Glycoconj J (2008) 25:595–602
DOI 10.1007/s10719-007-9093-5

SHORT COMMUNICATION

Significant rate accelerated synthesis of glycosyl azides and glycosyl 1,2,3-triazole conjugates

Rishi Kumar · Prakas R. Maulik · Anup Kumar Misra

Received: 27 August 2007 / Accepted: 20 November 2007 / Published online: 18 December 2007

Abstract An efficient and significantly rapid access of a series of glycosyl azides and glycosyl 1,2,3-triazole conjugates is reported using modified one-pot reaction conditions. In both cases yields were excellent and single diastereomers were obtained.

Keywords Glycosyl azides · Glycosyl triazoles · Glycosyl bromides · Click chemistry · One-pot

Introduction

Glycosyl azides are important classes of carbohydrate derivatives, which have been used as precursors for the synthesis of glycosyl amines [1, 2], N-glycopeptides [3], N-glycoproteins [4] and glycosyl heterocycles such as, 1,2,3-triazoles [5–7] etc. In some cases, glycosyl azides have been converted into glycosyl fluorides for their use in the synthesis of oligosaccharides and glycoconjugates [8]. Glycosyl azides have successfully been used in the solid-phase preparation of glycopeptides [9, 10]. They can also provide chiral templates for the synthesis of glycosyl amino acids (GAA), amino glycosyl phosphonic acid derivatives [11–13]. Glycosyl azides have successfully been applied as novel substrate for enzymatic transglycosylations [14].

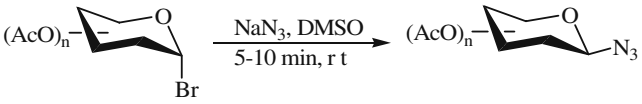
Glycosyl 1,2,3-triazole derivatives derived from glycosyl azides using "Click chemistry"[15–22] have appeared as useful molecules of medicinal interest because of their potential to act as inhibitors for galectins [23–26], RNA binding molecules [27] and carbonic anhydrase antagonists [28]. Most commonly, glycosyl triazole derivatives are prepared by the 1,3-dipolar cycloaddition of glycosyl azides and alkynes under "Click chemistry" conditions, which is a powerful technique for the preparation of triazole linked neoglycoconjugates [29], cyclodextrin analogs [30, 31] and linking of carbohydrate moieties with proteins to generate glycoconjugates [32, 33] in glycobiology research.

Recently, we are engaged in the preparation of several glycosyl triazole derivatives for their evaluation as RNA binding molecules and for this purpose we were looking for a faster reaction condition for the preparation of glycosyl azides and glycosyl 1,2,3-triazoles from glycosyl bromides. Conventionally, glycosyl azides are prepared by the stereospecific reaction of glycosyl halides with sodium azide in DMF at elevated temperature in a longer reaction time (12–20 h) [34, 35]. Heterogeneous phase-transfer reaction conditions have also been established for the preparation of glycosyl azides from glycosyl halides [36]. They can also be prepared from glycosyl acetates on treatment with trimethylsilyl azide in the presence of a Lewis acid [37]. Earlier, we have reported a one-pot reaction protocol for the preparation of glycosyl azides directly from unprotected reducing sugars under a phase-transfer conditions [38]. In this circumstance, we presumed that under the conventional reaction conditions sodium azide has a poor solubility in DMF, used as the solvent and as a result longer reaction time was required at about 80°C resulting in the possibility of the formation of a mixture of

CDRI communication no. 7340.

R. Kumar · P. R. Maulik
Molecular and Structural Biology,
Central Drug Research Institute,
Chattar Manzil Palace,
Lucknow 226001 UP, India

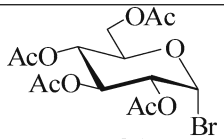
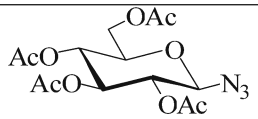
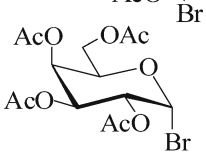
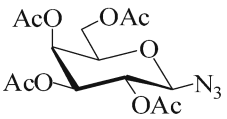
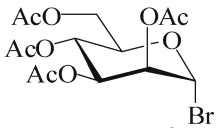
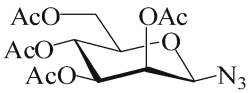
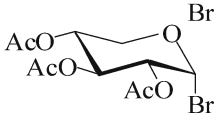
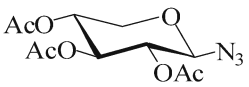
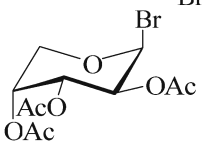
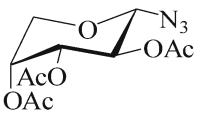
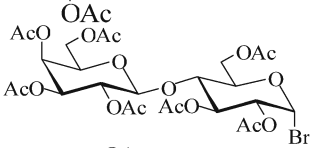
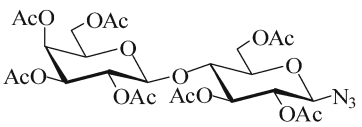
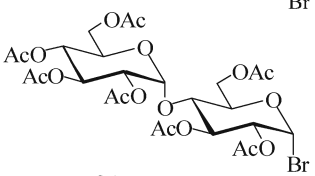
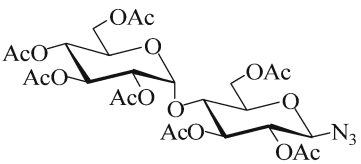
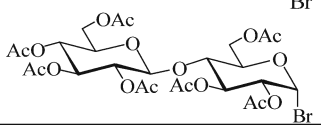
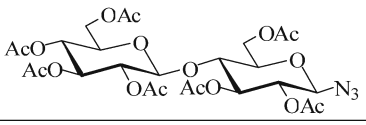
A. K. Misra (✉)
Medicinal and Process Chemistry Division,
Central Drug Research Institute,
Chattar Manzil Palace,
Lucknow 226001 UP, India
e-mail: akmisra69@rediffmail.com



