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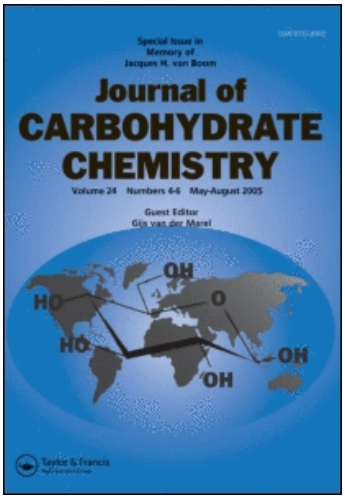

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NOVEL SYNTHESIS AND STRUCTURES OF AMINES AND TRIAZOLE-DERIVED GLYCOSIDE AND NUCLEOSIDE DERIVATIVES OF PHOSPHANYL SUGAR ANALOGS[1]

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ABSTRACT

3-Methyl-1-phenyl-2-phospholene and 1-phenyl-2-phospholene 1-oxides were converted into 2-bromo-3-hydroxy-3-methyl-1-phenylphospholane and 2-bromo-3-hydroxy-1-phenylphospholane 1-oxide (1-bromo-1,3,4-trideoxy-1,4-*C*-[(*R*,*S*)-phenylphosphinylidene]-*glycero*-tetrofuranose) by the action of bromine in aqueous medium. The bromo substituent of the phospholane was substituted by treatment with amines or an azide anion to afford novel glycoside derivatives of phosphanyl sugar analogs such as 2-amino-3-hydroxy-1-phenylphospholane (3,4-dideoxy-1,4-*C*-[(*R*,*S*)-phenylphosphinylidene]-*glycero*-tetrofuranosylamine) and 2-azido-3-hydroxy-3-methyl-1-phenylphospholane 1-oxides with retention of the configuration. The 1,3-dipolar cycloaddition of the 2-azido derivative of the phospholane with alkynes gave 3-hydroxy-3-methyl-1-phenyl-2-(triazol-1'-yl)phospholane 1-oxides as a novel triazole-derived nucleoside of phosphanyl sugar analogs. The structure of the glycoside and nucleoside derivatives of the phosphanyl sugar analogs prepared was deterimined from IR, NMR, and X-ray crystallography analysis.

INTRODUCTION

Normal sugar derivatives, represented by Haworth structures, have a heterocyclic structure with an oxygen atom in the hemiacetal ring. Replacement of the oxygen atom in

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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 In particular, hetero sugars in which the ring oxygen has been replaced by a nitrogen, sulfur, or selenium atom have been extensively studied and widely developed.[2] Synthesis of phosphanyl sugars, which belong to a category of pseudo sugar derivatives having a phosphorus atom instead of the oxygen atom in the hemiacetal ring of sugars, have been investigated by conventional methodology using sugar starting materials. However, the multistep synthesis methods required to prepare a wide variety of phosphanyl sugar derivatives such as glycosides and nucleosides in order to elucidate structure-activity relationships has limited their development. They have been mainly prepared 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, deprotection, etc.[3] The fact that amino and thio sugars are known to exist in nature, while phosphanyl sugar derivatives have not yet been found in naturally occurring products may also have delayed the development of phosphanyl sugar chemistry.

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In previous papers,[4,5] we reported the synthesis of phosphanyl sugar derivatives starting from 2- and 3-phospholene derivatives, having the unsaturated five membered phosphorus heterocycles. We are further interested in the synthesis of glycosides and/or nucleosides of phosphanyl sugars from phospholenes since *O*- and *N*-glycosides of normal sugars exist widely and play important biological roles in nature.[2] Moreover nucleosides such as azidothimidine (AZT), which is an anti-HIV agent with an N_3 substituent on the sugar moiety of the nucleoside,[6] are also biologically important substances. Thus, preparation of sugar derivatives such as glycosides and nucleosides for biological study represents an important research area of carbohydrate chemistry.[7] As bioactive nucleosides, ribavirin, deoxyfluridine, cytosine arabinoside, and 5-fluorodeoxyuridine as well as AZT are known as anti-influenza, or anti-tumor reagents and these nucleosides have normal sugar moieties.[8-11] In addition, some pseudo sugar nucleosides exist in nature and show interesting bioactivities such as anti-bacterial, anti-tumor, and anti-virus activities. Some examples are aristeromycin, cyclaradine, thiothymidine, thioddC, and dioxolane T;[12] however, no phosphanyl sugar nucleoside has been reported. The present paper deals with the synthesis and the structure determination of glycoside and nucleoside derivatives of phosphanyl sugar analogs using 2-phospholenes as the starting materials.

RESULTS AND DISCUSSION

Reaction of 3-methyl-1-phenyl-2-phospholene 1-oxide (**1A**) and 1-phenyl-2-phospholene 1-oxide (**1B**)[13] with bromine or *N*-bromoacetamide (NBA) in chloroform-water or

acetone-water at room temperature afforded a mixture of *threo* and *erythro* bromohydrin derivatives **2A** and **2B**. Fractional recrystallization of **2B** from chloroform-carbon tetrachloride afforded *threo* 2-bromo-3-hydroxy-1-phenylphospholane 1-oxide (*threo* **2B**; 1-bromo-1,3,4-trideoxy-1,4-*C*-[(*R*)-phenylphosphinylidene]-β-D-*glycero*-tetrofuranose and the enantiomer; mp 180-183 °C; yield 43%) and *erythro* 2-bromo-3-hydroxy-1-phenylphospholane 1-oxide (*erythro* **2B**; 1-bromo-1,3,4-trideoxy-1,4-*C*-[(*R*)-phenylphosphinylidene]-α-L-*glycero*-tetrofuranose and the enantiomer; mp 136-139 °C; yield 24%). Fractional recrystallization of a mixture of *erythro* and *threo* products **2A** (ca. 1 : 3), gave *threo* 2-bromo-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (*threo* **2A**) in 46% yield.[14]

Reaction of bromohydrin *erythro* **2B** with some primary and secondary amines at 40 °C afforded novel phosphanyl sugar *N*-glycosides, 2-amino-3-hydroxy-1-phenylphospholane 1-oxides (**3Ba-d**; 3,4-dideoxy-1,4-*C*-[(*R*)-phenylphosphinylidene]-α-L-*glycero*-tetrofuranosylamines and the enantiomers; Table 1). Treatment of bromohydrin *erythro* **2B** with triethylamine or primary and secondary amines at room temperature gave almost quantitatively *threo* 2,3-epoxy-1-phenylphospholane 1-oxide (*threo* **4B**; 1,2-anhydro-3,4-dideoxy-1,4-*C*-[(*R*)-phenylphosphinylidene]-β-L-*glycero*-tetrofuranose and the enantiomer). Epoxide *threo* **4B** was smoothly converted into *erythro* *N*-glycosides **3Ba-d** by the action of primary or secondary amines at 40 °C. At 40 °C, the reaction of **2B** with primary or secondary amines afforded *N*-glycosides of phosphanyl sugar analogs **3Ba-d** in one pot through intermediary 1,2-anhydro phosphanyl sugars **4B**. Therefore, retention of configuration at the C1 position of phosphanyl sugar analogs, *N*-glycosides **3Ba-d**, from **2B** are observed through different reaction conditions, with and without isolation of intermediate epoxide **4B**.

Acyl derivatives of α-D-glucopyranosyl bromide are known to be often converted by treatment of amines into 2-hydroxyglycals with elimination of hydrogen halide, instead of formation of *N*-glycosides by substitution of the halogen with amines.[15] An S_N1 type substitution reaction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with sodium iodide or silver fluoride is reported to give thermally more stable α or β anomer of the corresponding glucopyranosyl halide when neighbouring group participation of the 2-substituent is available.[16] On the other hand, β-D-glucopyranosyl fluoride was converted into the corresoponding methyl glucoside by treatment with methoxide via epoxide formation by participation of the *trans* 2-hydroxy group in the elimination of the fluoro group to give the 1,2-epoxide derivative, this method being called the Micheel synthesis.[17,18] Preparation of 1,2-anhydro-α-D-glucose or the corresponding tri-*O*-acetyl derivative ("Brigl's anhydride")[18] was carried out using careful ammonolysis of 3,4,6-tri-*O*-acetyl-α-D-glucopyra-

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1A 1B

Figure 1. Structure of phospholenes **1A** and **1B**.

