Evaluation of fluorine mediated intermolecular interactions in tetrafluorinated tetrahydroisoquinoline derivatives: Synthesis and Computational Studies

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[#]These authors have equal contributions

Supporting Information:

S1: Experimental:

The synthesis of compound **6** was carried out in two steps starting with **4** following the reaction scheme **2**.

S1.1: Synthesis of 5: In 100 ml dry round bottom flask, substituted secondary amide (**4**) (1.0 m equiv), 0.1 ml conc. HCl and 10 ml $POCl_3$ were added and the reaction mixture was refluxed for 4 hrs by using of anhydrous calcium chloride as a guard tube fitted to the condenser. After the completion of the reaction, $POCl_3$ and HCl were removed completely under high vacuum fitted with liquid nitrogen trap. The solid crude product (chloride salt (**5**), dark brown in colour) was directly used for the next step, without any further purification.

S1.2: Synthesis of 6: The chloride salt **5** was first dissolved in dry methanol and $NaBH_4$ (2.2 m equiv) were added. Then reaction mixture was refluxed for 2 hrs. Then the reaction mixture was cooled to 0 ^{o}C and water was added to decompose the excess $NaBH_4$. The product (**6**) was precipitated, filtered and dried. The crude product was purified by column chromatography using basic alumina as the stationary phase and 2-3% ethyl acetate in hexane as the mobile phase. Most of the products were found to be solid upon purification, but some of them were dense liquid at the room temperature. All the products (**6**) were characterized by ^{1}H, ^{13}C and ^{19}F NMR, differential scanning calorimetry (DSC), PXRD and FTIR spectroscopy (ESI). The produced compounds have been named as per the **scheme 3**.

S2: Powder X-ray diffraction (PXRD) analysis

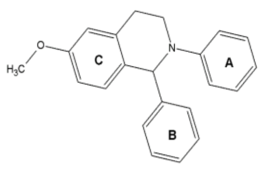
PXRD patterns of all the pure compounds were recorded on a Rigaku Ultima IV X-ray diffractometer using parallel beam geometry equipped with a Cu – Kα radiation, 2.5° Primary and secondary solar slits, 0.5° divergence slit with 10 mm height limit slit, sample rotation stage (120 rpm) attachment and DTex Ultra detector. The tube voltage and current applied were 40 kV and 40 mA. The data were collected over an angle range 5 to 50° with a scanning speed of 2° per minute with 0.02° step. The observed PXRD patterns have been compared (using WINPLOTR) (Roisnel and Rodriguez, 2000) with the simulated PXRD patterns generated from the crystal coordinates using Mercury (Macrae *et al.*, 2008).

S3: Single crystal analysis

Single crystals of suitable size and quality were grown by dissolving the compound in different solvents like acetone, methanol, ethanol, ethyl acetate, dichloromethane, acetonitrile, toluene or a mixture of solvents such as DCM/hexane, chloroform/hexane, ethyl acetate/hexane, methanol/hexane and acetone/hexane etc and subsequent slow evaporation of solvent at 4^{o} C or at RT. Single crystal X-ray diffraction data were collected using a Rigaku XtaLABmini X-ray diffractometer equipped with Mercury CCD detector with graphite monochromated Mo-Kα radiation (λ=0.71073 Å) at 100.0(2) K using ω scans. The data for 6-37 was collected using Bruker AXS KAPPA APEX II X-ray diffractometer with CCD detector and monochromated Mo-Kα radiation at 100.0(2) Kelvin. The data were reduced using Crystal Clear suite 2.0 (2013) and the space group determination was done using Olex2 (Dolomanov *et al.*, 2009). The crystal structures of 6-3 and 6-4 were solved using SHELXS (Sheldrick, 2008), 6-2 was solved using SIR2004 (Burla *et al.*, 2005) and all other compounds were solved using SHELXT (Sheldrick, 2015). All but one compounds were refined using SHELXL (Sheldrick, 2008), olex2.refine of Olex2 (Dolomanov *et al.*, 2004) suite was used to refine 6-2. All the hydrogen atoms were geometrically fixed and refined using the riding model. Multi-scan method was employed for absorption correction. Data collection, crystal structure solution and refinement details for all the compounds are listed in the manuscript. All the packing and interaction diagrams have been generated using Mercury 3.5 (Macrae *et al.*, 2008). Geometric calculations have been done using PARST (Nardelli, 1995) and PLATON (Spek, 2009).

S4: Crystallographic Modelling of Disorder

All the data sets were recorded at 100.0K. Only one compound (**6-23**) was found to be disordered. The phenyl ring attached to the N atoms is termed as the "A ring", the phenyl ring connected to the C=O group is termed as the "B ring" and the 3rd phenyl ring containing the –OMe groups is termed as the "C ring" in the structural descriptions in this manuscript (Scheme 4).



Scheme 4: Identification of various phenyl rings in the studied molecules.

The positional disorder has been found due 180^o rotation of phenyl ring (B ring) around C–C bonds in the molecule. The ratio of the occupancy of fluorophenyl ring B is 0.6557**:**0.3443. The structure was refined with 0.5 occupancy using PART command in SHELXL (Sheldrick, 2008). Thermal parameters of the atoms of the two parts, which belong to the same chemical environment, were constrained to be equal by EADP command in SHELXL (Sheldrick, 2008). Refinement of this structure (**6-23**) was done for two independent positions, namely **A** and **B** ('**A**' for higher occupancy and '**B**' for lower occupancy). For refinement, the positions of carbon atom in benzene ring for **A** and **B** were kept fixed using EXYZ command in SHELXL. For the atoms at the same position, thermal parameters were also constrained to be equal using EADP command in SHELXL (Sheldrick, 2008). All hydrogen atoms were then positioned geometrically and refined using a riding model with U_{iso}(H) = 1.2 U_{eq}(C,N). Except fluorine all other atoms in the minor conformer were refined isotopically and the thermal parameter of all the carbon atoms was constrained to the same value using EADP command in SHELXL (Sheldrick, 2008).

Powder X-ray diffraction

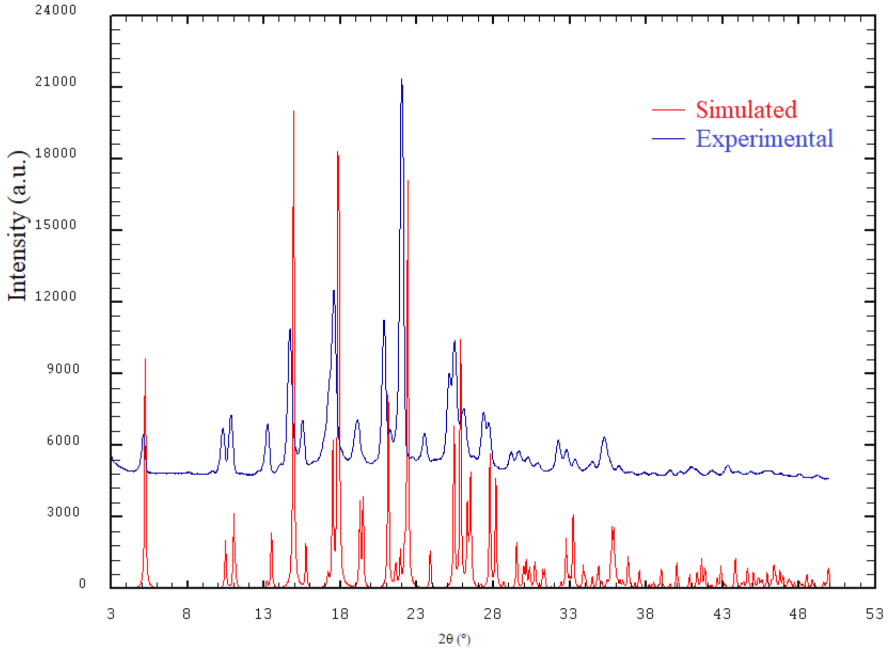


Figure S1: Comparison of experimental and simulated PXRD patterns of **6-1**

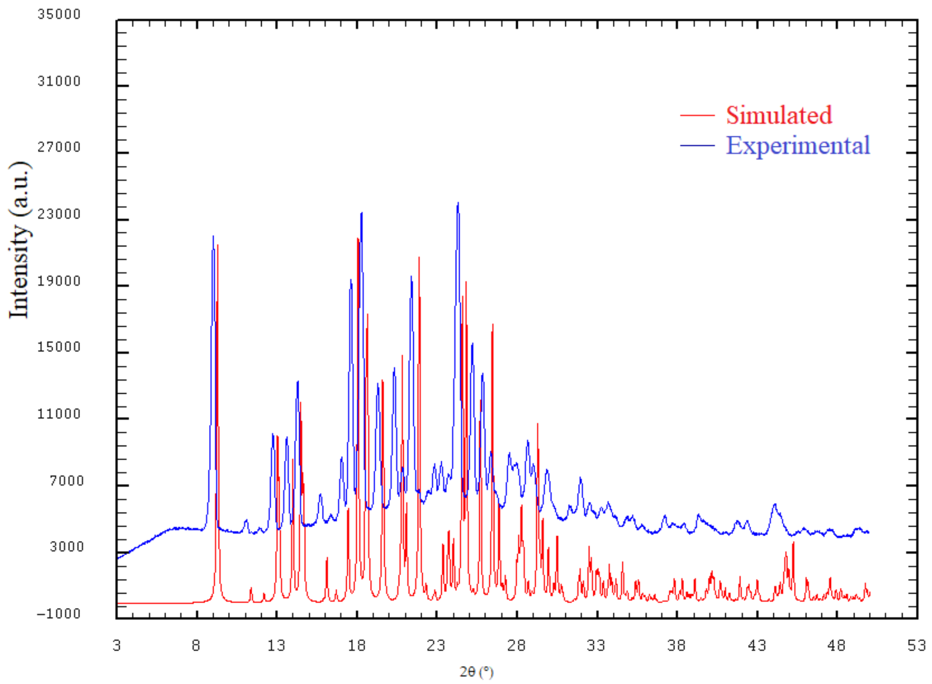


Figure S2: Comparison of experimental and simulated PXRD patterns of **6-2**

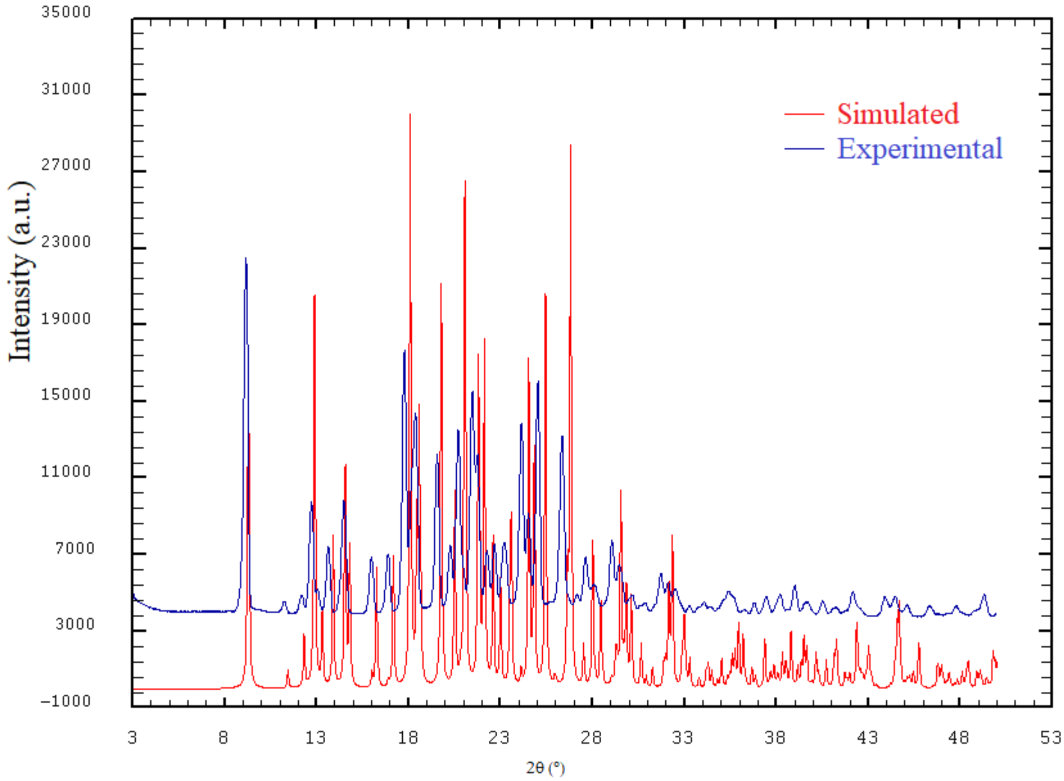


Figure S3: Comparison of experimental and simulated PXRD patterns of **6-3**

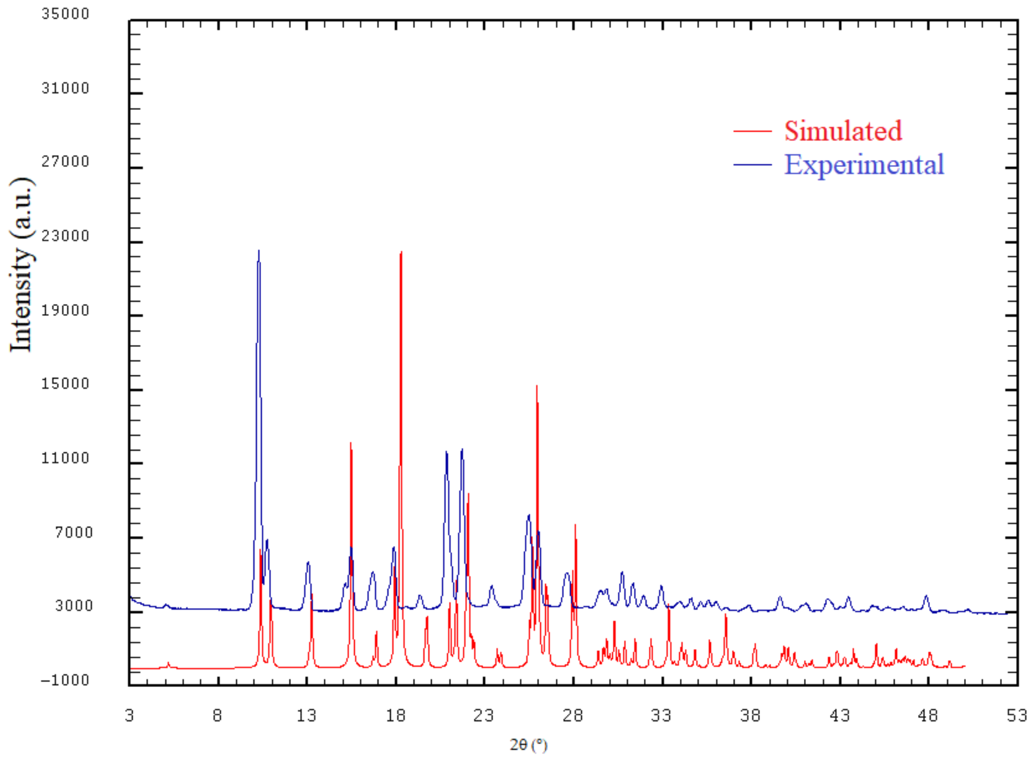


Figure S4: Comparison of experimental and simulated PXRD patterns of **6-4**

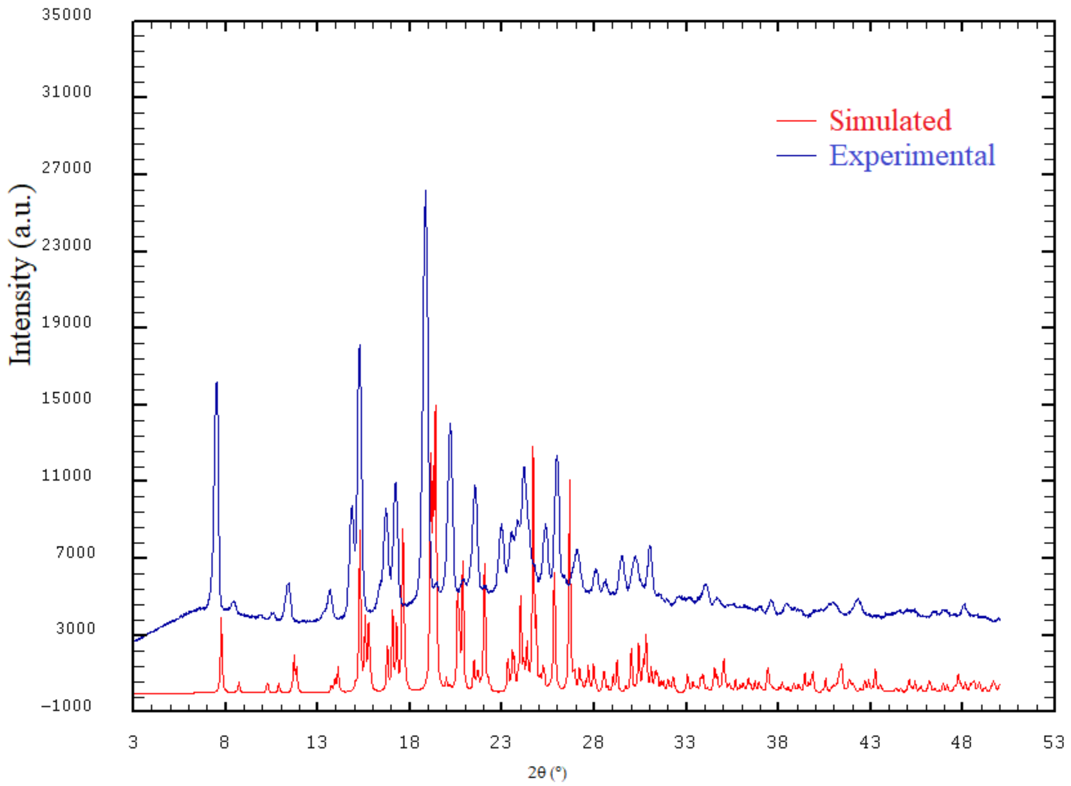


Figure S5: Comparison of experimental and simulated PXRD patterns of **6-5**

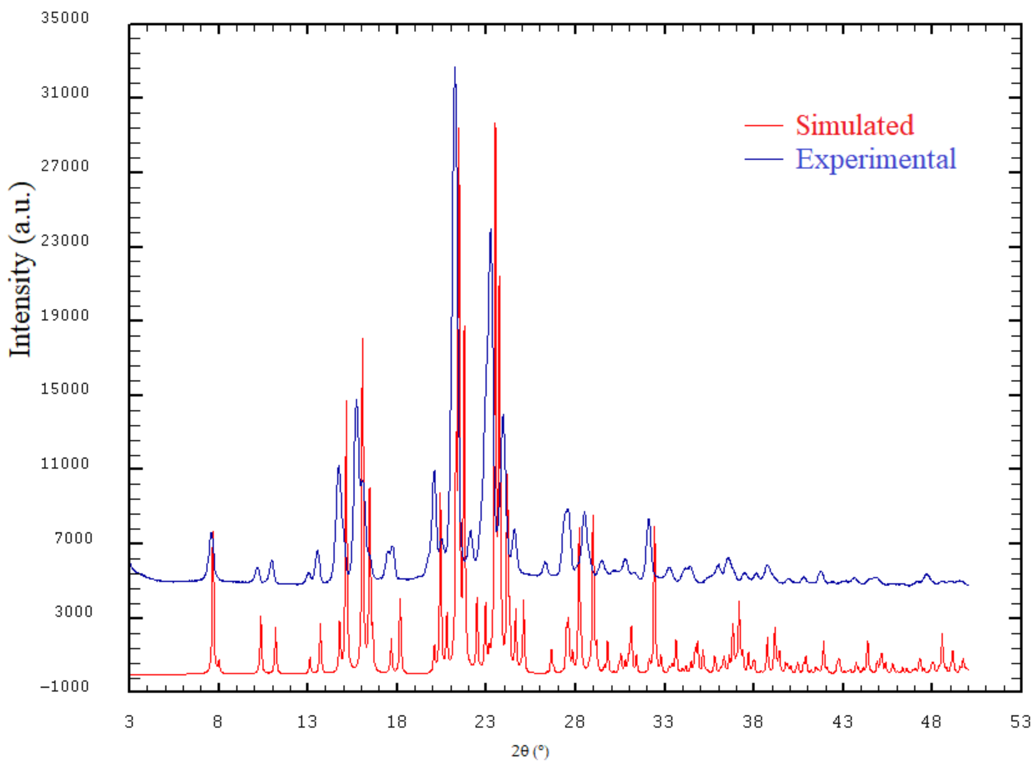


Figure S6: Comparison of experimental and simulated PXRD patterns of **6-6**

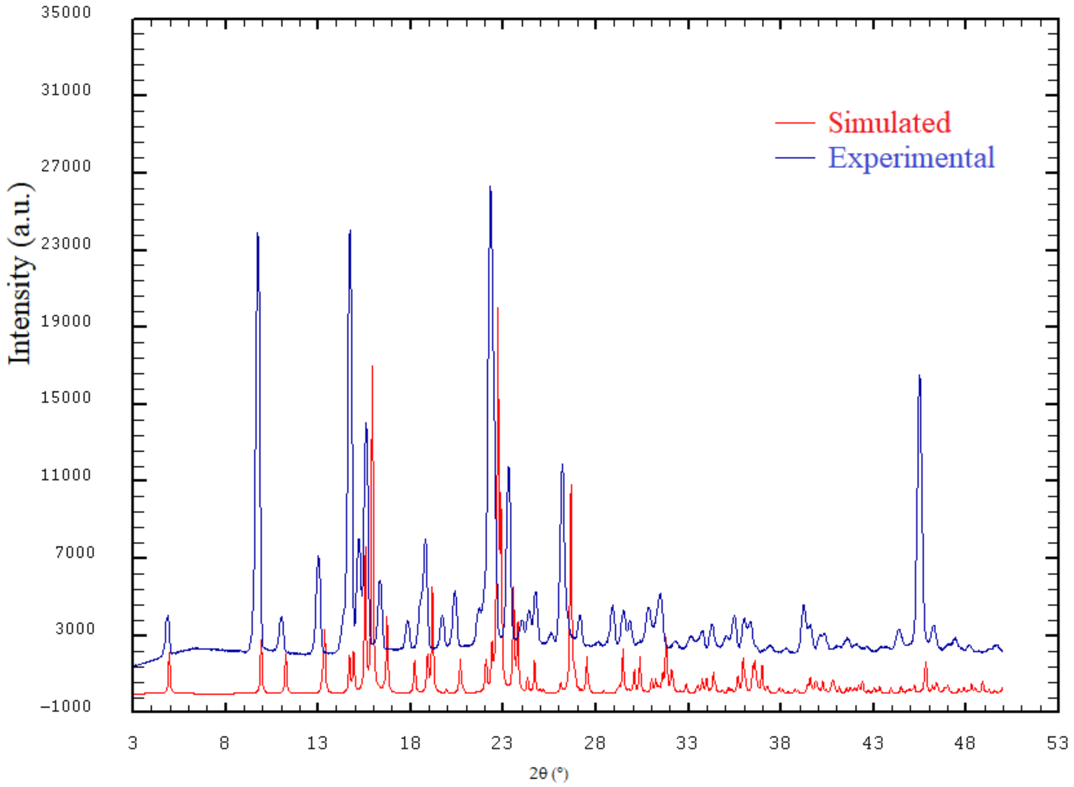


Figure S7: Comparison of experimental and simulated PXRD patterns of **6-7**

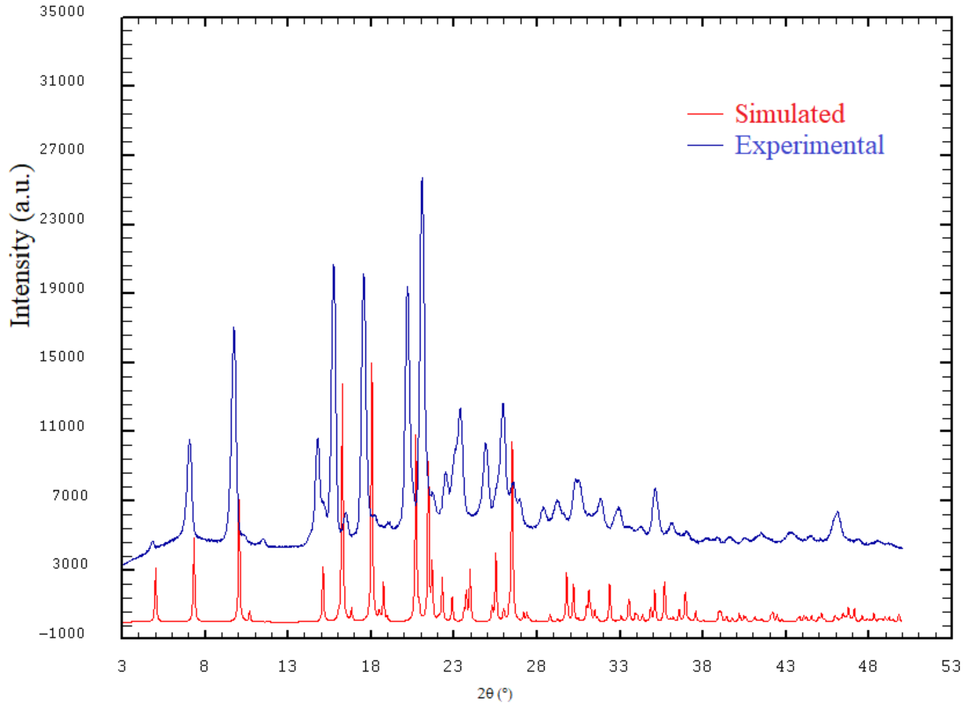


Figure S8: Comparison of experimental and simulated PXRD patterns of **6-8**

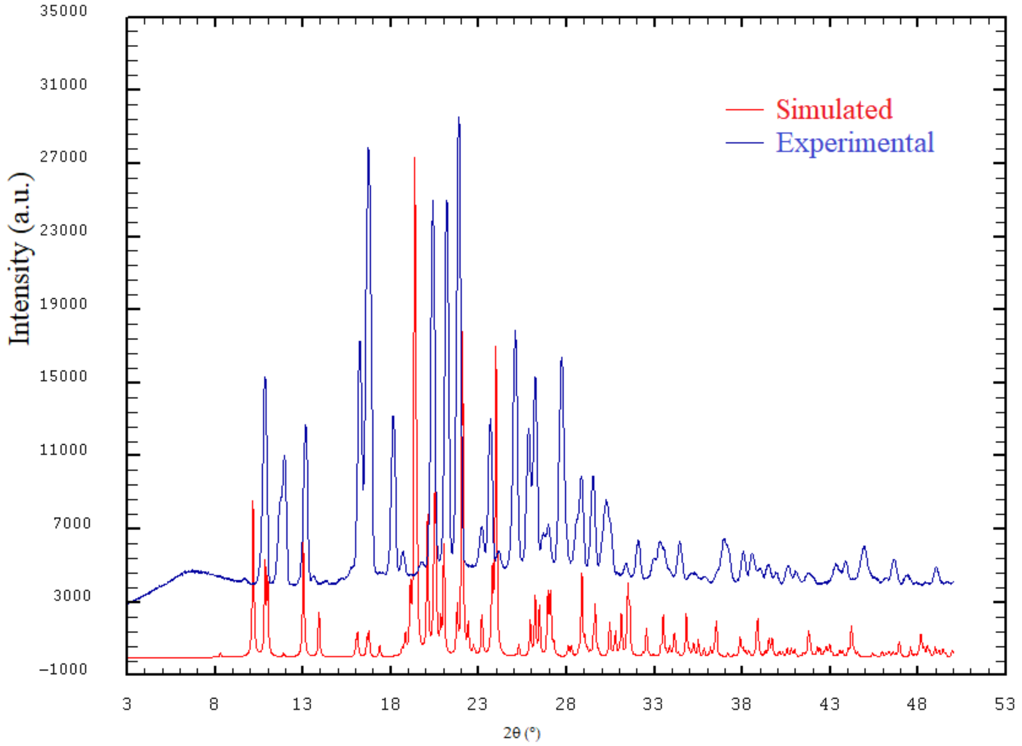


Figure S9: Comparison of experimental and simulated PXRD patterns of **6-9**

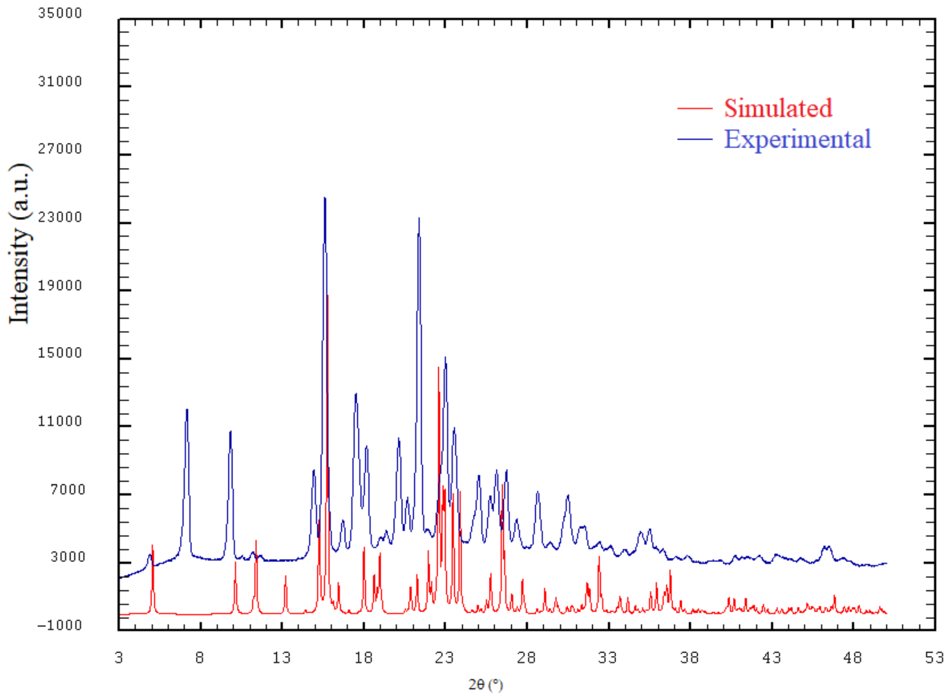


Figure S10: Comparison of experimental and simulated PXRD patterns of **6-13**

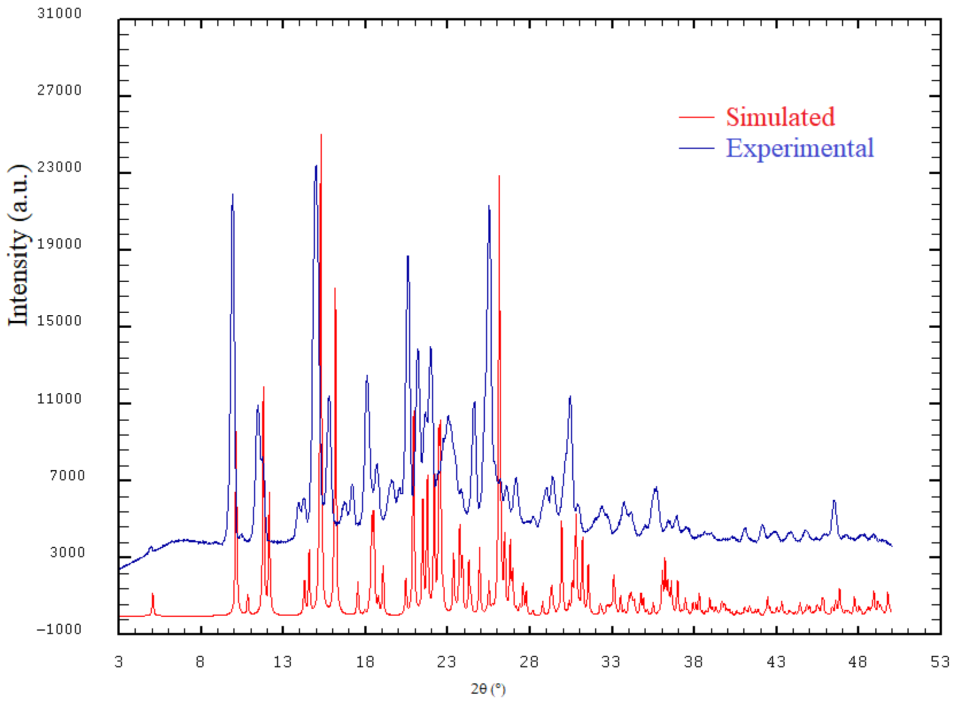


Figure S11: Comparison of experimental and simulated PXRD patterns of **6-16**

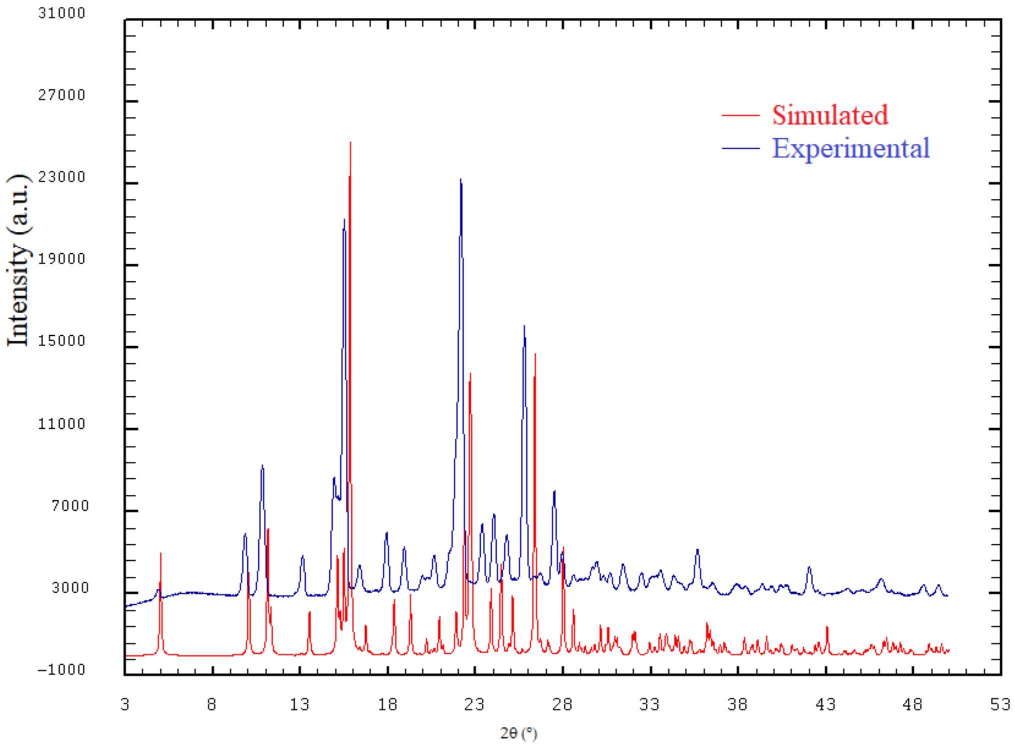


Figure S12: Comparison of experimental and simulated PXRD patterns of **6-19**

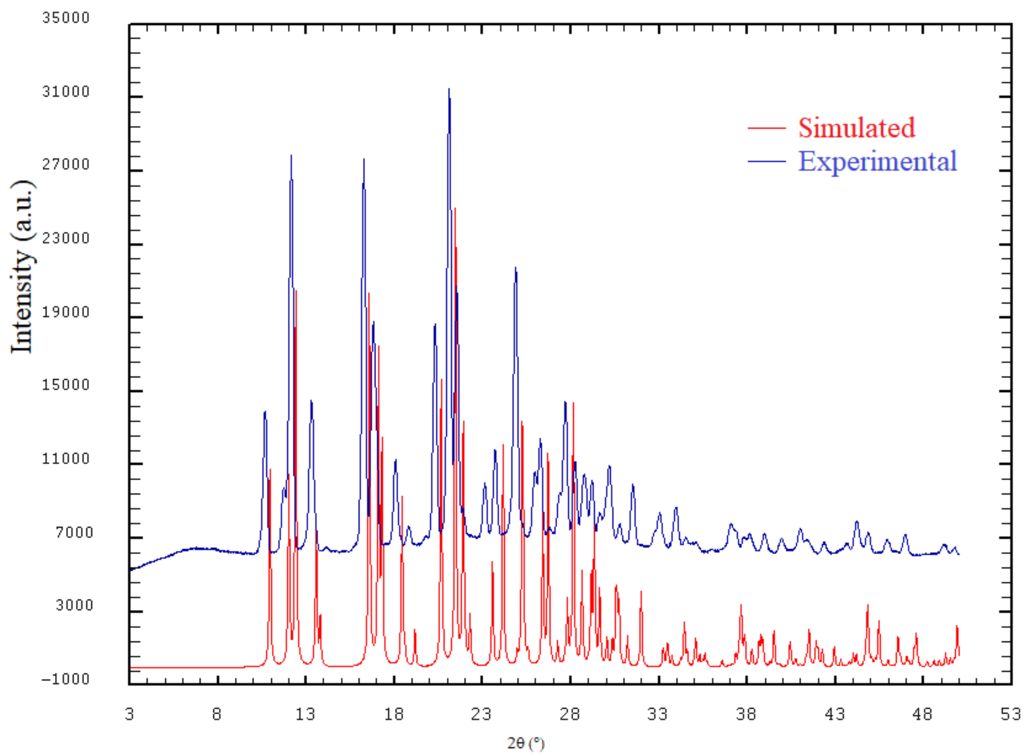


Figure S13: Comparison of experimental and simulated PXRD patterns of **6-21**

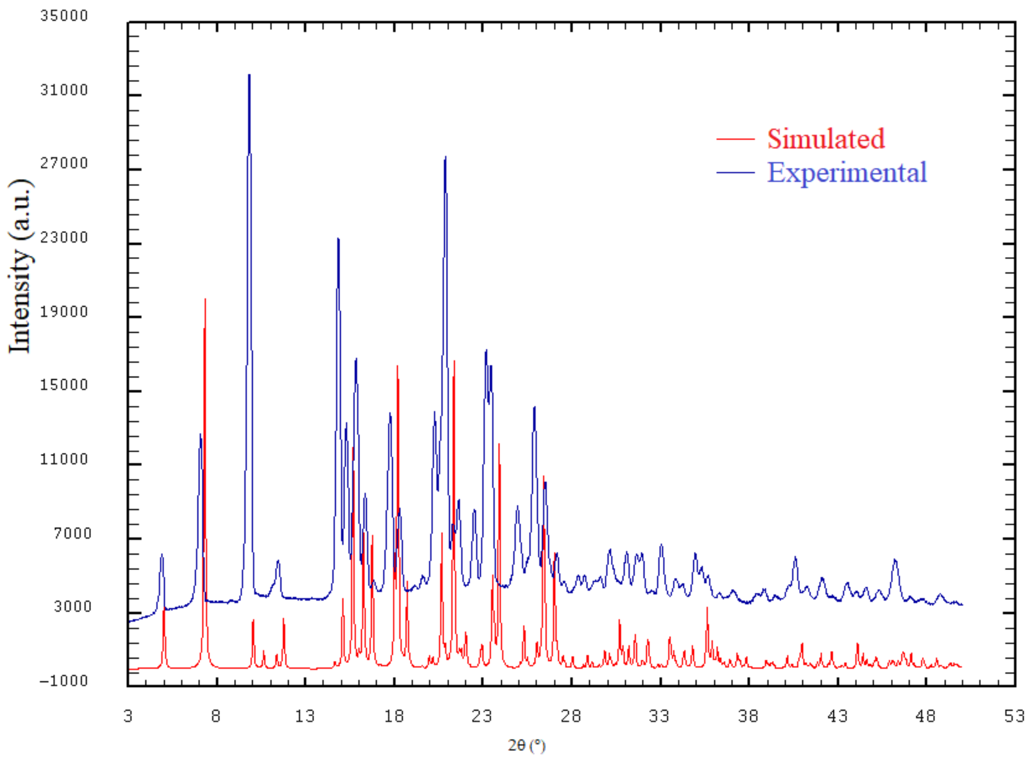


Figure S14: Comparison of experimental and simulated PXRD patterns of **6-23**

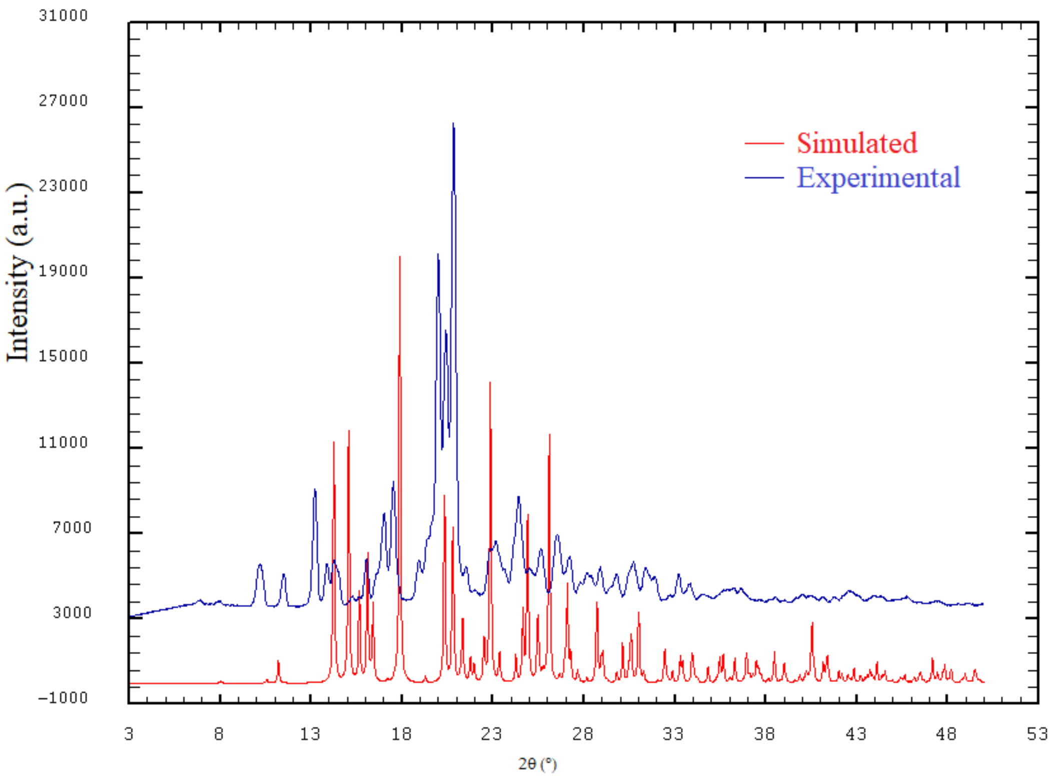


Figure S15: Comparison of experimental and simulated PXRD patterns of **6-25**

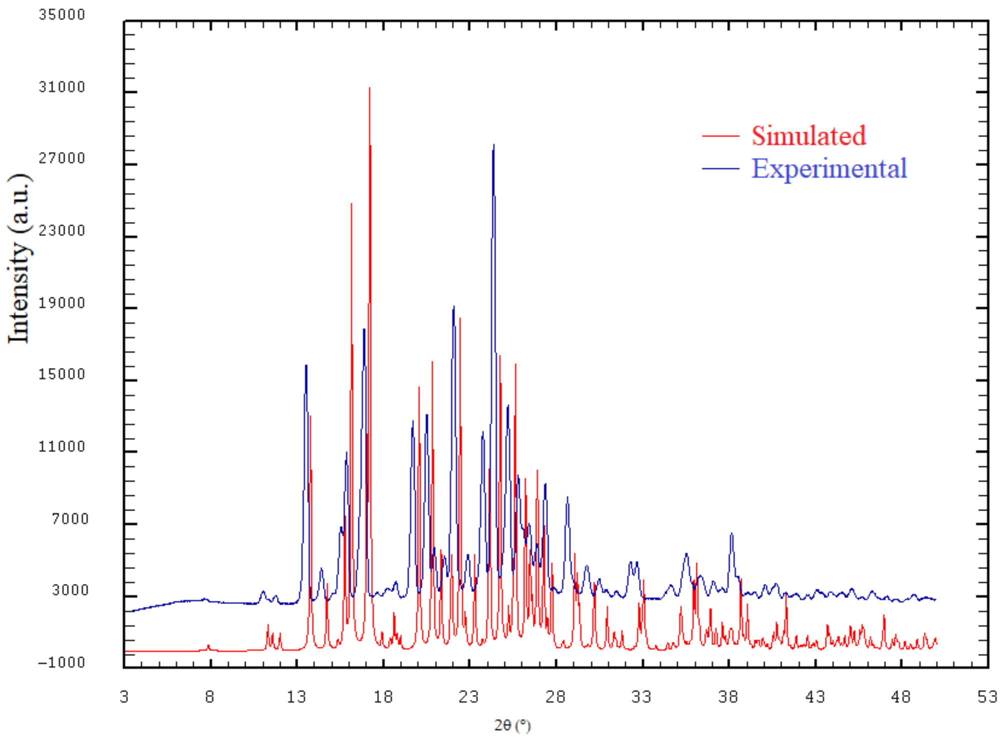


Figure S16: Comparison of experimental and simulated PXRD patterns of **6-30**

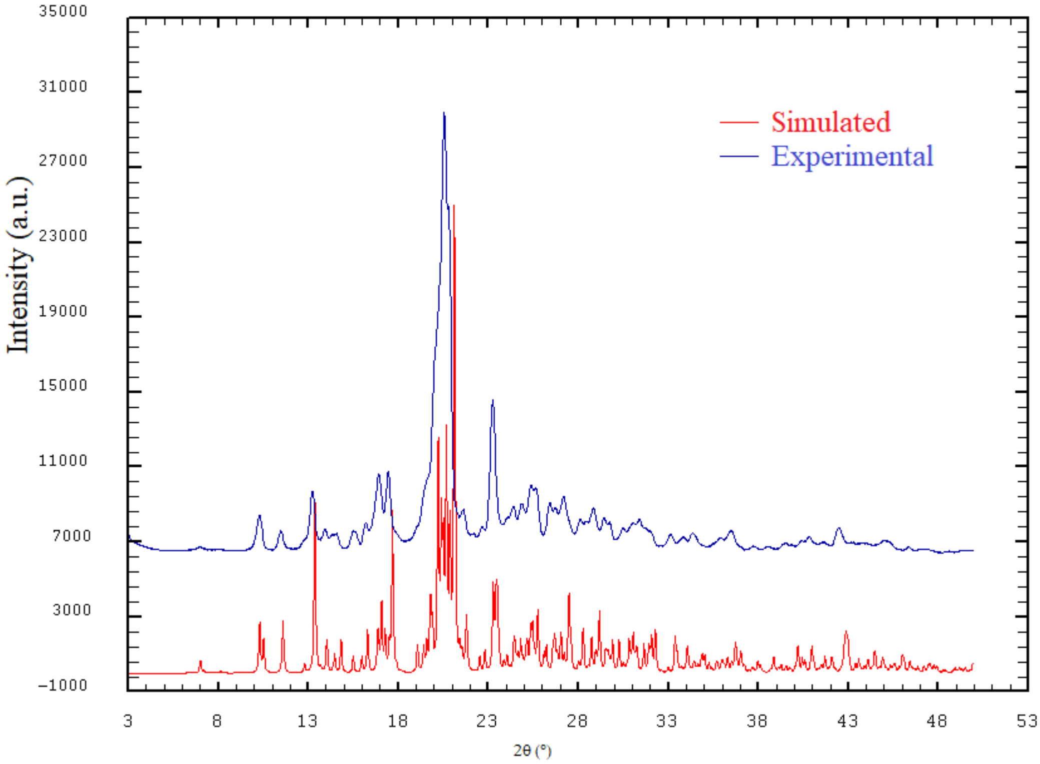


Figure S18: Comparison of experimental and simulated PXRD patterns of **6-33**

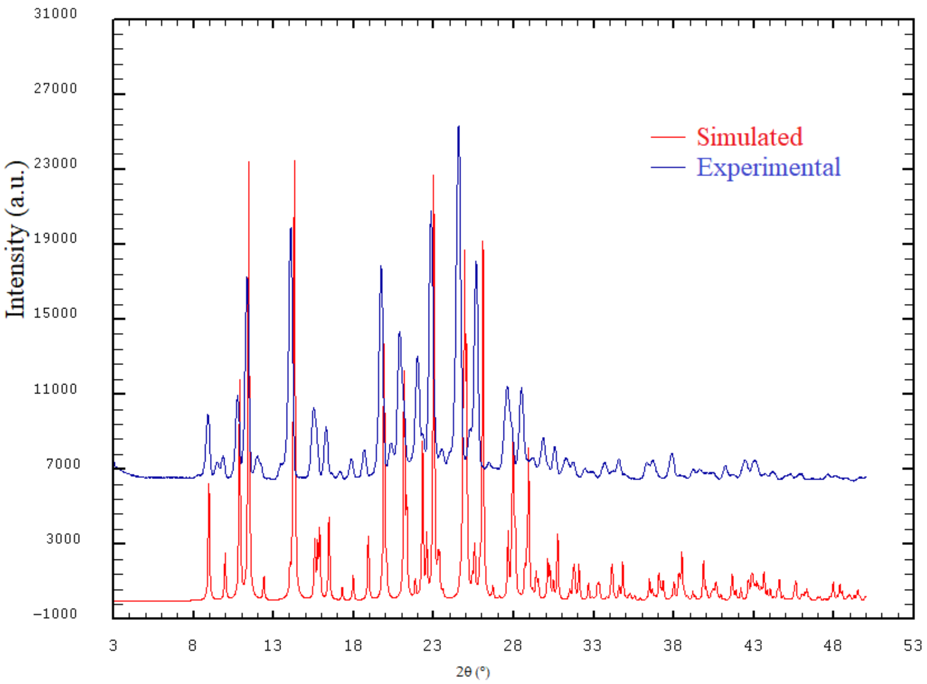


Figure S19: Comparison of experimental and simulated PXRD patterns of **6-34.**

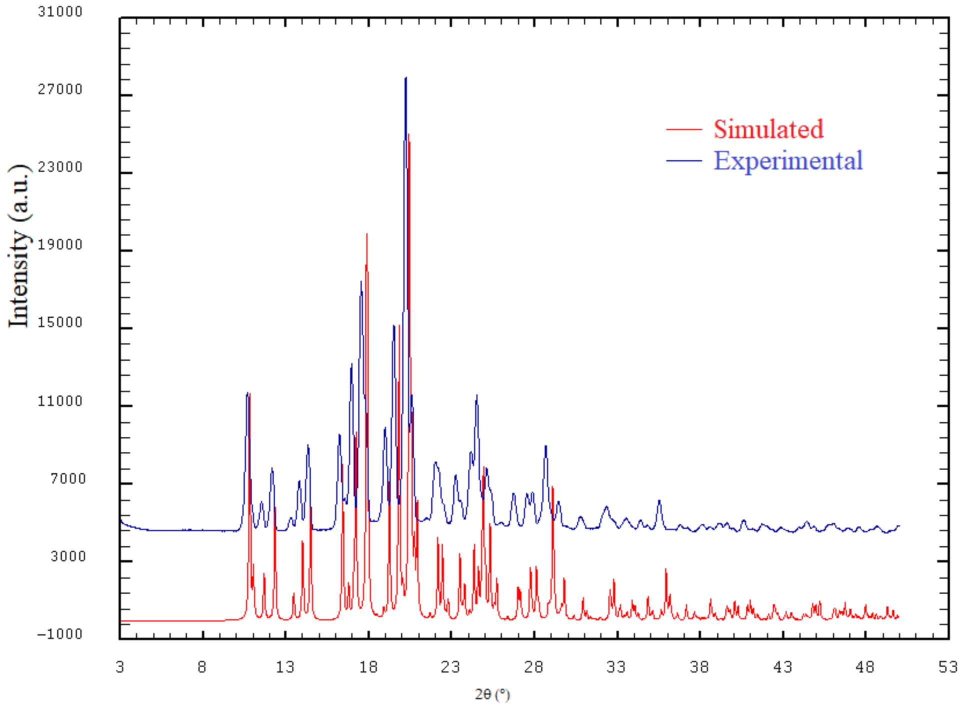


Figure S20: Comparison of experimental and simulated PXRD patterns of **6-37**

NMR

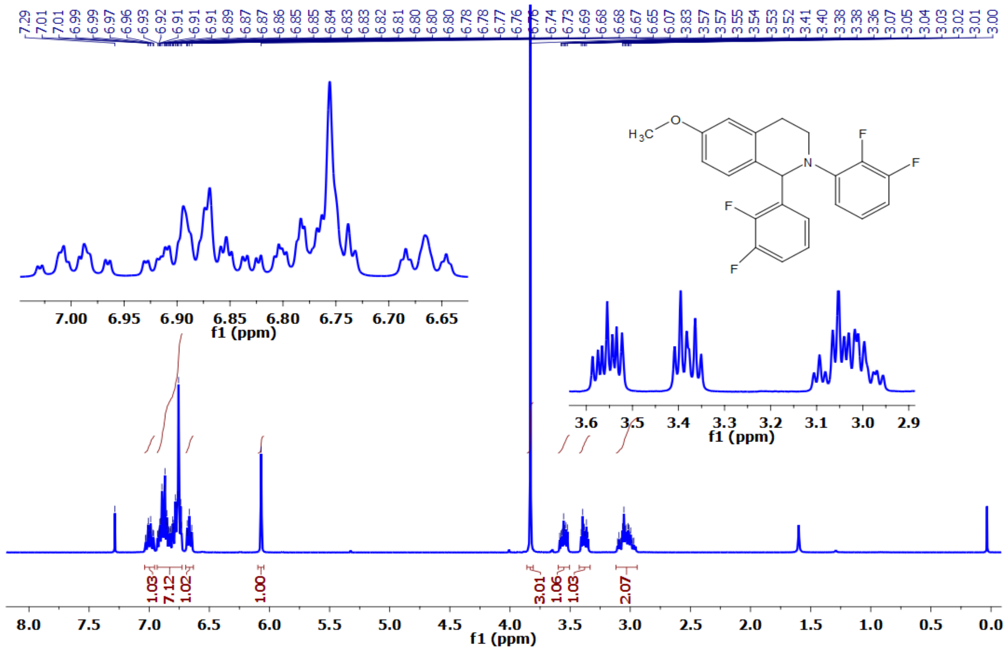


Figure S21(a): [1]H - NMR Spectra of 6-1, (400 MHz, $CDCl_3$) : δ (ppm) = 2.97 – 3.11 (m, 2H), 3.35 – 3.41 (m, 1H), 3.52-3.59 (m, 1H), 3.01 (s, 3H), 6.07 (d, 1H), 6.65-6.69 (m, 1H), 6.73-6.93 (m, 7H), 6.96-7.03 (m, 1H).

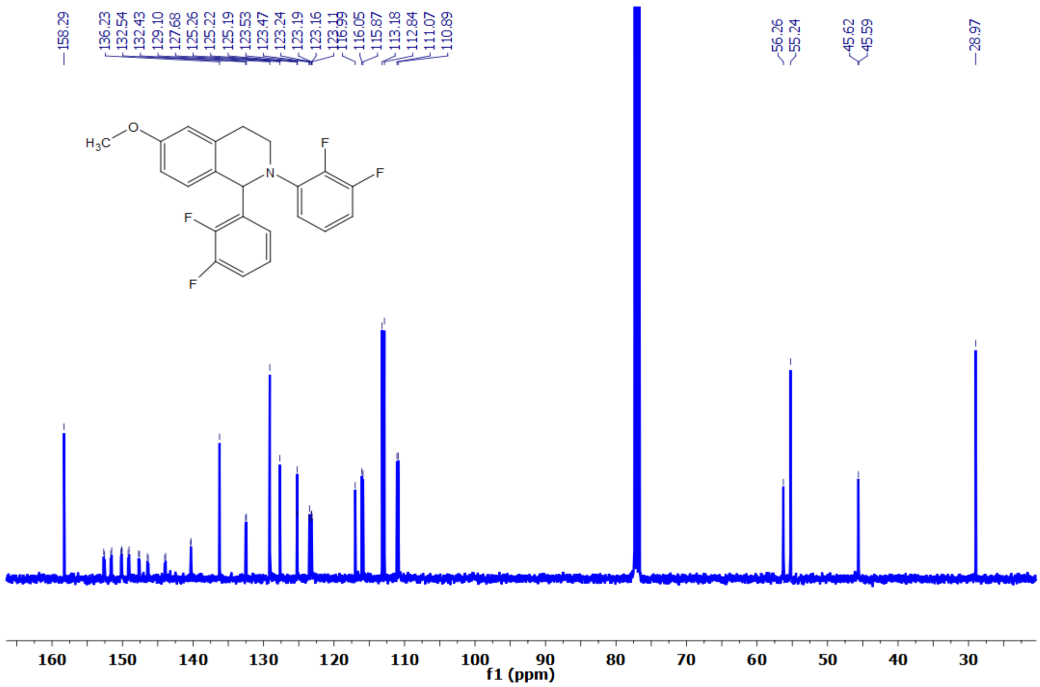


Figure S21(b): [13]C spectra of 6-1, (125 MHz, $CDCl_3$): δ (ppm) = 140.3505, 140.3023, 140.2832, 136.2484, 132.5498, 132.442, 129.1185, 127.6892, 125.2682, 125.2379, 125.2081, 123.54761, 23.5018, 123.4819, 123.437, 123.2536, 123.204, 123.1686, 123.1213, 117.0052, 116.0579, 115.8879, 113.1957, 112.8561, 111.0797, 110.9057, 56.2671, 55.2457, 45.6254, 45.5951, 28.976

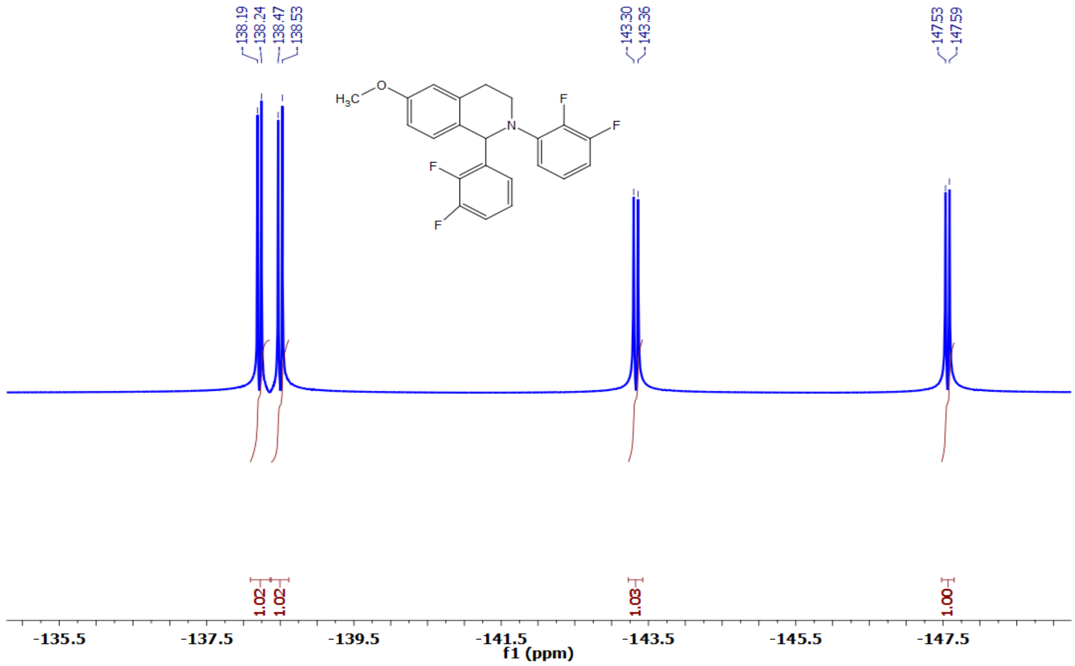


Figure S21(c): ^{19}**F- NMR Spectra of 6-1, (376 MHz, CDCl$_3$): δ (ppm)** = -147.56 (d,1F), -143.33 (d, 1F), -138.50 (d, 1F), -138.22 (d, 1F).

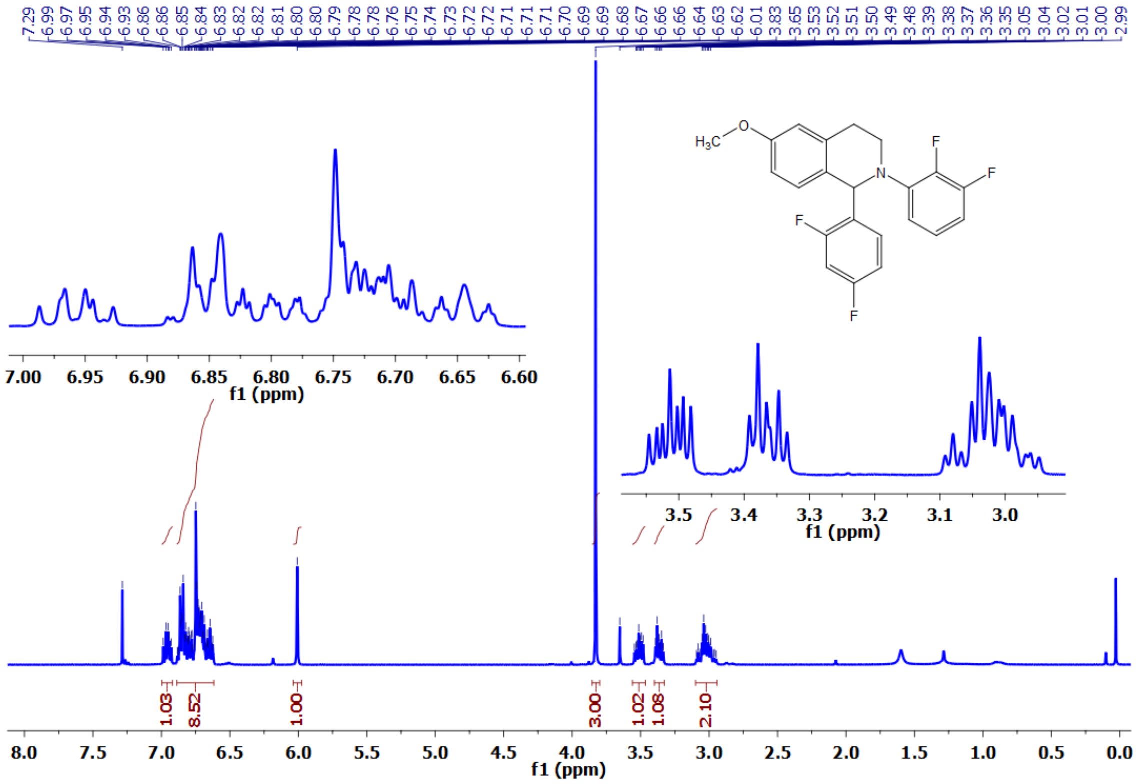


Figure S22(a): ^{1}**H - NMR Spectra of 6-2, (400 MHz, CDCl$_3$): δ (ppm)** = 2.95-3.09 (m, 2H), 3.33-3.39 (m, 1H), 3.48-3.55 (m, 1H), 3.83 (s, 3H), 6.01 (s, 1H), 6.62-6.8 (m, 8H), 6.93-6.99 (m, 1H).

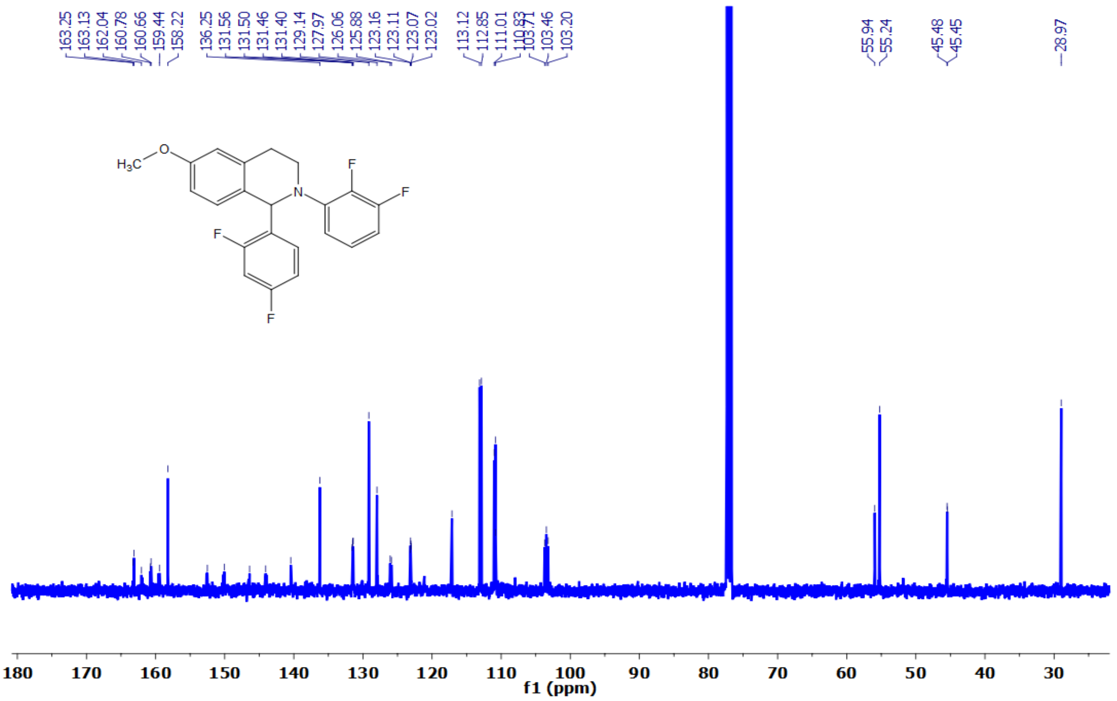


Figure S22(b): ^{13}C spectra of 6-2, (125 MHz, $CDCl_3$): δ (ppm) = 163.2643, 163.1452, 162.0573, 160.7945, 160.6728, 159.5794, 159.4624, 158.239, 152.6444, 152.5258, 150.1967, 150.0771, 146.4139, 144.0839, 143.9526, 140.4742, 140.4558, 140.4097, 140.3903, 136.261, 131.5722, 131.5151, 131.4773, 131.42, 129.1583, 127.9814, 126.0715, 126.0337, 125.9308, 125.8934, 123.1691, 123.1209, 123.0865, 123.037, 121.1256, 117.1314, 113.1342, 112.8601, 111.0525, 111.0186, 110.8446, 110.8088, 107.9867, 103.7238, 103.4717, 103.4606, 103.2091, 55.9516, 55.9304, 55.2479, 45.486, 45.4564, 28.9779.

