LONG CHAIN POLYETHYLENE ETHER GLYCOLS

AND

POLYMERIZATION

THE SYNTHESIS OF LONG CHAIN POLYETHYLENE ETHER GLYCOLS AND THE NATURE OF POLYMERIZATION

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 Master
of Science

McGill University May 1933

ACKNOWLEDGMENT

The writer desires to express his gratitude to Dr. Harold Hibbert for his kind advice and helpful criticism during the course of this research, and to Dr. Fritz Brauns for his many timely suggestions.

TABLE OF CONTENTS

INTRODUCTION 1

Theories of Polymerization 2

General Methods for Attacking the Problem of Polymerization 3

Nature of the Mechanism of Ethylene Oxide Polymerization 5

SURVEY OF LITERATURE AND PREVIOUS WORK 7

Synthesis of the Higher Polyethylene Glycol Ethers 13

EXPERIMENTAL METHODS AND DIFFICULTIES ENCOUNTERED 14

I. Synthesis and Isolation of the Di-Chloride Derivatives 15

II. Preparation of the Monosodium Salt ... 16

Purification of the Polyethylene Glycol Ethers 20

EXPERIMENTAL PART 23

Synthesis of Polyethylene Glycol Ether Dichlorides 23

Preparation of Triethylene Glycol Dichloride 23

Preparation of Hexaethylene Glycol Dichloride 25

Preparation of Nonaethylene Glycol Ether Dichloride 27

Preparation of Octadekaethylene Glycol Ether Dichloride 27

Synthesis of the Polyethylene Glycol Ethers 29

Synthesis of Nonaethylene Glycol Ether 29

Synthesis of Octadekaethylene Glycol. 30

Synthesis of Heptacosaethylene Glycol 32

IDENTIFICATION OF THE POLYETHYLENE GLYCOL ETHERS 33

Attempts to Prepare Esters of the Polyethylene Glycol Ethers 34

Attempts to Prepare an Ester of Octadekaethylene Glycol Ether 35

Determination of Hydroxyl in Heptacosaethylene Glycol Ether 36

CONCLUSIONS AND THEORETICAL DEDUCTIONS 37

REFERENCES 41

INTRODUCTION

The present research has been carried out with the view of obtaining further information on the nature of polymerization, and it was thought that it might pave the way towards a better understanding of such supermolecular compounds as cellulose, starch, etc. The initial work was begun some eight years ago in these laboratories and the writer is continuing the research from the point at which his predecessor, Mr. S. Z. Perry, left it.

Many of the basic substances used in industry represent supermolecular or polymerized compounds. Among the most common are cellulose, starch, rubber and resins. A great deal of study has already been devoted to the subject of the nature and properties of polymerized compounds and much progress made towards an understanding of the mechanism involved.

Probably one of the most important factors concerns the nature of the forces binding the units of these large molecules. Many theories and speculations have been put forward in this connection and these may be arranged conveniently as: Long Chain Theories, Theory of Large Rings and Association Theories.

Theories of Polymerization

Long Chain Theory - The supporters of the long chain theory maintain that polymerization proceeds in a step-wise manner by means of normal valency forces, which may, or may not, involve free end valencies. Reversibility, or depolymerization, in certain cases is to be expected but this property is exhibited only by a few of the known complex polymers. Hence, in order to account for this, it is assumed that the individual structural unit loses its identity in the polymer. This theory finds much support in a variety of data dealing with polymerization involving a -C-C- linkage, while in the case of polymers involving a -C-O-C- linkage, the evidence is much less complete. The data obtained in the present investigation provide valuable support in favor of the long chain theory of polymerization.

Large Ring Theory - For many years the large ring theory of polymerization had few supporters. The principal reason for this was the general acceptance of the principles involved in the Baeyer Strain Theory, which postulates that only five and six membered rings are stable and that any higher membered ring would not only be unstable but its formation highly improbable. However, when Ruzicka (1) succeeded in preparing large homocyclic carbon ring compounds which are exceedingly stable, the theory received valuable support. The existence of large rings indicated that the atoms are very probably not in the same plane, so that a long chain may assume the form of a flexible spiral, thus bringing the end groups close enough together to facilitate union. This is contrary to Baeyer's theory.

Association Theory - This theory assumes that polymerization is brought about under the influence of residual valencies, the nature of which, however, are ill-defined. The formation of the polymer by means of the residual valencies of the structural unit should in general indicate a weak union but the supporters of the theory assert that the strength of these accumulated residual valencies may be great enough to resist the disruptive powers of solvents, etc. It has also been suggested that under favorable circumstances the associated polymer may revert to the original individual unit.

General Methods for Attacking the Problem of Polymerization

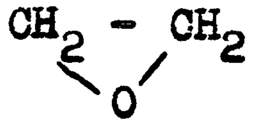
a. Isolation of the structural unit and reconversion into the polymer - This mode of attack is favored by those who believe in the residual valency theory. If the structural unit could be isolated and shown to have free valencies and a marked tendency to associate, then the association theory would receive valuable support. Work has been performed in this direction by Bergmann (2), Pictet (3), Hess (4), Irvine (5), and Pringsheim (6).

b. Study of the physical and colloidal properties of polymers - The most favored of the physical methods is that of X-ray analysis. This valuable method is of great assistance in determining the arrangement of the atoms or structural units in space. Its chief drawback is the fact that it is only applicable to crystalline polymers and unfortunately many important commercial polymers are not crystalline. Many colloidal properties of organic lyophilic sols have been studied and some evidence obtained as to their structure. Work of this nature has been performed by Staudinger (7), Meyer and Mark (8), and Whitby (9).

c. Study of the action of groups which appear to be nuclear centres in causing polymerization - Certain configurations such as unsaturated -C=C- linkages, oxygen bridged and oxide ring systems are said to provide nuclear centres for polymerization. These may be exemplified as follows: -

(i) Unsaturation $>C = C$ $>C = O$

(ii) Cyclic oxides



$CH_2 - CH_2$, O

(iii) Polyfunctional compounds $HOCH_2 - CHO$

Unsaturated linkages display the most marked effect in that polymerization sometimes occurs with explosive violence. This work has been examined by Bergmann (2) and Levene (10).

d. Study of cleavage and degradation products of polymers and their chemical properties - This method has been used with great success in the study of polysaccharides and related compounds by several chemists including Haworth (11), Freudenberg (12)and Hibbert (13).

