### **Supplementary Information**

# A cascading reaction sequence involving ligand-directed azaelectrocyclization and autooxidation-induced fluorescence recovery enables visualization of target proteins on the surfaces of live cells

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General Procedures. <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured at ambient temperature in an indicated solvent with JEOL JNM-LA 500 spectrometers. The chemical shifts in CDCl<sub>3</sub> are given in  $\delta$  value from tetramethylsilane (TMS) as an internal standard. ESI-Mass spectra were obtained on BRUKER microTOF-QII-HC. MALDI-TOF Mass spectra were taken on a SHIMADZU AXIMA-CFR mass spectrometer equipped with a nitrogen laser ( $\lambda = 337$  nm). Preparative separation was usually performed by column chromatography on silica gel (FUJI silysia LTD, BW-200 and BW-300) and by thin layer chromatography on silica gel (Merck, 20 x 20 cm, Silica gel 60 F<sub>254</sub>, 1 mm). Anhydrous DMF was purchased from Aldrich, and anhydrous THF and CH<sub>2</sub>Cl<sub>2</sub> were from NACALAI TESQUE INC., Kyoto. All other commercially available reagents were used without further purification. Fluorescence emission spectra were measured either on a JASCO FP-6500 spectrofluorometer.



Alcohol (10). To a solution of the aminoalcohol derived from 8 (51.1 mg, 168 µmol) in DMF (5.0 mL) were added 4-nitrophenyl ester 9 (64.7 mg, 168 µmol) and triethylamine (23.4 µL, 168 µmol) at room temperature and the mixture was stirred for 5 h at this temperature. The solution was concentrated *in vacuo* to give the crude product, which was purified by column chromatography on silica gel (5% MeOH in CHCl<sub>3</sub>) to give the alcohol 10 (39.7 mg, 43%, 2 steps from 8) as a yellow solid: MALDI-TOF-MS *m*/*z* calcd for C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 573.2, found 573.2; HRESI-MS *m*/*z* calcd for C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 573.2, found 573.2; HRESI-MS *m*/*z* calcd for C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 573.2, found 573.2; HRESI-MS *m*/*z* calcd for C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 573.2, found 573.2; HRESI-MS *m*/*z* calcd for C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 573.2, found 573.2; HRESI-MS *m*/*z* calcd for C<sub>33</sub>H<sub>30</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 573.2, found 573.1995; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  8.29 (s, 1H), 7.49-7.24 (m, 12H), 6.82 (t, 1H, *J* = 6.2 Hz), 6.79 (d, 1H, *J* = 16.7 Hz), 6.74 (d, 1H, *J* = 16.3 Hz), 5.96 (s, 1H), 5.55 (m, 1H), 4.55 (d, 2H, *J* = 4.3 Hz), 4.29 (q, 2H, *J* = 7.1 Hz), 4.02 (d, 2H, *J* = 4.9 Hz), 3.20 (d, 1H, *J* = 14.9 Hz), 2.92 (dd, 1H, *J* = 15.1, 3.8 Hz), 1.35 (t, 3H, *J* = 7.1 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>: Due to the multiple signals derived from the rotamers, those of representative were shown)  $\delta$  166.9, 151.4, 150.8, 140.3, 134.4, 131.0, 129.9, 128.14, 128.11, 127.27, 127.23, 126.4, 126.1, 123.8, 123.6, 121.2, 120.1, 119.9, 113,1, 109.9, 77.9, 77.2, 61.1, 59.9, 46.0, 45.5, 14.3.



