teen minutes at 25° resulted in formation of a derivative of IV, but V was recovered unchanged. The derivative of IV was obtained by diluting the reaction product with water, adjusting the *p*H to 7 and filtering off the precipitate which was then crystallized as white plates from hot dioxane, yield 200 mg., m. p. 177–178°.

Anal. Found: C, 71.95; H, 9.50; N, 3.07. Calcd. for $C_{26}H_{41}O_4N$: C, 72.35; H, 9.57; N, 3.25.

The derivative contained a lactone group and a basic nitrogen (forms insoluble hydrochloride).

Antibacterial and other properties of the lichesterinic acids and related substances will be reported in the near future.

Acknowledgment.—We are indebted to M. E. Auerbach and staff for much of the analytical work presented.

Summary

The antibacterial agent from *Arctium minus*, $C_{18}H_{24}O_6$, has been indicated to have an α-methylene butyrolactone type of structure. The antibacterial properties are attributed to this structural feature. In addition, the compound contains an ester group, an isolated double bond and two hydroxyl groups.

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK AND CO., INC.]

Streptomyces Antibiotics. XV. N-Methyl-L-glucosamine

BY FREDERICK A. KUEHL, JR., EDWIN H. FLYNN, FREDERICK W. HOLLY, RALPH MOZINGO AND KARL FOLKERS

The degradation of streptomycin resulting in the isolation of a hexosamine and its characterization as N-methyl-L-glucosamine has been reported[1]; the present paper contains a detailed account of these investigations and includes the results on an additional synthesis of N-methyl-L-glucosamine.

The cleavage of streptomycin by the action of methanol in the presence of hydrogen chloride to methyl streptobiosaminide dimethyl acetal hydrochloride and streptidine hydrochloride has been described.[2] Further cleavage of this streptobiosamine derivative is accomplished by the action of concentrated hydrochloric acid at the boiling point for two hours, which results in the decomposition of the nitrogen-free portion, leaving the hexosamine intact.

The hexosamine obtained by hydrolysis was acetylated to give the pentaacetyl derivative as a mixture of the α and β forms. From this mixture, a levorotatory pentaacetyl derivative, m. p. 160.5–161.5°, was obtained by repeated crystallization. This same derivative was obtained in better yield, however, from the crude acetylated product by treatment with zinc chloride and acetic anhydride.[3] Analyses and molecular weight determinations were in agreement with the molecular formula $C_{17}H_{25}NO_{10}$, and showed the presence of five acetyl groups.

Hydrolysis of this acetyl derivative with dilute hydrochloric acid yielded an amorphous hydrochloride which was crystallized from alcohol to give a product melting at 160–163° (dec.). Analyses and results of potentiometric titration were in agreement with the formula $C_7H_{15}NO_5 \cdot HCl$ containing an N-methyl group.[2] This compound reduced both Fehling and Tollens solutions. The hydrochloride was converted into the free base by treatment with silver oxide in methyl alcoholic solution. The free base was acetylated with acetic anhydride in methanol to give the N-acetyl derivative, m. p. 165–166°.

Since all these reactions were in agreement with those expected of a hexosamine, the hydrochloride was treated with phenylhydrazine for phenylosazone formation. A phenylosazone was formed and the methylamino group was eliminated; the reaction required prolonged heating to obtain a good yield. This phenylosazone, which decomposed at 205°,[4] was converted[5] into a phenylosotriazole[1,6] melting at 196–197°. The phenylosotriazole prepared from D-glucose melted at 196–197°; however, the specific rotations of the two phenylosotriazoles were equal in magnitude but opposite in sign. These results indicated that the hexosamine belongs to the L-series and the "natural" phenylosotriazole is phenyl-L-glucosotriazole (I).[1,6]

The position of the methylamino group was demonstrated by oxidation of the hexosamine with mercuric oxide to a nitrogen-containing acid which melted at 230–232° (dec.), the reported melting point of N-methyl-D-glucosamic acid.[7] Again, the rotation was equal in magnitude but opposite in sign, indicating that the acid is N-methyl-L-glucosamic acid (III) and that the hexosamine from streptomycin is N-methyl-L-glucosamine (II).

