A Convenient Synthesis of (2*R*)-1-Amino-1-deoxy-1-phosphinylglycerols

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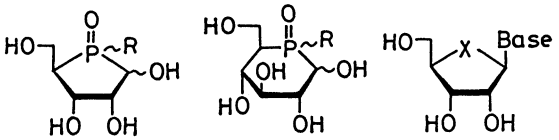
2,3-*O*-Isopropylidene-D-glyceraldehyde reacts with dimethylphosphine oxide in the presence of triethylamine to give separable (1*S*,2*R*)- and (1*R*,2*R*)-1-dimethylphosphinylglycerol (65 : 35), from which the (1*R*) and (1*S*) title compounds are respectively derived via 1-*O*-mesyl and 1-azido derivatives. The corresponding 1-dimethoxyphosphinylglycerols are similarly prepared. Structural and conformational assignments of these products are made on the basis of the ^{1}H NMR data and $[\alpha]_D$ values.

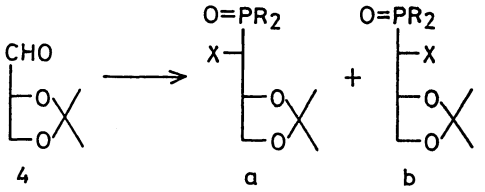
In view of a wide interest in their physicochemical properties and potential biological activity, sugar analogs having a phosphorus atom in the hemiacetal ring have been prepared in recent years;[1] e.g., analogs of D-ribofuranose **1** (R=Et, Ph, OH)[2] and D-glucopyranose **2** (R=Et, OH).[3] However, no nucleoside or nucleotide analogs of P-in-ring sugars have been reported so far, whereas some synthetic heteroatom-sugar and pseudo-sugar nucleosides have drawn considerable attention due to the unique physiological activity; e.g. **3** (X=S,[4] NAc,[5] CH_2[6]). We report herein a new type of simple (2*R*)-1-amino-1-phosphinylglycerols that can be readily prepared by a synthetic scheme potentially applicable to preparation of biologically important amino phosphonic acid derivatives,[7] as well as a series of P-in-ring sugar nucleosides.



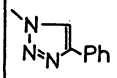
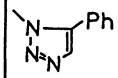
1 2 3

Results and Discussion

Paulsen et al.[8] briefly described that the addition of dimethyl phosphonate to 2,3-*O*-isopropylidene-D-glyceraldehyde (**4**) in the presence of a catalytic amount of sodium alkoxide gave a 41 : 59 mixture of (2*R*)-glycerol derivatives **6a** and **6b**, which were chromatographically inseparable and whose C-1 configuration (1*R* or 1*S*) remained unestablished. Although we also studied the reactivities of these phosphonates (see below), we have chosen a 1-dialkylphosphinyl-substituted (2*R*)-glycerol as a model compound for thorough investigation in view of later preparation of alkylphosphinyl-in-ring sugar nucleosides. Thus, condensation of **4** with dimethylphosphine oxide in the presence of triethylamine (TEA) gave a mixture of adducts **5a** and **5b** in a ratio of 35 : 65, which were separable by chromatography (84% isolated yield). The (1*R*) and (1*S*) configurations were assigned to **5a** and **5b**, respectively, on the basis of ^{1}H NMR spectra of these compounds as well as their derivatives (see below).



4 a b

R=Me	R=OMe	X
5	6	OH
7		OAc
8	9	OMs
	10	OTf
11	12	N_3
13	14	NH_2
15	16	NHAc
17	18	
19	20	
21	22	NHBu

Compounds **5a** and **5b** were readily led to acetates **7a** and **7b**, as well as mesylates **8a** and **8b**, respectively, by the usual method. The nucleophilic substitution reactions with azide anion took place smoothly for **8a** and **8b** (but not for **5a**,**b**) with C-1 inversion to give **11b** and **11a**, respectively. Compounds **11a** and **11b** were reduced to amino compounds **13a** and **13b**, respectively, which were characterized as acetamido derivatives **15a** and **15b**. Azido **11a** was easily led to the 1,2,3-triazolyl-substituted compounds **17a** and **19a** on treatment with phenylacetylene. Nucleophilic sub-

Table 1. ^{1}H (500 MHz) and ^{31}P (81 MHz) NMR Parameters for Selected Compounds in $CDCl_3$

