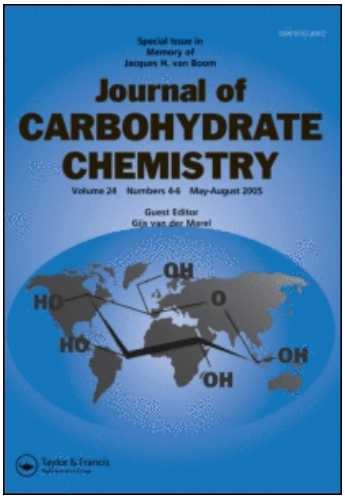

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Synthesis of *N*-(β-Glycopyrano-syl)azidoacetamides

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Synthesis of *N*-(β-Glycopyranosyl)azidoacetamides

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N-(β-Glycopyranosyl)azidoacetamides, mimetics of the widely distributed GlcNAc-Asn linkage in glycoproteins, have been synthesized in good yields starting from β-glycopyranosylamines in four steps involving selective *N*-chloroacetylation, peracetylation catalyzed by Na β-zeolite, displacement of the Cl group by NaN_3 in aqueous acetone, and Zemplen de-*O*-acetylation.

Keywords Azidoacetamide, Carbohydrate, β-Zeolite, *N*-Chloroacetylation

INTRODUCTION

The structural complexity and heterogeneity of the glycoprotein glycans and the difficulties involved in obtaining homogeneous glycoproteins from natural sources in sufficient amounts pose a considerable challenge to the correlation of their structure with myriad biologic functions.[1] In recent years we have witnessed a growing interest in the synthesis of selectively functionalized carbohydrate molecules for preparing structurally well-defined homogeneous neoglycoconjugates. Among these chemical ligating agents,[2] the azido derivatives (Fig. 1) are particularly attractive in view of (a) stability of the azide functionality under a wide variety of chemical and enzymatic[4] conditions, (b) ready conversion under mild conditions to more reactive and rather difficult to handle amino compounds, and (c) rapid, efficient, and selective reaction of alkyl azides with alkynes at room temperature under biologic conditions[5] to form 1,2,3-triazole derivatives. The 2-azidoethyl *O*-glycosides and the recently developed glycosylthiomethyl azides[2b] are mimetics of the linkage region in *O*-glycoproteins.

The β-*N*-glycosidic linkage of GlcNAc to Asn represents the most widely distributed carbohydrate-peptide bond[6] (Fig. 2). A large variety of glycan chains are

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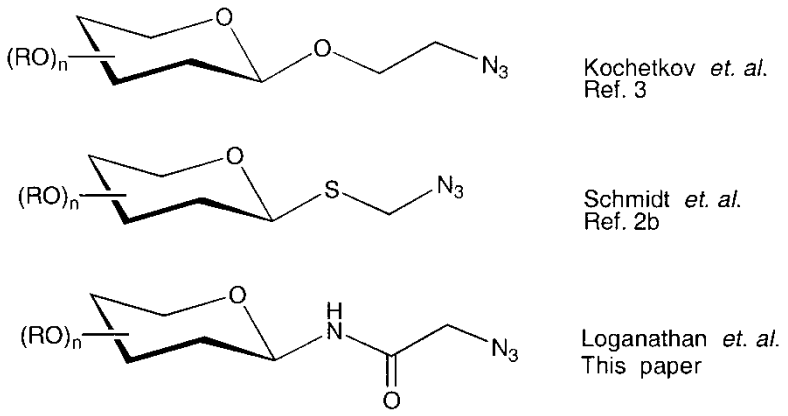


Figure 1: Azidoalkyl sugar derivatives.

found attached through this linkage to proteins with demonstrated biologic importance.[1a] There has, however, been no report on the use of *N*-linked azido derivatives for the preparation of neoglycoconjugates. Herein we report a simple and effective method for the synthesis of *N*-(β-glycopyranosyl)azidoacetamides, useful as chemical ligating agents, starting from glycopyranosylamines.