The conclusions were supported by synthesis of N-methyl-L-glucosamine from L-arabinose by two series of reactions. L-Arabinose (IV) was con-

(1) Kuehl, Flynn, Holly, Mozingo and Folkers, THIS JOURNAL, **68**, 536 (1946).

(2) Brink, Kuehl and Folkers, *Science*, **102**, 506 (1945).

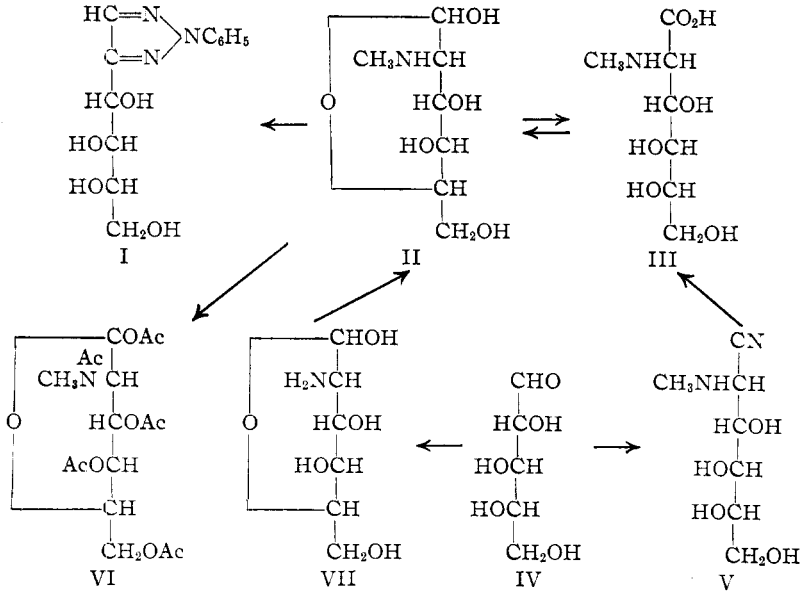
(3) It is assumed that the isomer obtained by the zinc chloride treatment is the α isomer; Gilman, "Organic Chemistry, An Advanced Treatise," 2nd ed., Vol. II, p. 1551, John Wiley and Sons, Inc., New York, 1943.

(4) L-Glucose phenylosazone, m. p. 205°; Fischer, *Ber.*, **23**, 374 (1890).

(5) Haskins, Hann and Hudson, THIS JOURNAL, **67**, 939 (1945).

(6) Wolfrom and Thompson, *ibid.*, **68**, 791 (1946).

(7) Votoček and Lukeš, *Chem. Listy*, **29**, 308 (1935); *Collection Czechoslov. Chem. Commun.*, **7**, 474 (1935).



verted by reaction with methylamine and hydrogen cyanide into a methylamino-nitrile (V). This nitrile was hydrolyzed with concentrated hydrochloric acid to N-methyl-L-glucosamic acid (III), which was then lactonized and reduced with sodium amalgam to N-methyl-L-glucosamine (II). The N-methyl-L-glucosamine was converted to a pentaacetyl derivative by treatment with acetic anhydride and pyridine. The synthetic N-methyl-L-glucosamic acid, the N-methyl-L-glucosamine hydrochloride, and its pentaacetyl derivative did not cause, on admixture, depression of the melting points of the corresponding compounds derived from streptomycin. The synthetic and "natural" compounds also had the same specific rotations.

Since the method of synthesis proved only the configurations about carbon atoms 3, 4 and 5, but not about carbon atom 2, in the hexosamine, D-glucosamine was methylated with dimethyl sulfate to give N-methyl-D-glucosamine. The hydrochloride and the pentaacetyl derivative of N-methyl-D-glucosamine melted at the same temperature as the corresponding derivatives of the hexosamine obtained from streptomycin; the specific rotations of the corresponding compounds were equal in magnitude but opposite in sign.

With the reported configuration about carbon atom 2 of D-glucosamine,[8] and the above data, it is concluded that the configuration about carbon atom 2 of the hexosamine from streptomycin and L-arabinose is also that of L-glucose, and that the degradation product is N-methyl-L-glucosamine.

Other workers[9] have described a synthesis of N-methyl-L-glucosamic acid which yielded the intermediate N-methylamine derivative of L-arabinose and the cyanohydrin (V) in crystalline form.

