D-Gulosamine from D-Xylose

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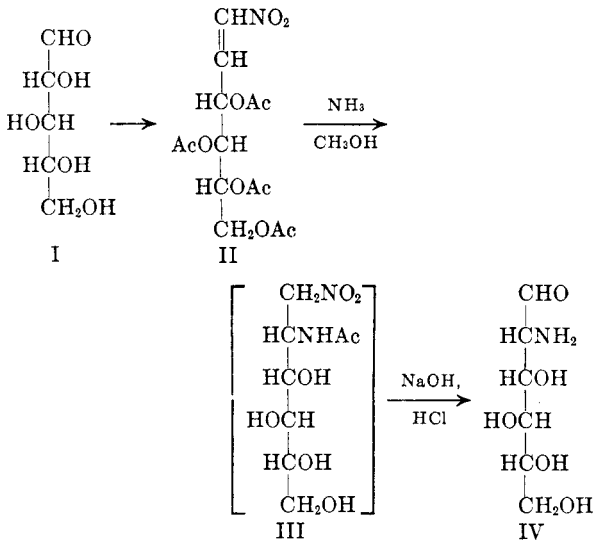
Recently, the synthesis of D-mannosamine[1,2] and D-glucosamine[2] from D-arabinose, by way of D-*arabino*-3,4,5,6-tetraacetoxy-1-nitro-1-hexene, has been described. The same sequence of reactions has now been applied to D-xylose to provide D-gulosamine hydrochloride in about 15% yield from the intermediate, acetoxylated nitroolefin.

D-Xylose (I) was converted first to D-*xylo*-3,4,5,6-tetraacetoxy-1-nitro-1-hexene (II) by condensation with nitromethane, acetylation, and treatment with sodium bicarbonate.[3] The action of methanolic ammonia on II gave an amorphous product, presumably a mixture of 2-acetamido-1,2-dideoxy-1-nitro-D-gulitol (III) and 2-acetamido-1,2-dideoxy-1-nitro-D-iditol, with the former predominating. The sodium salts of the mixture, on treatment with concentrated hydrochloric acid (Nef reaction[4,5]), yielded D-gulosamine (IV), isolated as the crystalline hydrochloride. Chromatography indicated that the epimeric D-idosamine also was formed in minor amount.



Increased interest in D-gulosamine has resulted from the observation that it occurs naturally as a component of the antibiotics streptothricin and streptolin B.[6] The amino sugar has been synthesized previously from D-galactosamine by configurational inversion at C_3,[7] and from D-xylose by condensation with hydrogen cyanide and aniline or *p*-toluidine, followed by controlled hydrogenation.[8] The complex mutarotation reported by Tarasiejska and Jeanloz[7] for D-gulosamine hydrochloride was not observed with our product, but rather our values agreed with the simple mutarotation reported by Kuhn and Bister.[8]

EXPERIMENTAL

D-*xylo*-3,4,5,6-Tetraacetoxy-1-nitro-1-hexene[3] (10.3 g., m.p. 114–115°) was covered with 100 ml. of methanol and the mixture was saturated with anhydrous ammonia at 0°. The resulting clear solution, protected from moisture with a drying tube, was allowed to warm to room temperature and stand overnight. Concentration in a stream of dry air then gave a dark brown sirup. This was extracted several times by trituration with chloroform and then heated at 90° and 1.5 mm. pressure to remove most of the acetamide. Decolorization in aqueous solution with carbon, concentration and drying over magnesium perchlorate at 1 mm. pressure yielded 7.1 g. of a light brown sirup. This was dissolved in 17 ml. of 2*N* sodium hydroxide and the solution added dropwise, with stirring, to 15 ml. of concd. hydrochloric acid. The resulting solution was cooled to 0°, saturated with hydrogen chloride, and the precipitated sodium chloride then removed by filtration (Whatman no. 42 paper). The filtrate was diluted sixfold with water, refluxed for 2 hr., decolorized and concentrated at reduced pressure to a sirup. Evaporation with ethanol then yielded a partly crystalline residue which, upon filtration with a small volume of methanol provided 3.2 g. of crude D-gulosamine hydrochloride, m.p. 157–163°.

The product at this stage was contaminated with ammonium chloride, presumably formed by the acid hydrolysis of unremoved acetamide. The inorganic salt was removed by chromatography over Amberlite IR-120 resin (3 × 27 cm.) as described by Kuhn and Bister.[8] The Fehling-positive, Nessler-negative fraction (100 to 775 ml. of eluate) yielded upon concentration 2 g. of D-gulosamine hydrochloride, m.p. 164–166° (dec. beginning at 150°) and $[\alpha]_D^{25}$ +15.4° (5 min.) → −9.8°, equil. in water, *c* 2.8. Several recrystallizations of this product from water by the addition of ethanol yielded 0.92 g. of pure D-gulosamine hydrochloride, m.p. 165–170° (dec. beginning at 153°) and $[\alpha]_D^{25}$ +24° (5 min.) → −19.1°, equil. in water (4 hr.), *c* 2.2. Kuhn and Bister[8] report m.p. 165–170° (dec. beginning at 150°) and $[\alpha]_D^{22}$ +32° (5 min.) → −19°, equil. in water (4 hr.), *c* 1, for D-gulosamine hydrochloride. Our synthetic product gave an x-ray powder diffraction pattern identical with that of naturally-occurring D-gulosamine hydrochloride obtained by the acid hydrolysis of streptolin-B.[6,9]