RESULTS AND DISCUSSION

Glycosylamines are chosen as synthons in the present work (Sch. 1) because these have a tendency to adopt β-anomeric configuration and, hence, the derived ligating agents would possess the natural *N*-glycosidic linkage. Moreover, a large number of glycosylamines have been prepared in reasonably good yields from both simple sugars and complex oligosaccharides by reaction with either ammonia in methanol[7a] or saturated ammonium bicarbonate in an aqueous medium.[7b] The Kochetkov amination procedure affords β-glycosylamines with >95%

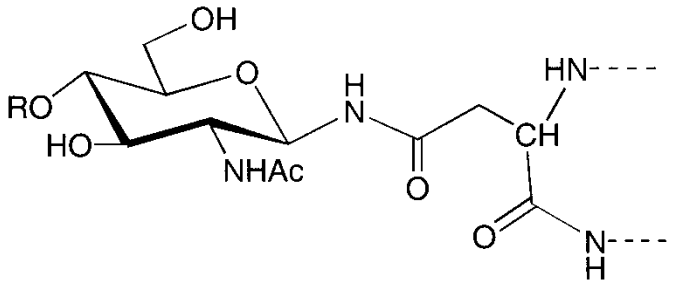
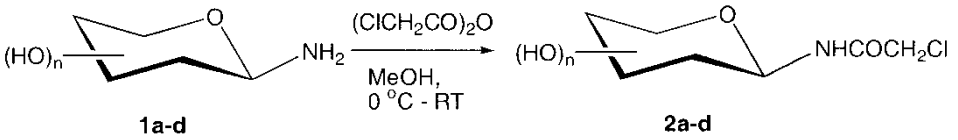


Figure 2: Linkage region of *N*-glycoproteins.

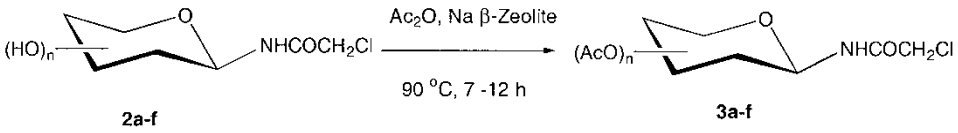


Scheme 1: Chloroacetylation of β-glycopyranosylamines.

stereoselectivity.[8] Glycopyranosylamines **1a**–**f** required for this study were prepared by one of these methods as indicated in the experimental section.

N-Chloroacetylation of β-glycopyranosylamines was first reported by Manger et al.[9] in 1M aqueous sodium bicarbonate medium using 10-fold excess of chloroacetic anhydride. This reaction has typically been performed in microgram scale and with glycosylamines derived from saccharides containing GlcNAc at the reducing end. A more general and preparative method was developed by Likhosherstov et al.[10] employing DMF as the medium and a slight excess of chloroacetic anhydride. Under these conditions, however, *O*-acylation also occurred, warranting an additional step of treatment with triethylamine before the isolation of the desired product. We have recently found that treatment of β-D-glycopyranosylamines **1a**–**b** with chloroacetic anhydride (1.7 equiv.) in dry methanol results in the separation of solid product, which could simply be filtered and recrystallized from aqueous methanol. The analytically pure chloroacetamido derivatives, **2a**–**b**, thus obtained in good yields were subsequently examined by X-ray crystallography, which revealed interesting differences in their structures.[11] Extension of this convenient and preparative method during the present work to the selective *N*-chloroacetylation of **1c**–**d** also afforded crystalline products in good yields (**2c**: 65%; **2d:** 69%). The reactions of amines **1e**–**f** derived from D-xylose and L-rhamnose, however, did not afford any solid product even after evaporation of the solvent.

The pure (**2a**–**d**) and crude (**2e**–**f**) chloroacetamido derivatives were then taken up for peracetylation (Sch. 2). Though acetylation of sugars is usually performed using acetic anhydride in pyridine, this method was not preferred in the present work in view of the potential nucleophilic displacement of the halo group in general by pyridine and its well-known toxicity. We have earlier demonstrated H β-zeolite as an efficient and environment-friendly solid acid catalyst for the peracetylation of mono- and disaccharides.[12] In the present study, peracetylation of **2a**–**f** was indeed brought about in good yields (Table 1)



Scheme 2: Preparation of fully acetylated *N*-(β-glycopyranosyl)chloroacetamides.

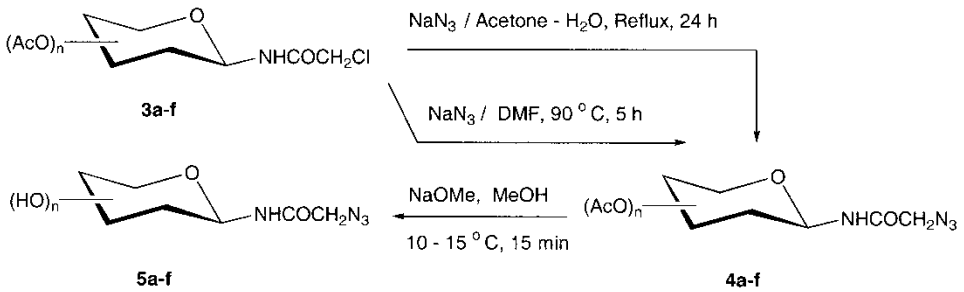
Table 1: Peracetylation of *N*-(β-glycopyranosyl)chloroacetamides.

