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METHYLATION OF POLYSACCHARIDES WITH DIMETHYL SULFATE[1]

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The recent publications by Kuhn and co-workers[2,3] on the methylation of carbohydrates using dimethyl sulfate, dimethyl sulfoxide (DMSO) and barium oxide and/or barium hydroxide prompts us to report similar work which we have been carrying out in this Laboratory simultaneously and independently.

In the earlier studies on methylation of carbohydrates[4,5] we have shown that sugars, oligosaccharides and most importantly, polysaccharides can be methylated by dissolving them in DMSO and treating the solutions with methyl iodide in presence of silver oxide

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1 This paper constitutes Part III of the series on Carbohydrate Methylations.

2 K. Wallenfels, G. Bechtler, R. Kuhn, H. Trischmann and H. Egge, Angew. Chem. (Int. edn.), 2, 515 (1963).

3 R. Kuhn and H. Trischmann, Chem. Ber., 96, 284 (1963).

4 H.C. Srivastava, S.N. Harshe and P.P. Singh, Indian J. Chem., 1, 304 (1963).

5 H.C. Srivastava, S.N. Harshe and P.P. Singh, Tetrahedron Letters, No. 27, 1869 (1963).

and drierite or barium oxide. The yields of the methylated products are excellent and in one step a high degree of methylation is achieved.

Falconer and Adams[6] and Hamilton and Kircher[7] have shown that oligosaccharides, which are soluble in tetrahydrofuran, and polysaccharide acetates can be methylated by dissolving them in tetrahydrofuran followed by portionwise addition of solid sodium hydroxide and dimethyl sulfate. This paper is concerned with the modification of the above procedure and it describes a general method whereby in one step almost complete methylation of polysaccharides can be achieved in near quantitative yields and without oxidative degradation of the polymers. The method is illustrated by methylation of starch and tamarind kernel polysaccharide (T.K.P.).

Methylation of Starch: Undegraded corn starch (1 g.) was dissolved in freshly distilled DMSO (70 ml.) and to the solution sodium hydroxide pellets (50 g.) and dimethyl sulfate (35 ml.) were added with stirring over a period of 8 hrs. For the first two hours the reaction was carried out at 20°C and in an atmosphere of nitrogen. After stirring for another 16 hrs., the reaction mixture was heated on a boiling water bath for one hour to decompose the methyl sulfate. Water (100 ml.) was added to dissolve the unreacted sodium hydroxide and the mixture, after cooling to 5°C, was neutralized with 10N sulfuric acid. The precipitated sodium sulfate was filtered off, the residue washed with chloroform and the

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6 E.L. Falconer and G.A. Adams, Can. J. Chem., 34, 338 (1956).

7 J.K. Hamilton and H.W. Kircher, J. Amer. Chem. Soc., 80, 4703 (1958)

aqueous filtrate extracted with chloroform in a liquid-liquid extractor for 12 hrs. The chloroform extract was dried (Na_2SO_4) and evaporated *in vacuo* to afford a buff coloured solid (1.24 g., OCH_3, 37.0%; Calcd. value: 45.6%). The product was fractionated by dissolving it in acetone and adding a small quantity of ethyl ether until turbidity appeared. The precipitated material was centrifuged off and the supernatant evaporated to give a light coloured solid. (1.15 g., 91% yield of theory; OCH_3, 42.3%).

Methylation of T.K.P.: T.K.P. (1.2 g.), purified twice *via* copper complexing, was methylated by dissolving in DMSO (100 ml.) and adding solid sodium hydroxide (50 g.) and dimethyl sulfate (35 ml.). The detailed experimental procedure was similar to that described under methylation of starch. Yield of the crude product was 1.5 g. (OCH_3, 39.9%; Calcd. value on the basis of a ratio of glucose:galactose:xylose as 8:2:3[8], 44.0%). It was fractionated with acetone and ethyl ether to afford a light coloured friable solid (1.4 g., 93% yield of theory; OCH_3, 41.5%).

Discussion:

The results of methylation of starch when compared with the results obtained by methylation with DMSO-BaO-CH_3I[5] show that the present method gives higher degree of methylation. This is corroborated by a very low degree of OH absorption (3400-3600 cm^{-1}) in the infrared by the methylated starch II (see Fig.1) as compared with I. Furthermore, the material II shows hardly any absorption at 1736 cm^{-1} indicating

8 H.C. Srivastava and Prem Pal Singh, unpublished results.

thereby that the starch is not oxidized during methylation with dimethyl sulfate, sodium hydroxide and DMSO.