Scheme 1 Fast preparation of glycosyl azides from glycosyl bromides

diastereomeric products. Earlier Alvarez and Alvarez [39] and Kacprzak [40] have performed azidation of various alkyl halides very efficiently using a slight excess of sodium azide in DMSO at room temperature. Therefore, we set out to explore the role of solvents such as, DMF, THF, 1,4-dioxane, DMSO etc in the reaction rate of per-*O*-acetyl-glucosyl azide formation from its corresponding bromide. After a series of experiments we were surprised to observe that the use of sodium azide (1.2 equiv.) in DMSO (5 mL/mmol of substrate) could furnish per-*O*-acetyl-glucosyl azide from per-*O*-acetyl-glucosyl bromide at room temperature within 10 min (Scheme 1). This may be explained by considering the high solubility of both reactants in DMSO could facilitate a fast S_N^2 reaction and thus resulted in the rapid formation of glucosyl azide. Under following similar reaction conditions, a series of glycosyl azides from glycosyl bromides have been prepared in excellent yield in a very short interval of time at room temperature (Table 1). Glycosyl bromides used for this reaction can be prepared from the reducing sugars following earlier reported protocols and can be used directly without any purification [41]. It is noteworthy that only β-glycosyl azides were obtained exclusively.

Table 1 Rapid access to glycosyl azides from glycosyl bromides[a]

Entry	Glycosyl bromides (**1**)	Glycosyl azides (**2**)	Time (min)	Yield (%)[b]	Ref
a			10	95	[17]
b			10	90	[17]
c			5	85	[25]
d			5	85	[26]
e			5	80	[19]
f			10	90	[17]
g			10	90	[17]
h			15	85	[27]

[a] All reactions were conducted at room temperature
[b] Isolated yield

After achieving glycosyl azides, we explored the possibility to extend the reaction for the direct preparation of glycosyl triazole following Sharpless "Click chemistry" condition in one-pot avoiding intermediate work-up step. Following literature reported protocols for the 1,3-cycloaddition reaction, preparation of glycosyl triazoles from glycosyl azides and alkynes usually take 10–16 h at an elevated temperature in water or organic solvents. Earlier a series of glucosyl-1,4-disubstituted 1,2,3-triazole derivatives were prepared by Akula *et al*. using the Sharpless $CuSO_4$/ascorbic acid system in water at 70°C in 8 h [42]. Chittabonia *et al*. reported direct formation of glycosyl triazole conjugates from reducing sugars or glycosyl acetate in a phase transfer reaction condition [43]. However, in our hands the reaction conditions resulted in a considerable amount of NH-triazole as a by product. In order to achieve the glycosyl triazole derivatives from glycosyl bromide in one-pot in a shorter reaction time, phenyl acetylene (1.5 equiv.), $CuSO_4{\cdot}5H_2O$ (2.5 mL, 1 M aq. solution) and sodium L-ascorbate (2.5 mL, 1 M aq. solution) were added to the reaction mixture after complete consumption of the glucosyl bromide and to our satisfaction, clean formation of glucosyl triazole formed in excellent yield within 30 min to 2 h at room temperature (Scheme 2). This one-pot reaction protocol has been generalized by preparing a series of glycosyl triazole derivatives directly from glycosyl bromides at room temperature (Table 2). It is clear that DMSO has a significant role in the reaction rate may be due to the fact that all reactants are highly soluble in DMSO, which led to the clean formation of products in a very short reaction time at room temperature. It is noteworthy that only single regioisomers of glycosyl 1,2,3-triazole derivatives (1,4-substituted triazoles) were formed under the reaction condition, which was further confirmed from nOe NMR experiments.

Conclusion

In summary we have developed an elegant methodology for the significant rapid access of glycosyl azides and glycosyl triazole conjugates from glycosyl bromides. Exceptionally fast preparation of glycosyl azides and triazoles from glycosyl bromides, a two-step, one-pot reaction protocol, aqueous reaction conditions are the key features of this method.

Experimental section

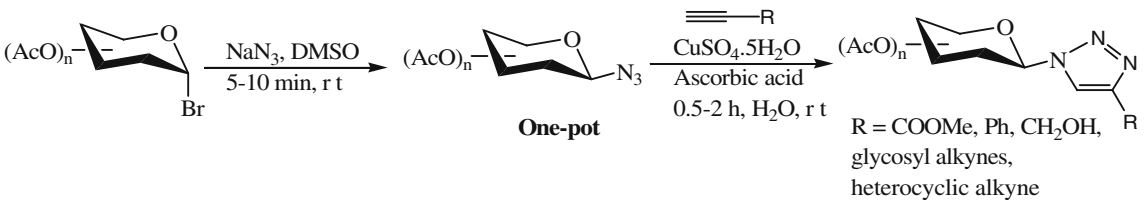
General methods General methods are same as described earlier [38].

General experimental protocol for the preparation of glycosyl azide To a solution of per-*O*-acetylated glycosyl bromide (1 mmol) in dry DMSO (5 mL) was added sodium azide (1.2 mmol) and the reaction was allowed to stir at room temperature for appropriate time (Table 1). The reaction mixture was diluted with water (25 mL) and extracted with EtOAc (25 mL). The organic layer was dried (Na_2SO_4) and evaporated to dryness to give per-*O*-acetylated glycosyl azide, which was purified either by crystallization or column chromatography over SiO_2. Products of all known compounds gave acceptable ^1H NMR and ^{13}C NMR spectra that matched the data reported in the cited references.

