Expedient and Facile One-Pot Syntheses of Triazole-Linked Glycoconjugates under Microwave Irradiation

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Abstract: Effective microwave assisted one-pot syntheses of triazole-*O*-glycoconjugates and triazolylglycosides involving sequential glycosylation and click chemistry are described.

Key words: one-pot synthesis, triazole glycoconjugates, multi-component, glycosylation, click chemistry, microwave irradiation

Glycoconjugates, sugar-linked proteins or lipids through O- or N-glycosidic linkage, play a crucial role in various life processes.[1] Synthetic organic chemistry has provided an array of methodologies for preparing glycoconjugates.[2] Introduction of unnatural glycosidic linkages, for example, triazolyl glycoconjugates, may provide stability towards hydrolysis of glycosidic bond while retaining the same geometry and spatial orientations of the natural glycoconjugates.[3] In addition to this, the modified linkage may be viable for further chemical transformations.[4]

The copper(I)-catalyzed Huisgen 1,3-dipolar cycloaddition reaction between organic azides and terminal alkynes has been proved to be a versatile synthetic route to 1,4-disubstituted 1,2,3-triazoles in recent years.[5] Because of the significant biological profile of triazoles, in respect to anti-HIV,[6] anti-allergic,[7] antibacterial,[8] herbicidal, and fungicidal activity,[9] this click reaction has emerged as an important topic of organic chemistry.[10] Moreover, triazole-linked glycoconjugates, in particular, were found to have various biological activities. Triazole-*O*-glycosides have long been used as fluorescence[11] probes and anticancer agents.[12] 1,2,3-Triazole glycosides have been evaluated for their ability to inhibit the enzymatic activity of glycosidases; they are also useful as antiviral, antiproliferative, and antidiabetic agents.[13] Quinoline coupled triazole sugar derivatives were found to have potent antitubercular activity in μg/mL level (Figure 1).[14] Mannosyl triazoles act as FimH antagonists and hence prevent urinary tract infection.[15] Glycosyl triazoles linked to 1,2,4-oxadiazole moiety show potent cell growth inhibition against NCI-H_{292} (lung carcinoma), HEp-2 (larynx carcinoma),[16] and when linked to α-keto carboxylic acids were identified as the potent protein tyrosine phosphatase 1B (PTP1B) inhibitors (Figure 1).[17] These few examples demonstrate the potency of triazolyl glycosides to be used as drugs in the near future. Thus, introduction of molecular diversity in the aglyconic part of triazolyl glycosides may lead to newer 'lead-molecules', which may be used for the treatment of various diseases.

Normally, 'click reactions' are efficient but time-consuming. Microwave heating, at controlled temperature and pressure may considerably reduce reaction time without promoting any side reactions. Thus, the synthesis of 1,4-disubstituted 1,2,3-triazoles under microwave irradiation may be a suitable alternative.[18] It features consecutive chemical transformation of alkyl halide to alkyl azide and subsequently to 1,2,3-triazoles, all in one pot.

One-pot sequential multi-component reactions (MCRs), which combine two or more completely different reactions in a single transformation, provide significant advantage over conventional stepwise synthesis avoiding tedious chromatographic purifications. Since carbohydrates have found wide applications as biopharmaceuticals or as inhibitors, carbohydrate-based one-pot MCR producing versatile and diastereomerically pure compounds is one of the most demanding methodology in diversity-oriented synthesis program. Due to the inherent

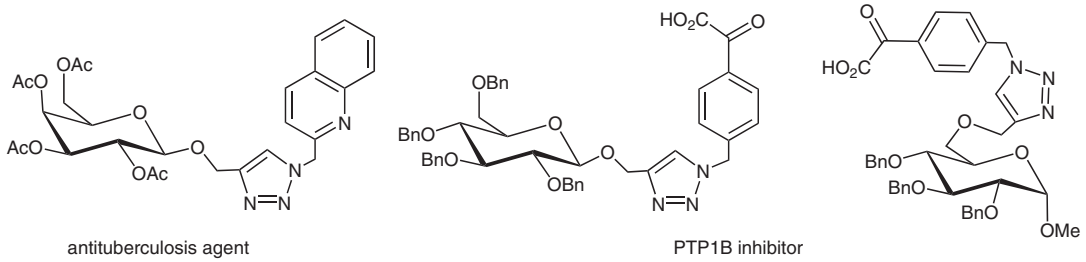

Figure 1 Examples of triazolyl glycosides having potent biological activity

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structural complexity of carbohydrates, the stereoselective incorporation of azide and/or alkyne in carbohydrate scaffold unleashes easy access to structurally diverse compounds. Here, we have revealed an integration of microwave-assisted glycosylation[19] and click chemistry to synthesize pure diastereomeric triazole-linked glycoconjugates in high yield. The glycosides formed through microwave-accelerated glycosylation of glycosyl donors underwent subsequent cycloaddition reaction. Copper(II), which promotes various donors for glycosylation after being reduced by KI to copper(I), catalyses the cycloaddition reaction. The reactions were fast and products were obtained in high yield as pure diastereomers.

Conventionally, the synthesis of triazole-*O*-glycoconjugates is a two-step process, the first of which involves Lewis acid promoted glycosylation[20] of glycosyl donors to obtain α- or β-anomers, followed by copper-mediated azide–alkyne cyclization to form glycoconjugates. This traditional method includes chromatographic purification of intermediates and hence the process is tedious and time-consuming. A recent one-pot approach to accomplish such glycoconjugates, carbohydrate-furan based hydroxytriazoles,[10c] involved cyclization of $TMSN_3$ and propargylglycoside, where Cu(I) was formed in situ via disproportionation of Cu(II) and Cu(0). Despite these advances, there is need to develop new methods to broaden the scope of this one-pot MCR. Our four-component one-pot tandem approach (Scheme 1) started with the preparation of mannose donor **2a**–**d**, which were in turn synthesized from peracylated sugar as reported earlier.[20,21]

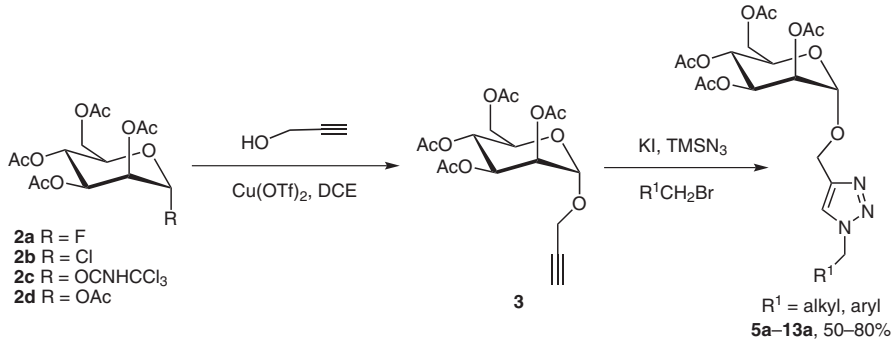
The terminal alkyne **3** participating in the cycloaddition reaction was generated in situ through copper(II)-promoted glycosylation of glycosyl donors and propargyl alcohol at different temperatures and under controlled microwave heating (Table 1, entries **1**–**12**). It is worthwhile to mention that in conventional procedure, the particular reaction requires 1–48 hours to complete at room temperature.

With the glycosyl chloride **2b**, the reaction was found to proceed smoothly in various solvents under microwave and showed the best yield in DCE. In the case of **2d**, the reaction was slow and elevation of reaction temperature did not significantly increase the yield. The thioglycosides did not participate in the reaction under the same experimental condition. All reactions were carried out using $Cu(OTf)_2$ (10 mol%) as promoter, while other Cu(II) salts like $CuSO_4$, $CuCl_2$, and $Cu(OAc)_2$ were not found to promote the glycosylation.