Pentaacetyl-N-methyl-L-glucosamine (VI) has also been synthesized by an alternate series of reactions. L-Arabinose was converted into crystalline L-glucosamine hydrochloride (VII) by treatment with ammonia and hydrogen cyanide followed by hydrolysis, lactonization and reduction. The L-glucosamine was treated with dimethyl sulfate in alkaline solution, and the product was acetylated to give pentaacetyl-N-methyl-L-glucosamine (VI).

(8) Haworth, Lake and Peat, *J. Chem. Soc.*, 271 (1939).

(9) Wolfrom, Thompson and Hooper, *Science*, **104**, 276 (1946); THIS JOURNAL, **68**, 2343 (1946).

Experimental

Pentaacetyl-N-methyl-α-L-glucosamine from the Hydrolysis of Methyl Streptobiosaminide Dimethyl Acetal Hydrochloride.[2]—A solution of 485 mg. of methyl streptobiosaminide dimethyl acetal hydrochloride in 5 ml. of concentrated hydrochloric acid was refluxed for two hours. The cooled reaction mixture was extracted with chloroform to remove oily decomposition products. The aqueous solution was then decolorized with Darco and concentrated *in vacuo*, yielding 278 mg. of a light tan residue which was acetylated with pyridine and acetic anhydride overnight at 5°. After concentration *in vacuo*, the residue was dissolved in water and the acetylated product was extracted with chloroform. The chloroform extract was washed with water, dried and concentrated to dryness. The residue was dissolved in ether, and 241 mg. of crystals separated, m. p. 134–137°. After several recrystallizations from chloroform–ether, the pentaacetyl-N-methyl-α-L-glucosamine melted at 160.5–161.5° (microblock), $[\alpha]^{25}D$ −100° (*c*, 0.70 in chloroform).

Conversion of the Mixture of Pentaacetyl-N-methyl-α and β-L-glucosamine to the α-Isomer.—A crude acetylation mixture, 3.169 g., m. p. 134–137°, prepared in the manner described above, was heated with 1 g. of zinc chloride in 50 ml. of acetic anhydride on a steam-bath for one hour. After removal of the acetic anhydride *in vacuo*, the residue was treated with water and chloroform. The chloroform phase was washed with water and distilled. The residue was dissolved in ether and 2.386 g. of crystals separated, m. p. 158–160°. One recrystallization of the product from chloroform–ether gave pentaacetyl-N-methyl-α-L-glucosamine, m. p. 160.5–161.5° (microblock), $[\alpha]^{25}D$ −100° (*c*, 0.70 in chloroform).

Anal. Calcd. for $C_{17}H_{25}NO_{10}$: C, 50.62; H, 6.25; N, 3.47; CH_3CO, 53.3; mol. wt., 403. Found: C, 50.51; H, 6.24; N, 3.76; CH_3CO, 49.2; mol. wt., 414 (cryoscopic in benzene).

N-Methyl-α-L-glucosamine Hydrochloride.—A solution of 329 mg. of pentaacetyl-N-methyl-α-L-glucosamine (from streptomycin) in 10 ml. of 10% hydrochloric acid was refluxed for two hours. The resulting light yellow solution was decolorized with Darco and concentrated *in vacuo* to an amorphous, hygroscopic residue, 190 mg. Needle-like crystals separated from an ethanol solution of the residue, m. p. 160–163° (dec., micro-block), $[\alpha]^{25}D$ −103° → −88° in twenty-four hours (*c*, 0.61 in water).

Anal. Calcd. for $C_7H_{15}NO_5 \cdot HCl$: C, 36.60; H, 7.02; N, 6.10; N-methyl, 6.5; mol. wt., 230. Found: C, 36.65; H, 6.86; N, 6.38; N-methyl, 6.8; eq. wt., 225 (potentiometric titration).

N-Methyl-L-glucosamine.—The free base was prepared by treating a methanolic solution of N-methyl-α-L-glucosamine hydrochloride (from streptomycin) with silver oxide and filtering the solution immediately through a pad of

Darco. Concentration of the filtrate *in vacuo* gave the free base as a colorless glass, $[\alpha]^{25}D$ −62° (*c*, 1.0 in methanol).

