxides and their decomposition. On occasion, commercial Cellosolve, stored exposed to daylight over a drying agent, became more than 0.2 normal in acidic decomposition products. From both Cellosolve and Carbitol, the bis-2,4-dinitrophenylhydrazone of glyoxal was isolated, the parent glyoxal being produced in the former case by an oxidation mechanism similar to that outlined by Wieland (80) or Clover (87).

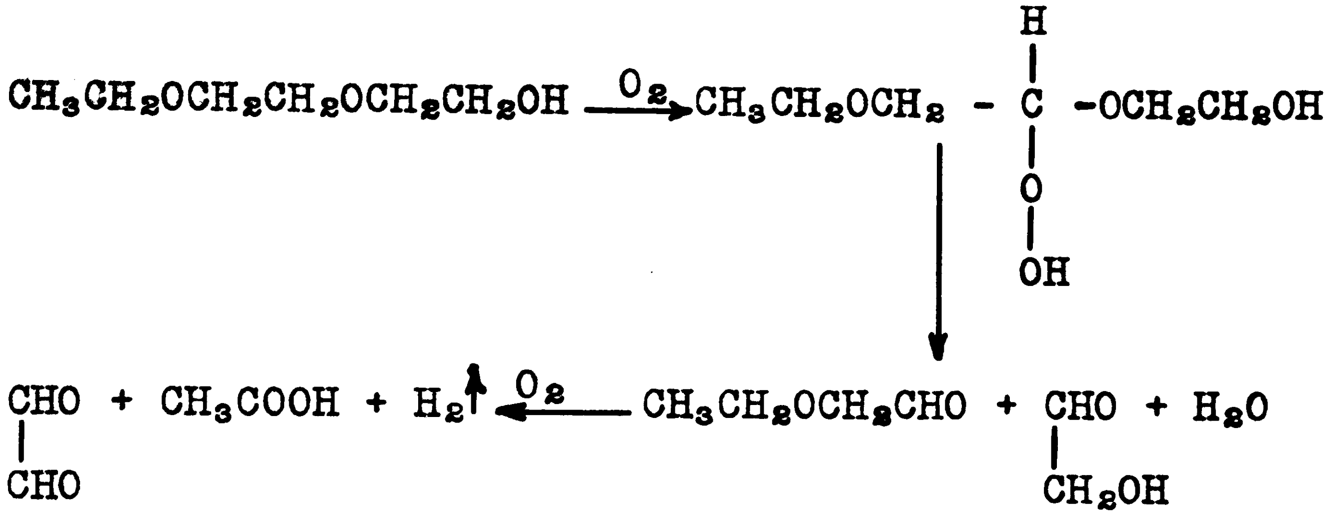


$$CH_3 - \overset{\overset{H}{|}}{\underset{\underset{\underset{OH}{|}}{\underset{O}{|}}}{C}} - OCH_2CH_2OH \longrightarrow CH_3COOH + CHO - CH_2OH + H_2\uparrow$$

The glycollic aldehyde postulated as an initial product would be oxidized to glyoxal either in the autooxidation process itself or by the 2,4-dinitrophenylhydrazine employed in the isolation (92). Milas (91) isolated glyoxal derivatives from the autooxidation of 1,4 dioxane and clearly demonstrated that the aldehyde formed by the oxidation was glycollic aldehyde.

In the case of the Carbitol, the isolation of the bis-2,4-dinitrophenylhydrazone of glyoxal is interesting for it indicates that the internal ether oxygen as well as that at the end of the molecule in the ethoxy group must be subject to autooxidation. The possible routes for the reaction are given in equations (A) and (B).

(A)

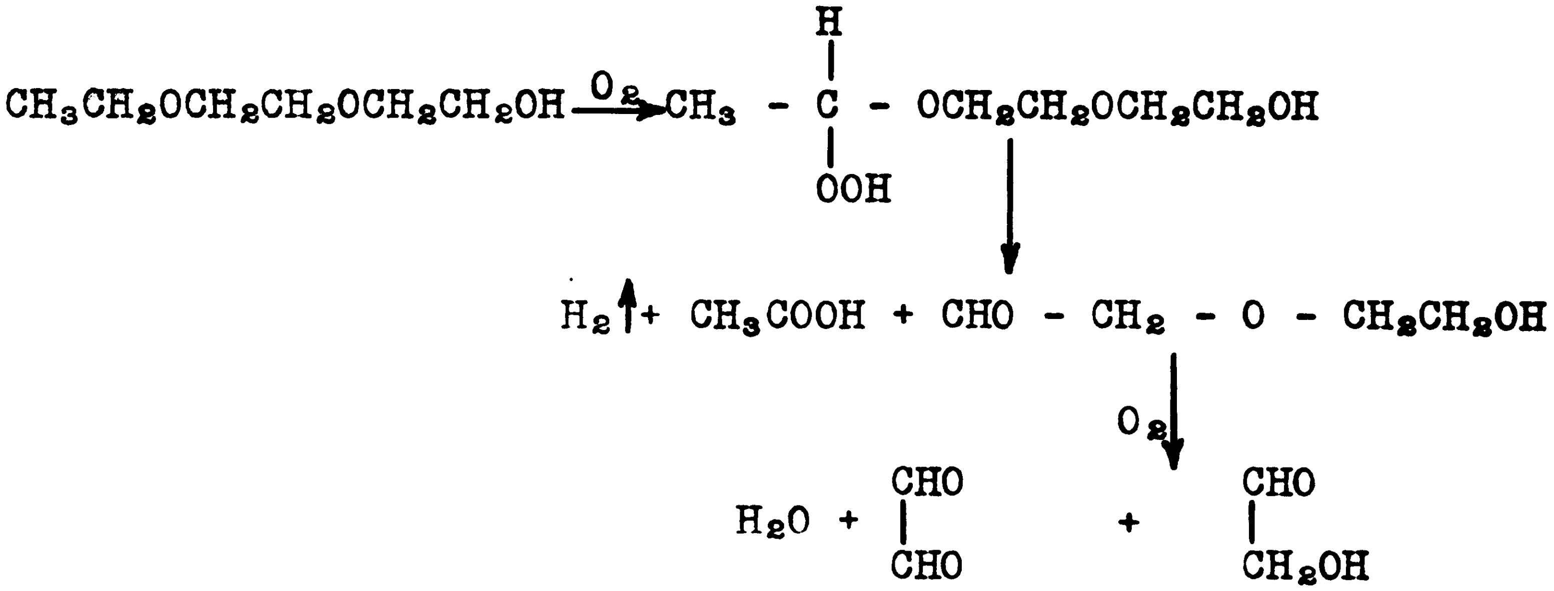


$$CH_3CH_2OCH_2CH_2OCH_2CH_2OH \xrightarrow{O_2} CH_3CH_2OCH_2-\overset{H}{\underset{\underset{OH}{O}}{C}}-OCH_2CH_2OH$$

$$\downarrow$$

$$\begin{matrix}CHO\\|\\CHO\end{matrix} + CH_3COOH + H_2\uparrow \xleftarrow{O_2} CH_3CH_2OCH_2CHO + \begin{matrix}CHO\\|\\CH_2OH\end{matrix} + H_2O$$

(B)



$$CH_3CH_2OCH_2CH_2OCH_2CH_2OH \xrightarrow{O_2} CH_3-\overset{H}{\underset{OOH}{C}}-OCH_2CH_2OCH_2CH_2OH$$

$$\downarrow$$

$$H_2\uparrow + CH_3COOH + CHO-CH_2-O-CH_2CH_2OH$$

$$\downarrow O_2$$

$$H_2O + \begin{matrix}CHO\\|\\CHO\end{matrix} + \begin{matrix}CHO\\|\\CH_2OH\end{matrix}$$

Since no acetaldehyde, ethoxyacetaldehyde (93) or β-hydroxyethoxyacetaldehyde was isolated, the end ethoxy group is represented as oxidizing to acetic acid in both of the alternative mechanisms, and the interior ether oxygen atom must undergo autooxidation. In either case, the end products would then be acetic acid and glyoxal or glycollic aldehyde. This inference requires proof, but present data render it plausible.

Means of removing these peroxides and their decomposition products are an important matter which henceforth must be considered in the purification of the Cellosolves and Carbitols. The use of fractional distillation is hazardous, tedious and unsatisfactory since the peroxides decompose with heat and the distillates are contaminated with decomposition products. A method such as described by Lipper (94), where the substance is treated with potassium hydroxide and potassium permanganate, should prove more effective. In the past Cellosolve and Carbitol have been characterized as possessing a "fruity" odor (24, 25), but in this investigation it was found that samples free from peroxides and aldehydes had no particular odor at all. It must be concluded that the "characteristic" odor was caused by traces of impurities. The presence or absence of peroxides in Cellosolve or Carbitol cannot be established by a simple physical constant such as refractive index (Table XVIII).

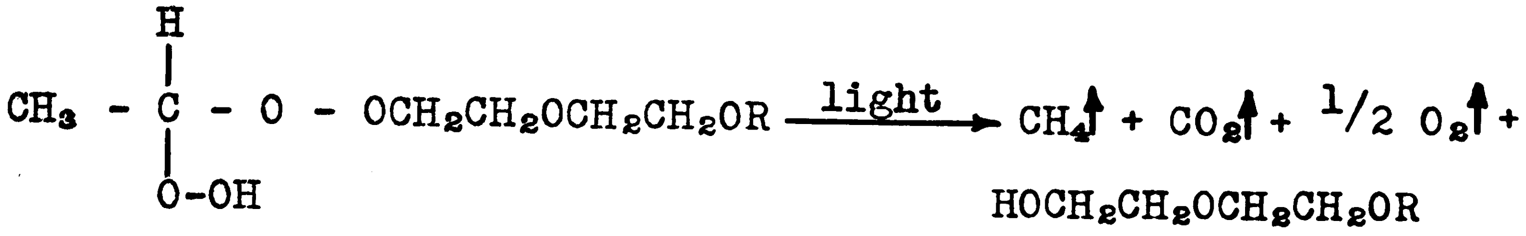
There is a certain amount of evidence in the literature which indicates that these peroxides have been encountered before without recognition. Liston and Dehn (37), preparing various dialkyl ethers of ethylene and diethylene glycol, found that during their formation, distillation and storage decomposition occurred, sometimes with

TABLE XVIII

REFRACTIVE INDICES OF CELLOSOLVE AND CARBITOL CONTAMINATED WITH PEROXIDES

Cellosolve		Carbitol	
Peroxide Normality	n_D^{20}	Peroxide Normality	n_D^{25}
-	1.4080	-	1.4254
0.0017	1.4080	0.0232	1.4256
0.0434	1.4080	0.0964	1.4256
0.2462	1.4090		

explosive violence. Distillation always gave high and low boiling fractions. The high boiling fraction might be accounted for by a peroxide decomposition suggested by Clover (87),

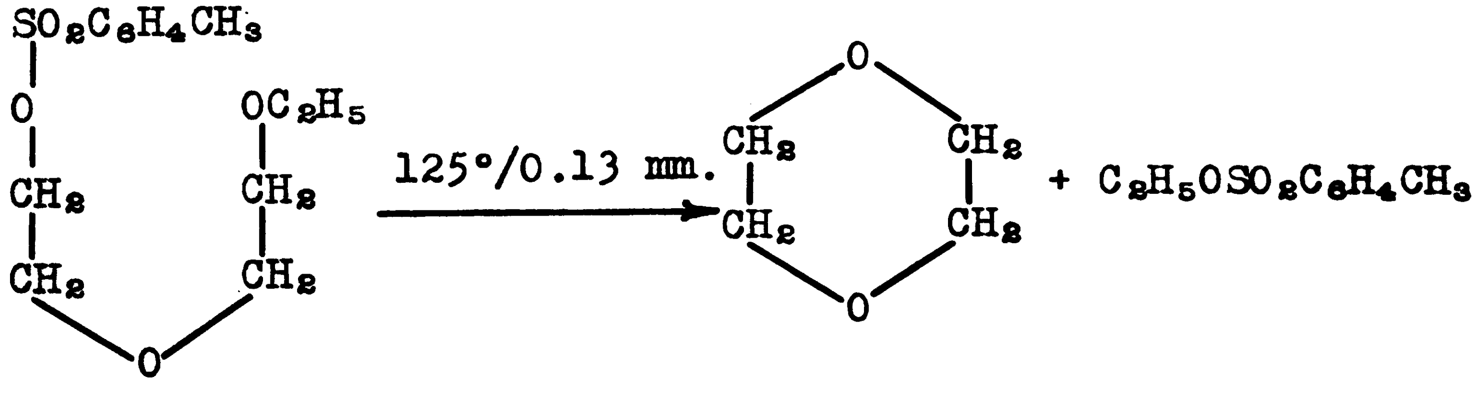


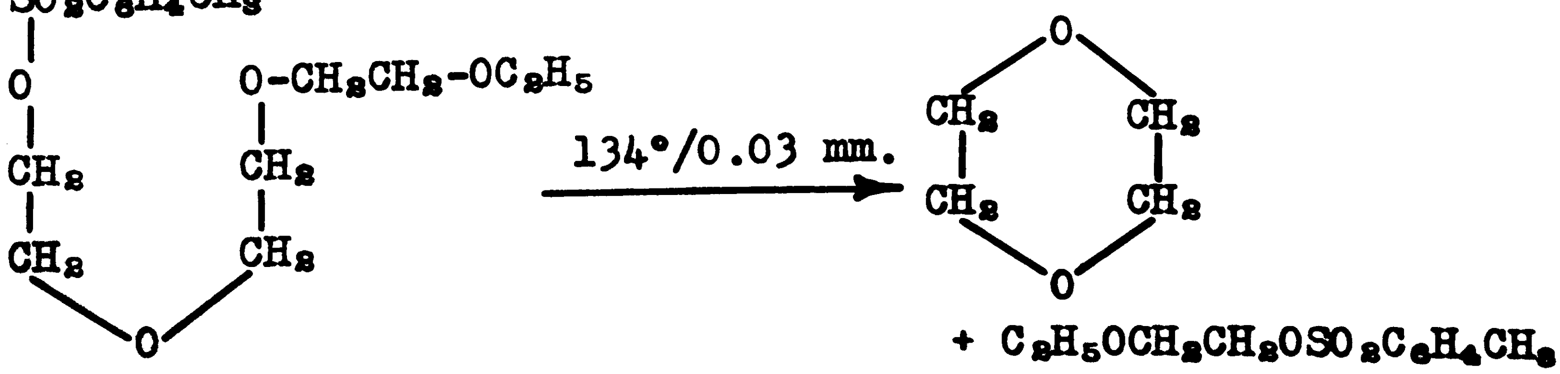
$$CH_3 - \underset{\displaystyle \overset{|}{O-OH}}{\overset{\displaystyle \underset{|}{H}}{C}} - O - OCH_2CH_2OCH_2CH_2OR \xrightarrow{light} CH_4\uparrow + CO_2\uparrow + {}^1/_2\ O_2\uparrow + HOCH_2CH_2OCH_2CH_2OR$$

yielding the corresponding monoether, which is known to have a higher boiling point than the diether (24, 25). On the other hand, the low boiling fractions might arise, at least in part, from other decomposition products such as acids or aldehydes or both. Gallaugher and Hibbert (20) noted that the dimethyl ether of diethylene glycol underwent thermal decomposition at the extremely low temperature of 60°, and contrasted sharply in this respect with the thermal stability of β,β'-dichloroethyl ether. But in the dimethyl ether there are three oxygen atoms capable of autooxidation while only one is present in the β,β'-dichloro derivative. Moreover, the oxygen atom in β,β'-dichloroethyl ether might not be so liable to peroxide formation because of the polar effects of the two chlorine atoms. When a sample of Carbitol which contained a small amount of ethylene glycol was treated with lead tetraacetate in glacial acetic acid, a steady consumption of the oxidant was noted (see Plot A, Fig. 2 and Table XVII). No sharp break (95) in the curve was obtained at two and one half days as would be expected if ethylene glycol was treated in glacial acetic acid along (Plot B). The observation shows that for some undetermined reason Carbitol is not entirely stable toward lead tetraacetate, whose action is often restricted to 1,2 glycol units. Although the instability might not cause great error in the estimation of ethylene glycol in Carbitol (40), it might well lead to complications if lead tetraacetate is employed to measure 1,2 glycols in hydroxyethyl cellulose ethers.

II. Thermal Decompositions in the Polyethylene Glycol Series

It was found that the p-tosyl esters of Carbitol and triethylene glycol monoethyl ether undergo in high yields a peculiar type of thermal decomposition at reduced pressure, which may be represented by the following equations:





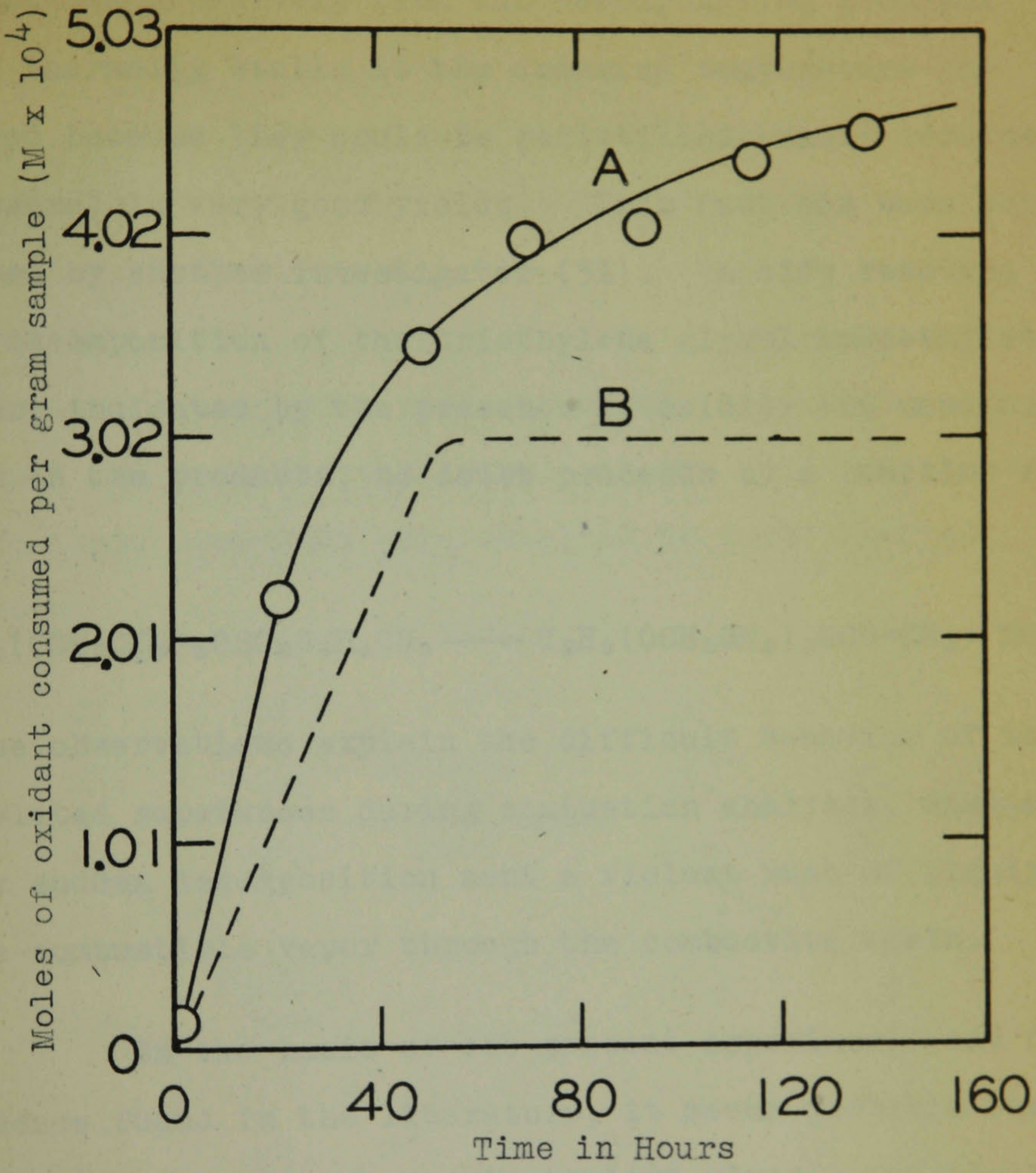


Fig. 2 (See Table XVII) The consumption of Lead Tetraacetate by Carbitol Containing Small Amounts of Ethylene Glycol.

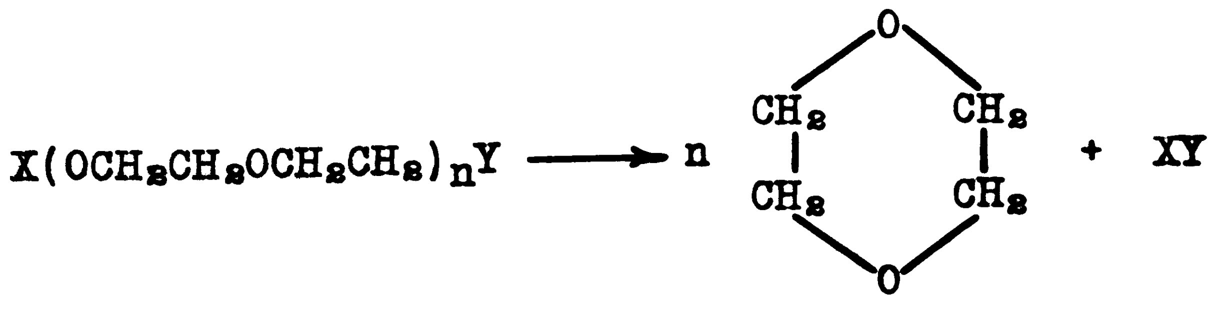
Plot A Actual results.
Plot B Theoretical results.

