Aminocyclitols. VII. A New Synthetic Route to *myo*-Inosamine-4

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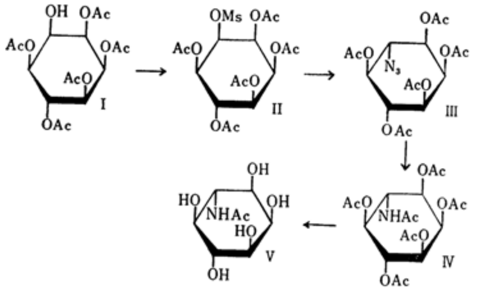
In a previous paper of this series,[1] the replacement of the mesyloxy group of 1-*O*-mesyl-*myo*-inositol pentaacetate by a highly nucleophilic azide ion has been described. In the present paper, the displacement of the mesyloxy group of (±)-2-*O*-mesyl-*epi*-inositol pentaacetate (II) by an azide ion is the main subject. II is prepared in 89% yield from (±)-1, 3, 4, 5, 6-penta-*O*-acetyl-*epi*-inositol (I)[2] by an ordinary procedure of mesylation.



The structure of II is substantiated by the NMR spectrum; as Fig. 1-A shows, the spectrum reveals a sharp signal at 7.85 τ, corresponding to an axial acetoxy group, and sharp signals with a 2 : 1 : 1 relative intensity at 7.94, 8.00 and 8.02 τ, corresponding to four equatorial acetoxy groups.[3] The protons of the mesyloxy group on C-2 reveals a sharp signal at 6.92 τ, as is to be expected from an axial mesyloxy group.[4]

II is then treated with sodium azide in boiling aqueous 2-methoxyethanol for 20 hr. Since the product has been partially deacetylated during the course of the reaction, the product is acetylated with acetic anhydride and pyridine to give the azido derivative (III), m. p. 149—150°C, in 47% yield; this shows an infrared absorption characteristic of an azide group at 2100 cm^{-1}.[5] III is reduced with Raney nickel in a hydrogen stream. The reduction product is further acetylated with acetic anhydride and pyridine, giving hexaacetyl-inosamine (IV), m. p. 235—237°C, in 58% yield. *N*-Acetyl-inosamine (V), m. p. 268—269°C (decomp.), is obtained by the selective deacetylation of IV with methanolic ammonia.

Since both of the vicinal acetoxy groups with respect to the mesyloxy group are located in anchimerically unassisted cis positions in II, the replacement of the mesyloxy group by an azide ion must occur through a direct S_N2 mechanism,[6] as has been shown in the case of 1, 3-di-*O*-acetyl-2-*O*-mesyl-*cis*-1, 2, 3-cyclohexanetriol.[4] Therefore, the product, IV, is probably identical with (±)-*myo*-inosamine-4 hexaacetate, which has been described by Anderson et al.[7] The configuration of IV is substantiated by its NMR spectrum. The NMR spectrum of IV, as shown in Fig. 1-B, reveals a sharp signal at 7.80 τ, corresponding to an axial acetoxy group, signals at 7.97 8.00 and 8.03 τ, with a 2 : 1 : 1 relative intensity corresponding to four equatorial acetoxy groups, and one at 8.10 τ, as is to be expected from an equatorial acetamido group.[3]

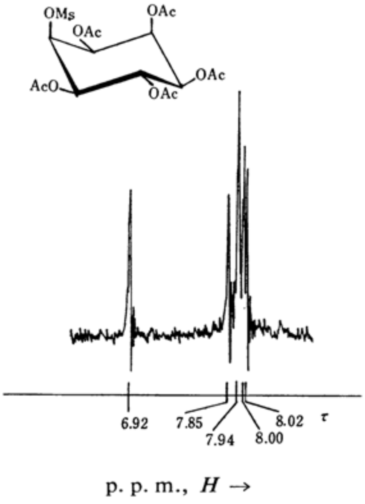


Fig. 1-A.

