1,2-Addition to Trifluoromethylated β-enamino diketones: Regioselective Synthesis of Trifluoromethyl-Containing Azomethine Pyrazoles and Isoxazoles

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SUPORTING INFORMATION

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General Information

The reagents used were obtain by commercial supplier without previous purification. Solvents were dried and purify according to recommend procedures.[1] All the reactions were monitored by thin-layer chromatography with Merck TLC silica gel plates and analyzed with UV light. All melting points were measured using a MQAPF-307 Microquímica apparatus using benzoic acid as internal standard. ^{1}H NMR, ^{13}C NMR, HSQC and HMBC experiments were run on Bruker avance III HD apparatus operating at ^{1}H 300 and 500 MHz and ^{13}C 75 and 125 MHz. Chemical shifts are reported in ppm using TMS as the internal standard for $CDCl_3$ in ^{1}H and ^{13}C. ESI(+)-MS and tandem ESI(+)-MS/MS were acquired using a hybrid high-resolution and high accuracy microTof (Q-TOF) mass spectrometer (Bruker). For ESI(+)-MS, the energy for the collision induced dissociations (CDI) was optimised for each component. For data acquisition and processing, the Q-TOF-control data analysis software (Bruker Scientific) was used. The single Crystal X-ray diffraction studies were based on X-ray intensity data measurements of compounds **2f** (CCDC: 1959494),[2a] **5dc** (CCDC: 1959495),[2b] **6fc** (CCDC: 1959496)[2c] were collected with a Bruker APEX II CCD area-detector diffractometer and graphitemonochromatized Mo-Ka radiation. The structure was solved by direct methods using SHELXS.[3] Subsequent Fourier-difference map analyses yielded the positions of the non-hydrogen atoms. Refinements were carried out the SHELXS package.[3] All refinements were made by full matrix least squares on *F2* with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were included in the refinement in calculated positions but the atoms (of hydrogens) that are commenting performing special bond were located in the Fourier map. The ORTEP diagram were drawn with 50% probability displacement ellipsoids using ORTEP-3 for Windows.[4]

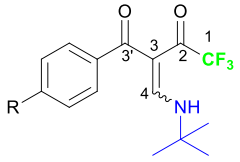
General Synthetic Procedure and Spectra Data.

Tertiary trifluoromethylated *β*-enamino diketones 1a-f.

General method. A solution of β-enamino ketone[5] (20 mmol, 1 equiv), anhydrous CH_2Cl_2 (6 mL), and pyridine (1.9 ml, 24.0 mmol, 1.2 equiv) was added dropwise to a stirred solution of trifluoracetic anhydride (3.5 mL, 24.0 mmol, 1.2 equiv) in CH_2Cl_2 (8 mL) at 0 °C under nitrogen atmosphere for 1 h. After warming to rt, the solution was stirred under reflux for 15 h. The organic layer was washed with a solution of H_2O–HCl (10:1; 1 x 20 mL) and with distilled H_2O (3 x 20 mL). Finally, the organic layer was dried over anhydrous sodium sulfate and evaporated under vacuum to afford the tertiary β-enamine diketones substrates **1a-f**. The spectral data of **1a-f** were in full accordance with those available in the literature.[5]

Secondary trifluoromethylated *β*-enamino diketones 2a-f.

General method. A mixture of compound **1** (**1a**: 3.16 g; **1b**: 2.71 g; **1c**: 3.01 g; **1d**: 2.89 g; **1e**: 3.05 g; **1f**: 3.50 g, 10.0 mmol, 1.0 equiv) and *tert*-butylamine (1.49 g, 20.0 mmol, 2.0 equiv) in dichloromethane (10 mL) was stirred at room temperature for 1 h. Then it was washed with distilled water (5 x 25 mL) and the organic layers were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was dissolved in hot ethanol (5 mL) and cooled to 0 °C which induced crystallization. The solid was filtered, washed with cold ethanol (20 mL) and dried under vacuum.



2a-f

Z:*E*

(*Z* and *E*)-4-(*tert*-Butylamino)-1,1,1-trifluoro-3-(4-nitrobenzoyl)-3-buten-2-one (**2a**): Yellow solid; 92% yield (3.17 g); *Z*/*E* ratio in $CDCl_3$: 25.4/74.6; mp 124.2-127.0 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) (***Z***) 1.39 (*s*, 9H, *t*-Bu), 7.76 (*d*, 1H, H^4, *J* = 14.7 Hz), 7.85 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 8.8 Hz), 8.30 (*d*, 2H, 4-$NO_2C_6H_4$, *J* = 8.8 Hz), 10.98 (*s*, 1H, N<u>H</u>); (***E***) 1.48 (*s*, 9H, *t*-Bu), 7.53 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 8.9 Hz), 8.13 (*d*, 1H, H^4, *J* = 14.3 Hz), 8.24 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 8.9 Hz), 11.33 (*s*, 1H, N<u>H</u>); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) (***Z***) 29.4 (C(<u>C</u>H_3)$_3$), 55.4 (<u>C</u>(CH_3)$_3$), 105.7 (C^3), 116.6 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 288.3 Hz), 123.6, 130.0, 144.6, 149.8 (4-NO_2-C_6H_4), 157.8 (C^4), 179.0 (*q*, C^2, $^{2}J_{C\text{-}F}$ = 35.4 Hz), 190.6 ($C^{3'}$); (***E***) 29.4 (C(<u>C</u>H_3)$_3$), 55.6 (<u>C</u>(CH_3)$_3$), 103.3 (C^3), 117.4 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 293.1 Hz), 123.3, 127.8, 146.9, 148.6 (4-NO_2-C_6H_4), 156.3 (C^4), 176.4 (*q*, C^2, $^{2}J_{C\text{-}F}$ = 32.9 Hz), 195.4 ($C^{3'}$); **HRMS** (ESI+): calcd for $C_{15}H_{16}F_3N_2O_4^+$, $[M+H]^+$: 345.1054, found 345.1061.

(*Z* and *E*)-3-Benzoyl-4-(*tert*-butylamino)-1,1,1-trifluoro-3-buten-2-one (**2b**): Light yellow solid; 88% yield (2.02 g); *Z*/*E* ratio in $CDCl_3$: 60.6/39.4; mp 93.2-95.7 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) (***Z***) 1.36 (*s*, 9H, *t*-Bu), 7.44-7.48 (*m*, 2H, C_6H_5), 7.54-7.57 (*m*, 1H, C_6H_5), 7.70-7.73 (*m*, 3H, H^4 and C_6H_5), 10.89 (*s*, 1H, NH); (***E***) 1.45 (*s*, 9H, *t*-Bu), 7.37-7.40 (*m*, 2H, C_6H_5), 7.44-7.48 (*m*, 3H, C_6H_5), 8.09 (*d*, 1H, H^4, *J* = 14,3 Hz), 11.01 (*s*, 1H, NH); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) (***Z***) 29.7 ($C(\underline{C}H_3)_3$), 55.1 ($\underline{C}(CH_3)_3$), 106.3 (C^3), 117.0 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 288.3 Hz), 128.6, 129.6, 132.6, 139.1 (C_6H_5), 157.9 (C^4), 179.4 (*q*, C^2, $^2J_{C\text{-}F}$ = 35.2 Hz), 192.8 ($C^{3'}$); (***E***) 29.7 ($C(\underline{C}H_3)_3$), 55.2 ($\underline{C}(CH_3)_3$), 104.0 (C^3), 117.6 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 293.2 Hz), 127.7, 128.2, 131.3, 141.0 (C_6H_5), 156.1 (C^4), 177.6 (*q*, C^2, $^2J_{C\text{-}F}$ = 32.5 Hz), 197.2 ($C^{3'}$); **HRMS** (ESI+): calcd for $C_{15}H_{17}F_3NO_2^+$, $[M+H]^+$: 300.1206, found 300.1220.

(*Z* and *E*)-4-(*tert*-Butylamino)-1,1,1-trifluoro-3-(4-methoxybenzoyl)-3-buten-2-one (**2c**): Orange solid; 82% yield (2.70 g); *Z*/*E* ratio in $CDCl_3$: 68.3/31.7; mp 120.4-122.1 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) (***Z***) 1.37 (*s*, 9H, *t*-Bu), 3.88 (*s*, 3H, 4-$OC\underline{H}_3$-C_6H_4), 6.96 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.7 Hz), 7.71 (*d*, 1H, H^4, *J* = 14.5 Hz), 7.75 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.7 Hz), 10.91 (*d*, 1H, NH, *J* = 12,9 Hz); (***E***) 1.43 (*s*, 9H, *t*-Bu), 3.85 (*s*, 3H, 4-$OC\underline{H}_3$-C_6H_4), 6.91 (*d*, 2H, 4-$OCH_3C_6H_4$, *J* = 8.9 Hz), 7.54 (*d*, 2H, 4-$OCH_3C_6H_4$, *J* = 8.7 Hz), 8.09 (*d*, 1H, H^4, *J* = 14.3 Hz), 10.75 (*d*, 1H, NH, *J* = 11.7 Hz); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) (***Z***) 29.6 ($C(\underline{C}H_3)_3$), 54.7 (4-$OC\underline{H}_3$-C_6H_4), 55.5 ($\underline{C}(CH_3)_3$), 106.3 (C^3), 117.0 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 288.4 Hz), 113.8, 131.6, 131.8, 163.3 (4-OCH_3-C_6H_4), 157.4 (C^4), 179.1 (*q*, C^2, $^2J_{C\text{-}F}$ = 34.9 Hz), 191.7 ($C^{3'}$); (***E***) 29.5 ($C(\underline{C}H_3)_3$), 54.8 (4-$OC\underline{H}_3$-C_6H_4), 55.3 ($\underline{C}(CH_3)_3$), 104.1 (C^3), 117.5 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 293.0 Hz), 113.5, 130.3, 133.2, 162.6 (4-OCH_3-C_6H_4), 155.7 (C^4), 177.5 (*q*, C^2, $^2J_{C\text{-}F}$ = 32.3 Hz), 195.6 ($C^{3'}$); **HRMS** (ESI+): calcd for $C_{16}H_{19}F_3NO_3^+$, $[M+H]^+$: 330.1312, found 330.1311.

(*Z* and *E*)-4-(*tert*-Butylamino)-1,1,1-trifluoro-3-(4-fluorbenzoyl)-3-buten-2-one (**2d**): Yellow solid; 87% yield (2.76 g); *Z*/*E* ratio in $CDCl_3$: 55.9/44.1; mp 113.2-114.8 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) (***Z***) 1.38 (*s*, 9H, *t*-Bu), 7.12-7.15 (*m*, 2H, 4-F-C_6H_4), 7.71 (*d*, 1H, H^4, *J* = 14.6 Hz), 7.74-7.77 (*m,* 2H, 4-F-C_6H_4), 10.91 (*s*, 1H, NH); (***E***) 1.45 (*s*, 9H, *t*-Bu), 7.04-7.08 (*m*, 2H, 4-F-C_6H_4), 7.48-7.51 (*m*, 2H, 4-F-C_6H_4), 8.09 (*d*, 1H, H^4, *J* = 14.3 Hz), 10.97 (*s*, 1H, NH); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) (***Z***) 29.6 ($C(\underline{C}H_3)_3$), 55.1 ($\underline{C}(CH_3)_3$), 106.0 (C^3), 116.9 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 288.5 Hz), 115.7 (*d,* 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 21.8 Hz), 131.9 (*d,* 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 9.1 Hz), 135.4 (*d,* 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 2.4 Hz), 157.5 (C^4), 165.4 (*d,* 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 253.9 Hz), 179.1 (*q*, C^2, $^2J_{C\text{-}F}$ = 35.2 Hz), 191.4 ($C^{3'}$); (***E***) 29.5 ($C(\underline{C}H_3)_3$), 55.2 ($\underline{C}(CH_3)_3$), 103.7 (C^3), 117.6 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 293.2 Hz),), 115.2 (*d,* 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.3 Hz), 130.2 (*d,* 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 9.1 Hz), 137.0 (*d,* 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.1 Hz), 156.1 (C^4), 164.6 (*d,* 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 251.5 Hz), 177.2 (*q*, C^2, $^2J_{C\text{-}F}$ = 32.5 Hz), 195.7 ($C^{3'}$); **HRMS** (ESI+): calcd for $C_{15}H_{16}F_4NO_2^+$, $[M+H]^+$: 318.1112, found 318.1110.

(*Z* and *E*)-4-(*tert*-Butylamino)-3-(4-chlorobenzoyl)-1,1,1-trifluor-3-buten-2-one (**2e**): Dark Yellow solid; 89% yield (2.96 g); *Z*/*E* ratio in $CDCl_3$: 51.7/48.3; mp 93.0-94.5 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) (***Z***) 1.38 (*s*, 9H, *t*-Bu), 7.34-7.45 (*m*, 6H, 4-Cl-C_6H_4 *E* and *Z*), 7.67-7.73 (*m*, 3H, 4-Cl-C_6H_4 *E* and *Z,* and H^4), 10.89 (*s*, 1H, NH); (***E***) 1.45 (*s*, 9H, *t*-Bu), 7.34-7.45 (*m*, 6H, 4-Cl-C_6H_4 *E* and *Z*), 8.09 (*d*, 1H, H^4, *J* = 14.3), 11.02 (*s*, 1H, NH); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) (***Z***) 29.7 ($C(\underline{C}H_3)_3$), 55.3 ($\underline{C}(CH_3)_3$), 103.6 (C^3), 116.8 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 288.4 Hz), 128.4, 130.8, 138.9, 139.3 (4-Cl-C_6H_4), 157.6 (C^4), 179.2 (*q*, C^2, $^2J_{C\text{-}F}$ = 35.2 Hz), 191.5 ($C^{3'}$); (***E***) 29.6 ($C(\underline{C}H_3)_3$), 55.4 ($\underline{C}(CH_3)_3$), 106.0 (C^3), 117.5 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 293.1 Hz), 128.9, 129.1, 137.2, 137.4 (4-Cl-C_6H_4), 156.1 (C^4), 177.1 (*q*, C^2, $^2J_{C\text{-}F}$ = 32.6 Hz), 196.0 ($C^{3'}$); **HRMS** (ESI+): calcd for $C_{15}H_{16}ClF_3NO_2^+$, $[M+H]^+$: 334.0816, found 334.0809.

(*Z* and *E*)-3-(4-bromobenzoyl)-4-(*tert*-butylamino)-1,1,1-trifluor-3-buten-2-one (**2f**): Yellow solid; 85% yield (3.21 g); *Z*/*E* ratio in $CDCl_3$: 51.4/48.6; mp 118.1-120.2 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) (***Z***) 1.38 (*s*, 9H, *t*-Bu), 7.33 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.6 Hz), 7.52 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.6 Hz), 7.70 (*d*, 1H, H^4, *J* = 14.6 Hz), 10.90 (*d*, 1H, NH, *J* = 11,9 Hz); (***E***) 1.45 (*s*, 9H, *t*-Bu), 7.59 (*s*, 4H, 4-Br-C_6H_4), 8.08 (*d*, 1H, H^4, *J* = 14.3), 11.05 (*d*, 1H, NH, *J* = 10.4 Hz); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) (***Z***) 29.7 ($C(\underline{C}H_3)_3$), 55.2 ($\underline{C}(CH_3)_3$), 103.7 (C^3), 116.9 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 288.4 Hz), 125.8, 129.2, 131.4, 139.8 (4-Br-C_6H_4), 157.6 (C^4), 179.3 (*q*, C^2, $^2J_{C\text{-}F}$ = 35.3 Hz), 191.7 ($C^{3'}$); (***E***) 29.6 ($C(\underline{C}H_3)_3$), 55.3 ($\underline{C}(CH_3)_3$), 106.0 (C^3), 117.6 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 293.2 Hz), 127.5, 131.0, 131.9, 138.0 (4-Br-C_6H_4), 156.2 (C^4), 177.1 (*q*, C^2, $^2J_{C\text{-}F}$ = 32.6 Hz), 196.1 ($C^{3'}$); **HRMS** (ESI+): calcd for $C_{15}H_{16}BrF_3NO_2^+$, $[M+H]^+$: 378.0311, found 378.0298.

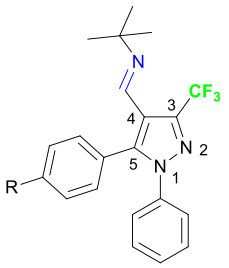
Analysis of the reactivity of trifluoromethylated *β*-enamino diketone 1a with phenylhydrazine: Formation of pyrazoles A and B.

General method. The preliminary analysis of cyclocondensation reaction of trifluoromethylated *β*-enamino diketone **1a** with phenylhydrazine was performed in according to the methodology described in literature.[6,7] The compound **1a** (0.316 g, 1.0 mmol, 1.0 equiv) was solubilized in MeCN (8 mL), added phenylhydrazine

(0.108 g, 1.0 mmol, 1.0 equiv) and the mixture was stirred under reflux for 24 h. Then it was washed with distilled water (75 mL), extracted with dichloromethane (3x20 mL) and the organic layers were dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure.

Analysis of the reactivity of trifluoromethylated β-enamino diketone 2a-f with phenylhydrazine.

General method. The analysis of cyclocondensation reaction of trifluoromethylated β-enamino diketone **2a-f** with phenylhydrazine was evaluated in according to the methodology described by da Silva *et al*.[8] The compound **2** (**2a**: 0.344 g; **2b**: 0.229 g; **2c**: 0.329 g; 2**d**: 0.317 g; **2e**: 0.334 g; **2f**: 0.378 g, 1.0 mmol, 1.0 equiv) was solubilized in MeCN (8 mL), then added phenylhydrazine (0.108 g, 1.0 mmol, 1.0 equiv) and boron trifluoride diethyl etherate solution 46.5% (0.400 mL, 1.5 mmol, 1.5 equiv). The mixture was stirred under reflux for 7 h. After that, reaction mixture was cooled to room temperature and the solvent was evaporated under vacuum. Then, the residue was washed with a solution of 3% of K_2CO_3 (25 mL), extracted with dichloromethane (3x20 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was dissolved in hot methanol (5 mL) and cooled to 0 °C which induced crystallization. The solid was filtered, washed with cold methanol (20 mL) and dried under vacuum.



3a-f

(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-5-(4-nitrophenyl)-1-phenyl-*1H*-pyrazole (**3a**): Yellow solid; 84% yield (0.351 g); mp 150.2-152.2 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) 1.13 (*s*, 9H, *t*-Bu), 7.19-7.21 (*m*, 2H, C_6H_5) 7.35-7.36 (*m*, 3H, C_6H_5), 7.50 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 8.8 Hz), 8.16 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 8.8 Hz), 8.26 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 58.4 (<u>C</u>(CH_3)$_3$), 118.9 (C^4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.2 Hz), 123.2 (4-NO_2-C_6H_4), 125.7, 129.2, 129.5, (C_6H_5), 132.1, 135.4 (4-NO_2-C_6H_4), 138.4 (C_6H_5), 141.2 (C^5), 142.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 144.7 (<u>C</u>H) 148.0 (4-NO_2-C_6H_4); **HRMS** (ESI+): calcd for $C_{21}H_{20}F_3N_4O_2^+$, $[M+H]^+$:417.1533, found 417.1522.

(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-1,5-diphenyl-*1H*-pyrazole (**3b**): Light yellow solid; 68% yield (0.222 g); mp 97.2-98.5 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) 1.17 (*s*, 9H, *t*-Bu), 7.22-7.25 (*m*, 4H, C_6H_5 A and B), 7.30-7.37 (*m*, 6H, C_6H_5 A and B), 8.15 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 58.0 (<u>C</u>(CH_3)$_3$), 118.5 (C^4), 121.5 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.0 Hz), 125.5, 128.4, 128.4, 128.5, 129.1, 129.3, 130.7 (C_6H_5 - A and B), 139.0 (C_6H_5 - B), 141.2 (*q*, C^3, $^2J_{C\text{-}F}$ = 36.9 Hz), 144.3 (C^5), 145.5 (<u>C</u>H); **HRMS** (ESI+): calcd for $C_{21}H_{21}F_3N_3^+$, $[M+H]^+$: 372.1682, found 372.1670.

(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-5-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazole (**3c**): White solid; 60% yield (0.244 g); mp 135.5-137.9 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.19 (*s*, 9H, *t*-Bu), 3.82 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4), 6.84 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), 7.17 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), 7.22-7.25 (*m*, 2H, C_6H_5), 7.29-7.33 (*m*, 3H, C_6H_5), 8.14 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 29.4 (C(<u>C</u>H_3)$_3$), 55.4 (4-O<u>C</u>H_3-C_6H_4), 58.0 (<u>C</u>(CH_3)$_3$), 113.9 (4-OCH_3-C_6H_4), 118.2 (C^4), 121.5 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.8 Hz), 120.4 (4-OCH_3-C_6H_4), 125.6, 128.4, 129.2 (C_6H_5), 132.0 (4-OCH_3-C_6H_4), 139.1 (C_6H_5), 141.1 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.6 Hz), 144.3 (C^5), 145.7 (<u>C</u>H) 160.3 (4-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{22}H_{23}F_3N_3O^+$, $[M+H]^+$: 402.1788, found 402.1789.

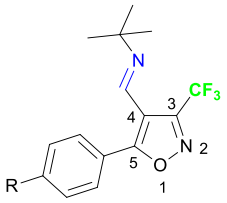
(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-5-(4-fluorophenyl)-1-phenyl-*1H*-pyrazole (**3d**): White solid; 81% yield (0.317 g); mp 124.9-126.8 °C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) 1.16 (*s*, 9H, *t*-Bu), 7.00-7.03 (*m*, 2H, 4-F-C_6H_4), 7.20-7.22 (*m*, 2H, C_6H_5), 7.24-7.27 (*m*, 2H, 4-F-C_6H_4), 7.32-7.33 (*m*, 3H, C_6H_5), 8.18 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 58.1 (<u>C</u>(CH_3)$_3$), 115.5 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 21.8 Hz), 118.4 (C^4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 124.5 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.5 Hz), 125.6, 128.6, 129.3 (C_6H_5), 132.8 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.4 Hz), 138.8 (C_6H_5), 141.4 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 143.1 (C^5), 145.2 (<u>C</u>H), 163.2 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 250.2 Hz); **HRMS** (ESI+): calcd for $C_{21}H_{20}F_4N_3^+$, $[M+H]^+$: 390.1588, found 390.1573.

(*E*)-4-[(*tert*-Butyl)iminomethyl]-5-(4-chlorophenyl)-3-trifluoromethyl-1-phenyl-*1H*-pyrazole (**3e**): Yellow solid; 71% yield (0.289 g); mp 117.1-119.0 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.16 (*s*, 9H, *t*-Bu), 7.17 (*d*, 2H, 4-Cl-C_6H_4, *J* = 9.0 Hz), 7.22-7.26 (*m*, 2H, C_6H_5), 7.28 (*d*, 2H, 4-Cl-C_6H_4, *J* = 9.0 Hz), 7.32-7.40 (*m*, 3H, C_6H_5), 8.14 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 58.1 (<u>C</u>(CH_3)$_3$), 118.8 (C^4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 126.6, 128.1 (4-Cl-C_6H_4), 128.6, 129.4, 129.6 (C_6H_5), 130.6, 134.3 (4-Cl-C_6H_4), 137.5 (C_6H_5), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 144.3 (C^5), 145.2 (<u>C</u>H); **HRMS** (ESI+): calcd for $C_{21}H_{20}ClF_3N_3^+$, $[M+H]^+$: 406.1292, found 406.1281.

(*E*)-5-(4-Bromophenyl)-4-[(*tert*-butyl)iminomethyl]-3-trifluoromethyl-1-phenyl-*1H*-pyrazole (**3f**): White solid; 77% yield (0.348 g); mp 115.8-117.2 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.17 (*s*, 9H, *t*-Bu), 7.15 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.7 Hz), 7.20-7.23 (*m*, 2H, C_6H_5), 7.32-7.35 (*m*, 3H, C_6H_5), 7.45 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.7 Hz), 8.18 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 58.2 (<u>C</u>(CH_3)$_3$), 118.5 (C^4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 123.8 (4-Br-C_6H_4), 125.6 (C_6H_5), 127.4 (4-Br-C_6H_4), 128.7, 129.3 (C_6H_5), 131.6, 132.4 (4-Br-C_6H_4), 138.7 (C_6H_5), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 142.8 (C^5), 145.2 (<u>C</u>H); **HRMS** (ESI+): calcd for $C_{21}H_{20}BrF_3N_3^+$, $[M+H]^+$: 450.0787, found 450.0790.

5-aryl 4-iminomethyl 3-trifluoromethyl isoxazoles 4a-f.

General method. The compound **2** (**2a**: 0.344 g; **2b**: 0.229 g; **2c**: 0.329 g; 2**d**: 0.317 g; **2e**: 0.334 g; **2f**: 0.378 g, 1.0 mmol, 1.0 equiv) was solubilized in MeCN (8 mL), added hydroxylamine hydrochloride (0.083 g, 1.2 mmol, 1.2 equiv) and boron trifluoride diethyl etherate solution 46.5% (0.400 mL, 1.5 mmol, 1.5 equiv). The mixture was stirred under reflux for 5 h. Next, reaction mixture was cooled to room temperature and the solvent was evaporated under vacuum. Then, the residue was washed with a solution of 3% of K_2CO_3 (25 mL), extracted with dichloromethane (3x20 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was dissolved in hot methanol (5 mL) and cooled to 0 °C which induced crystallization. The solid was filtered, washed with cold methanol (20 mL) and dried under vacuum.



4a-f

(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-5-(4-nitrophenyl)-isoxazole (**4a**): Light Yellow solid; 89% yield (0.305 g); mp 75.2-78.4 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.31 (*s*, 9H, *t*-Bu), 8.26 (*s*, 1H, C<u>H</u>), 8.35 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz), 8.43 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 59.4 (<u>C</u>(CH_3)$_3$), 114.5 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 123.8, 129.7, 132.1 (4-NO_2-C_6H_4), 142.8 (<u>C</u>H), 149.4 (4-NO_2-C_6H_4), 155.1 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.8 Hz), 167.8 (C^5); **HRMS** (ESI+): calcd for $C_{15}H_{15}F_3N_3O_3^+$, $[M+H]^+$: 342.1060, found 342.1078.

(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-5-phenyl-isoxazole (**4b**): Light yellow liquid; 63% yield (0.189 g); mp - °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.29 (*s*, 9H, *t*-Bu), 7.48-7.55 (*m*, 3H, C_6H_5), 7.93-7.96 (*m*, 2H, C_6H_5), 8.26 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.46 MHz, $CDCl_3$) δ (ppm) 29.2 (C(<u>C</u>H_3)$_3$), 58.8 (<u>C</u>(CH_3)$_3$), 112.8 (C^4), 119.9 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 271.9 Hz), 126.4, 128.3, 129.0, 131.6 (C_6H_5), 143.2 (<u>C</u>H), 154.3 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.5 Hz), 170.6 (C^5); **HRMS** (ESI+): calcd for $C_{15}H_{16}F_3N_2O^+$, $[M+H]^+$: 297.1215, found 297.1235.

(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-5-(4-methoxyphenyl)-isoxazole (**4c**): White solid; 78% yield (0.257 g); mp 92.2-93.6 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.29 (*s*, 9H, *t*-Bu), 3.89 (*s*, 3H, 4-O<u>C</u>H_3-C_6H_4), 7.01 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.99 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 8.24 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 55.6 (4-O<u>C</u>H_3-C_6H_4), 58.7 (<u>C</u>(CH_3)$_3$), 111.5 (C^4), 114.3, 119.0 (4-OCH_3-C_6H_4), 119.9 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 271.9 Hz), 130.1 (4-OCH_3-C_6H_4), 143.5 (<u>C</u>H), 154.4 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.4 Hz), 162.2 (4-OCH_3-C_6H_4), 170.6 (C^5); **HRMS** (ESI+): calcd for $C_{16}H_{18}F_3N_2O_2^+$, $[M+H]^+$: 327.1315, found 327.1318.

(*E*)-4-[(*tert*-Butyl)iminomethyl]-3-trifluoromethyl-5-(4-fluorophenyl)-isoxazole (**4d**): Light yellow liquid; 65% yield (0.205 g); mp - °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.30 (*s*, 9H, *t*-Bu), 7.17-7.23 (*m*, 2H, 4-F-C_6H_4), 8.09-8.14 (*m*, 2H, 4-F-C_6H_4), 8.24 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.46 MHz, $CDCl_3$) δ (ppm) 29.3 (C(<u>C</u>H_3)$_3$), 59.0 (<u>C</u>(CH_3)$_3$), 112.4 (C^4), 116.1 (*d*, $^2J_{C\text{-}F}$ = 22.0 Hz, 4-F-C_6H_4), 119.9 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.8 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}}$

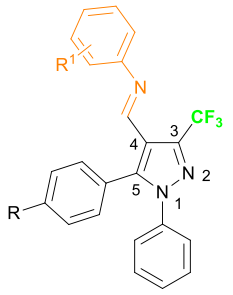
$_F$ = 3.3 Hz), 130.9 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.8 Hz), 143.1 (CH), 154.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.4 Hz), 164.7 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 253.6 Hz), 169.6 (C^5); **HRMS** (ESI+): calcd for $C_{15}H_{15}F_4N_2O^+$, $[M+H]^+$: 315.1115, found 315.1133.

(*E*)-4-[(*tert*-Butyl)iminomethyl]-5-(4-chlorophenyl)-3-trifluoromethyl-isoxazole (**4e**): White solid; 79% yield (0.262 g); mp 56.8-58.0 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.29 (*s*, 9H, *t*-Bu), 7.49 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 8.05 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 8.23 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 29.3 ($C(CH_3)_3$), 59.0 ($C(CH_3)_3$), 112.8 (C^4), 119.9 (*q*, CF_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 124.9, 129.2, 129.8, 138.0 (4-Cl-C_6H_4), 143.1 (CH) 154.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.4 Hz), 169.4 (C^5); **HRMS** (ESI+): calcd for $C_{15}H_{15}ClF_3N_2O^+$, $[M+H]^+$: 331.0820, found 331.0834.

(*E*)-5-(4-Bromophenyl)-4-[(*tert*-butyl)iminomethyl]-3-trifluoromethyl-isoxazole (**4f**): White solid; 83% yield (0.310 g); mp 66.6-69.1 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 1.29 (*s*, 9H, *t*-Bu), 7.65 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.99 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.23 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 29.3 ($C(CH_3)_3$), 59.1 ($C(CH_3)_3$), 112.9 (C^4), 119.8 (*q*, CF_3, $^1J_{C\text{-}F}$ = 272.1 Hz), 125.4, 126.5, 130.0, 132.1 (4-Br-C_6H_4), 143.1 (CH), 154.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.4 Hz), 169.5 (C^5); **HRMS** (ESI+): calcd for $C_{15}H_{15}BrF_3N_2O^+$, $[M+H]^+$: 375.0314, found 375.0332.

5-aryl-4-[(aryl)iminomethyl]-3-trifluoromethyl-*N*-phenylpyrazoles 5(aa-af)-5(fa-ff).

General method. The compound **2** (**2a**: 0.344 g; **2b**: 0.229 g; **2c**: 0.329 g; **2d**: 0.317 g; **2e**: 0.334 g; **2f**: 0.378 g, 1.0 mmol, 1.0 equiv) was solubilized in MeCN (8 mL), then added phenylhydrazine (0.108 g, 1.0 mmol, 1.0 equiv) and boron trifluoride diethyl etherate solution 46.5% (0.400 mL, 1.5 mmol, 1.5 equiv). The mixture was stirred under reflux for 7 h. In sequence, the reaction mixture was cooled to room temperature, added substituted anilines (3.0 mmol, 3.0 equiv) and stirred for 15 min. Then, the solvent was evaporated under vacuum and the residue was washed with a solution of 3% of K_2CO_3 (25 mL), extracted with dichloromethane (3x20 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was dissolved in hot ethyl ether (5 mL) and cooled to 0 °C which induced crystallization. The solid was filtered, washed with cold ethyl ether (20 mL) and dried under vacuum.



5(aa-af)-5(fa-ff)

(*E*)-3-Trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]-5-(4-nitrophenyl)-1-phenyl-*1H*-pyrazole (**5aa**): Yellow solid; 78% yield (0.366 g); mp 158.8-161.8 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.80 (*s*, 3H, 4-OCH_3-C_6H_4), 6.87 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.04 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.22-7.25 (*m*, 2H, C_6H_5), 7.35-7.38 (*m*, 3H, C_6H_5), 7.57 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.20 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.50 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.6 (4-OCH_3-C_6H_4), 114.5 (4-OCH_3-C_6H_4), 118.2 (C^4), 121.3 (*q*, CF_3, $^1J_{C\text{-}F}$ = 270.2 Hz), 122.2 (4-NO_2-C_6H_4), 123.4 (4-OCH_3-C_6H_4), 125.7, 129.3, 129.6 (C_6H_5), 132.2, 135.1 (4-NO_2-C_6H_4), 138.2 (C_6H_5), 142.1 (C^5), 142.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 144.1 (4-OCH_3-C_6H_4), 146.6 (CH), 148.2 (4-NO_2-C_6H_4), 158.9 (4-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}F_3N_4O_3^+$, $[M+H]^+$: 467.1326, found 467.1344.

(*E*)-3-Trifluoromethyl-5-(4-nitrophenyl)-1-phenyl-4-[(phenyl)iminomethyl]-*1H*-pyrazole (**5ab**): Orange solid; 65% yield (0.285 g); mp 147.4-150.3 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.01-7.04 (*m*, 2H, C_6H_5 A and B), 7.22-7.25 (*m*, 3H, C_6H_5 A and B), 7.32-7.39 (*m*, 5H, C_6H_5 A and B), 7.58 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.22 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.48 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.9 (C^4), 121.2 (*q*, CF_3, $^1J_{C\text{-}F}$ = 270.3 Hz), 120.7, 123.5, 125.7, 126.6, 129.3, 129.4, 129.6, 132.2, 134.9, 138.1 (C_6H_5 – A, B and 4-NO_2-C_6H_4), 142.4 (C^5), 142.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 148.3 (4-NO_2-C_6H_4), 149.1 (CH), 151.4 (C_6H_5 – B); **HRMS** (ESI+): calcd for $C_{23}H_{16}F_3N_4O_2^+$, $[M+H]^+$: 437.1220, found 437.1245.

(*E*)-3-Trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]-5-(4-nitrophenyl)-1-phenyl-*1H*-pyrazole (**5ac**): Yellow solid; 69% yield (0.321 g); mp 165.2-167.2 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.79 (*s*, 3H, 2-OCH_3-C_6H_4), 6.86-6.95 (*m*, 3H, 2-OCH_3-C_6H_4), 7.13-7.19 (*m*, 1H, 2-OCH_3-C_6H_4), 7.22-7.25 (*m*, 2H, C_6H_5), 7.35-

7.39 (*m*, 3H, C_6H_5), 7.62 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.18 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.57 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.9 (2-O<u>C</u>H_3-C_6H_4), 112.1 (2-OCH_3-C_6H_4), 118.2 (C^4), 120.5, 121.1 (2-OCH_3-C_6H_4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.2 Hz), 123.3 (4-NO_2-C_6H_4), 125.7 (C_6H_5), 127.3 (2-OCH_3-C_6H_4), 129.3, 129.6 (C_6H_5), 132.3, 134.8 (4-NO_2-C_6H_4), 138.2 (C_6H_5), 140.9 (2-OCH_3-C_6H_4), 142.2 (C^5), 142.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 148.1 (4-NO_2-C_6H_4), 150.3 (<u>C</u>H), 152.4 (2-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}F_3N_4O_3^+$, $[M+H]^+$: 467.1326, found 467.1349.

(*E*)-3-Trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-5-(4-nitrophenyl)-1-phenyl-*1H*-pyrazole (**5ad**): Orange solid; 69% yield (0.314 g); mp 161.8-165.7 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.00-7.03 (*m*, 4H, 4-F-C_6H_4), 7.22-7.25 (*m*, 2H, C_6H_5), 7.35-7.39 (*m*, 3H, C_6H_5), 7.56 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.22 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.46 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 116.1 (*d,* 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.6 Hz), 117.8 (C^4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.2 Hz), 122.3 (*d,* 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.4 Hz), 123.5 (4-NO_2-C_6H_4), 125.7, 129.4, 129.6 (C_6H_5), 132.1, 134.9 (4-NO_2-C_6H_4), 138.1 (C_6H_5), 142.4 (C^5), 142.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 147.3 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 2.9 Hz), 148.3 (4-NO_2-C_6H_4), 148.7 (<u>C</u>H), 161.7 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 245.8 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{15}F_4N_4O_2^+$, $[M+H]^+$: 455.1126, found 455.1154.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-5-(4-nitrophenyl)-1-phenyl-*1H*-pyrazole (**5ae**): Orange solid; 61% yield (0.286 g); mp 191.9-194.4 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.95 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.21-7.25 (*m*, 2H, C_6H_5), 7.30 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.35-7.39 (*m*, 3H, C_6H_5), 7.56 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.22 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.0 Hz), 8.45 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.7 (C^4), 121.2 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.2 Hz), 122.1 (4-Cl-C_6H_4), 123.6 (4-NO_2-C_6H_4), 125.7, 129.4, 129.5 (C_6H_5), 129.6 (4-Cl-C_6H_4), 132.1 (4-NO_2-C_6H_4), 132.3 (4-Cl-C_6H_4), 134.8 (4-NO_2-C_6H_4), 138.0 (C_6H_5), 142.6 (C^5), 142.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 148.4 (4-NO_2-C_6H_4), 149.4 (<u>C</u>H), 149.8 (4-Cl-C_6H_4); **HRMS** (ESI+): calcd for $C_{23}H_{15}ClF_3N_4O_2^+$, $[M+H]^+$: 471.0830, found 471.0846.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-5-(4-nitrophenyl)-1-phenyl-*1H*-pyrazole (**5af**): Yellow solid; 54% yield (0.278 g); mp 205.4-207.7 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.89 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.7 Hz), 7.21-7.25 (*m*, 2H, C_6H_5), 7.35-7.39 (*m*, 3H, C_6H_5), 7.45 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.7 Hz), 7.55 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 8.9 Hz), 8.21 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 8.9 Hz), 8.44 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.6 (C^4), 120.1 (4-Br-C_6H_4), 121.2 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.2 Hz), 122.5 (4-Br-C_6H_4), 123.6 (4-NO_2-C_6H_4), 125.7, 129.5, 129.6 (C_6H_5), 132.1 (4-NO_2-C_6H_4), 132.4 (4-Br-C_6H_4), 134.8 (4-NO_2-C_6H_4), 138.0 (C_6H_5), 142.6 (C^5), 142.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 148.4 (4-NO_2-C_6H_4), 149.5 (<u>C</u>H), 150.3 (4-Br-C_6H_4); **HRMS** (ESI+): calcd for $C_{23}H_{15}BrF_3N_4O_2^+$, $[M+H]^+$: 515.0325, found 515.0346.

(*E*)-3-Trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]-1,5-diphenyl-*1H*-pyrazole (**5ba**): White solid; 68% yield (0.288 g); mp 134.6-136.9 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.80 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 6.87 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.09 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), *7*.24-7.42 (*m*, 10H, C_6H_5 A and B), 8.35 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.6 (4-O<u>C</u>H_3-C_6H_4), 114.4 (4-OCH_3-C_6H_4), 117.8 (C^4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.2 (4-OCH_3-C_6H_4), 125.5, 128.1, 128.6, 128.7, 129.2, 129.7, 130.7, 138.7 (C_6H_5 – A and B), 141.4 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 145.0 (4-OCH_3-C_6H_4), 145.8 (C^5), 147.9 (<u>C</u>H), 158.5 (4-OCH_3-C_6H_5); **HRMS** (ESI+): calcd for $C_{24}H_{19}F_3N_3O^+$, $[M+H]^+$: 422.1475, found 422.1495.

(*E*)-3-Trifluoromethyl-1,5-diphenyl-4-[(phenyl)iminomethyl]-*1H*-pyrazole (**5bb**): White solid; 63% yield (0.247 g); mp 154.8-156.5 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.06-7.09 (*m*, 2H, C_6H_5 – B),7.16-7.21 (*m*, 1H, C_6H_5 – B), 7.27-7.42 (*m*, 12H, C_6H_5 A, B and C), 8.33 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.6 (C^4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.0 Hz), 120. 8, 125.5, 126.1, 127.9, 128.7, 128.8, 129.2, 129.2, 129.8, 130.7, 138.6 (C_6H_5 – A, B and C), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 146.2 (C^5), 150.1 (<u>C</u>H), 152.2 (C_6H_5 – C); **HRMS** (ESI+): calcd for $C_{23}H_{17}F_3N_3^+$, $[M+H]^+$: 392.1369, found 392.1387.

(*E*)-3-Trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]-1,5-diphenyl-*1H*-pyrazole (**5bc**): Light Yellow solid; 66% yield (0.276 g); mp 196.8-198.3 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.82 (*s,* 3H, 2-OC<u>H</u>$_3$-C_6H_4), 6.87-6.94 (*m*, 3H, 2-OCH_3-C_6H_4), 7.10-7.16 (*m*, 1H, 2-OCH_3-C_6H_4), 7.23-7.40 (*m*, 10H, C_6H_5 A and B), 8.38 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.2 (2-O<u>C</u>H_3-C_6H_4), 112.6 (2-OCH_3-C_6H_4), 117.9 (C^4), 121.0, 121.2 (2-OCH_3-C_6H_4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 125.5 (C_6H_5), 126.7 (2-OCH_3-C_6H_4), 127.9, 128.7, 128.7, 129.2, 129.7, 130.8, 138.7 (C_6H_5 – A and B), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 142.1 (2-OCH_3-C_6H_4), 146.0 (C^5), 151.6 (<u>C</u>H), 152.2 (2-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{19}F_3N_3O^+$, $[M+H]^+$: 422.1475, found 422.1487.

(*E*)-3-Trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-1,5-diphenyl-*1H*-pyrazole (**5bd**): Yellow solid; 69% yield (0.285 g); mp 150.0-151.9 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.98-7.09 (*m*, 4H, 4-F-C_6H_4),

7.24-7.43 (*m*, 10H, C_6H_5 A and B), 8.31 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 115.9 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.6 Hz), 117.5 (C^4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.3 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.3 Hz), 125.5, 127.9, 128.8, 128.8, 129.2, 129.9, 130.7, 138.6 (C_6H_5 – A and B), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.3 Hz), 146.2 (C^5), 148.1 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 2.9 Hz), 149.7 (<u>C</u>H), 161.4 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 244.7 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{16}F_4N_3^+$, $[M+H]^+$: 410.1275, found 410.1283.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-1,5-diphenyl-*1H*-pyrazole (**5be**): White solid; 68% yield (0.284 g); mp 158.5-160.3 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.01 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.24-7.43 (*m*, 12H, C_6H_5 A, B and 4-Cl-C_6H_4), 8.29 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.4 (C^4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.2, 125.5, 127.8 (4-Cl-C_6H_4) 128.8, 128.8, 129.2, 129.9, 130.7, 131.7, 138.6 (C_6H_5 – A and B), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 146.4 (C^5), 150.4 (<u>C</u>H), 150.5 (4-Cl-C_6H_4); **HRMS** (ESI+): calcd for $C_{23}H_{16}ClF_3N_3^+$, $[M+H]^+$: 426.0979, found 426.0989.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-1,5-diphenyl-*1H*-pyrazole (**5bf**): Yellow solid; 62% yield (0.272 g); mp 167.3-169.7 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.94 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.6 Hz), 7.27-7.45 (*m*, 12H, C_6H_5 A, B and 4-Br-C_6H_4), 8.29 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.4 (C^4), 119.5 (4-Br-C_6H_4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.6 (4-Br-C_6H_4), 125.5, 127.8, 128.8, 128.8, 129.2, 129.9, 130.6, (C_6H_5 – A and B), 132.2 (4-Br-C_6H_4), 138.5 (C_6H_5 – B), 141.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 146.4 (C^5), 150.4 (<u>C</u>H), 151.0 (4-Br-C_6H_5); **HRMS** (ESI+): calcd for $C_{23}H_{16}BrF_3N_3^+$, $[M+H]^+$: 470.0474, found 470.0507.

(*E*)-3-Trifluoromethyl-5-(4-methoxyphenyl)-4-[(4-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5ca**): Light Yellow solid; 63% yield (0.284 g); mp 140.0-143.2 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.80 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4 – B), 3.82 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4 – A), 6.86-6.90 (*m*, 4H, 4-OCH_3-C_6H_4 – A and B), 7.10 (*d*, 2H, 4-OCH_3-C_6H_4 – B, *J* = 9.0 Hz), 7.23 (*d*, 2H, 4-OCH_3-C_6H_4 – A, *J* = 8.9 Hz), 7.27-7.35 (*m*, 5H, C_6H_5), 8.34 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.4 (4-O<u>C</u>H_3-C_6H_4 – A), 55.6 (4-O<u>C</u>H_3-C_6H_4 – B), 114.2, 114.4 (4-OCH_3-C_6H_4 – A and B), 117.6 (C^4), 120.0 (4-OCH_3-C_6H_4 – A), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.2 (4-O<u>C</u>H_3-C_6H_4 – B), 125.5, 128.5, 129.2 (C_6H_5), 132.1 (4-O<u>C</u>H_3-C_6H_4 – A), 138.8 (C_6H_5), 141.3 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 145.1 (4-OCH_3-C_6H_4 – B), 145.8 (C^5), 148.2 (<u>C</u>H), 158.4, 160.6 (4-OCH_3-C_6H_4 – A and B); **HRMS** (ESI+): calcd for $C_{25}H_{21}F_3N_3O_2^+$, $[M+H]^+$: 452.1580, found 452.1600.

(*E*)-3-Trifluoromethyl-5-(4-methoxyphenyl)-1-phenyl-4-[(phenyl)iminomethyl]-*1H*-pyrazole (**5cb**): White solid; 62% yield (0.263 g); mp 136.5-139.2 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.82 (*s*, 3H, O<u>C</u>H_3), 6.88 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), 7.07-7.10 (*m*, 2H, C_6H_5 A and B), 7.16-7.24 (*m*, 3H, C_6H_5 A, B and 4-$OCH_3C_6H_4$), 7.27-7.36 (*m*, 7H, C_6H_5 A and B), 8.32 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.4 (4-O<u>C</u>H_3-C_6H_4), 114.2 (4-OCH_3-C_6H_4), 117.3 (C^4), 119.8 (4-OCH_3-C_6H_4), 120.8 (C_6H_5 – A or B), 121.2 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 125.5, 126.0, 128.6, 129.2, 129.2 (C_6H_5 – A and B), 132.1 (4-OCH_3-C_6H_4), 138.8 (C_6H_5 – A), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 146.2 (C^5), 150.3 (<u>C</u>H), 152.3 (C_6H_5 – B), 160.7 (4-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{19}F_3N_3O^+$, $[M+H]^+$: 422.1475, found 422.1500.

(*E*)-3-Trifluoromethyl-5-(4-methoxyphenyl)-4-[(2-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5cc**): White solid; 52% yield (0.233 g); mp 130.0-131.5 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.81 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4), 3.84 (*s*, 3H, 2-OC<u>H</u>$_3$-C_6H_4), 6.85-6.95 (*m*, 6H, 4-OCH_3-C_6H_4 and 2-OCH_3-C_6H_4), 7.11-7.17 (*m,* 1H, 2-OCH_3-C_6H_4), 7.24-7.28 (*m*, 3H, 4-OCH_3-C_6H_4 and 2-OCH_3-C_6H_4), 7.32-7.36 (*m*, 3H, 4-OCH_3-C_6H_4 and 2-OCH_3-C_6H_4), 8.37 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.4 (4-O<u>C</u>H_3-C_6H_4), 56.2, 112.4 (2-O<u>C</u>H_3-C_6H_4), 114.1 (4-OCH_3-C_6H_4), 117.6 (C^4), 119.8 (4-OCH_3-C_6H_4), 120.8, 121.2 (2-O<u>C</u>H_3-C_6H_4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.8 Hz), 125.6 (C_6H_5), 126.6 (2-OCH_3-C_6H_4), 128.6, 129.2 (C_6H_5), 132.2 (4-OCH_3-C_6H_4), 138.8 (C_6H_5), 141.4 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 142.2 (2-O<u>C</u>H_3-C_6H_4), 146.1 (C^5), 151.8 (<u>C</u>H), 152.2 (2-O<u>C</u>H_3-C_6H_4), 160.5 (4-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{25}H_{21}F_3N_3O_2^+$, $[M+H]^+$: 452.1580, found 452.1609.

(*E*)-3-Trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-5-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazole (**5cd**): Light Yellow solid; 56% yield (0.248 g); mp 126.7-129.0 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.83 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 6.89 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), 6.99-7.10 (*m*, 4H, 4-F-C_6H_4), 7.21-7.25 (*m*, 3H, 4-OC<u>H</u>$_3$-C_6H_4 and C_6H_5), 7.27-7.36 (*m*, 4H, C_6H_5), 8.30 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.4 (4-O<u>C</u>H_3-C_6H_4), 114.3 (4-OCH_3-C_6H_4), 115.9 (*d,* 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.5 Hz), 117.2 (C^4), 119.8 (4-OCH_3-C_6H_4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.8 Hz), 122.3 (*d,* 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.3 Hz), 125.5, 128.6, 129.2 (C_6H_5), 132.1 (4-OCH_3-C_6H_4), 138.7 (C_6H_5), 141.4 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 146.2 (C^5), 148.2 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 2.9 Hz), 150.0 (<u>C</u>H), 160.7 (4-OCH_3-C_6H_4), 161.4 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 244.7 Hz); **HRMS** (ESI+): calcd for $C_{24}H_{18}F_4N_3O^+$, $[M+H]^+$: 440.1381, found 440.1401.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-5-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazole (**5ce**): Orange solid; 59% yield (0.269 g); mp 153.3-155.1 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.83 (*s,* 3H, 4-OC$\underline{H}_3$-C_6H_4), 6.89 (*d*, 2H, 4-OCH$_3$-C_6H_4, *J* = 8.9 Hz), 7.02 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.20-7.24 (*m*, 3H, 4-OC$\underline{H}_3$-C_6H_4 and C_6H_5), 7.28-7.36 (*m*, 7H, 4-Cl-C_6H_4 and C_6H_5), 8.28 (*s*, 1H, C$\underline{H}$); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.4 (4-O$\underline{C}$H$_3$-C_6H_4), 114.3 (4-OCH$_3$-C_6H_4), 117.1 (C^4), 119.7 (4-OCH$_3$-C_6H_4), 121.3 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 269.8 Hz), 122.2 (4-Cl-C_6H_4), 125.5, 128.7, 129.2 (C_6H_5), 129.2, 131.6 (4-Cl-C_6H_4), 132.1 (4-OCH$_3$-C_6H_4), 138.7 (C_6H_5), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.3 Hz), 146.4 (C^5), 150.6 (C$\underline{H}$), 150.6 (4-Cl-C_6H_4), 160.7 (4-OCH$_3$-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}ClF_3N_3O^+$, $[M+H]^+$: 456.1085, found 456.1109.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-5-(4-methoxyphenyl)-1-phenyl-*1H*-pyrazole (**5cf**): Yellow solid; 52% yield (0.263 g); mp 161.3-162.9 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.82 (*s,* 3H, 4-OC$\underline{H}_3$-C_6H_4), 6.89 (*d*, 2H, 4-OCH$_3$-C_6H_4, *J* = 8.9 Hz), 6.96 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.19-7.25 (*m*, 3H, 4-OC$\underline{H}_3$-C_6H_4 and C_6H_5), 7.26-7.28 (*m*, 1H, C_6H_5), 7.32-7.36 (*m*, 3H, C_6H_5), 7.44 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.28 (*s*, 1H, C$\underline{H}$); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.4 (4-O$\underline{C}$H$_3$-C_6H_4), 114.3 (4-OCH$_3$-C_6H_4), 117.1 (C^4), 119.4 (4-Br-C_6H_4), 119.7 (4-OCH$_3$-C_6H_4), 121.3 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 270.0 Hz), 122.6 (4-Br-C_6H_4), 125.5, 128.7, 129.3 (C_6H_5), 132.1 (4-Br-C_6H_4), 132.2 (4-OCH$_3$-C_6H_4), 138.7 (C_6H_5), 141.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 146.5 (C^5), 150.7 (C$\underline{H}$), 151.2 (4-Br-C_6H_4), 160.8 (4-OCH$_3$-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}BrF_3N_3O^+$, $[M+H]^+$: 500.0580, found 500.0605.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-4-[(4-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5da**): Light Gray solid; 71% yield (0.316 g); mp 149.5-150.5 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.80 (*s,* 3H, 4-OC$\underline{H}_3$-C_6H_4), 6.87 (*d*, 2H, 4-OCH$_3$-C_6H_4, *J* = 9.0 Hz), 7.03-7.09 (*m*, 4H, 4-F-C_6H_4 and 4-OCH$_3$-C_6H_4), 7.23-7.25 (*m*, 1H, C_6H_5), 7.30-7.36 (*m*, 5H, 4-F-C_6H_4 and C_6H_5), 8.39 (*s*, 1H, C$\underline{H}$); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.6 (4-O$\underline{C}$H$_3$-C_6H_4), 114.4 (4-O$\underline{C}$H$_3$-C_6H_4), 115.9 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 21.9 Hz), 117.8 (C^4), 121.4 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.2 (4-O$\underline{C}$H$_3$-C_6H_4), 124.2 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.5 Hz), 125.6, 128.8, 129.3 (C_6H_5), 132.8 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.5 Hz), 138.6 (C_6H_5), 141.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 144.3 (C^5), 144.8 (4-O$\underline{C}$H$_3$-C_6H_4), 147.5 (C$\underline{H}$), 158.6 (4-O$\underline{C}$H$_3$-C_6H_4), 163.4 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 250.8 Hz); **HRMS** (ESI+): calcd for $C_{24}H_{18}F_4N_3O^+$, $[M+H]^+$: 440.1381, found 440.1396.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-1-phenyl-4-[(phenyl)iminomethyl]-*1H*-pyrazole (**5db**): Yellow solid; 58% yield (0.241 g); mp 135.7-137.7 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.04-7.09 (*m*, 4H, 4-F-C_6H_4 and C_6H_5 – A and B), 7.17-7.25 (*m*, 2H, C_6H_5 – A and B), 7.30-7.37 (*m*, 8H, 4-F-C_6H_4 and C_6H_5 – A and B), 8.37 (*s*, 1H, C$\underline{H}$); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 115.9 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 21.9 Hz), 117.5 (C^4), 120.8 (C_6H_5 – A or B), 121.3 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 270.0 Hz), 124.1 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.4 Hz), 125.6, 126.3, 128.9, 129.2, 129.3 (C_6H_5 – A and B), 132.8 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.6 Hz), 138.5 (C_6H_5), 141.9 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 144.7 (C^5), 149.8 (C$\underline{H}$), 152.0 (C_6H_5 – B), 163.4 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 251.0 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{16}F_4N_3^+$, $[M+H]^+$: 410.1275, found 410.1303.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-4-[(2-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5dc**): Light Brown solid; 61% yield (0.267 g); mp 125.6-127.1 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.81 (*s,* 3H, 2-OC$\underline{H}_3$-C_6H_4), 6.87-6.95 (*m*, 3H, 2-OCH$_3$-C_6H_4), 7.01-7.07 (*m*, 2H, 4-F-C_6H_4), 7.11-7.17 (*m*, 1H, 2-OCH$_3$-C_6H_4), 7.22-7.25 (*m*, 1H, C_6H_5), 7.33-7.38 (*m*, 5H, 4-F-C_6H_4 and C_6H_5), 8.44 (*s*, 1H, C$\underline{H}$); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.1 (2-O$\underline{C}$H$_3$-C_6H_4), 112.4 (2-O$\underline{C}$H$_3$-C_6H_4), 115.8 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 21.8 Hz), 117.8 (C^4), 120.9, 121.2 (2-O$\underline{C}$H$_3$-C_6H_4), 121.4 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 270.0 Hz), 124.1 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.4 Hz), 125.6 (C_6H_5), 126.9 (2-O$\underline{C}$H$_3$-C_6H_4), 128.8, 129.3 (C_6H_5), 133.0 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.6 Hz), 138.6 (C_6H_5), 141.7 (2-O$\underline{C}$H$_3$-C_6H_4), 141.9 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 144.5 (C^5), 151.2 (C$\underline{H}$), 152.3 (2-O$\underline{C}$H$_3$-C_6H_4), 163.4 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 250.5 Hz); **HRMS** (ESI+): calcd for $C_{24}H_{18}F_4N_3O^+$, $[M+H]^+$: 440.1381, found 440.1405.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-4-[(4-fluorophenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5dd**): Light Gray solid; 70% yield (0.316 g); mp 169.7-171.6 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.02-7.10 (*m*, 6H, 4-F-C_6H_4 – A and B), 7.23-7.25 (*m*, 1H, C_6H_5), 7.29-7.37 (*m*, 6H, 4-F-C_6H_4 – A and B), 8.34 (*s*, 1H, C$\underline{H}$); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 115.9 (*d*, 4-F-C_6H_4 – B, $^2J_{C\text{-}F}$ = 22.7 Hz), 115.9 (*d*, 4-F-C_6H_4 – A, $^2J_{C\text{-}F}$ = 21.9 Hz), 117.4 (C^4), 121.3 (*q*, $\underline{C}F_3$, $^1J_{C\text{-}F}$ = 270.0 Hz), 122.3 (*d*, 4-F-C_6H_4 – B, $^3J_{C\text{-}F}$ = 8.3 Hz), 124.1 (*d*, 4-F-C_6H_4 – A, $^4J_{C\text{-}F}$ = 3.5 Hz), 125.6, 128.9, 129.3 (C_6H_5), 132.8 (*d*, 4-F-C_6H_4 – A, $^3J_{C\text{-}F}$ = 8.5 Hz), 138.5 (C_6H_5), 141.8 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 144.7 (C^5), 147.9 (*d*, 4-F-C_6H_4 – B, $^4J_{C\text{-}F}$ = 2.9 Hz), 149.4 (C$\underline{H}$), 161.5 (*d*, 4-F-C_6H_4 – B, $^1J_{C\text{-}F}$ = 245.0 Hz), 163.5 (*d*, 4-F-C_6H_4 – A, $^1J_{C\text{-}F}$ = 251.2 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{15}F_5N_3^+$, $[M+H]^+$: 428.1181, found 428.1208.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-5-(4-fluorophenyl)-1-phenyl-*1H*-pyrazole (**5de**): Light Yellow solid; 67% yield (0.302 g); mp 150.9-152.5 ^{o}C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.99 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.04-7.10 (*m*, 2H, 4-F-C_6H_4), 7.22-7.25 (*m*, 1H, C_6H_5), 7.28-7.37 (*m*, 8H, 4-F-C_6H_4, 4-Cl-C_6H_4 and C_6H_5), 8.33 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 116.0 (*d*, 4-F-C_6H_4, $^{2}J_{C\text{-}F}$ = 22.0 Hz), 117.3 (C^4), 121.3 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 269.9 Hz), 122.1 (4-Cl-C_6H_4), 123.9 (*d*, 4-F-C_6H_4, $^{4}J_{C\text{-}F}$ = 3.6 Hz), 125.6, 128.9, 129.3 (C_6H_5), 129.4, 131.8 (4-Cl-C_6H_4), 132.8 (*d*, 4-F-C_6H_4, $^{3}J_{C\text{-}F}$ = 8.6 Hz), 138.4 (C_6H_5), 141.9 (*q*, C^3, $^{2}J_{C\text{-}F}$ = 38.2 Hz), 144.9 (C^5), 150.1 (<u>C</u>H), 150.3 (4-Cl-C_6H_4), 163.5 (*d*, 4-F-C_6H_4, $^{1}J_{C\text{-}F}$ = 251.3 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{15}ClF_4N_3^+$, $[M+H]^+$: 444.0885, found 444.0908.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-5-(4-fluorophenyl)-1-phenyl-*1H*-pyrazole (**5df**): Light Yellow solid; 60% yield (0.293 g); mp 158.8-159.9 ^{o}C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.93 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.04-7.10 (*m*, 2H, 4-F-C_6H_4), 7.22-7.25 (*m*, 1H, C_6H_5), 7.28-7.37 (*m*, 6H, 4-F-C_6H_4 and C_6H_5), 7.45 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.32 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 116.0 (*d*, 4-F-C_6H_4, $^{2}J_{C\text{-}F}$ = 22.0 Hz), 117.3 (C^4), 119.7 (4-Br-C_6H_4), 121.3 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 270.1 Hz), 122.5 (4-Br-C_6H_4), 123.9 (*d*, 4-F-C_6H_4, $^{4}J_{C\text{-}F}$ = 3.5 Hz), 125.6, 129.0, 129.4 (C_6H_5), 132.3 (4-Br-C_6H_4), 132.8 (*d*, 4-F-C_6H_4, $^{3}J_{C\text{-}F}$ = 8.5 Hz), 138.4 (C_6H_5), 141.9 (*q*, C^3, $^{2}J_{C\text{-}F}$ = 38.0 Hz), 144.9 (C^5), 150.1 (<u>C</u>H), 150.8 (4-Br-C_6H_4), 163.5 (*d*, 4-F-C_6H_4, $^{1}J_{C\text{-}F}$ = 251.3 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{15}BrF_4N_3^+$, $[M+H]^+$: 488.0380, found 488.0401.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5ea**): Light yellow solid; 61% yield (0.281 g); mp 155.9-159.0 ^{o}C; **^{1}H NMR** (500.13 MHz, $CDCl_3$) δ (ppm) 3.81 (*s,* 3H, 4-OC<u>H_3</u>-C_6H_4), 6.88 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), 7.08 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), 7.23-7.25 (*m*, 2H, C_6H_5), 7.26-7.28 (*m*, 2H, 4-Cl-C_6H_4), 7.33-7.36 (*m*, 5H, 4-Cl-C_6H_4 and C_6H_5), 8.39 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (125.76 MHz, $CDCl_3$) δ (ppm) 55.6 (4-O<u>C</u>H_3-C_6H_4), 114.4 (4-OCH_3-C_6H_4), 117.8 (C^4), 121.4 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 270.0 Hz), 122.2 (4-OCH_3-C_6H_4), 125.6 (C_6H_5), 126.7 (4-Cl-C_6H_4), 128.9, 128.9 (C_6H_5), 129.3, 132.2, 135.9 (4-Cl-C_6H_4), 138.5 (C_6H_5), 141.8 (*q*, C^3, $^{2}J_{C\text{-}F}$ = 38.0 Hz), 144.0 (C^5), 144.7 (4-OCH_3-C_6H_4), 147.4 (<u>C</u>H), 158.6 (4-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}ClF_3N_3O^+$, $[M+H]^+$: 456.1085, found 456.1097.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-1-phenyl-4-[(phenyl)iminomethyl]-*1H*-pyrazole (**5eb**): White solid; 55% yield (0.235 g); mp 175.6-176.4 ^{o}C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.05-7.08 (*m*, 2H, C_6H_5), 7.18-7.24 (*m*, 2H, C_6H_5), 7.29-7.37 (*m*, 10H, C_6H_5 A, B and 4-Cl-C_6H_4), 8.37 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.6 (C^4), 120.8 (C_6H_5 – A or B), 121.3 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 270.1 Hz), 125.6, 126.3 (C_6H_5 – A and B), 126.5 (4-Cl-C_6H_4), 129.0, 129.0, 129.2, 129.4, 132.2, 136.1, 138.4 (C_6H_5 – A, B and 4-Cl-C_6H_4), 142.0 (*q*, C^3, $^{2}J_{C\text{-}F}$ = 38.2 Hz), 144.4 (C^5), 149.6 (<u>C</u>H), 151.9 (C_6H_5 – B); **HRMS** (ESI+): calcd for $C_{23}H_{16}ClF_3N_3^+$, $[M+H]^+$: 426.0979, found 426.1008.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5ec**): Light gray solid; 59% yield (0.270 g); mp 162.2-167.2 ^{o}C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.82 (*s,* 3H, 2-OC<u>H_3</u>-C_6H_4), 6.87-6.95 (*m*, 4H, 2-OCH_3-C_6H_4 and 4-Cl-C_6H_4), 7.12-7.18 (*m*, 1H, 2-OCH_3-C_6H_4), 7.23-7.26 (*m,* 4H, 2-OCH_3-C_6H_4 and C_6H_5), 7.34-7.38 (*m*, 4H, 4-Cl-C_6H_4 and C_6H_5), 8.44 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.1 (2-O<u>C</u>H_3-C_6H_4), 112.3 (2-OCH_3-C_6H_4), 117.8 (C^4), 120.7, 121.2 (2-OCH_3-C_6H_4), 121.3 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 270.1 Hz), 125.6 (C_6H_5), 126.4 (4-Cl-C_6H_4), 126.9 (2-OCH_3-C_6H_4), 128.8, 128.9 (C_6H_5), 129.4, 132.3, 135.8 (4-Cl-C_6H_4), 138.5 (C_6H_5), 141.6 (2-OCH_3-C_6H_4), 142.0 (*q*, C^3, $^{2}J_{C\text{-}F}$ = 38.1 Hz), 144.2 (C^5), 151.1 (<u>C</u>H), 152.3 (2-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}ClF_3N_3O^+$, $[M+H]^+$: 456.1085, found 456.1102.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5ed**): Light brown solid; 60% yield (0.268 g); mp 155.1-157.2 ^{o}C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.01-7.05 (*m*, 4H, 4-F-C_6H_4), 7.24-7.28 (*m*, 2H, C_6H_5), 7.27-7.28 (*m*, 2H, 4-Cl-C_6H_4), 7.34-.737 (*m*, 5H, 4-Cl-C_6H_4 and C_6H_5), 8.35 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 115.9 (*d*, 4-F-C_6H_4, $^{2}J_{C\text{-}F}$ = 22.5 Hz), 117.5 (C^4), 121.3 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 270.0 Hz), 122.3 (*d*, 4-F-C_6H_4, $^{3}J_{C\text{-}F}$ = 8.2 Hz), 125.6 (C_6H_5), 126.5 (4-Cl-C_6H_4), 129.0, 129.0 (C_6H_5), 129.4, 132.1, 136.1 (4-Cl-C_6H_4), 138.4 (C_6H_5), 141.9 (*q*, C^3, $^{2}J_{C\text{-}F}$ = 38.1 Hz), 144.4 (C^5), 147.8 (*d*, 4-F-C_6H_4, $^{4}J_{C\text{-}F}$ = 2.9 Hz), 149.3 (<u>C</u>H), 161.5 (*d*, 4-F-C_6H_4, $^{1}J_{C\text{-}F}$ = 245.1 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{15}ClF_4N_3^+$, $[M+H]^+$: 444.0885, found 444.0912.

(*E*)-5-(4-Chlorophenyl)-4-[(4-chlorophenyl)iminomethyl]-3-trifluoromethyl-1-phenyl-*1H*-pyrazole (**5ee**): Light yellow solid; 54% yield (0.251 g); mp 163.8-165.7 ^{o}C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.00 (*d*, 2H, 4-Cl-C_6H_4 – B, *J* = 8.7 Hz), 7.23-7.25 (*m*, 2H, C_6H_5), 7.28-7.38 (*m*, 9H, 4-Cl-C_6H_4 – A and B, and C_6H_5), 8.33 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.3 (C^4), 121.2 (*q*, <u>C</u>F_3, $^{1}J_{C\text{-}F}$ = 270.0 Hz), 122.2 (4-Cl-C_6H_4 – B), 125.6 (C_6H_5), 126.4 (4-Cl-C_6H_4 – A), 129.1, 129.1 (C_6H_5), 129.4, 131.9, 132.1, 136.2 (4-Cl-C_6H_4 – A

and B), 138.3 (C_6H_5), 141.9 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.3 Hz), 144.6 (C^5), 150.0 (C<u>H</u>), 150.3 (4-Cl-C_6H_4 – B); **HRMS** (ESI+): calcd for $C_{23}H_{15}Cl_2F_3N_3^+$, $[M+H]^+$: 460.0590, found 460.0615.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-5-(4-chlorophenyl)-3-trifluoromethyl-1-phenyl-*1H*-pyrazole (**5ef**): Light yellow solid; 52% yield (0.261 g); mp 168.9-173.5 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.94 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.23-7.27 (*m*, 3H, 4-Cl-C_6H_4 and C_6H_5), 7.34-7.38 (*m*, 6H, 4-Cl-C_6H_4 and C_6H_5), 7.45 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.33 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.3 (C^4), 119.8 (4-Br-C_6H_4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.1 Hz), 122.5 (4-Br-C_6H_4), 125.6 (C_6H_5), 126.4 (4-Cl-C_6H_4), 129.1, 129.1 (C_6H_5), 129.4, 132.1 (4-Cl-C_6H_4), 132.3 (4-Br-C_6H_4), 136.2 (4-Cl-C_6H_4), 138.3 (C_6H_5), 142.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 144.6 (C^5), 150.0 (C<u>H</u>), 150.8 (4-Br-C_6H_4); **HRMS** (ESI+): calcd for $C_{23}H_{15}BrClF_3N_3^+$, $[M+H]^+$: 504.0084, found 504.0110.

(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5fa**): White solid; 74% yield (0.369 g); mp 172.6-176.1 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.81 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 6.88 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.08 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.19-7.25 (*m*, 4H, C_6H_5 and 4-Br-C_6H_4), 7.35-7.37 (*m*, 3H, C_6H_5), 7.50 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.6 Hz), 8.39 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.6 (4-O<u>C</u>H_3-C_6H_4), 114.4 (4-OCH_3-C_6H_4), 117.8 (C^4), 121.4 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.1 Hz), 122.2 (4-OCH_3-C_6H_4), 124.3 (4-Br-C_6H_4), 125.6 (C_6H_5), 127.1 (4-Br-C_6H_4), 128.9, 129.4 (C_6H_5), 131.9, 132.4 (4-Br-C_6H_4), 138.5 (C_6H_5), 141.9 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 144.0 (C^5), 144.7 (4-OCH_3-C_6H_4), 147.4 (C<u>H</u>), 158.6 (4-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}BrF_3N_3O^+$, $[M+H]^+$: 500.0580, found 500.0609.

(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(phenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5fb**): White solid; 57% yield (0.269 g); mp 179.3-184.2 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.05-7.08 (*m*, 2H, C_6H_5), 7.18-7.24 (*m*, 5H, C_6H_5 A, B and 4-Br-C_6H_4), 7.32-7.38 (*m*, 5H, C_6H_5 A, B and 4-Br-C_6H_4), 7.50 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.7 Hz), 8.37 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.6 (C^4), 120.8 (C_6H_5 – A or B), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.1 Hz), 124.4 (4-Br-C_6H_4), 125.6, 126.3 (C_6H_5 – A and B), 127.0 (4-Br-C_6H_4), 129.0, 129.2, 129.4 (C_6H_5 – A and B) 131.9, 132.4 (4-Br-C_6H_4), 138.4 (C_6H_5 – A), 142.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 144.4 (C^5), 149.6 (C<u>H</u>), 151.9 (C_6H_5 – B); **HRMS** (ESI+): calcd for $C_{23}H_{16}BrF_3N_3^+$, $[M+H]^+$: 470.0474, found 470.0506.

(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5fc**): Light Yellow solid; 68% yield (0.341 g); mp 177.5-179.4 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.82 (*s,* 3H, 2-OC<u>H</u>$_3$-C_6H_4), 6.87-6.95 (*m*, 4H, 2-OCH_3-C_6H_4 and 4-Br-C_6H_4), 7.12-7.18 (*m*, 1H, 2-OCH_3-C_6H_4), 7.23-7.25 (*m*, 2H, 2-OCH_3-C_6H_4 and C_6H_5), 7.35-7.38 (*m*, 4H, 2-OC<u>H</u>$_3$-C_6H_4 and C_6H_5), 7.48 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.5 Hz), 8.44 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.1 (2-O<u>C</u>H_3-C_6H_4), 112.3 (2-OCH_3-C_6H_4), 117.8 (C^4), 120.7, 121.2 (2-OCH_3-C_6H_4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.1 Hz), 124.2 (4-Br-C_6H_4), 125.6 (C_6H_5), 126.9 (2-OCH_3-C_6H_4), 128.9, 129.4 (C_6H_5), 131.8, 132.5 (4-Br-C_6H_4), 138.5 (C_6H_5), 141.6 (2-OCH_3-C_6H_4), 142.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 144.2 (C^5), 151.0 (C<u>H</u>), 152.3 (2-OCH_3-C_6H_4); **HRMS** (ESI+): calcd for $C_{24}H_{18}BrF_3N_3O^+$, $[M+H]^+$: 500.0580, found 500.0605.

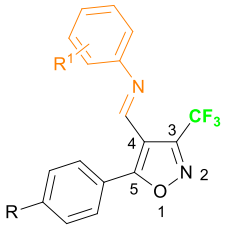
(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-1-phenyl-*1H*-pyrazole (**5fd**): Light brown solid; 65% yield (0.316 g); mp 143.9-147.0 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.99-7.05 (*m*, 4H, 4-F-C_6H_4), 7.18-7.25 (*m*, 4H, 4-Br-C_6H_4 and C_6H_5), 7.35-7.38 (*m*, 3H, C_6H_5), 7.51 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.6 Hz), 8.35 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 115.9 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.6 Hz), 117.4 (C^4), 121.3 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 269.9 Hz), 122.3 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.3 Hz), 124.5 (4-Br-C_6H_4), 125.6 (C_6H_5), 127.0 (4-Br-C_6H_4), 129.0, 129.4 (C_6H_5), 132.0, 132.3 (4-Br-C_6H_4), 138.4 (C_6H_5), 141.9 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 144.4 (C^5), 147.8 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 2.9 Hz), 149.3 (C<u>H</u>), 161.5 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 245.1 Hz); **HRMS** (ESI+): calcd for $C_{23}H_{15}BrF_4N_3^+$, $[M+H]^+$: 488.0380, found 488.0417.

(*E*)-5-(4-Bromophenyl)-4-[(4-chlorophenyl)iminomethyl]-3-trifluoromethyl-1-phenyl-*1H*-pyrazole (**5fe**): White solid; 66% yield (0.334 g); mp 163.2-164.4 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.00 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.19 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.7 Hz), 7.23-7.25 (*m*, 2H, C_6H_5), 7.30 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.36-7.38 (*m*, 3H C_6H_5), 7.51 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.7 Hz), 8.33 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.3 (C^4), 121.2 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.1 Hz), 122.2 (4-Cl-C_6H_4), 124.5 (4-Br-C_6H_4), 125.6 (C_6H_5), 126.9 (4-Br-C_6H_4), 129.0, 129.3 (C_6H_5), 129.4, 131.9 (4-Cl-C_6H_4), 132.0, 132.3 (4-Br-C_6H_4), 138.3 (C_6H_5), 142.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 144.6 (C^5), 149.9 (C<u>H</u>), 150.3 (4-Cl-C_6H_4); **HRMS** (ESI+): calcd for $C_{23}H_{15}BrClF_3N_3^+$, $[M+H]^+$: 504.0084, found 504.0111.

(*E*)-5-(4-Bromophenyl)-4-[(4-bromophenyl)iminomethyl]-3-trifluoromethyl-1-phenyl-*1H*-pyrazole (**5ff**): White solid; 60% yield (0.330 g); mp 171.5-174.3 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 6.93 (*d*, 2H, 4-Br-C_6H_4 – B, *J* = 8.8 Hz), 7.19 (*d*, 2H, 4-Br-C_6H_4 – A, *J* = 8.7 Hz), 7.23-7.25 (*m*, 2H, C_6H_5), 7.35-7.38 (*m*, 3H, C_6H_5), 7.45 (*d*, 2H, 4-Br-C_6H_4 – B, *J* = 8.8 Hz), 7.51 (*d*, 2H, 4-Br-C_6H_4 – A, *J* = 8.7 Hz), 8.33 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 117.3 (C^4), 119.8 (4-Br-C_6H_4 – B), 121.2 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 270.1 Hz), 122.5 (4-Br-C_6H_4 – B), 124.5 (4-Br-C_6H_4 – A), 125.6 (C_6H_5), 126.8 (4-Br-C_6H_4 – A), 129.0, 129.4 (C_6H_5), 132.0, 132.3, 132.3 (4-Br-C_6H_4 – A and B), 138.3 (C_6H_5), 142.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 144.6 (C^5), 150.0 (<u>C</u>H), 150.8 (4-Br-C_6H_4 – B); **HRMS** (ESI+): calcd for $C_{23}H_{15}Br_2F_3N_3^+$, $[M+H]^+$: 547.9579, found 547.9600.

General procedure of synthesis of 5-aryl-4-[(aryl)iminomethyl]-3-trifluoromethylisoxazoles 6(aa-af)-6(fa-ff).

General method. The compound **2** (**2a**: 0.344 g; **2b**: 0.229 g; **2c**: 0.329 g; 2**d**: 0.317 g; **2e**: 0.334 g; **2f**: 0.378 g, 1.0 mmol, 1.0 equiv) was solubilized in MeCN (8 mL), then added hydroxylamine hydrochloride (0.083 g, 1.2 mmol, 1.2 equiv) and boron trifluoride diethyl etherate solution 46.5% (0.530 mL, 2.0 mmol, 2.0 equiv). The mixture was stirred under reflux for 5 h. After that, reaction mixture was cooled to room temperature, added substituted anilines (3.0 mmol, 3.0 equiv) and stirred for 15 min. Then, the solvent was evaporated under vacuum and the residue was washed with a solution of 3% of K_2CO_3 (25 mL), extracted with dichloromethane (3x20 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated under reduced pressure and the obtained residue was dissolved in hot ethyl ether (5 mL) and cooled to 0 °C which induced crystallization. The solid was filtered, washed with cold ethyl ether (20 mL) and dried under vacuum.



6(aa-af)-6(fa-ff)

(*E*)-3-Trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]-5-(4-nitrophenyl)isoxazole (**6aa**): Yellow solid; 75% yield (0.292 g); mp 159.8-161.5 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.85 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4), 6.96 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.24 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 8.39 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz), 8.45 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz), 8.50 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.7 (4-O<u>C</u>H_3-C_6H_4), 114.2 (C^4), 114.8 (4-OCH_3-C_6H_4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.4 Hz), 122.6 (4-NO_2-C_6H_4), 124.0 (4-OCH_3-C_6H_4), 130.1, 131.9 (4-NO_2-C_6H_4), 143.1 (4-OCH_3-C_6H_4), 143.6 (<u>C</u>H), 149.5 (4-NO_2-C_6H_4), 155.1 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 159.8 (4-OCH_3-C_6H_4), 168.6 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}F_3N_3O_4^+$, $[M+H]^+$: 392.0853, found 392.0877.

(*E*)-3-Trifluoromethyl-5-(4-nitrophenyl)-4-[(phenyl)iminomethyl]isoxazole (**6ab**): Yellow solid; 71% yield (0.256 g); mp 141.3-142.8 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.19-7.22 (*m*, 2H, C_6H_5), 7.30-7.35 (*m*, 1H, C_6H_5), 7.45-7.47 (*m*, 2H, C_6H_5), 8.40 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz), 8.46 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz), 8.50 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 113.9 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.5 Hz), 121.0 (C_6H_5), 124.1 (4-NO_2-C_6H_4), 127.8, 129.6 (C_6H_5), 130.2, 131.7 (4-NO_2-C_6H_4), 146.4 (<u>C</u>H), 149.6 (4-NO_2-C_6H_4), 150.4 (C_6H_5), 155.1 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 169.2 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{11}F_3N_3O_3^+$, $[M+H]^+$: 362.0747, found 362.0769.

(*E*)-3-Trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]-5-(4-nitrophenyl)isoxazole (**6ac**): Yellow solid; 73% yield (0.287 g); mp 175.5-177.2 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.94 (*s*, 3H, 2-OC<u>H</u>$_3$), 6.98-7.08 (*m*, 3H, 2-OCH_3-C_6H_4), 7.27-7.31 (*m*, 1H, 2-OCH_3-C_6H_4), 8.38 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz), 8.62 (*s*, 1H, C<u>H</u>), 8.65 (*d*, 2H, 4-NO_2-C_6H_4, *J* = 9.2 Hz); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.1 (2-O<u>C</u>H_3-C_6H_4), 112.0 (2-OCH_3-C_6H_4), 114.1 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.5 Hz), 120.9, 121.3 (2-OCH_3-C_6H_4), 123.9 (4-NO_2-C_6H_4), 128.6 (2-OCH_3-C_6H_4), 130.2, 131.8 (4-NO_2-C_6H_4), 139.6 (2-OCH_3-C_6H_4), 147.5 (<u>C</u>H), 149.5 (4-NO_2-C_6H_4), 152.7 (2-OCH_3-C_6H_4), 155.2 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 168.8 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}F_3N_3O_4^+$, $[M+H]^+$: 392.0853, found 392.0883.

(*E*)-3-Trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-5-(4-nitrophenyl)isoxazole (**6ad**): Yellow solid; 70% yield (0.266 g); mp 157.7-159.6 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.10-7.23 (*m*, 4H, 4-F-C_6H_4), 8.41 (*s*, 4H, 4-NO_2-C_6H_4), 8.47 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 113.8 (C^4), 116.5 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.9 Hz), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.4 Hz), 122.7 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.5 Hz), 124.1, 130.1, 131.7 (4-NO_2-

C_6H_4), 146.0 (CH), 146.4 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.1 Hz), 149.6 (4-NO_2-C_6H_4), 155.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 162.3 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 247.6 Hz) 169.2 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}F_4N_3O_3^+$, $[M+H]^+$: 380.0653, found 380.0662.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-5-(4-nitrophenyl)isoxazole (**6ae**): Yellow solid; 72% yield (0.283 g); mp 162.8-165.6 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.14 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.40 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 8.41 (*s*, 4H, 4-NO_2-C_6H_4), 8.47 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 113.7 (C^4), 119.6 (*q*, CF_3, $^1J_{C\text{-}F}$ = 272.4 Hz), 122.3 (4-Cl-C_6H_4), 124.1 (4-NO_2-C_6H_4), 129.8 (4-Cl-C_6H_4), 130.2, 131.6 (4-NO_2-C_6H_4), 133.5 (4-Cl-C_6H_4), 146.7 (CH), 148.8 (4-Cl-C_6H_4), 149.7 (4-NO_2-C_6H_4), 155.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.2 Hz), 169.4 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}ClF_3N_3O_3^+$, $[M+H]^+$: 396.0357, found 396.0380.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-5-(4-nitrophenyl)isoxazole (**6af**): Yellow solid; 73% yield (0.319 g); mp 170.7-173.5 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.08 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.55 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.40 (*s*, 4H, 4-NO_2-C_6H_4), 8.47 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 113.7 (C^4), 119.6 (*q*, CF_3, $^1J_{C\text{-}F}$ = 272.4 Hz), 121.4, 122.6 (4-Br-C_6H_4), 124.1, 130.2, 131.6 (4-NO_2-C_6H_4), 132.7 (4-Br-C_6H_4), 146.8 (CH), 149.3 (4-Br-C_6H_4), 149.7 (4-NO_2-C_6H_4), 155.0 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.3 Hz), 169.5 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}BrF_3N_3O_3^+$, $[M+H]^+$: 439.9852, found 439.9882.

(*E*)-3-Trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]-5-phenylisoxazole (**6ba**): White solid; 78% yield (0.269 g); mp 77.6-78.5 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.84 (*s,* 3H, 4-OCH_3), 6.94 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), 7.22 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 8.9 Hz), *7*.53-7.60 (*m*, 3H, C_6H_5), 7.97-8.00 (*m*, 2H, C_6H_5), 8.49 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.7 (4-OCH_3-C_6H_4), 112.6 (C^4), 114.6 (4-OCH_3-C_6H_4), 119.9 (*q*, CF_3, $^1J_{C\text{-}F}$ = 271.9 Hz), 122.4 (4-OCH_3-C_6H_4), 126.2, 128.8, 129.2, 132.0 (C_6H_5), 143.9 (4-OCH_3-C_6H_4), 144.8 (CH), 154.2 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 159.2 (4-OCH_3-C_6H_5) 172.1 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{14}F_3N_2O_2^+$, $[M+H]^+$: 347.1002, found 347.1027.

(*E*)-3-Trifluoromethyl-5-phenyl-4-[(phenyl)iminomethyl]isoxazole (**6bb**): White solid; 74% yield (0.234 g); mp 103.0-104.3 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.17-7.20 (*m*, 2H, C_6H_5 B), 7.27-7.30 (*m*, 1H, C_6H_5 B), 7.39-7.44 (*m*, 2H, C_6H_5 – B), 7.53-7.60 (*m*, 3H, C_6H_5 – A), 7.97-8.01 (*m*, 2H, C_6H_5 – A), 8.48 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.4 (C^4), 119.8 (*q*, CF_3, $^1J_{C\text{-}F}$ = 272.0 Hz), 120.9, 126.1, 127.1, 128.8, 129.2, 129.4, 132.1 (C_6H_5 – A and B), 147.3 (CH), 151.2 (C_6H_5 – B), 154.2 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 172.6 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{12}F_3N_2O^+$, $[M+H]^+$: 317.0896, found 317.0915.

(*E*)-3-Trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]-5-phenylisoxazole (**6bc**): Light yellow solid; 77% yield (0.266 g); mp 80.3-81.3°C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.90 (*s,* 3H, 2-OCH_3), 6.96-7.06 (*m*, 3H, 2-OCH_3-C_6H_4), 7.20-7.25 (*m*, 1H, 2-OCH_3-C_6H_4), 7.51-7.59 (*m*, 3H, C_6H_5), 8.09-8.13 (*m*, 2H, C_6H_5), 8.60 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.1 (2-OCH_3-C_6H_4), 112.2 (2-OCH_3-C_6H_4), 112.5 (C^4), 119.8 (*q*, CF_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 121.2, 121.5 (2-OCH_3-C_6H_4), 126.2 (C_6H_5), 127.7 (2-OCH_3-C_6H_4), 128.8, 129.1, 132.0 (C_6H_5), 140.5 (2-OCH_3-C_6H_4), 149.0 (CH), 152.2 (2-OCH_3-C_6H_4), 154.3 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 172.1 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{14}F_3N_2O_2^+$, $[M+H]^+$: 347.1002, found 347.1035.

(*E*)-3-Trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-5-phenylisoxazole (**6bd**): Light yellow solid; 72% yield (0.242 g); mp 72.5-73.6 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.07-7.13 (*m*, 2H, 4-F-C_6H_4, *J* = 8.6 Hz), 7.17-7.22 (*m*, 2H, 4-F-C_6H_4), 7.54-7.62 (*m*, 3H, C_6H_5), 7.94-7.98 (*m*, 2H, C_6H_5), 8.46 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.3 (C^4), 116.2 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.6 Hz), 119.8 (*q*, CF_3, $^1J_{C\text{-}F}$ = 272.0 Hz), 122.5 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.4 Hz), 126.0, 128.8, 129.3, 132.2 (C_6H_5), 146.9 (CH), 147.8 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.0 Hz), 154.1 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 161.9 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 246.3 Hz), 172.7 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{11}F_4N_2O^+$, $[M+H]^+$: 335.0802, found 335.0824.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-5-phenylisoxazole (**6be**): White solid; 76% yield (0.265 g); mp 57.8-59.5 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.13 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.37 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.54-7.62 (*m*, 3H, C_6H_5), 7.93-7.97 (*m*, 2H, C_6H_5), 8.45 (*s*, 1H, CH); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.2 (C^4), 119.8 (*q*, CF_3, $^1J_{C\text{-}F}$ = 271.9 Hz), 122.3 (4-Cl-C_6H_4), 126.0, 128.8, 129.3 (C_6H_5), 129.5 (4-Cl-C_6H_4), 132.2 (C_6H_5), 132.7 (4-Cl-C_6H_4), 147.6 (CH), 149.5 (4-Cl-C_6H_4), 154.1 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 172.9 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{11}ClF_3N_2O^+$, $[M+H]^+$: 351.0507, found 351.0535.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-5-phenylisoxazole (**6bf**): Yellow solid; 71% yield (0.279 g); mp 100.7-101.4 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.07 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.52

(*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.57-7.62 (*m*, 3H, C_6H_5), 7.93-7.97 (*m*, 2H, C_6H_5), 8.45 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.2 (C^4), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.1 Hz), 120.6, 122.6 (4-Br-C_6H_4), 125.9, 128.8, 129.3, 132.3 (C_6H_5), 132.5 (4-Br-C_6H_4), 147.7 (<u>C</u>H), 150.0 (4-Br-C_6H_5), 154.1 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 172.9 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{11}BrF_3N_2O^+$, $[M+H]^+$: 395.0001, found 395.0029.

(*E*)-3-Trifluoromethyl-5-(4-methoxyphenyl)-4-[(4-methoxyphenyl)iminomethyl]isoxazole (**6ca**): Yellow solid; 78% yield (0.295 g); mp 86.5-87.1 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.86 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4 – B), 3.90 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4 – A), 6.94 (*d*, 2H, 4-OCH_3-C_6H_4 – B, *J* = 9.0 Hz), 7.05 (*d*, 2H, 4-OCH_3-C_6H_4 – A, *J* = 9.0 Hz), 7.22 (*d*, 2H, 4-OCH_3-C_6H_4 – B, *J* = 9.0 Hz), 8.04 (*d*, 2H, 4-OCH_3-C_6H_4 – A, *J* = 9.0 Hz), 8.46 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.6 (4-O<u>C</u>H_3-C_6H_4 – A), 55.7 (4-O<u>C</u>H_3-C_6H_4 – B), 111.3 (C^4), 114.6, 114.6 (4-OCH_3-C_6H_4 – A and B), 118.7 (4-OCH_3-C_6H_4 – A), 119.9 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.0 Hz), 122.4 (4-O<u>C</u>H_3-C_6H_4 – B), 130.6 (4-O<u>C</u>H_3-C_6H_4 – A), 144.1 (4-OCH_3-C_6H_4 – B), 145.2 (<u>C</u>H), 154.3 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.4 Hz), 159.1 (4-OCH_3-C_6H_4 – B), 162.5 (4-OCH_3-C_6H_4 – A), 171.9 (C^5); **HRMS** (ESI+): calcd for $C_{19}H_{16}F_3N_2O_3^+$, $[M+H]^+$: 377.1108, found 377.1130.

(*E*)-3-Trifluoromethyl-5-(4-methoxyphenyl)-4-[(phenyl)iminomethyl]isoxazole (6cb): Light Yellow solid; 73% yield (0.252 g); mp 88.7-89.9 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.90 (*s*, 3H, OC<u>H</u>$_3$-C_6H_4), 7.05 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.17-7.21 (*m*, 2H, C_6H_5), 7.27-7.30 (*m*, 1H, C_6H_5), 7.39-7.44 (*m*, 2H, C_6H_5), 8.05 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 8.45 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.6 (4-O<u>C</u>H_3-C_6H_4), 111.1 (C^4), 114.6, 118.5 (4-OCH_3-C_6H_4), 119.9 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.0 Hz), 120.9, 126.9, 129.4 (C_6H_5), 130.6 (4-OCH_3-C_6H_4), 147.7 (<u>C</u>H), 151.3 (C_6H_5), 154.3 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 162.7 (4-OCH_3-C_6H_4), 172.4 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{14}F_3N_2O_2^+$, $[M+H]^+$: 347.1002, found 347.1030.

(*E*)-3-Trifluoromethyl-5-(4-methoxyphenyl)-4-[(2-methoxyphenyl)iminomethyl]isoxazole (**6cc**): White solid; 77% yield (0.291 g); mp 81.8-82.9 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.89 (*s*, 3H, 4-OC<u>H</u>$_3$-C_6H_4), 3.91 (*s*, 3H, 2-OC<u>H</u>$_3$-C_6H_4), 6.96-7.05 (*m*, 5H, 2-OCH_3-C_6H_4 and 4-OCH_3-C_6H_4), 7.20-7.26 (*m*, 1H, 2-OCH_3-C_6H_4), 8.18 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.1 Hz), 8.56 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.6 (4-O<u>C</u>H_3-C_6H_4), 56.1 (2-O<u>C</u>H_3-C_6H_4), 111.1 (C^4), 112.1 (2-OCH_3-C_6H_4), 114.4 (4-OCH_3-C_6H_4), 118.7 (2-OCH_3-C_6H_4), 119.9 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.0 Hz), 121.2, 122.1, 127.6 (2-OCH_3-C_6H_4), 130.7, 140.7 (4-OCH_3-C_6H_4), 149.2 (<u>C</u>H), 152.3 (2-OCH_3-C_6H_4), 154.4 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.5 Hz), 162.6 (4-OCH_3-C_6H_4), 172.0 (C^5); **HRMS** (ESI+): calcd for $C_{19}H_{16}F_3N_2O_3^+$, $[M+H]^+$: 377.1108, found 377.1135.

(*E*)-3-Trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]-5-(4-methoxyphenyl)isoxazole (**6cd**): White solid; 72% yield (0.263 g); mp 98.3-99.0 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.90 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 7.04-7.21 (*m*, 6H, 4-F-C_6H_4 and 4-OCH_3-C_6H_4), 8.01 (*d*, 2H, 4-OC<u>H</u>$_3$-C_6H_4, *J* = 9.0 Hz), 8.43 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.7 (4-O<u>C</u>H_3-C_6H_4), 111.0 (C^4), 114.6 (4-OCH_3-C_6H_4), 116.2 (*d,* 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.6 Hz), 118.5 (4-OCH_3-C_6H_4), 119.9 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.0 Hz), 122.5 (*d,* 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.4 Hz), 130.6 (4-OCH_3-C_6H_4), 147.3 (*d,* 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 4.4 Hz), 147.3 (<u>C</u>H), 154.2 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.6 Hz), 161.8 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 246.0 Hz), 162.7 (4-OCH_3-C_6H_4), 172.6 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}F_4N_2O_2^+$, $[M+H]^+$: 365.0908, found 365.0938.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-5-(4-methoxyphenyl)isoxazole (**6ce**): Yellow solid; 70% yield (0.265 g); mp 95.5-98.8 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.90 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 7.06 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.13 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.37 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 8.00 (*d*, 2H, 4-OC<u>H</u>$_3$-C_6H_4, *J* = 9.0 Hz), 8.42 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.7 (4-O<u>C</u>H_3-C_6H_4), 110.9 (C^4), 114.7, 118.4 (4-OCH_3-C_6H_4), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.0 Hz), 122.3 (4-Cl-C_6H_4), 129.5 (4-Cl-C_6H_4), 130.7 (4-OCH_3-C_6H_4), 132.6 (4-Cl-C_6H_4), 148.0 (<u>C</u>H), 149.7 (4-Cl-C_6H_4), 154.2 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.6 Hz), 162.8 (4-OCH_3-C_6H_4), 172.7 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}ClF_3N_2O_2^+$, $[M+H]^+$: 381.0612, found 381.0637.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-5-(4-methoxyphenyl)isoxazole (**6cf**): Yellow solid; 69% yield (0.291 g); mp 123.5-124.6 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.90 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 7.04-7.08 (*m*, 4H, 4-OC<u>H</u>$_3$-C_6H_4 and 4-Br-C_6H_4), 7.52 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.00 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 8.42 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.7 (4-O<u>C</u>H_3-C_6H_4), 110.9 (C^4), 114.7, 118.4 (4-OCH_3-C_6H_4), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.1 Hz), 120.4, 122.6 (4-Br-C_6H_4), 130.7 (4-OCH_3-C_6H_4), 132.5 (4-Br-C_6H_4), 148.1 (<u>C</u>H), 150.2 (4-Br-C_6H_4), 154.2 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 162.8 (4-OCH_3-C_6H_4), 172.8 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}BrF_3N_2O_2^+$, $[M+H]^+$: 425.0107, found 425.0129.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-4-[(4-methoxyphenyl)iminomethyl]isoxazole (**6da**): White solid; 81% yield (0.295 g); mp 108.7-109.5 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.84 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4),

6.95 (*d*, 2H, 4-OCH$_3$-C$_6$H$_4$, *J* = 8.9 Hz), 7.20-7.27 (*m*, 4H, 4-F-C$_6$H$_4$ and 4-OCH$_3$-C$_6$H$_4$), 8.13-8.17 (*m*, 2H, 4-F-C$_6$H$_4$), 8.46 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, CDCl$_3$) δ (ppm) 55.7 (4-O<u>C</u>H$_3$-C$_6$H$_4$), 112.2 (C^4), 114.7 (4-O<u>C</u>H$_3$-C$_6$H$_4$), 116.4 (*d*, 4-F-C$_6$H$_4$, $^2J_{C\text{-}F}$ = 22.1 Hz), 119.8 (*q*, <u>C</u>F$_3$, $^1J_{C\text{-}F}$ = 272.1 Hz), 122.4 (4-O<u>C</u>H$_3$-C$_6$H$_4$), 122.5 (*d*, 4-F-C$_6$H$_4$, $^4J_{C\text{-}F}$ = 3.5 Hz), 131.3 (*d*, 4-F-C$_6$H$_4$, $^3J_{C\text{-}F}$ = 8.9 Hz), 143.7 (4-O<u>C</u>H$_3$-C$_6$H$_4$), 144.5 (<u>C</u>H), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 159.3 (4-O<u>C</u>H$_3$-C$_6$H$_4$), 164.8 (*d*, 4-F-C$_6$H$_4$, $^1J_{C\text{-}F}$ = 254.3 Hz), 170.7 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}F_4N_2O_2^+$, [M+H]$^+$: 365.0908, found 365.0926.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-4-[(phenyl)iminomethyl]isoxazole (**6db**): White solid; 75% yield (0.251 g); mp 111.8-112.4 ^{o}C; **^{1}H NMR** (300.06 MHz, CDCl$_3$) δ (ppm) 7.17-7.22 (*m*, 3H, C$_6$H$_5$), 7.25-7.32 (*m*, 2H, C$_6$H$_5$), 7.40-7.45 (*m*, 2H, 4-F-C$_6$H$_4$), 8.13-8.18 (*m*, 2H, 4-F-C$_6$H$_4$), 8.45 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, CDCl$_3$) δ (ppm) 112.0 (C^4), 116.5 (*d*, 4-F-C$_6$H$_4$, $^2J_{C\text{-}F}$ = 22.2 Hz), 119.8 (*q*, <u>C</u>F$_3$, $^1J_{C\text{-}F}$ = 272.2 Hz), 120.9 (C$_6$H$_5$), 122.4 (*d*, 4-F-C$_6$H$_4$, $^4J_{C\text{-}F}$ = 3.3 Hz), 127.2, 129.5 (C$_6$H$_5$), 131.4 (*d*, 4-F-C$_6$H$_4$, $^3J_{C\text{-}F}$ = 9.0 Hz), 147.2 (<u>C</u>H), 151.0 (C$_6$H$_5$), 154.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 164.9 (*d*, 4-F-C$_6$H$_4$, $^1J_{C\text{-}F}$ = 254.6 Hz), 171.2 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{11}F_4N_2O^+$, [M+H]$^+$: 335.0802, found 335.0829.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-4-[(2-methoxyphenyl)iminomethyl]isoxazole (**6dc**): Yellow solid; 79% yield (0.287 g); mp 107.5-108.7 ^{o}C; **^{1}H NMR** (300.06 MHz, CDCl$_3$) δ (ppm) 3.91 (*s,* 3H, 2-OC<u>H$_3$</u>-C$_6$H$_4$), 6.98-7.04 (*m*, 3H, 2-OCH$_3$-C$_6$H$_4$), 7.21-7.25 (*m*, 3H, 4-F-C$_6$H$_4$ and 2-OCH$_3$-C$_6$H$_4$), 8.32-8.35 (*m*, 2H, 4-F-C$_6$H$_4$), 8.57 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, CDCl$_3$) δ (ppm) 56.1 (2-O<u>C</u>H$_3$-C$_6$H$_4$), 112.1 (C^4), 112.1 (2-O<u>C</u>H$_3$-C$_6$H$_4$), 116.2 (*d*, 4-F-C$_6$H$_4$, $^2J_{C\text{-}F}$ = 22.0 Hz), 119.8 (*q*, <u>C</u>F$_3$, $^1J_{C\text{-}F}$ = 272.2 Hz), 121.1, 121.3 (2-O<u>C</u>H$_3$-C$_6$H$_4$), 122.6 (*d*, 4-F-C$_6$H$_4$, $^4J_{C\text{-}F}$ = 3.3 Hz), 128.0 (2-O<u>C</u>H$_3$-C$_6$H$_4$), 131.5 (*d*, 4-F-C$_6$H$_4$, $^3J_{C\text{-}F}$ = 8.9 Hz), 140.3 (2-O<u>C</u>H$_3$-C$_6$H$_4$), 148.5 (<u>C</u>H), 152.4 (2-O<u>C</u>H$_3$-C$_6$H$_4$), 154.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 164.9 (*d*, 4-F-C$_6$H$_4$, $^1J_{C\text{-}F}$ = 254.3 Hz), 170.8 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}F_4N_2O_2^+$, [M+H]$^+$: 365.0908, found 365.0923.