Both the ethyl and β-ethoxyethyl tosyl esters isolated almost quantitatively from the decomposition products were thermally stable at the cracking temperature employed because they could be redistilled (under reduced pressure) in very good yields. This fact has been confirmed by another investigator (51). A side reaction in the decomposition of the triethylene glycol monoethylether ester, indicated by the presence of acidity and unsaturation in the products, no doubt proceeds by a reaction such as,

$$C_2H_5(OCH_2CH_2)_3OSO_2C_6H_4CH_3 \longrightarrow C_2H_5(OCH_2CH_2)_2OCH{=}CH_2 + HOSO_2C_6H_4CH_3$$

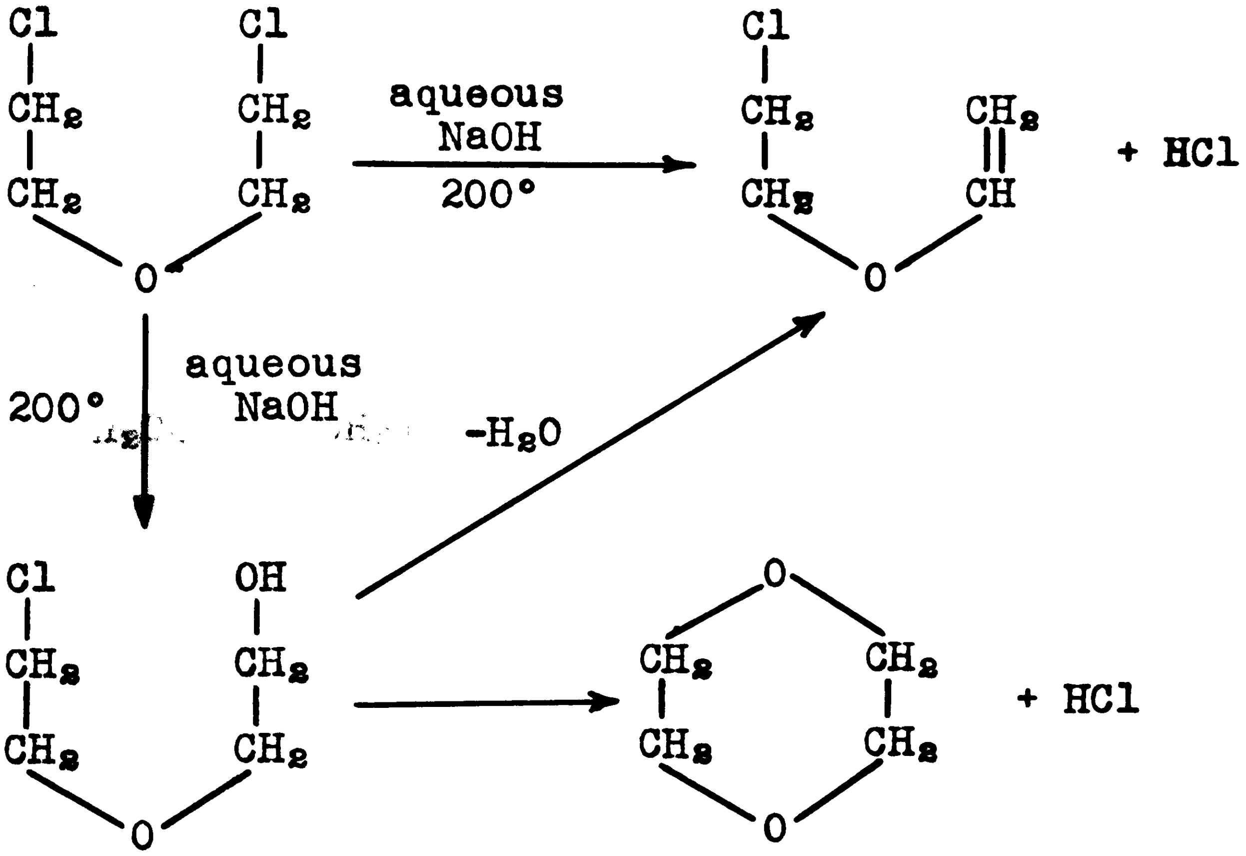
These observations explain the difficult behavior of the tosylated substances during combustion analyses, when a very sudden decomposition sent a violent rush of highly volatile combustible vapor through the combustion train.

On the basis of the present experiments and other evidence found in the literature, it seems probable that the thermal decomposition of polyethylene glycols and their derivatives proceeds at least to a large extent according to the general mechanism:

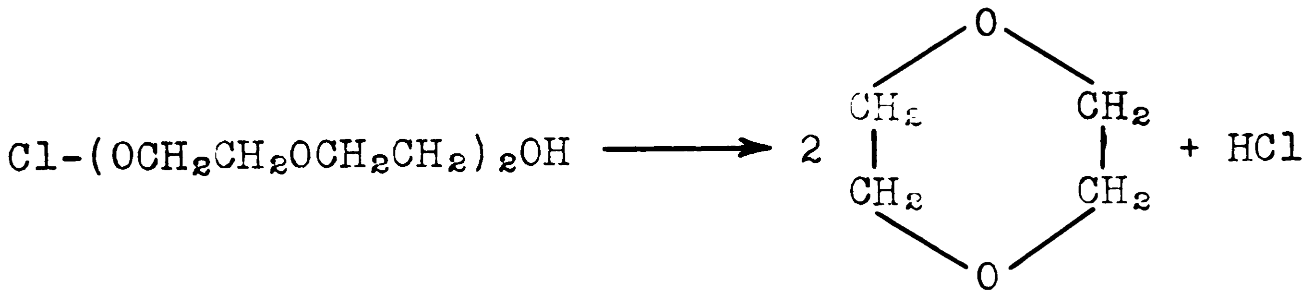


where n = 1, 2, 3, etc., X = H, alkyl, or β-alkoxylethyl, etc., and Y = halogen, alkoxyl, or $-OSO_2C_6H_4CH_3$, etc.

Direct support of this postulate is seen in the results Cretcher and his coworkers (96) obtained when they treated β,β'-dichloroethyl ether with aqueous sodium hydroxide at 200°. Very little of the desired divinyl ether was produced, the product largely consisting of 1,4-dioxane and β-chloroethyl vinyl ether. The reactions by which these compounds were obtained no doubt were as follows:



Butler and his coworkers (55) found that decomposition occurred during the high vacuum distillation of the tosylated monochlorohydrin of diethylene glycol. Liston and Dehn (37) obtained low boiling fractions when they distilled the diethers of diethylene glycol. Although these fractions might have arisen, at least in part, from peroxide decomposition, the very low yields of 30 and 40 percent of pure product recovered would more likely be explained by thermal cracking on distillation. Hibbert and Gallaugher (20) noted that the polyethylene glycols and their derivatives undergo thermal cracking, some at very low temperatures, yielding volatile, sweet smelling distillates, but unfortunately they failed to identify any decomposition products. The monochlorohydrin of tetraethylene glycol decomposed at 140° and on the basis of the decomposition of β,β'-dichloroethyl ether as noted by Cretcher (95) the reaction might have been of the general type proposed:

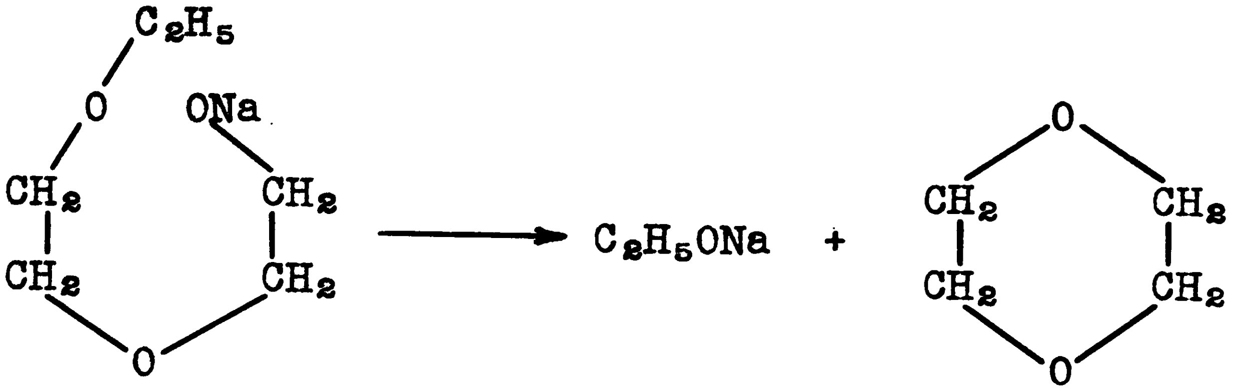


Since many investigators have found that the p-toluenesulfonate esters and the alkyl halides react similarly under the same conditions (52, 53, 97, 98), the suggested analogy between the two types of derivatives in this thermal reaction is therefore not without foundation.

Although no mechanism can be advanced without more information, decomposition might be connected with the ability of the polyethylene glycol chain to assume a coiled structure, the cross section of which would look like a 1,4-dioxane molecule. Hibbert (21) assumed some sort of intramolecular attraction between the two hydroxyl groups in diethylene glycol with the object of accounting for some of the anomalous physical properties of the compound. Hurd and Blunck (99) also proposed that an intramolecular hydrogen bridge existed to explain the products obtained in the low temperature pyrolysis of the carboxylic acid esters.

III. Preparations and Purifications

The first steps in the synthesis of the monoethyl ether of triethylene glycol was to prepare the sodium alcoholate of Carbitol. The addition of metallic sodium or of sodium methylate, to carefully purified, peroxide-free Carbitol, however, produced considerable decomposition as judged by the reddish-brown color immediately assumed by the mixture. Little improvement was noted when the experiment was repeated in a pure nitrogen atomosphere with the rigorous exclusion of moisture. On the basis of reactions already discussed, the decomposition might be connected with the formation of volatile products such as dioxane,

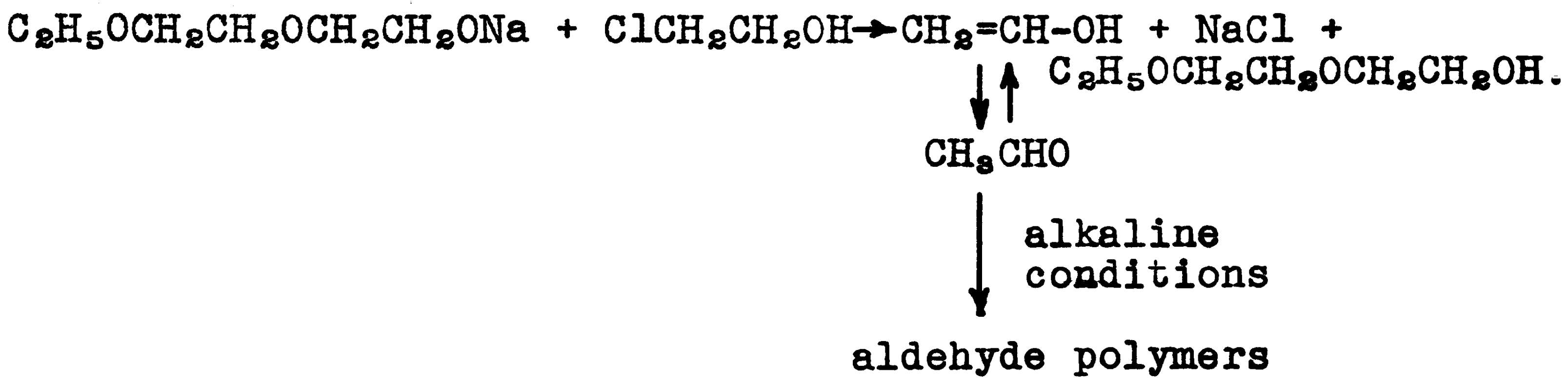


or with the formation of volatile cyclic acetals by reactions analogous to those recently discovered by Hurd and Botterson (100) for certain alpha halogen derivatives of ethylene and diethylene glycol in the presence of bases. No volatile matter, however, could be isolated from metallic sodium and Carbitol, even when the solution was kept at 170° under 15 mm. pressure. The nature of the colored products formed from sodium and Carbitol therefore remains obscure. Although the addition of ethylene chlorohydrin to the Carbitol-sodium system was also carried out with the rigorous exclusion of oxygen and moisture, the yield of the distilled monoethyl ether of triethylene glycol was only 29 percent based on sodium or 48 percent based on Carbitol consumed. This low yield might be attributed either to side reactions in the preparation of sodium Carbitolate or to thermal cracking during the isolation. Although the matter was not investigated, it is possible that the monoethyl ether during distillation partly decomposed to Cellosolve and dioxane by the cyclization already discussed. In the reaction of sodium methylate on β,β'-

dichloroethyl ether, Gallaugher and Hibbert (18) postulated a side reaction as follows:

$$Cl{-}CH_2CH_2OCH_2CH_2{-}Cl + 2CH_3ONa \rightarrow CH_2{=}CHOCH_2CH_2OCH_3 + 2NaCl + CH_3OH.$$

The same type of side reaction would account for the poor yields and color encountered in the present case:



$$C_2H_5OCH_2CH_2OCH_2CH_2ONa + ClCH_2CH_2OH \rightarrow CH_2{=}CH{-}OH + NaCl + C_2H_5OCH_2CH_2OCH_2CH_2OH.$$

$$CH_2{=}CH{-}OH \rightleftarrows CH_3CHO \xrightarrow{\text{alkaline conditions}} \text{aldehyde polymers}$$

When carefully purified starting materials were used, and the possibilities of peroxide formation and thermal cracking were carefully avoided, the preparation and purification of the tosyl esters and their iodine analogs proceeded normally. Analyses for iodine, however, could not be carried out with alcoholic solutions of potassium ethylate or potassium hydroxide because such solutions often failed to displace the halogen completely. With β-iodo-β'-ethoxyethyl ether, for example, Mahoney and Purves' (3a) sodium ethylate method of analysis gave iodine contents ranging from 38.0 to 51.7 percent, whereas the proper value of 52.0 percent was reliably obtained by the Carius method. Such low results were to be expected because various investigators (60, 61, 62, 64) have shown that β-halogen ethers were extremely stable substances, particularly the β-iodoethers.

The compounds prepared in this investigation were found to be pure by elemental analysis for carbon, hydrogen, and sulfur or iodine, and by the determination of molar refraction. In Table XIX and Fig. 3, data taken from Table III are supplemented by figures derived from the literature. No molar refractions for the tosylates could be calculated, because there were no data available on the atomic or group refractivity of the sulfonate ($-O-SO_2-$) unit in these compounds. The molar refractions when plotted against the number of ethylene oxide units per molecule give three straight lines whose slopes are A, 11.17, B, 10.93, and C, 11.00. These values are actually the contribution made per ethylene oxide unit to the molar refractions and they agree well with the calculated value of 10.88. A similar agreement was found by Hibbert for the polyethylene glycols (16, 19) and by others (65, 101) for other homologous series of linear polymers. Since the slope of the straight line for the tosylates is substantially the same as the slopes for the original monoethylethers and their iodo derivatives, it may be concluded that the observed molar refractions for the tosylates are correct within experimental error and afford further proof of purity. From these data and from tables of atomic refractivities, the average contribution of the sulfonate

TABLE XIX

(See Fig. 3 and 4)

SPECIFIC AND MOLAR REFRACTIONS IN THE POLYETHYLENE GLYCOL SERIES

Compound	n_D^{20}	Molar Refraction M_R Obser.	Molar Refraction M_R Calcd.(a)	Difference M_R (obser.) $-M_R$ (calcd.)
C_2H_5OH(b)	1.3610	12.92	12.96	- 0.04
$C_2H_5(OCH_2CH_2)OH$(c)	1.4074	23.88	23.84	+ 0.04
$C_2H_5(OCH_2CH_2)_2OH$(d)	1.4273	34.88	34.72	+ 0.16
$C_2H_5(OCH_2CH_2)_3OH$	1.4380	45.78	45.60	+ 0.18
$C_2H_5OSO_2C_6H_4CH_3$	1.5067 (35°)	51.04	-	-
$C_2H_5(OCH_2CH_2)OSO_2C_6H_4CH_3$	1.5032 (25°)	61.79	-	-
$C_2H_5(OCH_2CH_2)_2OSO_2C_6H_4CH_3$	1.4976 (25°)	72.80	-	-
$C_2H_5(OCH_2CH_2)_3OSO_2C_6H_4CH_3$	1.4959 (25°)	82.99	-	-
C_2H_5I(e)	1.5133(18.5°)	24.30	24.24	+ 0.06
$C_2H_5OCH_2CH_2I$(f)	1.4965	35.21	35.12	+ 0.09
$C_2H_5(OCH_2CH_2)_2I$	1.4908	46.24	45.99	+ 0.25
$C_2H_5(OCH_2CH_2)_3I$	1.4889	56.93	56.87	+ 0.06

(a) Atomic refractivity values were obtained from Gilman (82)
(b) Huntress and Mulliken (83b)
(c) Tallman (65)
(d) Seikel (40)
(e) Beilstein (98)
(f) Karvonen (64)

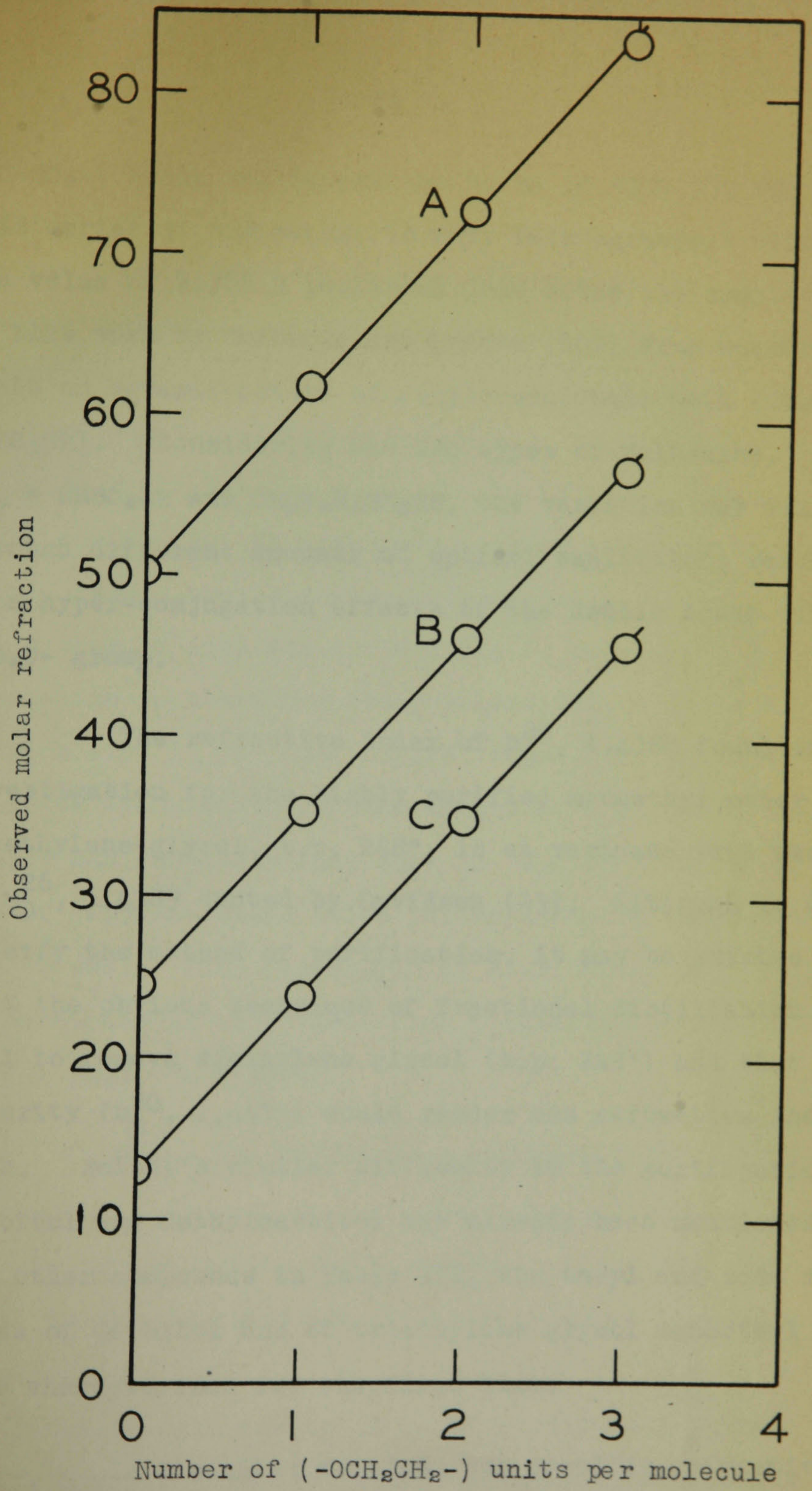


Fig. 3 (See Table XIX) Change in Molar Refraction per Ethylene Oxide Unit in Derivatives of the Polyethylene Glycols

Plot A	The tosyl esters of the monoethyl ethers
Plot B	The β-iodoethyl ethers
Plot C	The monoethyl ethers

($-O-SO_2-$) group was determined to be 10.53±0.35, for this series of compounds, in only fair agreement with the value of 9.7±0.2 published just after the completion of this work by Whitmore and Landau (102) from measurements on several esters of ethylenesulfonic acid ($CH_2 = CHSO_2OR$). Considering the two types of molecules, $CH_2 = CHSO_2OR$ and $CH_3C_6H_4SO_2OR$, the variation may arise through different amounts of optical exaltation, resulting from hyper-conjugation effects of the double bonds with the $-SO_2O-$ group.

The refractive index of n_D^{20}, 1.4380 found in this investigation for the highly purified monoethyl ether of triethylene glycol, b.p. 248°, is at variance with the value of n_D^{26}, 1.4389 quoted by Davidson (25). Although he did not specify the method of purification, it may be pointed out that the obvious technique of fractional distillation would fail to remove diethylene glycol (b.p. 245°) and that this impurity (n_D^{20}, 1.4475) would render his refractive index high. Seikel's similar difficulty in the purification of Carbitol and Methylcarbitol has already been mentioned. Of the other compounds in Table XIX, the tosyl and iodo derivatives of Carbitol and of triethylene glycol monoethyl ether were characterized for the first time.

In a similar fashion, the specific refractive indices of the various polyethylene glycol derivatives are plotted in Fig. 4, against the number of ethylene oxide units per molecule. The values for the monoethyl ethers show an increase as the series is ascended, but the increment decreases. This phenomenon was noted by Hibbert and Gallaugher (18) for the homologous series of polyethylene glycols, and was included in a generalization on specific refractive power by Smiles (103). However, the first members in the homologous series of tosyl esters and β-iodo ethers show a decrease in specific refractivity as the number of ethylene oxide units is increased, and are in opposition to the above observations and to other published results (18, 103). Refractive indices reported for the benzoate and p-nitrobenzoate esters of a number of Cellosolves and Carbitols (44) show no regular trend as the number of ethylene oxide units per molecule is increased from one to two. This result can be attributed only to impure preparations as is evident from a detailed consideration of the paper (44) itself.

