curve method and supported by cryoscopic molecular weight determinations and analysis of the dichlorides.

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Studies on Reactions Relating to Carbohydrates and Polysaccharides. LVII. The Synthesis of 90-Membered Oxyethylene and 186-Membered Oxyethylene Glycols[1]

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The Williamson ether synthesis described previously[3] has been used to synthesize further higher members of the polyoxyethylene glycol series, namely, the 90-membered and the 186-membered polyoxyethylene glycols $HO(CH_2CH_2O)_{90}H$ and $HO(CH_2CH_2O)_{186}H$, respectively.

These were synthesized by reaction of 2 moles of the respective monosodium salts of 42- and 90-membered oxyethylene glycols with one mole each of the 6-membered oxyethylene glycol dichloride.

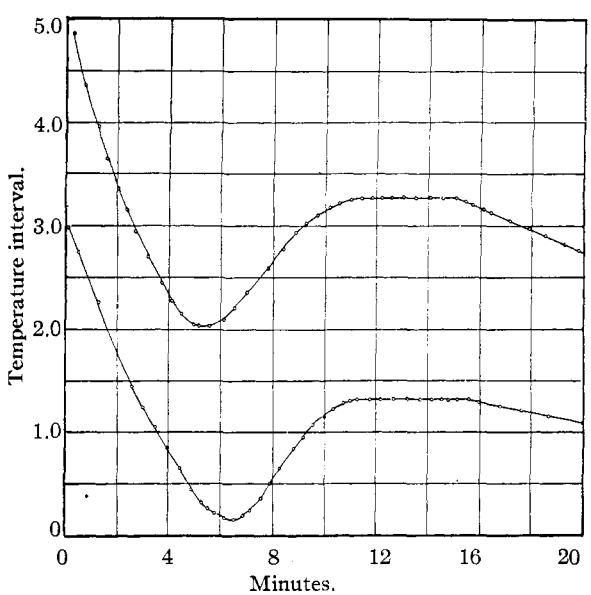

Fig. 1.—Time–temperature cooling curves of (a) 186-membered oxyethylene glycol (upper); (b) 90-membered oxyethylene glycol (lower).

Chlorine could not be detected in either of the isolated reaction products and their refractive indices gave the values to be expected for such higher members of this series.

Their purity was shown by the constancy of the freezing point following several recrystallizations. A further series of recrystallizations was carried out on the pure glycols and, while the final product represented only about 60% of the starting material, it was found that the freezing point of initial and final products was the same. Additional evidence of the purity of the 90- and 186-membered oxyethylene glycols was found in their time–temperature cooling curves (Fig. 1).

The preparation of derivatives of the two glycols suitable for end-group molecular weight determinations proved impracticable because the solubility and other physical characteristics of such derivatives were found to parallel those of the corresponding glycols so closely, even when large groups were attached, that their isolation in the pure state was rendered almost impossible.

Cryoscopic molecular weights, also, could not be employed as they had no significance due to the difficulty in measuring accurately the small freezing-point depression in question.[4]

The method of synthesis of the glycols together with the evidence of their purity, as shown by their physical properties, is strong evidence for the establishment of their molecular weights. Furthermore, the freezing points are shown to vary in a regular manner with the molecular weight and in ascendancy with a relationship developed by Lovell and Hibbert.[5]

The solubility characteristics of 90- and 186-membered glycols are the same as those of the lower members of the series. One of the most outstanding properties of these long chain compounds is their ready solubility in common solvents.

The birefringence observed[3] with the lower members of this series is shown in the photomicrograph

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(3) Fordyce, Lovell and Hibbert, THIS JOURNAL, **61**, 1905 (1939).

(4) An investigation of the determination of the molecular weights of the polyoxyethylene glycols by the "spinning top" method is being carried out by Professor McBain, Stanford University, and it is our intention to obtain supporting evidence from osmotic pressure measurements.

(5) Lovell and Hibbert, THIS JOURNAL, **61**, 1916 (1939).

of the extinction cross produced through crossed nicols by a thin film of 90-membered oxyethylene glycol when allowed to cool slowly. A similar effect has also been observed by Staudinger, Staudinger and Sauter[6] for higher molecular weight polyethylene oxides.

Experimental Part

The operations were carried out by the method described previously[3] and the same precautions taken to ensure purity and freedom from moisture of the necessary reagents. Because of the very small amounts of sodium required to form the sodium salts of the 42- and 90-membered polyoxyethylene glycols, respectively, it was necessary to carefully free these glycols from all trace of water prior to use. This was accomplished by passing a very fine stream of dry air through the glycol at 100° at a pressure of 0.010 mm. After four hours of this treatment the glycol was moisture free. The vacuum was then broken by admitting, very carefully, dried oxygen-free nitrogen and an atmosphere of the gas maintained in the flask throughout the sodium salt formation and the ensuing reaction with the dichloride.