(*E*)-3-Trifluoromethyl-5-(4-fluorophenyl)-4-[(4-fluorophenyl)iminomethyl]isoxazole (**6dd**): White solid; 76% yield (0.268 g); mp 92.6-94.2 ^{o}C; **^{1}H NMR** (300.06 MHz, CDCl$_3$) δ (ppm) 7.08-7.29 (*m*, 6H, 4-F-C$_6$H$_4$ – A and B), 8.09-8.14 (*m*, 2H, 4-F-C$_6$H$_4$ – A), 8.43 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, CDCl$_3$) δ (ppm) 111.9 (C^4), 116.3 (*d*, 4-F-C$_6$H$_4$ – A, $^2J_{C\text{-}F}$ = 22.8 Hz), 116.5 (*d*, 4-F-C$_6$H$_4$ – A, $^2J_{C\text{-}F}$ = 22.1 Hz), 119.7 (*q*, <u>C</u>F$_3$, $^1J_{C\text{-}F}$ = 272.1 Hz), 122.4 (*d*, 4-F-C$_6$H$_4$ – A, $^4J_{C\text{-}F}$ = 3.4 Hz), 122.5 (*d*, 4-F-C$_6$H$_4$ – B, $^3J_{C\text{-}F}$ = 8.5 Hz), 131.4 (*d*, 4-F-C$_6$H$_4$ – A, $^3J_{C\text{-}F}$ = 9.0 Hz), 146.7 (<u>C</u>H), 146.9 (*d*, 4-F-C$_6$H$_4$ – B, $^4J_{C\text{-}F}$ = 3.1 Hz), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 162.0 (*d*, 4-F-C$_6$H$_4$ – B, $^1J_{C\text{-}F}$ = 246.6 Hz), 164.9 (*d*, 4-F-C$_6$H$_4$ – A, $^1J_{C\text{-}F}$ = 254.7 Hz), 171.3 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}F_5N_2O^+$, [M+H]$^+$: 353.0708, found 353.0734.

(*E*)-4-[(4-Chlorophenyl)iminomethyl]-3-trifluoromethyl-5-(4-fluorophenyl)isoxazole (**6de**): Light Yellow solid; 71% yield (0.260 g); mp 100.1-101.7 ^{o}C; **^{1}H NMR** (300.06 MHz, CDCl$_3$) δ (ppm) 7.12 (*d*, 2H, 4-Cl-C$_6$H$_4$, *J* = 8.8 Hz), 7.23-7.28 (*m*, 2H, 4-F-C$_6$H$_4$), 7.38 (*d*, 2H, 4-Cl-C$_6$H$_4$, *J* = 8.8 Hz), 8.09-8.13 (*m*, 2H, 4-F-C$_6$H$_4$), 8.42 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, CDCl$_3$) δ (ppm) 111.8 (C^4), 116.5 (*d*, 4-F-C$_6$H$_4$, $^2J_{C\text{-}F}$ = 22.2 Hz), 119.7 (*q*, <u>C</u>F$_3$, $^1J_{C\text{-}F}$ = 272.2 Hz), 122.3 (4-Cl-C$_6$H$_4$), 122.3 (4-F-C$_6$H$_4$), 129.6 (4-Cl-C$_6$H$_4$), 131.4 (*d*, 4-F-C$_6$H$_4$, $^3J_{C\text{-}F}$ = 9.0 Hz), 132.9 (4-Cl-C$_6$H$_4$), 147.4 (<u>C</u>H), 149.4 (4-Cl-C$_6$H$_4$), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 165.0 (*d*, 4-F-C$_6$H$_4$, $^1J_{C\text{-}F}$ = 254.9 Hz), 171.5 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}ClF_4N_2O^+$, [M+H]$^+$: 369.0412, found 369.0439.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-3-trifluoromethyl-5-(4-fluorophenyl)isoxazole (**6df**): Yellow solid; 64% yield (0.265 g); mp 114.7-115.8 ^{o}C; **^{1}H NMR** (300.06 MHz, CDCl$_3$) δ (ppm) 7.06 (*d*, 2H, 4-Br-C$_6$H$_4$, *J* = 8.8 Hz), 7.23-7.29 (*m*, 2H, 4-F-C$_6$H$_4$), 7.53 (*d*, 2H, 4-Br-C$_6$H$_4$, *J* = 8.8 Hz), 8.08-8.13 (*m*, 2H, 4-F-C$_6$H$_4$), 8.42 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, CDCl$_3$) δ (ppm) 111.8 (C^4), 116.5 (*d*, 4-F-C$_6$H$_4$, $^2J_{C\text{-}F}$ = 22.2 Hz), 119.7 (*q*, <u>C</u>F$_3$, $^1J_{C\text{-}F}$ = 272.2 Hz), 120.8 (4-Br-C$_6$H$_4$), 122.3 (*d*, 4-F-C$_6$H$_4$, $^4J_{C\text{-}F}$ = 3.5 Hz), 122.6 (4-Br-C$_6$H$_4$), 131.4 (*d*, 4-F-C$_6$H$_4$, $^3J_{C\text{-}F}$ = 8.9 Hz), 132.6 (4-Br-C$_6$H$_4$), 147.5 (<u>C</u>H), 149.8 (4-Br-C$_6$H$_4$), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 165.0 (*d*, 4-F-C$_6$H$_4$, $^1J_{C\text{-}F}$ = 254.9 Hz), 171.6 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}BrF_4N_2O^+$, [M+H]$^+$: 412.9907, found 412.9935.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]isoxazole (**6ea**): Yellow solid; 78% yield (0.297 g); mp 98.2-98.8 ^{o}C; **^{1}H NMR** (300.06 MHz, CDCl$_3$) δ (ppm) 3.85 (*s,* 3H, 4-OC<u>H$_3$</u>-C$_6$H$_4$), 6.95 (*d*, 2H, 4-OCH$_3$-C$_6$H$_4$, *J* = 9.0 Hz), 7.22 (*d*, 2H, 4-OCH$_3$-C$_6$H$_4$, *J* = 9.00 Hz), 7.53 (*d*, 2H, 4-Cl-C$_6$H$_4$, *J* = 8.8 Hz), 8.08 (*d*, 2H, 4-Cl-C$_6$H$_4$, *J* = 8.8 Hz), 8.46 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, CDCl$_3$) δ (ppm) 55.7 (4-O<u>C</u>H$_3$-C$_6$H$_4$), 112.6 (C^4), 114.7 (4-OCH$_3$-C$_6$H$_4$), 119.8 (*q*, <u>C</u>F$_3$, $^1J_{C\text{-}F}$ = 272.1 Hz), 122.5 (4-OCH$_3$-C$_6$H$_4$), 124.7, 129.4, 130.2, 138.4 (4-Cl-C$_6$H$_4$), 143.6 (4-OCH$_3$-C$_6$H$_4$), 144.3 (<u>C</u>H), 154.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.5 Hz), 159.4 (4-OCH$_3$-C$_6$H$_4$), 170.5 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}ClF_3N_2O_2^+$, [M+H]$^+$: 381.0612, found 381.0629.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-4-[(phenyl)iminomethyl]isoxazole (**6eb**): White solid; 73% yield (0.255 g); mp 90.1-90.8 ^{o}C; **^{1}H NMR** (300.06 MHz, CDCl$_3$) δ (ppm) 7.17-7.20 (*m*, 2H, C$_6$H$_5$), 7.27-7.32 (*m*,

1H, C_6H_5), 7.40-7.45 (*m*, 2H, C_6H_5), 7.54 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.9 Hz), 8.09 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.9 Hz), 8.46 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.4 (C^4), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 120.9 (C_6H_5), 124.5 (4-Cl-C_6H_4), 127.3 (C_6H_5), 129.4 (4-Cl-C_6H_4), 129.5, (C_6H_5), 130.2, 138.6 (4-Cl-C_6H_4), 147.0 (<u>C</u>H), 150.9 (C_6H_5), 154.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 171.0 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{11}ClF_3N_2O^+$, $[M+H]^+$: 351.0507, found 351.0531.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]isoxazole (**6ec**): Yellow solid; 76% yield (0.290 g); mp 118.2-120.2 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.91 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 6.97-7.06 (*m*, 3H, 2-OCH_3-C_6H_4), 7.22-7.26 (*m*, 1H, 2-OCH_3-C_6H_4), 7.51 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.9 Hz), 8.26 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.9 Hz), 8.57 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.1 (2-O<u>C</u>H_3-C_6H_4), 112.0 (2-OCH_3-C_6H_4), 112.5 (C^4), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.4 Hz), 121.0, 121.3 (2-OCH_3-C_6H_4), 124.7 (4-Cl-C_6H_4), 128.0 (2-OCH_3-C_6H_4), 129.3, 130.3, 138.4 (4-Cl-C_6H_4), 140.1 (2-OCH_3-C_6H_4), 148.4 (<u>C</u>H), 152.4 (2-OCH_3-C_6H_4), 154.7 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.5 Hz), 170.6 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}ClF_3N_2O_2^+$, $[M+H]^+$: 381.0612, found 381.0626.

(*E*)-5-(4-Chlorophenyl)-3-trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]isoxazole (**6ed**): White solid; 69% yield (0.255 g); mp 101.4-103.8 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.08-7.21 (*m*, 4H, 4-F-C_6H_4), 7.54 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.9 Hz), 8.05 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.9 Hz), 8.43 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.3 (C^4), 116.3 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.8 Hz), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.1 Hz), 122.6 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.5 Hz), 124.5, 129.5, 130.2, 138.6 (4-Cl-C_6H_4), 146.6 (<u>C</u>H), 146.8 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 3.1 Hz), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 162.1 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 246.7 Hz), 171.1 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}ClF_4N_2O^+$, $[M+H]^+$: 369.0412, found 369.0441.

(*E*)-5-(4-Chlorophenyl)-4-[(4-chlorophenyl)iminomethyl]-3-trifluoromethylisoxazole (**6ee**): Yellow solid; 64% yield (0.247 g); mp 86.8-88.0 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.13 (*d*, 2H, 4-Cl-C_6H_4 – B, *J* = 8.7 Hz), 7.38 (*d*, 2H, 4-Cl-C_6H_4 – B, *J* = 8.7 Hz), 7.55 (*d*, 2H, 4-Cl-C_6H_4 – A, *J* = 8.7 Hz), 8.04 (*d*, 2H, 4-Cl-C_6H_4 – A, *J* = 8.7 Hz), 8.43 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.2 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 122.3 (4-Cl-C_6H_4 – B), 124.4, 129.5 (4-Cl-C_6H_4 – A), 129.6 (4-Cl-C_6H_4 – B), 130.2 (4-Cl-C_6H_4 – A), 133.0 (4-Cl-C_6H_4 – B), 138.7 (4-Cl-C_6H_4 – A), 147.3 (<u>C</u>H), 149.3 (4-Cl-C_6H_4 – B), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.0 Hz), 171.3 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}Cl_2F_3N_2O^+$, $[M+H]^+$: 385.0117, found 385.0130.

(*E*)-4-[(4-Bromophenyl)iminomethyl]-5-(4-chlorophenyl)-3-trifluoromethylisoxazole (**6ef**): White solid; 63% yield (0.270 g); mp 95.5-96.3 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.06 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.6 Hz), 7.52-7.56 (*m*, 4H, 4-Cl-C_6H_4 and 4-Br-C_6H_4), 8.04 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.7 Hz), 8.42 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.2 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 120.9, 122.6 (4-Br-C_6H_4), 124.4, 129.5, 130.2 (4-Cl-C_6H_4), 132.6 (4-Br-C_6H_4), 138.7 (4-Cl-C_6H_4), 147.4 (<u>C</u>H), 149.8 (4-Br-C_6H_4), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 38.1 Hz), 171.4 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}BrClF_3N_2O^+$, $[M+H]^+$: 428.9612, found 428.9641.

(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(4-methoxyphenyl)iminomethyl]isoxazole (**6fa**): Yellow solid; 72% yield (0.306 g); mp 105.4-106.1 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.84 (*s,* 3H, 4-OC<u>H</u>$_3$-C_6H_4), 6.94 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.22 (*d*, 2H, 4-OCH_3-C_6H_4, *J* = 9.0 Hz), 7.69 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.01 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.46 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 55.7 (4-O<u>C</u>H_3-C_6H_4), 112.7 (C^4), 114.7 (4-OCH_3-C_6H_4), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 122.5 (4-OCH_3-C_6H_4), 125.2, 126.9, 130.3, 132.4 (4-Br-C_6H_4), 143.6 (4-OCH_3-C_6H_4), 144.3 (<u>C</u>H), 154.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.7 Hz), 159.4 (4-OCH_3-C_6H_4), 170.6 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}BrF_3N_2O_2^+$, $[M+H]^+$: 425.0107, found 425.0135.

(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(phenyl)iminomethyl]isoxazole (**6fb**): Yellow solid; 69% yield (0.272 g); mp 108.4-109.1 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.17-7.20 (*m*, 2H, C_6H_5), 7.27-7.32 (*m*, 1H, C_6H_5), 7.40-7.45 (*m*, 2H, C_6H_5), 7.70 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8Hz), 8.01 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.45 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.4 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.3 Hz), 120.9 (C_6H_5), 125.0, 127.1 (4-Br-C_6H_4), 127.3, 129.5 (C_6H_5), 130.4, 132.4 (4-Br-C_6H_4), 147.0 (<u>C</u>H), 150.9 (C_6H_5), 154.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.8 Hz), 171.1 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{11}BrF_3N_2O^+$, $[M+H]^+$: 395.0001, found 395.0016.

(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(2-methoxyphenyl)iminomethyl]isoxazole (**6fc**): Yellow solid; 70% yield (0.297 g); mp 126.8-127.4 °C; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 3.91 (*s,* 3H, 2-OC<u>H</u>$_3$-C_6H_4), 6.97-7.05 (*m*, 3H, 2-OCH_3-C_6H_4), 7.22-7.27 (*m*, 1H, 2-OCH_3-C_6H_4), 7.67 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.19 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.57 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 56.1 (2-O<u>C</u>H_3-C_6H_4), 112.1 (2-OCH_3-C_6H_4), 112.6 (C^4), 119.8 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.3 Hz), 121.1, 121.3 (2-OCH_3-C_6H_4), 125.1, 127.0 (4-Br-C_6H_4), 128.0

(2-OCH_3-C_6H_4), 130.4, 132.2 (4-Br-C_6H_4), 140.1 (2-OCH_3-C_6H_4), 148.4 (C<u>H</u>), 152.4 (2-OCH_3-C_6H_4), 154.8 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.8 Hz), 170.7 (C^5); **HRMS** (ESI+): calcd for $C_{18}H_{13}BrF_3N_2O_2^+$, $[M+H]^+$: 425.0107, found 425.0142.

(*E*)-5-(4-Bromophenyl)-3-trifluoromethyl-4-[(4-fluorophenyl)iminomethyl]isoxazole (**6fd**): Light Yellow solid; 69% yield (0.286 g); mp 105.1-106.2 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.07-7.21 (*m*, 4H, 4-F-C_6H_4), 7.70 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.98 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.43 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.4 (C^4), 116.3 (*d*, 4-F-C_6H_4, $^2J_{C\text{-}F}$ = 22.7 Hz), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.2 Hz), 122.5 (*d*, 4-F-C_6H_4, $^3J_{C\text{-}F}$ = 8.5 Hz), 124.9, 127.1, 130.3, 132.5 (4-Br-C_6H_4), 146.6 (<u>C</u>H), 146.8 (*d*, 4-F-C_6H_4, $^4J_{C\text{-}F}$ = 2.9 Hz), 154.6 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 162.1 (*d*, 4-F-C_6H_4, $^1J_{C\text{-}F}$ = 246.8 Hz), 171.2 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}BrF_4N_2O^+$, $[M+H]^+$: 412.9907, found 412.9932.

(*E*)-5-(4-Bromophenyl)-4-[(4-chlorophenyl)iminomethyl]-3-trifluoromethylisoxazole (**6fe**): Light Yellow solid; 66% yield (0.284 g); mp 91.2-92.6 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.12 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.38 (*d*, 2H, 4-Cl-C_6H_4, *J* = 8.8 Hz), 7.71 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 7.97 (*d*, 2H, 4-Br-C_6H_4, *J* = 8.8 Hz), 8.42 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.3 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.3 Hz), 122.3 (4-Cl-C_6H_4), 124.9, 127.2 (4-Br-C_6H_4), 129.6 (4-Cl-C_6H_4), 130.3, 132.5 (4-Br-C_6H_4), 133.0 (4-Cl-C_6H_4), 147.3 (<u>C</u>H), 149.3 (4-Cl-C_6H_4), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.9 Hz), 171.4 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}BrClF_3N_2O^+$, $[M+H]^+$: 428.9612, found 428.9638.

(*E*)-5-(4-Bromophenyl)-4-[(4-bromophenyl)iminomethyl]-3-trifluoromethylisoxazole (**6ff**): Yellow solid; 67% yield (0.318 g); mp 102.6-106.1 ^oC; **^{1}H NMR** (300.06 MHz, $CDCl_3$) δ (ppm) 7.06 (*d*, 2H, 4-Br-C_6H_4 – B, *J* = 8.8 Hz), 7.53 (*d*, 2H, 4-Br-C_6H_4 – B, *J* = 8.8 Hz), 7.70 (*d*, 2H, 4-Br-C_6H_4 – A, *J* = 8.8 Hz), 7.96 (*d*, 2H, 4-Br-C_6H_4 – A, *J* = 8.8 Hz), 8.42 (*s*, 1H, C<u>H</u>); **^{13}C NMR** (75.45 MHz, $CDCl_3$) δ (ppm) 112.3 (C^4), 119.7 (*q*, <u>C</u>F_3, $^1J_{C\text{-}F}$ = 272.3 Hz), 120.9, 122.6, 124.8, 127.2, 130.3, 132.5, 132.6 (4-Br-C_6H_4 – A and B), 147.3 (<u>C</u>H), 149.8 (4-Br-C_6H_4 – B), 154.5 (*q*, C^3, $^2J_{C\text{-}F}$ = 37.8 Hz), 171.4 (C^5); **HRMS** (ESI+): calcd for $C_{17}H_{10}Br_2F_3N_2O^+$, $[M+H]^+$: 472.9106, found 472.9135.

Table S1 – X-ray crystallographic data of compound **2f**

Bond precision:	C-C = 0.0091 A	Wavelength=0.71073	
Cell:	a=16.298(10)	b=8.588(6)	c=12.152(8)
	alpha=90	beta=103.311(17)	gamma=90
Temperature:	297 K		
	Calculated	Reported	
Volume	1655.2(19)	1655.2(18)	
Space group	P 21/c	P 1 21/c 1	
Hall group	-P 2ybc	-P2ybc	
Moiety formula	C15 H15 Br F3 N O2	C15 H15 Br F3 N O2	
Sum formula	C15 H15 Br F3 N O2	C15 H15 Br F3 N O2	
Mr	378.18	378.19	
Dx,g cm-3	1.518	1.518	
Z	4	4	
Mu (mm-1)	2.518	2.518	
F000	760.0	760.0	
F000'	759.31		
h,k,lmax	22,11,16	22,11,16	
Nref	4520	4500	
Tmin,Tmax	0.604,0.860	0.593,0.874	
Tmin'	0.541		

Correction method= # Reported T Limits: Tmin=0.593 Tmax=0.874
AbsCorr = MULTI-SCAN

Data completeness= 0.996 Theta(max)= 29.260

R(reflections)= 0.0693(2034) wR2(reflections)= 0.1782(4500)

S = 0.893 Npar= 199

The crystal structure **2f** has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: CCDC-1959494.

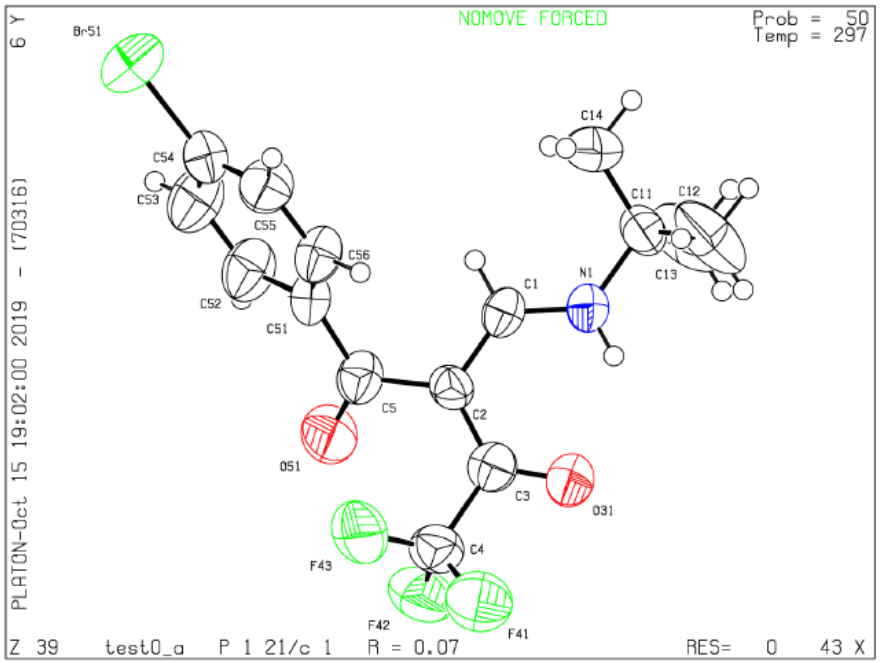


Figure S1 – ORTEP diagram of compound **2f**

Table S2 – X-ray crystallographic data of compound **5dc**

```
Bond precision:  C-C = 0.0015 A          Wavelength=0.71073

Cell:          a=9.0678(4)        b=10.6289(5)     c=11.4690(6)
               alpha=103.200(2)   beta=92.950(2)   gamma=110.440(2)
Temperature:   100 K

                 Calculated                Reported
Volume           997.94(8)                 997.94(8)
Space group      P -1                      P-1
Hall group       -P 1                      -P1
Moiety formula   C24 H17 F4 N3 O           C24 H17 F4 N3 O
Sum formula      C24 H17 F4 N3 O           C24 H17 F4 N3 O
Mr               439.41                    439.41
Dx,g cm-3        1.462                     1.462
Z                2                         2
Mu (mm-1)        0.117                     0.117
F000             452.0                     452.0
F000'            452.27
h,k,lmax         12,14,15                  12,14,15
Nref             5417                      5396
Tmin,Tmax        0.974,0.980               0.950,0.980
Tmin'            0.950

Correction method= # Reported T Limits: Tmin=0.950 Tmax=0.980
AbsCorr = MULTI-SCAN

Data completeness= 0.996          Theta(max)= 29.190

R(reflections)= 0.0354( 4849)     wR2(reflections)= 0.0943( 5396)

S = 1.027                 Npar= 289
```

The crystal structure **5dc** has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: CCDC-1959495.

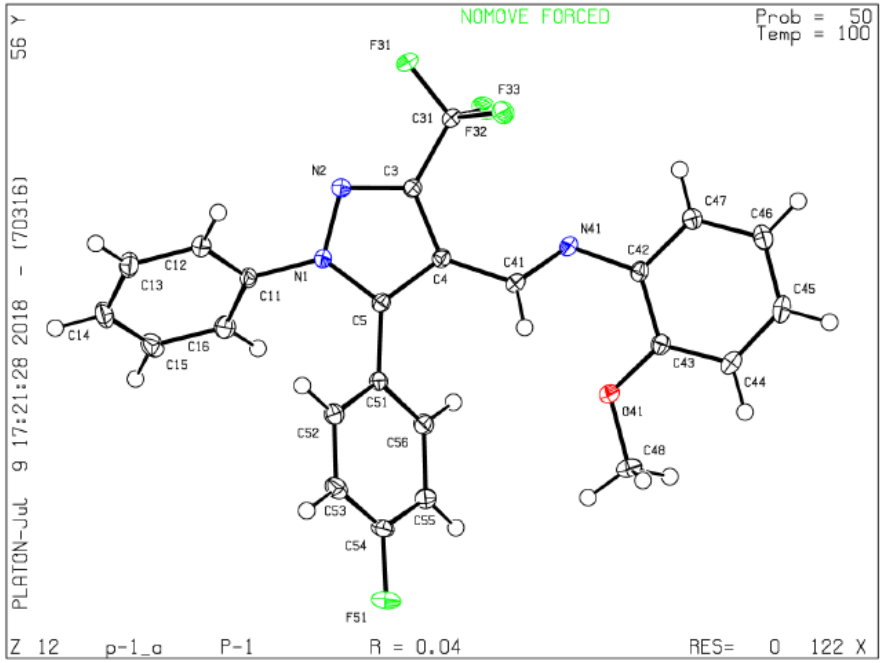


Figure S2 – ORTEP diagram of compound **5dc**

Table S3 – X-ray crystallographic data of compound **6fc**

Bond precision:	C-C = 0.0044 A	Wavelength=0.71073	
Cell:	a=12.889(2)	b=5.2686(10)	c=25.153(5)
	alpha=90	beta=97.851(6)	gamma=90
Temperature:	295 K		

	Calculated	Reported
Volume	1692.1(5)	1692.0(5)
Space group	P 21/n	P21/n
Hall group	-P 2yn	-P2yn
Moiety formula	C18 H12 Br F3 N2 O2	C18 H12 Br F3 N2 O2
Sum formula	C18 H12 Br F3 N2 O2	C18 H12 Br F3 N2 O2
Mr	425.20	425.21
Dx,g cm-3	1.669	1.669
Z	4	4
Mu (mm-1)	2.476	2.476
F000	848.0	848.0
F000'	847.33	
h,k,lmax	16,6,32	16,6,32
Nref	3764	3750
Tmin,Tmax	0.574,0.690	0.575,0.718
Tmin'	0.520	

Correction method= # Reported T Limits: Tmin=0.575 Tmax=0.718
AbsCorr = MULTI-SCAN

Data completeness= 0.996 Theta(max)= 27.200

R(reflections)= 0.0463(2246) wR2(reflections)= 0.1231(3750)

S = 1.019 Npar= 235

The crystal structure **6fc** has been deposited at the Cambridge Crystallographic Data Centre and allocated the deposition number: CCDC-1959496.

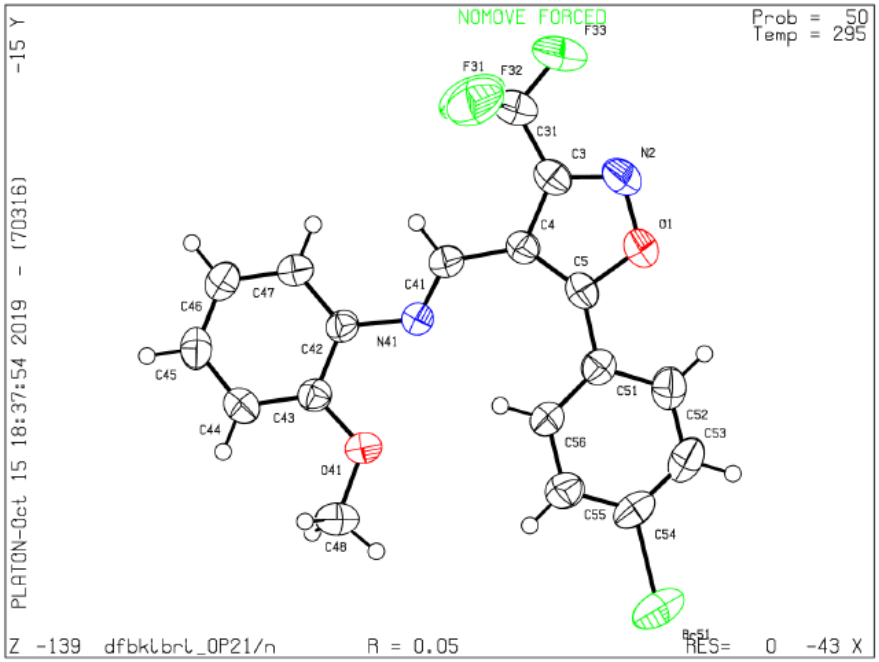


Figure S3 – ORTEP diagram of compound **6fc**

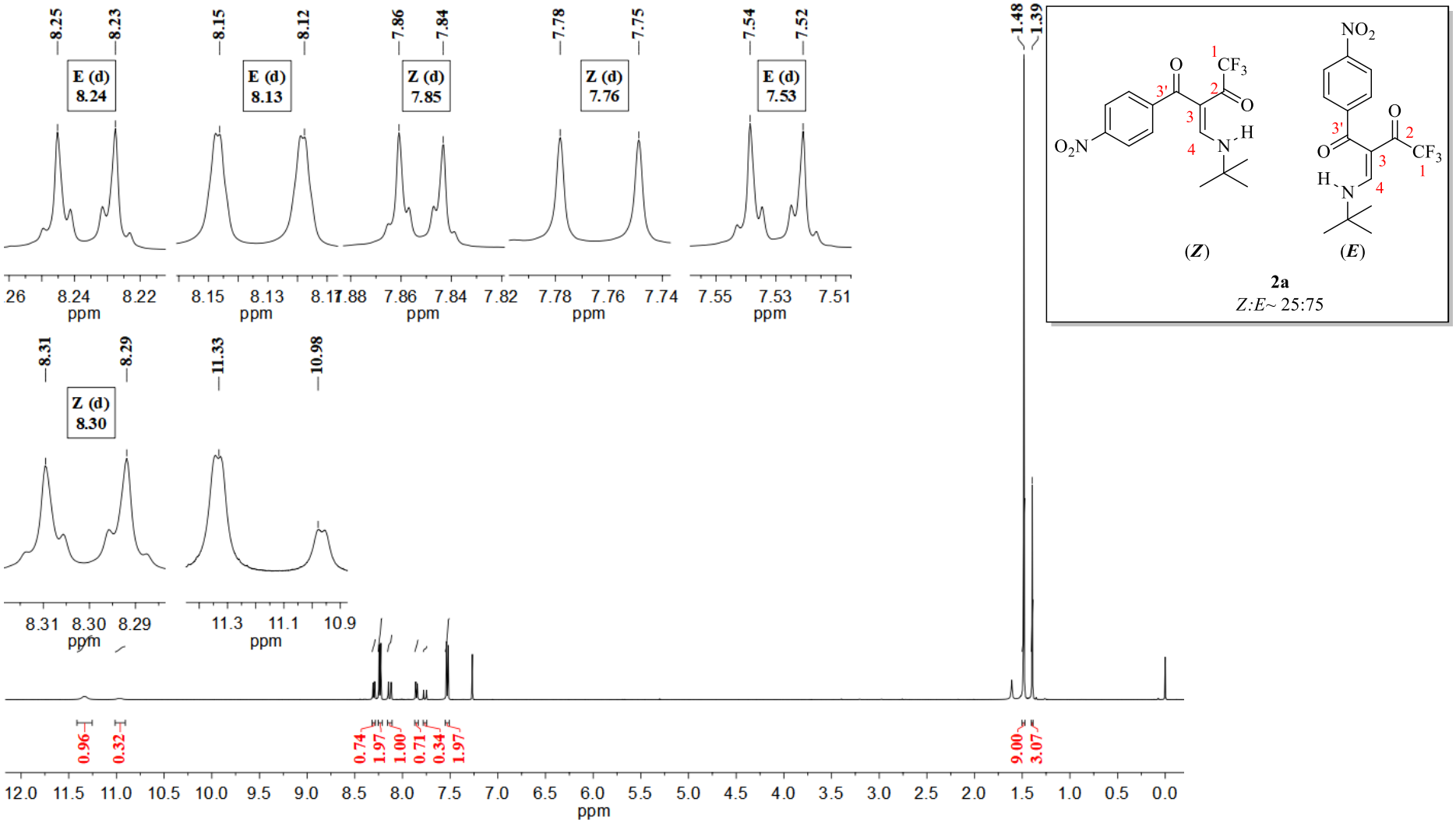


Figure S4 – ^{1}H NMR spectrum of compound **2a** in $CDCl_3$ at 500.13 MHz.

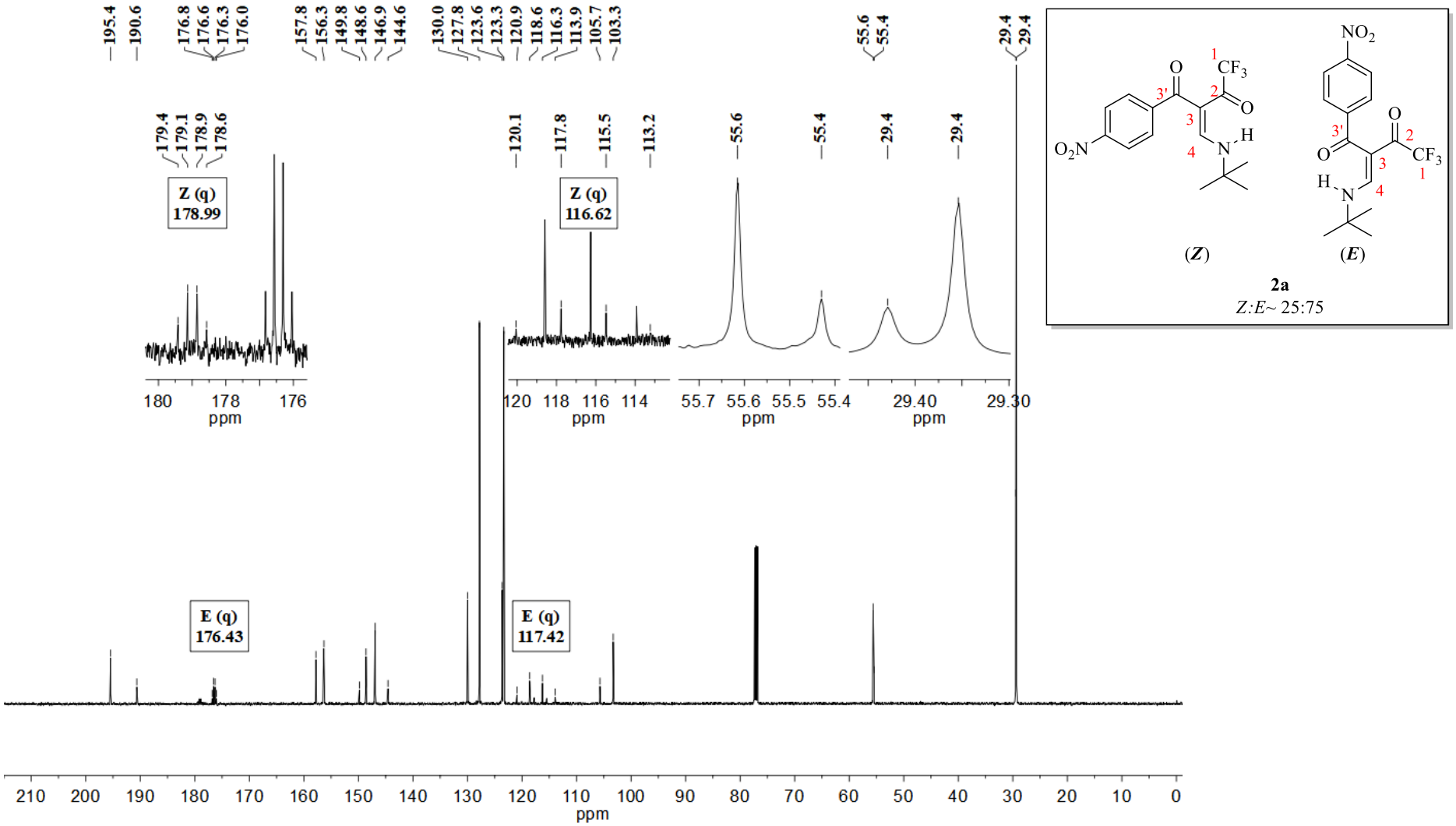


Figure S5 – ^{13}C NMR spectrum of compound **2a** in $CDCl_3$ at 125.76 MHz.

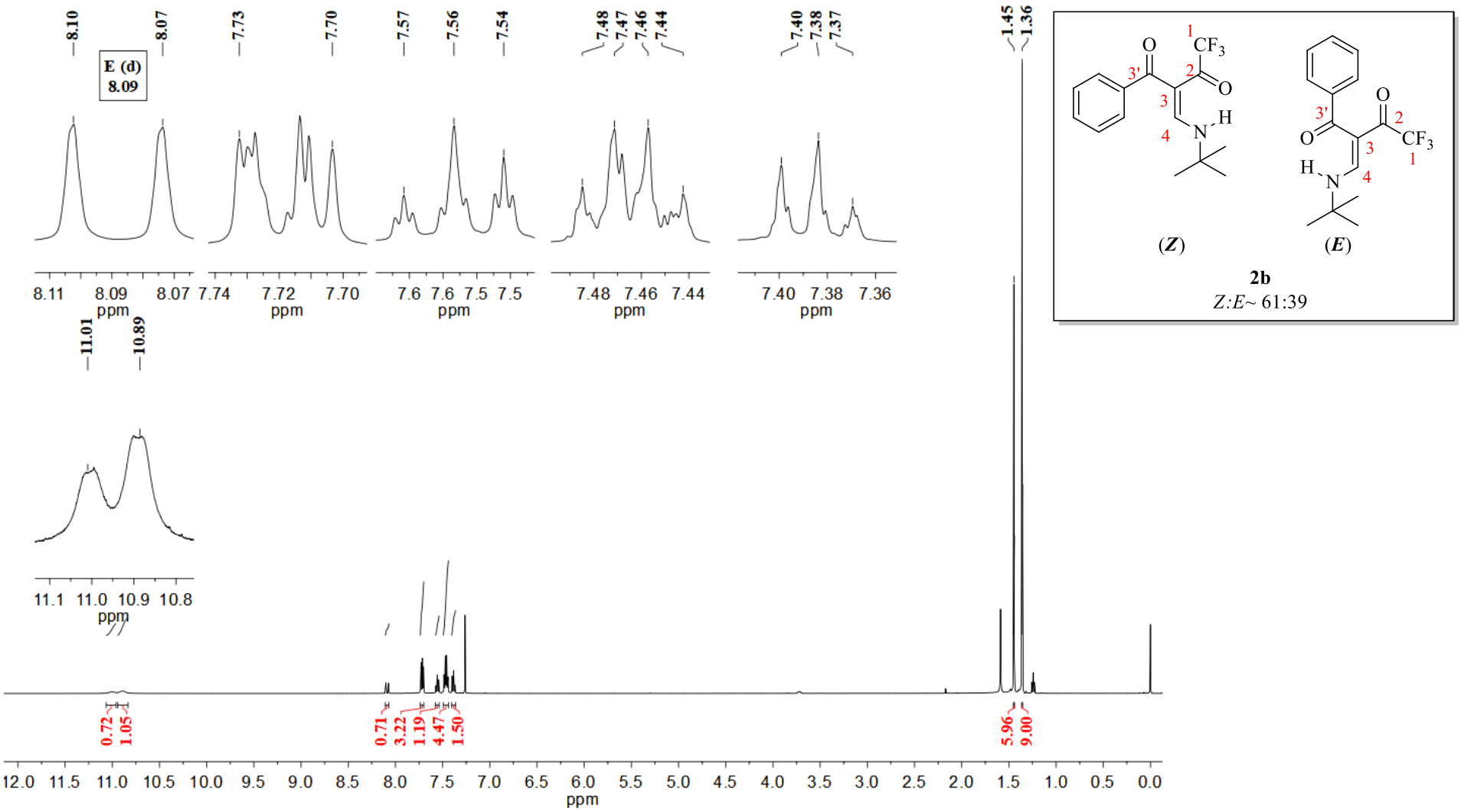


Figure S6 – ^{1}H NMR spectrum of compound **2b** in $CDCl_3$ at 500.13 MHz.

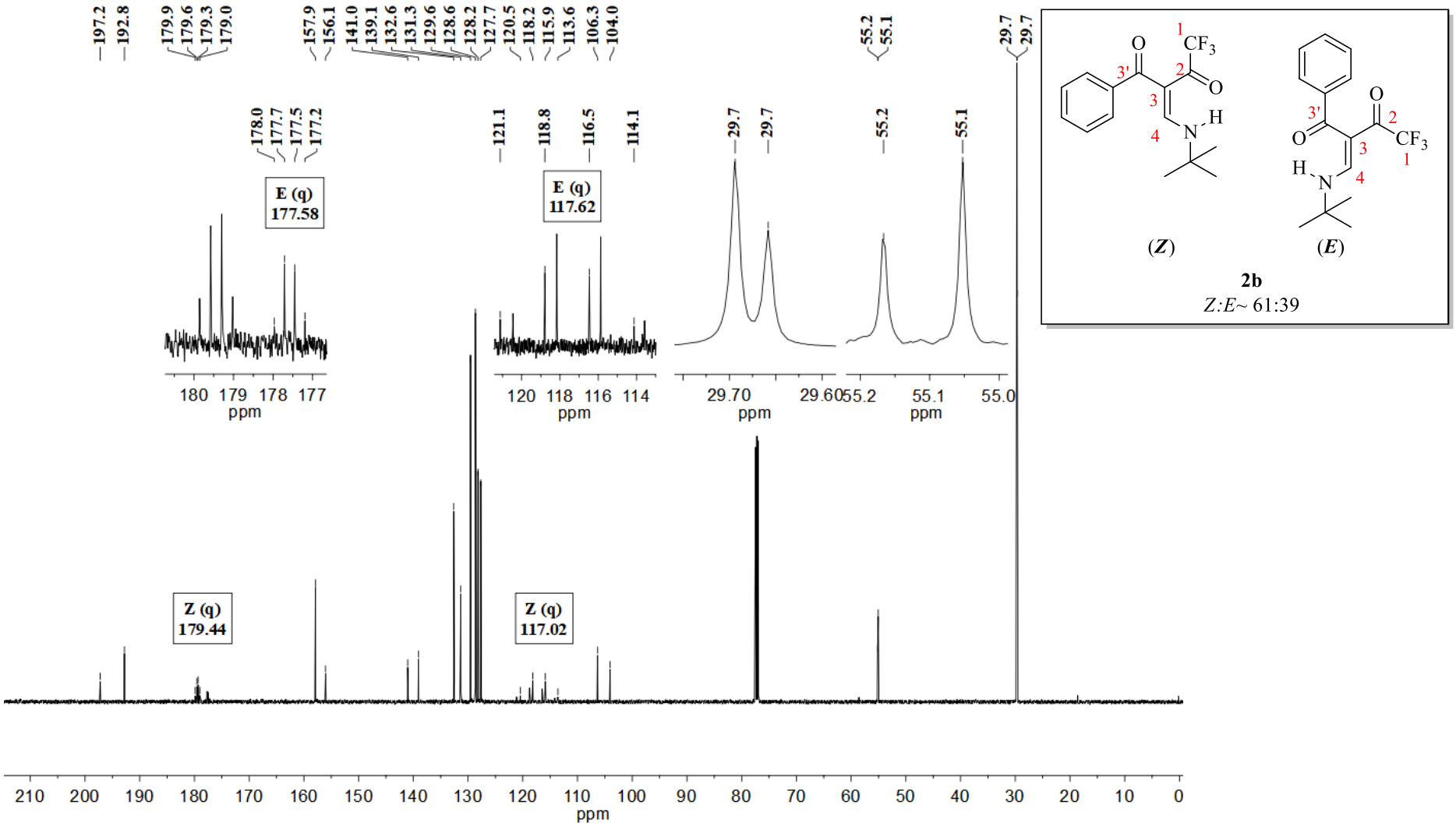
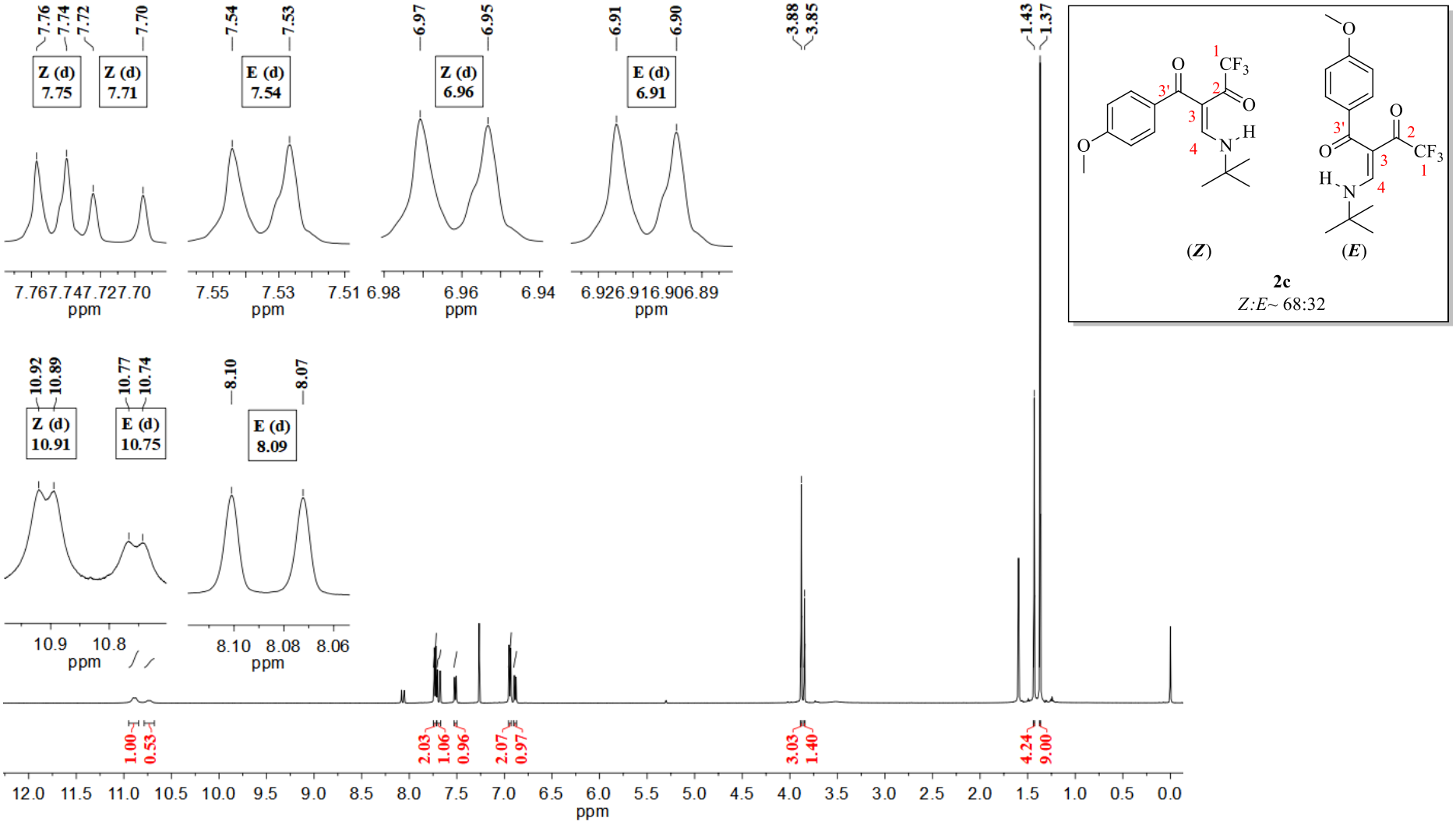


Figure S7 – ^{13}C NMR spectrum of compound **2b** in $CDCl_3$ at 125.76 MHz.


7.76
7.74
7.72
7.70
Z (d)
7.75
Z (d)
7.71
7.54
7.53
E (d)
7.54
6.97
6.95
Z (d)
6.96
6.91
6.90
E (d)
6.91
3.88
3.85
1.43
1.37
10.92
10.89
Z (d)
10.91
10.77
10.74
E (d)
10.75
8.10
8.07
E (d)
8.09
7.767.747.727.70
ppm
7.55
7.53
7.51
ppm
6.98
6.96
6.94
ppm
6.926.916.906.89
ppm
10.9
10.8
ppm
8.10
8.08
8.06
ppm
1.00
0.53
2.03
1.06
0.96
2.07
0.97
3.03
1.40
4.24
9.00
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
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6.5
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5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
(Z)
(E)
2c
Z:E~ 68:32

Figure S8 – ^{1}H NMR spectrum of compound **2c** in $CDCl_3$ at 500.13 MHz.

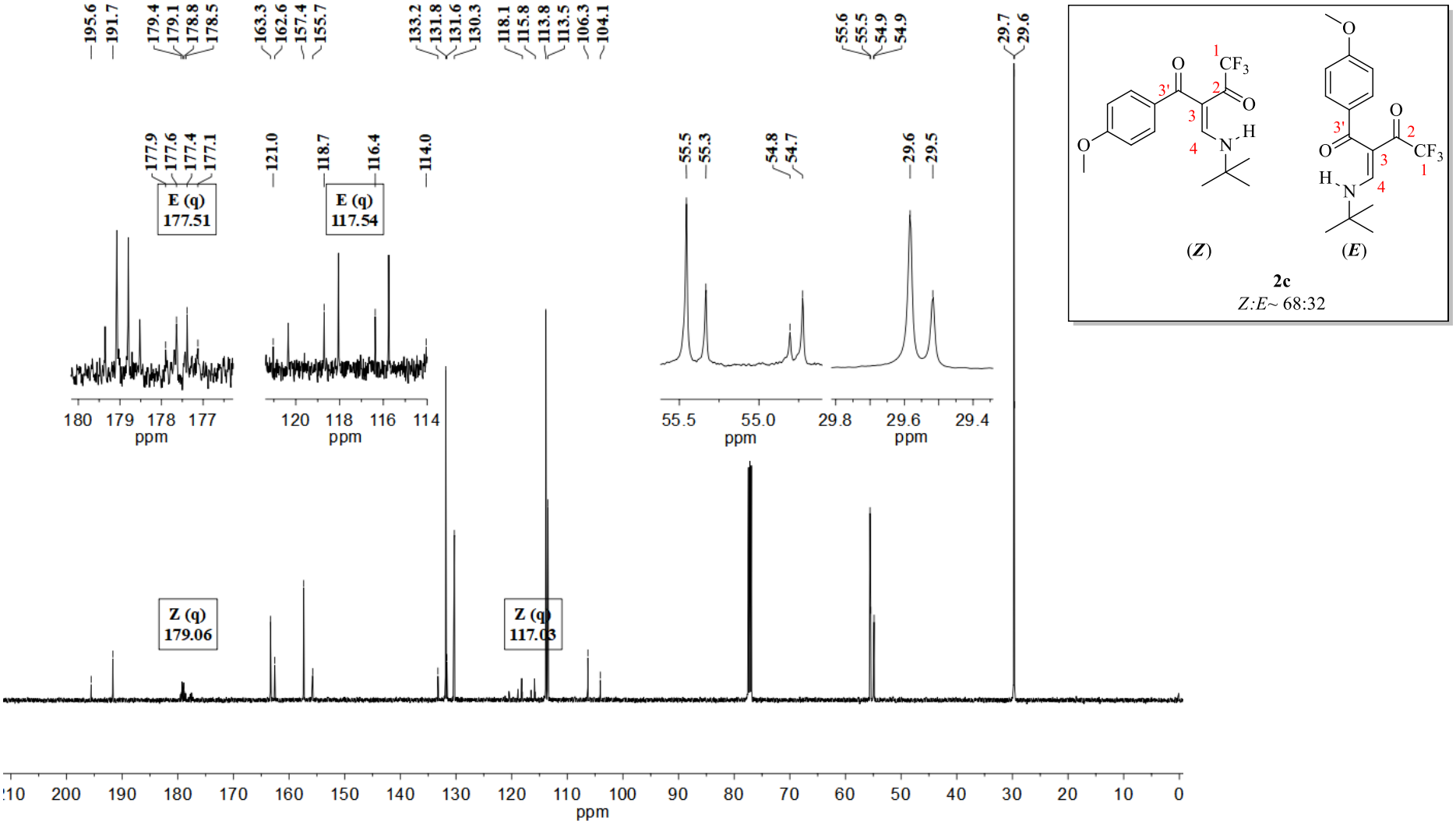


Figure S9 – ^{13}C NMR spectrum of compound **2c** in $CDCl_3$ at 125.76 MHz.

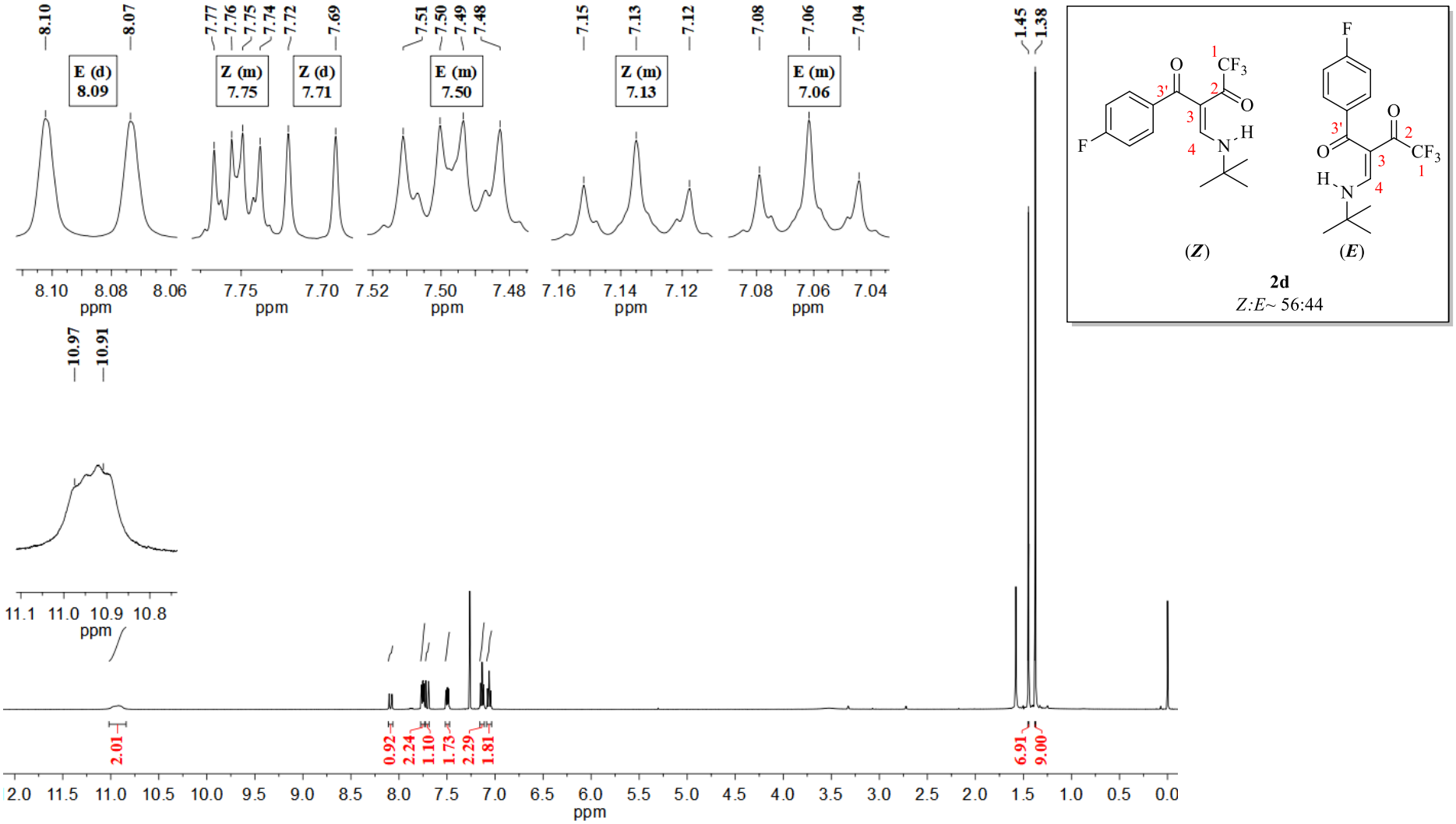

E (d) 8.09
Z (m) 7.75
Z (d) 7.71
E (m) 7.50
Z (m) 7.13
E (m) 7.06
(Z)
(E)
2d
Z:E~ 56:44
ppm

Figure S10 – ^{1}H NMR spectrum of compound **2d** in $CDCl_3$ at 500.13 MHz.

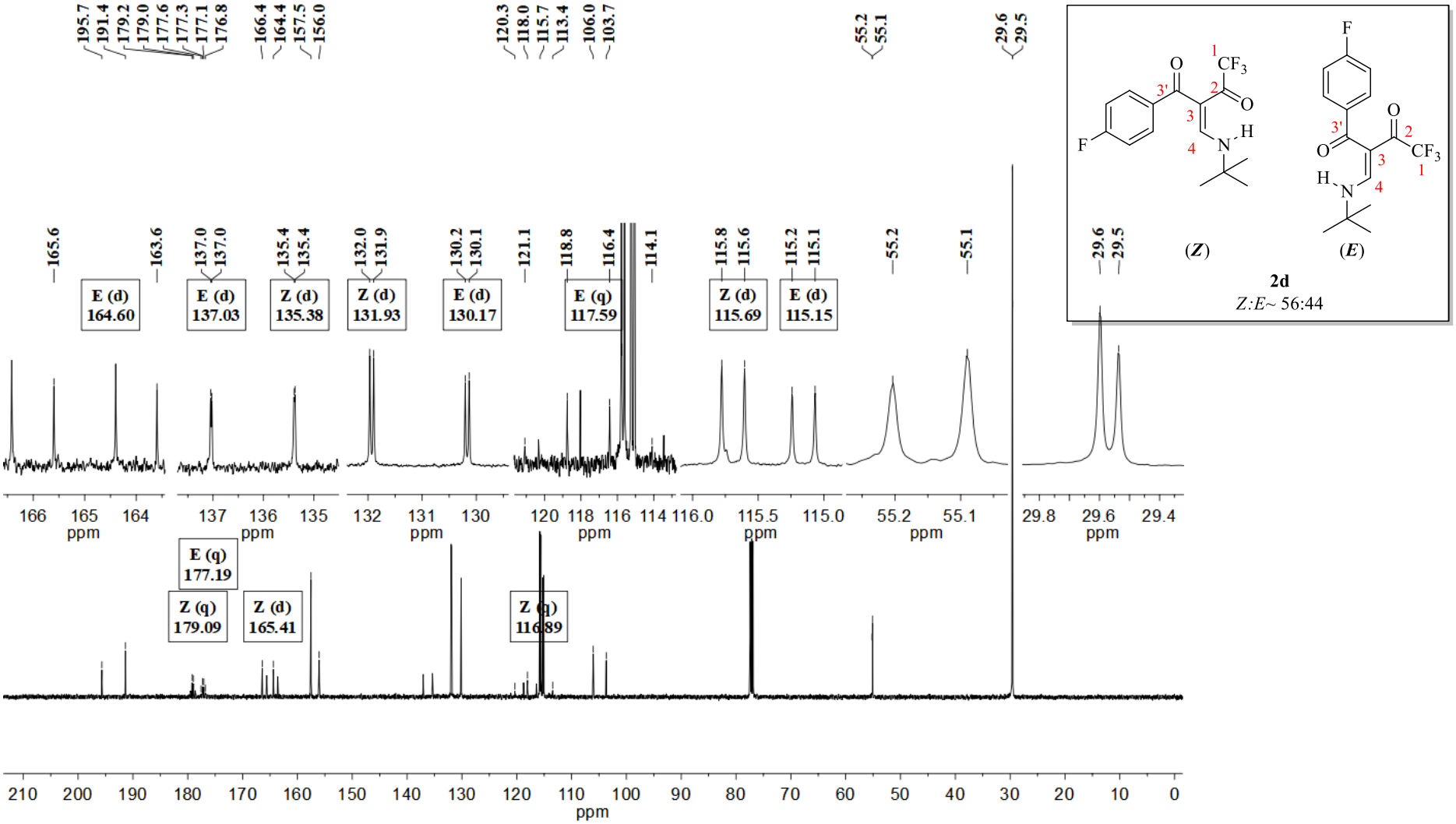


Figure S11 – ^{13}C NMR spectrum of compound **2d** in $CDCl_3$ at 125.76 MHz.

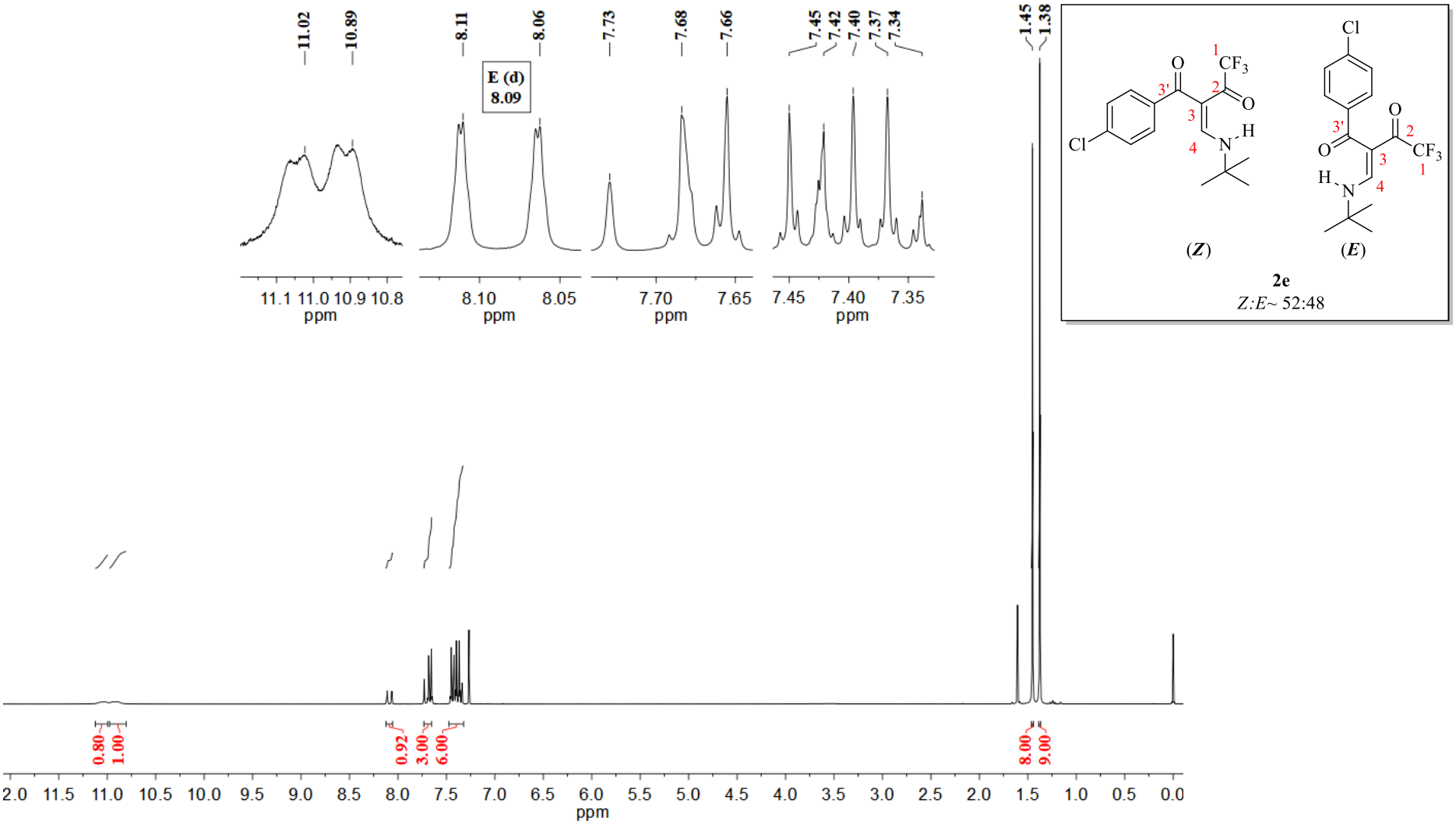


Figure S12 – ^{1}H NMR spectrum of compound **2e** in $CDCl_3$ at 500.13 MHz.

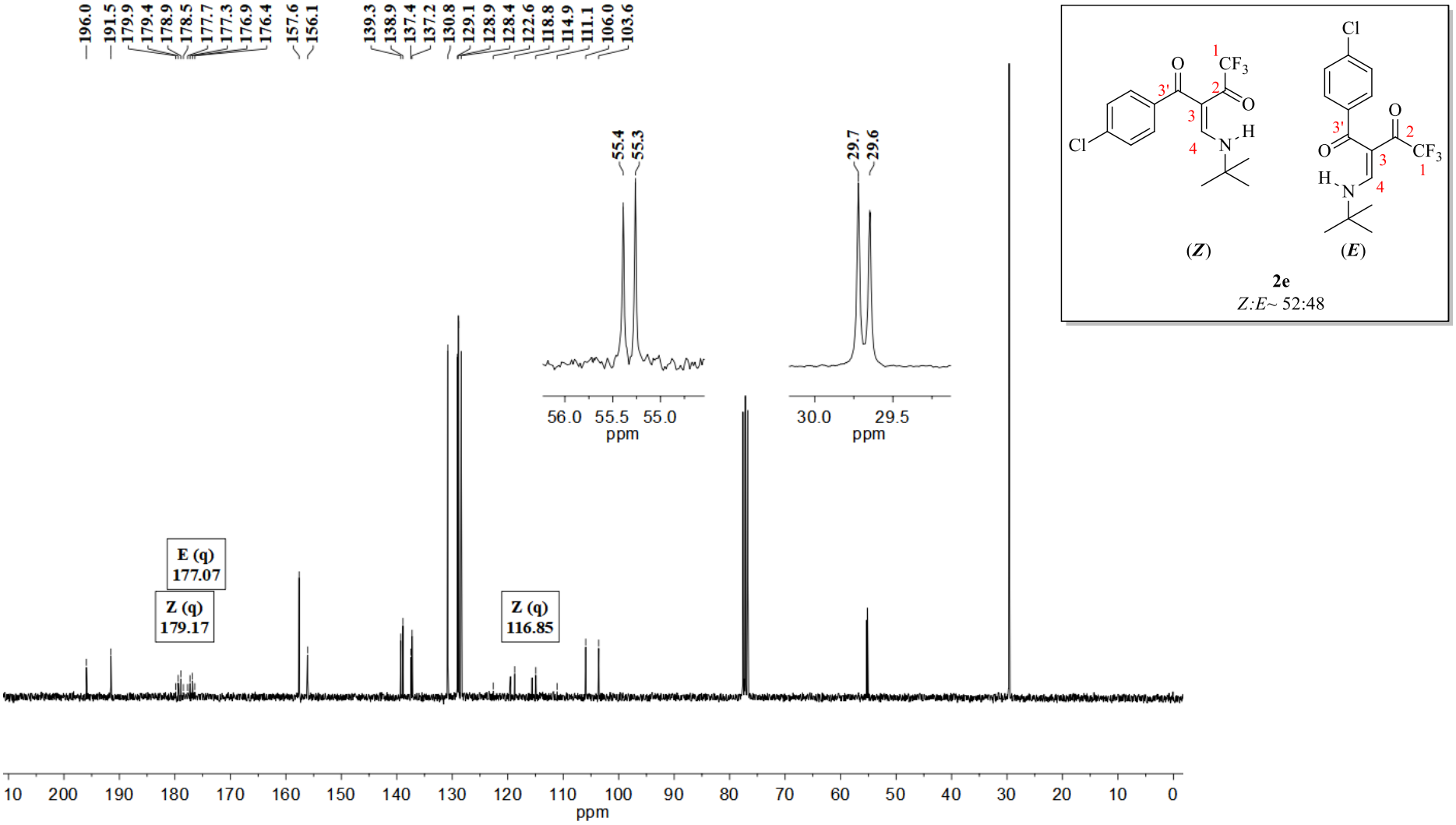


Figure S13 – ^{13}C NMR spectrum of compound **2e** in $CDCl_3$ at 125.76 MHz.

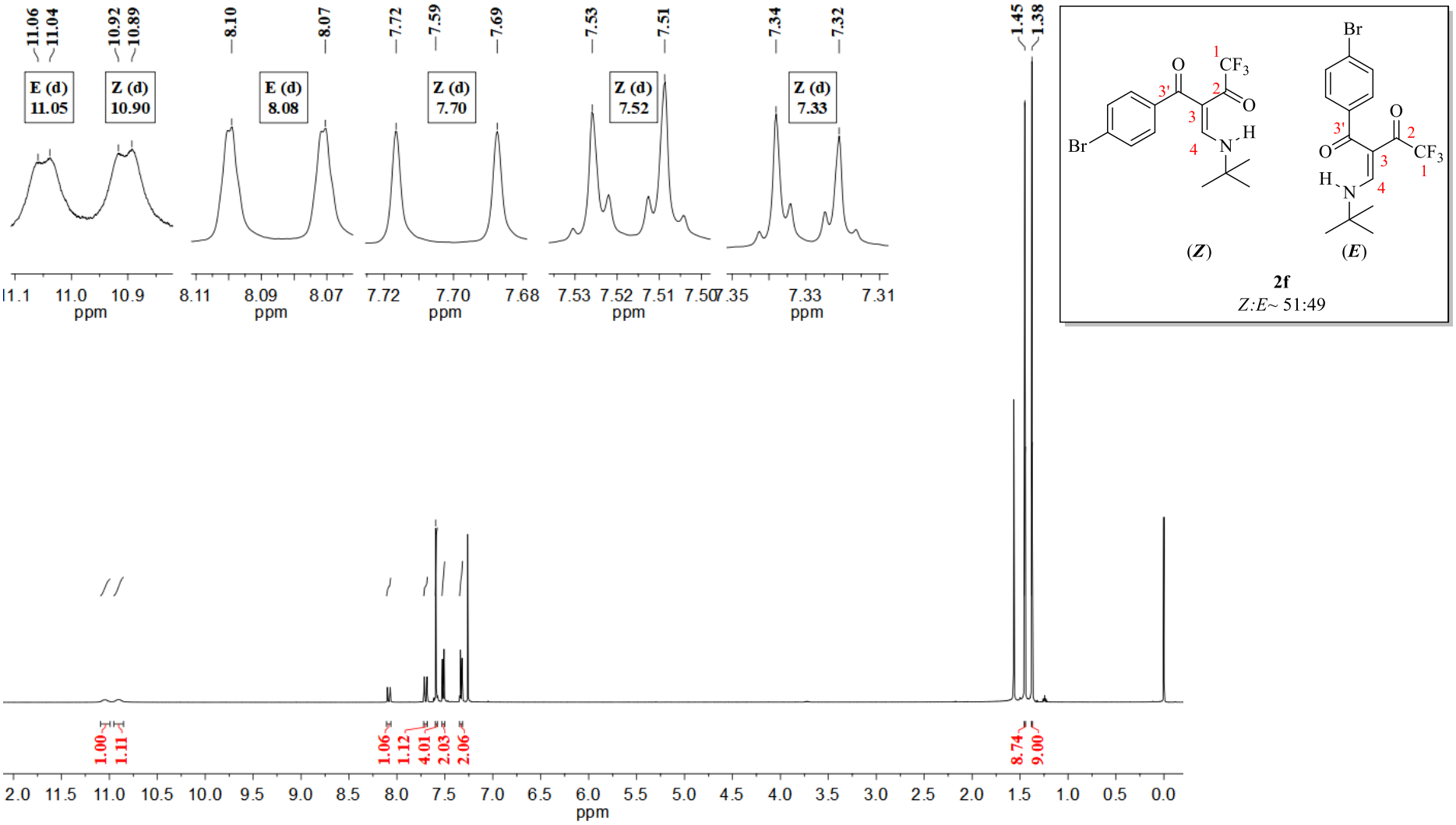


Figure S14 – ^{1}H NMR spectrum of compound **2f** in $CDCl_3$ at 500.13 MHz.

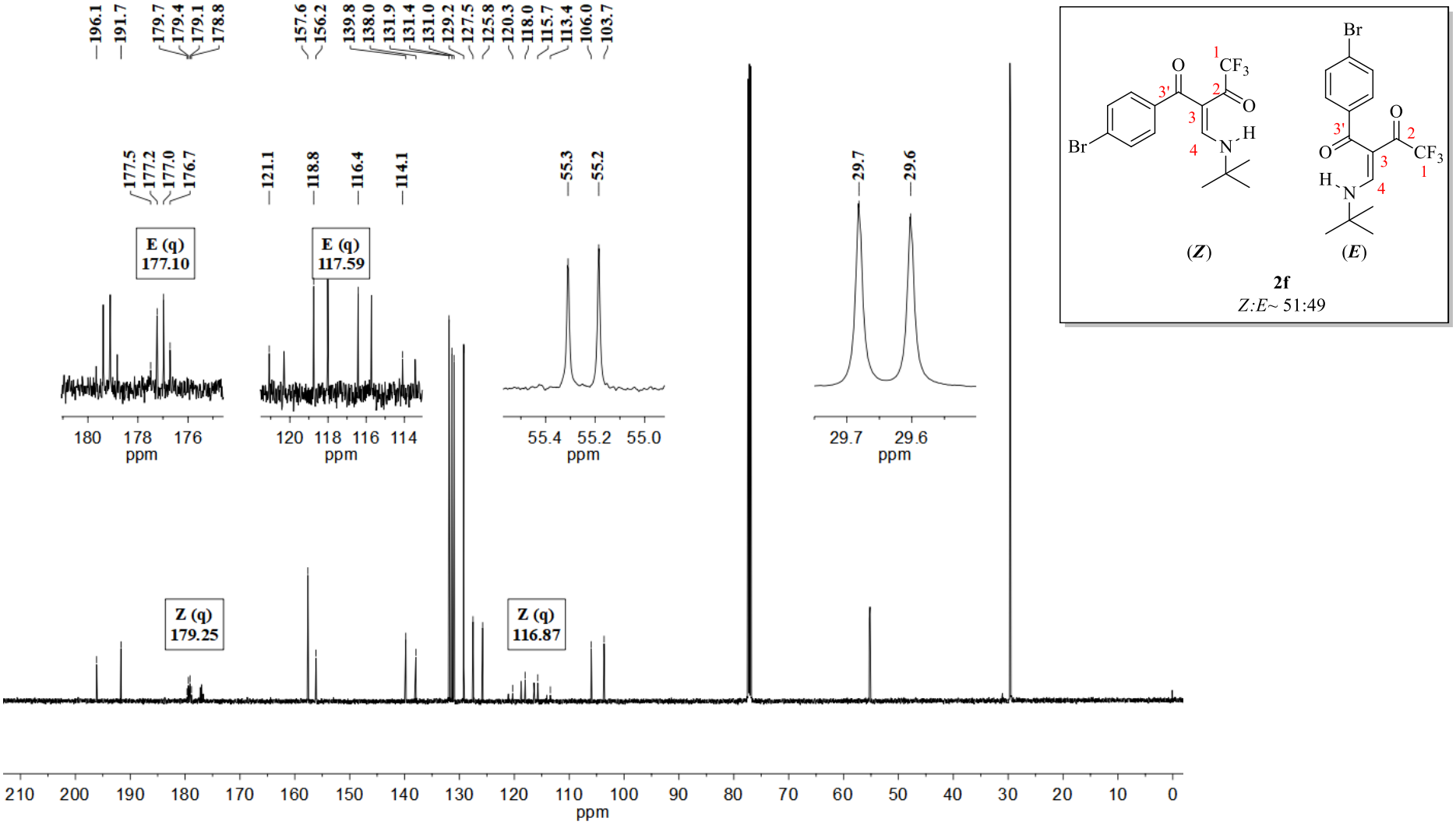
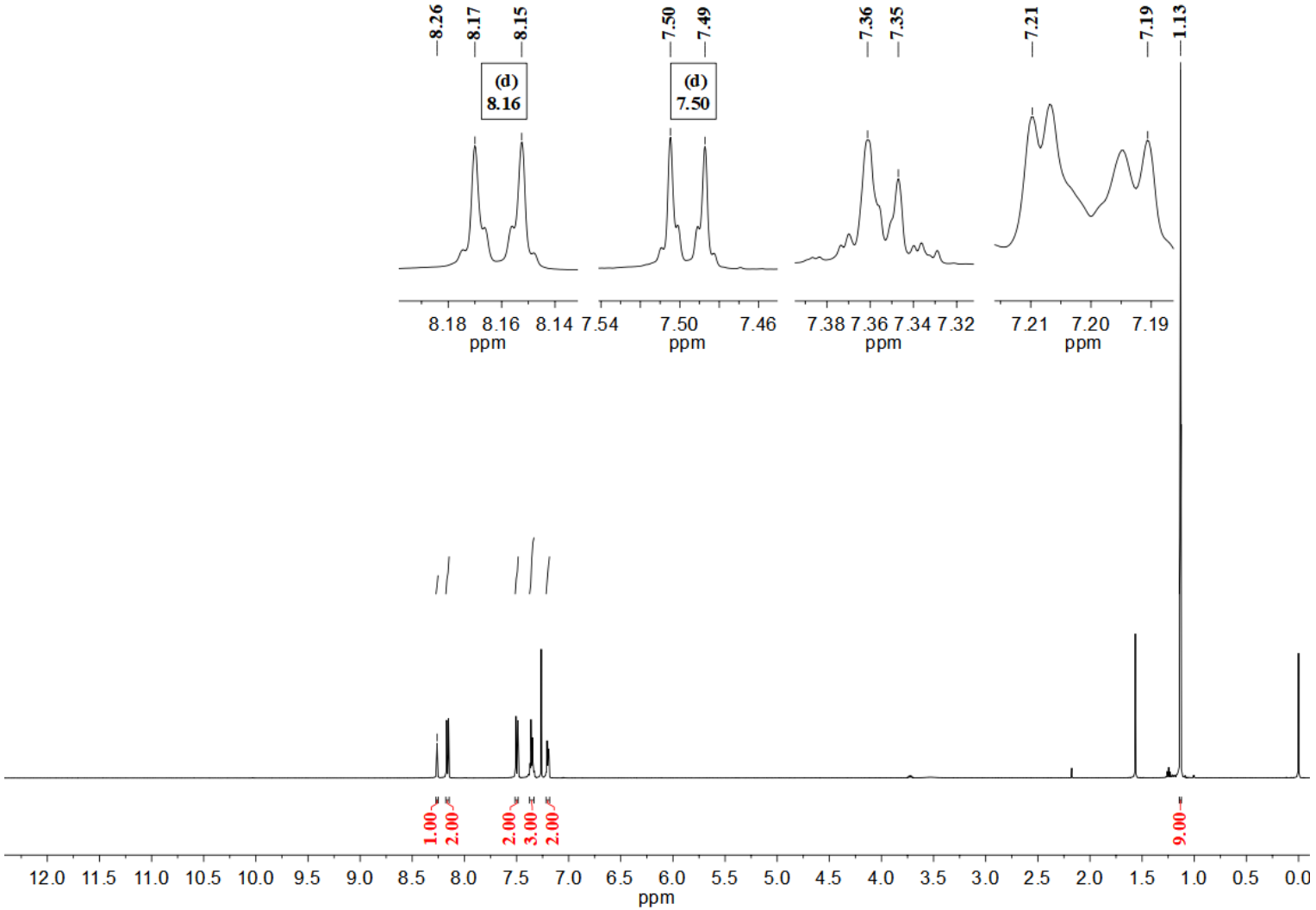
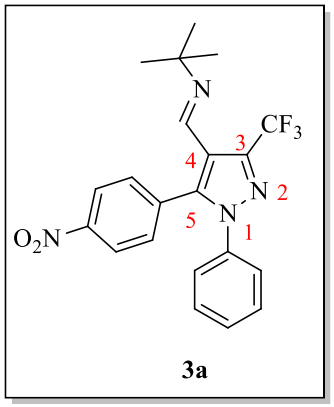


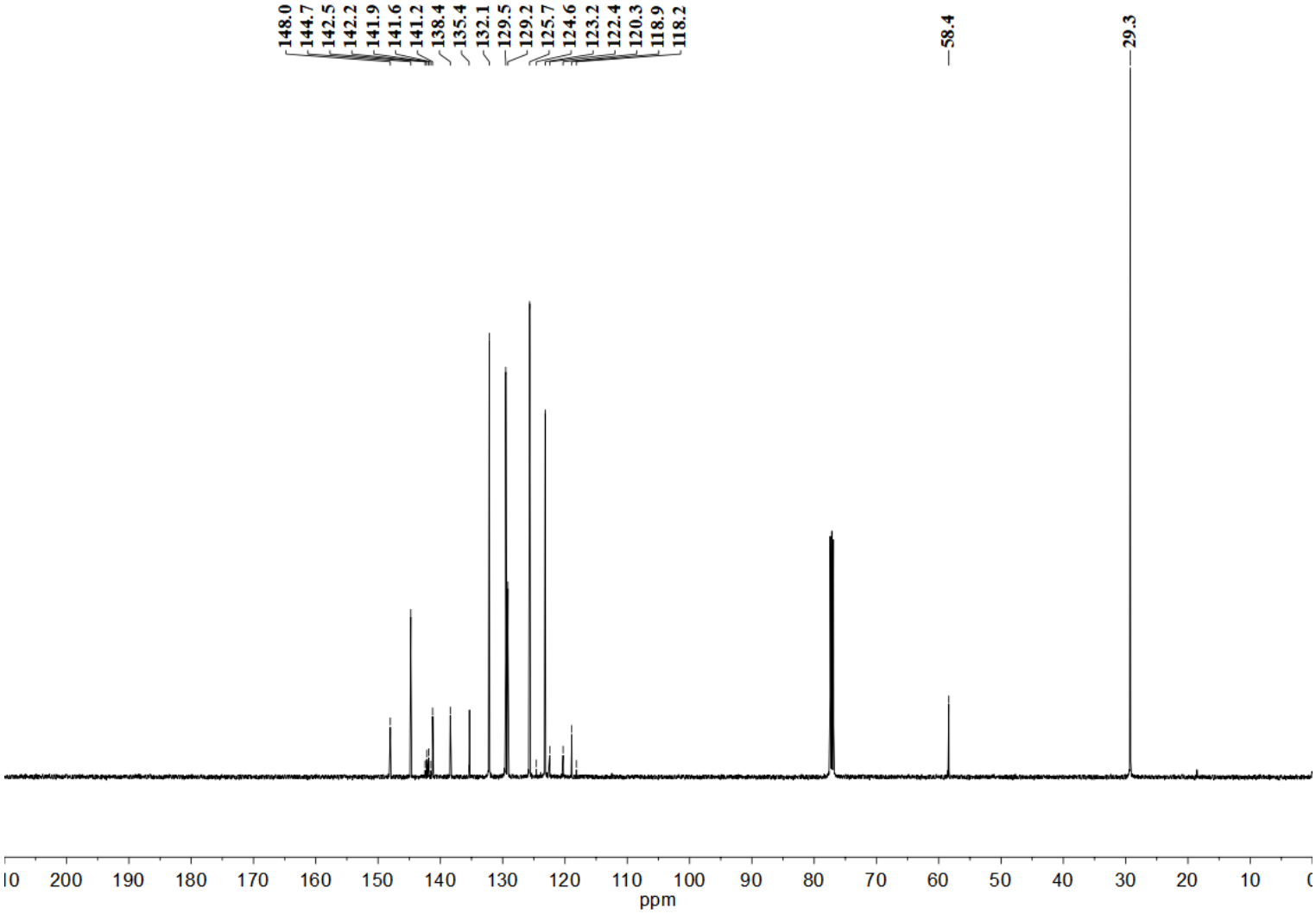
Figure S15 – ^{13}C NMR spectrum of compound **2f** in $CDCl_3$ at 125.76 MHz.

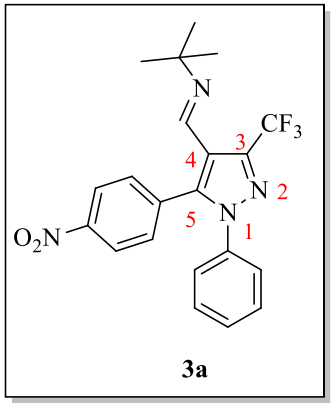




3a

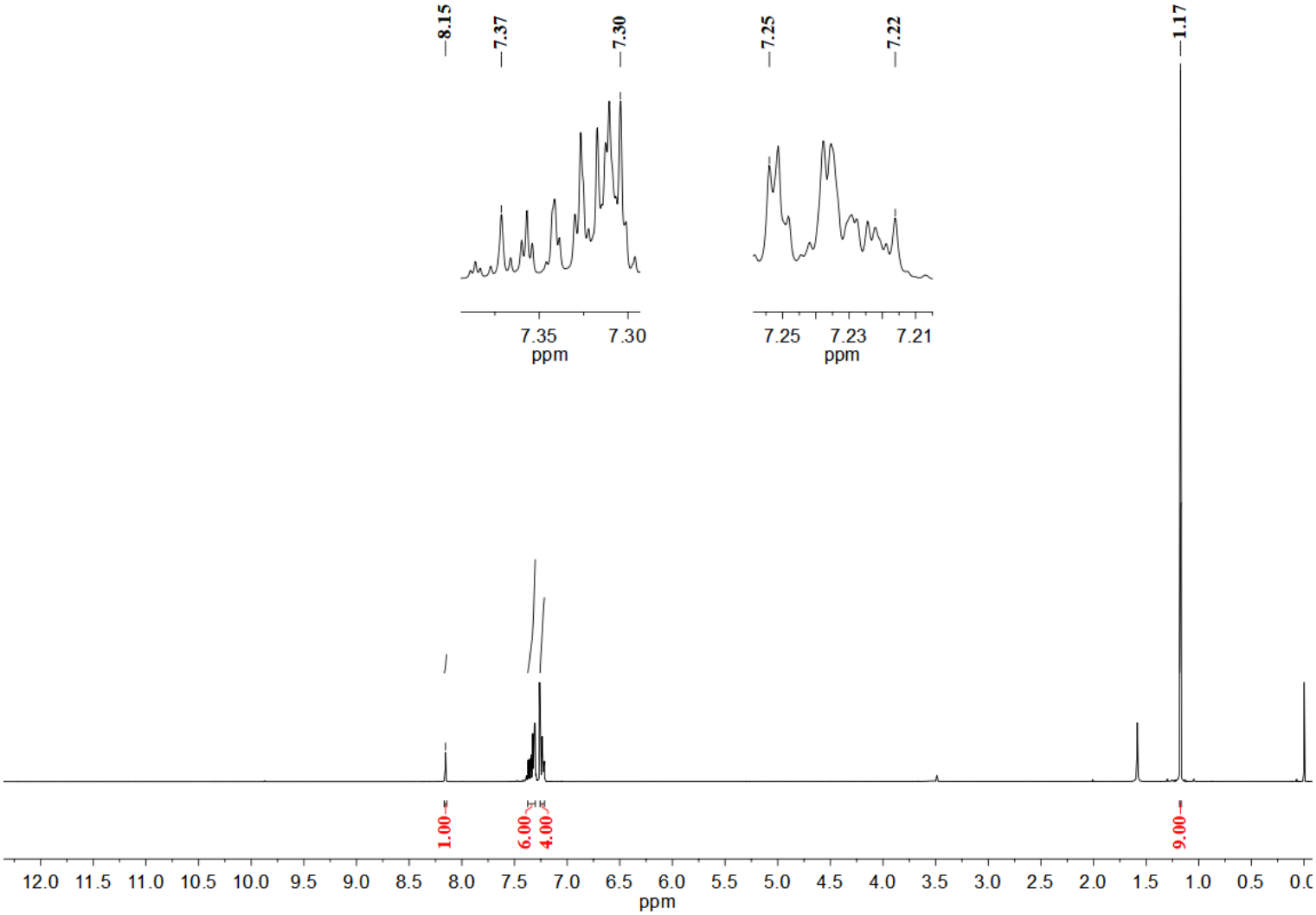
Figure S16 – ^{1}H NMR spectrum of compound **3a** in $CDCl_3$ at 500.13 MHz.

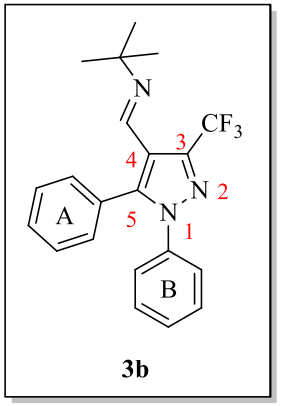




3a

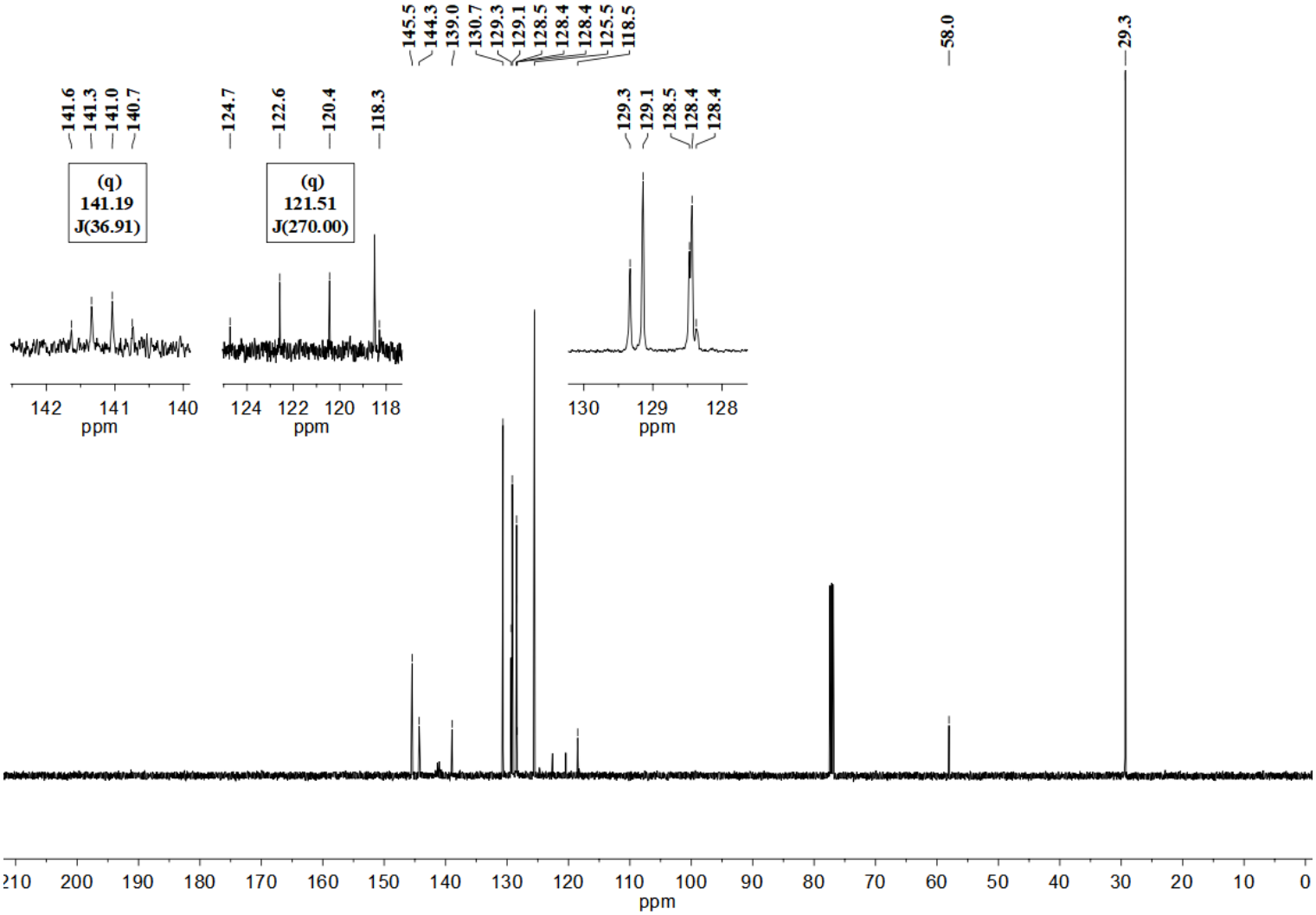
Figure S17 – ^{13}C NMR spectrum of compound **3a** in $CDCl_3$ at 125.76 MHz.





3b

Figure S18 – ^{1}H NMR spectrum of compound **3b** in $CDCl_3$ at 500.13 MHz.



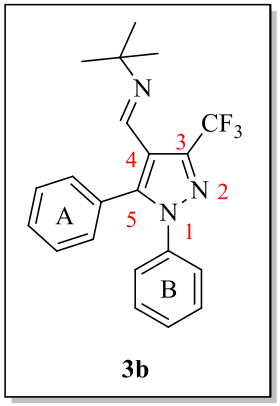
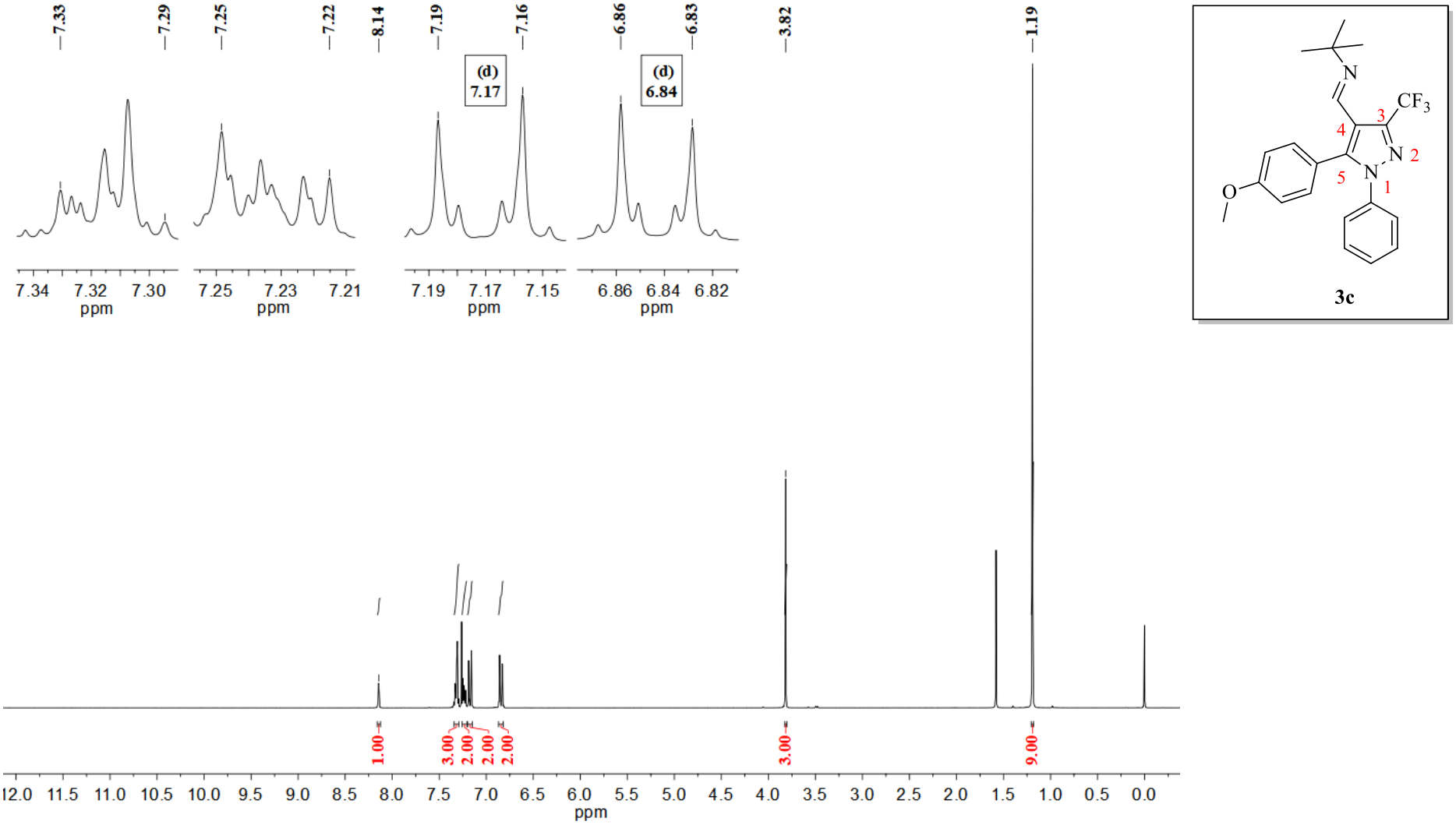


Figure S19 – ^{13}C NMR spectrum of compound **3b** in $CDCl_3$ at 125.76 MHz.


7.33
7.29
7.25
7.22
8.14
7.19
7.16
6.86
6.83
3.82
1.19
(d)
7.17
(d)
6.84
7.34 7.32 7.30
ppm
7.25 7.23 7.21
ppm
7.19 7.17 7.15
ppm
6.86 6.84 6.82
ppm
1.00
3.00
2.00
2.00
2.00
3.00
9.00
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
ppm

N
CF3
3
4
N
2
5
N
1
O

3c

Figure S20 – ^{1}H NMR spectrum of compound **3c** in $CDCl_3$ at 300.06 MHz.