Table 1 Effect of Microwave Irradiation on the Formation of **3**

Entry[a]	Donor	Solvent	Microwave irradiation	Time	Yield (%)[b] of **3**
1	**2a**	DCE	0 W, 25 °C	48 h	42
			0 W, 60 °C	2.5 h	56
			100 W, 60 °C	10 min	78
2	**2a**	Et_2O	0 W, 25 °C	48 h	0
			0 W, 60 °C	48 h	0
			100 W, 60 °C	60 min	0
3	**2a**	MeCN	0 W, 25 °C	48 h	0
			0 W, 60 °C	48 h	0
			100 W, 80 °C	60 min	0
4	**2b**	DCE	0 W, 25 °C	3 h	62
			100 W, 60 °C	8 min	79
5	**2b**	Et_2O	0 W, 25 °C	1.5 h	68
			100 W, 60 °C	10 min	73
6	**2b**	MeCN	0 W, 25 °C	2 h	28
			100 W, 80 °C	10 min	70
7	**2c**	DCE	0 W, 25 °C	2 h	60
			100 W, 60 °C	5 min	90
8	**2c**	Et_2O	0 W, 25 °C	2 h	62
			100 W, 60 °C	10 min	67
9	**2c**	MeCN	0 W, 25 °C	1 h	60
			100 W, 80 °C	12 min	62
10	**2d**	DCE	0 W, 25 °C	48 h	0
			100 W, 80 °C	15 min	60
11	**2d**	Et_2O	0 W, 25 °C	48 h	0
			100 W, 60 °C	15 min	5
12	**2d**	MeCN	0 W, 25 °C	48 h	0
			100 W, 80 °C	15 min	4

[a] Reactions were performed using **2a**–**d** (1 equiv), and propargyl alcohol (1 equiv) using $Cu(OTf)_2$ (10 mol%) in a microwave vial. Increase of molar concentration of the catalyst did not produce better result.
[b] Yield of isolated pure product (some losses during purification were unavoidable in certain cases).



Scheme 1 Copper-mediated consecutive glycosylation and click chemistry to synthesize triazole-*O*-glycoconjugates under microwave irradiation

Once we standardized the optimal condition for glycosylation, our attention was focused on the consecutive cyclization, and the results are summarized in Table 2. Entry 3 had been found to show the best yield. Increase in the amount of catalyst over 10 mol% did not change the overall yield significantly. However, it is observed that when the amount of catalyst was reduced from 10 mol% the yield of the reaction decreased considerably.

Table 2 Effect of Microwave Irradiation on the One-Pot Synthesis of **5a**

Entry	Donor	Solvent	Microwave irradiation	Time	Yield (%)[a] of **5a**
1[b]	**2c**	DCE	100 W, 60 °C 0 W, 25 °C	5 min 14 h	 82
2[c]	**2c**	DCE	100 W, 60 °C 100 W, 60 °C	5 min 3 min	 72
3[d]	**2c**	DCE	100 W, 60 °C 100 W, 60 °C	5 min 3 min	 88 (80)[e]

[a] Yield of isolated pure product (some losses during purification were unavoidable in certain cases).
[b] First step was performed in DCE using **2c** (1 equiv), and propargyl alcohol (1 equiv) using $Cu(OTf)_2$ (10 mol%) in microwave vial followed by stirring at r.t. with $CuSO_4$ (10 mol%) and sodium ascorbate in EtOH–H_2O (1:1, v/v) with corresponding alkyl halide and NaN_3.
[c] First step as described in method 'b', followed by microwave irradiation with metallic Cu, alkyl halide, and $TMSN_3$ as described.
[d] First step as described in method 'b', followed by microwave irradiation with KI, alkyl halide, and $TMSN_3$ as described.
[e] When performed with 8 mol% $Cu(OTf)_2$.

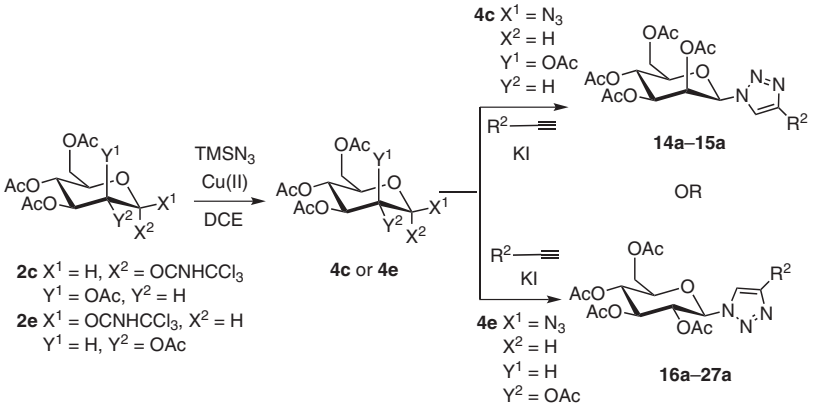
With this sequential one-pot procedure (Scheme 1), and its optimal conditions standardized, the scope of the method was investigated with different halides. The results are summarized in Table 3. Compound **3** formed through the activation of trichloroacetimidate donor **2** underwent cyclization with the organic azides when irradiated further (100 W, 3 min, 60 °C) with $TMSN_3$ and corresponding alkyl halide to produce triazole glycoconjugates (Table 3, entries 1–12) as pure diastereomers. Benzylic bromides (Table 3, entries 5–11), as well as other activated halides such as glycosyl bromide (Table 3, entry 12), gave desired 1,2,3-triazoles in good yield, whereas, in the case of aliphatic bromides, the yield was found to be poor.

Reasonable yields for aliphatic bromides were obtained only when the temperature was increased from 60 to 85 °C in the cyclization reaction. The copper(I) generated from copper(II) by adding KI accelerates the formation of alkyl azide, and at the same time catalyses the cycloaddition reactions. The reaction was highly regioselective and only 1,4-triazoles were obtained.

Next, our efforts were concentrated on the synthesis of triazolylglycosides, as illustrated in Scheme 2. The reaction of β-D-glucosyl azide to glucosyl triazole with complete retention of anomeric stereochemistry is known in the literature.[22] The reaction is slow and requires about 18–20 hours to reach completion at room temperature.

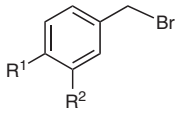
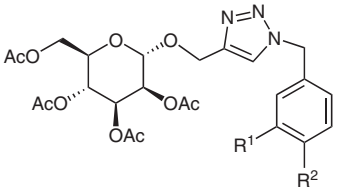
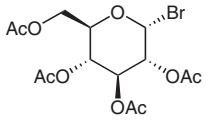
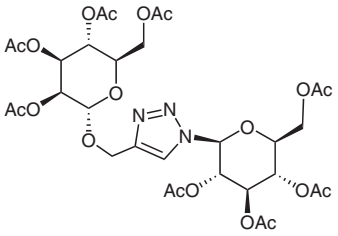
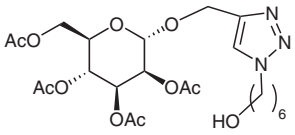
Glycosyl azides are normally formed through the stereoselective displacement of α-glycosyl halide with inorganic azide under homogeneous, phase-transfer or Lewis acid catalyzed reaction conditions.[23] With trichloroacetimidate **2c** and **2e** as starting materials and copper(II) as promoter, the glycosyl azides **4c** and **4e** were formed smoothly under microwave irradiation (100 W, 2 min, 60 °C) using $TMSN_3$ as acceptor. A participating group at C-2 did not direct the stereochemistry of anomeric bonds. In the presence of KI, copper(II) was reduced to copper(I) and glycosyl azide then underwent Huisgen 1,3-dipolar cycloaddition reaction with alkynes when further exposed to microwave irradiation (100 W, 3 min, 60 °C). The reaction sequence when performed without microwave, that is, at room temperature or at elevated temperature, required ~20 hours for completion with much lower yield. The reason may be due to the formation of bulkier triazole ring compared to glycosyl azide, which is stabilized due to anomeric effect. On completion of the reaction, all the volatiles were removed under reduced pressure, diluted with dichloromethane and washed with saturated aqueous solution of $Na_2S_2O_3$ to remove the iodine. On concentration pure products precipitated out (Table 4, entries 1–9, 11–12); no column chromatography was required.

