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Creation of 3,4-bis-triazolocoumarin–sugar conjugates via flourogenic dual click chemistry and their quenching specificity with silver(I) in aqueous media

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ABSTRACT

Fluorogenic click chemistry has recently emerged as an ingenious and powerful tool toward numerous biochemical purposes. We describe herein the use of dual click chemistry toward the fluorescence restoration of a fluorogenic coumarin on epimeric dipropargyl sugar scaffolds and their practical utility in selective metal ion detection. The dual click reactions were smoothly proceeded under microwave irradiation between silylated 3,4-di-*O*-propynyl gluco- or galactoside and 3-azidocoumarin, forming fluorescently reactivated bis-triazolocoumarins on sugar templates. Subsequent desilylation resulted in the OH-glycosides with desired water solubility. The following photochemical study disclosed that their fluorescence could be uniquely quenched by silver(I) in aqueous media with very minor responses to the addition of other metal ions. This research would presumably prompt the efficient creation of water soluble and potentially low toxic chemosensors via the fluorogenic dual click chemistry in using the universally existent sugars as the central scaffold.

1. Introduction

Fluorogenic chemistry, which is the ligation of fluorescently deactivated substrates with appropriate chemical handles for their fluorescence renaissance has recently received considerable interest in numerous biochemical studies. Among the many synthetic tools to realize such unique purpose, the 1,3-dipolar cycloaddition of terminal alkynes with organic azides promoted by Cu(I) (the representative reaction of click chemistry)[1,2] is emerging as the most applicable one due to its superior regioselectivity and high efficiency.[3] For instance, the fluorogenic click reaction has been successfully established in the combinatorial synthesis of fluorescent dyes,[4] cell imaging,[5] and the labeling of DNA[6] and virus.[7]

Coumarins are widely used chemical entities in photochemical studies owing to their synthetic convenience and validated biocompatibility. Indeed, the first fluorogenic click reaction was based on fluorescently quenched coumarin derivatives in which alkyne or azide functionalities were properly introduced.[4,8,9] While the subsequent click reaction took place, the electron density at the original azido or alkynyl position would be varied, which may result in the fluorescent restoration upon the formed triazolocoumarins. Enlightened by such ingenious strategy, we sought to create coumarin-based chemosensors[10] via fluorogenic click reaction.

Recent independent studies indicate that the development of fluorescent substrates based on sugar scaffolds is a viable strategy.[11,12] Apparently, sugars are naturally abundant, biocompatible, and low toxic raw materials with rich configurational and structural diversities. Furthermore, their promising water solubility may be considered as an essentially desirable feature for constituting sensors that are of practical detection uses. In the past decade, click chemistry has been fruitfully introduced into the synthesis of various triazolyl glycomimetics[13–15] involving sugar-based chemosensors.[11b–d,12] However, bis-triazolyl sugar derivatives wherein dual functional groups are simultaneously fixed on a glycosyl scaffold via click chemistry were scarcely developed.[16]

We have shown in a very recent study that bidentate bis-triazologlucosides prepared via dual click chemistry may exhibit unique photochemical properties.[17] With a continued interest in the development of triazole-functionalized sugar derivatives,[18] we present herein the construction of bis-triazolocoumarin–sugar conjugates in using fluorogenic dual click chemistry and their preliminary application in metal ion detection.

As illustrated in Fig. 1, a 3-azidocoumarin (**a**), which exhibits diminished fluorescence due to the existence of the electron-rich azide group on its 3-position[4] was employed as the fluorogenic

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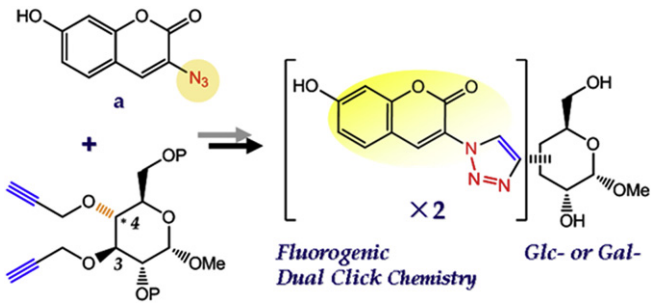