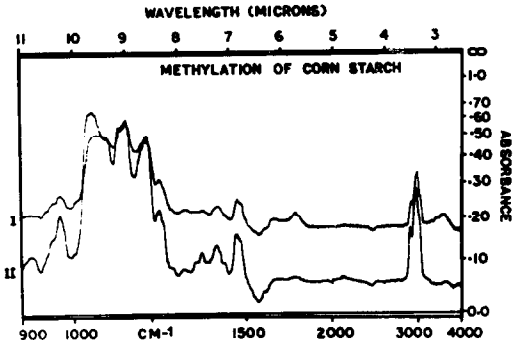

FIG.1

I AFTER ONE METHYLATION WITH DMSO, BaO & CH_3I

II AFTER ONE METHYLATION WITH DMSO, $(CH_3)_2SO_4$ & NaOH

It is of interest to note that Wallenfels et al[2] have methylated soluble starch, which is generally a degraded starch, with DMSO, dimethyl sulfate and BaO with excellent results but have observed that by their procedure it is not possible to methylate untreated starch. It is apparent from the results given above that undegraded starch can be methylated conveniently and efficiently by our method of methylation.

In connection with the constitutional studies on T.K.P., we had occasion to permethylate the polysaccharide. Complete methylation of the polysaccharide could not be achieved by the known methylation procedures. Thus, after three Haworth and six Purdie methylations,

the methoxyl content of the methylated product was only 37.7%. When the partially methylated polysaccharide was further methylated with dimethyl sulfate, DMSO and barium oxide[2,3], the methoxyl content was raised to 39.5%. Methylation of the partially methylated polysaccharide either by sodium, liquid ammonia and methyl iodide[9,10] or by N,N-dimethylformamide, methyl iodide and silver oxide[11] did not raise the methoxyl content beyond 40%. White and Rao[12] have also methylated T.K.P. and after seven Haworth methylations, the methylated product was obtained in 66% yield and had a methoxyl content of 42.3%. In contrast to the number of steps involved and the time spent on methylation in the above procedures, our method has given in just one step 93% yield of a product having a methoxyl content of 41.5%. Infrared spectra of the products obtained by methylation of T.K.P. by various methods are given in figure 2. It is apparent from these spectrograms that T.K.P. methylated by DMSO, sodium hydroxide and dimethyl sulfate has the minimum of unmethylated hydroxyl groups and carbonyl functions. This method has also been used in the methylation of a protein-amylose complex[13] isolated from the seeds of Pongamia glabra vent. As with starch and T.K.P., almost

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9 K. Freudenberg, E. Plankenhorn and H. Boppel, Ber., 71, 2435 (1938).

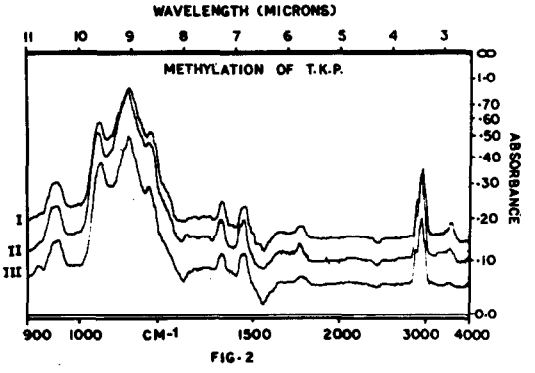
10 J.E. Hodge, S.A. Karjala and G.E. Hilbert, J. Amer. Chem. Soc., 73, 3312 (1951).

11 R. Kuhn, H. Trischmann and I. Löw, Angew. Chem., 67, 32 (1955).

12 E.V. White and P.S. Rao, J. Amer. Chem. Soc., 75, 2617 (1953).

13 H.C. Srivastava and S.N. Harshe, to be published.

complete methylation was achieved in a single step methylation.



FIG·2

I AFTER 3 HAWORTH AND 6 PURDIE METHYLATIONS
II I AFTFR ONE METHYLATION WITH DMSO,$(CH_3)_2SO_4$ & BaO+$Ba(OH)_2$
III AFTER ONE METHYLATION WITH DMSO,$(CH_3)_2SO_4$ & NaOH

As indicated in our earlier publication[5], DMSO is an excellent solvent for a variety of polysaccharides; consequently, our method of methylation should prove to be of general use in permethylating carbohydrate polymers. By analogy, the lower molecular weight carbohydrates, namely, the sugars, oligosaccharides and their derivatives, which are not sensitive to strong alkali, should be amenable to this methylation procedure. N,N-Dimethylformamide could be substituted or replaced in part for DMSO as the solvent medium for the reaction.

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