

NOTE

A Simplified Preparation of *N*-Acetyl-D-glucosamine

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N-Acetyl-D-glucosamine (*N*-acetyl-2-amino-2-deoxy-D-glucose) usually has been prepared by the method of White¹⁾, which utilizes the action of silver acetate and acetic anhydride on the hydrochloride in methanol and in the dark. Kuhn and Haber²⁾ acetylated D-glucosamine in *N,N*-dimethylformamide at low temperature and Roseman and Ludowieg³⁾ treated D-glucosamine hydrochloride, in dilute methanol, with acetic anhydride in the presence of Dowex-1. It is also prepared by the action of sodium acetate and acetic anhydride in methanol⁴⁾.

A simpler and cheaper method has been devised in the course of study of some D-glucosamine derivatives in our Laboratory, whereby *N*-acetyl-D-glucosamine of high purity is obtained in good yield. This procedure is based upon the finding that a suspension of D-glucosamine hydrochloride in an adequate volume of methanol gives a supersaturated solution of D-glucosamine when treated with an equivalent amount of sodium methoxide,** and that *N*-acetylation of the D-glucosamine is effected readily in this solution, without any catalytic substance, by treatment at room temperature with from one and a half to two equivalents of acetic anhydride. The methanolic supersaturated solutions of D-glucosamine, so formed, can be maintained for some time at room temperature in concentrations as high as 10% or some more, whereas its usual solubility is reported to be 1/38 in boiling methanol⁵⁾. Under adequate conditions, the yields of *N*-acetyl-D-glucosamine thus prepared are of quantitative level, and the crude preparations, m.p. ranging from 200° to 204°, are pure sufficiently for ordinary purposes. This method has been used in the preparations of a series of *N*-acylated derivatives of D-glucosamine with saturated fatty acids, the properties of which will be reported elsewhere.

EXPERIMENTAL

Ten grams of D-glucosamine hydrochloride, prepared from crab shell by the method of Purchase and Brauns⁶⁾, was placed in 80-100 ml. of methanol in which 1.1g.

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** Liberation of D-glucosamine from its salts has been reported (O. Westphal and H. Holzmann, *Ber.*, **75**, 1274 (1942)).

NOTE

of sodium had been dissolved. On gentle swirling, sodium chloride separated and was removed by filtration and washed with a small amount of methanol.* Acetic anhydride (7.0-9.4 g.) was added immediately to the supersaturated solution of D-glucosamine at, or slightly above, room temperature and the reaction mixture was shaken mechanically for 0.5-1 hr. Crystallization usually ensued immediately and was completed by standing overnight at icebox temperature. The crude *N*-acetyl-D-glucosamine (*N*-acetyl-2-amino-2-deoxy-D-glucose) was removed by filtration, washed with cold methanol and then ether, and dried over sulfuric acid (concd.) at room temperature; yield maximum 10g., m. p. ranged from 200° to 204°. Recrystallization was effected from the minimal quantity of water by the addition of ethanol and then ether to incipient turbidity. Colorless needles formed on standing at icebox temperature, m. p. 208° (uncorrected), $[\alpha]_D^{25}$ 40.5° (after 24 hr., *c* 1 water).

Anal. Calcd. for $C_8H_{15}O_6N$; C, 43.43; H, 6.84; N, 6.33. Found: C, 43.10; H, 6.82; N, 6.22.

Similar material was obtained when the sodium was replaced by an equivalent of sodium hydroxide. D-Galactosamine hydrochloride was acetylated by the method to yield *N*-acetyl-D-galactosamine (*N*-acetyl-2-amino-2-deoxy-D-galactose).

REFERENCES

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- (6) E. R. Purchase and C. E. Brauns, *Org. Syntheses*, **26**, 36 (1946).

* Rotatory value of D-Glucosamine in MeOH: $[\alpha]_D^{25}$ 34° (30 min.) 8° (24 hr.) (*c* 3 %).