General experimental protocol for the preparation of 4-substituted glycosyl 1,2,3-triazole To a solution of per-*O*-acetylated glycosyl bromide (1 mmol) in dry DMSO (5 mL) was added sodium azide (1.2 mmol) and the reaction was allowed to stir at room temperature for appropriate time (Table 1). To the reaction mixture were added appropriate alkyne (1.5 mmol), sodium L-ascorbate (2.5 mL, 1 M aq. soln) and $CuSO_4{\cdot}5H_2O$ solution (2.5 mL, 1 M aq. soln) and the reaction mixture was allowed to stir for appropriate time (Table 2). The reaction mixture was filtered and extracted with EtOAc (25 mL). The organic layer was dried (Na_2SO_4) and evaporated to dryness to give per-*O*-acetylated glycosyl triazole derivative, which was purified by column chromatography over SiO_2.

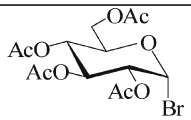
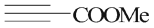
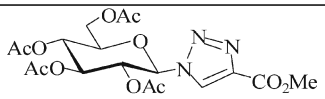
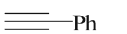
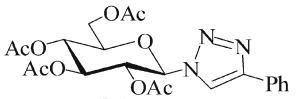
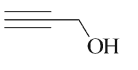
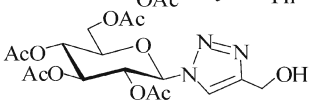
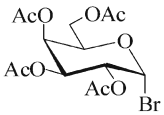
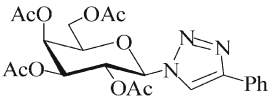
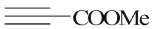
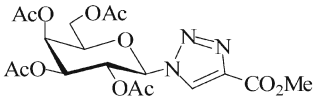
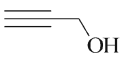
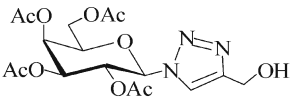
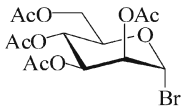
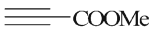
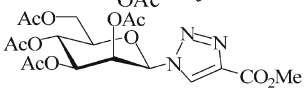
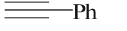
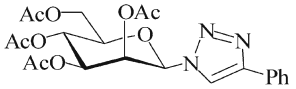
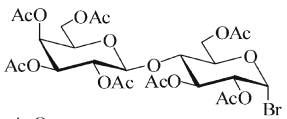
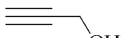
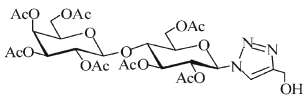
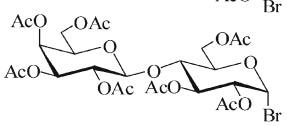
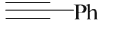
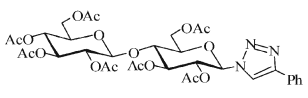
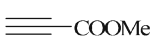
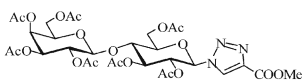
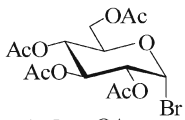
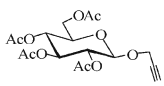
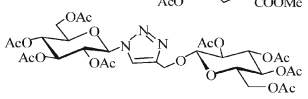
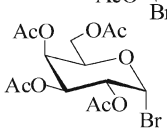
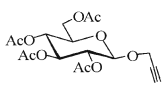
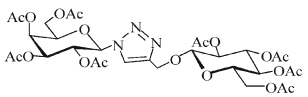
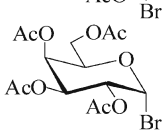
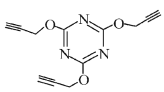
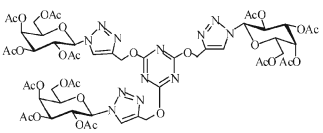
Spectral data for glycosyl triazole conjugates as follows.

Compound 3a: Oil; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.35 (s, 1 H, H-5′), 5.92 (d, *J*=8.9 Hz, 1 H, H-1), 5.47–5.36 (m, 2 H, H-2 and H-3), 5.22 (t, *J*=9.8 Hz, 1 H, H-4), 4.31 (dd, *J*=12.6, 4.9 Hz, 1 H, H-6_a), 4.15 (dd, *J*=12.6,



Scheme 2 One-pot rapid preparation of 4-substituted glycosyl 1,2,3-triazole conjugates from glycosyl bromides

Table 2 Two step, one-pot synthesis of glycosyl triazole derivatives from glycosyl bromides via *in situ* generation of glycosyl azides[a]

Entry	Glycosyl bromides (**1**)	Alkynes	Glycosyl azides (**3**)	Time (min)[b]	Yield (%)[c]
a				30	90
b				30	92
c				30	85
d				30	90
e				45	85
f				45	82
g				30	90[d]
h				30	92
i				90	80
j				90	90
k				90	85
l				120	90
m				120	92
n				120[e]	76

[a] All reactions were conducted at room temperature
[b] Time required after formation of glycosyl azides
[c] Isolated yield
[d] Reference [43]
[e] 70°C and two drops of *N,N*-diisopropylethyl amine.

1.9 Hz, 1 H, H-6_b), 4.06–4.0 (m, 1 H, H-5), 3.96 (s, 3 H, OCH_3), 2.09, 2.07, 2.03, 1.90 (4 s, 12 H, 4 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.4, 169.8, 169.3, 168.9 (4 *C*OCH$_3$), 160.5 (*C*OOCH$_3$), 140.6 (C-5′), 126.1 (C-4′), 85.9 (C-1), 75.4, 72.3, 70.4, 67.6, 61.4, 52.3 (COO*C*H$_3$), 20.6, 20.5 (2 C), 20.1 (4 CO*C*H$_3$); ESI-MS: *m/z*=480.3 $[M+Na]^+$; Anal. Calcd. for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; found: C, 47.10; H, 5.30.

