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Synthesis of (1 → 6)-carbodiimide-tethered pseudooligosaccharides *via* aza-Wittig reaction

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Abstract

The synthesis of unsymmetrical sugar carbodiimides through aza-Wittig coupling of sugar derived iminophosphoranes and isothiocyanates is reported. The reaction is particularly fast and efficient in the case of phosphoranylide derivatives of 6-azido-6-deoxysugars and glycosyl isothiocyanates, and has been exploited in the one-pot preparation of (1 → 6)-linked pseudodi- and trisaccharides incorporating carbodiimide bridges as convenient precursors for the corresponding ureido, thioureido, and guanidino derivatives. Kinetic considerations suggest that sugar phosphazides, formed in the early stages of the Staudinger reaction of triphenylphosphine and sugar azides, are the reactive intermediates.

Keywords: Sugar carbodiimides; Sugar isothiocyanates; Sugar iminophosphoranes; Sugar phosphazides; aza-Wittig reaction; Pseudooligosaccharide

1. Introduction

The synthesis and conformational behaviour of pseudooligosaccharides incorporating three-atom intermonosaccharide linkers of the pseudoamide type have been the subject of recent attention [1–6]. The interest for this family of compounds stems from the structural analogy of carboxamide, carbamic and thiocarbamic functionalities with the phosphodiester group present in many biologically important derivatives such as polynucleotides, oligo(glycosyl phosphates) and glycosyl phosphonucleosides. Thiourea segments have also been employed to connect two saccharide moieties in macrocyclic receptors [7] and cyclodextrin–glycopeptide conjugates [8], providing new conformational, complexing and solubility properties. The corresponding carbodiimide-linked pseudooligosaccharides appear as very attractive synthetic intermediates, since the carbodiimide group plays a pivotal role in the preparation of ureas, thioureas and

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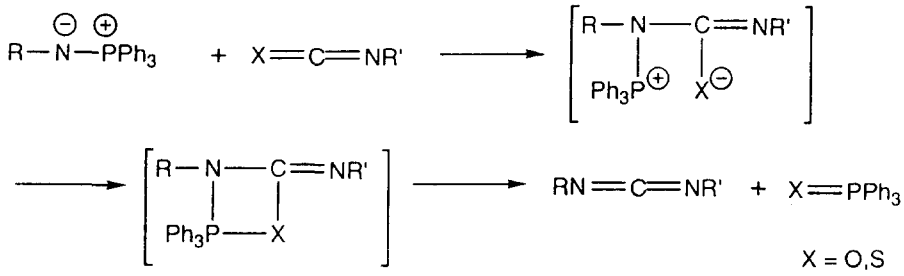


Scheme 1.

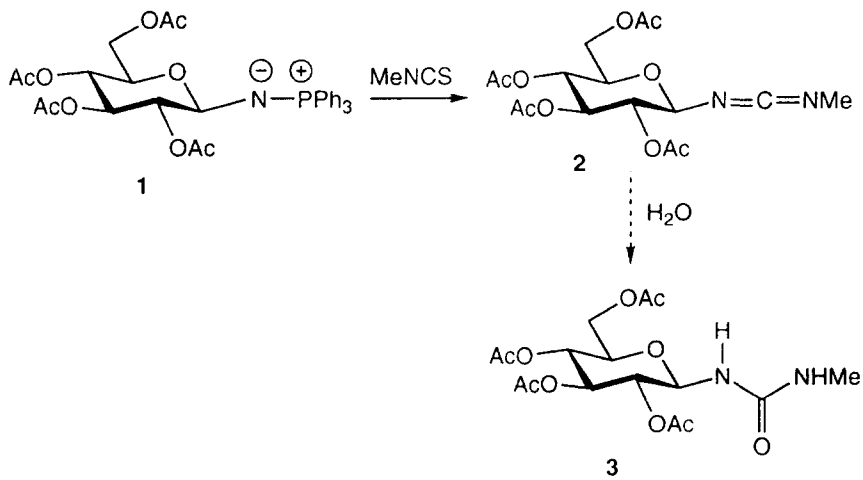
guanidines, among other functional groups, through standard transformations [9,10].

Despite the enormous synthetic potential of sugar carbodiimides, reports on them are very scarce [11–13] and there are no example of unsymmetrical sugar carbodiimides, probably because of the lack of suitable synthetic methodologies compatible with the polyfunctionality of carbohydrates. From the range of general methods available for the construction of the carbodiimide functional group [9,10,14–16], we have focused on the intermolecular aza-Wittig type reaction of iminophosphoranes (λ^5-phosphazenes, phosphine imines) and heterocumulenes [17,18], since it takes place under neutral conditions compatible with all common hydroxyl-protecting groups and may be conceived for convergent strategies in the synthesis of unsymmetrical complex structures [19]. Here, we report on the application of this reaction to the synthesis of (1 → 6)-linked glycosyl carbodiimidosugars. The mechanisms of the transformations are also discussed. Our interest is to disclose a general route of access to analogues of antigenic oligo(glycosyl phosphates) [20–24] useful for the development of diagnostic tests, vaccines or as enzyme inhibitors, by analogy with the promising results obtained with backbone-modified antisense oligonucleotides [25,26].

2. Results and discussion

The general mechanism of carbodiimide synthesis via aza-Wittig condensation is depicted in Scheme 1. Both isocyanates and their thio counterparts can undergo the desired transformation, with extrusion of triphenylphosphine oxide or thioxide, respectively. Nevertheless, we have favoured the use of sugar isothiocyanates as precursors because they can be readily prepared at multi-gram scale by isothiocyanation of sugar halides or amino sugars and safely stored and handled without the hazards associated with isocyanate chemistry [27,28]. Iminophosphoranes on their side are conveniently prepared by Staudinger reaction from the corresponding azides and triphenylphosphine [18,29].