Compd	Chemical shifts (δ)								Coupling constants (Hz)						
	H-1	H-2	H-3	H-3′	PMe_2[a]	CMe_2	X	^{31}P	$J_{1,2}$	$J_{1,P}$	$J_{2,3}$	$J_{2,3'}$	$J_{2,P}$	$J_{3,3'}$	$J_{1,X}$
5a	3.77	4.58	4.13	4.01	1.58,1.52	1.45,1.37	3.18[b]	46.3	3.9	6.9	6.8	6.4	3.7	8.5	6.9
5b	3.66	4.23	4.19[c]	4.10	1.58,1.56	1.41,1.33	5.28[b]	45.7	9.0	1.0	6.0	4.5	6.1	8.5	5.2
6a	3.87	4.45	4.08	3.94	(3.84,3.82)	1.45,1.38	2.82[b,d]	22.1	4.8	9.8	6.5	6.6	3.8	8.5	7.4
6b	4.12	4.37	4.13	4.07[f]	(3.82,3.82)	1.44,1.36	3.20[b,e]	22.9	4.7	8.3	6.0	6.5	3.5	8.8	4.3
7a	5.30	4.70	4.09	3.83	1.63,1.47	1.43,1.34	2.18[g]	43.1	3.4	9.0	6.8	5.4	2.8	8.8	
7b	5.26	4.55	4.14	3.97	1.60,1.52	1.42,1.36	2.18[g]	40.6	6.0	0.5	6.4	6.2	5.7	8.7	
8a	4.90	4.55	4.20	4.14	1.68,1.63	1.46,1.37	3.23[h]	43.7	6.2	8.0	6.7	5.6	2.4	9.5	
8b	5.00	4.53	4.11	4.05	1.67,1.64	1.45,1.37	3.23[h]	42.0	5.0	5.0	6.4	6.8	3.9	8.6	
9a	5.13	4.49	4.11	4.01	(3.89,3.86)	1.45,1.37	3.18[h]	16.3	3.2	11.9	6.6	7.3	1.8	8.7	
9b	4.87	4.47	4.15	4.05	(3.87,3.87)	1.47,1.38	3.20[h]	15.6	7.6	11.0	6.5	6.0	2.5	9.3	
11a	3.48	4.63	4.18	4.10	1.63,1.60	1.48,1.37		45.2	5.6	12.5	6.6	6.0	3.7	8.9	
11b	3.79	4.40	4.16	4.02	1.62,1.58	1.48,1.37		43.7	6.0	7.4	6.4	6.0	4.2	8.5	
12a	3.44	4.50	4.11	3.99	(3.88,3.85)	1.49,1.38		20.1	5.6	15.7	6.5	6.5	3.5	8.7	
12b	4.00	4.42	4.05	4.03	(3.85,3.84)	1.49,1.37		19.8	4.3	14.7	6.4	6.4	2.9	8.8	
15a	4.39	4.81	4.09	3.60	1.55,1.52	1.46,1.36	5.97[i,k]	44.6	1.4	11.5	7.1	6.8	4.3	8.4	9.8
15b	4.26	4.44	4.13[j]	3.86	1.70,1.43	1.44,1.35	7.68[i,l]	45.1	9.5	0.5	6.2	5.4	6.1	8.8	9.4
16a	4.57	4.58	4.06	3.62	(3.80,3.79)	1.44,1.36	5.95[i,m]	23.2	2.1	19.5	7.0	6.6	4.2	8.5	9.8
16b	4.72	4.38	4.06	4.03	(3.79,3.76)	1.43,1.33	6.18[i,l]	22.9	5.4	17.8	6.3	5.6	7.5	9.1	10.0
17a	5.05	5.03	4.20	3.71	1.69,1.51	1.42,1.39	8.12[n,o]	42.5	4.3	12.1	6.4	6.8	4.3	8.7	
19a	4.76	4.98	4.31	4.10	1.93,1.04	1.35,1.35	7.76[p,q]	45.7	9.3	15.1	6.0	7.7	2.5	9.4	
18a	5.20	4.84	4.15	3.63	(3.81,3.77)	1.36,1.32	8.15[n,o]	17.2	4.6	19.8	6.4	6.6	3.5	8.9	
20a	4.69	5.02	4.21	4.05	(3.79,3.75)	1.27,1.17	7.76[p,q]	16.8	9.4	16.9	6.2	6.0	1.9	9.3	
18b	5.12	4.75	4.04[j]	3.90	(3.90,3.68)	1.36,1.32	8.05[n,o]	19.6	7.0	18.2	6.2	5.0	5.7	9.3	
20b	4.91	4.93	4.10	4.10	(3.85,3.71)	1.33,1.10	7.75[p,q]	17.9	6.3	16.0	5.4	5.4	5.5	—	

