ESI for Upper-rim Functionalised Calix[4]arenes for Chemoselective Au^{3+} Detection

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General Information

All reactions were conducted in flame-dried glass apparatus under an atmosphere of nitrogen or argon. Water refers to distilled water, all commercially available chemicals and reagents were used as supplied. Melting points were recorded using open capillary tubes on melting point apparatus and are uncorrected. Infrared spectra were recorded either as a thin film or neat sample. ^{1}H- and ^{13}C-NMR spectra were recorded in Fourier transform mode at the field strength and deuterated solvent indicated. ^{1}H-spectra were recorded in ppm and referenced to the residual $CHCl_3$ signal located at δ 7.26 ppm. ^{13}C-NMR spectra were recorded in ppm and referenced to the residual $CHCl_3$ signal found at δ 77.00. Multiplicities in the NMR spectra are described as: s = singlet, d = doublet, t = triplet, q= quartet, m = multiplet, br = broad; coupling constants are reported in Hz. Ion mass/charge (*m/z*) ratios are reported as values in atomic mass units. Microwave reactions refer to a closed vessel microwave reactor 300W. Fluorimetric analyses were performed on a Perkin-Elmer LS45 fluorescence spectrometer, with all of the sample dilutions prepared using HPLC grade methanol and tetrahydrofuran. All of the commercially available salts were used 'as is', these included; sodium tetrachloroaurate(III) hydrate, cadmium(II) acetate hydrate, hydrogen hexachloroplatinate (IV) hydrate, mercury(II) chloride, silver(I) tetrafluoroborate, triphenylphosphinegold(I) chloride, sodium chloride, lithium chloride, calcium chloride, potassium hexafluorophosphate, magnesium chloride, tetraethylammonium tetrafluoroborate and cesium chloride.

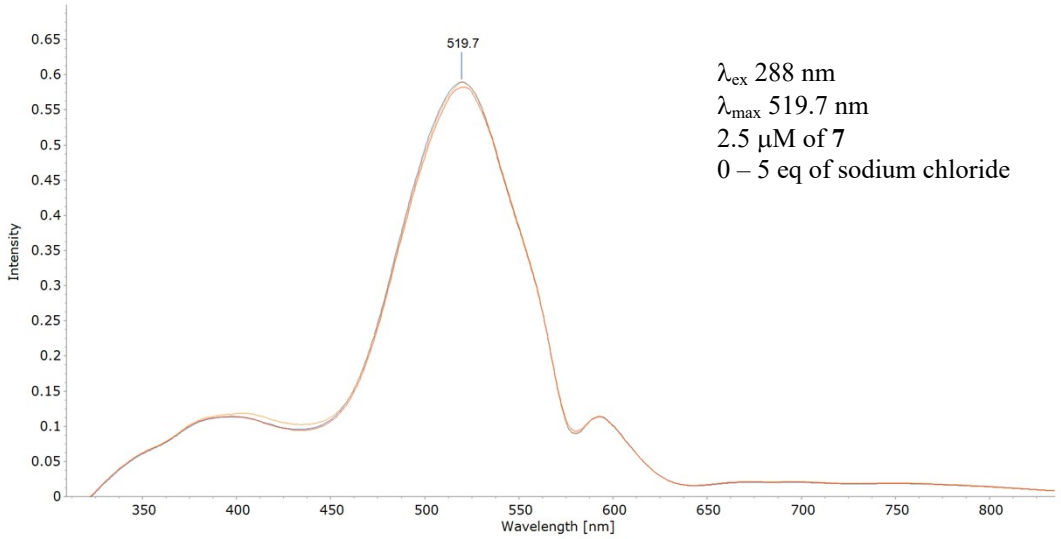


Figure 1. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of sodium chloride (0 – 5 equivalents).

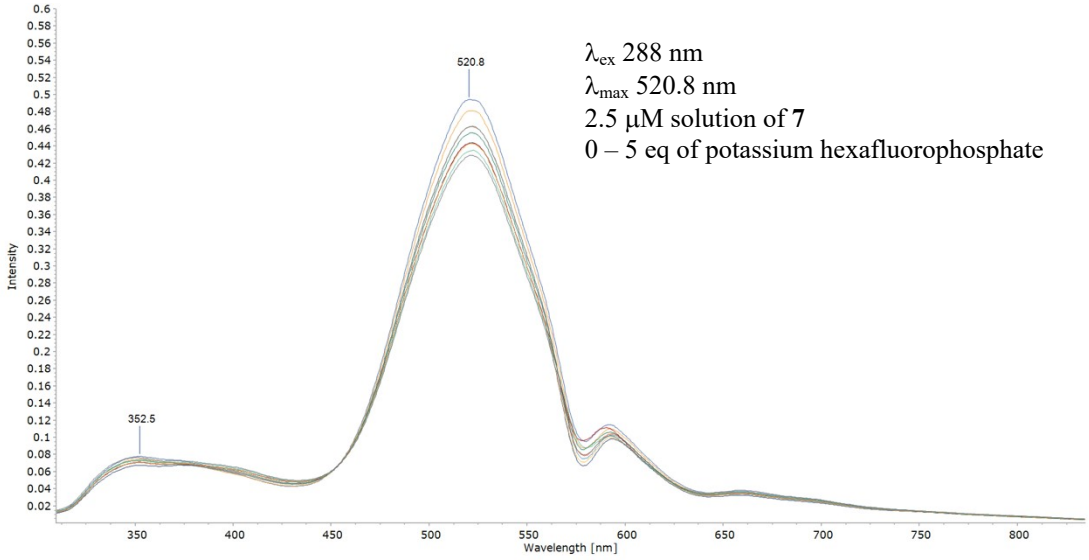


Figure 2. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of potassium hexafluorophosphate (0 – 5 equivalents).

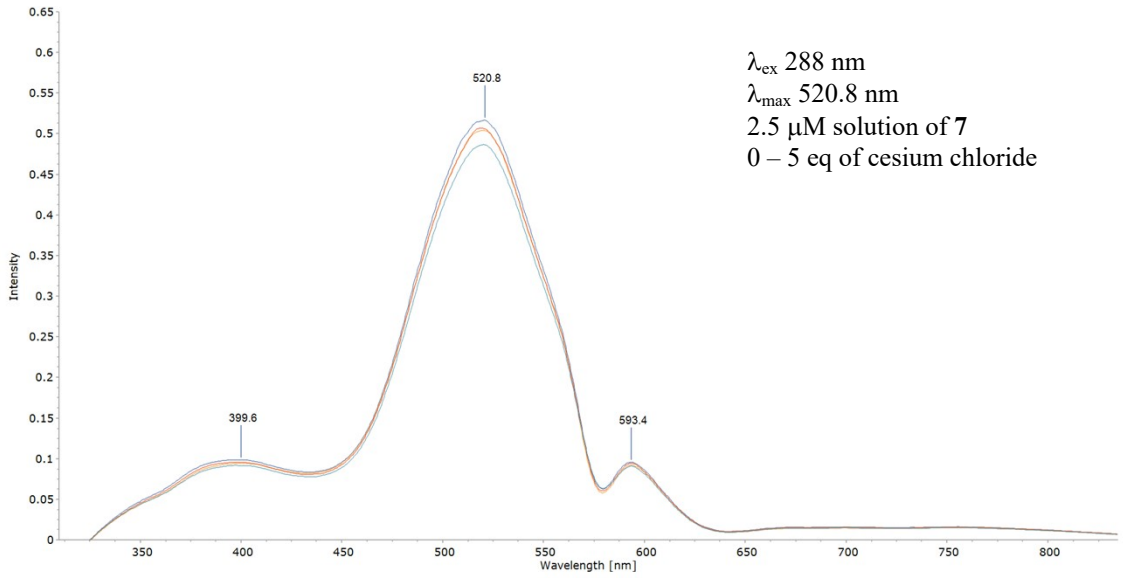


Figure 3. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of cesium chloride (0 – 5 equivalents).

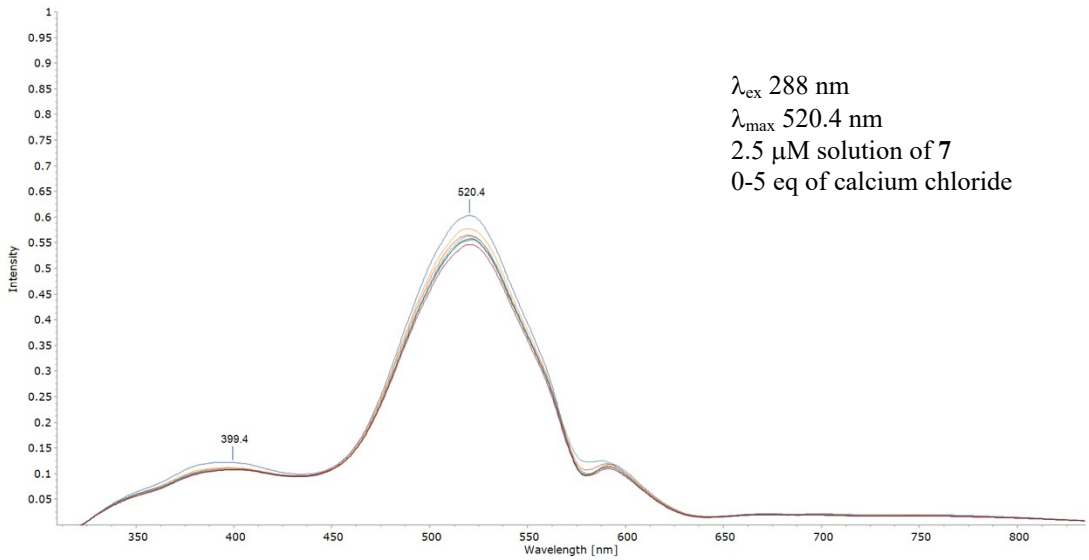


Figure 4. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of calcium chloride (0 – 5 equivalents).

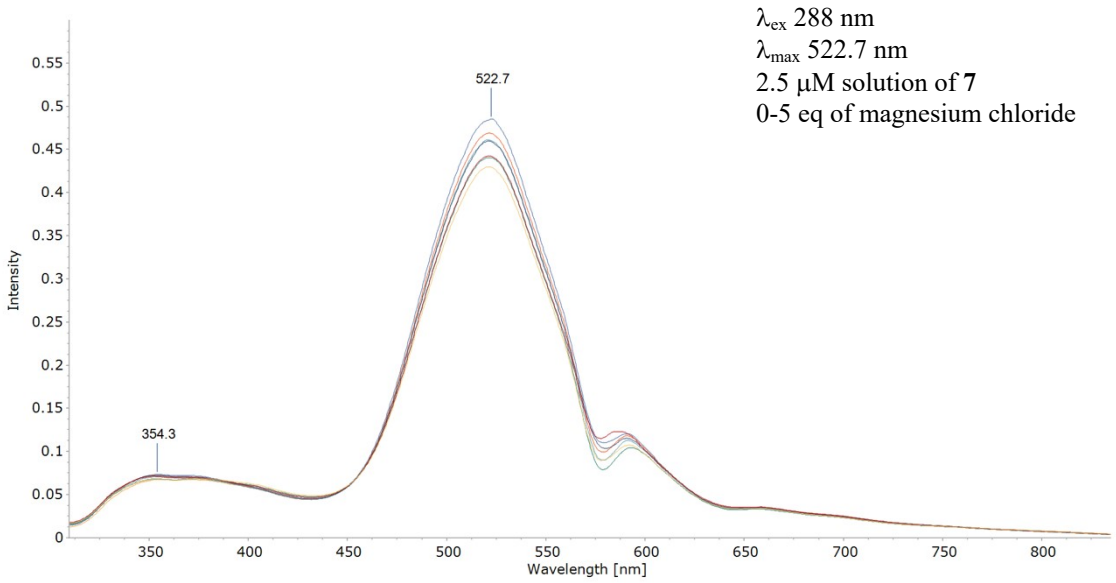


Figure 5. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of magnesium chloride (0 – 5 equivalents).

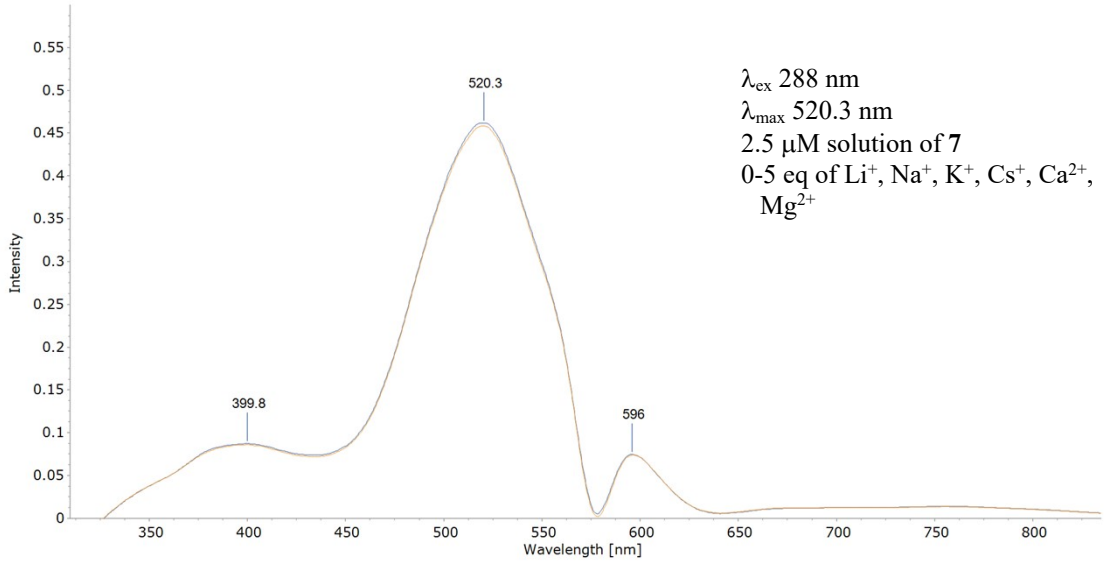


Figure 6. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of a mixture of Group 1 and 2 salts (0 – 5 equivalents).

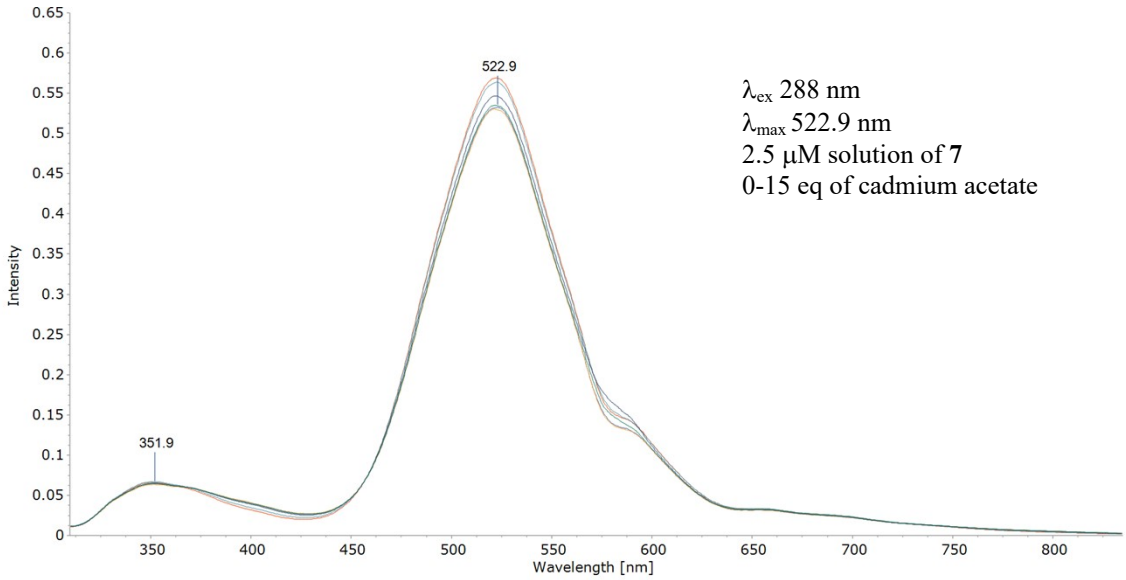


Figure 7. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of cadmium acetate (0 – 15 equivalents).

