Copper-Catalyzed Direct Synthesis of 3-Methylene-2-arylisoindolin-1-ones with Calcium Carbide as a Surrogate of Gaseous Acetylene

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1. Experimental Section

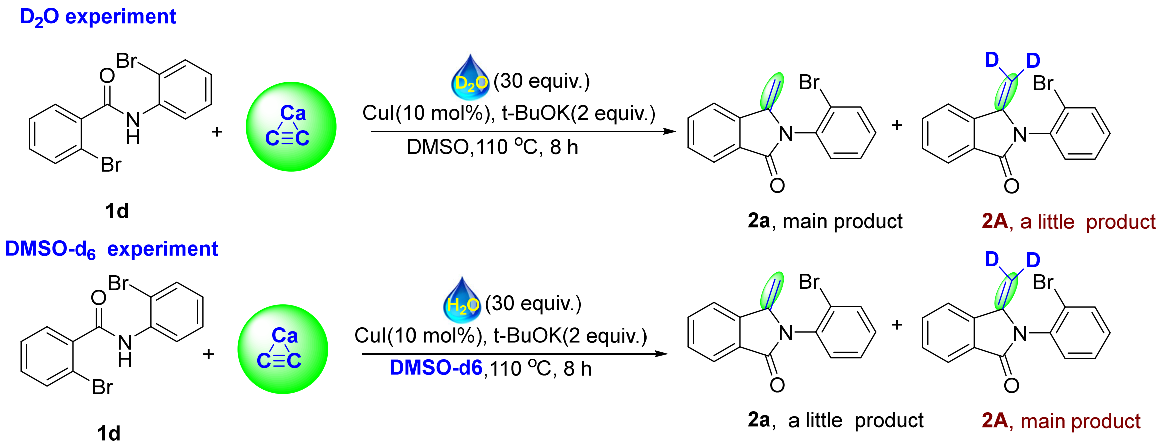
1.1 General Information

^{1}H NMR and ^{13}C NMR spectra were recorded on a Mercury-600 MB or 400 MB instrument using $CDCl_3$ as solvent and Me_4Si as internal standard. High-resolution mass spectra (HRMS) (ESI) were obtained with a Bruker Daltonics APEX II 47e and quadrupole Orbitrap Elite (Q-Exactive) mass spectrometer. Melting points were observed in an electrothermal melting point apparatus (X-5, Beijing Tech Instrument Co. Ltd, China). Calcium carbide was purchased from Macklin Chemical Company(China, purity: 98%), and ground into powder (ca. 50-100 mesh) in a ceramic mortarprior to use. Column chromatography was carried out on a flash chromatographic system using silica gel, and petroleum ether (60-90 ºC) and ethyl acetate as eluent. For thin layer chromatography (TLC), silica gel plates precoated with GF-254 were used. Various benzimidazoles were synthesized by the reactions of corresponding o-phenylenediamines and o-bromobenzaldehydes according to literature procedure[1].

1.2 Mechanism inquiry experiment

(a) H-atoms in products come from

To verify where H-atoms in products come from. We did an experiment of deuteration. On the basis of our experimental results of H-NMR. Thanks for the comments. To verify where H-atoms in products come from. We did an experiment of deuteration. On the basis of our experimental results of H-NMR. We realized that most of the H-atoms in products come from the same environment, we speculated that H-atoms in products comes from the solvent in reaction.



Scheme S1. Experiment of deuteration

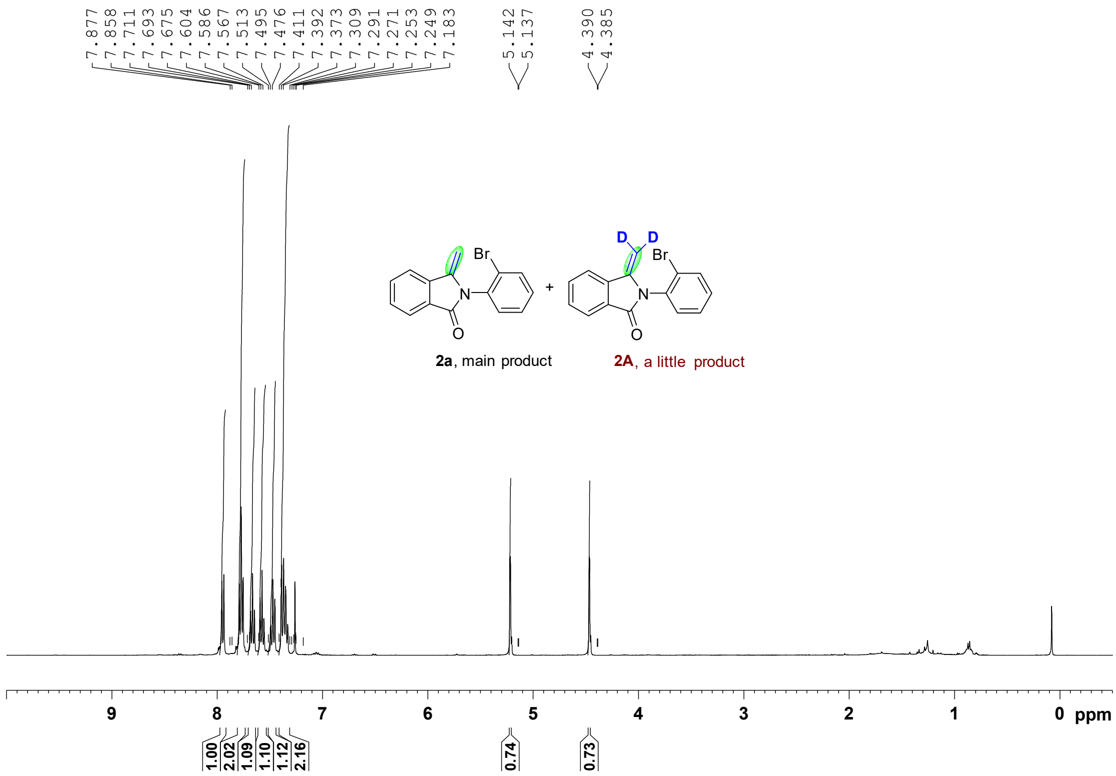


Figure S1. ¹H NMR (400 MHz, $CDCl_3$) of D_2O experiment

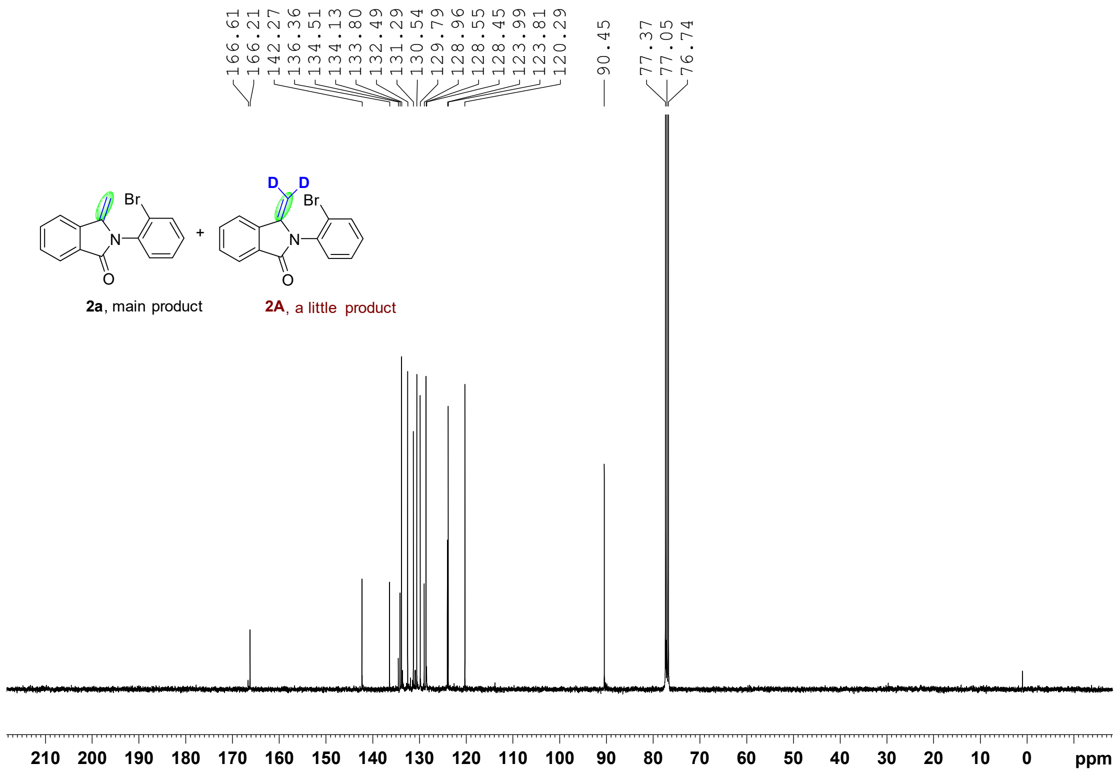


Figure S2. ^{13}C NMR (101 MHz, $CDCl_3$) of D_2O experiment

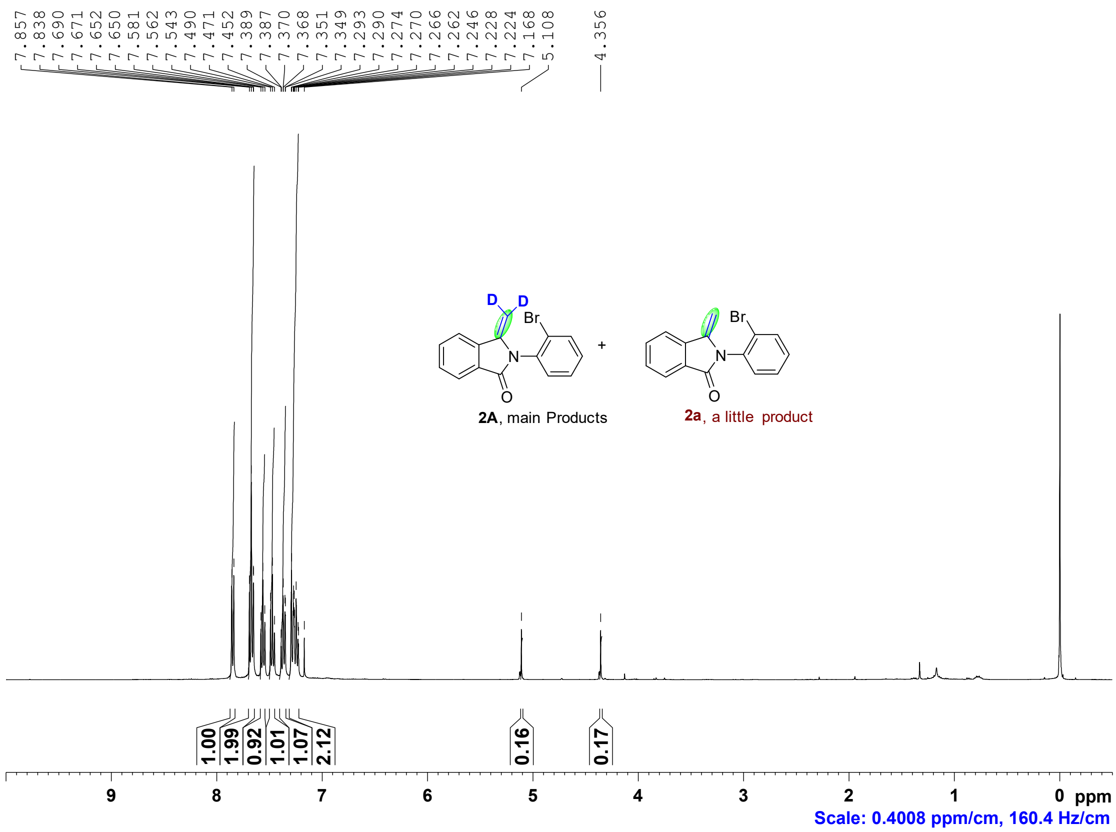


Figure S3. ^{1}H NMR (400 MHz, $CDCl_3$) of DMSO-d_6 experiment

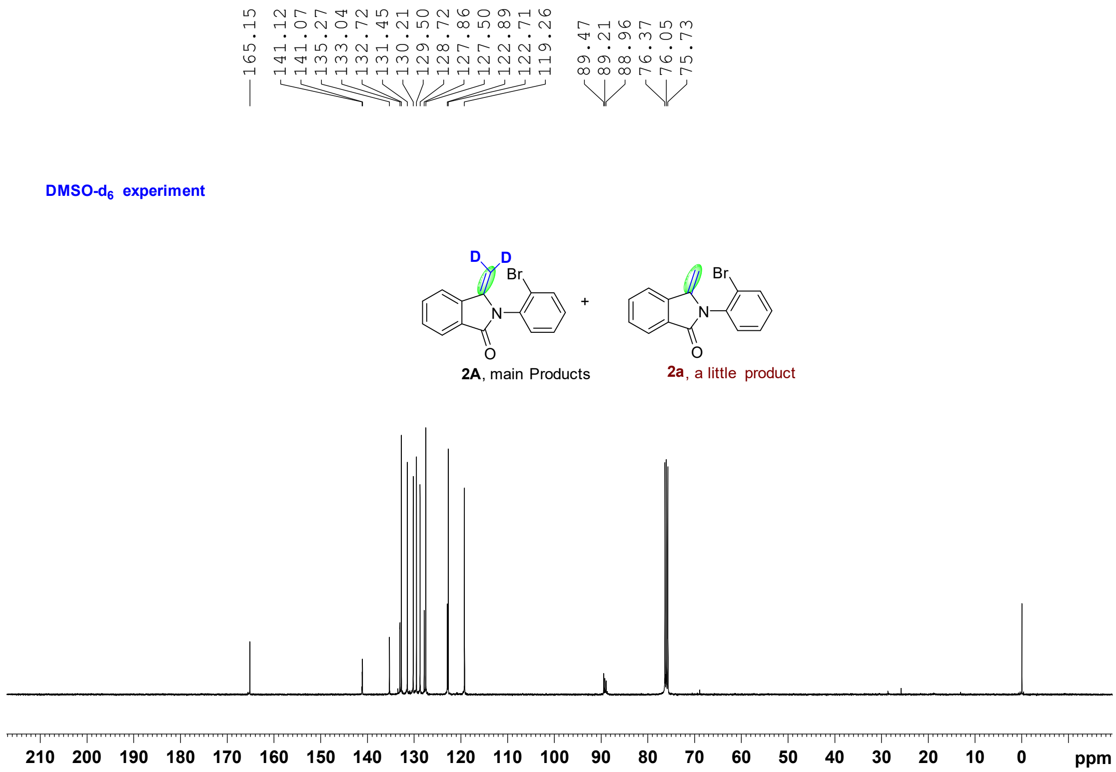
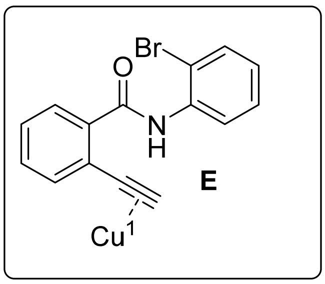


Figure S4. ^{13}C NMR (101 MHz, $CDCl_3$) of DMSO-d_6 experiment

(b)HRMS for Intermediate E

HRMS (ESI): m/z $(M\text{-}Cu+H)^+$ calcd for: $C_{15}H_{10}BrNO$: 300.0018; Found: 300.0015.



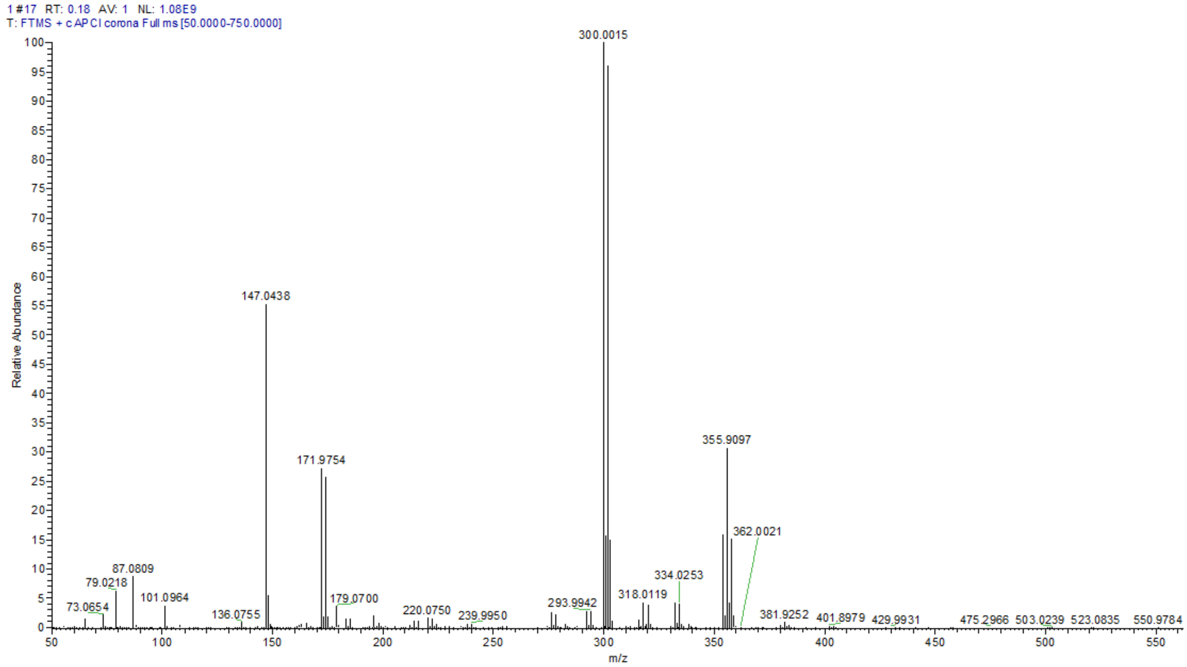
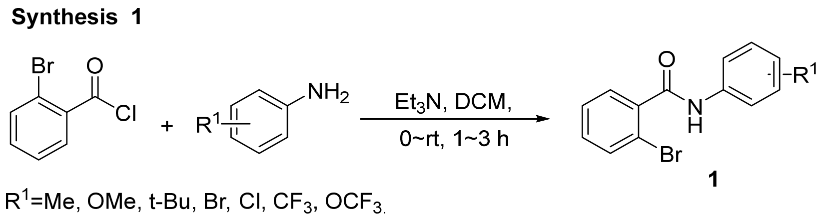


Figure S5. HRMS spectra for intermediate E

2. General Procedure

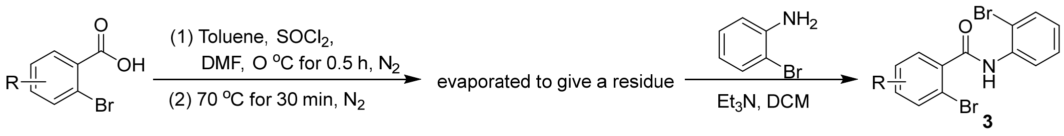
2.1 Synthesis Procedure of Substrates.



Scheme S2. Synthesis procedure of substrate **1**

The appropriate amine (5 mmol) was added dropwise to 2-bromobenzoyl chloride (1.10 g, 5.0 mmol) THF (20 mL) and NEt_3 (1.7 mL) at 0 ºC. After the addition of amine, the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was then poured into 30 mL of ethyl acetate and washed with saturated aqueous $NaHCO_3$ solution (30 mL) and brine (20 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated using a rotary evaporator under reduced pressure (20 mmHg). This resulted in the formation of a solid, which was then dried under high-vacuum conditions to afford the desired amide.

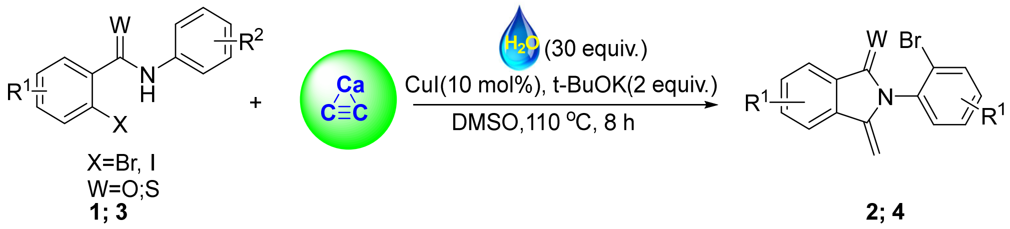
Synthesis 3



Scheme S3. Synthesis procedure of substrate **3**

Under nitrogen atmosphere, add 2 g (10 mmol) o-o-benzoic acid, 25 mL of toluene, 2 mL of alum dichloride, and several drops of DMF to a 50 mL eggplant-shaped flask, and stop heating after refluxing for 2-3 h. The solvent and sassium dichloride were evaporated to obtain a pale yellow oily liquid. Add 20 mL of dichloromethane, and simultaneously add 1.5 mL of benzylamine and 3 mL of triethylamine with a syringe under ice bath conditions. The reaction is basically completed by TLC, washed with 20 mL of hydrochloric acid for 2 times, and washed with saturated saline once. Acetyl acetate was recrystallized to obtain pure product 1.53 g (76%).

2.2 The General Procedure for the Synthesis of 3-methylene-2-arylisoindolin-1-ones 2x-4i

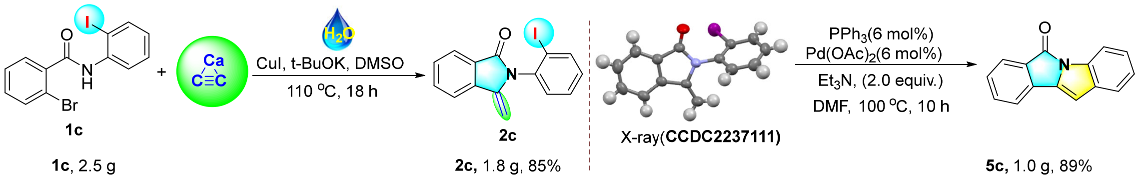


Scheme S4. Synthesis procedure of substrate **2** and **4**

2-Bromo-N-phenylbenzamide (0.2 mmol), calcium carbide (CaC_2)(0.8 mmol, 4.0 equiv), t-BuOK (0.4 mmol, 2 equiv), CuI (10 mol%) and H_2O(6 mmol, 30 equiv.) in 1 mL Dimethyl sulfoxide Were stirred at 110 °C for 8 h under the air atmosphere. After the completion of the reaction, the resulting mixture was filtered to remove the solid, and the liquor was extracted with ethyl acetate (3×10 mL), and washed with saturated brine (3×10 mL). The resulting organic phase was dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 20:1 to 6:1) as eluent to give the pure products.

2.3 Gram-Scale Synthesis of 2a and Pd-catalyzed Heck Annulation for Synthesis of Tetracyclic Isoindolinone Derivative

(a) Gram-Scale Synthesis of ***2a***



Scheme S5. Gram-scale synthesis of **2a**

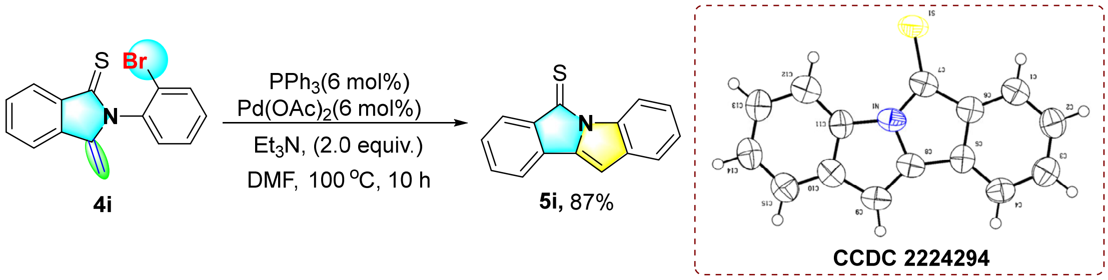
2-Bromo-N-phenylbenzamide (6.25 mmol), calcium carbide (CaC_2)(25 mmol, 4.0 equiv), t-BuOK (12.5 mmol, 2 equiv), CuI (10 mol%) and H_2O(187 mmol, 30 equiv.) in 30 mL Dimethyl sulfoxide Were stirred at 110 °C for 24 h under the air atmosphere. After the completion of the reaction, the resulting mixture was filtered to remove the solid, and the liquor was extracted with ethyl acetate (3×10 mL), and washed with saturated brine (3×10 mL). The resulting organic phase was dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 10:1) as eluent to give **2c** white solid the pure product.

(b) Pd-catalyzed Heck Annulation for Synthesis of Tetracyclic Isoindolinone Derivative

2c (1800 mg, 5.2 mmol), PPh_3(81mg, 0.3 mmol), $Pd(OAc)_2$(69 mg, 0.3 mmol) and Et_3N(1050 mg, 0.3 mmol) in 25 mL N, N-dimethylformamide were stirred at 100 ° C for 10 h. After the completion of the reaction, the resulting mixture was filtered to remove the solid, and the liquor was extracted with ethyl acetate (3×10 mL), and washed with saturated brine (3×10 mL). The resulting organic phase was dried with anhydrous sodium sulfate, and concentrated under reduced

pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 20:1) as eluent to give **5c** white yellow solid the pure product.

(c) Pd-catalyzed for Synthesis of ***5i***



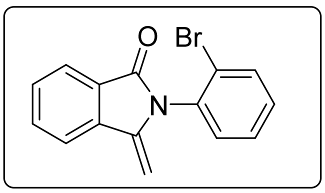
Scheme S6. Pd-catalyzed for synthsis of **5i**

4i (50 mg, 0.15 mmol), PPh_3(3 mg, 0.01 mmol), $Pd(OAc)_2$(2 mg, 0.01 mmol) and Et_3N(45 mg, 0.4 mmol) in 10 mL N, N-dimethylformamide were stirred at 100 ° C for 10 h. After the completion of the reaction, the resulting mixture was filtered to remove the solid, and the liquor was extracted with ethyl acetate (3×10 mL), and washed with saturated brine (3×10 mL). The resulting organic phase was dried with anhydrous sodium sulfate, and concentrated under reduced pressure. The residue was isolated by column chromatography using petroleum ether and ethyl acetate (v/v 20:1) as eluent to give **5i** brownish red solid pure product.

Analytical Data for Compounds **5i**

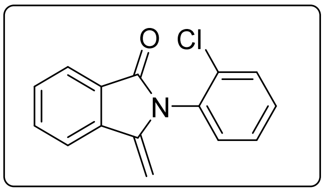
Brownish red crystals (32 mg, 87% yield). m.p.64-67 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (d, J =8.0 Hz, 1H), 7.82 (d, J = 4 Hz, 1H), 7.49-7.40 (m, 3H), 7.32-7.26 (m, 2H), 7.15 (t, J = 8 Hz, 1H), 6.57 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 188.9, 142.5, 141.9, 135.2, 134.9, 133.1, 132.0, 128.9, 127.7, 125.3, 125.2, 122.6, 120.5, 114.3, 104.1 ppm. **HRMS (ESI-TOF)** calc. for [$C_{15}H_9NS$ + H]+ : 236.0528; Found: 236.0524.

3. Analytical Data for Compounds 2a-5i



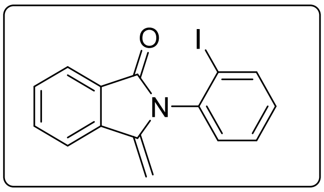
2-(2-bromophenyl)-3-methyleneisoindolin-1-one(2a)[2]

Yellow oil liquid (51 mg, 86% yield); **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.00-7.93 (m, 1H), 7.81-7.74 (m, 2H), 7.67 (td, J=7.5, 1.2 Hz, 1H), 7.58 (td, J =7.5, 1.1 Hz, 1H), 7.47 (td, J=7.6, 1.4 Hz, 1H), 7.40-7.34 (m, 2H), 5.22 (d, J=2.3 Hz, 1H), 4.47 (d, J=2.3 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ166.25, 142.23, 136.34, 134.52, 134.07, 133.79, 133.58, 132.51, 131.88, 131.27, 130.95, 130.84, 130.56, 129.79, 128.91, 128.55, 128.45, 123.99, 123.96, 123.80, 120.30, 90.55 ppm; HRMS (ESI-TOF) calc. for $[C_{15}H_{11}BrNO + H]^+$: 300.00162; Found: 300.00165.



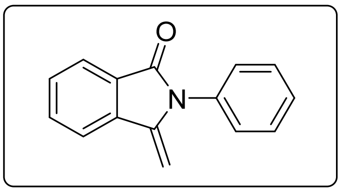
2-(2-chlorophenyl)-3-methyleneisoindolin-1-one(2b)

Yellow solid (39 mg, 76% yield). m.p. 104-107 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.77 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.66 (td, *J* = 7.4, 1.1 Hz, 1H), 7.61-7.54 (m, 2H), 7.45-7.36 (m, 3H), 5.21 (d, *J* = 2.3 Hz, 1H), 4.48 (d, *J* = 2.3 Hz, 1H); **^{13}C NMR** (150 MHz, $CDCl_3$) δ166.3, 142.3, 136.4, 133.9, 132.5, 132.4, 131.2, 130.6, 130.3, 129.7, 128.9, 127.8, 123.7, 120.2, 90.3 ppm; HRMS (ESI-TOF) calc. for $[C_{15}H_{10}ClNO + H]^+$: 256.0524; Found: 256.0527.



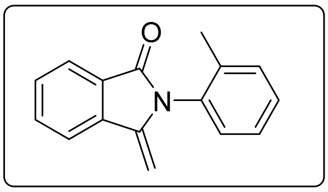
2-(2-iodophenyl)-3-methyleneisoindolin-1-one (2c)[3]

White solid (60 mg, 89% yield). m.p. 100-102 ºC; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 8.00-7.97 (m, 1H), 7.96(d, *J*=8.0 Hz, 1H), 7.77 (d, *J*=8.0 Hz, 1H), 7.68-7.63 (m, 1H), 7.58-7.54 (m, 1H), 7.51-7.47 (m, 1H), 7.35-7.32 (m, 1H), 7.19-7.15(m, 1H), 5.22 (d, *J*=4.0 Hz, 1H), 5.42 (d, *J*=4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ*166.1, 142.1, 140.1, 137.7, 136.3, 132.6, 130.7, 130.6, 129.8, 129.5, 129.0, 123.8, 120.4 ppm.



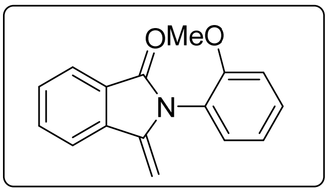
3-methylene-2-phenylisoindolin-1-one(2d)[4]

White solid (35 mg, 78%); m.p. 94-95 °C; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.92 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J*=8.0 Hz, 1H), 7.65(t, *J*=8.0 Hz, 1H), 7.58-7.49 (m, 3H), 7.43-7.37 (m, 3H), 5.23 (d, *J*=4.0 Hz, 1H), 4.80(d, *J*= 4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-*d*) *δ*166.7, 143.2, 136.2, 134.6, 132.3, 131.8, 129.7, 129.1, 128.9, 128.1, 126.6, 123.7, 123.6, 120.0, 90.5 ppm.



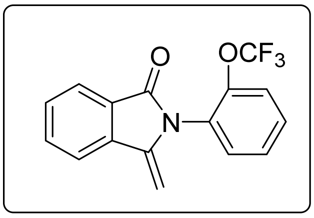
3-methylene-2-(o-tolyl)isoindolin-1-one(2e)

Colorless liquid (34 mg, 72% yield); **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.83-7.81 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.53 (t, J = 4.0, Hz, 1H), 7.45 (t, J = 4.0 Hz, 1H), 7.25-7.20 (m, 3H), 5.15-5.11 (m, 1H), 5.07(d, J = 4.0 Hz, 1H), 4.37(d, J = 4.0 Hz, 1H), 2.0 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 167.4, 166.5, 165.7, 142.9, 137.2, 136.5, 134.4, 133.4, 132.3, 132.0, 131.2, 129.7, 129.4, 129.3, 129.2,129.1, 128.7, 127.0 , 126.9, 123.7, 123.5, 120.52 , 90.4, 77.36, 17.8, 17.7(d, J = 4.0 Hz) ppm; HRMS (ESI-TOF) calc. for $[C_{16}H_{13}NO + H]^+$: 236.1069; Found: 236.1067.



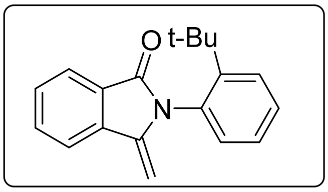
2-(2-methoxyphenyl)-3-methyleneisoindolin-1-one(2f)

White solid (43 mg, 86% yield). m.p. 111-114 °C; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.91 (d, J = 8.0 Hz, 1H), 7.74 (d, J = 8.0 Hz, 1H), 7.62 (t, J = 8.0 Hz, 1H), 7.54(t, J = 8.0 Hz, 1H), 7.44-7.39 (m, 1H), 7.27(d, J = 8.0 Hz, 1H), 7.09-7.05 (m, 2H), 5.15(d, J = 4.0 Hz, 1H), 4.53(d, J = 4.0 Hz, 1H), 3.76(s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.1, 141.9, 138.1, 136.4, 134.8, 133.2, 132.8, 131.7, 131.4, 130.6, 130.3, 130.0, 128.5, 128.4, 127.1, 124.5, 124.2, 123.9, 121.8, 120.4, 90.6, 55.9,55.8 ppm; **HRMS** (ESI-TOF) calc. for $[C_{16}H_{13}NO_2 + H]^+$: 252.1019; Found: 252.1015.



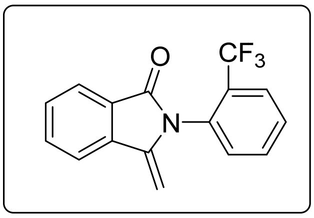
3-methylene-2-(2-(trifluoromethoxy)phenyl)isoindolin-1-one(2g)

White solid (45 mg, 75% yield). m.p. 121-124 °C; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.93(d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.65 (t, J=4.0, Hz, 1H), 7.55 (t, J=4.0 Hz, 1H), 7.51-7.45 (m, 2H), 7.44-7.41 (m, 2H), 5.22 (d, J = 4.0 Hz, 1H), 4.57 (d, J = 4.0 Hz, 1H); **^{19}F NMR** (376 MHz, Chloroform-d) δ -57.32; **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 166.2, 145.9(q, $^3J_{CF3}$=1 Hz),142.2, 136.4, 132.4, 131.1, 130.1, 119.7, 128.6, 127.4, 127.0, 123.6, 121.5, 120.2(q,$^1J_{CF3}$=257 Hz), 120.1, 90.2 ppm; HRMS (ESI): **HRMS** (ESI-TOF) calc. for [$C_{16}H_{10}$ F_3NO_2+ H]$^+$: 306.07363; Found: 306.07336.



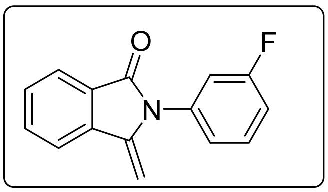
2-(2-(tert-butyl)phenyl)-3-methyleneisoindolin-1-one(2h)

White solid (33 mg, 60% yield). m.p. 101-103 °C; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.92 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.66-7.61 (m, 2H), 7.58-7.54 (m, 1H), 7.46-7.35 (m, 2H), 7.34-7.23 (m, 2H), 7.02-7.00 (m, 1H), 5.23 (d, *J* = 4.0 Hz, 1H), 4.8 (d, *J* = 4.0 Hz, 1H), 1.31(s, 9H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 168.0 , 149.6, 145.3 , 137.7 , 136.6, 133.0, 132.6 , 132.3 , 131.9, 131.3, 130.8, 129.7, 129.5 , 129.4 , 129.3 ,128.9, 128.8, 127.9,m 127.8, 127.6, 127.3, 123.6, 120.1, 91.9, 35.8, 31.8, 31.6, ppm; **HRMS** (ESI-TOF) calc. for [$C_{19}H_{19}NO$ + H]$^+$: 278.15395; Found: 278.15366.