a) Values in parenthesis are for $P(OMe)_2$. These signals are all doublets with J_{PMe}=12.9—13.2 Hz or J_{POMe}=10.7—11.0 Hz. b) HO-1. c) $J_{3,P}$=2.5 Hz. d, e) $J_{P,OH}$=15.0 and 10.2 Hz, respctively. f) $J_{3',P}$=1.0 Hz. g) AcO-1. h) MsO-1. i) HN-1. j) $J_{3,P}$=1.7 Hz. k, l, m) For AcN-1, δ=2.10, 2.05, and 2.08, respctively. n) H-5′. o) For protons of Ph(*o*) Ph(*m*) and Ph(*p*)-4′, δ=7.85, 7.44, and 7.35 (±0.01), respctively, $J_{o,m}$=8.0, $J_{m,p}$=7.4, $J_{o,p}$=1.2 Hz. p) H-4′. q) For protons of Ph-5′, δ=7.51—7.48.

stitution with an alkylamine was exemplified by the conversion of **8a** and **8b** into rather unstable butylamino derivatives **21b** and **21a**, respectively, but only in moderate yields.

According to the similar reaction schemes for phosphine oxides shown above, the mixture of the phosphonates **6a** and **6b** (41 : 59)[8] were led to the corresponding mesylates **9a** and **9b**. These mesylates did not yield the azido-substituted compounds **12b** and **12a**, which, however, were successfully prepared via unstable trifluoromethanesulfonates **10a** and **10b** derived from **6a** and **6b**, respectively. Compounds **12a** and **12b** were separable by chromatography and similarly led to the corresponding amino **14a,b**, acetamido **16a,b**, and triazolyl derivatives **18a,b** and **20a,b**. Compounds **10a** and **10b** were also led to butylamino derivatives **22b** and **22a**, respectively.

Structural Assignments and Conformational Analyses of Compounds 5—22a,b. Characteristic features observed in the ^{1}H NMR spectra of the major product **5b** and minor one **5a** and their respective, acetamido derivatives **15a** and **15b** are as follows: 1) The large $J_{1,2}$ and small $J_{1,P}$ of **5b** and **15b** strongly suggest the anti conformation of H-C(1)-C(2)-H and O=P-C(1)-H bonds,[1] whereas the medium or small $J_{1,2}$ and medium $J_{1,P}$ values of **5a** and **15a** are indicative of the gauche conformations of the above groups. 2) The presence of a medium, long-range coupling ($^4J_{3,P}$) in **5b** and **15b** suggests the W-shaped P-C(1)-C(2)-C(3)-H bond nearly on a plane. 3) The HO-1 and HN-1 signals of **5b** and **15b** appear at a significantly lower field compared with those of **5a** and **15a**, indicating the possibility of the presence of a certain extent of an intramolecular hydrogen bonding between HO-1 (or HN-1) and O=P groups in **5b** and **15b**. 4) Both $J_{2,3}$ and $J_{2,3'}$ values of all of these compounds can be regarded as relatively large.

Combination of these data led to the assignments of the C-1 configuration of **5a** and **5b** to be (*R*) and (*S*), respectively, with the most likely conformations (in $CDCl_3$ solution) illustrated in the Newman projection formulas in Fig. 1. The same assignments are applicable to the acetamido derivatives **15a** and **15b**. These NMR data are summarized in Table 1. The assignment of (1*S*) to the major product is in conformity with the already reported examples of the preponderant addition of some nucleophiles, such as allylic boronates,[9] to protected D-glyceraldehyde to give anti derivatives, which are in accordance with the Felkin-Ahn rule.[10]

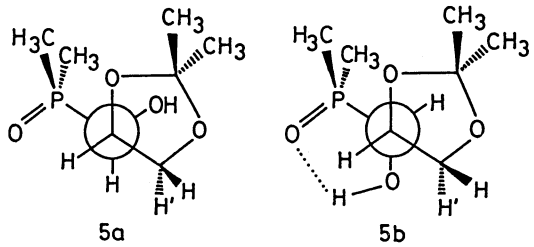


Fig. 1.