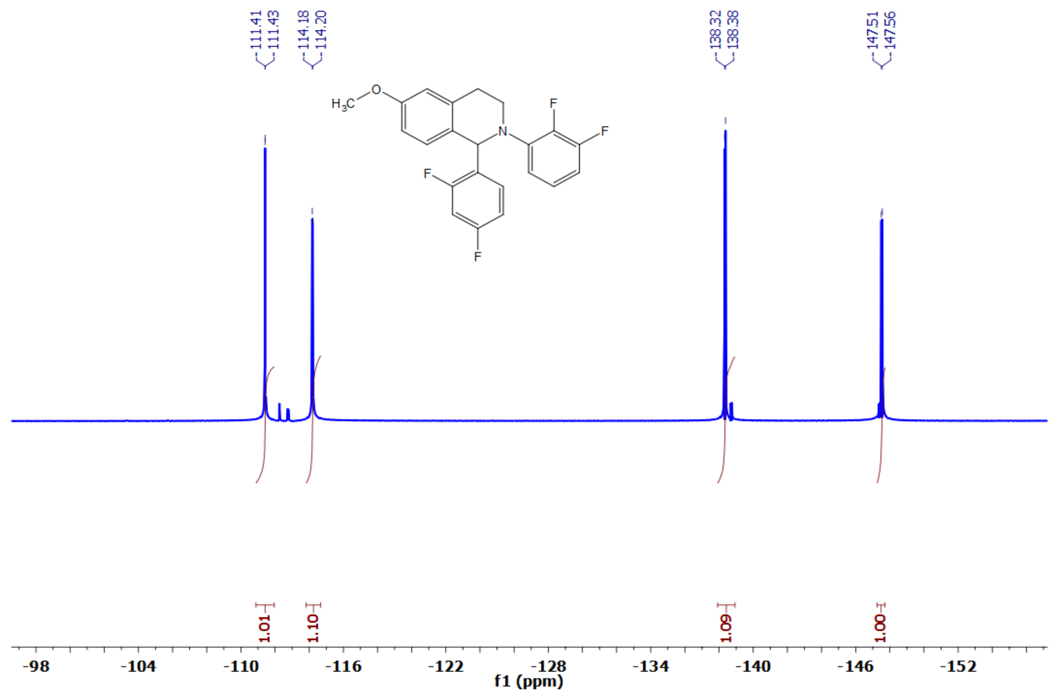


Figure S22(c): ^{19}F- NMR Spectra of 6-2, (376 MHz, $CDCl_3$): δ (ppm) = -147.54 (d, 1F), -138.35 (d, 1F), -114.19 (d, 1F), -111.42 (d, 1F).

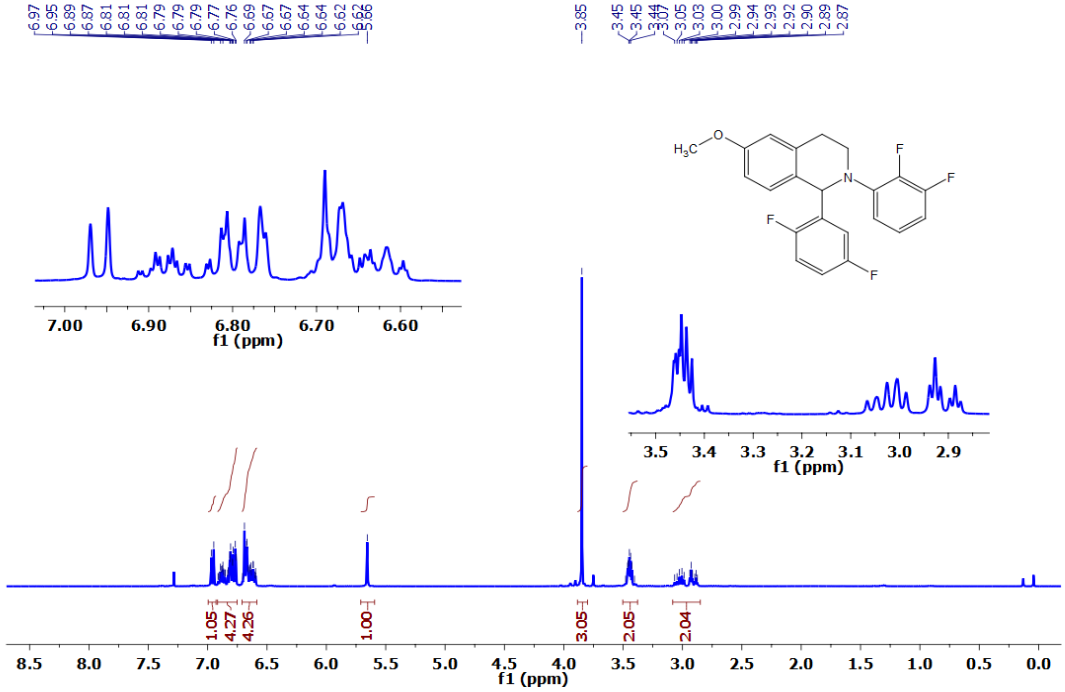


Figure S23(a): ^{1}**H - NMR Spectra of 6-3, (400 MHz, CDCl$_3$): δ (ppm)** = 2.87-3.07 (m, 2H), 3.40-3.48 (m, 2H), 3.85 (s, 3H), 5.66 (s, 1H), 6.59-6.71 (m, 4H), 6.76-6.91 (m, 4H), 6.96 (d, 1H).

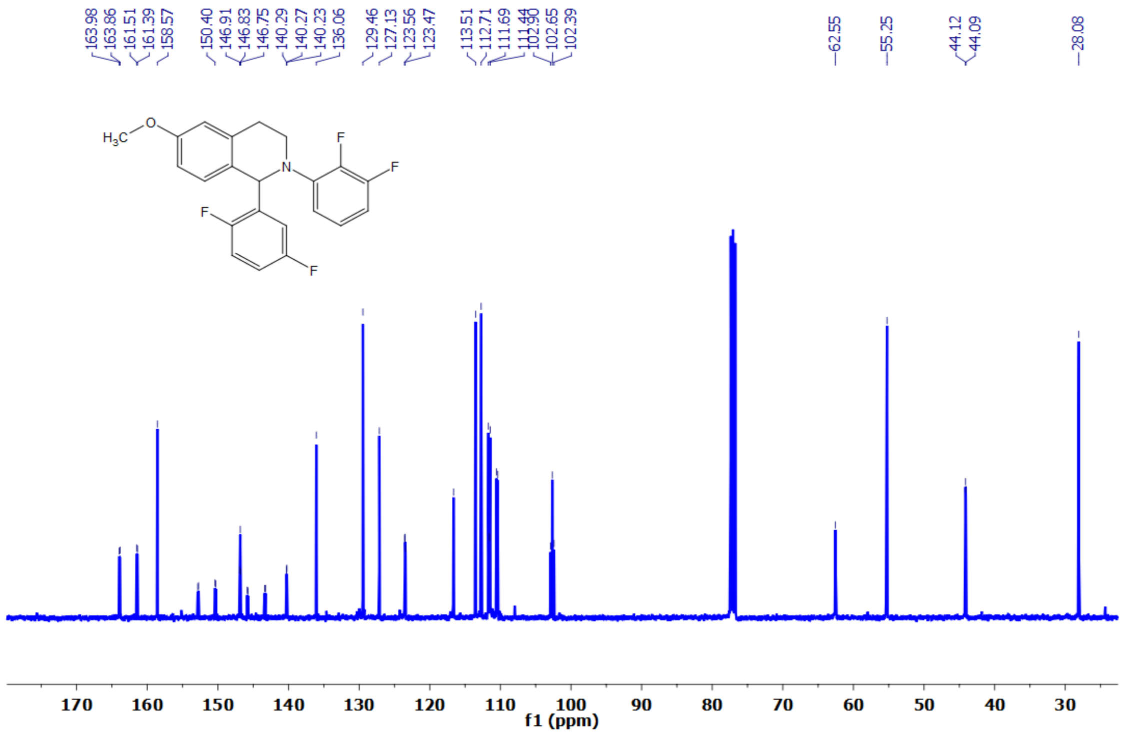


Figure S23(b): ^{13}**C spectra of 6-3, (125 MHz, CDCl$_3$): δ (ppm)** = 163.9979, 163.8735, 161.5272, 161.403, 158.5881, 152.8671, 152.7476, 150.4164, 150.2973, 146.922, 146.8442, 146.7683, 145.8594, 145.7261, 143.405, 143.2692, 140.3029, 140.2864, 140.2441, 140.2287, 136.0786, 129.4754, 127.1434, 123.5733, 123.5244, 123.4878, 123.439, 116.661, 116.6416, 116.6228, 113.5225, 112.7263, 111.703, 111.6366, 111.5175, 111.4516, 110.5475, 110.3728, 102.9128, 102.6596, 102.4074, 62.5743, 62.5558, 62.5417, 55.2557, 44.1281, 44.0989, 28.089

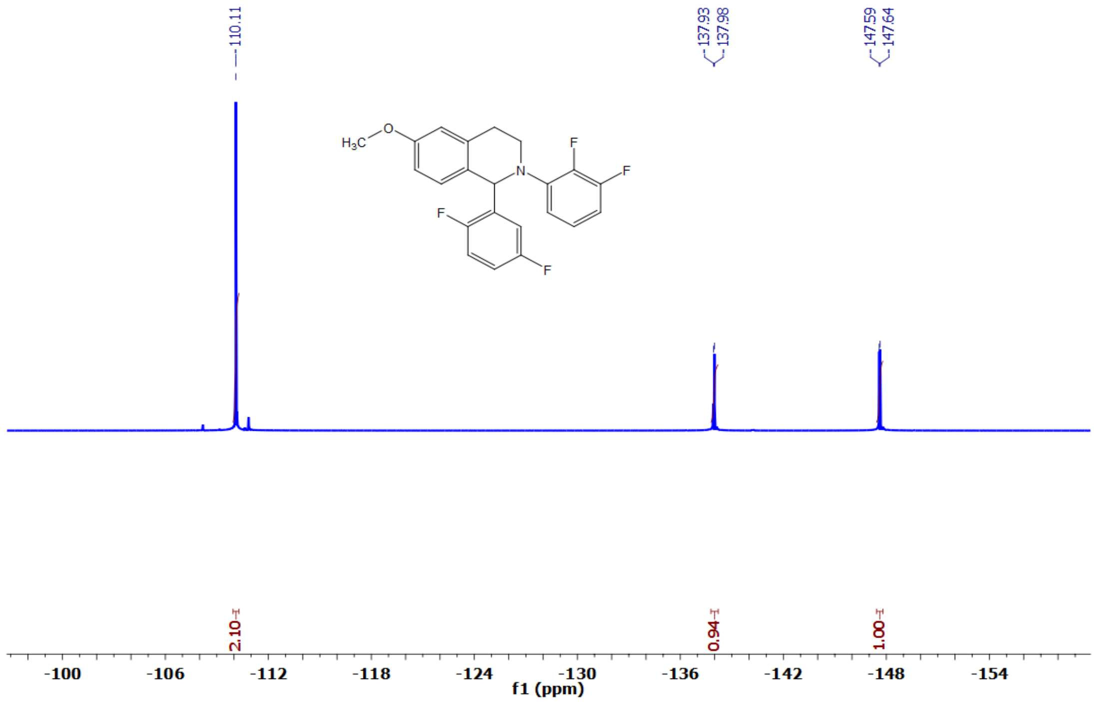


Figure S23(c): **^{19}F- NMR Spectra of 6-3, (376 MHz, $CDCl_3$): δ (ppm)** = -147.61 (d, 1F), -137.95 (d, 1F), -110.11 (s, 2F).

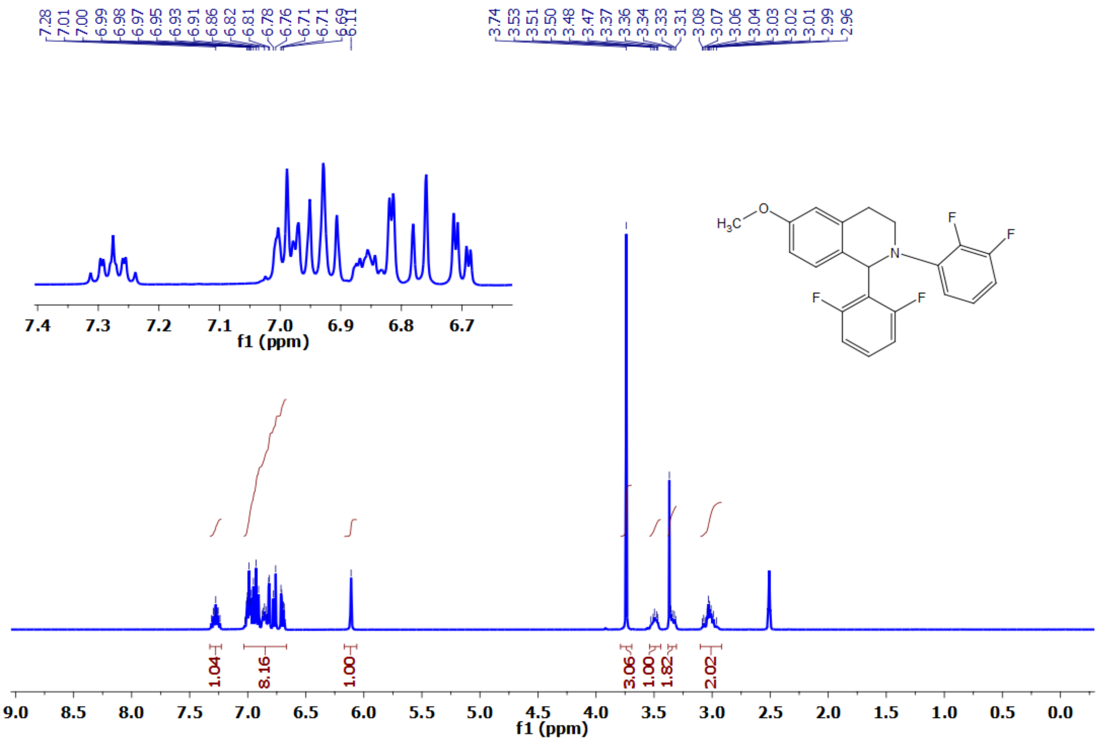


Figure S24(a): **^{1}H - NMR Spectra of 6-4, (400 MHz, $CDCl_3$): δ (ppm)** = 2.96-3.08 (m, 2H), 3.31-3.37 (m, 1H), 3.47-3.53 (m, 1H), 3.74 (s, 3H), 6.11 (s, 1H), 6.69-7.02 (m, 8H), 7.24-7.31 (m, 1H).

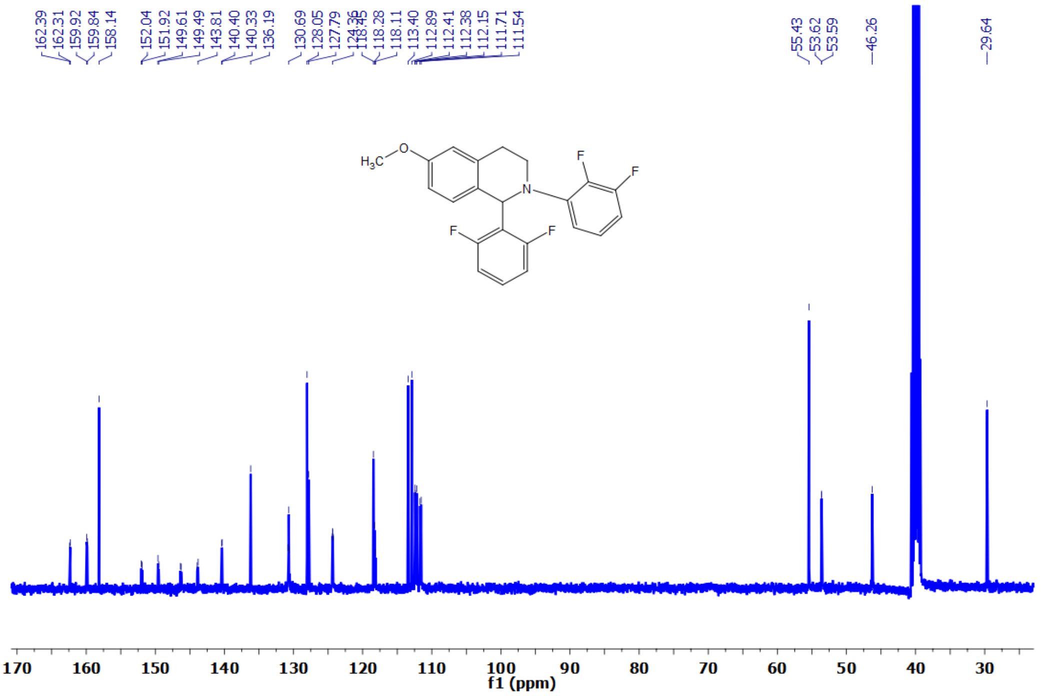


Figure S24(b): **^{13}C spectra of 6-4, (125 MHz, DMSO-d$_6$): δ (ppm)** = 162.4059, 162.3251, 159.9424, 159.8608, 158.1574, 152.0547, 151.9372, 149.6283, 149.5094, 146.4096, 146.2799, 143.9616, 143.8296, 140.41, 140.3971, 140.3458, 140.3338, 136.2066, 130.8043, 130.7, 130.5951, 128.0611, 127.8069, 124.4204, 124.3742, 124.3344, 124.2894, 118.4652, 118.2946, 118.1229, 113.4169, 112.9006, 112.4266, 112.3975, 112.1938, 112.1654, 111.7234, 111.5522, 55.4395, 53.6277, 53.5949, 46.2701, 29.65.

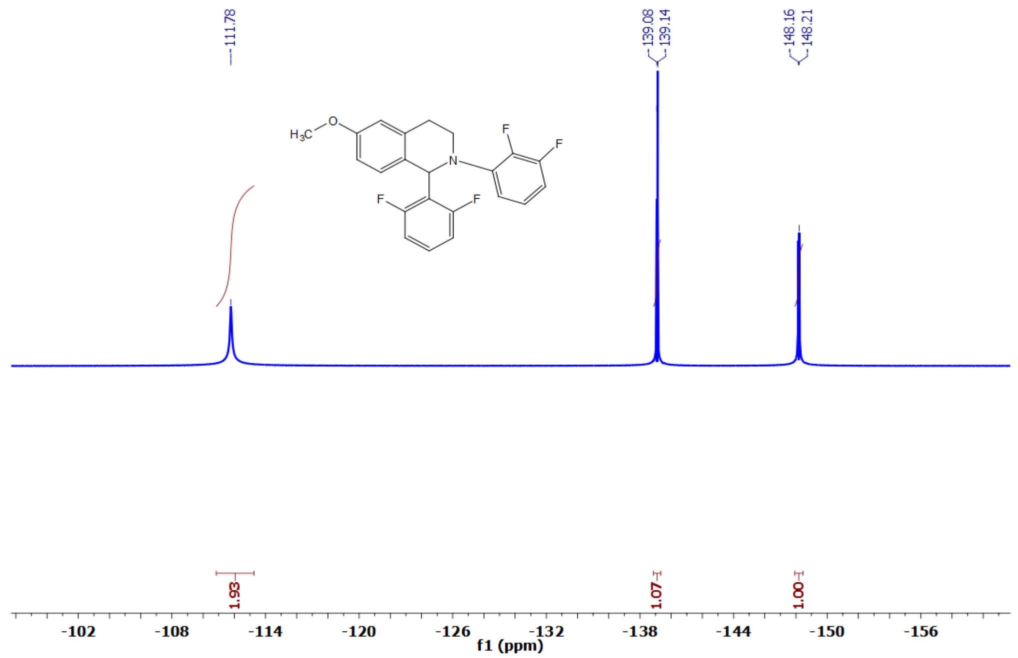


Figure S24(c): **^{19}F- NMR Spectra of 6-4, (376 MHz, DMSO-d$_6$): δ (ppm)** = -148.18 (d, 1F), -139.11 (1F), -111.78 (s, 2F).

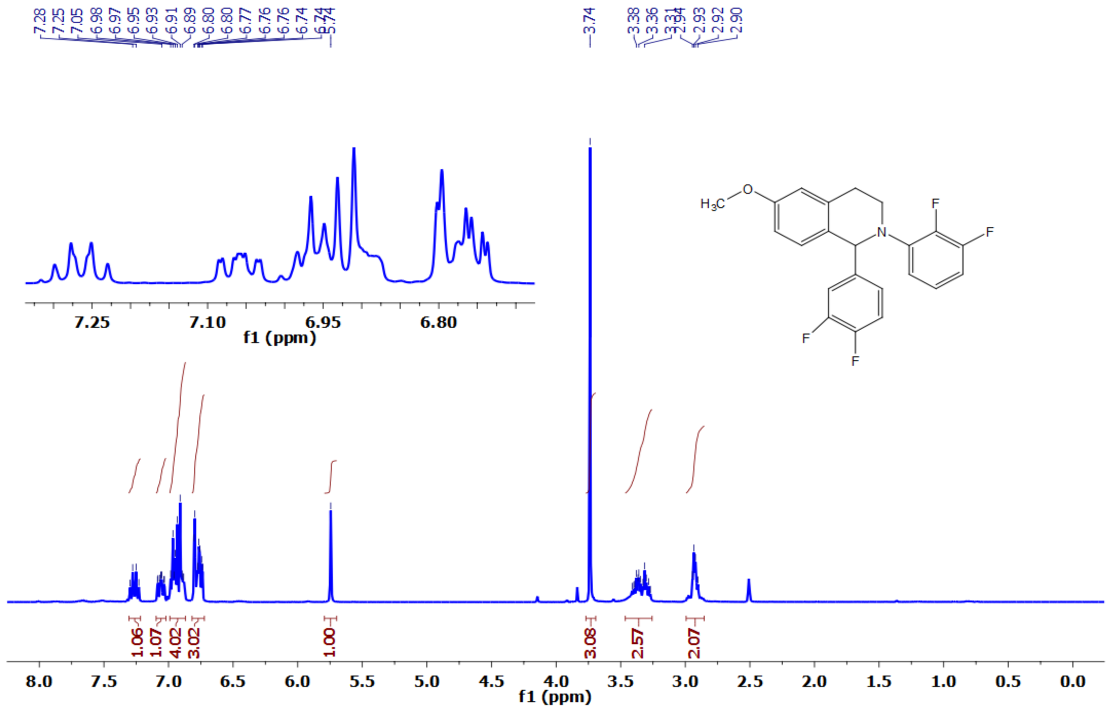


Figure S25(a): **^{1}H - NMR Spectra of 6-5, (400 MHz, DMSO-d_6): δ (ppm)** = 2.90-2.94 (m, 2H), 3.27-3.41 (m, 2H), 3.74 (s, 3H), 5.74 (s, 1H), 6.74-6.84 (m, 3H), 6.88-6.98 (m, 4H), 7.03-7.09 (m, 1H), 7.23-7.30 (m, 1H).

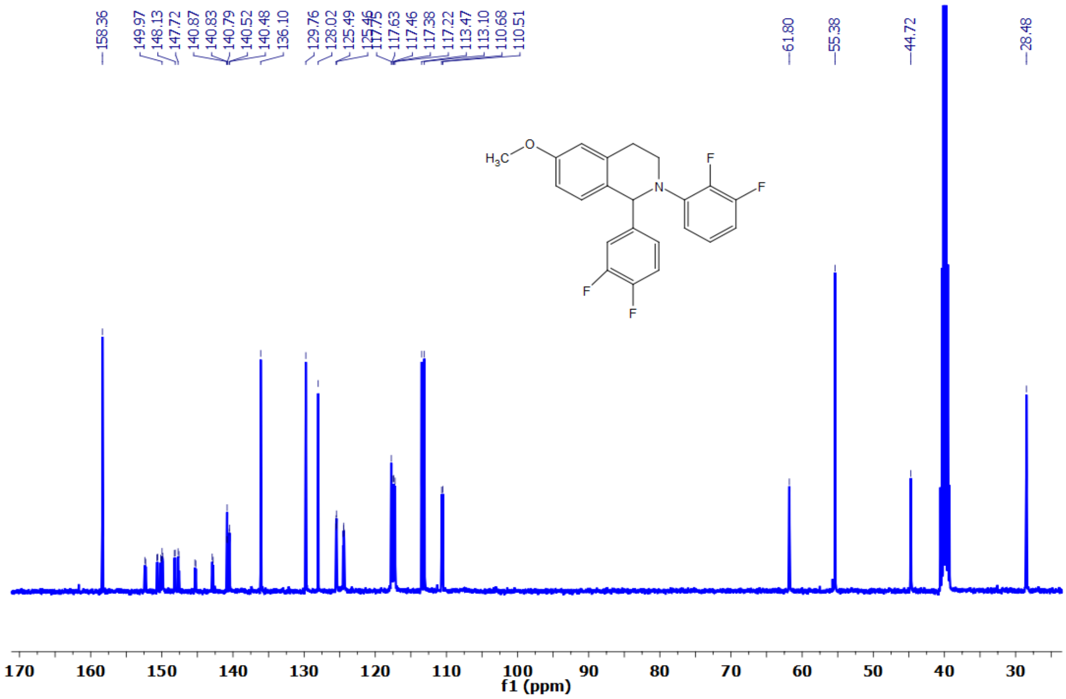


Figure S25(b): **^{13}C spectra of 6-5, (125 MHz, DMSO-d_6): δ (ppm)** = 158.3748, 152.4067, 152.289, 150.7142, 150.5891, 150.1723, 150.0478, 149.9834, 149.8646, 148.2709, 148.1449, 147.7323, 147.6078, 145.375, 145.24, 142.9351, 142.8019, 140.8822, 140.8424, 140.8047, 140.5534, 140.537 , 140.4964, 136.1171, 129.7743, 128.0319, 125.5334, 125.5019, 125.4712, 125.4411, 124.5241, 124.4788, 124.4378, 124.3939, 117.7629, 117.6416, 117.4716, 117.3988, 117.2302, 113.4864, 113.1126, 110.696, 110.5243, 61.833, 61.8116, 55.3872, 44.7462, 44.7305, 28.4844.

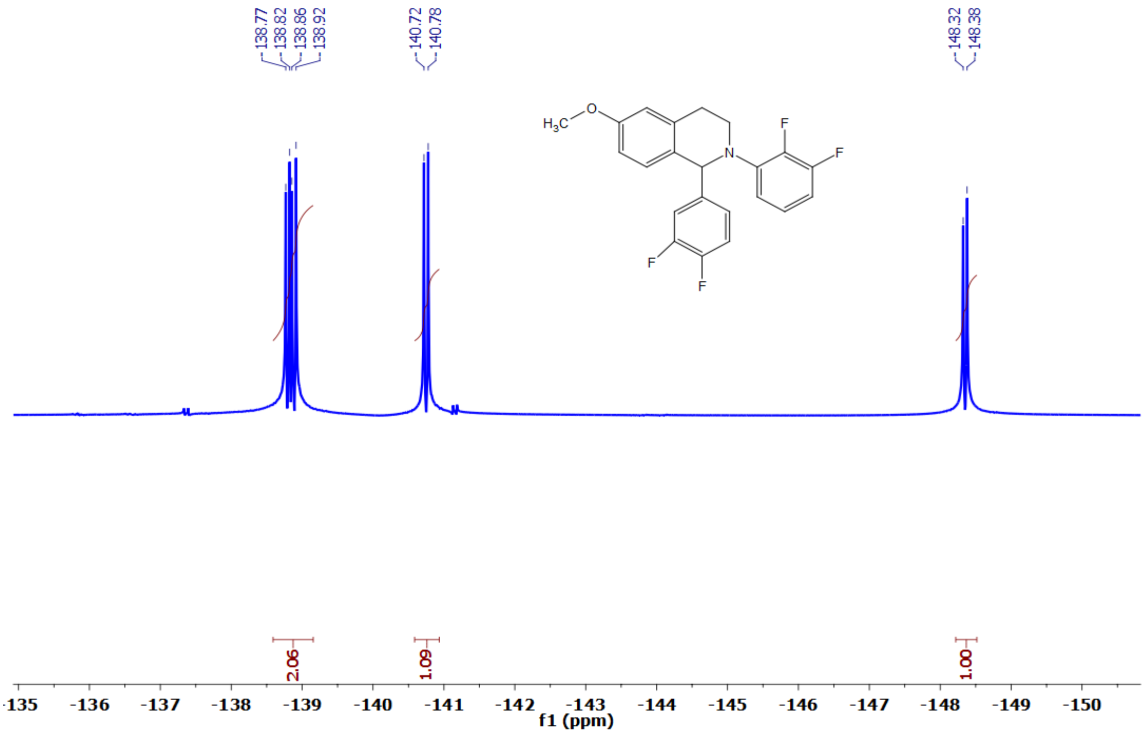


Figure S25(c): **[19]F- NMR Spectra of 6-5, (376 MHz, DMSO-d$_6$): δ (ppm)** = -148.35 (d, 1F), -140.75 (d, 1F), -138.84 (q, 2F).

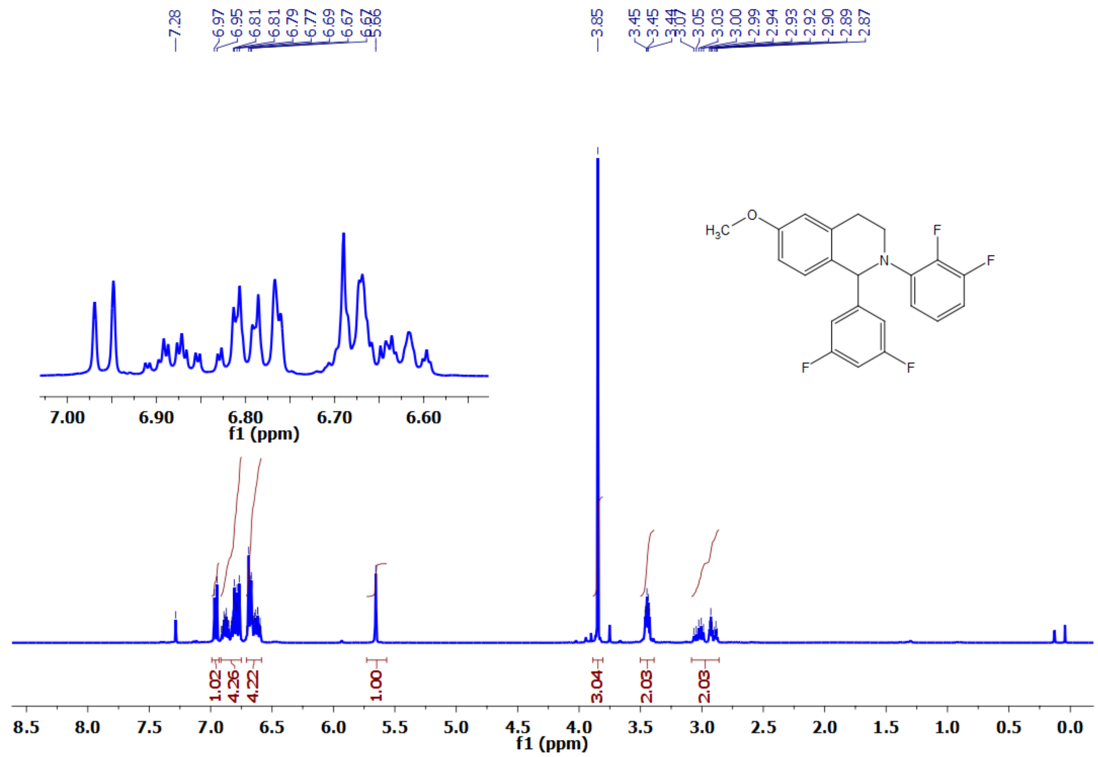


Figure S26(a): **[1]H - NMR Spectra of 6-6, (400 MHz, CDCl$_3$): δ (ppm)** = 2.89-3.07 (M, 2H), 3.43-3.46 (m, 2H), 3.85 (s, 3H), 5.66 (s, 1H), 6.59-6.71 (m, 4H), 6.76-6.91 (m, 4H), 6.96 (d, 1H).

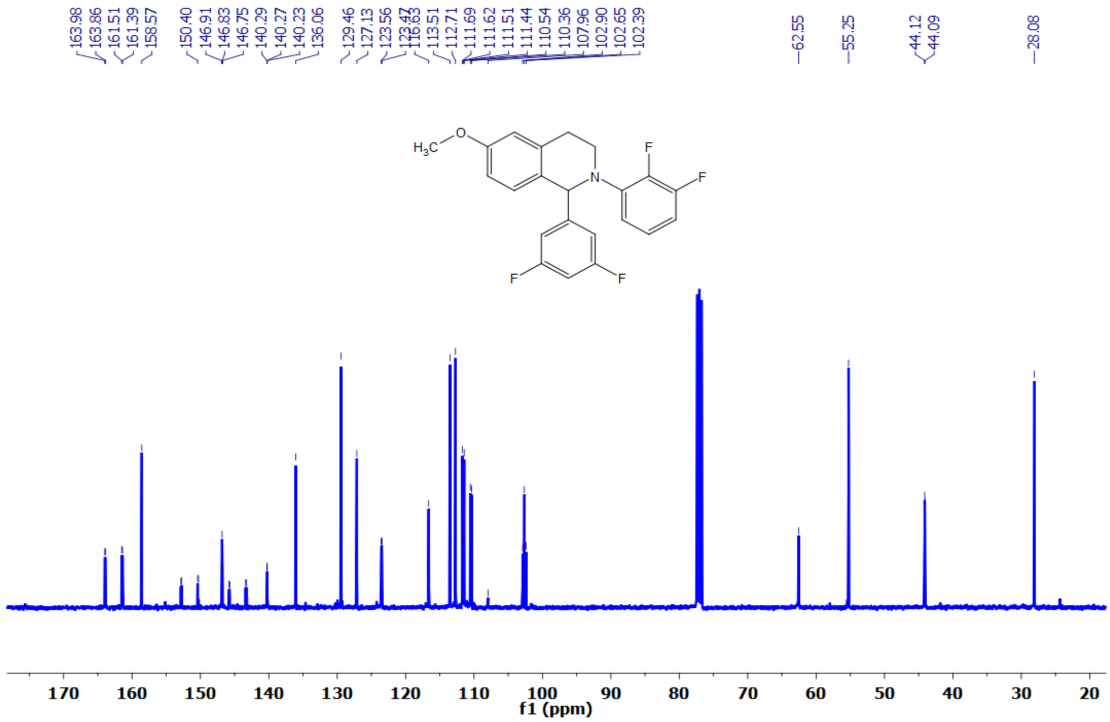


Figure S26(b): **^{13}C spectra of 6-6, (125 MHz, $CDCl_3$): δ (ppm)** = 163.9979, 163.8735, 161.5272, 161.403, 158.5881, 152.8671, 152.7476, 150.4164, 150.2973, 146.922, 146.8442, 146.7683, 145.8594, 145.7261, 143.405, 143.2692, 140.3029, 140.2864, 140.2441, 140.2287, 136.0786, 129.4754, 127.1434, 123.5733, 123.5244, 123.4878, 123.439, 116.661, 116.6416, 116.6228, 113.5225, 112.7263, 111.703, 111.6366, 111.5175, 111.4516, 110.5475, 110.3728, 102.9128, 102.6596, 102.4074, 62.5743, 62.5558, 62.5417, 55.2557, 44.1281, 44.0989, 28.089.

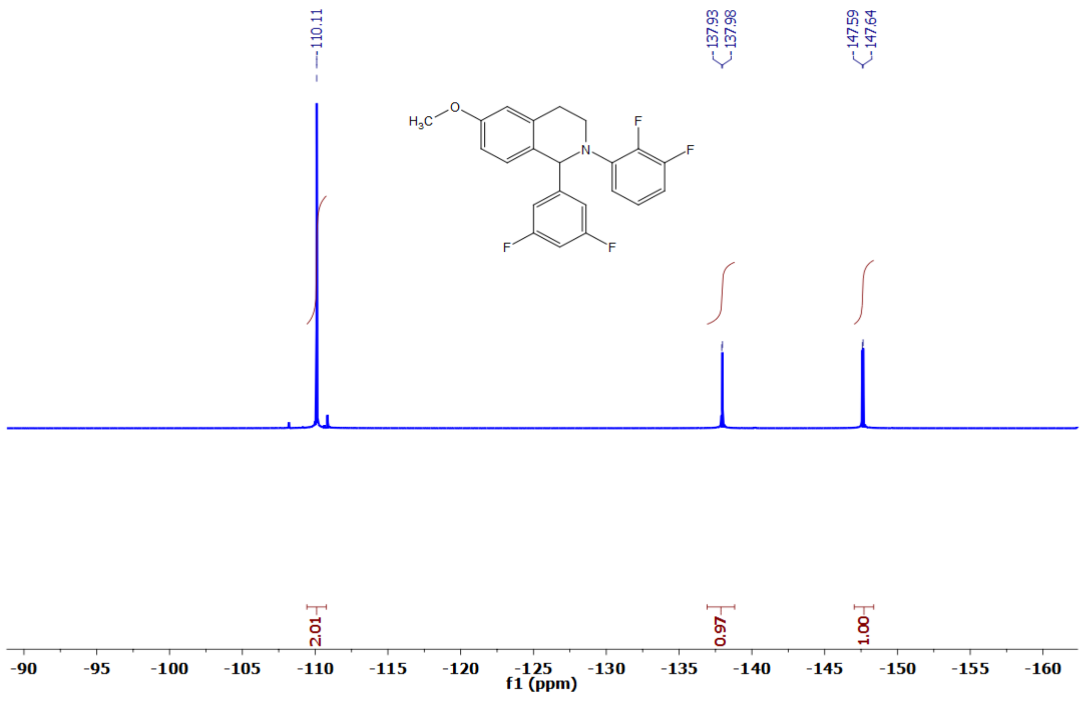


Figure S26(c): **^{19}F- NMR Spectra of 6-6, (376 MHz, $CDCl_3$): δ (ppm)** = -147.61 (d, 1F), -137.95 (d, 1F), -110.11 (s, 2F).

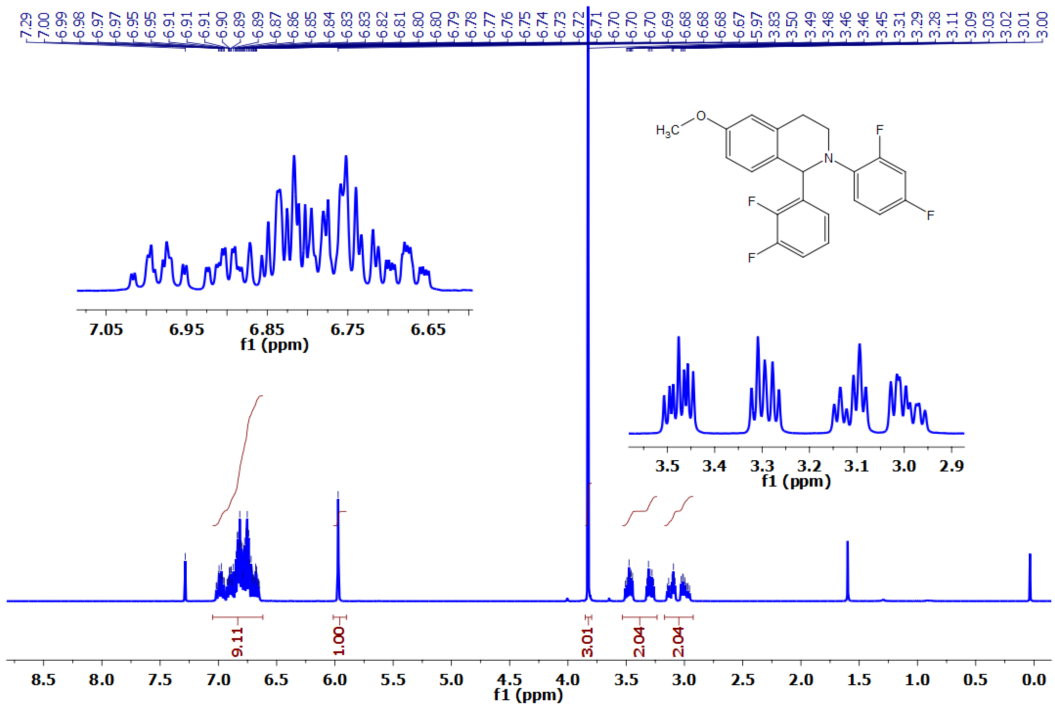


Figure S27(a): **^{1}H - NMR Spectra of 6-7, (400 MHz, $CDCl_3$): δ (ppm)** = 2.96-3.15 (m, 2H), 3.26-3.51 (m, 2H), 3.83 (s, 3H), 5.97 (s, 1H), 6.66-7.02 (m, 9H).

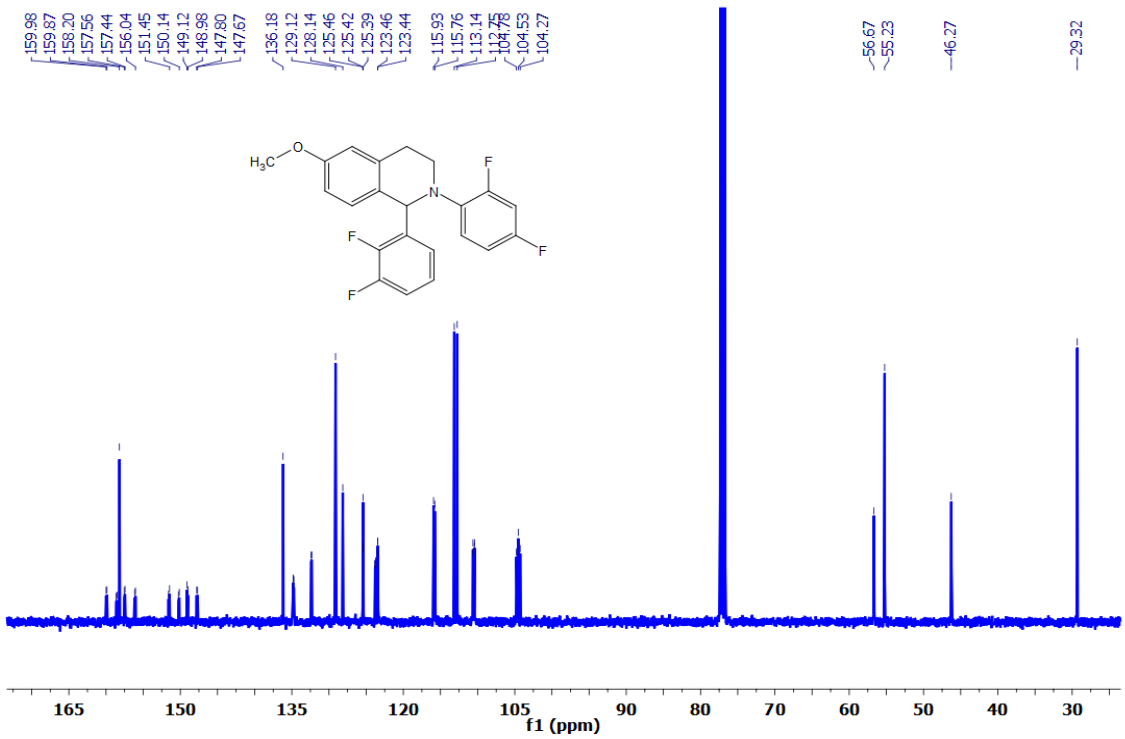


Figure S27(b): **^{13}C spectra of 6-7, (125 MHz, $CDCl_3$): δ (ppm)** = 132.3257, 129.1325, 128.1549, 125.4706, 125.4393, 125.4071, 123.8458, 123.8062, 123.7514, 123.712, 123.5172, 123.4721, 123.4519, 123.4072, 115.9467, 115.7759, 113.1539, 112.7614, 110.6766, 110.6403, 110.4635, 110.4251, 104.7911, 104.5434, 104.5336, 104.2868, 56.6832, 55.2402, 46.277, 46.2588, 29.3221

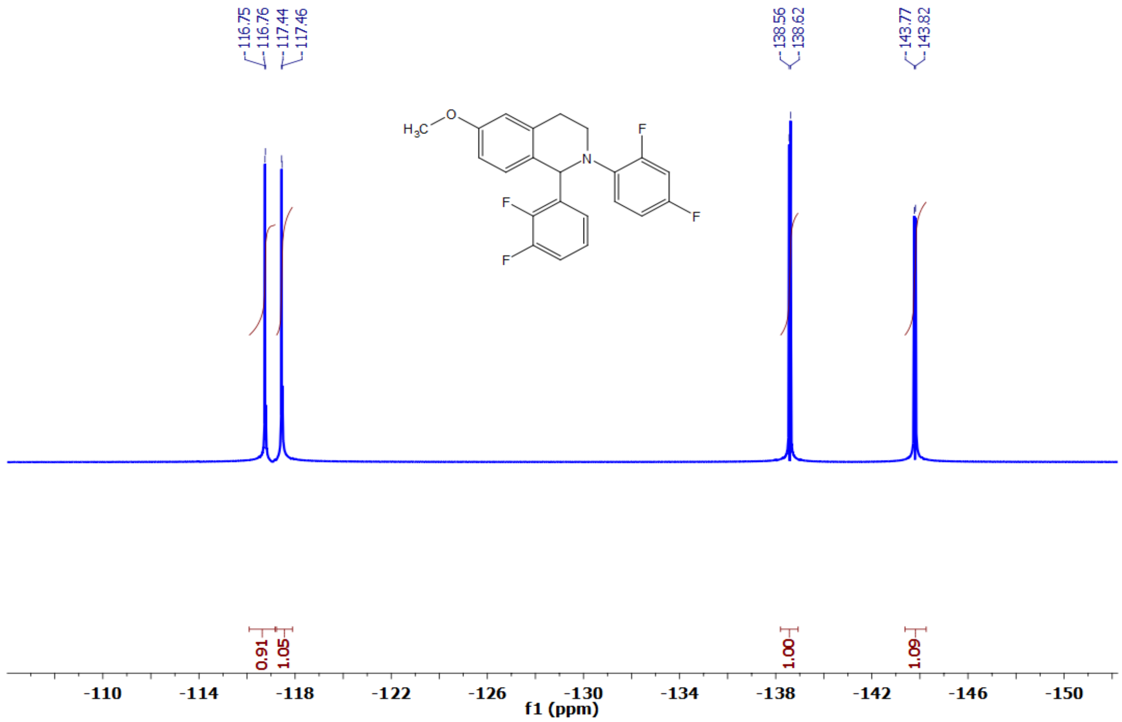


Figure S27(c): [19]**F- NMR Spectra of 6-7, (376 MHz, $CDCl_3$): δ (ppm) = -**143.80 (d, 1F), -138.59 (d, 1F), -117.45 (d, 1F), -116.75 (d, 1F).

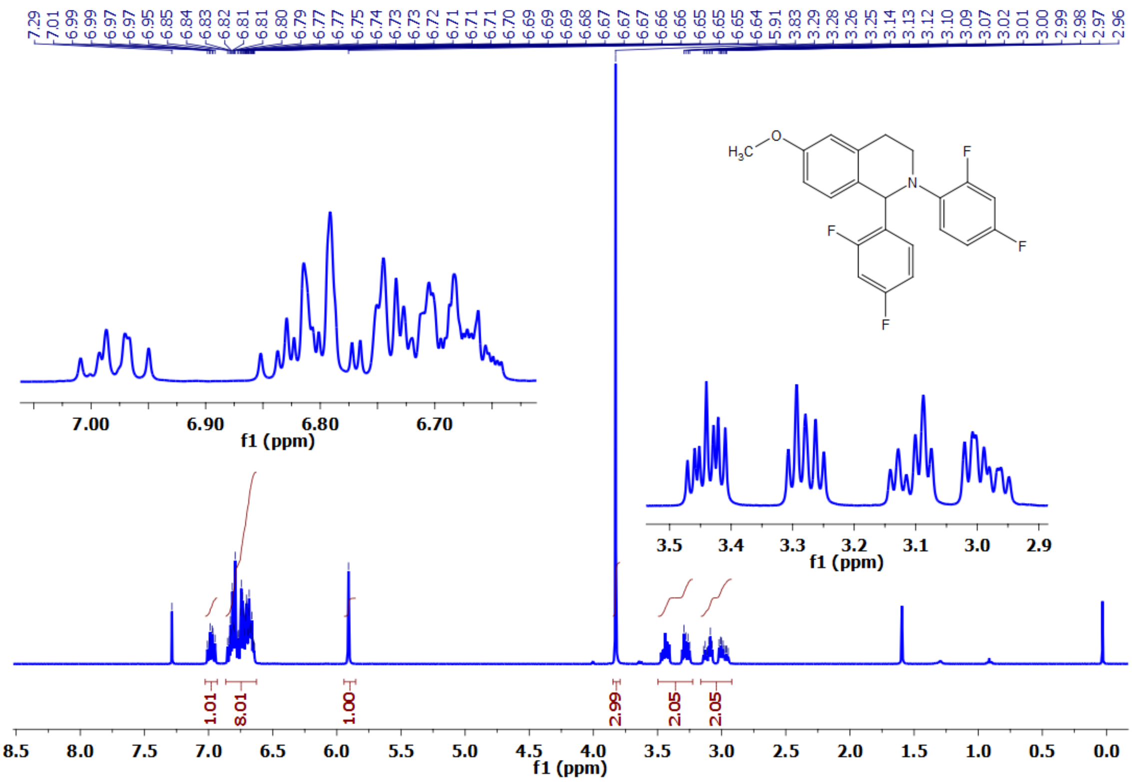


Figure S28(a): [1]**H - NMR Spectra of 6-8, (400 MHz, $CDCl_3$): δ (ppm)** = 2.953.14 (m, 2H), 3.25-3.47 (m, 2H), 3.83 (s, 3H), 5.91 (s, 1H), 6.64-6.85 (m, 8H), 6.95-7.01 (m, 1H).

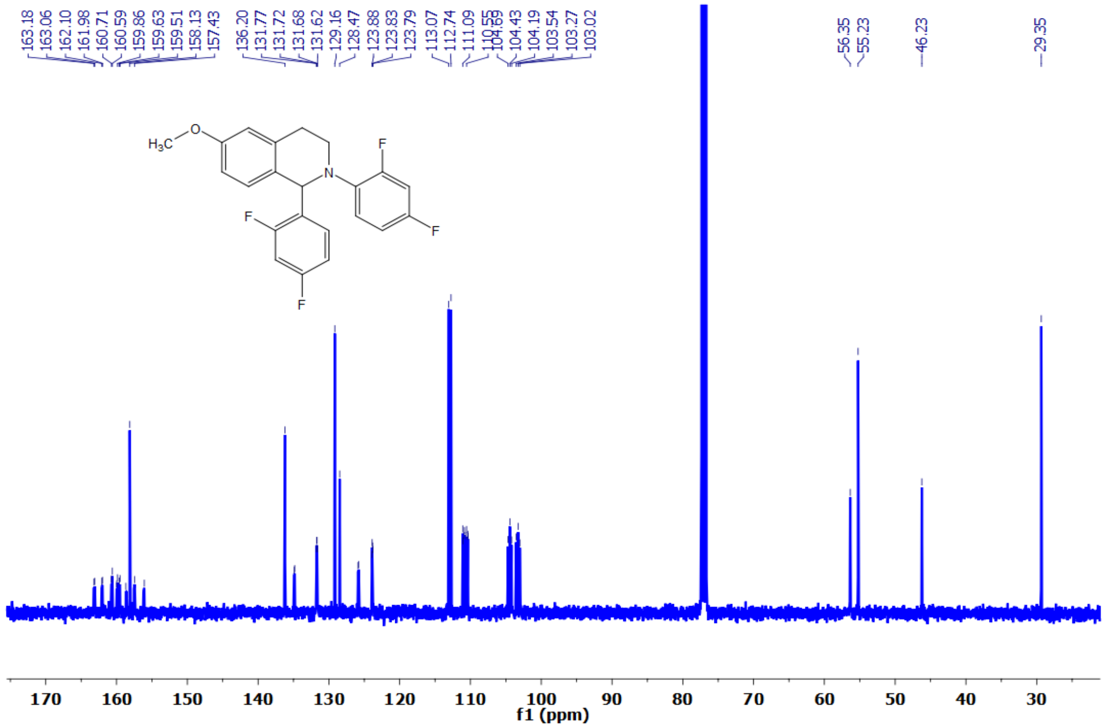


Figure S28(b): ^{13}C spectra of 6-8, (125 MHz, $CDCl_3$): δ (ppm) = 158.1502, 136.2116, 131.7878, 131.7295, 131.6934, 131.634, 129.179, 128.4822, 123.9361, 123.8957, 123.8398, 123.8011, 113.0873, 112.7562, 111.1041, 111.0684, 110.8957, 110.8595, 110.5962, 110.5599, 110.3824, 110.3449, 104.7048, 104.4554, 104.2007, 103.5488, 103.2977, 103.2843, 103.032, 56.3766, 56.3592, 55.2415, 46.2363, 46.2175, 29.359

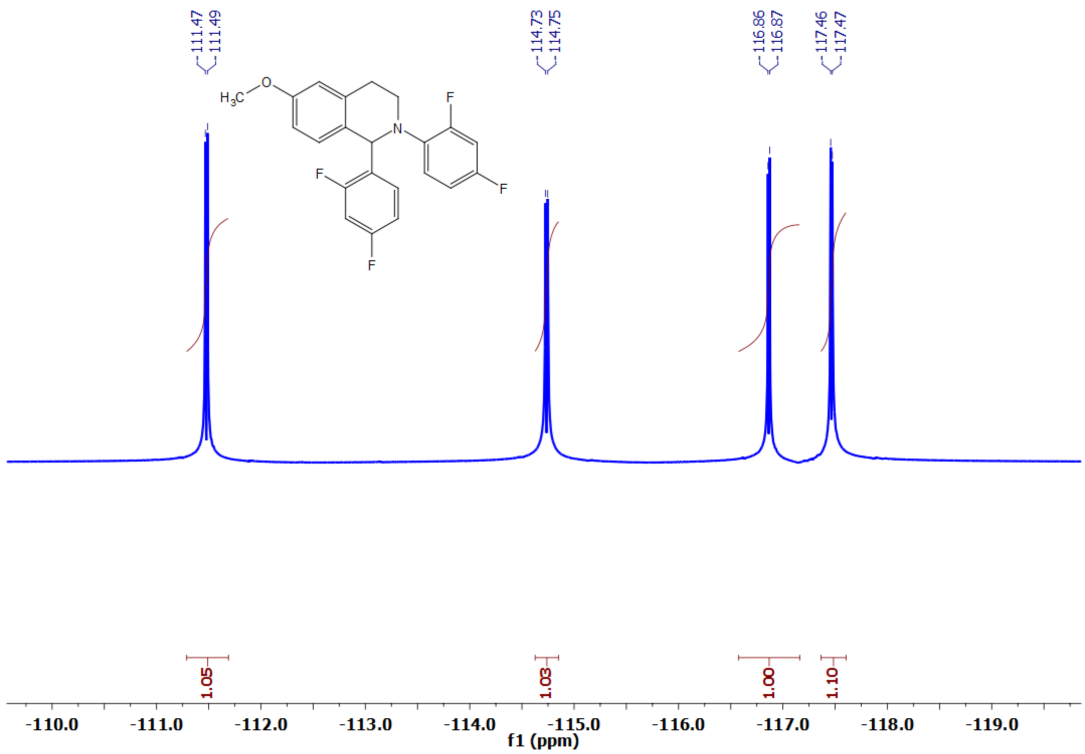


Figure S28(c): [19]**F- NMR Spectra of 6-8, (376 MHz, $CDCl_3$): δ (ppm)** = -117.46 (d, 1F), -116.86 (d, 1F), -114.74 (d, 1F), -114.48 (d, 1F).

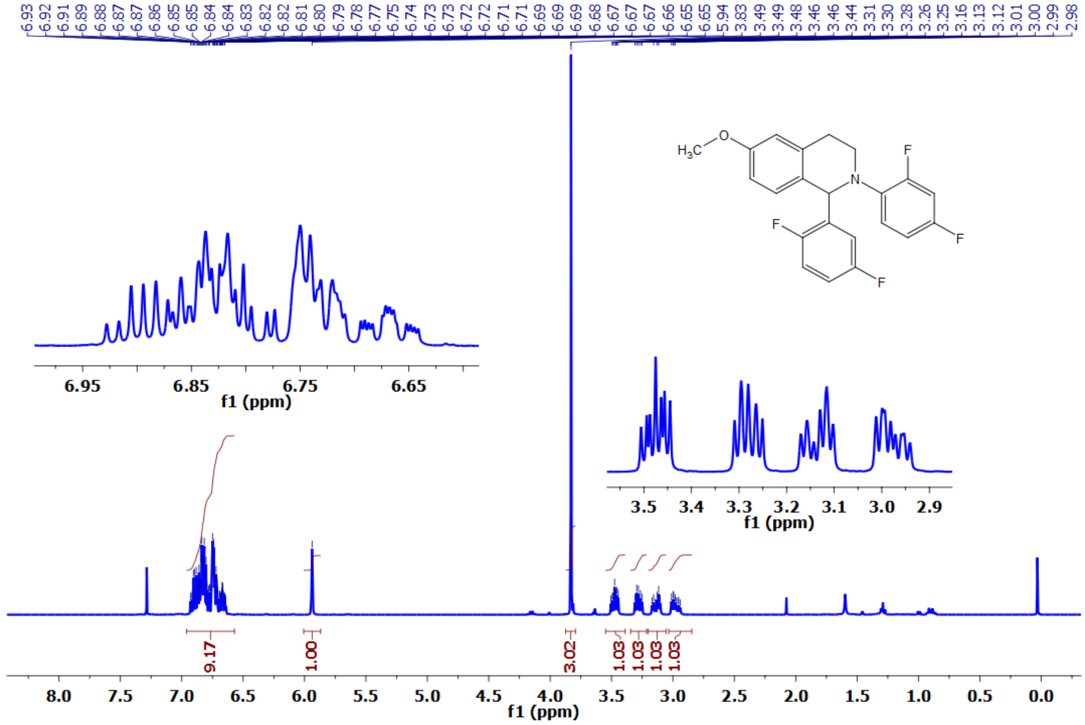


Figure S29(a): [1]**H - NMR Spectra of 6-9, (400 MHz, $CDCl_3$): δ (ppm)** = 2.94-3.01 (m, 1H), 3.10-3.17 (m, 1H), 3.25-3.31 (m, 1H), 3.44-3.51 (m, 1H), 3.83 (s, 3H), 6.64-6.93 (m, 9H).

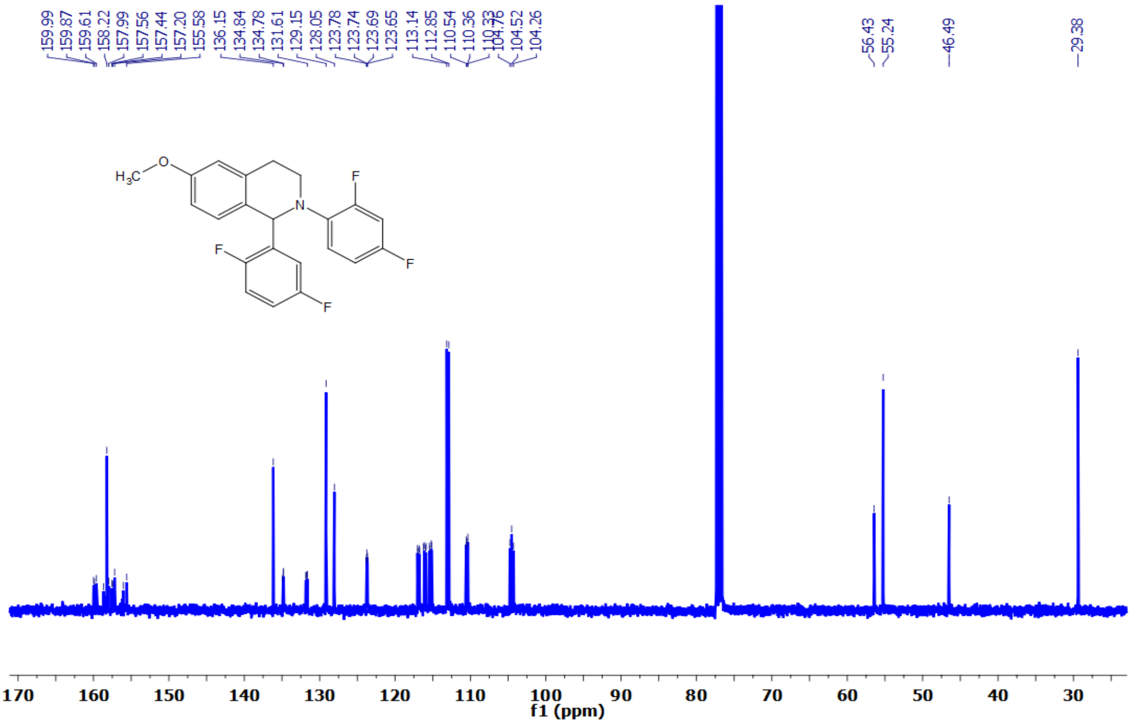


Figure S29(b): [13]**C spectra of 6-9, (125 MHz, $CDCl_3$): δ (ppm)** = 158.2382, 136.1658, 129.167, 128.0642, 123.7993, 123.7594, 123.7041, 123.6662, 117.028, 116.9836, 116.787, 116.7418, 116.2322, 116.1466, 115.9732, 115.8898, 115.4539, 115.3666, 115.2121, 115.1249, 113.1493, 112.8654, 110.5899, 110.5534, 110.3773, 110.3405, 104.7774, 104.5287, 104.2738, 56.4385, 55.25, 46.5222, 46.5025, 29.3865

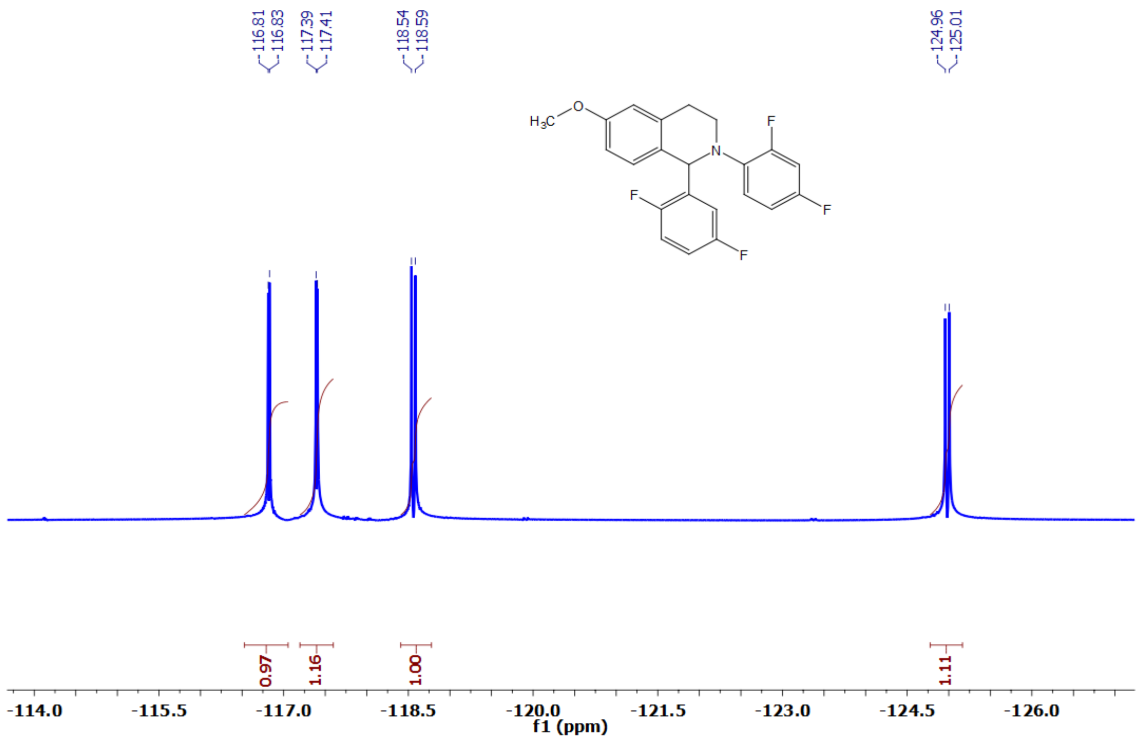


Figure S29(c): **^{19}F- NMR Spectra of 6-9, (376 MHz, $CDCl_3$): δ (ppm) =** -125.98 (d, 1F), -118.56 (d, F), -117.40 (d, 1F), -116.82 (d, 1F).

