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Note

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Nascent-HBr Catalyzed Removal of Orthogonal Protecting Groups in Aqueous Surfactants

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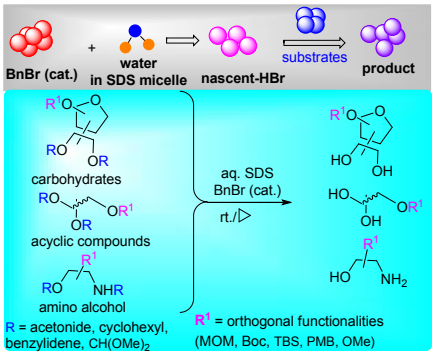
ABSTRACT:

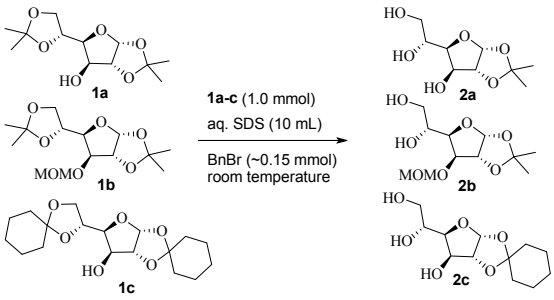


Organic reactions in the aqueous environment have recently emerged as a promising research area. The generation of nascent-HBr from the slow hydrolysis of the dispersed catalyst, benzyl bromide with the interior water present in the hydrophobic core of the confined micellar medium in aqueous surfactant is described for the first time. The sustained-release nascent-HBr enabled the chemoselective cleavages of acid-sensitive orthogonal functionalities present in carbohydrates, amino alcohols and hydroxylated acyclic compounds in good to excellent yields.

Masking and demasking of organic functional groups[1] with high chemoselectivity, mildness and efficiency is a challenging task in synthetic organic chemistry. It is due to the consequences of undesired breaking and making of bonds and side reactions, particularly for hydroxy, amine and polyhydroxylated compounds. In general, the protocols for orthogonal protection need to be milder because selective deprotection is governed by alternative cleavage mechanisms rather than by reaction rates. The functional groups, for example, acetals/ketals,[2] benzylidene, MOM/PMB/silyl ethers,[3] trityl,[4] and *tert*-butyl carbamate[5] etc. are extensively used in contemporary organic synthesis. The organic reactions in water as green media[6] have greatly attracted the attention of many researchers for many years. Although many methods for deprotection of the above-cited functional groups under acidic environments are well documented; however, the lacking of compatibility of several functionalities, mild reaction condition and proper solubility of organic compounds in water favored the reactions in organic solvents. Herein, we have demonstrated a remarkable report of the chemoselective cleavages of acid-sensitive orthogonal functionalities by the sustained-release nascent-HBr from the catalytic amount of benzyl bromide (BnBr) with the interior water present in the hydrophobic core of the confined micellar medium (micelle centre) in aqueous surfactant.[7a,b] Recently, Steflova et al. also reported that, SDS has a positive effect on the rate of cycloadditions reaction with highly hydrophobic compounds in aq. solution.[7c] In addition, the surfactant in water also acts as a phase-transfer catalyst for the shuttling of organic molecules and water into the micellar microenvironment from the solution and *vice versa* to facilitate the reaction.[8]

For the asymmetric synthesis of natural products and pharmaceutically active ingredients,[9] the most widely useful chiral pools, monosaccharides are generally encountered with multiple protection and deprotection steps to form the final targets.[10] In this context, we set out to explore our perspective for the chemoselective cleavage of 5,6-*O*-isopropylidene and cyclohexylidene functionalities of α-D-glucofuranosides (**1a-1c**) in aq. anionic surfactant, sodium dodecyl sulfate (SDS) and cationic surfactants, cetyltrimethylammonium bromide (CTAB), and dodecyl trimethylammonium bromide (DTAB); these are well-known to form self-assembled micelles in water. Initially, a set of reactions were performed in different concentrations (0.06, 0.10, 0.14, 0.18 and 0.22 M) of 10.0 mL aqueous anionic surfactant, SDS in the presence of BnBr (~0.15 mmol) as the precursor of the acid catalyst. Surprisingly, the reaction in 0.14 M aq. SDS provided the desired compound **2a-2c** exclusively without affecting 1,2-*O*-isopropylidene and cyclohexylidene as well as MOM group, mostly within 10-12 h at room temperature (Table 1). In a simple workup process, ethyl acetate was added as an external trigger to destabilise the micelles and the product was soluble in ethyl acetate, reducing interfacial tension. Encouraged by these observations, the same set of reactions was investigated in other aq. surfactants, CTAB, and DTAB; however, the result came out with a slower rate, longer reaction time and with comparatively lower yields (Figure S1, Table S1). The most effective results viewed at the concentration of ~0.14 M aq. SDS was further corroborated by the outcome of pH and specific conductance measurements of aq. SDS at different concentrations

Table 1. Nascent-HBr catalysed selective removal of 5,6-*O*-ketal



SDS Conc. (M)	Product	Time 3 h	4 h	5h	6 h	8 h	10 h	16 h
		Conversion yield (%)/*isolated yields						
0.06	2a	5	5	25	50	60	75	80
0.10		10	15	40	65	75	80	85
0.14		**10**	**25**	**40**	**60**	**80**	**>99/97***	-
0.18		-	5	25	45	55	60	75
0.22		-	5	15	35	55	70	75
0.06	2b	<5	5	10	15	35	45	60
0.10		<5	10	25	30	45	55	70
0.14		**5**	**20**	**45**	**65**	**75**	**80**	**95/90***
0.18		5	<10	20	25	35	55	70
0.22		-	<5	15	20	25	50	60
0.06	2c	-	5	15	20	30	40	45
0.10		-	5	20	25	35	50	55
0.14		**5**	**15**	**25**	**45**	**70**	**80**	**90/88***
0.18		-	5	10	25	45	50	65
0.22		-	-	5	15	20	30	45

(0.06-0.22 M) on various temperature (25, 40, 50, 60, 70, and 80 °C) (Figure S2, S3). In this study, surprisingly, the phenomenal abnormalities were observed in the concentration range 0.10-0.18 M (effective conc. ~0.14 M) of aqueous SDS; the formation of a compact domain of micelle in this range might be the reason for effective collisions leading to the formation of an activated complex for facilitating the chemical reaction.

These opportunistic and interesting consequences prompted us to find out the acidic behavior of nascent-HBr, formed *in situ* from the entrapment of catalytic amount of benzyl bromide in the micellar medium of aq. surfactant. The pH gradients overtime of 0.14 M aq. SDS solution (initial pH~7.88) gradually changes to acidic pH on the addition of various amounts of BnBr (Figure 1), indicating the slow-release nascent-HBr through hydrolysis. On a serious note, it is important to know that on continuous stirring for 24 h, the final pH of the solution reached to ~3.0 to 1.5 at 25 °C depending on the amount of catalyst.

To investigate the effective concentration of the catalyst, the endeavour for cleavage reaction of compound **1a** with different amounts of catalyst (0.05, 0.15, 0.25, 0.35, and 0.45 mmol) in 0.14 M aq. SDS at rt. (Figure S4) was executed. We found that 0.05-0.15 mmol BnBr (cat.) in 10 mL 0.14 M aq. SDS produced enough nascent-HBr for developing the acidic reaction medium (pH ~3.8-3.0) for selective and efficient hydrolysis of the ketal functionality in **1a-1c**.

Even though, 0.15 mmol BnBr in 10 mL 0.14 M aq. CTAB and DTAB each generated the pH ~1.4 within 10 h; however, the cleavage reactions were not as promising as SDS solution. In this regards, it is relevant to mention that the larger space between head ionic groups of SDS (anionic) micelles compared to those of CTAB and DTAB (cationic) facilitates the easier penetration of the organic molecules into the micelle core.[11]

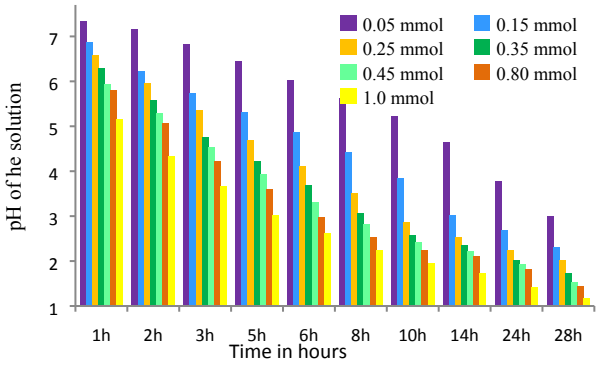


Figure 1. Study on pH gradient of freshly prepared aq. SDS (0.14 M, 10 mL, pH 7.88) upon addition of various concentration of BnBr (cat.) at 25 °C

Further attention was edified towards the generation of nascent-HCl from the catalyst benzyl chloride in aq. surfactant and its acid catalysing behaviour for the selective ketal deprotection of **1a**; nonetheless, the outcome of the reaction was not noteworthy. The higher average bond enthalpy of C–Cl (330 kJ/mol) bond than C–Br (275 kJ/mol) in benzyl bromide lowers the hydrolysis efficiency of benzyl chloride in aq. surfactant. Next, the effect of electrolyte on the rate of the cleavage reaction was examined, and it was noticed that with an increasing amount of electrolyte like NaCl, the rate of the cleavage reaction of **1a** decreases as the concentration of micelle in aq. surfactant reduces on the addition of electrolytes (Figure S5).[12]

The slow hydrolysis of BnBr for *in-situ* generation of hydrobromic acid was supported by the ^{1}H NMR study of 0.15 mmol of $PhCH_2Br$ (BnBr) dispersed in 1.0 mL 0.14 M SDS in D_2O in different time intervals with continuous stirring. In the ^{1}H NMR experiment, over a period of time, the shifting of signals at δ 7.00 and 4.16 ppm ($C_6\underline{H}_5$ and $C\underline{H}_2$, respectively) of $PhCH_2Br$ to δ7.23 and 4.48 ppm ($C_6\underline{H}_5$ and $C\underline{H}_2$) of $PhCH_2OH$ with a gradual increase of their intensities confirmed the slow hydrolysis of $PhCH_2Br$.