Compound 3b: [43] White solid, m.p. 195–198°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.02 (s, 1 H, H-5′), 7.85 (d, *J*=8.5 Hz, 2 H, Ar-H), 7.47–7.35 (m, 3 H, Ar-H), 5.94 (d, *J*=9.1 Hz, 1 H, H-1), 5.53 (t, *J*=9.4 Hz, 1 H, H-3), 5.44 (t, *J*=9.5 Hz, 1 H, H-2), 5.27 (t, *J*=9.3 Hz, 1 H, H-4), 4.32 (dd, *J*=12.6, 5.0 Hz, 1 H, H-6_a), 4.18 (dd, *J*=12.6, 2.0 Hz, 1 H, H-6_b), 4.06–4.0 (m, 1 H, H-5), 2.09, 2.08, 2.05, 1.89 (4 s, 12 H, 4 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.4, 169.8, 169.3, 168.9 (4 *C*OCH$_3$), 148.4 (C-5′), 129.8 (C-4′), 128.8–117.7 (Ar-*C*), 85.7 (C-1), 75.1, 72.7, 70.2, 67.7, 61.5, 20.6, 20.5 (2 C), 20.1 (4 CO*C*H$_3$); ESI-MS: *m/z*=498.2 $[M+Na]^+$; Anal. Calcd. for $C_{22}H_{25}N_3O_9$ (475.44): C, 55.58; H, 5.30; found: C, 55.40; H, 5.48.

Compound 3c: Oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.82 (s, 1 H, H-5′), 5.90 (d, *J*=9.0 Hz, 1 H, H-1), 5.46–5.43 (m, 2 H, H-2 and H-3), 5.25 (t, *J*=9.2 Hz, 1 H, H-4), 4.80 (br s, 2 H, CH_2OH), 4.30 (dd, *J*=12.6, 4.9 Hz, 1 H, H-6_a), 4.17 (dd, *J*=12.6, 2.0 Hz, 1 H, H-6_b), 4.08–4.0 (m, 1 H, H-5), 2.1, 2.08, 2.04, 1.89 (4 s, 12 H, 4 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.5, 169.9, 169.4, 169.1 (4 *C*OCH$_3$), 148.4 (C-5′), 120.2 (C-4′), 85.7, 75.0, 72.6, 70.3, 67.6, 61.5, 56.3, 20.6, 20.5 (2 C), 20.1 (4 CO*C*H$_3$); ESI-MS: *m/z*=452.4 $[M+Na]^+$; Anal. Calcd. for $C_{17}H_{23}N_3O_{10}$ (429.38): C, 47.55; H, 5.40; found: C, 47.36; H, 5.55.

Compound 3d: [43] White solid, m.p. 185–187°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.07 (s, 1 H, H-5′), 7.89–7.86 (m, 2 H, Ar H), 7.48–7.37 (m, 3 H, Ar H), 5.92 (d, *J*=9.4 Hz, 1 H, H-1), 5.66 (t, *J*=9.9 Hz, 1 H, H-2), 5.59 (d, *J*=3.1 Hz, 1 H, H-4), 5.30 (dd, *J*=10.3, 3.3 Hz, 1 H, H-3), 4.27–4.19 (m, 3 H, H-5 and H-6_{ab}), 2.27, 2.07, 2.02, 1.92 (4 s, 12 H, 4 COCH_3); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 169.9, 169.6, 169.4, 168.7 (4 *C*OCH$_3$), 148.0 (C-5′), 129.5 (C-4′), 128.4–117.4 (Ar *C*), 85.9 (C-1), 74.5, 71.3, 68.2, 67.3, 61.6, 21.1, 21.0, 20.9, 20.7 (4 CO*C*H$_3$); ESI-MS: *m/z*=498.3 $[M+Na]^+$; Anal. Calcd. for $C_{22}H_{25}N_3O_9$ (475.44): C, 55.58; H, 5.30; N, 8.84 found: C, 55.42; H, 5.50.

Compound 3e: White solid, m.p. 168–171°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.41 (s, 1 H, H-5′), 5.92 (d, *J*=9.2 Hz, 1 H. H-1), 5.57 (d, *J*=2.7 Hz, 1 H, H-4), 5.50 (t, *J*=9.3 Hz, 1 H, H-2), 5.27 (dd, *J*=10.3 and 3.3 Hz, 1 H, H-3), 4.30–4.24 (m, 1 H, H-5), 4.20–4.15 (m, 2 H, H-6_{ab}), 3.96 (s, 3 H, CH_3), 2.23, 2.04, 2.01, 1.90 (4 s, 12 H, 4 COCH_3); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.2, 169.8, 169.7, 169.0 (4 *C*OCH$_3$), 160.6 (*C*OOCH$_3$), 140.5 (C-5′), 126.2 (C-4′), 86.4 (C-1), 74.2, 70.4, 68.0, 66.7, 61.1 (C-1), 52.3 (COO*C*H$_3$), 20.5, 20.4 (2 C), 20.1 (4 CO*C*H$_3$); ESI-MS: *m/z*=480.1 $[M+Na]^+$; Anal. Calcd. for $C_{18}H_{23}N_3O_{11}$ (457.39): C, 47.27; H, 5.07; found: C, 47.08; H, 5.25.