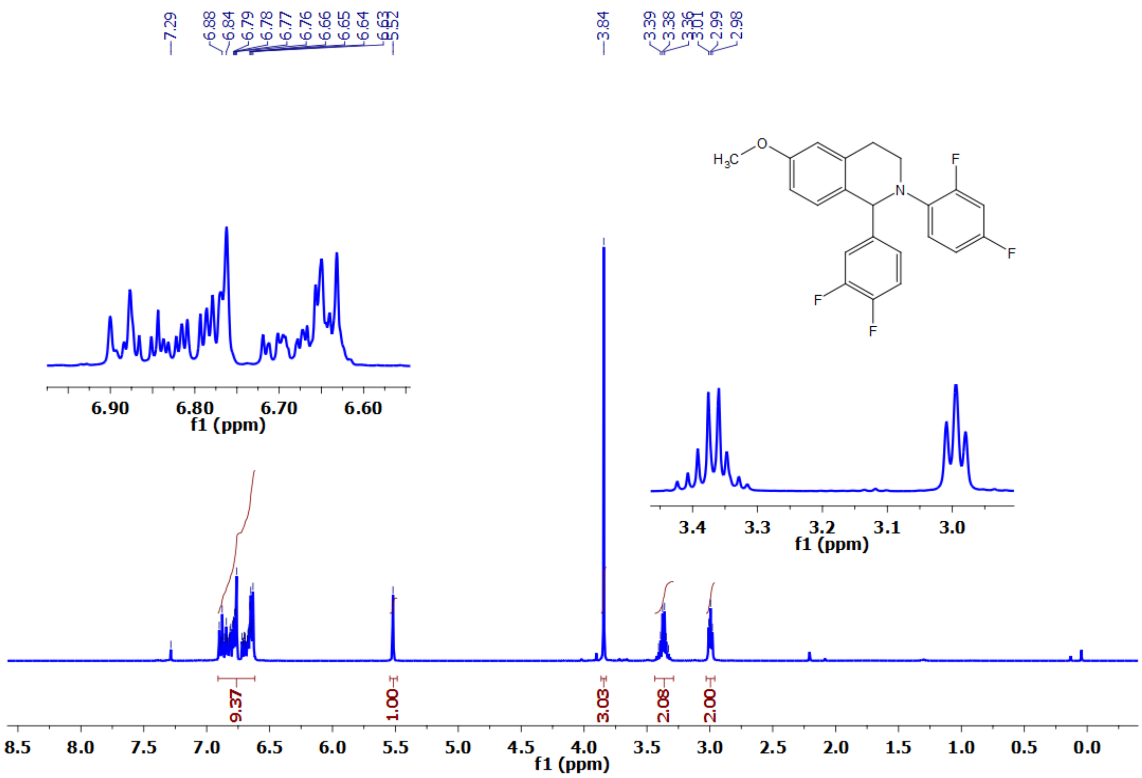


Figure S30(a): **^{1}H - NMR Spectra of 6-11, (400 MHz, $CDCl_3$): δ (ppm)** = 2.99 (t, 2H), 3.33-3.42 (m, 2H), 3.84 (s, 3H), 5.52 (s, 1H), 6.63-6.90 (m, 9H).

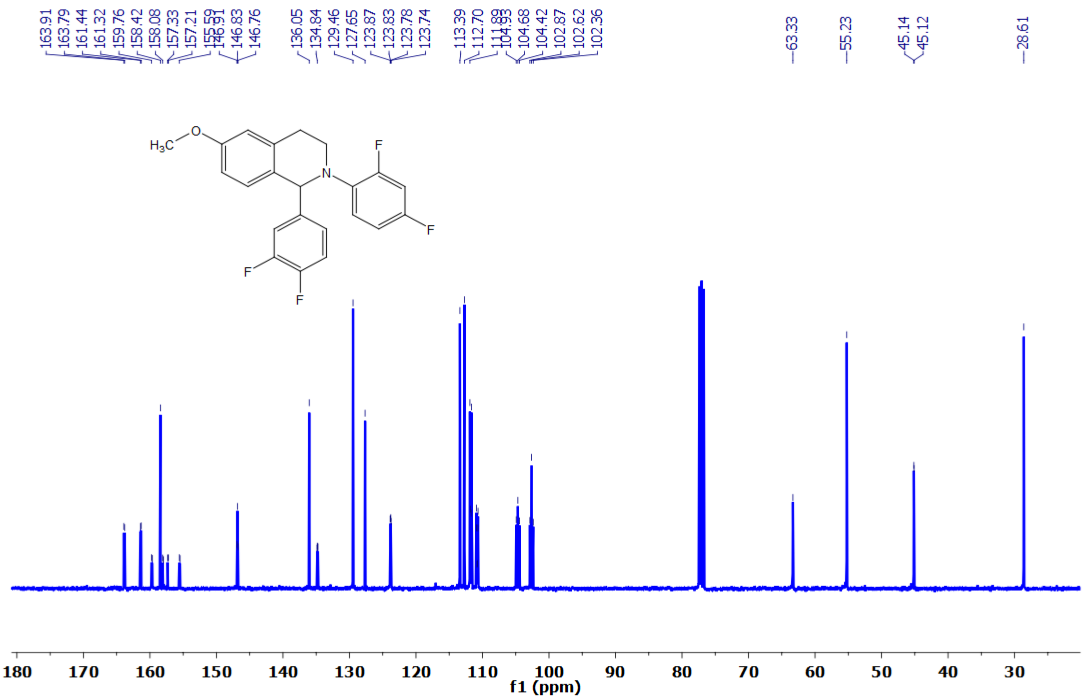


Figure S30(b): **^{13}C spectra of 6-11, (125 MHz, $CDCl_3$): δ (ppm)** = 163.9262, 163.8019, 161.4589, 161.334, 158.4407, 146.8491, 136.0594, 129.4738, 127.6644, 123.8876, 123.8433, 123.7957, 123.7512, 113.4051, 112.7144, 111.901, 111.8357, 111.7176, 111.6521, 110.9272, 110.9117, 110.6973, 110.6782, 104.9396, 104.6871, 104.4362, 102.8826, 102.6288, 102.3763, 63.3333, 55.2363, 45.1447, 45.1259, 28.6151

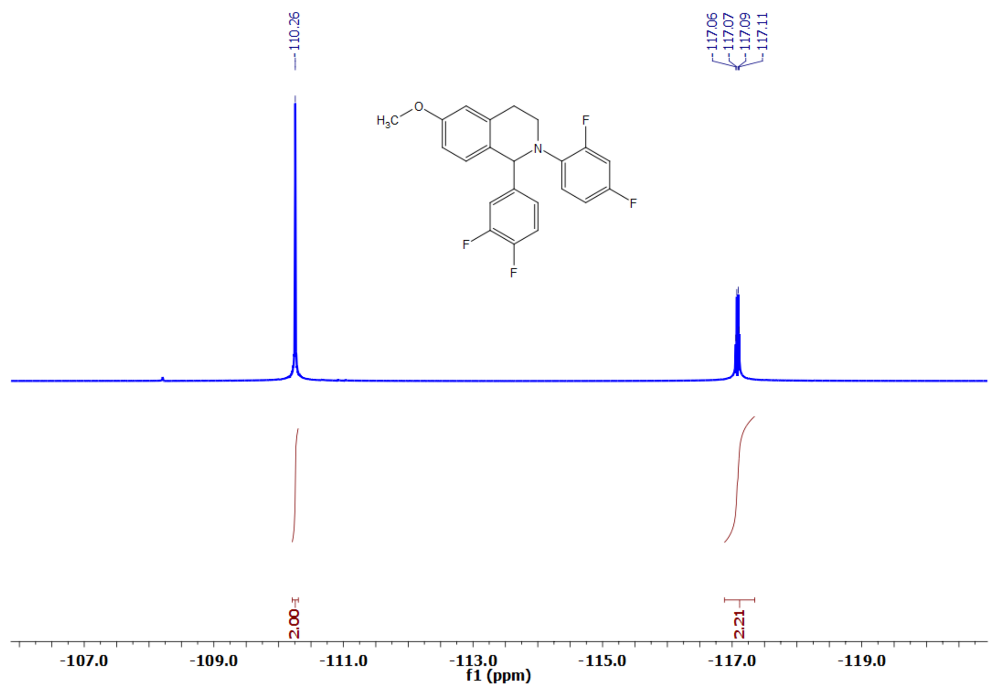


Figure S30(c): **^{19}F- NMR Spectra of 6-11, (376 MHz, $CDCl_3$): δ (ppm) =** -117.08 (q, 1F), -110.26 (s, 2F).

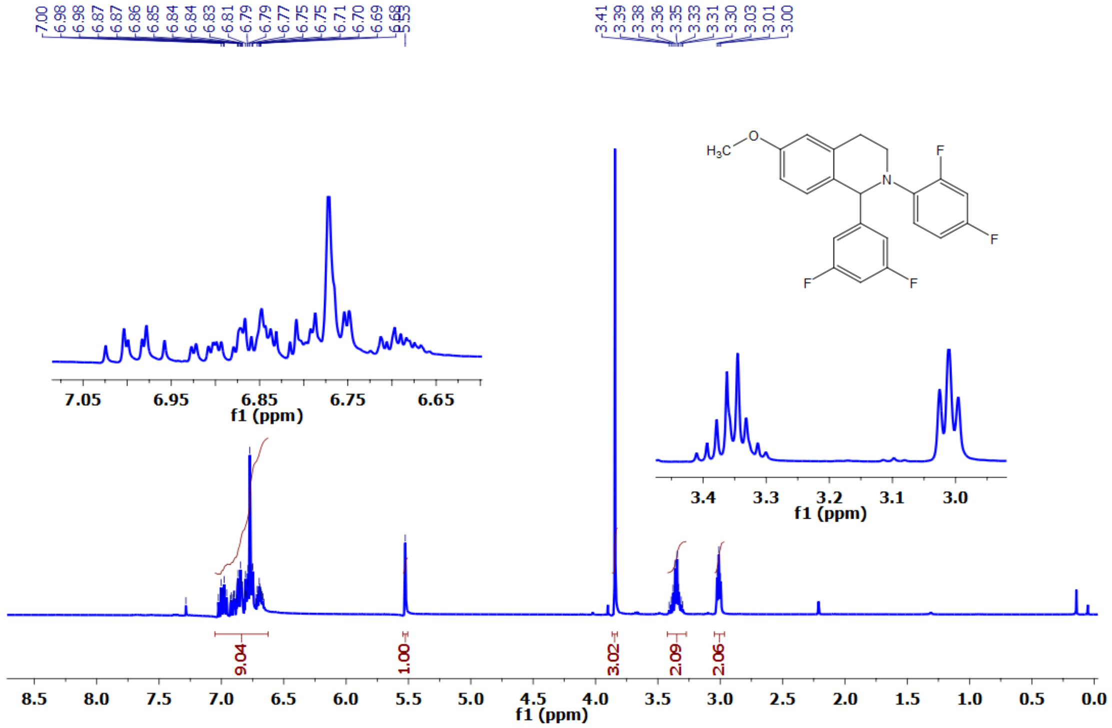


Figure S31(a): ^{1}**H - NMR Spectra of 6-12, (400 MHz, $CDCl_3$): δ (ppm)** = 3.01 (t, 2H), 3.30-3.41 (m, 2H), 3.84 (s, 3H), 5.53 (s, 1H), 6.66-7.02 (m, 9H),

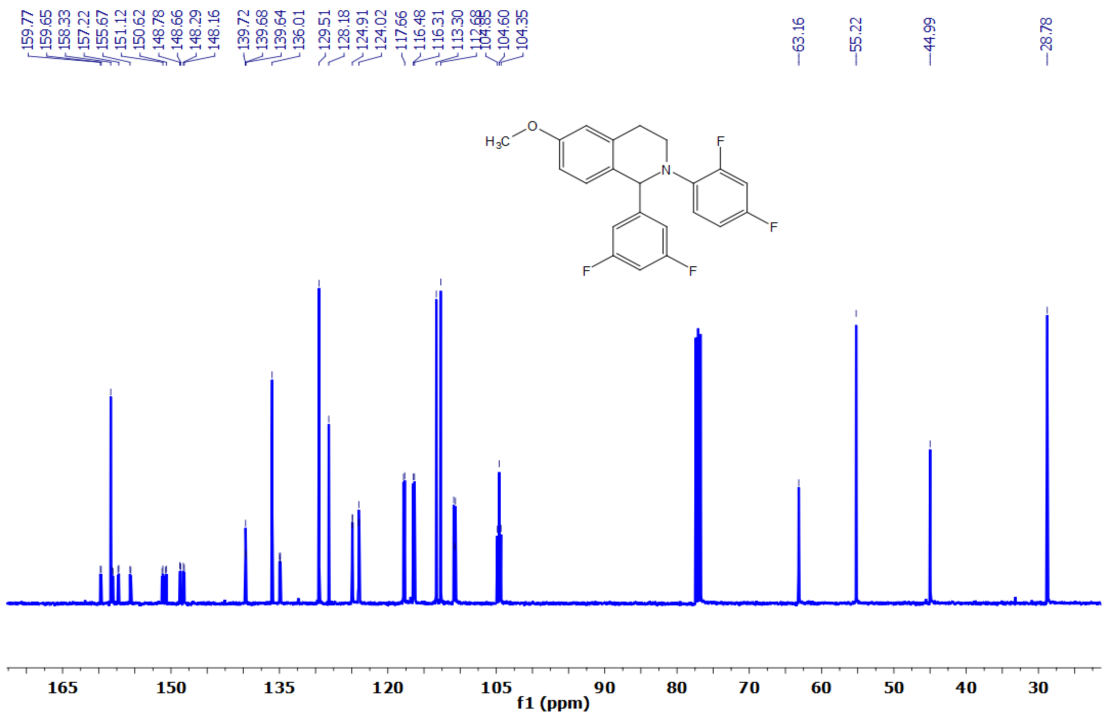


Figure S31(b): ^{13}**C spectra of 6-12, (125 MHz, $CDCl_3$): δ (ppm)** = 158.3502, 139.7366, 139.6959, 139.6555, 136.0236, 135.0064, 134.9193, 134.8748, 129.5213, 128.19, 124.9612, 124.9277, 124.9013, 124.8665, 124.0999, 124.0331, 123.9661, 117.8487, 117.6761, 116.4894, 116.3199, 113.3087, 112.6899, 110.9031, 110.8486, 110.709, 110.6546, 104.8647, 104.6118, 104.3613, 63.1706, 55.2263, 44.9993, 28.7867

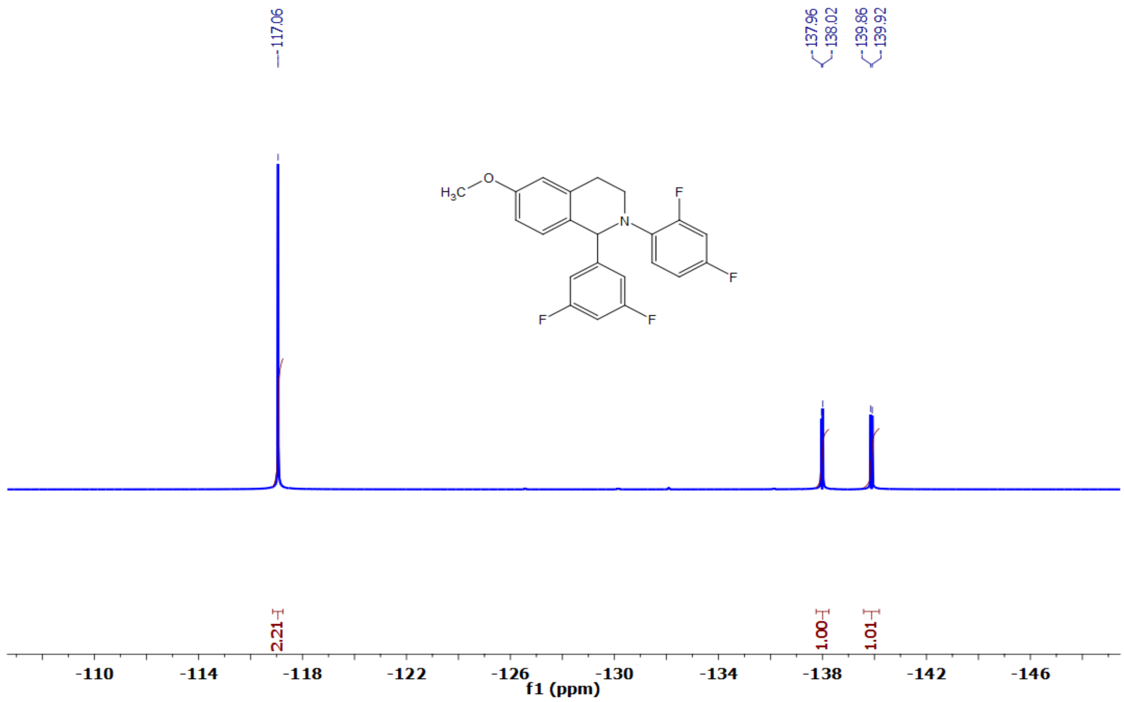


Figure S31(c): **^{19}F- NMR Spectra of 6-12, (376 MHz, $CDCl_3$): δ (ppm)** = -139.89 (d, 1F), -137.99 (d, 1F), -117.06 (s, 2F).

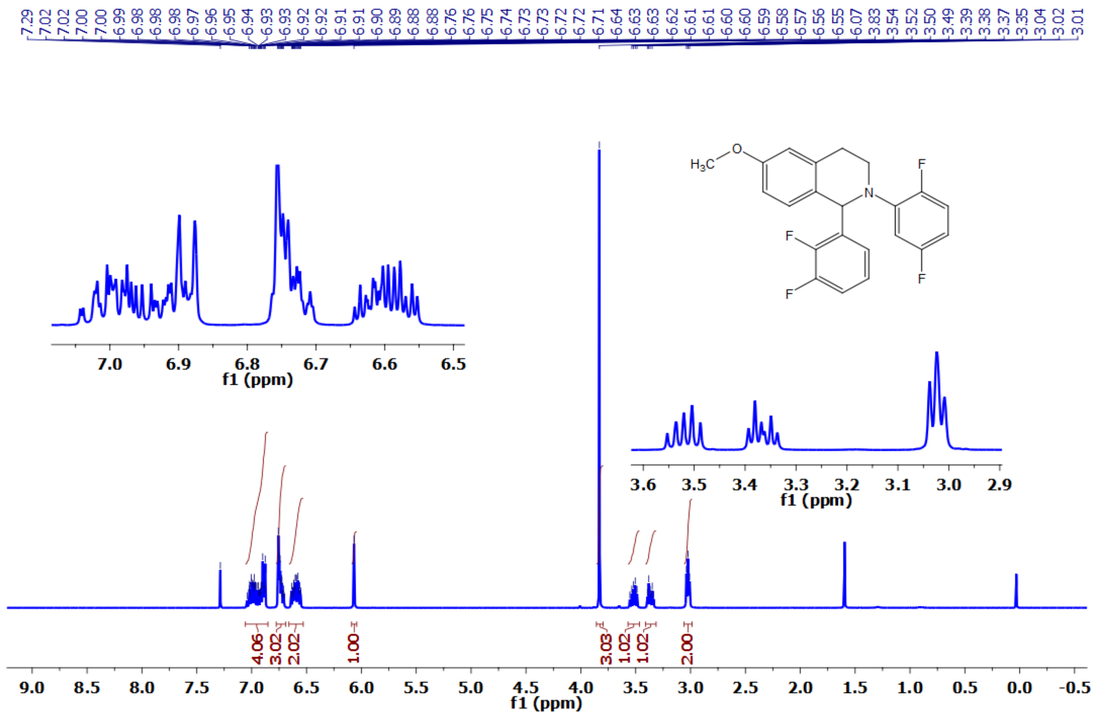


Figure S32(a): **^{1}H - NMR Spectra of 6-13, (400 MHz, $CDCl_3$): δ (ppm)** = 3.02 (t, 2H), 3.34-3.39 (m, 1H), 3.49-3.55 (m, 1H), 3.83 (s, 3H), 6.07 (s, 1H), 6.55-6.64 (m, 2H), 6.70-6.76 (m, 3H), 6.88-7.04 (m, 4H).

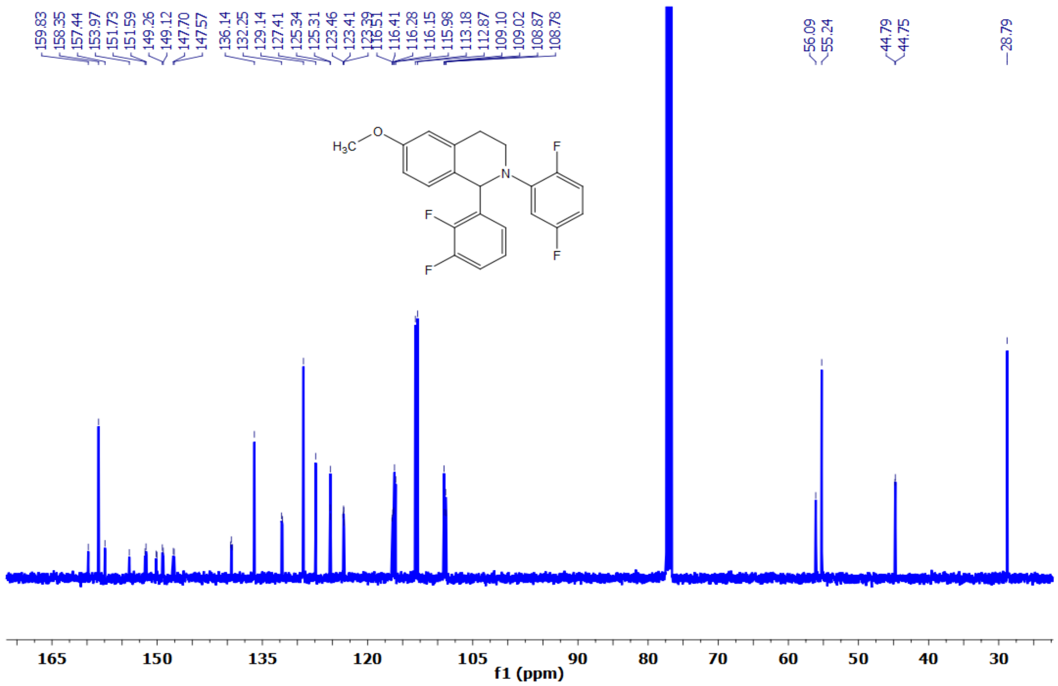


Figure S32(b): **[13]C spectra of 6-13, (125 MHz, $CDCl_3$): δ (ppm)** = 158.362, 139.4422, 139.4197, 136.1509, 132.2671, 132.1577, 129.1523, 127.4187, 125.353, 125.3217, 125.2907, 123.4736 , 123.4284, 123.4081, 123.363, 116.526, 116.4278, 116.291, 116.1889, 116.1668, 115.9963, 113.1974, 112.8862 , 109.1443, 109.116, 109.0354, 108.877, 108.7961, 56.1017, 55.2505, 44.7925, 44.7597, 28.7971

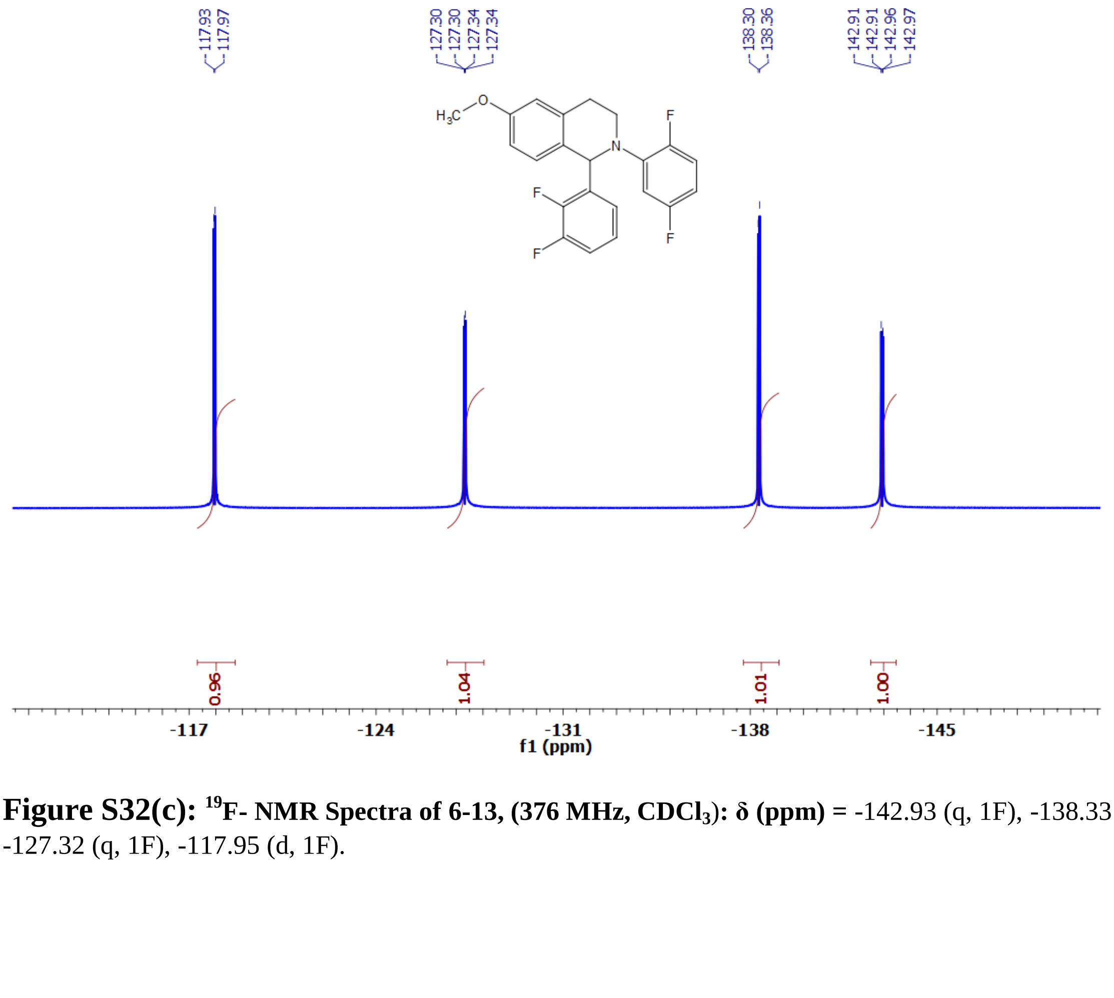


Figure S32(c): **[19]F- NMR Spectra of 6-13, (376 MHz, $CDCl_3$): δ (ppm) =** -142.93 (q, 1F), -138.33 (d, 1F), -127.32 (q, 1F), -117.95 (d, 1F).

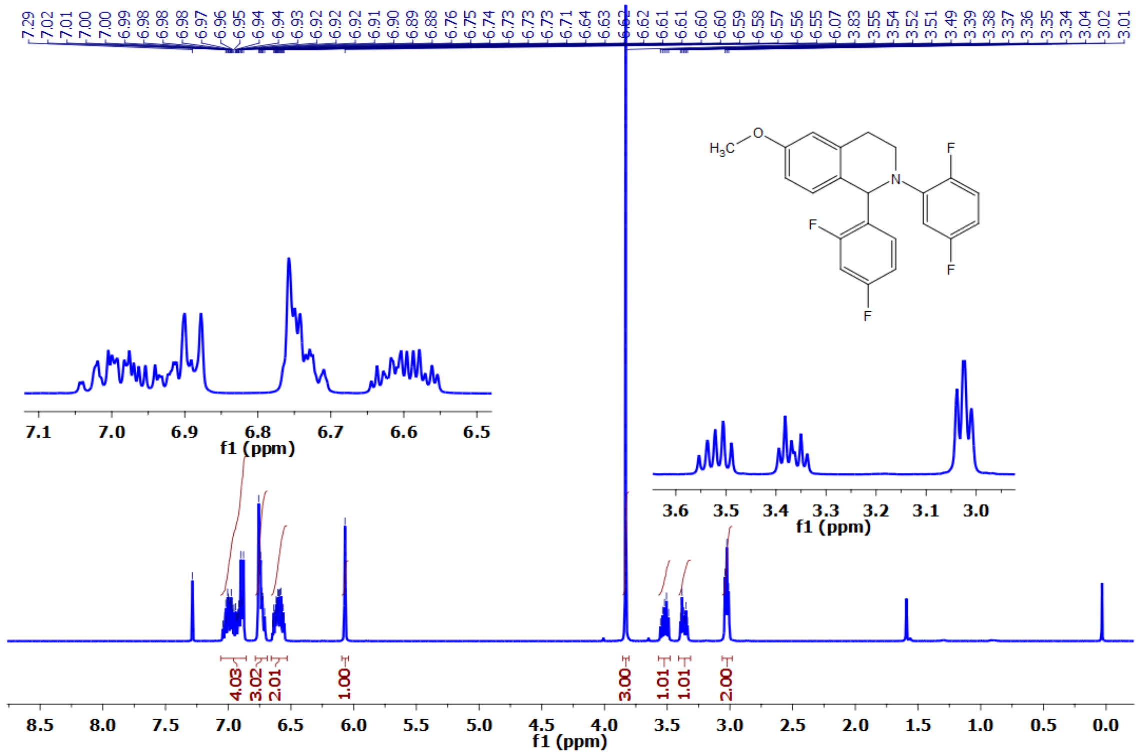


Figure S33(a): **^{1}H - NMR Spectra of 6-14, (400 MHz, $CDCl_3$): δ (ppm)** = 3.02 (t, 2H), 3.34-3.39 (m, 1H), 3.49-3.55 (m, 1H), 3.83 (s, 3H), 6.07 (s, 1H), 6.55-6.64 (m, 2H), 6.71-6.76 (m, 3H), 6.88-7.04 (m, 4H).

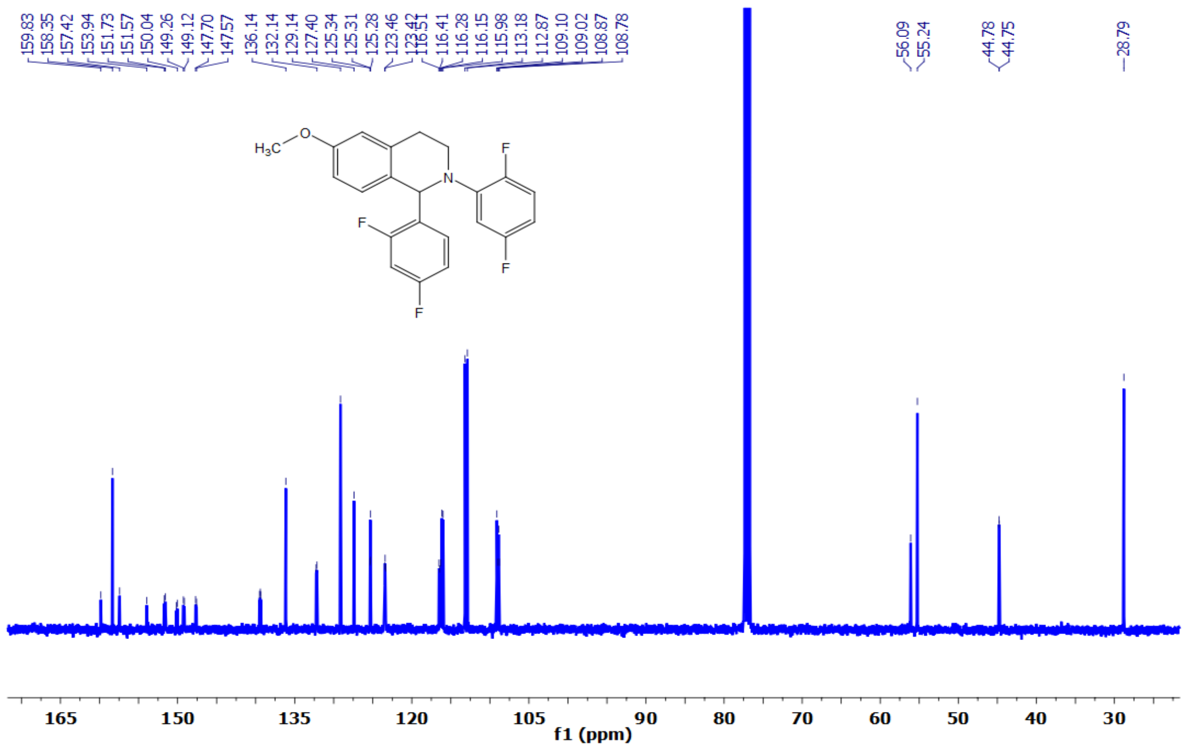


Figure S33(b): **^{13}C spectra of 6-14, (125 MHz, $CDCl_3$): δ (ppm)** = 158.3626, 136.1519, 132.2668, 132.1575, 129.153, 127.4169, 125.3543, 125.324, 125.2933, 123.4746, 123.4294, 123.4094 , 123.364, 116.5265, 116.4282, 116.2909, 116.1887, 116.1679, 115.9971, 113.1957, 112.8865, 109.1429, 109.1152, 109.035, 108.8779, 108.8642, 108.7958, 56.1007, 55.2493, 44.7885, 44.7568, 28.7965

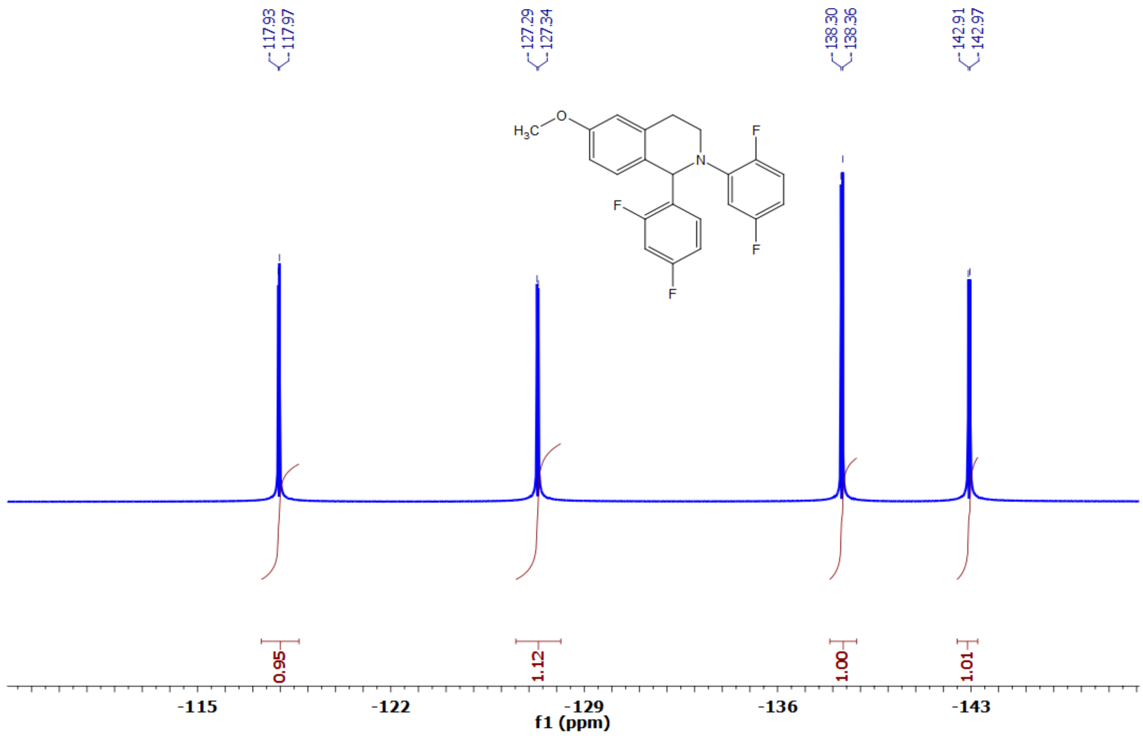


Figure S33(c): ^{19}**F- NMR Spectra of 6-14, (376 MHz, $CDCl_3$): δ (ppm)** = -142.94 (d, 1F), -138.33 (d, 1F), -127.31 (d, 1F), -117.95 (d, 1F)

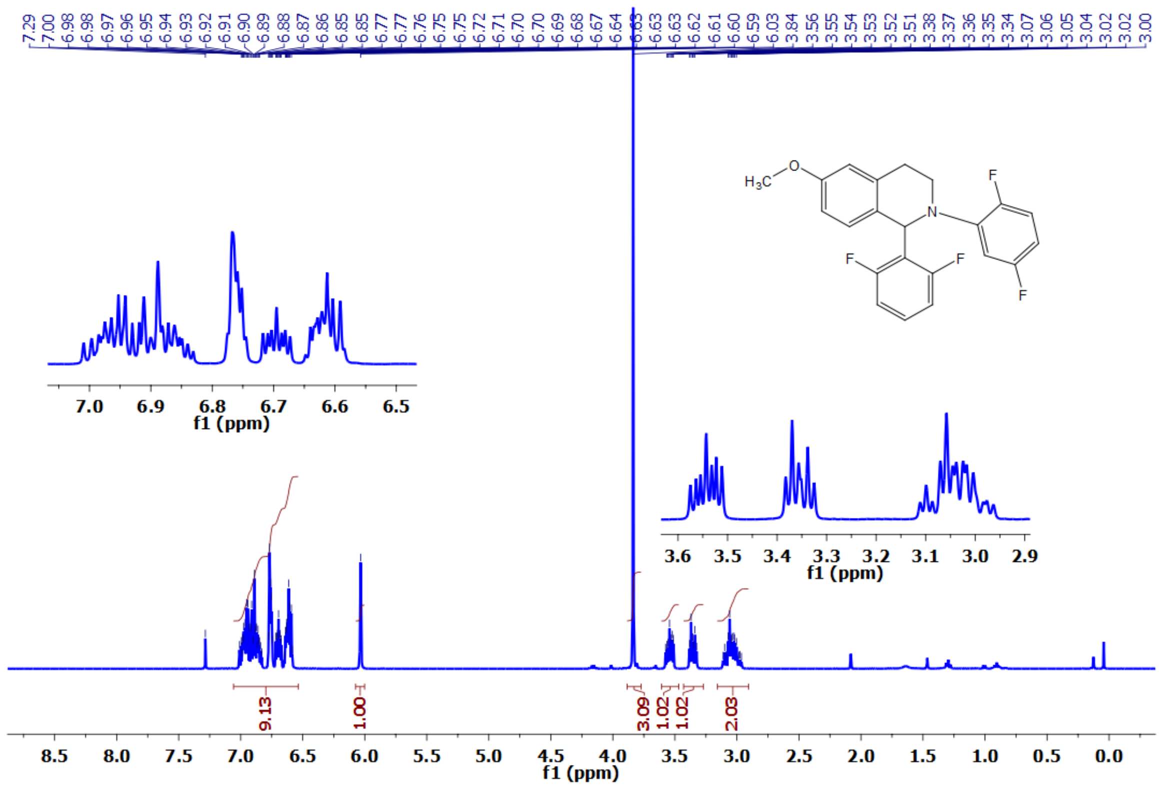


Figure S34(a): ^{1}**H - NMR Spectra of 6-16, (400 MHz, $CDCl_3$): δ (ppm)** = 2.96-3.11 (m, 2H), 3.33-3.38 (m, 1H), 3.51-3.58 (m, 1H), 3.84 (s, 3H), 6.03 (s, 1H), 6.58-7.01 (m, 9H).

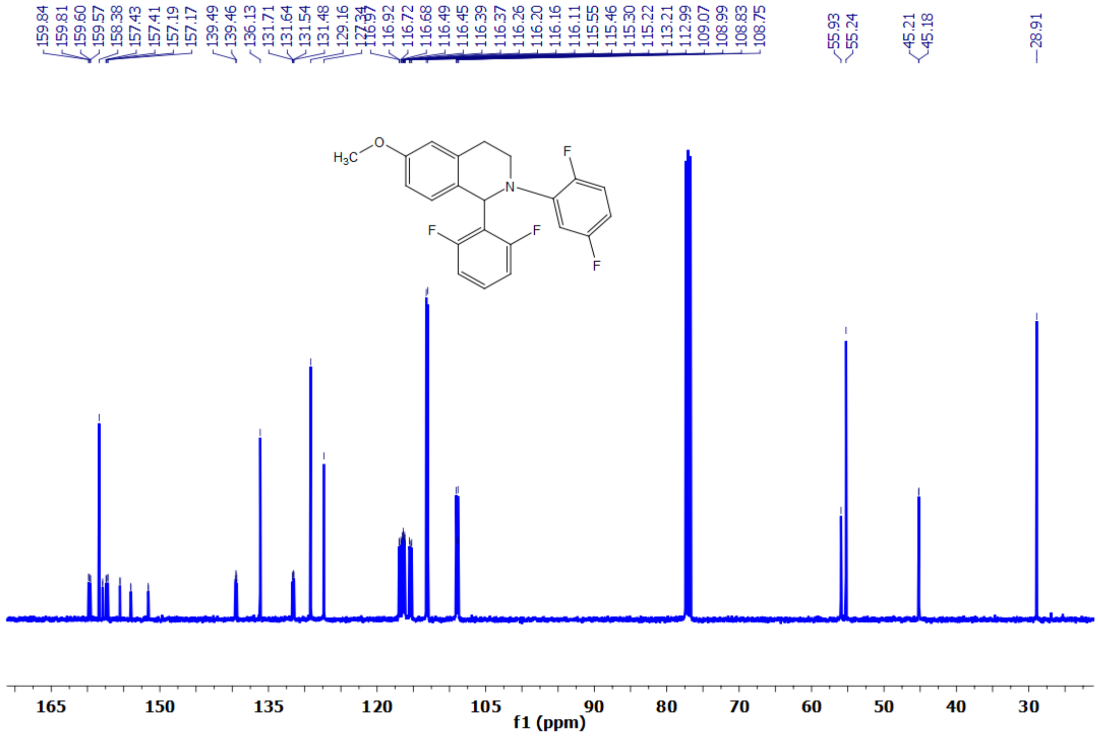


Figure S34(b): 13C spectra of 6-16, (125 MHz, $CDCl_3$): δ (ppm) = 158.399, 136.1484, 129.1789, 127.3537, 116.9789, 116.934, 116.736, 116.6916, 116.5045, 116.4663, 116.406, 116.3821, 116.2693, 116.21, 116.1695, 116.1248, 115.5601, 115.4733, 115.3178, 115.2314, 113.218, 113.0019, 109.1007, 109.0795, 109, 108.8454, 108.8255, 108.7606, 55.9354, 55.9085, 55.246, 45.2162, 45.1825, 28.9139

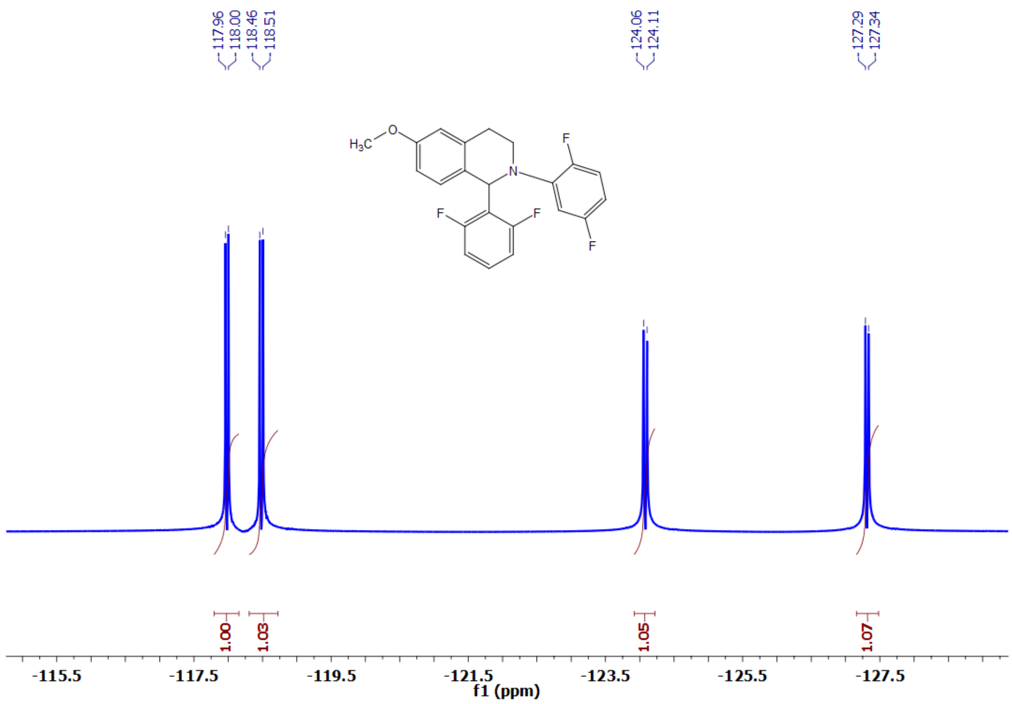


Figure S34(c): 19F- NMR Spectra of 6-16, (376 MHz, $CDCl_3$): δ (ppm) = -127.31 (d, 1F), -124.08 (d, 1F), -118.48 (d, 1F), -117.98 (d, 1F).

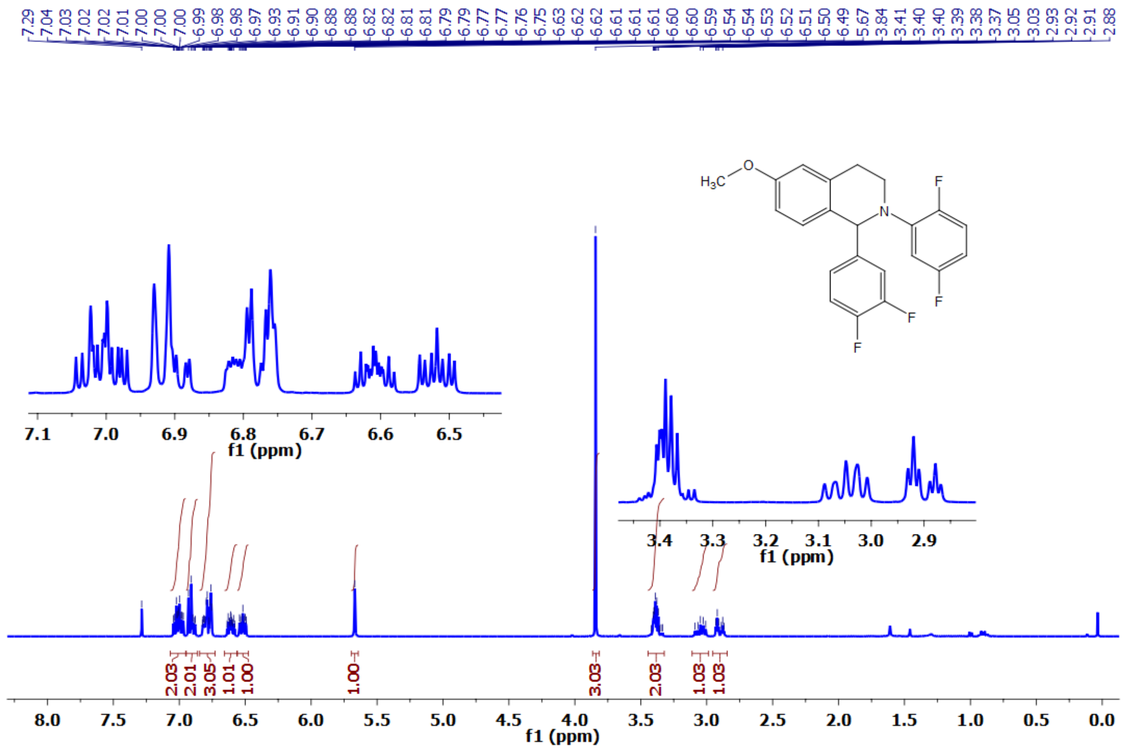


Figure S35(a): ^{1}**H - NMR Spectra of 6-17, (400 MHz, CDCl$_3$): δ (ppm)** = 2.87-3.09 (m, 2H), 3.33-3.42 (m, 2H), 3.84 (s, 3H), 5.67 (s, 1H), 6.49-6.54 (m, 1H), 6.58-6.64 (m, 1H), 6.75-6.82 (m, 3H), 6.88-6.93 (m, 2H), 6.97-7.04 (m, 2H).

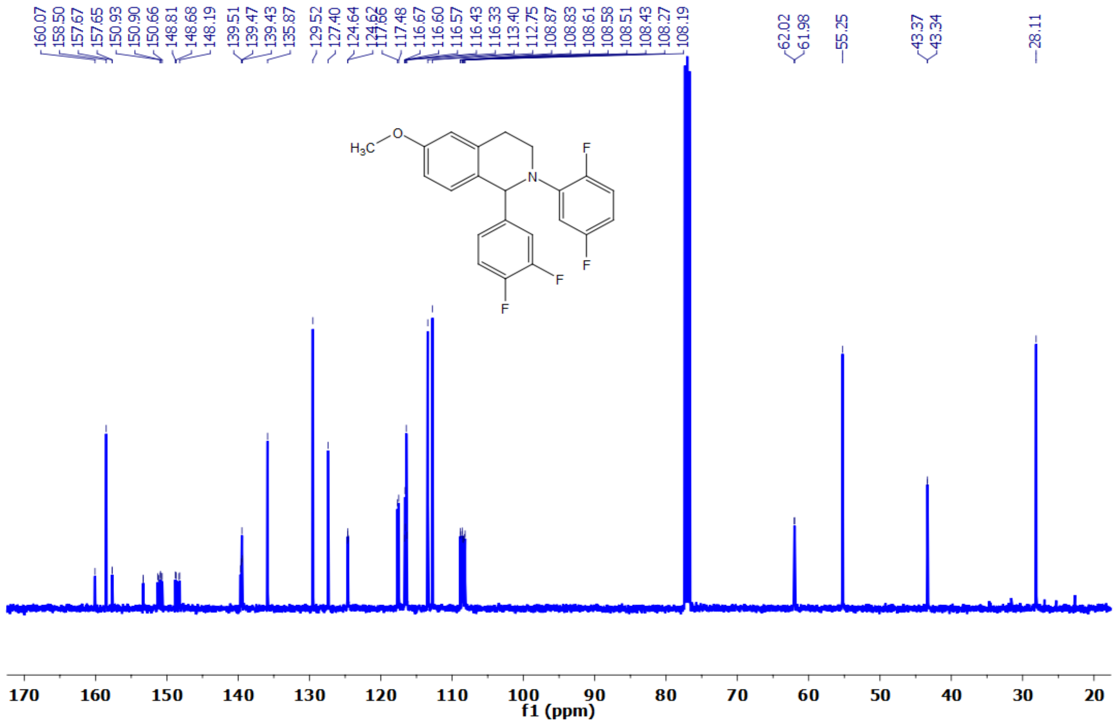


Figure S35(b): ^{13}**C spectra of 6-17, (125 MHz, CDCl$_3$): δ (ppm)** = 158.5217, 139.5785, 139.5295, 139.4905, 139.4737, 135.8837, 129.5355, 127.4108, 124.6912, 124.6569, 124.6312 , 124.5961, 117.6723, 117.4987, 116.6805, 116.6148, 116.5821, 116.4448, 116.3434, 113.4185, 112.7623, 108.8822, 108.8472, 108.6273, 108.5922, 108.5241, 108.4412, 108.285, 108.2027, 62.032, 61.9855, 55.2599, 43.3777, 43.3493, 28.1178

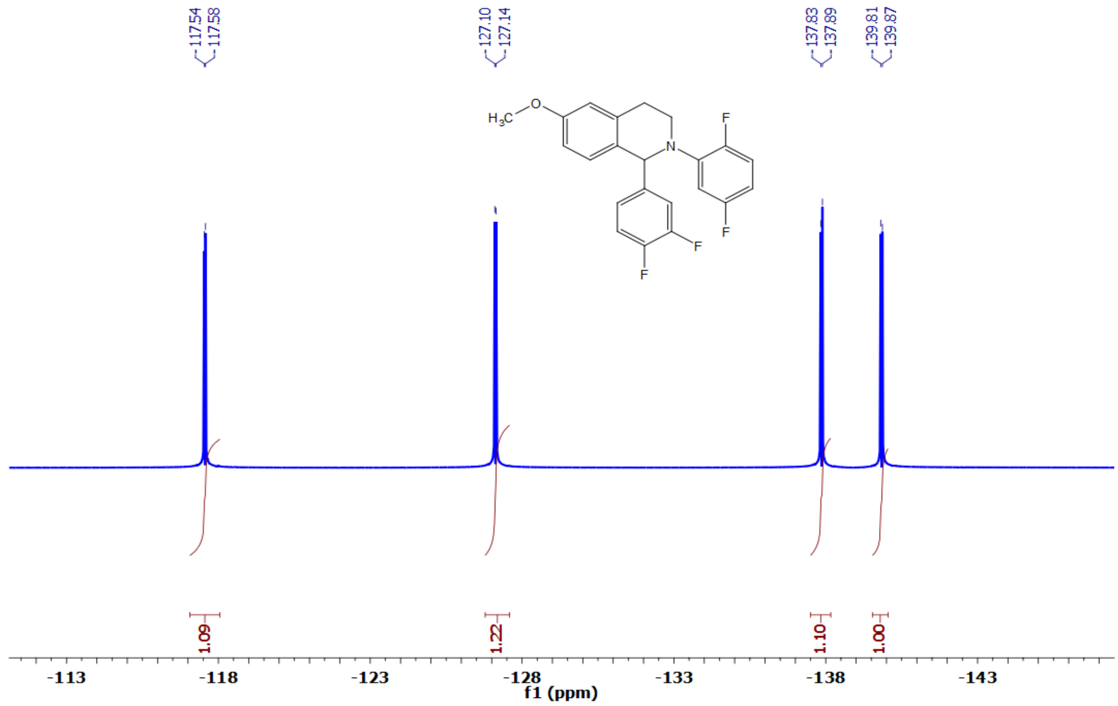


Figure S35(c): **[19]F- NMR Spectra of 6-17, (376 MHz, $CDCl_3$): δ (ppm)** = -139.84 (d, 1F), -137.86 (d, 1F), -127.12 (d, 1F), -117.56 (d, 1F).

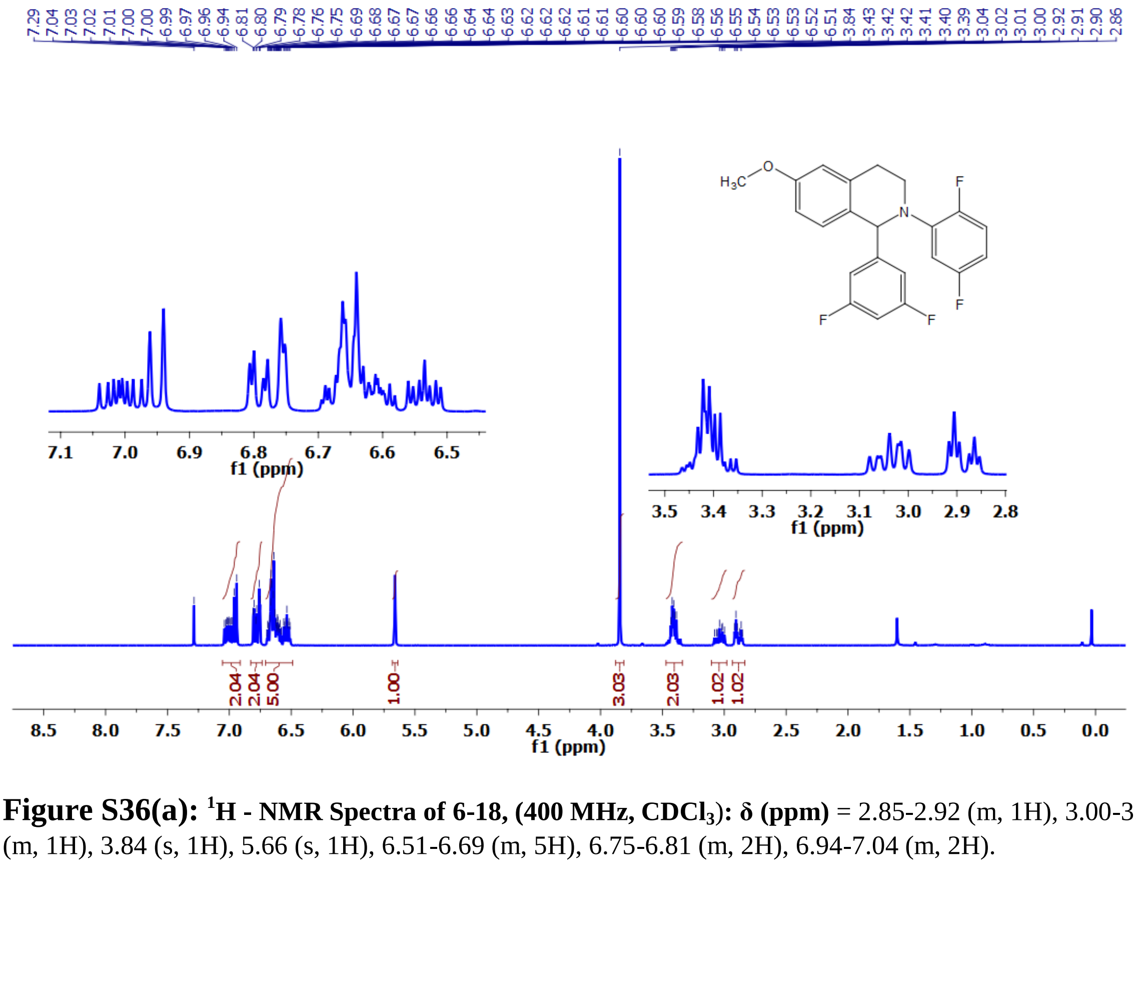


Figure S36(a): **[1]H - NMR Spectra of 6-18, (400 MHz, $CDCl_3$): δ (ppm)** = 2.85-2.92 (m, 1H), 3.00-3.08 (m, 1H), 3.84 (s, 1H), 5.66 (s, 1H), 6.51-6.69 (m, 5H), 6.75-6.81 (m, 2H), 6.94-7.04 (m, 2H).

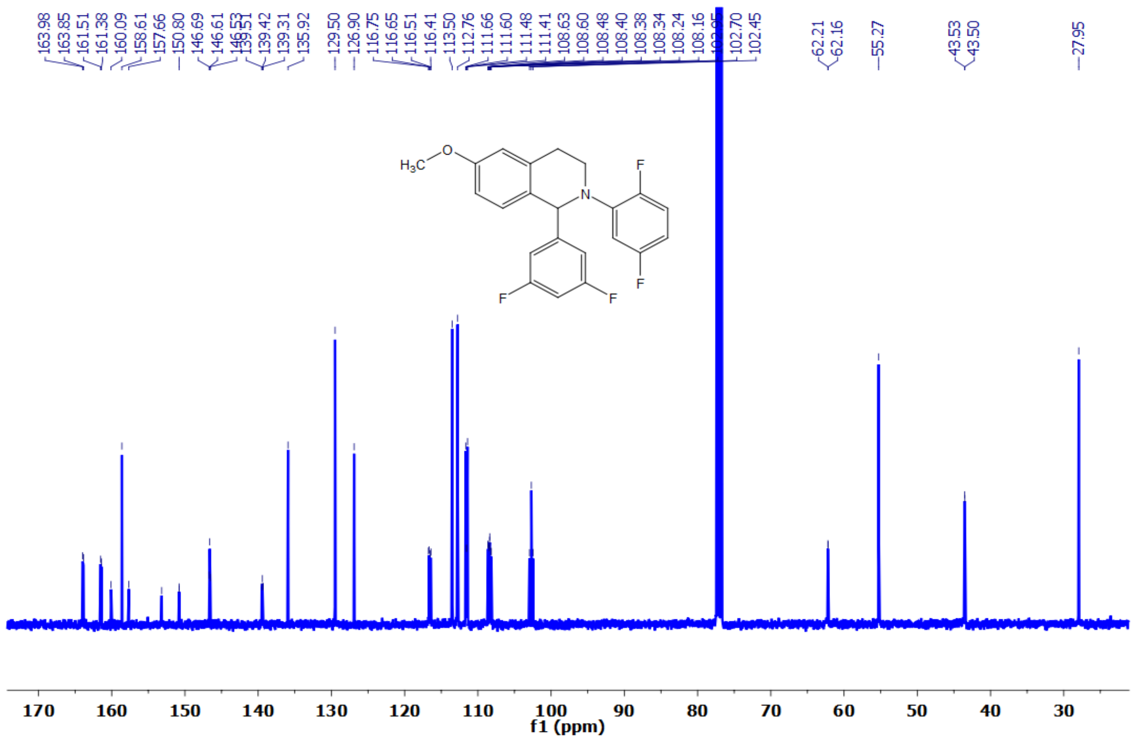


Figure S36(b): ^{13}**C spectra of 6-18, (125 MHz, $CDCl_3$): δ (ppm)** = 163.8677, 158.6226, 146.6237, 135.9373, 129.5117, 126.914, 116.7599, 116.6609, 116.5241, 116.423, 113.5094, 112.7716, 111.6754, 111.6096, 111.4912, 111.4249, 108.6432, 108.609, 108.4954, 108.411, 108.3883, 108.3528, 108.2558, 108.1744, 102.9633, 102.7099, 102.4582, 62.217, 62.1926, 62.1693, 55.2726, 43.5378, 43.5077, 27.957

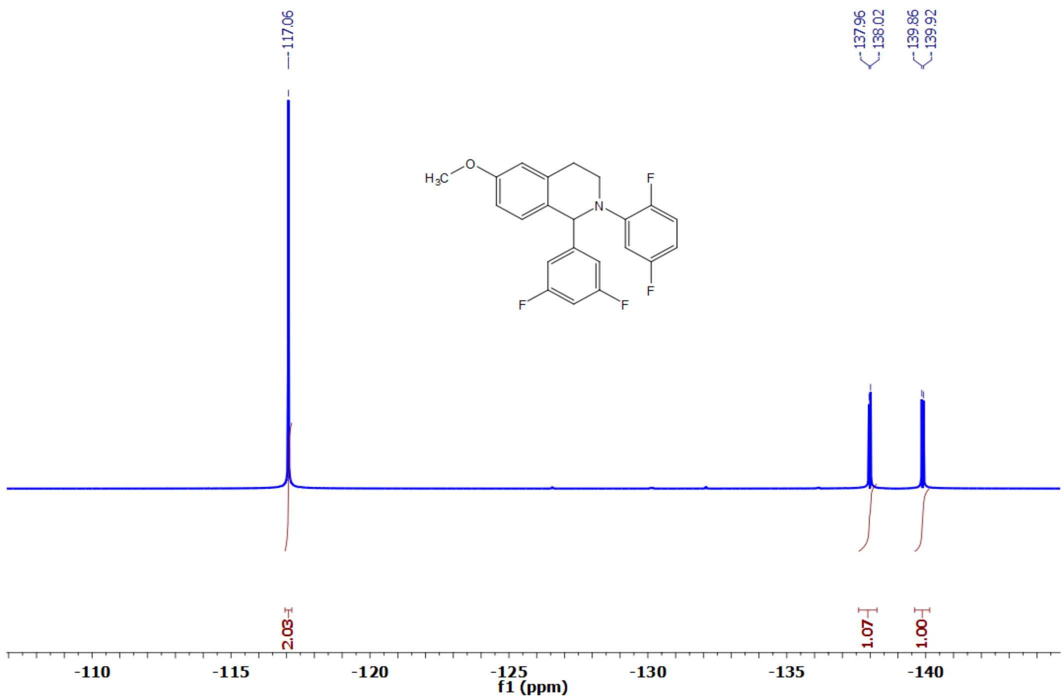


Figure S36(c): ^{19}**F- NMR Spectra of 6-18, (376 MHz, $CDCl_3$): δ (ppm)** = -139.89 (d, 1F), -137.99 (d, 1F), -117.06 (s, 2F).