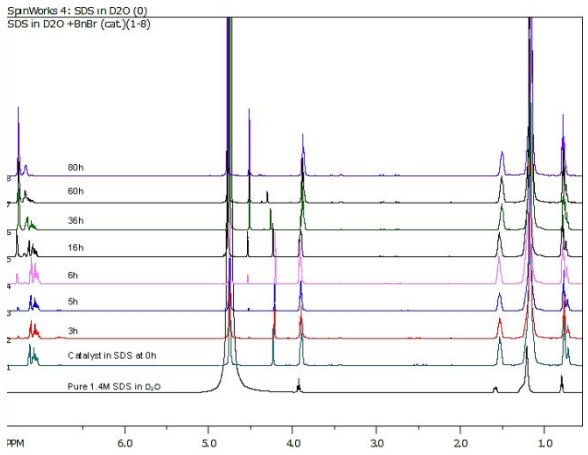


Figure 2. ^{1}H NMR of catalyst BnBr in 1.4M SDS solution in D_2O at a different time interval

Literature precedents reported that in aq. acidic medium (aq. H_2SO_4) the hydrolysis of SDS produces dodecanol (signal at δ ~3.5 ppm for $-\underline{CH_2}OH$) over a prolonged period.[13] Fortunately, in our method, no peaks were observed for dodecanol even after two days at 50 °C in the presence of a high concentration of catalyst (Figure 2).

To shed light on the excellent properties shown by the sustained-release nascent-HBr in the selective cleavage reaction, pH study was performed. The gradual addition of commercial 48% aq. HBr in different amounts (~ 0.04, 0.06, 0.07, 0.08 and 0.09 mmol) in 10 mL 0.14 M aq. SDS solution (initial ~pH 7.9) produced the instantaneous pH of the medium ~4.0, 3.2, 2.9, 2.4 and 2.1, respectively (inset A, Figure 3) that led to a either non-responsive or non-selective cleavage reaction.

From the NMR study, it was observed that the partial hydrolysis of 0.15 mmol BnBr (4.2 %) in 3 h in a D_2O solution of SDS generated 0.006 mmol of nascent-HBr (~pH 5.6) adequate to start the cleavage reaction. The complete hydrolysis of 0.15 mmol BnBr produced 0.15 mmol of nascent-HBr, making the SDS medium strong acidic (inset A and B, Figure 3). Thus, it can be seen that reaction time has a significant influence on the reaction yield, i.e. with an increase of time, yield increases even in the presence of a lower concentration of BnBr.

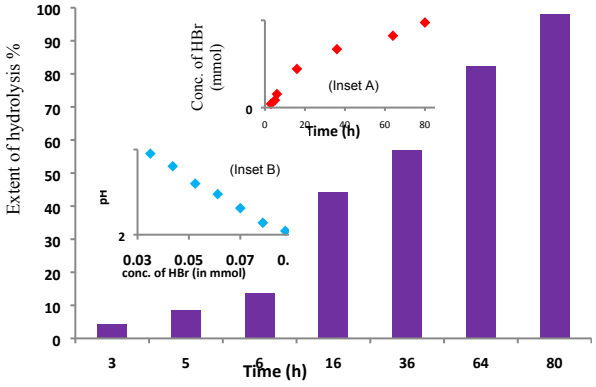


Figure 3. Rate of hydrolysis of BnBr in D_2O solution of SDS *vs.* time

Furthermore, the scope and limitation of the optimal reaction conditions were examined by adding the protected mannose, glucose, galactose and xylose derivatives (**1d-1j**) (1.0 mmol each) in presence of 0.1-0.15 mmol of BnBr in 10 mL SDS (Table 2: entry 1-8). It was gratifying to find that the acidic cleavages at rt. are highly selective at the 5,6-position, and produced **2d-2j** in 87-96% yield after chromatographic purification. The literature precedent demonstrated that 1,2-ketal cleavage at the anomeric position of glucose, galactose, xylose and sterically hindered 2,3-ketal of mannose derivatives require strong acidic medium. To our delight, the removal of said functionalities using nascent-HBr in a higher

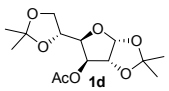
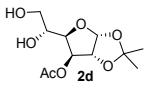
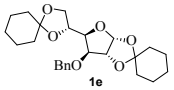
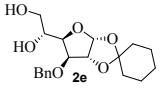
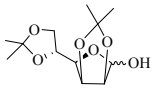
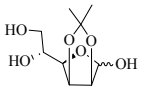
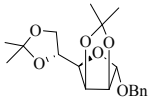
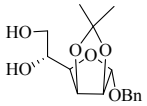
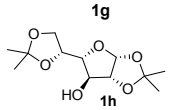
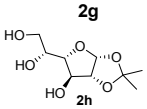
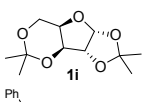
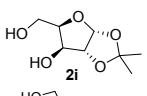
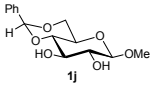
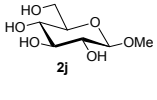
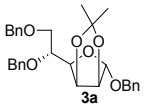
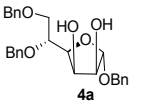
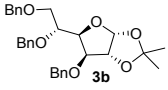
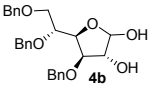
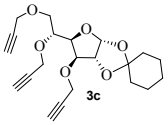
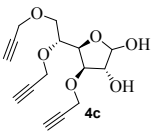
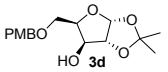
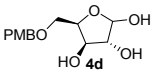
concentration of surfactant was achieved successfully at 45-50 °C yielding 79-85% of products (Table 2, entry 9-12) after purification. At a higher temperature, there may be the possibilities of decreasing the micellar number or their sizes[14] and subsequently the reduced solubility of hydrophobic organic compounds. The nascent-HBr mediated mild method for the deprotection of acid-sensitive ketal and acetal functionalities in open-chain hydroxylated as well as in amino alcohol derivatives proceeded smoothly with good results even in presence of TBS, MOM, *tert*-Boc and PMB group (Table 3). Herein, we are even more delighted to report that alkenes and alkynes under this condition remain unaffected from hydrohalogenation reactions. The substrates bearing acid-labile *t*-Boc and MOM group required longer time and higher reaction temperature.

For orthogonal protection study, the compound **14a** (1.0 mmol) containing both MOM and *t*-Boc functionalities was found to be highly stable at r.t. in presence of cat. BnBr (0.15 mmol) in 1.4 M aq. SDS (10 mL), however, there was lacking of tolerance of both the groups at ~45 °C in the above reaction medium (Table 3, entry 10).

In the meantime, we have attempted to optimize the cleavage reaction for a few selected compounds employing electron-donating and electron-withdrawing group substituted benzyl bromide (*p*-methyl benzyl bromide and p-nitrobenzyl bromide) as the source of nascent-HBr (Table S2). It is worthy to note that the rate and yield of the reaction are found to be higher for BnBr and *p*-MeBnBr compared to *p*-NO_2BnBr (BnBr ~ *p*-MeBnBr >> *p*-NO_2BnBr).

Further, the investigation with non-aromatic halides, *t*-BuBr has demonstrated the faster rate of cleavage of 5,6-ketals of glucose and 2,3-ketals of mannose in comparison to BnBr compromising the orthogonal selectivity for the functional groups TBS, PMB, and MOM. The systematic pH study of the four halides (BnBr, *p*-MeBnBr, *p*-NO_2BnBr and *t*-BuBr) in 1.4 M aq. SDS was conducted, and surprisingly, an initial burst-release HBr from the *t*-BuBr-mediated catalytic system (Figure S6) was observed leading to the generation of strong acidic environment in the confined micellar medium. The NMR studies of *t*-BuBr (Figure S7) hydrolysis in a D_2O solution of SDS revealed the faster release of nascent-HBr (Figure S8) relative to that of BnBr (Figure 3).

