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Efficient and selective azidation of *per-O*-acetylated sugars using ultrasound activation: Application to the one-pot synthesis of 1,2,3-triazole glycosides

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An inexpensive, simple and highly efficient process was developed for the selective anomeric azidation of protected sugars using a cooperative effect of iron catalysis and ultrasound activation, in the presence of $SO_2(N_3)_2$. The latter, as soluble azide source, is generated *in situ* by reaction of sodium azide and sulfuryl chloride under sonication. The obtained azidoglycosides undergo clean 1,3-dipolar cycloaddition with terminal alkynes under ultrasound activation to afford 1,2,3-triazole glycosides in high yields. These results illustrate that ultrasounds can significantly enhance the efficiency of both azidation and cycloaddition steps and lead to good overall yields. The stereo- and regioselectivity of the azidation and the 1,3-dipolar cycloaddition reactions have also been examined.

Introduction

Azidoglycosides represent an important class of reactive agents used for various chemical reactions including Staudinger reduction, Curtius and Schmidt rearrangements, and in 1,3-dipolar cycloadditions.[1] Given the chemical relevance of azidoglycosides as multifunctional reactive intermediates, the synthesis of these derivatives has long been the aim pursued by researchers from various fields.[1] Indeed, azidoglycosides were usefully used as precursors for the synthesis of amino sugars, glycosylamines, neoglycoconjugates such as *N*-glycopeptides, *N*-glycoproteins, heterocyclic compounds and for other biochemical applications.[1-3] Several methods have been reported for carbohydrates azidation at the anomeric position including Mitsunobu reaction on free anomeric hydroxy, Lewis acid-assisted azidation by addition on oxonium intermediates, transformation of 1,2-anhydro sugars and nucleophilic substitution at C1-stereocentre.[1] A widely applied strategy in carobohydrates is the nucleophilic substitution of glycosyl halides by azide ion. However, this methodology is limited by the instability of glycosyl halides which opened the way for a series of one pot procedures to avoid isolation and storage of these instable intermediates.[1,4] Among them, the direct preparation of azidoglycosides from glycosyl acetates by treatment with trimethylsilyl azide (TMSA) in the presence of a Lewis acid as the catalyst is the most convenient.[5] However, even if TMSA generally gave good azidation yields, its use is hampered by its instability, high sensitivity to hydrolysis and high cost, which limits large scale syntheses. Thus, to circumvent these drawbacks inexpensive and robust alternatives are required.[6]

Furthermore, the growing interest in azidoglycosides derivatives also rises from their high potential value as building blocks in Cu^I-catalyzed Huisgen cycloaddition.[7] Their utility in the synthesis of 1,2,3-triazolyl glycosides and the need for the development of efficient protocols towards effective glycosylation are of great interest. In this context, our group has devoted efforts in developing general protocols using unconventional ultrasound and microwave activations to overcome synthetic limitations in nucleoside synthesis.[8] Indeed, sonication[9] and microwaves[10] have emerged as powerful techniques to enhance reaction rates of a variety of chemical transformations. On the one hand, microwave-assisted synthesis is often performed without solvent for a better efficiency, thus making this method not ideally compatible for syntheses involving molecules with high polarity such as carbohydrates.[11] On the other hand, sonication can provide the required energy to increase the reactivity of carbohydrates/metal catalysts, towards the synthesis of highly functionalized glycosides and nucleosides.[8b,c]

In continuation of our investigations for the development of original routes to functionalized nucleosides and their biochemical applications,[12] we report herein an inexpensive, selective and robust

one-pot synthesis of functionalized triazolyl-glycosides through a Cu^{I}/Fe^{III} co-catalyzed sequential azidation, using *in situ* generated $SO_2(N_3)_2$, followed by a 1,3-dipolar cycloaddition between the azidoglycosides and various terminal alkynes under ultrasound activation. In our knowledge, carbohydrate azidation using this procedure with $SO_2(N_3)_2$ has not been reported before.[13]

Results and discussion

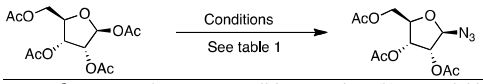
As a model reaction, we investigated the reactivity of ribose 1,2,3,5-*tetra*-*O*-acetate **1a** and $SO_2(N_3)_2$ in the presence of various catalysts, with and without ultrasound irradiation (Table 1). In a typical experiment, sulfuryl chloride (1 mmol) is added dropwise to a cold suspension of sodium azide (2 mmol) in dichloromethane (5 mL), the mixture is sonicated at room temperature and then **1a** (1 mmol) and the catalyst (20 mol%) were successively added with continuous sonication.

Optimization of the reaction parameters revealed that the treatment of **1a** with $SO_2(N_3)_2$ without catalyst under both magnetic stirring or ultrasound irradiation did not yield the desired product even with a prolonged reaction time (Table 1, entry 1). Interestingly, upon addition of a Lewis acid catalyst such as $AlCl_3$, the reaction led to **2a** in 59% yield, which can be further increased to 65% within shorter reaction time under US-irradiation (Table 1, entry 2). Encouraged by this result, we screened different Lewis acid catalysts in the presence of $SO_2(N_3)_2$. We found that $ZnCl_2$, $SnBr_4$, $InCl_3$ and $FeCl_2$ could also efficiently catalyze the azidation reaction and the yields were further increased by an additional 10% compared to $AlCl_3$ (Table 1, entries 3-6). $BF_3{\cdot}Et_2O$ was also found to be an excellent catalyst leading to 80% of **2a** (Table 1, entry 7). No ultrasound effect was observed in the case of $BF_3{\cdot}Et_2O$ because of its high solubility in CH_2Cl_2. The best result was obtained using $FeCl_3$, as a near quantitative yield was observed within a short reaction time under US-activation (96%, Table 1, entry 8). This result maybe explained by the high-energy effects of acoustic cavitation with the expected mechanical pulverization responsible for the optimal dissolution of suspended iron catalyst under sonication, compared to classical stirring. Furthermore, as shown in this reaction, 20 mol% of catalyst is required since the use of only 10 mol% of $FeCl_3$ induced a significant yield decrease (45%). It is worth noting that in all these experiments the yields were increased and reactions were significantly accelerated under ultrasound irradiation.

