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Synthesis of ν-triazole derivatives from anomeric sugar diazides

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Abstract

Staudinger reaction of acetylated glycopyranosylidene 1,1-diazides led to resonance-stabilized iminophosphoranes (phosphinimines) of 6,7-dihydro[3,4-*d*]-1,2,3-triazole. This unprecedented transformation involves β-elimination of acetic acid and cycloaddition of azide anion to the resulting C-2 double bond. Transformation of the new fused heterocyclic iminophosphoranes on treatment with aqueous ethanolic ammonia gives carboxamidine derivatives of ν-triazole bearing a chiral trihydroxypropyl side-chain. Crystal structure of 5-(D-*erythro*-1′,2′,3′-trihydroxypropyl)-1,2,3-triazole-4-carboxamidine was established by X-ray crystallography.

Keywords: Azido sugars; Glycopyranosylidene 1,1-diazides; Iminophosphoranes (phosphinimines); Pyrano[3,4-*d*]-1,2,3-triazole; Staudinger reaction; X-ray structure

Introduction

Iminophosphoranes (phosphinimines) of sugars [1], easily available by Staudinger reaction [2] of the corresponding azido compounds, are advantageous precursors of various *N*-containing carbohydrate derivatives (epimines, carbodiimides, cyclic carbamates, ureido- and guanidino sugars, etc.) [3–8]. Our interest in new synthetic pathways involving transformations via sugar phosphinimines has recently focused on the Staudinger reaction of bifunctional glycosyl azides (e.g. **1**–**4**) bearing an additional substituent at the anomeric carbon atom. As preliminaries of these studies, we have reported [9] the reaction of 2,3,4,6-tetra-*O*-acetyl-D-glucopyranosylidene 1,1-diazide (**1**) [10–12] with triphenylphosphine to give a novel ν-triazole-fused sugar phosphinimine (**5**). Recently, the anomalous Staudinger reactions of (1*R*)2,3,4,6-tetra-*O*-acetyl-1-azido-D-galactopyranosyl cyanide [13,14] and its carboxamide analogue [14] have been described [15]. Investigating the scope and limitations of these transformations, we now report on the further application of the Staudinger reaction to anomeric diazides (D-*gluco*, D-*galacto*, D-*manno* series).

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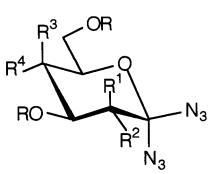
Table 1
^{1}H NMR data[a] (400 MHz) for compounds **5**–**7** and **9**

		Chemical shifts (δ)					P-phenyl					Coupling constants (Hz)			
Compound	Solvent	H-4	H-5	H-6a	H-6b	Ac	H_{ortho}	H_{para}	H_{meta}	NH_2	OH	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
5	$CDCl_3$	6.29 d	4.67 ddd	3.88 dd	3.69 dd	2.06 1.85	7.84	7.73	7.61			3.7	4.9	5.4	12.1
6	$CDCl_3$	6.38 d	4.71 ddd	4.19 dd	3.81 dd	1.97 1.89	7.83	7.73	7.61			2.6	4.6	7.4	11.9
7	$(CD_3)_2SO$	4.90 d	3.75 ddd	3.41 dd	3.29 dd					8.82 8.03	6.34 4.96 4.48	5.0	4.4	6.5	11.0
7	D_2O	5.18 d	4.08 ddd	3.75 dd	3.52 dd							5.7	3.9	7.0	11.9
9	D_2O	5.15 d	3.94 ddd	3.57 dd	3.50 dd							6.0	4.2	6.6	11.7

[a] Listed according to parent sugar numbering.

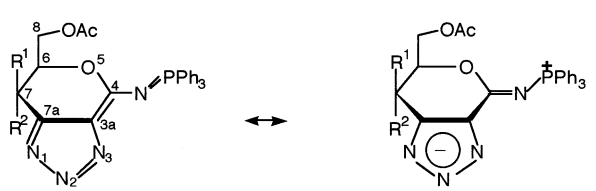
Results and discussion

We have found that the outcome of the reaction of **1** with triphenylphosphine is independent of the molar ratio of the reactants. Using triphenylphosphine in a slight excess (1.1 mol) **5** was obtained in a yield of 86%, while a large excess (3 mol) of triphenylphosphine afforded 82% yield of **5**, and the unreacted reagent could be recovered from the reaction mixture.



