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STUDIES ON NITRO SUGARS VII.[1] SYNTHESIS OF METHYL 2,3,5-TRIACETAMIDO-2,3,5-TRIDEOXY-β-D-PENTOFURANOSIDES VIA NITROOLEFIN

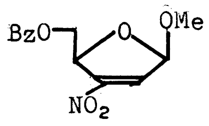
Tetsuyoshi TAKAMOTO, Hozumi TANAKA, Takayuki KAWAHARA
and Rokuro SUDOH
Department of Chemistry, Tokyo Institute of Technology,
O-okayama, Meguro-ku, Tokyo 152

Synthesis of methyl 5-azido-3-nitro-2,3,5-trideoxy-β-D-*glycero*-pent-2-enofuranoside (**7**) from methyl 5-*O*-benzoyl-3-deoxy-3-nitro-β-D-xylofuranoside (**2**) through five steps in 13% overall yield is described. The nitroolefin **7** was treated with hydrazoic acid in the presence of trace of sodium azide, followed by hydrogenation and N-acetylation, to give a diastereoisomeric mixture of four triacetamido furanoside derivatives.

It has been well known that pyranosides involving α-nitroolefin and *vic*-nitroacetate[2] system are readily susceptible to addition and substitution, respectively, on the syntheses of polyamino-,[3] branched-chain sugars,[4] etc.[5,6]

During the course of the studies, we have reported the synthetic method[7] of 3-deoxy-3-nitro-D-furanoses by the oxidation of the corresponding oxime with trifluoroperoxyacetic acid in an excellent yield, and also the preparation[8] of the reactive nitroolefin (**1**) which was readily applied to the formation of methyl 5-*O*-benzoyl-2,3-diacetamido-2,3-dideoxy-β-D-ribofuranoside.

Considering a synthetic usefulness and a limitation of nitro sugars in the field of carbohydrate chemistry, the successful synthesis of such key compounds with good stereochemical control and yield is quite important. As an extension of the synthetic studies of polyamino pentofuranosides, we now present the synthesis of a diastereoisomeric mixture of triacetamido derivatives[9] via 5-azido nitroolefin.



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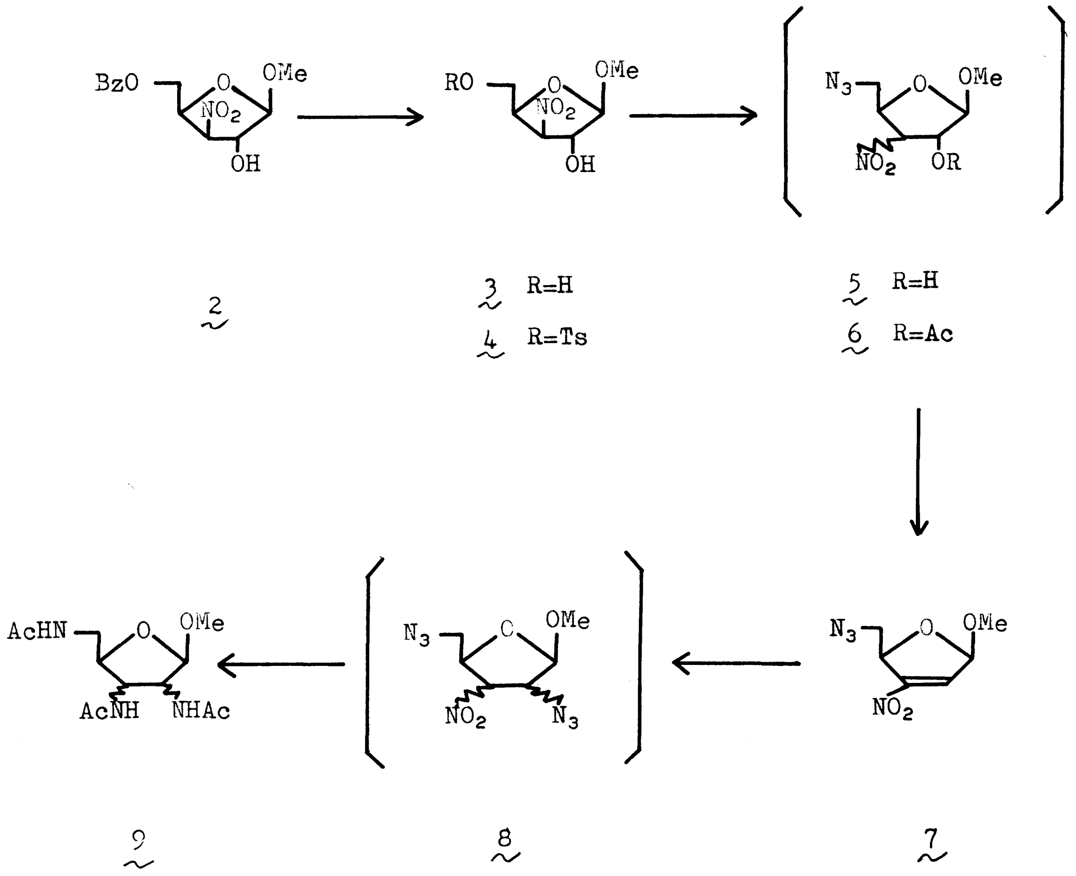