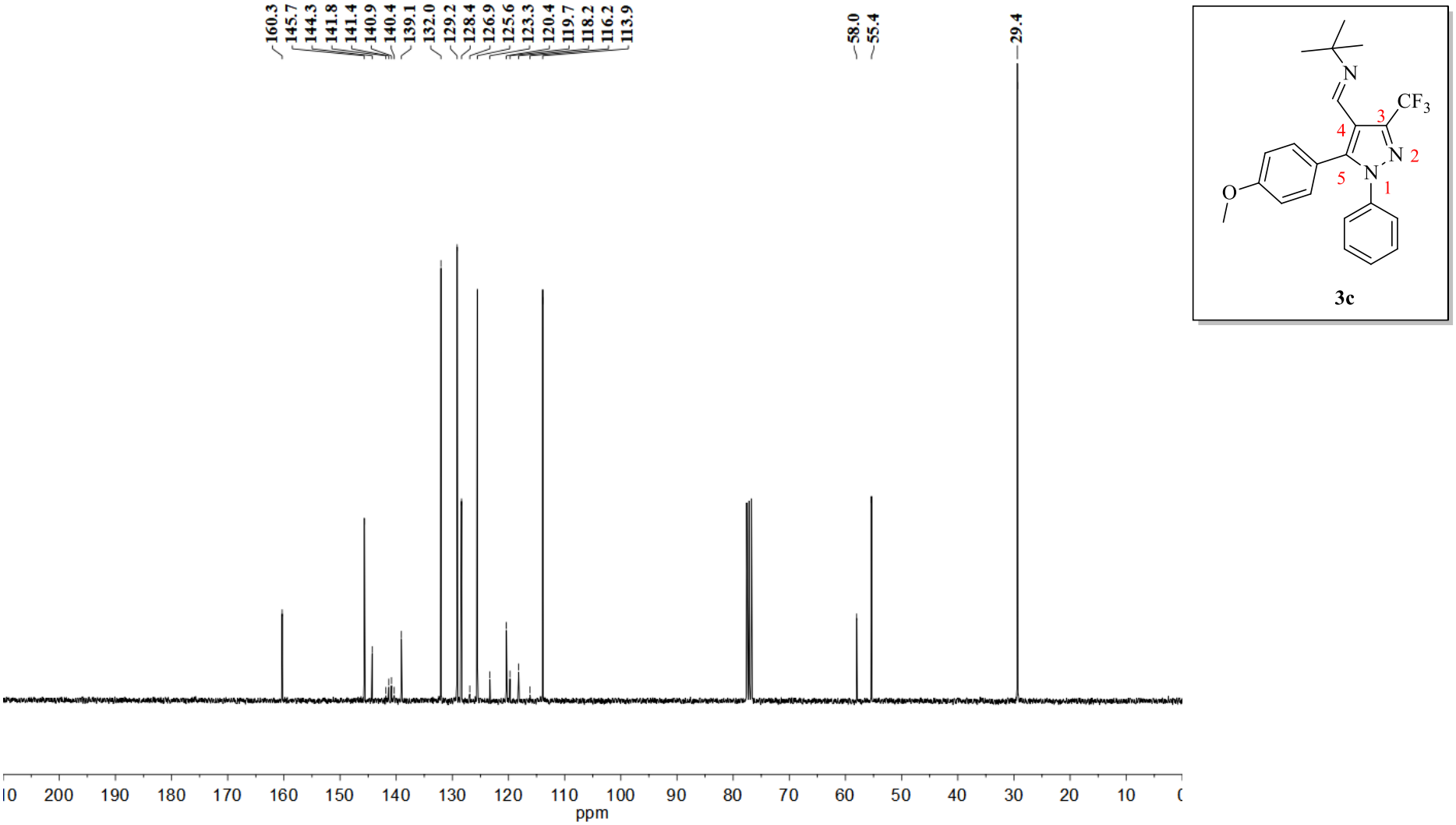


Figure S21 – ^{13}C NMR spectrum of compound **3c** in $CDCl_3$ at 75.45 MHz.

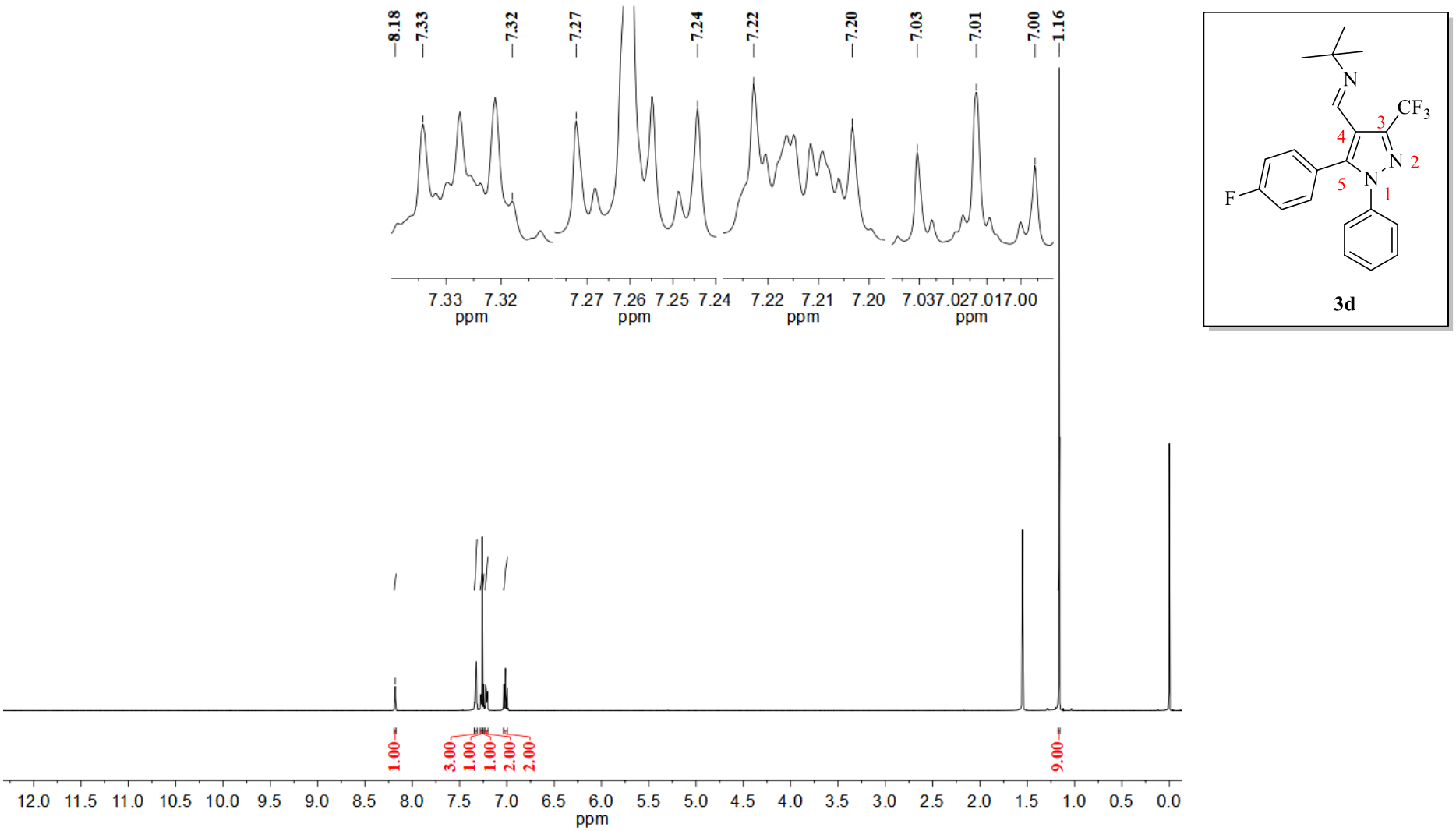


Figure S22 – ^{1}H NMR spectrum of compound **3d** in $CDCl_3$ at 500.13 MHz.

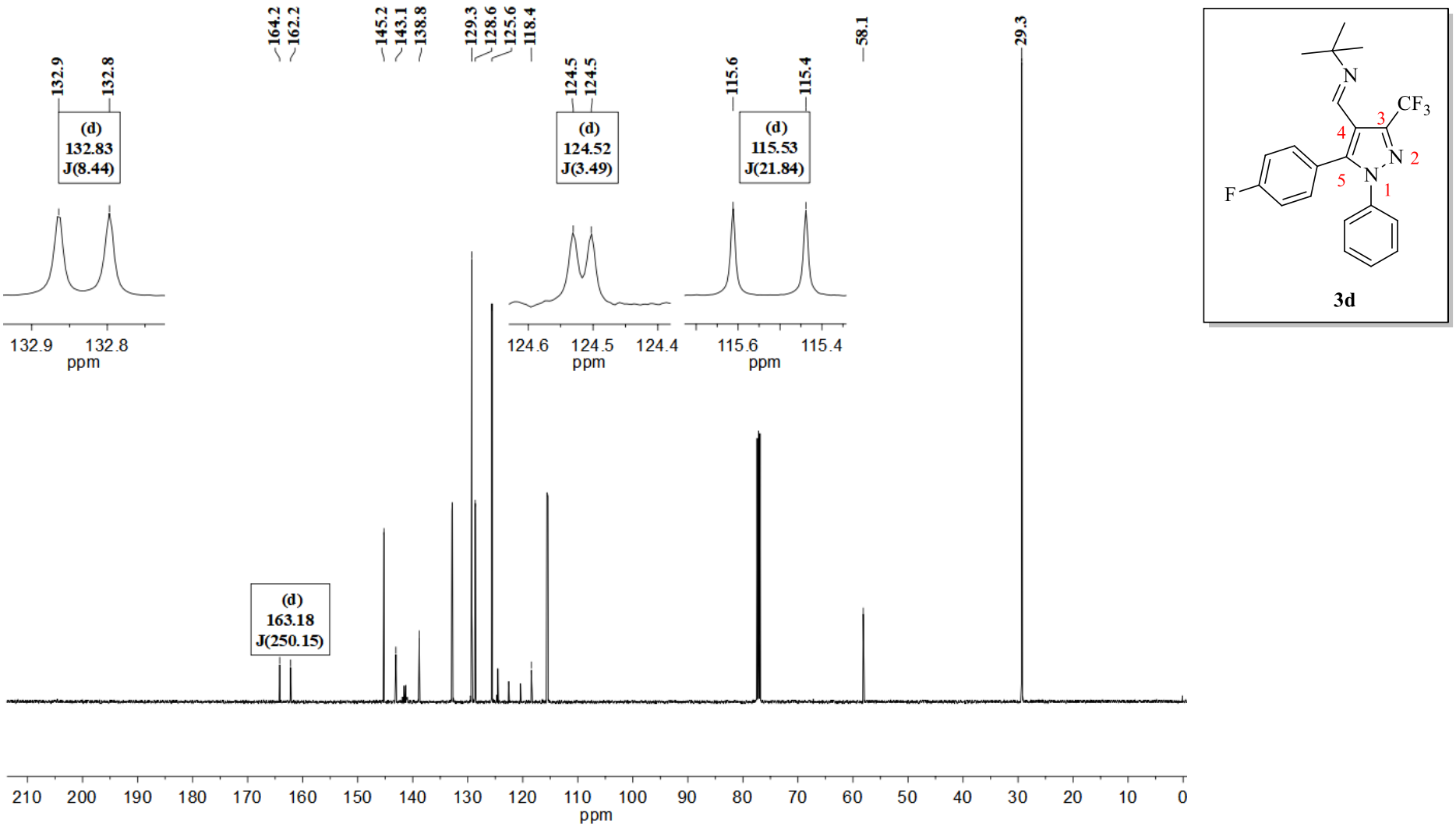
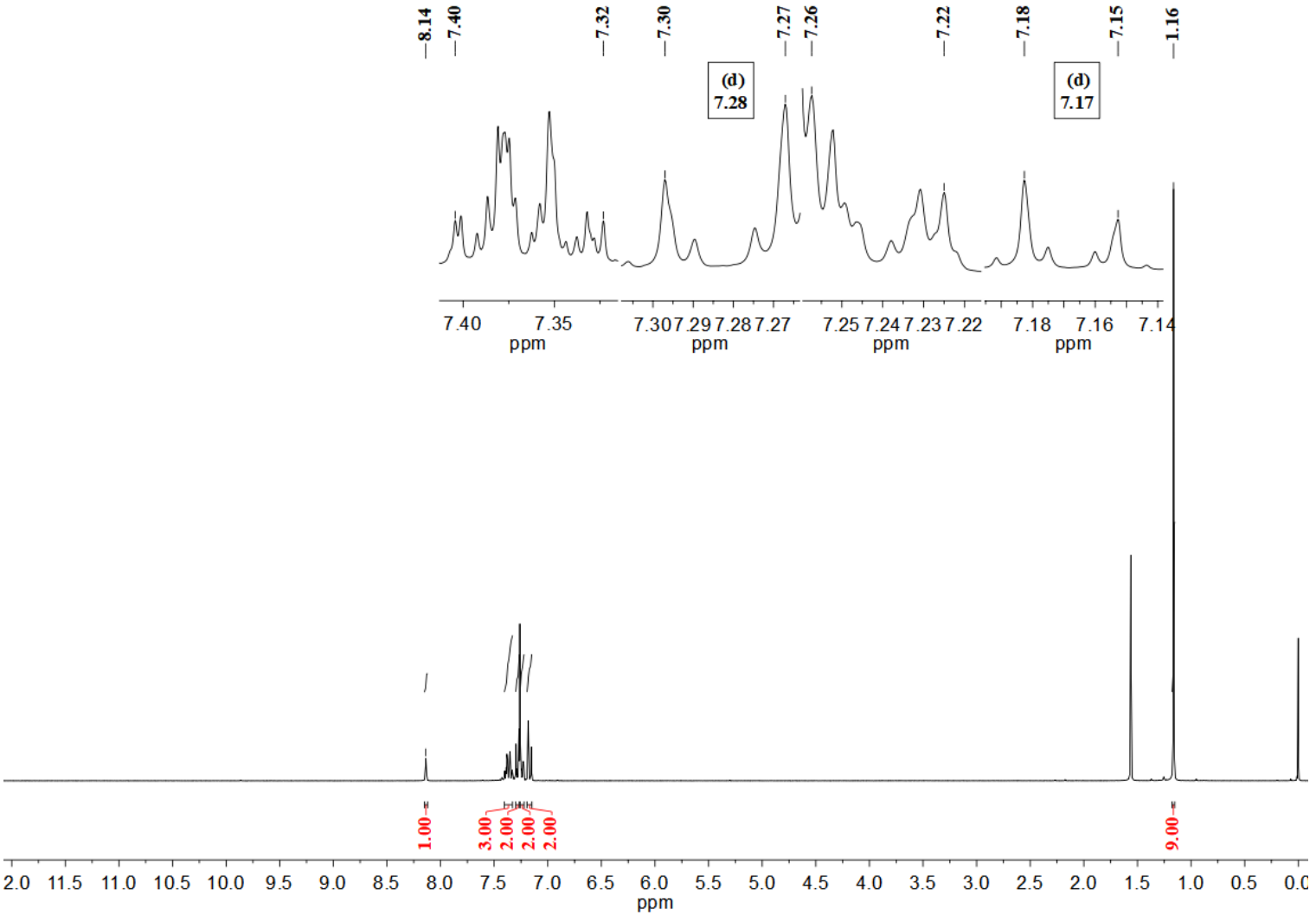
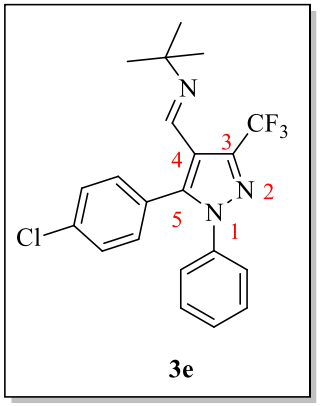


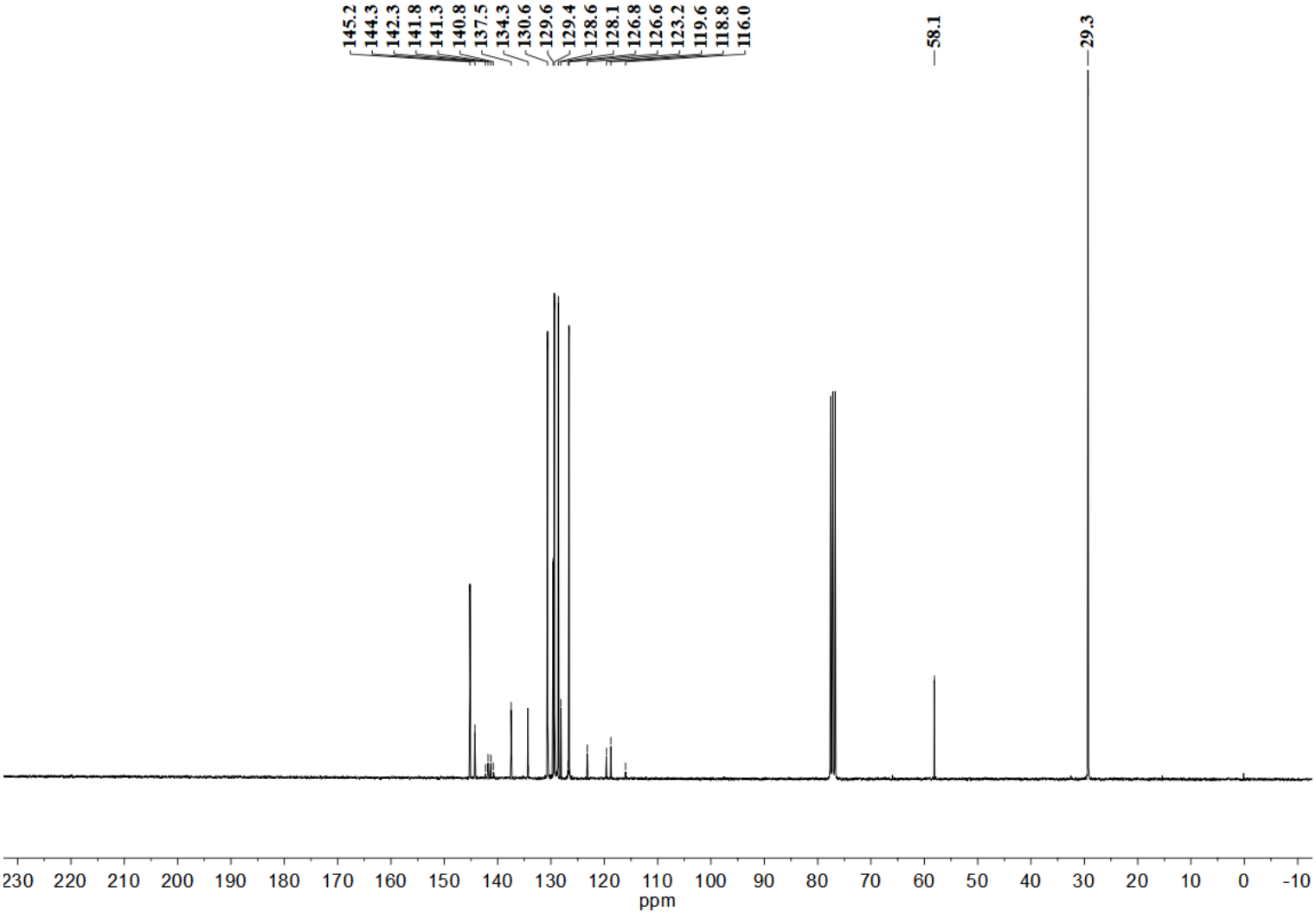
Figure S23 – ^{13}C NMR spectrum of compound **3d** in $CDCl_3$ at 125.76 MHz.

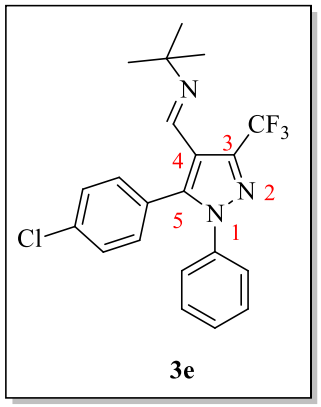

8.14
7.40
7.32
7.30
7.27
7.26
7.22
7.18
7.15
1.16
(d)
7.28
(d)
7.17
7.40
7.35
ppm
7.30
7.29
7.28
7.27
7.25
7.24
7.23
7.22
7.18
7.16
7.14
1.00
3.00
2.00
2.00
2.00
9.00
2.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm


N
CF3
3
4
N
2
5
N
1
Cl

3e

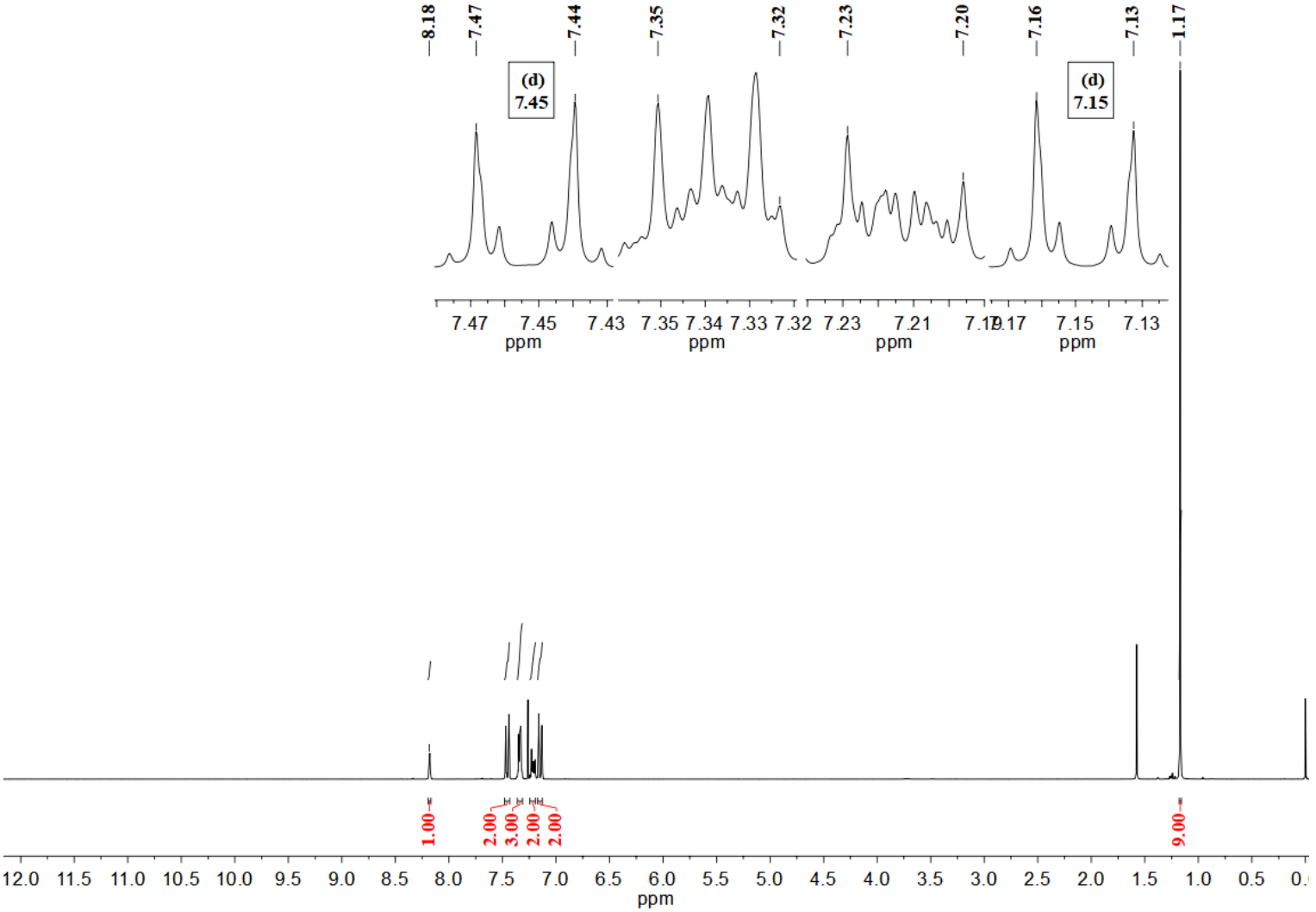
Figure S24 – ^{1}H NMR spectrum of compound **3e** in $CDCl_3$ at 300.06 MHz.

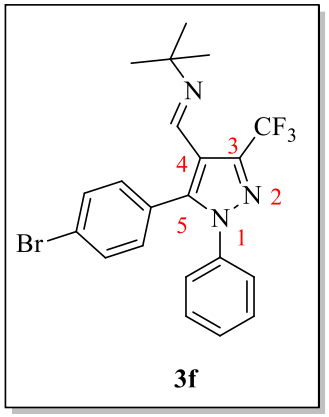




3e

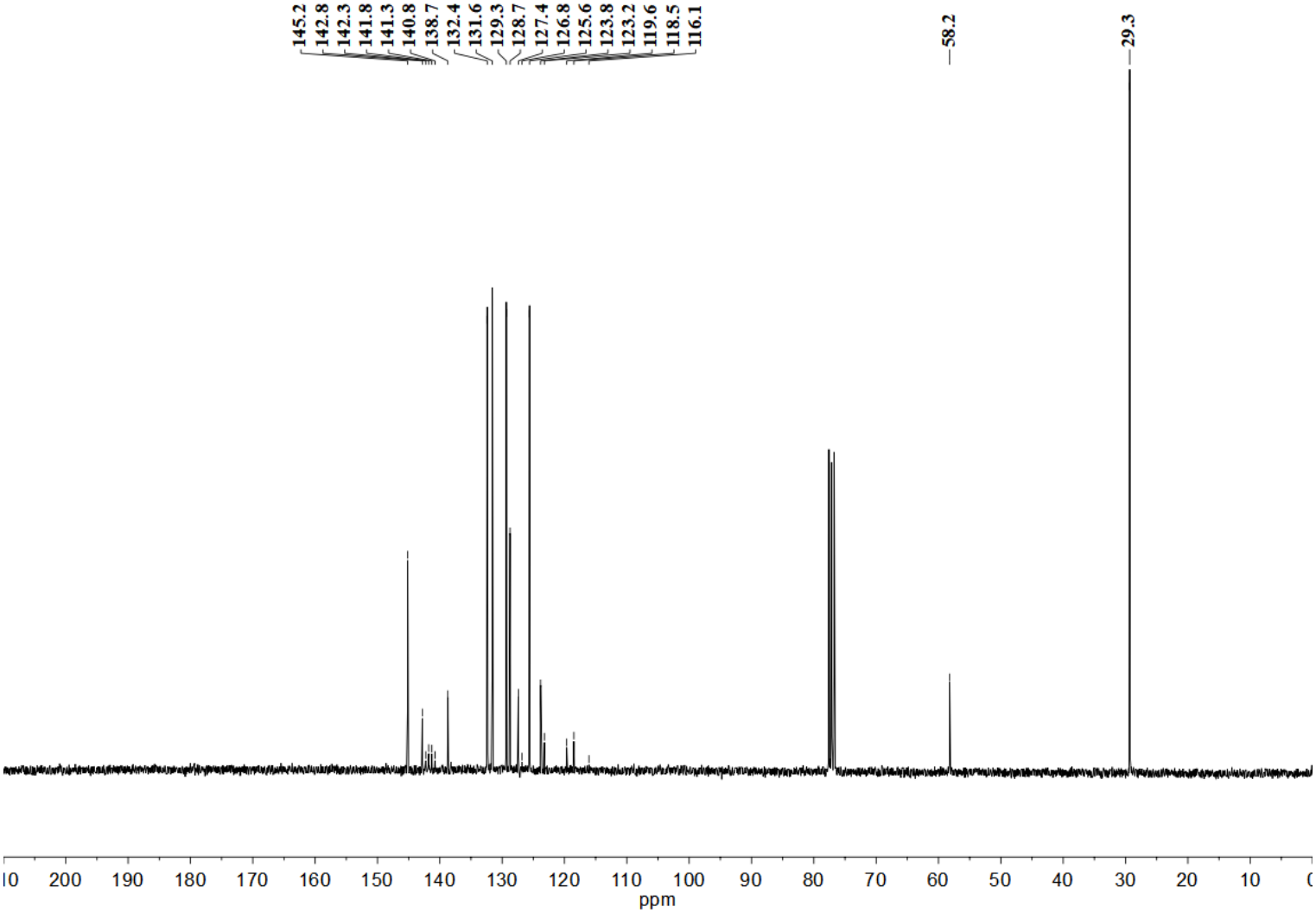
Figure S25 – ^{13}C NMR spectrum of compound **3e** in $CDCl_3$ at 75.45 MHz.





3f

Figure S26 – ^{1}H NMR spectrum of compound **3f** in $CDCl_3$ at 300.06 MHz.



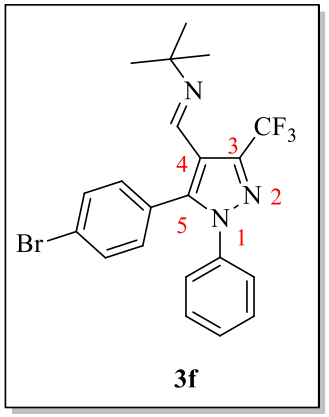


Figure S27 – ^{13}C NMR spectrum of compound **3f** in $CDCl_3$ at 75.45 MHz.

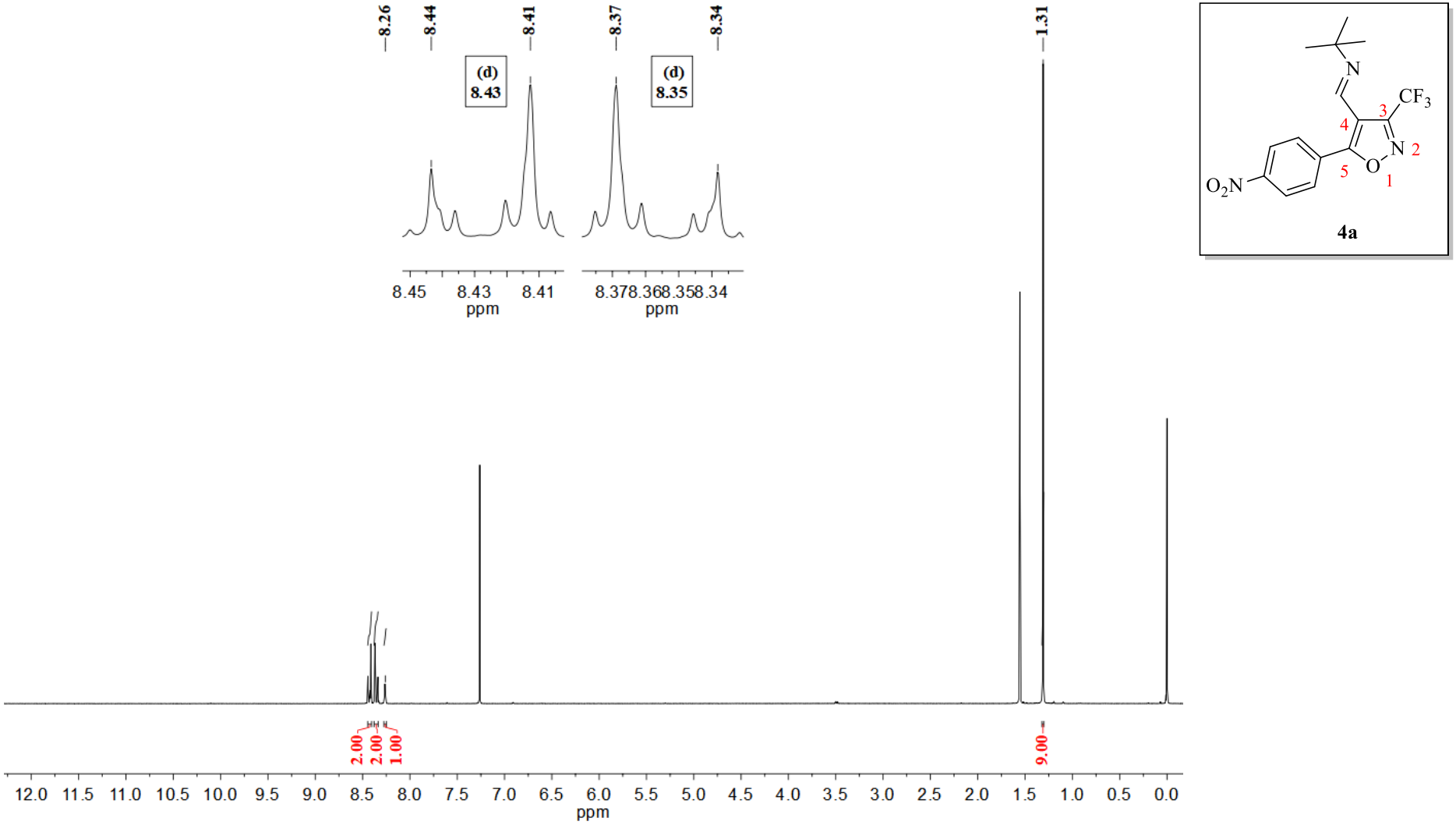
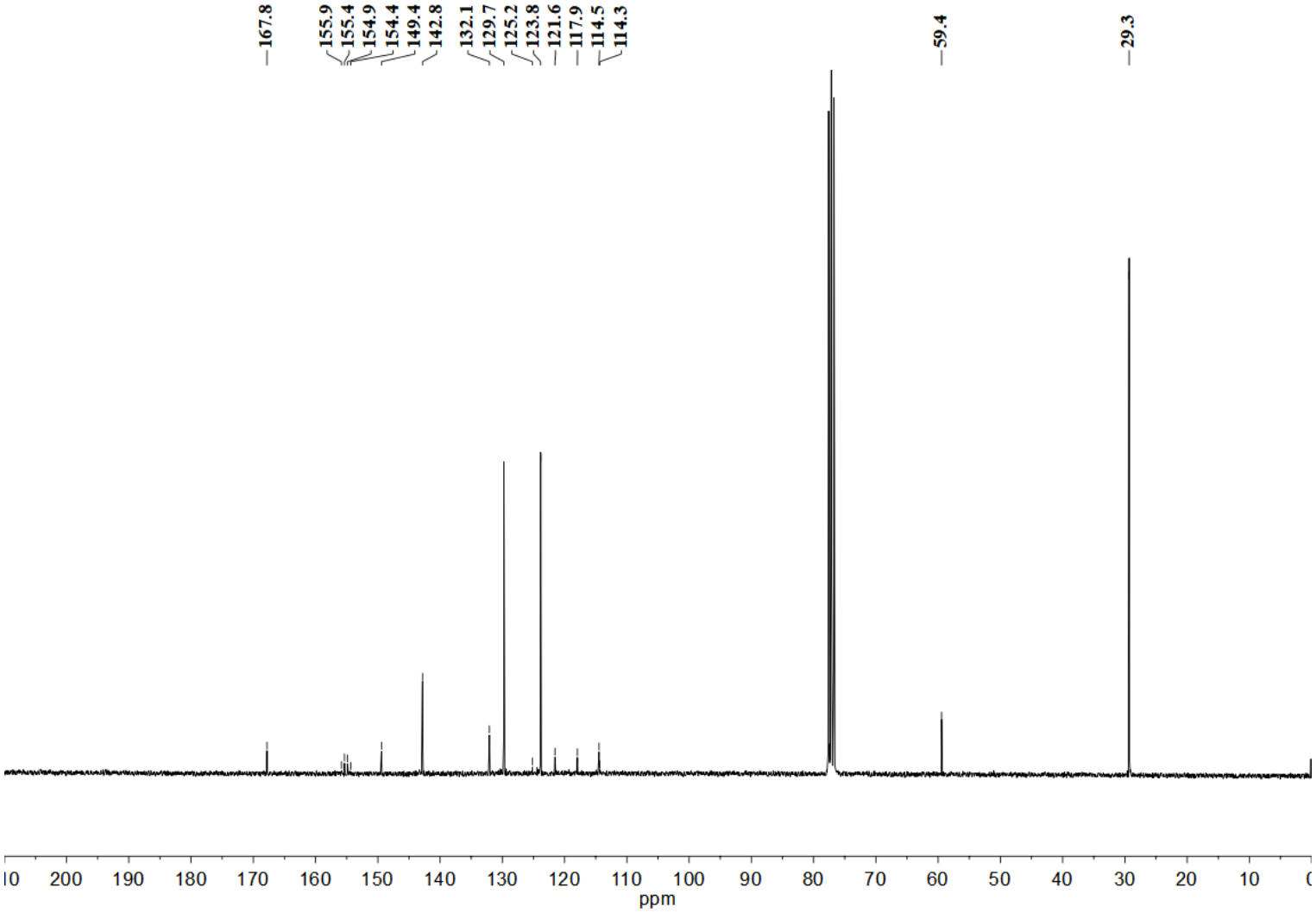
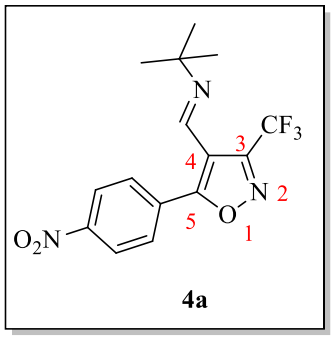


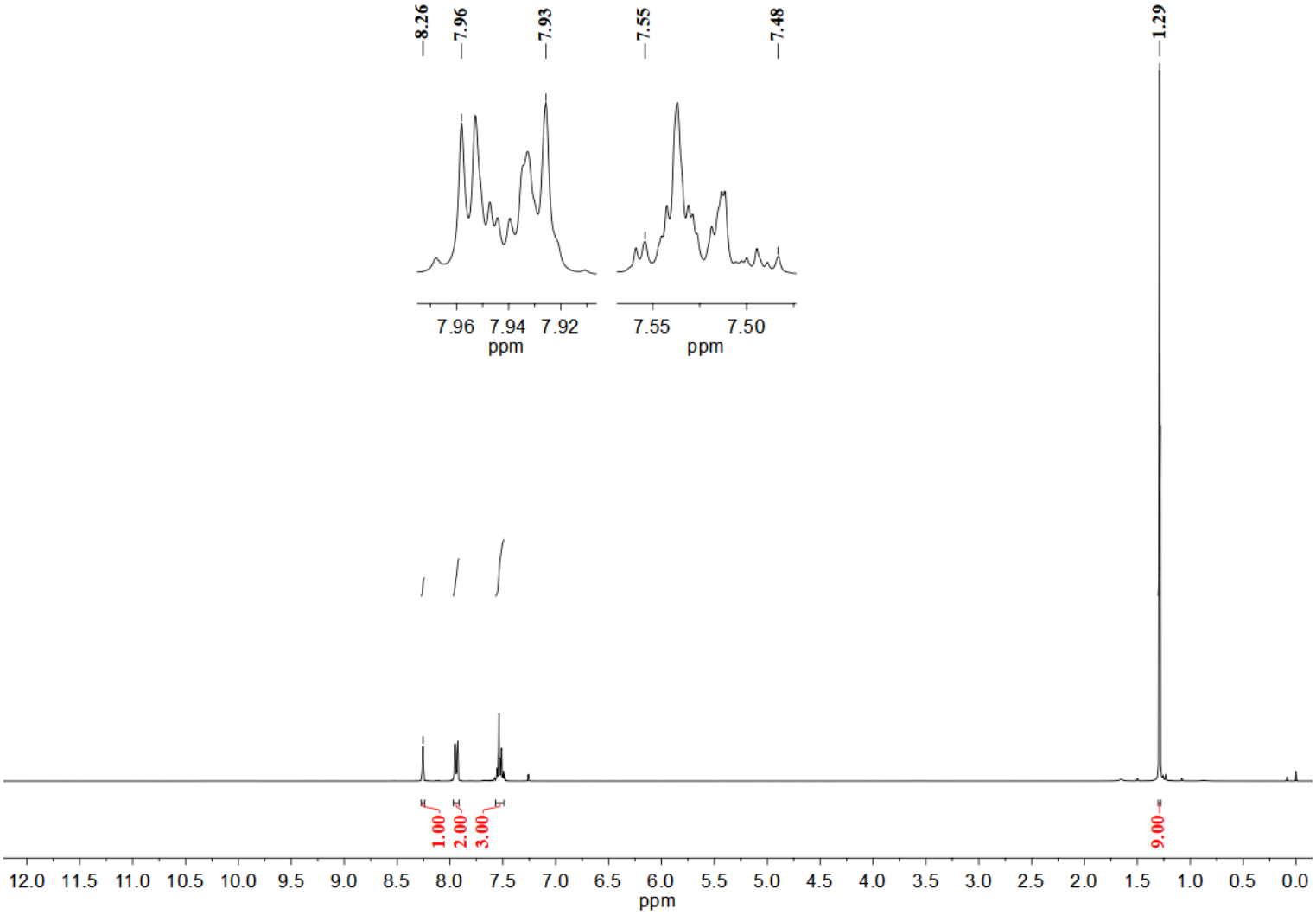
Figure S28 – ^{1}H NMR spectrum of compound **4a** in $CDCl_3$ at 300.06 MHz.

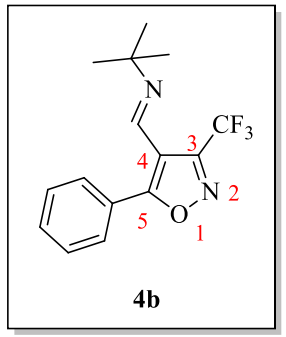




4a

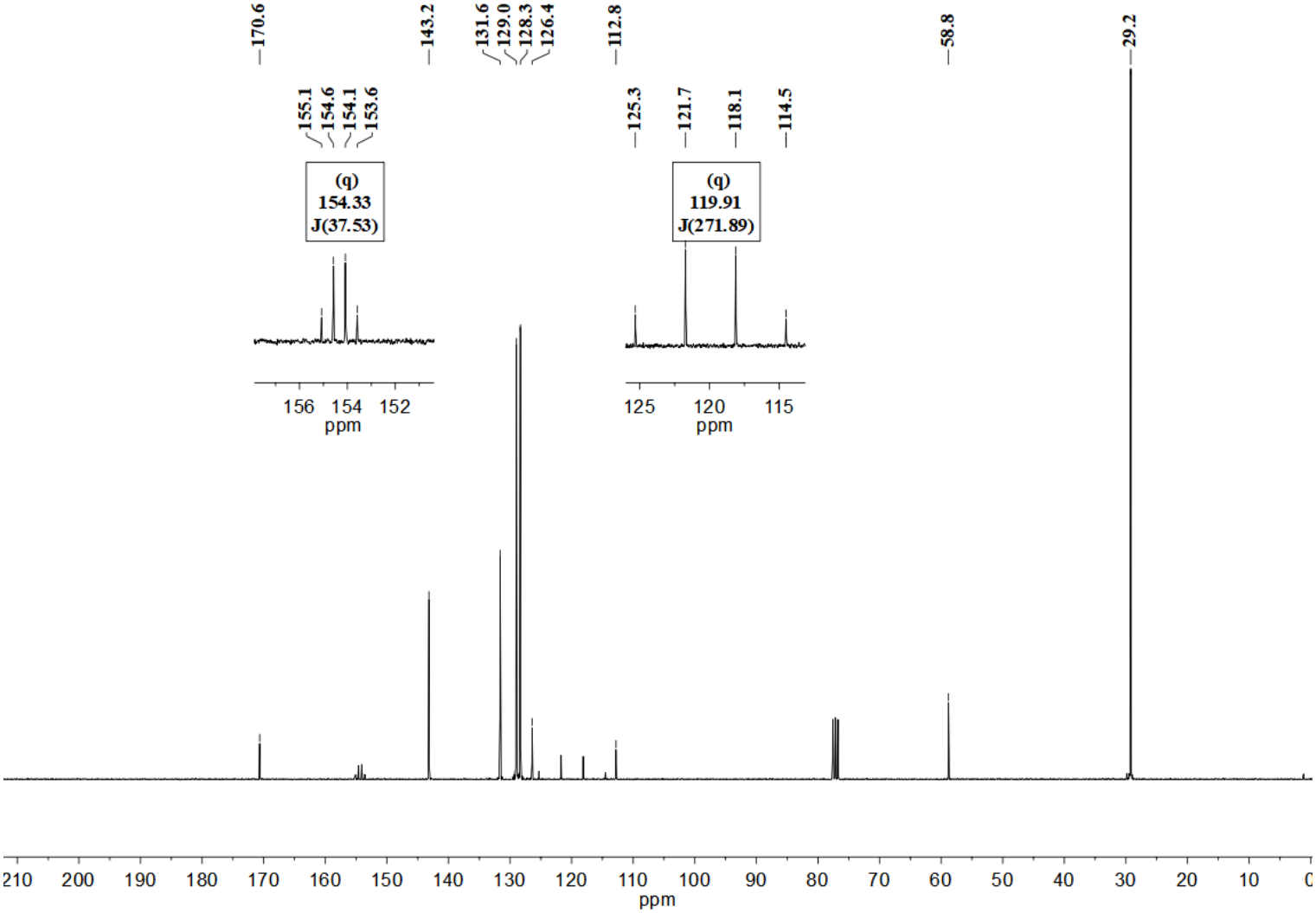
Figure S29 – ^{13}C NMR spectrum of compound **4a** in $CDCl_3$ at 75.45 MHz.

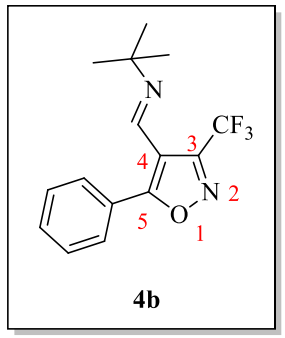




4b

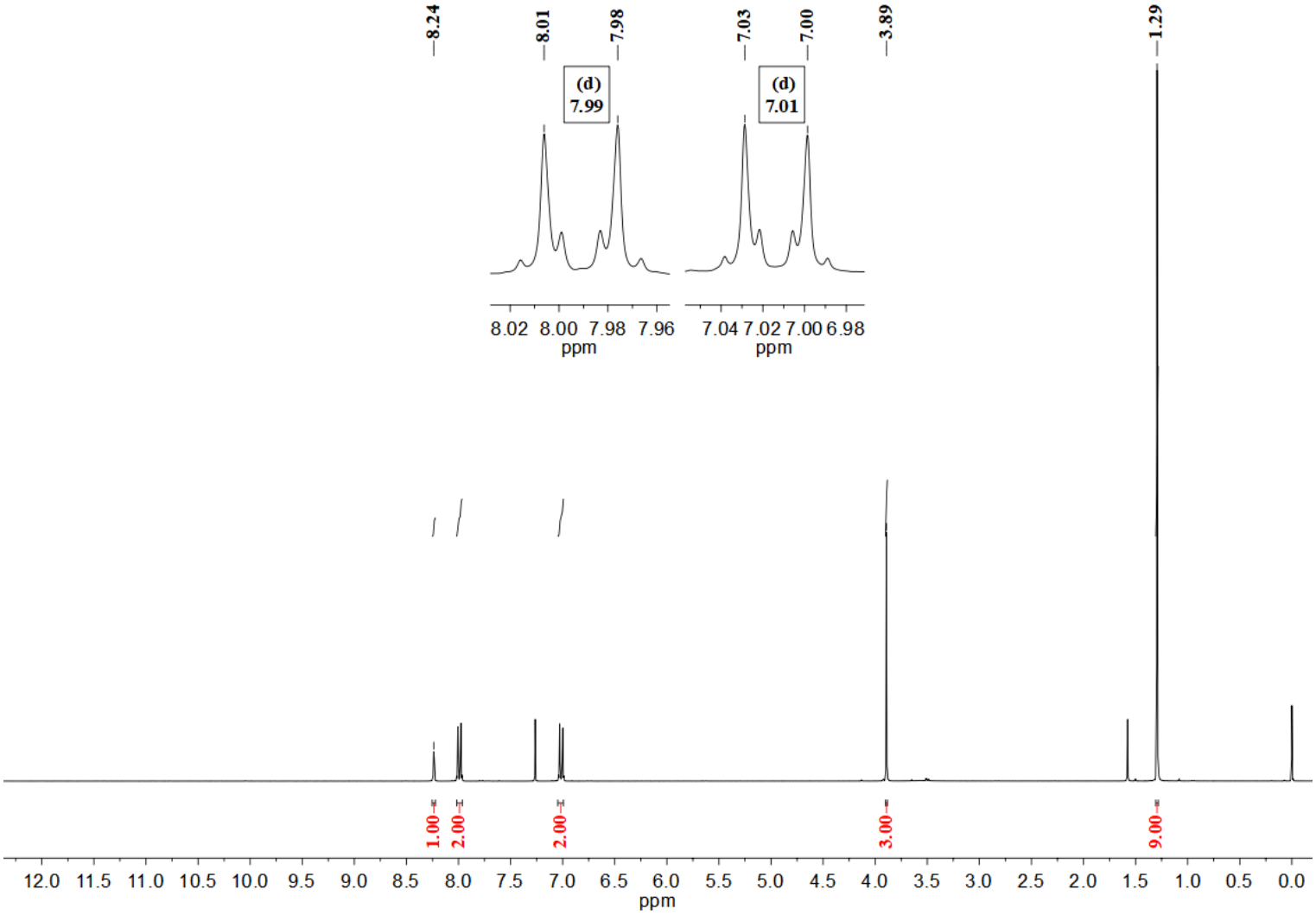
Figure S30 – ^{1}H NMR spectrum of compound **4b** in $CDCl_3$ at 300.06 MHz.

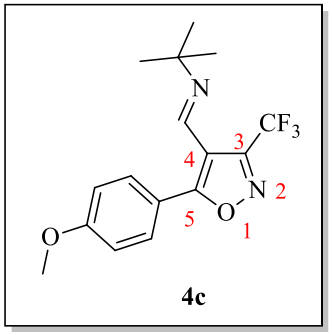




4b

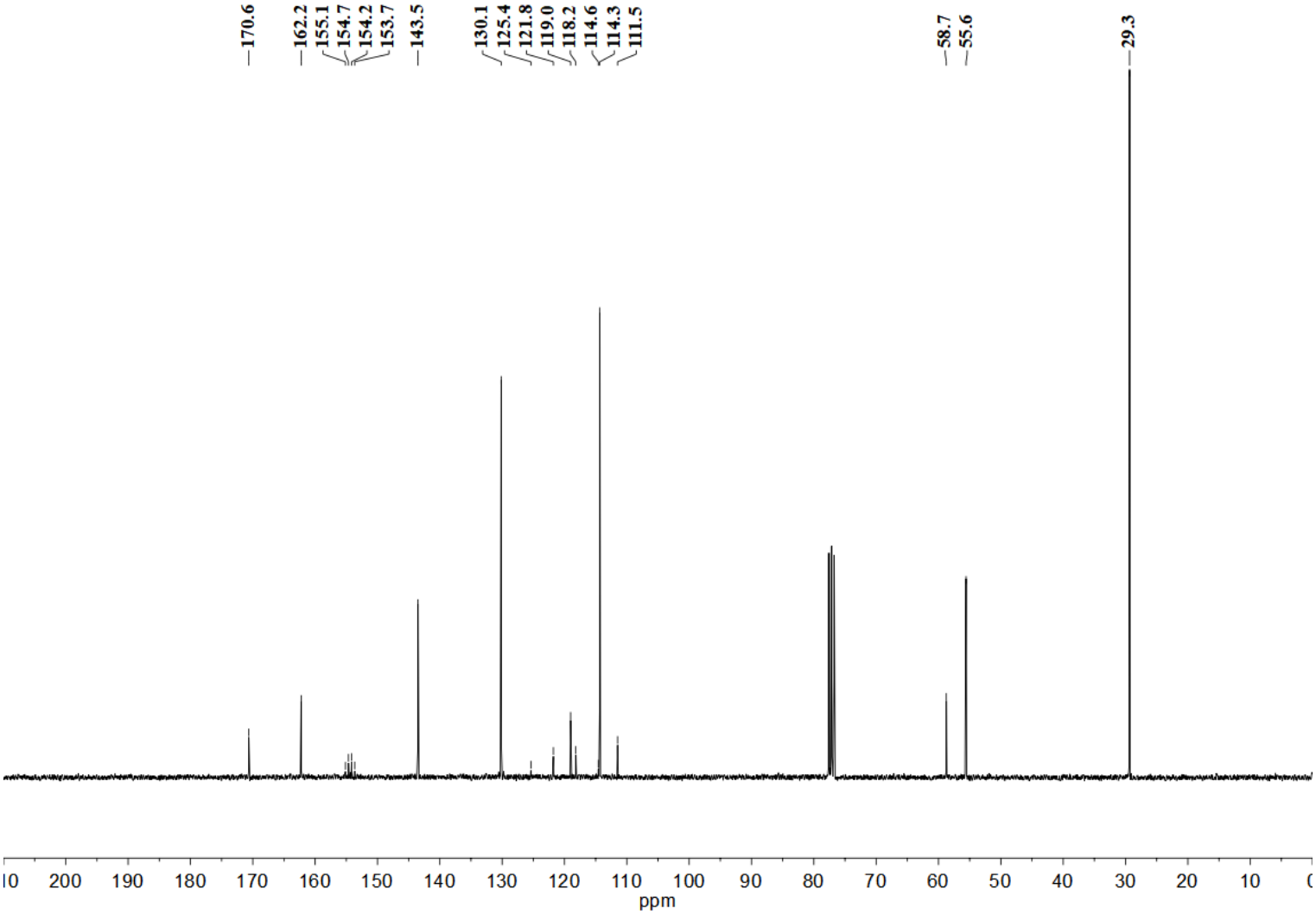
Figure S31 – ^{13}C NMR spectrum of compound **4b** in $CDCl_3$ at 75.45 MHz.





4c

Figure S32 – ^{1}H NMR spectrum of compound **4c** in $CDCl_3$ at 300.06 MHz.



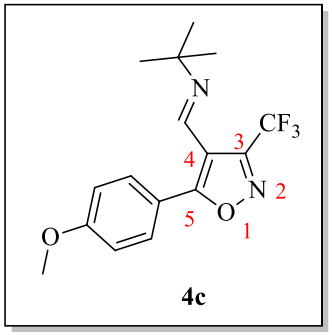
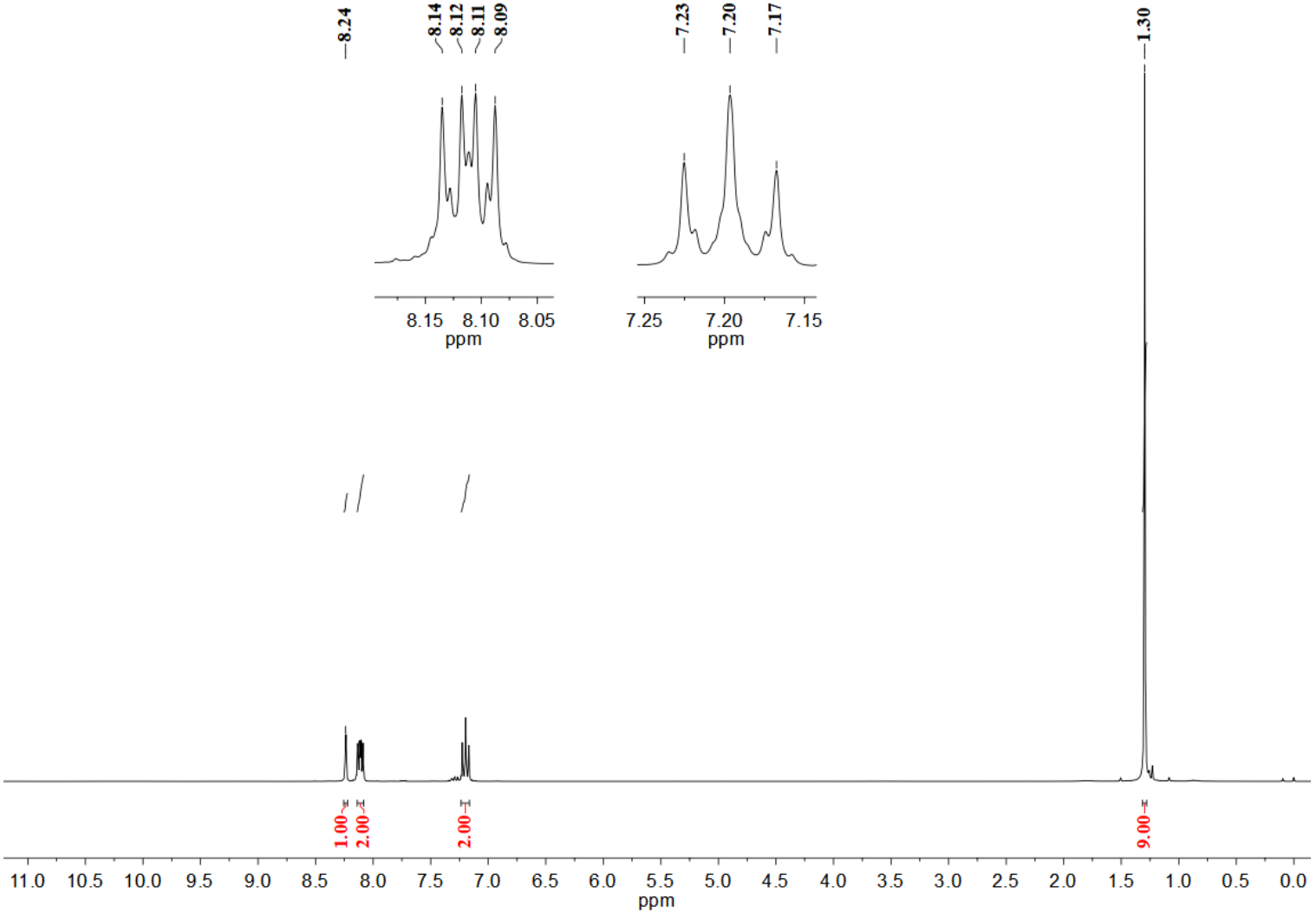
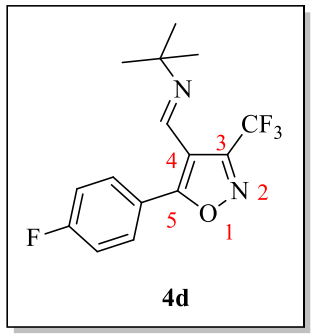


Figure S33 – ^{13}C NMR spectrum of compound **4c** in $CDCl_3$ at 75.45 MHz.





4d

Figure S34 – ^{1}H NMR spectrum of compound **4d** in $CDCl_3$ at 300.06 MHz.

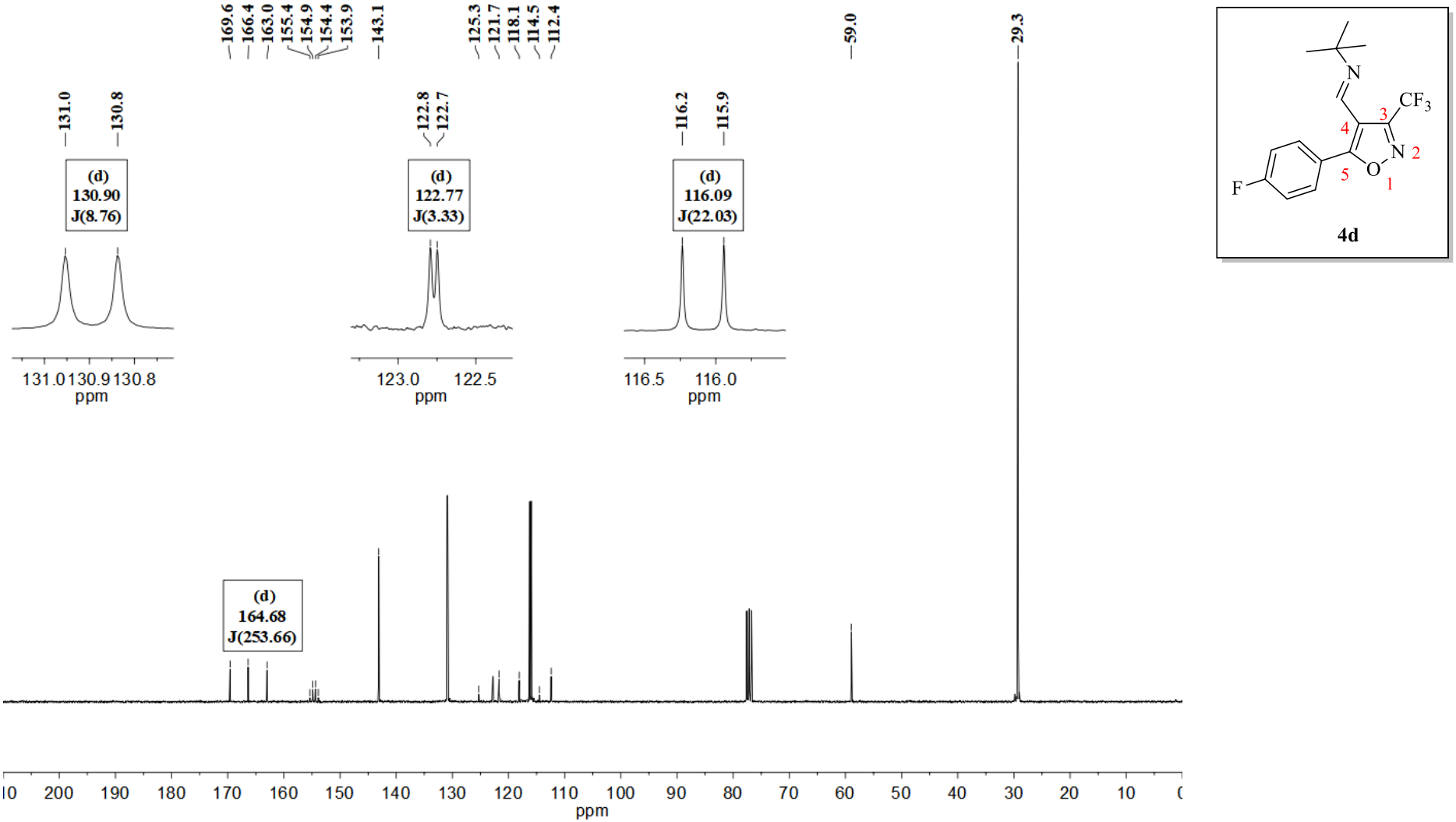


Figure S35 – ^{13}C NMR spectrum of compound **4d** in $CDCl_3$ at 75.45 MHz.

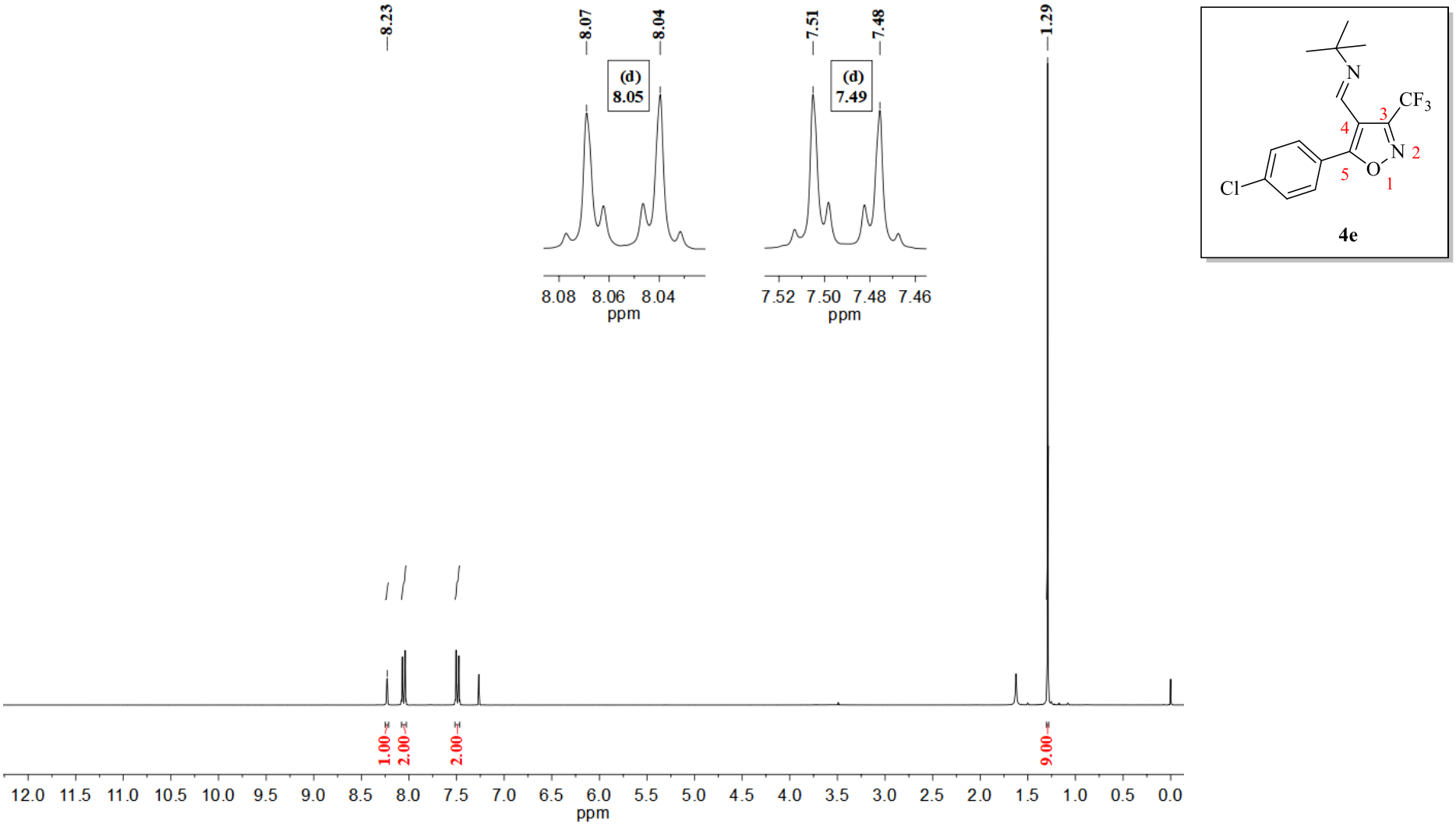


Figure S36 – ^{1}H NMR spectrum of compound **4e** in $CDCl_3$ at 300.06 MHz.

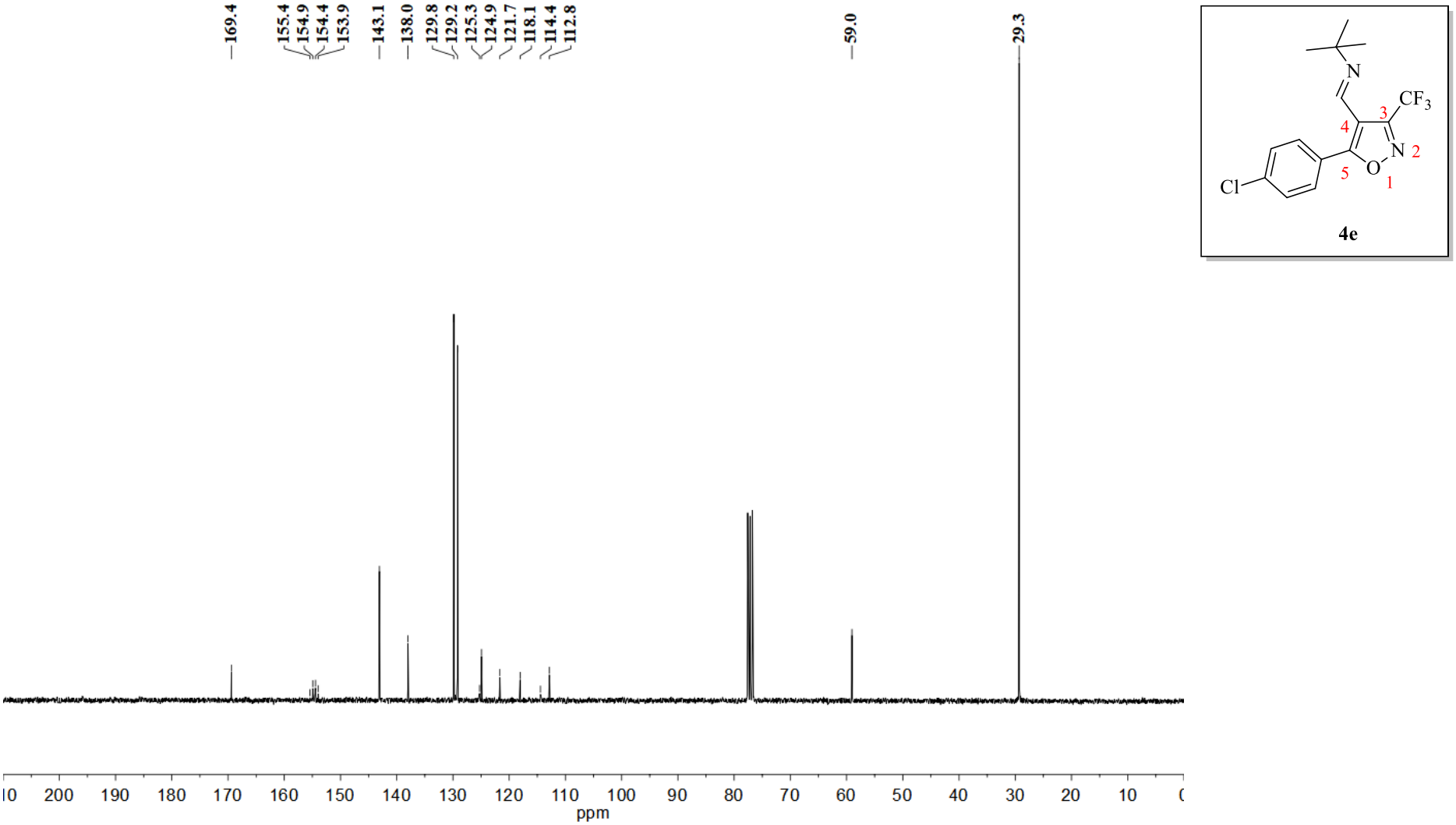


Figure S37 – ^{13}C NMR spectrum of compound **4e** in $CDCl_3$ at 75.45 MHz.

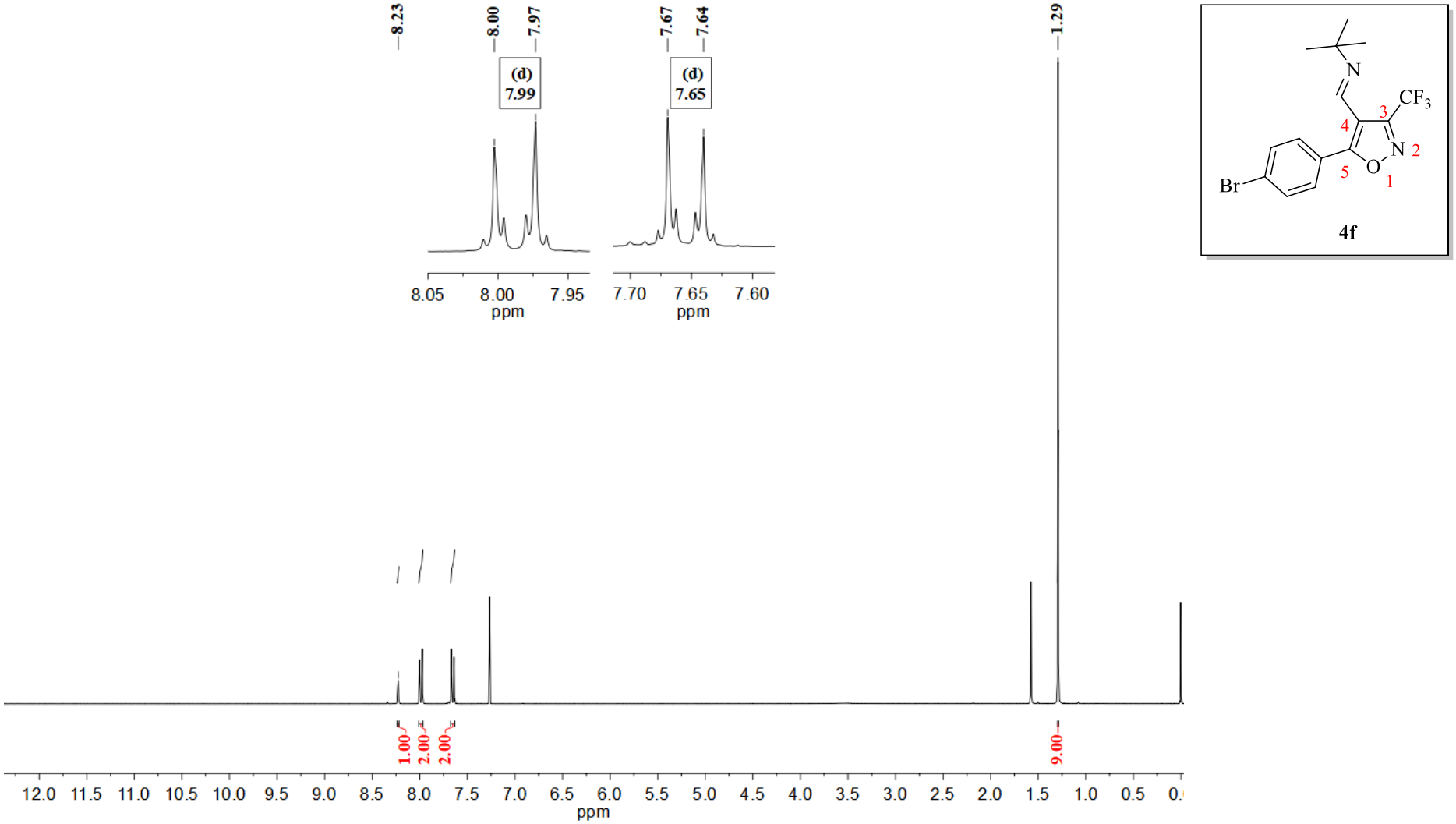


Figure S38 – ^{1}H NMR spectrum of compound **4f** in $CDCl_3$ at 300.06 MHz.

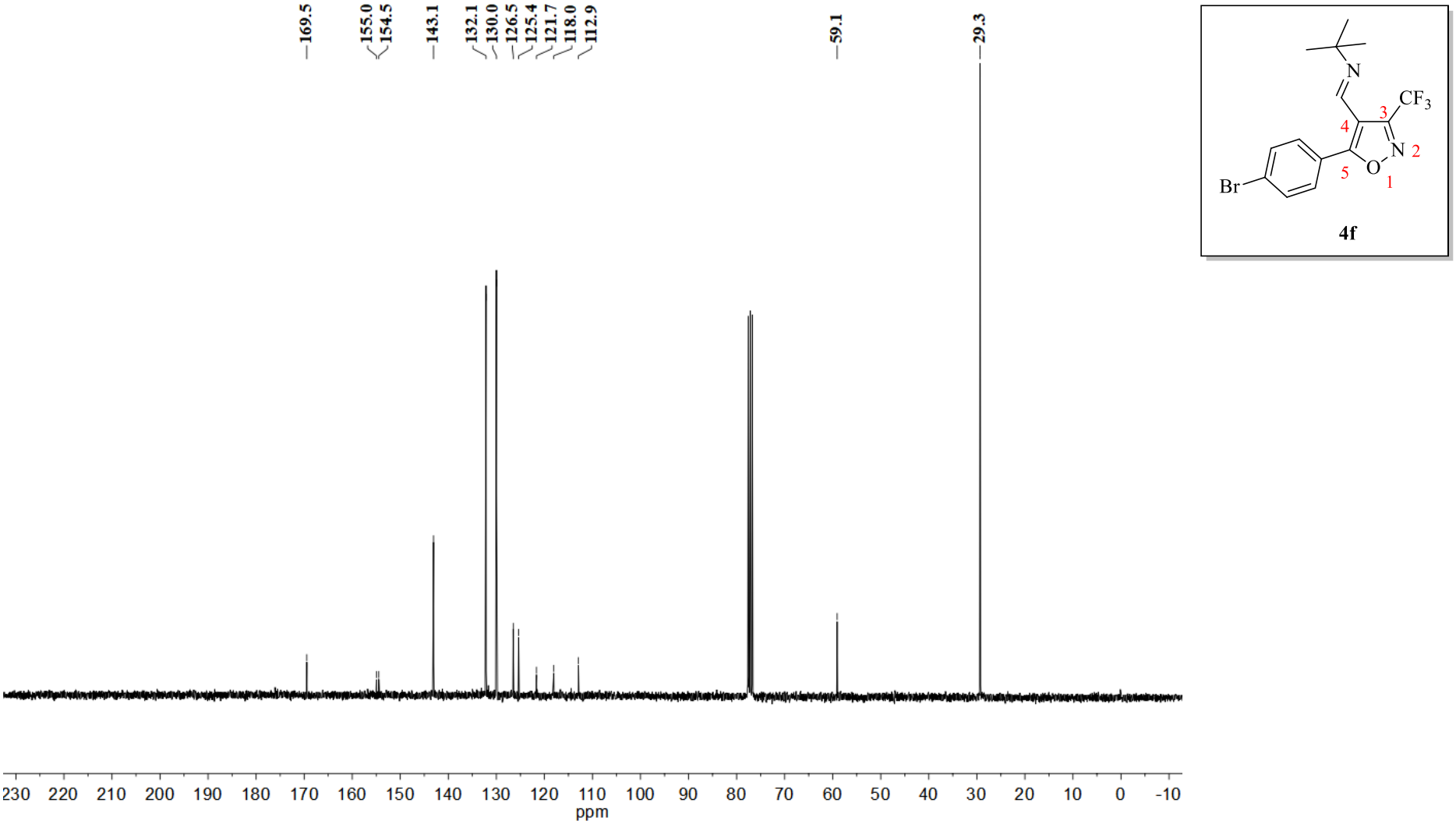


Figure S39 – ^{13}C NMR spectrum of compound **4f** in $CDCl_3$ at 75.45 MHz.

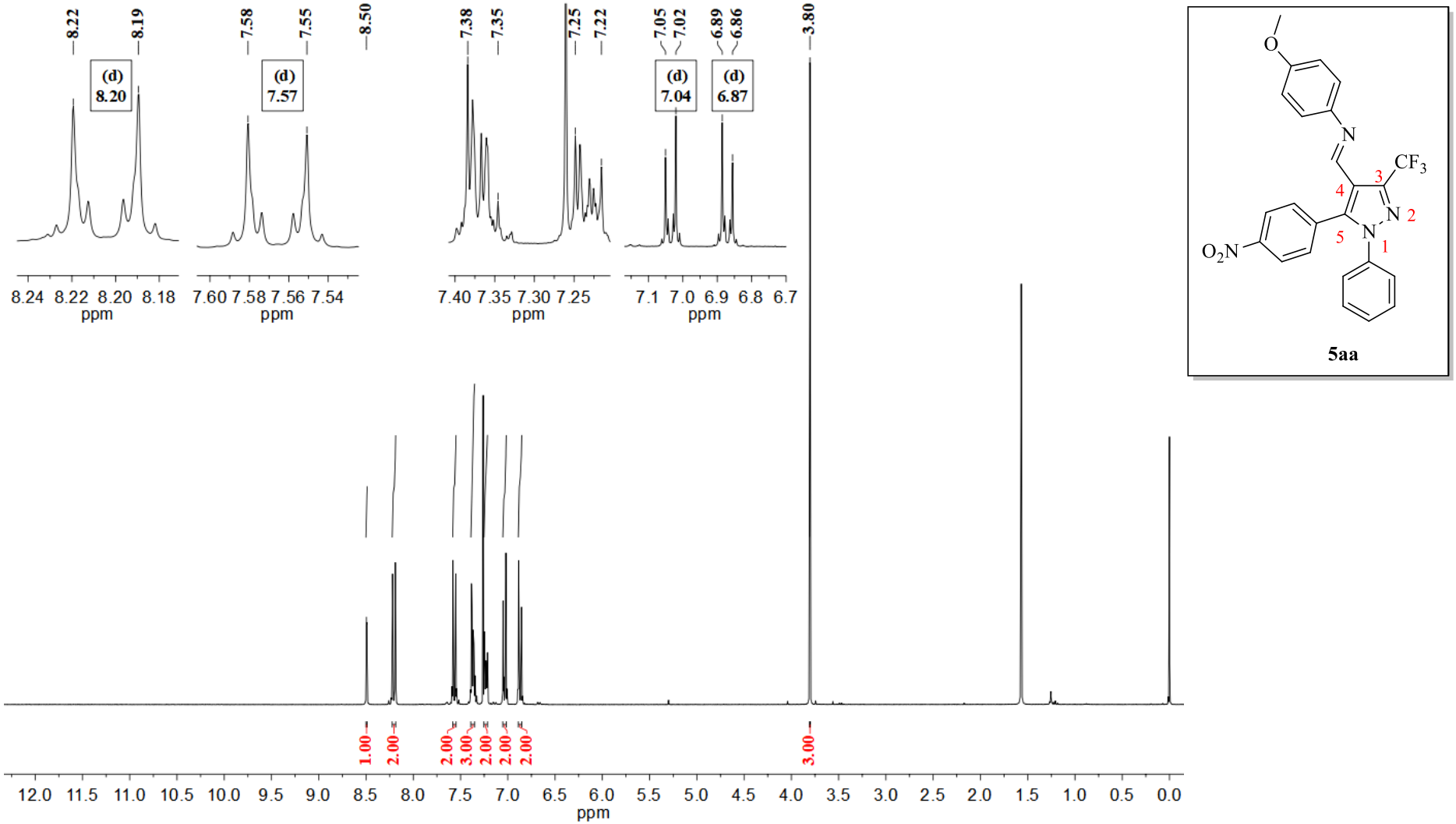
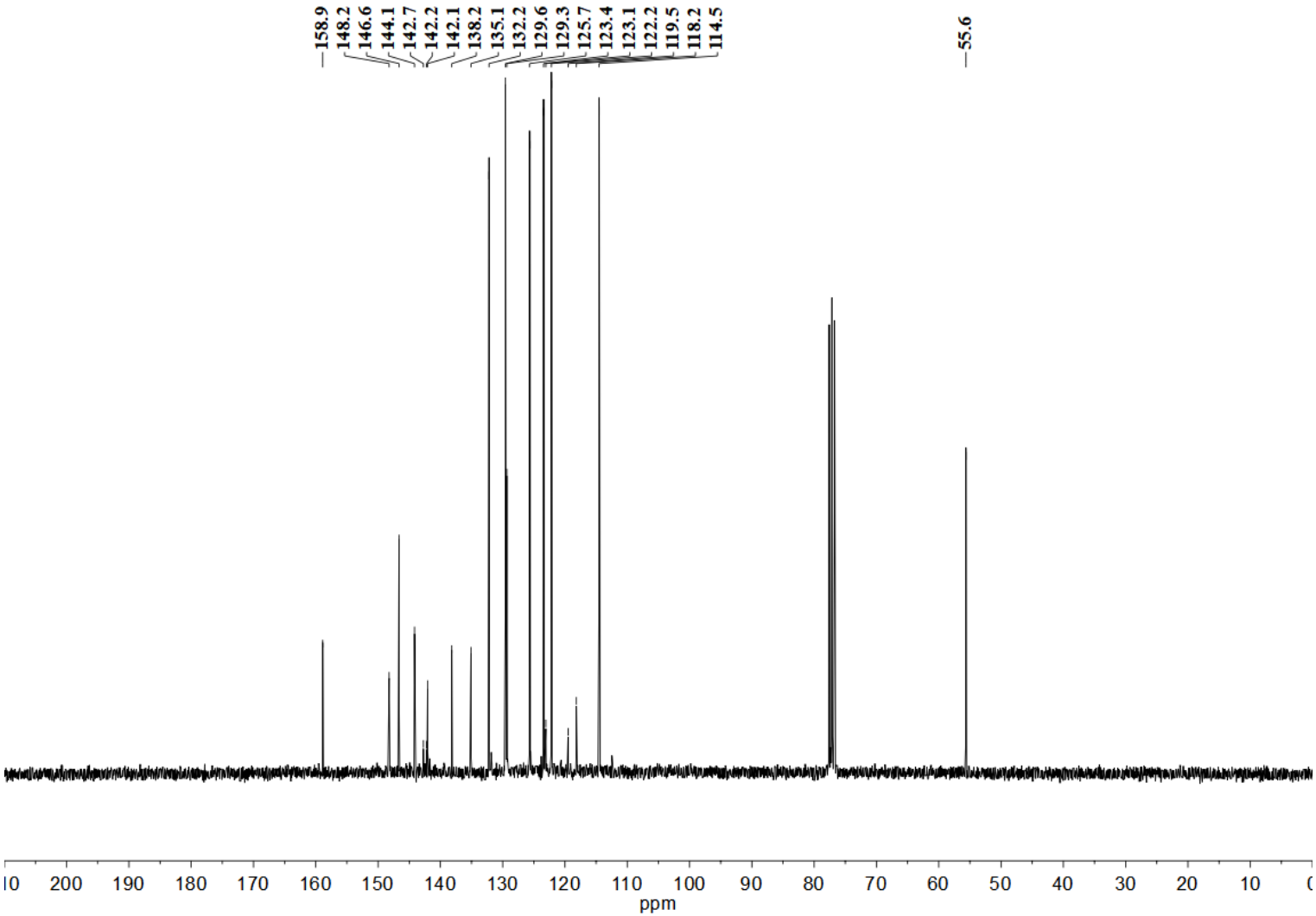
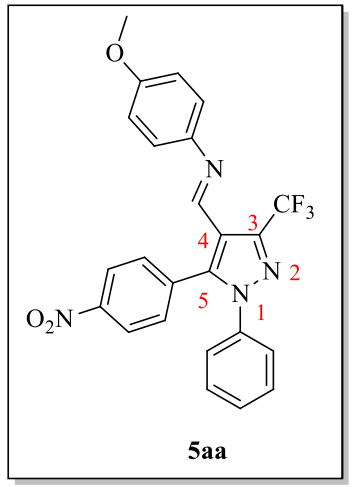


Figure S40 – ^{1}H NMR spectrum of compound **5aa** in $CDCl_3$ at 300.06 MHz.





5aa

Figure S41 – ^{13}C NMR spectrum of compound **5aa** in $CDCl_3$ at 75.45 MHz.

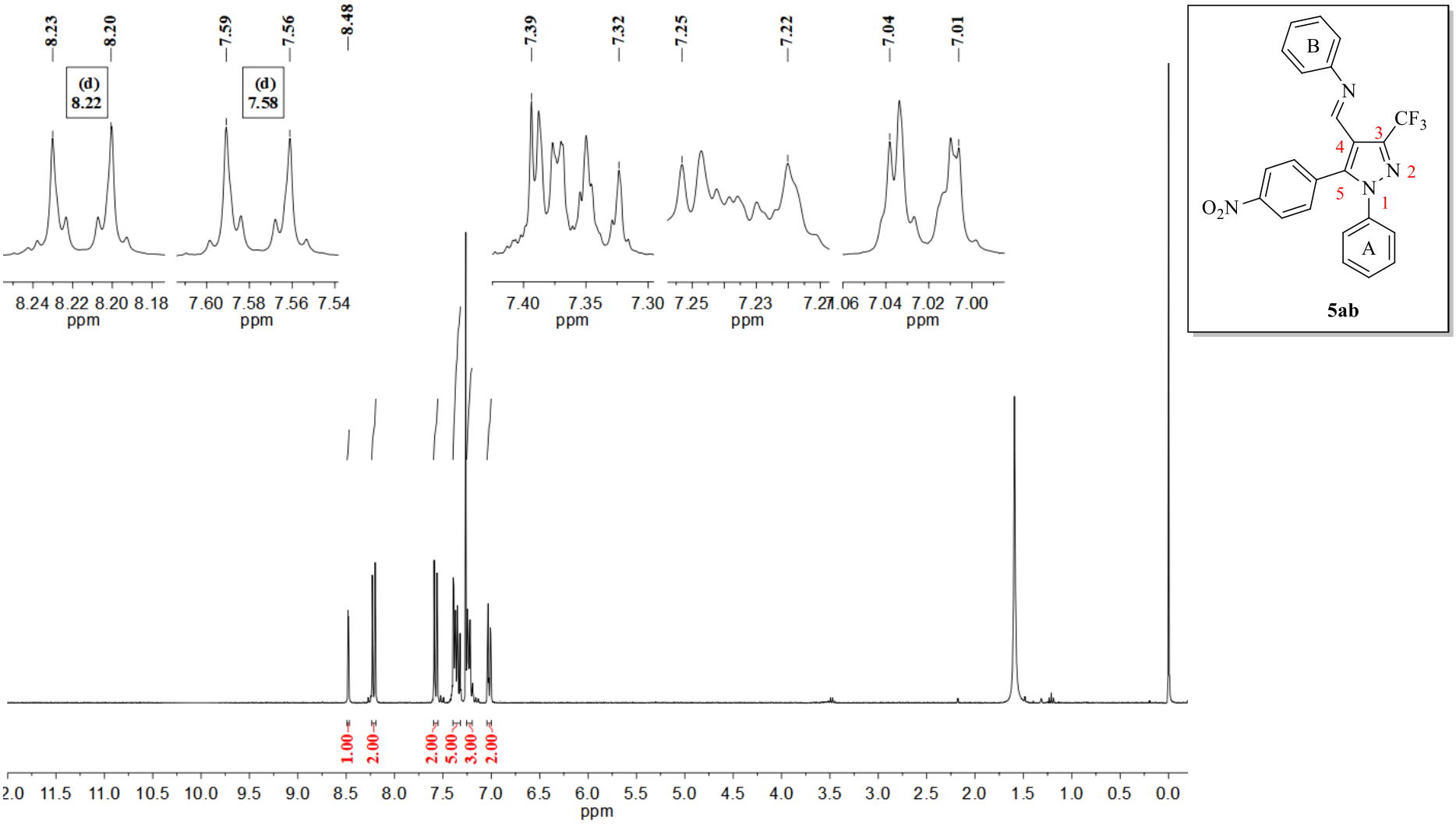
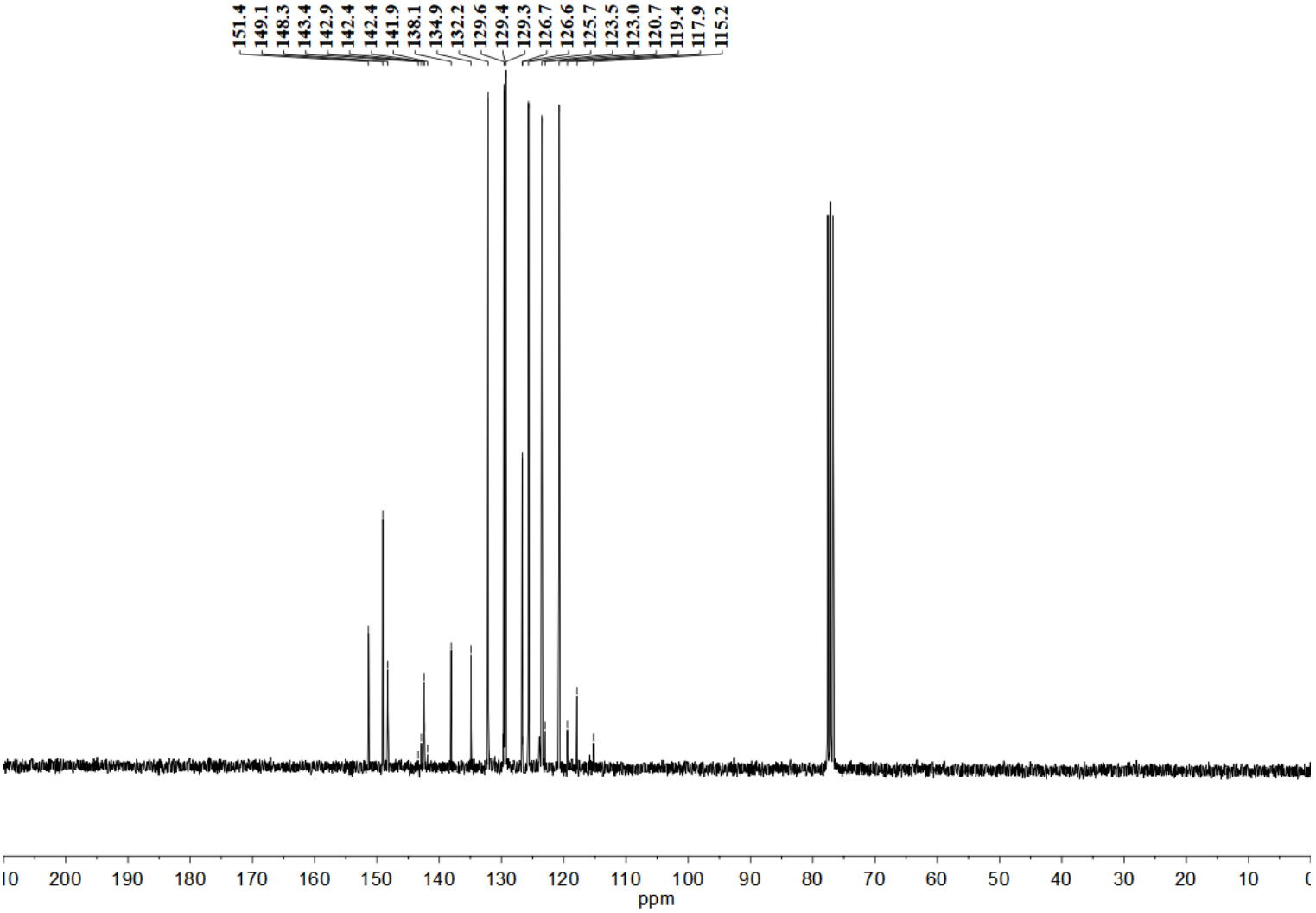


Figure S42 – ^{1}H NMR spectrum of compound **5ab** in $CDCl_3$ at 300.06 MHz.



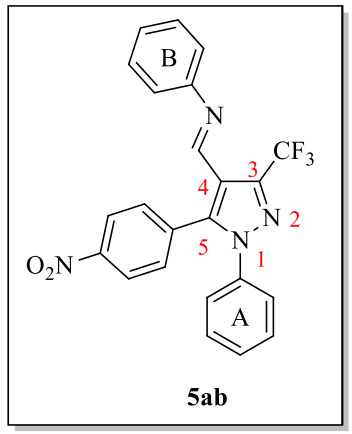


Figure S43 – ^{13}C NMR spectrum of compound **5ab** in $CDCl_3$ at 75.45 MHz.

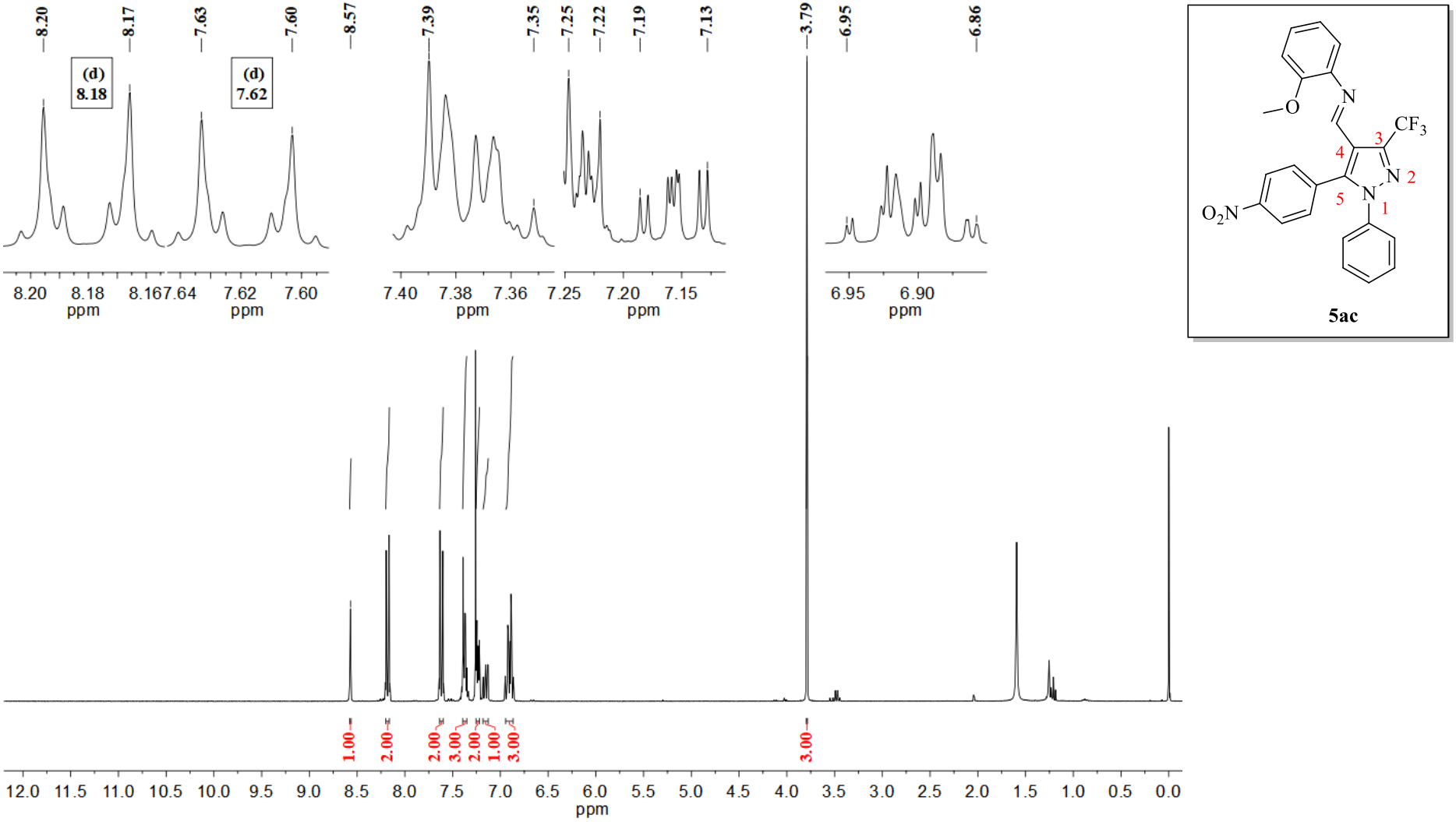
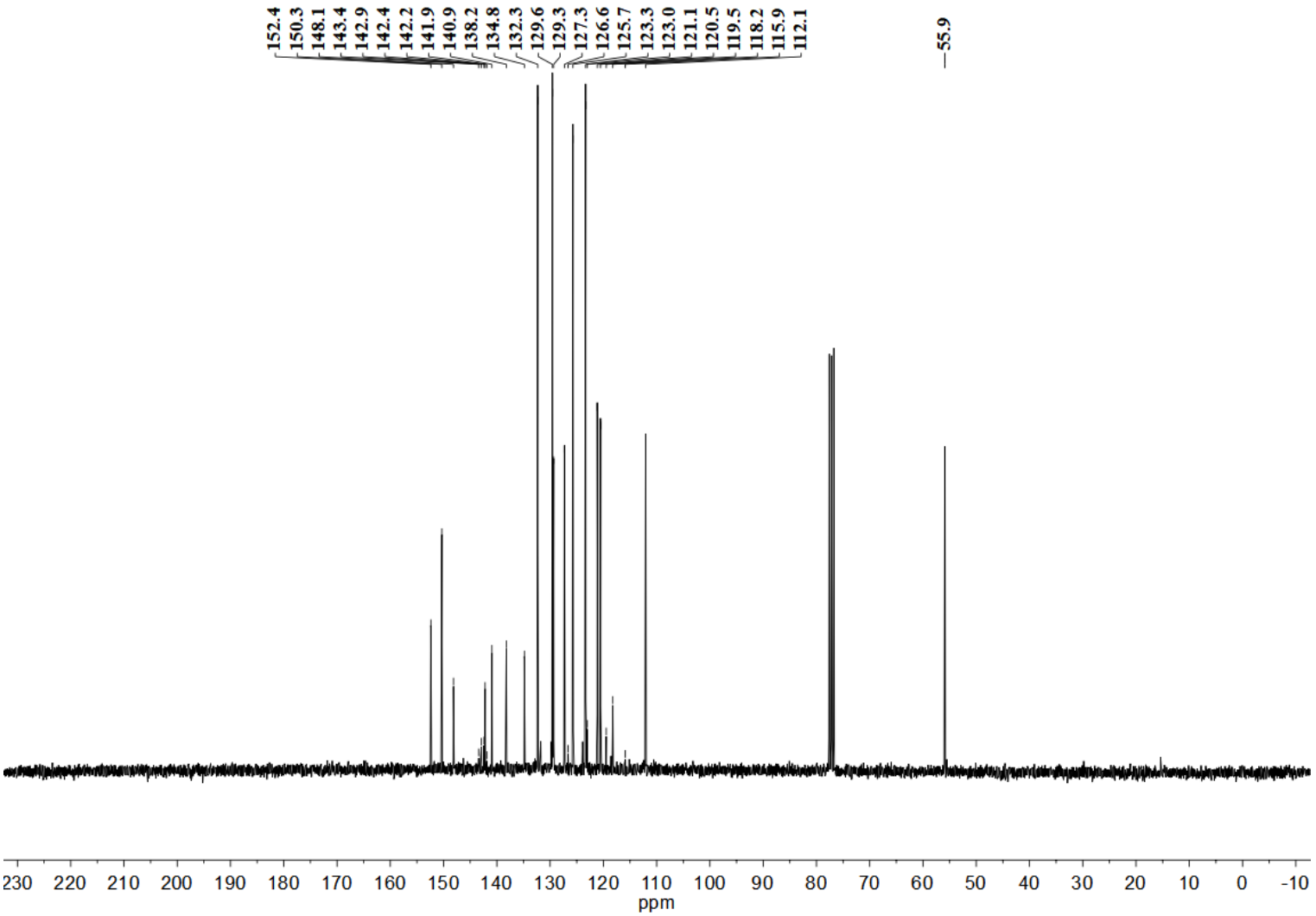
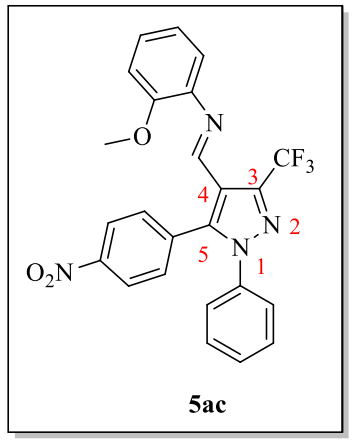


Figure S44 – ^{1}H NMR spectrum of compound **5ac** in $CDCl_3$ at 300.06 MHz.