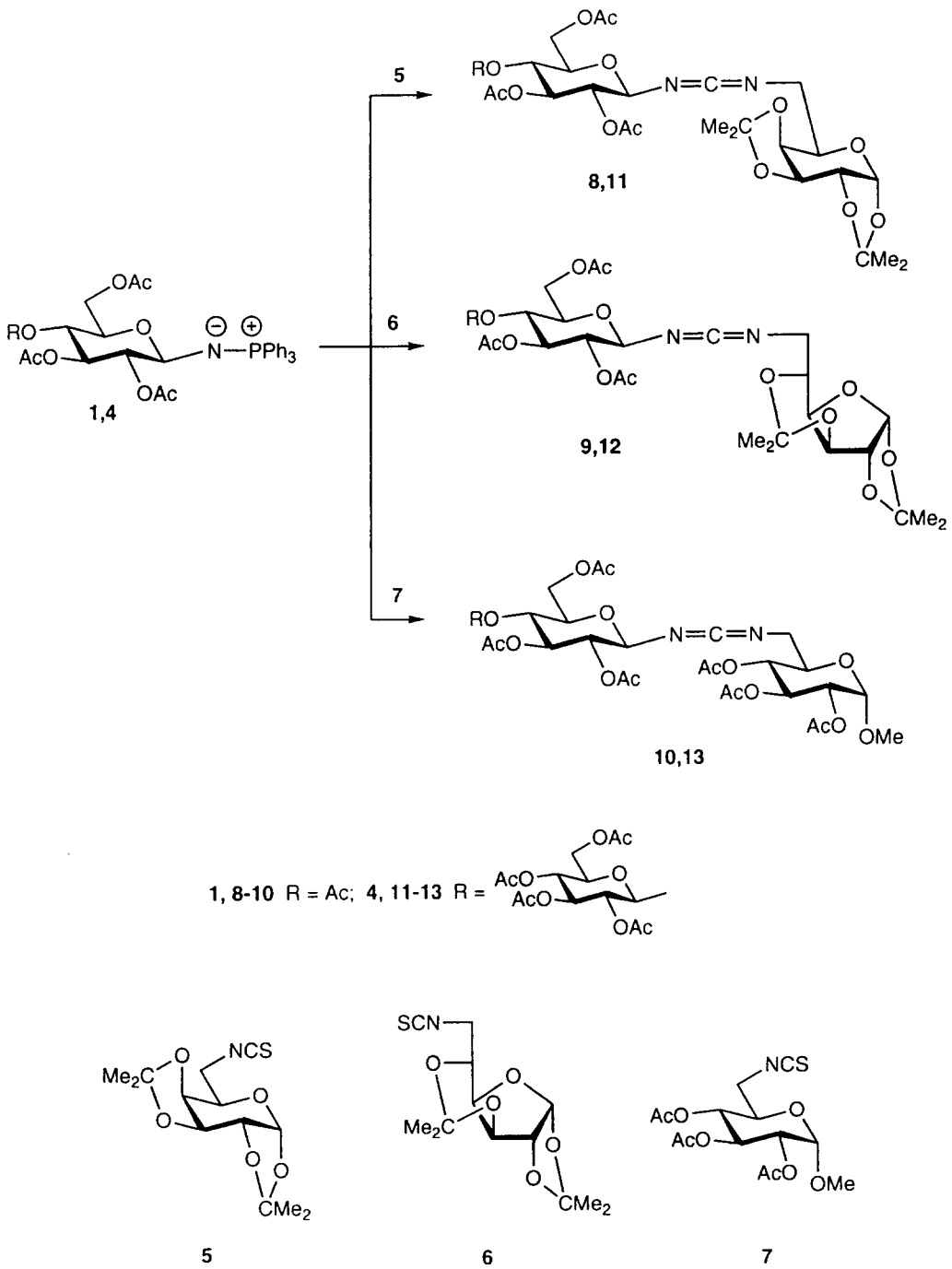
According to Scheme 1, two alternative synthetic strategies are possible, in principle, for the construc-



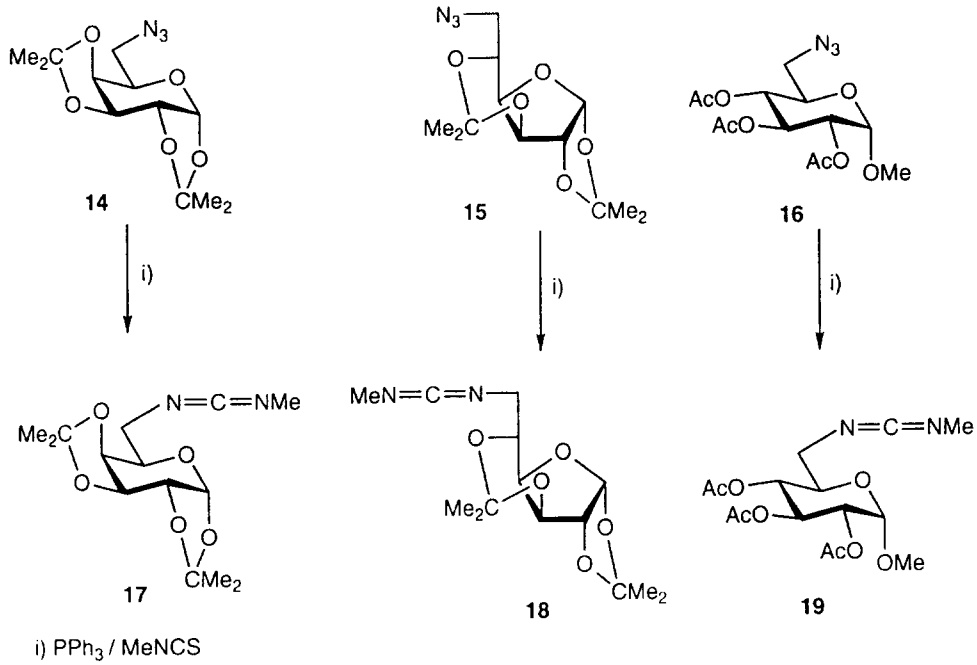
Scheme 2.

