NOVEL EFFICIENT SYNTHESIS AND STRUCTURAL ANALYSIS OF FURANOSE-TYPE PHOSPHONO SUGARS

Mitsuji Yamashita,* Akihiro Yabui, Tatsuo Oshikawa, Tadashi Hanaya,† and Hiroshi Yamamoto†

Department of Applied Chemistry, Faculty of Engineering, Shizuoka University, Hamamatsu 432, Japan

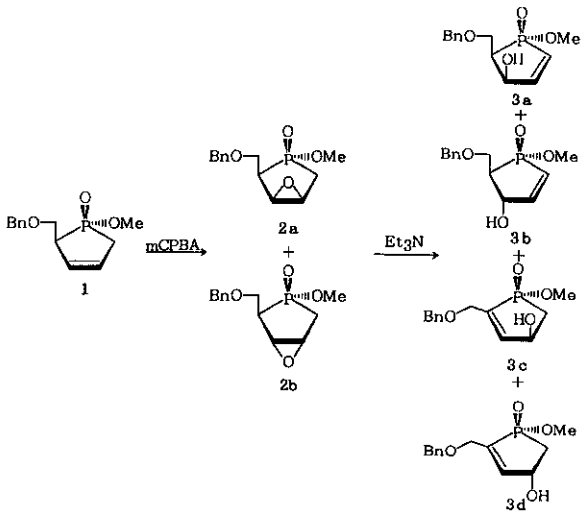
†Department of Chemistry, Faculty of Science, Okayama University, Okayama 700, Japan

Abstract-----Reaction of 2-benzyloxymethyl-1-methoxy-3-phospholene 1-oxide with mCPBA afforded 3,4-epoxyphospholane derivatives, whose isomerized allylic alcohols were *cis*-dihydroxylated by osmium(VIII) oxide-catalyzed oxidation to give ribo-, arabino-, xylo-, and lyxo-furanose-type phosphono sugars. The nmr data suggest a twist conformation.

Phosphono sugars, being of interest in the aspects related to syntheses and biological activities,[1,2] have been prepared mostly from sugar materials.[2,3] In our previous papers, we reported the novel synthesis of phosphono sugar *N*- and *C*-glycosides from none sugar materials such as 1-phenyl-2-phospholene and 1-alkoxy-3-phospholene 1-oxides, respectively.[4,5] This communication deals with an entirely novel and efficient synthesis of pentofuranose-type phosphono sugars *via* oxidation of a 3-phospholene 1-oxide derivative with mCPBA, base induced isomerization, and osmium (VIII) oxide-catalyzed diastereoselective *cis*-dihydroxylation, as well as structural elucidation of some of the pentofuranose-type phosphono sugars prepared.

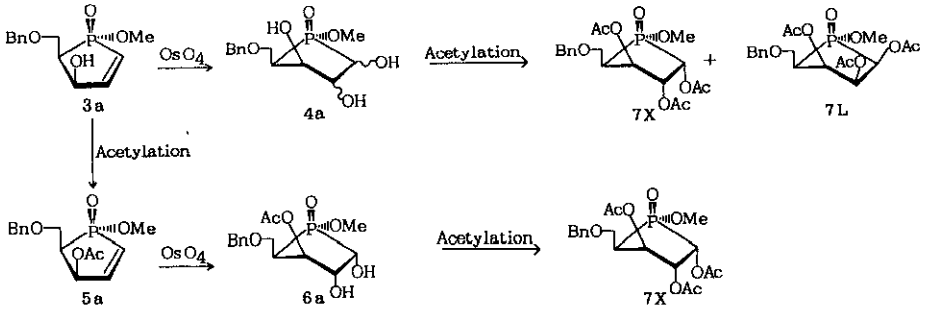
2-Benzyloxymethyl-1-methoxy-3-phospholene 1-oxide (1)[6] was treated with 3-chloroperbenzoic acid (mCPBA, 1.7 equiv.) in chloroform at 100 ℃ for 2 day to afford (3*R*, 4*S*)- and (3*S*, 4*R*)-2-benzyloxymethyl-3,4-epoxyphospholane 1-oxides (2a and 2b, respectively) in a quantitative yield (2a : 2b = 4 : 7).[7] Treatment of the mixture of 2a and 2b with triethylamine (1.0 equiv.) in ethanol at

100 ℃ for 2 day followed by separation by column chromatography on silica gel gave allylic alcohols 3a (18.4%), 3b (32.0%), 3c, and 3d (yield of 3c + 3d, 16.8%) (Scheme 1).[8]



Scheme 1. Isomerization of epoxides prepared from 3-phospholene (1).