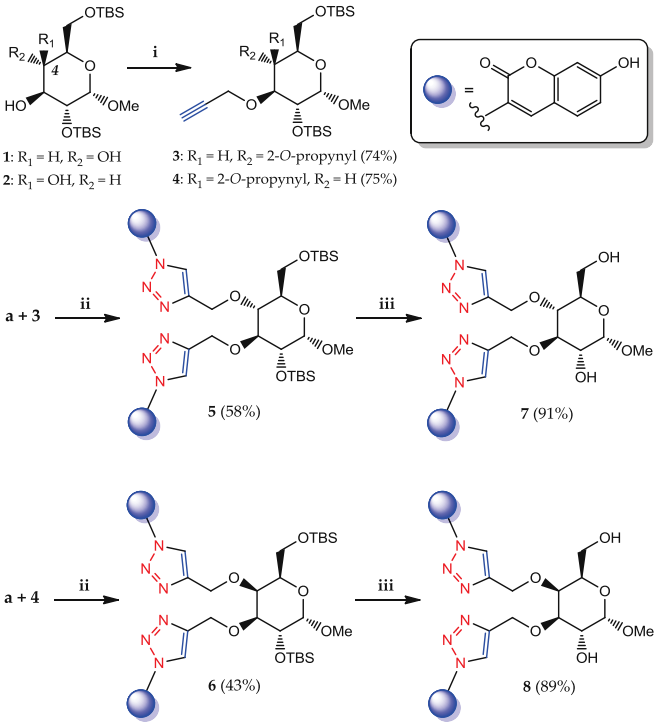
Fig. 1. Water soluble bis-triazolocoumarin–sugar conjugates formed by fluorogenic dual click chemistry.

substrate. This azide was then 'clicked' simultaneously onto the C3,4-positions of dipropargyl gluco- or galactosides, forming the fluorescence reactivated bis-triazolyl sugar intermediates. The desired hydroxyl glycosides with benign water solubility could be easily afforded by the following desilylation, which are envisioned applicable for the detection of metal ions in water.

2. Result and discussion

2.1. Synthesis

The 3-azidocoumarin (**a**, Fig. 1) utilized for click reaction was synthesized via a former literature report.[4a] For the preparation of C3,4-dipropargyl glycodonors, the known C2,6-silylated 1-*O*-methyl-α-D-glucoside **1** and galactoside **2** were used as the starting materials (Scheme 1).[19] Then, in the presence of 5.0 equiv NaH and 5.0 equiv propargyl bromide in dry DMF, the dipropargyl gluco- (**3**) and galactoside (**4**) were afforded in good yields of 74% and 75%, respectively. Notably, both glucosyl and galactosyl derivatives were prepared in order to evaluate whether their epimeric identity may render different optical properties of the synthesized glycoconjugates.



Scheme 1. Reagents and conditions: (i) NaH, propargyl bromide, DMF, 0 °C to rt; (ii) Na ascorbate (4.0 equiv) and $CuSO_4 \cdot 5H_2O$ (2.0 equiv), DMF/H_2O=3:1 (v/v), microwave irradiation, 60 °C; (iii) AcCl, MeOH, rt.

As it has been well-noticed that the microwave irradiation could serve as a potent accessory for enhancing the efficiency and greatly economizing the reaction time of click chemistry,[20] we chose to sequentially actualize the dual click reaction under such condition. All microwave-assisted reactions were performed in a Yalian (YL8023B1) microwave oven at 60 °C with a ramp time of 8 min. However, our initial attempt toward the microwave-assisted *Huisgen* [3+2] cycloaddition of compound **a** with **3** or **4** in the presence of catalytic amount of Na ascorbate (0.4 equiv) and $CuSO_4 \cdot 5H_2O$ (0.2 equiv) in a solvent mixture of DMF/water failed to yield the desired bis-triazolyl derivatives.

We noticed that besides the unreacted starting materials, two adjacent spots with equally strong fluorescence and similar polarities were observed by TLC monitoring under UV light (365 nm). This is in accordance with a previous study on sugar-based dual click reaction, which confirmed that mono-triazolyl intermediates would be generated on a dipropargyl template in prior to bis-triazoles.[21] Such spatial hindrance would successively render the sluggish reaction process en route to the desired bis-triazolyl products. Hence, it was proposed that the increase of catalyst loading would efficaciously lead to the formation of bis-triazoles in moderate-to-good yields in terms of the reactant structures.

