Near-Infrared Fluorophores Containing Benzo[*c*]heterocycle Subunits

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Supporting Information

Materials. Commercial reagents were purchased from Sigma Aldrich, Alfa Aesar, or GFS Chemicals, and used as received. Dry solvents were obtained using a solvent purification system (Innovative Technologies, Inc.), and handled under an argon atmosphere, unless otherwise noted. Flash chromatography was performed using SiliaFlash F60 (230-400 mesh) from Silicycle.

Instrumentation. Melting points were determined in open capillaries using a Mel-Temp II apparatus and are uncorrected. Proton nuclear magnetic resonance (1H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded on a Varian Mercury-300 (300 MHz) or an Inova-500 (500 MHz) NMR spectrometer. Chemical shifts for protons are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CHCl_3$: δ 7.27). Chemical shifts for carbon are reported in parts per million downfield from tetramethylsilane and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.0). Data are represented as follows: chemical shift, integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, sp = septet, m = multiplet), and coupling constants in Hertz (Hz). High-resolution mass spectra (HRMS) were obtained at the MIT Department of Chemistry Instrumentation Facility using a peak-matching protocol to determine the mass and error range of the molecular ion, employing either electron impact or electrospray as the ionization technique. Fluorescence spectra were measured on a SPEX Fluorolog-τ3 fluorimeter (model FL-321, 450 W Xenon lamp) using right-angle detection. Ultraviolet-visible absorption spectra were measured with an Agilent 8453 diode array spectrophotometer and corrected for background signal with a solvent-filled cuvette. Fluorescence quantum yields were determined by the optically dilute method[1] using cresyl violet perchlorate in methanol (Φ=0.54) or zinc phthalocyanine in 1% pyridine in toluene (Φ=0.30) as standards and were corrected for solvent refractive index and absorption differences at the excitation wavelength.

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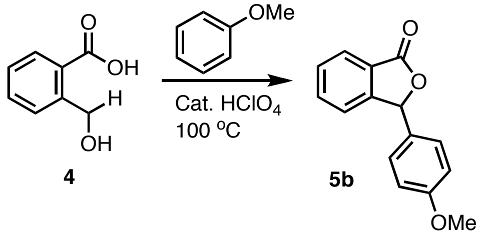
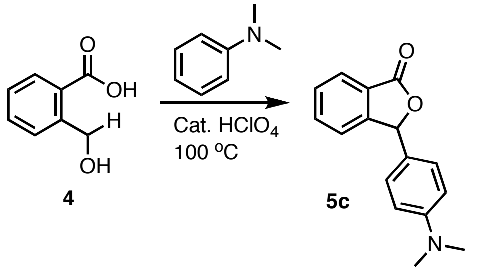
[1] Demas, J. N.; Crosby, G. A. *J. Phys. Chem.* **1971**, *75*, 991.
[2] Barili, P. L.; Scartoni, V. *J. Heterocycl.Chem.* **1985**, *22*, 1199.
[3] Al-Hamdany, R.; Al-Rawi, J. M.; Ibrahim, S. *J. Prakt. Chem.* **1987**, *329*, 126.
[4] Johnson, A. L. *J. Org. Chem.* **1976**, *41*, 1320.

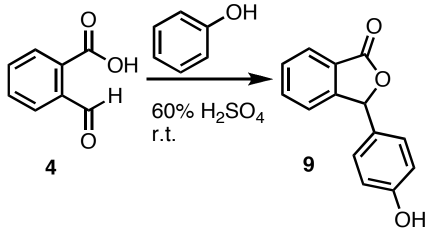
Synthetic Procedures



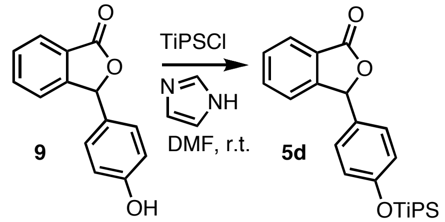
To a solution of **4** (5.0 g, 33 mmol) in anisole (10 ml, 92 mmol) were added 8 drops of 70% $HClO_4$, and the solution was stirred at 100 °C for 2 hours. After cooling, the reaction mixture was poured into water and stirred for 30 minutes. The sticky white product was collected by suction filtration and was washed with water and saturated sodium bicarbonate. Recrystalization from methanol afforded **5b** as white crystals (4.5 g, 19 mmol, 58% yield, Mp=117-118 °C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.97 (1H, d, 7.6 Hz), 7.67 (1H, td, 7.4 Hz, 1.2 Hz), 7.57 (1H, t, 7.6 Hz), 7.32 (1H, d, 7.6 Hz), 7.19 (2H, dm, 8.8 Hz), 6.90 (2H, dm, 8.8 Hz), 6.39 (1H, s), 3.82 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): 170.5, 160.3, 149.7, 134.2, 129.2, 128.7, 128.1, 125.8, 125.4, 122.9, 114.2, 82.6, 55.2. HRMS (ESI): 241.0853 [calc'd for $M+H^+$: 241.0859]. These values are consistent with data reported in the literature.[2]



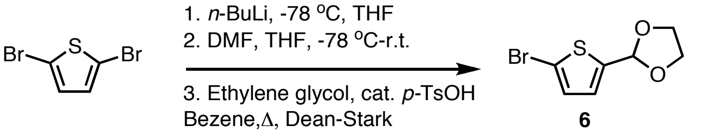
To a solution of **4** (4.0 g, 27 mmol) in *N*,*N*-dimethylaniline (8.2 ml, 65 mmol) were added 6 drops of 70% $HClO_4$, and the solution was stirred at 100 °C for 2 hours. After cooling, the reaction mixture was poured into water and stirred for 30 minutes. The light blue product was collected by suction filtration and was washed with water and saturated sodium bicarbonate. Recrystalization from acetone afforded **5c** as white crystals (3.4 g, 13 mmol, 48% yield, Mp= 193-195 °C) ^{1}H NMR (300 MHz, $CDCl_3$): 7.96 (1H, d, 7.6 Hz), 7.65 (1H, td, 7.5 Hz, 1.2 Hz), 7.55 (1H, t, 7.5 Hz), 7.33 (1H, d, 7.6 Hz), 7.10 (2H, dm, 8.8 Hz), 6.90 (2H, dm, 8.8 Hz), 6.37 (1H, s), 2.97 (6H, s). ^{13}C NMR (125 MHz, $CDCl_3$): 170.7, 151.1, 150.0, 134.0, 129.0, 128.7, 126.2, 125.4, 123.04, 123.02, 83.5, 40.3. HRMS (ESI): 254.1176 [calc'd for $M+H^+$: 254.1176].



4 (2.2 g, 15 mmol) was dissolved in 12 ml of 60% H_2SO_4 and stirred for 10 min at room temperature. Phenol (1.4 g, 15 mmol) was added in one portion, and the reaction mixture was stirred for an additional 2 hours at room temperature. The reaction mixture was then poured onto ice and stirred for 30 minutes. The white product was collected by suction filtration and washed with water and saturated sodium bicarbonate solution. Recrystalization from 20% aqueous ethanol afforded **9** as white crystals (3.1 g, 14 mmol, 93% yield, Mp = 161-163 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.97 (1H, d, 7.6 Hz), 7.67 (1H, td, 7.5 Hz, 1.2 Hz), 7.57 (1H, t, 7.2 Hz), 7.32 (1H, dq, 7.6 Hz, 0.9 Hz), 7.13 (2H, dm, 8.4 Hz), 6.90 (2H, dm, 8.6 Hz), 6.38 (1H, s), 5.13 (1H, s). ^{13}C NMR (125 MHz, $CDCl_3$): 170.9, 156.7, 149.7, 134.4, 129.4, 129.0, 128.1, 125.8, 125.6, 123.0, 115.9, 82.9. HRMS (ESI): 249.0526 [calc'd for M+Na^{+}: 249.0522]. These values are consistent with data reported in the literature.[3]

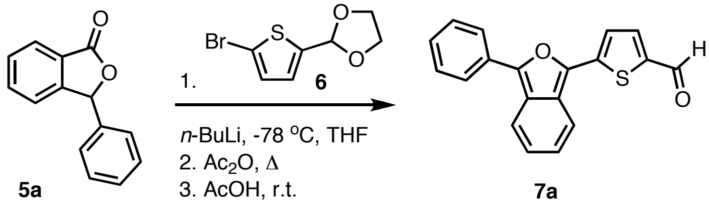


9 (5.1 g, 23 mmol) was dissolved in DMF (94 ml) along with imidazole (6.8 g, 0.10 mol) and triisopropylsilyl chloride (9.4 ml, 44 mmol), and the solution was stirred overnight at room temperature. The reaction mixture was then poured onto ice and stirred for one hour. The white solid was collected by suction filtration. Recrystalization from methanol afforded **5d** as a white crystalline solid (6.4 g, 18 mmol, 78% yield, Mp= 102-103 ^{o}C). ^{1}H NMR (300 MHz, $CDCl_3$): 7.97 (1H, d, 7.6 Hz), 7.66 (1H, td, 7.5 Hz, 1.2 Hz), 7.56 (1H, tt, 7.4 Hz, 0.8 Hz), 7.33 (1H, dq, 7.6 Hz, 1.1 Hz), 7.11 (2H, dm, 8.4 Hz), 6.87 (2H, dm, 8.7 Hz), 6.37 (1H, s), 1.26 (3H, sp, 6.8 Hz), 1.09 (18H, d, 6.7 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 170.5, 157.0, 149.7, 134.2, 129.2, 128.7, 128.5, 125.9, 125.5, 122.9, 120.2, 82.8, 17.8, 12.6. HRMS (ESI): 405.1855 [calc'd for M+Na^{+}: 405.1856].

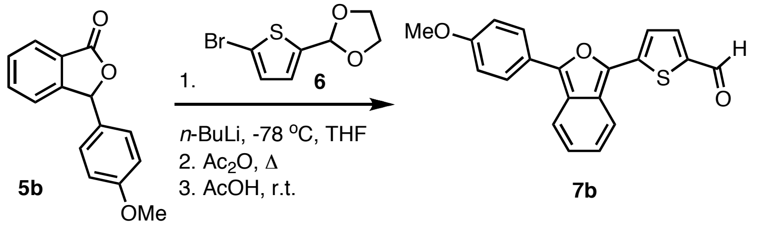


2,5-Dibromothiophene (6.0 g, 25 mmol) and dry THF (50 ml) were added to a vacuum dried Schlenk flask under argon and the solution was cooled to -78 °C. *n*-BuLi (15.6 ml 1.6M solution in hexanes, 25 mmol) was added dropwise and the solution was stirred at -78 °C for 90 minutes. A solution of dry DMF (2.5 ml, 32 mmol, distilled from NaH) in dry THF (10 ml) was added, and the reaction mixture was warmed to room temperature and stirred overnight. The reaction mixture was then poured onto saturated sodium bicarbonate and extracted with ethyl acetate. The organic fraction was washed with saturated sodium bicarbonate, water, and brine, dried over magnesium sulfate, and concentrated in vacuo. The resulting dark, viscous liquid was then dissolved in benzene (100 ml) along with ethylene glycol (3.2 ml, 57 mmol) and *p*-toluenesulfonic acid monohydrate (0.060 g, 0.32 mmol), and this solution was refluxed overnight in a flask equipped with a Dean-Stark trap. The reaction mixture was then cooled to room temperature, concentrated in vacuo, taken up in ethyl acetate and washed with saturated sodium bicarbonate and brine. The organic layer was dried over magnesium sulfate and concentrated in vacuo. The residue was purified by flash chromatography on silica gel (2:1 hexane:ethyl acetate) and then vacuum distillation (66-70 °C, 190 mtorr) to afford **6** as a clear liquid (2.2 g, 9.4 mmol, 38% yield) ^{1}H NMR (300 MHz, $CDCl_3$): 6.95 (1H, d, 3.8 Hz), 6.92 (1H, d, 3.8 Hz), 6.02 (1H s), 4.15-3.95 (4H, m). ^{13}C NMR (125 MHz, $CDCl_3$): 143.3, 129.4, 126.5, 113.5, 65.2 HRMS (ESI): 234.9417 [calc'd for $M+H^+$: 234.9423]. These values are consistent with data reported in the literature.[4]

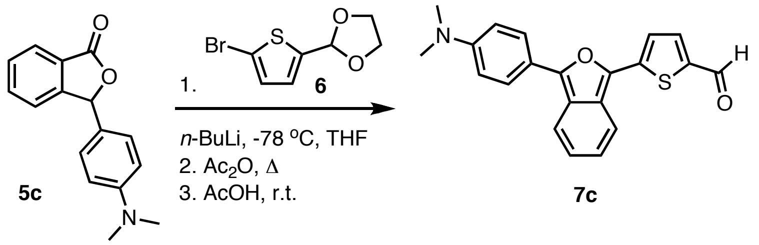
General procedure for synthesis of aldehydes **7a-d**



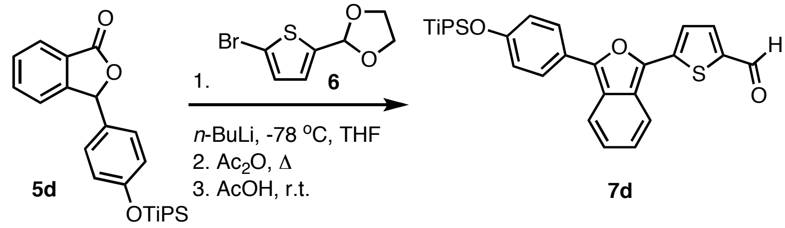
n-BuLi (1.4 ml of 1.6M solution in hexanes) was added to a solution of **6** (0.5 g, 2.1 mmol) in dry THF (7 ml) in a vacuum dried Schlenk flask at -78 °C under argon, and the solution was stirred at -78 °C for 2 hours. A solution of 3-phenylphthalide (0.45 g, 2.1 mmol) in dry THF (7 ml) was added dropwise, and the reaction mixture was stirred at -78 °C for an additional hour. Acetic anhydride (0.23 ml, 2.4 mmol) was added, and the solution was warmed to room temperature, and was then refluxed for 10 minutes. The reaction mixture was cooled to room temperature, and was then diluted with ethyl acetate and washed with saturated aqueous sodium bicarbonate and brine. The organic layer was dried over magnesium sulfate and concentrated in vacuo. Acetic acid (15 ml of 90% aqueous solution) was then added to the residue, and this solution was stirred under argon for 2 hours, and then poured into water and stirred for 30 minutes. The red solid was collected by suction filtration and washed with saturated aqueous sodium bicarbonate and water. Recrystallization from 5% aqueous methanol afforded **7a** as red crystals (0.26 g, 0.86 mmol, 41% yield, Mp = 150-152 °C) ^{1}H NMR (300 MHz, $CDCl_3$): 9.92 (1H, s), 7.99-7.92 (2H, m), 7.90 (1H, dt, 8.8 Hz, 1.2 Hz), 7.82-7.76 (2H, m), 7.58-7.49 (3H, m), 7.38 (1H, tt, 7.4 Hz, 1.2 Hz), 7.23-6.99 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): 182.3, 146.3, 142.3, 140.5, 137.4, 130.6, 129.1, 128.1, 127.2, 125.9, 125.3, 124.5, 122.4, 122.0, 120.6, 119.6, 99.8. HRMS (ESI): 305.0641[calc'd for M+H$^+$: 305.0631]



The reaction was carried out on a 2.1 mmol scale, and **7b** was obtained as a rusty red powder after recrystallization from ethanol (0.23 g, 0.69 mmol, 33% yield, Mp = 79-81 ^{o}C) ^{1}H NMR (300 MHz, CDCl$_3$): 9.90 (1H, s), 7.90 (2H, dt, 9.1 Hz, 2.2 Hz), 7.84 (1H, dt, 8.8 Hz, 1.0 Hz), 7.79-7.75 (2H, m), 7.51 (1H, d, 4.1 Hz), 7.18 (1H, ddd, 8.8 Hz, 3.0 Hz, 0.8 Hz), 7.11-7.02 (3H, m), 3.90 (3H, s). ^{13}C NMR (125 MHz, CDCl$_3$): 182.0, 159.5, 146.5, 142.4, 139.7, 137.9, 137.4, 127.0, 126.7, 125.2, 124.5, 123.4, 121.24, 121.20, 120.6, 119.3, 114.5, 55.3. HRMS (ESI): 335.0741 [calc'd for M+H$^+$: 335.0736]

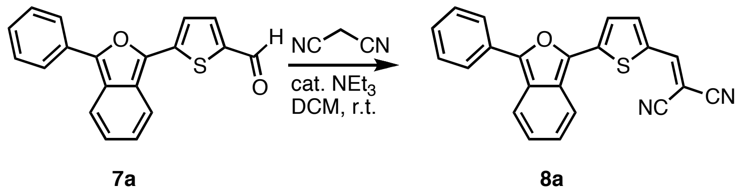


The reaction was carried out with 2.1 mmol of **6** and 1.8 mmol of **5c** in dry THF (40 ml)**,** and 20 ml of 90% aqueous acetic acid were used in the work up. The acetic acid solution was poured into water, and then small portions of saturated aqueous sodium bicarbonate were carefully added. The dark product was collected by suction filtration, and was washed with sodium bicarbonate and brine. Flash chromatography on silica gel (dichloromethane) afforded **7c** as a dark solid (0.38 g, 1.1 mmol, 61% yield) ^{1}H NMR (300 MHz, CDCl$_3$): 9.87 (1H, s), 7.88-7.82 (3H, m), 7.76-7.72 (2H, m), 7.46 (1H, d, 4.2 Hz), 7.17 (1H, ddd, 8.8 Hz, 6.5 Hz, 0.9 Hz), 7.04 (1H, ddd, 8.8 Hz 0.9 Hz), 6.83 (2H, dm, 8.8 Hz), 3.07 (6H, s). 182.0, 150.1, 148.2, 143.0, 139.1, 137.7, 137.2, 127.2, 126.7, 125.0, 124.6, 121.3, 120.7, 120.6, 119.4, 118.7, 112.3, 40.2. HRMS (ESI): 348.1051 [calc'd for M+H$^+$: 348.1053]

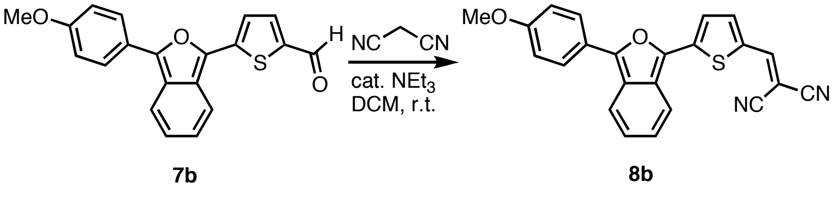


The reaction was carried out on a 2.1 mmol scale. After acetic acid workup, the reaction mixture was poured into water, stirred for 30 minutes, and then extracted with ethyl acetate. The organic layer was washed with saturated aqueous sodium bicarbonate and brine, and was then dried over magnesium sulfate and concentrated in vacuo. Flash chromatography on silica gel (2:1 hexane:ethyl acetate) afforded **7d** as a viscous red oil (0.47 g, 0.99 mmol, 47% yield) ^{1}H NMR (300 MHz, $CDCl_3$): 9.90 (1H, s), 7.88-7.82 (3H, m), 7.79-7.74 (2H, m), 7.52 (1H, d, 4.1 Hz), 7.18 (1H, ddd, 8.7 Hz, 6.3 Hz, 0.9 Hz), 7.12-7.00 (3H, m), 1.30 (3H, sp, 6.9 Hz), 1.15 (18H, d, 6.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 182.0, 156.4, 146.7, 142.5, 139.8, 137.9, 137.4, 127.0, 126.7, 125.2, 124.5, 123.7, 121.3, 121.2, 120.7, 120.6, 119.4, 17.9, 12.6. HRMS (ESI): 499.1733 [calc'd for $M+Na^+$: 499.1734]

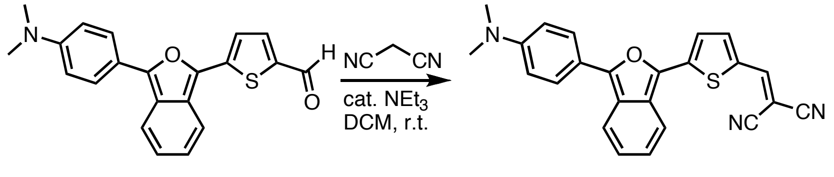
General Procedure for synthesis of dyes **8a-d**



7a (70 mg, 0.23 mmol) was dissolved in a solution of malonitrile (15 mg, 0.23 mmol) in dry dichloromethane (10 ml) and then 3 drops of triethylamine were added and the resulting solution was stirred overnight, under argon, at room temperature. The reaction mixture was then diluted with ethyl acetate, washed with water and brine, dried over magnesium sulfate, and concentrated in vacuo. Flash chromatography over silica gel (dichloromethane) afforded **8a** as a purple solid (62 mg, 0.18 mmol, 78% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 7.97-7.88 (3H, m), 7.72 (1H, d, 8.7 Hz), 7.66 (1H, s), 7.59 (1H, d, 4.3 Hz), 7.53 (2H, t, 7.2 Hz), 7.48 (1H, d, 4.3 Hz), 7.41 (1H, tt, 7.2 Hz, 1.3 Hz), 7.26-7.14 (2H, m). ^{13}C NMR (125 MHz, $CDCl_3$): 149.1, 148.2, 144.0, 140.2, 138.5, 132.5, 130.0, 129.2, 128.8, 128.3, 126.4, 125.9, 125.6, 122.8, 122.2, 121.0, 119.6, 114.9, 114.1, 73.3. HRMS (ESI): 353.0753 [calc'd for $M+H^+$: 353.0743]

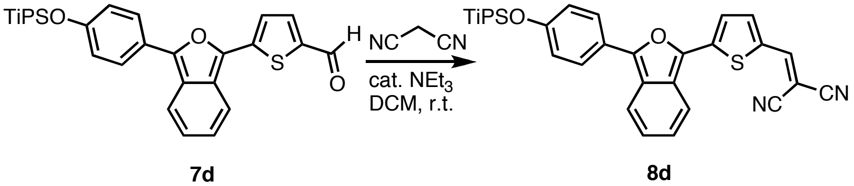


The reaction was carried out on a 0.18 mmol scale with 10 ml of dry dichloromethane. Flash chromatography over silica gel (dichloromethane) afforded **8b** as a purple solid (45 mg, 0.12 mmol, 67% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 7.96-7.87 (3H, m), 7.78 (1H, d, 8.7 Hz), 7.73 (1H, s), 7.66 (1H, d, 4.4 Hz), 7.52 (1H, d, 4.4 Hz), 7.31-7.24 (1H, m), 7.16 (1H, ddd, 8.8 Hz, 6.5 Hz 0.9 Hz), 7.07 (2H, dm, 8.9 Hz), 3.92 (3H, s). ^{13}C NMR (125 MHz, $CDCl_3$): 160.3, 149.0, 148.9, 144.4, 140.4, 137.9, 132.1, 128.5, 127.4, 126.3, 126.0, 123.0, 122.0, 121.6, 121.2, 119.6, 115.2, 114.8, 114.4, 72.5, 55.5. HRMS (ESI): 383.0845 [calc'd for $M+H^+$: 383.0849].