Chromatography of the initial, crude mixture of products on Whatman no. 1 paper with pyridine:ethyl acetate:acetic acid:water (5:5:1:3), in a cabinet saturated with pyridine:ethyl acetate:water (11:40:6),[10] showed two major products with $R_{glucosamine \cdot HCl}$ values of 1.06 and 1.30, respectively. Kuhn, Bister and Fischer[11] report values of 1.04 and 1.29, respectively, for D-gulosamine hydrochloride and D-idosamine hydrochloride in this solvent system.

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Formation of an Adduct of Triphenylboroxin and *p*-Phenylenediamine[1]

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Pyrolysis of the 1:1 adduct of boron trichloride and aniline is reported[5] to give good yields of 2,4,6-trichloro-1,3,5-triphenylborazine; hexaphenylborazine has been prepared[6] by pyrolysis of the adduct formed between phenyldichloroborane and aniline. Previous work in this laboratory[7] has shown that the 1:1 adduct of boron trichloride and *p*-phenylenediamine can be pyrolyzed to the cyclic trimer $(C_6H_5N_2B)_3$ and that pyrolysis of the 1:1 adduct of phenyldichloroborane and *p*-phenylenediamine leads to the monomeric $C_6H_4(NH)_2BC_6H_5$. We have extended this study to the pyrolysis of the 1:1 adduct of phenyldichloroborane and *p*-phenylenediamine.

The major products isolated from the pyrolysis of this adduct, whether the pyrolysis was done *in vacuo* or in refluxing xylene, were the mono- and dihydrochlorides of *p*-phenylenediamine and a new compound of formula $C_{54}H_{54}B_6N_6O_6$, which is best formulated as 2(triphenylboroxin)·3(*p*-phenylenediamine).

This compound melts at 167–168°, dissociates in benzene to form five moles of particles per mole of compound dissolved, dissociates to pure triphenylboroxin and *p*-phenylenediamine on heating *in vacuo* with the base appearing as a sublimate, and has an infrared spectrum very similar to a composite spectrum formed by combining the spectra of triphenylboroxin and *p*-phenylenediamine. Significant changes in the infrared spectrum of the compound, as compared with the composite spectrum, appear (1) in the N—H stretching vibrations of *p*-phenylenediamine where a shift from 2.98 μ to 2.90 μ and from 3.10 μ to 2.99 μ is observed (2), in the absorption at 7.54 μ which diminishes in intensity, and (3) in the boroxin ring absorption which is shifted from 14.5 μ to 14.85 μ.

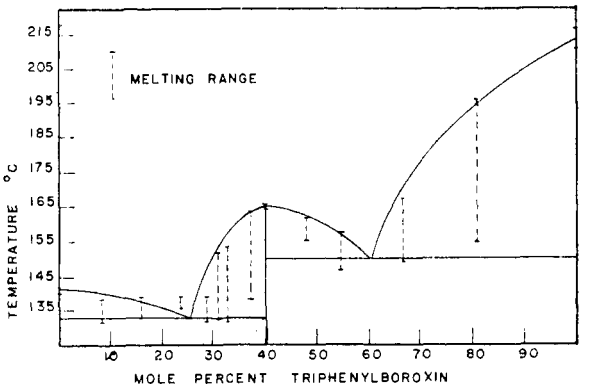

Fig. 1. Phase diagram of triphenylboroxin-*p*-phenylenediamine

The compound may be synthesized independently of the pyrolysis reaction by triturating triphenylboroxin and *p*-phenylenediamine in benzene in a 2:3 mole ratio and removing the benzene by vacuum distillation at room temperature. The phase diagram of the system triphenylboroxin–*p*-phenylenediamine indicates a congruently melting compound, m.p. 168°, at 40 mole% triphenylboroxin.

The presence of oxygen in the compound was not expected; care had been taken to avoid exposure of the system to moisture or the atmosphere. Residual moisture in the solvents used in working up the reaction mixture is the most likely source of the oxygen.

Similar compounds of the boroxin ring system and organic bases have been reported. Yabroff and Branch[8] have reported that simple amines will react to form adducts with phenylboric acid. Burg[9] reports a 1:1 compound of trimethylboroxin and trimethylamine. Snyder[10] reports a 1:1 compound of triphenylboroxin and pyridine and a 2:1 compound of triphenylboroxin and 3,6-diaminoacridine. The 2:3 compound of triphenylboroxin and *p*-phenylenediamine reported here is apparently of the same type as those reported by Burg, by Yabroff and Branch and by Snyder.

EXPERIMENTAL

Preparation of the 1:1 adduct. Phenyldichloroborane was prepared, following the method of Schupp,[11] by the chlorina-

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