To our delight, we discovered that in the presence of equivalently increased Na ascorbate (4.0 equiv) and $CuSO_4 \cdot 5H_2O$ (2.0 equiv), the microwave-assisted dual click reaction between azide **a** and sugar alkynes **3** and **4** could afford the desired bis-triazolyl gluco- (**5**, 58%) and galactoside (**6**, 43%) in moderate yields, respectively, within 30 min. However, further increase in catalyst loading and reaction time could not lead to the succeeding conversion of mono-triazolyl intermediates into the desired products. This could probably be ascribed to the excessive spatial hindrance of the bulky mono-triazolocoumarin formed on the neighboring C3- or C4-position of the sugar template, impeding the further acquisition of the bis-triazolyl glycoconjugates. Eventually, the hydroxyl-exposed glycosides **7** and **8** were furnished via desilylation of compounds **5** and **6** with AcCl in high yields of 90% and 89%, respectively.

2.2. Fluorescence study

The majority of current chemosensors encounter much limitation against practical use, such as their unsatisfactory water solubility and high toxicity to nature as well as to human body. Coumarin–sugar conjugates are essentially 'green' serving as sensor entities since both moieties are biocompatible and low toxic, while the latter also possesses benign water solubility. Furthermore, recent studies revealed that the triazole moiety could become an ion-binding site due to its nitrogen-rich structure.[11d,22] Taking into account such compelling evidence, we sought to assess the metal ion sensitivity of our prepared bis-triazolocoumarin–sugar conjugates.

To our delight, the fluorescence signals of both glycosides **7** and **8** could be measured directly in pure water, shown in Fig. 2. A broad emission band centered from approximately 400–550 nm (excited at 345 nm) was similarly observed for both compounds (Figs. 2A-**7**, Figs. 2B-**8**), which is in agreement with the feature of coumarins.[4] This supports that the fluorogenic dual click reaction employed in the present study could successfully restore the fluorescence of coumarin on sugar scaffolds. Moreover, the fluorescent intensity of glucoside **7** (Fig. 2A, blank-in red) is stronger than that of galactoside **8** (Fig. 2B, blank-in red), indicating that the epimeric identity of monosaccharide moiety may influence considerably the optical property of glycosyl bis-coumarins.

The ion-sensing property of the two glycosides in the presence of various metal cations was sequentially investigated. As shown in Fig. 2A, by adding 9 equiv of main group metal ions (Al^{3+}, Pb^{2+}),

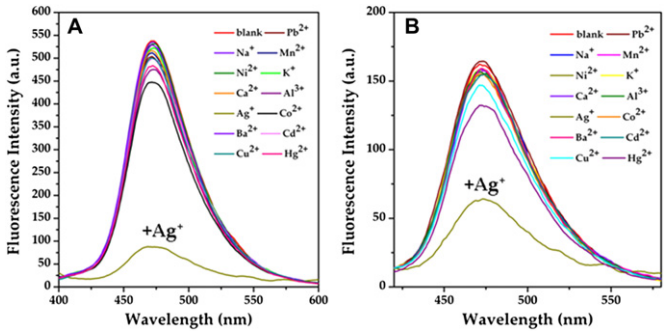


Fig. 2. Fluorescence spectra of (A) compound **7** (10 μM) upon addition of various NO_3^- salt (9.0 equiv) and (B) compound **8** (10 μM) upon addition of various NO_3^- salt (3.0 equiv) in water (λ_{ex}=345 nm).

alkali metal ions (Na^+, K^+), alkaline earth metal ions (Mg^{2+}, Ca^{2+}, Ba^{2+}), and transition metal ions (Cu^{2+}, Co^{2+}, Cd^{2+}, Mn^{2+}, Ni^{2+}, Zn^{2+}) to the aqueous solution of compound **7** (10 μM), its fluorescence remained approximately unchanged. In stark contrast, while Ag^+ (9 equiv) was added to the same solution, a remarkable quenching effect was observed. On the other hand, upon addition of 3 equiv (maximum) of Ag^+ to the aqueous solution of **8** (10 μM), its fluorescence could be significantly quenched, whereas unapparent variations in fluorescence intensity were observed when other metal ions (3 equiv) were added, shown in Fig. 2B.

