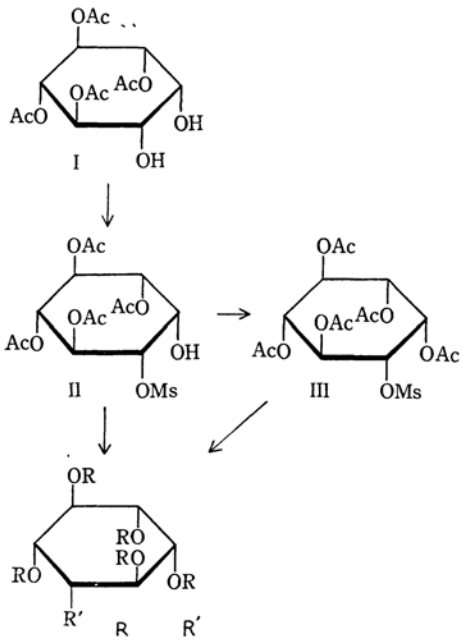
Aminocyclitols. IV. The New Synthesis of Inosamine

By Tetsuo SUAMI and Seiichiro OGAWA

(Received June 4, 1964)

In a previous paper[1] of this series, the displacement of the mesylate group of the 2-amino-1, 3-cyclohexanediol derivative with an azide ion has been described. The replacement of the mesylate group of *myo*-inositol by an azide ion will be studied and the synthesis of inosamine will be described in the present communication.



IV Ac N_3
V Ac NHAc
VI H NHAc
VII H $NH_3^+Cl^-$

The starting material for the synthesis is a known (±)-1, 4, 5, 6-tetra-*O*-acetyl-*myo*-inositol (I).[2] By treating I with one mole of methanesulfonyl chloride in pyridine, (±)-1, 4, 5, 6-tetra-*O*-acetyl-3-*O*-mesyl-*myo*-inositol (II), m. p. 207~208°C, is obtained in 72% yield. II is further acetylated with acetic anhydride and pyridine to give (±)-3-*O*-mesyl-*myo*-inositol pentaacetate (III), m. p. 159~161°C, in 88% yield. It is found that III is different in melting point and in infrared spectra from 2-*O*-mesyl-*myo*-inositol pentaacetate, m. p. 190~192°C which is prepared from 1, 3, 4, 5, 6-penta-*O*-acetyl-*myo*-inositol[3] by the ordinary procedure of mesylation. Since tosyl chloride attacks an equatorial hydroxyl group rather than an axial one in the *myo*-inositol derivative,[4] the attacking of mesyl chloride might take place in a similar manner; therefore, the assignment of the attaching point of the mesylate group to C-3 (or C-1) in II seems to be reasonable. This is further confirmed by the NMR spectrum of III, which reveals a sharp signal at 7.00 τ, as is expected from the protons of an equatorial mesylate group.[5]

When II is then treated with sodium azide in boiling aqueous 2-methoxyethanol for 15 hr., an oily product is obtained. As it has been partially deacetylated during the reaction with sodium azide, this product is acetylated with acetic anhydride and pyridine to yield IV, which shows the characteristic infrared absorption of an azide group at 2115 cm^{-1}. IV is reduced with hydrogen in the presence of Raney nickel. The reduction product shows the infrared absorption of an amide group at 1645 and 1570 cm^{-1}; accordingly, a migration of the acyl group from O to N must have occurred[6] during the course of the reduction. Further treatment with acetic anhydride and pyridine gave hexaacetyl-inosamine (V), m. p. 205~205.5°C in 43% yield from II.

V is also obtained from III by the procedure mentioned above.

The selective deacetylation of V with ammonia in methanol yields *N*-acetyl-inosamine (VI), m. p. 224~225°C. The hydrolysis of VI with 6 N hydrochloric acid gives inosamine hydrochloride (VII), which shows a single spot of R_f 0.18 in ascending paper chromatography in an ethyl acetate - pyridine - acetic

1) T. Suami and S. Ogawa, This Bulletin, **37**, 733 (1964).
2) S. J. Angyal, P. T. Gilham and C. G. Macdonald, *J. Chem. Soc.*, **1957**, 1417.
3) E. L. May, *J. Org. Chem.*, **17**, 286 (1952).
4) S. J. Angyal and L. Anderson, "Advances in Carbohydrate Chemistry," Vol. XIV, Academic Press, New York (1959), p. 167.
5) The NMR spectra of an axial and an equatorial mesylate groups in cyclohexanetriol were presented at the 17th Annual Meeting of the Chemical Society of Japan, Tokyo, April 1964.
6) G. Fordor and J. Kiss, *J. Am. Chem. Soc.*, **72**, 3495 (1950); L. Anderson and H. A. Lardy, ibid., **72**, 3141 (1950).

acid - water (5 : 5 : 3 : 1) system[7] at 20°C (R_f of D-glucosamine hydrochloride : 0.25).

Not enough examples of the reactions of the sulfoxylate group with sodium azide have been accumulated to predict the stereochemistry of the reaction product, but there are three possible configurations for V: hexaacetyl-*myo*-inosamine-(1),[8] *rac*-inosamine-(2),[9] and *muco*-inosamine-(1).[10] The melting point of V and the R_f value of VII are different from those of the former two. Therefore, hexaacetyl-*muco*-inosamine-(1) seems to be the most probable structure for V.

Department of Applied Chemistry
Faculty of Engineering
Keio University
Koganei-shi, Tokyo

7) F. G. Fischer and H. Dorfel, *Hoppe-Seyler's Z. physiol. Chem.*, **301**, 224 (1955).
8) F. W. Lichtenthaler, *Chem. Ber.*, **94**, 3071 (1961).
9) M. Nakajima, N. Kurihara and A. Hasegawa, ibid., **95**, 141 (1962).
10) M. Nakajima, A. Hasegawa and N. Kurihara, ibid., **95**, 2708 (1962).