We also observed that a strong Lewis acid, TMSOTf, did not efficiently catalyze the azidation and only significant degradation was noticed. Moreover, the use of other solvents such as acetonitrile, acetone and THF gave lower yields, which can be ascribed to their coordination properties responsible for catalyst deactivation.

The successful azidation of protected sugar **1a** clearly demonstrate the efficiency of this procedure. Moreover, this reaction, compared to other methodologies, do not liberate toxic gases and only non-toxic compounds were generated at the end of the reaction, e.g., sodium chloride and diacetyl sulphate (see Figure 1). Indeed, as proposed in figure 1, the reaction would start with a stereospecific β-facial addition of $SO_2(N_3)_2$ to the oxonium intermediate followed by nucleophilic attack of AcO^- to the sulfonylazide, with a concomitant release of azido-sugar **2a**. The second part of the mechanism probably involves the *O*-acetyl-sulfonyl azide as azido-donating group, with the ultimate elimination of Ac_2SO_4 and formation of **2a**.

Table 1. Optimization of the reaction conditions using Lewis acid and NaN_3/SO_2Cl_2



Entry[a]	Catalyst	Conditions	Time (h)	Yield (%)[b]
1	None	Stir.	24	0[c]
		US	2	0[c]
2	$AlCl_3$	Stir.	4	59
		US	0.75	65
3	$ZnCl_2$	Stir.	4	68
		US	0.75	73
4	$SnBr_4$	Stir.	4	69
		US	0.5	78
5	$InCl_3$	Stir.	3	70
		US	0.25	75
6	$FeCl_2$	Stir.	4	68
		US	0.25	80
7	$BF_3.Et_2O$	Stir.	3	81
		US	0.25	80
8	$FeCl_3$	Stir.	4	78
		US	0.25	89
		US	0.75	96
		US	1	45[d]
9	TMSOTf	US	0.25	-[e]

[a] Reactions were performed under stirring (Stir) or by sonication (US): NaN_3 (1 mmol), SO_2Cl_2 (0,5 mmol) and **1a** (1 mmol), catalyst (20 mol%), CH_2Cl_2 (5 mL). [b] Isolated yields. [c] Starting material was recovered. [d] Azidation of **1a** with 10 mol% of $FeCl_3$. [e] **1a** underwent complete conversion to unidentified products (degradation).

Under this optimized reaction conditions, the azidoglycoside **2a** was isolated as a pure β-anomer, presumably according to the mechanism shown in figure 1; the stereospecificity of the process being driven by the anchimeric participation of the acetate group in C2-position.

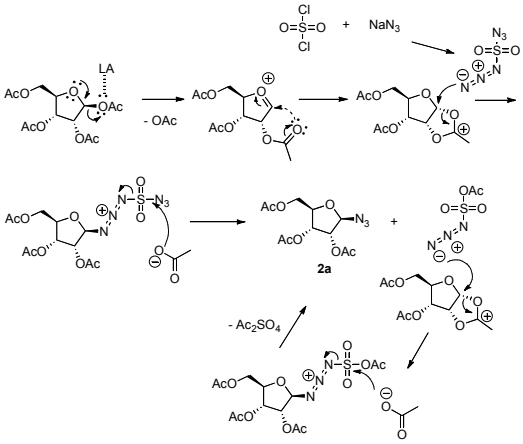
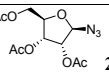
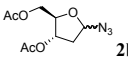
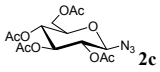
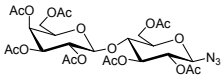
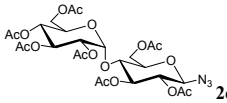


Figure 1. Proposed mechanism for the azidation reaction.

With this optimized reaction conditions in hand, the scope and limitations of this methodology were explored using various protected sugars. In general, all reactions between NaN_3/SO_2Cl_2 and various sugars, e.g., deoxyribose, glycopyranose, lactose

and maltose, were clean and the corresponding azido-derivatives were obtained in good yields (Table 2). The β-stereochemistry was maintained in all derivatives except in the case of deoxyribose **1b**, which gave a mixture of α- and β-anomers in 2/3 ratio, due to the lack of anchimeric assistance.

Sugar[a]	Azidoglycosides	Yield (%)[b]	Ratio α/β [c]
1a	 **2a**	96	0/100
1b	 **2b**	64	40/60
1c	 **2c**	72	0/100
1d	 **2d**	68	0/100
1e	 **2e**	67	0/100

[a] Reactions were performed on 1 mmol NaN_3, 0,5 mmol SO_2Cl_2 and 1 mmole of acetylated sugar **1** with 20 mol% of $FeCl_3$ in 5 mL of CH_2Cl_2, 45 min. [b] Isolated yields. [c] Based on ^{1}H NMR.

Confirmation of the stereochemistry at the anomeric centre of azidoglycosides **2a-2e** was clearly attested by ^{1}H NMR and ^{1}H 2D NOESY experiments. For example, as shown in figure 2, the β-configuration of **2a** was unambiguously evidenced by the chemical shift of H1' at 5.30 ppm, its coupling with H2' (J = 1.9 Hz) and a clear NOESY correlation between H1' and H4'. Similar correlations were observed between H1' and H3' for compounds **2c** and **2e** (Figure 2).