In conclusion, we have developed a novel $Cu(OTf)_2$/KI-mediated one-pot synthesis of 1,2,3-triazole bridged gly-



Scheme 2 Copper-mediated consecutive glycosylation and click chemistry to synthesize triazolylglycosides under microwave irradiation

Table 3 One-Pot Syntheses of Triazole-*O*-glycoconjugates under Microwave Irradiation

Entry	Glycoside	Alkyl halide	Triazole-*O*-glycoconjugate[a]	Yield (%) α/β
				
1	**2a**	**5** (R^1 = Me, R^2 = H)	**5a**	65 (1:0)
2	**2b**	**5**	**5a**	71 (1:0)
3	**2c**	**5**	**5a**	88 (1:0)
4	**2d**	**5**	**5a**	57 (1:0)
5	**2c**	**6** (R^1 = H, R^2 = H)	**6a**	70 (1:0)
6	**2c**	**7** (R^1 = NO_2, R^2 = H)	**7a**	68 (1:0)
7	**2c**	**8** (R^1 = H, R^2 = NO_2)	**8a**	66 (1:0)
8	**2c**	**9** (R^1 = CN, R^2 = H)	**9a**	69 (1:0)
9	**2c**	**10** (R^1 = F, R^2 = H)	**10a**	71 (1:0)
10	**2c**	**11** (R^1 = OMe, R^2 = H)	**11a**	70 (1:0)
11	**2c**	 **12**	 **12a**	61 (1:0)
12	**2c**	 **13**	 **13a**	46 (1:0)

[a] Reactions were performed using **2a**–**d** (1 equiv), propargyl alcohol (1 equiv), alkyl halide (1 equiv), and $Cu(OTf)_2$ (0.1 equiv) under microwave irradiation (100 W, 60 °C, 5 min) in a microwave vial followed by addition of KI (20 mg) and $TMSN_3$ (1 equiv), with a further irradiation of 3 min. Anhyd DCE was used as solvent. Products were characterized by spectroscopic and analytical data.
[b] Isolated yield after column chromatography (some losses during purification were unavoidable in certain cases). α/β-Ratio was confirmed by ^{1}H NMR spectroscopy.

coconjugates. Microwave irradiation significantly reduced reaction time and improved the overall yield. $Cu(OTf)_2$, used in the reaction protocol, plays dual role in promoting the glycosylation reaction and later on being reduced by KI, activates the C≡C bond to undergo 'click chemistry'. The methodology may have interesting implications on the construction of structurally diverse carbohydrate derived heterocycles.

All solvents were dried and purified according to standard methods prior to use. Analytical TLC was performed on silica gel 60 F254 Al plates. The spots were visualized by charring with 10% (v/v) H_2SO_4 in EtOH or detected using UV light. Column chromatography and flash column chromatography were performed on 60–120 and 230–400 mesh silica gel, respectively. ESI-MS (positive) was conducted using LC-ESI-Q-TOF Micro Mass spectrometer. The NMR spectra were taken on a Bruker 300/600 DPX spectrometer operating at 300/600 MHz for ^{1}H and 75/150 MHz for ^{13}C, respectively, with TMS as an internal standard unless and otherwise stated, and the chemical shifts are reported in δ units. The values of chemical shifts (δ) are given in ppm and coupling constants (*J*) in Hz. IR spectra were recorded on a Jasco FTIR (model 410) spectrophotometer either as neat or on KBr plates.

Table 4 One-Pot Syntheses of Triazolylglycosides at Room Temperature and Under Microwave Irradiation

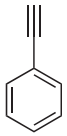
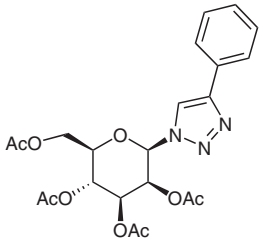
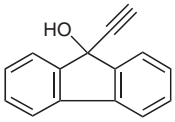
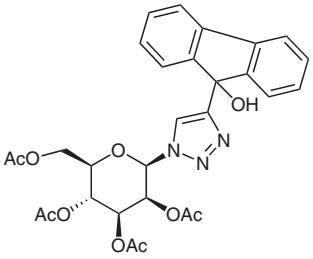
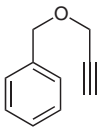
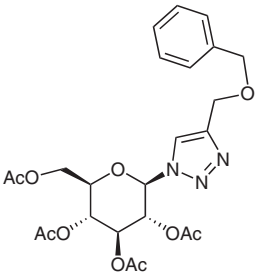
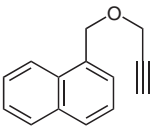
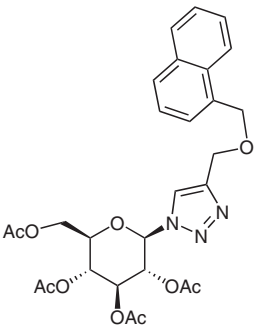
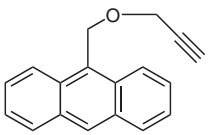
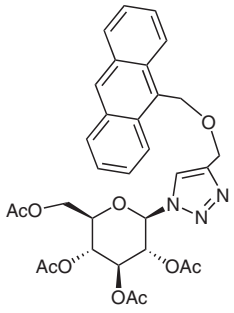
Entry	Thioglycoside	Alkyne	Triazolo-glycoconjugate[a]	Yield (%)[b]
1	**2c**	 **14**	 **14a**	91 (70)[c]
2	**2c**	 **15**	 **15a**	86
3	**2e**	 **16**	 **16a**	87
4	**2e**	 **17**	 **17a**	90
5	**2e**	 **18**	 **18a**	90

Table 4 One-Pot Syntheses of Triazolylglycosides at Room Temperature and Under Microwave Irradiation (continued)

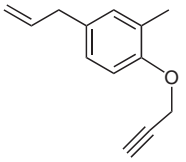
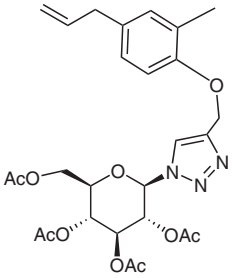
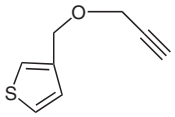
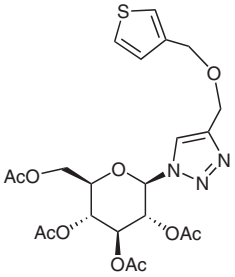
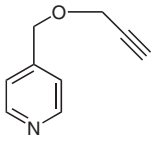
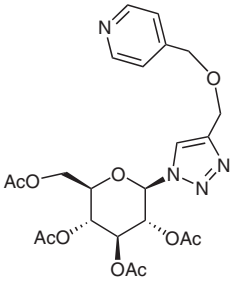
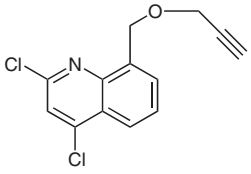
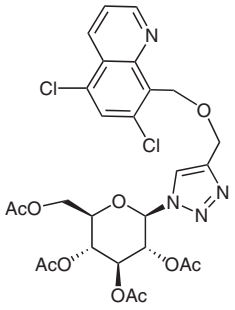
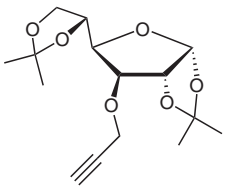
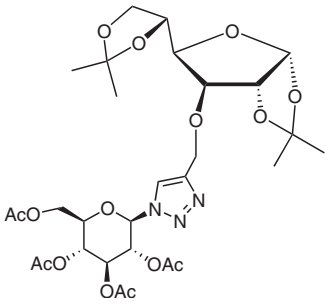
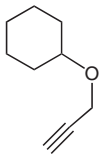
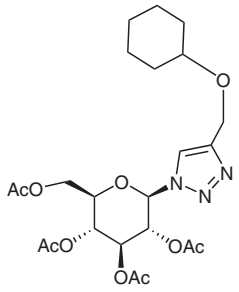
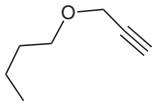
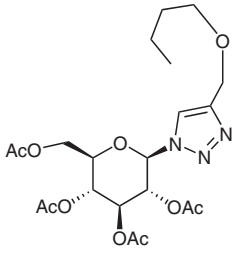
Entry	Thioglycoside	Alkyne	Triazolo-glycoconjugate[a]	Yield (%)[b]
6	**2e**	 **19**	 **19a**	75
7	**2e**	 **20**	 **20a**	80
8	**2e**	 **21**	 **21a**	79
9	**2e**	 **22**	 **22a**	80
10	**2e**	 **23**	 **23a**	91

