

Supporting information

A Detailed Study of the Intramolecular Hydroamination of *N*-(*ortho*-alkynyl)aryl-*N*'-Substituted Trifluoroacetamides and Bromodifluoroacetamides

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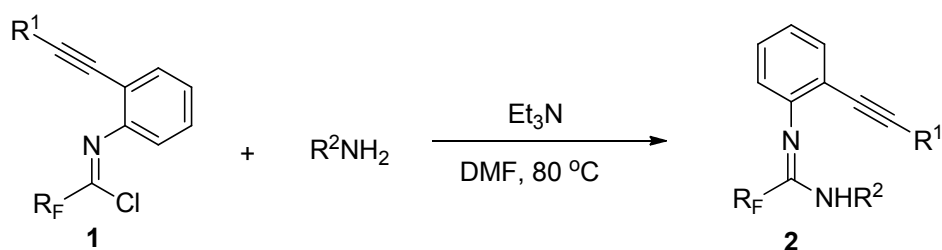
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General:

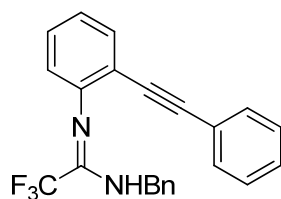
Melting points were measured on a Melt-Temp apparatus and uncorrected. ¹H NMR spectra were recorded in CDCl₃ on a Bruker AM-300 spectrometer (300 MHz) with TMS as internal standard. ¹³C NMR spectra were taken on a Bruker AM-400 (100 MHz) spectrometer. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Elemental analysis was performed by the Analytical Laboratory of Shanghai Institute of Organic Chemistry. Mass spectra were recorded by EI methods. HRMS (EI) was measured on Waters Micromass GCT Premier mass spectrometer. Solvents and reagents were purchased from commercial sources and used as received. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure and petroleum ether/ethyl acetate combination was used as the eluent.

1. Synthesis of **2** from the corresponding acetimidoyl chloride and amine.



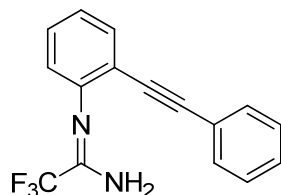
A 50 mL flask was charged fluorinated acetimidoyl chloride **1** (6 mmol), the corresponding amine (7.2 mmol), triethylamine (727 mg, 7.2 mmol), DMF (20 mL). The resulting mixture was stirred at $80\text{ }^\circ\text{C}$ for 2 h. Water (10 mL) was added to the mixture, which was then extracted with ethyl acetate ($20\text{ mL} \times 3$). The combined organic layers were washed by saturated salt water, dried over $MgSO_4$ and concentrated in vacuo, giving a residue which was subjected to silica gel chromatography to furnish the pure product **2**.

N-Benzyl-2,2,2-trifluoro-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2a**)



1H NMR (300 MHz, $CDCl_3$): δ 7.81 – 6.61 (m, 14H), 5.26 (brs, 1H), 4.47 (brs, 2H); MS (EI): m/z (%): 278 (20.83) [M^+], 91 (100.00); Anal. Calcd. for $C_{23}H_{17}F_3N_2$: C, 73.01; H, 4.53; N, 7.40; Found: C, 72.94; H, 4.65; N, 7.25; IR (film): ν 3426, 3063, 3030, 1680, 1530, 1493, 1206, 1148, 754 cm^{-1} .

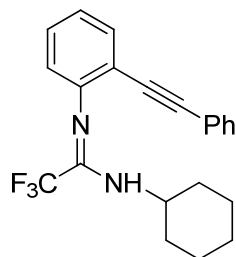
2,2,2-trifluoro-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2b**)



1H NMR (300 MHz, $CDCl_3$): δ 7.67 – 7.23 (m, 7H), 7.11 (t, $J = 7.6\text{ Hz}$, 1H), 6.96 (d, $J = 7.9\text{ Hz}$, 1H), 4.92 (brs, 2H); MS (EI): m/z (%): 288 (61.40) [M^+], 193 (100.00); HRMS (EI) Calcd. for $C_{16}H_{11}F_3N_2$: 288.0874, Found: 288.0880; IR (film): ν 3464, 3388, 3323, 3160, 1681, 1593, 1493,

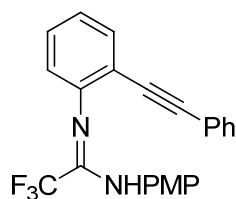
1424, 1209, 1166, 754 cm⁻¹.

N-Cyclohexyl-2,2,2-trifluoro-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2d**)



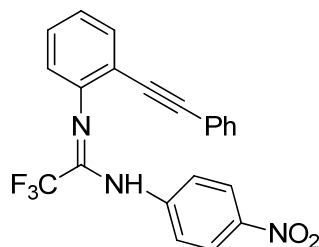
¹H NMR (300 MHz, CDCl₃): δ 7.82 – 6.34 (m, 9H), 4.88 (brs, 1H), 3.67 (brs, 1H), 2.31 – 1.80 (s, 2H), 1.80 – 0.93 (m, 8H); MS (EI): m/z (%): 370 (49.84) [M⁺], 288 (100.00); HRMS (EI) Calcd. for C₂₂H₂₁F₃N₂: 370.1657, Found: 370.1658; IR (film): ν 3285, 2922, 2851, 1655, 1544, 1187, 1151, 752 cm⁻¹.

2,2,2-Trifluoro-*N*-(4-methoxyphenyl)-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2e**)



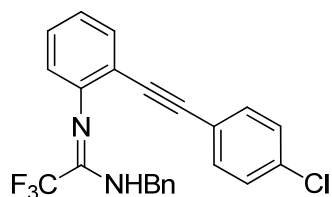
¹H NMR (300 MHz, CDCl₃): δ 8.85 – 6.10 (m, 14H), 3.73 (s, 3H); MS (EI): m/z (%): 394 (8.08) [M⁺], 204 (100.00); Anal. Calcd. for C₂₃H₁₇F₃N₂O: C, 70.04; H, 4.34; N, 7.10; Found: C, 70.21; H, 4.32; N, 7.06; IR (film): ν 3383, 3057, 2851, 1668, 1510, 1243, 1147, 1033, 754 cm⁻¹.

2,2,2-Trifluoro-*N*-(4-nitrophenyl)-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2g**)



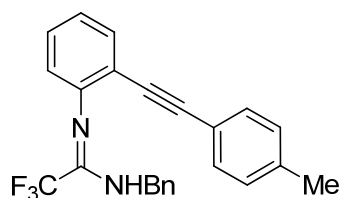
¹H NMR (300 MHz, CDCl₃): δ 8.54 – 6.61 (m, 14H); MS (EI): m/z (%): 409 (100.00) [M⁺]; Anal. Calcd. for C₂₂H₁₄F₃N₃O: C, 64.55; H, 3.45; N, 10.26; Found: C, 64.73; H, 3.54; N, 10.23; IR (film): ν 3377, 1682, 1580, 1541, 1508, 1337, 1163, 1128, 754 cm⁻¹.

N-benzyl-*N'*-(2-((4-chlorophenyl)ethynyl)phenyl)-2,2,2-trifluoroacetimidamide (**2h**)



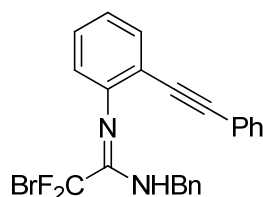
¹H NMR (300 MHz, CDCl₃): δ 7.68 – 6.62 (m, 13H), 5.29 (brs, 1H), 4.46 (brs, 2H); MS (EI): m/z (%): 412 (15.32) [M⁺], 91 (100.00); HRMS (EI) Calcd. for C₂₃H₁₆ClF₃N₂: 412.0954; Found: 421.0955; IR (film): ν 3426, 3057, 3030, 1678, 1530, 1493, 1207, 1147, 828, 751 cm⁻¹.

N-Benzyl-2,2,2-trifluoro-*N'*-(2-(*p*-tolylethynyl)phenyl)acetimidamide (**2i**)



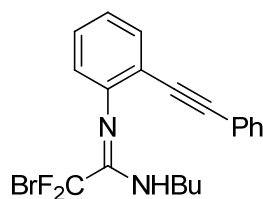
¹H NMR (300 MHz, CDCl₃): δ 7.59 – 6.71 (m, 13H), 5.25 (brs, 1H), 4.43 (brs, 2H), 2.36 (s, 3H); MS (EI): m/z (%): 392 (2.52) [M⁺], 204 (100.00); Anal. Calcd. for C₂₄H₁₉F₃N₂: C, 73.46; H, 4.88; N, 7.14; Found: C, 73.53; H, 4.89; N, 7.07; IR (film): ν 3426, 3068, 3035, 2927, 1681, 1526, 1510, 1207, 1147, 816, 750 cm⁻¹.

N-Benzyl-2-bromo-2,2-difluoro-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2j**)



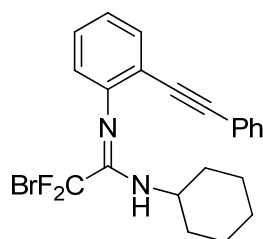
¹H NMR (300 MHz, CDCl₃): δ 7.60 – 6.87 (m, 14H), 5.22 (brs, 1H), 4.39 (brs, 2H); MS (EI): m/z (%): 438 (6.97) [M⁺], 91 (100.00); Anal. Calcd. for C₂₃H₁₇BrF₂N₂: C, 62.88; H, 3.90; N, 6.38; Found: C, 63.08; H, 3.92; N, 6.34; IR (film): ν 3426, 3063, 3052, 1673, 1520, 1493, 1170, 1110, 919, 857, 754 cm⁻¹.

2-Bromo-*N*-butyl-2,2-difluoro-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2k**)



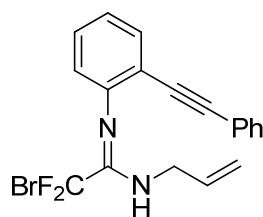
^1H NMR (300 MHz, CDCl_3): δ 7.50 – 6.87 (m, 9H), 4.93 (brs, 1H), 3.14 (brs, 2H), 1.49 (brs, 2H), 1.29 – 1.24 (m, 2H), 0.82(t, J = 6.9 Hz, 3H); MS (EI): m/z (%): 404 (4.22) [M^+], 187 (100.00); HRMS (EI) Calcd. for $\text{C}_{20}\text{H}_{19}\text{BrF}_2\text{N}_2$: 404.0700, Found: 404.0702; IR (film): ν 3421, 3057, 2959, 2932, 2862, 1673, 1523, 1493, 1174, 1112, 911, 755 cm^{-1} .

2-Bromo-*N*-cyclohexyl-2,2-difluoro-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2l**)



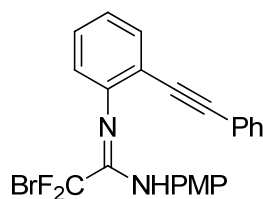
^1H NMR (300 MHz, CDCl_3): δ 7.50 – 6.87 (m, 9H), 4.83 (brs, 1H), 3.46 (brs, 1H), 1.99 (brs, 2H), 1.64 – 1.10 (m, 8H); MS (EI): m/z (%): 430 (31.10) [M^+], 98 (100.00); Anal. Calcd. for $\text{C}_{22}\text{H}_{21}\text{BrF}_2\text{N}_2$: C, 61.26; H, 4.91; N, 6.49; Found: C, 61.40; H, 4.95; N, 6.45; IR (film): ν 3415, 3046, 2931, 2854, 1668, 1515, 1493, 1472, 1170, 1110, 896, 754 cm^{-1} .

N-Allyl-2-bromo-2,2-difluoro-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2m**)



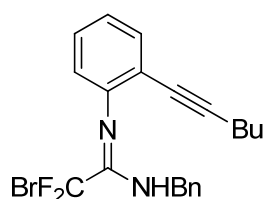
^1H NMR (300 MHz, CDCl_3): δ 7.78 – 6.63 (m, 9H), 5.84 (brs, 1H), 5.40 – 4.75 (m, 3H), 3.83 (brs, 2H); MS (EI): m/z (%): 388 (43.08) [M^+], 254 (100.00); HRMS (EI) Calcd. for $\text{C}_{19}\text{H}_{15}\text{BrF}_2\text{N}_2$: 388.0387, Found: 388.0393; IR (film): ν 3421, 3057, 3019, 1673, 1518, 1493, 1473, 1174, 1112, 924, 755 cm^{-1} .

2-Bromo-2,2-difluoro-*N*-(4-methoxyphenyl)-*N'*-(2-(phenylethynyl)phenyl)acetimidamide (**2n**)



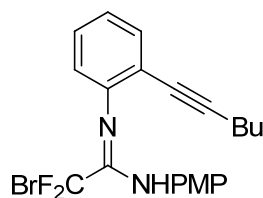
^1H NMR (300 MHz, CDCl_3): δ 9.14 – 6.28 (m, 14H), 4.00 (s, 3H); MS (EI): m/z (%): 454 (26.09) [M^+], 375 (100.00); Anal. Calcd. for $\text{C}_{23}\text{H}_{17}\text{BrF}_2\text{N}_2\text{O}$: C, 60.67; H, 3.76; N, 6.15; Found: C, 60.96; H, 3.93; N, 6.10; IR (film): ν 3388, 3063, 2829, 1673, 1582, 1510, 1442, 1240, 1146, 754 cm^{-1} .

N-Benzyl-2-bromo-2,2-difluoro-*N'*-(2-(hex-1-yn-1-yl)phenyl)acetimidamide (**2o**)



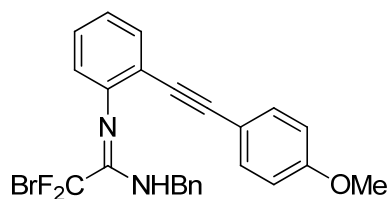
^1H NMR (300 MHz, CDCl_3): δ 7.51 – 6.55 (m, 9H), 5.06 (brs, 1H), 4.23 (brs, 2H), 2.51 – 2.01 (m, 2H), 1.71 – 1.10 (m, 4H), 0.84 (t, J = 5.7 Hz, 3H); MS (EI): m/z (%): 418 (3.57) [M^+], 91 (100.00); HRMS (EI) Calcd. for $\text{C}_{21}\text{H}_{21}\text{BrF}_2\text{N}_2$: 418.0856, Found: 418.0858; IR (film): ν 3421, 3068, 3053, 2954, 2932, 2873, 1674, 1520, 1477, 1171, 1116, 917, 749 cm^{-1} .

2-Bromo-2,2-difluoro-*N'*-(2-(hex-1-yn-1-yl)phenyl)-*N*-(4-methoxyphenyl)acetimidamide (**2p**)



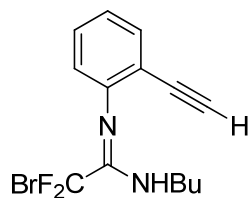
^1H NMR (300 MHz, CDCl_3): δ 7.64 – 5.87 (m, 9H), 3.73 (s, 3H), 2.68 – 2.21 (m, 2H), 1.81 – 1.37 (m, 4H), 1.11 – 0.68 (m, 3H); MS (EI): m/z (%): 434 (17.06) [M^+], 355 (100.00); Anal. Calcd. for $\text{C}_{21}\text{H}_{21}\text{BrF}_2\text{N}_2\text{O}$: C, 57.94; H, 4.86; N, 6.44; Found: C, 58.09; H, 4.95; N, 6.39; IR (film): ν 3383, 2954, 2927, 1668, 1504, 1240, 1147, 1085 cm^{-1} .

N-Benzyl-2-bromo-2,2-difluoro-*N'*-(2-((4-methoxyphenyl)ethynyl)phenyl)acetimidamide (**2q**)



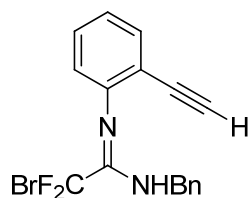
^1H NMR (300 MHz, CDCl_3): δ 7.63 – 6.60 (m, 13H), 5.20 (brs, 1H), 4.39 (brs, 2H), 3.83 (s, 3H); MS (EI): m/z (%): 468 (10.48) [M^+], 91 (100.00); Anal. Calcd. for $\text{C}_{24}\text{H}_{19}\text{BrF}_2\text{N}_2\text{O}$: C, 61.42; H, 4.08; N, 5.97; Found: C, 61.69; H, 4.14; N, 5.94; IR (film): ν 3431, 3068, 3035, 2927, 2829, 1673, 1605, 1510, 1474, 1248, 1173, 1108, cm^{-1} .

2-Bromo-*N*-butyl-*N'*-(2-ethynylphenyl)-2,2-difluoroacetimidamide (**2s**)



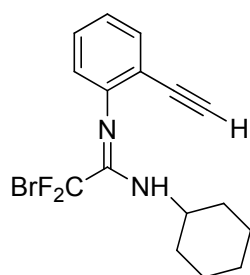
^1H NMR (300 MHz, CDCl_3): δ 7.44 – 6.84 (m, 4H), 4.93 (brs, 1H), 3.18 (s, 1H), 3.15 – 3.12 (m, 2H), 1.60 – 0.80 (m, 7H); MS (EI): m/z (%): 328 (30.58) [M^+], 116 (100.00); HRMS (EI) Calcd. for $\text{C}_{14}\text{H}_{15}\text{BrF}_2\text{N}_2$: 328.0387; Found: 328.0381;

N-Benzyl-2-bromo-*N'*-(2-ethynylphenyl)-2,2-difluoroacetimidamide (**2r**)



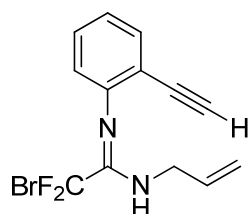
^1H NMR (300 MHz, CDCl_3): δ 7.44 – 6.84 (m, 9H), 5.24 (brs, 1H), 4.37 (brs, 2H), 3.19 (s, 1H); MS (EI): m/z (%): 362 (0.96) [M^+], 91 (100.00); HRMS (EI) Calcd. for $\text{C}_{17}\text{H}_{13}\text{BrF}_2\text{N}_2$: 362.0230; Found: 362.0228; IR (film): ν 3426, 3298, 3063, 3019, 2103, 1673, 1591, 1521, 1475, 1170, 1114, 917, 849, 750 cm^{-1} .

2-Bromo-*N*-cyclohexyl-*N'*-(2-ethynylphenyl)-2,2-difluoroacetimidamide (**2t**)



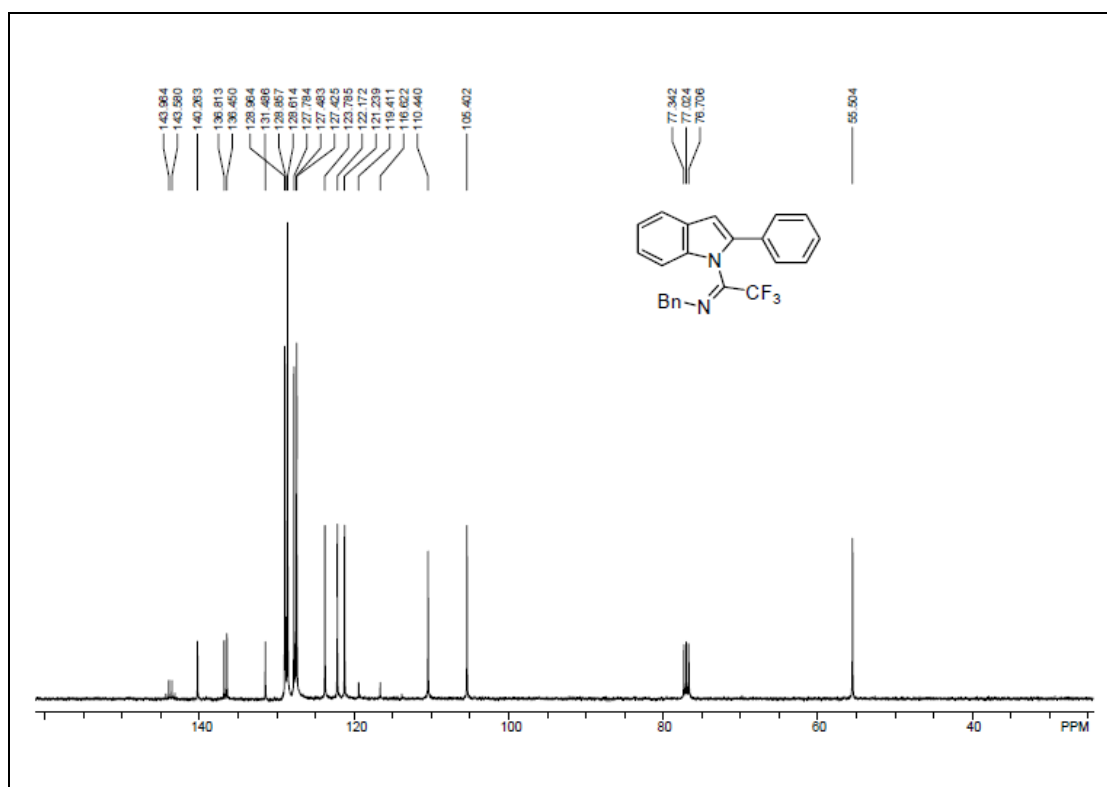
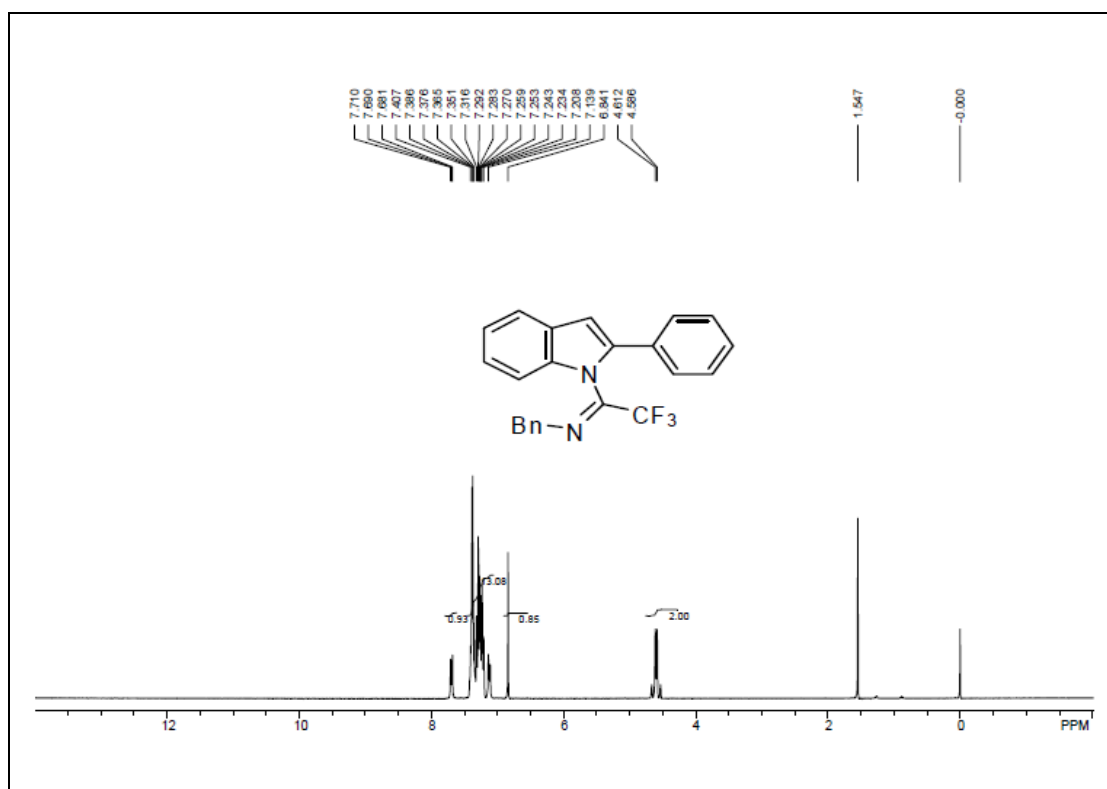
^1H NMR (300 MHz, CDCl_3): δ 7.44 – 6.84 (m, 4H), 4.80 (brs, 1H), 3.17 (s, 1H), 2.01-1.13 (m, 11H); MS (EI): m/z (%): 354 (4.50) [M^+], 55 (100.00); HRMS (EI) Calcd. for $\text{C}_{16}\text{H}_{17}\text{BrF}_2\text{N}_2$: 345.0543; Found: 345.0541; IR (film): ν 3415, 3310, 2932, 2855, 2018, 1670, 1592, 1518, 1474, 1171, 1113, 896 cm^{-1} .