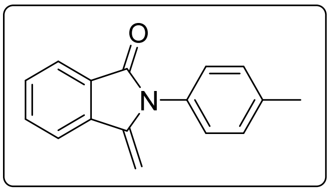
3-methylene-2-(2-(trifluoromethyl)phenyl)isoindolin-1-one(2i)

White solid (39 mg, 69% yield). m.p. 110-112 ºC; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.94 (d, *J*=8.0 Hz, 1H), 7.9 (d, *J*=8.0 Hz, 1H), 7.74-7.67 (m, 5H), 7.60 (t, *J*=8.0 Hz, 1H), 5.25 (d, *J*=4.0 Hz, 1H), 5.48 (d, *J*=4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 166.1, 141.8, 138.0, 136.3, 134.7, 133.1, 132.8, 131.3, 130.41(q, *J*=33 Hz),130.0, 128.46, 128.39, 128.36, 127.1(q, *J*=4 Hz), 123.9, 123.1 (q, *J*=271 Hz),120.3, 90.5 ppm. **HRMS** (ESI-TOF)calc. for [$C_{16}H_{10}F_3NO$+H]$^+$: 290.0787; Found: 290.0782.



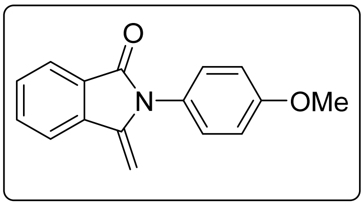
2-(3-fluorophenyl)-3-methyleneisoindolin-1-one(2j)

Colorless liquid (36 mg, 74% yield); ^{1}**H NMR** (400 MHz, Chloroform-d) δ 7.92 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.67 (t, J = 8.0 Hz, 1H), 7.58 (t, J = 8.0 Hz, 1H), 7.51-7.45 (m, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.15-7.14 (m, 2H), 5.27 (d, J = 4.0 Hz, 1H), 4.48 (d, J = 4.0 Hz, 1H); ^{19}**F NMR** (376 MHz, Chloroform-d) δ -111.14; ^{13}**C NMR** (101 MHz, Chloroform-d) δ 166.4, 162.9(d, J=246 Hz), 142.6, 136.2, 136.01(d, J=10 Hz), 132.5 (d, J=9 Hz) 129.9, 128.6, 123.8(d, J=3 Hz), 123.6, 120.1, 115.5(d, J=23 Hz), 115.0 (d, J=21 Hz), 90.6 ppm. **HRMS** (ESI-TOF) calc. for $[C_{15}H_{10}FNO+H]^{+}$: 240.0819; Found: 240.0813.



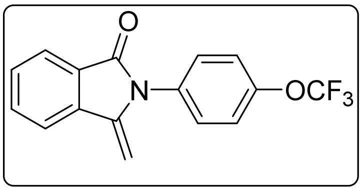
3-methylene-2-(p-tolyl)isoindolin-1-one(2k)[3]

White solid (42 mg, 88%); m.p. 130-133 °C; ^{1}**H NMR** (400 MHz, Chloroform-d) δ 7.90 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 4.0 Hz, 1H), 7.63-7.59 (m, 1H), 7.55-7.51 (m, 1H), 7.31-7.29 (m, 2H), 7.25-7.23 (m, 2H), 5.24 (d, J = 4.0 Hz, 1H), 4.47 (d, J = 4.0 Hz, 1H), 2.40 (s, 3H); ^{13}**C NMR** (101 MHz, Chloroform-*d*) δ 166.8, 143.2, 138.0, 136.2, 132.2, 131.9, 130.0, 129.7, 129.0, 127.9, 123.5, 120.0, 90.4, 21.3, 21.2 ppm; **HRMS** (ESI-TOF) calc. for $[C_{16}H_{13}NO +H]^{+}$: 236.10699; Found: 236.10674.



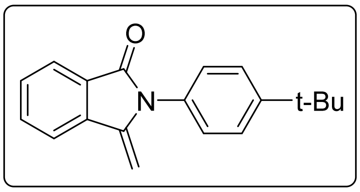
2-(4-methoxyphenyl)-3-methyleneisoindolin-1-one (2l)[5]

White solid (41 mg, 80%); m.p. 124-125 °C; ^{1}**H NMR** (400 MHz, Chloroform-d) δ 7.94 (d, J = 8.0 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.68-7.64 (m, 1H), 7.60-7.56 (m, 1H), 7.32-7.28 (m, 2H), 7.06-7.04 (m, 2H), 5.52 (d, J = 4.0 Hz, 1H), 4.77 (d, J = 4.0 Hz, 1H), 3.88 (s, 3H); ^{13}**C NMR** (101 MHz, Chloroform-*d*) δ 166.9, 159.2, 143.6, 136.1, 132.2, 129.7, 129.3, 129.0, 127.1, 123.5, 120.0, 114.7, 90.4, 55.6 ppm; **HRMS** (ESI-TOF) calc. for $[C_{16}H_{13}NO_2 +H]^{+}$: 252.1019; Found:252.1013.



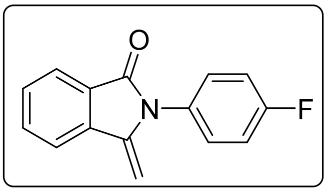
3-methylene-2-(4-(trifluoromethoxy)phenyl)isoindolin-1-one(2m)

White solid (57 mg, 93%), m.p. 112-113 °C; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.92 (d, J = 8.0 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.68-7.64 (m, 1H), 7.59-7.55(m, 1H), 7.44-7.42 (m, 2H), 7.36 (d, J=8.0 Hz, 2H); **^{19}F NMR** (376 MHz, Chloroform-d)δ -57.82; **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.6, 148.4, 142.8, 136.2, 133.1, 132.5, 129.9, 129.5, 128.6, 123.7, 121.8, 120.41(q, J=256 Hz), 120.1, 90.4 ppm.; **HRMS** (ESI-TOF) calc. for $[C_{16}H_{10}F_3NO_2 +H]^+$: 306.0736, Found:306.0732.



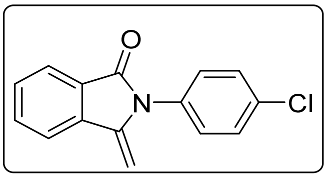
2-(4-(tert-butyl)phenyl)-3-methyleneisoindolin-1-one (2n)[6]

White solid (39 mg, 72%); m.p. 155-157 °C; **^{1}H NM**R (400 MHz, Chloroform-d) δ 7.91 (d, J = 8.0 Hz, 1H), 7.75 (d, J=8.0 Hz, 1H), 7.65-7.61(m, 1H), 7.56-7.53 (m, 3H), 7.51-7.29 (m, 2H), 5.22 (d, J=4.0 Hz, 1H), 4.83 (d, J= 4.0 Hz, 1H), 1.36 (s, 39H); **^{13}C NMR** (101 MHz, Chloroform-*d*) δ166.8, 150.9, 143.2, 136.3, 132.3, 131.8, 129.7, 129.0, 127.5, 126.4, 125.7, 123.5, 121.4, 120.2, 90.7, 34.8, 31.4 ppm; **HRMS** (ESI-TOF) calc. for $[C_{19}H_{19}NO +H]^+$: 278.1539, Found: 278.1532.



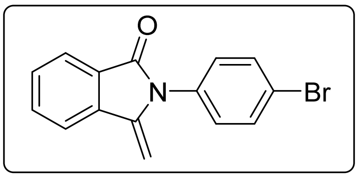
2-(4-fluorophenyl)-3-methyleneisoindolin-1-one (2o)[4]

White solid(40 mg, 85%), m.p. 107-108 °C; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.90 (d, J=8.0 Hz, 1H), 7.76 (d, J=8.0 Hz, 1H), 7.66-7.63 (m, 1H), 7.57-7.54 (m, 1H), 7.36-7.32 (m, 2H), 5.19 (d, J=4.0 Hz, 2H), 5.23 (d, J=4.0 Hz, 1H), 4.75 (d, J= 4.0 Hz, 1H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -113.19; **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.7, 162.0 (d, J=246 Hz), 143.1, 136.1, 132.4, 130.4(d, J=3 Hz), 129.9, 129.84, 129.82, 128.7, 123.6, 120.1, 116.3(d, J=33 Hz), 90.3 ppm. **HRMS** (ESI-TOF) calc. for $[C_{15}H_{10}FNO +H]^+$: 240.0819, Found: 240.0812.



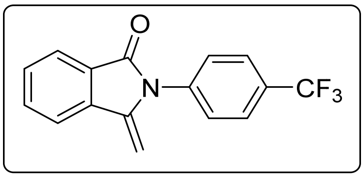
2-(4-chlorophenyl)-3-methyleneisoindolin-1-one (2p)[7]

White solid(40 mg, 80%); m.p. 118.2-119.4 °C; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.84 (d, J=8.0 Hz, 1H), 7.69 (d, J=8.0, 1.0 Hz, 1H), 7.60-7.56 (m, 1H), 7.51-7.47 (m, 1H), 7.43-7.39(m, 2H), 7.27-7.24 (m, 2H), 5.17 (d, J = 4.0 Hz, 1H), 4.72 (d, J = 4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.5 , 142.8 , 136.2 , 133.8 , 133.1 , 132.5 , 129.9 , 129.6 , 129.39, 128.7, 123.7, 120.1, 90.1 ppm; **HRMS** (ESI-TOF) calc. for $[C_{15}H_{10}ClNO +H]^+$: 256.05236; Found: 256.05232.



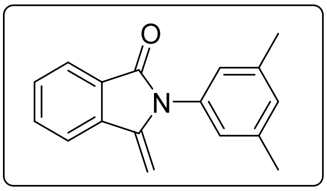
2-(4-bromophenyl)-3-methyleneisoindolin-1-one (2q)[5]

White solid (49 mg, 82%); m.p. 138-139°C;**^{1}H NMR** (400 MHz, Chloroform-d) δ 7.92 (d, J = 8.0 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.67-7.65 (m, 3H), 7.58 (t, J = 8.0 Hz, 1H), 7.28-7.26 (m, 2H), 5.23 (d, J = 4.0 Hz, 1H), 4.80 (d, J = 4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.5, 142.7, 136.2, 133.6, 132.6, 132.5 (d, J = 4.0 Hz), 129.9, 129.7, 128.7, 123.6, 121.9, 120.1, 90.5 ppm.



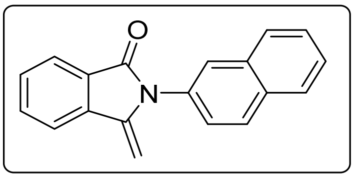
3-methylene-2-(4-(trifluoromethyl)phenyl)isoindolin-1-one(2r)[3]

White solid (43 mg, 76%), m.p. 116-117 °C; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.93 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.0 Hz, 3H), 7.69-7.66 (m, 1H), 7.60-7.26(m, 3H), 5.29 (d, J = 4.0 Hz, 1H), 4.86 (d, J = 4.0 Hz, 1H); **^{19}F NMR** (376 MHz, Chloroform-d)δ -62.55; **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.4, 142.4, 137.8, 136.2, 132.7, 123.76, 130.0, 129.9(d, J=33 Hz), 128.3, 126.3(q, J=4 Hz), 123.81(q, J=270 Hz), 120.2, 90.7 ppm. **HRMS** (ESI-TOF) calc. for $[C_{16}H_{10}F_3NO +H]^+$: 290.0787, Found: 290.0783.



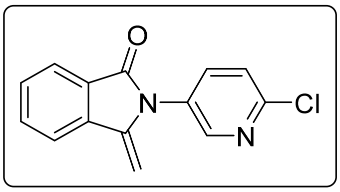
2-(3,5-dimethylphenyl)-3-methyleneisoindolin-1-one(2t)

White solid (38 mg, 76%), m.p. 94-96 °C; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.91 (d, *J*=8.0 Hz, 1H), 7.76-7.74 (m, 1H), 7.65-7.61(m, 1H), 7.57-7.53(m, 1H), 7.25-6.05(m, 1H), 6.97 (s, 2H), 5.21 (d, *J* =4.0 Hz, 1H), 4.77 (d, *J* =4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.8, 142.3, 139.1, 138.9, 137.4, 136.2, 134.3, 133.4, 132.2, 129.9, 129.7, 129.0, 125.8, 123.5, 120.0, 117.7, 90.5, 21.2 ppm; **HRMS** (ESI-TOF) calc. for $[C_{17}H_{15}NO +H]^{+}$: 250.1226, Found: 250.1220.



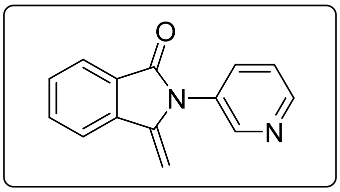
3-methylene-2-(naphthalen-2-yl)isoindolin-1-one(2u)[4]

White solid (37 mg, 69%); m.p. 143-144 °C; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.98 (t, *J*=8.0 Hz, 2H), 7.92-7.87 (m, 3H), 7.79 (d, *J*=8.0 Hz, 1H), 7.67 (t, *J*=8.0 Hz, 1H), 7.59 (d, *J*=8.0 Hz, 1H),7.57-7.53 (m, 2H), 7.50-7.47 (m, 1H), 5.27 (d, *J*=4.0 Hz, 1H), 4.87 (t, *J*=4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 166.09, 143.2, 136.2, 133.6, 132.7, 132.4, 132.0, 129.9, 129.3, 128.9, 128.1, 127.8, 127.1, 126.7, 126.6, 125.8, 123.7, 120.1, 90.7 ppm; **HRMS** (ESI-TOF) calc. for $[C_{19}H_{13}NO +H]^{+}$: 250.1226, Found: 250.1220.



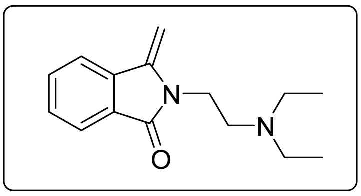
2-(6-chloropyridin-3-yl)-3-methyleneisoindolin-1-one(2v)[2]

White solid (35 mg, 68%); m.p. 115-118 °C; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 8.47 (d, *J* = 8.0 Hz, 1H), 7.92 (d, *J*=8.0 Hz, 1H), 7.79-7.73 (m, 2H), 7.70 (t, *J*=4.0 Hz, 1H), 7.59 (t, *J*=4.0 Hz, 1H), 7.50 (d, *J*=4.0 Hz, 1H), 5.30 (d, *J*= 4.0 Hz, 1H), 4.83 (d, *J*= 4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-*d*) *δ*166.5, 150.3, 148.8, 142.2, 138.1, 136.2, 132.9, 130.5, 130.2, 128.2, 124.9, 123.8, 120.3, 190.6 ppm.



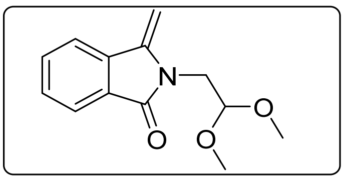
3-methylene-2-(pyridin-3-yl)isoindolin-1-one(2w)

White solid (32 mg, 72%); m.p. 120-125 °C; **^{1}H NMR** (400 MHz, Chloroform-d) δ 8.68-8.64 (m, 2H), 7.92 (d, *J*=8.0 Hz, 1H), 7.78-7.75(m, 2H), 7.68-7.64 (m, 1H), 7.59-7.55 (m, 1H), 7.48-7.45 (m, 1H), 5.27 (d, *J*=4.0 Hz, 1H), 4.81 (d, *J*= 4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-*d*) δ166.6, 149.1, 148.9, 142.3, 136.3, 135.6, 132.7, 131.5, 130.1, 128.5, 124.0, 123.7, 120.2, 90.6, 90.5 ppm; **HRMS** (ESI-TOF) calc. for $[C_{14}H_{10}N_2O +H]^+$: 223.0866, Found: 223.0862.



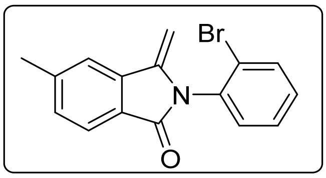
2-(2-(diethylamino)ethyl)-3-methyleneisoindolin-1-one(2y)

Yellow oil (43 mg, 89%); **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.79 (d, *J*=8.0 Hz, 1H), 7.66 (d, *J*=8.0 Hz, 1H), 7.54 (t, *J*=4.0 Hz, 1H), 7.46 (t, *J*=6.0 Hz, 1H), 5.18 (d, *J*=4.0 Hz, 1H), 4.89 (d, *J*=4.0 Hz, 1H), 3.86 (t, *J*=8.0 Hz, 2H), 2.69 (t, *J*=8.0 Hz, 2H), 2.63-2.58 (m, 4H), 1.03 (t, *J*=4.0 Hz,6H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 167.0 , 141.9.2 , 136.4 , 131.8 , 129.4 , 123.0 , 119.8, 88.6 , 50.4 , 47.5, 37.9, 12.1. ppm; **HRMS** (ESI-TOF) calc. for $[C_{15}H_{20}N_2O +H]^+$: 245.1648, Found: 245.1645.



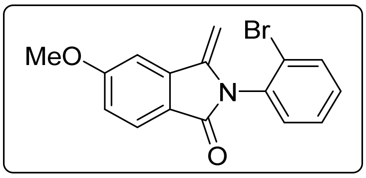
2-(2,2-dimethoxyethyl)-3-methyleneisoindolin-1-one(2z)

Yellow oil (29 mg, 64%); **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.84-7.82 (d, *J*=8.0 Hz, 1H), 7.69-7.67 (d, *J*=8.0 Hz, 1H), 7.59-7.56 (t, *J*=4.0 Hz, 1H), 7.51-7.47(t, *J*=8.0 Hz, 1H), 5.23-5.22(d, *J*=4.0 Hz, 1H), 5.02-5.01(d, *J*=4.0 Hz, 1H), 5.66-5.63 (t, *J*=4.0 Hz, 1H), 3.91-3.90(d, *J*=4.0 Hz, 2H), 3.41(s, 6H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 167.4, 142.0, 136.4, 132.0, 129.4, 128.9, 123.2, 119.9, 102.1, 89.7, 54.5, 54.4, 41.8 ppm; **HRMS** (ESI-TOF) calc. for $[C_{13}H_{15}NO_3 +H]^+$: 234.1124, Found: 234.1125



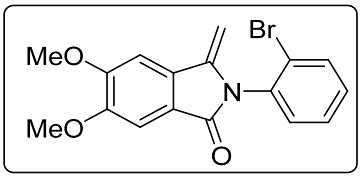
2-(2-bromophenyl)-5-methyl-3-methyleneisoindolin-1-one(4a)

White solid (51 mg, 82% yield). m.p. 80-91 ºC; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.82 (d, J = 8.0 Hz, 1H), 7.76-7.74 (m, 1H), 7.57 (s, 1H), 7.48-7.44 (m, 1H), 7.39-7.31 (m, 3H), 5.17 (d, J = 4.0 Hz, 1H), 4.41 (d, J = 4.0 Hz, 1H), 2.52 (t, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.1, 143.1, 142.2, 136.6, 134.1, 133.6, 131.1, 130.7, 130.4, 128.4, 126.4, 123.9, 123.5, 120.5, 89.9, 21.9, 21.8 ppm; **HRMS** (ESI-TOF) calc. for $[C_{16}H_{12}BrNO +H]^{+}$: 314.0175, Found: 314.0169.



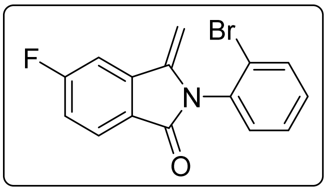
2-(2-bromophenyl)-5-methoxy-3-methyleneisoindolin-1-one(4b)

White solid (46 mg, 71% yield). m.p. 95-97 ºC; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.84 (d, J=8.0 Hz, 1H), 7.75 (d, J=8.0, 1.0 Hz, 1H), 7.48-7.43 (m,1H), 7.38-7.31 (m, 2H), 7.21 (d, J=8.0 Hz, 1H), 7.10-7.07 (m, 1H), 5.15 (d, J = 4.0 Hz, 1H), 4.42 (d, J = 4.0 Hz, 1H), 3.93 (m, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 166.1, 163.6, 142.2, 138.6, 134.2, 133.7, 131.4, 130.4, 128.6, 125.3, 124.1, 121.7, 116.5, 104.5, 90.1, 55.9, 55.8 ppm; **HRMS** (ESI-TOF) calc. for $[C_{16}H_{12}BrNO_2 +H]^{+}$: 330.0124, Found: 330.0118.



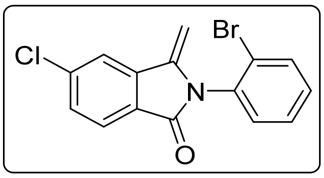
2-(2-bromophenyl)-5,6-dimethoxy-3-methyleneisoindolin-1-one(4c)

White solid (61 mg, 85% yield). m.p.112-114 ºC; **^{1}H NMR** (400 MHz, Chloroform-d) δ 7.75 (d, J=8.0 Hz, 1H), 7.48-7.45 (m, 1H), 7.38-7.32 (m, 3H), 7.19 (s, 1H), 5.08 (d, J=4.0 Hz, 1H), 4.38 (d, J=4.0 Hz, 1H), 4.02 (s, 3H), 3.98 (s, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) δ 168.6 , 166.4 , 153.3, 151.2, 142.2, 134.3, 1333.7, 131.4, 130.5, 130.3, 128.5, 124.1, 121.8, 104.9, 102.3, 102.2, 89.6, 56.4, 56.3 ppm; **HRMS** (ESI-TOF) calc. for $[C_{17}H_{14}BrNO_3+H]^{+}$:360.0229, Found:360.0223.



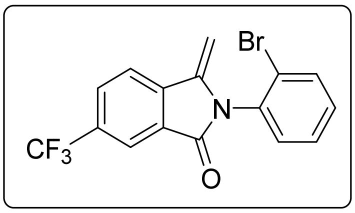
2-(2-bromophenyl)-5-fluoro-3-methyleneisoindolin-1-one(4d)

Colorless liquid(57 mg, 91% yield); **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.97-7.73 (m, 1H), 7.80-7.78 (m, 1H), 7.52-7.44 (m, 2H), 7.40-7.36 (m, 2H), 7.31-7.28 (m, 1H), 5.21 (d, *J* = 4.0 Hz, 1H), 4.53 (d, *J* = 4.0 Hz, 1H); **^{19}F NMR** (376 MHz, $CDCl_3$)δ -105.70; **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 165.8 (d, *J*=251 Hz), 165.1, 141.4 (d, *J*=4 Hz), 138.7 (d, *J*=10 Hz), 133.83, 133.79, 131.2, 130.6, 128.6, 126.0 (d, *J*=10 Hz), 125.01 (d, *J*=2Hz), 123.8, 117.5 (d, *J*=24 Hz), 107.5 (d, *J*=24 Hz), 91.4 ppm; **HRMS** (ESI-TOF) calc. for $[C_{15}H_9BrFNO+H]^+$: 317.9924, Found:317.9917.



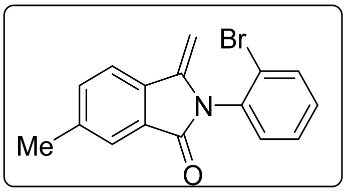
2-(2-bromophenyl)-5-chloro-3-methyleneisoindolin-1-one(4e)

White solid (61 mg, 93% yield). m.p.129-131 ºC; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.87 (d, *J*=8.0, 1.0 Hz, 1H), 7.77-7.74 (m, 2H), 7.55-7.53 (m, 1H), 7.49-7.45 (m, 1H), 7.37-7.33(m, 2H), 5.21 (d, *J* = 4.0 Hz, 1H), 4.50 (d, *J* = 4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 164.9, 140.9, 138.7, 137.6, 133.7, 133.6, 131.0, 130.5, 130.0, 128.5, 127.1, 124.9, 123.6, 120.5, 91.6, 91.5 ppm; **HRMS** (ESI-TOF) calc. for $[C_{15}H_9BrClNO +H]^+$: 333.9628, Found:333.9623.



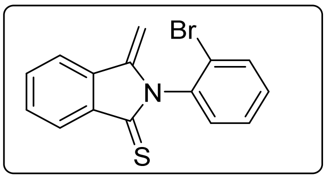
2-(2-bromophenyl)-3-methylene-6-(trifluoromethyl)isoindolin-1-one(4f)

White solid (57 mg, 79% yield). m.p.145-148 ºC; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 8.23 (s, 1H), 7.93-7.88 (m, 2H), 7.79-7.76 (m, 1H), 7.51-7.47 (m, 1H), 7.39-7.35 (m, 2H), 5.33 (d, *J* = 4.0 Hz, 1H), 4.60 (d, *J* = 4.0 Hz, 1H); **^{13}C NMR** (101 MHz, DMSO-d_6) *δ* 164.0, 163.9, 140.6, 139.2, 136.5, 133.4, 133.2, 131.6, 131.3, 130.5 (q, *J*=32 Hz), 129.1, 128.7, 126.9(q, *J*=4 Hz), 124.3, 123.8(q, *J*=27 Hz), 123.71(q, *J*=271 Hz), 123.0, 122.6, 120.1(q, *J*=4 Hz), 118.9(q, *J*=4 Hz), 90.4, 93.7 ppm.; **HRMS** (ESI-TOF) calc. for [$C_{16}H_9BrF_3NO$ +H]$^+$: 367.9892, Found: 367.9891.



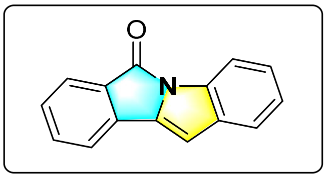
2-(2-bromophenyl)-6-methyl-3-methyleneisoindolin-1-one(4g)

White solid (46 mg, 73% yield). m.p.196-198 °C; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.76-7.74 (m, 2H), 7.65 (d, *J*=4.0, 1.0 Hz, 1H), 7.48-7.44 (m,2H), 7.38-7.31 (m, 2H), 5.14 (d, *J* = 4.0 Hz, 1H), 4.40 (d, *J* = 4.0 Hz, 1H), 2.49 (m, 3H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 166.4 , 142.3 , 140.2 , 134.2 , 133.8 , 133.7 , 133.5, 131.3 , 129.1 , 128.5 , 124.1 , 123.9 , 120.1 , 89.8, 21.7, 21.6 ppm; **HRMS** (ESI-TOF) calc. for [$C_{16}H_{12}BrNO$ +H]$^+$: 314.0175; Found: 314.0169.



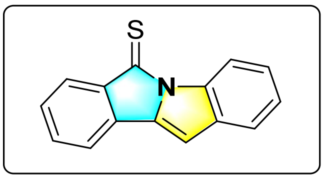
2-(2-bromophenyl)-3-methyleneisoindoline-1-thione(4i)

White solid (42 mg, 68%); m.p. 143-144 °C; **^{1}H NMR** (400 MHz, Chloroform-d) *δ* 7.94 (d, *J*=8.0 Hz, 1H), 7.76 (d, *J*=8.0 Hz, 2H), 7.64 (t, *J*=4.0 Hz, 1H), 7.55 (t, *J*=6.0 Hz, 1H), 7.46 (t, *J*=6.0 Hz, 1H), 7.38-7.32 (m, 2H), 5.21 (d, *J*=4.0 Hz, 1H), 4.45 (d, *J*=4.0 Hz, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ*166.6, 166.2, 142.2, 136.3, 134.6, 134.0, 133.8, 132.5, 131.3, 130.6, 129.8, 128.9, 128.6, 124.0, 123.9, 123.7, 120.3, 90.6 ppm; **HRMS** (ESI-TOF) calc. for [$C_{15}H_{10}BrNS$ +H]$^+$: 315.9967; Found: 315.9962.



6H-isoindolo[2,1-a]indol-6-one(5c)[1]

Yellow solid (1000 mg, 89% yield). m.p.157-158 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.88(d, *J* =8.0 Hz, 1H), 7.74 (d, *J* = 4 Hz, 1H), 7.51-7.49 (m, 2H), 7.43 (d, *J*=4 Hz, 1H), 7.357.25 (m, 2H), 7.15 (t, J = 8 Hz, 1H), 6.59 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 162.5, 138.7, 134.6, 134.4, 133.8, 133.6, 133.5, 128.7, 126.2, 125.1, 123.8, 122.2, 121.1, 113.2, 103.4, 103.3 ppm.



6H-isoindolo[2,1-a]indol-6-one(5i)

Red solid (32 mg, 87% yield). m.p.64-67 ºC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.45 (d, *J* =8.0 Hz, 1H), 7.82 (d, *J* = 4 Hz, 1H), 7.49-7.40 (m, 3H), 7.32-7.26 (m, 2H), 7.15 (t, J = 8 Hz, 1H), 6.57 (s, 1H); **^{13}C NMR** (101 MHz, Chloroform-d) *δ* 188.9, 142.5, 141.9, 135.2, 134.9, 133.1, 132.0, 128.9, 127.7, 125.3, 125.2, 122.6, 120.5, 114.3, 104.1 ppm. HRMS (ESI-TOF) calc. for $[C_{15}H_9NS + H]^+$: 236.0528; Found: 236.0524.

4. X-raySpectra of 2c, 5c and 5i.

4.1 Single crystal data for compound 2c

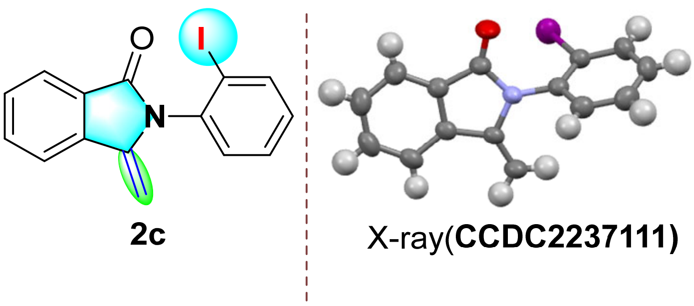


Figure S6. X-ray(CCDC2237111) Spectra of **2c**

Datablock wjl-1 - ellipsoid plot

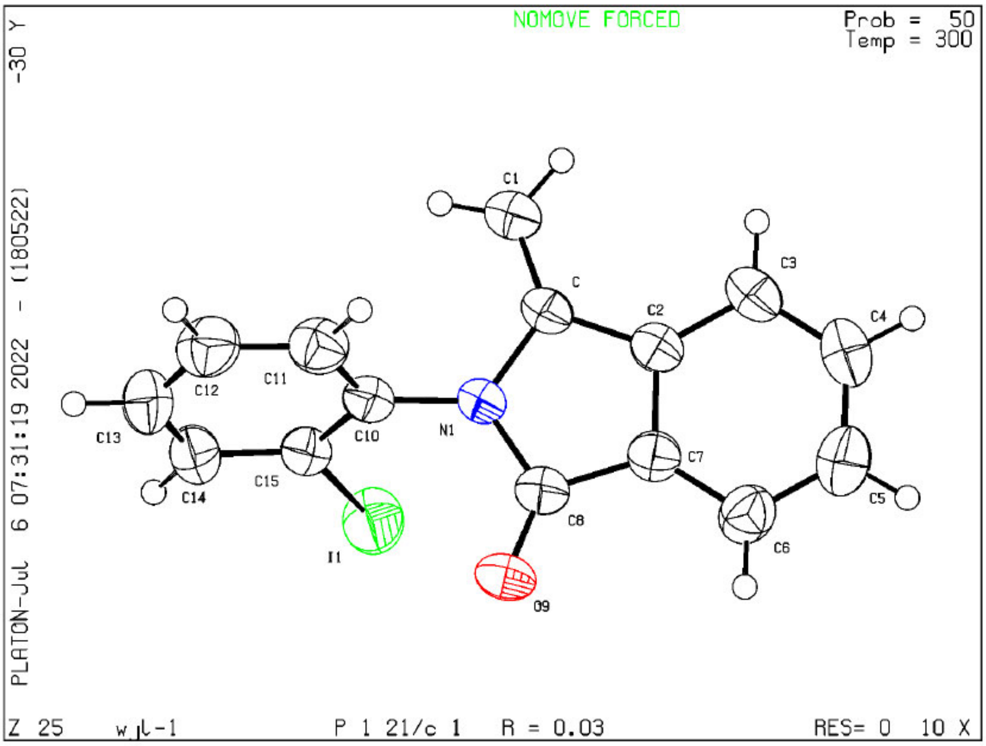


Figure S7. X-ray (CCDC2237111) Spectra of **2c**

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: wjl-1

Bond precision: C-C = 0.0049 A Wavelength=0.71073

Cell:	a=13.0551(6)	b=7.4021(3)	c=13.9932(6)
	alpha=90	beta=101.381(2)	gamma=90
Temperature:	300 K		

	Calculated	Reported
Volume	1325.65(10)	1325.65(10)
Space group	P 21/c	P 1 21/c 1
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C15 H10 I N O	C15 H10 I N O
Sum formula	C15 H10 I N O	C15 H10 I N O
Mr	347.14	347.14
Dx,g cm-3	1.739	1.739
Z	4	4
Mu (mm-1)	2.402	2.402
F000	672.0	672.0
F000'	670.34	
h,k,lmax	16,9,17	16,9,17
Nref	2772	2735
Tmin,Tmax	0.655,0.768	0.622,0.745
Tmin'	0.627	

Correction method= # Reported T Limits: Tmin=0.622 Tmax=0.745
AbsCorr = MULTI-SCAN

Data completeness= 0.987 Theta(max)= 26.578

R(reflections)= 0.0270(2437) wR2(reflections)= 0.0982(2735)

S = 0.997 Npar= 163

```
The following ALERTS were generated. Each ALERT has the format
       test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
```

Alert level G

```
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ..........        4.6 Low
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   0 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   1 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   0 ALERT type 2 Indicator that the structure model may be wrong or deficient
   1 ALERT type 3 Indicator that the structure quality may be low
   0 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

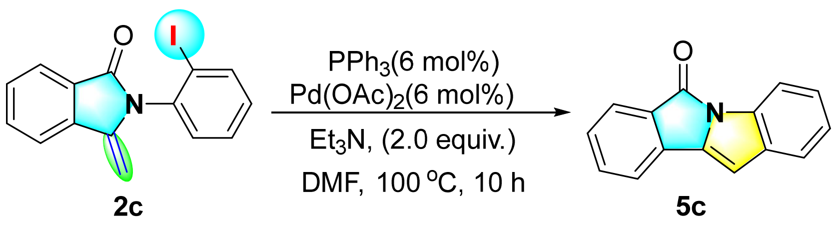
Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica*, *Journal of Applied Crystallography*, *Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E* or *IUCrData*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Figure S8. Single crystal data of **2c** (X-ray(CCDC2237111))

4.2 Single crystal data for compound 5c



2c, 1.8 g, 85%

5c, 1.0 g, 89%

Scheme S7. Synthesis of substrates **5c**

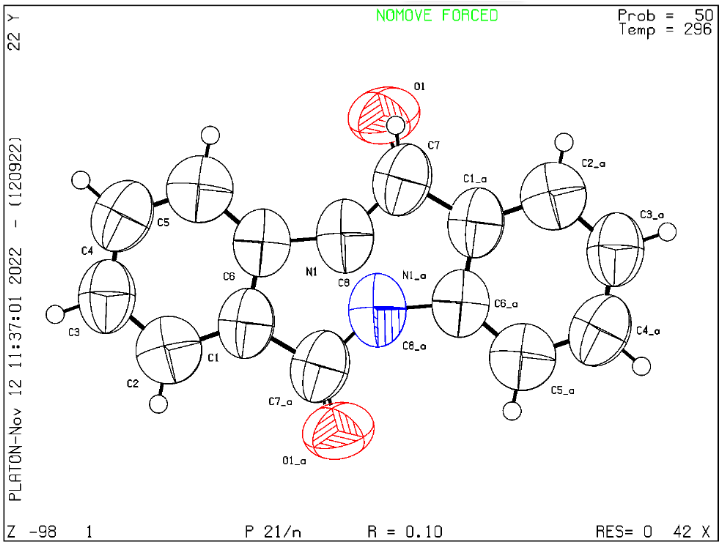


Figure S9. X-ray (CCDC2219270) Spectra of **5c**

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: 1

```
Bond precision:   C-C = 0.0093 A          Wavelength=0.71073

Cell:               a=6.52(2)     b=5.62(2)            c=14.76(5)
                    alpha=90      beta=94.416(5)       gamma=90
Temperature:        296 K

                 Calculated                 Reported
Volume           539(3)                     539(3)
Space group      P 21/n                     P 21/n
Hall group       -P 2yn                     -P 2yn
Moiety formula   C15 H9 N O                 ?
Sum formula      C15 H9 N O                 C15 H9 N O
Mr               219.23                     219.23
Dx,g cm-3        1.351                      1.350
Z                2                          2
Mu (mm-1)        0.085                      0.085
F000             228.0                      228.0
F000'            228.10
h,k,lmax         7,6,17                     7,6,17
Nref             943                        929
Tmin,Tmax        0.983,0.983                0.864,0.864
Tmin'            0.983

