1,3-Dipolar cycloaddition of alkynes to azides. Construction of operationally functional metal responsive fluorophores

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Supporting Information

Materials and Methods:

All chemicals were purchased from Aldrich Chemical, Acros, TCI America, or Fischer Scientific and used without purification unless otherwise specified. Column chromatography was performed using Standard Grade silica gel 60 Å, 32-63 µm (230 x 450 mesh) from Sorbent Technologies and the indicated eluent. Melting points were obtained using a Mel-Temp apparatus. All IR spectra were obtained using a Shimadzu FTIR-8400s spectrometer. Unless otherwise specified, NMR spectra were recorded at 298 K on a Varian Mercury spectrometer (300 MHz ¹H, 75 MHz ¹³C). Chemical shifts are reported in parts per million (ppm), using residual solvent as an internal standard. Data Reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet), coupling constant, and integration. Mass spectral analyses were provided by the Georgia Institute of Technology Mass Spectrometry Facility. All absorption spectra were collected using a Shimadzu UV-2401PC spectraphotometer. All emission spectra were acquired using a Shimadzu RF-5301PC spectrofluorophotometer. Elemental analyses were provided by Desert Analytics (Tucson, Az). Quantum yields were measured using standard procedures¹. In all cases, quinine sulfate was used as a standard and all solutions were purged with nitrogen prior to measurement.

Synthesis:

Warning: Sodium azide decomposes explosively above 275 °C and some organic azides are classified as highly explosive. To avoid danger appropriate safety measures must be taken all the time.

2-Trimethylsilanylethynylpyridine, 3-trimethylsilanylehynylpyridine², 4-triisopropylsilanylethynylpyridine and ((3,5-bis(trifluoromethyl)phenyl)ethynyl)trimethylsilane³ were prepared according to the literature.

4-Butoxyphenylazide (1): 4-butoxyaniline (5.61 g, 34.0 mmol) was added to a solution of 100 mL water and 100 mL conc. hydrochloric acid. Sodium nitrite (2.93 g, 42.5 mmol) dissolved in water (20 mL) was added dropwise at 0 °C and the solution was stirred for 1 h. After that (4.42 g, 68.0 mmol) sodium azide dissolved in water (20 mL) was added slowly at 0 °C and the mixture was stirred for additional 2 h. The solution was extracted with dichloromethane (3 x 50 mL) and the combined organic layers were washed with brine. The organic phase was dried over MgSO₄,

¹ "A Guide to Recording Fluorescence Quantum Yields." Horiba Jobin Yvon Ltd. Available online: http://www.jobinyvon.co.uk/ukdivisions/Fluorescence/plqy.htm

² T. A. Zeidan, S. V. Kovalenko, M. Manoharan, R. J. Clark, I. Ghiviriga, and I. V. Alabugin, *J. Am. Chem. Soc.* **2005**, *127*, 4270 – 4285.

³ M. Hauck, J. Schönhaber, A. J. Zucchero, K. I. Hardcastle, T. J. J. Müller, and U. H. F. Bunz, *J. Org. Chem.* **2007**, 72, 6714 – 6725.

the solvent was evaporated and the compound was dried in vacuo to give the desired product as a yellow oil (2.52 g, 39 %).

¹**H-NMR, CDCl₃** (δ , 300 Mz): 0.96 (t, 3H, J = 7.4 Hz); 1.50 (m, 2H, J = 7.5 Hz); 1.75 (m, 2H, J = 7.4 Hz); 3.92 (t, 2H, J = 6.5 Hz); 7.89 (dd, 4H). ¹³**C-NMR, CDCl₃** (δ , 75 Mz): 13.8, 19.2, 31.3, 68.0, 115.7, 119.9, 132.0, 156.5. **IR** (cm⁻¹): 822, 1244, 1377, 1456, 1503, 2108, 2853, 2923. **HRMS (EI+**): Calculated for C₁₀H₁₃N₃O 191.1059, found 191.1042.

4-[4-(3,5-Bis(trifluoromethyl)phenyl)-1*H***-1,2,3-triazol-1-yl]butoxybenzene (2):** ((3,5-bis(trifluoromethyl)phenyl)ethynyl)trimethylsilane (372 mg, 1.20 mmol) and potassium fluoride (208 mg, 3.6 mmol) were dissolved in methanol (1.0 mL) in a Schlenk tube. The solution was stirred for 2 h at room temperature. After that (191 mg, 1.00 mmol) 1, *tert*-butanol (3.0 mL) and water (3.0 mL) were quickly added. The solution was degassed three times using freeze/pump/thaw technique. Under flowing nitrogen CuSO₄ (3 mg, 1 mol %) and sodium ascorbate (24 mg, 10 mol %) were added. The mixture was stirred for 1 d at 50 °C. The reaction mixture was poured into ice. After 20 min the precipitate was filtered, washed with dilute sodium hydroxide solution (30 mL, 2N) and again washed with water (100 mL). The compound was dried at the oil pump over night to give the desired product (370 mg, 86 %)as a brown solid.

