SUPPORTING INFORMATION

Facile synthesis of the unknown 6,7-dihydrofuro[3,4-*c*]pyridines and 3,4-diaryloylpyridines from *N*-homopropargylic β-enaminones

Elif Serel Yilmaz,[a] Kerem Kaya[#b] and Metin Zora[*a]

[a] Department of Chemistry, Faculty of Arts and Science, Middle East Technical University, 06800 Ankara, Turkey

[b] Department of Chemistry, Faculty of Science, Istanbul Technical University, 34469 Istanbul, Turkey

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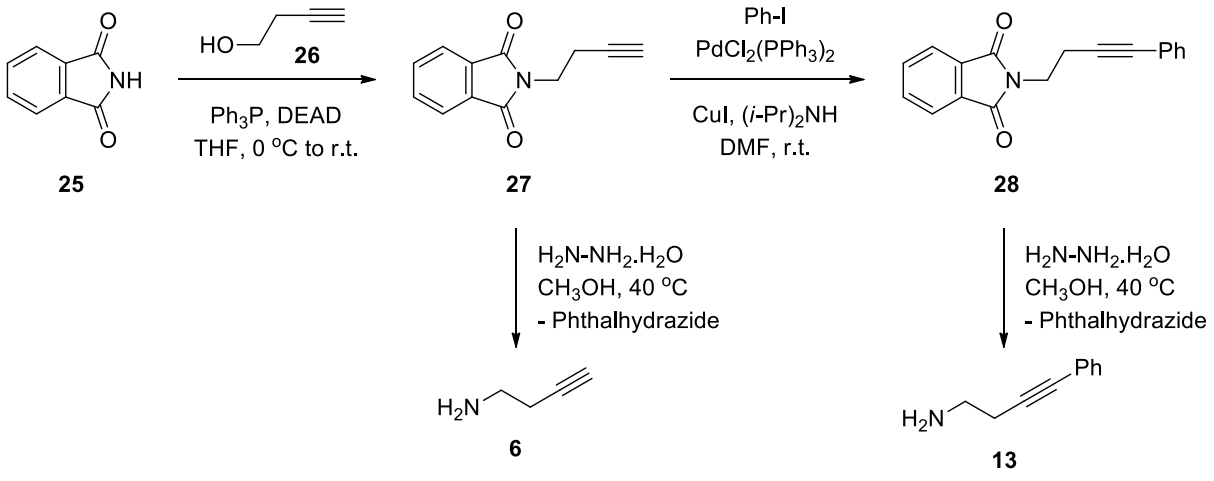
[#] Author to whom inquiries concerning the X-ray analysis should be directed
[*] Corresponding Author. E-mail address: zora@metu.edu.tr (M. Zora)

Experimental Section

General Information. ^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts were given in parts per million (ppm) relative to $CDCl_3$ (7.26 and 77.16 ppm in ^{1}H and ^{13}C NMR, respectively. Coupling constants (*J*) were given in hertz (Hz), and spin multiplicities were shown by the following symbols: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). Infrared (IR) spectra were obtained using attenuated total reflection (ATR). Band positions diagnostic for major functional groups were recorded in reciprocal centimeters (cm^{-1}). Mass spectra (MS) and high-resolution MS (HRMS) were obtained using electrospray ionization (ESI) or atmospheric pressure chemical ionization (APCI) with micro-Tof; *m/z* values are reported (for each measurement, the mass scale was recalibrated with sodium formate clusters, and samples were dissolved and measured in MeOH or CH_3CN). Flash chromatography was performed using thick-walled glass columns and "flash-grade" silica gel (230−400 mesh). TLC was accomplished by using commercially prepared 0.25 mm silica gel plates and visualization was effected with a short-wavelength UV lamp (254 nm). The relative proportions of solvents in chromatography solvent mixtures refer to the volume/volume ratio. All commercially available reagents were used directly without purification unless otherwise stated. All solvents used in reactions and chromatography were distilled and/or dried properly for purity. The inert atmosphere was created using slight positive pressure (ca. 0.1 psi) of argon. All glassware was dried in an oven prior to use.

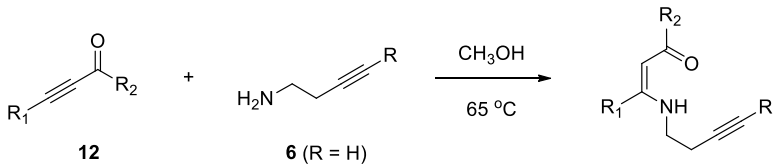
We prepared homopropargylamines **6** and **13** according to known literature procedures as depicted in Scheme S1.[1,2] Mitsunobi reaction between phthalimide (**25**) and 3-butyn-1-ol (**26**)

Scheme S1. Synthesis of Homopropargylamines **6** and **13**.



using Ph_3P and diethyl azodicarboxylate (DEAD) produced *N*-(3-butynyl)phthalimide (**27**).[1] Sonagashira cross coupling of **27** with iodobenzene under palladium catalysis yielded phenyl-substituted phthalimide **28**.[2] Subsequent deprotection with hydrazine monohydrate provided 4-phenylbut-3-yn-1-amine (**13**).[1,2] 3-Butynylamine (**6**) is commercially available but, if desired, it can be synthesized from *N*-(3-butynyl)phthalimide (**27**) by a similar deprotection step using hydrazine monohydrate (Scheme S1).[1,2] For the characterization data and/or the NMR spectra for these compounds, see references 1 and 2 and their Supporting Information.

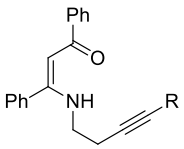
Scheme S2. Synthesis of *N*-Homopropargylic β-Enaminones **9** and **14**.[a]



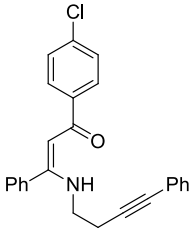
12
12a (R_1 = R_2 = Ph)

6 (R = H)
13 (R = Ph)

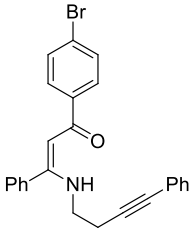
14 (R = H)
9 (R = Ph)



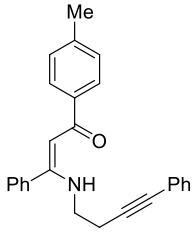
14a (R= H) (70%)
9a (R= Ph) (58%)



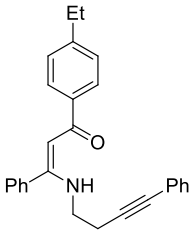
9b (54%)



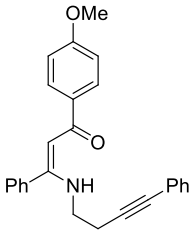
9c (26%)



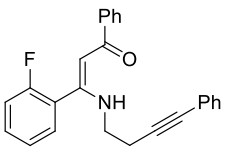
9d (37%)



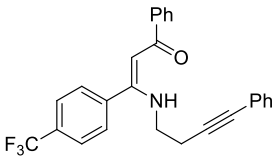
9e (18%)



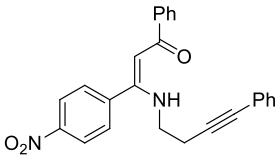
9f (60%)



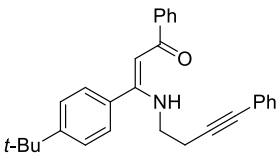
9g (49%)



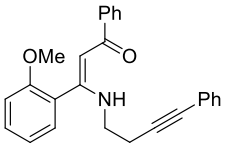
9h (51%)



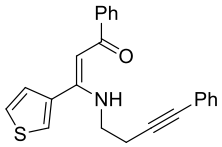
9i (44%)



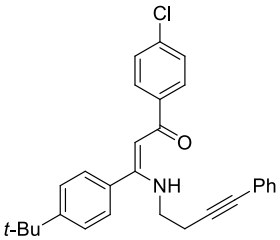
9j (84%)



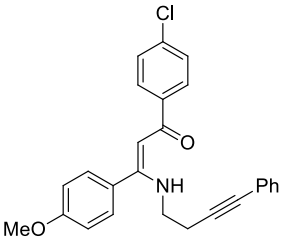
9k (25%)



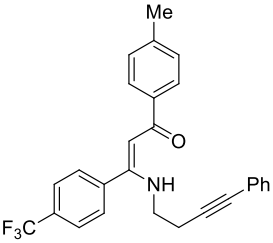
9l (24%)



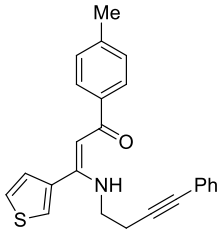
9m (23%)



9n (33%)



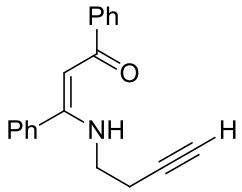
9o (32%)



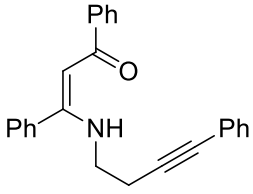
9p (18%)

[a]Isolated yields.

General Procedure 1. Synthesis of *N*-Homopropargylic β-Enaminones 9 or 14 (Scheme S2). To a stirred solution of the proper α,β-alkynic ketone **12** (1.94 mmol) in MeOH (10 mL) was added 3-butynylamine (**6**) (1.94 mmol) or 4-phenylbut-3-yn-1-amine (**13**) (1.94 mmol), and the resulting mixture was then refluxed until α,β-alkynic ketone **12** was completely consumed as monitored by routine TLC. After the reaction was over, the solvent was removed on a rotary evaporator, and ethyl acetate (50 mL) and a saturated NH_4Cl solution (50 mL) were added. After the layers were separated, the aqueous layer was extracted with ethyl acetate (3 x 50 mL). The combined organic layers were dried over $MgSO_4$ and evaporated on a rotary evaporator to give the crude product, which was purified by flash chromatography on silica gel using hexane/ethyl acetate (9:1 followed by 4:1) as the eluent to afford the corresponding *N*-homopropargylic β-enaminone **9** or **14**.

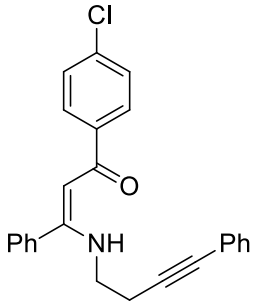


(*Z*)-3-(But-3-yn-1-ylamino)-1,3-diphenylprop-2-en-1-one (14a). 1,3-Diphenylprop-2-yn-1-one (**12a**) (376.0 mg, 1.83 mmol) and 3-butynylamine (**6**) (151.4 mg, 2.19 mmol) were employed to afford 353.7 mg (70%) of the indicated product **14a** as a yellow solid (R_f = 0.52 in 4:1 hexane/ethyl acetate; mp 112.0–113.3 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.45 (br s, 1H), 7.90 (dd, *J* = 8.0, 1.5 Hz, 2H), 7.51–7.36 (m, 8H), 5.79 (s, 1H), 3.39 (q, *J* = 6.8 Hz, 2H), 2.42 (td, *J* = 6.9, 2.6 Hz, 2H), 2.09 (t, *J* = 2.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (CO), 166.5 (C), 140.2 (C), 135.5 (C), 130.9 (C), 129.7 (CH), 128.7 (CH), 128.3 (CH), 127.8 (CH), 127.2 (CH), 94.1 (CH), 80.6 (C), 70.8 (CH), 43.4 (CH_2), 21.0 (CH_2) (Note that two CH peaks overlap on each other); IR (neat): 3284, 1571, 1546, 1478, 1440, 1334, 1295, 1215, 1144, 1083, 1056, 1025, 1002, 923, 792, 780, 745, 707, 688, 647, 617, 540, 508 cm^{-1}; MS (APCI, *m/z*): 276.14 $[M+H]^+$; HRMS (APCI) calcd. for $C_{19}H_{17}NO$: 276.1383 $[M+H]^+$, found: 276.1385.

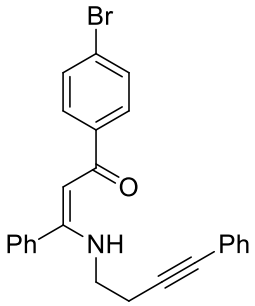


(*Z*)-1,3-Diphenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9a). 1,3-Diphenylprop-2-yn-1-one (**12a**) (400.0 mg, 1.94 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (281.7 mg, 1.94 mmol) were employed to afford 395.5 mg (58%) of the indicated product **9a** as a yellow solid (R_f = 0.43 in 4:1 hexane/ethyl acetate; mp 99.2–101.2 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.57 (br s, 1H), 7.94 (d, *J* = 6.3 Hz, 2H), 7.56–7.36 (m, 10H), 7.35–7.24 (m, 3H), 5.83 (s, 1H), 3.49 (q, *J* = 6.8 Hz, 2H), 2.66 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6 (CO), 166.5 (C), 140.2 (C), 135.5 (C), 131.8 (CH), 130.8 (CH), 129.6 (CH), 128.7 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 127.1 (CH), 123.3 (C), 94.1 (CH), 86.2 (C), 82.8 (C), 43.6 (CH_2), 23.0 (CH_2)

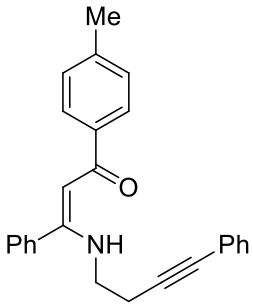
(Note that two CH peaks overlap on each other); IR (neat): 3058, 2945, 2928, 2870, 1770, 1700, 1594, 1567, 1487, 1468, 1436, 1392, 1355, 1321, 1291, 1256, 1175, 1146, 1115, 1083, 1058, 1024, 998, 971, 913, 865, 757, 736, 688, 616 cm^{-1}; MS (ESI, *m/z*): 352.17 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{21}NO$: 352.1696 $[M+H]^+$, found: 352.1694.



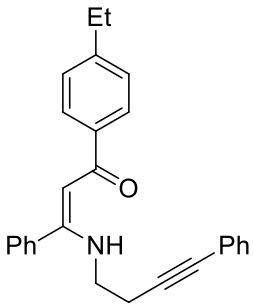
(*Z*)-1-(4-Chlorophenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9b). 1-(4-Chlorophenyl)-3-phenylprop-2-yn-1-one (**12b**) (236.7 mg, 0.98 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (142.3 mg, 0.98 mmol) were employed to afford 204.2 mg (54%) of the indicated product **9b** as a light brown oil (R_f = 0.53 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (br s, 1H), 7.84 (d, *J* = 8.5 Hz, 2H), 7.50–7.41 (m, 7H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.33–7.27 (m, 3H), 5.74 (s, 1H), 3.48 (q, *J* = 6.8 Hz, 2H), 2.65 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.2 (CO), 167.0 (C), 138.6 (C), 137.0 (C), 135.4 (C), 131.8 (CH), 129.8 (CH), 128.8 (CH), 128.6 (CH), 128.5 (CH), 128.3 (CH), 128.1 (CH), 127.9 (CH), 123.4 (C), 93.7 (CH), 86.1 (C), 82.9 (C), 43.7 (CH_2), 22.0 (CH_2); IR (neat): 3058, 3029, 2928, 1905, 1711, 1670, 1586, 1563, 1476, 1442, 1396, 1368, 1322, 1293, 1271, 1220, 1174, 1144, 1087, 1061, 1010, 913, 882, 845, 780, 754, 690, 666, 627, 614 cm^{-1}; MS (ESI, *m/z*): 386.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{20}ClNO$: 386.1306 $[M+H]^+$, found: 386.1311.



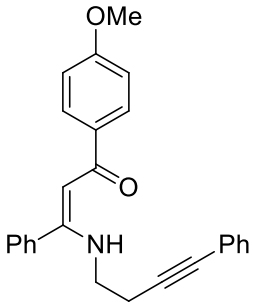
(*Z*)-1-(4-Bromophenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9c). 1-(4-Bromophenyl)-3-phenylprop-2-yn-1-one (**12c**) (326.0 mg, 1.14 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (165.5 mg, 1.14 mmol) were employed to afford 127.6 mg (26%) of the indicated product **9c** as a yellow solid (R_f = 0.49 in 4:1 hexane/ethyl acetate; mp 138.3–140.3 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.50 (s, 1H), 7.94 (dd, *J* = 7.9, 1.5 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.53–7.40 (m, 5H), 7.38–7.28 (m, 5H), 5.80 (s, 1H), 3.46 (q, *J* = 6.7 Hz, 2H), 2.66 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.8 (CO), 165.1 (C), 140.0 (C), 134.8 (C), 131.9 (CH), 131.7 (CH), 131.0 (CH), 129.5 (CH), 128.3 (CH), 128.0 (CH), 127.1 (CH), 123.9 (C), 123.2 (C), 94.1 (CH), 86.1 (C), 82.9 (C), 43.6 (CH_2), 22.0 (CH_2) (Note that two CH peaks overlap on each other); IR (neat): 3080, 3040, 2938, 2878, 1910, 1593, 1573, 1547, 1473, 1442, 1390, 1320, 1291, 1253, 1222, 1177, 1140, 1072, 1055, 1010, 915, 826, 779, 751, 691, 662, 622 cm^{-1}; MS (ESI, *m/z*): 430.08 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{20}{}^{79}BrNO$: 430.0801 $[M+H]^+$, found: 430.0792.



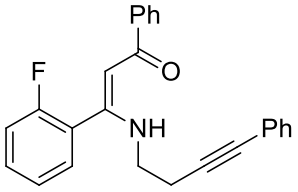
(*Z*)-3-Phenyl-3-((4-phenylbut-3-yn-1-yl)amino)-1-(*p*-tolyl)prop-2-en-1-one (9d). 3-Phenyl-1-(*p*-tolyl)prop-2-yn-1-one (**12d**) (302.8 mg, 1.37 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (198.9 mg, 1.37 mmol) were employed to afford 500.7 mg (37%) of the indicated product **9d** as an orange oil (R_f = 0.54 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.63 (br s, 1H), 7.92 (d, *J* = 8.1 Hz, 2H), 7.57–7.52 (m, 2H), 7.49 (s, 5H), 7.37– 7.31 (m, 3H), 7.26 (d, *J* = 7.9 Hz, 2H), 5.89 (s, 1H), 3.50 (q, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.8 Hz, 2H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.3 (CO), 166.1 (C), 141.0 (C), 137.4 (C), 135.5 (C), 131.6 (CH), 129.4 (CH), 128.8 (CH), 128.5 (CH), 128.1 (CH), 127.8 (CH), 127.7 (CH), 127.0 (CH), 123.2 (C), 93.7 (CH), 86.2 (C), 82.6 (C), 43.4 (CH_2), 21.8 (CH_3), 21.3 (CH_2); IR (neat): 3056, 3027, 2917, 2874, 1713, 1591, 1564, 1480, 1442, 1404, 1370, 1323, 1300, 1207, 1178, 1144, 1114, 1061, 1017, 998, 915, 885, 837, 755, 691, 670, 614 cm^{-1}; MS (ESI, *m/z*): 366.19 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{23}NO$: 366.1852 $[M+H]^+$, found: 366.1859.



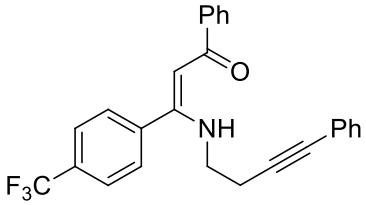
(*Z*)-1-(4-Ethylphenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9e). 1-(4-Ethylphenyl)-3-phenylprop-2-yn-1-one (**12e**) (352.5 mg, 1.50 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (217.8 mg, 1.50 mmol) were employed to afford 102.5 mg (18%) of the indicated product **9e** as a yellow oil (R_f = 0.51 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.54 (s, 1H), 7.89 (d, J = 8.2 Hz, 2H), 7.53–7.44 (m, 8H), 7.36– 7.23 (m, 4H), 5.84 (s, 1H), 3.49 (q, *J* = 6.7 Hz, 2H), 2.93–2.44 (m, 4H), 1.28 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6 (CO), 166.2 (C), 147.4 (C), 137.8 (C), 135.7 (C), 131.8 (CH), 129.5 (CH), 128.6 (CH), 128.2 (CH), 128.0 (CH), 127.9 (CH), 127.8 (CH), 127.3 (CH), 123.4 (C), 94.0 (CH), 86.3 (C), 82.7 (C), 43.6 (CH_2), 28.8 (CH_2), 22.0 (CH_2), 15.4 (CH_3); IR (neat): 3057, 3028, 2964, 2930, 2872, 1706, 1591, 1564, 1481, 1443, 1370, 1322, 1294, 1228, 1178, 1144, 1065, 1016, 915, 850, 791, 755, 693 cm^{-1}; MS (ESI, *m/z*): 380.20 $[M+H]^+$; HRMS (ESI) calcd. for $C_{27}H_{25}NO$: 380.2009 $[M+H]^+$, found: 380.2012.



(*Z*)-1-(4-Methoxyphenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9f). 1-(4-Methoxyphenyl)-3-phenylprop-2-yn-1-one (**12f**) (253.2 mg, 1.07 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (155.4 mg, 1.07 mmol) were employed to afford 244.9 mg (60%) of the indicated product **9f** as an orange solid (R_f = 0.34 in 4:1 hexane/ethyl acetate; mp 110.0–112.0 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (s, 1H), 7.90 (d, *J* = 8.7 Hz, 2H), 7.45 (br s, 7H), 7.32–7.20 (m, 3H), 6.91 (d, *J* = 8.8 Hz, 2H), 5.77 (s, 1H), 3.84 (s, 3H), 3.46 (q, 6.8 Hz, 2H), 2.64 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.9 (CO), 166.1 (C), 161.9 (C), 133.0 (C), 131.8 (CH), 129.6 (C), 129.1 (CH), 128.7 (CH), 128.3 (CH), 128.0 (CH), 128.0 (CH), 123.4 (C), 113.5 (CH), 93.7 (CH), 86.3 (C), 82.7 (C), 55.4 (OCH_3), 43.7 (CH_2), 22.1 (CH_2) (Note that two CH peaks overlap on each other); IR (neat): 3073, 2996, 2916, 2851, 1740, 1583, 1564, 1547, 1483, 1443, 1378, 1335, 1308, 1257, 1227, 1171, 1142, 1117, 1063, 1026, 994, 927, 836, 776, 756, 735, 706, 692, 669, 633 cm^{-1}; MS (ESI, *m/z*): 382.18 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{23}NO_2$:382.1802 $[M+H]^+$, found: 382.1800.

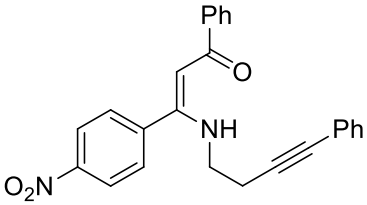


(*Z*)-3-(2-Fluorophenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9g). 3-(2-Fluorophenyl)-1-phenylprop-2-yn-1-one (**12g**) (197.7 mg, 0.88 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (127.8 mg, 0.88 mmol) were employed to afford 159.3 mg (49%) of the indicated product **9g** as a yellow oil (R_f = 0.49 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.55 (s, 1H), 7.99 (d, *J* = 7.1 Hz, 2H), 7.61–7.42 (m, 6H), 7.40–7.33 (m, 3H), 7.32–7.19 (m, 3H), 5.87 (s, 1H), 3.52 (q, *J* = 6.1 Hz, 2H), 2.72 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.9 (CO), 164.8 (C), 162.6 (d, ^1J = 248.2 Hz, CF) 140.0 (C), 137.5 (d, ^3J = 7.5 Hz, CH), 131.7 (CH), 131.0 (CH), 130.4 (d, ^3J = 8.2 Hz, CH), 128.28 (CH), 128.27 (CH), 128.0 (CH), 127.1 (CH), 123.7 (d, ^4J = 2.8 Hz, CH), 123.2 (C), 116.6 (d, ^2J = 21.0 Hz, C), 115.2 (d, ^2J = 22.5 Hz, CH), 94.0 (CH), 86.1 (C), 83.0 (C), 43.6 (CH_2), 22.0 (CH_2); IR (neat): 3059, 2929, 2877, 1710, 1664, 1595, 1571, 1523, 1474, 1433, 1370, 1327, 1299, 1197, 1176, 1158, 1127, 1056, 1024, 1001, 875, 791, 753, 689, 677, 632 cm^{-1}; MS (ESI, *m/z)*: 370.16 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{20}FNO$:370.1602 $[M+H]^+$, found: 370.1605.

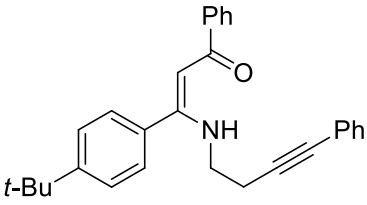


(*Z*)-1-Phenyl-3-((4-phenylbut-3-yn-1-yl)amino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (9h). 1-Phenyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (**12h**) (300.0 mg, 1.09 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (158.3 mg, 1.09

mmol) were employed to afford 233.2 mg (51%) of the indicated product **9h** as an orange oil (R_f = 0.51 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.50 (s, 1H), 7.94 (d, *J* = 6.5 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.52–7.38 (m, 5H), 7.38–7.22 (m, 3H), 5.81 (s, 1H), 3.43 (q, *J* = 6.6 Hz, 2H), 2.66 (t, *J* = 6.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.1 (CO), 164.9 (C), 139.9 (C), 139.1 (C), 131.8 (CH), 131.6 (q, ^2J = 32.6 Hz, CH), 131.1 (C), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 127.2 (CH), 125.7 (q, ^3J = 3.6 Hz, CH). 123.9 (q, ^1J = 272.3 Hz, CF_3), 123.3 (C), 94.2 (CH), 86.0 (C), 83.0 (C), 43.6 (CH_2), 22.1 (CH_2); IR (neat): 3057, 2937, 2879, 1712, 1670, 1595, 1561, 1502, 1488, 1444, 1406, 1370, 1320, 1226, 1165, 1108, 915, 850, 810, 754, 713, 688, 622 cm^{-1}; MS (ESI, *m/z*): 420.16 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{20}F_3NO$: 420.1570 $[M+H]^+$, found: 420.1560.

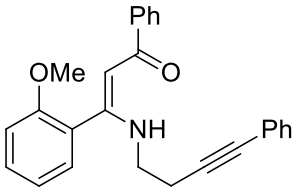


(*Z*)-3-(4-Nitrophenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9i). 3-(4-Nitrophenyl)-1-phenylprop-2-yn-1-one (**12i**) (243.3 mg, 0.97 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (140.8 mg, 0.97 mmol) were employed to afford 170.1 mg (44%) of the indicated product **9i** as a yellow oil (R_f = 0.41 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.42 (s, 1H), 8.30 (d, *J* = 8.6 Hz, 2H), 7.93 (d, *J* = 8.1 Hz, 2H), 7.64 (d, *J* = 8.6 Hz, 2H), 7.54–7.39 (m, 5H), 7.34–7.28 (m, 3H), 5.80 (s, 1H), 3.42 (q, *J* = 6.5 Hz, 2H), 2.67 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.2 (CO), 163.6 (C), 148.4 (C), 141.7 (C), 139.7 (C), 131.7 (CH), 131.3 (CH), 129.2 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 127.2 (CH), 123.9 (CH), 123.1 (C), 94.3 (CH), 85.9 (C), 83.1 (C), 43.7 (CH_2), 22.0 (CH_2); MS (ESI, m/z): 397.15 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{20}N_2O_3$: 397.1547 $[M+H]^+$, found: 397.1549.

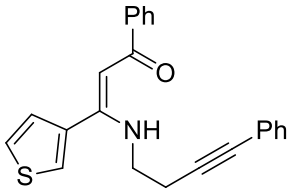


(*Z*)-3-(4-(*tert*-Butyl)phenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9j). 3-(4-(*tert*-Butyl)phenyl)-1-phenylprop-2-yn-1-one (**12j**) (213.0 mg, 0.81 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (117.6 mg, 0.81 mmol) were employed to afford 277.3 mg (84%) of the indicated product **9j** as a yellow oil (R_f = 0.54 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.58 (s, 1H), 7.93 (d, *J* = 7.1 Hz, 2H), 7.57–7.37 (m, 9H), 7.35–7.25 (m, 3H), 5.83 (s, 1H), 3.53 (q, *J* = 5.9 Hz, 2H), 2.68 (t, *J* = 5.9 Hz, 2H), 1.38 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6 (CO), 166.9 (C), 152.9 (C), 140.4 (C), 132.7 (C), 131.8 (CH), 130.8 (CH), 128.3 (CH), 128.3 (CH), 128.0 (CH), 127.7 (CH), 127.2 (CH), 125.6 (CH), 123.4 (C), 94.1 (CH), 86.3 (C), 82.8 (C), 43.7 (CH_2), 34.9 (C), 31.4

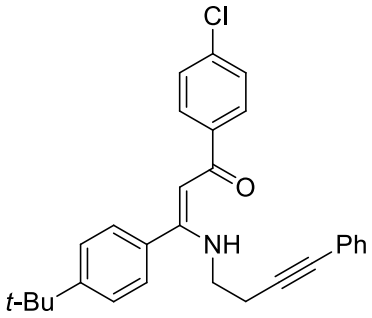
(CH_3), 22.1 (CH_2); IR (neat): 3056, 2960, 2904, 2868, 1712, 1579, 1552, 1497, 1485, 1365, 1327, 1295, 1267, 1224, 1149, 1108, 1057, 1022, 915, 840, 755, 689, 634 cm^{-1}; MS (ESI, *m/z*): 408.23 $[M+H]^+$; HRMS (ESI) calcd. for $C_{29}H_{29}NO$: 408.2322 $[M+H]^+$, found: 408.2317.



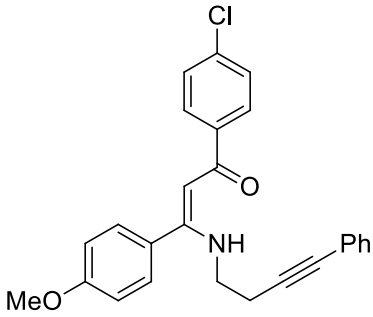
(*Z*)-3-(2-Methoxyphenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9k). 3-(2-Methoxyphenyl)-1-phenylprop-2-yn-1-one (**12k**) (339.6 mg, 1.44 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (209.1 mg, 1.44 mmol) were employed to afford 134.6 mg (25%) of the indicated product **9k** as a yellow oil (R_f = 0.39 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.64 (s, 1H), 7.81 (dd, *J* = 7.7, 1.7 Hz, 2H), 7.49–7.12 (m, 10H), 6.99–6.79 (m, 2H), 5.64 (s, 1H), 3.74 (s, 3H), 3.26 (d, *J* = 26.8 Hz, 2H), 2.54 (t, *J* = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.4 (CO), 164.0 (C), 156.0 (C), 140.3 (C), 131.7 (CH), 131.0 (CH), 130.6 (CH), 129.7 (CH), 128.2 (CH), 128.1 (CH), 127.9 (CH), 127.1 (CH), 124.3 (C), 123.4 (C), 120.9 (CH), 110.8 (CH), 93.4 (CH), 86.4 (C), 82.4 (C), 55.5 (OCH_3), 43.6 (CH_2), 21.5 (CH_2); IR (neat): 3055, 2936, 2875, 2836, 1734, 1594, 1568, 1548, 1521, 1483, 1453, 1368, 1326, 1296, 1270, 1239, 1178, 1147, 1115, 1082, 1057, 1022, 913, 835, 806, 690, 619 cm^{-1}; MS (ESI, *m/z*): 382.18 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{23}NO_2$: 382.1802 $[M+H]^+$, found: 382.1810.



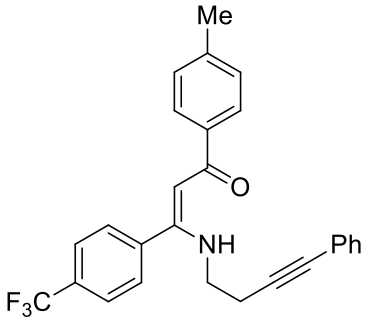
(*Z*)-1-Phenyl-3-((4-phenylbut-3-yn-1-yl)amino)-3-(thiophen-3-yl)prop-2-en-1-one (9l). 1-Phenyl-3-(thiophen-3-yl)prop-2-yn-1-one (**12l**) (263.0 mg, 1.24 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (204.7 mg, 1.41 mmol) were employed to afford 106.4 mg (24%) of the indicated product **9l**. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.96 (dd, *J* = 8.0, 3.6 Hz, 2H), 7.58–7.39 (m, 7H), 7.35–7.29 (m, 3H), 7.27–7.19 (m, 1H), 5.93 (s, 1H), 3.58 (q, *J* = 4.5 Hz, 2H), 2.69 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.6 (CO), 161.3 (C), 140.2 (C), 136.2 (C), 131.8 (CH), 130.8 (CH), 128.3 (CH), 128.0 (CH), 127.3 (CH), 127.1 (CH), 126.5 (CH), 125.8 (CH), 123.3 (C), 93.8 (CH), 86.2 (C), 82.8 (C), 43.7 (CH_2), 21.9 (CH_2) (Note that two CH peaks overlap on each other).



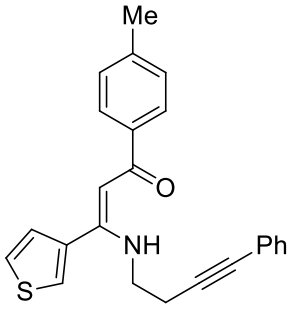
(*Z*)-3-(4-(*tert*-Butyl)phenyl)-1-(4-chlorophenyl)-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9m). 3-(4-(*tert*-Butyl)phenyl)-1-(4-chlorophenyl)prop-2-yn-1-one (**12m**) (422.0 mg, 1.42 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (206.2 mg, 1.42 mmol) were employed to afford 144.3 mg (23%) of the indicated product **9m** as an orange oil (R_f = 0.61 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 7.74 (d, *J* = 8.4 Hz, 2H), 7.39–7.30 (m, 4H), 7.30–7.21 (m, 4H), 7.21–7.13 (m, 3H), 5.65 (s, 1H), 3.41 (q, *J* = 6.6 Hz, 2H), 2.55 (t, *J* = 6.8 Hz, 2H), 1.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.9 (CO), 167.1 (C), 153.0 (C), 138.7 (C), 136.8 (C), 132.4 (C), 131.8 (CH), 128.6 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.6 (CH), 125.6 (CH), 123.3 (C), 93.7 (CH), 86.2 (C), 82.8 (C), 43.7 (CH_2), 34.9 (C), 31.3 (CH_3), 22.0 (CH_2); IR (neat): 3056, 2960, 2903, 2868, 1735, 1577, 1550, 1497, 1478, 1396, 1364, 1324, 1294, 1267, 1221, 1149, 1088, 1061, 1026, 910, 839, 773, 754, 730, 690, 671, 628 cm^{-1}; MS (ESI, *m/z*): 442.19 $[M+H]^+$; HRMS (ESI) calcd. for $C_{29}H_{28}ClNO$: 442.1932 $[M+H]^+$, found: 442.1924.



(*Z*)-1-(4-Chlorophenyl)-3-(4-methoxyphenyl)-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (9n). 1-(4-Chlorophenyl)-3-(4-methoxyphenyl)prop-2-yn-1-one (**12n**) (253.2 mg, 0.94 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (136.5 mg, 0.94 mmol) were employed to afford 129.0 mg (33%) of the indicated product **9n** as a yellow solid (R_f = 0.33 in 4:1 hexane/ethyl acetate; mp 72.1–74.1 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.88 (d, *J* = 8.5 Hz, 2H), 7.51–7.45 (m, 2H), 7.40 (t, *J* = 8.8 Hz, 4H), 7.34–7.28 (m, 3H), 6.99 (d, *J* = 8.6 Hz, 2H), 5.78 (s, 1H), 3.86 (s, 3H), 3.54 (q, *J* = 6.7 Hz, 2H), 2.68 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 186.7 (CO), 166.9 (C), 160.7 (C), 138.7 (C), 136.7 (C), 131.7 (CH), 129.3 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.5 (C), 123.3 (C), 114.0 (CH), 93.7 (CH), 86.2 (C), 82.8 (C), 55.4 (OCH_3), 43.7 (CH_2), 21.9 (CH_2); IR (neat): 3077, 2933, 2875, 2840, 1909, 1714, 1565, 1498, 1476, 1443, 1395, 1367, 1328, 1294, 1268, 1246, 1174, 1143, 1110, 1084, 1062, 1024, 1009, 917, 834, 816, 771, 757, 692, 666, 603 cm^{-1}. MS (ESI, *m/z*): 416.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{22}ClNO_2$: 416.1412 $[M+H]^+$, found: 416.1408.

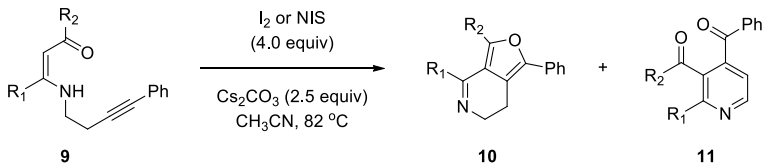


(*Z*)-3-((4-Phenylbut-3-yn-1-yl)amino)-1-(*p*-tolyl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (9o). 1-(*p*-Tolyl)-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-one (**12o**) (252.8 mg, 0.88 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (127.8 mg, 0.88 mmol) were employed to afford 122.1 mg (32%) of the indicated product **9o** as a yellow solid (R_f = 0.54 in 4:1 hexane/ethyl acetate; mp 86.4–88.4 °C). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.43 (s, 1H), 7.89–7.78 (m, 2H), 7.79–7.69 (m, 1H), 7.64–7.55 (m, 3H), 7.53–7.39 (m, 1H), 7.38–7.16 (m, 6H), 5.80 (s, 1H), 3.44 (q, *J* = 3.4 Hz, 2H), 2.67 (t, *J* = 6.6 Hz, 2H), 2.42 (s, 3H); IR (neat): 3058, 2947, 2891, 1717, 1660, 1585, 1561, 1488, 1464, 1406, 1320, 1300, 1232, 1163, 1121, 1067, 1057, 1016, 923, 857, 842, 809, 771, 753, 731, 693, 610 cm^{-1}; MS (ESI, *m/z*): 434.17 $[M+H]^+$; HRMS (ESI) calcd. for $C_{27}H_{22}F_3NO$: 434.1726 $[M+H]^+$, found: 434.1727.

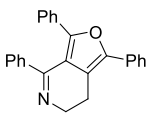


(*Z*)-3-((4-Phenylbut-3-yn-1-yl)amino)-3-(thiophen-3-yl)-1-(*p*-tolyl)prop-2-en-1-one (9p). 3-(Thiophen-3-yl)-1-(*p*-tolyl)prop-2-yn-1-one (**12p**) (255.0 mg, 1.13 mmol) and 4-phenylbut-3-yn-1-amine (**13**) (164.1 mg, 1.13 mmol) were employed to afford 75.6 mg (18%) of the indicated product **9p** as an orange oil (R_f = 0.51 in 4:1 hexane/ethyl acetate). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.40 (s, 1H), 7.72 (d, *J* = 8.1 Hz, 2H), 7.42–7.39 (m, 1H), 7.38–7.33 (m, 2H), 7.29 (dd, *J* = 4.9, 3.0 Hz, 1H), 7.20–7.15 (m, 3H), 7.11 (d, *J* = 6.4 Hz, 3H), 5.77 (s, 1H), 3.44 (q, *J* = 6.8 Hz, 2H), 2.57 (t, *J* = 6.9 Hz, 2H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.5 (CO), 161.1 (C), 141.2 (C), 137.5 (C), 136.3 (C), 131.8 (CH), 129.0 (CH), 128.3 (CH), 128.0 (CH), 127.4 (CH), 127.2 (CH), 126.5 (CH), 125.8 (CH), 123.3 (C), 93.7 (CH), 86.3 (C), 82.8 (C), 43.7 (CH_2), 22.0 (CH_3), 21.5 (CH_2); IR (neat): 3079, 3056, 3027, 2918, 2873, 1715, 1575, 1549, 1486, 1408, 1369, 1313, 1284, 1230, 1208, 1178, 1133, 1114, 1061, 1015, 796, 755, 689, 634, 613 cm^{-1}; MS (ESI, *m/z*): 372.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{21}NOS$: 372.1417 $[M+H]^+$, found: 372.1414.

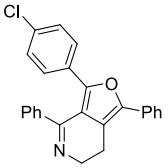
Scheme S3. Scope of the Cyclization of *N*-Homopropargylic β-Enaminones **9** Leading to 6,7-Dihydrofuro[3,4-*c*]pyridines **10** and/or 3,4-Diaryloylpyridines **11**.[a,b]



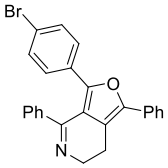
9 **10** **11**



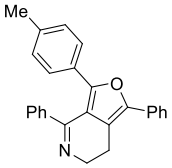
10a (30%) (29%)[c] [29%] [28%][d]



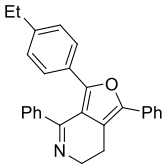
10b (26%)



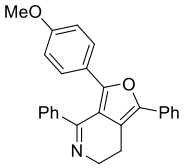
10c (19%)



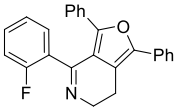
10d (33%)



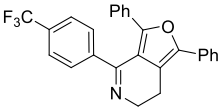
10e (33%)



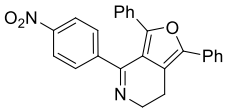
10f (22%)



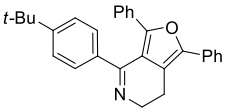
10g (19%) [50%]



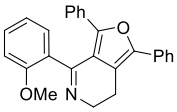
10h (27%)



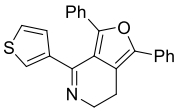
10i (12%) [29%]



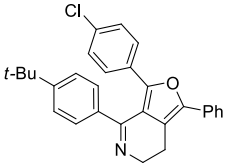
10j (26%)



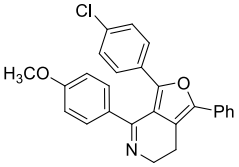
10k (55%)



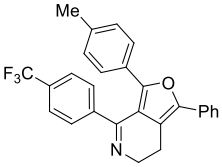
10l (34%)



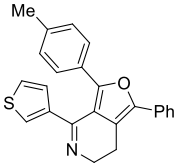
10m (12%) [33%]



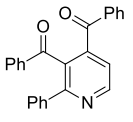
10n (12%)



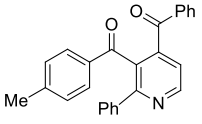
10o (11%) [30%]



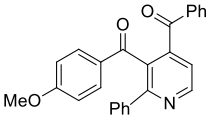
10p (25%)



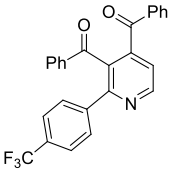
11a (10%) (13%)[c] [29%] (23%)[e]



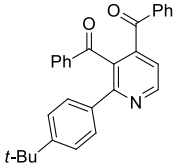
11d (9%)



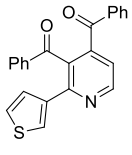
11f (20%)



11h (21%)



11j (12%)



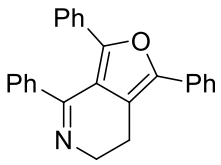
11l (11%)

[a]Isolated yields. [b]Yields obtained with I_2 are given in parentheses while those obtained with NIS are shown in square brackets. [c]Yield obtained from the reaction performed on a 1.99 mmol scale of **9a**. [d]Yield obtained from the reaction performed in DMF at 110 °C. [e]Yield obtained from the reaction carried out by using 2.5 equiv of I_2.