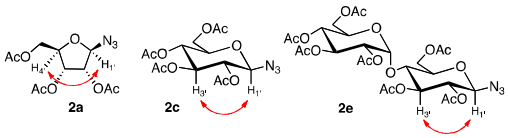
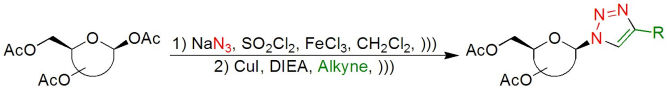


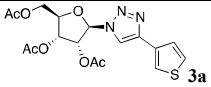
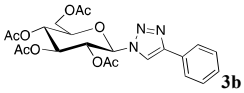
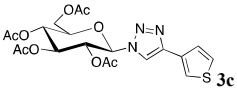
Figure 2: Example of significant NOESY correlations

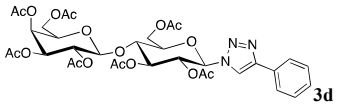
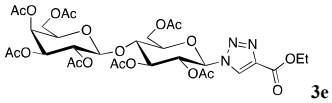
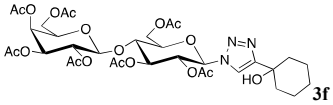
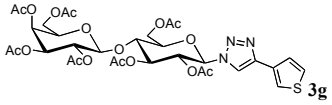
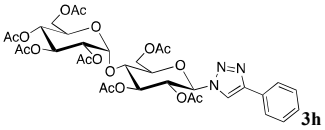
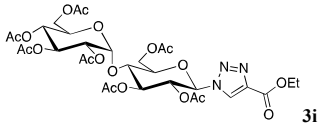
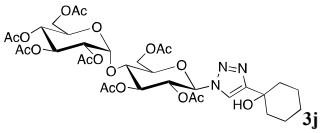
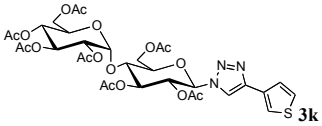
After establishing a viable route to prepare different azidoglycosides, we investigated a one-pot procedure to access functionalized 1,2,3-triazole glycosides starting from per-*O*-acetylated sugars. To this end, we investigated a one-pot sequential 1,3-dipolar cycloaddition step according to our previously developed protocol using alkyne/CuI/DIEA in CH_2Cl_2 under sonication.[8b,c] As shown in table 3, this sequential one-pot process was applied on per-*O*-acetylated sugars **1a** and **1c-e** with a range of alkynes. All experiments were performed in relatively short global times (1-3 h) and with good overall yields (60–86%). Moreover, the anomeric stereochemistry of all products remained unchanged during this transformation, as attested by NMR data. The stereo- and regio-chemistry of **3a-3i** were unambiguously confirmed by ^{1}H NMR, NOESY and HMBC experiments (Figure 3). For example, the β configuration of **3d** was clearly evidenced by the chemical shift of H1' at 6.38 ppm, the value of its coupling constant with H2' ($J_{1'-2'}$ = 8.7 Hz) and the NOESY correlation between H1' and H3'. The 1,4-substitution pattern of the triazole was confirmed by a NOESY correlation between H1' and H5-triazole. The ^{1}H-^{13}C HMBC spectrum of **3d** shows C1'-H5 and H5-C1 phenyl cross coupling, in accordance with the proposed structure.

Table 3: One-pot procedure under ultrasound activation.



1a, 1c, 1d, 1e **3a-3l**

Entry [a]	Alkyne	Product	Time (h)	Yield (%) [b]
1		 **3a**	1	89
2		 **3b**	2	62
3		 **3c**	1.5	68

4		 **3d**	3	60
5		 **3e**	2.5	65
6		 **3f**	2.5	67
7		 **3g**	2.5	64
8		 **3h**	3	62
9		 **3i**	2.5	66
10		 **3j**	2.5	65
11		 **3k**	3	68

[a] All reaction steps were monitored by TLC analysis, the first step of the azidation was carried out under sonication at room temperature, *O*-acetylated sugar **1** (1 mmol), NaN_3 (1 eq.)/SO_2Cl_2 (0,5 equiv), $FeCl_3$ (20 mol %), CuI (2 equiv), DIEA (2 equiv), alkyne (2 equiv). [b] Isolated yield

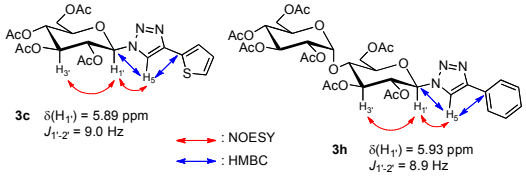


Figure 3: Significant NOESY and HMBC correlations

Conclusion

In conclusion, we have developed a new, inexpensive and efficient azidation method of per-*O*-acetylated sugar using commercially available sodium azide, sulfuryl chloride and iron chloride under sonication. The intermediate $SO_2(N_3)_2$, generated *in situ*, showed remarkable efficiency as a soluble azide source.[14] A cooperative

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effect of iron and copper co-catalysis and ultrasound activation was also successfully applied in a one-pot procedure to access functionalized triazole glycosides. Further investigations are currently under way to explore the efficiency of $SO_2(N_3)_2$ in the enantioselective azidation of asymmetric alcohols. Moreover, since triazole nucleosides demonstrated high promising bioactivities,[15,16] all the synthesized triazoles and their sugar-free analogues will be evaluated for their antiviral and antitumor activities.

Experimental section

General. All organic solvents were purchased from commercial sources and used as received or dried using standard procedures, unless otherwise stated. All chemicals were purchased from Aldrich, Merck or Alfa Aesar and used without further purification; thin layer chromatography (TLC) was performed on precoated Merck 60 GF254 silica gel plates and revealed by spraying (p-anisaldehyde or H_2SO_4/EtOH), and detection by means of UV light at 254 and 360 nm. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 200 MHz spectrometer. Mass spectra (ESI MS) were recorded on a Brucker (Daltonics Esquire 3000+). HRMS spectra were carried out on a ThermoFisher Q Exactive plus in ESI mode positive and negative depending on the compounds to identify. We use a pump syringe at a flow of 3ul/mn and with the mass spectrometer at a resolution of 140 000 at m/z 200 for best accuracy. The purity of compounds was further verified to be >95% by HPLC analysis using analytical columns Hypersil (C18 (ELITE), 4.6 mm x 250 mm) or Nucleosil (120-5C8 (HICHROM), 4.6 mm x 250 mm) with an isocratic elution of CH_3CN/H_2O, 90/10. The ultrasound-assisted reactions were carried out in a "Branson Bransonic® 5510 DTH UltraSonic Bath Cleaner", with a frequency of 40 kHz. The ultrasonic cleaner has a power consumption of 185W (399 × 371 × 401 mm) with liquid holding capacity of 9.5 L.

