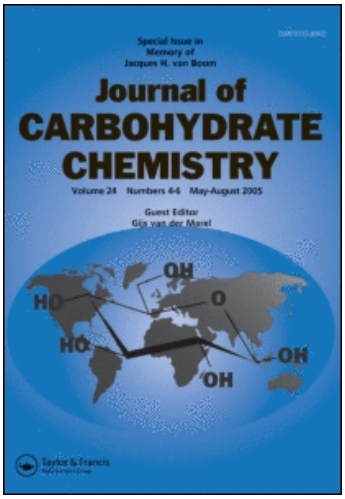

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[a] Department of Materials Chemistry, Faculty of Engineering, Shizuoka University, Hamamatsu, Japan
[b] Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York, U.S.A.

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NOVEL SYNTHESIS AND STRUCTURE OF PHOSPHANYL SUGAR DERIVATIVES[1]

Mitsuji Yamashita,[a]* Akihiro Yabui,[a] Kazumitsu Suzuki,[a] Yukihiro Kato,[a] Miyuki Uchimura,[a] Akihito Iida,[a] Hiroyuki Mizuno,[a] Koichi Ikai,[a] Tatsuo Oshikawa,[a] Laszlo Parkanayi,[b] and Jon Clardy[b]

a Department of Materials Chemistry, Faculty of Engineering, Shizuoka University, Hamamatsu 432, Japan

b Department of Chemistry, Baker Laboratory, Cornell University, Ithaca, New York 14853-1301, U.S.A.

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ABSTRACT

Some phosphanyl sugar derivatives, which are analogs of sugars having a phosphorus atom in place of the ring oxygen, were synthesized from 2- and 3-phospholenes as starting materials. Catalytic *cis*-dihydroxylation of 2-phospholene or 3-phospholene 1-oxide derivatives with osmium(VIII) oxide in the presence of a cooxidant afforded 3-deoxy- or 1-deoxy-tetrofuranose-type phosphanyl sugar derivatives, respectively. *cis*-Dihydroxylation of 4-acyloxy-2-phospholene 1-oxide derivatives gave tetrofuranose type phosphanyl sugar derivatives. Some of these derivatives of phosphanyl sugars were subjected to structural analyses using ^{1}H NMR and X-ray crystallography.

INTRODUCTION

Replacement of the oxygen atom in the hemiacetal ring of normal sugars by a hetero atom or a carbon atom leads to pseudo sugars, some of which have been widely investigated in the fields of synthetic, biological, and medicinal chemistry. In particular, hetero sugars in which the ring oxygen has been replaced by a nitrogen, sulfur, or selenium atom have been extensively studied and widely developed.[2] Although aza and thia sugars

are known to exist in nature, phosphanyl sugar derivatives, having a P atom in place of the ring oxygen, have not yet been found in naturally occurring products.

Phosphanyl sugars are of interest because of their potential biological activities.[3] Therefore phosphanyl sugar derivatives were of interest in the aspects related not only to syntheses and structures but also to biological activities. They have been mainly prepared to date from sugars as starting materials with suitable reaction sequences of OH group protections, functional group interconversions, C-P bond formation, cyclization with the P atom, and deprotection, as illustrated in Scheme 1.[3]

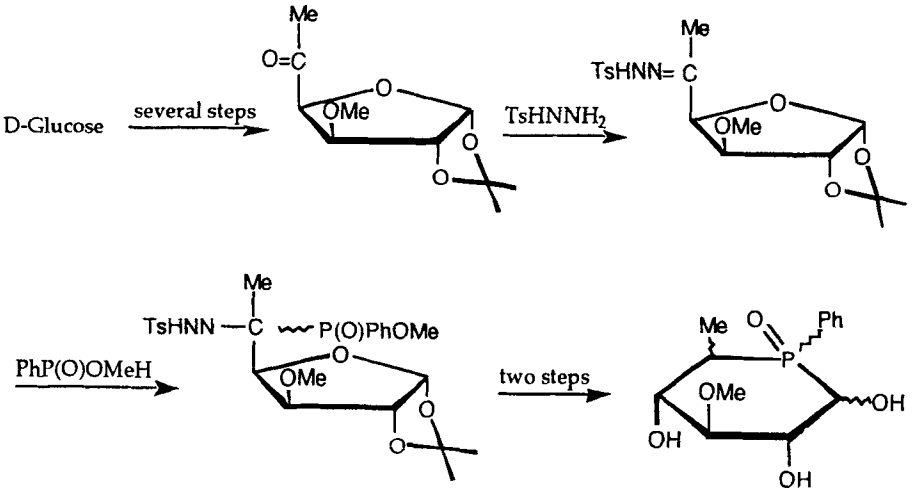
In our previous paper, we reported the *cis*-dihydroxylation of 2-phospholenes with a catalytic amount of osmium(VIII) oxide and cooxidants.[4] The present paper deals with further conversion of 2- and 3-phospholene 1-oxide derivatives to prepare and structurally analyze tetrofuranose-type phosphanyl sugar derivatives.[5]

RESULTS AND DISCUSSION

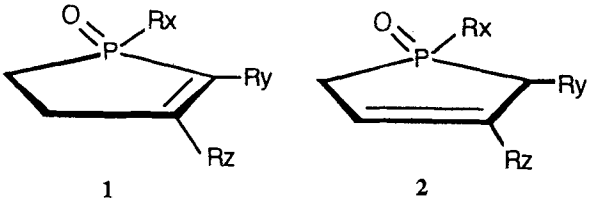
[4+2] Cycloaddition of phosphorus(III) halides to 1,3-dienes such as 1,3-butadiene, 1,3-pentadiene, and 2-methyl-1,3-butadiene followed by solvolysis is known to produce cyclic unsaturated phosphorus heterocycles, i.e., 2- or 3-phospholene 1-oxide derivatives **1** or **2**, respectively (Figure 1).[6] Modification of 3-phospholenes can occur by substitution reactions of the C-1 substituent.[5a,7]

Potassium permanganate is often used to introduce *cis*-dihydroxyl groups onto a carbon-carbon double. However, this reagent was inert toward the double bond of 2-phospholene 1-oxides **1a**, **1c**, and **1i**. Oxidation of 3-methyl-1-phenyl-2-phospholene 1-oxide (**1a**) in aqueous tetrahydrofuran with a catalytic amount of osmium(VIII) oxide and a chlorate as the cooxidant for 18 h at 45-50 ℃ afforded the vicinal *cis*-diol product 2,3-dihydroxy-3-methyl-1-phenylphospholane 1-oxide (**3a**) in 91 % yield (Table 1) and a minor component in a ratio of ca. 13:1 (w/w).[4] The major product **3a** was purified by chromatography on silica gel and isolated as a crystalline compound, whose single crystal X-ray structural analysis afforded an ORTEP drawing as shown in Figure 2. The *cis*-dihydroxylation proceeded in a highly diastereospecific manner and may be controlled by electron-repulsive interactions between the oxygen atom of the phosphoryl group (P=O) of the phospholene derivative and those of osmium(VIII) oxide.

Further investigation on the product ratio of the *cis*-dihydroxylation of 2-phospholene 1-oxides **1** with osmium(VIII) oxide revealed the ratio of major to minor product as shown in Table 2 together with δ values for ^{31}P NMR chemical shifts. Some X-ray single crystallographic data are presented on the following page.



Scheme 1



Rx=Alkyl, Aryl (e.g., Ph), Alkoxyl (e.g., OMe,OEt), Halogen, etc.
Ry,Rz=Alkyl (e.g., Me), Hydrogen, etc.

a; Rx=Ph, Ry=H, Rz=Me
b; Rx=Ph, Ry=Rz=H
c; Rx=OMe, Ry=H, Rz=Me
d; Rx=OMe, Ry=Rz=H
e; Rx=OEt, Ry=H, Rz=Me
f; Rx=OEt, Ry=Rz=H
g; Rx=O^{i}Pr, Ry=H, Rz=Me
h; Rx=O^{i}Pr, Ry=Rz=H
i; Rx=Ph, Ry=Me, Rz=H

Figure 1. Derivatives of 2- and 3-phospholene 1-oxides **1** and **2**, respectively.

Table 1. *cis*-Dihydroxylation of 2-phospholene 1-oxides **1a**, **1c**, and **1i**.

Phospholene	Reaction condition			Product		
No.	Reagent	Temperature (℃)	Time (h)	No.	Yield(%)	MS (*m/z*)[a]
1a	OsO_4-$KClO_3$	45-50	18	**3a**	91	226
1a	OsO_4-$NaClO_3$	45-50	18	**3a**	66	226
1a	OsO_4-$Ba(ClO_3)_2$	45-50	18	**3a**	65	226
1a	OsO_4-$^tBuO_2H$	45-50	24	**3a**	20	226
1b	OsO_4-$KClO_3$	35	48	**3b**	82	212
1c	OsO_4-$KClO_3$	55-60	24	**3c**	35	178
1i	OsO_4-$KClO_3$	45-50	18	**3i**	42	226

a. MS data indicate the molecular ion peak (M^+) in *m/z*.