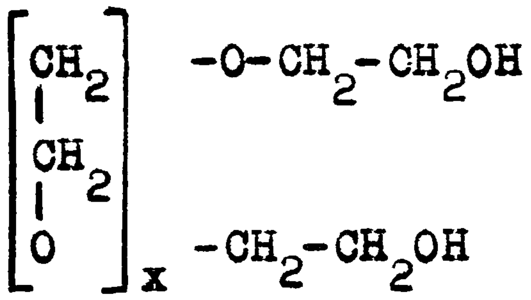
e. Synthesis of the structural unit - The only outstanding success in this method of attack is the work on synthetic rubber. But even here there is no certainty as to the mechanism of the conversion to the supermolecular state.

f. Direct synthesis of complex and natural polymers by a building process - This method probably offers the most conclusive evidence as to the mechanism of polymerization and the actual structure of the resulting polymer. By starting with a well-known compound capable of functioning as a structural unit and condensing it with itself by recognized procedures, the polymerization may be controlled, so that only normal valency forces are involved. Carothers (14) is attacking the problem from this angle and this is the method used by the writer in the present investigation.

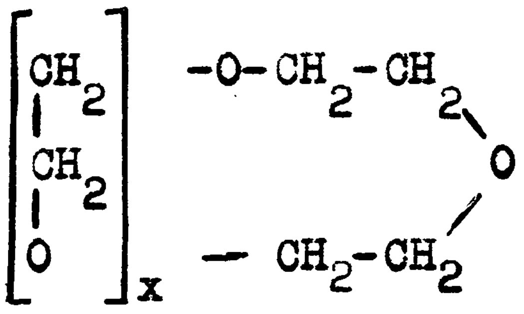
Nature of the Mechanism of Ethylene Oxide Polymerization

Ethylene oxide was adopted as the basic building unit in this study of polymerization, not only on account of its simplicity but also in view of the relation of the polymerized product to cellulose. However, one great difficulty with regard to the substance is that a mixture of polymers is always obtained. A consideration of the probable structure of polymerized ethylene oxide as a long chain polymer with terminal hydroxyl groups indicated a close relationship between the polyethylene glycol ethers* and the ethylene oxide polymers. If the polyethylene glycol ether series could be synthesized by recognized reactions and found to be identical with the polymers formed by the polymerization of ethylene oxide, valuable information as to the structure and mechanism of formation of the latter could probably be obtained. In any event the synthetic long chain polyethylene glycol ethers would serve as a valuable series of reference compounds. Their structure could be confirmed by formation of derivatives such as dihalides, etc. Furthermore an investigation of the physical properties such as viscosity, etc., of these chemically pure, long chain ethers might be expected to yield interesting data with reference to such important factors as the relation of viscosity to chain length and state of aggregation. The relation in structure between polyethylene glycol ethers and polyethylene oxides is shown below:

This series of compounds has been re-named " polyethylene ether glycols " as on the title page.



Polyethylene glycol



Polyethylene oxide

The fact that the polymers of ethylene oxide have now been shown by Perry and Hibbert (15)* to be long open chain polyethylene glycol ethers formed by a stepwise addition of each successive polymer to a new molecule of ethylene oxide lends added interest to the problem.

SURVEY OF LITERATURE AND PREVIOUS WORK

Würtz (16) prepared ethylene oxide by treating ethylene chlorhydrin with caustic potash at 125° C. He found that ethylene oxide containing just a trace of caustic potash polymerizes on standing.

Crafts (17) prepared the dimer of the corresponding ethylene sulphide by treating ethylene bromide with an alcohol solution of potassium hydrosulphide.

Roithner (18) prepared ethylene oxide by the method of Demole (19), which consists in dropping ethylene chloride on

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*page 102, line 19 - "nona" should read "deka" to hot caustic potash. He made a study of its properties and obtained a polymer in the same manner as Würtz, which he described as a crystalline solid with an observed molecular weight of twenty-three to thirty times that of the original ethylene oxide.

Careful measurements of several physical constants of ethylene oxide were made by Maass and Boomer (20).

Polyethylene glycol ethers were first prepared by Lourenco (21) in 1859 by heating ethylene glycol with ethylene bromide in a sealed tube at 115-120°C. He claimed to have obtained and separated polyethylene glycols as high as hexaethylene glycol. His work was repeated by Perry in these laboratories but with no satisfactory results.

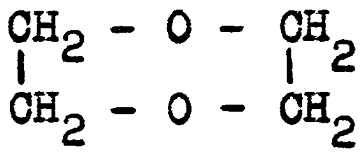
Würtz (22) prepared polyethylene glycols by heating ethylene glycol or water with ethylene oxide for several weeks.

Hibbert and Bilger (unpublished work) prepared polyethylene glycol ethers by heating ethylene glycol with a small amount of iodine which catalyses the reaction and causes a mole of water to separate from two moles of the glycol. The effect diminishes perceptibly with the higher polyethylene glycol ethers.

Würtz (23) prepared chlorhydrins by heating ethylene glycol, saturated with hydrochloric acid gas, in a sealed tube.

Carius (24), Fittig (25), and Strom (26) treated ethylene glycol with sulphur chloride and obtained chlorhydrins.

Lourenco (27) passed a stream of dry hydrogen chloride gas through warm polyethylene glycol ethers and obtained polyethylene glycol chlorhydrins. He also prepared the bromhydrins of the polyethylene glycols by heating ethylene bromide and ethylene glycol to 160°C. in a sealed tube. By heating these substances together at 160°C. at ordinary pressure, he obtained diethylene glycol bromhydrin, and diethylene oxide. To the latter he ascribed the formula:



Faworski (28) also obtained this compound as the main product in distilling ethylene glycol with sulphuric acid, and ascribed to it the same formula. This was confirmed by Clark (29) in 1912.

Staudinger (7) has recently published, in book-form, a very complete account of supermolecular compounds, principally the work of himself and co-workers, and devotes considerable space to the polyethylene oxides and related compounds. He attempted to determine the mechanism of their formation, but his results and conclusions are characterized by uncertainty and lack of correlation. He obtains certain velocity relationships with regard to polymerization and influence of catalysts.

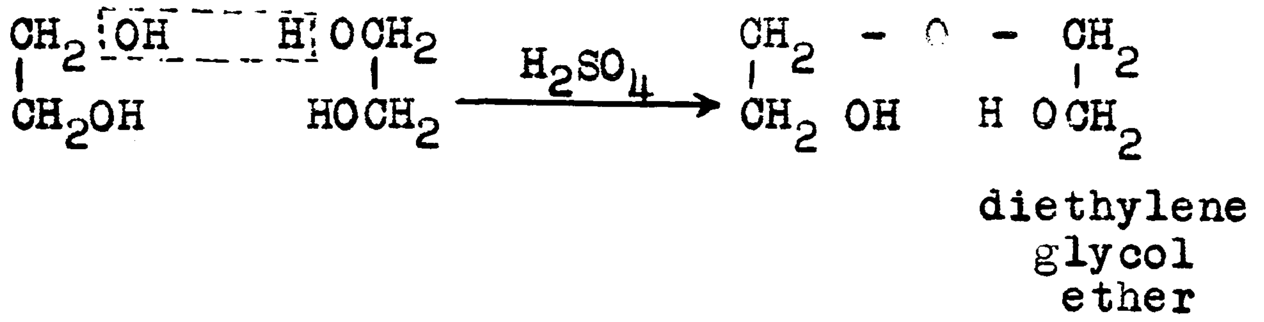
He was also able to separate the natural polymer into fractions having molecular weights assumed to be mean values of a series of polymers, the molecular weights of which lie above and below those obtained. His many attempts at depolymerization, however, resulted only in the formation of complex substances and decomposition products. He suggests a long chain formula:

