

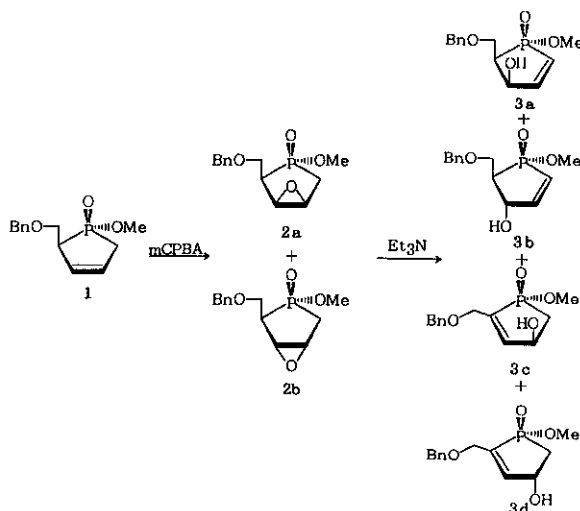
NOVEL EFFICIENT SYNTHESIS AND STRUCTURAL ANALYSIS OF  
FURANOSE-TYPE PHOSPHONO SUGARSMITSUJI YAMASHITA,\* AKIHIRO YABUI, TATSUO OSHIKAWA, TADASHI HANAYA,<sup>†</sup>  
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Abstract-----Reaction of 2-benzyloxymethyl-1-methoxy-3-phospholene 1-oxide with 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,<sup>1,2</sup> have been prepared mostly from sugar materials.<sup>2,3</sup> 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.<sup>4,5</sup> 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.

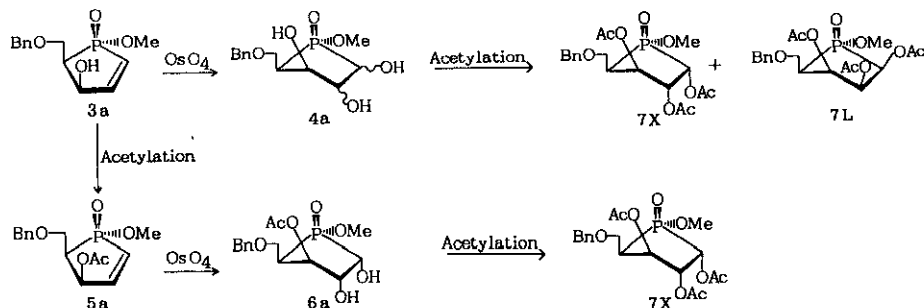
2-Benzyloxymethyl-1-methoxy-3-phospholene 1-oxide (1)<sup>6</sup> was treated with 3-chloroperbenzoic acid (mCPBA, 1.7 equiv.) in chloroform at 100 °C for 2 day to afford (3*R*, 4*S*)- and (3*S*, 4*R*)-2-benzyloxymethyl-3,4-epoxyphospholane 1-oxides (2a and 2b, respectively) in a quantitative yield (2a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

100 °C 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).<sup>8</sup>



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

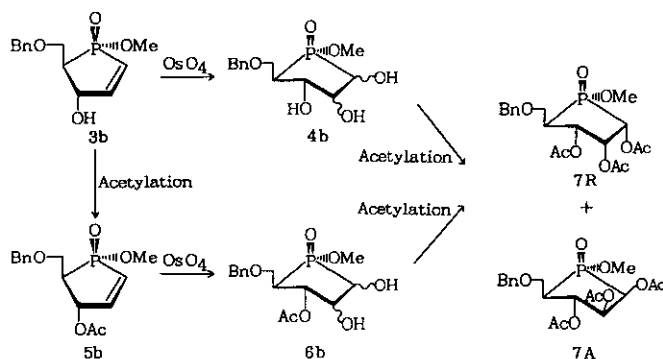
Osmium(VIII) oxide-catalyzed *cis*-dihydroxylation of compound (3a) with sodium chlorate at 40 °C followed by treatment with acetic anhydride in pyridine at room temperature afforded 1,2,3-tri-*O*-acetyl-5-*O*-benzyl-4-deoxy-[(*R*)-methoxyphosphinyl]- $\alpha$ -D-xylofuranose (7X) and - $\beta$ -D-lyxo-furanose (7L) in a ratio of 74 : 26 (7X, <sup>31</sup>P nmr (CDCl<sub>3</sub>)  $\delta$  = 51.6 ppm; 7L, <sup>31</sup>P nmr (CDCl<sub>3</sub>)  $\delta$  = 50.3 ppm; 7X + 7L, 78% from 3a).<sup>7</sup> 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  $\alpha$ -D-xylo- and  $\beta$ -D-lyxo-furanose-type phosphono sugars from 3a.

Osmium(VIII) oxide-catalyzed *cis*-dihydroxylation of compound (3b) at 40 °C 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]- $\alpha$ -*D*-ribofuranose (**7R**) and - $\beta$ -*D*-arabinofuranose (**7A**) in a ratio of 47 : 53 (**7R**,  $^{31}\text{P}$  nmr ( $\text{CDCl}_3$ )  $\delta$  = 49.3 ppm; **7A**,  $^{31}\text{P}$  nmr ( $\text{CDCl}_3$ )  $\delta$  = 47.9 ppm; **7R** + **7A**, 99% from **3b**).<sup>7</sup> Osmium(VIII) oxide-catalyzed *cis*-dihydroxylation of acetylated compound **5b** afforded product **7R** and **7A** (**7R** : **7A** = 59 : 41; **7R** + **7A**, 51% from **3b**)<sup>7</sup> upon acetylation.



Scheme 3. Preparation of  $\alpha$ -*D*-ribo- and  $\beta$ -*D*-arabino-furanose-type phosphono sugars from **3b**.

Table 1. Observed 500 MHz  $^1\text{H}$  nmr spectral parameters for compounds **7R** and **7A** in  $\text{CDCl}_3$ <sup>a)</sup>

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

Compd.	Coupling constant (Hz)												
	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,P}$	$J_{3,4}$	$J_{3,P}$	$J_{4,5}$	$J_{4,5'}$	$J_{4,P}$	$J_{5,5'}$	$J_{5,P}$	$J_{5',P}$	$J_{\text{POMe}}$
<b>7R</b>	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
<b>7A</b>	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 °C 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  $^1\text{H}$  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.<sup>9-12</sup>

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  $^1\text{H}$  and  $^{31}\text{P}$  nmr spectra.
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11. Conformation of 7R was determined based on the dihedral angles (ca.  $65^\circ$  and  $150^\circ$  for  $\text{P-C}_4\text{-C}_3\text{-H}_3$  and  $\text{P-C}_1\text{-C}_2\text{-H}_2$ , respectively) calculated from  $J_{3,\text{P}}$  and  $J_{2,\text{P}}$  by Karplus like equations.<sup>10</sup>
12. Conformation of 7A was determined based on the dihedral angles (ca.  $60^\circ$  and  $110^\circ$  for  $\text{P-C}_4\text{-C}_3\text{-H}_3$  and  $\text{P-C}_1\text{-C}_2\text{-H}_2$ , respectively) calculated from  $J_{3,\text{P}}$  and  $J_{2,\text{P}}$  by Karplus like equations.<sup>10</sup>
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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