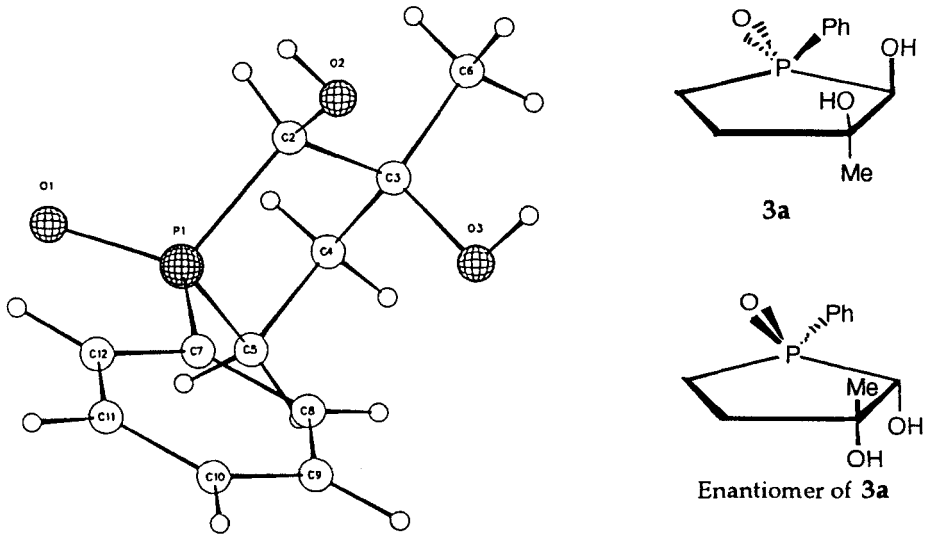


Figure 2. ORTEP Drawing of *cis*-diol **3a**[8] and representation of the enantiomers.

Table 2. *cis*-Dihydroxylation of 2-phospholene 1-oxides **1a-h** and the δ values and ratios of the diastereomeric *cis*-diols **3** and **3'**.

2-Phospholenes				*cis*-Diols **3** and **3'**			
No.	Rx	Ry	Rz	Yield(%)	^{31}P NMR δ (ppm)		Ratio of diols
					3	**3'**	**3** : **3'**
1a	Ph	H	Me	91	50.1	62.7	7.5 : 1.0
1b	Ph	H	H	82	48.9	60.4	1.4 : 1.0
1c	OMe	H	Me	65	70.8	68.6	3.1 : 1.0
1d	OMe	H	H	76	69.0	67.4	2.2 : 1.0
1e	OEt	H	Me	79	69.1	67.0	4.5 : 1.0
1f	OEt	H	H	83	67.5	66.5	3.4 : 1.0
1g	O^{i}Pr	H	Me	85	67.2	65.4	4.0 : 1.0
1h	O^{i}Pr	H	H	81	65.7	64.9	1.7 : 1.0

X-ray single crystallographic data:

Molecular formula: $C_{11}H_{15}O_3P$. Formula weight: 226.21.

Unit Cell Parameters: a=8.105(1) Å, b=17.029(3) Å, c=9.080(1) Å, β=113.38(1)°, V=1150.32(29) Å^3, Z=4, Space group: $P2_1/a$, F(000)=480.

Experimental conditions: λ (Cu-K$_\alpha$)=1.5418 Å, $P2_1$ four-circle diffractometer, Graphite monochrometor, Room temperature, ω-scan techinique, θ-range: 0-57°, Crystal size: 0.32 x 0.12 x 0.20 mm, D_x=1.306 gcm^{-3}, μ (Cu-K$_\alpha$)=20.1 cm^{-1}, Check reflections: -2 4 2; -3 3 2; -2 -4 3.

Data treatment: Total no. of intensities collected: 1805, Merging and averaging gave 1555 unique data (98 reflections were avaraged, R(I)=0.020), Observed reflections: 954 [I>3 σ (I) and I>100] (61.4 %).

Structure determination and refinement: Heavy atom method and Fourier techniques. Block-digital Least-squares. H-atoms of the OH groups were located in difference maps while the positions of the remaining H atoms were generated from assumed geometries. The H atoms were refined in 3 final least-squares cycles and they behaved well.

R factors: R=0.039 (R_w=0.051) for 954 observed reflections, GOF=0.165. R=0.064 for all (1555) data (R=0.059 excluding zeroes). Highest peak in final difference map: +576 (scale=1.8954).

The X-ray program used: K. Sugawara, M. Tsunakawa, M. Konishi, H. Kawaguchi, B. Krishanan, C.-H. He, and J. Clardy, *J. Org. Chem.*, **52**, 996 (1987).

Selected bond distances in Å: P(1)-C(2) 1.849(5), C(2)-C(3) 1.532(5), C(3)-C(4) 1.524(6), C(4)-C(5) 1.522(7). C(5)-P(1) 1.811(4), P(1)-O(1) 1.498(3), P(1)-C(7) 1.784(4).

Selected bond angles in degree: P(1)-C(2)-C(3) 105.2(3), C(2)-C(3)-C(4) 105.2(3), C(3)-C(4)-C(5) 108.0(3), C(4)-C(5)-P(1) 103.7(3), C(5)-P(1)-C(2) 95.5(2), O(1)-P(1)-C(2) 112.4(2), O(1)-P(1)-C(7) 110.7(2), C(5)-P(1)-C(7) 112.5(2), C(2)-P(1)-C(7) 110.5(2), O(1)-P(1)-C(5) 114.4(2).

Selected torsional angles in degree: P(1)-C(2)-C(3)-C(4) 35.5(4), C(2)-C(3)-C(4)-C(5)-51.3(4), C(3)-C(4)-C(5)-P(1) 41.5(4), C(5)-P(1)-C(2)-C(3)-10.8(3), C(2)-P(1)-C(5)-C(4)-17.0(3).

These data imply that the conformation of **3a** is in a $^3T_2$ form.

Figure 2 shows that the geometric relationship between P=O and 2-OH is *anti* and that of the two OHs is *syn*. The high diastereoselectivity may be due to a restricted direction of attack by OsO_4. Attack of OsO_4 may be affected by steric and electronic effects of substituents around the olefinic carbon atoms, e.g., P=O, P-Rx (Rx=Ph or OR; R=Me, Et, or ^{i}Pr), C-Ry (Ry=H), and C-Rz (Rz=H or Me) on the 2-phospholene ring. The relative order of electron withdrawing power for some groups attached to a tetracoordinated phosphorus atom is reported as follows: F ≒ CF_3>OPh>OMe ≒ Cl>Br>Et>NMe_2>Ph ≒ Me>^{t}Bu.[9] The result of diastereoselectivity for the *cis*-dihydroxylation of 2-phospholene derivatives shown in Table 2 may be well explained by electron repulsive interactions, being one of the most important factors for the stereoselectivity, between oxygen atoms of phosphoryl group (P=O) and attacking reagent OsO_4. The electron density of the oxygen atom of the P=O may be increased to afford P^+-O^- charge separation by the 3-methyl substituent (Rz=Me) larger than by the 3-H substituent (Rz=H). Hence the methyl substituent enhances the electron repulsive power of the P=O group toward OsO_4, therefore, *anti* diastereoselectivity for 3-methyl-2-phospholene derivatives (Rz=Me) (**1a**, **1c**, **1e**, and **1g**) becomes greater than that for the corresponding 3-unsubstituted derivatives (Rz=H) (**1b**, **1d**, **1f**, and **1h**). The result that the P-Ph substituent induced greater *anti* diastereoselectivity (Figure 3) than the P-OR substituent did in the 2-phospholene ring may also be explained by electron repulsive interaction and steric hindrance factors. Among the P-OR substituents for P-Rx, the order of the selectivity obtained in the present study was OMe ≒ O^{i}Pr<OEt. The σ * and the Es values of Taft's equation are reported as follows: Me=0.00 and 0.00, Et=-0.100 and -0.07, and ^{i}Pr=-0.190 and -0.47, respectively.[10] Therefore, based on the σ * values the order of the selectivity may be OMe<OEt<O^{i}Pr, while, based on the Es values the order may be OMe>OEt>O^{i}Pr. The observed stereoselectivity for the P-OR groups may be explained by either an electronic effect or steric effect of the alkyl group of P-OR, i.e., in the order of OMe ≒ O^{i}Pr<OEt. The