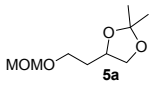
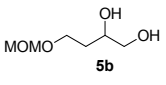
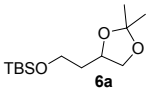
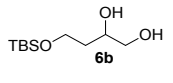
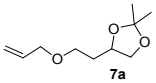
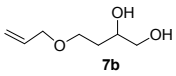
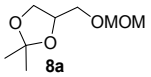
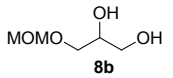
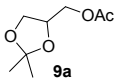
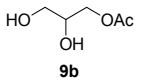
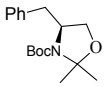
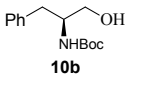
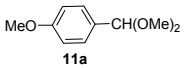
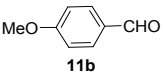
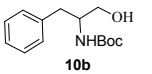
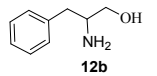
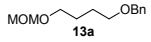
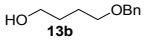
Table 2. Selective deprotection in compound **1d-1j** and **3a-3d**

Entry	Compound	Product	Catalyst	Time (h)	Yield %
1.	 **1d**	 **2d**	0.10	8	87
2.	 **1e**	 **2e**	0.15	16	95
3.	 **1f**	 **2f**	0.15	8	90
4.	 **1g**	 **2g**	0.15	9	87
5.	 **1h**	 **2h**	0.10	9	96
6.	 **1i**	 **2i**	0.10	9	94
7.	 **1j**	 **2j**	0.15	14	90
8.	 **3a**	 **4a**	0.15	11	84
9.	 **3b**	 **4b**	0.15	14	85
10.	 **3c**	 **4c**	0.15	17	82
11.	 **3d**	 **4d**	0.1	18	79

Reaction condition: aq. SDS (10-15 mL); **1d-1j** (1.0 mmol), rt; **3a** and **3b-3d** (0.50 mmol), 45-50 °C.

In general, at least 2-3 h is required for the inclusions or encapsulation of hydrophobic organic substrates and catalyst as guest molecules in the core of micelles (by overcoming the large hydrophilic-hydrophobic interface area) in aq. surfactants to initiate the reaction. The slow-release nascent-HBr gradually increases the proton (H^+) concentration towards the comparatively most reactive site of the molecule in acidic medium, causing the selective removal of the most acid-labile functionalities.

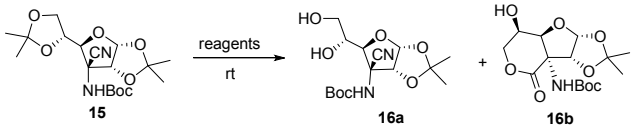
Table 3. Scope of deprotection in compounds **5a-13a**

Entry	Substrates	Product	Catalyst BnBr (mmol)	Time (h)	yield (%)
1.	 **5a**	 **5b**	0.10	9	81
2.	 **6a**	 **6b**	0.10	12	85
3.	 **7a**	 **7b**	0.10	12	93
4.	 **8a**	 **8b**	0.10	9	87
5.	 **9a**	 **9b**	0.10	7	75
6.	 **10a**	 **10b**	0.15	7	88
7.	 **11a**	 **11b**	0.10	8	92
8.	 **10b**	 **12b**	0.15	48	76
9.	 **13a**	 **13b**	0.15	24	93
10.	**14a**	**14b**	0.20	18	58

Reaction condition: 1.4 M aq. SDS (10-15 mL), **5a-11a** (1.0 mmol), rt; **10b, 13a** and **14a** (1.0 mmol), 45-50 °C.

Finally, the 5,6-*O*-isopropylidene acetal of the advanced building block **15** (preparation, supporting information, Scheme S1) was selectively removed by the newly developed mild and efficient catalyst system forming compound **16a** (80%) along with lactone **16b** (10%) *via* Pinner-cyclization of δ-hydroxy nitrile **16a**.[15] The

same deprotection of the acetal in traditional methods provided either less amount of desired product (**16a**) or a mixture of both (**16a** and **16b**) (Scheme 1). The structure of compound **16a** and **16b** was confirmed by NMR, Mass and FTIR spectroscopy.



Method	Reagents	Products	
		16a	16b
Method A	Amberlyst IR120 (H^+)/MeOH	40%	trace amount
Method B	*p*-TSA/MeOH	50%	40%
Method C	Nascent-HBr (cat.BnBr)	85%	10%

Scheme 1. Selective isopropylidene hydrolysis of δ-hydroxy nitrile derivative

Mechanistic considerations. The hydrophobic organic molecules in the water remain on the surface of the water where the limited collision of reacting partners inhibited the chemical reactions. Generally, the surfactant molecules approach to assemble into micelles (spherical aggregates) in water and maintain equilibrium with free surfactant monomers.[16] The literature report on high-resolution NMR experiments predicted that the center of the micelle is similar to liquid hydrocarbon and perhaps, the first few carbons from the ionic group, is exposed to the solvent, facilitating to penetrate water into the micelle core.[17] From our experimental results and the literature reports, we propose that the surfactant acts as a phase transfer catalyst in water for the dispersion of hydrophobic organic molecules, lowering the surface tension of water and interfacial tension between hydrophobic and hydrophilic materials whereas the interior water present in the hydrophobic micelle core assists in generating the nascent-HBr (Figure 4).[18]

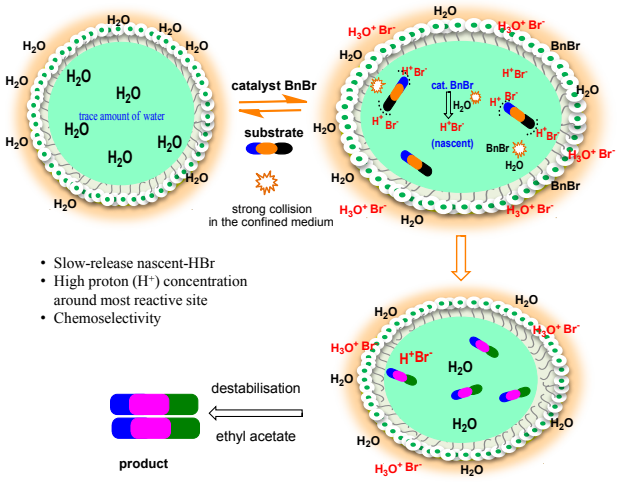


Figure 4: Pictorial diagram for the sequential steps involved in the chemoselective reaction

In summary, we have developed the micellar-assisted slow-release nascent-HBr from the dispersed catalyst BnBr in aqueous SDS. This catalytic system was successfully applied for chemoselective removal of acid-sensitive functionalities like ketals, acetals, MOM, *tert*-Boc functionalities present in carbohydrates, hydroxylated acyclic compounds and amino alcohol in good to excellent yield. We have also optimized the reactions using other halides, such as *p*-MeBnBr, *p*-NO_2BnBr and *t*-BuBr as sources of bromide and it was found that the rate of cleavage reaction was faster and the orthogonal selectivity was reduced with *t*-BuBr than that of BnBr and *p*-MeBnBr. The chemoselectivity and the tolerance toward orthogonal functionalities combined with the effective conversion in mild conditions, and the ease of the operation should make our catalytic system in aqueous medium potentially useful in the synthesis of natural product and active pharmaceutical ingredients.

EXPERIMENTAL SECTION:

General Information: NMR spectra were recorded on a Bruker Avance 500 spectrometer (500 MHz). Multiplicities are abbreviated as s = singlet, d = doublet, t = triplet, quart = quartet, quint = quintet, sext = sextet and m = multiplet. Optical rotation was measured at a concentration of g/100 mL with a Polarimeter (M/s Anton Paar, model: MCP-200). Mass spectra were recorded with an Agilent Technologies Q-TOF LC/MS G6520B mass spectrometer with the electrospray ionisation (ESI^+) technique. Perkin-Elmer Spectrum 65 FT-IR Spectrometer was used for recording IR spectra, and the values are expressed as % transmittance. Analytical thin-layer chromatography was performed on an Aluminum TLC plate, silica gel coated with fluorescent indicator F254 (1.0554, silica gel 60 F254, Merck). Elemental analysis (C/H/N/S) was performed by Euro Vector elemental analyser (EA-3000). Chromatographic separations were performed on a silica gel column by flash chromatography. Yields are given after purification unless differently stated. All the reagents and solvents were used as received without any further purification. Compounds were named following IUPAC rules as applied by Beilstein-Institute AutoNom (version 2.1) software for systematic names in organic chemistry. Compound **11a** was purchased from Sigma-Aldrich. All the starting materials are prepared in our laboratory and used for cleavage reaction.

General procedure for the synthesis of compounds 2a-2j, 4a-4d, and 5b-13b: The catalytic amount of benzyl bromide was added to a solution of protected compounds (**1a-1j**, **3a-3d**, and **5a-13a)** (shown in Table 2 and 3) in 10.0-15.0 mL aq. SDS solution with vigorous stirring at room temperature. On completion of the reaction monitoring through TLC, the reaction mixture was destabilised with ethyl acetate, and the two layers were separated. The organic layer was extracted and dried over Na_2SO_4, concentrated and purified through flash column chromatography using silica gel (200-400 mess) to offer the products **2a-2j**, **4a-4d**, and **5b-13b**.