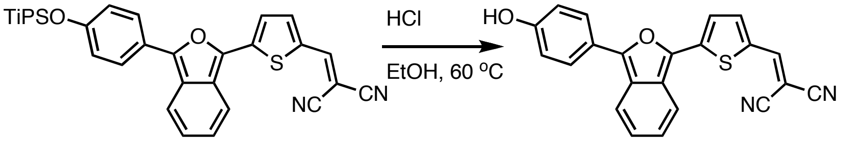
7c **8c**

The reaction was carried out on a 0.25 mmol scale with 15 ml of dry dichloromethane. Flash chromatography over silica gel (dichloromethane) afforded **8c** as a green solid (38 mg, 0.096 mmol, 38% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 7.94-7.86 (3H, m), 7.76 (1H, dt, 8.9 Hz, 0.9 Hz), 7.66 (1H, s), 7.61 (1H, d, 4.0 Hz), 7.44 (1H, d, 4.3 Hz), 7.31-7.24 (1H, m, obscured by solvent), 7.12 (1H, ddd, 8.8 Hz, 6.5 Hz, 0.9 Hz), 6.83 (2H, dm, 9.2 Hz), 3.10 (6H, s). ^{13}C NMR (125 MHz, DMF-d_7): 152.2, 151.8, 151.5, 144.8, 144.2, 138.1, 132.8, 130.2, 128.3, 127.8, 126.8, 123.2, 122.7, 122.3, 120.4, 118.4, 116.9, 116.3, 113.6, 70.9, 40.5. HRMS (ESI): 396.1170 [calc'd for $M+H^+$: 396.1170]



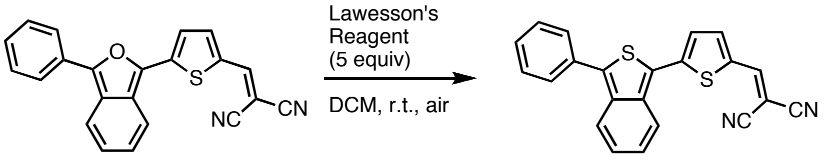
7d **8d**

The reaction was carried out on a 0.38 mmol scale with 15 ml dry dichloromethane. Flash chromatography over silica gel (dichloromethane) afforded **8d** as a purple solid (0.11 g, 0.21 mmol, 55% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 7.92-7.85 (3H, m), 7.78 (1H, d, 8.9 Hz), 7.73 (1H, s), 7.66 (1H, d, 4.4 Hz), 7.51 (1H, d, 4.3 Hz), 7.31-7.24 (1H, m), 7.15 (1H, ddd, 8.9 Hz, 6.3 Hz 0.9 Hz), 7.05 (2H, dm, 8.9 Hz), 1.30 (3H, sp, 7.0 Hz), 1.15 (18H, d, 7.0 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 157.2, 149.0, 148.9, 144.3, 140.4, 137.8, 132.0, 128.4, 127.3, 126.3, 125.9, 123.1, 122.0, 121.5, 121.3, 120.8, 119.5, 115.2, 114.3, 17.9, 12.7. HRMS (ESI): 547.1837 [calc'd for $M+Na^+$: 547.1846]



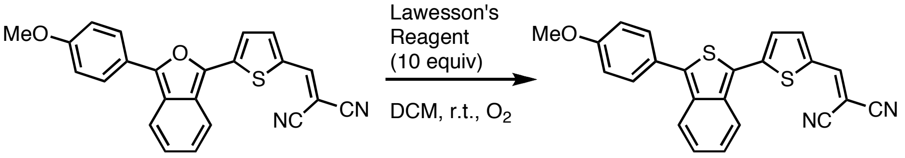
8d **11**

8d (13.5 mg, 0.026 mmol) was dissolved in ethanol (12 ml, 200 proof) at 60 °C. Hydrochloric acid (1.3 ml, 36%) was added and the solution was stirred at 60 °C under argon for 18 hours. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, and washed with water, saturated aqueous sodium bicarbonate, and brine, and was then dried over magnesium sulfate and concentrated in vacuo. Flash chromatography over silica gel (9:1 methylene chloride: ethyl acetate, then 2:1 ethyl acetate: hexane) afforded **11** as a blue solid (8.4 mg, 0.023 mmol, 88% yield). ^{1}H NMR (500 MHz, DMSO-d$_6$): 9.03 (1H, bs), 6.85 (1H, s), 6.53 (1H, d, 8.5 Hz), 6.42 (2H, d, 8.5 Hz), 6.32 (1H, d, 4.4 Hz), 6.22 (1H, d, 8.9 Hz), 6.08 (1H, d, 4.3 Hz), 5.88 (1H, t, 7.5 Hz), 5.77 (1H, t, 8.0 Hz), 5.65 (2H, d, 8.5 Hz). ^{13}C NMR (125 MHz, DMSO-d$_6$): 158.9, 150.6, 148.9, 143.2, 143.1, 137.2, 131.9, 129.0, 127.6, 126.3, 125.9, 122.0, 121.7, 121.3, 121.0, 119.3, 116.8, 115.8, 115.0, 70.2. HRMS (ESI): 367.0539 [calc'd for M-H$^-$: 367.0547]



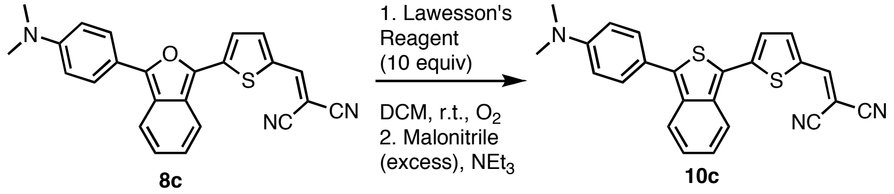
8a **10a**

Lawesson's reagent (7.5 mg, 0.019 mmol) was added to a solution of **8a** (11 mg, 0.031 mmol) in dry dichloromethane (10 ml) and the reaction was stirred open to air for 3 hours. Another portion of Lawesson's reagent (52 mg, 0.13 mmol) was added and the reaction mixture was stirred for an addition 4 hours, monitored by thin later chromatography (dichloromethane). When the starting material had been consumed, the reaction mixture was purified by flash chromatography over silica gel (dichloromethane) to afford **10a** as a purple solid (10 mg, 0.027 mmol, 87% yield) ^{1}H NMR (300 MHz, CDCl$_3$): 8.08 (1H, dt, 8.9 Hz, 0.9 Hz), 7.88 (1H, dt, 8.9 Hz, 0.9 Hz), 7.78 (1H, s), 7.74-7.67 (3H, m), 7.59-7.44 (4H, m), 7.37 (1H, ddd, 8.9 Hz, 6.5 Hz, 0.9 Hz), 7.23 (1H, ddd, 8.9 Hz, 6.5 Hz, 0.9 Hz). ^{13}C NMR (125 MHz, CDCl$_3$): 149.5, 148.9, 140.2, 139.7, 136.9, 136.0, 133.2, 132.9, 129.4, 129.3, 128.8, 127.4, 125.2, 125.0, 124.6, 122.1, 121.3, 114.7, 113.9, 74.6. HRMS (EI): 368.0429 [calc'd for M$^+$: 368.0436]

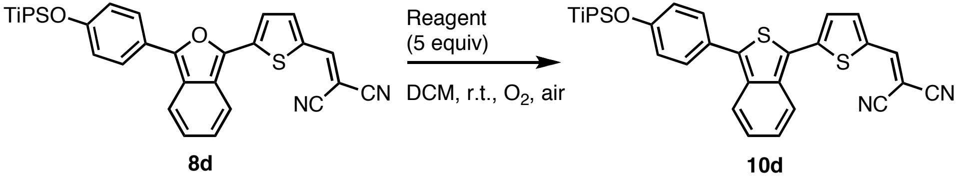


8b **10b**

8b (11 mg, 0.029 mmol) was dissolved in 10 ml of dry dichloromethane (10 ml) in a Schlenk flask along with Lawesson's reagent (55 mg, 0.14 mmol), and the solution was cooled to -78 °C. Anhydrous oxygen was bubbled through the solution for 5 minutes, after which the flask was sealed, and the reaction mixture was allowed to warm to room temperature and was stirred at room temperature for 3 hours. A second portion of Lawesson's reagent (55 mg, 0.14 mmol) was added and the reaction mixture was stirred at room temperature for 6 hours under an oxygen atmosphere. The reaction mixture was purified by flash chromatography over silica gel (dichloromethane) to afford **10b** as a purple solid (8.3 mg, 0.021 mmol, 72% yield). ^{1}H NMR (300 MHz, CDCl$_3$): 8.07 (1H, dt, 8.9 Hz, 0.9 Hz), 7.84 (1H, dt, 8.8 Hz, 0.9 Hz), 7.77 (1H, s), 7.71 (1H, d, 4.3 Hz), 7.63 (2H, d, 8.9 Hz), 7.48 (1H, d, 4.2 Hz), 7.36 (1H, ddd, 8.9 Hz, 6.5 Hz, 0.9 Hz), 7.21 (1H, ddd, 8.8 Hz, 6.5 Hz, 0.9 Hz), 7.08 (2H, dm, 8.9 Hz), 3.91 (3H, s). ^{13}C NMR (125 MHz, CDCl$_3$): 160.2, 149.4, 149.2, 140.7, 139.8, 136.9, 135.6, 132.9, 130.6, 127.4, 125.3, 125.3, 124.9, 124.7, 123.6, 122.2, 121.3, 114.8, 114.0, 74.0, 55.5. HRMS (EI): 398.0544 [calc'd for M$^+$: 398.0542]

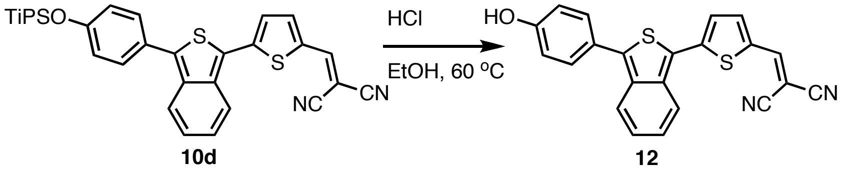


8c (7.0 mg, 0.018 mmol) and Lawesson's reagent (70 mg, 0.17 mmol) were dissolved in dry dichloromethane (7 ml) in a Schlenk flask and the solution was cooled to -78 °C. Anhydrous oxygen was bubbled through the reaction mixture for 5 minutes, after which the flask was sealed, and the reaction mixture was allowed to warm to room temperature and was stirred at room temperature for 7 hours. Malonitrile (80 mg, 2.4 mmol) was then added along with triethylamine (.1 ml) and the solution was stirred at room temperature under argon for 30 minutes. The reaction mixture was purified by flash chromatography over silica gel (dichloromethane) to afford **10c** as a blue solid (4.9 mg, 0.012 mmol, 67% yield). ^{1}H NMR (300 MHz, CDCl$_3$): 8.07 (1H, d, 8.9 Hz), 7.90 (1H, d, 8.8 Hz), 7.74 (1H, s), 7.68 (1H, d, 4.5 Hz), 7.59 (2H, d, 9.0 Hz), 7.45 (1H, d, 4.5 Hz), 7.35 (1H, ddd, 8.9 Hz, 6.3 Hz, 0.9 Hz), 7.18 (1H, ddd, 8.9 Hz, 6.5 Hz, 0.9 Hz), 6.85 (2H, d, 8.9 Hz), 3.08 (6H, s). ^{13}C NMR (125 MHz, DMF-d$_7$): 152.4, 152.2, 149.3, 143.6, 143.4, 138.1, 135.9, 134.0, 131.2, 128.8, 126.2, 125.9, 123.9, 123.0, 122.2, 121.0, 116.3, 115.8, 113.8, 73.5, 40.6. HRMS (EI): 411.0863 [calc'd for M$^+$: 411.0858]



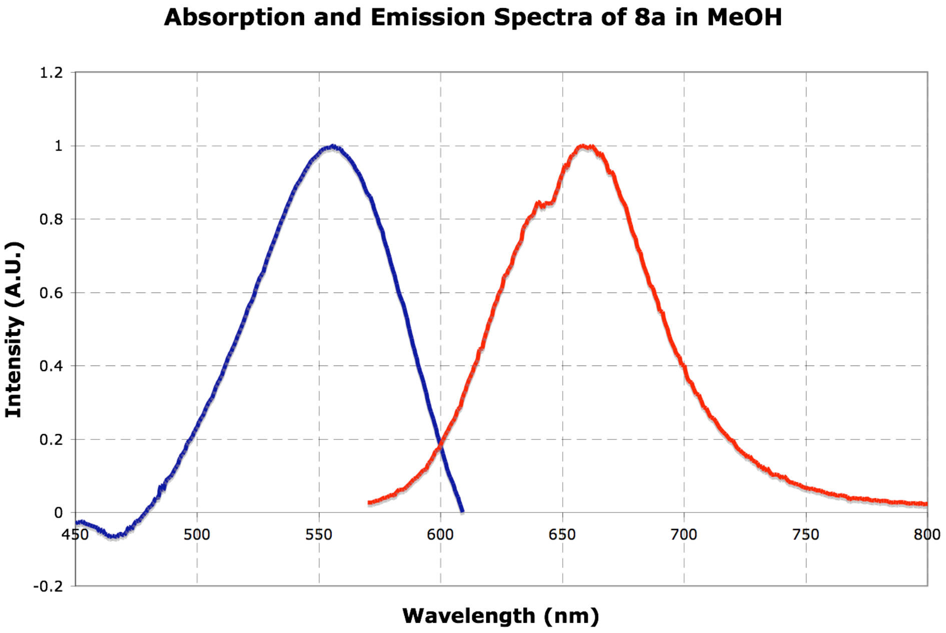
8d (13.7 mg, 0.026 mmol) and Lawesson's reagent (53 mg, 0.13 mmol) were dissolved in dry dichloromethane (10 ml) in a Schlenk flask and the solution was cooled to -78 °C.

Anhydrous oxygen was bubbled through the reaction mixture for 5 minutes, after which the flask was sealed, and the reaction mixture was allowed to warm to room temperature and was stirred at room temperature for 4 hours. The solution was then opened to air and stirred for an additional 3 hours at room temperature. The reaction mixture was purified by flash chromatography over silica gel (dichloromethane) to afford **10c** as a blue solid (13.3 mg, 0.025 mmol, 96% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 8.06 (1H, d, 8.9 Hz), 7.85 (1H, d, 8.9 Hz), 7.76 (1H, s), 7.70 (1H, d, 4.3 Hz), 7.55 (2H, d, 8.7 Hz), 7.47 (1H, d, 4.3 Hz), 7.35 (1H, ddd, 8.9 Hz, 6.5 Hz, 0.9 Hz), 7.20 (1H, ddd, 8.9 Hz, 6.3 Hz, 0.9 Hz), 1.31 (3H, sp, 7.0 Hz), 1.16 (18H, d, 7.1 Hz). ^{13}C NMR (125 MHz, $CDCl_3$): 157.1, 149.4, 149.2, 141.0, 139.8, 136.9, 135.6, 132.9, 130.5, 127.4, 125.5, 124.8, 124.7, 123.5, 122.3, 121.2, 120.7, 114.8, 114.0, 74.0, 17.9, 12.7. HRMS (EI): 540.1719 [calc'd for M^+: 540.1720]

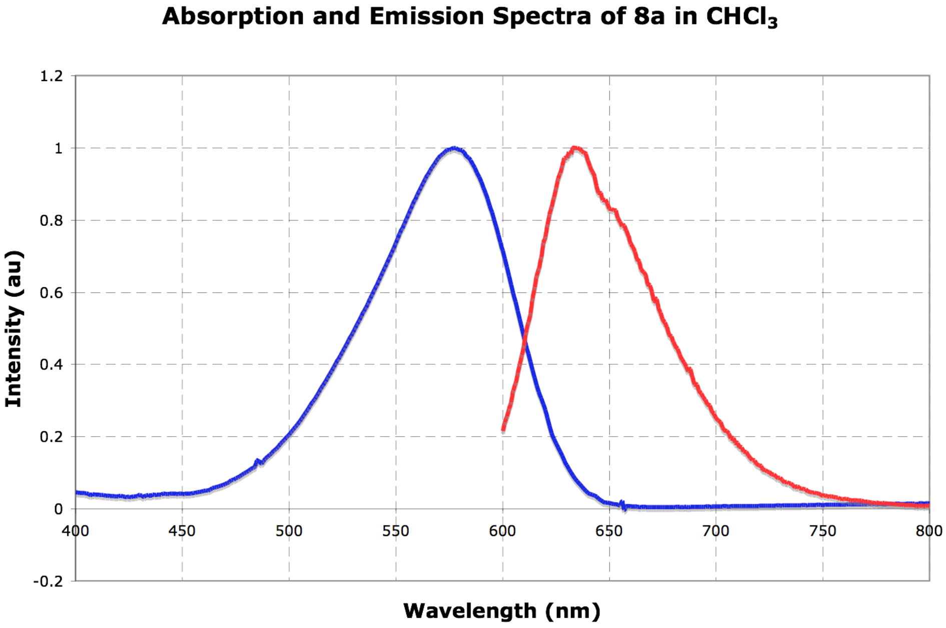


10d (34 mg, 0.063 mmol) was dissolved in ethanol (16 ml, 200 proof) at 60 °C. Hydrochloric acid (1.66 ml, 36%) was added and the reaction was stirred at 60 °C under argon for 18 hours. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, and washed with water, saturated aqueous sodium bicarbonate, and brine, and was then dried over magnesium sulfate and concentrated in vacuo. Flash chromatography (2:1 ethyl acetate:hexane) afforded **12** as a purple solid (13.5 mg, 0.035 mmol, 56% yield). ^{1}H NMR (500 MHz, DMSO-d_6): 9.17 (1H, s), 7.70 (1H, s), 7.10 (1H, dd, 8.9 Hz, 0.8 Hz), 7.04 (1H, d, 4.1 Hz), 6.95 (1H, dd, 8.9 Hz, 0.8 Hz), 6.83 (1H, dd, 4.1 Hz, 0.9 Hz), 6.67 (2H, d, 8.7 Hz), 6.54 (1H, dd, 8.9 Hz, 6.3 Hz), 6.38 (1H, dd, 8.9 Hz, 6.3 Hz), 6.09 (2H, d, 8.7 Hz). ^{13}C NMR (125 MHz, DMSO-d_6): 158.6, 151.7, 147.4, 142.3, 140.6, 136.2, 134.6, 132.8, 130.6, 127.7, 125.4, 125.11, 122.9, 122.5, 122.3, 120.8, 116.5, 115.1, 114.4, 72.4. HRMS (ESI): 383.0310 [calc'd for $M-H^-$: 383.0318]