General Procedure 2. Cyclization of *N*-Homopropargylic β-Enaminones 9 Leading to 6,7-Dihydrofuro[3,4-*c*]pyridines 10 and/or 3,4-Diaryloylpyridines 11 (Scheme S3). The proper *N*-homopropargylic β-enaminone **9** (0.28 mmol) in acetonitrile (4.0 mL) was stirred at room temperature under argon and then molecular iodine (1.12 mmol) and Cs_2CO_3 (0.70 mmol) were added to the reaction mixture. The resulting mixture was then refluxed until *N*-homopropargylic β-enaminone **9** was completely consumed as monitored by routine TLC. After the reaction was over, the solvent was removed on a rotary evaporator, and ethyl acetate (40 mL) and a saturated aqueous solution of $Na_2S_2O_3$ (15 mL) were added. After the layers were separated, the aqueous layer was extracted with ethyl acetate (2 x 30 mL). The combined organic layers were dried over $MgSO_4$ and evaporated on a rotary evaporator to give the crude product, which was purified by flash chromatography on silica gel using 4:1 hexane/ethyl acetate as the eluent to afford the corresponding 6,7-dihydrofuro[3,4-*c*]pyridine **10** and/or 3,4-diaryloylpyridine **11**.

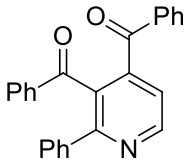
1,3,4-Triphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10a) and (2-phenylpyridine-3,4-diyl)bis(phenylmethanone) (11a). (*Z*)-1,3-Diphenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9a**) (98.4 mg, 0.28 mmol), I_2 (284.3 mg, 1.12 mmol) and Cs_2CO_3 (228.1 mg, 0.70 mmol) were employed. Two fractions were isolated. First fraction yielded 10.2 mg (10%) of the indicated product **11a** as a brown solid (R_f = 0.18 in 4:1 hexane/ethyl acetate; mp 156.5–158.5 °C). Second fraction afforded 29.4 mg (30%) of the indicated product **10a** as a yellow solid (R_f = 0.09 in 4:1 hexane/ethyl acetate; mp 119.2–121.2 °C).

This reaction was also performed on a larger scale as summarized below: 1,3-Diphenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9a**) (700 mg, 1.99 mmol), I_2 (2021 mg, 7.96 mmol) and Cs_2CO_3 (1618 mg, 4.98 mmol) were employed in 15 ml acetonitrile. Two fractions were isolated. First fraction yielded 92 mg (13%) of the indicated product **11a** as a brown solid (R_f = 0.18 in 4:1 hexane/ethyl acetate). Second fraction afforded 200 mg (29%) of the indicated product **10a** as a yellow solid (R_f = 0.09 in 4:1 hexane/ethyl acetate).



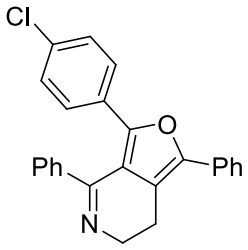
10a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 7.4 Hz, 2 H), 7.52 (dd, *J* = 17.9, 7.6 Hz, 4 H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.33–7.27 (m, 1H), 7.27–7.16 (m, 3H), 7.24 (d, *J* = 7.1 Hz, 2H), 7.13 (d, *J* = 7.6 Hz, 2H), 4.04 (t, *J* = 6.6 Hz, 2H), 3.00 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (C), 151.2 (C), 145.9 (C), 138.0 (C), 130.6 (C), 129.6 (CH), 129.5 (C), 128.9 (CH), 128.30 (CH), 128.25 (CH), 128.1 (CH), 127.7 (CH), 127.5 (CH), 125.1 (CH), 120.0 (C), 115.2 (C), 49.2 (CH_2), 20.3 (CH_2) (Note that two CH peaks overlap on each other); IR (neat): 3050, 2940, 1656, 1582, 1557, 1485, 1444,

1402, 1323, 1262, 1066, 958, 906, 760, 727, 684, 660 cm^{-1}; MS (ESI, *m/z*): 356.16 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{19}NO$: 350.1539 $[M+H]^+$, found: 350.1549.



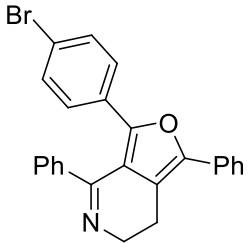
11a: ^1H NMR (400 MHz, $CDCl_3$) δ 8.93 (d, *J* = 4.9 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 2H), 7.61 (t, *J* = 7.5 Hz, 1H), 7.57–7.48 (m, 4H), 7.44 (dd, *J* = 15.8, 6.5 Hz, 3H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.24–7.14 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9 (CO), 195.3 (CO), 158.0 (C), 150.0 (CH), 147.9 (C), 138.9 (C), 137.2 (C), 135.7 (C), 134.2 (CH), 133.9 (C), 133.4 (CH), 130.4 (CH), 129.5 (CH), 129.4 (CH), 129.2 (CH), 128.8 (CH), 128.4 (CH), 128.3 (CH), 120.9 (CH); IR (neat): 3058, 2021, 1980, 1731, 1656, 1593, 1576, 1554, 1492, 1448, 1392, 1314, 1275, 1250, 1178, 1148, 1074, 1023, 1001, 971, 957, 929, 860, 814, 781, 759, 686, 664, 624, 611 cm^{-1}; MS (ESI, *m/z*): 364.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{17}NO_2$: 364.1332 $[M+H]^+$, found: 364.1326.

3-(4-Chlorophenyl)-1,4-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10b). (*Z*)-1-(4-Chlorophenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9b**) (85.3 mg, 0.22 mmol), I_2 (223.4 mg, 0.88 mmol) and Cs_2CO_3 (179.2 mg, 0.55 mmol) were employed to afford 22.0 mg (26%) of the indicated product **10b** as a yellow solid (R_f = 0.14 in 4:1 hexane/ethyl acetate; mp 128.6–130.6 °C).



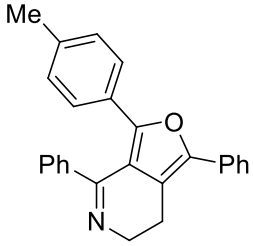
10b: ^1H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.4 Hz, 2H), 7.57–7.44 (m, 4H), 7.39–7.29 (m, 2H), 7.23–7.16 (m, 2H), 7.10 (dd, *J* = 27.2, 8.7 Hz, 4H), 3.99 (t, *J* = 6.5 Hz, 2H), 2.96 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (C), 151.0 (C),150.2 (C),146.5 (C), 134.6 (C), 130.4 (C), 130.2 (C), 129.5 (CH), 129.0 (CH), 128.6 (CH), 128.5 (CH), 128.2 (CH), 128.0 (CH), 125.3 (CH), 119.6 (C), 115.4 (C), 48.7 (CH_2), 20.2 (CH_2) (Note that two CH peaks overlap on each other); IR (neat): 3057, 2932, 2849, 1732, 1663, 1557,1484, 1444, 1397, 1238, 1087, 1011, 926, 833, 760, 691, 526, 481 cm^{-1}; MS (ESI, *m/z*): 384.12 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{18}ClNO$: 384.1150 $[M+H]^+$, found: 384.1149.

3-(4-Bromophenyl)-1,4-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10c). (*Z*)-1-(4-Bromophenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9c**) (108.0 mg, 0.25 mmol), I_2 (253.8 mg, 1.00 mmol) and Cs_2CO_3 (205.3 mg, 0.63 mmol) were employed to afford 20.3 mg (19%) of the indicated product **10c** as a yellow solid (R_f = 0.18 in 4:1 hexane/ethyl acetate; mp 191.0–193.0 °C).

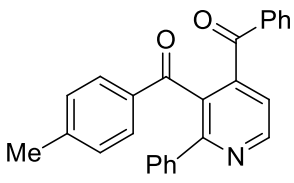


10c: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 7.2 Hz, 2H), 7.47–7.37 (m, 2H), 7.36–7.29 (m, 3H), 7.25–7.06 (m, 7H), 3.92 (t, J = 6.3 Hz, 2 H), 2.89 (t, J = 6.2 Hz, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (C), 151.7 (C), 146.3 (C), 136.7 (C), 131.3 (CH), 130.5 (C), 130.1 (CH), 129.5 (C), 129.0 (CH), 128.9, (CH), 128.5 (CH), 128.0 (CH), 127.8 (CH), 125.3 (CH), 124.2 (C), 119.7 (C), 114.9 (C), 49.2 (CH_2), 20.6 (CH_2); IR (neat): 2962, 1583,1552, 1486,1444, 1404, 1258, 1066, 1010, 790, 688 cm^{-1}; MS (ESI, *m/z*): 428.07 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{18}{}^{79}BrNO$: 428.0645 $[M+H]^+$, found: 428.0653.

1,4-Diphenyl-3-(*p*-tolyl)-6,7-dihydrofuro[3,4-*c*]pyridine (10d) and (4-benzoyl-2-phenylpyridin-3-yl)(*p*-tolyl)methanone (11d). (*Z*)-3-Phenyl-3-((4-phenylbut-3-yn-1-yl)amino)-1-(*p*-tolyl)prop-2-en-1-one (**9d**) (111 mg, 0.30 mmol), I_2 (304.6 mg, 1.20 mmol) and Cs_2CO_3 (244.4 mg, 0.75 mmol) were employed. Two fractions were isolated. First fraction yielded 10.5 mg (9%) of the indicated product **11d** as an orange oil (R_f = 0.18 in 4:1 hexane/ethyl acetate). Second fraction afforded 36.0 mg (33%) of the indicated product **10d** as a brown oil (R_f = 0.09 in 4:1 hexane/ethyl acetate).



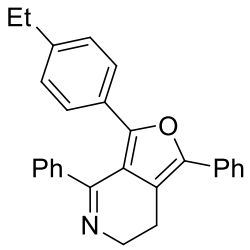
10d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.5 Hz, 2H), 7.57–7.48 (m, 3H), 7.38–7.26 (m, 3H), 7.23–7.10 (m, 4H), 6.93 (d, J = 8.0 Hz, 2H), 4.00 (t, J = 6.5 Hz, 2H), 2.96 (t, J = 6.6 Hz, 2H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8 (C), 151.7 (C), 145.6 (C), 138.4 (C), 138.0 (C), 130.6 (C), 129.7 (CH), 128.9 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 128.1 (CH), 127.5 (CH), 126.9 (C), 125.1 (CH), 119.9 (C), 114.7 (C), 49.2 (CH_2), 21.4 (CH_3), 20.4 (CH_2); IR (neat): 3050, 3030, 2941, 2915, 2556, 1733, 1659, 1599, 1561, 1489, 1443, 1401, 1317, 1261, 1231, 1176, 1068, 1042, 1010, 958, 924, 906, 819, 760, 730, 641 cm^{-1}; (ESI, *m/z*): 364.17 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{21}NO$: 364.1696 $[M+H]^+$, found: 364.1706.



11d: ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.11 (d, J = 4.9 Hz, 1H), 8.00 (d, J = 8.4 Hz, 2H), 7.86–7.77 (m, 1H), 7.73 (dd, J = 6.5, 3.1 Hz, 2H), 7.65 (dd, J = 8.0, 1.9 Hz, 3H), 7.60 (d, J = 4.9 Hz, 1H), 7.46–7.40 (m, 4H), 7.20 (d, J = 8.0 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.4 (CO), 195.3 (CO), 157.9 (C), 149.9 (CH), 147.7 (C), 144.4 (C), 139.0 (C), 135.8 (C), 134.8 (C), 134.1 (CH), 134.0 (CH), 130.4 (C), 129.7 (CH), 129.3 (CH), 129.1 (CH), 128.7 (CH), 128.4 (CH), 120.8 (CH), 21.8 (CH_3) (Note that two CH peaks overlap on each other); IR (neat): 3059, 2953, 2922, 2853, 1730, 1658, 1600, 1577, 1549, 1450, 1392, 1316,

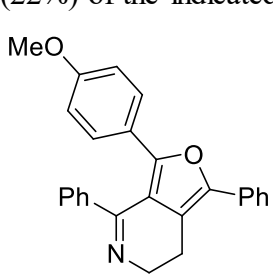
1277, 1251, 1177, 1149, 1100, 1065, 1022, 981, 970, 929, 841, 820, 784, 764, 734, 711, 692, 667, 626, 609 cm^{-1}; MS (ESI, *m/z*): 378.15 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{19}NO_2$: 378.1489 $[M+H]^+$, found: 378.1487.

3-(4-Ethylphenyl)-1,4-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10e). (*Z*)-1-(4-Ethylphenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9e**) (100.2 mg, 0.26 mmol), I_2 (264.0 mg, 1.04 mmol) and Cs_2CO_3 (211.8 mg, 0.65 mmol) were employed to afford 32.4 mg (33%) of the indicated product **10e** as a dark brown oil (R_f = 0.14 in 4:1 hexane/ethyl acetate).



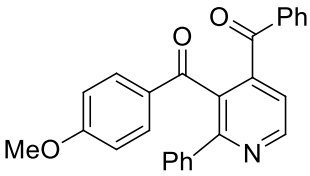
10e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.9 Hz, 2H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.38–7.26 (m, 3H), 7.20–7.08 (m, 3H), 6.93 (d, *J* = 8.2 Hz, 2H), 4.02 (t, *J* = 6.6 Hz, 2H), 2.99 (t, *J* = 6.6 Hz, 2H), 2.55 (q, 7.6 Hz, 2H), 1.16 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4 (C), 158.1 (C), 147.3 (C), 146.7 (C), 132.6 (C), 130.4 (C), 129.9 (CH), 129.5 (CH), 129.2 (CH), 128.9 (CH), 128.8 (CH), 128.5 (CH), 127.8 (CH), 125.8 (C), 125.5 (CH), 117.2 (C), 113.9 (C), 45.8 (CH_2), 28.8 (CH_2), 20.2 (CH_2), 15.4 (CH_3); IR (neat): 3055, 3031, 2963, 2928, 2870, 1713, 1599, 1569, 1491, 1446, 1415, 1335, 1312, 1256, 1237, 1175, 1103, 1018, 963, 910, 835, 763, 728, 691, 644 cm^{-1}; (ESI, *m/z*): 378.19 $[M+H]^+$; HRMS (ESI) calcd. for $C_{27}H_{23}NO$: 378.1852 $[M+H]^+$, found: 378.1852.

3-(4-Methoxyphenyl)-1,4-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10f) and (4-benzoyl-2-phenylpyridin-3-yl)(4-methoxyphenyl)methanone (11f). (*Z*)-1-(4-Methoxyphenyl)-3-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9f**) (133.0 mg, 0.35 mmol), I_2 (355.3 mg, 1.40 mmol) and Cs_2CO_3 (286.7 mg, 0.88 mmol) were employed. Two fractions were isolated. First fraction yielded 26.9 mg (20%) of the indicated product **11f** as a yellow solid (R_f = 0.08 in 4:1 hexane/ethyl acetate; mp 164.1–166.1 °C). Second fraction afforded 29.2 mg (22%) of the indicated product **10f** as a yellow oil (R_f = 0.04 in 4:1 hexane/ethyl acetate).



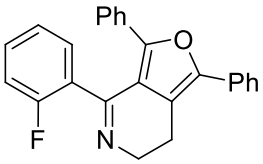
10f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.53 (d, *J* = 7.1 Hz, 2H), 7.51–7.44 (m, 2H), 7.38–7.27 (m, 3H), 7.24–7.11 (m, 3H), 6.62 (d, *J* = 8.9 Hz, 2H), 4.00 (t, *J* = 6.5 Hz, 2 H), 2.97 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (C), 160.0 (C), 145.8 (C), 136.8 (C), 130.5 (C), 130.4 (C), 130.0 (CH), 129.0 (CH), 128.8 (CH), 128.4 (CH), 127.7 (C), 125.2 (CH), 122.2 (CH), 119.3 (C), 114.0 (C), 113.5 (CH), 55.4 (OCH_3), 48.4 (CH_2), 20.4 (CH_2) (Note that two CH peaks overlap on each other); IR (neat):

3054, 2917, 2836, 1737, 1658, 1598, 1503, 1445, 1420, 1395, 1355, 1251, 1175, 1149, 1101, 1074, 1026, 962, 928, 914, 833, 765, 733, 694, 672, 644, 603 cm^{-1}; MS (ESI, *m/z*): 380.17 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{21}NO_2$: 380.1645 $[M+H]^+$, found: 380.1654.



11f: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.94 (d, *J* = 5.0 Hz, 1H), 7.73 (d, *J* = 7.2 Hz, 2H), 7.62–7.48 (m, 3H), 7.47–7.38 (m, 4H), 7.36–7.29 (m, 1H), 7.23–7.13 (m, 3H), 6.94 (t, *J* = 7.5 Hz, 1H), 6.60 (d, *J* = 8.4 Hz, 1H), 3.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5 (CO), 195.1 (CO), 156.4 (C), 155.8 (C), 150.2 (CH), 147.4 (C), 137.1 (C), 135.9 (C), 134.3 (C), 134.0 (C), 132.9 (CH), 131.6 (CH), 130.7 (CH), 130.2 (CH), 129.4 (CH), 128.7 (CH), 127.9 (CH), 120.9 (CH), 110.4 (CH), 54.4 (OCH_3); IR (neat): 3060, 2935, 2837, 1731, 1664, 1597, 1582, 1550, 1494, 1449, 1435, 1392, 1317, 1250, 1178, 1152, 1127, 1090, 1073, 1046, 1022, 1002, 961, 925, 855, 813, 752, 705, 690, 656, 622 cm-^{1}; MS (ESI, *m/z*): 394.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{19}NO_3$: 394.1438 $[M+H]^+$, found: 394.1434.

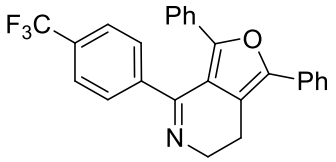
4-(2-Fluorophenyl)-1,3-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10g). (*Z*)-3-(2-Fluorophenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9g**) (124.4 mg, 0.34 mmol), I_2 (345.2 mg, 1.36 mmol) and Cs_2CO_3 (276.9 mg, 0.85 mmol) were employed to afford 23.7 mg (19%) of the indicated product **10g** as a light brown solid (R_f = 0.23 in 4:1 hexane/ethyl acetate; mp 120.9–122.9 °C).



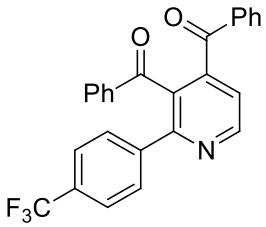
10g: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 7.1 Hz, 2H), 7.40 (d, *J* = 7.3 Hz, 2H), 6.95–7.30 (m, 9H), 6.87 (d, *J* = 7.0 Hz, 1H), 3.90 (t, *J* = 6.19 Hz, 2H), 2.85 (t, *J* = 6.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.0 (d, ^3J = 4.3 Hz, C), 162.0 (d, ^1J = 103.6 Hz, CF), δ 151.5 (C), 146.3 (C), 140.0 (d, ^3J = 7.6 Hz, CH), 130.4 (C), 129.7 (C), 129.5 (d, ^3J = 7.3 Hz, CH), 129.0 (CH), 128.7 (CH), 128.4 (CH), 127.9 (CH), 127.7 (CH), 125.2 (CH), 124.3 (CH), 119.6 (C), 116.5 (d, ^2J = 22.4 Hz, CH), 115.3 (d, ^2J = 22.5 Hz, C), 114.9 (C), 49.3 (CH_2), 20.2 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ -112.82; IR (neat): 3057, 2919, 2849, 1734, 1666, 1568, 1490, 1442, 1325, 1216, 1195, 1066, 1017, 969, 894, 878, 807, 765, 740, 690 cm-^{1}; (ESI, *m/z*): 368.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{18}FNO$: 368.1445 $[M+H]^+$, found: 368.1440.

1,3-Diphenyl-4-(4-(trifluoromethyl)phenyl)-6,7-dihydrofuro[3,4-*c*]pyridine (10h) and (2-(4-(trifluoromethyl)phenyl)pyridine-3,4-diyl)bis(phenylmethanone) (11h). (*Z*)-1-Phenyl-3-((4-phenylbut-3-yn-1-yl)amino)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**9h**) (91.3 mg, 0.22 mmol), I_2 (223.4 mg, 0.88 mmol) and Cs_2CO_3 (179.2 mg, 0.55 mmol) were employed.

Two fractions were isolated. First fraction yielded 24.8 mg (27%) of the indicated product **10h** as a yellow solid (R_f = 0.23 in 4:1 hexane/ethyl acetate; mp 172.5–174.5 °C). Second fraction afforded 20.2 mg (21%) of the indicated product **11h** as a dark brown oil (R_f = 0.20 in 4:1 hexane/ethyl acetate).

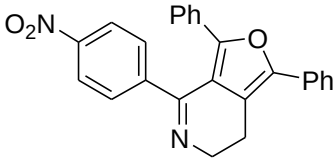


10h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, J = 7.9 Hz, 2H), 7.59 (d, J = 8.0 Hz, 2H), 7.48 (t, J = 7.7 Hz, 2H), 7.42–7.32 (m, 3H), 7.21– 7.14 (m, 3H), 7.11 (d, J = 7.4 Hz, 2H), 4.03 (t, J = 6.6 Hz, 2H), 2.96 (t, J = 6.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (C), 152.2 (C), 146.5 (C), 140.8 (C), 131.7 (q, ^2J = 32.4 Hz, C), 130.4 (C), 129.3 (C), 129.2 (q, ^3J = 20.9 Hz, CH), 129.0 (CH), 129.1 (q, ^4J = 3.8 Hz, CH), 129.0 (CH), 128.5 (CH), 128.0 (CH), 126.1 (q, ^1J = 237.1 Hz, CF_3), 125.3 (CH), 125.1 (CH), 119.3 (C), 114.9 (C), 49.2 (CH_2), 20.2 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.79; IR (neat): 3058, 2970, 2909, 2854, 1667, 1618, 1563, 1488, 1446, 1407, 1320, 1157, 1117, 1064, 1015, 923, 846, 762, 728, 687 cm^{-1}; (ESI, *m/z*): 418.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{18}F_3NO$: 418.1413 $[M+H]^+$, found: 418.1406.



11h: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (d, J = 4.9 Hz, 1H), 7.62 (d, J = 7.1 Hz, 2H), 7.45 (d, J = 8.4 Hz, 2H), 7.36 (d, J = 7.1 Hz, 2H), 7.33–7.25 (m, 4H), 7.21 (t, J = 7.5 Hz, 2H), 7.08–7.02 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6 (CO), 194.9 (CO), 156.5 (C), 150.2 (CH), 147.8 (C), 142.3 (C), 137.0 (C), 135.5 (C), 134.4 (CH), 134.3 (C), 133.8 (CH), 130.9 (q, ^2J = 32.6 Hz, C), 130.4 (CH), 129.7 (CH), 129.4 (CH), 128.8 (CH), 128.6 (CH), 126.6 (q, ^1J = 271.2 Hz, CF_3), 125.3 (q, ^3J = 3.4 Hz, CH), 121.6 (CH); ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.84; IR (neat): 3059, 2924, 2851, 1734, 1661, 1619, 1596, 1580, 1552, 1491, 1449, 1410, 1320, 1260, 1164, 1110, 1063, 1016, 961, 926, 845, 783, 760, 705, 690, 658, 604 cm^{-1}; MS (ESI, *m/z*): 432.12 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{16}F_3NO_2$: 432.1206 $[M+H]^+$, found: 432.1210.

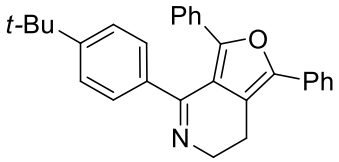
4-(4-Nitrophenyl)-1,3-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10i). (*Z*)-3-(4-Nitrophenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9i**) (70.0 mg, 0.18 mmol), I_2 (182.7 mg, 0.72 mmol) and Cs_2CO_3 (146.6 mg, 0.45 mmol) were employed to afford 8.5 mg (12%) of the indicated product **10i** as an orange solid (R_f = 0.12 in 4:1 hexane/ethyl acetate; mp 211.3–213.3 °C).



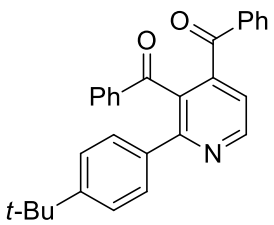
10i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.6 Hz, 2H), 7.72 (d, J = 7.6 Hz, 4H), 7.49 (t, J = 7.7 Hz, 2H), 7.38 (t, J = 7.4 Hz, 1H), 7.24-7.07 (m, 5H), 4.08 (t, J = 6.6 Hz, 2H), 3.03 (t, J = 6.6

Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1 (C), 148.9 (C), 147.1 (C), 130.8 (C), 130.0 (CH), 129.9 (C), 129.6 (CH), 129.1 (CH), 128.8 (CH), 128.6 (CH), 128.3 (CH), 128.1 (C), 126.7 (C), 125.4 (CH), 123.5 (CH), 118.4 (C), 114.6 (C), 48.5 (CH_2), 20.1 (CH_2); IR (neat): 3036, 2928, 2903, 2849, 2380, 2287, 1911, 1893, 1730, 1628, 1598, 1565, 1515, 1491, 1447, 1409, 1346, 1319, 1158, 1103, 1065, 1029, 1014, 960, 922, 906, 864, 843, 764, 727, 691, 650, 612 cm^{-1}; MS (ESI, *m/z*): 395.14 $[M+H]^+$; HRMS (ESI) calcd. for $C_{25}H_{18}N_2O_3$:395.1390 $[M+H]^+$, found: 395.1384.

4-(4-(*tert*-Butyl)phenyl)-1,3-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10j) and (2-(4-(*tert*-Butyl)phenyl)pyridine-3,4-diyl)bis(phenylmethanone) (11j). (*Z*)-3-(4-(*tert*-Butyl)phenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9j**) (195.5 mg, 0.48 mmol), I_2 (487.3 mg, 1.92 mmol) and Cs_2CO_3 (391.0 mg, 1.20 mmol) were employed. Two fractions were isolated. First fraction yielded 24.2 mg (12%) of the indicated product **11j** as a brown oil (R_f = 0.25 in 4:1 hexane/ethyl acetate). Second fraction afforded 50.6 mg (26%) of the indicated product **10j** as a yellow oil (R_f = 0.14 in 4:1 hexane/ethyl acetate).



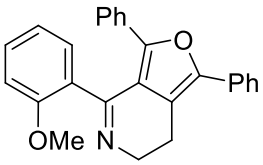
10j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.52 (t, *J* = 7.7 Hz, 2H), 7.46–7.39 (m, 2H), 7.33 (d, *J* = 8.3 Hz, 1H), 7.21–7.09 (m, 5H), 4.16 (t, *J* = 6.5 Hz, 2H), 3.20 (t, *J* = 6.4 Hz, 2H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.8 (C), 154.2 (C), 153.7 (C), 146.4 (C), 132.9 (C), 130.2 (C), 129.3 (C), 129.0 (CH), 128.7 (CH), 128.6 (CH), 128.5 (CH), 127.9 (CH), 127.8 (CH), 125.3 (CH), 125.2 (CH), 118.9 (C), 115.2 (C), 47.8 (CH_2), 34.8 (C), 31.2 (CH_3), 20.3 (CH_2); IR (neat): 3056, 2960, 2904, 2865, 1714, 1603, 1556, 1491, 1446, 1395, 1356, 1338, 1268, 1156, 1107, 1072, 1025, 965, 909, 865, 836, 765, 721, 691 cm^{-1}; (ESI, m/z): 406.22 $[M+H]^+$; HRMS (ESI) calcd. for $C_{29}H_{27}NO$:406.2165 $[M+H]^+$, found: 406.2157.



11j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 4.9 Hz, 1H), 7.81 (d, *J* = 7.2 Hz, 2H), 7.63–7.57 (m, 2H), 7.53 (d, *J* = 7.2 Hz, 2H), 7.49–7.36 (m, 4H), 7.37–7.29 (m, 2H), 7.24–7.13 (m, 3H), 1.20 (s, 9H); IR (neat): 3058, 2961, 2903, 2867, 1718, 1659, 1596, 1579, 1548, 1392, 1317, 1259, 1069, 1016, 926, 838, 807, 792, 703, 670 cm^{-1}; MS (ESI, m/z): 420.20 $[M+H]^+$; HRMS (ESI) calcd. for $C_{29}H_{25}NO_2$:420.1958 $[M+H]^+$, found: 420.1955.

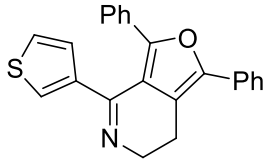
4-(2-Methoxyphenyl)-1,3-diphenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10k). (*Z*)-3-(2-Methoxyphenyl)-1-phenyl-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9k**) (114.9 mg,

0.30 mmol), I_2 (304.6 mg, 1.20 mmol) and Cs_2CO_3 (244.4 mg, 0.75 mmol) were employed to afford 62.6 mg (55%) of the indicated product **10k** as a red solid (R_f = 0.05 in 4:1 hexane/ethyl acetate; mp 77.0–79.0 °C).

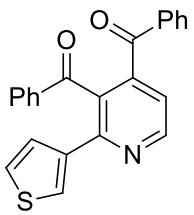


10k: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.7 Hz, 2H), 7.58–7.50 (m, 3H), 7.45–7.38 (m, 3H), 7.32 (d, *J* = 7.4 Hz, 2H), 7.25–7.16 (m, 2H), 6.97 (d, *J* = 8.5 Hz, 1H), 6.72 (d, *J* = 8.0 Hz, 1H), 4.27 (br s, 2H), 3.92 (s, 3H), 3.37 (t, *J* = 6.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4 (C), 162.5 (C), 158.7 (C), 148.9 (C), 137.1 (C), 133.7 (C), 131.2 (CH), 129.3 (CH), 129.2 (CH), 129.1 (CH), 128.7 (CH), 128.4 (CH), 127.4 (CH), 125.9 (CH), 121.4 (CH), 116.0 (C), 114.8 (C), 113.9 (C), 112.4 (CH), 57.1 (OCH_3), 44.9 (CH_2), 20.2 (CH_2); IR (neat): 3476, 3421, 3052, 2929, 2834, 1595, 1554, 1487, 1430, 1336, 1246, 1154, 1013, 909, 863, 749, 689 cm^{-1}; MS (ESI, m/z): 380.16 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{21}NO_2$: 380.1645 $[M+H]^+$, found: 380.1649.

1,3-Diphenyl-4-(thiophen-3-yl)-6,7-dihydrofuro[3,4-*c*]pyridine (10l) and (2-(thiophen-3-yl)pyridine-3,4-diyl)bis(phenylmethanone) (11l). (*Z*)-1-Phenyl-3-((4-phenylbut-3-yn-1-yl)amino)-3-(thiophen-3-yl)prop-2-en-1-one (**9l**) (108.0 mg, 0.30 mmol), I_2 (304.6 mg, 1.20 mmol) and Cs_2CO_3 (244.4 mg, 0.75 mmol) were employed. Two fractions were isolated. First fraction yielded 12.2 mg (11%) of the indicated product **11l** as a brown oil (R_f = 0.20 in 4:1 hexane/ethyl acetate). Second fraction afforded 39.9 mg (34%) of the indicated product **10l** as a brown solid (R_f = 0.09 in 4:1 hexane/ethyl acetate; mp 126.0–128.0 °C).



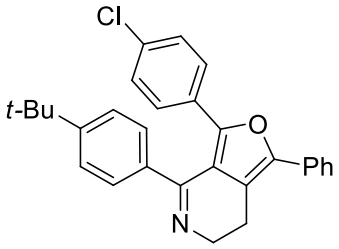
10l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.58 (m, 2H), 7.40 (d, *J* = 6.8 Hz, 2H), 7.32–7.00 (m, 8H), 3.90 (t, *J* = 6.03 Hz, 2H), 2.88 (t, *J* = 6.1 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3 (C), 152.5 (C), 146.4 (C), 138.7 (C), 130.3 (C), 129.6 (C), 129.0 (CH), 128.8 (CH), 128.6 (CH), 128.4 (CH), 128.1 (CH), 127.9 (CH), 127.7 (CH), 125.6 (CH), 125.3 (CH), 119.4 (C), 115.7 (C), 48.2 (CH_2), 20.3 (CH_2); IR (neat): 3052, 2926, 2846, 1566, 1489, 1444, 1421, 1319, 1226, 1067, 1016, 968, 930, 901, 837, 797, 767, 765, 689 cm^{-1}; (ESI, m/z): 356.11 $[M+H]^+$; HRMS (ESI) calcd. for $C_{23}H_{17}NOS$: 356.1104 $[M+H]^+$, found: 356.1098.



11l: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (d, *J* = 5.0 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 2H), 7.65 (d, *J* = 7.4 Hz, 2H), 7.57–7.53 (m, 1H), 7.52–7.45 (m, 3H), 7.42 (d, *J* = 5.0 Hz, 1H), 7.37 (d, *J* = 5.0 Hz, 1H), 7.34–7.26 (m, 3H), 7.24–7.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.9 (CO), 194.9 (CO), 152.3 (C), 149.4 (C), 147.9 (C), 137.0 (C), 135.6 (C), 134.3 (C), 133.7 (CH), 133.6 (CH), 130.5 (CH),

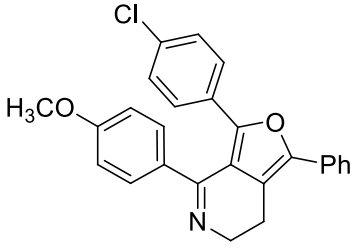
129.4 (CH), 129.1 (CH), 128.8 (CH), 128.6 (CH), 128.2 (CH), 127.8 (CH), 126.4 (CH), 120.9 (CH); IR (neat): 3057, 2921, 2852, 1727, 1658, 1594, 1547, 1423, 1374, 1351, 1314, 1257, 1176, 1149, 1071, 1023, 1000, 978, 927, 848, 795, 777, 706, 685, 642; MS (APCI, *m/z*): 370.09 $[M+H]^+$; HRMS (APCI) calcd. for $C_{23}H_{15}NO_2S$: 370.0896 $[M+H]^+$, found: 370.0896.

4-(4-(*tert*-Butyl)phenyl)-3-(4-chlorophenyl)-1-phenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10m). (*Z*)-3-(4-(*tert*-Butyl)phenyl)-1-(4-chlorophenyl)-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9m**) (100.1 mg, 0.23 mmol), I_2 (233.5 mg, 0.92 mmol) and Cs_2CO_3 (189.0 mg, 0.58 mmol) were employed to afford 12.1 mg (12%) of the indicated product **10m** as a yellow solid (R_f = 0.14 in 4:1 hexane/ethyl acetate; mp 158.5–160.5 °C).



10m: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.3 Hz, 2H), 7.55–7.43 (m, 2H), 7.35 (d, *J* = 8.0 Hz, 3H), 7.22–6.98 (m, 6H), 3.97 (t, *J* = 6.5 Hz, 2H), 2.94 (t, *J* = 6.5 Hz, 2H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.4 (C), 153.5 (C), 150.5 (C), 146.3 (C), 134.6 (C), 134.2 (C), 130.4 (C), 129.5 (CH), 129.0 (CH), 128.2 (CH), 127.9 (CH), 127.8 (CH), 125.22 (CH), 125.18 (CH), 119.8 (C), 115.9 (C), 49.0 (CH_2), 34.8 (C), 31.3 (CH_3), 20.3 (CH_2) (Note that one CH peak and one C peak overlap on each other); IR (neat): 3053, 2955, 2931, 2903, 2868, 2849, 1990, 1666, 1603, 1554, 1482, 1461, 1413, 1395, 1358, 1329, 1266, 1228, 1178, 1122, 1087, 1067, 1011, 962, 921, 908, 830, 763, 738, 689, 666, 655, 631 cm^{-1}; MS (ESI, *m/z*): 440.18 $[M+H]^+$; HRMS (ESI) calcd. for $C_{29}H_{26}ClNO$: 440.1776 $[M+H]^+$, found: 440.1770.

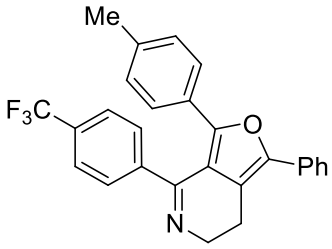
3-(4-Chlorophenyl)-4-(4-methoxyphenyl)-1-phenyl-6,7-dihydrofuro[3,4-*c*]pyridine (10n). (*Z*)-1-(4-Chlorophenyl)-3-(4-methoxyphenyl)-3-((4-phenylbut-3-yn-1-yl)amino)prop-2-en-1-one (**9n**) (103.5 mg, 0.25 mmol), I_2 (253.8 mg, 1.00 mmol) and Cs_2CO_3 (205.3 mg, 0.63 mmol) were employed to afford 12.4 mg (12%) of the indicated product **10n** as a light brown oil (R_f = 0.05 in 4:1 hexane/ethyl acetate).



10n: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.6 Hz, 2H), 7.50 (dd, *J* = 17.5, 8.3 Hz, 4H), 7.42–7.33 (m, 1H), 7.16 (dd, *J* = 28.0, 8.6 Hz, 4H), 6.73 (d, *J* = 8.7 Hz, 2H), 3.98 (t, *J* = 6.4 Hz, 2H), 3.78 (s, 3H), 2.99 (t, *J* = 6.3 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6 (C), 162.6 (C), 153.3 (C), 147.2 (C), 147.2 (C), 135.2 (C), 131.1 (CH), 129.8 (CH), 129.1 (CH), 128.4 (CH), 128.3 (C), 127.6 (C), 125.4 (CH), 118.9 (C), 115.2 (C), 114.1 (CH), 55.7 (OCH_3), 47.4 (CH_2), 20.4 (CH_2) (Note that two CH

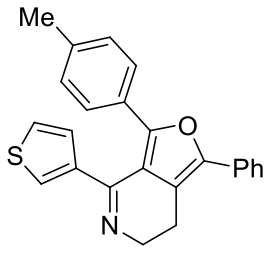
peaks overlap on each other); IR (neat): 3055, 2930, 2837, 1721, 1658, 1597, 1511, 1446, 1419, 1354, 1335, 1305, 1249, 1171, 1089, 1025, 962, 924, 907, 831, 763, 730, 709, 690, 605 cm^{-1}; MS (ESI, *m/z*): 414.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{26}H_{20}ClNO_2$: 414.1255 $[M+H]^+$, found: 414.1252.

1-Phenyl-3-(*p*-tolyl)-4-(4-(trifluoromethyl)phenyl)-6,7-dihydrofuro[3,4-*c*]pyridine (10o). (*Z*)-3-((4-Phenylbut-3-yn-1-yl)amino)-1-(*p*-tolyl)-3-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (**9o**) (96.0 mg, 0.22 mmol), I_2 (223.4 mg, 0.88 mmol) and Cs_2CO_3 (179.2 mg, 0.55 mmol) were employed to afford 10.5 mg (11%) of the indicated product **10o** as a yellow solid (R_f = 0.23 in 4:1 hexane/ethyl acetate; mp 194.0–196.0 °C).



10o: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.0 Hz, 2H), 7.51 (d, *J* = 7.6 Hz, 2H), 7.40 (d, *J* = 6.4 Hz, 2H), 7.33 (d, *J* = 7.5 Hz, 2H), 7.30–7.24 (m, 1H), 7.01–6.94 (m, 2H), 6.83 (d, *J* = 7.0 Hz, 2H), 3.94 (t, *J* = 6.4 Hz, 2H), 2.88 (t, *J* = 6.4 Hz, 2H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (C), 151.8 (C), 146.0 (C), 141.4 (C), 139.0 (C), 131.3 (q, ^2J = 32.3 Hz, C), 130.5 (C), 129.0 (CH), 128.8 (CH), 128.7 (CH), 128.3 (CH), 127.7 (C), 126.6 (CH), 125.2 (CH), 125.0 (q, ^3J = 3.4 Hz, CH), 124.1 (q, ^1J = 191.6 Hz, CF_3), 119.3 (C), 114.6 (C), 49.5 (CH_2), 21.3 (CH_3), 20.3 (CH_2); ^{19}F NMR (282 MHz, $CDCl_3$) δ -62.72; IR (neat): 3036, 2923, 2850, 1611, 1567, 1493, 1446, 1407, 1322, 1265, 1166, 1109, 1065, 1016, 924, 909, 839, 819, 763, 690 cm^{-1}; MS (ESI, *m/z*): 432.16 $[M+H]^+$; HRMS (ESI) calcd. for $C_{27}H_{20}F_3NO$: 432.1570 $[M+H]^+$, found: 432.1565.

1-Phenyl-4-(thiophen-3-yl)-3-(*p*-tolyl)-6,7-dihydrofuro[3,4-*c*]pyridine (10p). (*Z*)-3-((4-Phenylbut-3-yn-1-yl)amino)-3-(thiophen-3-yl)-1-(*p*-tolyl)prop-2-en-1-one (**9p**) (64.0 mg, 0.17 mmol), I_2 (172.6 mg, 0.68 mmol) and Cs_2CO_3 (140.1 mg, 0.43 mmol) were employed to afford 15.7 mg (25%) of the indicated product **10p** as a red oil (R_f = 0.09 in 4:1 hexane/ethyl acetate).



10p: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.50–7.40 (m, 2H), 7.38–7.30 (m, 2H), 7.19–7.14 (m, 3H), 6.99 (d, *J* = 7.8 Hz, 2H), 4.01 (br s, 2H), 3.08 (t, *J* = 5.5 Hz, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.2 (C), 149.9 (C), 148.0 (C), 141.4 (CH), 136.0 (C), 130.8 (C), 130.4 (C), 129.5 (CH), 129.3 (CH), 129.0 (CH), 128.7 (C), 128.5 (CH), 127.5 (CH), 125.7 (CH), 125.3 (CH), 116.3 (C), 113.8 (C), 43.9 (CH_2), 21.7 (CH_3), 20.2 (CH_2); IR (neat): 3056, 3034, 2917, 2851, 1715, 1632, 1602, 1493, 1445, 1419, 1349, 1306, 1238, 1177, 1147, 1106, 1071, 1034, 1019, 972, 922, 877, 838, 820,

763, 744, 714, 691, 627 cm^{-1}; MS (ESI, *m/z*): 370.13 $[M+H]^+$; HRMS (ESI) calcd. for $C_{24}H_{19}NOS$: 370.1260 $[M+H]^+$, found: 370.1260.

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

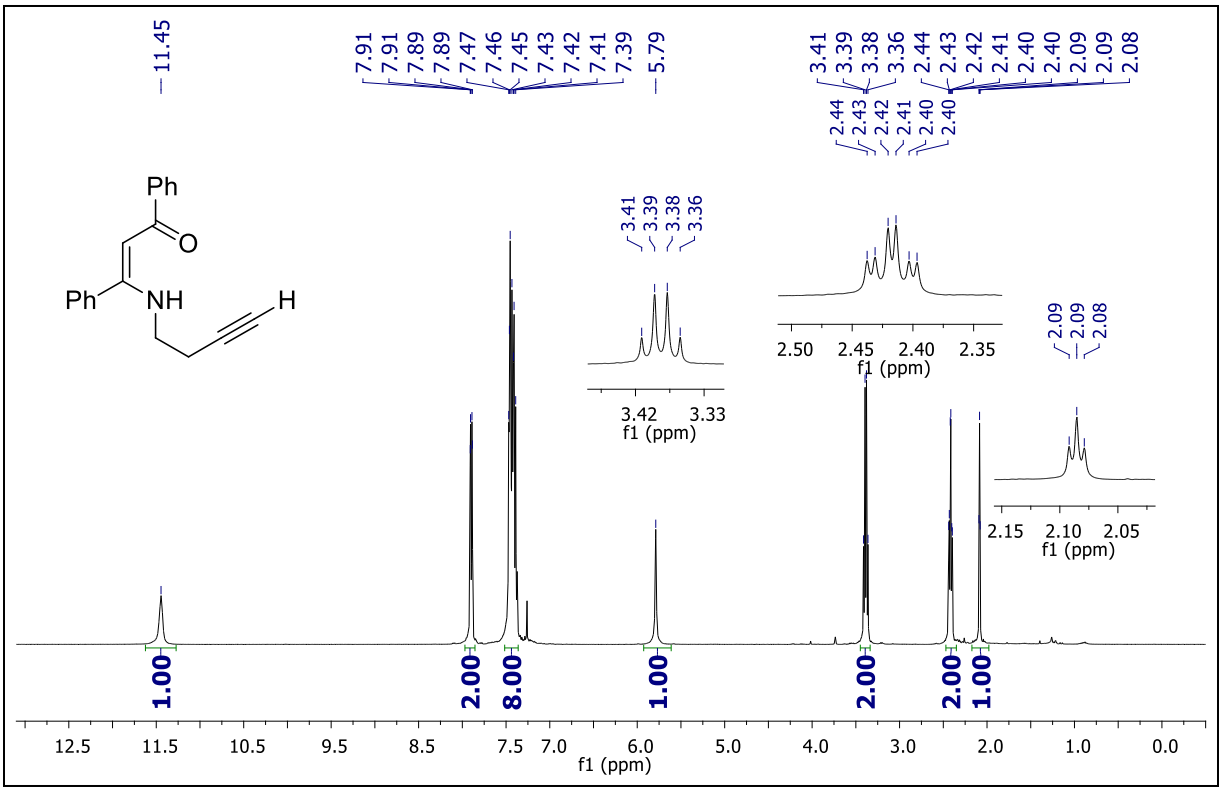


Figure S1. ^{1}H NMR Spectrum of compound **14a**.