Compound 3f: White solid, m.p. 148–150°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.87 (s, 1 H, H-5′), 5.87 (d, *J*=9.3 Hz, 1 H, H-1), 5.56 (d, *J*=2.6 Hz, 1 H, H-4), 5.54 (t, *J*=9.5 Hz, 1 H, H-2), 5.27 (dd, *J*=10.2, 3.4 Hz, 1 H, H-3), 4.80 (br s, 2 H, CH_2OH), 4.27–4.22 (m, 1 H, H-5), 4.18–4.13 (m, 2 H, H-6_{ab}), 2.22, 2.05, 2.02, 1.90 (4 s, 12 H, 4 COCH_3); ^{13}C NMR ($CDCl_3$, 50 MHz): δ 170.8, 170.5, 170.3, 169.6 (4 *C*OCH$_3$), 148.9 (C-5′), 120.9 (C-4′), 86.3 (C-1), 74.2, 71.1, 68.4, 67.4, 61.7, 56.3, 20.9 (2 C), 20.8, 20.6 (4 CO*C*H$_3$); ESI-MS: *m/z*=452.4 $[M+Na]^+$; Anal. Calcd. for $C_{17}H_{23}N_3O_{10}$ (429.38): C, 47.55; H, 5.40; found: C, 47.37; H, 5.58.

Compound 3h: Oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.03 (s, 1 H, H-5′), 7.88–7.82 (m, 2 H, Ar H), 7.47–7.36 (m, 3 H, Ar H), 6.22 (br s, 1 H, H-1), 5.81 (br s, 1 H, H-2), 5.39–5.31 (m, 2 H, H-3 and H-4), 4.37 (dd, *J*=12.5, 5.9 Hz, 1 H, H-6_a), 4.22 (dd, *J*=12.5, 2.0 Hz, 1 H, H-6_b), 4.05–4.0 (m, 1 H, H-5), 2.12, 2.10, 2.01 (3 s, 12 H, 4 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.6, 169.7, 169.6, 168.9 (4 *C*OCH$_3$), 147.7 (C-5′), 130.0 (C-4′), 128.9–118.4 (Ar C), 84.8 (C-1), 75.7, 70.7, 68.9, 64.9, 62.2, 20.7, 20.6, 20.5, 20.4 (4 CO*C*H$_3$); ESI-

MS: *m/z*=498.5 $[M+Na]^+$; Anal. Calcd. for $C_{22}H_{25}N_3O_9$ (475.44): C, 55.58; H, 5.30; N, 8.84 found: C, 55.40; H, 5.46.

Compound 3i: Oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.73 (s, 1 H, H-5″), 5.84 (d, *J*=9.0 Hz, 1 H, H-1), 5.42–5.39 (m, 2 H, H-2 and H-3), 5.36 (d, *J*=3.0 Hz, 1 H, H-4′), 5.13 (dd, *J*=10.3, 7.8 Hz, 1 H, H-2′), 5.0 (dd, *J*=10.4, 3.4 Hz, 1 H, H-3′), 4.79 (br s, 2 H, CH_2OH), 4.54 (d, *J*=7.8 Hz, 1 H, H-1′), 4.50 (d, *J*=12.3 Hz, 1 H, H-6_a), 4.18–4.10 (m, 3 H, H-4, H-5 and H-6_b), 3.97–3.90 (m, 3 H, H-5′ and H-$6'_{ab}$), 2.16, 2.10, 2.08, 2.07, 2.06, 1.97, 1.88 (7 s, 21 H, 7 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.3 (2 C), 170.1, 169.5 (2 C), 169.2, 169.1 (7 *C*OCH$_3$), 148.3 (C-5″), 120.1 (C-4″), 101.0 (C-1′), 85.5 (C-1), 77.2, 75.9, 75.5, 72.5, 70.8 (2 C), 69.0, 66.6, 61.7, 60.8, 56.5, 20.6 (2 C), 20.5 (3 C), 20.2 (2 C) (7 CO*C*H$_3$); ESI-MS: *m/z*=740.6 $[M+Na]^+$; Anal. Calcd. for $C_{29}H_{39}N_3O_{18}$ (717.63): C, 48.54; H, 5.48; found: C, 48.35; H, 5.72.

Compound 3j: [43] Oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.95 (s, 1 H, H-5″), 7.84–7.81 (m, 2 H, Ar H), 7.45–7.35 (m, 3 H, Ar H), 5.90 (d, *J*=8.8 Hz, 1 H, H-1), 5.49–5.44 (m, 2 H, H-2 and H-3), 5.38 (d, *J*=2.7 Hz, 1 H, H-4′), 5.13 (dd, *J*=10.3, 7.8 Hz, 1 H, H-2′), 5.02 (dd, *J*=10.4, 3.4 Hz, 1 H, H-3′), 4.57 (d, *J*=7.8 Hz, 1 H, H-1′), 4.52 (d, *J*=12.4 Hz, 1 H, H-6_a), 4.22–4.11 (m, 3 H, H-4, H-5 and H-6_b), 4.0–3.93 (m, 3 H, H-5′ and H-$6'_{ab}$), 2.17, 2.11, 2.08, 2.07, 2.06, 1.97, 1.88 (7 s, 21 H, 7 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.2 (2 C), 170.0 (2 C), 169.5 (2 C), 169.2 (7 *C*OCH$_3$), 148.3 (C-5″), 129.8 (C-4″), 128.8–117.9 (Ar C), 101.0 (C-1′), 85.5 (C-1), 75.9, 75.6, 72.6, 70.8 (2 C), 70.4, 69.0, 66.6, 61.8, 60.8, 20.6 (2 C), 20.4 (3 C), 20.2 (2 C) (7 CO*C*H$_3$); ESI-MS: *m/z*=786.2 $[M+Na]^+$; Anal. Calcd. for $C_{34}H_{41}N_3O_{17}$ (763.69): C, 53.47; H, 5.41; found: C, 53.30; H, 5.60.