tion of a carbodiimide tether between positions C-1 and C-6 of per-*O*-protected aldohexose precursors: (a) the reaction of glycosyl phosphinimines with 6-deoxy-6-isothiocyanato sugars and (b) the converse reaction of glycosyl isothiocyanates and 6-deoxy-6-triphenylphosphoranylideneamino sugars.

Using methyl isothiocyanate as a model substrate, the aza-Wittig condensation with the known, crystalline 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl phosphinimine **1** [13,30] was first attempted. No reaction was observed after three days at room temperature in toluene. Refluxing a stoichiometric mixture of the reagents for 2 h, the corresponding glucosyl carbodiimide **2** was obtained (Scheme 2) in moderate yield (40%). An increase in the relative proportion of either **1** or methyl isothiocyanate, or longer reaction times, led to a decrease in the yield of **2**, with formation of several by-products (not isolated), which



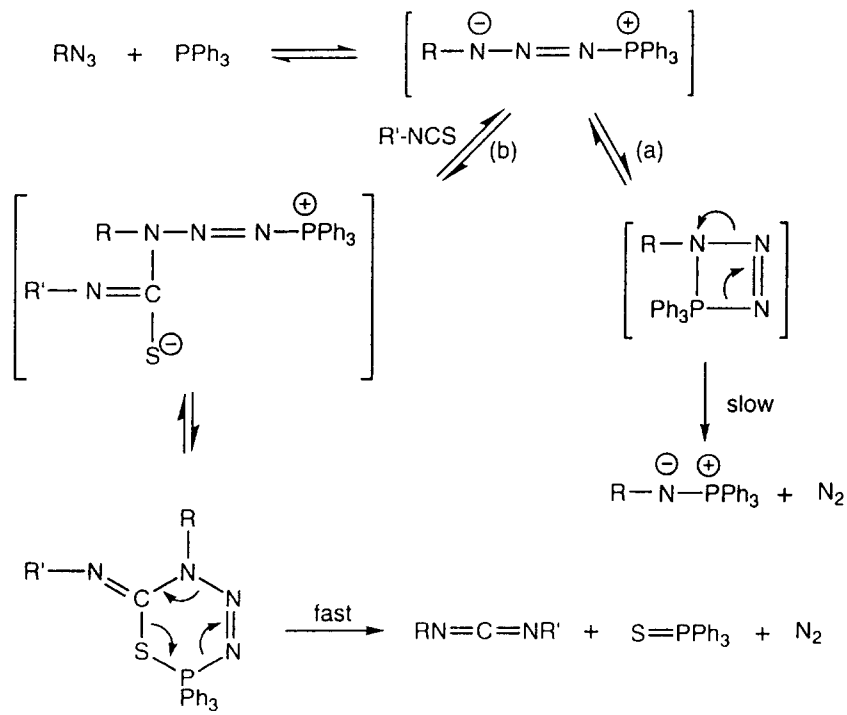
Scheme 3.



Scheme 4.

complicated the purification step. In fact, both unreacted iminophosphoranes and isothiocyanates are able to react with the formed carbodiimide [31,32]. Compound **2** was stable enough to be isolated in pure form. Nevertheless, formation of the glucosylurea **3**, resulting from nucleophilic addition of water to the carbodiimido group occurred to some extent during the chromatographic process, which was minimised by using short columns and short separation times.

Under the above optimal conditions, **1** underwent intermolecular aza-Wittig reaction with the 6-deoxy-6-isothiocyanato derivatives of 1,2:3,4-di-*O*-isopro-



Scheme 5.

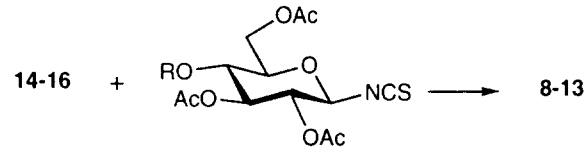
pylidene-α-D-galactopyranose **5** [33,34], 1,2:3,5-di-*O*-isopropylidene-α-D-glucofuranose **6** [33,35] and methyl 2,3,4,-tri-*O*-acetyl-α-D-glucopyranoside **7** [33,34] to give the corresponding carbodiimide-bridged pseudodisaccharides **8–10** in 25–35% yield. Likewise, the hepta-*O*-acetyl-β-cellobiosyl phosphinimine **4** [30] afforded the pseudotrisaccharide carbodiimides **11–13** (Scheme 3).

The lower reactivity of glycosyl phosphinimines towards the aza-Wittig reaction with isothiocyanates as compared to alkyl iminophosphoranes [17,18] must be ascribed to the particular electronic properties of the anomeric position of carbohydrates. The electron withdrawing (-I) effect of the glycopyranosyl ring results in a stabilisation of the negatively charged anomeric nitrogen atom, with a subsequent decrease in the rate of formation of the key betaine intermediate (Scheme 1).