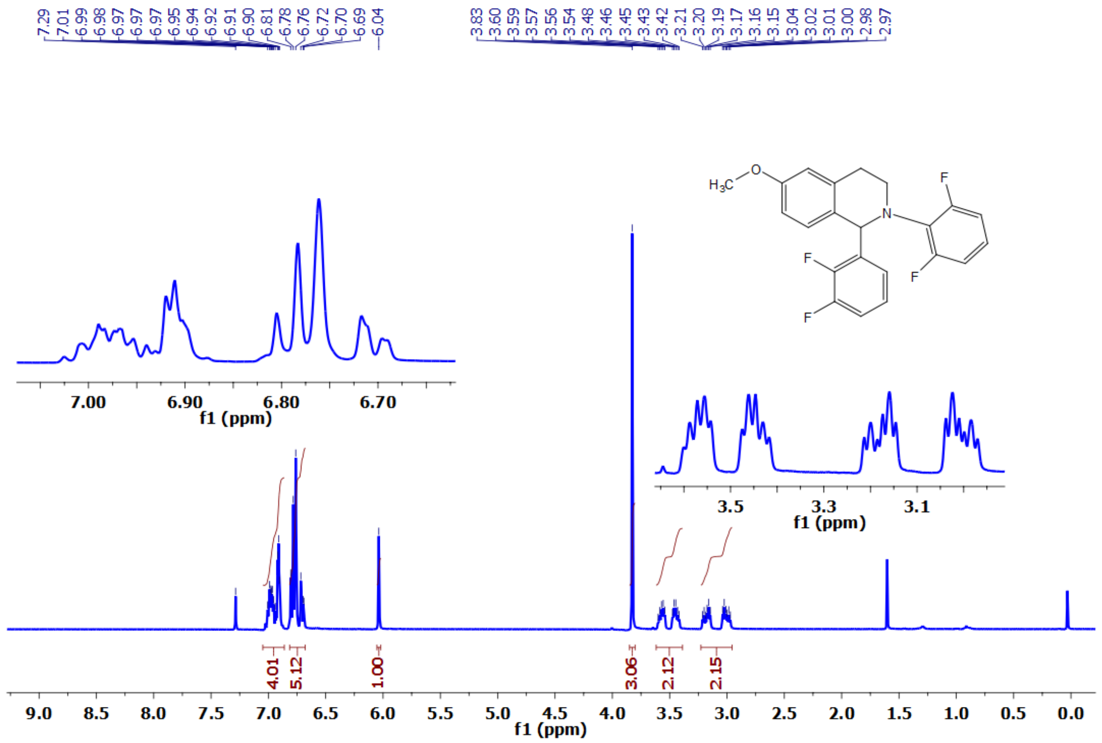


Figure S37(a): **^{1}H - NMR Spectra of 6-19, (400 MHz, $CDCl_3$): δ (ppm)** = 2.97-3.21 (m, 2H), 3.42-3.60 (m, 2H), 3.83 (s, 3H), 6.04 (s, 1H), 6.69-6.81 (m, 5H), 6.90-7.01 (m, 4H).

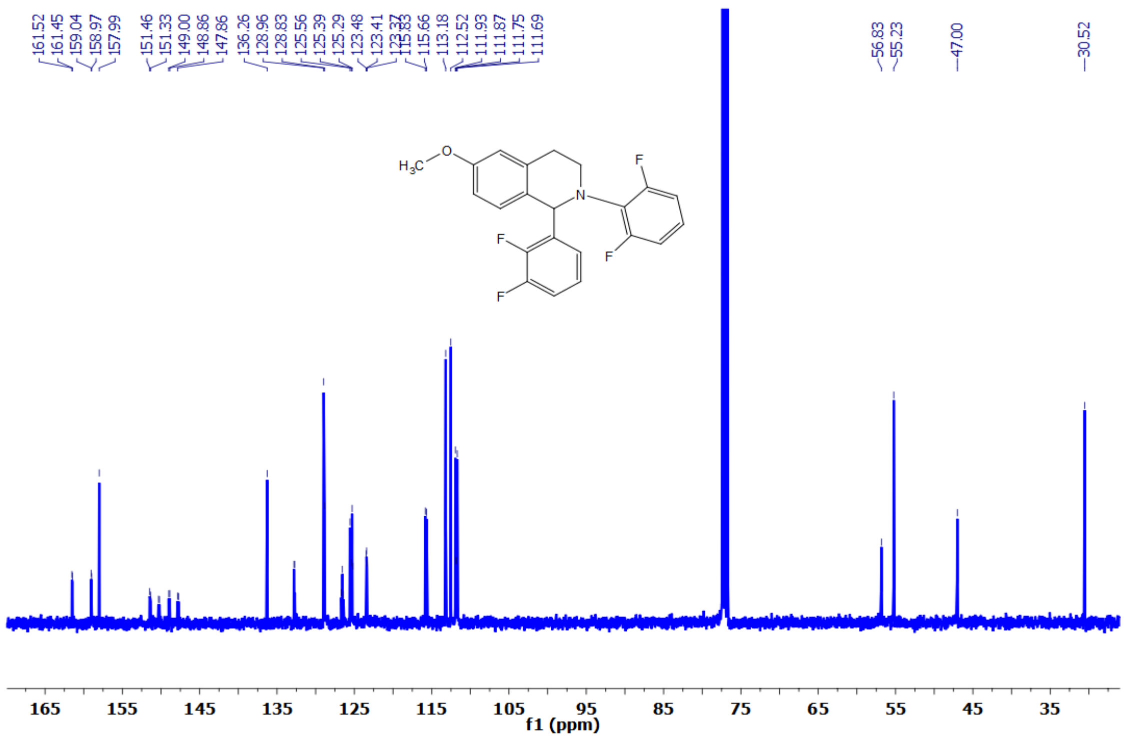


Figure S37(b): **^{13}C spectra of 6-19, (125 MHz, $CDCl_3$): δ (ppm)** = 161.5399, 161.4706, 159.0612, 158.9919, 158.0112, 136.2792, 132.8241, 132.7193, 128.9769, 128.8457, 126.5574, 125.6024, 125.5718, 125.5398, 125.4008, 125.2988, 125.1964, 123.4892, 123.4435, 123.4242, 123.3796, 115.8398, 115.6701, 113.1877, 112.5363, 111.9442, 111.8815, 111.7609, 111.6985, 56.8354, 55.2414, 47.0103, 30.5232

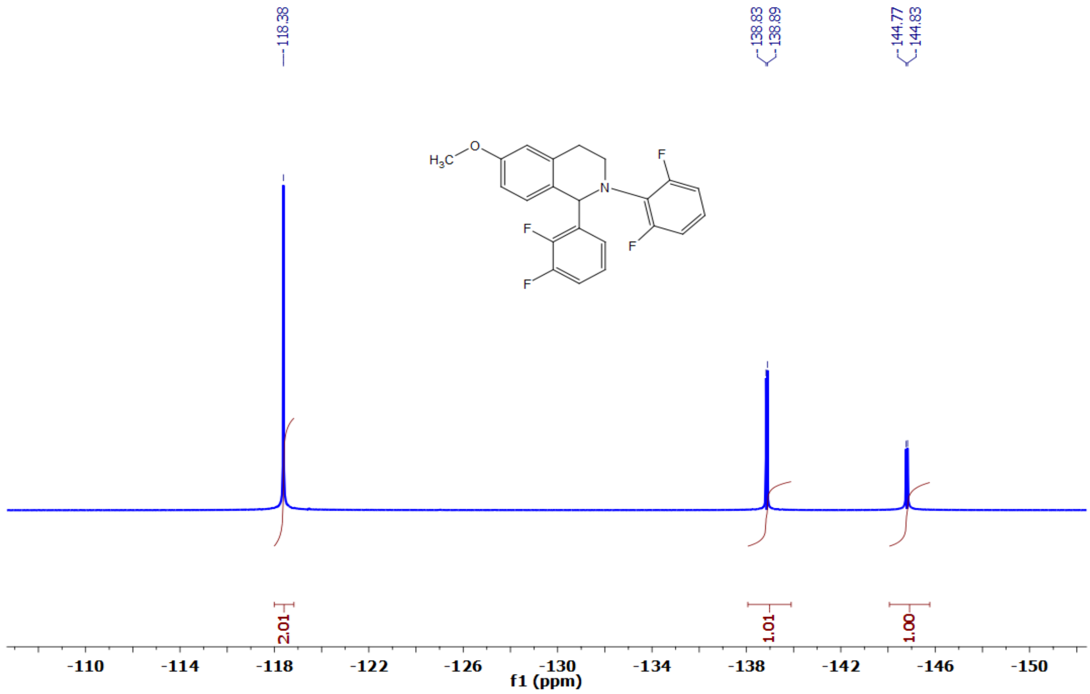


Figure S37(c): [19]**F- NMR Spectra of 6-19, (376 MHz, $CDCl_3$): δ (ppm)** = -144.80 (d, 1F), -138.86 (d, 1F), -118.38 (s, 2F),

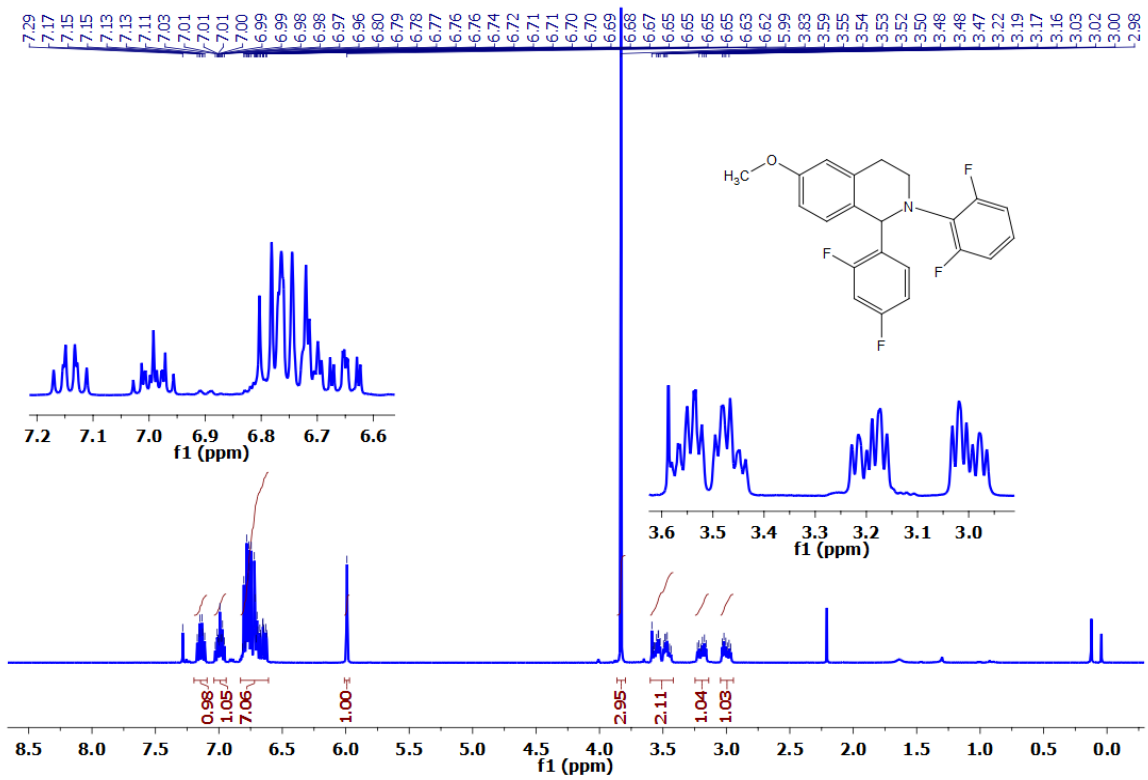


Figure S38(a): [1]**H - NMR Spectra of 6-20, (400 MHz, $CDCl_3$): δ (ppm)** = 2.96-3.03 (m, 1H), 3.16-3.23 (m, 1H), 3.44-3.59 (m, 2H), 3.83 (s, 3H), 5.99 (s, 1H), 6.62-6.81 (m, 7H), 6.96-7.03 (m, 1H), 7.11-7.17 (m, 1H).

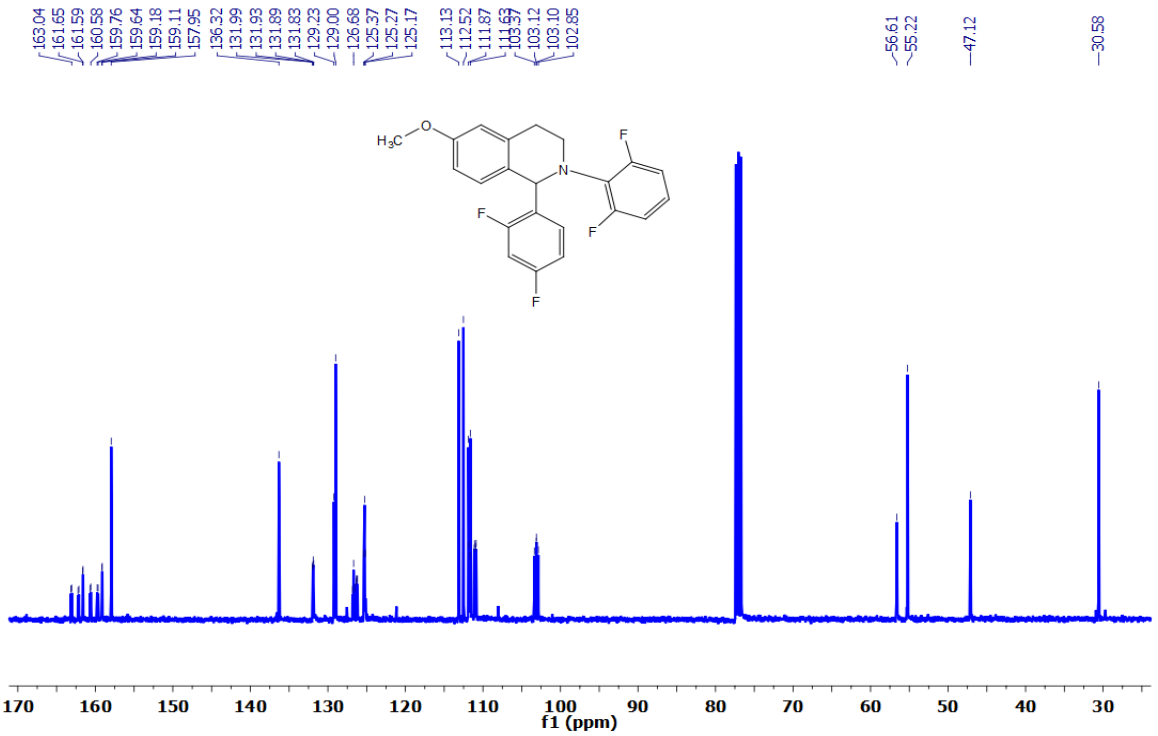


Figure S38(b): ^{13}**C spectra of 6-20, (125 MHz, CDCl$_3$): δ (ppm)** = 161.6719, 161.6035, 159.1929, 159.1239, 157.968, 136.3342, 132.0024, 131.944, 131.9071, 131.8488, 129.2411, 129.014, 126.697, 125.3858, 125.2835, 125.1817, 113.1469, 112.5307, 111.8857, 111.8231, 111.7019, 111.6397, 111.1317, 111.0956, 110.9241, 110.8878, 103.3822, 103.13, 103.1165, 102.8658, 56.6206, 55.2269, 47.1528, 47.1285, 47.1054, 30.5821

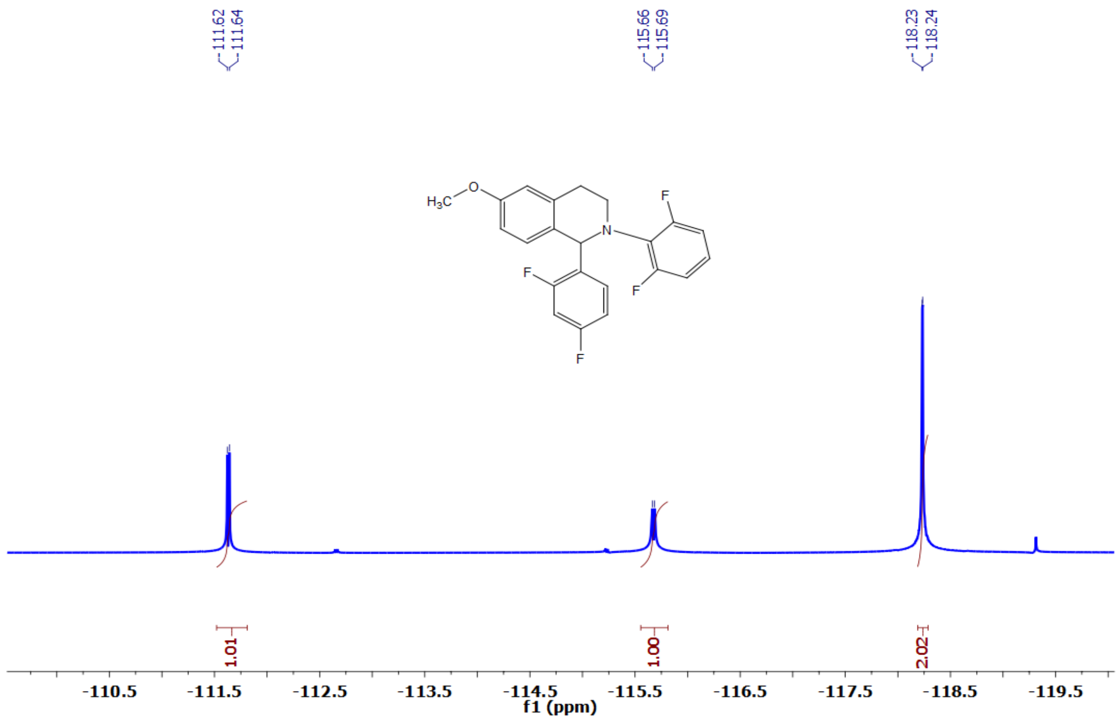


Figure S38(c): ^{19}**F- NMR Spectra of 6-20, (376 MHz, CDCl$_3$): δ (ppm)** = -118.23 (d, 2F), -115.67 (d, 1F), -111.63 (d, 1F).

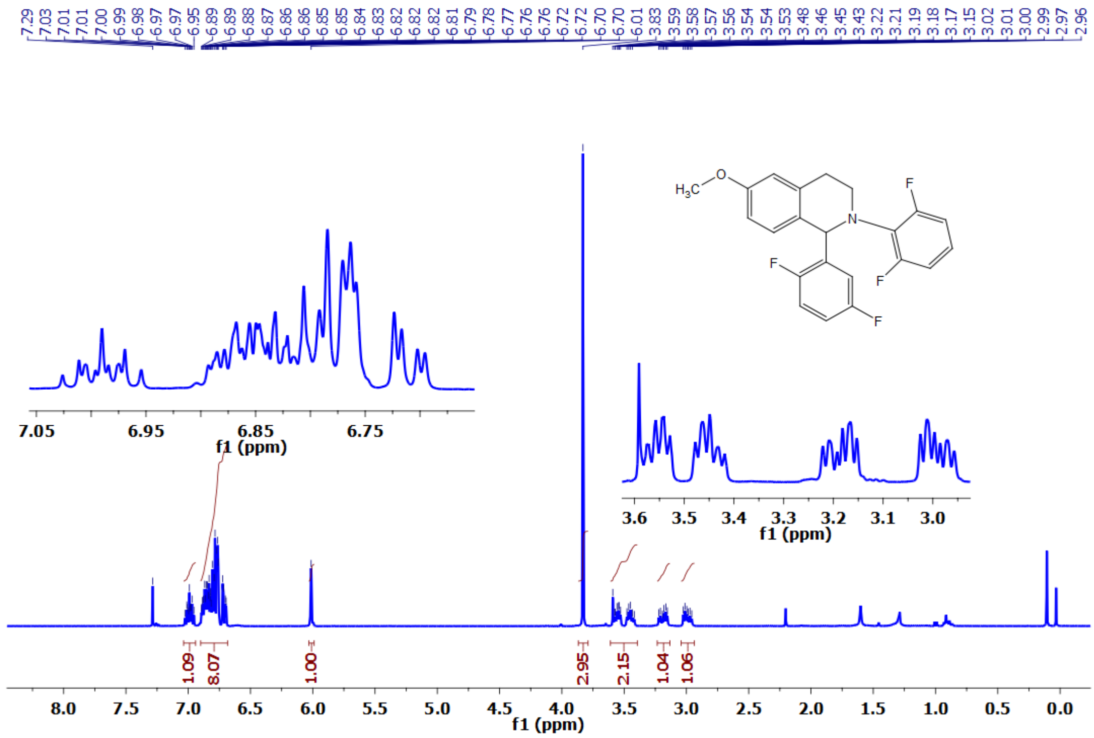


Figure S39(a): **^{1}H - NMR Spectra of 6-21, (400 MHz, $CDCl_3$): δ (ppm)** = 2.96-3.02 (m, 1H), 3.15-3.22 (m, 1H), 3.42-3.59 (m, 2H), 3.83 (s, 3H), 6.01 (s, 1H), 6.70-6.89 (m, 8H), 6.95-7.03 (m, 1H).

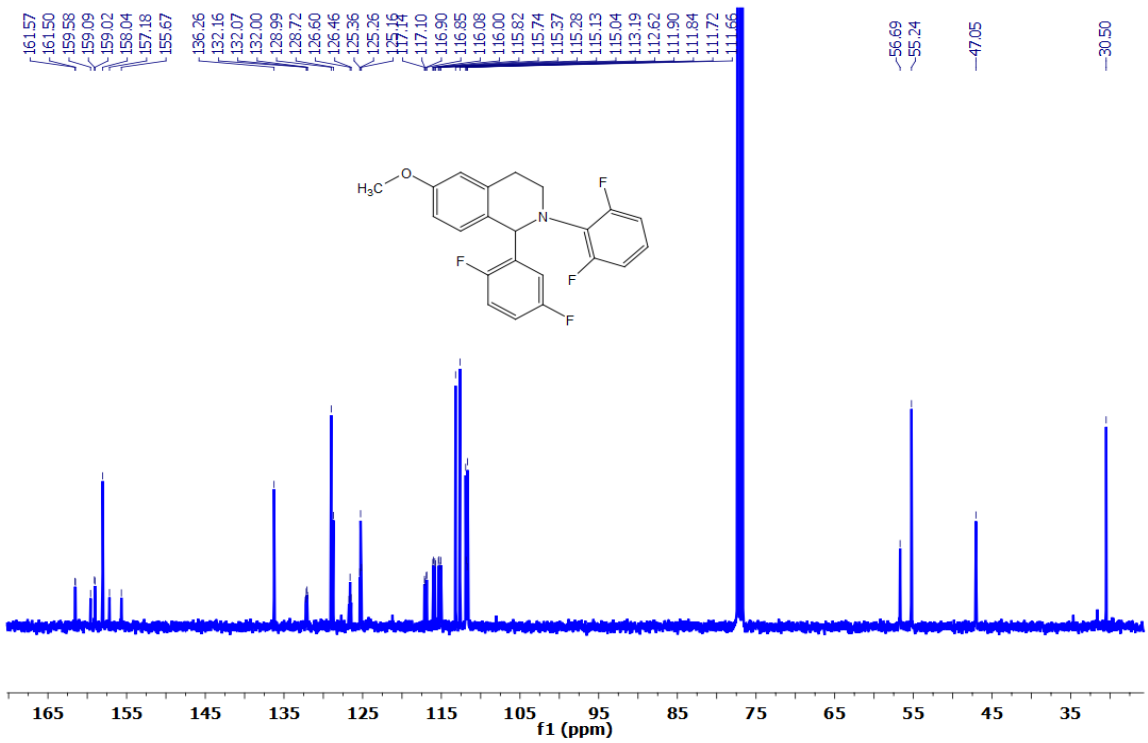


Figure S39(b): **^{13}C spectra of 6-21, (125 MHz, $CDCl_3$): δ (ppm)** = 161.587, 161.5192, 159.107, 159.0398, 158.0555, 136.2768, 129.0085, 128.7347, 126.6123, 125.3779, 125.2759, 125.1747, 117.1542, 117.1094, 116.9125, 116.868, 116.0945, 116.0096, 115.8378, 115.752, 115.3848, 115.2985, 115.1411, 115.0558, 113.2015, 112.6369, 111.9159, 111.8526, 111.7334, 111.6701, 56.6991, 55.2491, 47.0814, 47.0601, 30.5055

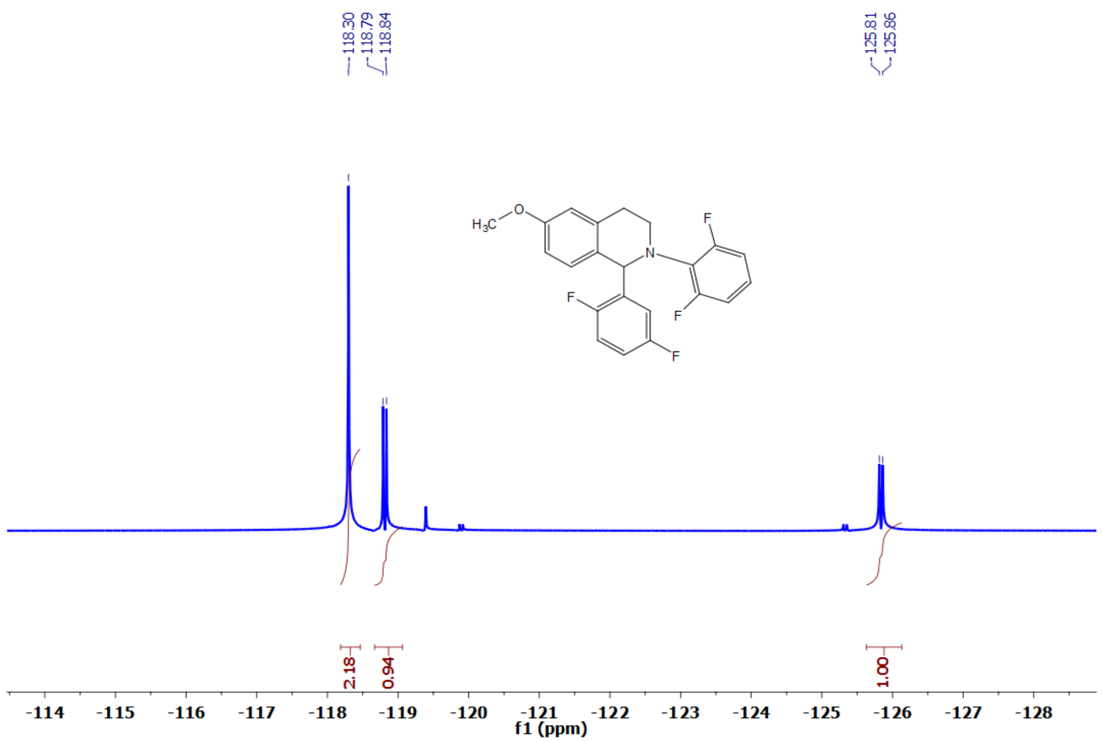


Figure S39(c): **19F- NMR Spectra of 6-21, (376 MHz, $CDCl_3$): δ (ppm)** = -125.83 (d, 1F), -118.81 (d, 1F), -118.30 (s, 2F)

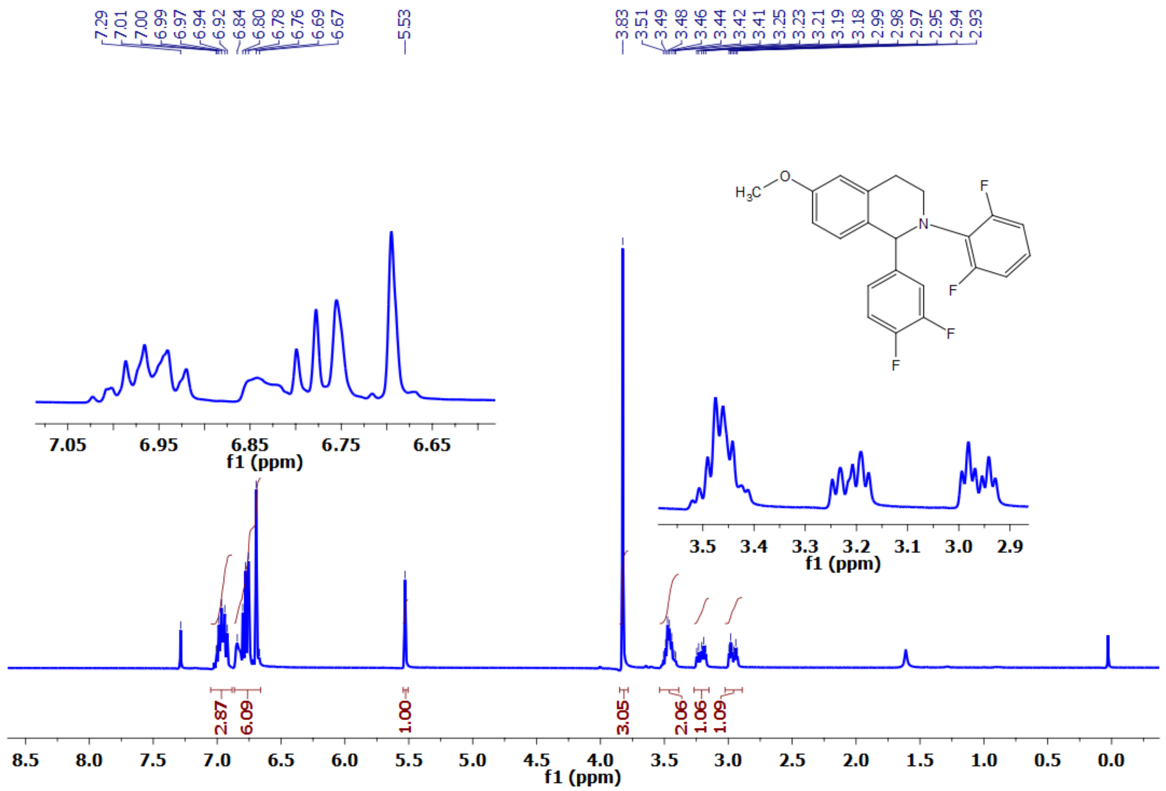


Figure S40(a): **1H - NMR Spectra of 6-23, (400 MHz, $CDCl_3$): δ (ppm)** = 2.93-2.99 (m, 1H), 3.18-3.25 (m, 1H), 3.41-3.51 (m, 2H), 3.83 (s, 3H), 5.53 (s, 1H), 6.67-6.84 (m, 6H), 6.92-7.01 (m, 3H).

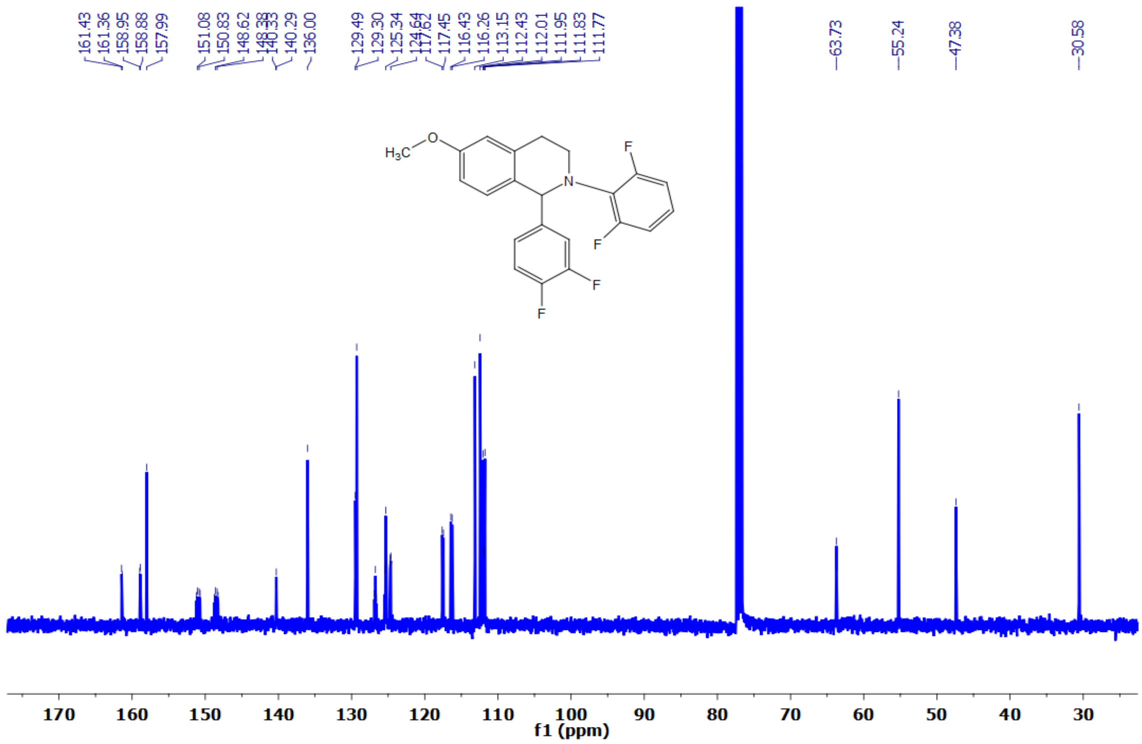


Figure S40(b): **^{13}C spectra of 6-23, (125 MHz, $CDCl_3$): δ (ppm)** = 161.4475, 158.9693, 158.901, 158.0049, 140.3086, 136.021, 129.5039, 129.3123, 126.7538, 125.4568, 125.3553, 125.2533 , 124.7504, 124.7169, 124.6896, 124.655, 117.6336, 117.4618, 116.4448, 116.2755, 113.1626, 112.4428 , 112.0242, 111.9614, 111.8398, 111.779, 63.7396, 55.2523 , 47.3864, 30.5817

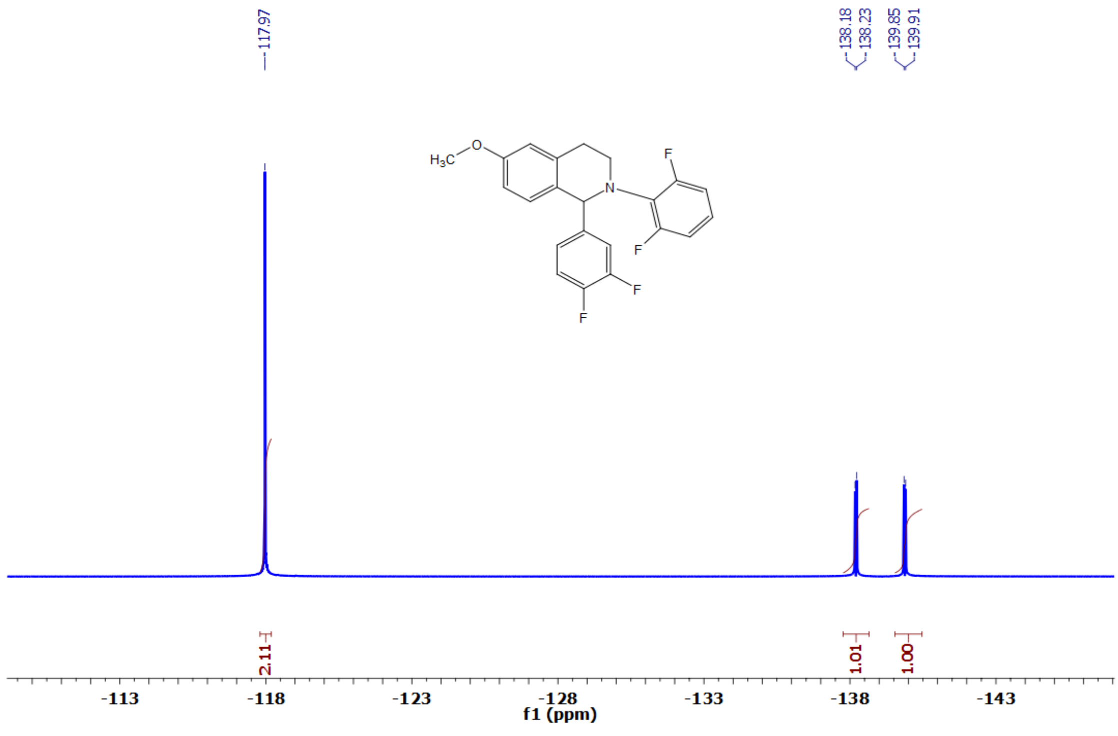


Figure S40(c): **^{19}F- NMR Spectra of 6-23, (376 MHz, $CDCl_3$): δ (ppm)** = -139.88 (d, 1F), -138.20 (d, 1F), -117.97 (s, 2F).

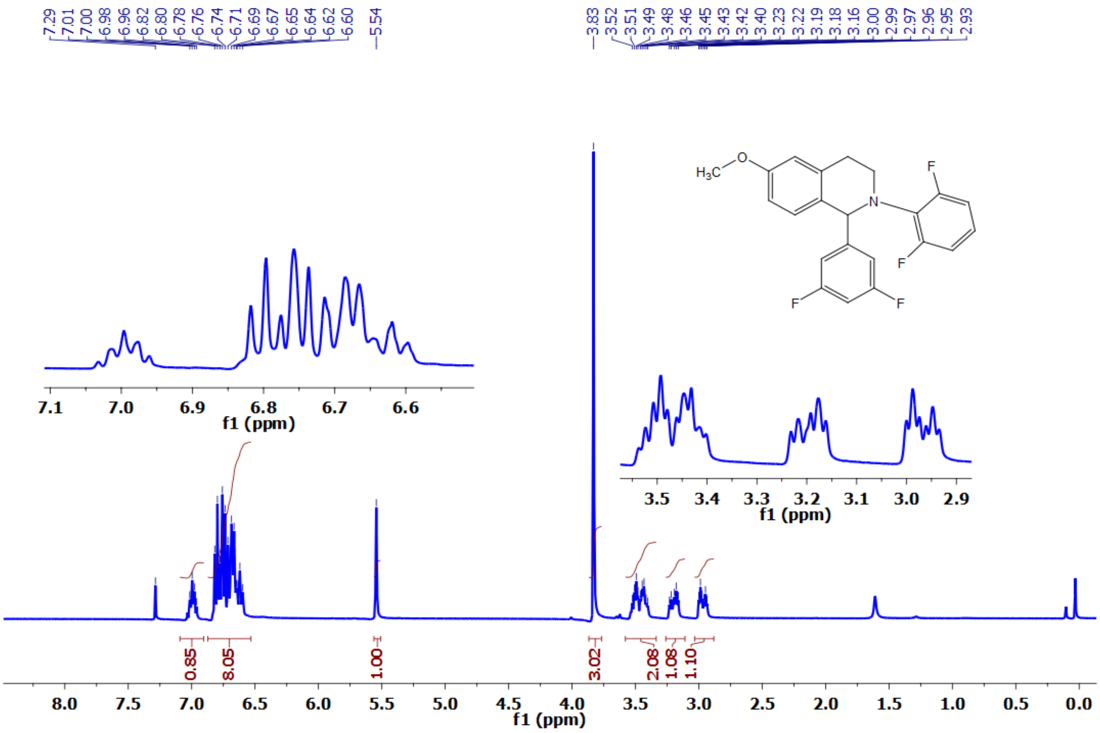


Figure S41(a): ^{1}**H - NMR Spectra of 6-24, (400 MHz, $CDCl_3$): δ (ppm)** = 2.93-3.00 (m, 1H), 3.16-3.23 (m, 1H), 3.40-3.52 (m, 2H), 3.83 (s, 3H), 5.54 (s, 1H), 6.60-6.82 (m, 8H), 6.96-7.01 (m, 1H).

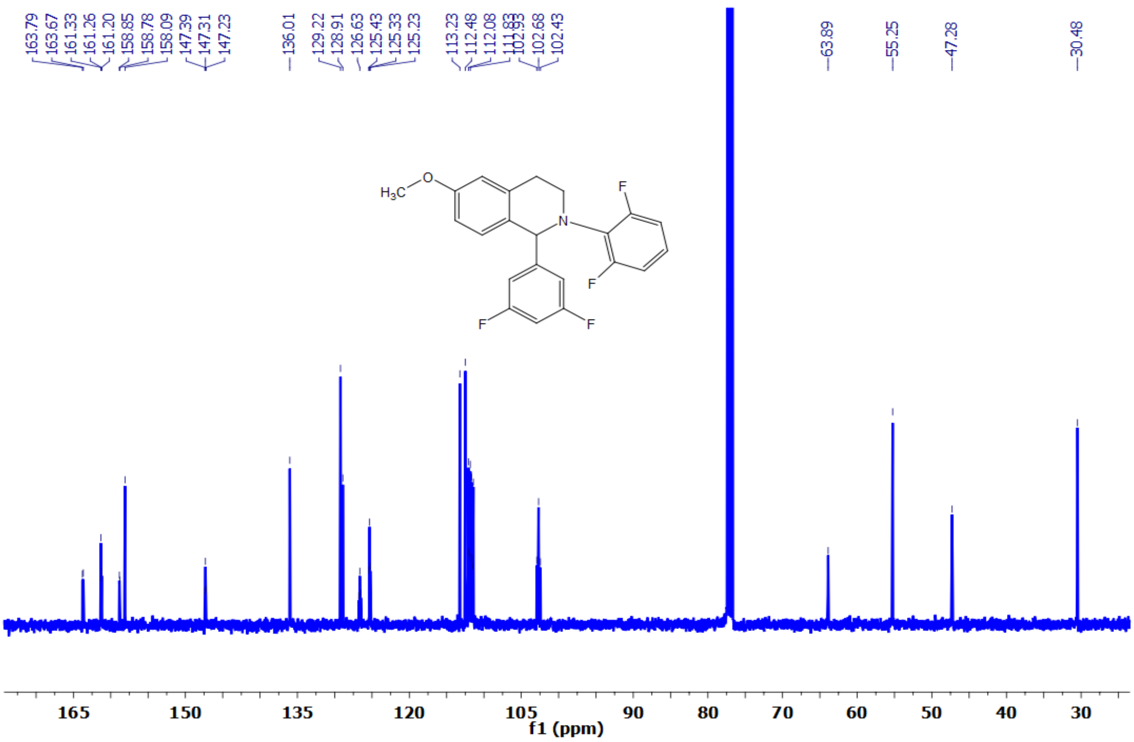


Figure S41(b): ^{13}**C spectra of 6-24, (125 MHz, $CDCl_3$): δ (ppm)** = 163.8111, 163.687, 161.3441, 161.2734, 161.2206, 158.8652, 158.1078, 147.3292, 136.0224, 129.2329, 128.9205, 126.6486, 125.4462, 125.3443, 125.2411, 113.2441, 112.4982, 112.0893, 112.0269, 111.9068, 111.8443, 111.6783, 111.6145, 111.4972, 111.4311, 102.9459, 102.6923, 102.4384, 63.8966, 55.2531, 47.305, 47.2843, 47.2649, 30.4855.

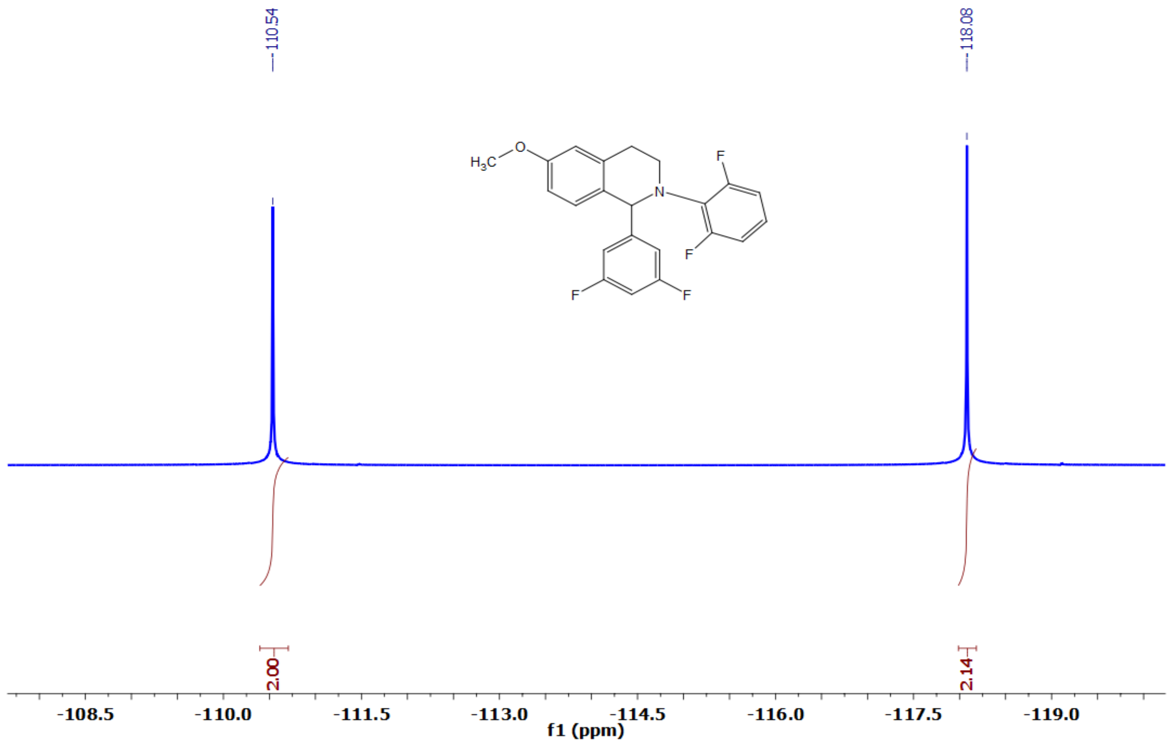


Figure S41(c): **^{19}F- NMR Spectra of 6-24, (376 MHz, $CDCl_3$): δ (ppm)** = -118.08 (s, 2F), -110.54 (s, 2F).

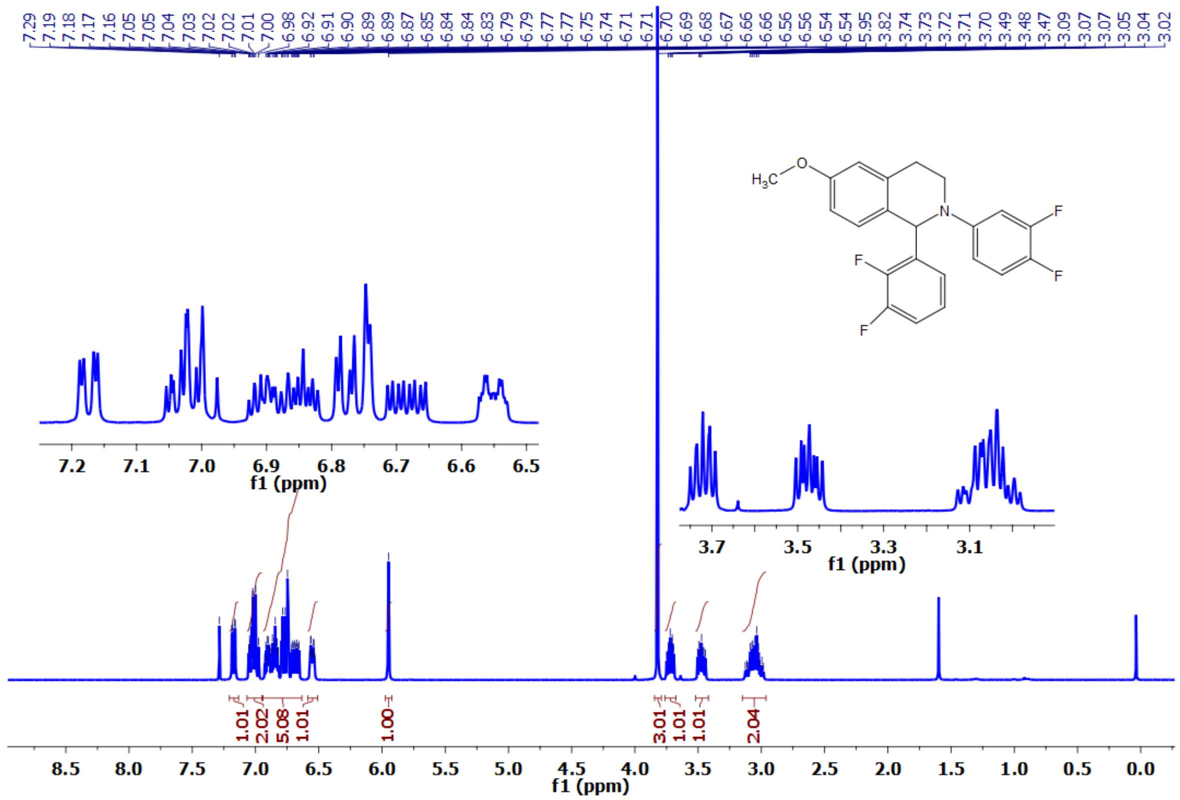


Figure S42(a): **^{1}H - NMR Spectra of 6-25, (400 MHz, $CDCl_3$): δ (ppm)** = 2.98-3.13 (m, 2H), 3.44-3.50 (m, 1H), 3.69-3.80 (m, 1H), 3.82 (s, 3H), 5.95 (s, 1H), 6.54-6.57 (m, 1H), 6.66-6.92 (m, 5H), 6.98-7.05 (m, 2H), 7.17 (dd, 1H).

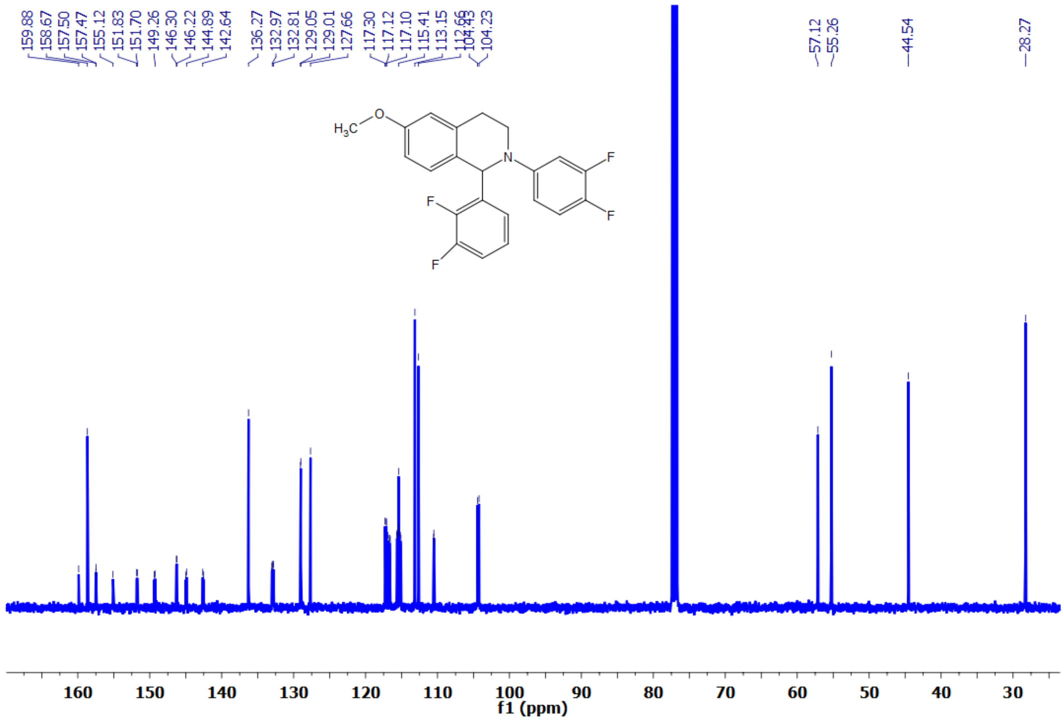


Figure S42(b): **^{13}C spectra of 6-25, (125 MHz, $CDCl_3$): δ (ppm)** = 158.6904, 146.3389, 146.3184, 146.26, 136.2896, 132.9813, 132.8212, 129.0617, 129.0214, 127.6712, 117.3097, 117.2923, 117.1343, 117.1168, 116.9261, 116.8431, 116.6731, 116.5899, 115.6772, 115.6327, 115.4282, 115.3847, 115.34, 115.1845, 115.0978, 113.1612, 112.669, 110.5519, 110.5224, 110.5006, 110.4705, 104.4463 , 104.2407, 57.1279, 55.2684, 44.5458, 28.2698

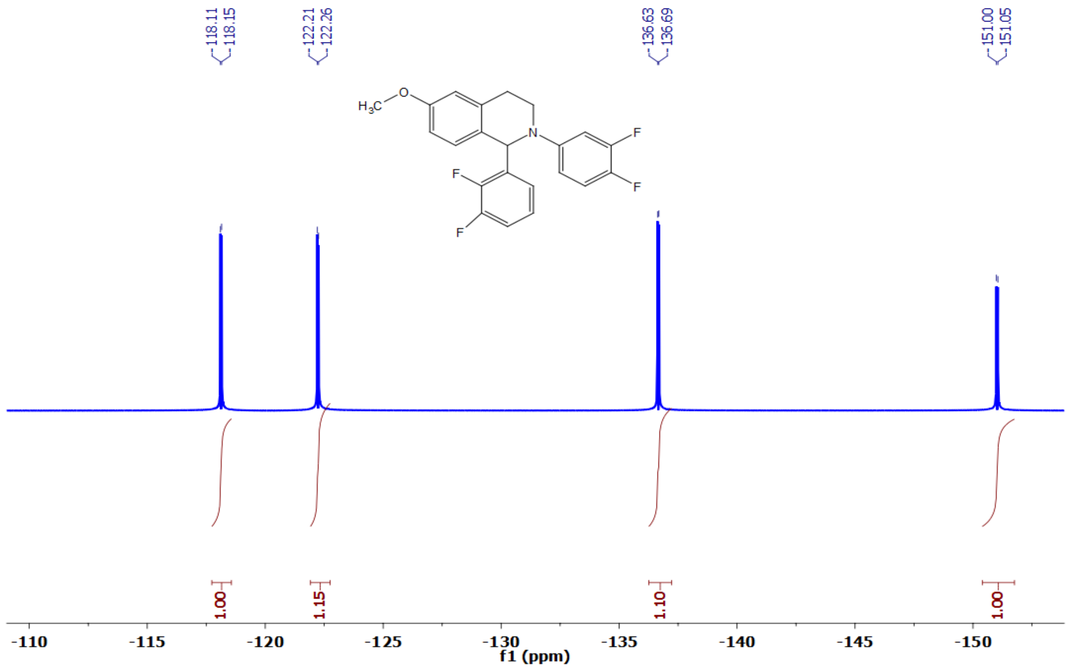


Figure S42(c): **^{19}F- NMR Spectra of 6-25, (376 MHz, $CDCl_3$): δ (ppm)** = -151.03 (d, 1F), -136.66 (d, 1F), -122.23 (d, 1F), -118.13 (d, 1F).

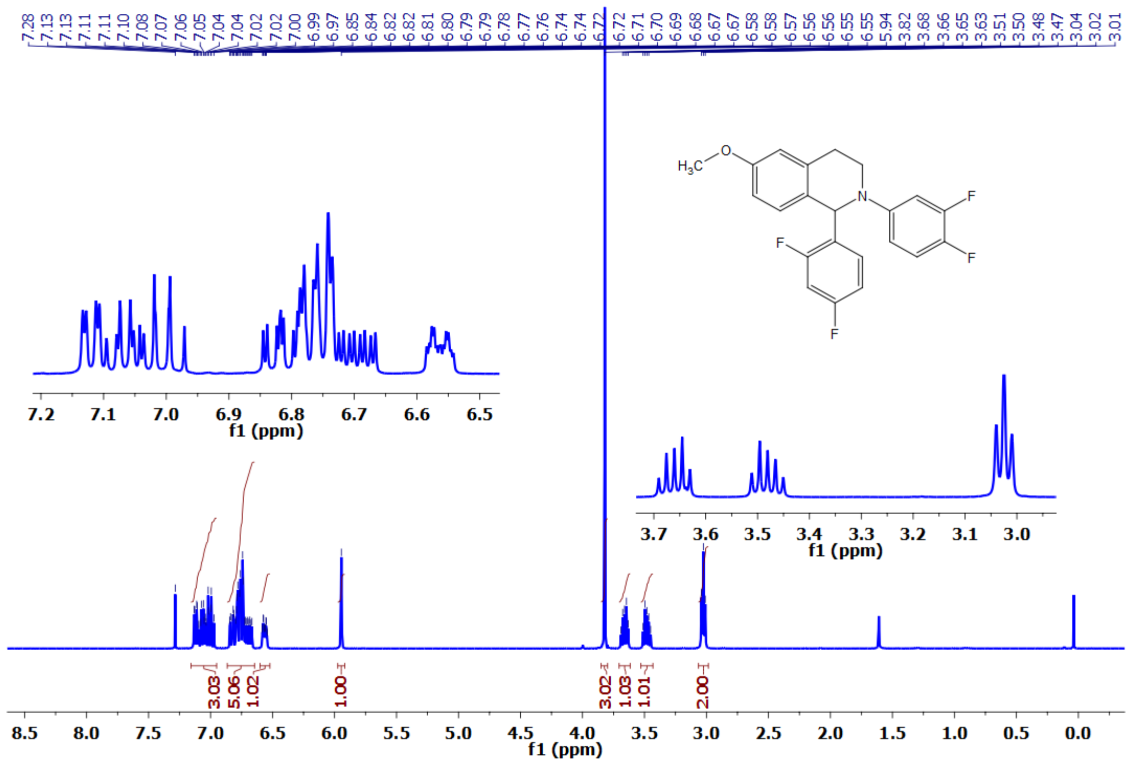


Figure S43(a): ^{1}**H - NMR Spectra of 6-26, (400 MHz, $CDCl_3$): δ (ppm)** = 3.02 (t, 2H), 3.45-3.51 (m, 1H), 3.63-3.69 (m, 1H), 3.82 (s, 3H), 5.94 (s, 1H), 6.54-6.58 (m, 1H), 6.67-6.85 (m, 5H), 6.97-7.13 (m, 3H).

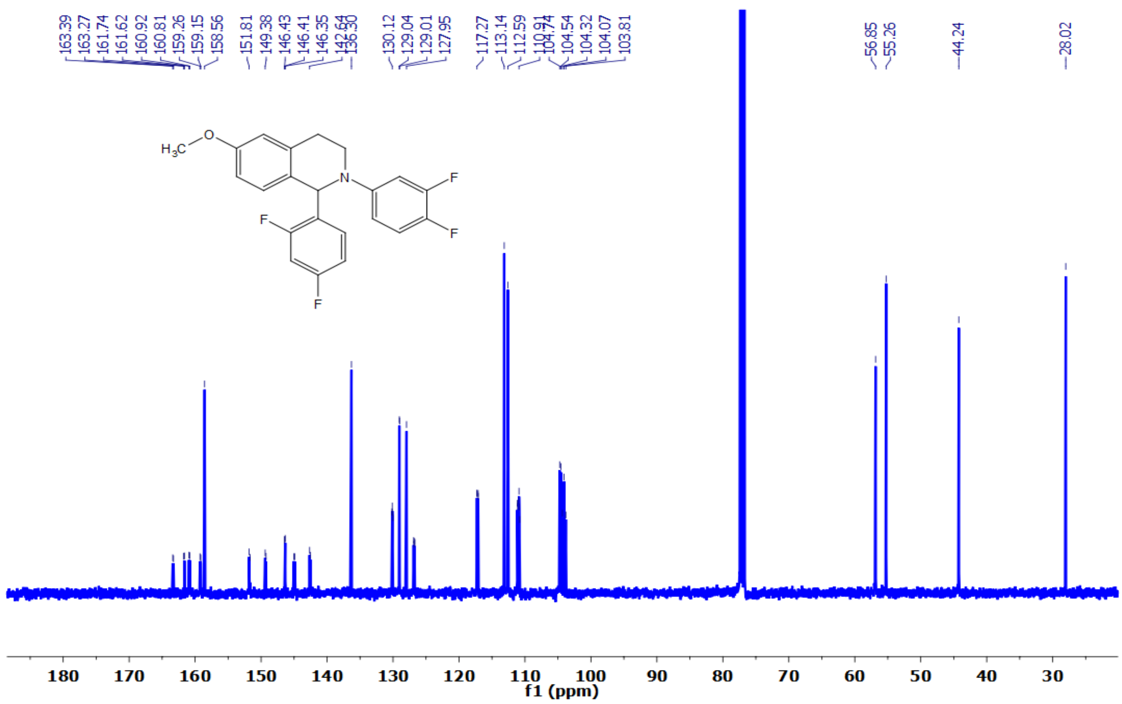


Figure S43(b): ^{13}**C spectra of 6-26, (125 MHz, $CDCl_3$): δ (ppm)** = 158.5802, 146.4449, 146.4252, 146.3662, 136.3172, 130.1887, 130.1313, 130.0943, 130.037, 129.0582, 129.023, 127.9664, 126.8855, 126.7477, 126.7109, 117.282, 117.2681, 117.1071, 117.093, 113.156, 112.5996, 111.1649, 111.1287, 110.9551, 110.9178, 110.8984, 110.8674, 110.8462, 110.8154, 104.7551, 104.5509, 104.3341, 104.0771, 103.8205, 56.8572, 55.2628, 44.2432, 28.0271.

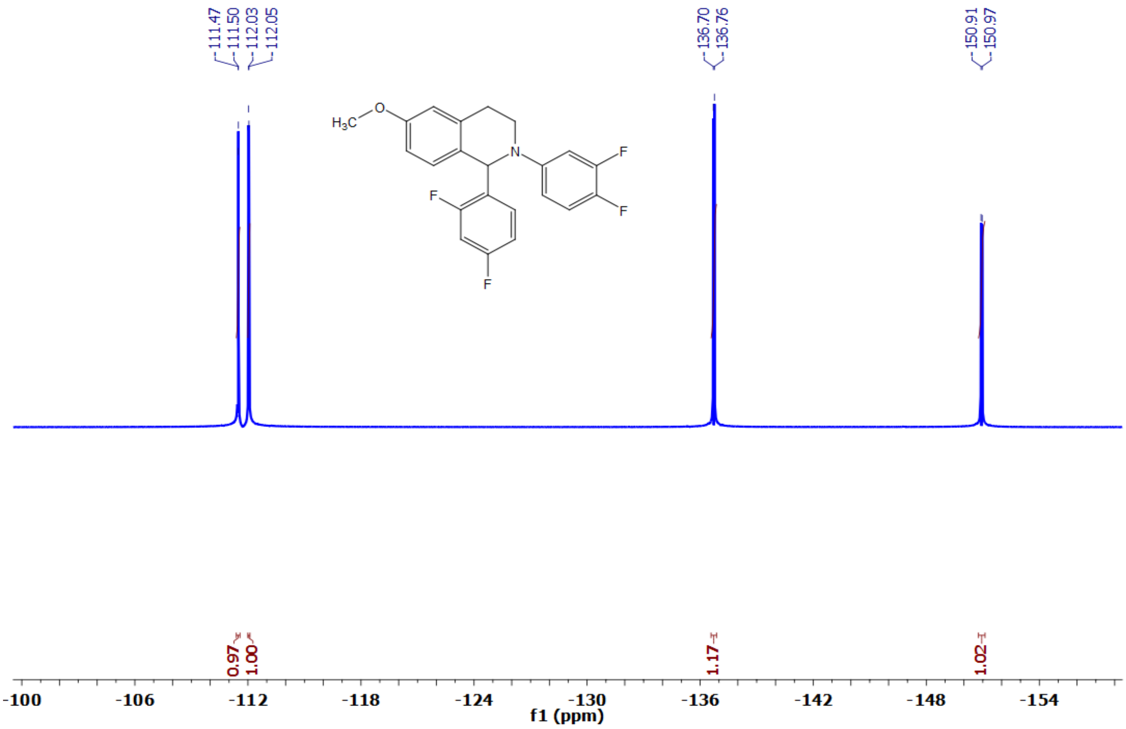


Figure S43(c): [19]**F- NMR Spectra of 6-26, (376 MHz, $CDCl_3$): δ (ppm)** = -150.94 (d, 1F), -136.73 (d, 1F), -112.04 (d, 1F), -118.48 (d, 1F).