N-Allyl-2-bromo-*N'*-(2-ethynylphenyl)-2,2-difluoroacetimidamide (**2u**)

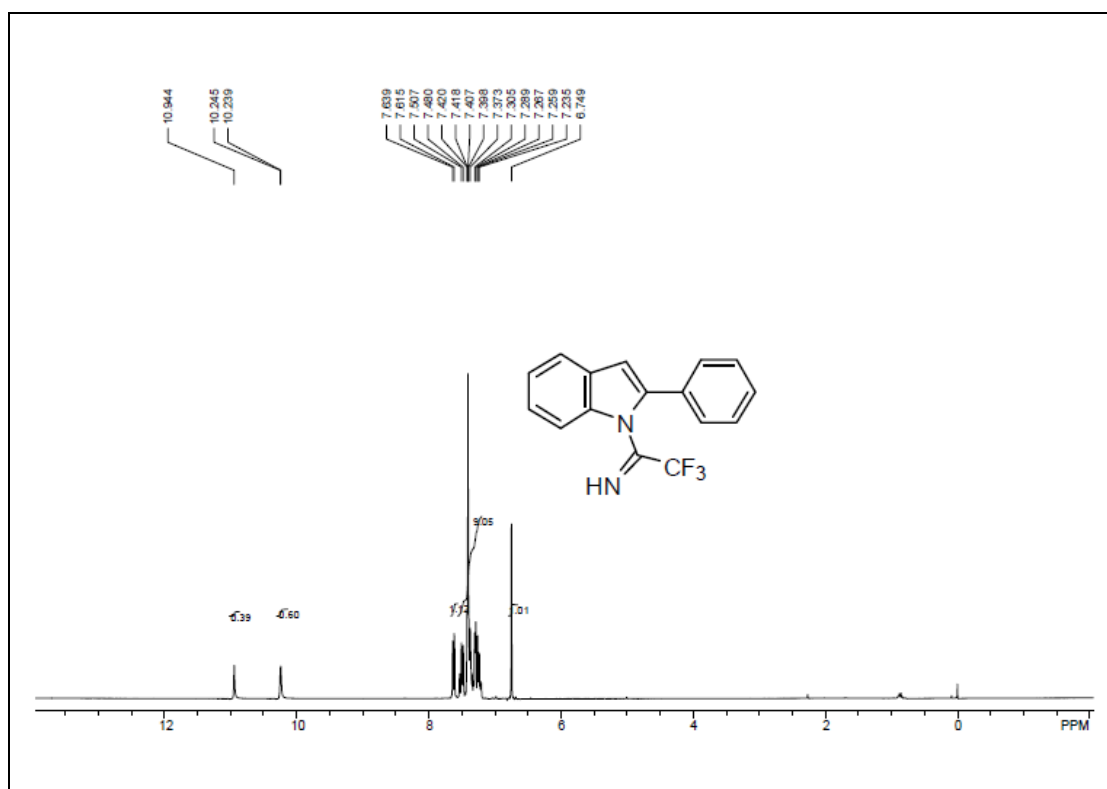


^1H NMR (300 MHz, CDCl_3): δ 7.44 – 6.80 (m, 4H), 5.85 (brs, 1H), 5.21 – 5.14 (m, 3H), 3.82 (brs, 2H), 3.19 (s, 1H); MS (EI): m/z (%): 312 (36.27) [M^+], 115 (100.00); HRMS (EI) Calcd. for $\text{C}_{13}\text{H}_{11}\text{BrF}_2\text{N}_2$: 312.0074; Found: 312.0076; IR (film): ν 3428, 3301, 3063, 2911, 2097, 1676, 1522, 1475, 1174, 924 cm^{-1} .

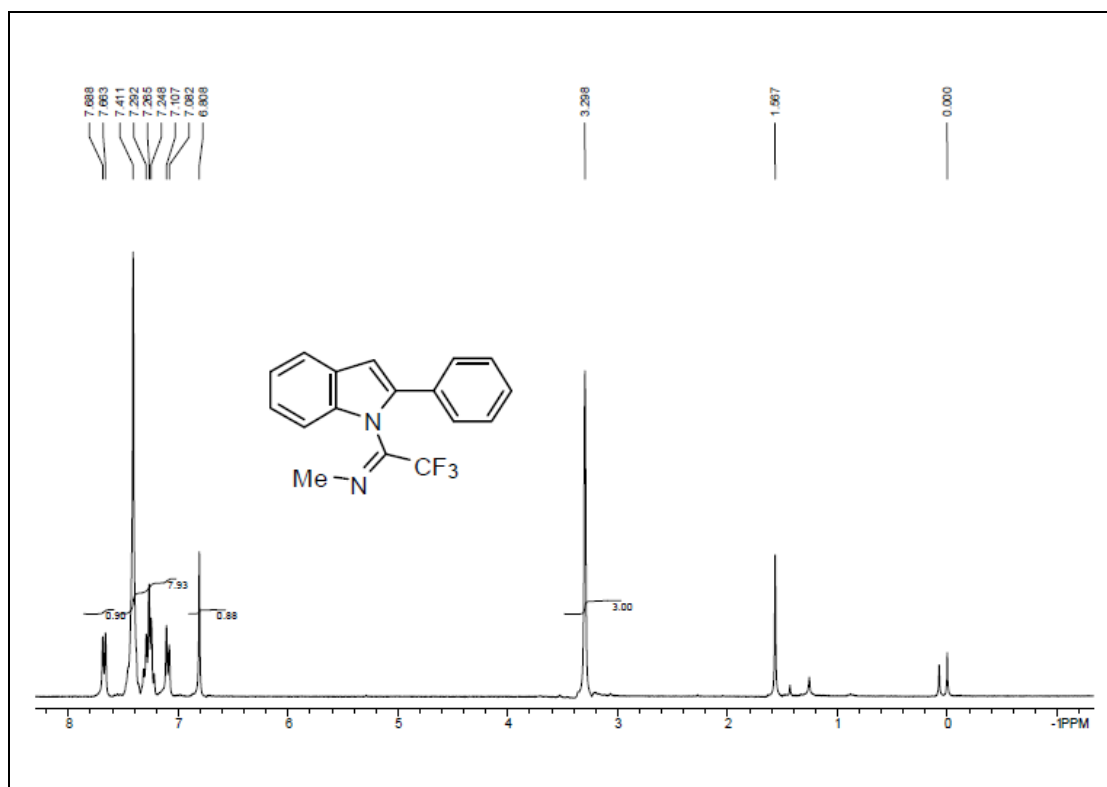
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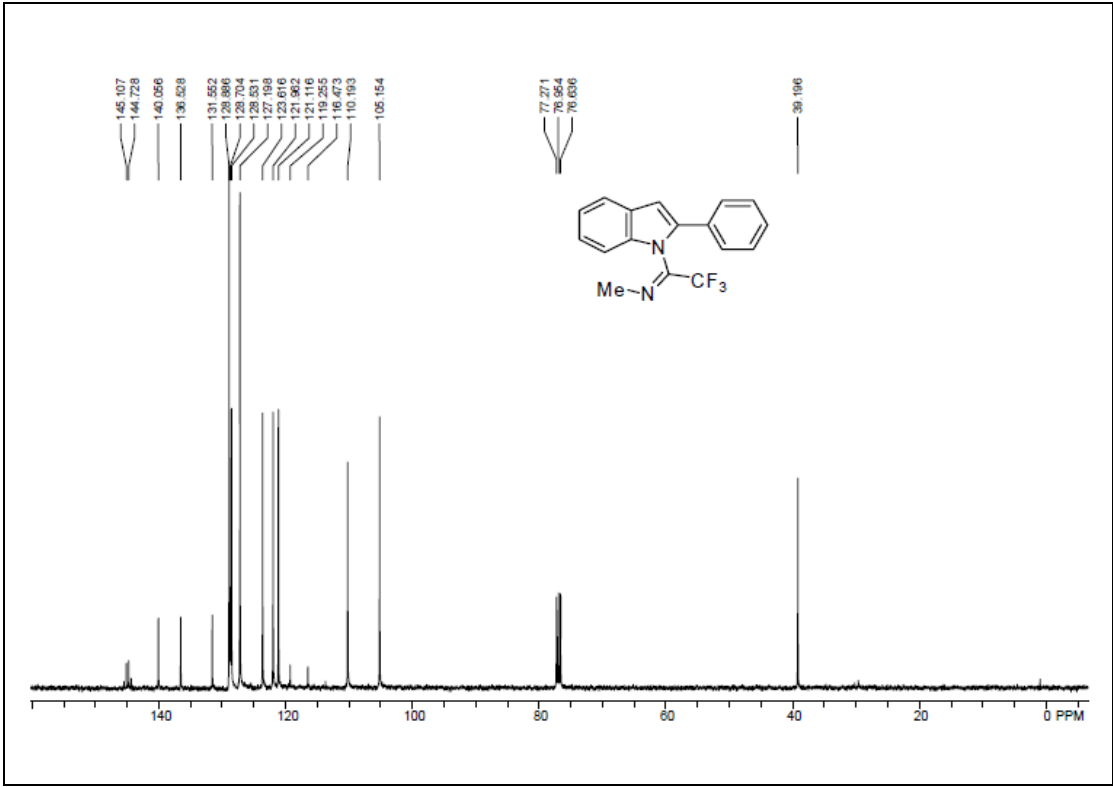


3b

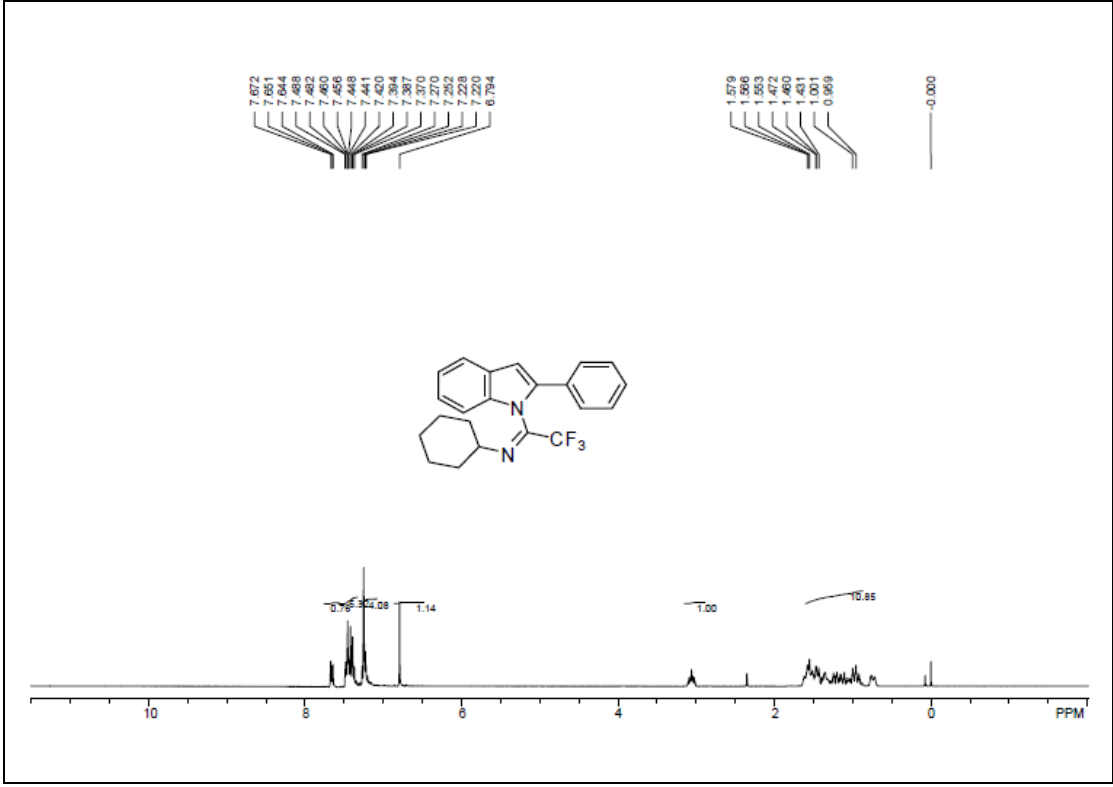


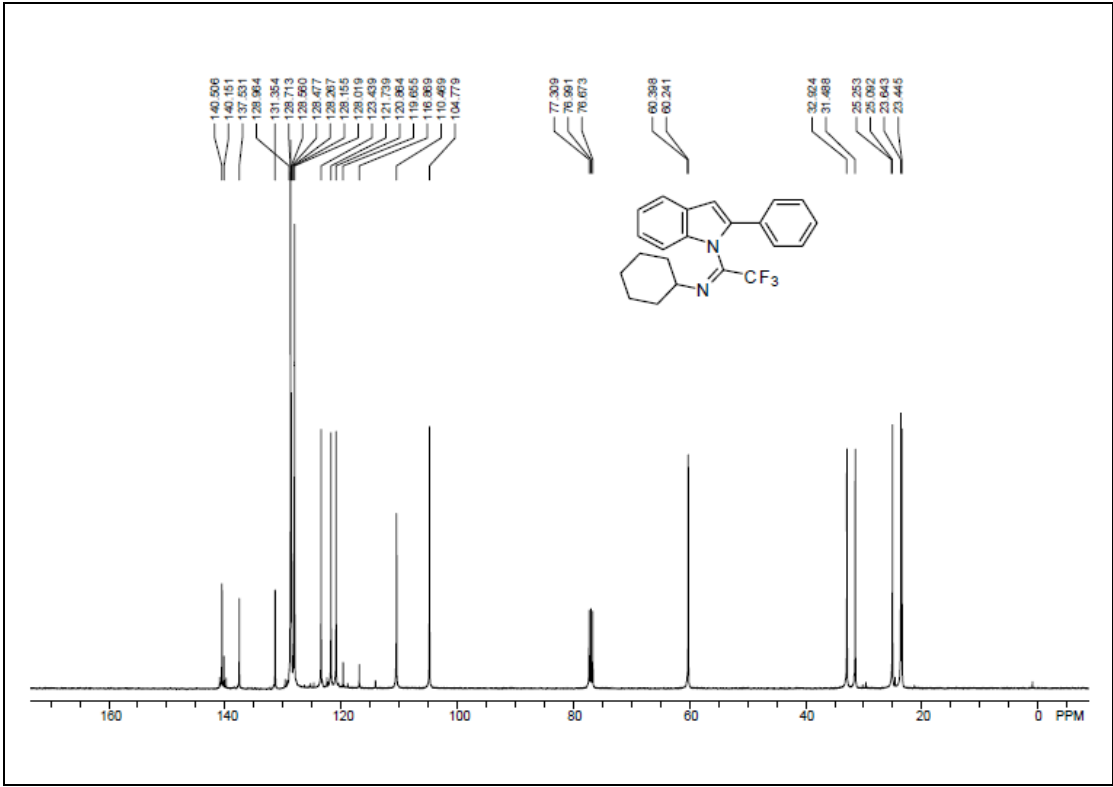
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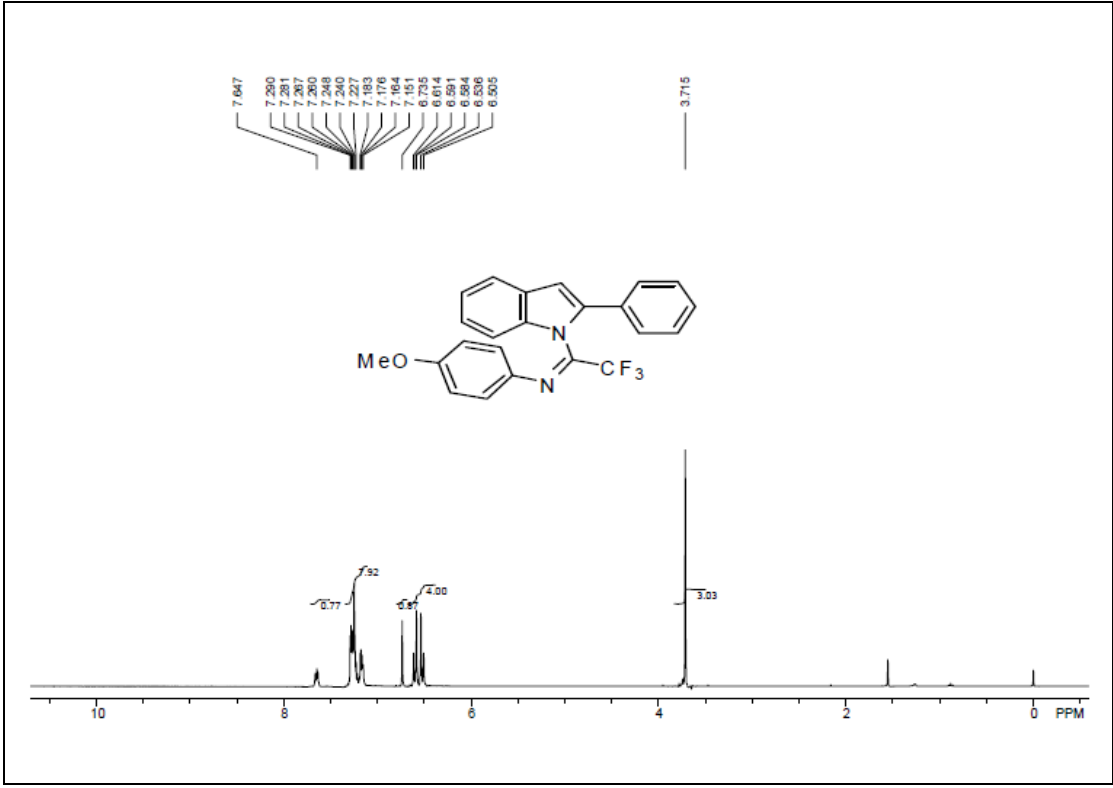