General procedure for the synthesis of azidoglycoside (2a-e). To a cold suspension of sodium azide (2 mmol) in dichloromethane (5 mL), sulfuryl chloride (1mmol) is added drop wise. After the completion of the addition the mixture is sonicated for few minutes, and then the acetylated sugar **1a-e** (2 mmol) and Lewis acid catalyst (20 mol %) are added to the mixture. The reaction mixture is sonicated during 45 min. After the completion of the reaction (TLC monitoring), the mixture was diluted with dichloromethane and washed with a saturated aqueous solution of $NaHCO_3$. The organic layer was washed with water (2×10 mL), dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The residue was subjected to purification by silica gel column chromatography [Cyclohexane-EtOAc (9:1)] to give the pure azidoglycoside **2a-e**.

2a. Colorless oil; R_f = 0.73 (cyclohexane-AcOEt: 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.99 (s, 3H, Ac), 2.04 (s, 6H, 2Ac), 4.06 (dd, *J* = 11.9, 4.0 Hz, 1H, H5'), 4.20-4.40 (m, 2H, H4' et H5'), 5.05 (dd, *J* = 4.8, 1.9 Hz, 1H, H2'), 5.25 (dd, *J* = 6.7, 4.8 Hz, 1H, H3'), 5.30 (d, *J* = 1.9 Hz, 1H, H1'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.3, 20.4, 20.6, 62.9, 70.4, 74.4, 79.3, 92.6, 169.3, 169.5, 170.5; MS (ES) m/z = 324.1 $[M+Na]^+$.

2b. Yellow oil; R_f = 0.74 (cyclohexane-AcOEt : 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 2.02 (s, 3H, OAc), 2.05 (s, 3H, OAc), 2.10-2.47 (m, 2H, 2H2'), 3.96-4.30 (m, 3H H4' and 2H5'), 5.03 (m, 0.6H, H3' α), 5,16 (m, 0.4H, H3' β), 5.54 (d, *J* = 6.2 Hz, 1H, H1'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.8, 21.0, 38.6, 63.6, 74.0, 83.0, 91.9, 170.5, 170.8; MS (ES) m/z = 266.1 $[M+Na]^+$.

2c. White solid; Mp = 124-125°C; R_f = 0.45 (cyclohexane-AcOEt: 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.94 (s, 3H, OAc), 1.97 (s, 3H, OAc), 2.01 (s, 3H, OAc), 2.04 (s, 3H, OAc), 3.72-3.80 (m, 1H, H5'), 4.09 (dd, *J* = 12.4, 2.0 Hz, 1H, H6'), 4.22 (dd, *J* = 12.5, 4.5 Hz, 1H, H6'), 4.61 (d, *J* = 8.9 Hz, 1H, H1'), 4.89 (t, *J* = 9.0 Hz, 1H, H2'), 4.99-5.21 (m, 2H, H4' and H3'); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.5 (2C), 20.7 (2C), 61.7, 67.9, 70.6, 72.6, 74.0, 87.8, 169.2, 169.3, 170.0, 170.5; MS (ES) m/z = 396.2 $[M+Na]^+$; HRMS calcd for $C_{14}H_{19}N_3O_9Na^+$ 396.10135, found 396.10110.

2d. White foamy solid; Mp = 88-89°C; Rf = 0.40 (cyclohexane-AcOEt: 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.93 (s, 3H, OAc), 2.01-2.03 (m, 12H, 4OAc), 2.10-2.12 (m, 6H, 2OAc), 3.64-3.88 (m, 3H, H4'and 2H6'), 4.04-4.15 (m, 3H, 2H6'' and H1'), 4.44-4.50 (m, 2H, H5' and H2'), 4.60 (d, *J* = 8.6 Hz, 1H, H4''), 4.78-4.95 (m, 2H, H5'' and H3'), 5.02-5.22 (m, 2H, H2'' and H3''), 5.31 (d, *J* = 3.3 Hz, 1H, H1''); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.6, 20.7 (2C), 20.7 (2C), 20.8 (2C), 20.9, 60.9, 61.8, 66.7, 69.1, 70.8, 71.0, 71.0, 72.6, 74.9, 75.8, 87.7, 101.2, 169.1, 169. 5, 169.7, 170.1, 170.2, 170.3, 170.4; MS (ES) m/z = 684.1 $[M+Na]^+$; HRMS calcd for $C_{26}H_{35}N_3O_{17}$ (-N_3) 619.18688, found 619.18750.

2e. White foamy solid; Mp = 66-67 °C; R_f = 0.40 (cyclohexane-AcOEt: 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.97-2.12 (m, 21H, 7OAc), 3.71-3.79 (m, 1H, H4'), 3.87-4.04 (m, 3H, 2H6' and H1'), 4.16-4.26 (m, 2H, 2H6''), 4.48 (dd, *J* = 12.3, 2.5 Hz, 1H, H5'), 4.65-4.85 (m, 3H, H2', H4'' and H5''), 5.02 (t, *J* = 9.8 Hz, 1H, H3''), 5.18-5.38 (m, 3H, H3', H2'' and H1''); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.6 (4C), 20.7, 20.8, 20.9, 61.5, 62.6, 68. 0, 68.7, 69.3, 70.1, 71.6, 72.4, 74.3, 75.1, 87.5, 95.8, 169.5, 169.5, 170.0, 170.1, 170.4, 170.5, 170.6; MS (ES) m/z = 684.3 $[M+Na]^+$; HRMS calcd for $C_{26}H_{35}N_3O_{17}$ (-N_3) 619.18688, found 619.18713.