Characterization data of compound 2a-2j:

1,2-O-Isopropylidene-α-D-glucofuranose (2a):[19] white solid, 97% (213.4 mg); mp156-160 °C; ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6 (99:1) δ (ppm): 5.92 (d, 1H, J = 3.4 Hz), 4.83 (d, 1H, J = 3.4 Hz), 4.52 (d, 1H, J = 4.4 Hz), 4.49 (d, 1H, J = 3.4 Hz), 4.30 (br s, 1H), 4.05-3.92 (m, 2H), 3.80-3.75 (m, 1H), 3.65-3.62 (m, 2H), 1.48 (s, 3H), 1.30 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$/DMSO-d_6) δ (ppm): 111.2, 104.9, 85.1, 80.4, 74.7, 69.7, 64.2, 26.7, 26.1.

1,2-O-Isopropylidene-3-O-methoxymethyl-α-D-glucofuranose (2b):[20] colorless semisolid, 90% (237 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.84 (d, 1H, J = 3.5 Hz), 4.68 (ABq, 2H, J = 6.4 Hz), 4.51 (d, 1H, J = 3.5 Hz), 4.16 (br d, 1H, J = 2.4 Hz), 4.06 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.6 Hz), 3.89-3.84 (m, 1H), 3.79 (dd, 1H, J_1 = 2.6 Hz, J_2 = 11.7 Hz), 3.67 (dd, 1H , J_1 = 5.8 Hz, J_2 = 11.7 Hz), 3.37 (s, 3H), 1.43 (s, 3H), 1.25 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 111.9, 105.1, 96.9, 83.3, 80.9, 79.7, 68.6, 64.2, 56.1, 26.6, 26.1.

1,2-O-Cyclohexylidene-α-D-glucofuranose (2c):[21] white solid, yield = 88% (229 mg); mp 148-152°C; ^{1}H NMR (500 MHz, $CDCl_3$/DMSO-d_6 (99:1)) δ (ppm): 5.92 (d, 1H, J = 3.5 Hz), 4.78 (d, 1H, J = 3.5 Hz), 4.51 (d, 1H J = 6.3 Hz), 4.48 (d, 1H, J = 3.5 Hz), 4.30 (br s, 1H), 4.01-3.99 (m, 2H), 3.84-3.80 (m, 1H), 3.68-3.61 (m, 2H), 1.72-1.43 (m, 10H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$/DMSO-d_6 (99:1)) δ (ppm): 112.0, 104.6, 84.6, 80.2, 74.9, 69.7, 64.2, 36.3, 35.5, 24.8, 23.8, 23.5.

3-O-Acetyl-1,2-O-isopropylidene-α-D-glucofuranose (2d):[22] colorless semisolid, 87% (228 mg), ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.91 (d, 1H, J = 3.4 Hz), 5.27 (br s, 1H), 4.60 (d, 1H, J = 3.4 Hz), 4.18 (dd, 1H, J_1 = 2.6 Hz, J_2 = 9.0 Hz), 3.86 (dd, 1H, J_1 = 2.6 Hz, J_2 = 11.7 Hz), 3.73 (dd, 1H, J_1 = 6.3 Hz, J_2 = 11.7 Hz), 3.68-3.63 (m, 1H), 2.18 (s, 2H), 2.16 (s, 3H), 1.52 (s, 3H), 1.32 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 171.2, 112.3, 104.8, 83.0, 79.1, 68.1, 64.0, 29.7, 26.5, 26.1, 20.6.

3-O-Benzyl-1,2-O-cyclohexylidene-α-D-glucofuranose (2e):[23] colorless, viscous liquid, 95% (332 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.39-7.30 (m, 5H), 5.95 (d, 1H, J = 3.5 Hz), 4.74 (d, 1H, J = 11.6 Hz), 4.63 (d, 2H, J = 3.1 Hz), 4.56 (ABq, 1H, J = 10.9 Hz), 4.14-4.10 (m, 2H), 4.03-3.97 (m, 1H), 3.81 (dd, 1H , J_1 = 3.5 Hz, J_2 =11.6 Hz), 3.69 (dd, 1H, J_1 = 5.0 Hz, J_2 =11.6 Hz), 1.71-1.33 (m, 10H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 137.2,

128.8-127.2 (5C), 112.5, 104.7, 82.1, 81.6, 79.8, 72.1, 69.3, 64.4, 36.3, 35.7, 24.8, 23.8, 23.5.

2,3-O-Isopropylidene-α-D-manno-furanose (2f):[20] white semisolid, 90% (211 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.28 (s, 1H), 4.82-4.79 (m, 1H), 4.53 (d, 1H, J = 5.9 Hz,), 4.35 (br s, 1H), 4.20 (br s, 1H), 4.06 (d, 1H, J = 7.5 Hz), 3.88 (br s, 1H), 3.74 (d, 1H, J = 11.2 Hz), 3.65 (d, 1H, J = 11.2 Hz), 3.51-3.48 (m, 1H), 1.38 (s, 3H), 1.26 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 112.5, 100.8, 85.3, 79.8, 78.7, 69.5, 63.7, 25.9, 24.6.

1-O-Benzyl-2,3-O-isopropylidene-α-D-manno-furanose (2g):[24] white crystal, 87% (270 mg), mp 80-82°C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.37-7.28 (m, 5H), 5.11 (s, 1H), 4.85 (t, 1H , J = 4.4 Hz), 4.63 (d, 1H , J = 5.7 Hz), 4.62 (d, 1H, J = 11.3 Hz), 4.50 (d, 1H, J = 12.0 Hz), 4.01-3.94 (m, 1H), 3.95 (dd, 1H, J_1 = 3.3 Hz, J_2 = 7.9 Hz), 3.82 (dd, 1H, J_1 = 3.3 Hz, J_2 = 11.3 Hz), 3.69-3.63 (m, 1H), 3.07 (br s, 1H), 2.40 (br s, 1H), 1.48 (s, 3H), 1.33 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 137.3, 128.5-127.9 (5C), 112.7, 105.4, 84.8, 80.1, 79.2, 70.3, 69.2, 64.4, 25.9, 24.6.

1,2-O-Isopropylidene-α-D-galactofuranose (2h):[25] colorless viscous liquid, 96% (211 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.86 (d, 1H, J = 3.6 Hz), 4.75 (s, 1H), 4.52 (d, 1H, J = 3.6 Hz), 4.23-4.16 (m, 2H), 4.06 (br s, 1H) 3.94 (d, 1H, J = 7.3 Hz), 3.80 (br s, 1H), 3.69 (d, 1H, J = 11.6 Hz), 3.60 (dd, 1H, J_1 = 4.2 Hz, J_2 = 11.6 Hz), 1.45 (s, 3H), 1.26 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 112.9, 105.2, 87.7, 87.0, 75.4, 71.0, 63.1, 26.8, 26.1.

1,2-O-Isopropylidene-α-D-xylofuranose (2i):[20] colorless viscous liquid, 94% (178 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.98 (d, 1H, J = 3.5 Hz), 4.51 (d, 1H, J = 3.5 Hz), 4.30 (s, 1H), 4.17 (dd, 1H, J_1 = 4.0 Hz, J_2 = 6.9 Hz), 4.05 (d, 1H, J = 11.2 Hz), 4.02 (d, 1H, J = 11.2 Hz), 3.71 (br s, 1H), 1.49 (s, 3H), 1.32 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 111.8, 104.7, 85.4, 79.1, 76.3, 60.8, 26.7, 26.1.

Methyl-β-D-glucopyranoside (2j):[26] white solid, 90% (174 mg), mp 195-199°C; ^{1}H NMR (500 MHz, D_2O) δ (ppm): 4.68 (d, 1H, J = 3.6 Hz), 3.74 (dd, 1H, J_1 = 2.4 Hz, J_2 = 11.8 Hz), 3.63 (dd, 1H, J_1 = 5.6 Hz, J_2 = 11.8 Hz), 3.61-3.53 (m, 2H), 3.44 (dd, 1H, J_1 = 3.6 Hz, J_2 = 9.5 Hz), 3.29 (s, 3H), 3.26 (d, 1H, J = 9.5 Hz).

Characterization data of compounds (4a-4d):

1,5,6-Tri-O-benzyl-α-D-mannofuranose (4a): viscous liquid, 84% (378 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.25-7.11 (m, 15H), 4.81 (d, 1H, J = 11.4 Hz), 4.72 (d, 1H, J = 11.4 Hz), 4.52 (s, 1H), 4.51 (s, 1H), 4.46-4.38 (m, 2H), 4.33 (s, 1H), 3.82 (s, 1H), 3.69-3.59 (m, 2H), 3.57-3.47 (m, 2H), 3.27-3.21 (m, 1H), 2.75 (br s, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm):139.2, 139.1, 137.7, 129.4-128.7 (15C), 99.2, 76.9, 75.8, 75.7, 75.6, 74.5, 72.0, 71.6, 70.1; $[\alpha]_D^{25}$ -40.0 (c = 0.8, $CHCl_3$); LC-MS (ESI$^+$) *m/z* Calcd. for $[C_{27}H_{30}O_6]^+$: 450.20 $(M)^+$, Found: 450.49; Elemental analysis Anal. Calcd for C27H30O6: C, 71.98; H, 6.71. Found: C, 71.87; H, 6.79.