The disappointingly low yields of the glycosyl phosphinimine approach prompted us to examine the alternative coupling of anomeric isothiocyanate groups and iminophosphorane functionalities located at the primary C-6 position. Although the Staudinger reaction has become popular in carbohydrate chemistry for the transformation of azido sugars into amino sugars [33,36,37], except in the case of the stable glycosyl derivatives, the iminophosphorane intermediates are generally hydrolysed in situ. Only a few examples of monosaccharides bearing a triphenylphosphoranylideneamino group at a non-anomeric position have been fully characterised [30,38–40].

The reaction of the 6-azido-6-deoxy sugars **14–16** [33] and triphenylphosphine in toluene with strict exclusion of water required long reaction times. After 24 h, some starting azide remained unreacted (TLC). Moreover, extensive hydrolysis occurred during the attempted isolation of the iminophosphoranes, with formation of the corresponding amino sugars [33] and triphenylphosphine oxide. Noteworthily, in the presence of methyl isothiocyanate, the overall transformations **14–16** → **17–19** (Scheme 4) were completed within 1 h, with isolated yields higher than 80%, suggesting an alternative mechanistic pathway.

It has been shown [18,29,41,42] that the Staudinger reaction proceeds via a transient phosphazide [3]



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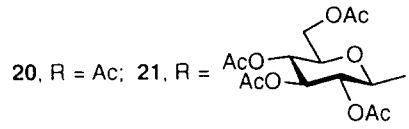

Scheme 6.

derivative, that further rearranges into the iminophosphorane with thermal splitting of nitrogen (Scheme 5, route a). In our case, the second step is very slow under the reaction conditions. The phosphazide might then act directly as the nucleophile in the aza-Wittig type reaction with isothiocyanates, giving rise to a new α,δ-zwitterionic intermediate that undergo fast transformation into the final reaction products through a six-membered cyclic intermediate (Scheme 5, route b). The much higher stability of the thioxo phosphorous (V) derivative as compared to the imino analogue probably accounts for the dramatic increase in the reaction rate.

Reactions of the sugar azides **14–16** with peracetylated β-D-glucopyranosyl and β-cellobiosyl isothiocyanates **20** and **21** [27,28,43] after addition of triphenylphosphine, following the above methodology, were even faster than for methyl isothiocyanate (Scheme 6). Virtually, quantitative transformations were achieved within 10 min (TLC), with isolated yields of the resulting carbodiimides **8–13** ranging from 70 to 90%. The increased reactivity towards nucleophiles of isothiocyanate groups at the anomeric position of carbohydrates has already been noticed and is in agreement with a higher contribution of the $R-N^{-}-C^{+}=S$ form to the ground state [27].

The structure of the new compounds were established on the basis of their spectroscopic (Tables 1 and 2 and Section 3), FABMS and analytical data. The presence of the carbodiimido group in compounds **2**, **8–13** was confirmed by the characteristic IR absorption at 2150–2135 cm^{-1} and ^{13}C chemical shift at 141.2–137.0 ppm (δ_{NCN}). The high field shift of the C-1′ and C-6 resonances in the pseudooligosaccharides **8–13** (Table 2) and of the corresponding protons H-1′ and H-6a,6b, as compared to the parent

[3] Although in the literature, the unit P=N-N=N is usually designated as phosphazide, the term triazenophosphorane has been proposed recently to avoid misleading, as this moiety does not contain an azide function. See Ref. [42].

sugars, is in agreement with the (1 → 6)-bridge. It should be mentioned that although carbodiimides, similarly to allenes, can exhibit geometrical isomerism, the interconversion barriers are generally lower than those observable by NMR spectroscopy. In fact, no significant widening of the spectral lines were observed for compounds **2**, **8–13** in chloroform-d_6 at 233 K.

In conclusion, we have shown that phosphoranylidene derivatives of 6-azido-6-deoxy sugars, probably with phosphazide structure, and glycosyl isothiocyanates are ideally suited to undergo aza-Wittig type

Table 1
^{1}H NMR data (500 MHz, $CDCl_3$) for carbodiimides **2**, **8–13**, **17–19**