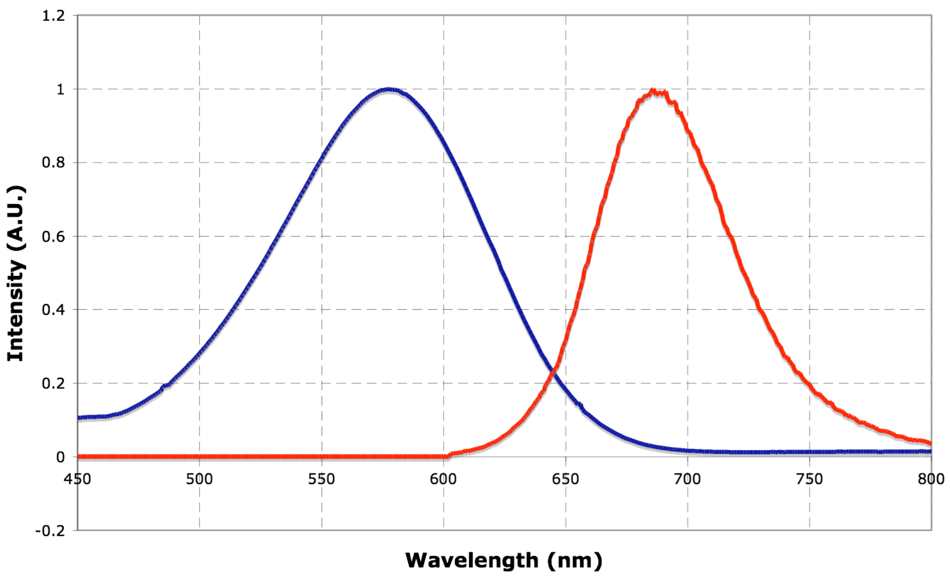
Absorption and Emission Spectra of 8a-c, 10a-c, 11, and 12



Abs λ_{max} = 556 nm; Em λ_{max} = 658 nm; Φ = 0.077

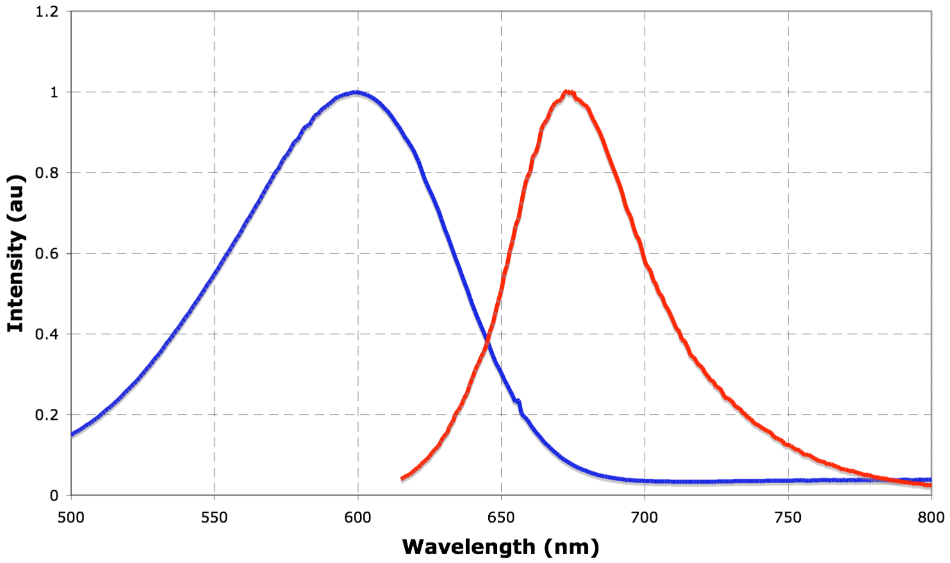


Abs λ_{max} = 578 nm; Em λ_{max} = 635 nm; Φ = 0.075



Absorption and Emssion spectra 8b in MeOH

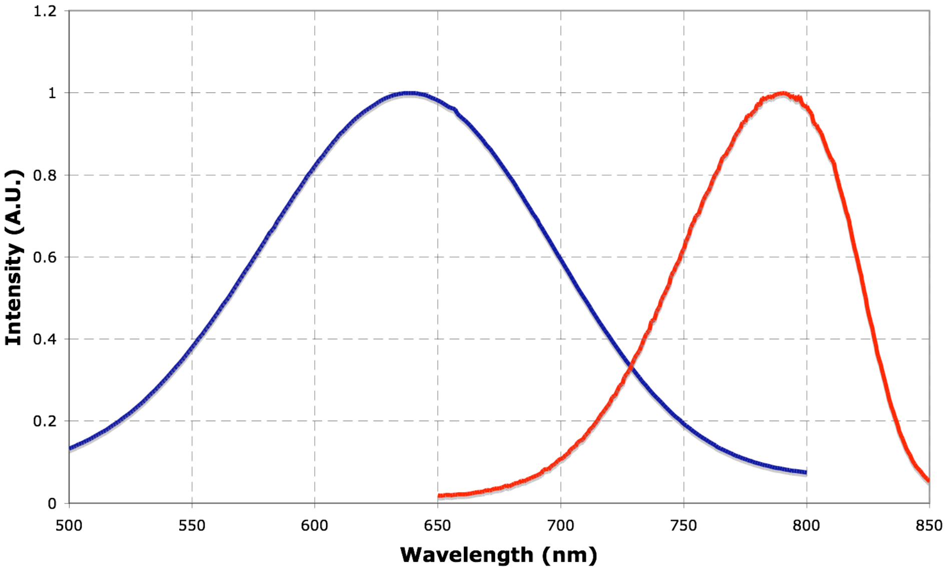
Abs λ_{max} = 578 nm; Em λ_{max} = 686 nm; Φ = 0.078



Absorption and Emission spectra for 8b in $CHCl_3$

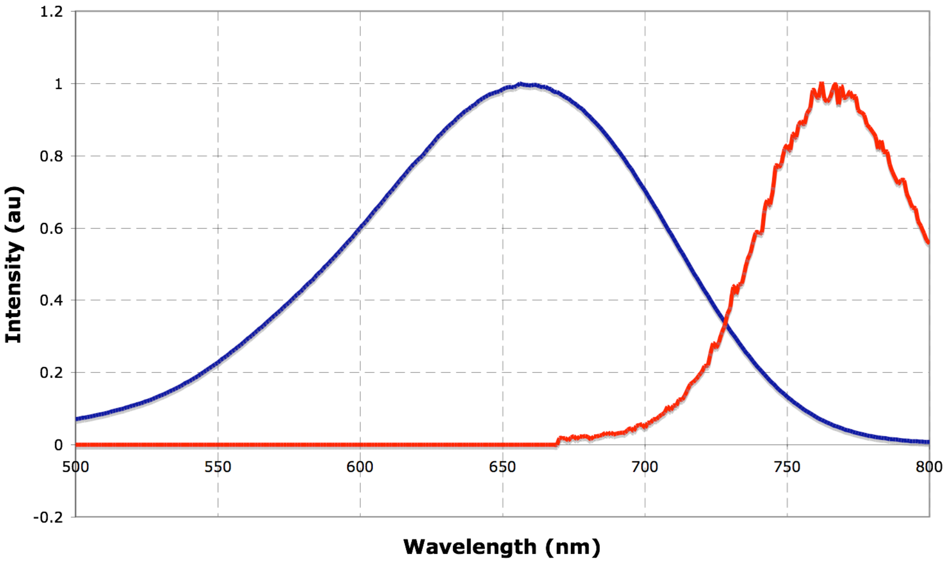
Abs λ_{max} = 599 nm; Em λ_{max} = 675 nm; Φ = 0.16

Absorption and Emission Spectra of 8c in MeOH

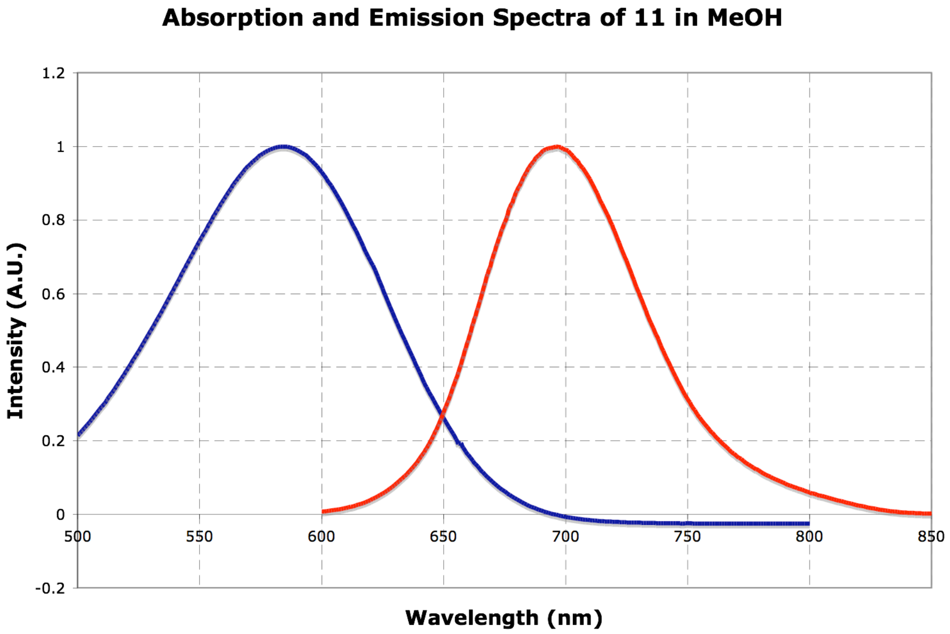


Abs λ_{max} = 637 nm; Em λ_{max} = 790 nm; Φ = 0.0055

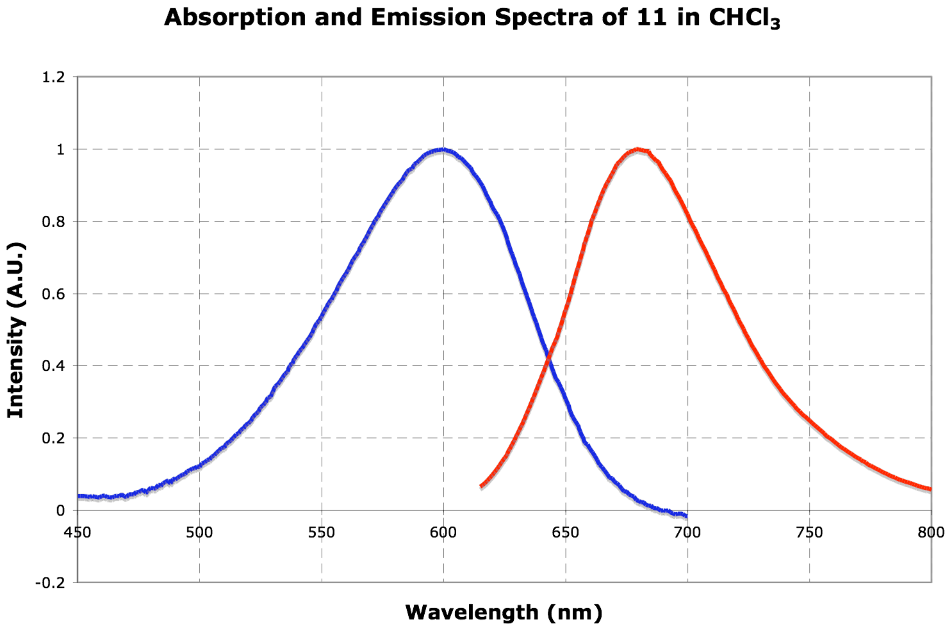
Absorption and Emission Spectra of 8c in $CHCl_3$



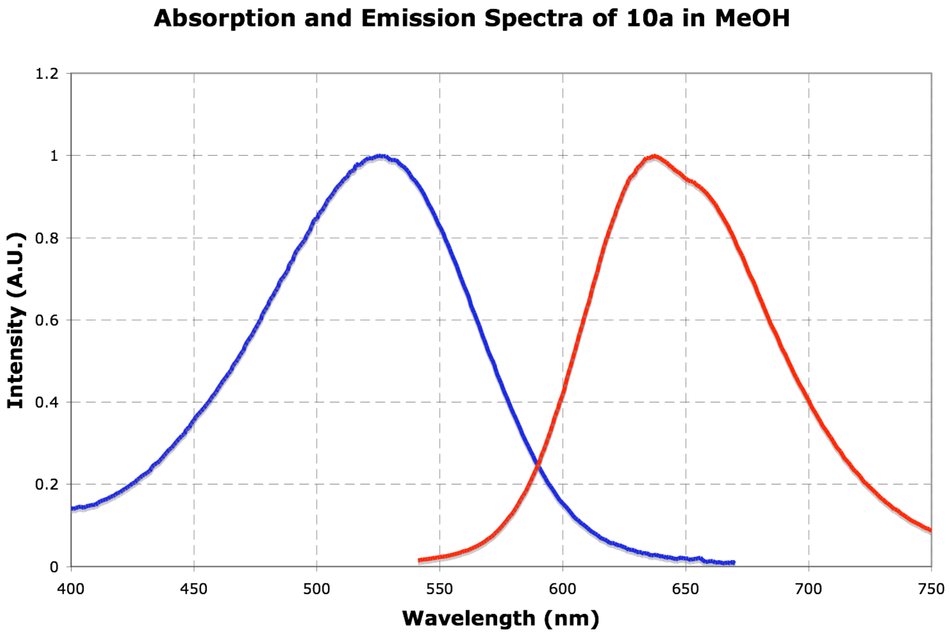
Abs λ_{max} = 656 nm; Em λ_{max} = 762 nm; Φ = 0.046



Abs λ_{max} = 584 nm; Em λ_{max} = 696 nm; Φ = 0.049

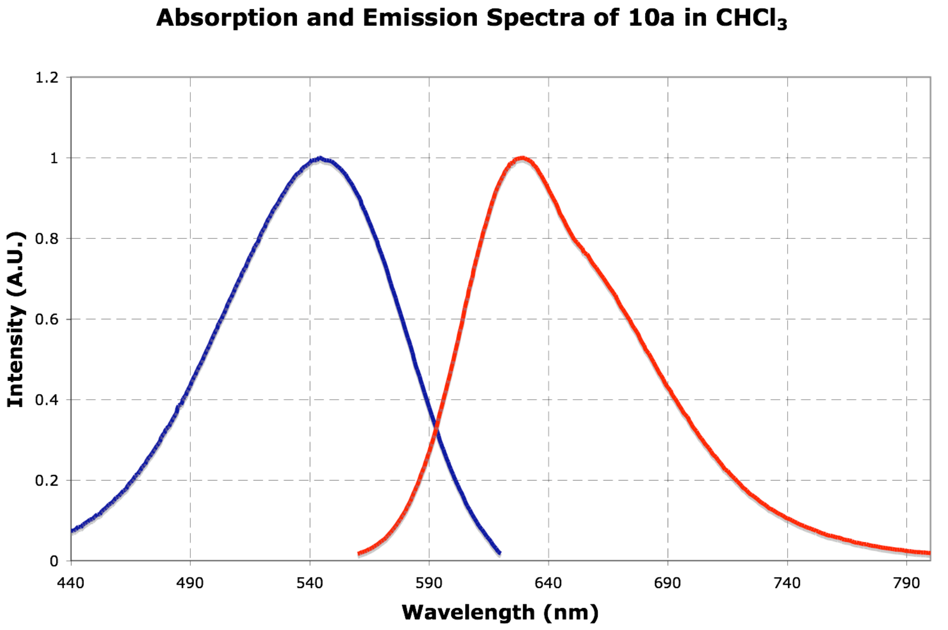


Abs λ_{max} = 600 nm; Em λ_{max} = 679 nm; Φ = 0.12



Absorption and Emission Spectra of 10a in MeOH

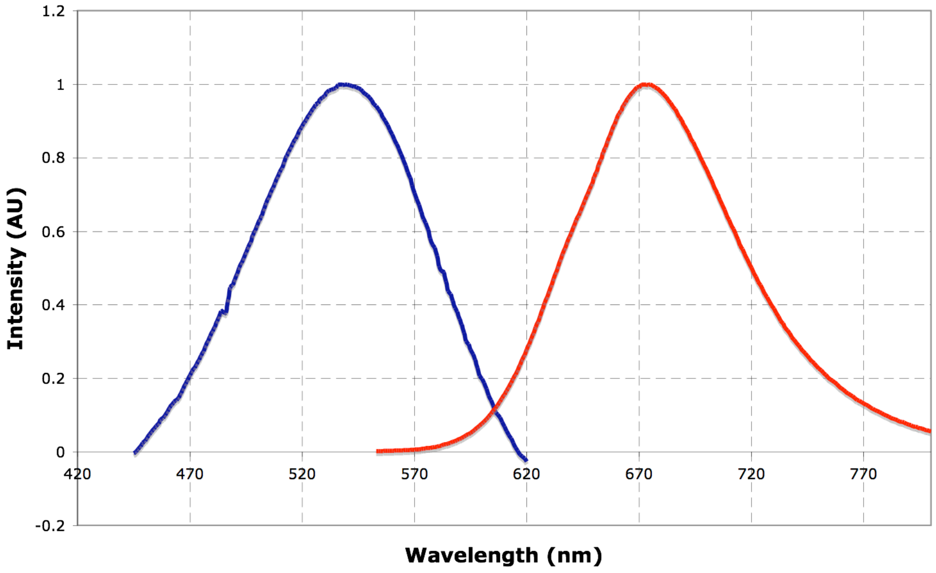
Abs λ_{max} = 525 nm; Em λ_{max} = 637 nm; Φ = 0.061



Absorption and Emission Spectra of 10a in $CHCl_3$

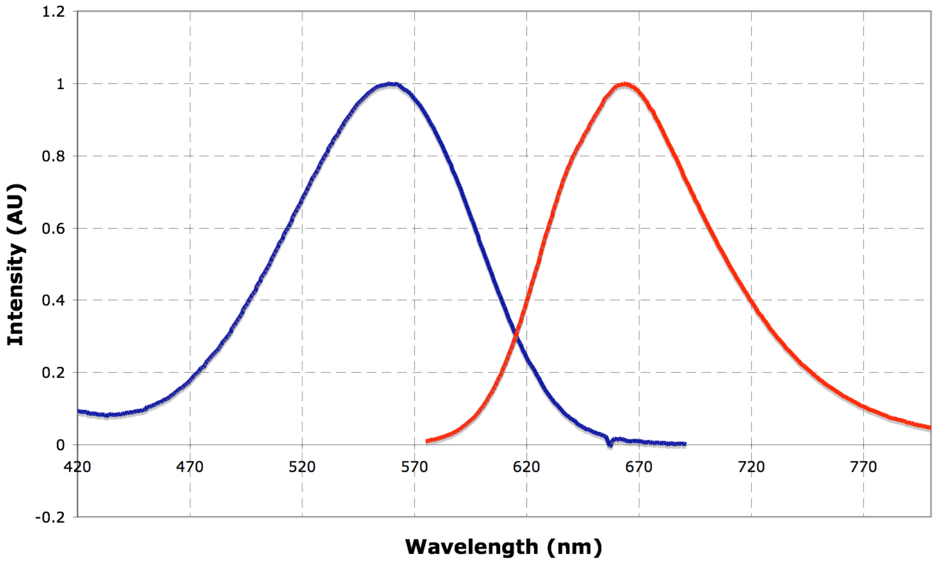
Abs λ_{max} = 544 nm; Em λ_{max} = 629 nm; Φ = 0.079

Absorption and Emission Spectra of 10b in MeOH

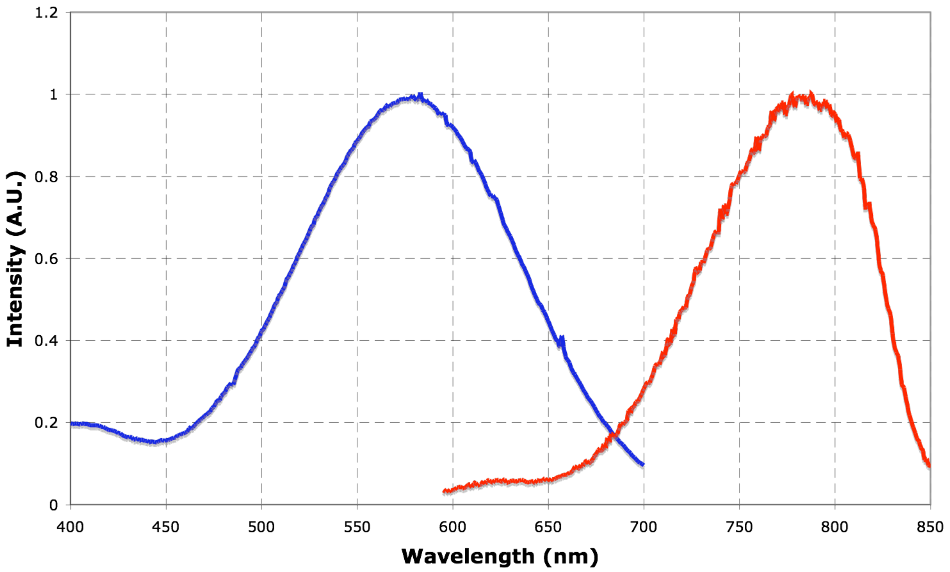


Abs λ_{max} = 537 nm; Em λ_{max} = 672 nm; Φ = 0.046

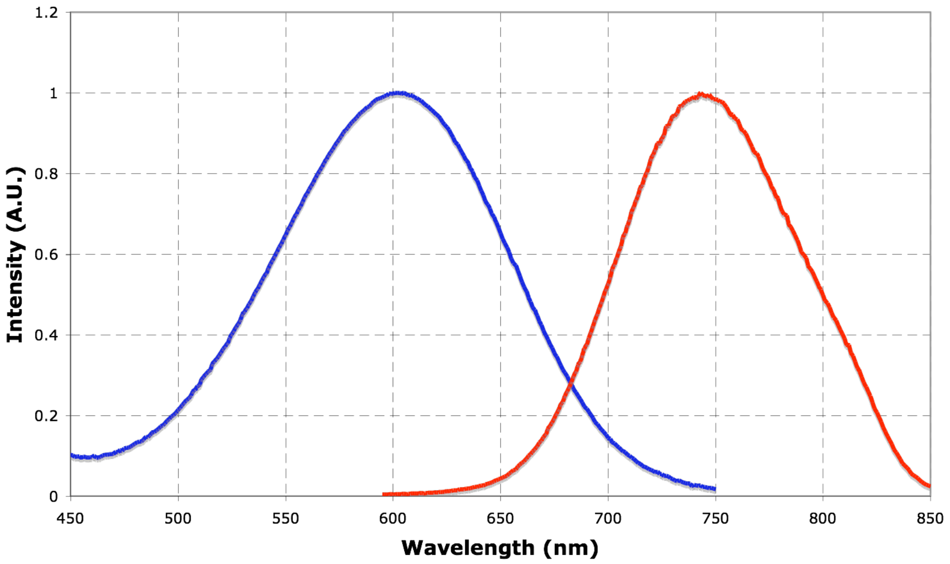
Absorption and Emission Spectra of $10b$ in $CHCl_3$