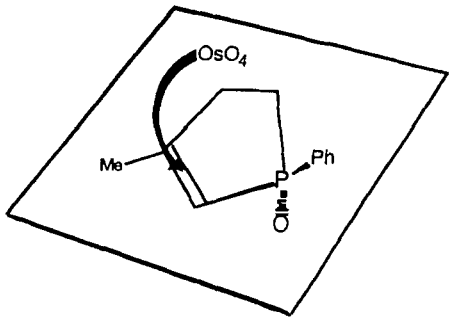
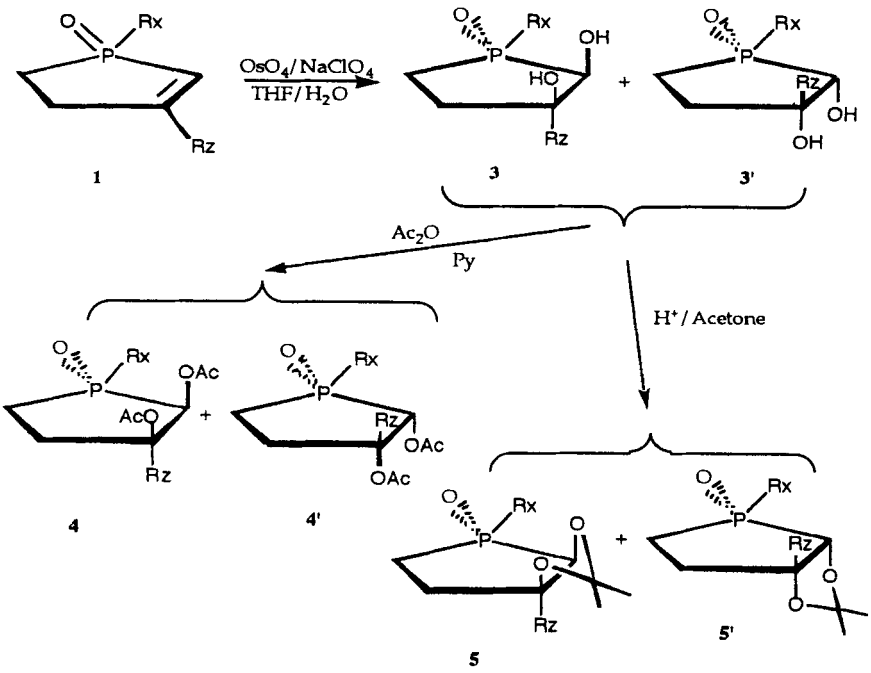


Figure 3. Schematic representation of osmium(VIII) oxide which attacks from the reverse side of P=O bond of a 2-phospholene 1-oxide.

prolonged reaction time (longer than about 48 h) allowed the further oxidation reaction of the *cis*-diols produced to afford ketone and aldehyde derivatives being recognized by ^{1}H NMR and TLC on silica gel.

Acetylation and acetonidation of 2,3-*cis*-dihydroxy-1-(substituted)-3-(substituted or unsubstituted)-phospholane 1-oxides (**3a-h** and **3'a-h**) were performed by the treatment with acetic anhydride/pyridine and with H^+/acetone, respectively, to afford 2,3-*cis*-di-acetoxy-1-(substituted)-3-(substituted or unsubstituted)-phospholane 1-oxides (**4a-h** and **4'a-h**) and 2,3-isopropylidenedioxy-1-(substituted)-3-(substituted or unsubstituted)-phospholane 1-oxides (**5a-h** and **5'a-h**), respectively, in quantitative yields (Scheme 2). Conversion of diols **3** and **3'** to diacetates **4** and **4'** and acetonides **5** and **5'** confirmed further that the *cis*-dihydroxylation of the olefin of 2-phospholenes **1** by OsO_4 yielded mainly **3** (minor product **3'**). The olefin of the 2-phospholene derivatives should be somewhat electron deficient because of the highly electron-withdrawing property of the P=O group. Therefore, potassium permanganate was not a powerful enough oxidizing agent for such an electron poor olefin.

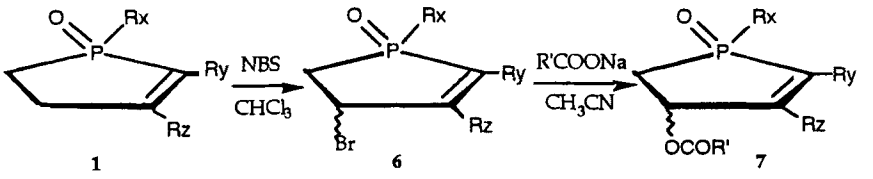
Introduction of an acyloxyl group at the 4-position of 2-phospholene 1-oxide derivatives **1b** (Rx=Ph, Ry=Rz=H), **1c** (Rx=OMe, Ry=H, Rz=Me), **1d** (Rx=OMe, Ry=Rz=H), **1e** (Rx=OEt, Ry=H, Rz=Me), and **1f** (Rx=OEt, Ry=Rz=H) was carried out by allylic bromination of the substrate with NBS to prepare bromides **6b**, **6c**, **6d**, **6e**, and **6f** followed by acyloxylation to give 4-acyloxy-2-phospholene 1-oxide derivatives **7b** (Rx=Ph, Ry=Rz=H, R'=Me), **7c** (Rx=OMe, Ry=H, Rz=Me, R'=Me), **7c'** (Rx=OMe, Ry=H, Rz=Me, R'=Ph), **7d** (Rx=OMe, Ry=Rz=H, R'=Me), **7e** (Rx=OEt, Ry=H, Rz=Me, R'=Me), **7e'** (Rx=OEt, Ry=H, Rz=Me, R'=Ph), **7f** (Rx=OEt, Ry=Rz=H, R'=Me), and **7f'** (Rx=OEt, Ry=Rz=H, R'=Ph), respectively. Compounds **7** were then

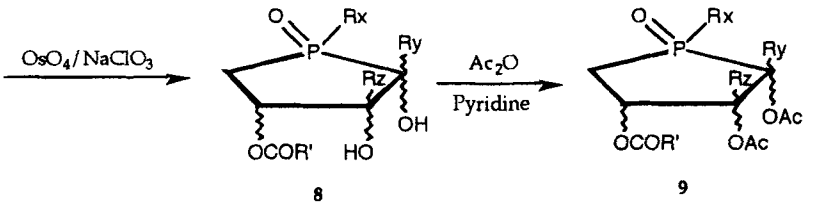


Scheme 2

treated with a catalytic amount of OsO_4 and cooxidant $NaClO_3$ as mentioned above to prepare tetrofuranose type phosphanyl sugar derivatives **8b**, **8c**, **8c'**, **8d**, **8e**, **8e'**, **8f**, and **8f'** which were further acetylated to give triacylates **9b** (Rx=Ph, Ry=Rz=H, R'=Me), **9c** (Rx=OMe, Ry=H, Rz=Me, R'=Me), **9c'** (Rx=OMe, Ry=H, Rz=Me, R'=Ph), **9d** (Rx=OMe, Ry=Rz=H, R'=Me), **9e** (Rx=OEt, Ry=H, Rz=Me, R'=Me), **9e'** (Rx=OEt, Ry=H, Rz=Me, R'=Ph), **9f** (Rx=OEt, Ry=Rz=H, R'=Me), and **9f'** (Rx=OEt, Ry=Rz=H, R'=Ph) (Scheme 3 and Table 3).

There are four possible diastereoisomers for 2,3,4-triacetoxy-3-methyl-1-phenylphospholane 1-oxide **9d** produced by *cis*-dihydroxylation of **7d** prepared from **1d** leading to a mixture of four sets of NMR. The product analyses for **9d** by ^{31}P, ^{13}C, and ^{1}H NMR revealed that the product triacetate **9d** showed three sets of signals, respectively. Similar results were observed for **9f** and **9f'**. The ^{31}P NMR spectrum of **9d** gave three peaks at δ 59.2, 61.7, and 62.8 ppm in the area ratio of ca. 2:1:2 for three of the four diastereoisomers. The ^{13}C NMR spectrum of triacetate **9d** showed three doublet peaks for the C-5 carbon at δ 29.2 (J=89.6 Hz), 29.3 (J=88.2 Hz), and 29.7 (J=88.2 Hz) ppm. Three components were also easily recognized in the 400 MHz ^{1}H NMR spectrum of **9d** [δ =





1b, 6b: Rx=Ph, Ry=Rz=H; **1c, 6c:** Rx=OMe, Ry=H, Rz=Me;
1d, 6d: Rx=OMe, Ry=Rz=H; **1e, 6e:** Rx=OEt, Ry=H, Rz=Me;
1f, 6f: Rx=OEt, Ry=Rz=H.
7b-9b: Rx=Ph, Ry=Rz=H, R'=Me; **7c-9c**: Rx=OMe, Ry=H, Rz=Me, R'=Me;
7c'-9c': Rx=OMe, Ry=H, Rz=Me, R'=Ph; **7d-9d**: Rx=OMe, Ry=Rz=H, R'=Me;
7e-9e: Rx=OEt, Ry=H, Rz=Me, R'=Me; **7e'-9e'**: Rx=OEt, Ry=H, Rz=Me, R'=Ph;
7f-9f: Rx=OEt, Ry=Rz=H, R'=Me; **7f'-9f'**: Rx=OEt, Ry=Rz=H, R'=Ph.