Table 1. Phosphanyl sugar *N*-glycosides prepared.

Starting material	NR^1R^2 R^3			Reaction condition		Product		
	R^1	R^2	R^3	Solvent	Temp(°C)	No.	Mp(°C)	Yield(%)
erythro **2B**	Me	H	H	MeOH-H_2O	40	*erythro* **3Ba**	Syrup	56
erythro **2B**	*i*-Pr	H	H	MeOH	40	*erythro* **3Bb**	138.5-140	75
erythro **2B**	*t*-Bu	H	H	MeOH	40	*erythro* **3Bc**	184-185	55
erythro **2B**	Et	Et	H	MeOH	40	*erythro* **3Bd**	Syrup	84
erythro **2B**	Et	Et	Et	Et_3N	rt[a)]	*threo* **4B**	Syrup	100
threo **2B**	Et	Et	Et	Et_3N	rt[a)]	*erythro* **4B**	116-118	91
threo **4B**	*i*-Pr	H	H	MeOH	40	*erythro* **3Bb**	138.5-140	100
erythro **4B**	Et	Et	Et	MeOH	40			NR[a)]

a. rt, room temperature; NR, No reaction.

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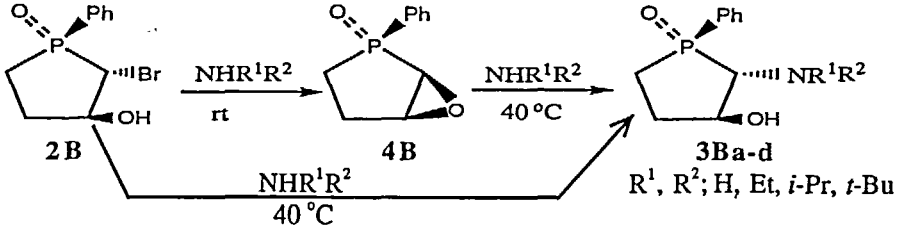
nosyl chloride. Therefore, facile epoxide formation followed by substitution with a nucleophile to give an *N*-glycoside from phosphanyl sugar derivative **2B** by an amine base treatment may be a unique feature in carbohydrate chemistry, because substitution of a halogen of acetylated glycosyl halides most generally occurs by participation of a 2-acetoxy group.



Scheme 1. Preparation of *N*-glycosides of phosphanyl sugars **3Ba-d**.

Table 2. Observed ^{1}H NMR (500 MHz) parameters for compound **3Bc** in $CDCl_3$.[a)]

Chemical shift δ (ppm)											
H1	H2	H3	H3'	H4	H4'	*t*-Bu	OH	NH	*o*-Ph	*m*-Ph	*p*-Ph
2.82	3.97	2.47	1.78	2.33	2.05	0.92	1.86	2.98	7.75	7.50	7.53

Coupling constant (Hz)[b)]			
$J_{1,2}$ = 8.3	$J_{1,P}$ = 4.9		
$J_{2,3'}$ = 9.6	$J_{2,3}$ = 5.0	$J_{2,P}$ = 5.0	
$J_{3,P}$ =25.0	$J_{3,3'}$ =13.2	$J_{3,4'}$ = 8.4	$J_{3,4}$ = 3.6
$J_{3',4}$ = 7.8	$J_{3',P}$ ≒ 8	$J_{3',4'}$ =11.0	$J_{4,4'}$ ≒16
			$J_{4,P}$ = 8.0
			$J_{4',P}$ ≒26

a. Measured on a VXR-500 instrument (Okayama University) at 21 °C.
b. Coupling constants for aromatic protons are omitted.

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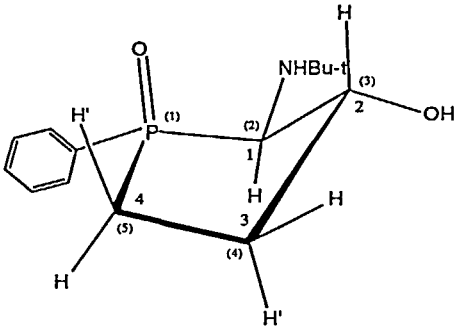

Figure 2. Favorable conformation (^2E) of *N*-glycoside **3Bc** based on ^{1}H NMR ($CDCl_3$) analysis. (Numbers outside the parenthesis correspond to carbohydrate nomenclature numbering while those within the parenthesis correspond to heterocycle nomenclature numbering, respectively.)

The structure of 1-*N*-*t*-butyl-3,4-dideoxy-1,4-*C*-[(*S*)-phenylphosphinylidene]-β-D-*glycero*-tetrofuranosylamine and its enantiomer was established for phosphanyl sugar **3Bc** by analysis of its 500 MHz ^{1}H NMR spectrum (Table 2). The $J_{1,2}$ value of 8.3 Hz shows that C-1—H-1 and C-2—H-2 bonds are diaxial, whereas the small $J_{1,P}$ value of 4.9 Hz indicates a *trans* relationship of C-1—H-1 and P=O bonds.[19,20] The ^{1}H NMR analysis reveals that *N*-glycoside **3Bc** exisits predominantly in the ^2E conformation in the solution (Figure 2).

Reaction of the *threo* 2-bromo derivative, *threo* **2A**, with sodium azide in DMF for 24 h at 70 °C afforded *threo* 2-azido-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (*threo* **3Aa**; 1-azido-1,3,4-trideoxy-2-methyl-1,4-*C*-[(*R*)-phenylphosphinylidene]-β-D-*glycero*-tetrofuranose and its enantiomer) in 87% yield. Hydrogenolysis of the azido derivative, *threo* **3Aa**, with an atmospheric pressure of H_2 in the presence of Pd/C catalyst for 24 h at room temperature gave the corresponding *threo* 2-amino derivative, 2-amino-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (*threo* **3Ab**; 3,4-dideoxy-2-methyl-1,4-*C*-[(*R*)-phenylphosphinylidene]-α-L-*glycero*-tetrofuranosylamine and the enantiomer), in 99% yield (Scheme 2). These products **3Aa**, **3Ab**, and **3Ba-d** are *N*-glycosides of phosphanyl sugar analogs. The structure of *threo* 2-bromo- and *threo* 2-azido-3-methyl-1-phenylphospholane 1-oxides (**2A** and **3Aa**) are shown in Figures 3 and 4, respectively. The retention of the configuration for the reaction of **2A** to afford **3Aa** may be explained by the formation of the intermediate epoxide **4A**.

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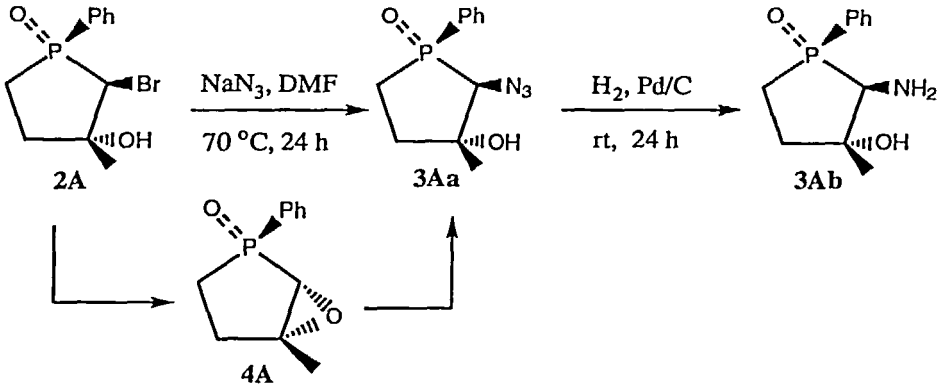

Scheme 2. Preparation of *N*-glycosides **3Aa** and **3Ab**.