Since the Cellosolves and Carbitols readily undergo autooxidation and many of their derivatives decompose to some extent during purification by fractional distillation, it may be concluded that the accuracy of much earlier physical data (44, 45, 46, 47, 48, 104) is open to criticism. The inference appears to be particularly well-founded for the Carbitol series, for the fractional distillations

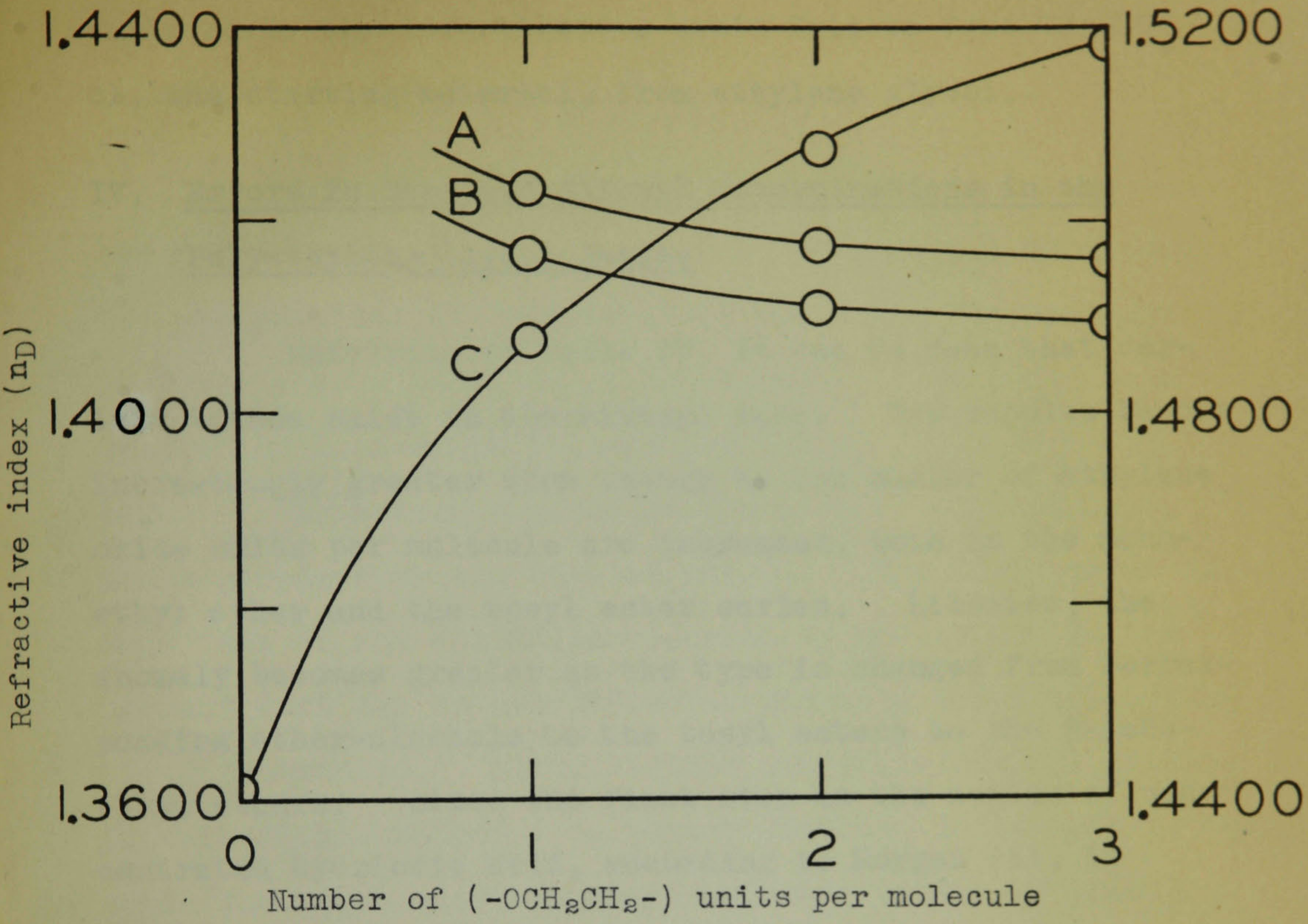


Fig. 4 (See Table XIX) Variation in refractive index with the number of ethylene oxide units per molecule

Plot A	Right hand ordinate, the tosyl esters, n_D at 25°
Plot B	Right hand ordinate, the β-iodoethers, n_D at 20°
Plot C	Left hand ordinate, the monoethyl ethers, n_D at 20°

employed by the investigators would fail to free Carbitol, the starting material, from ethylene glycol.

IV. Errors in Standard Alkoxyl Determinations in the Polyethylene Glycol Series

Referring to Table IV, it can be seen that certain trends exist in the alkoxyl data. The results become increasingly greater than theory as the number of ethylene oxide units per molecule are increased, both in the monoethyl ether and the tosyl ester series. Likewise, the anomaly becomes greater as the type is changed from corresponding ether-alcohols to the tosyl esters to the β-iodoethyl ethers. Since the first step in the action of concentrated hydriodic acid, according to Morgan (5), is

$$ROCH_2CH_2OH + 3\ HI \longrightarrow RI + ICH_2CH_2I + 2\ H_2O$$

these trends become understandable. As the number of ethylene oxide units ($-OCH_2CH_2-$) per molecule increase, there is greater chance for more ethylene diiodide to form and consequently more ethyl iodide. The tosyl ester group being readily replaced by iodine, would result in more ethylene diiodide, other conditions being the same. When the β-iodoethyl ethers are considered, there is already one iodine atom in position so that ethylene diiodide should form most readily. By recalculating some of Morgan's data on the amount of ethyl iodide collected to a percent ethoxy basis from percent (-OCH_2CH_2-), the results shown in Table XX were obtained.

Inspection shows that the anomaly increases as the number of ethylene oxide units per molecule increases. The substitution of certain ether and ester for hydroxyl groups causes a decrease in the anomaly. No doubt some generalizations might be made concerning these facts on the basis of the modern electronic theories of organic reactions proposed by the English school. The differences in magnitude of the anomalies reported by Morgan and in the present work may be attributed to slightly different analytical procedures. Since neither procedure for the conventional alkoxyl method gave proper results, it is safe to conclude that such analyses are inherently worthless when applied to compounds containing the (-OCH_2CH_2-) unit.

V. Relative Rates of Solvolysis and of Iodination among Tosylated Polyethylene Glycol Monoethyl Ethers

Pure samples of the tosyl esters of ethanol, Cellosolve, Carbitol and triethylene glycol monoethyl ether were separately dissolved in sufficient 95 percent aqueous methanol to provide a 1000-fold molar excess of water. The course of the overall solvolysis reaction was determined by following the increase in acidity. Although it was expected that these conditions would ensure pseudo first order kinetics (97), the study was not planned with the idea of investigating

TABLE XX

DATA OBTAINED BY MORGAN[a] IN THE ANALYSIS OF POLYETHYLENE GLYCOL DERIVATIVES

Compound	Range of differences between % found and % calculated values (Found - Calc.)
Ethylene glycol ($HOCH_2CH_2OH$)	43.0 - 58.7
Diethylene glycol ($H(OCH_2CH_2)_2OH$)	71.4 - 61.1
Polyethylene oxide ($H(OCH_2CH_2)_{91}OH$)	61.4 - 87.1
Ethylene glycol di-o-pentacetyl d-gluconate ($C_2H_4O_2(C_6H_6O_6(COCH_3)_5)_2$	3.53 - 4.55
2-Phenoxyethanol ($C_6H_5OCH_2CH_2OH$)	18.2 - 29.1
1,4-dioxane ($(C_2H_4O)_2$)	88.9 - 92.5
β-Methoxyethanol-1 ($CH_3OCH_2CH_2OH$)	45.6 - 50.0
Methoxyethyl oleate ($CH_3OC_2H_4OOC_{18}H_{33}$)	7.72 - 9.34
β-Ethoxyethyl-o-benzoyl benzoate ($C_6H_5OOC_6H_4COOC_2H_4OC_2H_5$)	8.80 - 10.0
Diethylene glycol dicresyl ether ($C_7H_7OC_2H_4OC_2H_4OC_7H_7$)	14.2 - 21.4
β,β'-dichloroethyl ether ($(ClCH_2CH_2)_2O$	48.8 - 52.1
Triethylene glycol di-2-ethyl hexoate ($C_6H_{12}O_2(C_7H_5COO)_2$)	19.7 - 25.5

(a) Ref. (5)

the detailed mechanism of the solvolysis. The data contained in Tables V, VI, VII and VIII give reasonable straight line rate plots (Fig. 5) as they should for first order reactions. The limit of error in the titrations was ±0.05 cc. of 0.0098 N sodium hydroxide and by calculation it can be demonstrated that, for solvolysis below 10 percent, the total error in the log c values may vary from 14 to 8 percent. When the percent solvolysis lay between 10 and 20 percent, the log c values may be in error by 8 to 4 percent of the values given. All the points in Fig. 5, together with those which are not reproduced (see Tables V to VIII), lie within experimental error on the straight lines, the error being least in the cases of the fastest reaction, the solvolysis of ethyl-p-toluenesulfonate. These measurements would have been of much more absolute value had they been carried out under conditions such that the reactions proceeded more rapidly. The specific reaction rate constants (k_1), in moles reacted/liter/hour, were as follows: for ethyl p-toluenesulfonate, 0.1239; for 2-ethoxyethyl p-toluenesulfonate-1, 0.0173; for 2(β-ethoxyethoxy)ethyl p-toluenesulfonate-1, 0.0232; and for 2(β-ethoxyethoxyethoxy)ethyl p-toluenesulfonate-1, 0.0192. Since calculation shows that these rates may be in error by 10 percent, no significant differences exist between the k_1 values for the three beta-substituted esters. There can be no doubt, however, that ethyl p-toluenesulfonate under-

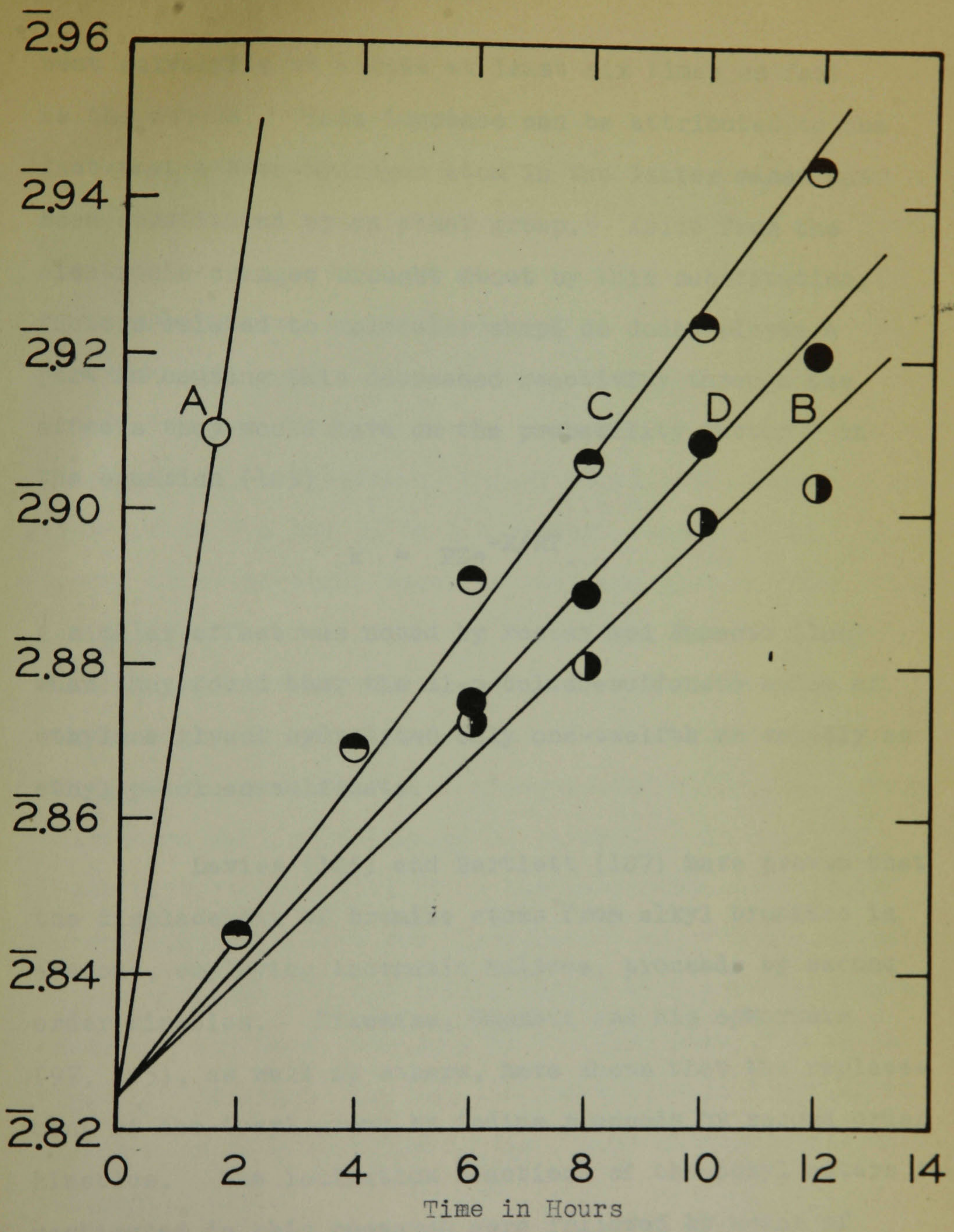


Fig. 5 (See Tables V to VIII) Solvolysis of 0.0015 molar solutions of various p-toluenesulfonates in a large excess of 95% aqueous methanol at 65±1°

Plot A ○ Ethyl p-toluenesulfonate
Plot B ◐ β-Ethoxyethyl p-toluenesulfonate-1
Plot C ◓ 2(β-Ethoxyethoxy) ethyl p-toluenesulfonate-1
Plot D ● 2(β-Ethoxyethoxyethoxy) ethyl p-toluenesulfonate-1

Ordinates log of concentration of unreacted ester went solvolysis at a rate at least six times as fast as the others. This increase can be attributed to the fact that a beta-hydrogen atom in the latter cases has been substituted by an ether group. Aside from the electronic changes brought about by this substitution, factors related to molecular shape no doubt played a part in causing this decreased reactivity through the effects they would have on the probability factor P in the equation (105)

$$k = PZe^{-E/RT}.$$

A similar effect was noted by Foster and Hammett (106) when they found that the di-p-toluenesulfonate ester of ethylene glycol hydrolyzed only one-twelfth as rapidly as ethyl p-toluenesulfonate.

Davies (105) and Bartlett (107) have proven that the displacement of bromine atoms from alkyl bromides in acetone, employing inorganic halides, proceeds by second order kinetics. Likewise, Hammett and his coworkers (97, 105), as well as others, have shown that the replacement of the tosyl group by iodine proceeds by second order kinetics. The iodination reactions of the tosyl esters investigated in this research were followed by means of changes in the refractive index of acetonyl acetone solutions. The data obtained, calculated on the basis of second order kinetics, are to be found in Tables IX, X, XI, and XII and are summarized in Fig. 6. Since the refractometer readings are accurate only to $\Delta n_D^{22} = \pm 0.1 \times 10^{-3}$, examination of the data reveals that the error for individual readings, in the case of the iodination of ethyl p-toluenesulfonate, ranged from 16.7 to 5.1 percent, as the reaction proceeded. The similar range for tosylated Cellosolve was from 100 to 6.5 percent for tosylated Carbitol and 2(β-ethoxyethoxyethoxy) ethyl p-toluenesulfonate from 100 to 7.4 and 33 to 6.1 percent respectively. A second order reaction requires that the plot of time versus $\log \frac{b}{a} \frac{(a-x)}{(b-x)}$ pass through the origin and the results (Fig. 6) show that the experimental points all fall within the limits of error on such straight lines. The slopes of these lines on the basis of experimental error have a calculated maximum variation of 15 percent. In order to check further the validity of the assumption of overall second order kinetics for these reactions, the concentrations of the tosylate and the sodium iodide were equalized in two cases and the data (Tables XIII and XIV) were plotted in Fig. 7. Straight line relationships between time and the bimolecular rate function $\frac{x}{(a-x)}$, were obtained within experimental error.

It is important to point out that the values of (k_s) obtained for these reactions are not absolute. They were obtained only as overall reaction rate constants

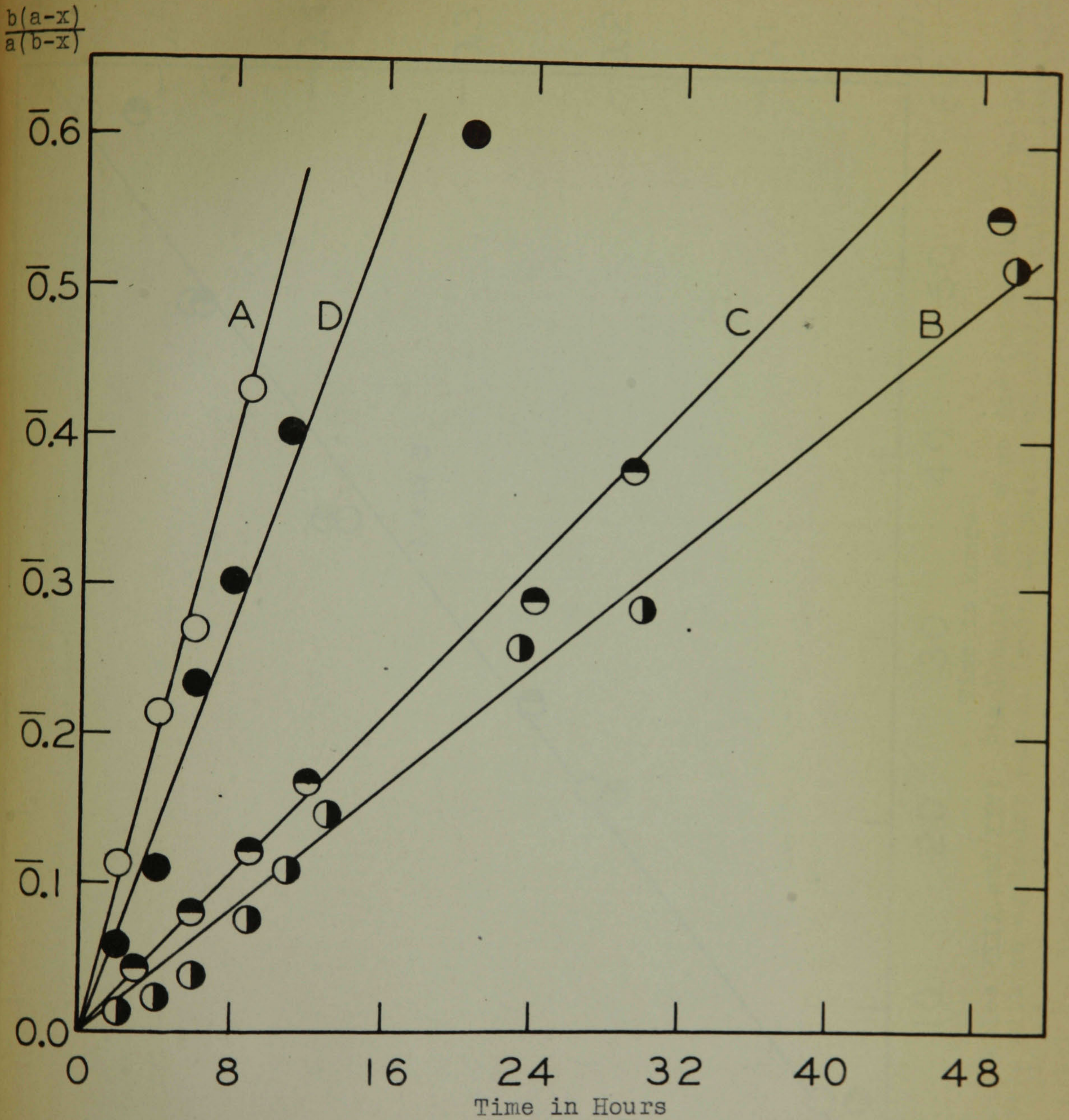


Fig. 6 (See Tables IX, X, XI and XII). Bimolecular rate of iodination of 0.1 molar solutions of various p-toluenesulfonate esters by an 0.3 molar solution of sodium iodide in acetonylacetone at 22±0.5°

Plot A ○ Ethyl p-toluenesulfonate
Plot B ◑ β-Ethoxyethyl p-toluenesulfonate-1
Plot C ◓ 2(β-Ethoxyethoxy) ethyl p-toluenesulfonate-1
Plot D ● 2(β-Ethoxyethoxyethoxy) ethyl p-toluenesulfonate-1

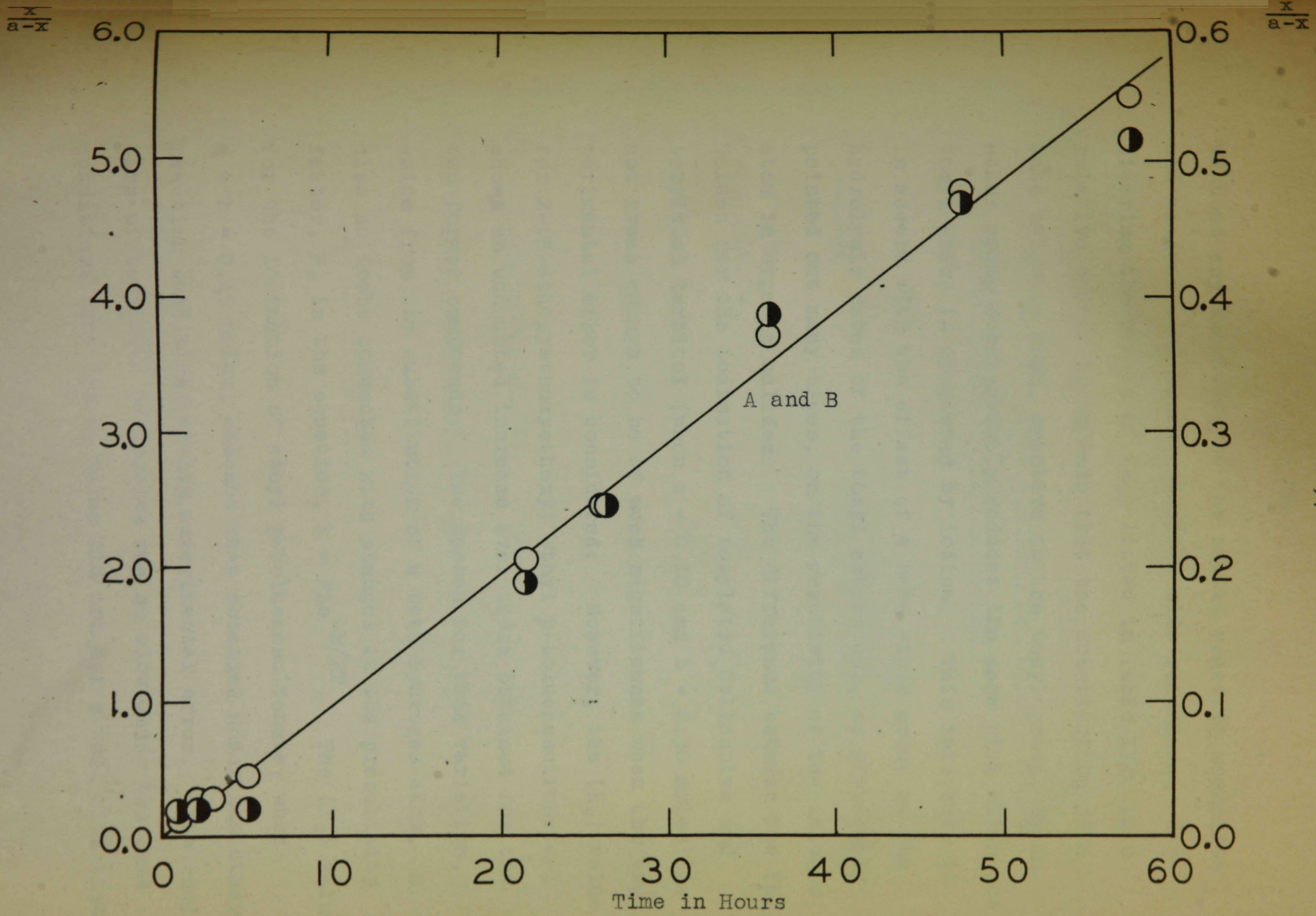


Fig. 7 (See Tables XIII and XIV) Bimolecular rate plot for iodination of p-toluenesulfonate esters with an equimolar amount (a=b=0.15 moles) of sodium iodide in acetonylacetone at 22±0.5°

Plot A ○ Ethyl p-toluenesulfonate, left hand ordinate

Plot B ◐ β-Ethoxyethyl p-toluenesulfonate-l right hand ordinate without any knowledge of the actual reaction mechanism and without considering possible side reactions. Considering the values of (k_2) listed in Table XXI, in a relative sense, it appears that the substitution of a beta hydrogen atom, relative to the tosyl group, by an ether group substantially reduces the ease with which the tosyl group is displaced by iodine. This inference is in accord with the effect of a beta ether group on the hydrolysis rates of the tosyl esters and, as previously pointed out many times, on the reactivity of the halogen atom in organic halides. The difference between the (k_2) values for the iodination of tosylated Cellosolve and tosylated Carbitol (when a = 0.10 and b = 0.30 moles) is not great enough to be of much significance when the experimental error is considered. However, the (k_2) value for 2-(β-ethoxyethoxyethoxy) ethyl p-toluenesulfonate-1 shows an undoubted increase over those obtained for the two former compounds. The reason for this variation, aside from the substitution of a beta hydrogen atom, is also no doubt connected with changes in the probability factor, P, in the equation, $k = PZe^{-E/RT}$. The (k_2) value for the iodination of ethyl p-toluenesulfonate, when a = b = 0.15 moles, checked that obtained under the other reaction conditions within experimental error. The iodination of tosylated Cellosolve was so slow under the same conditions that the k_2 value did not agree well with that

TABLE XXI

OVERALL SPECIFIC REACTION RATE CONSTANTS (k_2) FOR THE IODINATION OF p-TOLUENESULFONATE ESTERS IN THE PRESENCE OF SODIUM IODIDE IN ACETONYLACETONE AT 22±0.5°

Compound	Concentration of Reactants Moles/Liter Ester (a)	 Sodium Iodide (b)	k_2*
$C_2H_5OSO_2C_6H_4CH_3$	0.10	0.30	0.563
	.15	.15	.660
$C_2H_5OCH_2CH_2OSO_6C_6H\ CH_3$	.10	.30	.121
	.15	.15	.063
$C_2H_5(OCH_2CH_2)_2OSO_2C_6H_4CH_3$	.10	.30	.151
$C_2H_5(OCH_2CH_2)_3OSO_2C_6H_4CH_3$	.10	.30	.360

* Moles/liter/hour

obtained earlier (Table XXI). Since other factors such as salt concentrations, co-precipitation of salt with sodium p-toluenesulfonate and changes in ester concentration (97, 105) are known to affect the (k_2) values by as much as 10 percent, the iodinations should have been carried out under conditions such that they proceeded more rapidly. In these circumstances the experimental error would have been greatly reduced.