Scheme 3

Table 3. Preparation of 4-acyloxy-2-phospholene 1-oxides and 4-acyloxy-2,3-*cis*-dihydroxyphospholane 1-oxides.

2-Phospholenes	Substituents			R'	Yield of products (%)			
No.	Rx	Ry	Rz		**6**	**7**	**8**	**9**
1b	Ph	H	H	Me	100	61	45	69
1c	OMe	H	Me	Me	100	55	71	75
1c	OMe	H	Me	Ph		67	41	78
1d	OMe	H	H	Me	98	75	63	68
1e	OEt	H	Me	Me	100	90	74	80
1e	OEt	H	Me	Ph		83	69	76
1f	OEt	H	H	Me	100	51	51	52
1f	OEt	H	H	Ph		93	93	46

3.73 (J=11.27 Hz), 3.79 (J=11.18 Hz), and 3.80 (J=11.19 Hz) ppm in an intensity ratio of ca. 2:2:1]. From these observations, it seems that OsO_4 attacks the olefin double bond of a 2-phospholene 1-oxide predominantly from the side opposite to the P=O oxygen, being the less electron-repulsive side (Figure 3). Cha and coworkers reported that OsO_4 reacted with an oxygen containing olefin, an allylic chiral alcohol, from the opposite side of oxo-substituents linked at the allylic chiral center.[11] Therefore, attack of OsO_4 may be controlled electron-repulsively by the oxygen atoms of P=O and 4-acyloxyl groups of phospholene derivatives **7**. For a diastereomer having P=O and 4-OCOR' (R'=Me or Ph) groups on the same side of the 2-phospholene heterocycle, OsO_4 may predominantly attack from the opposite side of these two diastereoselectively important groups. However, for a diastereomer having P=O and 4-OCOR' groups at the opposite side of the 2-phospholene heterocycle, OsO_4 may attack from either opposite side of a P=O or a 4-OCOR' group. Hence the structures of the three racemic products observed by NMR will have configurations shown in Figure 4. Compound **9d**β**DT** corresponds to 1,2,3-*O*-triacetyl-1,4-*C*-[(*S*)-methoxyphosphinylidene]-β-D-*threo*-tetrofuranose and the enantiomer, having the P=O and the 4-OAc on the same side and the P=O and the 2-OAc (3-OAc) on the opposite side of the phosphanyl sugar heterocycle. Compound **9d**α**LE** corresponds to 1,2,3-*O*-triacetyl-1,4-*C*-[(*S*)-methoxyphosphinylidene]-α-L-*erythro*-tetrofuranose and the enantiomer, having the P=O, the 4-OAc, and the 2- OAc (3-OAc) on the opposite side of the heterocycle. Compound **9d**β**LT** corresponds to 1,2,3-*O*-triacetyl-1,4-*C*-[(*S*)-methoxyphosphinylidene]-β-L-*threo*-tetrofuranose and the enantiomer, having the P=O and the 4-OAc on the opposite side and the P=O and the 2-OAc (3-OAc) on the same side of the heterocycle. The *cis*-dihydroxylation reagent OsO_4 may suffer from an electron-repulsive effect more effectively by P=O than by OAc. Therefore, compounds **9d**β**DT** and **9d**α**LE** are the major components, whereas, **9d**β**LT** is the minor one (Figure 4).

1-(Substituted)-3-(substituted or unsubstituted)-3-phospholene 1-oxides **2** were *cis*-dihydroxylated by the action of a catalytic amount of OsO_4 in the presence of $NaClO_3$ in THF-H_2O (1:1) for 2d at 30-40 ℃ to afford diastereomeric 3,4-dihydroxy-1-(substituted)-3-(substituted or unsubstituted)-phospholane 1-oxides **10** and **10'** in good to excellent yields. Diols **10** and **10'** were converted to their isopropylidene derivatives by treatment with acetone under acidic conditions to give **11** and **11'**, respectively (Scheme 4 and Table 4).

The *syn* or *anti* relationship between the P=O and the 2,3-*O*-isopropylidene groups of acetonides **11** (*anti*) and **11'** (*syn*) was determined from NMR data. When the relationship between P=O and C-H in P-C-C-H linkage is *anti* (i.e., H is *syn* to O), the proton in the *cis* diaxal 1,3-relation to the P=O group is deshielded,[12] and resonates at the lower field than

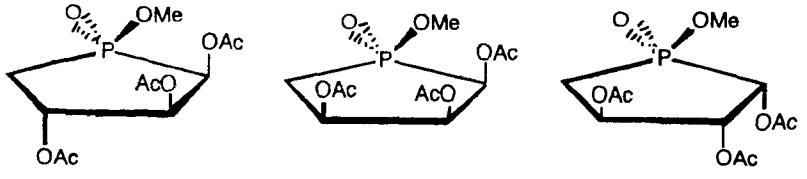
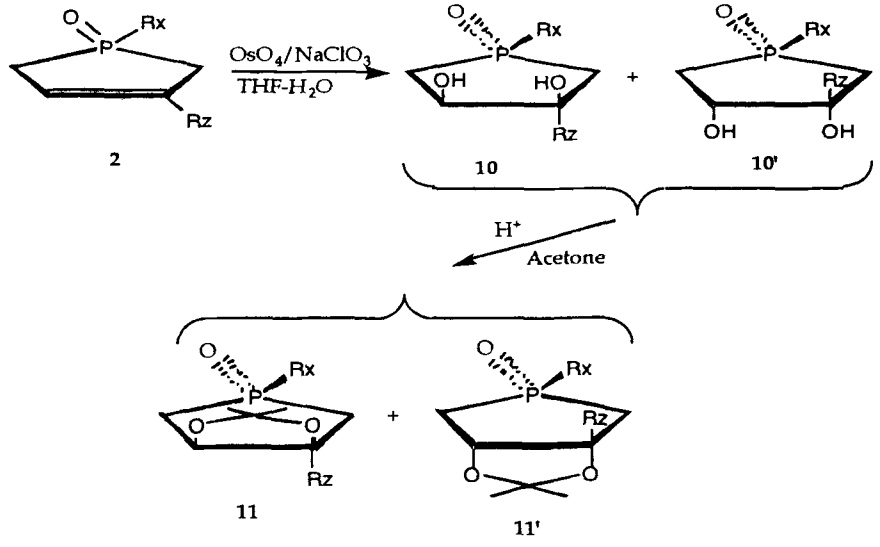


Figure 4. Possible structures for tetrofuranose type phosphanyl sugars prepared.



a: Rx=Ph, Rz=Me; **b**: Rx=Ph, Rz=H; **c**: Rx= α -Np, Rz=H; **d**: Rx=OMe, Rz=Me; **e**: Rx=OMe, Rz=H; **f**: Rx=O^{i}Pr, Rz=H.

Scheme 4

would an *anti* proton. The proton chemical shift of *anti* isomer **11** is at lower field than that of *syn* isomer **11'**. The structures of *syn* and *anti* isomers were further confirmed using a shift reagent technique with tris(dipivalometanato)europium [Eu(dpm)$_3$] for compounds **11b** and **11b'**. The larger downfield shift for the *ortho* hydrogens of the phenyl group and the smaller downfield shift for 3,4-hydrogens of the phospholane ring were observed for compound **11b** compared with those downfield shifts for compound **11b'** when up to ca. 20 mol % of Eu(dpm)$_3$ was used. The observation resembled quite well the shift tendency observed for the *anti* isomer of 3,4-oxo-1-phenylphospholane 1-oxide (**12**).[13]

Table 4. *cis*-Dihydroxylation of 3-phospholene 1-oxides **2**.