As mentioned in Micheel's method[17,18] for the preparation of glycosides of normal sugars, sodium methoxide in methanol converts β-D-glucopyranosyl fluoride into methyl β-D-glucopyranoside via a 1,2-epoxide ring-opening. 1,6-Anhydro-β-D-glucopyranose is usually obtained when phenolic glycosides undergo alkaline hydrolysis. The formation of 1,6-anhydro glucose derivatives is explained by a mechanism where an attack by the 6-hydroxyl group occurs at the C1 position of intermediary 1,2-anhydride formed instead of the attack at the C2 position of the epoxide.[21-23] The epoxide ring opening of 1,2-anhydro phosphanyl sugar **4A** or **4B** to afford 1-azido or 1-amino phosphanyl sugar *N*-glycoside may be attributable to a strong electron-withdrawal property of the P=O group, by which

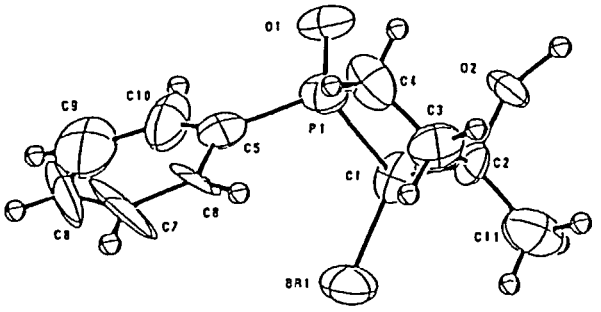

Figure 3. ORTEP drawing of 2-bromo compound **2A**.[24]

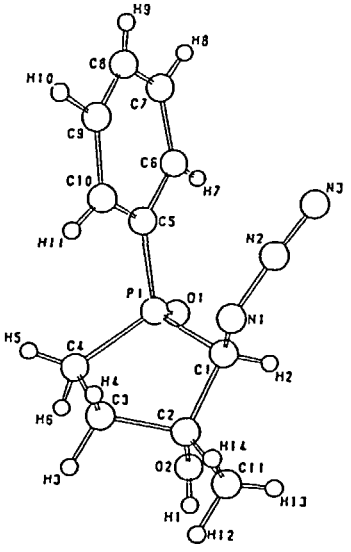

Figure 4. ORTEP drawing of 2-azido compound **3Aa**.[25]

the C1 position of the 1,2-anhydride becomes more electrophilic than the C2 position for the attack of amines or azide ion, although the C1 position is sterically more hindered by the phenyl group than is the C2 position.

For the preparation of nucleosides, the following two major methodologies are usually applied: (a) the substitution reaction of a leaving substituent on an anomeric carbon

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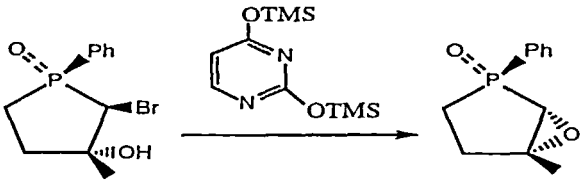
atom by an activated nucleic acid base; (b) the cyclization of glycosyl ureas or glycosyl amines of sugar derivatives by a condensation reaction with acrylamides or the dipolar cycloaddition with dipolarophiles such as alkynes to form nucleic acid bases or nitrogen heterocycles.[26-32]



Scheme 3. Formation of epoxide **4A** from **2A** by treatment with TMS-pyrimidine.

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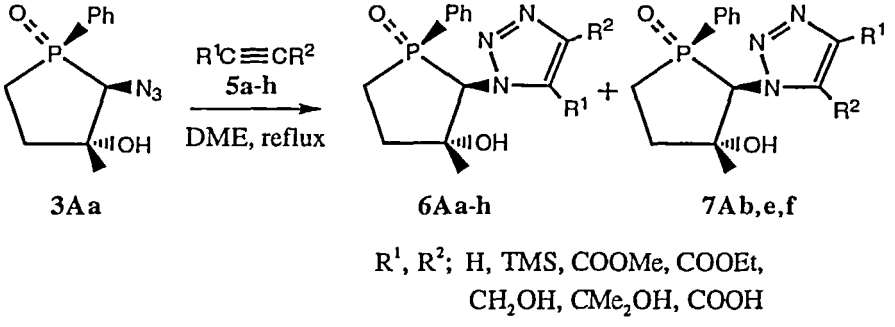
Reaction of 2-bromo-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (**2A**) with trimethylsilylated pyrimidine was carried out according to the method (a); however, the reaction afforded only intramolecular substitution reaction product, epoxide **4A**, instead of an intermolecular substitution reaction product, a pyrimidine nucleoside.

1,3-Dipolar cycloaddition of azido derivative, *threo* **3Aa**, with alkynes **5a-h** in 1,2-dimethoxyethane (DME) under reflux afforded regioisomeric phosphanyl sugar nucleoside analogs **6Aa-h** and **7Ab,e,f** having a triazole ring as the nitrogen heterocyclic nucleus depending on the substituents on the alkyne derivatives (Scheme 4 and Table 3).



Scheme 4. Preparation of nucleosides of phosphanyl sugar analogs **6A** and **7A**.

Disubstituted alkynes **5c**, **5d**, **5g**, and **5h** afforded triazole derivatives **6Ac**, **6Ad**, **6Ag**, and **6Ah**, respectively, whose structures were determined by ^{1}H, ^{13}C, and ^{31}P NMR

Table 3. Phosphanyl sugar nucleoside analogs having a triazole ring as the nitrogen heterocyclic nucleus.

Alkyne			Reaction	Phosphanyl sugar nucleoside analogs			
No.	R^1	R^2	time(h)	No.	Yield(%)	Ratio of **6A** : **7A**	mp(°C)
5a	H	$SiMe_3$	12	**6Aa**	64.9	**6Aa** only[a]	222
5b	H	COOMe	12	**6Ab+7Ab**	66.6	1 : 1[b]	221-223[d]
5c	COOMe	COOMe	18	**6Ac**	88.2	------	205-207
5d	COOEt	COOEt	24	**6Ad**	79.4	------	175-176
5e	H	CH_2OH	48	**6Ae+7Ae**	66.0	1 : 1[c]	224-226[e]
5f	H	CMe_2OH	96	**6Af+7Af**	50.9	3 : 1[c]	198-202[0]
5g	CH_2OH	CH_2OH	72	**6Ag**	66.0	------	206
5h	COOH	COOH	24	**6Ah**	55.2	------	175

a. Isolated by crystallization.
b. Based on the ratios of 3-Me group and the olefin protons by ^{1}H NMR.
c. Isolated by column chromatography on silica gel.
d. Melting point for **7Ab**.
e. Melting point for **7Ae**.
f. Melting point for **6Af**.

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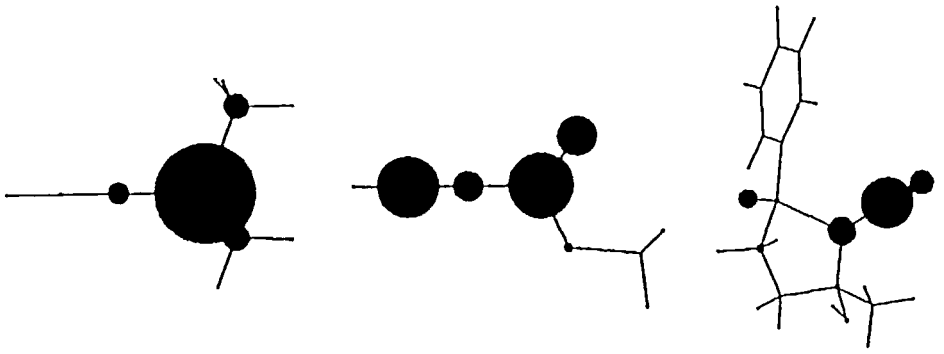
spectral analysis. Typical observations for triazole derivatives **6Ad** compared with azido derivative **3Ad** in NMR are as follows: down field chemical shift of N-CH for triazole **6Ad** (5.57 ppm) was observed compared with that for azido **3Ad** (4.00 ppm) by ^{1}H NMR ($CDCl_3$); triazole sp^2 carbon atoms were observed for **6Ad** at 131.79 and 138.34 ppm by ^{13}C NMR ($CDCl_3$); and only one signal was observed for **6Ad** at 70.49 ppm by ^{31}P NMR ($CDCl_3$).