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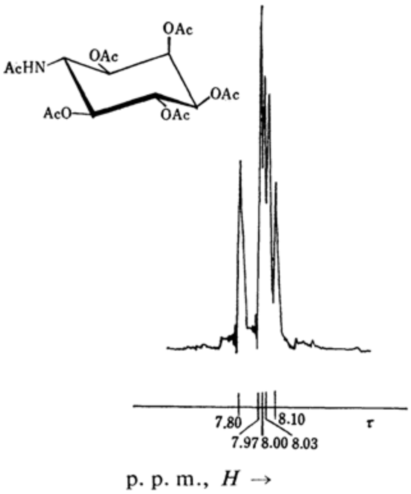

Fig. 1-B.

Experimental

All melting points were measured on a Mitamura Riken micro hot plate. The NMR spectra were determined at a frequency of 60 Mc. p. s. with Japan Electron Optics JNM-C-60 and Hitachi Model H-6013 spectrometers in deuteriochloroform. Tetramethylsilane was used as an internal reference, and peak positions were given in τ-values.

(±)-2-*O*-Mesyl-*epi*-inositol Pentaacetate (II).—To a mixture of 2.3 g. of (±)-1,3,4,5,6-penta-*O*-acetyl-*epi*-inositol and 30 ml. of pyridine, 1.0 g. of methanesulfonyl chloride was added under agitation at 0°C. After it had settled overnight in a refrigerator, the mixture was added to 45 ml. of ice cold water. The precipitate was then collected by filtration. The crude product (2.7 g.) was recrystallized from methanol to give 2.4 g. (89%) of needles melting at 196—197°C.

Found: C, 43.52; H, 5.36; S, 6.63. Calcd. for $C_{17}H_{24}O_{13}S$: C, 43.59; H, 5.16; S, 6.85%.

(±)-4-Deoxy-4-azido-*myo*-inositol Pentaacetate (III).—A mixture of 2.0 g. of II, 0.9 g. of sodium azide and 50 ml. of 80% aqueous 2-methoxyethanol was refluxed for 20 hr. The mixture was then evaporated to dryness in vacuo. The residue was repeatedly extracted with ethanol. The combined ethanol extract was evaporated, and the residue was added to a mixture of 20 ml. of acetic anhydride and 20 ml. of pyridine. The mixture was then evaporated in vacuo, and the residue was recrystallized twice from ethanol to give 0.84 g. of needles (46.6%) melting at 149.5—150°C.

Found: C, 46.47; H, 5.33; N, 10.07. Calcd. for $C_{16}H_{21}N_3O_{10}$: C, 46.26; H, 5.10; N, 10.12%.

(±)-Hexaacetyl-*myo*-inosamine-4 (IV).—A solution of 0.68 g. of III in 100 ml. of ethanol was hydrogenated with Raney nickel T4[8] in hydrogen at an initial pressure of 50 p. s. i. g. for 20 hr. Then the catalyst was removed by filtration, and the filtrate was evaporated in vacuo. The residue was acetylated with a mixture of acetic anhydride and pyridine. The crude product was repeatedly recrystallized from ethanol to give 0.33 g. of needles melting at 235—237°C. (Lit. m. p. 236—239°C).[7] (Found: C, 50.12; H, 5.71; N, 3.25%.)

(±)-*N*-Acetyl-*myo*-inosamine-4 (V). — A 0.4 g. portion of IV was added to 50 ml. of methanol which had been previously saturated with ammonia. After it had settled overnight at room temperature, the mixture was evaporated under reduced pressure. The residue was washed with ethanol and then recrystallized from a mixture of ethanol and water (2:1), giving 0.18 g. (92.7%) of needles melting at 268—269°C (decomp.). [Lit. m. p. 270—271°C (decomp.)].[7] (Found: C, 43.54; H, 7.08; N, 6.40%.)

Paper Chromatography. — IV was hydrolyzed with boiling 6 N hydrochloric acid for 6 hr. Then the hydrolyzate was evaporated to dryness in vacuo. The residue was developed in an acetic acid - ethyl acetate - pyridine - water (3:5:5:1) system[9] in ascending paper chromatography. The hydrochloride showed a single spot of R_f 0.24 at 22°C (R_f of D-glucosamine hydrochloride: 0.46). R_f/R_f glucosamine: 0.52 (Lit. R_f DL-*myo*-inosamine-4/R_f glucosamine: 0.53).[10]

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