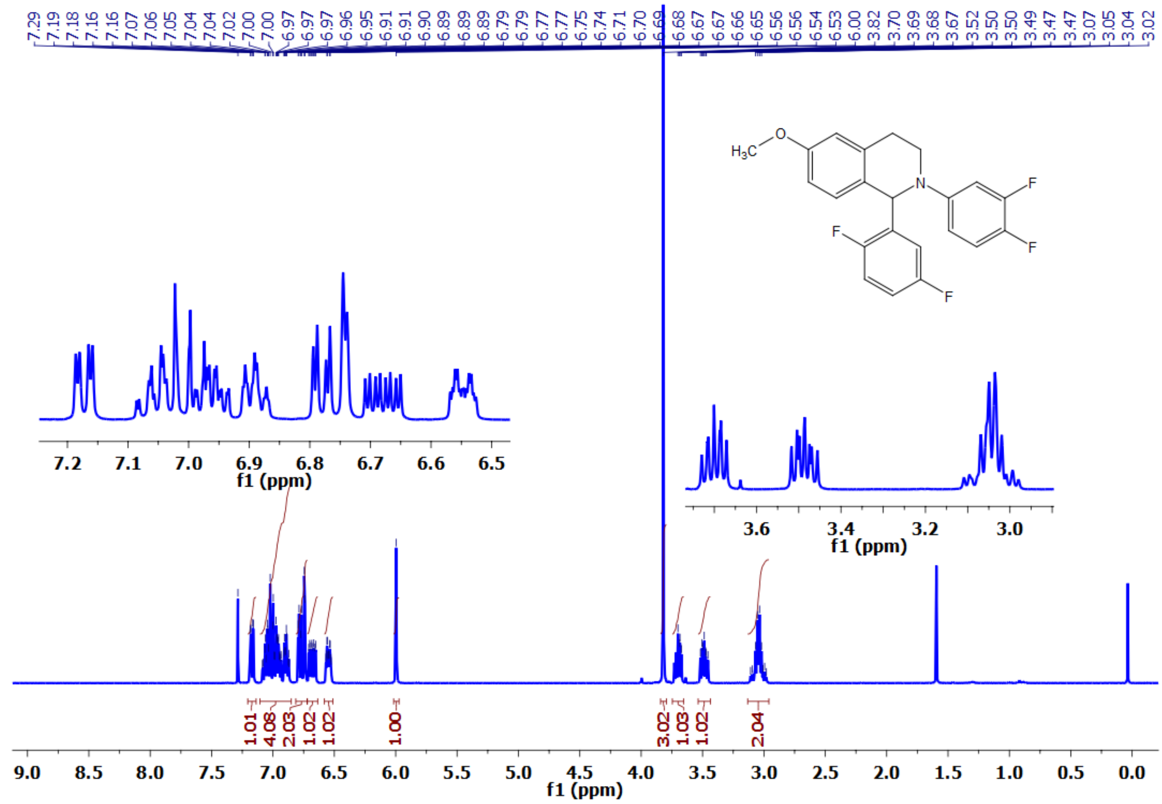


Figure S44(a): [1]**H - NMR Spectra of 6-27, (400 MHz, $CDCl_3$): δ (ppm)** = 2.98-3.11 (m, 2H), 3.46-3.52 (m, 1H), 3.67-3.70 (m, 1H), 3.82 (s, 3H), 6.00 (s, 1H), 6.53-6.57 (m, 1H), 6.65-6.71 (m, 1H), 6.77 (dt, 2H), 6.87-7.09 (m, 4H), 7.17 (dd, 1H)

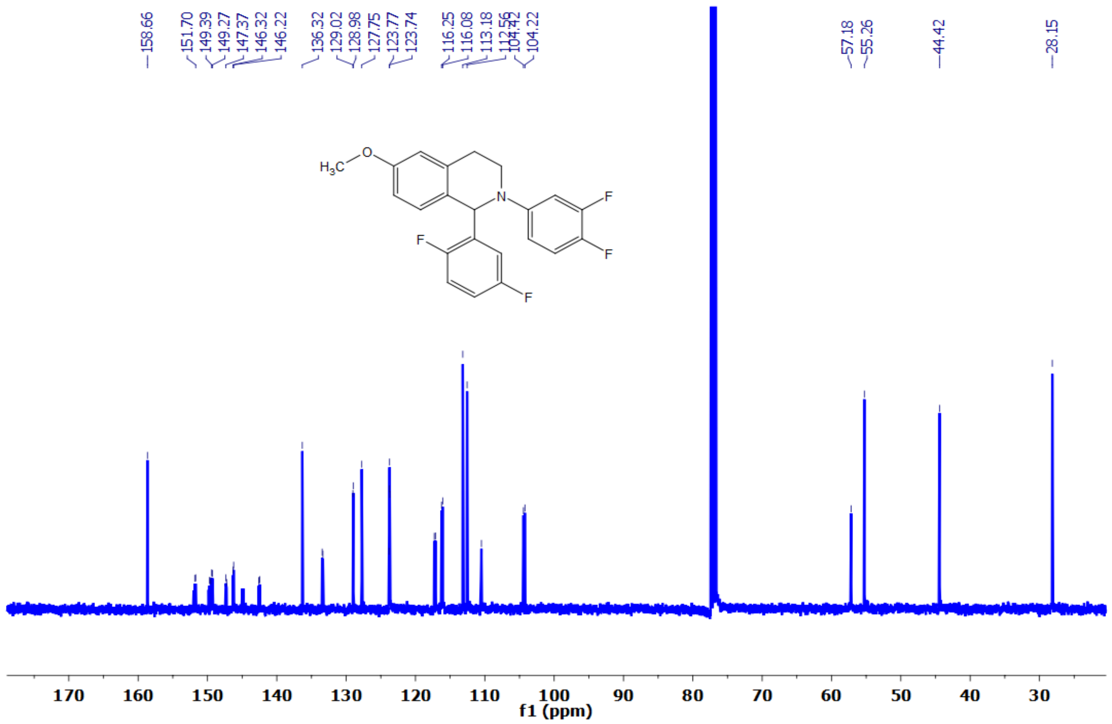


Figure S44(b): [13]**C spectra of 6-27, (125 MHz, $CDCl_3$): δ (ppm)** = 158.6814, 136.3416, 133.4769, 133.3734, 129.0355, 128.9949, 127.7655, 123.8263, 123.7798, 123.7535, 123.7171, 117.3231, 117.3064, 117.1461, 117.1311, 116.2612, 116.0896, 113.1919, 112.5718, 110.5599, 110.5301, 110.5053, 110.4778, 104.4368, 104.2319, 57.1856, 55.2684, 44.4251 , 28.16

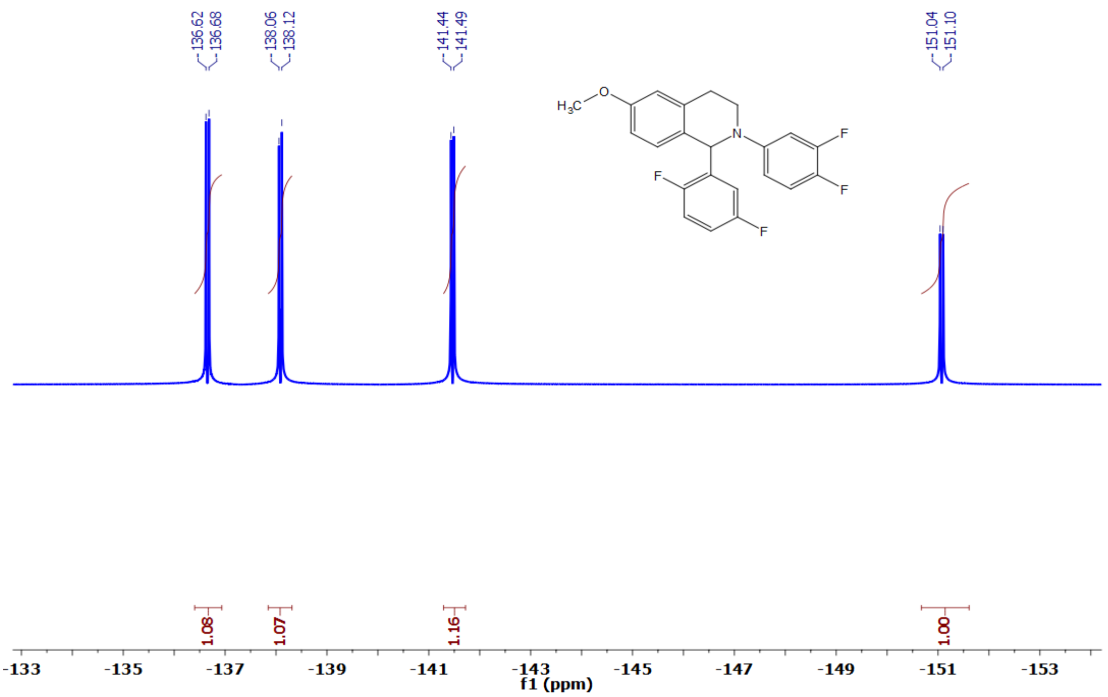


Figure S44(c): [19]**F- NMR Spectra of 6-27, (376 MHz, $CDCl_3$): δ (ppm)** = -151.07 (d, 1F), -141.46 (d, 1F), 138.09 (d, 1F), -136.65 (d, 1F).

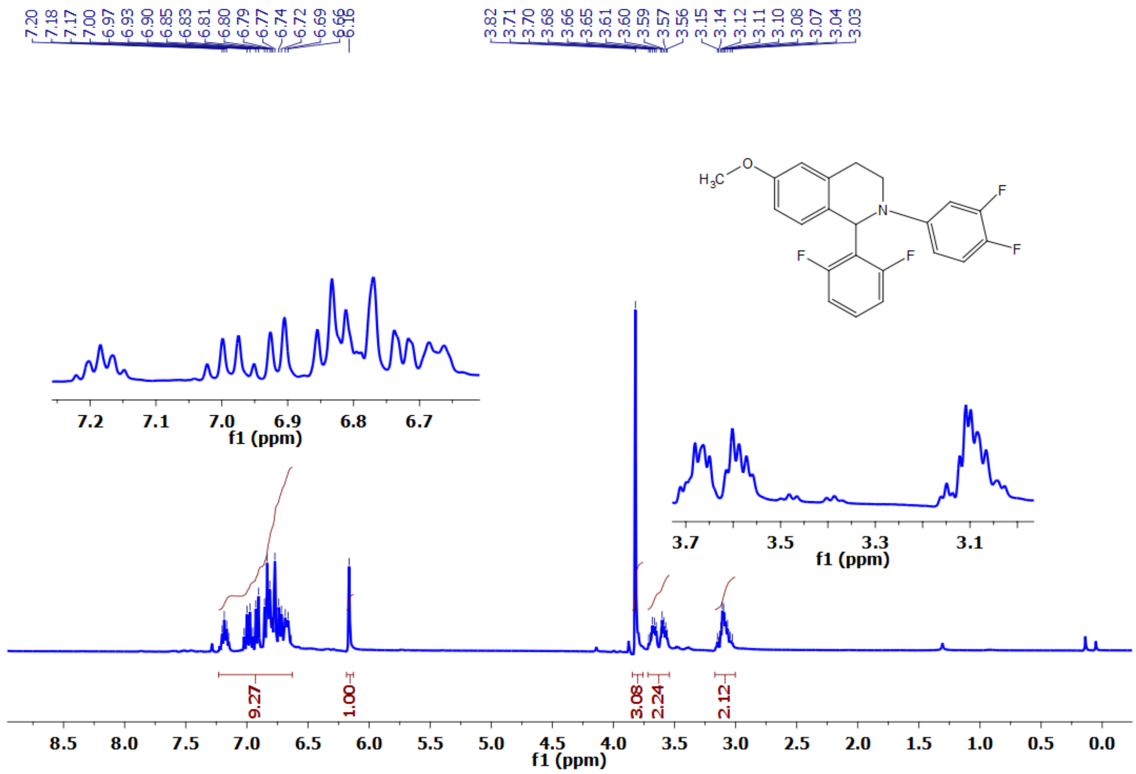


Figure S45(a): **^{1}H - NMR Spectra of 6-28, (400 MHz, $CDCl_3$): δ (ppm)** = 3.03-3.15 (m, 2H), 3.56-3.71 (m, 2H), 3.82 (s, 3H), 6.16 (s, 1H), 6.63-7.20 (m, 9H).

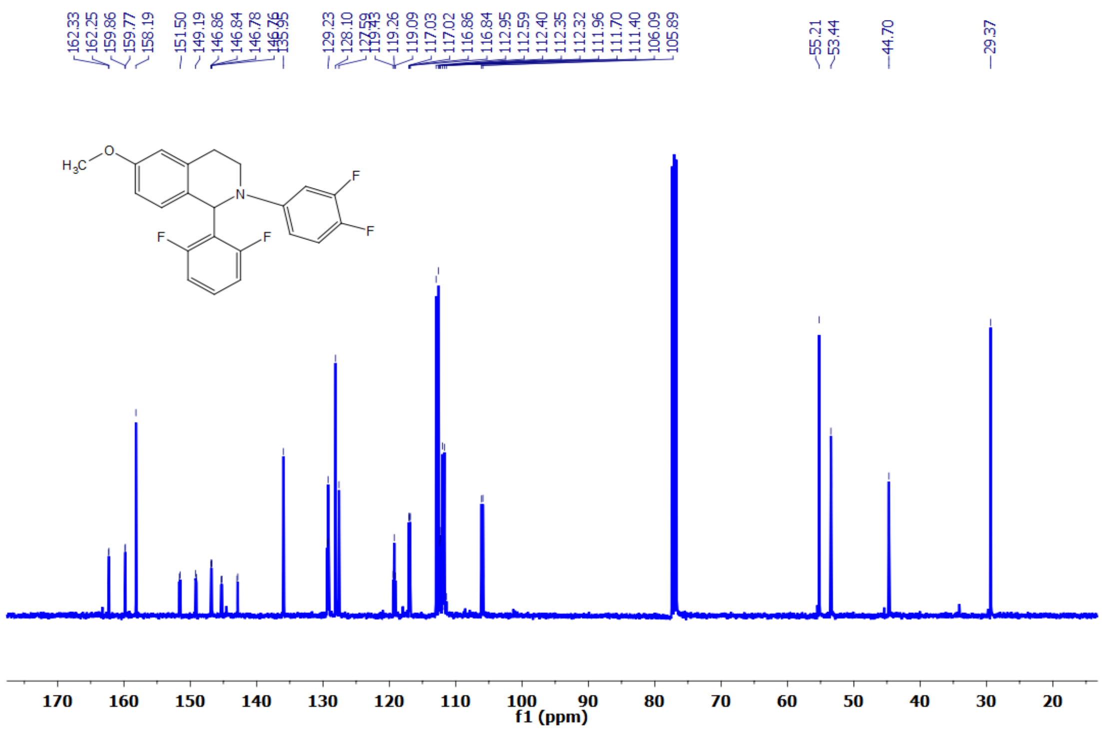


Figure S45(b): **^{13}C spectra of 6-28, (125 MHz, $CDCl_3$): δ (ppm)** = 162.3437, 162.2626, 159.8724, 159.7912, 158.2029, 146.7977, 146.7767, 135.9632, 129.3547, 129.2478, 129.1406, 128.1109, 127.6082, 119.2716, 117.046, 117.0296, 116.8713, 116.8549, 112.9604, 112.6009, 112.4105, 112.3807, 112.3597, 112.329, 111.9758, 111.955, 111.7336, 111.7105, 106.1064, 105.9075, 55.2136, 53.4525, 44.7341, 44.7082, 44.6833, 29.3771.

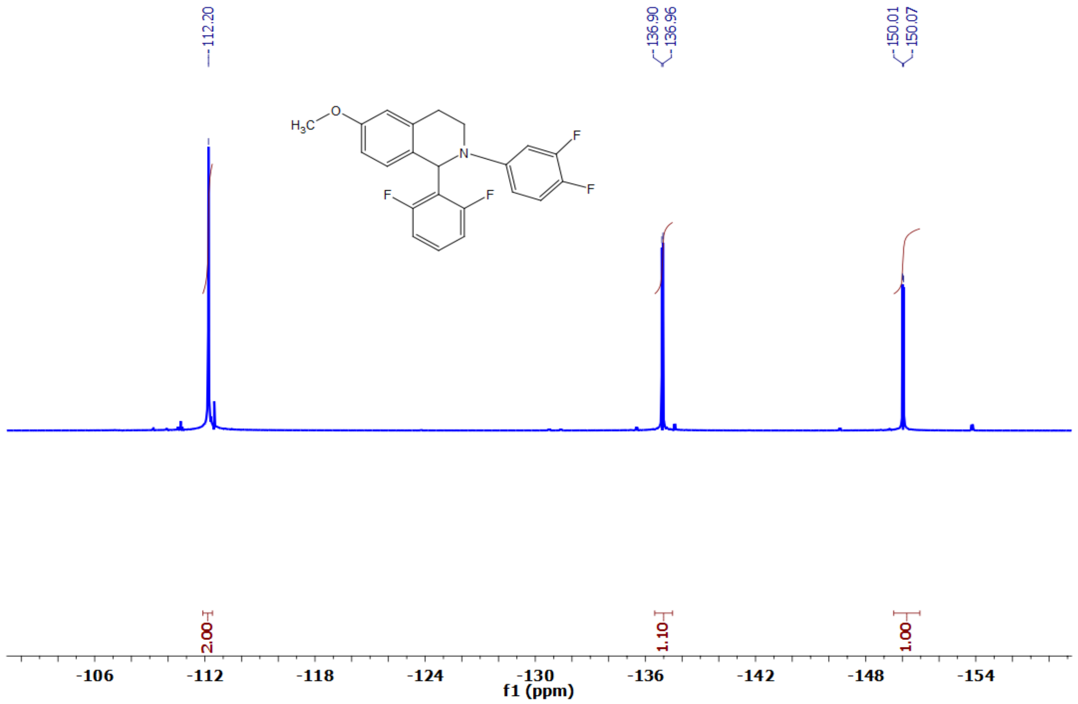


Figure S45(c): **[19]F- NMR Spectra of 6-28, (376 MHz, $CDCl_3$): δ (ppm)** = -150.04 (d, 1F), -136.93 (d, 1F), -112.20 (s, 2F).

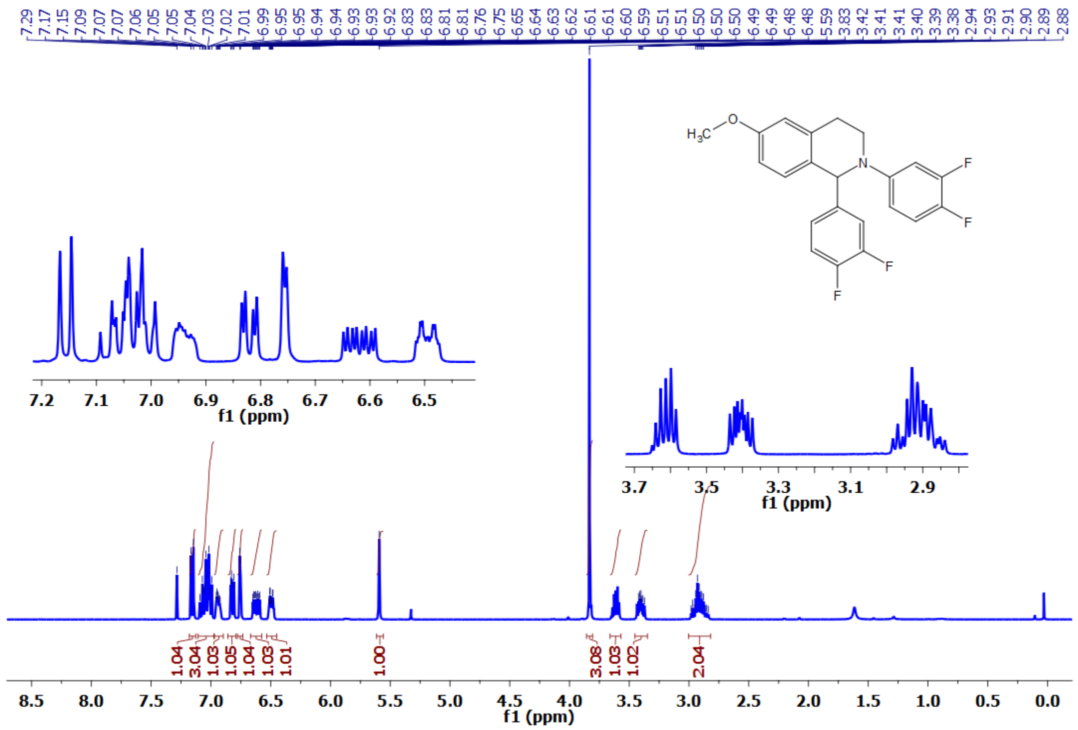


Figure S46(a): **[1]H - NMR Spectra of 6-29, (400 MHz, $CDCl_3$): δ (ppm)** = 2.84-2.98 (m, 2H), 3.37-3.42 (m, 1H), 3.58-3.65 (m, 1H), 3.83 (s, 3H), 5.59 (s, 1H), 6.48-6.52 (m, 1H), 6.59-6.65 (m, 1H), 6.76 (d, 1H), 6.82 (dd, 1H), 6.92-6.95 (m, 1H), 6.99-7.09 (m, 3H), 7.16 (d, 1H).

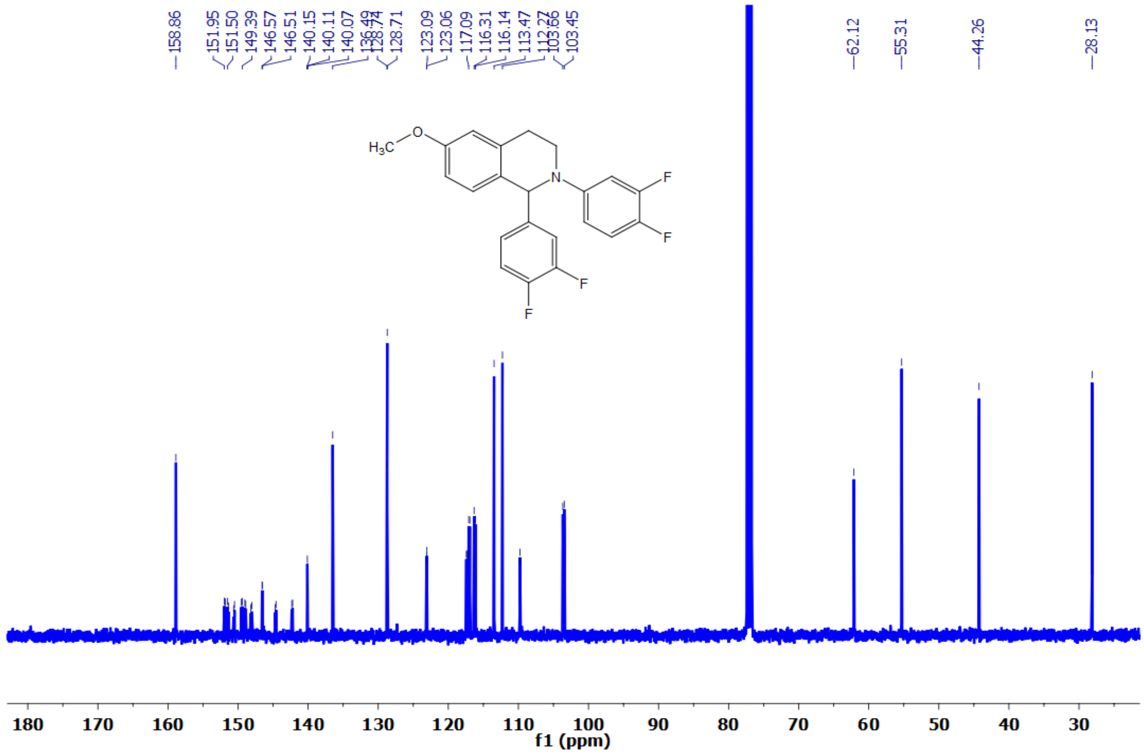


Figure S46(b): **[13]C spectra of 6-29, (125 MHz, $CDCl_3$): δ (ppm)** = 158.8831, 146.6052, 146.5863, 146.5258, 140.1245, 140.0875, 136.5095, 128.7564, 128.7289, 123.1362, 123.1026 , 123.0754, 123.0409, 117.46, 117.4417, 117.2833, 117.2667, 117.1077, 116.9363, 116.3283, 116.1507, 113.481 1, 12.2844, 109.8031, 109.773, 109.7502, 109.7201, 103.6689, 103.4633, 62.125, 55.3132, 44.2708, 28.1371.

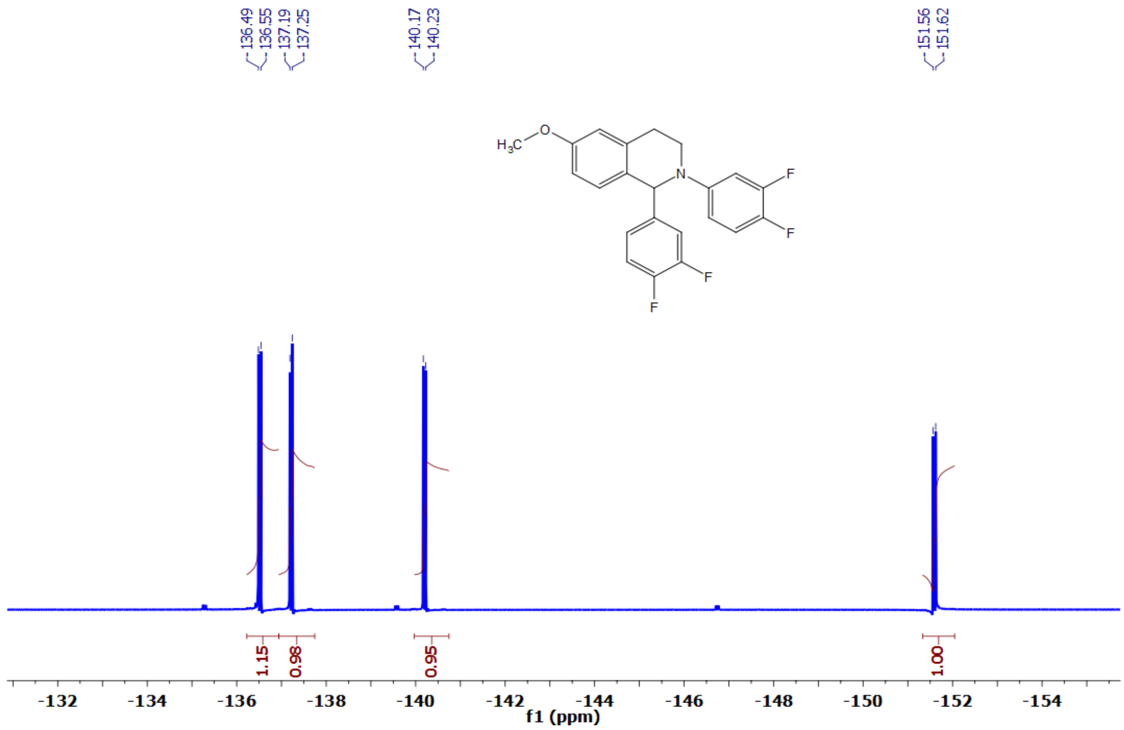


Figure S46(c): **[19]F- NMR Spectra of 6-29, (376 MHz, $CDCl_3$): δ (ppm)** = -151.59 (d, 1F), -140.20 (d, 1F), -137.22 (d, 1F), -136.52 (d, 1F),

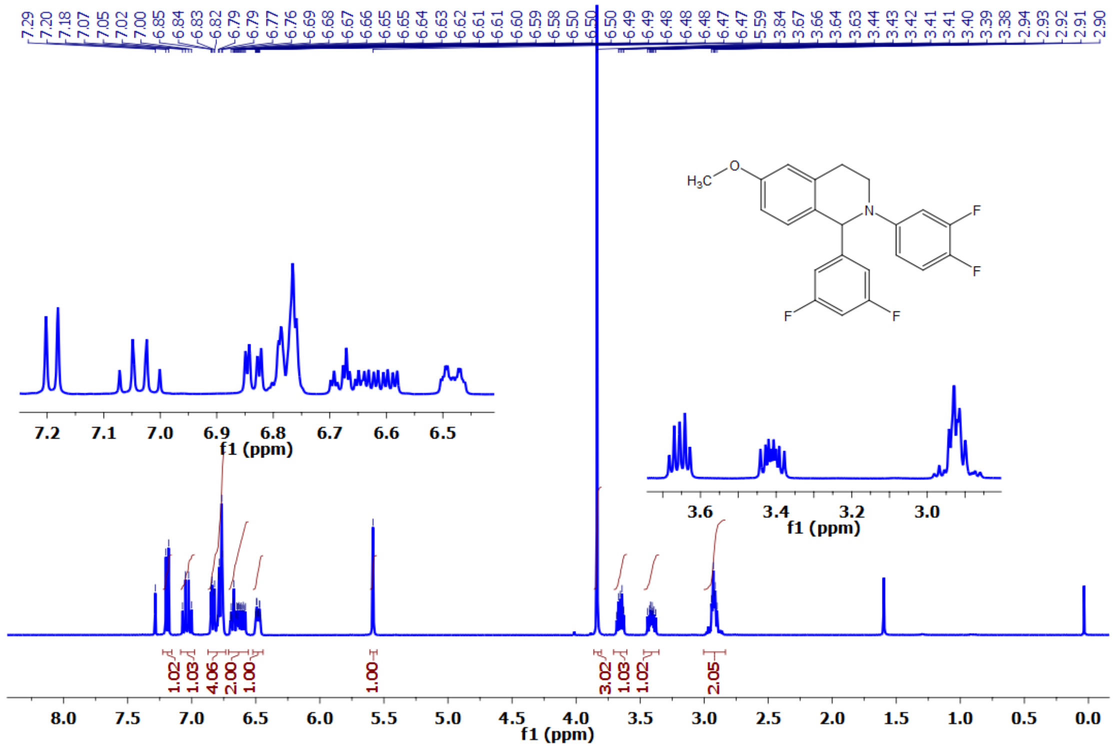


Figure S47(a): ^{1}H - NMR Spectra of 6-30, (400 MHz, $CDCl_3$): δ (ppm) = 2.90-2.94 (m, 2H), 3.38-3.44 (m, 1H), 3.63-3.68 (m, 1H), 3.84 (s, 3H), 5.59 (s, 1H), 6.46-6.50 (m, 1H), 6.58-6.70 (m, 2H), 6.56- 6.58 (m, 4H), 7.04 (q, 1H), 7.19 (d, 1H).

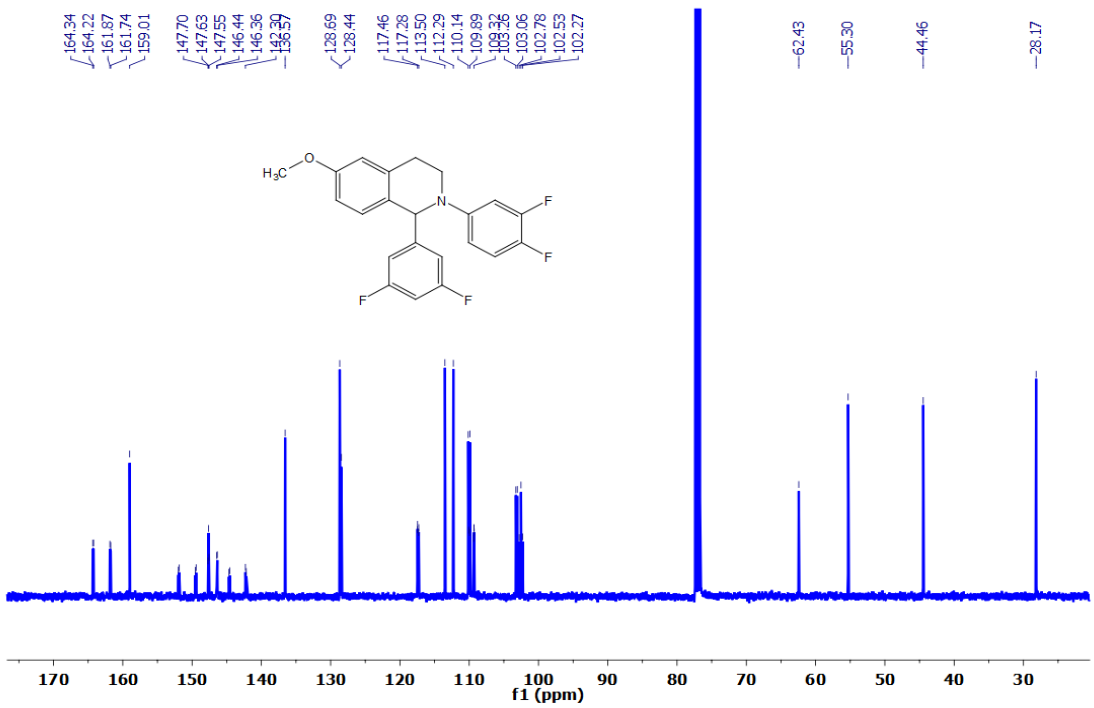


Figure S47(b): ^{13}C spectra of 6-30, (125 MHz, $CDCl_3$): δ (ppm) = 164.3574, 164.2325, 161.8837, 161.7593, 159.025, 147.7171, 147.6439, 147.5705, 146.4541, 146.4349, 146.3741, 146.3551, 136.5832, 128.7009, 128.4526, 117.4866, 117.4715, 117.3113, 117.2953, 113.5187, 112.3013, 110.153, 110.086, 109.9686, 109.8986, 109.3665, 109.3365, 109.3141, 109.2852, 103.276, 103.067, 102.7925, 102.539, 102.2847, 62.4372, 62.4193, 55.3092, 44.4723, 28.173

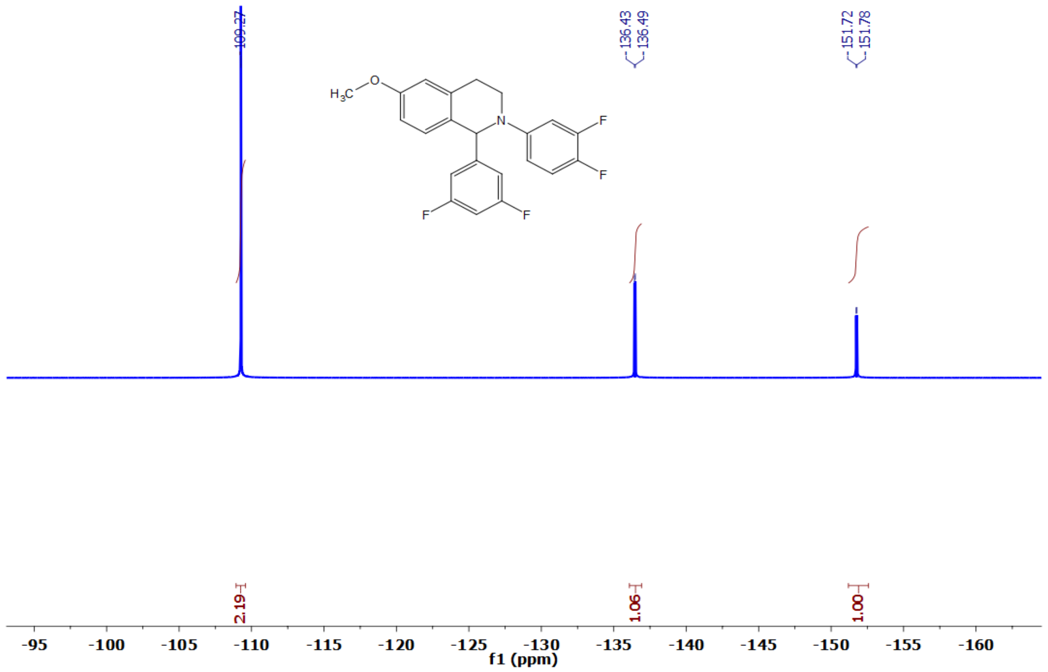


Figure S47(c): **[19]F- NMR Spectra of 6-30, (376 MHz, $CDCl_3$): δ (ppm)** = -151.75 (d, 1F), -136.46 (d, 1F), -109.27 (s, 2F).

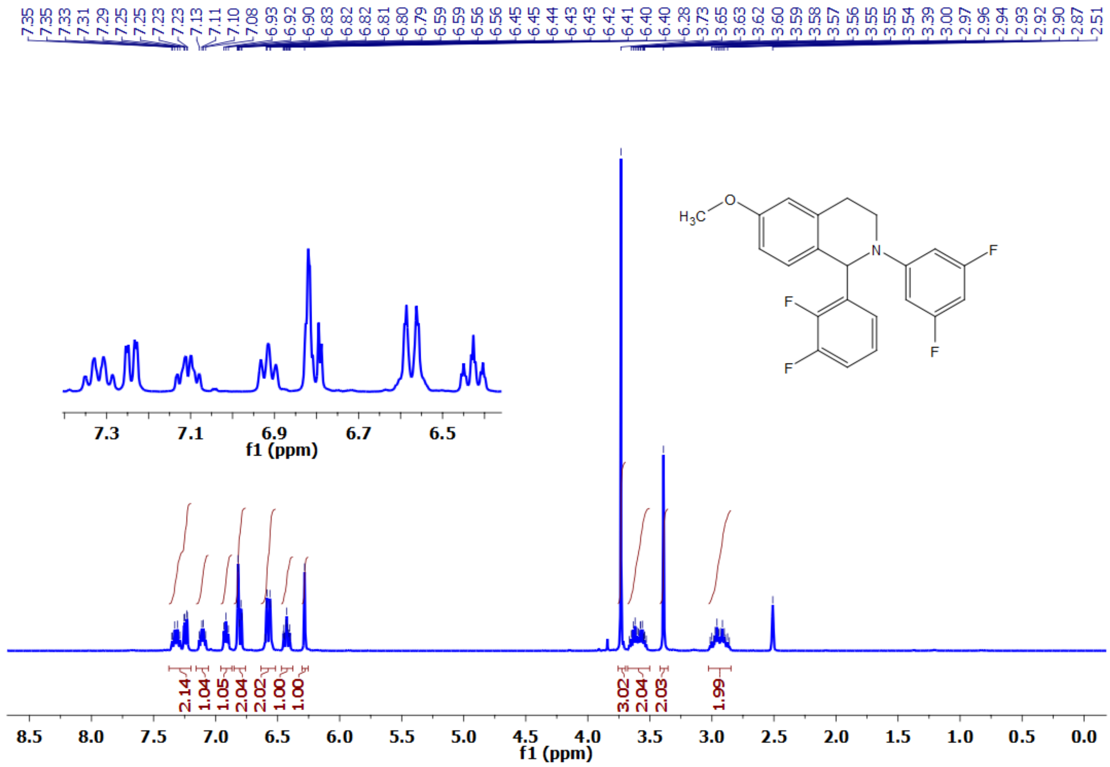


Figure S48(a): **[1]H - NMR Spectra of 6-31, (400 MHz, DMSO-d6): δ (ppm)** = 2.86-3.01 (m, 2H), 3.53-3.66 (m, 2H), 3.73 (s, 3H), 6.28 (s, 1H), 6.40-6.45 (m, 1H), 6.56-6.60 (m, 2H), 6.79-6.83 (m, 2H), 6.92 (t, 1H), 7.10 (q, 1H), 7.23-7.35 (m, 2H).

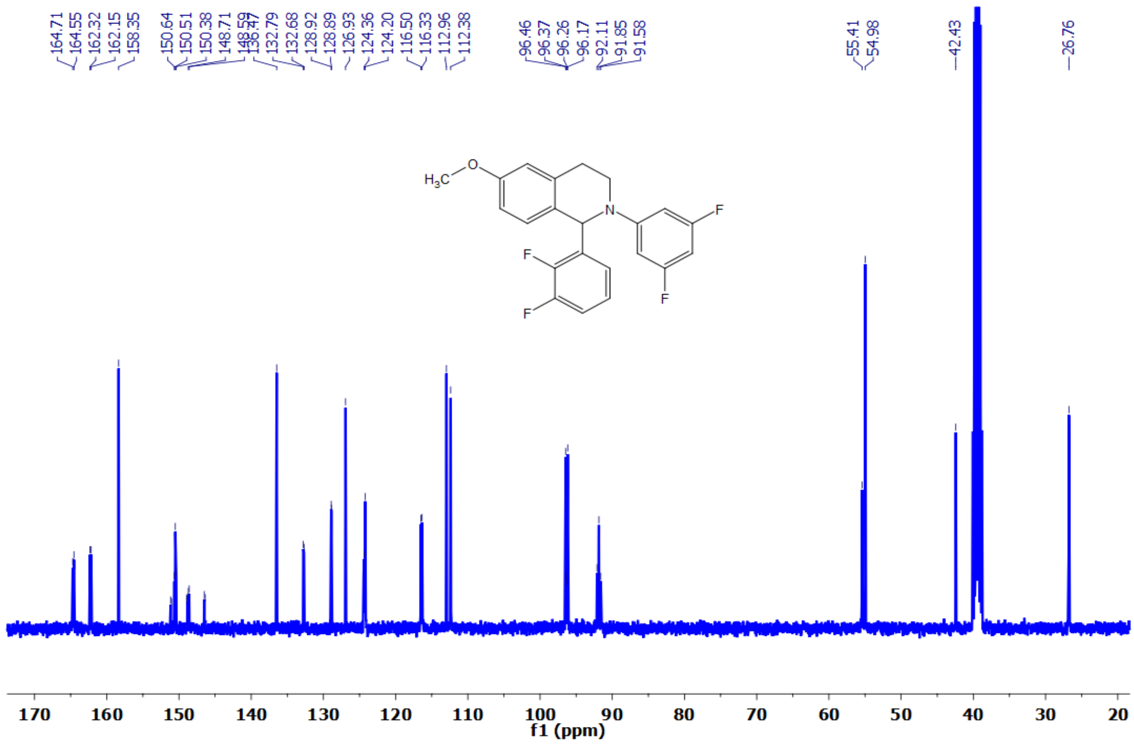


Figure S48(b): **^{13}C spectra of 6-31, (125 MHz, DMSO-d6): δ (ppm)** = 164.7146 , 164.5478, 162.3195, 162.1536, 158.3529, 150.5099, 136.4728, 132.7877, 132.6856, 128.9225, 128.889 , 126.93, 124.3856, 124.3653, 124.2316, 124.2053, 116.4997, 116.3309, 112.9622, 112.3773, 96.4629, 96.1715, 91.849, 55.4093, 55.4004, 54.9821, 42.4312, 26.7673.

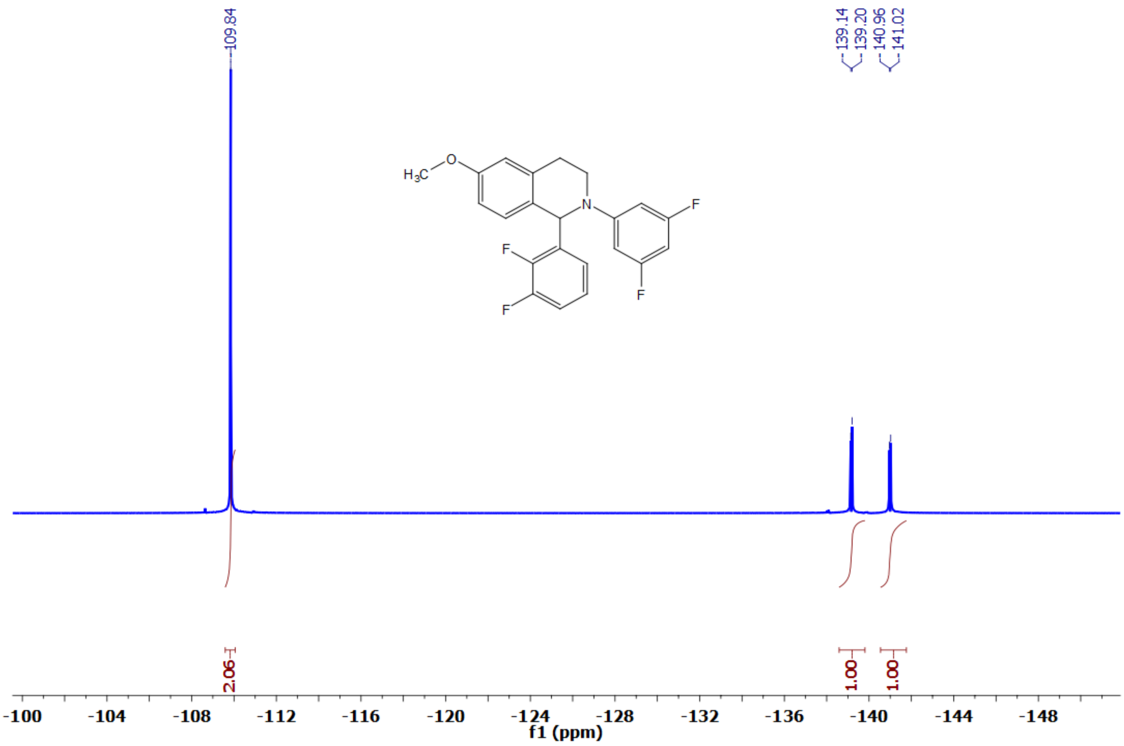


Figure S48(c): **^{19}F- NMR Spectra of 6-31, (376 MHz, DMSO-d6): δ (ppm)** = -140.99 (d, 1F), -139.17 (d, 1F), -109.84 (s, 2F)

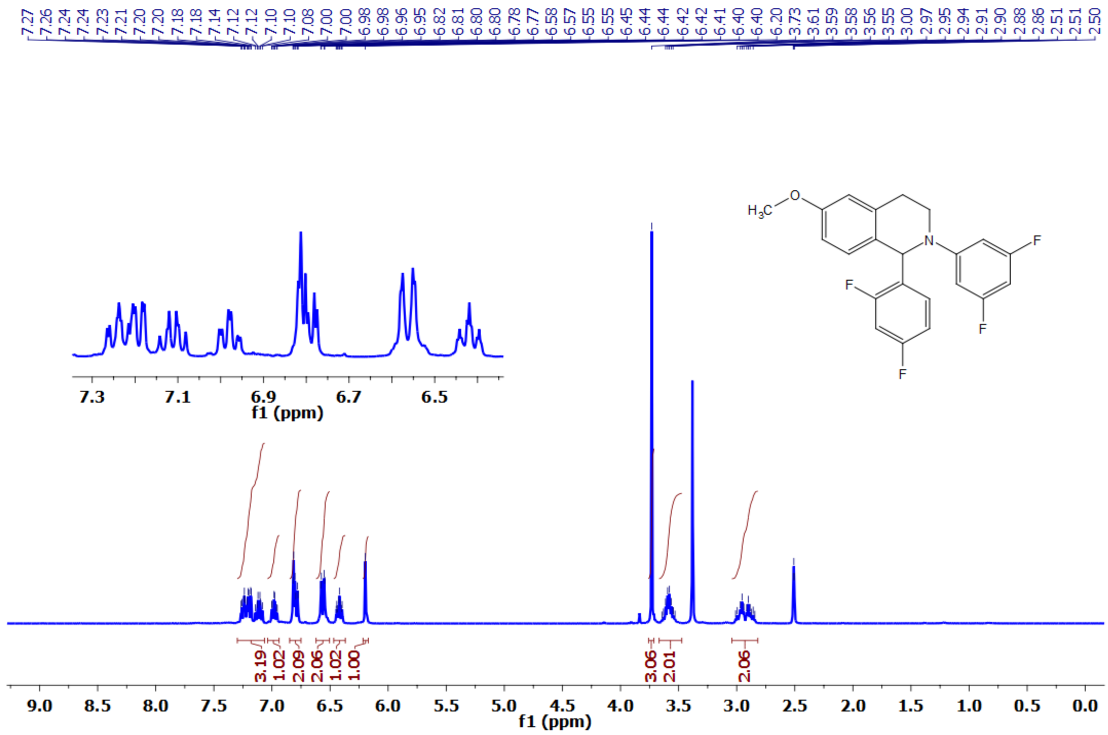


Figure S49(a): **^{1}H - NMR Spectra of 6-32, (400 MHz, DMSO-d6): δ (ppm)** = 2.84-3.01 (m, 2H), 3.53-3.64 (m, 2H), 3.73 (s, H), 6.20 (s, 1H), 6.40-6.45 (m, 1H), 6.55-6.59 (m, 1H), 6.77-6.82 (m, 2H), 6.95-7.00 (dt, 1H), 7.08-7.14 (m, 1H), 7.18-7.27 (m, 2H).

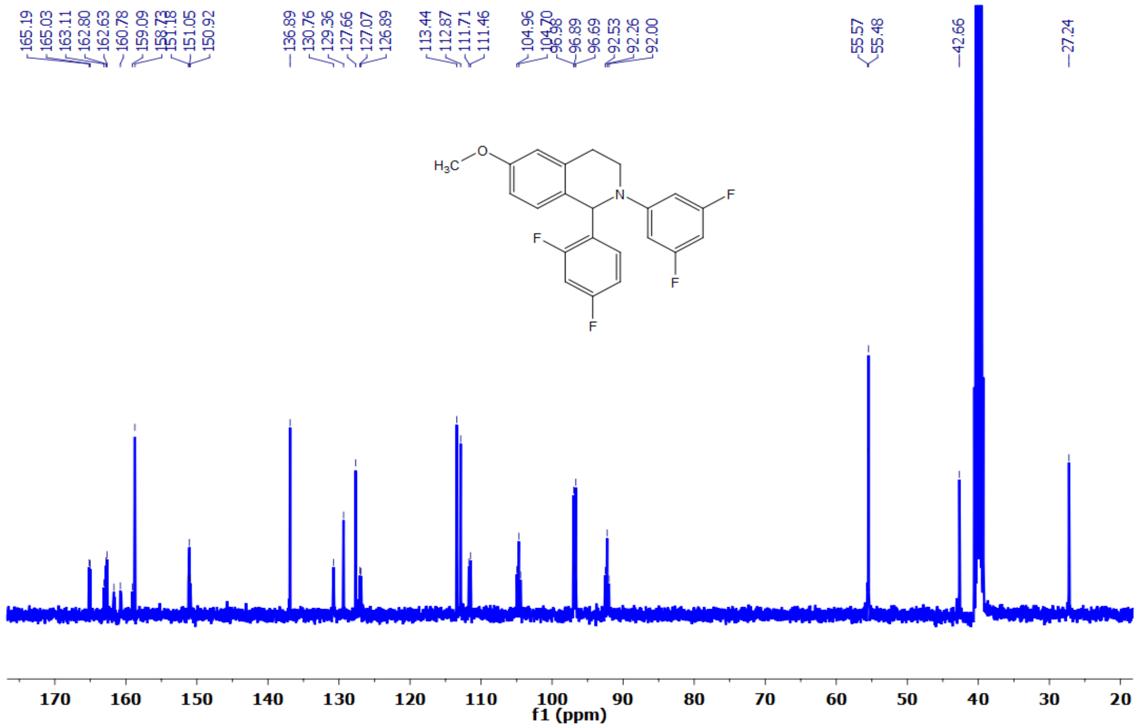


Figure S49(b): **^{13}C spectra of 6-32, (125 MHz, DMSO-d6): δ (ppm)** = 165.2087 , 165.0428, 162.8168, 162.6493, 158.7474, 151.0669, 136.904, 130.8718, 130.8182, 130.7756, 130.7202 , 129.4015, 129.3717, 127.6721, 127.0803, 126.9058, 113.4485, 112.8827, 111.7181, 111.6838 , 111.5107, 111.4771, 104.968, 104.7077, 104.4486, 96.9891, 96.9013, 96.6976, 92.5373, 92.272, 55.5755, 55.4843, 42.6691, 27.2432

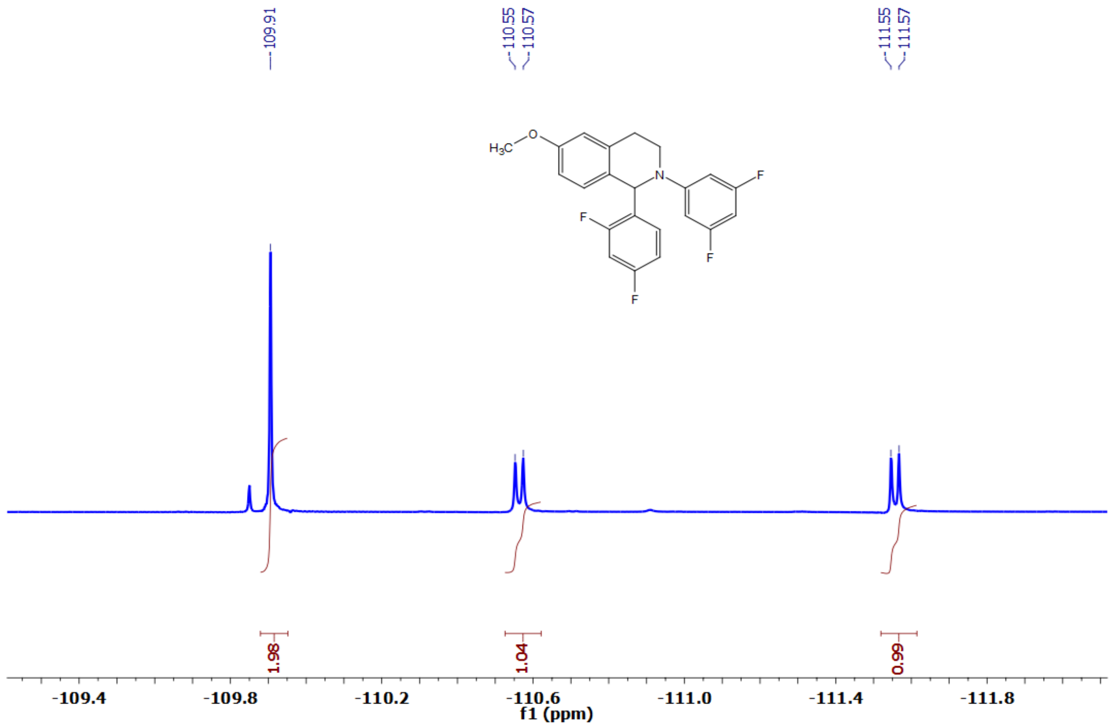


Figure S49(c): **^{19}F- NMR Spectra of 6-32, (376 MHz, DMSO-d6): δ (ppm)** = -111.56 (d, 1F), -110.56 (d, 1F), -109.91 (s, 2F).

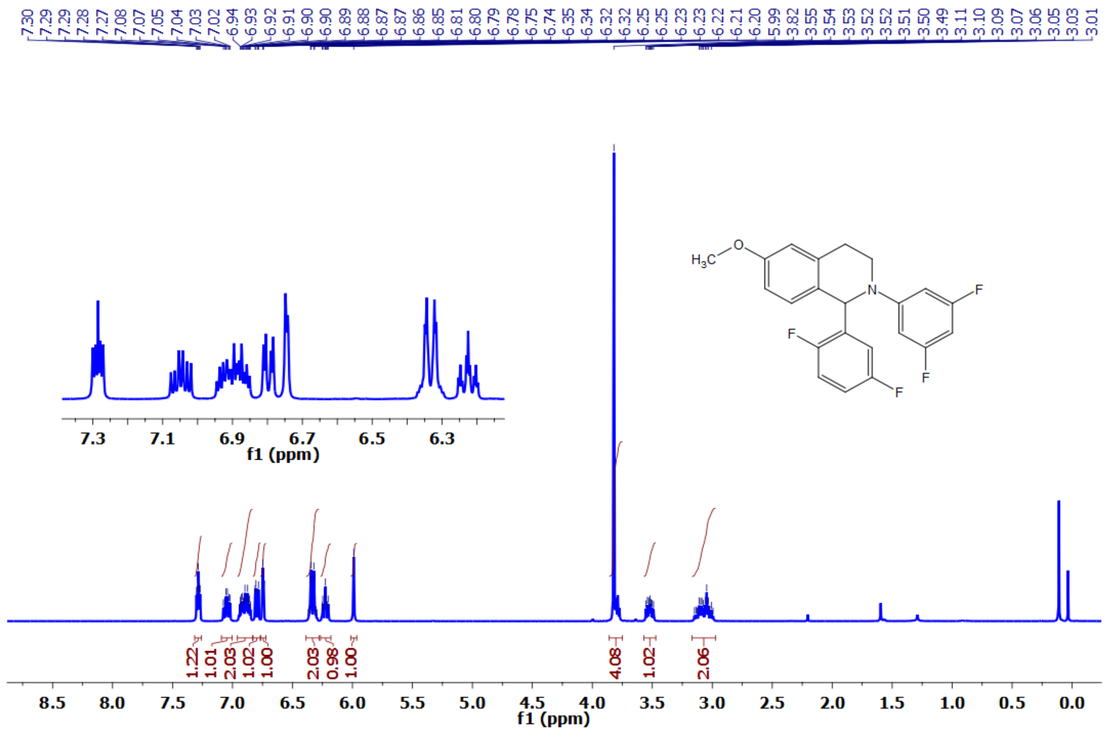


Figure S50(a): **^{1}H - NMR Spectra of 6-33, (400 MHz, $CDCl_3$): δ (ppm)** = 2.99-3.15 (m, 2H), 3.49-3.55 (m, 1H), 3.77-3.80 (m, 1H), 3.82 (s, 3H), 5.99 (s, 1H), 6.23 (tt, 1H), 6.62-6.35 (m, 2H), 6.75 (d, 1H), 6.79 (dd, 1H), 6.85-6.94 (m, 2H), 7.02-7.08 (m, 1H), 7.27-7.30 (m, 1H).

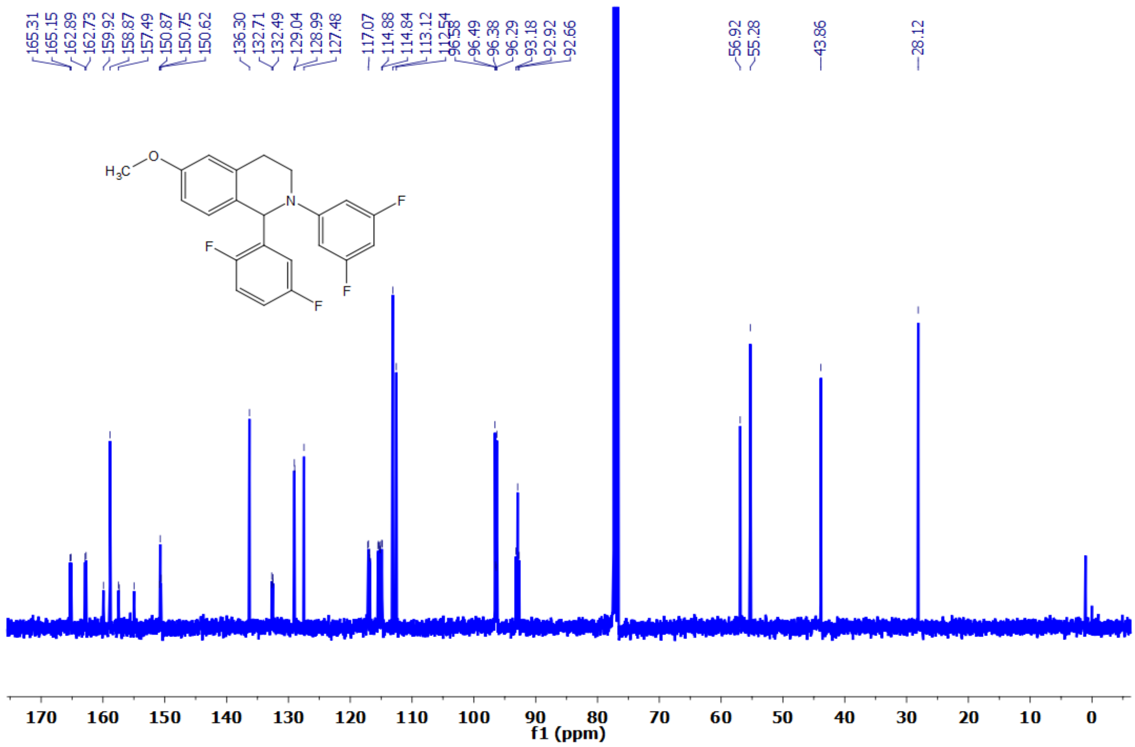


Figure S50(b): ^{13}**C spectra of 6-33, (125 MHz, DMSO-d6): δ (ppm)** = 165.3256, 165.1646, 162.9052, 162.7444, 158.8852, 150.7624, 150.633, 136.3202, 132.7242, 132.5013, 129.0524, 127.4921, 117.1645, 117.0795, 116.9118, 116.829, 115.5337, 115.4467, 115.293, 115.2057, 115.1417, 115.0983, 114.892, 114.8484, 113.1372, 112.5532, 96.5914, 96.503, 96.3873, 96.2991, 93.1865, 92.9271, 92.6672, 56.9223, 55.2908, 43.8646, 28.1254

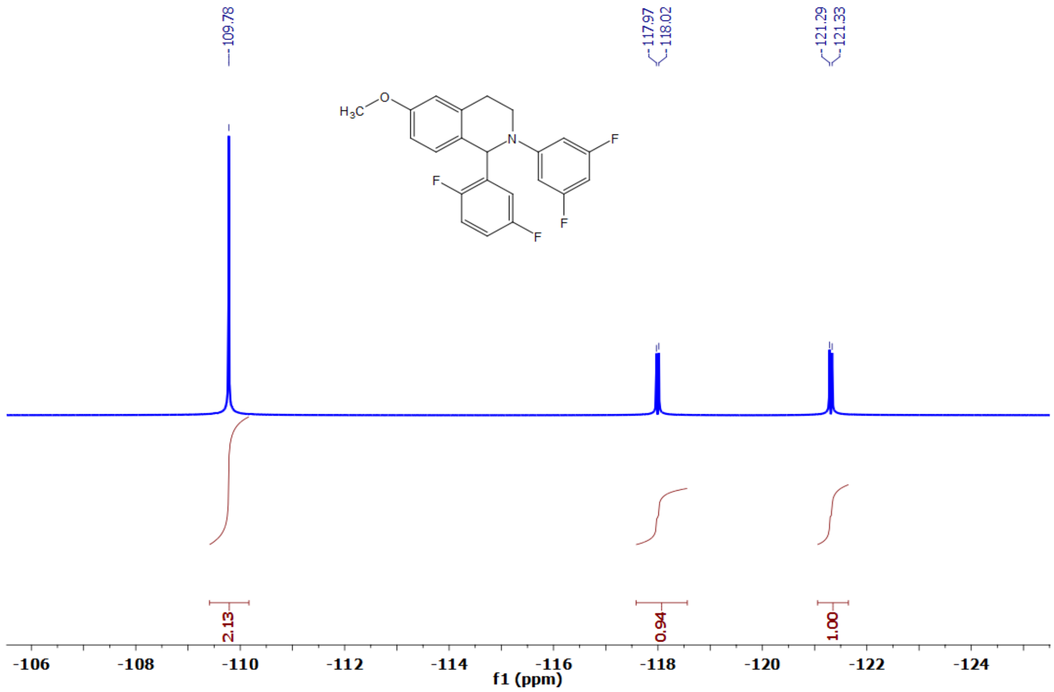


Figure S50(c): ^{19}**F- NMR Spectra of 6-33, (376 MHz, $CDCl_3$): δ (ppm)** = -121.31 (d, 1F), -117.99 (d, 1F), -109.78 (s, 2F).

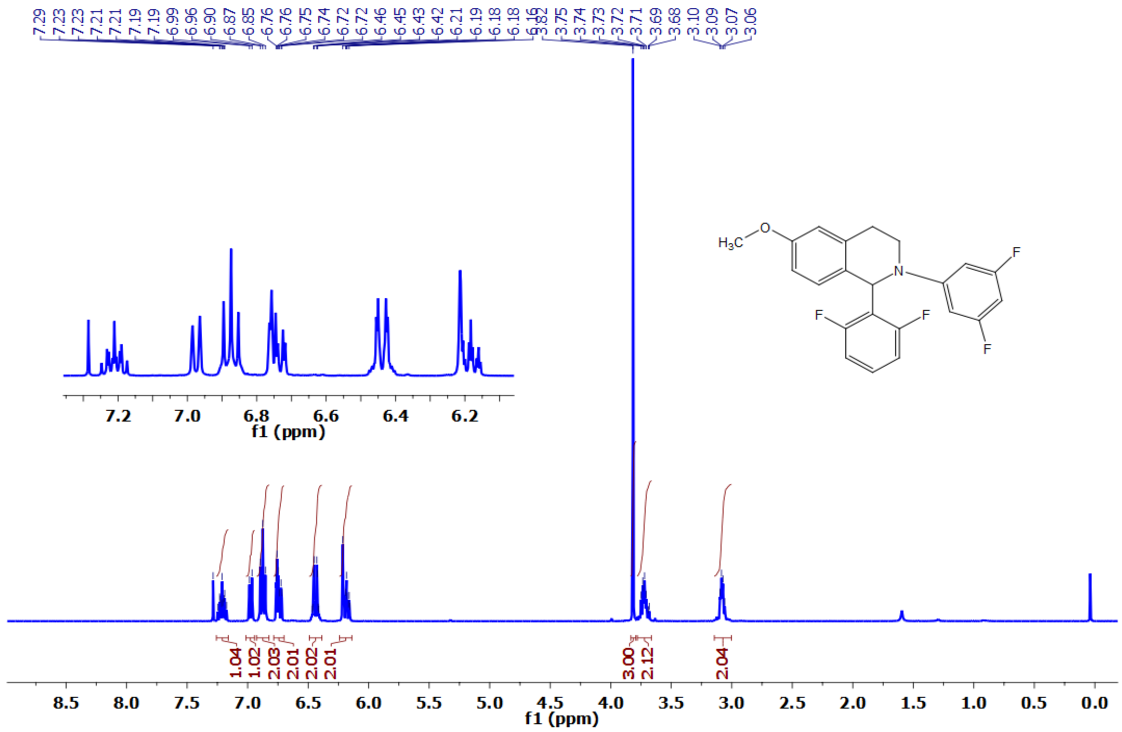


Figure S51(a): **^{1}H - NMR Spectra of 6-34, (400 MHz, $CDCl_3$): δ (ppm)** = 3.06-3.10 (m, 2H), 3.68-3.75 (m, 2H), 3.82 (s, 3H), 6.21 (s, 1H), 6.16-6.19 (m, 1H), 6.41-6.47 (m, 2H), 6.72-6.76 (m, 2H), 6.87 (t, 2H), 6.97 (d, 1H), 7.17-7.25 (m, 1H).