	Unit[a]	Chemical shifts (δ)						
		H-1	H-2	H-3	H-4	H-5	H-6a	H-6b
2	I	4.64d	4.92t	5.15t	5.07t	3.71ddd	4.20dd	4.11dd
8[b]	I	5.55d	4.33dd	4.61dd	4.22d	3.84bdd	3.60dd	3.27dd
	II	4.82d	4.98t	5.19t	5.10t	3.74ddd	4.23dd	4.13dd
9	I	5.98d	4.57d	4.23d	4.27dd	3.66td	3.50dd	3.45dd
	II	4.73d	4.94dd	5.18t	5.09t	3.74ddd	4.24dd	4.13dd
10	I	4.95d	4.85dd	5.47dd	5.01dd	3.87dt	3.42d	
	II	4.27d	4.97t	5.19t	5.14t	3.78ddd	4.26dd	4.17dd
11[c]	I	5.52d	4.32dd	4.60dd	4.17dd	3.83m	3.57dd	3.26dd
	II	4.81d	4.86t	5.15t	3.77t	3.65m	4.47bd	4.02dd
	III	4.49d	4.92t	5.13t	5.05t	3.63m	4.32dd	4.03dd
12	I	5.98d	4.57d	4.22d	4.26dd	3.66m	3.49dd	3.43dd
	II	4.51d	4.92t	5.15t	3.78t	3.66m	4.98bd	4.10dd
	III	4.71d	4.85t	5.14t	5.06t	3.66m	4.37dd	4.04dd
13	I	4.93d	4.85dd	5.46dd	4.99t	3.86dt	3.40d	
	II	4.69d	4.92dd	5.16t	3.82t	3.67ddd	4.52dd	4.11dd
	III	4.51d	4.86t	5.14t	5.06t	3.65ddd	4.37dd	4.04dd
17	I	5.49d	4.27dd	4.56dd	4.16dd	3.80ddd	3.41dd	3.22dd
18	I	5.99d	4.58d	4.21d	4.31dd	3.66td	3.44dd	3.35dd
19[b]	I	4.97d	4.88dd	5.48t	5.02t	3.86dt	3.33d	
		Coupling constants (Hz)						
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$
2	I	9.2	9.2	9.2	9.2	4.8	2.3	12.4
8	I	5.0	2.5	7.9	0	8.3	4.8	13.1
	II	8.7	8.7	8.7	8.7	4.7	2.3	12.3
9	I	3.7	0	3.4	7.0	3.6	7.0	13.8
	II	8.7	9.5	9.5	9.5	4.8	2.3	12.5
10	I	3.5	10.3	9.4	10.0	4.2	4.2	–
	II	8.8	9.4	9.4	9.4	4.7	2.3	12.5
11	I	4.9	2.4	7.8	1.8	8.4	4.8	13.1
	II	8.7	8.7	8.7	8.7	0	4.9	12.1
	III	8.1	8.1	8.1	8.1	4.1	2.0	12.5
12	I	3.7	0	3.8	7.0	3.6	7.0	13.8
	II	8.0	8.9	8.9	8.9	–	5.0	12.9
	III	8.6	9.3	9.3	9.3	4.3	1.9	12.5
13	I	4.0	10.3	9.4	9.4	4.4	4.4	–
	II	8.7	7.6	7.6	7.6	1.9	4.8	12.1
	III	7.9	7.9	7.9	7.9	4.4	2.2	12.6
17	I	5.0	2.4	7.9	7.9	8.1	5.1	3.2
18	I	3.8	0	3.8	3.8	3.4	7.1	13.4
19	I	3.6	9.9	9.9	9.9	4.4	4.4	–

[a]Units I, II, and III refer to the unprimed, primed and double primed sugar rings, respectively. [b]At 300 MHz.

Table 2
^{13}C NMR data (125.7 MHz, $CDCl_3$) for carbodiimides **2**, **8–13**, **17–19**

	Unit[a]	Chemical shifts (δ)					
		C-1	C-2	C-3	C-4	C-5	C-6
2	I	84.8	72.9	73.0	68.2	73.7	61.9
8[b]	I	96.2	70.4	70.6	70.9	67.3	46.1
	II	84.9	72.6	73.0	68.1	73.5	61.9
9	I	106.2	83.7	74.8	80.0	71.2	47.9
	II	84.7	72.5	72.8	68.0	73.5	61.7
10	I	96.6	70.5	69.8	69.4	67.9	46.1
	II	84.6	72.6	72.8	68.0	73.6	61.7
11[c]	I	96.2	70.7	70.6	71.0	67.5	46.2
	II	84.9	72.0	73.0	76.5	74.4	62.0
	III	100.9	71.6	72.9	67.7	73.5	61.5
12	I	106.2	83.7	74.4	79.9	71.8[d]	47.9
	II	84.6	72.5	72.7	76.1	74.8	61.7[e]
	III	100.6	71.2	72.8	65.8	71.4[d]	61.4[e]
13	I	96.7	70.7	69.9	69.6	68.0	46.3
	II	84.6	71.6	72.9	76.1	74.6	61.7
	III	100.7	71.9	72.9	67.8	72.6	61.5
17	I	96.3	70.5	70.7	71.2	67.8	46.4
18	I	106.2	83.8	74.9	80.2	71.5	48.4
19[b]	I	96.5	70.7	69.5	69.8	68.1	46.6

[a]Units I, II, and III refer to the unprimed, primed, and double primed sugar rings, respectively. [b]At 75.5 MHz. [c]At 100.6 MHz. [d,e]Assignments may be reversed.

condensation under mild conditions. The reactive sugar phosphazides are generated in situ, and further C=N bond formation takes place within minutes with total control of the anomeric configuration.

3. Experimental

General methods.—A Perkin-Elmer Model 141 MC polarimeter and 1 dm tubes were used for measurement of specific rotations. Infrared spectra were recorded on a Bomem Michelson MB-120 FTIR spectrophotometer. ^1H and ^{13}C NMR spectra were recorded at 500 (125.7), 400 (100.6) and 300 (75.5) MHz with, respectively, Bruker 500 AMX and DRX, 400 DRX and 300 AMX spectrometers. Chemical shifts are given in ppm with reference to Me_4Si as internal standard. Assignments of ^1H and ^{13}C signals were assisted by 2D COSY and HETCOR experiments. FABMS were taken in a Kratos MS-80 RFA instrument. The operating conditions were the following: the primary beam consisted of xenon atoms with a maximum energy of 8 keV; the samples were dissolved in *m*-nitrobenzyl alcohol, and the positive ions were separated and accelerated over a potential of 7 kV; sodium iodide was added as cationising agent. TLC was performed with E. Merck precoated TLC plates, Silica Gel $30F_{245}$, with visualisation by UV light and by charring with 10% H_2SO_4. Flash chromatography was carried out with Silica Gel 60 (E. Merck, 230–400 mesh). Typically for 0.5 g of reaction mixture a 4×2.5 cm filter was used, with separation times of 15–20 min. Microanalyses were performed by the Instituto de Investigaciones Químicas (CSIC, Sevilla).