^{1}H NMR ($CDCl_3$) spectra for **6Ae** and **7Ae** showed the olefinic proton signals at 7.86 and 7.36 ppm, respectively, suggesting that the more polarized isomer resonates at lower field than the less polarized isomer does. Trimethylsilylacetylene (**5a**) gave nucleo- side **6Aa** (70.39 ppm by ^{31}P NMR, $CDCl_3$) selectively as the sole regioisomer,[33] whereas methyl propiolate (**5b**) produced nucleoside **6Ab** and **7Ab** in a 1:1 ratio. Frontier π-electron densities were obtained for **5a**, **5b**, and 2-azidophospholane derivative **3Aa** by an MO calculation using MOPAC PM3 (Stuart)[34] as shown in Figure 5. For TMS derivative **5a** the unsubstituted *sp* carbon atom has almost no π-electron density while the substituted one exclusively has π-electron density. For propiolate **5b** the unsubstituted *sp* carbon



Trimethylsilylacetylene (**5a**) Methyl propiolate (**5b**) 2-Azidophospholane **3Aa**

Figure 5. Comparisons of π-electron densities of trimethylsilylacetylene (**5a**), methyl propiolate (**5b**), and 2-azidophospholane derivative **3Aa** based on MO calculations using MOPAC PM3 (Stuart).

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atom has a larger π-electron density than that of substituted *sp* carbon atom. Both effects of steric hindrance and electron density caused by the TMS group of **5a** may introduce the predominant formation of nucleoside **6Aa**. In contrast to **5a**, methyl propiolate (**5b**) has a larger electron density on the unsubstituted and less hindered *sp* carbon, hence 1:1 regio-isomeric products **6Ab** and **7Ab** are formed. Triazolyl phosphanyl sugar nucleosides **6A** and **7A** are the first ribavirin type pseudo sugar nucleosides reported.

Phosphanyl sugar nucleoside analog **6Ad** was purified by recrystallization from chloroform, affording a good single crystal. The X-ray analysis of **6Ad** revealed the structure of the novel nucleoside of the phosphanyl sugar as shown by the ORTEP drawing in Figure 6 and afforded bond lengths, bond angles, and torsion angles as shown in Table 4.

EXPERIMENTAL

General methods. Melting points were determined by a Yanagimoto MP-S2 micro-melting point apparatus and are reported uncorrected. ^{1}H NMR spectra were recorded on Japan Electron Optics Laboratory (JEOL) JNM-EX90 (at 90 MHz), JEOL JNM-EX270 (at 270 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 spectra were recorded on a JEOL EX90 (at 22.40 MHz)

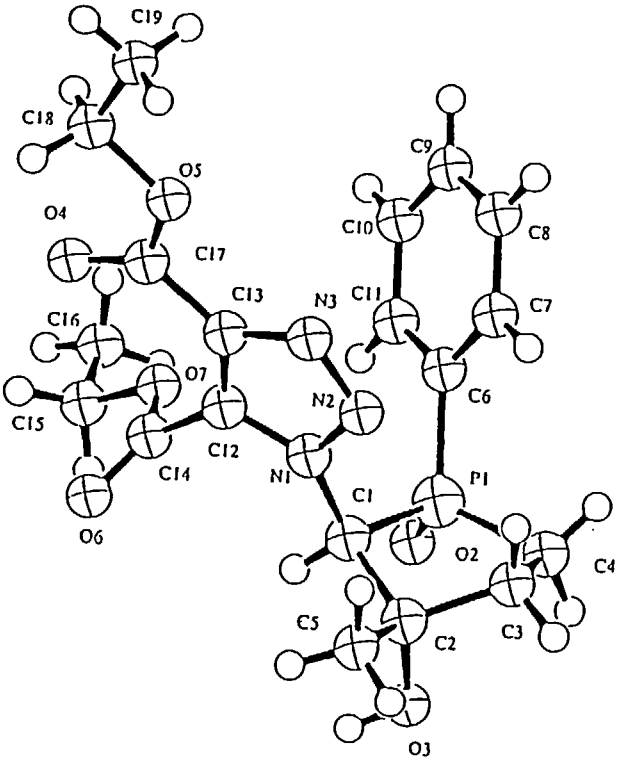

Figure 6. ORTEP drawing of the nucleoside analog of phosphanyl sugar **6Ad** having a triazole nucleus.[35]

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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 Japan Spectroscopic Co. Ltd. (JASCO) FT/IR-8000 and A-3 spectrophotometers. MS spectra were measured using a 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) as the detector, column, and solvent, respectively. X-ray crystallographies for single crystals were performed using Rigaku AFC7R and AFC5S diffractometers.

2-Phospholene 1-oxides **1A** and **1B** were prepared according to reported methods via cycloaddition reaction of 2-methyl-1,3-butadiene and 1,3-butadiene, respectively, with phosphorus trichloride.[36-40]

Table 4. Selected bond lengths, bond angles, and torsion angles for compound **6Ad.**[35]

Selected bond length		Selected bond angle		Selected torsion angle	
Bond	Length (Å)	Bond	Angle (°)	Bond	Angle (°)
P(1)-O(2)	1.496	O(2)-P(1)-C(1)	112.1	P(1)-C(1)-C(2)-C(3)	39.2
P(1)-C(1)	1.857	O(2)-P(1)-C(6)	111.0	C(1)-C(2)-C(3)-C(4)	-48.9
P(1)-C(4)	1.806	C(1)-P(1)-C(6)	108.7	C(2)-C(3)-C(4)-P(1)	34.8
C(1)-C(2)	1.566	P(1)-C(1)-C(2)	103.7	C(3)-C(4)-P(1)-C(1)	-9.5
C(2)-C(3)	1.548	C(1)-C(2)-C(3)	105.4	C(4)-P(1)-C(1)-C(2)	-17.4
P(1)-C(6)	1.799	C(2)-C(3)-C(4)	107.8	P(1)-C(1)-N(1)-N(2)	-77.4
C(1)-N(1)	1.467	P(1)-C(1)-N(1)	114.2	C(2)-C(1)-N(1)-N(2)	42.7
N(1)-N(2)	1.367	C(2)-C(1)-N(1)	115.6	C(2)-C(1)-N(1)-C(12)	-142.7
N(2)-N(3)	1.305	N(1)-N(2)-N(3)	107.2	N(1)-N(2)-N(3)-C(13)	-0.9
N(3)-C(13)	1.359	C(1)-N(1)-N(2)	121.8	N(2)-N(3)-C(13)-C(12)	0.3
C(12)-C(13)	1.359	C(1)-N(1)-C(12)	127.8	N(3)-C(13)-C(12)-N(1)	0.3
N(1)-C(12)	1.338	N(2)-N(3)-C(13)	108.5	C(13)-C(12)-N(1)-N(2)	-0.9
C(6)-C(7)	1.392	N(3)-C(13)-C(12)	109.2	C(12)-N(1)-N(2)-N(3)	1.1
C(7)-C(8)	1.385	C(13)-C(12)-N(1)	105.0	P(1)-C(6)-C(7)-C(8)	179.7
C(8)-C(9)	1.355	C(4)-P(1)-C(6)	111.0	P(1)-C(6)-C(11)-C(10)	-179.7
C(9)C(10)	1.371	P(1)-C(6)-C(7)	122.8	C(6)-C(7)-C(8)-C(9)	1.4
C(10)-C(11)	1.382	P(1)-C(6)-C(11)	119.4	C(7)-C(8)-C(9)-C(10)	-2.0
C(11)-C(6)	1.377	C(6)-C(7)-C(8)	119.7	C(8)-C(9)-C(10)-C(11)	1.9
C(13)-C(17)	1.477	C(7)-C(8)-C(9)	120.5	C(9)-C(10)-C(11)-C(6)	-1.3
C(12)-C(14)	1.496	C(8)-C(9)-C(10)	121.5	C(10)-C(11)-C(6)-C(7)	0.7
C(17)-O(4)	1.194	C(9)-C(10)-C(11)	119.5	C(11)-C(6)-C(7)-C(8)	-0.8
C(2)-O(3)	1.423	C(10)-C(11)-C(6)	120.2	N(3)-C(13)-C(17)-O(5)	2.4
C(2)-C(5)	1.519	C(11)-C(6)-C(7)	119.4	C(17)-C(13)-C(12)-C(14)	0.5