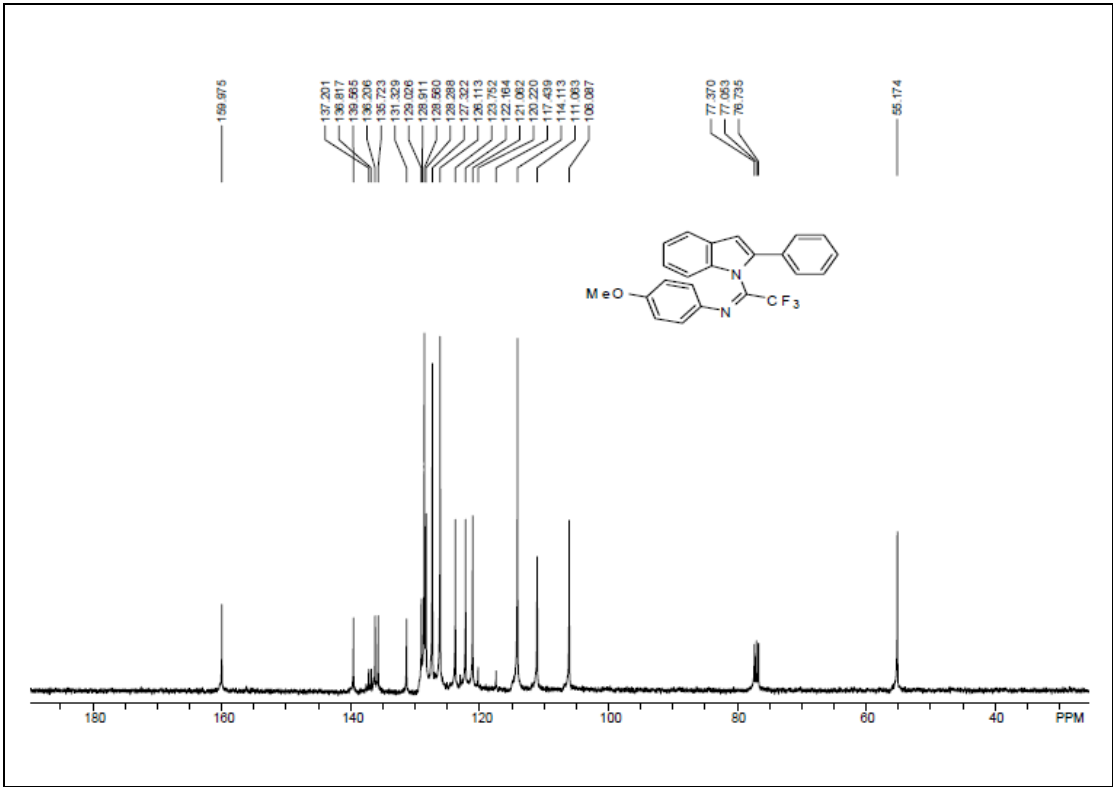
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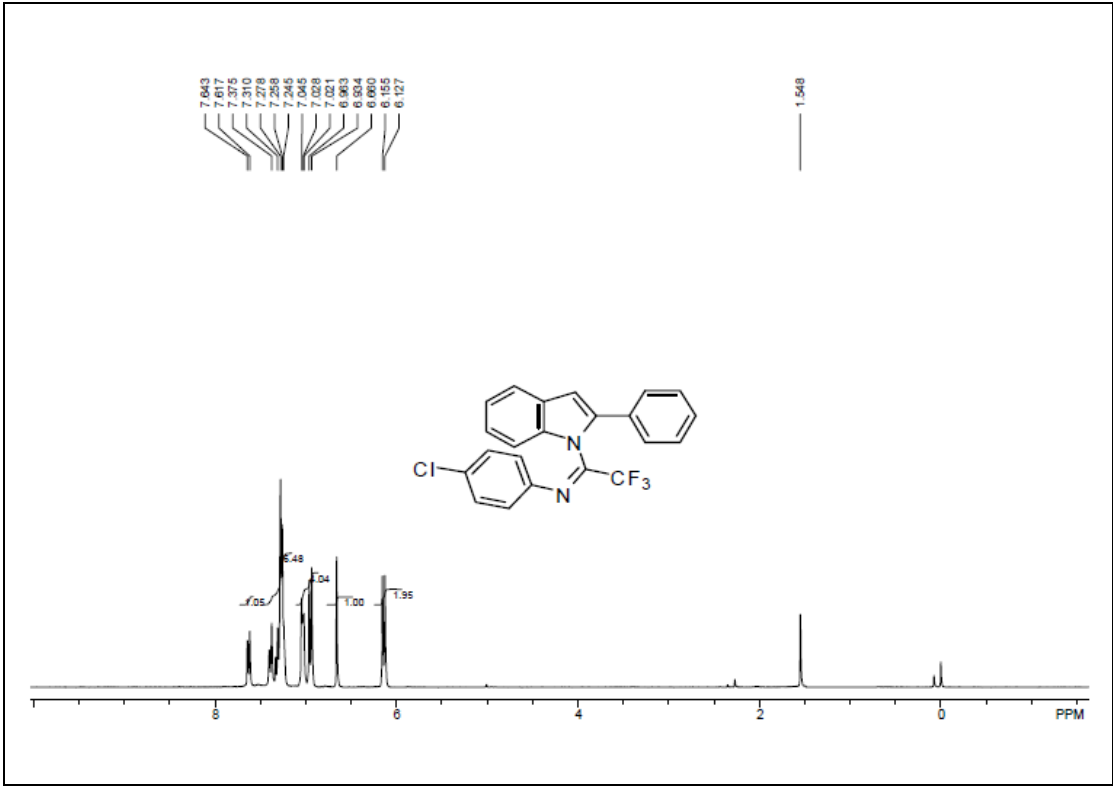


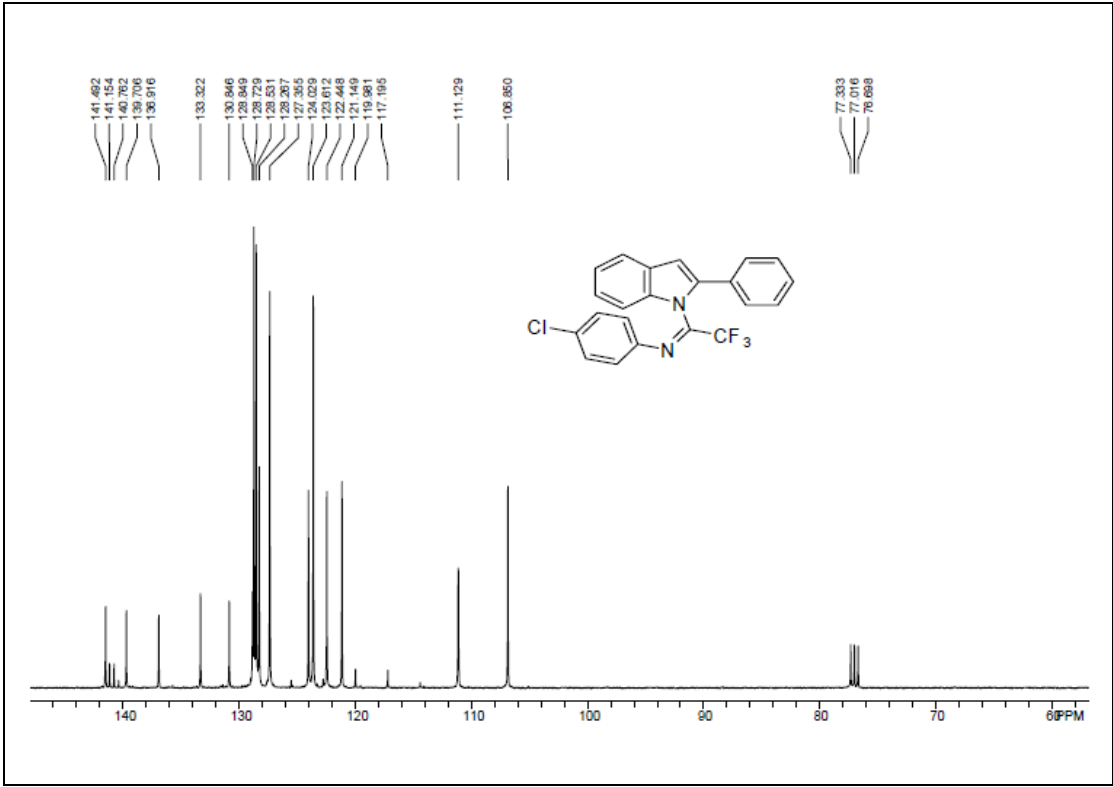
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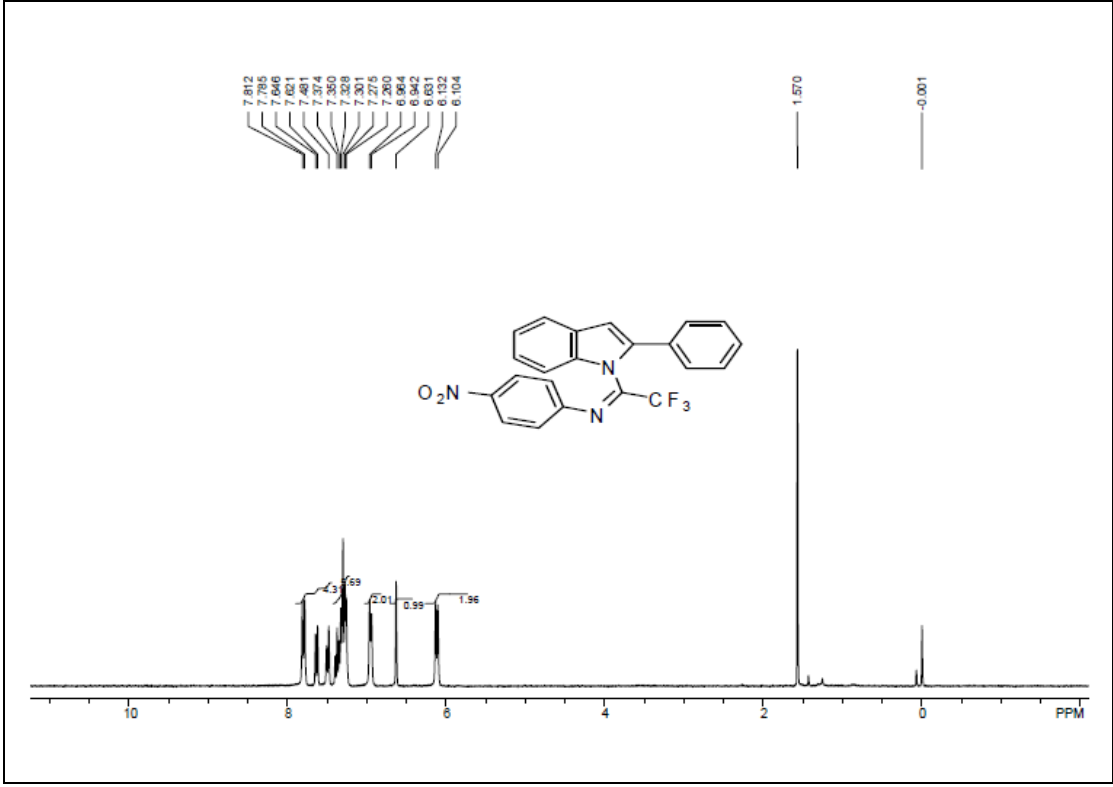


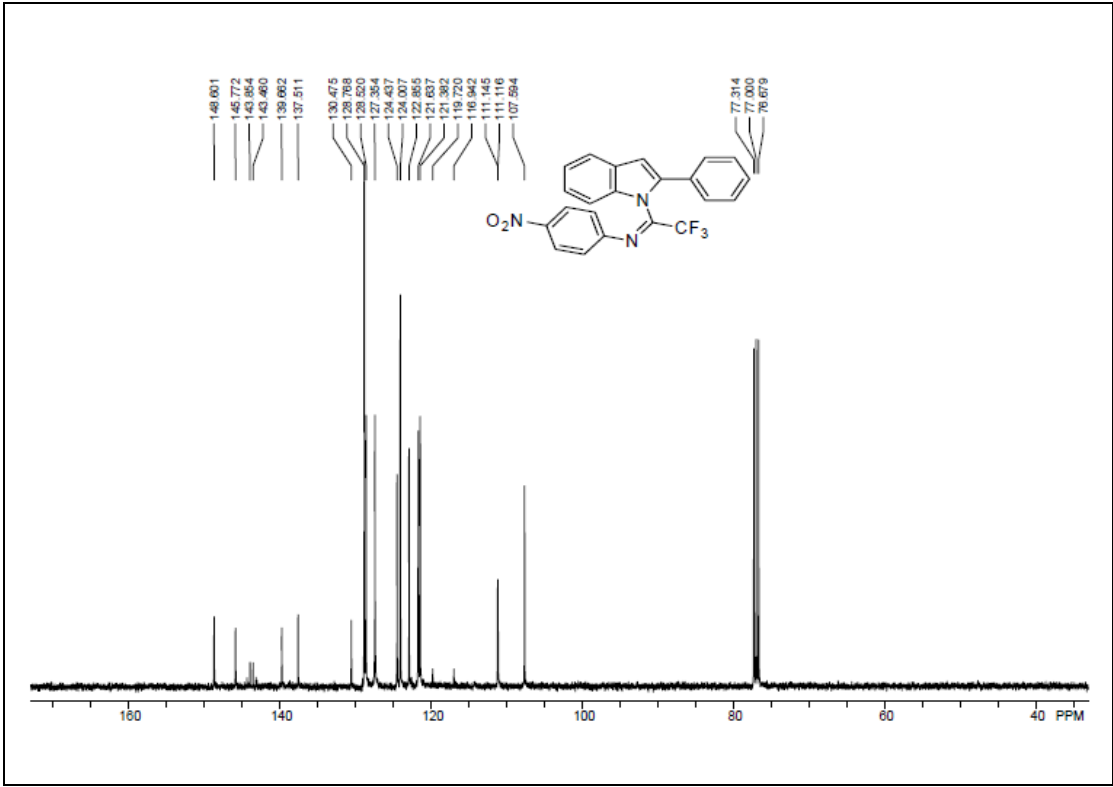
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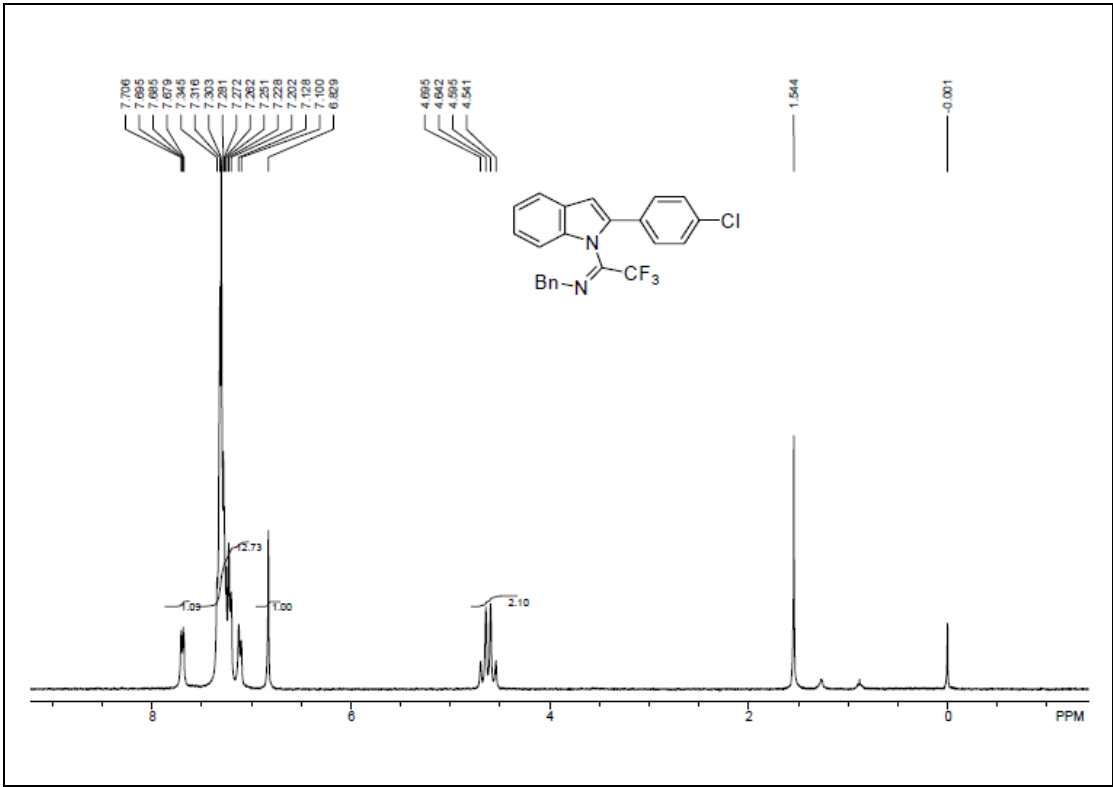


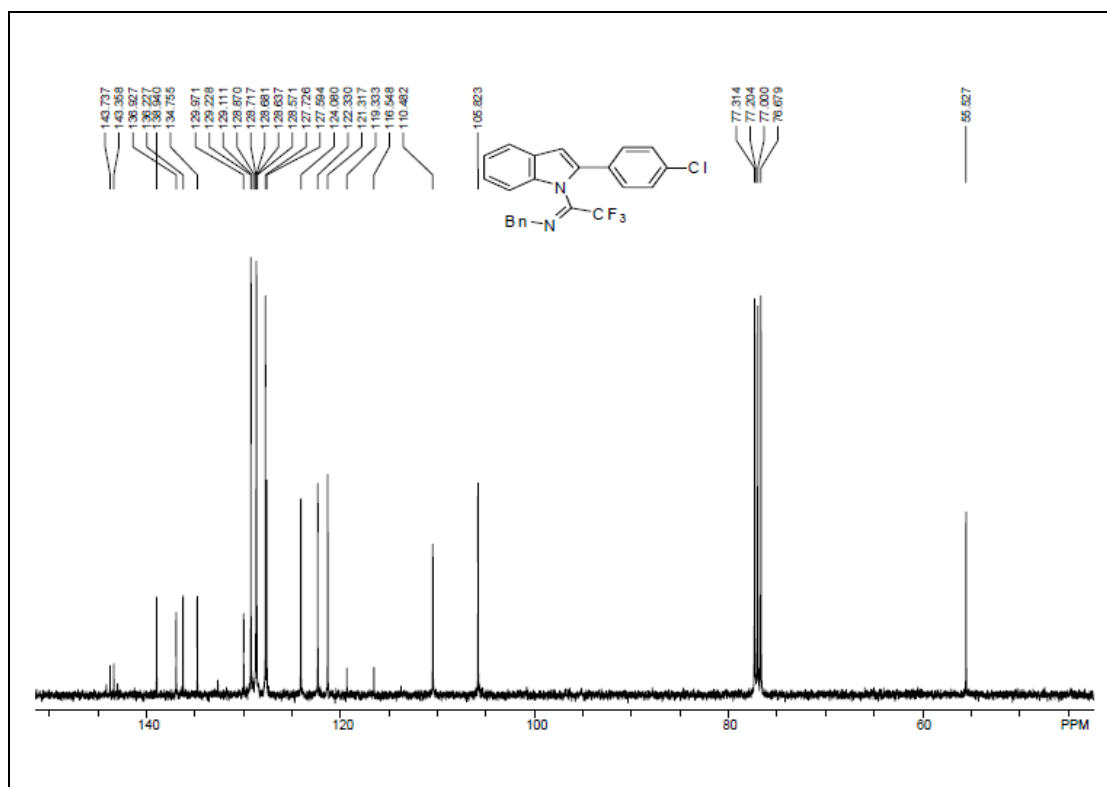
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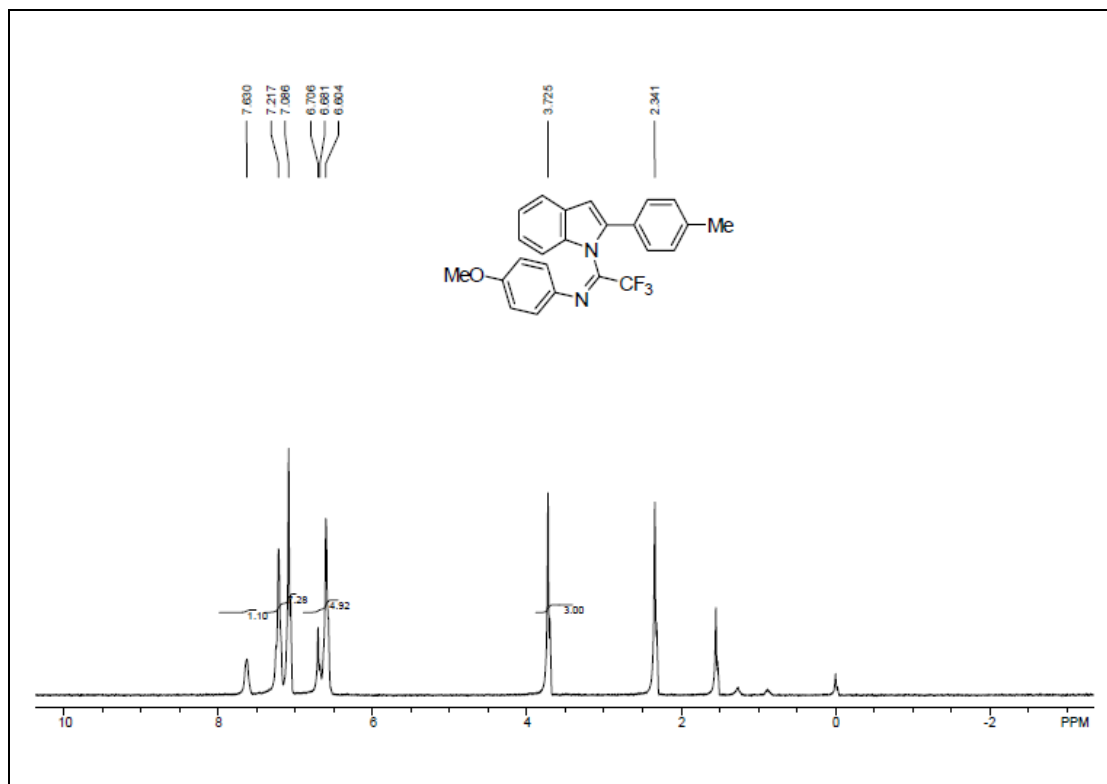