Table 4 One-Pot Syntheses of Triazolylglycosides at Room Temperature and Under Microwave Irradiation (continued)

Entry	Thioglycoside	Alkyne	Triazolo-glycoconjugate[a]	Yield (%)[b]
11	**2e**	 **24**	 **24a**	79
12	**2e**	 **25**	 **25a**	69

[a] Reactions were performed using **2c** or **2e** (1 equiv), $TMSN_3$ (1 equiv), and $Cu(OTf)_2$ (0.1 equiv) under microwave irradiation (100 W, 60 °C, 2 min) in a microwave vial followed by addition of KI (20 mg) and alkyne (1 equiv), with a further irradiation of 3 min. Anhyd DCE was used as solvent. Products were characterized by spectroscopic and analytical data.
[b] Isolated yield. In most cases the product precipitated out (some product may be lost during filtration).
[c] Isolated yield without the use of microwave; required 20 h at r.t.

Triazole-*O*-glycoconjugates 5a–13a; General Procedure

A solution of trichloroacetimidate **2c** (0.1 mmol) and propargyl alcohol (0.1 mmol) in anhyd DCE (10 mL) was stirred at r.t. with powdered molecular sieves (4 Å, 20 mg) for 10 min, at the end of which $Cu(OTf)_2$ (3.6 mg, 0.01 mmol) was added. The mixture was then exposed to 100 W microwave irradiation maintaining a constant temperature of 60 °C for 5 min, in a microwave vial. When TLC (eluent: hexane–EtOAc, 3:2) indicated complete consumption of the starting materials, alkyl halide (0.1 mmol), KI (20 mg), $TMSN_3$ (11.5 mg, 0.1 mmol), and DCE (5 mL) were added, and the mixture irradiated further (100 W, 60 °C) for 3 min. The mass was then filtered, concentrated, diluted with CH_2Cl_2 (30 mL), and washed thoroughly with aqueous $Na_2S_2O_3$ and then purified by column chromatography (eluent: hexane–EtOAc, 5:1) (Table 3).

5a

Yield: 48 mg (88%); thick glass.

IR (neat): 3626, 3475, 3141, 2941, 2431, 2116, 1747, 1515, 1437, 1371, 1225, 1133 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.11 (s, 3 H, $COCH_3$), 2.15 (s, 3 H, $COCH_3$), 2.36 (s, 3 H, CH_3), 4.04 (m, 1 H, H-5), 4.07 (m, 1 H, H_A-6), 4.28 (m, 1 H, H_B-6), 4.65 (d, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.81 (d, *J* = 12.0 Hz, 1 H, OCH_2Ar), 4.93 (s, 1 H, H-1), 5.22 (s, 1 H, H-2), 5.28 (m, 1 H, H-4), 5.29 (m, 1 H, H-3), 5.49 (s, 2 H, NCH_2Ar), 7.20–7.28 (m, 4 H, Ar), 7.48 (s, 1 H, Ar).

^{13}C NMR (150 MHz $CDCl_3$): δ = 20.60 ($COCH_3$), 20.61 ($COCH_3$), 20.70 ($COCH_3$), 20.80 ($COCH_3$), 53.99 (CH_2), 61.04 (CH_2), 62.23 (CH_2), 65.95 (CH), 68.57 (CH), 68.94 (CH), 69.33 (CH), 96.86 (CH), 122.68 (CH), 128.18 (CH), 129.78 (CH), 131.26 (C), 138.73 (CH), 143.72 (C), 169.63 ($COCH_3$), 169.83 ($COCH_3$), 169.94 ($COCH_3$), 170.61 ($COCH_3$).

HRMS (ESI): *m/z* calcd for $C_{25}H_{31}N_3O_{10}$ + Na $[M + Na]^+$: 556.1907; found: 556.1937.

6a

Yield: 37 mg (70%); thick glass.

IR (neat): 3472, 3141, 2948, 1748, 1437, 1371, 1228, 1133, 1050 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.11 (s, 3 H, $COCH_3$), 2.15 (s, 3 H, $COCH_3$), 4.05–4.13 (m, 2 H), 4.25–4.31 (m, 1 H), 4.65 (d, *J* = 12.3 Hz, 1 H, OCH_2Ph), 4.82 (d, *J* = 12.3 Hz, 1 H, OCH_2Ph), 4.93 (s, 1 H), 5.22 (s, 1 H), 5.25–5.30 (m, 2 H), 5.44 (s, 2 H), 7.27–7.50 (m, 6 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.47 (2 × $COCH_3$), 20.56 ($COCH_3$), 20.66 ($COCH_3$), 53.99 (CH_2), 60.85 (CH_2), 62.09 (CH_2), 65.81 (CH), 68.45 (CH), 68.81 (CH), 69.19 (CH), 96.71 (CH), 122.76 (CH), 127.97 (CH), 128.62 (CH), 128.97 (CH), 134.26 (C), 143.64 (CH), 169.50 ($COCH_3$), 169.69 ($COCH_3$), 169.79 ($COCH_3$), 170.47 ($COCH_3$).

HRMS (ESI): *m/z* calcd for $C_{24}H_{29}N_3O_{10}$ + Na $[M + Na]^+$: 542.1751; found: 542.1726.

7a

Yield: 39 mg (68%); thick glass.

IR (neat): 3472, 3142, 2943, 1748, 1605, 1525, 1434, 1353, 1228, 1134, 1049 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.99 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.11 (s, 3 H, $COCH_3$), 2.15 (s, 3 H, $COCH_3$), 4.05–4.08 (m, 2 H), 4.12–4.13 (m, 1 H), 4.69 (d, *J* = 12.6 Hz, 1 H, OCH_2Ar), 4.86 (d, *J* = 12.3 Hz, 1 H, OCH_2Ar), 4.94 (s, 1 H), 5.21 (s, 1 H), 5.29–5.31 (m, 2 H), 5.67 (s, 2 H), 7.44–8.28 (m, 5 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.61 (2 × $COCH_3$), 20.70 ($COCH_3$), 20.79 ($COCH_3$), 53.11 (CH_2), 60.99 (CH_2), 62.25 (CH_2),

65.93 (CH), 68.66 (CH), 68.87 (CH), 69.32 (CH), 96.84 (CH), 123.07 (CH), 124.31 (CH), 128.67 (CH), 141.37 (CH), 144.41 (C), 148.04 (CH), 169.62 (*C*OCH$_3$), 169.94 (*C*OCH$_3$), 170.02 (*C*OCH$_3$), 170.64 (*C*OCH$_3$).

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}N_4O_{12}$ + Na [M + Na]$^+$: 587.1601; found: 587.1562.

8a

Yield: 38 mg (66%); thick glass.