N - *Methyl* - N' - *(2, 3, 4, 6 - tetra* - O - *acetyl* - β - D - *glucopyranosyl)carbodiimide* (**2**).—To a soln of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl phosphinimine [13,30] (**1**, 300 mg, 0.5 mmol) in dry toluene (3 mL) was added methyl isothiocyanate (38 mg, 0.5 mmol) and the mixture was refluxed for 2 h. Monitoring by TLC (1:1 light petroleum ether–EtOAc) showed the formation of two compounds. After conc, the residue was purified by flash chromatography using first toluene and then 1:1 light petroleum ether–EtOAc to give **2** (78 mg, 40%). Further elution with EtOAc provided *N*-methyl-*N'*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)urea (**3**, 16 mg, 20%). Data for **2**: syrup, $[\alpha]_D^{20}$ −115.4° (c 1.0, CH_2Cl_2); R_f 0.49 (1:1 light petroleum ether–EtOAc); IR (KBr) 2944, 2155, 1755, 1377, 1227, and 1036 cm^{-1}; NMR: ^1H (500 MHz, $CDCl_3$) Table 1 and δ 2.98 (NMe), 2.05, 2.03, 1.98, and 1.96 (4 s, each 3 H, 4 Ac); ^{13}C (125.5 MHz, $CDCl_3$) Table 2 and δ 170.6, 170.3, 169.4, 169.3 (4 CO), 136.4 (N=C=N), 31.9 (NMe), and 20.6 (4 C, 4 MeCO); FABMS *m/z* 409 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{16}H_{22}N_2O_9$: C, 49.74; H, 5.74; N, 7.25. Found: C, 49.71; H, 5.69; N, 7.26. Data for **3**: amorphous solid, $[\alpha]_D^{20}$ +11.4° (c 1.1, CH_2Cl_2); R_f 0.24 (1:3 light petroleum ether–EtOAc); IR (KBr) 3366, 2949, 1750, 1661, 1564, 1373, 1227, and 1036 cm^{-1}; NMR: ^1H (300 MHz, $CDCl_3$): δ 6.81 (bs, 1 H, NH), 5.92 (bd, 1 H, $J_{NH,1}$ 8.9 Hz, NH), 5.33 (t, 1 H, $J_{2,3} = J_{3,4}$ 9.5 Hz, H-3), 5.14 (dd, 1 H, $J_{1,2}$ 9.5 Hz, H-1), 5.07 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.92 (t, 1 H, H-2), 4.31 (dd, 1 H, $J_{5,6a}$ 4.7 Hz, $J_{6a,6b}$ 12.5 Hz, H-6a), 4.11 (dd, 1 H, $J_{5,6b}$ 2.0 Hz, H-6b), 3.85 (ddd, 1 H, H-5), 2.77 (s, 3 H, NMe), 2.08, 2.07, 2.04, and 2.03 (4 s, each 3 H, 4 Ac); ^{13}C (75.5 MHz, $CDCl_3$) δ 171.2, 170.7, 169.8, 169.6 (4 CO ester), 158.2 (CO urea), 80.0 (C-1), 73.0 (C-5), 72.6 (C-3), 70.4 (C-2), 68.2 (C-4), 61.8 (C-6), 27.0 (NMe), and 20.6 (4 C, 4 *Me*CO); FABMS *m/z* 427 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{16}H_{24}N_2O_{10}$: C, 47.52; H, 5.98; N, 6.93 Found: C, 47.43; H, 5.81; N, 7.00.

General procedure for the preparation of sugar carbodiimides.—(a) To a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl phosphinimine (**1**) [13,30] or 2,3,6,2',3',4',6'-hepta-*O*-acetyl-β-cellobio-

syl phosphinimine (**4**) [13,30] (0.5 mmol) in dry toluene (3 mL) was added the corresponding isothiocyanate **5**, **6** or **7** [33–35] (0.5 mmol). The reaction mixture was refluxed for 2 h, then concentrated and the residue purified by flash chromatography using first toluene to elute most unreacted triphenylphosphine and triphenylphosphine thioxide and then the(b) solvent indicated in each case. Compounds **8–13** were thus isolated in 25–35% yield.

(b) To a soln of triphenylphosphine (1.1 mmol) and the corresponding isothiocyanate derivative (methyl, **20** or **21**) [27,28,43] (1.1 mmol) in dry toluene (3 mL) was added the azido derivative (**14**, **15** or **16**) [33,35] (1.0 mmol) in dry toluene (3 mL). The mixture was stirred at room temperature for 10–40 min, then concentrated and the residue purified by flash chromatography as above. The yields of pure carbodiimides **8–13** and **17–19** are indicated hereinafter.

*6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-[3-(2',3',4',6'-tetra-*O*-acetyl-β-*D*-glucopyranosyl)carbodiimido]-α-*D*-galactopyranose* (**8**).—Yield: 618 mg (91%), syrup, $[\alpha]_D^{20}$ −51.5° (c 0.8, CH_2Cl_2); R_f 0.50 (3:1 Et_2O–CCl_4); IR (KBr) 2988, 2938, 2143, 1753, 1377, 1221, and 1069 cm^{-1}; NMR: ^1H (300 MHz, $CDCl_3$) Table 1 and δ 2.08, 2.06, 2.02, 2.00 (4 s, each 3 H, 4 Ac), 1.56, 1.44, 1.35, and 1.33 (4 s, each 3 H, 2 CMe_2); ^{13}C (75.5 MHz, $CDCl_3$) Table 2 and δ 170.2, 169.8, 169.3 (2 C) (4 CO), 137.9 (N=C=N), 109.5, 108.7 (2 CMe_2), 26.0, 25.8, 24.8, 24.3 (2 CMe_2), and 20.5 (4 C, 4 *Me*CO); FABMS *m/z* 637 (70%, $[M + Na]^+$). Anal. Calcd. for $C_{27}H_{38}N_2O_{14}$: C, 52.76; H, 6.23; N, 4.56. Found: C, 52.78; H, 6.41; N, 4.59.