Mp: 134 − 136 °C.

¹**H-NMR, CDCl₃** (δ , 300 Mz): 0.99 (t, 3H, J = 7.3 Hz); 1.52 (m, 2H, J = 7.3 Hz); 1.80 (m, 2H, J = 7.4 Hz); 4.02 (t, 2H, J = 6.5 Hz); 7.03 (d, 2H, J = 9.0 Hz); 7.66 (d, 2H, J = 8.9 Hz); 7.84 (s, 1H); 8.25 (s, 1H); 8.34 (s, 2H).

¹³C-NMR, CDCl₃ (δ, 75 Mz): 13.8, 19.2, 31.2, 68.2, 115.4, 118.9, 121.7 (m), 122.2, 123.2 (q, J = 3.6 Hz), 125.6 (m), 129.8, 132.3 (q, J = 0.4 Hz), 132.5, 145.5, 159.8.

IR (cm⁻¹): 721, 1281, 1377, 1460, 2853, 2922.

HRMS (EI+): Calculated for C₂₀H₁₇N₃OF₆ 429.1276, found 429.1254.

Elemental analysis: Calculated for $C_{20}H_{17}N_3OF_6$: C 55.95, H 3.99, N 9.79 %; found: C 55.81, H 3.12, N 9.45 %.

4-[4-(2-Pyridyl)-1*H***-1,2,3-triazol-1-yl]butoxybenzene (3):** 2-Trimethylsilylethynylpyridine (210 mg, 1.20 mmol) and potassium fluoride (208 mg, 3.60 mmol) were dissolved in methanol (1 ml) in a schlenk tube. The solution was stirred for 2 h at room temperature. After that **1** (191 mg, 1.00 mmol), *tert*-butanol (3 mL) and water (3 mL) were quickly added. The solution was degassed three times using freeze/pump/thaw technique. Under flowing nitrogen CuSO₄ (3 mg, 1 mol %) and sodium ascorbate (24 mg, 10 mol %) were added. The mixture was stirred for 2 d at 50 °C. The reaction mixture was poured into ice. After 20 min the precipitate was filtered, washed with dilute sodium hydroxide solution (30 mL, 2N) and again washed with water (100 mL). The compound was dried at the oil pump over night to give the desired product (270 mg, 92 %) as a brown solid.

Mp: 98 - 100 °C. ¹**H-NMR, CD₂Cl₂** (δ , 300 Mz): 0.99 (t, 3H, J = 7.4 Hz); 1.52 (m, 2H, J = 7.6 Hz); 1.80 (m, 2H, J = 7.9 Hz); 4.04 (t, 2H, J = 6.5 Hz); 7.05 (d, 2H, J = 9.1 Hz); 7.28 (m, 1H); 7.71 (d, 2H, J = 9.1 Hz); 7.83 (t, 1H, J = 7.6 Hz); 8.21 (d, 1H, J = 7.9 Hz); 8.56 (s, 1H); 8.60 (d, 1H, J = 4.9 Hz). ¹³C-NMR, CDCl₃ (δ , 75 Mz): 13.8, 19.2, 31.1, 68.1, 115.3, 120.0, 120.4, 122.0, 123.0, 130.2, 136.9, 148.7, 149.4, 150.0, 159.5. **IR** (cm⁻¹): 721, 1377, 1456, 1518, 2853, 2922. **HRMS** (EI+): Calculated for C₁₇H₁₈N₄O 294.1481, found 294.1423. **Elemental analysis**: Calculated for C₁₇H₁₈N₄O: C 69.37, H 6.16, N 19.03 %; found: C 69.04, H 5.37, N 18.46 %.

4-[4-(3-Pyridyl)-1*H***-1,2,3-triazol-1-yl]butoxybenzene (4):** 3-Trimethylsilylethynylpyridine (210 mg, 1.20 mmol) and potassium fluoride (208 mg, 3.60 mmol) were dissolved in methanol (1 mL) in a Schlenk tube. The solution was stirred for 2 h at room temperature. After that **1** (191 mg, 1.00 mmol), *tert*-butanol (3 mL) and water (3 mL) were quickly added. The solution was degassed three times using freeze/pump/thaw technique. Under flowing nitrogen CuSO₄ (3 mg, 1 mol %) and sodium ascorbate (24 mg, 10 mol %) were added. The mixture was stirred for 1 d at 50 °C. The reaction mixture was poured into ice. After 20 min the precipitate was filtered, washed with dilute sodium hydroxide solution (30 mL, 2N) and again washed with water (100 mL). The compound was dried at the oil pump over night to give the desired product (240 mg, 82 %) as an orange solid.

Mp: 139 - 140 °C.