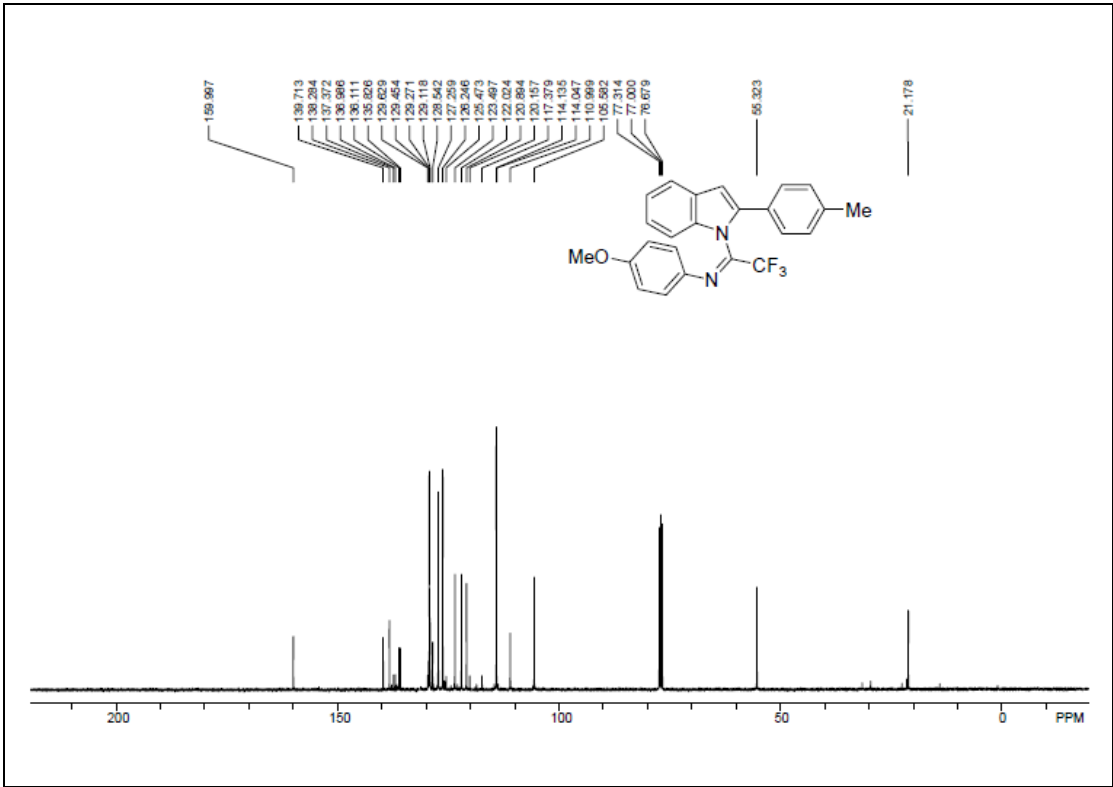
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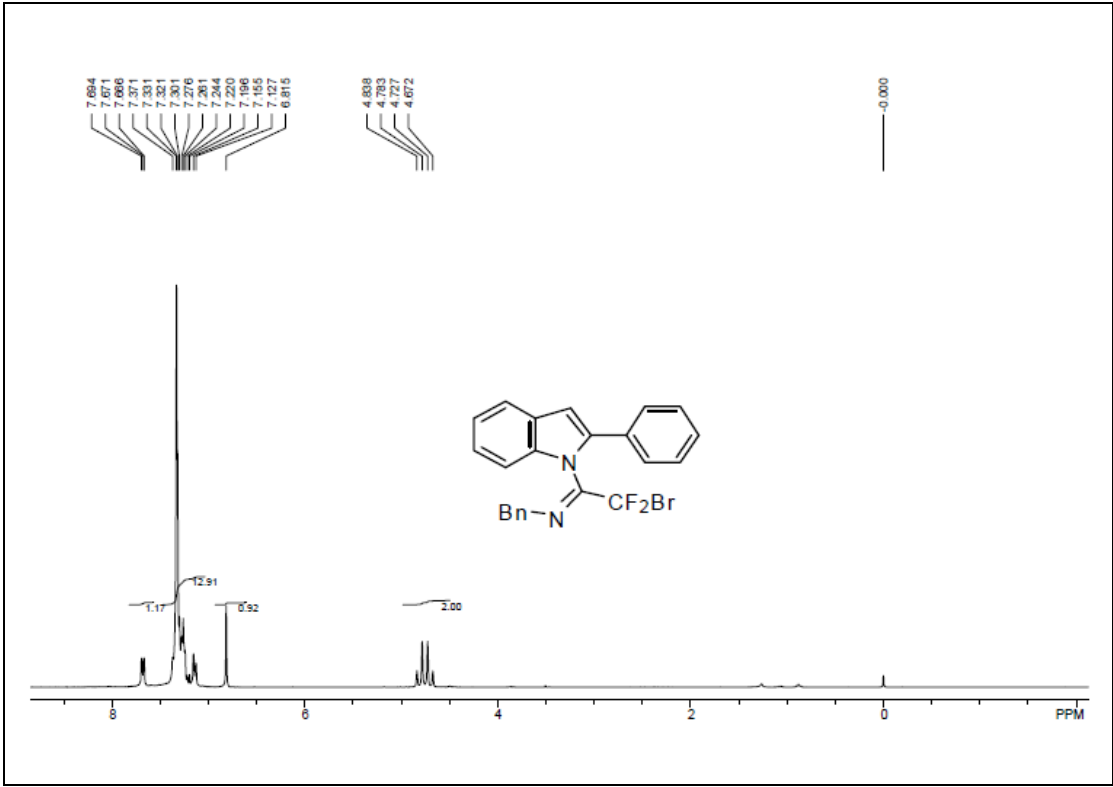


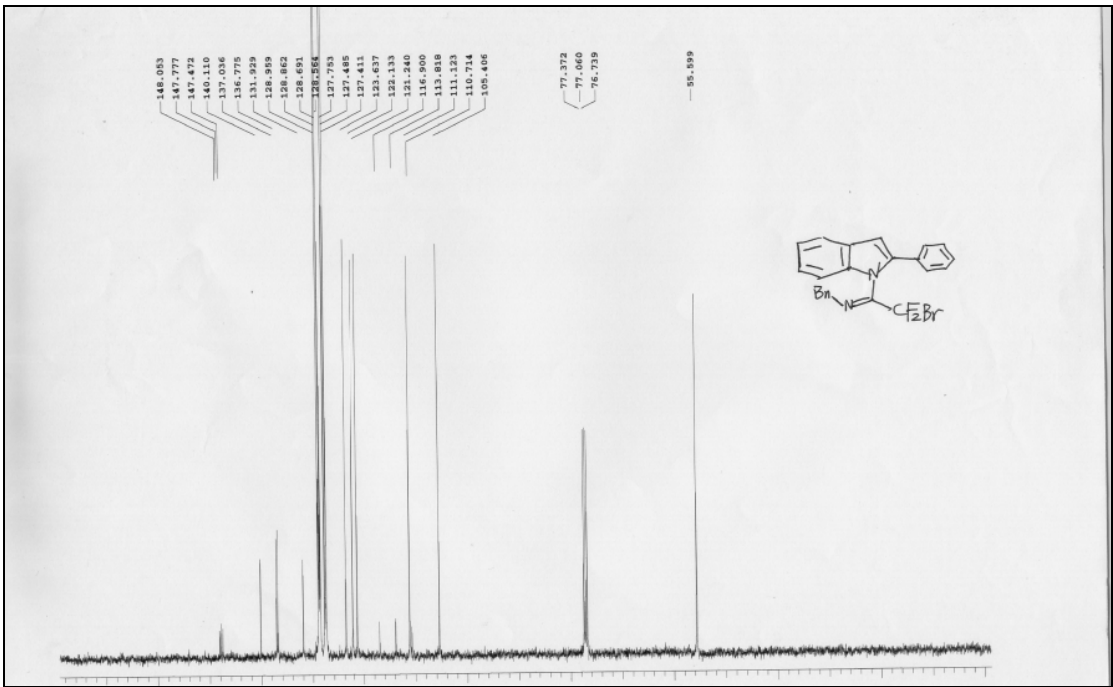
3i



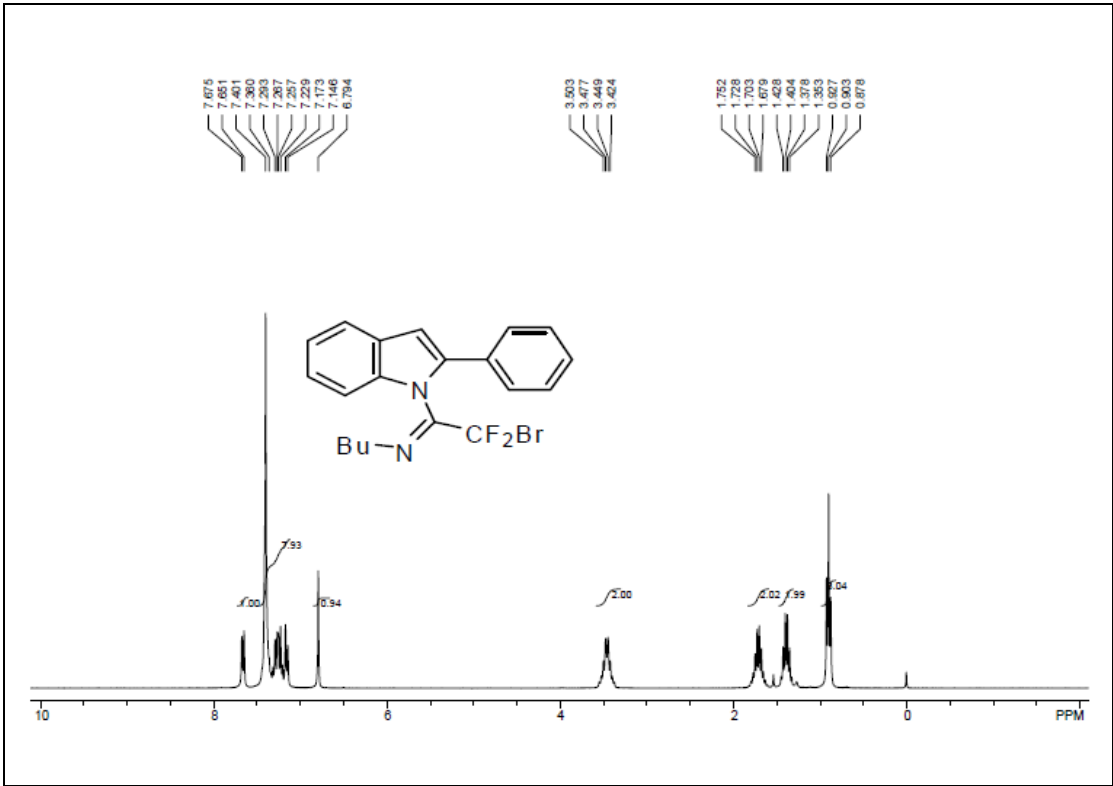


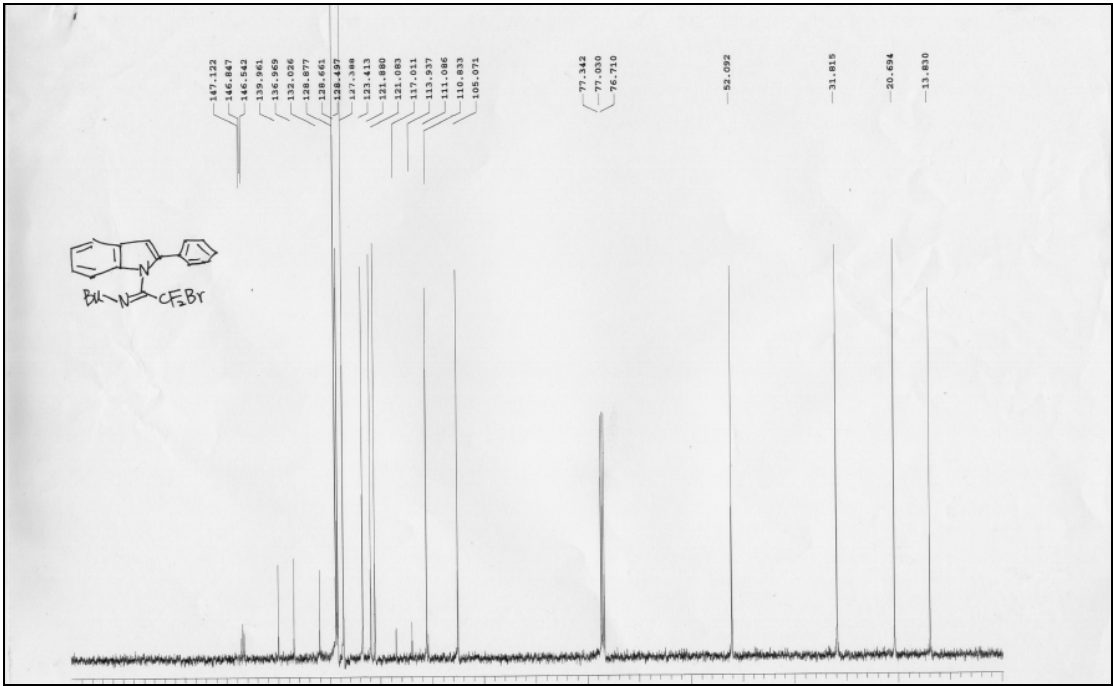
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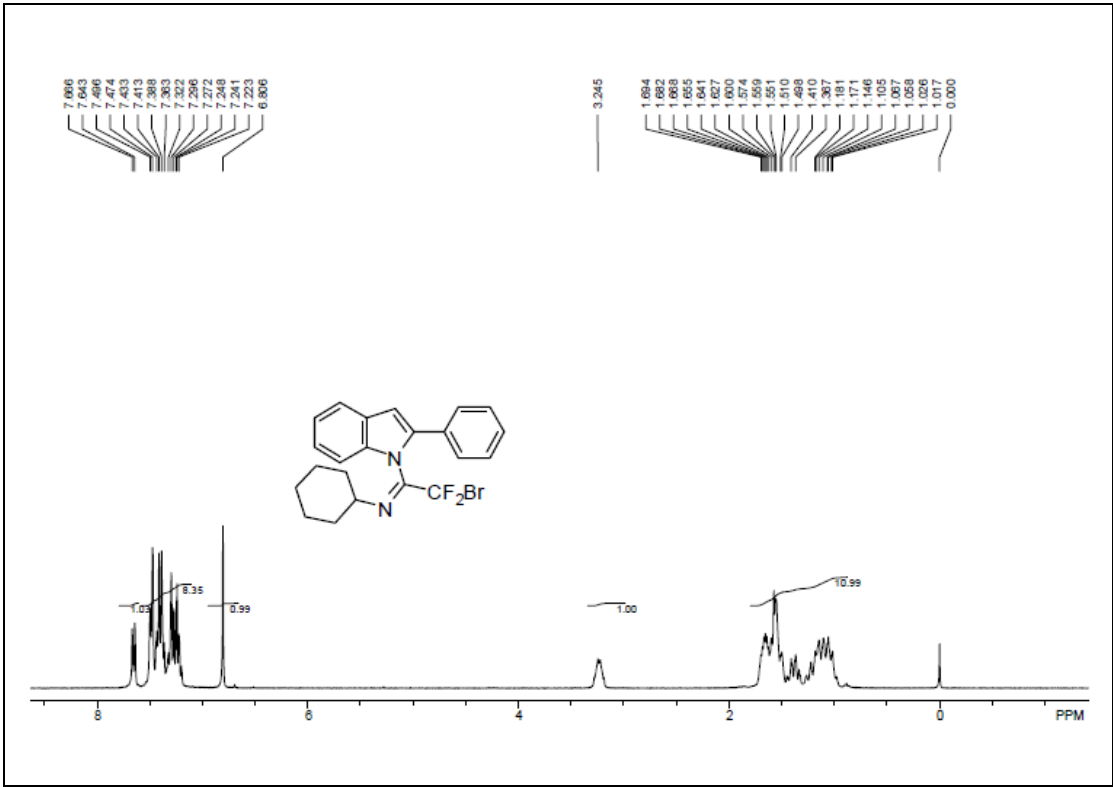