3,5,6-Tri-O-benzyl-α-D-glucofuranose (4b):[27] colorless semisolid, 85% (382 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.23-7.15 (m, 15H), 4.94 (br s, 1H), 4.67 (dd, 2H, J_1 = 8.0 Hz, J_2 = 11.6 Hz), 4.56 (d, 1H, J = 11.6 Hz), 4.50 (br s, 2H), 4.45-4.42 (m, 2H), 4.41 (d, 1H, J = 6.3 Hz), 4.39-4.36 (m, 1H), 4.29 (s, 1H), 4.03-3.98 (m, 1H), 3.95 (d, 1H , J = 10.6 Hz), 3.79 (d, 1H, J = 10.6 Hz), 3.62 (dd, 1H, J_1 = 5.4 Hz, J_2 = 10.6 Hz); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 138.8 (2C), 138.5, 138.0, 137.8, 128.3 (2C), 128.2, 127.6 (3C), 127.4 (3C), 125.8, 107.7, 82.9, 80.2, 78.3, 78.3, 73.3, 72.5, 71.9, 70.8, 70.7, 69.5 (2C).

3,5,6-Tri-O-propargyl-α-D-glucofuranose (4c): colorless semisolid, 82% (241 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.50 (br s, 1H), 4.39-4.36 (m, 1H), 4.32-4.27 (m, 5H), 4.25-4.21 (m, 2H), 4.12 (m, 1H), 4.01 (d, 1H, J = 10.6 Hz), 3.95 (d, 1H, J = 10.6 Hz), 3.94 (m, 1H), 3.75-3.72 (m, 1H), 3.69-3.66 (m, 1H), 2.44 (br s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 96.8, 83.2, 79.6, 79.5, 79.4, 77.5, 75.4, 75.0 (2C), 74.5, 74.3, 69.9, 58.7, 57.9, 57.3; $[\alpha]_D^{25}$ +25.0 (c = 1.2, $CHCl_3$); LC-MS (ESI$^+$) *m/z* Calcd. for $[C_{15}H_{18}O_6]^+$: 294.11 $(M)^+$, Found: 294.23. Elemental analysis Anal. Calcd for C15H18O6: C, 61.22; H, 6.17. Found: C, 61.19; H, 6.22.

5-O-(4-Methoxybenzyl)-α-D-xylofuranose (4d): colorless semisolid, 79% (213 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.73-7.70 (m, 2H), 7.54-7.51 (m, 2H), 5.82 (d, 1H, J = 6.3 Hz), 4.99 (d, 2H, J = 16.1 Hz), 4.92 (d, 2H, J = 10.4 Hz), 4.67 (s, 1H), 4.32 (d, 2H, J = 11.5 Hz), 4.30 (s, 3H), 4.09 (d, 1H, J = 6.3 Hz); $[\alpha]_D^{25}$ +28.0 (c = 0.9, $CHCl_3$); LC-MS (ESI$^+$) *m/z* Calcd. for $[C_{13}H_{18}O_6]^+$: 270.11 $(M)^+$, Found: 270.33; Elemental analysis Anal. Calcd for C13H18O6: C, 57.77; H, 6.71. Found: C, 57.83; H, 6.80.

Characterization data of compounds (5b-13b)

(±)-4-(methoxymethoxy)butane-1,2-diol (5b):[28] colorless semisolid, 81% (350 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.63 (s, 2H), 4.19-4.15 (m, 1H), 4.03 (t, 1H, J = 6.9 Hz), 3.76-3.73 (m, 2H), 3.62-3.59 (m, 2H), 3.40-3.36 (m, 1H), 3.34 (s, 3H), 1.93-1.77 (m, 2H).

(±)-5-((tert-Butyldimethylsilyl)oxy)pentane-1,2-diol (6b):[29] colorless liquid, 85% (127 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 3.88-3.83 (m, 1H), 3.82-3.77 (m, 1H), 3.74 (t, 2H, J = 5.4 Hz), 3.56-3.51 (m, 1H), 3.46-3.41 (m, 1H), 3.40-3-35 (m, 1H), 1.60-1.56 (m, 2H), 0.81 (s, 9H), -0.01 (s, 6H).

(±)-4-(Allyloxy)butane-1,2-diol (7b):[30] colorless viscous liquid, 93% (204 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.96-5.86 (m, 1H), 5.28-5.19 (m, 2H), 4.12 (dd, 1H, J_1 = 6.9 Hz, J_2 = 14.4 Hz), 4.01 (d, 2H, J = 5.2 Hz), 3.95-3.89 (m, 1H), 3.69-3.62 (m, 2H), 3.55-3.49 (m, 1H), 3.10 (s, 1H), 1.89-1.80 (m, 1H), 1.75-1.68 (m, 1H).

(±)-3-(Methoxymethoxy)propane-1,2-diol (8b):[31] colorless viscous liquid, 87% (118 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.67 (s, 2H), 3.89 (br s, 1H), 3.71 (t, 2H, J = 8.6 Hz), 3.67-3.59 (m, 2H), 3.40 (s, 3H), 2.95 (br s, 1H), 2.15 (br s, 1H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 97.2, 70.7, 70.5, 63.9, 55.6.

(±)-2,3-Dihydroxypropyl acetate (9b):[32] colorless viscous liquid, 75% (100 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) : 4.12 (quintet, 2H), 3.92 (br s, 2H), 3.67 (d, 1H, J = 11.4 Hz), 3.57 (dd, 1H, J_1 = 5.9 Hz, J_2 = 11.4 Hz), 3.48 (br s, 1H), 2.10 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 171.9, 70.6, 65.0, 63.5, 21.0.

tert-Butyl(S)-(1-hydroxy-3-phenylpropan-2-yl)carbamate

(10b):[33] white solid, 88% (221 mg); mp 93-98 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) : 7.29-7.17 (m, 5H), 5.18 (br s, 1H), 3.86 (s, 1H), 3.59 (dd, 1H, J_1 = 3.8 Hz, J_2 = 11.2 Hz), 3.50 (dd, 1H, J_1 = 4.3 Hz , J_2 = 10.3 Hz), 2.81 (d, 2H, J = 6.5 Hz), 1.39 (s, 9H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 156.2, 138.0, 129.3 (2C), 128.6 (2C), 126.3, 79.5, 63.5, 53.6, 37.4, 28.4 (3C);

4-Methoxybenzaldehyde (11b): colorless liquid, 92% (125 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.88 (s, 1H), 7.83 (d, 2H, J = 8.2 Hz), 7.00 (d, 2H, J = 8.2 Hz), 3.90 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 190.8, 164.4, 132.0 (2C), 130.0, 114.0 (2C), 55.5.

(S)-2-Amino-3-phenylpropan-1-ol (12b):[34] white solid, 76% (115 mg); m. 93-95 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) : 7.33-7.17 (m, 5H), 3.65 (dd, 1H, J_1 = 3.2 Hz, J_2 = 10.7 Hz), 3.40 (dd, 1H, J_1 = 7.9 Hz, J_2 = 10.7 Hz), 3.14 (dd, 1H, J_1 = 5.3 Hz, J_2 = 12.6 Hz), 2.80 (dd, 1H, J_1 = 5.3 Hz, J_2 = 12.6 Hz), 2.54 (dd, 1H, J_1 = 8.7 Hz, J_2 = 12.6 Hz), 2.33 (br s, 2H).

(4-(Benzyloxy)butan-1-ol (13b):[35] colorless viscous liquid, 93% (167 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.39-7.32 (m, 5H), 4.52 (s, 2H), 3.60 (t, 2H, J = 5.7 Hz), 3.51 (t, 2H, J = 5.4 Hz), 1.71 (m, 2H), 1.64 (m, 2H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 138.3, 128.5 (2C), 127.8 (2C), 127.7, 72.9, 70.3, 62.2, 29.7, 26.5.

Methyl 2-amino-3-hydroxypropanoate (14b):[36] colorless semisolid, 58% (69 mg), ^{1}H NMR (500 MHz, D_2O/CD_3OD (19:1)), δ (ppm): 4.19 (br s, 1H), 3.99 (d, 1H, J = 12.9 Hz), 3.89 (d, 1H, J = 12.5 Hz), 3.74 (s, 3H).

Methods for 5,6-*O*-isopropylidene cleavage of compound 15 (Scheme 1)

Method A: To a solution of compound **15** (500 mg, 1.30 mmol) in methanol (10.0 mL), Amberlite IR120 (H^+) (100 mg) was added and stirred slowly at room temperature for 24 h. The reaction mixture was filtered off, the filtrate was concentrated and purified using silica gel flash column chromatography to get the diol **16a**.

Method B: To a solution of compound **15** (500 mg, 1.30 mmol) in methanol (10.0 mL), a catalytic amount of *p*TSA (22.3 mg, 0.13 mmol) was added and stirred at room temperature for 24 hr. The solvent was removed, and the residue was partitioned between EtOAc and water. The organic layer was separated, washed with satd. $NaHCO_3$, brine, and dried over anhydrous Na_2SO_4 and concentrated. The crude residue was purified using silica gel flash column chromatography to afford the diol **16a** and lactone **16b**.

Method C: To a compound **15** (500 mg, 1.30 mmol) in 1.4 M SDS

solution (10.0 mL), a catalytic amount of BnBr (0.15 mmol) was added and stirred for 24h at room temperature. Ethyl acetate was added to the reaction mixture, the organic layer was separated, dried over anh. Na_2SO_4, concentrated and purified using silica gel flash column chromatography to form diol **16a** and lactone **16b**.