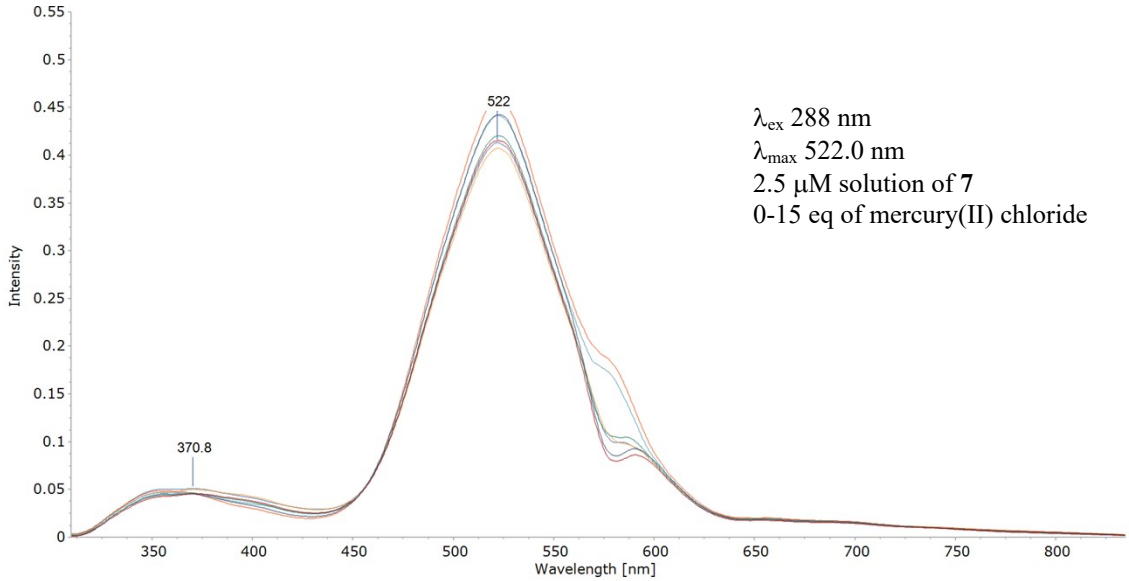


Figure 8. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of mercury(II) chloride (0 – 15 equivalents).

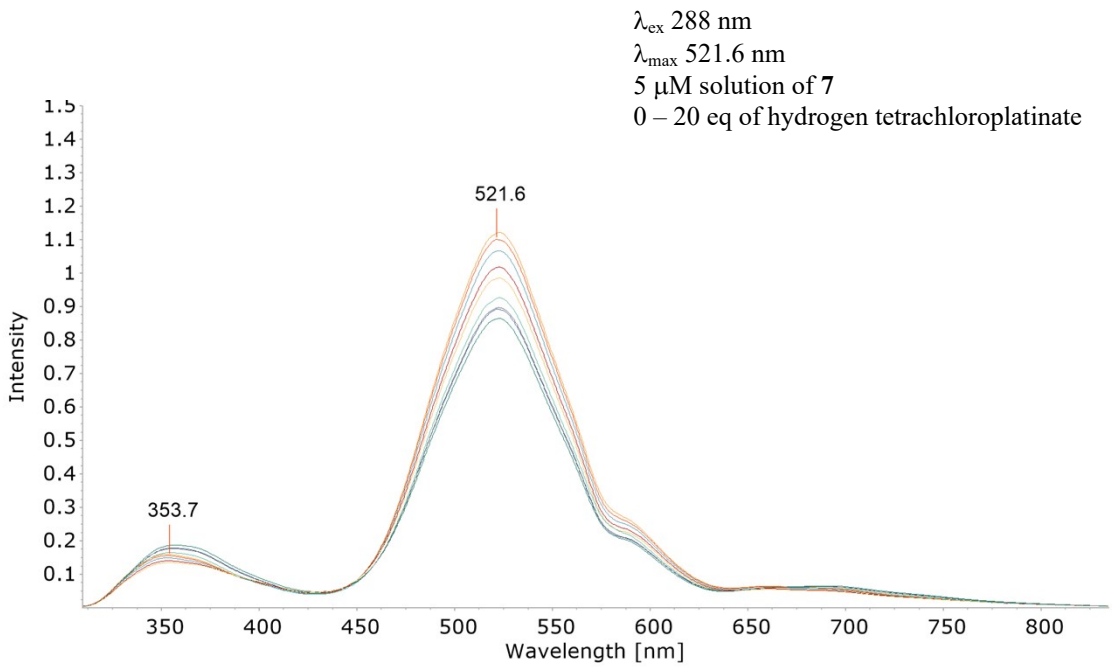


Figure 9. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 5 µM, methanol) with increasing equivalents of hydrogen tetrachloroplatinate (0 – 20 equivalents).

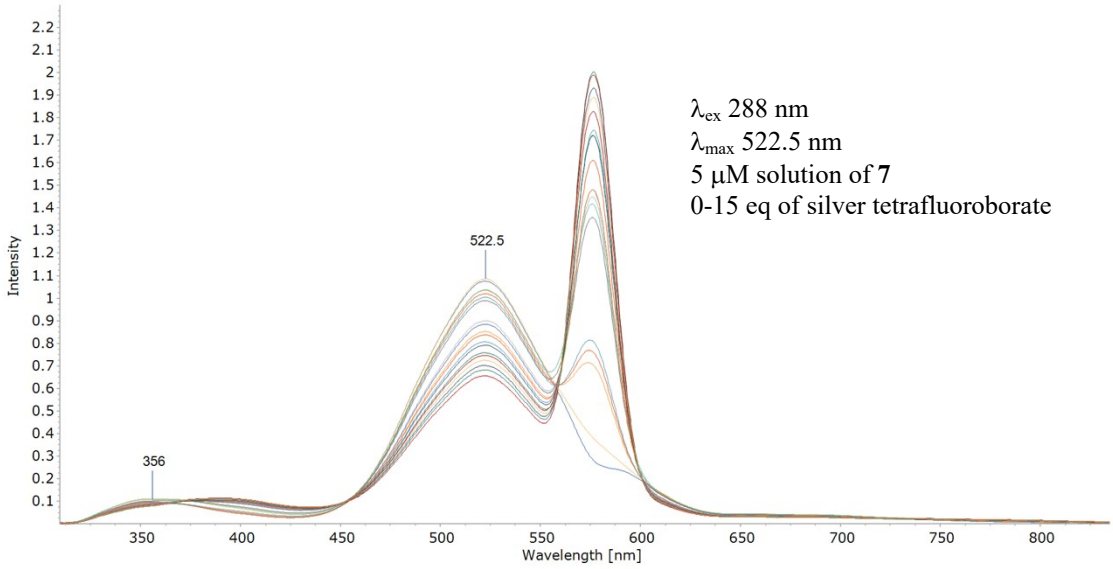


Figure 10. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 5 µM, methanol) with increasing equivalents of silver tetrafluoroborate (0 – 15 equivalents).

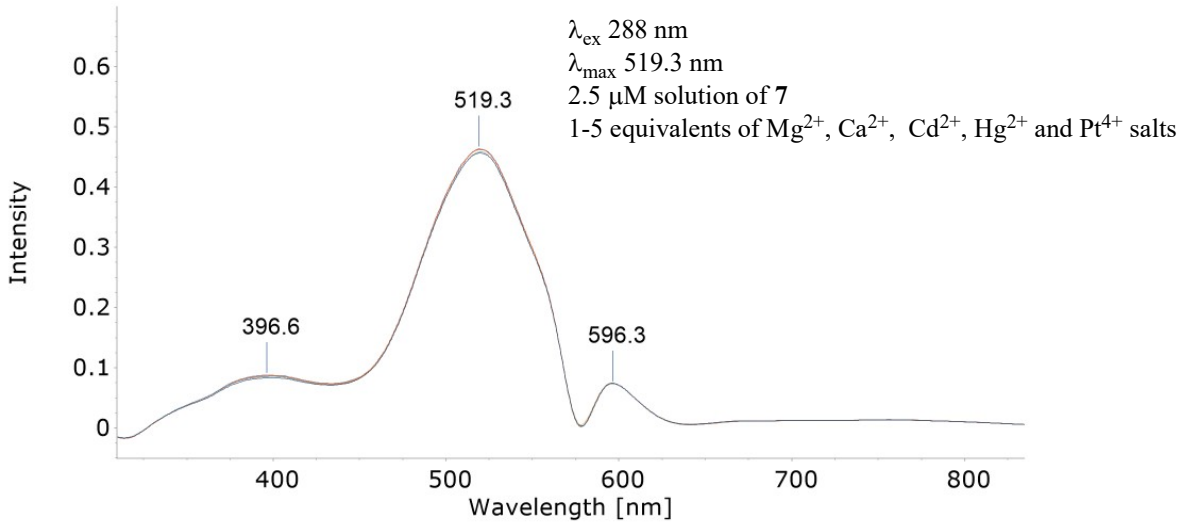


Figure 11. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 5 μM, methanol) with increasing equivalents of Mg^{2+}, Ca^{2+}, Pt^{4+}, Cd^{2+} and Hg^{2+} salts (1 – 5 equivalents).

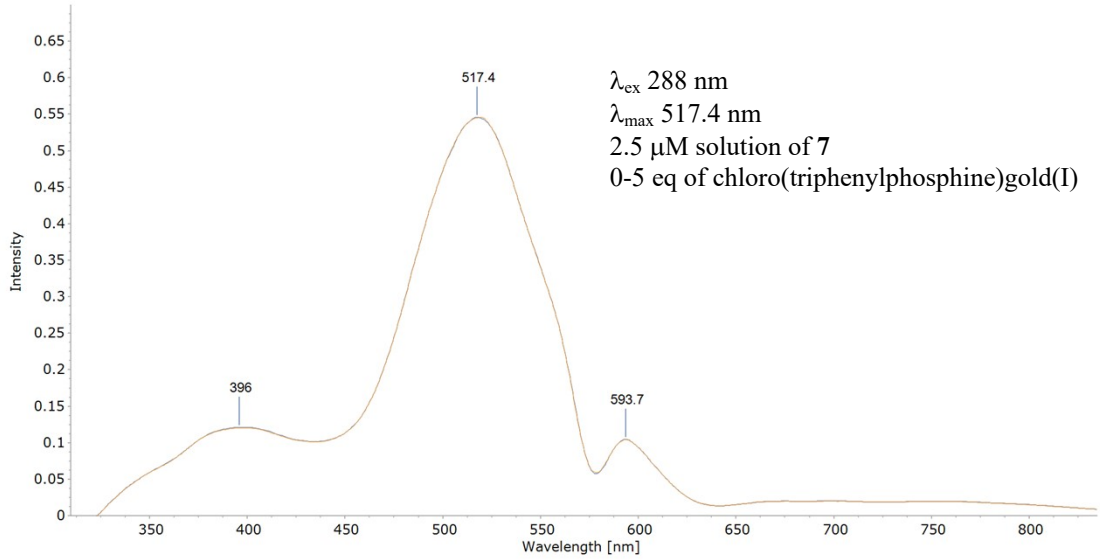


Figure 12. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of chloro(triphenylphosphine)gold(I) (0 – 5 equivalents).

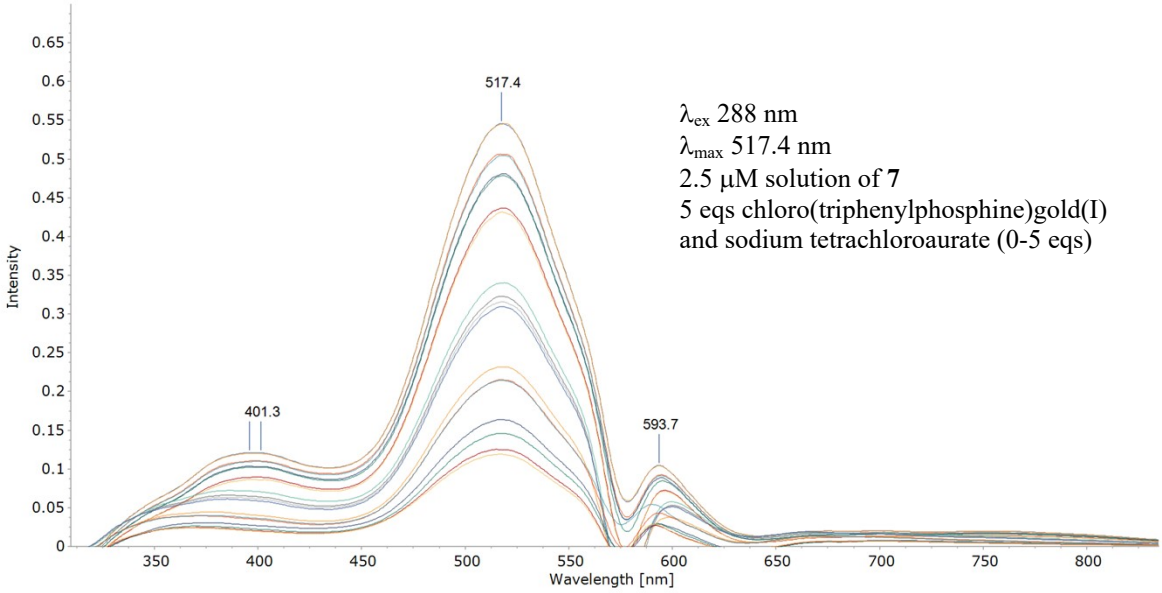


Figure 13. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 µM, methanol) with increasing equivalents of chloro(triphenylphosphine)gold(I) (5 equivalents) and sodium tetrachloroaurate (0 – 5 equivalents).

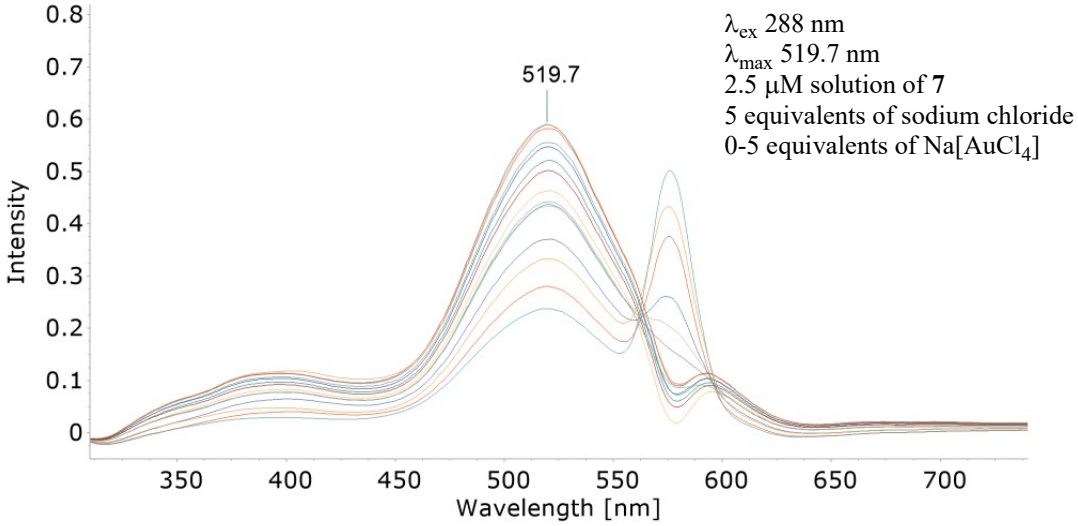


Figure 14. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 µM, methanol) with sodium chloride (5 equivalents) and subsequent addition of 1-5 equivalents of sodium tetrachloroaurate.

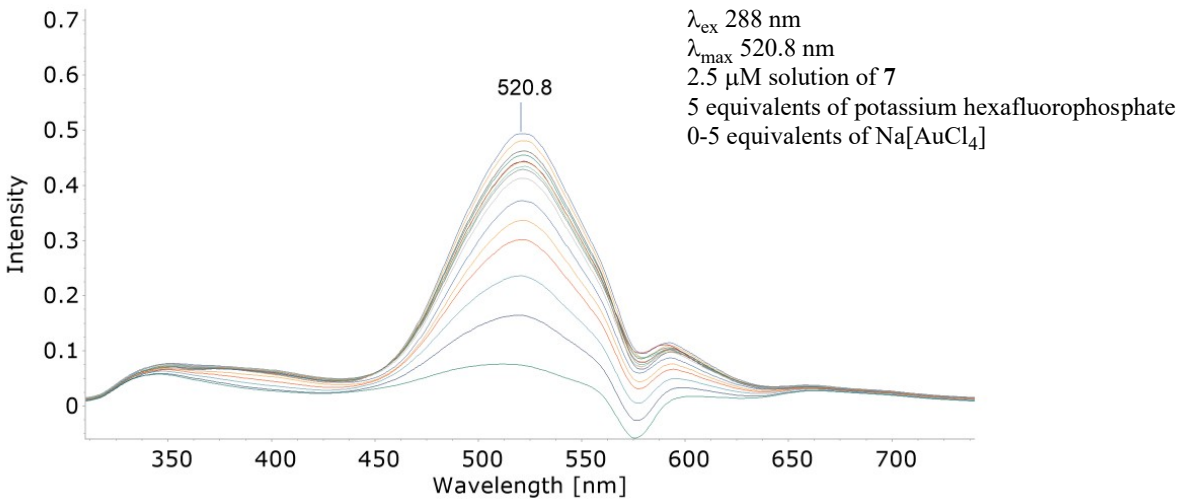


Figure 15. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 µM, methanol) with potassium hexafluorophosphate (5 equivalents) and subsequent addition of 0-5 equivalents of sodium tetrachloroaurate.