N-Acetyl-N-methyl-L-glucosamine.—A solution of 136 mg. of N-methyl-α-L-glucosamine hydrochloride (from streptomycin) in methanol was filtered through a pad of silver oxide and Darco. The filtrate was adjusted to a volume of 30 ml. with methanol and 0.1 ml. of acetic anhydride was added. After standing four hours at room temperature, the solvent was removed *in vacuo*. A solution of the residue in chloroform–methanol deposited 61 mg. (77%) of crystals. N-Acetyl-N-methyl-L-glucosamine was obtained by recrystallization from the same solvents, m. p. 165–166° (micro-block), $[\alpha]^{25}D$ −51° (*c*, 0.40 in water).

Anal. Calcd. for $C_9H_{17}NO_6$: C, 45.94; H, 7.31; N, 5.95. Found: C, 45.80; H, 7.53; N, 6.45.

Phenyl-L-glucosazone.—A solution of 534 mg. of N-methyl-α-L-glucosamine hydrochloride (from streptomycin), 1.0 g. of phenylhydrazine hydrochloride and 1.5 g. of sodium acetate in 15 ml. of water containing 1.0 ml. of saturated sodium bisulfate solution was refluxed for three hours. Crystal formation was observed after two hours of boiling. The mixture was cooled, the crystals were removed by filtration, and the filtrate was refluxed again for four two-hour intervals, the crystalline phenylosazone being removed after each interval. A total of 371 mg. (45%) of product was obtained. Recrystallization of this product from alcohol–water gave the phenylosazone, m. p. 195–196° (dec., micro-block), 205° (dec., capillary).

Anal. Calcd. for $C_{18}H_{22}N_4O_4$: C, 60.32; H, 6.19; N, 15.63. Found: C, 60.17; H, 6.11; N, 15.62.

Phenyl-L-glucosotriazole.—A solution of 260 mg. of phenyl-L-glucosazone and 780 mg. of copper sulfate pentahydrate in 20 ml. of water and 10 ml. of isopropyl alcohol containing 1.0 ml. of 1 *N* sulfuric acid was refluxed one hour. After refluxing, the solution was concentrated *in vacuo* to a volume of 8 ml. and the precipitate was removed by centrifuging. The precipitate was dissolved in 10 ml. of hot methanol and treated with Darco. On cooling, 45 mg. (24%) of crystalline product was deposited. One recrystallization of this product from methanol–water gave phenylosotriazole, m. p. 196–197° (micro-block), $[\alpha]^{25}D$ +82° (*c*, 0.83 in pyridine). On admixture with authentic phenyl-D-glucosotriazole, m. p. 196–197° (micro-block), the melting point was depressed to 186–188° (micro-block).

Anal. Calcd. for $C_{12}H_{15}N_3O_4$: C, 54.33; H, 5.70; N, 15.84. Found: C, 54.31; H, 5.49; N, 16.20.

N-Methyl-L-glucosamic Acid from the Oxidation of N-Methyl-α-L-glucosamine with Mercuric Oxide.—An aqueous solution of 58 mg. of N-methyl-α-L-glucosamine hydrochloride (from streptomycin) was filtered through a pad of silver oxide and Darco. The filtrate (5 ml.) containing the free base was heated on a steam-bath with 300 mg. of yellow mercuric oxide for fifteen minutes with occasional shaking. The solution was then refluxed for five minutes and filtered while hot. Mercuric ion was removed by treatment with hydrogen sulfide followed by filtration through a small amount of Darco. When the filtrate was concentrated *in vacuo*, 49 mg. of a partially crystalline residue was obtained, which was crystallized from methanol–water to give 32 mg. (60%) of N-methyl-L-glucosamic acid, m. p. 223–225° (dec., micro-block). A recrystallization from the same solvents gave N-methyl-L-glucosamic acid, m. p. 230–232° (dec., micro-block), $[\alpha]^{25}D$ −4.6° → −7.3° in twenty-four hours (*c*, 1.8 in 0.6 *N* hydrochloric acid). A mixed melting point determination with authentic N-methyl-L-glucosamic acid, m. p. 231–232° (dec., micro-block), showed no depression.