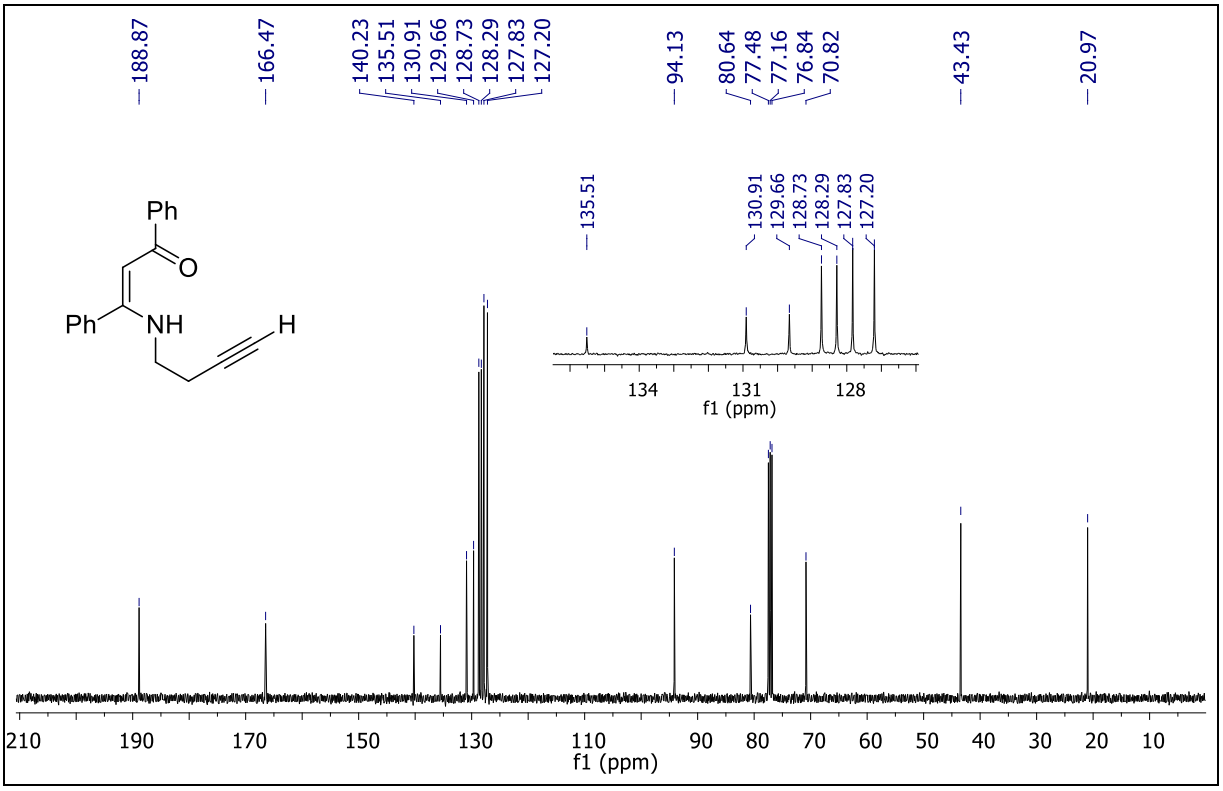


Figure S2. ^{13}C NMR Spectrum of compound **14a**.

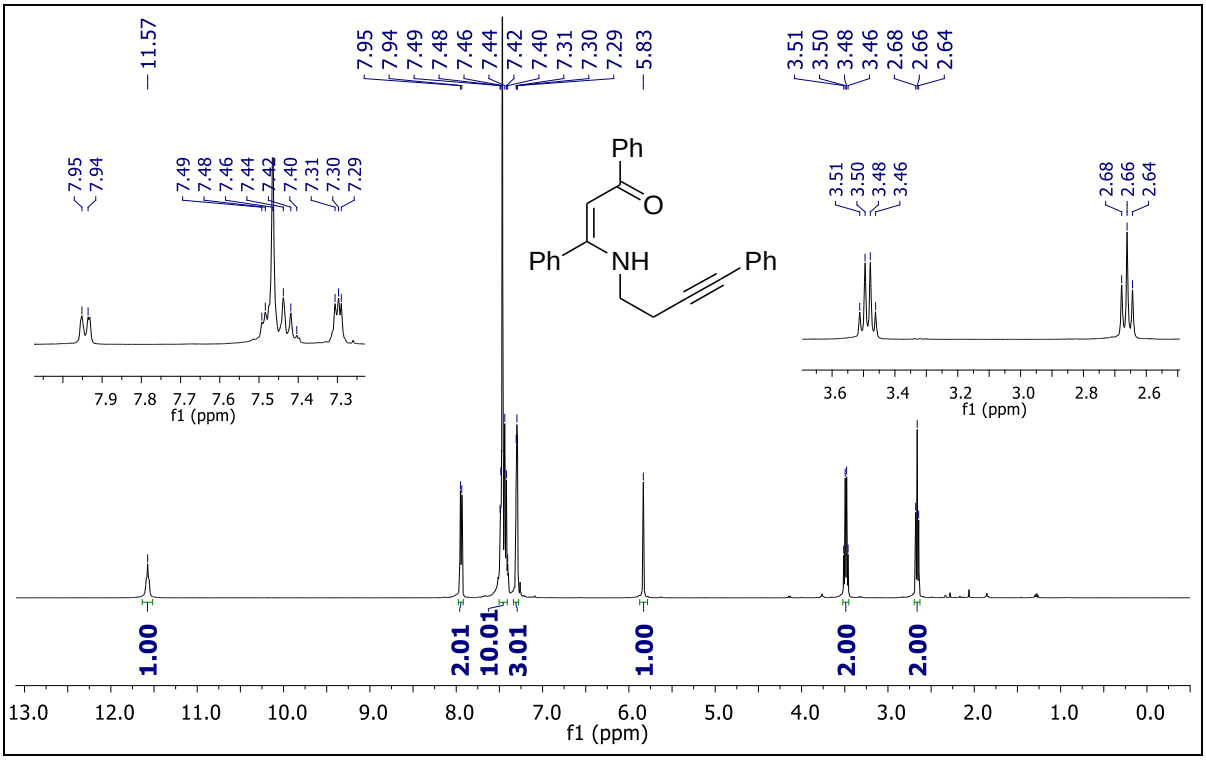


Figure S3. ^{1}H NMR Spectrum of compound **9a**.

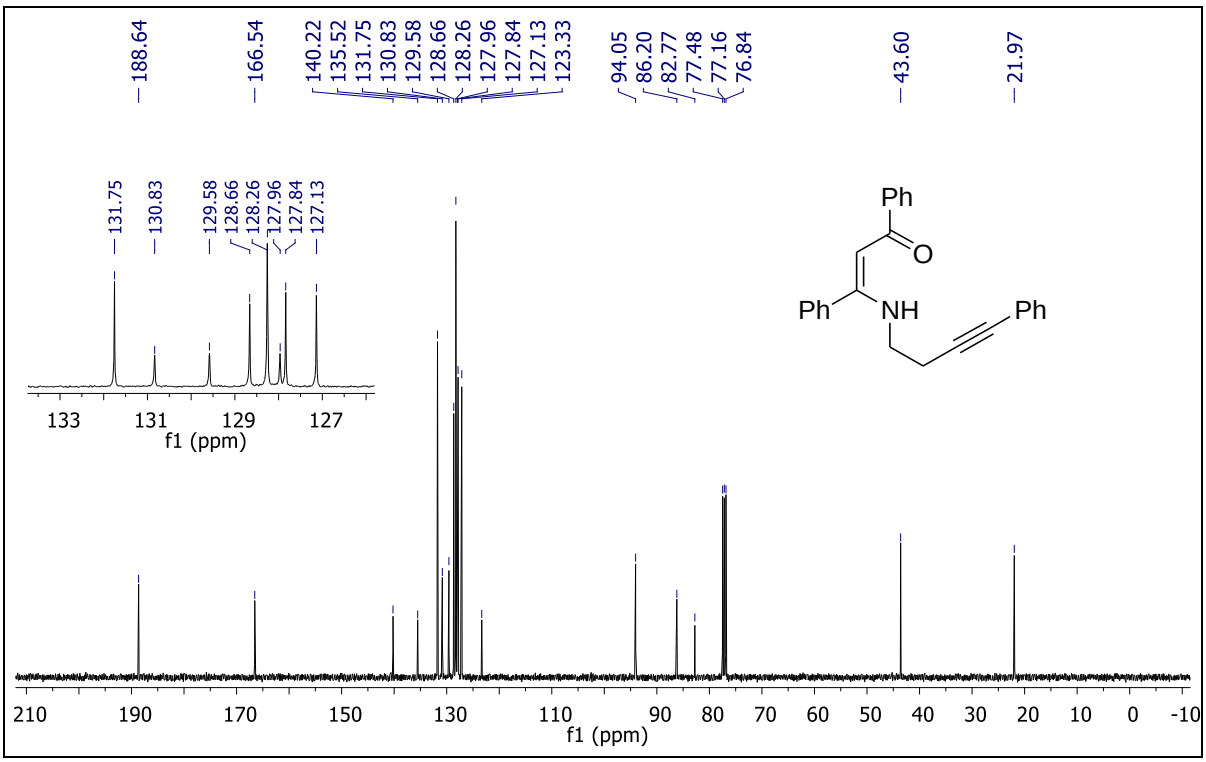


Figure S4. ^{13}C NMR Spectrum of compound **9a**.

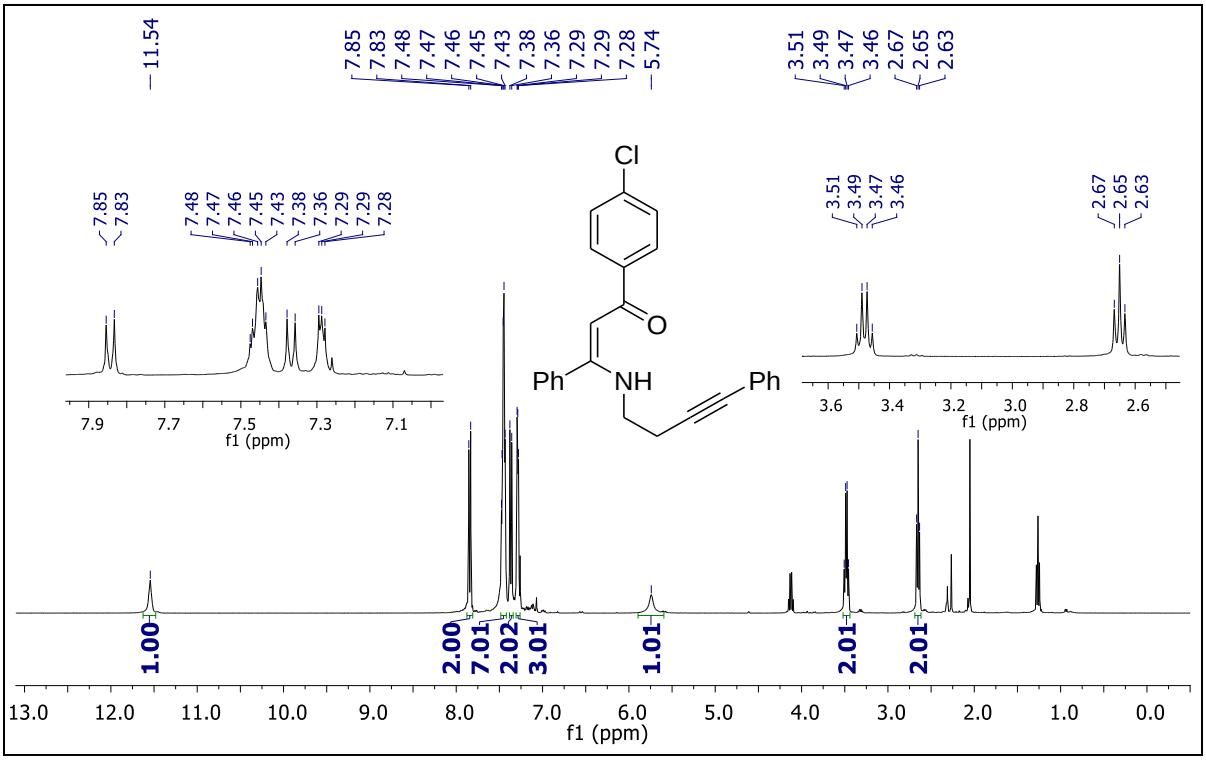


Figure S5. ^{1}H NMR Spectrum of compound **9b**.

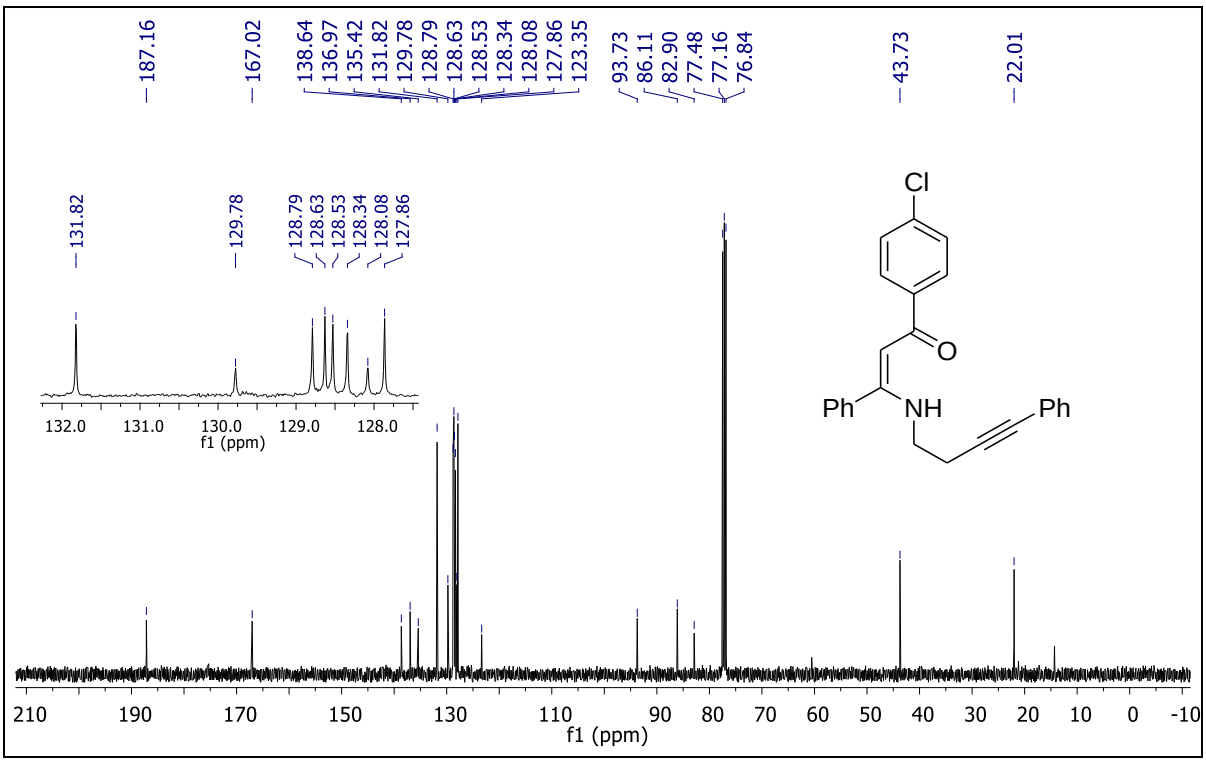


Figure S6. ^{13}C NMR Spectrum of compound **9b**.

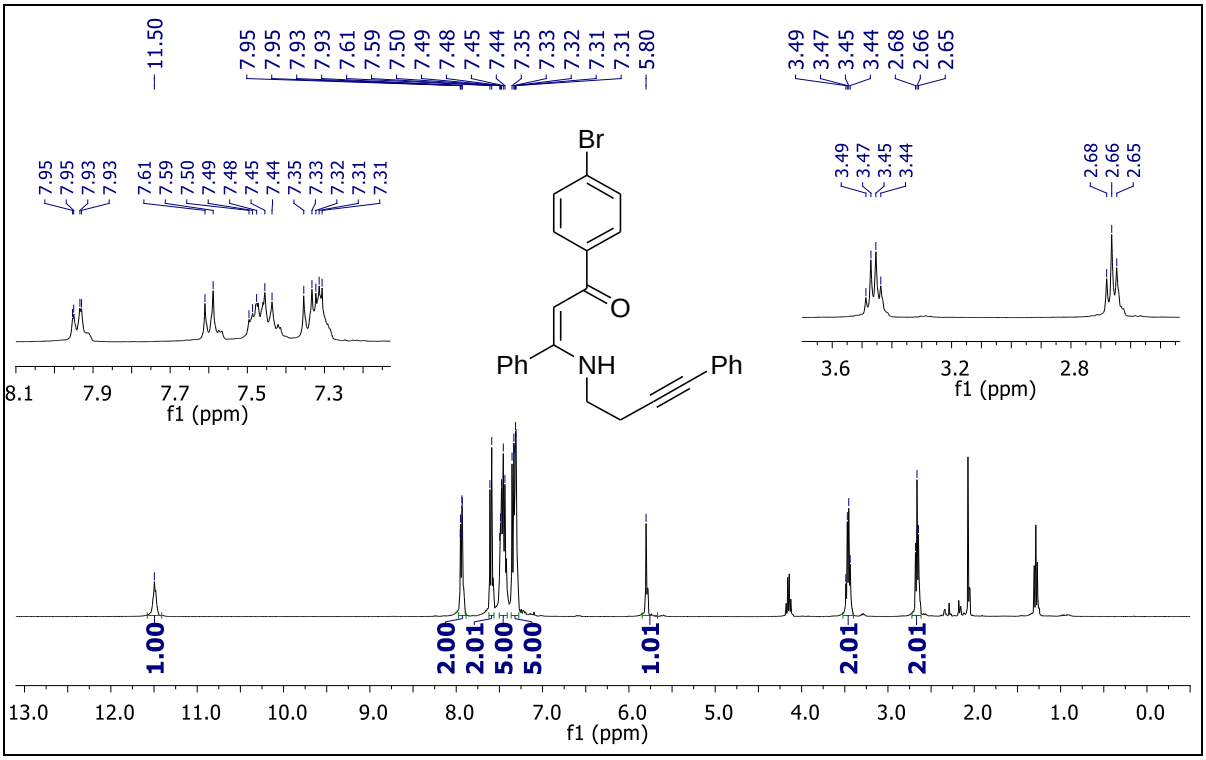


Figure S7. ^{1}H NMR Spectrum of compound **9c**.

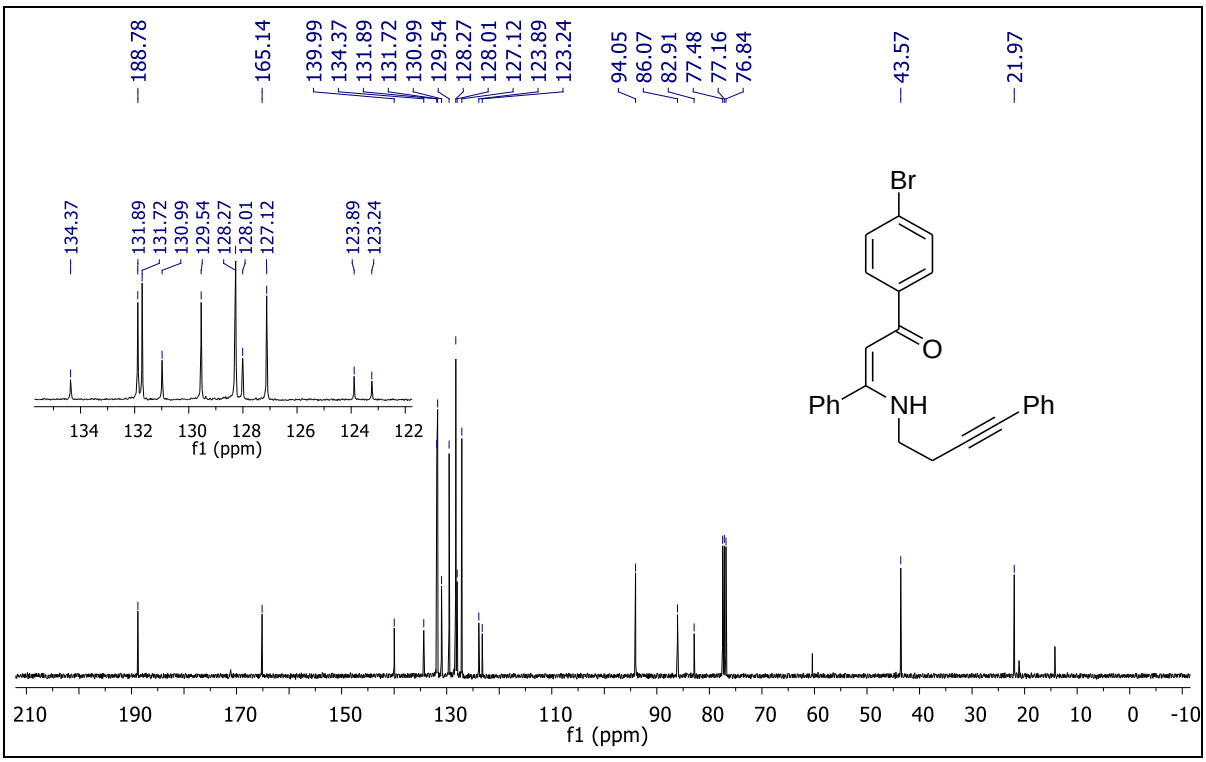


Figure S8. ^{13}C NMR Spectrum of compound **9c**.

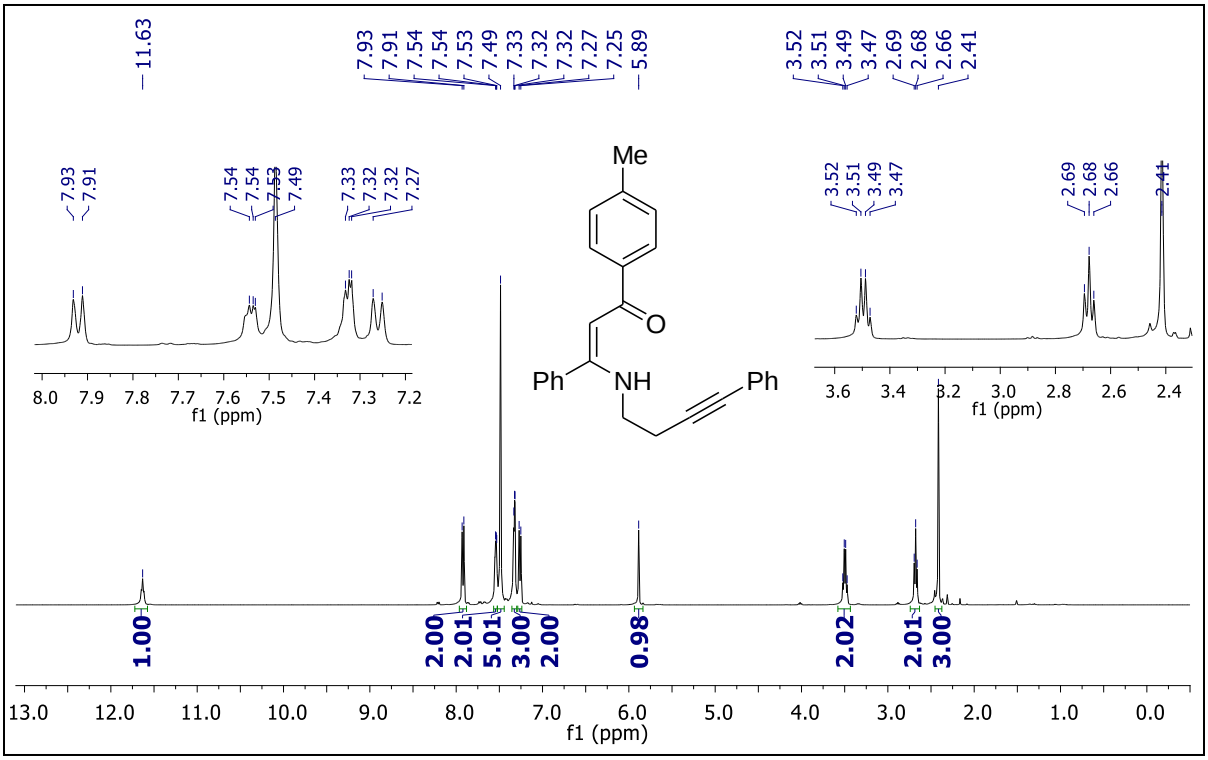


Figure S9. ^{1}H NMR Spectrum of compound **9d**.

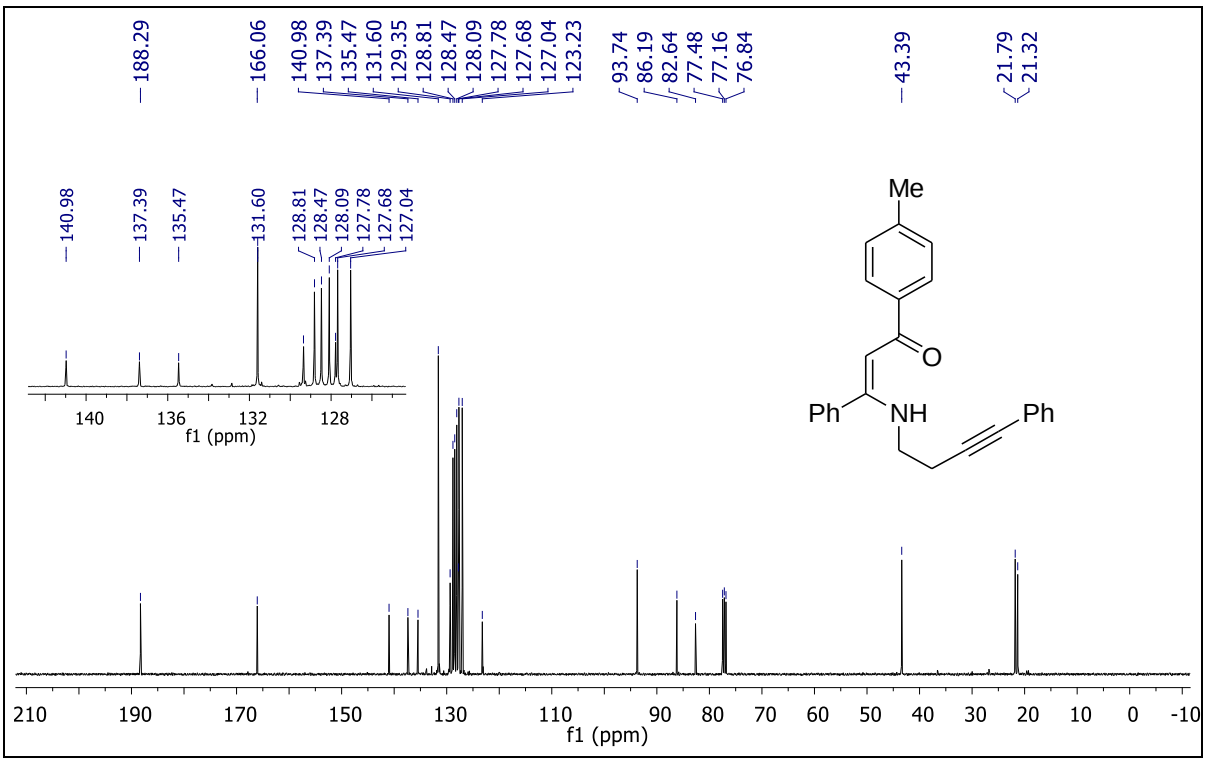


Figure S10. ^{13}C NMR Spectrum of compound **9d**.

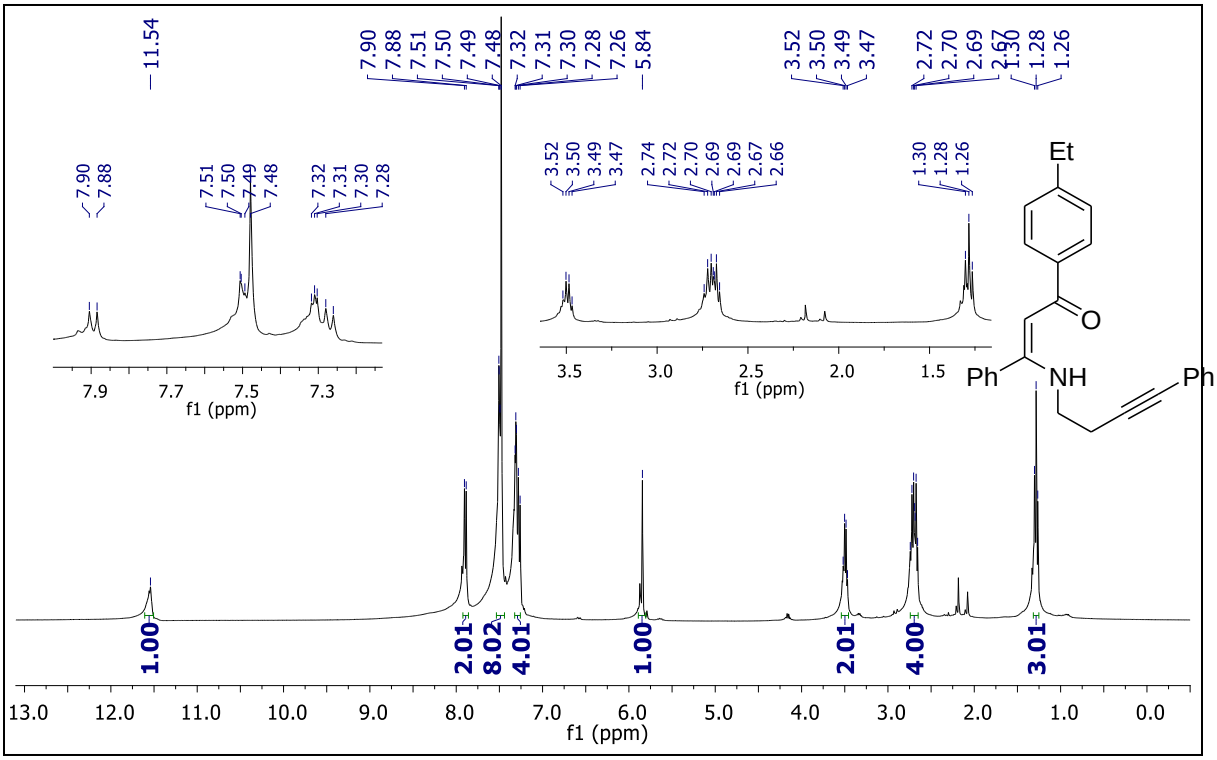


Figure S11. ^{1}H NMR Spectrum of compound **9e**.

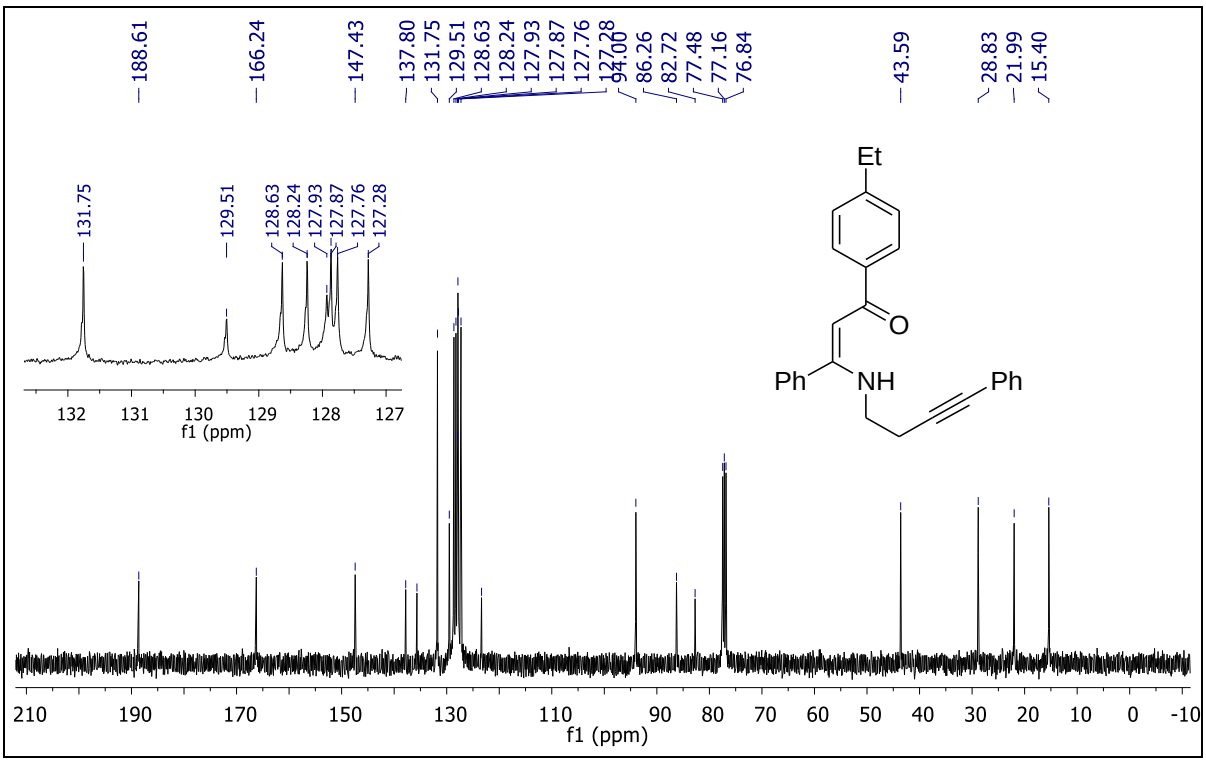


Figure S12. ^{13}C NMR Spectrum of compound **9e**.

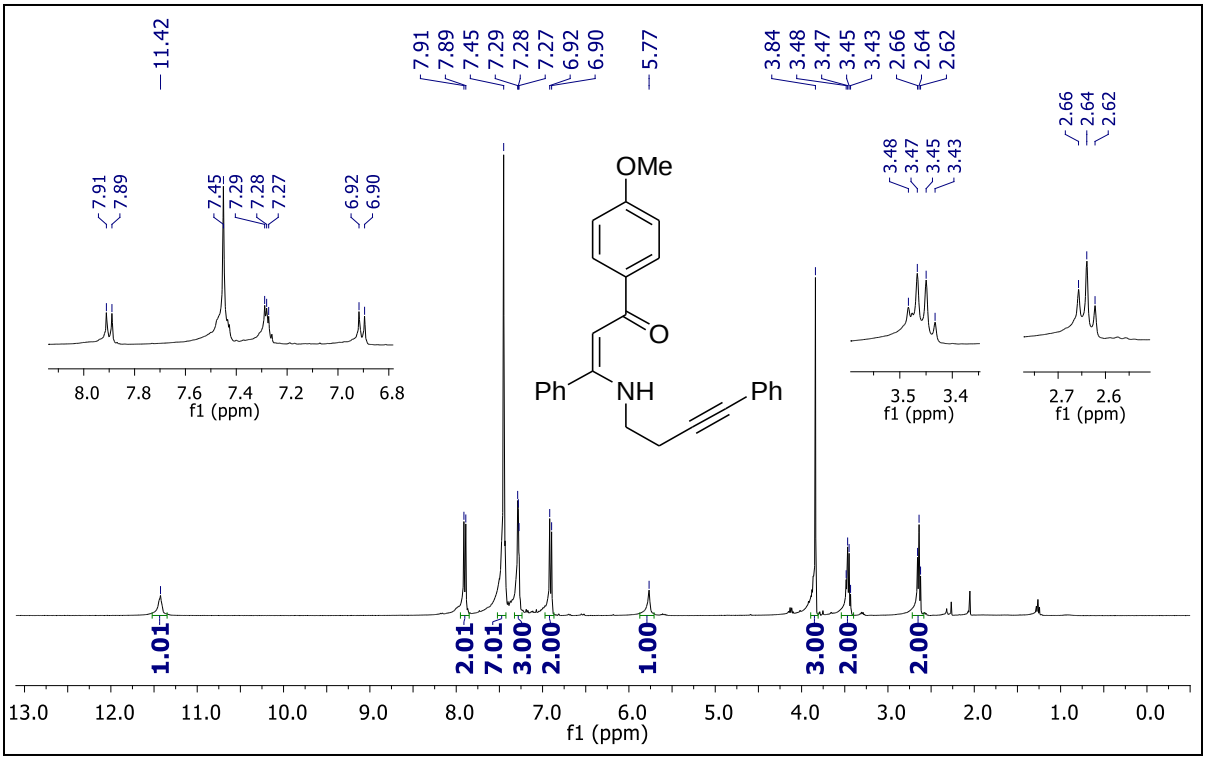


Figure S13. ^{1}H NMR Spectrum of compound **9f**.

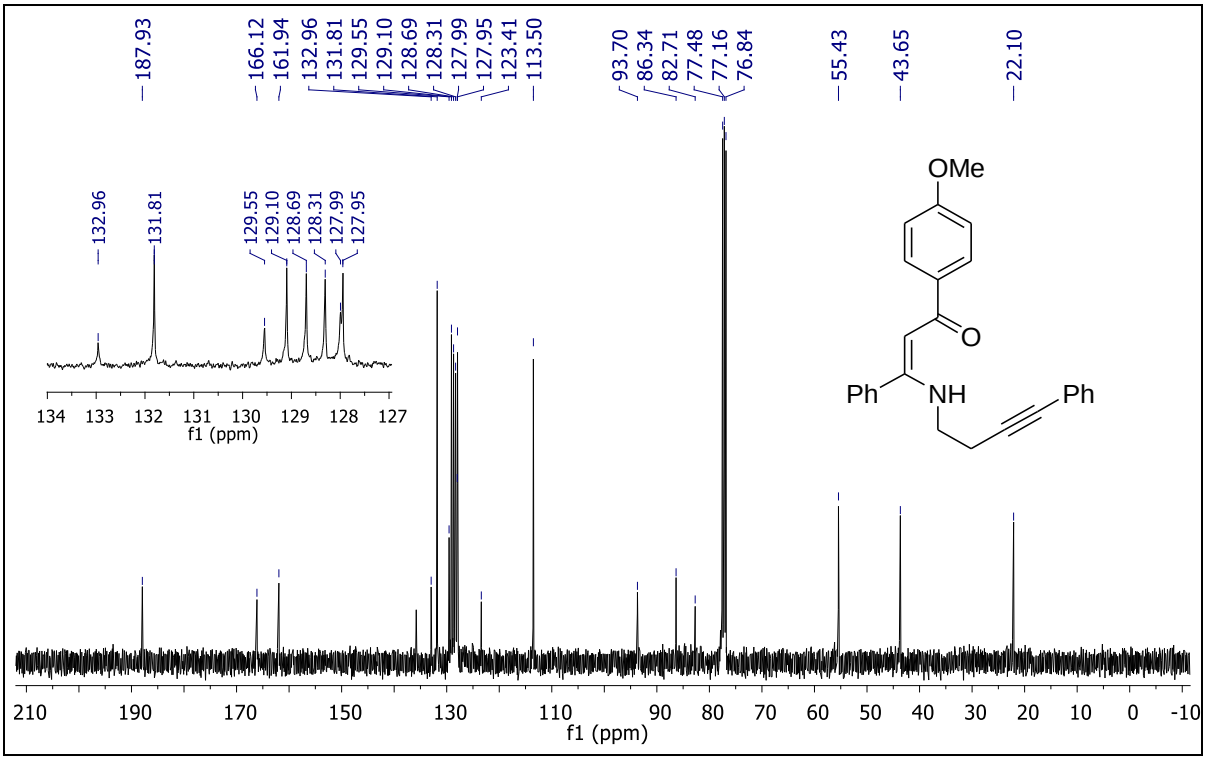


Figure S14. ^{13}C NMR Spectrum of compound **9f**.

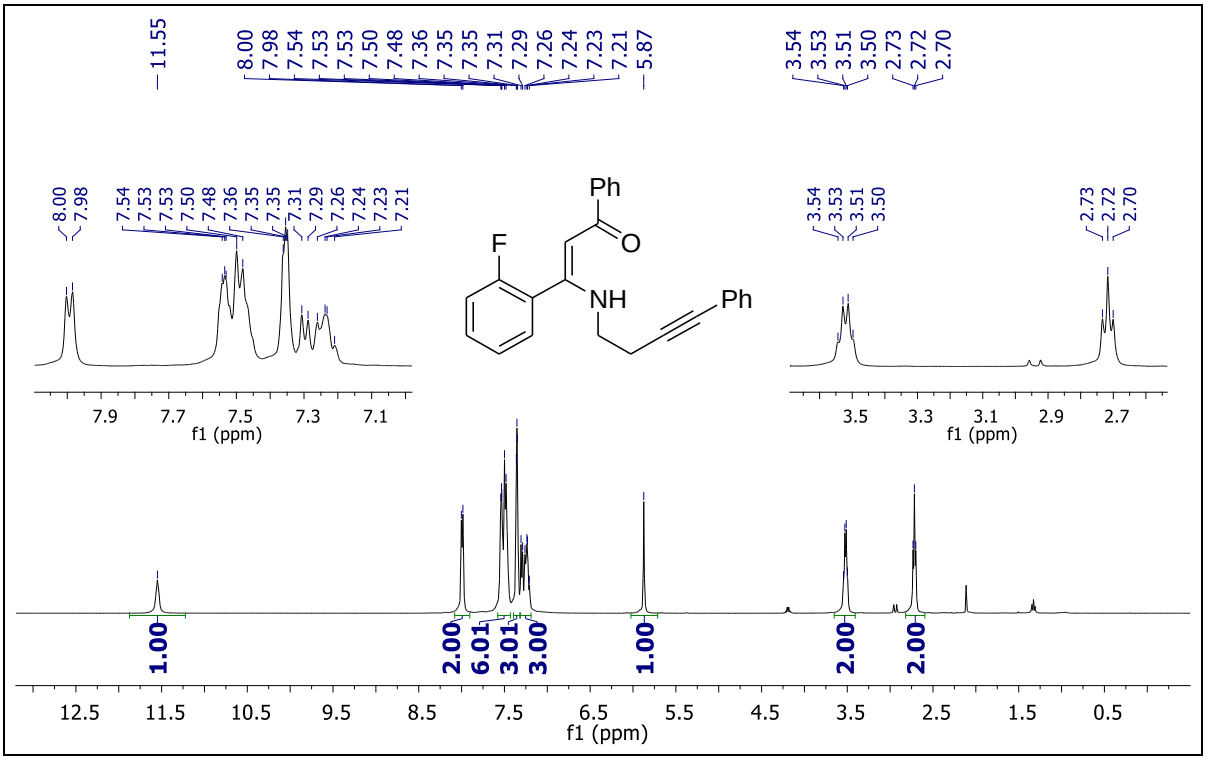


Figure S15. ^{1}H NMR Spectrum of compound **9g**.