1 R = Ac, $R^1 = R^3 = H$, $R^2 = R^4 = OAc$
2 R = Ac, $R^1 = R^4 = OAc$, $R^2 = R^3 = H$
3 R = Ac, $R^1 = R^4 = H$, $R^2 = R^3 = OAc$
4 R = Bn, $R^1 = R^3 = H$, $R^2 = R^4 = OBn$

The novelty of the transformation **1**→**5** prompted the extension of this reaction to the analogous D-*manno* and D-*galacto* configured glycopyranosylidene 1,1-diazides (**2** and **3**, respectively) [12]. Reaction of **2** with triphenylphosphine in dry ether at room temperature (rt) gave the same compound (**5**), as obtained from **1**, in accord with the reaction mechanism suggested earlier [9] involving β-elimination of acetic acid and cycloaddition of azide anion to the resulting C-2 double bond. On treatment with triphenylphosphine, the D-*galacto* diazide **3** gave the epimeric fused triazole derivative **6**, which exhibited very similar NMR signals to those of **5** (Tables 1 and 2). The ^{31}P NMR spectra of **5** and **6** exhibited signals at δ 23.87 and 24.13, respectively, which are downfield shifted with respect to the ^{31}P chemical shift value in sugar phosphinimines, but are at much a higher field than that of aminophosphonium salts [4,5]. This is in good agreement with the resonance-stabilized structure of **5** and **6** revealed by the X-ray analysis of **5** [16]. As a consequence of their delocalized electronic structure, **5** and **6** show quite low reactivity. Thus, they do not react with cumulated double-bond systems, e.g., with carbon dioxide, in contrast to simple sugar phosphinimines.



5 R^1 = H, R^2 = OAc
6 R^1 = OAc, R^2 = H

Table 2
^{13}C and ^{31}P NMR data[a] for compounds **5**–**7**, **9** and **11**

Compound	Solvent	C-1	C-2	C-3	C-4	C-5	C-6	OCH_2Ph	CH_3CO	CH_3CO	P-phenyl C_{ipso}	C_{ortho}	C_{meta}	C_{para}	P
5	$CDCl_3$	164.97	132.36	144.83	63.59	82.09	61.66		170.13	20.95	123.96	133.08	129.54	134.22	23.87
		8.1	*14.0*	*2.2*					169.98	20.40	*102.4*	*10.8*	*13.2*	*3.0*	
6	$CDCl_3$	165.23	133.36	146.22	61.46	81.25	61.41		169.91	20.66	123.98	133.06	129.51	134.22	24.13
		8.5	*14.0*	*2.5*					169.15	20.56	*102.2*	*11.1*	*13.3*	*2.6*	
7	D_2O	161.80	134.65	149.32	70.86	77.20	65.24								
9	D_2O	161.59	134.47	149.84	70.75	77.05	65.21								
11	$CDCl_3$	173.36	79.90	81.22	78.89	70.87	71.19	74.65							
								74.37							
								73.40							
								72.72							

[a] Listed according to parent sugar numbering. Chemical shifts (δ) given in ppm. Heteronuclear ^{31}P, ^{13}C couplings (Hz) italicized. Recorded at 101 MHz (^{13}C) and 162 MHz (^{31}P), respectively.

Attempted deacetylation of the triazole-fused sugar phosphinimines (**5** and **6**) by the Zemplén method gave very complex mixtures that could not be analysed. However, reaction of **5** with ethanolic aqueous ammonia could be well monitored by TLC showing the formation of two products besides triphenylphosphine oxide. The product isolated in 48% yield after 2 days reaction proved to be 5-(D-*erythro*-1′,2′,3′-trihydroxypropyl)-1,2,3-triazole-4-carboxamidine (**7**). Work-up of the reaction mixture at this stage by dry column flash chromatography [17] led to the isolation of the minor product **8** in the form of its acetic acid salt. NMR data for **7** and **8** revealed very similar molecular structures of both compounds having the same trihydroxypropyl side chain. In the case of **7** the structure was corroborated by X-ray analysis which proved the conservation of the D-*erythro* configuration, as well as the symmetrical, delocalized structure of the carboxamidinium moiety. In addition to the geometrical parameters, (e.g. the N–N and N–C multiple bond lengths fall in the range 1.324(2)–1.351(2) Å, as seen from Table 6), the electronic structure of the ν-triazole-ring depicted as **7** is substantiated by the hydrogen bond network (Fig. 1) in which all endocyclic nitrogen atoms N-3, N-4 and N-5 act exclusively as acceptors. The complex hydrogen bond network in which all proton donor moieties participate in six intermolecular contacts formed between the homochiral molecules accounts for the high packing coefficient of 0.78 and crystal density of 1.60 g/cm^3 found for **7**.

