# Fe/ppm Cu Nanoparticles as a Recyclable Catalyst for Click Reactions in Water at Room Temperature

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## I. General Information

Unless otherwise noted, all reactions were performed under an atmosphere of argon. All commercially available reagents were used without further purification. A 2 wt % TPGS-750-M/H<sub>2</sub>O solution was prepared by dissolving TPGS-750-M in water (degassed with argon prior to mixing, HPLC grade). A solution of TPGS-750-M can be purchased from Sigma Aldrich® (catalog numbers 733857 and 763918). TPGS- 750-M was made as previously described.<sup>1</sup> Analytical thin layer chromatography (TLC) was performed using Silica Gel 60 F254 plates (Merck, 0.25 mm thick). The developed chromatogram was analyzed by UV lamp (254 nm). UV inactive compounds were visualized using aqueous potassium permanganate (KMnO<sub>4</sub>), ninhydrin staining, aqueous phosphomolybdic acid, or butanolic vanillin and developed with a heat gun. Flash chromatography was performed using Silicycle Siliaflash® P60 Unbounded Grade Silica: Particle size: 40-60 µm, Pore size: 60 Å. <sup>1</sup>H and <sup>13</sup>C NMR data were recorded at 297.8 K on a Agilent® Technologies 400 MHz or Varian Unity Inova® 500 MHz.The FID was processed using MestReNova (release: 10.0). Chemical shifts in <sup>1</sup>H NMR spectra are reported in parts per million (ppm) on the  $\delta$  scale with the residual <sup>1</sup>H resonance from deuterated chloroform set at 7.26 ppm. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sext = sextet, sep = septet, m = multiplet, br = broad, dt = doublet of triplets, dd = doublet of doublets, td = triplet of doublets, ddd = doublet of doublet of doublets), coupling constant in hertz (Hz), and integration. Chemical shifts of <sup>13</sup>C NMR spectra were referenced through the chloroform <sup>13</sup>C resonance reported at 77.16 ppm from the central peak on the  $\delta$  scale according to IUPAC recommended secondary referencing method<sup>2</sup> and the manufacturer's protocols. Reactions were deemed complete by TLC or via GC-MS. GCMS data were recorded on a 5975C Mass Selective Detector, coupled with a 7890A Gas Chromatograph (Agilent Technologies). A capillary column HP-5MS cross-linked 5% phenylmethylpolysiloxanediphenyl column (30 m x 0.250 mm, 0.25 micron, Agilent Technologies) was employed. Helium was used as carrier gas at a constant flow of 1 mL/min.

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2) (a) Harris, R. K.; Becker, E. D.; Cabral de Menezes, S. M.; Goodfellow, R.; Granger, P. *Pure Appl. Chem.* **2001**, *73*, 1795–1818. (b) Harris, R. K.; Becker, E. D.; Cabral de Menezes, S. M.; Granger, P.; Hoffman, R. E.; Zilm, K. W. *Pure Appl. Chem.* **2008**, *80*, 59–84.

### II. Experimental Procedures

General procedure A for CuAAC reactions. In a flame dried 10 mL microwave reaction vial, FeCl<sub>3</sub> (4.1 mg, 5 mol %) was added under anhydrous conditions. The reaction vial was closed with a rubber septum and the mixture was evacuated and backfilled with argon three times. Dry THF (0.7 mL) and CuOAc in THF (0.061 mL, 1000 ppm; 1 g/L) were added to the vial and the mixture was stirred for 10 min at rt, after which MeMgCl in THF (0.75 mL, 7.5 mol %; 0.5 M) was added to the reaction mixture. While maintaining an inert atmosphere, THF was evaporated under reduced pressure. An aqueous solution of 2 wt % TPGS-750-M (1.0 mL) was then added to the vial followed by sequential addition of alkyne (0.5 mmol), azide (0.6 mmol, 1.2 equiv), and triethylamine (0.0349 mL, 0.25 mmol, 0.5 equiv). The mixture was stirred vigorously at rt. After complete consumption of starting material, as monitored by TLC or GC-MS, EtOAc (1 mL) was added to the reaction mixture, which was then stirred gently for 5 min (NOTE : vigorous stirring or shaking in the reaction flask or in a separatory funnel during the exctraction process resulted in the formation of an intractable emulsion with consequent reductions in isolated yields). Stirring was stopped and the organic layer was separated with the aid of a centrifuge. The organic layer was removed and the extraction process was repeated two additional times. The combined organic layers were dried over anhydrous magnesium or sodium sulfate, or flushed through a plug of dried silica gel. The solvent was then evacuated under reduced pressure to obtain crude material which was purified by flash chromatography over silica gel using EtOAc/hexanes as eluent.