Characterization data of compound 16a and 16b:

***tert-butyl ((3aR,5S,6R,6aR)-6-cyano-5-((R)-1,2-dihydroxyethyl)-2,2-dimethyltetrahydrofuro[2,3-d][1,3]dioxol-6-yl)carbamate* (*16a*):** colorless semisolid, 85% (357 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.95 (d, 1H, J = 3.6 Hz), 5.68 (br s, 1H), 5.08 (s, 1H), 4.12 (dd, 1H, J_1 = 3.6 Hz, J_2 = 9.3 Hz), 3.90 (d, 2H, J = 9.3 Hz), 3.73 (dd, 1H, J_1 = 5.1 Hz, J_2 = 11.2 Hz), 1.56 (s, 3H), 1.49 (s, 5H), 1.37 (s, 3H), 1.25 (s, 4H); ^{13}C{^{1}H} NMR (125 MHz, CD_3OD) δ (ppm): 156.2 (Boc, C=O), 113.0 (CN), 107.0, 106.9, 85.4, 84.7, 82.5, 80.1, 72.4, 64.9, 28.1 (3C), 27.2 (2C); $[\alpha]_D^{25}$ 32.0 (c = 0.9, $CHCl_3$); FTIR (KBr): 3414 (OH, NH), 1731.1 (>C=O Boc) and 2242 (less intense CN) cm^{-1}; LC-MS (ESI$^+$) *m/z* $[C_{15}H_{24}NaN_2O_7]^+$ 367.15; Found 367.24; Elemental analysis Anal. Calcd for C15H24N2O7: C, 52.32; H, 7.02; N, 8.13. Found: C, 52.49; H, 7.15; N, 8.21.

***tert-butyl ((3aR,4aS,5R,8aR,8bR)-5-hydroxy-2,2-dimethyl-8-oxotetrahydro-6H-[1,3]dioxolo[4',5':4,5]furo[3,2-c]pyran-8a(8H)-yl)carbamate* (*16b*):** colorless semisolid, 10% (41 mg); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.94 (d, J = 3.4 Hz, 1H), 5.76 (br s, 1H), 4.84 (s, 1H), 4.75 (d, 1H, J = 3.4 Hz), 4.50-4.45 (m, 1H), 4.02 (dt, 1H, J = 3.4, 11.6 Hz), 3.94-3.89 (m, 1H), 3.21 (s, 1H), 1.60 (s, 3H), 1.44 (s, 12H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 172.2 (lactone C=O), 154.9 (Boc, C=O), 114.6, 105.2, 85.7, 84.0, 83.8, 82.1, 66.8, 62.0, 28.1 (3C), 27.3, 27.2; $[\alpha]_D^{25}$ +45.0 (c = 1.3, $CHCl_3$); FTIR (KBr): 3432.2 (OH, NH), 1784.9 (C=O lactone), 1710.1 (C=O Boc) cm^{-1}; LC-MS (ESI$^+$) *m/z* $[C_{15}H_{23}NaNO_8]^+$ 368.13, Found 368.19; Elemental analysis Anal. Calcd for C15H23NO8: C, 52.17; H, 6.71; N, 4.06. Found: C, 52.29; H, 6.81; N, 4.11.

Preparation and characterization of starting materials:

Characterization data of compounds (**1a-1j**):

***1,2:5,6-Di-O-isopropylidene-α-D-glucofuranose (1a).*[37]** white solid, 77% (15.0 g); mp 107-110 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.95 (br s, 1H), 4.54 (br s, 1H), 4.38-4.31 (m, 2H), 4.20-4.14 (m, 1H), 4.09-4.05 (m, 1H), 3.97 (dd, 1H, J_1 = 4.6 Hz, J_2 = 9.4 Hz), 2.70 (s, 1H), 1.50 (s, 3H), 1.44 (s, 3H), 1.36 (s, 3H), 1.32 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 111.8, 109.7, 105.3, 85.1, 81.1, 75.2, 73.4, 67.6, 26.9, 26.8, 26.2, 25.1.

***1,2:5,6-Di-O-isopropylidene-3-O-methoxymethyl-α-D-glucofuranose (1b).*[38]** colorless semisolid, 79% (3.16 g); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.85 (d, 1H, J = 3.5 Hz), 4.71 (s, 2H), 4.56 (d, 1H, J = 3.5 Hz), 4.29-4.23 (m, 1H), 4.20 (d, 1H, J = 2.7 Hz), 4.08 (dd, 2H, J_1 = 3.5 Hz, J_2 = 6.3 Hz), 3.96 (dd, 1H, J_1 = 5.6 Hz, J_2 = 8.6 Hz), 3.39 (s, 3H), 1.48 (s, 3H), 1.40 (s, 3H), 1.32 (s, 3H), 1.30 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 111.8, 109.1, 105.2, 95.9, 83.2, 81.0, 78.9, 72.2, 67.5, 55.7, 26.8 (2C), 26.2, 25.3.

***1,2:5,6-Di-O-cyclohexylidene-α-D-glucofuranose (1c).*[39]** white solid 69% (7.0 g); mp 134-137°C, ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.97 (d, 1H, J = 3.4 Hz), 4.53 (d, 1H, J = 3.4 Hz), 4.36-4.33 (m, 2H), 4.16 (dd, 1H, J_1 = 6.3 Hz, J_2 = 8.6 Hz), 4.06 (dd, 1H, J_1 = 2.4 Hz, J_2 = 8.6 Hz), 3.97 (dd, 1H, J_1 = 5.4 Hz, J_2 = 8.6 Hz), 1.77-1.49 (m, 20H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 112.2, 104.3, 84.6, 81.3, 80.2, 64.2, 40.1, 39.9, 39.7, 39.6, 36.3, 35.6, 34.6, 25.0, 24.8, 24.0, 23.7, 23.5.

***3-O-Acetyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (1d).*[40]** white solid, 70% (2.19 g); mp 61-65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.80 (d, 1H, J = 3.4 Hz), 5.16 (br s, 1H), 4.44 (d, 1H, J = 3.4 Hz), 4.16-4.10 (m, 2H), 3.99 (dd, 1H, J_1 = 4.9 Hz, J_2 = 8.5 Hz), 3.94 (dd, 1H, J_1 = 4.9 Hz, J_2 = 8.5 Hz), 2.03 (s, 3H), 1.43 (s, 3H), 1.33 (s, 3H), 1.24 (s, 3H), 1.23 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 169.4, 112.0, 109.1, 104.9, 83.2, 79.9, 75.5, 72.3, 66.9, 26.7, 26.6, 26.0, 25.1, 20.7.

***3-O-Benzyl-1,2:5,6-di-O-cyclohexylidene-α-D-glucofuranose (1e).*[41]** colorless semisolid, 82% (1.87 g); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.39-7.31 (m, 5H), 5.90 (d, 1H, J = 3.3 Hz), 4.71 (d, 1H, J_1 = 11.5 Hz), 4.69 (d, 1H, J_1 = 11.5 Hz), 4.58 (d, 1H, J = 3.3 Hz), 4.40-4.37 (m, 1H), 4.12 (dd, 2H, J_1 = 4.2 Hz, J_2 = 7.8 Hz), 4.05 (d, 1H, J = 3.3 Hz), 4.00 (dd, 1H, J_1 = 5.5 Hz, J_2 = 8.7 Hz), 1.58 (m, 20H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): δ 137.7, 128.4 (2C), 127.8, 127.6, 112.4, 109.6, 104.9, 82.3, 81.7, 81.5, 79.6, 72.3, 72.1, 67.2, 36.6, 36.5, 35.7, 34.9, 25.2, 24.9, 24.1, 23.9, 23.9, 23.6.

***2,3:5,6 Di-O-isopropylidene-D-manno-furanose (1f).*[42]** white solid, 89%; (1.84 g); mp 121-125 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):5.38 (s, 1H), 4.82 (dd, 1H, J_1 = 3.5 Hz, J_2 = 5.5 Hz), 4.62 (d, 1H, J = 5.5 Hz), 4.41 (dd, 1H, J_1 = 5.8 Hz, J_2 = 11.5 Hz), 4.19 (dd, 1H, J_1 = 3.5 Hz, J_2 = 7.6 Hz), 4.11-4.03 (m, 2H), 2.80 (d, 1H, J = 2.2 Hz), 1.48 (s, 3H), 1.47 (s, 3H), 1.39 (s, 3H), 1.33 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 112.6, 109.1, 101.1, 85.4, 80.2, 79.6, 73.2, 66.5, 26.8, 25.8, 25.1, 24.4.

***1-O-Benzyl-2,3:5,6-di-O-isopropylidene-α-D-manno-furanose (1g).*[43]** white crystal; 82% (2.16 g); mp 81-83 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):7.37-7.29 (m, 5H), 5.07 (s, 1H), 4.80 (dd, 1H, J_1 = 4.2 Hz, J_2 = 5.5 Hz), 4.66 (d, 1H, J = 5.5 Hz), 4.63 (s, 1H), 4.48 (dd, 1H, J_1 = 5.5, J_2 = 7.8 Hz), 4.43-4.38 (m, 1H), 4.11 (t, 1H, J = 7.8 Hz), 3.98-3.90 (m, 2H), 1.46 (s, 6H), 1.38 (s, 3H), 1.32 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 137.3, 128.5-127.8 (5C), 112.6, 109.3, 105.6, 85.1, 80.4, 79.5, 73.1, 69.1, 66.9, 26.9, 25.8, 25.2, 24.5.