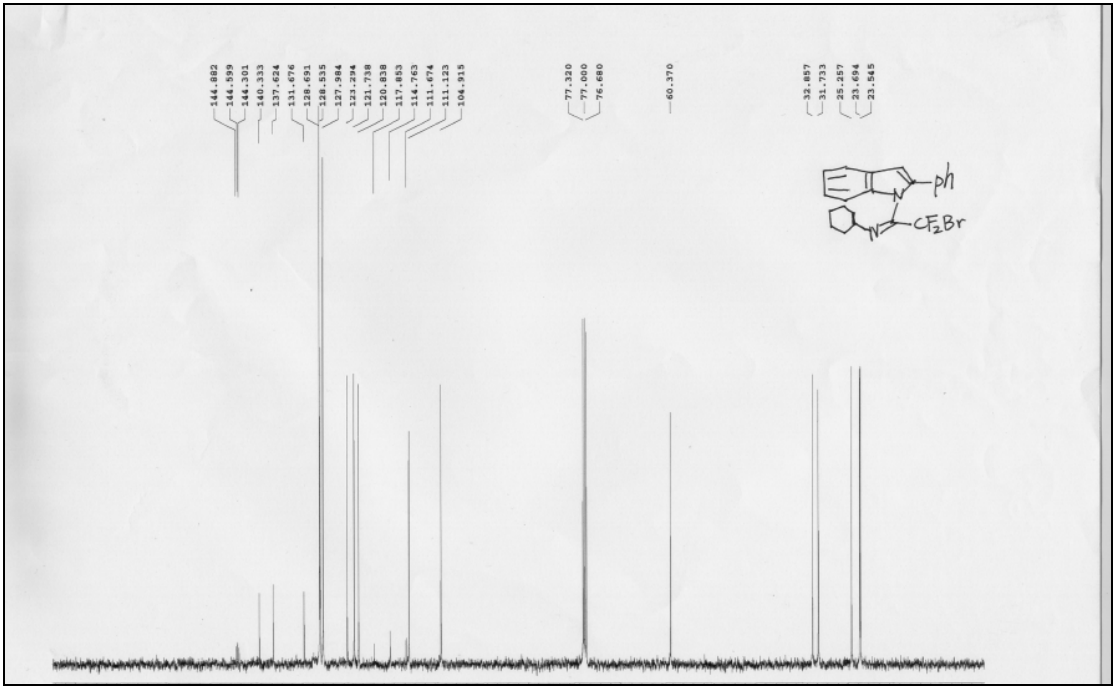
3k



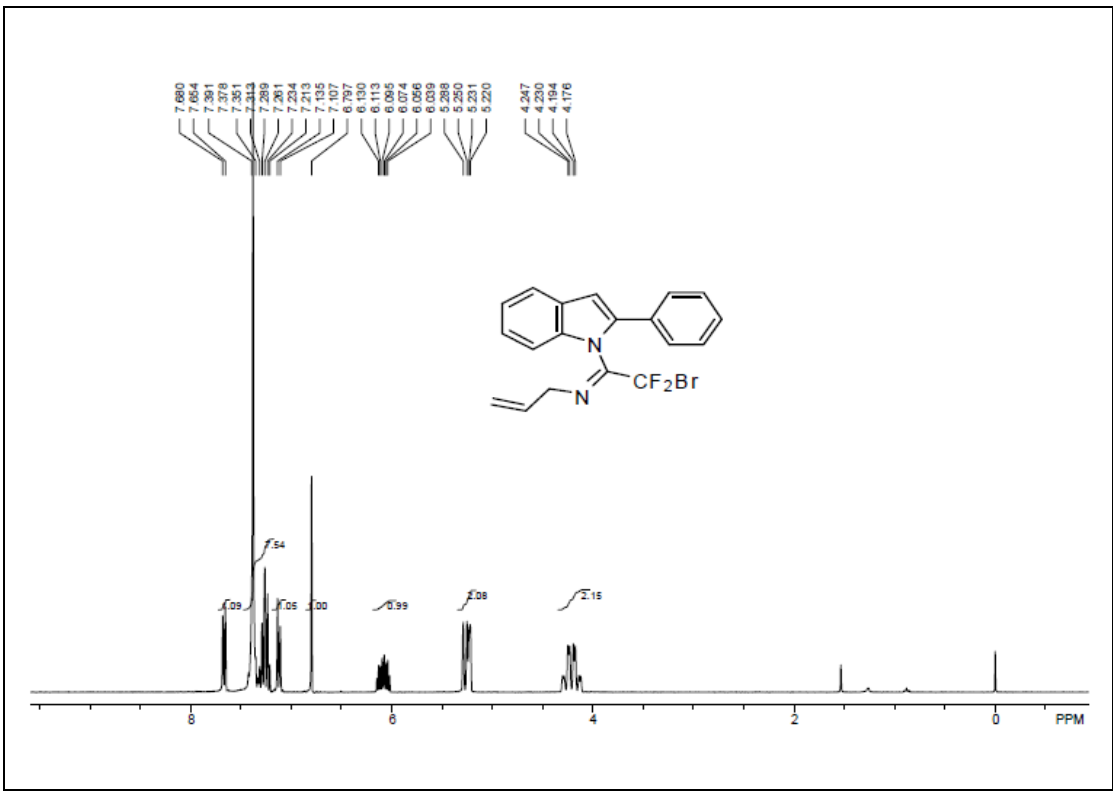


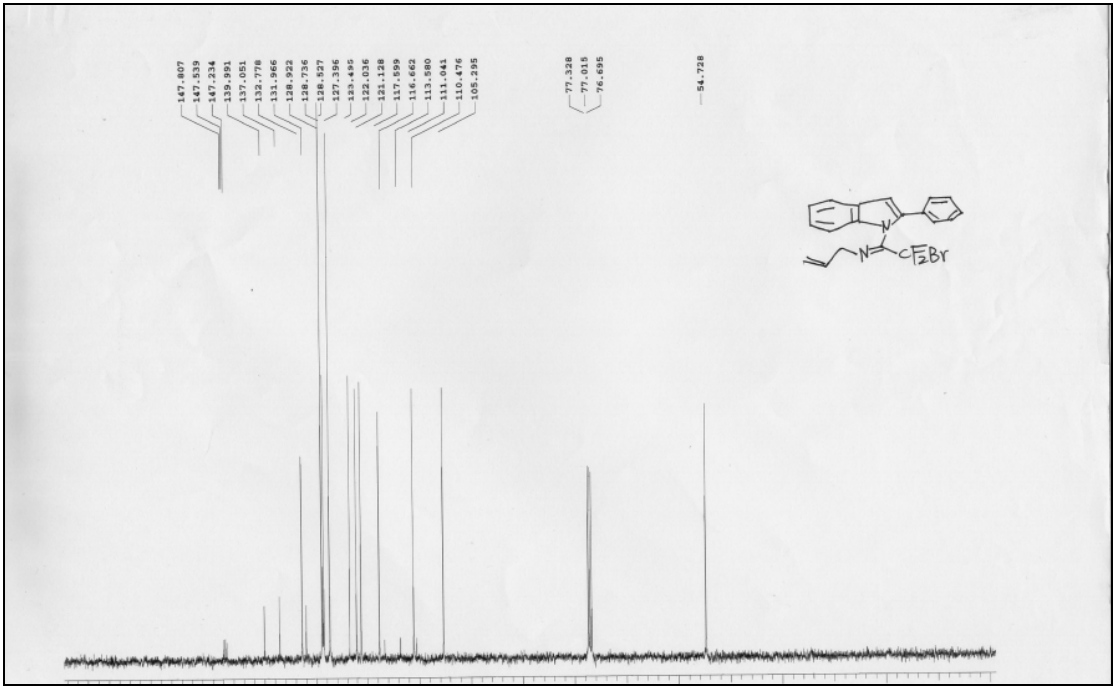
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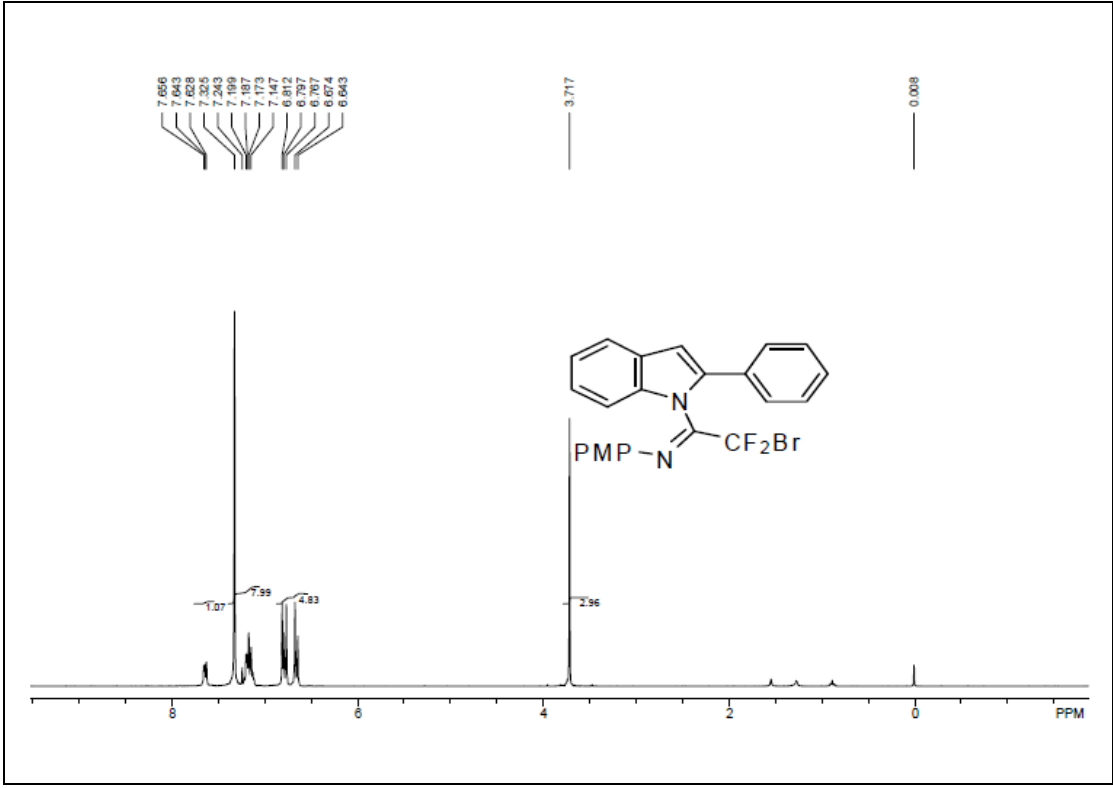


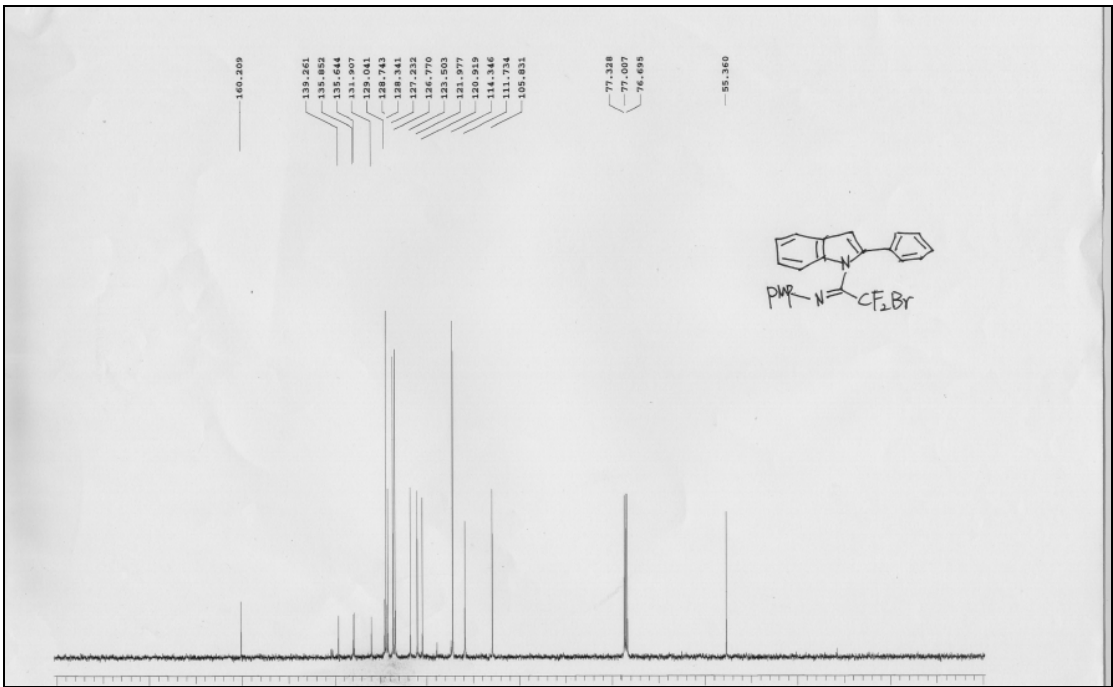
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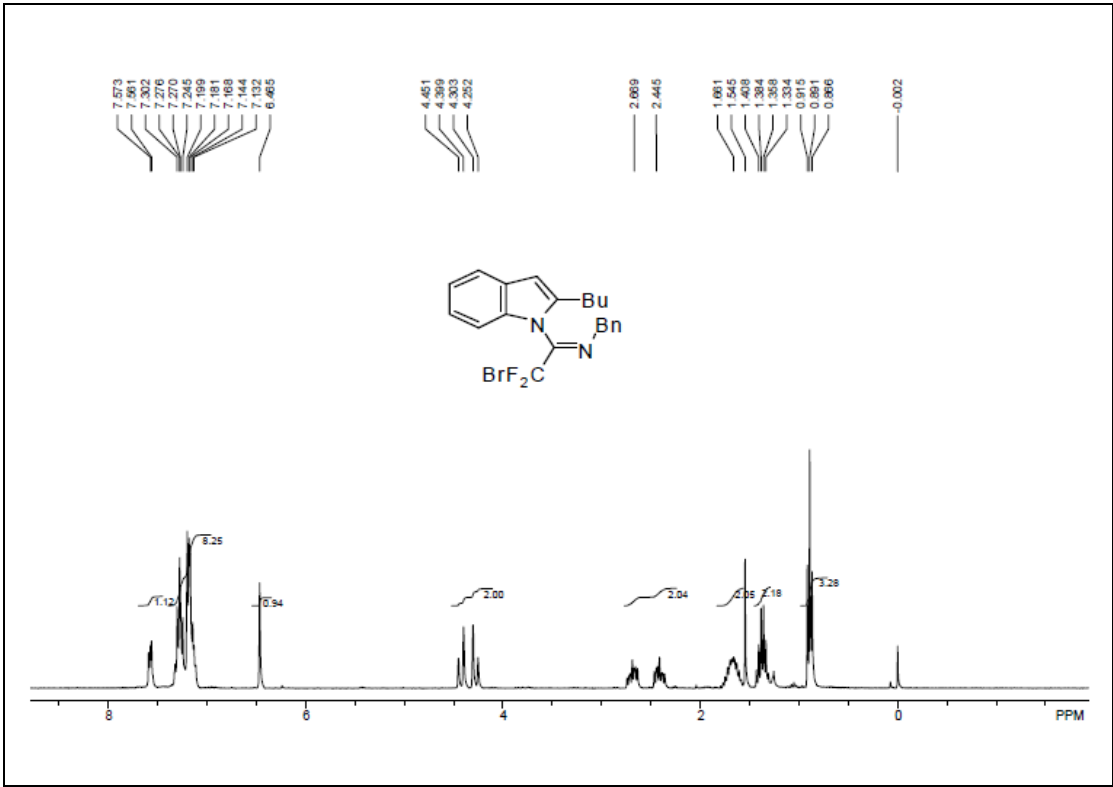


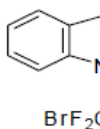
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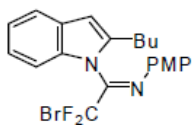


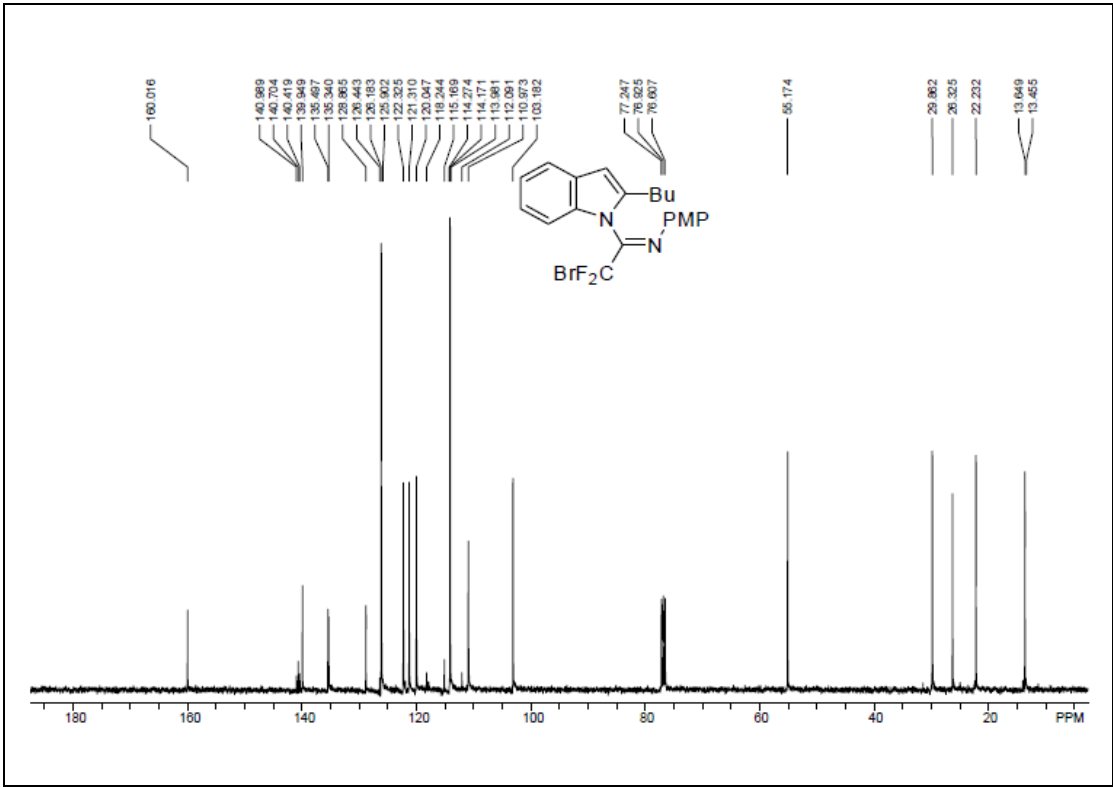
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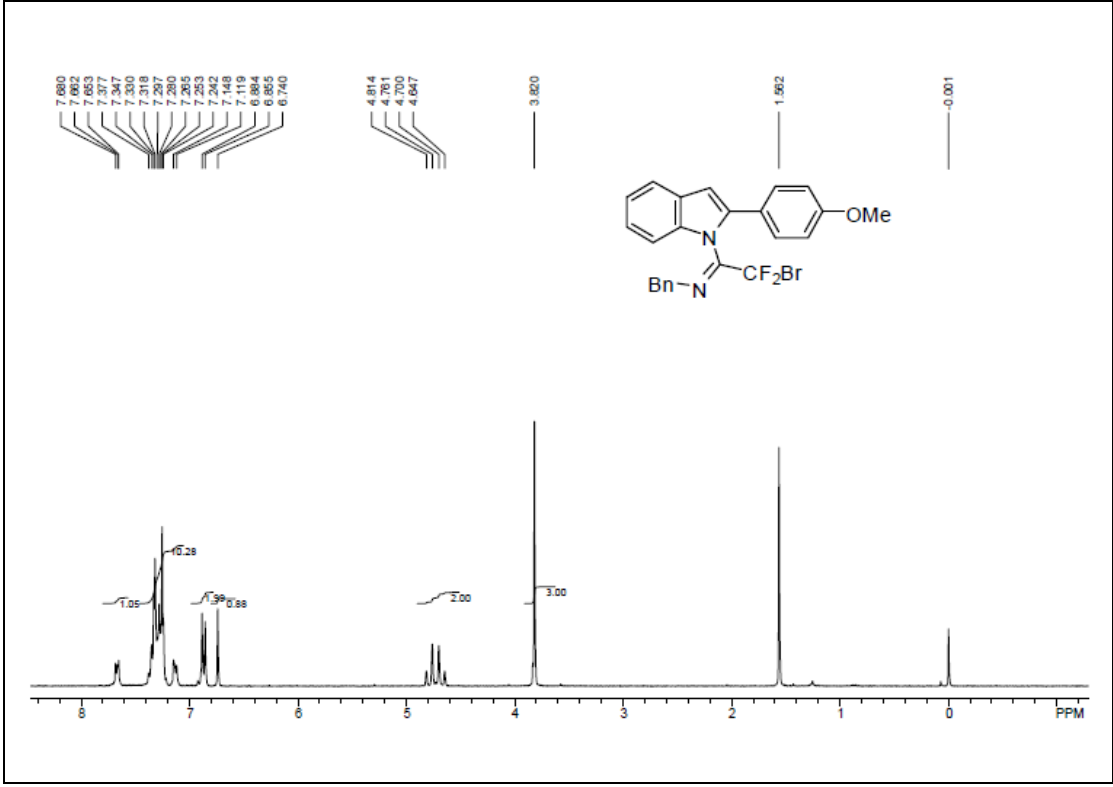


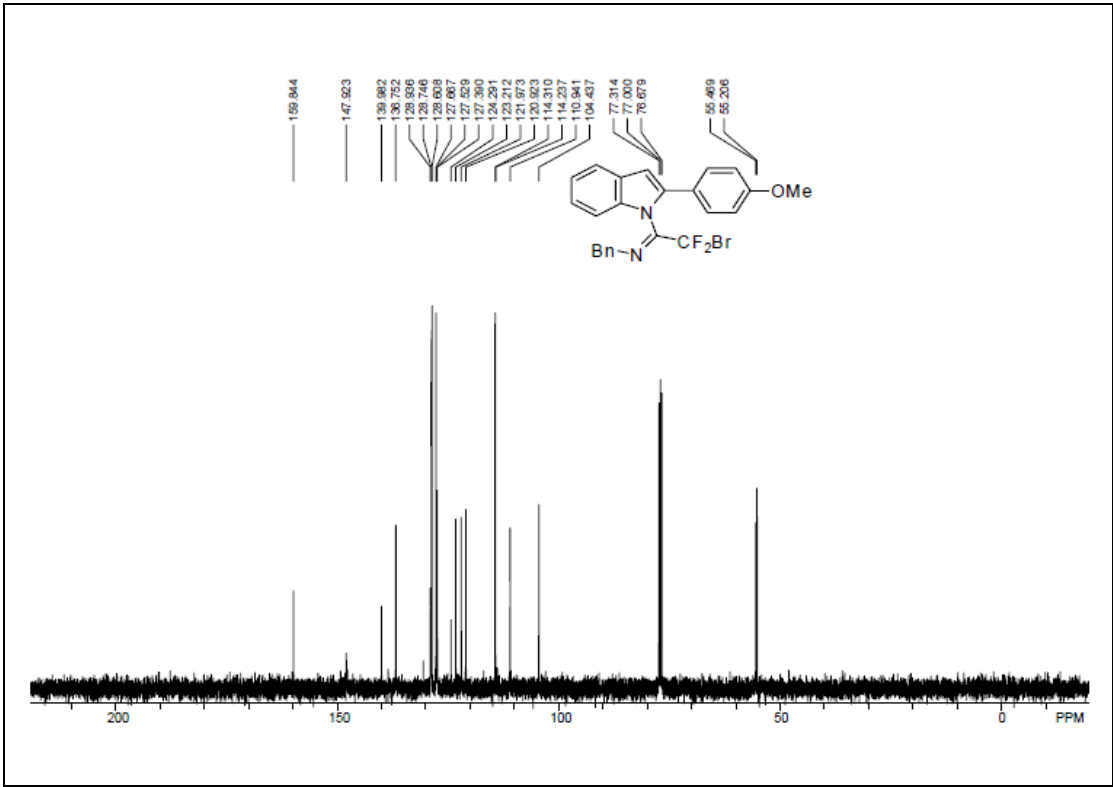
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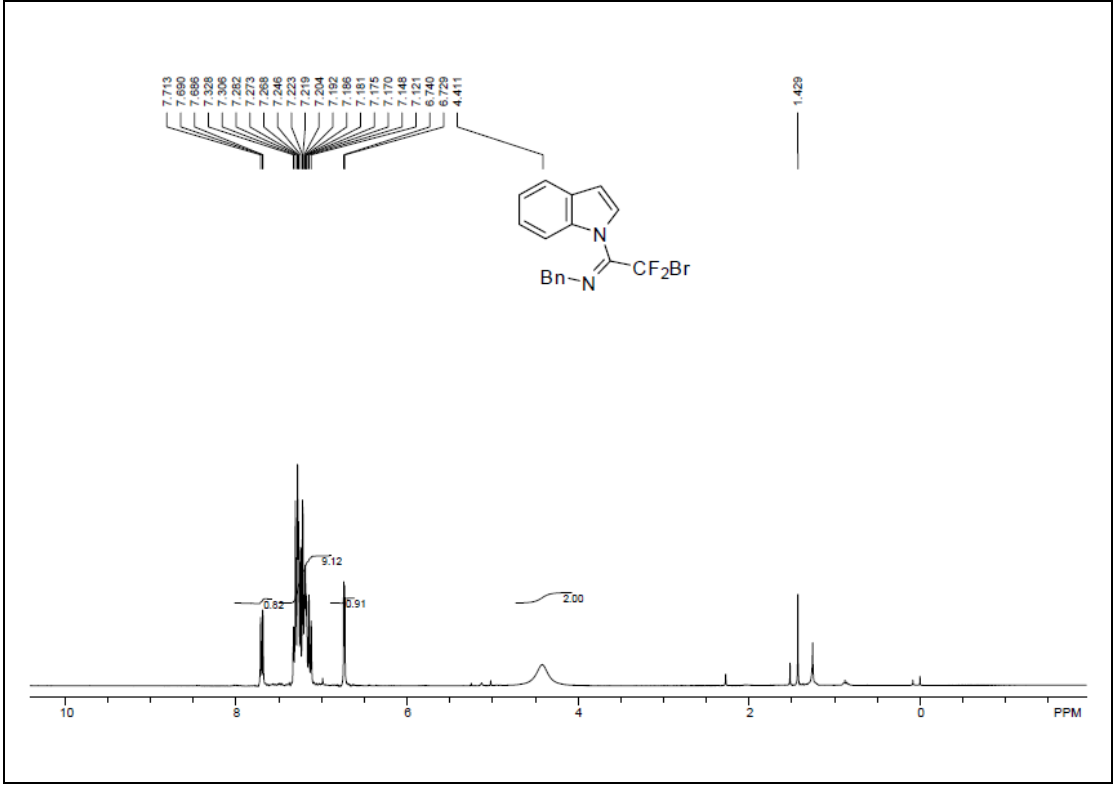