**Preparation of Fe/ppm Cu nanoparticles.** In a tared flame dried two-neck round-bottomed flask, anhydrous pure FeCl<sub>3</sub> (121.7 mg, 0.75 mmol) and CuOAc (1.839 mg, 0.015 mmol) were placed under an atmosphere of dry argon. The flask was closed with a septum, and dry THF (10 mL) was added. The reaction mixture was stirred for 10 min at rt. While maintaining a dry atmosphere at rt, MeMgCl (2.25 mL, 1.125 mmol; 0.5 M solution) in THF was very slowly (1 drop/two sec) added to the reaction mixture. After complete addition of the Grignard reagent, the reaction mixture was stirred for an additional 30 min at rt. An appearance of a dark-brown coloration was indicative of generation of nanomaterial. The stir bar was removed and THF was evaporated under reduced pressure at rt followed by washing the mixture with dry pentane to provide a light brown-colored nanopowder. The nanomaterial was dried under reduced pressure at rt for 10 min (603 mg) and could then be used directly for CuAAC reactions under micellar conditions. Dividing the starting mass of CuOAc by the final weight in the flask yields CuOAc concentration in the isolated catalyst: 1.839 mg CuOAc/603 mg NPs = 0.305 mg CuOAc/100 mg NPs which equates to 0.061 mg (1000 ppm Cu for 0.5 mmol substrate)/20 mg NPs.

Determination of Cu concentration in isolated catalyst.

$$[CuOAc] = \frac{1.839 \text{ mg CuOAc}}{603 \text{ mg NPs}} = \frac{0.305 \text{ mg CuOAc}}{100 \text{ mg NPs}}$$

0.5mmol substrate×0.001 equiv CuOAc {1000 ppm Cu}×122.59 FW CuOAc = 0.061 mg CuOAc for 0.5 mmol scale reaction

 $\frac{100 \text{ mg NPs}}{0.305 \text{ mg CuOAc}} \times 0.061 \text{ mg CuOAc} = 20 \text{ mg NPs}$ 

**General procedure B for CuAAC reaction with aged catalyst.** In a flame dried 10 mL microwave reaction vial, aged nanomaterial (20 mg) and vitamin C (8.8 mg, 0.05 mmol) were added. The reaction vial was closed with a rubber septum and the mixture was evacuated and backfilled with argon three times. An aqueous solution of 2 wt % TPGS-750-M (1.0 mL) was added to the vial. After 24 h stirring at rt, while maintaining the inert atmosphere, alkyne (0.5 mmol), azide (0.6 mmol, 1.2 equiv), and triethylamine (0.0349 mL, 0.25 mmol, 0.5 equiv) were added. The mixture was stirred vigorously at rt. After complete consumption of starting material, as monitored by TLC or GC-MS, EtOAc (1 mL) was added to the reaction mixture, which was stirred gently for 5 min (NOTE : vigorous stirring or shaking in the reaction flask or in a separatory funnel during the exctraction process resulted in the formation of an intractable emulsion with consequent reductions in isolated yields). Stirring was stopped and the organic layer was separated two additional times. The combined organic layers were dried over anhydrous magnesium sulfate or sodium sulfate, or flushed through a plug of dried silica gel. The solvent was then evacuated under reduced pressure to obtain crude material which was purified by flash chromatography over silica gel using EtOAc/hexanes as eluent.

#### III. Analytical Data for Triazole Products

(2) 1-Benzyl-4-phenyl-1*H*-1,2,3-triazole. Isolated as a white powdery crystal (99%).  $R_f = 0.33$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.79-7.81 (m, 2H), 7.66 (s, 1H), 7.37-7.42 (m, 5H), 7.30-7.33 (m, 3H), 5.59 (s, 2H). Melting point: 123-125 °C.