$$---CH_2-CH_2-O-(CH_2-CH_2-O)_x-CH_2-CH_2-O---$$

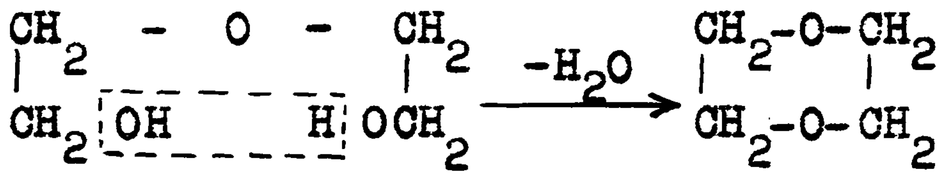
for the polymers and assumes as one possible explanation that instead of free end valencies the products isolated may be mixtures of hydrated oxides; i.e., a mixture of polyethylene glycol ethers:

$$HO-CH_2-CH_2-O-(CH_2-CH_2-O)_x-CH_2-CH_2OH$$

That polyethylene glycol ethers may be dehydrated, finds support in the work of Faworski (28). The formation of diethylene oxide from ethylene glycol obviously suggests a dehydration process. This may be assumed to take place through an intermediate stage thus:



$$\begin{array}{llll} CH_2 & OH \quad H & OCH_2 \\ | & & | \\ CH_2OH & & HOCH_2 \end{array} \xrightarrow{H_2SO_4} \begin{array}{llll} CH_2 & - O - & CH_2 \\ | & & | \\ CH_2 & OH \quad H & OCH_2 \end{array}$$



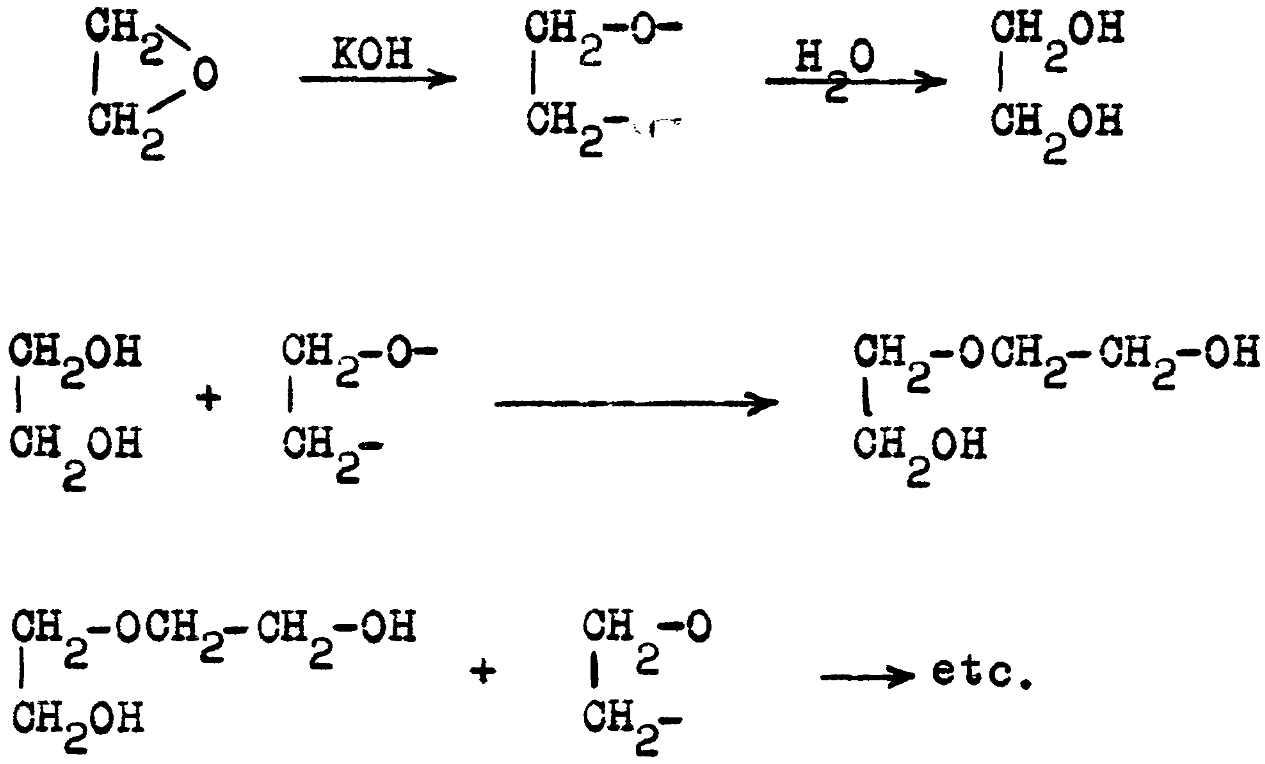
Diethylene oxide

This suggested that if diethylene glycol be treated with concentrated sulphuric acid, diethylene oxide should be obtained. Experimental evidence justified this assumption and ethylene glycol along with polyethylene glycols, similar to those obtained in the iodine condensation, were obtained as by-products.

S. Z. Perry (unpublished work) has carried out during the last three years an extensive series of investigations with a view to the direct synthesis of the higher polyethylene glycol ethers, as a result of which it was found possible to synthesize the lower members of the series. The various methods investigated were all based on the general principle of an interaction between one mole of the dichloride of a polyethylene glycol ether with two moles of the monosodium salt of a polyethylene glycol ether, with the subsequent elimination of two moles of sodium chloride.

A greater part of his primary research was spent in attempts to discover the best way of bringing about such interaction with a good yield and a suitable method of isolation. In one series of experiments in his earlier work he prepared the metallic salt of the glycol by the direct action of sodium, with a fair measure of success. However, he later modified the process by using sodium methylate in place of metallic sodium, the former reacting with the polyethylene glycols. The resulting methyl alcohol was then removed by distillation under reduced pressure. A third method was the use of sodium hydroxide which forms sodium derivatives when heated with the glycol-ether to a high temperature. He found the sodium methylate process to be the most suitable and used this for the synthesis of a number of the lower polyethylene glycol ethers, namely those within the range of diethylene to dekaethylene glycol inclusive (with the exception of the nonaethylene glycol).