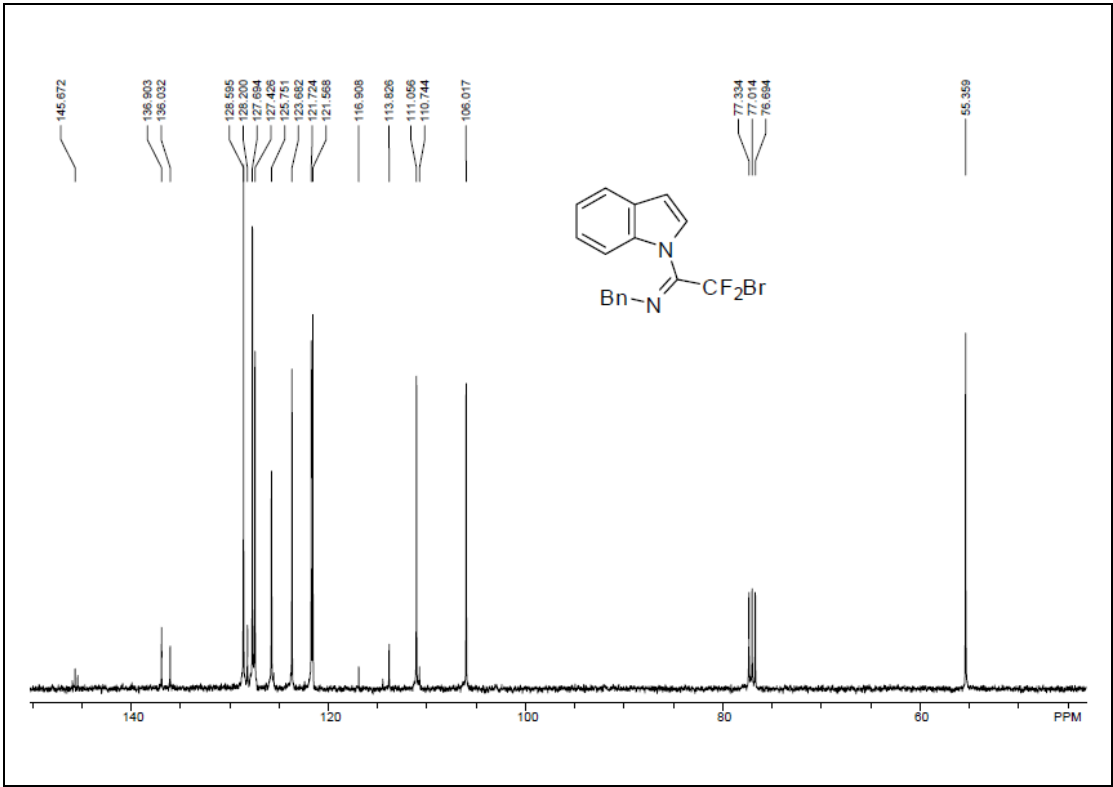
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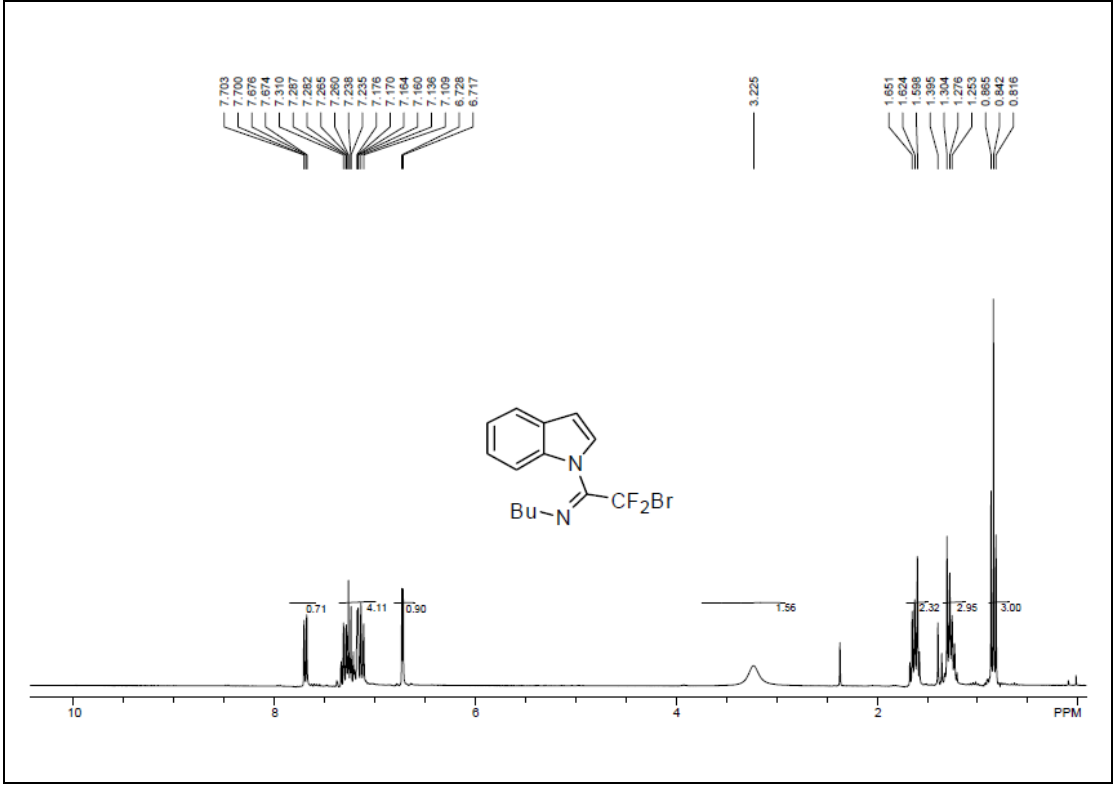


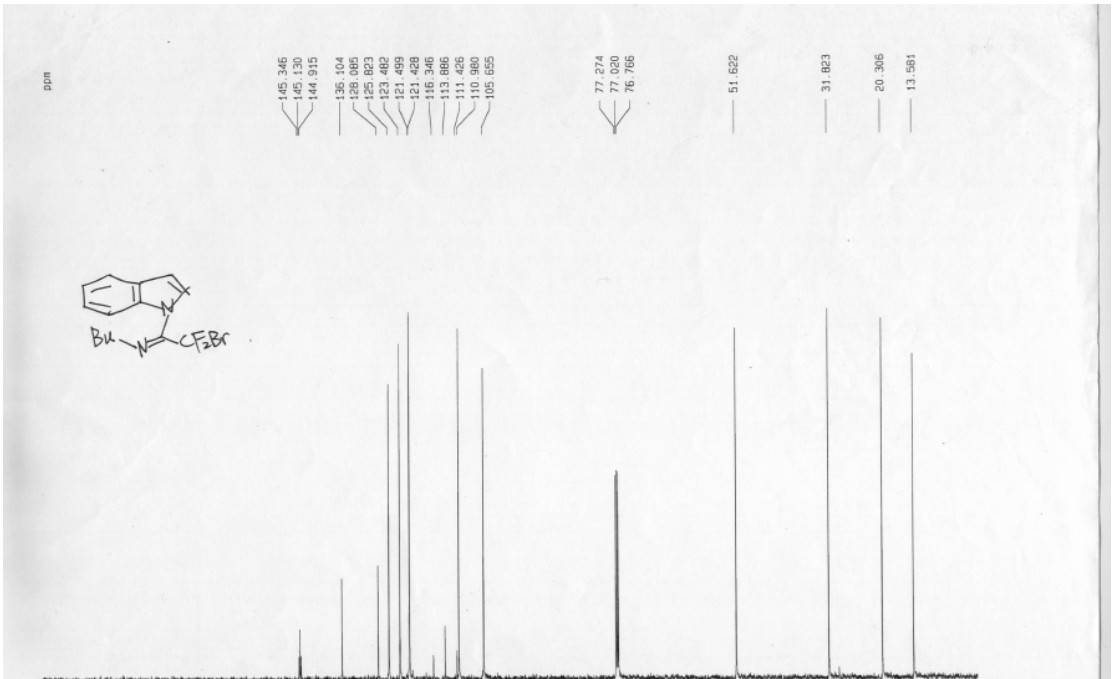
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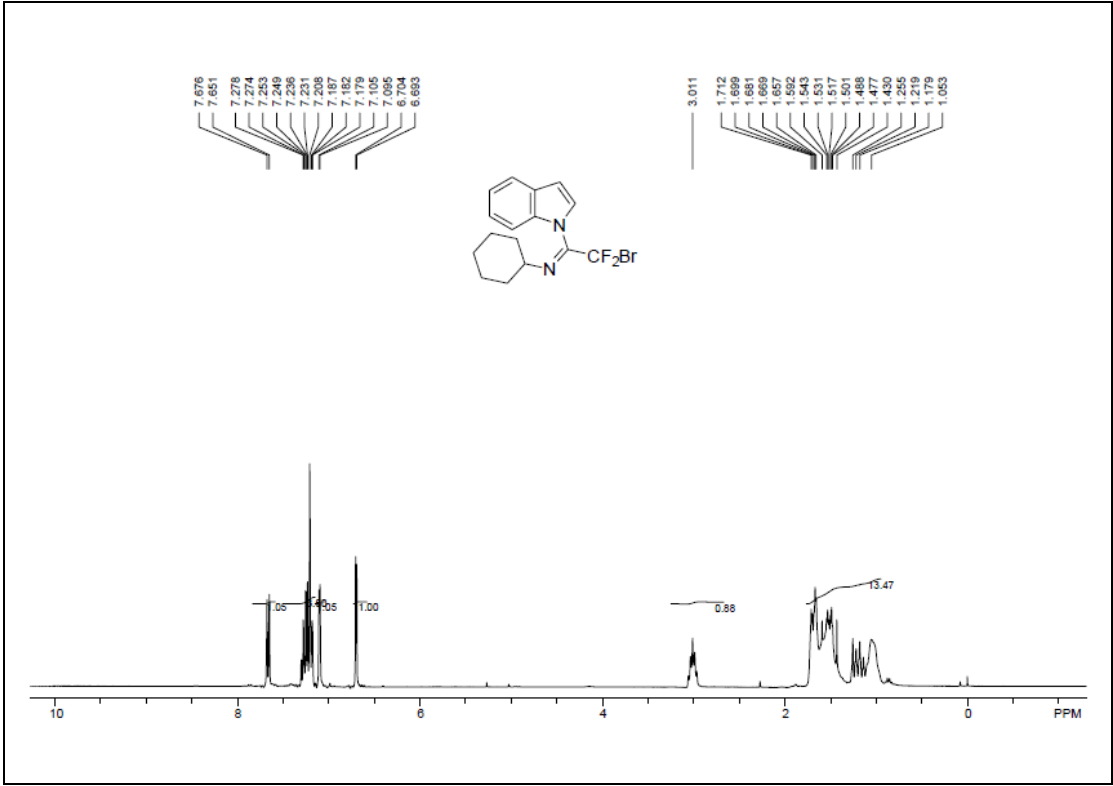


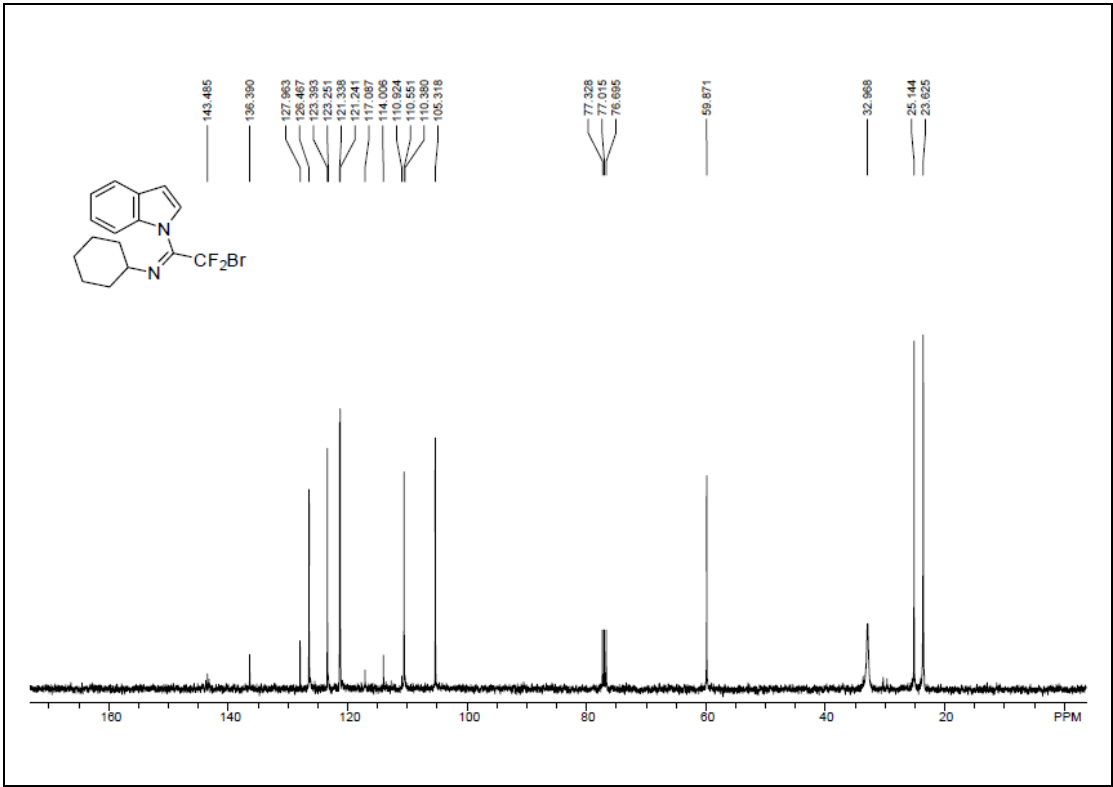
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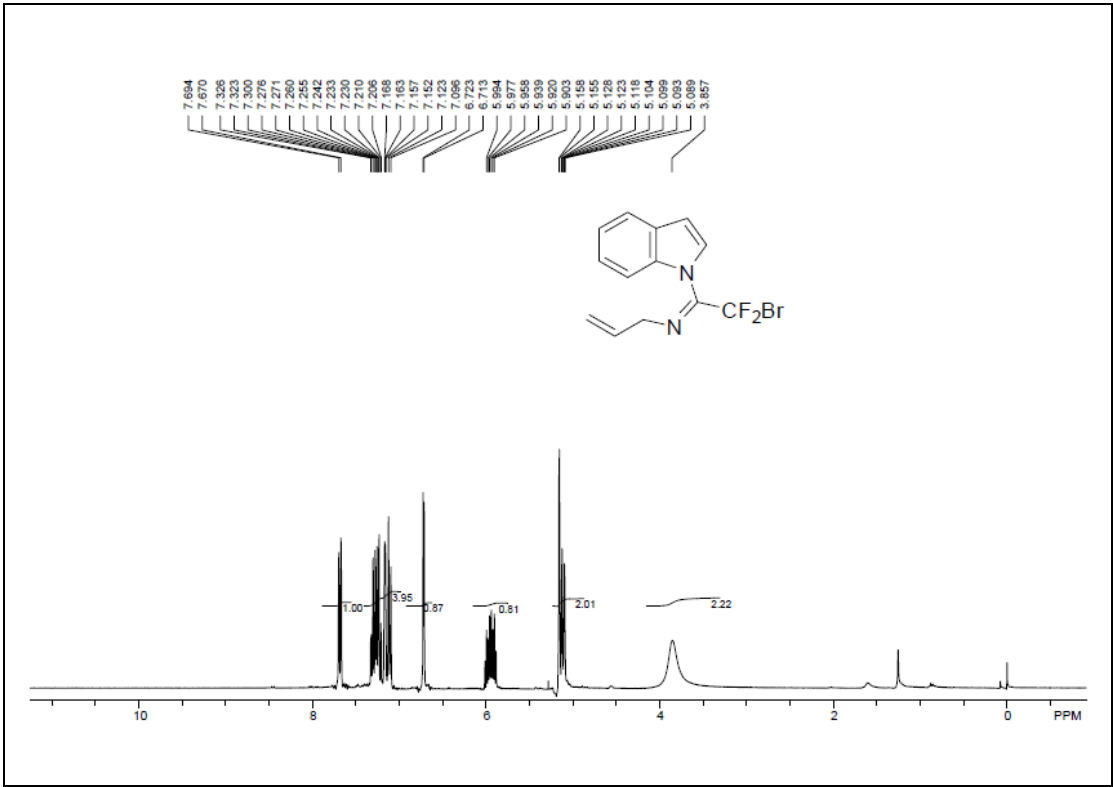


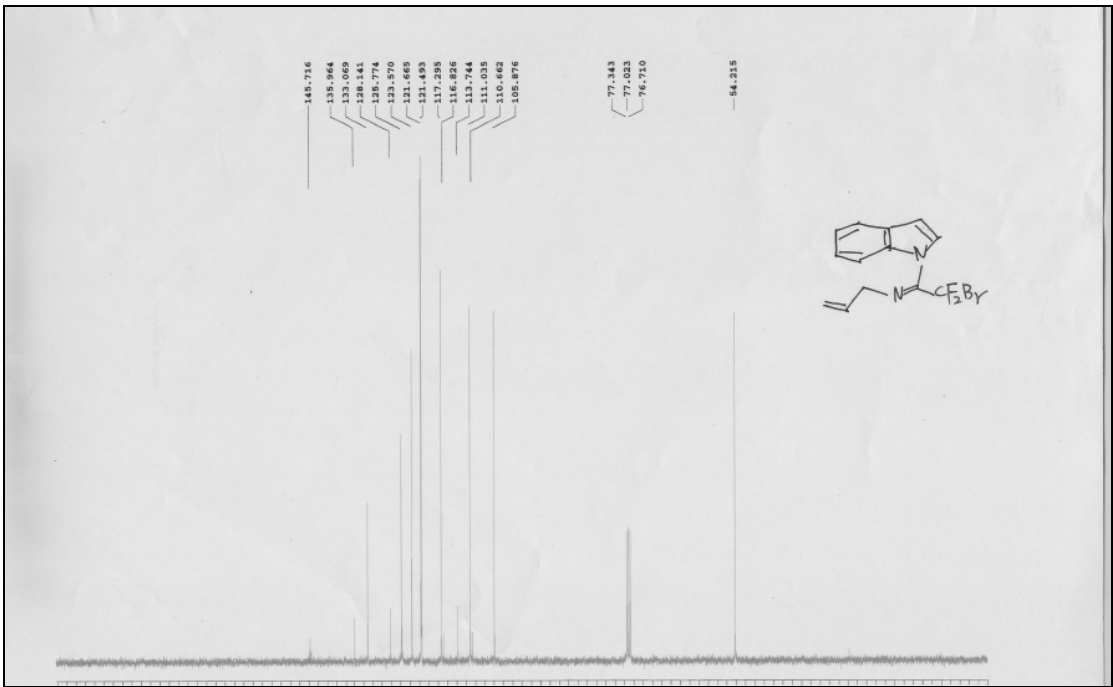
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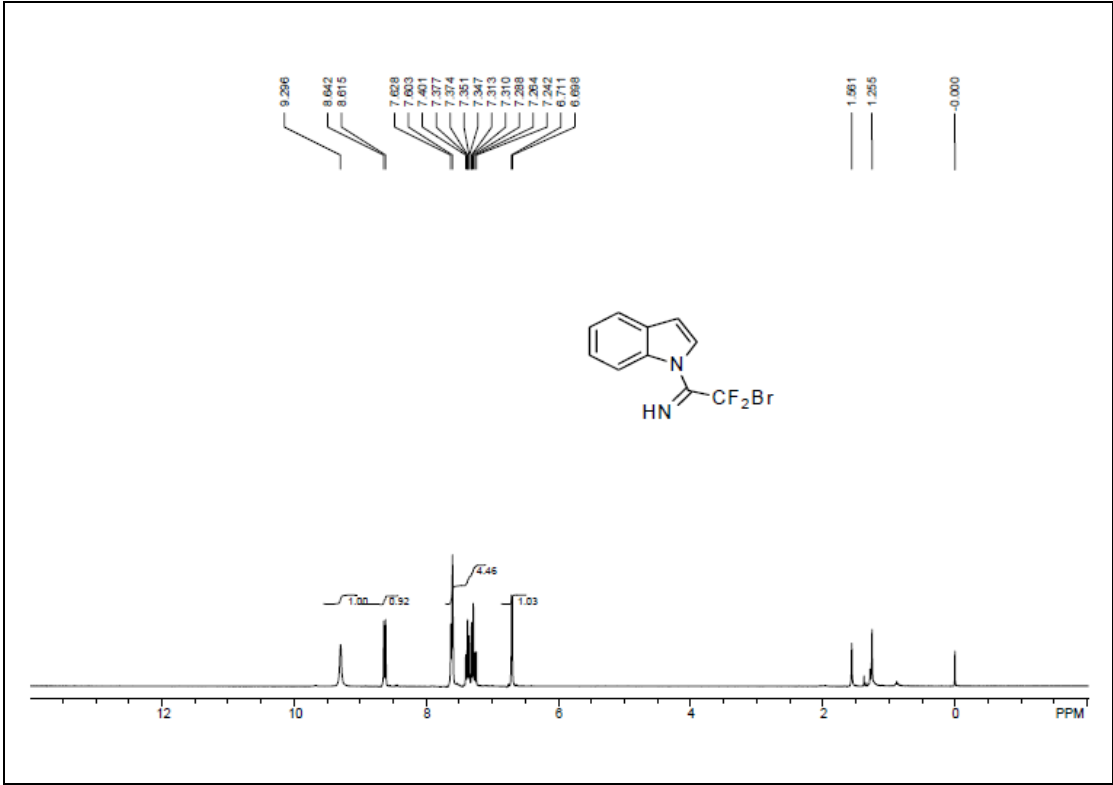