These characteristic ^{1}H NMR features are not observable for the rest of the products, presumably because of the absence of certain, predominant conformations in solution at 21 °C. However, a close relationship is observed between the specific rotations of the C-1 diastereomers of the separated phosphine oxides and phosphonates. Namely, $[\alpha]_D$ of the **a**-series of compounds **5**, **7**, **8**, **11**, **12**, **15**, and **16** all shows negative values, whereas the values of the **b**-series of these corresponding compounds are positive (except for **5b**). On the ground of this characteristic features and the mode of the nucleophilic addition and the subsequent reactions observed for **5a**/**5b** and **15a**/**15b**, the same configurations (1*R*)/(1*S*) would be assignable to the corresponding phosphonates **6a**(minor)/**6b**(major), **16a**/**16b** and other related compounds. Their NMR data are summarized in Table 1. Although the ^{31}P signals of all of (1*S*) compounds appear at slightly higher field than those of the corresponding (1*R*) diastereomers (except for the case of **6a**,**6b**), the exact reasons for this difference have remained to be clarified.

These synthetic and spectral findings described so far are believed to be valuable information on preparations and structural assignments of similar α-hydroxy and α-amino phosphinyl compounds.

Experimental

Melting points are uncorrected. All reactions were performed under an argon atmosphere and monitored by TLC (Merck silica gel 60F, 0.25 mm) with an appropriate solvent system [(*A*) 1 : 1 AcOEt-hexane, (*B*) 1 : 9 EtOH-AcOEt, (*C*) 1 : 14 MeOH-$CHCl_3$, (*D*) 1 : 9 MeOH-$CHCl_3$, (*E*) 1 : 9 EtOH-benzene] unless otherwise specified. Chromatographic separation was carried out on a column of silica gel (Wako C-200). Solid products were recrystallized from AcOEt-hexane. Optical rotations were measured with a Nihon-Bunko DIP-4 polarimeter at 25 °C. The ^{1}H and ^{31}P NMR spectra were measured in $CDCl_3$ with Varian VXR-500 and VXR-200 instruments (500 and 81 MHz, respectively, SC-NMR Lab., Okayama Univ.) at 21 °C. Chemical shifts are reported as δ values relative to tetramethylsilane (internal standard for ^{1}H) and 85% phosphoric acid (external standard for ^{31}P). The assignments of signals of diastereomers were confirmed by 2D COSY measurements. These NMR data together with assignments of all signals are summarized in Table 1. The mass spectra were taken on an A.E.I. MS 50 ultrahigh resolution instrument and were given in terms of *m*/*z* (rel intensity) compared with the base peak.

(1*R*,2*R*)- and (1*S*,2*R*)-1-(Dimethylphosphinyl)-2,3-*O*-isopropylideneglycerol (5a, 5b). A mixture of dimethylphosphine oxide[11] (1.56 g), **4**[12] (3.00 g) and TEA (1.11 ml) in dry $CHCl_3$ (2 ml) was stirred at 20 °C for 3 h and then chromatographed to give (1*S*)-compd **5b** (2.30 g, 55%) and (1*R*)-isomer **5a** (1.20 g, 29%).

5a: Colorless prisms, mp 144.5—146 °C; R_f 0.14 (*B*); $[\alpha]_D$ −14° (*c* 0.34, $CHCl_3$); MS *m/z* 209 (M+1, 0.6), 193 (20), 108 (100). Found: *m/z* 209.0944. Calcd for $C_8H_{18}O_4P$: M+1, 209.0943.

5b: Colorless needles, mp 116—117 °C; R_f 0.22 (*B*); $[\alpha]_D$ −23° (*c* 0.71, $CHCl_3$); MS *m/z* 209 (M+1, 0.5), 193 (31), 108 (100). Found: *m/z* 209.0935. Calcd for $C_8H_{18}O_4P$: M+1, 209.0943.