IR (neat): 3144, 2950, 1748, 1533, 1437, 1533, 1437, 1361, 1228, 1134, 1049 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.98 (s, 3 H, COCH$_3$), 2.04 (s, 3 H, COCH$_3$), 2.11 (s, 3 H, COCH$_3$), 2.15 (s, 3 H, COCH$_3$), 4.07–4.12 (m, 2 H), 4.26–4.30 (m, 1 H), 4.69 (d, *J* = 12.3 Hz, 1 H, OC*H*$_2$Ar), 4.86 (d, *J* = 12.3 Hz, 1 H, OC*H*$_2$Ar), 4.95 (s, 1 H), 5.22 (s, 1 H), 5.30 (s, 2 H), 5.67 (s, 2 H), 7.63–8.26 (m, 5 H, Ar).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 20.53 (2 × CO*C*H$_3$), 20.63 (CO*C*H$_3$), 20.66 (CO*C*H$_3$), 53.99 (CH$_2$), 60.85 (CH$_2$), 62.09 (CH$_2$), 65.81 (CH), 68.45 (CH), 68.81 (CH), 69.19 (CH), 96.71 (CH), 122.76 (CH), 127.97 (CH), 128.62 (CH), 128.97 (CH), 134.26 (C), 143.64 (CH), 169.50 (*C*OCH$_3$), 169.69 (*C*OCH$_3$), 169.79 (*C*OCH$_3$), 170.47 (*C*OCH$_3$).

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}N_4O_{12}$ + Na [M + Na]$^+$: 587.1601; found: 587.1601.

9a

Yield: 38 mg (69%); thick glass.

IR (neat): 3473, 3141, 2948, 2231, 2110, 1747, 1615, 1433, 1371, 1228, 1134 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.99 (s, 3 H, COCH$_3$), 2.04 (s, 3 H, COCH$_3$), 2.12 (s, 3 H, COCH$_3$), 2.16 (s, 3 H, COCH$_3$), 4.04–4.13 (m, 2 H), 4.29 (dd, *J* = 5.1, 12.0 Hz, 1 H), 4.68 (d, *J* = 12.6 Hz, 1 H, OC*H*$_2$Ar), 4.86 (d, *J* = 12.3 Hz, 1 H, OC*H*$_2$Ar), 4.94 (m, 1 H), 5.21 (s, 1 H), 5.29–5.31 (m, 2 H), 5.62 (s, 2 H), 7.38 (d, *J* = 8.1 Hz, 1 H, Ar), 7.58 (s, 1 H, Ar), 7.70 (d, *J* = 8.4 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 20.49 (2 × CO*C*H$_3$), 20.59 (CO*C*H$_3$), 20.68 (CO*C*H$_3$), 53.23 (CH$_2$), 60.77 (CH$_2$), 62.12 (CH$_2$), 65.77 (CH), 68.50 (CH), 68.75 (CH), 69.16 (CH), 96.67 (CH), 112.53 (C), 118.00 (C), 123.06 (CH), 128.35 (2 × CH), 132.75 (2 × CH), 139.49 (C), 144.11 (C), 169.50 (*C*OCH$_3$), 169.82 (*C*OCH$_3$), 169.89 (*C*OCH$_3$), 170.52 (*C*OCH$_3$).

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{28}N_4O_{10}$ + Na [M + Na]$^+$: 567.1703; found: 567.1720.

10a

Yield: 39 mg (71%); thick glass.

IR (neat): 3473, 3141, 2950, 1749, 1606, 15512, 1436, 1372, 1229, 1134, 1051 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.98 (s, 3 H, COCH$_3$), 2.03 (s, 3 H, COCH$_3$), 2.11 (s, 3 H, COCH$_3$), 2.15 (s, 3 H, COCH$_3$), 4.06–4.09 (m, 2 H), 4.28 (dd, *J* = 5.1, 12.3 Hz, 1 H), 4.65 (d, *J* = 12.3 Hz, 1 H, OC*H*$_2$Ar), 4.83 (d, *J* = 12.3 Hz, 1 H, OC*H*$_2$Ar), 4.93 (s, 1 H), 5.21 (s, 1 H), 5.22–5.31 (m, 3 H), 5.52 (s, 2 H), 7.01–7.51 (m, 5 H, Ar).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 20.59 (2 × CO*C*H$_3$), 20.68 (CO*C*H$_3$), 20.77 (CO*C*H$_3$), 53.41 (CH$_2$), 61.04 (CH$_2$), 62.25 (CH$_2$), 65.98 (CH), 68.63 (CH), 68.93 (CH), 69.35 (CH), 96.87 (CH), 115.99 (CH), 116.28 (CH), 122.67 (CH), 129.96 (CH), 130.07 (CH), 130.20 (C), 130.24 (C), 143.97 (C), 169.62 (*C*OCH$_3$), 169.85 (*C*OCH$_3$), 169.95 (*C*OCH$_3$), 170.60 (*C*OCH$_3$).

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{28}N_3O_{10}$ + Na [M + Na]$^+$: 560.1656; found: 560.1615.

11a

Yield: 39 mg (70%); thick glass.

IR (neat): 3474, 3141, 2948, 2843, 2433, 2116, 1748, 1613, 1515, 1438, 1371, 1228, 1133 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.98 (s, 3 H, COCH$_3$), 2.03 (s, 3 H, COCH$_3$), 2.11 (s, 3 H, COCH$_3$), 2.15 (s, 3 H, COCH$_3$), 3.81 (s, 3 H, OCH$_3$), 4.06–4.07 (m, 2 H), 4.28 (dd, *J* = 5.1, 12.3 Hz, 1 H), 4.64 (d, *J* = 12.3 Hz, OC*H*$_2$Ar, 1 H), 4.81 (d, *J* = 12.3 Hz, OC*H*$_2$Ar, 1 H), 4.93 (s, 1 H), 5.22 (s, 1 H), 5.28–5.30 (m, 2 H), 5.47 (s, 2 H), 6.92 (d, *J* = 8.7 Hz, 2 H, Ar), 7.25 (d, *J* = 8.4 Hz, 2 H, Ar), 7.47 (s, 1 H, Ar).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 20.35 (2 × CO*C*H$_3$), 20.44 (CO*C*H$_3$), 20.54 (CO*C*H$_3$), 53.41 (CH$_2$), 54.98 (CH$_3$), 60.71 (CH$_2$), 61.95 (CH$_2$), 65.66 (CH), 68.31 (CH), 68.73 (CH), 69.06 (CH), 96.61 (CH), 114.19 (2 × CH), 122.53 (CH), 126.14 (C), 129.47 (2 × CH), 143.37 (C), 159.61 (C), 169.42 (*C*OCH$_3$), 169.60 (*C*OCH$_3$), 169.69 (*C*OCH$_3$), 170.37 (*C*OCH$_3$).

HRMS (ESI): *m*/*z* calcd for $C_{25}H_{31}N_3O_{11}$ + Na [M + Na]$^+$: 572.1856; found: 572.1868.

12a

Yield: 47 mg (61%); thick glass.

IR (neat): 3644, 3149, 2961, 2360, 2118, 1756, 1643, 1435, 1435, 1372, 1229, 1134, 1041 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.88 (s, 3 H, COCH$_3$), 1.99 (s, 3 H, COCH$_3$), 2.04 (s, 3 H, COCH$_3$), 2.08 (s, 3 H, COCH$_3$), 2.11 (s, 3 H, COCH$_3$), 2.13 (s, 3 H, COCH$_3$), 2.15 (s, 3 H, COCH$_3$), 4.00–4.19 (m, 4 H), 4.30–4.36 (m, 2 H), 4.69 (d, *J* = 12.3 Hz, 1 H), 4.86 (d, *J* = 12.6 Hz, 1 H), 4.93 (s, 1 H), 5.23–5.47 (m, 6 H), 5.87–5.90 (m, 1 H), 7.86 (s, 1 H, Ar).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 19.93 (CO*C*H$_3$), 20.34 (CO*C*H$_3$), 20.47 (2 × CO*C*H$_3$), 20.50 (2 × CO*C*H$_3$), 20.59 (CO*C*H$_3$), 20.65 (CO*C*H$_3$), 60.53 (CH$_2$), 61.33 (CH$_2$), 62.18 (CH$_2$), 65.81 (CH), 67.48 (CH), 68.55 (CH), 68.83 (CH), 69.15 (CH), 70.16 (CH), 72.34 (CH), 74.93 (CH), 85.54 (CH), 96.63 (CH), 121.43 (CH), 144.04 (C), 168.72(*C*OCH$_3$), 169.17 (*C*OCH$_3$), 169.54 (*C*OCH$_3$), 169.72 (2 × *C*OCH$_3$), 169.75 (*C*OCH$_3$), 170.35 (*C*OCH$_3$), 170.54 (*C*OCH$_3$).