The transformation of **5** can be explained by the nucleophilic attack of ammonia at the anomeric carbon followed by the opening of the pyranoid ring and deacetylation to give the intermediate triphenylphosphoranylidene-carboxamidine (**8**). Hydrolysis of **8**—as shown by NMR as well as by preparative experiment—results in the formation of amidine **7** with the elimination of tri-

phenylphosphine oxide. Under analogous conditions, the D-*galacto* ν-triazolo-pyranosyl phosphinimine (**6**) furnished the amidine **9** differing from **7** only in the absolute configuration of C-4 (according to the parent sugar numbering).

The transformation of glycopyranosylidene 1,1-diazides with triphenylphosphine to give a dihydropyrano[3,4-*d*]-ν-triazole ring system requires the presence of a good leaving group attached at C-3 in order to facilitate the formation of a C-2–C-3 double bond by 1,2-elimination [9]. Therefore, replacing acetoxy groups by benzyloxy moieties having lower nucleofugacity may very much influence the outcome of the reaction. Indeed, the benzylated diazide (**4**) [10,12] disappeared only with an excess of triphenylphosphine (1.5 mol) within 4 days, resulting in a multicomponent mixture that could be partially separated by column chromatography to give, unexpectedly, 2,3,4,6-tetra-*O*-benzyl-D-mannono-1,5-lactone (**10**) and 2,3,4,6-tetra-*O*-benzyl-D-mannonamide (**11**) in moderate yields (22 and 17%, respectively) in addition to triphenylphosphine oxide. Structures of **10** and **11** were proved by NMR data in accordance with the literature [18,19].

The mechanism of the reaction may be interpreted by the pathway presented in Scheme 1. The *gluco* configured cation **12**, formed from **4** by the Staudinger reaction of one of the azido groups and subsequent elimination of an azide anion, cannot be stabilised by β-elimination as in the case of the acetyl analogue [9] because the benzyloxy group is a worse leaving group. Instead, deprotonation and protonation—involving the 1,2-unsaturated intermediate **13**—may either regenerate **12** or give the *manno* configured cation **14**. Hydrolysis of **14** (which seems to be the thermodynamically favoured intermediate) during the chromatographic separation may furnish both the cyclic lactone (**10**) and the acyclic mannonamide (**11**).

In conclusion, the anomalous Staudinger reaction of acetylated glycopyranosylidene diazides with triphenylphosphine results in the formation of fused heterocyclic iminophosphoranes containing 6,7-dihydropyrano[3,4-*d*]-1,2,3-triazole ring-system, not formed from the corresponding benzylated derivatives. On treatment with ethanolic ammonia, these unprecedented sugar-derived iminophosphoranes gave in good yields new ν-triazole derivatives substituted by a chiral trihydroxypropyl chain.

Table 3
Crystal data and structure refinement[a]

Empirical formula	$C_6H_{11}N_5O_3$
Formula weight	201.20
Temperature (K)	293(2)
Radiation and wavelength (Å)	Cu K_α; $\lambda = 1.54180$
Crystal system	orthorhombic
Space group	$P2_12_12_1$
Unit cell dimensions	
a (Å)	6.210(1)
b (Å)	7.097(1)
c (Å)	18.904(1)
V (Å^3)	833.14(18)
Z	4
D_{calc} (Mg/m^3)	1.604
Absorption coefficient, μ (mm^{-1})	1.116
$F(000)$	424
Crystal description	colourless, plate
Crystal size (mm)	$0.25 \times 0.25 \times 0.05$
Theta range for data collection (°)	$4.68 \le \theta \le 75.91$
Index ranges	$-7 \le h \le 7$; $-8 \le k \le 8$; $-23 \le l \le 23$
Reflections collected	2180
Completeness to 2θ (%)	99.9
Independent reflections	1728 [$R_{int} = 0.0183$]
Absorption correction	semi-empirical from psi-scans
Max./min. transmission	0.9463 and 0.7678
Refinement method	full-matrix least squares on F^2
Data/restraints/parameters	1728/0/139
Goodness-of-fit on F^2	1.056
Extinction coefficient	0.0050 (11)
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.0394$, $wR_2 = 0.1045$
R indices (all data)	$R_1 = 0.0400$, $wR_2 = 0.1049$
Absolute structure parameter	0.1(3)
Max. and mean shift/esd	0.000, 0.000
Largest difference peak and hole (e Å^{-3})	0.432 and −0.267