Entry	Reactant	Sugar	Time (hr)	Product	Yield (%)[a]
1	**2a**	Glc	8	**3a**[16]	87
2	**2b**	Gal	10	**3b**[16]	76
3	**2c**	Man	10	**3c**[16]	79
4	**2d**	GlcNAc	12	**3d**[16]	81
5	**2e**	Xyl	8	**3e**	60
6	**2f**	L-Rha	7	**3f**	40

[a]Corresponds to the isolated pure product.

by using even the commercially available sodium form as such under heating. After completion of reaction as shown by the disappearance of the starting material on TLC, filtration of the catalyst followed by simple work-up afforded the products **3a**–**d** in pure form, while chromatographic purification was required only for the products derived from the crude chloroacetamido derivatives **2e**–**f**. All compounds **3a**–**f** were characterized based on their physical and spectral data.

Displacement of the chloro group in **3a**–**f** by azide was carried out initially using NaN_3 in dry DMF medium at 90°C to obtain the azidoacetamido derivatives, **4a**–**f** (Sch. 3). All these compounds exhibited the characteristic azide group stretching in their IR spectrum around 2100 cm^{-1}, and the signal due to the methylene carbon appeared typically around δ 52.5 ppm upfield, shifted from a value of about 42 ppm observed for that of the corresponding chloroacetamido derivatives. Though the TLC monitoring of the reaction indicated the near disappearance of the starting material in these reactions, product recovery was not efficient as reflected in the moderate yields obtained (Table 2). Satisfyingly, replacement of DMF by aqueous acetone as employed recently in similar displacement reactions[2b,13] led to considerable yield improvement (Sch. 3, Table 2). De-*O*-acetylation of **4a**–**f** was accomplished quantitatively by treatment with NaOMe (0.5 equiv.) in methanol for 15 min to furnish the free azidoacetamido derivatives **5a**–**f**.



Scheme 3: Preparation of fully acetylated *N*(β-glycopyranosyl)azidoacetamides.

Table 2: Conversion of chloro- to azidoacetamido sugars.

				Yield (%)[a]	
Entry	**Reactant**	**Sugar**	**Product**	**Method A**	**Method B**
1	**3a**	Glc	**4a**	80	95
2	**3b**	Gal	**4b**	68	92
3	**3c**	Man	**4c**	67	83
4	**3d**	GlcNAc	**4d**[14]	70	91
5	**3e**	Xyl	**4e**	65	81
6	**3f**	L-Rha	**4f**	N.P.	91

Method A: NaN_3/DMF; Method B: NaN_3/Acetone-H_2O; N.P: Not performed.
[a]Corresponds to the isolated pure product.

All the fully acetylated and the free azidoacetamido derivatives, except **4d** and **5d**, synthesized in the present study are hitherto unknown. Compound **4d** has earlier been obtained[14] by reacting relatively expensive lithium azide in dry acetone at 60°C to 65°C for 16 hr with the corresponding chloroacetamido derivative, **3d**, which in turn was prepared from 2-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl azide by catalytic reduction. De-*O*-acetylation of **4d** was performed using 10% triethylamine in aqueous methanol to give **5d** in only 85% yield. No other azidoacetamido derivatives have been prepared using this method. More importantly, the methodology employed has several limitations. Catalytic reduction of fully acetylated glycosyl azides is known to be complicated by inter- or intramolecular migration of an *O*-acetyl group to yield undesired 1-*N*-amido derivatives.[15] Although the Staudinger reaction of glycosyl azides serves as an alternative method, the phosphinimine intermediate formed shows poor reactivity in some cases resulting in low yield or formation of an inseparable mixture of anomeric chloroacetamido derivatives.[16]

In conclusion, the title compounds have been synthesized starting from β-glycopyranosylamines using a simple and convenient set of reactions, including the readily available sodium β-zeolite catalyzed peracetylation, which is reported for the first time. The use of a non-nucleophilic catalyst in place of the typically employed pyridine would be particularly suitable for the peracetylation of more labile bromo- and iodoacetamido sugar derivatives. Alternatively, the free *N*-(β-glycopyranosyl)chloroacetamides prepared in two steps from parent sugars could be transformed to a variety of protected derivatives prior to their conversion to the corresponding azidoacetamido sugars.