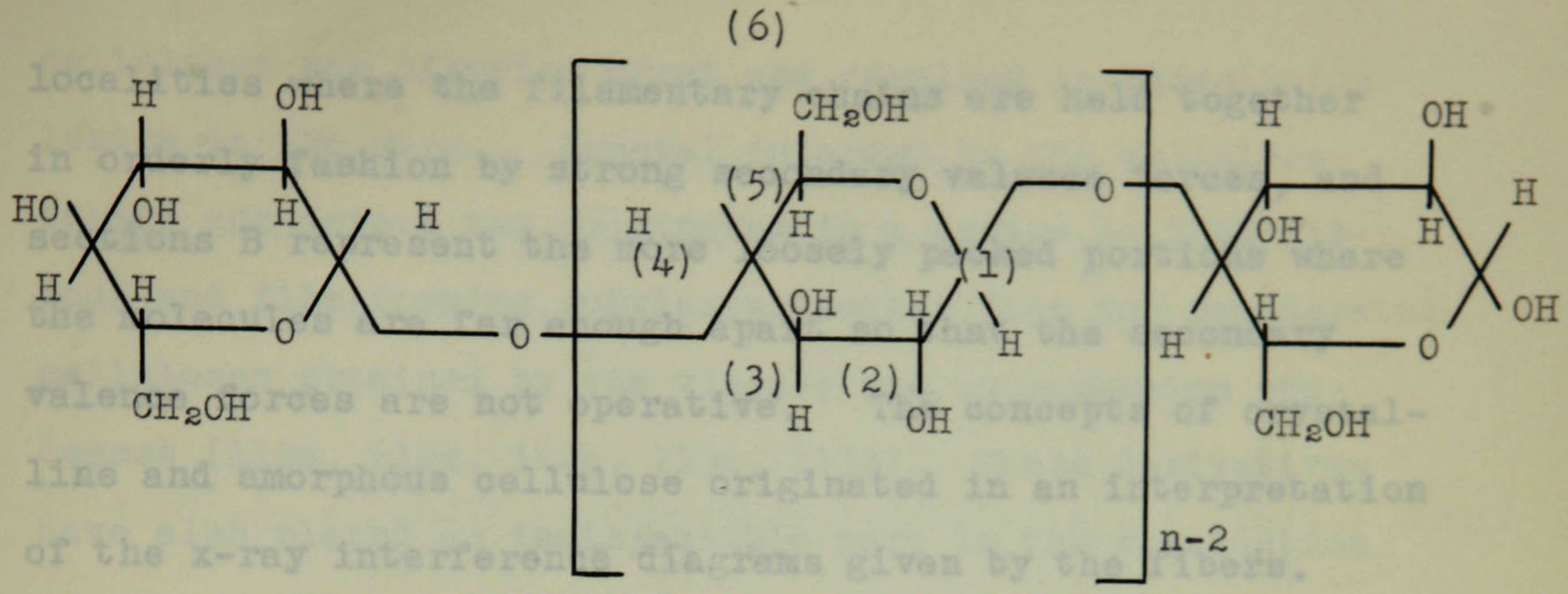
PART II

APPLICATION OF THE TOSYLATION-IODINATION REACTION TO A HYDROXYETHYL CELLULOSE

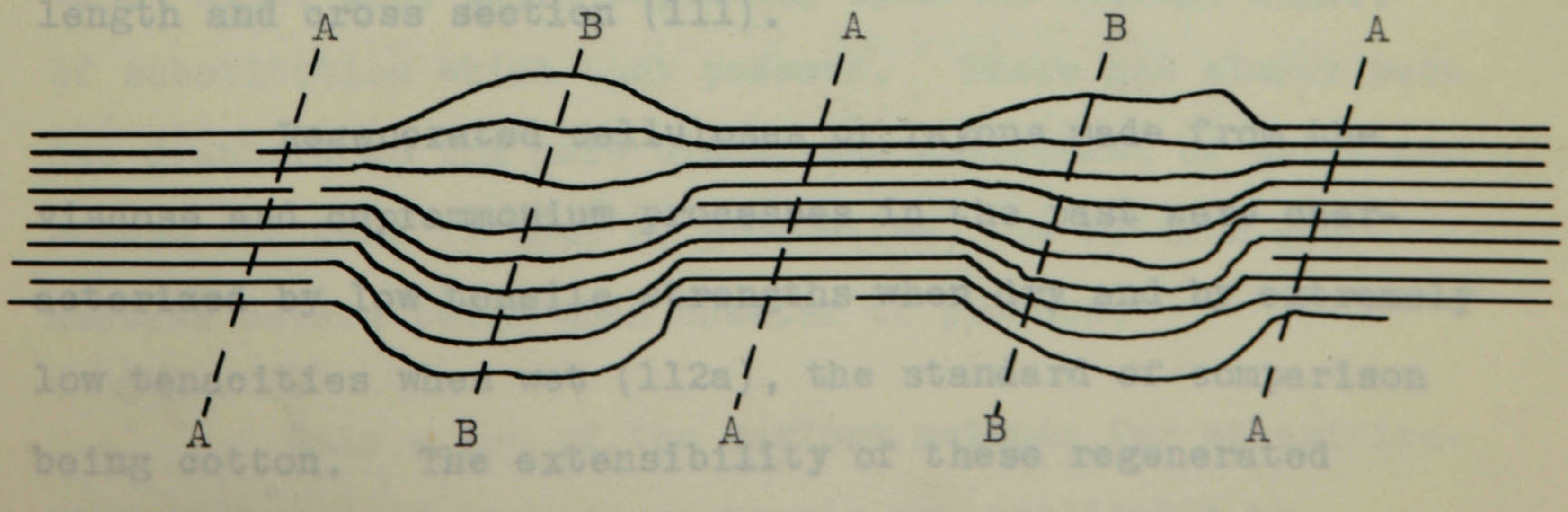
HISTORICAL INTRODUCTION

Although a detailed discussion of the literature on cellulose itself is far beyond the scope of this thesis, a brief summary will facilitate a review of the alkali soluble hydroxyethyl ethers of cellulose. Two very recent and well presented works, one by Ott (108) and the other by Wise (109) contain complete and comprehensive surveys of the general chemistry of cellulose.

The basic structure of the macromolecule has been established, by chemical and physical methods, to be a linear polymer of anhydro d-glucose units. The units are connected through β-glucosidic 1,4-oxygen bridges, leaving two secondary hydroxyl groups, in the second and third positions, and the primary hydroxyl group, in the sixth position, free in every d-glucose unit. The end groups are supposedly the only dissimilar units in any molecule. On one end of the chain there is a d-glucose unit which has an aldehyde reducing group on the first carbon atom, and on the other end the d-glucose units has three free secondary hydroxyl groups in the second, third and fourth positions respectively. The following structural formula has been accepted for cellulose containing (n) structural units.



These filamentary macromolecules or primary valence chains may form various types of crystal lattice by close orderly lateral associations between the chains, brought about by strong secondary valence forces. The resulting structure, when the molecules are so grouped together, are called micelles or crystallites. The modern fringe micelle theory proposes that the filamentary macromolecules run through these submicroscopic crystallite regions and also through more loosely packed or amorphous regions (110). The theory calls for a diagrammatic representation for fibrous cellulose as follows, each line corresponding to a single macromolecule.



The cross sections A represent closely packed crystalline localities where the filamentary chains are held together in orderly fashion by strong secondary valence forces, and sections B represent the more loosely packed portions where the molecules are far enough apart so that the secondary valence forces are not operative. The concepts of crystalline and amorphous cellulose originated in an interpretation of the x-ray interference diagrams given by the fibers. Such diagrams, together with a knowledge of the bond angles and lengths joining adjacent atoms, make it possible to calculate the actual dimensions and angles of the unit cell which exists in the crystalline regions.

Cellulosic material from various sources is made up of varying amounts of these so-called crystalline and amorphous varieties, native celluloses being high while regenerated celluloses and many derivatives are low in crystallinity. Physical and chemical examinations have proven that cellulose fibers have many submicroscopic voids or holes distributed more or less at random throughout their length and cross section (111).

Regenerated celluloses or rayons made from the viscose and cuprammonium processes in the past were characterized by low tensile strengths when dry and by extremely low tenacities when wet (112a), the standard of comparison being cotton. The extensibility of these regenerated celluloses was likewise great and resulted in undesirable lustre in the yarn. General interest in the cellulose ethers and esters has originated in a desire to find fibrous and film-forming substances better than the regenerated celluloses obtained by the viscose and cuprammonium processes (112a, 112b, 112c, 113a, 113b). These derivatives have also played an indispensible part in the elucidation of the structure of cellulose itself (108, 109), and, more recently, industry has become extremely interested in them as plastic, lacquer, coating, and sizing ingredients (114, 115, 116).

The ethers have been found to possess many of the desirable properties of the better known esters and also some which the esters do not have (112a). Unlike esters, most ethers are stable to light, storage, high concentrations of alkali, and heat. They are less flammable and, like esters, are soluble in water, dilute caustic soda and a wide variety of organic solvents (112a, 112b, 112c, 113a, 113b, 114, 115), depending upon the average degree of substitution which they possess. There has always been one drawback to the more widespread employment of cellulose ethers and that is cost of production, the nitrate and acetate esters being much cheaper to produce.

Only a few of the various methods for etherification employed in organic synthesis are applicable to cellulose (117, 118). In general, inorganic acid esters such as dimethyl sulfate or ethyl or benzyl chloride are the etherifying agents, and aqueous caustic soda is usually used to neutralize the resulting acids and to act as a catalyst (117).

$$\left[C_6H_7O_2(OH)_3\right]_x + 2xNaOH + 2xRX \rightarrow \left[C_6H_7O_2(OH)(OR)_2\right]_x + 2xNaX + 2xH_2O$$

In addition to aqueous inorganic bases, organic bases are occasionally employed, pyridine having been used successfully for preparing the trityl ethers of cellulose (119, 120), and quaternary bases for methyl and ethyl ethers by Bock (121, 122). Various organic and inorganic salts have also been substituted for bases (123, 124), but industrially only the aqueous caustic soda process has hitherto proven to be economically feasible. Uniform alkali cellulose may be obtained by immersing the pulp in a large bulk of aqueous alkali and by pressing or centrifuging the mass to remove the excess. The composition of the alkali cellulose is very important (30, 117, 118), since the ratio of water to alkali influences, the speed of the etherification reaction and the extent of the etherification or degree of substitution attained. The ratio of cellulose to water also determines to some degree the extent of the side reactions, while the character of those side reactions in turn depends upon the alkali to water ratio. The water in the cellulose acts in two ways (117); first, as a solvent and carrier for the sodium hydroxide and, second, as a swelling agent which loosens up the structure of the cellulose fiber. The penetration and diffusion of the alkylating agent is thereby facilitated. The swelling effect is of course supplemented by the action of the strong sodium hydroxide, which causes mercerization or hydration of the cellulose.

Ordinarily, the etherification is heterogeneous in nature (117), but when carried out in quaternary ammonium bases is homogeneous provided the etherifying agent, the cellulose, and the products are all soluble (121, 122). In the heterogeneous systems the cellulose hydroxyl groups are surrounded by an aqueous phase and it is necessary for the etherifying agent to disperse in the caustic solution, to diffuse through the various cracks, canals, and finer interstices or void spaces (111), in order to reach the potential reaction centers of the internal surfaces. Such a diffusion process depends upon the molecular size of the alkylating agent, on its solubility in the alkali solution, and on the concentration of the latter. The temperature and pressure at which etherification is carried out likewise affect the diffusion phenomena. Only a relatively few hydroxyl groups on the surface of the cellulose fibers react in the initial phase and a low substituted layer results. This layer swells, but does not dissolve in the aqueous alkali and excess etherifying agent. Since reaction in subsequent layers of the fiber depends upon diffusion through this gellified, swollen layer (117, 125), it is necessary to distinguish between velocity of reaction and speed of propagation in the reaction zone. The former refers to the case where the hydroxyl groups and the etherifying agent are in contact, and is comparable with the velocity of a homogeneous reaction. The latter term refers to the speed with which the reaction front travels from layer to layer, as determined by diffusion conditions. Initially at least, the reactions in the presence of aqueous alkali are of a topochemical nature, whose type is dependent upon the ratio of the two velocities (117). When the propagation is slow the reaction is macroheterogeneous. When the alkylating agent is in the gaseous state, diffusion is rapid, and it may be assumed that the surfaces of the smallest physical structural units are attacked at once. This is a microheterogeneous reaction and might almost be termed permutoid (quasihomogeneous). If a product undergoes a rather high degree of swelling on its surface, agitation helps to dissolve or disperse it and thereby allows propagation to continue (117), but on the other hand too much agitation causes excessive hydrolysis of the alkylating agent. The degree of substitution finally obtained depends also on the amount of alkylating agent employed, particularily, if the agent is a solvent for the reaction. In general, high temperatures during alkylation increase both the reaction velocity and speed of propagation, although not necessarily in the same ratio. High temperatures favor a highly substituted outer layer, whereas, a more uniform conversion throughout the fiber tends to result at lower temperatures.

All etherifying agents of the ester or halide type are subject to alkaline hydrolysis under the conditions employed and are thus used up simultaneously in two competing reactions (117), whose relative rates influence the whole course of the etherification. When hydrolysis occurs at a rate faster than etherification, more alkali and etherifying agent have to be continuously added. The usual side reactions are,

$$RX + NaOH \longrightarrow ROH + NaX,$$
$$RX + ROH + NaOH \longrightarrow ROR + NaX + H_2O$$

and the second is favored by high alkali concentrations in the alkali cellulose (125, 126, 127, 128, 129). The first reaction reaches a maximum near 20 percent alkali concentration, increasing at smaller (117, 130) and decreasing with larger concentrations. It decreases as the ratio of alkylating agent to alkali in the system increases. It also increases as rate of agitation is increased, as the reaction temperature is raised, and as the reaction time is prolonged. Unfortunately, conditions which cut down the undesirable side reactions also tend to limit the etherification reaction, and, in most instances the set of conditions adopted is the compromise giving the best overall results.

A thorough search of the literature and consultation of reviews on cellulose ethers (115, 131, 132) revealed no articles concerning hydroxyethyl cellulose prior to 1933 (133). However, numerous patents had been issued concerning them (124, 126, 130, 134, 135, 136, 137, 138, 139) prior to this date. The first hydroxyethyl cellulose, prepared from ethylene oxide and cellulose, was made and described by Hubert in 1920 (139), but there was not much interest in such products until the work of Shorigin and Rymashewskaja (133, 140, 141), Schorger (126, 127, 128, 129), and Schorger and Shoemaker (142) was published. Since a reliable means for the determination of the average degree of substitution of hydroxyethyl cellulose ethers was not developed until 1946 (5), the literature values are probably in error and are quoted below only for comparative purposes.

Some preparations of the hydroxyethyl ethers of cellulose employ ethylene chlorohydrin (134, 135), others ethylene oxide (121, 125, 142, 143, 144, 145, 146), and in others either etherifying agent may equally well be applied (116, 122, 126, 127, 128, 129, 132, 147, 148, 149, 150). Cotton linters, high alpha wood pulp cellulose, regenerated cellulose, and pretreated cellulose may be used. Pretreated cellulose refers to material which has undergone some special acid or alkaline treatment and which is often somewhat degraded.

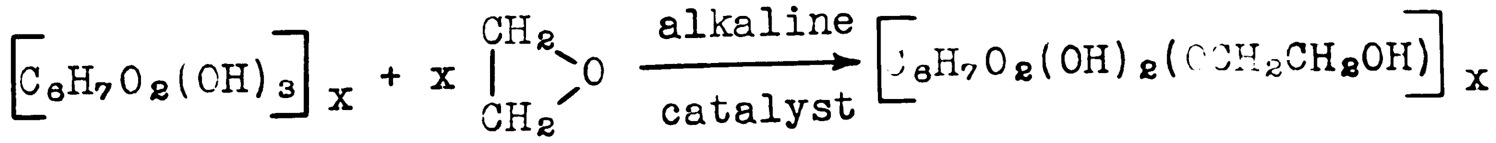
The reaction of cellulose with ethylene oxide (108b, 116, 117, 126, 127, 128, 129) is a notable exception to the general etherification process already outlined. Ethylene oxide is capable of entering into a direct addition with fibrous cellulose, although with extreme slowness, and some type of alkaline catalyst is usually employed. The catalyst may be caustic soda or a wide variety of other organic and inorganic bases or salts (121, 124, 144, 145, 150), and may be employed in amounts ranging from that of the dry cellulose to as little as 0.25 percent (144, 145). The function of the catalyst is to swell the cellulosic material, thus promoting a more uniform reaction, to speed up the overall reaction, and sometimes to degrade the cellulose, as when caustic soda is used. No degradation may occur with small amounts of organic bases. Commercially caustic soda is probably the most widely employed catalyst and the cellulose is usually converted into alkali cellulose in a conventional manner. The concentration of caustic soda solution quoted for the conversion varies greatly from source to source and so does the alkali cellulose aging time and temperature, providing any aging is done at all. These variables greatly effect the solubility, viscosity (30, 117, 126, 127, 128, 129, 150), and solution stability (143) of the final products. A caustic soda solution of approximately 30 percent is regarded as best for preparing alkali cellulose when low substituted, alkali-soluble, hydroxyethyl ethers are sought (126, 127, 128, 129, 150). If the mercerizing solution is more dilute, excessive side reactions leading to the formation of ethylene glycol diethylene glycol, 1,4 dioxane, and other polyethylene glycols result (116, 121, 124, 125, 126, 127, 128, 129). If the caustic soda solution is more than 30 percent, the reaction is retarded. The alkali cellulose is placed in a rotating autoclave and 11 to 20 percent by weight of ethylene oxide, based on the original cellulose, either in the liquid or gaseous state is admitted, usually after the autoclave has been evacuated. After a reaction period varying from one-half to two hours, a product is obtained that is soluble in 5 to 15 percent sodium hydroxide. The reaction is quite exothermic and in order to carry it out, preferably around 45° to 60°, it may be necessary to employ external cooling (126, 127, 128, 129). Other catalysts such as sodium chloride, potassium acetate or pyridinium hydrohalides may replace the caustic soda (121, 124). In this event the reaction is slower, less heat is liberated per unit time, and thermal control is easier. The autoclave may be operated either above or below atmospheric pressure and the ethylene oxide is usually admitted at a rate only slightly above that at which it reacts. Heat may or may not be employed depending on the other reaction conditions, such as pressure, amount of oxide employed, and upon the degree of substitution desired. The etherification may be carried out in the presence of inert solvents such as 1,4 dioxane, acetone or benzol (121, 142) which may improve the uniformity of the product, but which usually diminish the reaction rate.

The maximum solubility of these alkali-soluble ethers is usually attained in 10 percent sodium hydroxide. If less than 11 percent ethylene oxide, based on the starting cellulose, is employed during the etherification, then the product is less soluble in dilute alkali and it may be necessary to chill the mixture at temperatures below 0° to attain clear, filterable solutions (126, 127, 128, 129). Alternatively, the dried cellulose ethers may be heated to temperatures in the neighborhood of 100° to 120° for periods between three and one-half to twenty-four hours (149), or they may be treated with mineral acid (149). Presumably, both of these treatments increase the solubility by promoting some type of undetermined chemical degradation. As a rule, these alkali-soluble hydroxyethyl cellulose ethers are said to contain substantially less than one hydroxyethyl group per glucose unit (126, 127, 128, 129, 132). Many times it is stated that the best derivatives contain 0.5

hydroxyethyl groups per glucose unit.