(3) 1-Benzyl-4-butyl-1*H*-1,2,3-triazole. Isolated as a clumpy white solid (99%).  $R_f = 0.28$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.32-7.38 (m, 3H), 7.23-7.25 (m, 2H), 7.17 (s, 1H), 5.48 (s, 2H), 2.68 (t, J = 8 Hz, 2H), 1.61 (p, J = 7.5 Hz, 2H), 1.35 (sext, J = 7.5 Hz, 2H), 0.90 (t, J = 7.5 Hz, 3H). Melting point: 55-56 °C.



(4) 1-Benzyl-4-hexyl-1*H*-1,2,3-triazole. Isolated as a fluffy white crystalline solid (96%).  $R_f = 0.32$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.32-7.37 (m, 3H), 7.23-7.24 (m, 2H), 7.17 (s, 1H), 5.47 (s, 2H), 2.67 (t, J = 7.5 Hz, 2H), 1.62 (p, J = 7.5 Hz, 2H), 1.25-1.33 (m, 6H), 0.85 (t, J = 6.5 Hz, 3H). Melting point: 45-47 °C.



**(5) 1-Benzyl-4-(3-chloropropyl)-1H-1,2,3-triazole.** Isolated as a flaky off-white solid (99%). R<sub>f</sub> = 0.21 (1:3 EtOAc: hexanes). **NMR** <sup>1</sup>**H (CDCl<sub>3</sub>, 500 MHz, δ):** 7.34-7.40 (m, 3H), 7.25-7.27 (m, 2H), 7.24 (s, 1H), 5.50 (s, 2H), 3.56 (t, J = 6.5 Hz, 2H), 2.86 (t, J = 7.5 Hz, 2H), 2.15 (p, J = 7 Hz, 2H).

$$HO \rightarrow N = N$$

(6) 2-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)propan-2-ol. Isolated as a white powdery solid (99%).  $R_f = 0.31$  (2:25 MeOH:  $CH_2Cl_2$ ). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.35-7.39 (m, 3H), 7.34 (s, 1H), 7.27 (dd, J = 8, 2.5 Hz, 2H), 5.49 (s, 2H), 2.54 (s, 1H), 1.60 (s, 6H). Melting point: 73-75 °C.



(7) 1-Benzyl-4-(3-((triisopropylsilyl)oxy)propyl)-1*H*-1,2,3-triazole. Isolated as a colorless, viscous oil (83%).  $R_f = 0.37$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.34-7.38 (m, 3H), 7.24-7.26 (m, 2H), 7.19 (s, 1H), 3.70 (t, J = 6.5 Hz, 2H), 2.79 (t, J = 7.5 Hz, 2H), 1.89 (p, J = 7.5 Hz, 2H), 1.03 (s, 18H). NMR <sup>13</sup>C (CDCl<sub>3</sub>, 101 MHz,  $\delta$ ): 148.60, 135.08, 129.18, 128.74, 128.11, 120.81, 62.53, 54.13, 32.52, 22.22, 18.15, 12.06. HRMS: 396.2447 ([M+Na<sup>+</sup>] calc), 396.2462 ([M+Na<sup>+</sup>] found).



(8) 1-Benzyl-4-(2-((*t*-butyldimethylsilyl)oxy)ethyl)-1*H*-1,2,3-triazole. Isolated as a colorless, viscous oil (76%). R<sub>f</sub> = 0.26 (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz, δ): 7.39-7.43 (m, 3H), 7.31-7.32 (m, 3H), 5.54 (s, 2H), 3.88 (t, J = 6.5 Hz, 2H), 2.96 (t, J = 6.5 Hz, 2H), 0.86 (t, 9H), 0.00 (t, 6H). NMR <sup>13</sup>C (CDCl<sub>3</sub>, 101 MHz, δ): 145.97, 134.95, 129.19, 128.77, 128.24, 121.92, 62.34, 54.16, 29.62, 25.98, 18.32, -5.32. HRMS: 340.1821 ([M+Na<sup>+</sup>] calc), 340.1817 ([M+Na<sup>+</sup>] found).