Alkyne-aldehyde (4). To a solution of the alcohol 10 (10.0 mg, 18.2 µmol) obtained above in dry CH<sub>2</sub>Cl<sub>2</sub> (1.0 mL) was added Dess-Martin periodinane (11.6 mg, 27.2 µmol) and the mixture was stirred at room temperature for 20 min. The solution was filtered and the filtrate was concentrated *in vacuo* to give the crude product, which was rapidly purified by column chromatography on silica gel (5% MeOH in CHCl<sub>3</sub>) to give the aldehyde **4** as a yellow solid (7.2 mg, 72%): MALDI-TOF-MS *m/z* calcd for C<sub>33</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 571.2 found 571.2; HRESI-MS *m/z* calcd for C<sub>33</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 571.2 found 571.2; HRESI-MS *m/z* calcd for C<sub>33</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 571.2 found 571.2; HRESI-MS *m/z* calcd for C<sub>33</sub>H<sub>28</sub>N<sub>2</sub>NaO<sub>6</sub> (M+Na)<sup>+</sup> 571.1845, found 571.1834; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  10.16 (d, 1H, *J* = 7.0 Hz), 8.35 (s, 1H), 7.54-7.26 (m, 13H), 7.06 (d, 1H, *J* = 16.7 Hz), 6.67 (d, 1H, *J* = 7.1 Hz), 5.93 (s, 1H), 5.56 (m, 1H), 4.37 (q, 2H, *J* = 7.1 Hz), 4.05 (d, 2H, *J* = 3.9 Hz), 3.21 (d, 1H, *J* = 15.0 Hz), 2.94 (dd, 1H, *J* = 16.0, 4.0 Hz), 1.39 (t, 3H, *J* = 7.2 Hz); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>: Due to the multiple signals derived from the rotamers, those of representative were shown)  $\delta$  191.3, 167.0, 156.1, 151.4, 150.7, 141.0, 133.3, 131.0, 129.9, 128.5, 128.1, 127.4, 127.3, 126.4, 126.1, 123.8, 123.6, 121.2, 119.9, 113.1, 109.9, 78.0, 77.2, 62.1, 46.1, 45.7, 11,0.



Azide (12). To a solution of H-Orn(N<sub>3</sub>)-OH (43 mg, 270 µmol) in dry DMF (100 µL) was added 4-[4-(dimethylamino)phenylazo]benzoic acid succinimidyl ester and triethylamine (380 µL) at room temperature, and the mixture was stirred overnight at this temperature. After the solution was concentrated *in vacuo*, the crude mixture was purified by column chromatography on silica gel (17% MeOH in CHCl<sub>3</sub>) to give the azide 12 as a bright red solid (111 mg, quant): MALDI-TOF-MS *m/z* calcd for C<sub>20</sub>H<sub>24</sub>N<sub>7</sub>O<sub>3</sub> (M+H)<sup>+</sup> 410.2, found 410.6; HRESI-MS *m/z* calcd for C<sub>20</sub>H<sub>23</sub>N<sub>7</sub>NaO<sub>3</sub> (M+Na)<sup>+</sup> 432.1760, found 432.1754; <sup>1</sup>H NMR (500 MHz, CD<sub>3</sub>OD)  $\delta$  7.90 (d, 2H, *J* = 6.2 Hz), 7.84 (d, 2H, *J* = 8.5 Hz), 7.79 (d, 2H, *J* = 7.9 Hz), 1.68 (brs, 2H); <sup>13</sup>C NMR (125 MHz, CD<sub>3</sub>OD)  $\delta$  173.8, 167.7, 155.2, 152.8, 143.6, 133.4, 128.2, 125.5, 122.2, 111.5, 53.3, 50.9, 40.2, 29.2, 25.2.



**Amine (13).** To a solution of **11** (16 mg, 21  $\mu$ mol) in CH<sub>2</sub>Cl<sub>2</sub> (1.5 mL) was added TFA (370  $\mu$ L) at 0 °C and the mixture were stirred at this temperature for 20 min. The solution was neutralized with saturated aqueous NaHCO<sub>3</sub> and the mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub>. The organic layers were combined, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated, and concentrated *in vacuo* to give the crude diamine, which was subjected to the acylation without further purification.