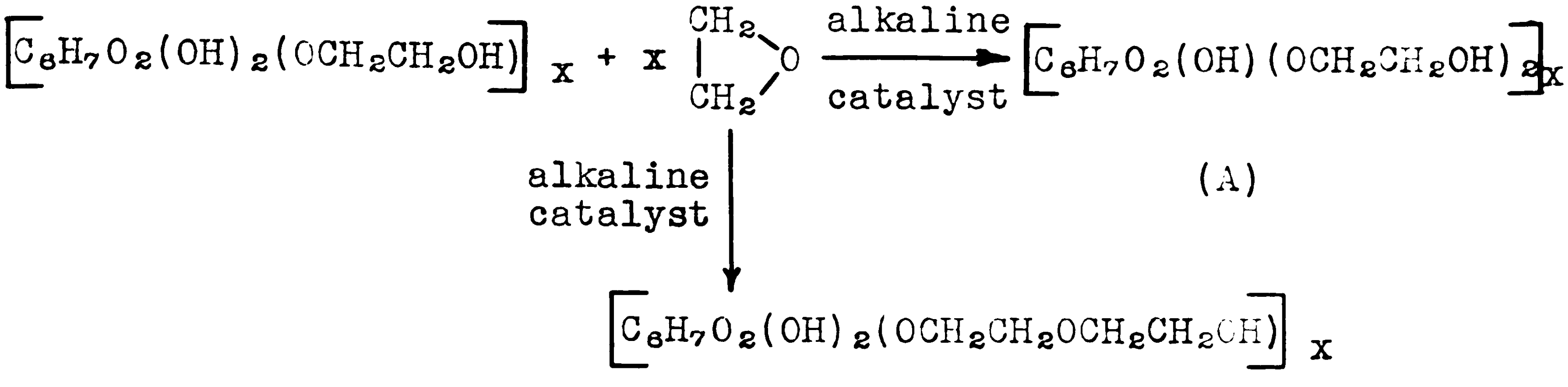
The water-soluble hydroxyethyl ethers are prepared in the same general manner as the alkali soluble types (126, 127, 128, 129). In these cases however, the alkali cellulose is first aged (133), treated by heat (148) or is prepared from a pretreated, degraded cellulose (146). Larger amounts of ethylene oxide, up to 85 percent of the dry weight of the cellulose, are employed (30) and the reaction is carried out under pressure and external heat (133). Water-soluble ethers in most instances are claimed to have an average degree of substitution greater than one (125, 133, 140). As the substitution increases from one to three, the water solubility increases and the products become increasingly soluble in organic solvents (140). Such products are easily obtained by heating regenerated cellulose with excess ethylene oxide at 100° under pressure (126, 127, 128, 129), no alkali or other catalyst being required under these conditions.

The condensation of cellulose with ethylene oxide may be represented as follows:



$$\left[C_6H_7O_2(OH)_3\right]_x + x \begin{matrix}CH_2\\ |\\ CH_2\end{matrix}\!>O \xrightarrow[\text{catalyst}]{\text{alkaline}} \left[C_6H_7O_2(OH)_2(OCH_2CH_2OH)\right]_x$$

Any subsequent condensation may occur either at the remaining hydroxyl groups of the cellulose, or at the newly formed hydroxyethyl groups (Condensations A and B).



$$[C_6H_7O_2(OH)_2(OCH_2CH_2OH)]_x + x\,(CH_2CH_2O) \xrightarrow[\text{catalyst}]{\text{alkaline}} [C_6H_7O_2(OH)(OCH_2CH_2OH)_2]_x \quad \text{(A)}$$

$$[C_6H_7O_2(OH)_2(OCH_2CH_2OH)]_x + x\,(CH_2CH_2O) \xrightarrow[\text{catalyst}]{\text{alkaline}} [C_6H_7O_2(OH)_2(OCH_2CH_2OCH_2CH_2OH)]_x \quad \text{(B)}$$

(A)

(B)

To date there has been no means of determining which of the condensations (A or B) actually occurs, or whether both courses are followed simultaneously. The reaction with ethylene oxide should, in the gaseous state at least, be microheterogeneous or quasihomogeneous in nature, for ethylene oxide is a small molecule (117). This consideration leads to the unproven inference that the hydroxyethyl groups would be uniformly distributed through the mass of the cellulose and that the condensation would be mostly of the type A, at least at low substitutions. Condensations employing liquid ethylene chlorohydrin are no doubt of a macroheterogeneous nature (117) and high local substitutions in the cellulose would perhaps favor products with a higher content of type B.

Condensations of cellulose with ethylene chlorohydrin (126, 127, 128, 129, 134, 135) have been carried out in the same general fashion as those employing ethylene oxide, but with the difference that alkali is required to neutralize the by-product hydrochloric acid as well as to act as a catalyst. The use of alkali in the chlorohydrin condensation is thus imperative rather than optional. Ethylene chlorohydrin generally reacts more slowly and in a less exothermic way than ethylene oxide. When, for example, mercerizing liquor of 30 percent is called for in an ethylene oxide process, 40 percent is required in a parallel process employing the chlorohydrin. Anhydrous ethylene chlorohydrin yields better results than its azeotrope with water. When other conditions are similar, the resulting hydroxyethyl celluloses are usually similar in physical and chemical properties to those prepared from ethylene oxide (126, 127, 128, 129). Both low substituted, alkali-soluble, and higher substituted, water and organo soluble derivatives have been prepared from chlorohydrin (148). Consideration of the equation for the initial reaction of the chlorohydrin with cellulose,

$$\left[C_6H_7O_2(OH)_3\right]_x + x\ ClCH_2CH_2OH + x\ NaOH \xrightarrow[\text{alkali}]{\text{excess}}$$

$$\left[C_6H_7O_2(OH)_2(OCH_2CH_2OH)\right]_x + x\ NaCl + x\ H_2O$$

shows that subsequent condensation may proceed along either or both of the two paths (A) and (B) already suggested for the ethylene oxide reaction. The side reactions are also of the same general character (116, 121, 124, 125, 126, 127, 128, 129).

The alkali-soluble, water insoluble hydroxyethyl ethers may be purified by precipitation from alkaline solutions by adding dilute acid and then thoroughly washing the precipitated products with water (126, 127, 128, 129). Water-soluble ethers, depending upon their average degree of substitution, are purified in different ways. If the ether is water soluble but insoluble in organic solvents, it may be precipitated by pouring the aqueous solution into a large volume of acetone or alcohol (126, 127, 128, 129, 133). If soluble in water, various organic solvents and aqueous alcohol, purification must be by dialysis or electrodialysis (146). The water-soluble hydroxyethyl ethers, in contrast to some of the water-soluble methyl or ethyl cellulose ethers, are soluble in hot as well as in cold water. The alkali-soluble ethers may be converted into films, threads, and other shaped objects by coagulating their alkaline solutions in an acid bath of the same type employed in the viscose process (135, 142). Lilienfeld (135) has enumerated several reasons why the manufacture of films and filaments by his alkali-soluble hydroxyethyl cellulose is superior to the viscose process. The ethers are stable both in the dry state and in alkaline solution, and may be transported or stored in either condition. They are very uniform and their alkaline solutions are colorless, odorless and free from impurities or by-products which would contaminate the coagulating baths. When coagulation is carried out, no sulfur separates out of solution into the films, thus no bleaching operation is required. Finally there are no noxious, poisonous gases evolved in the coagulation process.

Richter (143) and others (126, 127, 128, 129), however, have noticed that some of the alkali-soluble hydroxyethyl ethers form unstable solutions which gel on standing. The instability of such solutions is associated with a number of manufacturing variables such as type of cellulose employed, pretreatment of the cellulose, method of preparing the alkali cellulose and the conditions of etherification (143). Any change brought about in these variables which tends to cause degradation of the cellulose results in derivatives which have higher solution stabilities. Richter further records that mixtures of hydroxyethyl ethers give solutions with the physical stability characteristic of the highest stability component.

The hydroxyethyl ethers of cellulose are found to be chemically more reactive, in general, than cellulose itself. A number of derivatives have been prepared but there is nothing of importance on record as to their properties or characterization (30, 131). Benzoyl chloride in the presence of aqueous alkali yields a hydroxyethyl ether benzoate (116, 126, 127, 128, 129, 142), which is said to be similar to the product obtained by partly esterifying cellulose with benzoyl chloride and then etherifying the product with ethylene oxide or chlorohydrin. The mixed ester ethers might be employed for films and filaments. The stearate and xanthate esters have been mentioned (131, 142). Shorigin and Rymashewskaja (133) describe the preparation of the triacetate of a water soluble hydroxyethyl cellulose by the acetic acid, acetic anhydride, sulfuric acid method. Schorger and Shoemaker (142) and also Sönnerskog (151, 152) make mixed ethers by using ethylene oxide and either methyl or ethyl chloride. These etherifying agents are employed either separately or simultaneously in the presence of aqueous alkali with about the same end results, insofar as the properties of the products are concerned. Since no reliable method of analysis was available, Sönnerskog (151) could not correlate properties accurately with degree or uniformity of substitution. Dreyfus (134) notes that a decomposition occurs when hydroxyethyl ethers are treated with concentrated hydrohalogen acids, phosphorous iodide and water, or dilute hydrohalogen acids under pressure. The decompositions yield ethylene glycol or its derivatives.

As already discussed in Part I of this thesis, no reliable method for analyzing hydroxyethyl type compounds, including hydroxyethyl ethers of cellulose, was known until 1946 (5, 151), when Morgan (5) analyzed several hydroxyethyl cellulose ethers, probably for the first time with some degree of certainty. Although Morgan's modified Zeisel method still remains to be checked by independent means for the cellulose ethers, it appears to be very reliable for simple compounds of similar structure. Earlier estimations (5, 30, 116) employed the ordinary alkoxyl determination together with other methods which likewise are of questionable value. Nikitin and Rudneva (116) attempted to obtain the average degree of substitution by using ordinary elemental analysis for carbon and hydrogen content. This method is not reliable, for appreciable increments in the average degree of substitution result in changes in the percent carbon and hydrogen which lie well within the analytical error. The fact that the hydroxyethyl substitution obtained by the erroneous Zeisel method was supported by the carbon and hydrogen values also discredits the precision of elemental analysis as an analytical tool. Neither of these methods seems to be better than a calculation of hydroxyethyl substitution from the gain in weight which occurs during the etherification. Davis (30) proposed a wet combustion method, employing concentrated chromic acid, for determining the substitution, but it is difficult to see what the advantage of this method over ordinary elemental analysis would be.

Shorigin and Rymashewskaja (133) also employed iodine numbers to estimate the extent to which hydroxyethyl cellulose ethers and their derivatives have been degraded, although they found in their work on the glycerol ethers of cellulose (140, 141) that the iodine number was not reliable, since glycerol itself exhibited an appreciable iodine number (141). It was believed that the glycerol ether groups in the cellulose derivatives were being oxidized by iodine in the presence of alkali.

Although the number of hydroxyethyl groups in a cellulose ether can now be estimated with some confidence by Morgan's method (5), the task of determining the position and uniformity of the substitution still remains. There is also the problem of determining whether or not condensation of ethylene oxide occurs on a hydroxyethyl group giving polyethylene glycol side chains (mechanism B) instead of only simple hydroxyethyl groups (mechanism A). It seems that the former might well occur, for Davis (30) has reported derivatives containing from 3 to 6 ethylene oxide units, and Morgan (5), derivatives containing up to 4 groups per glucose residue.

In an attempt to answer the above questions for a commercial alkali-soluble hydroxyethyl cellulose ether, it was decided to apply the tosylation-iodination technique developed by Purves and his coworkers for cellulose acetates (2, 4, 153) and for the methyl and ethyl ethers of cellulose (3). Oldham and Rutherford, working with sugar derivatives (1), established the fact that tosyl groups in the number six or primary hydroxyl position were quantitatively replaced by iodine when the esters were heated with excess sodium iodide in acetone solution. Tosyl groups occupying the positions of the secondary hydroxyl groups were in contrast not affected. Irvine and Rutherford (154) and Oldham (155) likewise found that in nitrated sugar derivatives the nitrate group in the sixth position was quantitatively replaced by iodine under the same conditions. Murray and Purves (156) then demonstrated that the same reaction applied to cellulose nitrate. Tosyl groups in the primary positions could also be replaced by chlorine, the reagent necessary for this substitution being pyridine hydrochloride in pyridine solution at 100° (157).

Purves and his collaborators (2, 4, 153) condensed technical cellulose acetates (average substitution 2.44 acetyl and 0.56 hydroxyl groups per glucose unit) in a dilute pyridine solution with a large excess of tosyl chloride.

The reaction was homogeneous in nature. At various time intervals portions were removed from the reaction mixture and the tosylated samples were isolated, purified, and analyzed for sulfur content. A rate plot of tosyl content versus reaction time was constructed. During the first three hours a very rapid reaction took place, then the rate diminished markedly. By extrapolating this rate curve back to zero time after a nearly flat portion of the curve was reached, it was possible to estimate the number of free hydroxyl groups involved in the initial rapid tosylation. This number checked the number of primary hydroxyl groups found by applying the iodination or the chlorination reaction to samples removed after the initial rapid tosylation had ceased. The free hydroxyl groups present in the second and third positions of the cellulose acetate were found by difference between the total hydroxyl groups (0.56 moles per glucose unit) and those on the number six position (0.20 moles). Gardner and Purves (4) by a kinetic analysis of the later portions of the tosylation rate curve, were able to differentiate quantitatively between the free hydroxyls available in the number two and number three secondary positions. This advance was possible because these two positions were tosylated at very different rates. The mode of substitution, random or bunched, on the secondary positions (153) was determined by lead tetraacetate oxidation, since one mole of oxidant was consumed every time an unsubstituted 2,3 glycol unit existed in a glucose residue. During the tosylation no loss or wandering of the acetate groups occurred, but the pyridine hydrochloride formed as a by-product very slowly replaced tosyl groups by chlorine. This reaction became appreciable after tosylation had proceeded for about a week at 20°.

The same general technique was employed by Mahoney and Purves (3) for studying the methyl and ethyl ethers of cellulose. However, periodate oxidation was used to determine the uniformity of substitution on the two secondary hydroxyl positions. No loss in alkoxyl groups was noted and the chlorination side reaction did not become evident until a number of weeks of tosylation had elapsed. In studying some of the water and dilute alkali soluble ethers, heterogeneous reaction mixtures were encountered so no attempt was made to use a kinetic approach to distinguish free hydroxyls in the two secondary positions. It was nevertheless possible to determine the free primary and the combined free secondary hydroxyl groups. In one case, the tosylation reaction was carried out in a highly swollen, apparently homogeneous gel system and appeared to proceed in a normal fashion. The usual kinetic approach was applied with success to obtain the number of unsubstituted hydroxyl groups in the two secondary positions and the reaction rates were in the same relative order as those observed for tosylation in homogeneous solution.

The following experiments explore the application of the tosylation-iodination and tosylation-chlorination methods to a technical, alkali-soluble hydroxyethyl cellulose.

EXPERIMENTAL

I. Materials and Reagents

Various samples of commercial hydroxyethyl cellulose ethers were available for this investigation: Ceglin (H), Ceglin (E.S. type H.), Ceglin (17443-B), Cellosize (W.S. 100) and Cellosize (W.S. 1000). The Ceglins were contributed by the Sylvania Industrial Corporation, now the Sylvania Division of the American Viscose Corporation, and the Cellosizes by the Carbide and Carbon Chemical Corporation. The ethers were passed through a laboratory Wiley mill and were reduced to particles which passed a 60 mesh sieve. The air-dry samples were stored in tightly stoppered bottles and moisture contents were obtained when desired as the percentage loss in weight occasioned by heating at 105°-110° for two hours.

All reagents employed were invariably purified as described in Part I, since cellulose derivatives frequently contaminate themselves by an avid absorption of any accessible impurities.

II. Methods of Analysis

Sulfur and Halogen Determinations

The sulfur and halogen determinations were all carried out by the Carius combustion method (73b, 73c).

It was found during the course of the analytical work (Parts I and II) that the amount of nitric acid employed for the 20 mg. to 30 mg. samples was of critical importance. When 0.5 cc. or less of nitric acid was used no explosions of bomb tubes resulted, and over 90 consecutive analyses were carried out without incident. Whenever the amount of acid was over 0.5 cc., explosion of the combustion tubes resulted in nearly every case.

Determination of Hydroxyethyl Content

Morgan's modified alkoxyl estimation (5) was employed; each estimation required 20 cc. of freshly distilled constant boiling hydriodic acid (sp. gr. 1.70; b.p. 126°-127°), and sample weights as large as 0.20 g. to 0.40 g., since hydroxyethyl contents were always low. The number of ethylene oxide units per glucose unit were calculated employing the following equation where (x) is the number of groups.

$$\%(OCH_2CH_2) = \frac{4404(x)}{162.14 + 44.04(x)}$$

Table XXII illustrates the results for three hydroxyethyl celluloses.

III. Examination of the Hydroxyethyl Cellulose Ethers for Peroxide Oxygen

The various hydroxyethyl ethers were examined in

TABLE XXII

ETHYLENE OXIDE CONTENT AND AVERAGE DEGREE OF SUBSTITUTION FOR THREE HYDROXYETHYL CELLULOSE ETHERS

Sample	Solubility type	%(OCH_2CH_2)	Average number of ethylene oxide groups per glucose residue
Ceglin (H)	alkali-soluble	6.17	0.242
		5.54	0.216
Ceglin (E.S. type H)	alkali-soluble	10.58	0.435
		10.93	0.451
Cellosize (W.S. 100)	water-soluble	28.12	1.439
		28.27	1.451

a qualitative way by the method of Liebhafsky and Sharkey (77) which was described in Part I. One gram of dry Cellosize (W.S. 100) and 1 g. of sodium bicarbonate were placed in a 125 cc. glass stoppered Erlenmeyer flask, then 25 cc. of pure glacial acetic acid was added, followed by 1 cc. of potassium iodide solution (0.4 g. KI/cc.). After washing down the sides with 5 cc. of distilled water, the flask was loosely stoppered and kept in the dark for five minutes, together with a reagent blank. No iodine was liberated by the presence of the Cellosize, not even the minute amount found in the reagent blank, which indicated no peroxide type oxygen. Samples of Cellosize (W.S. 1000), Ceglin (H), Ceglin (17443-B) and Ceglin (E.S. type H.) were also investigated, but no peroxide oxygen was indicated in any case. Both the water-soluble Cellosizes were soluble in the reaction mixture, but the Ceglins were not.

Samples were then treated in an acidified (dil. H_2SO_4) aqueous media with ferrous and thiocyanate ions (88, 158); no peroxide oxygen was indicated by the lack of the usual red coloration caused by ferric ion. The qualitative benzidine test (159), using a saturated aqueous solution of benzidine and a 10 percent aqueous solution of copper sulfate was also tried, but no peroxide type oxygen could be detected.

IV. Iodine Consumption by Hydroxyethyl Cellulose Ethers in Alkaline Hypoiodite Solutions

In two sets of experiments a high alpha cellulose wood pulp and Ceglin (H) (containing 0.23 moles of ethylene oxide groups/glucose unit) were immersed in alkaline hypoiodite as described by Harris and his coworkers (160, 161) for the estimation of reducing groups in hydro- and oxycelluloses. Accurately weighed samples, approximate to 1 g. over dry, were placed in 125 cc. glass stoppered Erlenmeyer flasks, then 10 cc. of a 0.05 M sodium borate buffer (pH 9.2 at 25°) and 20 cc. of an approximately 0.03 M iodine solution (0.02 g. KI/cc.) were added; the flask was tightly stoppered and placed in a constant temperature bath at 25.5°±0.1° for six hours. At the end of this time the mixtures were acidified with 10 cc. of 0.1 N hydrochloric acid and the available iodine was immediately titrated with 0.01293 N sodium thiosulfate, using starch solution as indicator. The difference between these titrations and the titration required by a reagent blank gave the amounts of 0.01293 N iodine consumed in six hours. The sample was then quantitatively recovered on a Büchner funnel, washed thoroughly with water to remove all traces of reagents, dried by solvent exchange through dry ethanol and ether, and finally dried until all traces of ethanol and ether had disappeared. Second treatments were then carried out as already described on the recovered samples and the amount of iodine consumed at the end of twelve hours was taken as the sum of the consumptions found for the first and second six hour treatments. Proceeding in this way, the iodine consumptions were determined for times of six, twelve, eighteen and twenty-four hours. The results are given in Table XXIII. The iodine number (cc. of 0.1 N iodine consumed per gram sample was then calculated as follows:

$$\frac{\text{cc. of iodine consumed by sample} \times 0.01293}{0.1 \times \text{sample weight}} = \text{iodine number}$$

The results are listed in Table XXIV.

In two further series of investigations, the water-soluble Cellosize (W.S. 100) (containing 1.45 moles of ethylene oxide/glucose unit) and highly purified Cellosolve (see Part I) were examined for their action toward alkaline hypoiodite. Accurately weighed samples (approx. 1 g. for Cellosize and 0.18 g. for Cellosolve) were transferred to 200 cc. volumetric flasks and 60 cc. of 0.05 M sodium borate buffer and 120 cc. of 0.03 M iodine solution were accurately added from a buret. The final volume was made up to the mark with distilled water. The flasks containing the Cellosize samples were shaken for a few minutes until solution was complete, and then were immersed together with the Cellosolve solutions in a bath regulated

TABLE XXIII

CONSUMPTION OF IODINE FROM ALKALINE HYPOIODITE SOLUTION BY HIGH ALPHA CELLULOSE WOOD PULP AND CEGLIN (H)

	Cc. of 0.01293 N Iodine consumed per sample			
Reaction time in hours	High Alpha Cellulose Wood Pulp		Ceglin (H)	
	(1) 1.2301 g.	(2) 0.9792 g.	(1) 1.1719 g.	(2) 1.0481 g.
6	5.25	4.30	5.85	5.40
12	9.45	7.60	11.45	11.05
18	11.90	9.55	16.80	16.90
24	13.70	10.80	20.70	21.40

TABLE XXIV

(see Fig. 9)

VARIATION IN IODINE NUMBERS OF HIGH ALPHA CELLULOSE WOOD PULP AND CEGLIN (H) WITH TIME

Reaction time in hours	Iodine Number					
	High Alpha Cellulose Wood Pulp			Ceglin H		
	(1)	(2)	(Av.)	(1)	(2)	(Av.)
6	0.55	0.57	0.56	0.65	0.67	0.66
12	0.99	1.00	1.00	1.26	1.36	1.31
18	1.25	1.26	1.26	1.86	2.08	1.97
24	1.44	1.43	1.44	2.28	2.64	2.46

at 25.5°±0.1°. At various time intervals 10 cc. portions of the reaction mixtures were pipetted into a flask containing 15 cc. of water and 5 cc. of 0.1 N hydrochloric acid. The iodine was immediately titrated with 0.01293 N sodium thiosulfate, with the results given in Table XXV. The iodine number was then calculated as

$$\frac{200\text{x}0.01293\text{x}(\text{cc. of thio./10 cc. blank - cc. of thio./10 cc. unknown})}{\text{Sample weight}}$$

and the results are shown in Table XXVI.