General procedure for one-pot synthesis of 1,2,3-triazolyl glycosides. To a cooled suspension of sodium azide (2 mmol) in dichloromethane (5 ml), sulfuryl chloride (1 mmol) is added drop wise. After the completion of the addition the mixture was sonicated at room temperature. The sugar derivative (2 mmol) and anhydrous $FeCl_3$ catalyst (20 mol %) were added and sonication continued. After reaction completion (TLC monitoring), the alkyne (4 mmol), CuI (4 mmol) and diisopropylethylamine (4 mmol) were added to the mixture and then left under sonication. After completion of the reaction (TLC monitoring), the mixture was diluted with dichloromethane and successively washed with a saturated solution of NH_4Cl and water (2×10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography (Cyclohexane-EtOAc 8:2 to 5:5) to afford the triazolyl glycosides **3**.

3a. Foam; Mp: 96-97°C; R_f = 0.39 (cyclohexane-AcOEt: 1-1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.99 (s, 3H, OAc), 2.06 (s, 6H, 2OAc), 4.16 (dd, *J* = 12.2, 4.2 Hz, 1H, H5'), 4.35 (dd, *J* = 12.6, 3.0

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Hz, 1H, H5'), 4.39-4.47 (m, 1H, H4'), 5.56 (t, *J* = 5.3 Hz, 1H, H3'), 5.82 (dd, *J* = 5.0, 3.8 Hz, 1H, H2'), 6.12 (d, *J* = 3.7 Hz, 1H, H1'), 7.29-7.39 (m, 2H, H-thienyl), 7.60-7.66 (m, 1H, H-thienyl), 7.80 (s, 1H, *H*-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δppm: 20.4, 20.5, 20.7, 62.8, 70.7, 74.3, 80.9, 90.0, 118.5, 121.6, 125.7, 126.5, 131.2, 144.3, 169.3, 169.4, 170.4; MS (ES) *m/z* = 432.1 $[M+Na]^+$, 841.2 $[2M+Na]^+$; HRMS: calcd for $C_{17}H_{19}N_3O_7SH^+$ 410.10165, found 410.10151.

3b. White solid; Mp: 212-213°C; R_f = 0.40 (cyclohexane-AcOEt: 1-1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.87 (s, 3H, OAc), 2.03-2.07 (m, 9H, 3OAc), 3.99-4.18 (m, 2H, H6' and H5'), 4.33 (dd, *J* = 12.6, 5.0 Hz, 1H, H6''), 5.27 (t, *J* = 9.4 Hz, 1H, H3'), 5.39-5.58 (m, 2H, H-2'and H-4'), 5.94 (d, *J* = 8.8 Hz, 1H, H1'), 7.34-7.47 (m, 3H, H-phenyl), 7.81-7.85 (m, 2H, H-phenyl), 8.02 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.3, 20.6, 20.7, 20.8, 61.7, 67.8, 70.3, 72.8, 75.2, 85.9, 117.9, 126.0 (2C), 128.7, 129.0 (2C), 130.0, 148.6, 169.1, 169.5, 170.0, 170.6; MS (ES) *m/z* = 498.2 $[M+Na]^+$, 973.5 $[2M+Na]^+$; HRMS calcd for $C_{22}H_{26}N_3O_9$ 476.16636, found 476.16675.

3c. Beige solid; Mp = 209-210°C; R_f = 0.43 (cyclohexane-AcOEt: 7:3); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.86 (s, 3H, OAc), 2.02-2.06 (M, 9H, 3OAc), 3.98-4.16 (m, 2H, H6' and H5'), 4.27 (dd, *J* = 12.6, 5.0 Hz, 1H, H6'), 5.25 (t, *J* = 9.6 Hz, 1H, H4'), 5.38-5.95 (m, 2H, H3' and H2'), 5.93 (d, *J* = 9.1 Hz, 1H, H1'), 7.35-7.45 (m, 2H, H-thienyl), 7.70 (dd, J = 2.9, 1.3 Hz, 1H, H-thienyl), 7.91 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.2, 20.6, 20.6, 20.7, 61.7, 67.8, 70.3, 72.8, 75.1, 85.8, 117.6, 121.9, 125.9, 126.5, 131.2, 144.7, 169.0, 169.4, 169.9, 170.5; MS (ES) *m/z* = 504.0 $[M+Na]^+$, 985.1 $[2M+Na]^+$; HRMS calcd for $C_{20}H_{24}N_3O_9S$ 482.12278, found 482.12308.

3d. White solid; Mp = 165-166°C; R_f = 0.30 (cyclohexane-AcOEt : 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.85 (s, 3H, OAc), 1.95 (s, 3H, OAc), 2.04-2.07 (m, 12H, 4OAc), 2.14 (s, 3H, OAc), 3.86-3.95 (m, 3H, H4' and 2H6'), 4.02-4.18 (m, 3H, 2H6'' and H5'), 4.44-4.55 (m, 2H, H2' and H4'), 4.96 (dd, *J* = 10.4, 3.4 Hz, 1H, H5"), 5.12 (dd, *J* = 10.4, 7.7 Hz, 1H, H3'), 5.34-5.52 (m, 3H, H2'', H3'' and H1''), 5.88 (d, *J* = 8.8 Hz, 1H, H1'), 7.31-7.44 (m, 3H, H-phenyl), 7.77-7.82 (m, 2H, H-phenyl), 7.93 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.3, 20.6, 20.7 (2C), 20.7, 20.8, 20.8, 60.9, 61.9, 66.7, 69.1, 70.5, 70.9, 71.0, 72.7, 75.6, 76.0, 85.6, 101.1, 117.9, 125.9 (2C), 128.6, 128.9 (2C), 129.9, 148.3, 169.1, 169.3, 169.5, 170.1, 170.1, 170.3, 170.4; HRMS calcd for $C_{34}H_{42}N_3O_{17}$ 764.25087, found 764.25061.