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***erythro* And *threo* 2-bromo-3-hydroxy-1-phenylphospholane 1-oxides (2B).** To 1-phenyl-2-phospholene 1-oxide **1B** (3.68 g, 20.7 mmol) in acetone (10 mL)-water (20 mL) was added NBA (4.28 g, 1.5 eq) and stirred at room temperature until the brownish color of the solution disappeared, and the completion of the reaction was confirmed by TLC. Removal of the solvent and addition of carbon tetrachloride to the residue afforded a solid product, whose recrystallization from chloroform-carbon tetrachloride afforded 2.43 g (8.84 mmol) of *threo* **2B** (yield 43%). Fractional crystallization of the

mother liquid from chloroform-carbon tetrachloride gave 1.38 g (5.02 mmol) of *erythro* **2B** (yield 24%).

For *threo* **2B**: mp 180-183 °C; ^{1}H NMR ($CDCl_3$) δ 2.0-2.8 (m, 4H, CH_2-CH_2), 4.1-4.8 (m, 2H, C<u>H</u>Br-C<u>H</u>OH), 5.7-6.0 (brs, 1H, OH), 7.3-8.0 (m, 5H, Ph); IR ν (KBr) 3200 (OH), 1440 (P-Ph), 1180 (P=O), 540 (C-Br); 750 (P-C); MS (*m/z*) 275(M^+), 277 (M^+ +2).

Anal. Calcd for $C_{10}H_{12}BrO_2P$ (275.1): C, 43.66; H, 4.40; P, 11.26. Found: C, 43.78; H, 4.29; P, 11.20.

For *erythro* **2B**: mp 136-139 °C; ^{1}H NMR ($CDCl_3$) δ 1.4-2.8 (m, 4H, CH_2-CH_2), 3.9-4.3 (m, 2H, CHBr), 4.7 (dm, 1H, $^2J_{HP}$=16 Hz, C<u>H</u>OH), 5.8-6.1 (brs, 1H, OH), 7.3-8.0 (m, 5H, Ph); IR ν (KBr) 3250 (OH), 1440 (P-Ph), 1180 (P=O), 540 (C-Br).

***threo* Bromo-3-methyl-3-hydroxy-1-phenylphospholane 1-oxide (*threo* 2A).** To 3-methyl-1-phenyl-2-phospholene 1-oxide **1A** (5.53 g, 28.8 mmol) in chloroform-water (1/4 v/v, 25 mL) was added bromine (3.0 mL, 2 eq) and the reaction mixture stirred for 3 d at room temperature. Work-up of the reaction mixture and fractional recrystallization from ethyl acetate gave 3.83 g (13.2 mmol) of *threo* **2A** in 46% yield; mp 150-152 °C. ^{1}H NMR ($CDCl_3$) δ 1.67 (s, 3H, Me), 1.9-2.8 (m, 4H, CH_2CH_2), 4.24 (d, 1H, $^2J_{HP}$=5.10 Hz, 5.56 (brs, 1H, OH), 7.3-8.0 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 25.46 (d, J_{CP}=64.83 Hz, C-5), 26.01 (d, $^3J_{CP}$=6.68 Hz, Me), 35.72 (d, $^2J_{CP}$=3.34 Hz, C-4), 50.12 (d, J_{CP}=65.50 Hz, C-2), 79.43 (d, $^3J_{CP}$=12.70 Hz, C-3), 128.02 (d, $^3J_{CP}$=12.03 Hz, *m*-Ph), 131.88 (d, $^2J_{CP}$=8.70 Hz, *o*-Ph), 132.43 (d, $^4J_{CP}$=2.69 Hz, *p*-Ph); ^{31}P NMR ($CDCl_3$) δ 68.937; IR ν (KBr) 3150 (OH).

***erythro* 2-(*N,N'*-Diethylamino)-3-hydroxy-1-phenylphospholane 1-oxide (*erythro* 3Bd).** Reaction of bromohydrin **2B** (89.4 mg, 0.325 mmol) with excess *N,N'*-diethylamine (2 mL) in methanol (3 mL) for 2 d at 40 °C gave *N*-glycoside product *erythro* **3Bd**. Removal of the volatile materials from the reaction mixture followed by washing the chloroform solution of the resulting residue with diluted sodium hydroxide (3 mL), further extraction of the water layer with chloroform, and chromatography of the residue on silica gel gave pure product **3Bd** (72.9 g, 0.273 mmol) in 84% yield. ^{1}H NMR ($CDCl_3$) δ 0.95 (t, 6H, *J*=7.0 Hz, 2 x $CH_2C\underline{H}_3$), 1.5-2.6 (m, 4H, CH_2CH_2), 2.7-3.3 (m, 5H, C<u>H</u>NEt_2, 2 x $C\underline{H}_2CH_3$), 3.6-4.0 (brs, 1H, OH), 4.3-4.8 (m, 1H, C<u>H</u>OH), 7.4-8.1 (m, 5H, Ph); IR ν (neat) 3300 (OH), 1440 (P-Ph), 1185 (P=O); MS (*m/z*) 267 (M^+).

The same procedure gave amino derivatives of phosphanyl sugar glycosides.

For methylamine derivative **3Ba**: ^{1}H NMR ($CDCl_3$) δ 1.3-2.6 (m, 4H, CH_2CH_2), 2.32 (s, 3H, NMe), 2.76 (d, 1H, *J*=7.0 Hz, CH), 3.5-4.0 (m, 3H, NH, CHOH), 7.1-8.0 (m, 5H, Ph); IR ν (neat) 3300 (OH, NH), 1445 (P-Ph), 1180 (P=O), 770 and 700 (Ph); MS (*m/z*) 226 (M^+).

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For isopropylamine derivative **3Bb**: ^{1}H NMR ($CDCl_3$) δ 0.87 (2d, 5H, J=6.0 Hz, C<u>Me</u>$_2$H), 1.5-3.1 (m, 5H, CH, CH_2CH_2, CMe$_2$<u>H</u>), 3.4-4.3 (brs, 2H, NH, OH), 7.4-8.0 (m, 5H, Ph); IR ν (KBr) 3250, 3450 (OH, NH), 1440 (P-Ph), 1160 (P=O), 770 and 700 (Ph); MS (*m/z*) 254 (M^+).

For *tert*-butylamine derivative **3Bc**: ^{1}H NMR ($CDCl_3$) data are shown in Table 2. IR ν (KBr) 3280, 3250 (OH, NH), 1440 (P-Ph), 1160 (P=O), 770 and 700 (Ph); MS (*m/z*) 268 (M^+).

***erythro* 2,3-Epoxy-1-phenylphospholane 1-oxide (*erythro* 4B).** *threo* Bromohydrin **2B** (1.31 g, 4.75 mmol) was treated with triethylamine (4 mL) in methanol (10 mL) for 2 d at room temperature. The reaction mixture was concentrated *in vacuo* and the residue was dissolved into chloroform (40 mL), whose solution was washed with aqueous sodium hydrogencarbonate solution (10 mL) and water (2 x 10 mL) and dried and concentrated under reduced pressure to give crystalline product *erythro* **4B** (recrystallized from carbon tetrachloride; 0.897 g, 4.31 mmol) in 91% yield; mp 116-118 °C. ^{1}H NMR ($CDCl_3$) δ 1.6-3.0 (m, 4H, CH_2CH_2), 3.39 (dd, $^2J_{HP}$=30 Hz, P(O)CH), 3.7-4.0 (m, 1H, CH_2C<u>H</u>), 7.2-8.0 (m, 5H, Ph); IR ν (KBr) 1440 (P-Ph), 1240 and 835 (epoxide), 1200 (P=O).