V. Tosylation of Alkali-soluble Ceglin (E.S. Type H)

Preparation of Tosyl Esters Requiring Twenty-One Hours or more Reaction Time

Ceglin (E.S. type H.), 14.88 g. air-dry or 14.0 g. oven-dry (0.077 moles containing 0.231 moles of free hydroxyl groups), was dissolved in 350 g. of a 5 percent (by wt.) sodium hydroxide solution with stirring under a nitrogen atmosphere at 10°. The Ceglin was reprecipitated in ribbons and pellets of highly swollen gel by pouring the alkali solution into 1.5 liters of aqueous acetic acid (50-50 by volume) with gentle stirring. After coagulation had taken place the mass was stirred vigorously by mechanical means for twenty minutes. The highly swollen gel particles and acidic supernatent liquors were poured into an 8" x 10" muslin bag which had been laundered many times.

TABLE XXV

CONSUMPTION OF IODINE FROM AN ALKALINE HYPOIODITE SOLUTION BY CELLOSIZE (W.S. 100) AND CELLOSOLVE

Reaction time in hours	Cc. of 0.01293 N thiosulfate required per 10 cc. alliquot of alkaline hypoiodite solution				
	Reagent Blank	Cellosize (W.S. 100)		Cellosolve	
		(1) 0.9448 g.	(2) 0.9498 g.	(1) 0.1819 g.	(2) 0.1810 g.
6	13.90	13.20	13.15	13.80	13.90
20	13.83	12.10	12.10	13.50	13.60
26	13.80	11.80	11.75	13.45	13.50
44	13.70	10.80	10.75	13.10	13.15

TABLE XXVI

(see Fig. 9)

VARIATION IN IODINE NUMBERS OF CELLOSIZE (W.S. 100) AND CELLOSOLVE WITH TIME

Reaction Time in hours	Iodine Number					
	Cellosize (W.S. 100)			Cellosolve		
	(1)	(2)	(Av.)	(1)	(2)	(Av.)
6	1.92	2.04	1.98	1.42	-	1.42
20	4.65	4.63	4.64	3.56	4.63	3.91
26	5.46	5.56	5.51	4.28	4.63	4.46
44	7.48	7.61	7.55	7.84	8.17	8.00

The gel retained in this bag was washed with distilled water until the effluent had the same pH as the water used (pH, 5.7), and, after being drained as free of water as possible, was transferred carefully to a 2 liter round bottom flask. The weights of the dry bag before and after use showed that it had retained no significant amount of gel. While in the flask, the gel was solvent exchanged into dry pyridine, using vacuum distillation and continuous addition of fresh dry pyridine. To follow the removal of the water, 1 cc. of the pyridine distillate was added at intervals to 1 cc. of dry petroleum ether (b.p. 30°-50°) and the gradual decrease in the formation of two layers was observed. When they no longer formed, the refractive index of the pyridine distillate was checked until that of pure, dry pyridine, n_D^{20}, 1.5090, was obtained, then the distillation was stopped. The vacuum was regulated during the distillation, so that the heating bath temperature never exceeded 60°. The Ceglin-dry pyridine gel particles were cooled to 5° and 274.1 g. (1.44 moles) of tosyl chloride, dissolved in enough additional chilled pyridine to give a total weight of pyridine of 1540 g. (19.46 moles), was added to them. The reaction flask was tightly stoppered, set in a constant temperature bath at 25°±0.1° and periodically was shaken vigorously by hand. After twenty-one and one-half hours, when the system had passed through an intermediate homogeneous to the second heterogeneous state, 100 cc. to 150 cc. samples were removed at various times after shaking the mixture to ensure uniformity. The esters were isolated by pouring the samples slowly into 1.5 liters of rapidly stirred distilled water which was cooled to 5°-10°. A further 500 cc. of distilled water, some of which was used to wash the sampling beaker, was added to the precipitation vessel. After recovery on a sintered glass funnel, the esters were washed repeatedly with fresh distilled water, with stirring and filtration, until both the wash water and the products were free from chlorine ions and pyridine. The products were dried by solvent exchange through dry methanol and dry ether; final drying before analysis being carried out *in vacuo* (0.6 mm.) over phosphorous pentoxide for at least two days at room temperature. Analyses of each ester are in Table XXVII.

Preparation of Tosyl Esters requiring less than Twenty-one Hours Reaction Time

The procedure employed in these cases were exactly as described above, with the exceptions that the reprecipitated Ceglin gels were washed and filtered on a sintered glass funnel, and that one-seventh of each of the reactants were employed, their relative concentrations being kept the same. Each tosylation required 2 g. (0.033 moles of free hydroxyl groups) of dry Ceglin, 39.5 g. (0.206 moles) of tosyl chloride and 220 g. (2.78 moles) of pyridine. The ester in each case was isolated by pouring the entire reaction mixture into 2.5 liters of rapidly stirred, cooled, distilled water and an additional 500 cc. of water was employed for washing the reaction flasks. The analysis of the products are in Table XXVII.

By employing the following set of three simultaneous equations, it was possible to calculate the average number of chlorine (x), tosyl (y) and ethylene oxide (z) groups per glucose unit in those esters that were completely analyzed (Table XXVII).

$$\% \text{ Cl} = \frac{3550x}{162.14 + 18.5x + 154\,y + 44.04z}$$

$$\% \text{ S} = \frac{3206y}{162.14 + 18.5x + 154y + 44.04z}$$

$$\% \ (\text{OCH}_2\text{CH}_2) = \frac{4404z}{162.14 + 18.5x + 154y + 44.04z}$$

The gradual loss of ethylene oxide groups as tosylation proceeded was plotted against two different time scales in Fig. 8, and from the curves the number (z) of ethylene oxide groups in the other intermediate esters was estimated. This information gave the value for (z) in the first two of the above equations, and the corresponding degree of chlorine and tosyl substitution was then easily obtained (Table XXVIII).

TABLE XXVII

ANALYSIS OF TOSYL ESTERS OF CEGLIN (E.S. TYPE H) FOR SULFUR, CHLORINE AND ETHYLENE OXIDE

Ester Sample	Reaction Time	% S	Aver.	% Cl	Aver.	$\%\ OCH_2CH_2$	Aver.
Unreacted Ceglin	Hours 0	0		0		10.58 10.93	10.76
M	1	9.16 9.06 9.42	9.21	Trace		-	-
N	3	10.66 10.65 10.72	10.68	0.146 0.137	0.142	-	-
O	5	10.87 10.98 10.86	10.90	0.136 0.100	0.112	4.24 4.25 4.05	4.18
P	7	10.92 10.88 10.93	10.92	0.302 0.225 0.252	0.259	-	-
Q	9	11.00 10.89 11.16	11.02	0.333 0.382 0.263	0.326	-	-
R	12	10.95 10.95	10.95	0.448 0.470 0.378	0.432	-	-
A	21.5	11.80 11.67 11.56	11.68	0.706 0.744 0.638	0.696	3.05 3.07 2.68	2.93
B	Days 2	11.76 11.80 12.26	11.94	1.158 1.156 1.118	1.143	1.98 2.00 2.03	2.00
C	3	11.98 11.92 11.94	11.95	1.378 1.375 1.380	1.377	-	-
D	5	11.99 12.06 12.01	12.02	1.807 1.845	1.826	-	-
E	8	12.31 12.03	12.17	2.379 2.413 2.340	2.377	-	-
F	12	11.92 11.90 11.82	11.88	2.873 2.870	2.872	-	-
G	20	11.90 11.82 11.79	11.84	3.659 3.717 3.584	3.653	1.54 1.56 1.60	1.57
H	40	11.60 11.68	11.64	4.546 4.497	4.522	1.35 1.50 1.62	1.49

TABLE XXVIII

(See fig. 8, 10, and 11)

THE AVERAGE DEGREES OF SUBSTITUTION OF VARIOUS TOSYL ESTERS OF CEGLIN (E.S. TYPE H)

Ester Sample	Reaction time	Average Substitution of Groups per Glucose unit		
		OCH_2CH_2 (z)	Tosyl (y)	Chlorine (x)
Unreacted	Ceglin	0.443	-	-
	Hours			
M	1	.425(a)	0.93	-
N	3	.390(a)	1.228	0.010
O	5	.362	1.278	.011
P	7	.345(a)	1.274	.029
Q	9	.332(a)	1.297	.039
R	12	.320(a)	1.279	.044
A	21.5	.279	1.466	.071
	Days			
B	2	.184	1.516	.130
C	3	.165(a)	1.510	.158
D	5	.155(a)	1.535	.210
E	8	.152(a)	1.515	.274
F	12	.150(a)	1.511	.323
G	20	.146	1.508	.420
H	40	.137	1.470	.494

(a) Values interpolated from Fig. 8.

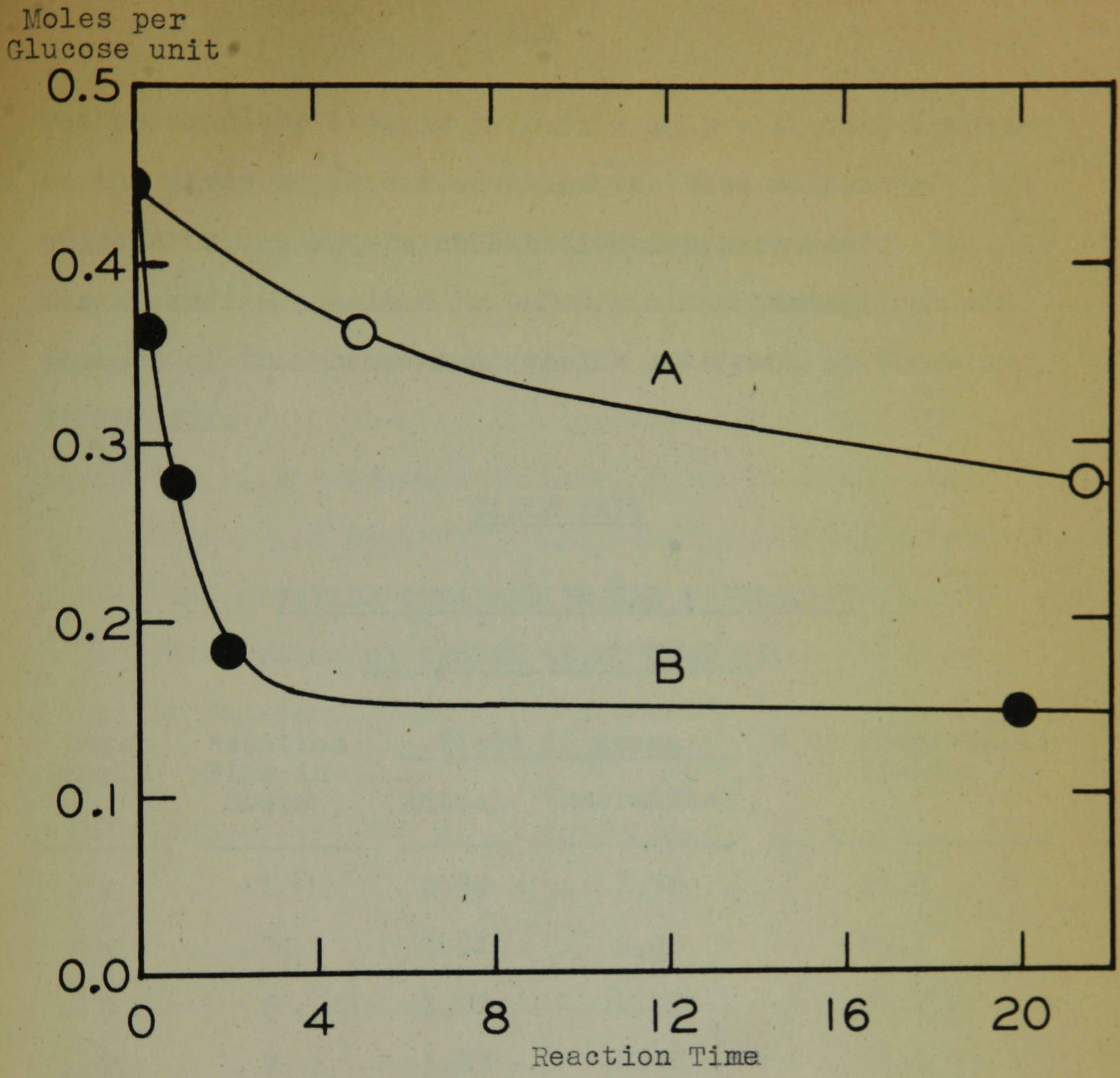


Fig. 8 (See Table XXVIII) Change in Ceglin Tosyl Ester Ethylene Oxide Content with Tosylation Time.

Plot A ○ Time in hours.
Plot B ● Time in days.

The denominator (162.14 + 18.5x + 154y + 44.04z) common to the three equations equalled the base molecular weights of the esters as substitution proceeded. It was therefore possible to calculate the theoretical and percent of the theoretical yields obtained, as shown in Table XXIX.

TABLE XXIX

YIELDS OBTAINED IN THE TOSYLATION OF CEGLIN (E.S. TYPE H)

Ester Sample	Reaction Time in Hours	Yield in grams		% of Theoretical Yield
		Actual	Theoretical	
M	1	3.39	3.56	95.3
N	3	3.81	4.06	94.1
O	5	3.78	4.12	91.7
P	7	3.83	4.06	94.4
Q	9	3.82	4.14	92.3
R	12	3.91	4.11	95.1

VI. Chlorination of Ceglin and its Tosyl Esters, B, P. and G (2).

A. To a 100 cc. flask containing 60 cc. of dry, purified pyridine in which 2 g. (0.055 moles) of dry hydrogen chloride had been dissolved, 2 g. (0.011 moles) of dry

Ceglin (E.S. Type H) containing 0.443 ethylene oxide groups per glucose unit was added. The Ceglin did not dissolve but became swollen. The mixture was warmed under anhydrous conditions at 85° for four hours; no significant coloration occurred. Isolation of the product was accomplished by pouring the mixture into 600 cc. of cold distilled water, collecting the highly swollen precipitate on a sintered glass funnel, washing with water until free from chlorine ions and pyridine, and then drying by solvent exchange through dry methanol and dry ether. Final drying before analysis was accomplished in a vacuum dessicator (0.6 mm. pressure) over phosphorous pentoxide for at least two days at room temperature.

Anal. Calcd. for 0.443 groups: (OCH_2CH_2), 10.75;
Found: (OCH_2CH_2), 10.69, 10.77%.
Chlorination in the standard conditions used had therefore displaced no ethylene oxide groups from Ceglin.

B. A sample, 0.94 g. (0.0023 moles) of Ceglin tosyl ester B dissolved in 20 cc. of dry pyridine was mixed with 1.5 g. (0.0411 moles) of dry hydrogen chloride dissolved in 30 cc. of dry pyridine. The ester precipitated as the pyridine hydrochloride solution was added. After heating as before at 85° for four hours, during which no significant color developed, the mixture was poured into 600 cc. of cold distilled water to precipitate the product as a solid ball.

When a solution of this crude product, in 100 cc. of dry pyridine and 5 cc. of water, however, was poured into a large bulk of distilled water for reprecipitation and purification, no precipitation resulted and the mixture remained homogeneous. The pyridine present was neutralized with dilute sulfuric acid (10 percent by wt.) and some translucent gel formed, but when washed and isolated in a dark, hard, horny state it weighed less than 0.1 g. No yields or analytical data could be obtained on this apparently water soluble product.

C. The Ceglin tosyl ester P was chlorinated as in the previous case, employing 1.2 g. (0.0032 moles) of the ester. This ester was not initially soluble in pyridine as ester B was, but formed a highly viscous, ropy transparent gel. After reaction, the mixture was poured into 200 cc. of dry, redistilled petroleum ether (b.p. 30°-50°). The product together with excess pyridine hydrochloride was recovered as a filter cake which was washed with cold water to remove the excess pyridine hydrochloride. Very highly swollen transparent gel particles resulted which had to be washed by gravity on an ordinary filter paper. Since water soluble organic solvents, such as the alcohols or acetone, caused further swelling and partial solution they were not used. After drying <u>in vacuo</u> over phosphorous pentoxide, the product was a hard, horny, grey material which had thoroughly impregnated and sized the filter paper which had sustained it. A total of 0.674 g. was obtained but no analytical work was attempted because of its unsatisfactory physical condition and its contamination with filter paper. By assuming a total of approximately 1.228 primary hydroxyl groups in the original Ceglin (E.S. Type H), the product from P would contain 0.345 ethylene oxide groups, 0.076 tosyl groups and 1.228 chlorine groups per glucose unit and the theoretical yield would be 0.678 g. On this basis approximately 100 percent of the theoretical yield was obtained.

D. When 1.2 g. (0.0029 moles) of the Ceglin tosyl ester G, which was initially soluble in pyridine, was heated with pyridine hydrochloride exactly as ester P had been, a product which was light tan color and granular was obtained with the same isolation technique. This product did not swell or dissolve in water or in the ordinary organic solvents even when they contained some water. The yield was 0.984 g.

Anal. Found: S, 9.30, 9.40; Cl, 8.51, 8.65; (OCH_2CH_2), 1.99, 1.74, 1.68%.

Based on these analysis the product contained 0.819 chlorine groups, 0.982 tosyl groups and 0.132 ethylene oxide groups per glucose unit, and the theoretical yield was 0.982 g. The actual yield was therefore 100 percent of the theoretical.

VII. Iodination of Ceglin Tosyl Ester N (156)

A 250 cc. flask containing 200 cc. of pure dry redistilled acetonyl acetone, 4 g. (0.0267 moles) of dry C.P. sodium iodide and 2.42 g. (0.0066 moles) of Ceglin tosyl ester N was heated at 115° to 120° for twelve hours. The ester was not completely soluble in the reaction mixture, which developed a deep-red color. The partially insoluble product and the supernatent liquid were poured into 1.8 liters of ice water with rapid stirring. The granular, slightly yellow precipitate was recovered on a sintered glass funnel and was repeatedly washed with water, then three times with deci-normal thiosulfate and finally with water until all traces of iodide ion, free iodine and acetonylacetone had been removed. The iodo derivative was dried in vacuo (0.6 mm.) over phosphorous pentoxide for two days at room temperature. Yield 1.84 g.

Anal. Found: S, 1.19, 1.15; I, 41.30, 41.40; (OCH_2CH_2), 5.43, 5.44, 5.29%.

Based on these analyses and neglecting the original trace of chlorine (0.14 percent), the product contained 0.996 iodine groups, 0.114 tosyl groups, and 0.373 ethylene oxide groups per glucose residue and the theoretical yield was 2.0 g. Actually 92 percent of the theory was isolated.

DISCUSSION OF EXPERIMENTAL RESULTS

I. Action of Alkaline Hypoiodite on Hydroxyethyl Cellulose

The three qualitative tests for peroxide oxygen, acetic acid-potassium iodide, ferrous and thiocyanate ions in dilute sulfuric acid, and the benzidine tests, all gave negative results when applied to several different hydroxyethyl celluloses. Therefore, at least when examined, there was no peroxide oxygen present in the samples. Since they had been stored one year in the laboratory and for an indeterminate period at the place of manufacture, prior to the tests, the negative results cannot be assumed to be necessarily valid for freshly prepared specimens, particularily when similar, simple hydroxyethyl structures readily form peroxides (see Discussion in Part I).

When carrying out the potassium iodide test for peroxides, it was noted that hydroxyethyl celluloseethers often failed to liberate even the minute amounts of iodine shown in the blanks. This observation suggested that any trace of iodine liberated by peroxide might have been immediately reduced by traces of aldehyde groups originating in the decomposition of peroxides previously present. The alkaline hypoiodite method of estimating aldehyde groups in celluloses (160, 161) was therefore applied to the hydroxycelluloses with the results summarized in Tables XXIV and XXVI and in Fig. 9. The reduction of alkaline hypoiodite by aldehyde groups in cellulosic material should be over in about six hours under the conditions used in the experimental work, any further consumption of oxidant being the result of side reactions (160, 161). It was found that the consumption continued rapidly after six hours in the case of Cellosize (W.S. 100) and Cellosolve, and more slowly in the case of Ceglin (H). Plots (A) and (B) (Fig. 9) were not exactly comparable to plots (C) and (D), because the former referred to one treatment in homogeneous systems while the latter were obtained in heterogeneous systems by repeated treatments with fresh full strength hypoiodite, however, despite this difference in reaction conditions, it was apparent that Ceglin (H), Cellosize (W.S. 100) and Cellosolve exhibit higher iodine numbers than the high alpha cellulose wood pulp, taken as an arbitrary standard, at six hours. Somewhat higher iodine numbers might be expected for the hydroxyethyl celluloses because the manufacturing methods usually employed in their preparation could cause degradation with the formation of a few aldehyde groups (30, 117, 126, 127, 128, 129, 150). Nevertheless, the long continued increase in plots (A) and (C) and their persistent divergence from plot (D), indicated that some other type of reaction was also proceeding. Plot (B) for pure Cellosolve showed definitely that the hydroxyethyl ether group in itself was unstable in some unknown manner to alkaline hypoiodite. It seemed justifiable then to infer that the hydroxyethyl groups in hydroxyethyl cellulose were unstable to alkaline hypoiodite. The fact that Cellosize (W.S. 100) (substitution 1.44) consumed much more iodine than Ceglin (H) (substitution 0.23) may be in part a result of the difference in hydroxyethyl content. Of course the difference may also be partially due to different reaction rates caused by the fact that the conditions were homogeneous in one case and heterogeneous in the other. Although the observations failed to decide whether or not traces of aldehyde groups were present in the hydroxyethyl celluloses, they were amply sufficient to discredit the use of the iodine number to assess the degradation incurred in their preparation (30, 117, 126, 127, 128, 129, 150). As already mentioned, the unreliability of the iodine number of glycerol ethers of cellulose was demonstrated by other workers (141).