Anal. Calcd. for $C_7H_{15}NO_6$: C, 40.20; H, 7.28; N, 6.69. Found: C, 40.12; H, 7.25; N, 6.93.

Pentaacetyl-N-methyl-α-D-glucosamine.—Five grams of α-D-glucosamine hydrochloride was dissolved in 25.0 ml. of 1.0 *N* sodium hydroxide. Two and five-tenths milliliters of dimethyl sulfate was added and the solution was shaken at room temperature for one-half hour. The water was removed *in vacuo* and the residue was triturated with 10 ml. of ethanol. The ethanol-soluble fraction was acetylated by treatment at 5° with pyridine and acetic anhydride. After standing twelve hours, the solution was concentrated *in vacuo*. The residue was dissolved in water, and the solution was extracted several times with chloroform. The combined chloroform extracts were washed with 5% aqueous sodium bicarbonate, dilute hydrochloric acid and water. After drying the extract and removing the solvent *in vacuo*, the residue was heated with 1 g. of zinc chloride in 25 ml. of acetic anhydride for one hour on a steam-bath. After removal of the acetic anhydride *in vacuo*, the residue was treated with water and chloroform. The chloroform layer was washed with water and distilled. An ether solution of the residue deposited 2.4 g. of crystals, m. p. 145–146°, $[\alpha]^{25}D$ +99° (*c*, 0.7 in chloroform). Purification was accomplished by recrystallization alternately from methanol and chloroform–ether, followed finally by chromatography on acid-washed alumina. The pentaacetyl-N-methyl-α-D-glucosamine melted at 160.5–161.5° (micro-block), $[\alpha]^{25}D$ +101° (*c*, 0.60 in chloroform).

Anal. Calcd. for $C_{17}H_{25}NO_{10}$: C, 50.62; H, 6.25; N, 3.47; CH_3CO, 53.3. Found: C, 50.66; H, 6.38; N, 3.54; CH_3CO, 50.16.

N-Methyl-α-D-glucosamine Hydrochloride.—A solution of 1.67 g. of pentaacetyl-N-methyl-α-D-glucosamine in 10 ml. of 2.5 *N* hydrochloric acid was refluxed for one hour. The reaction mixture was cooled, decolorized with Darco, and concentrated to dryness. The product was dissolved in a minimum amount of ethanol, and the solution deposited 820 mg. of crystals of N-methyl-α-D-glucosamine hydrochloride, m. p. 164–166° (dec., micro-block), $[\alpha]^{25}D$ +104° → +89° in twenty-four hours (*c*, 1.07 in water).

Anal. Calcd. for $C_7H_{15}NO_5 \cdot HCl$: C, 36.60; H, 7.02; N-methyl, 6.5. Found: C, 36.79; H, 6.70; N-methyl, 6.6.

N-Methyl-L-glucosamic Acid from L-Arabinose.—A solution of 500 g. of L-arabinose in 625 ml. of a 33% solution of methylamine in water was kept at room temperature for one week. To the solution, 1.8 g. of potassium cyanide was added. The mixture was cooled in an ice-bath and 182 ml. of anhydrous hydrogen cyanide was added at such a rate that the temperature remained at 35–40°. The addition required twenty minutes. Twenty-five minutes after completion of the addition of the hydrogen cyanide, the solution was cooled to −5° and it was added slowly to 2.5 liters of concentrated hydrochloric acid which had been cooled to −5°. The temperature was maintained below 10° throughout the addition. After remaining in an ice-bath for four hours, the solution was kept at room temperature for twenty hours.

The dark-colored mixture was concentrated to a thick sirup. This and all subsequent concentrations were done under reduced pressure and below 50°. The sirup was dissolved in 500 ml. of water and reconcentrated to a sirup. One liter of alcohol was added and removed. The residue was dissolved in 500 ml. of water and the solution was concentrated to a thick sirup. Two liters of water was added, and sufficient barium hydroxide octahydrate was added so that the *p*H of the solution remained above *p*H 10 during the subsequent concentration (more being added during the concentration to maintain this *p*H). The mixture was partly concentrated under reduced pressure (about 500 ml. of water was removed) and then allowed to stand fifteen hours at room temperature. The solution was diluted to 5 liters with water, and the barium was precipitated with 50% sulfuric acid. The barium sulfate was removed by centrifugation; the cake was washed twice with two volumes of water and the washings were added to the main solution. Sulfate and chloride ions were removed (solution about *p*H 5) by the addition of 1200 g. of lead monoxide. The lead salts and unchanged lead monoxide were removed by filtration and were washed twice with water. The solution was saturated with hydrogen sulfide, the precipitated lead sulfide was removed by filtration, and the filtrate was concentrated to a thick sirup. The addition of four volumes of methanol to the sirup