To the azide **12** (8.7 mg, 21 umol) obtained above were added the 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC · HCl, 4.0 mg, 21 µmol), pentafluorophenol (3.9 mg, 21 µmol), and triethylamine (2.1 mg, 21 µmol) in dry CH<sub>2</sub>Cl<sub>2</sub>(1.0 mL) at room temperature. After the mixture was stirred for 2 h, the crude diamine (21 µmol) derived from 11 in dry CH<sub>2</sub>Cl<sub>2</sub>(100 µL) was further added, and the resulting mixture was stirred overnight at room temperature. The solution was concentrated *in vacuo*, and the crude mixture was purified by preparative TLC on silica gel (67 % ethyl acetate in hexane) to give the amine 13 as a bright red solid (10.3 mg, 52% for 2 steps from 11): MALDI-TOF-MS m/z calcd for C<sub>52</sub>H<sub>61</sub>N<sub>9</sub>NaO<sub>6</sub>Si  $(M+Na)^+$  958.5, found 959.3; HRESI-MS *m/z* calcd for C<sub>52</sub>H<sub>61</sub>N<sub>9</sub>NaO<sub>6</sub>Si (M+Na)^+ 958.4412, found 958.4398; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) & 7.90-7.86 (m, 6H), 7.67 (m, 4H), 7.43-7.34 (m, 6H), 7.11 (d, 2H, J = 8.5Hz), 6.79 (t, 1H, J = 6.0 Hz), 6.76 (d, 2H, J = 9.2 Hz), 6.60 (d, 1H, J = 16.6 Hz), 6.58(d, 2H, J = 8.5 Hz), 6.48 (d, 1H, J = 16.2 Hz), 4.69-4.62 (m, 1H), 4.55 (d, 2H, J = 5.9 Hz), 4.37 (t, 2H, J = 4.8 Hz), 3.74 (t, 2H, J = 4.7 Hz), 3.62 (t, 2H, J = 4.9 Hz), 3.49 (t, 2H, J = 5.3 Hz), 3.30 (m, 2H), 3.10 (s, 6H), 2.03-1.75 (brm, 2H), 1.69-1.65 (brm, 2H), 1.05 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) & 171.3, 167.2, 166.7, 155.3, 152.9, 146.7, 143.7, 140.3, 135.6, 134.8, 133.7, 133.3, 130.3, 129.8, 128.0, 127.8, 127.7, 127.5, 125.5, 122.3, 117.1, 115.0, 111.5, 69.6, 69.2, 63.7, 61.4, 53.0, 51.1, 40.3, 39.5, 30.4, 26.8, 25.0, 19.2.



**Coumarin derivative 14.** To a solution of **13** (3.3 mg, 3.5  $\mu$ mol) obtained above in dry CH<sub>2</sub>Cl<sub>2</sub> (500  $\mu$ L) were added HATU (2.0 mg, 5.3  $\mu$ mol) and 7-(dimethylamino)coumarin-3-carboxylic acid

(1.1 mg, 4.3 µmol) at room temperature. After the mixture was stirred at this temperature for 10 min, triethylamine (740 nL, 5.3 µmol) was added to the solution and stirred at room temperature overnight. The resulting mixture was concentrated *in vacuo* to give the crude product, which was directly purified by preparative TLC on silica gel (5% MeOH in CHCl<sub>3</sub>) to give the coupling product 14 as a bright red solid (3.3 mg, 79%): MALDI-TOF-MS m/z calcd for C<sub>66</sub>H<sub>74</sub>N<sub>10</sub>NaO<sub>9</sub>Si  $(M+Na)^+$  1201.5, found 1201.5; HRESI-MS m/z calcd for  $C_{66}H_{74}N_{10}NaO_9Si$   $(M+Na)^+$  1201.5308, found 1201.5289; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  10.9 (s, 1H), 8.76 (s, 1H), 7.90 (d, 2H, J = 8.9 Hz), 7.87 (d, 2H, J = 9.3 Hz), 7.85 (d, 2H, J = 8.5 Hz), 7.68-7.65 (m, 6H), 7.45 (d, 1H, J = 9.0 Hz), 7.44-7.32 (m, 6H), 7.28 (d, 2H, J = 8.6 Hz), 6.87 (t, 1H, J = 6.0 Hz), 6.74 (d, 2H, J = 9.2 Hz), 6.68 (d, 1H, J = 16.5 Hz), 6.67 (dd, 1H, J = 2.4, 8.7 Hz), 6.61 (d, 1H, J = 16.3 Hz), 6.52 (d, 1H, J = 2.1Hz), 4.68-4.64 (m, 1H), 4.53 (d, 2H, J = 5.9 Hz), 4.38 (t, 2H, J = 4.8 Hz), 3.76 (t, 2H, J = 4.8 Hz), 3.66-3.59 (m, 4H), 3.46 (q, 4H, J = 7.2 Hz), 3.33-3.27 (m, 2H), 3.09 (s, 6H), 2.03-1.81 (brm, 2H),1.71-1.61 (brm, 2H), 1.26 (t, 6H, 7.2 Hz), 1.05 (s, 9H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>: Due to the multiple signals derived from the rotamers, those of representative were shown)  $\delta$  171.3, 170.0, 166.7, 163.1, 161.1, 157.8, 155.3, 152.9, 148.5, 143.7, 141.4, 138.3, 135.6, 135.5, 134.3, 133.2, 132.8, 131.4, 130.0, 129.9, 129.1, 128.0, 127.8, 127.7, 127.4, 125.5, 122.3, 120.4, 119.8, 111.5, 110.2, 108.7, 96.7, 69.6, 69.2, 63.8, 61.3, 53.0, 51.1, 45.2, 40.3, 39.5, 30.3, 26.8, 25.0, 19.2, 12.5.