Compound 3k: Oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 8.31 (s, 1 H, H-5″), 5.93 (d, *J*=8.9 Hz, 1 H, H-1), 5.43–5.31 (m, 3 H, H-2, H-3 and H-4′), 5.16–5.08 (m, 1 H, H-2′), 5.01–4.94 (m, 1 H, H-3′), 4.57–4.48 (m, 3 H, H-1′, H-4, H-6_a), 4.19–4.05 (m, 4 H, H-5′, H-6_b and H-$6'_{ab}$), 3.95 (s, 3 H, COO*C*H$_3$), 3.93–3.87 (m, 1 H, H-5), 2.17, 2.12, 2.08, 2.06, 2.05, 1.98, 1.89 (7 s, 21 H, 7 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.5, 170.3, 170.1, 170.0, 169.6, 169.4, 169.0 (7 *C*OCH$_3$), 160.6 (*C*OOCH$_3$), 140.4 (C-5″), 126.2 (C-4″), 100.9 (C-1′), 85.6 (C-1), 77.02, 76.0, 75.4, 72.2, 70.9, 70.6, 69.0, 66.6, 60.8 (2 C), 52.3 (COO*C*H$_3$), 20.8, 20.6 (2 C), 20.5 (2 C), 20.4, 20.2 (7 CO*C*H$_3$); ESI-MS: *m/z*=768.1 $[M+Na]^+$; Anal. Calcd. for $C_{30}H_{39}N_3O_{19}$ (745.64): C, 48.32; H, 5.27; found: C, 48.15; H, 5.46.

Compound 3l: White solid, m.p. 130–132°C; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.83 (m, 1 H, H-5″), 5.90 (d, *J*=8.8 Hz, 1 H, H-1), 5.45–5.42 (m, 2 H, H-2, H-3), 5.25 (t, *J*=9.7 Hz, 1 H, H-4), 5.20 (t, *J*=9.4 Hz, 1 H, H-2′), 5.10 (t, *J*=9.6 Hz, 1 H, H-3′), 4.96 (t, *J*=8.1 Hz, 1 H, H-4′), 4.95–4.78 (AB_q, *J*=12.9 Hz each, 2 H, CH_2O), 4.57 (d, *J*=7.9 Hz, 1 H, H-1′), 4.32–4.27 (m, 2 H, H-6_a and H-$6'_a$), 4.22–4.13 (m, 2 H, H-6_b and H-$6'_b$), 4.05–4.0 (m, 1 H, H-5), 3.78–3.75 (m, 1 H, H-5′), 2.12, 2.08, 2.07, 2.04, 2.02, 1.98, 1.97, 1.90 (8 s, 24 H, 8 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.7, 170.4, 170.2 (2 C), 169.8 (2 C), 169.3, 169.0 (8 *C*OCH$_3$), 144.2 (C-5″), 121.9 (C-4″), 98.8 (C-1′), 85.8 (C-1), 75.2, 72.6, 72.4, 71.7, 71.1, 70.4, 68.4, 67.7, 61.9, 61.7, 61.5, 20.7 (2 C), 20.5 (4 C), 20.0 (2 C) (8 CO*C*H$_3$); ESI-MS: *m/z*=782.2 $[M+Na]^+$; Anal. Calcd. for $C_{31}H_{41}N_3O_{19}$ (759.66): C, 49.01; H, 5.44; N, 5.53; found: C, 48.82; H, 5.70.

Compound 3m: Oil; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.86 (s, 1 H, H-5″), 5.89 (d, *J*=9.2 Hz, 1 H, H-1), 5.57 (d, *J*=3.1 Hz, 1 H, H-4), 5.52 (t, *J*=9.5 Hz, 1 H, H-2), 5.26 (dd, *J*=10.5 and 3.4 Hz, 1 H, H-3), 5.20 (t, *J*=9.4 Hz, 1 H, H-2′), 5.07 (t, *J*=9.5 Hz, 1 H, H-3′), 5.0 (t, *J*=8.0 Hz, 1 H, H-4′), 4.96–4.78 (AB_q, *J*=12.8 Hz each, 2 H, CH_2O), 4.60 (d, *J*=8.0 Hz, 1 H, H-1′), 4.32–4.09 (m, 5 H, H-5, H-6_{ab} and H-$6'_{ab}$), 3.81–3.78 (m, 1 H, H-5′), 2.23, 2.11, 2.02, 1.98, 1.97, 1.91, 1.89 (7 s, 24 H, 8 COCH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.6, 170.2, 170.1, 169.8, 169.7, 169.4, 169.3, 169.2 (8 *C*OCH$_3$), 144.2 (C-5″), 121.8 (C-4″), 98.8 (C-1′), 86.2 (C-1), 74.0, 72.6, 71.7, 71.0, 70.5, 68.3, 67.9, 66.8, 61.8, 61.7, 61.1, 20.6 (2 C), 20.5 (3 C), 20.4 (2 C), 20.1 (8 CO*C*H$_3$); ESI-MS: *m/z*=782.3 $[M+Na]^+$; Anal. Calcd. for $C_{31}H_{41}N_3O_{19}$ (759.66): C, 49.01; H, 5.44; N, 5.53; found: C, 48.80; H, 5.65.

Compound 3n: Oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.04 (br s, 3 H), 5.89 (d, *J*=9.2 Hz, 3 H), 5.61 (br s, 3 H), 5.56–5.52 (m, 3 H), 5.28 (dd, *J*=10.3 and 3.2 Hz, 3 H), 4.28–4.22 (m, 3 H), 4.18 (m, 6 H), 2.23, 2.04, 2.01, 1.87 (4 s, 36 H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.7 (3 C), 170.3 (3 C), 170.0 (3 C), 169.8 (3 C), 169.0 (3 C), 142.9 (3 C), 122.3 (3 C), 86.2 (3 C), 74.0 (3 C), 70.7 (3 C), 67.8 (3 C), 66.8 (3 C), 61.5 (3 C), 61.1 (3 C), 20.6 (3 C), 20.4 (6 C), 20.2 (3 C); ESI-MS: *m/z*=1363.4 [M]; 1386.2 $[M+Na]^+$; Anal. Calcd. for $C_{31}H_{41}N_3O_{19}$ (759.66): $C_{54}H_{66}N_{12}O_{30}$ (1363.16): C, 47.58; H, 4.88; found: C, 47.40; H, 5.10.