3-Phospholenes			Diols **10** and **10'**		Acetonides **11** (*anti*) and **11'** (*syn*)					
No.	Rx	Rz	Y (%)[a]	Mp (℃)	Y (%)[a]	Ratio	Mp (℃)		^{1}H, ^{13}C, or ^{31}P NMR[b]	
						11:**11'**	**11**	**11'**	**11**	**11'**
2a	Ph	Me	79	146-157	--	---	---	---	---	---
2b	Ph	H	78	134-140	72	34:38[c]	74-79	131-133	5.00(14.7)[d]	4.80(16.0)[d]
2c	α-Np	H	58	163-170	88	49 : 39[c]	94-96	---	5.00(19.7)[d]	---
2d	OMe	Me	100	---	70	3.5: 1.0[e]	---	---	4.36(34.9)[d]	4.29(28.7)[d]
									3.77(11.2)[f]	3.72 (11.0)[f]
2e	OMe	H	100	---	84	7.8: 1.0[e]	---	---	4.70(26.4)[d]	4.62(25.9)[d]
									3.71(11.4)[f]	3.64(11.0)[f]
									74.7[g]	72.6[g]
2f	O^{i}Pr	H	78	---	59	2.0: 1.0[e]	---	---	69.59(6.7)[h]	70.14(6.0)[h]

a. Y (%) means either total yield of diols **10** and **10'** or acetonides **11** and **11'**.
b. Data show chemical shift and coupling constant of ^{1}H NMR unless otherwise noted.
c. Isolated product ratio.
d. Chemical shift value for H-C-C-P. Value in the parentheses shows the H-C-C-P coupling constant $^3J_{HP}$.
e. Peak ratio on NMR.
f. Chemical shift value for Me-O-P. Value in the parentheses shows the H-C-O-P coupling constant $^3J_{HP}$.
g. Value of ^{31}P NMR chemical shift.
h. Value of ^{13}C NMR chemical shift for P-O-C. Value in the parentheses shows the P-O-C coupling constant $^2J_{PC}$.

The shift reagent experiment shows that compounds **11b** and **11b'** are *anti* and *syn* diastereoisomers, respectively (see Experimental).

The diastereoselectivity for *cis*-dihydroxylation of 3-phospholene 1-oxides with OsO_4 predominantly proceeded to give *anti* diastereomer **11** over *syn* isomer **11'**. This may be brought about by electron repulsive interaction between the oxygen atom of the P=O group and OsO_4. Nevertheless, the ratio of *anti* to *syn* from 3-phospholene 1-oxides was reduced compared with the ratio from 2-phospholene 1-oxides. Here again the steric effect of the substituent at the phosphorus atom seems to exert a secondary effect on the ratio.

The synthesis of pentofuranose type phosphanyl sugar derivatives, glycosides and nucleosides of phosphanyl sugars, and structure and biological activity of phosphanyl sugars being prepared by applying the present method will be reported hereafter.

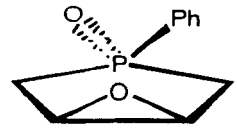


Figure 5. *anti* Epoxide **12**.

EXPERIMENTAL

General methods. Melting points were determined with a Yanagimoto MP-S2 micro-melting point apparatus and were uncorrected. ^{1}H NMR were recorded on Hitachi R-24B (at 60 MHz), Japan Electron Optics Laboratory (JEOL) JNM-EX90 (at 90 MHz), JEOL JNM-EX400 (at 400 MHz), and Varian VXR-500 (at 500 MHz) spectrometers using $CDCl_3$ and TMS as the solvent and the internal standard, respectively. ^{13}C NMR were recorded on a JEOL EX90 (at 22.40 MHz) spectrometer using $CDCl_3$ and TMS as the solvent and the internal standard, respectively. ^{31}P NMR spectra were measured by JEOL JNM-EX90 (at 36.18 MHz) and Varian VXR-500 spectrometers using $CDCl_3$ and H_3PO_4 as the solvent and the external standard, respectively. IR were recorded on a Japan Spectroscopic Co. Ltd. (JASCO) A-3 spectrophotometer. MS spectra were measured by Hitachi RMU7M GC-MS mass spectrometer. HPLC were carried out using JASCO UNIFLOW-211 with UVIDEC-100-H, FINEPAC SIL, and MeOH-$CHCl_3$ (1:20 (v/v)) as the detector, column, and solvent, respectively. Phospholene 1-oxides (2- and 3-) **1** and **2**, respectively, were prepared according to the reported methods via cycloaddition reaction of 1,3-dienes (1,3-butadiene, 1,3-pentadiene, and 2-methyl-1,3-butadiene) and phosphorus trihalide (phosphorus trichloride and phosphorus tribromide) or phenylphosphonous dichloride.[4,6,14-16] Conversion of an alkoxyl substituent on the phosphorus atom of 2- and 3-phospholenes to a chloro substituent followed by Grignard coupling reaction of the 1-chloro-2- and 1-chloro-3-phospholene 1-oxides with phenylmagnesium bromide afforded 1-phenyl-2- and 1-phenyl-3-phospholene 1-oxides.[5a,7,14a,17]

***cis*-Dihydroxylation of 3-methyl-1-phenyl-2-phospholene 1-oxide (1a).** 2-Phospholene 1-oxide **1a** (2.89 g, 15.1 mmol), OsO_4 (0.10 g, 0.39 mmol), and potassium chlorate (2.63 g, 21.5 mmol) were dissolved in THF (17 mL) and water (33 mL) and the solution was stirred for 18 h at 45-50 ℃. Removal of the solvent *in vacuo* followed by extraction of the residue with chloroform (30 mL), dehydration with sodium sulfate, and evaporation of chloroform afforded the product, *cis*-2,3-dihydroxy-3-methyl-1-phenylphospholane 1-oxide (**3a**, 3.11 g, 13.8 mmol), in 91% yield. Purification by

column chromatography on silica gel and recrystallization from carbon tetrachloride afforded the major and the minor components in a ratio of ca. 13:1 (w/w). The major puroduct **3a** formed pure single crystals; mp 185-188 ℃; ^{1}H NMR ($CDCl_3$) δ 1.45 (d, 3H, J_{PH}=2.0 Hz, CH_3), 1.75-2.85 (m, 4H, CH_2-CH_2), 3.80 (d, 1H, J_{PH}=2.0 Hz, P-CH), 4.60 (s, 2H, 2OH), 7.5-7.9 (m, 5H, Ph); ^{31}P NMR ($CDCl_3$) δ 50.1; IR ν (KBr) 3375 (OH), 1450 (P-Ph), 1150 (P=O), 750 (P-C); MS (*m/z*) 125 (100%, PhP(O)H), 226 (48%, M^+).

Anal. Calcd for $C_{11}H_{15}O_3P$ (226.17): C, 58.42; H, 6.69; P, 13.68. Found: C, 58.48; H, 6.66; P, 13.64.

The minor product **3a'**; mp 173-175 ℃; ^{1}H NMR ($CDCl_3$) δ 1.40 (d, 3H, J_{PH}=1.8 Hz, CH_3), 1.9-3.0 (m, 4H, CH_2-CH_2), 3.75 (d, 1H, J_{PH}=1.3 Hz, P-CH), 4.60 (s, 2H, 2OH), 7.3-7.8 (m, 5H, Ph); ^{31}P NMR ($CDCl_3$) δ 62.7; IR ν (KBr) 3375 (OH), 1450 (P-Ph), 1150 (P=O), 750 (P-C); MS (*m/z*) 125 (100%, PhP(O)H), 226 (30%, M^+).

Anal. Calcd for $C_{11}H_{15}O_3P$ (226.17): C, 58.42; H, 6.69; P, 13.68. Found: C, 57.98; H, 6.68; P, 13.22.

***cis*-Dihydroxylation of 1-phenyl-2-phospholene 1-oxide (1b).** 2-Phospholene 1-oxide **1b** (2.63 g, 14.8 mmol), OsO_4 (0.032 g, 0.12 mmol), and sodium chlorate (2.66 g, 25.0 mmol) were dissolved in THF (20 mL) and water (40 mL) and the solution was stirred for 48 h at 35 ℃. Removal of the solvent *in vacuo* followed by extraction of the residue with chloroform (50 mL), dehydration with sodium sulfate, evaporation of chloroform, and column chromatography on silica gel afforded *cis*-2,3-dihydroxy-1-phenylphospholane 1-oxide (**3b**, 2.58 g, 12.2 mg) in 82% yield; mp 142-149 ℃; ^{1}H NMR ($CDCl_3$) δ 1.4-2.6 (m, 4H, CH_2-CH_2), 3.4-4.7 (m, 2H, P-CH-CH), 5.90 (bs, 2H, 2OH), 7.1-8.0 (m, 5H, Ph); IR ν (KBr) 3430 (OH), 1440 (P-Ph), 1170 (P=O), 750 (P-C); MS (*m/z*) 125 (100%, PhP(O)H), 212 (30%, M^+).