Correction method= # Reported T Limits: Tmin=0.864 Tmax=0.864
AbsCorr = MULTI-SCAN

Data completeness= 0.985          Theta(max)= 24.930

R(reflections)= 0.1006( 393)                          wR2(reflections)=
                                                      0.3217( 929)
S = 1.037                 Npar= 71
```

```
The following ALERTS were generated. Each ALERT has the format
       test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
```

```
Alert level C
PLAT026_ALERT_3_C Ratio Observed / Unique Reflections (too) Low ..       42% Check
PLAT031_ALERT_4_C Refined Extinction Parameter Within Range of ...     2.667 Sigma
PLAT084_ALERT_3_C High wR2 Value (i.e. > 0.25) ..................       0.32 Report
PLAT148_ALERT_3_C s.u. on the       a    - Axis is (Too) Large ....    0.020 Ang.
PLAT148_ALERT_3_C s.u. on the       b    - Axis is (Too) Large ....   0.0200 Ang.
PLAT148_ALERT_3_C s.u. on the       c    - Axis is (Too) Large ....    0.050 Ang.
PLAT234_ALERT_4_C Large Hirshfeld Difference C1         --C2      .     0.16 Ang.
PLAT260_ALERT_2_C Large Average Ueq of Residue Including        O1     0.117 Check
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............    0.00929 Ang.
```

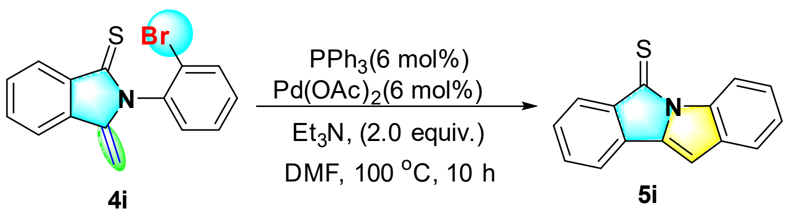
```
Alert level G
PLAT168_ALERT_4_G The CIF-Embedded .res File Contains EXYZ Records          1 Report
PLAT171_ALERT_4_G The CIF-Embedded .res File Contains EADP Records          1 Report
PLAT230_ALERT_2_G Hirshfeld Test Diff for    O1         --C7      .       5.1 s.u.
PLAT300_ALERT_4_G Atom Site Occupancy of O1          Constrained at       0.5 Check
PLAT300_ALERT_4_G Atom Site Occupancy of N1          Constrained at       0.5 Check
PLAT300_ALERT_4_G Atom Site Occupancy of C8          Constrained at       0.5 Check
PLAT300_ALERT_4_G Atom Site Occupancy of H7          Constrained at       0.5 Check
PLAT301_ALERT_3_G Main Residue  Disorder ..............(Resd  1  )        18% Note
PLAT764_ALERT_4_G Overcomplete CIF Bond List Detected (Rep/Expd) .      1.25 Ratio
PLAT767_ALERT_4_G INS Embedded LIST 6 Instruction Should be LIST 4    Please Check
PLAT883_ALERT_1_G No Info/Value for _atom_sites_solution_primary .    Please Do !
PLAT965_ALERT_2_G The SHELXL WEIGHT Optimisation has not Converged    Please Check
PLAT967_ALERT_5_G Note: Two-Theta Cutoff Value in Embedded .res ..      50.0 Degree
```

```
  0 ALERT level A = Most likely a serious problem - resolve or explain
  0 ALERT level B = A potentially serious problem, consider carefully
  9 ALERT level C = Check. Ensure it is not caused by an omission or oversight
 13 ALERT level G = General information/check it is not something unexpected

  1 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
  3 ALERT type 2 Indicator that the structure model may be wrong or deficient
  7 ALERT type 3 Indicator that the structure quality may be low
 10 ALERT type 4 Improvement, methodology, query or suggestion
  1 ALERT type 5 Informative message, check
```

Figure S10. Single crystal data of **5c** (X-ray (CCDC2219270))

4.3 Single crystal data for compound **5i**



Scheme S8. Synthesis of substrates **5i**

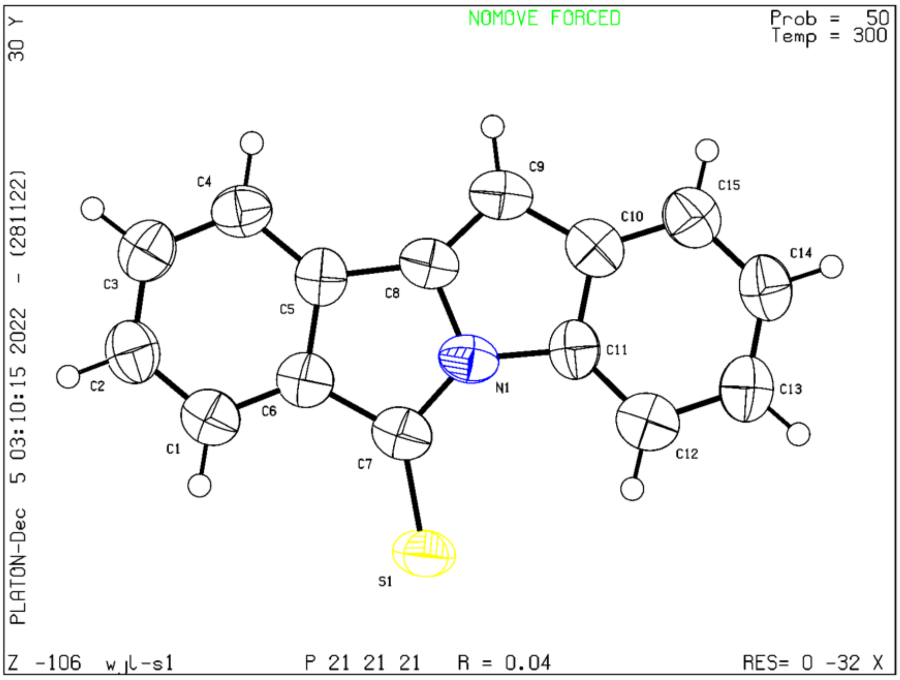


Figure S11. X-ray (CCDC 2224294) Spectra of **5i**

checkCIF/PLATON report

You have not supplied any structure factors. As a result the full set of tests cannot be run.

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No syntax errors found. CIF dictionary Interpreting this report

Datablock: wjl-s1

Bond precision: C-C = 0.0070 A Wavelength=0.71073

Cell:	a=13.5296(8)	b=17.6839(10)	c=4.6966(2)
	alpha=90	beta=90	gamma=90
Temperature:	300 K		

	Calculated	Reported
Volume	1123.69(10)	1123.69(10)
Space group	P 21 21 21	P 21 21 21
Hall group	P 2ac 2ab	P 2ac 2ab
Moiety formula	C15 H9 N S	C15 H9 N S
Sum formula	C15 H9 N S	C15 H9 N S
Mr	235.29	235.29
Dx,g cm-3	1.391	1.391
Z	4	4
Mu (mm-1)	0.260	0.260
F000	488.0	488.0
F000'	488.65	
h,k,lmax	16,21,5	16,21,5
Nref	2205[1321]	1753
Tmin,Tmax	0.954,0.974	0.673,0.745
Tmin'	0.949	

Correction method= # Reported T Limits: Tmin=0.673 Tmax=0.745
AbsCorr = MULTI-SCAN

Data completeness= 1.33/0.80 Theta(max)= 26.020

R(reflections)= 0.0432(1541) wR2(reflections)= 0.1133(1753)

S = 1.149 Npar= 154

```
The following ALERTS were generated. Each ALERT has the format
       test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.
```

Alert level A

```
PLAT029_ALERT_3_A _diffrn_measured_fraction_theta_full value Low .      0.856 Why?
```

Author Response: The completeness of data is less than the usual 99-100% for this compound, however it is only the very high angle data that is incomplete and above 0.75 angstroms we have 100% coverage. This will always be a problem with area detector data that is not truncated.

Alert level C

```
PLAT340_ALERT_3_C Low Bond Precision on  C-C Bonds ..............      0.007 Ang.
```

Alert level G

```
PLAT941_ALERT_3_G Average HKL Measurement Multiplicity ..........       3.7 Low
```

```
   1 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   1 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   1 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   0 ALERT type 2 Indicator that the structure model may be wrong or deficient
   3 ALERT type 3 Indicator that the structure quality may be low
   0 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

Figure S12. Single crystal data of **5i** (X-ray (CCDC 2224294))

5. References

[1](a)Long Y, She Z, Liu X, et al. Synthesis of 1-aminoisoquinolines by gold (III)-mediated domino reactions from 2-alkynylbenzamides and ammonium acetate. *J Org Chem.* **2013**, *78*(6): 2579-2588. (b)Marques C S, Peixoto D, Burke A J. Transition-metal-catalyzed intramolecular cyclization of amido (hetero) arylboronic acid aldehydes to isoquinolinones and derivatives. *RSC Adv.* **2015**, *5*(26): 20108-20114.

[2] Dai X J, Liu M, Zhang J Y, et al. A Facile Direct Synthesis of 3-Methyleneisoindolin-1-ones by Annulation of Methyl 2-Acylbenzoates with Amines. *ChemistrySelect*. **2019**, *4*(15): 4458-4461

[3] Wei W, Chen Z, Lin Y, et al. Synthesis of Isoindolinones through Intramolecular Amidation of ortho-Vinyl Benzamides. *Adv Synth & Catal.* **2020**, *362*(10): 1972-1976.

[4]Sharma S, Nayal O S, Sharma A, et al. Tin (II) triflate catalysed synthesis of 3-methyleneisoindolin-1-ones[J]. *ChemistrySelect*, **2019**, *4(6)*: 1985-1988.

[5]Zhou B, Hou W, Yang Y, et al. Rhodium (III)-Catalyzed Amidation of Aryl Ketone O-Methyl Oximes with

Isocyanates by C□ H Activation: Convergent Synthesis of 3-Methyleneisoindolin-1-ones[J]. Chemistry–A European Journal, 2013, 19(15): 4701-4706.

[6]Gao B, Liu S, Lan Y, et al. Rhodium-catalyzed cyclocarbonylation of ketimines via C–H bond activation[J]. Organometallics, 2016, 35(10): 1480-1487.

[7]Albano G, Giuntini S, Aronica L A. Synthesis of 3-Alkylideneisoindolin-1-ones via sonogashira cyclocarbonylative reactions of 2-ethynylbenzamides[J]. The Journal of organic chemistry, 2020, 85(15): 10022-10034.

