

# The Preparation and Properties of 2, 3, 4, 6-Tetraethyl- $\alpha$ -ethyl-*D*-glucoside<sup>1</sup>

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Numerous research studies have been devoted to the alkylation of the carbohydrates. The first methylating agent, introduced by Purdie and Irvine (1), to be applied successfully to  $\alpha$ -methyl-*D*-glucoside was methyl iodide in the presence of silver oxide suspended in methyl alcohol. Somewhat later, Haworth (2) obtained comparable results by the use of methyl sulfate in the presence of aqueous sodium hydroxide. West (3) modified the Haworth procedure by using carbon tetrachloride as a solvent during the initial stages of the alkylation and succeeded in methylating *D*-glucose directly. Subsequently, using liquid ammonia as the solvent, Muskat (4) developed a method which permitted the use of either methyl iodide or methyl sulfate in the direct methylation of *D*-glucose. Padgett (5), by the use of modified Haworth and Irvine procedures, prepared and described 2,3,4,6-tetraethyl- $\alpha$ -methyl-*D*-glucoside. As his starting material, he used  $\alpha$ -methyl-*D*-glucoside. The present study was undertaken with the hope of obtaining 2,3,4,6-tetraethyl- $\alpha$ -ethyl-*D*-glucoside by the direct ethylation of *D*-glucose.

Numerous variations of four different methods were investigated in the preparation of 2,3,4,6-tetraethyl- $\alpha$ -ethyl-*D*-glucoside. *D*-Glucose was treated with ethyl sulfate dissolved in carbon tetrachloride and neutralized with (a) aqueous sodium hydroxide, (b) normal butyl amine, (c) alcoholic sodium ethoxide, and (d) alcoholic sodium hydroxide. Some of the results obtained by the use of these different alkalies are given in Table I.

TABLE I. RELATIVE EFFECT OF THE DIFFERENT ALKALIES

Method	First Step	Second Step	Base	Yield	% Yield	Remarks
a.1.	55°C.	70°C.	NaOH	1 g.	2.3	Rod stirrer
2.	70°C.	85°C.	NaOH	3 g.	6.8	Better stirring
3.	60°C.	82°C.	NaOH	7 g.	15.8	Good agitation
b.	65°C.	80°C.	C <sub>4</sub> H <sub>9</sub> NH <sub>2</sub>	8 g.	18.0	Tarry product
c.	65°C.	80°C.	Et.ONa	1 g.	2.3	Good agitation
d.	65°C.	80°C.	Alc. NaOH	2 g.	4.5	Good agitation

Although 18 g. of material were obtained by Method b, the product contained an appreciable amount of tarry products; and the optimum conditions for ethylation were as follows: Twenty-five grams of *D*-glucose was dissolved in 15 cc. of water and added to a three-liter

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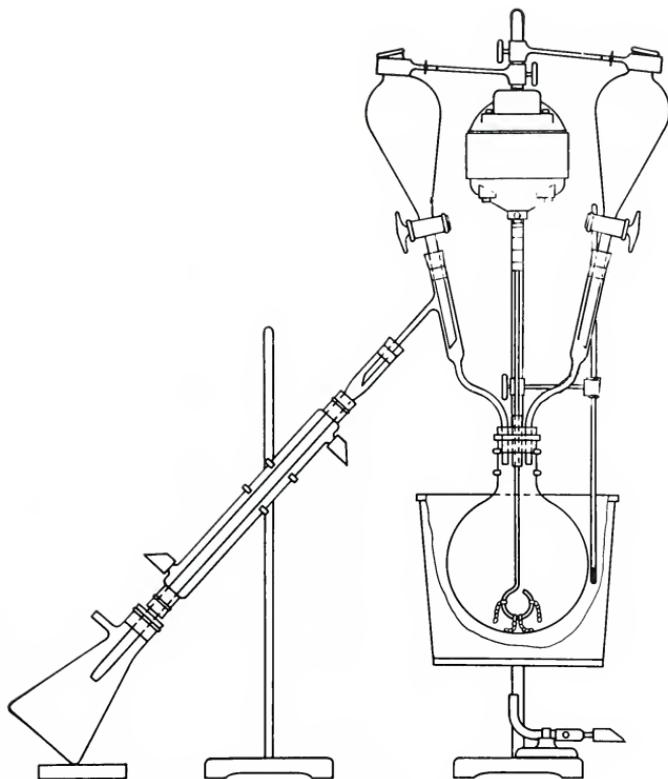


Fig. 1.

round-bottom flask which was equipped for vigorous agitation (Figure 1). Then 125 cc. of ethyl sulfate was dissolved in 125 cc. of carbon tetrachloride and added to the glucose solution. The mixture was agitated, the temperature of the bath raised of  $65^{\circ}\text{C}.$ , and aqueous sodium hydroxide (340 g. NaOH dissolved in water and diluted to one liter) added dropwise from the dropping funnel until the carbon tetrachloride had distilled. One to one and one-half hours were required for this operation. Then, 500 cc. of 8.5 N sodium hydroxide was added rather rapidly through the other dropping funnel and the temperature of the bath raised to  $85^{\circ}\text{C}.$  The bath was maintained at about this temperature while 220 cc. of ethyl sulfate was added at the rate of about two drops per second. When the addition of the ethyl sulfate was completed, the temperature of the water bath was raised to boiling and held there for about thirty minutes, and the bath was then allowed to cool.