***1,2:5,6-Di-O-isopropylidene-α-D-galactofuranose (1h).*[44]** colorless, viscous liquid; 55% (1.95 g); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.81 (s, 1H), 4.49 (s, 1H), 4.29-4.23 (m, 1H), 4.00-3.98 (m, 2H), 3.75 (m, 1H), 3.73 (br t, 1H, J = 7.2 Hz), 1.46 (s, 3H), 1.36 (s, 3H), 1.29 (s, 3H), 1.25 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 113.1, 109.7, 105.0, 87.3, 86.8, 75.6, 68.3, 65.6, 27.1, 26.4, 25.8, 25.3.

***1,2:3,5-Di-O-isopropylidene-α-D-xylofuranose (1i).*[45]** colorless solid, 60% (1.77 g); mp 43-45 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):6.00 (d, 1H, J = 3.4 Hz), 4.52 (d, 1H, J = 3.3 Hz), 4.26 (br s, 1H), 4.13-4.01 (m, 3H), 1.49 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H), 1.32 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 111.6, 105.2, 97.4, 84.6, 73.1, 71.6, 60.1, 28.9, 26.7, 26.1, 25.9.

***Methyl 4,6-benzylidene-β-D-glucopyranoside (1j).*[46]** white solid, 87% (2.30 g); mp 197-201 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm):7.39 (d, 2H, J = 8.4 Hz), 7.26 (s, 1H), 6.80 (d, 2H, J = 8.7 Hz), 5.47 (s, 1H), 4.76 (d, 1H, J = 3.5 Hz), 4.26 (dd, 1H, J_1 = 4.2 Hz, J_2 = 10.1 Hz), 3.90 (t, 1H, J = 10.1 Hz), 3.80 (s, 3H), 3.78-3.74 (m, 1H), 3.72 (d, 1H, J = 10.1 Hz), 3.47 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 160.3, 129.4, 127.5, 113.6, 101.8, 99.8, 96.1, 80.8, 72.8, 71.8, 68.8, 62.3, 55.5, 55.2.

Characterization data of compounds (3a-3d):

1,5,6-Tri-O-benzyl-2,3-O-isopropylidene-α-D-manno-furanose (3a). A solution of 2,3-*O*-isopropylidine-α-D-manno-furanose (0.5 g, 4.5 mmol) (**2f**) in DMF (5.0 mL), sodium hydride (60 % w/w in mineral oil, 0.46 g, 22.7 mmol) was added at 0 ºC and stirred at room temperature for 1 h. Again, the reaction mixture was cooled to the 0 ºC followed by the addition of benzyl bromide (1.4 mL, 22.5 mmol) and *tetra*-butyl ammonium iodide (catalytic amount) and stirred at room temperature for 10 h. The reaction mixture was suspended in ice cold water (10.0 mL), and extracted with EtOAc (2×10.0 mL). The combined organic layers were dried over sodium sulfate and concentrated under vacuum. The remaining crude was purified by column chromatography (EtOAc: petroleum ether 15%) to afford **3a** as a colorless semi solid, 88% (1.81 g). ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.36-7.24 (m, 15H), 4.95 (d, 1H, J = 11.5 Hz), 4.81 (d, 1H, J = 11.5 Hz), 4.73 (d, 1H, J = 11.5 Hz), 4.71 (s, 1H), 4.61 (ABq, 2H, J = 11.5 Hz), 4.54 (d, 1H, J = 11.5 Hz), 4.26 (t, 1H, J = 6.3 Hz), 4.21 (d, 1H, J = 6.3 Hz), 3.80 (d, 1H, J = 10.3 Hz), 3.72 (dd, 1H, J_1 = 6.3 Hz, J_2 = 10.3 Hz), 3.66-3.62 (m, 1H), 3.54 (t, 1H, J = 7.6 Hz), 1.55 (s, 3H), 1.40 (s, 3H); ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ (ppm): 138.4, 138.0, 136.9, 128.5-127.6 (15C), 110.8, 96.0, 79.9, 75.7, 74.5, 74.3, 73.5 (2C), 70.2, 70.1, 27.6, 26.2. $[\alpha]_D^{25}$ +27.0 (c = 0.8, $CHCl_3$); LC-MS (ESI$^+$) *m/z* Calcd for $[C_{30}H_{34}O_6]^+$: 490.24 (M)$^+$, Found: 490.31; Elemental analysis Anal.Calcd for C30H34O6: C, 73.45; H, 6.99. Found: C, 73.53; H, 7.01.

***3,5,6-Tri-O-benzyl-1,2-O-isopropylidene-α-D-glucofuranose (3b).*[47]** colorless semisolid, 91% (2.72 g); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.30-7.23 (m, 15H), 5.91 (d, 1H, J = 3.5 Hz), 4.82 (d, 1H, J = 11.2 Hz), 4.63 (d, 1H, J = 11.2 Hz), 4.60 (d, 1H, J = 3.5 Hz), 4.58 (s, 2H), 4.48 (d, 2H, J = 11.2 Hz), 4.30 (dd, 1H, J_1 = 3.5 Hz, J_2 = 9.3 Hz), 4.13 (d, 1H, J = 3.5 Hz), 4.09-4.04 (m, 1H), 3.91 (d, 1H, J = 10.5 Hz), 3.68 (dd, 1H, J_1 = 5.6 Hz, J_2 = 10.5 Hz), 1.48 (s, 3H), 1.30

(s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 138.7 (3C), 138.5, 137.6, 128.4 (3C), 128.3 (2C), 128.2, 127.9 (2C), 127.8, 127.6, 127.5, 127.4 (2C), 111.8, 105.1, 81.8 (2C), 79.0, 75.5, 73.4, 72.7, 72.0, 71.3, 26.8, 26.3.

1,2-O-Cyclohexylidene-3,5,6-tri-O-propargyl-α-D-glucofuranose (3c). 1,2-*O*-Cyclohexylidene-α-D-glucofuranose (1.30 g, 3.8 mmol) (**2c**) was dissolved in dry DMF (5.0 mL) and sodium hydride (1.02 g, 19.0 mmol) was added at 0 ºC and stirred at room temperature for 1h. Propargyl bromide (2.2 mL, 23.0 mmol) was introduced at 0 ºC and the mixture was warmed to room temperature and stirred for 12 h. The reaction mixture was reverse-quenched with ice and diluted with EtOAc (3×10.0 mL). The combined organic layers were dried over sodium sulfate and evaporated. The residue was chromatographed on silica gel (elution with EtOAc-petroleum ether 25%) as a colorless semisolid, 66% (1.31 g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.88 (d, 1H, J = 3.4 Hz), 4.61 (br s, 1H), 4.44-4.40 (m, 1H), 4.33-4.26 (m, 3H,), 4.22-4.14 (m, 4H), 3.97-3.93 (m, 2H), 3.65-3.61 (m, 1H), 2.52 (s, 1H), 2.45 (d, 2H, J = 8.5 Hz), 1.60-1.35 (m, 10H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 112.6, 104.6, 81.4, 81.2, 80.0, 79.7, 79.1, 78.4, 75.1, 74.5, 74.3, 70.3, 58.6, 57.8 (2C), 57.7, 36.3, 35.8, 24.8, 23.8, 23.5. $[\alpha]_D^{25}$ -41.0 (c = 1.3, $CHCl_3$); LC-MS (ESI^+) *m/z* Calcd for $[C_{21}H_{26}O_6]^+$: 374.17 $(M)^+$, Found: 374.28; Elemental analysis Anal. Calcd for C21H26O6: C, 67.36; H, 7.00. Found: C, 67.47; H, 6.97.

1,2-O-Isopropylidene-5-O-(4-methoxybenzyl)-α-D-xylofuranose (3d).[48] colorless semisolid, 68% (1.37 g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.25 (d, 2H, J = 8.0 Hz), 6.89 (d, 2H, J = 8.5 Hz), 5.99 (d, 1H, J = 3.5 Hz), 4.68-4.64 (m, 2H), 4.59-4.47 (m, 1H), 4.41 (d, 1H, J = 11.2 Hz), 4.28-4.21 (m, 1H), 4.00 (d, 1H, J = 3.5 Hz), 3.92 (dd, 1H, J_1 =5.5 Hz, J_2 = 11.2 Hz), 3.83-3.80 (m, 1H), 3.81 (s, 3H), 1.48 (s, 3H), 1.33 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm):159.6, 129.5 (2C), 129.0, 114.0 (2C), 111.7, 105.1, 82.5, 82.4, 79.9, 71.5, 61.0, 55.3, 26.8, 26.3; $[\alpha]_D^{25}$ -32 (c = 1.0, $CHCl_3$), LC-MS (ESI^+) *m/z* Calcd. for $[C_{16}H_{22}O_6]^+$: 310.14 $(M)^+$, Found: 310.22; Elemental analysis Anal. Calcd for C16H22O6: C, 61.92; H, 7.15. Found: C, 62.01; H, 7.19.