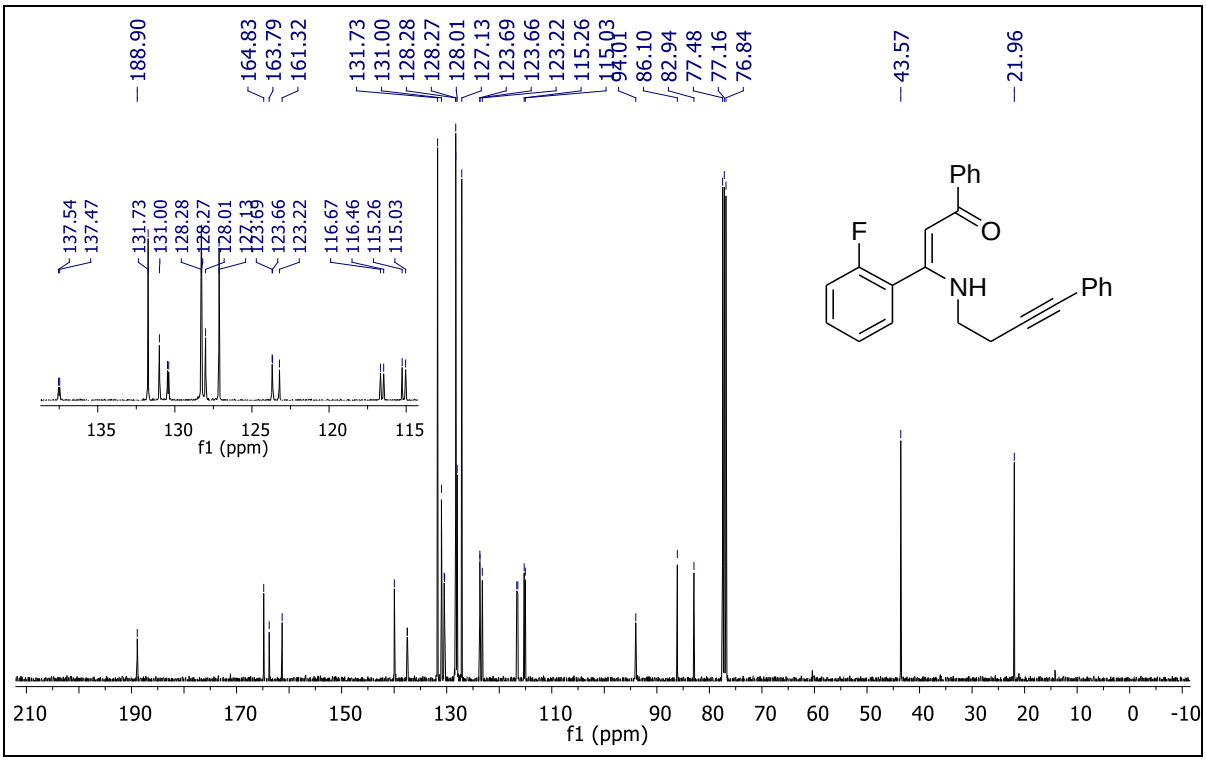


Figure S16. ^{13}C NMR Spectrum of compound **9g**.

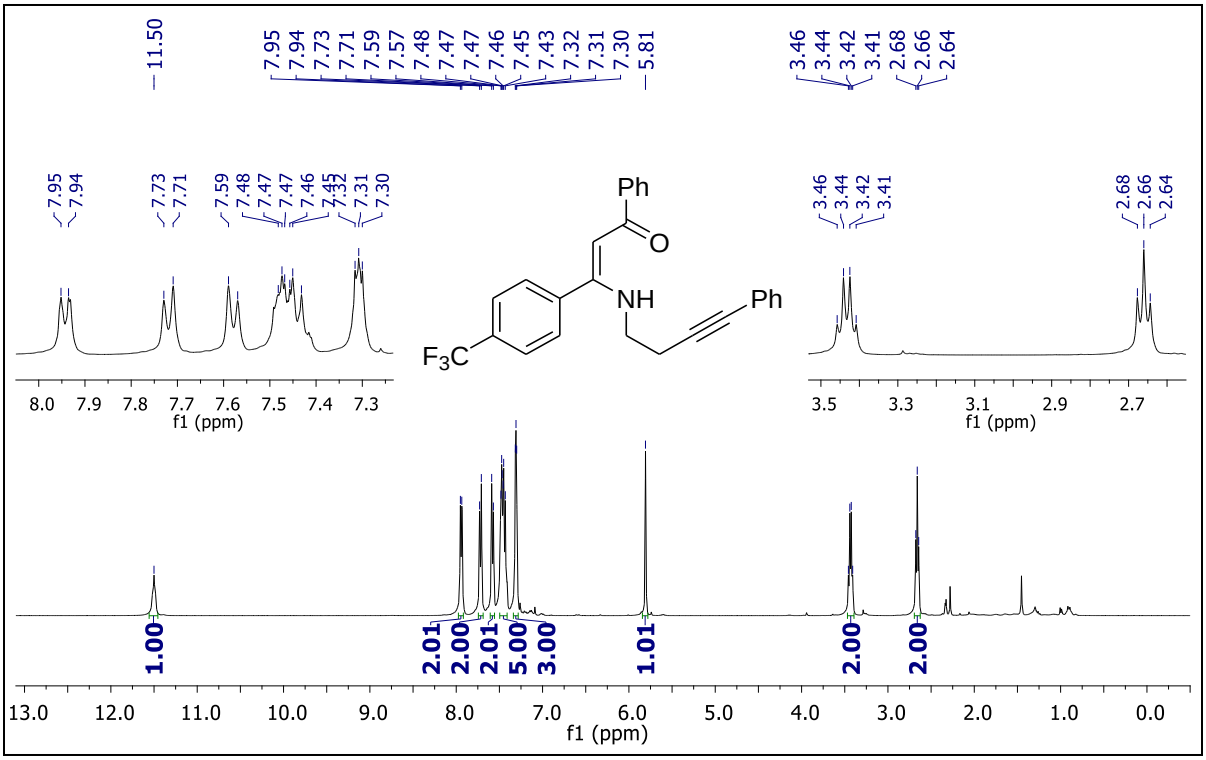


Figure S17. ^{1}H NMR Spectrum of compound **9h**.

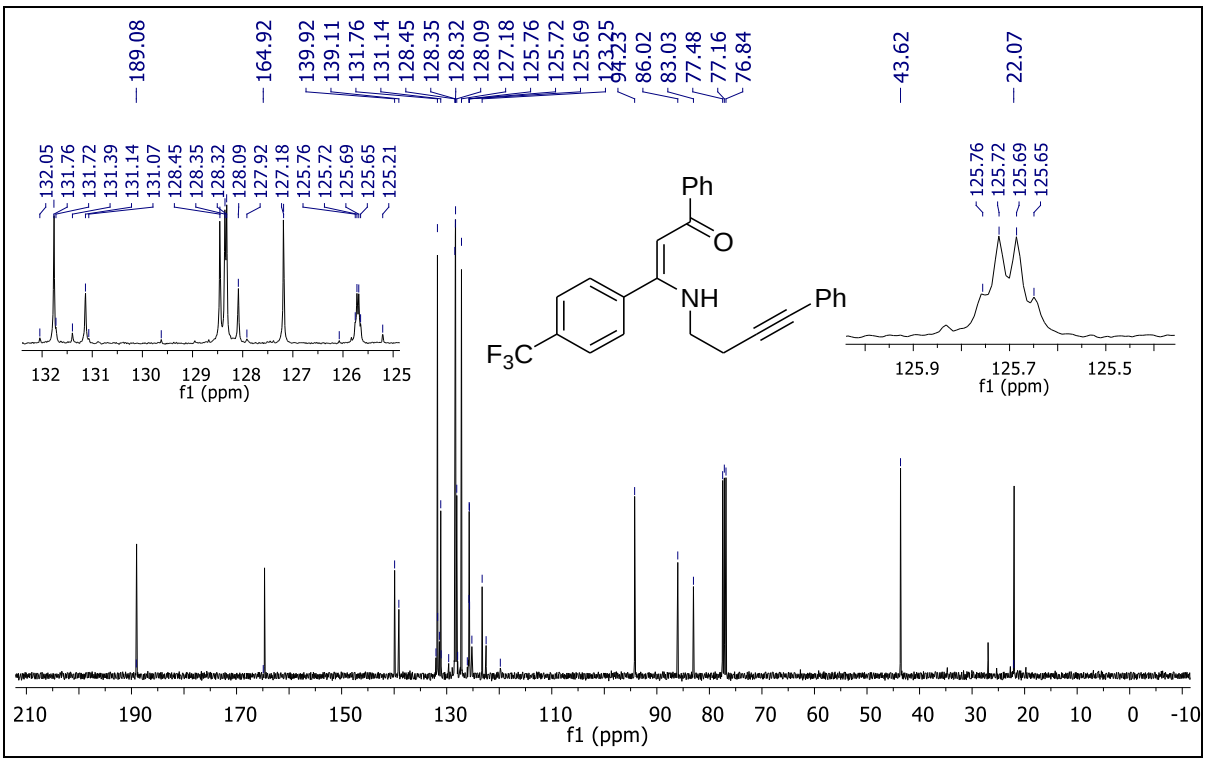


Figure S18. ^{13}C NMR Spectrum of compound **9h**.

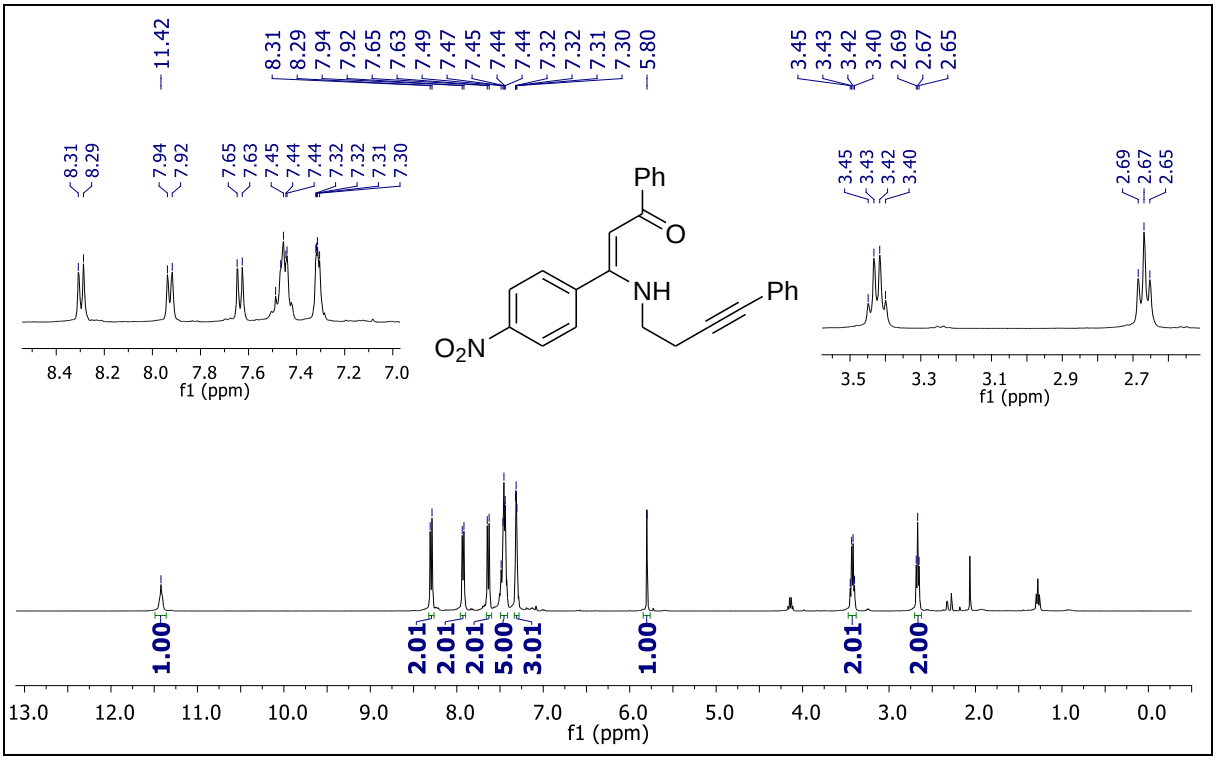


Figure S19. ^{1}H NMR Spectrum of compound **9i**.

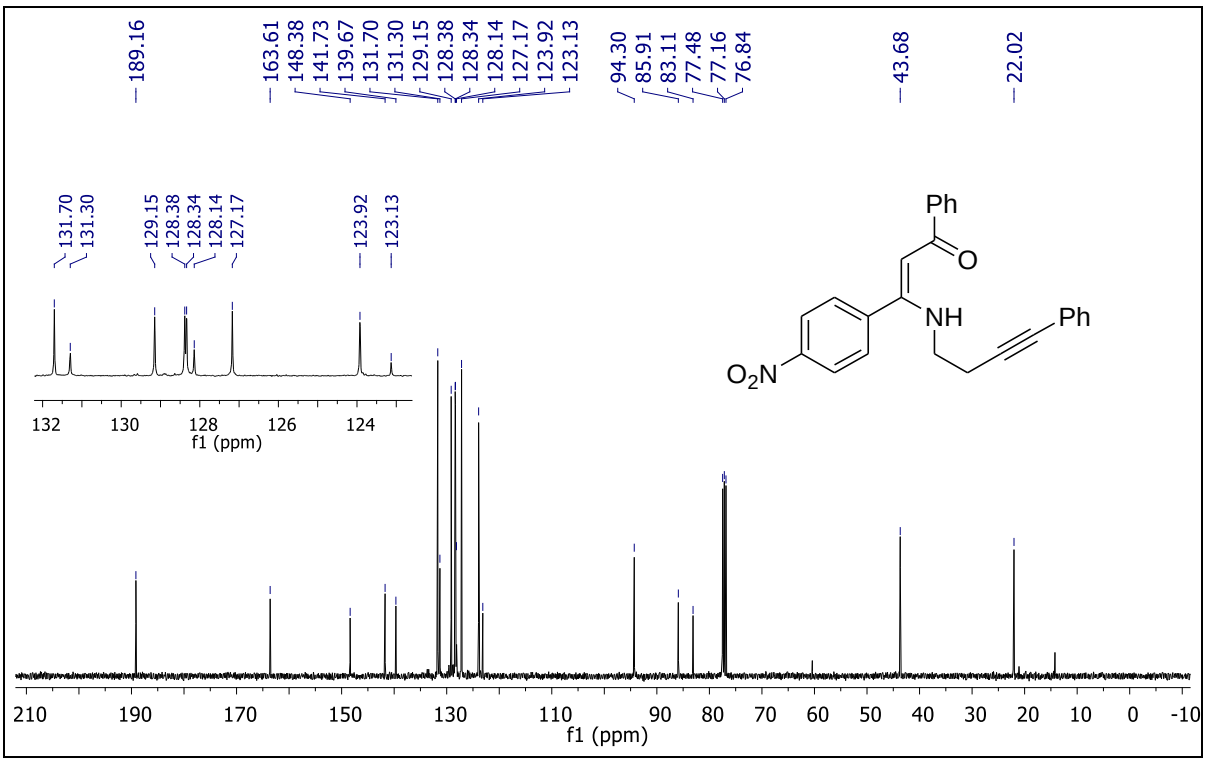


Figure S20. ^{13}C NMR Spectrum of compound **9i**.

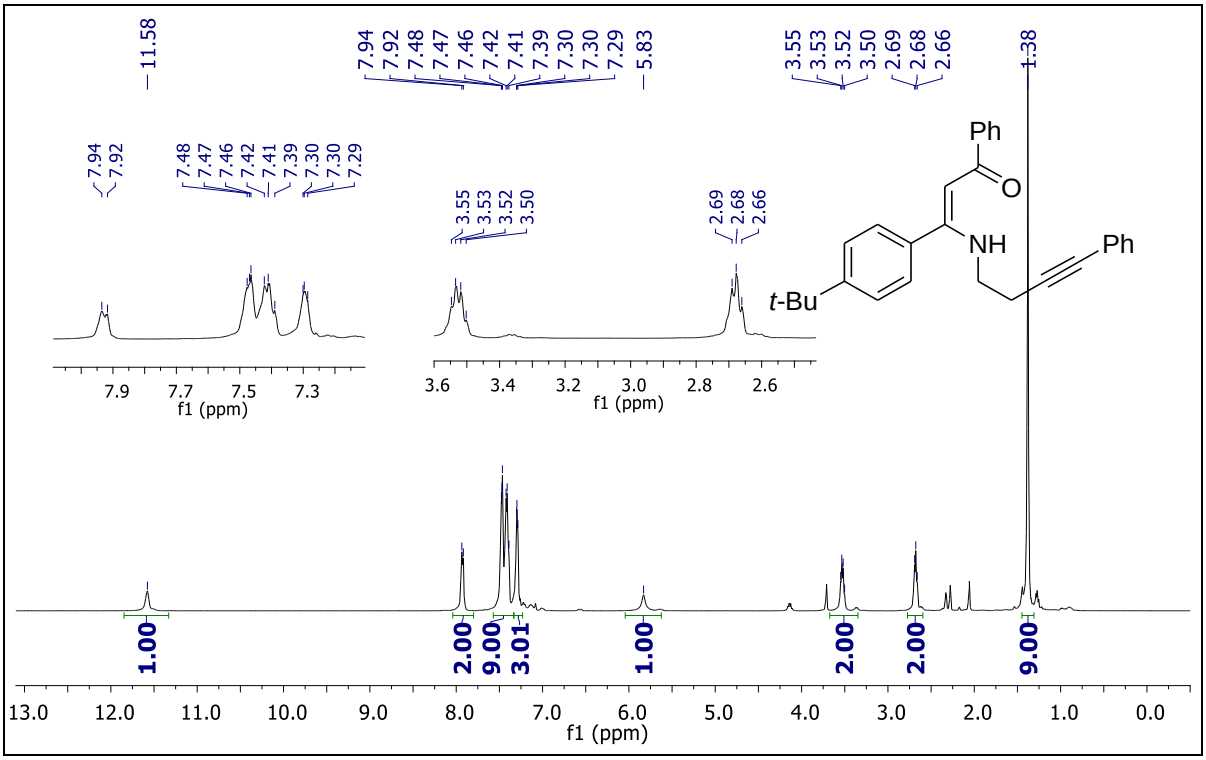


Figure S21. ^{1}H NMR Spectrum of compound **9j**.

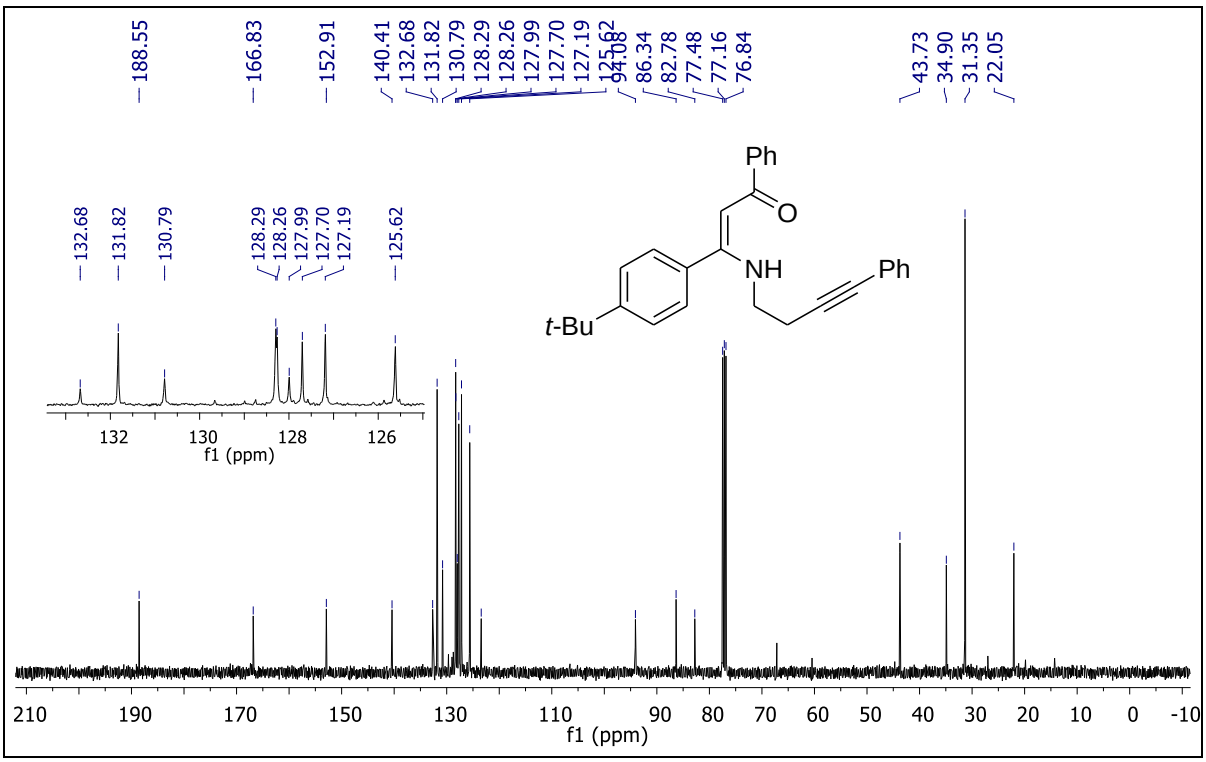


Figure S22. ^{13}C NMR Spectrum of compound **9j**.

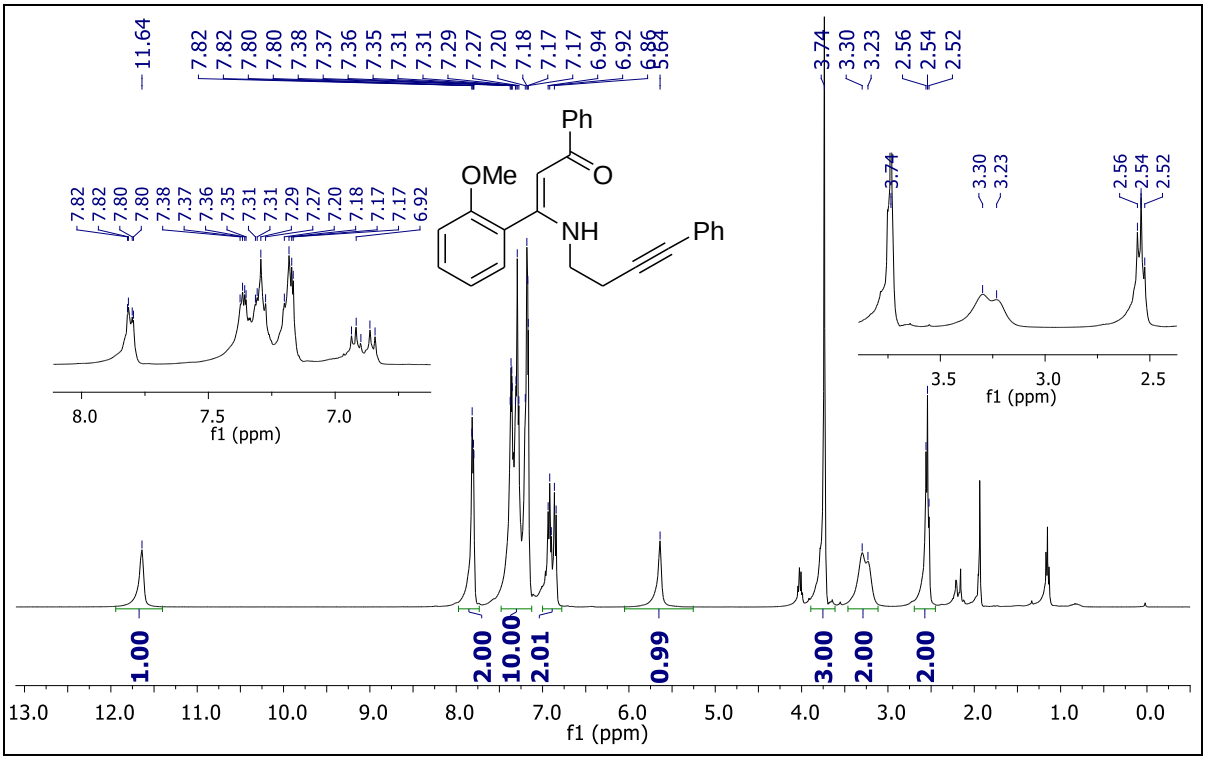


Figure S23. ^{1}H NMR Spectrum of compound **9k**.

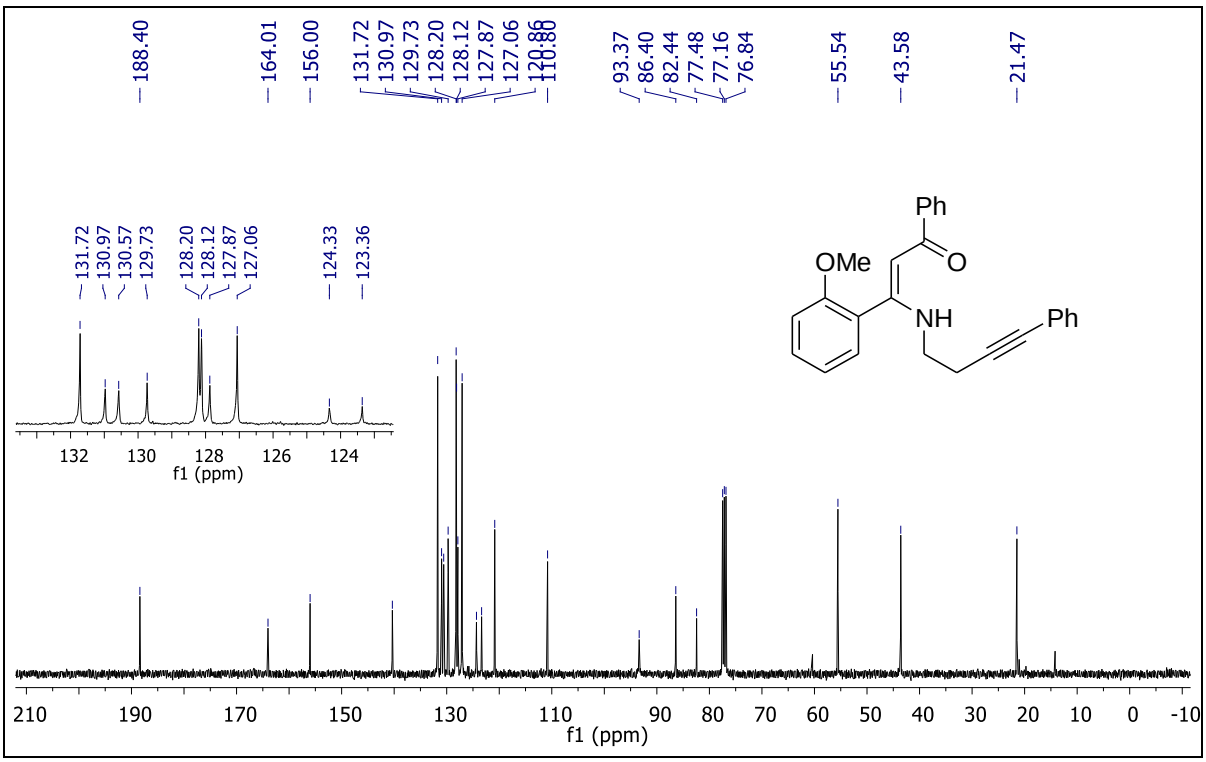


Figure S24. ^{13}C NMR Spectrum of compound **9k**.

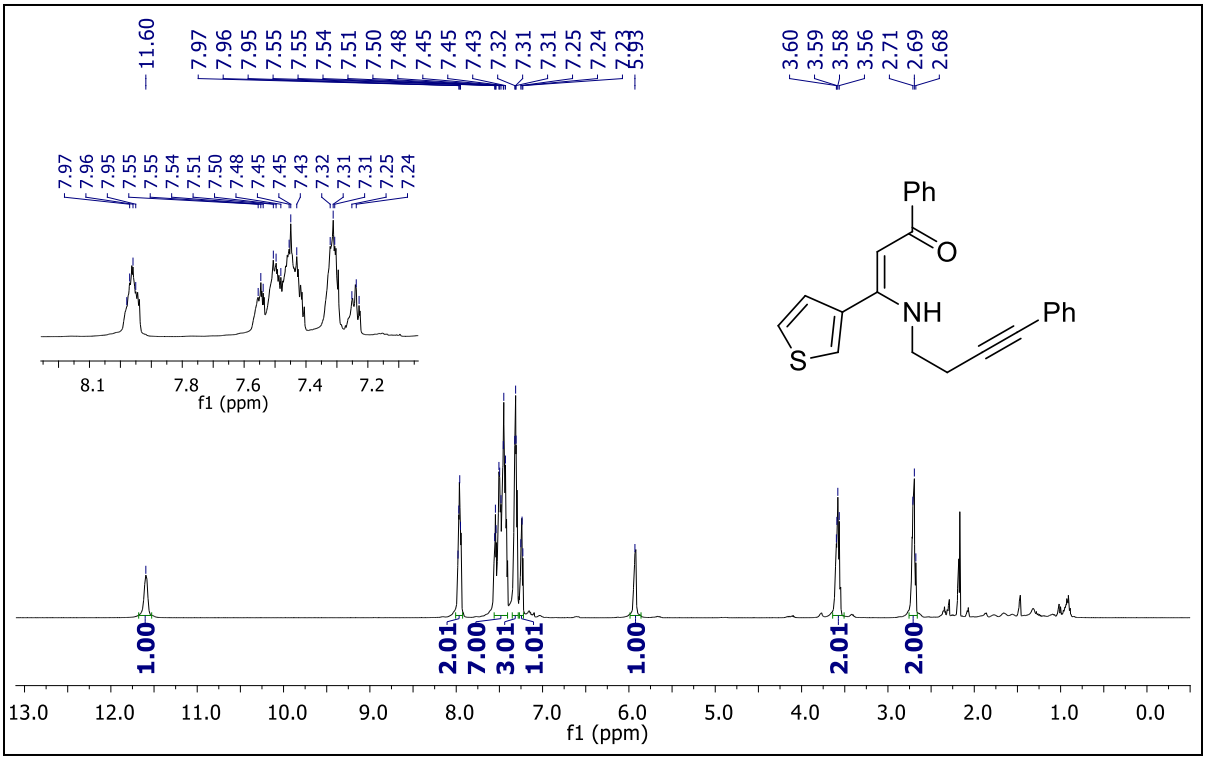


Figure S25. ^{1}H NMR Spectrum of compound **9l**.

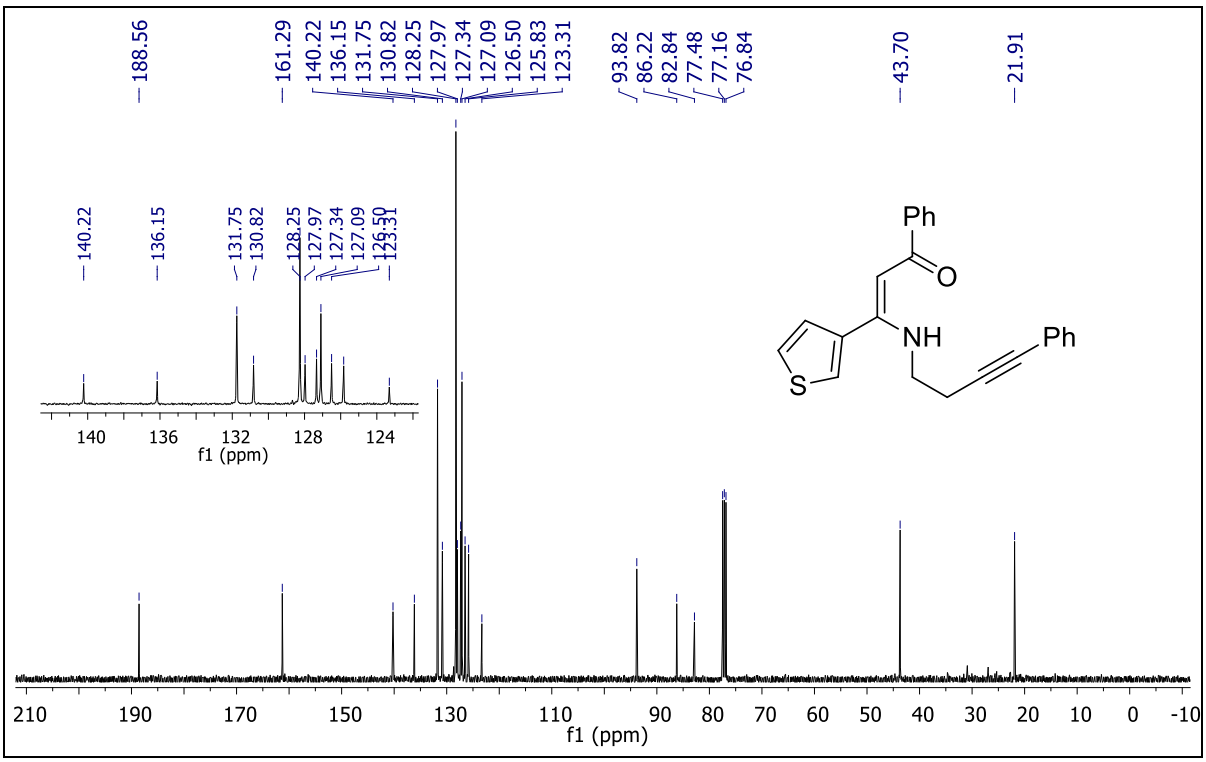


Figure S26. ^{13}C NMR Spectrum of compound **9l**.

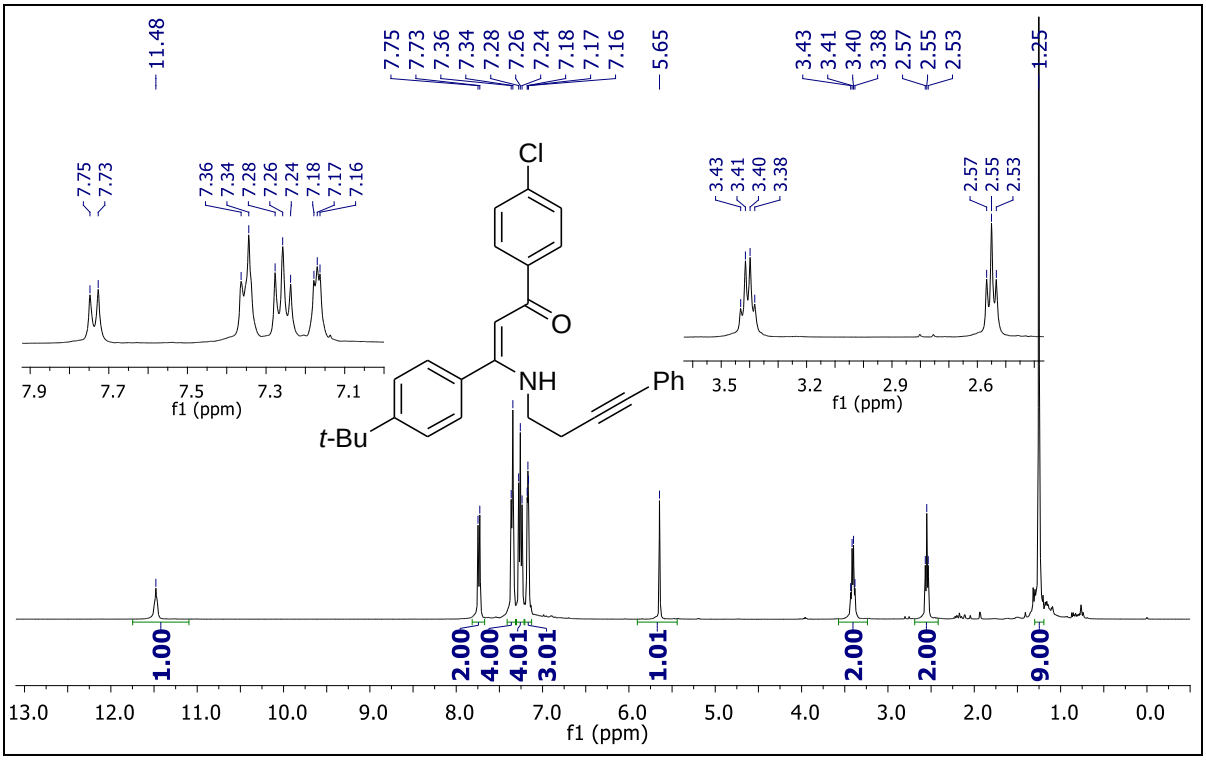


Figure S27. ^{1}H NMR Spectrum of compound **9m**.

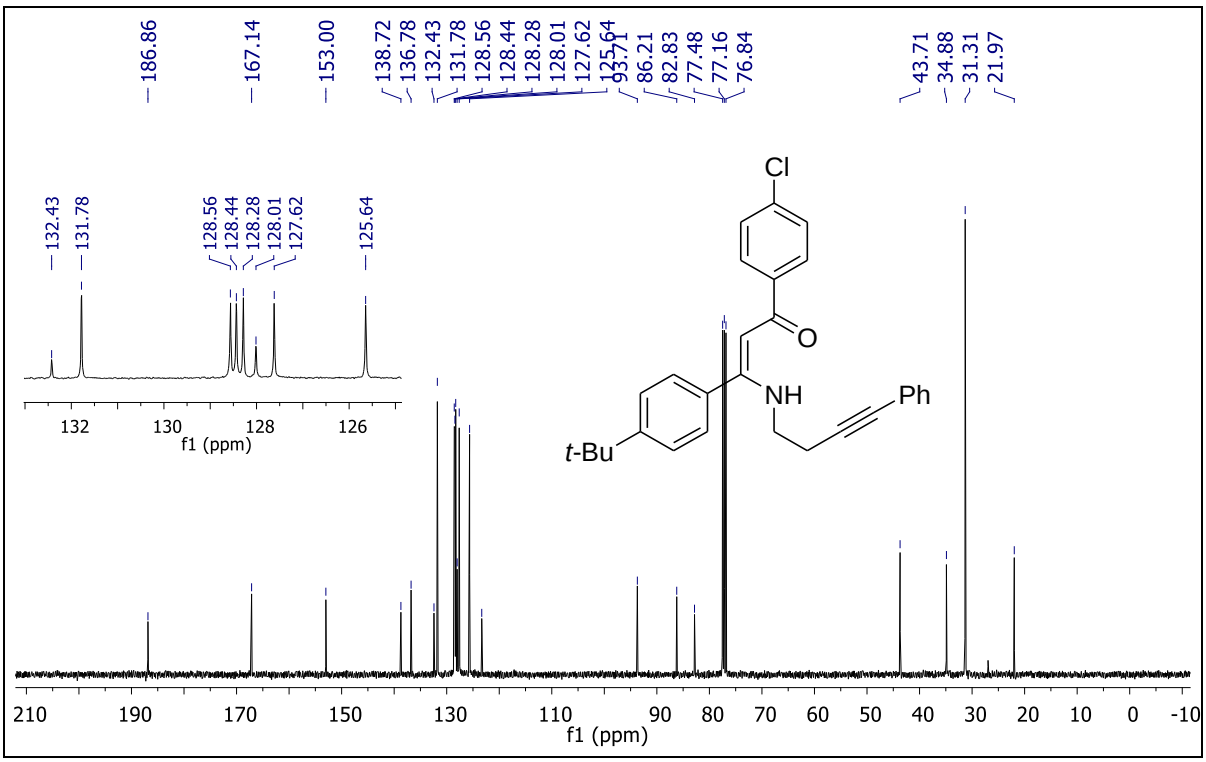


Figure S28. ^{13}C NMR Spectrum of compound **9m**.

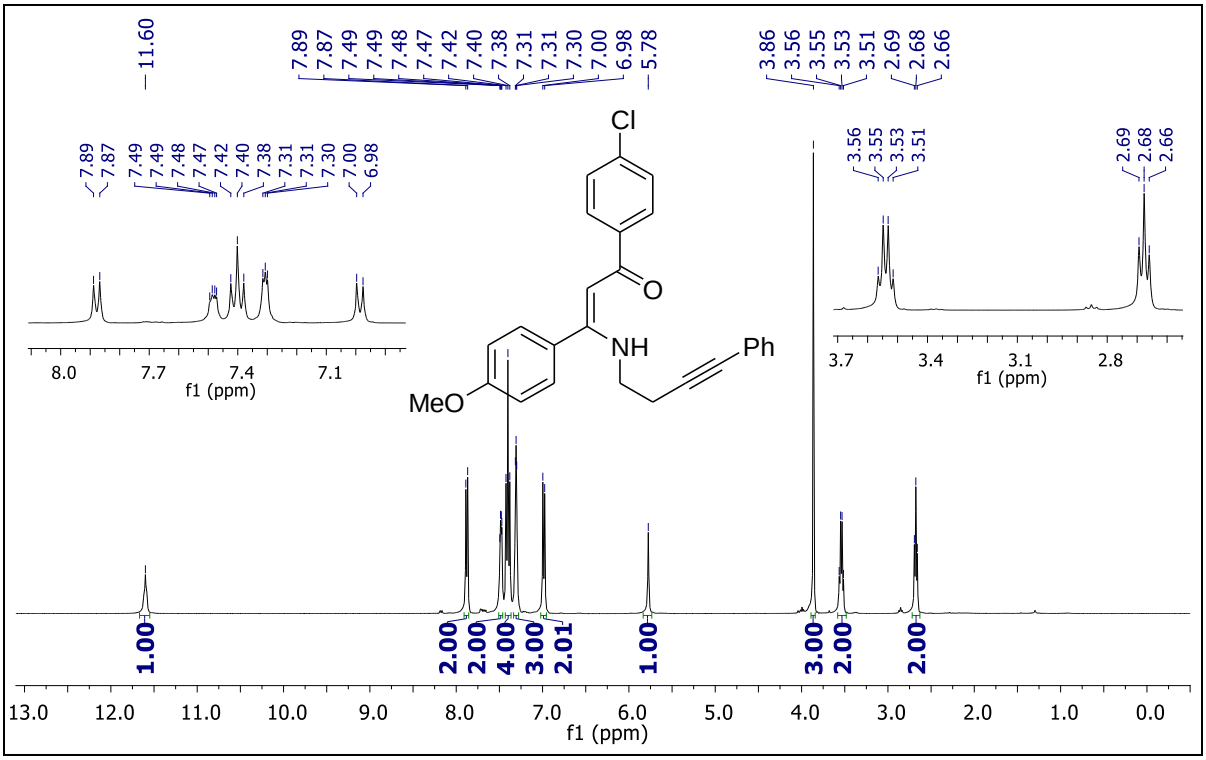


Figure S29. ^{1}H NMR Spectrum of compound **9n**.