In a more recent investigation on the nature of the products formed in the reaction of aqueous alkali with ethylene oxide, Perry has obtained definite evidence which justifies the graphic formula for the polyethylene glycol ethers as used in this research. He has shown that ethylene oxide will not polymerize in the presence of dry caustic potash while the reaction proceeds readily if there is moisture, or a glycol, or polyethylene glycol ether present. Also the degree and rate of polymerization is governed by time and concentration factors. The polymerization of ethylene oxide under the influence of aqueous alkali may be represented as follows:



Synthesis of the Higher Polyethylene Glycol Ethers

In the present investigation considerable time and effort was spent on the purification and isolation of considerable quantities of pure hexaethylene glycol ether from the crude products left by Mr. Perry.

The best conditions were then ascertained, after numerous experiments, for preparing the dichlorides of the product and of the higher ethers. This work was followed in turn by experiments on the preparation of the monosodium salt of the glycol ethers; the condensation between them and the dichlorides; and later the development of new methods of isolation and purification of the polyethylene glycol ether synthesized in this way.

The following new products have been prepared, isolated in a pure state and certain conclusions as to their structure arrived at.

Nonaethylene glycol ether*
Octadekaethylene glycol ether
Heptacosaethylene glycol ether
Nonaethylene glycol ether dichloride
Octadekaethylene glycol ether dichloride

EXPERIMENTAL METHODS AND DIFFICULTIES ENCOUNTERED

The numerous difficulties encountered in this work necessitated various side investigations, especially with respect to the isolation and purification of the final polyethylene glycol ether.

The synthesis of the higher from the lower polyethylene glycol ethers involves two main processes:

I. Synthesis, isolation and purification of the long-chain dichloropolyethylene glycol ethers,

II. Synthesis of the monosodium salts of the polyethylene glycol ether and interaction of one mole of I with two moles of II to give a higher ether. Isolation and purification of the latter.

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*See foot-note page 7

I. Synthesis and Isolation of the Dichloride Derivatives

In agreement with the data obtained by Mr. Perry, the reagents finally used in this preparation were thionyl chloride and pyridine. It was found very important to use only anhydrous materials, and to note that thionyl chloride hydrolyses very readily. The polyethylene glycol ethers were dried by repeated distillation under diminished pressure and finally placed in a vacuum desiccator over concentrated sulphuric acid.

The apparatus for the preparation of the dichlorides consisted of a three-neck flask fitted with a water-cooled condenser, mercury-sealed mechanical stirrer and a dropping funnel. The condenser was closed with a calcium chloride tube and all joints were of ground glass to avoid any discoloration caused by rubber or cork stoppers.

In general, a large excess of thionyl chloride was found to increase the yield. The rate, and time of addition of the thionyl chloride and the reaction-temperature varied with each substance and the optimum conditions could only be ascertained by carrying out a number of runs, in each of which one of the above factors was varied in turn; the difficulties were more pronounced in the case of the higher glycol ethers, especially in connection with the purification of the final product.

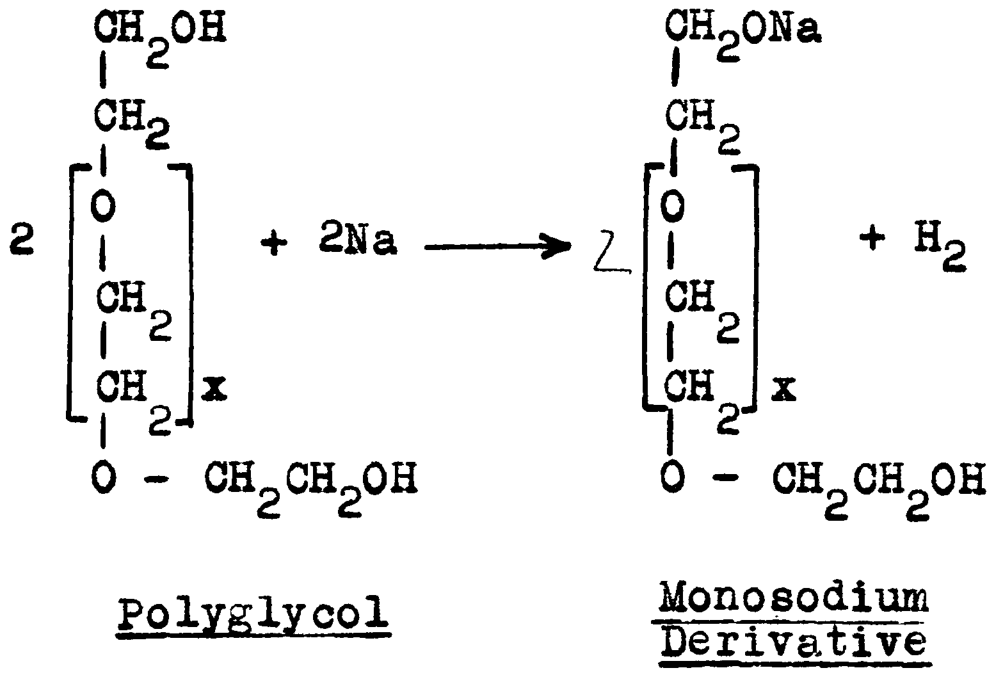
II. Preparation of the Monosodium Salt

The monosodium derivatives of the polyethylene glycol ethers were prepared originally by the action of metallic sodium on the polyethylene glycol ether at room temperature. The apparatus was the same as that used in the dichloride preparation.

The polyethylene glycol, in large excess, was placed in the flask and covered with a layer of absolute ether to prevent oxidation taking place during the reaction. Metallic sodium (theoretical amount) was added, with vigorous stirring, in the form of small freshly-cut pieces over a period of time. The reaction velocity, measured by the rate at which the sodium dissolved, was extremely slow, requiring as long as two days. During this period the reaction mixture became very viscous and difficult to stir, but solution was effected with a minimum of discoloration.

The improved process, developed by the author, and which was afterwards used in all of the preparations of the monosodium derivatives, made use of an inactive nitrogen atmosphere and the greater reaction velocity associated with higher temperatures. In this case the polyethylene glycol ether was placed in the three-necked flask and stirred vigorously while a stream of nitrogen was led beneath the surface of the liquid, the flask being placed in a hot water bath, kept at constant temperature.