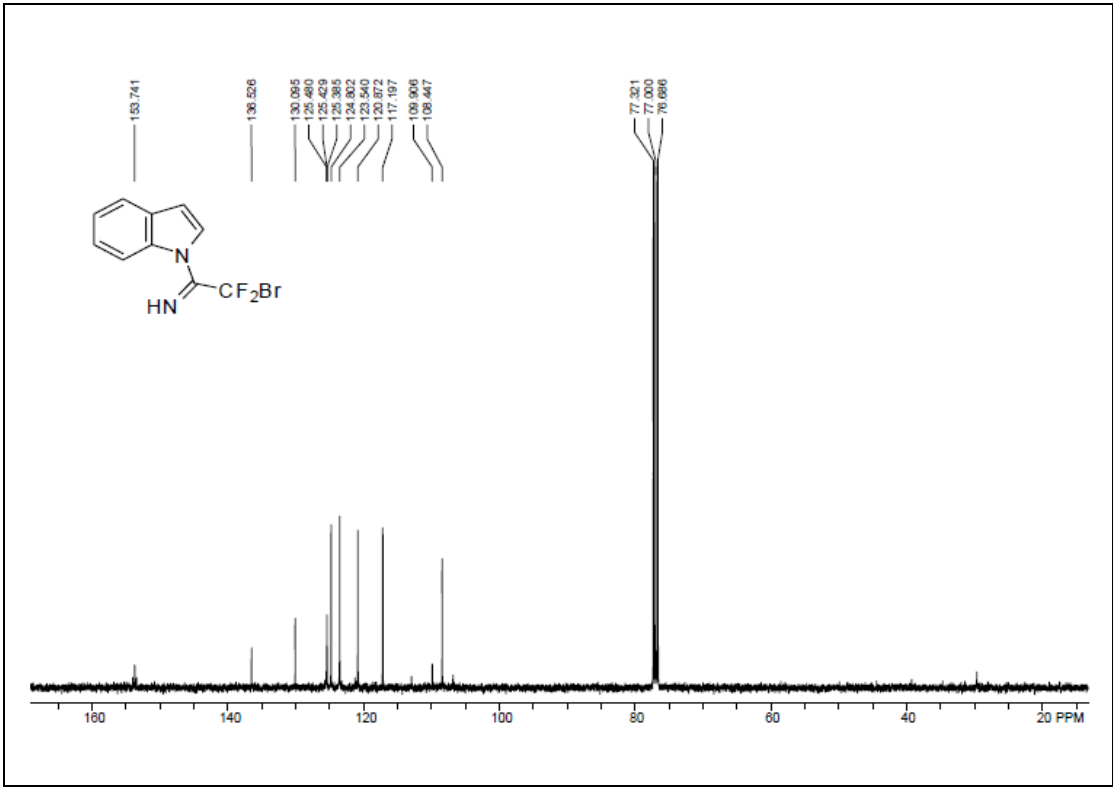
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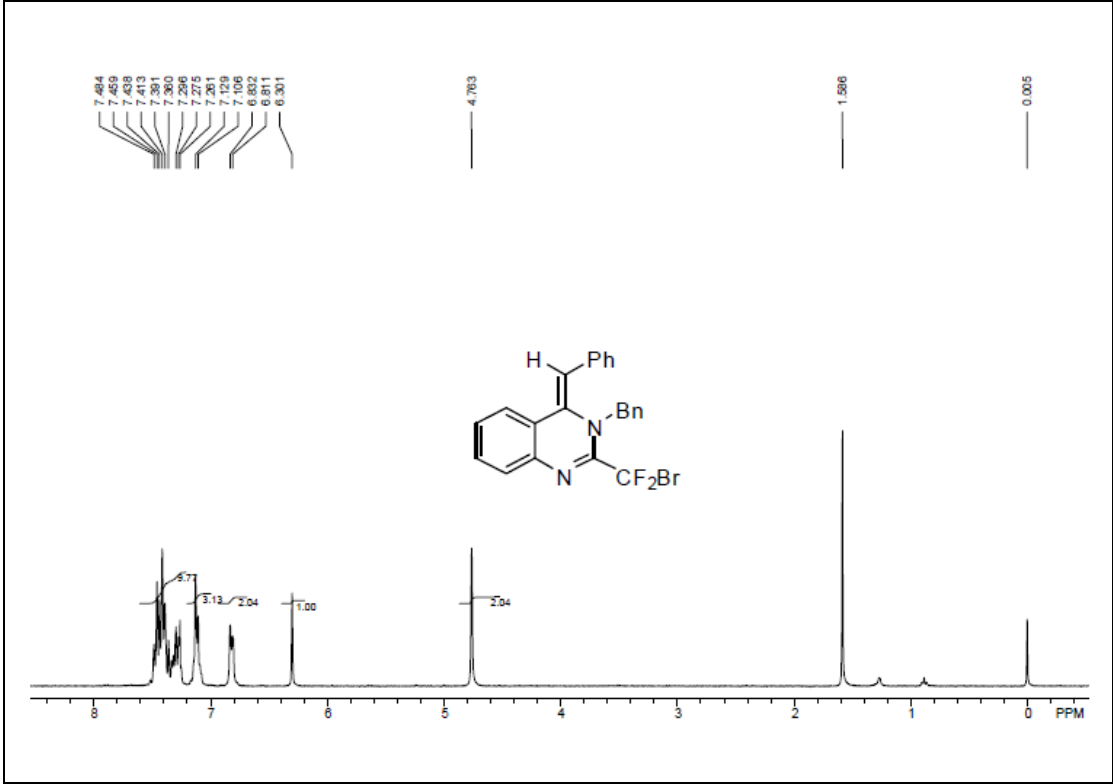


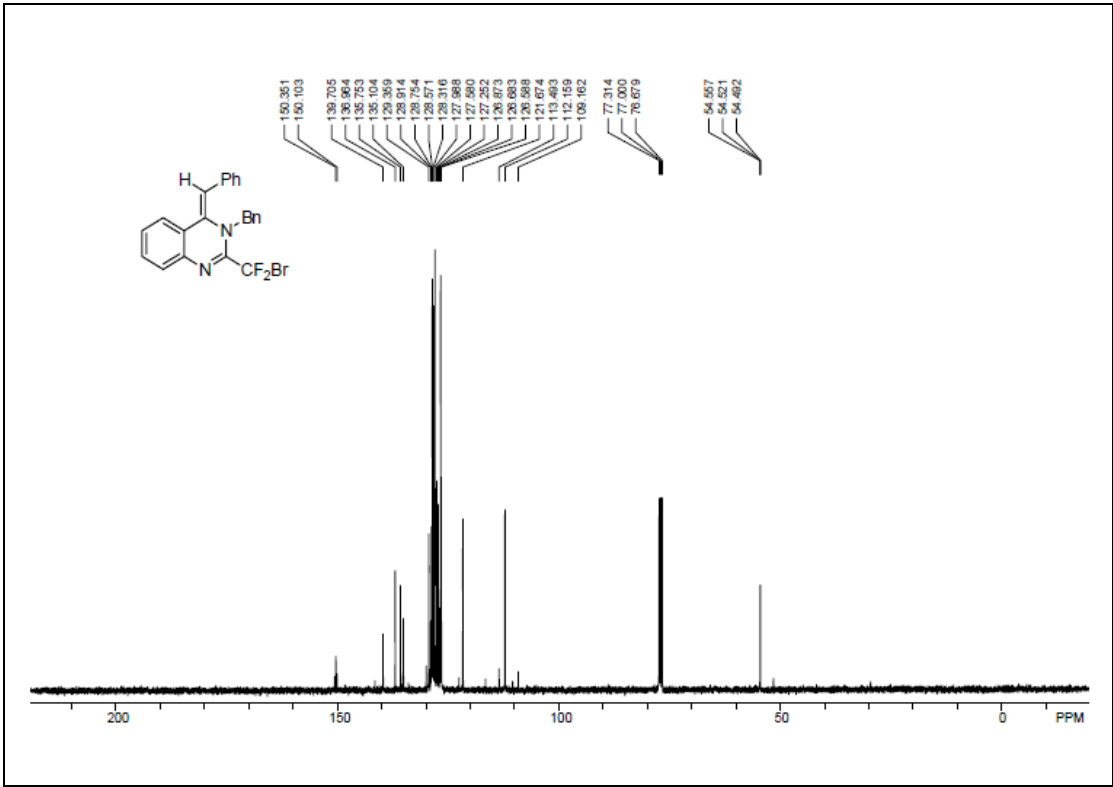
3v



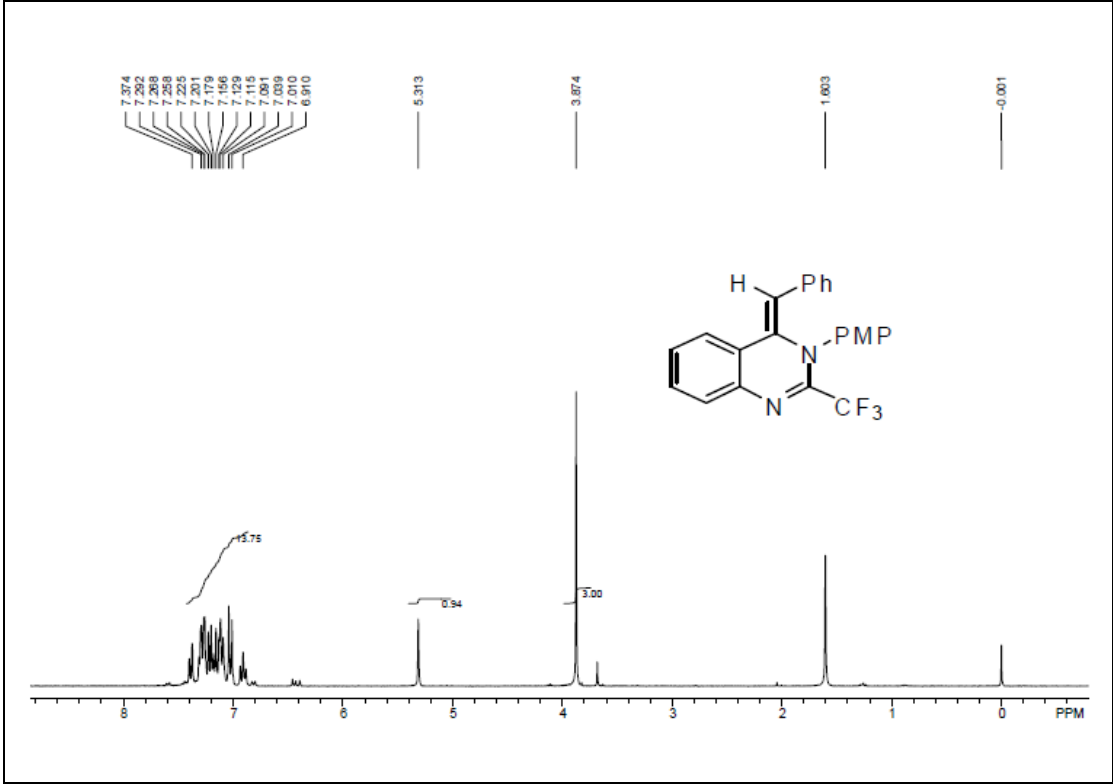


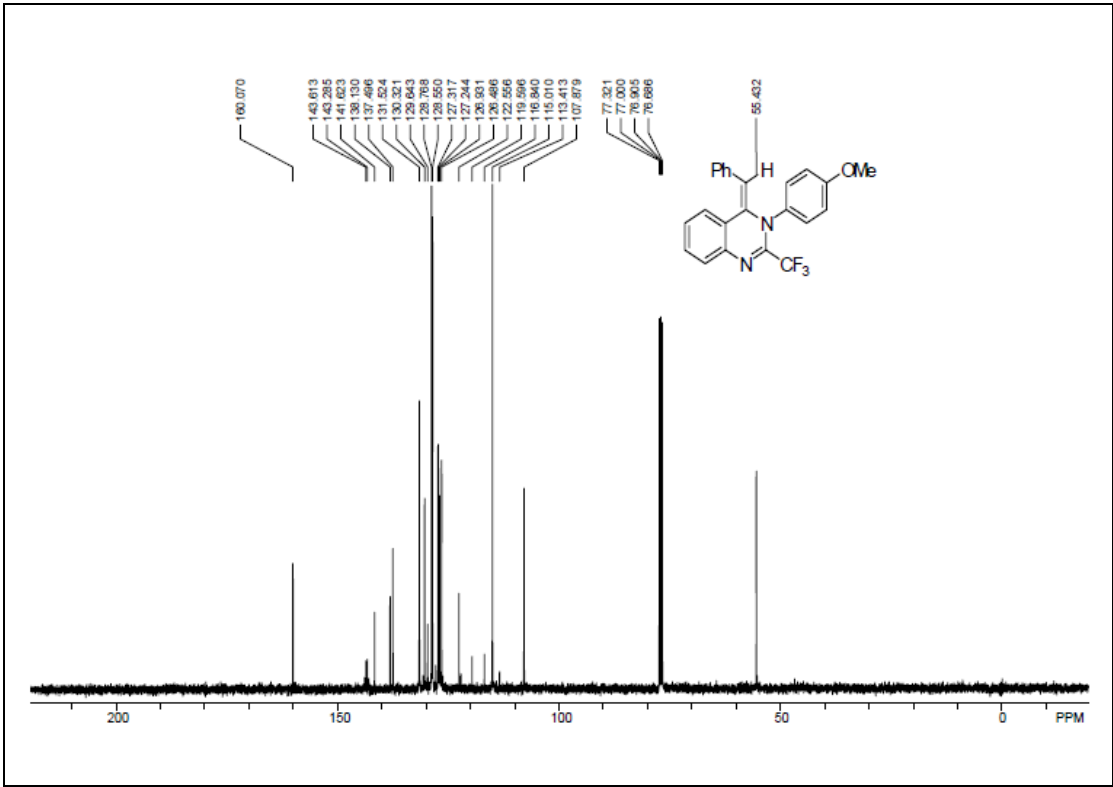
4j'