(1*R*,2*R*)- and (1*S*,2*R*)-1-(Dimethoxyphosphinyl)-2,3-*O*-isopropylideneglycerol (6a, 6b).[8] A mixture of dimethyl phosphonate (2.3 ml), **4** (4.0 g) and TEA (1.5 ml, 11 mmol) was stirred at 20 °C for 1.5 h, concentrated in vacuo and chromatographed to give an inseparable mixture of **6a** and **6b** (41 : 59) as a colorless oil (4.74 g, 79%) (cf. lit,[8] 52% yield using sodium methoxide as base); R_f 0.10 (*A*), 0.25 (AcOEt).

(1*R*,2*R*)- and (1*S*,2*R*)-1-*O*-Acetyl-1-(dimethylphosphinyl)-2,3-*O*-isopropylideneglycerol (7a, 7b). A. A mixture of **5b** (301 mg), acetic anhydride (0.40 ml) and dry pyridine (2.4 ml) was stirred at 20 °C for 22 h, worked up and chromatographed to give (1*S*)-compd **7b** as colorless hygroscopic crystals (307 mg, 85%), mp 72—75 °C (in sealed capillary); R_f 0.41 (*B*); $[\alpha]_D$ +29° (*c* 0.57, $CHCl_3$); MS *m/z* 251 (M+1, 1.0), 235 (83), 150 (56), 133 (100). Found: *m/z* 251.1047. Calcd for $C_{10}H_{20}O_5P$: M+1, 251.1048.

B. Similarly, **5a** gave (1*R*)-isomer **7a** as colorless hygroscopic crystals (79%), mp 69—72 °C (in sealed capillary); R_f 0.46 (*B*); $[\alpha]_D$ −27° (*c* 0.54, $CHCl_3$); MS *m/z* 235 (M-CH_3, 82), 150 (81), 133 (99), 107 (100). Found: *m/z* 235.0736. Calcd for $C_9H_{16}O_5P$: M−CH_3, 235.0736.

(1*R*,2*R*)- and (1*S*,2*R*)-1-(Dimethylphosphinyl)-2,3-*O*-isopropylidene-1-*O*-mesylglycerol (8a, 8b). A. To a solution of **5b** (120 mg) and γ-collidine (0.152 ml) in dry CH_2Cl_2 (1.4 ml) was dropwise added mesyl chloride (0.070 ml) at 0 °C. The mixture was stirred at 20 °C for 4 h and worked up to give (1*S*)-compd **8b** as colorless prisms (137 mg, 83%), mp 111—112 °C; R_f 0.33 (*C*); $[\alpha]_D$ +27° (*c* 0.63, $CHCl_3$); MS *m/z* 287 (M+1, 0.9), 271 (100), 133 (77). Found: *m/z* 287.0715. Calcd for $C_9H_{20}O_6SP$: M+1, 287.0718.

B. Similarly, **5a** gave (1*R*)-isomer **8a** as a colorless oil (86%); R_f 0.42 (*C*); $[\alpha]_D$ −29° (*c* 0.67, $CHCl_3$); MS *m/z* 287 (M+1, 0.3), 271 (88), 133 (62), 107 (100). Found: *m/z* 287.0747. Calcd for $C_9H_{20}O_6SP$: M+1, 287.0718.

(1*R*,2*R*)- and (1*S*,2*R*)-1-(Dimethoxyphosphinyl)-2,3-*O*-isopropylidene-1-*O*-mesylglycerol (9a, 9b). Similarly, mesylation of **6a,b** gave an inseparable mixture of **9a** and **9b** as a colorless oil (91%); R_f 0.21 (*A*); MS *m/z* 319 (M+1, 0.4), 303 (100), 165 (95),139 (39). Found: *m/z* 319.0613. Calcd for $C_9H_{20}O_8SP$: M+1, 319.0616.

(1*R*,2*R*)- and (1*S*,2*R*)-1-(Dimethoxyphosphinyl)-2,3-*O*-isopropylidene-1-*O*-(trifluoromethylsulfonyl)glycerol (10a, 10b). Trifluoromethanesulfonic anhydride (0.156 ml) was added, at −15 °C, to a solution of **6a,b** (150 mg), γ-collidine (0.010 ml) and pyridine (0.10 ml) in dry $CHCl_3$ (6 ml). The mixture was stirred at −15 °C for 20 min and then worked up to give an inseparable mixture of **10a** and **10b** as a pale yellow oil (209 mg, 90%); R_f 0.40 (*A*); ^1H NMR (60 MHz) δ=1.34, 1.42 (3H each, 2s, CMe_2), 3.88 (6H, d, *J*=11.8 Hz, 2MeO), 4.0—4.2 (2H, m, H-3,3′), 4.48 (1H, m, H-2), 4.93 (0.6H, dd, $J_{1,P}$=10, $J_{1,2}$=8 Hz, H-1 of **10b**), 5.27 (0.4H, dd, $J_{1,P}$=11, $J_{1,2}$=3 Hz, H-1 of **10a**). The product was unstable and therefore immediately used for the next step.