The metallic sodium was then added carefully, and while it dissolved with much greater rapidity it left the solution more discolored. The mixture could be stirred much more easily at the higher temperatures and the reaction readily controlled so that it proceeded at an even rate. The evolution of hydrogen could be readily noted and this also aided in preventing oxidation. The reaction is a displacement one and may be represented as follows: -

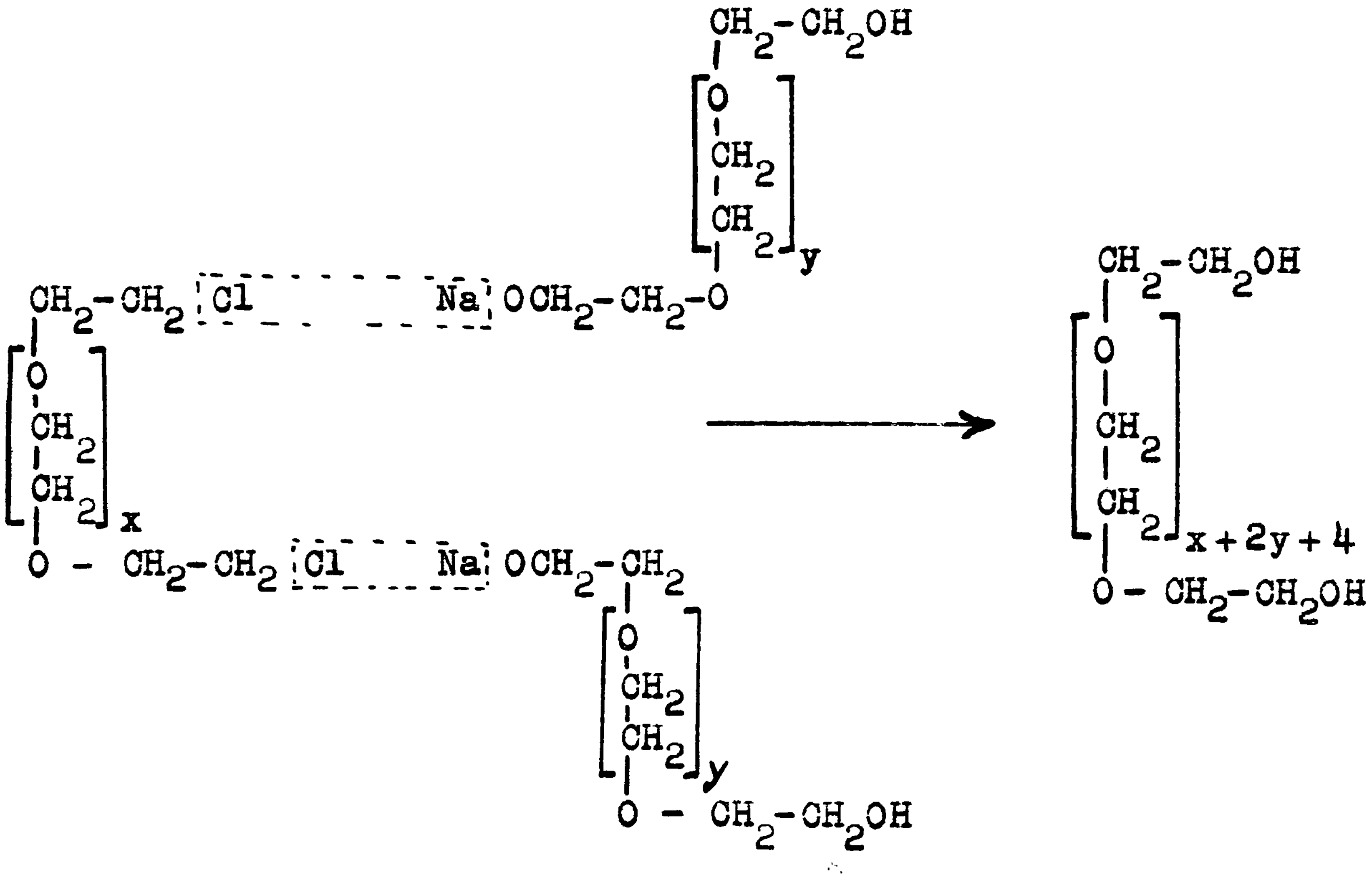


Any disodium salt which forms, presumably, breaks up spontaneously to the monosodium derivative when a large excess of the glycol is present.

The dark yellow to dark brown color which is formed during the preparation of the monosodium derivative disappears partly during the dichloride addition, and to a still greater degree during the condensation reaction. The color disappearance was also facilitated by allowing the temperature to increase slowly and at an even rate.

The preparation of the monosodium derivative and the ensuing condensation with the dichloro derivative were always run as a continuous reaction in the same apparatus described above.

During the actual condensation, dry nitrogen gas was passed into the reaction mixture, containing the monosodium salt dissolved in an excess of the polyethylene glycol ether. The dichloride was run in from the funnel, keeping the temperature identical with that at which the monosodium derivative was formed, namely room temperature. An oil bath was used instead of a water bath. After all the dichloride had been added, the bath temperature was raised considerably and vigorous stirring continued. No reaction was noted until a definite temperature was reached, generally about 150°C, and this occurred instantaneously with sodium chloride precipitating rapidly. The reaction product was held at this temperature for some time and then filtered to remove sodium chloride crystals. The filtrate was extracted in a continuous all-glass extractor and the extracts shaken with charcoal (for lower members only). For polyglycol ethers which are liquid at ordinary temperature, the solvent was removed by distillation and the original polyglycol ether recovered by vacuum distillation, The residue was fractionally distilled at very low pressures, using a Megavac oil pump in series with a Langmuir mercury pump and obtaining in this way a colorless, very viscous oil. The reaction may be represented as follows: -



where x may be 1, 2, 3, 4, etc., y may be 1, 2, 3, 4, etc. and x and y may, or may not, have the same value.

The rate of condensation was greatly improved by adding the dichloride at 90°C. and then allowing the temperature to rise only very slowly after the entire dichloride addition had been completed. The reaction then took place gradually as shown by the even rate of salt precipitation and gradual change in color from dark brown to a pale cream or white. The temperature was held constant for a short time at the highest point reached, the neutral reaction then obtained showing that all the sodium derivative had reacted. The mixture was poured into the continuous extractor without filtering and then extracted with ether, in this way obtaining an extract free from inorganic salts and avoiding loss of material through filtration.

Purification of the Polyethylene Glycol Ethers

For polyethylene glycol ethers which are solid at ordinary temperature the ether extracts were not shaken with charcoal. In these cases the ether was evaporated and the original glycol (if a liquid) removed by vacuum distillation. The residue, which was usually dark yellow or yellowish red, solidified on cooling. It was melted, again placed in the extractor, and repeatedly fractionally extracted. In this process, the receiver was replaced at regular intervals and it was found that the first fraction of the extract was lighter in color than the original, the next fraction less so, etc. The fractions were all again extracted separately and the process repeated until a colorless product was obtained. These colorless fractions were now kept in a cool place, covered by a layer of ether. After several days the polyethylene glycol ether separated out as well-characterized crystals, the impurities being left behind in the mother liquor of the various fractions.

Attempts to purify the solid polyethylene glycol ethers by the use of solvents were unsuccessful, due to their high solubility in the usual organic solvents. By precipitation from a mixture of benzene and ligroin an oil was obtained, which still retained the yellow color. Fractional distillation in vacuum always resulted in decomposition and excessive charring. A great deal of time was spent in a search for better methods of purification before the fractional extraction method was developed and this finally proved to be the most satisfactory.