Acknowledgments Instrumentation facilities from SAIF, CDRI is gratefully acknowledged. R.K. thanks CSIR, New Delhi for providing a Senior Research Fellowship. This project was partly funded by Ramanna Fellowship (AKM), Department of Science and Technology (DST), New Delhi, India.

References

1. Garcia-Lopez, J.J., Santoyo-Gonzalez, F., Vargas-Berenguel, A.: Efficient one-pot syntheses of chloroacetyl and S-acetylmercaptoacetyl N-glycosides from glycosyl azides. Synlett, 265–266 (1997)
2. Garcia-Lopez, J.J., Santoyo-Gonzalez, F., Vargas-Berenguel, A., Gimenez-Martinez, J.J.: Synthesis of cluster N-glycosides based on a β-cyclodextrin core. Chem. Eur. J. **5**, 1777–1784 (1999)
3. Malkinson, J.P., Falconer, R.A., Toth, I.: Synthesis of *C*-terminal glycopeptides from resin-bound glycosyl azides via a modified Staudinger reaction. J. Org. Chem. **65**, 5249–5252 (2000)
4. Thiem, J., Wiemann, T.: Combined chemoenzymatic synthesis of N-glycoprotein building blocks. Angew. Chem. Int. Ed. Engl. **29**, 80–82 (1990)
5. Gyorgydeak, Z., Szilagyi, L., Paulsen, H.: Synthesis, structure and reactions of glycosyl azides. J. Carbohydr. Chem. **12**, 139–163 (1993)
6. Al-Masoudi, N.A., Al-Soud, Y.A.: Synthesis of 1′-β-D-glucopyranosyl-1,2,3-triazole-4,5-dimethanol-4,5-bis(isopropylcarbamate) as potential antineoplastic agent. Tetrahedron Lett. **43**, 4021–4022 (2002)
7. Al-Masoudi, N.A., Al-Soud, Y.A.: New glycosyl-(carboxamide)-1,2,3-triazole-*N*-nucleosides: synthesis and antitumor activity. Nucleosides Nucleotides Nucleic Acids **21**, 361–375 (2002)
8. Broder, W., Kunz, H.: A new method of anomeric protection and activation based on the conversion of glycosyl azides into glycosyl fluorides. Carbohydr. Res. **249**, 221–241 (1993)
9. Anisfeld, S.T., Lansbury Jr., P.T.: A convergent approach to the chemical synthesis of asparagine-linked glycopeptides. J. Org. Chem. **55**, 5560–5562 (1990)
10. Kunz, H., Dombo, B.: Solid phase synthesis of peptides and glycopeptides on polymeric supports with allylic anchor groups. Angew. Chem., Int. Ed. Engl. **27**, 711–713 (1988)
11. Kunz, H., Pfrengle, W.: Asymmetric synthesis on carbohydrate templates: stereoselective Ugi-synthesis of alpha-amino acid derivatives. J. Am. Chem. Soc. **110**, 651–652 (1998)
12. Laschat, S., Kunz, H.: Carbohydrates as chiral templates: stereoselective synthesis of (R)- and (S)-a-aminophosphonic acid derivatives. Synthesis 90–95 (1992)
13. Kunz, H., Sager, W.: Diastereoselective strecker synthesis of α-aminonitriles on carbohydrate templates. Angew. Chem., Int. Ed. Engl. **26**, 557–559 (1987)
14. Fialova, P., Carmona, A.T., Robina, I., Ettrich, R., Sedmera, P., Prikrylova, V., Petraskova-Husakova, L., Kren, V.: Glycosyl azide-a novel substrate for enzymatic transglycosylations. Tetrahedron Lett. **46**, 8715–8718 (2005)
15. Hotha, S., Kashyap, S.: Click chemistry inspired synthesis of *pseudo*-oligosaccharides and amino acid glycoconjugates. J. Org. Chem. **71**, 364–367 (2006)
16. Dominique, R., Das, S.K., Roy, R.: Alkenyl O- and C-glycopyranoside homodimerization by olefin metathesis reaction. Chem. Commun. 2437–2438 (1998)
17. Billing, J.F., Nilsson, U.J.: C_2-symmetric macrocyclic carbohydrate/amino acid hybrids through copper(I)-catalyzed formation of 1,2,3-triazoles. J. Org. Chem. **70**, 4847–4850 (2005)
18. Dondoni, A., Giovanninni, P.P., Massi, A.: Assembling heterocycle-tethered *C*-glycosyl and α-amino acid residues via 1,3-dipolar cycloaddition reactions. Org. Lett. **6**, 2929–2932 (2004)
19. Marmuse, L., Nepogodiev, S.A., Field, R.A.: "Click chemistry" en route to pseudo-starch. Org. Biomol. Chem. **3**, 2225–2227 (2005)
20. Patch, R.J., Chen, H., Pandit, C.R.: Multivalent templated saccharides: convenient syntheses of spacer-linked 1,1′-Bis -and 1,1′,1″-Tris-β-glycosides by the glycal epoxide glycosidation method. J. Org. Chem. **62**, 1543–1546 (1997)
21. Dedola, S., Nepogodiev, S.A., Field, R.A.: Recent applications of the CuI-catalysed Huisgen azide-alkyne 1,3-dipolar cycloaddition reaction in carbohydrate chemistry. Org. Biomol. Chem. **5**, 1006–1017 (2007)
22. Dondoni, A.: Triazole: the Keystone in glycosylated molecular architectures constructed by a click reaction. Chem. Asian J. **2**, 700–708 (2007)
23. Tejler, J., Skogman, F., Leffler, H., Nilsson, U.J.: Synthesis of galactose-mimicking 1*H*-(1,2,3-triazol-1-yl)-mannosides as selective galectin-3 and 9N inhibitors. Carbohydr. Res. **342**, 1869–1875 (2007)
24. Larsen, K., Thygesen, M.B., Guillaumie, F., Willats, W.G.T., Jensen, K.J.: Solid-phase chemical tools for glycobiology. Carbohydr. Res. **341**, 1209–1234 (2006)
25. Tejler, J., Tullberg, E., Frejd, T., Leffler, H., Nilsson, U.J.: Synthesis of multivalent lactose derivatives by 1,3-dipolar cycloadditions: selective galectin-1 inhibition. Carbohydr. Res. **341**, 1353–1362 (2006)
26. Salameh, B.A., Leffler, H., Nilsson, U.J.: 3-(1,2,3-Triazol-1-yl)-1-thio-galactosides as small, efficient, and hydrolytically stable inhibitors of galectin-3. Bioorg. Med. Chem. Lett. **15**, 3344–3346 (2005)
27. Thomas, J.R., Liu, X., Hergenrother, P.J.: Size-specific ligands for RNA hairpin loops. J. Am. Chem. Soc. **127**, 12434–12435 (2005)
28. Wilkinson, B.L., Bornaghi, L.F., Houston, T.A., Innocenti, A., Supuran, C.T., Poulsen, S.A.: A novel class of carbonic anhydrase inhibitors: glycoconjugate benzene sulfonamides prepared by "click-tailing". J. Med. Chem. **49**, 6539–6548 (2006)
29. Perez-Balderas, F., Ortega-Munoz, M., Morales-Sanfrutos, J., Hernandez-Mateo, F., Calvo-Flores, F.G., Calvo-Asin, J.A., Isac-Garcia, J., Santoyo-Gonzalez, F.: Multivalent neoglycoconjugates by regiospecific cycloaddition of alkynes and azides using organic-soluble copper catalysts. Org. Lett. **5**, 1951–1954 (2003)
30. Bodine, K.D., Gin, D.Y., Gin, M.S.: Synthesis of readily modifiable cyclodextrin analogues via cyclodimerization of an alkynyl-azido trisaccharide. J. Am. Chem. Soc. **126**, 1638–1639 (2004)