[a] Weighting scheme used: $w = 1/[\sigma^2(F_o^2) + (0.0680*P)^2 + 0.28*P]$ where $P = [\text{Max}\ (F_o^2, 0) + 2*F_c^2]/3$. Extinction correction formula: $F_c^* = kF_c[1 + 0.001 \times F_c^2\lambda^3/\sin(2\theta)]^{-1/4}$.

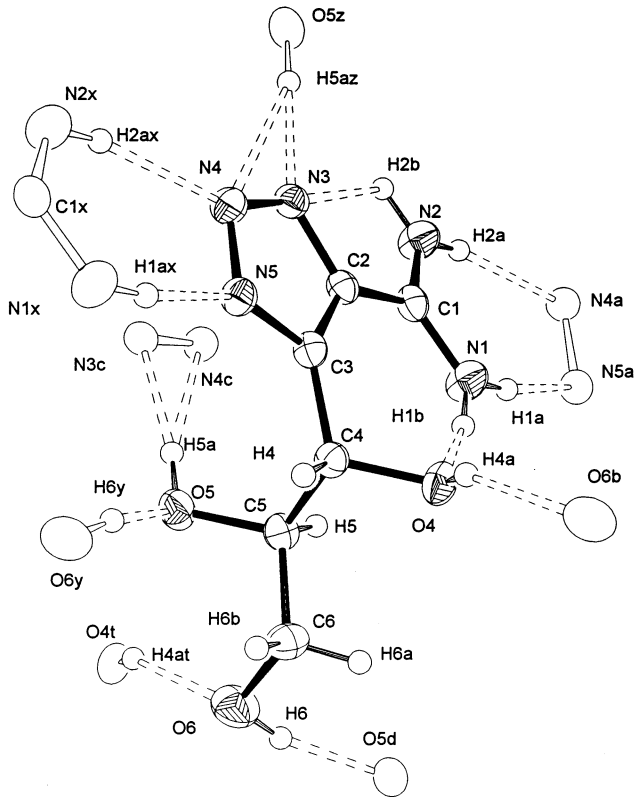
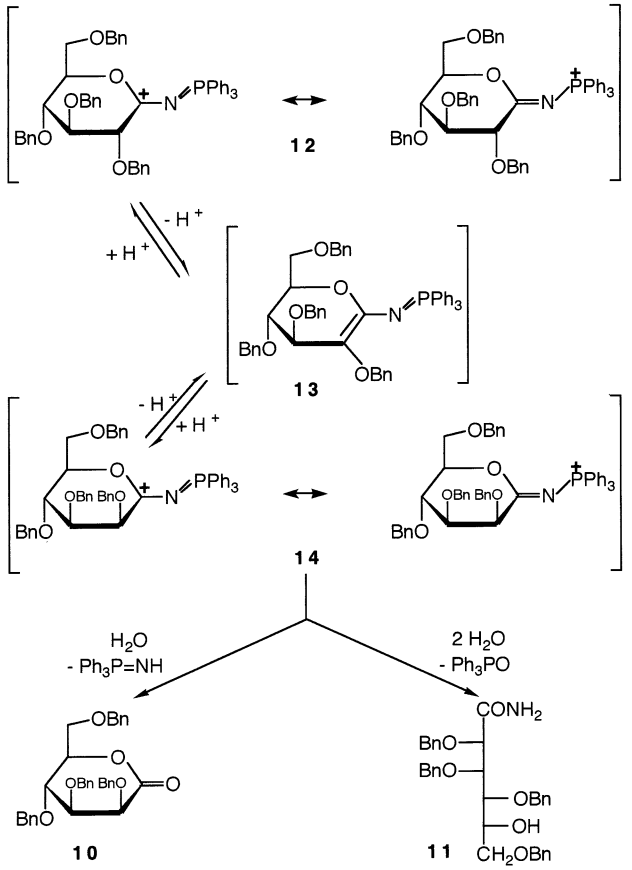


Fig. 1. Perspective view of **7**, showing the hydrogen contacts.