The mixture was extracted with six 100 cc. portions of chloroform, and the extracts were dried with anhydrous sodium sulfate, decolorized by treatment with Norite, and filtered. The chloroform was removed by distillation under diminished pressure, and a light yellow sirup of crude 2,3,4,6-tetraethyl- $\alpha$ -ethyl-*D*-glucoside was obtained. The sirup was rectified in a modified Podbielniak column (Figure 2) to give a colorless

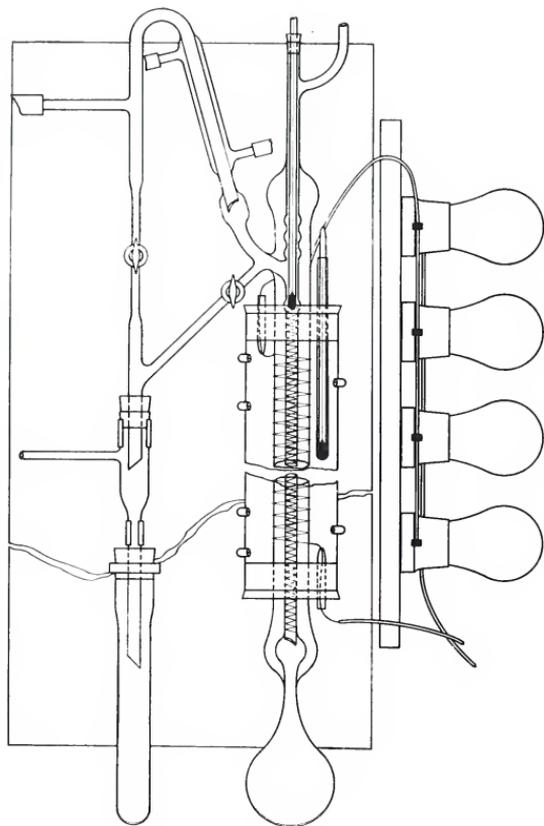


Fig. 2.

liquid which boiled at  $99.8^{\circ}\text{C}$ . at 0.2 mm. Its refractive index was found to be 1.4462 at  $25^{\circ}\text{C}$ . The average yield was seven grams. This product, when subjected to hydrolysis, gave the 2,3,4,6-tetraethyl-*D*-glucose described by Padgett (5).

The optimum conditions for the second step in the ethylation were determined by making a study of the ethylation of  $\alpha$ -methyl-*D*-glucoside with ethyl sulfate in the presence of aqueous sodium hydroxide. The method of West and the method of Haworth were both studied. Some of these results are given in Table II.

The procedure used in Experiment 1a was as follows: Twenty-seven grams of  $\alpha$ -methyl-*D*-glucoside was placed in the ethylation flask. To this was added 500 cc. of 8.5 N sodium hydroxide solution, the temperature of the bath was raised to  $80^{\circ}\text{C}$ ., and 220 cc. of ethyl sulfate was added at the rate of about two drops per second. When the addition was completed, the temperature of the water bath was raised to boiling and maintained at that temperature for about thirty minutes and the bath allowed to cool. The product was isolated and purified as previously indicated. The average yield of crude material was 17 g.

In Experiment 2b, 27 g. of  $\alpha$ -methyl-*D*-glucoside was placed in the

TABLE II.

Experiment	Bath Temperature	Method of	Base Used	Yield	% Yield
1a	80°C.	West	8.5 N NaOH	17 g.	39.4
b	80°C.	West	12.5 N NaOH	10 g.	23.2
c	80°C.	West	24.5 N NaOH	3 g.	6.9
2a	80°C.	Haworth	12.5 N NaOH	9 g.	18.6
b	80°C.	Haworth	8.5 N NaOH	16 g.	37.1

ethylation flask and 100 cc. of 8.5 N sodium hydroxide added to facilitate stirring. The temperature of the water bath was then raised to 80°C., and 220 cc. of ethyl sulfate was added at the rate of about two drops per second, while an additional amount (400 cc.) of 8.5 N sodium hydroxide was added at the rate of about four drops per second, or at such a rate as to maintain a slightly alkaline solution. This addition usually required about two hours. The bath temperature was then raised to boiling and maintained at that temperature for about thirty minutes and the bath allowed to cool. The product was isolated and purified as previously described. The yields were 16 to 20 g.

### Summary

The following factors appear to be involved in the preparation of 2,3,4,6-tetraethyl- $\alpha$ -ethyl-*D*-glucoside: (1) vigorous agitation, (2) a suitable base in the proper concentration, and (3) the optimum temperature.

### Bibliography

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