6. ^{1}H, ^{13}C and ^{19}F NMR Spectra for Products **2a-5i**

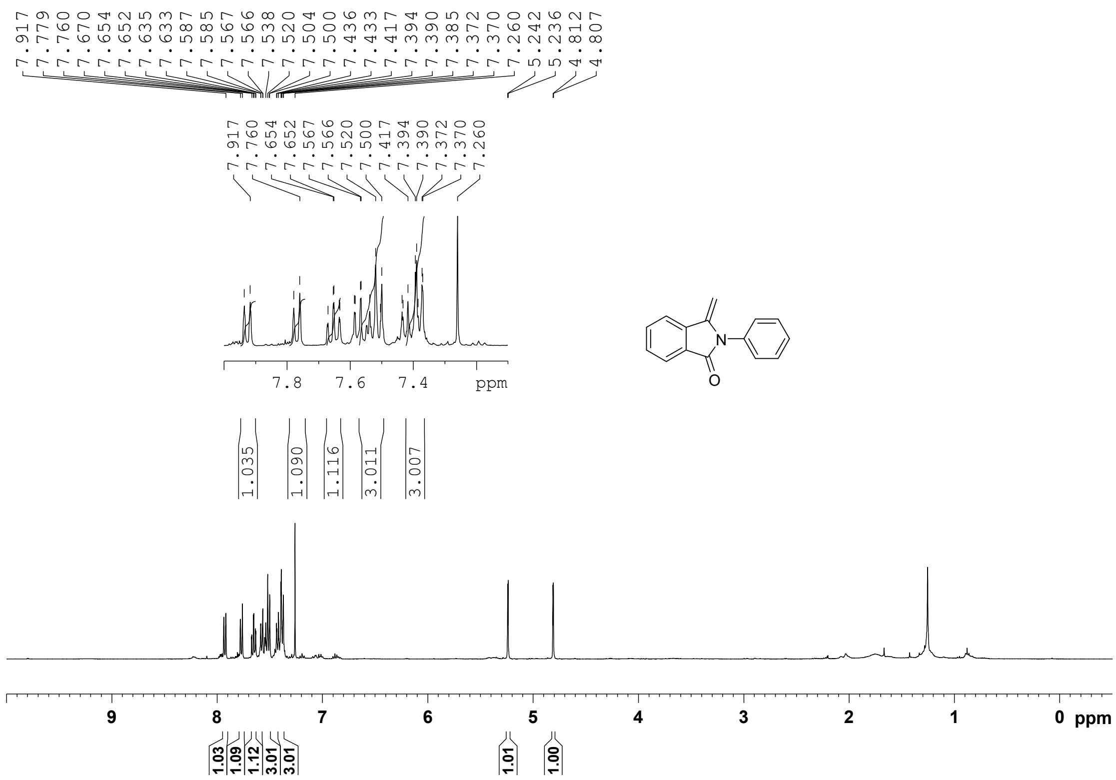

Figure S13. ^{1}H NMR (400 MHz, $CDCl_3$) of **2a**

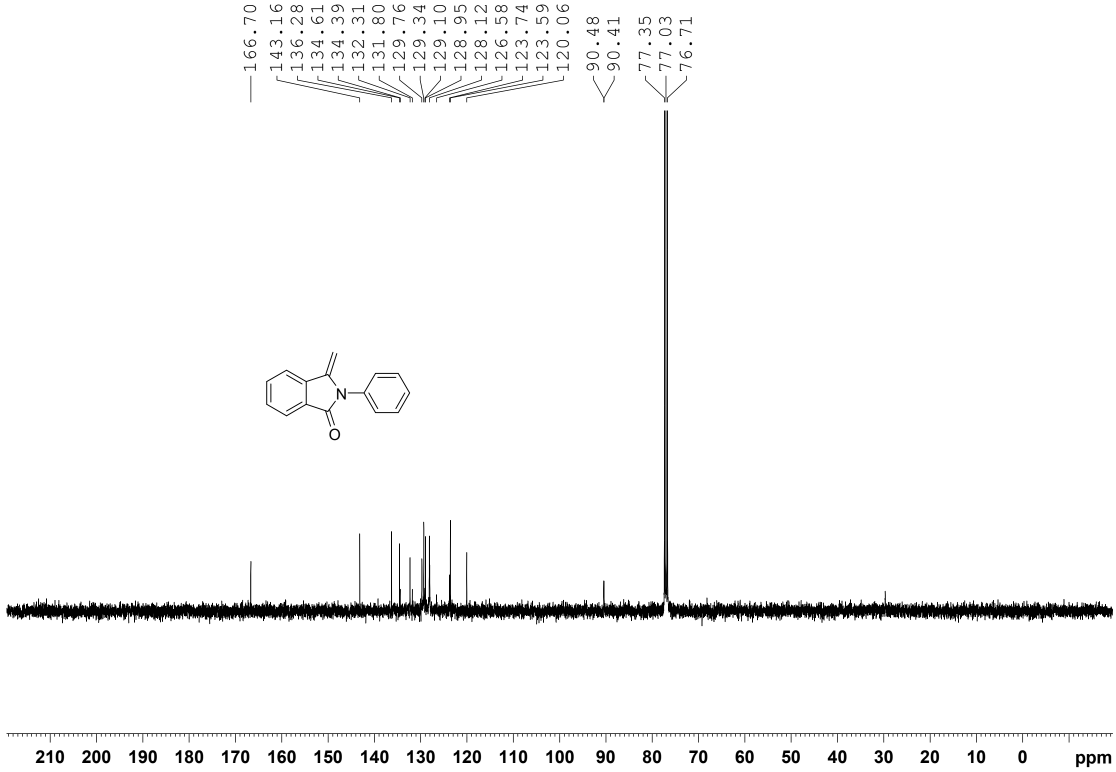

Figure S14. ^{13}C NMR (101 MHz, $CDCl_3$) of **2a**

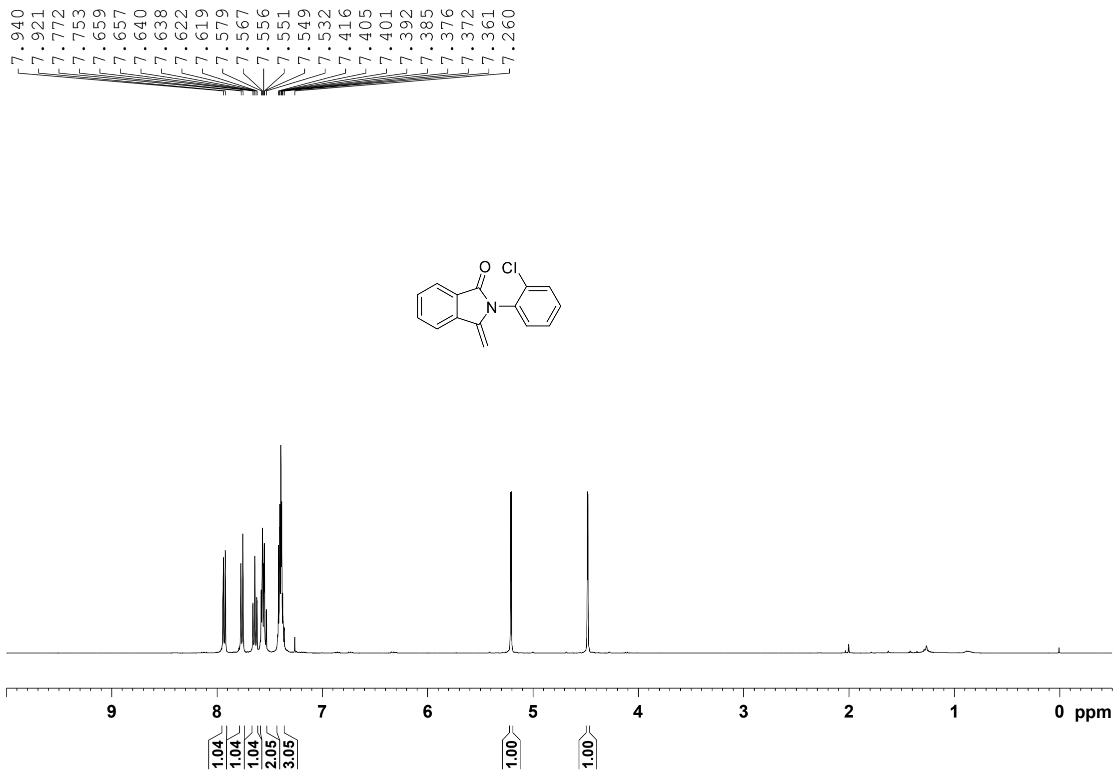

Figure S15. ^{1}H NMR (400 MHz, $CDCl_3$) of **2b**

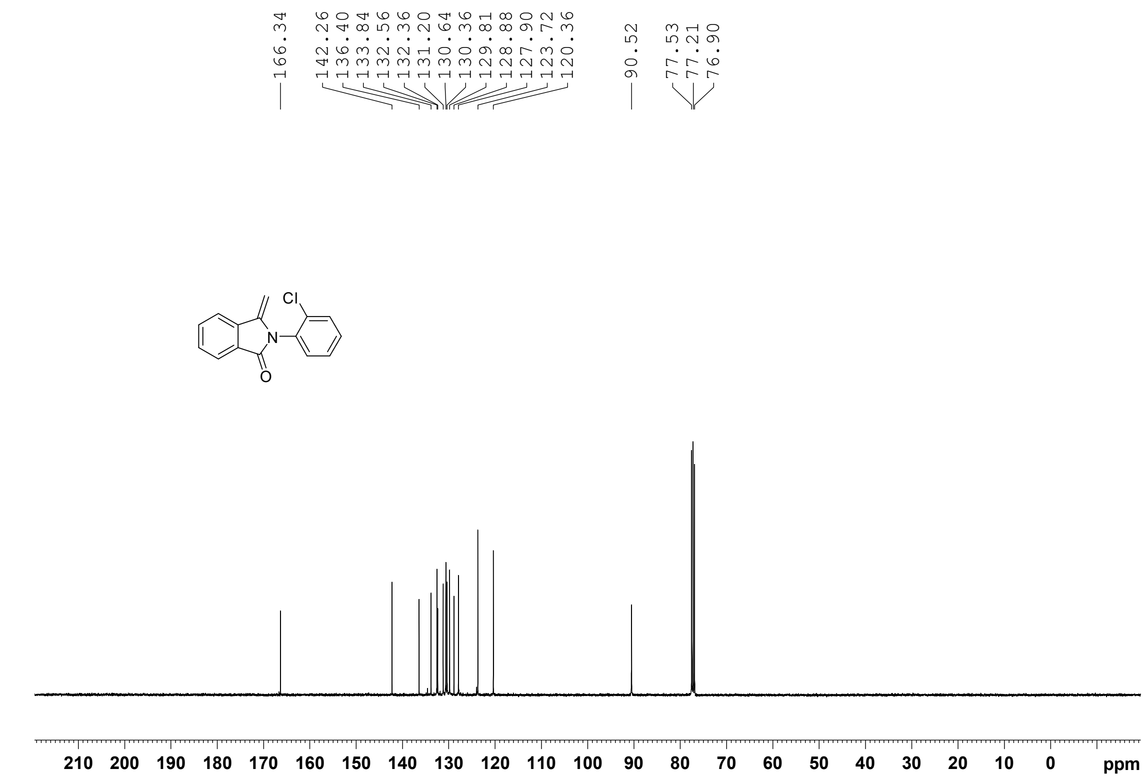

Figure S16. ^{13}C NMR (101 MHz, $CDCl_3$) of **2b**

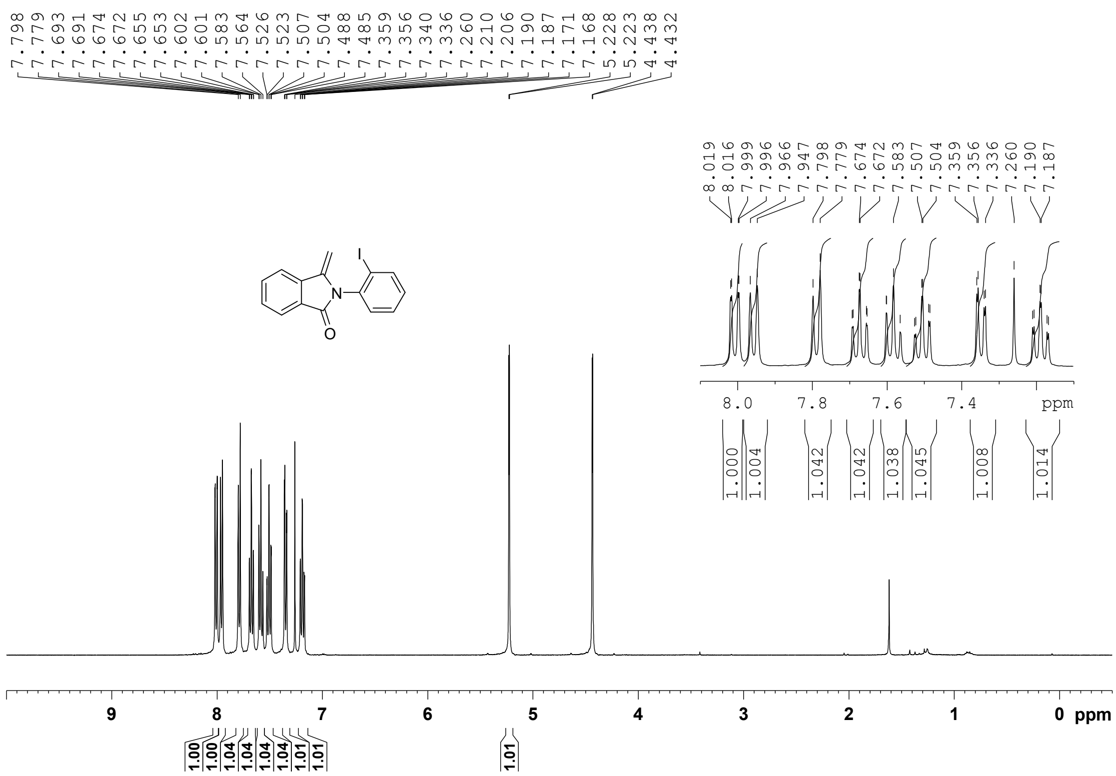

Figure S17.1H NMR (400 MHz, $CDCl_3$) of of **2c**

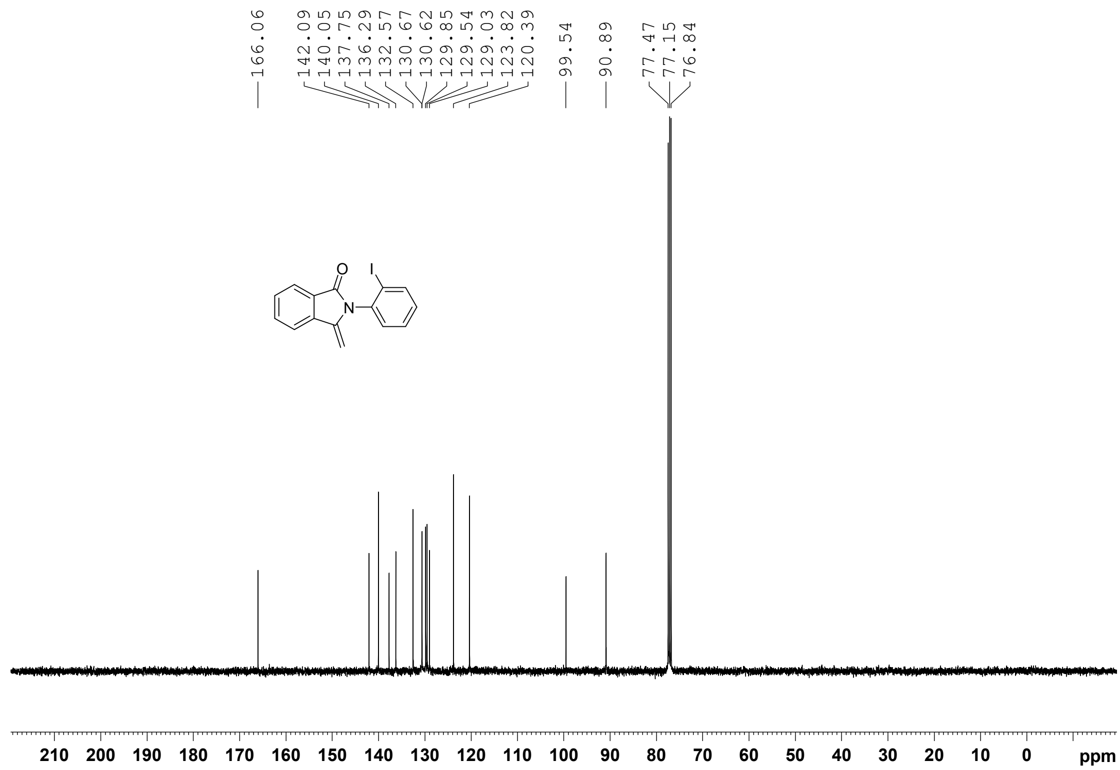

Figure S18. ^{13}C NMR (101 MHz, $CDCl_3$) of **2c**

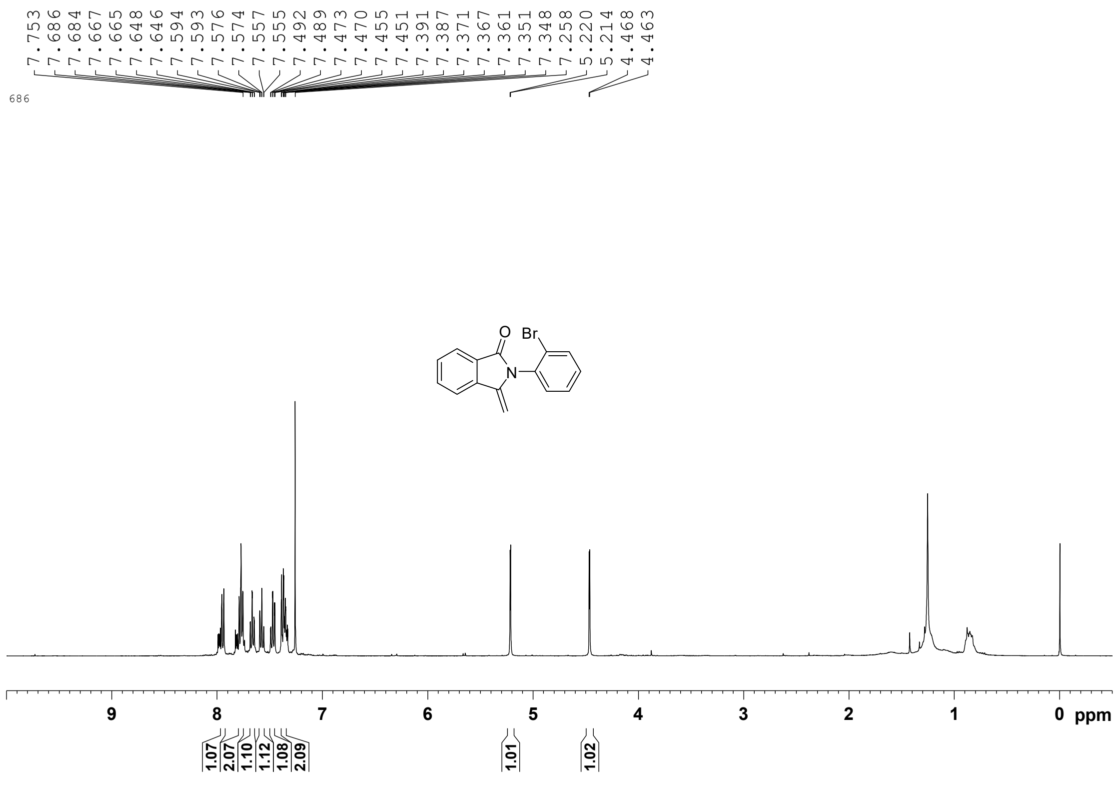

Figure S19. ^{1}H NMR (400 MHz, $CDCl_3$) of **2d**

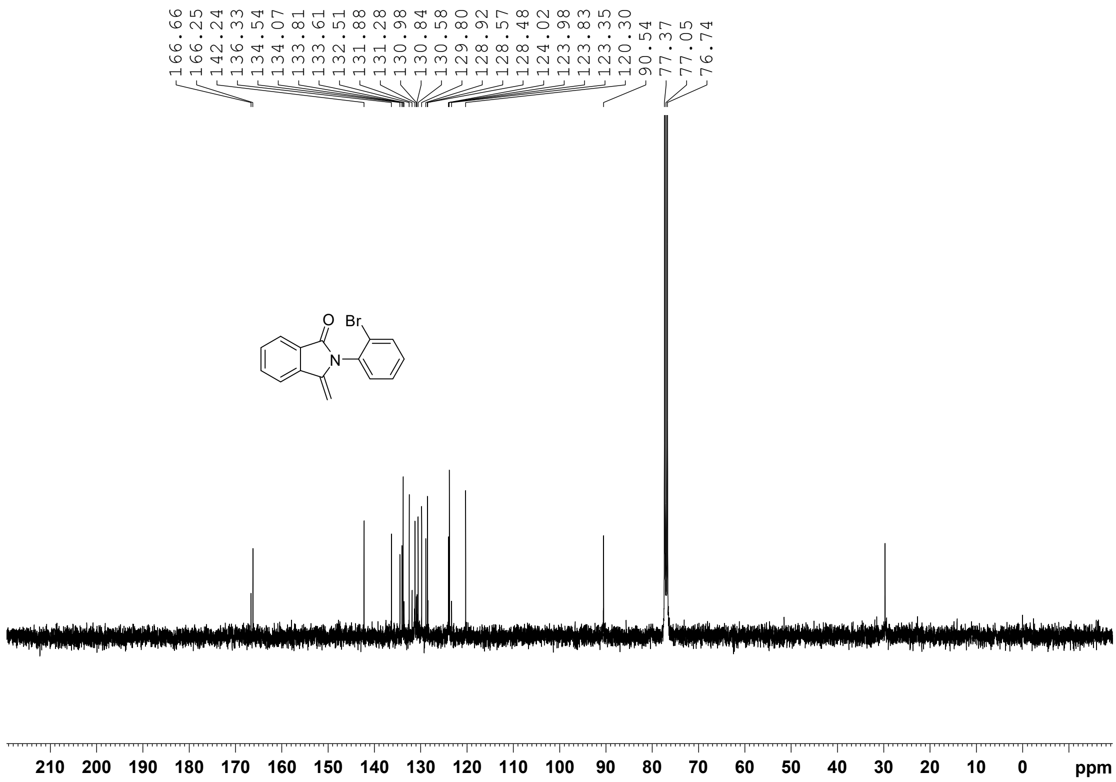

Figure S20. ^{13}C NMR (101 MHz, $CDCl_3$) of **2d**

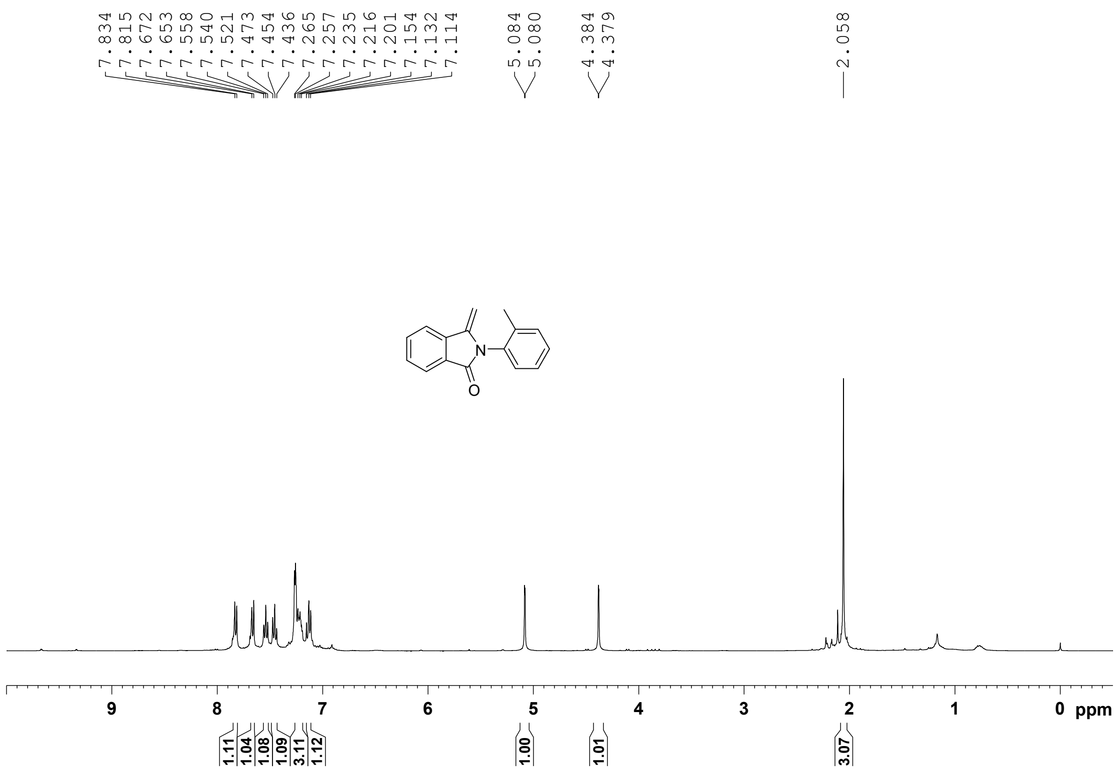

Figure S21. ^{1}H NMR (400 MHz, $CDCl_3$) of **2e**

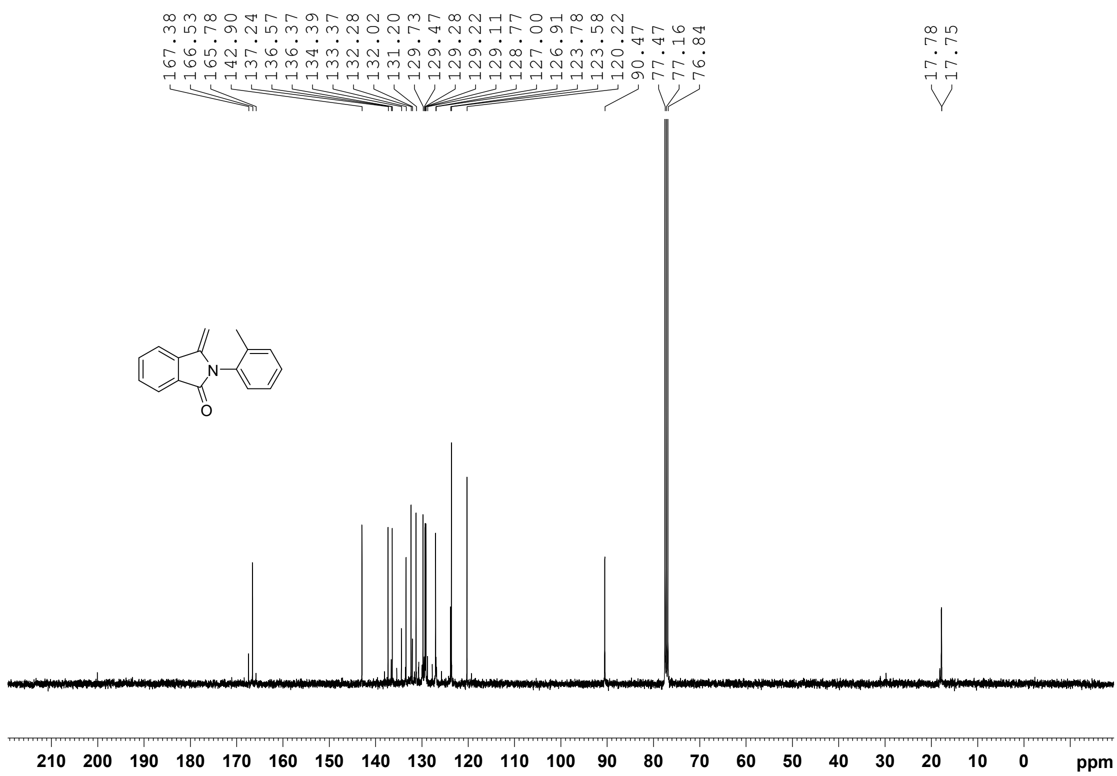

Figure S22. ^{13}C NMR (101 MHz, $CDCl_3$) of **2e**

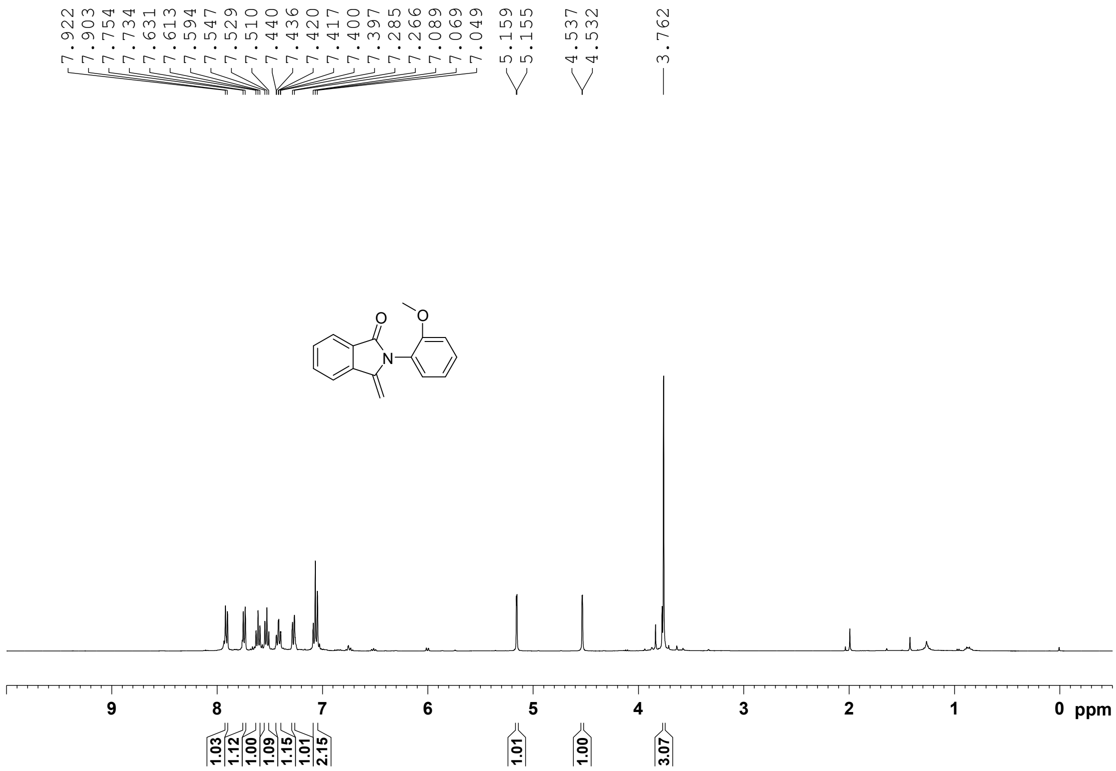

Figure S23. ^{1}H NMR (400 MHz, $CDCl_3$) of **2f**

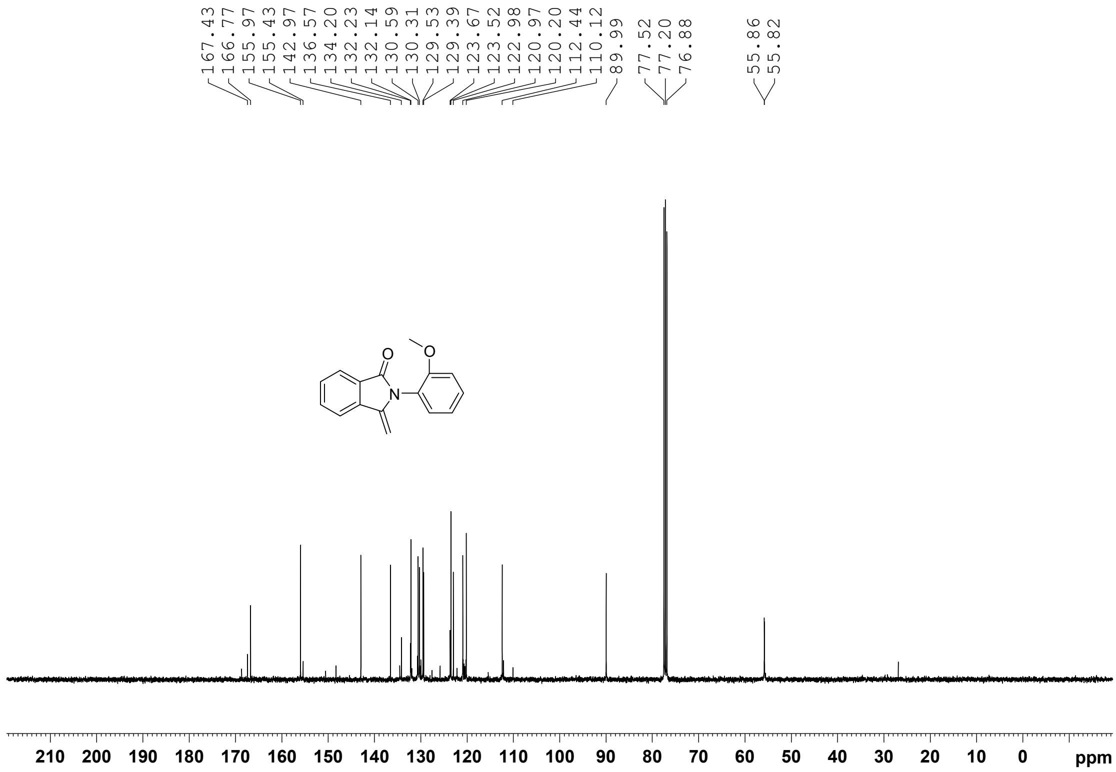

Figure S24. ^{13}C NMR (101 MHz, $CDCl_3$) of **2f**

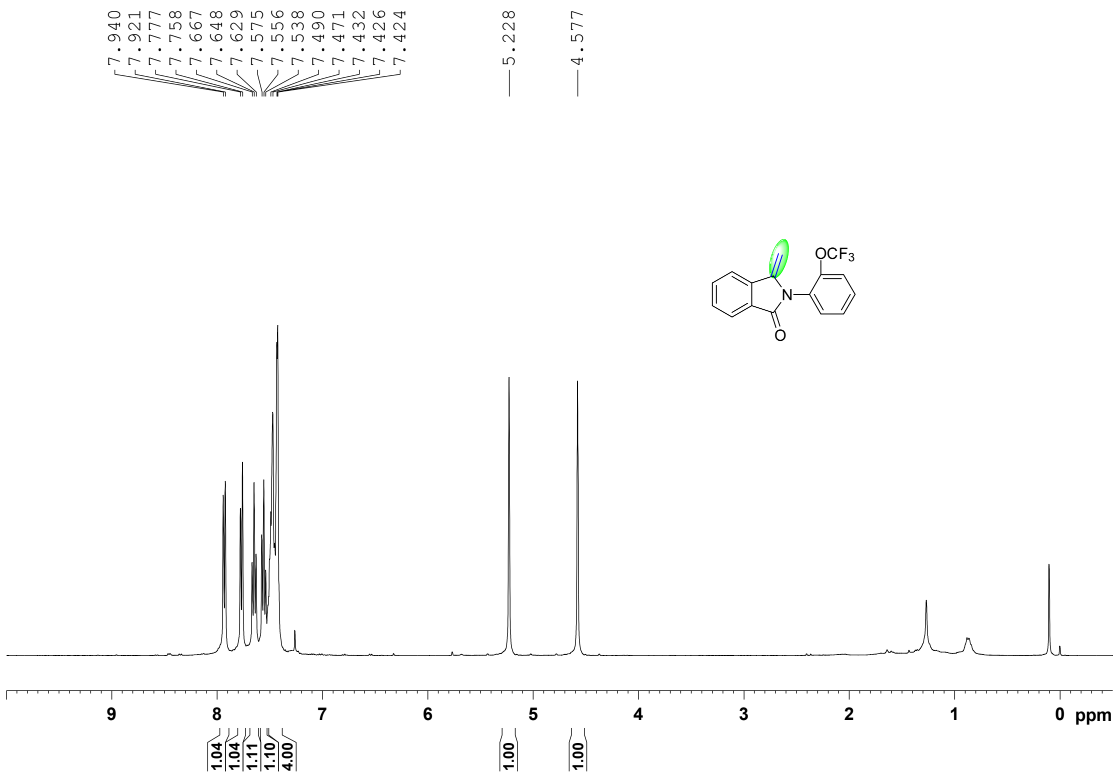

Figure S25. ^{1}H NMR (400 MHz, $CDCl_3$) of **2g**

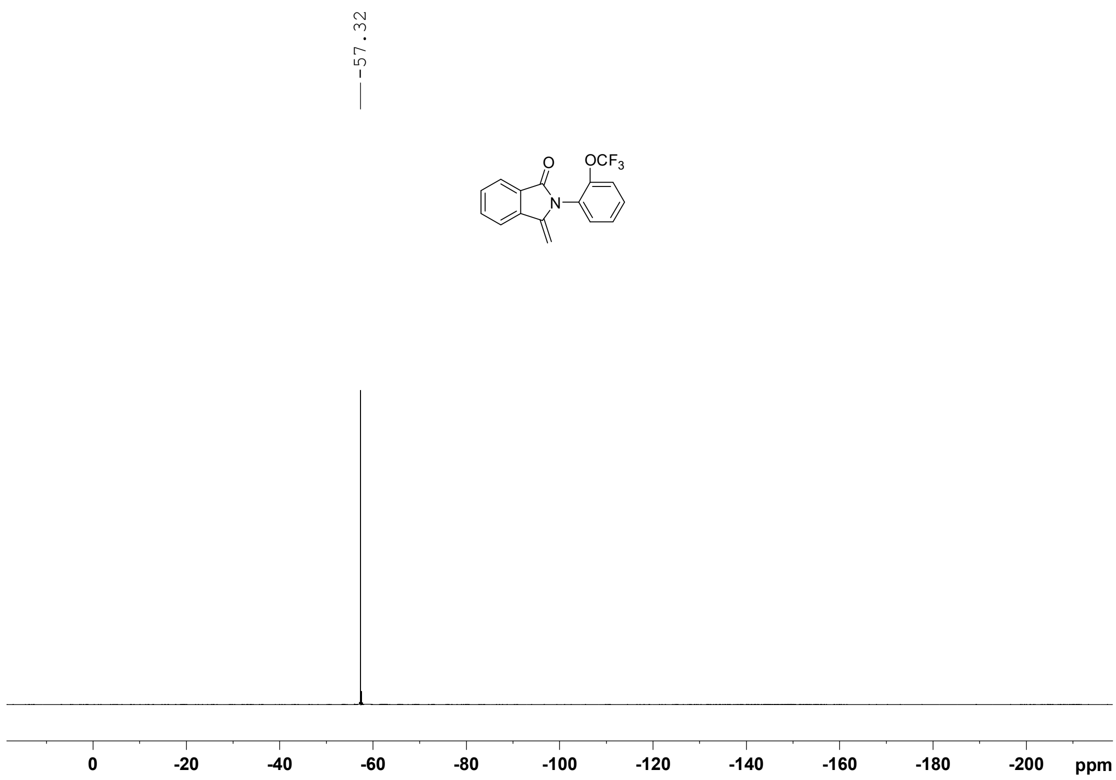

Figure S26. ^{19}F NMR (376 MHz, $CDCl_3$) of **2g**

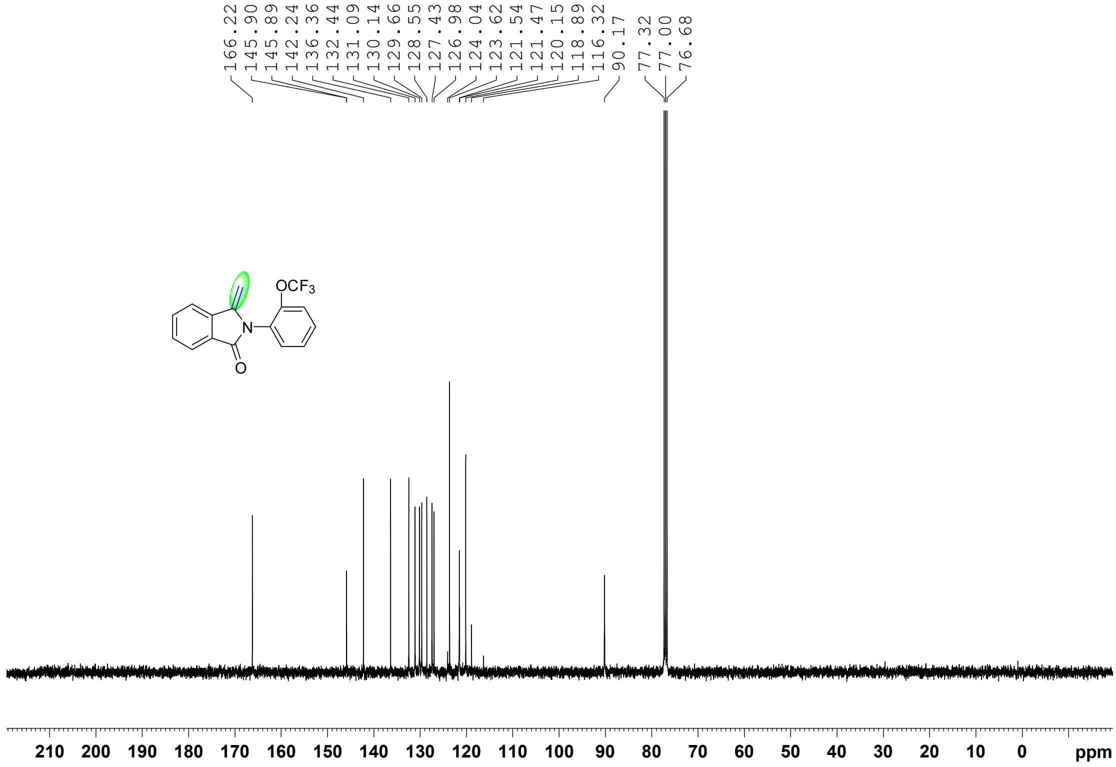