EXPERIMENTAL

Thin layer chromatograms were performed on 25 mm E. Merck silica gel plates (60F-254). Detection was done by spraying the plates with 10% sulfuric acid in ethanol and heating on a hot plate. Column chromatography was performed

using silica gel (230–400 mesh) under flash conditions using a mixture of ethyl acetate and hexane. Melting points were determined on a Toshniwal melting point apparatus and are uncorrected. Optical rotation was measured at 30°C on a JASCO-DIP 200 digital polarimeter using a cell of 10 mm length. Infrared spectra were recorded on a Shimadzu R-470 spectrophotometer. NMR spectra were recorded on a Bruker AV400 spectrometer. ESI-MS spectra were measured on a Micromass Q-Tof mass spectrometer. All sugars used were purchased from Sigma-Aldrich USA or from Pfanstiehl Laboratories Inc. USA and used as such: Beta zeolite (Na form) was obtained from Süd-Chemie India Ltd., New Delhi, and activated by heating to 250°C prior to use. Chloroacetic anhydride and NaN_3 were purchased from Acros Organics, Belgium. Glycopyranosylamines **1a–c** and **1e** were obtained as crystalline solids using the procedure of Isbell & Frush,[7a] and **1d** and **1f** were prepared by the Kochetkov amination method.[7b] Toluene, acetone, ethyl acetate, hexane, chloroform, dichloromethane, methanol, and Ac_2O were of laboratory grade, and all were distilled once before use. Dry methanol was prepared by using Mg and iodine, dry DMF was prepared by treatment with CaH_2, and both these solvents were further dried over 4 Å molecular sieves.

General Procedure for the Chloroacetylation of β-Glycopyranosylamines (1a–f)

The procedure recently reported[11] for the selective *N*-chloroactylation of **1a–b** was extended to **1c–f**. Products derived from **1c–d** were separated out from the reaction mixture as solids and were purified by crystallization from aqueous methanol. Both these products were fully characterized based on their physical and spectral data and their comparison with those reported in literature.[10] In the case of **1e–f** where no solid product separation was noticed, the reaction mixture was concentrated to dryness. The syrup obtained was washed with ethyl acetate to remove anhydride or acid impurities and used as such for the next step.

General Procedure for the Preparation of Fully Acetylated *N*-(β-Glycopyranosyl)chloroacetamides (3a–f)

A mixture of *N*-chloroacetylated glycopyranosylamine (1.5 mmol) and activated Na β-zeolite (0.7 g) was placed in a 100 mL RB flask to which acetic anhydride (12 mmol) was added. The mixture was heated for 7 to 12 hr at 90°C under stirring. Following completion of the reaction as shown by TLC analysis using ethyl acetate/hexane (1:1) as the eluent, the contents of the flask were cooled to room temperature. The solid mass was diluted with chloroform (50 mL), refluxed for 15 min, and filtered to remove the catalyst, which was extracted two more times with refluxing chloroform (50 mL each) for better recovery of

the product. The combined filtrate was concentrated under reduced pressure, co-evaporated with toluene to remove unreacted acetic anhydride, and recrystalized from ethyl acetate-hexane mixture (1:1) to obtain analytically pure product. All the products obtained were fully characterized based on their physical and spectral data and their comparison with those reported in literature.[16]

N-(2,3,4-Tri-O-acetyl-β-D-xylopyranosyl)chloroacetamide (3e)

M.p 175°C; $[\alpha]_D = 9.2$ (c 1, $CHCl_3$); IR(ν, cm^{-1}): 3435, 2954, 1758, 1673, 1591, 1382, 1353, 1224, 1067, 1040, 992; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.43 (d, 1H, J = 9.0 Hz, NH), 5.32 (t, 1H, J = 9.4 Hz, H-3), 5.15 (t, 1H, J = 9.0 Hz, H-1), 5.00–4.96 (m, 2H, H-4 & H-2), 4.11 (m, 1H, H-5a), 4.07 and 4.01 (AB q, 2H, -CH_2Cl), 3.47 (t, 1H, J = 11.0 Hz, H-5b), 2.07, 2.06, and 2.05 ppm (3s, 9H, 3 × -COCH_3); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.8, 169.9, 169.8, 167.0 (-NHCO-), 78.9 (C-1), 72.0, 70.3, 68.8, 64.5 (C-6), 42.2 (-CH_2Cl), 20.7, 20.6, 20.5 (3 × −COCH_3); ESI-MS: Calcd for C_{13} H_{18} N O_8 Cl Na ($[M + Na]^+$): 374.0623. Found 374.0619.