Scheme 1.

Experimental

General methods.—TLC was performed on aluminium sheets coated with Silica Gel 60 F_{254} (E. Merck); detection by UV light and charring with H_2SO_4. Column chromatography and dry column flash chromatography [17] were carried out on Silica Gel 60 (E. Merck, 230–400 mesh). Melting points were measured in a Büchi apparatus and are uncorrected. Optical rotations were determined with a Zeiss Polamat A polarimeter at 25 °C. IR spectra were taken with a Nicolet FT 205 spectrometer and the Raman spectra on a Nicolet 950 FT Raman spectrometer. NMR spectra were recorded on a Varian VXR-400 spectrometer. Spectral assignments were based on standard 1D and 2D NMR methods. Chemical shifts of the ^{31}P NMR spectra refer to 85% aqueous phosphoric acid. FAB mass spectra were obtained with VG ZAB-SEQ mass spectrometer using a 3-nitrobenzylalcohol matrix.

X-ray data[1].—Unit cell parameters of **7** were determined by least squares of setting angles of 25 ($36.34 \leq \theta \leq 41.60°$) reflections. Intensity data were collected on an Enraf–Nonius CAD4 diffractometer (graphite monochromator; Cu–K_α radiation, $\lambda = 1.54180$ Å) at 293(2) K in the range $4.68 \leq \theta \leq 75.91°$ (index range $-7 \leq h \leq 7$; $-8 \leq k \leq 8$; $-23 \leq l \leq 23$) using ω–2θ scans. The intensities of three standard reflections were monitored regularly every 60 min. The intensities of the standard reflections remained constant within the experimental error throughout the data collection. The structure was solved by direct methods [20] and refined by anisotropic full matrix least-squares on F^2 [21]. Crystal data and refinement details are shown in Table 3. Hydrogen atomic positions were calculated from assumed geometries,

[1] Tables of atomic coordinates, bond lengths, and bond angles have been deposited with the Cambridge Crystallographic Data Centre under the deposit No CCDC 113397. These tables may be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, UK, CB2 1EZ.

which allowed the C–H, N–H and O–H distances to be refined. Neutral atomic scattering factors and anomalous scattering factors were taken from [22]. Final atomic parameters for non-hydrogen atoms are listed in Table 4. The geometry parameters of hydrogen bonds are given in Table 5, while bond lengths and relevant torsion angles are given in Tables 6 and 7.

*(6*R,7S*) - 6 - Acetoxymethyl - 7 - acetoxy - 4-(triphenylphosphoranylideneamino) - 6,7 - di - hydropyrano[3,4-*d*]-1,2,3-triazole* (**5**).—(a) To a stirred solution of **1** [10,12] (192 mg, 0.463 mmol) in dry Et_2O (3 mL), was added a solution of PPh_3 (134 mg, 0.511 mmol) in the same solvent (2 mL). Precipitation of the product started within 5 min. The reaction mixture was stored in a cool dark place for 1 night then filtered and washed with dry Et_2O (2 mL) to give **5** as pale yellow crystals; 210 mg (86%), mp 193–194 °C. Recrystallisation from a $CHCl_3$ solution on saturation with Et_2O gave nice colourless needles, mp 199–200 °C; $[\alpha]_D + 8°$ (*c* 2.3, $CHCl_3$), + 17° (*c* 2, AcOH); IR (KBr): 1750, 1613, 1574, 729, and 695 cm^{-1}; Raman (solid): 1608, 1592, 1584, 1575, 1026, and 1002 cm^{-1}. FABMS: *m/z* 529 $[M + H]^+$. Anal. Calcd for $C_{28}H_{25}N_4O_5P$ (528.52): C, 63.63; H, 4.77; N, 10.60; P, 5.86. Found: C, 63.31; H, 4.89; N, 10.31; P, 5.58.