3e. Yellow solid; Mp = 208-209°C; R_f = 0.23 (cyclohexane-AcOEt : 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.38 (t, *J* = 7.1 Hz, 3H, CH_3), 1.85 (s, 3H, OAc), 1.94 (s, 3H, OAc), 2.03-2.08 (m, 12H, 4OAc), 2.14 (s, 3H, OAc), 3.90-3.97 (m, 3H, H4' and 2H6'), 4.07-4.17 (m, 3H, 2H6'' and H5'), 4.34-4.54 (m, 4H, H2', H4'' and CH_2), 4.95 (dd, *J* = 10.4, 3.4 Hz, 1H, H5''), 5.11 (dd, *J* =10.4, 7.7 Hz, 1H, H3'), 5.35-5.40 (m, 3H, H3'', H2'' and H1''), 5.89 (d, *J* = 8.8 Hz, 1H, H1'), 8.29 (s, 1H, H-triazole). ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 14.2, 20.1, 20.5, 20.6 (4C), 20.7, 60.8, 61.5, 61.6, 66.6, 69.0, 70.6, 70.8, 70.8, 72.2, 75.5, 76.1, 85.6, 101.0, 126.2, 140.7, 160.2, 169.0, 169.1, 169.4, 170.0, 170.0, 170.1, 170.3; HRMS calcd for $C_{31}H_{42}N_3O_{19}$ 760.24070, found 760.24097.

3f. White solid; Mp = 154-155 °C; R_f = 0.16 (cyclohexane-AcOEt: 1:1), ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.30-2.14 (m, 31H, 7OAc and H-cyclohexyl), 2.44 (br, 1H, O*H*), 3.85-4.00 (m, 3H, H4' and 2H6'), 4.07-4.17 (m, 3H, 2H6'' and H5'), 4.43-4.53 (m, 2H, H2' and H4''), 4.95 (dd, *J* = 10.4, 3.4 Hz, 1H, H5''), 5.11 (dd, *J* = 10.4, 7.7 Hz, 1H, H3'), 5.33-5.43 (m, 3H, H2'', H3'' and H1''), 5.74-5.85 (m, 1H, H1'), 7.61 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.2, 20.6, 20.7, 20.7, 20.8, 20.9, 22.0, 25.4, 38.0, 60.9, 61.9, 66.7, 69.1, 69.6, 70.7, 70.9, 71.0, 72.6, 75.7, 75.9, 85.6, 101.2, 118.4, 126.0, 169.1, 169.2, 169.6, 170.1, 170.2, 170.3, 170.4; HRMS calcd for $C_{34}H_{48}N_3O_{18}$ 786.29274, found 786.29285.

3g. White solid; ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.84 (s, 3H, OAc), 2.00-2.11 (m, 18H, 6OAc), 3.93-4.29 (m, 6H, H4', 2H6', 2H6'' and H5'), 4.47 (dd, 1H, *J* = 12.3 and 2.0 Hz, H2'), 4.87 (dd, 1H, *J* = 10.5, 4.0 Hz, H4''), 5.06 (t, 1H, *J* = 9.8 Hz, H5''), 5.32-5.47 (m, 4H, H3', H2'', H3'' and H1''), 5.92 (d, 1H, *J* = 8.8 Hz, H1'), 7.36 (dd, *J* = 5.0, 2.9 Hz, 1H, H-thienyl), 7.42 (dd, *J* = 5.0, 1.3 Hz, 1H, H-thienyl), 7.69 (dd, *J* = 2.8, 1.3 Hz, 1H, H-thienyl), 7.81 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.2, 20.6, 20.7, 20.8, 20.8, 20.8, 61.5, 62.5, 67.9, 68.8, 69.2, 70.0, 70.9, 72.5, 75.2, 75.4, 85.3, 95.9, 117.6, 121.8, 125.8, 126.5, 131.1, 144.5, 169.3, 169.4, 169.9, 170.3, 170.6; HRMS calcd for $C_{32}H_{40}N_3O_{17}$ 770.20729, found 770.20728.

3h. White solid; R_f = 0.51 (cyclohexane-AcOEt: 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.84 (s, 3H, OAc), 2.00-2.11 (m, 18H, 6OAc), 3.94-4.52 (m, 6H, H4', 2H6', 2H6'' and H5'), 4.48 (dd, *J* = 12.4, 2.3 Hz, 1H, H2'), 4.87 (dd, *J* = 10.5, 4.0 Hz, 1H, H4''), 5.06 (t, *J* = 9.8 Hz, 1H, H5''), 5.32-5.53 (m, 4H, H3', H2'', H3'' and H1''), 5.93 (d, *J* = 8.9 Hz, 1H, H1'), 7.29-7.45 (m, 3H, H-phenyl), 7.79-7.83 (m, 2H, H-phenyl), 7.92 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.3, 20.7, 20.8 (3C), 20.9, 20.9, 61.5, 62.6, 68.0, 68.9, 69.3, 70.1, 70.9, 72.6, 75.3, 75.4, 85.4, 96.0, 117.9, 125.9 (2C), 128.7, 129.0 (2C), 129.9, 148.4, 169.4, 169.5, 170.0, 170.0, 170.4, 170.6, 170.6; HRMS calcd for $C_{34}H_{42}N_3O_{17}$ 764.25087, found 764.25049.

3i. Yellow solid; Mp =144-145°C; R_f = 0.33 (cyclohexane-AcOEt : 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.39 (t, *J* = 7.1 Hz, 3H, CH_3), 1.85 (s, 3H, OAc), 2.00-2.12 (m, 18H, 6OAc), 3.93-4.10 (m, 3H, 2H6' and H6''), 4.14-4.28 (m, 3H, 4.2 Hz, H6', H5' and H4'), 4.35-4.52 (m, 3H, H4'' and O*C*H_2CH$_3$), 4.86 (dd, *J* = 10.5, 4.0 Hz, 1H, H5''), 5.06 (t, *J* = 9.9 Hz, 1H, H3'), 5.24-5.36 (m, 2H, H2'' and H3''), 5.41-5.46 (m, 2H, H2' and H1''), 5.94 (d, *J* = 9.1 Hz, 1H, H1'), 8.26 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, DMSO-d_6) δ ppm: 14.1, 19.9, 20.3, 20.4, 20.4, 20.5, 20.5, 20.6, 60.9, 61.4, 62.7, 67.7, 68.2, 68.9, 69.5, 70.9, 73.1, 74.0, 83.8, 95.7, 128.3, 139.6, 159.8, 168.9, 169.2, 169.5, 169.7, 169.9, 170.0, 170.1; HRMS calcd for $C_{31}H_{42}N_3O_{19}$ 760.24070, found 760.24060.