Azide-aldehyde (6). To a solution of the coupling product 14 (1.0 mg, 830 nmol) obtained above in THF (500 µL) were added acetic acid (1.0 M in THF, 800 nL, 800 nmol) and TBAF (1.0 M in THF, 830 nL, 830 nmol) at 0 °C. After the resulting mixture was warmed to room temperature and stirred for 2 h, the mixture was extracted with CHCl<sub>3</sub>. The organic layers were combined, washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>, filtrated, and concentrated *in vacuo* to give the crude product, which was rapidly purified by preparative TLC on silica gel (5% MeOH in CHCl<sub>3</sub>) to give the allyl alcohol as a bright red solid (380 µg, 47%). The product was unstable and immediately oxidized after rapidly confirming the structure by MS and <sup>1</sup>H NMR: MALDI-TOF-MS *m/z* calcd for C<sub>50</sub>H<sub>56</sub>N<sub>10</sub>NaO<sub>9</sub> (M+Na)<sup>+</sup> 963.4, found 963.4; HRESI-MS *m/z* calcd for C<sub>50</sub>H<sub>56</sub>N<sub>10</sub>NaO<sub>9</sub> (M+Na)<sup>+</sup> 963.4130, found 963.4108; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  10.9 (s, 1H), 8.77 (s, 1H), 7.88-7.83 (m, 6H), 7.69 (d, 2H, *J*=8.2 Hz), 7.59 (d, 1H, *J*=9.3 Hz), 7.40 (2H, *J*=8.6 Hz), 6.93 (t, 1H, *J*=5.8Hz), 6.74 (d, 2H, *J*=

9.1 Hz), 6.78-6.58 (m, 3H), 6.53 (brs, 1H), 4.67 (m, 1H), 4.59 (d, 2H, *J* = 5.6 Hz), 4.30 (m, 2H), 3.75 (m, 2H), 3.64 (m, 4H), 3.47 (q, 4H, *J* = 7.2 Hz), 3.33(m, 2H), 3.04 (s, 6H), 2.06-1.79 (brm, 2H), 1.67 (brm, 2H), 1.26 (t, 6H, *J* = 7.2 Hz).

To a solution of the allyl alcohol obtained above (200 µg, 210 nmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (500 µL) was added Dess-Martin periodinane (140 µg, 320 nmol) and the mixture was stirred at room temperature for 20 min. The solution was filtered and the filtrate was concentrated *in vacuo* to give the crude product, which was rapidly purified by preparative TLC on silica gel (5% MeOH in CHCl<sub>3</sub>) to give the desired aldehyde **6** as a bright red solid (190 µg, 93%), being pure enough to be used for subsequent labeling studies after the rapid MS and <sup>1</sup>H NMR analysis: MALDI-TOF-MS m/z calcd for C<sub>50</sub>H<sub>54</sub>N<sub>10</sub>NaO<sub>9</sub> (M+Na)<sup>+</sup> 961.4 found 961.4; HRESI-MS m/z calcd for C<sub>50</sub>H<sub>54</sub>N<sub>10</sub>NaO<sub>9</sub> (M+Na)<sup>+</sup> 961.3973, found 961.3969; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  11.01 (s, 1H), 10.17 (d, 1H, J = 7.2 Hz), 8.77 (s, 1H), 7.88 (d, 2H, J = 9.0Hz), 7.87 (d, 2H, 9.1 Hz), 7.85 (d, 2H, J = 8.9 Hz), 7.76 (d, 2H, J = 8.7 Hz), 7.50 (d, 1H, J = 7.8 Hz), 7.46 (d, 2H, J = 9.3 Hz), 6.68 (dd, 1H, J = 2.2, 8.9 Hz), 6.53 (d, 1H, J = 2.2 Hz), 4.63 (m, 1H), 4.30 (m, 2H), 4.22 (m, 2H), 3.77 (t, 2H, J = 4.7 Hz), 3.61 (m, 2H), 3.48 (q, 4H, J = 7.2 Hz), 3.35 (m, 2H), 3.09 (s, 6H), 2.10-1.80 (brm, 2H), 1.70 (brm, 2H), 1.26 (t, 6H, J = 7.2 Hz).