This preliminarily suggests that the 3,4-bis-triazolocoumarin–sugar conjugates could be regarded as novel chemical entities for the development of water soluble Ag^+ sensor. In addition, we postulate that the specific quenching property might be ascribed to the heavy metal effect of silver(I), that is, preferable in size compared to other metal ions upon coordination with the ligands (**7** and **8**).

The glucoside **7** was then selected for detailed fluorescence assessments. As displayed in Fig. 3A, when increasing amounts of Ag^+ from 0 to 9.0 equiv was added to the aqueous solution of compound **7** (10 μM), the corresponding fluorescence intensity decreased gradually and finally reached its quenching plateau at the highest concentration (9.0 equiv of Ag^+). This signifies that the fluorescence of compound **7** is quenched by silver(I) in a concentration-dependent manner.

In addition, a competition experiment was conducted, shown in

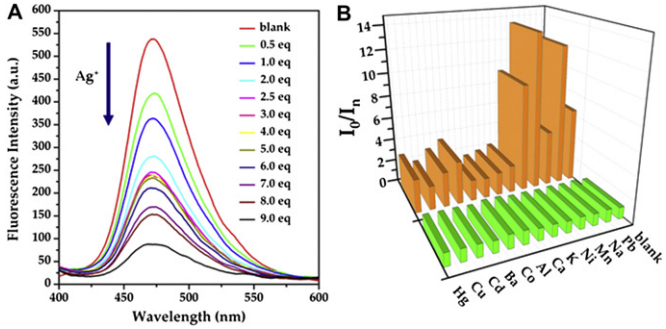


Fig. 3. (A) Fluorescence spectrum of compound **7** (10 μM) upon addition of Ag^+ ion (from top to bottom: 0, 0.5, 1.0, 2.0, 2.5, 3.0, 4.0, 5.0, 6.0, 7.0, 8.0, 9.0 equiv, λ_{ex}=345 nm) in water; (B) Fluorescence intensity change profile of compound **7** (10 μM) with selected cations (9.0 equiv) in the absence (green) or presence (orange) of Ag^+ (90 μM) in water (λ_{ex}=345 nm). The I_0/I_n ratio represents the fluorescence quenching efficiency, where I_0 is the fluorescence intensity of compound **7** alone and I_n is its fluorescence intensity upon addition of metal ions.

Fig. 3B. The I_0/I_n ratio, which represents the fluorescence quenching efficiency of competing metal ion (9.0 equiv)–ligand **7** mixtures (in water) in the absence (green columns) and presence (orange columns) of Ag^+ was compared. Clearly, the existence of the representative selection of competing metal ions in aqueous solution of **7** (10 μM, green columns) are not influential toward its corresponding fluorescence intensity as their quenching efficiency is parallel with that of compound **7** alone (blank). However, when 9.0 equiv of Ag^+ was successively added to these mixtures (orange columns), the corresponding quenching efficiencies increased in distinct modes. Obviously, in the presence of Pb^{2+}, Mn^{2+}, and Ni^{2+}, the fluorescence of **7** may be more efficiently quenched by Ag^+, whereas other selected metal ions lowered its quenching efficiency comparing to the blank experiment.

The accumulation of silver ion is noted to bring on deleterious impact to both environment and human health.[22b] Hence, the sensitive detection of Ag^+ in both natural and physiological environments is highly desirable. Since there are rare chemosensors that may give unique response to silver(I)[23] over other metal ions in aqueous media, the bis-triazolocoumarin–sugar conjugates prepared in this study may potentially constitute a new class of chemical entities for the development of Ag^+ chemosensors with good water solubility.

3. Conclusion

In summary, we have demonstrated herein for the first time that by a microwave-assisted dual click reaction, the fluorogenic 3-azidocoumarin could be rapidly introduced onto a 3,4-dipropargyl gluco- or galactosyl scaffold with restored fluorescence. Subsequent desilylation led to water soluble sugar-bis-triazolocoumarin conjugates which are applicable toward selective metal ion (Ag+) detection in aqueous media via fluorescence spectroscopy. Consequently, this study would presumably furnish new insights into the development of novel water soluble, and potentially biocompatible optical sensors based on the structurally and configurationally diverse sugar scaffolds in using microwave-assisted fluorogenic dual click chemistry as an ingenious synthetic tool.