Anal. Calcd for $C_{10}H_{11}O_2P$ (194.2): C, 61.86; H, 5.71; P, 15.95 Found: C, 61.73; H, 5.64; P, 15.82.

***threo* 2-Azido-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (*threo* 3Aa).** *threo* 2-Bromo-3-hydroxy-3-methyl-1-phenylphosphlane 1-oxide (*threo* **2A**, 1.36 g, 4.71 mmol) was stirred for 1 d at 70 °C with sodium azide in DMF (30 mL). Removal of volatile materials from the reaction mixture followed by washing of the chloroform solution (50 mL) of the residue with water (3 x 20 mL) and removal of the solvent afforded crystalline azido derivative *threo* **3Aa** (1.03 g, 4.10 mmol) in 87% yield; mp 174-176 °C. ^{1}H NMR ($CDCl_3$) δ 1.53 (s, 3H, Me), 1.6-2.6 (m, 4H, CH_2CH_2), 4.00 (d, 1H, $^2J_{HP}$=1.98 Hz, CHN_3), 5.80 (brs, 1H, OH), 7.4-8.0 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 24.24 (d, $^3J_{CP}$=7.35 Hz, Me), 26.39 (d, J_{CP}=63.48 Hz, C-5), 36.23 (d, $^2J_{CP}$=4.68 Hz, C-4), 67.89 (d, J_{CP}=72.84 Hz, C-2), 78.45 (d, $^2J_{CP}$=12.03 Hz, C-3), 128.60 (d, $^3J_{CP}$=11.37 Hz, *m*-Ph), 129.24 (d, J_{CP}=93.54 Hz, *x*-Ph), 131.54 (d, $^2J_{CP}$=9.36 Hz, *o*-Ph), 132.61 (d, $^4J_{CP}$=2.67 Hz, *p*-Ph); ^{31}P NMR ($CDCl_3$) δ 67.286; IR ν (KBr) 3150 (OH), 2120 (N_3).

***threo* (*1R,2S,3R*)-2-(4',5'-Diethoxycarbonyl-1'H-1',2',3'-triazol-1'-yl)-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (6Ad).** A mixture of 2-azido-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (*threo* **3Aa**, 0.202 g, 0.804

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mmol) and diethyl acetylenedicarboxylate (0.203 g, 1.19 mmol) in DME (3 mL) was refluxed for 1 d. The solvent was then removed *in vacuo* and chromatography on silica gel afforded 0.269 g (0.638 mmol) of triazole derivarive of nucleoside of phosphanyl sugar **6Ad** in 79% yield; mp 175-176 °C. ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 3H, Me), 1.33 and 1.36 (2t, 6H, J=6.6 Hz, 2 x $OCH_2C\underline{H}_3$), 2.4-3.0 (m, 4H, CH_2CH_2), 4.32 and 4.41 (2q, 4H J=6.6 Hz, 2 x $OC\underline{H}_2CH_3$), 5.57 (d, 1H, $^2J_{HP}$=9.99 Hz, CH), 6.15 (brs, 1H, OH), 7.3-7.8 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 13.69 and 13.90 (2s, 2 x $OCH_2\underline{C}H_3$), 23.45 (d, $^3J_{CP}$=6.68 Hz, Me), 24.82 (d, J_{CP}=68.16 Hz, C-5, 37.56 (d, $^2J_{CP}$=4.68 Hz, C-4), 61.55 and 63.07 (2s, 2 x $O\underline{C}H_2CH_3$), 68.05 (d, J_{CP}=66.82 Hz, C-2), 79.89 (d, $^2J_{CP}$= 16.04 Hz, C-3), 127.84 (d, J_{CP}=93.56 Hz, *x*-Ph), 128.02 (d, $^3J_{CP}$=12.03 Hz, *m*-Ph), 131.14 (d, $^2J_{CP}$=10.01 Hz, *o*-Ph), 131.79 (d, $^3J_{CP}$=2.02 Hz, triazole C-5'), 132.52 (d, $^4J_{CP}$=2.69 Hz, *p*-Ph), 138.34 (s, triazole C-4'), 158.00 and 159.40 (2s, 2 x $\underline{C}OOCH_2$-CH_3); ^{31}P NMR ($CDCl_3$) δ 70.490.

Anal. Calcd for $C_{19}H_{24}N_3O_6P$ (421.4): C, 54.15; H, 5.74; N, 9.97, P, 7.35. Found: C, 54.02; H, 5.66; N, 5.87; P, 9.83.

The same procedure gave triazole derivatives of phosphanyl sugar nucleosides **6A** and **7A**.

For (trimethylsilyl)acetylene adduct **6Aa**: ^{1}H NMR ($CDCl_3$) δ 0.12 (s, 9H, TMS), 1.46 (s, 3H, Me), 2.3-3.3 (m, 4H, CH_2CH_2), 5.31 (d, 1H, $^2J_{HP}$=9.48 Hz, CH), 6.36 (brs, 1H, OH), 7.2-7.7 (m, 5H, Ph), 7.34 (s, 1H, triazole H); ^{13}C NMR ($CDCl_3$) δ 0.00 (s, TMS), 23.98 (d, J=6.68 Hz, Me), 25.24 (d, J=62.83 Hz, C-5), 37.98 (d, J=4.00 Hz, C-4), 68.93 (d, J=68.84 Hz, C-2), 79.73 (d, J=16.71 Hz, C-3), 127.88 (d, J=92.89 Hz, *x*-Ph), 128.00 (d, J=11.86 Hz, *m*-Ph), 130.85 and 145.74 (2s, triazole C-4' and C-5'), 130.93 (d, J=10.01 Hz, *o*-Ph), 132.37 (d, J=2.67 Hz, *p*-Ph); ^{31}P NMR ($CDCl_3$) δ 68.257.

Anal. Calcd for $C_{16}H_{24}N_3O_2PSi$ (349.4): C, 54.99; H, 6.92; N, 12.02. Found: C, 54.69; H, 6.86; N, 11.90.

For methyl propiolate adducts **6Ab** and **7Ab**: ^{1}H NMR ($CDCl_3$) δ 1.31 and 1.53 (2s, 6H, 2 x Me), 2.2-3.1 (m, 8H, CH_2CH_2), 3.76 and 3.83 (2s, 3H, COOMe for **6Ab** and **7Ab**), 4.93 (brs, 2H, 2x OH), 5.44 and 6.23 (2d, 1H, J=90.3 and 9.12 Hz, CH for **6Ab** and **7Ab**), 7.2-7.9 (m, 5H, Ph), 7.71 and 8.30 (2s, 1H, triazole H for **6Ab** and **7Ab**).

Anal. Calcd for $C_{15}H_{18}N_3O_4P$ (335.3): C, 53.73; H, 5.41; N, 12.53. Found: C, 53.52; H, 5.32; N, 12.38.

For dimethyl acetylenedicarboxylate adduct **6Ac**: ^{1}H NMR ($CDCl_3$) δ 1.33 (s, 3H, Me), 2.5-3.1 (m, 4H, CH_2CH_2), 3.89 and 3.98 (2s, 5H, 2 x COOMe), 5.64 (d, 1H,

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J=10.56 Hz, CH), 6.48 (brs, 1H, PH), 7.2-7.9 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 23.40 (d, J=60.3 Hz, Me), 24.98 (d, J=64.83 Hz, C-5), 37.63 (d, J=3.34 Hz, C-4), 52.42 and 53.61 (2s, 2 x COO<u>Me</u>), 68.12 (d, J=66.17 Hz, C-2), 79.86 (d, J=16.04 Hz, C-3), 127.78 (d, J=93.56 Hz, x-Ph), 128.06 (d, J=11.36 Hz, m-Ph), 131.08 (d, J=10.04 Hz, o-Ph), 131.72 (d, J=1.32 Hz, triazole C-5'), 132.60 (d, J=3.34 Hz, p-Ph), 138.19 (s, triazole C-4'), 158.30 and 159.73 (2s, 2 x <u>C</u>OOMe); ^{31}P NMR ($CDCl_3$) δ 69.908.