**One-pot sequence of cRGDyK-directed "switched on" labeling on cell surface.** To a solution of the azide-aldehyde **4** in DMSO (1.0 mL, 9.0 x  $10^{-3}$  M) was added cyclic RGDyK peptide in DMSO (1.0 mL, 9.0 x  $10^{-3}$  M) at room temperature. The mixture was stirred at room temperature for 30 min to give the DIBO-derivatized RGDyK peptide, which was analyzed by MS and immediately subjected to the strain-releasing click reaction: MALDI-TOF-MS *m/z* calcd for C<sub>60</sub>H<sub>67</sub>N<sub>11</sub>O<sub>13</sub> (M)<sup>+</sup> 1149.5, found 1149.5.

To the reaction mixture of the DIBO-cRGDyK peptide obtained above was added the azide-aldehyde **6** in DMSO (10  $\mu$ L, 1.0 x 10<sup>-2</sup> M) at room temperature, and the mixture was stirred at 55 °C for 5 min (final reaction concentrations: DIBO-cRGDyK peptide: 3.3 x 10<sup>-3</sup> M, **6**: 3.3 x 10<sup>-3</sup> M) to give the aldehyde probe **7**. The reaxtion mixture was used directly in the following labeling experiments: MALDI-TOF-MS *m/z* calcd for C<sub>110</sub>H<sub>121</sub>N<sub>21</sub>O<sub>22</sub> (M)<sup>+</sup> 2086.9, found 2086.9.

RAW264.7 and Hep3B cells were cultured in DMEM medium (Sigma) supplemented with 10% (v/v) FBS at 37 °C in a 5% CO<sub>2</sub>-incubator. Cells were seeded at 2 x 10<sup>5</sup> cells/well in 50  $\mu$ L of DMEM, and placed for 6 h. After the medium was removed, the solution of the aldehyde probe 7, which were obtained above and diluted to a concentration of 1 x 10<sup>-5</sup> M in PBS (70  $\mu$ L containing 0.05% DMSO (v/v)), were added to the cell cultures at 37 °C under 5% CO<sub>2</sub> atmosphere. The resulting cells were immediately (within 1 min) and directly analyzed by confocal microscopy.



**Fig. SI-1**  $^{1}$ H NMR spectrum of **10**.

248.Carbon-1-1.als single pulse decoupled gated NOE 2012-12-04 21:17:40 13C carbon.jxp 135.77 MHz 7.87 KHz 4.21 Hz 2.6214 3146.54 Hz 14912 0.8336 sec 2.000 sec 2.000 sec ppm Hz 1H 30.0 c CDCL3 0.00 pp 0.12 H 58 ΗI 0000.0 70. a 65. a 60. a 55. a 50. a 45. a 40. a 35. a 30. a 25. a 20. a 15. a 10. a 05. a 90. 0 95. 0 90. 0 75. 0 70. 0 65. 0 60. 0 55. 0 50. 0 45. 0 40. 0 35. 0 30. 0 25. 0 20. 0 15. 0 10. 0 5. 0 0.0 14.2600 9718.84 8499.84 1268.63 1268.63 70,2235 77,2235 77,2235 77,2235 77,2235 77,2235 77,052 77, uments and SettingsYAll UsersYDocumentsYdataYNMR DataYkitadaniY248 Carbon-1-1.als 113-6928.011 137-0505 113-0505 152,00002 122,0200 122,020 122,021 12,021 123,021 123,020 123,020 123,020 123,020 123,020 123,020 123,020 123,020 123,020 123,020 123, single pulse decoupled gated NOE C:YDoc 991 -

### **Fig. SI-2** $^{13}$ C NMR spectrum of 10.



### **Fig. SI-3** <sup>1</sup>H NMR spectrum of **4**.

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### **Fig. SI-4** $^{13}$ C NMR spectrum of 4.

197 pure proton-1-1.als single pulse 2012-10-09 13:11:50 1H 500.16 MHz 500.16 MHz 500.16 Hz 500.16 Hz 500.11 Hz 500.16 Hz 500.00 sec 1H 3.00 usec 1H 3.00 usec 1H 3.00 usec 1H 3.00 usec 2.00 ppm 0.00 ppm 0.00 ppm 0.00 ppm 0.00 ppm 0.00 ppm

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**Fig. SI-5** <sup>1</sup>H NMR spectrum of **12**.