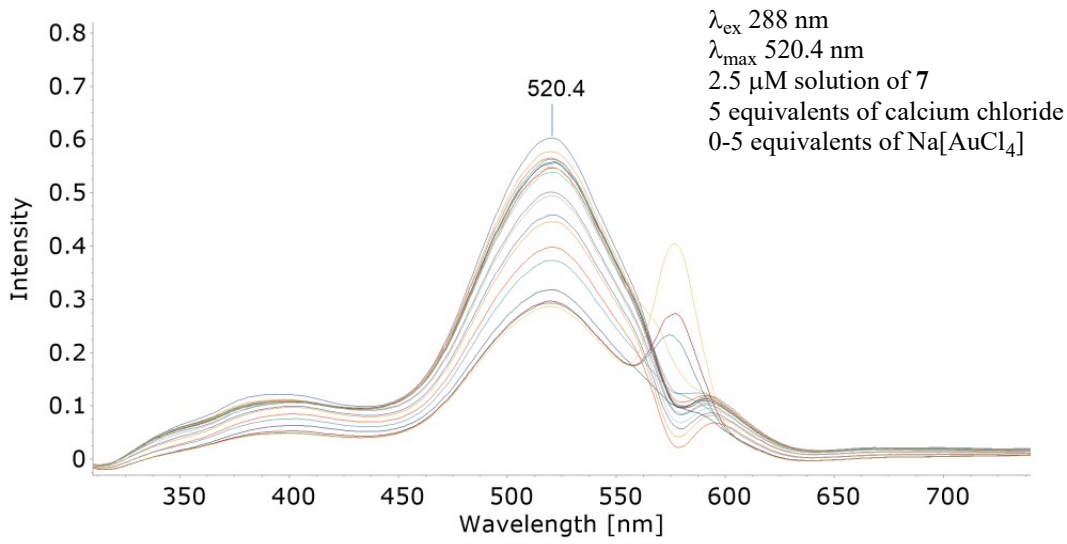


Figure 16. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 µM, methanol) with calcium chloride (5 equivalents) and subsequent addition of 0-5 equivalents of sodium tetrachloroaurate

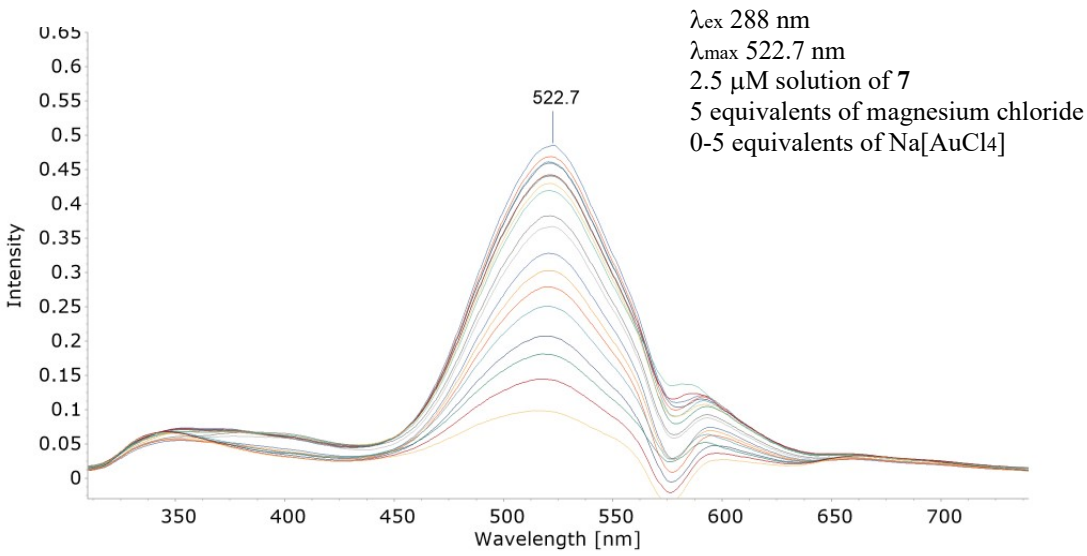


Figure 17. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 µM, methanol) with magnesium chloride (5 equivalents) and subsequent addition of 0-5 equivalents of sodium tetrachloroaurate.

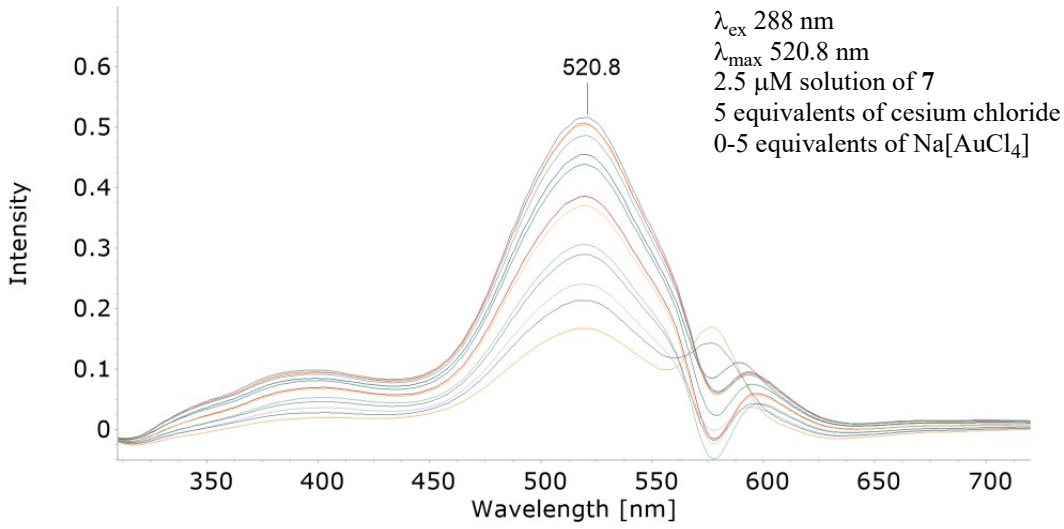


Figure 18. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 µM, methanol) with cesium chloride (5 equivalents) and subsequent addition of 1-5 equivalents of sodium tetrachloroaurate.

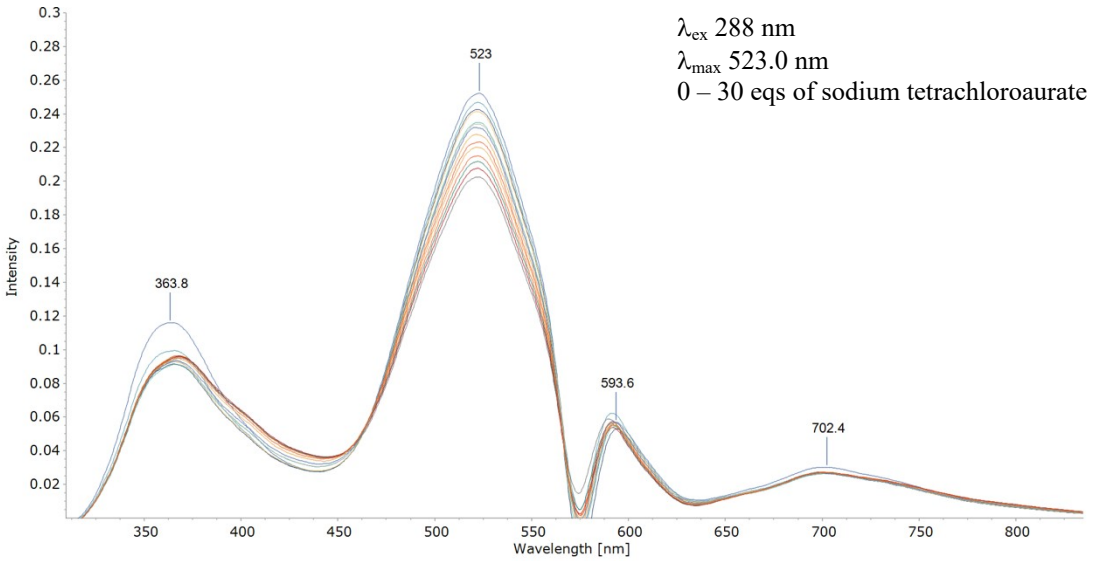


Figure 19. Fluorescent spectrum of alkyne-hydrogenated **7** (λ_{ex} 288 nm, 2 μM, methanol) with increasing equivalents of sodium tetrachloroaurate (0 – 30 equivalents).

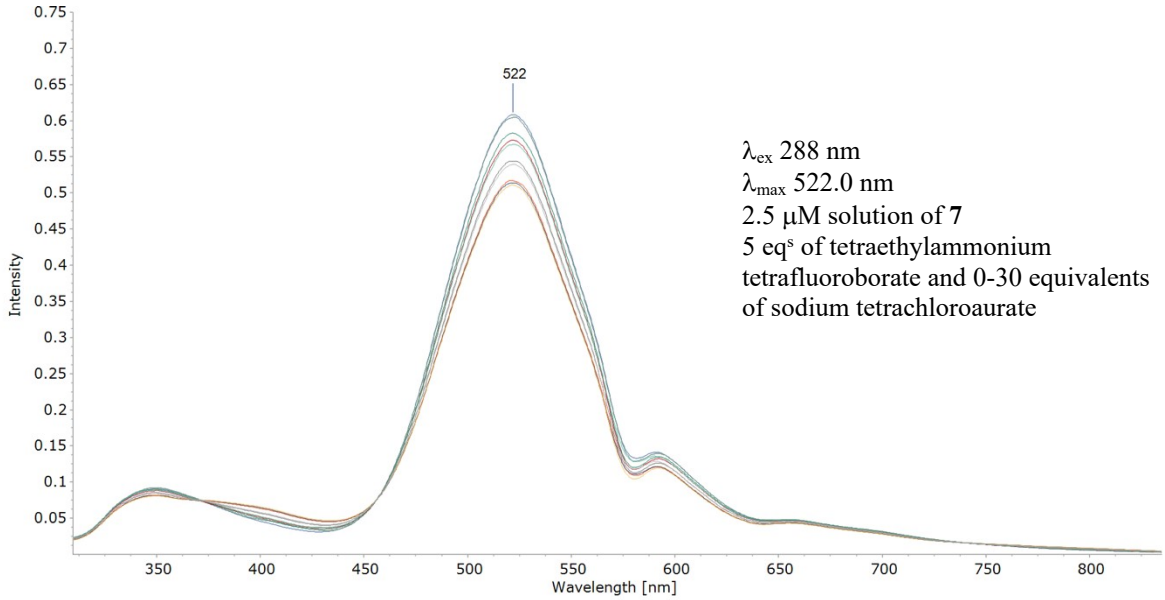


Figure 20. Fluorescent spectrum of **7** (λ_{ex} 288 nm, 2.5 μM, methanol) with tetraethylammonium tetrafluoroborate (5 equivalents) and increasing equivalents of sodium tetrachloroaurate (0 – 30 equivalents).

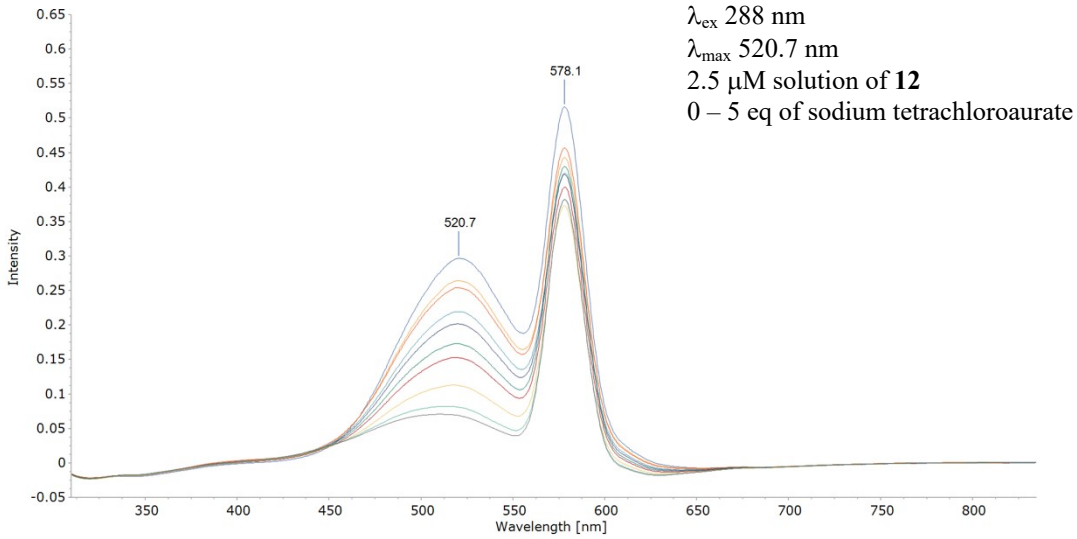


Figure 21. Fluorescent spectrum of *para*-nitrophenylacetylene derived **12** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of sodium tetrachloroaurate (0 – 5 equivalents).

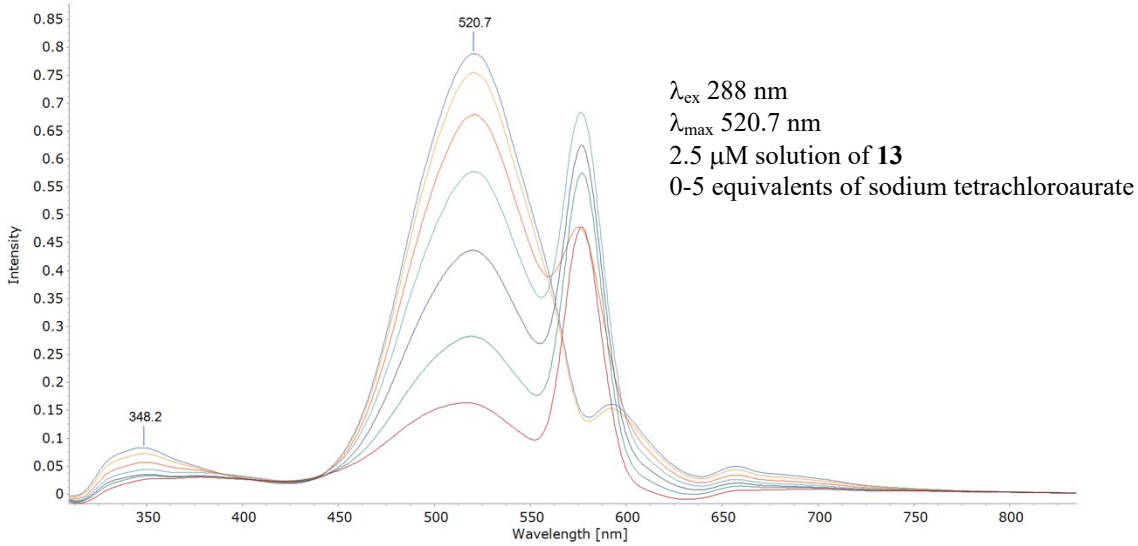


Figure 22. Fluorescent spectrum of *para*-methoxyphenyl-derived **13** (λ_{ex} 288 nm, 2.5 μM, methanol) with increasing equivalents of sodium tetrachloroaurate (0 – 5 equivalents).

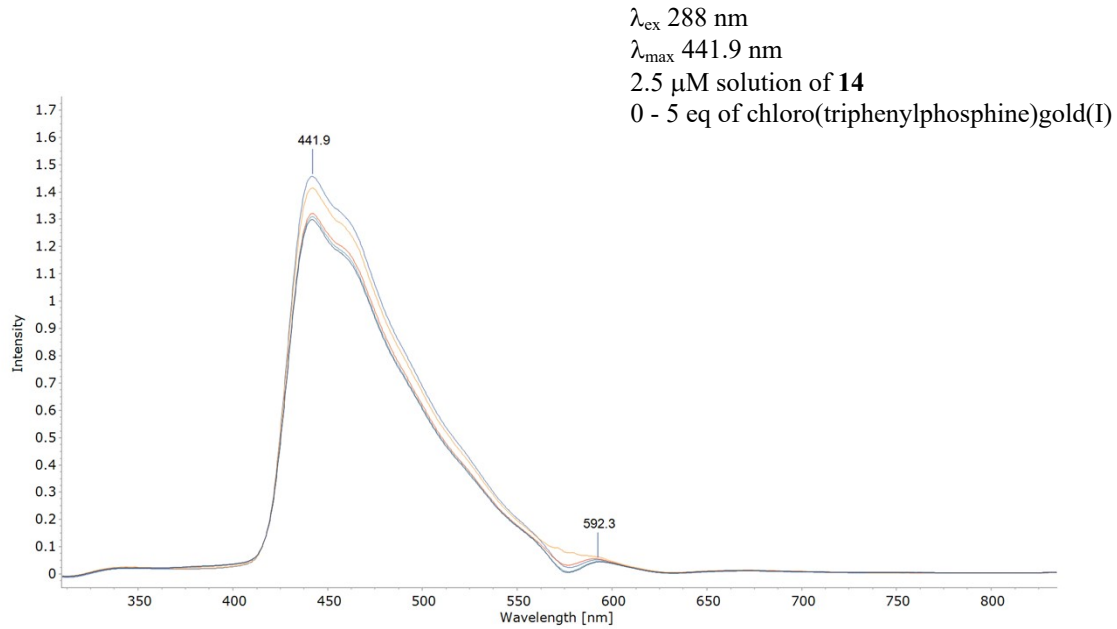


Figure 23. Fluorescent spectrum of 9-(4-ethynylphenyl)anthracene-derived **14** (λ_{ex} 288 nm, 2.5 µM, methanol) with increasing equivalents of chloro(triphenylphosphine)gold(I) (0 – 5 equivalents).