Figure S27. ^{13}C NMR (101 MHz, $CDCl_3$) of **2g**

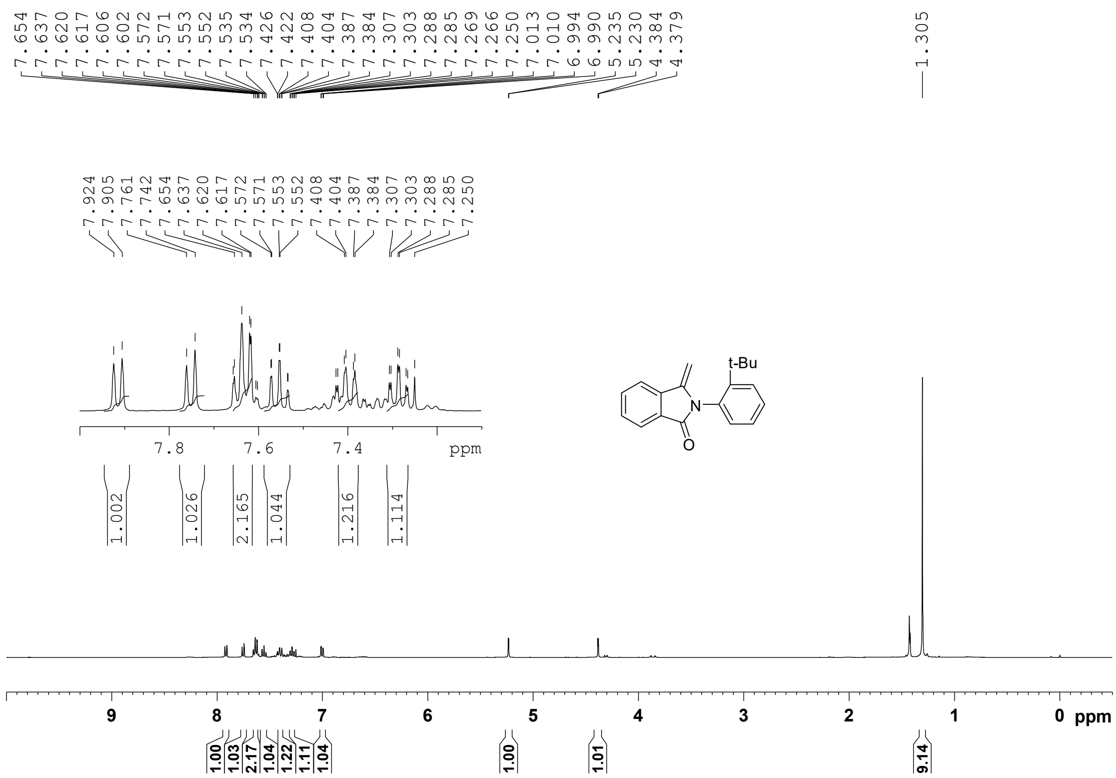

Figure S28.[1]H NMR (400 MHz, $CDCl_3$) of **2h**

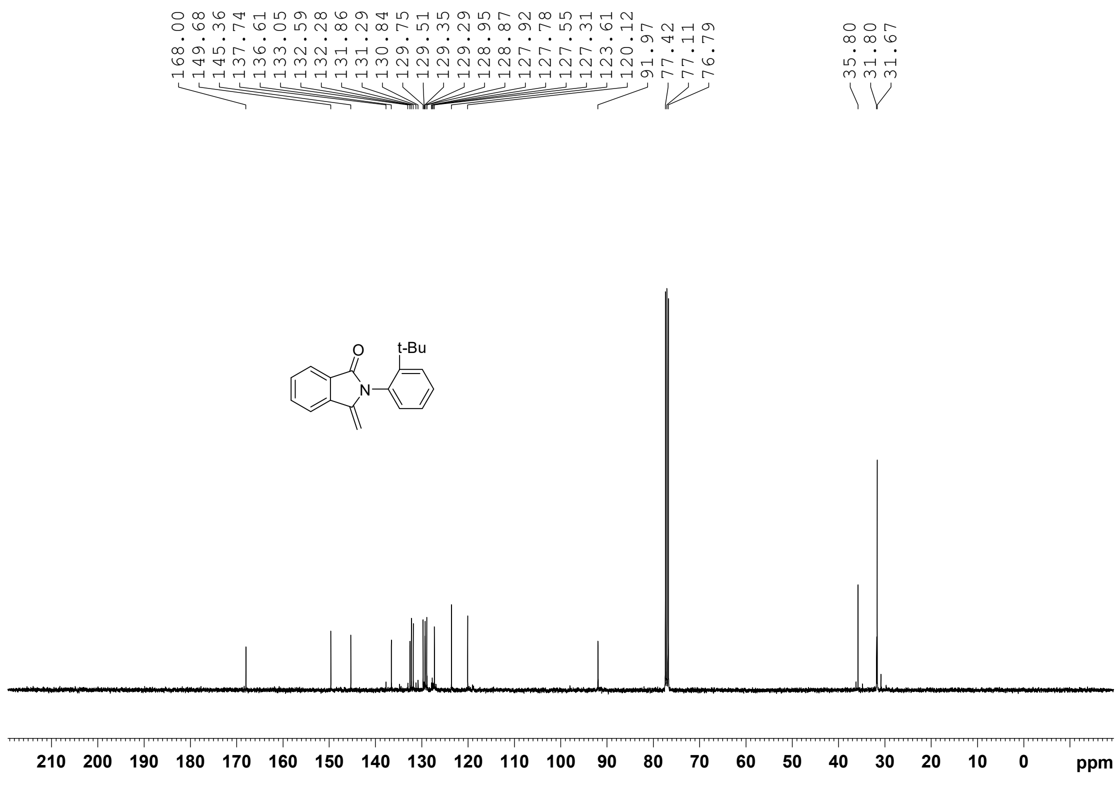

Figure S29. ^{13}C NMR (101 MHz, $CDCl_3$) of **2h**

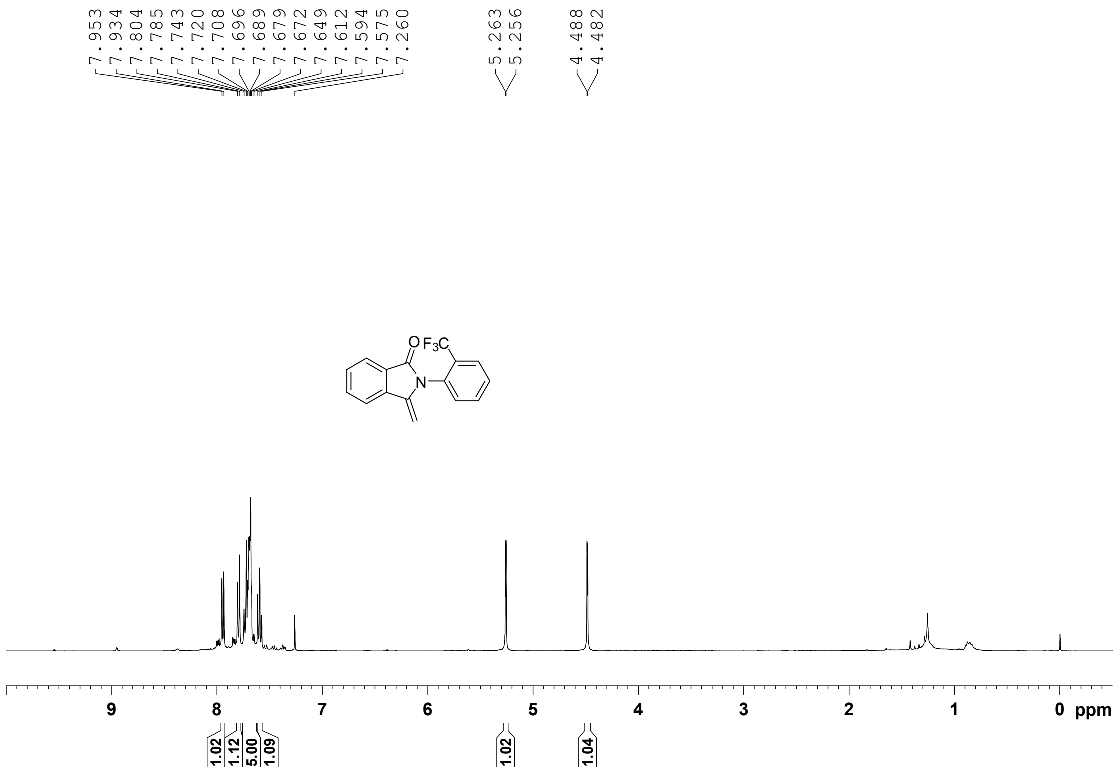

Figure S30. ^{1}H NMR (400 MHz, $CDCl_3$) of **2i**

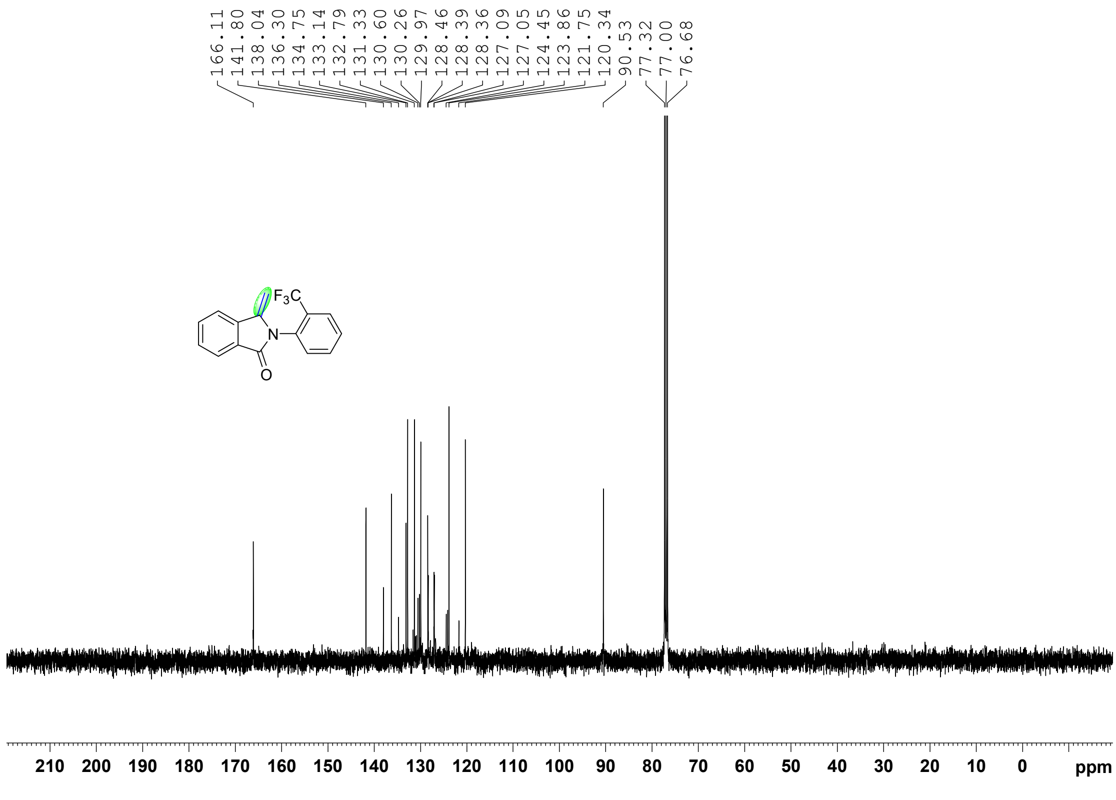

Figure S31. ^{13}C NMR (101 MHz, $CDCl_3$) of **2i**

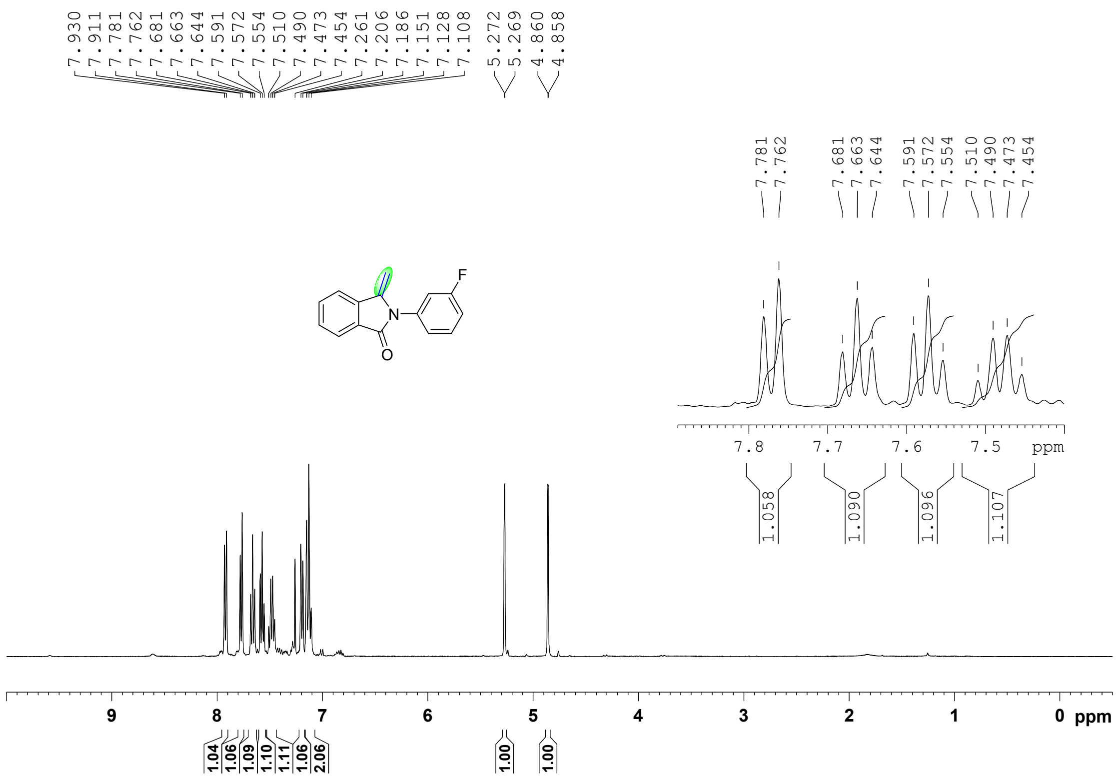

Figure S32. ^{1}H NMR (400 MHz, $CDCl_3$) of **2j**

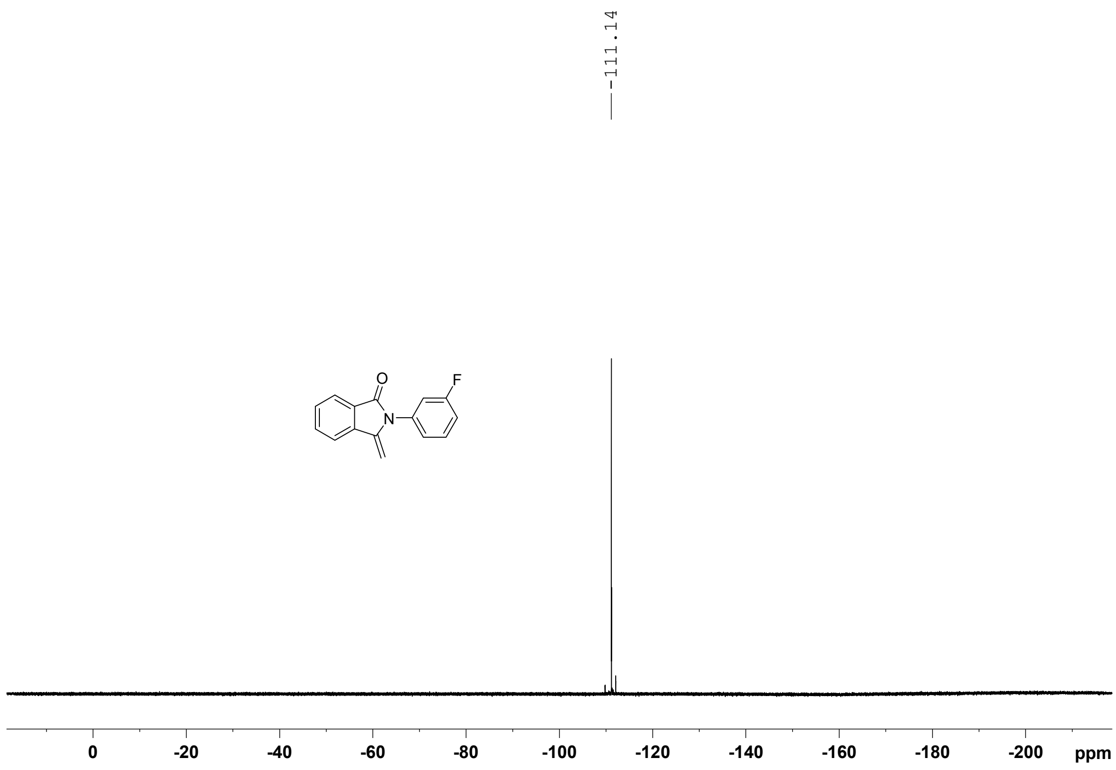

Figure S33. ^{19}F NMR (376 MHz, $CDCl_3$) of **2j**

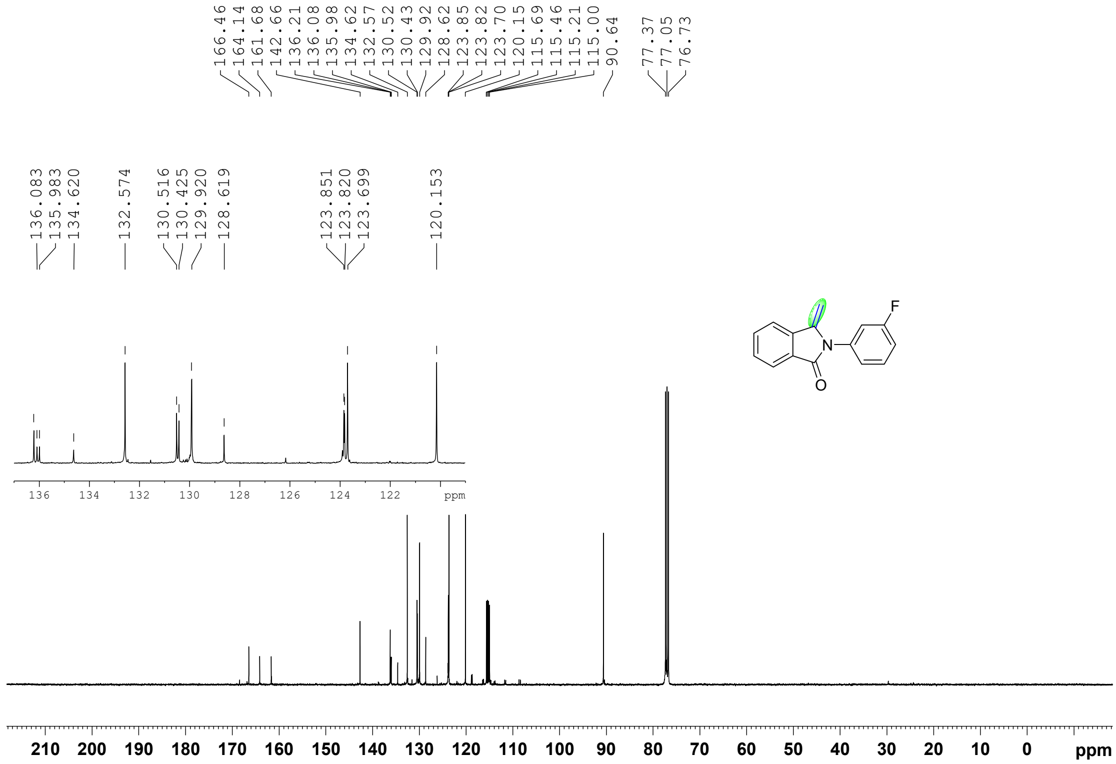

Figure S34. ^{13}C NMR (101 MHz, CDCl$_3$) of **2j**

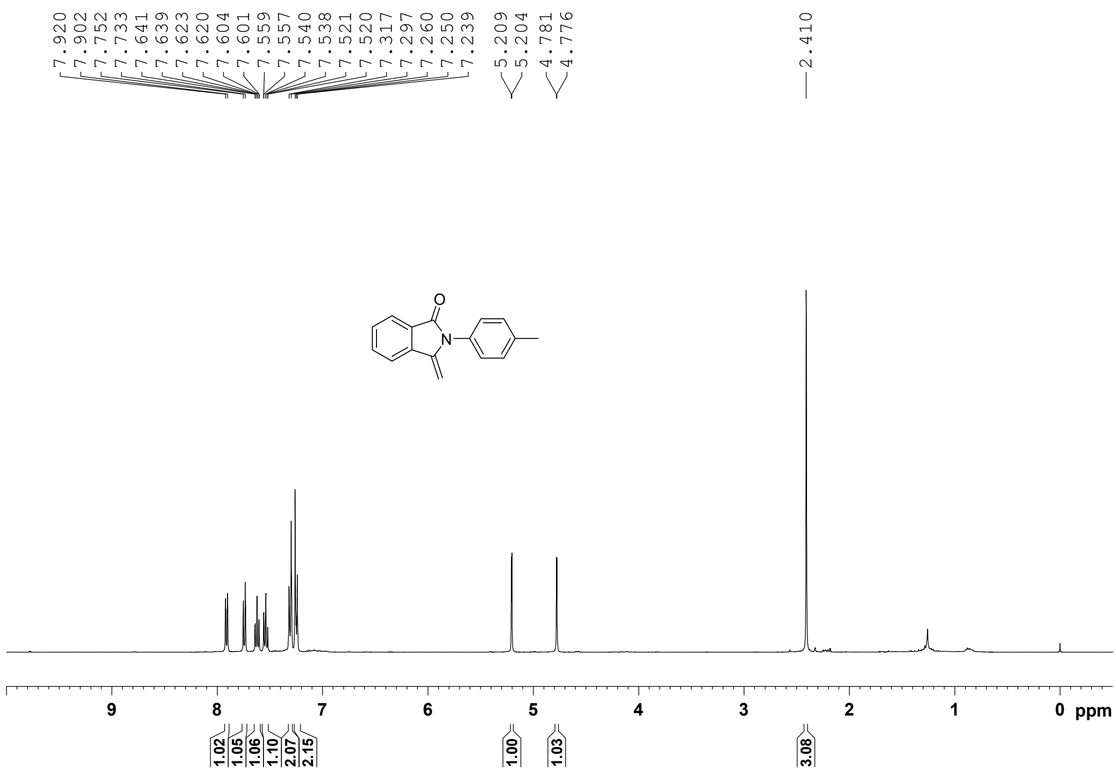

Figure S35.^{1}H NMR (400 MHz, CDCl$_3$) of **2k**

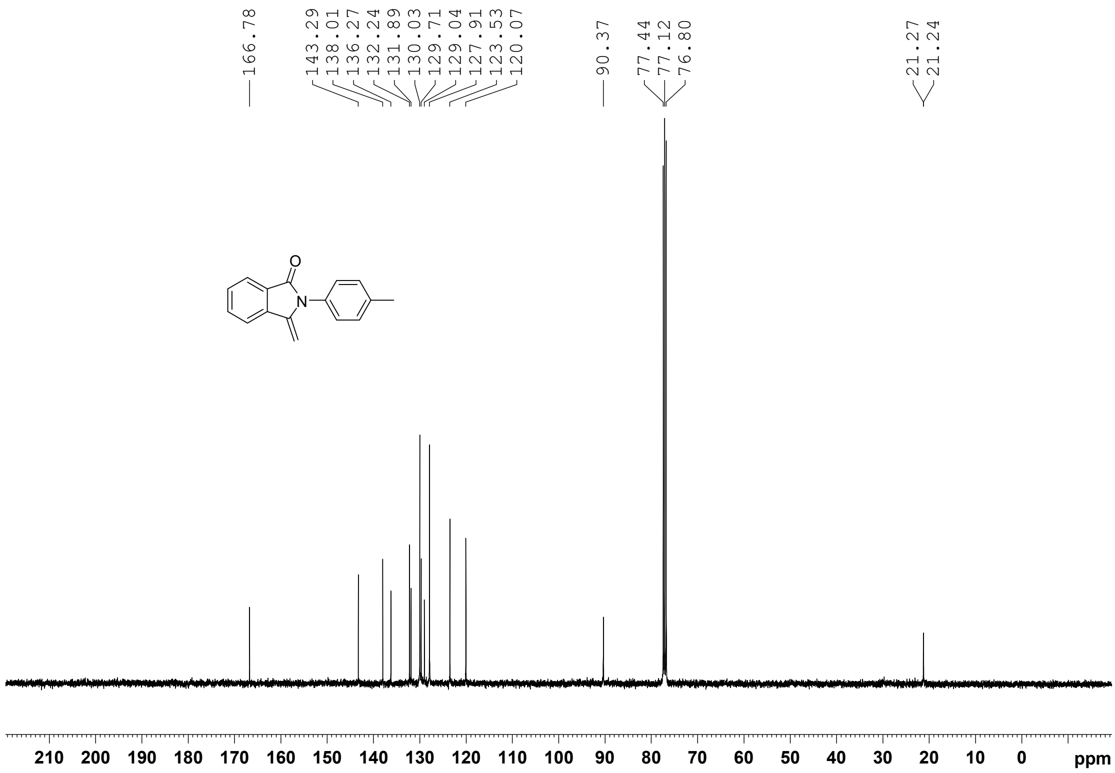

Figure S36. ^{13}C NMR (101 MHz, $CDCl_3$) of **2k**

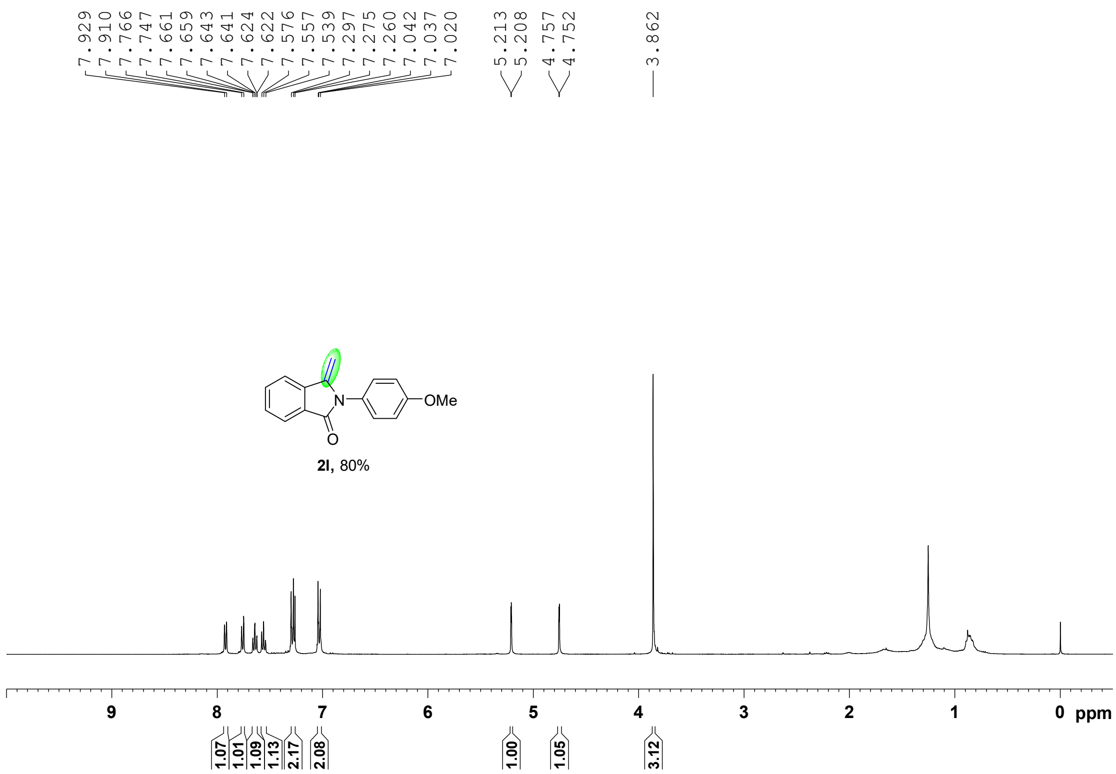

Figure S37. ^{1}H NMR (400 MHz, $CDCl_3$) of **2l**

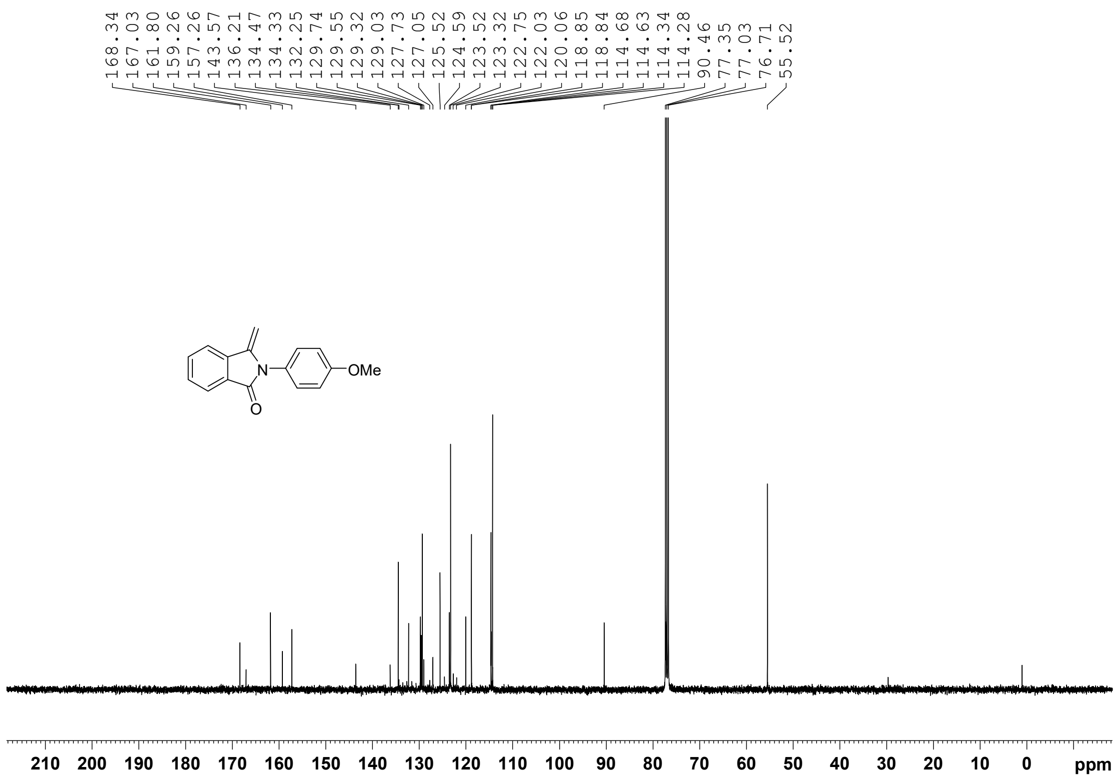

Figure S38. ^{13}C NMR (101 MHz, $CDCl_3$) of **2l**

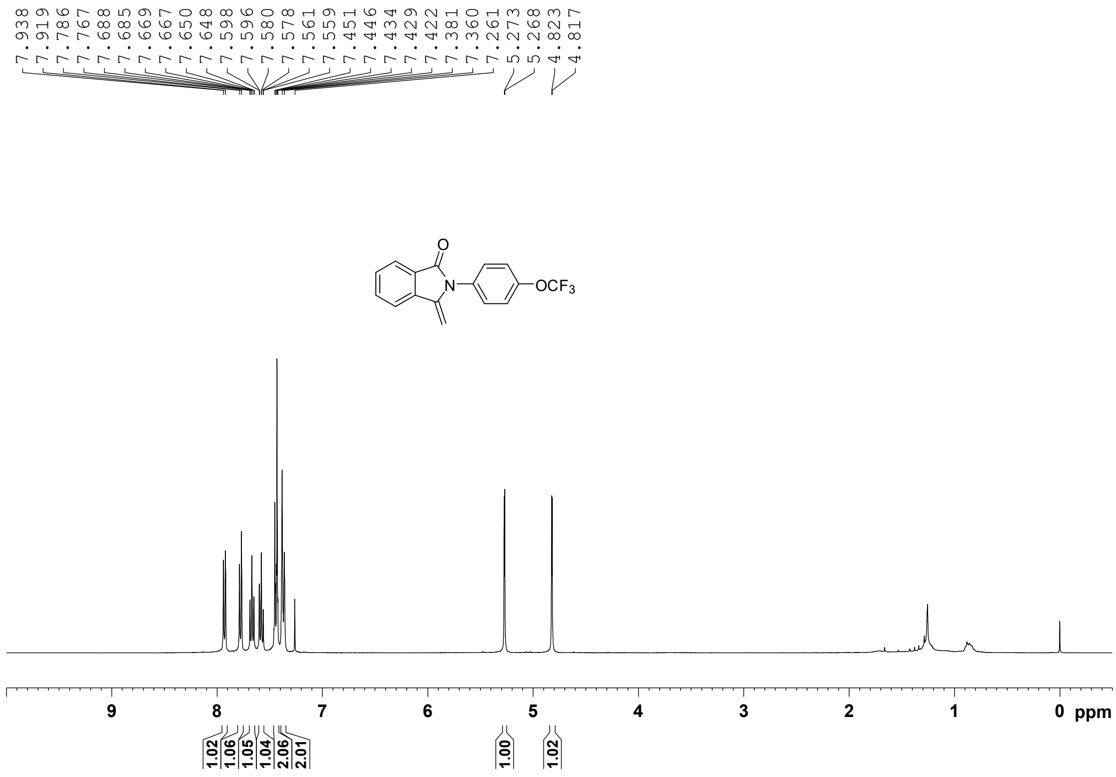

Figure S39. ^{1}H NMR (400 MHz, $CDCl_3$) of **2m**

Figure S40. ^{19}F NMR (376 MHz, $CDCl_3$) of **2m**

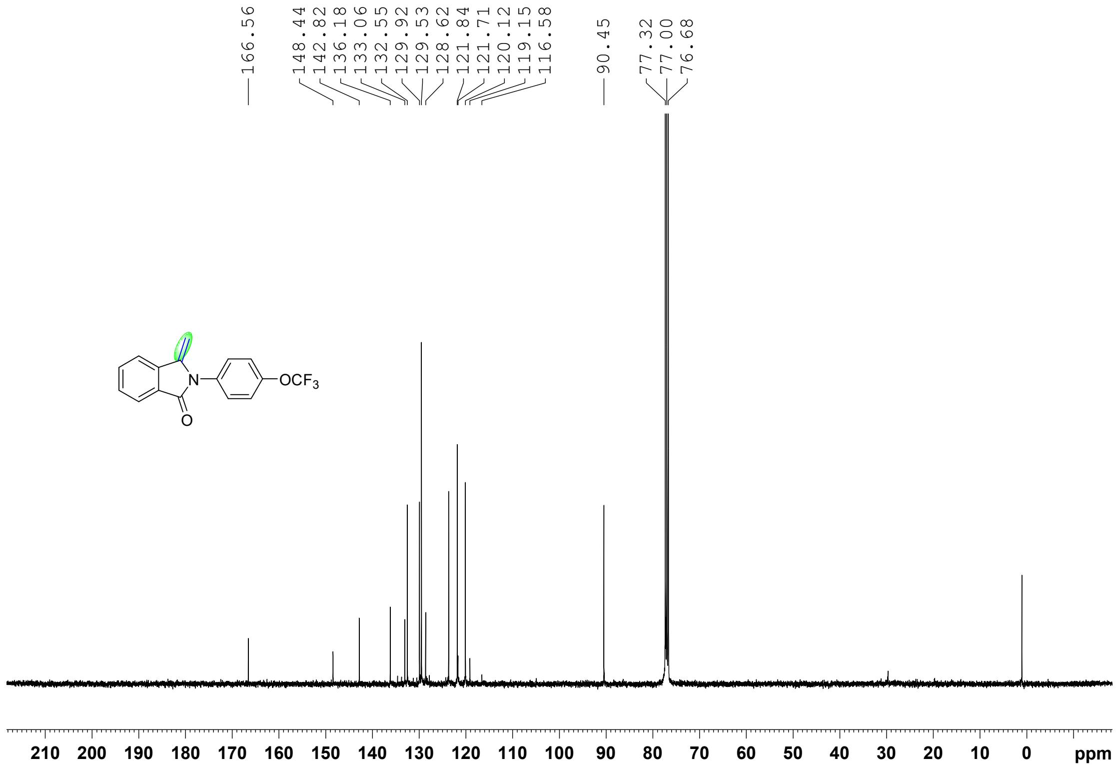

Figure S41. ^{13}C NMR (101 MHz, $CDCl_3$) of **2m**

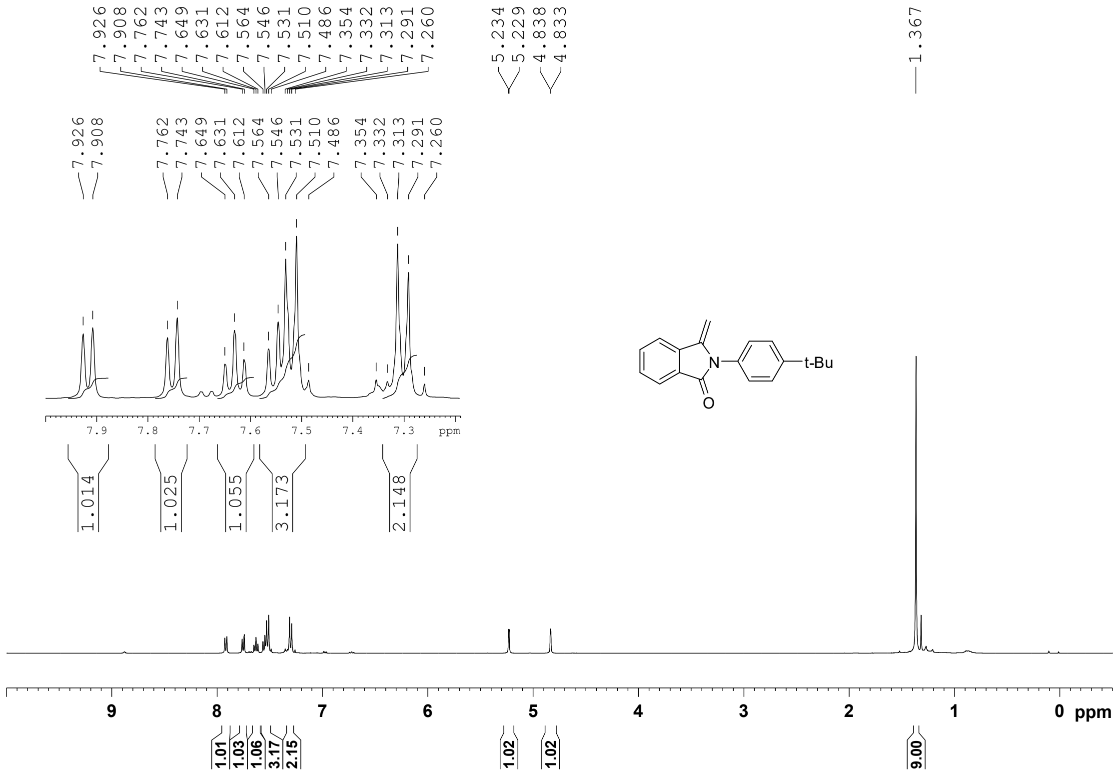

Figure S42. ^{1}H NMR (400 MHz, CDCl3) of **2n**