5ac

Figure S45 – ^{13}C NMR spectrum of compound **5ac** in $CDCl_3$ at 75.45 MHz.

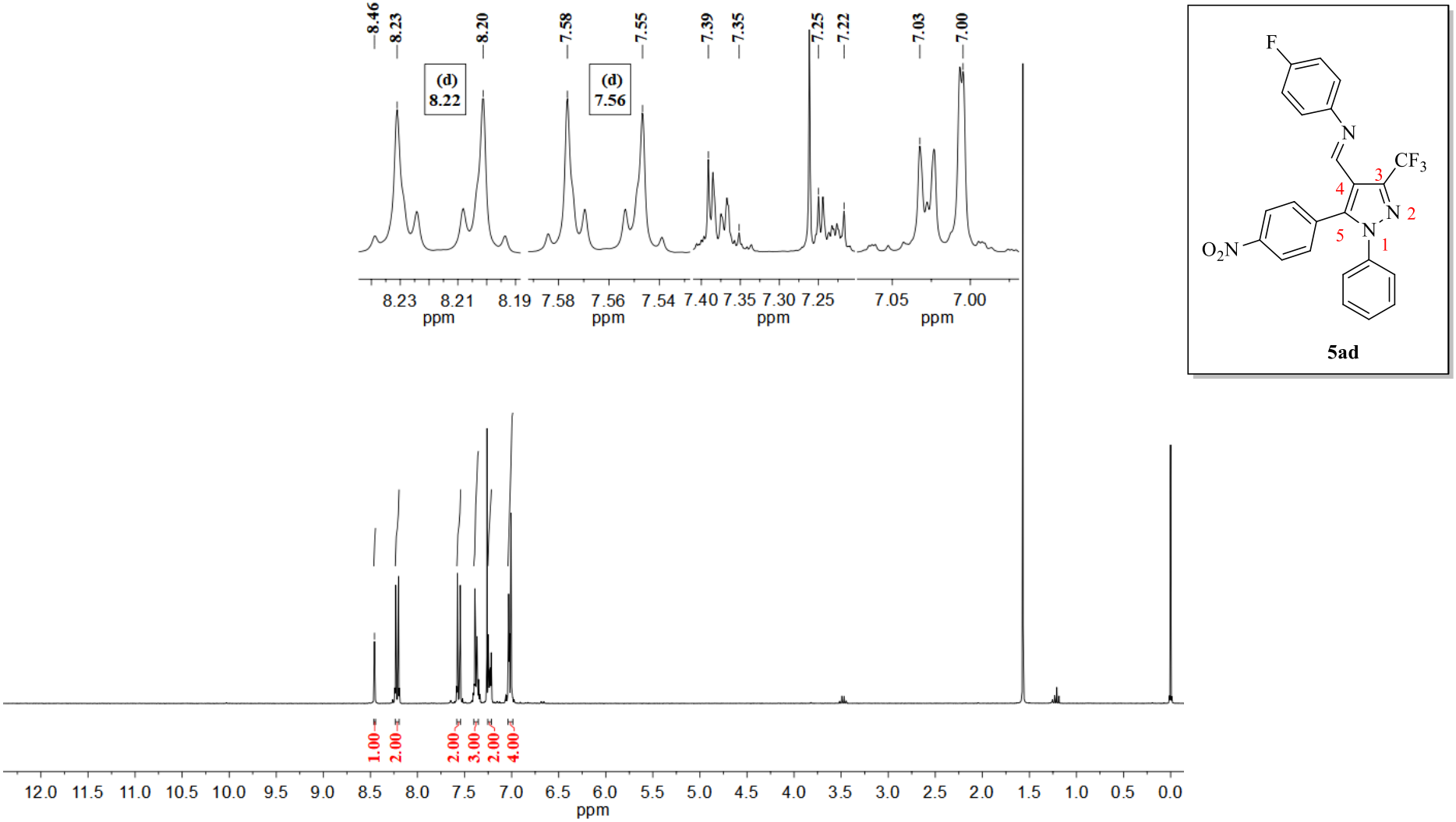


Figure S46 – ^{1}H NMR spectrum of compound **5ad** in $CDCl_3$ at 300.06 MHz.

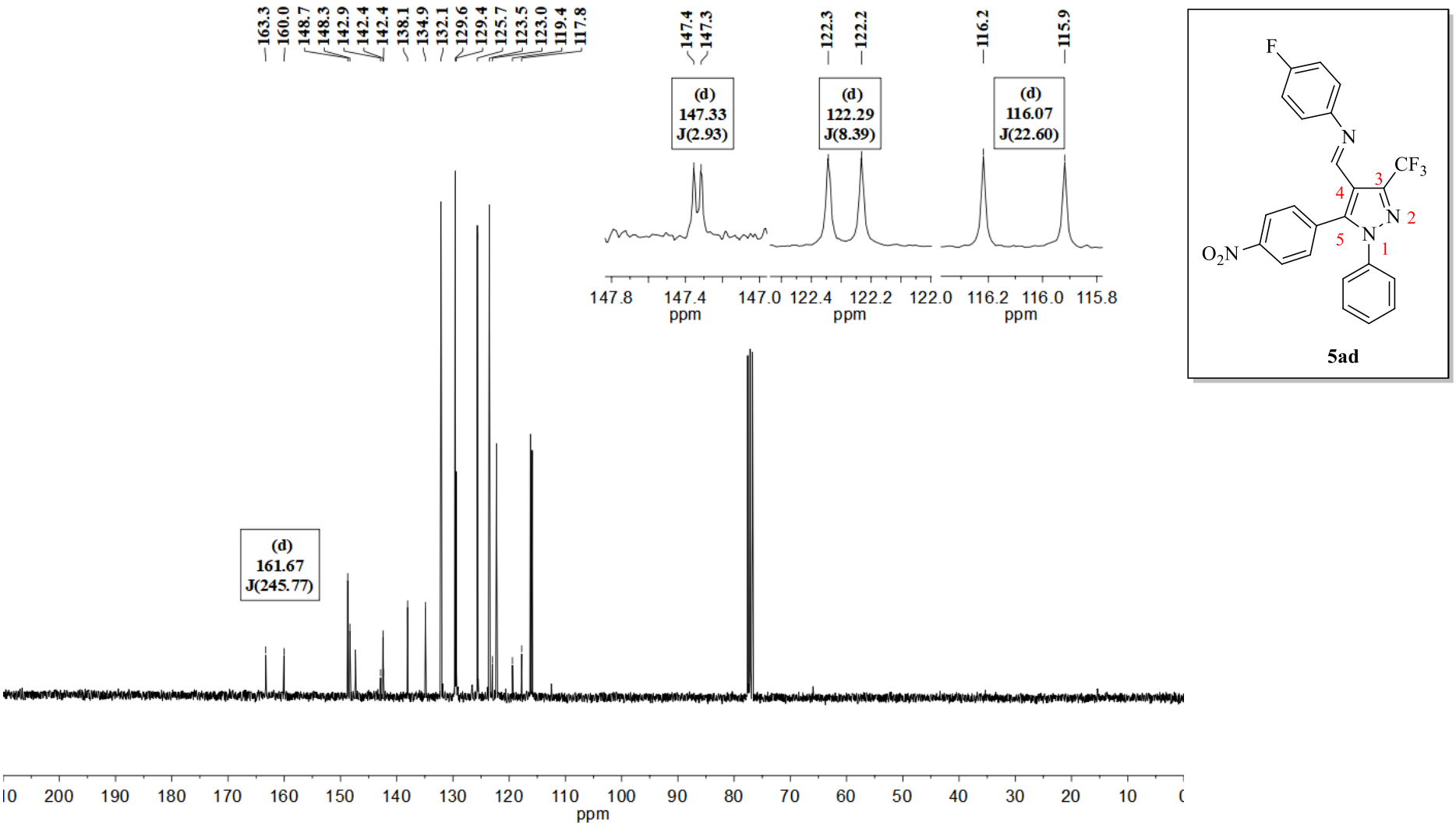


Figure S47 – ^{13}C NMR spectrum of compound **5ad** in $CDCl_3$ at 75.45 MHz.

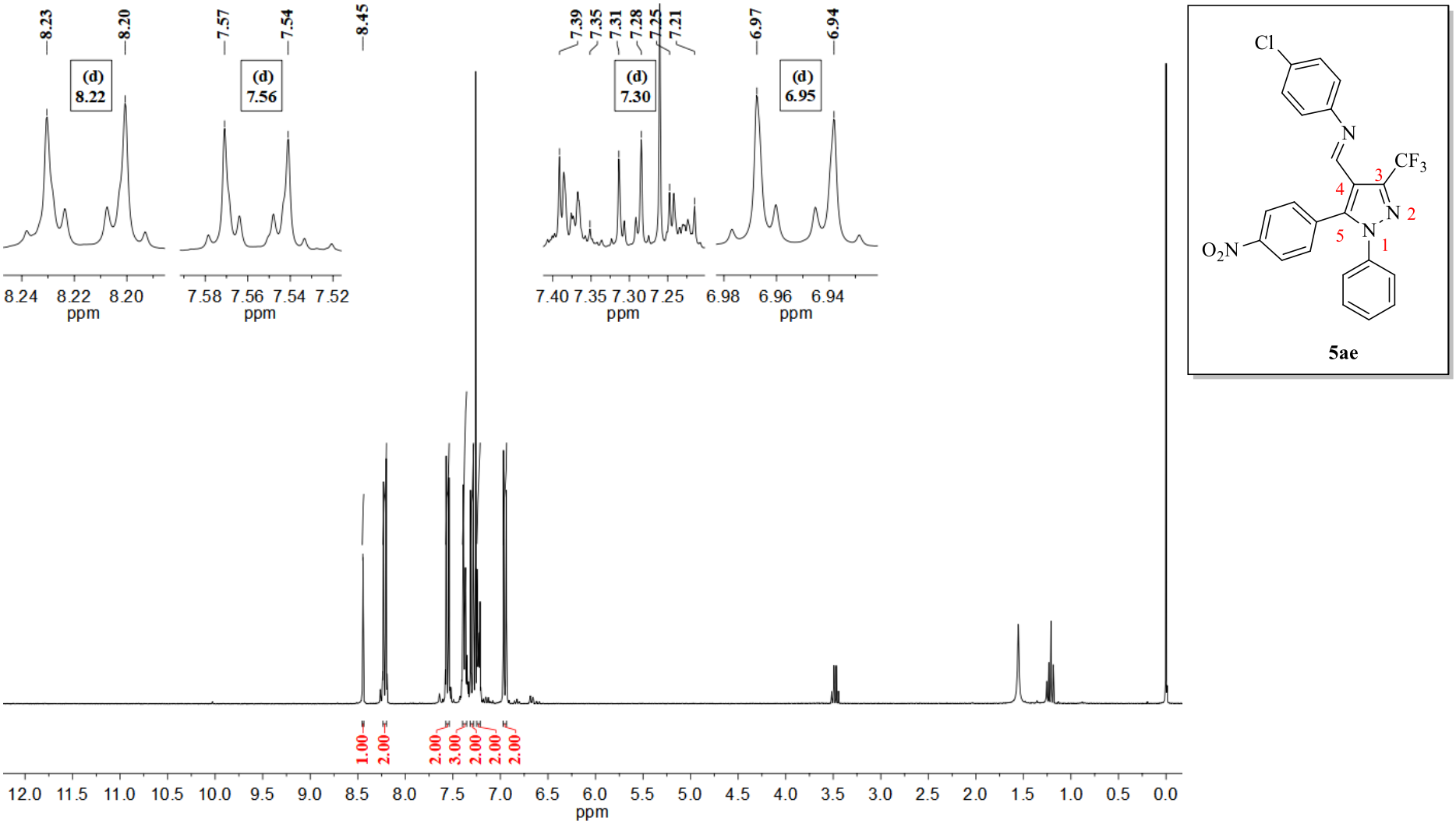
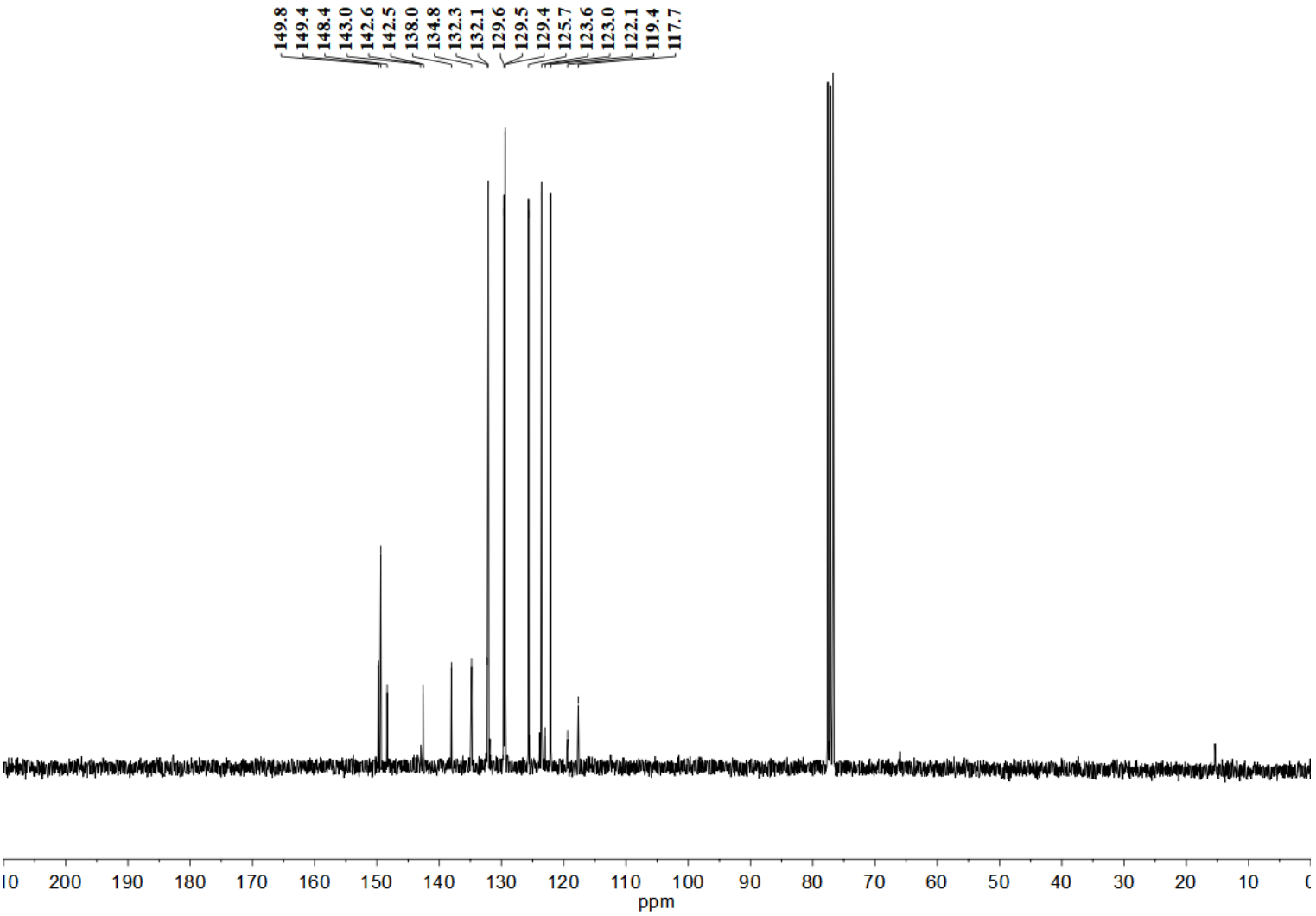
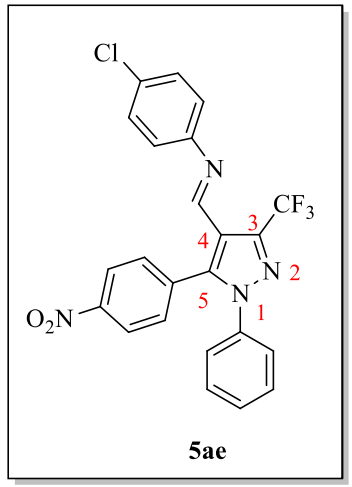


Figure S48 – ^{1}H NMR spectrum of compound **5ae** in $CDCl_3$ at 300.06 MHz.





5ae

Figure S49 – ^{13}C NMR spectrum of compound **5ae** in $CDCl_3$ at 75.45 MHz.

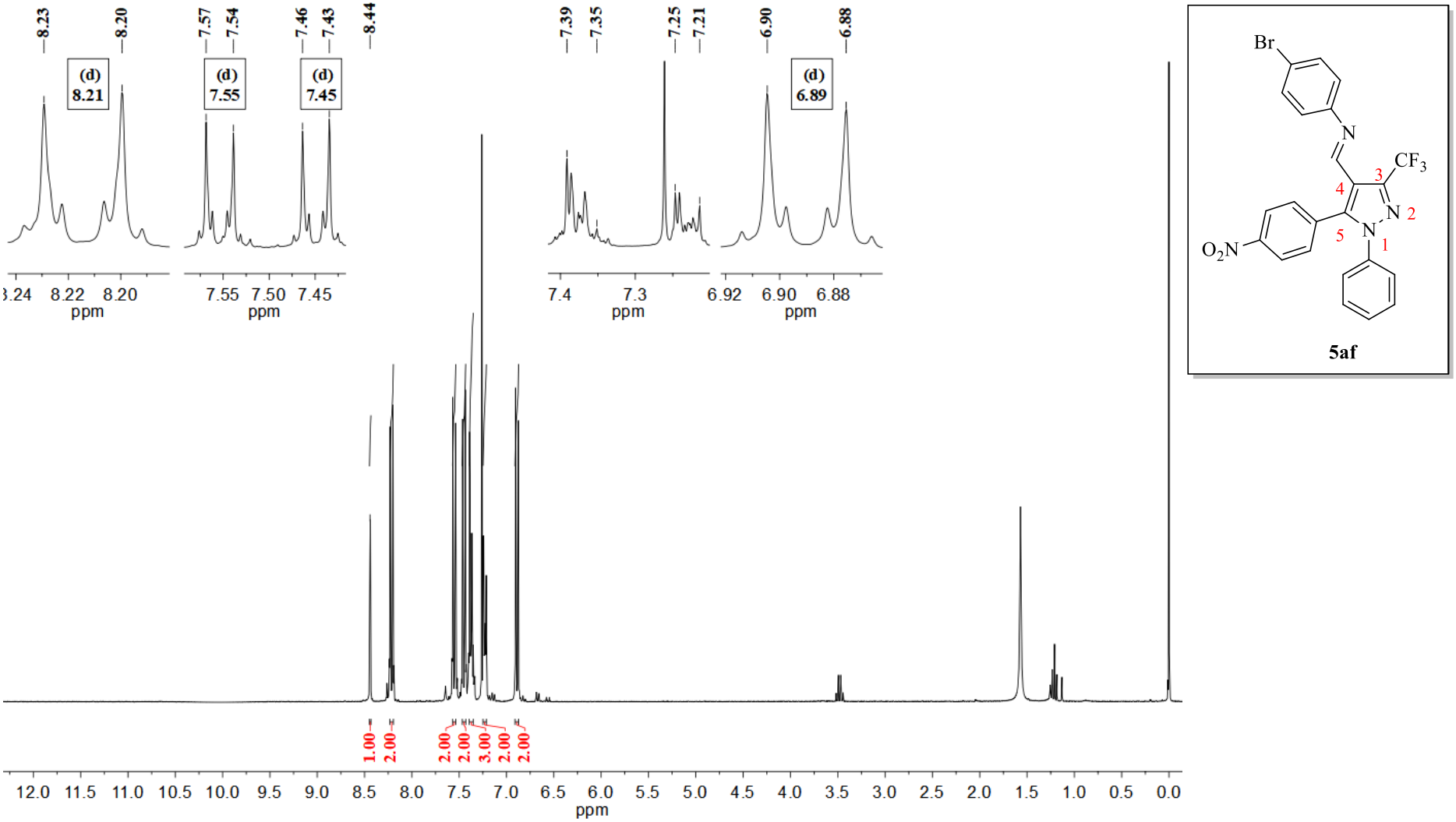
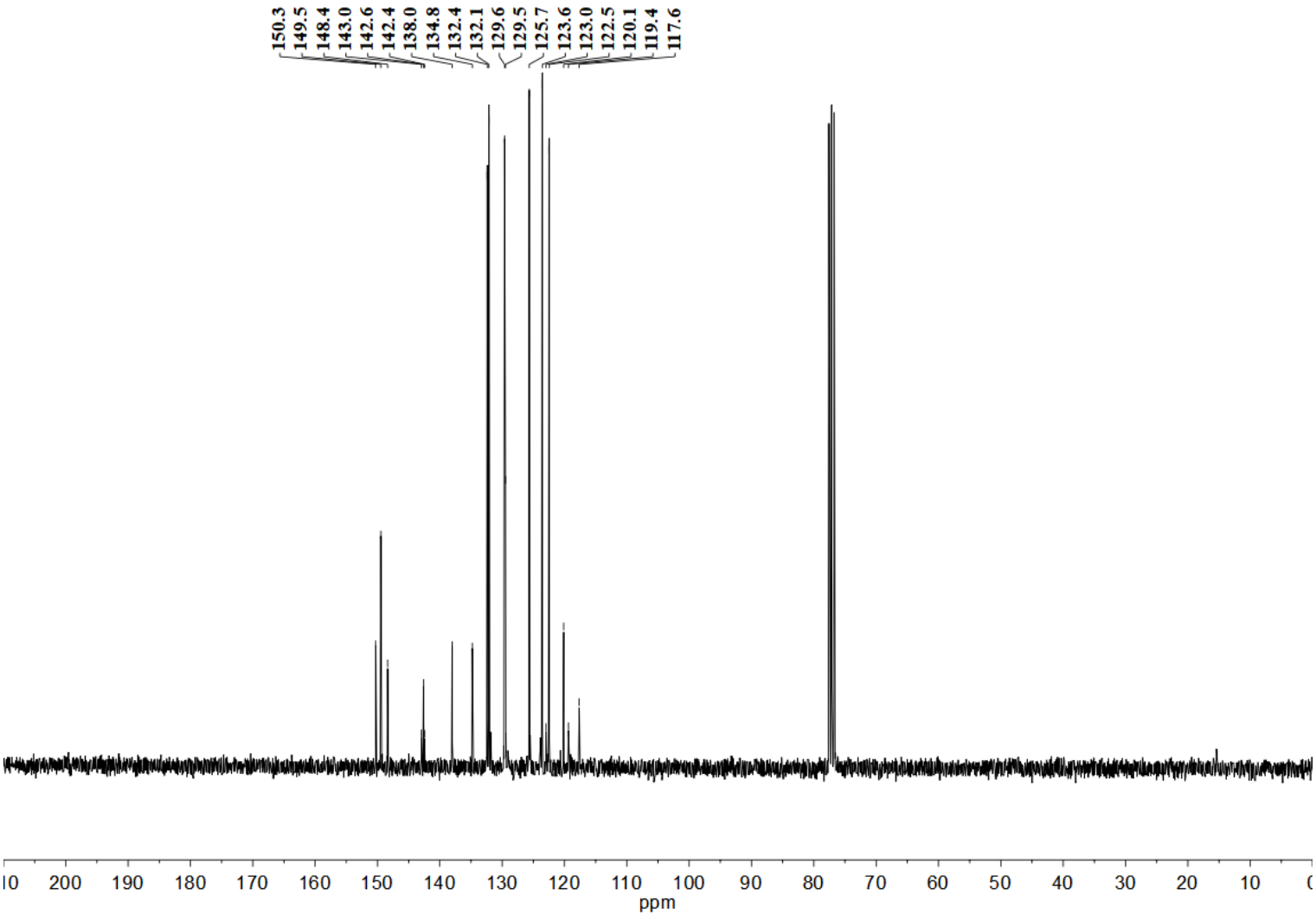


Figure S50 – ^{1}H NMR spectrum of compound **5af** in $CDCl_3$ at 300.06 MHz.



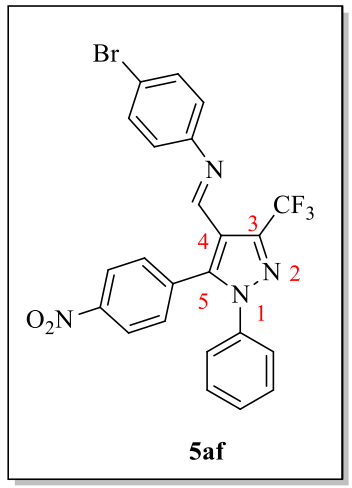
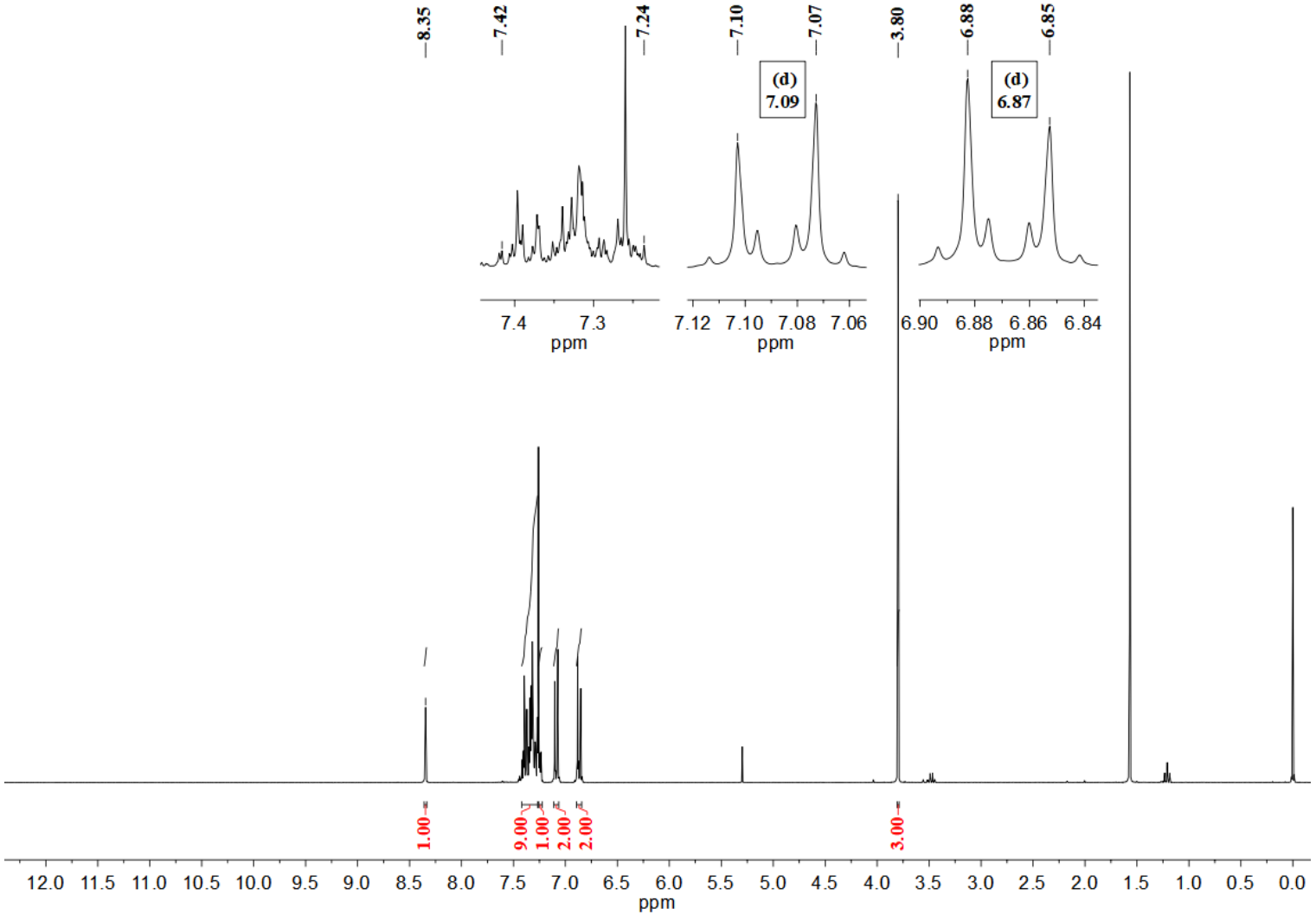


Figure S51 – ^{13}C NMR spectrum of compound **5af** in $CDCl_3$ at 75.45 MHz.



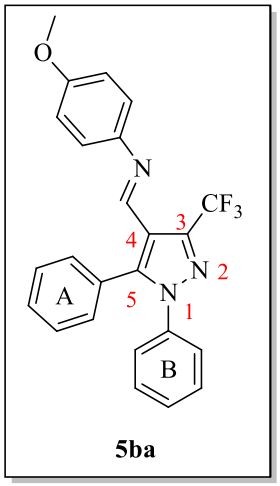
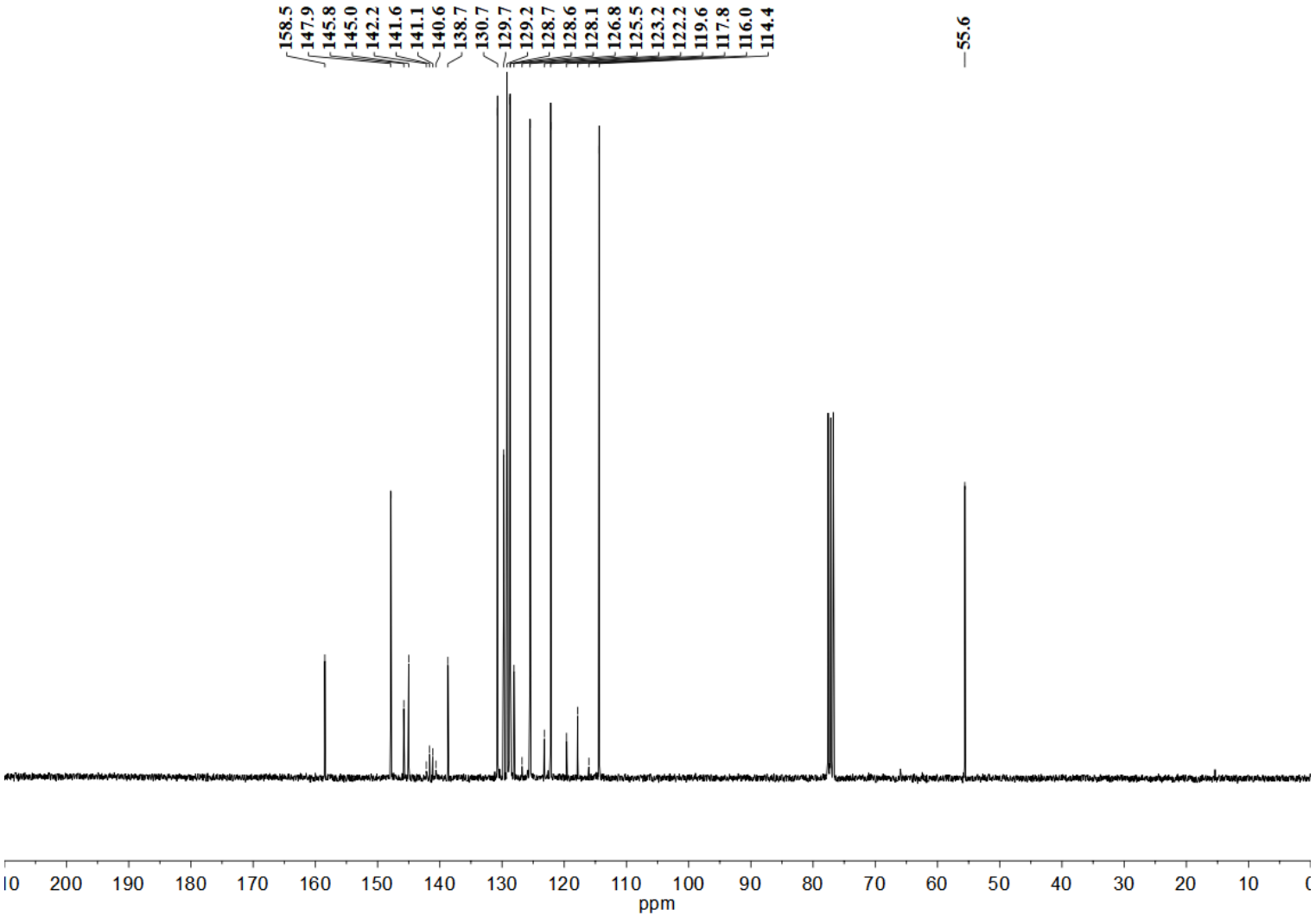
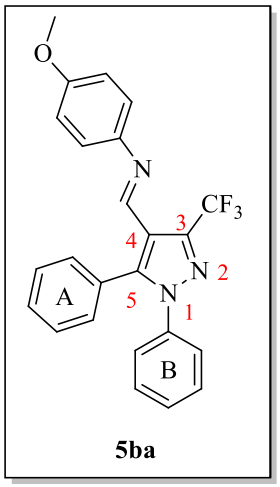


Figure S52 – ^{1}H NMR spectrum of compound **5ba** in $CDCl_3$ at 300.06 MHz.





5ba

Figure S53 – ^{13}C NMR spectrum of compound **5ba** in $CDCl_3$ at 75.45 MHz.

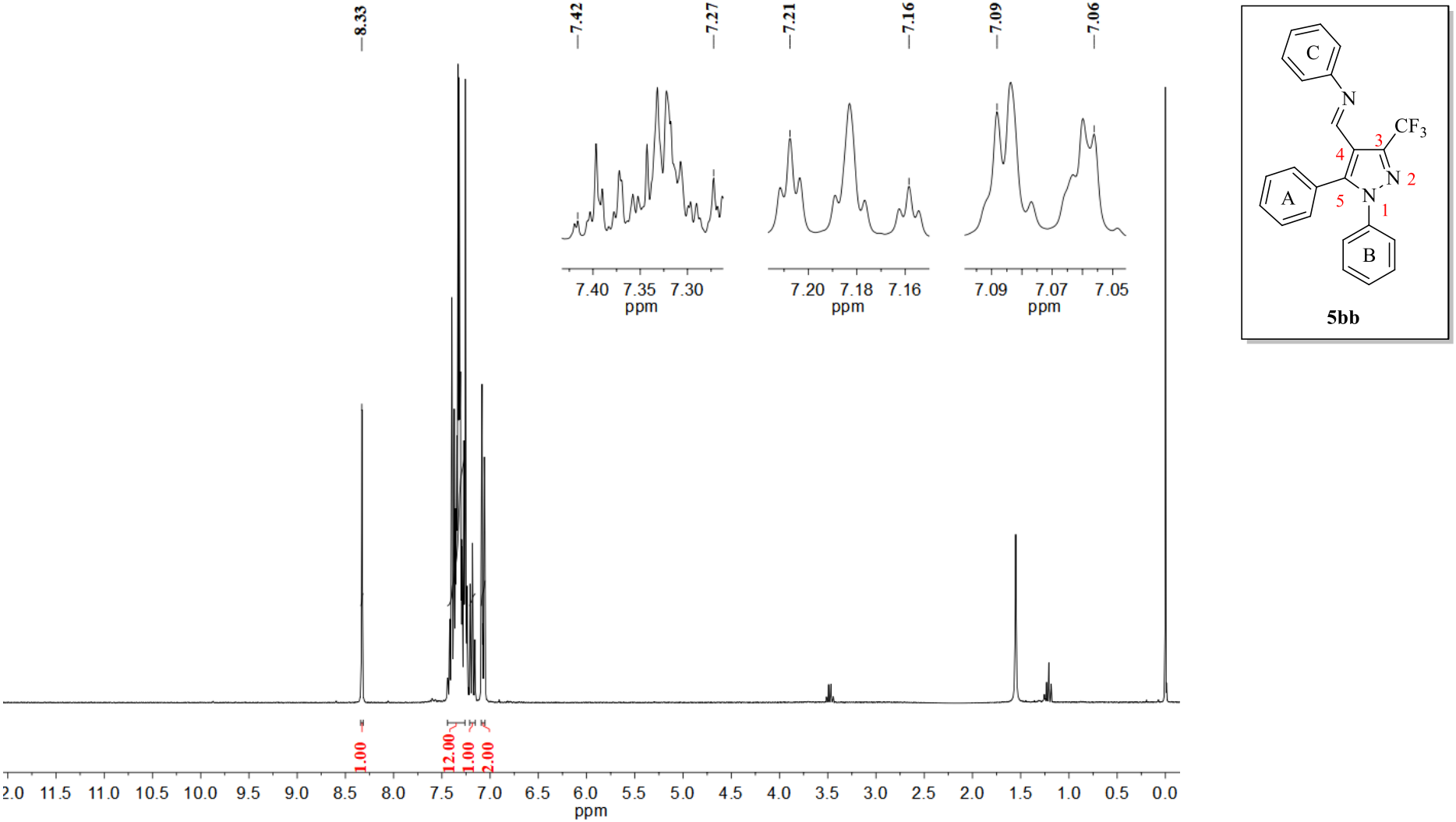
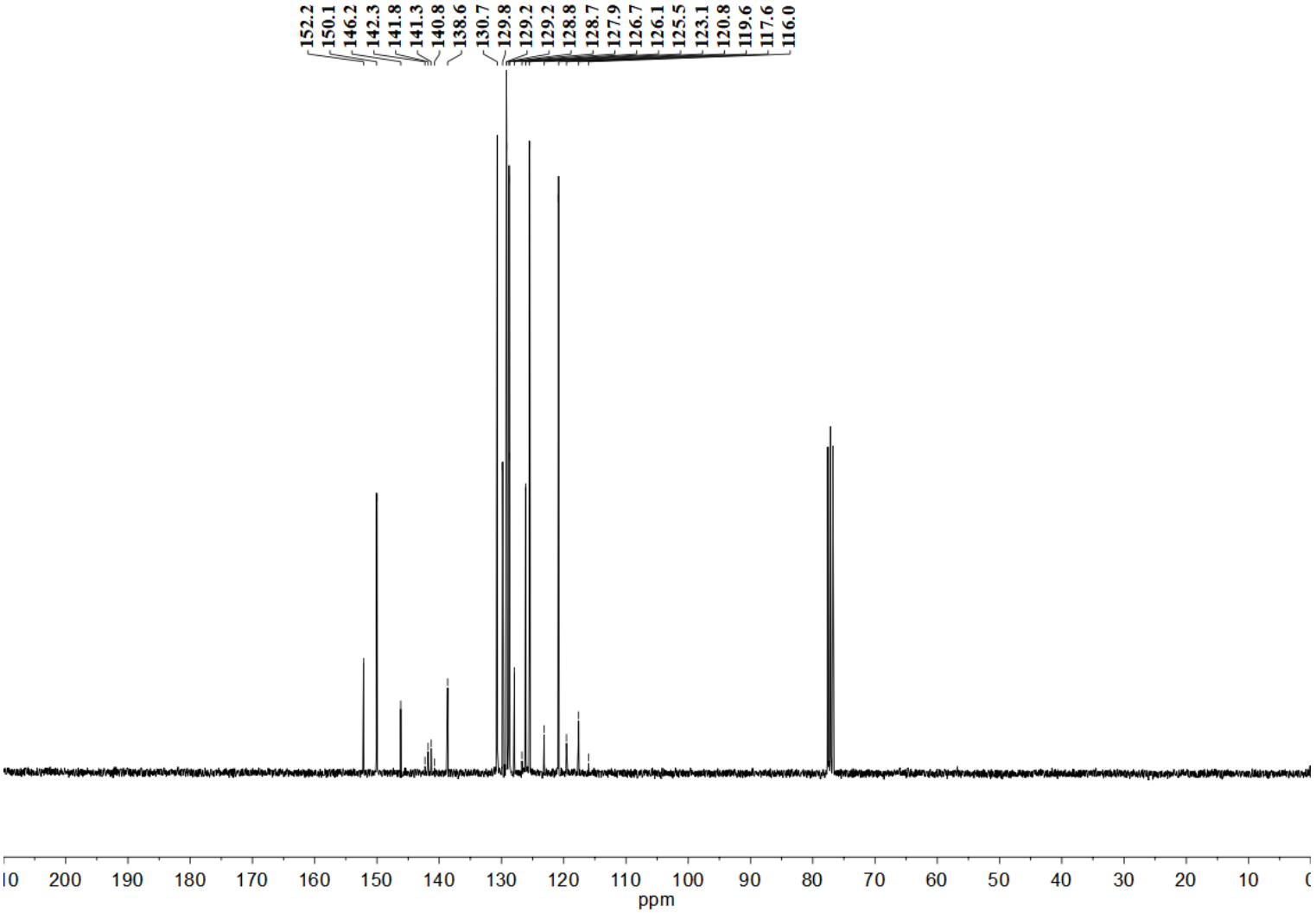
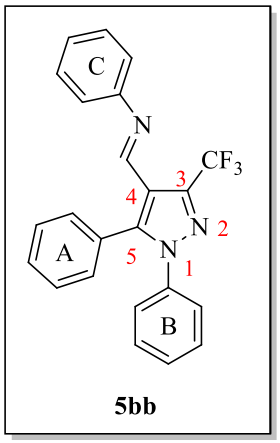


Figure S54 – ^{1}H NMR spectrum of compound **5bb** in $CDCl_3$ at 300.06 MHz.





5bb

Figure S55 – ^{13}C NMR spectrum of compound **5bb** in $CDCl_3$ at 75.45 MHz.

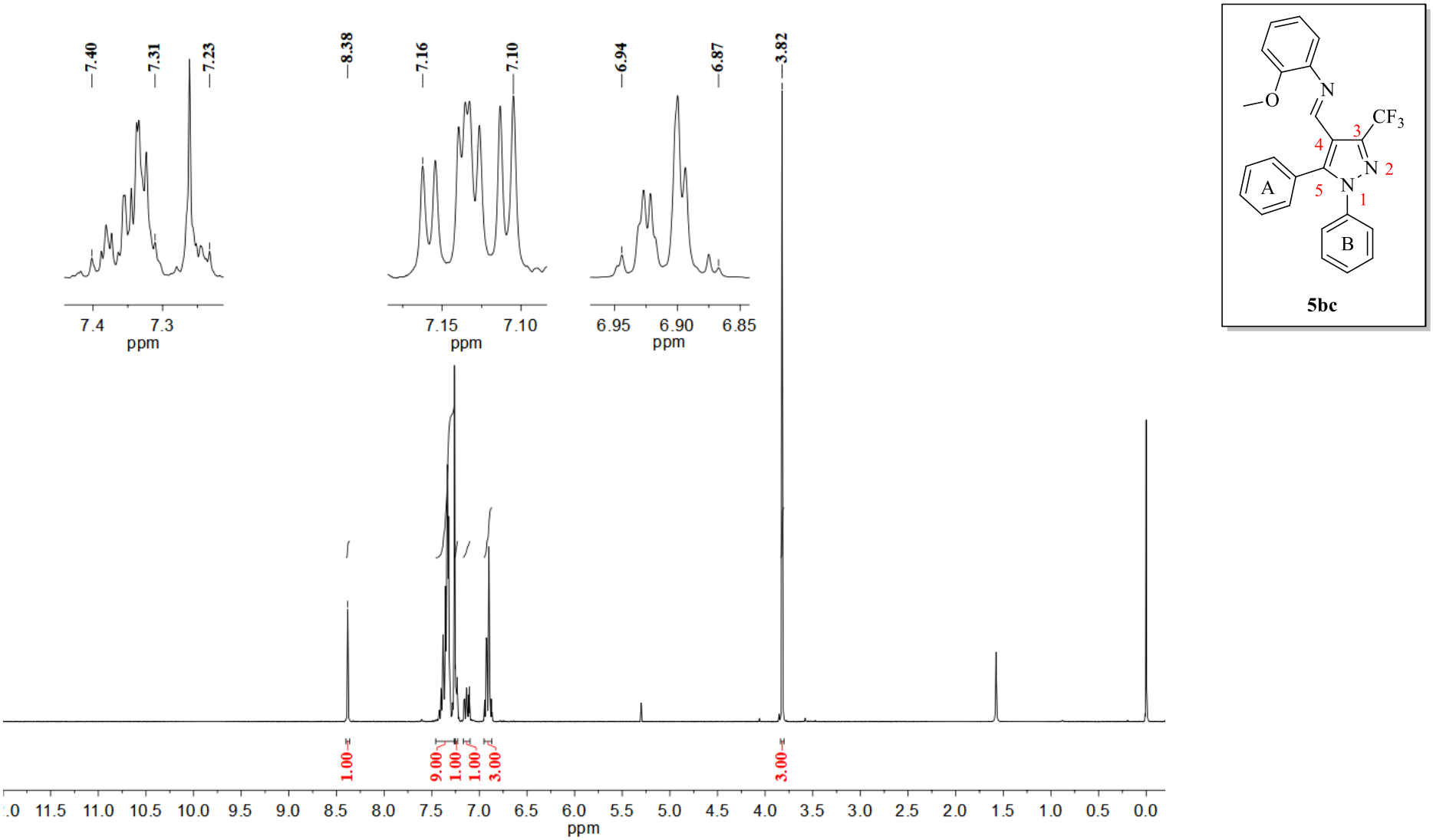
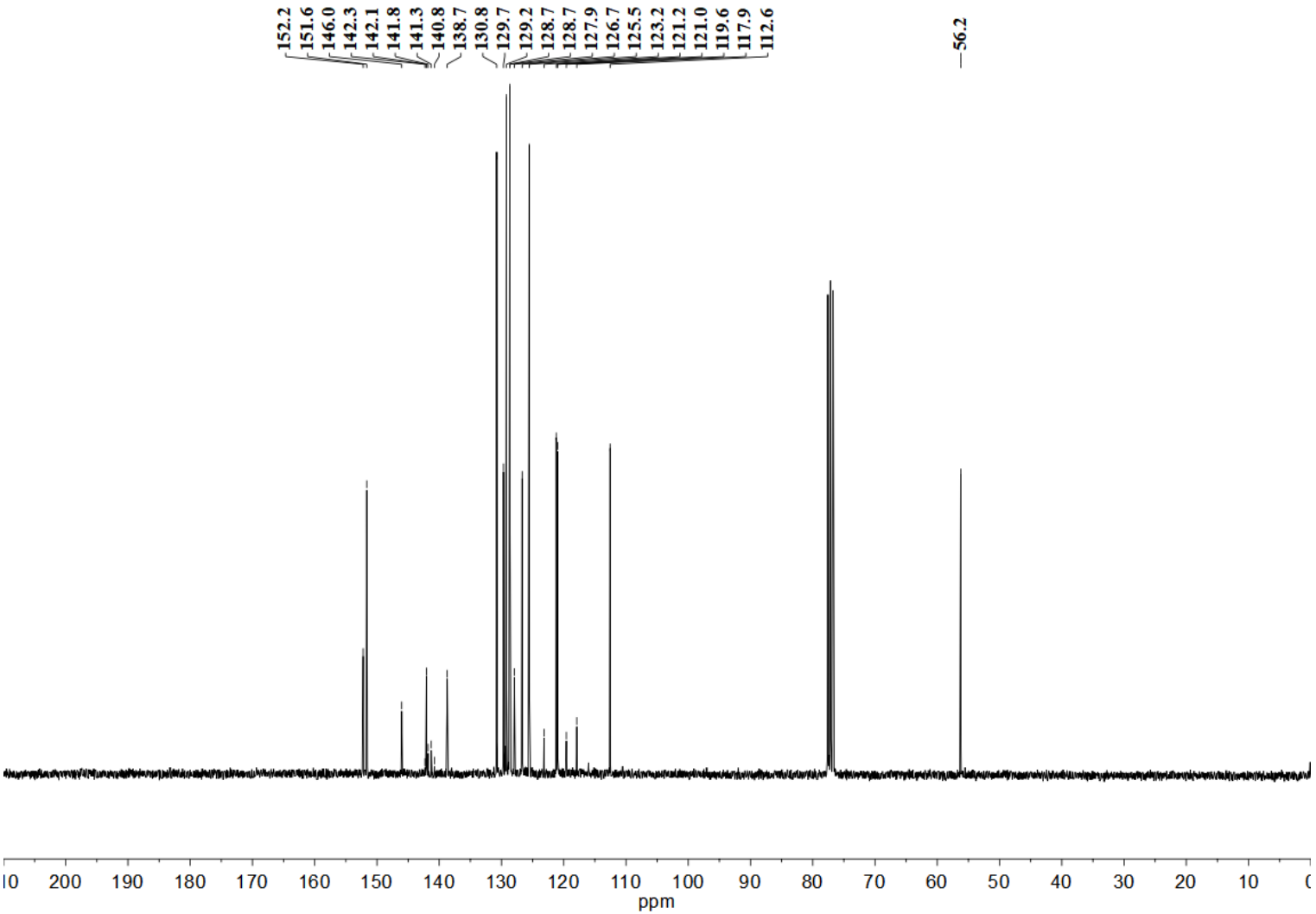
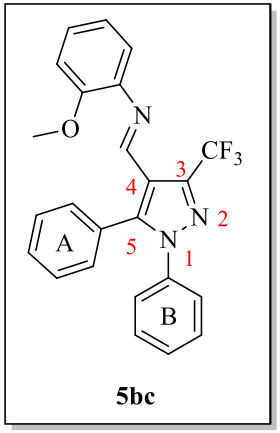


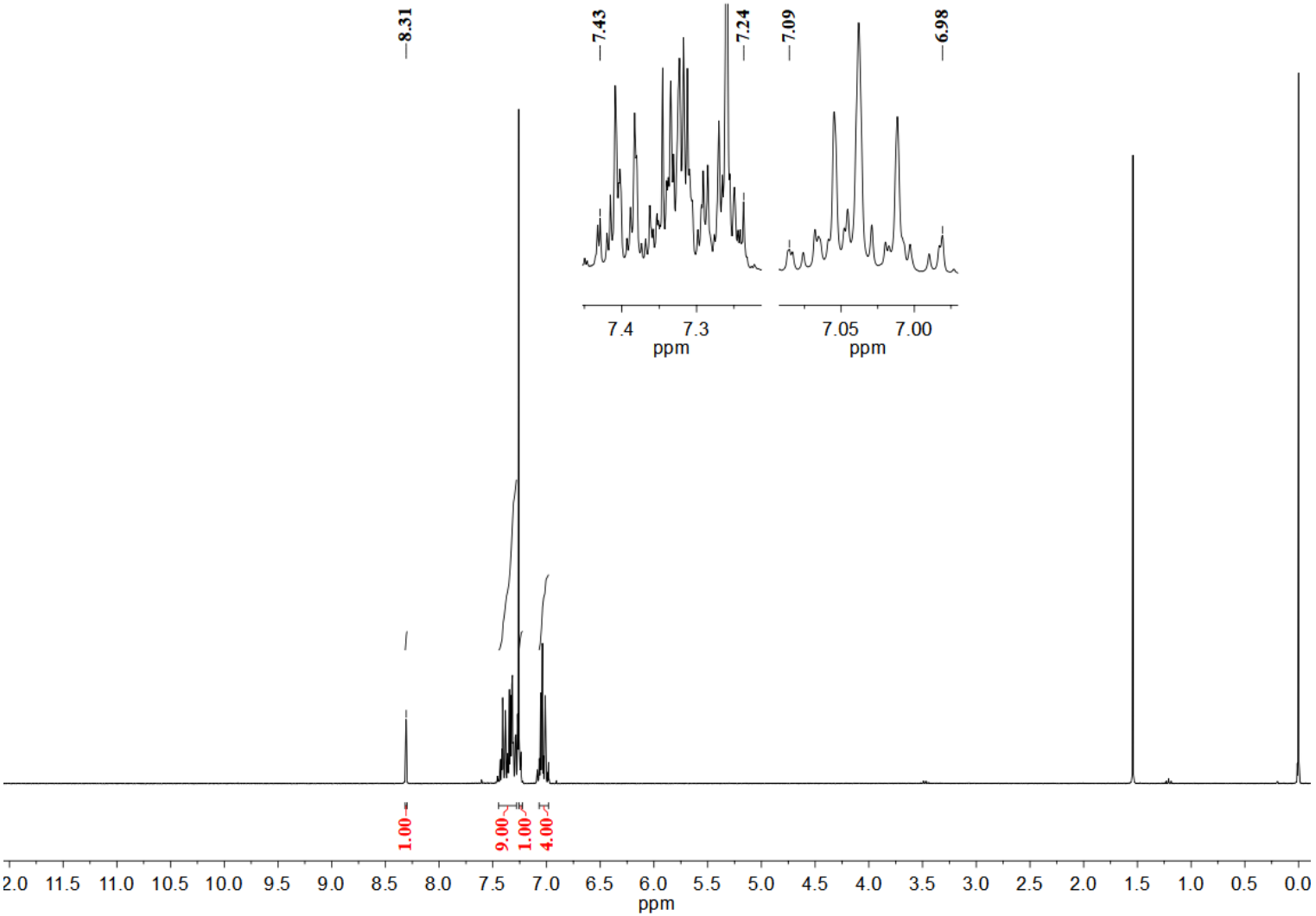
Figure S56 – ^{1}H NMR spectrum of compound **5bc** in $CDCl_3$ at 300.06 MHz.

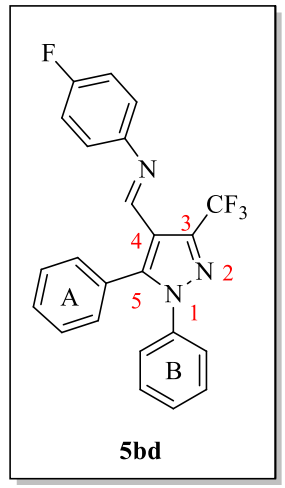




5bc

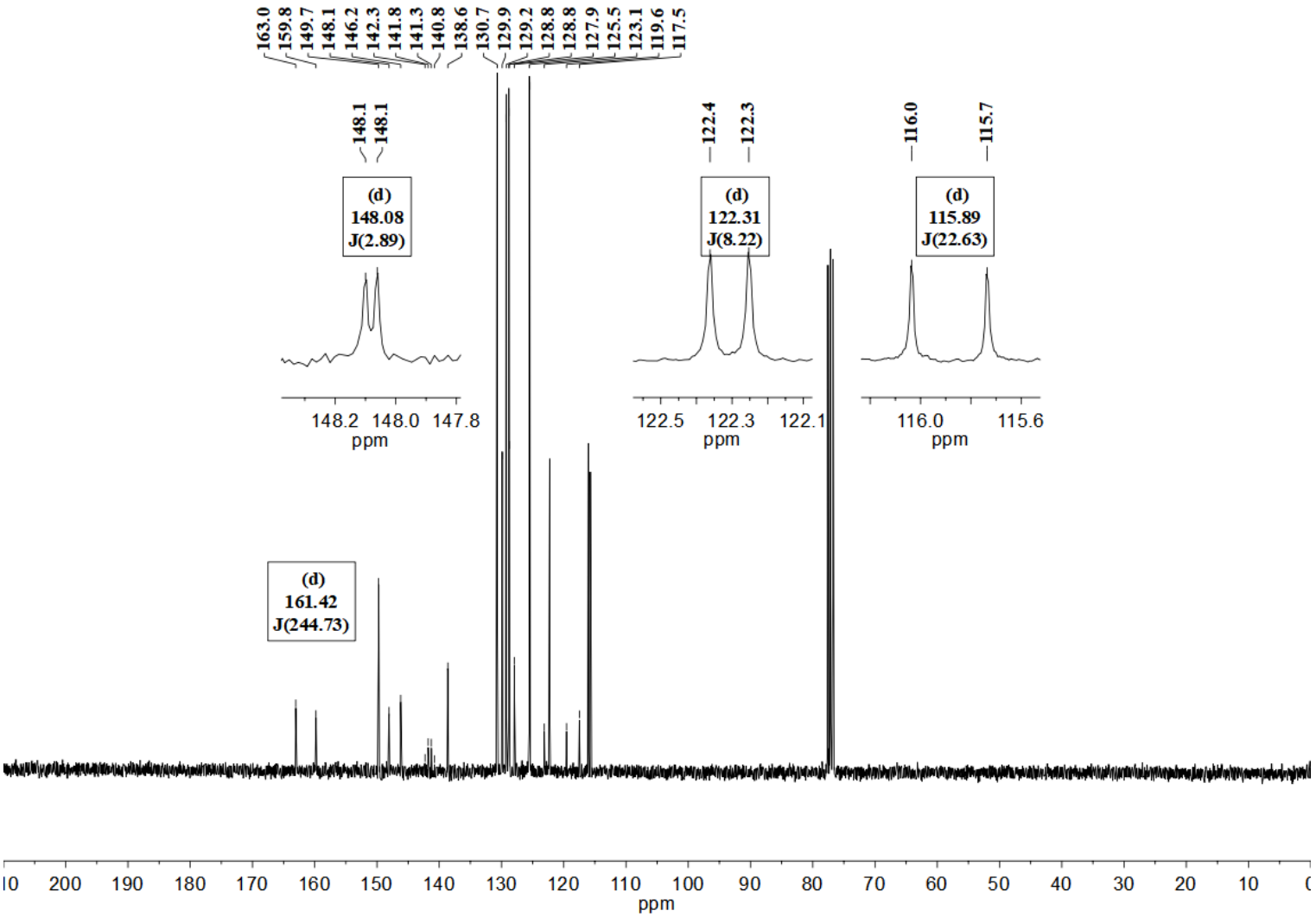
Figure S57 – ^{13}C NMR spectrum of compound **5bc** in $CDCl_3$ at 75.45 MHz.





5bd

Figure S58 – ^{1}H NMR spectrum of compound **6d** in $CDCl_3$ at 300.06 MHz.



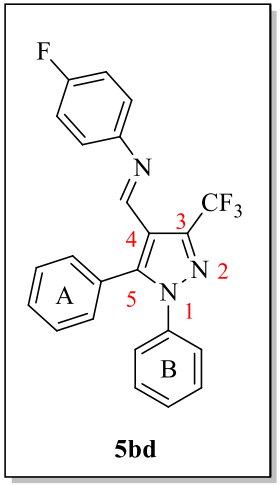


Figure S59 – ^{13}C NMR spectrum of compound **5bd** in $CDCl_3$ at 75.45 MHz.

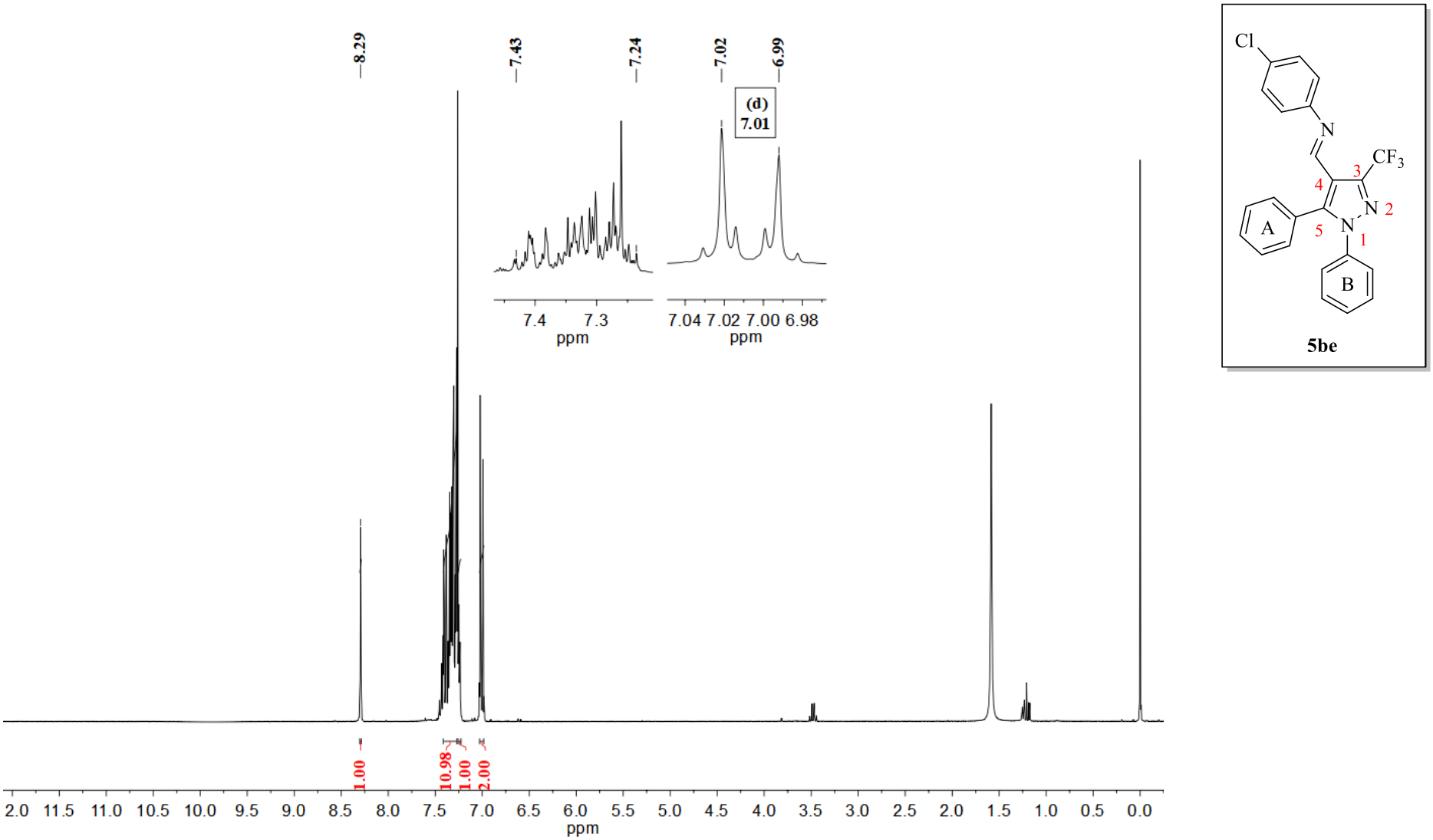
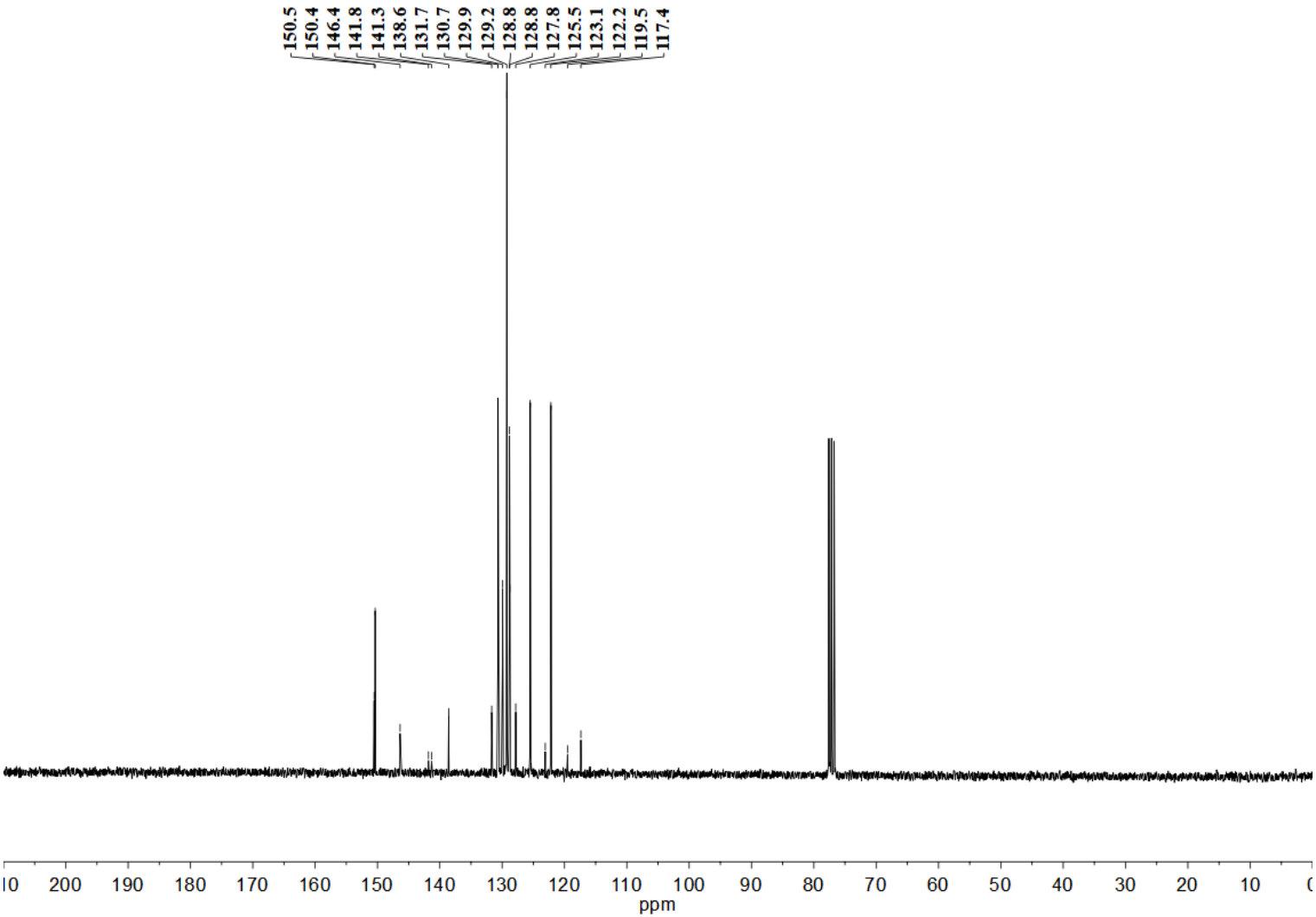


Figure S60 – ^{1}H NMR spectrum of compound **5be** in $CDCl_3$ at 300.06 MHz.



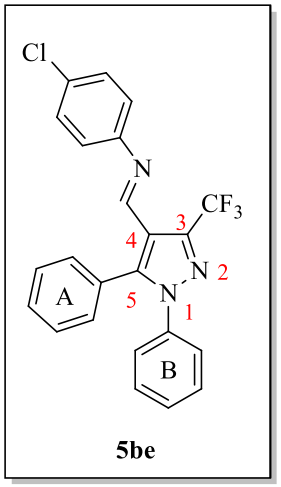
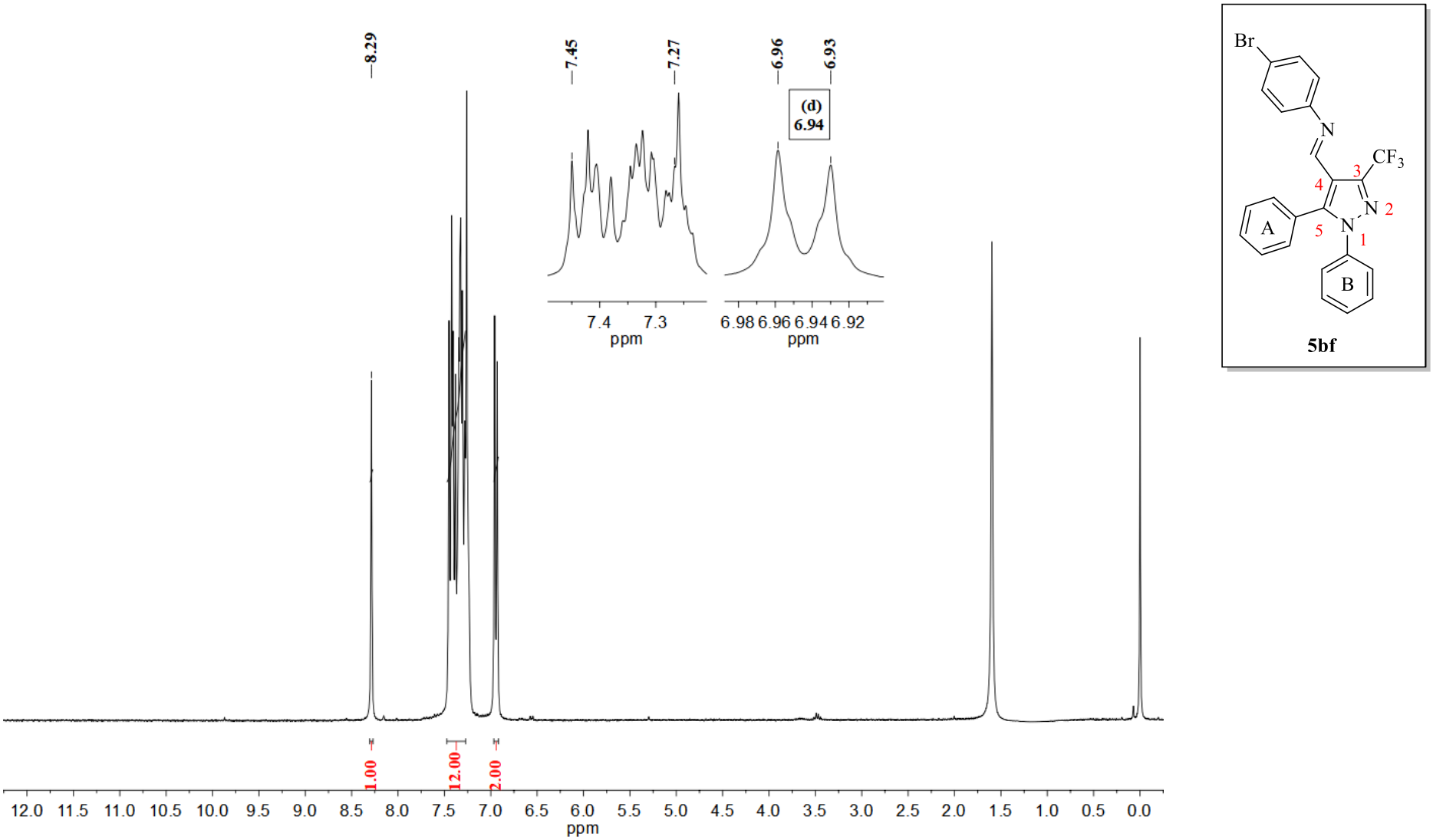
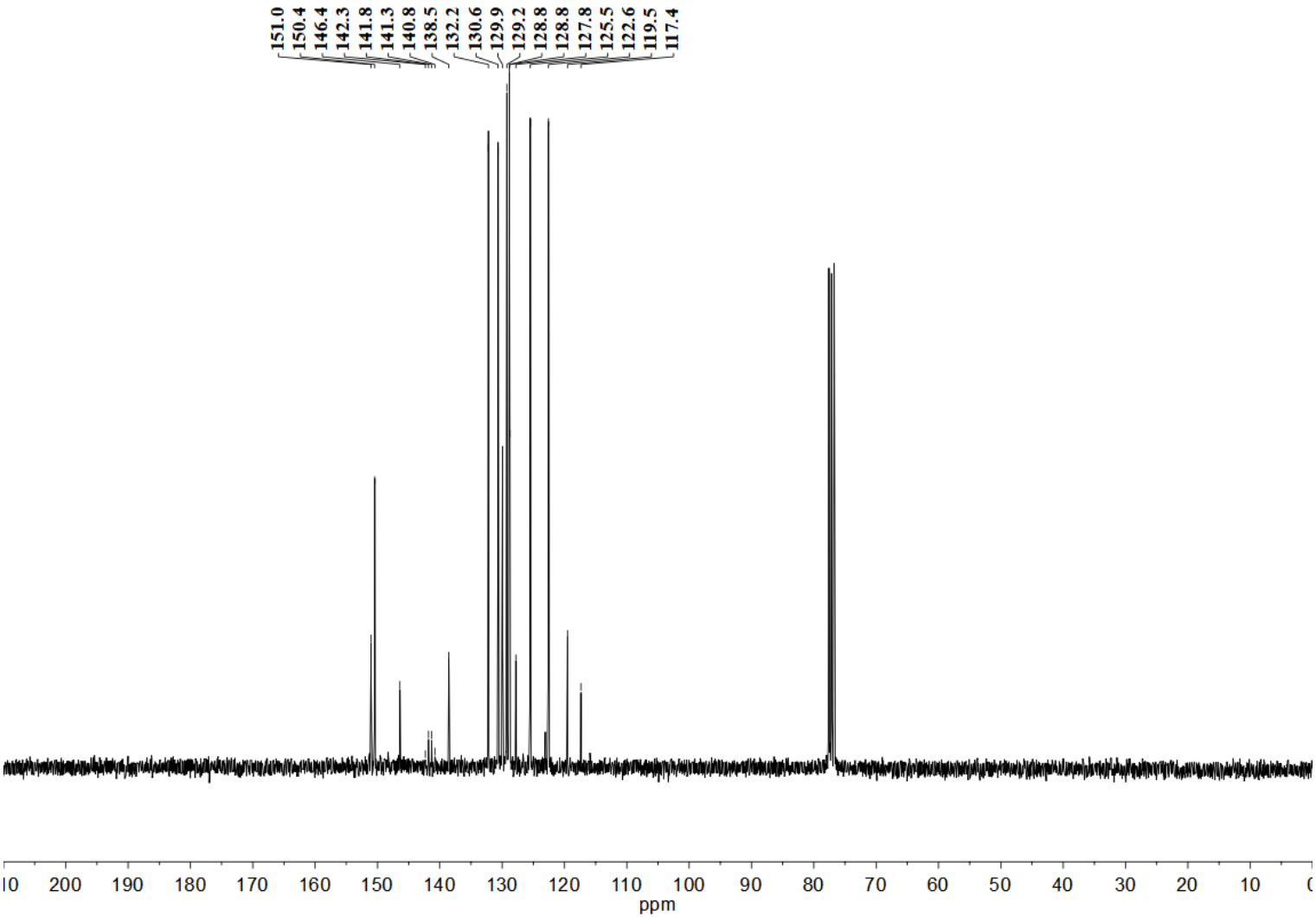


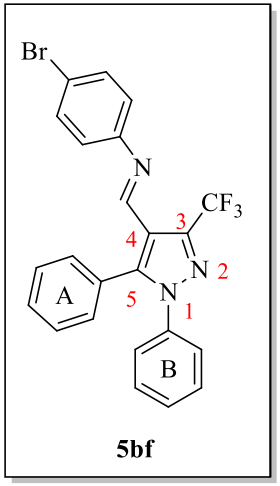
Figure S61 – ^{13}C NMR spectrum of compound **5be** in $CDCl_3$ at 75.45 MHz.



5bf

Figure S62 – ^{1}H NMR spectrum of compound **5bf** in $CDCl_3$ at 300.06 MHz.





5bf

Figure S63 – ^{13}C NMR spectrum of compound **5bf** in $CDCl_3$ at 75.45 MHz.

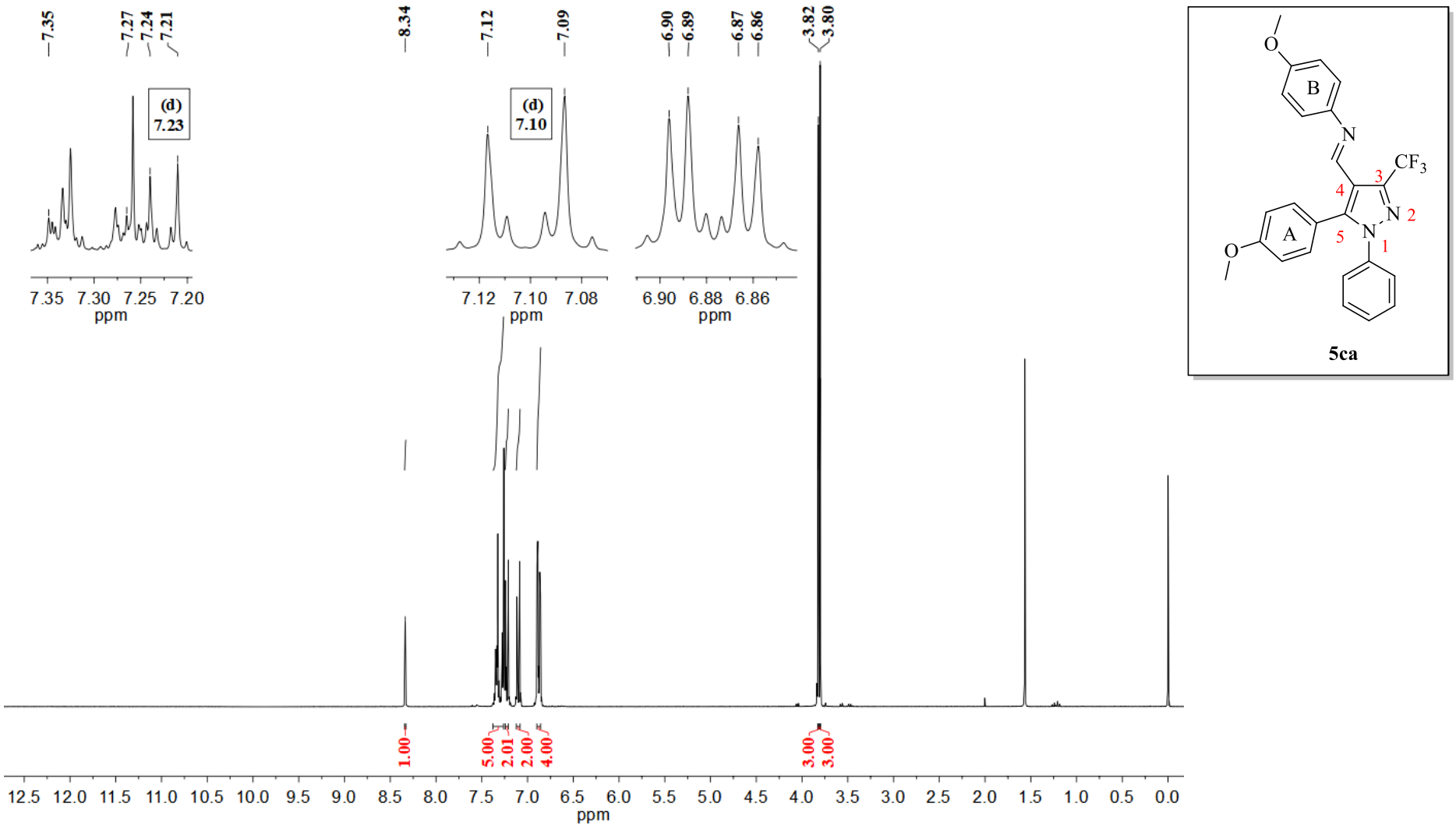
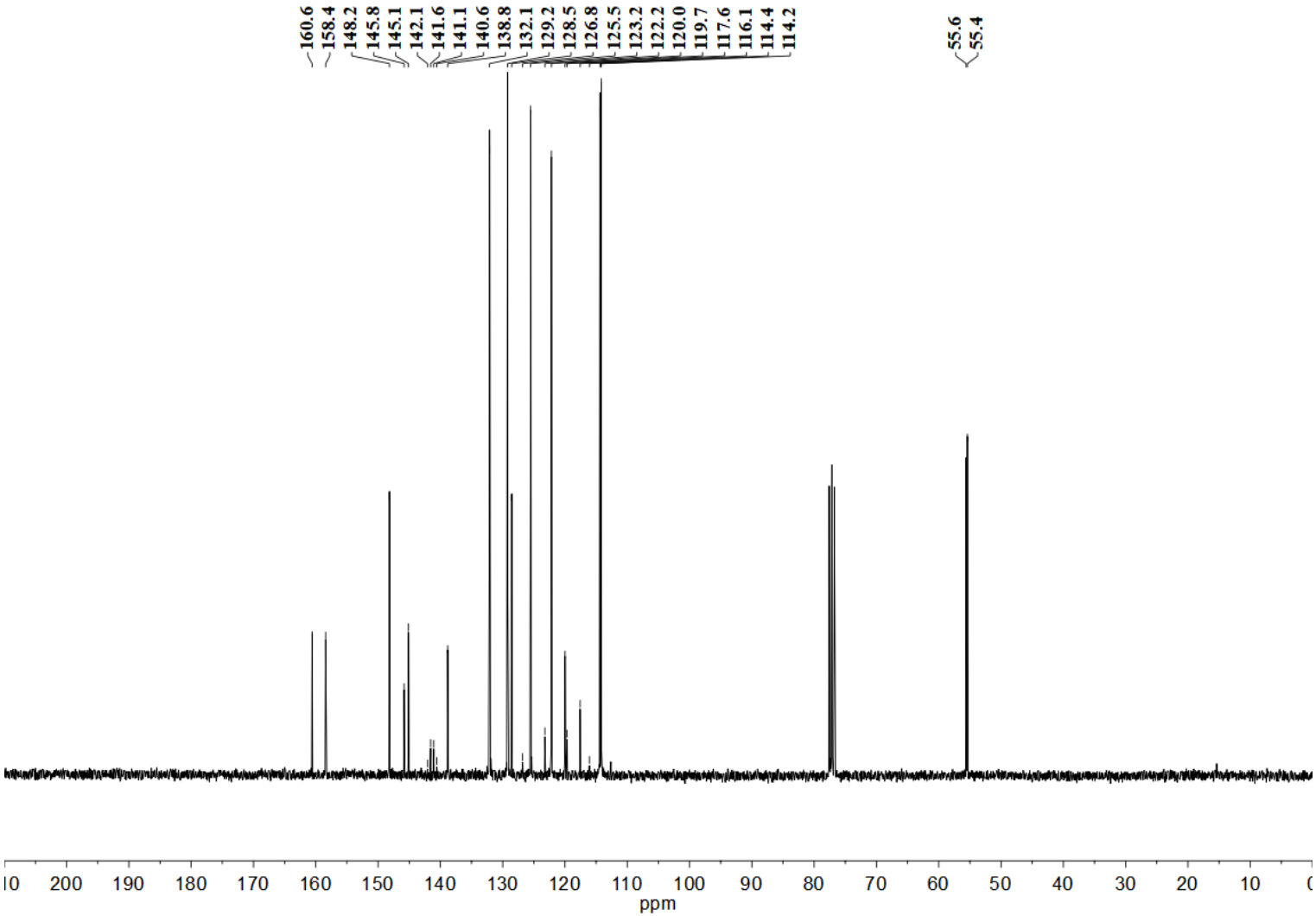
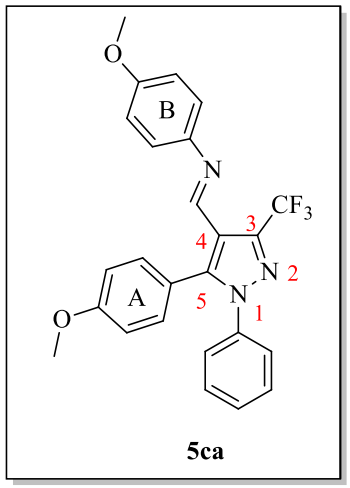


Figure S64 – ^{1}H NMR spectrum of compound **5ca** in $CDCl_3$ at 300.06 MHz.





5ca

Figure S65 – ^{13}C NMR spectrum of compound **5ca** in $CDCl_3$ at 75.45 MHz.

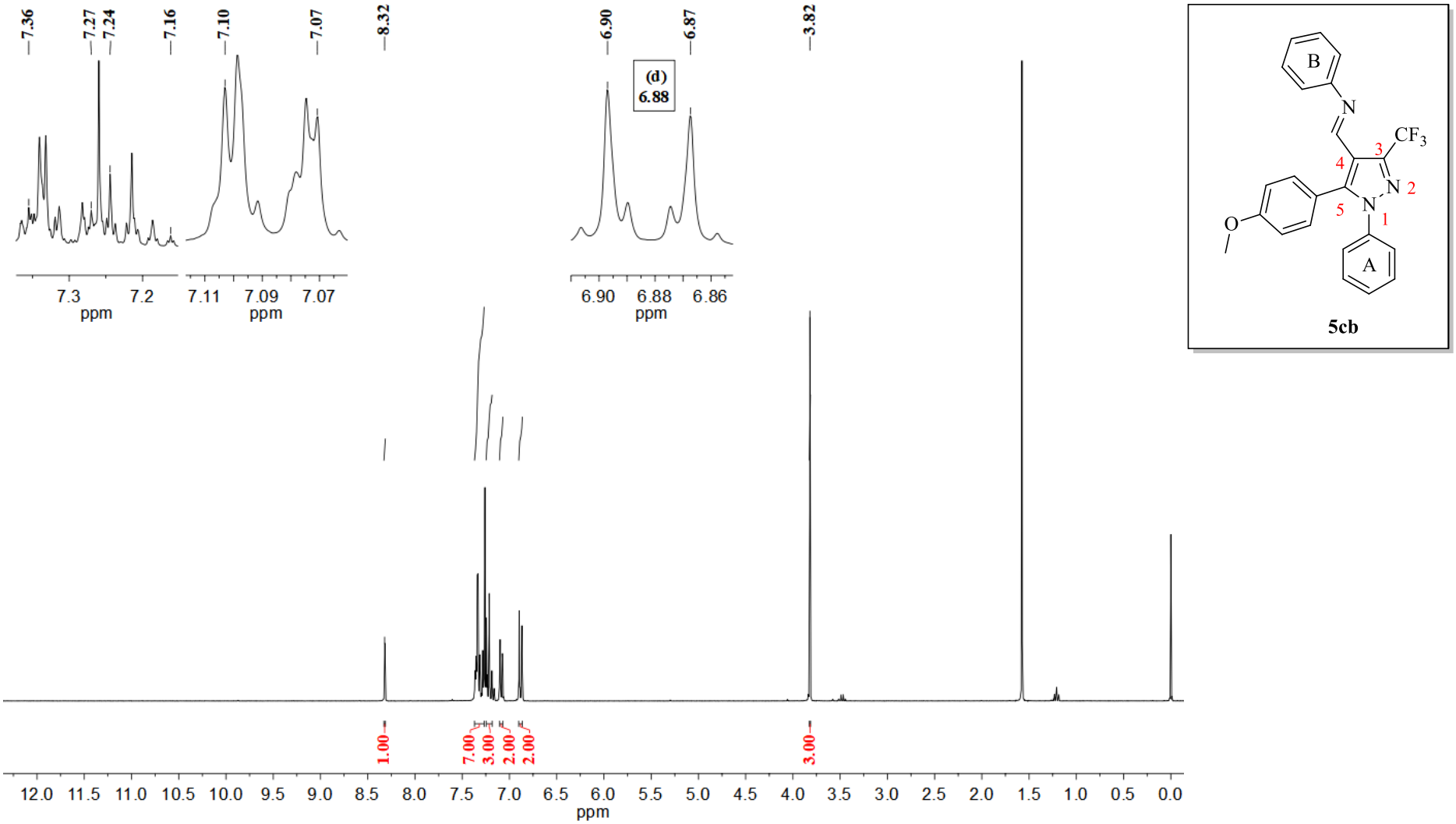


Figure S66 – ^{1}H NMR spectrum of compound **5cb** in $CDCl_3$ at 300.06 MHz.

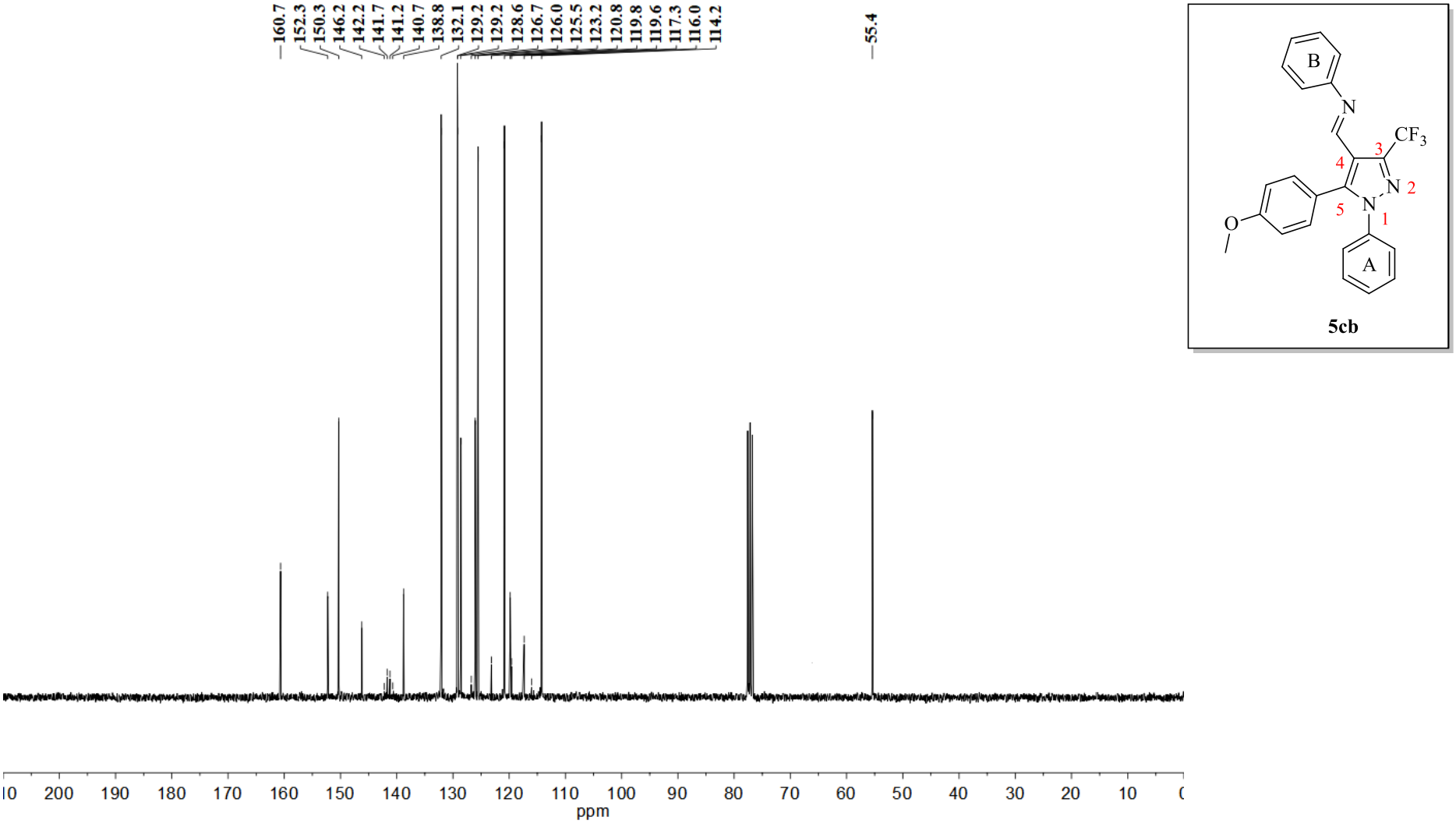


Figure S67 – ^{13}C NMR spectrum of compound **5cb** in $CDCl_3$ at 75.45 MHz.

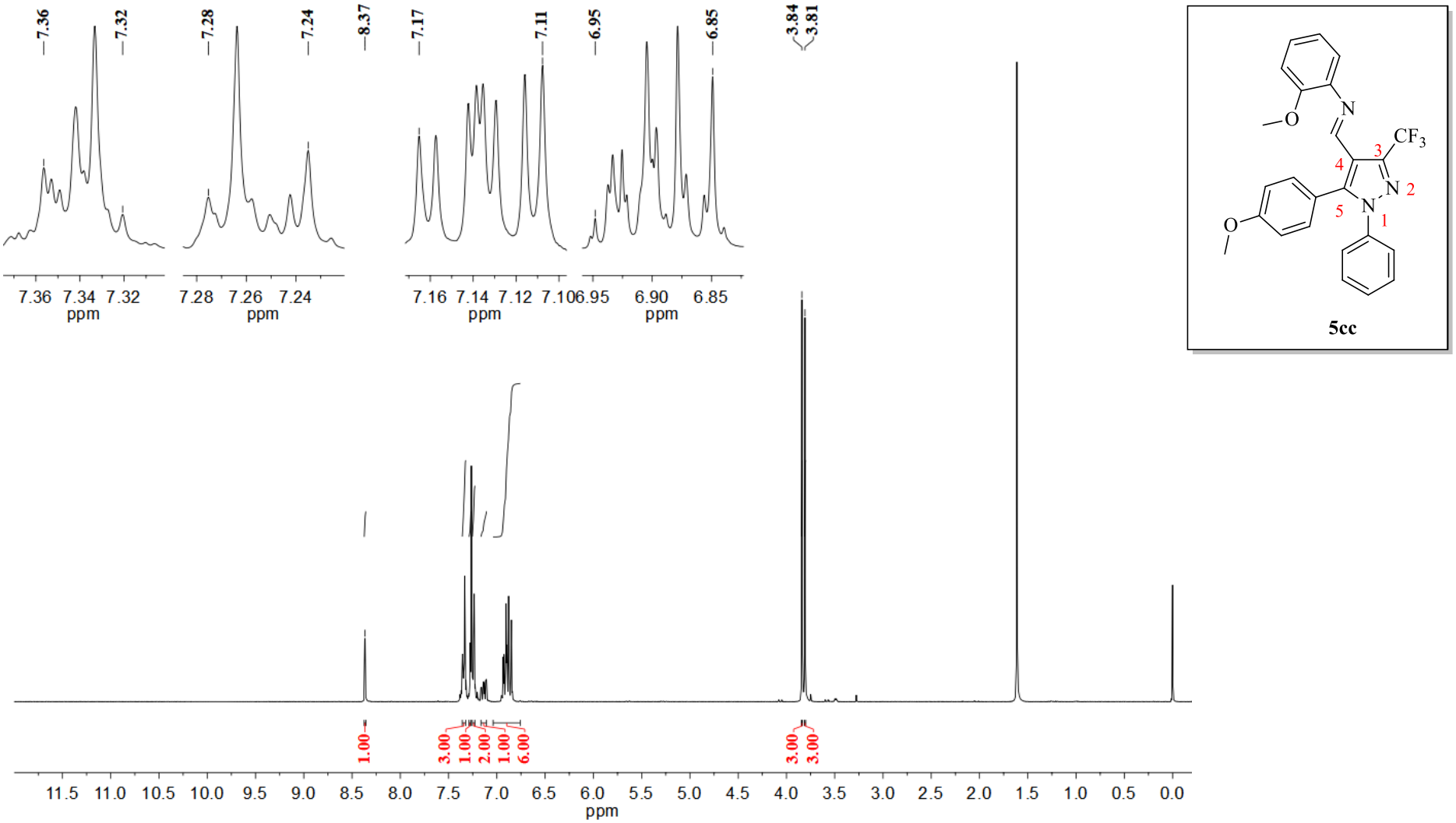
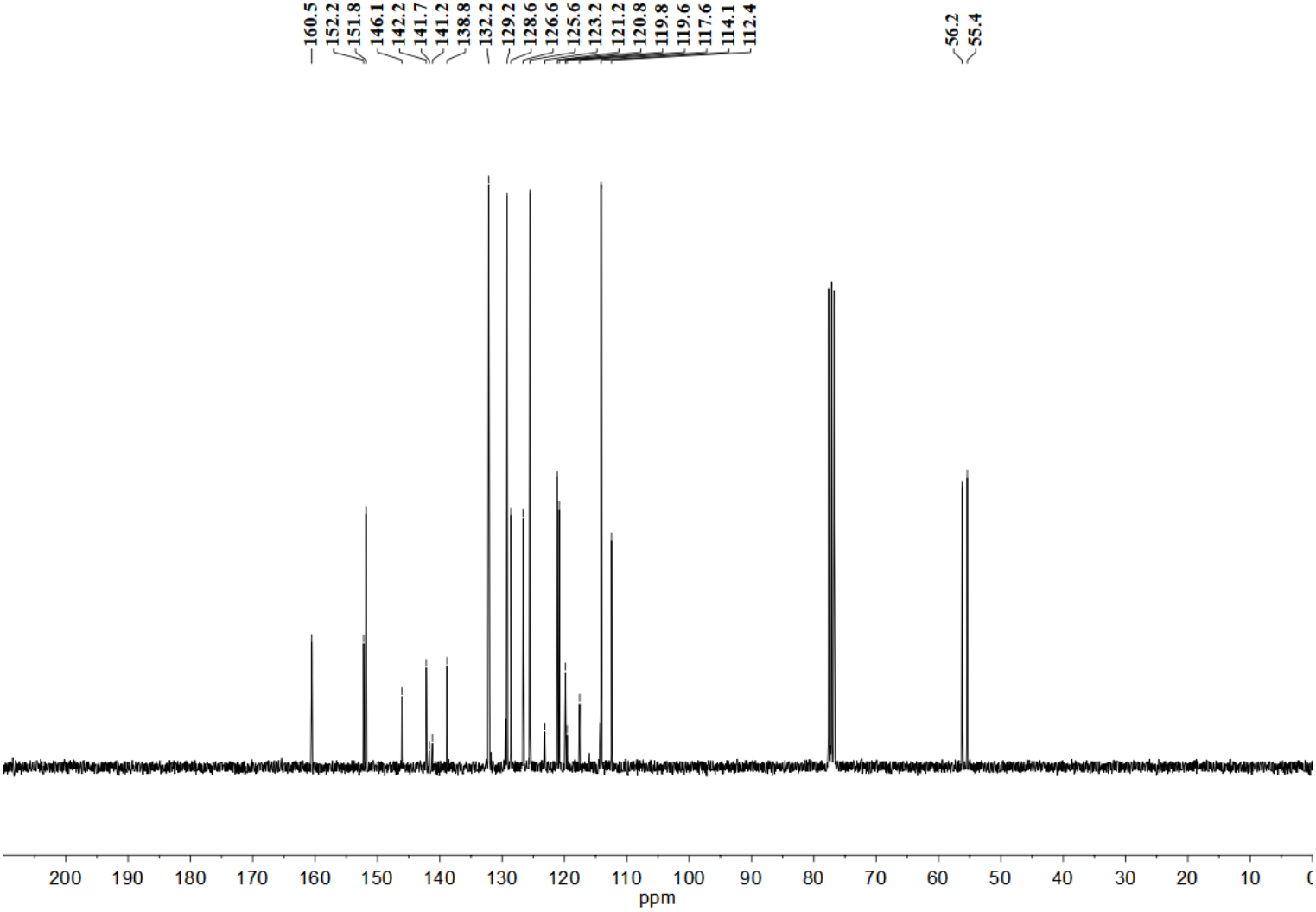


Figure S68 – ^{1}H NMR spectrum of compound **5cc** in $CDCl_3$ at 300.06 MHz.