Synthesis of the 90-Membered Oxyethylene Glycol, $HO(CH_2CH_2O)_{90}H$.—42-Membered oxyethylene glycol (20.0 g., 0.0108 mole) was placed in a 50-cc. side-arm distilling flask and dried as described above. Metallic sodium (0.25 g., 0.0108 mole), which had been cut and weighed under petroleum ether (b. p. 30–50°), was added in one addition at 80° to the glycol, kept under a nitrogen atmosphere. The reaction mixture was stirred by a mercury seal type of stirrer and a slow stream of nitrogen was kept flowing constantly through the side arm. After stirring for eleven hours at 80° the temperature was raised during two hours to 135° and then stirred at this temperature for a further three hours to complete the sodium salt formation. Hexaoxyethylene glycol dichloride (1.91 g., 0.006 mole, 10% excess) was then added at 135°, dropwise, to the glycol solution of the sodium during a twenty-five minute period and stirring continued for a further nineteen hours until the solution reacted neutral to phenolphthalein.

The reaction mixture was cooled, mixed with four volumes of dioxane, centrifuged and, after decanting from the precipitated potassium chloride, the dioxane removed at 100° (0.15 mm.).

The residual oil was dissolved in 100 cc. of methanol, 350 cc. of ether added and then decolorized by stirring for four hours with charcoal (3 g.). After filtration, the crude crystalline glycol was obtained by cooling to −11° in a brine-bath. The product was filtered, washed with anhydrous ether, redissolved in a mixture of methanol (100 cc.) and ether (350 cc.) and recrystallized at −11°.

Repeated recrystallizations under the same conditions to constant freezing point gave the pure 90-membered oxyethylene glycol (8.0 g., 36.7%); f. p., 40.6°; $n^{60°}D$ 1.4570.

(6) Staudinger, Staudinger and Sauter, *Z. physik. Chem.*, **B37**, 403 (1937).

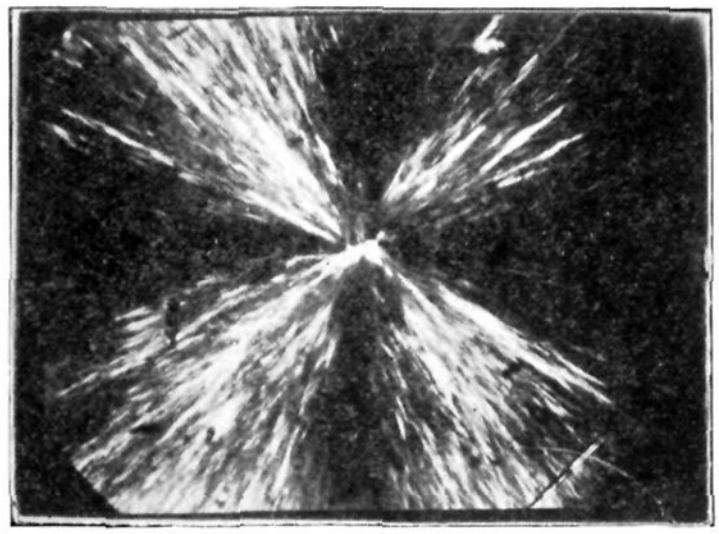

Fig. 2.

Synthesis of 186-Membered Oxyethylene Glycol, $HO(CH_2CH_2O)_{186}H$.—The 90-membered oxyethylene glycol (14.3 g., 0.0036 mole), contained in a 50-cc. side-arm distilling flask, was dried as above under vacuum in a nitrogen atmosphere. Metallic sodium (0.08 g., 0.0035 mole) which had been cut and weighed under petroleum ether (30–50°) was added in one addition at 80°. The reaction mixture was stirred with a mercury seal type of stirrer and a dry nitrogen atmosphere maintained throughout the reaction. After stirring for seventeen and one-half hours at 80° the temperature was raised during one hour to 135° and stirring continued at that temperature for an additional five and one-half hours to complete the sodium salt formation. Hexaoxyethylene glycol dichloride (0.60 g., 0.00188 mole, 4% excess) was then added dropwise during a period of five minutes and stirring continued at the same temperature for six and one-half hours until neutral (phenolphthalein). The reaction mixture was cooled, dissolved in four volumes of anhydrous dioxane, centrifuged and after decanting from the precipitated potassium chloride the dioxane then removed at 100° (15 mm.).

The residual oil was dissolved in 135 cc. of methanol and 35 cc. of ether added, the solution decolorized by stirring for three hours with charcoal and the crystalline glycol isolated by cooling to −11°. It was filtered, washed with anhydrous ether, then dissolved in methanol (135 cc.), ether (35 cc.) added, and recrystallized again by cooling. After ten or eleven such crystallizations to constant freezing point, pure 186-membered oxyethylene glycol was obtained: yield, 4.72 g. (47% of theoretical); f. p., 44.1°; $n^{60°}D$ 1.4572.

Summary

1. The syntheses of 90-membered oxyethylene glycol, $HO(CH_2CH_2O)_{90}H$, and 186-membered oxyethylene glycol, $HO(CH_2CH_2O)_{186}H$, are described.

2. The time–temperature cooling curves of the recrystallized products serve to indicate their purity.

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