II. Tosylation of Alkali-Soluble Ceglin (E.S. Type H)

The general pattern of the tosylation technique developed by Purves and his coworkers (2, 3, 4) for certain cellulose derivatives was employed for investigating Ceglin (E.S. type H). The material consisted of white flocks that were freely soluble to a viscous solution in cold caustic soda and were insoluble in water, which, however swelled them. They were also insoluble in dry pyridine and even after prolonged shaking the persistence of white cores

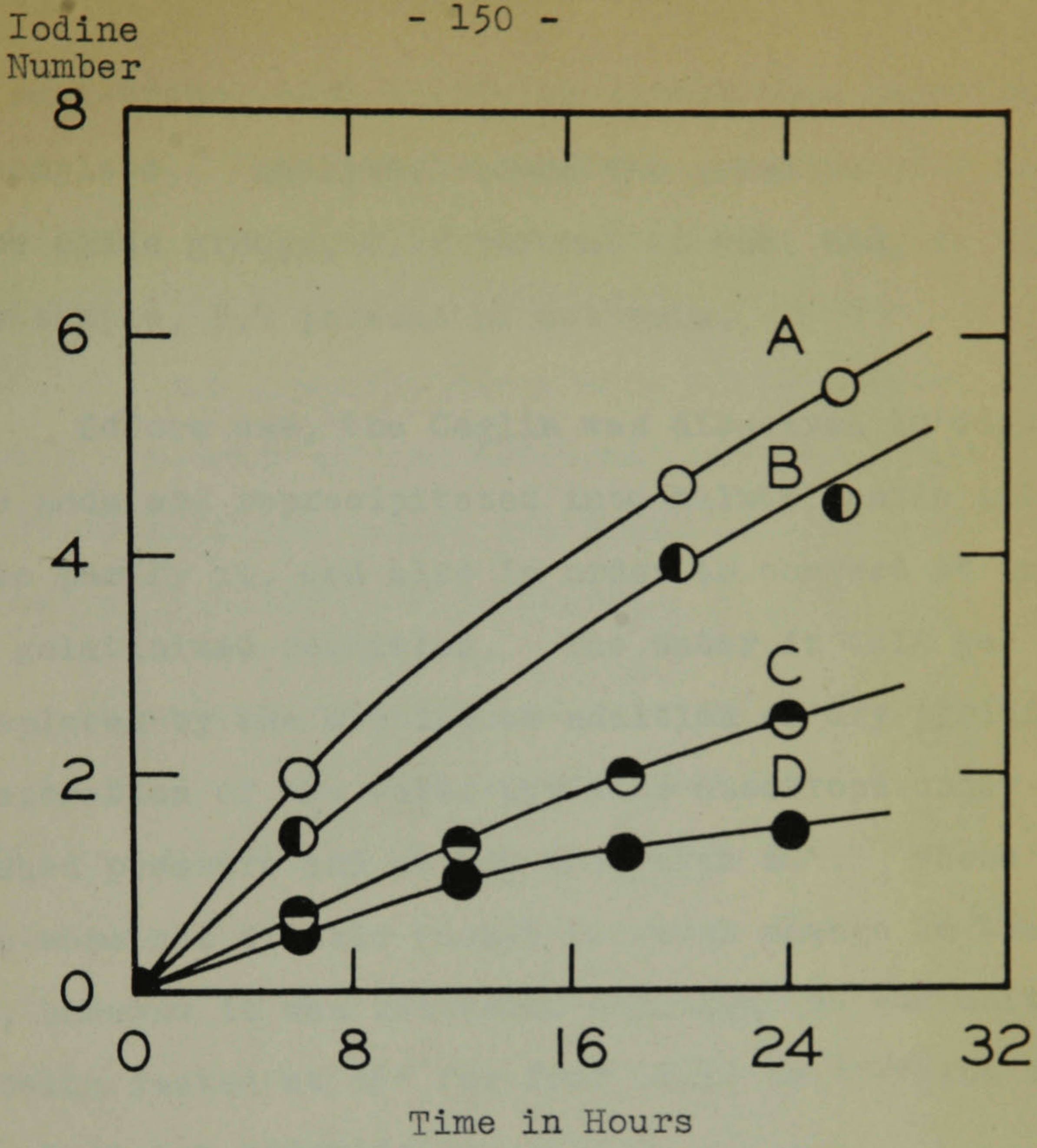


Fig. 9 (See Tables XXIV and XXVI) Rate of Reduction of Alkaline Hypoiodite by Hydroxyethyl Cellulose Ethers and Cellosolve.

Plot A ○ Cellosize (W.S. 100)
Plot B ◐ Cellosolve
Plot C ⊖ Ceglin H
Plot D ● High Alpha Cellulose Wood Pulp

in the semi-translucent particles showed that gelation was incomplete. Analyses showed the presence of 0.443 ethylene oxide groups, 0.12 percent of ash, and, in the air-dry sample, 5.9 percent of moisture.

Before use, the Ceglin was dissolved in dilute caustic soda and reprecipitated into dilute acetic acid in order to purify it, and also in order to convert it into a highly gelatinized condition. The water in this gel was then replaced by the continuous addition of dry pyridine and evaporation of the water-pyridine azeotrope under diminished pressure and at not more than 60°. These conditions were not drastic enough to cause change in the Ceglin, because it was recovered unchanged in composition after being heated at 85° for four hours in pyridine containing hydrogen chloride.

Although the transparent Ceglin-dry pyridine gel was not initially soluble at 25° in the large excess (6.03 moles based on total free hydroxyl groups in the Ceglin) of tosyl chloride in dry pyridine used for tosylation, after a reaction time of approximately twelve hours at 25° the system became homogeneous, all gel particles disappearing. After fifteen to twenty-one hours, depending upon the extent of the intermittent agitation applied, the system again became heterogeneous and deposited a highly swollen rather dark colored gel, which was uniformly dispersed by shaking, but not dissolved. In order to minimize sampling difficulties, small individual tosylation runs were made for reaction times under twenty-one hours and a single, larger-scale mixture, from which on shaking uniform samples could be recovered, was prepared for longer time periods. Table XXX, gives a summary of the physical changes observed in the reaction mixtures during the tosylation and notes the appearance of isolated tosyl esters.

Data from Table XXVIII, plotted in Figures 10 and 11, as well as some preliminary experiments, demonstrated that side reactions, resulting in chlorination and loss of ethylene oxide, accompanied tosylation. These results were accepted as trustworthy because they were obtained by analytical methods extensively tested in Part I of this Thesis, and which in the present case were always the mean of concordant duplicate or triplicate estimations (Table XXVII). The smooth nature of the substitution curves drawn through each individual point (Fig. 8, 10 and 11) and the consistantly high yields of esters, 92-95 percent of the theoretical (Table XXIX), also gave strong support to the conclusion that the analytical techniques were valid to one or two units in the second decimal place.

Considering first the side reaction whereby ethylene oxide groups were lost, Fig. 11 (Table XXVIII) indicated that approximately 63 percent of the original 0.44 moles per glucose unit disappeared during the first four to five days.

TABLE XXX

PHYSICAL STATE OF CEGLIN (E.S. Type H) TOSYLATED FOR VARIOUS TIMES

Ester Sample	Reaction Time	Physical State	
		Reaction Mixture	Isolated Ester
	Hours		
M	1	No color, large gel particles.	A gradual change from entirely hard white pellets and ribbons in (M) to mostly white fibers in (P).
N	3	Color gradually increasing to a slight yellow. The gel particles gradually disperse or dissolve until (R) contains only one or two small pieces	
O	5		
P	7		
Q	9		White and fibrous
R	12		
A	21.5	Slightly yellow. Apparently homogeneous	
	Days		
B	2	Dark colored gel phase separates in gradually increasing amounts. The color of the whole reaction mixture changes from light yellow at 2 days to dark red-brown at 40 days. The gel will in all cases disperse on shaking	
C	3		
D	5		Fibers assume a progressively deepening tan color.
E	8		
F	12		
G	20		
H	40		

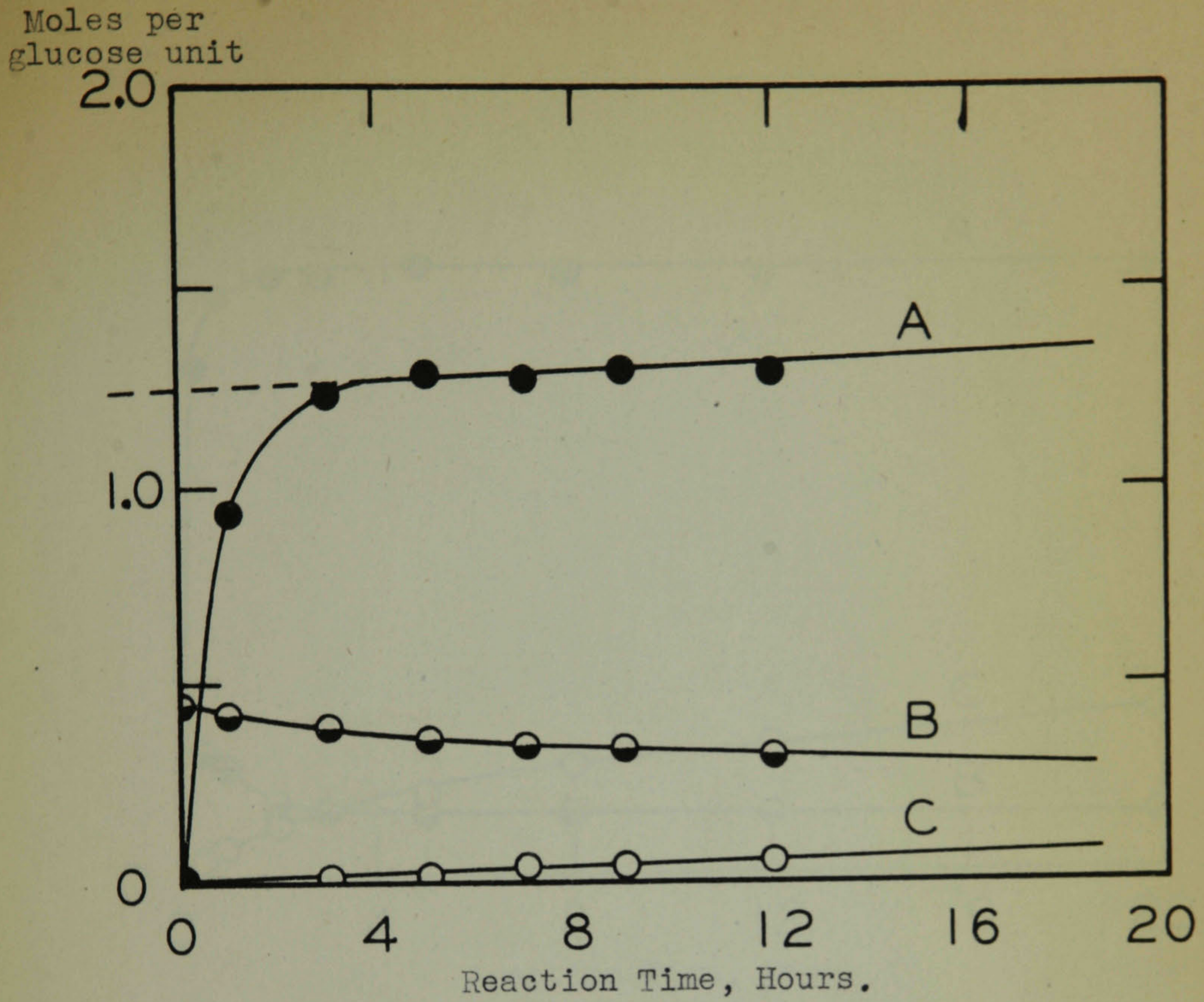


Fig. 10 (See Table XXVIII) Changes with Time in Hours in the Substituent Groups during Tosylation of Ceglin (E.S. Type H).

Plot A ● Moles of Tosyl Groups
Plot B ◒ Moles of Ethylene Oxide Groups
Plot C ○ Moles of Chlorine Groups

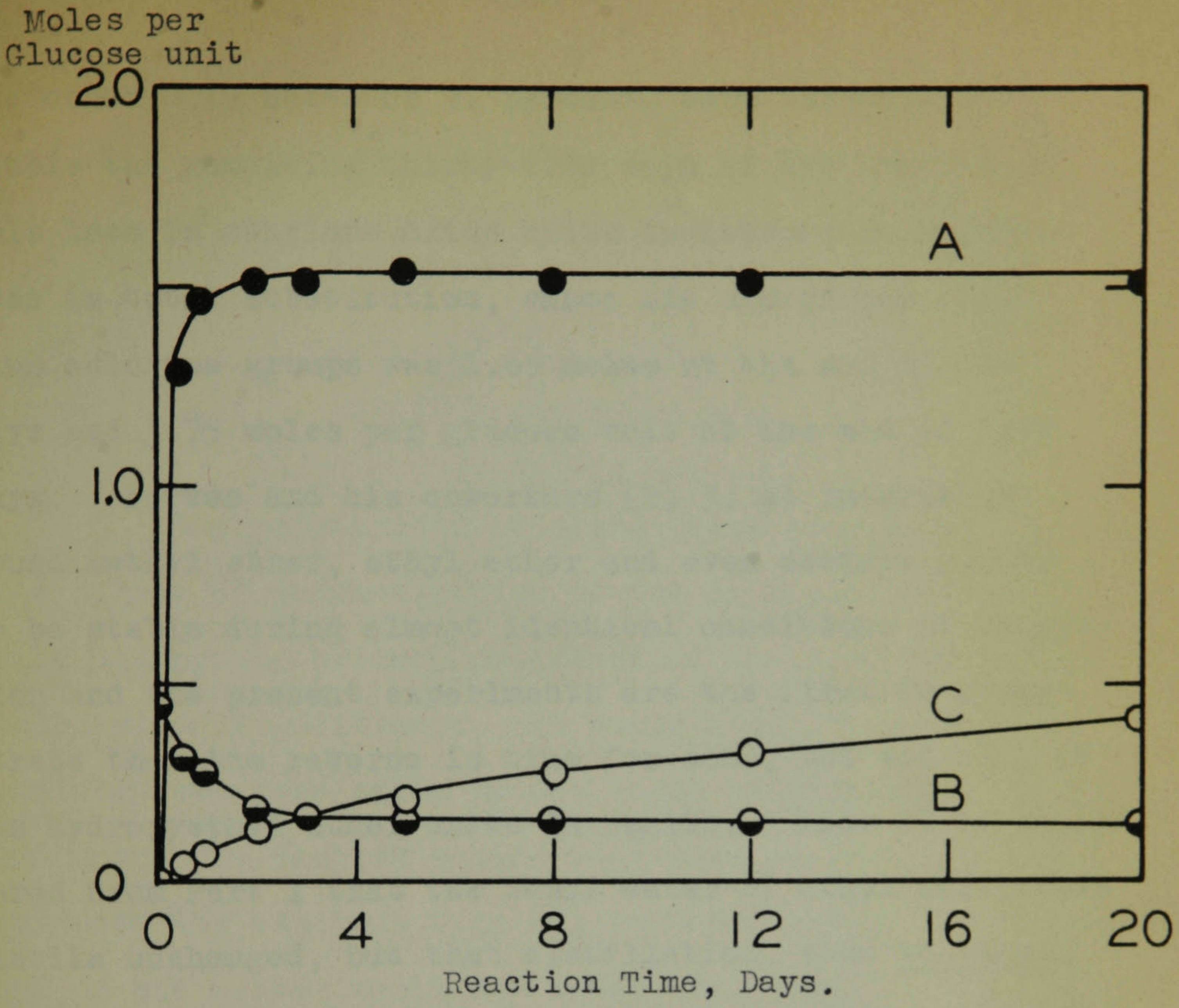
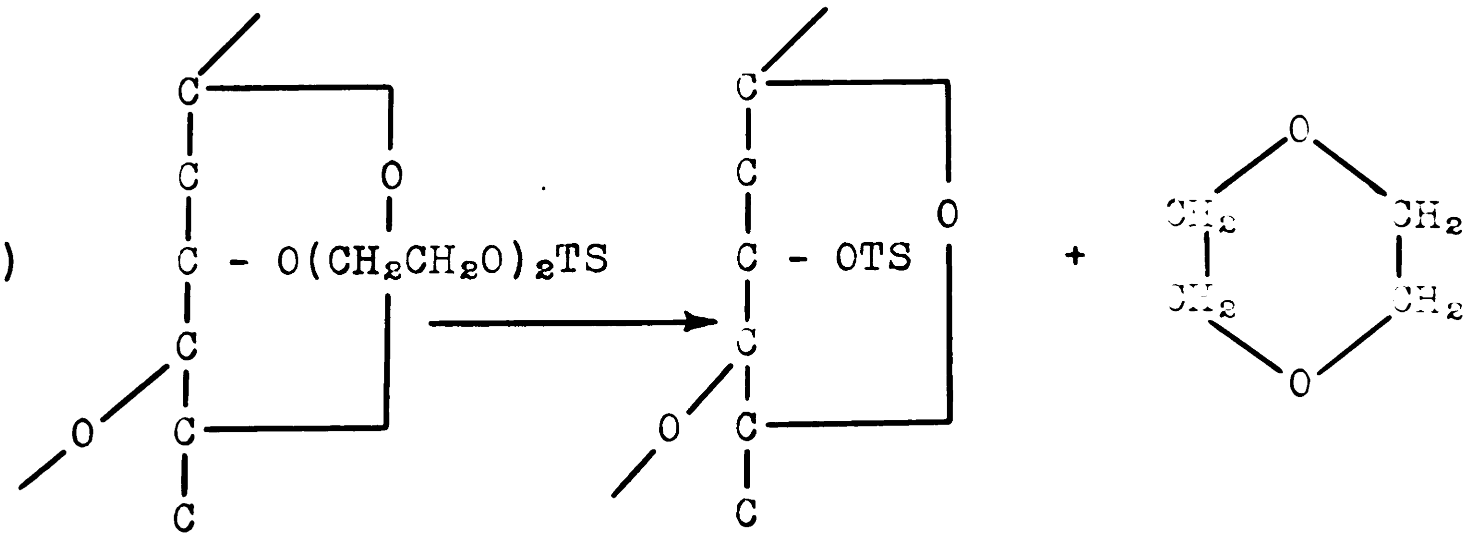


Fig. 11 (See Table XXVIII) Changes with Time in Days in the Substituent Groups during Tosylation of Ceglin (E.S. Type H).

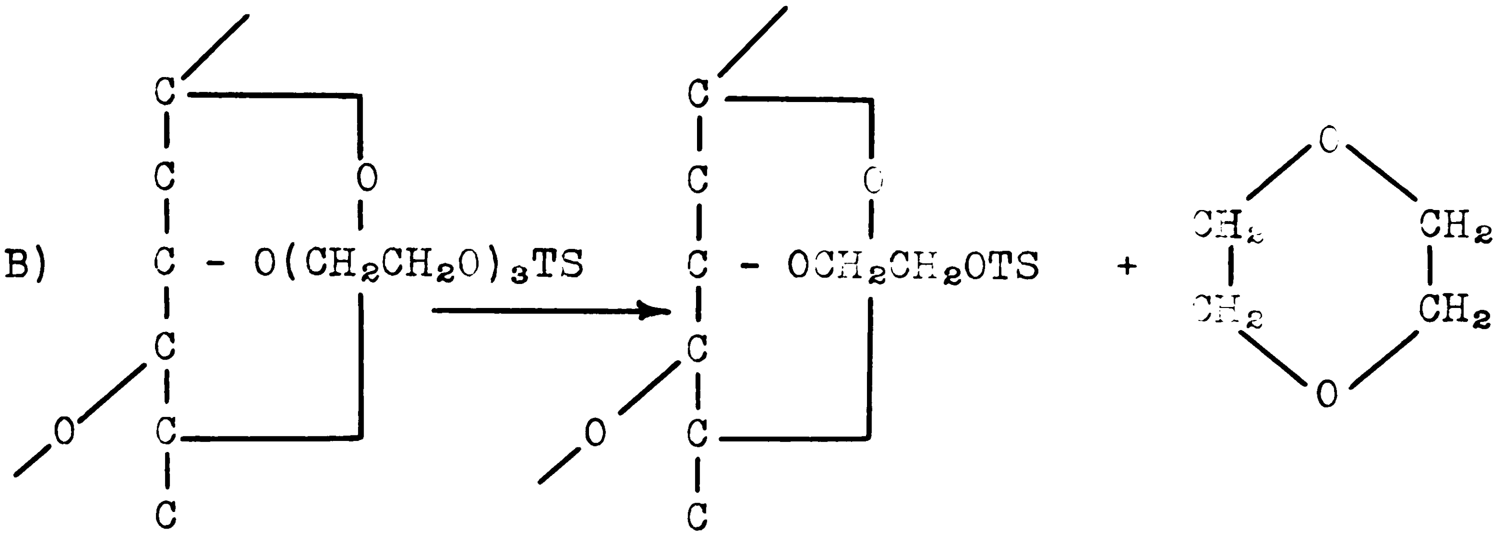
Plot A ● Moles of Tosyl Groups
Plot B ◒ Moles of Ethylene Oxide Groups
Plot C ○ Moles of Chlorine Groups

The other 0.15 moles or 37 percent, were practically stable the remaining thirty-five days of the tosylation. This loss in ethylene oxide units occasioned no apparent loss in total substitution, since the sum of the tosyl plus chlorine groups was 1.65 moles at the end of two days and 1.75 moles per glucose unit at the end of five days. Purves and his coworkers (2, 3, 4) invariably found methyl ether, ethyl ether and even acetate groups to be stable during almost identical conditions of tosylation and the present experiments are the first to demonstrate that the reverse is true for some, but not all, of the hydroxyethyl ether units in Ceglin. When it is remembered from Part I that the tosyl ester of ethyl Cellosolve distils unchanged, but that distillation, even <u>in vacuo</u>, of the Carbitol and triethylene glycol homologous eliminated 1,4 dioxane in nearly quantitative yield, it is reasonable to suggest that the present loss is connected with a break down of ethylene oxide chains. The tosyl groups would be retained in the cellulose structure in one or both of the ways illustrated.