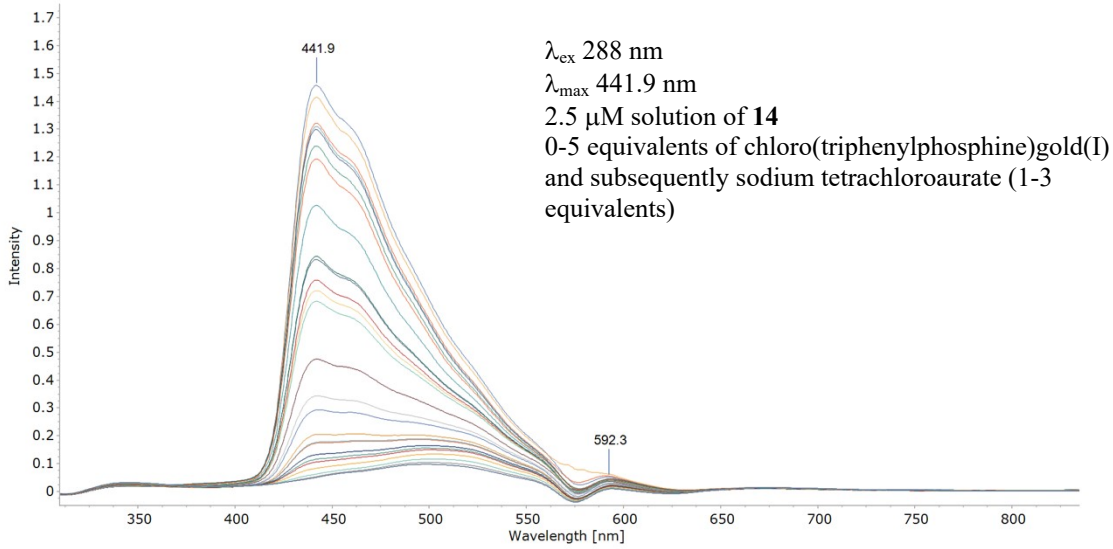


Figure 24. Fluorescent spectrum of anthracene derived **14** (λ_{ex} 288 nm, 2.5 µM, methanol) with increasing equivalents of chloro(triphenylphosphine)gold(I) (0 – 5 equivalents) with subsequent addition of sodium tetrachloroaurate (1-3 equivalents)

Synthesis of 7: 1-[4-[3-[[5-(dimethylamino)naphthalen-1-yl]sulfonylamino]phenyl]phenyl]-3-[[17-[[[4-(2-phenylethynyl)phenyl]carbamoylamino]methyl]-25,26,27,28-tetra(propan-2-yloxy)-5-pentacyclo [19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(25),3,5,7(28),9(27),10,12,15(26),16,18,21,23-dodecaenyl]methyl]urea

To a solution of **4**[1] (25 mg, 0.022 mmol) in anhydrous *N,N*-dimethylformamide (0.5 mL) was added CuI (1.2 mg, 20 mol%), $PdCl_2(PPh_3)_2$ (1 mg, 7 mol%), tri-*tert*-butylphosphine (8 µL of 1M solution in toluene, 20 mol%) and dry piperidine (30 µL, 10 eq^n). To this was added a solution of phenylacetylene (2.4 µL, 0.023 mmol) in anhydrous *N,N*-dimethylformamide (100 µL) over 4 hours *via* a syringe pump. The reaction mixture was stirred at room temperature for an additional 15 hours under argon. After which TLC analysis (diethyl ether) indicated consumption of **4**. The reaction mixture was diluted with ethyl acetate (10 mL), washed successively with water (5 x 5 mL), dilute sodium bicarbonate (1 x 5 mL) and brine. The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. The residue was re-dissolved in dichloromethane (1 mL) and filtered through a pad of silica gel (eluting with diethyl ether) affording **5**. This was used 'as is' in the next step. 3-(Dansylamino)-phenylboronic acid **6** (15 mg, 0.04 mmol), $PdCl_2(PPh_3)_2$ (0.8 mg, 5 mol%), tri-*tert*-butylphosphine (5 µL of 1M solution in toluene, 10 mol%) and anhydrous potassium carbonate (9 mg, 0.066 mmol) was added to a solution of **5** in anhydrous *N,N*-dimethylformamide (250 µL) contained within a Biotage microwave vial (200-500 µL capacity). The reaction solvent/tube was purged with argon and heated (after sealing with an aluminium crimp cap with a PTFE lined rubber seal) in the microwave synthesiser at 100 °C for 30 min. After cooling to room temperature, the reaction was diluted with ethyl acetate (10 mL) and washed with water (5 x 5 mL). The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash chromatography (2:1 hexanes-diethyl ether) afforded **7** as an amorphous yellow solid (10.2 mg, 35% from **4**). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.56 (s, 1H), 8.42 (s, 1H), 8.16 (d, 1H, *J* 6.81 Hz), 7.52-7.34 (m, 5H), 7.30-7.27 (m, 3H), 7.11 (d, 4H, *J* 7.98 Hz), 7.02-6.92 (m, 10H), 6.82 (m, 4H), 6.12 (s, 4H), 5.89 (m, 2H), 4.40 (d, 4H, *J* 12.90 Hz), 3.99 (t, 4H, *J* 6.58 Hz), 3.78 (d, 4H, *J* 11.38 Hz), 3.61 (t, 4H, *J* 6.26 Hz), 3.09 (d, 4H, *J* 12.90 Hz), 2.85 (s, 6H), 2.02-1.84 (m, 8H), 1.05 (t, 6H, *J* 7.22 Hz), 0.86 (t, 6H, *J* 7.20 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 161.3, 157.8, 157.2, 154.8, 152.2, 141.9, 139.8, 139.0 137.2, 136.7, 134.5, 133.7, 132.6, 132.5, 132.2, 131.7, 131.0, 130.5, 129.9, 129.7, 129.0, 128.6, 128.2, 127.5, 125.4, 123.7, 123.4, 122.2, 120.3, 120.0, 119.7, 118.9, 116.9, 115.5, 89.9, 88.7, 77.4, 76.7, 45.5, 42.5, 31.0, 23.6, 23.0, 10.8, 9.9 ppm; FT-IR (neat) 2965, 2928, 2155, 1732, 1658, 1463, 1253, 1014 cm^{-1}; HRMS (ES): calcd. for $C_{82}H_{85}N_6O_8S$ [M + H$^+$] 1313.6144; found 1313.6150

Synthesis of 8: 1-[(4-butoxyphenyl)methyl]-3-[4-[3-[[5-(dimethylamino)naphthalen-1-yl] sulfonylamino]phenyl]phenyl]urea

Part A. Trifluoroacetic acid (950 mg, 8.4 mmol) and triethylsilane (1.7 mL, 11.2 mmol) was added to a mixture of 4-butoxybenzaldehyde (500 mg, 2.8 mmol) and 4-iodophenylurea (800 mg, 3.1 mmol) in anhydrous toluene (10 mL). The suspension was stirred at room temperature for an additional 15 hours under nitrogen. The reaction was diluted with ethyl acetate (50 mL) and quenched by addition of dilute sodium bicarbonate solution (20 mL). After stirring for 15 min, a white precipitate separated which was filtered, washed with ethyl acetate (10 mL) and water afforded 1-(4-butoxybenzyl)-3-(4-iodophenyl)urea as an amorphous white solid (590 mg, 50%) which was used directly in the next step. ^{1}H NMR (d_6-acetone, 400 MHz) δ 8.02 (s, 1H), 7.32 (d, 2H, *J* 8.9 Hz), 7.13 (d, 2H, *J* 8.8 Hz), 7.03 (d, 2H, *J* 8.7 Hz), 6.64 (d, 2H, *J* 8.7 Hz), 6.03 (s, 2H), 4.09 (d, 2H, *J* 4.9 Hz), 3.74 (t, 2H *J* 6.5 Hz), 1.51 (dt, 2H, *J* 14.4, 6.5 Hz), 1.26 (dd, 2H, *J* 15.1, 7.5 Hz), 0.73 (t, 3H, *J* 7.4 Hz) ppm; ^{13}C NMR (d_6-acetone, 75 MHz) δ 158.5, 155.4, 140.9, 137.6, 132.2, 128.8, 128.7, 120.4, 120.4, 114.4, 114.3, 83.1, 67.4, 42.8, 31.2, 18.9, 13.2 ppm; FT-IR (neat) 3012, 2928, 1715, 1685, 1640, 1445, 1217, 1011, 855 cm^{-1}; HRMS (ES): calcd. for $C_{18}H_{21}N_2O_2I$ [M] 424.0648; found 424.0645.

Part B. 3-(Dansylamino)-phenylboronic acid (25 mg, 0.067 mmol), $PdCl_2(PPh_3)_2$ (0.3 mg, 5 mol%), tri-*tert*-butylphosphine (5 μL of 1M solution in toluene, 10 mol%) and anhydrous potassium carbonate (28 mg, 0.2 mmol) were added to a solution of the product from Part A above (34 mg, 0.08 mmol) in anhydrous *N,N*-dimethylformamide (500 μL) in a Biotage microwave vial (200-500 μL capacity). The reaction solution/tube was purged with argon and heated (after sealing with an aluminium crimp cap with a PTFE lined rubber seal) in the microwave synthesiser at 110 °C for 120 min. The reaction mixture was diluted with ethyl acetate (10 mL) and washed with water (5 x 5 mL). The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash chromatography on silica gel (hexanes-ethyl acetate, 40%) afforded **8** as an amorphous pale yellow solid (16 mg, 32%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.37 (t, 2H, *J* 8.2 Hz), 8.09 (d, 1H, *J* 7.3 Hz), 7.40 (t, 1H, *J* 8.0 Hz), 7.28 (t, 1H, *J* 7.9 Hz), 7.14 – 7.01 (m, 6H), 6.95 (dd, 4H, *J* 14.2, 6.6 Hz), 6.82 (d, 1H, *J* 7.0 Hz), 6.67 (d, 2H, *J* 8.5 Hz), 5.71 (s, 1H), 4.19 (d, 2H, *J* 5.2 Hz), 3.76 (t, 2H, *J* 6.5 Hz), 2.73 (s, 6H), 1.70 – 1.52 (m, 2H), 1.41 – 1.27 (m, 2H), 0.86 (t, *J* 7.4 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.6, 156.2, 141.5, 138.6, 137.2, 134.7, 130.7, 130.5, 129.8, 129.6, 128.9, 128.7, 127.5, 123.4, 120.3, 119.7, 119.6, 114.7, 67.9, 45.6, 43.9, 29.9, 19.4, 14.0 ppm; FT-IR (neat) 2918, 2955, 1698, 1673, 1646, 1452, 1218, 1012 cm^{-1}; HRMS (ES): calcd. for $C_{36}H_{38}N_4O_4S$ [M] 622.2614; found 622.2620.

Synthesis of 12: 1-[4-[3-[[5-(dimethylamino)naphthalen-1-yl]sulfonylamino]phenyl]phenyl]-3-[[17-[[[4-[2-(4-nitrophenyl)ethynyl]phenyl]carbamoylamino]methyl]-25,26,27,28-tetra(propan-2-yloxy)-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(25),3,5,7(28),9(27),10,12,15(26),16,18,21,23-dodecaenyl]methyl]urea

Part A. Under an argon atmosphere, a solution of **4**[1] (40 mg, 0.035 mmol) in anhydrous *N,N*-dimethylformamide (2 mL) was charged with CuI (1.4 mg, 20 mol%), $PdCl_2$ (1.3 mg, 5 mol%), PPh_3 (4 mg, 50 mol%) and dry piperidine (100 μL). To this was added a solution of 4-nitrophenylacetylene (6.8 mg, 0.046 mmol) in anhydrous *N,N*-dimethylformamide (100 μL) over 1 hour *via* syringe pump. The reaction mixture was stirred at room temperature for an additional 15 hours under argon. Subsequent TLC analysis (diethyl ether) indicated complete consumption of starting material **3**. The reaction mixture was diluted with ethyl acetate (10 mL), washed successively with water (5 x 5 mL), dilute sodium bicarbonate (1 x 5 mL) and brine. The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash column chromatography (DCM-MeOH, gradient 0.2-2%) afforded the desired product as an amorphous white solid (30 mg, 73%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.23 (d, 2H, *J* 8.9 Hz), 8.04 (bs, 2H), 7.75 (bs, 1H), 7.68 (d, 2H, *J* 8.9 Hz), 7.48 (d, 2H, *J* 8.8 Hz), 7.35-7.22 (m, 4H), 7.02-6.85 (m, 4H), 6.72 (m, 2H, *J* 9.2 Hz), 6.12 (bs, 4H, *J* 6.4 Hz), 4.4 (d, 4H, *J* 13.0 Hz), 3.93 (m, 4H), 3.68 (bd, 4H), 3.56 (t, 4H, *J* 6.1 Hz), 3.07 (d, 4H, *J* 13.0 Hz), 1.93-1.76 (m, 8H), 1.00 (t, 6H, *J* 7.3 Hz), 0.81 (t, 6H, *J* 6.7 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 157.6, 156.9, 156.8, 154.6, 146.8, 140.5, 137.7, 136.6, 133.6, 132.8, 132.2, 132.1, 132.0, 130.8, 128.95, 128.85, 125.1, 123.8, 122.04, 122.0, 119.35, 115.5, 95.5, 87.1, 85.45 77.3, 76.6, 42.4, 31.1, 23.7, 23.1, 11.0, 10.0 ppm; FT-IR (neat) 2932, 2919, 2134, 1708, 1668, 1212, 1038 cm^{-1}; HRMS (ES): calcd. for $C_{64}H_{66}N_5O_8I$ [M] 1159.3956; found 1159.3952.