Treatment of methyl 5-*O*-benzoyl-3-deoxy-3-nitro-*β*-*D*-xylofuranoside (**2**) (297 mg, 1 mmol) with sodium methoxide followed by column chromatography gave methyl 3-deoxy-3-nitro-*β*-*D*-xylofuranoside (**3**), {mp 119-120°C, $[\alpha]_D^{20}$ -95.9° (c 1, acetone)} in 73% yield.

Selective sulfonylation of **3** (139 mg, 1 mmol) in chloroform gave methyl 3-deoxy-3-nitro-5-*O*-p-toluenesulfonyl-*β*-*D*-xylofuranoside (**4**), {mp 90-91°C, $[\alpha]_D^{20}$ -15.8° (c 1, acetone)} in 44% yield which was treated with sodium azide in dimethylsulfoxide at 70°C followed by column chromatography to give the azido derivative (**5**) in 65% yield. On the substitution reaction, the epimerization at C-3 position took place through aci-form under the basic condition to give an epimeric mixture of xylo- and ribo-furanoside.10) However, the following acetylation and elimination11) afforded a single product: methyl 5-azido-3-nitro-2,3,5-trideoxy-*β*-*D*-*glycero*-pent-2-enofuranoside (**7**), {mp 64-64.5°C; $[\alpha]_D^{20}$ +232°12) (c 1, acetone)} in 60% yield. As $J_{1,4}$=$J_{2,4}$=1.2 Hz, and $J_{1,4}$=4.4 and $J_{2,4}$=1.2 Hz on methyl 5-*O*-benzoyl-2,3-dideoxy-*α*- and *β*-*D*-*glycero*-

Table 1. 100 MHz P.m.r. data of methyl 3-deoxy-3-nitro-β-D-pentofuranoside derivatives (Me_4Si as an internal standard)

	Chemical Shift (ppm)							Coupling Constant (Hz)							
Compound	H^1	H^2	H^3	H^4	H^5	$H^{5'}$	OCH_3	J_{12}	J_{23}	J_{34}	J_{45}	$J_{45'}$	$J_{55'}$	J_{14}	J_{24}
3^a	4.83	4.40	5.09	?	3.65	3.65	3.35	0	5.2	7.3	5.0	5.0	-	-	-
4^b	4.86	4.53	5.09	4.90	4.16	4.28	3.26	0	4.5	7.8	3.8	4.0	10.8	-	-
7^b	5.70	7.15	-	5.31	2.74	2.72	3.63	3.7	-	-	1.7	1.7	3.4	3.7	0.7

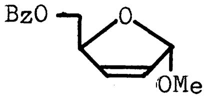
a: in CD_3OD b: in $CDCl_3$

pent-2-enofuranoside (10 and 11, respectively),[13)] long-range couplings were clearly observed on the p.m.r. spectrum of 7 as shown in Table 1.