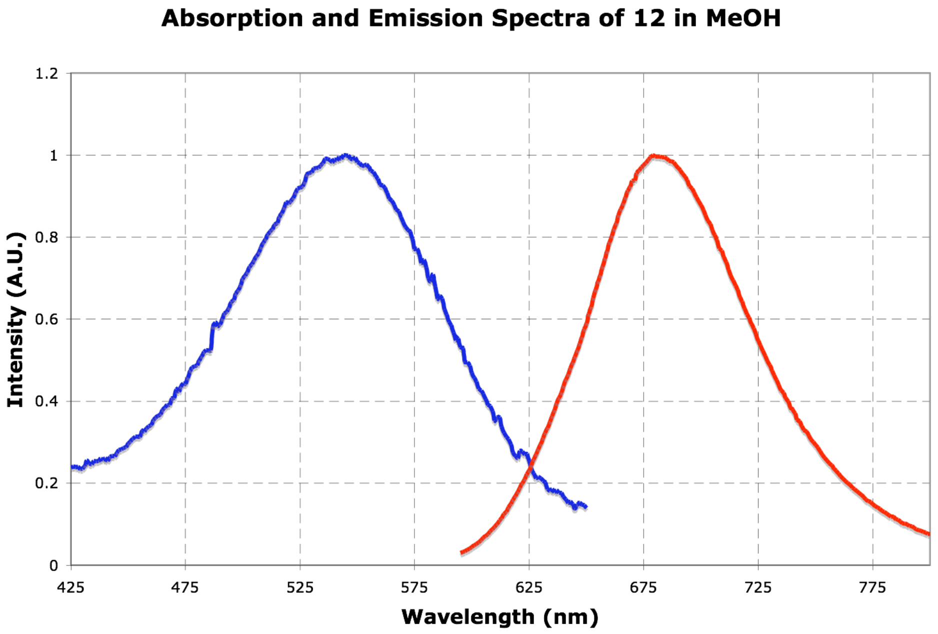
Abs λ_{max} = 559 nm; Em λ_{max} = 663 nm; Φ = 0.099


Absorption and Emission Spectra for 10c in MeOH

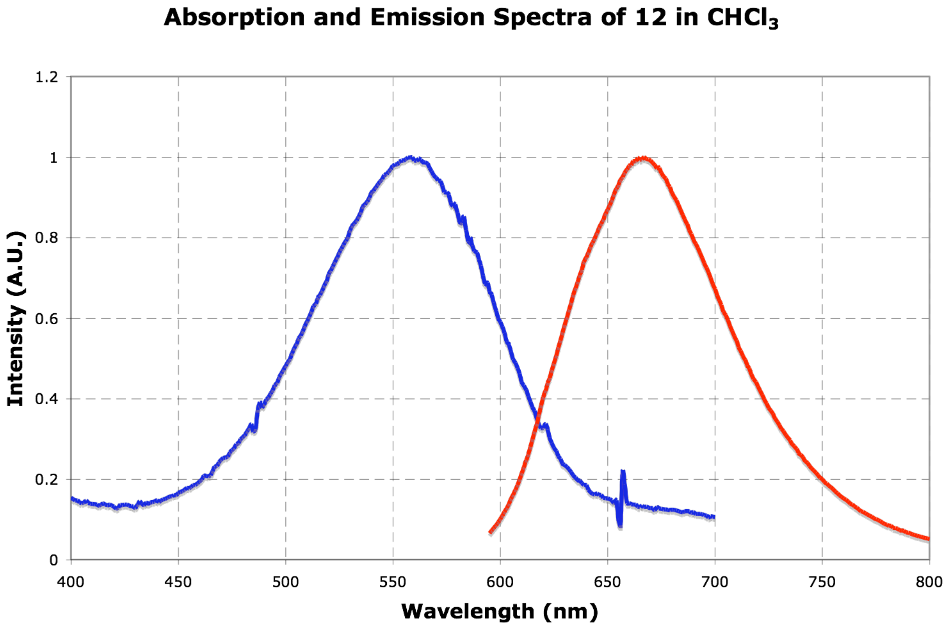
Abs λ_{max} = 579 nm; Em λ_{max} = 785 nm; Φ = 0.0015


Absorption and Emission Spectra of 10c in $CHCl_3$

Abs λ_{max} = 604 nm; Em λ_{max} = 743 nm; Φ = 0.021



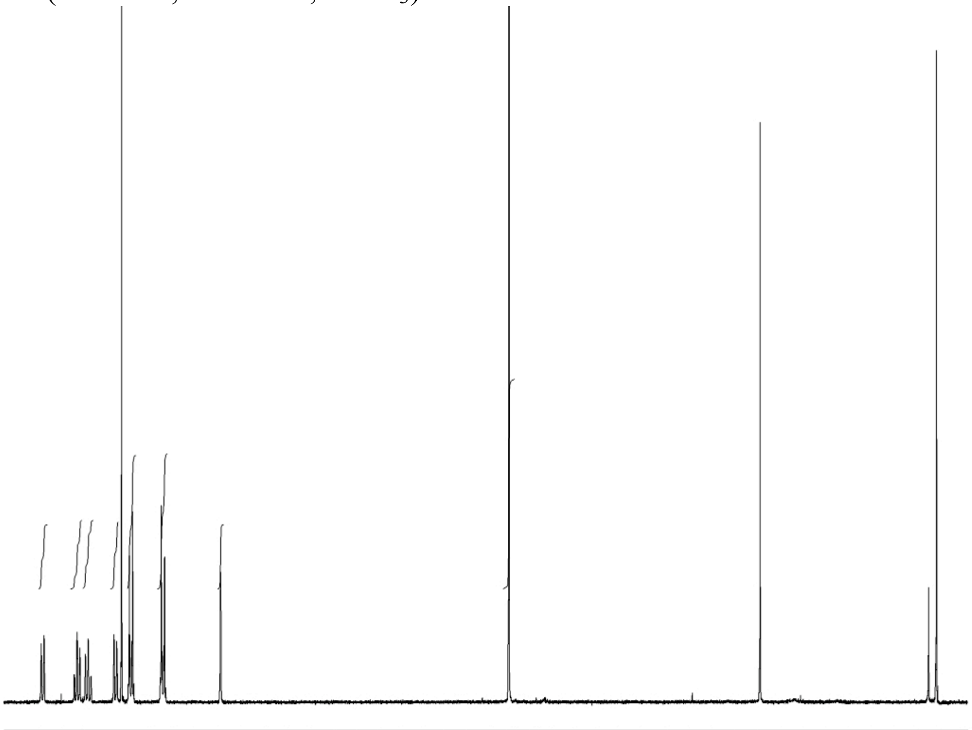
Abs λ_{max} = 545 nm; Em λ_{max} = 684 nm; Φ = 0.023



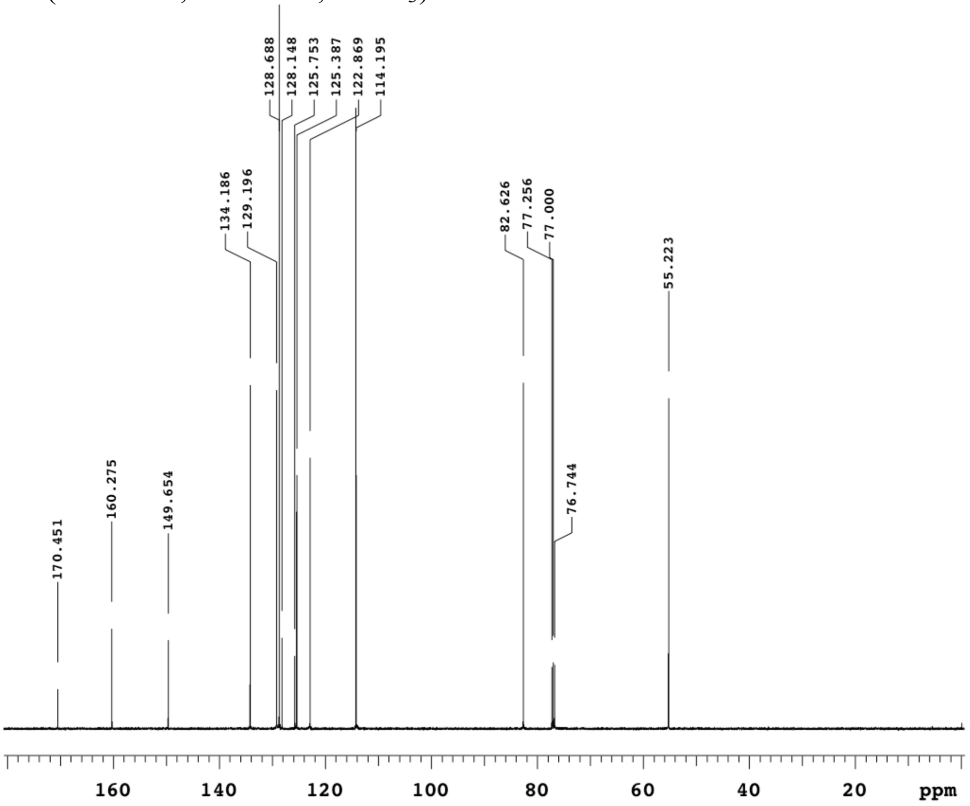
Abs λ_{max} = 559 nm; Em λ_{max} = 667 nm; Φ = 0.071

^{1}H and ^{13}C NMR Spectra

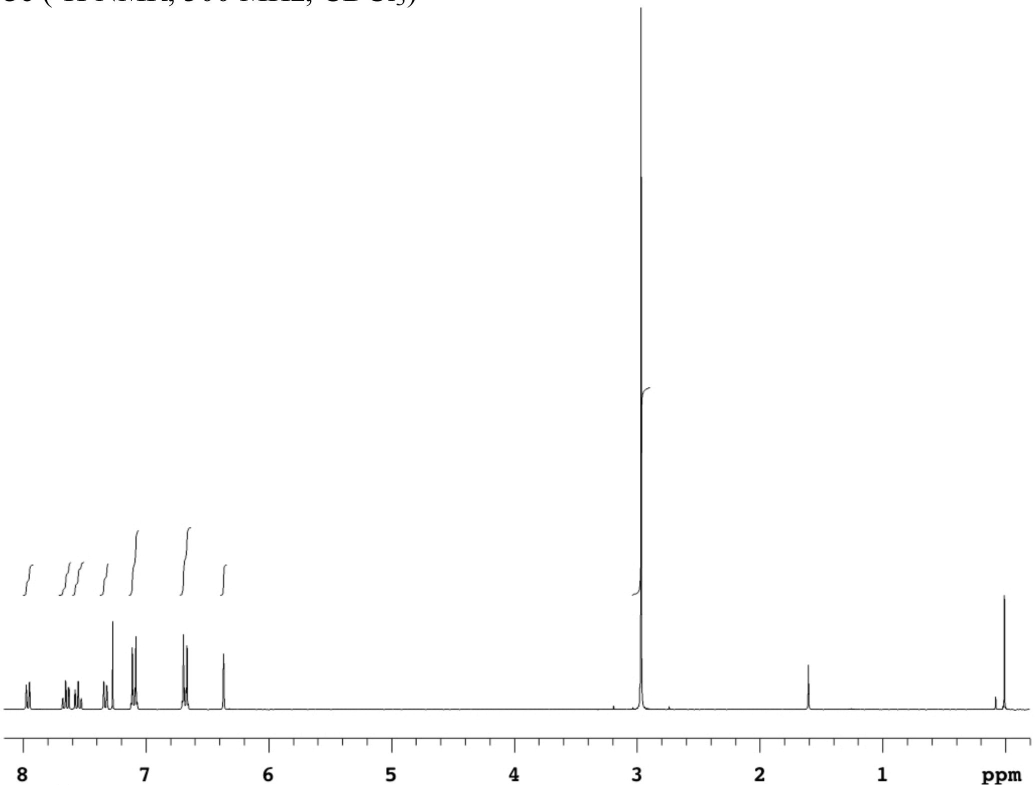
5b (^{1}H NMR, 300 MHz, CDCl$_3$)



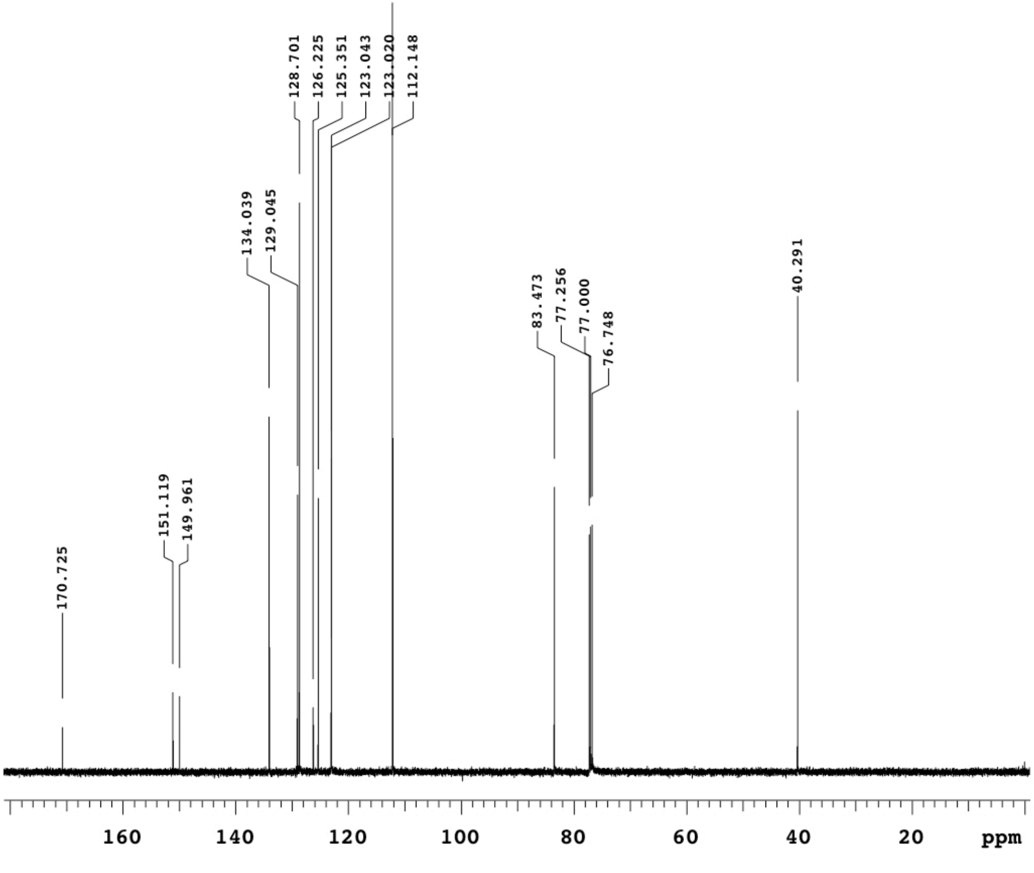
5b (^{13}C NMR, 500 MHz, CDCl$_3$)



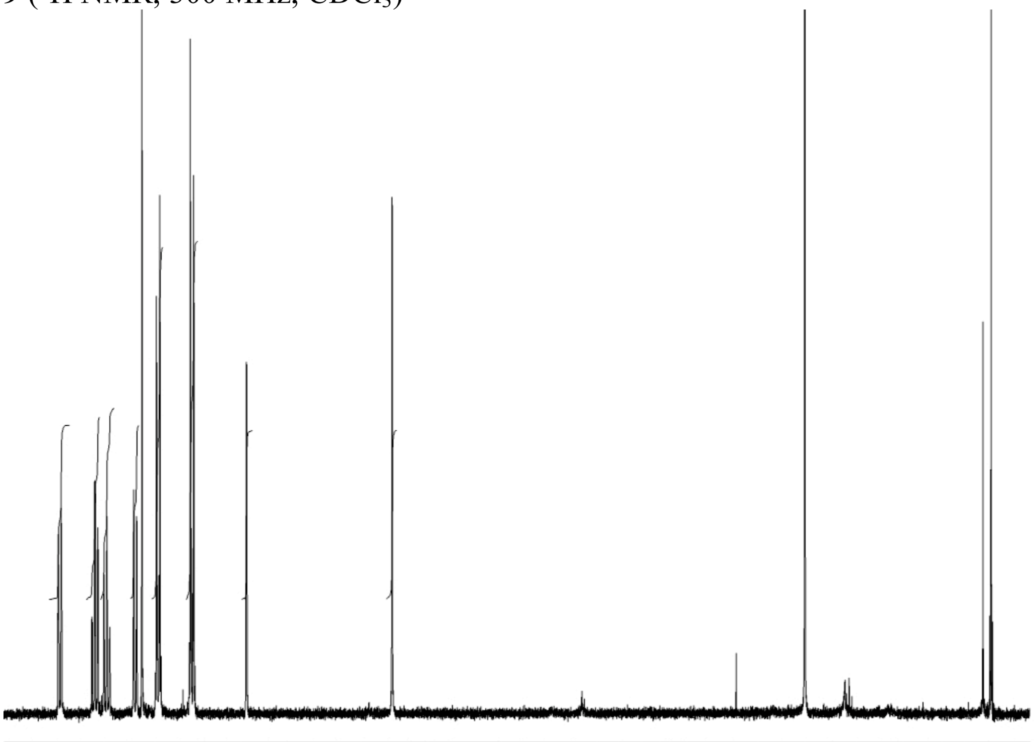
5c (^{1}H NMR, 300 MHz, CDCl$_3$)



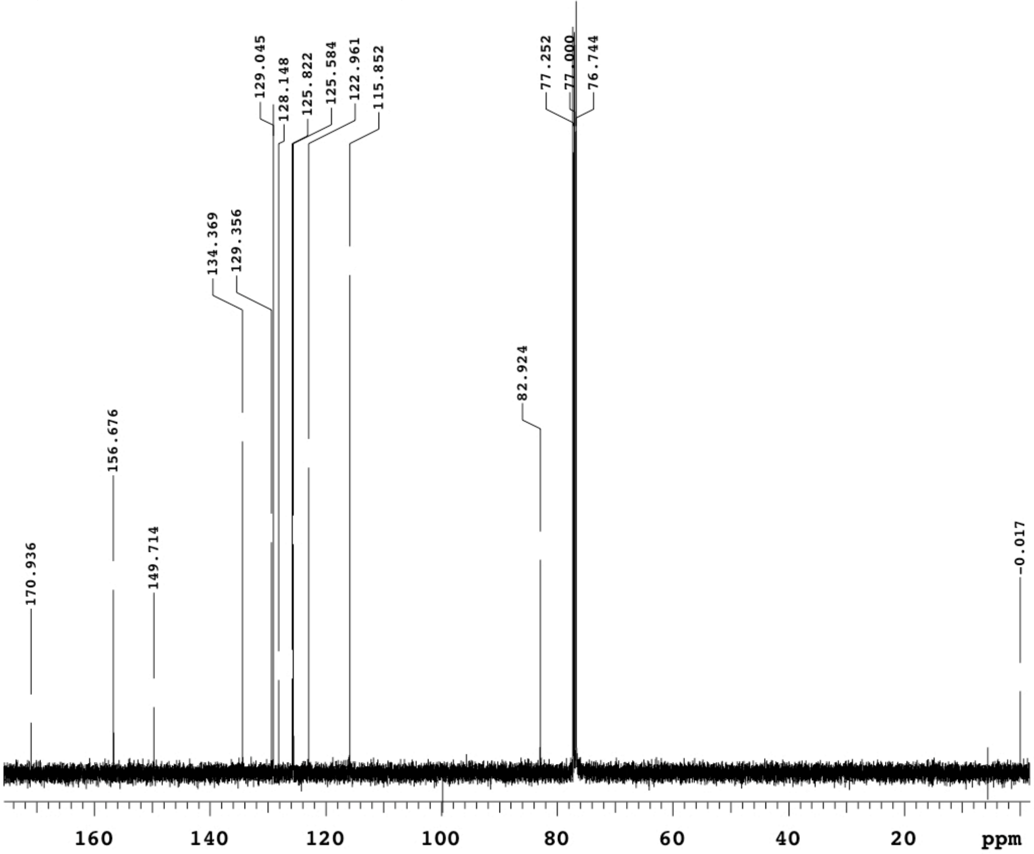
5c (^{13}C NMR, 125 MHz, CDCl$_3$)