Part B. Under an argon atmosphere, 3-(dansylamino)-phenylboronic acid **6** (16.6 mg, 0.044 mmol), $PdCl_2$ (0.38 mg, 10 mol%), PPh_3 (1.2 mg, 20 mol%) and dry potassium carbonate (9.1 mg, 0.066 mmol) was added to the product from Part A above in anhydrous *N,N*-dimethylformamide (500 μL) contained within a Biotage microwave vial (200-500 μL capacity). The reaction solution/tube was purged with argon and heated (after sealing with an aluminium crimp cap with a PTFE lined rubber seal) in the microwave synthesiser at 80 °C for 60 min. The reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (5 x 5 mL). The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash chromatography (DCM / MeOH, gradient 0.1-1.2%) afforded **12** as an amorphous yellow solid (11.5 mg, 39%, overall yield 56%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.41 (bs, 1H), 8.31 (bs, 1H), 8.12 (d, 2H, *J* 8.1 Hz), 8.04 (d, 2H, *J* 8.5 Hz), 7.57 (dd, 4H, *J* 12.0, 7.9 Hz), 7.54-7.45 (m, 4H), 7.41-7.35 (m, 5H), 7.11-7.08 (m, 6H), 7.02-6.81 (m, 6H), 6.78 (t, 2H, *J* 7.1 Hz), 6.07 (d, 4H, *J* 5.5 Hz), 4.36 (d, 4H, *J* 13.1 Hz), 3.95 (t, 4H, *J* 6.8 Hz), 3.81 (bs, 2H), 3.74 (bs, 2H), 3.57 (t, 4H, *J* 6.5 Hz), 3.05 (dd, 4H, *J* 13.1, 6.1 Hz), 2.78 (s, 6H), 2.01-1.76 (m, 8H), 1.01 (t, 6H, *J* 6.5 Hz), 0.82 (t, 6H, *J* 7.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.5, 156.8, 156.6, 154.4, 151.8, 141.5, 139.4, 138.7, 136.8, 136.5, 134.0, 133.3, 132.2, 131.9, 130.8, 130.2, 129.6, 128.7, 128.3, 127.9, 127.2, 125.1, 123.0, 121.9, 120.0, 119.7, 119.4, 118.5, 115.1, 89.6, 88.4, 77.1, 76.4, 45.1, 40.5, 30.7, 23.3, 22.7, 10.5, 9.6 ppm; FT-IR (neat) 2971, 2921, 2144, 1712, 1668, 1455, 1222, 1012 cm^{-1}; HRMS (ESI): calcd. for $C_{82}H_{84}N_7O_{10}S$ [M + H^+] 1358.5995; found 1358.6000

Synthesis of 13: 1-[4-[3-[[5-(dimethylamino)naphthalen-1-yl]sulfonylamino]phenyl]phenyl]-3-[[17-[[[4-[2-(4-methoxyphenyl)ethynyl]phenyl]carbamoylamino]methyl]-25,26,27,28-tetra(propan-2-yloxy)-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(25),3,5,7(28),9(27),10,12,15(26),16,18,21,23-dodecaenyl]methyl]urea

Part A. Under an argon atmosphere, a solution of **4** (45 mg, 0.04 mmol) in anhydrous *N,N*-dimethylformamide (2 mL) was added CuI (1.4 mg, 20 mol%), $PdCl_2$ (1.3 mg, 5 mol%), PPh_3 (4 mg, 50 mol%) and dry piperidine (100 µL). To this was added a solution of 4-methoxyphenylacetylene (6.3 mg, 0.048 mmol) in anhydrous *N,N*-dimethylformamide (100 µL) over 1 hour *via* a syringe pump. The reaction mixture was stirred at room temperature for an additional 15 hours under argon. TLC analysis (diethyl ether) indicated complete consumption of starting material **3**. The reaction mixture was diluted with ethyl acetate (10 mL) and washed successively with water (5 x 5 mL) and brine. The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash column chromatography (DCM-MeOH, gradient 0.2-2%) afforded the desired product as an amorphous solid (35 mg, 74%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.0 (bs, 2H), 7.53 (d, 2H), 7.25 (d, 2H, *J* 8.5 Hz), 6.99-6.88 (m, 4H), 6.81-6.68 (m, 4H), 6.73 (t, 2H, *J* 11.1 Hz), 6.35 (bs, 2H), 6.05 (s, 4H), 4.43 (d, 4H, *J* 12.9 Hz), 3.93 (t, 4H, *J* 6.3 Hz), 3.74 (2s, 4H), 3.7 (bs. 3H), 3.65 (m, 4H), 3.08 (d, 4H, *J* 12.9 Hz), 2.00-1.78 (m, 8H), 1.01 (t, 6H, *J* 7.4 Hz), 0.81 (t, 6H, *J* 7.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.6, 157.7, 157.0, 156.3, 154.6, 139.1, 139.0, 137.7, 136.6, 133.5, 133.15, 133.0, 132.2, 131.9, 129.4, 128.9, 125.13, 125.1, 122.0, 121.85, 119.7, 117.5, 115.8, 114.4, 114.1, 88.7, 88.3, 85.3, 77.3, 76.6, 55.4, 42.4, 31.0, 23.6, 23.1, 10.95, 10.0 ppm; FT-IR (neat) 2965, 2936, 2142, 1716, 1655, 1446, 1210, 1022 cm^{-1}; HRMS (ES): calcd. for $C_{65}H_{69}N_4O_7I$ [M] 1144.4211; found 1144.4214.

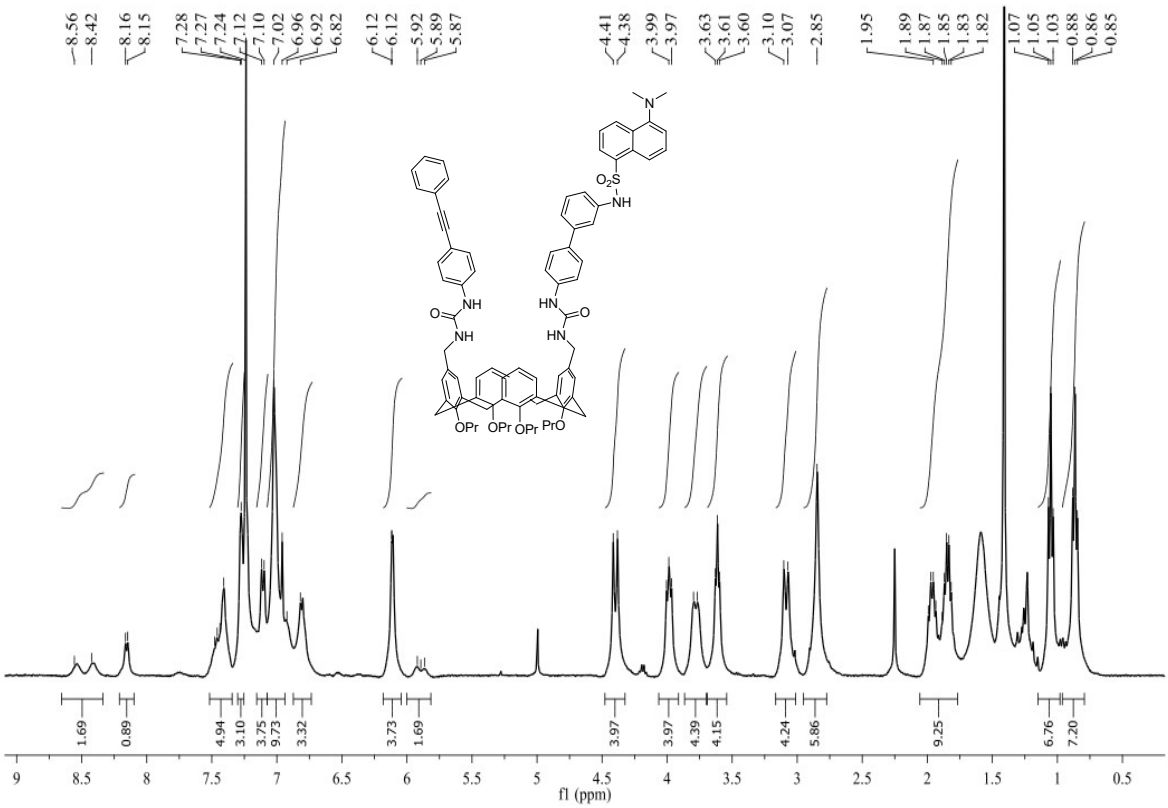
Part B. Under an argon atmosphere, 3-(dansylamino)-phenylboronic acid (22 mg, 0.06 mmol), $PdCl_2$ (0.5 mg, 11 mol%), PPh_3 (1.3 mg, 20 mol%) and dry potassium carbonate (12.5 mg, 0.066 mmol) was added to a solution of the product from Part A above in anhydrous *N,N*-dimethylformamide (500 µL) in a Biotage microwave vial (200-500 µL capacity). The reaction mixture was purged with argon and heated (after sealing with aluminium crimp cap with PTFE lined rubber seal) in the microwave synthesiser at 80 °C for 60 min. The reaction mixture was diluted with ethyl acetate (20 mL) and washed with water (5 x 5 mL). The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash chromatography (DCM / MeOH, gradient 0.2-1.5%) afforded **13** (25 mg, 62%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.48 (d, 1H, *J* 8.4 Hz), 8.34 (d, 1H, *J* 8.4 Hz), 8.17 (d, 2H, *J* 7.3 Hz), 7.58-7.29 (m, 8H), 7.22 (d, 1H, *J* 8.6 Hz), 7.15 (d, 2H, *J* 7.8 Hz), 7.11-6.98 (m, 6H), 6.85 (m, 6H), 6.55 (s, 1H), 6.45 (t, 2H, *J* 8.8 Hz), 6.11 (d, 4H, *J* 3.2 Hz), 4.41 (d, 4H, *J* 12.9 Hz), 4.0 (t, 4H, *J* 6.8 Hz), 3.87-3.72 (m, 7H), 3.63 (t, 4H, *J* 6.7 Hz), 3.10 (d, 4H, *J* 12.9 Hz), 2.85 (s, 6H), 2.02-1.82 (m, 8H), 1.06 (t, 6H, *J* 7.4 Hz), 0.88 (t, 6H, *J* 7.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 159.5, 157.6, 156.6, 154.6, 141.7, 139.1, 137.7, 136.5, 134.3, 132.9, 132.2, 130.7, 130.3, 130.0, 129.6, 128.9, 128.5, 127.3, 125.2, 123.3, 122.0, 120.1, 119.6, 118.9, 117.3, 115.4, 113.9, 112.5, 112.2, 108.2, 95.1, 88.5, 77.8, 77.2, 55.2, 45.3, 42.4, 30.8, 23.3, 22.8, 10.6, 9.7 ppm; FT-IR (neat) 2977, 2931, 2128, 1702, 1674, 1442, 1212, 1018 cm^{-1}; HRMS (ESI): calcd. for $C_{83}H_{87}N_6O_9S$ [M + H$^+$] 1343.6250; found 1343.6255

Synthesis of 14: 1-[4-[2-(4-anthracen-9-ylphenyl)ethynyl]phenyl]-3-[[17-[[[4-[3-[[5-(dimethylamino)naphthalen-1-yl]sulfonylamino]phenyl]phenyl]carbamoylamino]methyl]-25,26,27,28-tetra(propan-2-yloxy)-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(25),3,5,7(28),9(27),10,12,15(26),16,18,21,23-dodecaenyl]methyl]urea

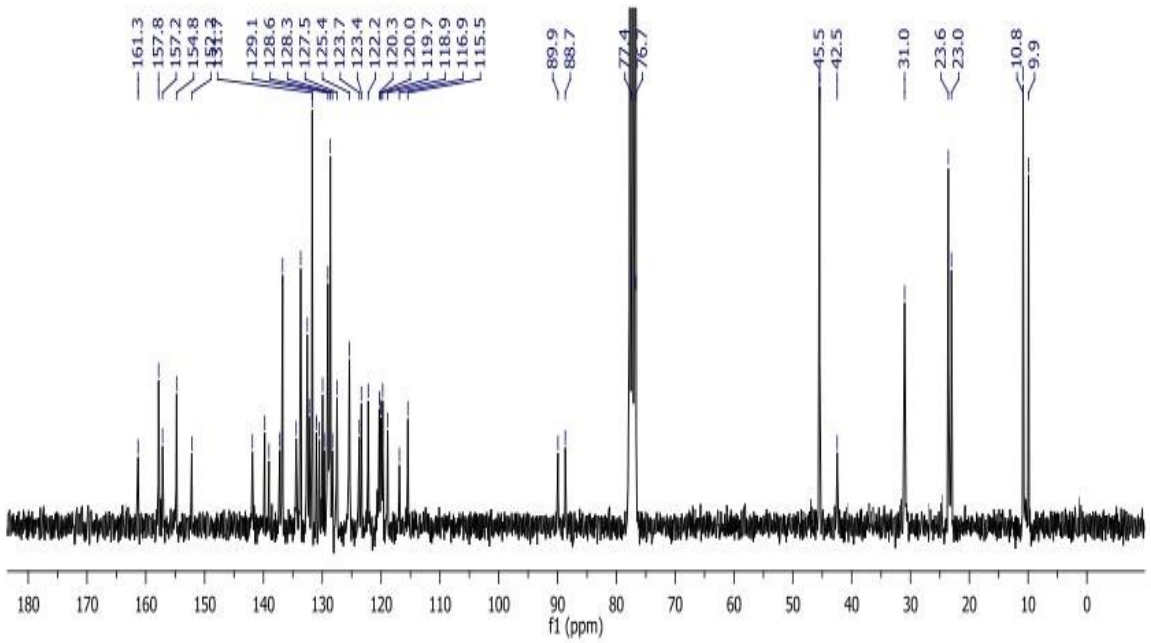
Part A. Under an argon atmosphere, 5-(dimethylamino)-N-(3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)naphthalene-1-sulfonamide (45 mg, 0.1 mmol), (dppf)$PdCl_2$ (7 mg, 10 mol%), and dry cesium fluoride (45 mg, 0.3 mmol) were added to a solution of **4** (95 mg, 0.08 mmol) in anhydrous *N,N*-dimethylformamide (2 mL). The reaction mixture was purged with argon and heated in a Biotage tube (sealed with an alumnium crimp lid) at 60 °C for 18 hours. The reaction mixture was diluted with DCM (20 mL), washed with water (5 x 5 mL), dilute sodium bicarbonate and brine. The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash chromatography (DCM / MeOH, gradient 0.5-2%) afforded the desired product as an amorphous solid (59 mg, 56%). ^{1}H NMR ($CDCl_3$, 300 MHz) δ 8.47 (d, 1H, *J* 8.4 Hz), 8.35 (d, 1H, *J* 8.7 Hz), 8.19 (d, 1H, *J* 7.4 Hz), 7.80 (s, 1H), 7.65 (s, 1H), 7.44-7.37 (m, 2H), 7.21-6.90 (m, 15H), 6.79 (d, 2H, *J* 8.5 Hz), 6.11 (s, 4H), 4.41 (d, 4H, *J* 13.0 Hz), 4.00 (t, 4H, *J* 6.6 Hz), 3.76 (bs, 4H), 3.62 (t, 4H, *J* 6.7 Hz), 3.09 (d, 4H, *J* 13.0 Hz), 2.83 (d, 6H, *J* 4.4 Hz), 2.06-1.78 (m, 8H), 1.07 (t, 6H, *J* 7.4 Hz), 0.89 (t, 6H, *J* 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 157.8, 156.83, 156.8, 156.8, 154.64, 154.6, 139.5, 138.9, 137.9, 136.8, 133.5, 132.6, 131.8, 131.4, 130.0, 128.8, 127.5, 127.1, 126.7, 125.8, 125.1, 125.0 122.3, 122.0, 119.7, 117.8, 117.6, 101.1, 85.9, 85.8, 77.3, 76.6, 42.4, 31.0, 23.6, 23.0, 10.9, 9.9 ppm; FT-IR (neat) 3120, 2945, 2935, 1715, 1684, 1668, 1430, 1211, 988 cm^{-1}; HRMS (ESI): calcd. for $C_{74}H_{79}N_6O_8SI$ [M] 1338.4725; found 1338.4725.

Part B. Under an argon atmosphere, to a solution of the product from Part A (36 mg, 0.027 mmol) in anhydrous *N,N*-dimethylformamide (2 mL) was added CuI (0.3 mg, 6 mol%), (dppf)$PdCl_2$ (1.1 mg, 5 mol%) and dry piperidine (50 µL). To this mixture was added a solution of 9-ethynylanthracene (12 mg, 0.05 mmol) in anhydrous *N,N*-dimethylformamide (100 µL) was added dropwise. The reaction mixture was stirred at room temperature for additional 15 hours under argon after which it was diluted with ethyl acetate (20 mL), washed successively with water (5 x 5 mL) and brine. The organic phase was dried over magnesium sulphate, filtered and the solvent removed under reduced pressure. Purification *via* flash column chromatography (DCM-MeOH, gradient 0.5-2%) afforded **14** as a pale brown waxy solid (23 mg, 58%). ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.51 (d, 1H, *J* 6.6 Hz), 8.38 (s, 1H), 8.34 (d, 1H, *J* 8.5 Hz), 8.21 (d, 1H, *J* 8.5 Hz), 8.05 (d, 1H, *J* 6.6 Hz), 7.99 (d, 4H, *J* 11.1 Hz), 7.51-7.40 (m, 6H), 7.16 (d, 2H, *J* 8.4 Hz),7.12-6.95 (m, 8H), 6.90-6.72 (m, 4H), 6.25 (s, 1H), 6.14 (d, 4H, *J* 4.9 Hz), 4.40 (d, 4H, *J* 13.0 Hz), 3.99 (t, 4H, *J* 5.6 Hz), 3.79 (bs, 4H), 3.62 (t, 4H, *J* 5.9 Hz), 3.09 (d, 4H, *J* 13.0 Hz), 2.73 (s, 6H), 2.02-1.79 (m, 8H), 1.05 (t, 6H, *J* 7.3 Hz), 0.86 (t, 6H, *J* 7.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 160.9, 157.5, 156.7, 154.5, 151.9, 141.4, 139.9, 138.8, 136.5, 134.2, 134.0, 133.4, 132.3, 131.9, 131.1, 130.7, 130.1, 129.6, 129.3, 128.8, 128.6, 127.3, 126.7, 126.5, 125.7, 125.1, 123.5, 123.0, 121.9, 120.2, 119.9, 119.5, 118.5, 117.5, 116.9, 115.2, 101.3, 85.4, 77.2, 76.7, 45.3, 42.5, 40.7, 30.9, 23.5, 22.9, 10.8, 9.9 ppm; FT-IR (neat) 2951, 2922, 2128, 1709, 1664, 1437, 1217, 1011 cm^{-1}; HRMS (ESI): calcd. for $C_{96}H_{93}N_6O_8S$ [M + H] 1489.6770; found 1489.6778.