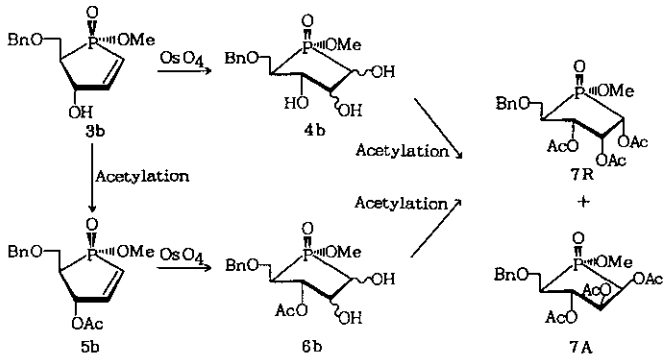
Osmium(Ⅷ) oxide-catalyzed *cis*-dihydroxylation of compound (3a) with sodium chlorate at 40 ℃ followed by treatment with acetic anhydride in pyridine at room temperature afforded 1,2,3-tri-*O*-acetyl-5-*O*-benzyl-4-deoxy-[(*R*)-methoxyphosphinyl]-α-D-xylofuranose (7X) and -β-D-lyxo-furanose (7L) in a ratio of 74 : 26 (7X, ^{31}P nmr ($CDCl_3$) δ = 51.6 ppm; 7L, ^{31}P nmr ($CDCl_3$) δ = 50.3 ppm; 7X + 7L, 78% from 3a).[7] In contrast osmium(Ⅷ) oxide-catalyzed *cis*-dihydroxylation of acetylated compound (5a) afforded diastereoselectively a sole product (7X) (87% from 3a) after the successive acetylation. This stereoselectivity can be explained by steric and electro-repulsive effects of the oxo-substituents of the heterocycle on the attack of osmium(Ⅷ) oxide.



Scheme 2. Preparation of α-D-xylo- and β-D-lyxo-furanose-type phosphono sugars from 3a.

Osmium(Ⅷ) oxide-catalyzed *cis*-dihydroxylation of compound (3b) at 40 ℃ followed by treatment

with acetic anhydride in pyridine at room temperature gave 1,2,3-tri-*O*-acetyl-5-*O*-benzyl-4-deoxy-[(*R*)-methoxyphosphinyl]-α-D-ribofuranose (7R) and -β-D-arabinofuranose (7A) in a ratio of 47 : 53 (7R, ^{31}P nmr ($CDCl_3$) δ = 49.3 ppm; 7A, ^{31}P nmr ($CDCl_3$) δ = 47.9 ppm; 7R + 7A, 99% from 3b).[7] Osmium(VIII) oxide-catalyzed *cis*-dihydroxylation of acetylated compound 5b afforded product 7R and 7A (7R : 7A = 59 : 41; 7R + 7A, 51% from 3b)[7] upon acetylation.



Scheme 3. Preparation of α-D-ribo- and β-D-arabino-furanose-type phosphono sugars from 3b.

Table 1. Observed 500 MHz ^{1}H nmr spectral parameters for compounds 7R and 7A in $CDCl_3$[a)]

Compd.	Chemical Shift (δ)							
	H1	H2	H3	H4	H5	H5'	OMe	Ac-1,2,3
7R	5.20	5.69	5.26	2.72	3.84	3.68	3.86	1.98, 2.10, 2.13
7A	5.35	5.12	5.56	2.42	3.89	3.77	3.84	2.00, 2.04 2.15

Compd.	Coupling constant (Hz)											
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{3,P}$	$J_{4,5}$	$J_{4,5'}$	$J_{4,P}$	$J_{5,5'}$	$J_{5,P}$	$J_{5',P}$	J_{POMe}
7R	4.8	7.8	3.3	30.1	10.6	3.1	8.2	5.8	17.9	9.3	11.2	20.1	11.1
7A	5.5	6.2	9.3	4.9	9.0	4.5	7.8	7.3	16.5	9.8	19.8	16.9	11.1

a) Measured by a Varian VXR-500 instrument (the SC-NMR Lab., Okayama Univ.) at 21 ℃ using TMS as the internal standard.

The structure of compounds (7R) and (7A) was established by means of complete assignments and analyses of chemical shifts and coupling constants of all ^{1}H nmr signals measured at the 500 MHz (Table 1). Compounds (7R) and (7A) are considered to exist preponderantly in the $^3T_2$ conformation in the solution.[9-12]

Compounds (7X, 7L, 7R, and 7A) are the phosphono sugars prepared first from a phospholene by the present novel efficient method. We are currently working further on the efficient and selective syntheses of phosphono sugar derivatives and on the conformational analyses.

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6. Compounds 1-7 consist of racemates, and the structure formulae represent one (*R*-form) of the enantiomers.
7. Ratios of products were determined by ^{1}H and ^{31}P nmr spectra.
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11. Conformation of 7R was determined based on the dihedral angles (*ca.* 65° and 150° for P-C_4-C_3-H_3 and P-C_1-C_2-H_2, respectively) caluculated from $J_{3,P}$ and $J_{2,P}$ by Karplus like equations.[10] Conformation of 7A was determined based on the dihedral angles (*ca.* 60° and 110° for P-C_4-C_3-H_3 and P-C_1-C_2-H_2, respectively) caluculated from $J_{3,P}$ and $J_{2,P}$ by Karplus like equations.[10]
12. The nmr parameters of 7R and 7A closely resembled those of structurally and conformationally similar D-ribofuranose analogs: T. Hanaya and H. Yamamoto, *Bull. Chem. Soc. Jpn.*, 1989, 62, 2320.

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