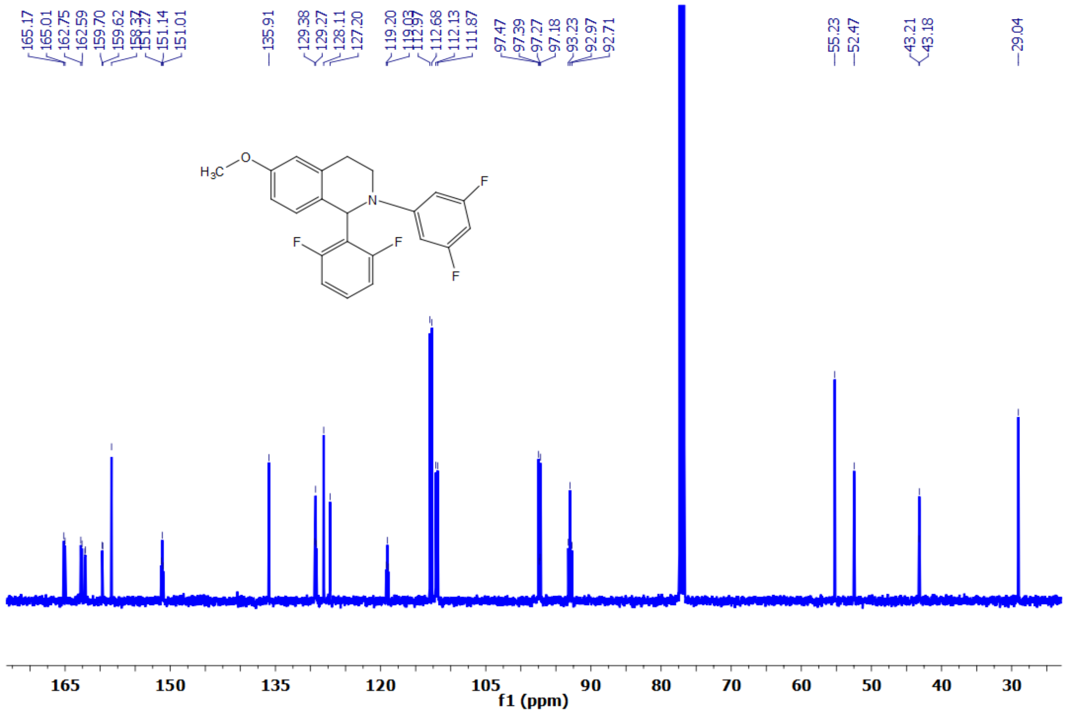


Figure S51(b): **^{13}C spectra of 6-34, (125 MHz, DMSO-d6): δ (ppm)** = 165.1872, 165.0265, 162.7717, 162.6095, 162.1865, 162.1043, 159.7177, 159.6367, 158.3852, 151.1537, 135.9268, 129.39, 129.2834, 129.1749, 128.1255, 127.2164, 119.0477, 112.9806, 112.6969, 112.1487, 111.8814, 97.4845, 97.2825, 97.1947, 93.2452, 92.9853, 92.7248, 55.2418, 52.4782, 43.2195, 43.1858, 43.1514, 29.0501

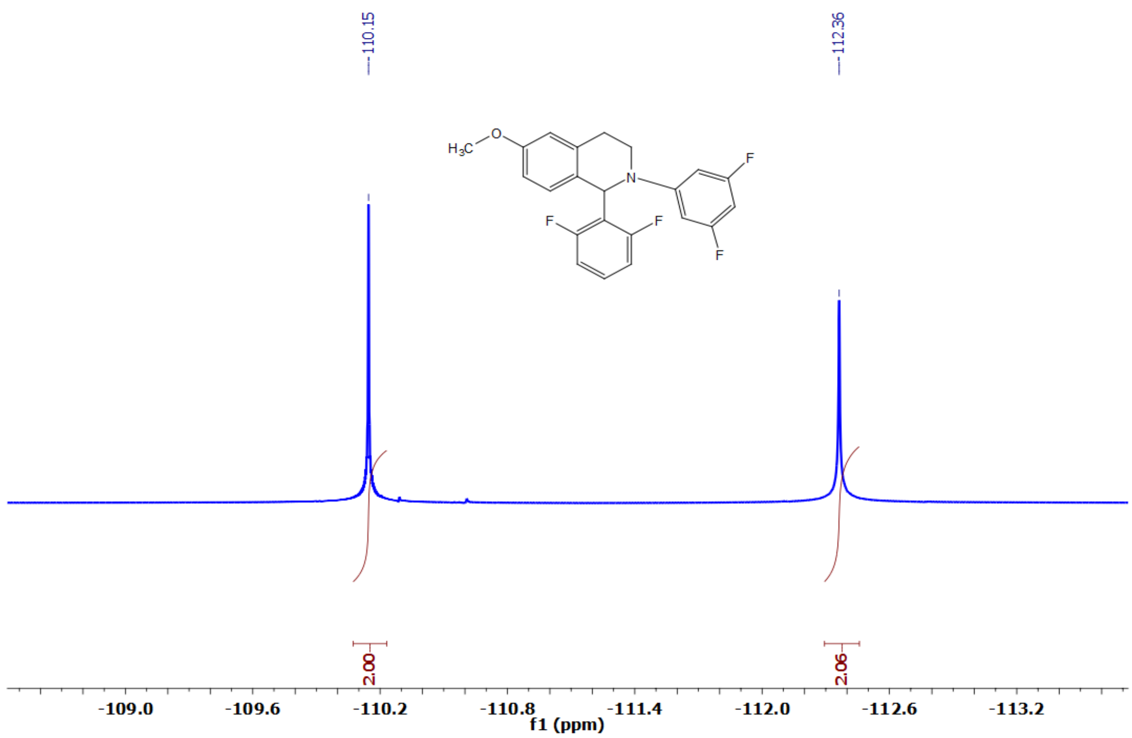


Figure S51(c): **[19]F- NMR Spectra of 6-34, (376 MHz, $CDCl_3$): δ (ppm)** = -112.36 (s, 2F), -110.15 (s, 2F).

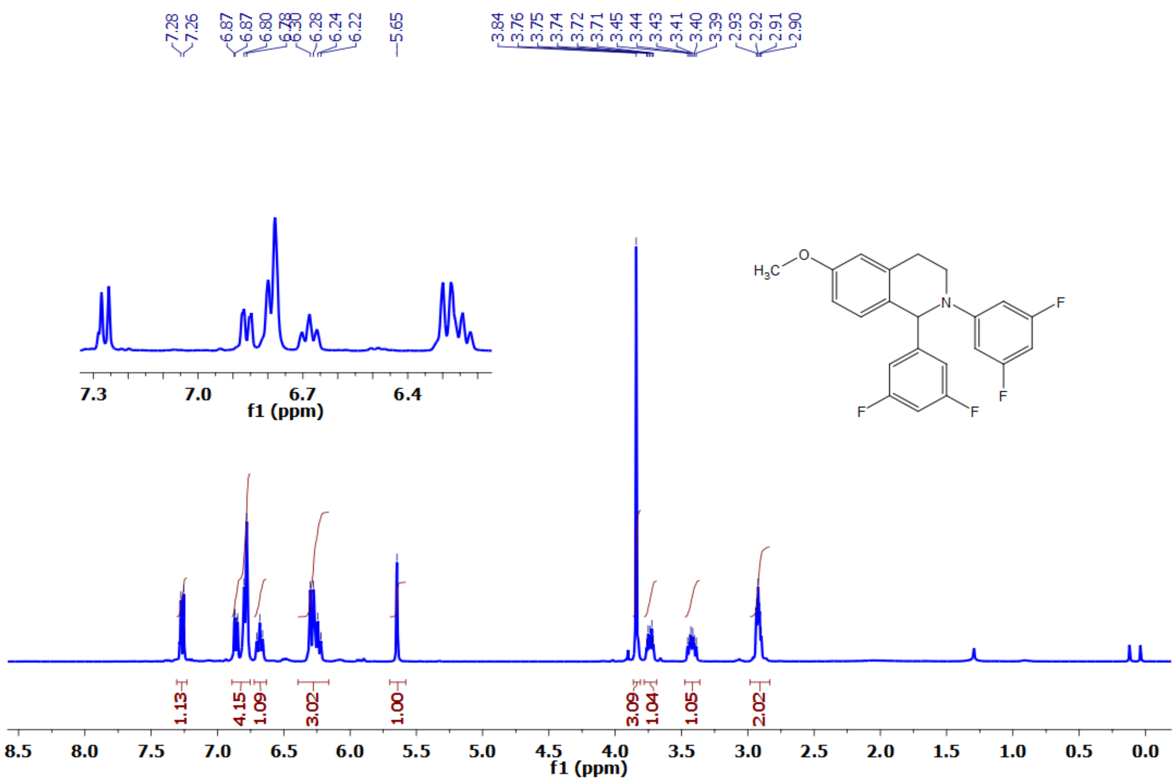


Figure S52(a): **[1]H - NMR Spectra of 6-36, (400 MHz, $CDCl_3$): δ (ppm)** = 2.90-2.93 (m, 2H), 3.39-3.45 (m, 1H), 3.71-3.76 (m, 1H), 3.84 (s, 3H), 5.65 (s, 1H), 6.22-6.30 (m, 3H), 6.68 (t, 1H), 6.78-6.87 (m, 4H), 7.27 (d, 1H).

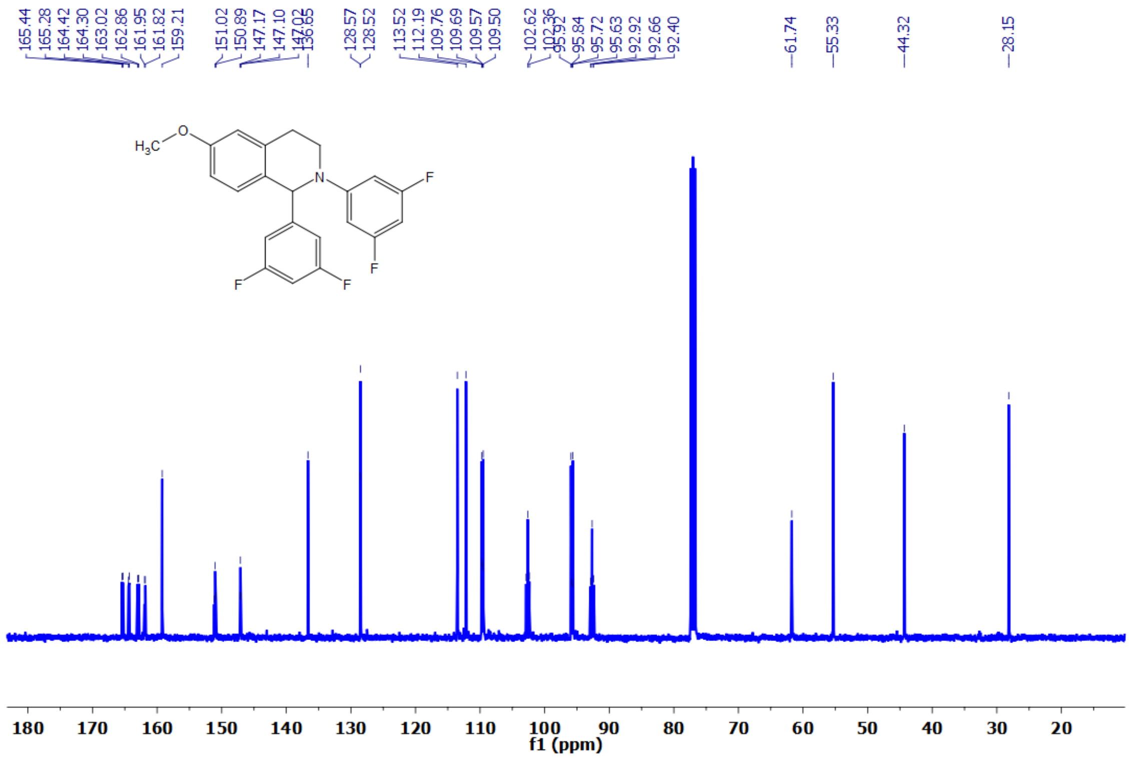


Figure S52(b): **^{13}C spectra of 6-36, (125 MHz, DMSO-d6): δ (ppm)** = 165.298, 162.8765 , 161.9638, 159.2273, 151.0408, 147.1139, 136.6639, 128.584, 128.5358, 113.535, 112.2048, 109.7739, 109.7059, 109.5887, 109.5183, 102.8849, 102.6322, 102.3788, 95.9364, 95.6433, 92.9302, 92.6685, 61.7647, 61.7477, 55.3365, 44.3314, 28.1614.

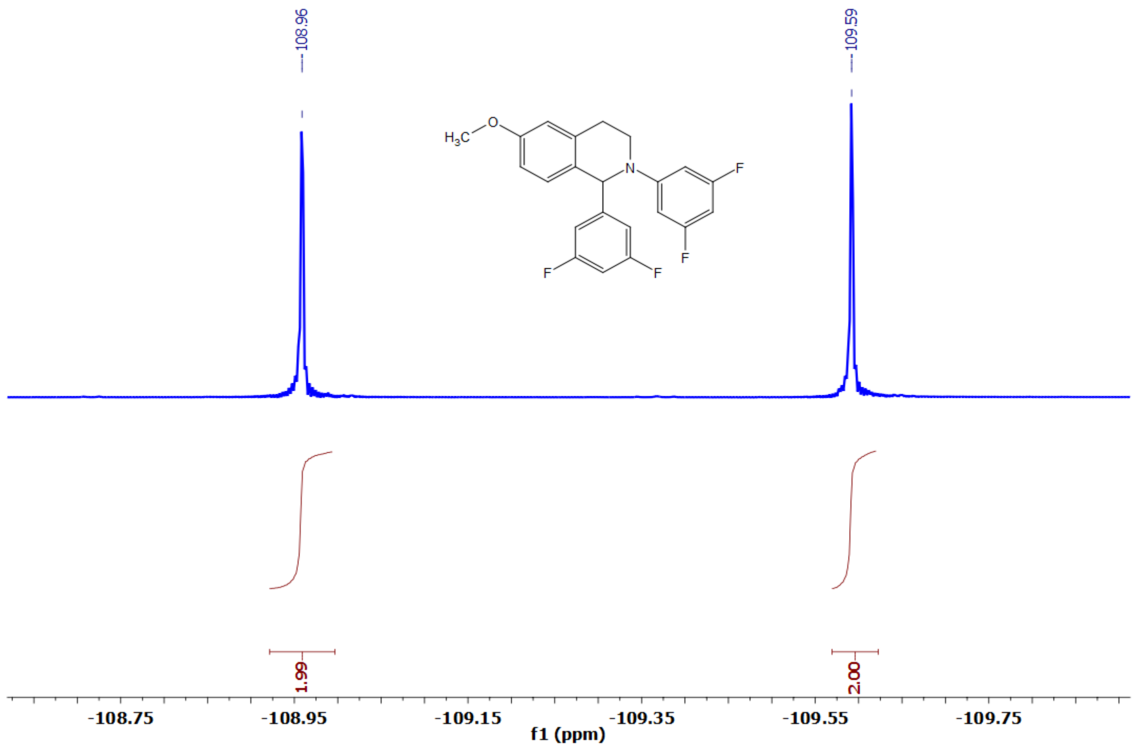


Figure S52(c): **^{19}F- NMR Spectra of 6-36, (376 MHz, $CDCl_3$): δ (ppm)** = -109.59 (s, 2F), -108.96 (s, 2F).

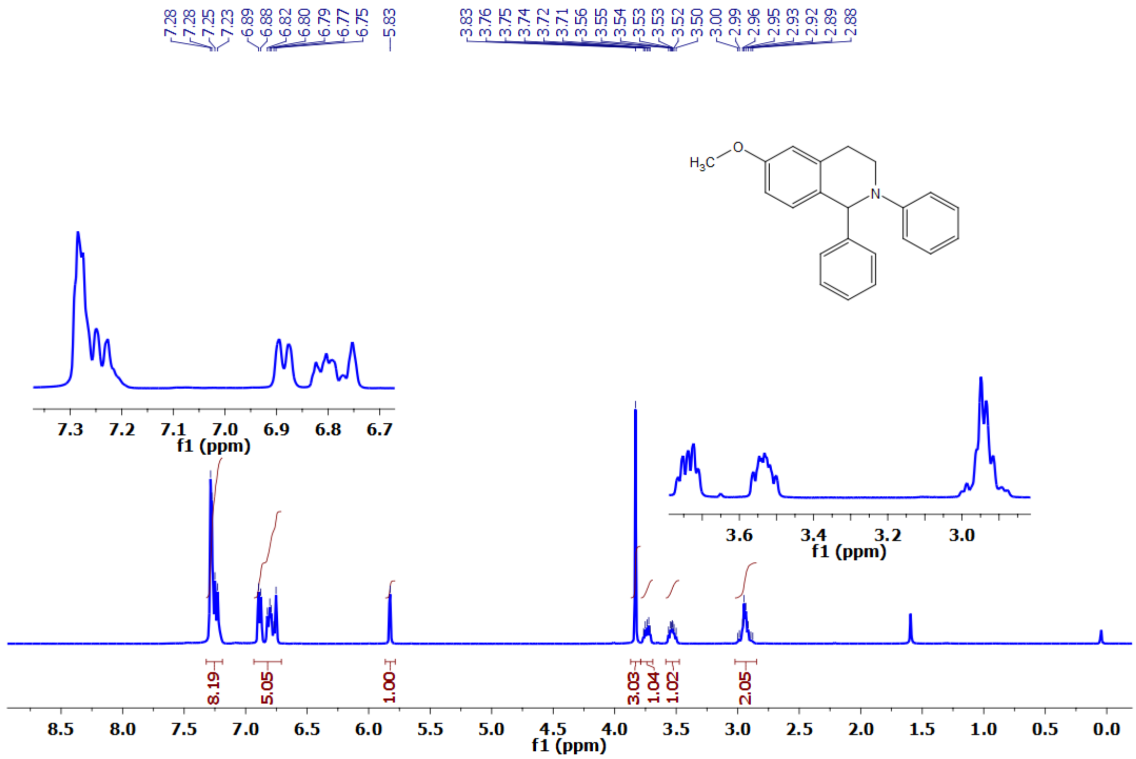


Figure S53(a): ^{1}**H - NMR Spectra of 6-37, (400 MHz, CDCl$_3$): δ (ppm)** = 2.88-3.00 (m, 2H), 3.50-3.56 (m, 1H), 3.71-3.76 (m, 1H), 3.83 (s, 3H), 5.83 (s, 1H), 6.75-6.89 (m, 5H), 7.23-7.28 (m, 8H).

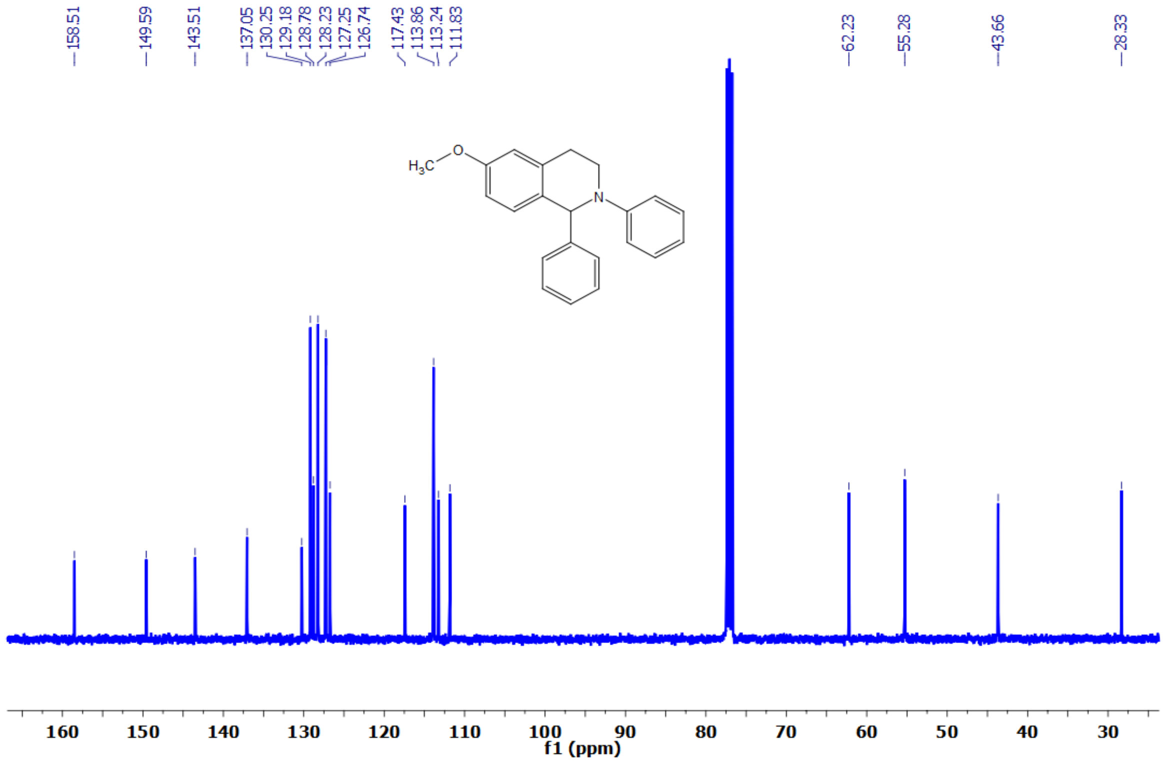


Figure S53(b): ^{13}**C spectra of 6-37, (125 MHz, CDCl$_3$): δ (ppm)** = 158.5286, 149.6021, 143.5241, 137.0621, 130.2639, 129.1893, 128.796, 128.2425, 127.2657, 126.7504, 117.4422, 113.8709, 113.2491, 111.842, 62.2405, 55.2892, 43.6698, 28.3337