(b) Reaction of **1** (122 mg, 0.295 mmol) and PPh_3 (235 mg, 0.897 mmol) in dry Et_2O (9 mL) was performed as described in (a). After filtration of **5** (128 mg, 82%; mp 192–193 °C) the mother liquor was concentrated and the residue extracted with petroleum ether. Evaporation of the solvent gave unreacted PPh_3 (147 mg, 63%), identical with an authentic sample.

Table 4
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$)

	x	*y*	*z*	U_{eq} [a]
C-1	347(3)	5582(2)	5377(1)	23(1)
C-2	361(3)	3530(2)	5406(1)	21(1)
C-3	526(3)	2282(2)	5973(1)	21(1)
C-4	879(3)	2521(2)	6754(1)	22(1)
C-5	3200(3)	3138(3)	6933(1)	24(1)
C-6	3573(3)	2975(3)	7726(1)	29(1)
O-4	−514(2)	3905(2)	7062(1)	29(1)
O-5	4730(2)	1931(2)	6602(1)	32(1)
O-6	5747(2)	3368(2)	7912(1)	40(1)
N-1	255(3)	6563(2)	5960(1)	33(1)
N-2	436(3)	6446(2)	4760(1)	32(1)
N-3	241(2)	2490(2)	4809(1)	23(1)
N-4	304(3)	692(2)	4995(1)	25(1)
N-5	469(3)	543(2)	5700(1)	25(1)

[a] U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

(c) Reaction of **2** [12] (94 mg, 0.227 mmol) and PPh_3 (66 mg, 0.25 mmol) in dry Et_2O as described above gave **5** (80 mg, 67%), mp 198–200 °C (from $CHCl_3/Et_2O$), identical with the product in (a).

*(6*R,7R*) - 6 - Acetoxymethyl - 7 - acetoxy - 4-(triphenylphosphoranylideneamino) - 6,7 - di - hydropyrano[3,4-*d*]-1,2,3-triazole* (**6**).—Reaction of **3** [12] (216 mg, 0.52 mmol) and PPh_3 (157 mg, 0.6 mmol) was carried out as described for the preparation of **5** to give **6** as a pale yellow solid; 197 mg (71%), mp 190–192 °C (from CH_2Cl_2/Et_2O); $[\alpha]_D - 38°$ (*c* 0.9, AcOH); IR (KBr): 1750, 1744, 1605, 1572, 730, and 692 cm^{-1}; FABMS: *m/z* 529 $[M + H]^+$. Anal. Calcd for $C_{28}H_{25}N_4O_5P$ (528.52): C, 63.63; H, 4.77; N, 10.60. Found: C, 63.40; H, 4.80; N, 10.39.

Table 5
Geometry parameters for hydrogen bonds

D–H···A[symm.]	D–H (Å)	H···A (Å)	D···A (Å)	<D–H···A (°)
N-1–H-1b···O-4[*x*, *y*, *z*]	0.88	2.02	2.849(2)	157.0
N-1–H-1a···N-5[*x*, *y*+1, *z*]	0.88	2.00	2.871(2)	168.3
N-2–H-2a···N-4[*x*, *y*+1, *z*]	0.89	2.18	3.047(2)	164.8
O-4–H-4a···O-6[*x*−1, *y*, *z*]	0.82	2.12	2.850(2)	147.9
O-5–H-5a···N-3[*x*+1/2, −*y*+1/2, −*z*+1]	0.92	1.80	2.716(2)	172.0
O-5–H-5a···N-4[*x*+1/2, −*y*+1/2, −*z*+1]	0.92	2.61	3.475(2)	156.8
O-6–H-6···O-5[*x*+1, *y*+1/2, −*z*+3/2]	0.91	1.81	2.707(2)	164.8
N-2–H-2b···N-3[*x*, *y*, *z*]	0.89	2.48	2.812(2)	102.2

Table 6
Bond distances (Å)

Atom 1	Atom 2	Dist. (Å)	Atom 1	Atom 2	Dist. (Å)
C-1	N-1	1.305(2)	C-1	N-2	1.319(2)
C-1	C-2	1.457(2)	C-2	N-3	1.351(2)
C-2	C-3	1.394(2)	C-3	N-5	1.338(2)
C-3	C-4	1.503(2)	C-4	O-4	1.432(2)
C-4	C-5	1.544(2)	C-5	O-5	1.424(2)
C-5	C-6	1.520(2)	C-6	O-6	1.423(2)
N-3	N-4	1.324(2)	N-4	N-5	1.341(2)