(1*R*,2*R*)- and (1*S*,2*R*)-1-Azido-1-deoxy-1-(dimethylphosphinyl)-2,3-*O*-isopropylideneglycerol (11a, 11b). A. A mixture of **8b** (430 mg) and sodium azide (981 mg) dissolved in dry DMF (14 ml) was stirred at 115—120 °C for 4 h, diluted with CH_2Cl_2 (150 ml) and filtered. The filtrate was triturated with AcOEt and purified by chromatography, affording (1*R*)-compd **11a** as a colorless oil (310 mg, 88%); R_f 0.25 (*E*); $[\alpha]_D$ −6.6° (*c* 0.64, $CHCl_3$); MS *m/z* 218 (M−CH_3, 24), 149 (81), 101 (100). Found: *m/z* 218.0695. Calcd for $C_7H_{13}N_3O_3P$: M−CH_3, 218.0695.

B. Similaryl, **8a** gave (1*S*)-isomer **11b** as colorless needles (76%), mp 91—92.5 °C; R_f 0.22 (*E*); $[\alpha]_D$ +12° (*c* 0.54, $CHCl_3$); MS *m/z* 218 (M−CH_3, 31), 191 (33), 149 (39), 101 (100). Found: *m/z* 218.0692. Calcd for $C_7H_{13}N_3O_3P$: M-CH_3, 218.0695.

(1*R*,2*R*) and (1*S*,2*R*)-1-Azido-1-deoxy-1-(dimethoxyphosphinyl)-2,3-*O*-isopropylideneglycerol (12a, 12b). The mixture **10a,b** (209 mg) was treated with sodium azide (109 mg) in dry DMF (1.2 ml) at 0 °C for 3 h and then worked up.

12a: Colorless needles (65 mg, 44%), mp 54—55 °C; R_f 0.25 (*A*); $[\alpha]_D$ −50° (*c* 0.56, $CHCl_3$); MS *m/z* 250 (M−CH_3, 18), 165 (5), 101 (100). Found: *m/z* 250.0591. Calcd for $C_7H_{13}N_3O_5P$: M−CH_3, 250.0593.

12b: Colorless oil (45 mg, 30%); R_f 0.30 (*A*); $[\alpha]_D$ +6.8° (*c* 0.68, $CHCl_3$); MS *m/z* 250 (M−CH_3, 18), 165 (5), 101 (100). Found: *m/z* 250.0589. Calcd for $C_7H_{13}N_3O_5P$: M−CH_3, 250.0593.

(1*R*,2*R*)- and (1*S*,2*R*)-1-Acetamido-1-deoxy-1-(dimethylphosphinyl)-2,3-*O*-isopropylideneglycerol (15a, 15b). A. A solution of **11a** (100 mg) in methanol (4 ml) was hydrogenated in the presence of 10% Pd-C (113 mg) at 20 °C for 3 h. After filtration of the catalyst, the filtrate was concentrated in vacuo to give (1*R*)-1-amino compd **13a** as a colorless oil (89 mg, 100%); R_f 0.06 (*E*); ^1H NMR (60 MHz) δ=1.35, 1.43 (3H each, 2s, CMe_2), 1.50, 1.54 (3H each, 2d, *J*=13.0 Hz, PMe_2), 2.9—3.1 (2H, m, NH_2), 3.8—4.3 (3H, m, H-1,3,3′), 4.65 (1H, m, H-2). Compound **13a** (89 mg) was treated with acetic anhydride (0.12 ml) in pyridine (1 ml) at 20 °C for 3 h, giving (1*R*)-compd **15a** as colorless needles (80 mg, 75%), mp 168—170 °C; R_f 0.25 (*E*); $[\alpha]_D$ −44 °C (*c* 0.53, $CHCl_3$); MS *m/z* 234 (M−CH_3, 9.0), 149 (100), 132 (54). Found: *m/z* 234.0894. Calcd for $C_9H_{17}NO_4P$: M−CH_3, 234.0896.