Anal. Calcd for $C_{10}H_{13}O_3P$ (212.29): C, 56.61; H, 6.18; P, 14.60. Found: C, 56.70; H, 6.16; P, 14.54.

Yields, isomer ratios, and chemical shift values (δ) of ^{31}P NMR ($CDCl_3$) for compounds **3a-h** and **3'a-h** thus prepared were summarized in Table 2.

2,3-Diacetoxy-3-methyl-1-phenylphospholane 1-oxide (4a). To a dried pyridine (5 mL) solution of 2,3-*cis*-dihydroxyl derivative **3a** (0.25 g, 1.1 mmol) was added acetic anhydride (3 mL) and the solution was left for 24 h at room temperature. Then to the reaction mixture was added chloroform (40 mL) and the organic phase was washed with water (2 × 20 mL). It was dried over sodium sulfate and then filtered. Evaporation of the volatile materials *in vacuo* afforded product **4a** (0.32 g, 1.0 mmol) in 94% yield; ^{1}H NMR ($CDCl_3$) δ 1.55 (s, 3H, CH_3), 1.75, 2.10 (2s, 6H, 2AcO), 2.2-3.0 (m, 4H, CH_2-CH_2), 5.10 (d, 1H, J_{PH}=9.0 Hz, P-CH), 7.4-8.2 (m, 5H, Ph); IR ν (neat) 1740

(C=O), 1442 (P-Ph), 1380 (O-CO-CH_3), 1250 (P=O), 750 (P-C); MS (*m/z*) 125 (100%, PhP(O)H), 310 (28%, M^+).

Yields, isomer ratios, and chemical shift values (δ) of ^{31}P NMR ($CDCl_3$) for compounds **3a-h** and **3'a-h** thus prepared were summarized in Table 2.

2,3-Isopropylidenedioxy-3-methyl-1-phenylphospholane 1-oxide (5a). To an anhydrous acetone (16 mL) solution of 2,3-*cis*-dihydroxyl derivative **3a** (0.90 g, 4.0 mmol) was added anhydrous copper (II) acetate (1.59 g) and conc sulfuric acid (0.08 mL), and the solution was stirred for 48 h at room temperature. After completion of the acetonide forming reaction (checked by TLC, usually 24-48 h) the solution was neutralized with calcium hydroxide and then filtered. Evaporation of acetone followed by extraction of the residue with chloroform and reevaporation of the solvent afforded acetonide **5a** (1.06 g, 4.0 mmol) quantitatively; ^1H NMR ($CDCl_3$) δ 1.30 (s, 3H, CH_3), 1.40, 1.65 (2s, 6H, CMe_2), 2.0-2.9 (m, 4H, CH_2-CH_2), 4.40 (d, 1H, J_{PH}=11.0 Hz, P-CH), 7.4-8.0 (m, 5H, Ph); IR ν (neat) 1440 (P-Ph), 1260 (P=O), 1215 (CMe_2), 750 (P-C); MS (*m/z*) 125 (100%, PhP(O)H), 266 (30%, M^+).

Similarly, diacetates **4** and acetonides **5** were prepared (Table 5).

4-Bromo-1-phenyl-2-phospholene 1-oxide (6b). A carbon tetrachloride (30 mL) solution of 2-phospholene 1-oxide **1b** (1.70 g, 9.57 mmol), NBS (1.74 g, 9.79 mmol), and a catalytic amount of benzoyl peroxide was refluxed under a nitrogen atmosphere for 3 h. After completion of the allylic bromination, the reaction mixture was cooled with ice and the formed insoluble material was filtered off. The mother liquor was washed with sodium hydrogencarbonate solution (10 mL) and the aqueous layer was extracted with chloroform (2 × 6 mL). The combined organic layers were dried over sodium sulfate and then concentrated to give 4-bromo derivative **6b** (2.46 g, 9.57 mmol) in quantitative yield; ^1H NMR ($CDCl_3$) δ 2.0-3.4 (m, 2H, P-CH_2), 4.9-5.6 (m, 1H, Br-CH), 6.40 (ddm, 1H, J_{HH}=8.0 Hz, J_{HP}=34.0 Hz, P-CH=), 6.80 (dm, 0.5H, J_{HH}=8.0 Hz, 0.5×C-CH=), 7.3-8.2 (m, 5.5H, Ph, 0.5×C-CH=); IR ν (neat) 1440 (P-Ph), 1210 (P=O).

4-Benzoyloxy-1-ethoxy-3-methyl-2-phospholene 1-oxide (7e'). A solution of 4-bromo-1-ethoxy-3-methyl-2-phospholene 1-oxide (**6e**) (2.80 g, 11.7 mmol) and sodium benzoate (2.40 g, 17 mmol) in acetonitrile (10 mL) was heated under reflux for 2 d. The insoluble material was filtered off and the mother liquor was concentrated *in vacuo*. The residue was column chromatographed on silica gel to afford benzoyloxyl derivative **7e'** (2.72 g, 9.71 mmol) in 83% yield; ^1H NMR ($CDCl_3$) δ 1.35 (t, 3H, *J*=7.0 Hz, O-CH_2-$\underline{CH_3}$), 2.04 (s, 3H, C-Me), 1.7-3.0 (m, 2H, P-CH_2), 4.13, 4.15 (2dq, 2H,

Table 5. Diacetates **4** and acetonides **5** prepared.

2-Phospholenes			4				5		
No.	Rx	Rz	Yield (%)	^{1}H NMR δ [a] (ppm)	IR ν [b] (cm^{-1})	MS [c] (*m/z*)	Yield (%)	IR ν [d] (ppm)	MS [c] (*m/z*)
1a	Ph	Me	94	1.75, 2.10	1740, 1250	310	100	1260	266
1b	Ph	H	89	1.80, 2.20	1730, 1250	296	76	1170	252
1c	OMe	Me	80	1.88, 2.13	1720, 1240	264	70	1220	220
1d	OMe	H	76	1.84, 2.05	1730, 1220	250	82	1230	206
1e	OEt	Me	85	1.90, 2.10	1720, 1240	278	83	1220	234
1f	OEt	H	88	1.95, 2.15	1730, 1230	264	90	1230	220
1g	O^{i}Pr	Me	82	1.92, 2.10	1730, 1240	292	95	1240	248
1h	O^{i}Pr	H	78	1.99, 2.14	1740, 1250	278	84	1230	234

a. Values show the absorption by acetyl groups.
b. The first and second values mean C=O and P=O frequencies.
c. Molecular ion peak (M^+).
d. Value shows P=O frequencies.

J_{HH}=J_{HP}=7.0 Hz, O-C<u>H</u>$_2$-CH$_3$), 5.43, 5.6-6.0 (bs, m, 1H, C<u>H</u>-OBz), 6.0 (dm, 1H, J_{HP}= 20.0 Hz, P-CH=), 7.2-8.2 (m, 5H); IR ν (neat) 1725 (C=O), 1240 (P=O), 1040 (P-O-C).

4-Benzoyloxy-1-ethoxy-2,3-dihydroxy-3-methylphospholane 1-oxide (8e'). 4-Benzoyloxy-1-ethoxy-3-methyl-2-phospholene 1-oxide (**7e'**) (2.72 g, 9.72 mmol) was *cis*-dihydroxylated with osmium(VIII) oxide (30 mg, 0.12 mmol) and sodium chlorate (1.74 g, 17 mmol) by a similar procedure to that mentioned above for the synthesis of *cis*-diol **3b** to give 4-benzoyloxy-1-ethoxy-2,3-dihydroxyl derivative **8e'** (2.10 g, 6.70 mmol) in 69% yield. Recrystallization of product **8e'** from carbon tetrachloride afforded a pure major diastereomer (1.24 g, 3.96 mmol) in 41% yield; 140-147 ℃; ^{1}H NMR ($CDCl_3$) δ 1.26 (t, 3H, *J*=7.8 Hz, O-CH$_2$-C<u>H</u>$_3$), 1.40 (s, 3H, C-Me), 1.8-3.0 (m, 2H, P-CH$_2$), 4.11 (dq, 2H, J_{HH}=J_{HP}=7.8 Hz, O-C<u>H</u>$_2$-CH$_3$), 3.9-4.6 (m, 1H, P-CH), 4.5-5.4 (bs, 2H, 2OH), 5.40 (ddm, J_{HH}=5.0 Hz, J_{HP}=29.0 Hz, 1H, C<u>H</u>-OBz), 7.2-8.2 (m, 5H); IR ν (neat) 1730 (C=O); MS (*m/z*) 93(100%, EtOP(O)H), 314 (8%, M^+).

Anal. Calcd for $C_{14}H_{19}O_6P$ (314.28): C, 53.50; H, 6.09; P, 9.86. Found: C, 53.61; H, 6.10; P, 9.75.