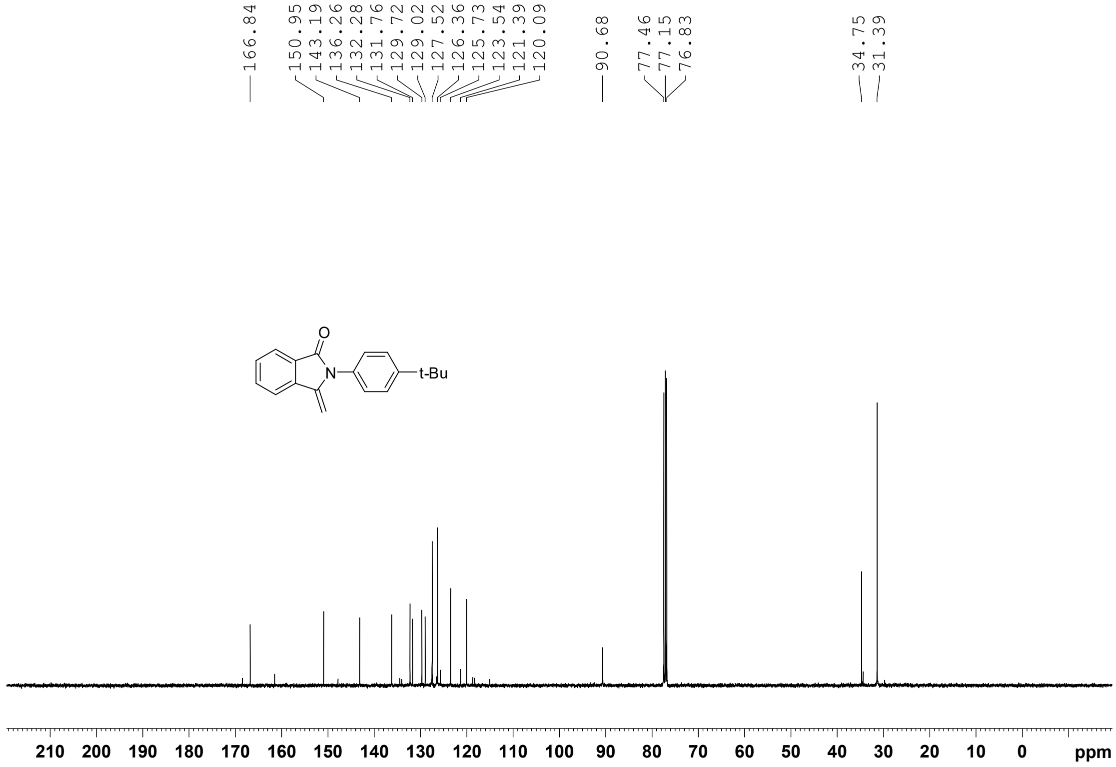

Figure S43. ^{13}C NMR (101 MHz, $CDCl_3$) of **2n**

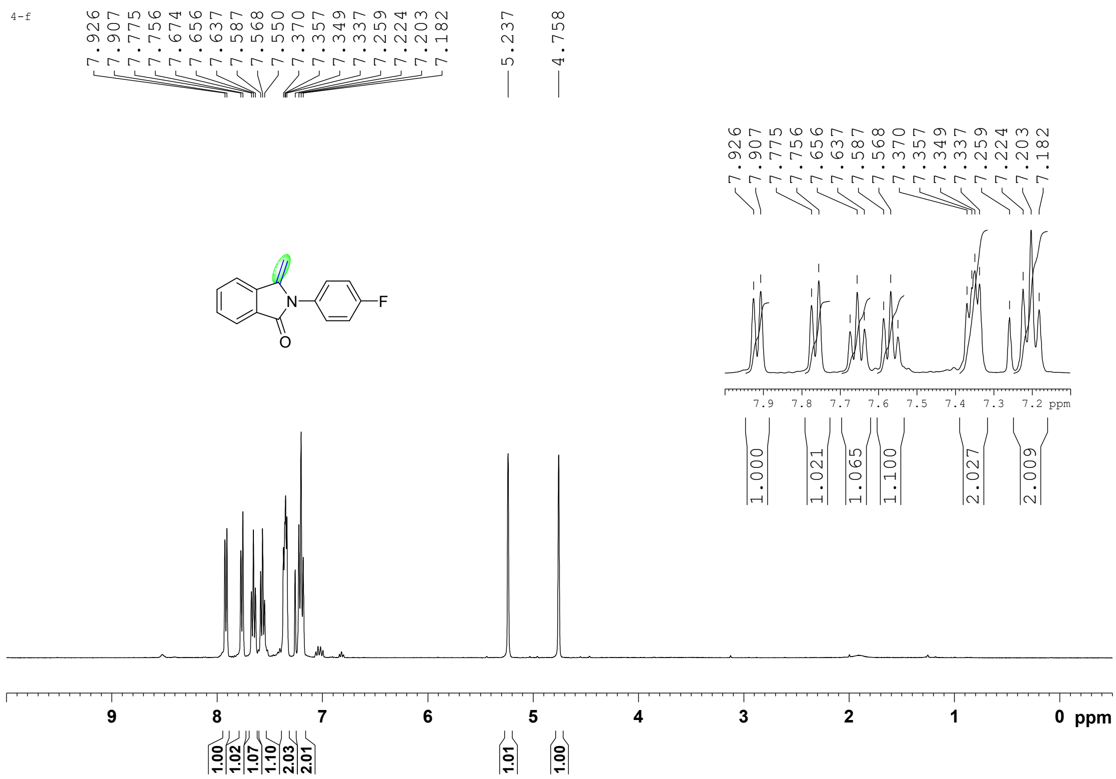

Figure S44. ^{1}H NMR (400 MHz, $CDCl_3$) of **2o**

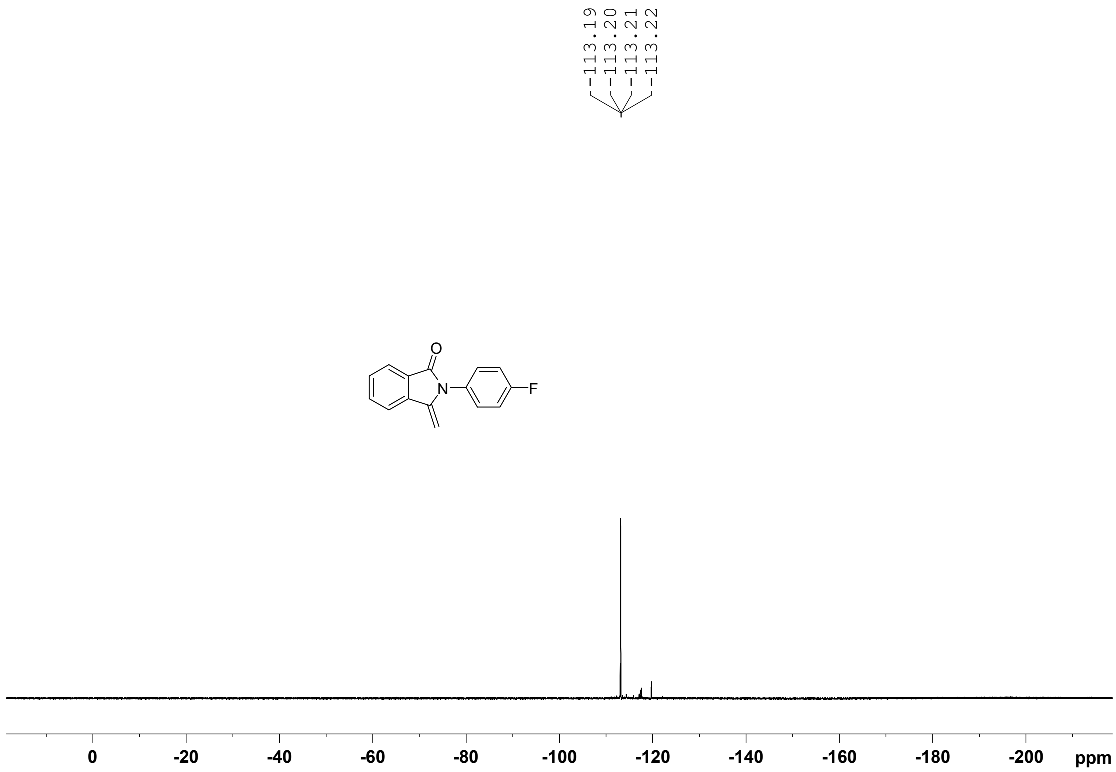

Figure S45. ^{19}F NMR (376 MHz, $CDCl_3$) of **2o**

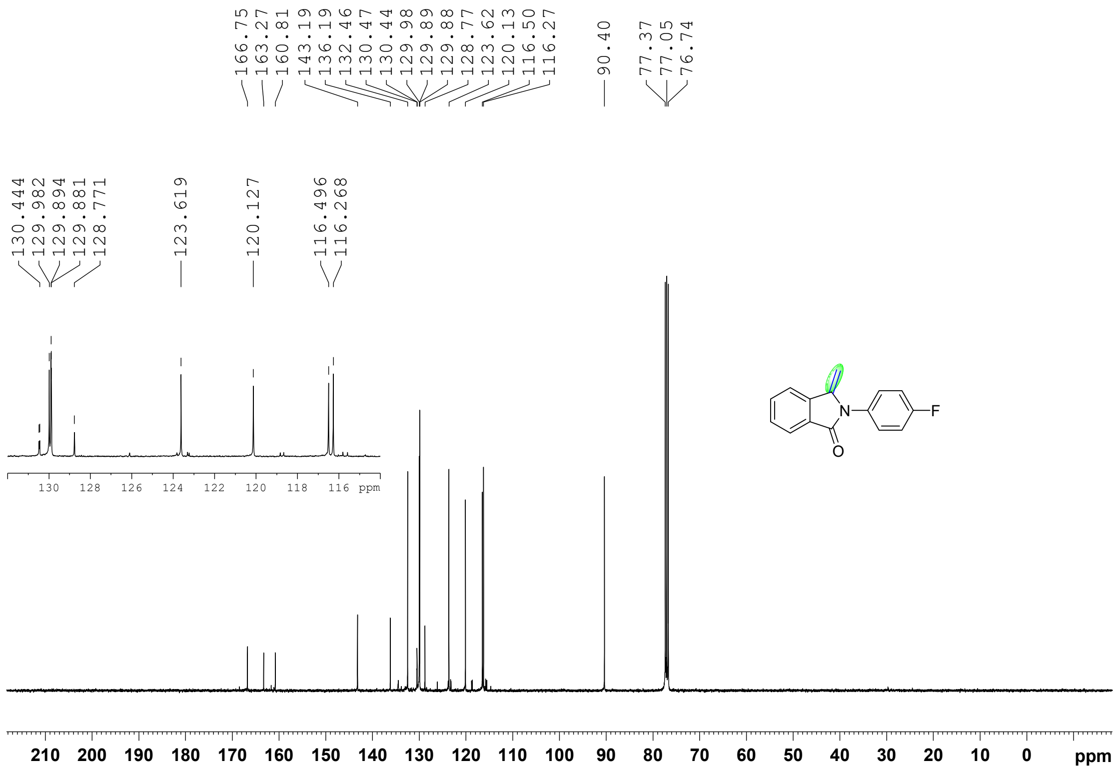

Figure S46. ^{13}C NMR (101 MHz, $CDCl_3$) of **2o**

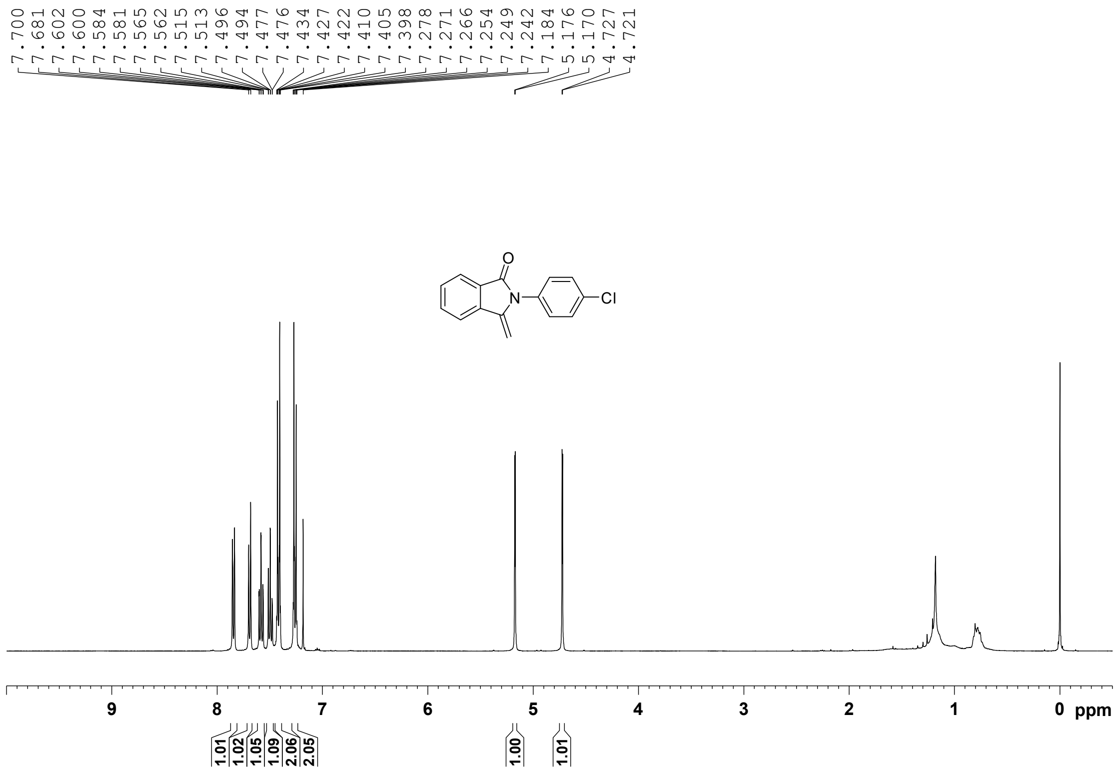

Figure S47. ^{1}H NMR (400 MHz, $CDCl_3$) of **2p**

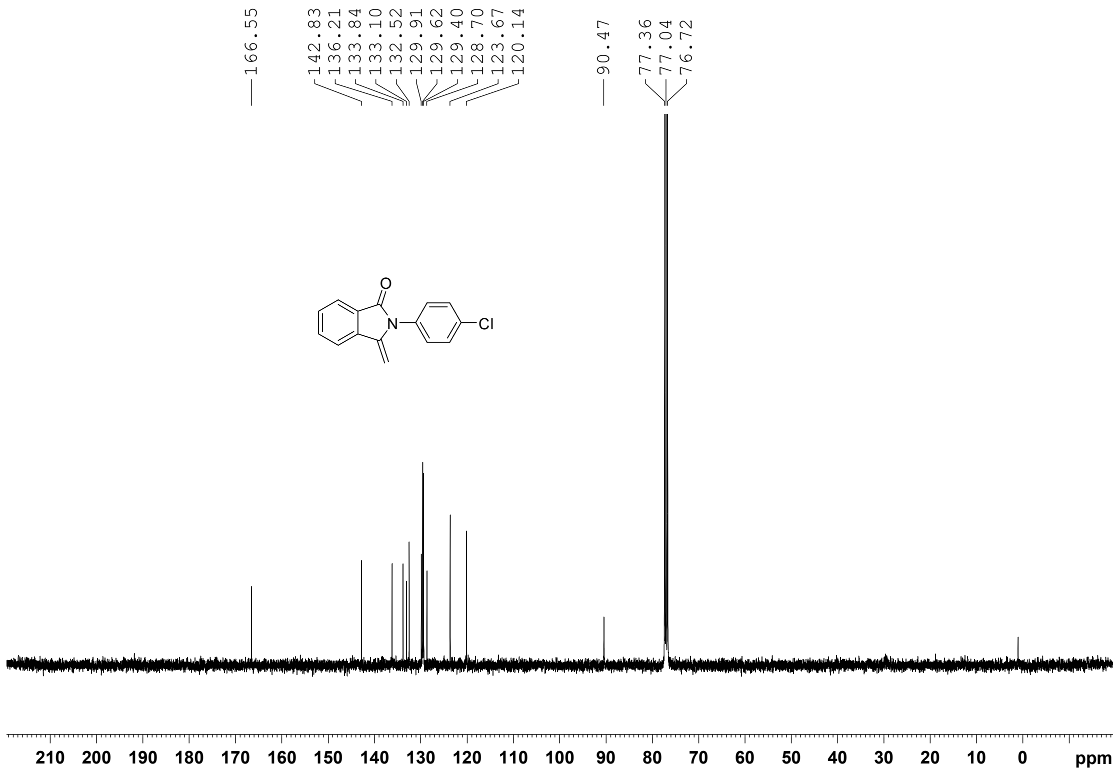

Figure S48. ^{13}C NMR (101 MHz, $CDCl_3$) of **2p**

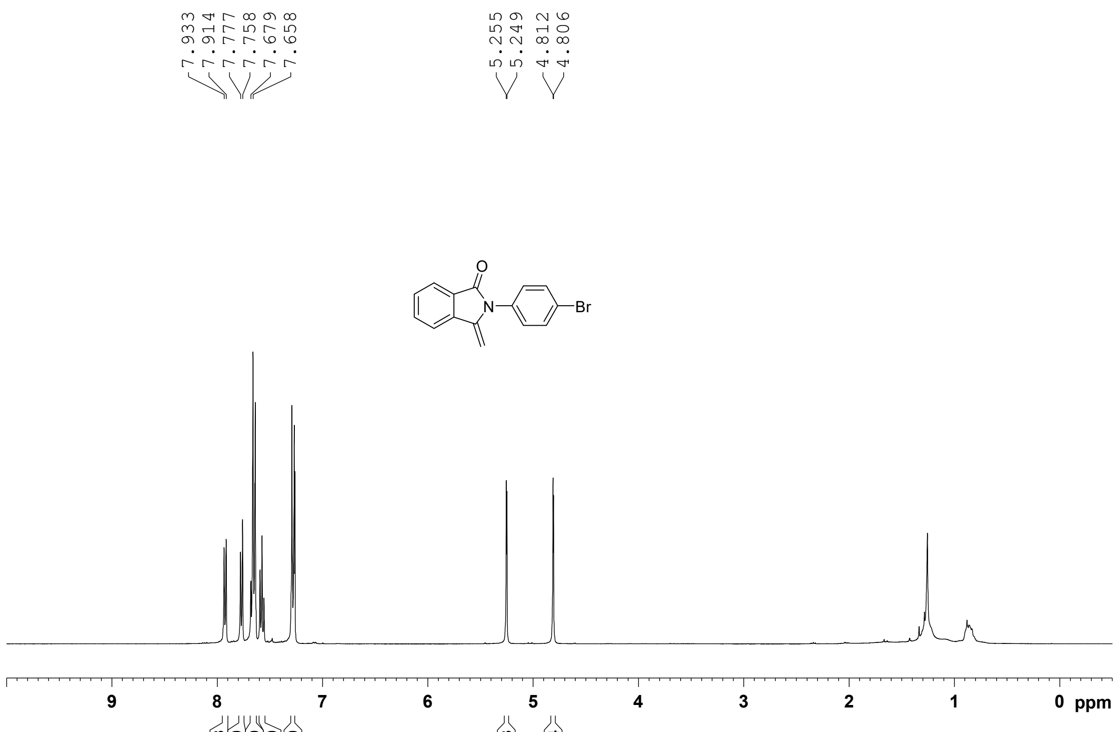

Figure S49. ^{1}H NMR (400 MHz, $CDCl_3$) of **2q**

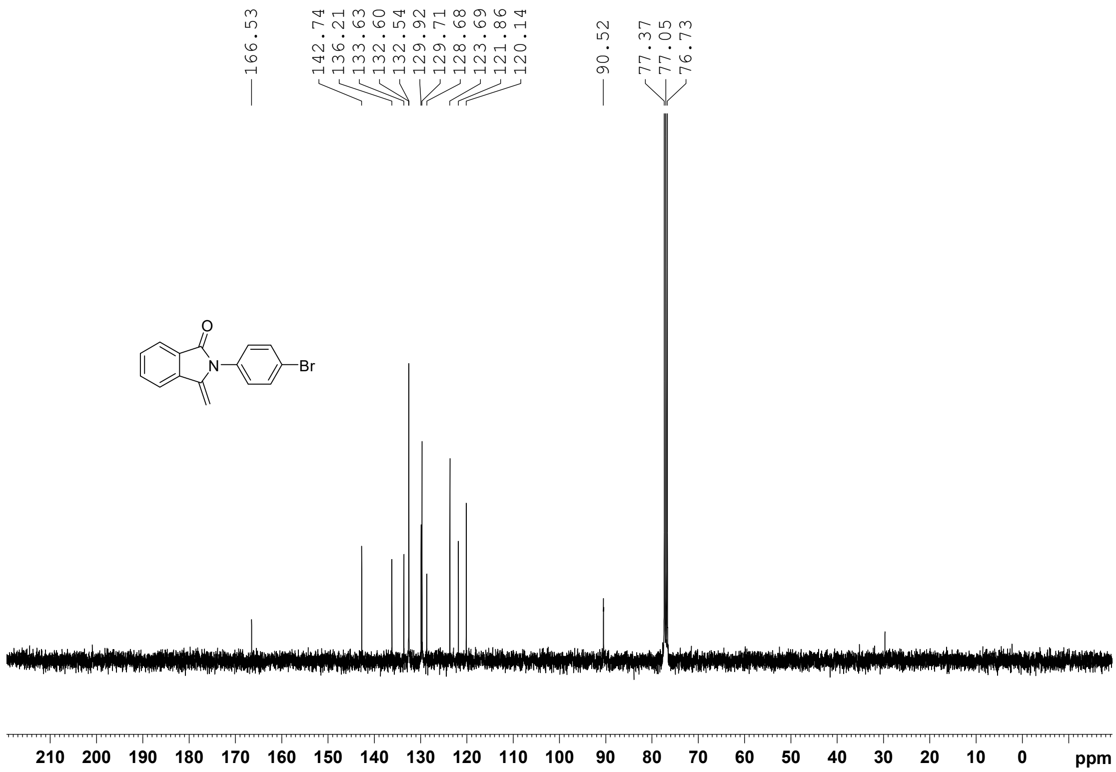

Figure S50. ^{13}C NMR (101 MHz, $CDCl_3$) of **2q**

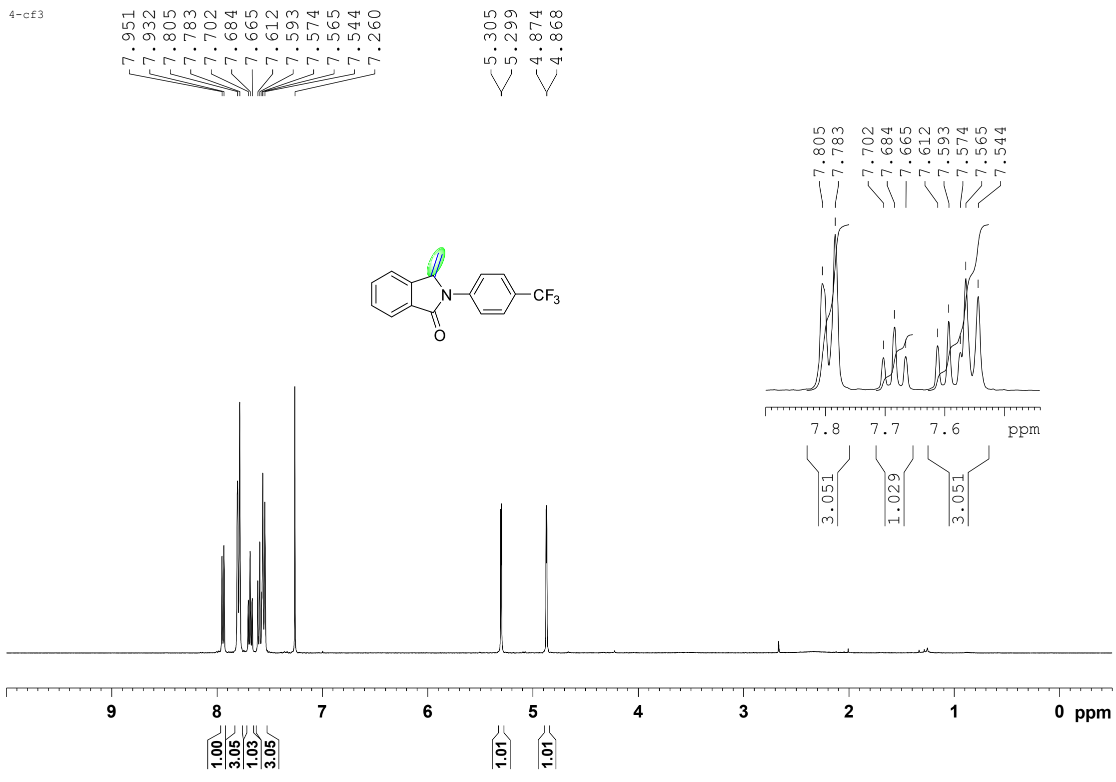

Figure S51. ^{1}H NMR (400 MHz, $CDCl_3$) of **2r**

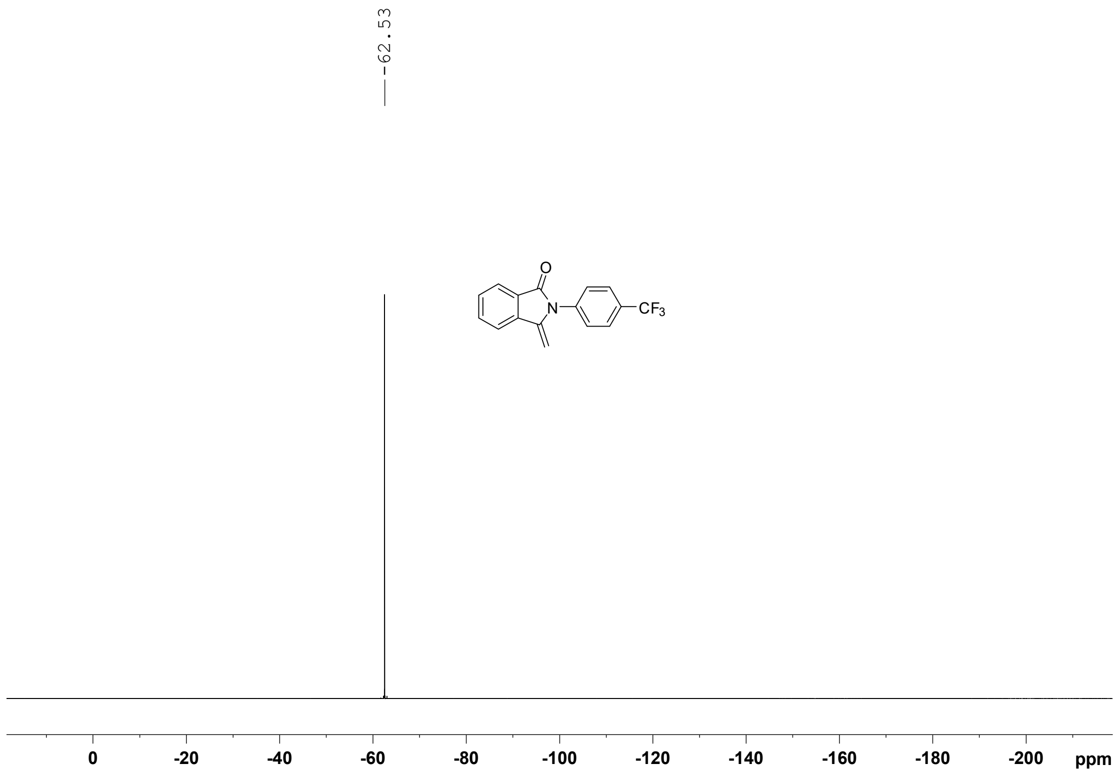

Figure S52. ^{19}F NMR (376 MHz, $CDCl_3$) of **2r**

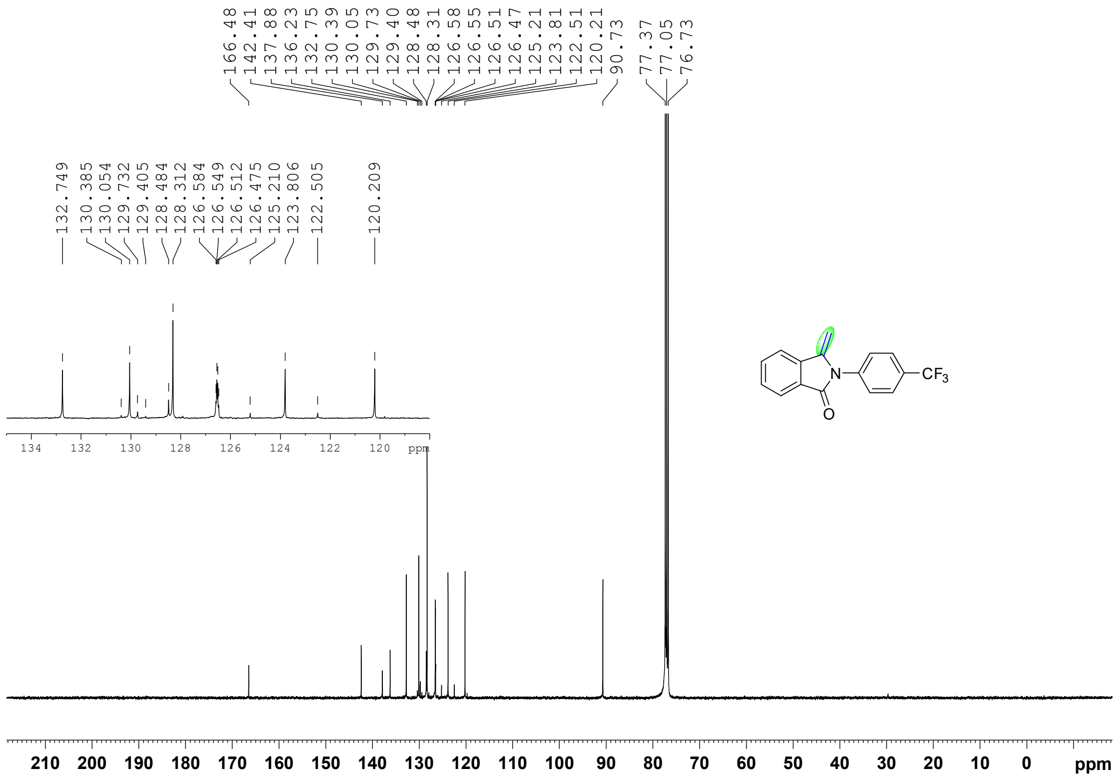

Figure S53. ^{13}C NMR (101 MHz, $CDCl_3$) of **2r**

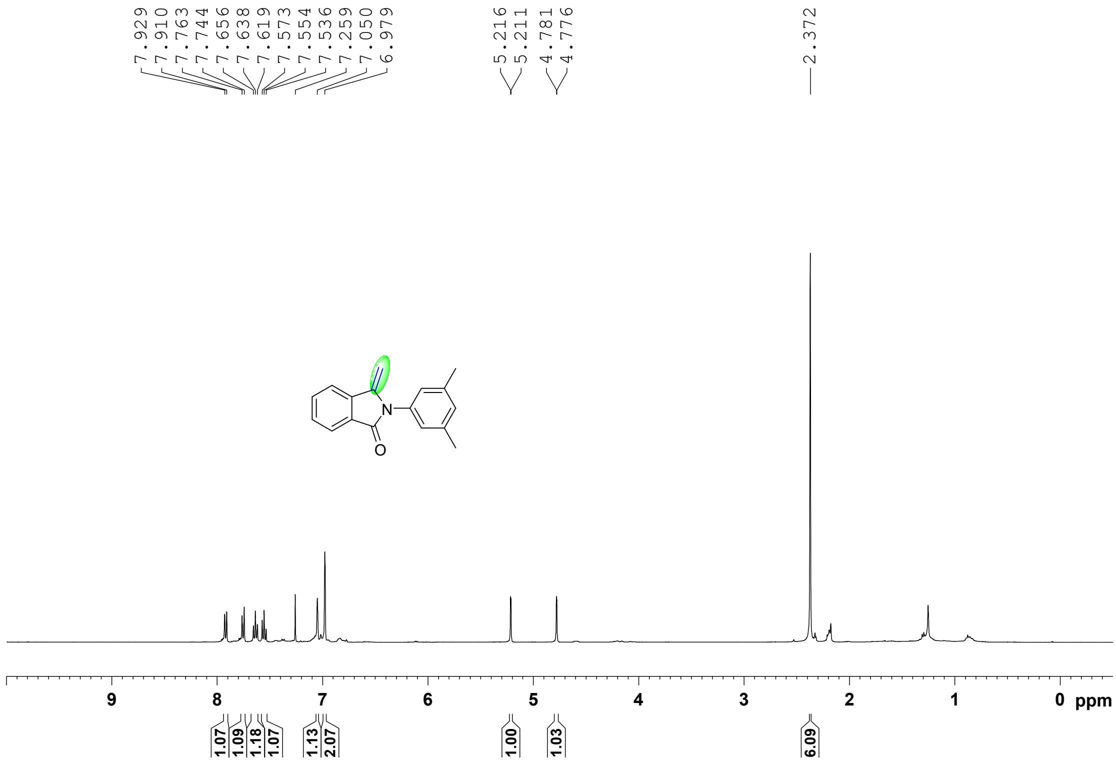

Figure S54. ^{1}H NMR (400 MHz, $CDCl_3$) of **2t**

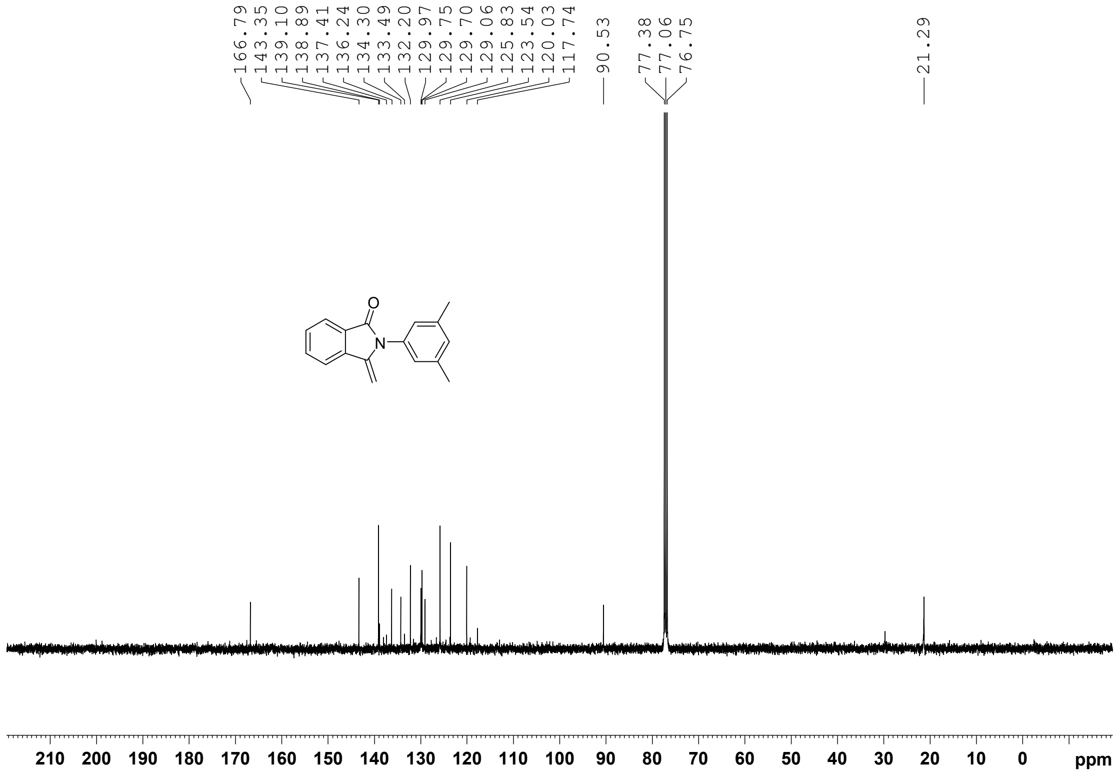

Figure S55. ^{13}C NMR (101 MHz, $CDCl_3$) of **2t**

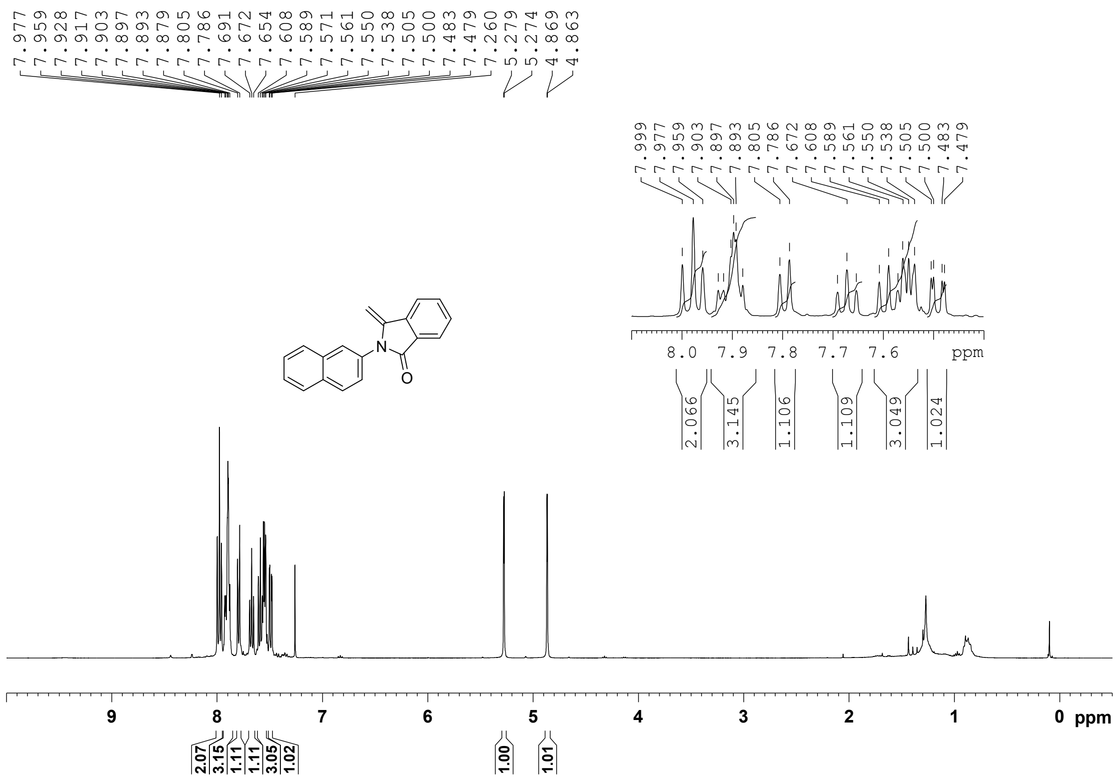

Figure S56. ^{1}H NMR (400 MHz, $CDCl_3$) of **2u**

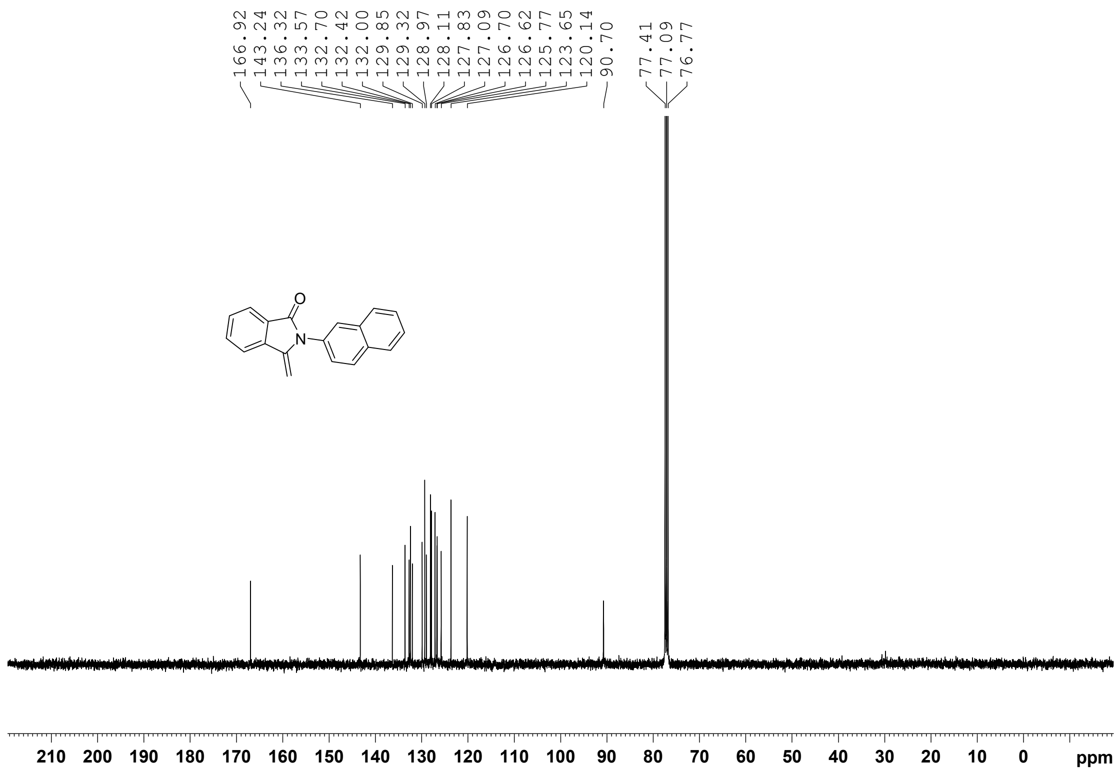

Figure S57. ^{13}C NMR (101 MHz, $CDCl_3$) of **2u**