*6-Deoxy-1,2:3,5-di-*O*-isopropylidene-6-[3-(2',3',4',6'-tetra-*O*-acetyl-β-*D*-glucopyranosyl)carbodiimido]-α-*D*-glucofuranose* (**9**).—Yield: 527 mg (78%); $[\alpha]_D^{20}$ +9.6° (c 0.9, CH_2Cl_2); R_f 0.51 (1:1 hexanes–EtOAc); IR (KBr) 2988, 2934, 2149, 1755, 1373, 1225, and 1034 cm^{-1}; NMR: ^1H (500 MHz, $CDCl_3$) Table 1 and δ 2.08, 2.07, 2.02, 1.99 (4 s, each 3 H, 4 Ac), 1.47, 1.37, 1.36, and 1.32 (4 s, each 3 H, 2 CMe_2); ^{13}C (125.5 MHz, $CDCl_3$) Table 2 and δ 170.4, 170.0, 169.1 (4 C, 4 CO), 136.8 (N=C=N), 112.1, 101.0 (2 CMe_2), 29.4, 26.9 (2 C), 26.3 (2 CMe_2), 23.8, 23.7, 20.5, and 20.4 (4 *Me*CO); FABMS *m/z* 637 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{27}H_{38}N_2O_{14}$: C, 52.76; H, 6.23; N, 4.56. Found: C, 52.76; H, 6.28; N, 4.42.

*Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[3-(2',3',4',6'-tetra-*O*-acetyl-β-*D*-glucopyranosyl)carbodiimido]-α-*D*-glucopyranoside* (**10**).—Yield: 534 mg (72%); $[\alpha]_D^{20}$ +65.2° (c 1.9, CH_2Cl_2); R_f 0.27 (1:1 hexanes–EtOAc); IR (KBr) 2944, 2851, 2151, 1748, 1225, and 1045 cm^{-1}; NMR: ^1H (500 MHz, $CDCl_3$) Table 1 and δ 3.43 (s, 3 H, OMe), 2.09, 2.08, 2.06, 2.04, 2.03, 2.02, and 2.01 (7 s, each 3 H, 7 Ac); ^{13}C (125.5 MHz, $CDCl_3$) Table 2 and δ 170.4, 170.0, 169.9, 169.8, 169.3, 169.1 (7 C, 7 CO), 137.1 (N=C=N), 55.5 (OMe), 20.5 (2 C), 20.4 (3 C), and 20.3 (2 C) (7 *Me*CO); FABMS *m/z* 697 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{28}H_{38}N_2O_{17}$: C, 49.85; H, 5.68; N, 4.15. Found: C, 49.80; H, 5.61; N, 3.93.

*6-Deoxy-1,2:3,4-di-*O*-isopropylidene-6-[3-[2,3,6-tri-*O*-acetyl-4-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-β-*D*-glucopyranosyl]carbodiimido]-α-*D*-galactopyranose* (**11**).—Yield: 749 mg (83%); $[\alpha]_D^{20}$ −28.8° (c 1.2, CH_2Cl_2); R_f 0.37 (Et_2O); IR (KBr) 2992, 2944, 2145, 1759, 1383, 1231, and 1047 cm^{-1}; NMR: ^1H (400 MHz, $CDCl_3$) Table 1 and δ 2.12, 2.08, 2.05, 2.02, 2.00 (6 H), 1.97 (6 s, 21 H, 7 Ac), 1.54, 1.42, 1.34, and 1.32 (4 s, each 3 H, 2 CMe_2); ^{13}C (100.6 MHz, $CDCl_3$) Table 2 and δ 170.5, 170.4, 170.2, 169.9, 169.6, 169.3, 169.1 (7 CO), 138.4 (N=C=N), 109.6, 108.8 (2 CMe_2), 26.1, 25.9, 25.0, 24.4 (2 CMe_2), 20.9, 20.7 (2 C), 20.6 (4 C) (7 *Me*CO); FABMS *m/z* 925 (70%, $[M + Na]^+$). Anal. Calcd. for $C_{39}H_{54}N_2O_{22}$: C, 51.88; H, 6.03; N, 3.10. Found: C, 51.89; H, 6.11; N, 3.11.

*6-Deoxy-1,2:3,5-di-*O*-isopropylidene-6-[3-[2,3,6-tri-*O*-acetyl-4-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-β-*D*-glucopyranosyl]carbodiimido]-α-*D*-glucofuranose* (**12**).—Yield: 695 mg (70%); $[\alpha]_D^{20}$ +15.0° (c 1.0, CH_2Cl_2); R_f 0.43 (1:1 hexanes–EtOAc); IR (KBr) 2924, 2853, 2147, 1755, 1373, 1229, and 1044 cm^{-1}; NMR: ^1H (500 MHz, $CDCl_3$) Table 1 and δ 2.17, 2.13, 2.10, 2.09, 2.07, 2.05, 2.02 (7 s, each 3 H, 7 Ac), 1.50, 1.30, 1.25, and 1.20 (4 s, each 3 H, 2 CMe_2); ^{13}C (125.5 MHz, $CDCl_3$) Table 2 and δ 170.2, 170.0, 169.9, 169.5, 169.3, 169.0, 168.8 (7 CO), 137.0 (N=C=N), 112.1, 101.0 (2 CMe_2), 29.4, 26.9, 26.2, 26.8 (2 CMe_2), 20.5, 20.4, and 20.2 (7 *Me*CO); FABMS *m/z* 925 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{39}H_{54}N_2O_{22}$: C, 51.88; H, 6.03; N, 3.10. Found: C, 51.62; H, 5.88; N, 3.12.