N-(2,3,4-Tri-O-acetyl-β-L-rhamnopyranosyl)chloroacetamide (3f)

M.p 122°C; $[\alpha]_D = 2.2$ (c 1, $CHCl_3$); IR (ν, cm^{-1}): 3391, 2924, 1754, 1691, 1530, 1370, 1258, 1228, 1058, 977; ^{1}H-NMR ($CDCl_3$): δ 7.20 (br d, 1H, NH), 5.49 (d, 1H, J = 9.2 Hz, H-1), 5.38 (m, 1H, H-2), 5.11–5.01 (m, 2H, H-3 and H-4), 4.08 (m, 2H, CH_2Cl), 3.67 (m, 1H, H-5), 2.25, 2.08, 2.00 (3s, 9H, 3 × COCH_3), 1.26 ppm (d, CH_3); ^{13}C-NMR ($CDCl_3$): 170.1, 169.8, (3 × COCH_3), 165.3 (NHCO), 76.7 (C-1), 75.9, 72.5, 71.3, 70.0, 42.4 (CH_2Cl), 20.7, 20.6, 20.5 ppm (3 x COCH_3), 17.4 (CH_3); ESI-MS: Calcd for C_{14} H_{20} N O_8 Cl Na ($[M + Na]^+$): 388.0775. Found 388.0778.

General Procedure for the Preparation of Fully Acetylated *N*-(β-Glycopyranosyl)azidoacetamides (4a–f)

Method A: (NaN_3/DMF)

To the peracetylated *N*-(β-glycopyranosyl)chloroacetamide (**3a**–**f**) (1 mmol) taken in a 100 mL RB flask was added to dry DMF (8 mL) followed by the addition of NaN_3 (5 mmol). The reaction mixture was heated to 90°C under stirring. Progress of the reaction was monitored by TLC using ethyl acetate and hexane (1:1) as the eluent. After 5 hr, the reaction mixture was cooled and diluted with ethyl acetate. The ethyl acetate solution was washed with water several times, dried over sodium sulfate, and concentrated to dryness to obtain a syrupy or solid product.

Method B: (NaN_3/Acetone–H_2O)

To the peracetylated *N*-(*β*-glycopyranosyl)chloroacetamide (**3a–f**) (1 mmol) taken in a 100 mL RB flask was added acetone (15 mL) and water (7 mL), followed by the addition of NaN_3 (5 mmol). The reaction mixture was refluxed for 24 hr. The reaction mixture was then cooled and diluted with ethyl acetate. The organic layer was separated, dried over sodium sulfate, and concentrated to dryness to obtain a syrupy or solid product.

General Procedure for the Preparation of *N*-(β-Glycopyranosyl)azidoacetamides (5a–f)

The peracetylated *N*-(*β*-glycopyranosyl)azidoacetamide (1 mmol) was dissolved in 10 mL of dry MeOH cooled to 10°C to 15°C. To this solution, freshly prepared NaOMe (1 M, 0.5 mL) was added and stirred for 15 min. The reaction mixture was then treated with IR-120 ion-exchange resin. After filtration of the resin, the filtrate was concentrated to give syrup in quantitative yield.

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)azidoacetamide (4a)

$[\alpha]_D = 4.1$ (c 1, $CHCl_3$); IR (ν, cm^{-1}): 3328, 2944, 2112, 1750, 1677, 1532, 1376, 1213, 1036, 906; ^{1}H-NMR ($CDCl_3$): δ 7.18 (d, 1H, J = 9.2 Hz, NH), 5.33 (t, 1H, J = 9.5 Hz, H-3), 5.24 (t, 1H, J = 9.3 Hz, H-1), 5.09 (t, 1H, J = 9.7 Hz, H-4), 4.99 (t, 1H, J = 9.5 Hz, H-2), 4.31 (dd, 1H, J = 4.2 & 12.5 Hz, H-6a), 4.10 (m, 1H, H-6b), 4.02 and 3.96 (ABq, CH_2N_3), 3.86 (m, 1H, H-5), 2.10, 2.07, 2.05, 2.04 ppm (4s, 12H, 4 × COCH_3); ^{13}C-NMR ($CDCl_3$): δ 170.8, 170.6, 169.8, 169.5 (4 × *C*OCH$_3$), 167.5 (NH*C*O), 78.1 (C-1), 73.8, 72.6, 70.4, 68.1, 61.6 (C-6), 52.5 (*C*H$_2$N$_3$), 20.6–20.5 ppm (4 × CO*C*H$_3$); ESI-MS: Calcd for C_{16} H_{22} N_4 O_{10} Na ($[M + Na]^+$): 453.1234. Found 453.1223.