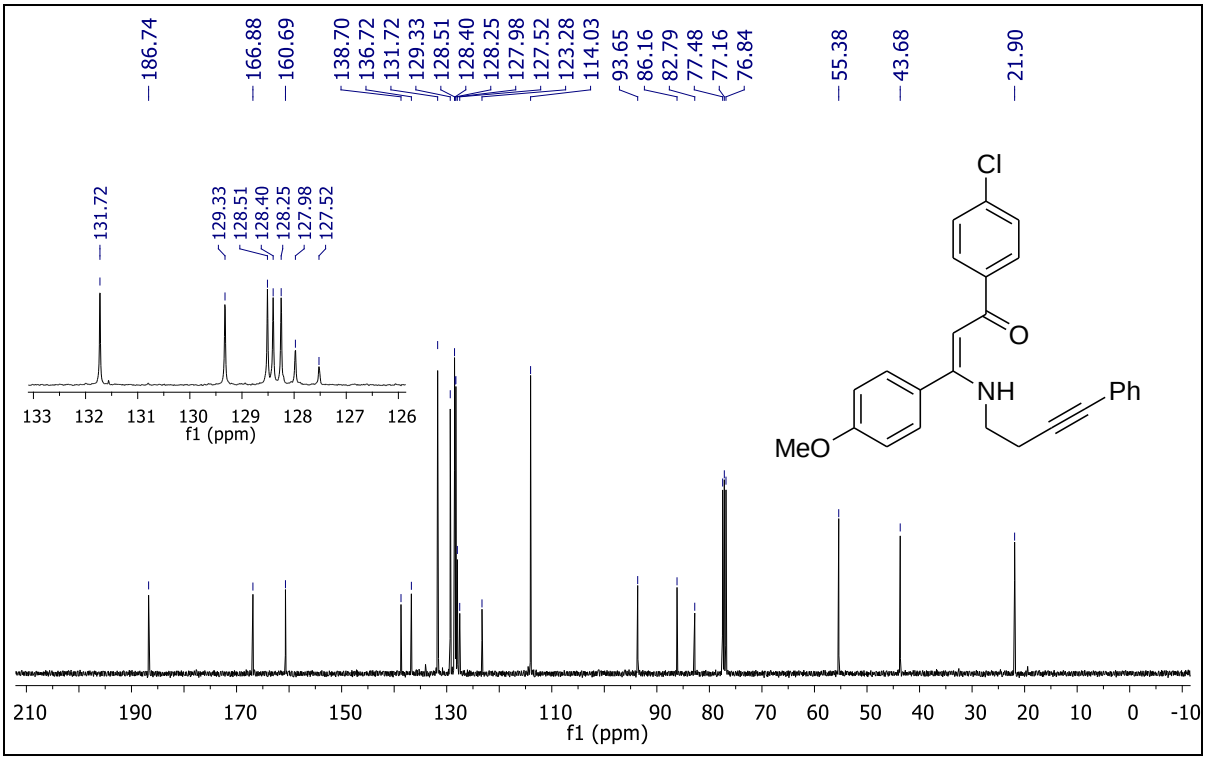


Figure S30. ^{13}C NMR Spectrum of compound **9n**.

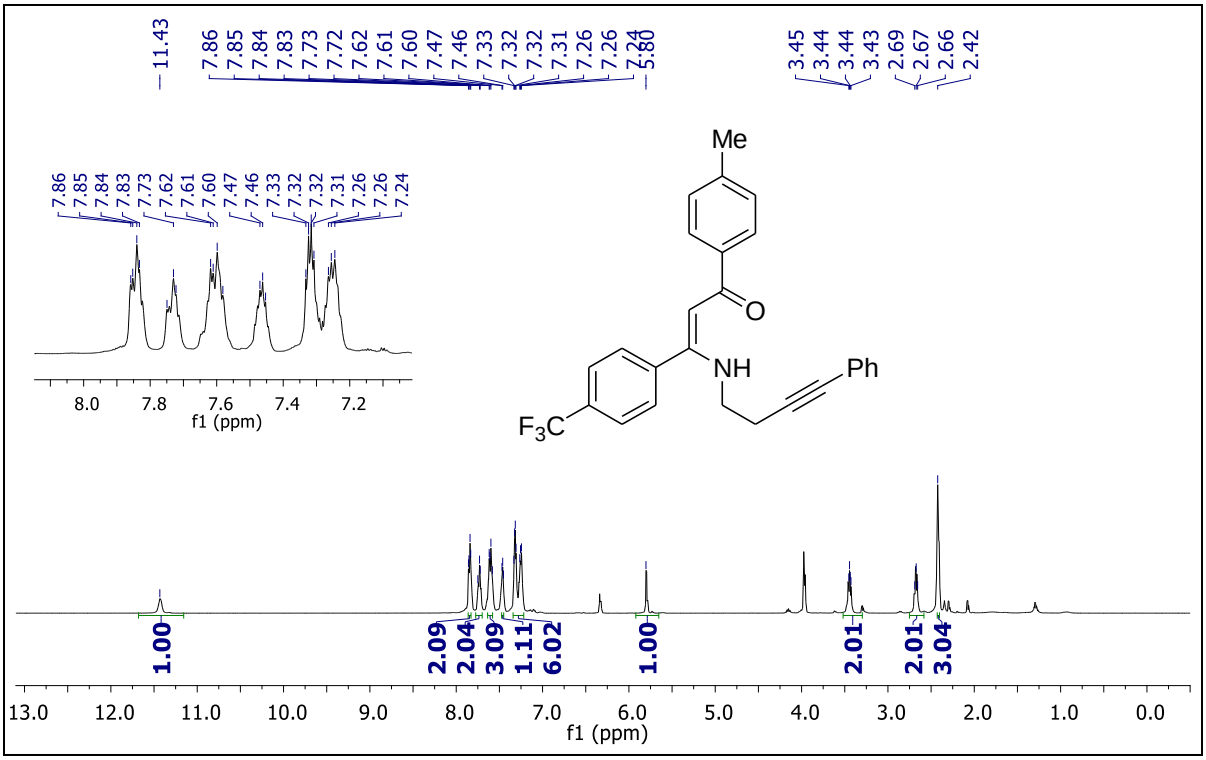


Figure S31. ^{1}H NMR Spectrum of compound **9o**.

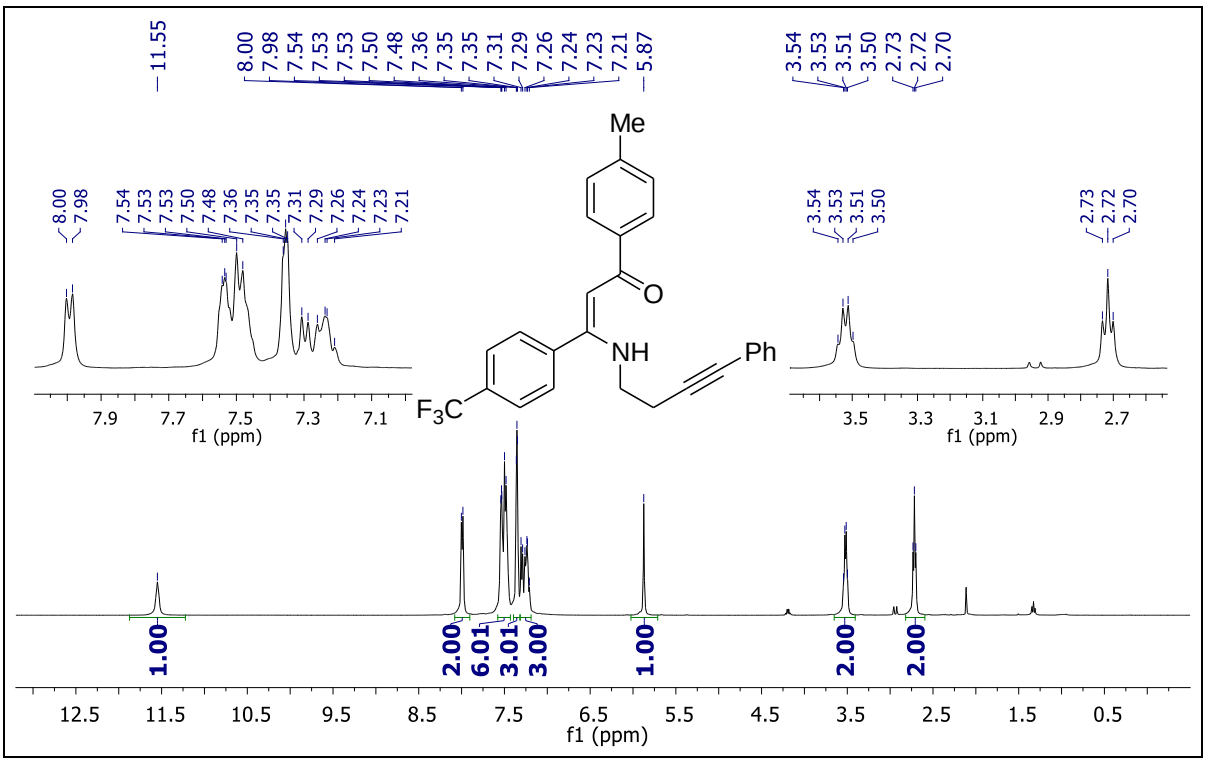


Figure S32. ^{1}H NMR Spectrum of compound **9o**.

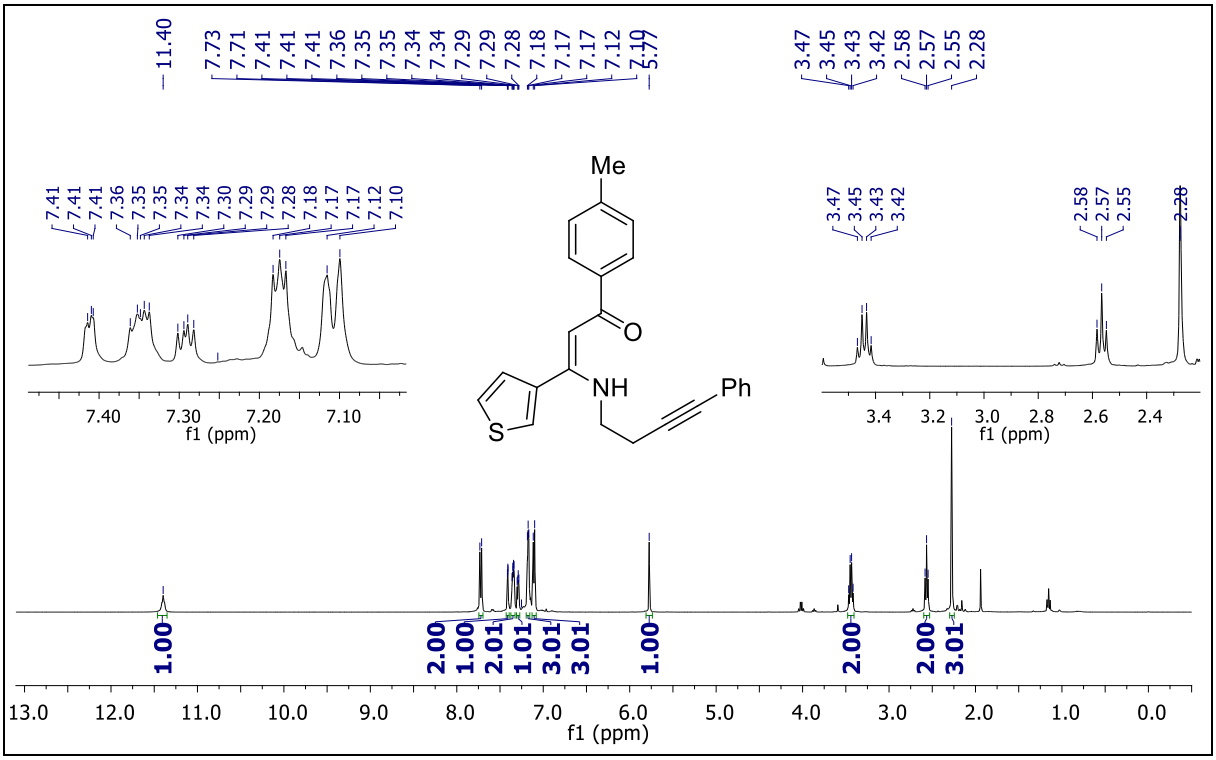


Figure S33. ^{1}H NMR Spectrum of compound **9p**.

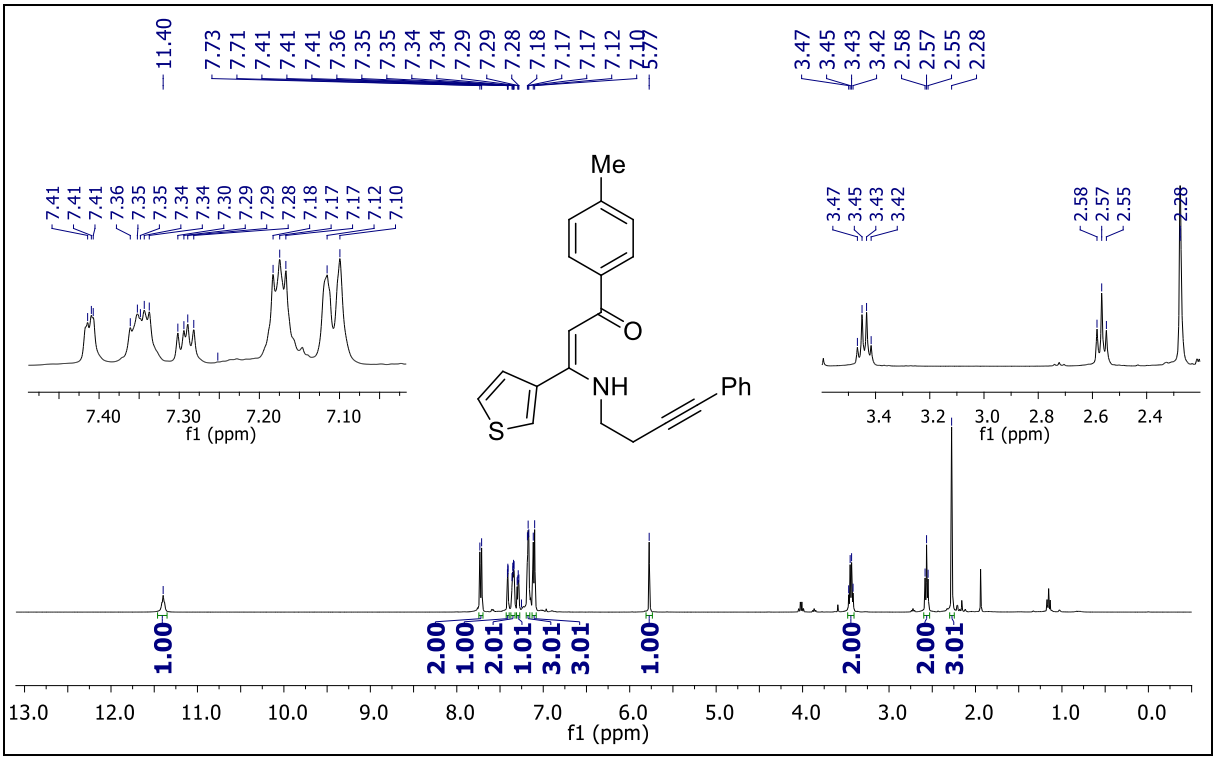


Figure S34. ^{13}C NMR Spectrum of compound **9p**.

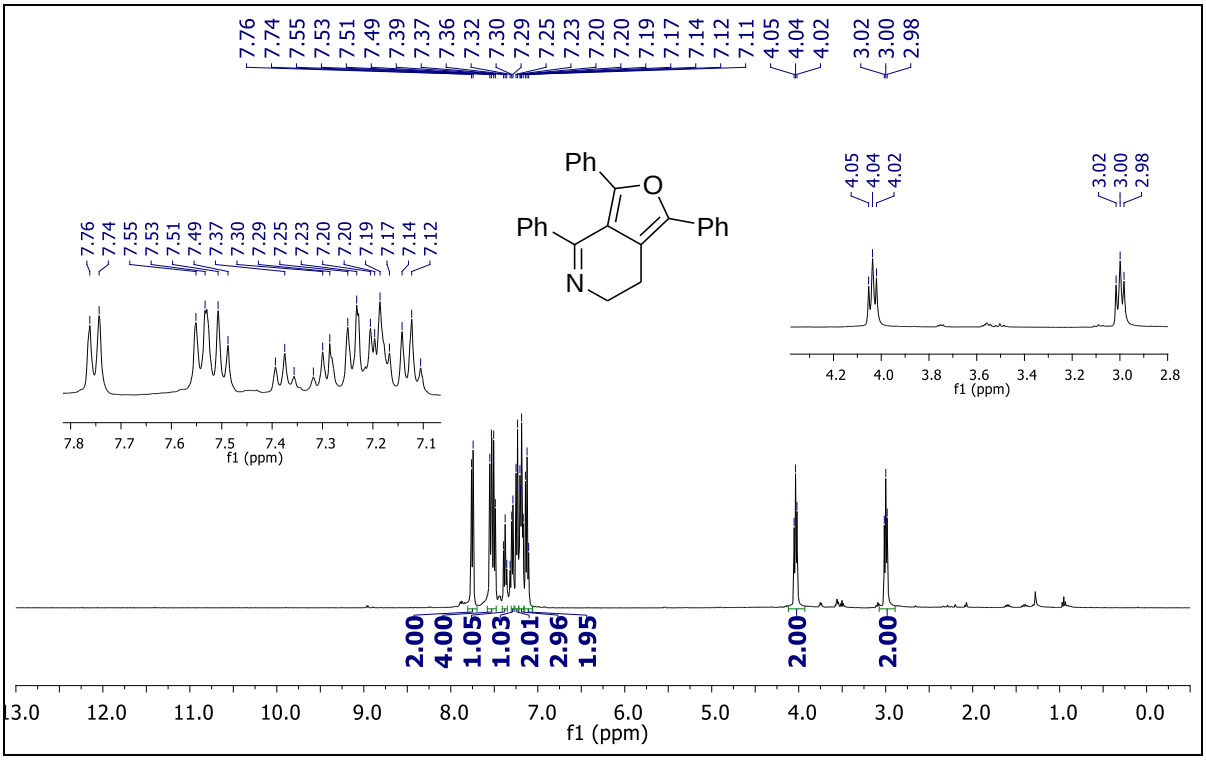


Figure S35. ^{1}H NMR Spectrum of compound **10a**.

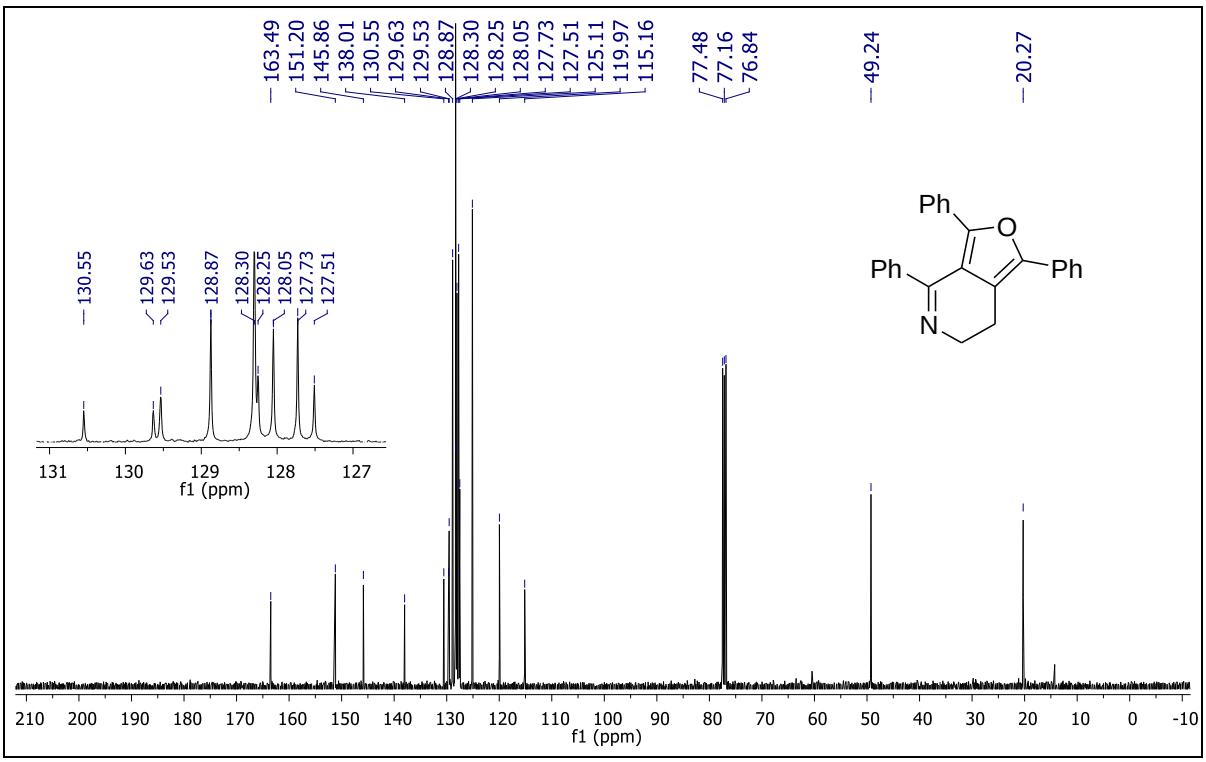


Figure S36. ^{13}C NMR Spectrum of compound **10a**.

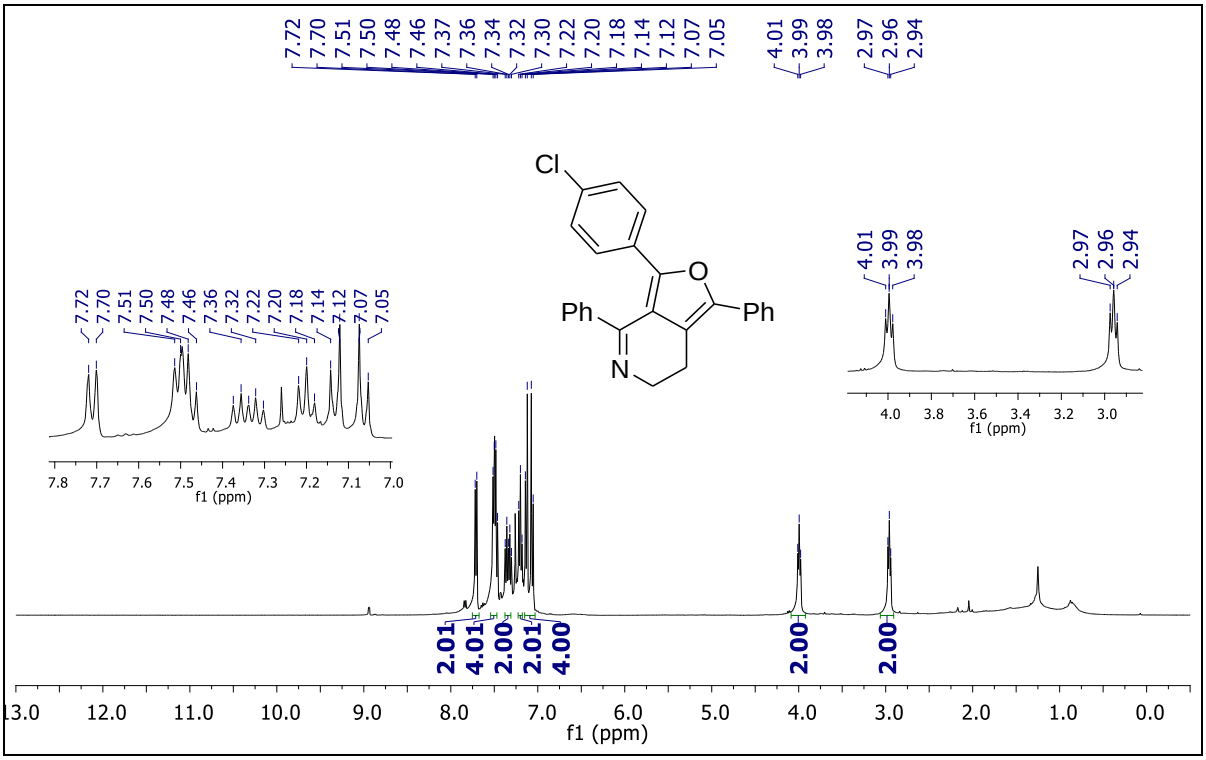


Figure S37. ^{1}H NMR Spectrum of compound **10b**.

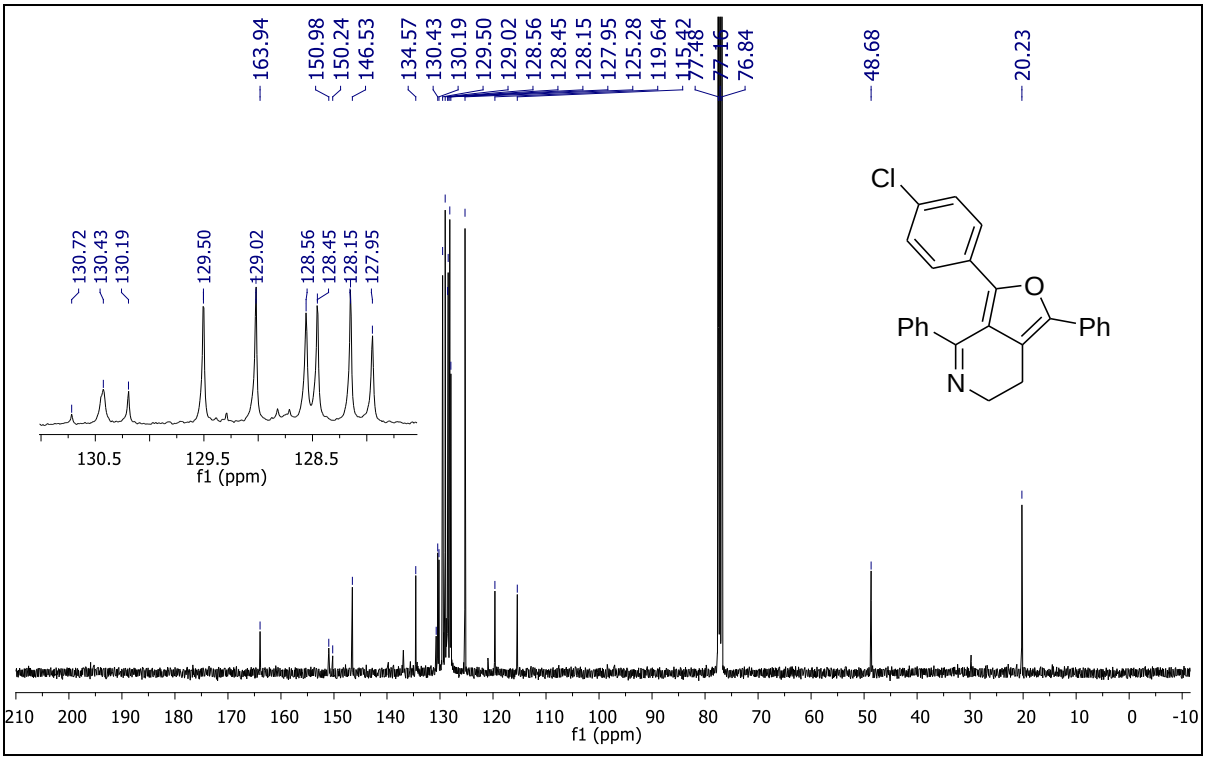


Figure S38. ^{13}C NMR Spectrum of compound **10b**.

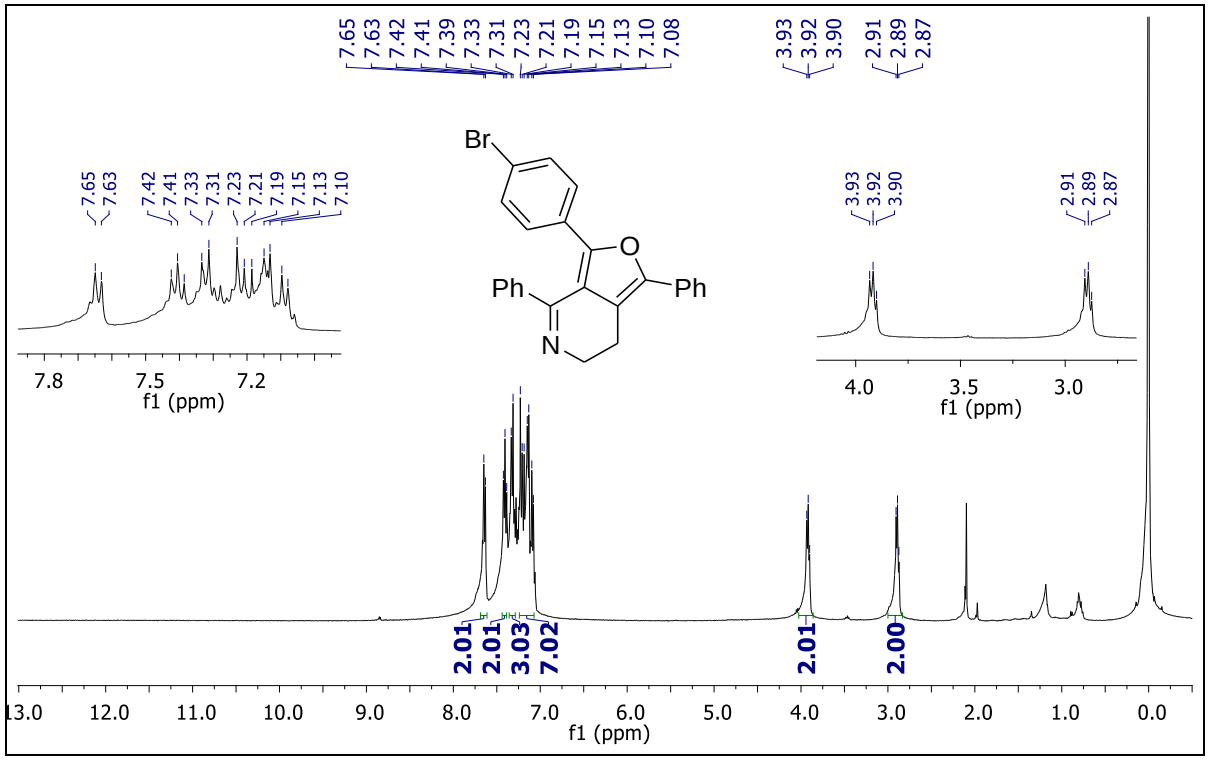


Figure S39. ^{1}H NMR Spectrum of compound **10c**.

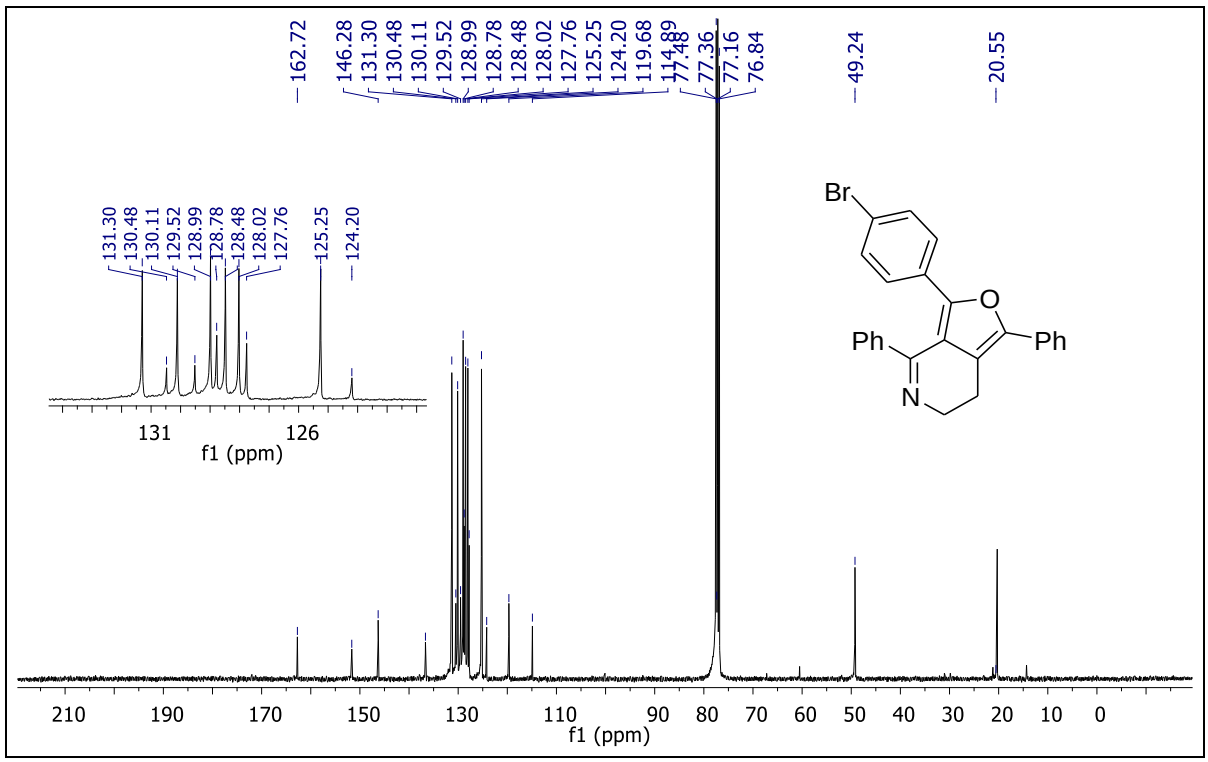


Figure S40. ^{13}C NMR Spectrum of compound **10c**.

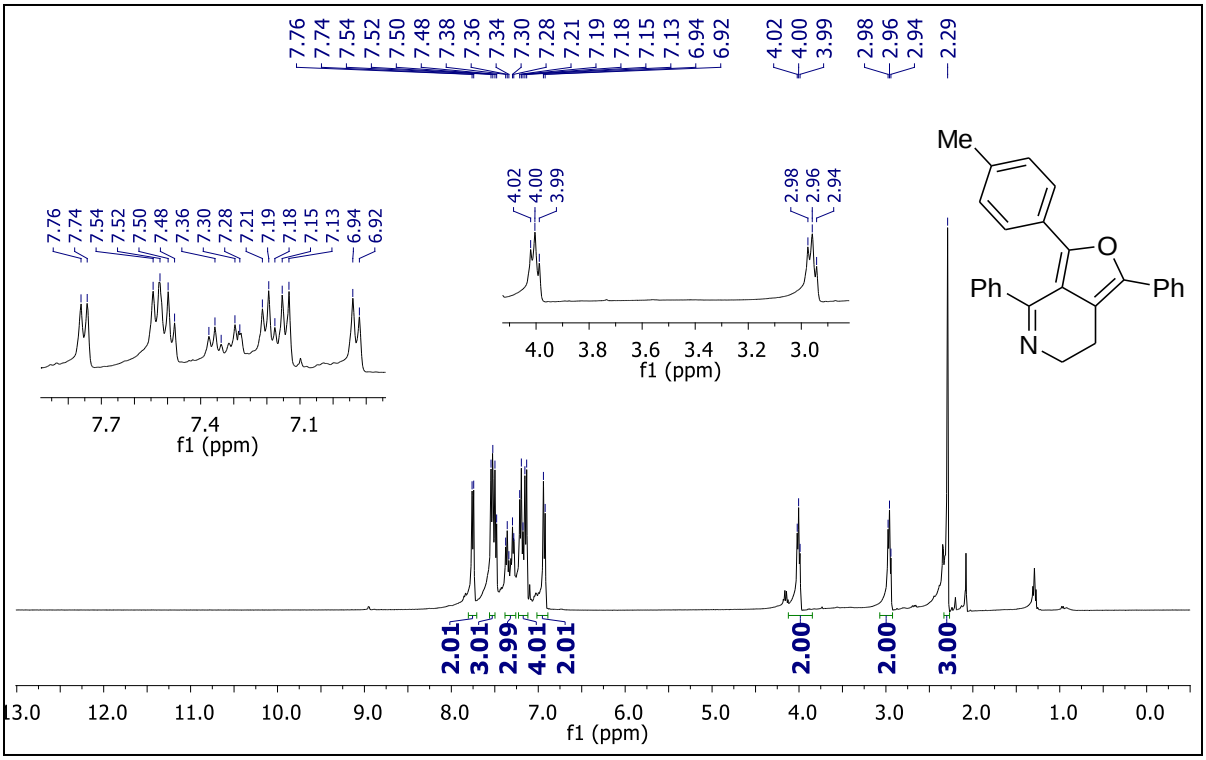


Figure S41. ^{1}H NMR Spectrum of compound **10d**.

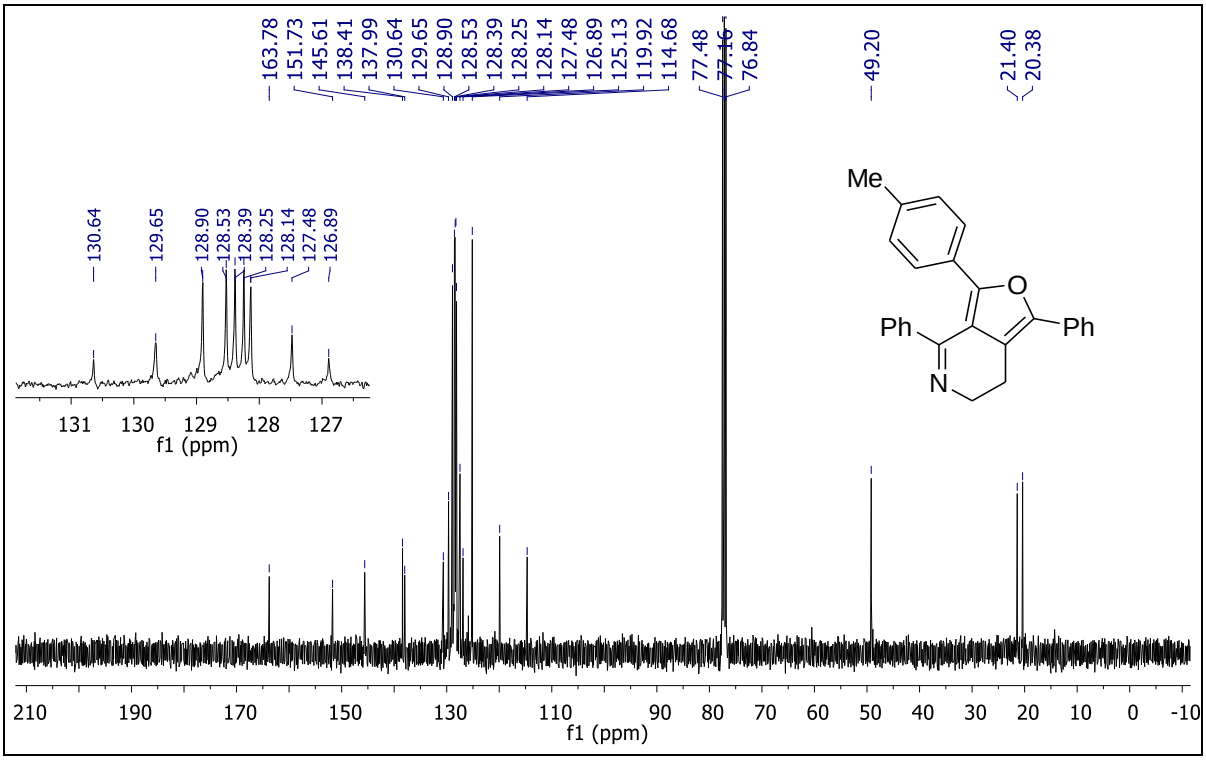


Figure S42. ^{13}C NMR Spectrum of compound **10d**.

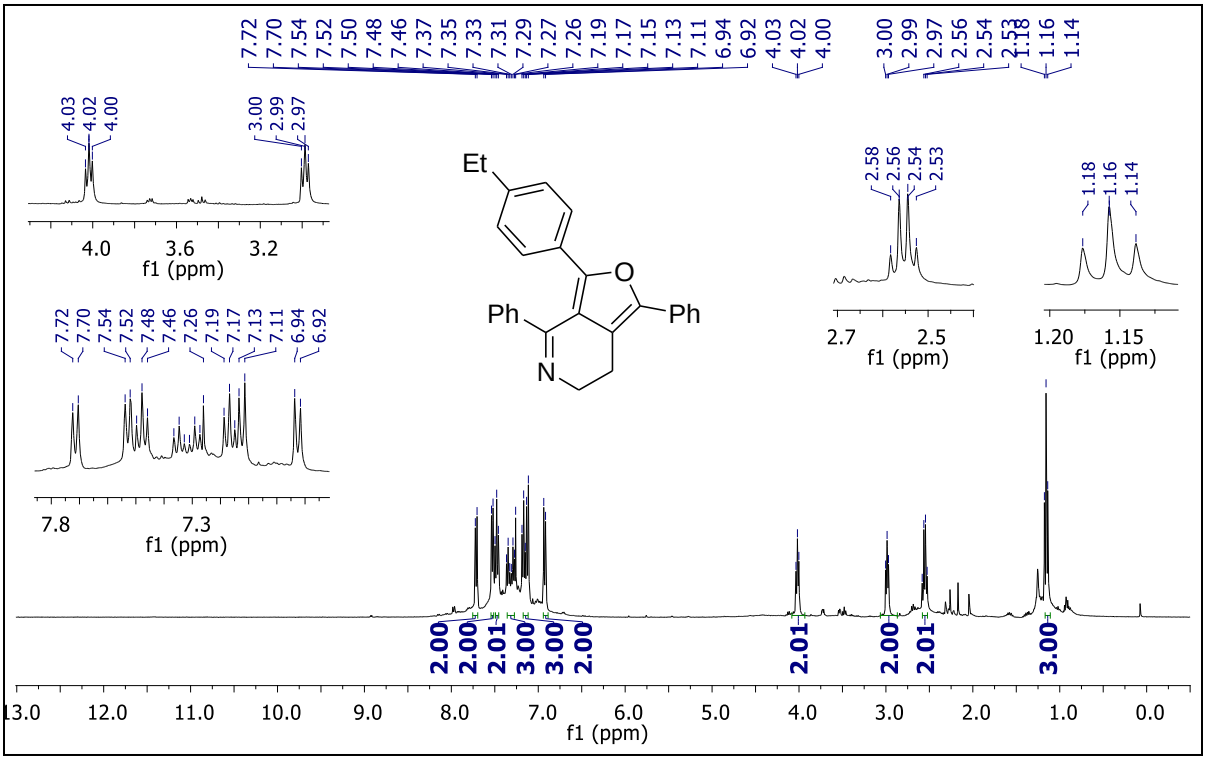


Figure S43. ^{1}H NMR Spectrum of compound **10e**.

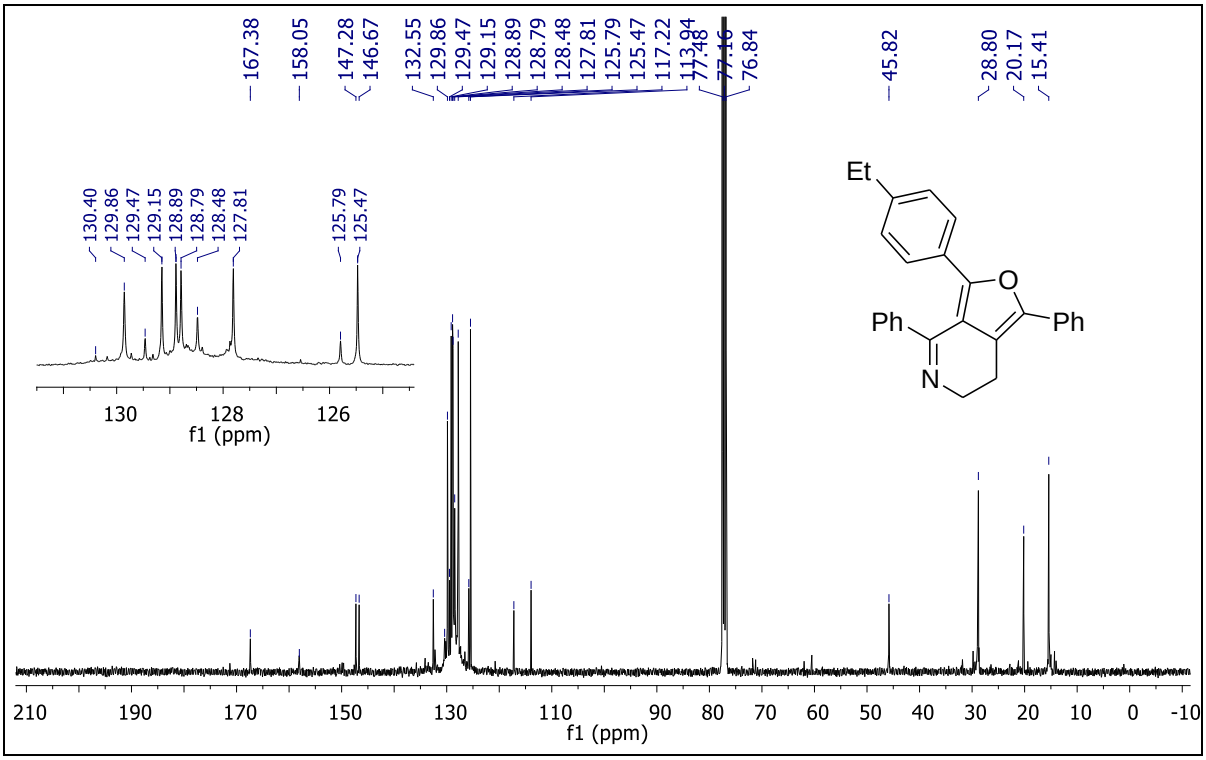


Figure S44. ^{13}C NMR Spectrum of compound **10e**.