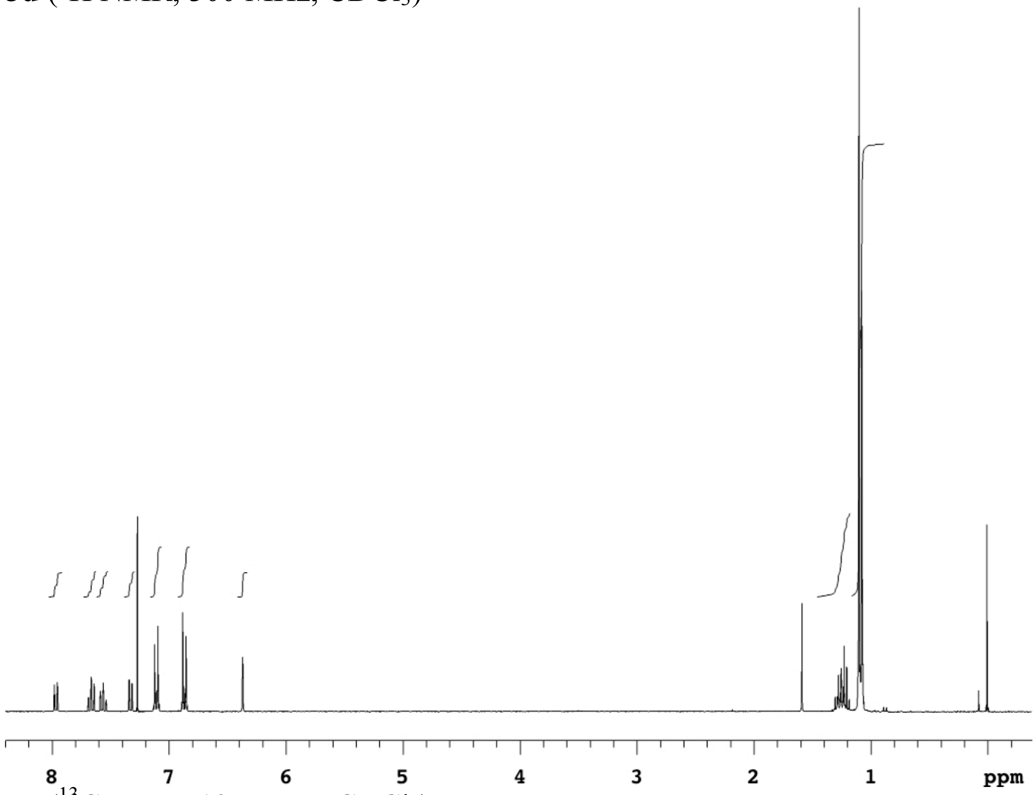
9 (^{1}H NMR, 300 MHz, CDCl$_3$)



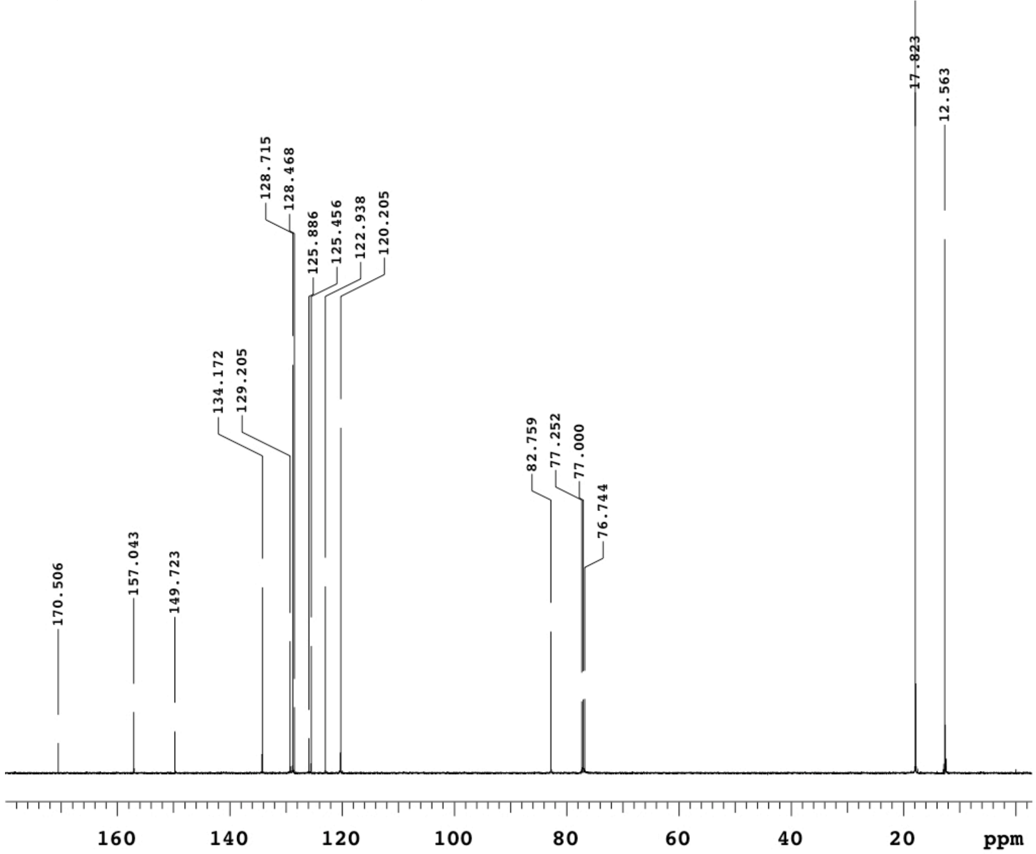
9 (^{13}C NMR, 125 MHz, CDCl$_3$)



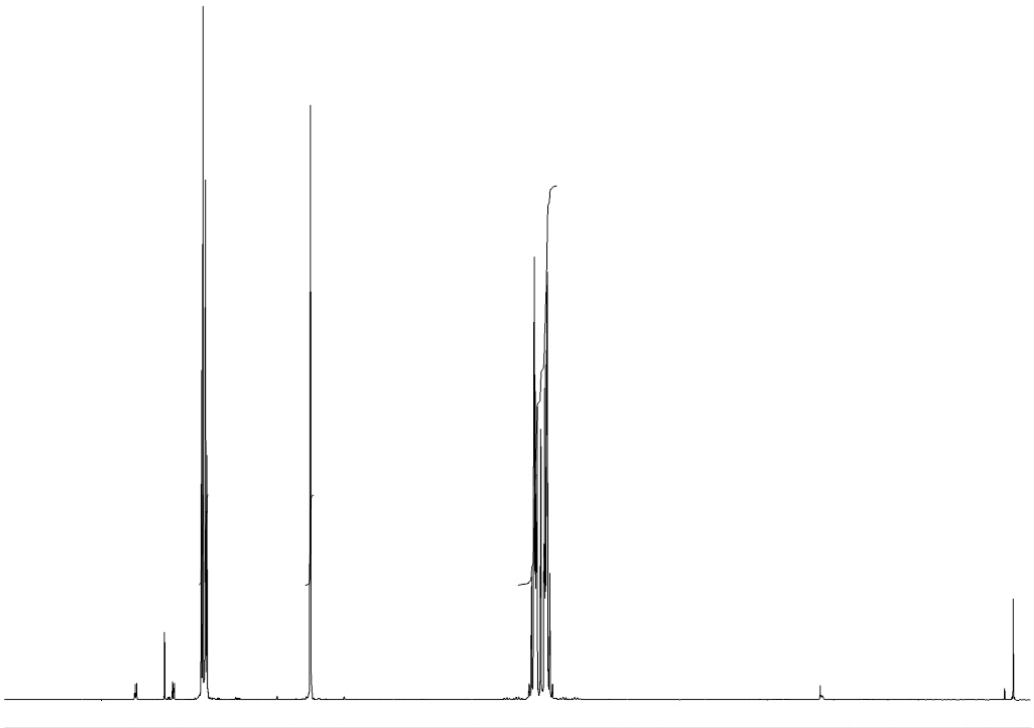
5d (^{1}H NMR, 300 MHz, CDCl$_3$)



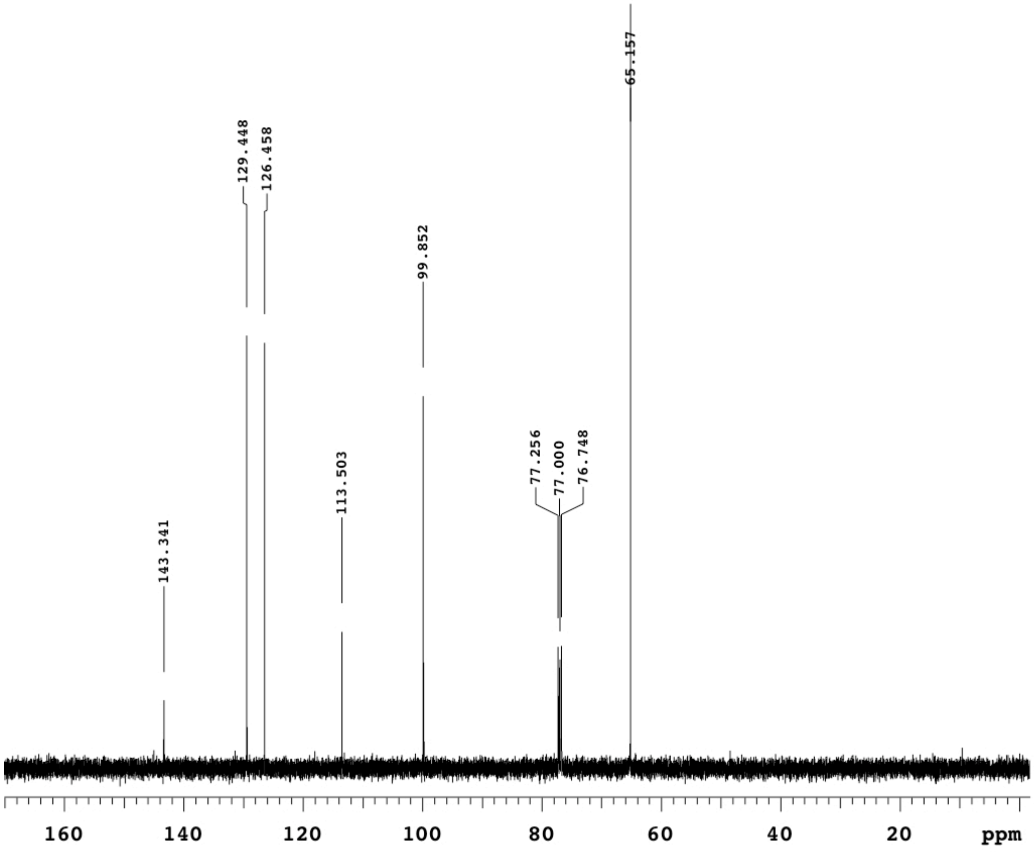
5d (^{13}C NMR, 125 MHz, CDCl$_3$)



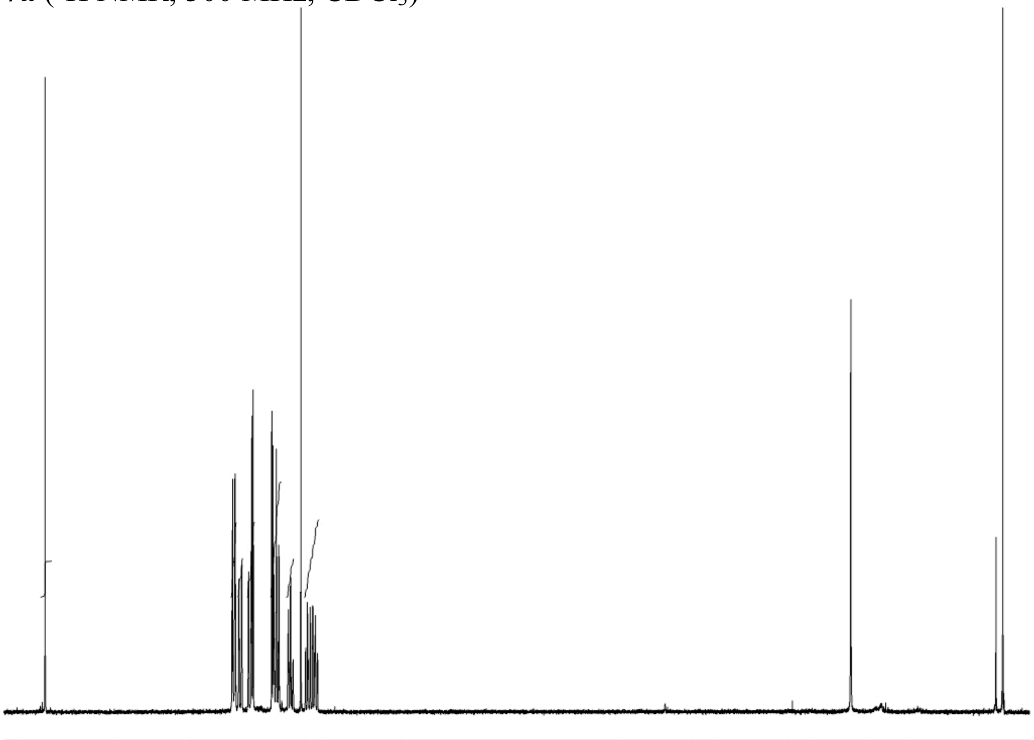
6 (^{1}H NMR, 300 MHz, CDCl$_3$)



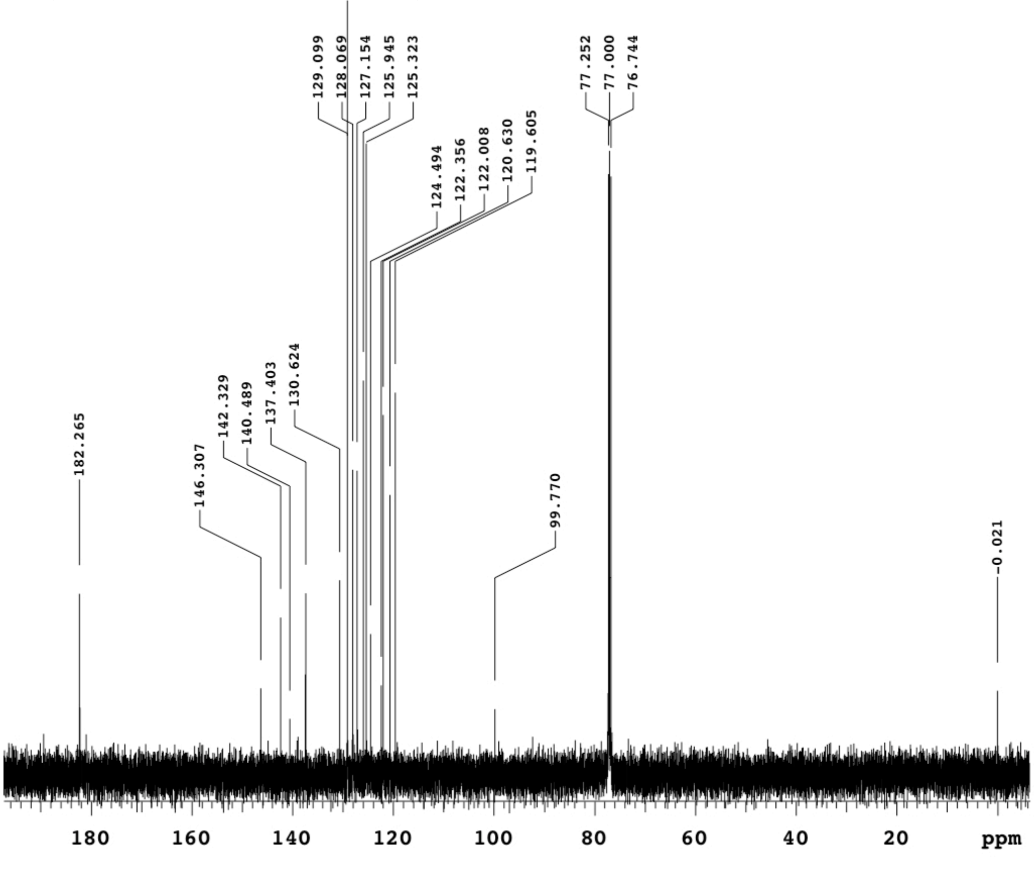
6 (^{13}C NMR, 125 MHz, CDCl$_3$)



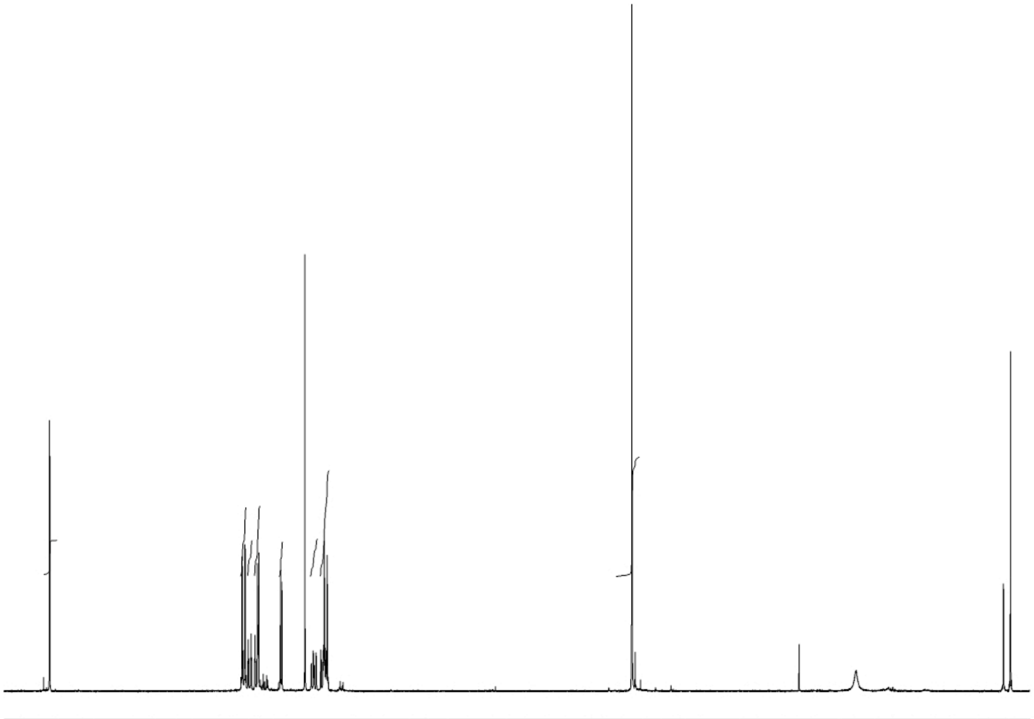
7a (^{1}H NMR, 300 MHz, CDCl$_3$)



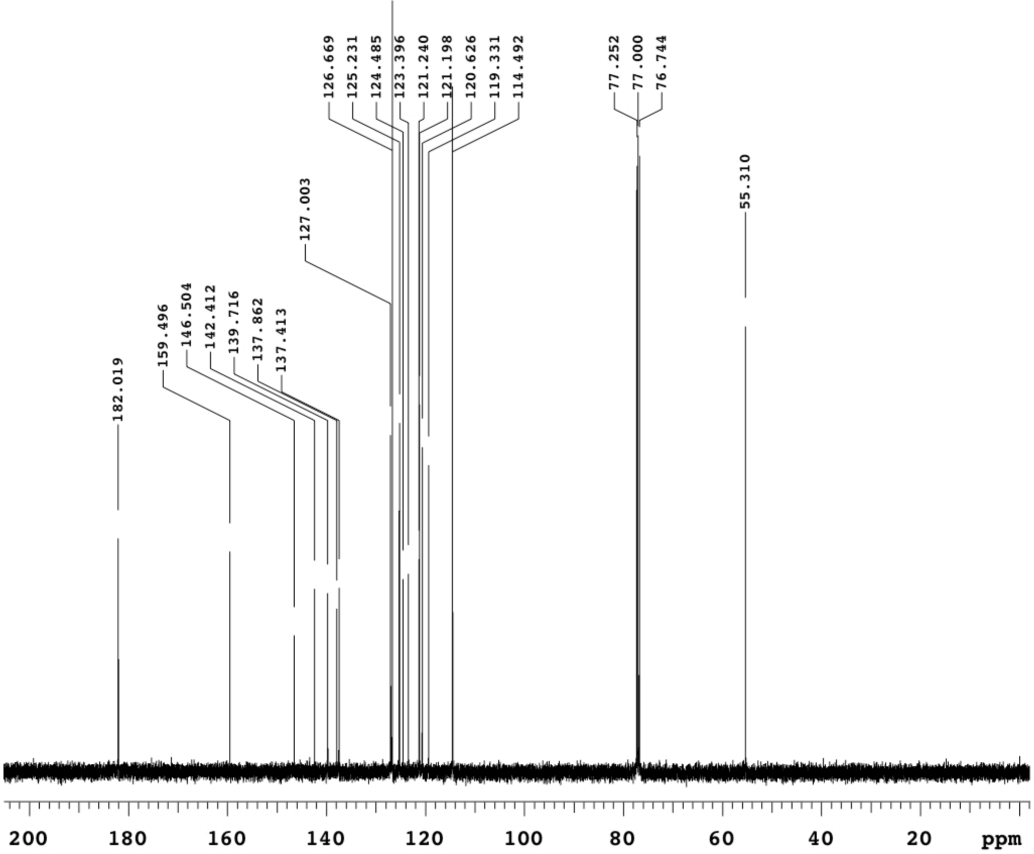
7a (^{13}C NMR, 125 MHz, CDCl$_3$)