N-(2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl)azidoacetamide (4b)

$[\alpha]_D = 25.9$ (c 1, $CHCl_3$); IR (ν, cm^{-1}): 3396, 3072, 2112, 1740, 1680, 1545, 1443, 1366, 1232, 1049, 905; ^{1}H-NMR ($CDCl_3$): δ 7.19 (d, 1H, J = 8.6 Hz, NH), 5.45 (s, 1H, H-4), 5.26–5.10 (m, 3H, H-1, H-2 & H-3), 4.20–4.04 (m, 3H, H-6a, H-6b and H-5), 4.02 and 3.97 (ABq, CH_2N_3), 2.16, 2.07, 2.05, 2.01 ppm (4s, 12H, 4 × COCH_3); ^{13}C-NMR ($CDCl_3$): δ 171.1, 170.3, 170.0, 169.7 (4 × *C*OCH$_3$), 167.4, 78.4 (C-1), 72.5, 70.7, 68.2, 67.1, 61.1 (C-6), 52.5 (*C*H$_2$N$_3$), 20.6–20.4 ppm (4 × CO*C*H$_3$).; HR MS: ESI-MS; Calcd for C_{16} H_{22} N_4 O_{10} Na ($[M + Na]^+$): 453.1234. Found 453.1387.

N-(2,3,4,6-Tetra-O-acetyl-β-D-mannopyranosyl)azidoacetamide (4c)

$[\alpha]_D = -5.3$ (c 1, $CHCl_3$); IR (ν, cm^{-1}): 3380, 2946, 2112, 1750, 1686, 1548, 1363, 1228, 1053, 903; ^{1}H-NMR ($CDCl_3$): δ 6.99 (d, 1H, J = 9.3 Hz, NH), 5.55 (d 1H, J = 9.2 Hz, H-1), 5.37 (m, 1H, H-2), 5.25 (t, 1H, J = 9.9 Hz, H-4), 5.13

(dd, 1H, J = 3.3 and 10.2 Hz, H-3), 4.31 (dd, 1H, J = 5.2 and 12.4 Hz, H-6a), 4.11 (dd, 1H, J = 2.0 and 12.4 Hz, H-6b), 4.04 (s, 2H, CH_2N_3), 3.80 (m, 1H, H-5), 2.27, 2.12, 2.06, 2.00 ppm (4s, 12H, 4 × COCH_3); ^{13}C-NMR ($CDCl_3$): δ 170.6, 170.3, 169.8, 169.6 (4 × COCH$_3$), 166.1 (NHCO), 76.0 (C-1), 74.4, 71.4, 69.9, 65.2, 62.2 (C-6), 52.4 (CH$_2$N$_3$), 20.8–20.5 ppm (4 × COCH$_3$); ESI-MS: Calcd for C_{16} H_{22} N_4 O_{10} Na ($[M + Na]^+$): 453.1234. Found 453.1228.

N-(3,4,6-Tri-O-acetyl 2-acetamido-2-deoxy-β-D-glucopyranosyl)azidoacetamide(4d)

$[\alpha]_D = -1.7$ (c 1, $CHCl_3$), [Lit.,[14] −2.1 (c 1.06, $CHCl_3$)]; (IR (ν, cm^{-1}): 3360, 2112, 1744, 1684, 1657, 1587, 1548, 1382, 1260, 1222, 1078, 1056, 905; ^{1}H-NMR ($CDCl_3$): δ 7.75 (d, 1H, J = 8.1 Hz, NH), 6.05 (d, 1H, J = 7.9 Hz, NH), 5.16 (t, 1H, J = 9.7 Hz, H-4), 5.12–5.02 (m, 2H, H-3 & H-1), 4.31 (dd, 1H, J = 4.2 and 12.5 Hz, H-6a), 4.26–4.14 (m, 1H, H-2), 3.97 and 3.91 (ABq, -CH_2N_3), 3.80 (m, 1H, H-5), 2.12, 2.11, 2.07, (3s, 9H, 3 × COCH_3), 1.98 ppm (s, 3H, NHCOCH_3); ^{13}C-NMR ($CDCl_3$): 172.0, 171.9, 170.6, 169.2, 168.0 (-NHCO), 80.3 (C-1), 73.7, 72.9, 67.7, 61.7 (C-6), 53.3 (C-2), 52.5 (CH$_2$N$_3$), 23.0, 20.7, 20.6, 20.5 (4 × COCH$_3$); ESI-MS: Calcd for C_{16} H_{24} N_5 O_9 ($[M + H]^+$): 430.1573. Found 430.1468.