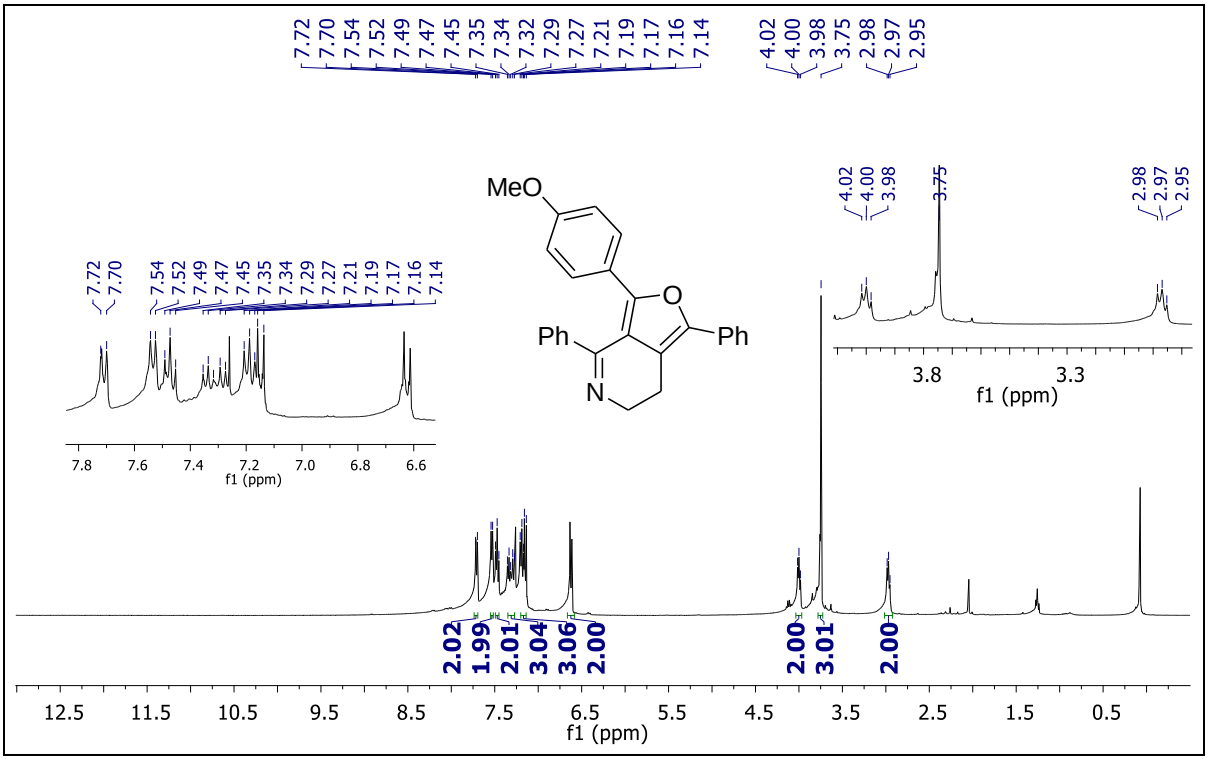


Figure S45. ^{1}H NMR Spectrum of compound **10f**.

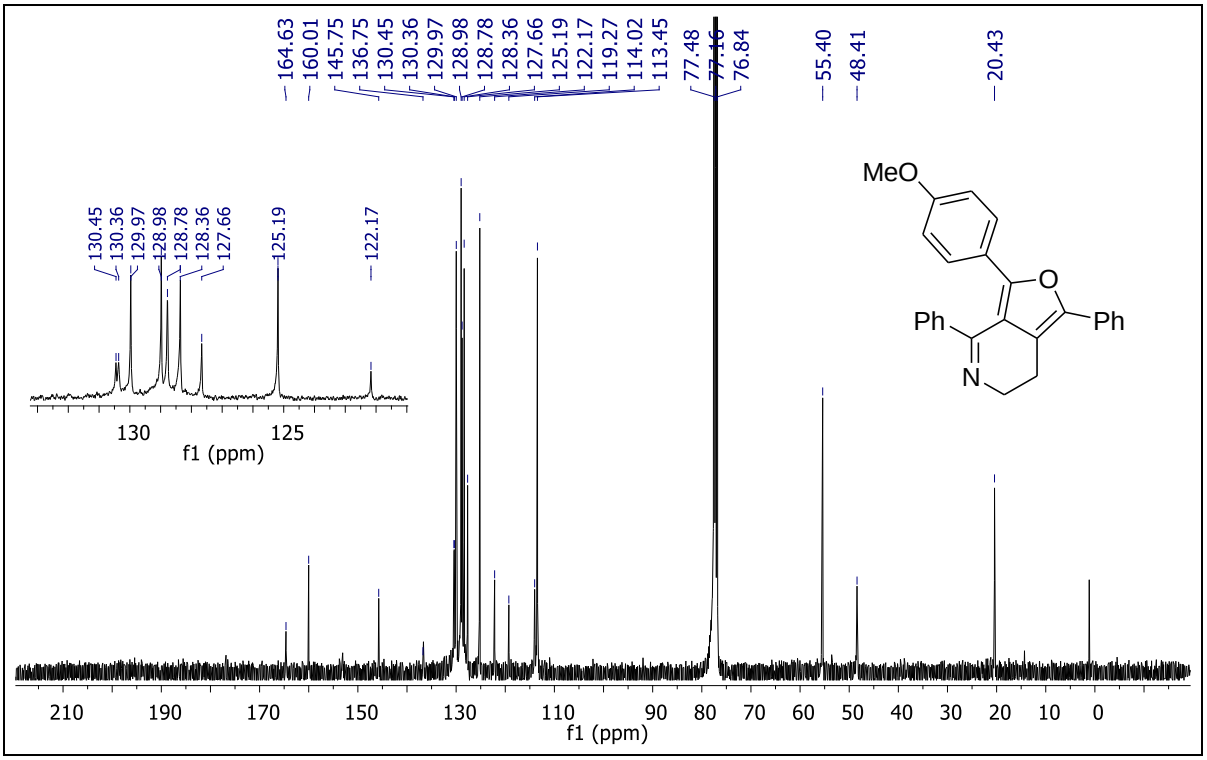


Figure S46. ^{13}C NMR Spectrum of compound **10f**.

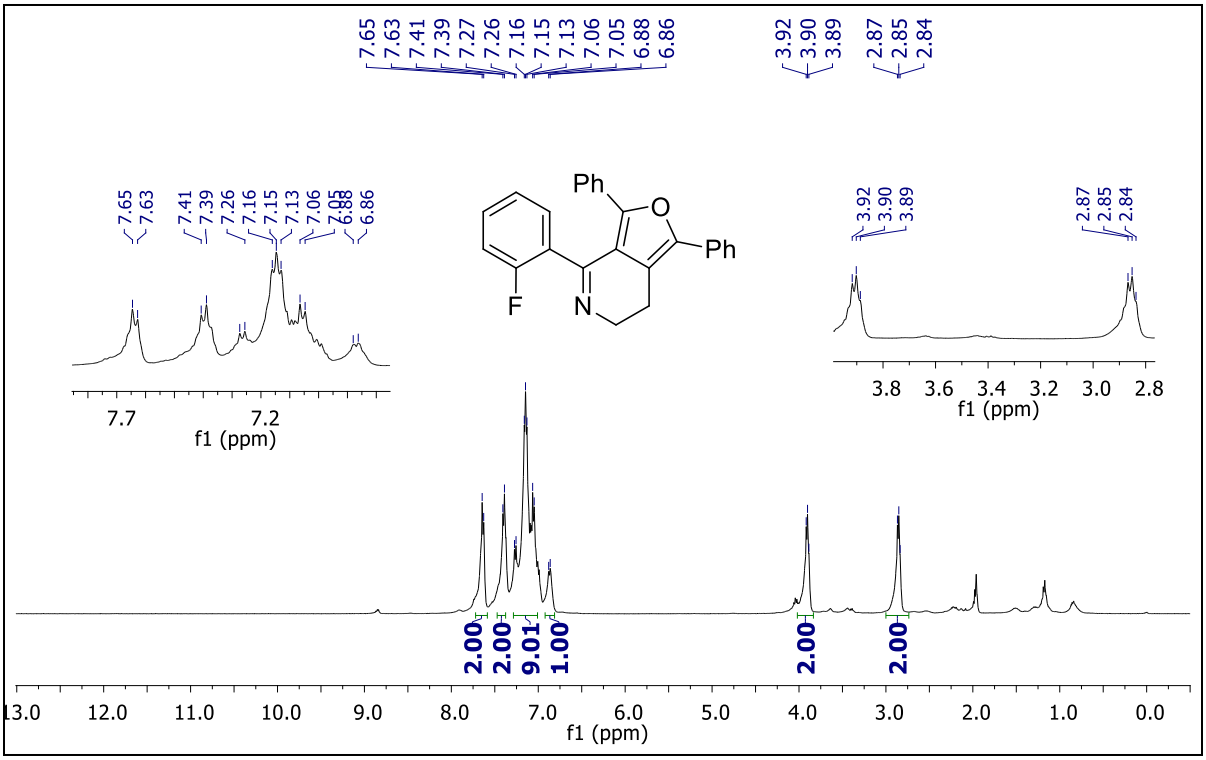


Figure S47. ^{1}H NMR Spectrum of compound **10g**.

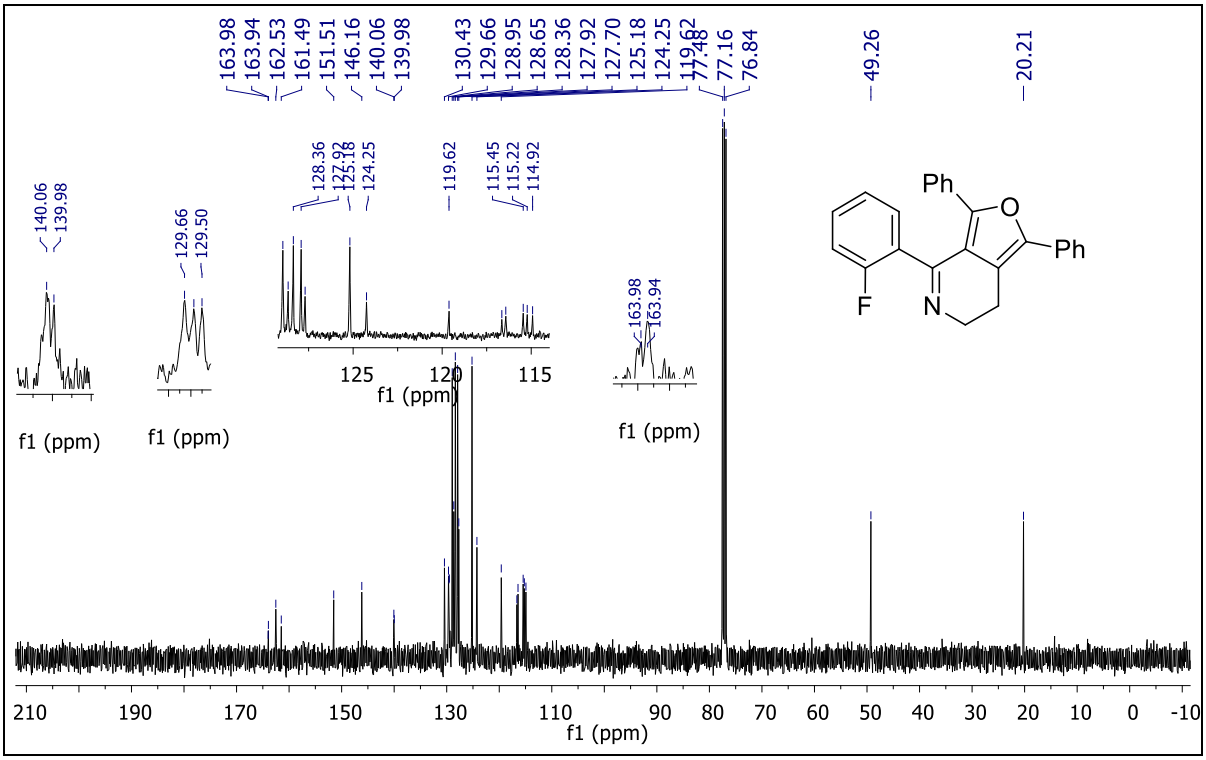


Figure S48. ^{13}C NMR Spectrum of compound **10g**.

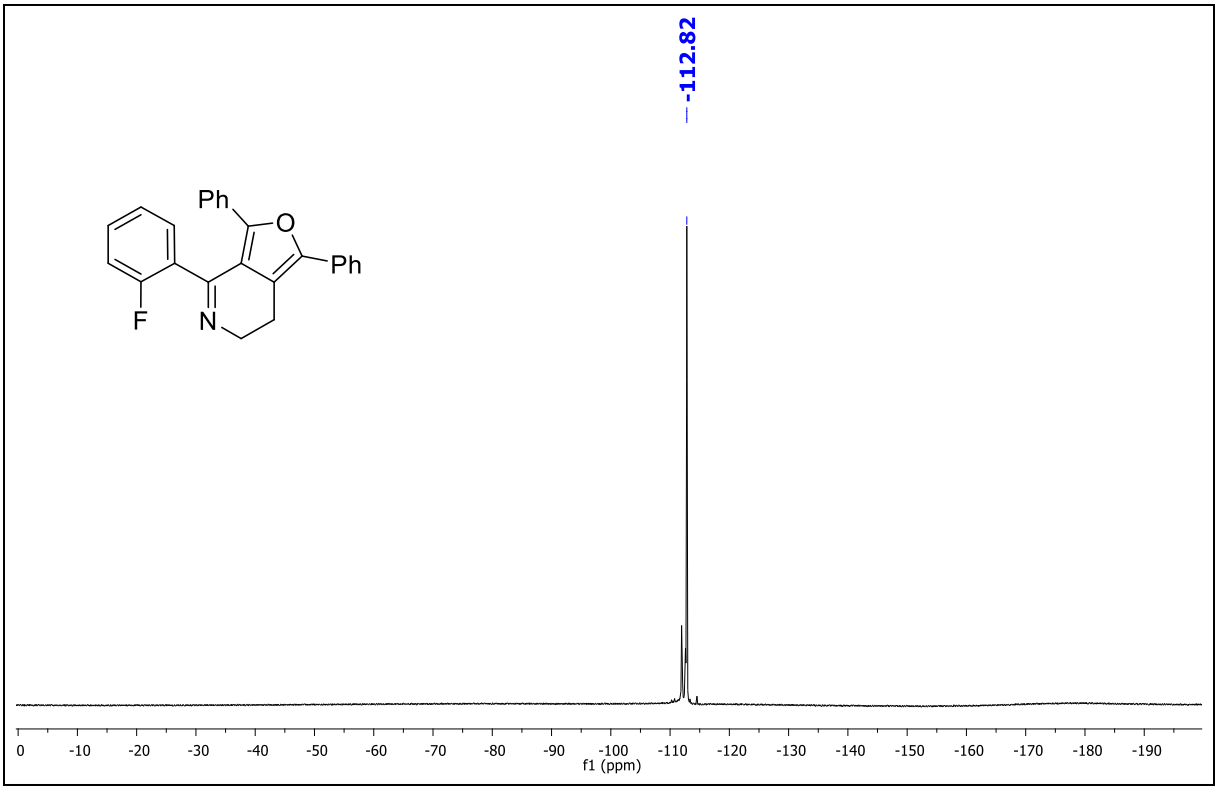


Figure S49. ^{19}F NMR Spectrum of compound **10g**.

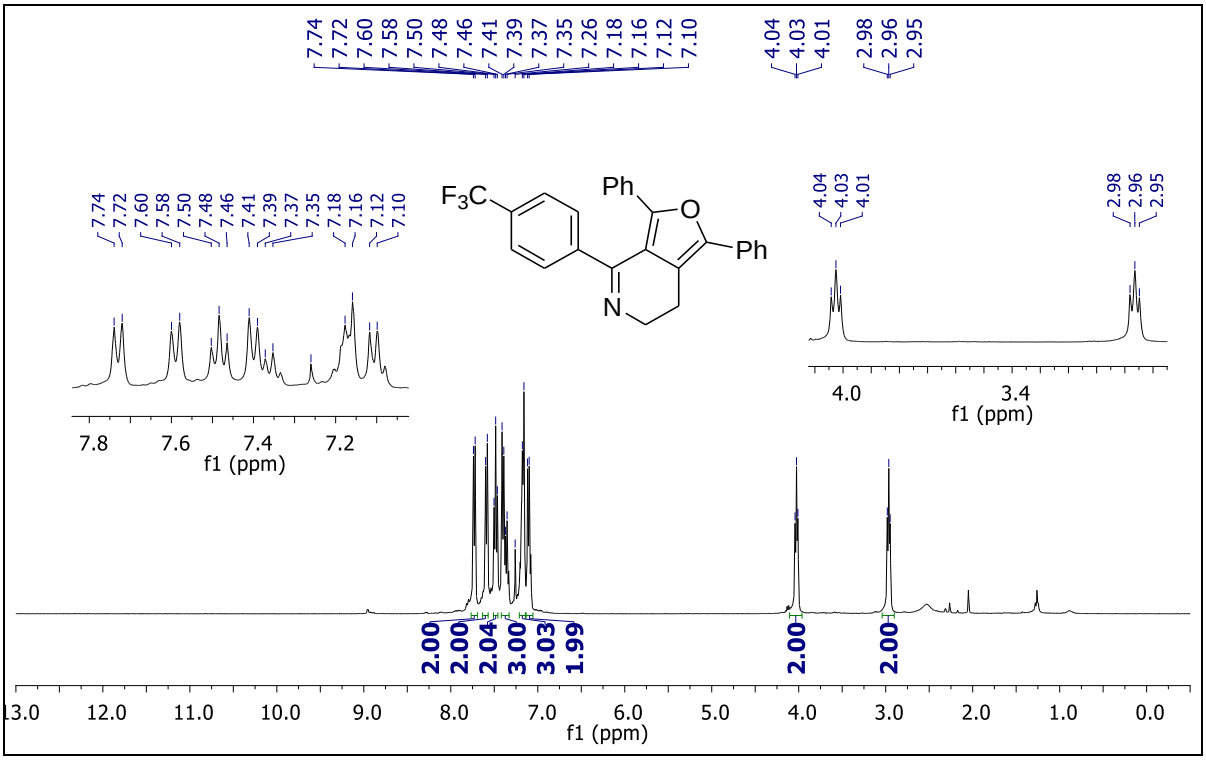


Figure S50. ^{1}H NMR Spectrum of compound **10h**.

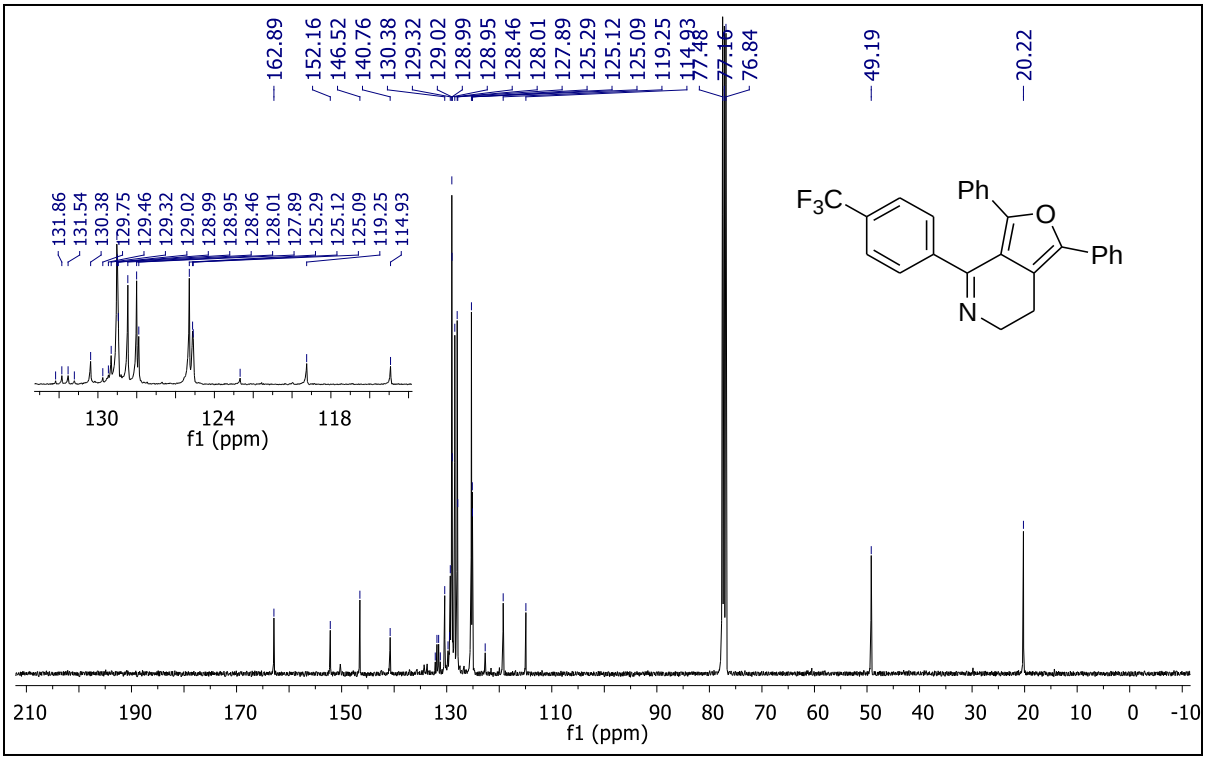


Figure S51. ^{13}C NMR Spectrum of compound **10h**.

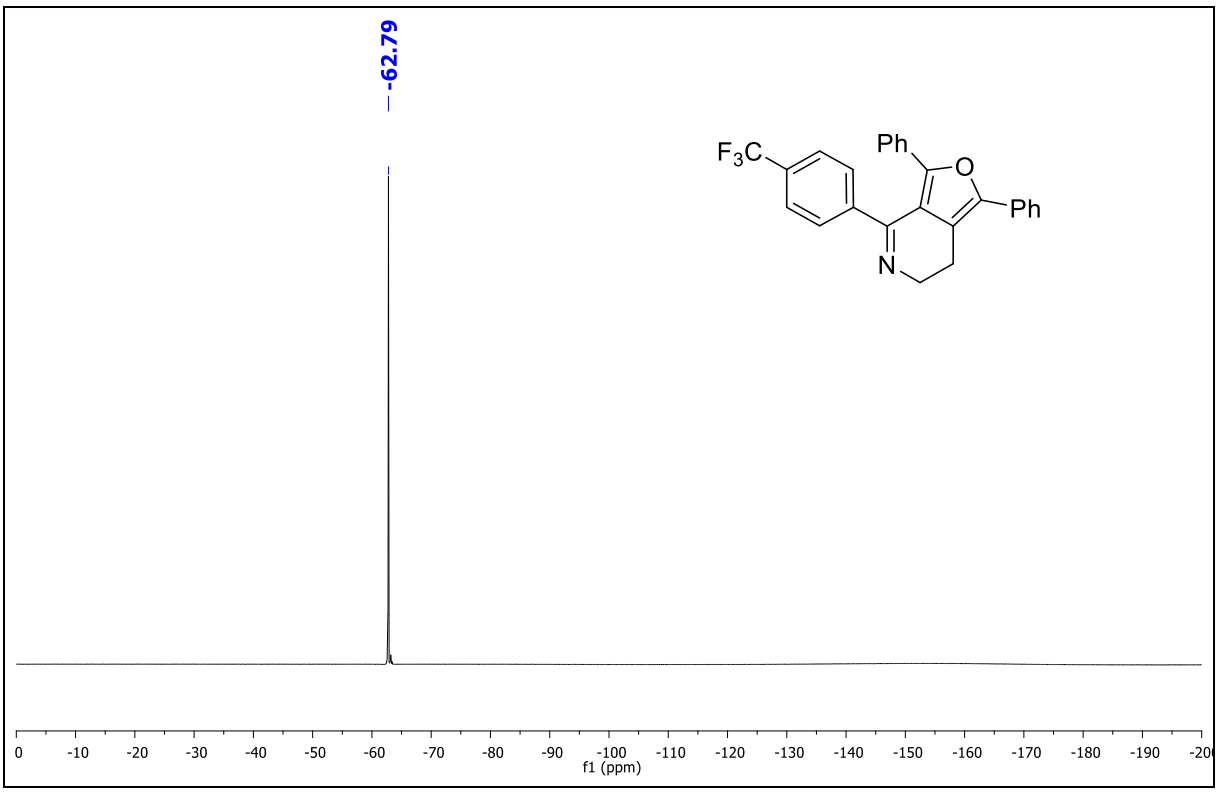


Figure S52. ^{19}F NMR spectrum of compound **10h**.

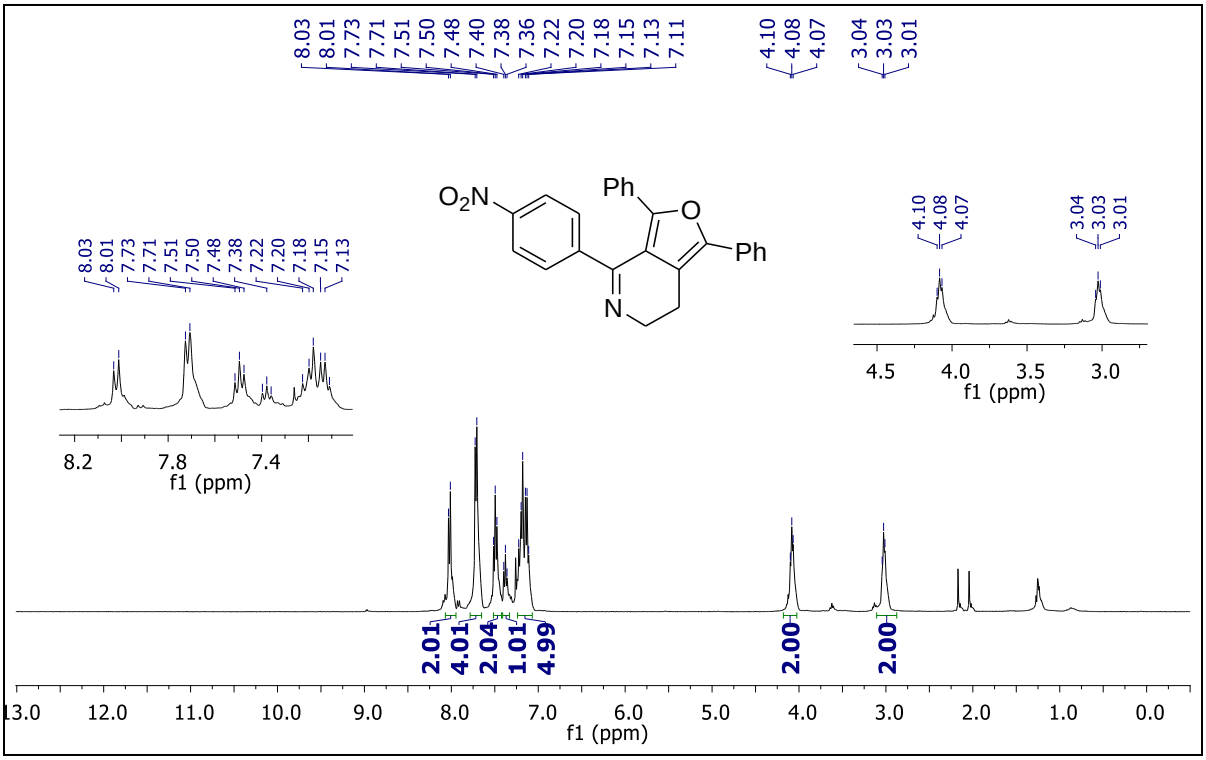


Figure S53. ^{1}H NMR Spectrum of compound **10i**.

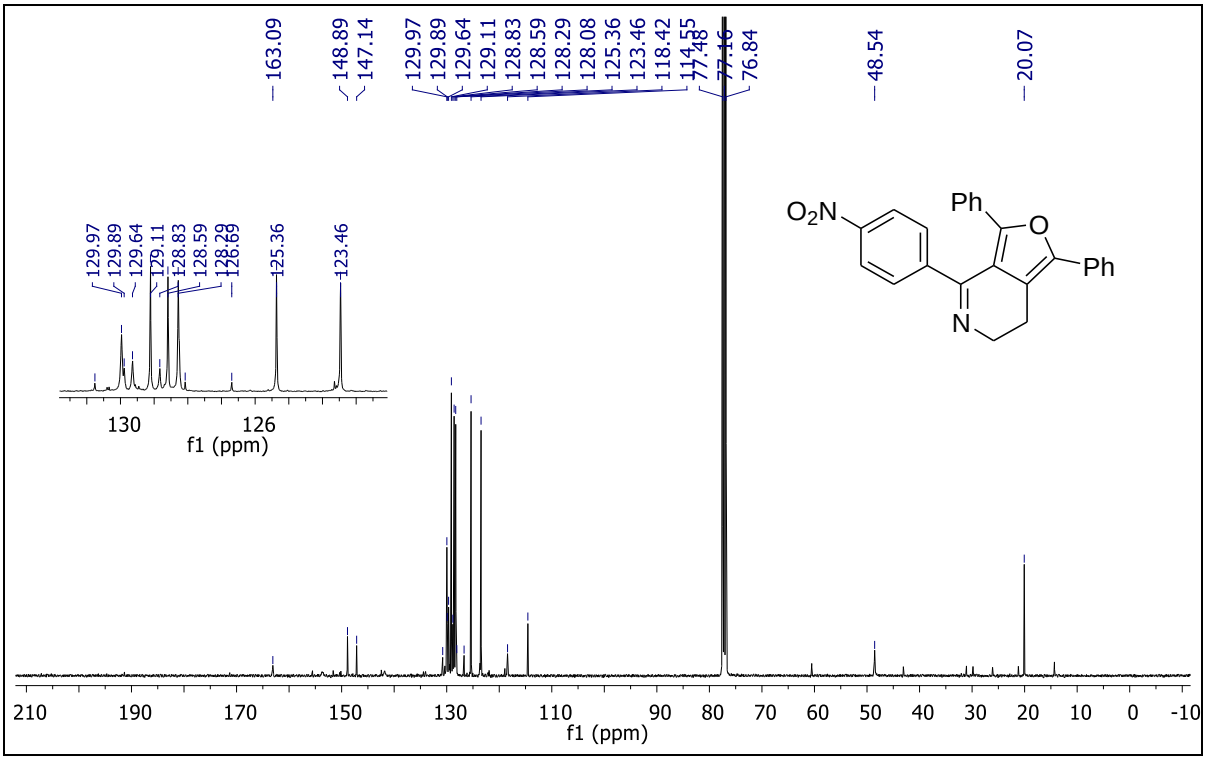


Figure S54. ^{13}C NMR Spectrum of compound **10i**.

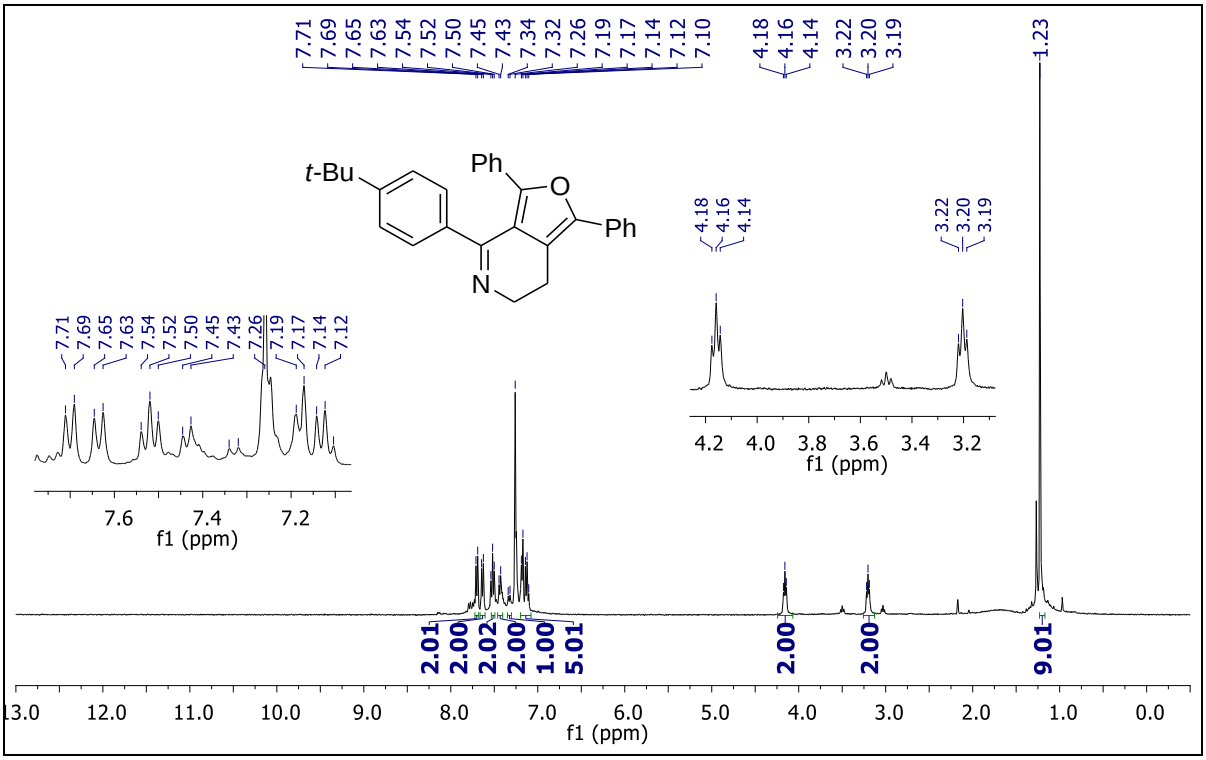


Figure S55. ^{1}H NMR Spectrum of compound **10j**.

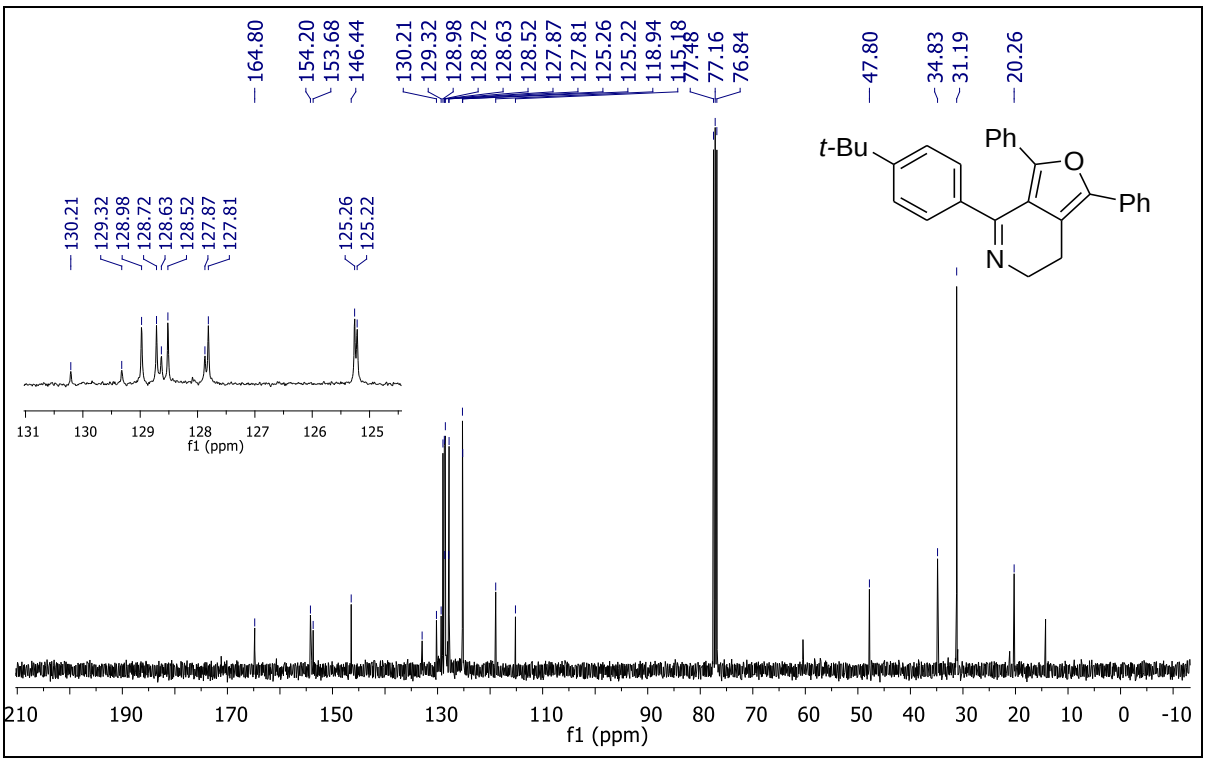


Figure S56. ^{13}C NMR Spectrum of compound **10j**.

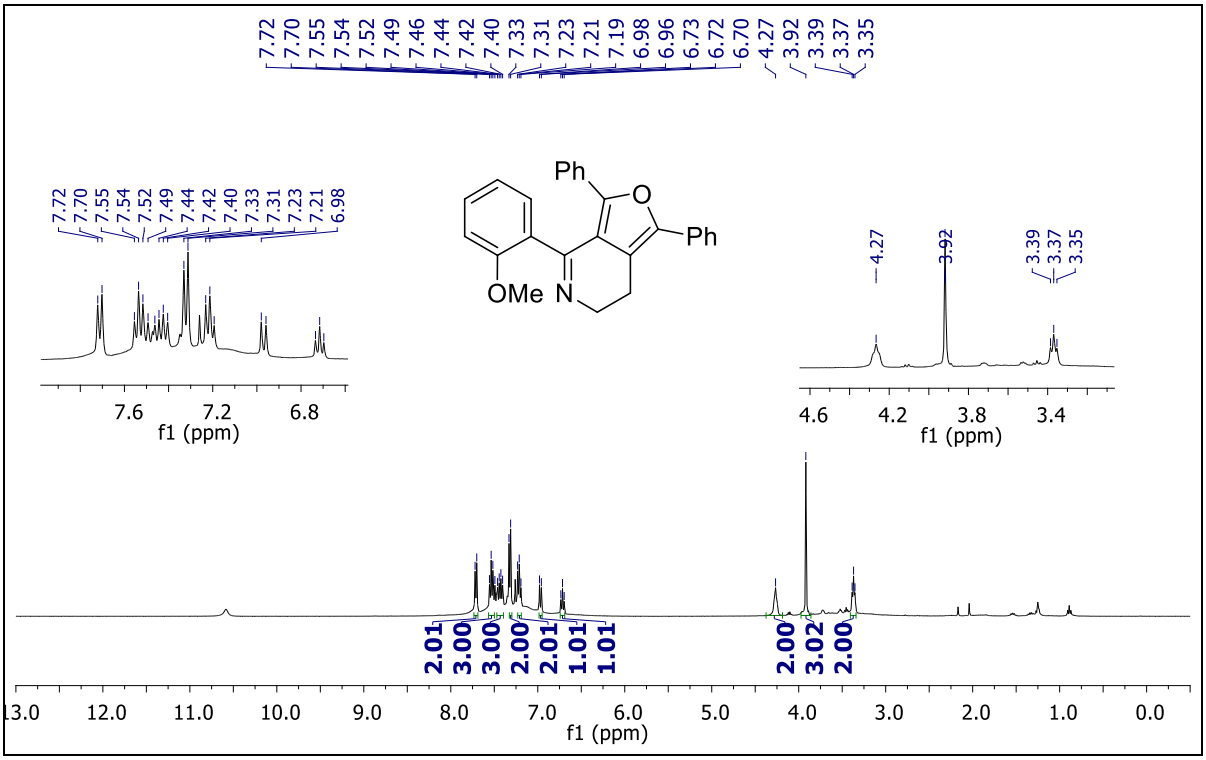


Figure S57. ^{1}H NMR Spectrum of compound **10k**.

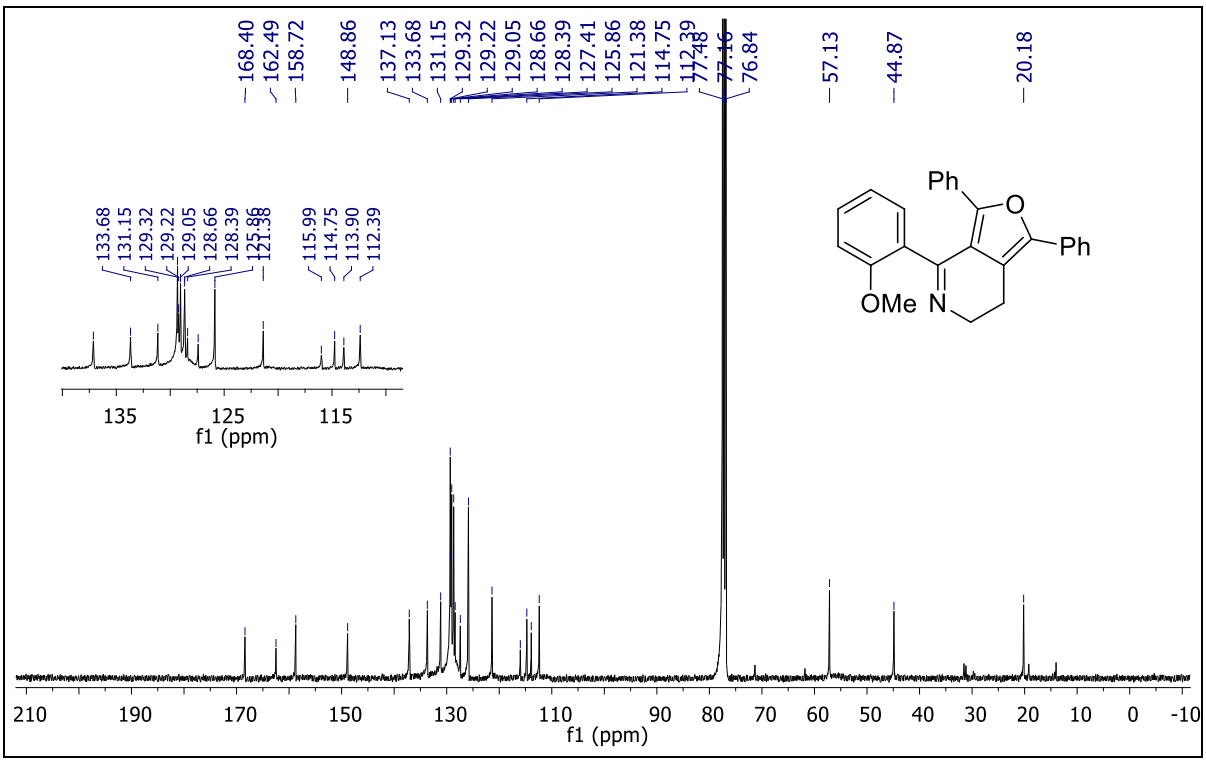


Figure S58. ^{13}C NMR Spectrum of compound **10k**.