Since the polyethylene glycols beoome more soluble, with increasing molecular weight, in the solvent used, it is possible to separate the original polyglycol from the product by fractional extraction if the original polyglycol is a solid. It could not be removed by distillation due to decomposition which takes place.

The greatest difficulty encountered was that in connection with the requisite distillations in high vacuum. As the substances concerned were very viscous oils, sharp boiling points were impossible at the very low pressures and high temperatures used. Repeated fractionations were necessary in order to obtain a fair estimate of the boiling point. In the case of the separation of a distillable liquid polyethylene glycol ether from that of a non-distillable solid member, great care was required to prevent charring of the latter. A Woods metal bath was used in most cases, but it was difficult to keep the bath temperature constant and hence continual attention was necessary in order to prevent superheating. As the distillations were usually operated at a pressure of several microns, distillation had to be conducted at a very slow rate in order to avoid marked variation in pressure. Asbestos rope insulation was used on all distilling flasks and this made it very difficult to watch the distilling action in the flask.

The ground glass joints of the condensation apparatus could not be opened when the reaction mixture was hot and hence often had to be warmed in order to allow of the transfer from flask to extractor.

The preparation of derivatives of the solid polyethylene glycols usually resulted in oils which would not crystallize.

EXPERIMENTAL PART

Synthesis of Polyethylene Glycol Ether Dichlorides

Commercial triethylene glycol was purified in the following way. 400 gm. of triethylene glycol (commercial) was distilled under reduced pressure using an oil pump. The fraction collected boiled constantly at 120°C./3 mm. 370 gm. of the product were obtained which was redistilled several times to eliminate any H_2O and placed in a vacuum desiccator.

Preparation of Triethylene Glycol Dichloride

20 gm. of triethylene glycol were dissolved in 20 gm. of dry pyridine and placed in a three-necked flask having ground glass joints and fitted with a water-cooled reflux condenser, mercury-sealed mechanical stirrer and a dropping funnel.

40 gm. of thionyl chloride were added through the dropping funnel during the course of three hours, vigorous stirring being maintained throughout the reaction. No external heat was applied, the temperature being controlled by occasionally surrounding the flask with a water bath. When the pyridine salt separated, the temperature of the reaction mixture was raised in order to dissolve it. After the final addition, a few chips of porous plate were added to facilitate

the evolution of sulphur dioxide. The contents had become yellowish brown in color.

The reaction mixture was poured into three times its own volume of cold water when a brown oil separated out. The latter was extracted repeatedly with ether in a separatory funnel, the extracts carefully neutralized with sodium bicarbonate and then dried for two days over anhydrous sodium sulphate. The ether was distilled off and the residual oil fractionated under reduced pressure with the following results: -

Fraction 1	75-90°C./6 mm.,	wt. 3 gm. approx.
Fraction 2	90-100°C./5 mm.	wt. 5 gm. approx.
Fraction 3	100-105°C./4 mm.	wt. 19 gm. approx.

In order to obtain a sharp fraction a Hempel column was then used with the following results:

Fraction 1	up to 95°C./5 mm.,	wt. 5 gm. approx.
Fraction 2	101-102°C./5 mm.	wt. 20 gm.

The product, Fraction 2, was a colorless, odorless, viscous oil; yield, 80% of the theoretical.

Analysis (Stepanov Method): 0.1976 gm. of substance used 20.95 cc. N/10 $AgNO_3$. Found: Cl, 37.60%. 0.2106 gm. of substance used 22.36 cc. N/10 $AgNO_3$. Found: Cl, 37.67%.

Calculated for $C_6H_{12}O_2Cl_2$ (187), 37.97%.

Preparation of Hexaethylene Glycol Dichloride

The preparation of this product was a more difficult problem. The hexaethylene glycol used had been prepared by Mr. Perry and was in the crude state. It was purified by repeated fractionations using the mercury pump, until the product obtained boiled constantly at 160-163° C./0.003-0.005 mm.

Using the same apparatus as for the previous experiment, 70 gm. of hexaethylene glycol were dissolved in 40 gm. of dry pyridine. To this mixture 65 gm. of thionyl chloride were added slowly over a period of three hours with vigorous stirring. The flask was surrounded by a water bath at room temperature which sufficed to control the reaction.

After the final addition, chips of porous plate were added and the temperature of the bath raised to 80°C. for fifteen minutes during which time vigorous evolution of sulphur dioxide took place. The reaction mixture became reddish-brown in color. It was poured into twice its volume of cold water and the dark oil separating was extracted repeatedly with ether. The ether extracts were neutralized with sodium bicarbonate after which the ether solution was shaken continuously (on a mechanical shaker) for two days with Darco decolorizing charcoal and 25 gm. of pure metallic mercury. When removed from the shaker, the solution contained a fine black suspension of mercuric sulphide which passed through an ordinary filter. It was removed by passing through a charcoal filter formed by depositing Darco decolorising carbon from an ether suspension on to a fine-pore fluted filter paper. The ether solution was then dried over anhydrous sodium sulphate, after which the ether was distilled off and the residual pale yellow oil distilled under reduced pressure. Only a few cubic centimeters of low boiling substances were obtained, the remainder boiling constantly at 165-170°C./0.008-0.012 mm. Redistillation gave a colorless oil which boiled at 164-166°C./0.009 mm. wt. 60 gm., yield 75% of theoretical.

Analysis: 0.1984 gm. of substance used 12.43 cc. N/10 $AgNO_3$. Found: Cl, 22.25%. 0.2108 gm. of substance used 13.25 cc. N/10 $AgNO_3$. Found: Cl, 22.29%. Calculated for $C_{12}H_{24}O_5Cl_2$ (319), 22.39%.

In the earlier preparation the crude product was always obtained in the form of a turbid dark yellow oil, the turbidity being due to the presence of finely divided solid particles. In later work, it was found that this turbidity disappeared on raising the reaction-temperature and maintaining same until all sulphur dioxide had been evolved. The dark yellow color (presumably due to the presence of sulphur) was removed later, at least in large measure, by shaking with a mixture of Darco charcoal and mercury as indicated above.

Preparation of Nonaethylene Glycol Ether Dichloride

The same apparatus was used. 20 gm. of nonaethylene glycol ether were dissolved in 10 gm. of pyridine and 13 gm. of thionyl chloride slowly added during the course of three hours, after which chips of porous plate were added and the mixture heated to 90°C. for ten minutes. The dark-red reaction mixture was poured into cold water, the oil separating out extracted with ether, and washed with sodium bicarbonate solution, then with water. It was then shaken with metallic mercury and Darco charcoal for two days. After filtration and removal of the ether, the residual oil was distilled with the use of a Megavac oil pump in series with a Langmuir mercury pump. After several distillations a colorless oil, b.p. 183-186°C./0.005 mm., was obtained, wt. 8.9 gm., yield 44.5% of theor.