Characterization data of compounds (5a-13a):

(±)-4-(3-(Methoxymethoxy)propyl)-2,2-dimethyl-1,3-dioxolane (5a).[49] yellowish liquid, 95% (1.96 g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.60 (s, 2H), 4.20 (quintet, 1H), 4.05 (t, 1H, J = 6.9 Hz), 3.61 (t, 2H, J = 5.5 Hz,), 3.56 (t, 1H, J = 7.5 Hz), 3.34 (s, 3H), 1.93-1.77 (m, 2H), 1.39 (s, 3H), 1.34 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 108.1, 96.0, 73.4, 69.1, 64.0, 54.6, 33.5, 26.6, 25.3.

(±)-tert-Butyl(3-(2,2-dimethyl-1,3-dioxolan-4-yl)propoxy) dimethylsilane (6a).[50] colorless oil, 80% (2.51g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.13 (quintet, 1H), 4.01 (t, 1H, J = 6.8 Hz), 3.37-4.36 (m, 2H), 3.50 (t, 1H, J = 7.4 Hz), 1.83-1.75 (m, 1H), 1.74-1.64 (m, 1H), 1.34 (s, 3H), 1.30 (s, 3H), 0.84 (s, 9H), 0.003 (s, 6H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 108.0, 73.6, 69.6, 59.7, 36.5, 26.8, 25.7 (3C), 25.6 (2C), 18.0, -5.5.

(±)-4-(2-(Allyloxy)ethyl)-2,2-dimethyl-1,3-dioxolane (7a).[51] colorless oil, 75% (1.46 g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.96-5.82 (m, 1H), 5.27 (d, 1H, J = 16.5 Hz), 5.17 (br t, 1H, J = 9.2 Hz), 4.22-4.15 (m, 1H), 4.09-4.03 (m, 1H), 3.99-3.91 (m, 2H), 3.59-3.48 (m, 3H), 1.86-1.80 (m, 2H), 1.40 (s, 3H), 1.35 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 134.7, 116.7, 108.5, 73.8, 71.8, 69.6, 66.9, 33.8, 26.9, 25.7.

(±)-4-((Methoxymethoxy)methyl)-2,2-dimethyl-1,3-dioxolane (8a).[31] colorless viscous liquid, 78% (2.77 g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.67 (s, 2H), 4.31 (quintet, 1H), 4.09 (t, 1H, J = 6.8 Hz), 3.74 (t, 1H, J = 6.8 Hz), 3.59 (br d, 2H, J = 5.7 Hz), 3.37 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 109.5, 96.7, 74.7, 68.6, 66.6, 55.3, 26.8, 25.4.

(±)-(2,2-Dimethyl-1,3-dioxolan-4-yl)methyl acetate (9a).[52] colorless liquid, 82% (2.58 g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 4.33 (quintet, 1H), 4.18 (dd, 1H, J_1 = 4.4 Hz, J_2 = 11.6 Hz), 4.11-4.04 (m, 2H), 3.74 (dd, 1H, J_1 = 6.2 Hz, J_2 = 8.5 Hz), 2.10 (s, 3H), 1.44 (s, 3H), 1.37 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 170.8, 109.9, 73.6, 66.4, 64.9, 26.6, 25.3, 20.8.

(S)-tert-Butyl 4-benzyl-2,2-dimethyloxazolidine-3-carboxylate (10a). The *tert*-butyl (S)-(1-hydroxy-3-phenylpropan-2-yl)carbamate (1.0 g, 3.9 mmol) (**10b**) was dissolved in dry acetone (7.0 mL), 2,2-dimethoxypropane (2.1 mL, 17.2 mmol) and boron trifluoride etherate ($BF_3.OEt_2$, 30 µL, 0.2 mmol) was added. The reaction was stirred for 3 h. The reaction was neutralized with aq. $NaHCO_3$, extracted with ethyl acetate and the solvent was removed under reduced pressure. The compound was purified through column chromatography (EtOAc/petroleum ether, 25%) to get yellowish liquid **10a** (93%, 1.94 g); $[\alpha]_D^{25}$ -36.0 (c = 1.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.32-7.14 (m, 5H), 4.04 (d, 1H, J = 7.6 Hz), 3.74-3.71 (m, 2H), 3.17 (dd, 1H, J_1 = 11.0 Hz, J_2 = 11.0 Hz), 2.65-2.62 (m, 1H), 1.67-1.44 (m, 15H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 151.6, 138.5, 129.5, 129.2, 128.6, 128.4, 126.4, 93.9, 79.5, 66.0, 59.1, 39.7, 28.5, 27.5, 26.8, 24.5, 23.2. LC-MS (ESI^+) *m/z* Calcd for $[C_{17}H_{25}NO_3]^+$: 291.18 $(M)^+$, Found: 291.20; Elemental analysis Anal. Calcd for C17H25NO3: C, 70.07; H, 8.65; N, 4.81. Found: C, 70.11; H, 8.71; N, 4.77.

((4-(Methoxymethoxy)butoxy)methyl)benzene (13a).[53] colorless liquid, 78% (1.53 g); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.34-7.31 (m, 5H), 4.60 (br s, 2H), 4.50 (br s, 2H), 3.53 (t, 2H, J = 5.7 Hz), 3.50 (t, 2H, J = 5.3 Hz), 3.34 (s, 3H), 1.69 (m, 4H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 138.6, 128.3 (2C), 127.6, 127.5 (2C), 96.4, 72.9, 70.1, 67.5, 55.1, 26.6, 26.5.

(S)-methyl 2-((tert-butoxycarbonyl)amino)-3-(methoxymethoxy)propanoate (14a).[54] yellowish, semisolid, 78% (300 mg); ^1H NMR (500 MHz, $CDCl_3$), δ (ppm): 5.52 (d, 1H, J = 8.2 Hz), 4.59 (s, 2H), 4.46 (d, 1H, J = 8.1 Hz), 3.99 (d, 1H, J = 9.8 Hz), 3.77 (s, 3H), 3.74 (d, 1H, J = 10.2 Hz), 3.32 (s, 3H), 1.45 (s, 9H).

Characterization data of compound 15: (Scheme shown in supporting information)

Synthesis of 1,2:5,6-di-O-isopropylidene-3-deoxy-3-amino-3-cyano-α-D-glucofuranose (18).[55] yellowish semisolid, 50% (3.22 g). ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.92 (d, 1H, J = 7.1 Hz), 4.78 (d, 1H, J = 3.0 Hz), 4.36 (quintet, 1H), 4.18 (dd, 1H, J_1 = 6.3 Hz, J_2 = 8.7 Hz), 4.00 (dd, 1H, J_1 = 3.9 Hz, J_2 = 9.1 Hz), 3.68 (d, 1H, J = 8.7 Hz), 2.18 (br s, 2H), 1.57 (s, 3H), 1.46 (s, 3H), 1.38 (s, 3H) 1.38 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$): 118.6, 113.7, 110.1, 103.9, 83.3, 81.6, 75.0, 67.5, 62.7, 26.7, 26.4, 26.3, 24.8.

1,2:5,6-Di-O-isopropylidene-3-deoxy-3-N-tert-butyloxycarbonyl-3-cyano-α-D-glucofuranose (15). 1,2:5,6-Di-*O*-isopropylidene-3-deoxy-3-amino-3-cyano-α-D-glucofuranose (**18**) (1.0 g, 3.5 mmol) was dissolved in acetonitrile (2.0 mL) followed by addition of di-*tert*-butyl dicarbonate (1.2 mL, 5.2 mmol) and 4-dimethylaminopyridine (0.825 g, 0.5 mmol) and stirred at rt. for 24 h. The reaction mixture was partitioned between EtOAc and water. The organic layer was dried over sodium sulfate, evaporated and purified through column chromatography (EtOAc:Petroleum ether, 25%) to furnish pure yellowish semisolid compound **15** (85%, 1.68 g). $[\alpha]_D^{25}$ +31.0 (c = 1.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 5.91 (d, 1H, J = 2.3 Hz), 5.43 (s, 1H), 5.28 (s, 1H), 4.43 (s, 1H), 4.20 (t, 1H, J = 8.0 Hz), 4.03 (s, 1H), 3.77 (d, 1H, J = 5.9 Hz), 1.54 (s, 6H), 1.49 (s, 9H), 1.39 (s, 3H), 1.36 (s, 3H); $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ (ppm): 153.7, 116.3, 113.8, 110.6, 104.2, 82.2, 81.5, 79.4, 74.3, 67.5, 62.2, 28.2, 26.7, 26.5, 26.4, 24.7 (3C); FTIR (KBr): 3414 (NH), 2242 (CN), 1731 (CO) cm^{-1}; LC-MS (ESI^+) *m/z* $[C_{18}H_{28}N_2O_7Na]^+$: 407.18 $[M+Na]^+$, Found: 407.41; Elemental analysis Anal. Calcd for C18H28N2O7: C, 56.24; H, 7.34; N, 7.29. Found: C, 56.32; H, 7.29; N, 7.24.

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Supporting Information Available. NMR spectra of all the synthesized compounds and other optimization data. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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