yielded a brown crystalline product which was collected and washed with methanol. The product was dissolved in 200 ml. of hot water, 5 g. of Darco was added, and the solution was filtered. To the hot filtrate, 250 ml. of methanol was added. The amino acid crystallized slowly from the hot solution; after cooling in ice, 48.2 g. of N-methyl-L-glucosamic acid was obtained, m. p. 230–232° (dec., micro-block), $[\alpha]^{25}D$ −5° → −8° in forty hours (*c*, 1.0 in 2.5% hydrochloric acid).

Anal. Calcd. for $C_7H_{15}NO_6$: C, 40.20; H, 7.28; N, 6.69. Found: C, 40.35; H, 7.37; N, 6.88.

The methanol filtrates were concentrated to dryness and the residue was treated as before; an additional 31.3 g. of N-methyl-L-glucosamic acid, m. p. 228–230° (dec., micro-block) was obtained.

N-Methyl-L-glucosamic Acid Lactone Hydrochloride.—Eight grams of N-methyl-L-glucosamic acid (prepared from L-arabinose) was suspended in 75 ml. of absolute alcohol and dry hydrogen chloride was passed into the suspension for thirty minutes. A heavy crystalline precipitate formed at first and slowly dissolved. After standing at room temperature for twenty hours, the solution was concentrated under reduced pressure. The lactone hydrochloride remained as an oil, $[\alpha]^{25}D$ −6° → −3° in twenty-four hours, (*c*, 1.1 in 0.1 *N* hydrogen chloride in ethanol).

Pentaacetyl-N-methyl-α-L-glucosamine from the Reduction of N-Methyl-L-glucosamic Acid Lactone.—The lactone hydrochloride described above was dissolved in 75 ml. of water. To the solution, 65 g. of 2.5% sodium amalgam was added at 0–5° with agitation during a one-hour period. Dilute hydrochloric acid was added concurrently with the amalgam so that the solution remained at *p*H 2–4 during the addition. The solution was concentrated under reduced pressure. To the oil and sodium chloride remaining, 80 ml. of pyridine and 50 ml. of acetic anhydride were added with cooling. After the mixture had remained at about 0° for twenty hours, it was concentrated under reduced pressure. The residue was dissolved in 50 ml. of water, and the aqueous solution was extracted three times with 30 ml. of chloroform. The chloroform extract was washed twice with 30 ml. of 5% sodium bicarbonate solution, once with 30 ml. of 5% hydrochloric acid, and once with 30 ml. of water. Fifty milliliters of benzene was added to the extract and the solvent was removed under reduced pressure. The residue was dissolved in 50 ml. of ether, and a crystalline precipitate formed when the solution was cooled by ice. The crystals were collected on a filter, washed with ether, and recrystallized from a mixture of chloroform and ether to yield 0.5 g. of pentaacetyl-N-methyl-α-L-glucosamine, m. p. 161–162° (micro-block), $[\alpha]^{25}D$ −98° (*c*, 0.558 in methanol).

Anal. Calcd. for $C_{17}H_{25}NO_{10}$: C, 50.62; H, 6.25; N, 3.47. Found: C, 50.84; H, 6.20; N, 3.59.

N-Methyl-α-L-glucosamine Hydrochloride.—Five grams of pentaacetyl-N-methyl-α-L-glucosamine (derived from L-arabinose) was suspended in 150 ml. of 2.5 *N* hydrochloric acid, and the solution was refluxed for two and one-half hours. When concentrated under reduced pressure, the solution yielded an oily residue which crystallized slowly. Recrystallization of the product from a mixture of methanol and ether yielded 2 g. of the hydrochloride. A 1-g. sample was dissolved in water, treated with Darco, and the resulting colorless solution was concentrated under reduced pressure to a sirup. The addition of ethanol to the oil yielded 0.6 g. of crystalline N-methyl-α-L-glucosamine hydrochloride, m. p. 168–170° (dec., capillary), $[\alpha]^{25}D$ −105° → −87° in twenty-four hours (*c*, 0.90 in water).

