Synthesis and Properties of 6-Deoxy-6-mercapto-D-glucosamine

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6-Deoxy-6-mercapto-D-glucosamine hydrochloride was synthesized from N-anisylidene-1,3,4-tri-O-acetyl-6-O-tosyl-D-glucosamine, and some of its properties were compared with those of D-glucosamine hydrochloride.

Recently, the pharmaceutical importance of D-glucosamine has been recognized. Andrew J. Schmitz, Jr. and Michael Carlozzi reported that the antibiotic tetracycline mixed with D-glucosamine gave higher blood levels than tetracycline hydrochloride. The antitumor activity of D-glucosamine was suggested by J. H. Quastel and A. Cantero and H. A. Ball et al. Many derivatives of glucosamine were synthesized and the number of new ones is now increasing.

The present paper reports the preparation of 6-deoxy-6-mercapto-D-glucosamine which has not yet been described in the literature. The synthetic route is represented by the following series of reactions.

N-Anisylidene-1,3,4-tri-O-acetyl-6-O-tosyl-D-glucosamine (II) was prepared from N-anisylidene-D-glucosamine by the method of Ch. J. Morel, who reported the synthesis of 6-deoxy-D-glucosamine. The replacement of tosyl group by thioacetyl group was first reported by J. H. Chapman and L. N. Owen. Application of this reaction to compound II could provide N-anisylidene-1,3,4-tri-O-acetyl-6-deoxy-S-acetyl-6-thio-D-glucosamine (III) in 72% yield. The infrared spectrum in KBr pellet of compound III showed bands at 1760 cm⁻¹ and 1699 cm⁻¹, indicative of C=O vibration of O-acetyl group (−O−C−CH₃) and S-acetyl group (−S−O−C−CH₃) respectively.

The hydrolysis of N-anisylidene group of compound III in acetone solution gave 1,3,4-tri-O-acetyl-6-deoxy-S-acetyl-6-thio-D-glucosamine hydrochloride (IV). The compound IV exhibited a characteristic ultraviolet absorption spectrum in aqueous solution with a maximum at 229 μ (ε 5200), which is attributable to the thioacetyl group. The β-configuration of compound IV was determined from the infrared absorption spectrum (in KBr), which showed two bands at 909 and 895 cm⁻¹ and showed no distinct band between 860 and 800 cm⁻¹.

Deacetylation of compound IV with N-methanolic hydrogen chloride gave 6-deoxy-6-mercapto-D-glucosamine hydrochloride (V), which showed a positive nitroprusside test for the mercapto group and a positive red tetrazolium test for the reducing group. It is a well known fact that 2-aminohexoses do...
hardly produce the methylglycoside by refluxing in dilute methanolic hydrogen chloride. The infrared absorption spectrum of compound V in KBr pellet (Fig. 1) showed a band at 2555 cm\(^{-1}\), characteristic of SH group. The bands at 895, 823 and 768 cm\(^{-1}\) probably indicate \(\alpha\)-pyranose configuration. The specific rotatory power was \([\alpha]_D^{19} +98^\circ \rightarrow +76^\circ\) (after 5 hours) (c, 1.2\% in water), while \(\alpha\)-D-glucosamine hydrochloride was reported\(^4\) to have \([\alpha]_D^{19} +100^\circ \rightarrow +72.5^\circ\) (in water). The compound V showed a single spot with \(R_F\) value of 0.41 on a paper chromatogram using a mixture of n-butanol, acetic acid, water (4:1:2 V.) as the developing solvent, and ninhydrin or aniline hydrogen phthalate solution as spraying reagent. On the same paper chromatogram, \(\alpha\)-D-glucosamine hydrochloride showed two spots with \(R_F\) values of 0.26 and 0.30 (weaker)\(^9\).

**EXPERIMENTAL**

**N-Anisylidene-1,3,4-tri-O-acetyl-6-O-tosyl-\(\beta\)-D-glucosamine (II).**

This compound was prepared as described by Ch. J. Morel\(^6\) and showed m.p. 202\(^\circ\)C, \([\alpha]_D^{19} +99^\circ\) (c, 0.5\% in CCHCl\(_3\)).

**N-Anisylidene-1,3,4-tri-O-acetyl-6-deoxy-6-mercapto-\(\beta\)-D-glucosamine (III).**

A solution of II (3 g) and dry potassium thiolacetate (1.5 g) in acetone (50 ml) was refluxed for 6 hours. The solid was filtered off and washed with acetone, then the filtrate and washings were evaporated to dryness in vacuo. The residue was dissolved in chloroform and washed with a little water and the solvent was removed in vacuo. Recrystallization of the residue from methanol gave needle crystals (1.8 g), m.p. 162\(^\circ\)C, \([\alpha]_D^{19} +84^\circ\) (c, 0.5\% in CHCl\(_3\)).

**N-Anisylidene-1,3,4-tri-O-acetyl-6-deoxy-S-acetyl-6-thio-\(\beta\)-D-glucosamine Hydrochloride (IV).**

A solution of III (2 g) in acetone (50 ml) was heated to boiling, and to this solution 5N hydrochloric acid (1 ml) was added. After standing in a refrigerator for 3 hours, the crystalline precipitate formed was filtered. The crude product (1.5 g) was dissolved in 15 ml of water and, after the insoluble substance was removed by filtration, the solution was concentrated in vacuo to dryness. The residue was recrystallized from ethanol to give needle crystals (0.7 g), m.p. 210\(^\circ\)C (with decomposition), \([\alpha]_D^{17} +3.9^\circ\) (c, 6.5\% in water).

**N-Anisylidene-1,3,4-tri-O-acetyl-6-deoxy-S-acetyl-6-thio-\(\beta\)-D-glucosamine Hydrochloride (V).**

A solution of III (2 g) in acetone (50 ml) was refluxed for 4 hours in \(n\)-methanolic hydrogen chloride (25 ml) under CO\(_2\) gas. The solution was concentrat-
ed in vacuo to form needle crystals which were filtered off and washed with cold ethanol. The yield was 0.24 g. It showed m.p. 180°C (with decomposition).

Calcld. for C_{6}H_{13}NO_{4}S·HCl: C, 31.10; H, 6.09; N, 6.05%.

This compound is readily soluble in water, soluble in methanol and slightly soluble in ethanol and n-butanol.

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