2,3-Diacetoxy-4-benzoyloxy-1-ethoxyphospholane 1-oxide (9f'). 4-Benzoyloxy-1-ethoxy-2,3-dihydroxy-2-phospholene 1-oxide (**8f'**) (3.15 g, 10.5 mmol)

was peracetylated with acetic anhydride in anhydrous pyridine by a similar procedure to that mentioned above for the preparation of diacetate **4a** to prepare 2,3-diacetoxy-4-benzoyloxyl derivative **9f'** (1.86 g, 4.83 mmol) in 46% yield; ^{31}P NMR ($CDCl_3$) δ 48.9, 50.9, 52.4 (three isomeric components); ^{1}H NMR ($CDCl_3$) δ 1.38 (2t, 3H, J=7.07 Hz, O-CH_2-C$\underline{H}_3$), 2.07, 2.11, 2.15, 2.17, 2.19 (5s, 6H, 2Ac), 1.80-3.00 (m, 2H, P-CH_2), 4.00-4.50 (m, 2H, O-C$\underline{H}_2$-CH_3), 5.04-5.90 (m, 3H, P-CH-CH-CH), 7.20-7.75 (m, *m*-Ph, *p*-Ph), 7.95-8.35 (m, 2H, *o*-Ph); ^{13}C NMR ($CDCl_3$) δ 16.20, 16.47 (2s, $OCH_2\underline{C}H_3$), 20.19, 20.28, 20.40 (2s, 2C(O)$\underline{C}H_3$), 29.80, 30.17, 30.34 (3d, J_{CP}=88.21, 88.88, 86.87 Hz, P-CH_2), 62.77, 62.86, 62.98 (3d, J_{CP}=6.78, 6.78, 6.70 Hz, O-CH_2), 64.9-72.5 (complex peaks for three Cs, P-$\underline{C}$H-$\underline{C}$H-$\underline{C}$H), 128.35, 128.44, 128.61, 128.73 (4s, *p*-Ph, *m*-Ph), 129.60, 129.69, 130.29 130.38 (2s, *o*-Ph), 133.42, 133.54, 134.25, 134.37 (4s, *x*-Ph), 164.98, 165.37 (2s, $\underline{C}$(O)Ph), 169.61, 169.79 (6s, $\underline{C}$(O)CH_3).

Anal. Calcd for $C_{17}H_{21}O_8P$ (384.33): C, 53.13; H, 5.51; P, 8.06. Found: C, 53.34; H, 5.36; P, 8.29.

Similarly, 4-bromides **6**, 4-acylates **7**, 2,3-dihyroxy-4-acylates **8**, and 2,3,4-triacylates **9** were prepared (Tables 3 and 6).

***cis*-Dihydroxylation of 1-phenyl-3-phospholene 1-oxide (2b). Preparation of 3,4-dihydroxy-1-phenylphospholane 1-oxide (10b and 10b').** 1-Phenyl-3-phospholene 1-oxide (**2b**) (0.338 g, 1.90 mmol) was *cis*-dihydroxylated with osmium(VIII) oxide (26.7 mg, 0.11 mmol, 5.5 mol%) and sodium chlorate (0.32 g, 3.00 mmol, 1.6 eq) by a similar procedure to that mentioned above for the synthesis of *cis*-diol **3b** to prepare 3,4-dihydroxy-1-phenylphospholane 1-oxide (**10b** and **10b'**) (0.313 g, 1.47 mmol) in 78% yield; 134-140 ℃; ^{1}H NMR ($CDCl_3$) δ 2.0-2.6 (m, 4H, CH_2-P-CH_2), 4.0-4.7 (m, 2H, CH-CH), 4.70 (bs, 2H, 2OH), 7.1-8.1 (m, 5H, Ph); IR ν (KBr) 3300 (OH), 1440 (P-Ph), 1170 (P=O); MS (*m/z*) 125 (100%, PhP(O)H), 211 (12%, M^+-1).

Anal. Calcd for $C_{10}H_{13}O_3P$ (212.19): C, 56.61; H, 6.18; P, 14.60. Found: C, 56.49; H, 6.03; P, 14.77.

3,4-Dihydroxy-1-methoxy-3-methylphospholane 1-oxide (10d and 10d'). 1-Methoxy-3-methyl-3-phospholene 1-oxide (**2d**) (0.564 g, 3.86 mmol) was *cis*-dihydroxylated with osmium(VIII) oxide (5.5 mol%) and sodium chlorate (1.6 eq) by a similar procedure to that mentioned above for the synthesis of *cis*-diol **3b** to give 3,4-dihydroxy-1-methoxy-3-methylphospholane 1-oxide (**10d** and **10d'**) in quantitative yield; ^{1}H NMR ($CDCl_3$) δ 1.38, 1.42 (2s, 3H, CH_3), 1.69-2.44 (m, 4H, CH_2-P-CH_2), 3.70 (d, 1/4.5×3H, J=11.18 Hz, OMe (minor)), 3.75 (d, 3/4.5×3H, J=11.45 Hz, OMe (major)), 3.40-4.30 (m, 3H, C-H, 2OH).

Table 6. 4-Bromides **6**, 4-acylates **7**, 2,3-dihyroxy-4-acylates **8**, and 2,3,4-triacylates **9** prepared.

2-Phospholenes			R' of acyl	Spectral data (NMR, IR, or MS)					
	Substituents								
No.	Rx	Rz		**6**[a]	**7**[b]		**8**[c]	**9**[d]	
1b	Ph	H	Me	4.9-5.6	1740	2.08	4.7-5.5	1755, 1230	354
1c	OMe	Me	Me	4.5-5.2	1745	2.05	4.7-5.8		322
1c	OMe	Me	Ph		1725	---	4.9-5.8		384
1d	OMe	H	Me	4.5-5.2	1740	2.08	5.0-5.5	59.2, 61.7, 62.8	(2:1:2)[f]
1e	OEt	Me	Me	4.5-5.1	1745	2.06	4.7-5.5	1745, 1230	336
1e	OEt	Me	Ph		1725	---	314[e]	1725, 1220	398
1f	OEt	H	Me	4.5-5.3	1740	2.10	4.7-5.8	49.5, 50.8, 51.2[f]	
1f	OEt	H	Ph		1725	---	4.9-5.8	48.9, 50.9, 52.4[f]	

a. Value shows ^{1}H NMR ($CDCl_3$) chemical shift δ (ppm) for CH-Br.
b. The first and second values mean IR (C=O) absorption ν (cm^{-1}) and ^{1}H NMR ($CDCl_3$) (OAc) chemical shift δ (ppm), respectively, for the 4-acyl group.
c. Value shows ^{1}H NMR ($CDCl_3$) chemical shift δ (ppm) for CH-OCOR' unless otherwise noted.
d. The first, second, and third values mean IR (C=O) and IR (P=O) absorptions ν (cm^{-1}) and MS (*m/z*) for the M^+ peak, respectively, unless otherwise noted.
e. Molecular ion peak (*m/z*) for M^+.
f. Value shows ^{31}P NMR ($CDCl_3$) chemical shift δ (ppm). Value in the parentheses shows the ratio of peak intencity.

3,4-Isopropylidenedioxy-1-phenylphospholane 1-oxide (11b and 11b'). 3,4-Dihydroxyl derivatives **10b** and **10'b** (0.430 g, 2.03 mmol) were treated with acetone by a similar procedure to that mentioned above for the synthesis of 2,3-isopropylidenedioxy-3-methyl-1-phenylphospholane 1-oxide (**5a**) to give 3,4-isopropylidenedioxy-1-phenyl-phospholane 1-oxide (**11b** and **11b'**), whose fractional recrystallization gave crystalline *anti* and *syn* diastereoisomers, **11b** (0.176 g, 0.698 mmol, 34% yield; as the second fraction from column chromatography on silica gel) and **11b'** (0.194 g, 0.769 mmol, 38% yield; as the first fraction from the chromatography), respectively.

11b (*anti*); 74-79 ℃; ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 6H, CMe_2), 2.1-3.8 (m, 4H, CH_2-P-CH_2), 5.00 (dm, 2H, J_{HP}=15.0 Hz, CH-CH), 7.4-8.1 (m, 5H, Ph); MS (*m/z*) 125 (100%, PhP(O)H), 252 (24%, M^+).