*Methyl 2,3,4-tri-*O*-acetyl-6-deoxy-6-[3-[2,3,6-tri-*O*-acetyl-4-*O*-(2',3',4',6'-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-β-*D*-glucopyranosyl]carbodiimido]-α-*D*-glucopyranoside* (**13**).—Yield: 751 mg (71%); $[\alpha]_D^{20}$ +44.5° (c 1.6, CH_2Cl_2); R_f 0.19 (1:1 hexanes–EtOAc); IR (KBr) 2947, 2149, 1755, 1371, 1227, and 1047 cm^{-1}; NMR: ^1H (500 MHz, $CDCl_3$) Table 1 and δ 3.42 (s, 3 H, OMe), 2.14, 2.09, 2.07, 2.03, 2.02, 2.01, and 1.99 (7 s, 30 H, 10 Ac); ^{13}C

(125.5 MHz, $CDCl_3$) Table 2 and δ 170.3–168.9 (10 CO), 137.4 (N=C=N), 55.6 (OMe), and 20.7–20.3 (10 C, 10 *Me*CO); FABMS *m/z* 985 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{40}H_{54}N_2O_{25}$: C, 49.90; H, 5.65; N, 2.91. Found: C, 50.20; H, 5.58; N, 2.64.

6 - Deoxy - 1, 2:3, 4 - di - O - isopropylidene - 6 - (3 - methylcarbodiimido) - α - D - galactopyranose (**17**).— Yield: 230 mg (72%); $[\alpha] -103.5°$ (c 1.0, CH_2Cl_2); R_f 0.45 (1:5 Et_2O–CCl_4); IR (KBr) 2985, 2957, 2135, 1385, 1252, 1167, and 1070 cm^{-1}; NMR: ^1H (500 MHz, $CDCl_3$) Table 1 and δ 2.91 (s, 3 H, N′Me), 1.48, 1.39, 1.28, and 1.27 (4 s, each 3 H, 2 CMe_2); ^{13}C (125.5 MHz, $CDCl_3$) Table 2 and δ 141.2 (N=C=N), 109.3, 108.6 (2 CMe_2), 32.7 (NMe), 25.9, 25.8, 24.9, and 24.3 (2 CMe_2); FABMS *m/z* 299 (100%, $[M + H]^+$), 321 (80, $[M + Na]^+$). Anal. Calcd. for $C_{14}H_{22}N_2O_5$: C, 56.36; H, 7.43; N, 9.39. Found: C, 56.33; H, 7.41; N, 9.39.

6 - Deoxy - 1, 2:3, 5 - di - O - isopropylidene - 6 - (3 - methylcarbodiimido) - α - D - glucofuranose (**18**).—Yield: 229 mg (70%); $[\alpha]_D^{20} +22.3°$ (c 0.9, CH_2Cl_2); R_f 0.60 (15:1 CCl_4–acetone); IR (KBr) 2986, 2934, 2139, 1377, 1221, and 1080 cm^{-1}; NMR: ^1H (500 MHz, CDC13) Table 1 and δ 2.95 (s, 3 H, N′Me), 1.50, 1.40, 1.39, and 1.35 (4 s, each 3 H, 2 CMe_2); ^{13}C (125.5 MHz, $CDCl_3$) Table 2 and δ 140.6 (N=C=N), 112.1, 100.9 (2 CMe_2), 32.6 (NMe), 27.0, 26.3, 23.9, and 23.8 (2 CMe_2); FABMS *m/z* 321 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{14}H_{22}N_2O_5$: C, 56.36; H, 7.43; N, 9.39. Found: C, 56.58; H, 7.80; N, 9.12.

Methyl 2, 3, 4 - tri - O - acetyl - 6 - deoxy - 6 - (3 - methylcarbodiimido) - α - D - glucopyranoside (**19**).— Yield: 295 mg (75%); $[\alpha]_D^{20} +107.7°$ (c 1.0, CH_2Cl_2); R_f 0.36 (1:2 hexanes–EtOAc); IR (KBr) 2988, 2934, 2141, 1751, 1223, and 1045 cm^{-1}; NMR: ^1H (300 MHz, $CDCl_3$) Table 1 and δ 3.44 (s, 3 H, OMe), 2.97 (s, 3 H, N′Me), 2.07, 2.04, and 2.01 (3 s, each 3 H, 3 Ac); ^{13}C (75.5 MHz, $CDCl_3$) Table 2 and δ 169.9, 169.4 (2 C) (3 CO), 140.3 (N=C=N), 55.3 (OMe), 32.0 (MeN), and 20.5 (3 C, 3 *Me*CO); FABMS *m/z* 381 (100%, $[M + Na]^+$). Anal. Calcd. for $C_{15}H_{22}N_2O_8$: C, 50.28; H, 6.19; N, 7.82. Found: C, 50.27; H, 6.10; N, 7.56.

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