Reaction of **5** *with aqueous ethanolic ammonia.*—(a) A solution of **5** in a mixture of concd aq ammonia (4 mL) and EtOH (8 mL) was stored at rt for 2 d. Monitoring by TLC (3:2:1:1 BuOAc–AcOH–EtOH–H_2O) showed no starting material but the formation of two products (R_f 0.5 and 0.3) besides Ph_3PO (R_f 0.9). The mixture was concentrated and dried by co-evaporation with EtOH. The residue was then crystallised from EtOH (4 mL) at 0 °C to give 5-(D-*erythro*-1′,2′,3′-trihydroxypropyl)-1,2,3-triazole-4-carboxamidine (**7**, 39 mg, 48%); beige solid, R_f 0.3 (3:2:1:1 BuOAc–AcOH–EtOH–H_2O); mp 210–211 °C. Recrystallisation by adding acetone to a concd aq solution of **7** gave colourless crystals, mp 214 °C; $[\alpha]_D + 4°$ (*c* 2, H_2O); IR (KBr): 3600–2400 (broad), 1694, and 1576 cm^{-1}; Raman (solid) 1649 and 1576 cm^{-1}, FABMS: *m/z* 202 $[M + H]^+$. Anal. Calcd for $C_6H_{11}N_5O_3$ (201.19): C, 35.82; H, 5.51; N, 34.81. Found: C, 35.61; H, 5.54; N, 34.28.

The EtOH mother liquor was then subjected to dry column flash chromatography [17] using acetone–AcOH mixtures with increasing proportion of the latter from 95:5 to 5:1. Eluted first was Ph_3PO (73 mg, 66%, mp 150–153 °C) identical with an authentic sample. Eluted second was 5-(D-*erythro*-1′,2′,3′-trihydroxypropyl) - 1,2,3 - triazole - 4 - (triphenylphosphoranylidene-carboxamidinium acetate (**8**·AcOH), as a white solid, R_f 0.5 (3:2:1:1 BuOAc–AcOH–EtOH–H_2O); mp 182 °C (dec); $[\alpha]_D + 11°$ (*c* 2, AcOH); IR (KBr): 3600–2400 (broad), 1690, 1570, 730, and 697 cm^{-1}. ^1H NMR (D_2O, 400 MHz): δ 5.36 (d, 1H, $J_{4,5}$ 5.8 Hz, H-4); 3.97 (ddd, 1H, H-5); 3.55 (dd, 1H, $J_{5,6a}$ 3.8 Hz, H-6a); 3.41 (dd, 1H, $J_{5,6b}$ 6.9 Hz, $J_{6a,6b}$ 12.0 Hz, H-6b). (A repeated ^1H NMR measurement after 2 weeks indicated a complete conversion of **8**·AcOH into **7**). Anal. Calcd for $C_{26}H_{28}N_5O_5P$ (521.53): C, 52.21; H, 5.41; N, 13.43. Found: C, 52.56; H, 5.53; N, 12.95.

(b) On treatment of **5** (211 mg, 0.4 mmol) with a mixture of concd aq ammonia (4 mL) and EtOH (8 mL) for 2 days, **7** (36 mg, mp 210–211 °C) was obtained by crystallisation from EtOH as described in (a). The ethanolic filtrate was concentrated and the residue, dissolved in water (3 mL), was stirred for 5 days. TLC (3:2:1:1 BuOAc–AcOH–EtOH–H_2O) showed the transformation of the intermediate **8** (R_f 0.5) into **7** (R_f 0.3). The separated crystals were then filtered to give Ph_3PO (90 mg, 81%, mp 148–151 °C), identical with an authentic sample. The aq filtrate was concentrated and the residue crystallised from EtOH to afford an additional crop of **7**, 32 mg, mp 206–210 °C, total yield 68 mg (85%).

