XLV.—*The Preparation of α- and β-Methylglucoside.*

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Being recently engaged on work in which α-methylglucoside was required in some quantity, we attempted to simplify Emil Fischer's method of preparation (*Ber.*, 1895, **28**, 1151), and found that this compound can be far more easily obtained merely by boiling pure glucose with methyl alcohol and hydrogen chloride under reflux, than by means of sealed tubes. We then discovered that Bourquelot (*Ann. Chim.*, 1915, **3**, 298) had already prepared α-methylglucoside by boiling glucose with methyl alcohol containing 0·25% of hydrogen chloride for 80 hours, obtaining a yield of about one-tenth the glucose used, and that Hudson (*J. Amer. Chem. Soc.*, 1925, **47**, 266), in consequence of Bourquelot's work, had prepared methylxyloside and some similar compounds in an analogous way but in a much shorter time. These preparations, being incidental, are not indicated in the titles of the papers and so may easily be overlooked. At this stage we received "Organic Syntheses," Vol. VI, in which the preparation of α-methyl-*d*-glucoside is described, p. 64. According to the method there given, a total yield of 48·5—49·5% of the theoretical may be obtained by boiling glucose for, altogether, 228 hours—nearly 10 days—with methyl alcohol containing 0·25% of hydrogen chloride, but this, the most recent procedure, does not seem to us to be by any means the best, and therefore it may be of use to others if we describe the process which we have found to be the most advantageous. It has been arrived at after a considerable number of trials, in which the time of boiling and the quantity of hydrogen chloride present were varied, the operations being controlled by the polarimeter.

The quality of the glucose is an important factor in the success of the preparation. We used that supplied by the British Drug Houses as *dextrose pure anhydrous.* Of this material, 200 g. were dissolved in 400 g. (half the quantity recommended by Fischer) of methyl alcohol, carefully dried over lime and containing 3% of hydrogen chloride. The rotation of the resulting mixture, determined as soon as possible after the glucose had gone into solution, was $\alpha^{17°}_{5461}$ (100 mm.) = *ca.* + 10°. The solution was then boiled on the water-bath under reflux for 4½ hours, 5 g. of good animal charcoal having been added 10 minutes before the end of this time. The rotation had then risen to *ca.* + 36° and longer boiling produced little further change. In another experiment, after 24 hours' boiling, the rotation was + 41·5°.

(A) The solution was then filtered rapidly and cooled in ice-water with occasional stirring. In the course of ¾ hour the reaction mixture formed a thick paste. The α-methylglucoside was filtered off and, after being washed with a little methyl alcohol, dried on porous plate. The yield was 82 g. of m. p. *ca.* 163°.

(B) From the mother-liquor some 200 c.c. were distilled off. The residue, after treatment with charcoal as before and cooling in ice-water, etc., yielded another 44 g. of α-methylglucoside having m. p. 155—160°; making a total yield of 126 g. of crude product (61·5% of the theoretical after only a short period of boiling).

(C) From this crude yield, after recrystallisation from methyl alcohol (140 g. requires 350 c.c. of alcohol) and working up of the mother-liquors, 92 g. of pure α-methylglucoside were obtained of m. p. 165—166° and rotation $[\alpha]^{12·5°}_{D}$ (c = 1·0443 in water) = +157·9°.

(D) The mother-liquor from (B), cooled in a freezing mixture and seeded with β-methylglucoside, yielded, on standing over-night, 16 g. of crude β-methylglucoside of m. p. 98—100°.

(E) The mother-liquor from (C), on standing, gave, without seeding, 3 g. of crude β-methylglucoside of m. p. 104—105°.

The crude products from (D) and (E) on recrystallisation from methyl alcohol yielded 10·2 g. of β-methylglucoside of m. p. 107—108° and rotation $[\alpha]_D^{15°}$ ($c = 0{\cdot}303$ in water) $= -26{\cdot}38°$. This, recrystallised from methyl alcohol, gave 4·8 g. of pure β-methylglucoside of m. p. 110° and rotation $[\alpha]_D^{15°}$ ($c = 0{\cdot}276$ in water) $= -31{\cdot}97°$.

It will readily be understood that there is a disproportionate loss in recrystallising an easily soluble substance like β-methylglucoside in small quantity, but it appears from our experiments that with a total time of boiling of only 4½ hours it is quite easily possible to obtain 42·6% of the theoretical yield of α-methylglucoside and at least 2·5% of the theoretical yield of β-methylglucoside or 45·1% in all. From the mother-liquors still further quantities of both the α- and the β-derivative may be obtained, but their recovery is probably not worth the time spent upon it, unless the mother-liquors from several preparations are worked up together.

If, after stage (B), the mother-liquors are boiled, with addition of more hydrogen chloride, under reflux for a further period, more α-methylglucoside is produced at the expense of β-methylglucoside, and the yield of the former can be increased. In this way, aiming at a maximum production of α-methylglucoside, we succeeded, in several preparations, in raising the yield to 75% of the theoretical, but this increased yield does not repay the trouble it involves.

Although we have described the above experiment to show what may be obtained after 4½ hours' boiling, the best practical procedure for the preparation of α-methylglucoside would be to boil over-night and work up the product next morning.

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