Anal. Calcd for $C_{17}H_{20}N_3O_6P$ (390.3): C, 52.31; H, 4.39; N, 10.77. Found: C, 52.18; H, 4.26; N, 10.69.

For propargyl alcohol adduct **6Ae**: ^{1}H NMR ($CDCl_3$) δ 1.26 (s, 3H, Me), 2.2-3.1 (m, 4H, CH_2CH_2), 4.40 (s, 2H, C<u>H</u>$_2$OH), 50.1 (d, 1H, J=8.95 Hz, CH), 7.2-7.8 (m, 5H, Ph), 7.86 (s, 1H, triazole H).

Anal. Calcd for $C_{14}H_{18}N_3O_3P$ (307.3): C, 54.72; H, 5.90; N, 13.67. Found: C, 54.44; H, 5.65; N, 13.46.

For propargyl alcohol adduct **7Ae**: ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 3H, Me), 2.2-3.1 (m, 4H, CH_2CH_2), 3.57 (s, 2H, C<u>H</u>$_2$OH), 5.03 (d, 1H, J=8.95 Hz, CH), 7.2-7.8 (m, 5H, Ph), 7.36 (s, 1H, triazole H).

Anal. Calcd for $C_{14}H_{18}N_3O_3P$ (307.3): C, 54.72; H, 5.90; N, 13.67. Found: C, 54.53; H, 5.71; N, 13.55.

For 3-methyl-1-butyn-3-ol adduct **6Af**: ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 3H, Me), 1.37 (s, 6H, 2 x C<u>Me</u>$_2$OH), 20.-3.2 (m, 4H, CH_2CH_2), 5024 (d, 1H, J=90.3 Hz, CH), 7.3-7.8 (m, 5H, Ph), 7.44 (s, 1H, triazole H); ^{31}P NMR ($CDCl_3$) δ 70.782.

Anal. Calcd for $C_{16}H_{22}N_3O_3P$ (335.3): C, 57.31; H, 6.61; N, 12.53. Found: C, 57.19; H, 6.56; N, 12.41.

For 3-methyl-1-butyn-3-ol adduct **7Af**: ^{1}H NMR ($CDCl_3$) δ 1.39 (s, 3H, Me), 1.46 and 1.57 (2s, 6H, 2 x C<u>Me</u>$_2$OH), 2.2-3.3 (m, 4H, CH_2CH_2), 5.85 (d, 1H, J=8.95 Hz, CH), 7.05 (s, 1H, triazole H), 7.2-7.8 (m, 5H, Ph); ^{31}P NMR ($CDCl_3$) δ 72.918.

Anal. Calcd for $C_{16}H_{22}N_3O_3P$ (335.3): C, 57.31; H, 6.61; N, 12.53. Found: C, 57.04; H, 6.48; N, 12.34.

For 2-butyn-1,4-diol adduct **6Ag**: ^{1}H NMR (CD_3OD) δ 1.20 (s, 3H, Me), 2.2-3.3 (m, 4H, CH_2CH_2), 4.42 and 4.67 (2s, 4H, 2 x C<u>H</u>$_2$OH), 5.11 (d, 1H, J=11.45 Hz, CH), 7.2-7.8 (m, 5H, Ph); ^{13}C NMR (CD_3OD) δ 23.89 (d, J=6.00 Hz, Me), 25.24 (d, J=66.15 Hz, c-5), 39.17 (d, J=4.68 Hz, C-4), 51.98 and 55.33 (2s, 2 x CH_2OH), 68.68 (d, J=70.18 Hz, C-2), 80.83 (d, J=17.38 Hz, C-3), 129.55 (d, J=93.56 Hz, x-Ph), 132.30 (d, J=9.34 Hz, o-Ph), 133.67 (d, J=2.67 Hz, p-Ph), 137.03 (d, J=1.99 Hz, triazole C-5'), 144.92 (s, triazole C-4').

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Anal. Calcd for $C_{15}H_{20}N_3O_4P$ (337.3): C, 53.41; H, 5.98; N, 12.46. Found: C, 53.22; H, 5.74; N, 12.32.

For acetylenedicarboxylic acid adduct **6Ah**: ^{1}H NMR (CD_3OD) δ 1.32 (s, 3H, Me), 2.2-3.1 (m, 4H, CH_2CH_2), 5.76 (d, 1H, J=11.36 Hz, CH), 7.2-7.8 (m, 5H, Ph); ^{13}C NMR (CD_3OD) δ 23.91 (d, J=6.68 Hz, Me), 25.43 (d, J=68.16 Hz, C-5), 39.30 (d, J=4.01 Hz, C-4), 70.15 (d, J=68.19 Hz, C-2), 80.80 (d, J=16.03 Hz, C-3), 129.42 (d, J=11.36 Hz, *m*-Ph), 132.14 (d, J=10.03 Hz, *o*-Ph), 133.91 (d, J=2.67 Hz, *p*-Ph).

Anal. Calcd for $C_{15}H_{16}N_3O_6P$ (365.3): C, 49.32; H, 4.41; N, 11.50. Found: C, 49.11; H, 4.36; N, 11.42.

***threo* 2-Amino-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (3Ab).** Catalytic hydrogenolysis of *threo* 2-azido-3-hydroxy-3-methyl-1-phenylphospholane 1-oxide (*threo* **3Aa**, 0.896 g, 3.57 mmol) in methanol (10 mL) in the presence of 10% Pd/C at atmospheric pressure of hydrogen followed by filtration of the catalyst, removal of the solvent under reduced pressure, and column chromatography on silica gel gave the *N*-glycoside of phosphanyl sugar, **3Ab** (0.795 g, 3.53 mmol, recrystallized from benzene) in 99% yield; mp 163-164 °C. ^{1}H NMR ($CDCl_3$) δ 1.34 (s, 3H, Me), 1.8-2.8 (m, 4H, CH_2CH_2), 3.39 (d, 1H, $^2J_{HP}$=5.72 Hz, CH), 7.3-7.9 (m, 5H, Ph); ^{13}C NMR ($CDCl_3$) δ 23.39 (d, $^3J_{CP}$=8.02 Hz, Me), 25.97 (d, J_{CP}=62.16 Hz, C-5), 35.77 (d, $^2J_{CP}$=5.33 Hz, C-4), 60.58 (d, J_{CP}=75.53 Hz, C-2), 79.04 (d, $^2J_{CP}$=11.36 Hz, C-3), 127.84 (d, J_{CP}=93.56 Hz, *x*-Ph), 128.30 (d, $^3J_{CP}$=11.35 Hz, *m*-Ph), 131.58 (d, $^3J_{CP}$=8.69 Hz, *o*-Ph), 132.08 (d, $^4J_{CP}$=2.67 Hz, *p*-Ph); ^{31}P NMR ($CDCl_3$) δ 68.257; IR ν (KBr) 3040-3600 (br, OH, NH).

Anal. Calcd for $C_{11}H_{15}NO_2P$ (224.2): C, 58.92; H, 6.74; N, 6.25; P, 13.81. Found: C, 58.78; H, 6.14; N, 6.13; P, 13.98.