3j. White solid; R_f = 0.22 (cyclohexane-AcOEt: 1:1); ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.31-2.11 (m, 31H, 7OAc and 5CH_2-cyclohexyl), 2.44 (br, 1H, O*H*), 3.92-4.28 (m, 6H, H4', 2H6', 2H6'' and H5'), 4.47 (dd, *J* = 12.2, 2.3 Hz, 1H, H2'), 4.86 (dd, *J* = 10.5,

4.0 Hz, 1H, H4''), 5.05 (t, *J* = 9.8 Hz, 1H, H5''), 5.26-5.49 (m, 4H, H3', H2'', H3'' and H1''), 5.86 (d, *J* = 9.1 Hz, 1H, H1'), 7.61 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, DMSO-d_6) δ ppm: 19.9, 20.3, 20.4, 20.5 (2C), 20.5, 20.6, 20.7, 21.7, 25.2, 37.4, 37.9, 61.4, 62.9, 67.7, 67.9, 68.2, 68.9, 69.4, 70.8, 73.4, 73.8, 74.4, 83.3, 95.7, 120.1, 156.0, 168.6, 169.2, 169.5, 169.7, 169.9, 170.0, 170.1; HRMS calcd for $C_{34}H_{48}N_3O_{18}$ 786.29274, found 786.29291.

3k. White solid; ^{1}H NMR (200 MHz, $CDCl_3$) δ ppm: 1.95 (s, 3H, OAc), 2.04 (s, 3H, OAc), 2.05-2.08 (m, 12H, 4OAc), 2.15 (s, 3H, OAc), 3.86-3.97 (m, 3H), 4.08-4.19 (m, 3H), 4.44-4.54 (m, 2H), 4.96 (dd, *J* = 10.4, 3.3 Hz, 1H), 5.13 (dd, *J* = 10.3, 7.8 Hz, 1H), 5.36-5.51 (m, 3H), 5.86 (d, *J* = 8.8 Hz, 1H), 7.35-7.43 (m, 2H), 7.68-7.69 (m, 1H), 7.82 (s, 1H, H-triazole); ^{13}C NMR (50 MHz, $CDCl_3$) δ ppm: 20.3, 20.5, 20.7, 20.7, 20.7, 20.8, 60.9, 61.8, 66.6, 69.1, 70.50, 70.9, 70.9, 72.7, 75.7, 76.0, 85.6, 101.1, 117.6, 121.8, 125.8, 126.5, 131.1, 144.5, 169.1, 169.3, 169.5, 170.1, 170.1, 170.2, 170.4; HRMS calcd for $C_{32}H_{40}N_3O_{17}$ 770.20729, found 770.20721.

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1 For review see: (a) Z. J. Witczak, *Carbohydr. Chem.* 2010, **36**, 176-193; (b) Z. Györgydeak, J. Thiem, *Adv. Carbohydr. Chem. BioChem.*, 2006, **60**, 103-182; (c) For recent review on reactivity of organic azides see: (e) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.*, 2005, **44**, 5188-5240

2 (*a*) M. Meldal, C. W. Tornøe, *Chem. Rev.*, 2008, **108**, 2952-3015; (*b*) S. Deng, U. Gangadharmath, C-W. Tom Chang, *J. Org. Chem.*, 2006, **71**, 5179-5185; (c) A. Marra, A. Vecchi, C. Chiappe, B. Melai, A. Dondoni, *J. Org. Chem.*, 2008, **73**, 2458-2461.

3 (*a*) O. Boutureira, G. J. L. Bernardes, *Chem. Rev.*, 2015, DOI: 10.1021/cr500399p; (b) Z. Lei, J. Wang, Y. Tian, G. Song, G. Zhao, H. Xu, *Dyes and Pigments*, 2015, **113**, 627-633. (c) B. Cobucci-Ponzano, F. Conte, E. Bedini, M. M. Corsaro, M. Parrilli, G. Sulzenbacher, A. Lipski, F. D. Piaz, L. Lepore, M. Rossi, M. Moracci, *Chemistry&Biology*, 2009, **16**, 1097-1108.

4 (a) R. Kumar, P. Tiwari, P. R. Maulik, A. K. Misra, *Eur. J. Org. Chem.*, 2006, 74-79. (b) M. L. Lepage, A. Bodlenner, P. Compain, *Eur. J. Org. Chem*, 2013, 1963-1972.

5 (a) K. El Akri, K. Bougrin, J. Balzarini, A. Faraj, A.; Benhida, R. *Bioorg. Med. Chem. Lett.*, 2007, **17**, 6656-6659; (b) C. Loukou, M. Tosin, H. Müller-Bunz, P. V. Murphy, *Carbohydr. Res.*, 2007, **342**, 1953-1959; (c) M. Spadafora, V. Y. Postupalenko, V. V. Shvadchak, A. S. Klymchenko, Y. Mély and A. Burger, *Tetrahedron*, 2009, **65**, 7809–7816.

6 For other alternatives see: (a) T. Tanaka, H. Nagai, M. Noguchi, A. Kobayashia, S-I Shoda, *Chem. Commun.*, 2009, 3378-3379; (b) M. Farrell, J. Zhou, P. V. Murphy, *Chem. Eur. J.*, 2013, **19**, 14836-14851; (c) S. B. Salunke, N. S. Babu, C. T. Chen, *Chem. Commun.*, 2011, **47**, 10440–10442;

7 (*a*) C. O. Kappe, E. Van der Eycken, *Chem. Soc. Rev.*, 2010, **39**, 1280-1290; (*b*) A. K. Feldman, B. Colasson, V. V. Fokin, *Org. Lett.*, 2006, **6**, 3897-3899; (*c*) P. Appukkuttan, W. Dehaen, V. V. Fokin, E. Van der Eycken, *Org. Lett.*, 2004, **6**, 4223-4225; (d) K. Kacprzak, *Synlett*, 2005, **6**, 943-946.