(9) 1-Benzyl-4-(((*tert*-butyldimethylsilyl)oxy)methyl)-1*H*-1,2,3-triazole. Isolated as a colorless, viscous oil (74%).  $R_f = 0.34$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.32 (s, 1H), 7.27-7.30 (m, 3H), 7.19 (dd, J = 7.5, 2 Hz, 2H), 5.44 (s, 2H), 4.76 (s, 2H), 0.81 (s, 9H), 0.00 (s, 6H). NMR <sup>13</sup>C (CDCl<sub>3</sub>, 101 MHz,  $\delta$ ): 134.93, 129.19, 128.79, 128.09, 121.62, 114.62, 58.11, 54.23, 26.01, 18.47, - 5.14. HRMS: 326.1665 ([M+Na<sup>+</sup>] calc), 326.1673 ([M+Na<sup>+</sup>] found).



(10) 4-(1-Benzyl-1*H*-1,2,3-triazol-4-yl)-*N*,*N*-dimethylaniline. Isolated as a maroon crystalline solid (93%).  $R_f = 0.40$  (1:1 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.66 (d, J = 9 Hz, 2H), 7.52 (s, 1H), 7.35-7.40 (m, 3H), 7.30 (d, J = 8 Hz, 2H), 6.74 (d, J=9 Hz, 2H), 5.55 (s, 2H), 2.97 (s, 6H). Melting point: 193-195 °C.



(11) 1-(2-Fluorobenzyl)-4-phenyl-1*H*-1,2,3-triazole. Isolated as a white powdery crystal (99%).  $R_f = 0.29$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz, δ): 7.81 (dd, J = 8.5, 1.5 Hz, 2H), 7.76 (s, 1H), 7.30-7.42 (m, 5H), 7.15 (q, J = 10 Hz, 2H), 5.64 (s, 2H). Melting point: 91-92 °C.



(12) 4-((4-Phenyl-1*H*-1,2,3-triazol-1-yl)methyl)benzonitrile. Isolated as a white powder (91%).  $R_f = 0.30$  (1:1 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.81 (dd, J = 8.5, 1.5 Hz, 2H), 7.72 (s, 1H), 7.68 (d, J = 8.5 Hz, 2H), 7.32-7.43 (m, 5H), 5.65 (s, 2H). Melting point: 132-134 °C.



(13) Methyl 4-((4-phenyl-1*H*-1,2,3-triazol-1-yl)methyl)benzoate. Isolated as an off-white crystalline solid (25%).  $R_f = 0.39$  (1:1 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 8.05 (d, J = 8.5 Hz, 2H), 7.81 (dd, J = 8.5, 1.5 Hz, 2H), 7.69 (s, 1H), 7.31-7.42 (m, 5H), 5.64 (s, 2H), 3.92 (s, 3H). Melting point : 156-158 °C.

$$Ph \xrightarrow{N=N}_{N} ( CH_3) CH_3$$

**(14) 1-Decyl-4-phenyl-1***H***-<b>1,2,3-triazole.** Isolated as a flaky white powder (23%). R<sub>f</sub> = 0.38 (1:3 EtOAc: hexanes). **NMR** <sup>1</sup>**H** (**CDCl**<sub>3</sub>, **500 MHz**, **δ**): 7.84 (d, J = 7.5 Hz, 2H), 7.74 (s, 1H), 7.42 (t, J = 8 Hz, 2H), 7.32 (t, J = 6.5 Hz, 1H), 4.39 (t, J = 7 Hz, 2H), 1.94 (p, J = 7 Hz 2H), 1.26-1.35 (m, 14H), 0.87 (t, J = 7 Hz, 3H).



(15) 1-Benzyl-4-(2-fluorophenyl)-1*H*-1,2,3-triazole. Isolated as a white crystalline solid (86%).  $R_f = 0.32$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 8.31 (td, J = 7.6, 2.0 Hz, 1H), 7.86 (d, J = 3.7 Hz, 1H), 7.42 – 7.22 (m, 7H), 7.13 – 7.08 (m, 1H), 5.60 (s, 2H). Melting point: 96-98 °C.