149-13C-4.als single pulse decoupled gated NOE 2011-11-22 17:40:42 13C single pulse dec 13C 77 MHz 7.87 KHz 7.87 KHz 4.21 Hz 2.821 Hz 2.821 Hz 2.821 A 31446.06 Hz 2.8336 sec 1.2000 sec 1.2000 sec 24.1 c CDCL3 77.00 ppm 4.20 Hz 58 DFILE COMNT COMNT COMNT OBJUC OBBRO Wdc 0.0 10.0 20.0 ₽₽81.62 15,25.7944 19742 30.0 €652.01 40.0 53.3259 53.3259 50.0 60.09 8250.78 70.0 77.2575 77.0000 76.7520 80.0 ntsYdataYNMR DataYkitadaniY149-13C-4.als 90.0 100.0 110.0 ₩ZS₩'III ----120.0 122.1544 128.2494 128.2494 130.0 .... 133\*3810 single pulse decoupled gated NOE 140.0 S778.641 ---and Settings¥All Users¥Doc 150.0 1971.831 160.0 9247.761 ----170.0 2279.871 -----180.0 C:¥Doc 190.0

### **Fig. SI-6** $^{13}$ C NMR spectrum of **12**.

253pure\_proton-1-1.als single\_pulse 2012-10-11 21:21:33 1H 500.16 MHz 500.16 MHz 500.14 6.01 Hz 52428 7507.51 Hz 6.9835 sec 5.0000 sec 6.70 usec 2.1 30.0 c 0.00 ppm 0.12 Hz 44 DFILE COMNT COMNT OBRUC OBRUC OBRIN OBFRQ OBFUC COMNT COMNT OBFUC OBFUC OBFUC OBFUC OBFUC OBFUC COMTO OBFUC COMNT OBFUC 000000 1.0599 1.65999 1.65999 1.6599 1.6599 1.6599 1.6599 1.6599 1.6599 1.6599 Mdd 0.0 3.2896 0.5 3,3036 1763.5 17 1.0 - 5 \$203.5 8003.5 2.145 2.140 2.0 4'2482 4'22482 4'2248 4'248 2.5 3.0 C: YDocuments and SettingsYAll UsersYDocumentsYdataYNMR DataYkitadaniY253pure\_proton-1-1.als 2'0e0 2:053 3.5 070.S 4.0 2961 4.5 2.024 811.1 5.0 5.5 6.0 6.5 086'1 3.175 101.5 1,055 1,055 7.0 2978.7 0888.7 186' 6089.7 2288.7 1278.7 1888.7 8588.7 8588.7 6.125 single\_pulse 7.5 3.957 0688.7 2668.7 2652858 8.0 1.9034 1606

**Fig. SI-7**  $^{1}$ H NMR spectrum of **13**.

253.Carbon-1-2.als single pulse decoupled gated NOE 1 2012-10-16 21:09:49 D carbon.jxp 135.77 MHz 7.87 KHz 4.21 Hz 4.21 Hz 3.3768 9308.18 Hz 14978 0.8336 sec 2.0000 sec 3.13 usec H 3.13 usec H 3.0.0 c CDCL3 0.00 pm 0.12 Hz 58

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### **Fig. SI-8** $^{13}$ C NMR spectrum of **13**.

1872nd\_proton-1-1.als single\_pulse 2012-06-01 21:11:03 1H 500.16 MHz 500.16 MHz 500.1 Hz 6.01 Hz 5.01 Hz 5.01 Hz 5.01 Hz 5.01 Hz 5.428 6.9835 sec 5.0000 sec 5.0000 sec 1H 30.0 c CDCL3 0.00 ppm 0.00 ppm 0.00 ppm

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**Fig. SI-9**  $^{1}$ H NMR spectrum of **14**.

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### **Fig. SI-10** $^{13}$ C NMR spectrum of 14.



**Fig. SI-11** <sup>1</sup>H NMR spectrum of TBDPS-deprotected compound of 14.

azide-aldehyde\_proton-1-1.als single\_pulse 2013-01-30 16:27:08 114 proton.jxp 500.16 MHz 50.01 Hz 52.41 KHz 6.01 Hz 52.428 7507.51 Hz 6.9835 sec 6.9835 sec 6.9835 sec 5.0000 sec 1H 3.00 usec 1H 3.00 usec 0 ppm 0.12 Hz 56

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### **Fig. SI-12** $^{1}$ H NMR spectrum of 6.

single\_pulse