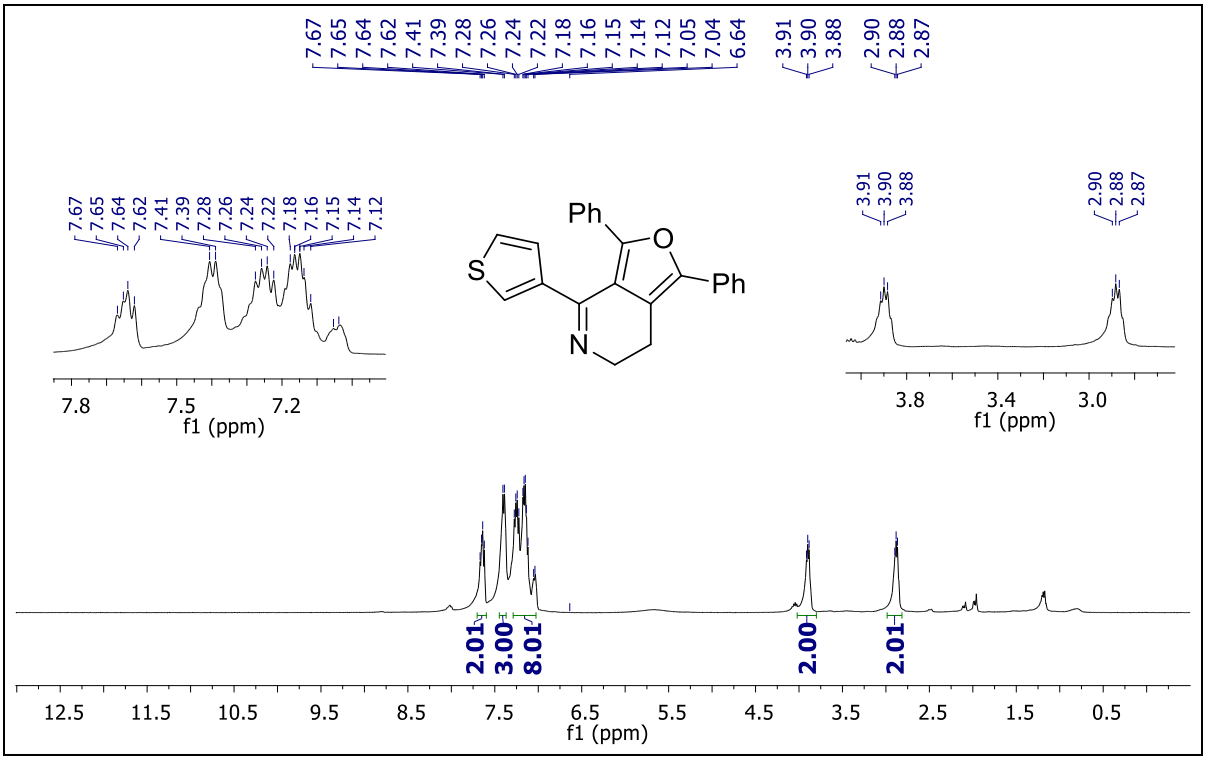


Figure S59. ^{1}H NMR Spectrum of compound **10l**.

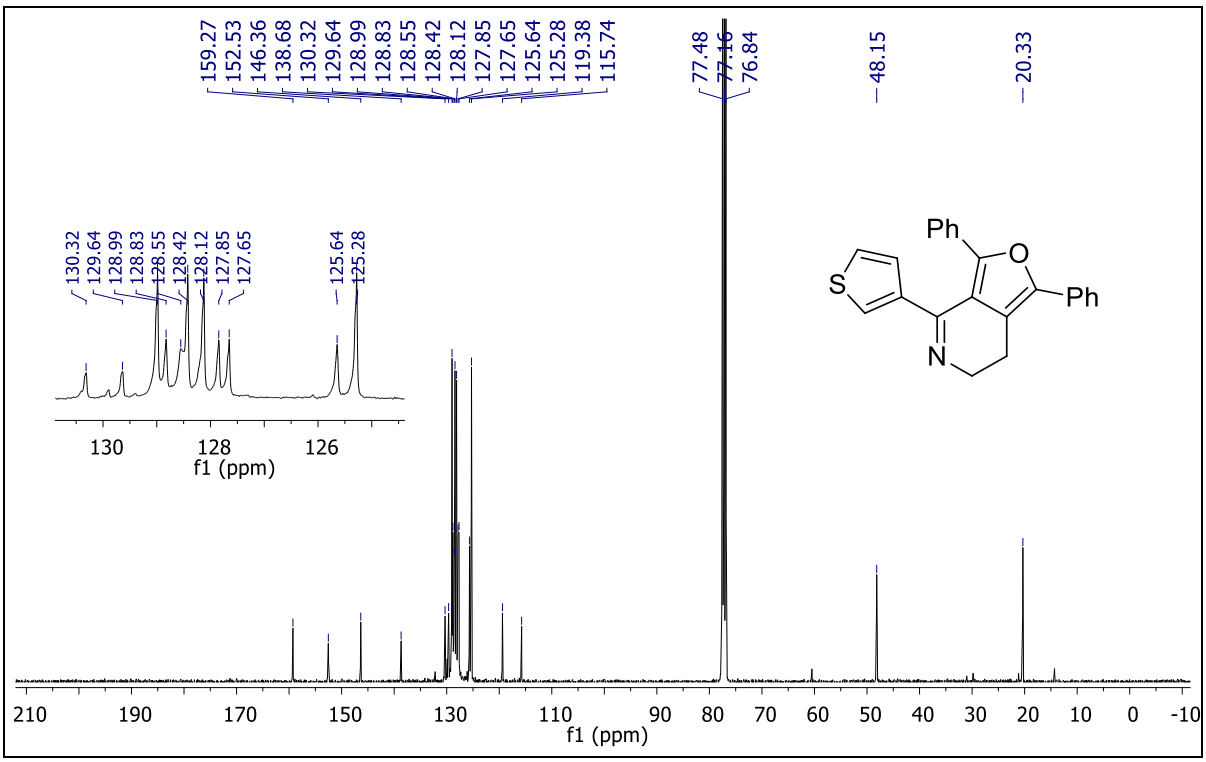


Figure S60. ^{13}C NMR Spectrum of compound **10l**.

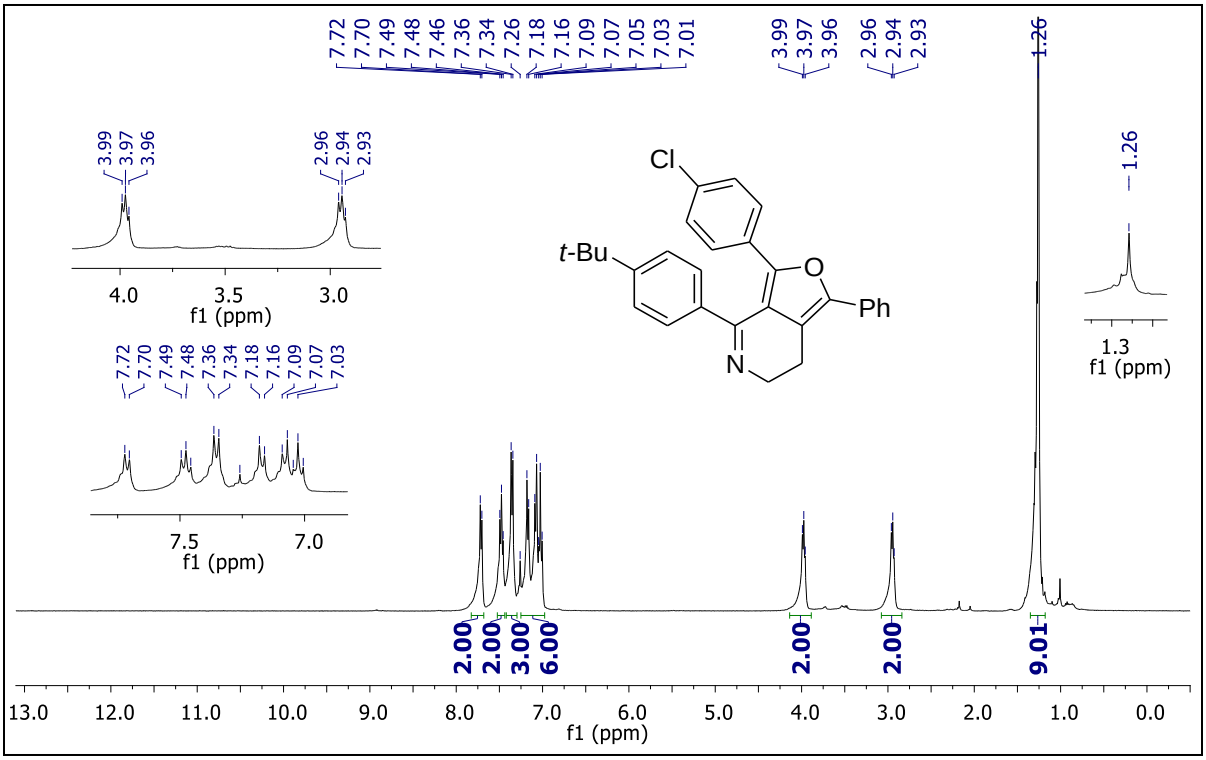


Figure S61. ^{1}H NMR Spectrum of compound **10m**.

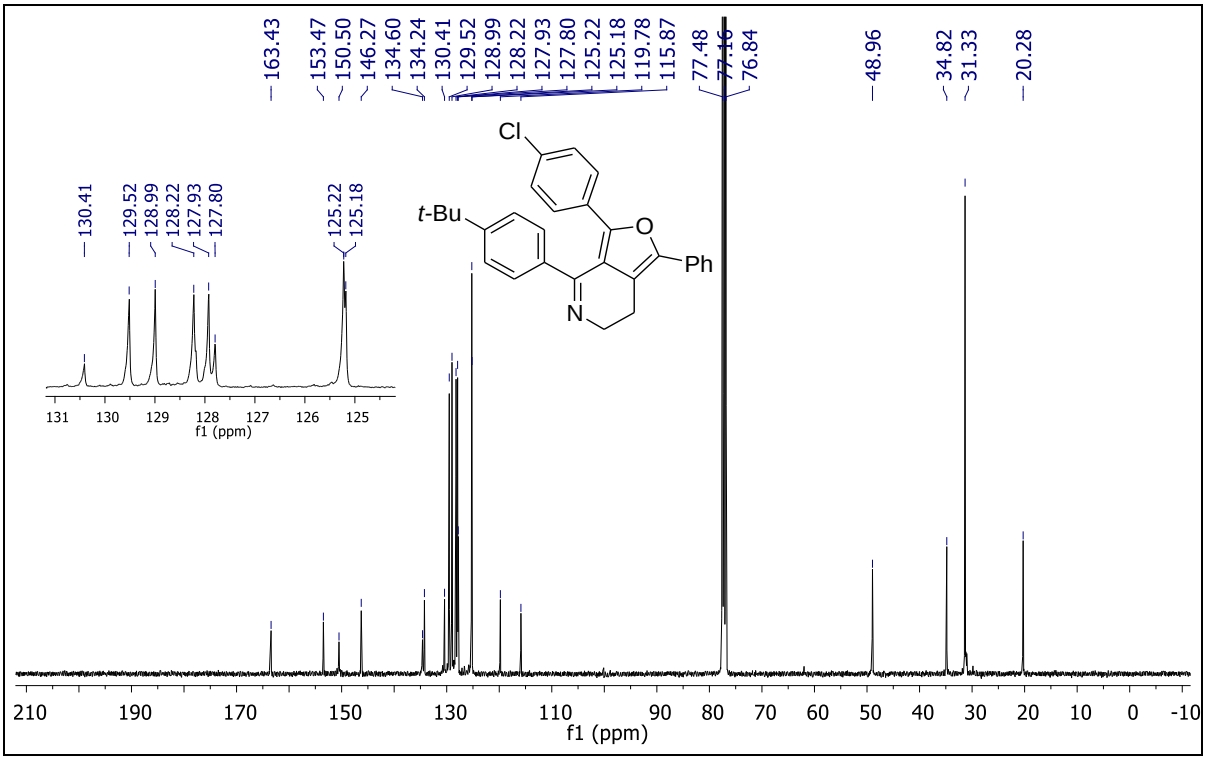


Figure S62. ^{13}C NMR Spectrum of compound **10m**.

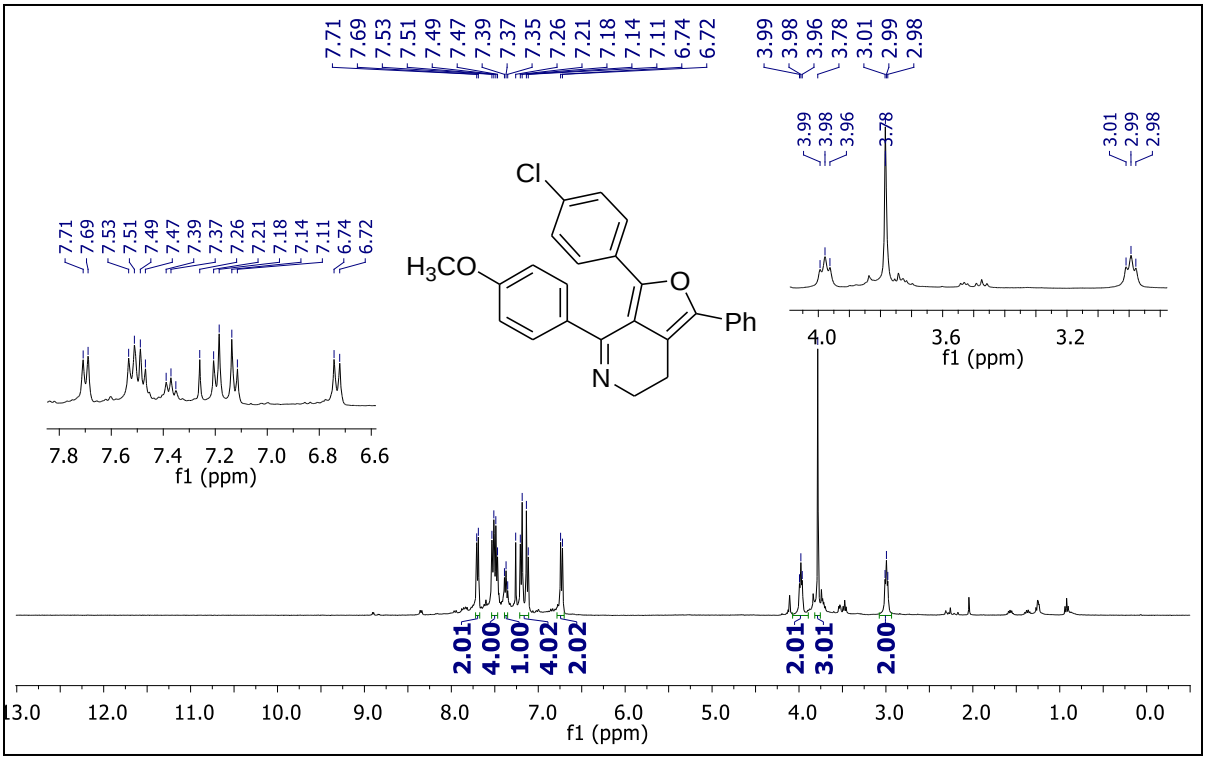


Figure S63. ^{1}H NMR Spectrum of compound **10n**.

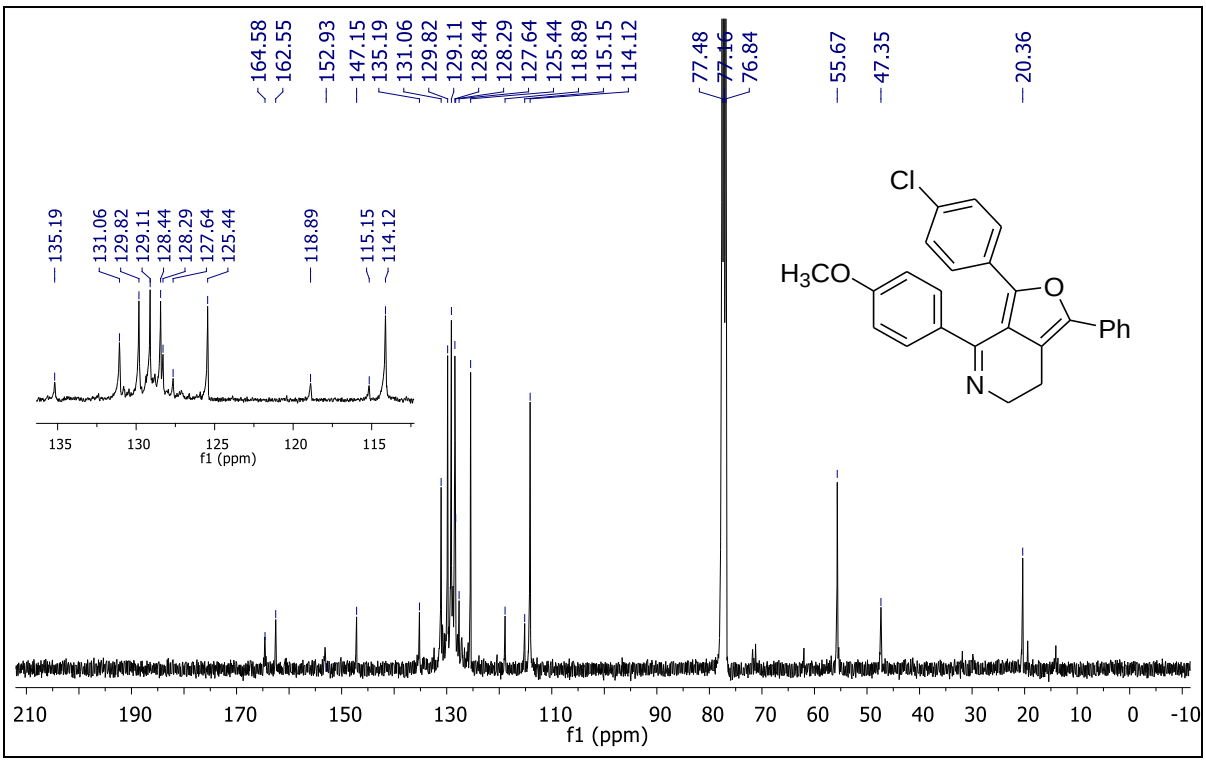


Figure S64. ^{13}C NMR Spectrum of compound **10n**.

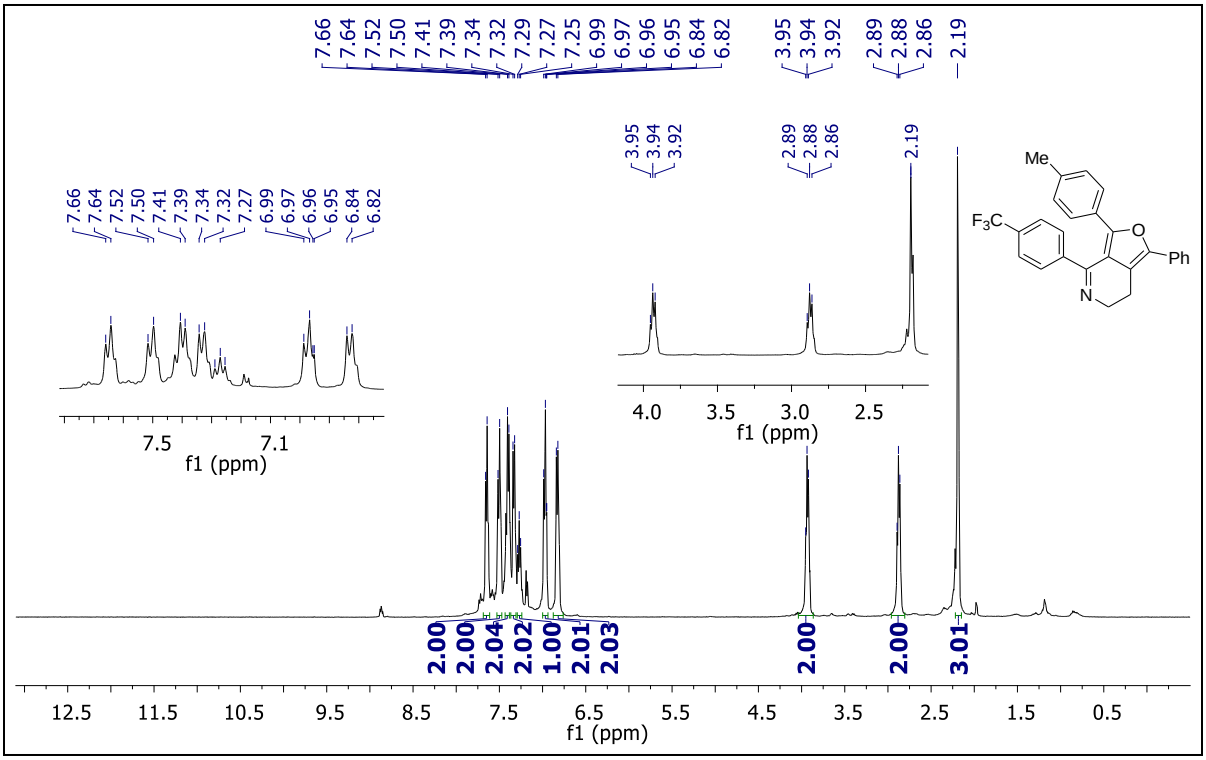


Figure S65. ^{1}H NMR Spectrum of compound **10o**.

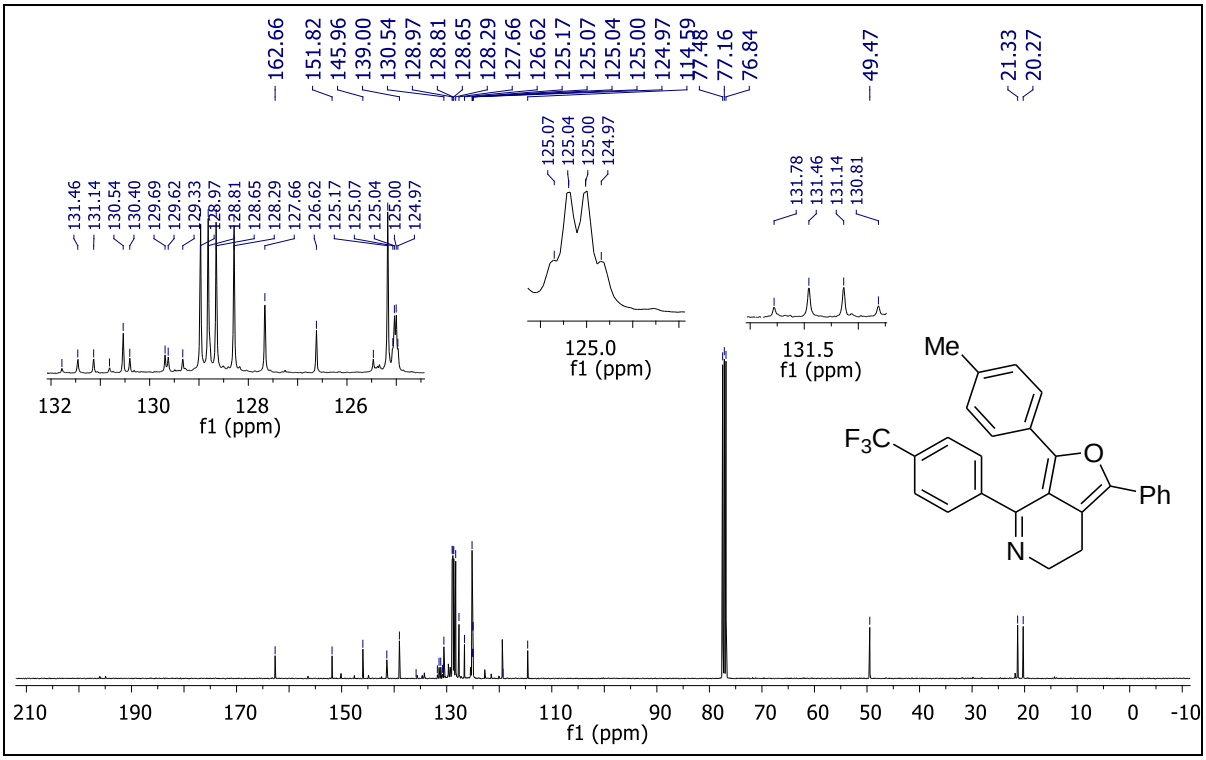


Figure S66. ^{13}C NMR Spectrum of compound **10o**.

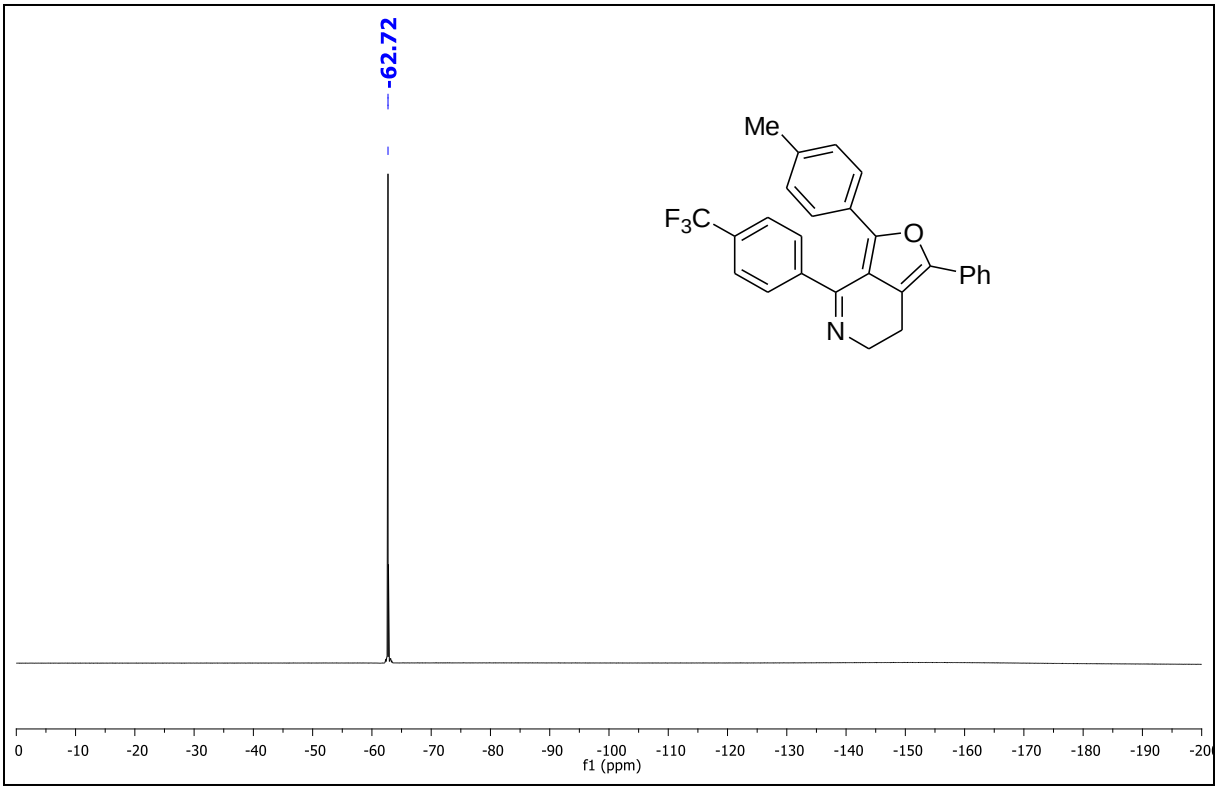


Figure S67. ^{19}F NMR Spectrum of compound **10o**.

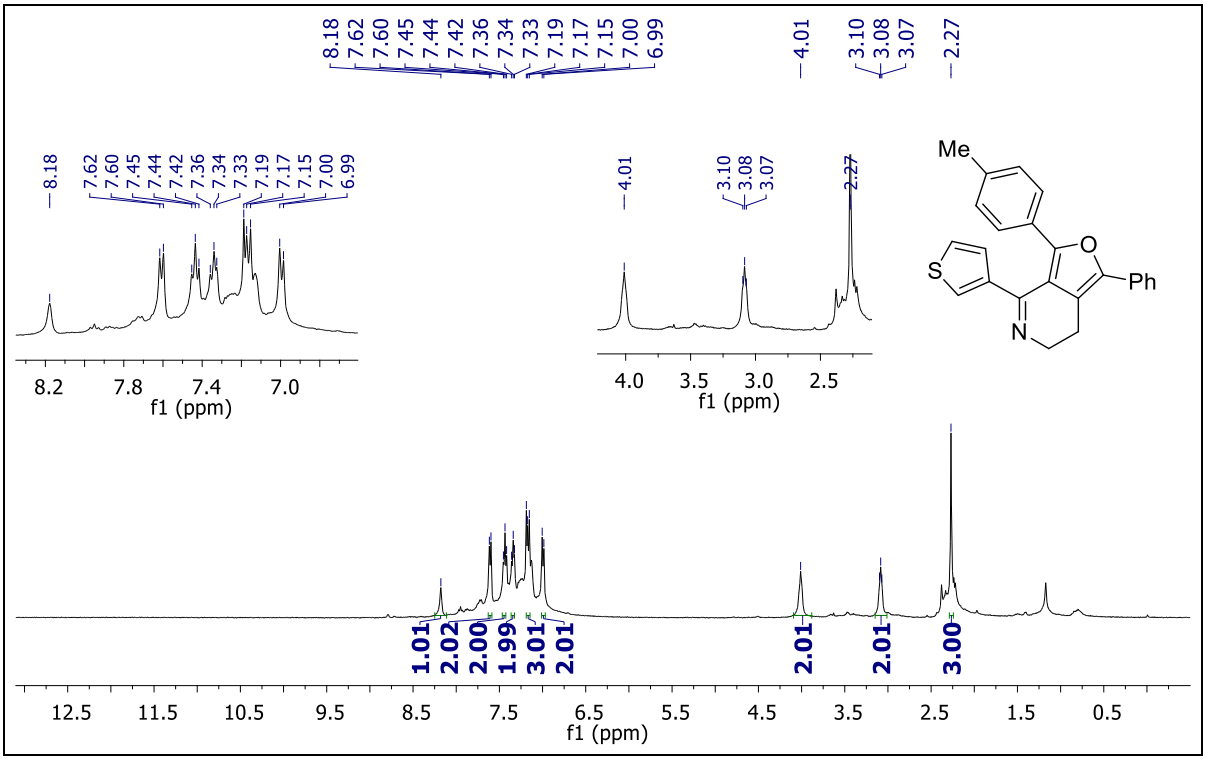


Figure S68. ^{1}H NMR Spectrum of compound **10p**.

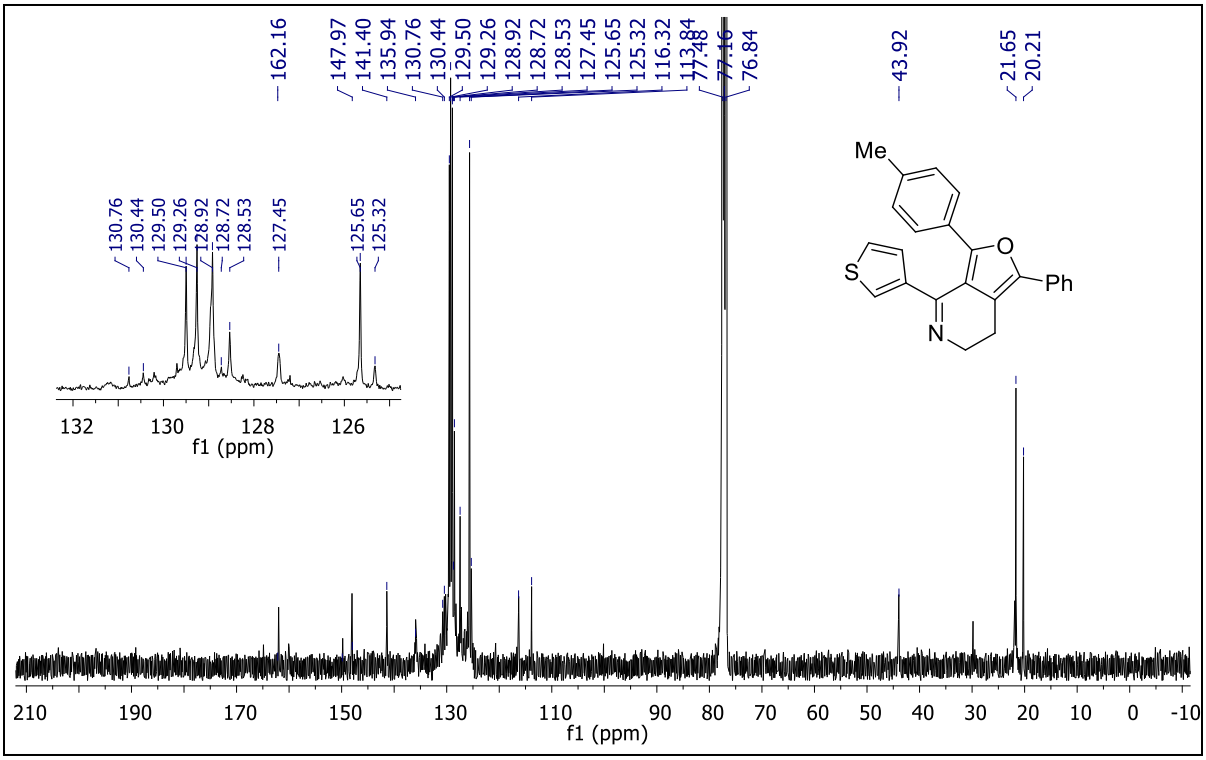


Figure S69. ^{13}C NMR Spectrum of compound **10p**.

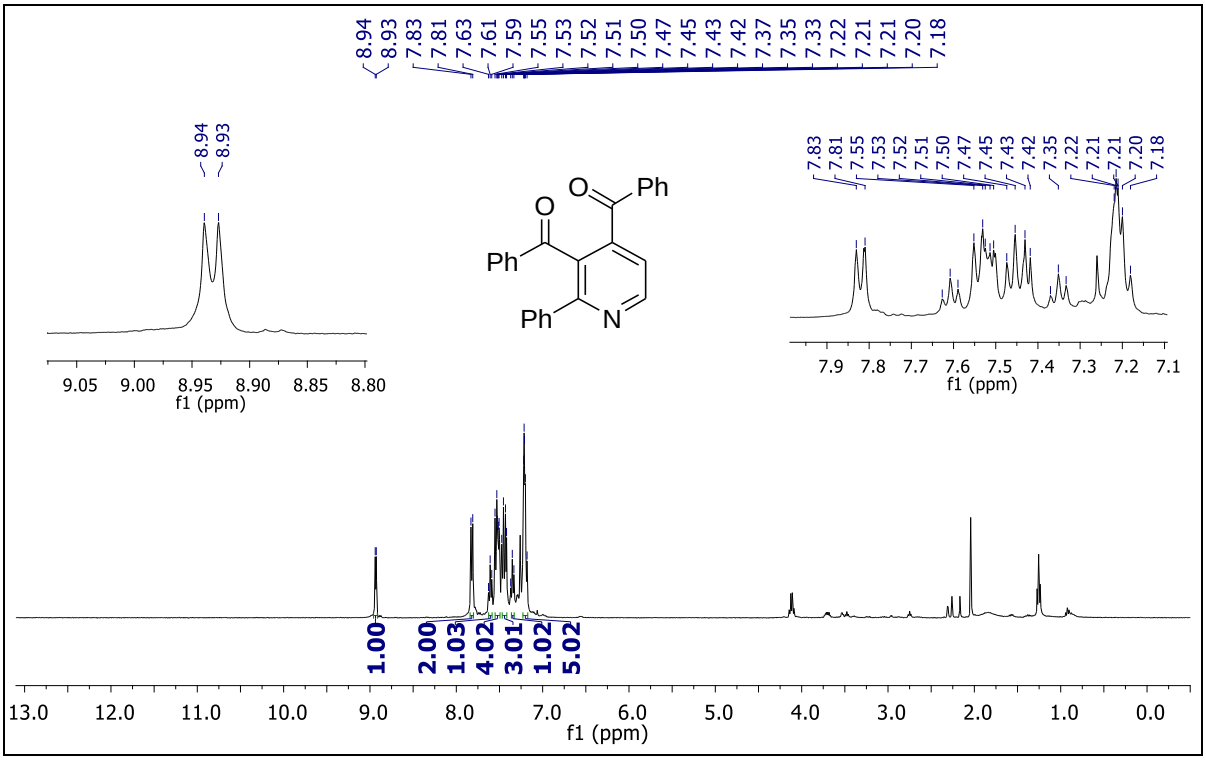


Figure S70. ^{1}H NMR Spectrum of compound **11a**.

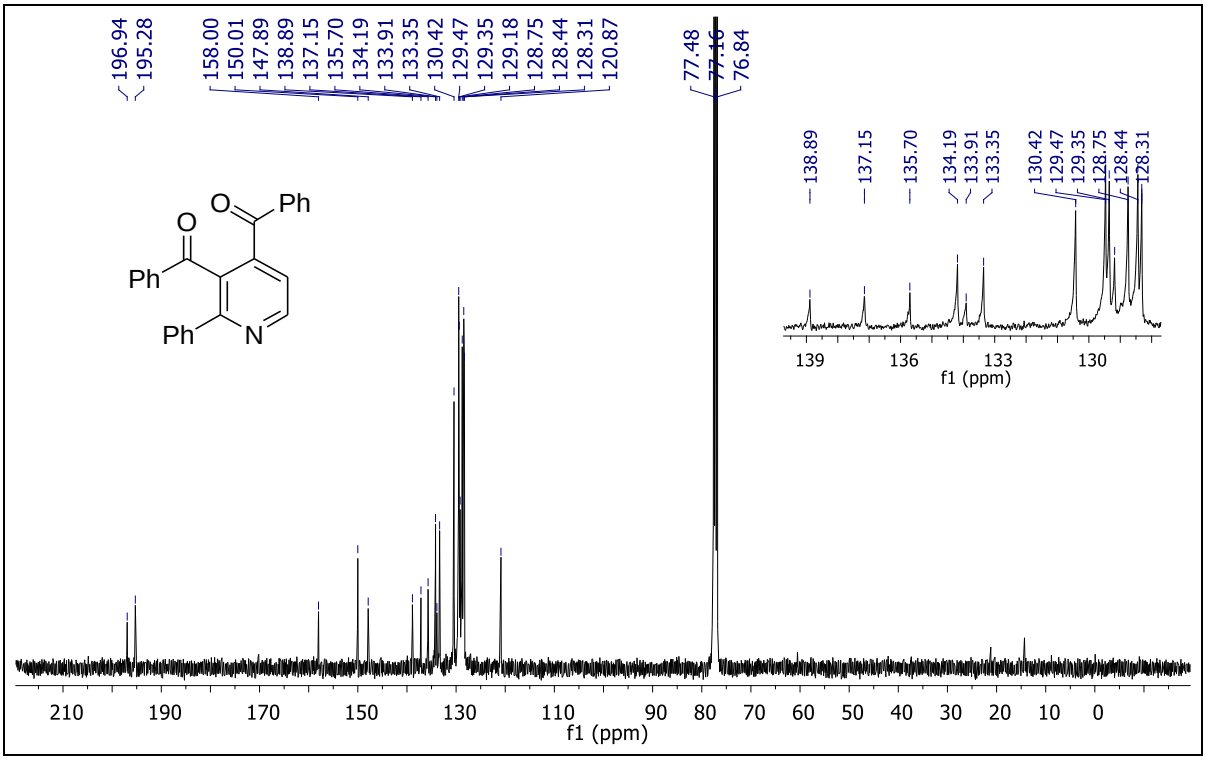


Figure S71. ^{13}C NMR Spectrum of compound **11a**.

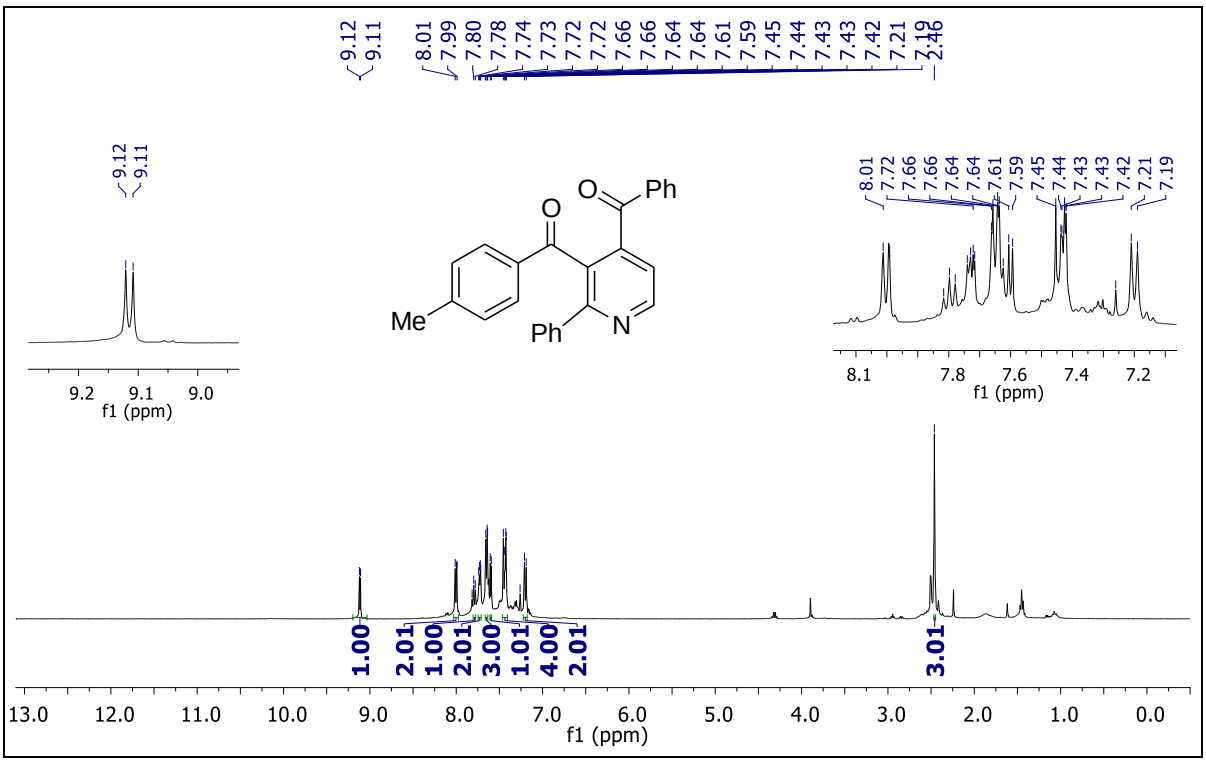


Figure S72. ^{1}H NMR Spectrum of compound **11d**.