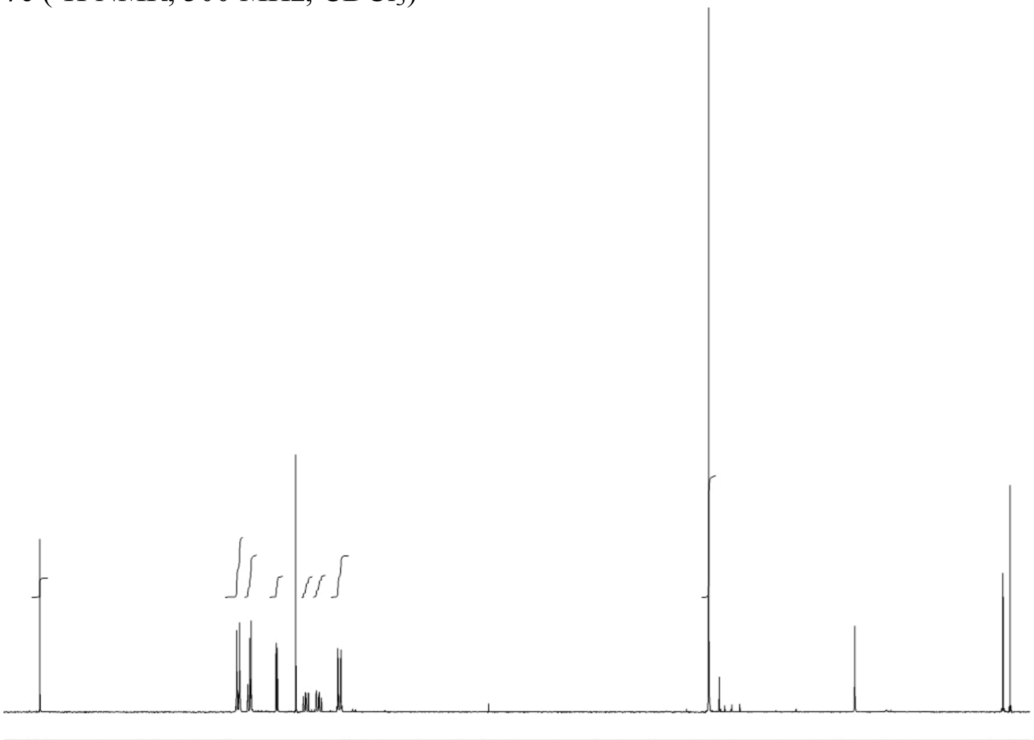
7b (^{1}H NMR, 300 MHz, CDCl$_3$)



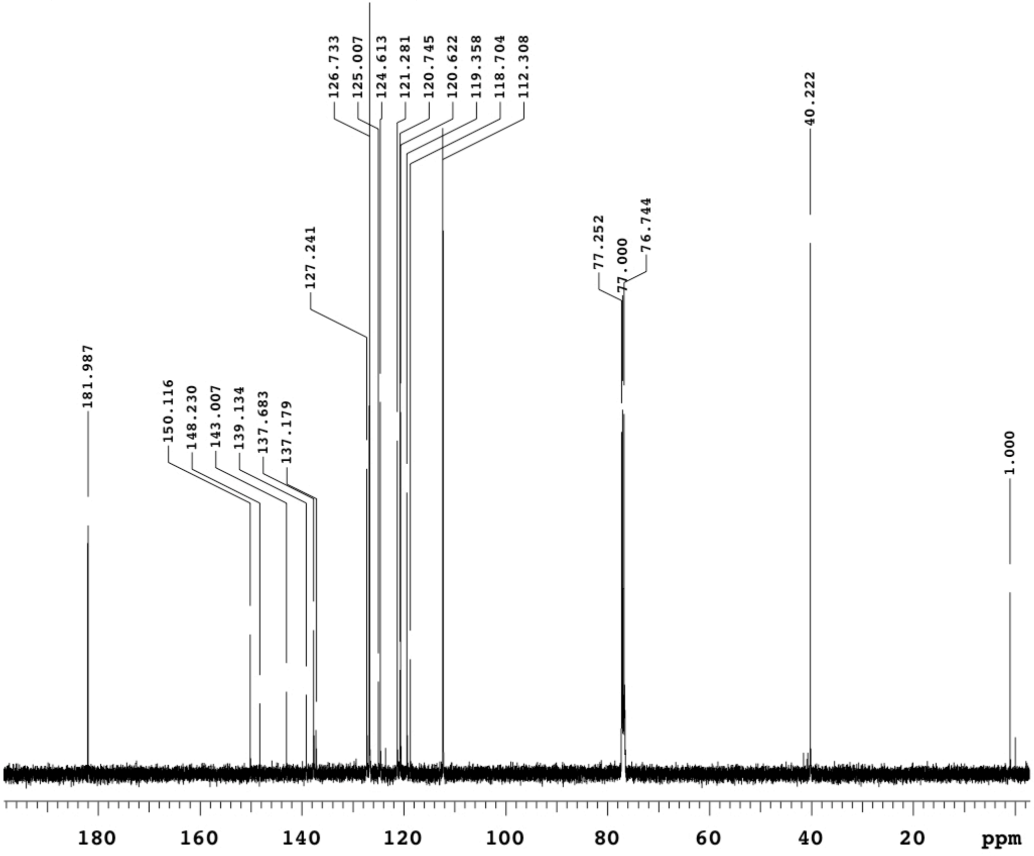
7b (^{13}C NMR, 125 MHz, CDCl$_3$)



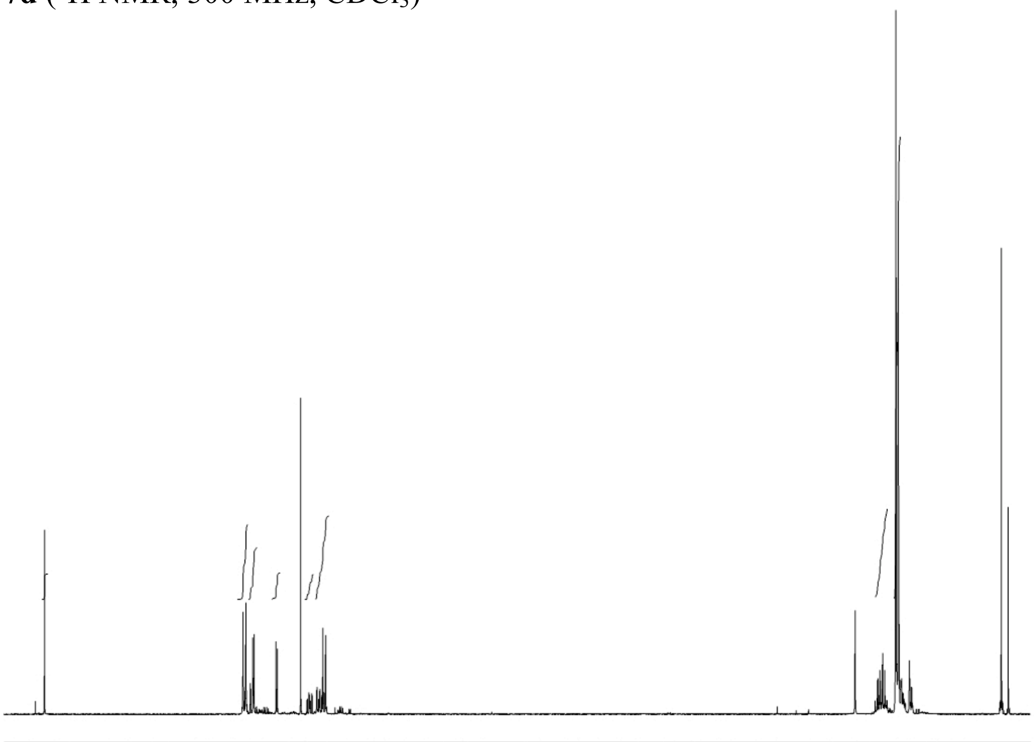
7c (^{1}H NMR, 300 MHz, $CDCl_3$)



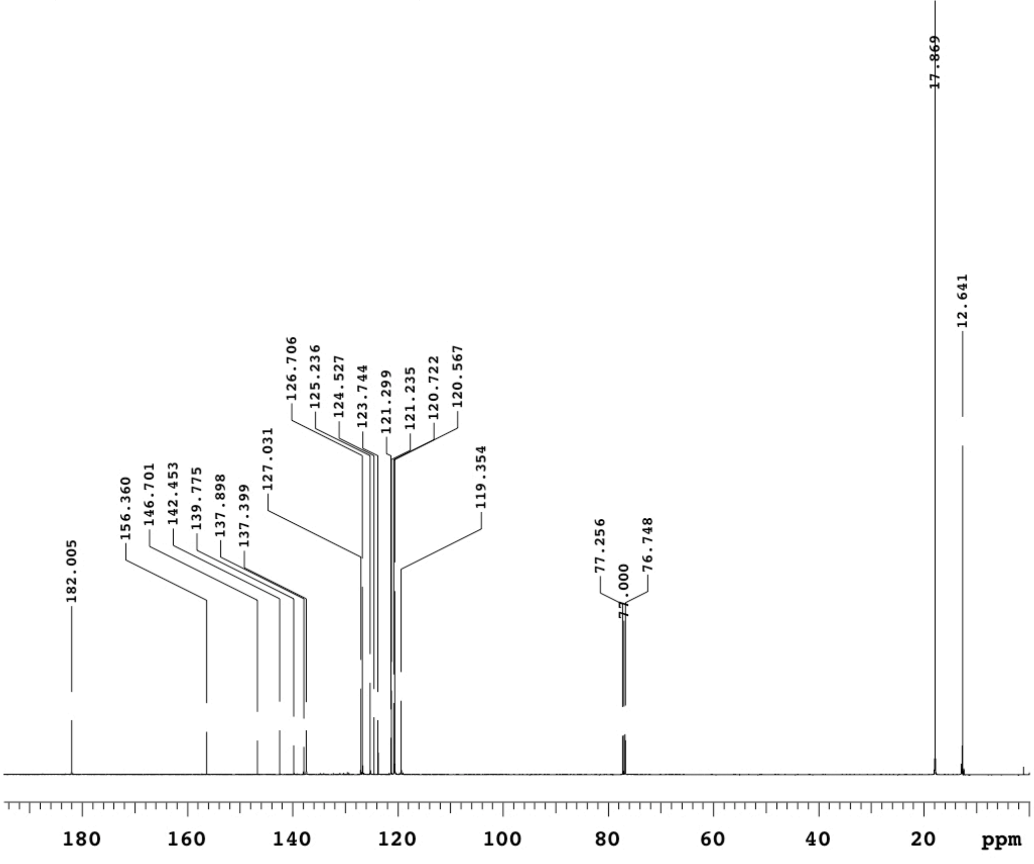
7c (^{13}C NMR, 125 MHz, $CDCl_3$)



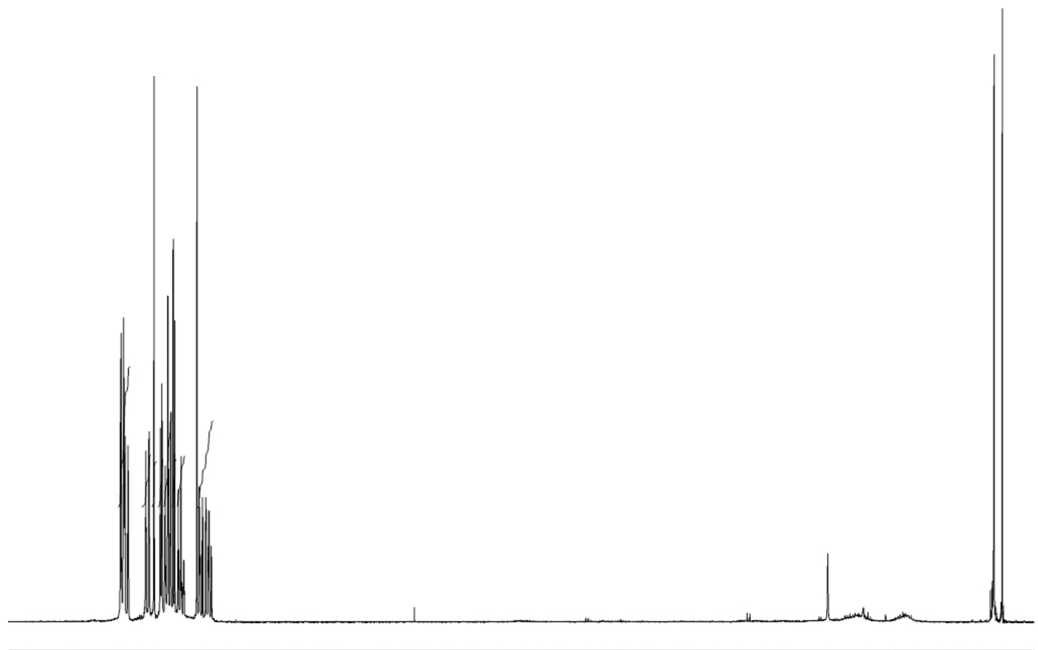
7d (^{1}H NMR, 300 MHz, CDCl$_3$)



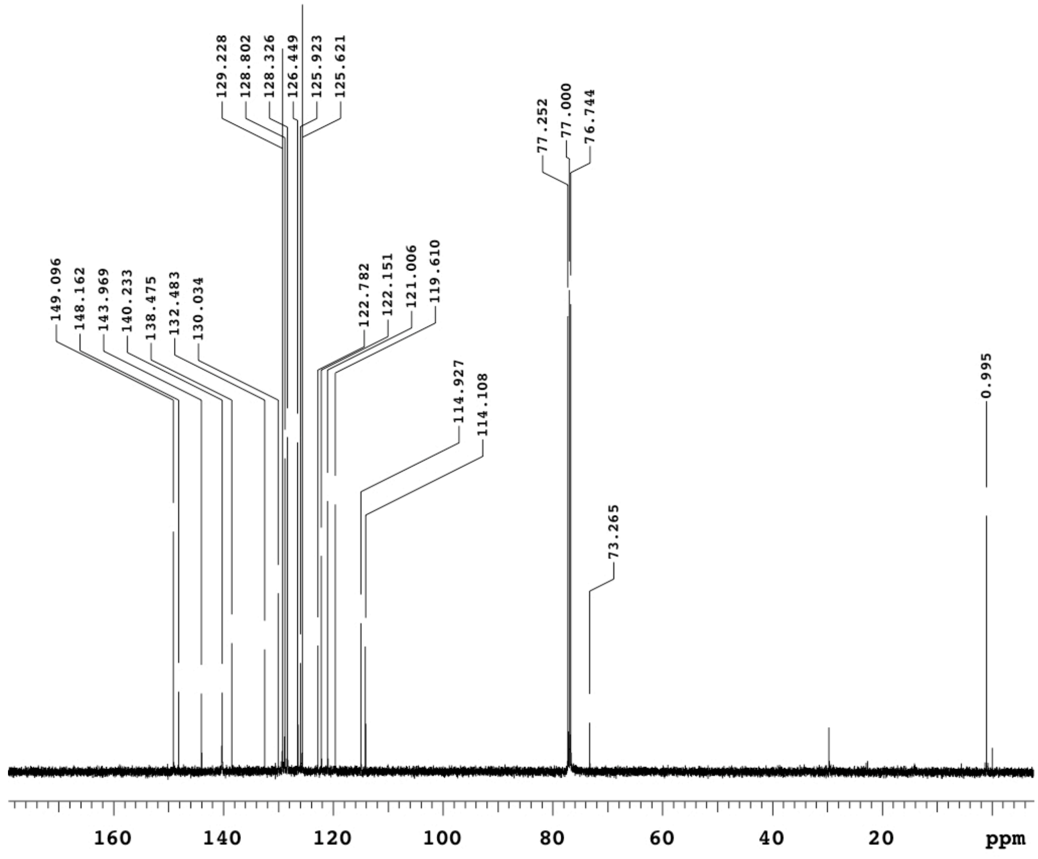
7d (^{13}C NMR, 125 MHz, CDCl$_3$)



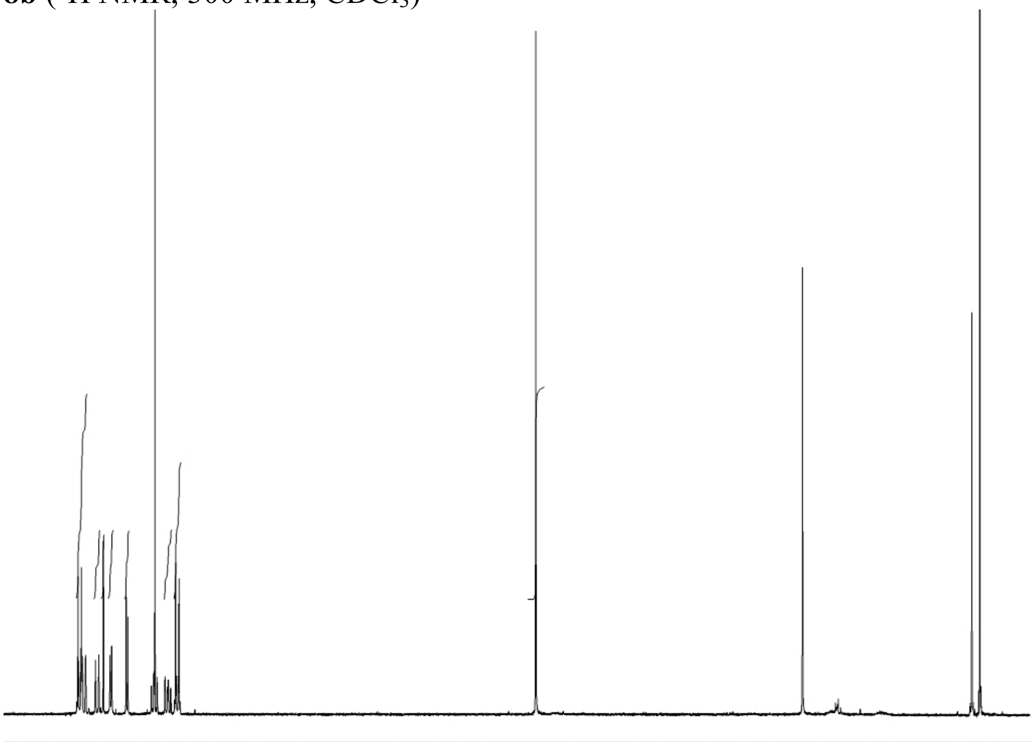
8a (^{1}H NMR, 300 MHz, CDCl$_3$)



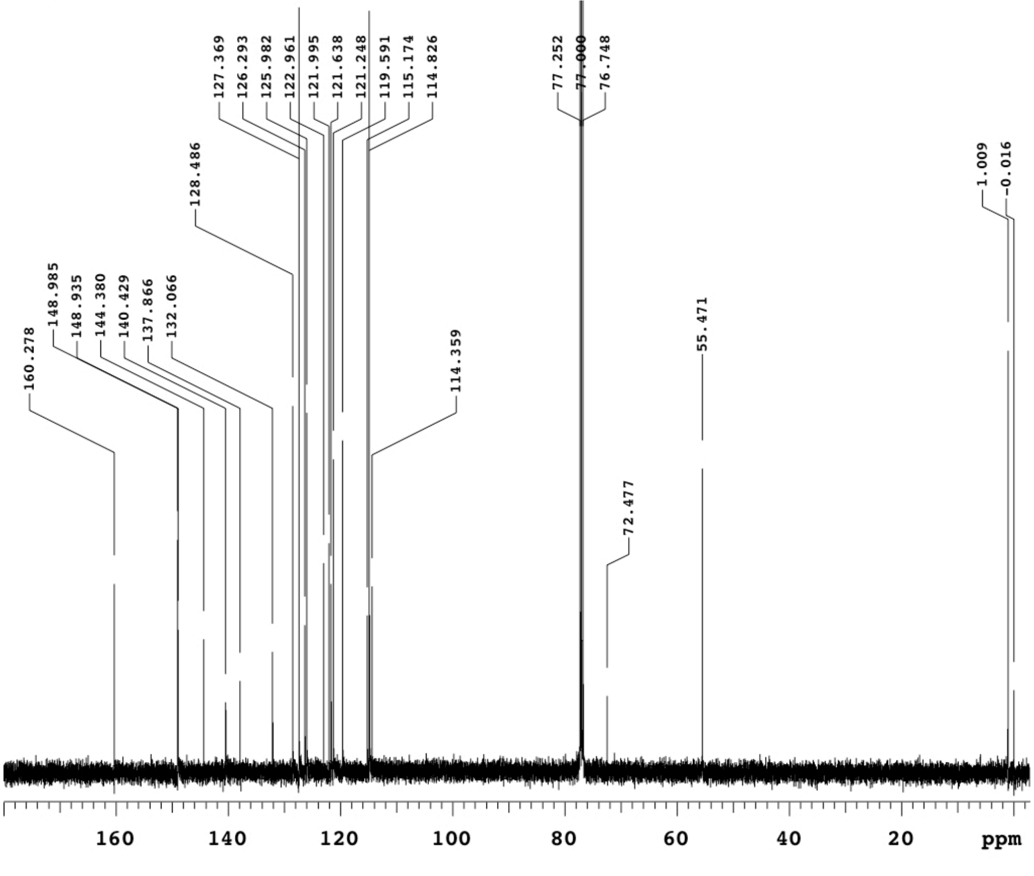
8a (^{13}C NMR, 125 MHz, CDCl$_3$)