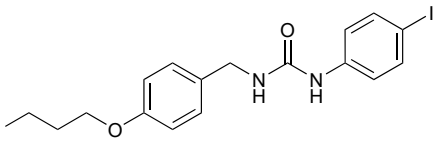
^{1}H-NMR of **7** (400 MHz, $CDCl_3$)



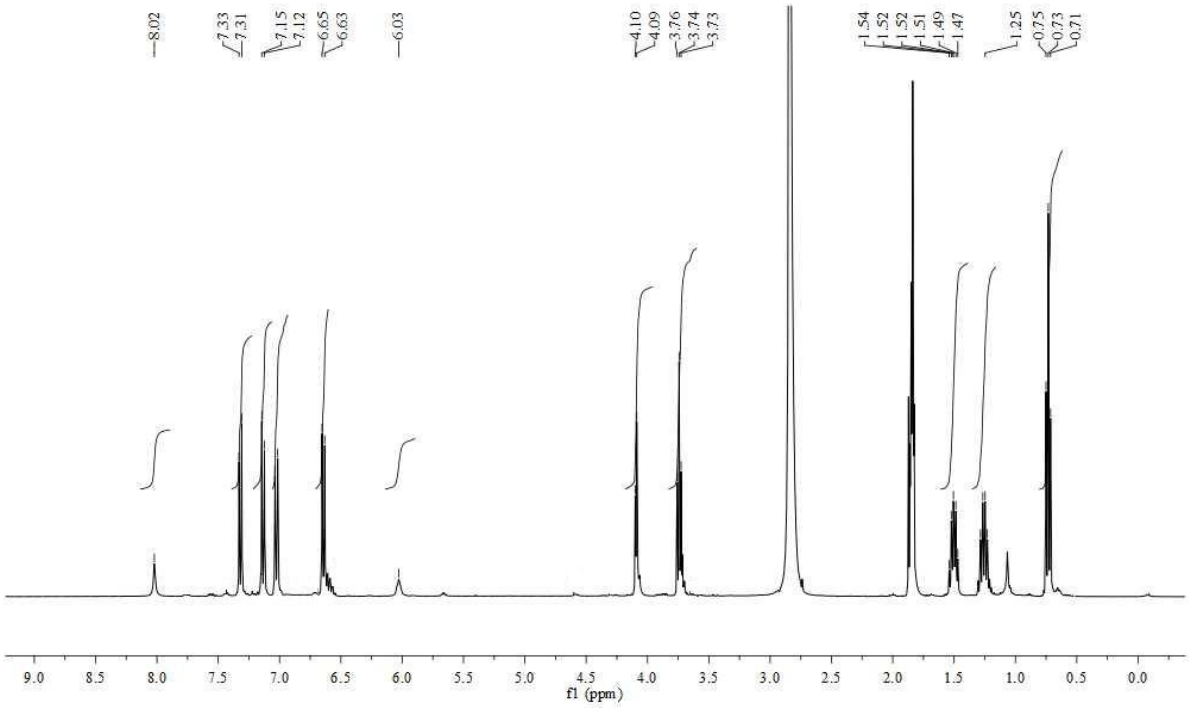
^{13}C-NMR of **7** (75 MHz, $CDCl_3$)



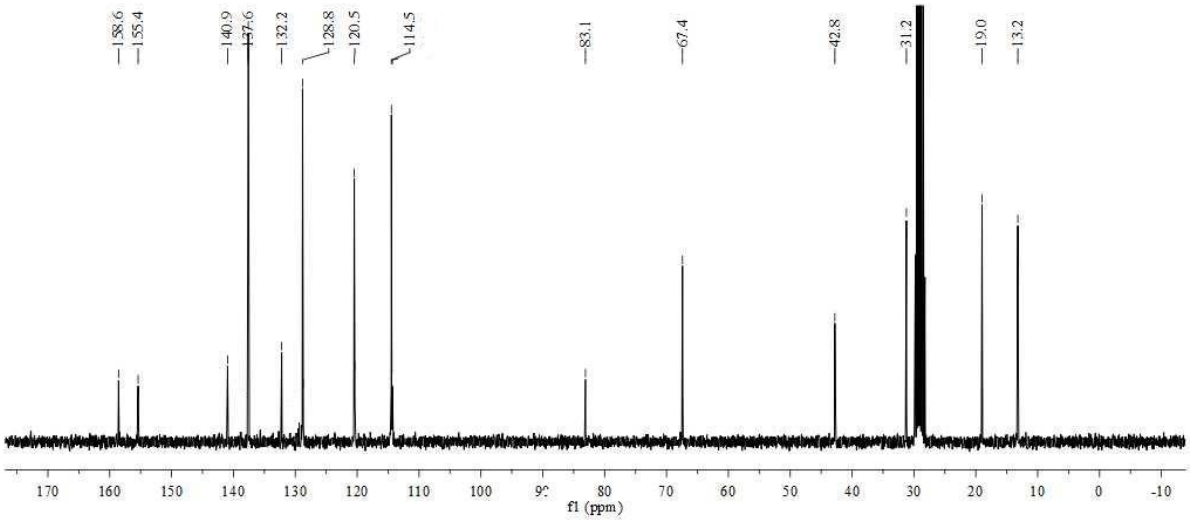
1-[(4-butoxyphenyl)methyl]-3-(4-iodophenyl)urea



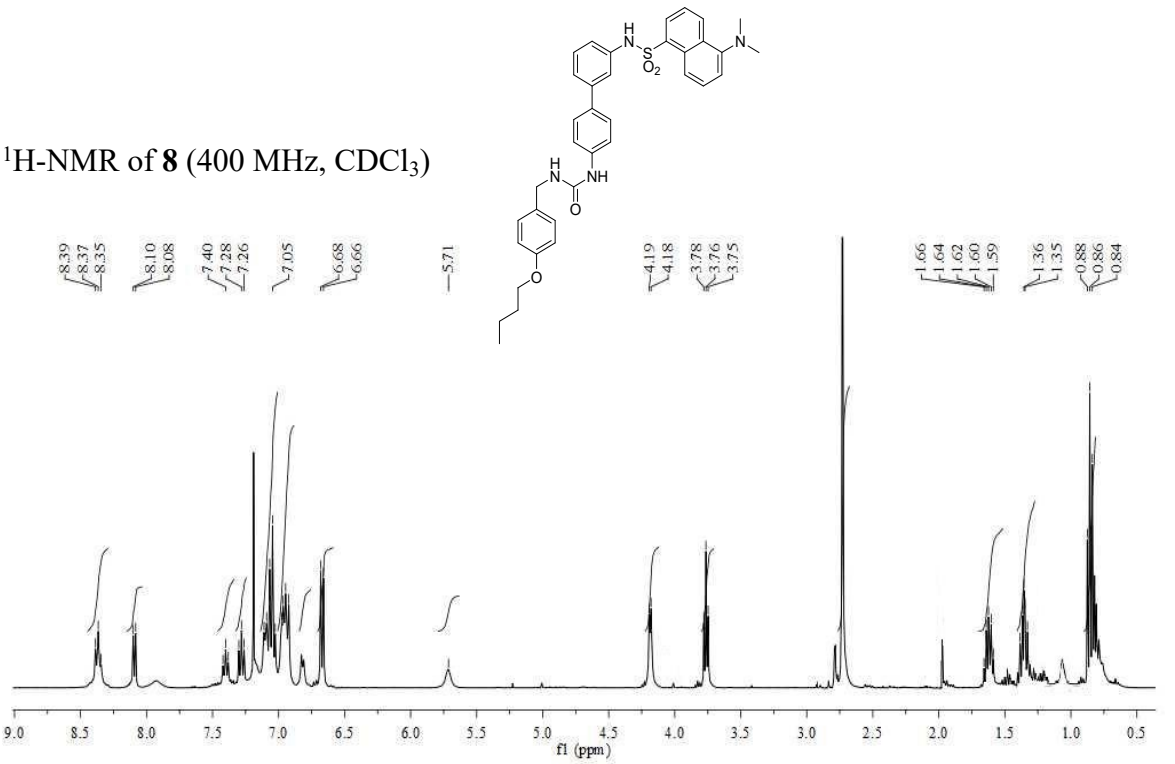
^{1}H NMR Acetone-D_6 (400 MHz)



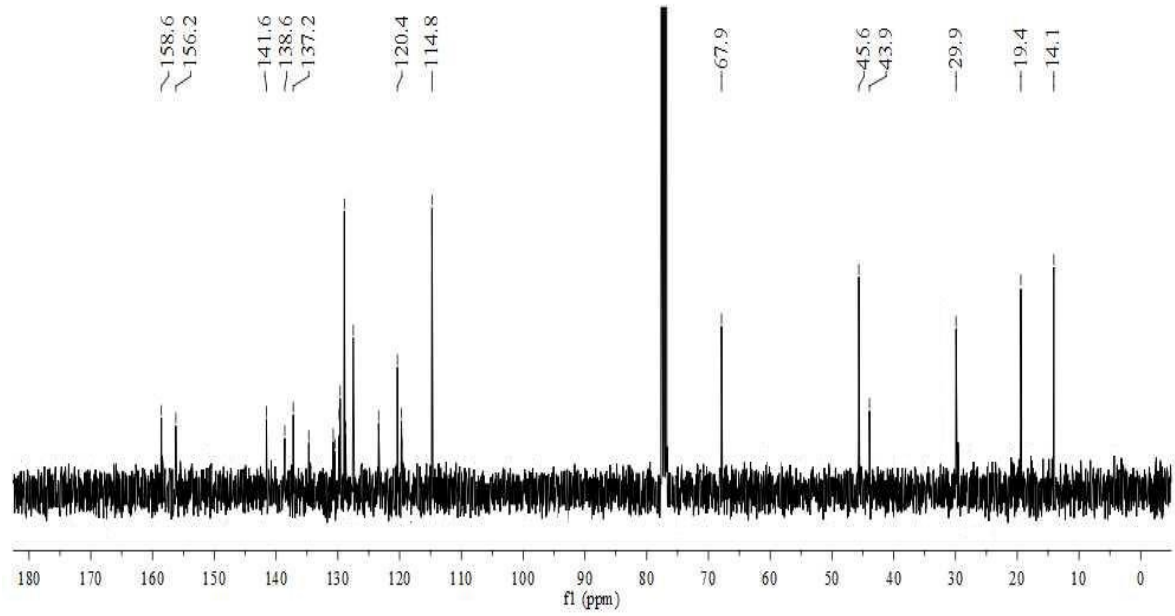
^{13}C NMR Acetone-D_6 (75 MHz)

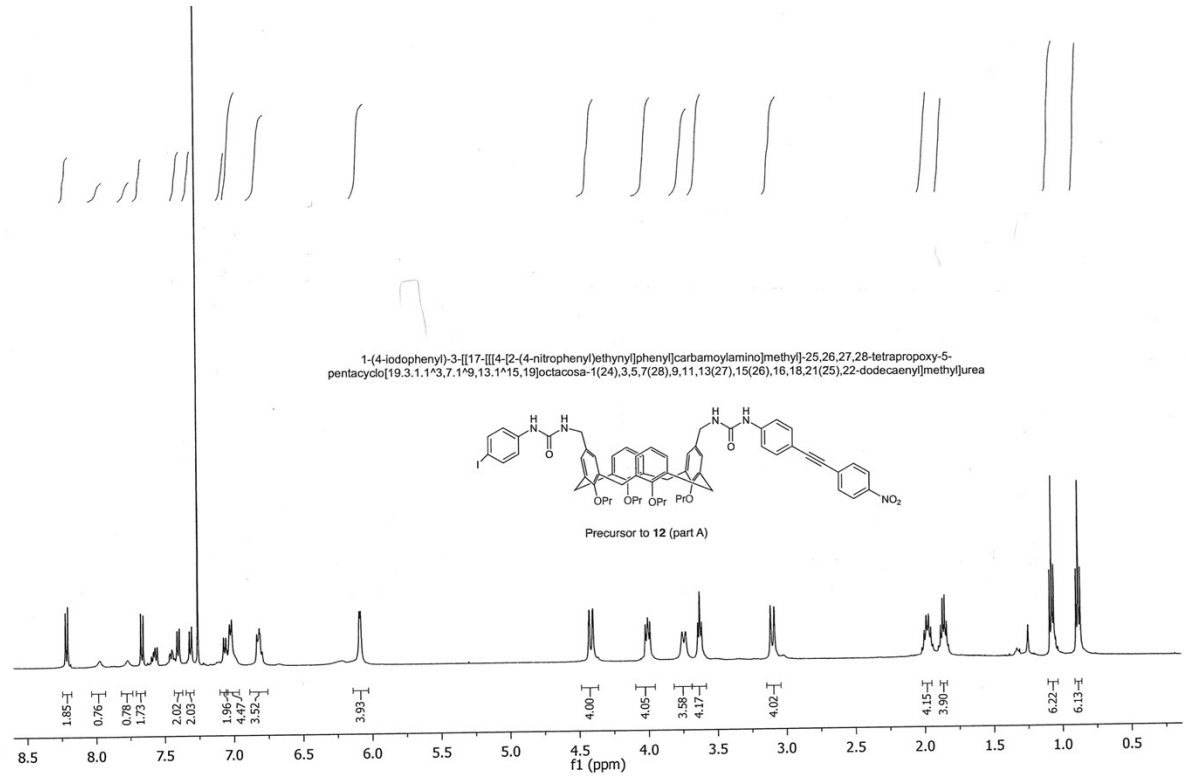


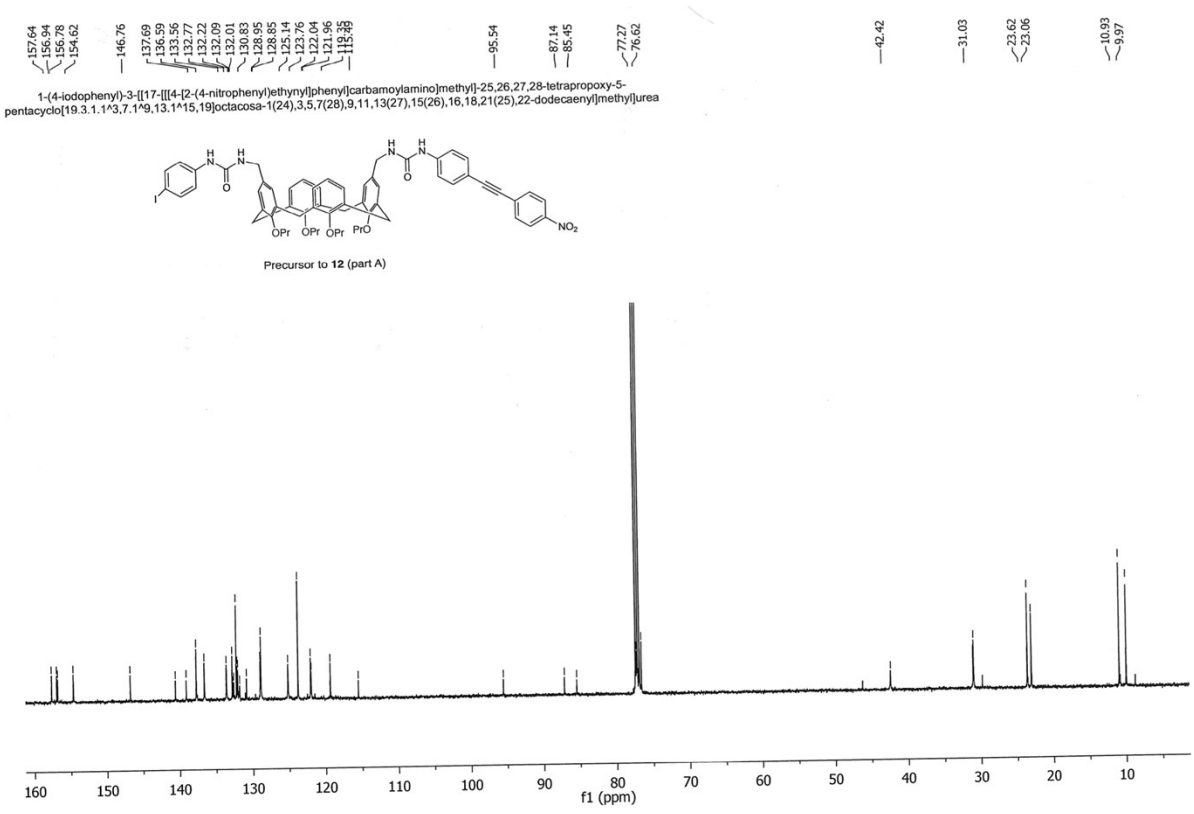
^{1}H-NMR of **8** (400 MHz, $CDCl_3$)