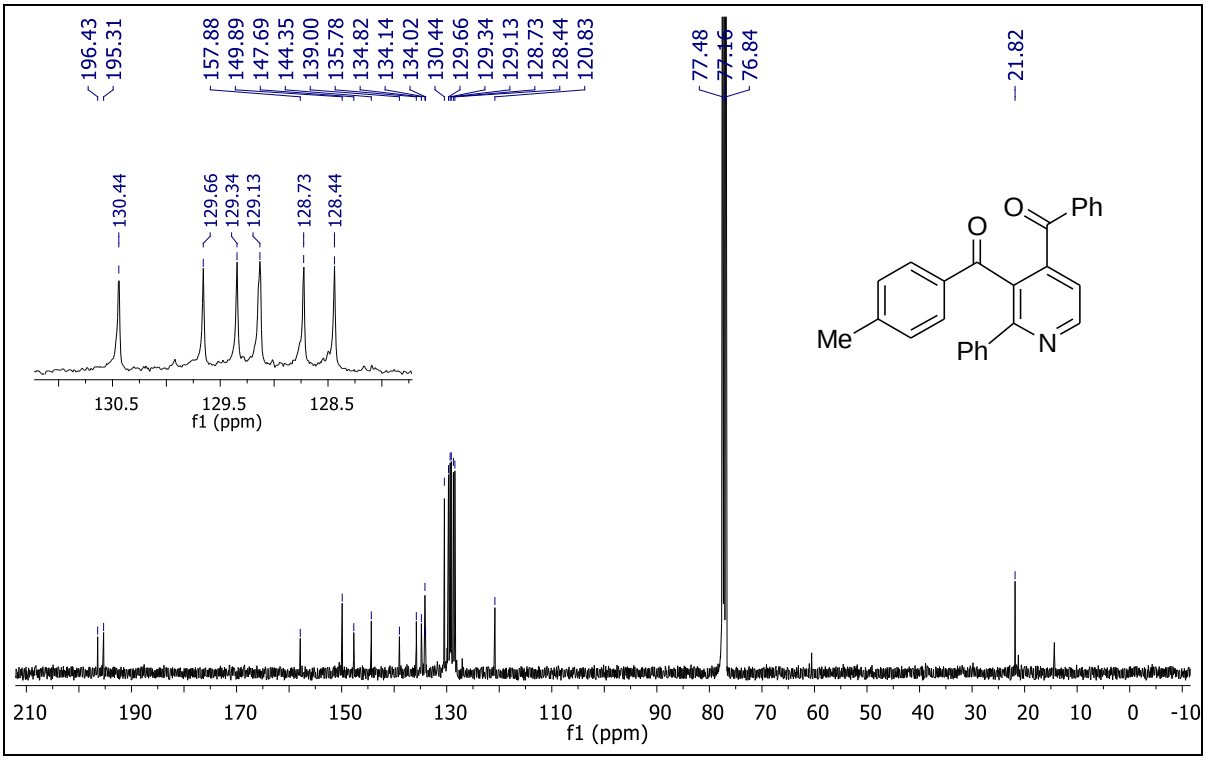


Figure S73. ^{13}C NMR Spectrum of compound **11d**.

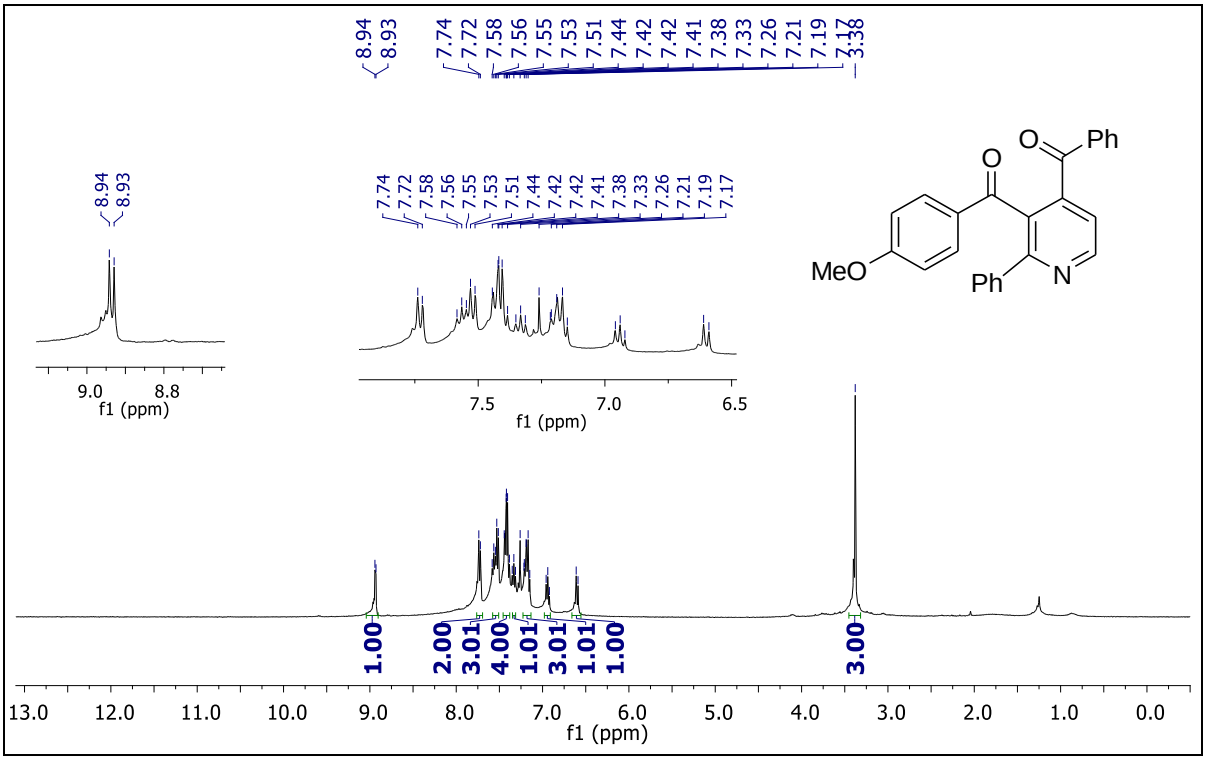


Figure S74. ^{1}H NMR Spectrum of compound **11f**.

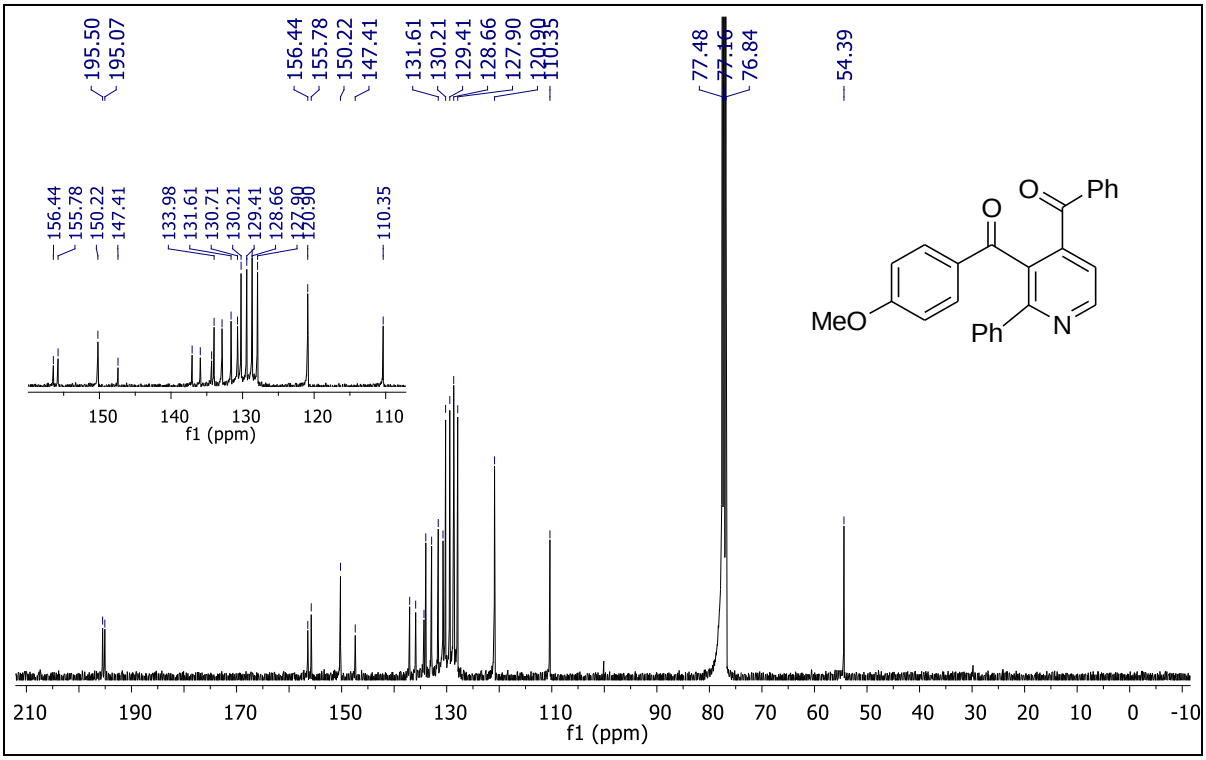


Figure S75. ^{13}C NMR Spectrum of compound **11f**.

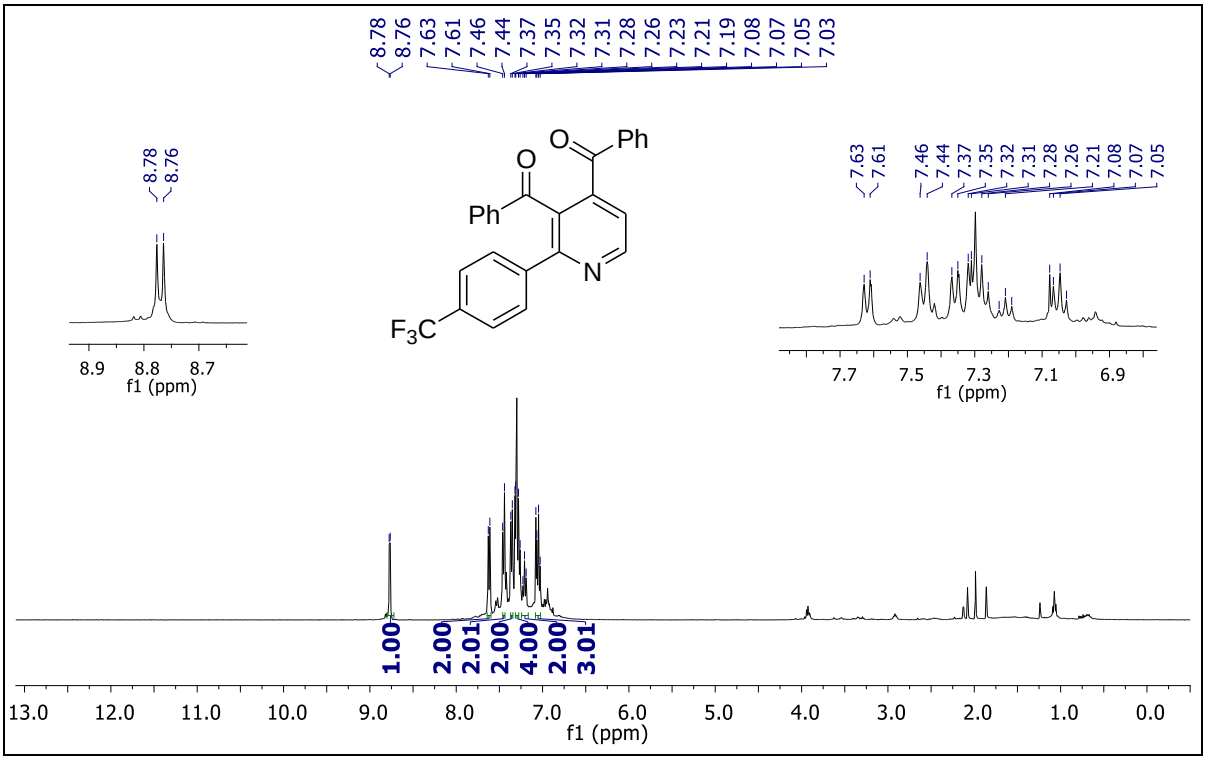


Figure S76. ^{1}H NMR Spectrum of compound **11h**.

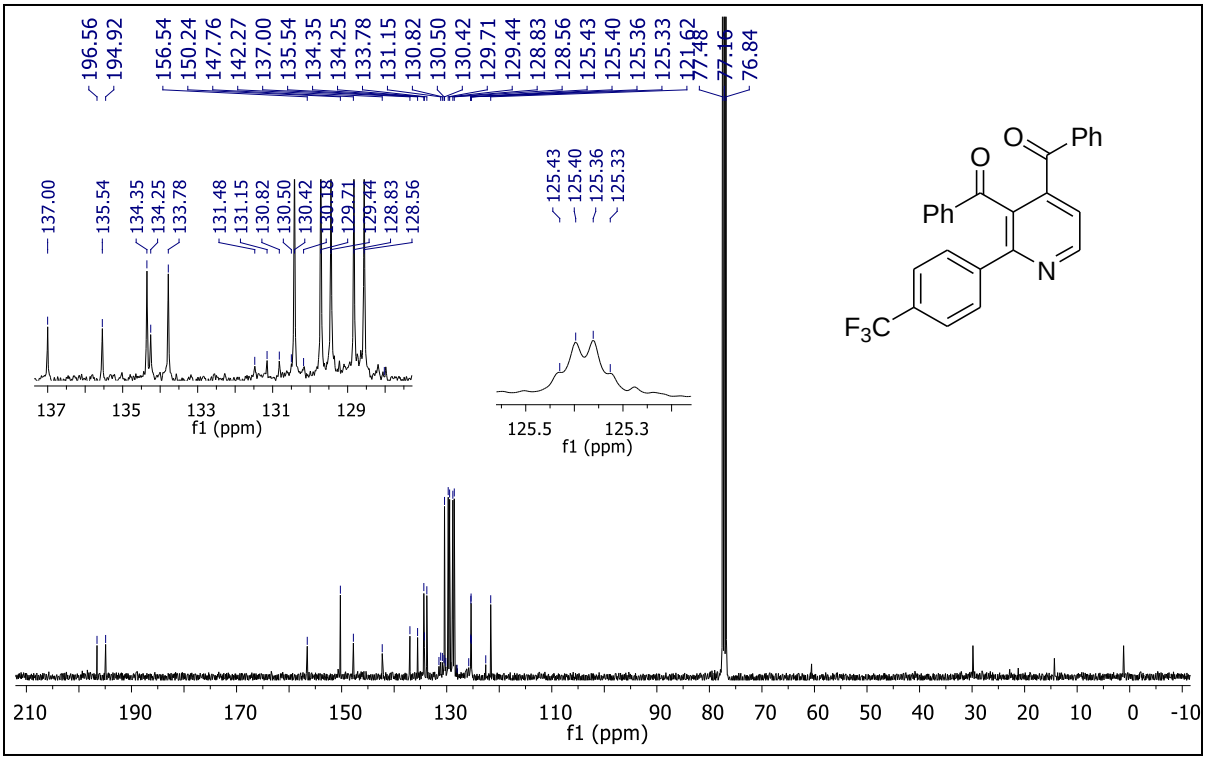


Figure S77. ^{13}C NMR Spectrum of compound **11h**.

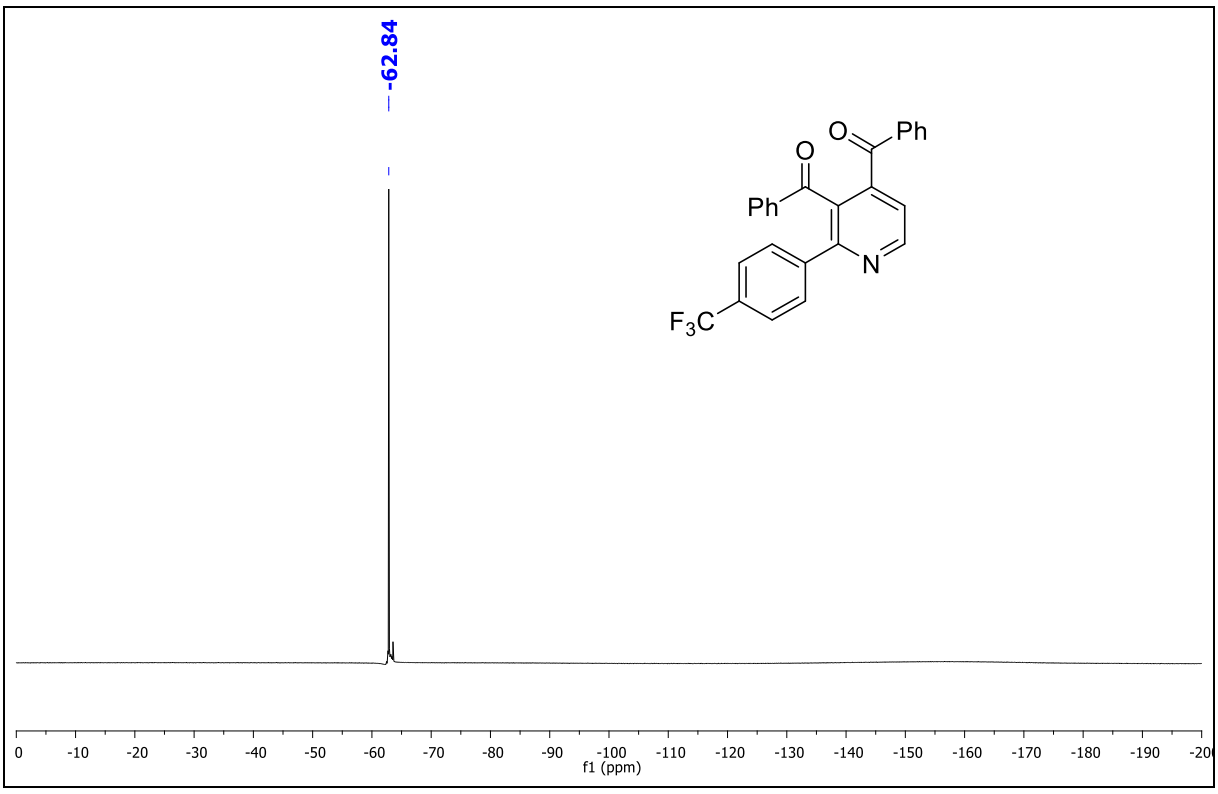


Figure S78. ^{19}F NMR Spectrum of compound **11h**.

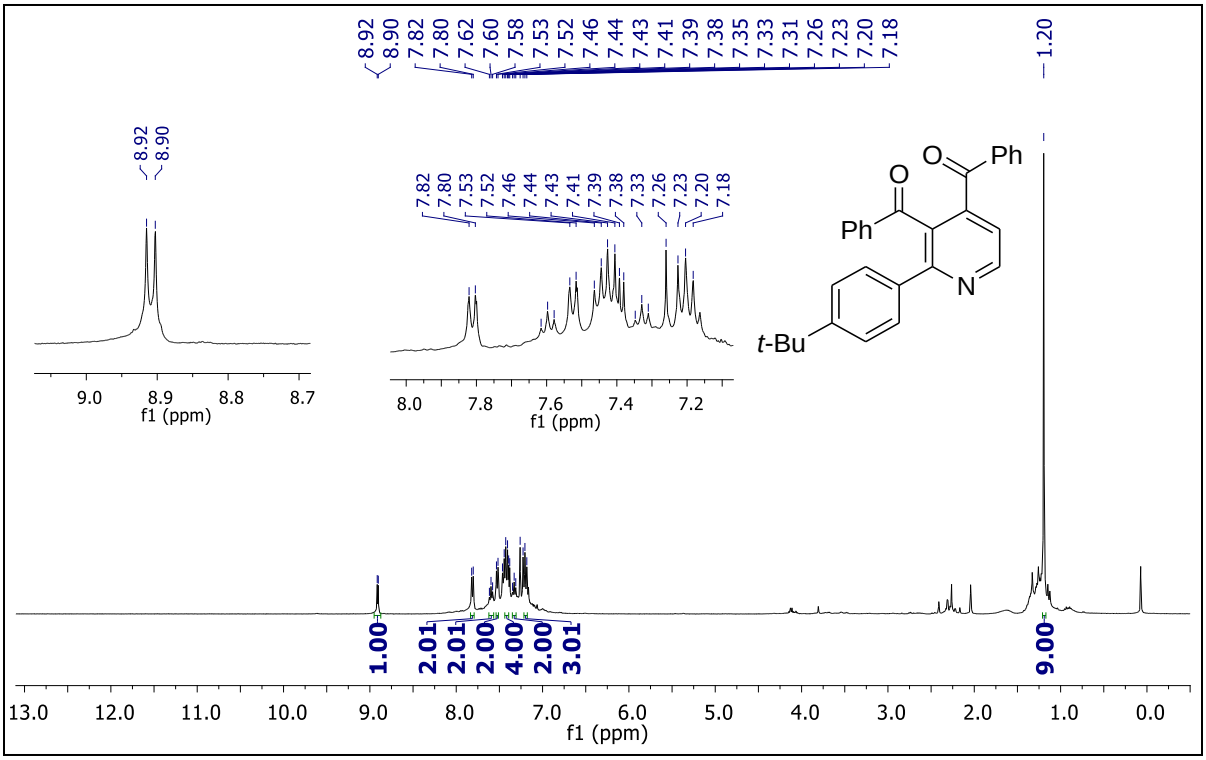


Figure S79. ^{1}H NMR Spectrum of compound **11j**.

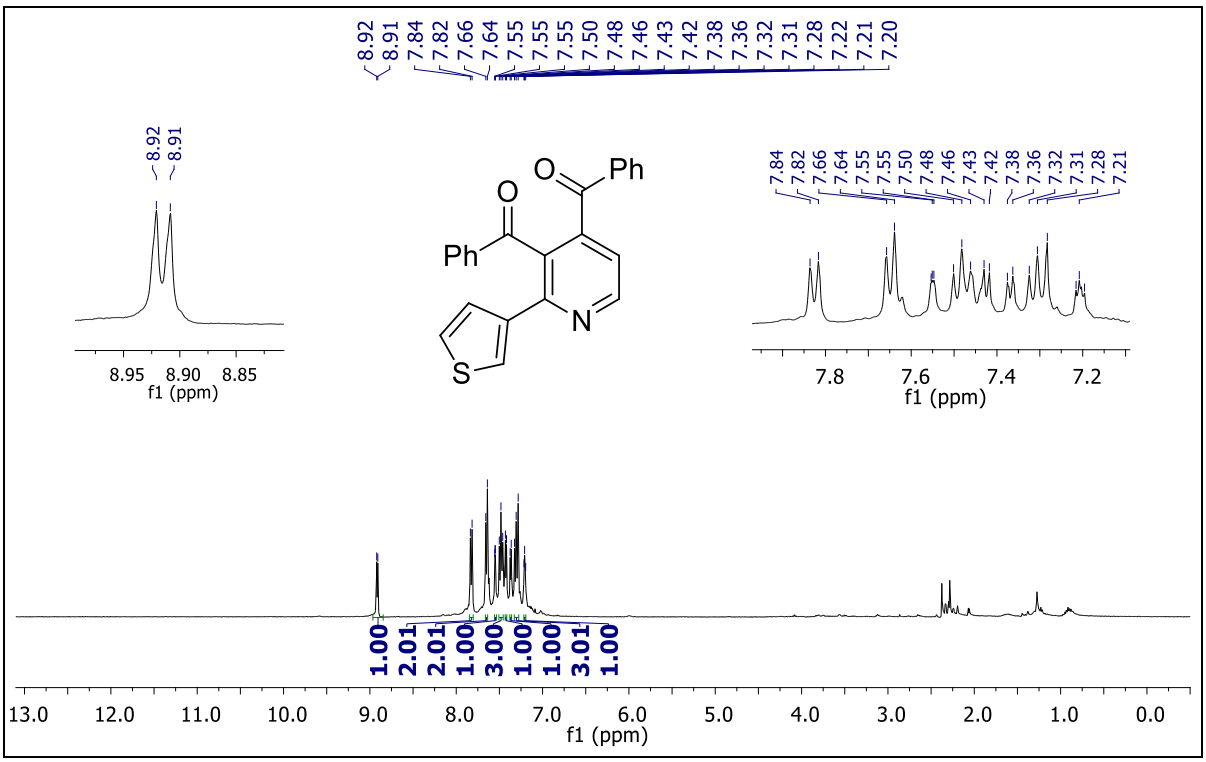


Figure S80. ^{1}H NMR Spectrum of compound **11l**.

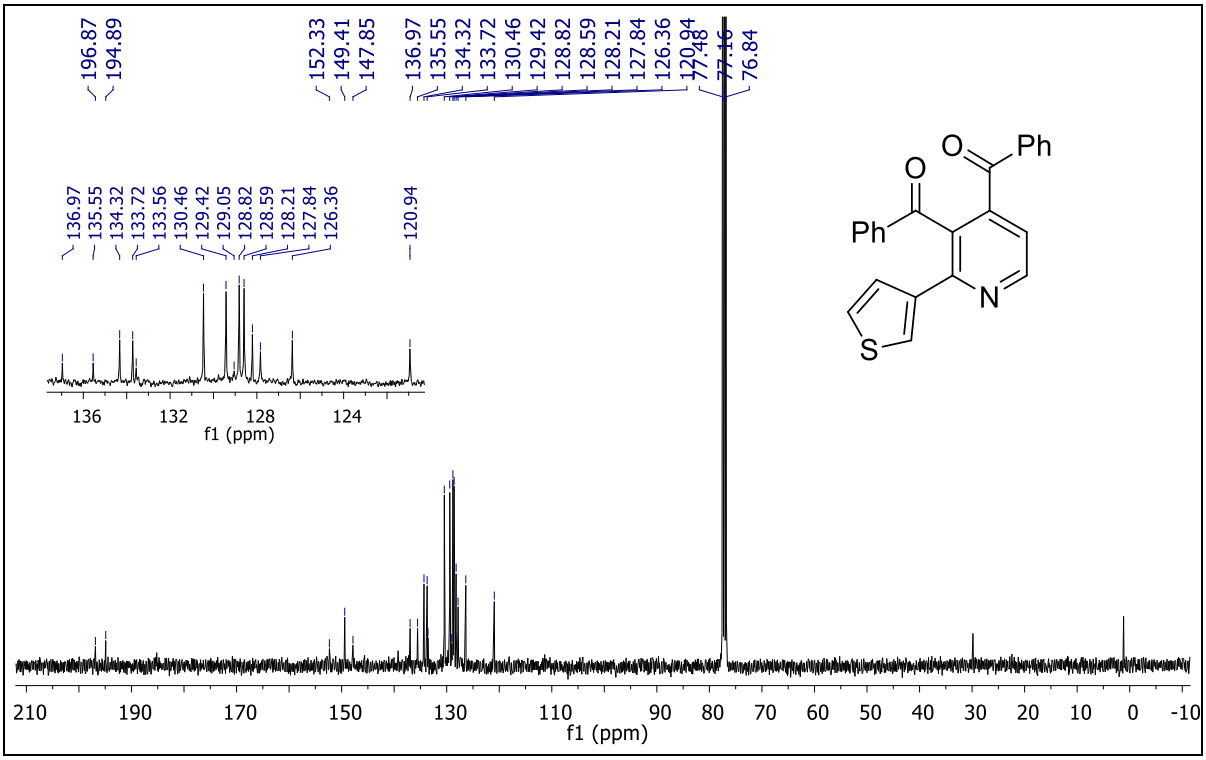


Figure S81. ^{13}C NMR Spectrum of compound **11l**.

X-Ray Crystallographic Data for CCDC 2379026

Crystal Structure Report for MZ (Compound 10a)

A specimen of $C_{25}H_{19}NO$ was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

Table S1. Data collection details for MZ.

Axis	dx/mm	2θ/°	ω/°	φ/°	χ/°	Width/°	Frames	Time/s	Wavelength/Å	Voltage/kV	Current/mA	Temperature/K
Omega	54.401	9.80	-177.51	-160.34	54.70	1.00	194	15.00	0.71076	50	30.0	297
Omega	54.401	9.80	-177.51	64.74	54.70	1.00	194	15.00	0.71076	50	30.0	297
Omega	54.401	8.70	-178.61	-72.00	54.70	1.00	194	15.00	0.71076	50	30.0	297
Omega	54.401	8.70	-178.61	0.00	54.70	1.00	194	15.00	0.71076	50	30.0	297
Omega	54.401	8.70	-178.61	144.00	54.70	1.00	194	15.00	0.71076	50	30.0	297
Phi	54.401	8.70	16.08	0.00	54.70	1.00	360	15.00	0.71076	50	30.0	297
Phi	54.401	8.70	-178.67	0.00	54.70	1.00	360	15.00	0.71076	50	30.0	297

A total of 1690 frames were collected. The total exposure time was 7.04 hours. The frames were integrated with the Bruker SAINT software package using a wide-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 68102 reflections to a maximum θ angle of 25.16° (0.84 Å resolution), of which 3352 were independent (average redundancy 20.317, completeness = 99.1%, R_{int} = 13.84%, R_{sig} = 6.17%) and 1807 (53.91%) were greater than $2\sigma(F^2)$. The final cell constants of a = 15.1533(19) Å, b = 9.0554(11) Å, c = 15.2139(19) Å, β = 115.586(3)°, volume = 1882.9(4) $Å^3$, are based upon the refinement of the XYZ-centroids of 9956 reflections above 20 σ(I) with 5.371° < 2θ < 41.51°. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.873.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group P 1 21/c 1, with Z = 4 for the formula unit, $C_{25}H_{19}NO$. The final anisotropic full-matrix least-squares refinement on F^2 with 320 variables converged at R1 = 5.88%, for the observed data and wR2 = 13.02% for all data. The goodness-of-fit was 1.094. The largest peak in the final difference electron density synthesis was 0.133 $e^-/Å^3$ and the largest hole was -0.153 $e^-/Å^3$ with an RMS deviation of 0.033 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.233 g/cm^3 and F(000), 736 e^-.

Table S2. Sample and crystal data for MZ.

Identification code	MZ
Chemical formula	$C_{25}H_{19}NO$

Formula weight	349.41 g/mol
Temperature	297(0) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	P 1 21/c 1
Unit cell dimensions	a = 15.1533(19) Å α = 90° b = 9.0554(11) Å β = 115.586(3)° c = 15.2139(19) Å γ = 90°
Volume	1882.9(4) $Å^3$
Z	4
Density (calculated)	1.233 g/cm^3
Absorption coefficient	0.075 mm^{-1}
F(000)	736

Table S3. Data collection and structure refinement for MZ.

Theta range for data collection	2.69 to 25.16°
Index ranges	-18<=h<=18, -10<=k<=10, -18<=l<=18
Reflections collected	68102
Independent reflections	3352 [R(int) = 0.1384]
Coverage of independent reflections	99.1%
Absorption correction	Multi-Scan
Structure solution technique	direct methods
Structure solution program	SHELXS-1997 (Sheldrick, 1997)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	3352 / 0 / 320

Goodness-of-fit on F^2	1.094	
Final R indices	1807 data; $I>2\sigma(I)$	R1 = 0.0588, wR2 = 0.1040
	all data	R1 = 0.1400, wR2 = 0.1302
Weighting scheme	$w=1/[\sigma^2(F_o^2)+(0.0374P)^2+0.7429P]$ where $P=(F_o^2+2F_c^2)/3$	
Largest diff. peak and hole	0.133 and -0.153 eÅ^{-3}	
R.M.S. deviation from mean	0.033 eÅ^{-3}	

Table S4. Atomic coordinates and equivalent isotropic atomic displacement parameters (Å^2) for MZ.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
O1	0.57858(12)	0.3098(2)	0.47288(12)	0.0537(5)
N1	0.66660(19)	0.4508(3)	0.78810(16)	0.0690(7)
C7	0.51715(19)	0.2619(3)	0.5139(2)	0.0502(7)
C11	0.64616(19)	0.3786(3)	0.62881(18)	0.0497(7)
C20	0.72912(18)	0.4378(3)	0.51293(17)	0.0481(7)
C8	0.55651(19)	0.3038(3)	0.60821(19)	0.0516(7)
C13	0.7061(2)	0.4312(3)	0.72848(19)	0.0542(7)
C6	0.43008(19)	0.1831(3)	0.44966(19)	0.0496(7)
C10	0.65640(19)	0.3808(3)	0.54361(18)	0.0496(7)
C14	0.8129(2)	0.4546(3)	0.76812(18)	0.0547(7)
C1	0.3920(2)	0.1956(3)	0.3493(2)	0.0600(8)
C21	0.7720(2)	0.5745(4)	0.5439(2)	0.0591(8)
C19	0.8725(3)	0.3699(4)	0.7396(2)	0.0646(9)
C5	0.3801(2)	0.0921(3)	0.4872(2)	0.0611(8)
C9	0.5231(3)	0.2902(4)	0.6872(2)	0.0646(9)
C24	0.8299(2)	0.4033(4)	0.4289(2)	0.0710(10)
C23	0.8722(3)	0.5389(4)	0.4605(2)	0.0743(10)
C25	0.7581(2)	0.3529(4)	0.4541(2)	0.0601(8)
C4	0.2971(2)	0.0187(4)	0.4263(3)	0.0713(9)

	x/a	y/b	z/c	U(eq)
C22	0.8430(2)	0.6251(4)	0.5174(2)	0.0707(9)
C12	0.5610(3)	0.4260(4)	0.7510(3)	0.0757(10)
C15	0.8578(3)	0.5623(4)	0.8394(2)	0.0741(9)
C2	0.3095(2)	0.1209(4)	0.2891(3)	0.0753(10)
C3	0.2610(3)	0.0329(4)	0.3275(3)	0.0752(10)
C18	0.9717(3)	0.3904(5)	0.7802(3)	0.0808(10)
C16	0.9566(3)	0.5832(5)	0.8788(3)	0.0906(11)
C17	0.0139(3)	0.4971(5)	0.8496(3)	0.0928(12)

Table S5. Bond lengths (Å) for MZ.

C19-H12	0.88(3)	C21-H13	0.94(2)
C24-H16	0.94(3)	C5-H5	0.95(3)
C4-H4	0.95(3)	C12-H7B	0.95(3)
C22-H14	0.96(3)	C17-H10	0.96(3)
C23-H15	0.97(3)	C15-H8	0.97(3)
C2-H2	0.97(3)	C25-H17	0.98(3)
C3-H3	0.98(3)	C18-H11	0.98(4)
C1-H1	0.99(3)	C9-H6B	0.99(3)
C16-H9	0.99(4)	C9-H6A	1.05(3)
C12-H7A	1.05(3)	N1-C13	1.296(3)
C7-C8	1.349(3)	C15-C16	1.364(5)
C4-C3	1.365(4)	O1-C10	1.366(3)
C1-C2	1.367(4)	C19-C18	1.369(5)
C18-C17	1.369(5)	C11-C10	1.371(3)
C5-C4	1.371(4)	C24-C23	1.372(5)
C23-C22	1.373(5)	C2-C3	1.374(4)
C16-C17	1.375(5)	C24-C25	1.377(4)
C21-C22	1.380(4)	C20-C21	1.383(4)
C6-C1	1.384(4)	C20-C25	1.388(4)
C14-C19	1.389(4)	O1-C7	1.395(3)
C6-C5	1.397(4)	C14-C15	1.397(4)
C11-C8	1.427(3)	C7-C6	1.446(4)
C20-C10	1.464(3)	N1-C12	1.466(4)
C11-C13	1.470(4)	C13-C14	1.479(4)
C8-C9	1.497(4)	C9-C12	1.518(4)

Table S6. Bond angles (°) for MZ.

C10-O1-C7	108.07(18)	C13-N1-C12	117.8(2)
C8-C7-O1	108.3(2)	C8-C7-C6	135.4(2)
O1-C7-C6	116.2(2)	C10-C11-C8	106.6(2)
C10-C11-C13	134.4(2)	C8-C11-C13	119.1(2)
C21-C20-C25	118.9(3)	C21-C20-C10	121.0(2)
C25-C20-C10	120.1(3)	C7-C8-C11	108.0(2)
C7-C8-C9	133.1(3)	C11-C8-C9	118.9(2)
N1-C13-C11	120.0(3)	N1-C13-C14	116.7(2)
C11-C13-C14	123.1(2)	C1-C6-C5	117.2(3)
C1-C6-C7	122.0(2)	C5-C6-C7	120.8(2)
O1-C10-C11	109.1(2)	O1-C10-C20	115.3(2)
C11-C10-C20	135.6(3)	C19-C14-C15	117.6(3)
C19-C14-C13	122.6(3)	C15-C14-C13	119.8(3)
C2-C1-C6	121.6(3)	C2-C1-H1	120.2(15)
C6-C1-H1	118.2(15)	C22-C21-C20	120.5(3)
C22-C21-H13	119.3(16)	C20-C21-H13	120.1(15)
C18-C19-C14	121.3(4)	C18-C19-H12	120.0(17)
C14-C19-H12	118.6(18)	C4-C5-C6	120.7(3)
C4-C5-H5	121.8(16)	C6-C5-H5	117.5(16)
C8-C9-C12	106.3(3)	C8-C9-H6A	110.4(14)
C12-C9-H6A	110.1(14)	C8-C9-H6B	110.4(15)
C12-C9-H6B	110.2(15)	H6A-C9-H6B	109.(2)
C23-C24-C25	120.3(3)	C23-C24-H16	121.(2)
C25-C24-H16	118.(2)	C24-C23-C22	120.0(3)

C24-C23-H15	123.(2)	C22-C23-H15	117.(2)
C24-C25-C20	120.3(3)	C24-C25-H17	122.8(15)
C20-C25-H17	116.8(15)	C3-C4-C5	120.9(3)
C3-C4-H4	121.8(16)	C5-C4-H4	117.3(16)
C23-C22-C21	120.0(3)	C23-C22-H14	121.2(17)
C21-C22-H14	118.7(17)	N1-C12-C9	114.7(3)
N1-C12-H7A	110.2(18)	C9-C12-H7A	108.0(18)
N1-C12-H7B	107.3(18)	C9-C12-H7B	110.8(18)
H7A-C12-H7B	105.(2)	C16-C15-C14	120.8(4)
C16-C15-H8	122.(2)	C14-C15-H8	117.(2)
C1-C2-C3	120.2(3)	C1-C2-H2	120.4(16)
C3-C2-H2	119.3(16)	C4-C3-C2	119.3(3)
C4-C3-H3	119.7(16)	C2-C3-H3	120.9(16)
C19-C18-C17	120.0(4)	C19-C18-H11	118.(2)
C17-C18-H11	122.(2)	C15-C16-C17	120.4(4)
C15-C16-H9	122.(2)	C17-C16-H9	117.(2)
C18-C17-C16	120.0(4)	C18-C17-H10	121.3(19)
C16-C17-H10	118.7(19)		

Table S7. Anisotropic atomic displacement parameters (Å^2) for MZ.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U_{11} + ... + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
O1	0.0559(12)	0.0656(12)	0.0472(11)	-0.0031(10)	0.0295(10)	-0.0059(10)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
N1	0.093(2)	0.0667(17)	0.0654(16)	-0.0117(13)	0.0517(15)	-0.0164(14)
C7	0.0540(17)	0.0516(17)	0.0558(18)	0.0047(14)	0.0340(16)	-0.0001(14)
C11	0.0647(18)	0.0462(16)	0.0466(16)	-0.0021(13)	0.0320(14)	-0.0029(14)
C20	0.0557(17)	0.0527(18)	0.0410(15)	0.0022(13)	0.0258(13)	-0.0022(14)
C8	0.0623(18)	0.0509(17)	0.0529(18)	-0.0007(14)	0.0356(15)	-0.0033(15)
C13	0.076(2)	0.0446(17)	0.0535(17)	0.0033(14)	0.0393(17)	-0.0017(15)
C6	0.0498(17)	0.0527(17)	0.0542(18)	0.0002(14)	0.0298(15)	0.0045(14)
C10	0.0525(17)	0.0533(17)	0.0461(16)	-0.0025(14)	0.0243(15)	-0.0033(14)
C14	0.070(2)	0.0504(18)	0.0448(16)	0.0039(14)	0.0258(15)	-0.0008(16)
C1	0.065(2)	0.065(2)	0.058(2)	-0.0036(17)	0.0343(18)	-0.0077(17)
C21	0.073(2)	0.058(2)	0.0568(18)	0.0010(16)	0.0376(17)	-0.0018(17)
C19	0.078(3)	0.059(2)	0.057(2)	0.0016(18)	0.0286(19)	0.0007(19)
C5	0.063(2)	0.062(2)	0.058(2)	0.0095(17)	0.0254(18)	-0.0030(17)
C9	0.083(3)	0.070(2)	0.060(2)	-0.0035(19)	0.0492(19)	-0.010(2)
C24	0.086(2)	0.085(3)	0.064(2)	0.0068(19)	0.0524(19)	0.009(2)
C23	0.063(2)	0.094(3)	0.073(2)	0.016(2)	0.0360(19)	-0.007(2)
C25	0.072(2)	0.066(2)	0.0540(18)	-0.0037(16)	0.0383(17)	-0.0071(18)
C4	0.069(2)	0.065(2)	0.084(3)	0.0137(19)	0.037(2)	-0.0101(18)
C22	0.079(2)	0.068(2)	0.068(2)	-0.0010(19)	0.0349(19)	-0.018(2)
C12	0.102(3)	0.081(3)	0.078(2)	-0.019(2)	0.070(2)	-0.017(2)
C15	0.077(3)	0.075(2)	0.062(2)	-0.0125(19)	0.022(2)	-0.005(2)
C2	0.073(2)	0.092(3)	0.058(2)	-0.001(2)	0.026(2)	-0.012(2)

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C3	0.070(2)	0.070(2)	0.077(3)	-0.004(2)	0.024(2)	-0.0151(19)
C18	0.070(3)	0.092(3)	0.075(2)	0.004(2)	0.027(2)	0.010(2)
C16	0.077(3)	0.092(3)	0.082(3)	-0.017(2)	0.015(2)	-0.007(2)
C17	0.064(3)	0.106(3)	0.090(3)	0.005(3)	0.016(2)	-0.001(3)

Table S8. Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å^2) for MZ.

	x/a	y/b	z/c	U(eq)
H6A	0.446(2)	0.287(3)	0.6572(17)	0.067(8)
H6B	0.5504(18)	0.199(3)	0.7260(19)	0.069(9)
H5	0.4067(18)	0.082(3)	0.556(2)	0.060(8)
H4	0.2667(19)	-0.043(3)	0.4555(19)	0.074(9)
H1	0.4261(18)	0.260(3)	0.3217(18)	0.067(8)
H2	0.2844(19)	0.130(3)	0.219(2)	0.073(9)
H3	0.203(2)	-0.023(3)	0.285(2)	0.079(10)
H7A	0.522(2)	0.518(4)	0.711(2)	0.101(12)
H7B	0.547(2)	0.421(3)	0.806(2)	0.085(10)
H12	0.8454(18)	0.301(3)	0.6954(19)	0.059(9)
H11	1.011(3)	0.327(4)	0.759(2)	0.111(13)
H9	0.991(3)	0.656(4)	0.931(3)	0.124(14)
H8	0.816(2)	0.619(4)	0.861(2)	0.096(11)
H10	1.084(2)	0.512(3)	0.880(2)	0.092(11)
H17	0.7230(18)	0.260(3)	0.4295(18)	0.064(9)
H14	0.873(2)	0.718(3)	0.5420(19)	0.073(10)
H16	0.851(2)	0.341(4)	0.393(2)	0.098(12)
H15	0.926(2)	0.576(4)	0.448(2)	0.104(11)
H13	0.7519(17)	0.635(3)	0.5823(18)	0.059(8)

REFERENCES

1. Shen, S.; Hadley, M.; Ustinova, K.; Pavlicek, J.; Knox, T.; Noonepallas, S.; Tavares, M. T.; Zimprich, C. A.; Zhang, G.; Robers, M. B.; Barinka, C.; Kozikowski, A. P.; Villagra, A. Discovery of a New Isoxazole-3-hydroxamate-Based Histone Deacetylase 6 Inhibitor SS-208 with Antitumor Activity in Syngeneic Melanoma Mouse Models. *J. Med. Chem.* **2019**, *62*, 8557–8577.

2. Fragkiadakis, M.; Kidonakis, M.; Zorba, L.; Stratakis, M. Synthesis of 3-Keto Pyridines from the Conjugated Allenone – Alkynylamine Oxidative Cyclization Catalyzed by Supported Au Nanoparticles. *Adv. Synth. Catal.* **2020**, *362*, 964–968.