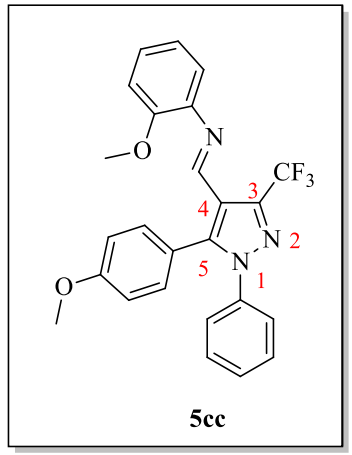


Figure S69 – ^{13}C NMR spectrum of compound **5cc** in $CDCl_3$ at 75.45 MHz.

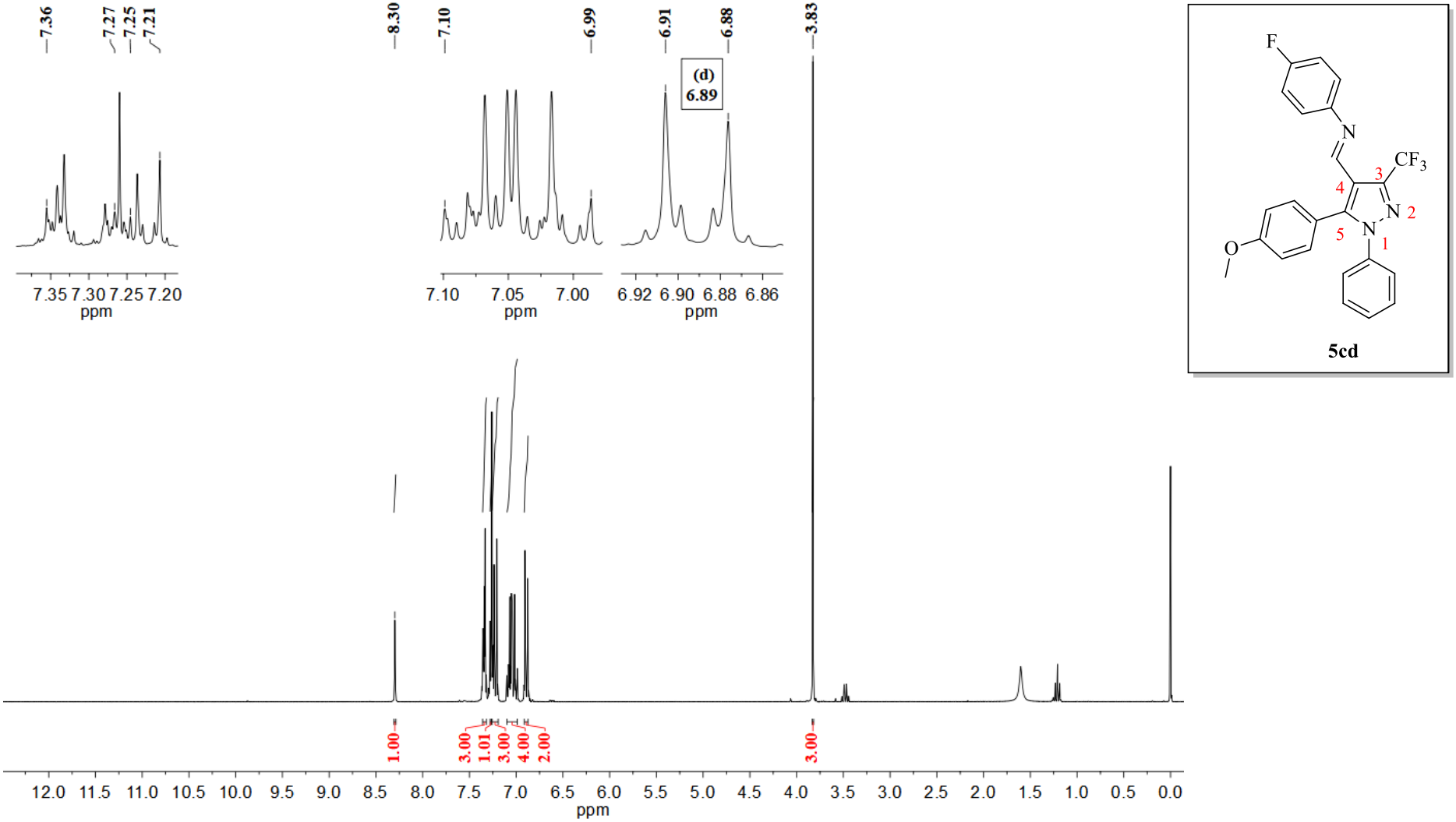


Figure S70 – ^{1}H NMR spectrum of compound **5cd** in $CDCl_3$ at 300.06 MHz.

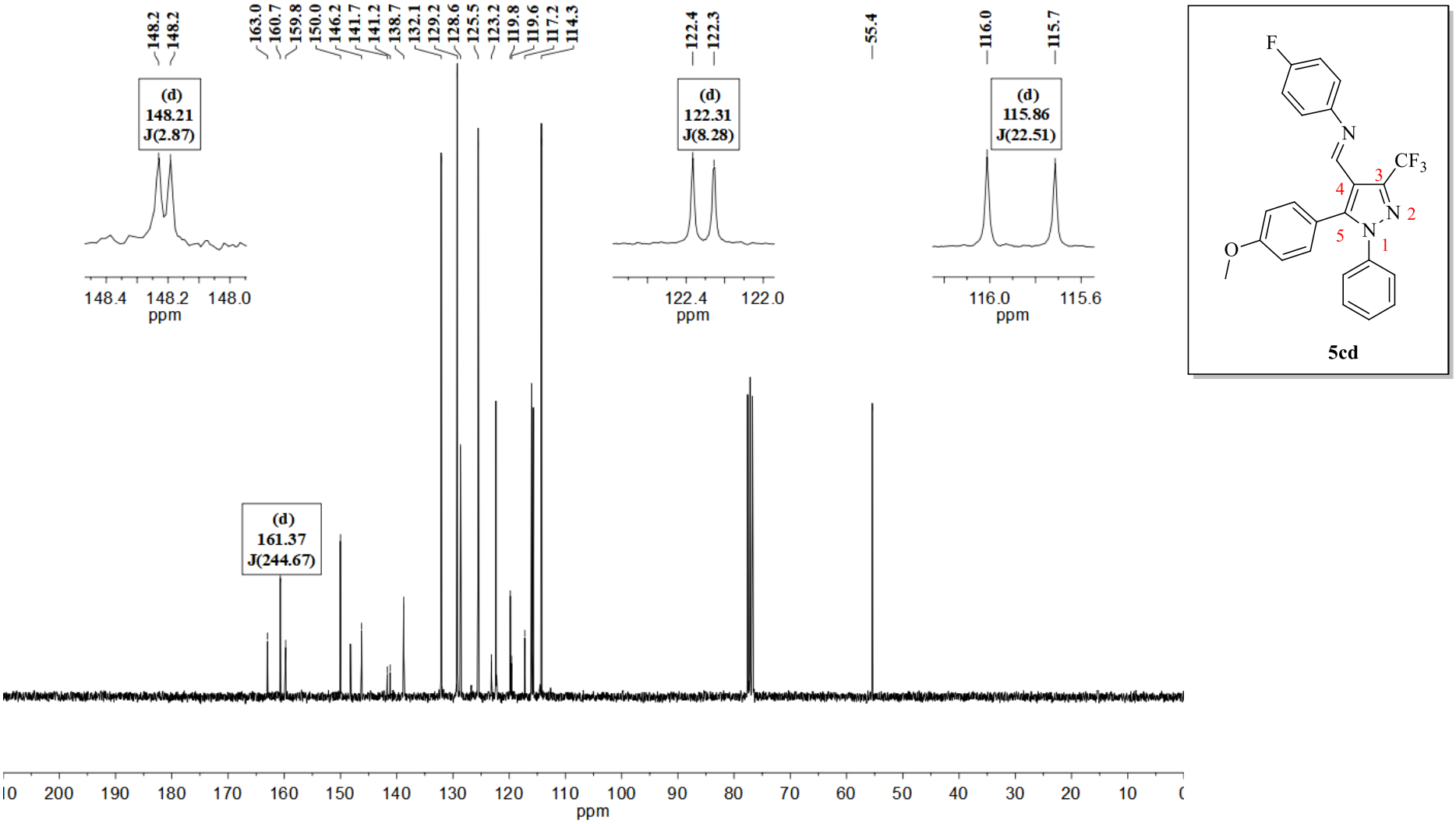


Figure S71 – ^{13}C NMR spectrum of compound **5cd** in $CDCl_3$ at 75.45 MHz.

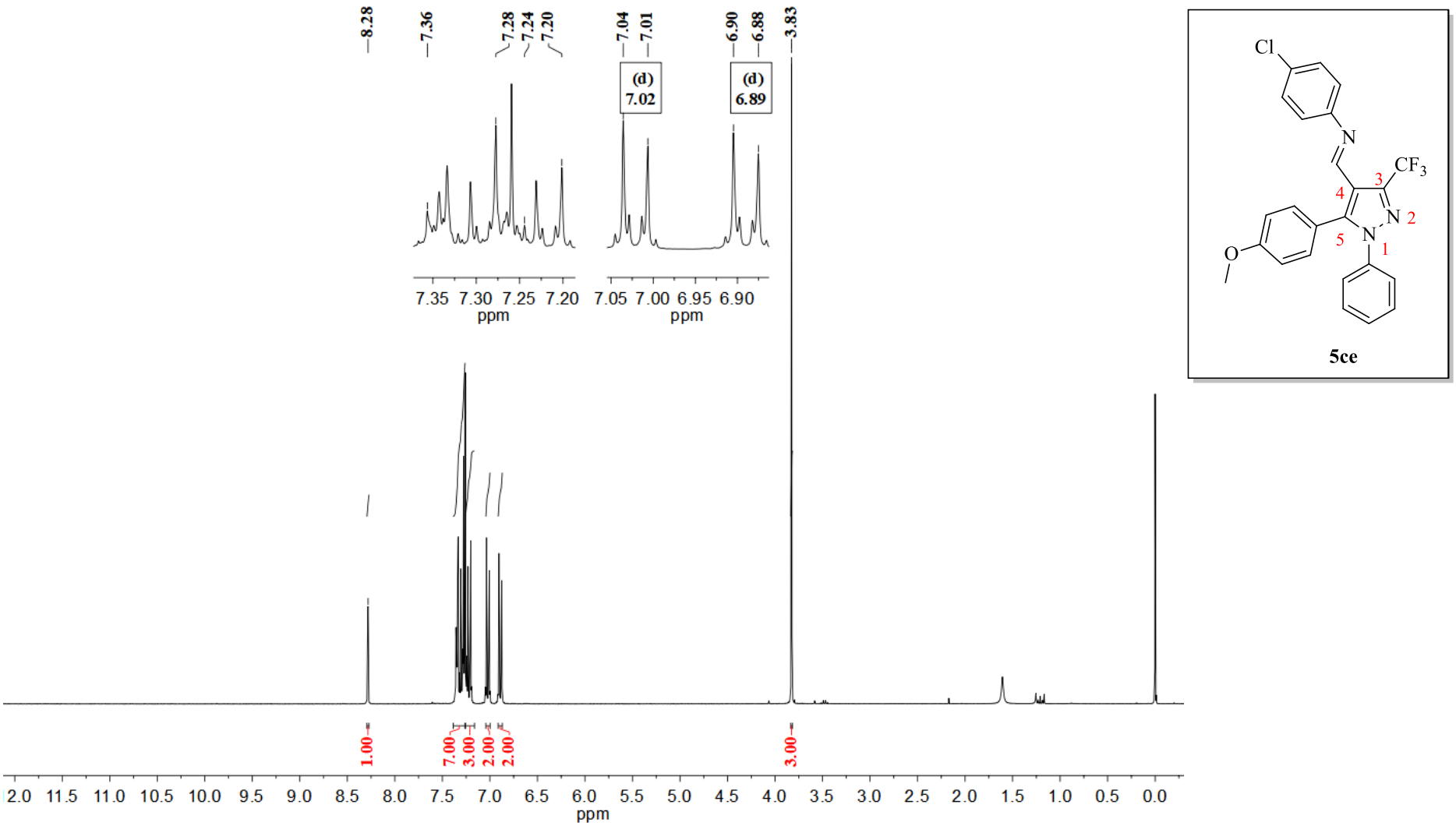
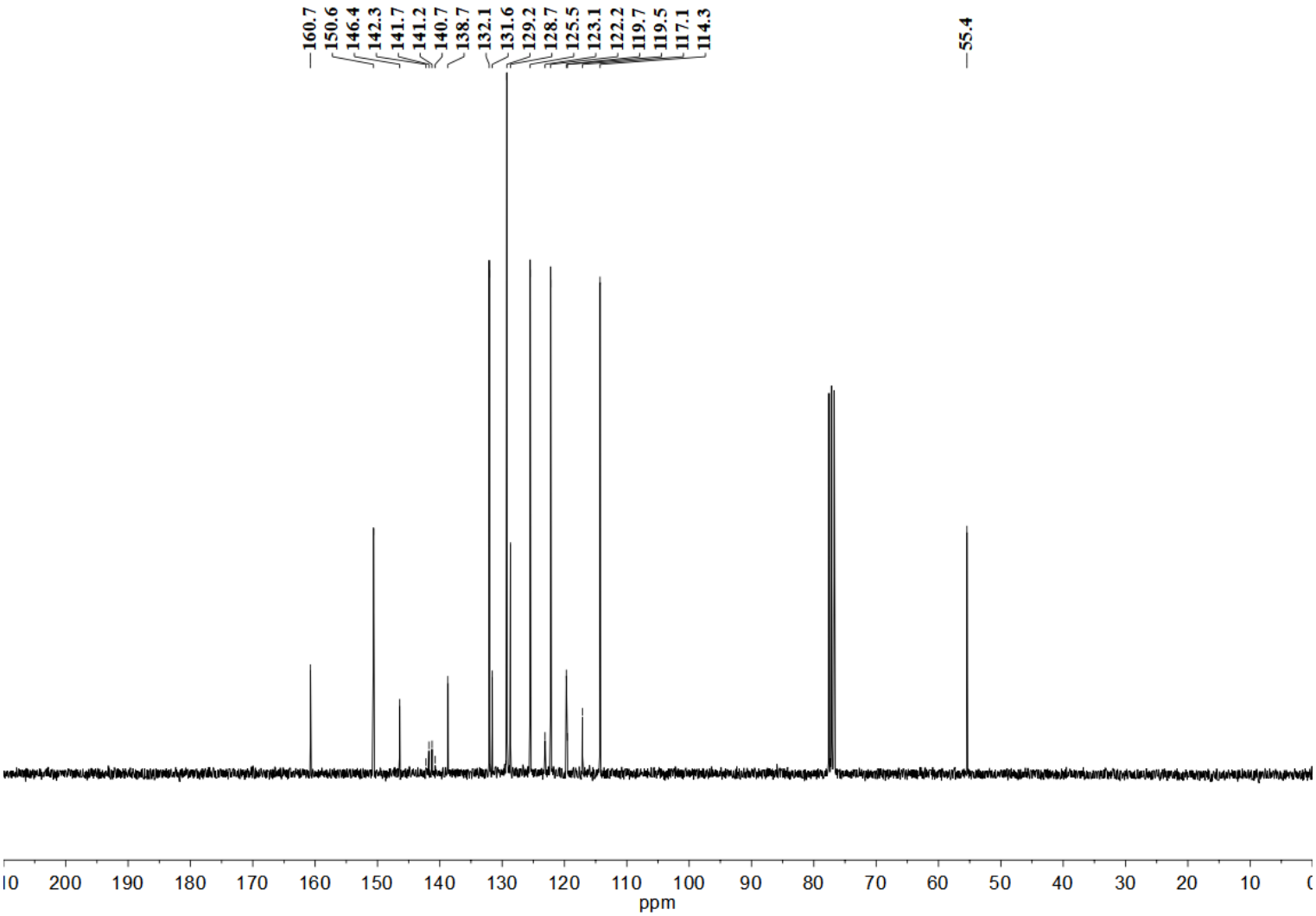


Figure S72 – ^{1}H NMR spectrum of compound **5ce** in $CDCl_3$ at 300.06 MHz.



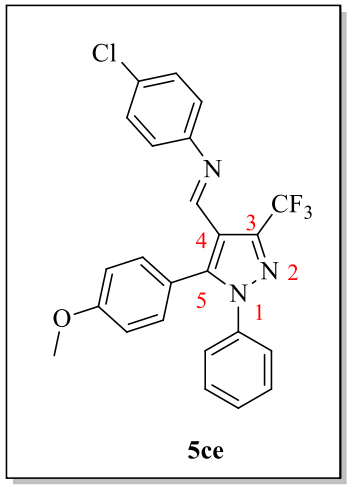


Figure S73– ^{13}C NMR spectrum of compound **5ce** in $CDCl_3$ at 75.45 MHz.

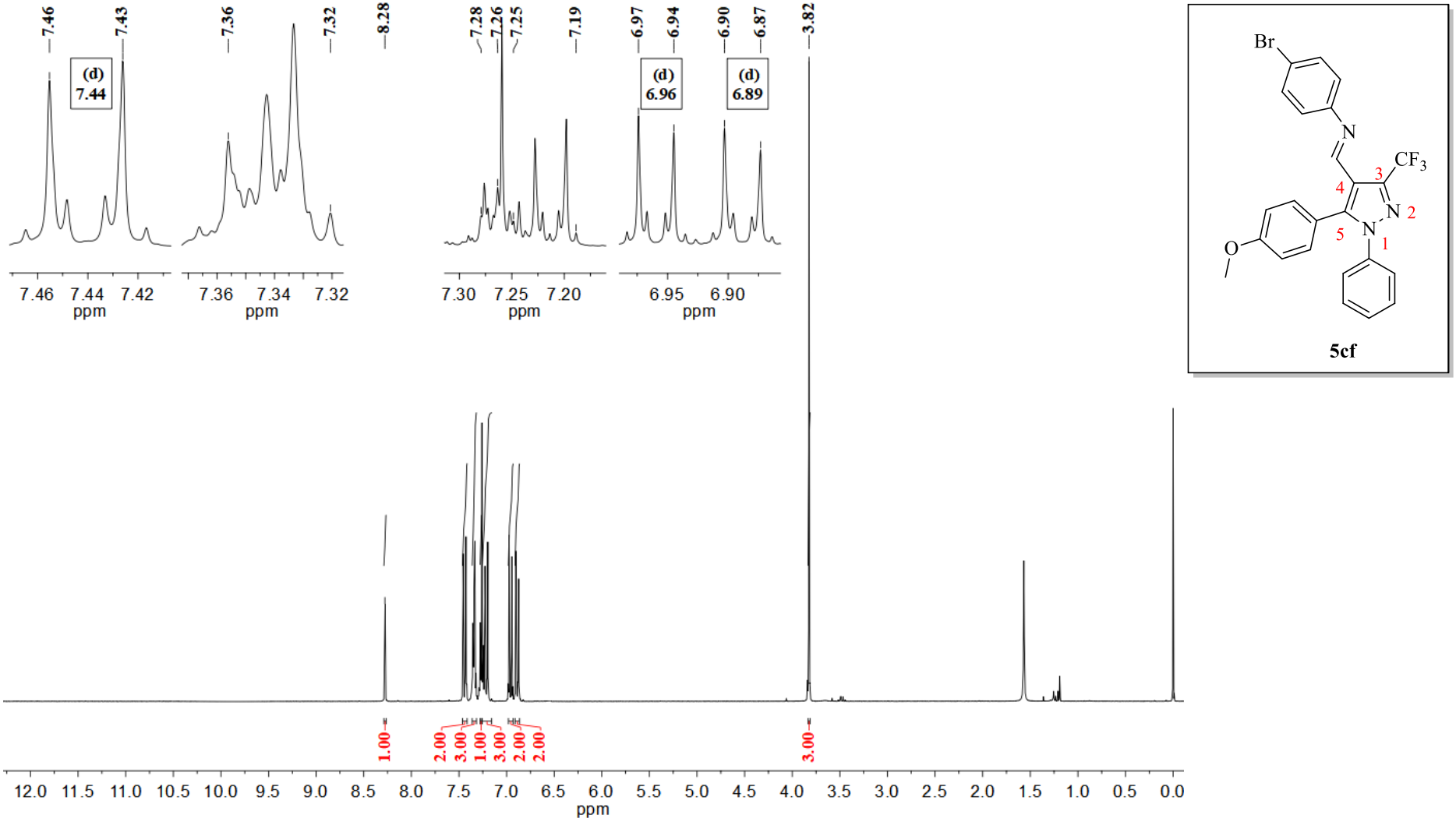
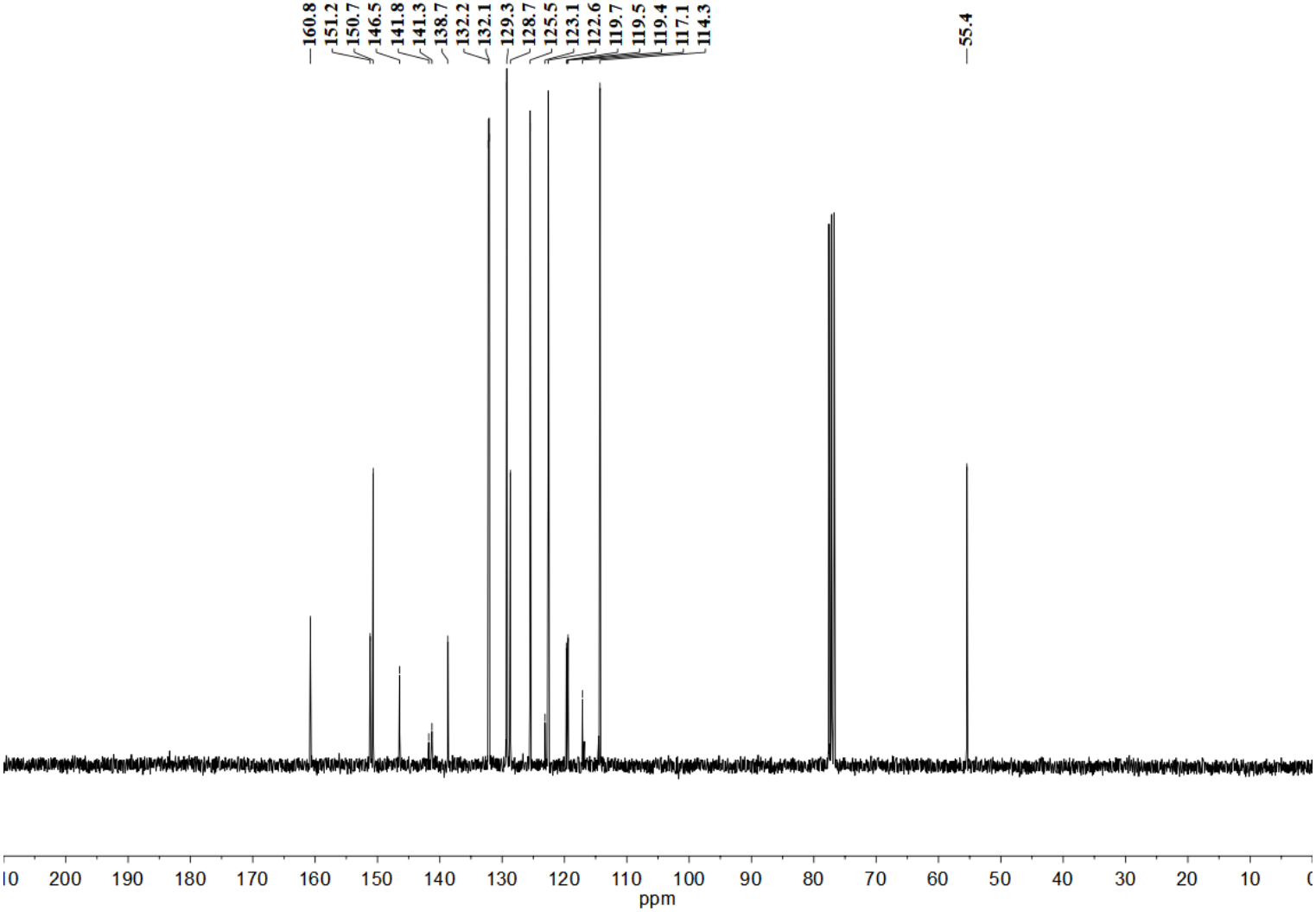


Figure S74 – ^{1}H NMR spectrum of compound **5cf** in $CDCl_3$ at 300.06 MHz.



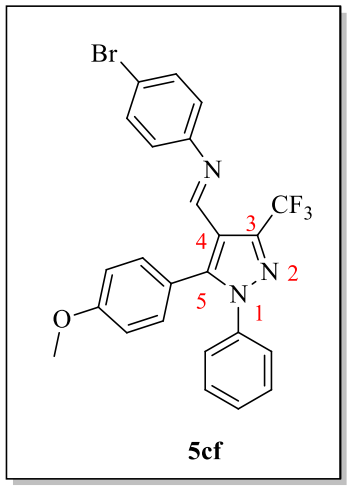


Figure S75 – ^{13}C NMR spectrum of compound **5cf** in $CDCl_3$ at 75.45 MHz.

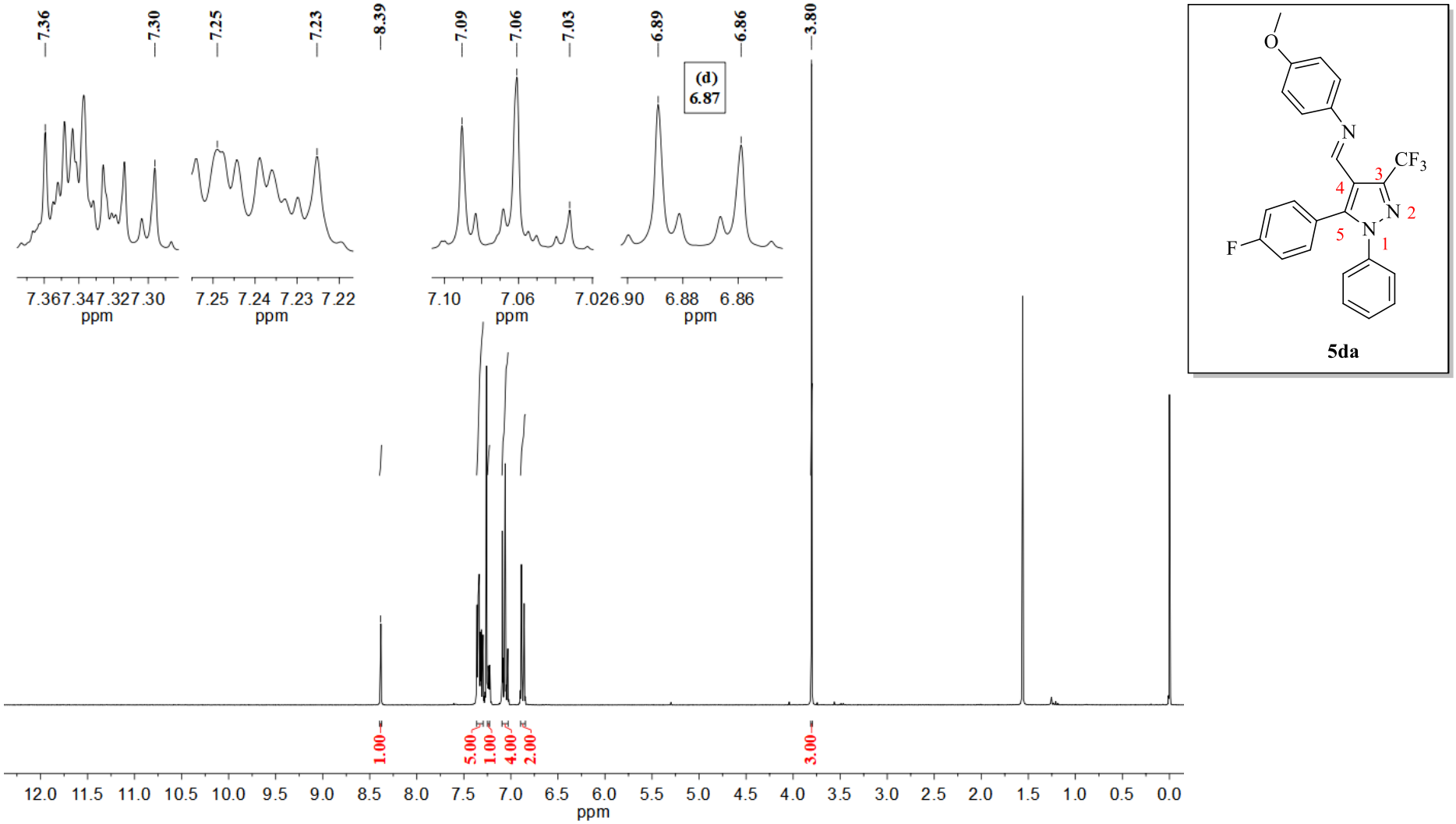


Figure S76 – ^{1}H NMR spectrum of compound **5da** in $CDCl_3$ at 300.06 MHz.

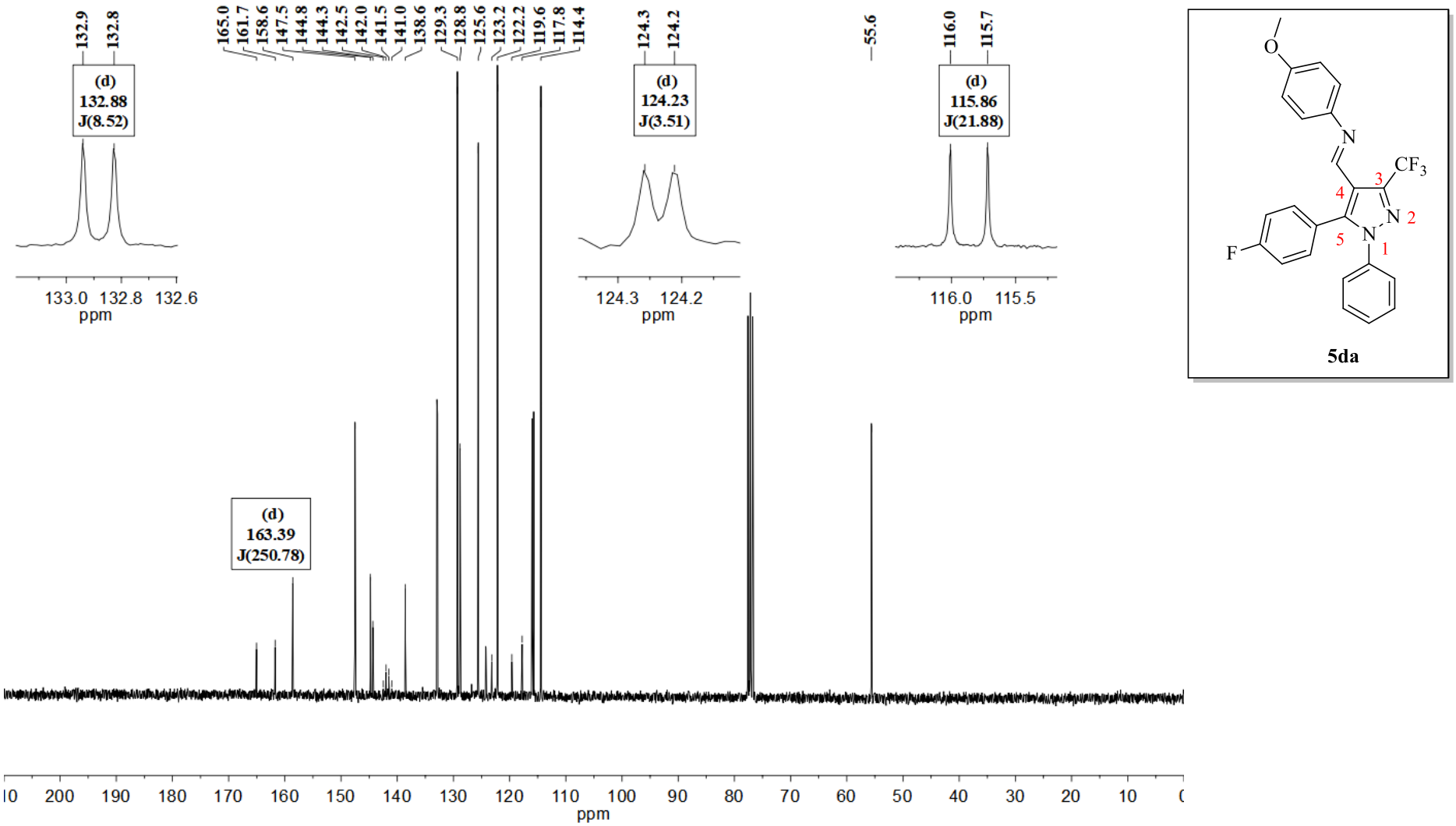


Figure S77 – ^{13}C NMR spectrum of compound **5da** in $CDCl_3$ at 75.45 MHz.

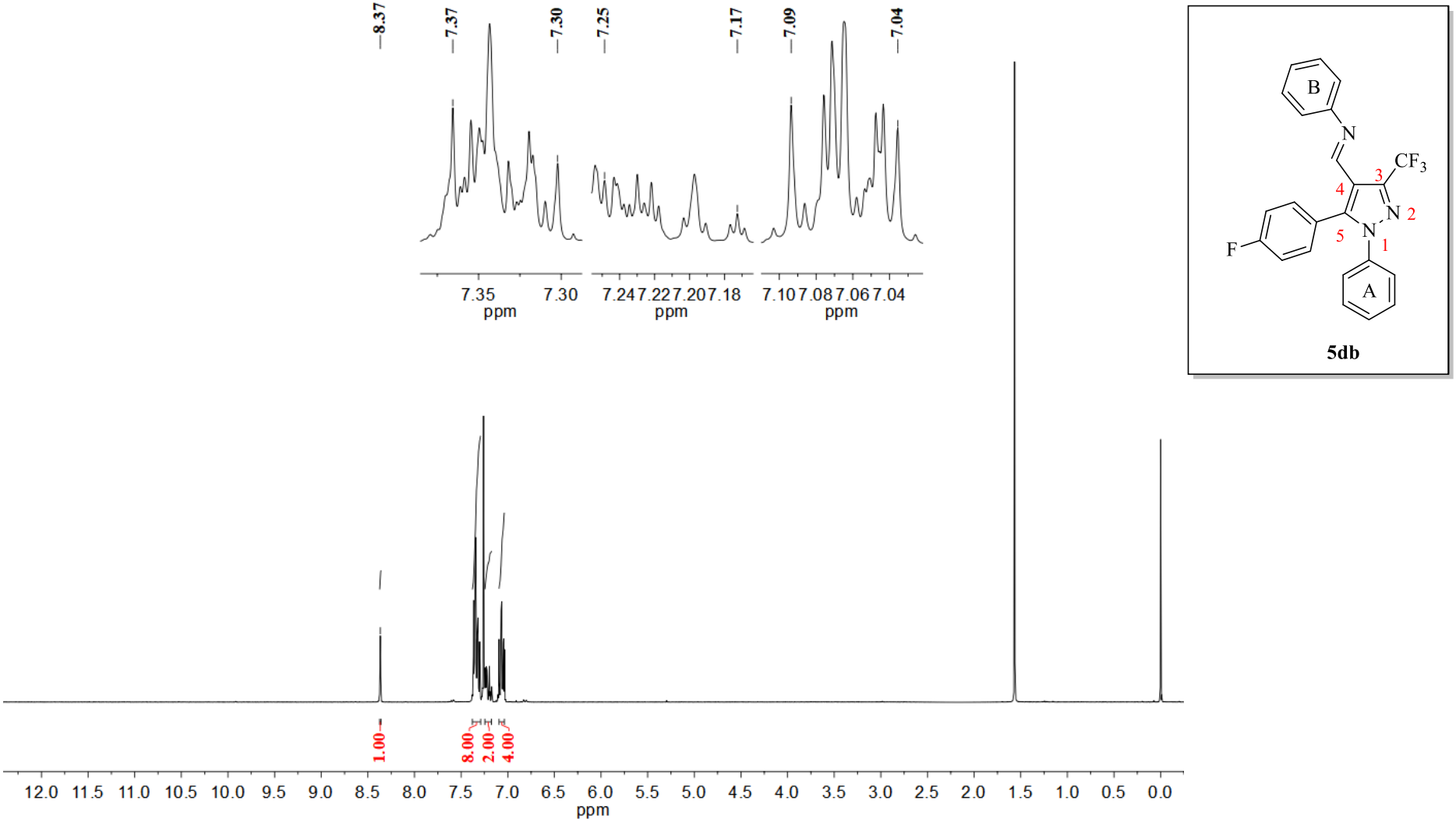


Figure S78 – ^{1}H NMR spectrum of compound **5db** in $CDCl_3$ at 300.06 MHz.

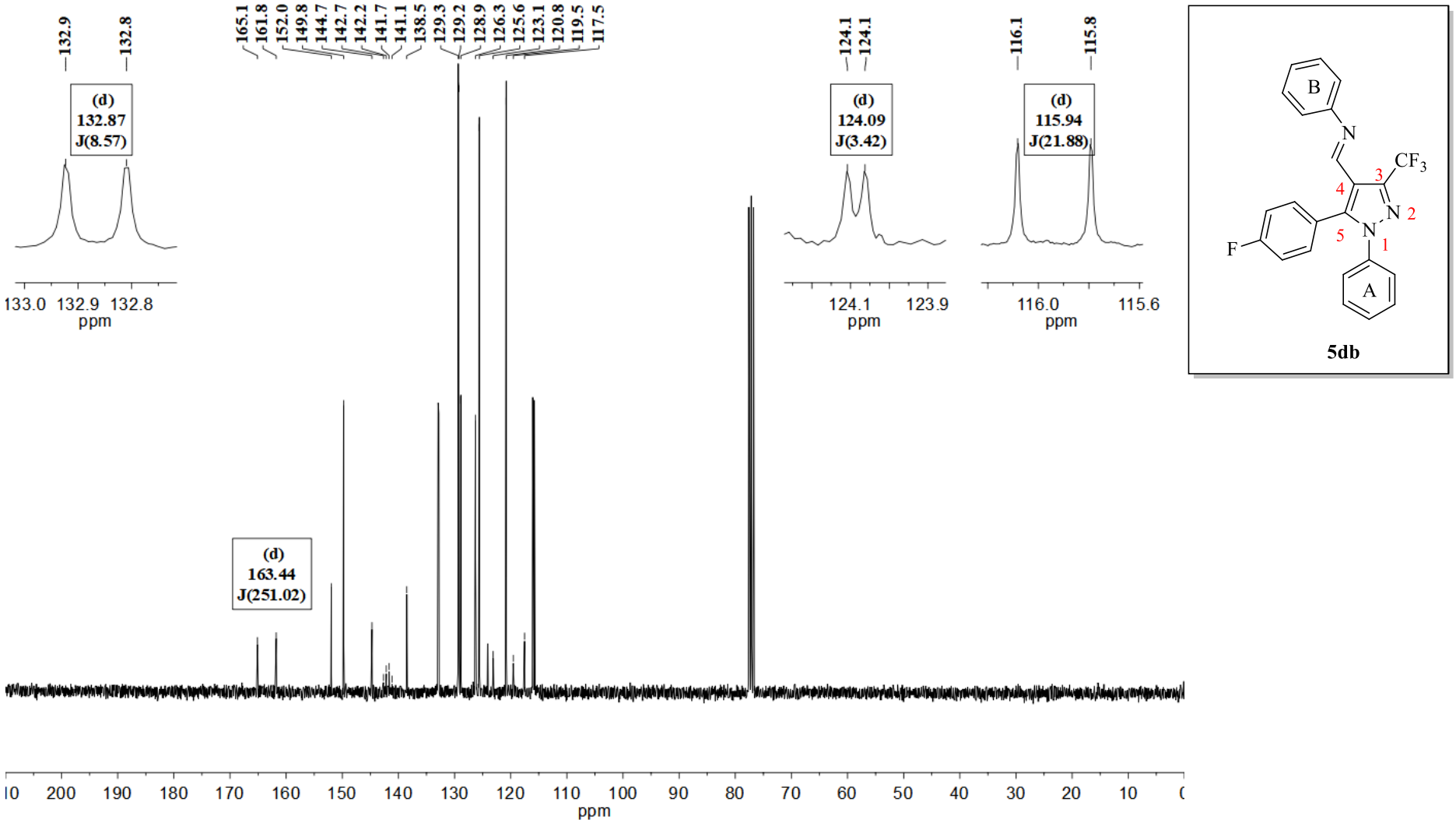


Figure S79 – ^{13}C NMR spectrum of compound **5db** in $CDCl_3$ at 75.45 MHz.

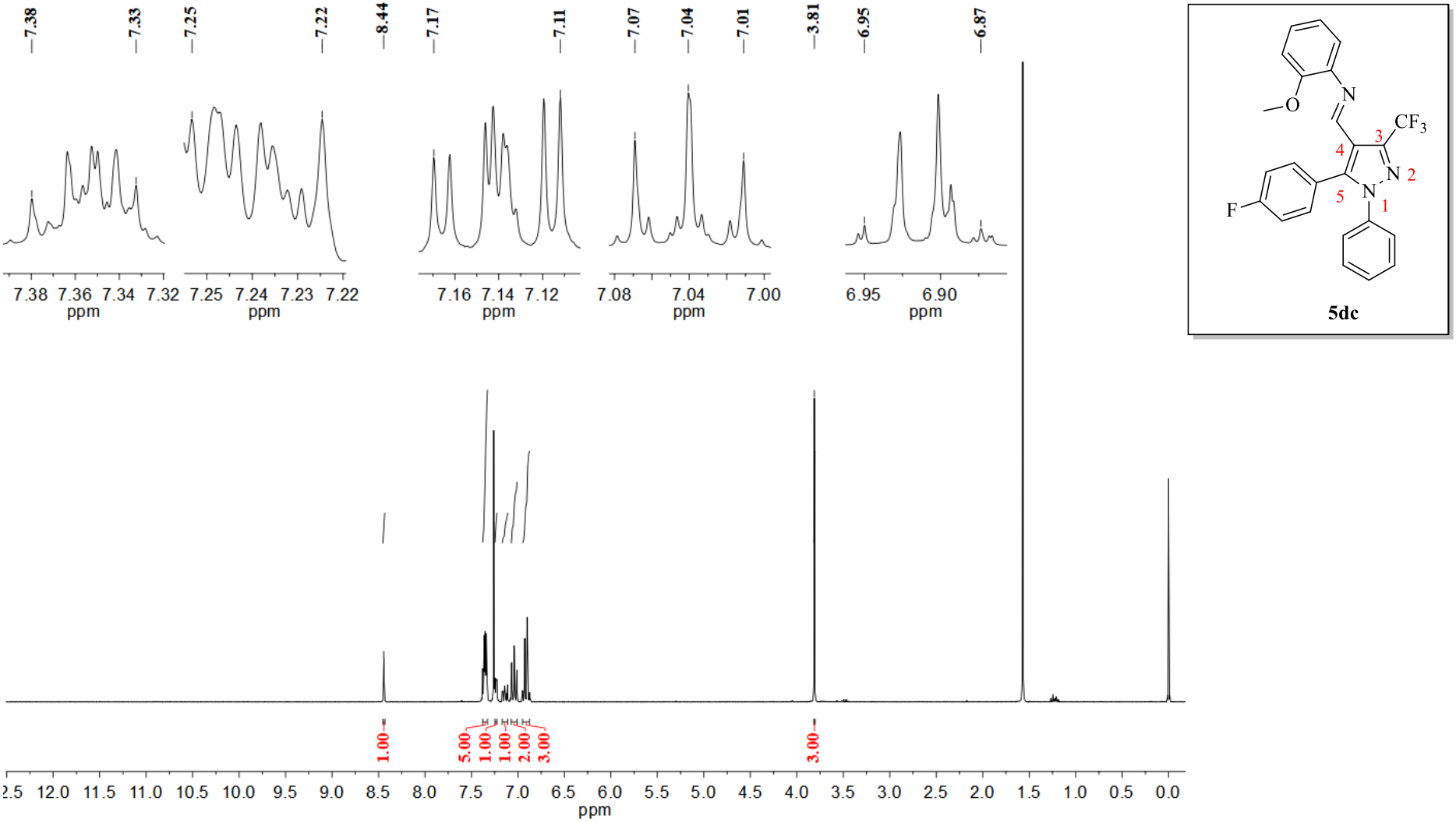


Figure S80 – ^{1}H NMR spectrum of compound **5dc** in $CDCl_3$ at 300.06 MHz.

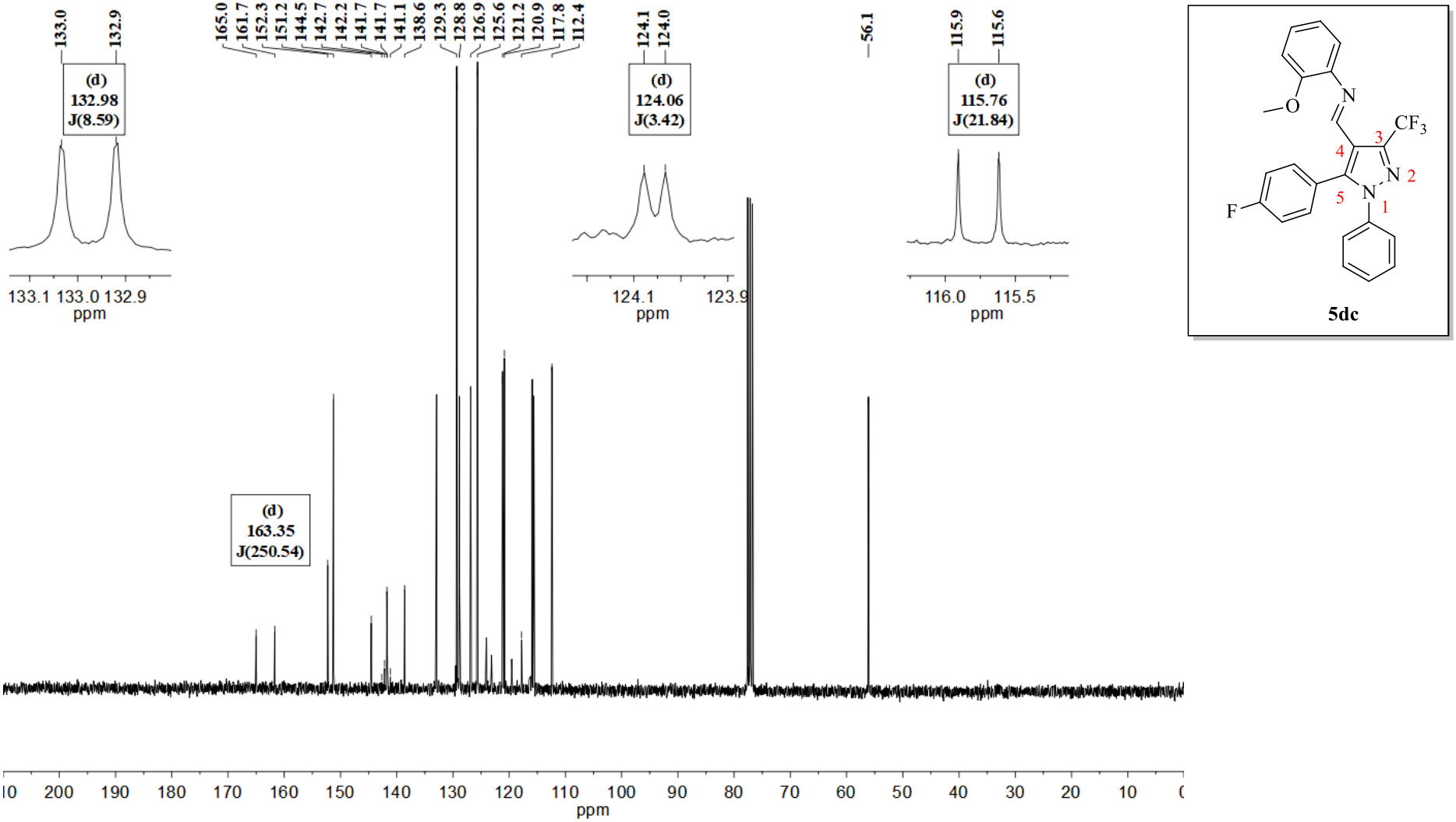


Figure S81 – ^{13}C NMR spectrum of compound **5dc** in $CDCl_3$ at 75.45 MHz.

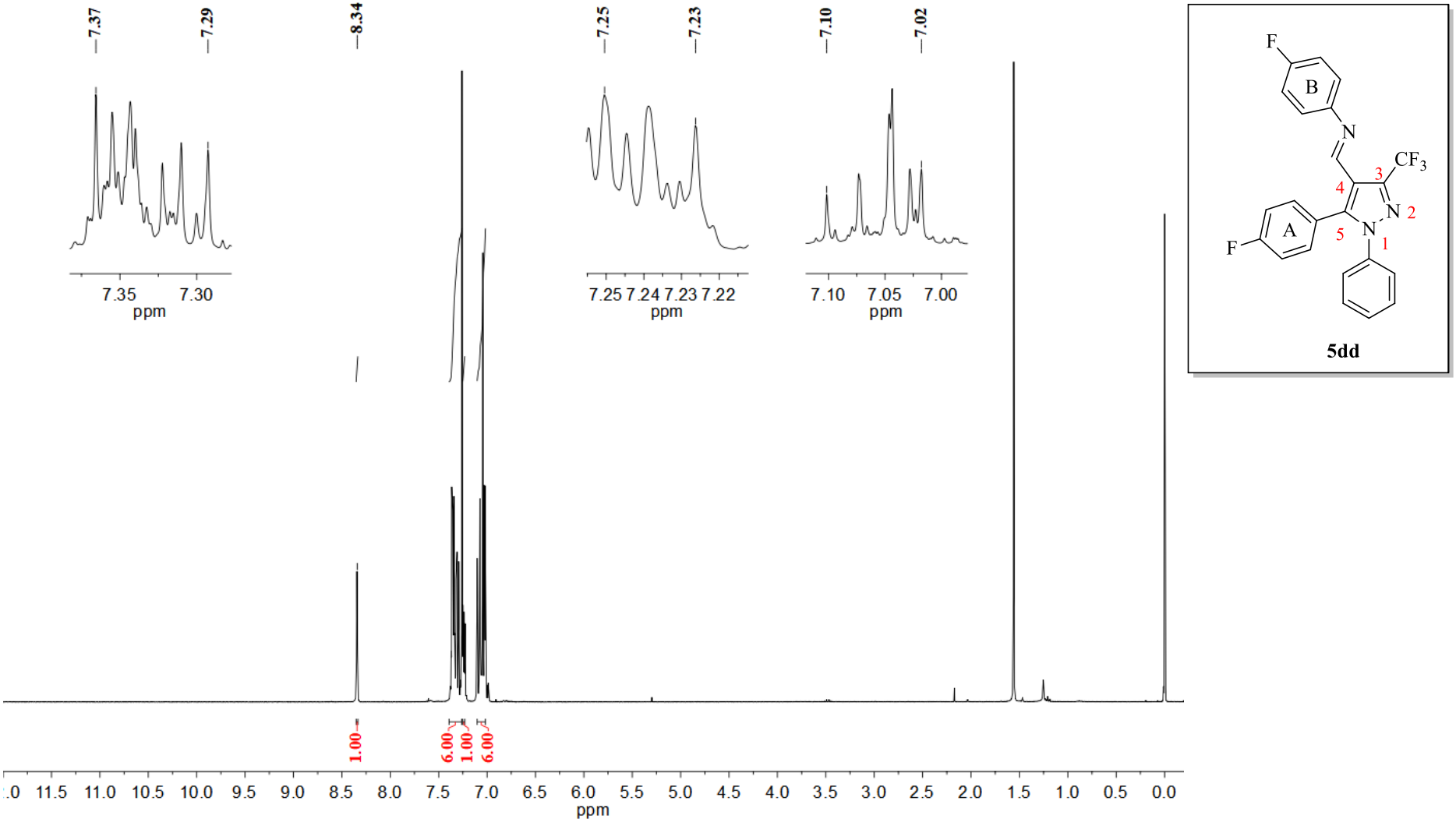


Figure S82 – ^{1}H NMR spectrum of compound **5dd** in $CDCl_3$ at 300.06 MHz.

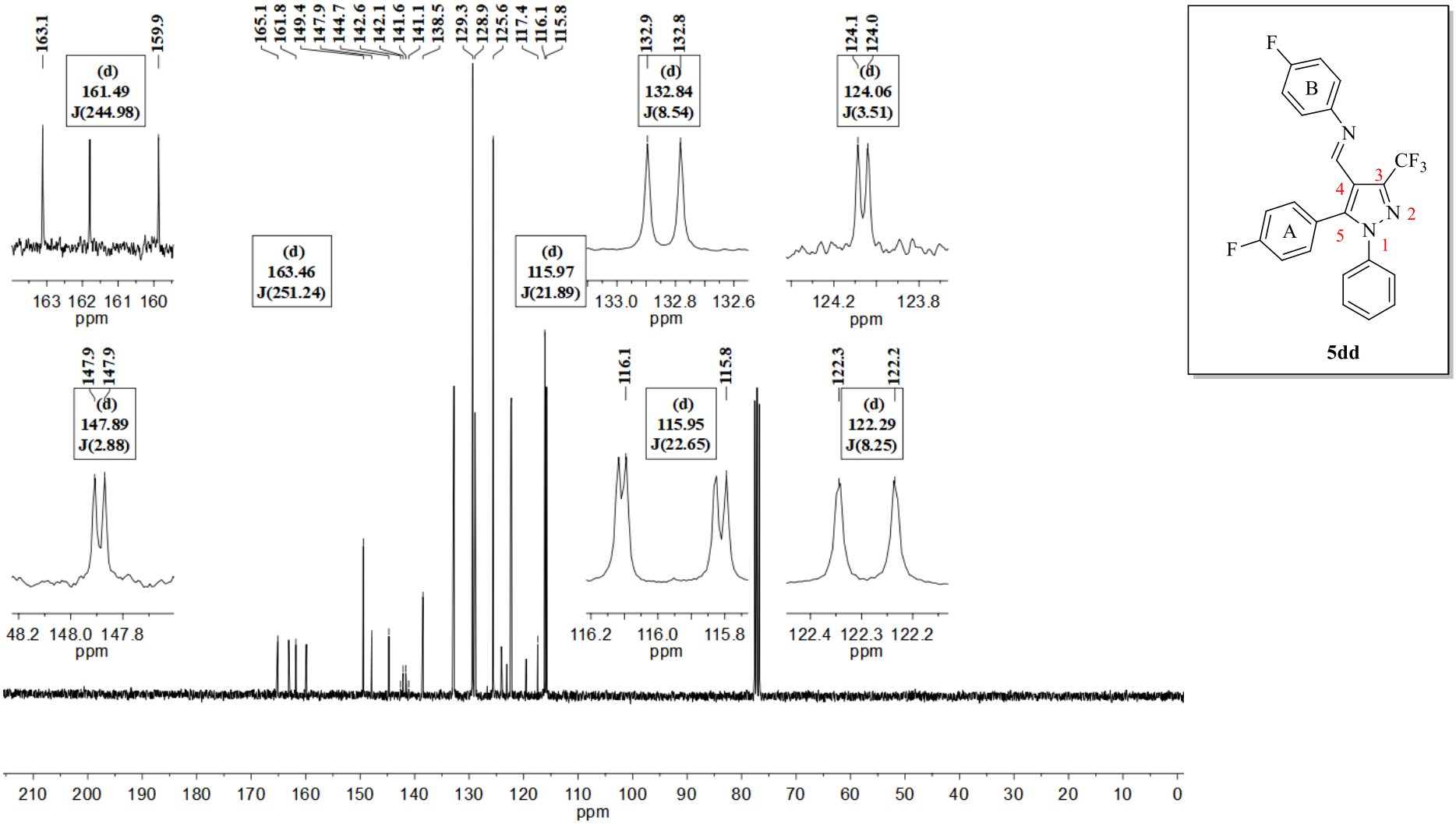


Figure S83 – ^{13}C NMR spectrum of compound **5dd** in $CDCl_3$ at 75.45 MHz.

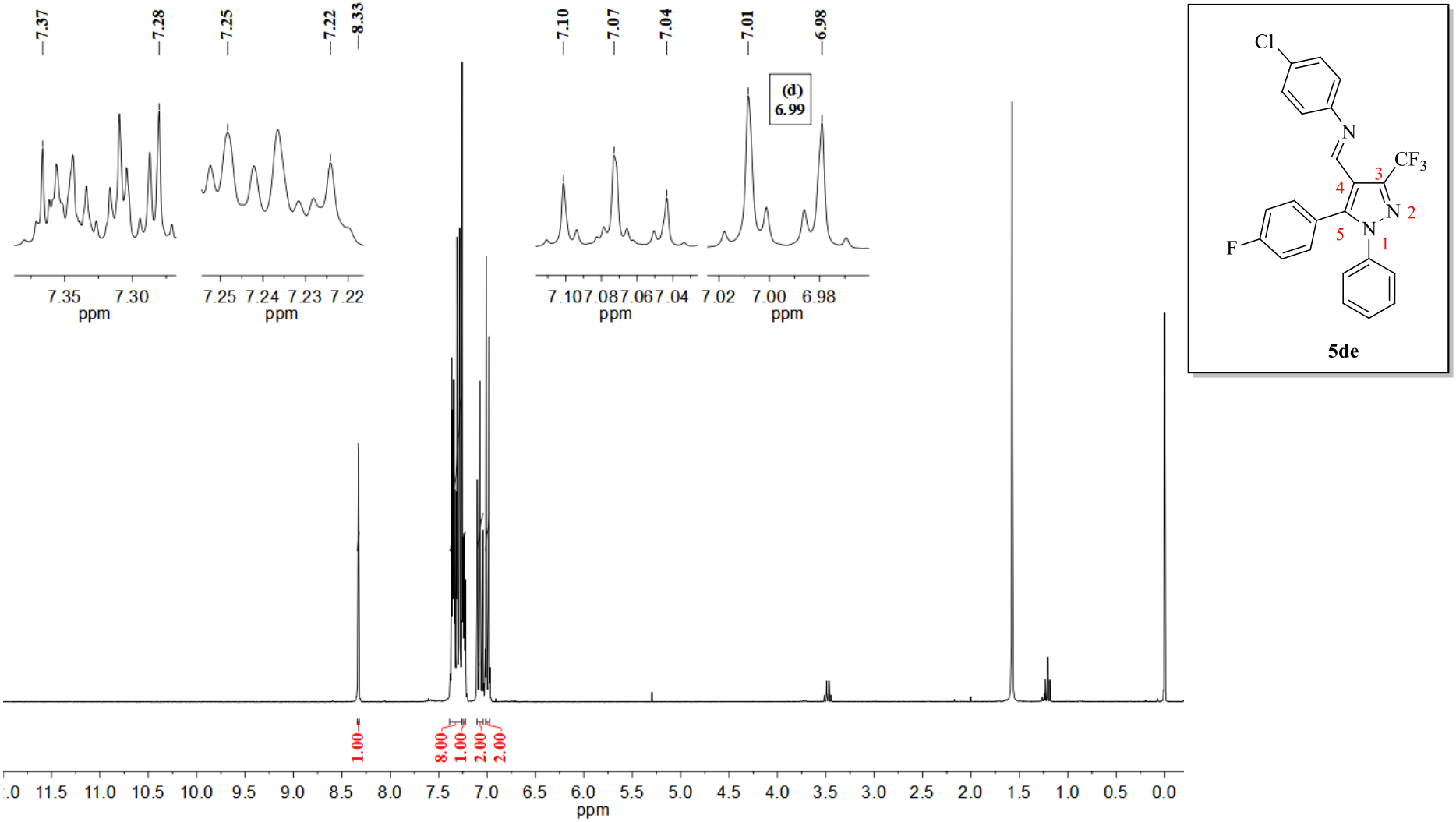


Figure S84 – ^{1}H NMR spectrum of compound **5de** in $CDCl_3$ at 300.06 MHz.

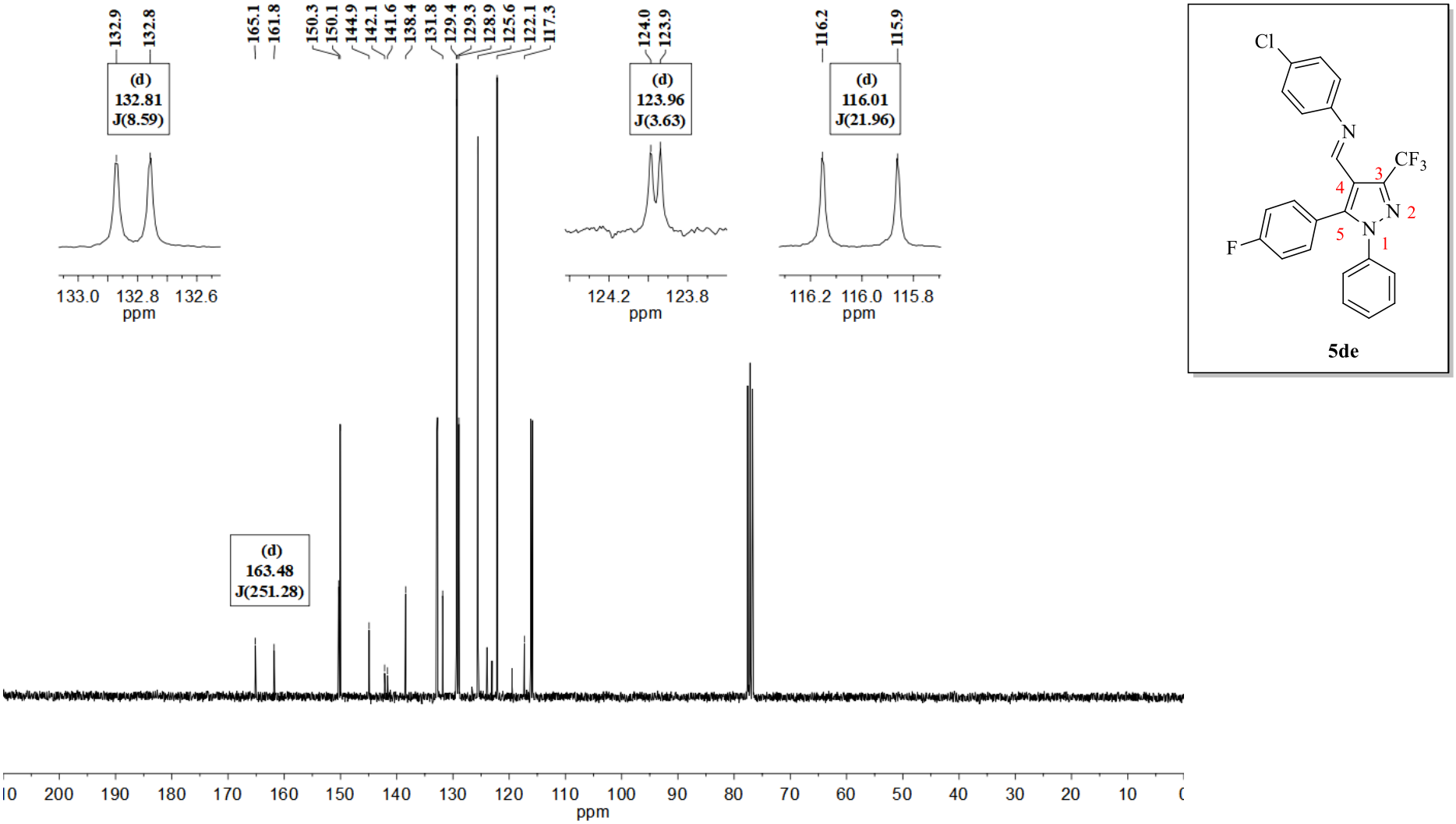


Figure S85 – ^{13}C NMR spectrum of compound **5de** in $CDCl_3$ at 75.45 MHz.

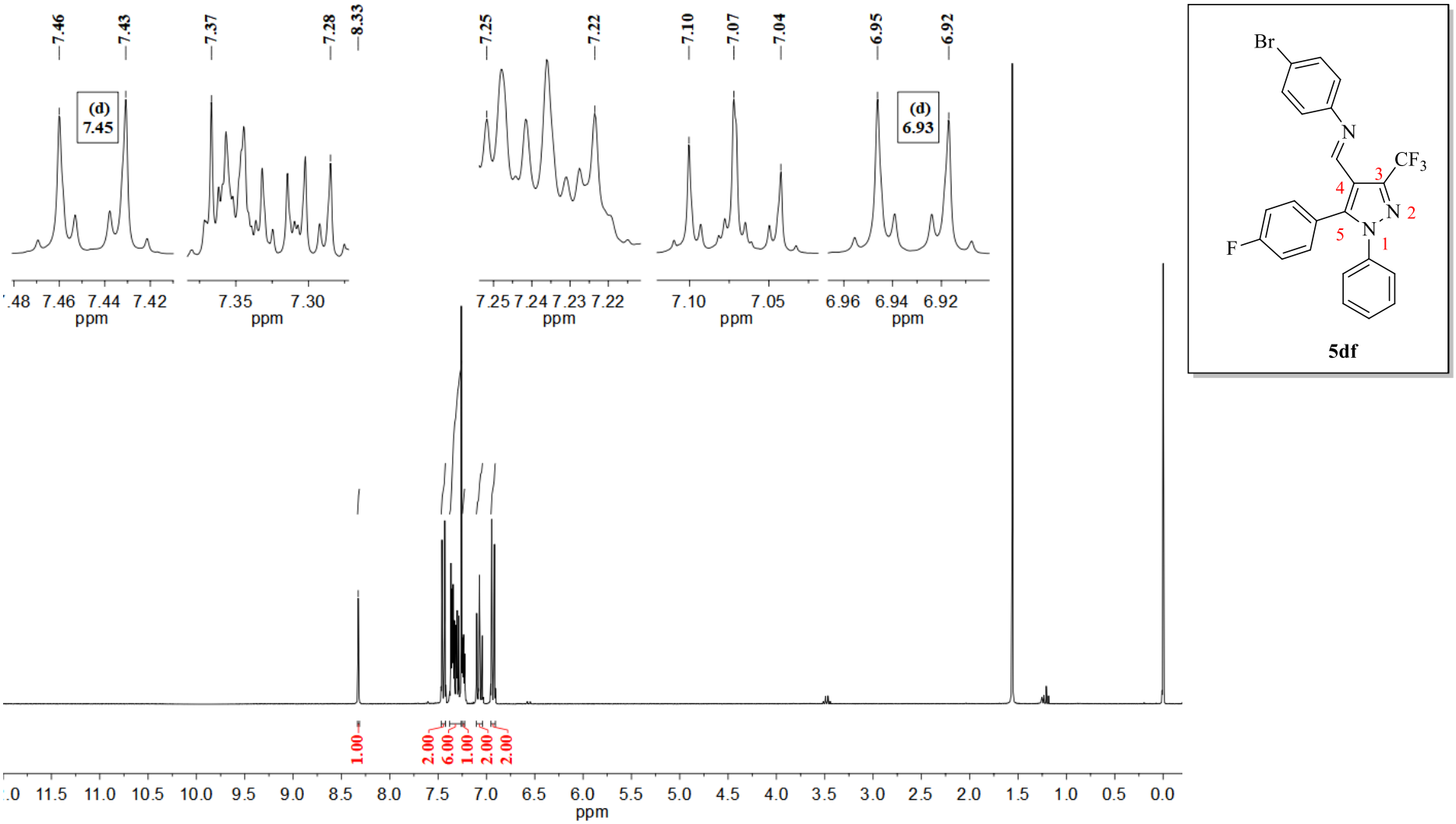


Figure S86 – ^{1}H NMR spectrum of compound **5df** in $CDCl_3$ at 300.06 MHz.

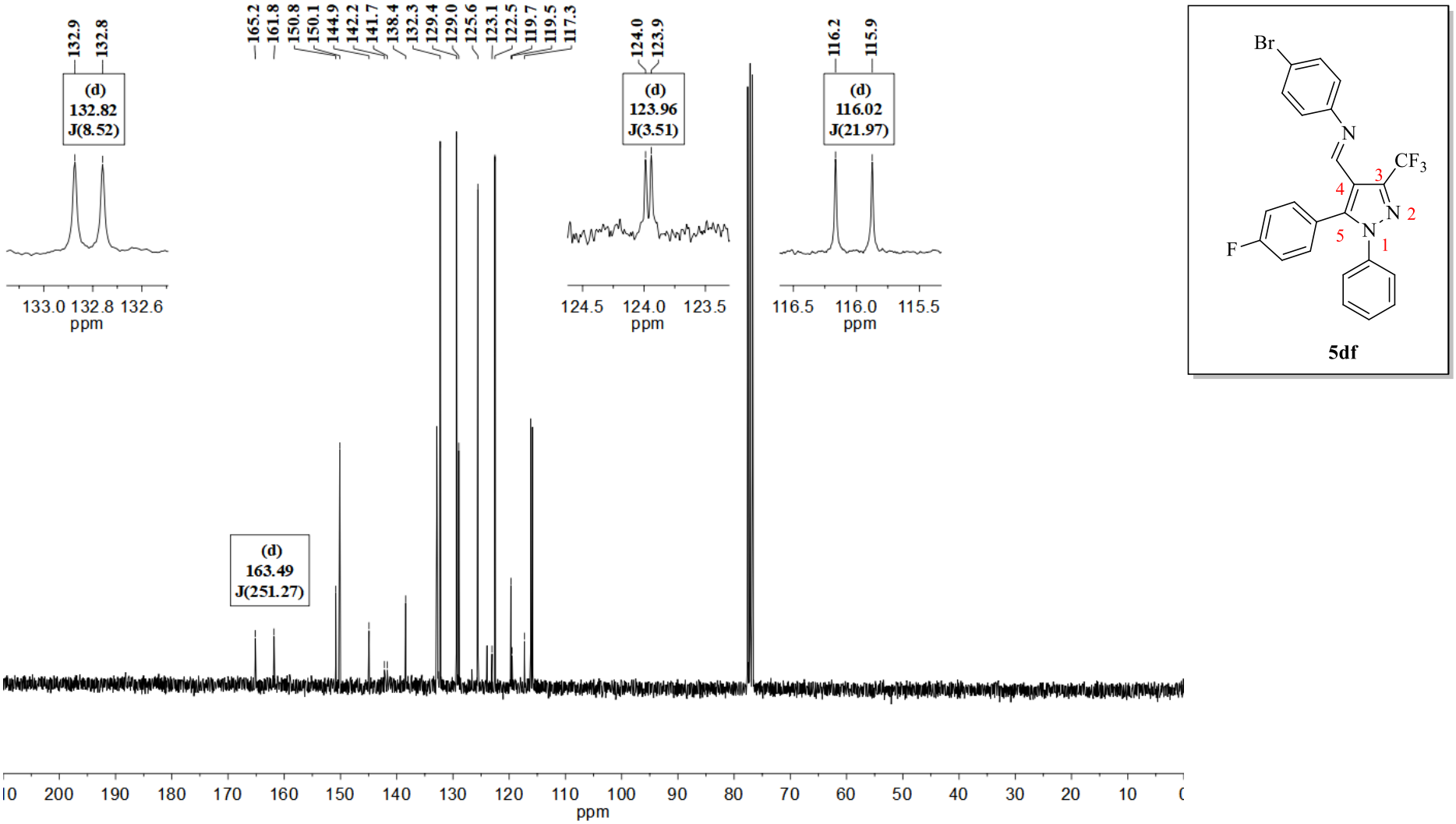


Figure S87 – ^{13}C NMR spectrum of compound **5df** in $CDCl_3$ at 75.45 MHz.

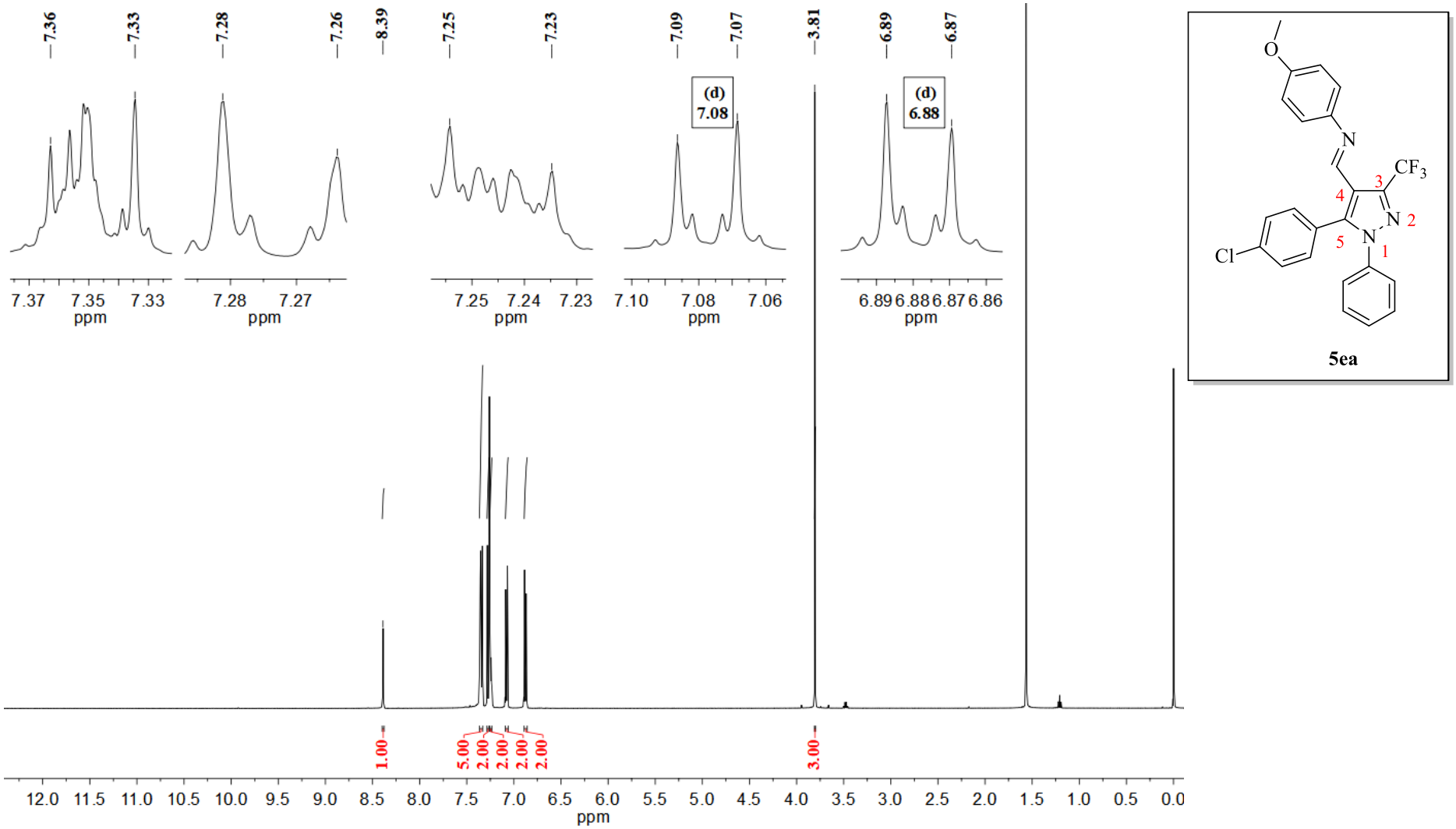
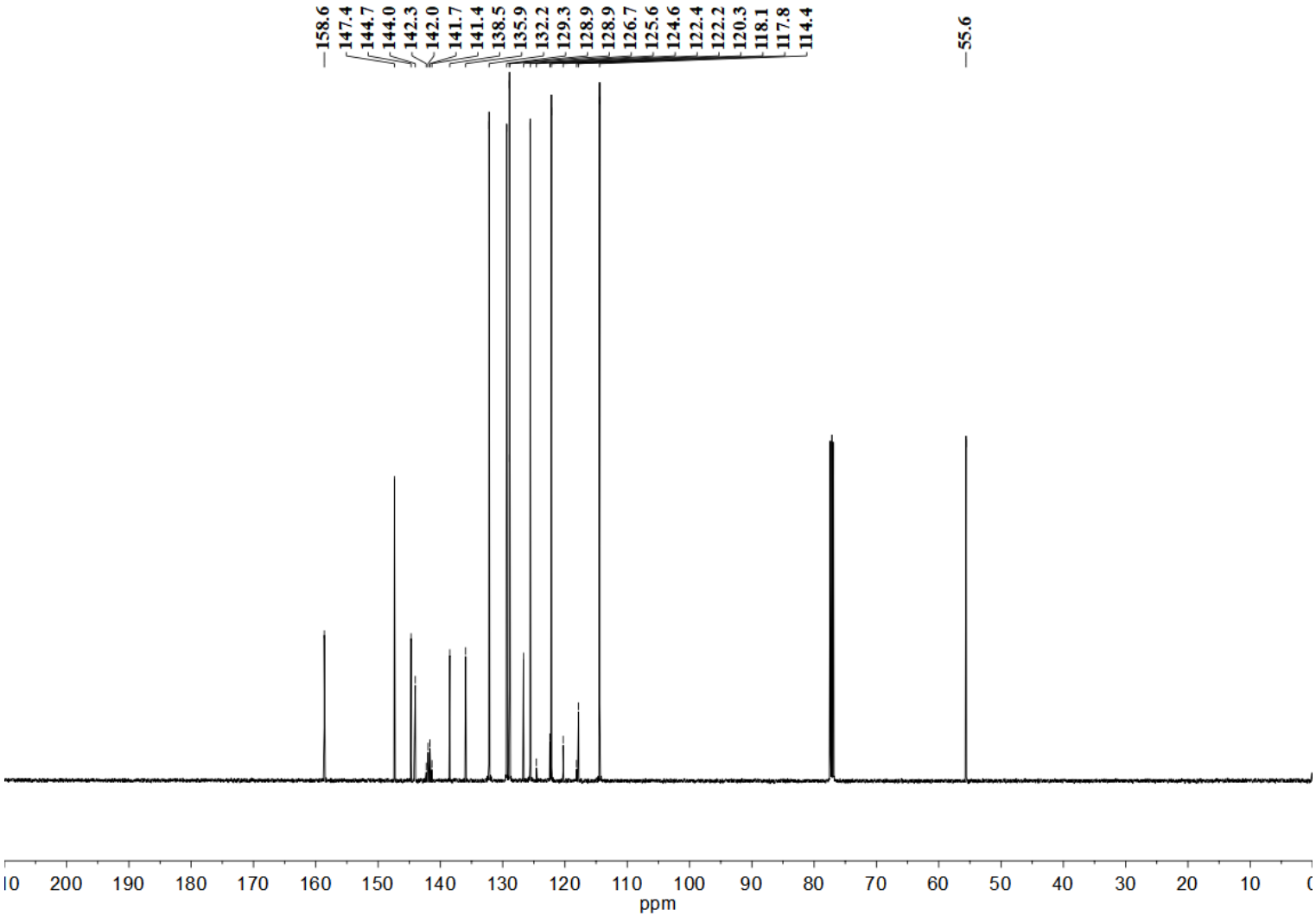


Figure S88– ^{1}H NMR spectrum of compound **5ea** in $CDCl_3$ at 500.13 MHz.



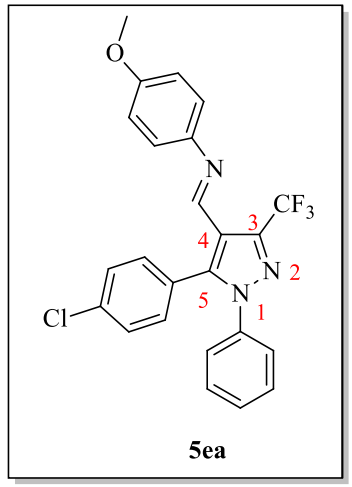


Figure S89 – ^{13}C NMR spectrum of compound **5ea** in $CDCl_3$ at 125.76 MHz.

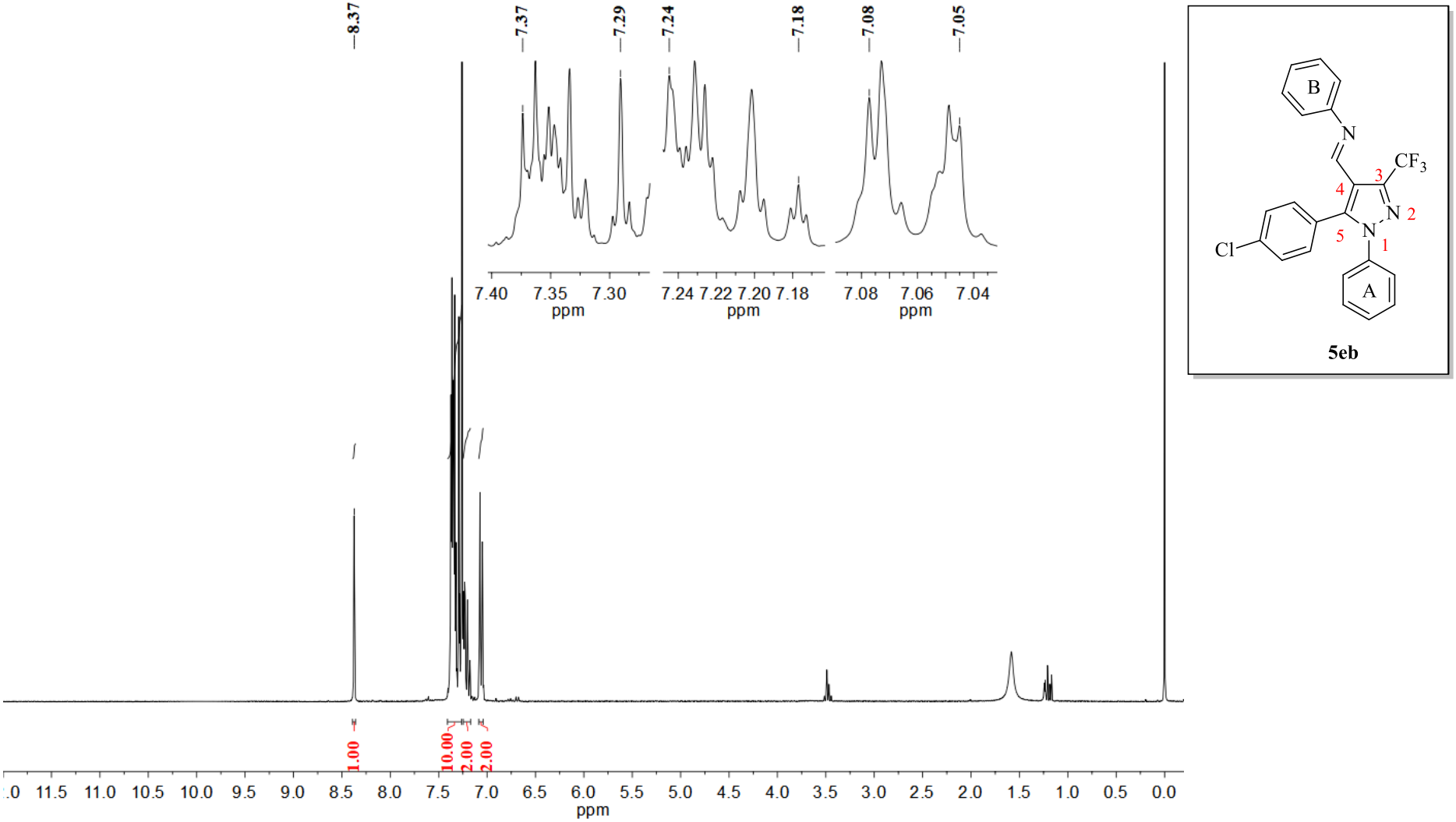
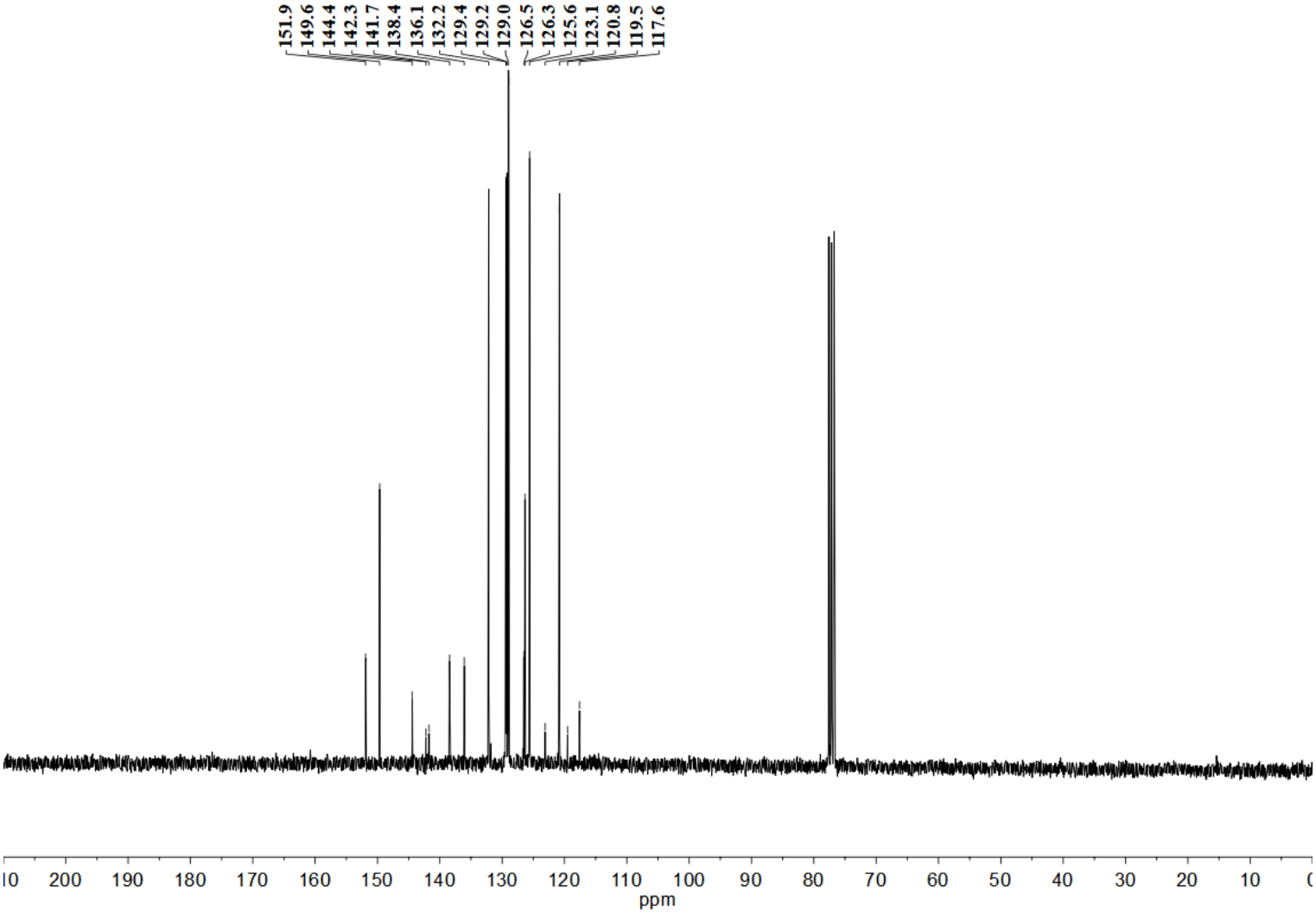


Figure S90 – ^{1}H NMR spectrum of compound **5eb** in $CDCl_3$ at 300.06 MHz.



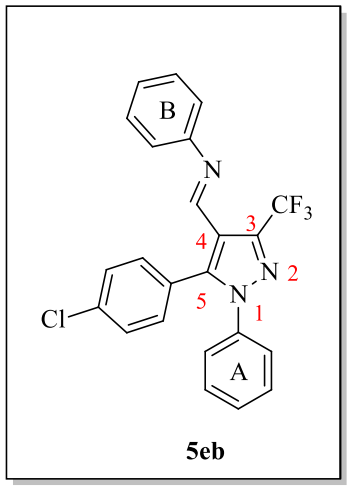


Figure S91 – ^{13}C NMR spectrum of compound **5eb** in $CDCl_3$ at 75.45 MHz.

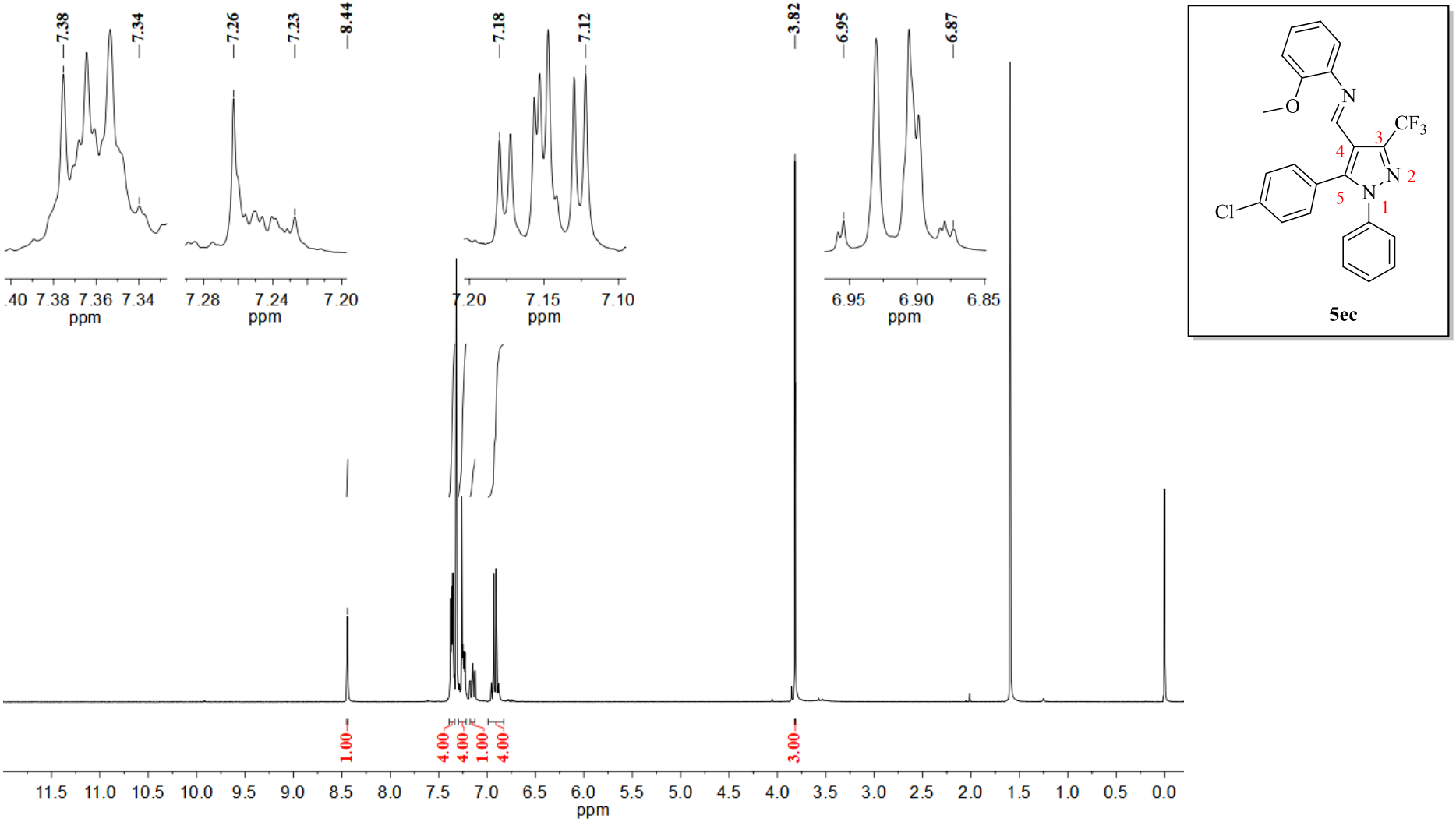


Figure S92 – ^{1}H NMR spectrum of compound **5ec** in $CDCl_3$ at 300.06 MHz.

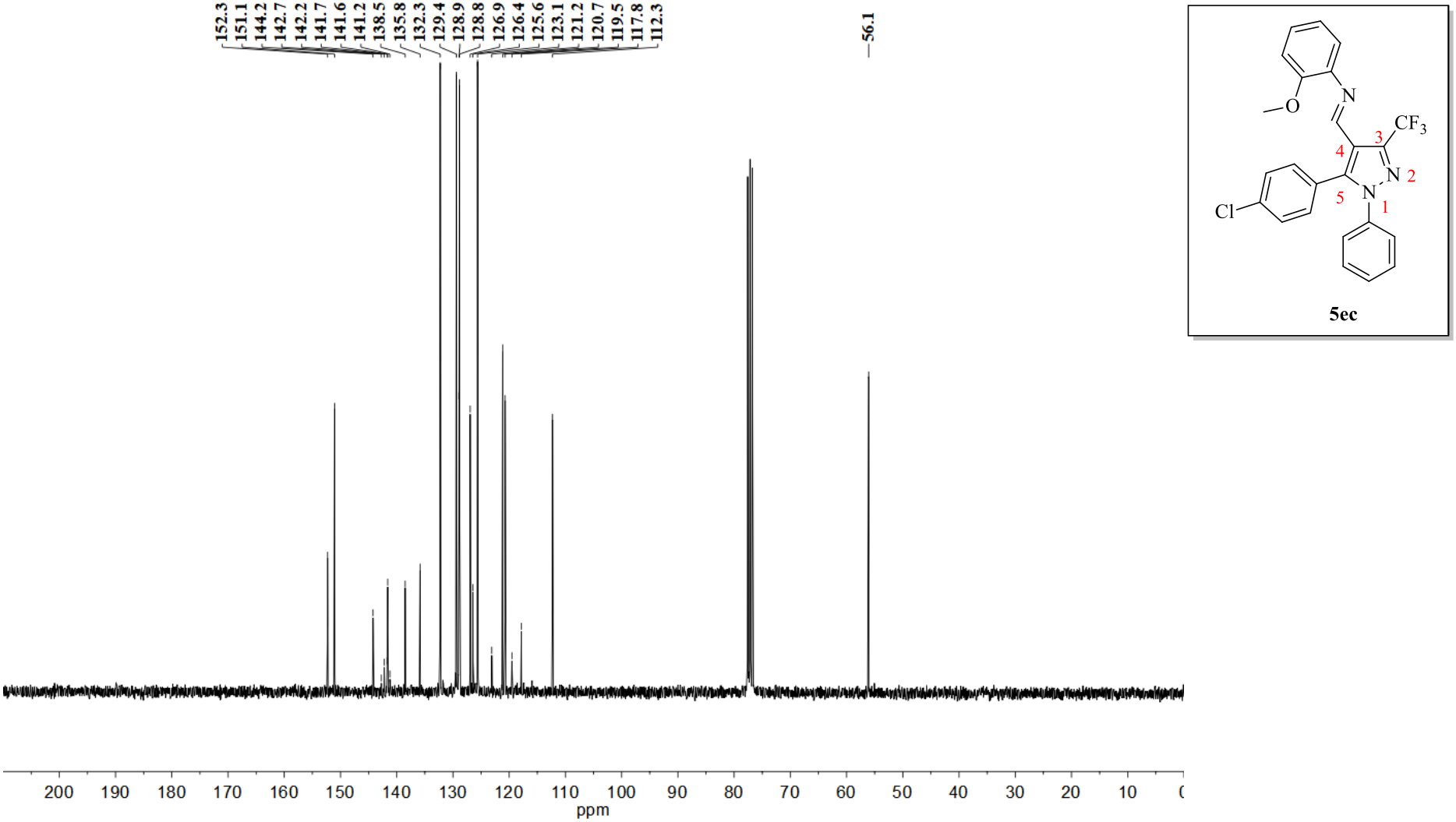


Figure S93 – ^{13}C NMR spectrum of compound **5ec** in $CDCl_3$ at 75.45 MHz.