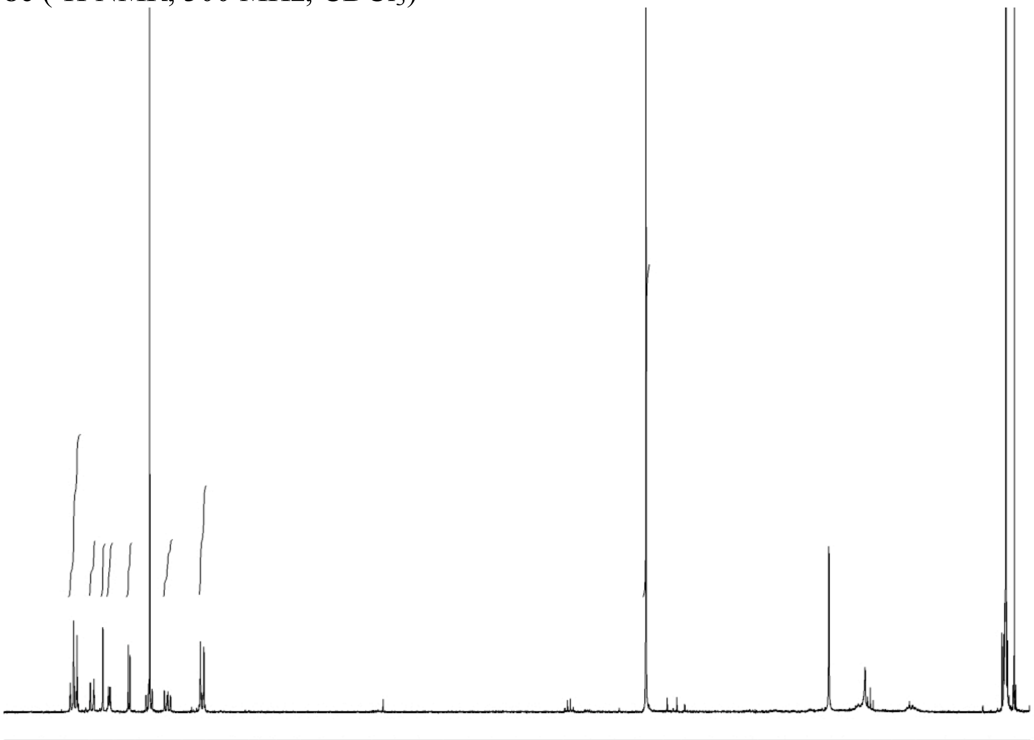
8b (^{1}H NMR, 300 MHz, $CDCl_3$)



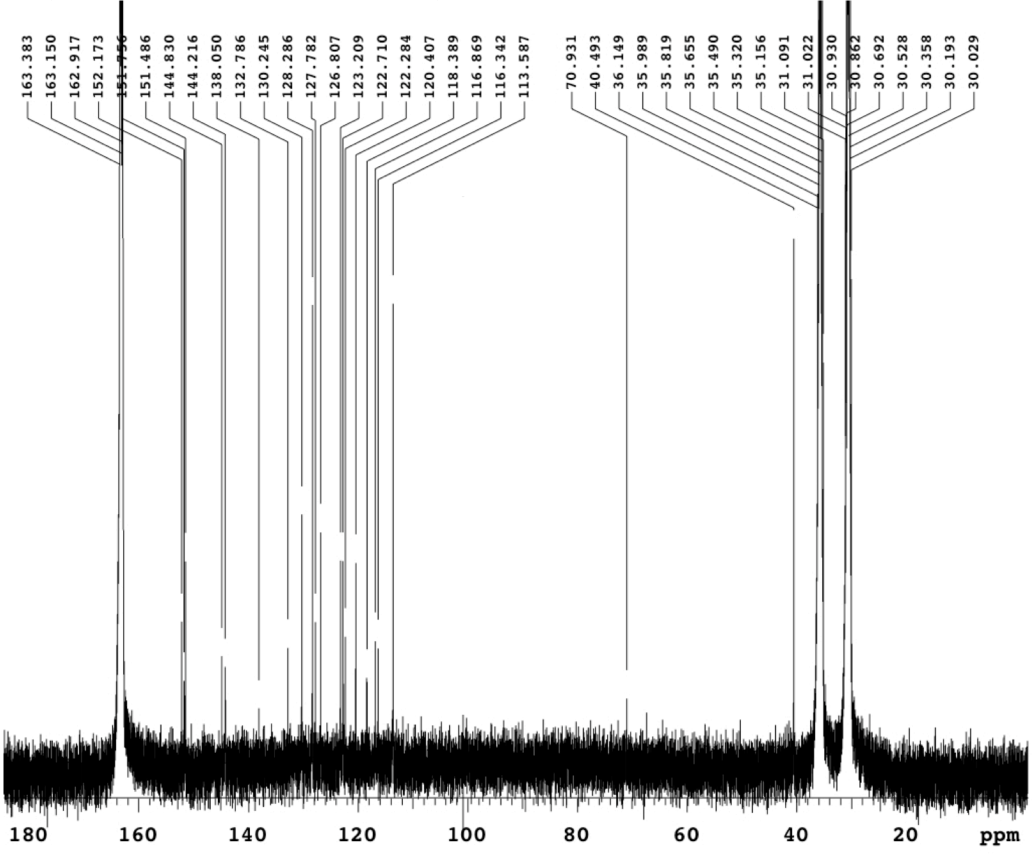
8b (^{13}C NMR, 125 MHz, $CDCl_3$)



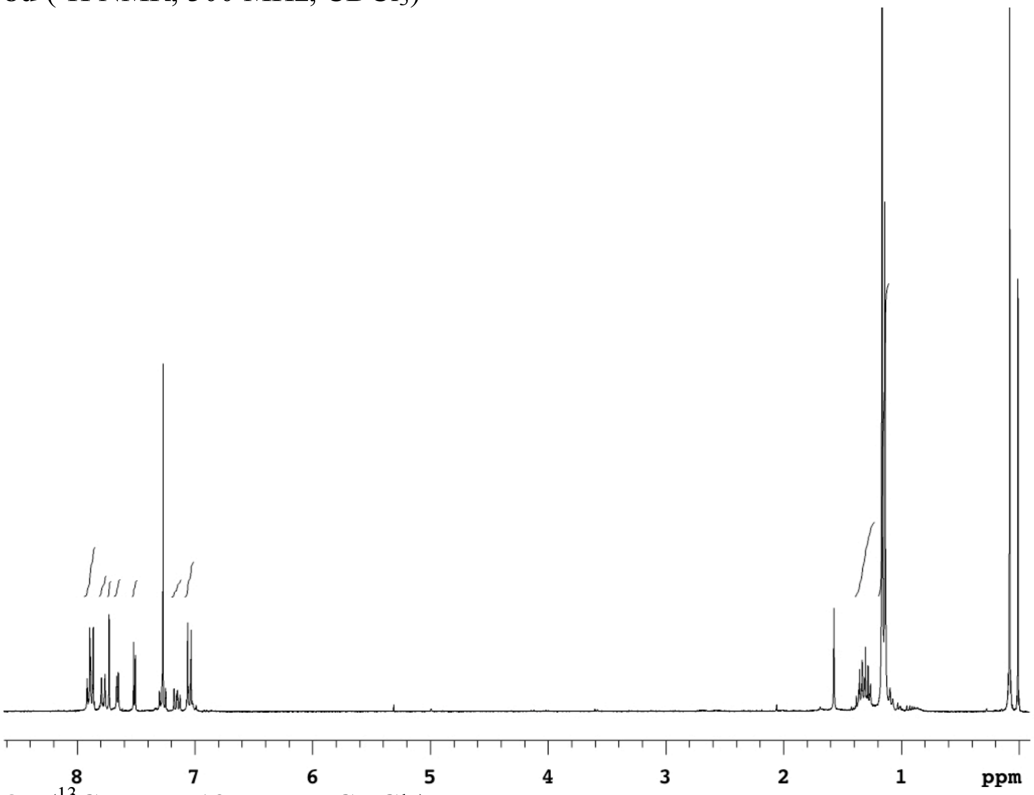
8c (^{1}H NMR, 300 MHz, CDCl$_3$)



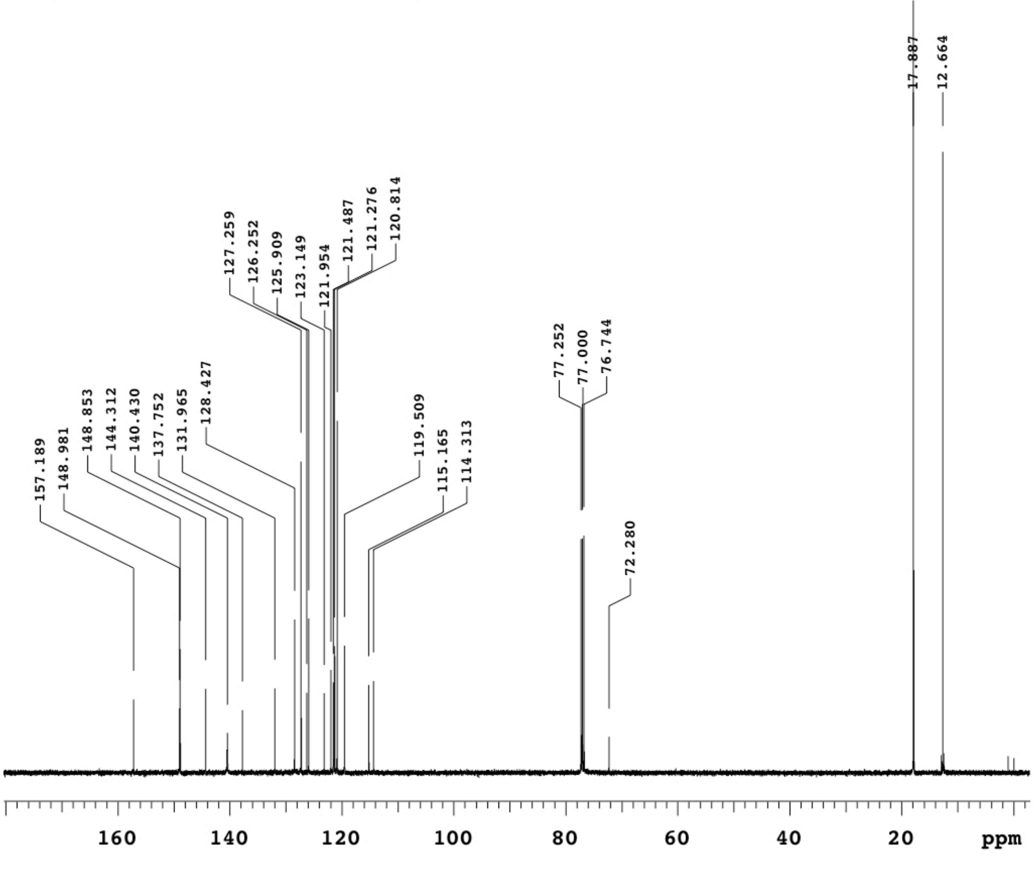
8c (^{13}C NMR, 125 MHz, DMF-d$_7$)



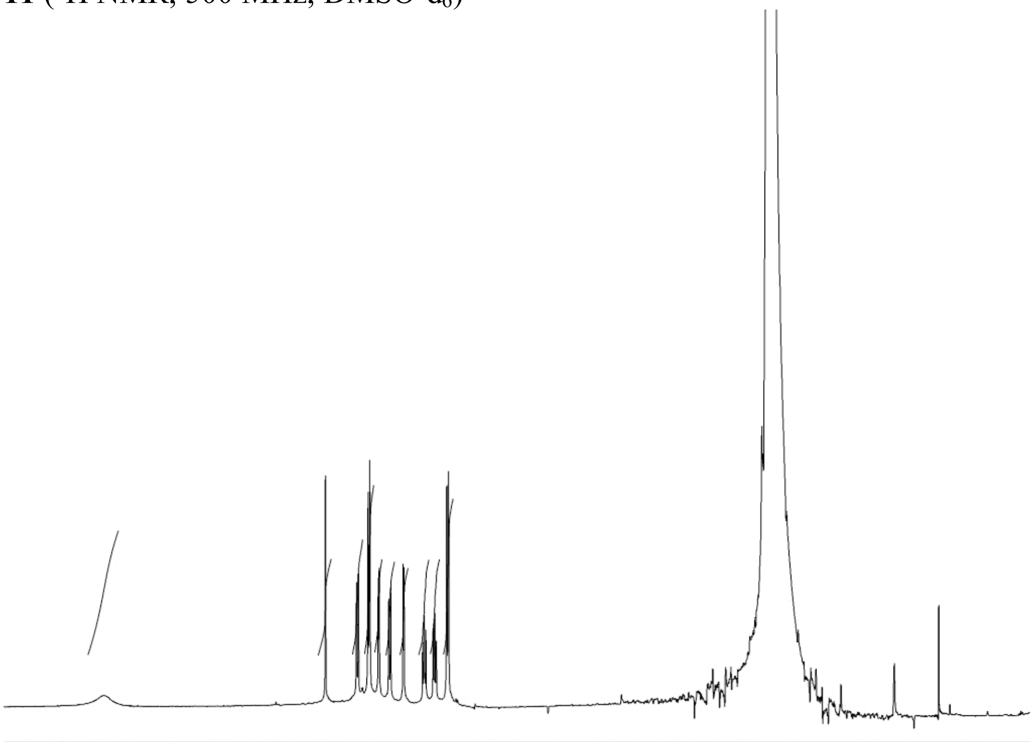
8d (^{1}H NMR, 300 MHz, CDCl$_3$)



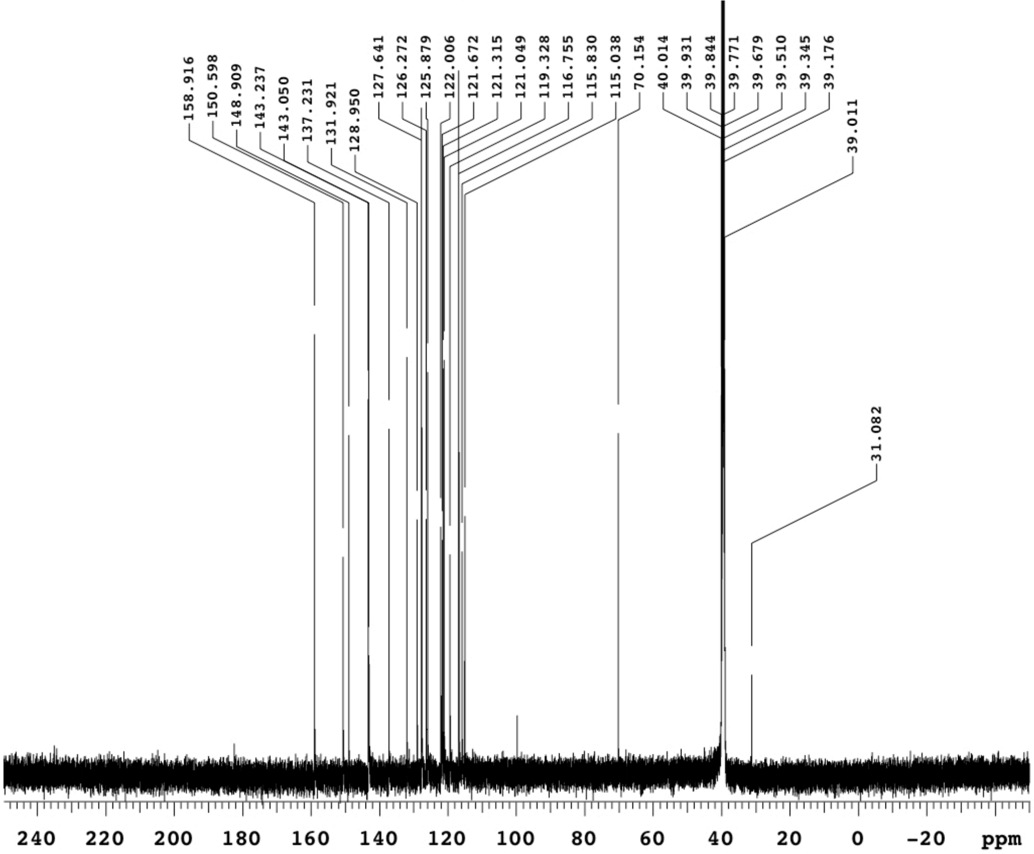
8d (^{13}C NMR, 125 MHz, CDCl$_3$)



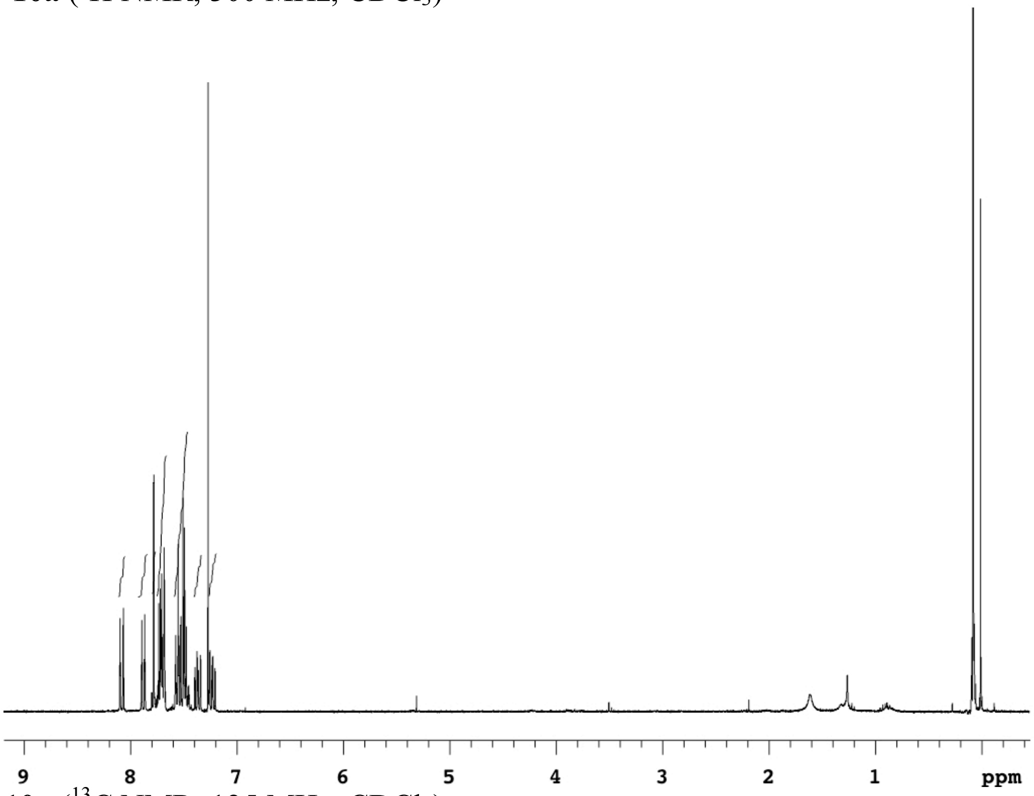
11 (^{1}H NMR, 500 MHz, DMSO-d$_6$)