N-(2,3,4-Tri-O-acetyl-β-D-xylopyranosyl)azidoacetamide (4e)

$[\alpha]_D = 2.4$ (c 1, $CHCl_3$); IR (ν, cm^{-1}): 3312, 2944, 2128, 1740, 1673, 1526, 1372, 1232, 1078, 1036, 899; ^{1}H-NMR ($CDCl_3$): δ 7.18 (d, 1H, J = 9.0 Hz, NH), 5.33 (t, 1H, J = 9.2 Hz, H-3), 5.15 (t, 1H, J = 9.1 Hz, H-1), 5.00 (m, 1H, H-4), 4.93 (t, 1H, J = 9.2 Hz, H-2), 4.10 (m, 1H, H-5a), 4.02 and 3.97 (ABq, CH_2N_3), 3.47 (m, 1H, J = 9.8 Hz, H-5b), 2.10, 2.08, 2.06 ppm (3s, 9H, 3 × COCH_3); ^{13}C-NMR ($CDCl_3$): δ 171.0, 169.9, 169.8 (3 × COCH$_3$), 167.6 (NHCO), 78.6 (C-1), 72.0, 70.5, 68.9, 64.5, 52.5 (CH$_2$N$_3$), 20.7–20.6 ppm (3 × COCH$_3$); ESI-MS: Calcd for C_{13} H_{18} N_4 O_8 Na ($[M + Na]^+$): 481.1022. Found 481.1021.

N-(2,3,4-Tri-O-acetyl-β-L-rhamnopyranosyl)azidoacetamide (4f)

$[\alpha]_D = 12.6$ (c 1, $CHCl_3$); IR (ν, cm^{-1}): 3391, 2924, 2099, 1755, 1685, 1529, 1372, 1257, 1228, 1079, 1061, 975; ^{1}H-NMR ($CDCl_3$): δ 6.94 (d, 1H, J = 9.2 Hz, NH), 5.52 (d, 1H, J = 9.2 Hz, H-1), 5.37 (m, 1H, H-2), 5.12–5.02 (m, 2H, H-3 and H-4), 4.05 (s, 2H, CH_2N_3), 3.67 (m, 1H, H-5), 2.27, 2.09, 2.01 (3s, 9H, 3 × COCH_3), 1.27 ppm (d, 3H, J = 6.1 Hz, CH_3); ^{13}C-NMR ($CDCl_3$): 170.4–169.9, (3 × COCH$_3$), 166.2 (NHCO), 76.5 (C-1), 75.6, 73.6, 71.3, 70.1, 52.5 (CH$_2$N$_3$), 21.0–20.5 ppm (3 × COCH$_3$), 17.4 (CH$_3$); ESI-MS: Calcd for C_{14} H_{20} N_4 O_8 Na ($[M + Na]^+$): 395.1179. Found 395.1192.

N-(β-D-Glucopyranosyl)azidoacetamide (5a)

$[\alpha]_D = -61.4$ (c 1, H_2O); IR (ν, cm^{-1}): 3408, 2880, 2112, 1683, 1542, 1278, 1075, 1014, 902; ^{1}H-NMR (D_2O): δ 4.89 (d, 1H, J = 9.1 Hz, H-1), 3.98 (s, 2H, CH_2N_3), 3.75 (dd, 1H, J = 2.0 and 12.3 Hz, H-6a), 3.60 (dd, 1H, J = 4.9 and 12.3 Hz, H-6b), 3.46–3.38 (m, 2H, H-4 and H-5) 3.35–3.27 ppm (m, 2H, H-2 & H-3); ^{13}C-NMR (D_2O): δ 174.2 (NH*C*O), 81.7 (C-1), 80.1, 78.8, 74.1, 71.6, 62.9 (C-6), 51.3 (*C*H_2N_3); ESI-MS: Calcd for C_8 H_{14} N_4 O_6 Na ($[M + Na]^+$): 285.0811. Found 285.0833.

N-(β-D-Galactopyranosyl)azidoacetamide (5b)

$[\alpha]_D = 14.5$ (c 1, H_2O); IR (ν, cm^{-1}): 3397, 2920, 2118, 1683, 1547, 1423, 1384, 1262, 1085, 784; ^{1}H-NMR (D_2O): δ 4.86 (d, 1H, J = 8.7 Hz, H-1), 4.00 (s, 2H, CH_2N_3), 3.88 (d, 1H, J = 3.0 Hz, H-4), 3.72–3.53 ppm (m, 5H, H-2, H-3, H-5, H-6a, and H-6b); ^{13}C-NMR (D_2O): δ 171.8 (NH*C*O), 79.8 (C-1), 76.9, 73.4, 69.3, 68.7, 61.0 (C-6), 51.8 ppm (*C*H_2N_3); ESI-MS: Calcd for C_8 H_{14} N_4 O_6 Na ($[M + Na]^+$): 285.0811. Found 285.0807.