4. Experimental section

4.1. General

All purchased chemicals and reagents are of high commercially available grade. Solvents were purified by standard procedures. ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-400 spectrometer in $CDCl_3$ or DMSO-d_6 solutions using tetramethylsilane as the internal standard (chemical shifts in ppm). Microwave-assisted reactions were performed in a Yalian (YL8023B1) system at 60 °C with a ramp time of 8 min. All reactions were monitored by TLC (thin-layer chromatography) with detection by UV or by spraying with 6 N H_2SO_4 and charring at 300 °C. Optical rotations were measured using a Perkin–Elmer 241 polarimeter at rt and a 10-mm 1-mL cell. High resolution mass spectra (HRMS) were recorded on an MA1212 instrument using standard conditions (ESI, 70 eV). All UV–vis absorption and fluorescence emission spectra were recorded with Ocean Optics USB2000+ and HORIBAJOBIN YVON FluoroMAX-4 spectrophotometer.

4.2. General procedure for O-propargylation

To a solution of 2,6-hydroxyl-protected sugars in anhydrous DMF at 0 °C, NaH (5.0 equiv) was added and the mixture was stirred for 20 min. Then propargyl bromide (5.0 equiv) was added dropwise and the reaction mixture was warmed to rt and stirred for another 12 h. DMF was removed in vacuum and the resulting residue was diluted with EtOAc, washed successively with water and brine. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to give a crude product, which was purified by column chromatography.

*4.2.1. Methyl 2,6-di-O-tert-butyldimethylsilyl-3,4-di-O-propargyl-α-D-glucopyranoside (**3**).* From compound **1** (422 mg, 1 mmol), column chromatography (EtOAc/petroleum ether, 1:10) afforded **3** as a yellow syrup (368 mg, 74%). R_f=0.7 (EtOAc/cyclohexane, 1:10). $[\alpha]_D^{25}$ +65 (*c* 3.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ=4.91 (d, *J*=3.7 Hz, 1H), 4.42–4.16 (m, 4H), 3.95–3.79 (m, 2H), 3.52 (m, 2H), 3.38 (m, 1H), 3.36 (s, 3H), 3.22 (t, *J*=9.3 Hz, 1H), 2.44 (m, 2H), 0.85 (m, 18H), 0.06 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=97.4, 80.1, 79.9, 79.8, 78.6, 74.5, 74.0, 73.5, 70.8, 62.4, 59.9, 58.3, 54.5, 25.9, 25.8, 25.7, 18.2, 17.9, −4.2, −4.5, −5.2, −5.4, −5.5.

*4.2.2. Methyl 2,6-di-O-tert-butyldimethylsilyl-3,4-di-O-propargyl-α-D-galactopyranoside (**4**).* From compound **2** (800 mg, 1.9 mmol), column chromatography (EtOAc/petroleum ether, 1:10) afforded **4** as a yellow syrup (708 mg, 75%). R_f=0.5 (EtOAc/petroleum ether, 1:10).

4.3. General procedure for microwave-assisted click reaction

To a solution of sugar alkyne (1.0 equiv) and azidocoumarin (2.0 equiv) in DMF/water (15 mL/3 mL) were added Na ascorbate (4.0 equiv) and $CuSO_4 \cdot 5H_2O$ (2.0 equiv). This mixture was then transferred into a Yalian (YL8023B1) microwave oven and stirred at 60 °C with a ramp time of 8 min and hold time of 30 min. After removal of the solvent in vacuum, the residue was diluted with CH_2Cl_2 and washed with brine. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated to give a crude product, which was purified by column chromatography.