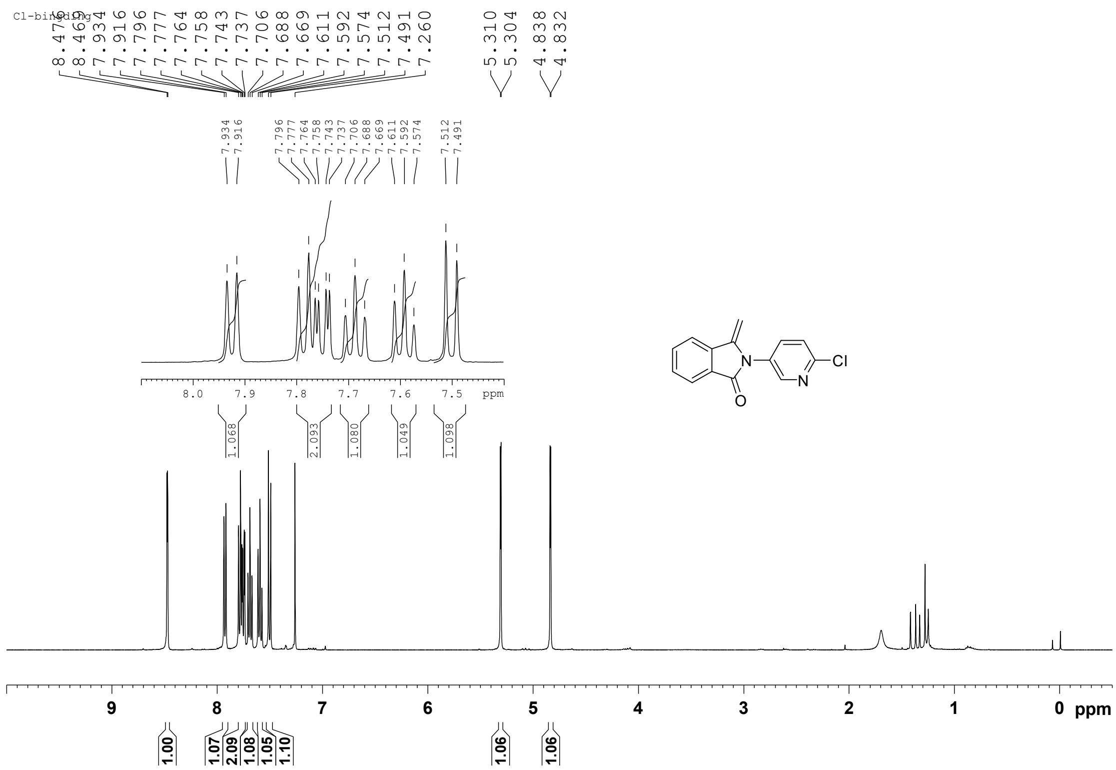

Figure S58. ^{1}H NMR (400 MHz, $CDCl_3$) of **2v**

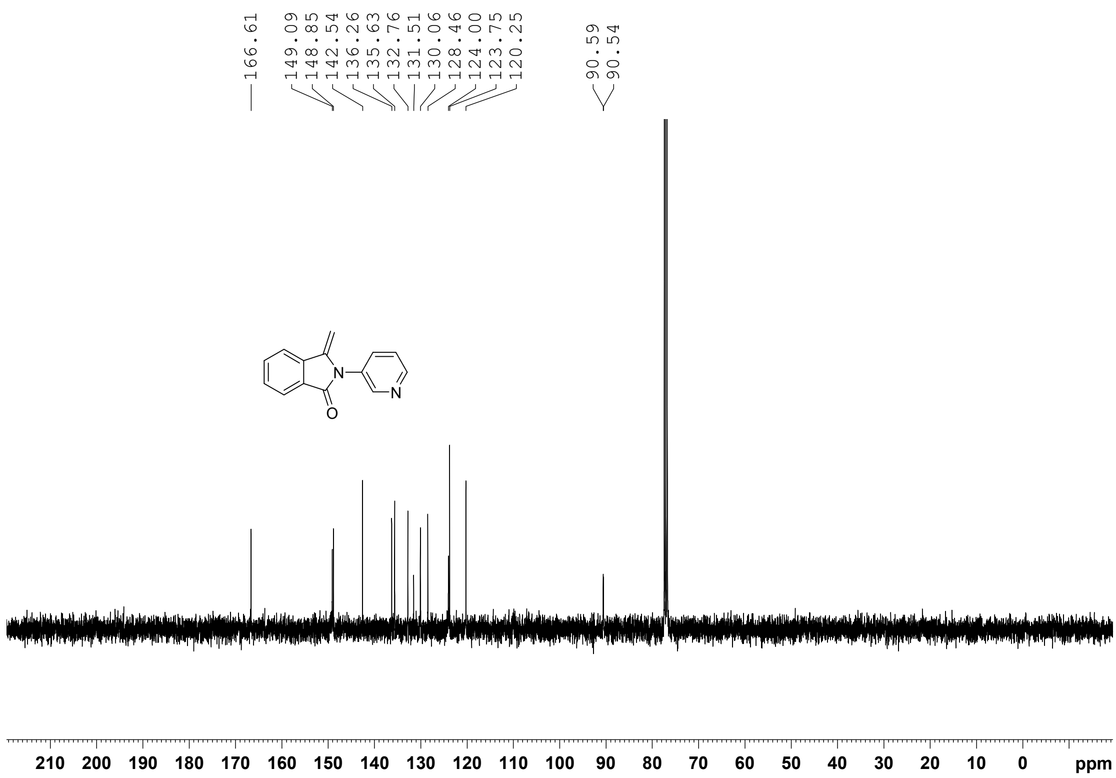

Figure S59. ^{13}C NMR (101 MHz, $CDCl_3$) of **2v**

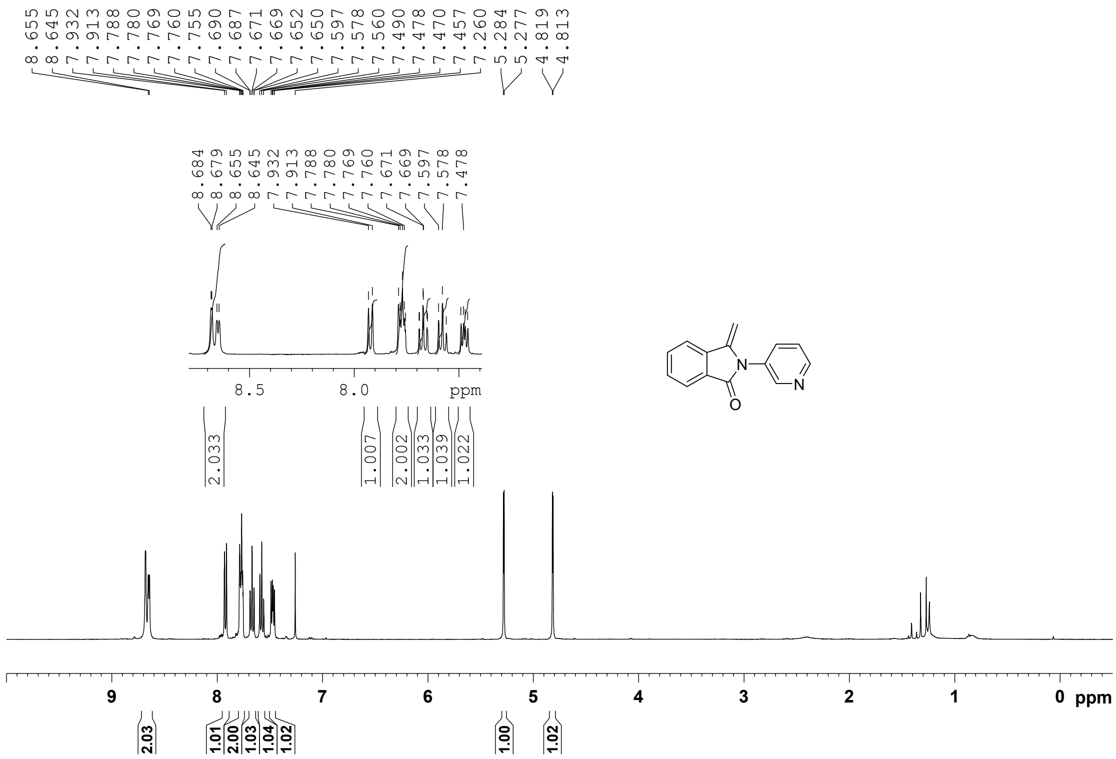

Figure S60. ^{1}H NMR (400 MHz, $CDCl_3$) of **2w**

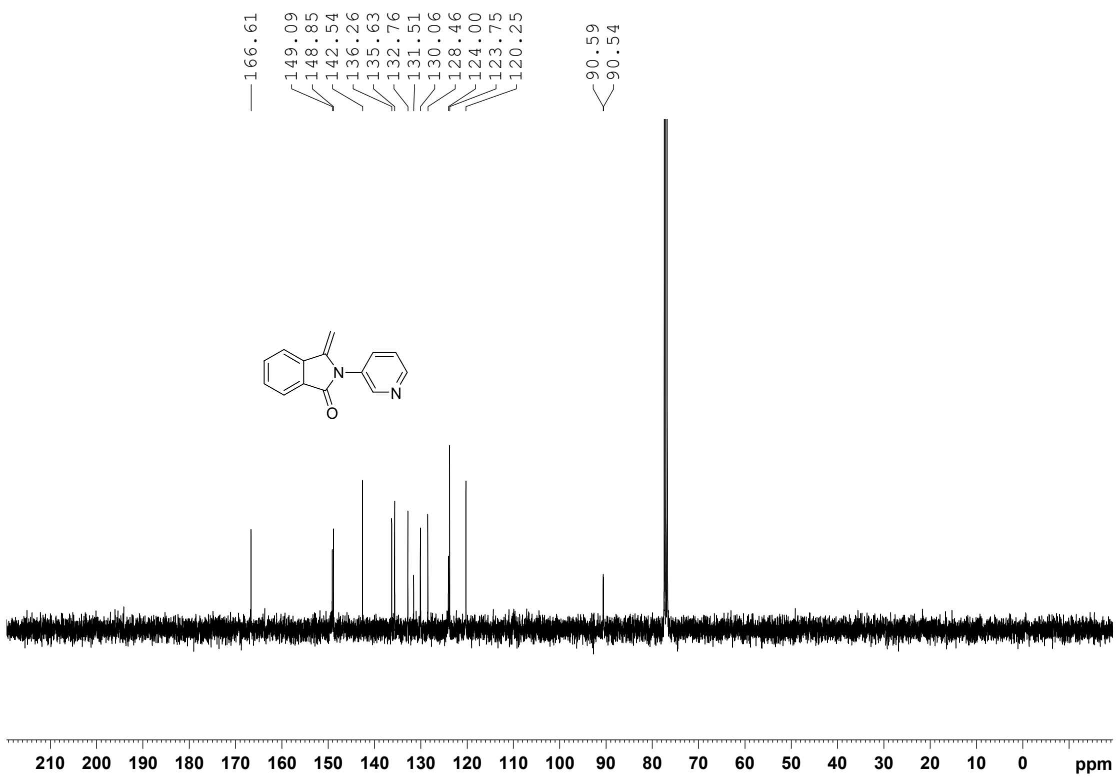

Figure S61. ^{13}C NMR (101 MHz, $CDCl_3$) of **2w**

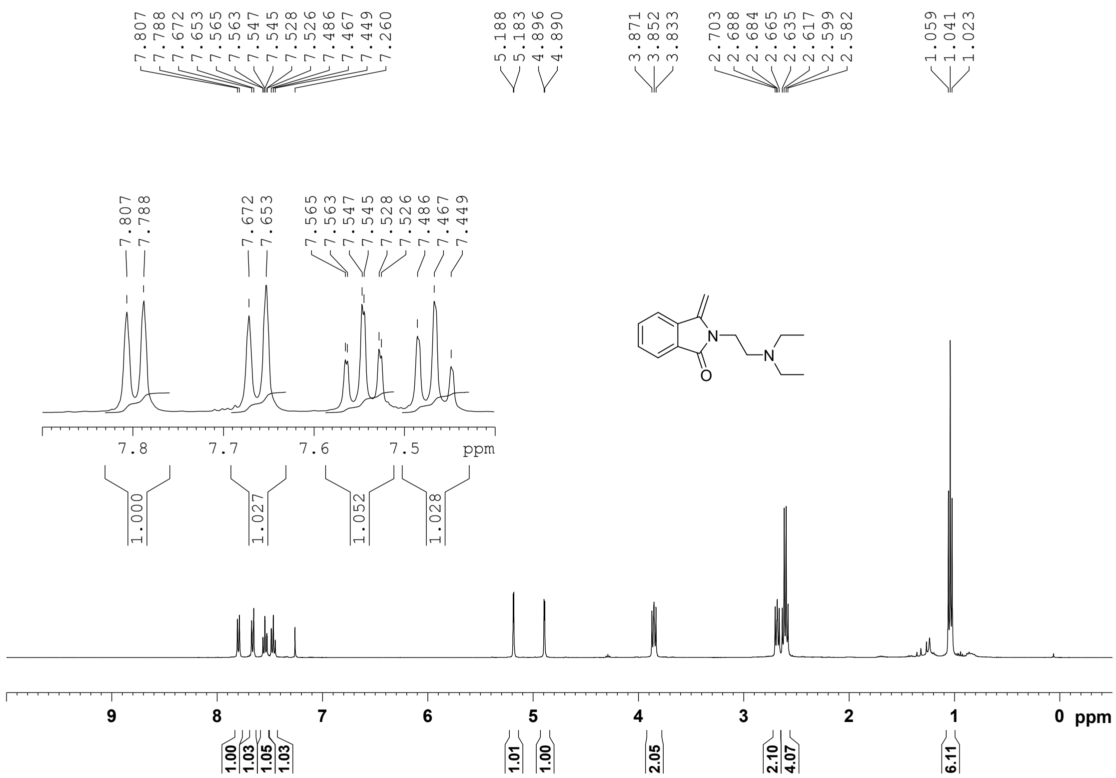

Figure S62. ^{1}H NMR (400 MHz, $CDCl_3$) of **2y**

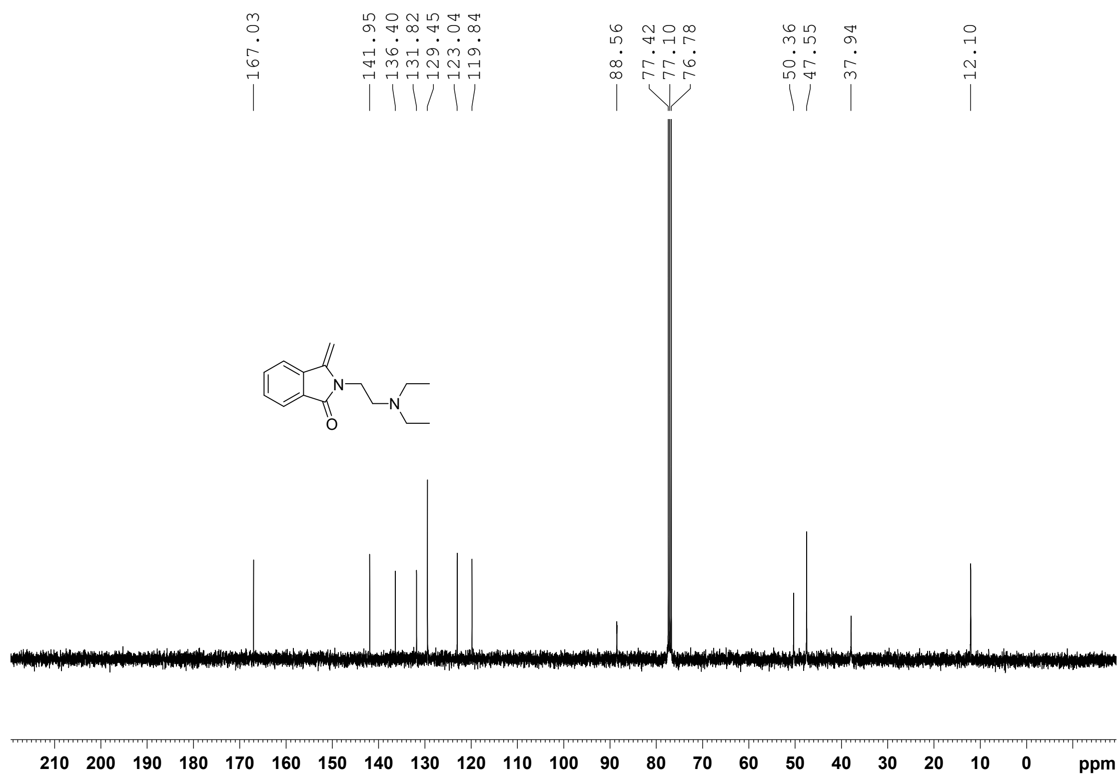

Figure S63. ^{13}C NMR (101 MHz, $CDCl_3$) of **2y**

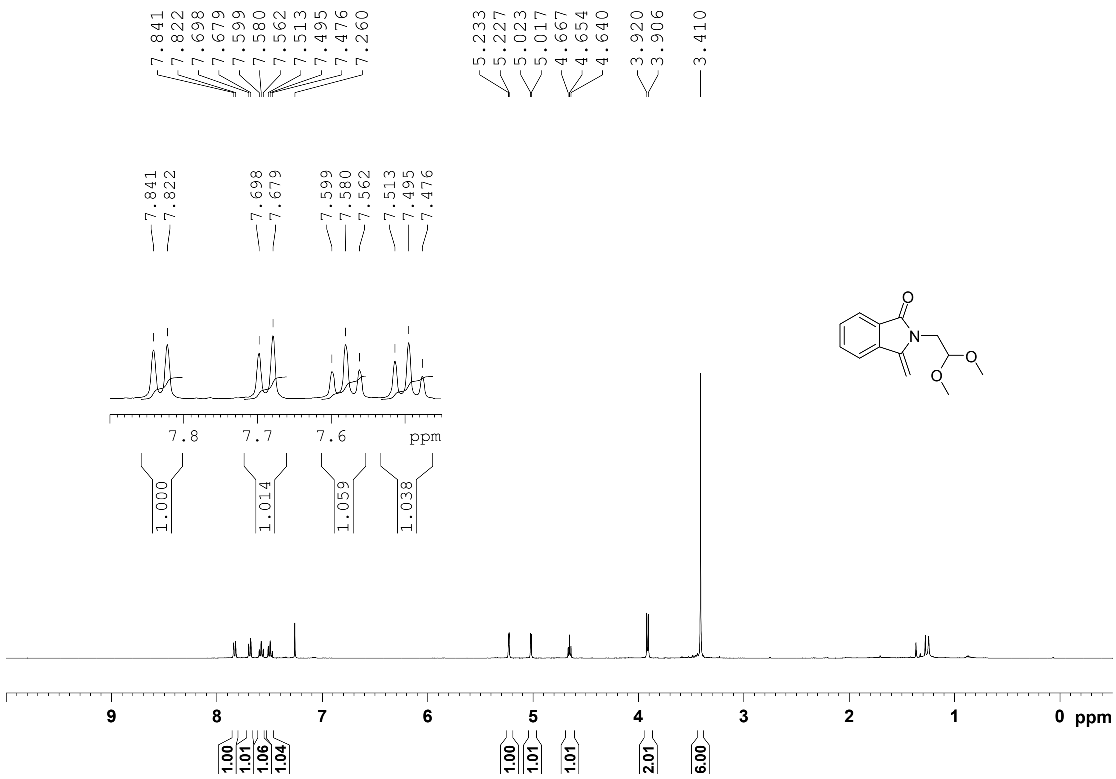

Figure S64. ^{1}H NMR (400 MHz, $CDCl_3$) of **2z**

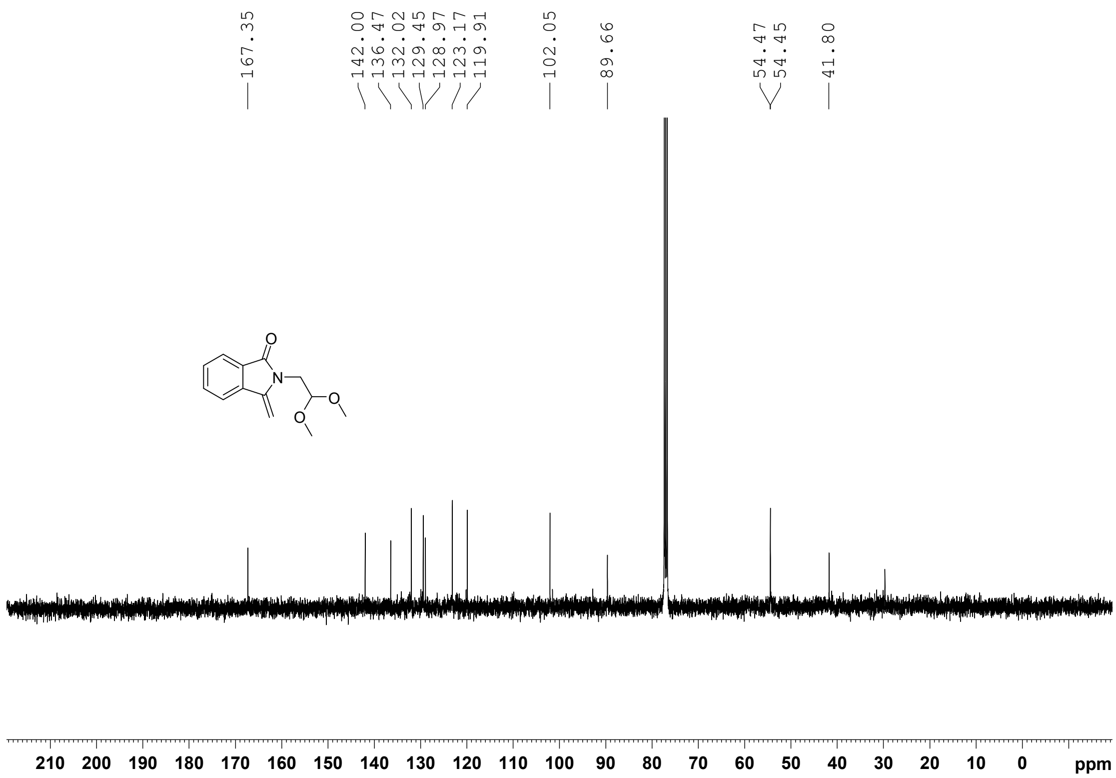

Figure S65. ^{13}C NMR (101 MHz, $CDCl_3$) of **2z**

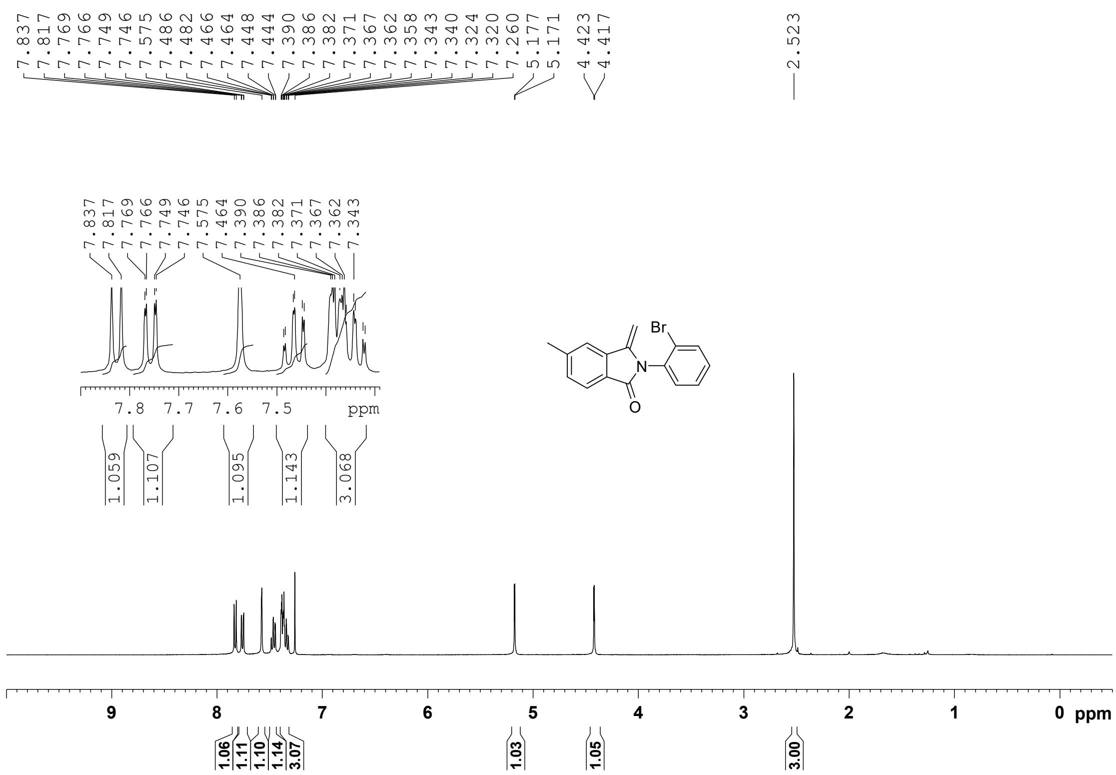

Figure S66. ^{1}H NMR (400 MHz, $CDCl_3$) of **4a**

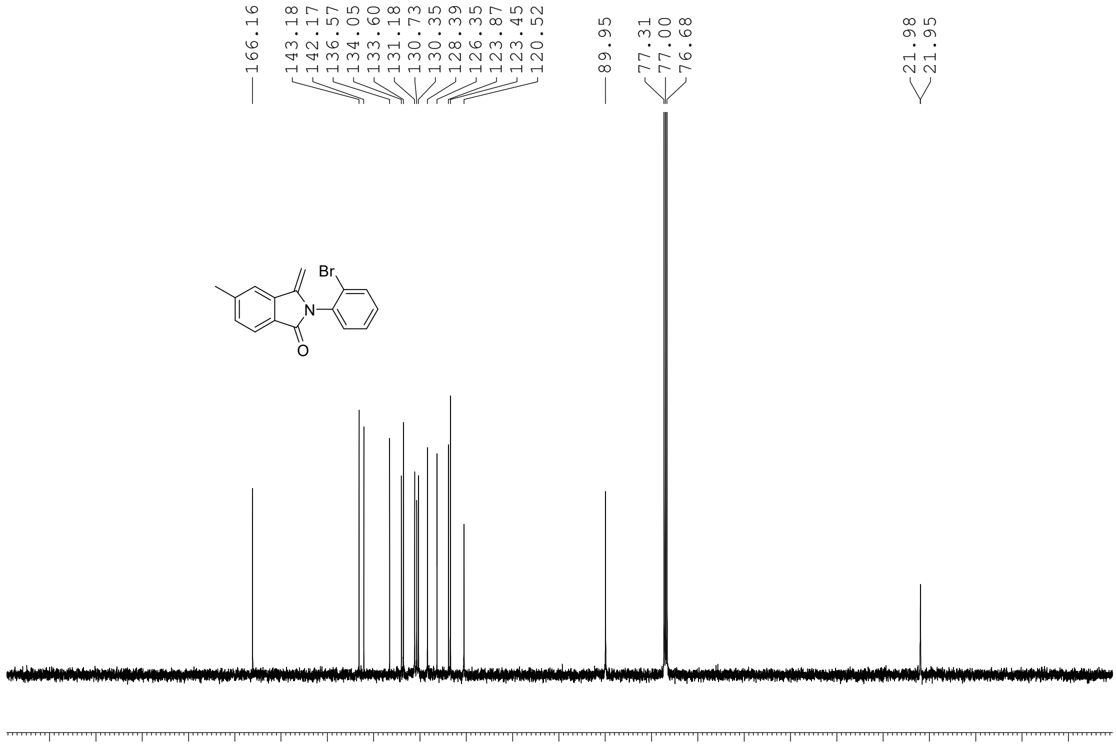

Figure S67. ^{13}C NMR (101 MHz, $CDCl_3$) of **4a**

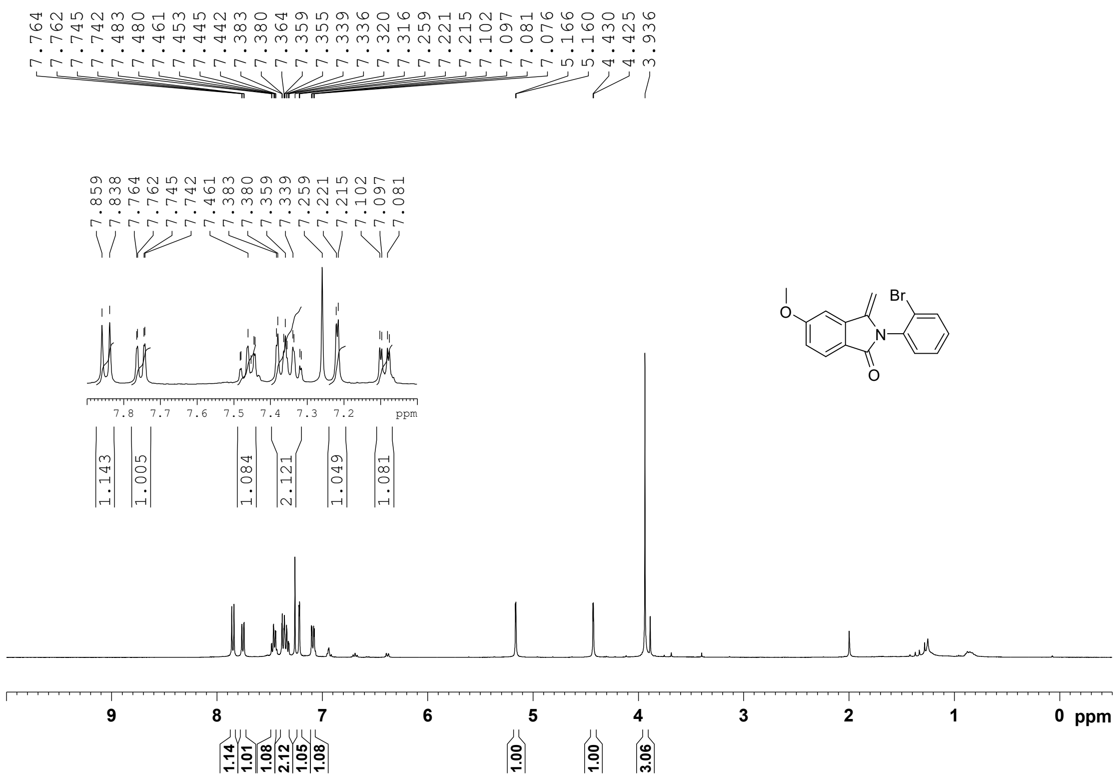

Figure S68. ^{1}H NMR (400 MHz, $CDCl_3$) of **4b**

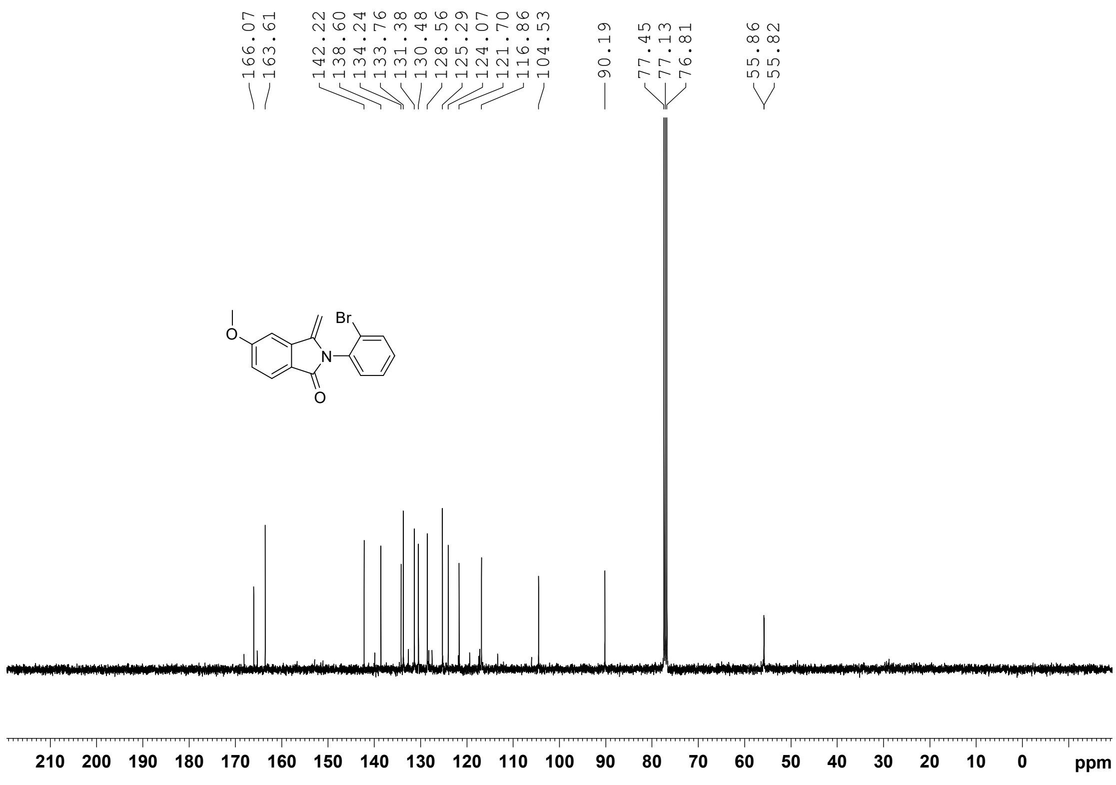

Figure S69. ^{13}C NMR (101 MHz, $CDCl_3$) of **4b**

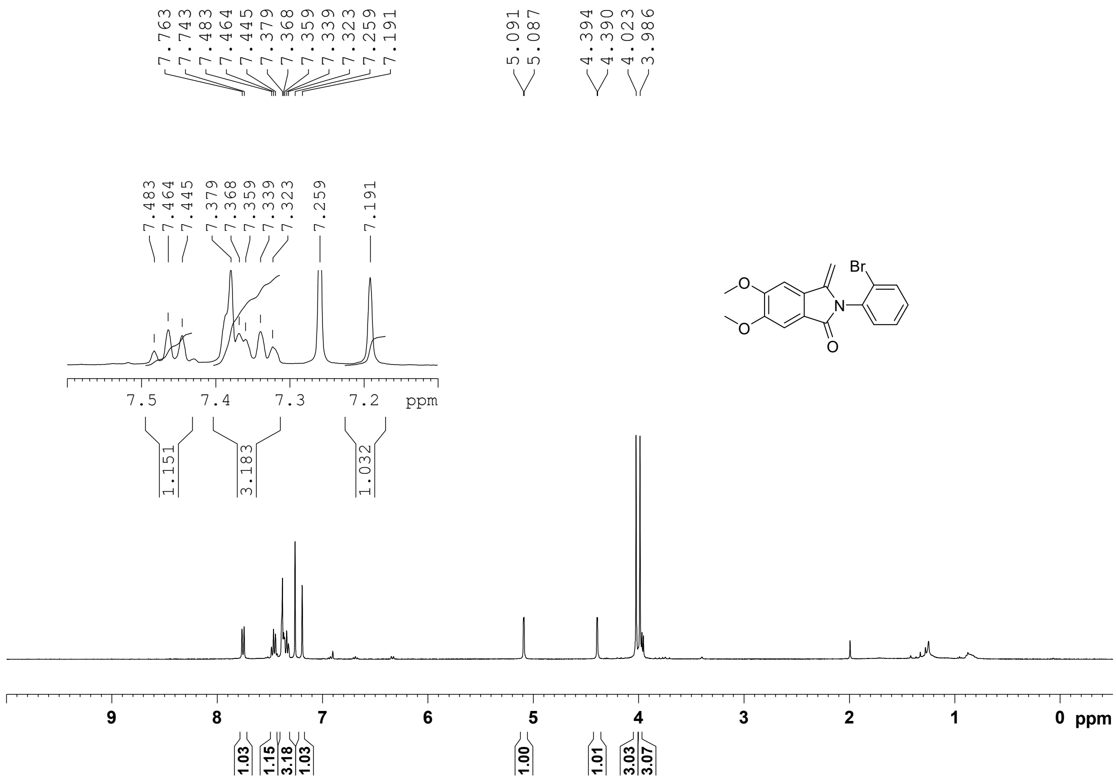

Figure S70.^{1}H NMR (400 MHz, $CDCl^3$) of **4c**

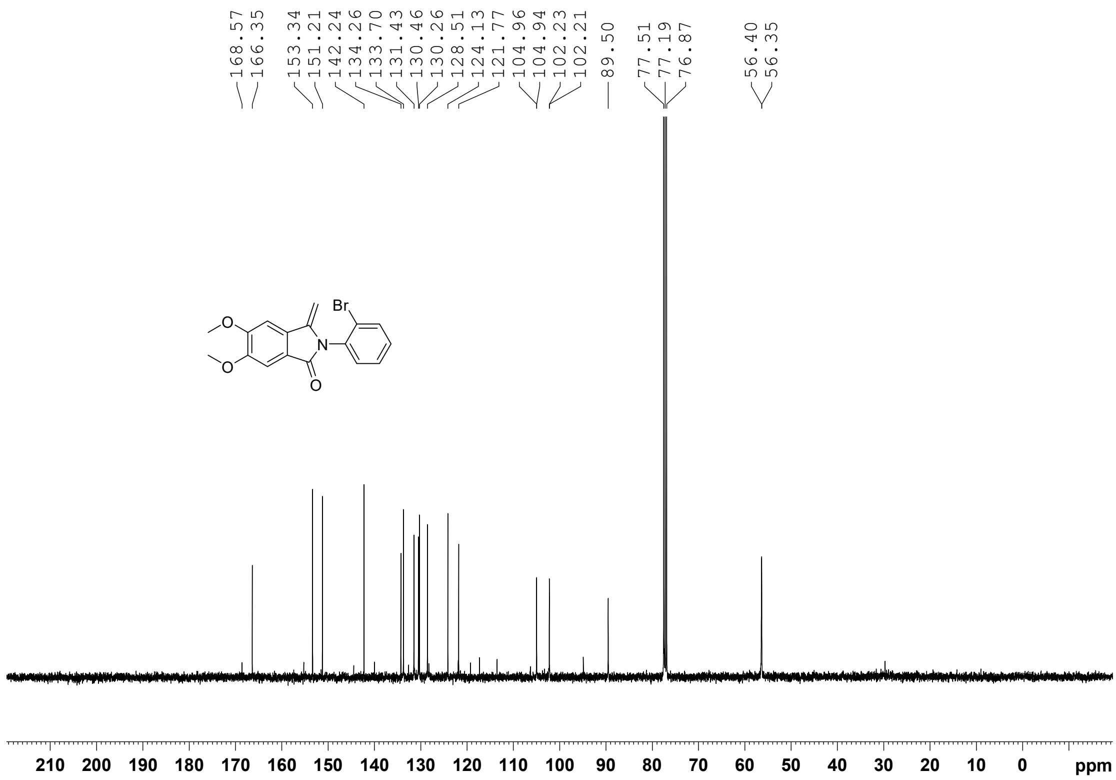

Figure S71. ^{13}C NMR (101 MHz, $CDCl_3$) of **4c**

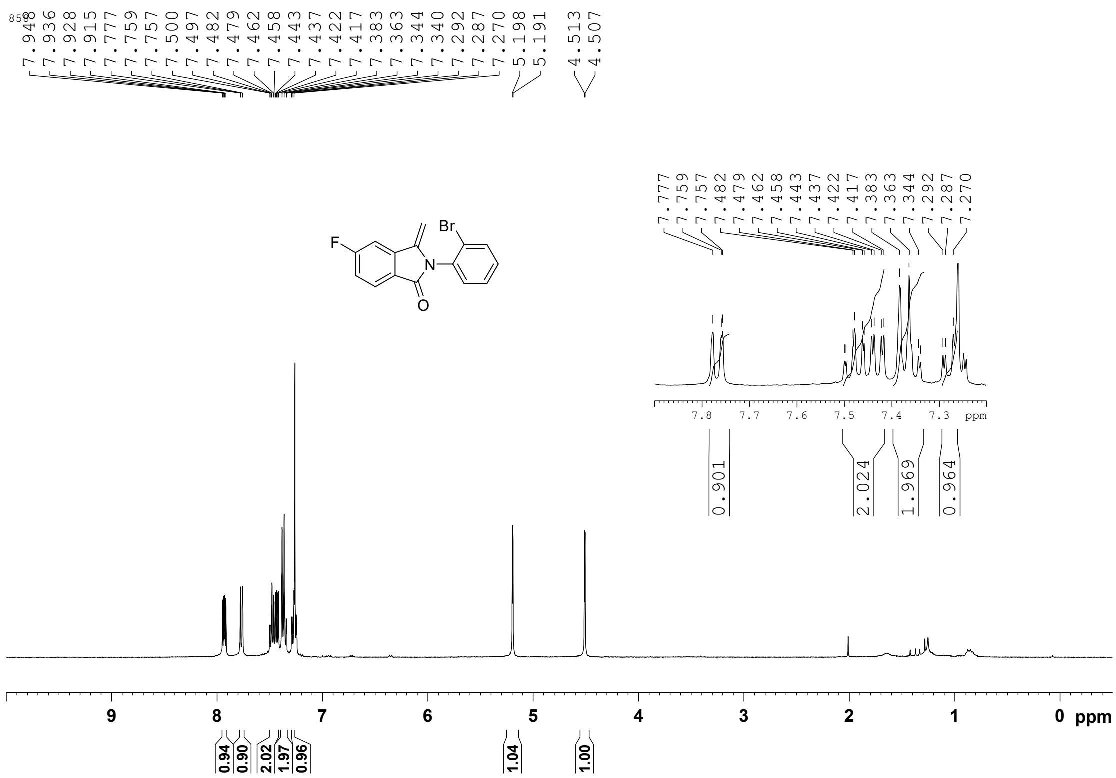

Figure S72. ^{1}H NMR (400 MHz, $CDCl_3$) of **4d**