31. Hoogenboom, R., Moore, B.C., Schubert, U.S.: Synthesis of star-shaped poly(e-caprolactone) via 'click' chemistry and 'supramolecular click' chemistry. Chem. Commun. 4010–4012 (2006)
32. Roy, R., Das, S.K., Santoyo-Gonzalez, F., Hernandez-Mateo, F., Dam, T.K., Brewer, C.F.: Synthesis of "sugar-rods" with phytohemagglutinin cross-linking properties by using the palladium-catalyzed sonogashira reaction. Chem. Eur. J. **6**, 1757–1762 (2000)
33. Fazio, F., Bryan, M.C., Blixt, O., Paulson, J.C., Wong, C.H.: Synthesis of sugar arrays in microtiter plate. J. Am. Chem. Soc. **124**, 14397–14402 (2002)
34. Gyorgydeak, Z., Szilagyi, L., Paulsen, H.: Synthesis, structure and reactions of glycosyl azides. J. Carbohydr. Chem. **12**, 139–163 (1993)
35. Sabesan, S., Neira, S.: Synthesis of glycosyl phosphates and azides. Carbohydr. Res. **223**, 169–185 (1992)
36. Tropper, F.D., Andersson, F.O., Braun, S., Roy, R.: Phase transfer catalysis as a general and stereoselective entry into glycosyl azides from glycosyl halides. Synthesis 618–620 (1992)
37. Kunz, H., Sager, W., Schanzenbach, D., Decker, M.: Carbohydrates as chiral templates: stereoselective strecker synthesis of D-α-amino nitriles and acids using O-pivaloylated D-galactosylamine as the auxiliary. Liebigs Ann. Chem. **1991**, 649–654 (1991)
38. Kumar, R., Tiwari, P., Maulik, P.R., Misra, A.K.: A generalized protocol for the one-pot preparation of glycosyl azides and thioglycosides directly from unprotected reducing sugars under phase transfer reaction conditions. Eur. J. Org. Chem. 74–79 (2006)
39. Alvarez, S.G., Alvarez, M.T.: A practical procedure for the synthesis of alkyl azides at ambient temperature in dimethyl sulfoxide in high purity and yield. Synthesis 413–414 (1997)
40. Kacprzak, K.: Efficient one-pot synthesis of 1,2,3-triazoles from benzyl and alkyl halides. Synthesis 943–946 (2005)
41. Kartha, K.P.R., Jennings, H.J.: A simplified one-pot preparation of acetobromo sugars from reducing sugars. Carbohydr. Chem. **9**, 777–781 (1990)
42. Akula, R.A., Temelkoff, D.P., Artis, N.D., Norris, P.: Rapid access to glucopyranosyl-1,2,3-triazoles via Cu(I)-catalyzed reactions in water. Heterocycles **63**, 2719–2725 (2004)
43. Chittabonia, S., Xie, F., Wang, Q.: One-pot synthesis of trizole-linked glycoconjugates. Tetrahedron Lett. **46**, 2331–2336 (2005)
44. Gyorgydeak, Z., Paulsen, H.: Syntheses of β-D-mannopyranosyl azides; investigation of the anomeric structures. Liebigs Ann. Chem. **1977**, 1987–1991 (1977)
45. El Meslouti, A., Beaupere, D., Demailly, G., Uzan, R.: One-pot stereoselective synthesis of glycosyl azides via 1,2-cyclic sulfite. Tetrahedron Lett. **35**, 3913–3916 (1994)
46. Dunstan, D., Hough, L.: Syntheses of cellobiosyl, maltosyl, and lactosyl derivatives of asparagines. Carbohydr. Res. **23**, 17–21 (1972)