*4.3.1. Bis-triazolocoumarin-2,6-O-TBDMS-1-O-methyl-α-D-pyranoglucoside conjugate (**5**).* From compound **3** (61.4 mg, 0.12 mmol) and **a** (60 mg, 0.3 mmol), column chromatography (EtOAc/petroleum ether, 1:2) afforded **5** as a light yellow solid (65.5 mg, 58.8%). $[\alpha]_D^{25}$ +42 (*c* 0.2, water); ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.96 (br s, 2H), 8.61 (d, *J*=2.0 Hz, 1H), 8.54 (s, 1H), 8.47 (d, *J*=3.2 Hz, 2H), 7.51–7.48 (m, 2H), 6.97 (br s, 1H), 6.94 (d, *J*=3.2 Hz, 3H), 5.01 (t, *J*=12.0 Hz, 1H), 4.90 (dd, *J*=4.0, 12.8 Hz, 1H), 4.85 (dd, *J*=7.6, 13.2 Hz, 1H), 4.79 (d, *J*=12.8 Hz, 1H), 4.73 (dd, *J*=3.2, 6.4 Hz, 1H), 4.06–3.97 (m, 1H), 3.87–3.73 (m, 2H), 3.63–3.40 (m, 3H), 3.32 (s, 3H), 0.93–0.87 (m, 18H), 0.16–0.04 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.0, 162.4, 156.3, 154.8, 145.3, 145.0, 134.5, 130.3, 124.2, 123.5, 119.4, 119.3, 115.1, 110.8, 110.7, 103.2, 80.9, 79.2, 73.7, 71.3, 65.9, 64.3, 62.3, 54.8, 26.0, 25.9, 18.3, 18.1, −3.6, −4.0, −4.2, −5.1, −5.4; HR(ESI)MS: calcd for $C_{43}H_{56}N_6O_{12}Si_2$+Na: 927.3392; found: 927.3391.

*4.3.2. Bis-triazolocoumarin-2,6-O-TBDMS-1-O-methyl-α-D-pyranogalacoside conjugate (**6**).* From compound **4** (100 mg, 0.2 mmol) and **a** (81.6 mg, 0.4 mmol), column chromatography (EtOAc/petroleum ether, 1:2) afforded **6** as a light yellow solid (77.8 mg, 43.1%). $[\alpha]_D^{25}$ −77 (*c* 0.1, water); ^{1}H NMR (400 MHz, $CDCl_3$): δ=9.72 (br s, 2H), 8.41–8.33 (m, 2H), 8.20–8.16 (m, 2H), 7.22 (d, *J*=8.8 Hz, 2H), 6.69–6.64 (m, 4H), 5.04 (d, *J*=11.6 Hz, 1H), 4.78–4.74 (m, 2H), 4.65 (d, *J*=11.6 Hz, 2H), 4.60–4.57 (m, 1H), 3.99 (d, *J*=10.0 Hz, 1H), 3.78 (dd, *J*=2.0, 9.6 Hz, 2H), 3.71 (s, 1H), 3.60–3.54 (m, 2H), 3.47 (t, *J*=6.4 Hz, 1H), 3.17 (s, 3H), 0.75 (s, 9H), 0.67 (s, 9H), 0.00 (s, 6H), −0.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.0, 162.5, 156.4, 156.3, 154.8, 145.5, 144.8, 134.6, 130.3, 124.4, 124.1, 119.3, 119.2, 115.0, 110.6, 110.5, 103.1, 98.6, 78.8, 76.3, 72.2, 70.9, 66.7, 64.2, 55.2, 26.0, 25.8, 18.2, 18.1, −4.5, −5.4; HR(ESI)MS: calcd for $C_{43}H_{56}N_6O_{12}Si_2$+Na: 927.3392; found: 927.3391.

4.4. General procedure for desilylation

To a solution of silylated glycoside (1.0 equiv) was added AcCl (3.0 equiv) and the mixture was stirred for 3 h at rt. Then the solvent was removed in vacuum and the residue was directly purified by column chromatography to afford the desired products.

*4.4.1. Bis-triazolocoumarin-1-O-methyl-α-D-pyranoglucoside conjugate (**7**).* From compound **5** (60 mg, 0.07 mmol), column chromatography (CH_2Cl_2/MeOH, 10:1) afforded **7** as a light yellow solid (41.3 mg, 91.2%). $[\alpha]_D^{25}$ +11 (*c* 0.1, water); ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.65–8.58 (m, 4H), 7.80 (d, *J*=7.6 Hz, 2H), 6.96 (d, *J*=8.4 Hz, 2H), 6.90 (s, 2H), 5.06 (d, *J*=12.0 Hz, 1H), 4.91 (d, *J*=12.4 Hz, 1H), 4.86 (d, *J*=9.6 Hz, 1H), 4.85–4.81 (m, 2H), 3.81 (t, *J*=8.8 Hz, 1H), 3.64 (d, *J*=11.6 Hz, 1H), 3.54 (dd, *J*=4.0, 11.6 Hz, 1H), 3.43–3.38 (m, 3H), 3.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.8, 156.4, 154, 7, 144.7, 144.6, 136.3, 130.9, 124.9, 124.7, 119.1, 114.4, 110.1, 102.1, 97.1, 79.3, 78.1, 72.7, 71.0, 64.9, 63.1, 60.3, 54.2; HR(ESI)MS: calcd for $C_{31}H_{28}N_6O_{12}$+Na: 699.1663; found: 699.1663.