Anal. Calcd. for $C_7H_{15}O_5N \cdot HCl$: C, 36.60; H, 7.02; N, 6.10. Found: C, 36.75; H, 6.90; N, 6.24.

L-Glucosamine Hydrochloride.—Dry hydrogen chloride was passed into a suspension of 10 g. of L-glucosamic acid[10] in 100 ml. of absolute alcohol until the solution was saturated at 50–60°. The acid dissolved slowly and a crystalline precipitate formed which redissolved partially as addition of hydrogen chloride to the mixture was continued. After the mixture had remained at room temperature for twenty-four hours, the solvent was removed under reduced pressure. A mixture of a crystalline material and an oil was obtained.

The mixture of oil and crystals was dissolved in 100 ml. of water, the solution was cooled to 5°, and 70 g. of 2.5% sodium amalgam was added to the solution with vigorous agitation during a thirty-minute period. The temperature of the solution was maintained at about 5°. During the addition of the amalgam, 2 *N* sulfuric acid was added concurrently at such a rate that the solution was kept at about *p*H 4. The mercury was removed and the solution was concentrated under reduced pressure. To the residue, 80 ml. of acetic anhydride and 100 ml. of pyridine were added, and the mixture was left at 0° for twenty-four hours and then concentrated to a thick oil. The oil was dissolved in water and the aqueous solution was extracted with three 50-ml. portions of chloroform. The chloroform extract was washed with 5% sodium bicarbonate, 2.5 *N* hydrochloric acid and water, and then concentrated to a thick oil.

A solution of the oil in 75 ml. of 2.5 *N* hydrochloric acid was refluxed for thirty minutes. Treatment of the dark colored solution with 1 g. of Darco gave a brown solution which was concentrated to a thick sirup that crystallized slowly. Methanol was added and the crystalline material was collected on a filter and washed successively with methanol and ether. A total of 1.82 g. of crystalline L-glucosamine hydrochloride was obtained. A sample was recrystallized from methanol, $[\alpha]^{27}D$ −73° (*c*, 2.05 in water).

Anal. Calcd. for $C_6H_{14}NO_5Cl$: C, 33.42; H, 6.54; N, 6.50. Found: C, 33.60; H, 6.82; N, 6.61.

Pentaacetyl-N-methyl-L-glucosamine from L-Glucosamine.—A solution prepared by dissolving 250 mg. of L-glucosamine hydrochloride in 1.3 ml. of 1 *N* sodium hydroxide was shaken for fifteen minutes with 0.13 ml. of dimethyl sulfate and was then concentrated under reduced pressure. The residue was treated with 5 ml. of acetic anhydride and 5 ml. of pyridine at room temperature for one hour. The solution was concentrated under reduced pressure and the residue was rubbed with 2 ml. of water at 0°. The crystalline product obtained was removed by centrifugation, washed with water, dried and recrystallized from a mixture of chloroform and ether. Fifty milligrams of pentaacetyl-N-methyl-L-glucosamine, m. p. 152–155° (micro-block) was obtained as a mixture of the α and β forms. Treatment of the mixture with zinc chloride in acetic anhydride yielded pentaacetyl-N-methyl-α-L-glucosamine, m. p. 161–162°; a mixture with an authentic sample melted at 161–162°.

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Summary

Methyl streptobiosaminide dimethyl acetal hydrochloride, a degradation product of streptomycin, has been degraded to a new hexosamine which has been identified as N-methyl-L-glucosamine.

N-Methyl-L-glucosamine has been synthesized from L-arabinose by reaction with methylamine and hydrogen cyanide, followed by hydrolysis, lactonization and reduction.

L-Glucosamine has been synthesized similarly from L-arabinose and methylated to N-methyl-L-glucosamine.

(10) Fischer and Leuchs, *Ber.*, **35**, 3802 (1902).

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