N-(β-D-Mannopyranosyl)azidoacetamide (5c)

$[\alpha]_D = 4.1$ (c 1, H_2O); IR (ν, cm^{-1}): 3400, 2921, 2851, 2117, 1603, 1541, 1416, 1384, 1259, 1081, 797; ^{1}H-NMR (D_2O): δ 5.18 (s, 1H, H-1), 4.01 (s, 2H, CH_2N_3), 3.85 (m, 1H, H-2), 3.80 (dd, 1H, J = 1.8 and 12.3 Hz, H-6a), 3.65–3.58 (m, 2H, H6b and H-3), 3.50 (t, 1H, J = 9.7 Hz, H-4), 3.38 ppm (m, 1H, H-5); ^{13}C-NMR (D_2O): δ 170.8 (NH*C*O), 77.9 (C-1), 77.6, 73.3, 70.1, 66.4, 60.9 (C-6), 51.7 (*C*H_2N_3); ESI-MS: Calcd for C_8 H_{14} N_4 O_6 Na ($[M + Na]^+$): 285.0811. Found 285.0814.

N-(2-Acetamido-2-deoxy-β-D-glucopyranosyl)azidoacetamide (5d)

$[\alpha]_D = 38.7$ (c 1, H_2O); [Lit.,[14] 37.8 (c 1, H_2O)]; IR (ν, cm^{-1}): 3333, 3264, 2849, 2108, 1681, 1655, 1543, 1425, 1384, 1292, 1251, 1090, 1041, 892; ^{1}H-NMR (D_2O): δ 5.01 (d, 1H, J = 9.6 Hz, H-1), 3.98 and 3.91 (ABq, 2H, CH_2N_3), 3.84–3.72 (m, 2H, H-6a & H-2), 3.67 (dd, 1H, J = 4.3 and 12.2 Hz, H-6b), 3.55 (m, 1H, H-3), 3.49–3.36 (m, 2H, H-5 and H-4), 1.93 ppm (s, 3H, COCH_3); ^{13}C-NMR (D_2O): δ 175.0, 172.0, 78.7 (C-1), 77.7, 74.0, 69.6, 60.6 (C-6), 54.3 (C-2), 51.0 (*C*H_2N_3), 22.0 ppm (CO*C*H_3); ESI-MS: Calcd for C_{10} H_{17} N_5 O_6 Na ($[M + Na]^+$): 326.1077. Found 326.1062.

N-(β-D-Xylopyranosyl)azidoacetamide (5e)

$[\alpha]_D = 11.6$ (c 1, H_2O); IR (ν, cm^{-1}): 3412, 2923, 2117, 1680, 1547, 1423, 1384, 1262, 1085, 784, 701; ^{1}H-NMR (D_2O): δ 4.83 (d, 1H, J = 8.9 Hz, H-1), 3.99 (s, 2H, CH_2N_3), 3.84 (dd, 1H, J = 5.4 and 11.4 Hz, H-5a), 3.52 (m, 1H, H-4), 3.40 (t, 1H, J = 9.0 Hz, H-3), 3.33 (t, 1H, J = 8.9 Hz, H-2), 3.29 ppm (t, 1H, H-5b); ^{13}C-NMR (D_2O): δ 171.7, 80.0 (C-1), 76.5, 71.5, 68.9, 66.9, 51.7

(CH_2N_3); ESI-MS: Calcd for C_7 H_{12} N_4 O_5 Na ($[M + Na]^+$): 255.0705. Found 255.0714.

N-(β-L-Rhamnopyranosyl)azidoacetamide (5f)

$[\alpha]_D = -62.5$ (c 1, H_2O); IR (ν, cm^{-1}): 3401, 2922, 2117, 1681, 1538, 1423, 1384, 1262, 1071 1023, 801; ^{1}H-NMR (D_2O): δ 5.12 (s, 1H, H-1), 3.98 (m, 2H, CH_2N_3), 3.82 (m, 1H, H-2), 3.54 (dd, 1H, J = 3.4 and 9.7 Hz, H-3), 3.37 (m, 1H, H-5), 3.25 (t, 1H, J = 9.6 Hz, H-4), 1.16 ppm (d, 3H, J = 6.1 Hz, CH_3); ^{13}C-NMR (D_2O): δ 170.7, 77.4 (C-1), 73.8, 72.9, 71.6, 70.0, 51.5 (CH_2N_3), 16.7 ppm (CH_3); ESI-MS: Calcd for C_8 H_{14} N_4 O_5 Na ($[M + Na]^+$): 269.0862. Found 269.0854.

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