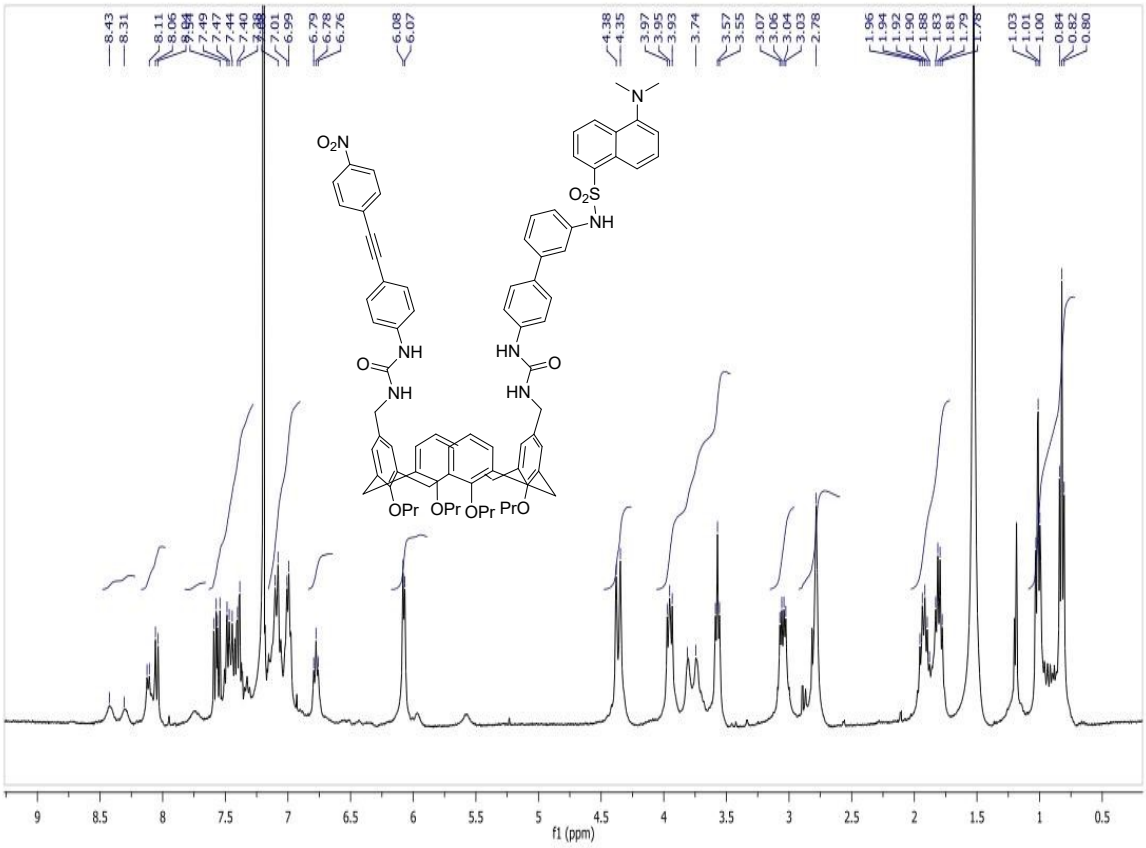
^{13}C-NMR of **8** (75 MHz, $CDCl_3$)



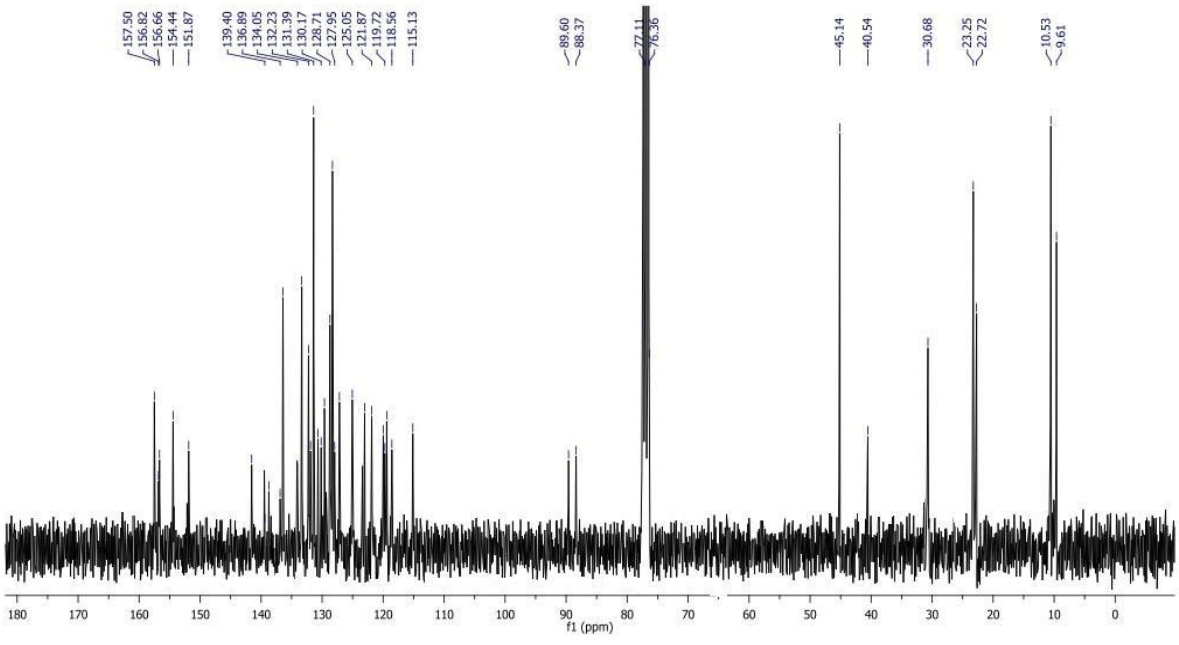

1-(4-iodophenyl)-3-[[17-[[[4-[2-(4-nitrophenyl)ethynyl]phenyl]carbamoylamino]methyl]-25,26,27,28-tetrapropoxy-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(24),3,5,7(28),9,11,13(27),15(26),16,18,21(25),22-dodecaenyl]methyl]urea
Precursor to 12 (part A)
1.85
0.76
0.78
1.73
2.02
2.03
1.96
4.47
3.52
3.93
4.00
4.05
3.58
4.17
4.02
4.15
3.90
6.22
6.13
f1 (ppm)

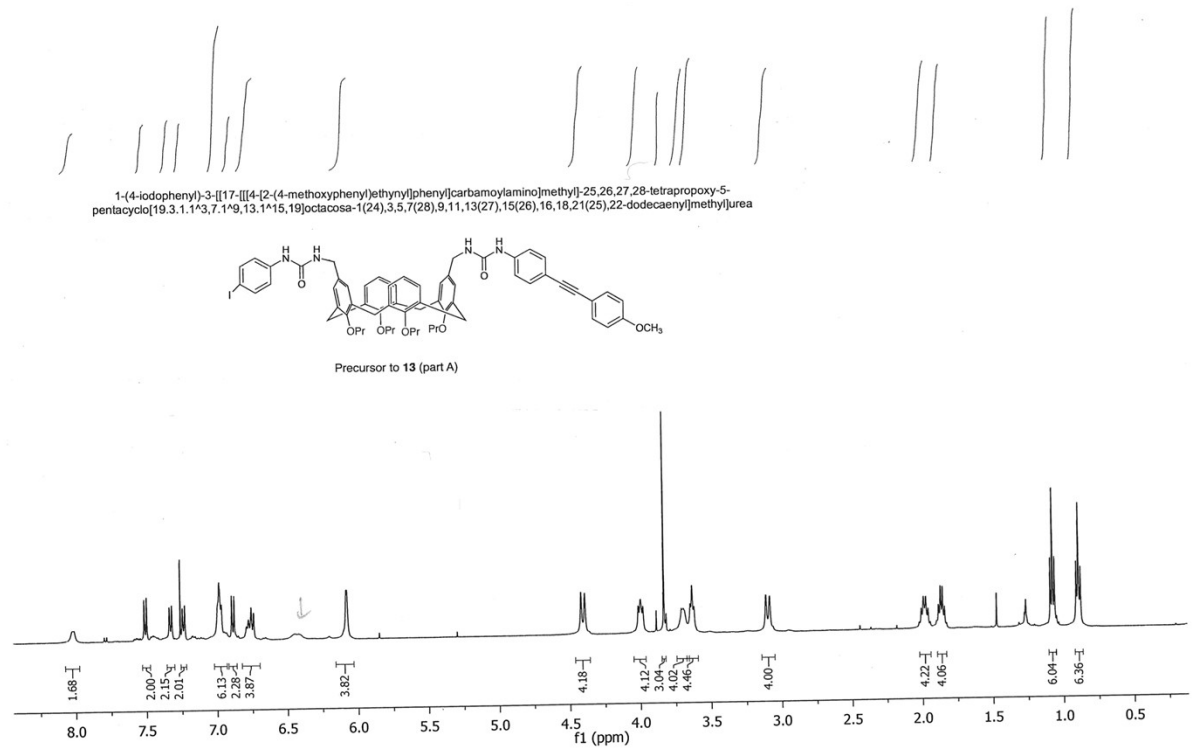

157.64
156.94
156.78
154.62
146.76
137.69
136.59
133.56
132.77
132.22
132.09
132.01
130.83
128.95
128.85
125.14
123.76
122.04
121.96
95.54
87.14
85.45
77.27
76.62
42.42
31.03
23.62
23.06
10.93
9.97
1-(4-iodophenyl)-3-[[17-[[[4-[2-(4-nitrophenyl)ethynyl]phenyl]carbamoylamino]methyl]-25,26,27,28-tetrapropoxy-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(24),3,5,7(28),9,11,13(27),15(26),16,18,21(25),22-dodecaenyl]methyl]urea
Precursor to 12 (part A)
f1 (ppm)

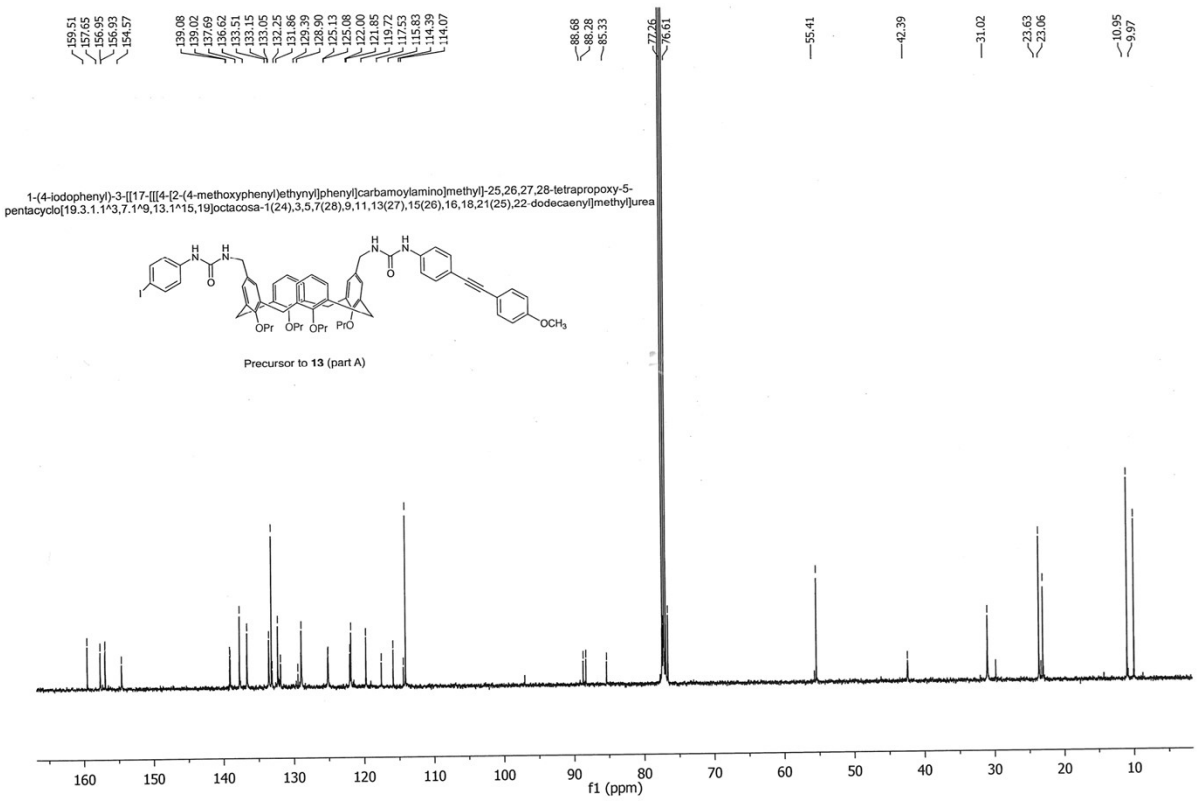
^{1}H-NMR of **12** (400 MHz, $CDCl_3$)



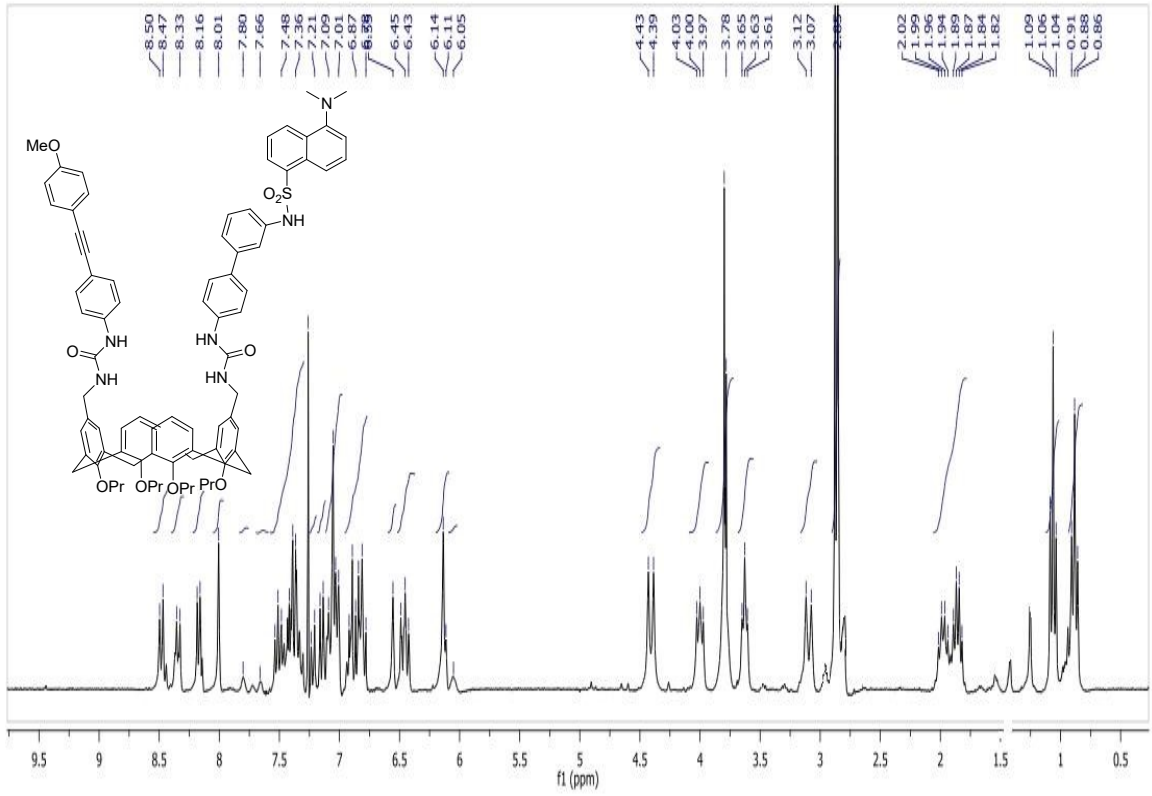
^{13}C-NMR of **12** (75 MHz, $CDCl_3$)