(A)



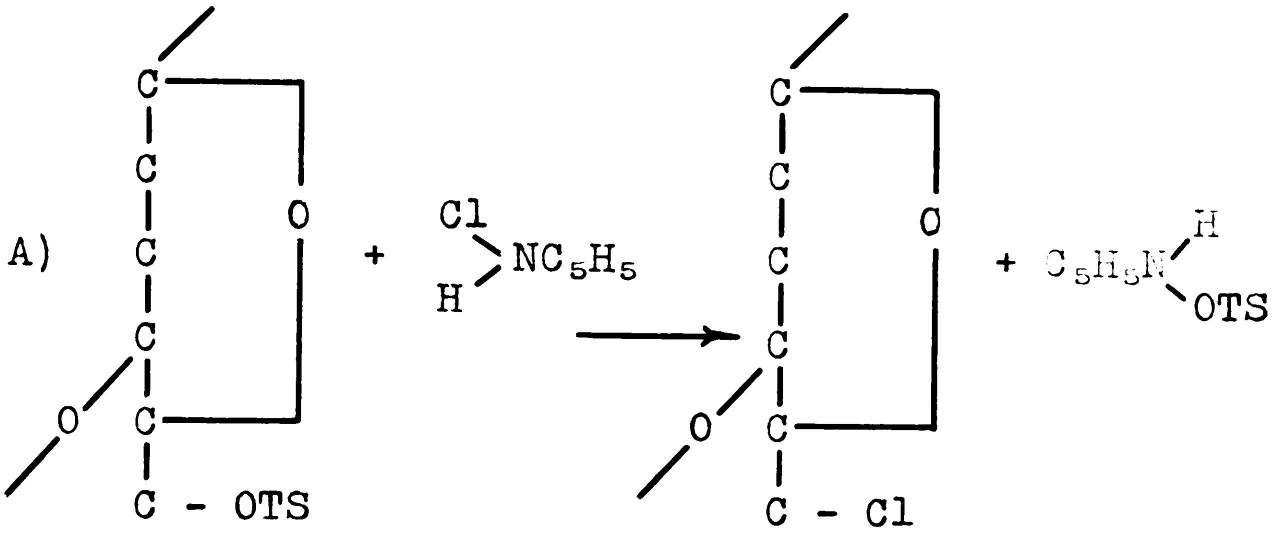
(B)



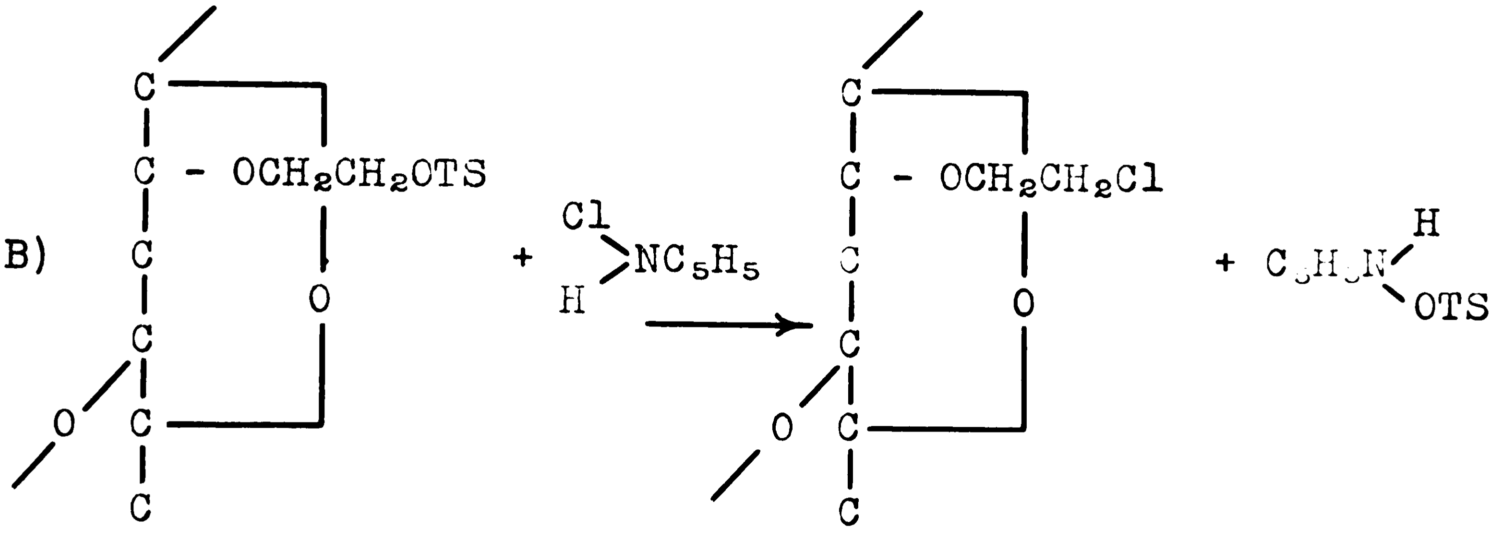
The polymerized ethylene oxide groups, not limited to a degree of polymerization of two or three necessarily, could occupy the primary or either of the secondary cellulosic hydroxyl positions. It would also follow that the remaining ethylene oxide groups would be directly attached in a monomeric fashion to the cellulose nucleus and would represent the residues from odd membered chains. The breakdown of the latter would not alter the number of tosyl groups attached to primary alcohol units. On the other hand, even numbered chains might be completely eliminated and in this case the terminal primary tosyl group would reappear, either as a primary or a secondary unit according to the original attachment to the cellulose. According to these ideas the original Ceglin contained <u>at least</u> 0.148 ethylene oxide units directly attached to cellulose and <u>not more than</u> 0.295 units in a polymerized condition. No direct evidence was obtained to support these speculations.

The chlorination side reaction probably took place in the conventional manner, by the action of the by-product pyridine hydrochloride on the primary tosyl groups as shown.

(A)



(B)



The tosyl group could be on polymerized ethylene oxide chains and the ethylene oxide units could occupy any combination of the free positions in the cellulose. Again no experimental evidence is available for these assumptions and it is possible that both the chlorination and the loss in ethylene oxide might be the result of some single unknown reaction. The apparent difference in the reaction rates, however, (Fig. 11, plots B and C) argues against this possibility. Chlorination has not been found to take place at such a rapid rate during the tosylation of other cellulose derivatives (2, 3, 4).

The extent of the side reactions was not too great during the first five to eight hours (Fig. 10). If it be assumed that an extrapolation of the later portion of the tosylation curve (A) to zero time would not be seriously altered by these side reactions, the tentative conclusion is that there were originally about 1.22 rapidly reacting primary hydroxyl groups per glucose residue (2, 3a). This conclusion would also be based on the further assumption that the primary hydroxyl groups, both those in the primary cellulosic positions and those of the hydroxyethyl units, would react rapidly while the Ceglin was in a gel state, although probably not at the same rate (see Discussion on Part I). Some precedent for this assumption is found in the work by Mahoney and Purves (3a), and in the very recent work by Honeyman (162), where certain heterogeneous tosylations of cellulose esterified the full complement of primary hydroxyl groups after six hours reaction time. Since cellulose has only 1.0 primary hydroxyl groups per glucose unit, and the number apparently present in the Ceglin was 1.22, it follows that 0.22 moles represent primary hydroxyethyl groups attached to the secondary positions of the cellulose. The actual number of such groups in these positions would be greater if they included polymers.

The application of kinetic theory to the tosylation rate plot, during the first five or six days, to determine relative amounts of tosylation at the two secondary cellulose hydroxyl groups (3a, 4) was not considered advantageous, since the reaction was heterogeneous in nature, and since the side reactions became seriously large within the first day (Fig. 11).

III. Chlorination and Iodination of the Tosyl Esters of Ceglin (E.S. Type H)

The iodination reaction, preferably (2, 3, 4, 156), and the chlorination reaction (2, 157) have both been employed to estimate tosylated primary in presence of tosylated secondary hydroxyl groups in cellulose derivatives and sugars. On account of the rapid chlorination side reaction, it was probably impractical to apply the iodination to many of the Ceglin tosyl esters. The small amount of chlorine in the three hour tosyl ester (N) (0.14 percent or 0.01 atoms per glucose unit) however, could be neglected and this sample was iodinated by a procedure similar to that used by Murray and Purves (156). Heating at 115° to 120° for a period of twelve hours was considered sufficient to displace tosyl groups which might be in a β position to an ether oxygen link, and thus less reactive, than the ordinary primary tosyl group (See Discussion of Part I).

The iodination proceeded in over 90 percent yield to give a slightly yellow powder which however contained only 1.0 moles of iodine per glucose unit, where 1.22 moles had been expected (Table XXXI, column 3) from the tosylation rate plot (Fig. 10). Moreover, the results were anomalous in that they showed a loss in total (tosyl plus halogen) group substitution during iodination of 0.13 groups per glucose unit. The chlorination reaction (2, 157) served as a check on these results. Since a loss of ethylene oxide took place during the tosylation reaction, the action of the chlorination conditions on Ceglin itself was investigated, in order to determine if pyridine hydrochloride acted as an ether cleaving agent. This property of the hydrochloride has been extensively studied by Prey (163). It was found that pyridine hydrochloride in pyridine solution, at least under the conditions of tosylation and chlorination of immediate interest did not remove ethylene oxide groups. The latter, then, were stable until they became substituted by a tosyl or chlorine group. Replacements of primary tosyl by chlorine were then carried out on the Ceglin tosyl esters (B) and (P), but water soluble, or very highly water swollen gels, resulted which could not be separated quantitatively and dried. A similar type of difficulty, although in less acute form, was experienced by Cramer (2) with 6-chloro-tosyl cellulose acetate. Ceglin tosyl ester (G) finally gave a good product in almost 100 percent of the theoretical yield and its composition is reproduced in Table XXXI.

Comparison of the last two lines in the Table shows that the chlorination occasioned a loss in total

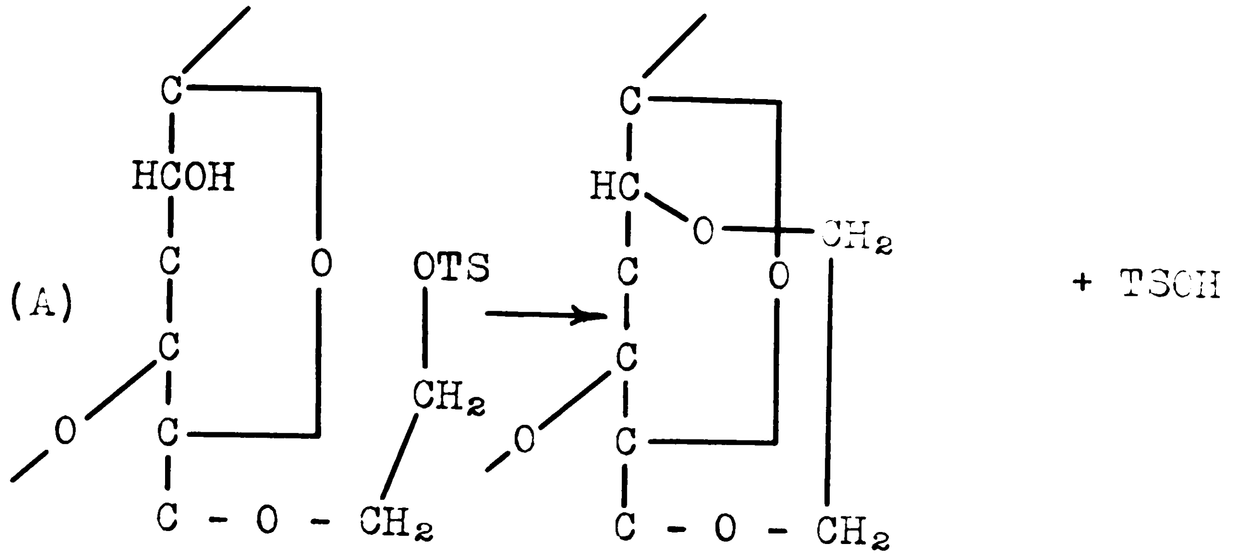
TABLE XXXI

SUBSTITUTIONS IN THE TOSYLATION-HALOGENATION REACTIONS

Sample	Moles per glucose unit $-OCH_2CH_2-$	Tosyl	Iodo	Primary OH	Secondary Tosyl
Original[(a)]	0.44	1.22	-	1.22	-
N (3 hours)	0.39	1.23	0.01	-	-
N Iodinated	0.37	0.11	1.00	1.00	0.11
			Chloro		
G (20 days)	0.15	1.51	0.42	-	-
G Chlorinated	0.13	0.98	0.82	0.82	0.98

(a) Tosylation plot extrapolated to zero time substitution (tosyl plus chlorine groups) of 0.13 moles per glucose unit, or identical in magnitude with the loss already noted during iodination. Both replacements of tosyl also brought about an apparent loss of 0.02 moles of ethylene oxide units, although in this case the differences were within the analytical error. The most striking feature of the chlorination, however, was the fact that only 0.82 atoms of halogen were introduced, whereas the minimum number of primary tosyl groups theoretically capable of replacement is 1.0 per glucose unit. This large discrepancy, which could not reasonably be attributed to the use of conditions inadequate for a complete replacement, pointed to the occurrence of an unsuspected side reaction. Although no evidence was obtained as to the nature of this side reaction, esters of p-toluene sulfonic acid are well-known alkylating agents in basic media. Let it be assumed that the 0.15 moles of tosylated hydroxyethyl groups not eliminated during tosylation slowly alkylated hydroxyl groups of the cellulose at some stage of the reactions, as the following reactions illustrate, such an assumption would result in the formation of cyclic ethers of ethylene glycol, the hydroxyethyl group being retained while either tosyl or halogen, or both, were eliminated. The observed loss of 0.13 units of tosyl plus halogen in the chlorination and iodination reactions on this basis would decrease the molar amount of primary tosyl groups from 1.0 to 0.87, where 0.82 moles were actually found.

(A)



(B)

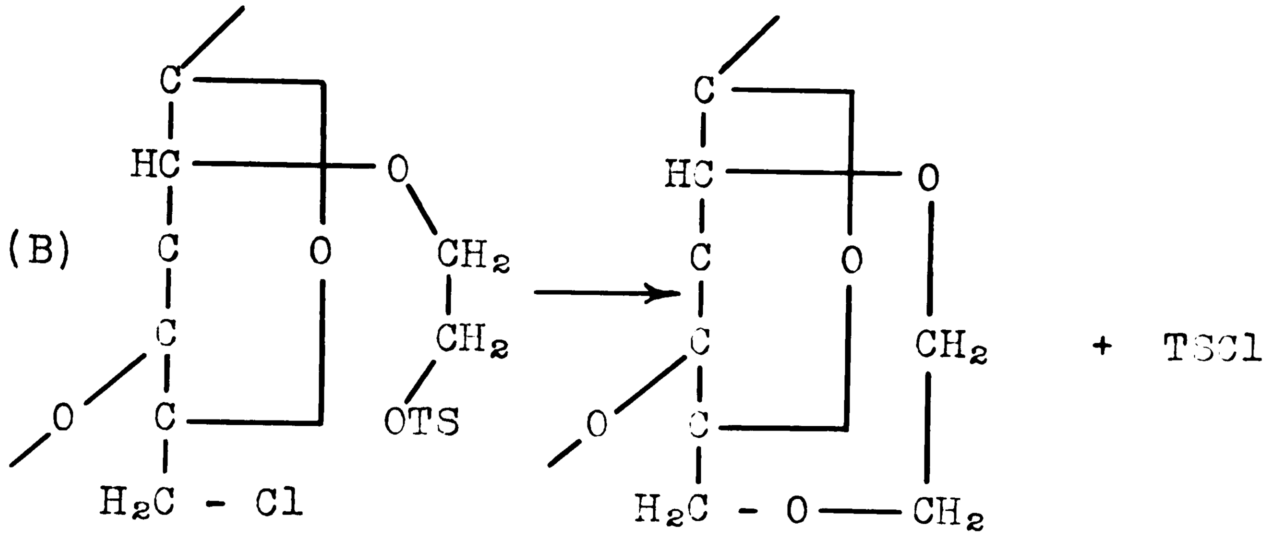


Table XXXII records an arbitrary distribution, found by trial and error, of monomeric and dimeric hydroxyethyl groups in the Ceglin; the only merit of the Table being to illustrate the nature of the assumptions put forward in this Discussion. The original material is supposed to have a total of (0.05 plus 0.10) 0.15 positions substituted by the double unit $-CH_2-CH_2O-CH_2-CH_2-OH$ which during tosylation is gradually eliminated as 1,4-dioxane, the tosyl groups concerned becoming located on the corresponding alcohol groups of the cellulose. This process is appreciable after three hours and is complete within twenty days, the loss from the secondary positions decreasing the amount of

TABLE XXXII

ILLUSTRATING A POSSIBLE MOLAR DISTRIBUTION OF HYDROXYETHYL GROUPS IN CEGLIN (E.S. TYPE H)

	Primary Positions		Secondary Positions			
Sample	Single	Double	Single	Double	Total	Primary Hydroxyl
Original	0.02	0.05	0.12	0.10	0.44	1.22(a)
				Found	0.44	1.22
N (3 hours)	0.02	0.04	0.12	0.08	0.38	1.06(b)
				Found	0.39	1.00
G (20 days)	0.02	0.0	0.12	0.0	0.14	0.86(b)
				Found	0.15	0.82

(a) From rapid initial tosylation (Fig. 11)

(b) Assuming all tosylated single hydroxyethyl groups (0.14 moles) alkylated primary hydroxyl positions.

primary tosyl (primary hydroxyl) toward unity. Although single hydroxyethyl units are not eliminated as dioxane, their tosylates or halides alkylate primary hydroxyl positions, or, if already bound to the latter, secondary positions. In either eventuality the number of primary tosyl groups capable of replacement by halogen is still further diminished.

This study of the tosylation of a Ceglin and the halogenation of the products has failed to determine in an exact way the locations in the cellulose structure of the hydroxylethyl units. It has, however, revealed for the first time the lability of part of these units and some of the difficulties to be overcome before the structural problem is solved. Another major research, preferably based upon more highly substituted hydroxyethyl celluloses than that used on the present occasion, is required to elucidate the anomalies encountered.

CLAIMS TO ORIGINAL RESEARCH

1. The following compounds were prepared in the pure state for the first time and were characterized.

   2-(β-ethoxyethoxy) ethyl p-toluenesulfonate-1

   2-(β-ethoxyethoxyethoxy) ethyl p-toluenesulfonate-1

   β-iodo-β'-ethoxy diethyl ether

   β-iodo-β'-ethoxyethoxy diethyl ether

   The β-iodoethyl ether was prepared by a method not previously employed; and 2-(β-ethoxyethoxyethoxy) ethanol-1 was purified and characterized for the first time.

2. Data for the specific and molar refractivities of the series ethanol, Cellosolve, Carbitol and the monoethyl ether of triethylene glycol, for their tosyl esters and β-iodo ethers were confirmed, corrected and extended. The specific refractivities increased in the first series but decreased in the latter two cases with increasing molecular weight. The molar refraction values in each series increased at the rate of 11.05 ± 0.12 per ethylene oxide unit, and the contribution of the $-O-SO_2-$ group to the molar refraction of the tosyl esters was found to be 10.53 ± 0.35.

3. The tosyl esters of the monoethyl ethers of diethylene glycol and triethylene glycol were found to undergo a

cyclization reaction in very high yields when heated under vacuum; giving 1,4 dioxane and ethyl p-toluenesulfonate in the first case and 1,4 dioxane plus β-ethoxy ethyl p-toluenesulfonate in the second.

4. The relative rates of solvolysis and iodination of the p-toluenesulfonate esters of ethanol, Cellosolve, Carbitol and the monoethyl ether of triethylene glycol were determined. The first member of the series reacted much more rapidly than the others, which contained an ether oxygen atom in the position β to the tosyl group.

5. It was shown that Cellosolve and two commercial hydroxyethyl cellulose ethers were unstable to alkaline hypoiodite, the use of which to estimate aldehyde groups in hydroxyethyl celluloses is therefore no longer admissable. The dimethyl ether of ethylene glycol, methyl Cellosolve, Cellosolve and Carbitol were found to decompose spontaneously by peroxide formation in ordinary storage conditions. No peroxides were detected in the monoethyl ether of triethylene glycol or in hydroxyethyl celluloses.

6. The tosylation-iodination and chlorination reactions were applied to a commercial hydroxyethyl cellulose for the first time. With reservations, at least 0.23

moles of the original 0.44 were assigned to secondary cellulosic hydroxyl positions. Unexpected side reactions were noted and two-thirds of the total ethylene oxide content of the ether was found to be unstable under normal tosylation conditions.

SUMMARY

1. The monoethyl ethers of ethylene glycol (Cellosolve) and diethylene glycol (Carbitol) were shown to form peroxides readily, especially in air and light. This property, together with the presence of ethylene glycol and diethylene glycol, makes Carbitol in particular a substance difficult to purify and to maintain in a pure form. On the other hand the monoethyl ether of triethylene glycol and hydroxyethyl ethers of cellulose were not found to contain peroxides.

2. Although the reaction between pure Carbitol and sodium formed colored decomposition products, the solution with pure ethylene chlorohydrin gave a rather poor yield of triethylene glycol monoethyl ether. Published values for the density and refractive index were corrected to D_{20}^{20}, 1.0211 and n_D^{20}, 1.4380 respectively.

3. The p-toluenesulfonates of Carbitol and triethylene glycol monoethyl ether were obtained for the first time as pure oils, D_{25}^{25}, 1.1599, n_D^{25}, 1.4976; and D_{25}^{25}, 1.1698, n_D^{25}, 1.4959 respectively. Both esters, when attempts were made to purify them by distillation in the region of 125°-135°/0.03-0.13 mm. decomposed to give high yields of 1,4 dioxane together with nearly

quantitative yields of ethyl p-toluenesulfonate in the first case and of Cellosolve p-toluenesulfonate in the second. Rate studies of the solvolysis of the sulfonates in 95 percent methanol at 65° showed that ethyl p-toluenesulfonate reacted about six times as rapidly as its three higher homologs. Pseudo unimolecular rate constants were obtained for the overall solvolysis reaction.

4. The replacement of the p-toluenesulfonyl group in the above four esters by iodine proceeded easily with iodide in acetonyl acetone, the overall rates agreed with second-order reactions and a minimum rate was observed for Cellosolve p-toluenesulfonate. The latter replacement constituted a new method of preparation for pure β-iodo ethyl ether. The higher homologs prepared for the first time, were β-ethoxy-β'-iodo diethyl ether, b.p. 40°-42°/0.15 mm., n_D^{20}, 1.4908, n_D^{25}, 1.4881 and D_{25}^{25}, 1.5210; and β-ethoxyethoxy-β'-iodo diethyl ether, b.p. 97°-98°/0.15 mm., n_D^{20}, 1.4889, n_D^{25}, 1.4870 and D_{25}^{25}, 1.4557.

5. In the series ethanol, Cellosolve, Carbitol and the monoethyl ether of triethylene glycol the molar refraction increased by uniform increments of 10.95±0.05 with each additional ethylene oxide unit. A similar increment was observed for the corresponding series of

iodides and of p-toluenesulfonates. The molar refraction of the $-O-SO_2-$ group in this series of tosyl esters was calculated for the first time and found to be 10.53 ± 0.35. In contrast to results in the alcohol series, specific refractive indices in the p-toluenesulfonyl and iodide series decreased with increase in molecular weight.

6. The stability of the higher iodides toward alkali was great and the polyethylene oxide monoethyl ethers gave abnormally high ethoxyl values in the standard alkoxyl estimation. This tendency was enhanced for the corresponding iodides and p-toluenesulfonates.

7. The consumption of alkaline hypoiodite by hydroxyethyl celluloses, Cellosize (W.S. 100) and Ceglin (H), increased steadily with time, indicating that side reactions were consuming iodine. Pure Cellosolve exhibited a similar behavior and showed that the hydroxyethyl group itself must be unstable to alkaline hypoiodite. By inference the side reaction, causing increasing iodine numbers in the cases of hydroxyethyl celluloses, would be due to the instability of the hydroxyethyl groups. The iodine number method of determining aldehyde groups when applied to hydroxyethyl celluloses, is therefore unreliable.

8. The tosylation-iodination or chlorination reaction was applied to Ceglin (E.S. type H) containing an average of 0.44 moles of ethylene oxide per glucose unit. The results, although complicated by unexpected side reactions of an unknown character leading to rapid loss in ethylene oxide during tosylation, and to loss of tosyl and halogen groups during iodination and chlorination, may indicate that there are a minimum of 0.23 ethylene oxide units on the secondary Ceglin cellulosic hydroxyl groups. The ethylene oxide groups appear to be of two different types, one relatively unstable and the other relatively stable to the tosylation-halogenation reaction conditions. About two-thirds of the original 0.44 groups are of the unstable type.

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