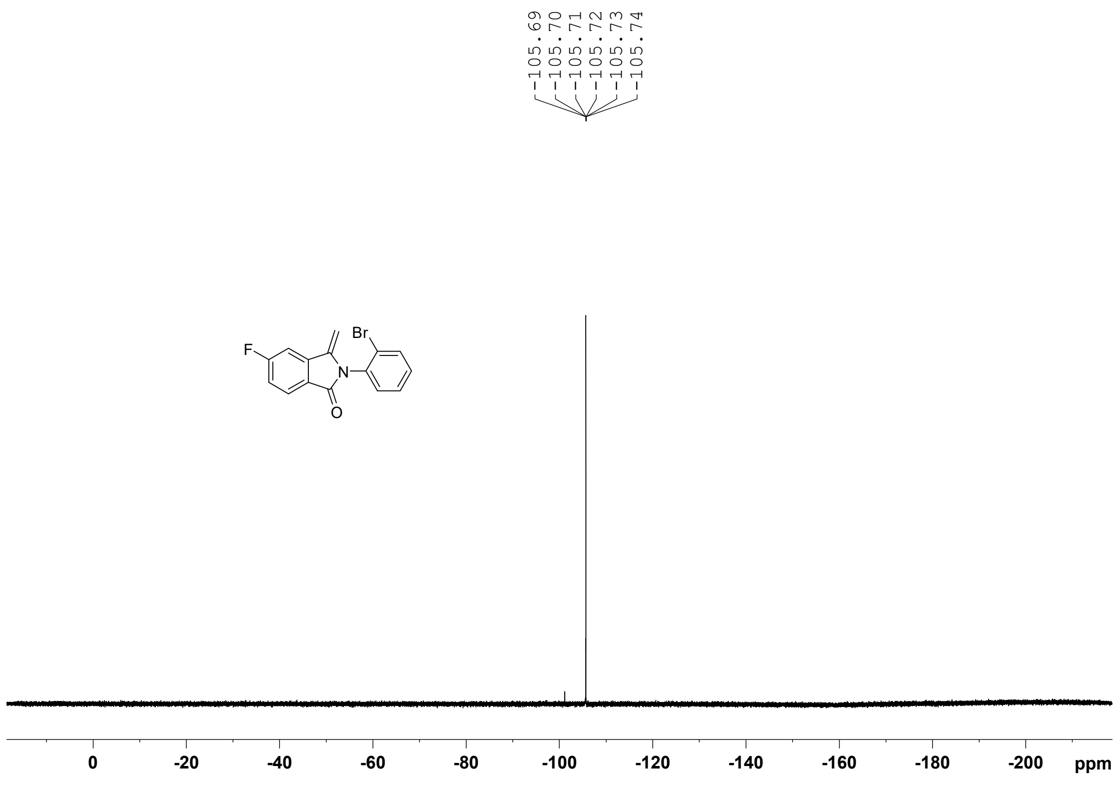

Figure S73. ^{19}F NMR (376 MHz, $CDCl_3$) of **4d**

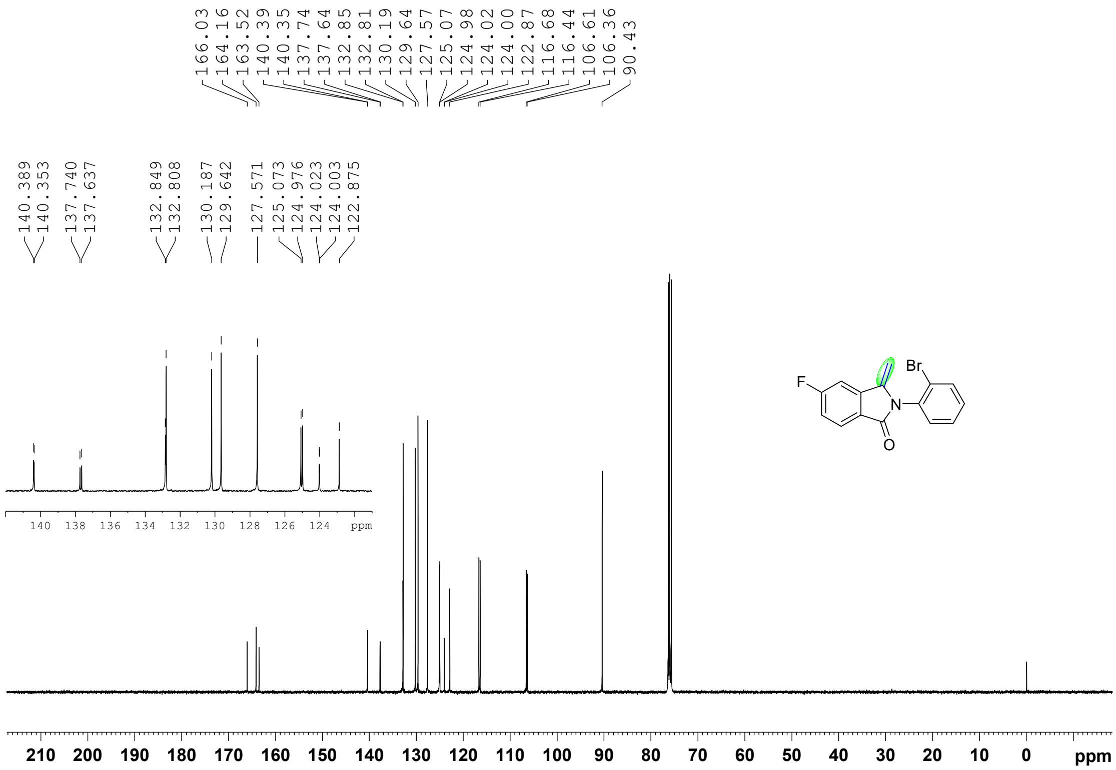

Figure S74. ^{13}C NMR (101 MHz, $CDCl_3$) of **4d**

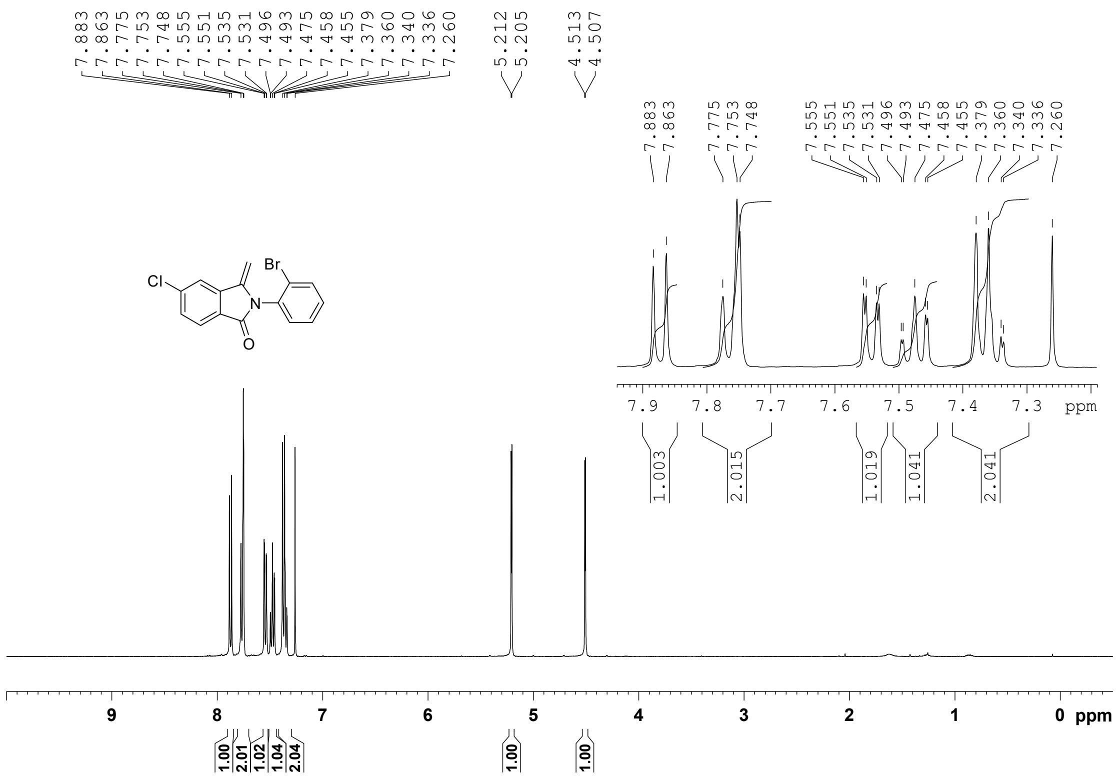

Figure S75. ^{1}H NMR (400 MHz, $CDCl_3$) of **4e**

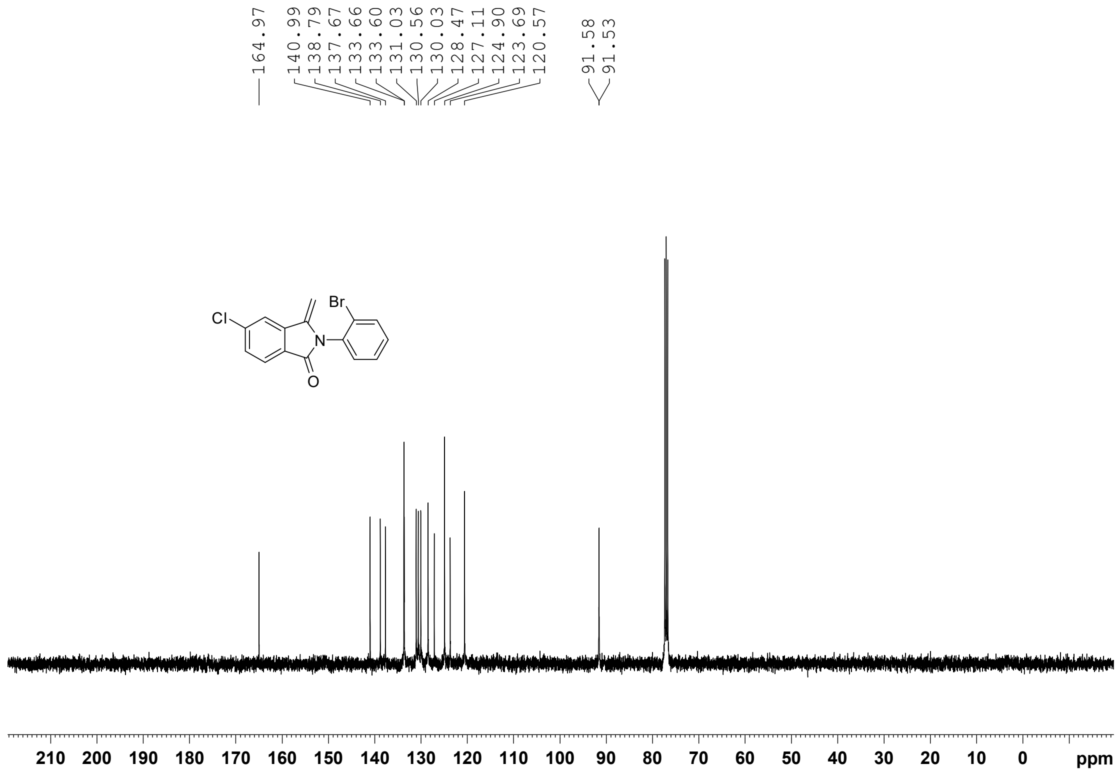

Figure S76. ^{13}C NMR (101 MHz, $CDCl_3$) of **4e**

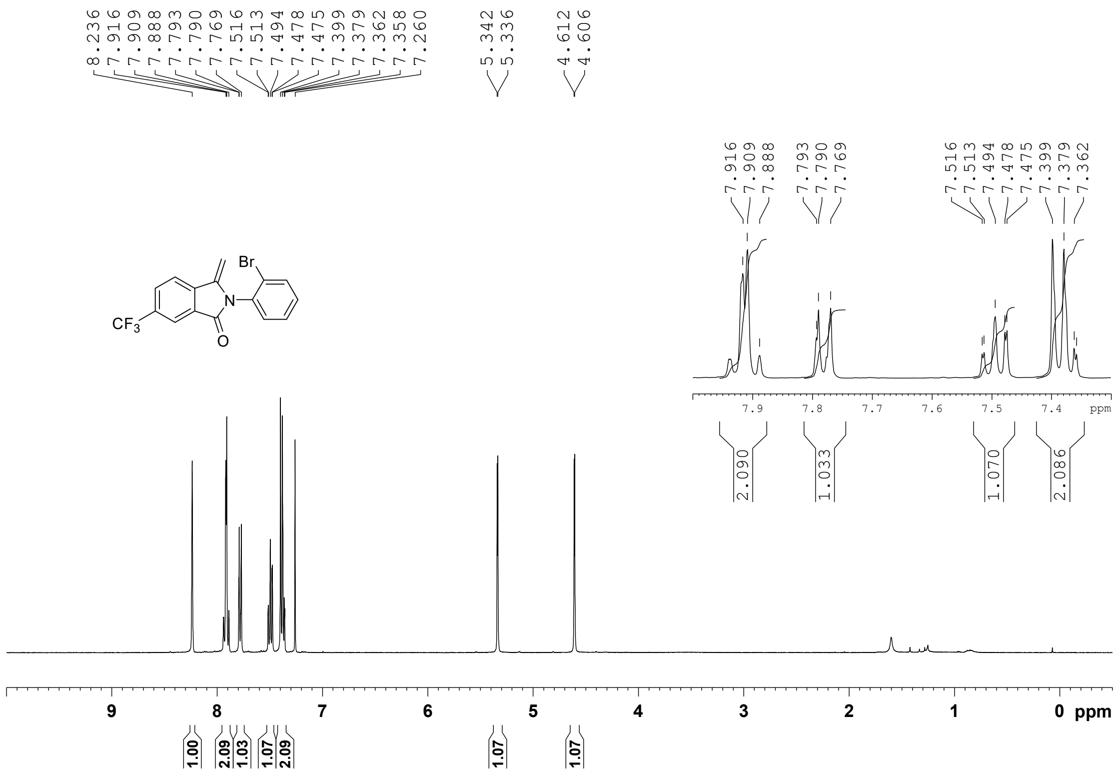

Figure S77. ^{1}H NMR (400 MHz, $CDCl_3$) of **4f**

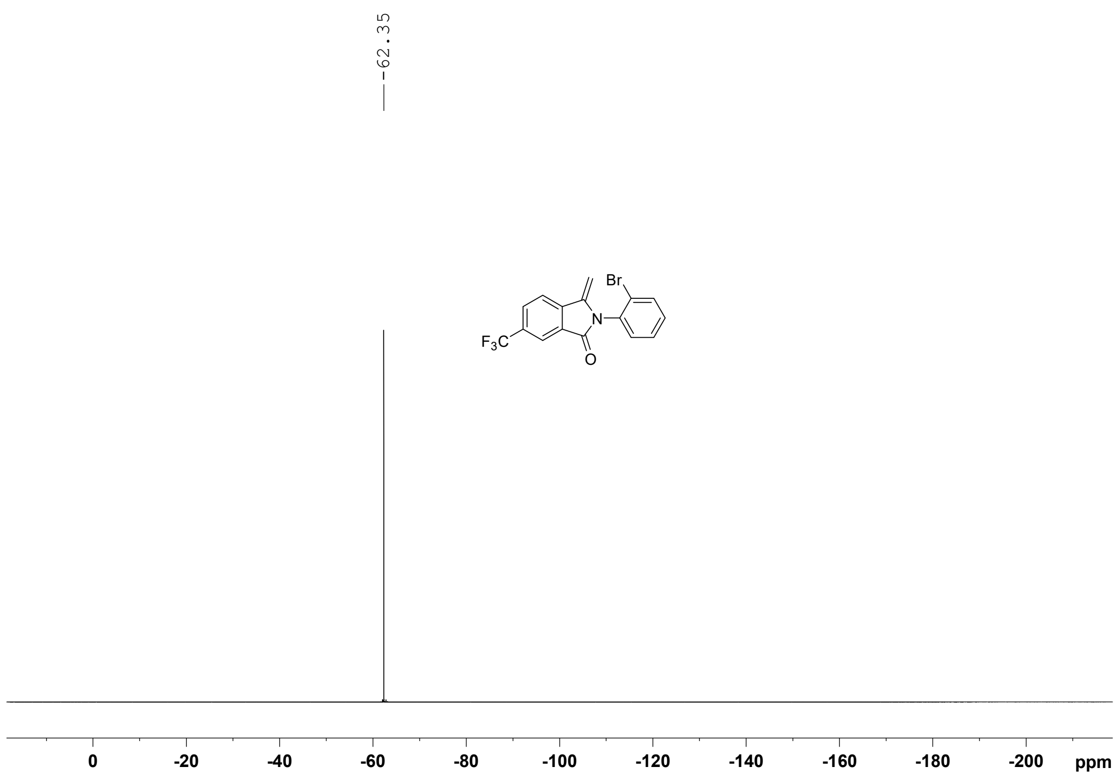

Figure S78. ^{19}F NMR (376 MHz, $CDCl_3$) of **4f**

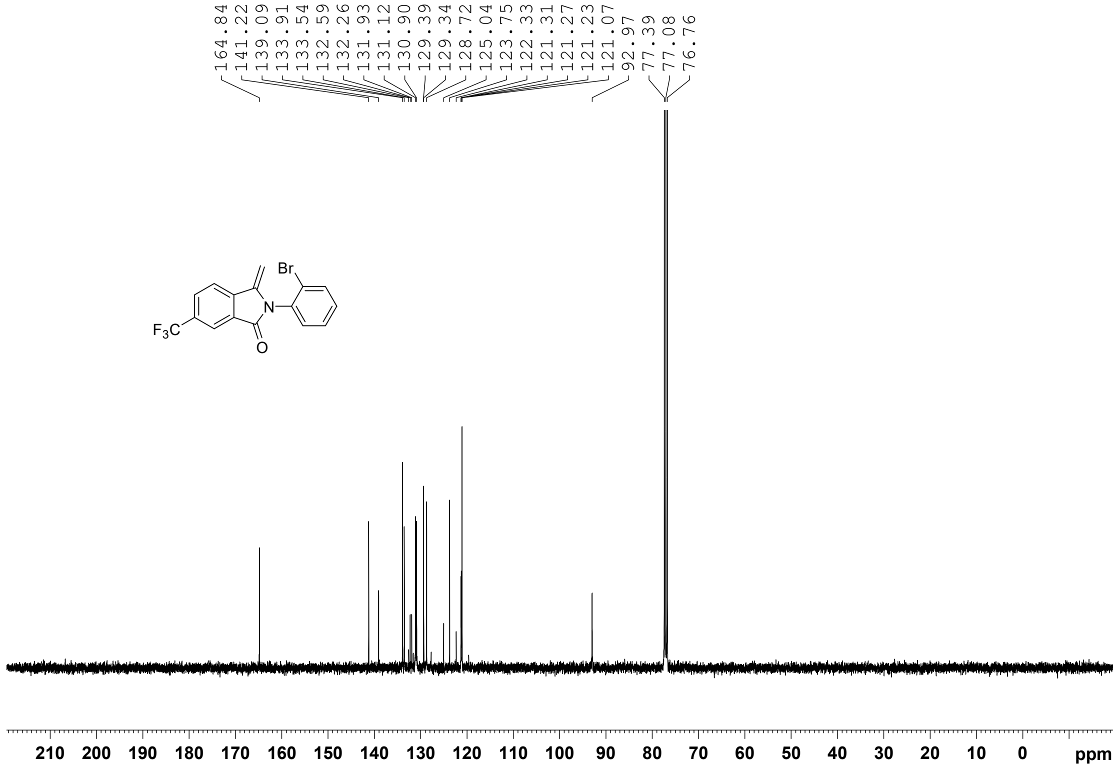

Figure S79. ^{13}C NMR (101 MHz, $CDCl_3$) of **4f**

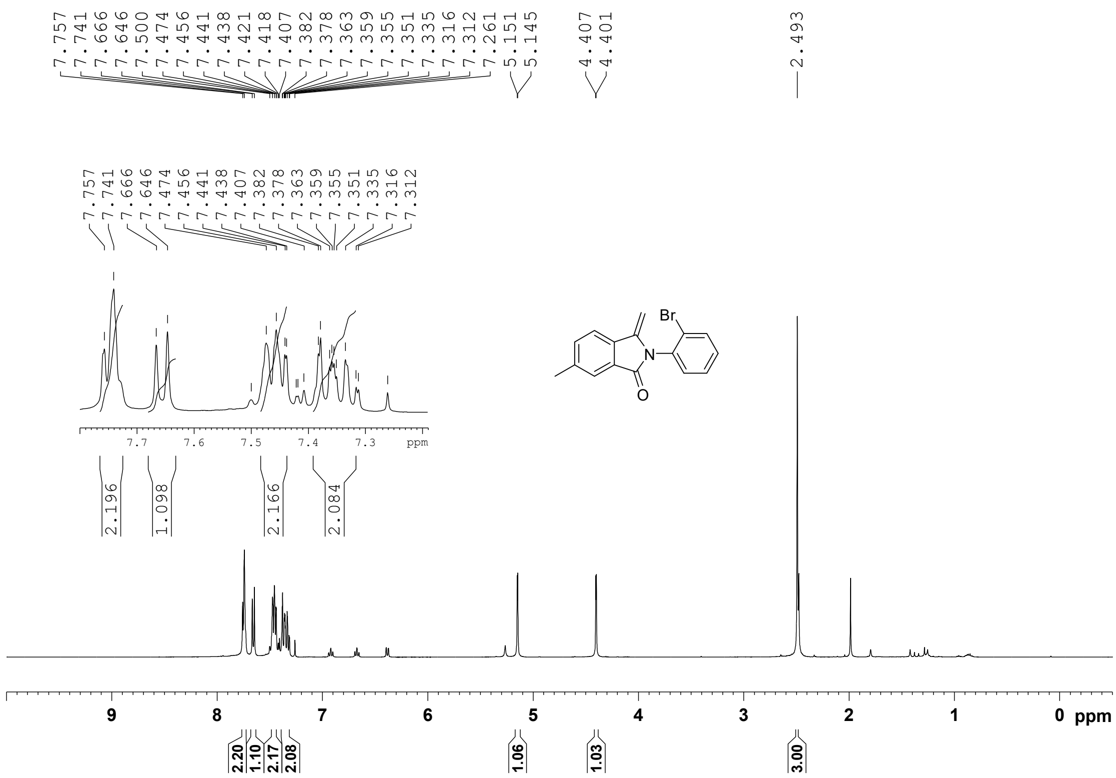

Figure S80.[1]H NMR (400 MHz, $CDCl_3$) of **4g**

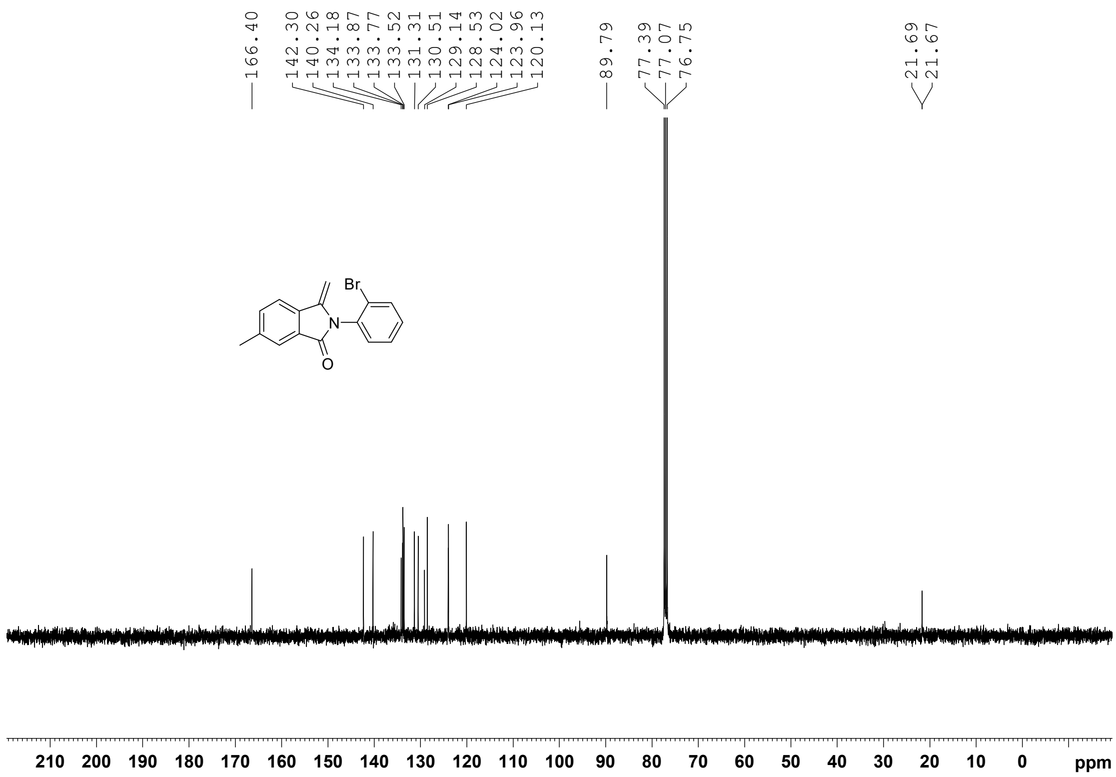

Figure S81. ^{13}C NMR (101 MHz, $CDCl_3$) of **4g**

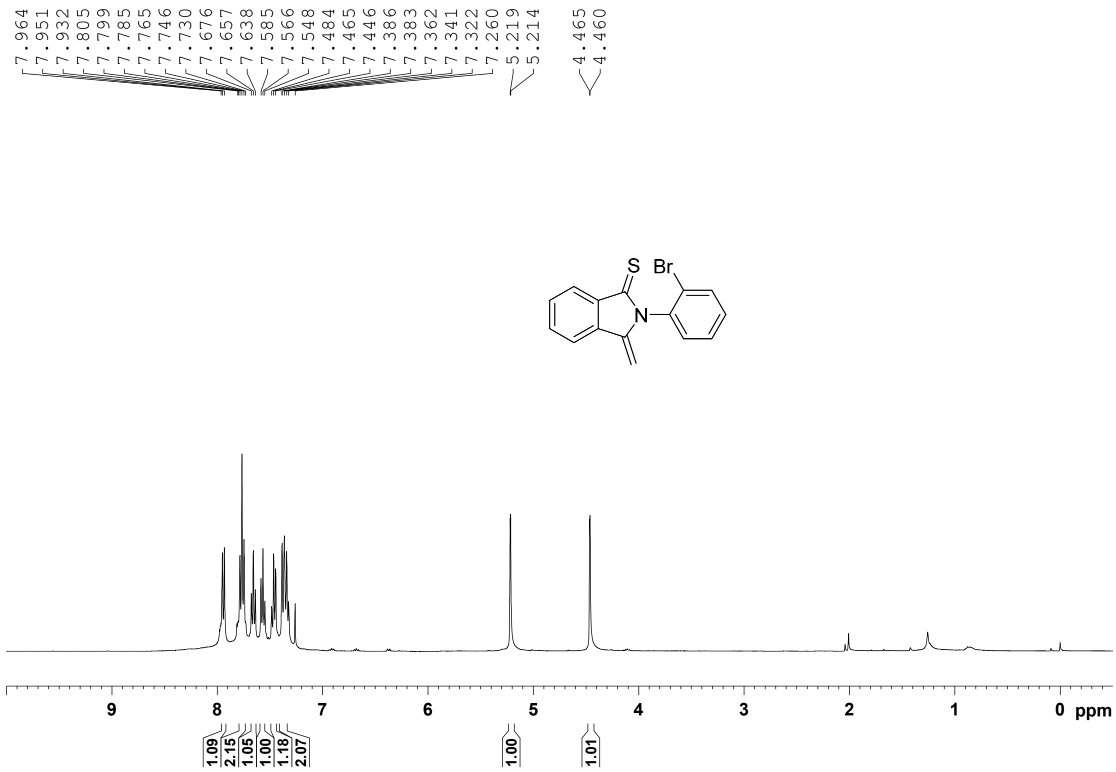

Figure S82. ^{1}H NMR (400 MHz, $CDCl_3$) of **4i**

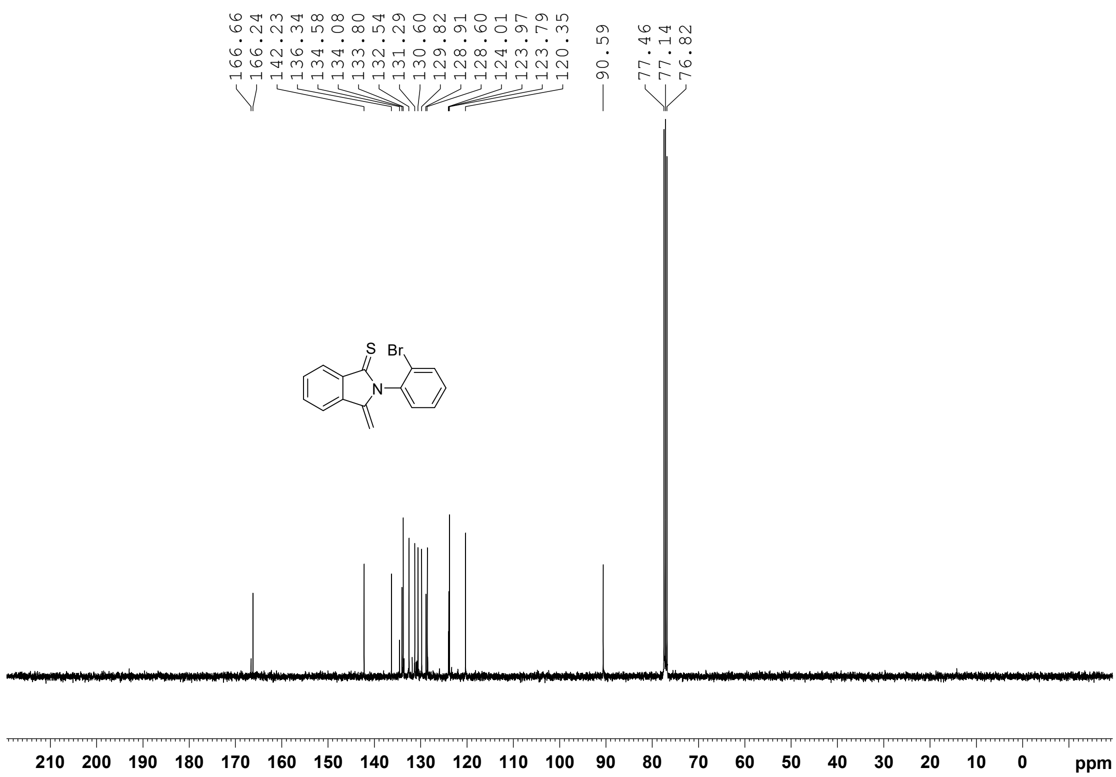

Figure S83. ^{13}C NMR (101 MHz, $CDCl_3$) of **4i**

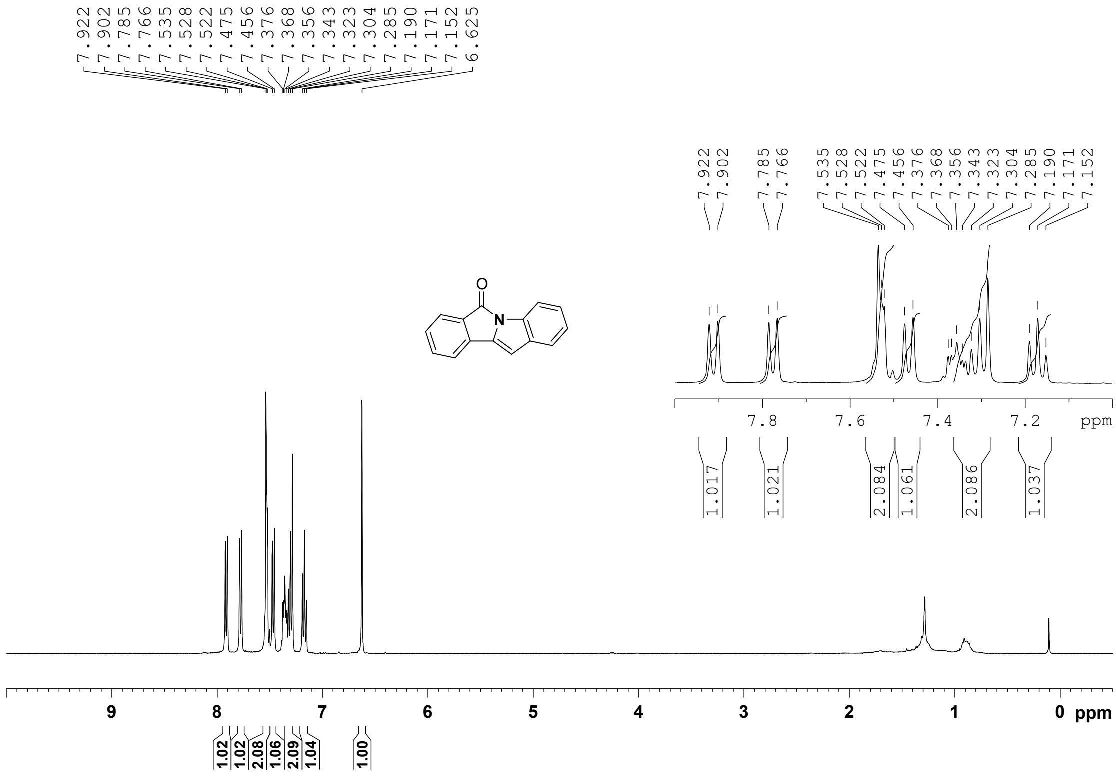

Figure S84. ^{1}H NMR (400 MHz, $CDCl_3$) of **5c**

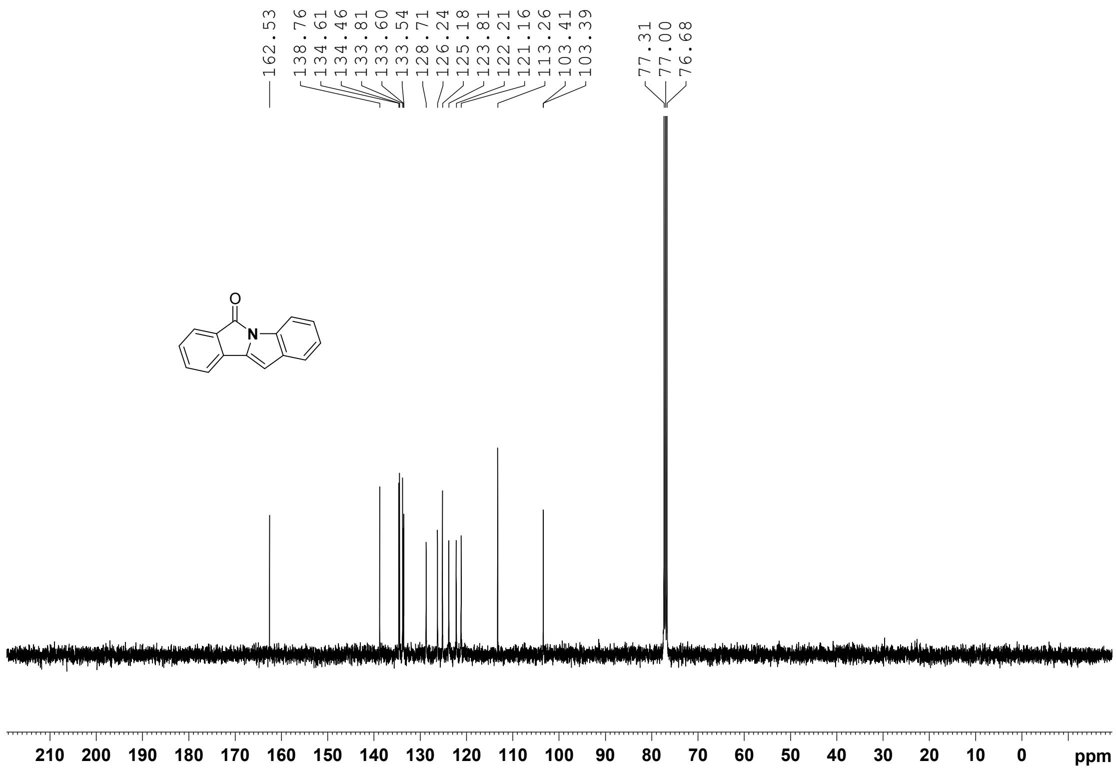

Figure S85. ^{13}C NMR (101 MHz, $CDCl_3$) of **5c**

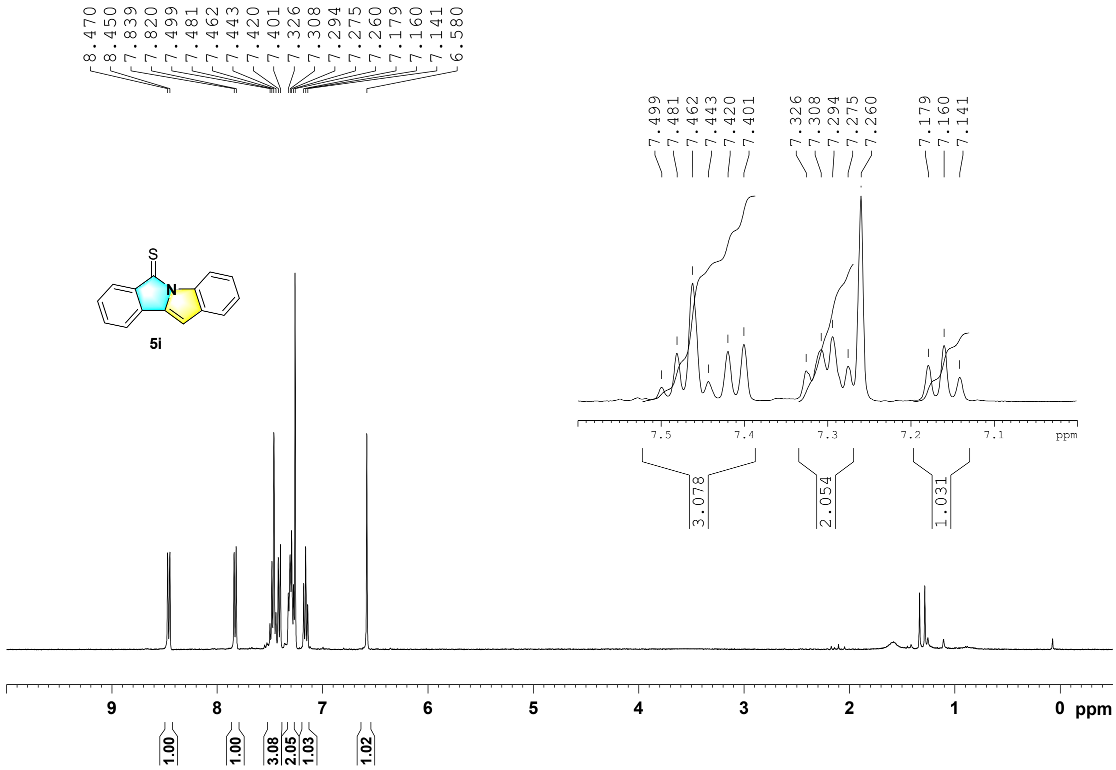

Figure S86. ^{1}H NMR (400 MHz, $CDCl_3$) of **5i**

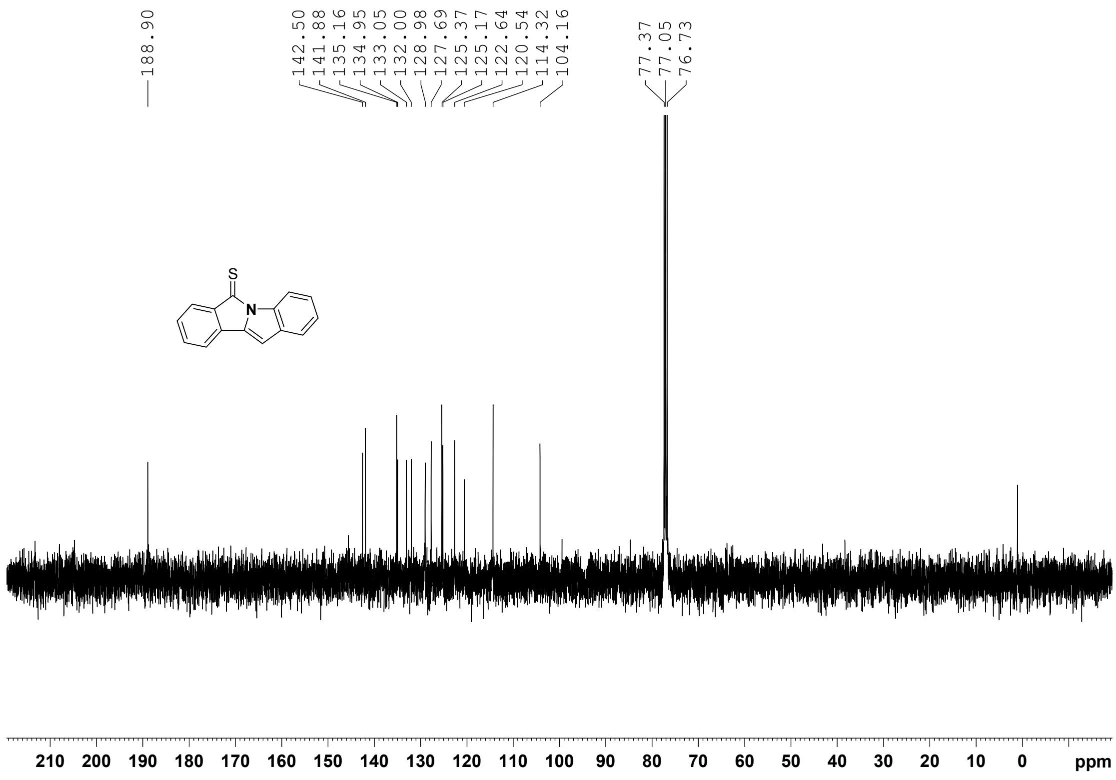

Figure S87. ^{13}C NMR (101 MHz, $CDCl_3$) of **5i**