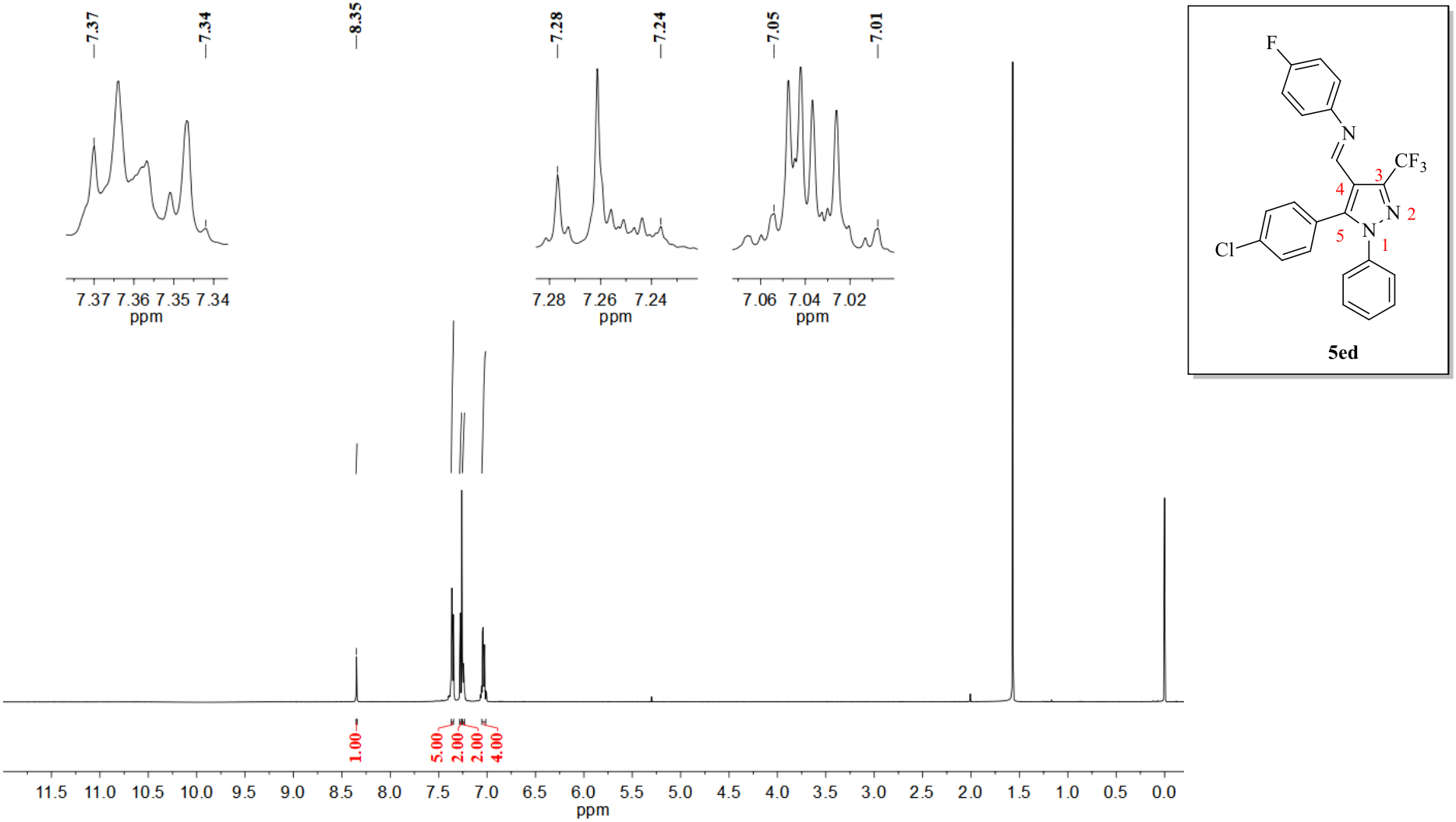


Figure S94 – ^{1}H NMR spectrum of compound **5ed** in $CDCl_3$ at 300.06 MHz.

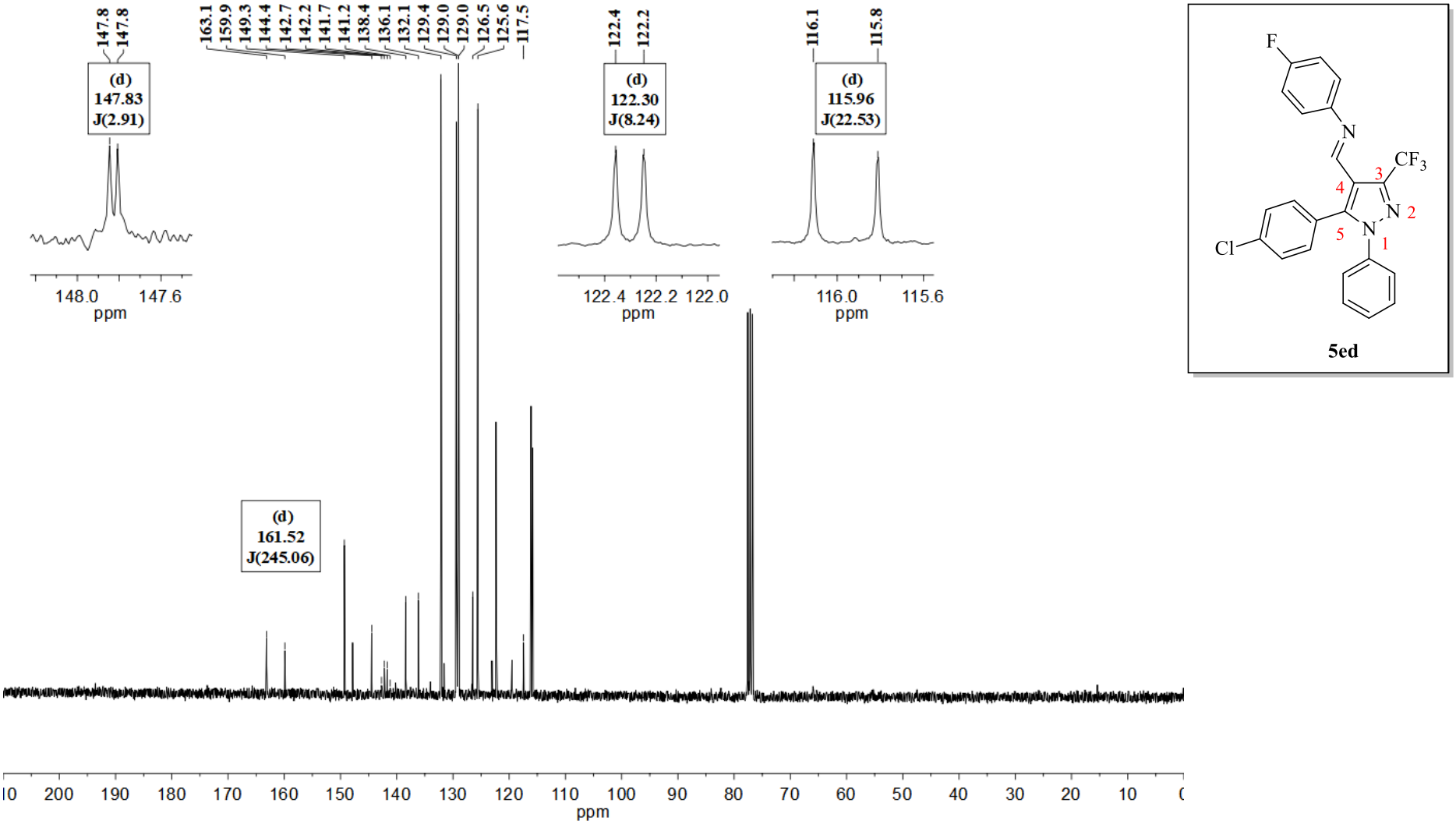


Figure S95 – ^{13}C NMR spectrum of compound **5ed** in $CDCl_3$ at 75.45 MHz.

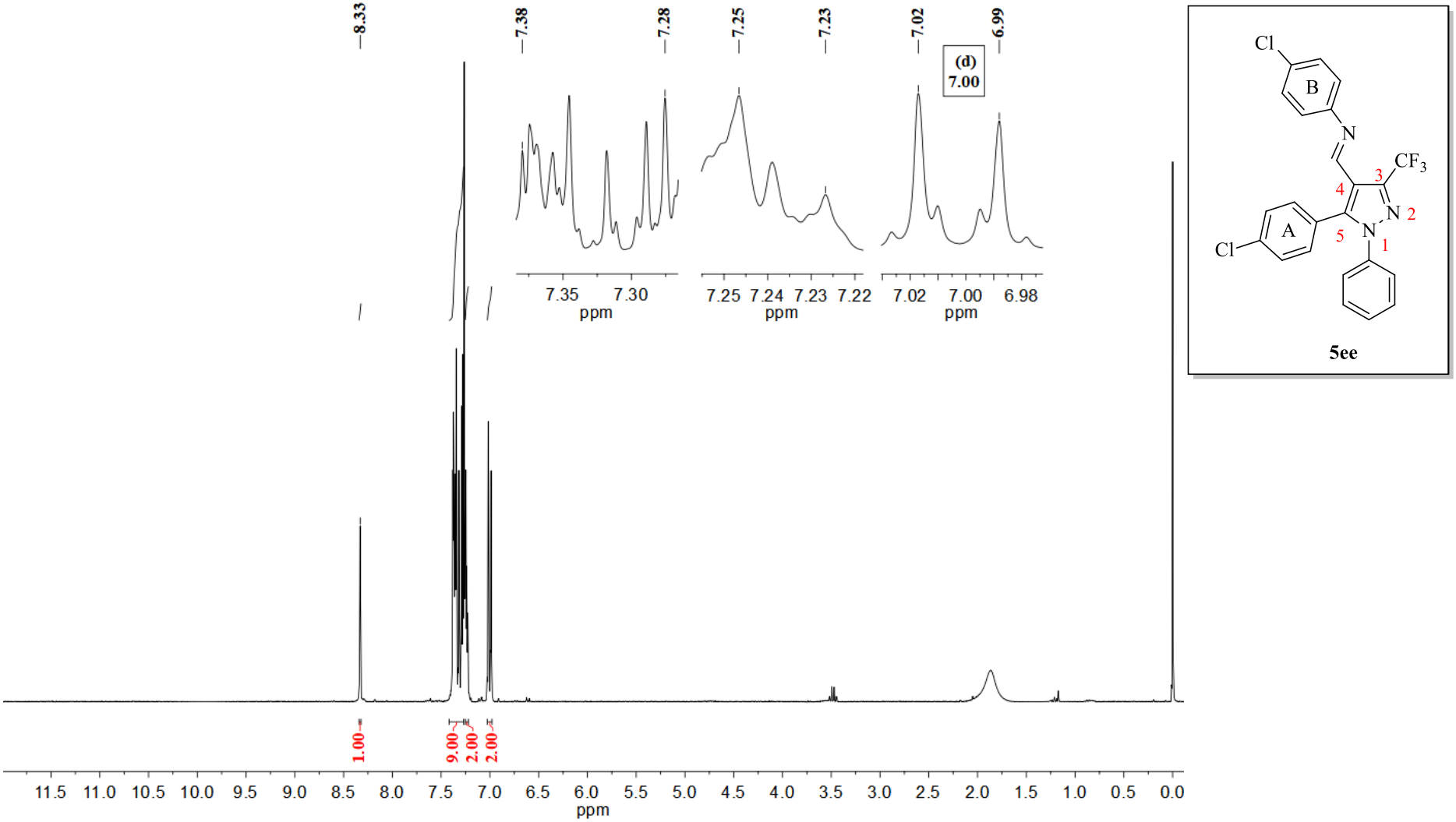
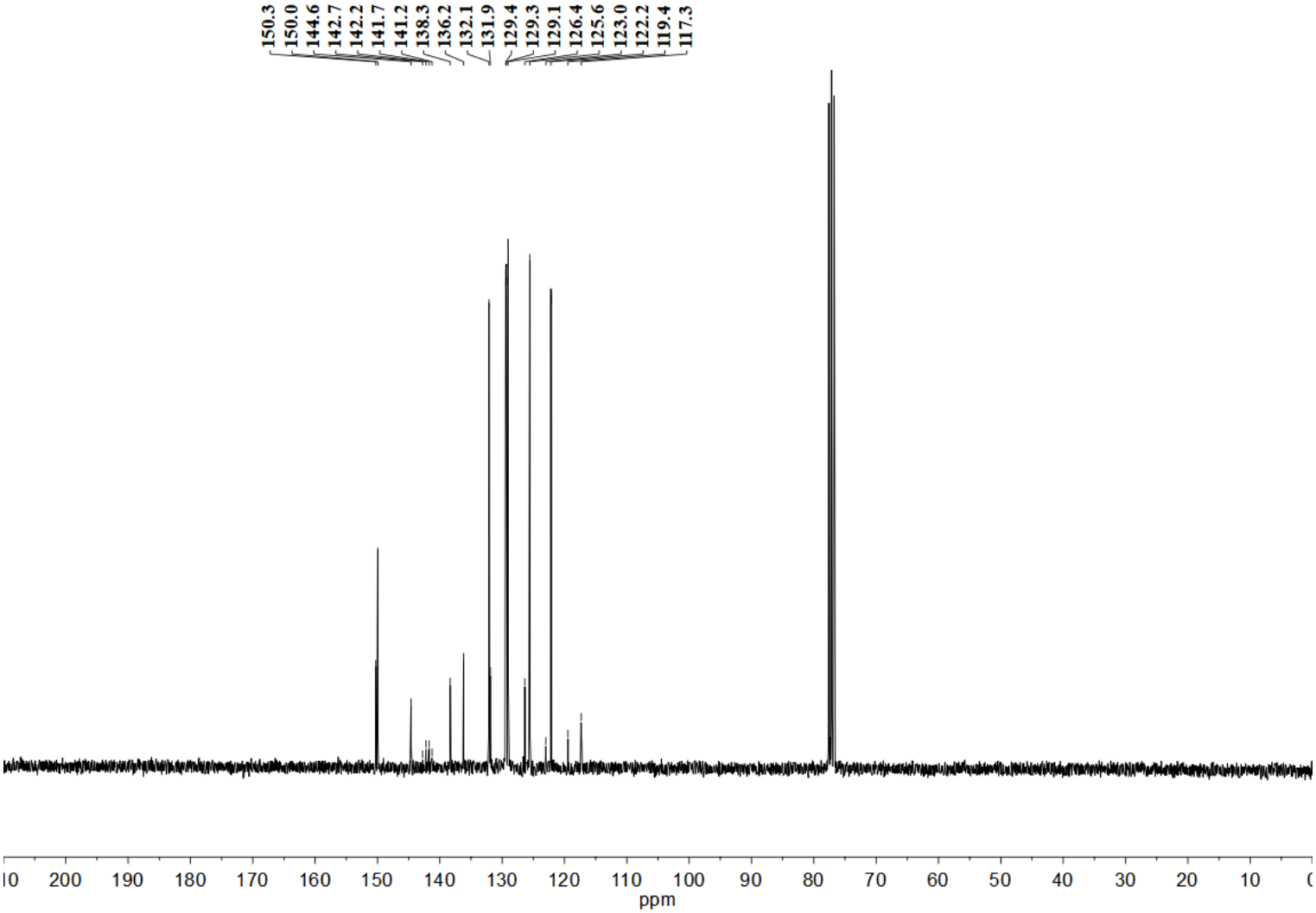


Figure S96 – ^{1}H NMR spectrum of compound **5ee** in $CDCl_3$ at 300.06 MHz.



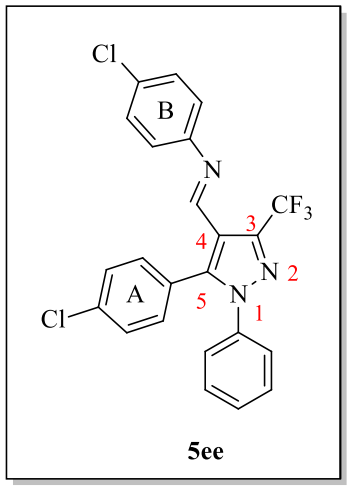


Figure S97 – ^{13}C NMR spectrum of compound **5ee** in $CDCl_3$ at 75.45 MHz.

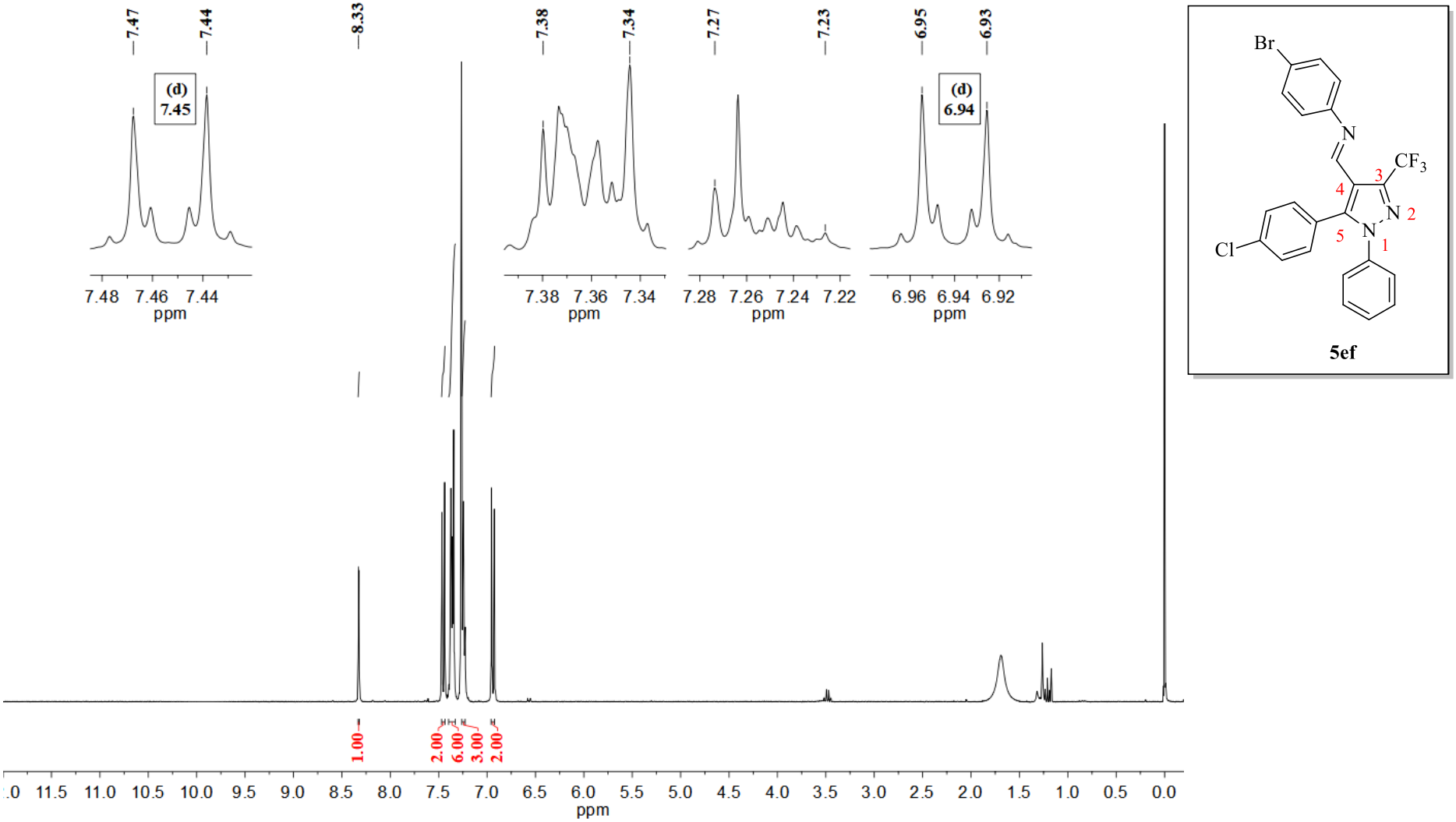


Figure S98 – ^{1}H NMR spectrum of compound **5ef** in $CDCl_3$ at 300.06 MHz.

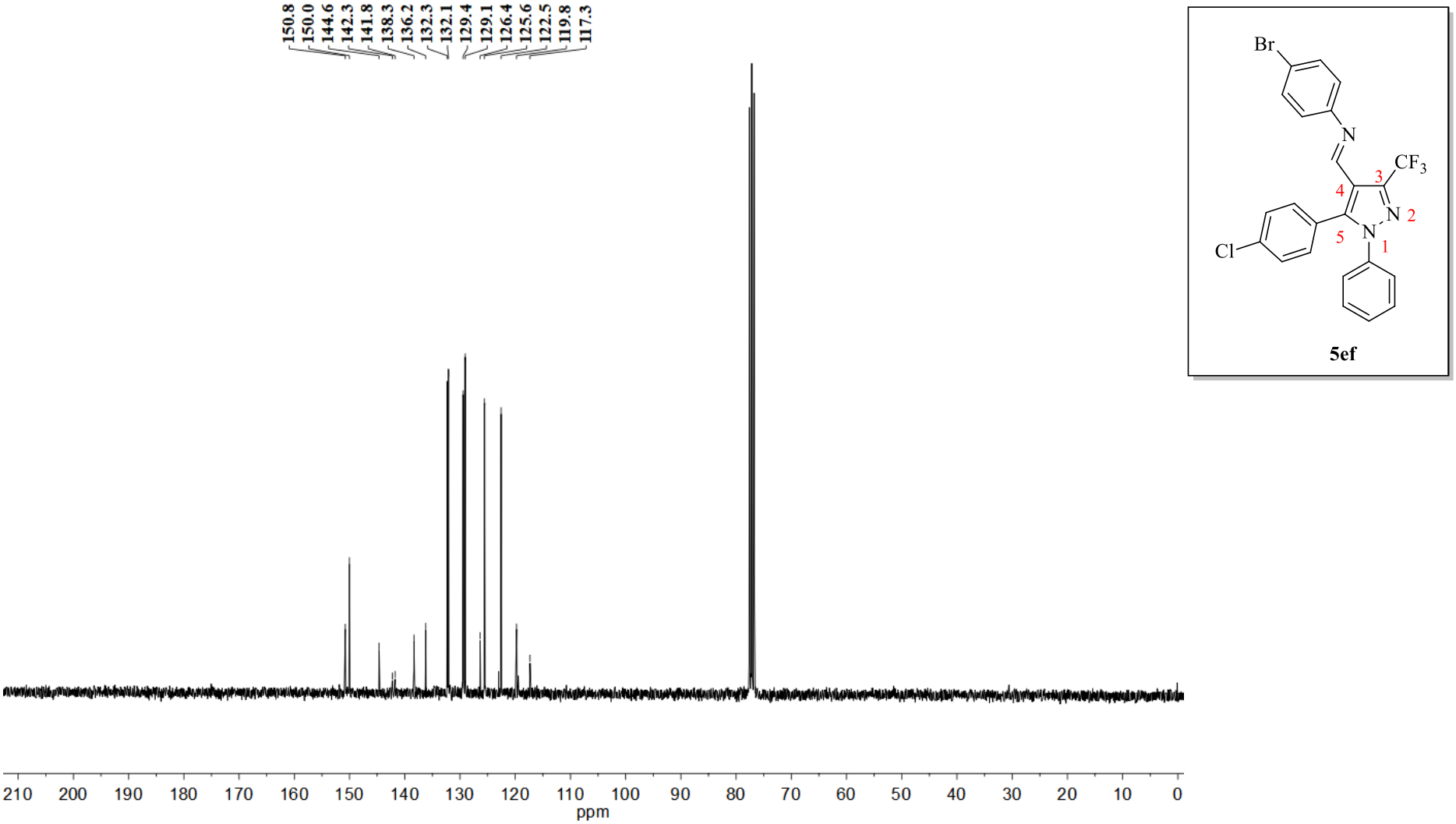


Figure S99 – ^{13}C NMR spectrum of compound **5ef** in $CDCl_3$ at 75.45 MHz.

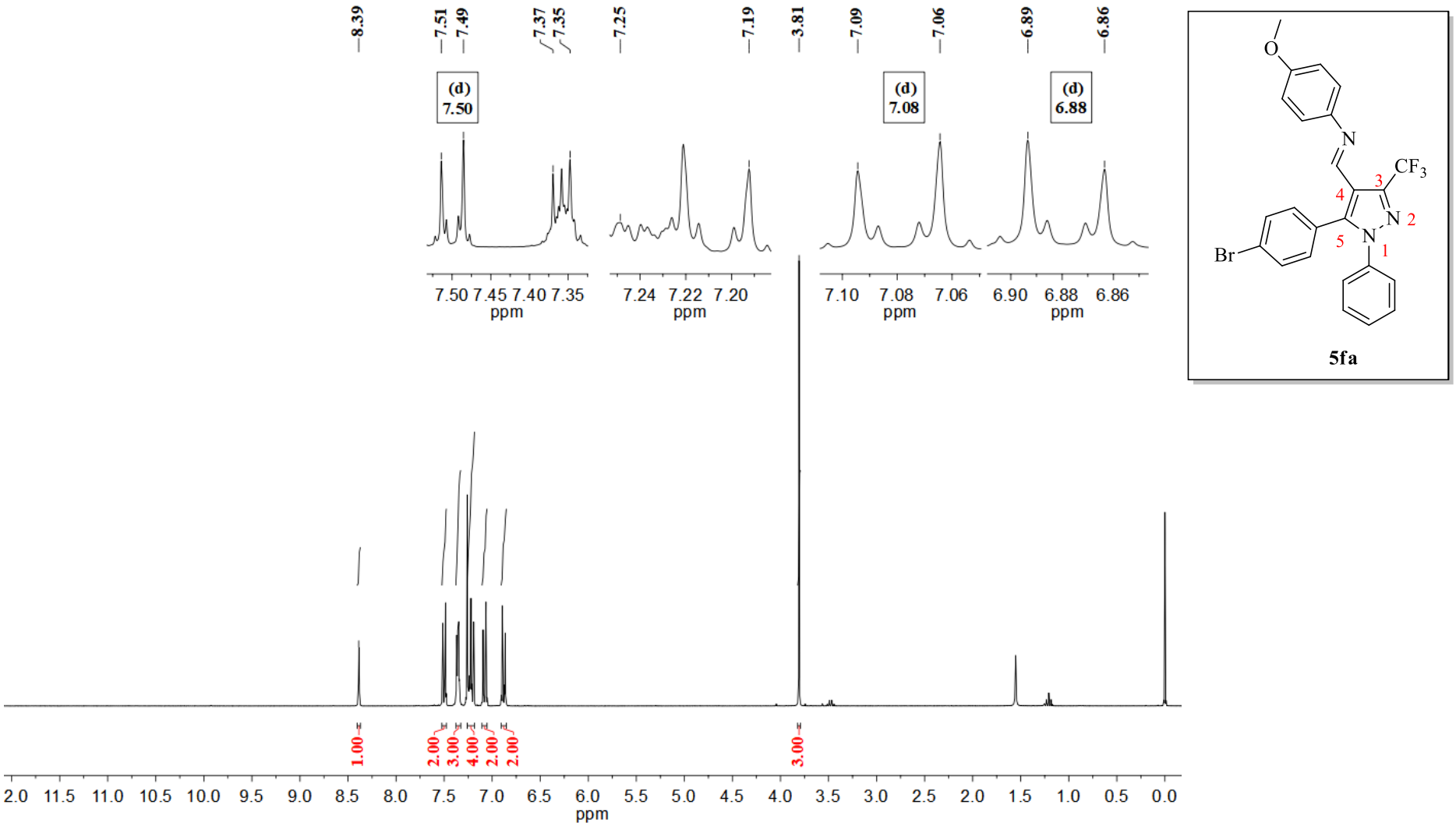
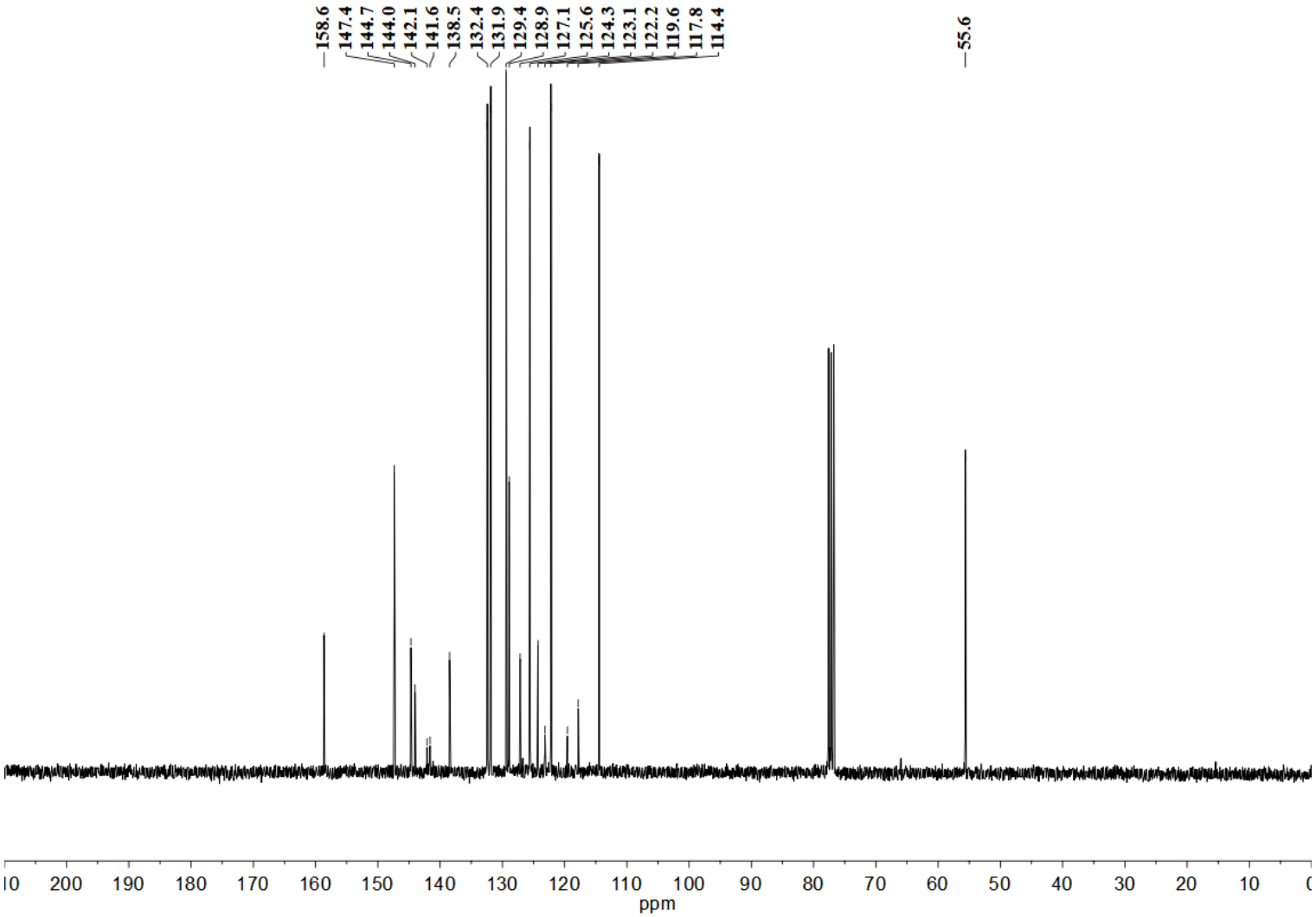
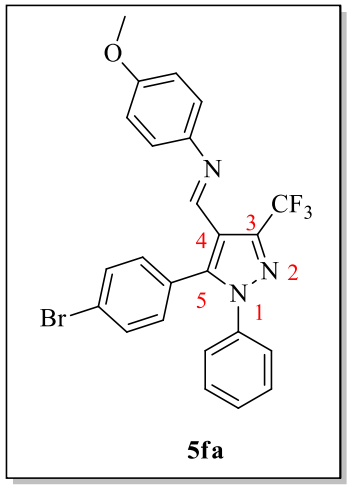


Figure S100 – ^{1}H NMR spectrum of compound **5fa** in $CDCl_3$ at 300.06 MHz.





5fa

Figure S101 – ^{13}C NMR spectrum of compound **5fa** in $CDCl_3$ at 75.45 MHz.

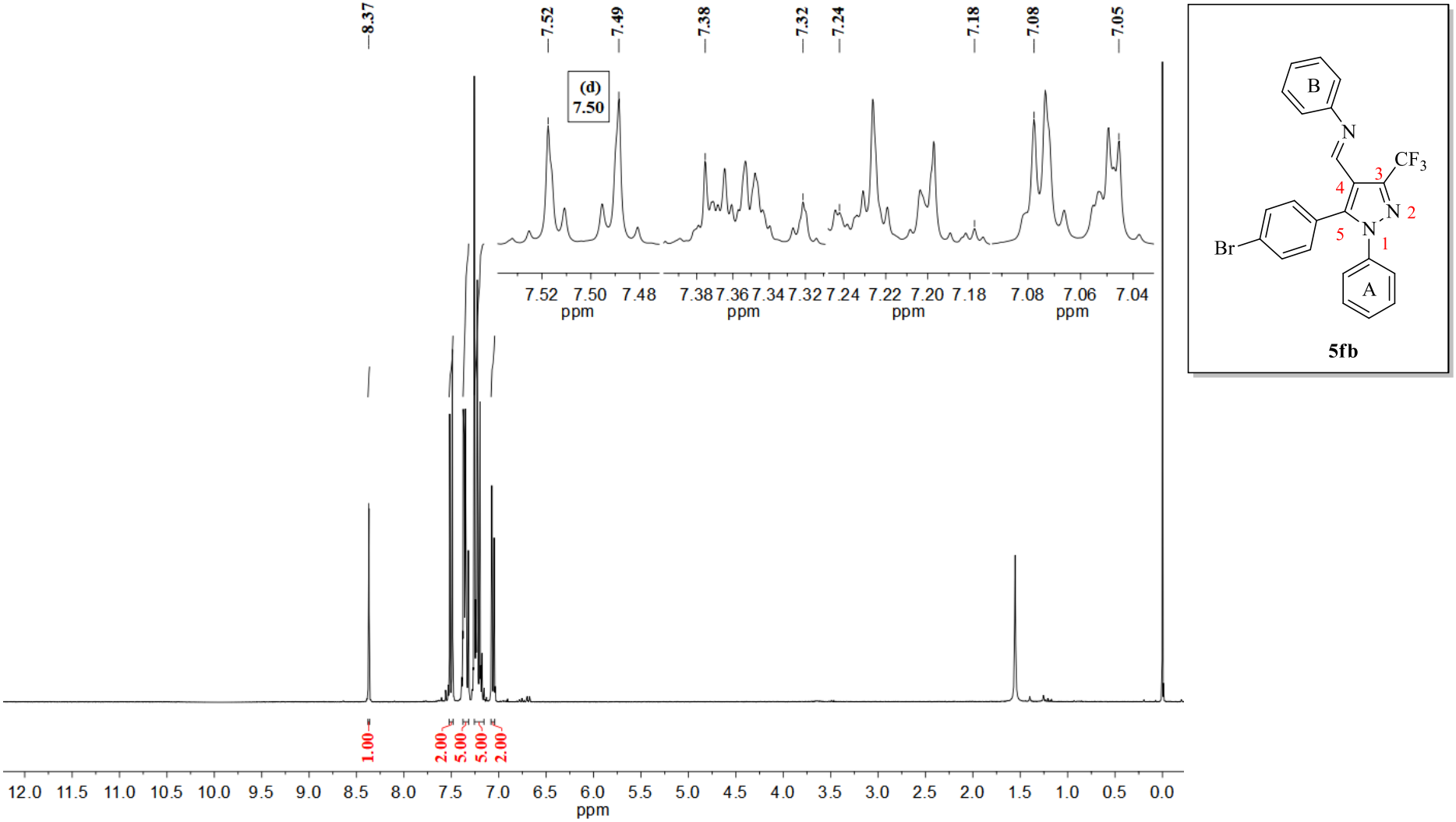
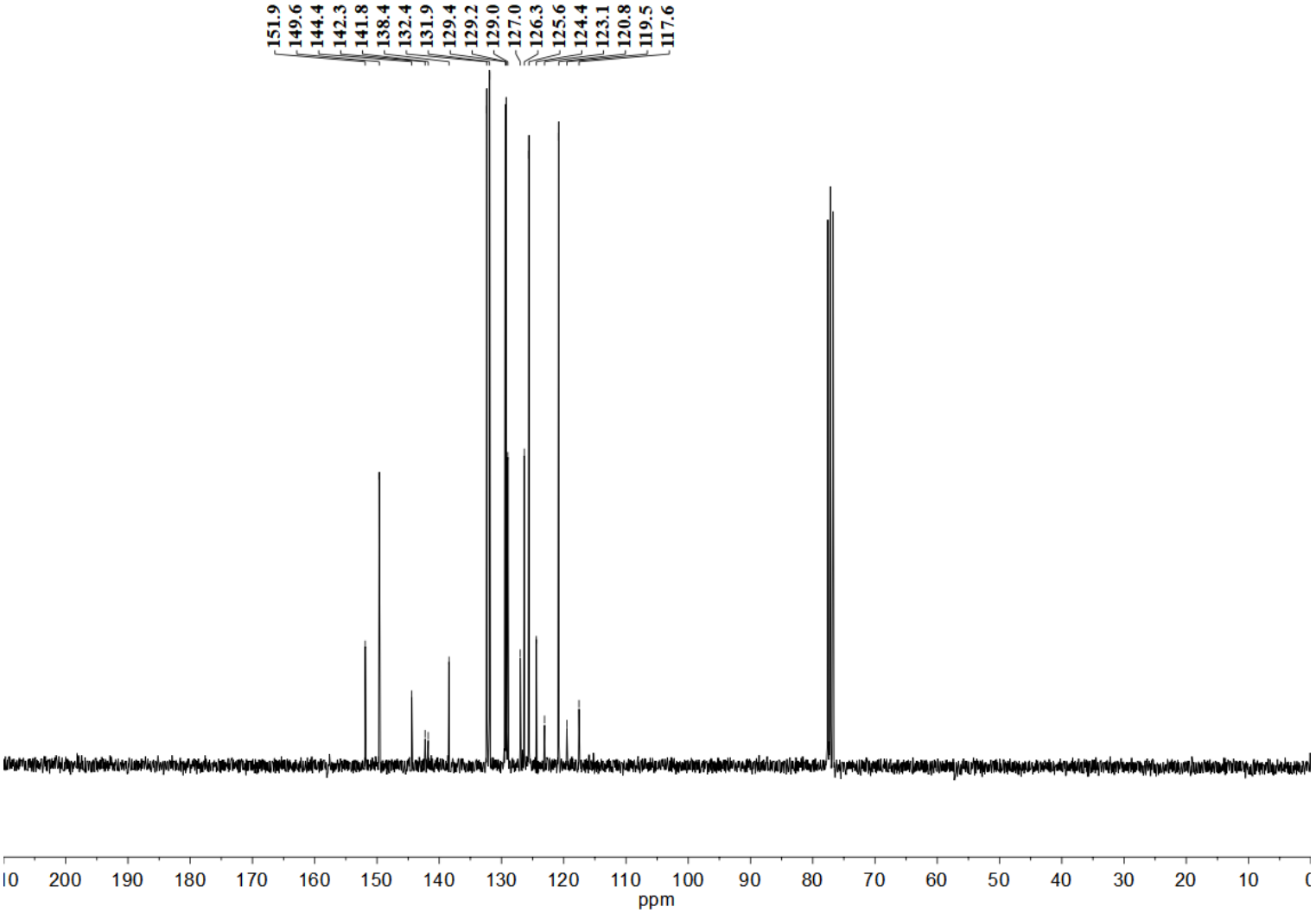
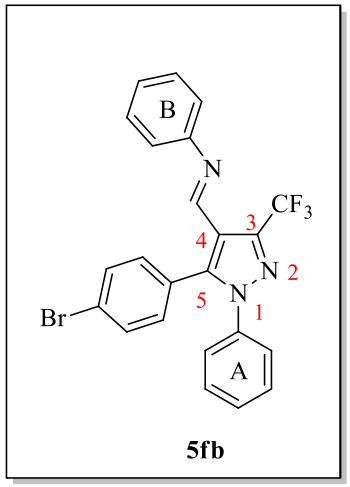


Figure S102 – ^{1}H NMR spectrum of compound **5fb** in $CDCl_3$ at 300.06 MHz.





5fb

Figure S103 – ^{13}C NMR spectrum of compound **5fb** in $CDCl_3$ at 75.45 MHz.

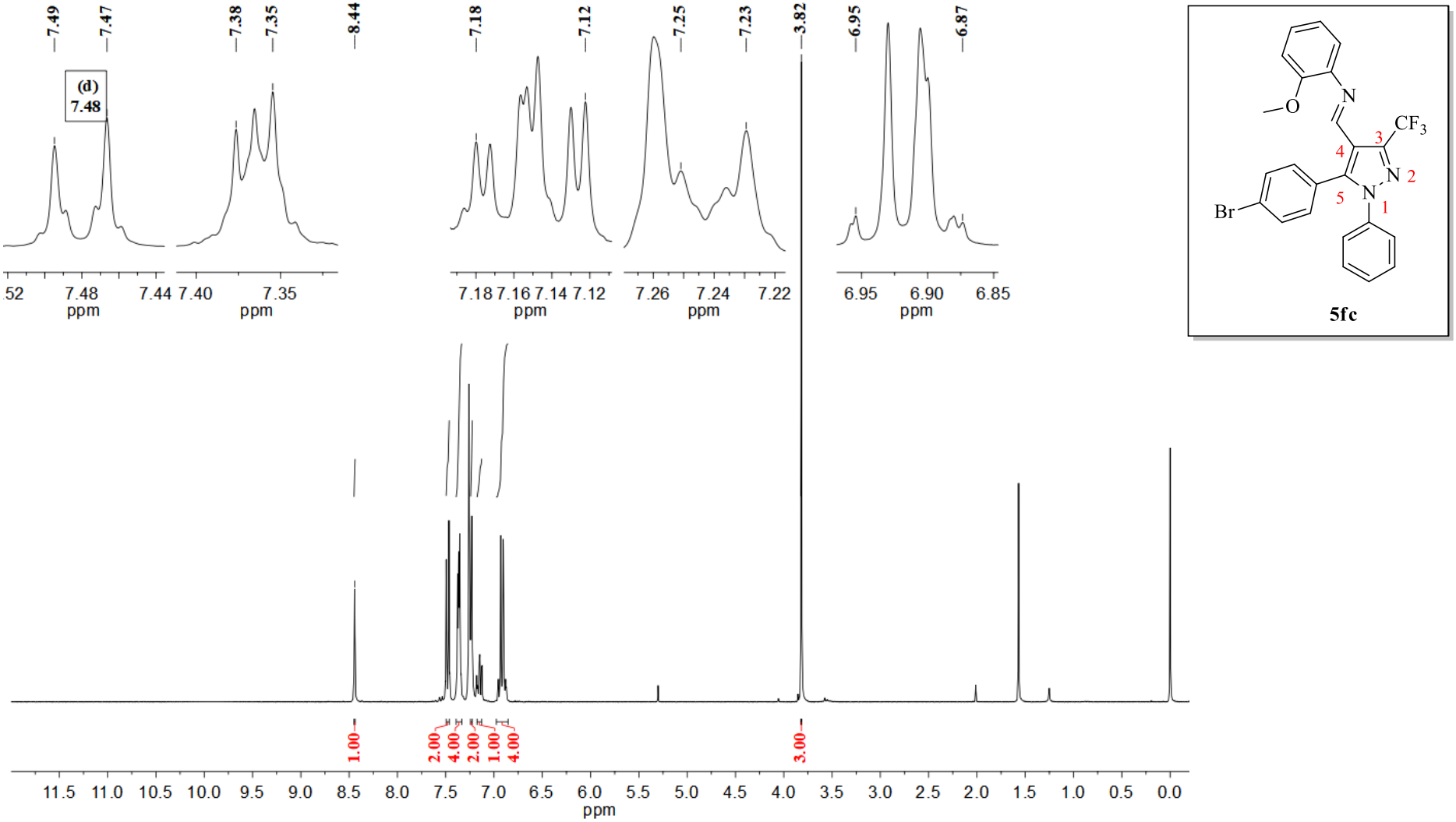
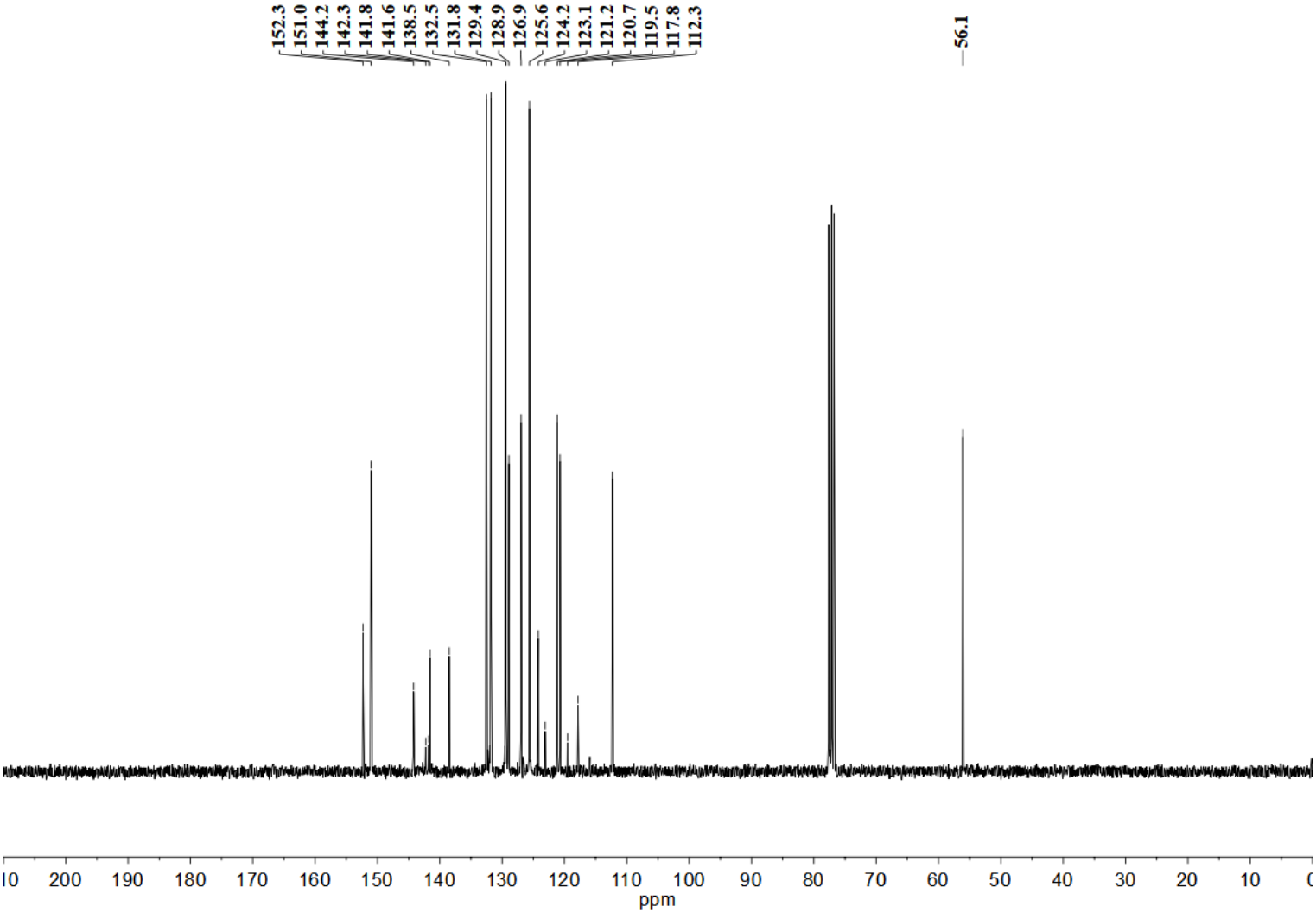
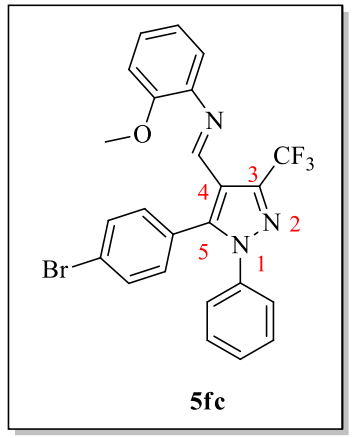


Figure S104 – ^{1}H NMR spectrum of compound **5fc** in $CDCl_3$ at 300.06 MHz.





5fc

Figure S105 – ^{13}C NMR spectrum of compound **5fc** in $CDCl_3$ at 75.45 MHz.

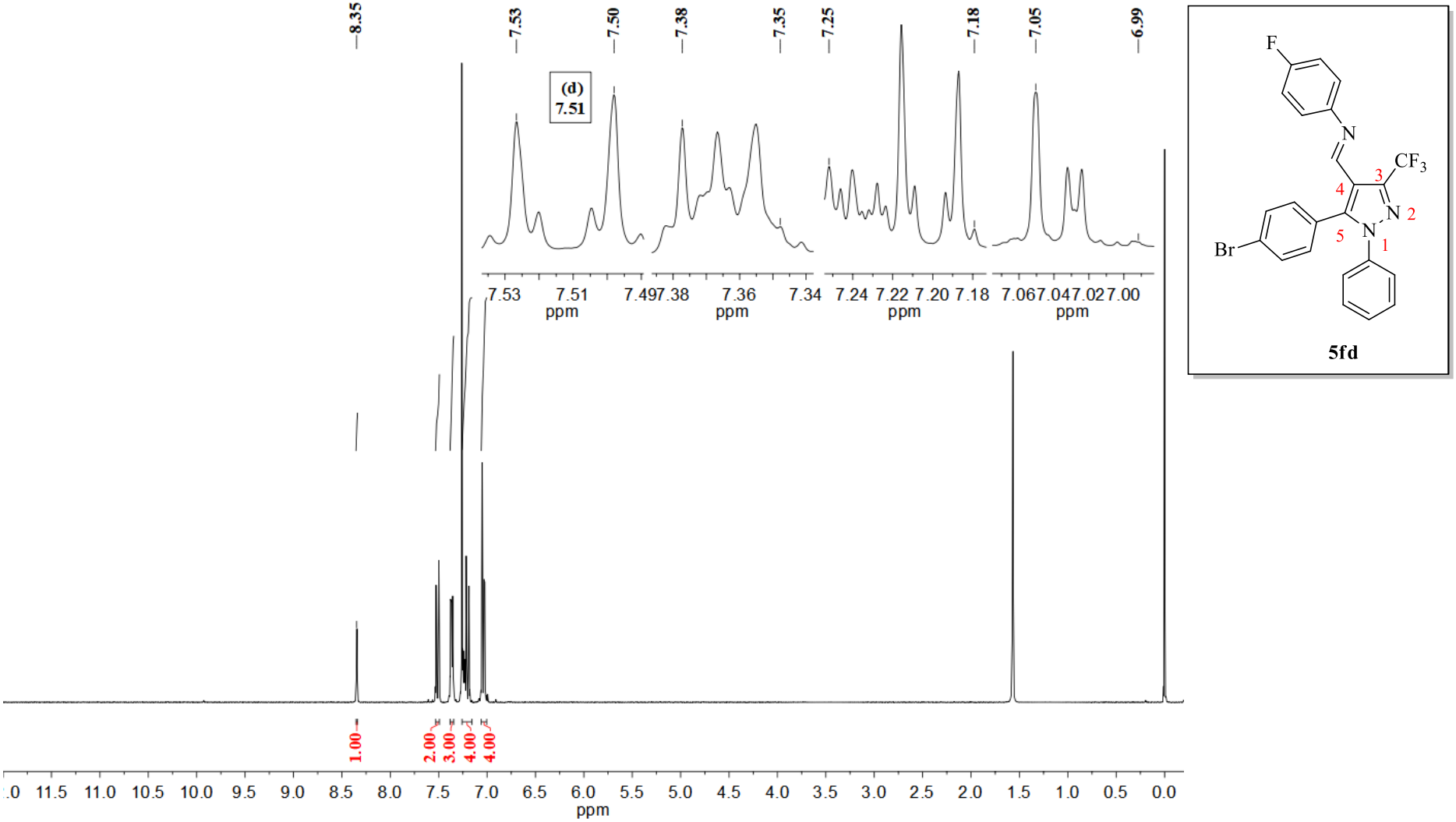


Figure S106 – ^{1}H NMR spectrum of compound **5fd** in $CDCl_3$ at 300.06 MHz.

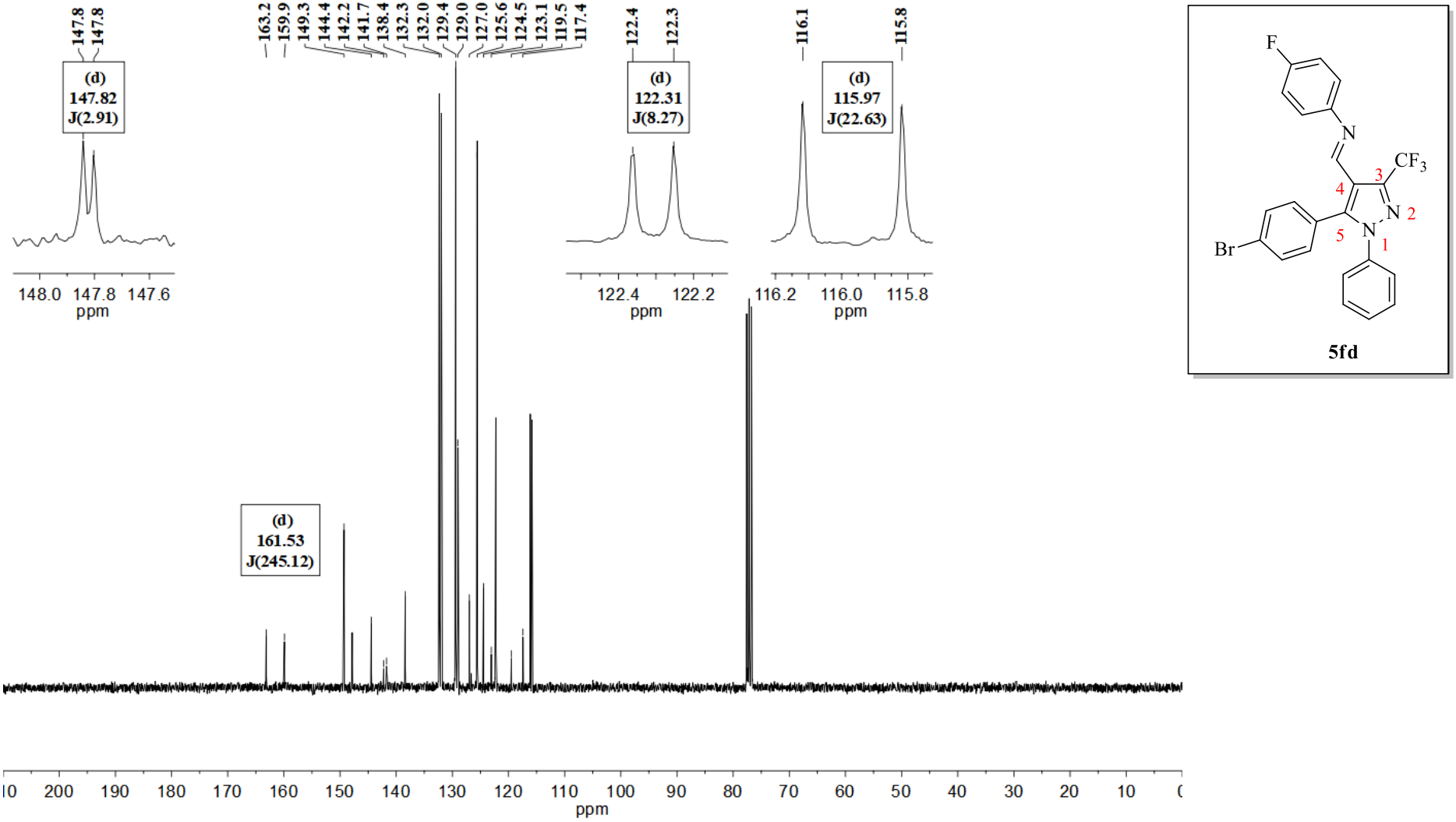


Figure S107 – ^{13}C NMR spectrum of compound **5fd** in $CDCl_3$ at 75.45 MHz.

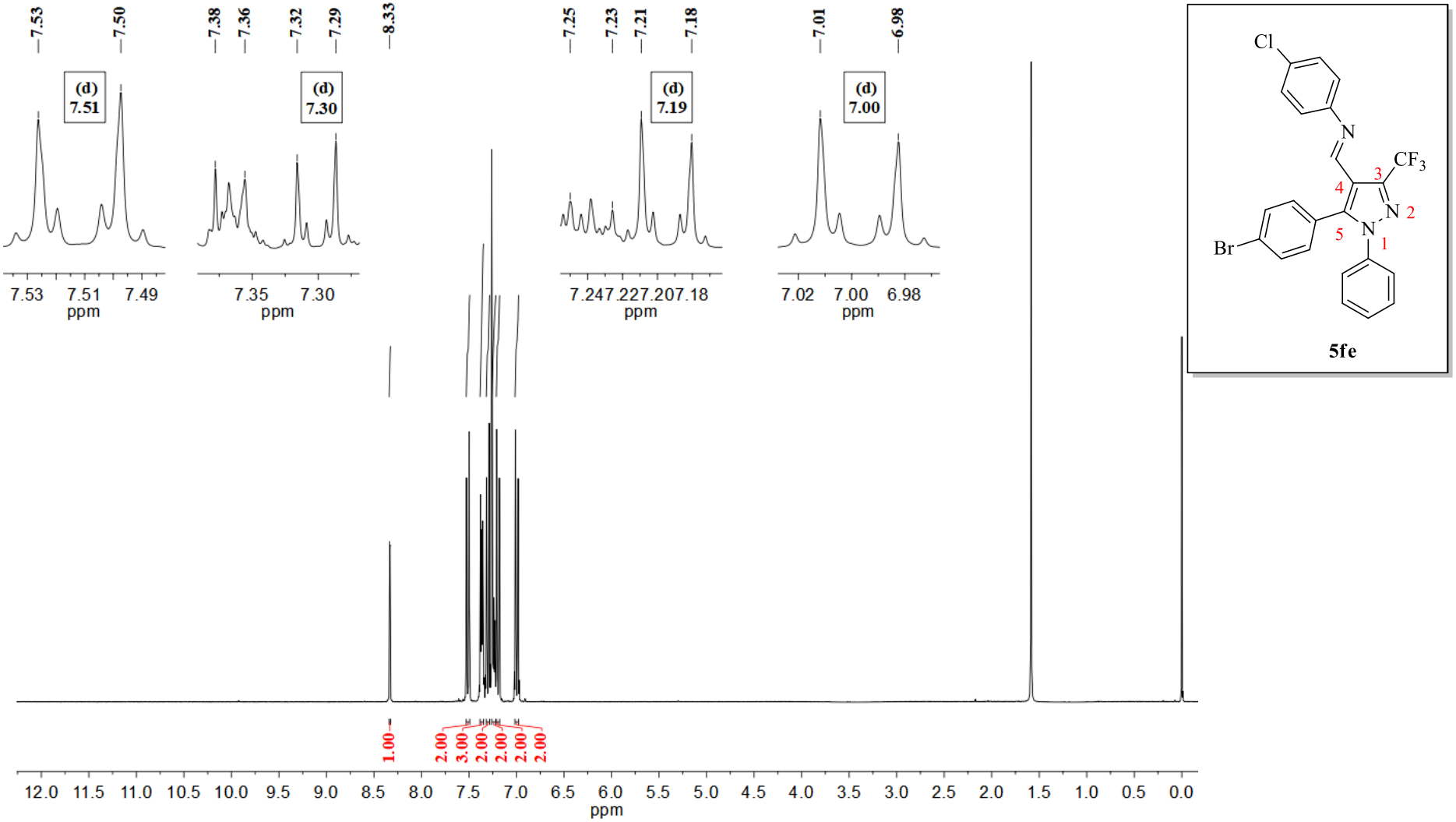
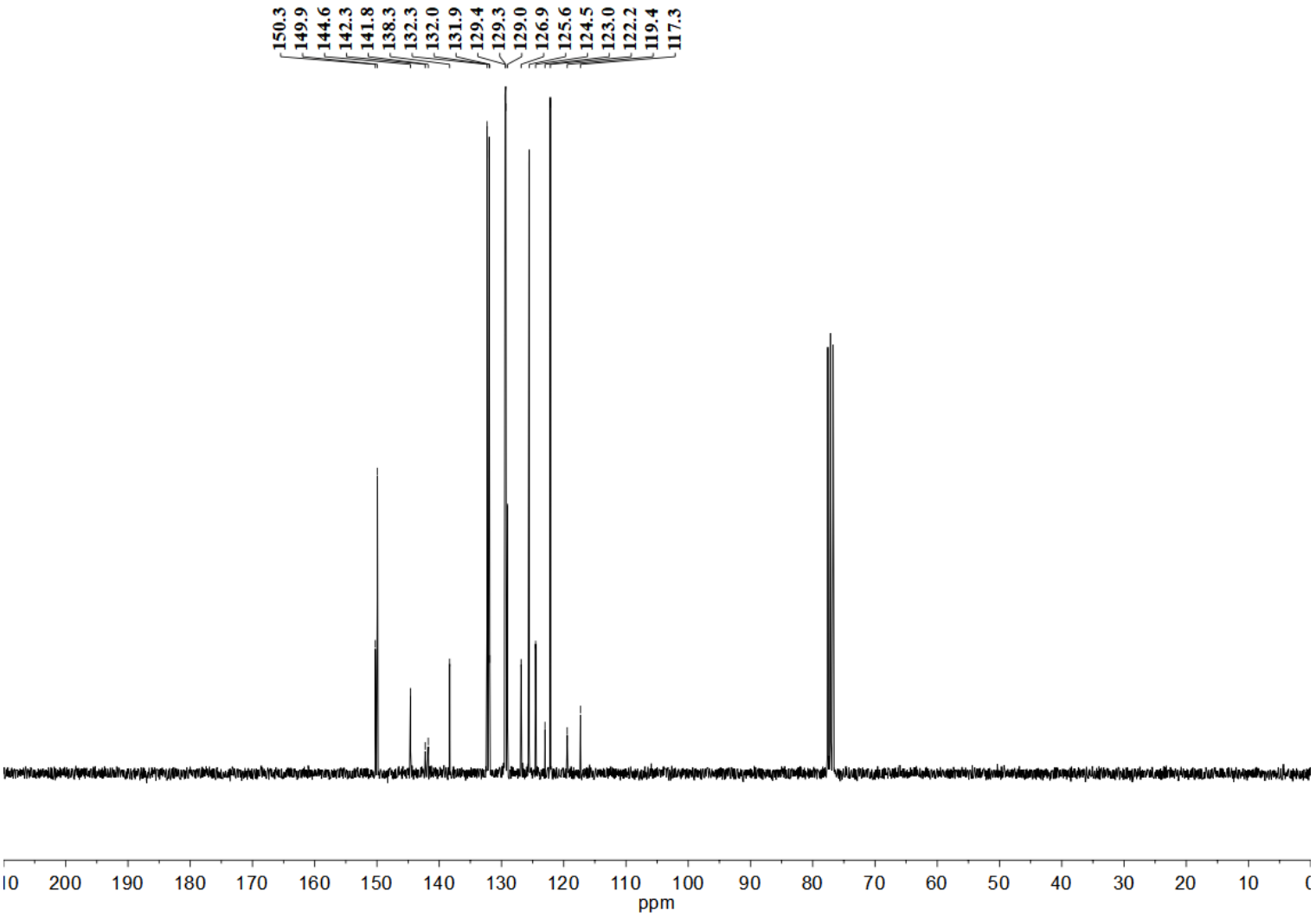


Figure S108 – ^{1}H NMR spectrum of compound **5fe** in $CDCl_3$ at 300.06 MHz.



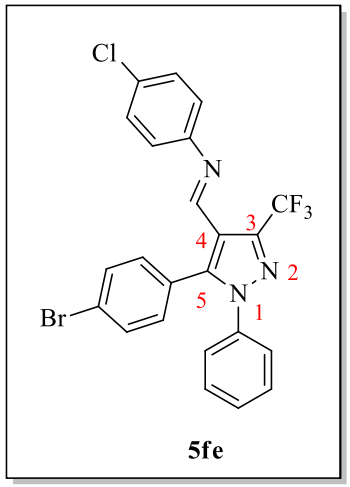


Figure S109 – ^{13}C NMR spectrum of compound **5fe** in $CDCl_3$ at 75.45 MHz.

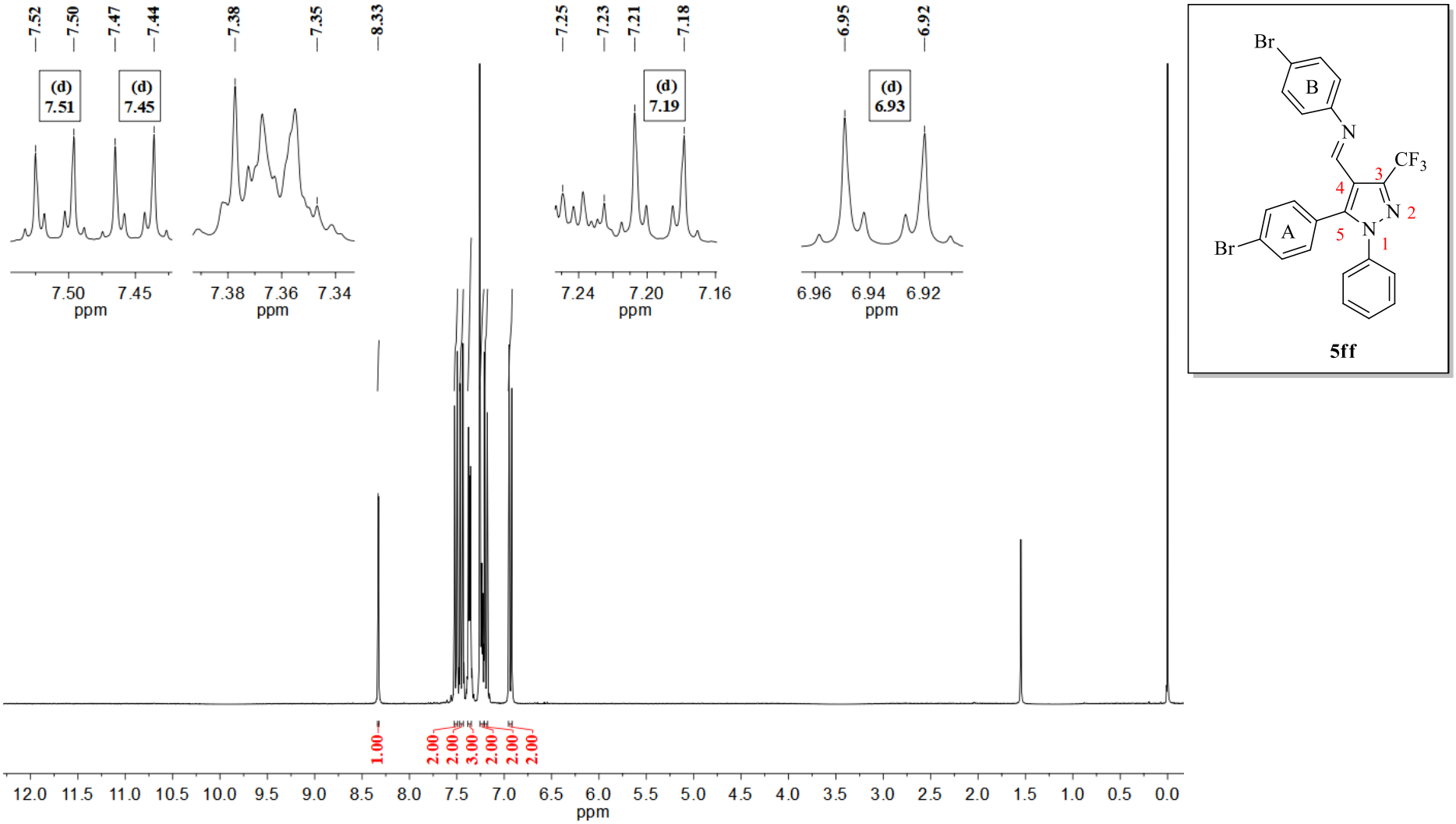
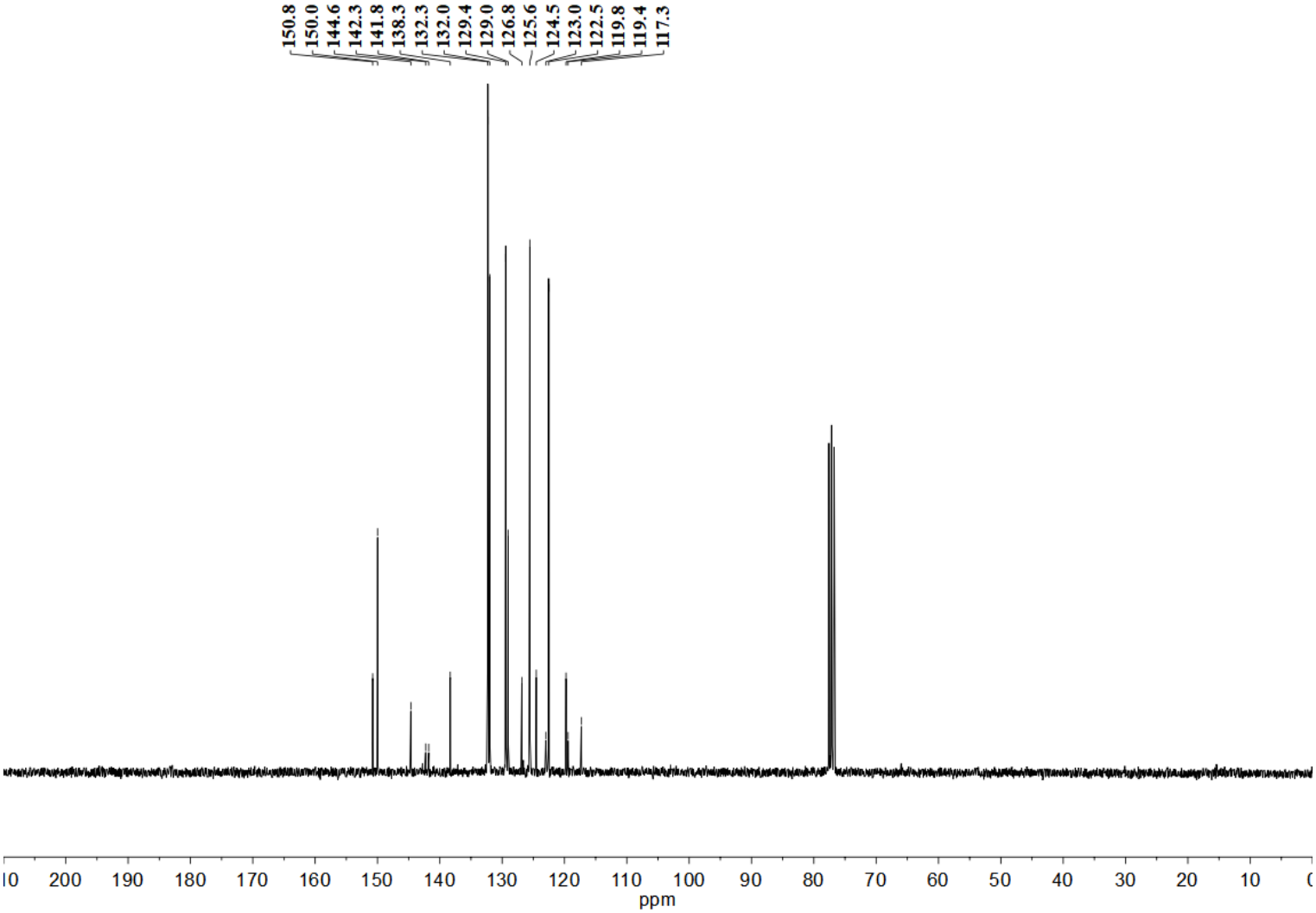


Figure S110 – ^{1}H NMR spectrum of compound **5ff** in $CDCl_3$ at 300.06 MHz.



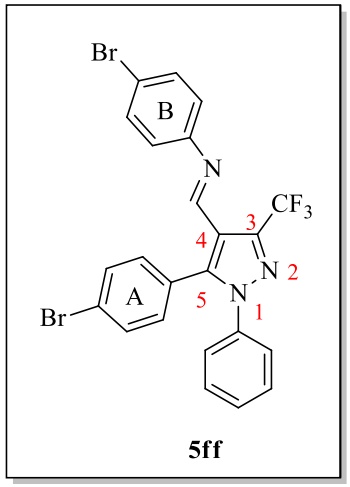


Figure S111 – ^{13}C NMR spectrum of compound **5ff** in $CDCl_3$ at 75.45 MHz.

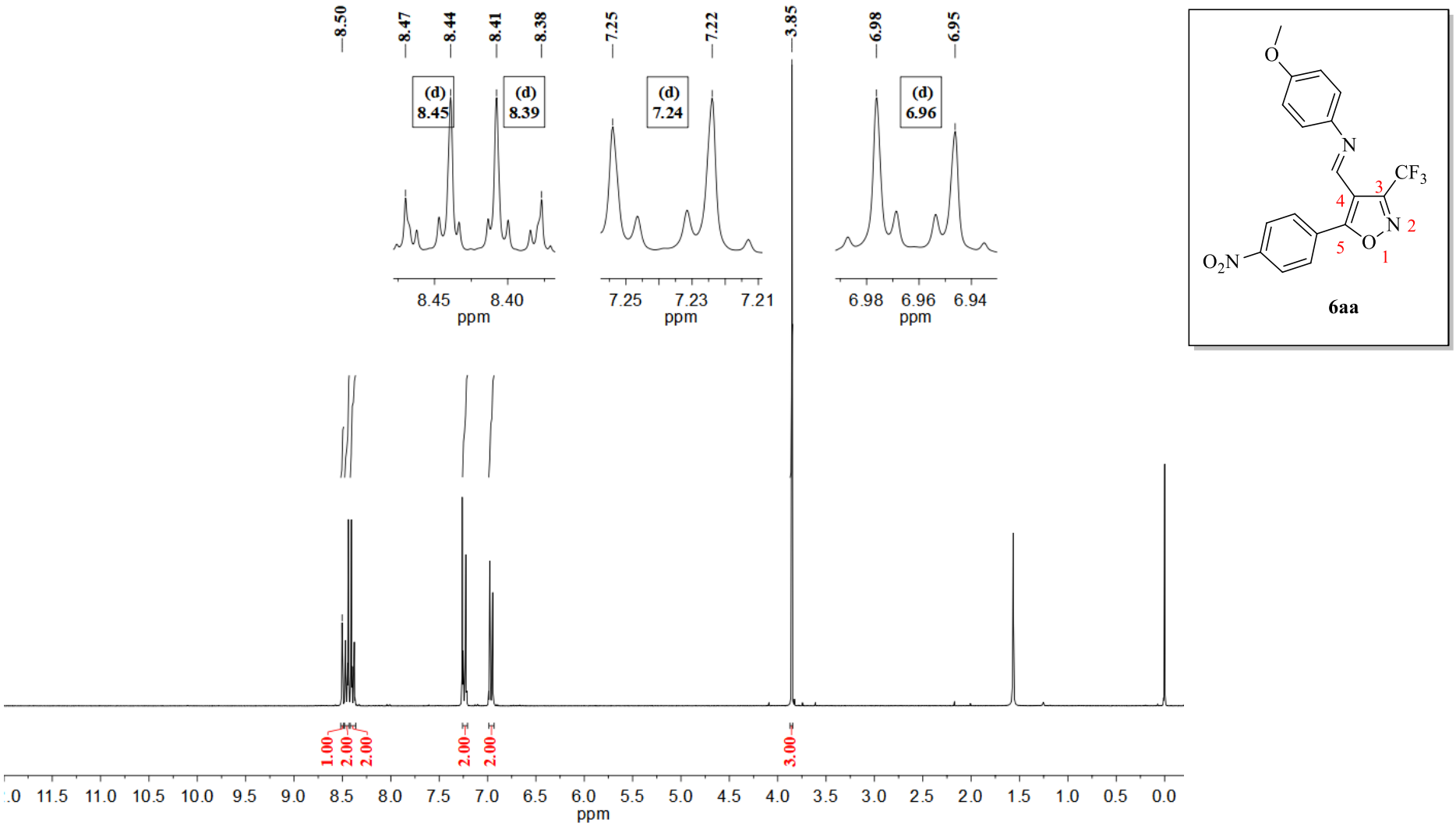


Figure S112 – ^{1}H NMR spectrum of compound **6aa** in $CDCl_3$ at 300.06 MHz.

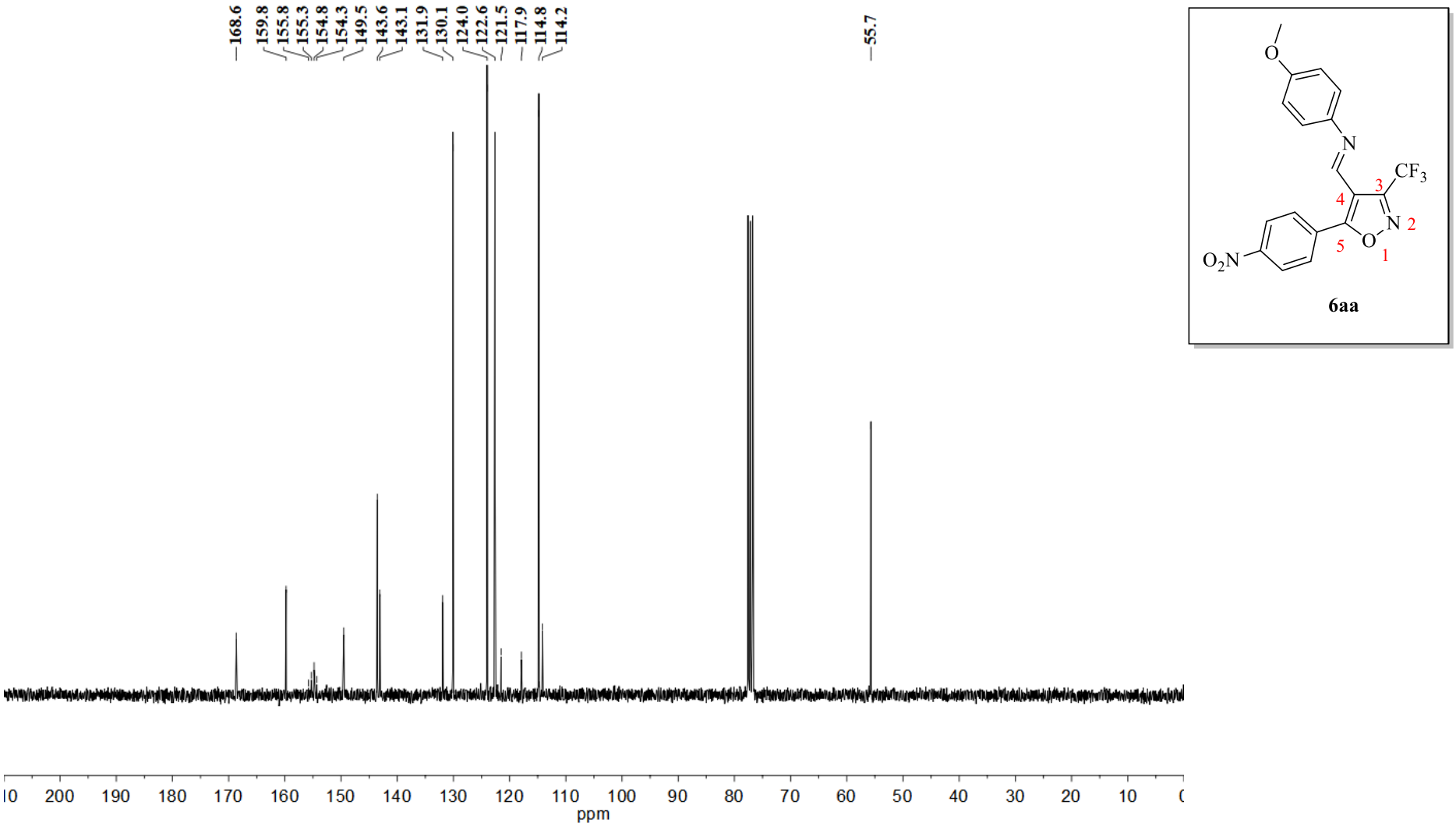


Figure S113 – ^{13}C NMR spectrum of compound **6aa** in $CDCl_3$ at 75.45 MHz.

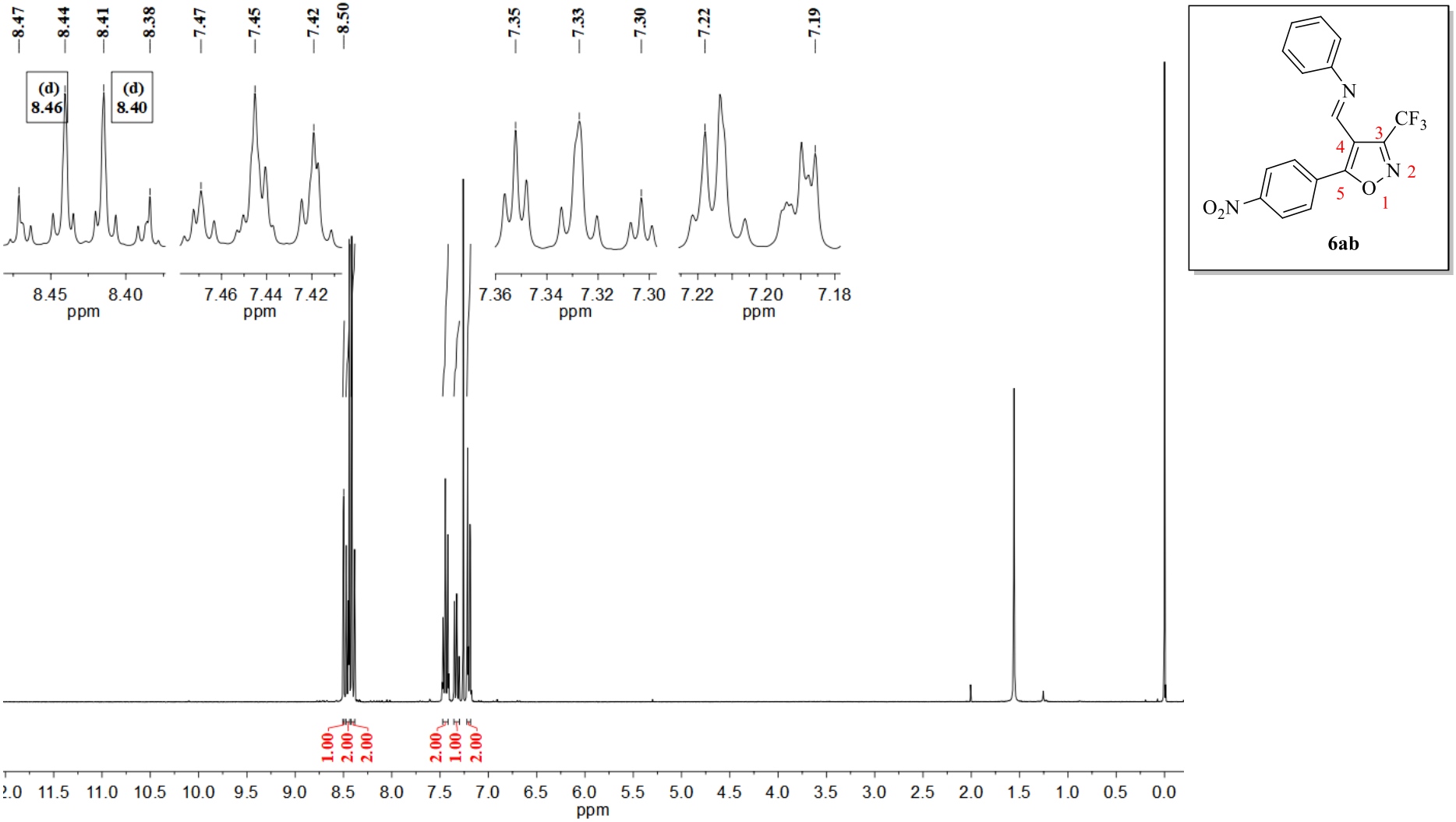
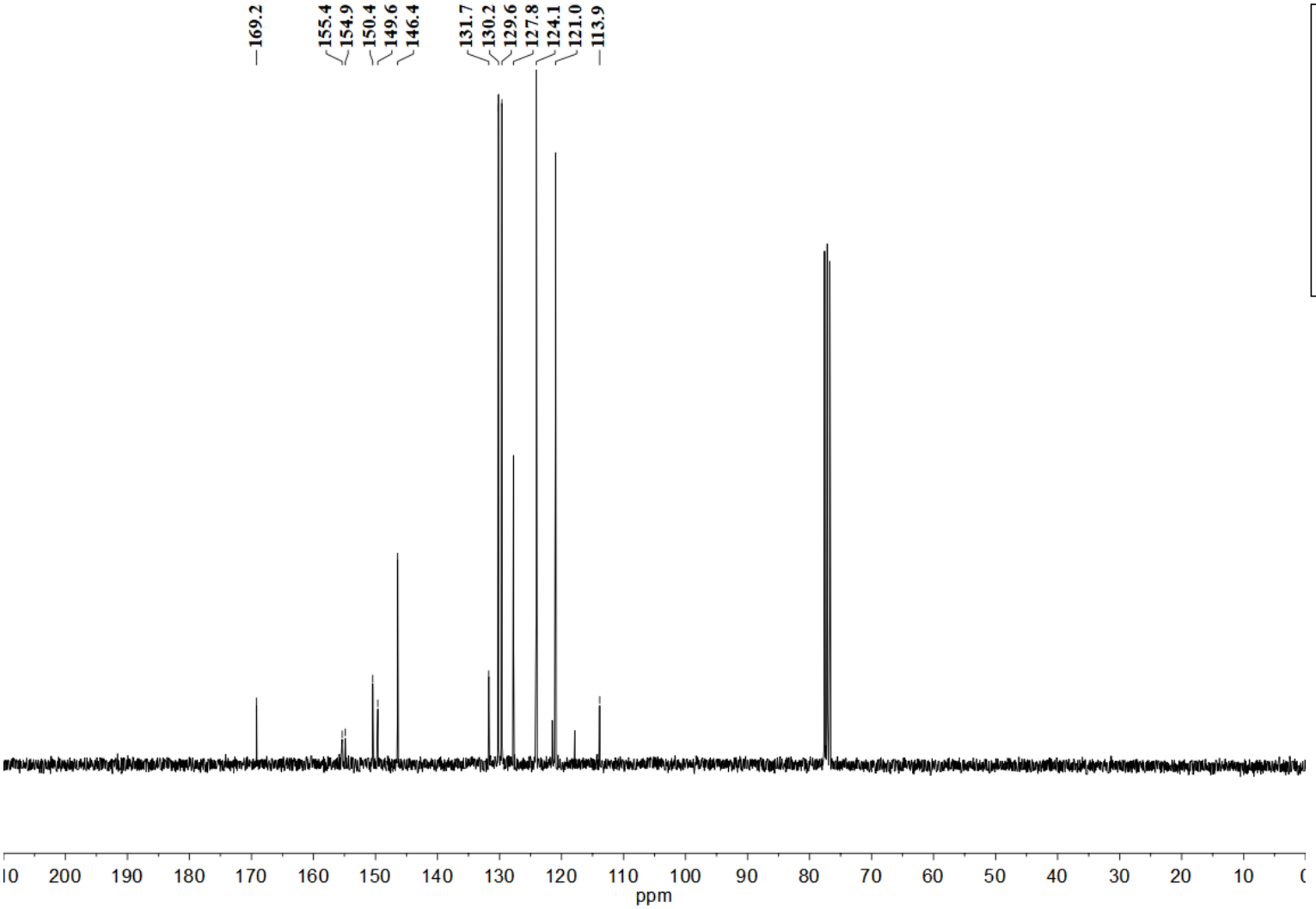


Figure S114 – ^{1}H NMR spectrum of compound **6ab** in $CDCl_3$ at 300.06 MHz.



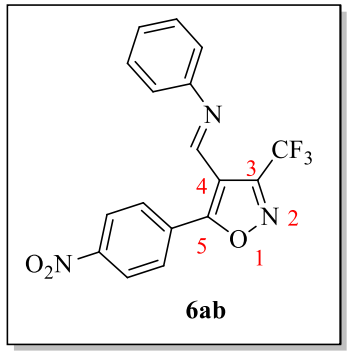


Figure S115 – ^{13}C NMR spectrum of compound **6ab** in $CDCl_3$ at 75.45 MHz.

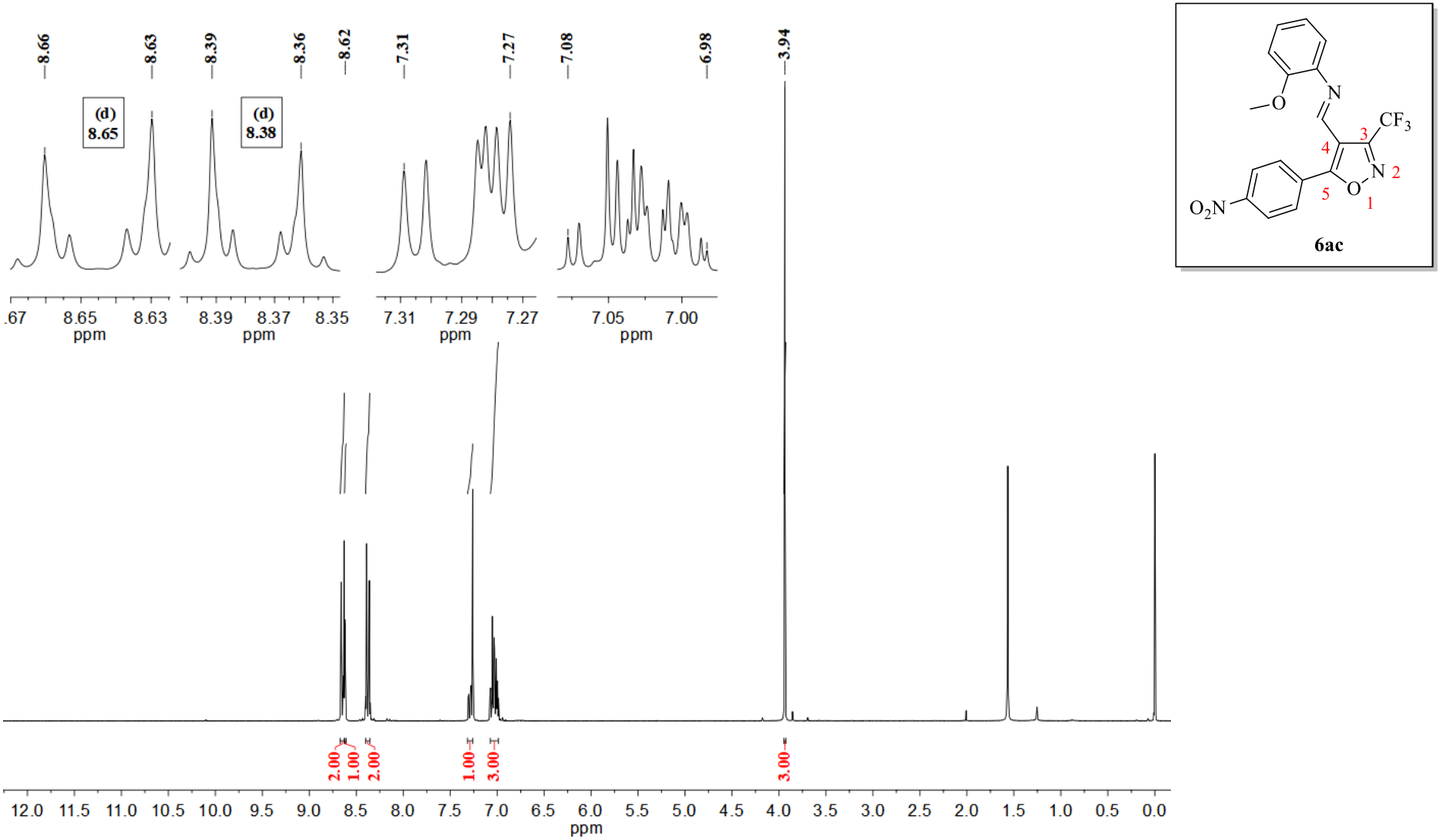


Figure S116 – ^{1}H NMR spectrum of compound **6ac** in $CDCl_3$ at 300.06 MHz.

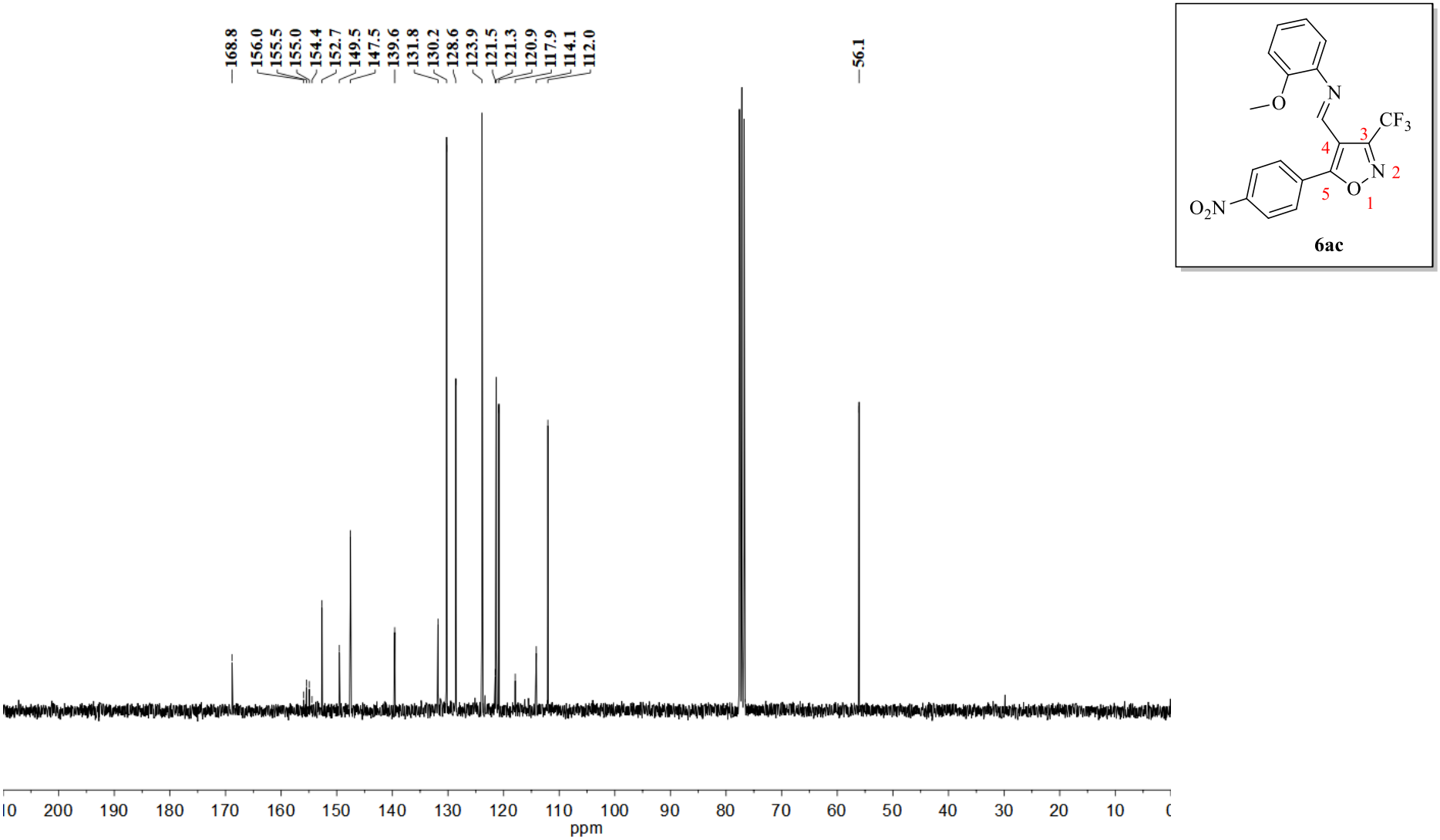


Figure S117 – ^{13}C NMR spectrum of compound **6ac** in $CDCl_3$ at 75.45 MHz.

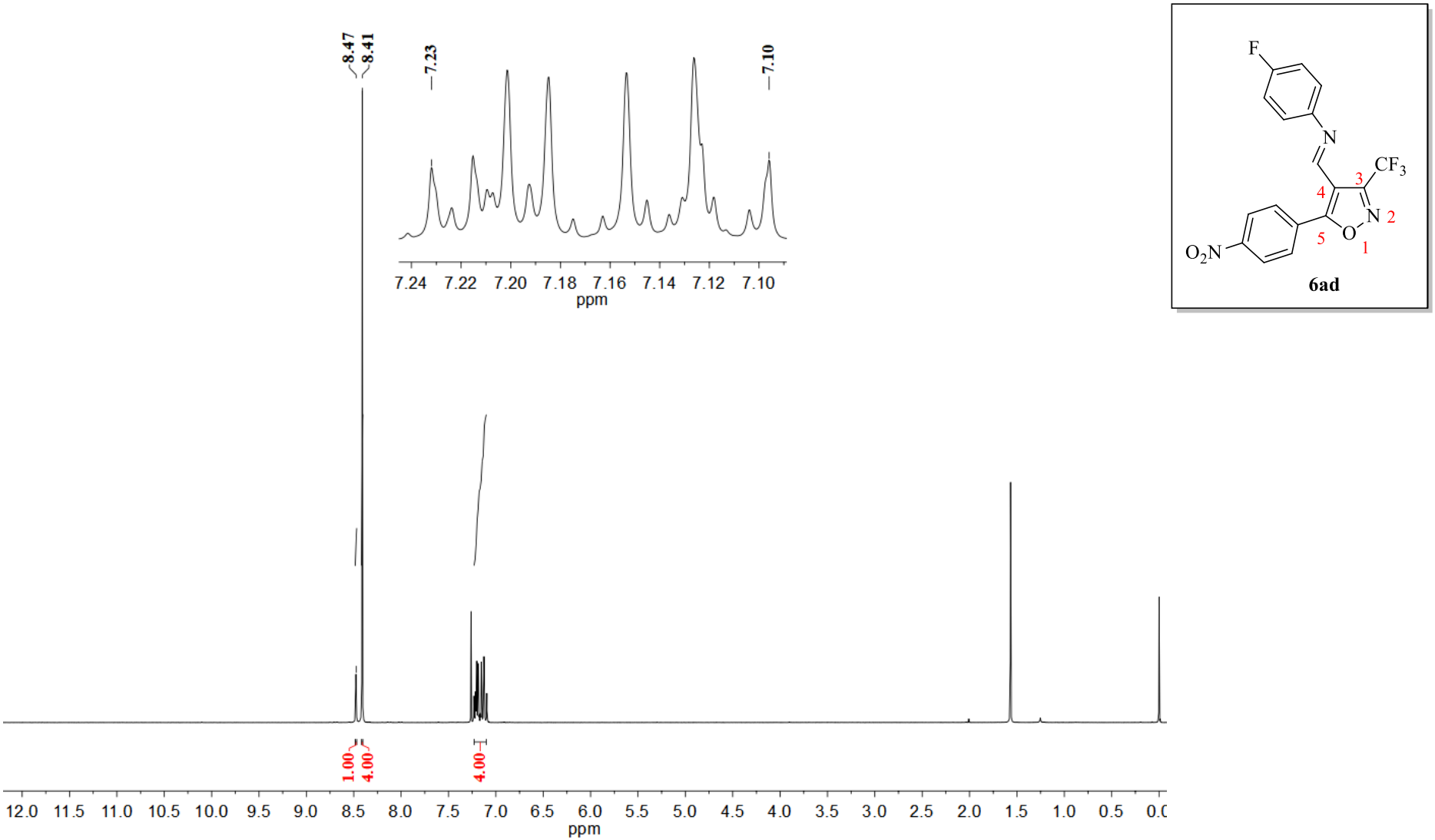


Figure S118 – ^{1}H NMR spectrum of compound **6ad** in $CDCl_3$ at 300.06 MHz.

