Biochemical Studies on Carbohydrates

CCXVIII. N-Acetyl-4,6-benzylidene-glucosamine

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N-Acetylglucosamine was condensed with benzaldehyde under the conditions, which Wood¹⁾ had preferred for synthesis of 4,6-benzylidene-glucose, with a yield reaching 90% of theory. The product (**I**) reduced Fehling reagent and consumed the calculated amount of iodine. Hence, in it, the glycosidic OH of N-acetylglucosamine is not participant in the condensation. It further proved to possess another OH in a free state. By successive methylations with dimethylsulfate, a monomethyl (**II**) and a dimethyl (**III**) derivative were produced. And hydrolysis of the latter derivative with 60% acetic acid gave a methylglycoside of N-acetyl-monomethyl-glucosamine (**IV**), which changed into a monomethylglucosamine hydrochloride (**V**) in turn on boiling with 2.5 *N* HCl. **V** melted and rotated D-light identically as 3-methyl-glucosamine hydrochloride (Neuberger²⁾) did, and mixed melting point test showed no depression. **IV** reduced neither alkaline iodine nor periodate, but was levorotatory contrary to the dextrorotatory N-acetyl-3-methyl- α -methyl-glucosaminide (Neuberger²⁾), so that it is assumed as N-acetyl-3-methyl- β -methyl-glucosaminopyranoside.

Therefore **I** is concluded to be N-acetyl-4,6-benzylidene-glucosamine.

II gave N-acetyl- β -methyl-glucosaminopyranoside (Zilliken *et al.*³⁾) (**VI**) when hydrolyzed with hot 60% acetic acid.

EXPERIMENTAL

N-Acetyl-4,6-benzylidene-glucosamine. 10 g. of fine powdered anhydrous *N*-acetylglucosamine, 40 g. of freshly fused and powdered zinc chloride and 200 cc. of freshly distilled benzaldehyde were shaken together for 12 hours at room temperature. The mixture was poured into 250 cc. of iced water and stood for several hours. The white pasty precipitate was kneaded with 200 cc. of iced water, filtered off and agitated in 500 cc. of petroleum ether, and the insoluble crystalline residue was brought onto a suction funnel.

It was heated with 1.5 l. of abs. methanol under reflux on boiling water until it dissolved entirely, and filtered quickly while hot. The filtrate was distilled in vacuo to about 300 cc. and placed in a refrigerator. The crystalline deposit was washed with ice-chilled methanol. About 8 g. of crystals (soft long needles) was yielded. Recrystallization from abs. methanol did not elevate the melting point. From the mother fluids was obtained about 4 g. of crystals of similar appearance. F.P., 214–215° (decomp.); $[\alpha]_D^{25} +10.0^\circ$ (c 1.0; pyridine; final). Found: N, 4.55; CH_3CO , 14.02; OH, 10.72; iodine use as glucose, 57.0. $\text{C}_{15}\text{H}_{19}\text{O}_6\text{N}$ requires N, 4.53; CH_3CO , 13.90; OH, 11.00; iodine use as glucose, 58.00. Soluble in pyridine, dioxane, alkaline methanol and ethanol and hot plain methanol. Slightly soluble in hot ethanol and CHCl_3 . Insoluble in water.

N-Acetyl-4,6-benzylidene- β -methyl-glucosaminide. 5 g. of N-acetyl-4,6-benzylidene-glucosamine was dissolved in 50 cc. of ice-chilled methanolic 2 *N* NaOH, and after addition of 1.8 cc. of dimethylsulfate, shaken under continuous cooling until it reduced Fehling reagent no more, followed by pouring into 500 cc. of iced water. After several hours the mixture containing some deposit was filtered. The filtrate was concentrated, and when crystals began to appear, it was placed in a refrigerator to complete crystallization. The deposit (crystals in long needles) was recrystallized from 50 cc. of methanol. Yield 2 g. (38% of theory). F.P. 252–253° (decomp.). $[\alpha]_D^{18} -40^\circ$ (c 1.0; CHCl₃). It did not reduce Fehling reagent and smelled of benzaldehyde on boiling with 60% acetic acid or 1 *N* HCl. Found: N, 4.26; CH₃CO, 12.9; OH, 5.42; CH₃O, 10.25. C₁₆H₂₁O₆N requires N, 4.33; CH₃CO, 13.6; OH, 5.27; CH₃O, 9.6.

N-Acetyl-4,6-benzylidene-3-methyl- β -methyl-glucosaminide. 3.5 g. of N-acetyl-4,6-benzylidene- β -methyl-glucosaminide was dissolved in 150 cc. of dioxane, warmed to 50°C and treated with ten portions of 15 cc. dimethylsulfate and of 33 cc. 30% NaOH at 10-minute intervals. After standing for a few hours at room temperature, the mixture was poured into a large volume of iced water, and the crystalline precipitate was filtered off with suction. The crystalline material was recrystallized from ethanol. Soft fine needles weighing 2.9 g. (79% of theory) were yielded. F.P. 208–209° (decomp.). $[\alpha]_D^{15} -76.0^\circ$ (c 1.0; CHCl₃). Found: N, 4.1; CH₃O, 17.6. C₁₇H₂₃O₆N requires N, 4.2; CH₃O, 18.4.

N-Acetyl-3-methyl- β -methyl-glucosaminide. 0.65 g. of N-acetyl-4,6-benzylidene-3-methyl- β -methyl-glucosaminide was suspended in 15 cc. of 60% acetic acid and refluxed on boiling water. The clear solution given in 7 minutes was further heated for 15 minutes. When cold it was diluted with three volumes of water, and after exhaustion with three 15 cc. portions of chloroform, distilled in vacuo, and the crystalline residue was recrystallized from 5 cc. of ethanol. 0.30 g. (62.5% of theory) of crystals in fine needles was given. F.P. 164–165°. $[\alpha]_D^{17} -58.4^\circ$ (c 1.4; H₂O). Found: N, 5.8; CH₃O, 24.5; OH, 11.2. C₁₀H₁₉O₆N requires N, 5.6; CH₃O, 24.9; OH, 10.1. The substance did not reduce alkaline iodine and sodium metaperiodate.

3-Methyl-glucosamine hydrochloride. 2 g. of N-acetyl-3-methyl- β -methyl-glucosaminide was hydrolyzed by heating with 50 cc. of 2.5 *N* HCl under reflux at 100°C for 4 hours. The brown solution was decolorized with charcoal, and the filtrate was concentrated to dryness, dissolved in 15 cc. of hot methanol and allowed to cool. Crystallization was processed by addition of acetone in small portions—fine needles. Yield 1.2 g. (60% of theory). F.P. 214–215° (decomp.). $[\alpha]_D^{25} +120^\circ$ (5 min.), $+92.0^\circ$ (10 h.; eq. val.) [c 1.2; H₂O]. Found: N, 6.1; CH₃O, 12.7. C₁₇H₁₅O₅N·HCl requires N, 6.1; CH₃O, 13.5. This product melted also at 214–215°, when mixed with the one prepared according to Neuberger.²⁾

N-Acetyl- β -methyl-glucosaminide. 1 g. of N-acetyl-4,6-benzylidene- β -methyl-glucosaminide was hydrolyzed with 60% acetic acid and further treated as N-acetyl-4,6-benzylidene-3-methyl- β -methyl-glucosaminide was. The crystals given—needles—weighed 0.47 g. (64.5% of theory). F.P. 197–198°. $[\alpha]_D^{20}$

—42.5° (c 1.0; H₂O).

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References

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