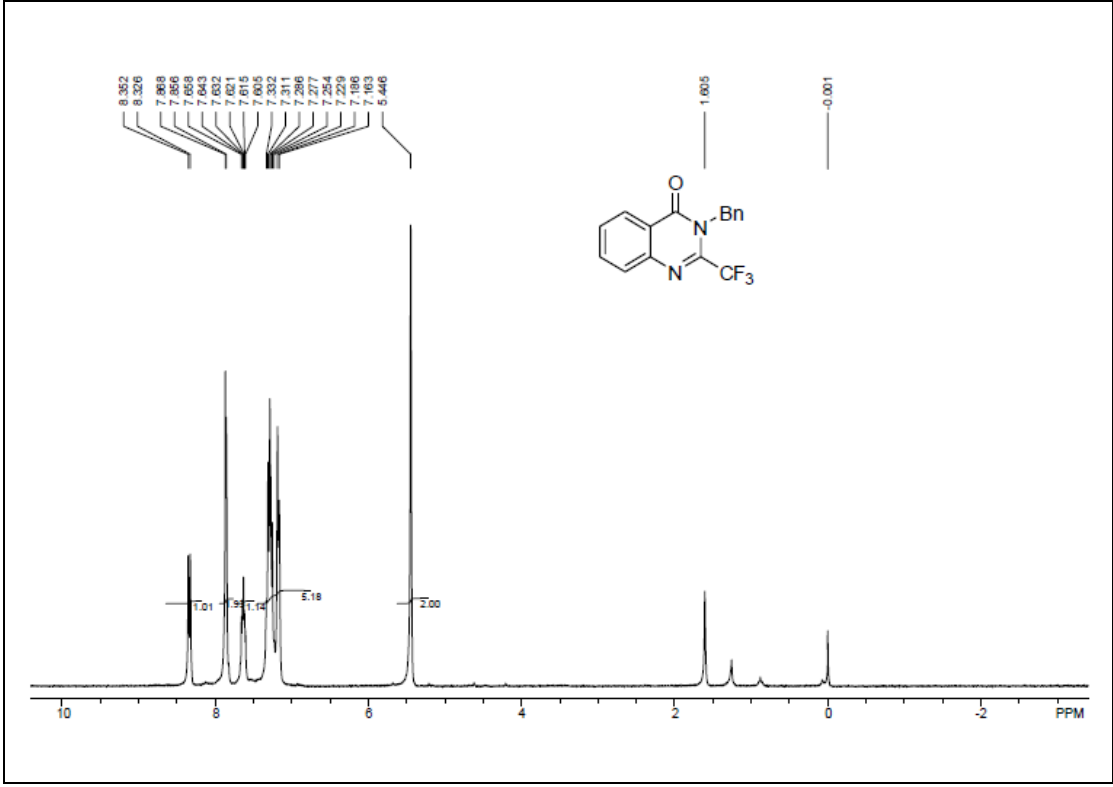


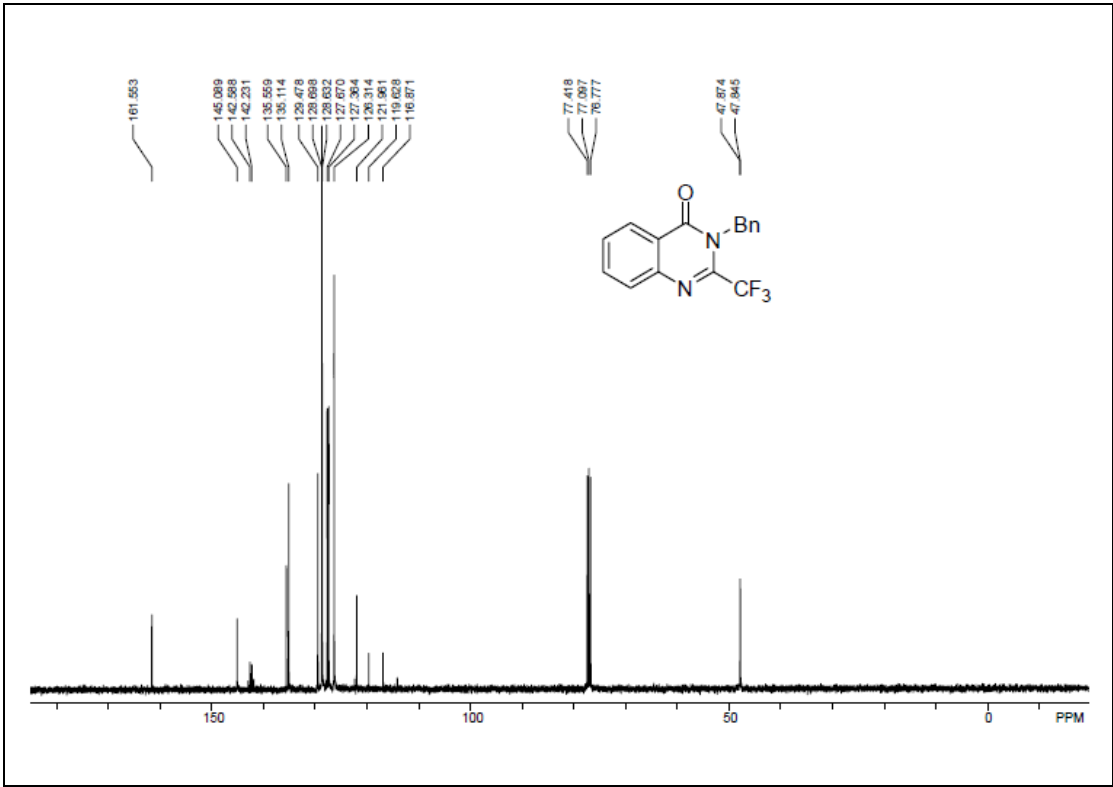
4e



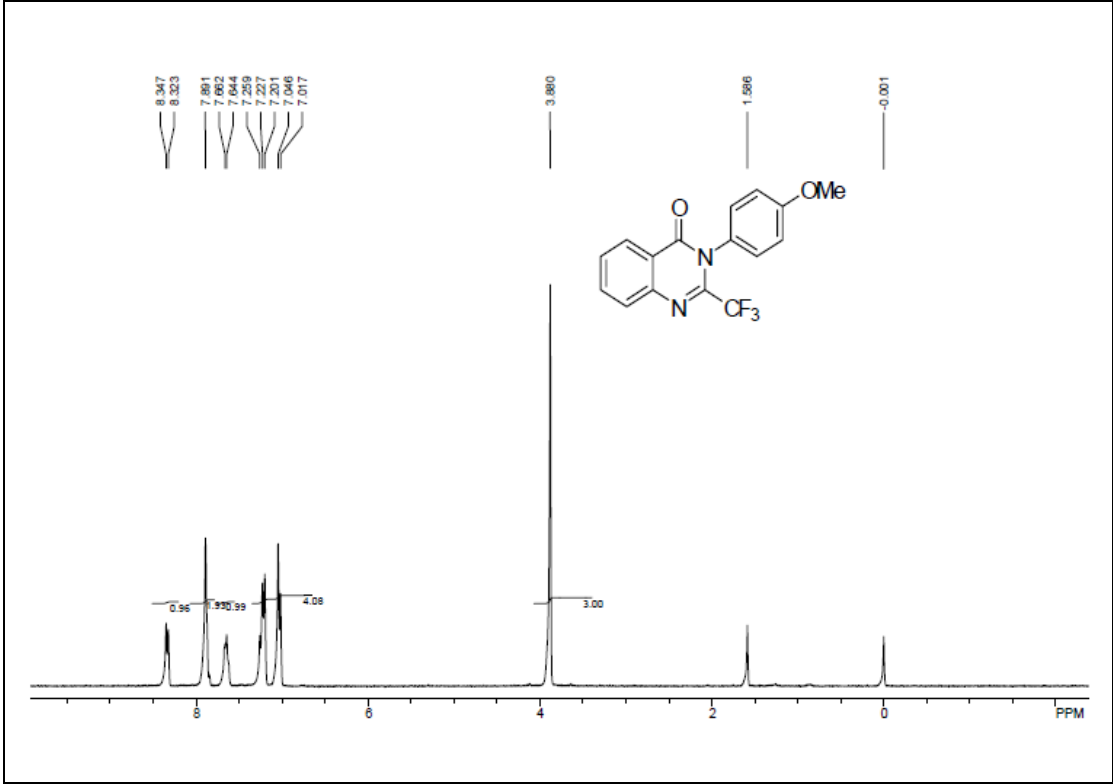


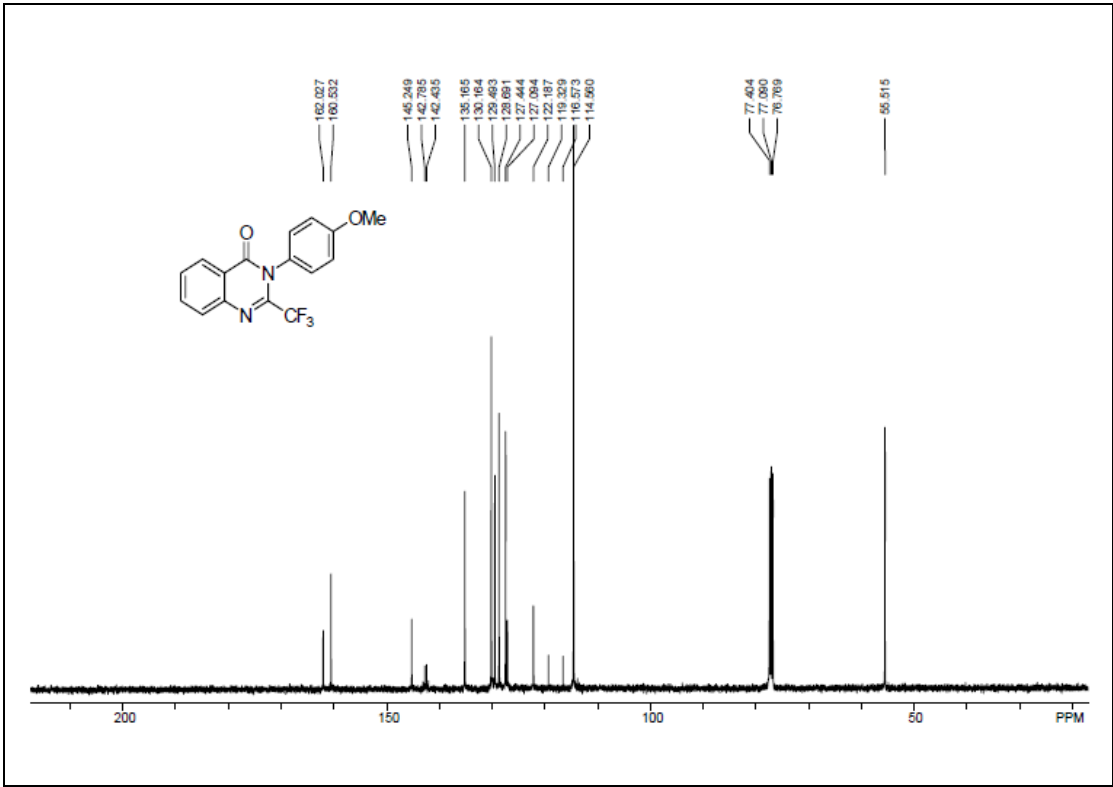
6a



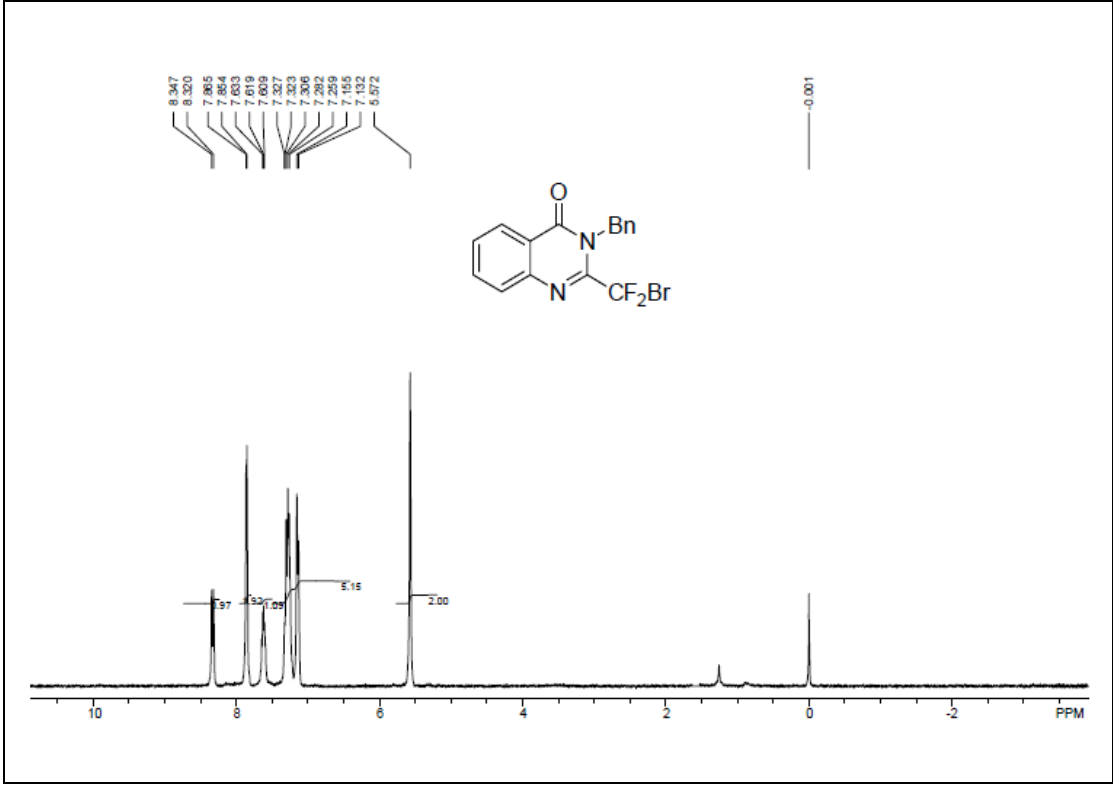


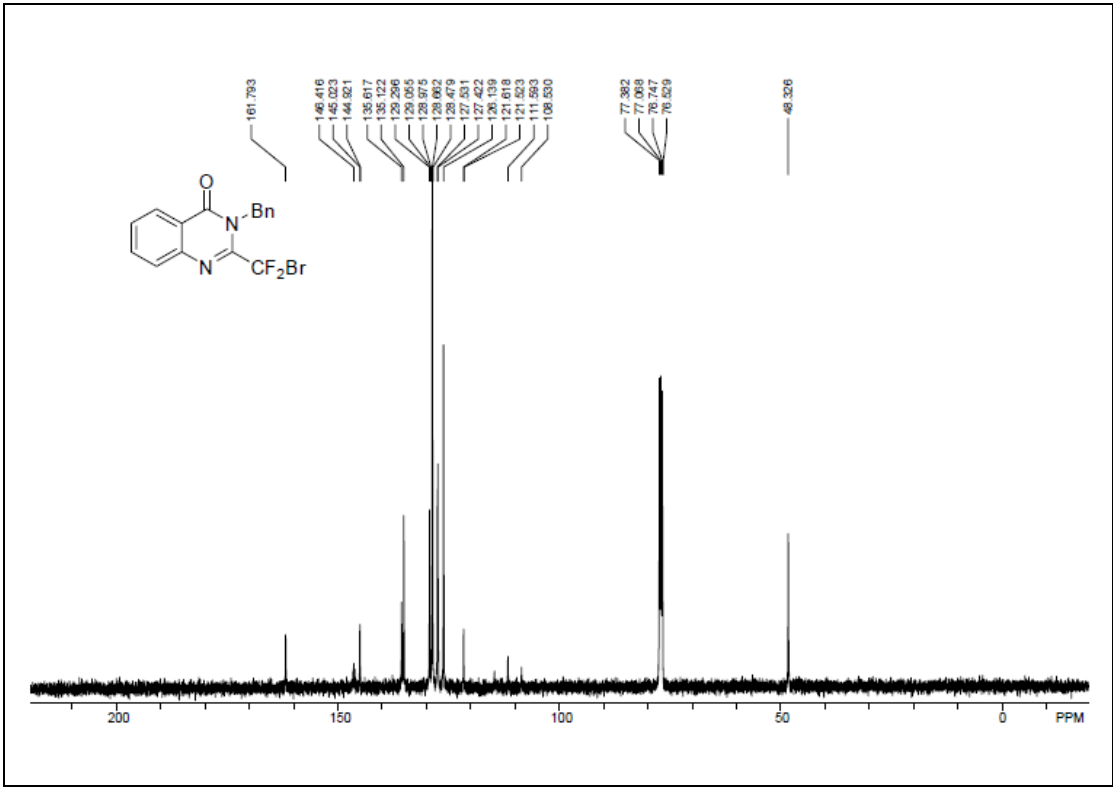
6b



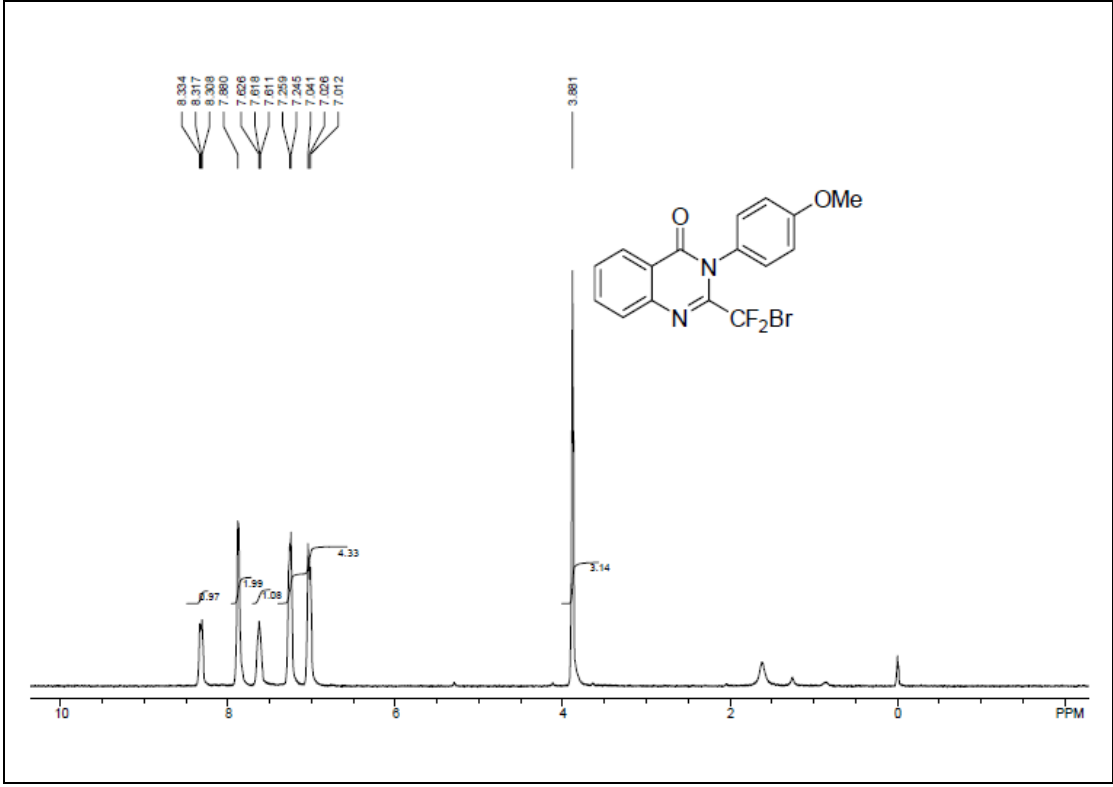


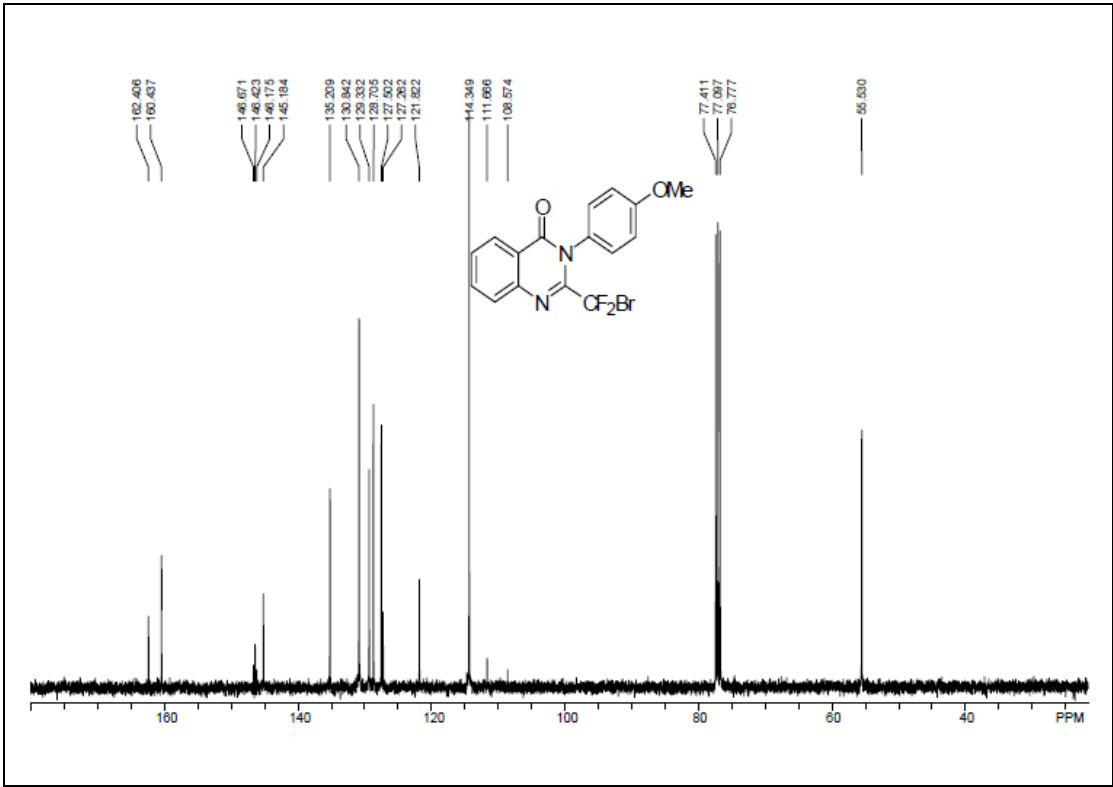
6c



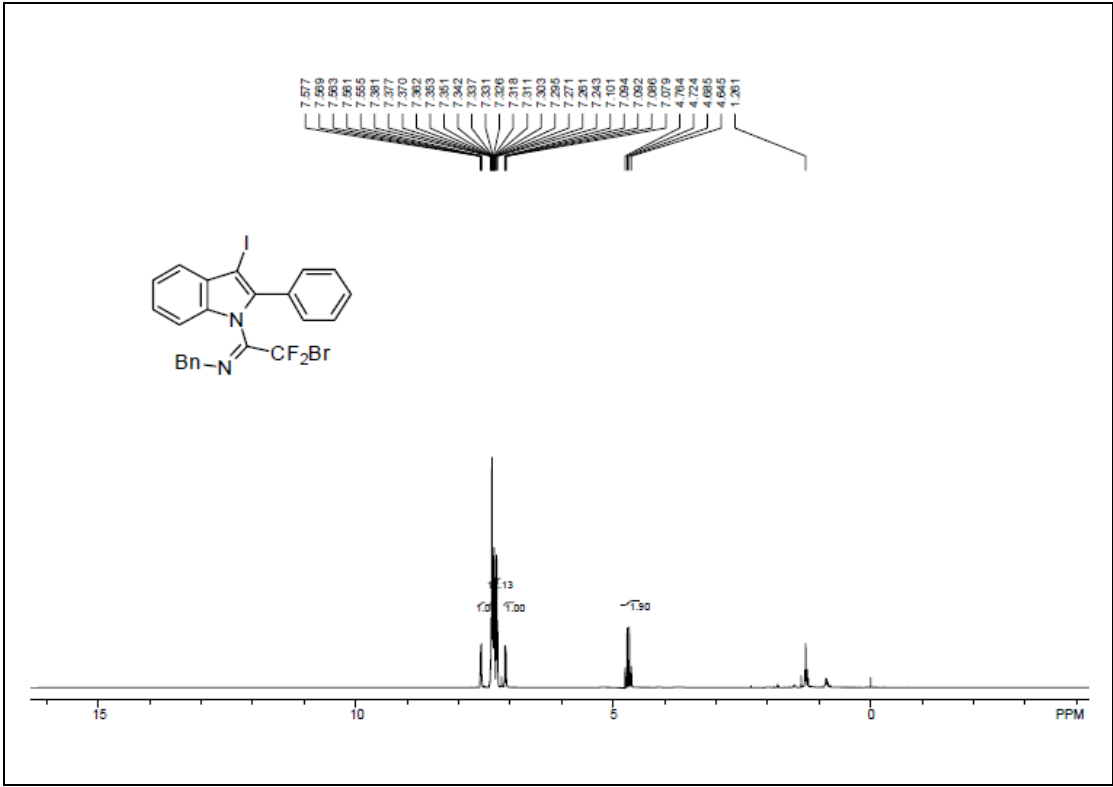


6d





3w



Chemical structure of compound 10: BrCC(F)c1n(c2ccccc2c3ccccc13)I

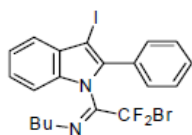
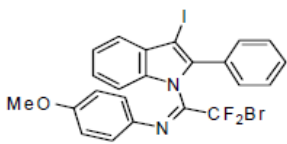
¹H NMR spectrum (CDCl₃) of compound 10. The spectrum shows peaks corresponding to the structure, with integration values indicated below the peaks.

Chemical shifts (ppm) listed above the spectrum:

- 7.937, 7.549, 7.546, 7.474, 7.470, 7.465, 7.455, 7.457, 7.444, 7.417, 7.411, 7.389, 7.384, 7.374, 7.371, 7.366, 7.353, 7.338, 7.334, 7.320, 7.298, 7.295, 7.225, 7.143, 7.124, 3.452, 3.433, 3.412, 3.394, 3.374, 1.715, 1.712, 1.698, 1.695, 1.685, 1.677, 1.665, 1.649, 1.631, 1.535, 1.409, 1.390, 1.372, 1.353, 1.344, 1.325, 1.290, 1.270, 0.922, 0.904, 0.885, 0.010

Integration values indicated below the peaks:

- 1.00
- 1.99
- 2.00
- 2.04
- 2.73

 $3y$ 

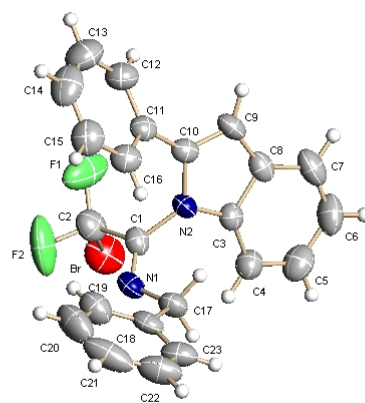
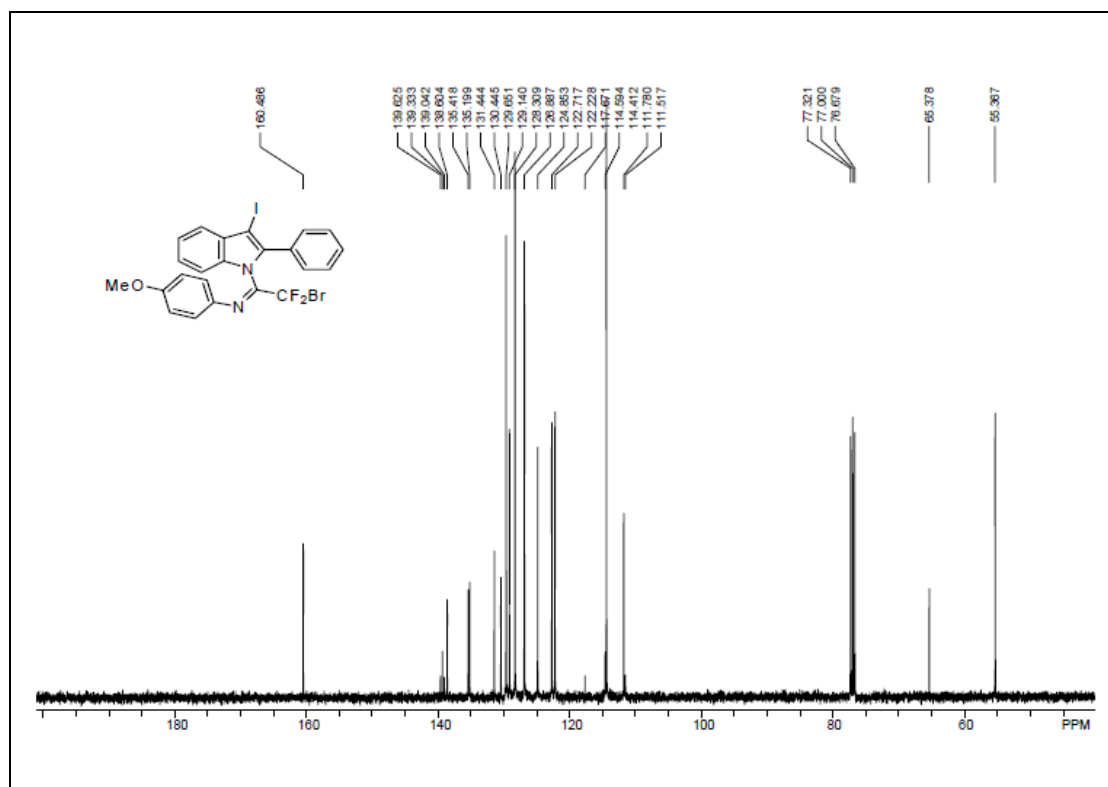


Figure 1. X-Ray Crystal Structure of **3j**

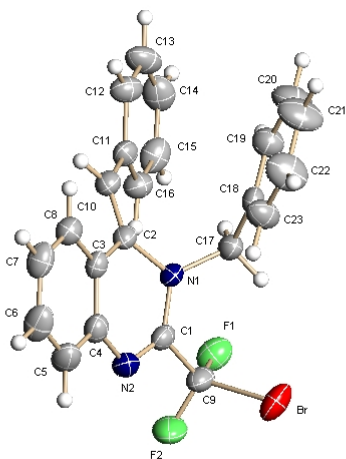


Figure 2. X-Ray Crystal Structure of **4j'**

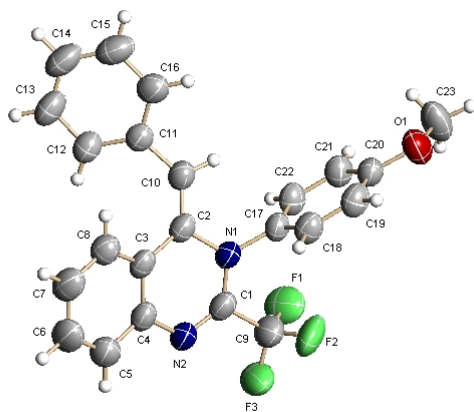


Figure 3. X-Ray Crystal Structure of **4e**