IR SPECTRA

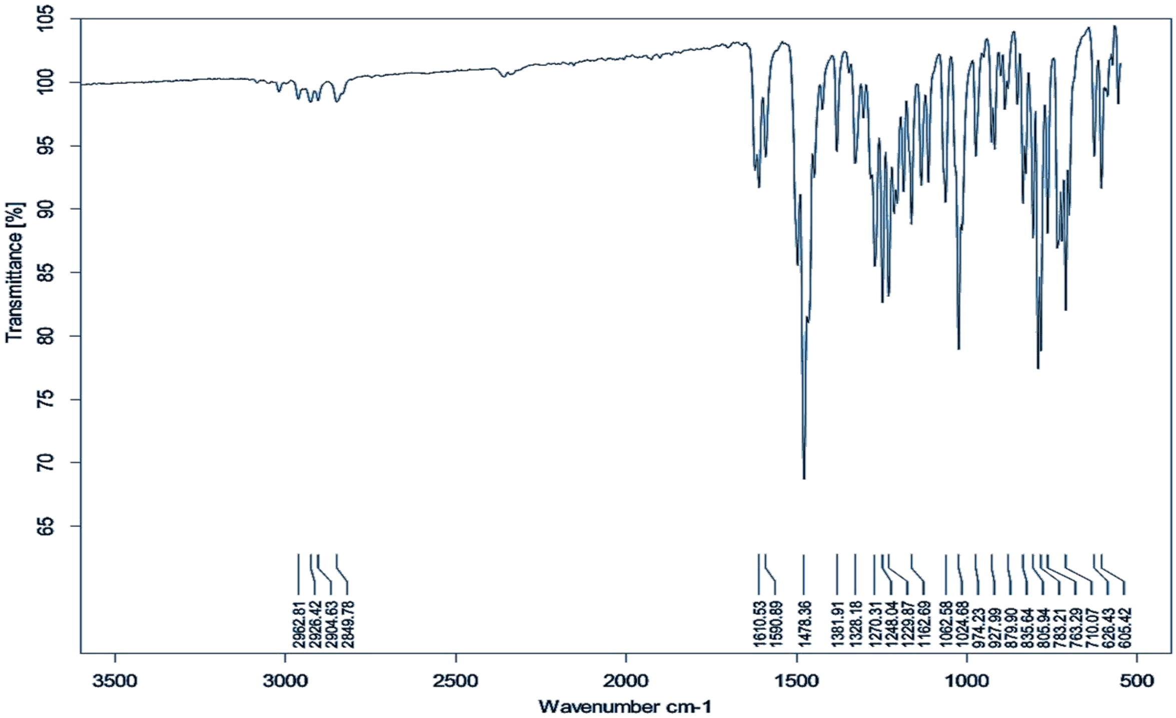


Figure S54: FT-IR Spectra of 6-1

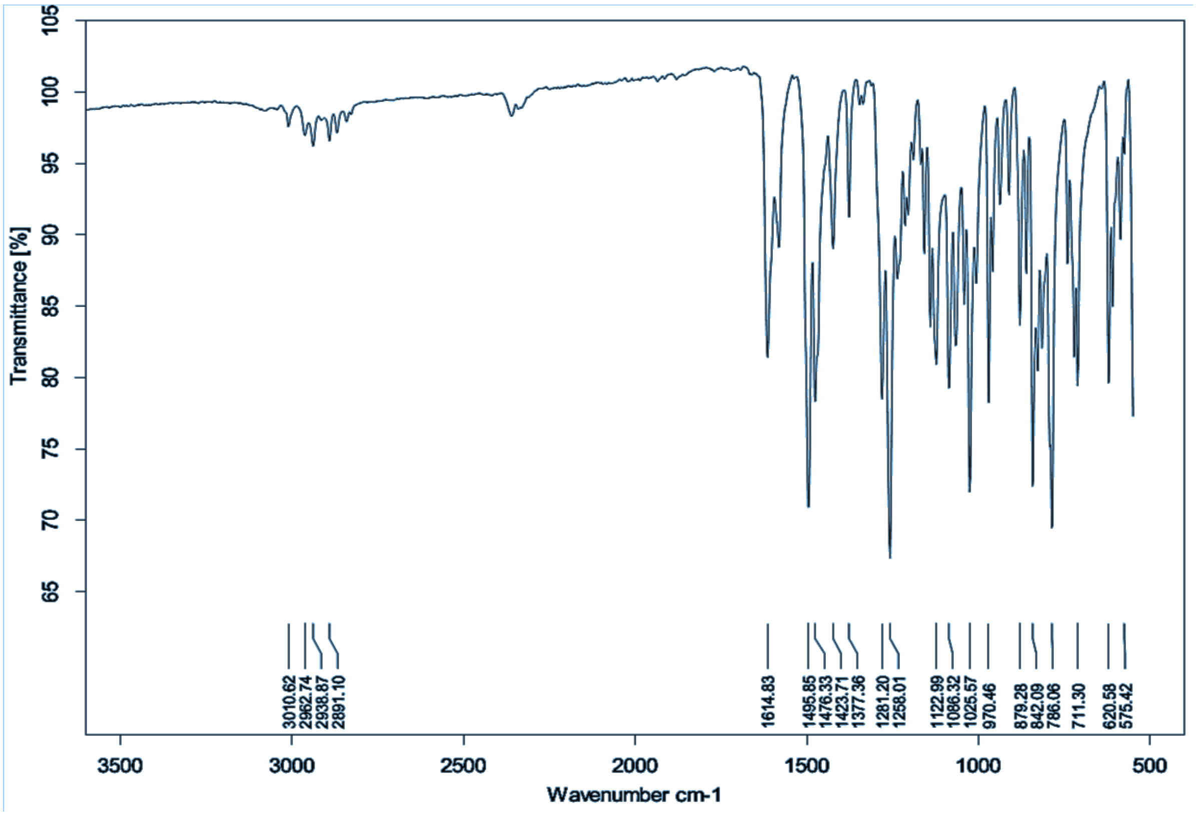


Figure S55: FT-IR Spectra of 6-2

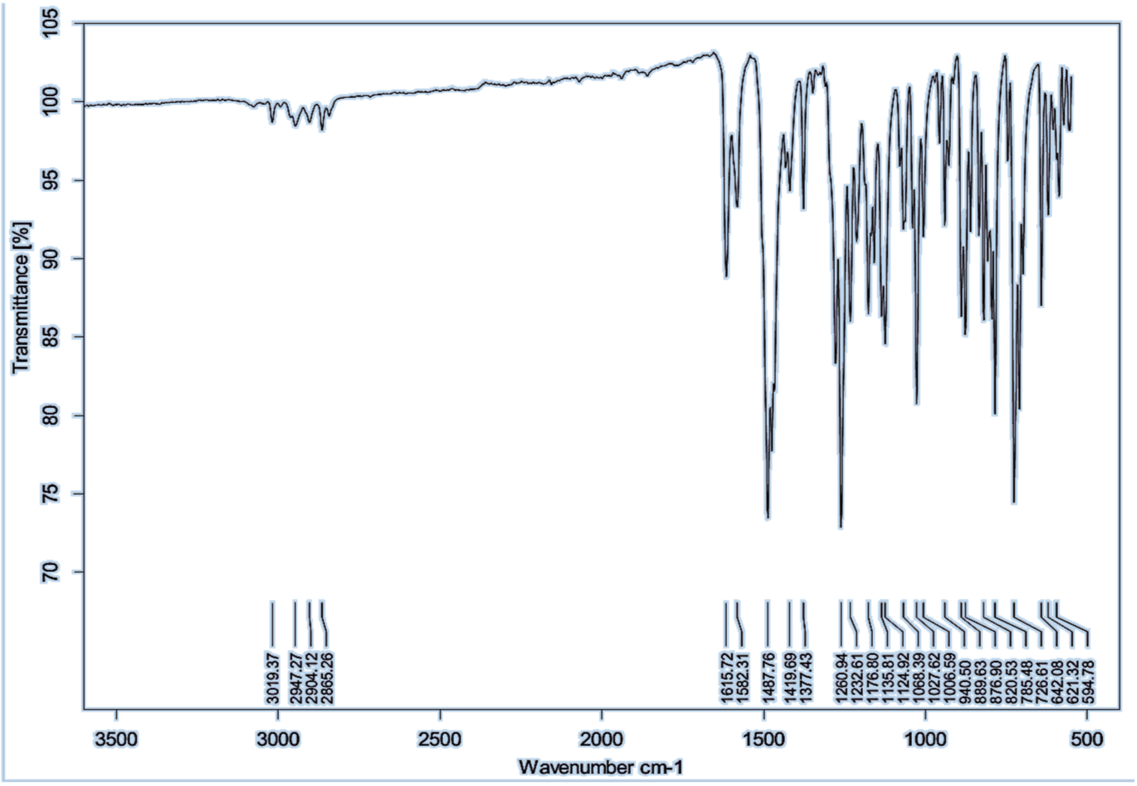


Figure S56: IR-spectra of 6-3

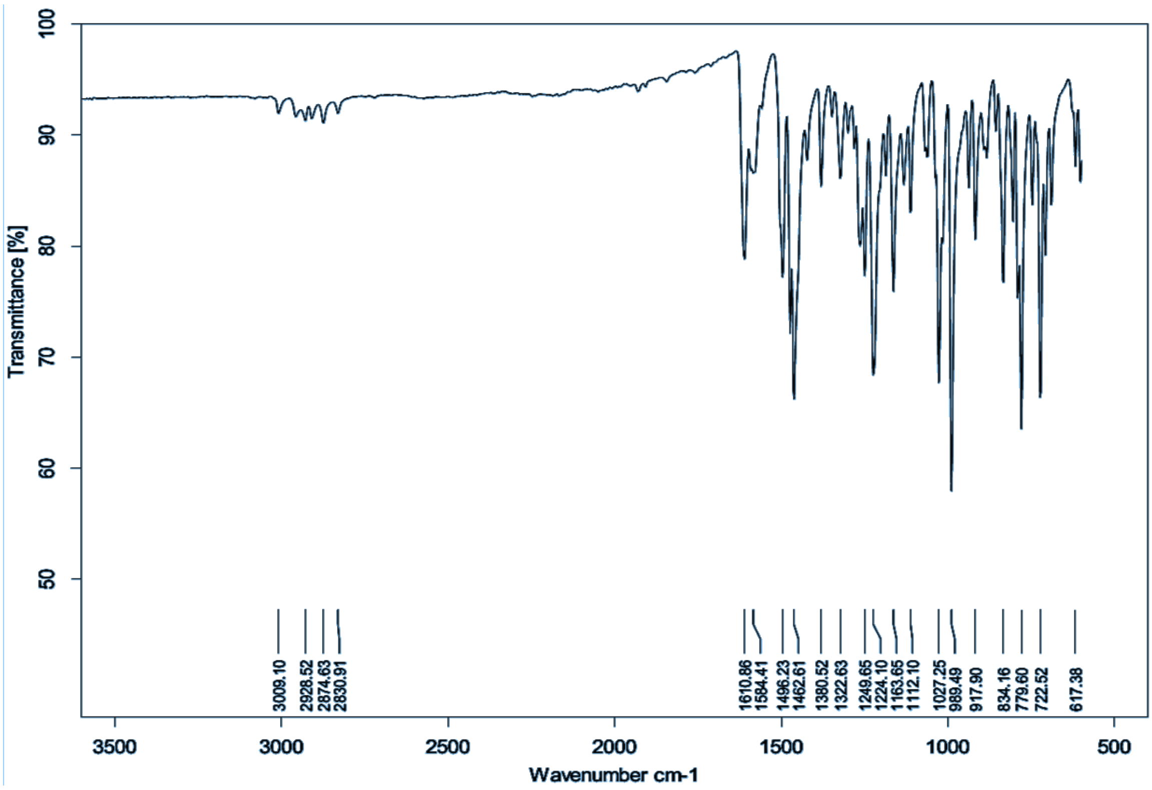


Figure S57: IR-spectra of 6-4

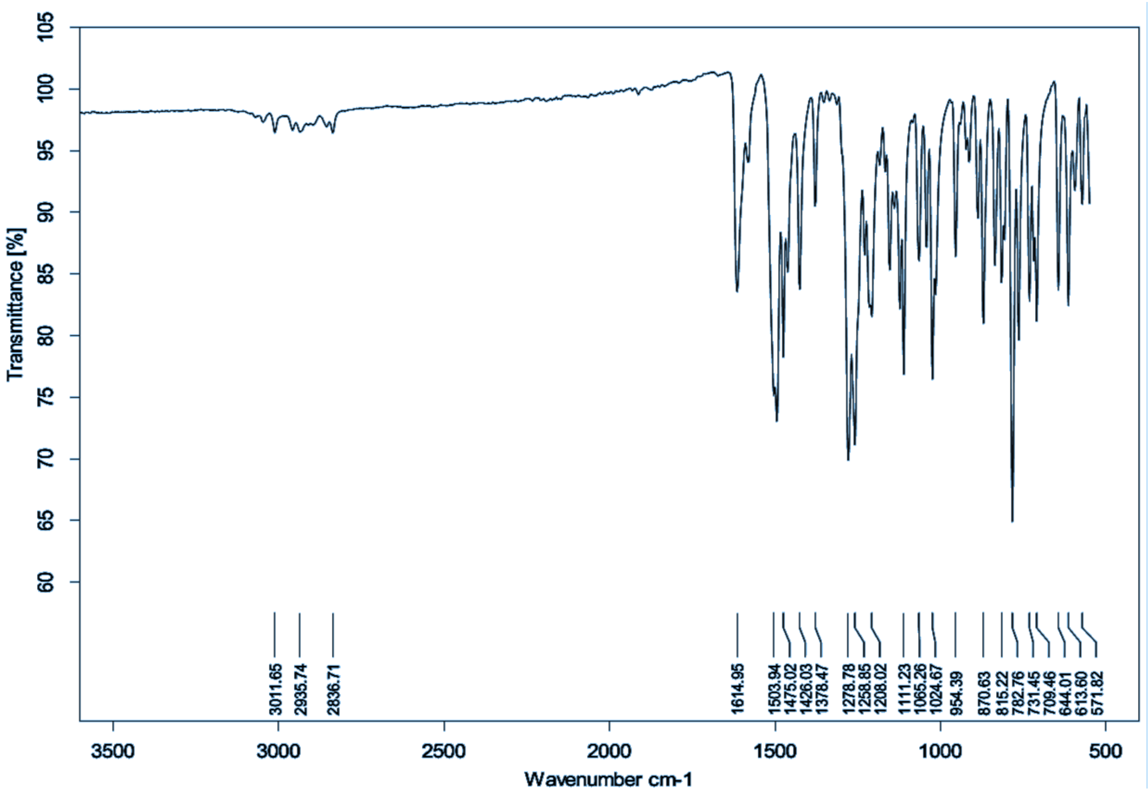


Figure S58: IR-spectra of 6-5

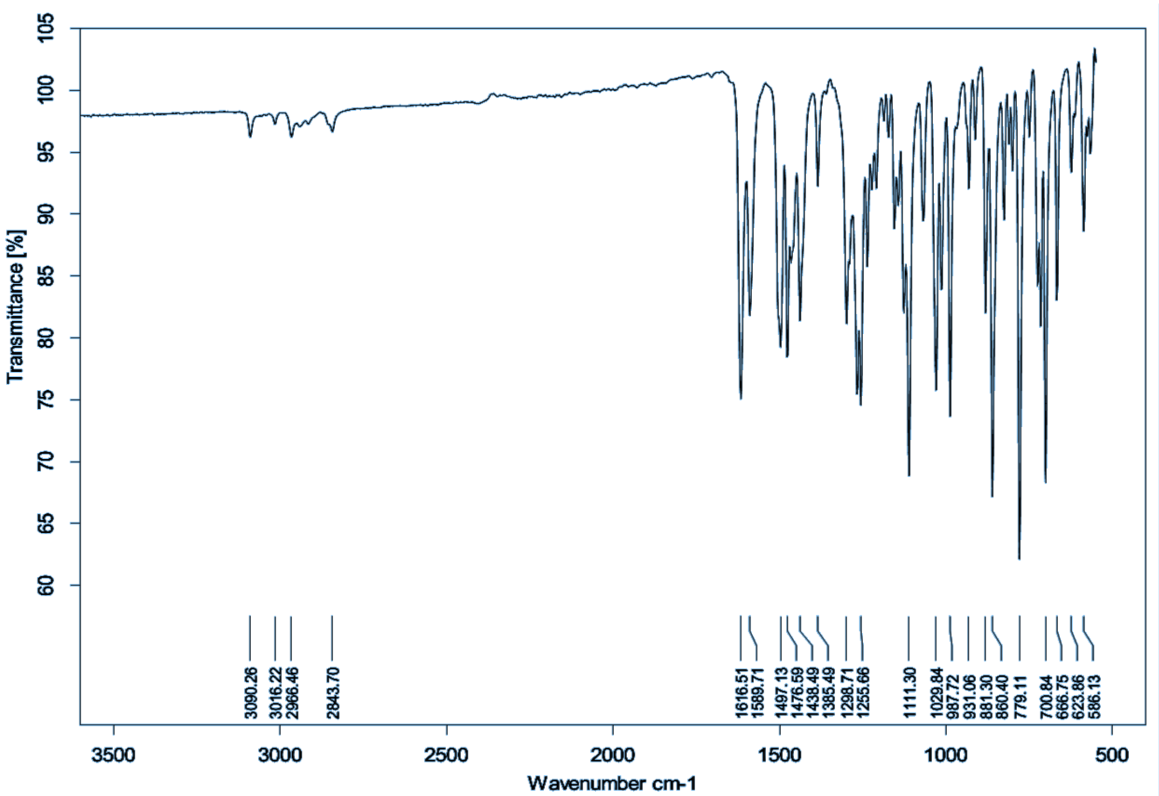


Figure S59: IR-spectra of 6-6

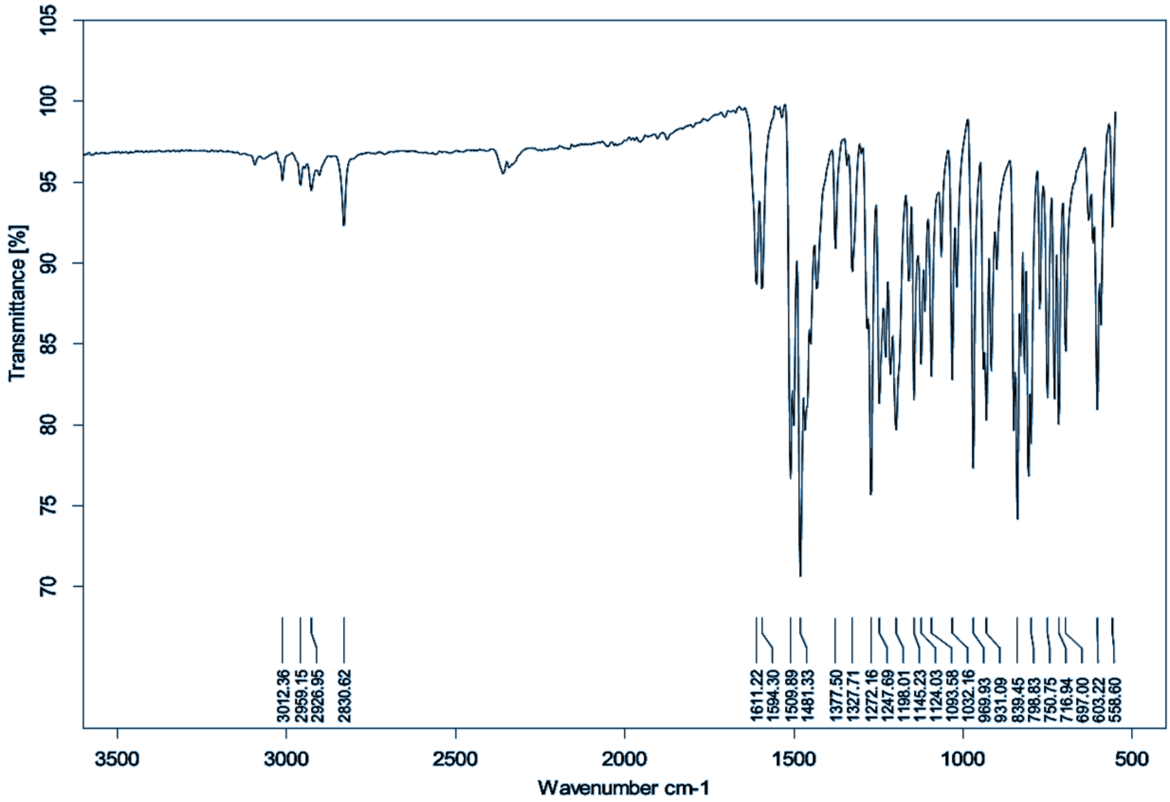


Figure S60: IR-spectra of 6-7

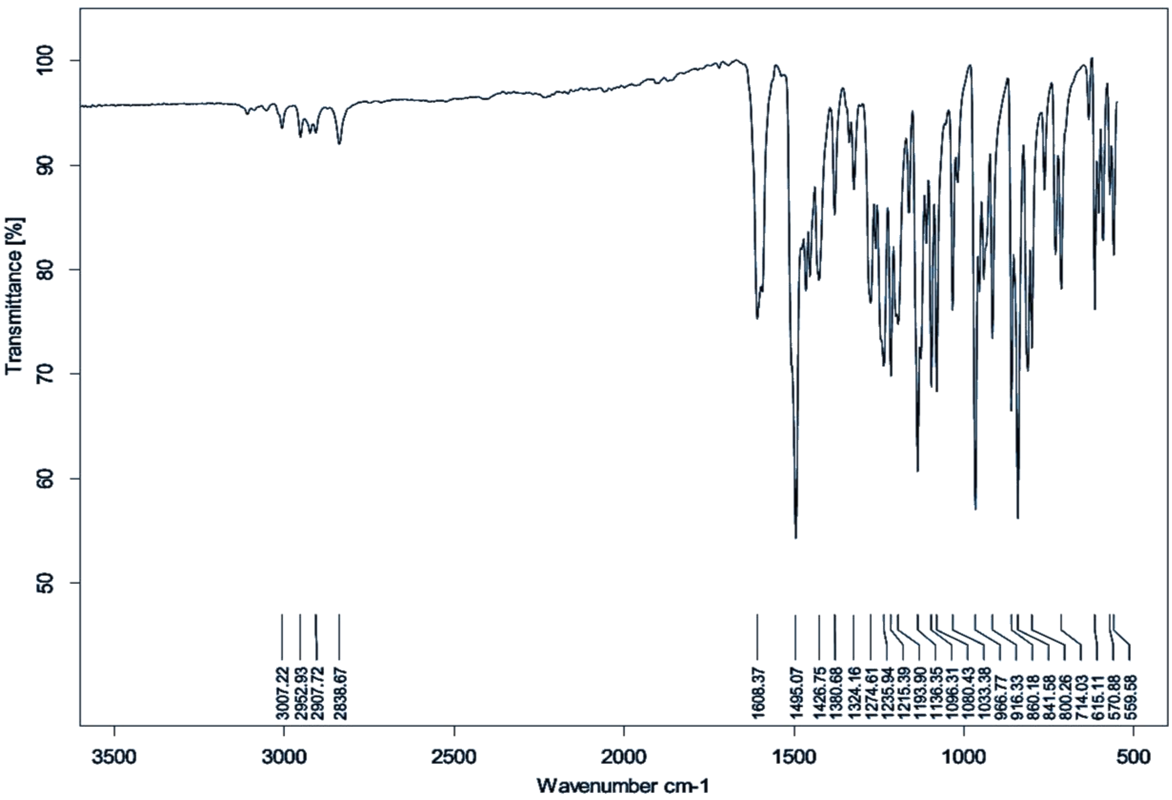


Figure S61: IR-spectra of 6-8

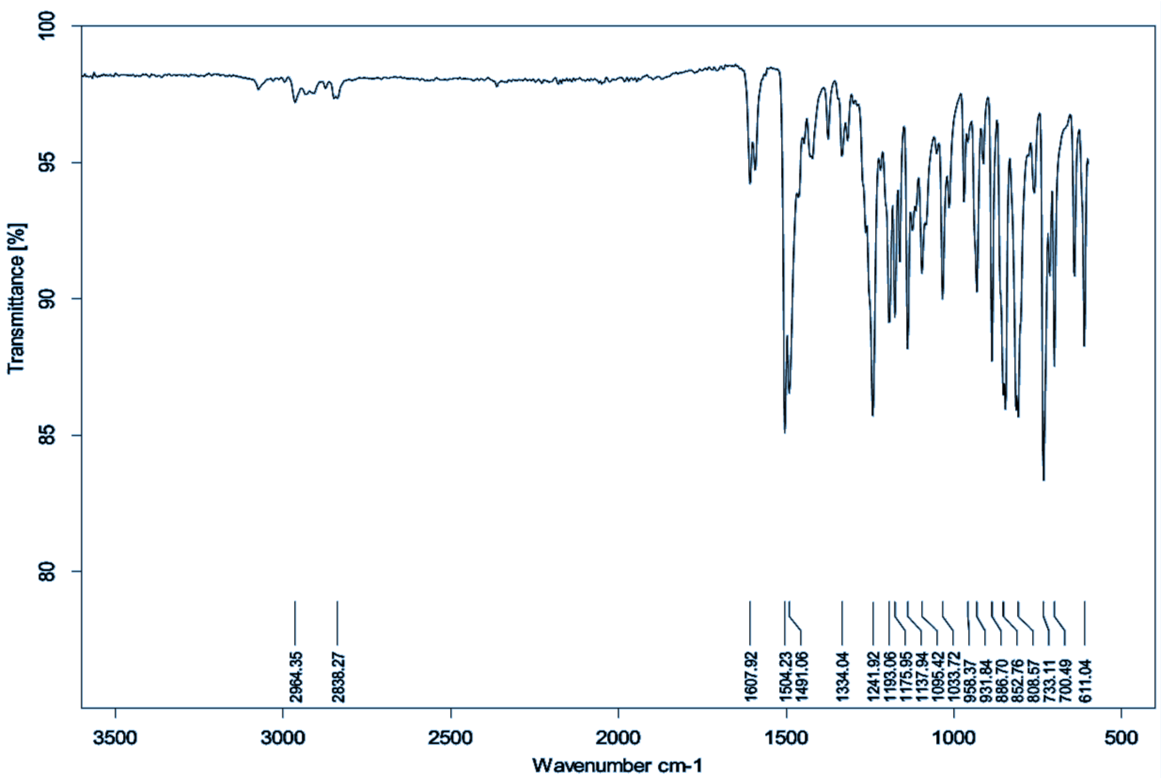


Figure S62: IR-spectra of 6-9

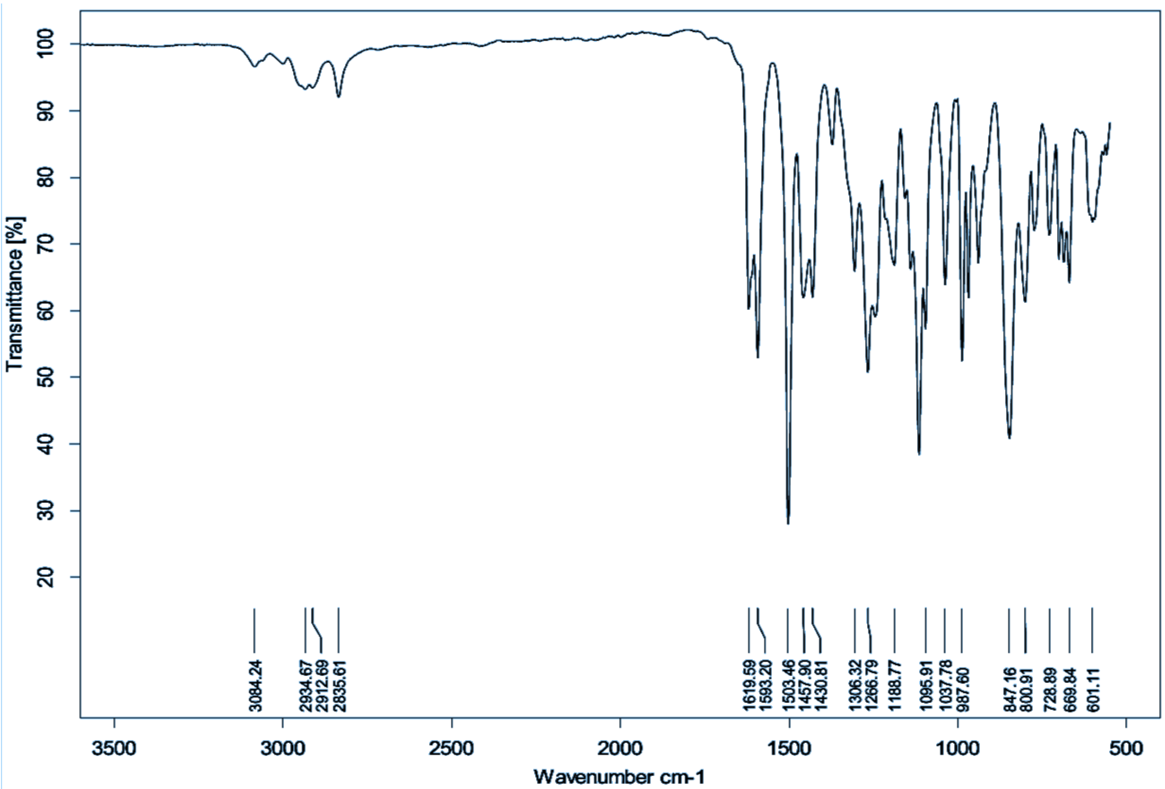


Figure S63: IR-spectra of 6-11

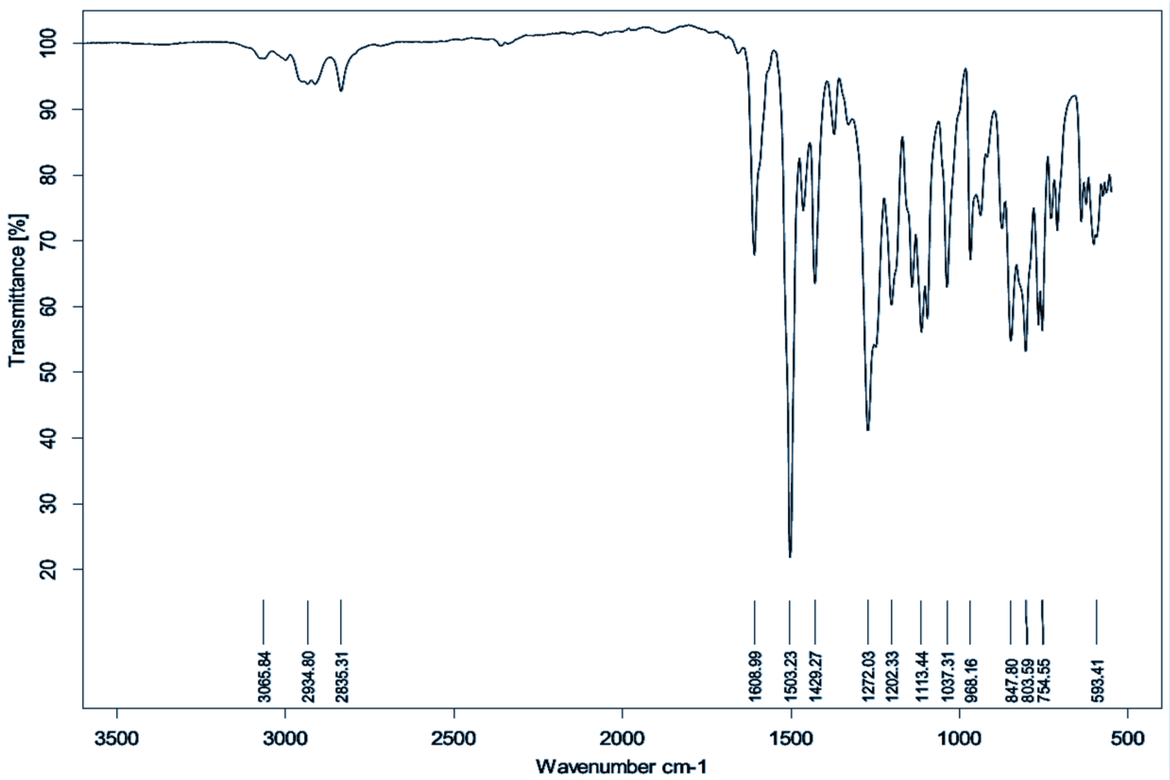


Figure S64: IR-spectra of 6-12

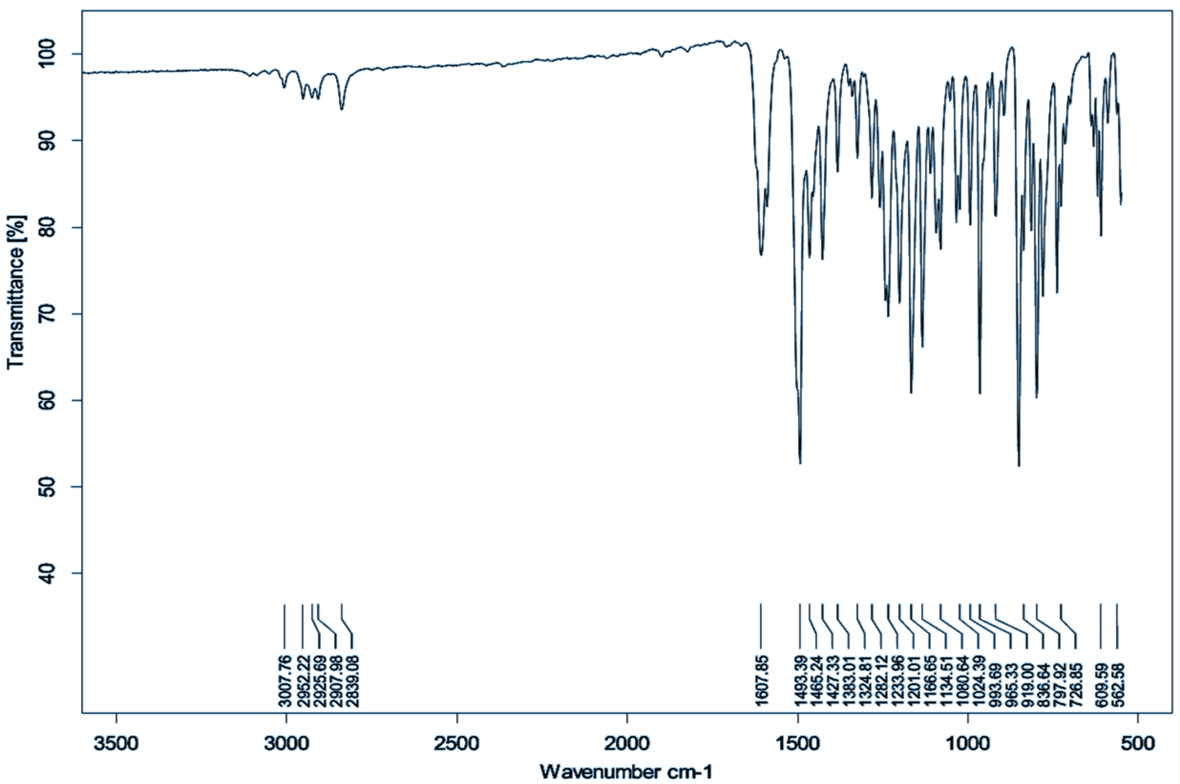


Figure S65: FT-IR - spectra of 6-13

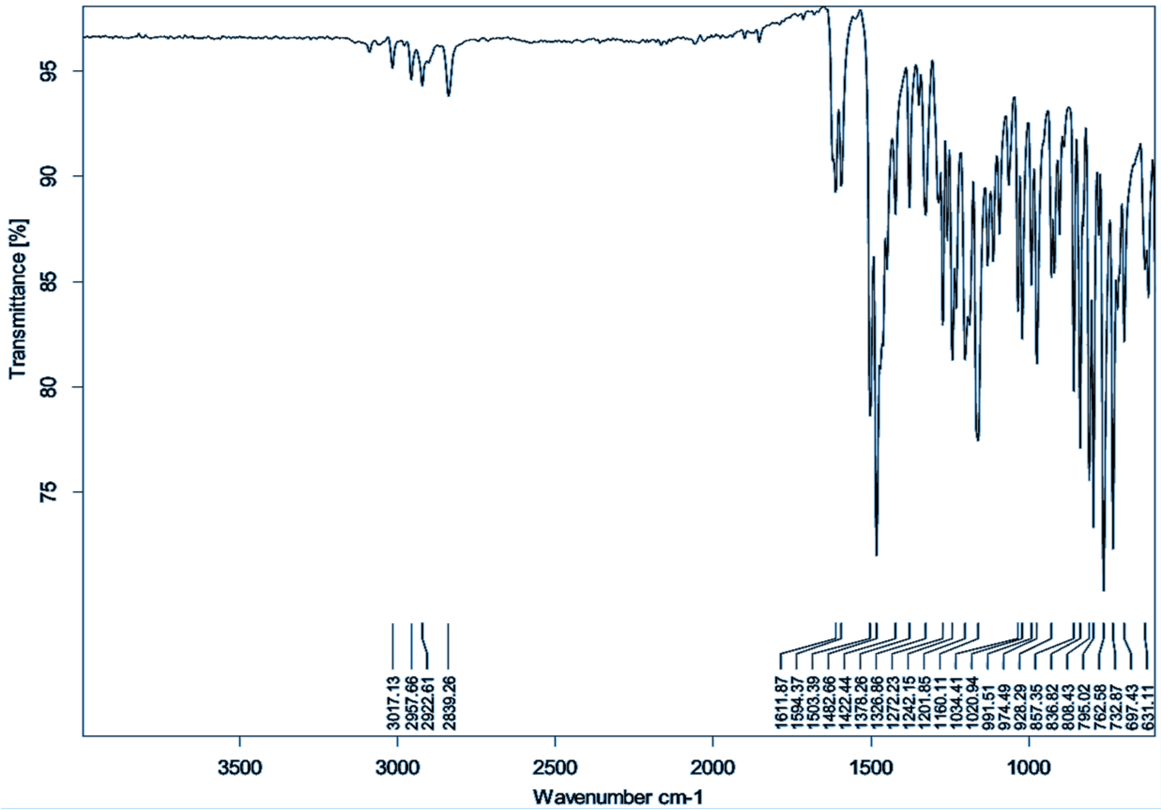


Figure S66: FT-IR - spectra of 6-14

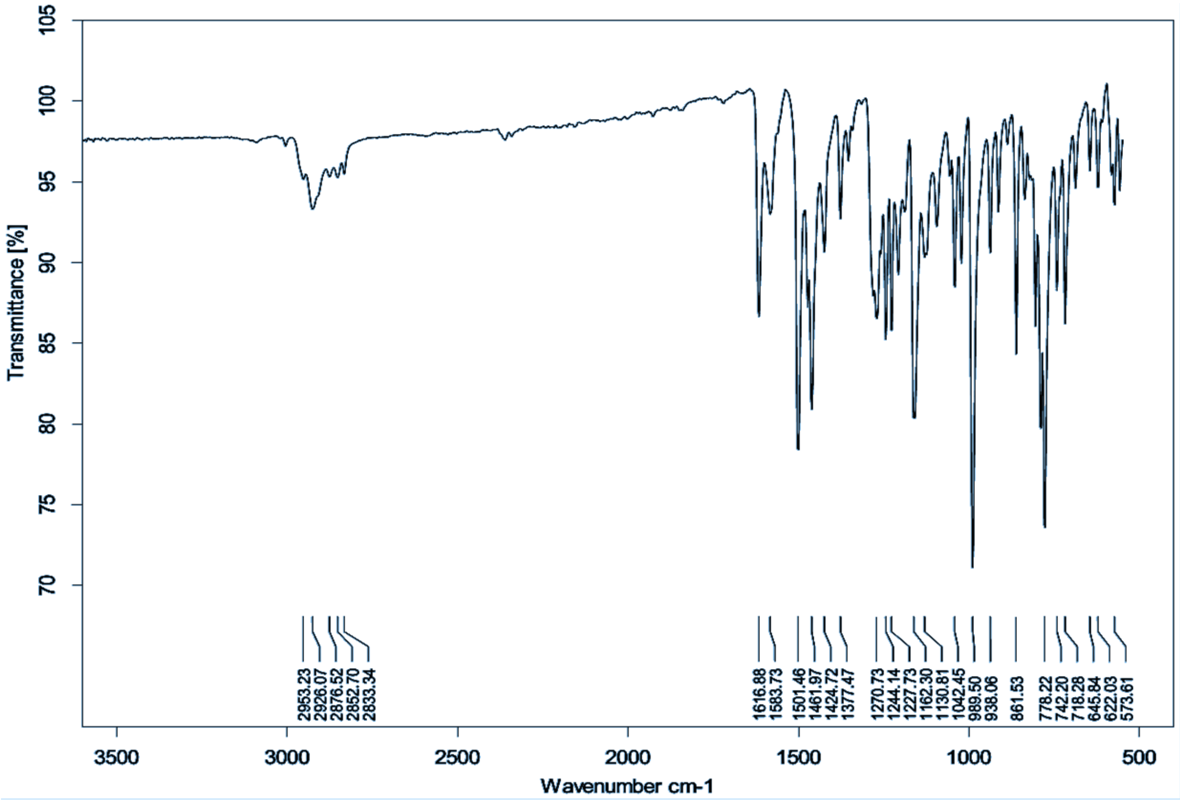


Figure S67: FT-IR - spectra of 6-16

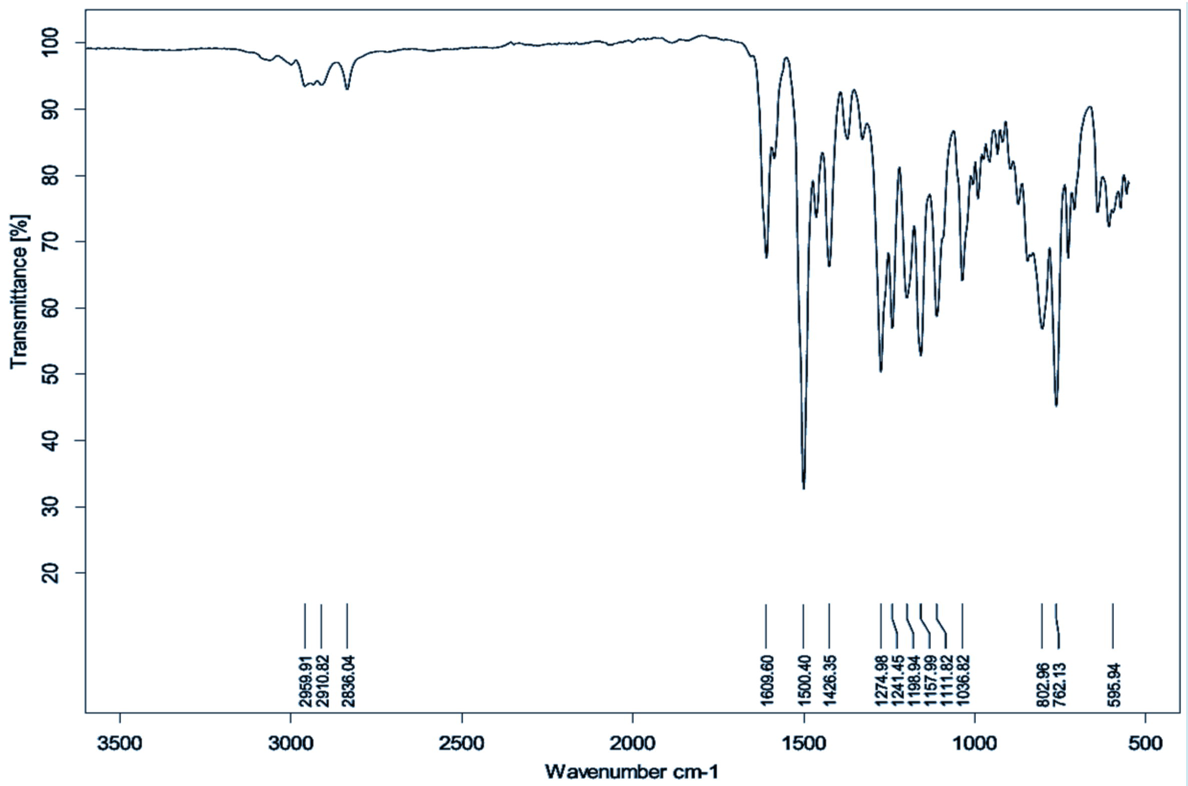


Figure S68: FT-IR - spectra of 6-17

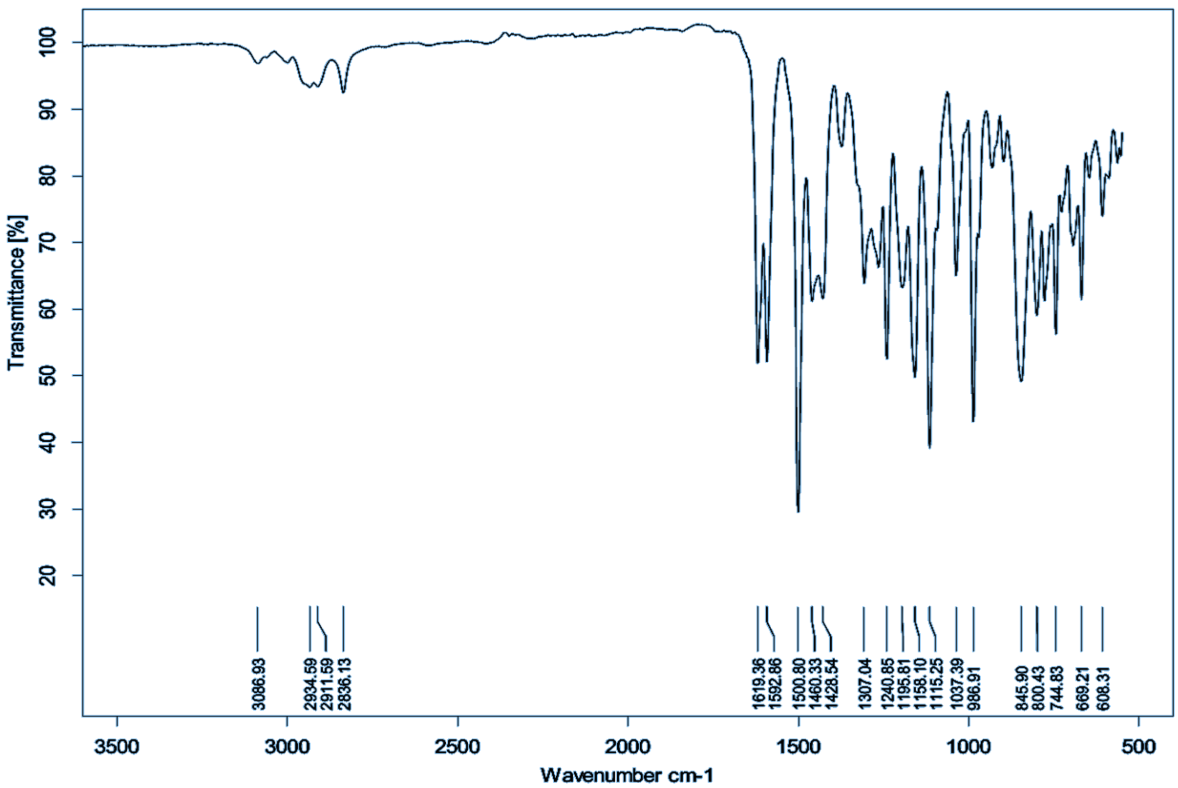


Figure S69: FT-IR - spectra of 6-18

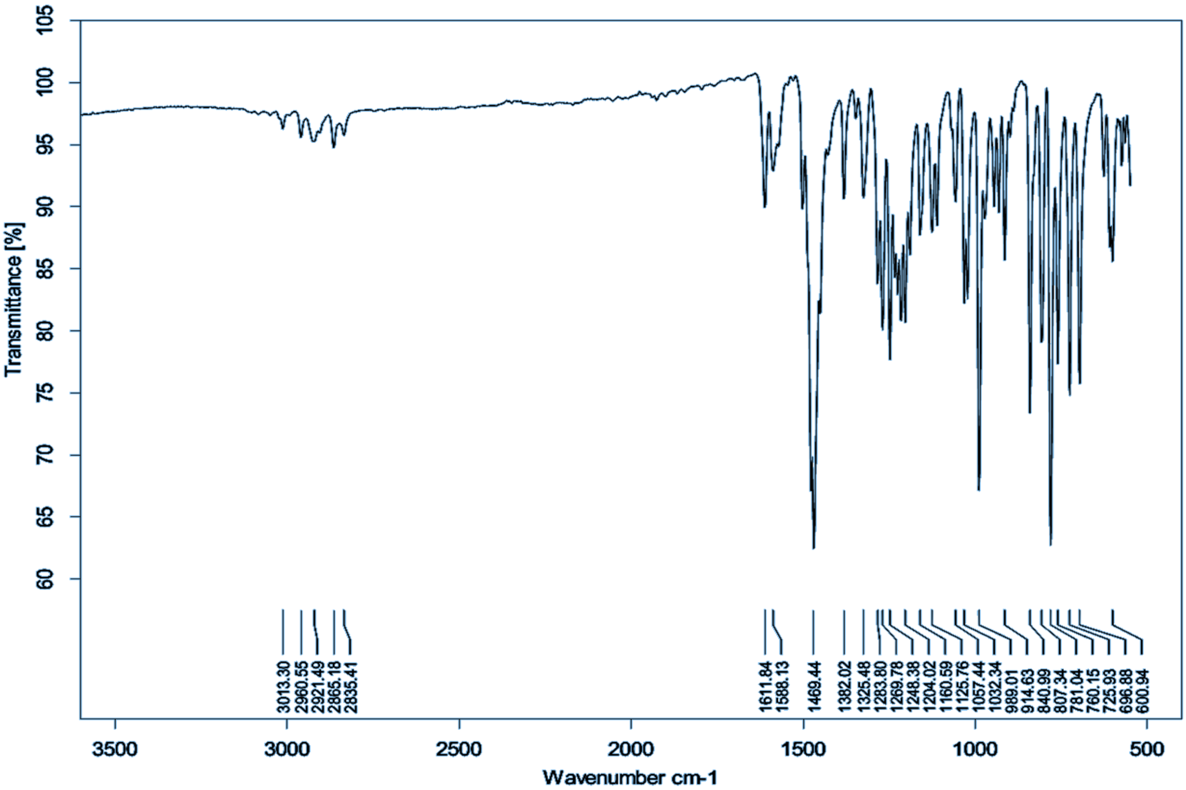


Figure S70: FT-IR - spectra of 6-19

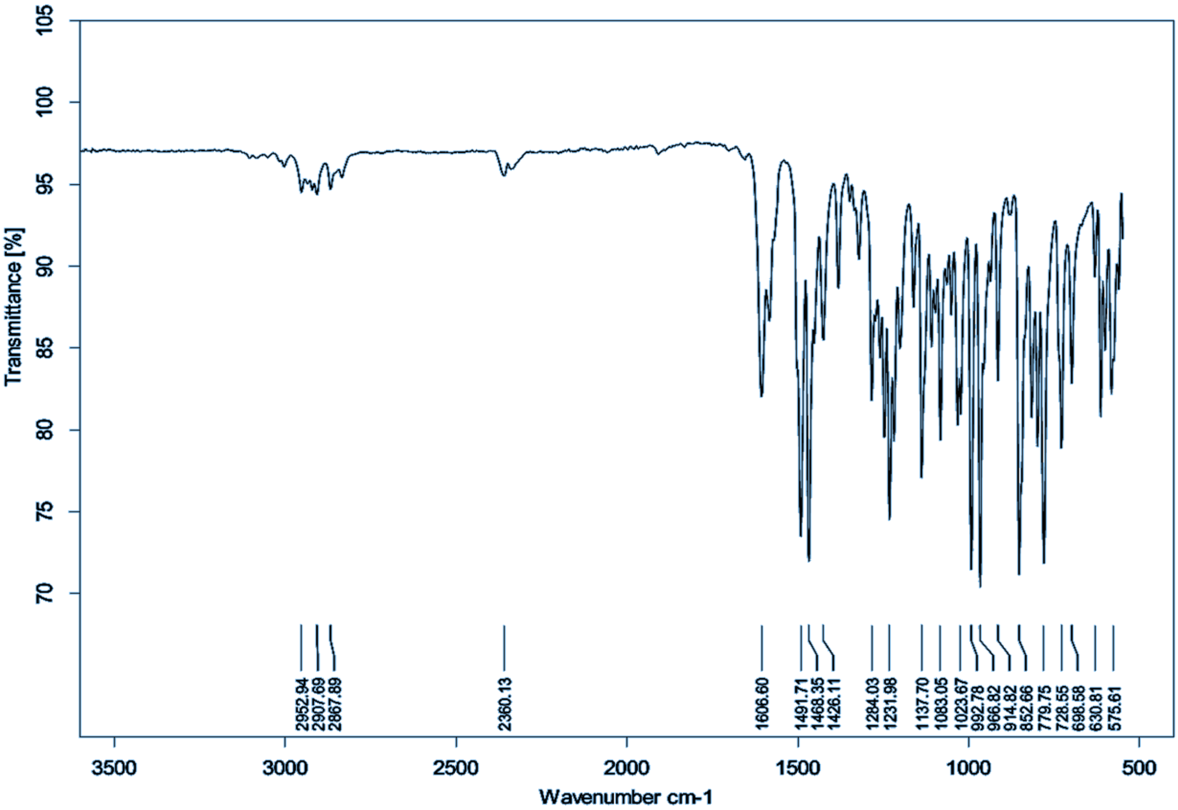


Figure S71: FT-IR - spectra of 6-22

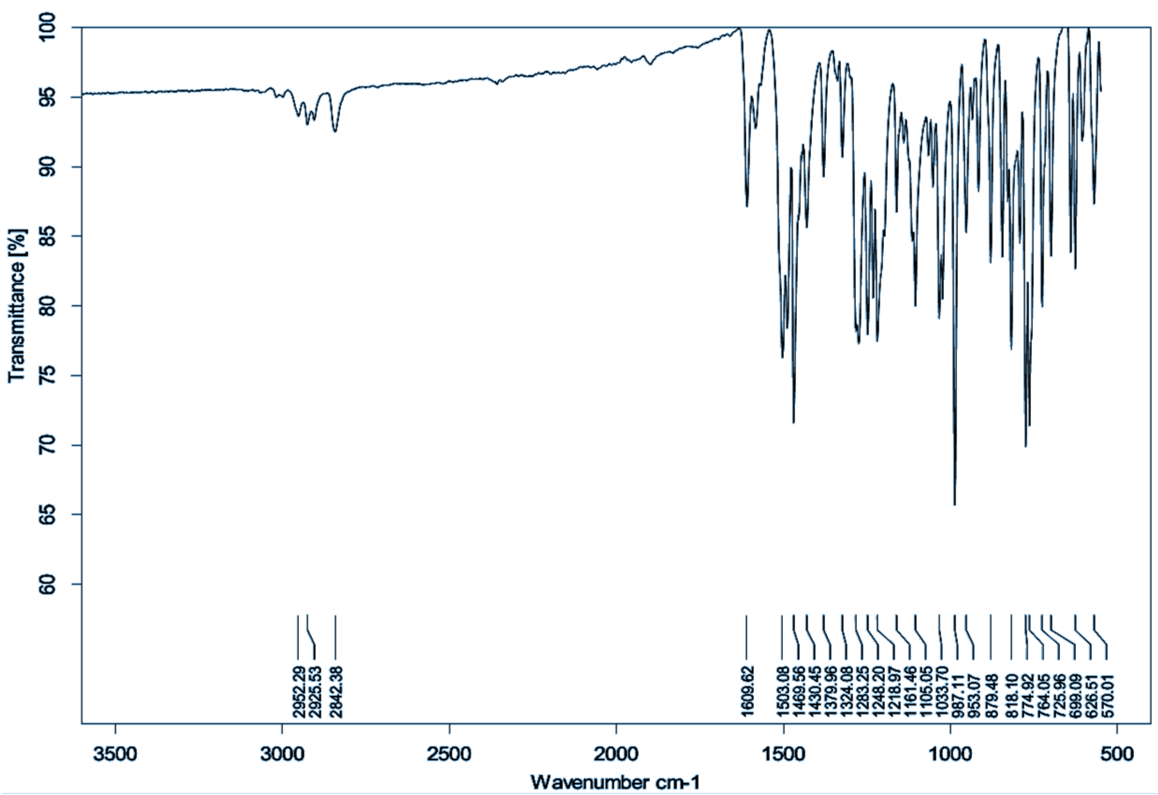


Figure S72: FT-IR - spectra of 6-23

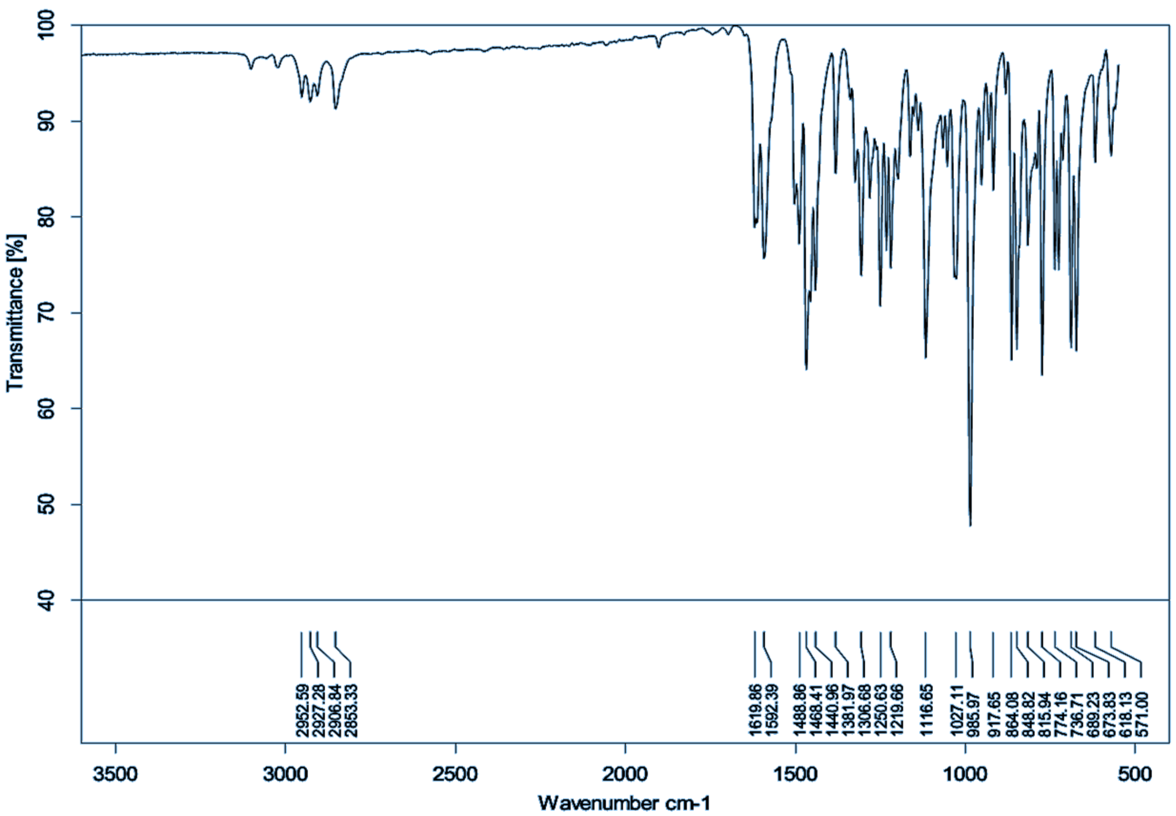


Figure S73: FT-IR - spectra of 6-24

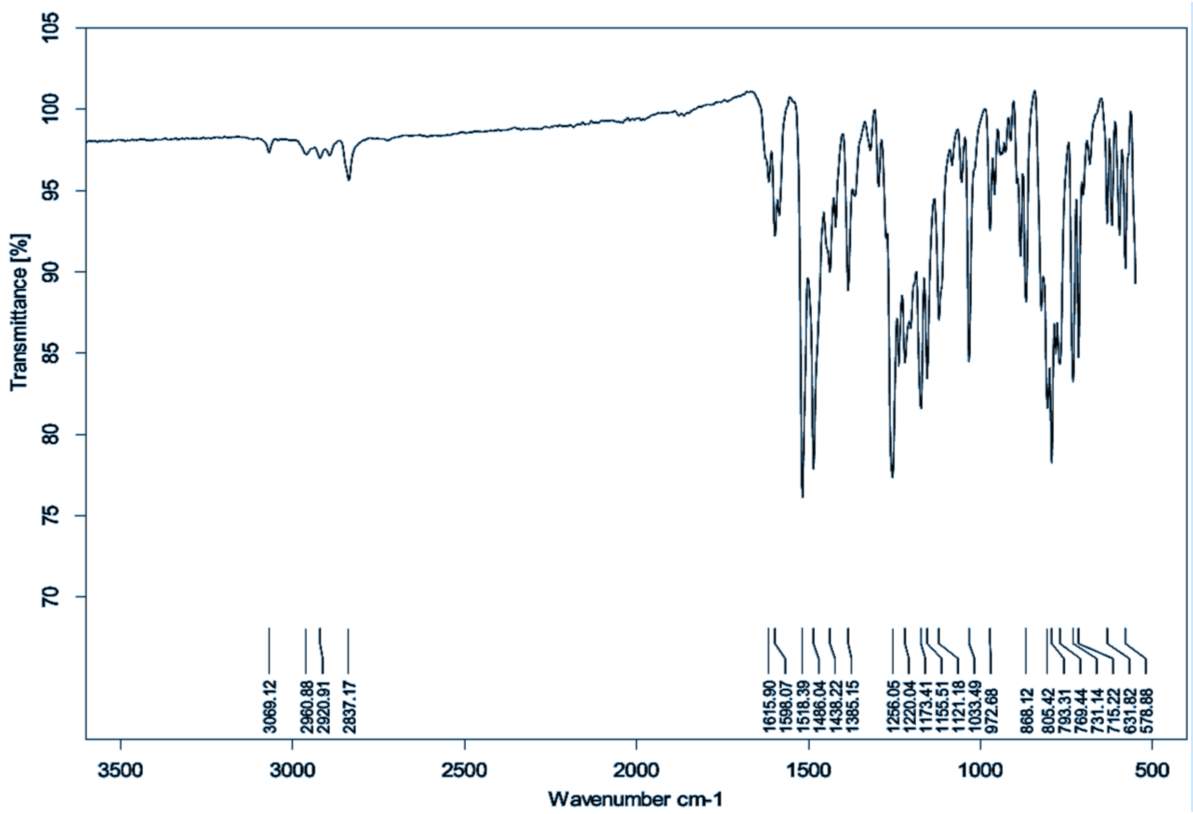


Figure S74: FT-IR - spectra of 6-25

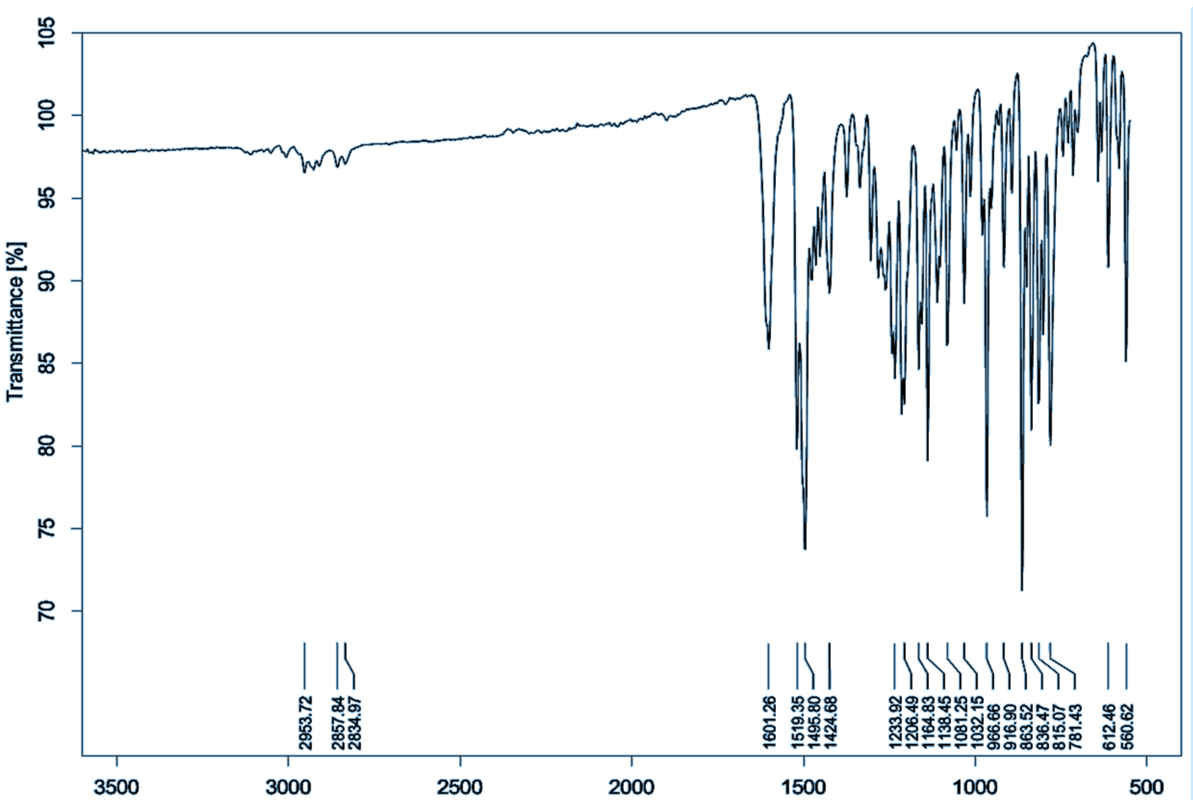


Figure S75: FT-IR - spectra of 6-26

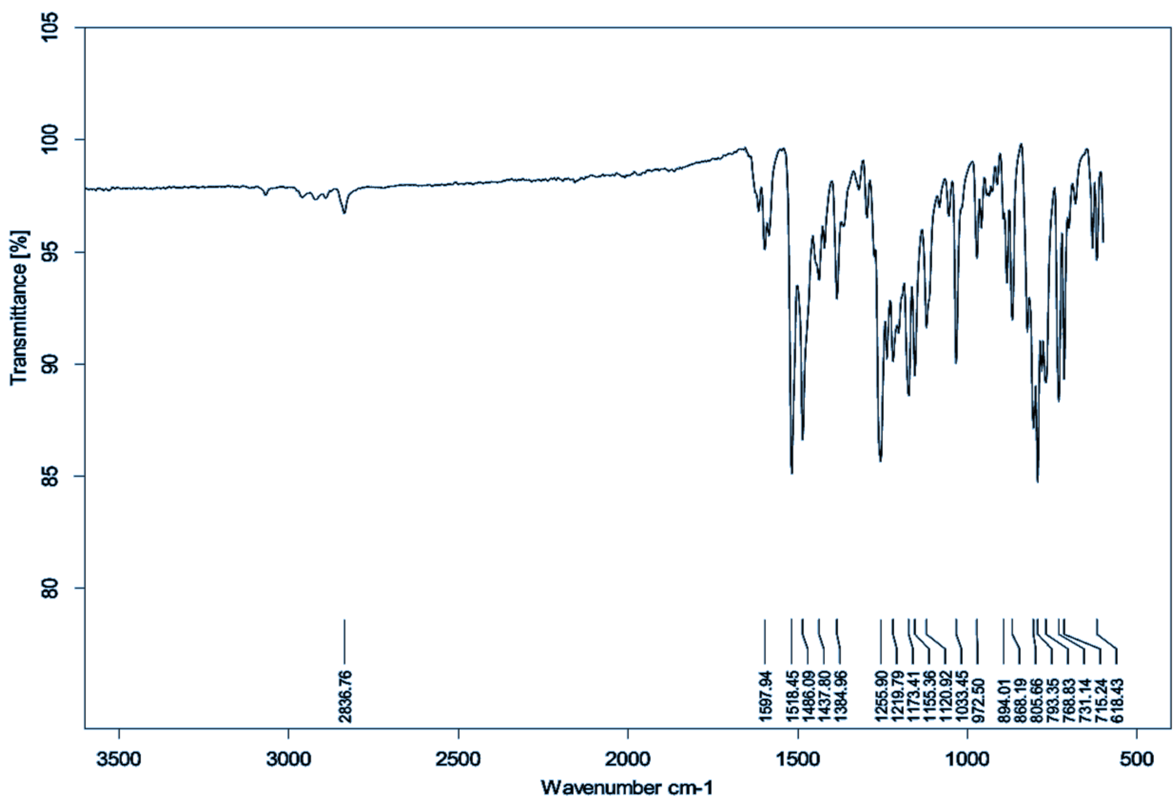


Figure S76: FT-IR - spectra of 6-27

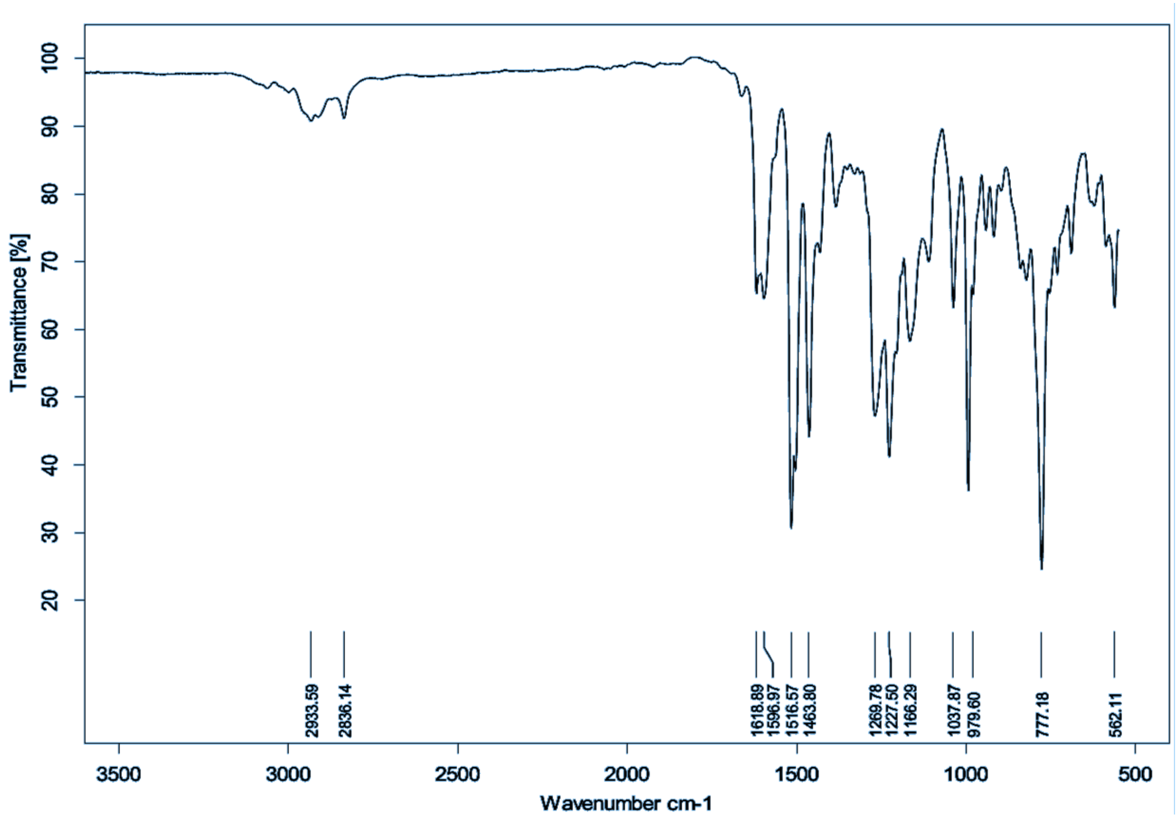


Figure S77: FT-IR - spectra of 6-28

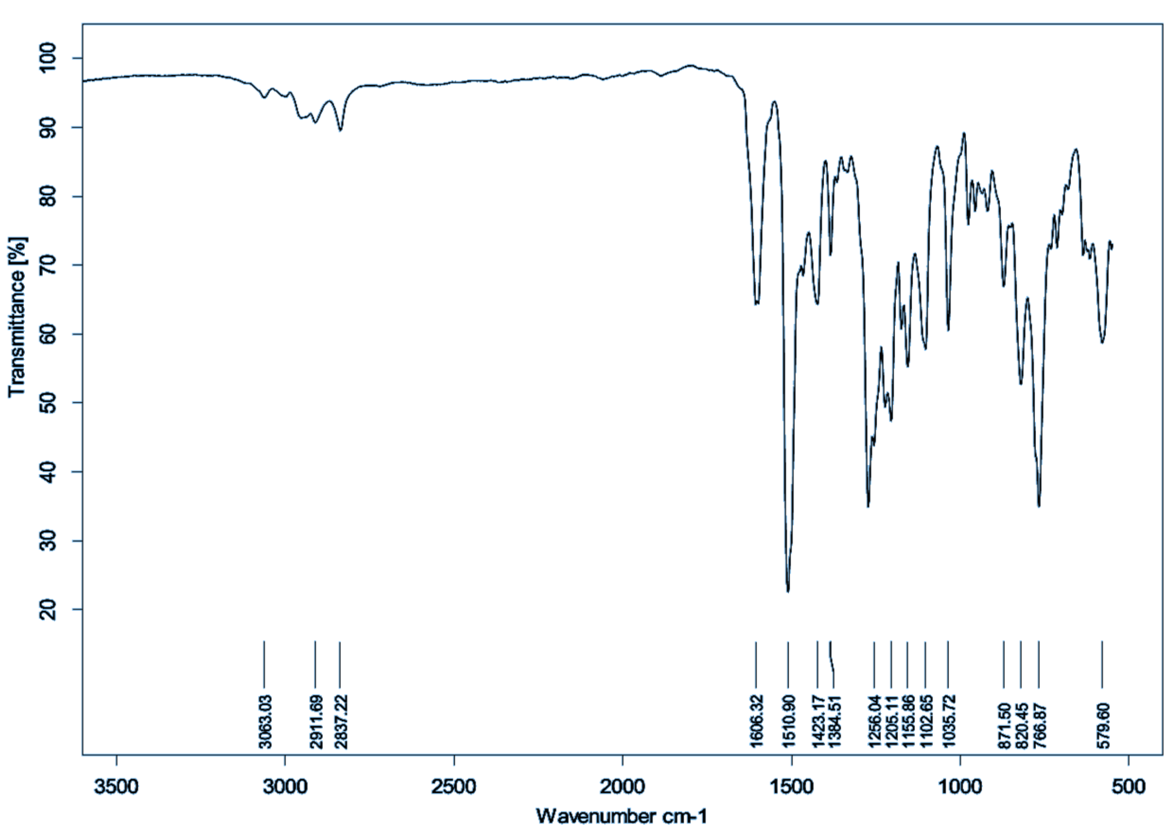


Figure S78: FT-IR - spectra of 6-29

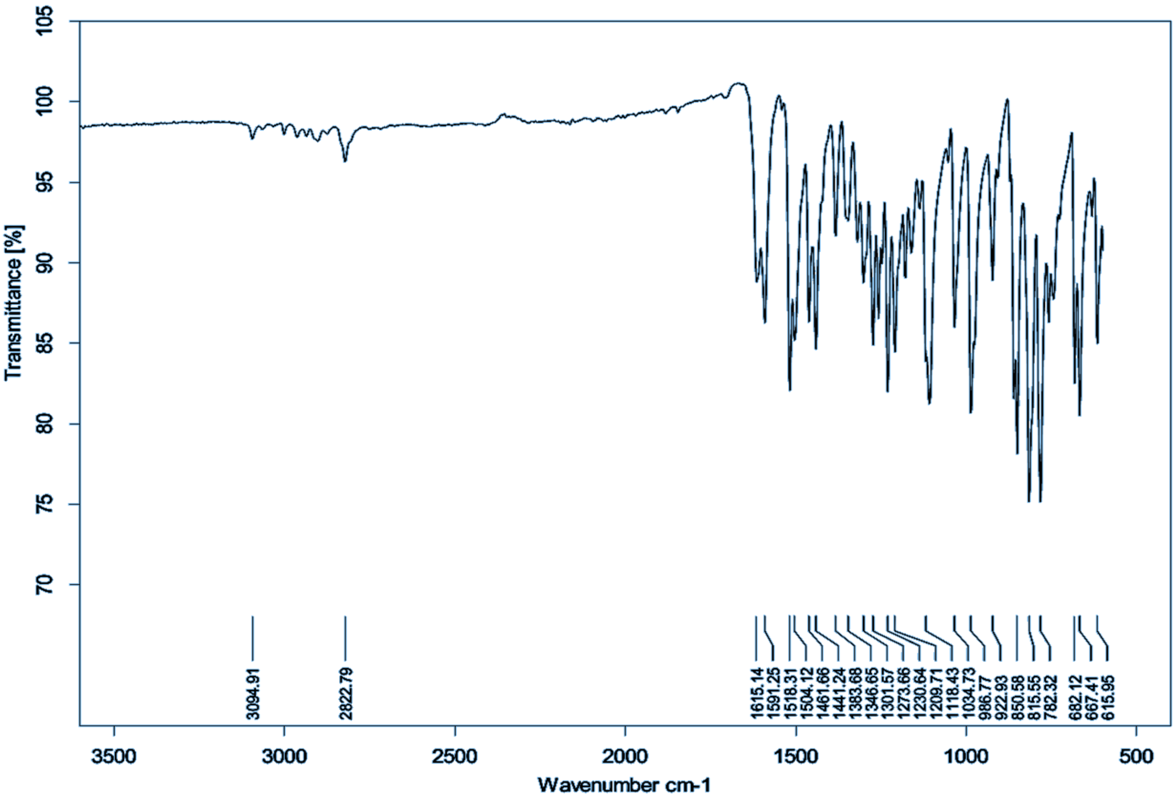


Figure S79: FT-IR - spectra of 6-30

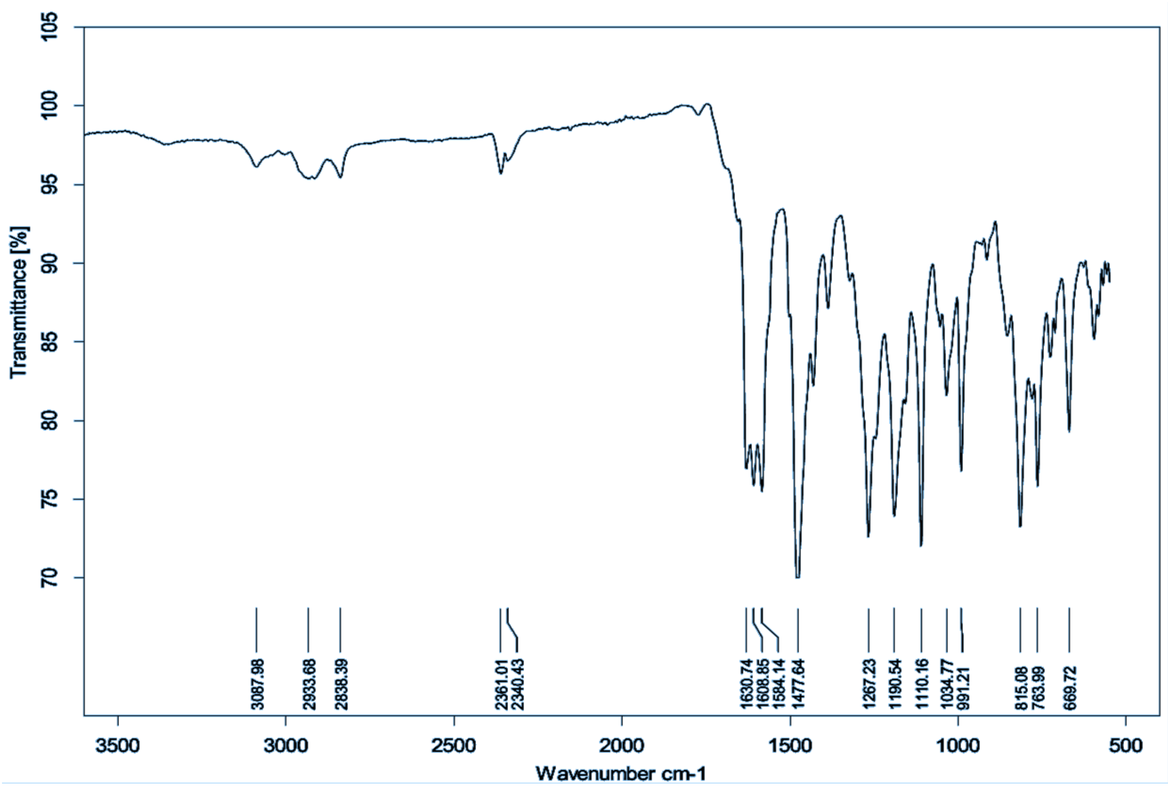


Figure S80: FT-IR - spectra of 6-31

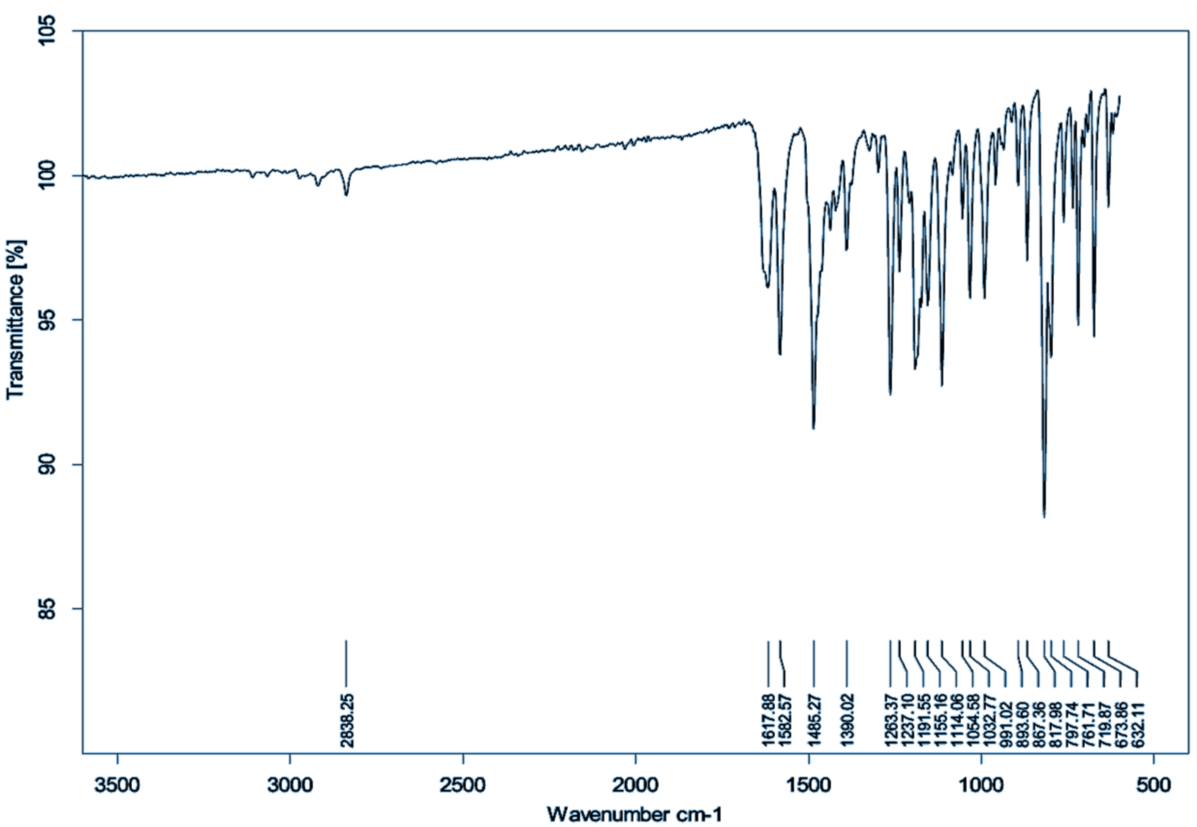


Figure S81: FT-IR - spectra of 6-33

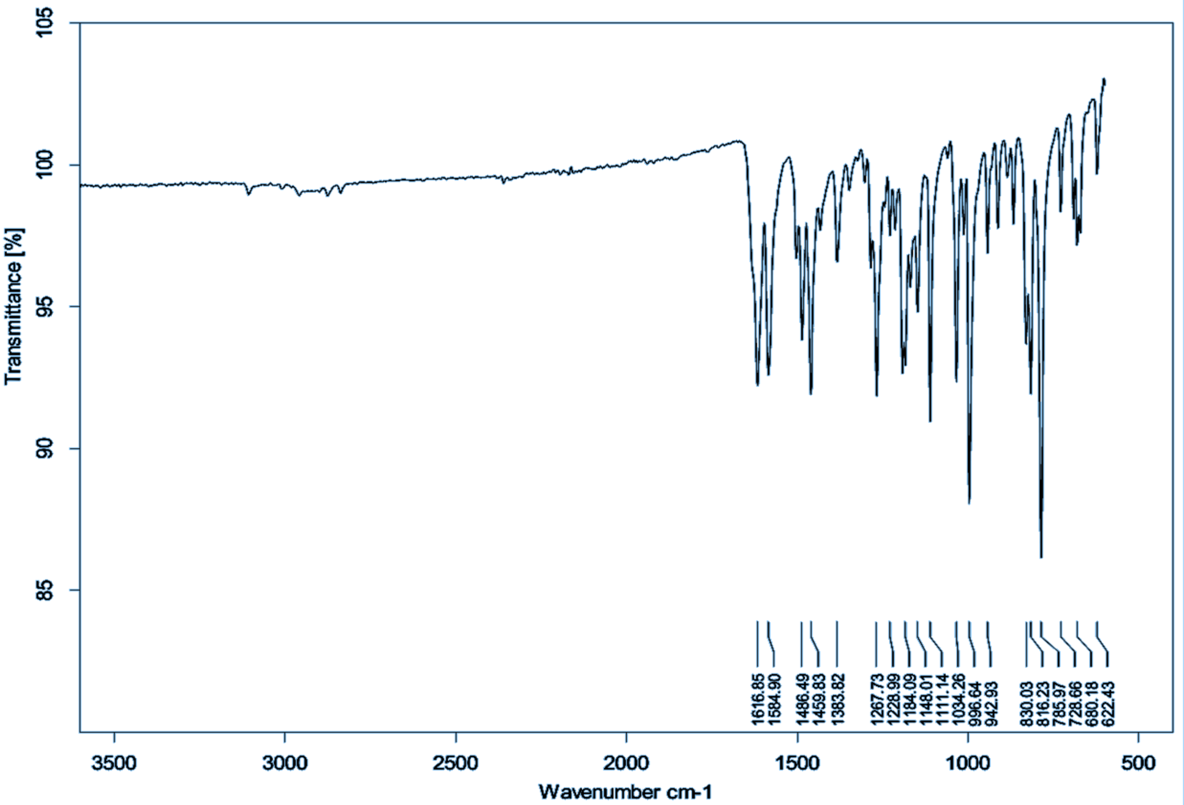


Figure S82: FT-IR - spectra of 6-34

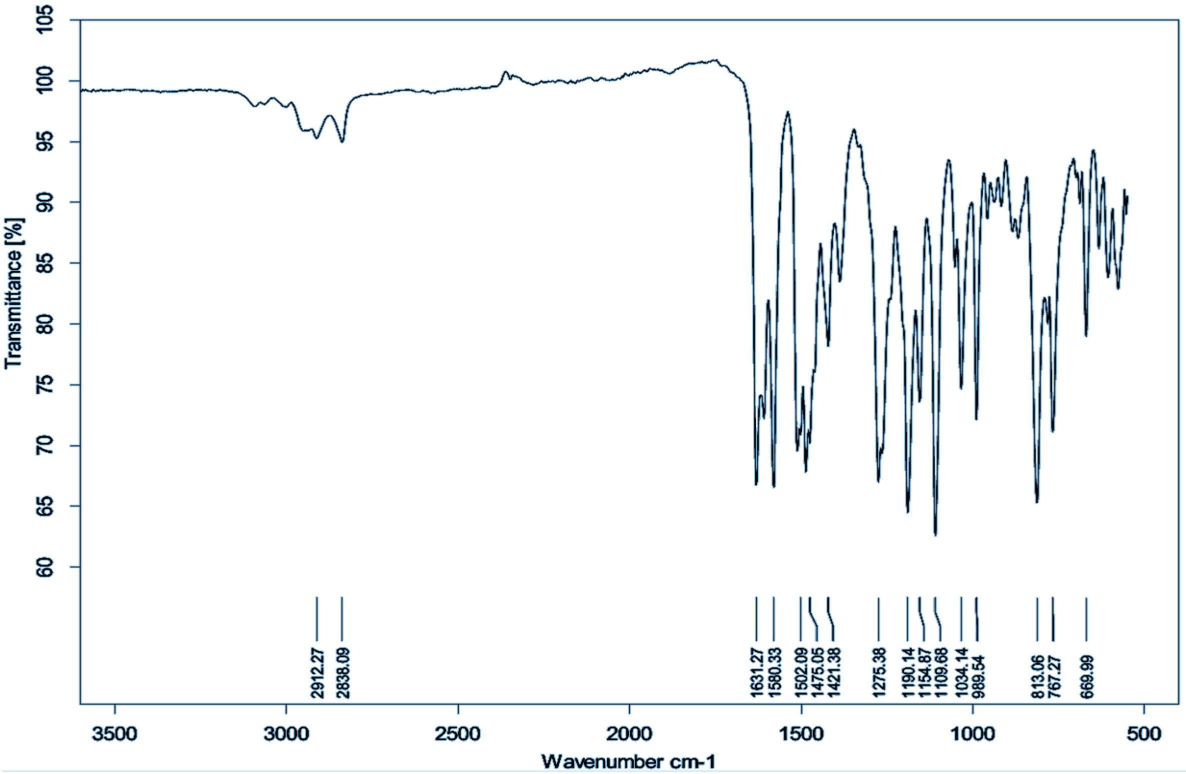


Figure S83: FT-IR - spectra of 6-35

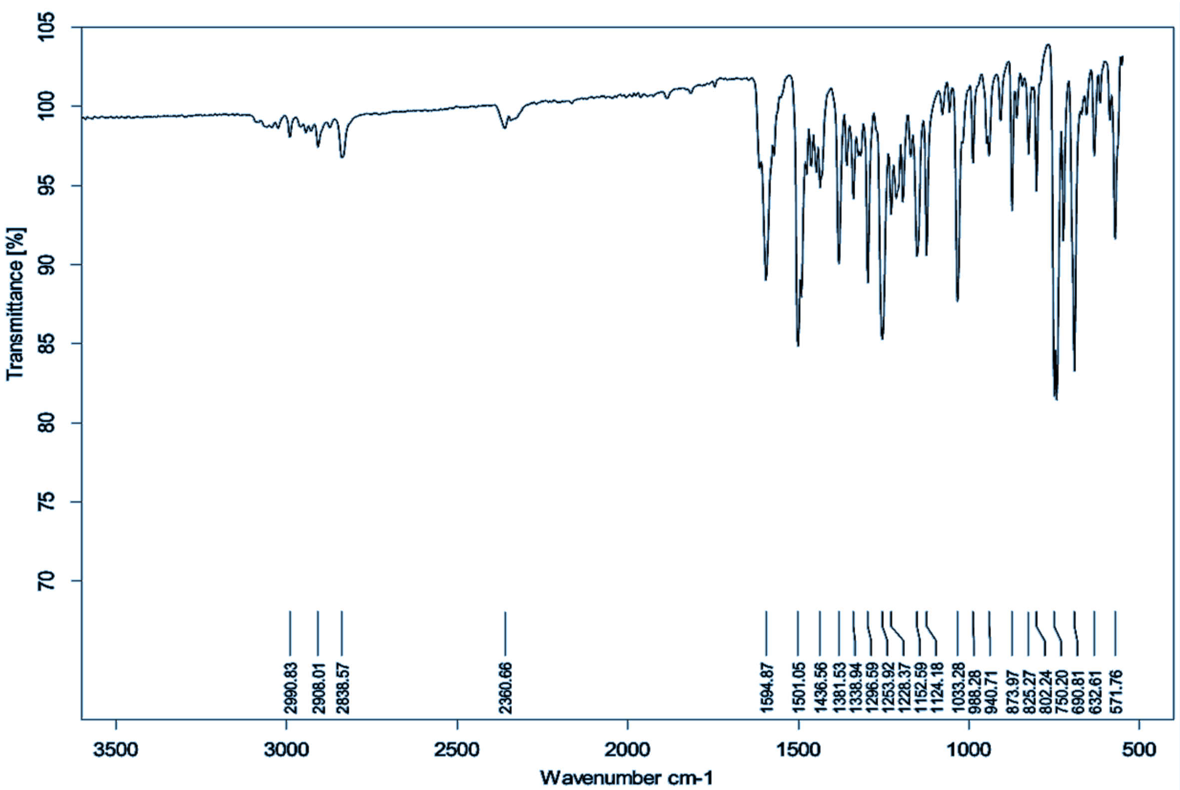


Figure S84: FT-IR - spectra of 6-37

Differential Scanning Calorimetry (DSC)