Analysis: 0.2110 gm. of substance used 9.47 cc. N/10 $AgNO_3$. Found: Cl, 15.92%. 0.2006 gm. of substance used 8.96 cc. N/10 $AgNO_3$. Found: Cl, 15.88%. Calculated for $C_{18}H_{36}O_8Cl_2$ (451), 15.74%.

Great care is necessary in the distillation to avoid charring and decomposition.

Preparation of Octadekaethylene Glycol Ether Dichloride

20 gm. of octadekaethylene glycol were dissolved in 10 gm. of dry pyridine and 10 gm. of thionyl chloride added during a period of three hours. Porous plate chips were

then added and the temperature of the bath raised rapidly to 70°C. Since the reaction mixture began to turn dark very rapidly the contents of the flask were poured immediately into cold water. An emulsion formed which was difficult to break up so the entire product was extracted with ether for two days in a continuous extraction apparatus. The ether extract was washed with sodium bicarbonate solution, then with water, shaken with metallic mercury and charcoal, and dried over sodium sulphate. After filtration, the ether was removed and the residual product, which had a pale yellow color was heated to 100°C. at a pressure of 10 mm. The residual oil, on cooling, solidified to a yellow mass; the latter was extracted fractionally with ether in a continuous extractor for two days and, upon evaporation of the ether, a light yellow crystalline solid was obtained. The latter was melted, placed in a continuous extractor and fractionally extracted by changing the receivers at regular intervals. Each fraction was lighter in color than the succeeding one, and repetition of this process finally yielded a colorless oil which was covered with a layer of ether and allowed to stand in the cold room. After two days a white crystalline solid separated, m.p. 20-22°C. approx., wt. 6.6 gm., yield 33% of theoretical.

Analysis: 0.2200 gm. of substance used 5.30 cc.

N/10 $AgNO_3$. Found: Cl, 8.57%. 0.2124 gm. of substance used 5.18 cc. N/10 $AgNO_3$. Found: Cl, 8.65%. Calculated for $C_{36}H_{72}O_{17}Cl_2$ (849), 8.38%.

The higher-membered dichlorides were found to be less soluble in ether.

Synthesis of the Polyethylene Glycol Ethers

Synthesis of Nonaethylene Glycol Ether

The apparatus used was the same in each case and consisted of a ground glass three-necked flask fitted as in the case of the dichloride preparation except that the dropping funnel was combined with a gas inlet tube which led to the bottom of the flask.

Method

250 gm. of dry redistilled triethylene glycol were placed in the flask, the latter immersed in an oil bath kept at 80°C. and a slow current of dry nitrogen bubbled through the liquid throughout the reaction. 20 gm. of metallic sodium were then added, with vigorous stirring, in small pieces during a period of three hours. The mixture turned brownish yellow, hydrogen gas being evolved continuously. After about 12 hours, the sodium had dissolved completely and 85 gm. of triethylene glycol dichloride were then added

through the dropping funnel during a period of one hour. Stirring was continued for a further hour, the temperature being maintained throughout at 80° C. During the next hour the temperature was raised slowly to 160° C., the reaction mixture steadily becoming lighter in color due to separation of the sodium chloride. The bath temperature was maintained at 160° C. for two hours, the light yellow mixture then giving a neutral reaction.

The reaction product was poured into a continuous liquid extractor, in which all joints were of ground glass, and the product extracted with dry ether for about 24 hours, leaving a large residue of salt.

After removal of the ether, the residual oil was fractionated by distillation under reduced pressure, first with an oil pump and later with a high-vacuum mercury pump.

200 gm. of triethylene glycol were recovered and further distillation of the residual oil gave, on careful fractionation, a colorless distillate, b.p. 209-212° C./0.008 mm., wt. 90 gm., yield 50%. of theoretical.

Synthesis of Octadekaethylene Glycol

Using the apparatus described above, the following procedure was used:

300 gm. of hexaethylene glycol (2-1/2 times the

theoretical) were placed in the flask from which the air had been displaced previously by nitrogen.

10 gm. of fresh-cut metallic sodium were added, with vigorous agitation, during two hours, the outside bath being maintained at 90°C. After continued heating and stirring for 24 hours at this temperature, the sodium had dissolved completely to form a brownish colored solution.

65 gm. of hexaethylene glycol dichloride were then added during a period of two hours at 90°C., the temperature of the bath then raised, during one hour, to 180°C. and then held at 165°C. for three hours, when the contents had a neutral reaction. The color of the liquid had gradually changed to a light cream, due to the separation of sodium chloride.

The reaction mixture was transferred to an extractor and extracted with ether leaving the salt behind.

The ether was evaporated and the residual oil distilled in high vacuum in order to recover the unused hexaethylene glycol, b.p. 176°C./0.009 mm., amounting to 208 gm. The temperature of the remaining oil was raised to 220°C. at 0.004 mm. for several minutes and the product allowed to cool when it solidified to a solid yellow mass.

The crude solid was melted and poured into a continuous ether extractor and the ether extracts removed at about three hour intervals. Each successive fraction was lighter in color than the following one and by repeating this process several times and allowing final fractions to stand under dry ether for several days, the octadekaethylene glycol separated in clusters of white needles, m.p. 25°C., wt. 110 gm. yield, 63% (theoretical).

Synthesis of Heptacosaethylene Glycol

The condensation reaction was carried out in the same manner but using in this case nonaethylene glycol ether dichloride and the monosodium salt of nonaethylene glycol ether.

45 gm. of nonaethylene glycol (5 times the theoretical amount) were placed in a flask and 0.5 gm. of fresh-cut metallic sodium added with stirring during the course of two hours, the outside bath being kept at 95°C. After stirring for sixteen hours at 95°C. all of the sodium had dissolved, a dark brown solution having been formed.

6 gm. of nonaethylene glycol dichloride were then added to the mixture over a period of one hour at 95°C. after which the temperature was increased to 180°C. during one hour and then maintained at 170°C. for two hours. The solution gave a neutral reaction and possessed a reddish-yellow instead of the usual cream color.

The crude mixture was extracted with ether, the ether evaporated and the residual oil distilled in high vacuum in order to recover the unchanged nonaethylene glycol. Although the distillation was conducted very carefully at a temperature of 225°C./0.01 mm., with an outside bath temperature of 265°C., it was difficult to avoid some decomposition and slight charring.

28 gm. of nonaethylene glycol were recovered, the temperature being finally raised to 270°C./0.06 mm. after which the residual oil was cooled and then solidified to a reddish brown mass. This solid was melted and submitted to fractional extraction with dry ether over a period of 48 hours. The final fractions (Fractions 4 and 5) were allowed to stand under ether for several days, when pure heptacosaethylene glycol separated in clusters of white needle crystals. M.p. 35°C. approx., wt. 8 gm., yield, 61.5%.of theoretical.