B. Similar hydrogenation of **11b** gave (1*S*)-isomer **13b** as a colorless oil (100%); R_f 0.27 (*D*); ^1H NMR (60 MHz) δ=1.34, 1.42 (3H each, 2s, CMe_2), 1.56 (6H, d, *J*=13.0 Hz, PMe_2), 2.9—3.1 (2H, m, NH_2), 3.8—4.4 (4H, m, H-1,2,3,3′). Similar acetylation of **13b** with acetic anhydride in pyridine gave the (1*S*)-isomer **15b** as colorless crystals (77%), mp 169—171 °C; R_f 0.33 (*D*); $[\alpha]_D$ +44° (*c* 0.45, $CHCl_3$); MS *m/z* 234 (M−CH_3, 13), 149 (100), 114 (56). Found: *m/z* 234.0889. Calcd for $C_9H_{17}NO_4P$: M−CH_3, 234.0896.

(1*R*,2*R*)- and (1*S*,2*R*)-1-Acetamido-1-deoxy-1-(dimethoxyphosphinyl)-2,3-*O*-isopropylideneglycerol (16a, 16b). A. Hydrogenation of **12a** (49 mg) gave (1*R*)-1-amino compd **14a** as a colorless oil (44 mg, 100%); R_f 0.04 (*A*); ^1H NMR (60 MHz), δ=1.33, 1.40 (3H each, 2s, CMe_2), 2.9—3.2 (2H, m, NH_2), 3.6—4.2 (3H, m, H-1,3,3′), 3.80 (6H, d, *J*=10.8 Hz, 2MeO), 4.35 (1H, m, H-2). Acetylation of **14a** gave (1*R*)-compd **16a** as a colorless oil (89%); R_f 0.04 (*A*); $[\alpha]_D$ −19° (*c* 0.33, $CHCl_3$); MS *m/z* 282 (M+1, 0.3), 181 (100), 139 (24). Found: *m/z* 282.1101. Calcd for $C_{10}H_{21}NO_6P$: M+1, 282.1107.

B. Hydrogenation of **12b** gave (1*S*)-1-amino isomer **14b** as a colorless oil (100%); R_f 0.04 (*A*); ^1H NMR (60 MHz) δ=1.33, 1.43 (3H each, 2s, CMe_2), 2.8—3.3 (2H, m, NH_2),

3.4—4.1 (3H, m, H-1,3,3′), 3.83 (6H, d, J=10.8 Hz, 2MeO), 4.30 (1H, m, H-2). Acetylation of **14b** gave the (1*S*)-isomer **16b** as colorless needles (76%), mp 71—73 °C; R_f 0.06 (*A*); $[\alpha]_D$ +9.4° (*c* 0.51, $CHCl_3$); MS *m/z* 282 (M+1, 0.4), 181 (100), 139 (24). Found: *m/z* 282.1096. Calcd for $C_{10}H_{21}NO_6P$: M+1, 282.1107.

(1*R*,2*R*)-1-Deoxy-1-(dimethylphosphinyl)-2,3-*O*-isopropylidene-1-(4- and 5-phenyl-1,2,3-triazol-1-yl)glycerol (17a, 19a). A. A mixture of **11a** (30 mg) and phenylacetylene (0.5 ml) was stirred at 120 °C for 0.5 h, evaporated in vacuo and chromatographed to give 4-phenyl- **17a** and 5-phenyltriazolyl compd **19a**.[13]

17a: Colorless needles (22 mg, 51%), mp 158—159 °C; R_f 0.23 (*E*); MS *m/z* 335 (M^+, 31), 235 (42), 229 (54), 206 (46), 77 (100). Found: *m/z* 335.1396. Calcd for $C_{16}H_{22}N_3O_3P$: M, 335.1399.

19a: Colorless needles (19 mg, 44%), mp 153—154 °C; R_f 0.33 (*E*); MS *m/z* 335 (M^+, 0.8), 258 (43), 235 (36), 207 (23), 78 (100). Found: *m/z* 335.1376. Calcd for $C_{16}H_{22}N_3O_3P$: M, 335.1399.