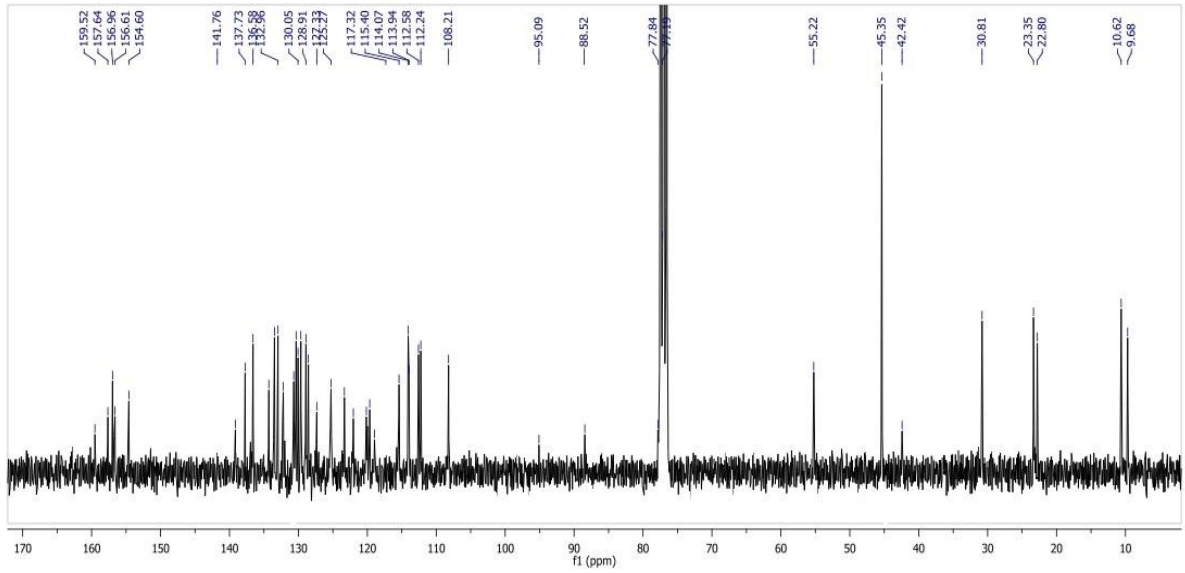

1-(4-iodophenyl)-3-[[17-[[[4-[2-(4-methoxyphenyl)ethynyl]phenyl]carbamoylamino]methyl]-25,26,27,28-tetrapropoxy-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(24),3,5,7(28),9,11,13(27),15(26),16,18,21(25),22-dodecaenyl]methyl]urea
Precursor to 13 (part A)
1.68
2.00
2.15
2.01
6.13
2.28
3.87
3.82
4.18
4.12
3.04
4.02
4.46
4.00
4.22
4.06
6.04
6.36
f1 (ppm)

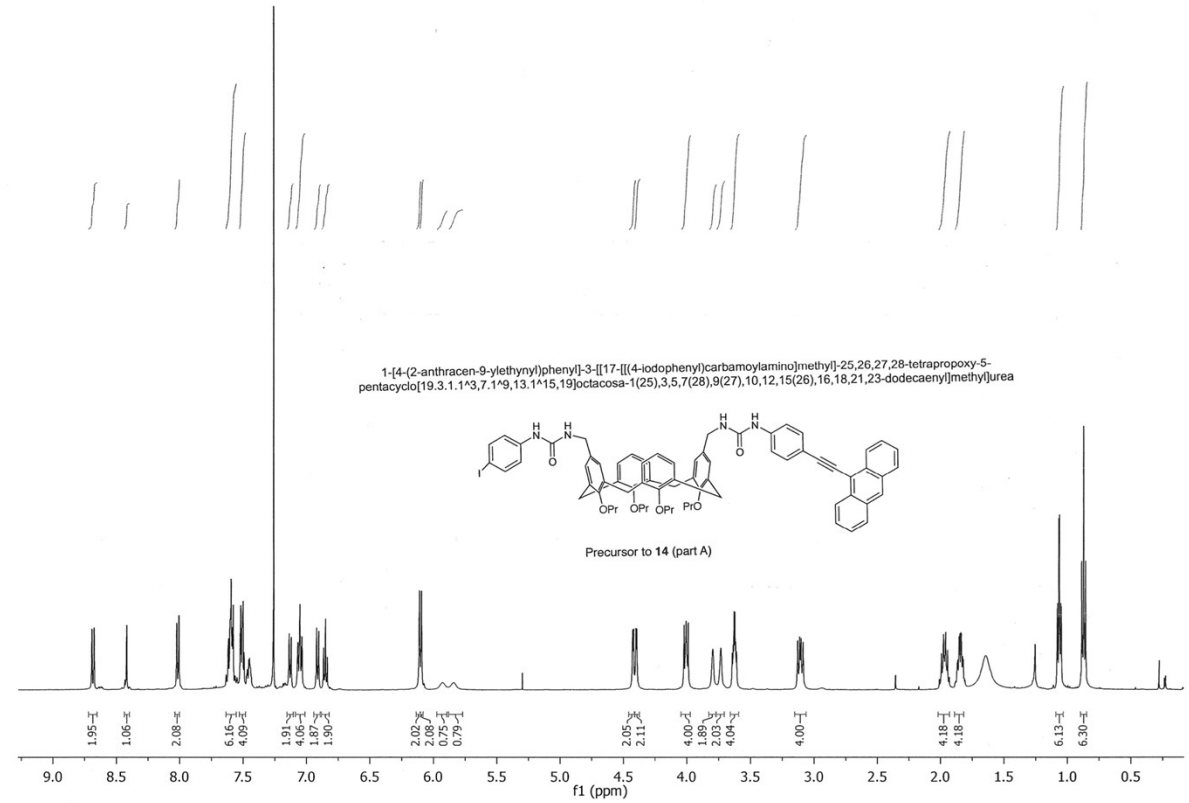

159.51
157.65
156.95
156.93
154.57
139.08
139.02
137.69
136.62
133.51
133.15
133.05
132.25
131.86
129.39
128.90
125.13
125.08
122.00
121.85
119.72
117.53
115.83
114.39
114.07
88.68
88.28
85.33
77.26
76.61
55.41
42.39
31.02
23.63
23.06
10.95
9.97
1-(4-iodophenyl)-3-[[17-[[[4-[2-(4-methoxyphenyl)ethynyl]phenyl]carbamoylamino]methyl]-25,26,27,28-tetrapropoxy-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(24),3,5,7(28),9,11,13(27),15(26),16,18,21(25),22-dodecaenyl]methyl]urea
Precursor to 13 (part A)
f1 (ppm)

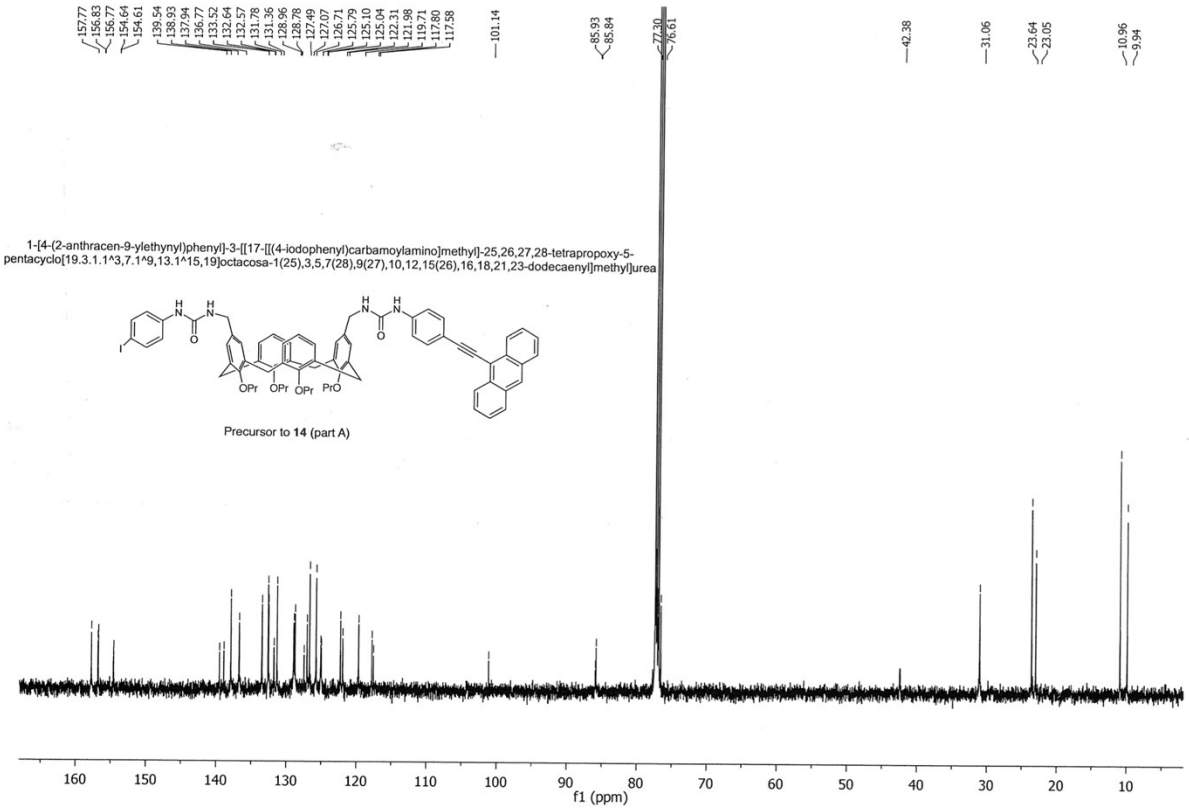
^{1}H-NMR of **13** (400 MHz, $CDCl_3$)



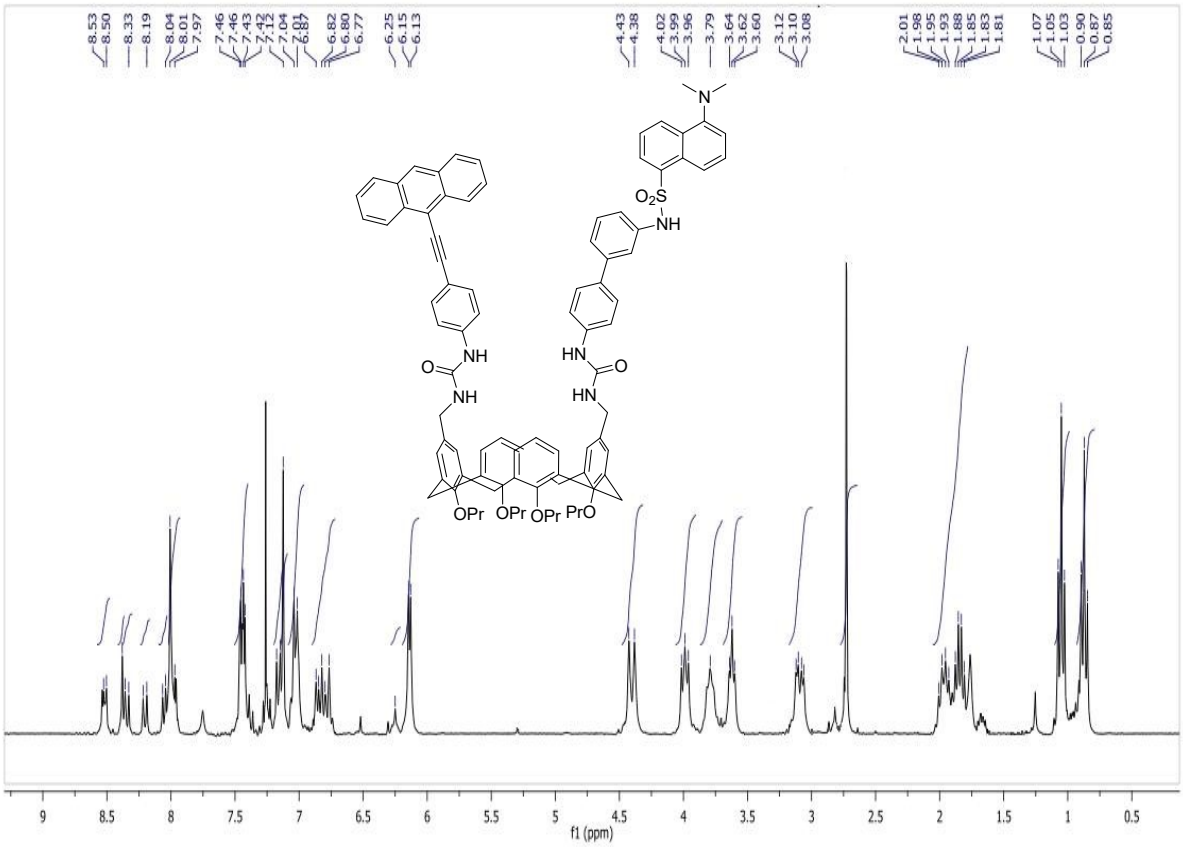
^{13}C-NMR of **13** (75 MHz, $CDCl_3$)



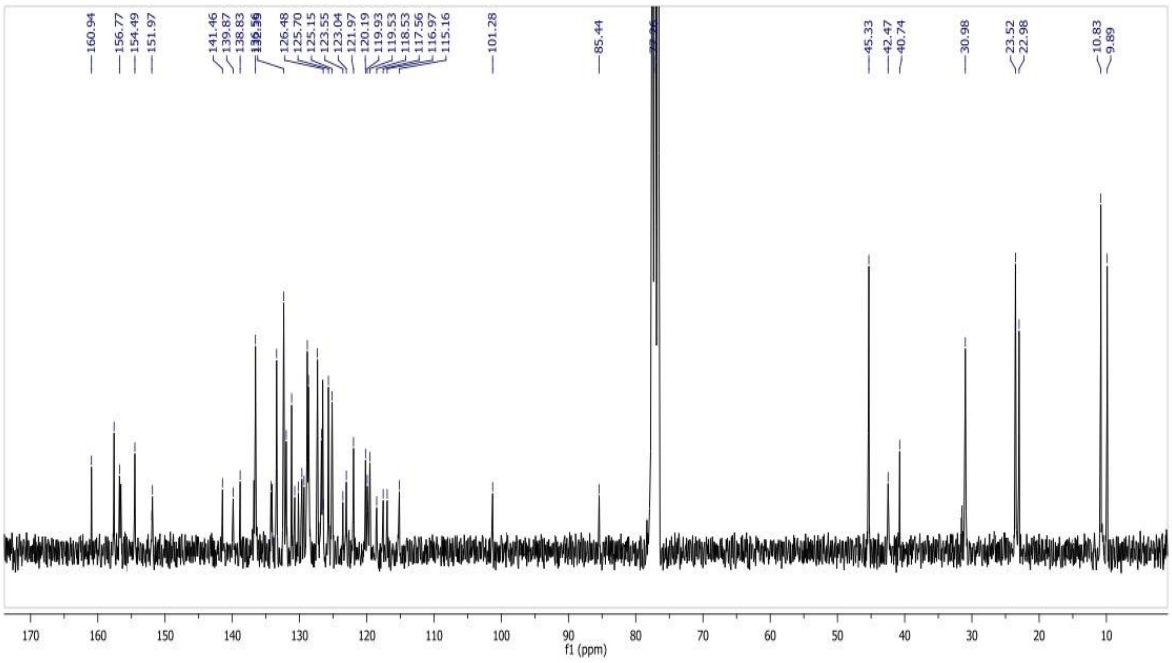

1-[4-(2-anthracen-9-ylethynyl)phenyl]-3-[[17-[[(4-iodophenyl)carbamoylamino]methyl]-25,26,27,28-tetrapropoxy-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(25),3,5,7(28),9(27),10,12,15(26),16,18,21,23-dodecaenyl]methyl]urea
Precursor to 14 (part A)
1.95
1.06
2.08
6.16
4.09
1.91
4.06
1.87
1.90
2.02
2.08
0.75
0.79
2.05
2.11
4.00
1.89
2.03
4.04
4.00
4.18
4.18
6.13
6.30
f1 (ppm)


157.77
156.83
156.77
154.64
154.61
139.54
138.93
137.94
136.77
133.52
132.64
132.57
131.78
131.36
128.96
128.78
127.49
127.07
126.71
125.79
125.10
125.04
122.31
121.98
119.71
117.80
117.58
101.14
85.93
85.84
77.30
76.61
42.38
31.06
23.64
23.05
10.96
9.94
1-[4-(2-anthracen-9-ylethynyl)phenyl]-3-[[17-[[(4-iodophenyl)carbamoylamino]methyl]-25,26,27,28-tetrapropoxy-5-pentacyclo[19.3.1.1^3,7.1^9,13.1^15,19]octacosa-1(25),3,5,7(28),9(27),10,12,15(26),16,18,21,23-dodecaenyl]methyl]urea
Precursor to 14 (part A)
f1 (ppm)

^{1}H-NMR of **14** (400 MHz, $CDCl_3$)



^{13}C-NMR of **14** (75 MHz, $CDCl_3$)



References

1 M. Rezankova, J. Budka, J. Miksatko, V. Eigner, I. Cisarova, P. Curinova and P. Lhotak, *Tetrahedron*, 2017, **73**, 742; R. A. Brimage, G.-H. Gipson, S. P. Bew, S. V. Sharma and S. Thurston, *Org. Lett.,* 2009, **11**, 2483.