HRMS (ESI): *m*/*z* calcd for $C_{31}H_{41}N_3O_{19}$ + Na [M + Na]$^+$: 782.2232; found: 782.2218.

13a

Yield: 25 mg (46%); thick glass.

IR (neat): 3462, 3142, 2936, 2865, 2109, 1748, 1439, 1372, 1228, 1135 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.37–1.6 (m, 8 H), 1.99 (s, 3 H, COCH$_3$), 2.04 (s, 3 H, COCH$_3$), 2.13 (s, 3 H, COCH$_3$), 2.16 (s, 3 H, COCH$_3$), 3.63 (t, *J* = 6.45 Hz, 2 H), 4.05–4.14 (m, 2 H), 4.31 (dd, *J* = 12.15, 5.1 Hz, 1 H), 4.36–4.41 (m, 2 H), 4.68 (d, *J* = 12.3 Hz, 1 H), 4.86 (d, *J* = 12.3 Hz, 1 H), 4.96 (m, 1 H), 5.25–5.35 (m, 3 H), 7.59 (s, 1 H, Ar).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 20.52 (2 × CO*C*H$_3$), 20.61 (CO*C*H$_3$), 20.70 (CO*C*H$_3$), 24.90 (CH$_2$), 25.97 (CH$_2$), 29.98 (CH$_2$), 32.11 (CH$_2$), 50.13 (CH$_2$), 60.92 (CH$_2$), 62.15 (CH$_2$), 62.21 (CH$_2$), 65.87 (CH), 68.52 (CH), 68.91 (CH), 69.28 (CH), 96.67 (CH), 122.73 (CH), 143.27 (C), 169.60 (*C*OCH$_3$), 169.90 (*C*OCH$_3$), 169.97 (*C*OCH$_3$), 170.63 (*C*OCH$_3$).

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{35}N_3O_{11}$ + Na [M + Na]$^+$: 552.2169; found: 552.2186.

Triazolyl Glycoconjugates 14a–25a; General Procedure

A solution of trichloroacetimidate **2c** or **2e** (0.1 mmol) and TMSN$_3$ (0.1 mmol) in anhyd DCE (10 mL) was stirred at r.t. with powdered

molecular sieves (4 Å, 20 mg) for 10 min, at the end of which $Cu(OTf)_2$ (0.01 mmol) was added. The mixture was then exposed to 100 W microwave irradiation maintaining a constant temperature of 60 °C for 2 min, in a microwave vial. When TLC (eluent: hexane–EtOAc, 3:2) indicated complete consumption of the starting materials, KI (20 mg), alkyne (0.1 mmol), and DCE (5 mL) were added and the mixture irradiated (100 W, 60 °C) further for 3 min. The mass was then filtered, concentrated, diluted with CH_2Cl_2 (30 mL) and washed thoroughly with aqueous $Na_2S_2O_3$. Pure compounds precipitated out directly from solution, no column chromatography was required (Table 4).

14a[23a]

Yield: 44 mg (91%); white solid; mp 177–179 °C.

IR (KBr): 3483, 3089, 1749, 1455, 1369, 1262, 1225, 1095, 1068 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 2.01 (s, 3 H, $COCH_3$), 2.11 (s, 9 H, 3 × $COCH_3$), 3.98–4.03 (m, 1 H), 4.23 (dd, *J* = 2.1, 12.5 Hz, 1 H), 4.38 (dd, *J* = 6, 12.6 Hz, 1 H), 5.29–5.42 (m, 2 H), 5.8–5.81 (m, 1 H), 6.19 (s, 1 H), 7.36–7.96 (m, 5 H, Ar), 7.99 (s, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.41 ($CO\mathit{C}H_3$), 20.50 ($CO\mathit{C}H_3$), 20.59 ($CO\mathit{C}H_3$), 20.67 ($CO\mathit{C}H_3$), 62.23 (CH_2), 65.02 (CH), 68.89 (CH), 70.74 (CH), 75.67 (CH), 84.75 (CH), 118.41 (CH), 125.71 (CH), 125.83 (CH), 128.41 (CH), 128.62 (CH), 128.85 (CH), 130.03 (C), 147.71 (C), 168.94 ($\mathit{C}OCH_3$), 169.56 ($\mathit{C}OCH_3$), 169.71 ($\mathit{C}OCH_3$), 170.48 ($\mathit{C}OCH_3$).

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{25}N_3O_9$ + Na $[M + Na]^+$: 498.1489; found: 498.1486.

15a

Yield: 51 mg (86%); brown solid; mp 192–194 °C.

IR (KBr): 3492, 3252, 3080, 1752, 1446, 1374, 1230, 1090 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.98 (s, 3 H, $COCH_3$), 2.09 (s, 2 H, 2 × $COCH_3$), 2.12 (s, 3 H, $COCH_3$), 3.99–4.06 (m, 1 H), 4.18 (dd, *J* = 2.1, 12.6 Hz, 1 H), 4.35–4.42 (m, 1 H), 5.25–5.43 (m, 2 H), 5.80–5.89 (m, 1 H), 6.20 (s, 1 H), 7.22–7.72 (m, 9 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.40 ($CO\mathit{C}H_3$), 20.52 ($CO\mathit{C}H_3$), 20.59 ($CO\mathit{C}H_3$), 20.64 ($CO\mathit{C}H_3$), 62.10 (CH_2), 65.22 (CH), 68.74 (CH), 69.04 (CH), 75.52 (CH), 84.25 (CH), 120.19 (CH), 124.84 (CH), 128.31 (CH), 128.61 (CH), 129.01 (CH), 130.03 (CH), 131.58 (CH), 133.64 (CH), 136.98 (C), 139.75 (C), 144.05 (C), 147.78 (C), 163.28 (C), 168.96 ($\mathit{C}OCH_3$), 169.61 ($\mathit{C}OCH_3$), 169.74 ($\mathit{C}OCH_3$), 170.51 ($\mathit{C}OCH_3$).

HRMS (ESI): *m*/*z* calcd for $C_{29}H_{29}N_3O_{10}$ + Na $[M + Na]^+$: 602.1751; found: 602.1748.

16a

Yield: 46 mg (87%); white solid; mp 128–130 °C.

IR (KBr): 3483, 3088, 2360, 1748, 1455, 1368, 1256, 1224, 1097, 1068 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 2.08 (s, 3 H, $COCH_3$), 3.99–4.01 (m, 1 H), 4.15 (dd, *J* = 1.8, 12.6 Hz, 1 H), 4.30 (dd, *J* = 4.8, 12.6 Hz, 1 H), 4.59 (s, 2 H), 4.69 (s, 2 H), 5.24 (t, *J* = 9.6 Hz, 1 H), 5.41–5.46 (m, 2 H), 5.87–5.90 (d, *J* = 9.0 Hz, 1 H), 7.29–7.38 (m, 5 H, Ar), 7.80 (s, 1 H, Ar).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.17 ($CO\mathit{C}H_3$), 20.50 ($CO\mathit{C}H_3$), 20.52 ($CO\mathit{C}H_3$), 20.67 ($CO\mathit{C}H_3$), 60.53 (CH_2), 61.50 (CH_2), 63.35 (CH_2), 67.65 (CH), 70.27 (CH), 72.47 (CH_2), 72.60 (CH), 75.07 (CH), 85.72 (CH), 120.88 (CH), 127.84 (CH), 127.96 (CH), 128.45 (CH), 137.60 (C), 146.00 (C), 168.92 ($\mathit{C}OCH_3$), 169.34 ($\mathit{C}OCH_3$), 169.90 ($\mathit{C}OCH_3$), 170.49 ($\mathit{C}OCH_3$).