*4.4.2. Bis-triazolocoumarin-1-O-methyl-α-D-pyranogalacoside conjugate (**8**).* From compound **6** (60 mg, 0.07 mmol), column chromatography (CH_2Cl_2/MeOH, 10:1) afforded **8** as a light yellow solid (40.3 mg, 89.0%). $[\alpha]_D^{25}$ −43 (*c* 0.1, water); ^{1}H NMR (400 MHz, $CDCl_3$): δ=11.17 (br s, 2H), 8.52 (br s, 4H), 7.72 (br s, 2H), 6.90 (br s, 4H), 5.23–4.98 (m, 2H), 4.74 (br s, 5H), 3.81 (br s, 2H), 3.65–3.58 (m, 2H), 3.22–3.14 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=162.6, 156.3, 154.5, 144.8, 136.4, 130.9, 124.9, 124.7, 119.2, 114.3, 110.2, 102.1, 97.6, 77.8, 76.6, 72.7, 69.4, 65.7, 63.1, 60.0, 54.5; HR(ESI)MS: calcd for $C_{31}H_{28}N_6O_{12}$+Na: 699.1663; found: 699.1662.

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Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.03.068.

References and notes

1. (a) Kolb, H. C.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 2004–2021; (b) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596–2599.
2. Tornoe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057–3064.
3. Le Droumaguet, C.; Wang, C.; Wang, Q. *Chem. Soc. Rev.* **2010**, *39*, 1233–1239.
4. (a) Sivakumar, K.; Xie, F.; Cash, B. M.; Long, S.; Barnhill, H. N.; Wang, Q. *Org. Lett.* **2004**, *6*, 4603–4606; (b) Xie, F.; Sivakumar, K.; Zeng, Q.; Bruckman, M. A.; Hodges, B.; Wang, Q. *Tetrahedron* **2008**, *64*, 2906–2914.
5. (a) Beatty, K. E.; Liu, J. C.; Xie, F.; Dieterich, D. C.; Schuman, E. M.; Wang, Q.; Tirrell, D. A. *Angew. Chem., Int. Ed.* **2006**, *45*, 7364–7367; (b) Neef, A. B.; Schultz, C. *Angew. Chem., Int. Ed.* **2009**, *48*, 1498–1500.
6. Gierlich, J.; Burley, G. A.; Gramlich, P. M. E.; Hammond, D. M.; Carell, T. *Org. Lett.* **2006**, *8*, 3639–3642.
7. Wang, Q.; Chan, T. R.; Hilgraf, R.; Fokin, V. V.; Sharpless, K. B.; Finn, M. G. *J. Am. Chem. Soc.* **2003**, *125*, 3192–3193.
8. Zhou, Z.; Fahrni, C. J. *J. Am. Chem. Soc.* **2004**, *126*, 8862–8863.
9. Varazo, K.; Le Droumaguet, C.; Fullard, K.; Wang, Q. *Tetrahedron Lett.* **2009**, *50*, 7032–7034.
10. (a) Chandrasekhar, V.; Bag, P.; Pandey, M. D. *Tetrahedron* **2009**, *65*, 9876–9883; (b) He, G.; Zhang, X.; He, C.; Zhao, X.; Duan, C. *Tetrahedron* **2010**, *66*, 9762–9768.
11. (a) Xie, J.; Ménand, M.; Maisonneuve, S.; Métivier, R. *J. Org. Chem.* **2007**, *72*, 5980–5985; (b) Maisonneuve, S.; Fang, Q.; Xie, J. *Tetrahedron* **2008**, *64*, 8716–8720; (c) David, O.; Maisonneuve, S.; Xie, J. *Tetrahedron Lett.* **2007**, *48*, 6527–6530; (d) Zhang, Y.-J.; He, X.-P.; Hu, M.; Li, Z.; Shi, X.-X.; Chen, G.-R. *Dyes and Pigments* **2011**, *88*, 391–395.
12. Hsieh, Y.-C.; Chir, J.-L.; Wu, H.-H.; Wu, A.-T. *Tetrahedron Lett.* **2010**, *51*, 109–111.
13. Aragão-Leoneti, V.; Campo, V. L.; Gomes, A. S.; Field, R. A.; Carvalho, I. *Tetrahedron* **2010**, *66*, 9475–9492.
14. (a) Lu, W.-Y.; Sun, X.-W.; Zhu, C.; Xu, J. H.; Lin, G.-Q. *Tetrahedron* **2010**, *66*, 750–757; (b) Neto, V.; Granet, R.; Krausz, P. *Tetrahedron* **2010**, *66*, 4633–4646;