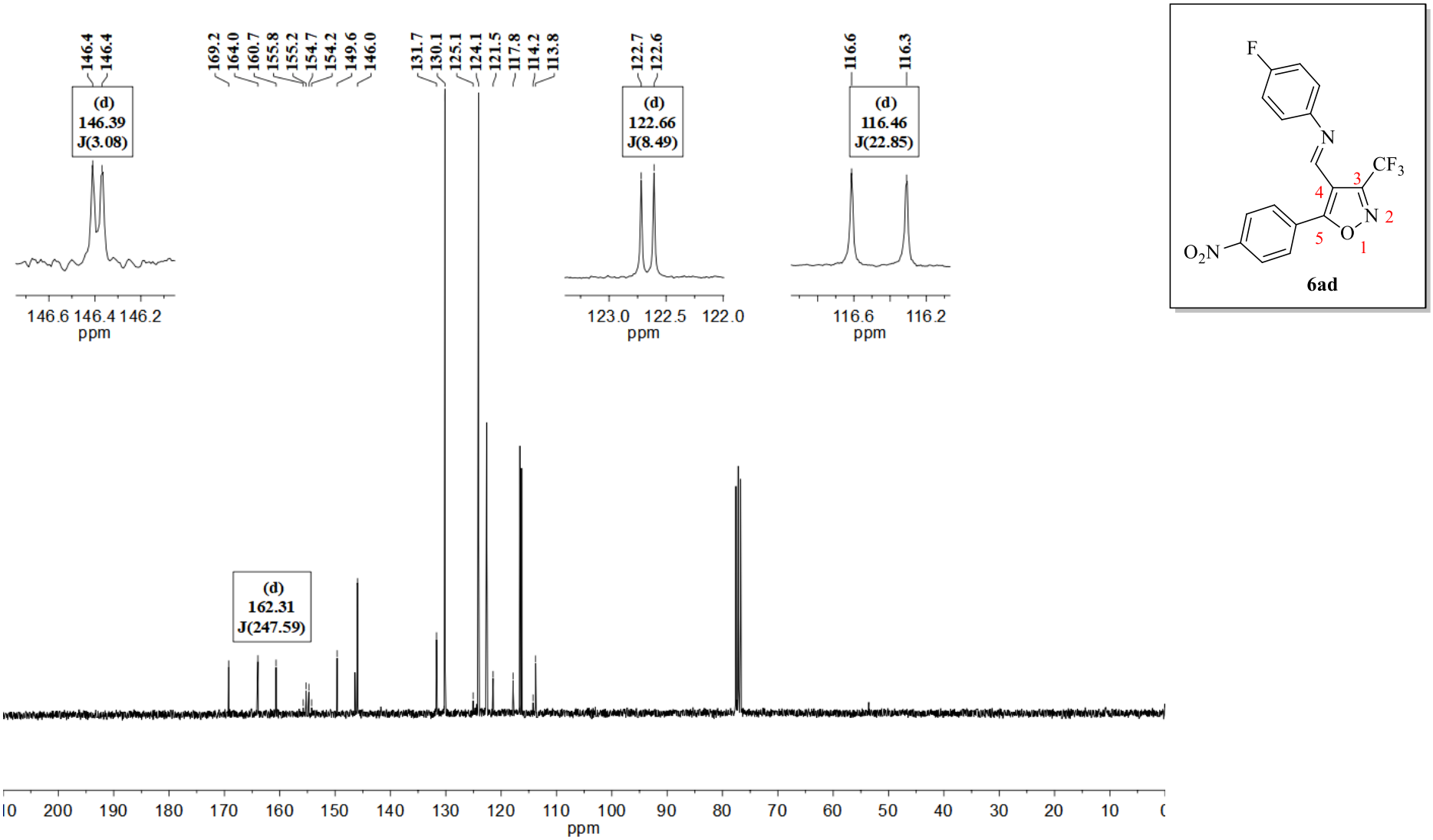


Figure S119 – ^{13}C NMR spectrum of compound **6ad** in $CDCl_3$ at 75.45 MHz.

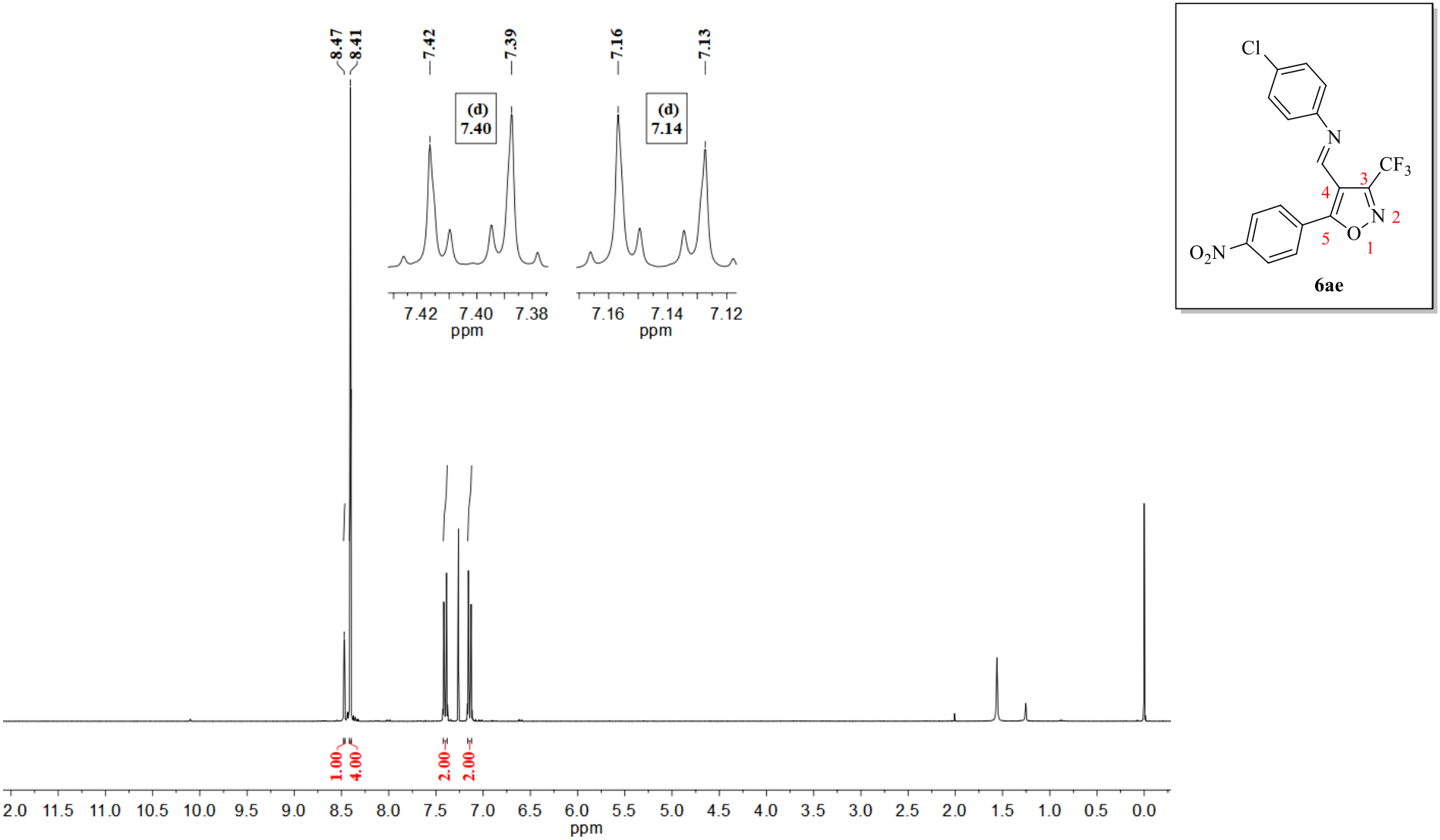


Figure S120 – ^{1}H NMR spectrum of compound **6ae** in $CDCl_3$ at 300.06 MHz.

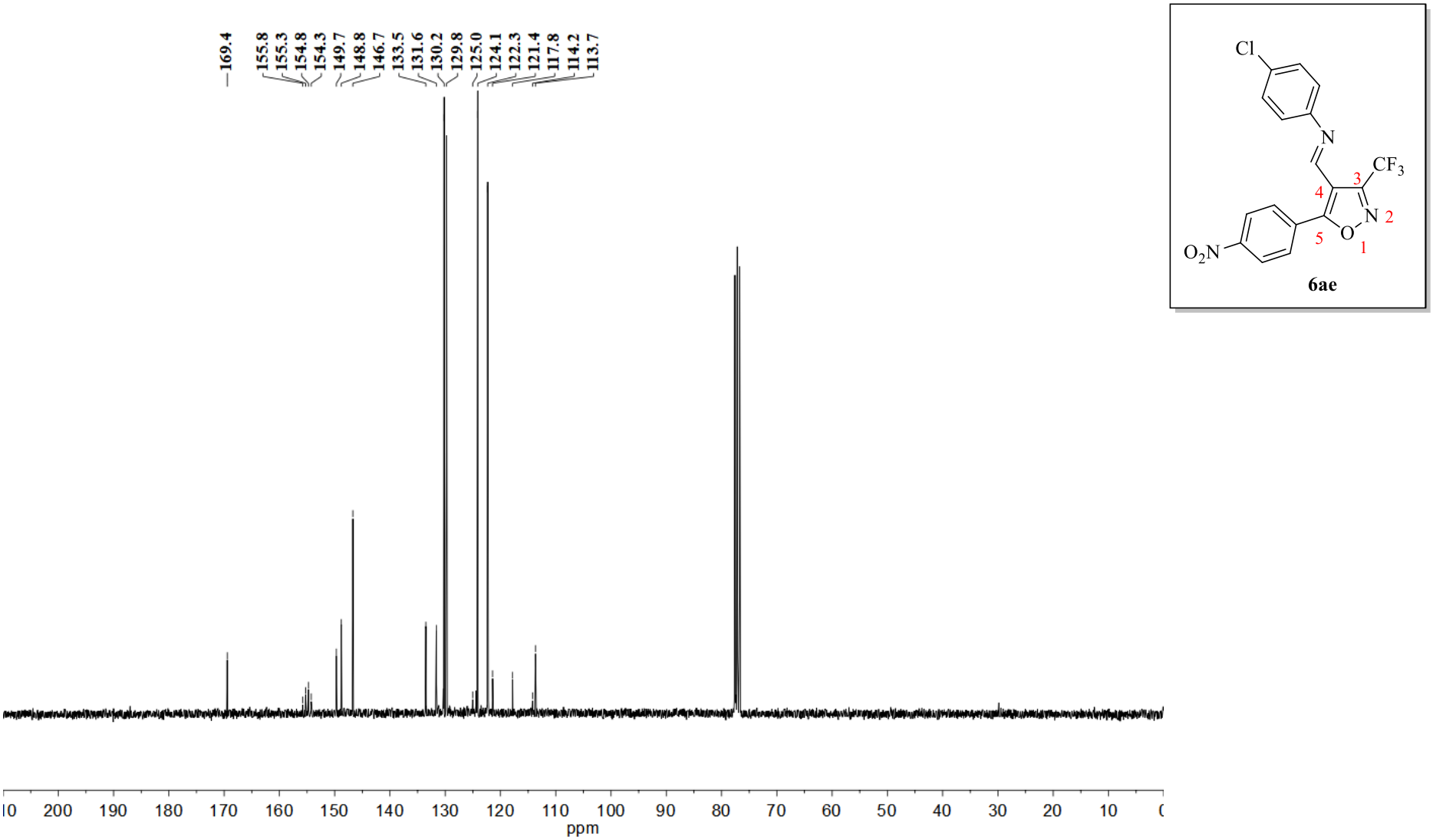


Figure S121 – ^{13}C NMR spectrum of compound **6ae** in $CDCl_3$ at 75.45 MHz.

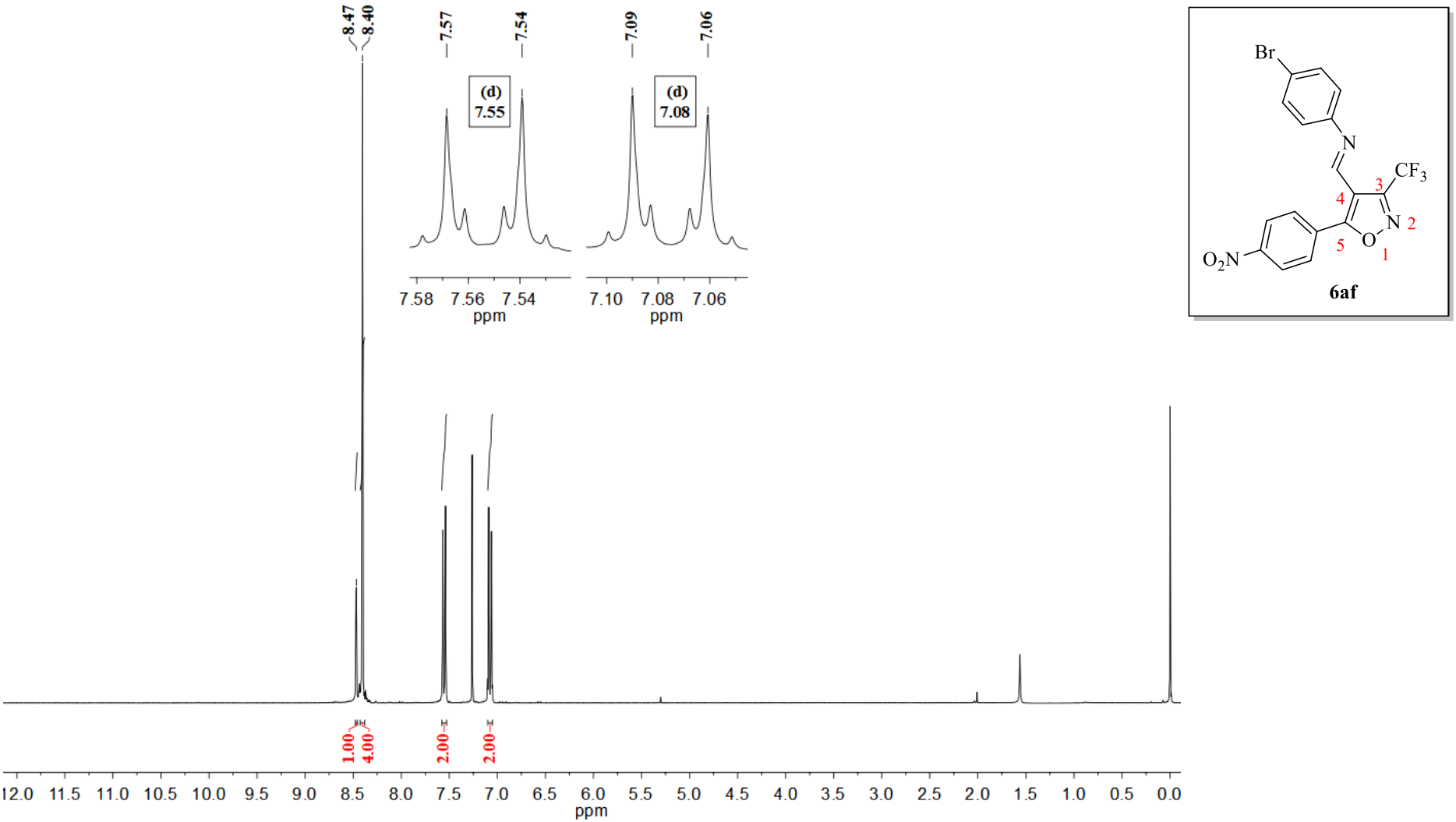
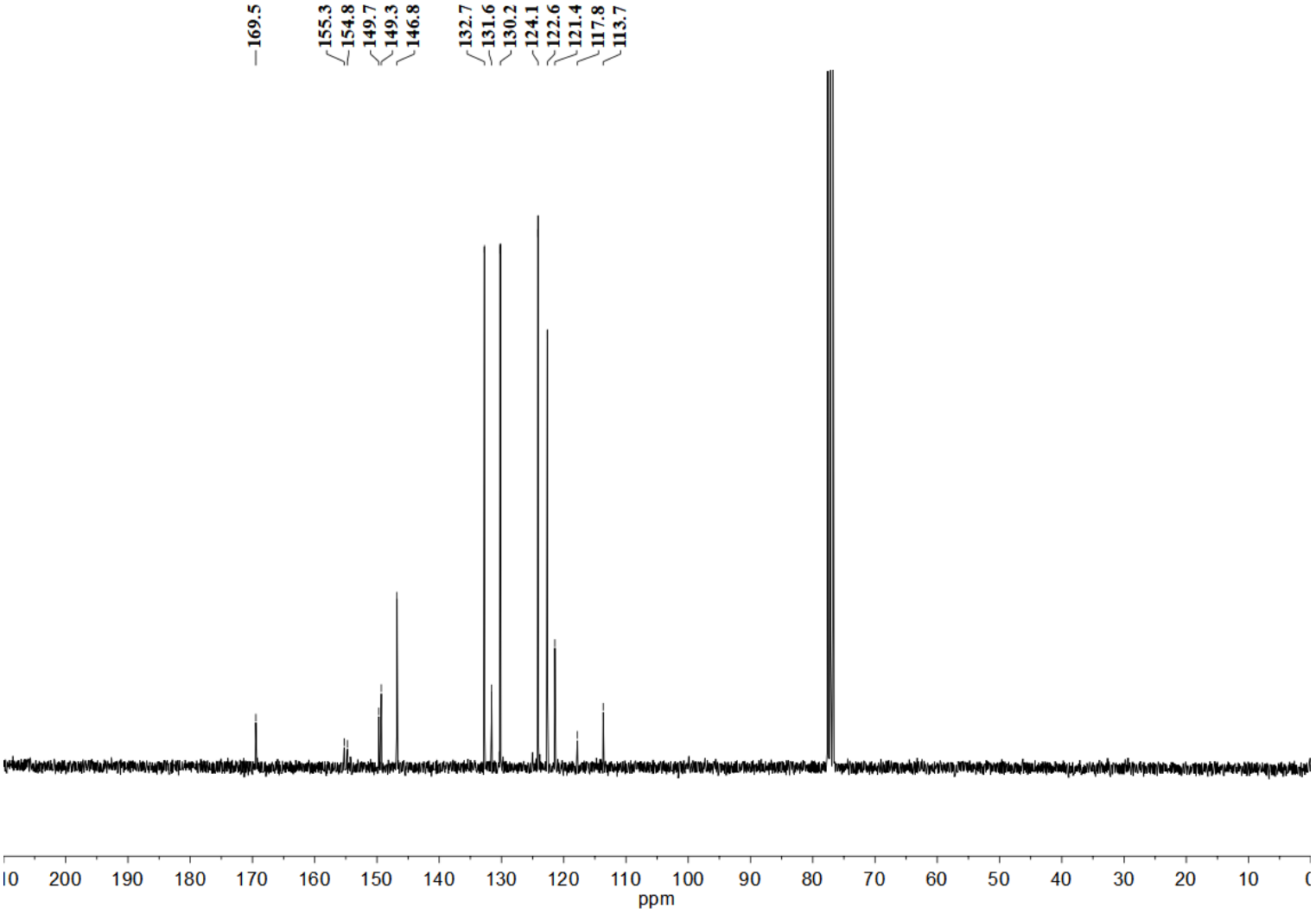


Figure S122 – ^{1}H NMR spectrum of compound **6af** in $CDCl_3$ at 300.06 MHz.



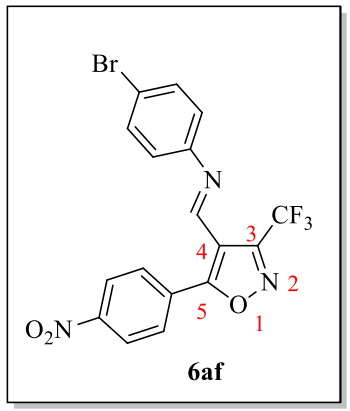


Figure S123 – ^{13}C NMR spectrum of compound **6af** in $CDCl_3$ at 75.45 MHz.

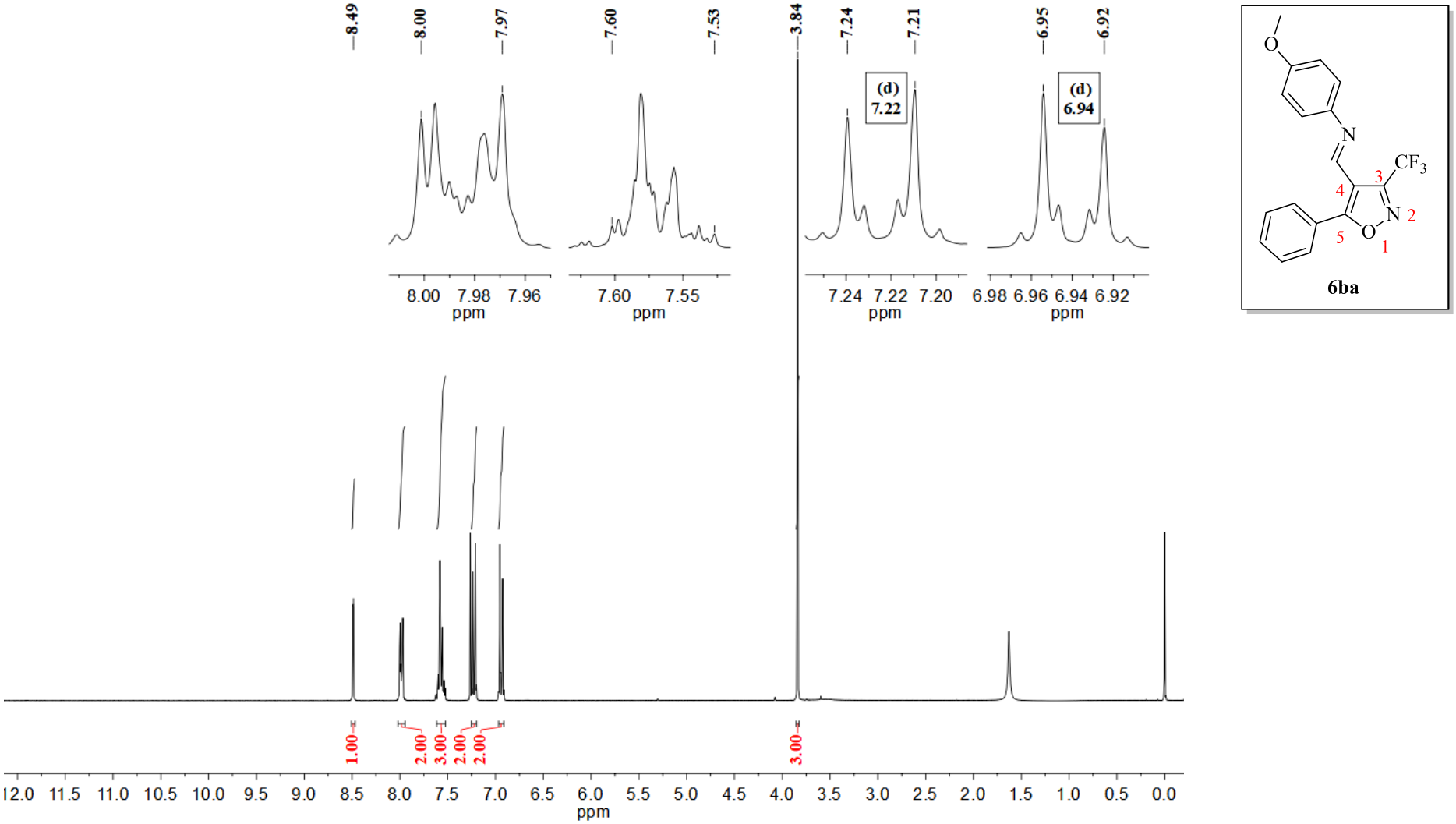
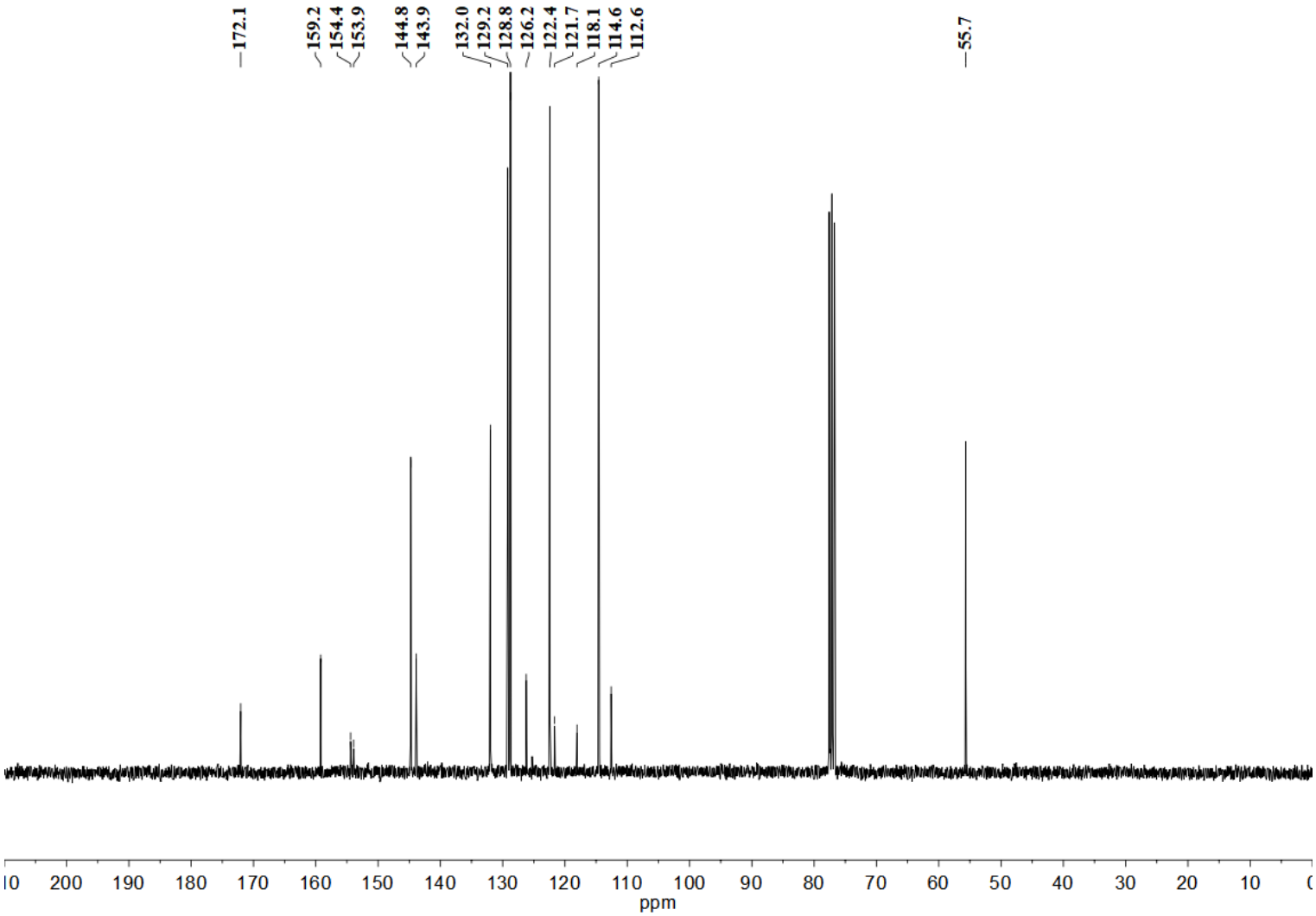
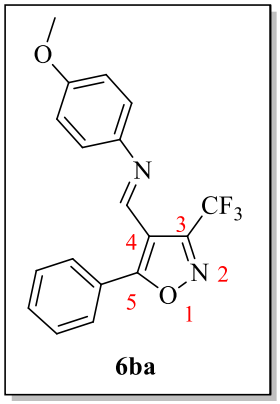


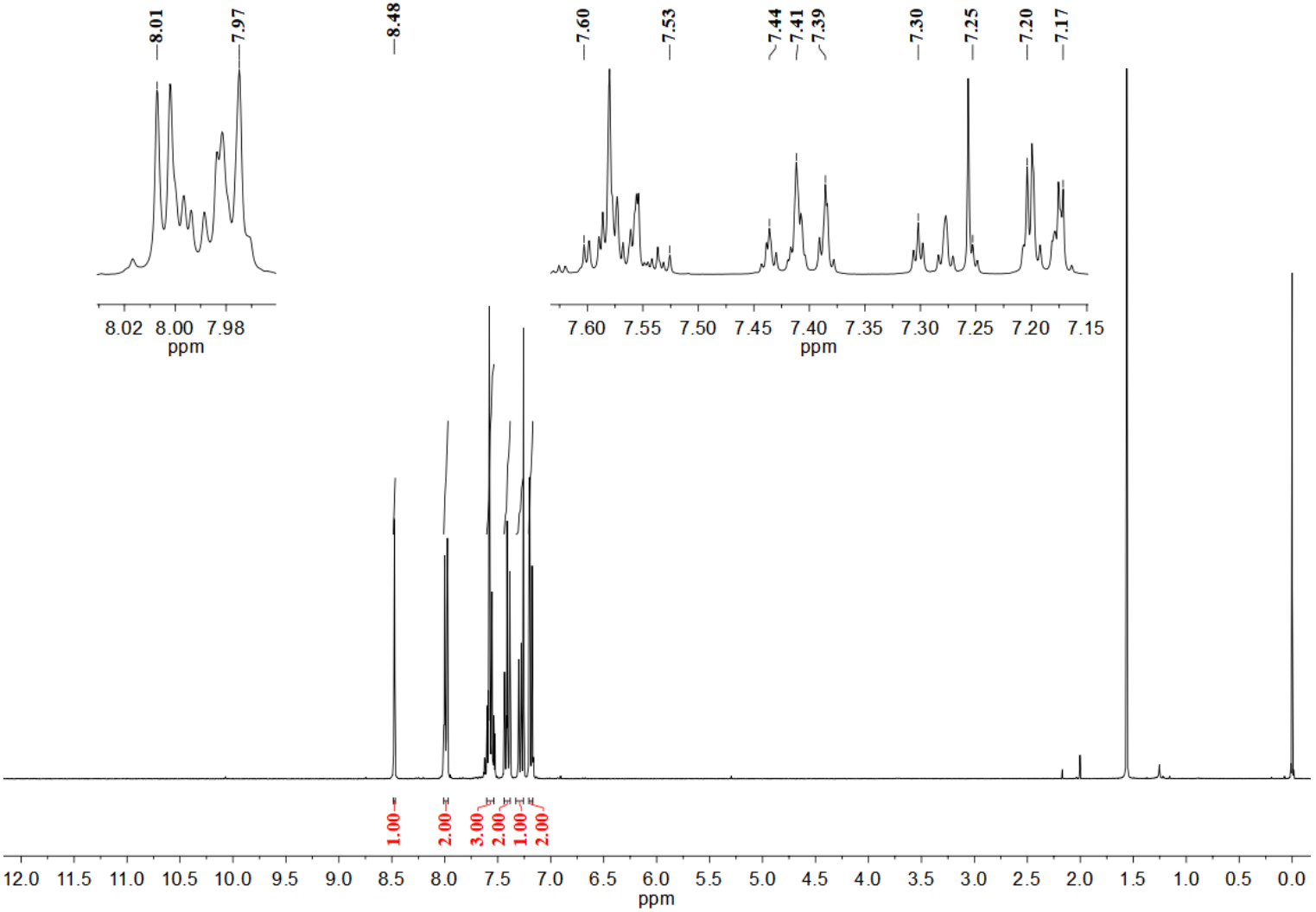
Figure S124 – ^{1}H NMR spectrum of compound **6ba** in $CDCl_3$ at 300.06 MHz.





6ba

Figure S125 – ^{13}C NMR spectrum of compound **6ba** in $CDCl_3$ at 75.45 MHz.



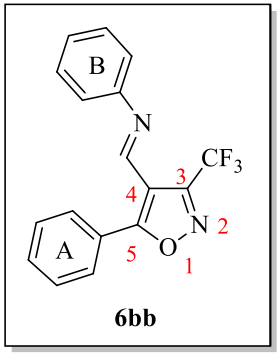
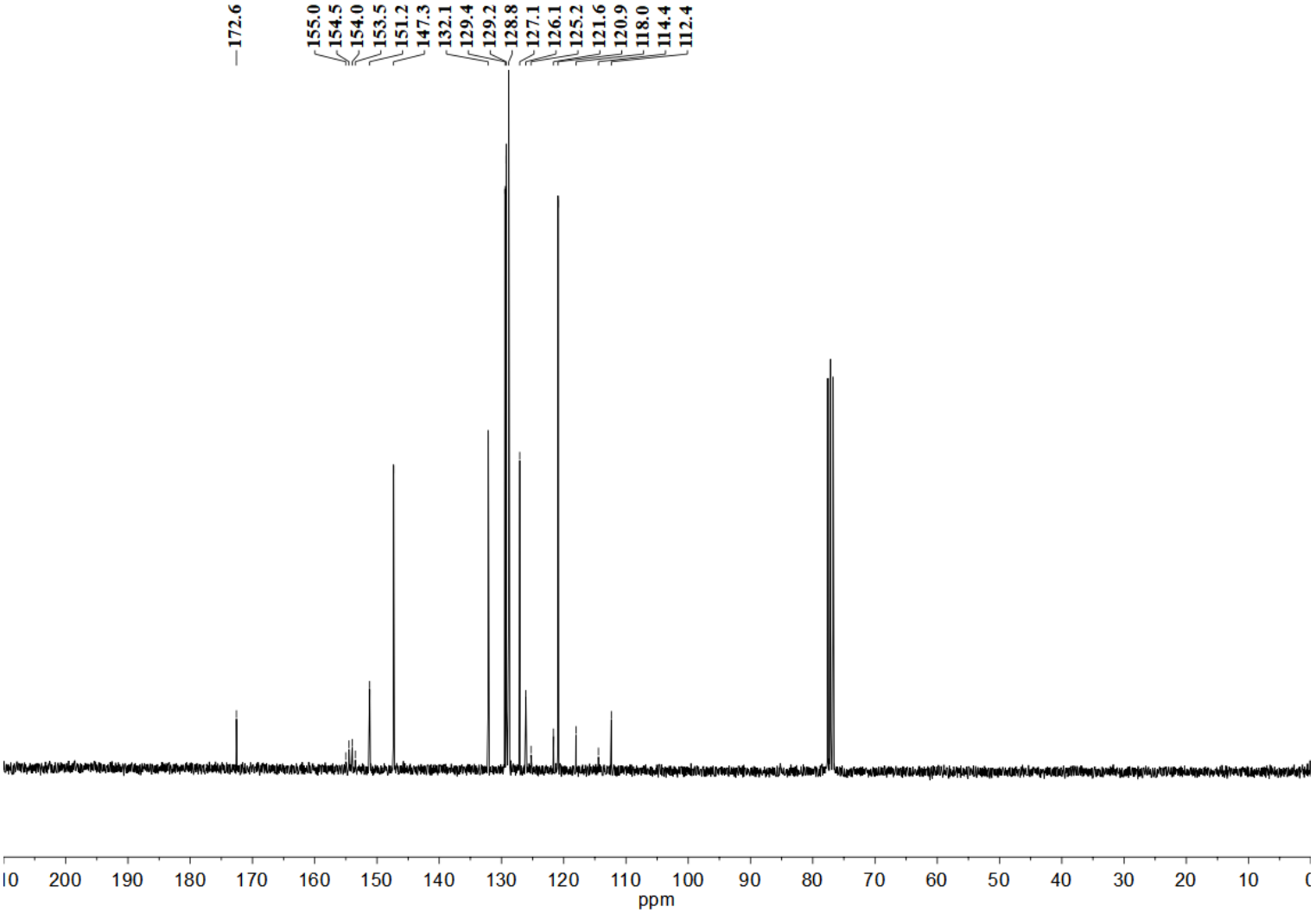
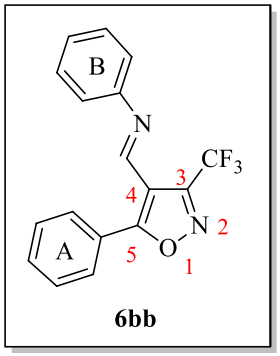


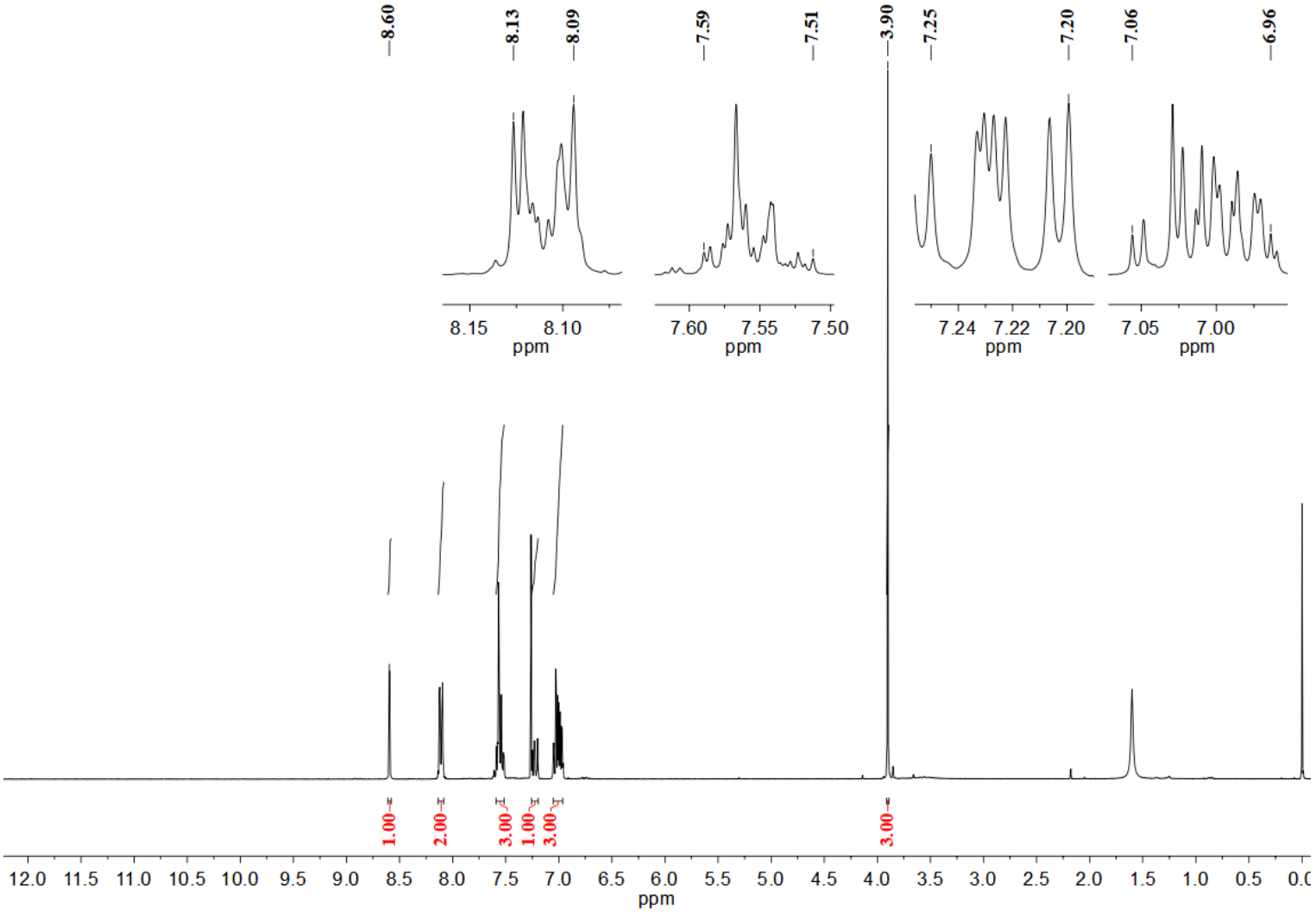
Figure S126 – ^{1}H NMR spectrum of compound **6bb** in $CDCl_3$ at 300.06 MHz.





6bb

Figure S127 – ^{13}C NMR spectrum of compound **6bb** in $CDCl_3$ at 75.45 MHz.



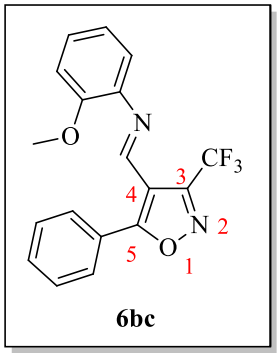
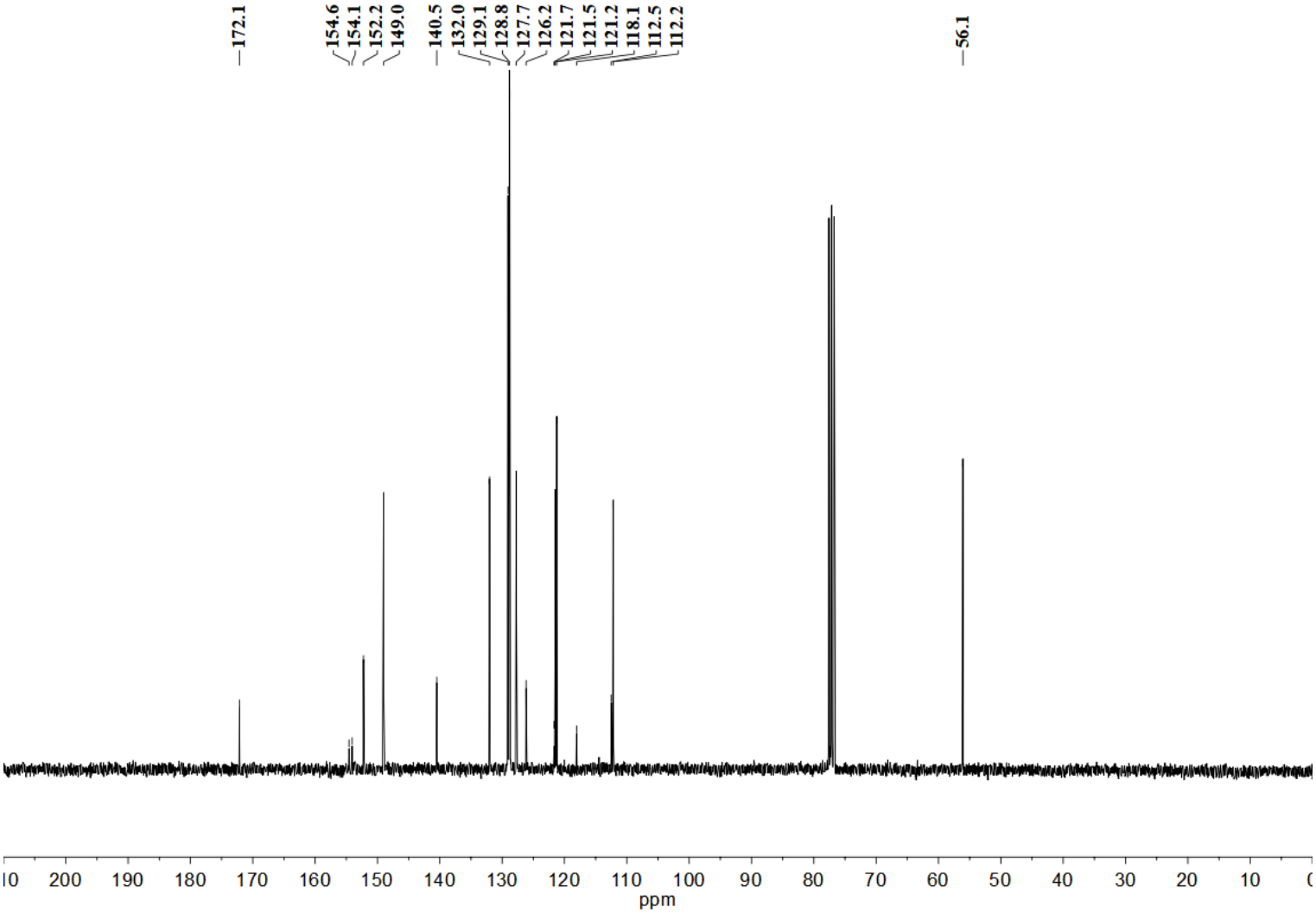


Figure S128 – ^{1}H NMR spectrum of compound **6bc** in $CDCl_3$ at 300.06 MHz.



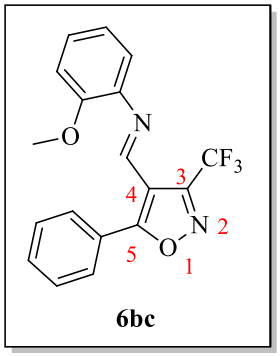
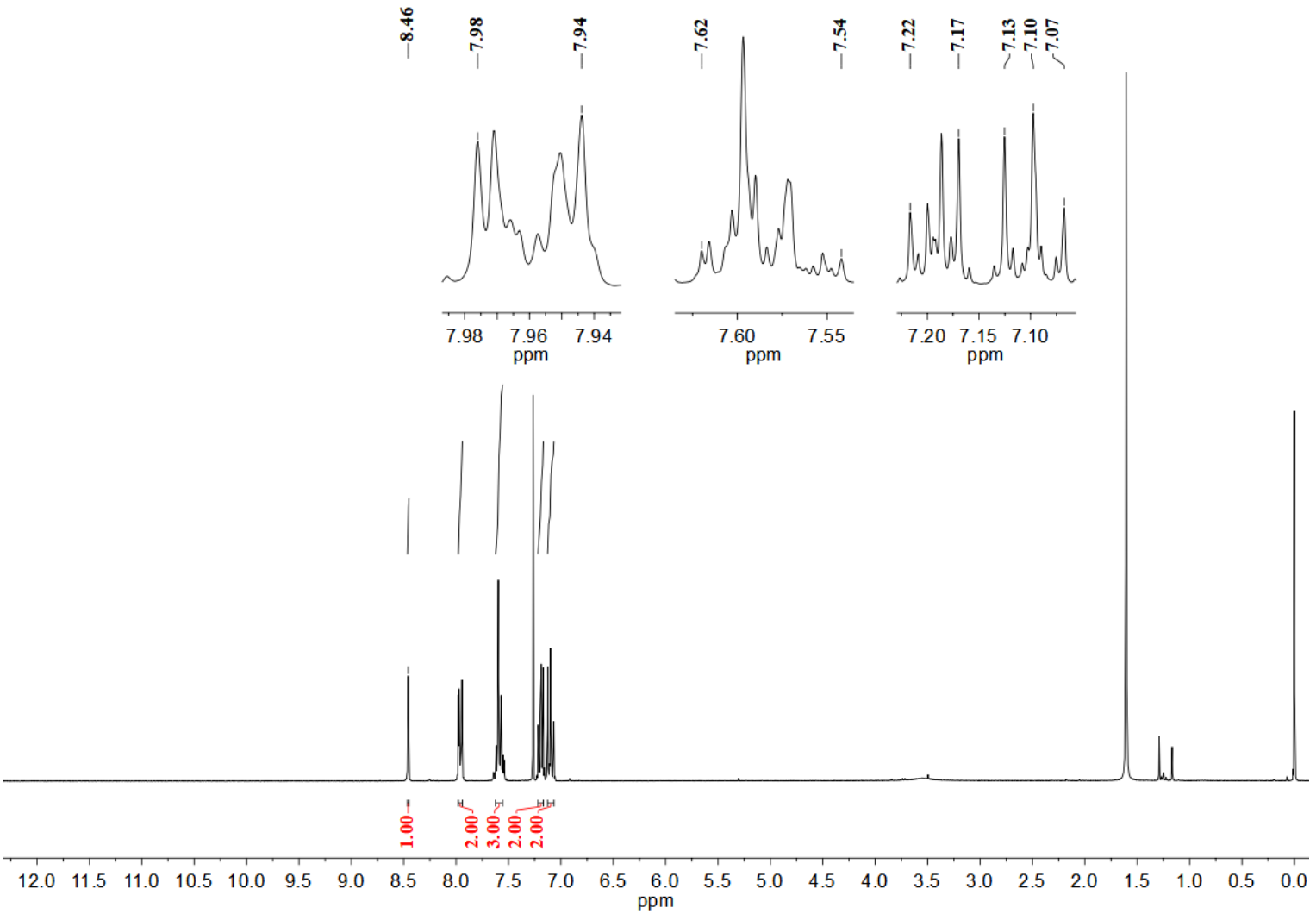


Figure S129 – ^{13}C NMR spectrum of compound **6bc** in $CDCl_3$ at 75.45 MHz.



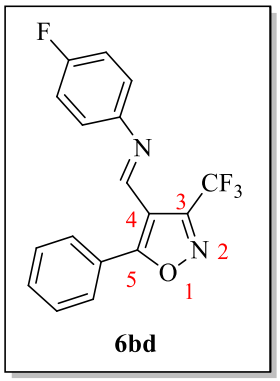
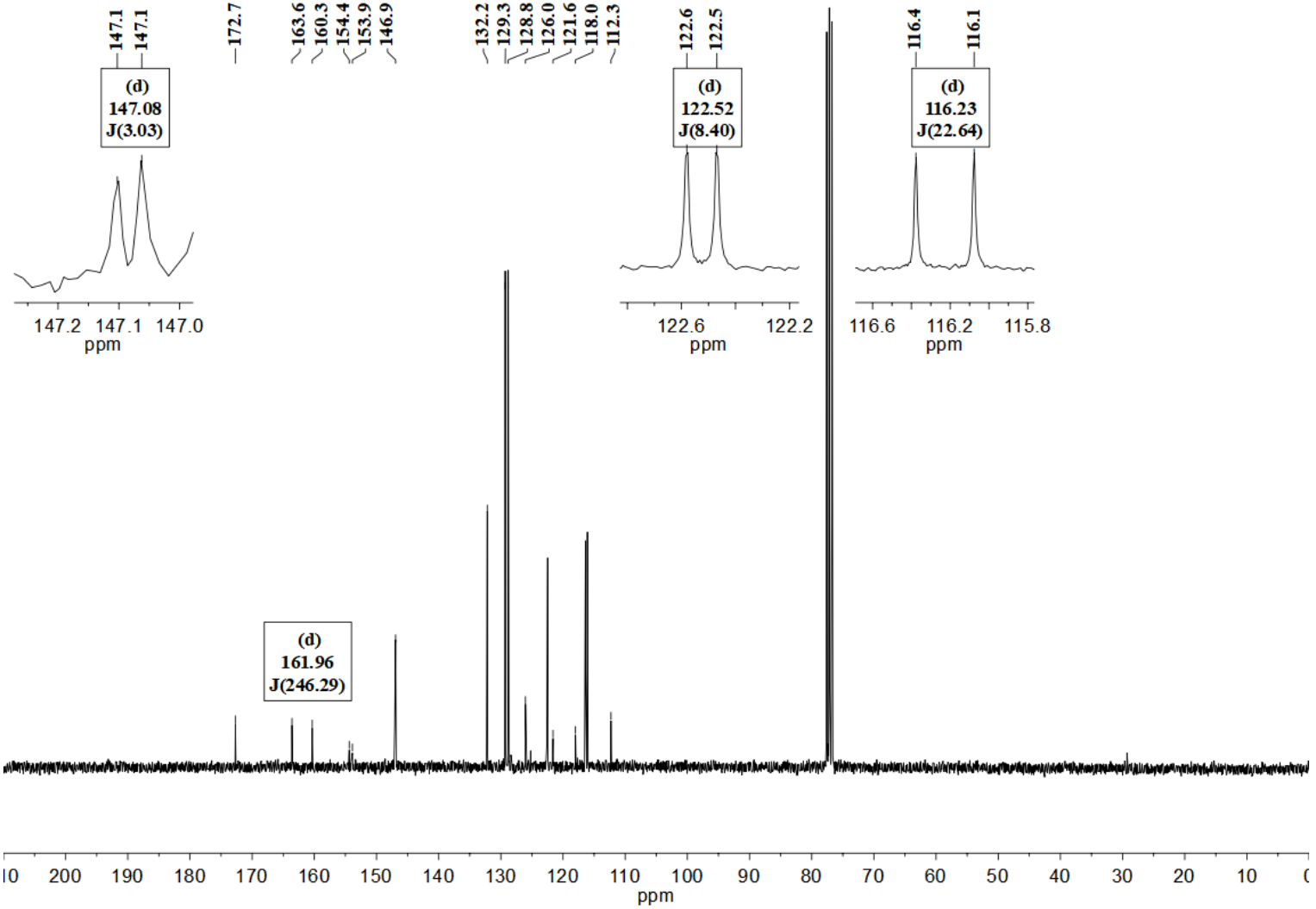


Figure S130 – ^{1}H NMR spectrum of compound **6bd** in $CDCl_3$ at 300.06 MHz.



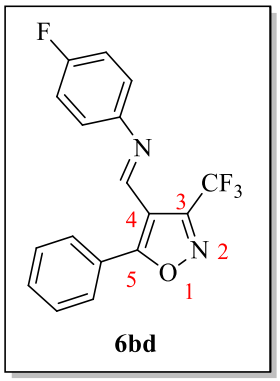
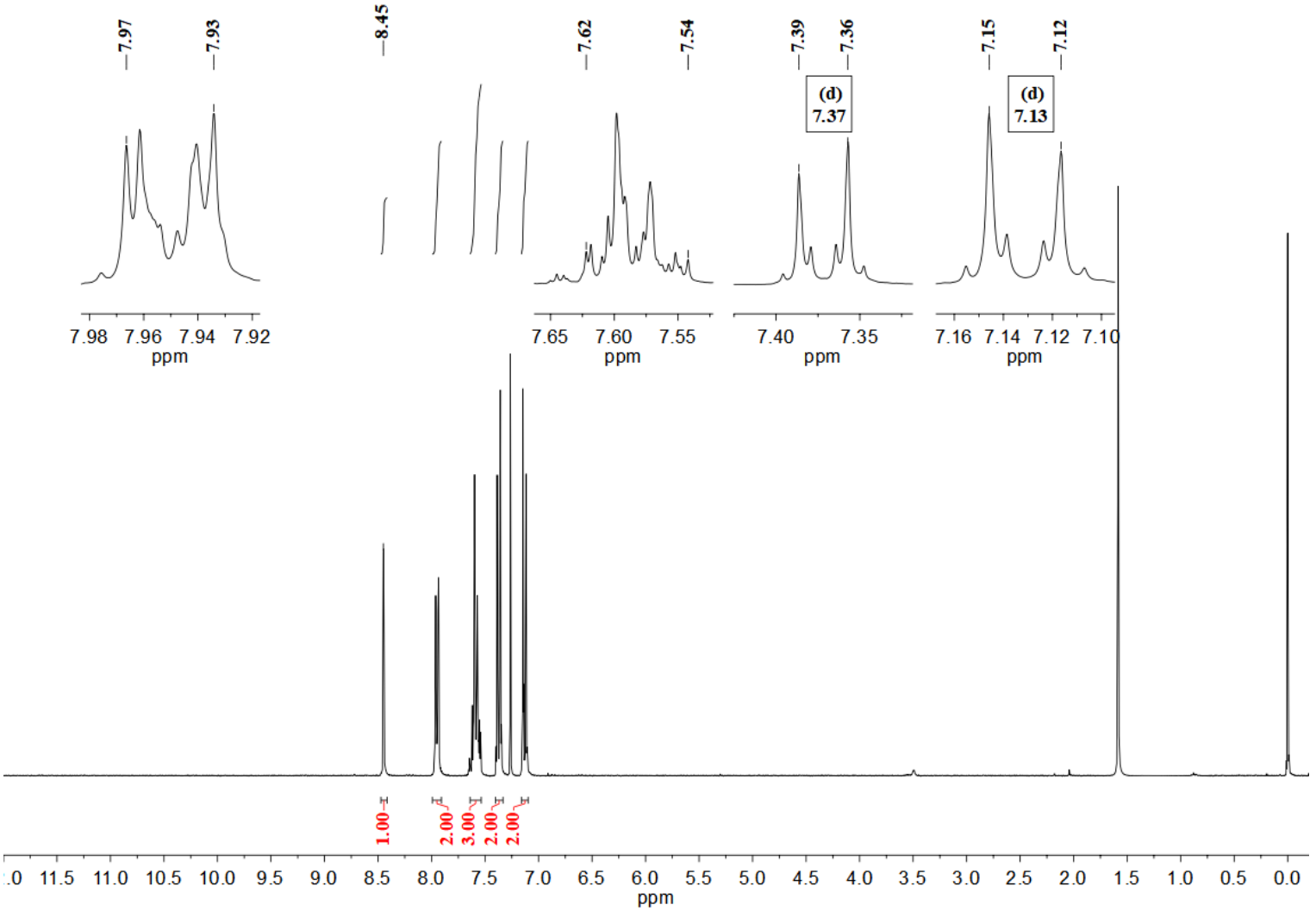


Figure S131 – ^{13}C NMR spectrum of compound **6bd** in $CDCl_3$ at 75.45 MHz.



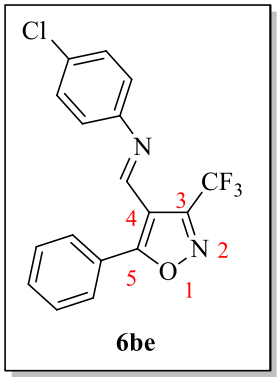
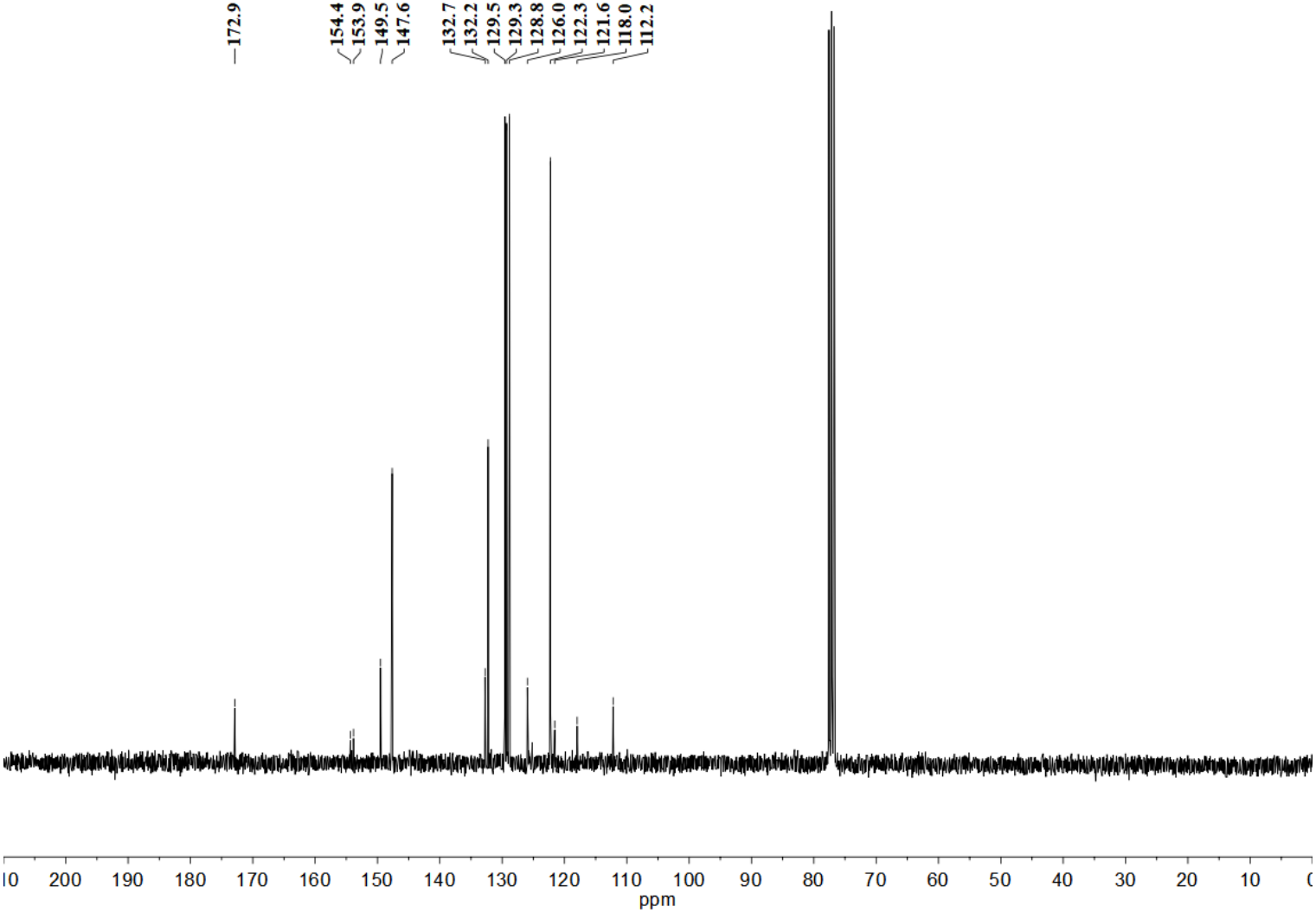
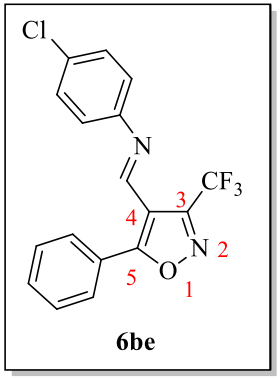


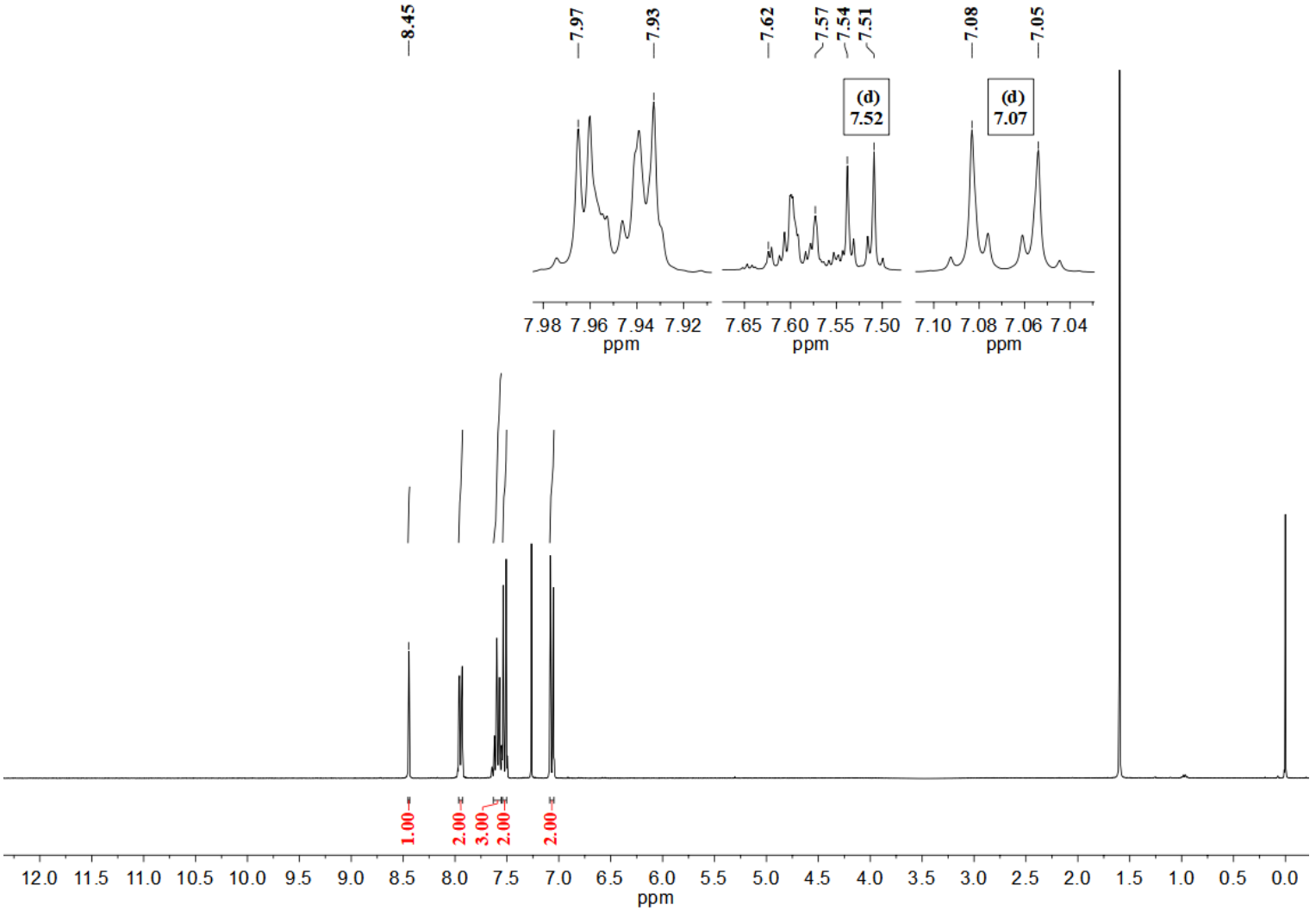
Figure S132 – ^{1}H NMR spectrum of compound **6be** in $CDCl_3$ at 300.06 MHz.





6be

Figure S133 – ^{13}C NMR spectrum of compound **6be** in $CDCl_3$ at 75.45 MHz.



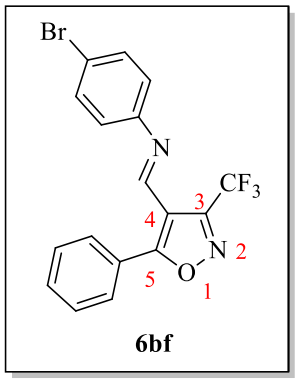
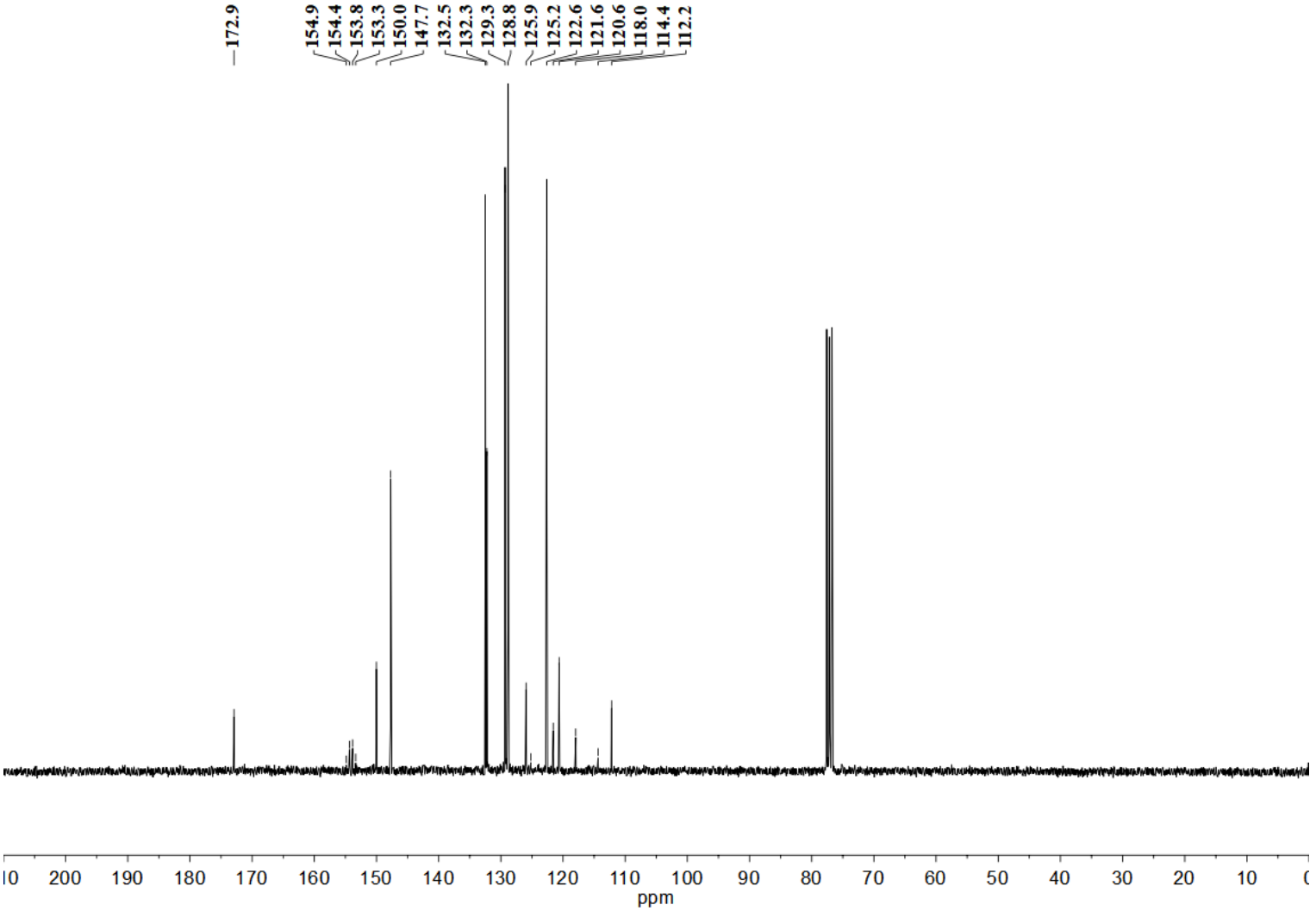


Figure S134 – ^{1}H NMR spectrum of compound **6bf** in $CDCl_3$ at 300.06 MHz.



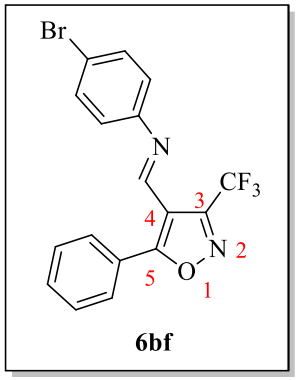


Figure S135 – ^{13}C NMR spectrum of compound **6bf** in $CDCl_3$ at 75.45 MHz.

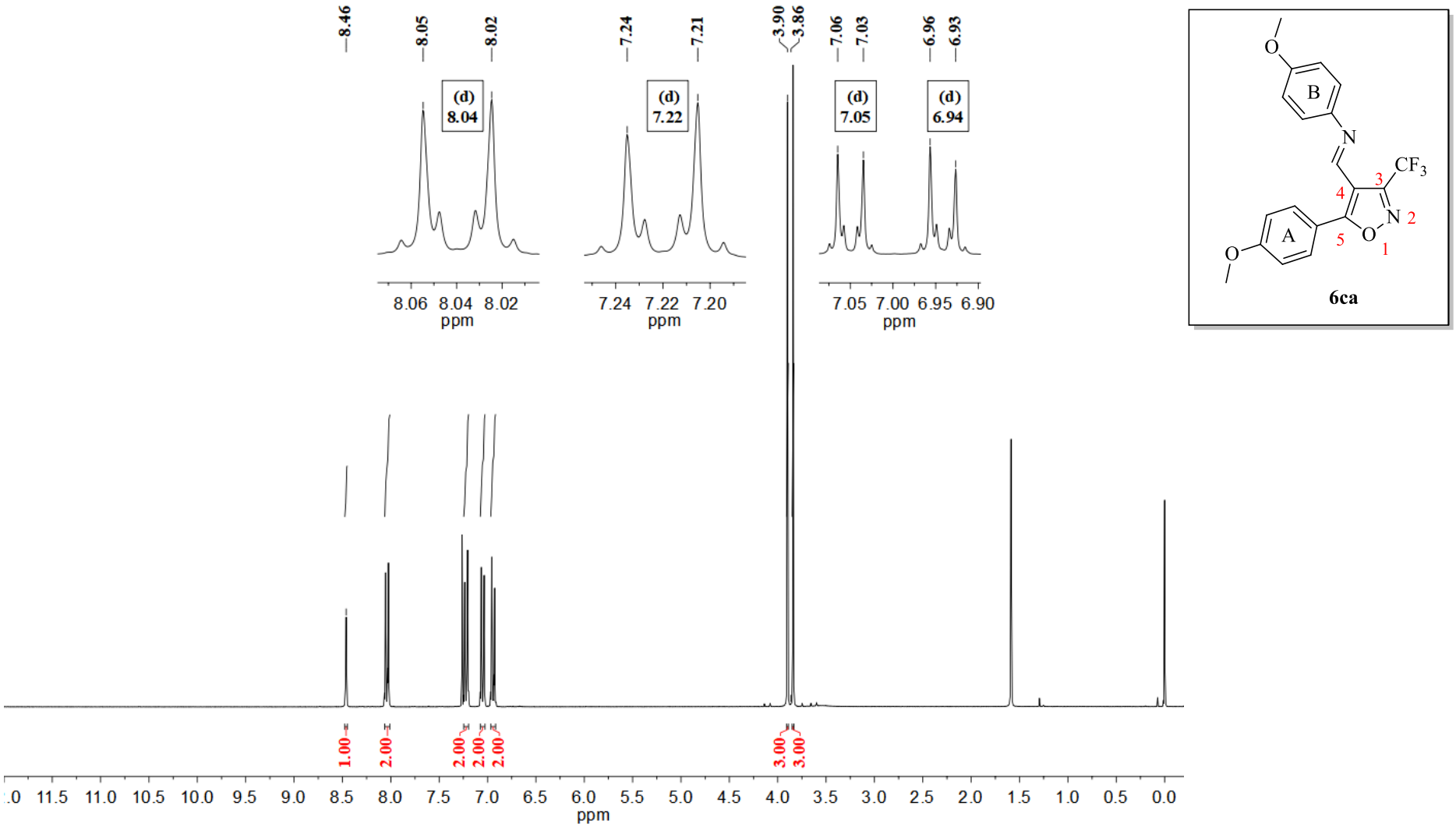


Figure S136 – ^{1}H NMR spectrum of compound **6ca** in $CDCl_3$ at 300.06 MHz.

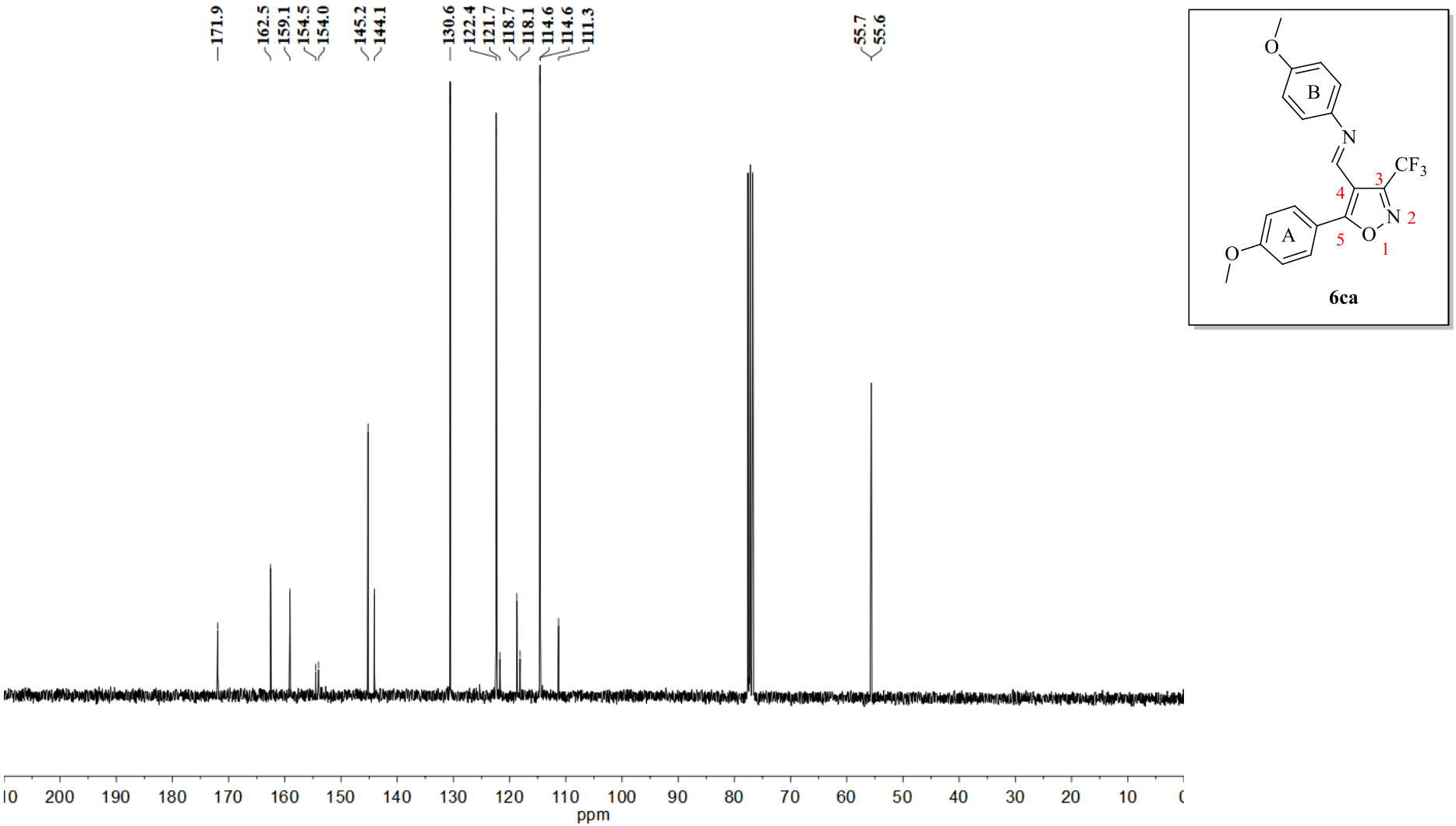


Figure S137 – ^{13}C NMR spectrum of compound **6ca** in $CDCl_3$ at 75.45 MHz.

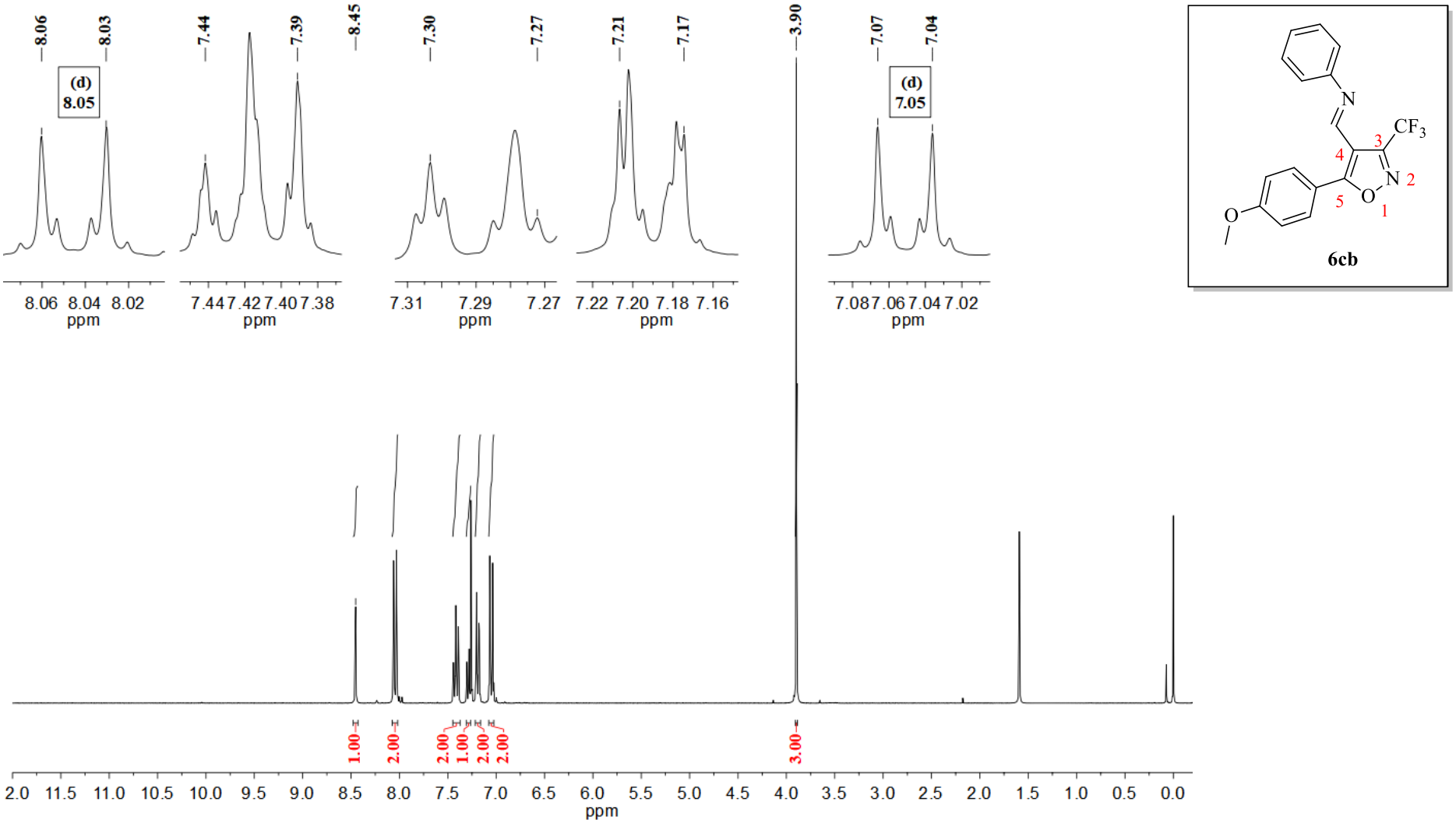
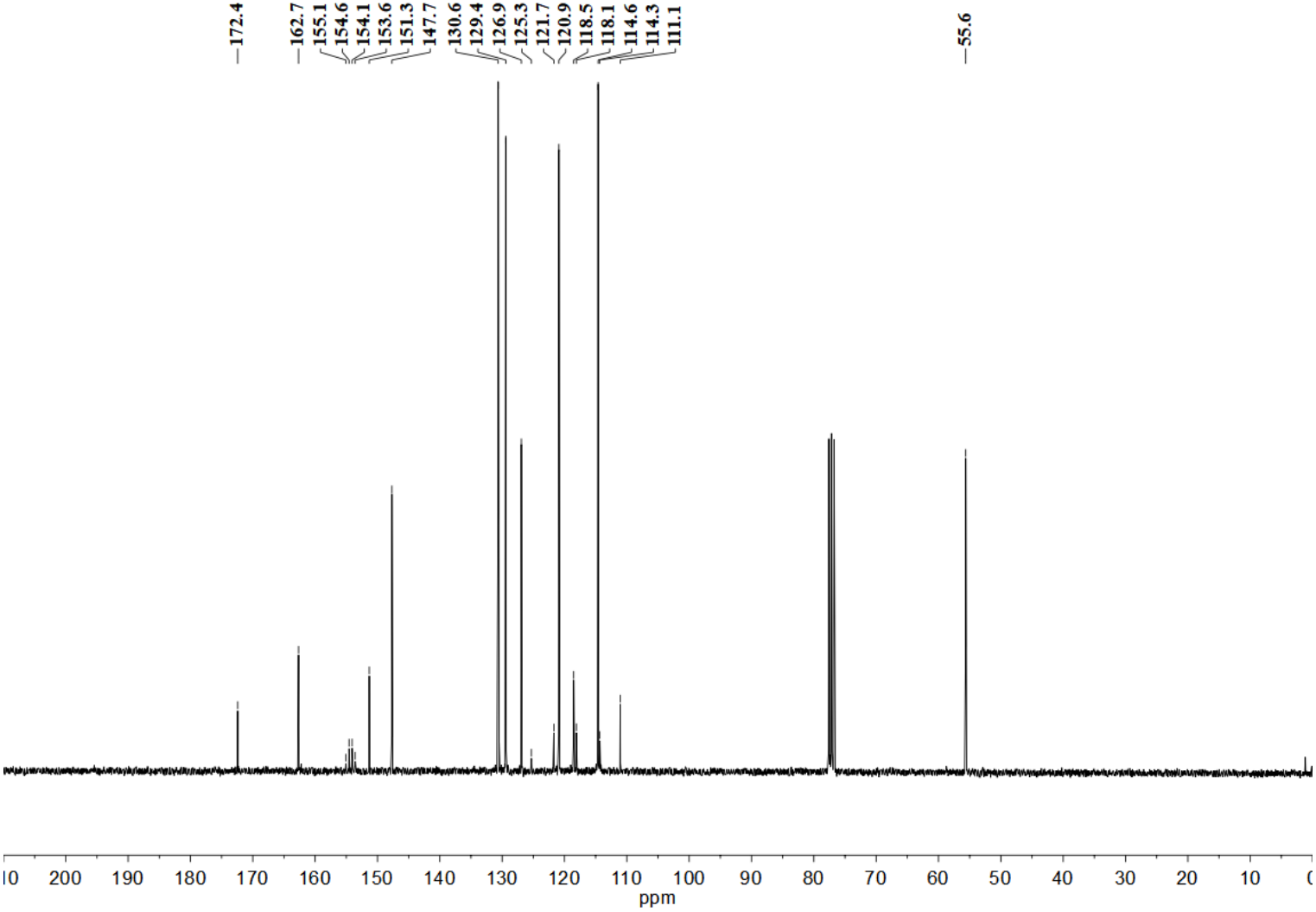


Figure S138 – ^{1}H NMR spectrum of compound **6cb** in $CDCl_3$ at 300.06 MHz.



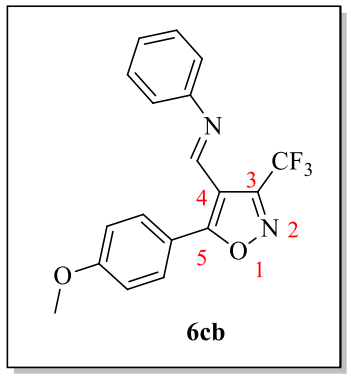


Figure S139 – ^{13}C NMR spectrum of compound **6cb** in $CDCl_3$ at 75.45 MHz.

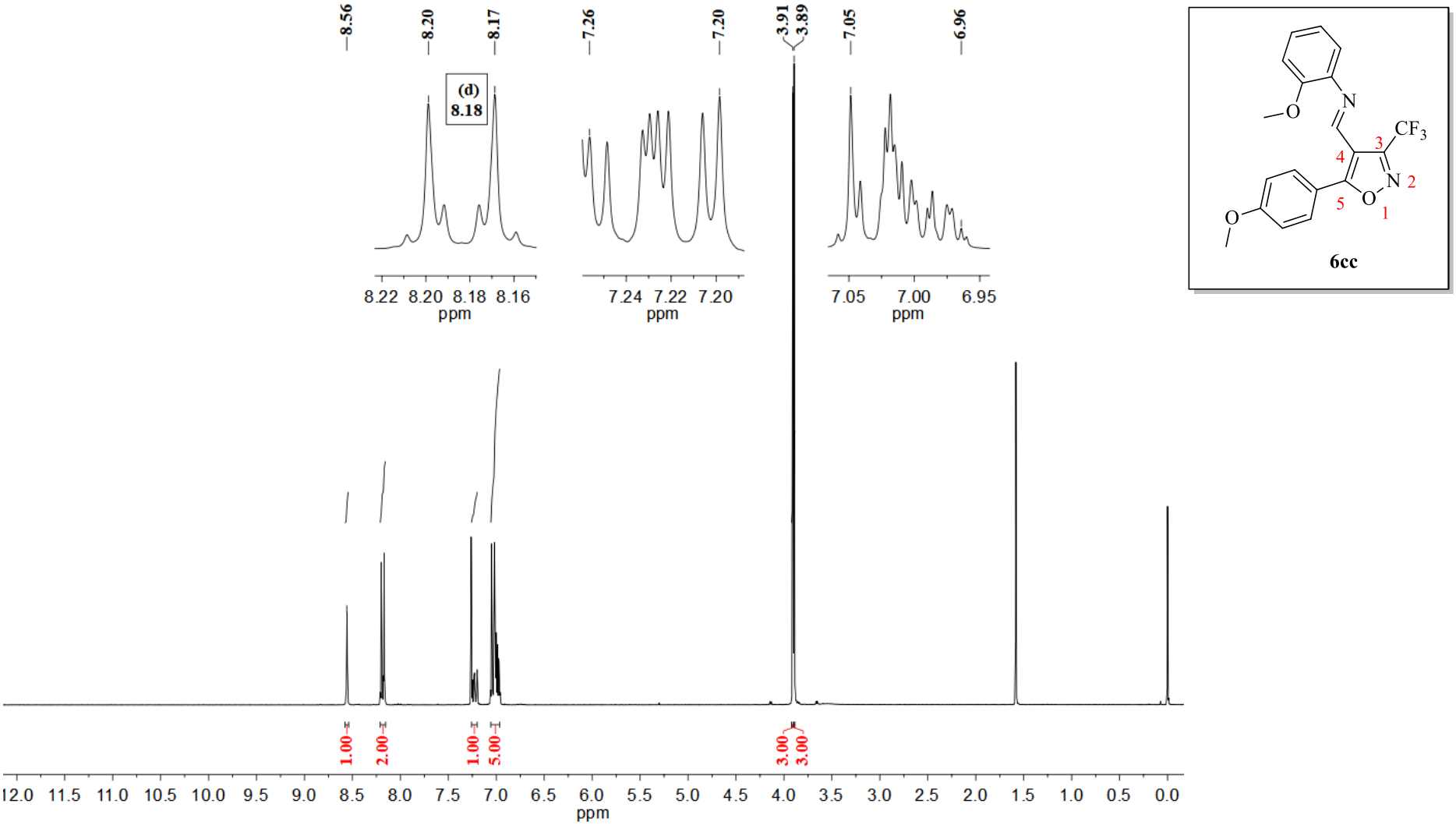


Figure S140 – ^{1}H NMR spectrum of compound **6cc** in $CDCl_3$ at 300.06 MHz.

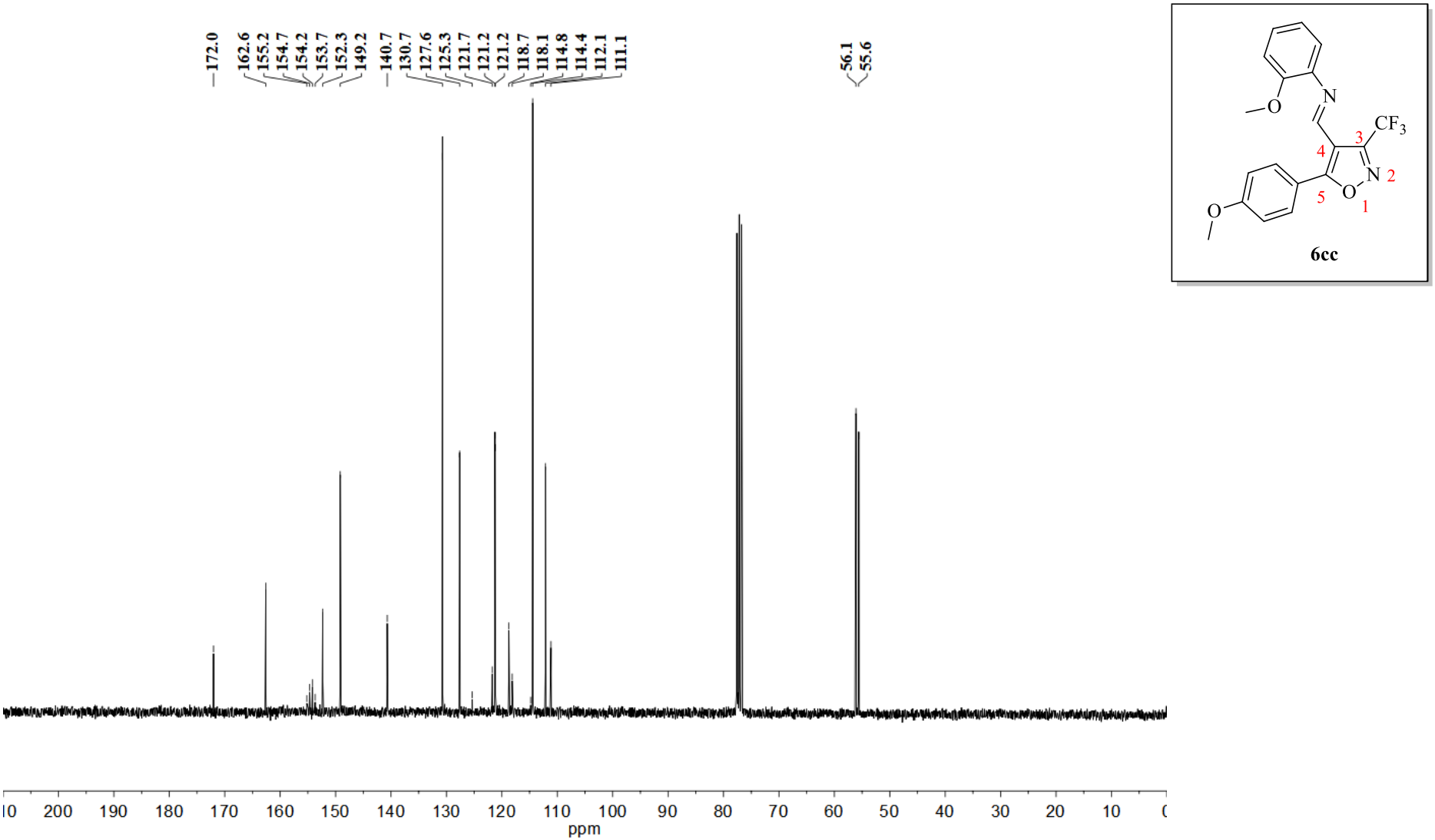


Figure S141 – ^{13}C NMR spectrum of compound **6cc** in $CDCl_3$ at 75.45 MHz.

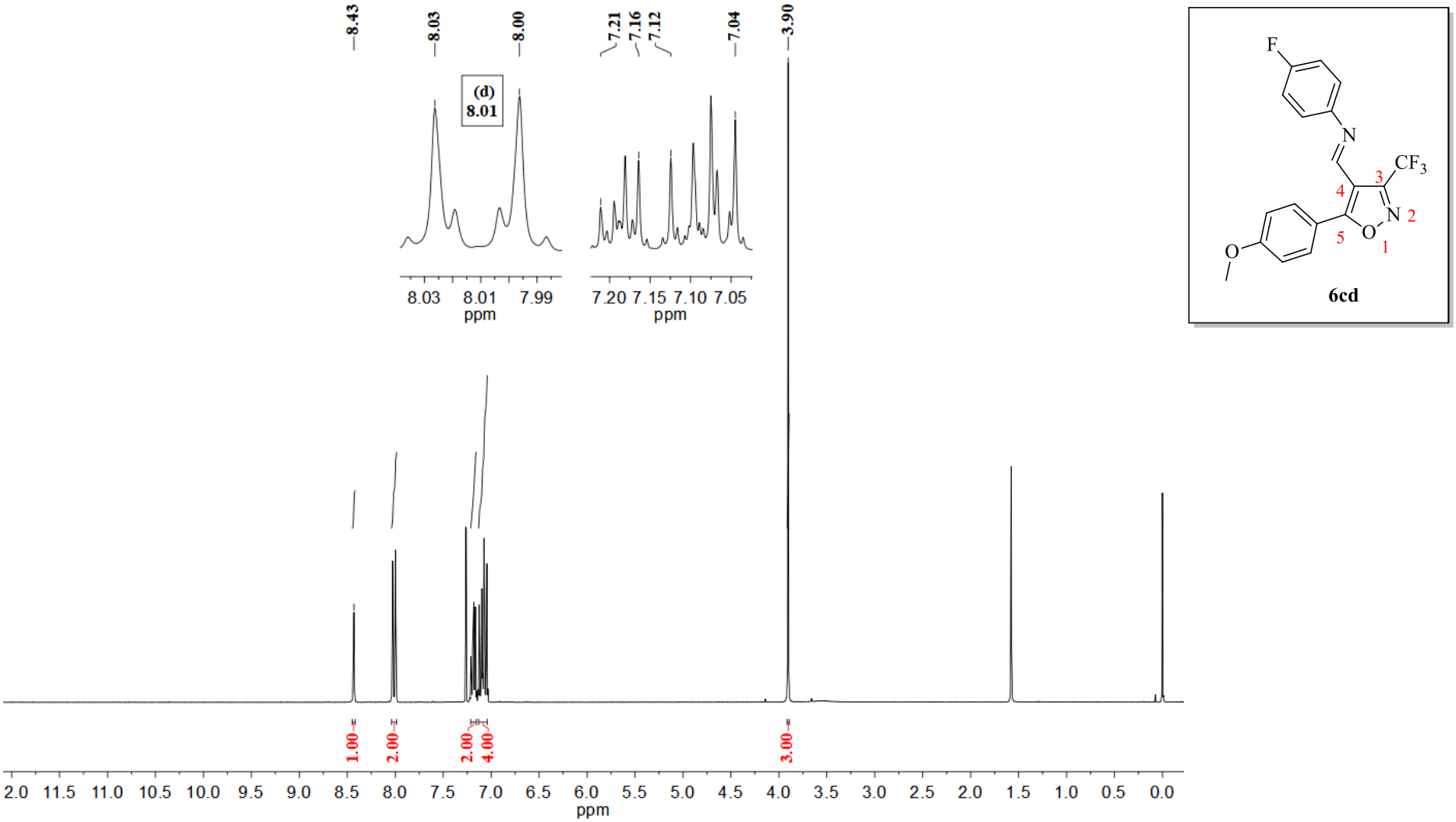


Figure S142 – ^{1}H NMR spectrum of compound **6cd** in $CDCl_3$ at 300.06 MHz.

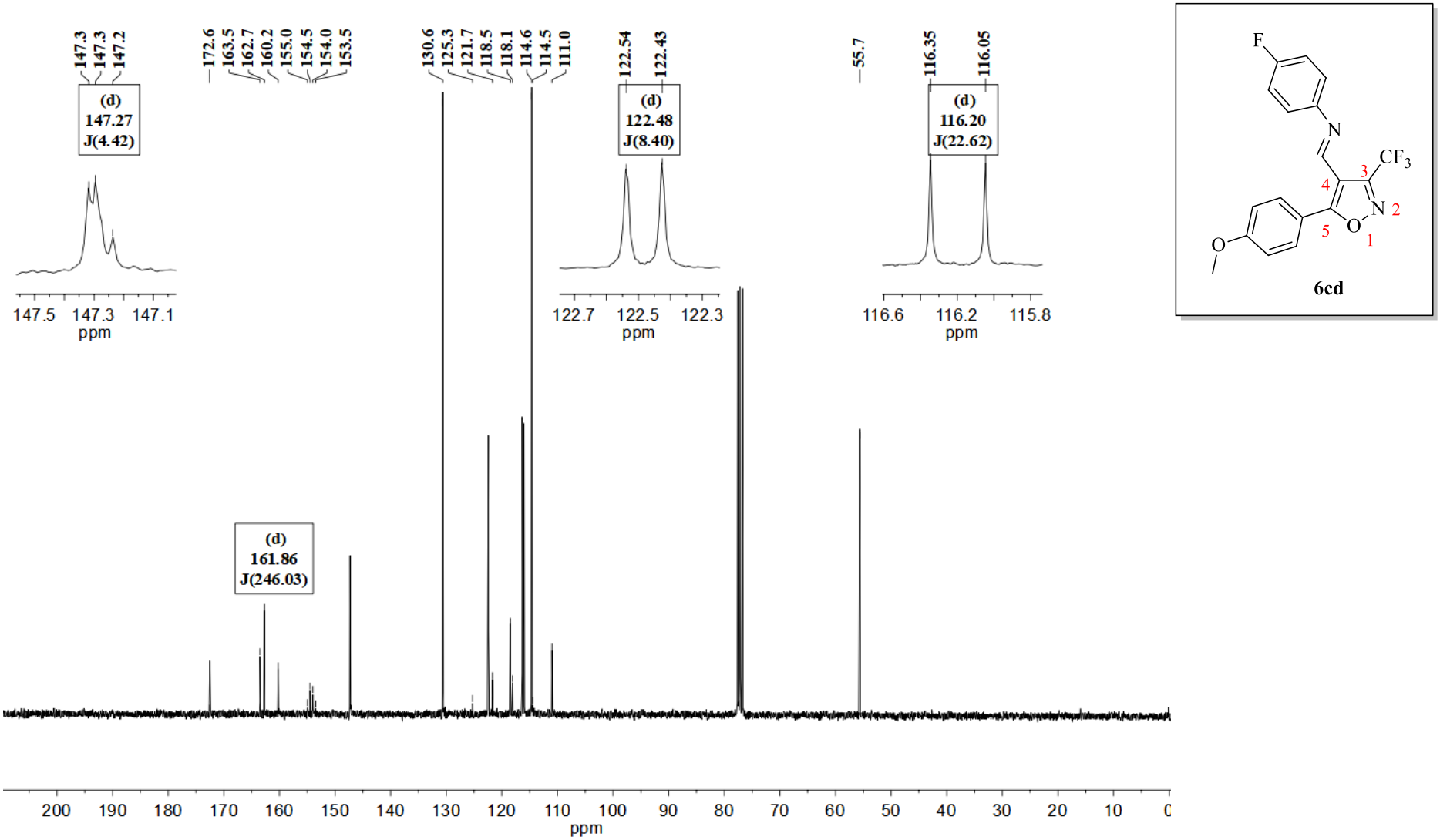


Figure S143 – ^{13}C NMR spectrum of compound **6cd** in $CDCl_3$ at 75.45 MHz.