HRMS (ESI): *m*/*z* calcd for $C_{24}H_{29}N_3O_{10}$ + Na $[M + Na]^+$: 542.1751; found: 542.1786.

17a

Yield: 52 mg (90%); white solid; mp 113–115 °C.

IR (KBr): 3474, 3074, 1748, 1512, 1455, 1375, 1227, 1095, 1067, 1041 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.87 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.07 (s, 6 H, 2 × $COCH_3$), 3.96–4.00 (m, 1 H), 4.11–4.15 (m, 2 H), 4.29 (dd, *J* = 4.8, 12.6 Hz, 1 H), 4.75 (s, 2 H), 5.03 (s, 2 H), 5.21–5.27 (m, 1 H), 5.39–5.45 (m, 2 H), 5.87–5.90 (m, 1 H), 7.42–7.56 (m, 4 H), 7.80 (s, 1 H), 7.84–7.88 (m, 2 H), 8.10 (d, *J* = 8.1 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.98 (CH_3), 20.34 (2 × CH_3), 20.48 (CH_3), 61.33 (CH_2), 63.18 (CH_2), 64.46 (CH_2), 70.16 (CH), 70.59 (CH), 72.42 (CH), 74.72 (CH), 85.44 (CH), 121.00 (CH), 123.85 (CH), 125.05 (CH), 125.65 (CH), 126.12 (CH), 126.66 (CH), 128.35 (CH), 128.64 (CH), 131.55 (C), 132.97 (C), 145.75 (C), 168.72 ($\mathit{C}OCH_3$), 169.20 ($\mathit{C}OCH_3$), 169.74 ($\mathit{C}OCH_3$), 170.31 ($\mathit{C}OCH_3$).

HRMS (ESI): *m*/*z* calcd for $C_{28}H_{31}N_3O_{10}$ + Na $[M + Na]^+$: 592.1907; found: 592.1916.

18a

Yield: 57 mg (90%); yellow solid; mp 108–110 °C.

IR (KBr): 3478, 3074, 1749, 1371, 1225, 1097, 1040 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.06 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 3.98–4.01 (m, 1 H), 4.13 (d, *J* = 12.0 Hz, 1 H), 4.28 (dd, *J* = 4.8, 12.5 Hz, 1 H), 5.2–5.26 (m, 1 H), 5.39–5.47 (m, 2 H), 5.58 (s, 2 H), 5.87–5.90 (m, 1 H), 7.45–7.58 (m, 4 H, Ar), 7.79 (s, 1 H), 8.02 (d, *J* = 8.1 Hz, 1 H, Ar), 8.35 (d, *J* = 9.0 Hz, 1 H, Ar), 8.48 (s, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.05 (CH_3), 20.40 (CH_3), 20.52 (CH_3), 20.59 (CH_3), 61.39 (CH_2), 63.51 (CH_2), 64.41 (CH_2), 67.50 (CH), 70.25 (CH), 72.49 (CH), 74.81 (CH), 85.54 (CH), 121.14 (CH), 124.12 (2 × C), 124.87 (2 × CH), 126.22 (2 × CH), 128.01 (C), 128.49 (CH), 128.89 (2 × CH), 130.89 (2 × C), 131.26 (2 × C), 145.94 (C), 168.79 ($\mathit{C}OCH_3$), 169.25 ($\mathit{C}OCH_3$), 169.81 ($\mathit{C}OCH_3$), 170.39 ($\mathit{C}OCH_3$).

HRMS (ESI): *m*/*z* calcd for $C_{32}H_{33}N_3O_{10}$ + Na $[M + Na]^+$: 642.2064; found: 642.2054.

19a

Yield: 44 mg (75%); white solid; mp 115–117 °C.

IR (KBr): 3466, 3086, 1752, 1740, 1520, 1458, 1367, 1256, 1235, 1222, 1142, 1042 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.84 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 3.33 (d, *J* = 7.2 Hz, 2 H), 3.87 (s, 3 H, OCH_3), 3.98–4.01 (m, 1 H), 4.14 (dd, *J* = 1.8, 12.3 Hz, 1 H), 4.29 (dd, *J* = 5.4, 12.6 Hz, 1 H), 5.07–5.11 (m, 2 H), 5.22–5.28 (m, 2 H), 5.39–5.46 (m, 2 H), 5.87 (d, *J* = 9.0 Hz, 1 H), 5.91–5.98 (m, 1 H), 6.7 (dd, *J* = 1.8, 8.4 Hz, 1 H), 6.73 (d, *J* = 1.8 Hz, 1 H), 6.93 (d, *J* = 7.8 Hz, 1 H), 7.87 (s, 1 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.12 ($CO\mathit{C}H_3$), 20.49 ($CO\mathit{C}H_3$), 20.52 ($CO\mathit{C}H_3$), 20.67 ($CO\mathit{C}H_3$), 39.8 (CH_2), 55.78 (CH_3), 61.50 (CH_2), 63.24 (CH_2), 67.62 (CH), 70.18 (CH), 72.67 (CH), 75.05 (CH), 85.67 (CH), 112.35 (CH), 114.68 (CH), 115.73 (CH), 120.47 (CH), 121.33 (CH), 134.00 (C), 137.46 (C), 145.24 (C), 145.80 (C), 149.61 (C), 168.82 ($\mathit{C}OCH_3$), 169.32 ($\mathit{C}OCH_3$), 169.92 ($\mathit{C}OCH_3$), 170.51 ($\mathit{C}OCH_3$).

HRMS (ESI): *m*/*z* calcd for $C_{27}H_{33}N_3O_{11}$ + Na $[M + Na]^+$: 598.2013; found: 598.2008.

20a
Yield: 43 mg (80%); white solid; mp 124–126 °C.

IR (KBr): 3480, 3119, 1755, 1549, 1446, 1417, 1374, 1229, 1155, 1099 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 3.98–4.03 (m, 1 H), 4.14 (dd, *J* = 1.8, 12.5 Hz, 1 H), 4.30 (dd, *J* = 5.1, 12.6 Hz, 1 H), 4.59 (s, 2 H), 4.67 (s, 2 H), 5.21–5.27 (m, 1 H), 5.39–5.47 (m, 2 H), 5.86–5.89 (m, 1 H), 7.11 (d, *J* = 4.8 Hz, 1 H, Ar), 7.27–7.33 (m, 2 H, Ar), 7.89 (s, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.77 (CH_3), 20.15 (CH_3), 20.19 (CH_3), 20.29 (CH_3), 61.23 (CH_2), 62.70 (CH_2), 66.89 (CH_2), 67.34 (CH), 70.05 (CH), 72.23 (CH), 74.45 (CH), 85.17 (CH), 120.94 (CH), 123.11 (CH), 125.77 (CH), 127.18 (CH), 138.44 (C), 145.45 (C), 168.55 (*C*OCH_3), 169.08 (*C*OCH_3), 169.56 (*C*OCH_3), 170.13 (*C*OCH_3).

HRMS (ESI): *m*/*z* calcd for $C_{22}H_{27}Cl_2N_3O_{10}S$ + Na [M + Na]$^+$: 548.1315; found: 548.1277.

21a
Yield: 42 mg (79%); white solid; mp 105–107 °C.