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24. X-ray data for measurement and analysis of structure of **2A**:

Rigaku AFC5S X-ray diffractometer with four-axis goniometer was used. Crystal data: Empirical formula, $C_{11}H_{14}O_2BrP$; Crystal color, Habit, colorless, prismatic; Crystal dimensions, 1.00 x 0.90 x 1.00 mm; Crystal system, monoclinic; Lattice type, primitive; No. of reflections used for unit cell determination (2θ range), 25 (29.94-34.76 °); Omega scan peak width at half-height, 0.24°; Lattice parameters, a=15.02 Å, b=10.134 Å, c=20.28 Å, α=90.00 °, β=107.3 °, γ= 90.00 °, V=2948.72 Å^3; Space group, $P2_1/a$ (#14); Z value, 4; D_{calc}, 1.571 g/cm^3; F_{000}, 1400; μ (MoK α), 31.29 cm^{-1}. Intensity measurments: Diffractometer, Rigaku AFC5S; Radiation, MoK α (λ=0.71069 Å), graphite monochromated; Attenuator, Ni foil (factors=2.3, 5.2, 11.7); Take-off angle, 6.0°; Detector aperture, 6.0 mm horizontal, 6.0 mm vertical; Diameter of beam collimator, 0.5 mm; Crystal to detector distance 400 mm; Temperature 22 ℃; Scan type, ω-2θ; Scan rate, 32.0° /min (in ω)-up to 2 rescans; Scan width, (1.00 +0.30 tan θ)°; $2\theta_{max}$, 55.0°; No. of reflections measured, total 6150, unique 5862 corrections, Lorentz-polarization. Structure solution and refinement: Structure solution, Direct methods (TEXSAN); Refinement, full-matrix least-squares; Function minimized, $\Sigma w(|Fo|-|Fc|)^2$; Least squares weights, $1/\sigma^2(Fo)=4Fo^2/\sigma^2(Fo^2)$; p-factor, 0.03; Anomalous dispersion, all non-hydrogen atoms; No. observations ($I > 3.00\,\sigma(I)$), 1426; No. variables, 307; Reflection/Parameter ratio, 4.64; Residuals: R; Rw, 0.083; 0.090; Goodness of fit indicator, 2.82; Max shift/Error in final cycle, 0.39; Maximum peak in final diff. map, 1.19 e$^-$/Å^3; Minimum peak in final diff. map, -0.73 e$^-$/Å^3.

X-ray structure data for **2A**.

Selected bond distances in Å: P(1)-C(2) 1.86, P(1)-C(5) 1.80, C(2)-C(3) 1.54, C(3)-C(4) 1.55, C(4)-C(5) 1.47.

Selected bond angles in degree: C(2)-P(1)-C(5) 94, P(1)-C(2)-C(3) 103, C(2)-C(3)-C(4) 104, C(3)-C(4)-C(5) 108, P(1)-C(5)-C(4) 108.

Selected torsional angles in degree: P(1)-C(2)-C(3)-C(4) 43, P(1)-C(5)-C(4)-C(3) 31, C(2)-P(1)-C(5)-C(4) -4, C(2)-C(3)-C(4)-C(5) -49, C(3)-C(2)-P(1)-C(5) -24.

These data imply that the conformation of **2A** may be in a ^2E form.

25. X-ray data for measurement and analysis of structure of **3Aa**:

Rigaku AFC5S X-ray diffractometer with four-axis goniometer was used. Crystal data: Empirical formula, $C_{11}H_{14}N_3O_2P$; Crystal color, Habit, colorless, prismatic; Crystal dimensions, 0.16 x 0.82 x 0.98 mm; Crystal system, monoclinic; Lattice type, primitive; No. of reflections used for unit cell determination (2θ range), 23 (20.1-29.7 °); Omega scan peak width at half-height, 0.21°; Lattice parameters, a=25.18 Å, b=9.834 Å, c=14.415 Å, α=90.00 °, β=122.23 °, γ= 90.00 °, V=3020 Å^3; Space group, C2/c (#15); Z value, 8; D_{calc}, 1.630 g/cm^3; F_{000}, 1520; μ (MoK α), 7.19 cm^{-1}. Intensity measurments: Diffractometer, Rigaku AFC5S; Radiation, MoK α (λ=0.71069 Å), graphite monochromated; Attenuator, Ni foil (factors=2.3, 5.2, 11.7); Take-off angle, 6.0°; Detector aperture, 6.0 mm horizontal, 6.0 mm vertical; Diameter of beam collimator, 0.5 mm; Crystal to detector distance 400 mm; Temperature 22 ℃; Scan type, ω-2θ; Scan rate, 32.0° /min (in ω)-up to 2 rescans; Scan width, (1.15 + 0.30 tan θ)°;

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$2\theta_{max}$, 55.0° ; No. of reflections measured, total 3768, unique 3684 corrections, Lorentz-polarization. Structure solution and refinement: Structure solution, Direct methods (TEXSAN); Refinement, full-matrix least-squares; Function minimized, $\Sigma w(|Fo|-|Fc|)^2$; Least squares weights, $1/\sigma^2(Fo)=4Fo^2/\sigma^2(Fo^2)$; p-factor, 0.03; Anomalous dispersion, all non-hydrogen atoms; No. observations ($I > 3.00\sigma(I)$), 1100; No. variables, 163; Reflection/Parameter ratio, 6.75; Residuals: R; Rw, 0.215; 0.301; Goodness of fit indicator, 7.53; Max shift/Error in final cycle, 1.35; Maximum peak in final diff. map, 6.54 $e^-/Å^3$; Minimum peak in final diff. map, -0.88 $e^-/Å^3$.

X-ray structure data for **3Aa**.

Selected bond distances in Å: P(1)-C(1) 1.85(3), C(1)-C(2) 1.56(5), C(2)-C(3) 1.54(4), C(3)-C(4) 1.43(5), C(4)-P(1) 1.84(4).

Selected bond angles in degree: P(1)-C(1)-C(2) 101(2), C(1)-C(2)-C(3) 105(3), C(2)-C(3)-C(4) 111(3), C(3)-C(4)-P(1) 105(3), C(4)-P(1)-C(1) 96(2).

Selected torsional angles in degree: P(1)-C(2)-C(3)-C(4) -43(3), C(1)-C(2)-C(3)-C(4) 51(4), C(2)-C(3)-C(4)-P(1) -30(4), C(3)-C(4)-P(1)-C(1) 3(3), C(4)-P(1)-C(1)-C(2) 24(2).

These data imply that the conformation of **3Aa** may be in a ^2E form.

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35. X-ray data for measurement and analysis of structure of **6d**.

Rigaku AFC7R X-ray diffractometer with four-axis goniometer was used. Crystal data: Empirical formula, $C_{19}H_{24}N_3O_6P$; Formula weight, 421.39; Crystal color, Habit, colorless, prismatic; Crystal dimensions, 020x0.20x0.30 mm; Crystal system, monoclinic; Lattice type, primitive; No. of reflections used for unit cell determination (2θ range), 25 (54.5-57.0 °); Omega scan peak width at half-height, 0.22°; Lattice parameters, a=14.243 Å, b=10.494 Å, c=14.486 Å, β=98.138 °, V=1589.6 $Å^3$; Space group, $P2_1/n$ (#9); Z value, 4; D_{calc}, 1.306 g/cm^3; F_{000}, 888.00; μ (CuKα), 14.86 cm^{-1}. Intensity measurments: Diffractometer, Rigaku AFC7R; Radiation, CuKα (λ=1.54178 Å), graphite monochromated; Attenuator, Ni foil (factors=1.00, 9.48, 9.48, 9.43); Take-off angle, 6.0°; Detector aperture, 9.0 mm horizontal, 13.0 mm vertical; Crystal to detector distance 235 mm; Temperature 20.0 ℃; Scan type, ω-2θ; Scan rate, 16.0 °/min (in ω)-up to 3 scans; Scan width, (1.78 +0.30 tan θ)°; $2\theta_{max}$, 120.1°; No. of reflections measured, total 3537; Corrections, Lorentz-polarization. Structure solution and refinement: Structure

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solution, Direct methods (SHELXS86); Refinement, full-matrix least-squares; Function minimized, $\Sigma w(|Fo|-|Fc|)^2$; Least squares weights, $1/\sigma^2(Fo)= 4Fo^2/\sigma^2(Fo^2)$; p-factor, 0.00; Anomalous dispersion, all non-hydrogen atoms; No. observations ($I > 3.00\,\sigma(I)$), 2337; No. variables, 358; Reflection/Parameter ratio, 6.53; Residuals: R; Rw, 0.056; 0.043; Goodness of fit indicator, 3.19; Max shift/Error in final cycle, 2.73; Maximum peak in final diff. map, 0.36 $e^-/Å^3$; Minimum peak in final diff. map, -0.34 $e^-/Å^3$.

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 IEZ, UK.

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