(1*R*,2*R*)- and (1*S*,2*R*)-1-Deoxy-1-(dimethoxyphosphinyl)-2,3,-*O*-isopropylidene-1-(4- and 5-phenyl-1,2,3-triazol-1-yl)-glycerol (18a,b, 20a,b). A. Similarly, **12a** (30 mg) gave 4-phenyl- **18a** and 5-phenyltriazolyl compd **20a**.[13]

18a: Colorless oil (25 mg, 60%); R_f 0.12 ($CHCl_3$); MS *m/z* 367 (M^+, 42), 352 (43), 267 (44), 238 (16), 43 (100). Found: *m/z* 367.1298. Calcd for $C_{16}H_{22}N_3O_5P$: M, 367.1297.

20a: Colorless oil (16 mg, 38%); R_f 0.08 ($CHCl_3$); MS *m/z* 367 (M^+, 3.1), 352 (30), 267 (20), 239 (31), 149 (100). Found: *m/z* 367.1280. Calcd for $C_{16}H_{22}N_3O_5P$: M, 367.1297.

B. Similarly, **12b** gave 4-phenyl- **18b** and 5-phenyltriazolyl compd **20b**.[13]

18b: Colorless needles (58%), mp 111—112 °C; R_f 0.13 (*A*); MS *m/z* 367 (M^+, 9.2), 352 (18), 281 (21), 171 (36), 93 (100). Found: *m/z* 367.1293. Calcd for $C_{16}H_{22}N_3O_5P$: M, 367.1297.

20b: Colorless oil (41%); R_f 0.08 (*A*).

(1*R*,2*R*)- and (1*S*,2*R*)-Butylamino-1-deoxy-1-(dimethylphosphinyl)-2,3-*O*-isopropylideneglycerol (21a, 21b). A. A mixture of **8b** (30 mg) and butylamine (0.5 ml) was heated at 150 °C for 4 h in a sealed tube and then evaporated in vacuo. The residue was triturated with AcOEt and chromatographed to give (1*R*)-compd **21a** as a pale yellow oil (13 mg, 47%); R_f 0.25 (*E*); ^{1}H NMR (60 MHz) δ=0.89 (3H, m, CH_3-C_3-N-1), 1.2—1.8 (4H, m, CH_2CH_2-C-N-1), 1.34, 1.40 (3H each, 2s, CMe_2), 1.44 (6H, d, J=13.0 Hz, PMe_2), 2.20 (1H, brs, NH-1, D_2O exchangeable), 2.5—2.9 (2H, m, CH_2N-1), 3.7—4.2 (3H, m, H-1,3,3′), 4.60 (1H, m, H-2).

B. Similarly, **8a** gave (1*S*)-isomer **21b** as a pale yellow oil (37%); R_f 0.28 (*E*); ^{1}H NMR (60 MHz) δ=0.89 (3H, m, CH_3-C_3-N-1), 1.2—1.8 (4H, m, CH_2CH_2-C-N-1), 1.33, 1.38 (3H each, 2s, CMe_2), 1.55 (6H, d, J=13.0 Hz, PMe_2), 1.95 (1H, brs, NH-1, D_2O exchangeable), 2.5—2.9 (2H, m, CH_2N-1), 3.7—4.3 (3H, m, H-1,3,3′), 4.55 (1H, m, H-2).

(1*R*,2*R*)- and (1*S*,2*R*)-Butylamino-1-(dimethoxyphosphinyl)-2,3-*O*-isopropylideneglycerol (22a, 22b). Compd **10a,b** (138 mg) was treated with butylamine (0.10 ml) in acetonitrile (2 ml) at 20 °C for 1.5 h, giving an inseparable mixture of **22a,b** as a colorless oil (14 mg, 13%); R_f 0.19 (*A*); ^{1}H NMR (60 MHz) δ=0.90 (3H, m, CH_3-C_3-N-1), 1.2—1.6 (4H, m, CH_2CH_2-C-N-1), 1.33, 1.41 (3H each, 2s, CMe_2), 1.88 (1H, brs, NH-1, D_2O exchangeable), 2.5—2.9 (2H, m, CH_2N-1), 3.7—4.35 (4H, m, H-1,2,3,3′), 3.78 (6H, d, J=11.0 Hz, 2MeO).

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