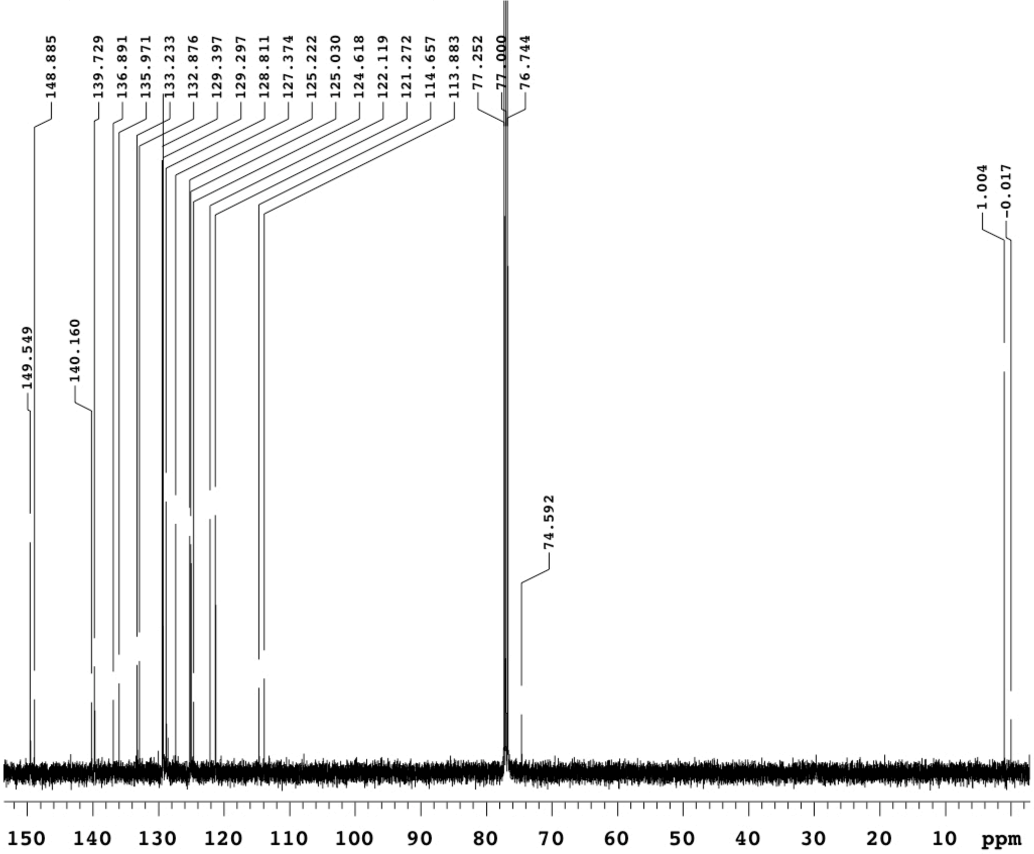
11 (^{13}C NMR, 125 MHz, DMSO-d$_6$)



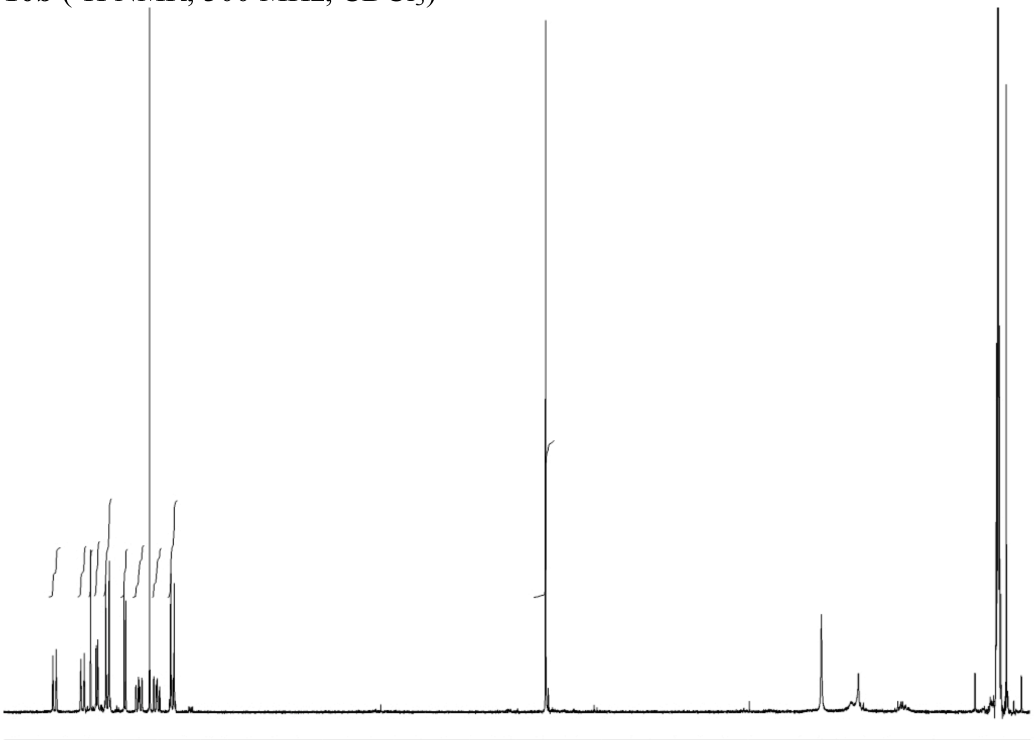
10a (^{1}H NMR, 300 MHz, CDCl$_3$)



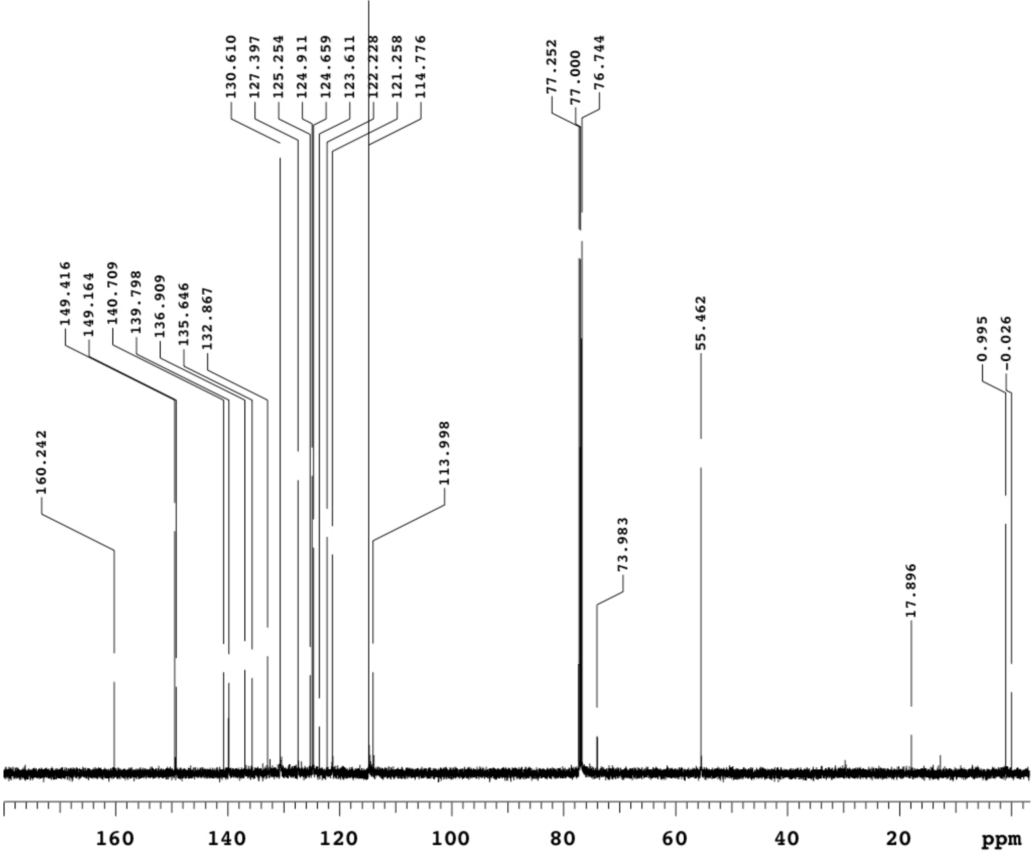
10a (^{13}C NMR, 125 MHz, CDCl$_3$)



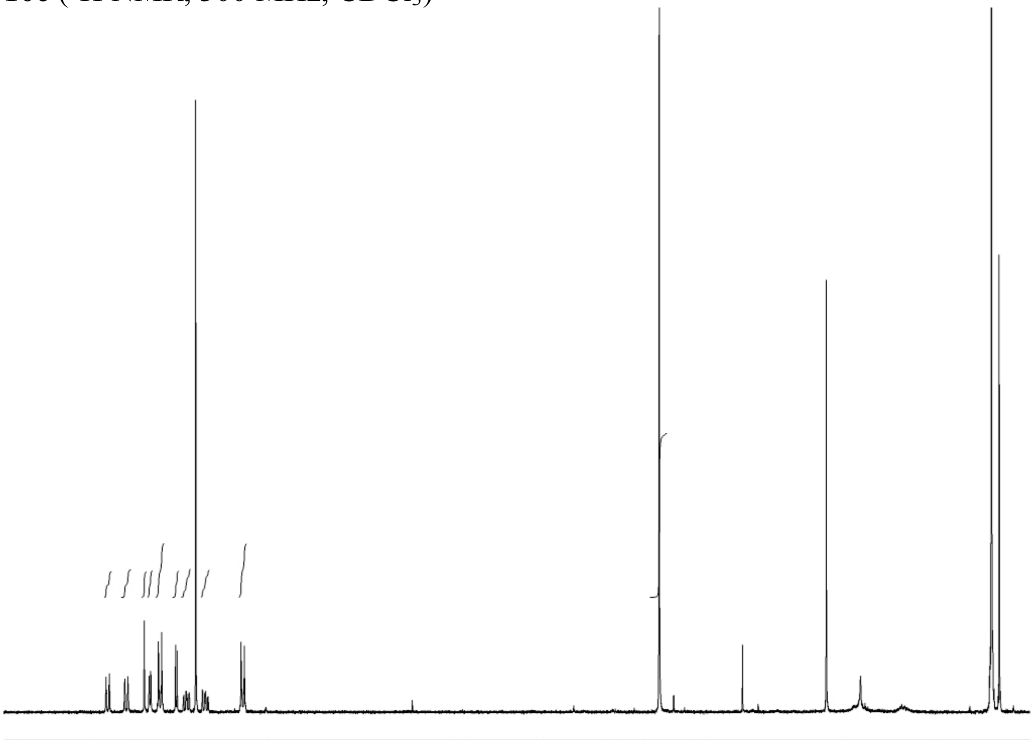
10b (^{1}H NMR, 300 MHz, CDCl$_3$)



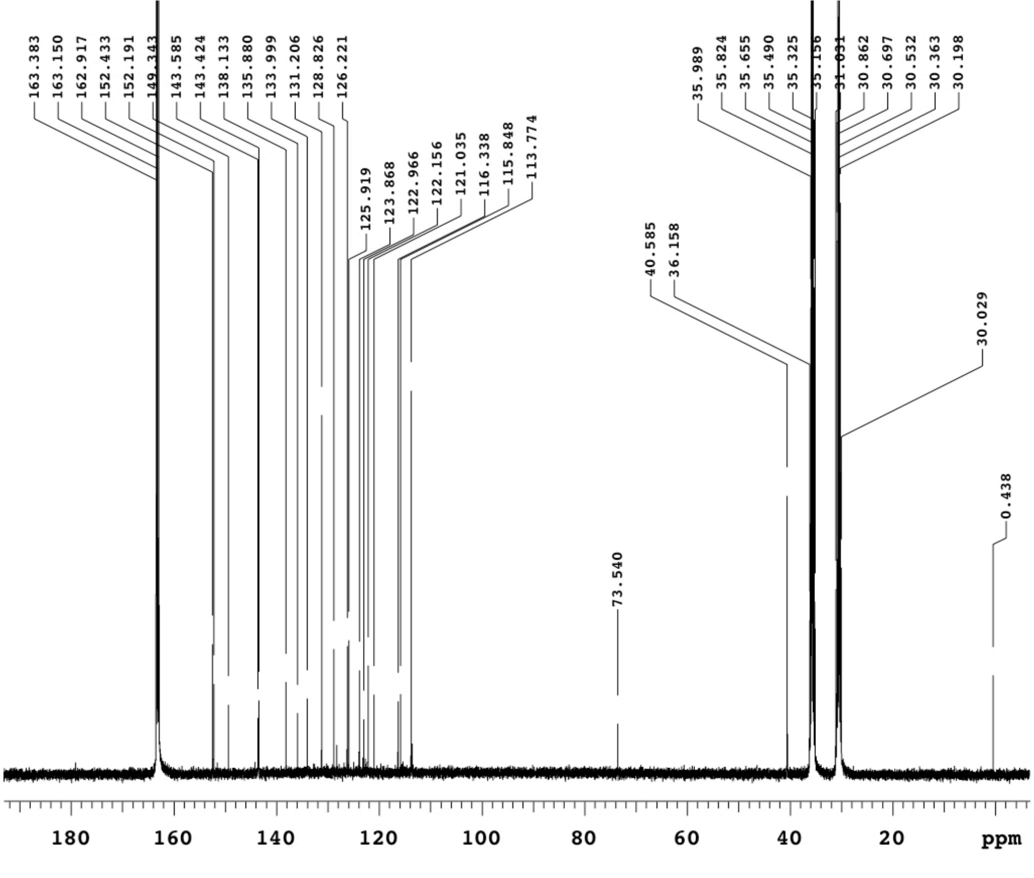
10b (^{13}C NMR, 125 MHz, CDCl$_3$)



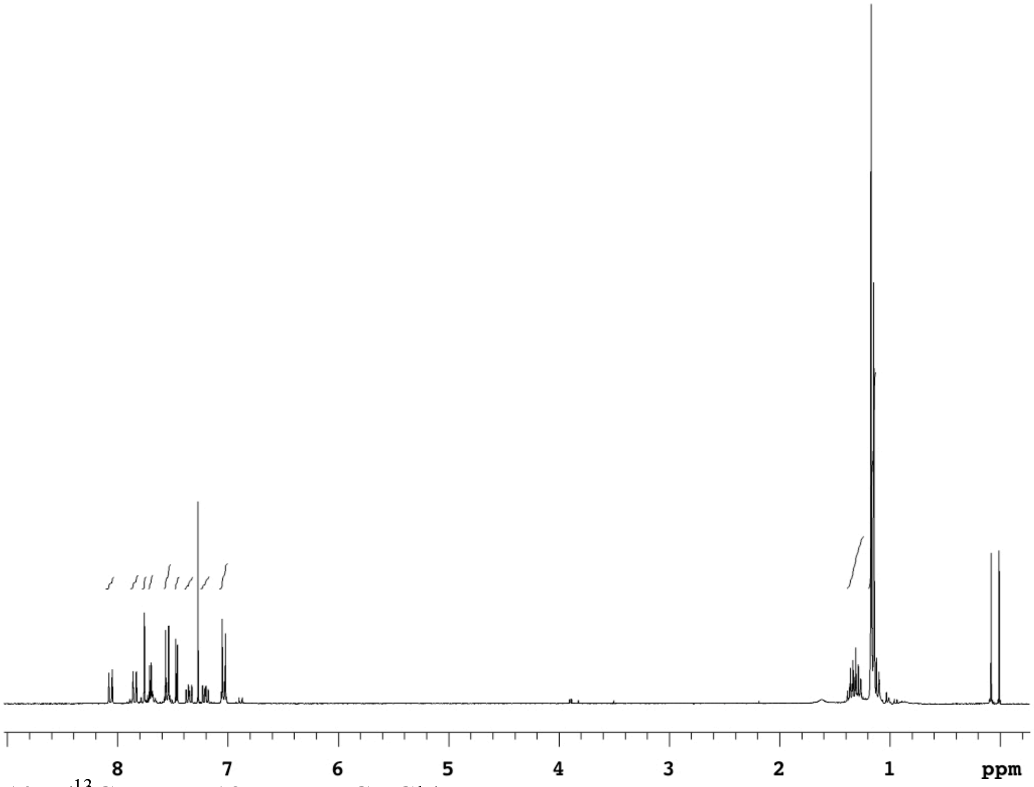
10c (^{1}H NMR, 300 MHz, CDCl$_3$)



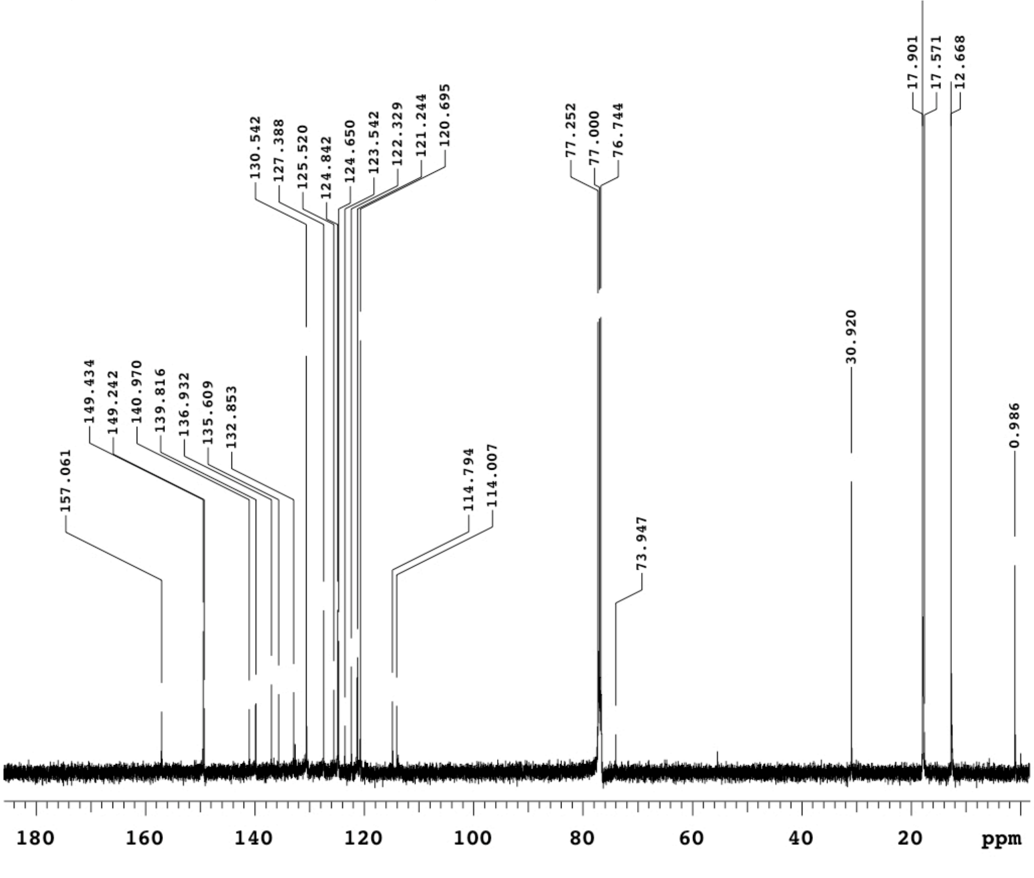
10b (^{13}C NMR, 125 MHz, DMF-d$_7$)



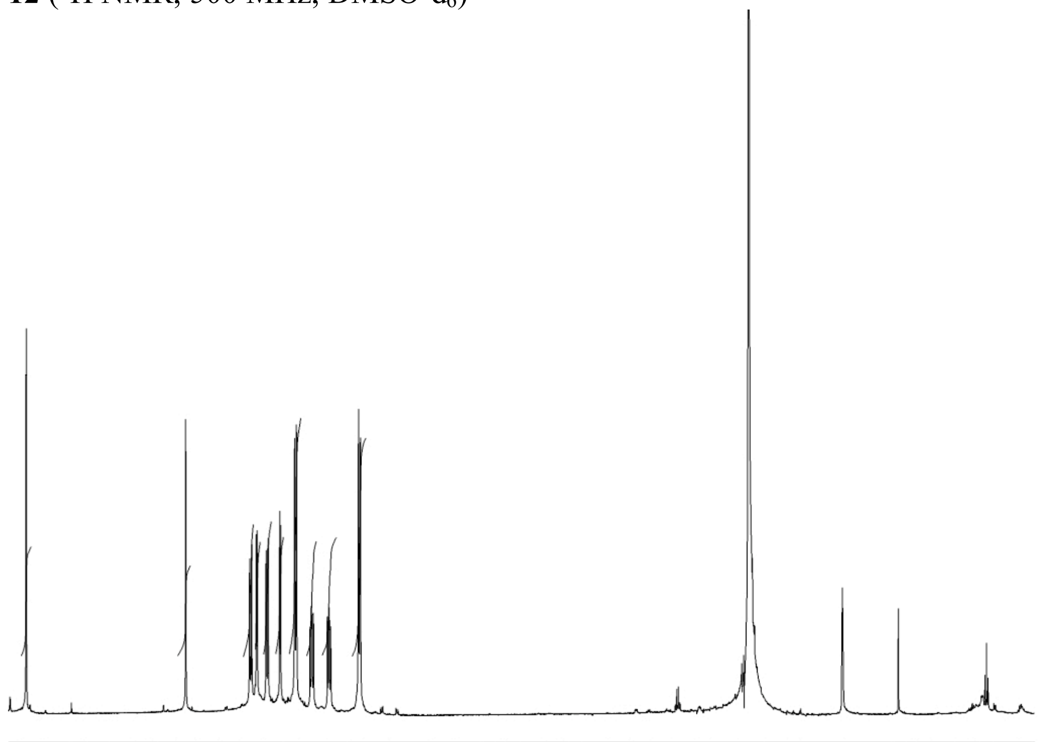
10d (^{1}H NMR, 300 MHz, CDCl$_3$)



10d (^{13}C NMR, 125 MHz, CDCl$_3$)



12 (^{1}H NMR, 500 MHz, DMSO-d_6)



12 (^{1}H NMR, 500 MHz, CDCl$_3$)