IR (KBr): 3472, 3083, 1747, 1600, 1564, 1379, 1366, 1224, 1092, 1033 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.08 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 4.00–4.05 (m, 1 H), 4.13–4.18 (m, 1 H), 4.32 (dd, *J* = 5.1, 12.6 Hz, 1 H), 4.60 (s, 2 H), 4.74 (s, 2 H), 5.22–5.28 (m, 1 H), 5.40–5.48 (m, 2 H), 5.89–5.92 (m, 1 H), 7.28–7.30 (m, 2 H, Ar), 7.85 (s, 1 H), 8.59 (d, *J* = 4.5 Hz, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.99 (CH_3), 20.35 (CH_3), 20.38 (CH_3), 20.51 (CH_3), 61.38 (CH_2), 63.69 (CH_2), 67.53 (CH), 70.25 (CH), 70.29 (CH_2), 72.37 (CH), 74.94 (CH), 85.59 (CH), 121.01 (CH), 121.76 (2 × CH), 145.19 (C), 146.81 (C), 149.66 (2 × CH), 168.79 (*C*OCH_3), 169.22 (*C*OCH_3), 169.71 (*C*OCH_3), 170.31 (*C*OCH_3).

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{28}N_4O_{10}$ + Na [M + Na]$^+$: 543.1703; found: 543.1714.

22a
Yield: 51 mg (80%); yellowish white solid; mp 140–142 °C.

IR (KBr): 3473, 3136, 3097, 2940, 1749, 1601, 1583, 1487, 1457, 1371, 1224, 1096, 1042 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.88 (s, 3 H, $COCH_3$), 2.04 (s, 3 H, $COCH_3$), 2.08 (s, 3 H, $COCH_3$), 2.10 (s, 3 H, $COCH_3$), 3.99–4.04 (m, 1 H), 4.15 (dd, *J* = 1.8, 12.5 Hz, 1 H), 4.3 (dd, *J* = 5.1, 12.5 Hz, 1 H), 4.23–5.30 (m, 1 H), 5.39–5.53 (m, 2 H), 5.66 (s, 2 H), 5.91 (d, *J* = 9.0 Hz, 1 H), 7.54–9.02 (m, 5 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.16 (CH_3), 20.50 (2 × CH_3), 20.65 (CH_3), 61.51 (CH), 67.64 (CH_2), 67.72 (CH_2), 70.15 (CH), 72.77 (CH), 75.01 (CH), 85.65 (CH), 122.03 (CH), 126.70 (C), 127.00 (C), 127.75 (3 × CH), 133.41 (CH), 143.52 (C), 145.08 (C), 149.60 (C), 150.90 (C), 168.83 (*C*OCH_3), 169.31 (*C*OCH_3), 169.91 (*C*OCH_3), 170.47 (*C*OCH_3).

HRMS (ESI): *m*/*z* calcd for $C_{26}H_{26}Cl_2N_4O_{10}$ + Na [M + Na]$^+$: 647.0924; found: 647.0927.

23a
Yield: 62 mg (91%); white foam.

IR (KBr): 3508, 2990, 2941, 2361, 1756, 1456, 1375, 1227, 1166, 1073 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.31 (s, 3 H, CH_3), 1.39 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.49 (s, 3 H, CH_3), 1.88 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 3.99–4.33 (m, 8 H), 4.59 (d, *J* = 3.3 Hz, 1 H), 4.76–4.86 (m, 2 H), 5.20–5.89 (m, 5 H), 7.88 (s, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.08 (CH_3), 20.45 (CH_3), 20.48 (CH_3), 20.62 (CH_3), 25.36 (CO*C*H_3), 26.15 (CO*C*H_3), 26.74 (CO*C*H_3), 26.85 (CO*C*H_3), 62.48 (CH_2), 63.79 (CH_2), 67.27 (CH_2), 67.61 (CH), 70.22 (CH), 70.36 (CH), 72.55 (CH), 75.15 (CH), 81.03 (CH), 81.77 (CH), 82.52 (CH), 85.73 (CH), 105.21 (CH), 108.99 (C), 111.80 (C), 120.86 (CH), 145.73 (C), 168.85 (*C*OCH_3), 169.31 (*C*OCH_3), 169.84 (*C*OCH_3), 170.41 (*C*OCH_3).

HRMS (ESI): *m*/*z* calcd for $C_{29}H_{41}N_3O_{15}$ + Na [M + Na]$^+$: 694.2435; found: 694.2432.

24a
Yield: 41 mg (79%); yellow solid; mp 148–150 °C.

IR (KBr): 3483, 3080, 2936, 2853, 1748, 1454, 1368, 1227, 1097, 1039 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 1.21–1.33 (m, 6 H), 1.74–1.76 (m, 2 H), 1.88 (s, 3 H, $COCH_3$), 1.93–1.95 (m, 2 H), 2.03 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 3.36–3.39 (m, 1 H), 3.98–4.01 (m, 1 H), 4.14 (dd, *J* = 1.9, 12.5 Hz, 1 H), 4.30 (dd, *J* = 4.8, 12.5 Hz, 1 H), 4.67 (2 s, 2 H), 5.24 (t, *J* = 9.6 Hz, 1 H), 5.40–5.48 (m, 2 H), 5.88 (d, *J* = 9.0 Hz, 1 H), 7.77 (s, 1 H, Ar).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 20.18 (CO*C*H_3), 20.50 (CO*C*H_3), 20.52 (CO*C*H_3), 20.67 (CO*C*H_3), 24.09 (CH_2), 24.10 (CH_2), 25.69 (CH_2), 32.05 (CH_2), 32.15 (CH_2), 61.24 (CH_2), 61.53 (CH_2), 67.67 (CH), 70.21 (CH), 72.70 (CH), 75.02 (CH), 85.64 (CH), 120.57 (CH), 147.05 (C), 168.89 (*C*OCH_3), 169.33 (*C*OCH_3), 169.91 (*C*OCH_3), 170.50 (*C*OCH_3).

HRMS (ESI): *m*/*z* calcd for $C_{23}H_{33}N_3O_{10}$ + Na [M + Na]$^+$: 534.2064; found: 534.2072.

25a
Yield: 34 mg (69%); yellow solid; mp 118–120 °C.

IR (KBr): 3482, 3087, 2962, 2874, 1748, 1445, 1371, 1222, 1114, 1042 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 0.92 (t, *J* = 7.35 Hz, 3 H, CH_3), 1.32–1.44 (m, 2 H, CH_3CH_2), 1.54–1.64 (m, 2 H, $CH_3CH_2CH_2$), 1.88 (s, 3 H, $COCH_3$), 2.03 (s, 3 H, $COCH_3$), 2.07 (s, 3 H, $COCH_3$), 2.09 (s, 3 H, $COCH_3$), 3.51 (t, *J* = 6.6 Hz, 3 H, OCH_2CH_3), 3.99–4.03 (m, 1 H), 4.13–4.17 (m, 1 H), 4.30 (dd, *J* = 5.1, 12.5 Hz, 1 H), 5.21–5.28 (m, 1 H), 5.39–5.49 (m, 2 H), 5.88–5.91 (m, 1 H), 7.78 (s, 1 H, Ar).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.60 (CH_3), 18.95 (CH_2), 19.85 (CO*C*H_3), 20.21 (CO*C*H_3), 20.25 (CO*C*H_3), 20.36 (CO*C*H_3), 31.35 (CH_2), 61.32 (CH_2), 63.75 (CH_2), 67.43 (CH), 70.05 (CH), 70.20 (CH_2), 72.38 (CH), 74.59 (CH), 85.26 (CH), 120.62 (CH), 145.96 (C), 168.61 (*C*OCH_3), 169.14 (*C*OCH_3), 169.64 (*C*OCH_3), 170.23 (*C*OCH_3).

HRMS (ESI): *m*/*z* calcd for $C_{21}H_{31}N_3O_{10}$ + Na [M + Na]$^+$: 508.1907; found: 508.1921.

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