IDENTIFICATION OF THE POLYETHYLENE GLYCOL ETHERS

Inasmuch as the usual combustion analyses for carbon and hydrogen do not serve to distinguish one polyethylene glycol ether from another, together with the fact that molecular weight determinations leave much to be desired when carried out on higher polymers, it was felt that other derivatives should be prepared, the analysis of which would provide definite information as to the identity of the long chain ethers.

Attempts to Prepare Esters of the Polyethylene Glycol Ethers

A considerable amount of time and effort was spent in an attempt to prepare a crystalline ester of the various polyethylene glycol ethers. Unfortunately such derivatives as the benzoates, the bromobenzoates and the nitrobenzoates of the lower ethers, up to, and including, the dekaethylene glycol ether, appear to be liquids at the ordinary temperature, and the same seems to be true of the higher members such as the heptacosaethylene glycol ether.

A further difficulty was met with in the attempt to prepare esters such as the p-chlorobenzoate and p-toluyl sulphonate. Following the usual procedure of dissolving the glycol ether in pyridine and allowing this to react at ordinary temperatures for 24 hours with a pyridine solution of the acyl chloride (for example, p-chlorobenzoyl chloride), it was found that the crystalline product isolated by pouring the reaction product into water was p-chlorobenzoic anhydride and not the expected di-ester of the glycol. No explanation of this abnormal behavior can be offered at the moment. Apparently p-toluene sulphonchloride would seem to be the best reagent to use for the purpose of identification but the entire matter calls for much further study.

Attempts to prepare an Ester of Octadekaethylene Glycol Ether

Four experiments were tried in each of which 1 gm. of the glycol was dissolved in 3 gm. dry pyridine and then mixed with

(a) 3 gm. of p-nitrobenzoyl chloride
(b) 2 gm. of p-chlorobenzoyl chloride
(c) 1.5 gm. of 2,4 dinitrobenzoyl chloride, and
(d) 1 gm. of p-toluene sulphonchloride

respectively, each previously dissolved in 5 cc. pyridine.

The experiments were carried out in well-stoppered flasks and the mixture allowed to stand for 24 hours. Ice-water was added to the reaction product in each case.

(a) yielded an orange-red oil, while with (b) and (c) a white solid and with (d) a dark-red semi-solid product, respectively, were obtained.

Investigation of (b)

The product was filtered, washed with water, dried, dissolved in benzene, the solution refluxed for ten minutes with Darco charcoal, filtered and allowed to cool slowly. Colorless needle crystals having a silver lustre, separated, m.p. 191°C., wt. 1.2 gm.

Analysis (Carius Method): 0.0446 gm. substance gave 0.04286 gm. AgCl. Found: Cl, 23.76%. 0.1012 gm. substance gave 0.09700 gm. AgCl. Found: Cl, 23.77%. Calculated for $C_{14}H_8O_3Cl_2$ (295), 24.06%.

A mixture of the product with an authentic sample of the anhydride melted at 194-195°C.

Investigation of (d)

The product isolated (presumably the p-toluene sulphonate) was extremely soluble in the usual organic solvents. It was crystallized finally from ether in the form of colorless crystals, m.p. 67-68°C. The amount obtained was not sufficient for analysis.

At the same time attempts to prepare the diparachlorobenzoate of heptacosaethylene glycol also resulted only in formation of the β-chlorobenzoic anhydride, m.p. 197°C.

Analysis: 0.9660 gm. of substance gave 0.09256 gm. of AgCl. Found: Cl = 23.7%. 0.7800 gm. of substance gave 0.07494 gm. AgCl. Found: Cl, 23.71%. Calculated for $C_{14}H_8O_3Cl_2$ (295), 24.06%.

Determination of Hydroxyl in Heptacosaethylene Glycol Ether

The heptacosaethylene glycol ether was thoroughly dried in an Abderhalden for 48 hours and weighed in a closed flask immediately after removing it. A mixture of acetic anhydride and pyridine was made up in the proportion of 24 gm. of the former to 176 gm. of the latter. The excess acetic anhydride, after the addition of 10 cc. of above mixture to the sample and heating for 15 minutes on the water bath, was converted to acetic acid with water and titrated with normal sodium hydroxide. The method of Verley and Bölsing (30) was used in this determination.

Analysis: 1.1168 gm. of substance used 1.91 cc. N NaOH. Found: -OH, 2.91%. 0.8947 gm. of substance used 1.57 cc. N NaOH. Found: -OH, 2.98%. Calculated for $C_{54}H_{108}O_{26}(OH)_2$ (1206), 2.81%.

CONCLUSIONS AND THEORETICAL DEDUCTIONS

The mode of synthesis employed, the analysis of the dichlorides, and the "acetyl value" obtained for the polyethylene glycol ethers would seem to clearly establish their identity, in spite of the failure to isolate other suitable derivatives capable of serving for their further identification.

It must be admitted that the experimental work and analytical proof of structure is not nearly as complete as the author desired. However, due to the nature of the reactions and technique employed in the synthesis the work must necessarily advance at a slow rate, for, if forced, more time and energy is lost than gained. This was the experience of the writer at the outset of this work. It was also his intention to carry out physical measurements such as molecular weight determinations, viscosities, etc., but time did not permit. As already pointed out carbon and hydrogen analyses offer no indication of purity or identity and it will be necessary both to prepare well-characterized derivatives and also to determine carefully the physical properties in order to establish definitely the purity of the products in question.

Thus far it has been found that the synthesis of the solid polyethylene glycol ethers,using the dichloride, can be carried out more readily than that of the liquid members. On the other hand, the yield of dichloride, using the thionyl chloride method of synthesis, decreases with increase in molecular weight. The success of the future synthesis of still longer chain derivatives is thus dependent on the development of an improved technique for the preparation of the dichlorides and it is possible that the latter can be prepared more satisfactorily at room, or even lower temperatures.

The discoloration of the crude polyethylene glycol ether appears to be due to side reactions brought about under the influence of the sodium so that with the higher members, where less sodium is required, less discoloration should occur. Sodium alcoholate could be used in place of metallic sodium but this would involve the use of a mercury-sealed stirrer capable of being operated under reduced pressure for the purpose of removing the alcohol and such procedure is very inconvenient.

Ring Closure

It is the writer's regret that not enough time was available to attempt the isolation of ring compounds from the higher glycol ethers. Observations already made indicate that by the action of active metals on the dihalide derivatives of the polyethylene glycols ring closure can probably be brought about. The methods of Ruzicka (1) are also applicable in this connection. Presumably it should also be possible to synthesize not only heterogeneous single chain polymers but also polymers comprising mixed homogeneous single chains.

It should be mentioned that in a number of experiments trouble was caused by the use of an impure thionyl chloride. The colorless material in question was purchased as a pure product but apparently contained some sulphur derivative which interfered with the normal course of the reaction.

At present, indications point to the successful application of the processes already developed to the synthesis of the higher members of the polyethylene glycol ether series with the formation of substances of molecular weights approaching those of various natural substances.

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