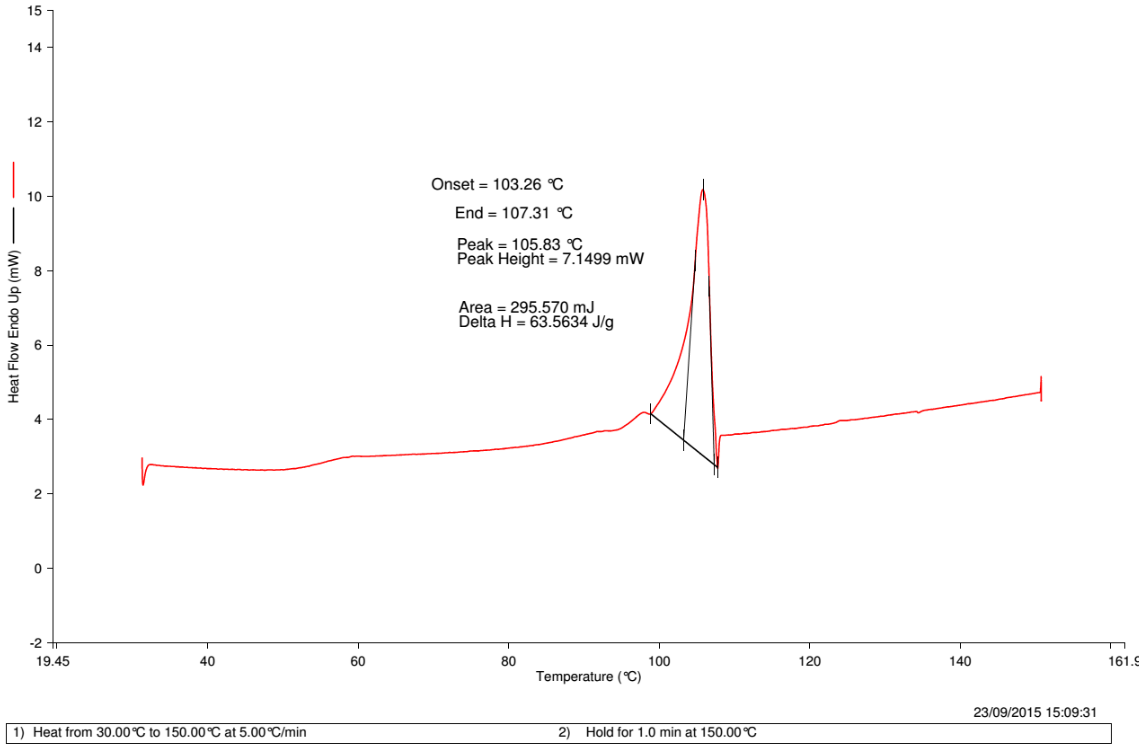


Figure S85: DSC of 6-1

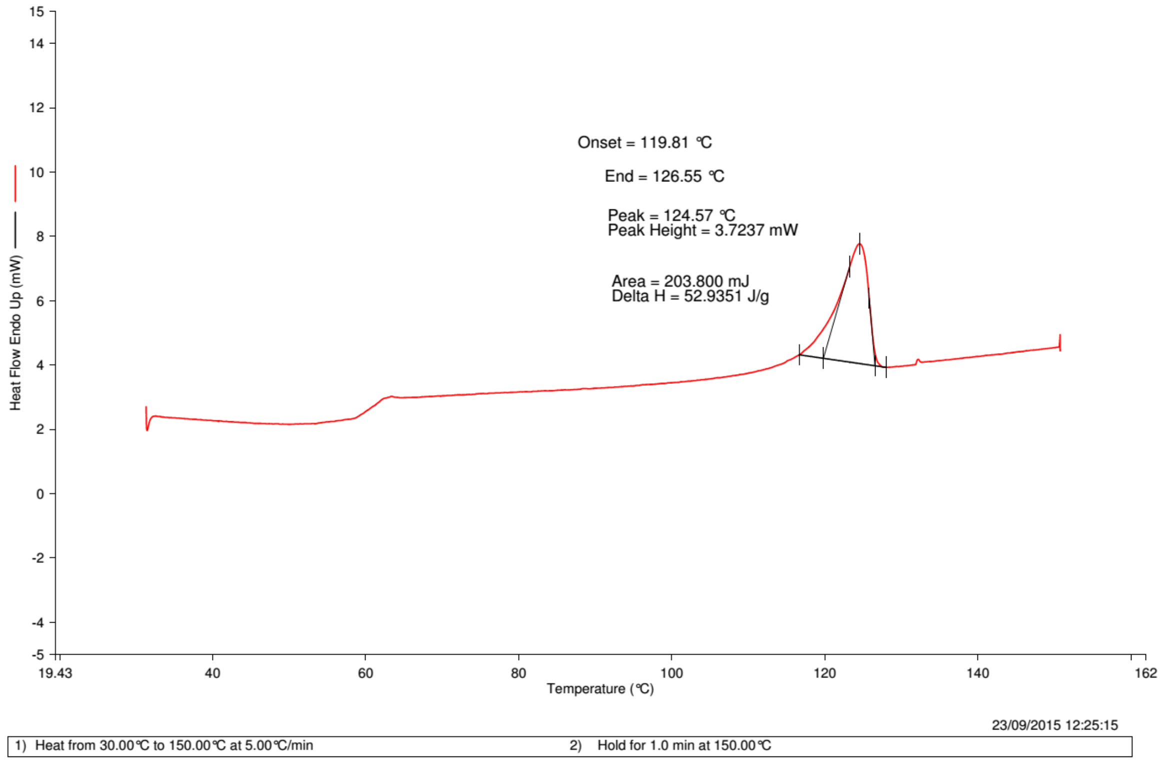


Figure S86: DSC of 6-2

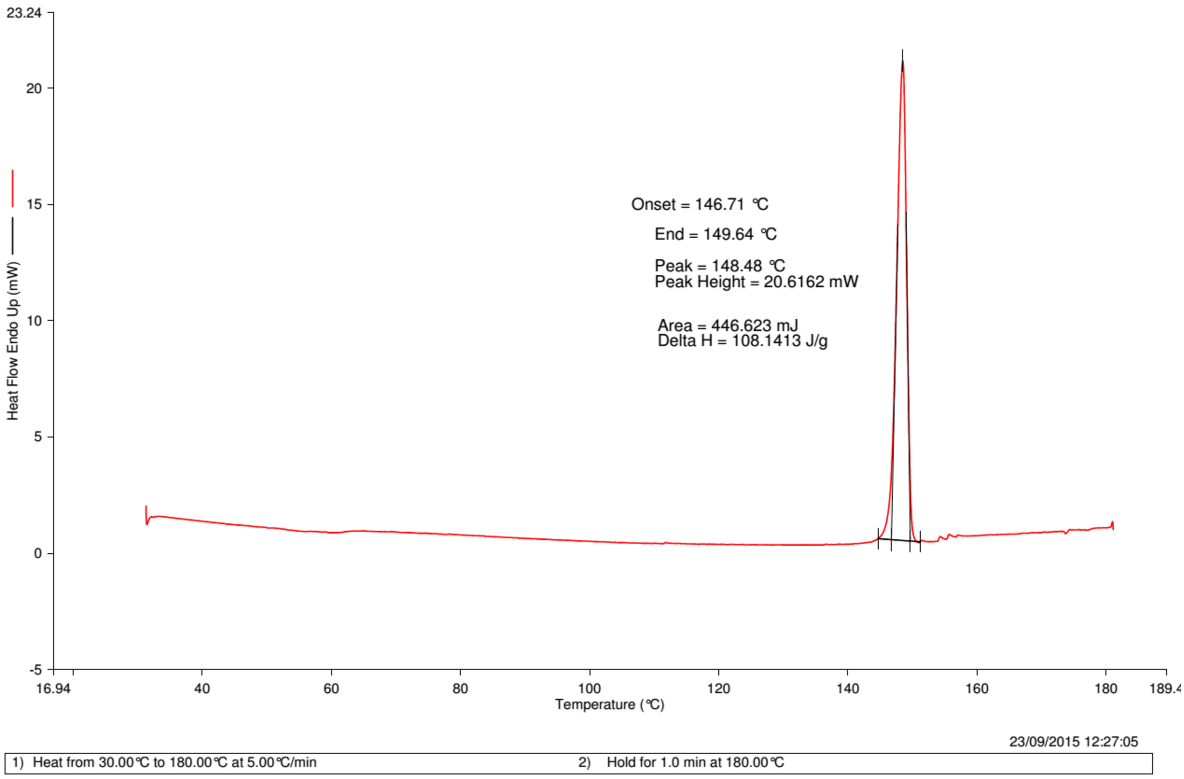


Figure S87: DSC of 6-3

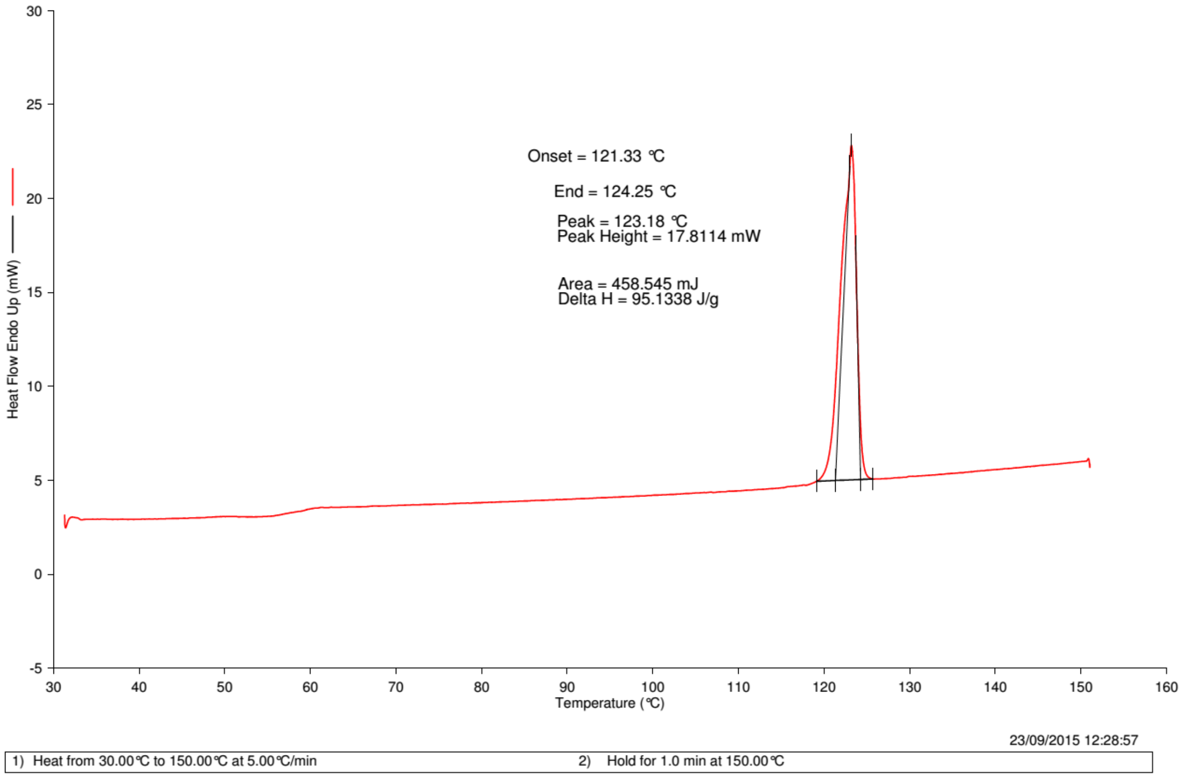


Figure S88: DSC of 6-4

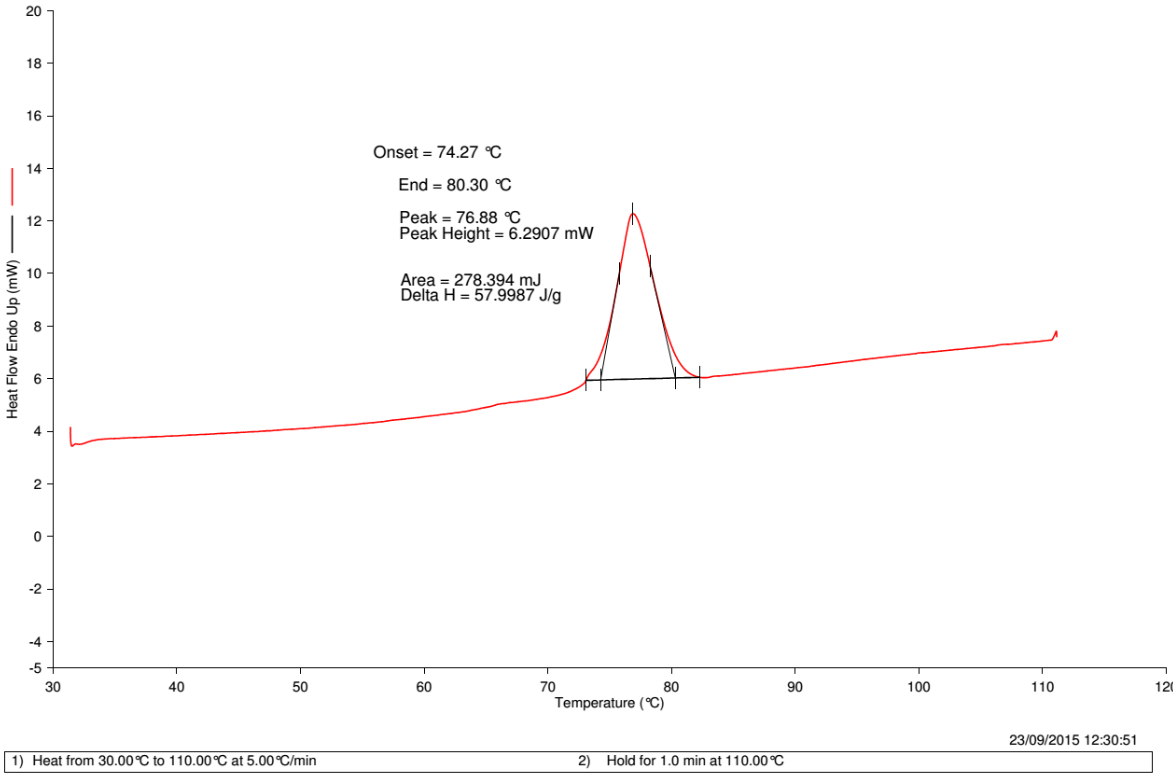


Figure S89: DSC of 6-5

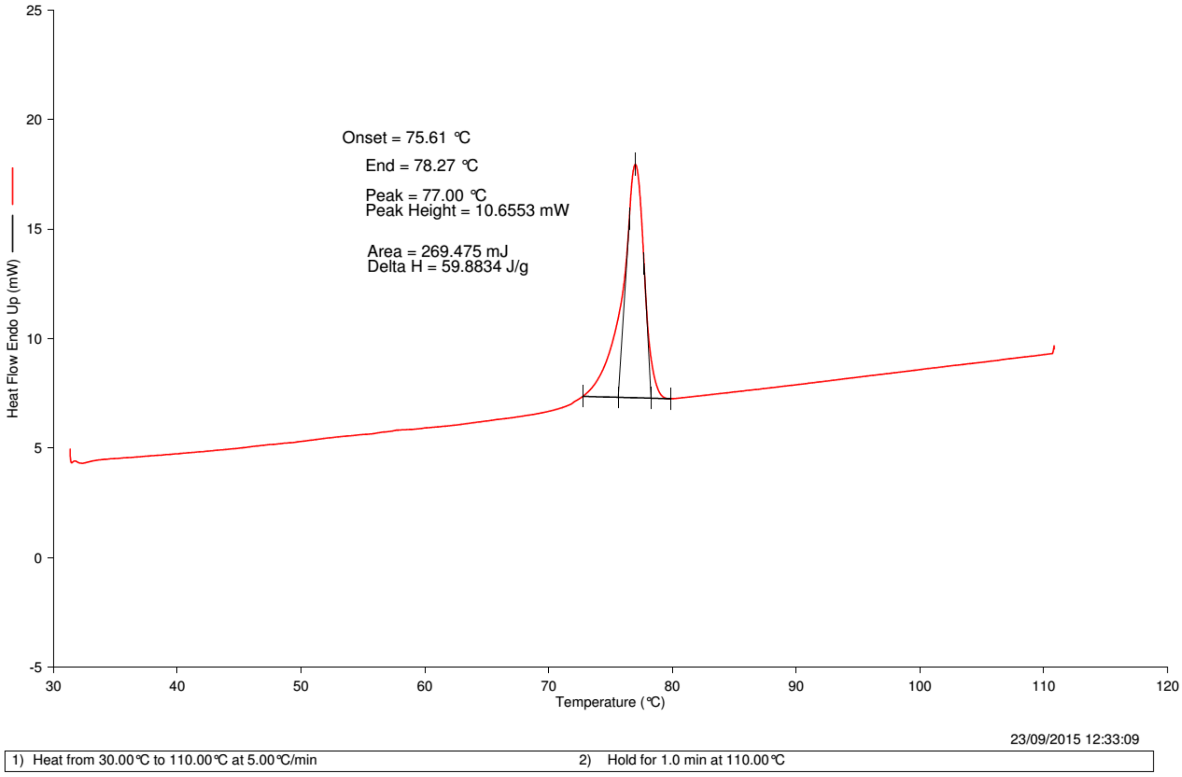


Figure S90: DSC of 6-6

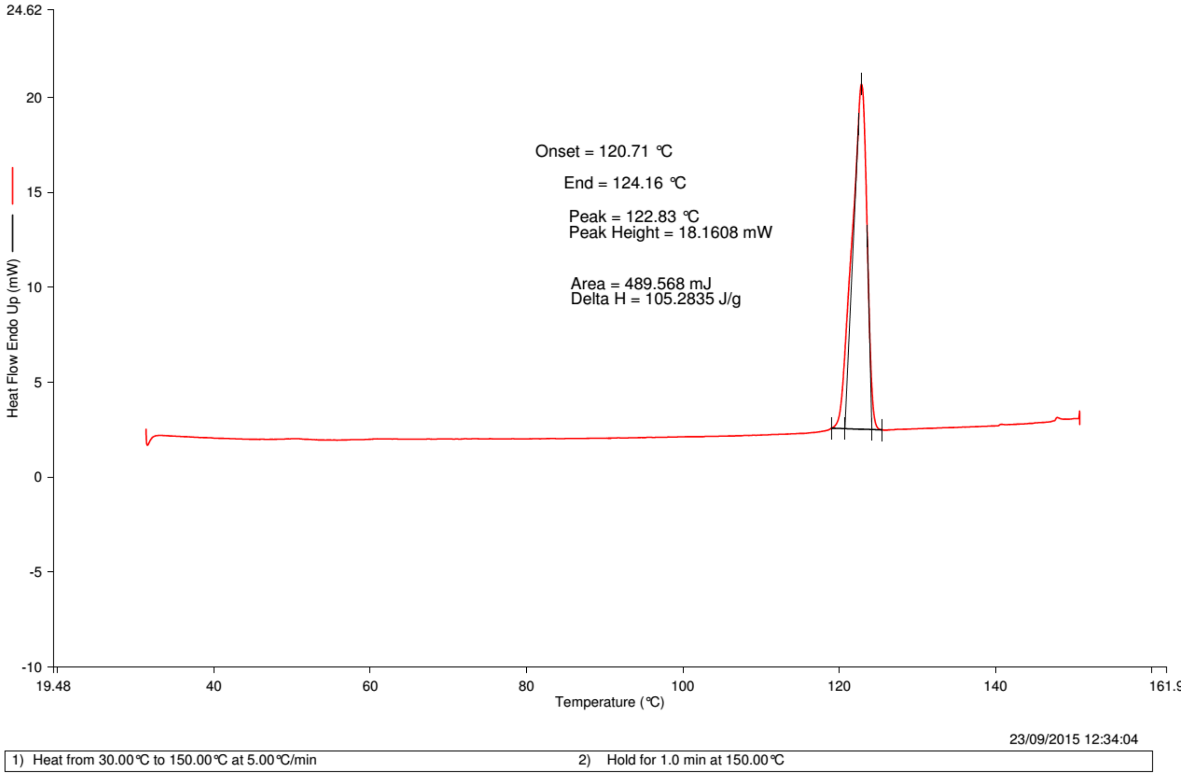


Figure S91: DSC of 6-7

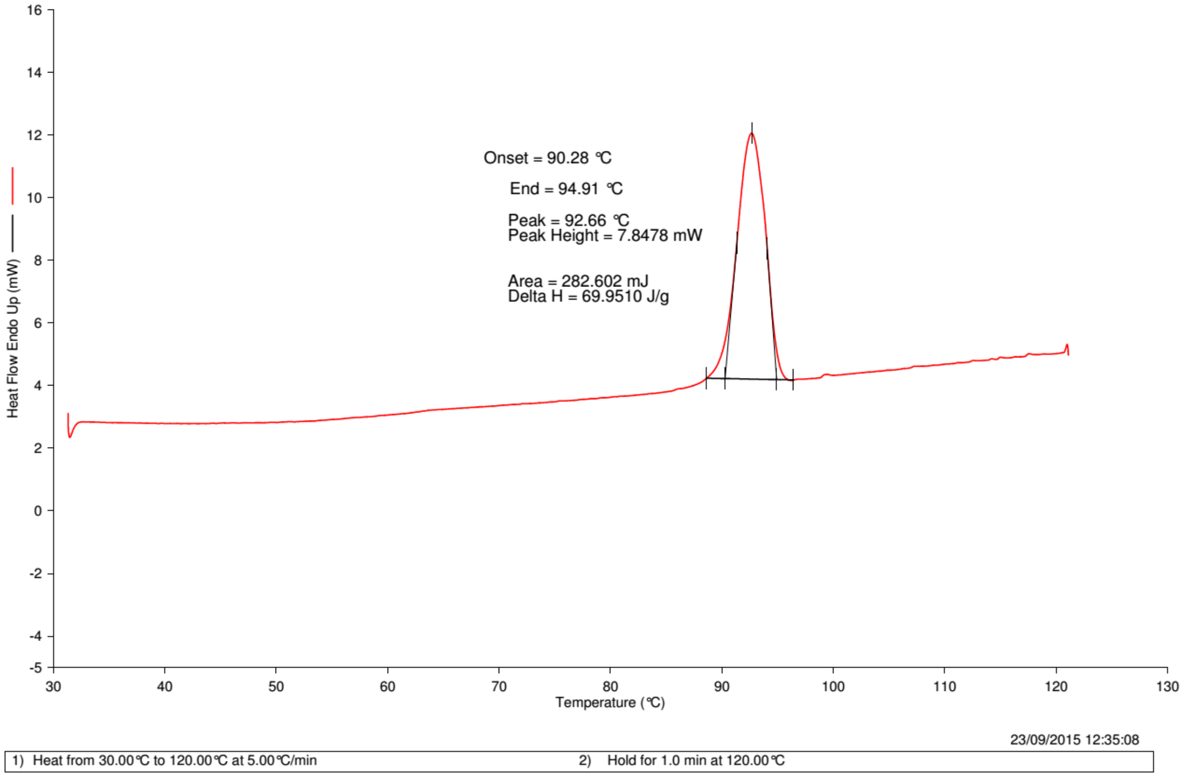


Figure S92: DSC of 6-8

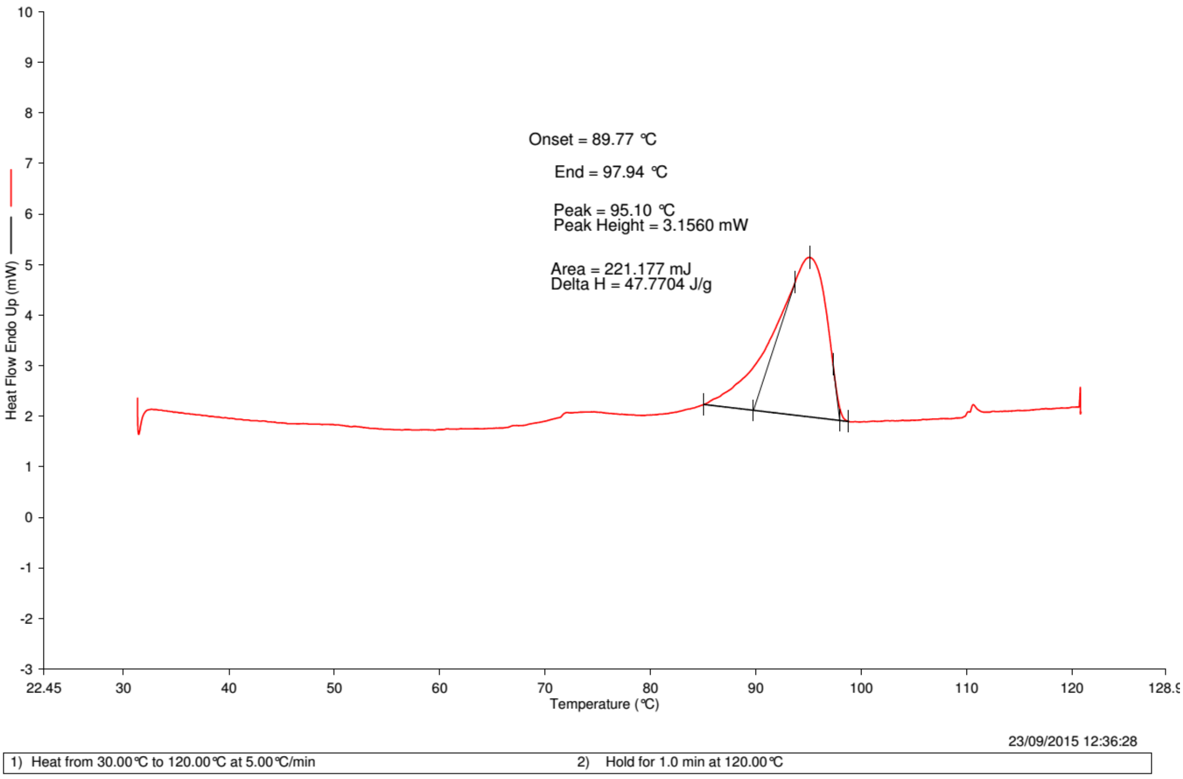


Figure S93: DSC of 6-9

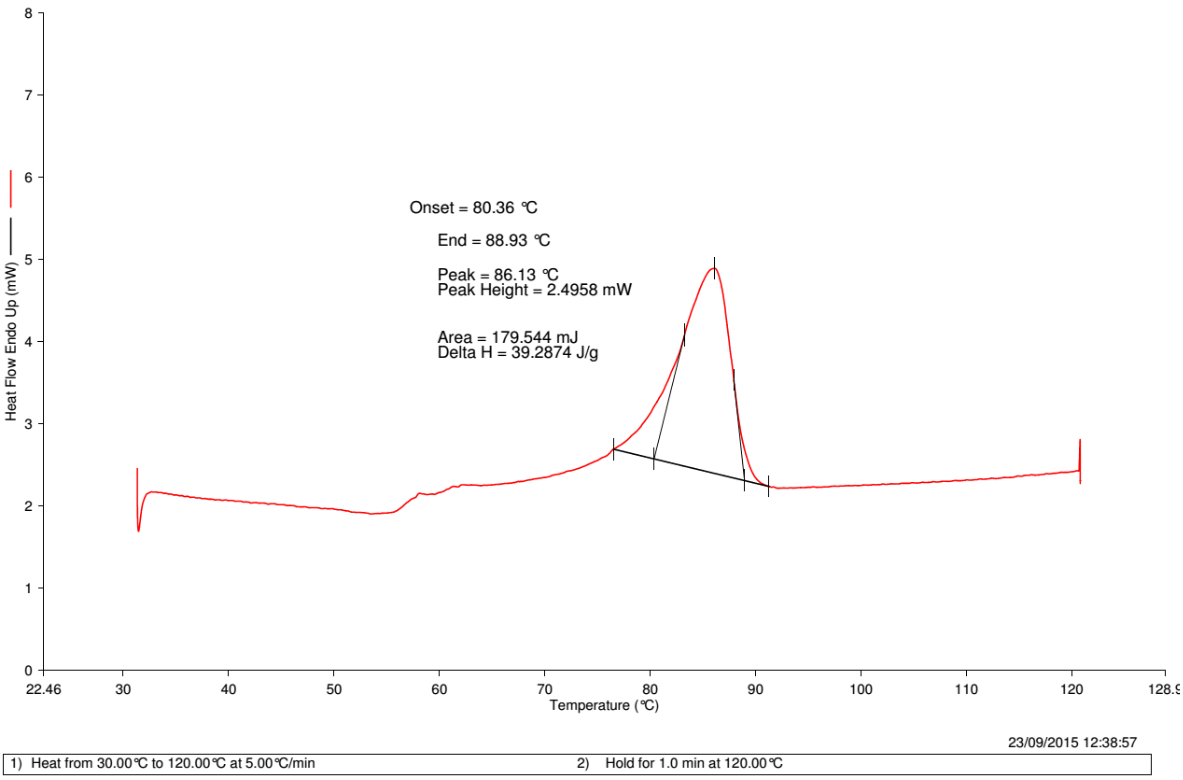


Figure S94: DSC of 6-13

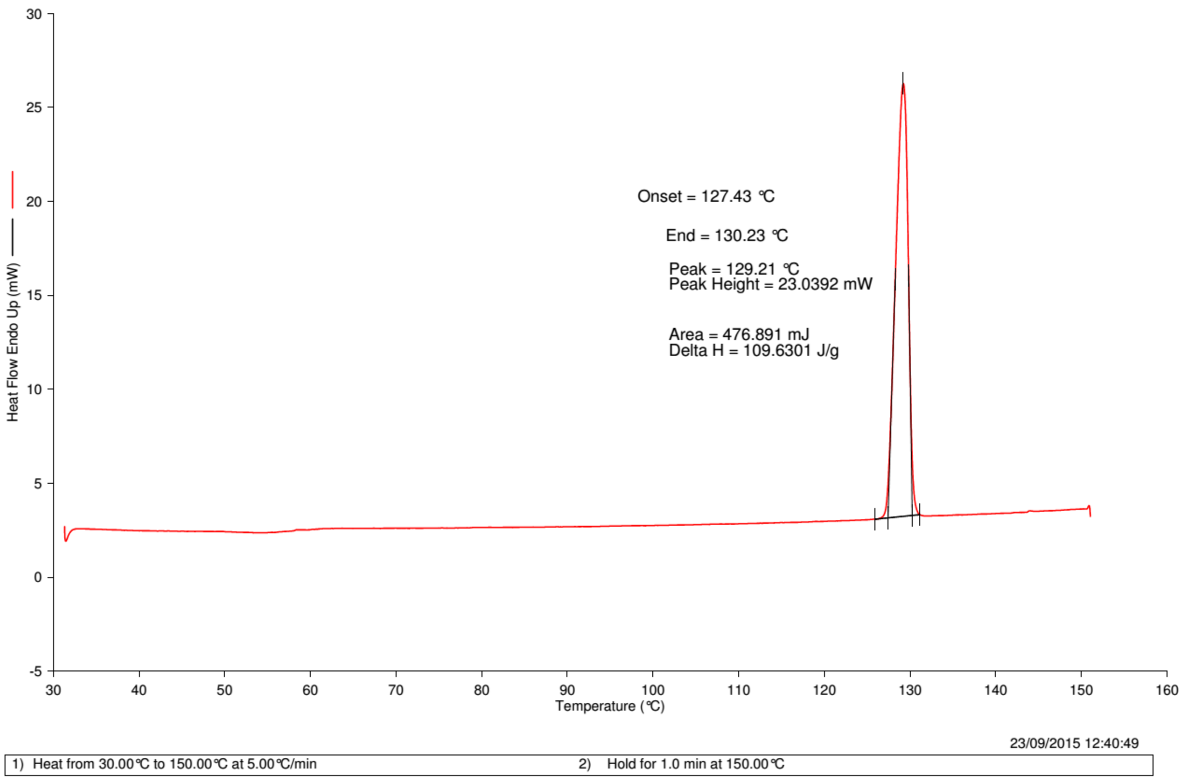


Figure S95: DSC of 6-14

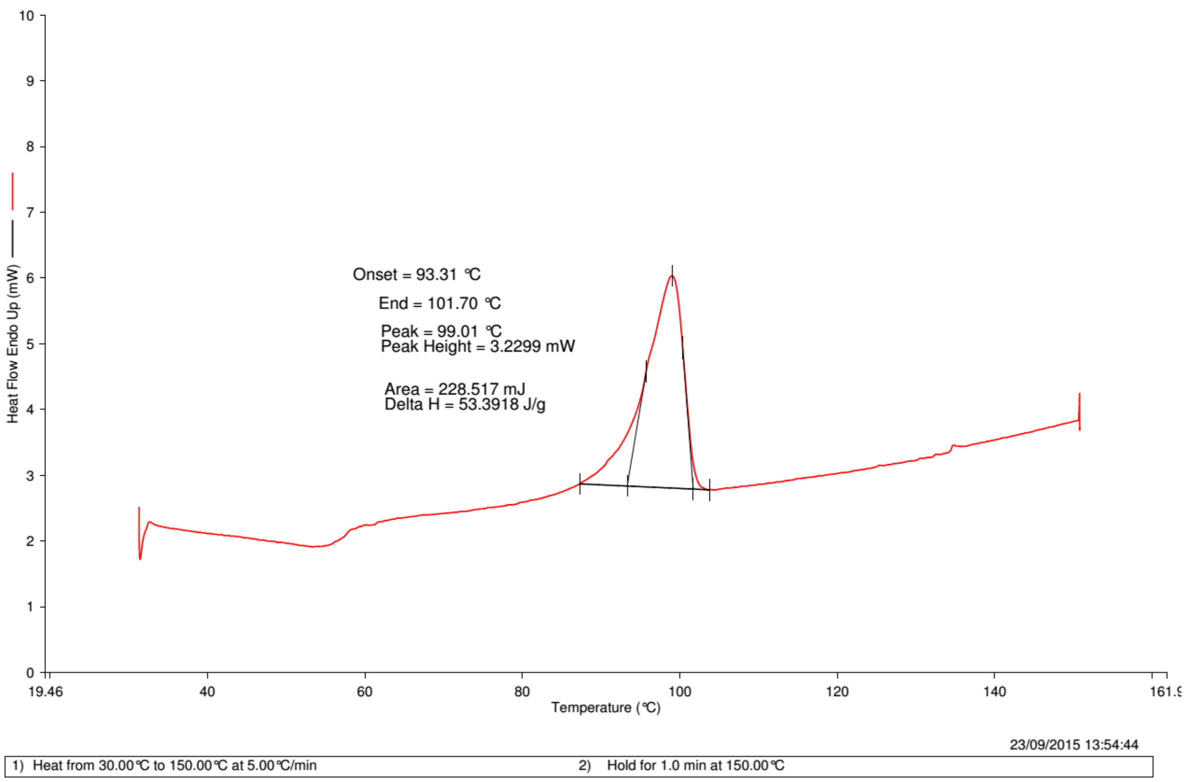


Figure S96: DSC of 6-16

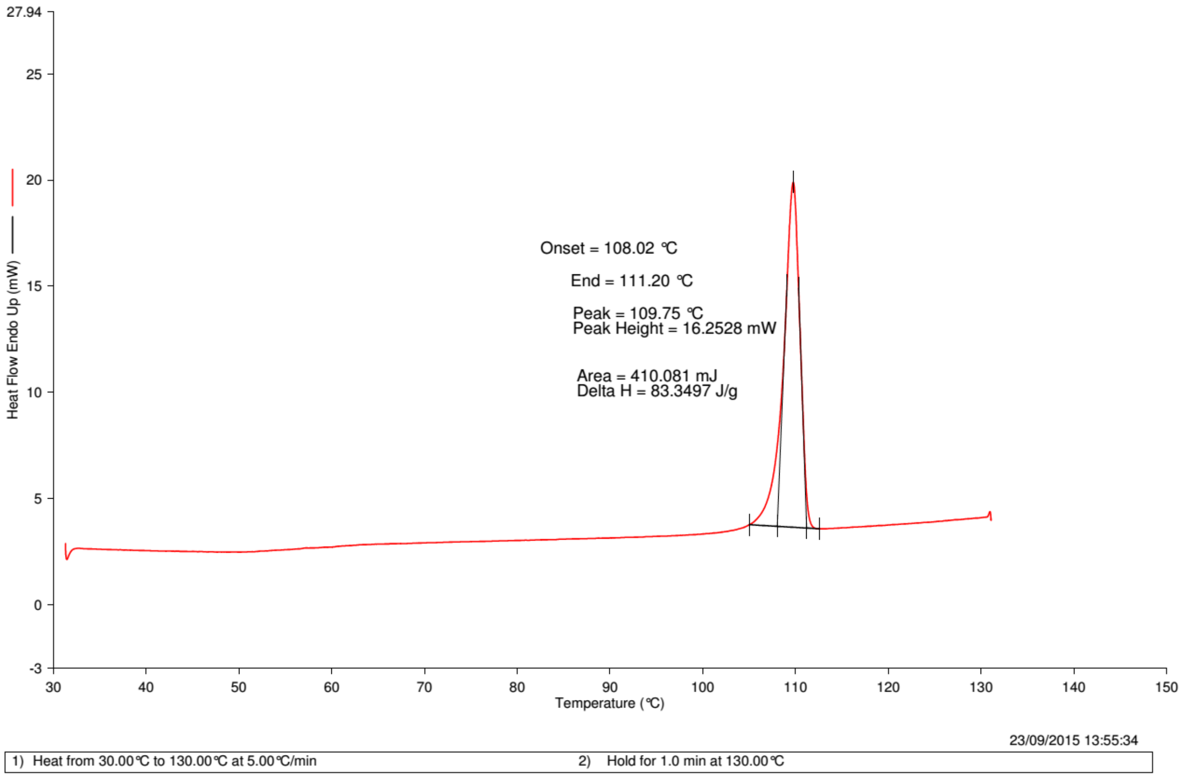


Figure S97: DSC of 6-19

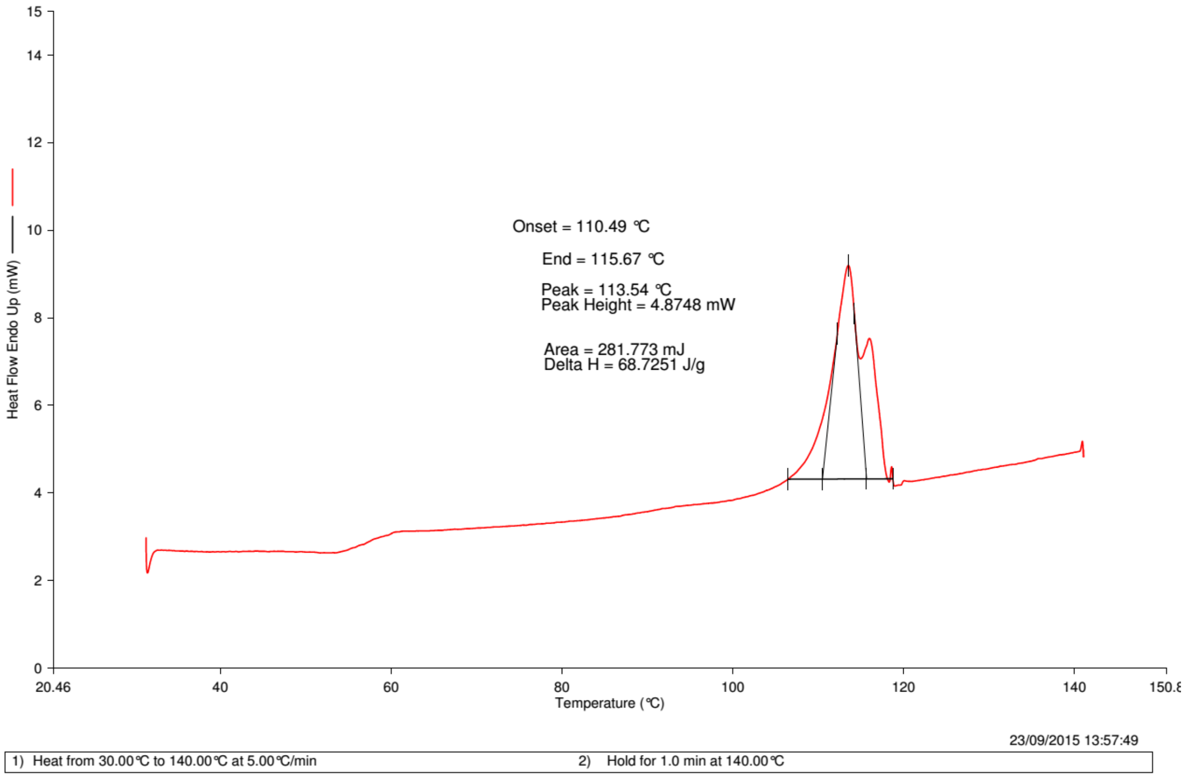


Figure S98: DSC of 6-21

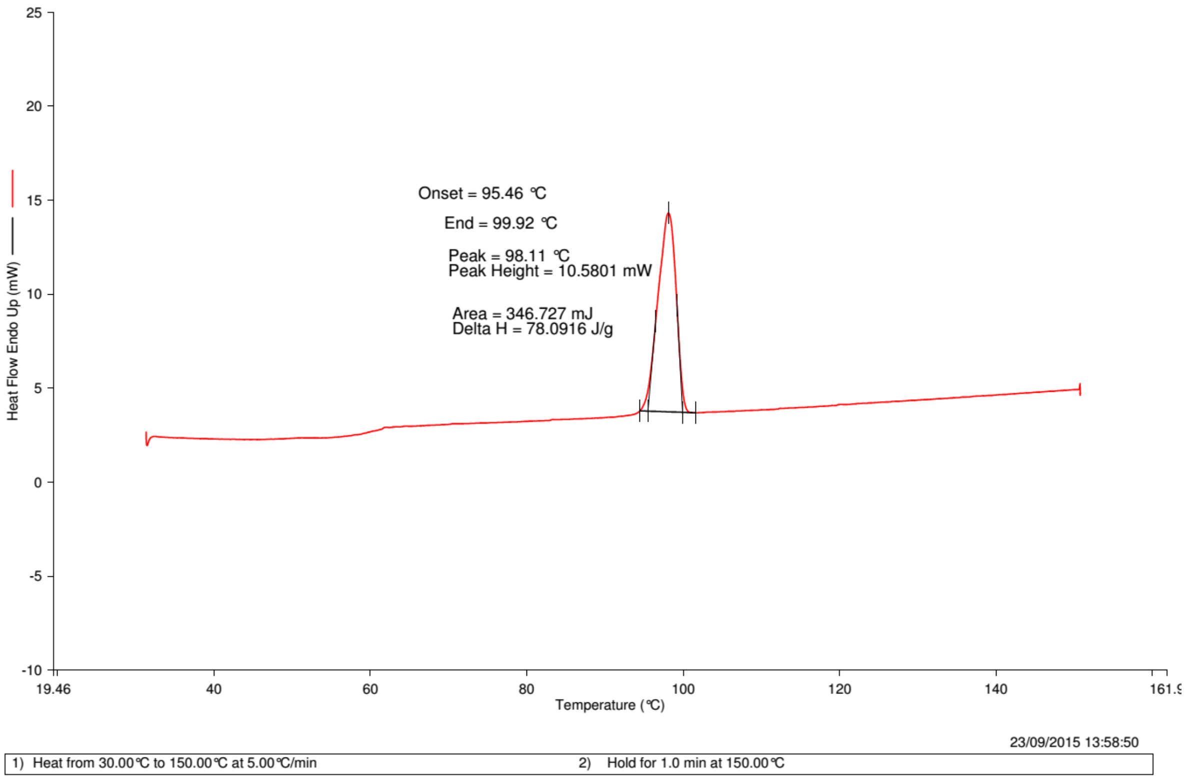


Figure S99: DSC of 6-23

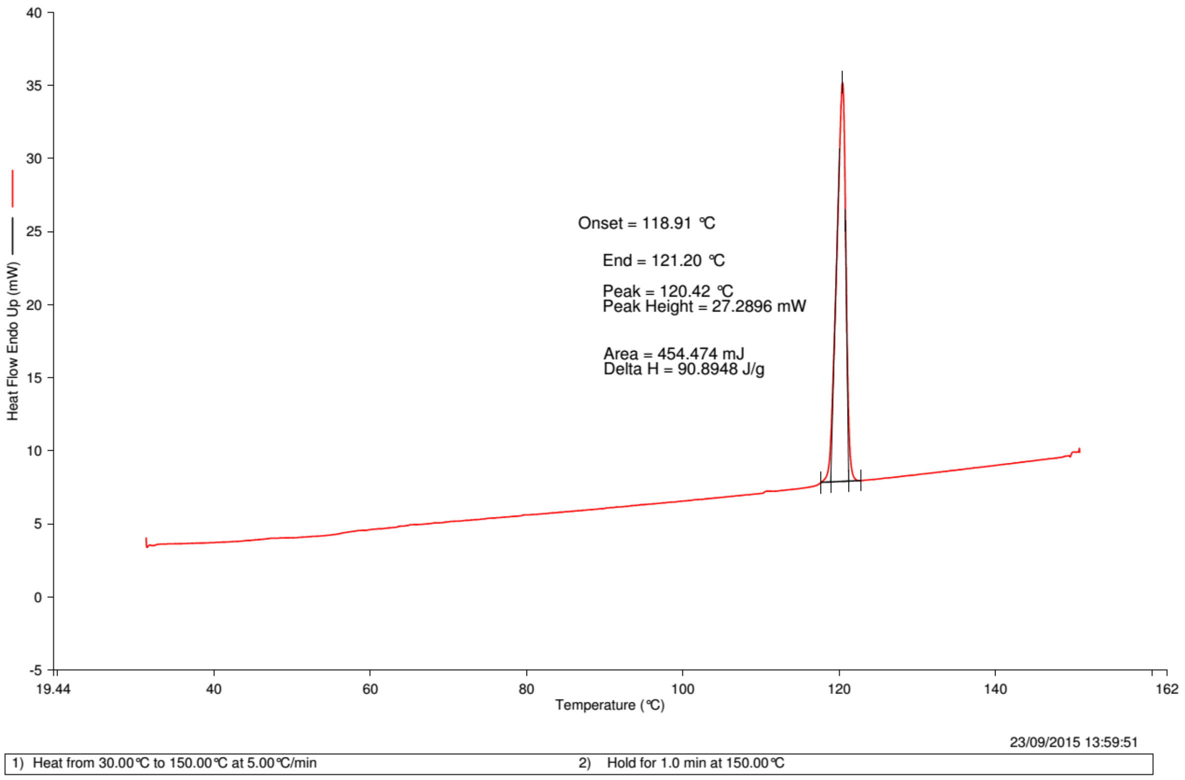


Figure S100: DSC of 6-24

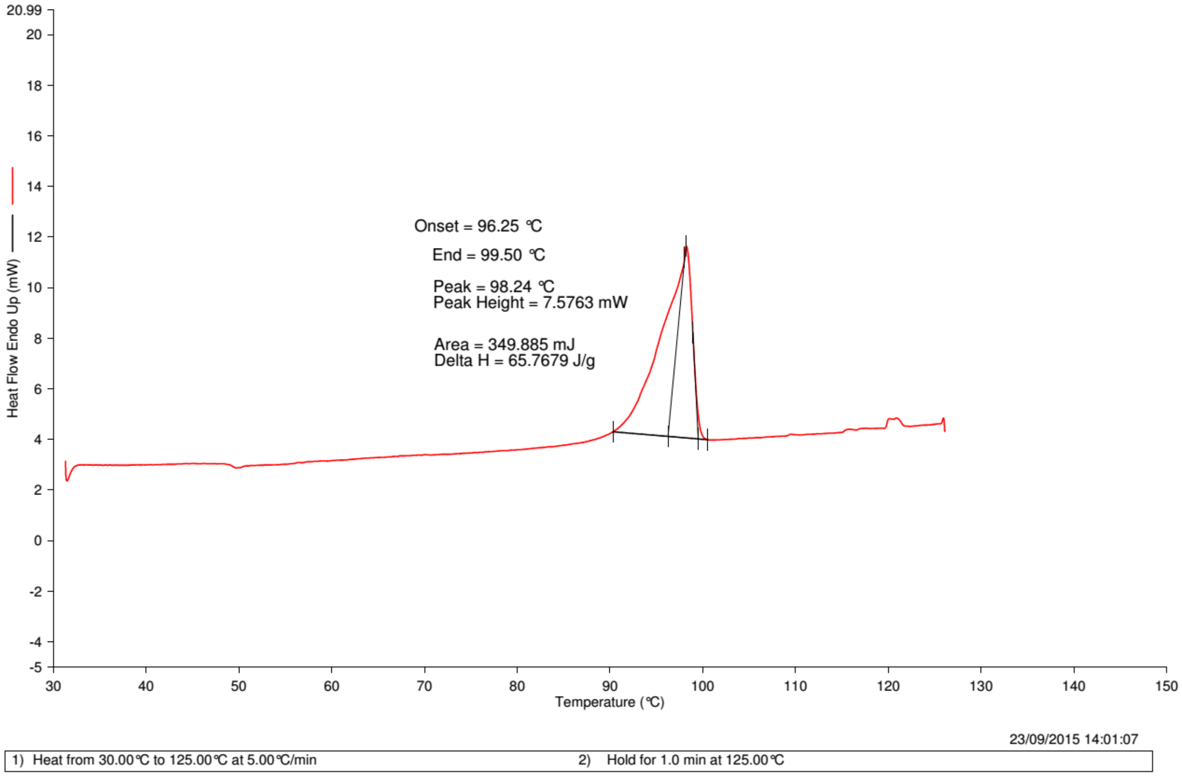


Figure S101: DSC of 6-25

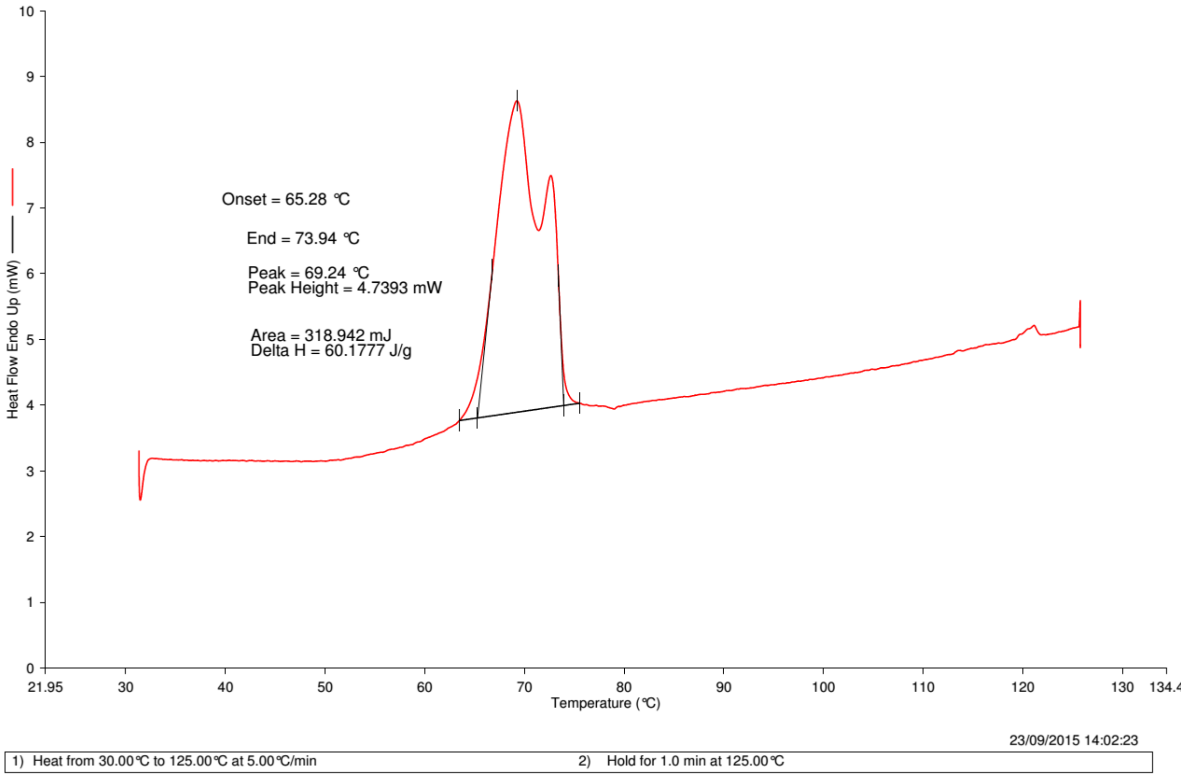


Figure S102: DSC of 6-26

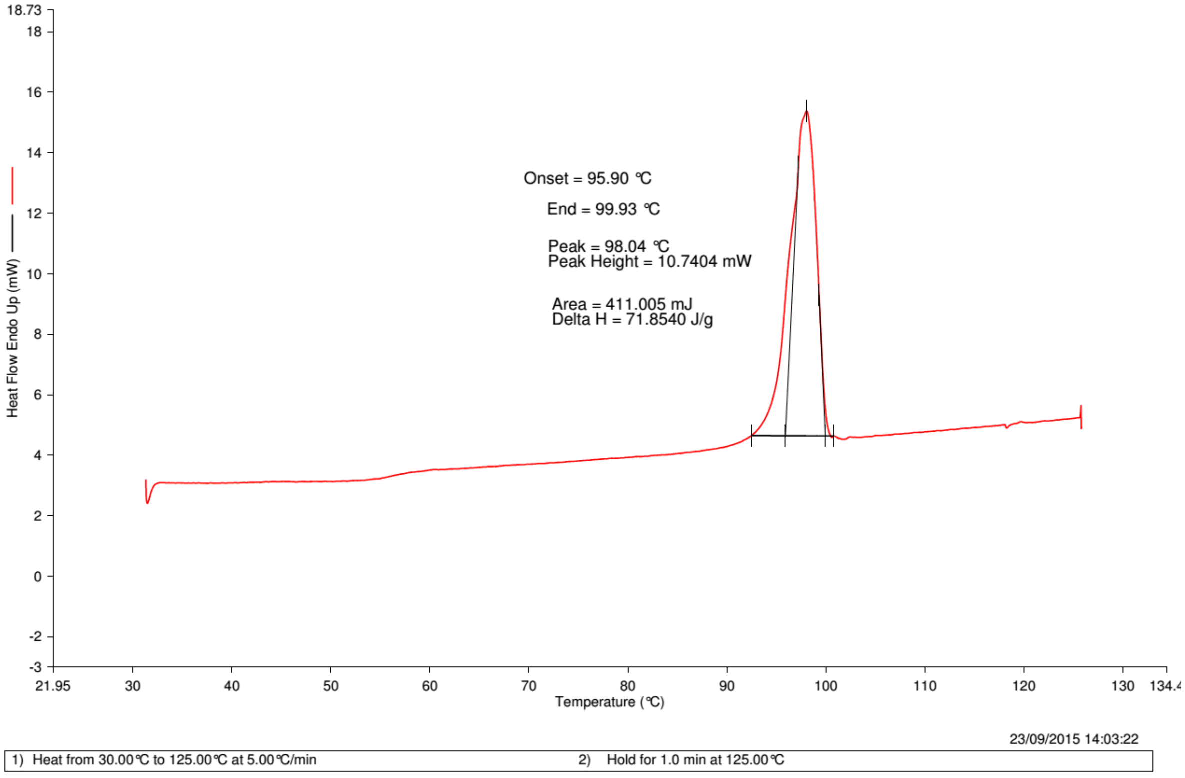


Figure S103: DSC of 6-27

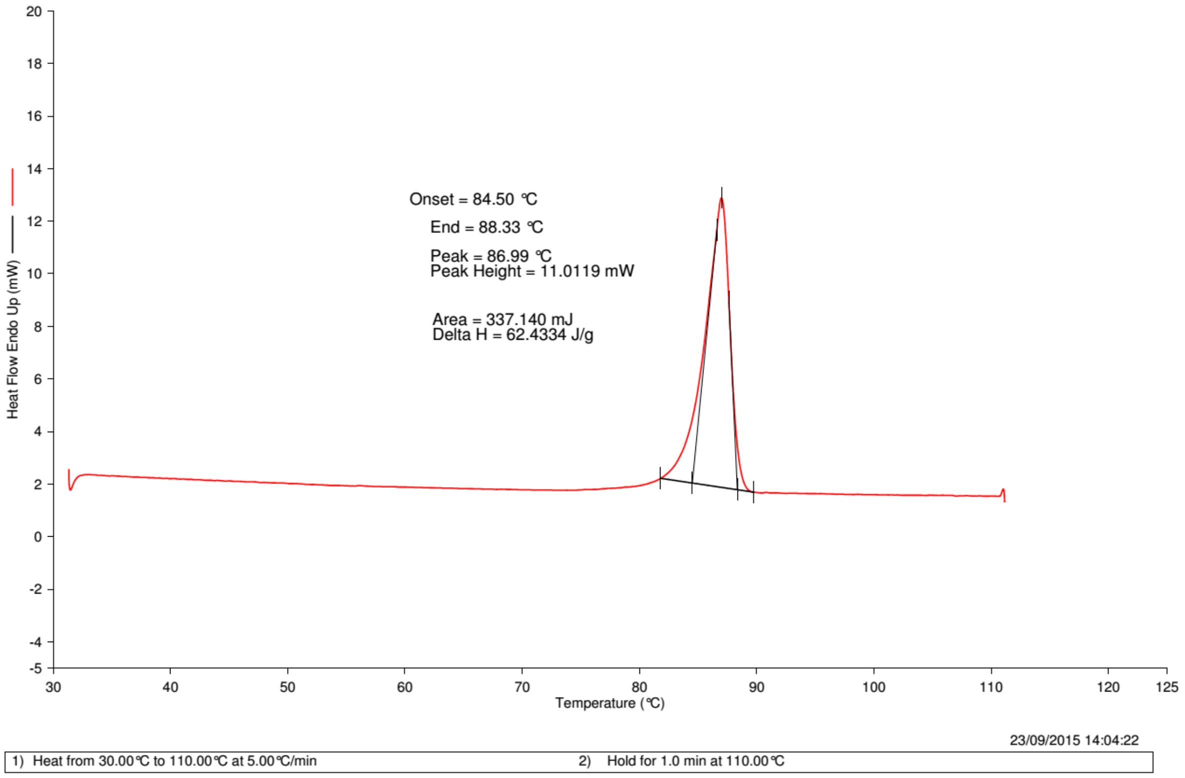


Figure S104: DSC of 6-30

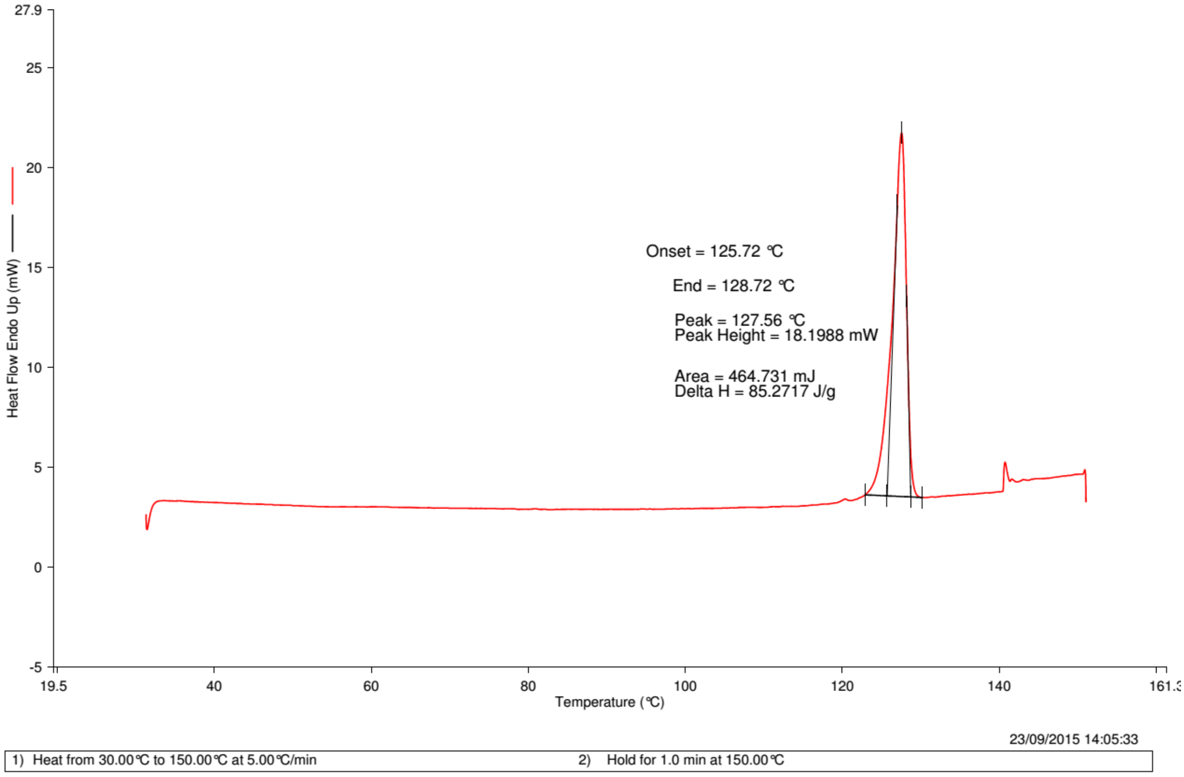


Figure S105: DSC of 6-33

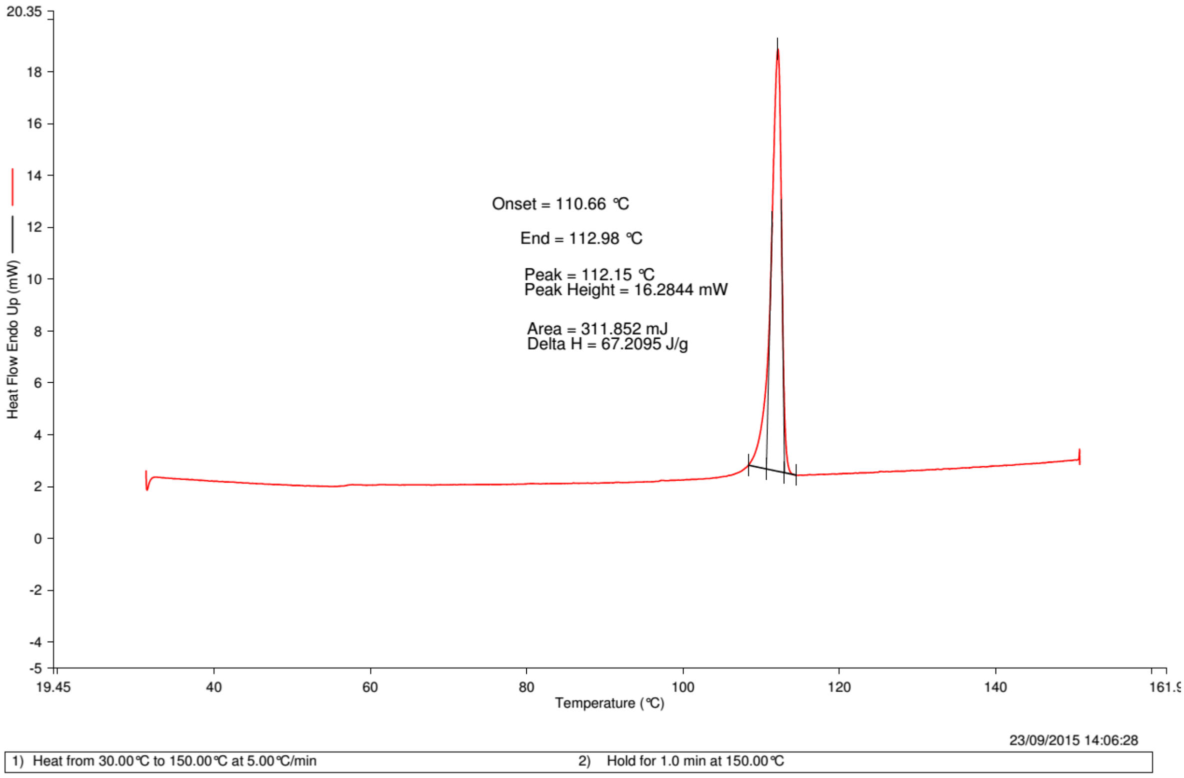


Figure S106: DSC of 6-34

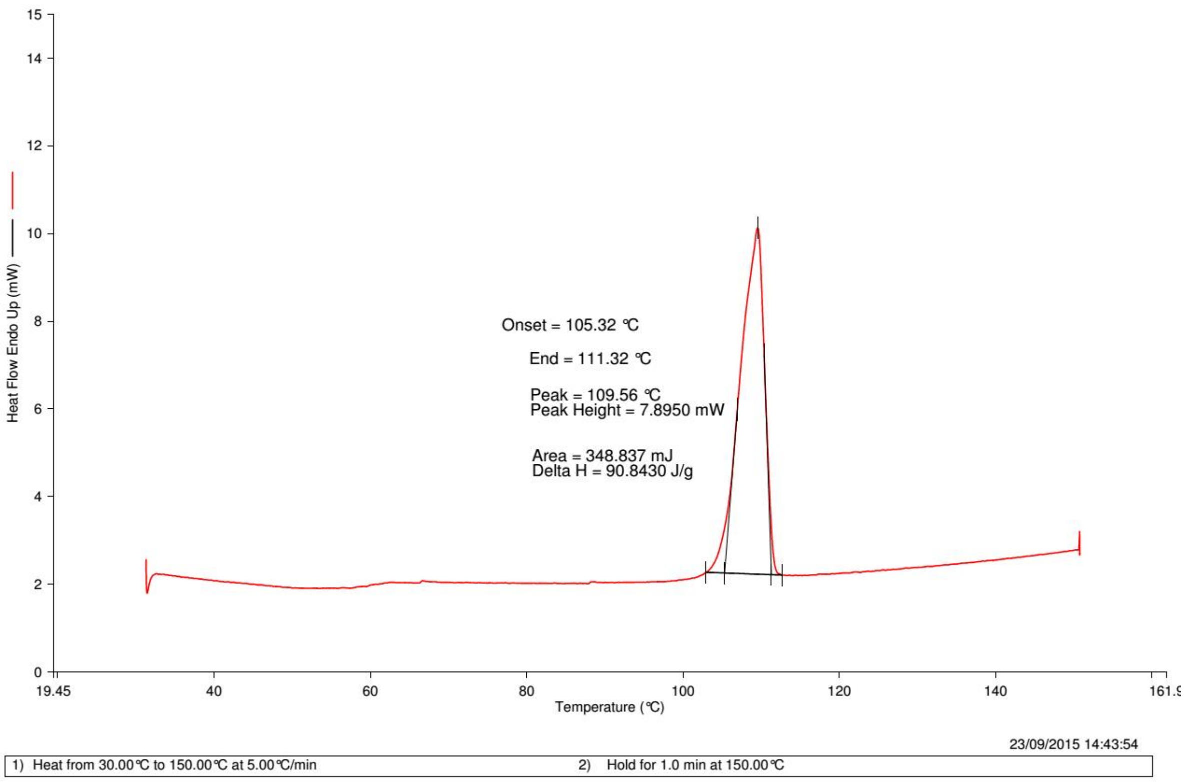
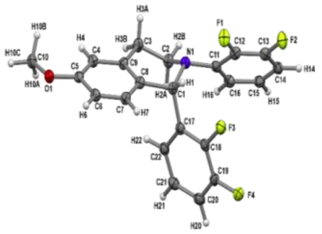
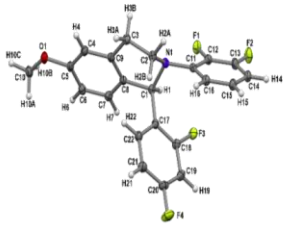
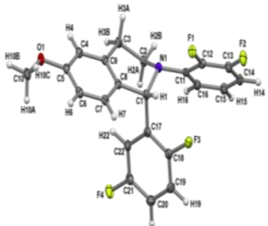


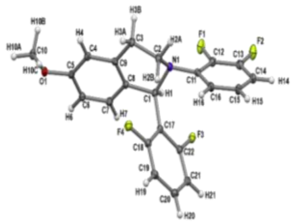
Figure S107: DSC of 6-37

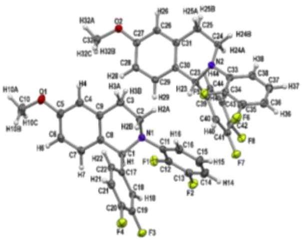


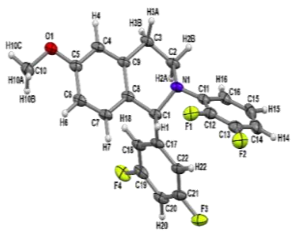




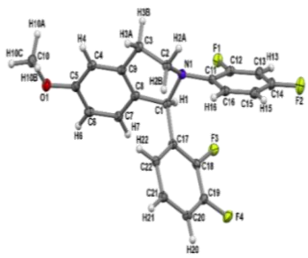
a **b** **c**

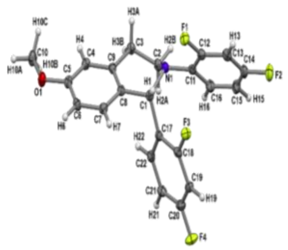


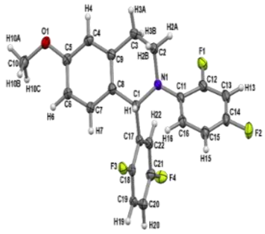




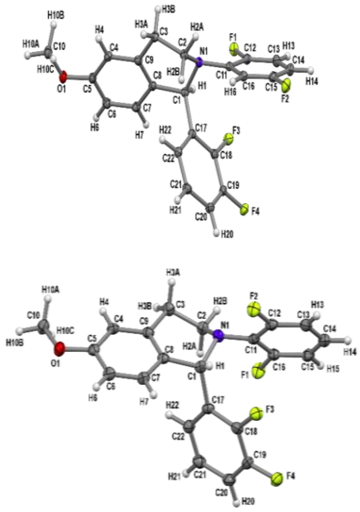
d **e** **f**

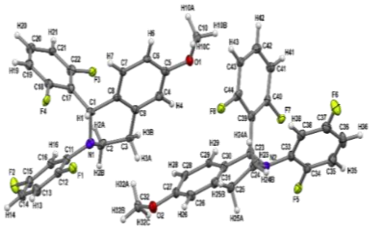




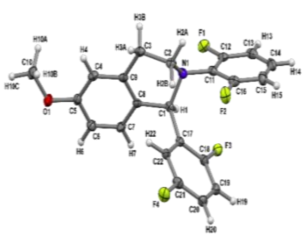


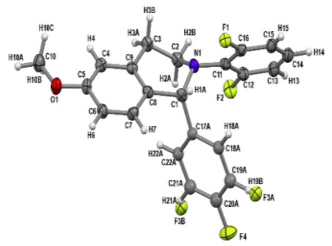
g **h** **i**

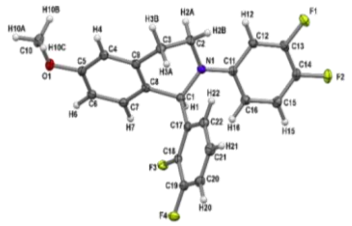




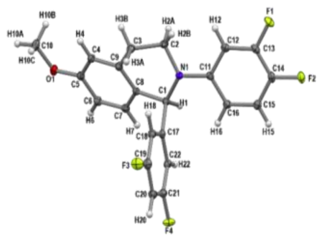
j **k** **l**

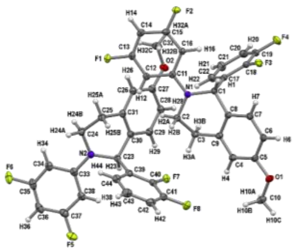


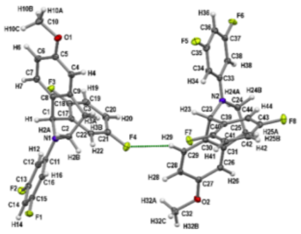




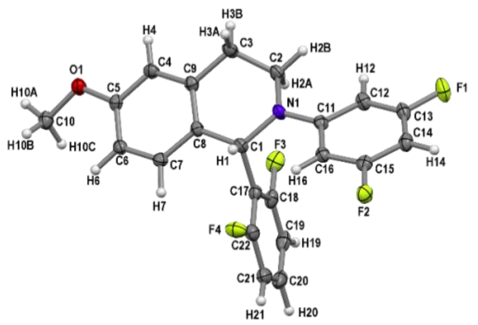
m **n** **o**

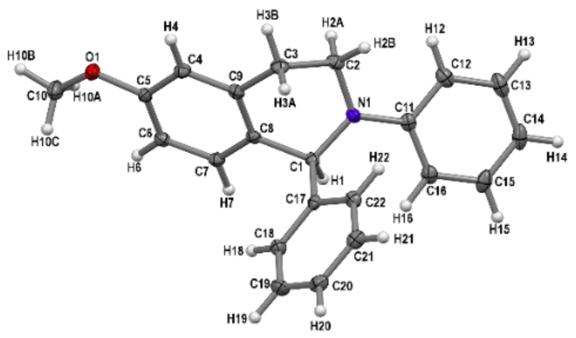






p **q** **r**





s **t**

Figure S108: a: ORTEP of **6-1** drawn with 50% ellipsoidal probability. **b:** ORTEP of **6-2** drawn with 50% ellipsoidal probability. **c:** ORTEP of **6-3** drawn with 50% ellipsoidal probability. **d:** ORTEP of **6-4** drawn with 50% ellipsoidal probability. **e:** ORTEP of **6-5** drawn with 50% ellipsoidal probability. **f:** ORTEP of **6-6** drawn with 50% ellipsoidal probability. **g:** ORTEP of **6-7** drawn with 50% ellipsoidal probability. **h**: ORTEP of 6-9 drawn with 50% ellipsoidal probability. **i:** ORTEP of **6-9** drawn with 50% ellipsoidal probability. **j:** ORTEP of

6-13 drawn with 50% ellipsoidal probability. **k:** ORTEP of **6-16** drawn with 50% ellipsoidal probability. **l:** ORTEP of **6-19** drawn with 50% ellipsoidal probability. **m:** ORTEP of **6-21** drawn with 50% ellipsoidal probability. **n:** ORTEP of **6-23** drawn with 50% ellipsoidal probability. **o:** ORTEP of **6-25** drawn with 50% ellipsoidal probability. **p:** ORTEP of **6-30** drawn with 50% ellipsoidal probability. **q:** ORTEP of **6-31** drawn with 50% ellipsoidal probability. **r**: ORTEP of **6-33** drawn with 50% ellipsoidal probability. **s:** ORTEP of **6-34** drawn with 50% ellipsoidal probability. **t:** ORTEP of **6-37** drawn with 50% ellipsoidal probability.

Table S4: Intermolecular interaction Energies

S. No.	Compound	ΔE H-F Dimer (Kcal/mol)	ΔE H-H Dimer (Kcal/mol)	(H-F dimer)-(H-H dimer)
1	6_1	-5.595650766	-5.61054	0.014892
2	6_2	-6.34252231	-7.24684	0.904317
3	6_2	-6.23578624	-5.04921	-1.18658
4	6_2	-1.512013779	2.363175	-3.87519
5	6_2	-9.11129849	-8.51026	-0.60104
6	6_2	-2.188494349	-1.46582	-0.72268
7	6_3	-9.16543009	-8.45733	-0.7081
8	6_3	-7.848089259	-7.1813	-0.66679
9	6_3	-2.210777045	-1.21552	-0.99526
10	6_3	-6.802425953	-5.66076	-1.14167
11	6_3	-4.209668037	-3.67474	-0.53493
12	6_4	-6.858066579	-7.35943	0.50136
13	6_5	-5.642066667	-5.77356	0.131497
14	6_5	-2.482646659	-1.95803	-0.52462
15	6_5	-2.506156257	-1.69603	-0.81013
16	6_6	-8.254860506	-7.45509	-0.79977
17	6_6	-1.173843555	-0.221	-0.95284
18	6_6	-8.262831187	-7.49454	-0.76829
19	6_6	-4.23801208	-3.68539	-0.55262
20	6_7	-1.230880303	-1.00733	-0.22355
21	6_7	-6.800862742	-6.09154	-0.70932
22	6_7	-10.23707847	-9.42417	-0.81291
23	6_8	-3.27340171	-3.52366	0.250258
24	6_8	-1.206847951	-1.06697	-0.13988
25	6_9	-2.768616463	-2.45855	-0.31006
26	6_9	-0.890932615	-0.26271	-0.62822
27	6_9	-5.596248015	-5.11676	-0.47948
28	6_9	-2.753582777	-2.46468	-0.28891
29	6_13	-6.831952851	-6.40833	-0.42363
30	6_13	-10.02400904	-9.29979	-0.72422
31	6_13	-6.831951766	-6.40832	-0.42363
32	6_16	-2.139205767	-3.48425	1.345045
33	6_16	-7.799419375	-7.34845	-0.45097
34	6_16	-5.954897137	-6.4968	0.541903
35	6_16	-1.861249074	-2.05862	0.197372
36	6_16	-5.954905257	-6.44021	0.485303
37	6_16	-5.9549051	-6.24453	0.289625
38	6_16	-7.799427638	-7.34846	-0.45097
39	6_19	-10.04539009	-9.19249	-0.8529
40	6_19	-5.552135367	-5.04775	-0.50439
41	6_19	-5.552135981	-5.04775	-0.50439
42	6_21	-5.106083422	-4.19756	-0.90853
43	6_21	-5.106083767	-4.19755	-0.90853
44	6_21	-1.917554169	-0.97721	-0.94035

45	6_23	-6.624533658	-7.28422	0.659687
46	6_23	-6.600788917	-6.06395	-0.53684
47	6_25	-4.775515479	-3.48665	-1.28886
48	6_25	-3.835721024	-2.72015	-1.11557
49	6_30	-1.498313002	-1.09391	-0.4044
50	6_30	-4.109781382	-3.67483	-0.43495
51	6_30	-3.45644777	-1.46913	-1.98731
52	6_30	-2.956137654	-1.51694	-1.4392
53	6_31	-13.93352217	-12.4626	-1.47093
54	6_31	-5.685554728	-4.59239	-1.09316
55	6_31	-4.89651888	-3.49577	-1.40075
56	6_31	-5.6855518	-4.60452	-1.08103
57	6_31	-1.502590502	-0.86897	-0.63362
58	6_31	-1.12466039	-0.32001	-0.80465
59	6_31	-4.081186131	-3.55629	-0.5249
60	6_33	1.745951272	-1.13974	2.885687
61	6_33	3.230084368	0.601909	2.628175
62	6_33	-1.820689497	-5.3921	3.571411
63	6_33	-6.137086948	-9.13571	2.998626
64	6_33	-3.124364168	-6.15321	3.028844
65	6_33	2.508191235	2.757678	-0.24949
66	6_33	-1.073778531	-4.76507	3.691287
67	6_33	-10.59898228	-3.31603	-7.28295
68	6_33	-1.895359209	-5.4098	3.514443
69	6_33	-0.95431439	-0.67097	-0.28334
70	6_33	-0.954316898	-0.67097	-0.28335
71	6_34	-3.714484153	-2.96025	-0.75424

References:

Burla, M.; Caliandro, R; Camalli, M.; Carrozzini, B.; Cascarano, G.; De C.; Liberato; Giacovazzo, C.; Polidori, G.; Spagna, R. SIR2004: An Improved Tool for Crystal Structure Determination and Refinement. *J. Appl. Crystallogr.* **2005**, *38*, 381-388.

CrystalClear2.0, Rigaku Corporation, Tokyo, Japan, **2013**.

Dolomanov, O.V.; Bourhis, L.J.; Gildea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Cryst*. **2009**, *42*, 339-341.

Macrae, C. F.; Bruno, I. J.; Chisholm, J. A.; Edgington, P. R.; McCabe, P.; Pidcock, E.; Rodriguez-Monge, L.; Taylor, R.; Streek, J.; Wood, P. A *J. Appl. Crystallogr.* **2008**, *41*, 466–470.

Nardelli, M. *J. Appl. Crystallogr*. **1995**, *28*, 569.

Roisnel T.; Rodriguez-Carvajal, J. WinPLOTR: a Windows tool for powder diffraction patterns analysis Materials Science Forum, Proceedings of the Seventh European Powder Diffraction Conference (EPDIC 7), **2000**, 118-123.

Sheldrick, G.M.; *Acta Crystallogr.* **2008**, *A64*, 112-122.

Sheldrick, G.M.; *Acta Crystallogr*. **2015**. *A71*, 3-8.

Spek, A. L. *Acta Crystallogr.* **2009**, *D65*, 148–155.