8 (*a*) R. Guezguez, K. Bougrin, K. El Akri, R. Benhida, *Tetrahedron Lett.*, 2006, **47**, 4807-4811; (*b*) M. Driowya, A. Puissant, G. Robert, P. Auberger, R. Benhida, K. Bougrin, *Ultrason. Sonochem.*, 2012, **19**, 1132-1138; (*c*) H. Marzag, G. Robert, M. Dufies, K. Bougrin, P. Auberger, R. Benhida, *Ultrason. Sonochem.*, 2015, **22**, 15-21. (d) Driowya, M.; Bougrin, K.; Benhida. *Synth. Commun.*, 2013, **43**, 1808–1817. (e) V. Malnuit, M. Duca, A. Manout, K. Bougrin, R. Benhida, *Synlett*, 2009, **13**, 2123-2128.

9 (a) S. D. Lepore, Y. J. He, *J. Org. Chem*., 2003, 68, 8261-8263; (b) A. R. Gholap, K. Venkatesan, D. Daniel, R. J. Lahoti, K. V. Srinivasan, *Green Chem.*, 2003, **6**, 693-696; (c) M.-Y. Chen, K.-C. Lu, A. S.-Y. Lee, C.-C Lin, *Tetrahedron Lett.*, 2002, 43, 2777-2780; (d) Y. G. Adewuyi, Ind. Eng. Chem. Res., 2001, **40**, 4681-4715; (e) N. Kardos, N., J.-L. Luche, *Carbohydr. Res.*, 2001, **332**, 115-131.

10 (a) C. O. Kappe, A. Stadler, In Methods and Principles in Medicinal Chemistry; R. Mannhold, H. Kubinyi, G. Folkers, Eds.; VCH: Weinheim, Germany, 2005, Vol. 409, p 139; (b) J. P. Tierney, P. Lidstrom, Microwave Assisted Organic Synthesis; Eds., Blackwell, Oxford, UK, 2005, Vol. 280, p 89; (c) K. Bougrin, A. Loupy, M. Soufiaoui, *J. Photochem. Photobiol. C: Photochem. Rev.*, 2005, **6**, 139-167; (d) K. Bougrin, M. Soufiaoui, G. Bashiardes, Microwaves in Cycloadditions. In "Microwaves in Organic Synthesis", Loupy, A. 2nd (ed), Wiley-VCH, Weinheim, 2006, Vol. 2, p 524; (e) K. Bougrin, R. Benhida, Microwave-assisted cycloadditions reactions. In A. De la Hoz, A. Loupy, Eds, Microwaves in organic synthesis, 3rd Eds. Wiley-VCH, Weinheim, 2012, Vol. 2, pp 737-809. (f) H. Marzag, A. Saber, K. Bougrin, R. Benhida, *Curr Org Chem*, 2014, **18**, 2139-2180.

11 (a) I. Idri, J. L. Havet, J. M. Garcia Fernandez, C. Ferroud, C. Porte, *Food Chem.*, 2012, **134**, 1527-1532; (b) A. Corsaro, U. Chiacchio, V. Pistara, G. Romeo, *Curr. Org. Chem.*, 2004, *8*, 511-538.

12 (*a*) D. Dziuba, V. Y. Postupalenko, M. Spadafora, A. S. Klymchenko, V. Guérineau, Y. Mély, R. Benhida, A. Burger, J. Am. Chem. Soc., 2012, 134, 10209–10213; (*b*) M. Duca, V. Malnuit, F. Barbault, R.

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Benhida, *Chem. Commun.,* 2010, **46**, 6162-6164; (*c*) V. Malnuit, M. Duca, A. Manout, K. Bougrin, R. Benhida, Synlett, 2009, 13, 2123-2128; (*d*) M. Spadafora, M. Mehiri, A. Burger, R. Benhida, *Tetrahedron Lett.*, 2008, 49, 3967-3971; (*e*) K. El Akri, K. Bougrin, J. Balzarini, A. Faraj, R. Benhida, *Bioorg. Med. Chem. Lett.* 2007, **17**, 6656-6659; (f) M. Spadafora, M. Mehiri, A. Burger, R. Benhida, *Tetrahedron Lett.*, 2008, **49**, 3967-3971.

13 For characterization of sulfuryl diazide see: X. Zeng, H. Beckers, E. Bernhardt, H. Willner, *Inorg. Chem.*, 2011, **50**, 8679-8684.

14 **Caution**!. Sulfonyl azides are potentially hazardous and explosive! Therefore, safety precautions are highly recommended particularly for large-scale syntheses (X. Zeng, H. Beckers, E. Bernhardt, H. Willner, Inorg. Chem., 2011, 50, 8679–8684).

15 (*a*) Y. Fan, Y. Xia, J. Tang, F. Ziarelli, F. Qu, P. Rocchi, J. Iovanna, L. Peng, *Chem. Eur. J.*, 2012, **18**, 2221-2225; (*b*) Y. Xia, Y. Liu, J. Wan, M. Wang, P. Rocchi, F. Qu, J. Iovanna, L. Peng, *J. Med. Chem.*, 2009, **52**, 6083-6096; (*c*) Y. Xia, Y. Liu, P. Rocchi, M. Wang, Y. Fan, F. Qu, J. Iovanna, L. Peng, *Cancer Lett.*, 2012, **318**, 145-153; (*d*) Y. Xia, M. Wang, O. Demaria, J. Tang, P. Rocchi, F. Qu, J. Iovanna, L. Alexopoulou, L. Peng, *J. Med. Chem.*, 2012, **55**, 5642-5646.

15 (*a*) J. Broggi, H. Kumamoto, S. Berteina-Raboin, S. P. Nolan, L. A. Agrofoglio, *Eur. J. Org. Chem.*, 2009, **12**, 1880-1888; (*b*) J. Broggi, N. Joubert, S. Diez-Gonzalez, S. Berteina-Raboin, T. Zevaco, S. P. Nolan, L. A. Agrofoglio, *Tetrahedron*, 2009, **65**, 1162-117.

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