*5-(*D-threo-*1′,2′,3′-Trihydroxypropyl)-1,2,3-triazole-4-carboxamidine* (**9**).—A solution of **6** in a mixture of concd aq ammonia (6 mL) and EtOH (12 mL) was left to stand for 2 days, then concentrated. The residue was stirred with water (8 mL) for a week, then decanted. The aq soln was concentrated to a small volume (1–2 mL) and mixed with acetone to give **9** (65 mg, 59%), as pale yellow crystals, mp 207–210 °C, R_f 0.3 (3:2:1:1 BuOAc–AcOH–EtOH–H_2O); $[\alpha]_D - 4°$ (*c* 2.4, H_2O); IR (KBr): 3600–2400 (broad), 1685, and 1577 cm^{-1}; FABMS: *m/z* 202 $[M + H]^+$. Anal. Calcd for $C_6H_{11}N_5O_3$ (201.19): C, 35.82; H, 5.51; N, 34.81. Found: C, 35.49; H, 5.56; N, 34.31.

Table 7
Relevant torsion angles (°)

Atom 1	Atom 2	Atom 3	Atom 4	Torsion angle
N-3	C-2	C-3	N-5	−0.9(2)
C-2	C-3	N-5	N-4	0.8(2)
N-3	N-4	N-5	C-3	−0.4(2)
C-2	N-3	N-4	N-5	−0.1(2)
C-3	C-2	N-3	N-4	0.6(2)
N-1	C-1	C-2	C-3	−8.0(3)
N-2	C-1	C-2	C-3	171.7(2)
C-1	C-2	C-3	N-5	−179.6(2)
N-3	C-2	C-3	C-4	174.4(2)
C-1	C-2	C-3	C-4	−4.3(3)
C-2	C-3	C-4	O-4	48.7(3)
C-2	C-3	C-4	C-5	−71.6(2)
O-4	C-4	C-5	O-5	−175.3(1)
C-3	C-4	C-5	O-5	−51.3(2)
C-3	C-4	C-5	C-6	−168.8(2)
O-5	C-5	C-6	O-6	54.8(2)
C-4	C-5	C-6	O-6	174.8(2)

The water-insoluble part of the reaction mixture was extracted with EtOAc, then after evaporation of the solvent the residue crystallised from cyclohexane to give Ph_3PO (103 mg, 68%), mp 153–155 °C, identical to an authentic sample.

Reaction of **4** *with* Ph_3P.—To a solution of **4** [12] (331 mg, 0.545 mmol) in dry Et_2O (3 mL), was added Ph_3P (227 mg, 0.82 mmol) in the same solvent (4 mL) and the mixture was stirred at rt for 4 days. TLC (9:1 CH_2Cl_2–acetone) showed a complex reaction mixture with the main spots of R_f 0.9, 0.35 (detectable by charring with H_2SO_4) and Ph_3PO (R_f 0.2). The mixture was concentrated and separated by column chromatography using first CH_2Cl_2 as eluent, then CH_2Cl_2–acetone mixtures with increasing proportion of the latter from 9:1 to 1:1. Eluted first was 2,3,4,6-tetra-*O*-benzyl-D-mannono-1,5-lactone (**10**, 63 mg, 22%), colourless crystals mp 82–84 °C (from Et_2O), R_f 0.9 (9:1 CH_2Cl_2–acetone); $[\alpha]_D \sim 0°$ (*c* 3, $CHCl_3$), IR (KBr): 1773, 690, and 752 cm^{-1}. Lit [18] mp 83–83.5 °C, $[\alpha]_D - 0.5°$ (*c* 10.5, $CHCl_3$); lit [19] mp 83.5–85 °C. ^1H and ^{13}C NMR data corresponded well with published data [18,19]. Eluted second was 2,3,4,6-tetra-*O*-benzyl-D-mannonamide (**11**, 51 mg, 17%), white solid, mp 130–133 °C (from Et_2O–petroleum ether), R_f 0.35 (9:1 CH_2Cl_2–acetone); $[\alpha]_D + 14°$ (*c* 1.8, $CHCl_3$). Lit [19] mp 132–134 °C, $[\alpha]_D + 15.8°$ (*c* 0.55, $CHCl_3$). IR (KBr): 3440, 1645, 738, and 695 cm^{-1}. The ^1H NMR data were in good agreement with published data [19]. Eluted third was Ph_3PO (396 mg, 99%), mp 152–154 °C (from cyclohexane), identical to an authentic sample.

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