11b' (*syn*); 131-133 ℃; ^{1}H NMR ($CDCl_3$) δ 1.33, 1.57 (2s, 6H, CMe_2), 2.3-2.8 (m, 4H, CH_2-P-CH_2), 4.80 (dm, 2H, J_{HP}=16.0 Hz, CH-CH), 7.4-7.9 (m, 5H, Ph); IR

Table 7. Chemical shits values (δ , ppm) with shift reagent $Eu(dpm)_3$ (mol %).[a]

11b (*anti*)			**11b'** (*syn*)			**12** (*anti*)		
mol%	Chemical shift		mol%	Chemical shift		mol%	Chemical shift	
	o-H	3,4-H		*o*-H	3,4-H		*o*-H	3,4-H
0	7.79(---)	5.00(---)	0	7.71(---)	4.80(---)	0	7.79(---)	3.71(---)
5.2	8.16(0.37)	5.06(0.06)	5.8	7.89(0.18)	4.94(0.14)	7.5	8.19(0.40)	3.86(0.15)
11.4	8.61(0.82)	5.11(0.11)	14.7	8.13(0.42)	5.07(0.27)	14.3	8.61(0.82)	4.00(0.29)
17.1	8.93(1.14)	5.14(0.14)	20.0	8.36(0.65)	5.14(0.34)	21.5	9.36(1.57)	4.32(0.61)

a. Value in the parentheses is the difference of δ (ppm).

(KBr) ν 1450 (P-Ph), 1210 (P=O), 760, 700 (Ph); MS (*m/z*) 125 (100%, PhP(O)H), 252 (16%, M^+).

Anal. Calcd for $C_{13}H_{17}O_3P$ (252.25): C, 61.90; H, 6.79; P, 12.28. Found: C, 61.72; H, 6.96; P,12.47.

3,4-Isopropylidenedioxy-1-methoxyphospholane 1-oxide (11e and 11e'). 3,4-Dihydroxyl derivatives **10e** and **10'e** (0.268 g, 1.61 mmol) were treated with acetone by a similar procedure to that mentioned above for the synthesis of 2,3-isopropylidenedioxy-3-methyl-1-phenylphospholane 1-oxide (**5a**) to give 3,4-isopropylidenedioxy-1-phenylphospholane 1-oxide (**11e** and **11e'**, 0.279 g, 1.35 mmol, 84% yield); ^{31}P NMR ($CDCl_3$) δ 72.6, 74.7 (ratio of intensity=1 : 7.8); ^1H NMR ($CDCl_3$) δ 1.20, 1.40 (2s, 6H, CMe_2), 1.80-2.20 (m, 4H, CH_2-P-CH_2), 3.64 (d, 1/8.8×3H, J=11.00 Hz, OMe (minor)), 3.71 (d, 7.8/8.8×3H, J=11.36 Hz, OMe (major)), 4.70 (dm, 2H, J=26.59 Hz, CH-CH).

Data for diols **10** and **10'** and acetonides **11** and **11'** similarly prepared are summarized in Table 4.

Shift reagent experiment for compounds 11b, 11b', and 12 with Eu(dpm)$_3$. Shift reagent $Eu(dpm)_3$ was added to $CDCl_3$ solutions of compounds **11b**, **11b'**, and *anti* 3,4-oxo-1-phenylphospholane 1-oxide (**12**)[13] in a range of 0-ca.20 mol %. The results obtained are summarized in Table 7.

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REFERENCES AND NOTES

1. Presented at the *XVIIIth International Carbohydrate Symposium*, Milan, Italy, July 21-26, 1996.
2. R. Goto, S. Inokawa, A. Sera, and S.Otani in *Tantorui no Kagaku (Chemistry of Monosaccharides)*, Maruzen, Tokyo, 1988.
3. a) M. Yamashita, Y. Nakatsukasa, M. Yoshikane, H. Yoshida, T. Ogata, and S. Inokawa, *Carbohydr. Res.*, **59**, C12 (1977). b) M. Yamashita, Y. Nakatsukasa, H. Yoshida, T. Ogata, S. Inokawa, K. Hirotsu, and J. Clardy, *Ibid.*, **70**, 247 (1979). c) M. Yamada and M. Yamashita, *Ibid.*, **95**, C9 (1981). d) M. Yamashita, M. Yamada, K. Tsunekawa, T. Oshikawa, K. Seo, and S. Inokawa, *Ibid.*, **121**, C4 (1983). e) Idem, *Ibid.*, **122**, C1 (1983). f) M. Yamashita, M. Yamada, M. Sugiura, H. Nomoto, and T. Oshikawa, *Nippon Kagaku Kaishi*, 1207 (1987). g) H. Yamamoto and S. Inokawa, *Adv. Carbohydr. Chem. Biochem.*, **42**, 135 (1984).
4. M. Yamashita, M. Uchimura, A. Iida, L. Parkanayi, and J. Clardy, *J. Chem. Soc., Chem. Commun.*, 569 (1988). One of the two minor components (fractions separated by column chromatography on silica gel) reported in reference 4 was the mixture of the major and the minor components which melted at 152-158 ℃; MS (*m/z*) 125 (100%, PhP(O)H), 226 (35%, M^+).
   Anal. Calcd for $C_{11}H_{15}O_3P$ (226.17): C, 58.42; H, 6.69; P, 13.68. Found: C, 57.98; H, 6.50; P, 12.92.
5. a) K. Ikai, A. Iida, and M. Yamashita, *Synthesis*, 595 (1989). b) M. Yamashita, A. Iida, K. Ikai, T. Oshikawa, T. Hanaya, and H. Yamamoto,*Chem. Lett.*, 407 (1992). c) A. Yabui, M. Yamashita, T. Oshikawa, T. Hanaya, and H. Yamamoto, *Ibid.*, 93 (1993). d) M. Yamashita, K. Ikai, C. Takahashi, and T. Oshikawa, *Phosphorus, Sulfur, and Silicon*, **79**, 293 (1993). e) M. Yamashita, A. Iida, H. Mizuno, Y. Miyamoto, T. Morishita, N. Sata, K. Tsunekawa, A. Yabui, and T. Oshikawa, *Heteroat. Chem.*, **4**, 553 (1993). f) M. Yamashita, A. Yabui, T. Oshikawa, and A. Kakehi, *Chem. Lett.*, 23 (1994). g) M. Yamashita, A. Yabui, T. Oshikawa, T. Hanaya, and H. Yamamoto, *Heterocycles*, **38**, 1449 (1994).
6. a) J. Emsley and D. Hall in *The Chemistry of Phosphorus*, Harper & Row, London, 1976, p 157. b) L. D. Quin and T. P. Barket, *J. Chem. Soc., Chem. Commun.*, 788 (1967). c) W. B. McCormack, *Org. Syn.*, **43**, 73 (1963).
7. O. Korpium, R. A. Lewis, J. Chickors, and K. Mislow, *J. Am. Chem. Soc.*, **90**, 4842 (1968).
8. Tables of atomic coordinates, bond lengths, and bond angles have been deposited with the Cambridge Crystallographic Data Centre. These tables may be obtained on request from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK.
9. J. Emsley and D. Hall in *The Chemistry of Phosphorus*, Harper & Row, London, 1976, p 75.

10. N. Inamoto in *Hannou Sokudoron Nyumon (Introduction to Reaction Kinetics)*, Hirokawa Publishing Co. Ltd., Tokyo, 1969, pp 50-51.
11. J. K. Cha, W. J. Christ, and Y. Kishi, *Tetrahedron*, **40**, 2247 (1984).
12. L. D. Quin in *The Heterocyclic Chemistry of Phosphorus*, Wiley-Interscience, New York, 1981, p 350.
13. a) R. Bodalski, T. Janecki, Z. Gatdecki, and M. Gtowka, *Phosphorus and Sulfur*, **14**, 15 (1982). b) M. Yamashita, A. Yabui, A. Iida, K. Hanioka, H. Mori, M. Uchimura, K. Ikai, T. Oshikawa, J. Kobayashi, to be published.
14. a) K. Hunger, U. Hasserodt, and F. Korte, *Tetrahedron*, **20**, 1563 (1964). b) G. Kresze, J. Firl, H. Zimmer, and U. Wollnic, *Tetrahedron*, **20**, 1593 (1964).
15. L. D. Quin, J. P. Gratz, and T. P. Barket, *J. Org. Chem.*, **33**, 1034 (1968).
16. a) L. D. Quin in *1,4-Cycloaddition Reactions: The Diels-Alder Reaction in Heterocyclic Syntheses*, Ed., by J. Hamer, Academic Press, New York, 1967, Chapt. 3. b) L. D. Quin in *The Heterocyclic Chemistry of Phosphorus*, Wiley-Interscience, New York, 1981, Chapt. 2. c) J. Emsley and D. Hall in *The Chemistry of Phosphorus*, Harper & Row Publishers, London, 1976, Chapt. 4.
17. R. F. Hudson in *Structure and Mechanism in Organophosphorus Chemistry*, Academic Press Inc., London, 1965, p 283.