¹**H-NMR, CDCl₃** (δ , 300 Mz): 0.98 (t, 3H, J = 7.3 Hz); 1.51 (m, 2H, J = 7.6 Hz); 1.80 (m, 2H, J = 7.4 Hz); 4.01 (t, 2H, J = 6.5 Hz); 7.03 (d, 2H, J = 8.9 Hz); 7.40 (t, 1H, J = 6.0 Hz); 7.66 (d, 2H, J = 8.9 Hz); 8.17 (s, 1H); 8.27 (d, 1H, J = 7.9 Hz); 8.60 (s, 1H); 9.06 (s, 1H).

¹³C-NMR, CDCl₃ (δ, 75 Mz): 13.8, 19.2, 31.1, 68.1, 115.3, 118.2, 122.19, 123.8, 126.6, 130.0, 133.1, 145.1, 147.1, 149.4, 159.6.

IR (cm⁻¹): 721, 1377, 1460, 2853, 2922.

HRMS (EI+): Calculated for C₁₇H₁₈N₄O 294.1481, found 294.1507.

Elemental analysis: Calculated for $C_{17}H_{18}N_4O$: C 69.37, H 6.16, N 19.03 %; found: C 68.45, H 5.18, N 18.26 %.

4-[4-(4-Pyridyl)-1*H***-1,2,3-triazol-1-yl]butoxybenzene (5):** 4-Triisopropylsilylethynylpyridine (310 mg, 1.20 mmol) and (568 mg, 1.80 mmol) tetrabutylammonium fluoride were dissolved in THF (0.5 mL) in a Schlenk tube. The solution was stirred for 2 h at room temperature. After that (191 mg, 1.00 mmol) 1, *tert*-butanol (3 mL) and water (3 mL) were quickly added. The solution was degassed three times using freeze/pump/thaw technique. Under flowing nitrogen CuSO₄ (3 mg, 1 mol %) and sodium ascorbate (24 mg, 10 mol %) were added. The mixture was stirred for 1 d at 50 °C. The reaction mixture was poured into ice. After 20 min the precipitate was filtered, washed with dilute sodium hydroxide solution (30 mL, 2N) and again washed with water (100 mL). The compound was dried at the oil pump over night to give the desired product (174 mg, 59 %) as a beige-brown solid.

Mp: 158 − 160 °C.

¹**H-NMR, acetone-d6** (δ , 300 Mz): 0.98 (t, 3H, J = 7.4 Hz); 1.51 (m, 2H, J = 7.6 Hz); 1.79 (m, 2H, J = 7.2 Hz); 4.09 (t, 2H, J = 6.5 Hz); 7.16 (d, 2H, J = 9.1 Hz); 7.84 (d, 2H, J = 9.1 Hz); 7.89 (d, 2H, J = 4.5 Hz); 8.65 (d, 2H, J = 4.3 Hz); 9.09 (s, 1H).

¹³**C-NMR, THF-d8** (δ, 75 Mz): 14.1, 20.0, 32.2, 68.7, 116.0, 120.5, 121.1, 122.4, 131.3, 139.2, 146.2, 151.1, 160.4.

IR (cm⁻¹): 721, 820, 839, 1377, 1458, 2853, 2922.

HRMS (EI+): Calculated for $C_{17}H_{18}N_4O$ 294.1481, found 294.1470 **Elemental analysis**: Calculated for $C_{17}H_{18}N_4O$: C 69.37, H 6.16, N 19.03 %; found: C 69.36, H 4.68, N 18.49 %.

Supporting Table: Photophysical Properties of 2-5

	3	4	5	2
Quantum Yield	< 0.01	-	< 0.01	-
$\lambda_{ m max}$ (ab) in nm	287	265	269	269
ε in I mol ⁻¹ cm ⁻¹	18600	21700	27700	25300
λ_{max} (em) in nm	484	-	486	-
Stokes shift in cm ⁻¹	14200	-	16600	-
	3 + Zn	4 + Zn	5 + Zn	2 + Zn
Quantum Yield	0.07	< 0.01	0.14	0.05
λ_{max} (ab) in nm	326	269	269/317	254
λ_{max} (em) in nm	498	-	496	412
Stokes shift in cm ⁻¹	10600	-	17000/11400	15100

Supporting Experiment 1. Absorption spectra after addition of metal salts to compound 2.



Supporting Experiment 2. Titration of 2 with trifluoroacetic acid as observed in emission.



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Supporting Experiment 4. Titration of 5a with trifluoroacetic acid in absorption (top) and emission (bottom).



Supporting Experiment 5. Metal reactivity of **4** with different metal cations in emission (top) and absorption (bottom).





Supporting Experiment 6. Titration of 4 with trifluoroacetic acid as shown in emission.

Supporting Experiment 7. ¹H-NMR spectrum (top) and ¹³C-NMR spectrum (bottom) of **2**.



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Supporting Experiment 8. ¹H-NMR spectrum (top) and ¹³C-NMR spectrum (bottom) of **3**.



Supporting Experiment 9. ¹H-NMR spectrum (top) and ¹³C-NMR spectrum (bottom) of **4**.



Supporting Experiment 10. ¹H-NMR spectrum (top) and ¹³C-NMR spectrum (bottom) of **5a**.