As reported on a previous paper,[8)] the nitroolefin reacts with hydrazoic acid[14)] in chloroform to afford a kinetically controlled single product. But no reaction was observed on nitroolefin 7 under the same condition. Addition of catalytic amount of sodium azide[15)] to the reaction mixture gave in 92% yield a syrupy diastereoisomeric mixture of the diazido derivatives (8), which is consist of possible four isomers confirmed by the p.m.r. spectrum.[16)]

Catalytic hydrogenation of 8 (122 mg, 0.5 mmol) with Pd-C in the presence of acetic anhydride (1.5 ml) in methanol (20 ml) afforded in 34% yield a mixture of the corresponding amorphous triacetamido derivatives (9)[17)] which showed 3275 (NH), 1650 and 1565 cm^{-1} (Amide) on the i.r. spectrum and gave a reasonable elemental analysis.

Consequently, on such an addition reaction of hydrazoic acid to nitroolefin in a furanoside system, no alkaline medium should be employed to avoid the reversible reaction. The considerable difference on reactivity between 1 and 7 will be further studied.



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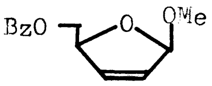

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References and Notes

1) Part VI, T. Takamoto and R. Sudoh, Bull. Chem. Soc. Japan, **48**, 3413 (1975).

2) *vic*-Nitroacetate is liable to eliminate acetic acid to give α-nitroolefin; H. H. Baer and L. Urbas, "The Chemistry of the nitro and nitroso groups" Part 2, ed. by H. Feuer, Interscience Publishers, New York, N. Y. (1970), p. 171.

3) F. J. M. Rajabalee, Synthesis, 359 (1971).

4) T. Sakakibara, S. Kumazawa, and T. Nakagawa, Bull. Chem. Soc. Japan, **43**, 2655 (1970).

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6) T. Nakagawa, T. Sakakibara, and S. Kumazawa, Tetrahedron Lett., 1645 (1970).

7) T. Takamoto, R. Sudoh, and T. Nakagawa, Tetrahedron Lett., 2053 (1971).

8) T. Takamoto, H. Tanaka, and R. Sudoh, Chem. Lett., 1125 (1972).

9) Two tribenzamido derivatives were prepared via epimino furanoside and were separated; J. Hildesheim, J. Cléophax, A. Sépulchre, and S. D. Géro, Carbohyd. Res., **9**, 315 (1969).

10) One of the epimers formed a little more than the other (in the ratio of ca. 3:2). However, identification is not done yet.

11) Acetylation of **5** with acetic anhydride in pyridine diluted with benzene gave a mixture of the corresponding O-acetate **6** and nitroolefin **7**, which was immediately converted to **7** by reflux with sodium bicarbonate in benzene.

12) There is no regularity with respect to specific rotation in the series of 2-enofuranoside, such as -100° and -102° (in chloroform) for *α*-**10** and *β*-anomer **11**, respectively.

13) R. U. Lemieux, K. A. Watanabe, and A. A. Pavia, Can. J. Chem., **47**, 4413 (1969).

14) Nucleophilic addition of weak acid such as HN_3 and HCN to nitroolefin in pyranoside series gives thermodynamically less stable product exclusively; T. Sakakibara and R. Sudoh, Chem. Comm., 69 (1974).

15) Although sodium azide is insoluble in chloroform, an equilibrium was likely reached for at least 30 hr. Such a result was obtained on 5-*O*-benzoyl-nitroolefin **1**.

16) Four singlets were observed in the region (δ 3.3-3.5) of methoxy protons.

17) Each isomer was not separated.

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