**(16) 4-((4-(2-Fluorophenyl)-1***H***-1,2,3-triazol-1-yl)methyl)benzonitrile.** Isolated as a white crystalline solid (83%). R<sub>f</sub> = 0.43 (1:1 EtOAc:hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, **500** MHz, δ): 8.30 (td, *J* = 7.6, 1.9 Hz, 1H), 7.92 (d, *J* = 3.6 Hz, 1H), 7.68 – 7.66 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.34 – 7.29 (m, 1H), 7.26 (td, *J* = 8.0, 1.4 Hz, 1H), 7.12 (ddd, *J* = 11.1, 8.2, 1.2 Hz, 1H), 5.66 (s, 2H). NMR <sup>13</sup>C (CDCl<sub>3</sub>, 125 MHz, δ): 160.34, 158.37, 142.17, 139.99, 133.03, 129.77, 129.71, 128.45, 127.92, 127.89, 124.83, 124.80, 123.02, 122.91, 118.36, 118.25, 115.89, 115.72, 112.94, 105.13, 53.55. Melting point: 137-138 °C. HRMS : 301.0865 ([M+Na<sup>+</sup>] calc), 301.0869 ([M+Na<sup>+</sup>] found).



(17) 4-(2-Fluorophenyl)-1-phenethyl-1*H*-1,2,3-triazole. Isolated as an off-white flaky powder (72%). R<sub>f</sub> = 0.31 (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 8.29 (td, *J* = 7.6, 2.0 Hz, 1H), 7.70 (d, *J* = 3.7 Hz, 1H), 7.35 – 7.21 (m, 4H), 7.17 – 7.14 (m, 2H), 7.13 – 7.09 (m, 1H), 4.66 (t, *J* = 7.3 Hz, 2H), 3.27 (t, *J* = 7.3 Hz, 2H). NMR <sup>13</sup>C (CDCl<sub>3</sub>, 125 MHz,  $\delta$ ): 137.11, 129.37, 129.30, 129.00, 128.85, 127.98, 127.95, 127.28, 124.73, 124.70, 123.18, 123.07, 115.84, 115.67, 51.86, 36.94. Melting point: 79-81 <sup>°</sup>C. HRMS: 290.1069 ([M+Na<sup>+</sup>] calc), 290.1066 ([M+Na<sup>+</sup>] found).



(18) 1-Benzyl-4-(3,5-bis(trifluoromethyl)phenyl)-1*H*-1,2,3-triazole. Isolated as a white powder (69%).  $R_f = 0.38$  (1:3 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 8.25 (s, 2H), 7.81 (s, 1H), 7.80 (s, 1H), 7.39-7.44 (m, 3H), 7.3 (dd, J = 7.5, 2 Hz, 2H), 5.62 (s, 2H). Melting point: 123-125 °C.

(19) 1-Phenethyl-4-phenyl-1*H*-1,2,3-triazole. Isolated as a white crystal (91%).  $R_f = 0.49$  (1:1 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.76 (dd, J = 8.5, 1.5 Hz, 2H), 7.46 (s, 1H), 7.41 (t, J = 8 Hz, 2H), 7.25-7.34 (m, 4H), 7.14 (d, J = 8 Hz, 2H), 4.64 (t, J = 7 Hz, 2H), 3.26 (t, J = 7 Hz, 2H). Melting point: 130-131 °C.



(20) 1-(4-Methoxybenzyl)-4-phenyl-1*H*-1,2,3-triazole. Isolated as a brownish white shiny crystalline solid (89%).  $R_f = 0.47$  (1:1 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.79 (dd, J = 8, 1 Hz, 2H), 7.62 (s, 1H), 7.39 (t, J = 7.5 Hz, 2H), 7.25-7.32 (m, 3H), 6.91 (dt, J = 9, 2 Hz, 2H), 5.50 (s, 2H), 3.81 (s, 3H). Melting point: 118-119 °C. HRMS: 288.1113 ([M+Na<sup>+</sup>] calc), 288.1116 ([M+Na<sup>+</sup>] found).