(c) Song, S.-X.; Zhang, H.-L.; Kim, C.-G.; Sheng, L.; He, X.-P.; Long, Y.-T.; Li, J.; Chen, G.-R. *Tetrahedron* **2010**, *66*, 9974–9980; (d) Broggi, J.; Joubert, N.; Díez-González, S.; Berteina-Raboin, S.; Zevaco, T.; Nolan, S. P.; Agrofoglio, L. A. *Tetrahedron* **2009**, *65*, 1162–1170; (e) Adamo, M. F. A.; Pergoli, R.; Moccia, M. *Tetrahedron* **2010**, *66*, 9242–9251.
15. (a) Kumar, K. K.; Kumar, R. M.; Subramanian, V.; Das, T. M. *Carbohydr. Res.* **2010**, *345*, 2297–2304; (b) Anand, N.; Jaiswal, N.; Pandey, S. K.; Srivastava, A. K.; Tripathi, R. P. *Carbohydr. Res.* **2011**, *346*, 16–25.
16. Garcia, L.; Maisonneuve, S.; Xie, J.; Guillot, R.; Dorlet, P.; Rivière, E.; Desmadril, M.; Lambert, F.; Pilicar, C. *Inorg. Chem.* **2010**, *49*, 7282–7288.
17. Song, Z.; He, X.-P.; Jin, X.-P.; Gao, L.-X.; Sheng, L.; Zhou, Y.-B.; Li, J.; Chen, G.-R. *Tetrahedron Lett.* **2011**, *52*, 894–898.
18. (a) Lin, L.; Shen, Q.; Chen, G.-R.; Juan, X. *Bioorg. Med. Chem.* **2008**, *16*, 9757–9763; (b) Zhang, Y.-J.; He, X.-P.; Li, C.; Li, Z.; Shi, D.-T.; Gao, L.-X.; Qiu, B.-Y.; Shi, X.-X.; Tang, Y.; Li, J.; Chen, G.-R. *Chem. Lett.* **2010**, *39*, 1261–1263; (c) Yang, J.-W.; He, X.-P.; Zhao, H.; Gao, L.-X.; Zhang, W.; Shi, X.-X.; Tang, Y.; Li, J.; Chen, G.-R. *Bull. Korean Chem. Soc.* **2010**, *31*, 3359–3365; (d) Song, Z.; He, X.-P.; Li, C.; Gao, L.-X.; Wang, Z.-X.; Tang, Y.; Xie, J.; Li, J.; Chen, G.-R. *Carbohydr. Res.* **2011**, *346*, 140–145; (e) He, X.-P.; Li, C.; Jin, X.-P.; Song, Z.; Zhang, H.-L.; Zhu, C.-J.; Shen, Q.; Zhang, W.; Sheng, L.; Shi, X.-X.; Tang, Y.; Li, J.; Chen, G.-R.; Xie, J. *New J. Chem.* **2011**, *35*, 622–631.
19. Halmos, T.; Montserret, R.; Filippi, J.; Antonakis, K. *Carbohydr. Res.* **1987**, *170*, 57–69.
20. Caddick, S.; Fitzmaurice, R. *Tetrahedron* **2009**, *65*, 3325–3355.
21. Ziegler, T.; Hermann, C. *Tetrahedron Lett.* **2008**, *49*, 2166–2169.
22. (a) Kumar, A.; Pandey, P. S. *Tetrahedron Lett.* **2009**, *50*, 5842–5845; (b) Hung, H.-C.; Cheng, C.-W.; Wang, Y.-Y.; Chen, Y.-J.; Chung, W.-S. *Eur. J. Org. Chem.* **2009**, 6360–6366.
23. Liu, L.; Zhang, G.; Xiang, J.; Zhang, D.; Zhu, D. *Org. Lett.* **2008**, *10*, 4581–4584.