(21) 1-Benzyl-4-(((2,7,8-trimethyl-2-(4,8,12-trimethyltridecyl)chroman-6-yl)oxy)methyl)-1*H*-1,2,3-triazole. Isolated as an off-white flaky wax (84%).  $R_f = 0.64$  (1:1 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.55 (s, 1H), 7.37-7.41 (m, 3H), 7.30-7.31 (m, 2H), 5.55 (s, 2H), 4.83 (s, 2H), 2.55 (t, J = 7 Hz, 2H), 2.16 (s, 3H), 2.11 (s, 3H), 2.07 (s, 3H), 1.72-1.84 (m, 2H), 1.05-1.58 (m, 26H), 0.83-0.87 (m, 12H). NMR <sup>13</sup>C (CDCl<sub>3</sub>, 101 MHz,  $\delta$ ): 148.19, 147.81, 145.55, 134.73, 129.27, 128.91, 128.28, 127.97, 126.09, 123.07, 122.55, 117.73, 75.00, 66.58, 54.35, 40.23, 40.19, 39.50, 37.59, 37.52, 37.42, 32.91, 32.84, 31.35, 31.30, 28.12, 24.96, 24.59, 24.00, 22.88, 22.78, 21.18, 20.76, 19.90, 19.83, 13.04, 12.18, 11.96. HRMS: 624.2505 ([M+Na<sup>+</sup>] calc), 624.4506 ([M+Na<sup>+</sup>] found).



(22) 1-Benzyl-4-((2*E*,6*E*,10*E*,14*E*,18*E*,22*E*,26*E*,30*E*)-3,7,11,15,19,23,27,31,35-nonamethylhexatriaconta-2,6,10,14,18,22,26,30,34-nonaen-1-yl)-1*H*-1,2,3-triazole. Isolated as a flaky off-white solid (88%).  $R_f = 0.55$  (1:1 EtOAc: hexanes). NMR <sup>1</sup>H (CDCl<sub>3</sub>, 500 MHz,  $\delta$ ): 7.34-7.36 (m, 3H), 7.24-7.26 (m, 2H), 7.16 (s, 1H), 5.49 (s, 2H), 5.08-5.14 (m, 9H), 2.73 (t, J = 7.5 Hz, 2H), 2.33 (q, J = 7.5 Hz, 2H), 1.94-2.07 (m, 32H), 1.68 (s, 3H), 1.60 (s, 22H), 1.55 (s, 1H), 1.52 (s, 3H). NMR <sup>13</sup>C (CDCl<sub>3</sub>, 101 MHz,  $\delta$ ): 136.47, 135.20, 135.13, 135.08, 135.05, 135.02, 131.40, 129.17, 128.72, 128.08, 124.52, 124.39, 124.36, 124.30, 124.20, 123.18, 120.75, 54.10, 39.89, 39.86, 39.80, 27.92, 26.89, 26.84, 26.80, 26.75, 26.08, 25.86, 17.84, 16.21, 16.18, 16.15. Melting point: 61-63 °C. HRMS: 808.6485 ([M+Na<sup>+</sup>] calc), 808.6509 ([M+Na<sup>+</sup>] found).

### IV. E Factor and Recycling Study

The initial reaction was set up according to the general procedure. After 8 h, the aqueous solution was extracted three times with EtOAc (0,8 mL), placed in a 10 mL round bottom flask, and the solvent was removed via rotary evaporation. The crude product was purified by flash column chromatography as described previously using EtOAc/hexane to provide the desired compound.

Re-use of surfactant solution: The vial was charged with NEt<sub>3</sub> and a new alkyne/azide pair via syringe. The reaction mixture was evacuated and backfilled with argon three times and then was allowed to stir vigorously at rt for 8 h. The product was extracted with EtOAc (0,4 mL). The organic solvent was evaporated via rotary evaporation. The crude product was purified flash column chromatography as described previously using EtOAc/hexane to provide the desired compound.

E Factor calculation: Note: density of EtOAc = 0.902 g/mL

$$E Factor = \frac{Waste (mg)}{Product (mg)} = \frac{0.722 + 0.361 + 0.361 + 0.361}{0.108 + 0.110 + 0.108 + 0.114} = 4.1$$

# V. <sup>1</sup>H NMR and <sup>13</sup>C NMR Spectra for products





































