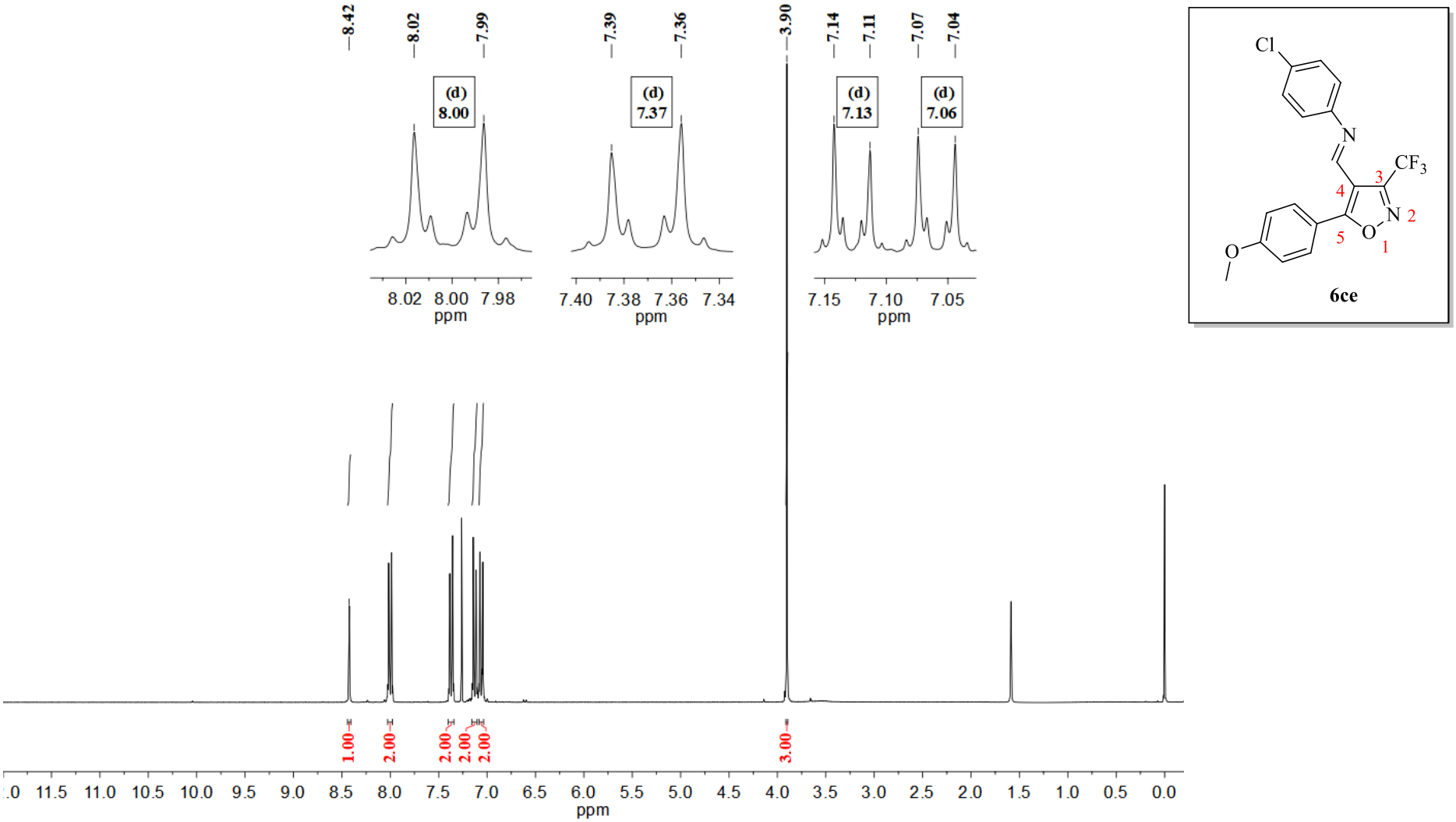


Figure S144 – ^{1}H NMR spectrum of compound **6ce** in $CDCl_3$ at 300.06 MHz.

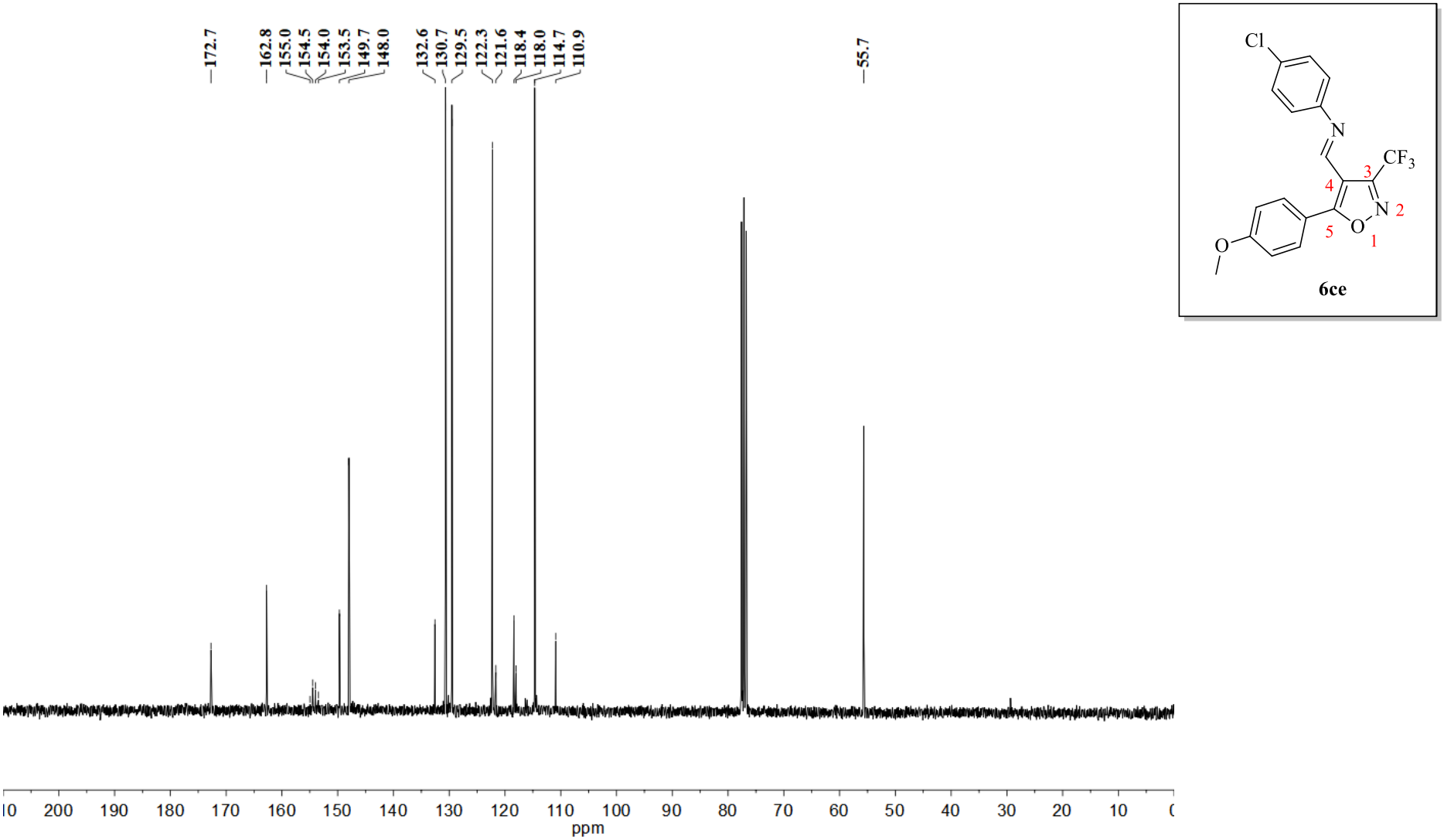


Figure S145 – ^{13}C NMR spectrum of compound **6cee** in $CDCl_3$ at 75.45 MHz.

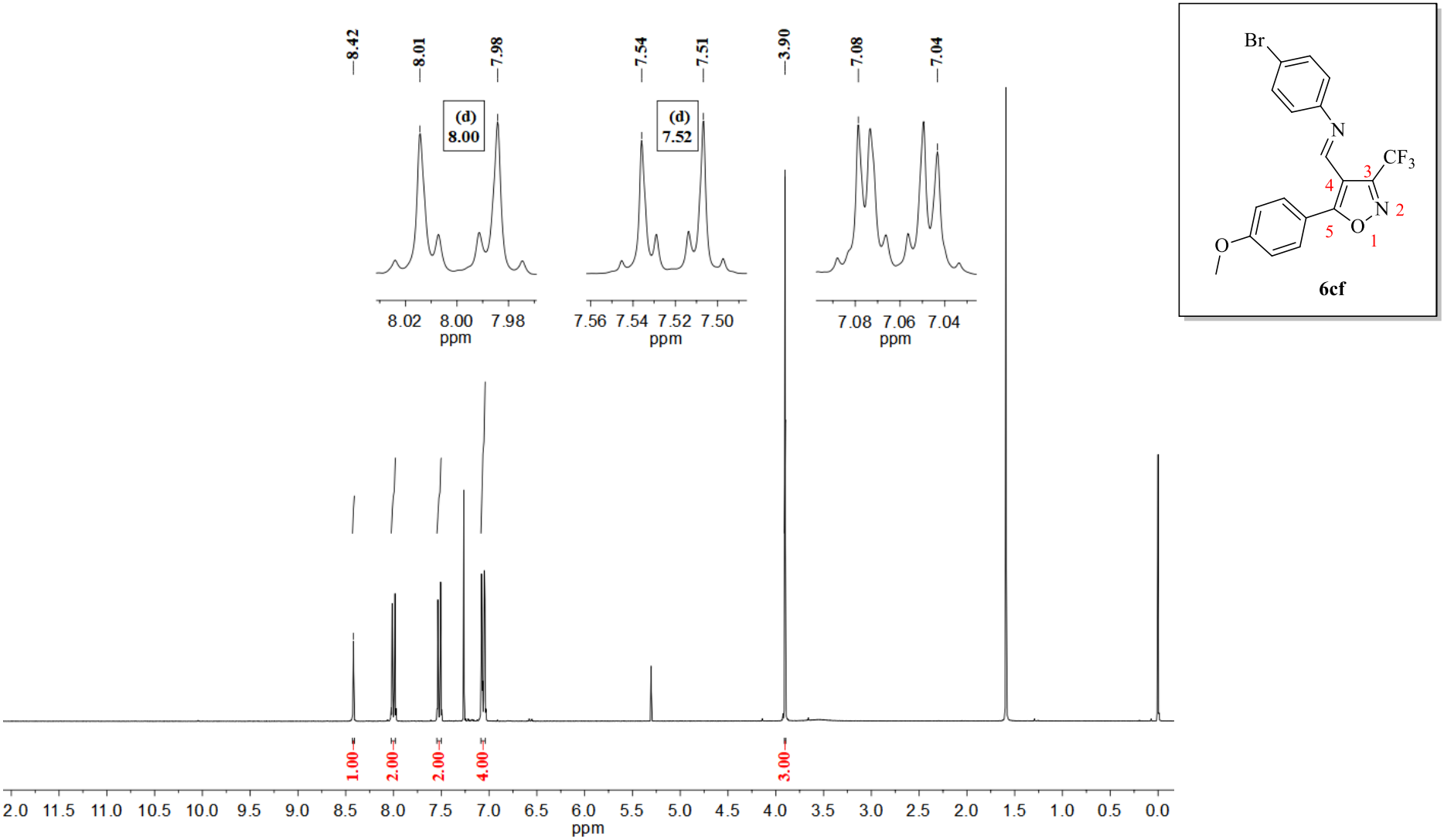


Figure S146 – ^{1}H NMR spectrum of compound **6cf** in $CDCl_3$ at 300.06 MHz.

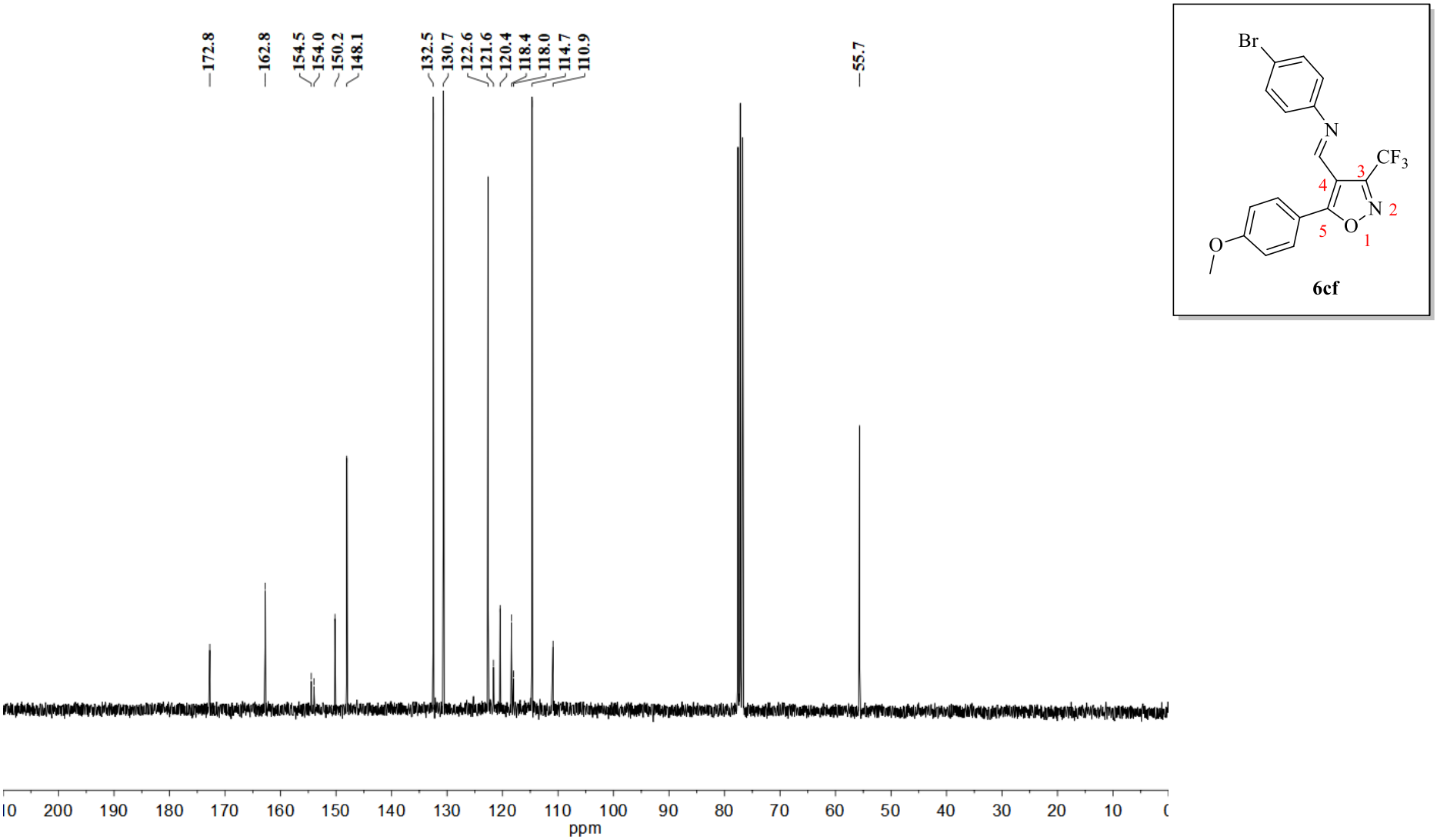


Figure S147 – ^{13}C NMR spectrum of compound **6cf** in $CDCl_3$ at 75.45 MHz.

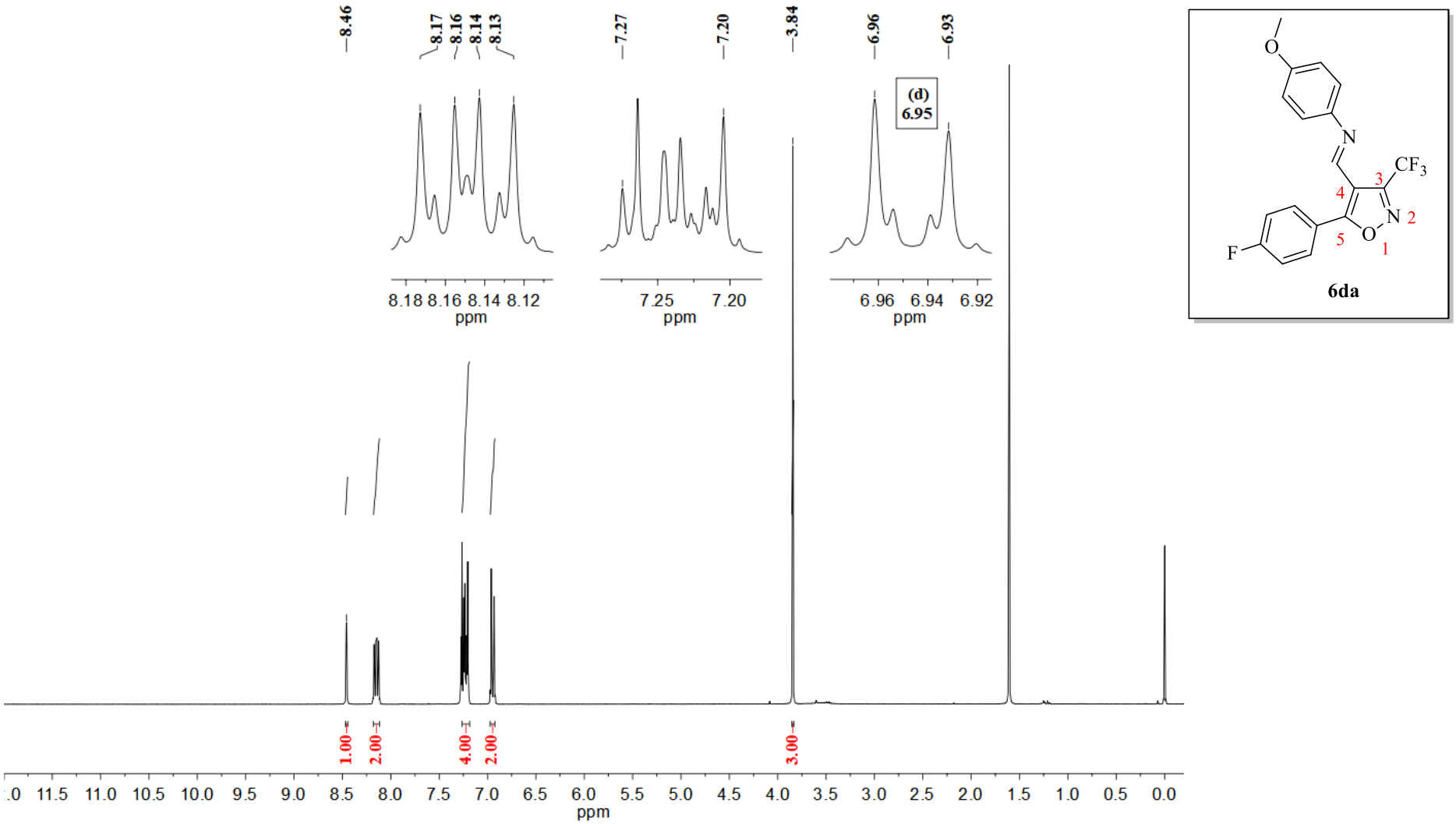


Figure S148 – ^{1}H NMR spectrum of compound **6da** in $CDCl_3$ at 300.06 MHz.

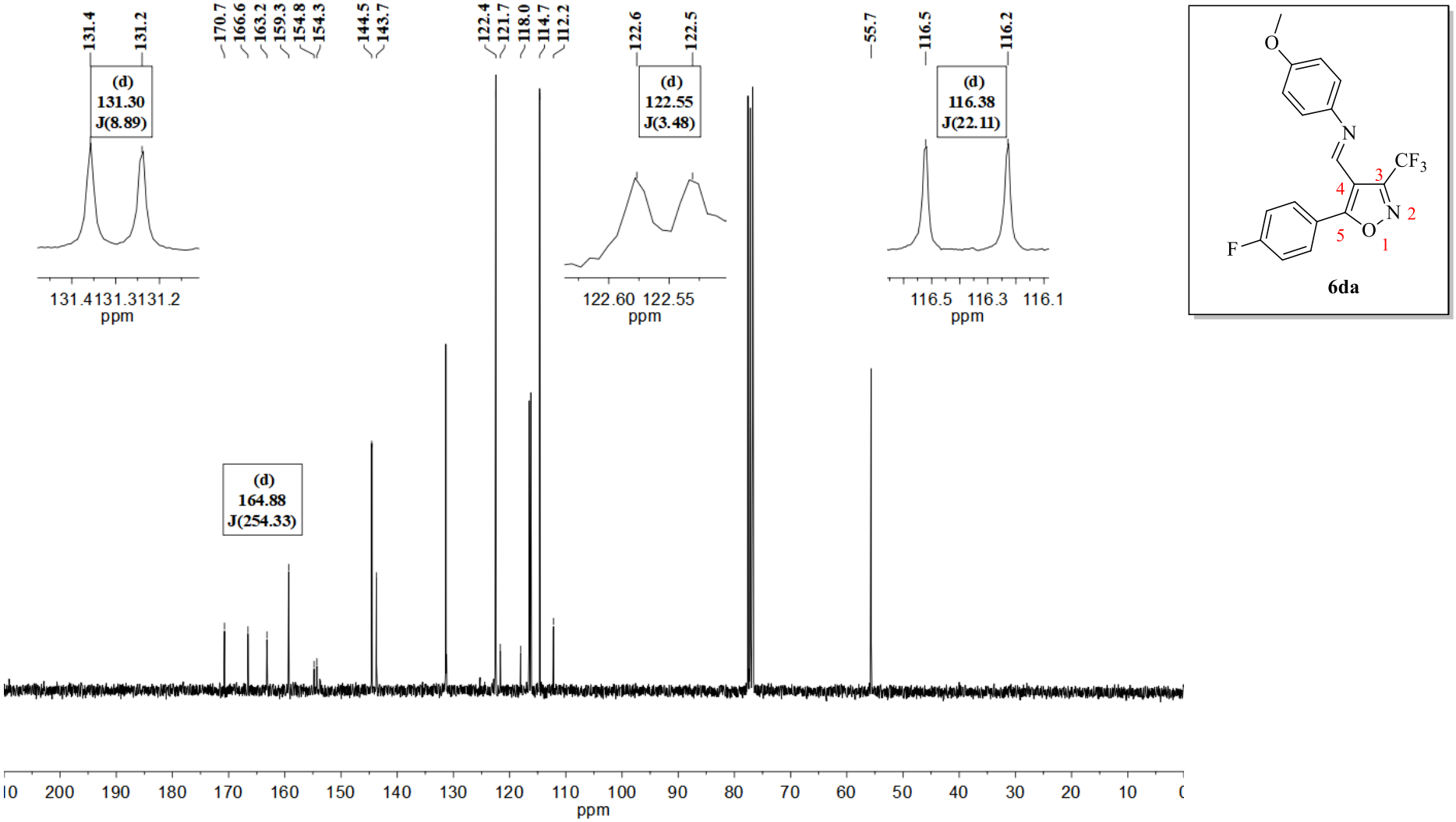


Figure S149 – ^{13}C NMR spectrum of compound **6da** in $CDCl_3$ at 75.45 MHz.

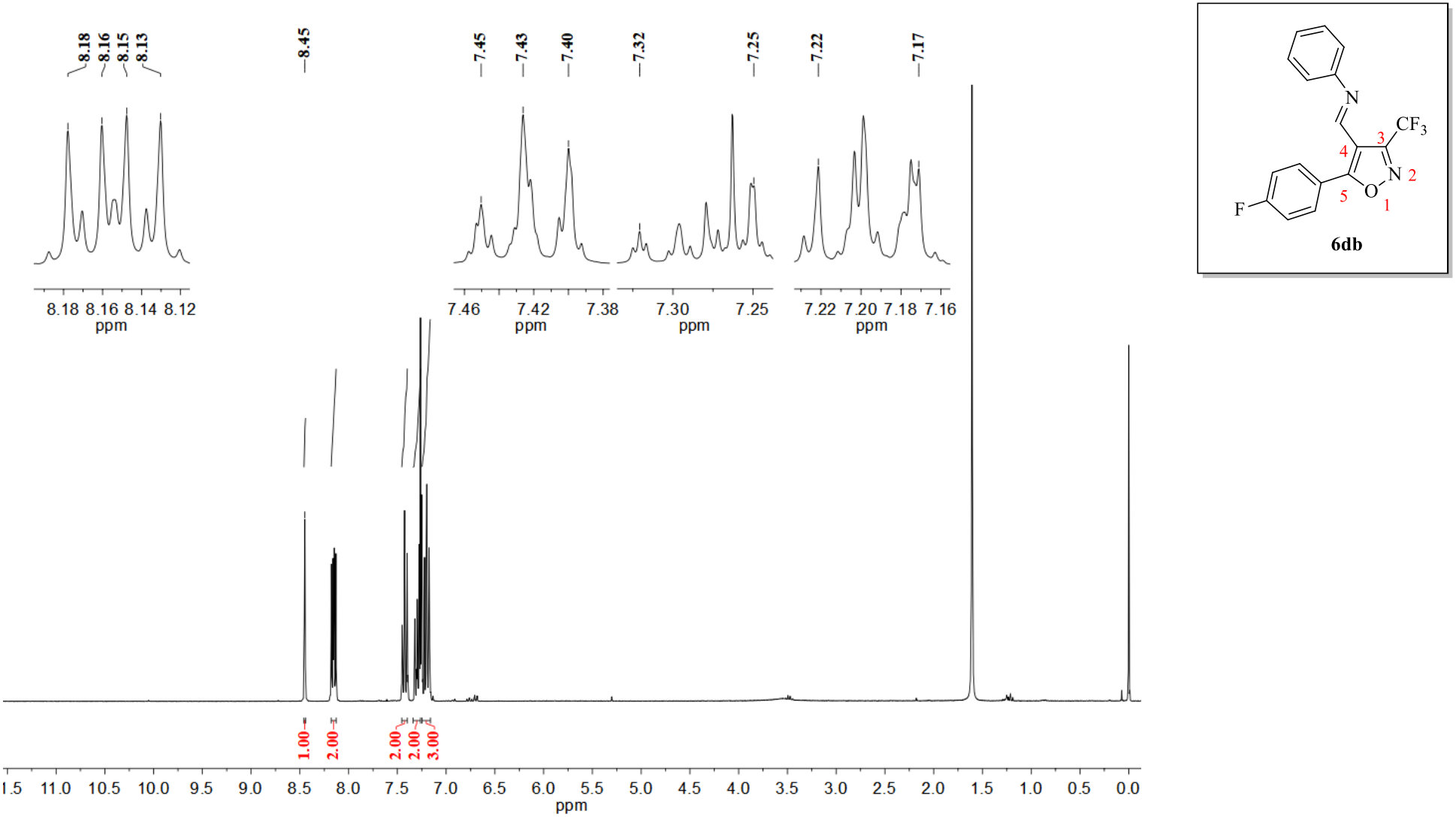


Figure S150 – ^{1}H NMR spectrum of compound **6db** in $CDCl_3$ at 300.06 MHz.

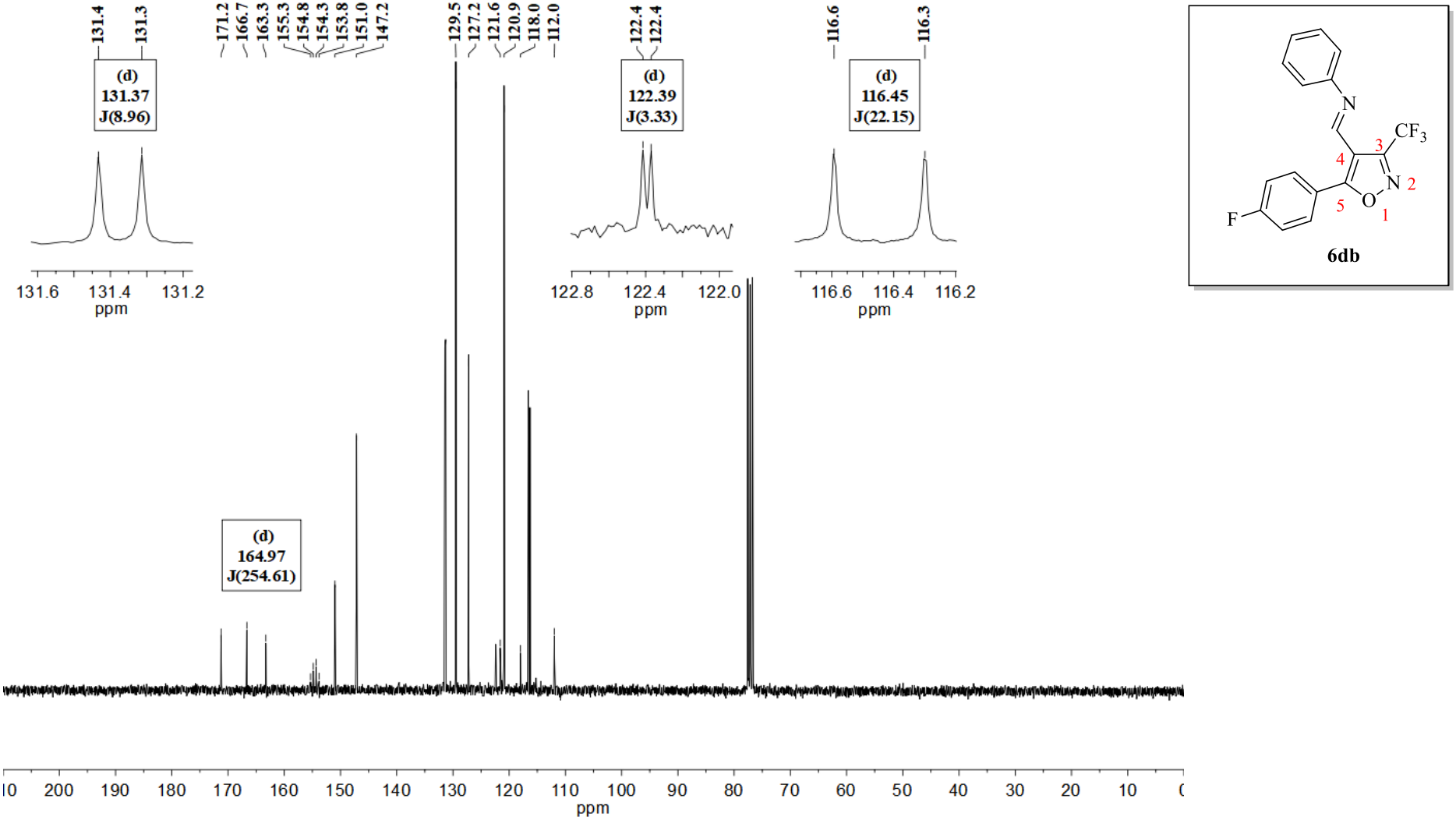


Figure S151 – ^{13}C NMR spectrum of compound **6db** in $CDCl_3$ at 75.45 MHz.

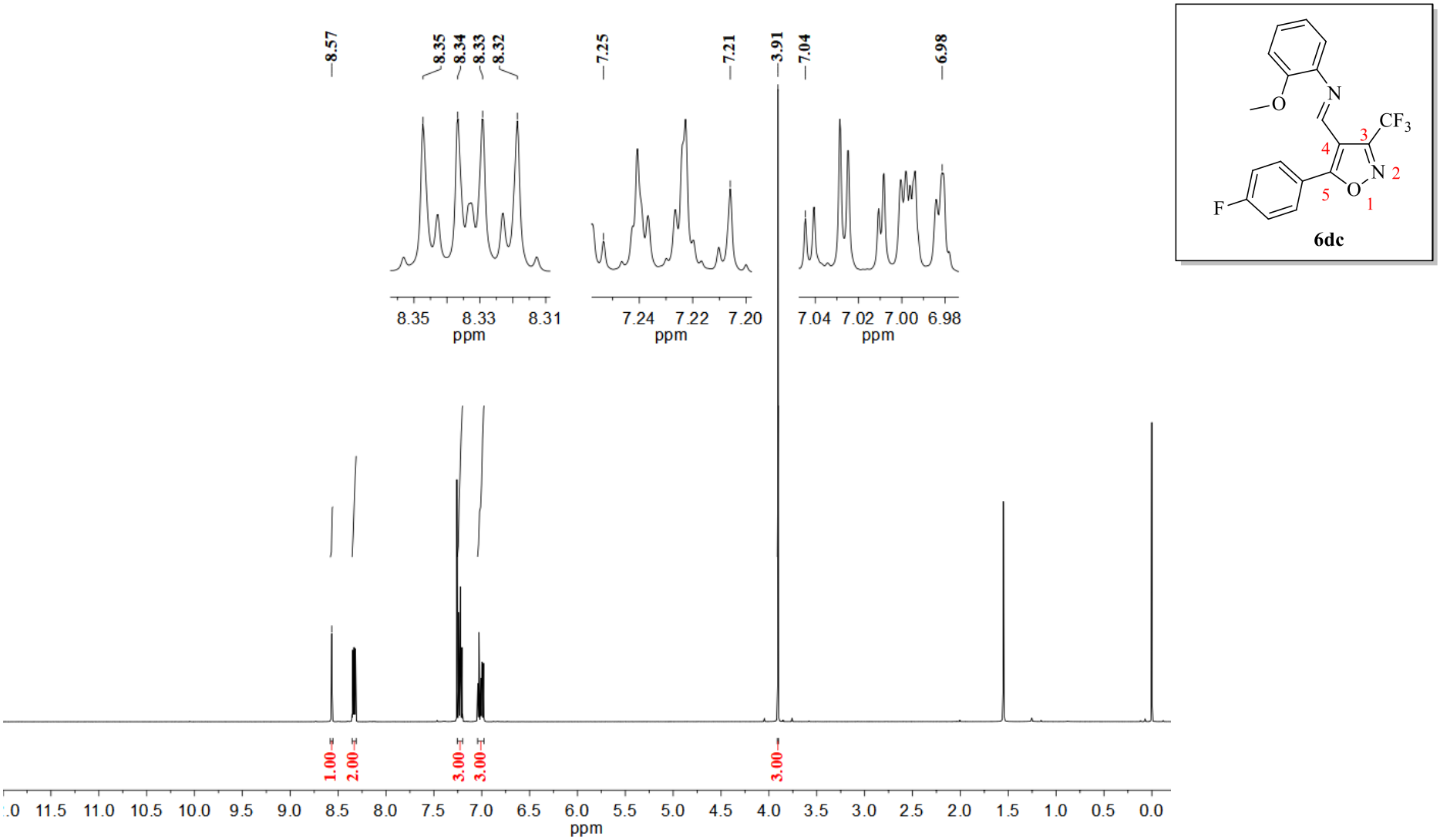


Figure S152 – ^{1}H NMR spectrum of compound **6dc** in $CDCl_3$ at 300.06 MHz.

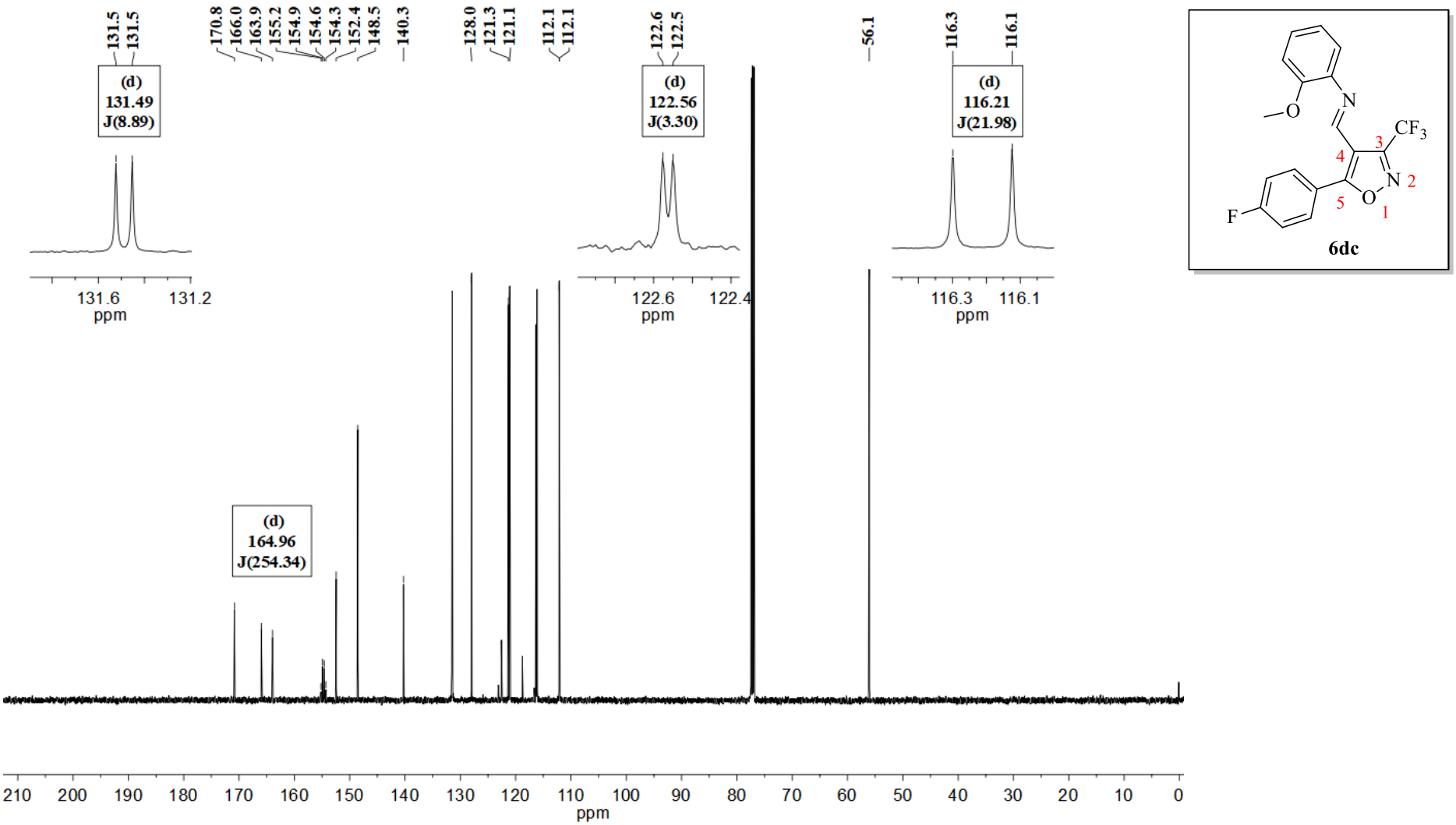


Figure S153 – ^{13}C NMR spectrum of compound **6dc** in $CDCl_3$ at 75.45 MHz.

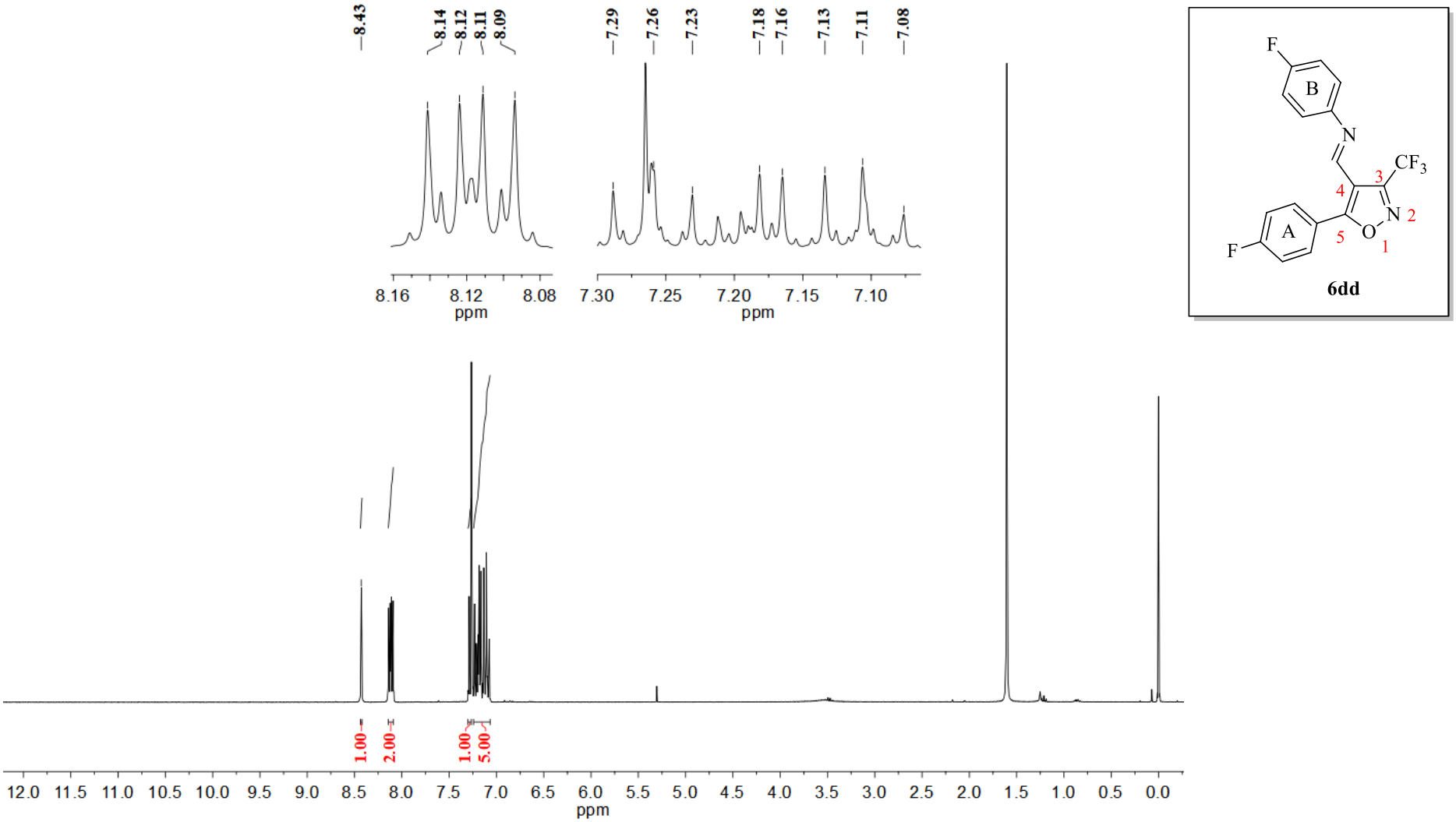


Figure S154 – ^{1}H NMR spectrum of compound **6dd** in $CDCl_3$ at 300.06 MHz.

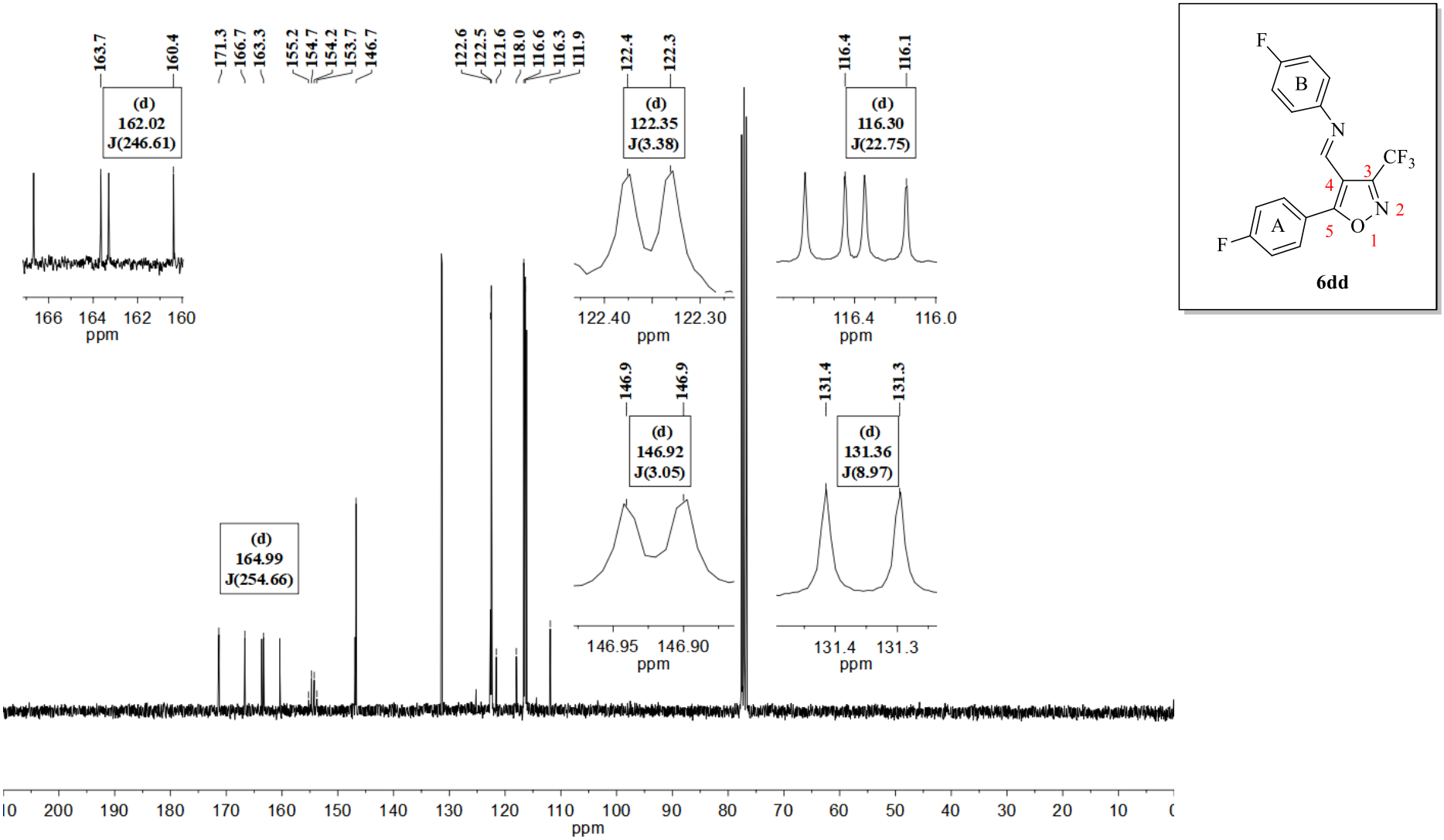


Figure S155 – ^{13}C NMR spectrum of compound **6dd** in $CDCl_3$ at 75.45 MHz.

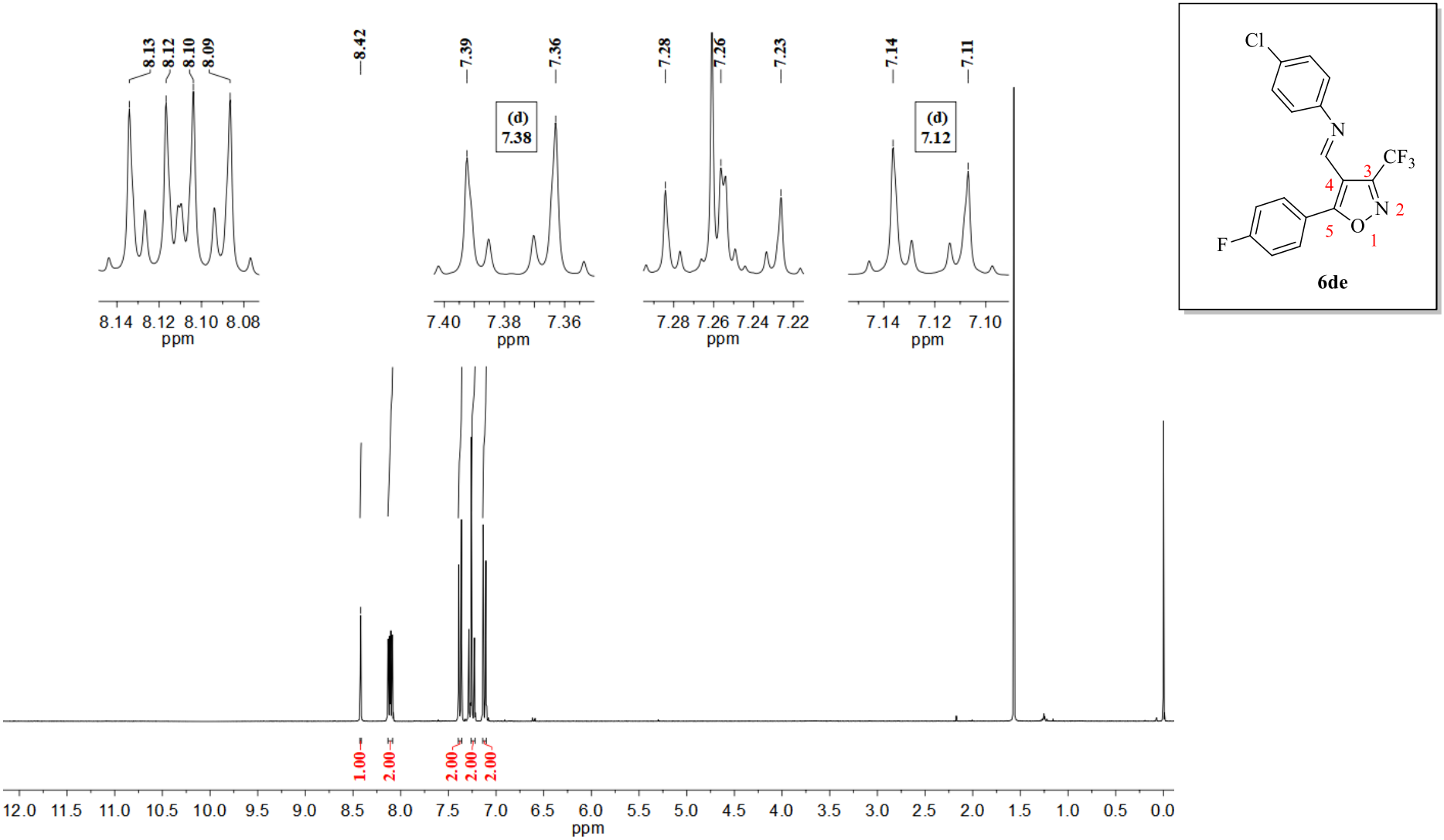


Figure S156 – ^{1}H NMR spectrum of compound **6de** in $CDCl_3$ at 300.06 MHz.

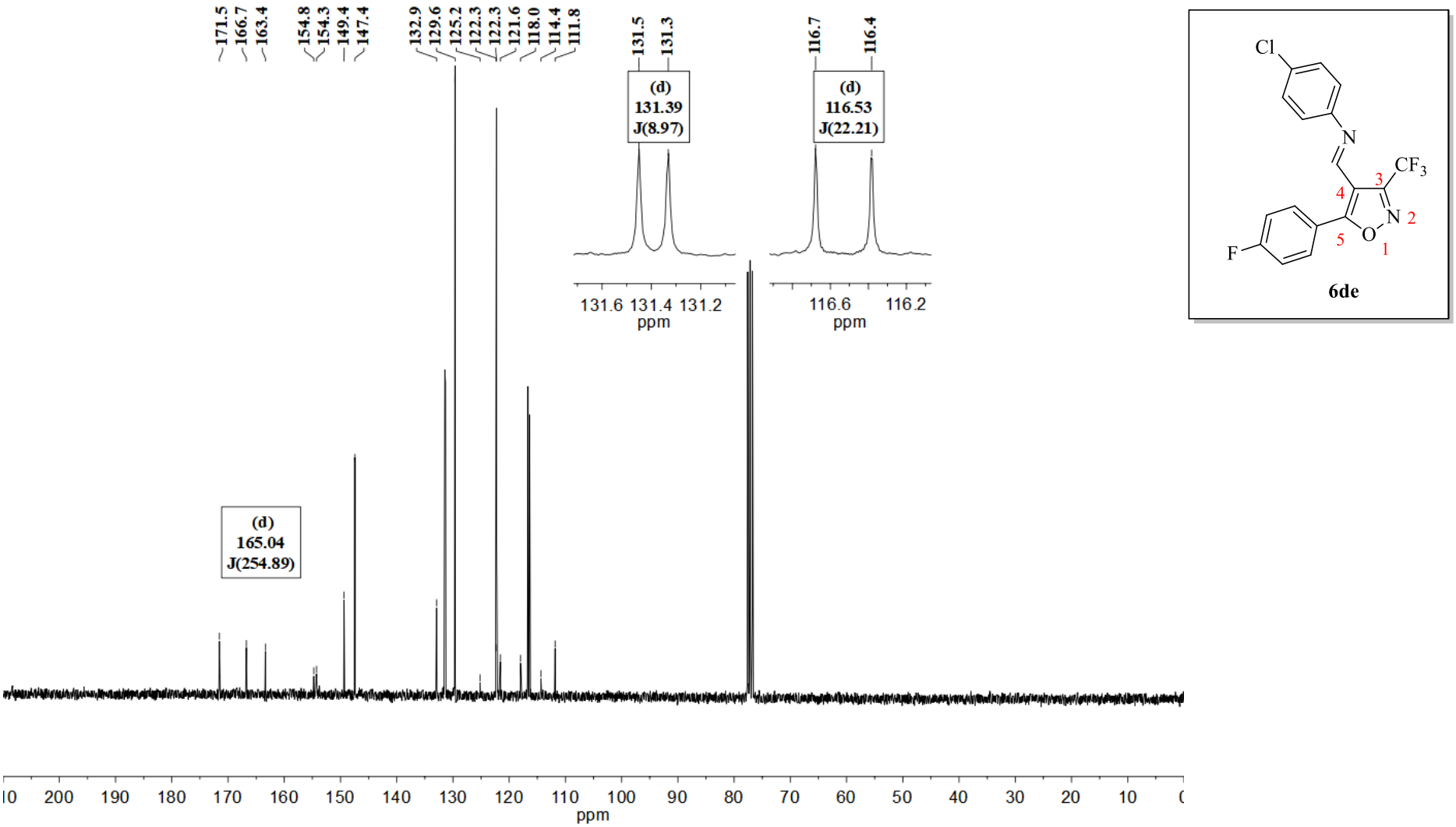


Figure S157 – ^{13}C NMR spectrum of compound **6de** in $CDCl_3$ at 75.45 MHz.

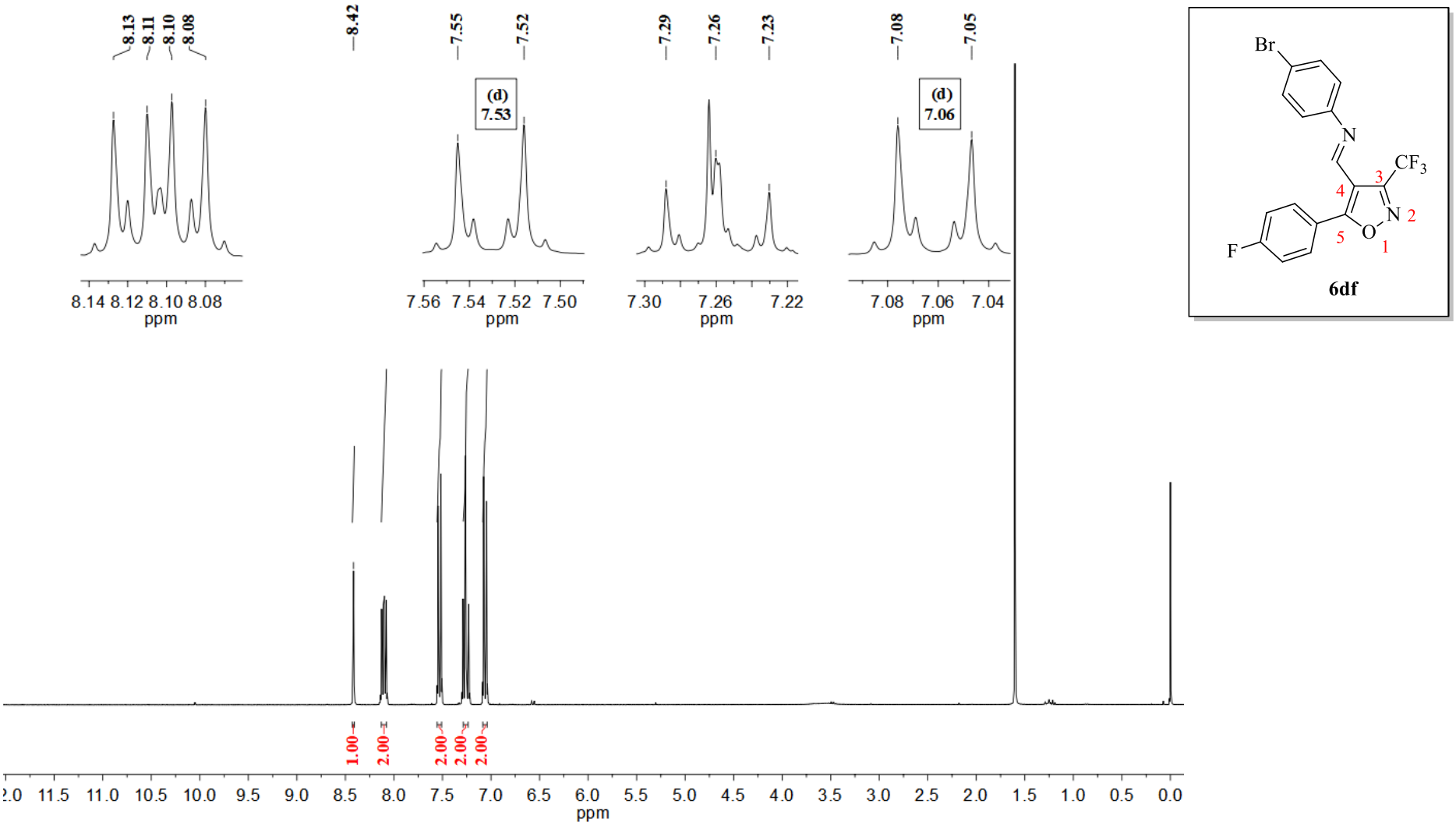


Figure S158 – ^{1}H NMR spectrum of compound **6df** in $CDCl_3$ at 300.06 MHz.

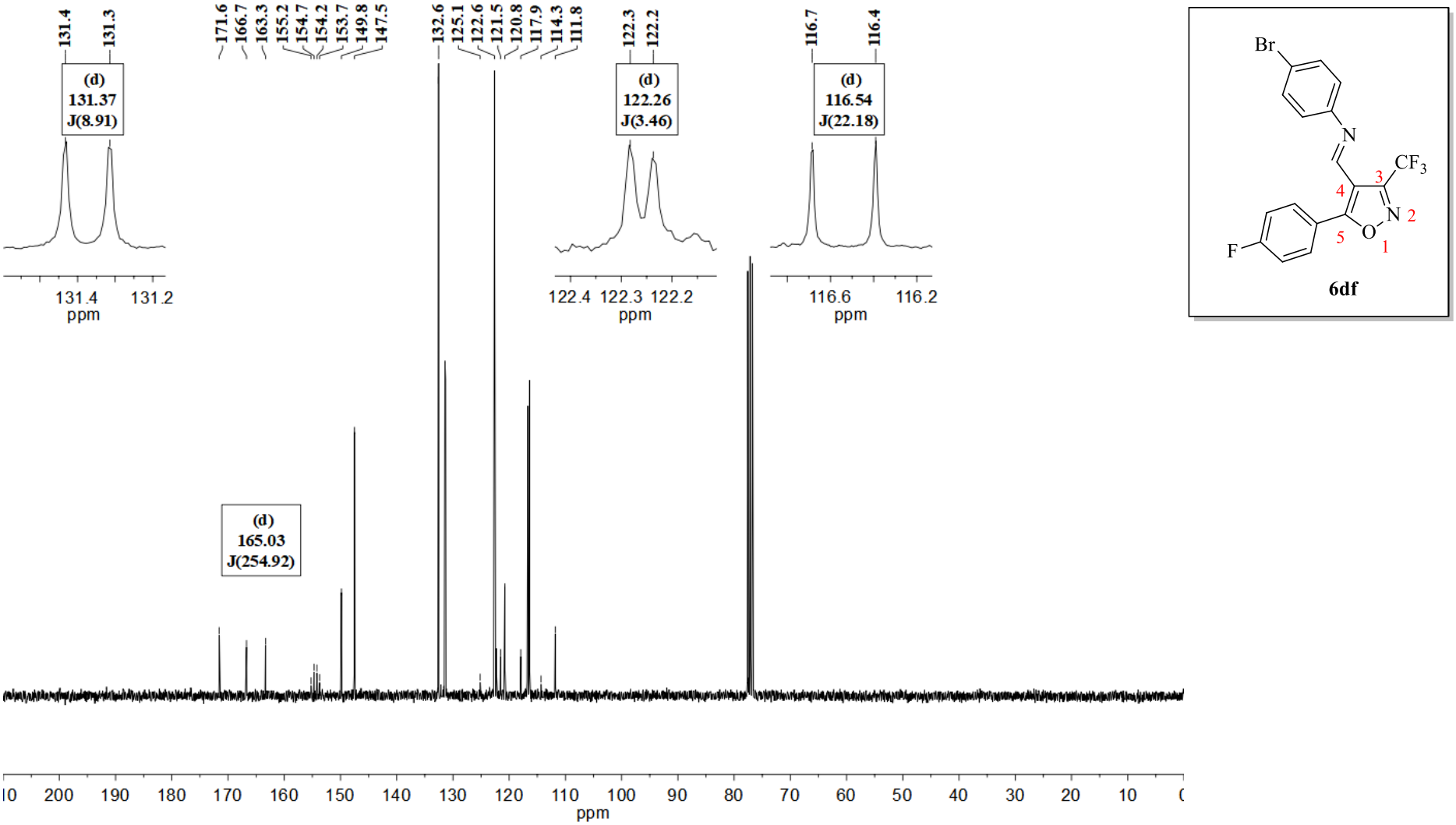


Figure S159 – ^{13}C NMR spectrum of compound **6df** in $CDCl_3$ at 75.45 MHz.

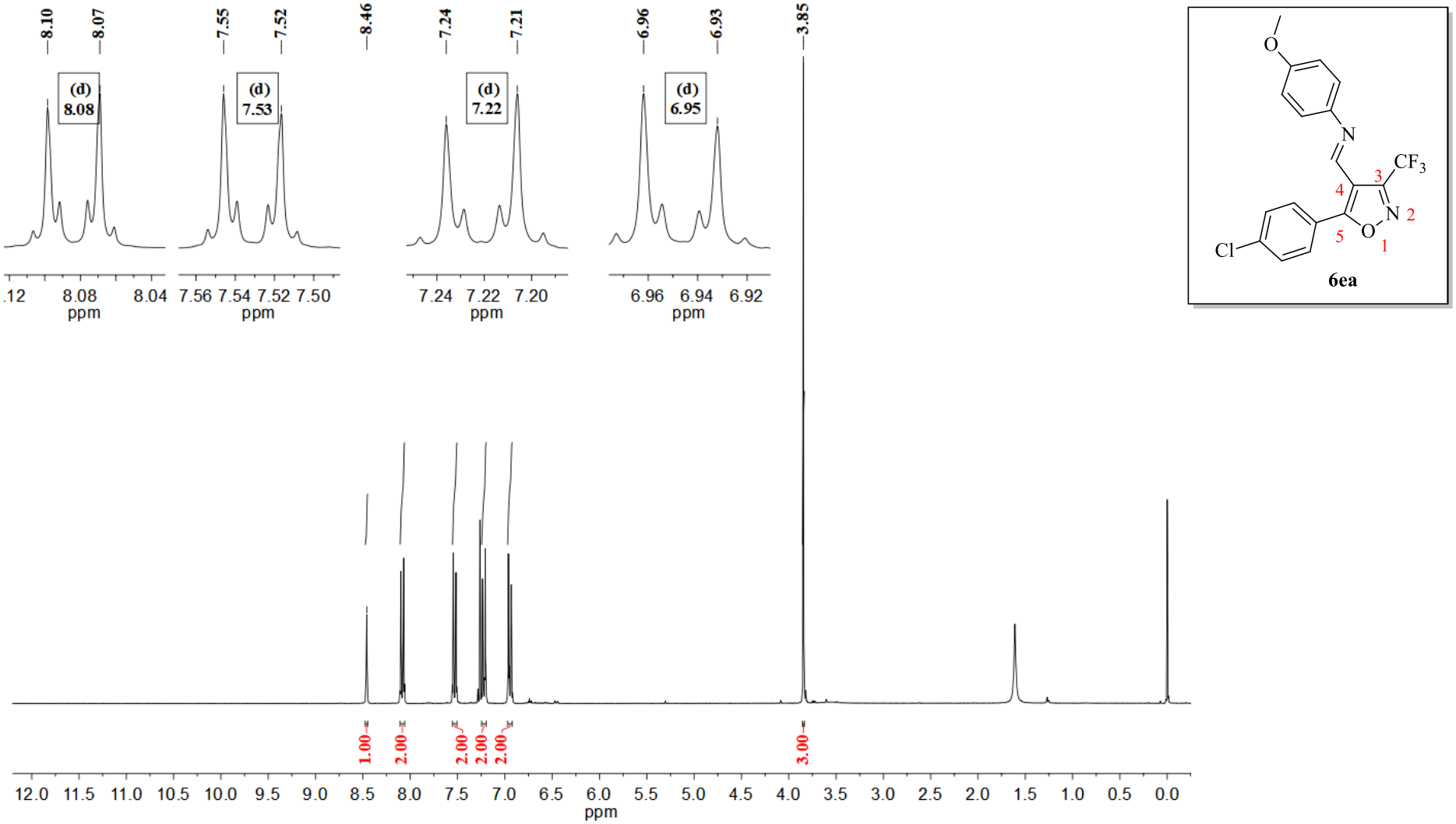
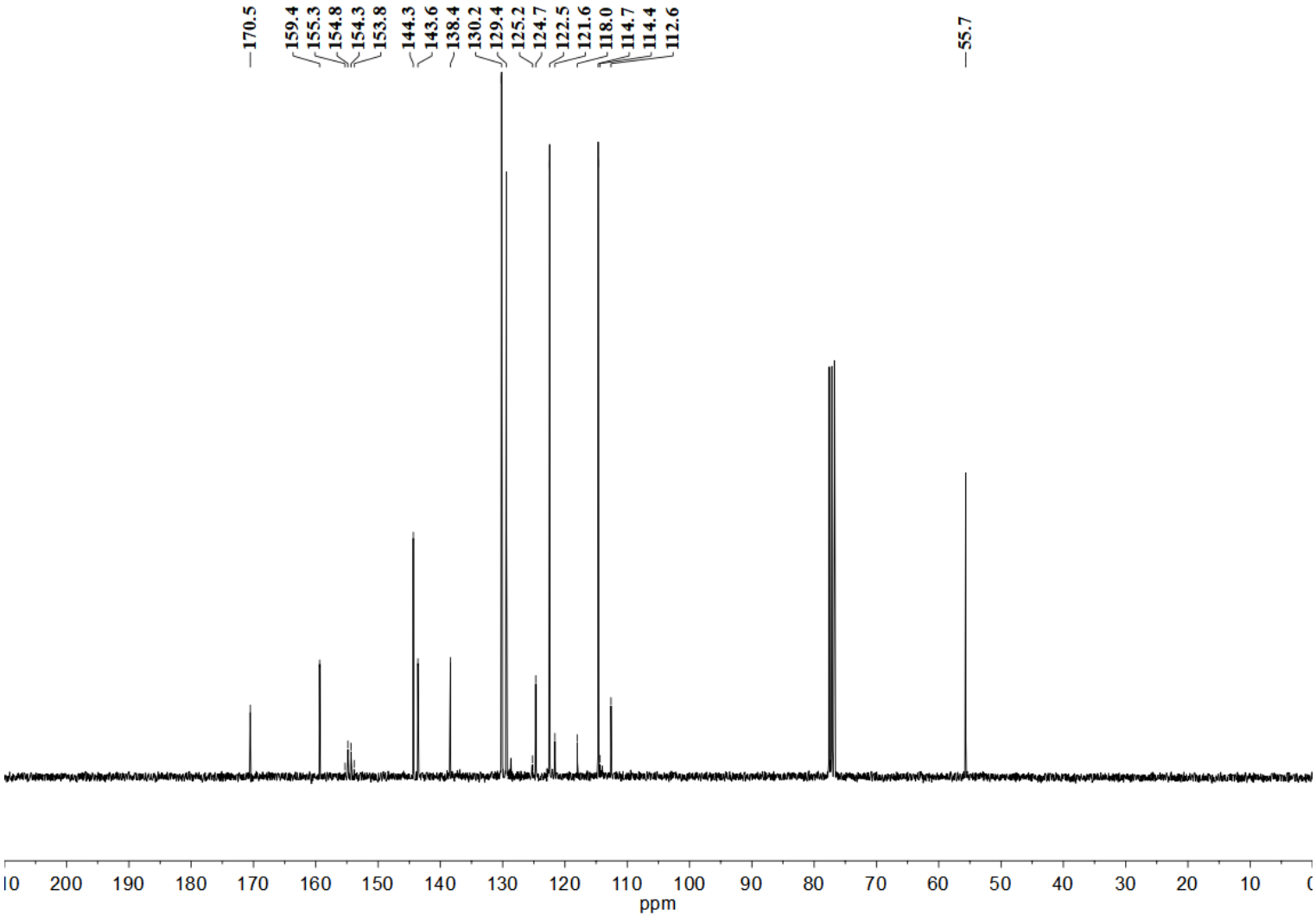
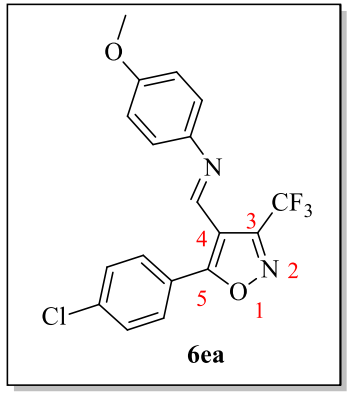


Figure S160 – ^{1}H NMR spectrum of compound **6ea** in $CDCl_3$ at 300.06 MHz.





6ea

Figure S161 – ^{13}C NMR spectrum of compound **6ea** in $CDCl_3$ at 75.45 MHz.

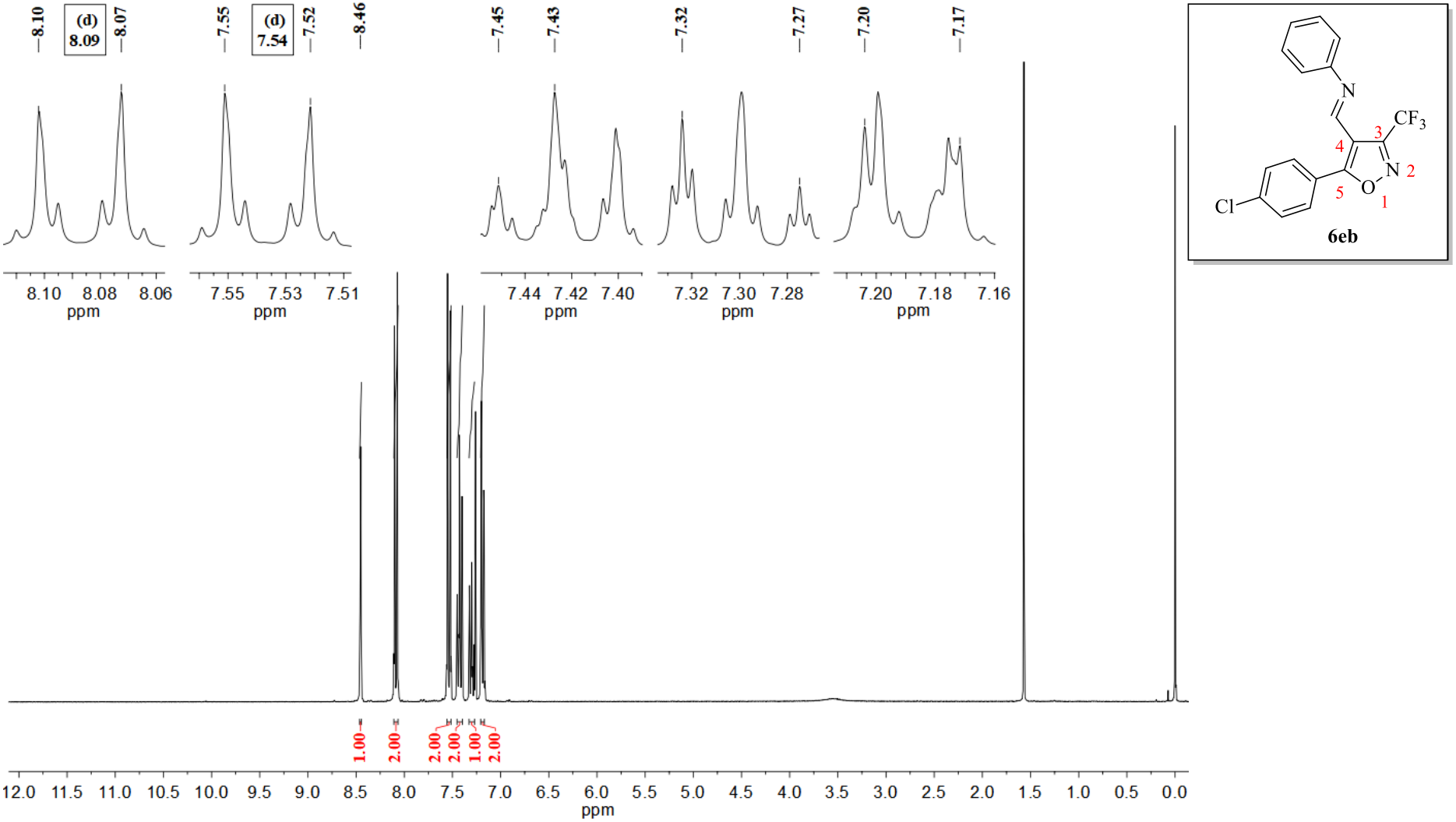


Figure S162 – ^{1}H NMR spectrum of compound **6eb** in $CDCl_3$ at 300.06 MHz.

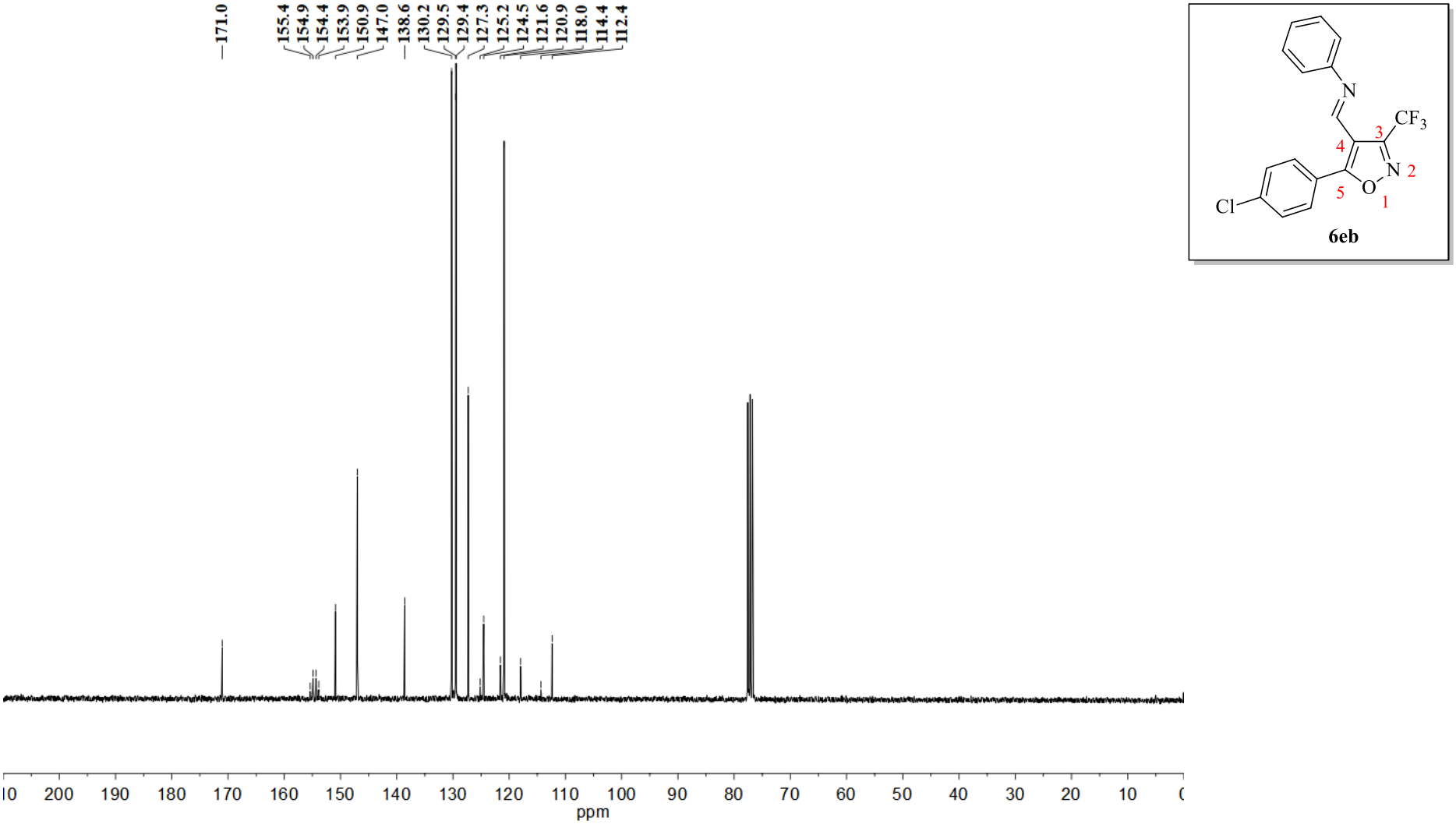


Figure S163 – ^{13}C NMR spectrum of compound **6eb** in $CDCl_3$ at 75.45 MHz.

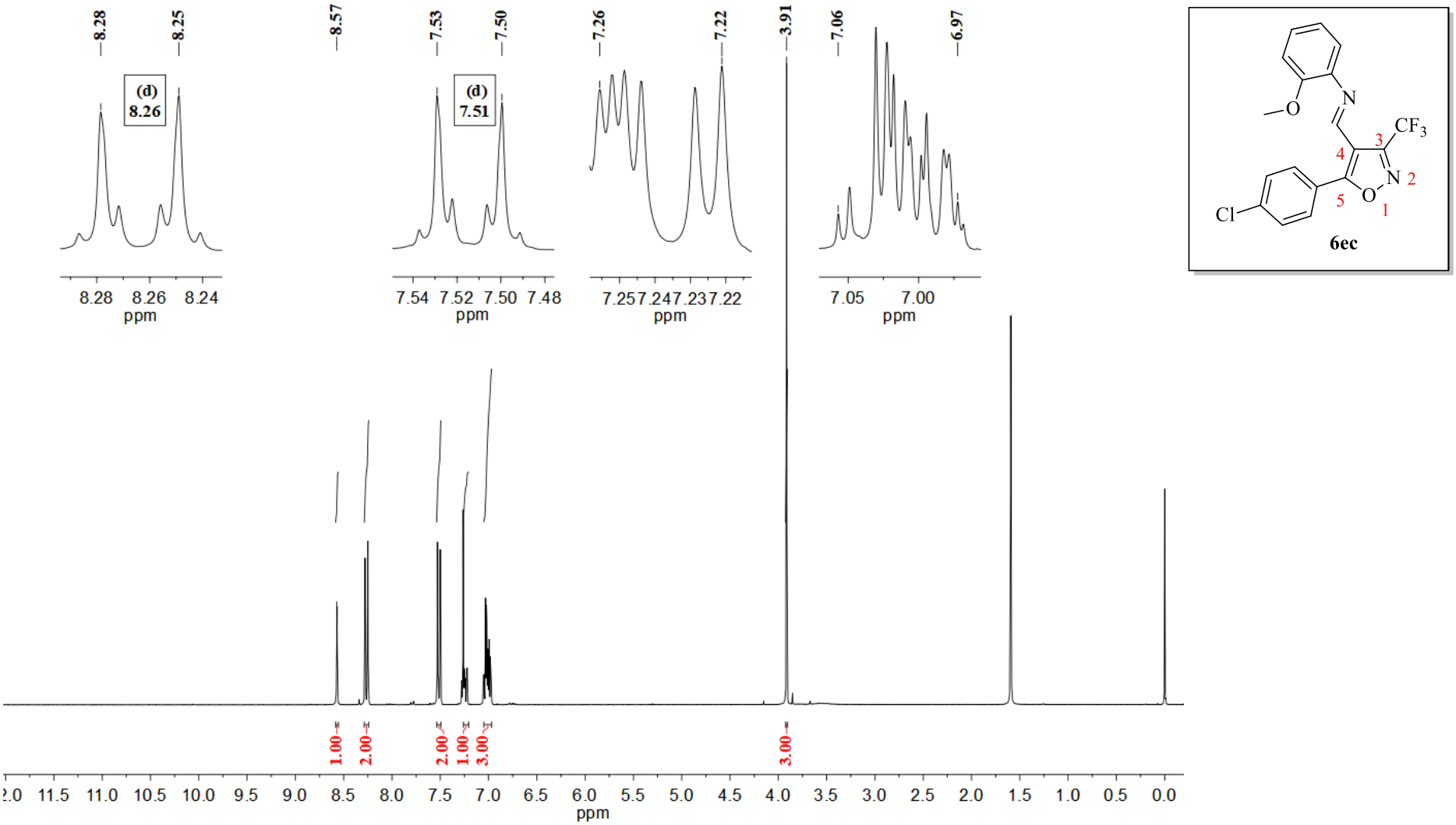


Figure S164 – ^{1}H NMR spectrum of compound **6ec** in $CDCl_3$ at 300.06 MHz.

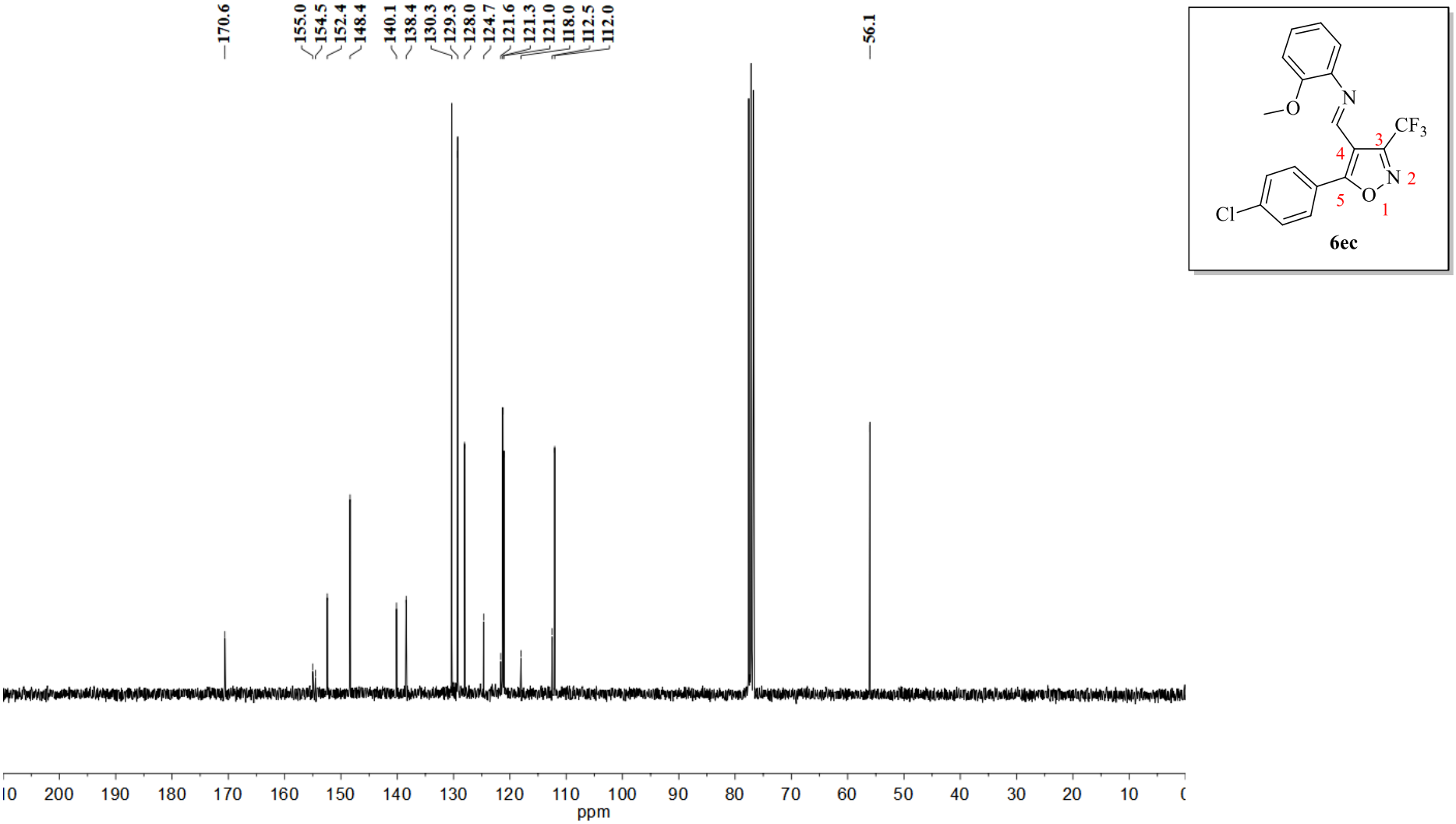


Figure S165 – ^{13}C NMR spectrum of compound **6ec** in $CDCl_3$ at 75.45 MHz.

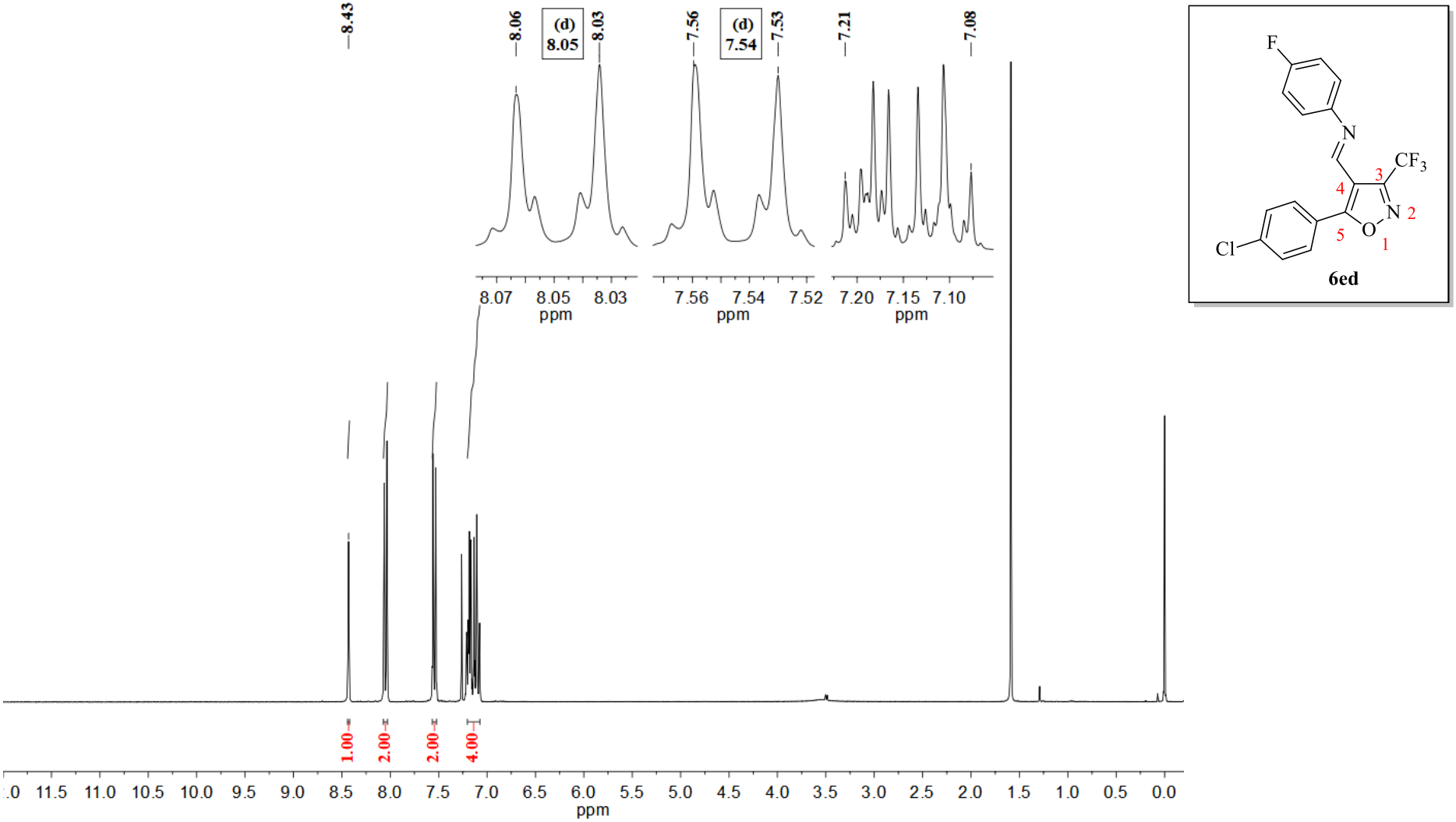


Figure S166 – ^{1}H NMR spectrum of compound **6ed** in $CDCl_3$ at 300.06 MHz.

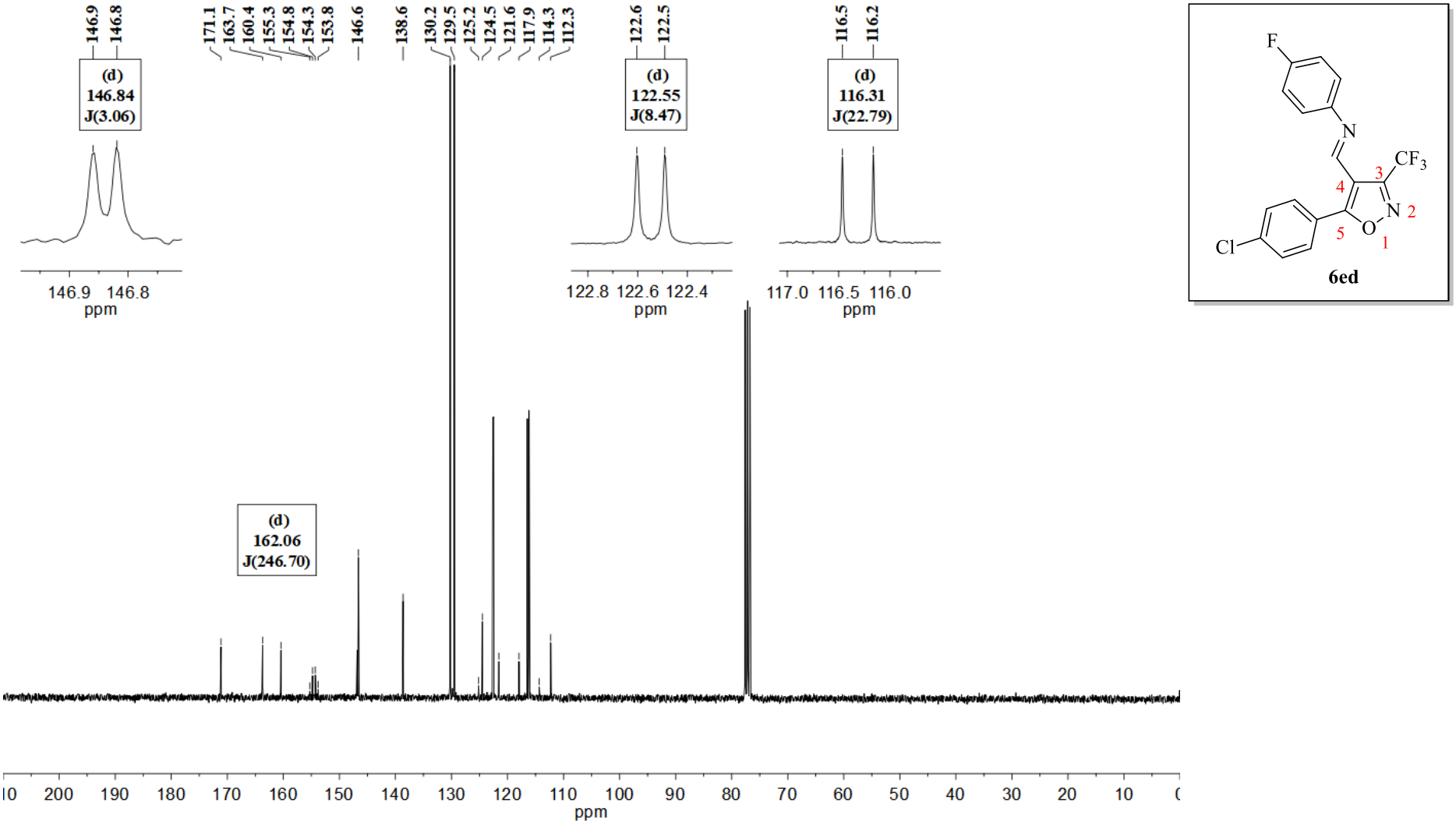


Figure S167 – ^{13}C NMR spectrum of compound **6ed** in $CDCl_3$ at 75.45 MHz.

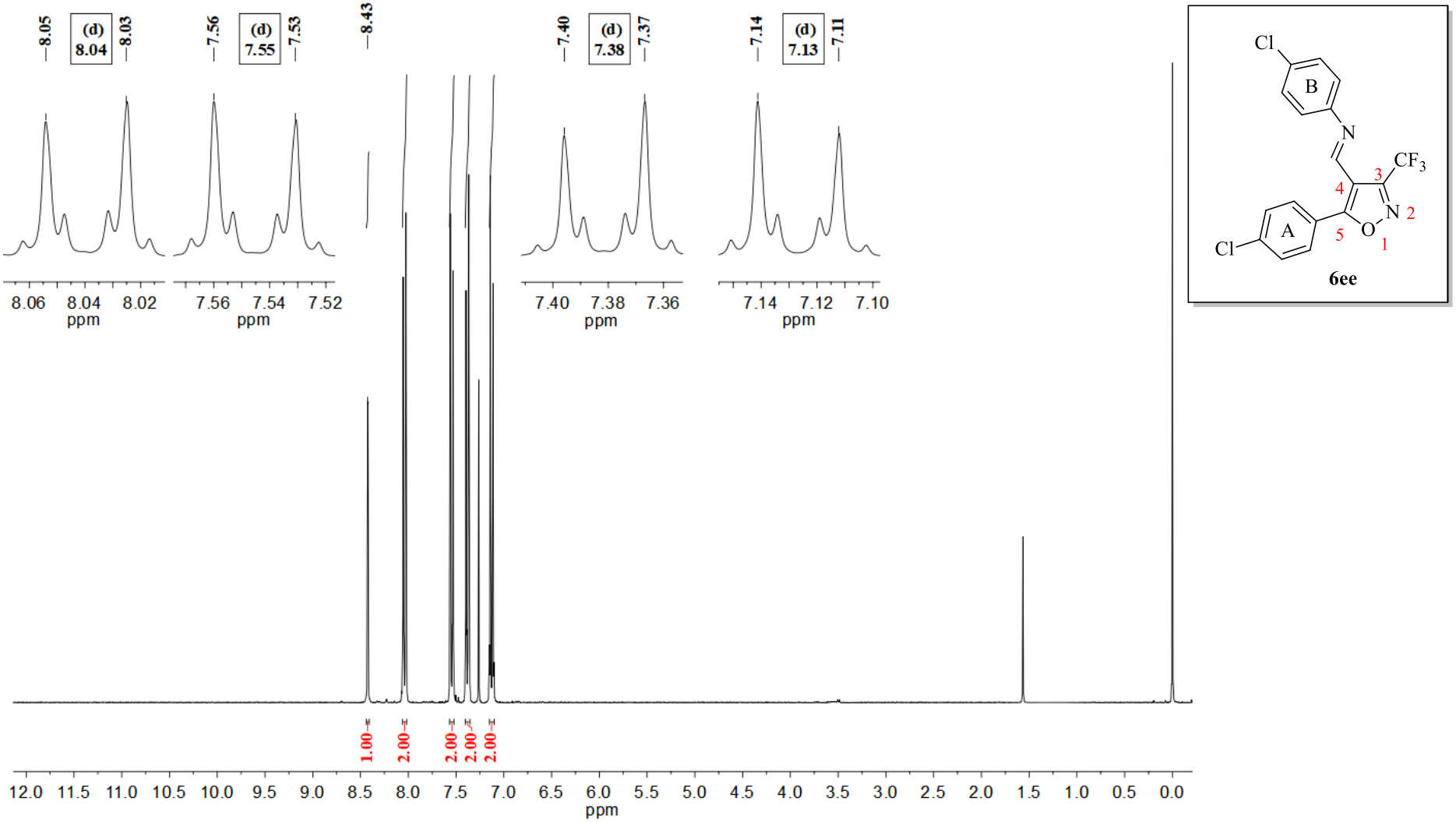


Figure S168 – ^{1}H NMR spectrum of compound **6ee** in $CDCl_3$ at 300.06 MHz.

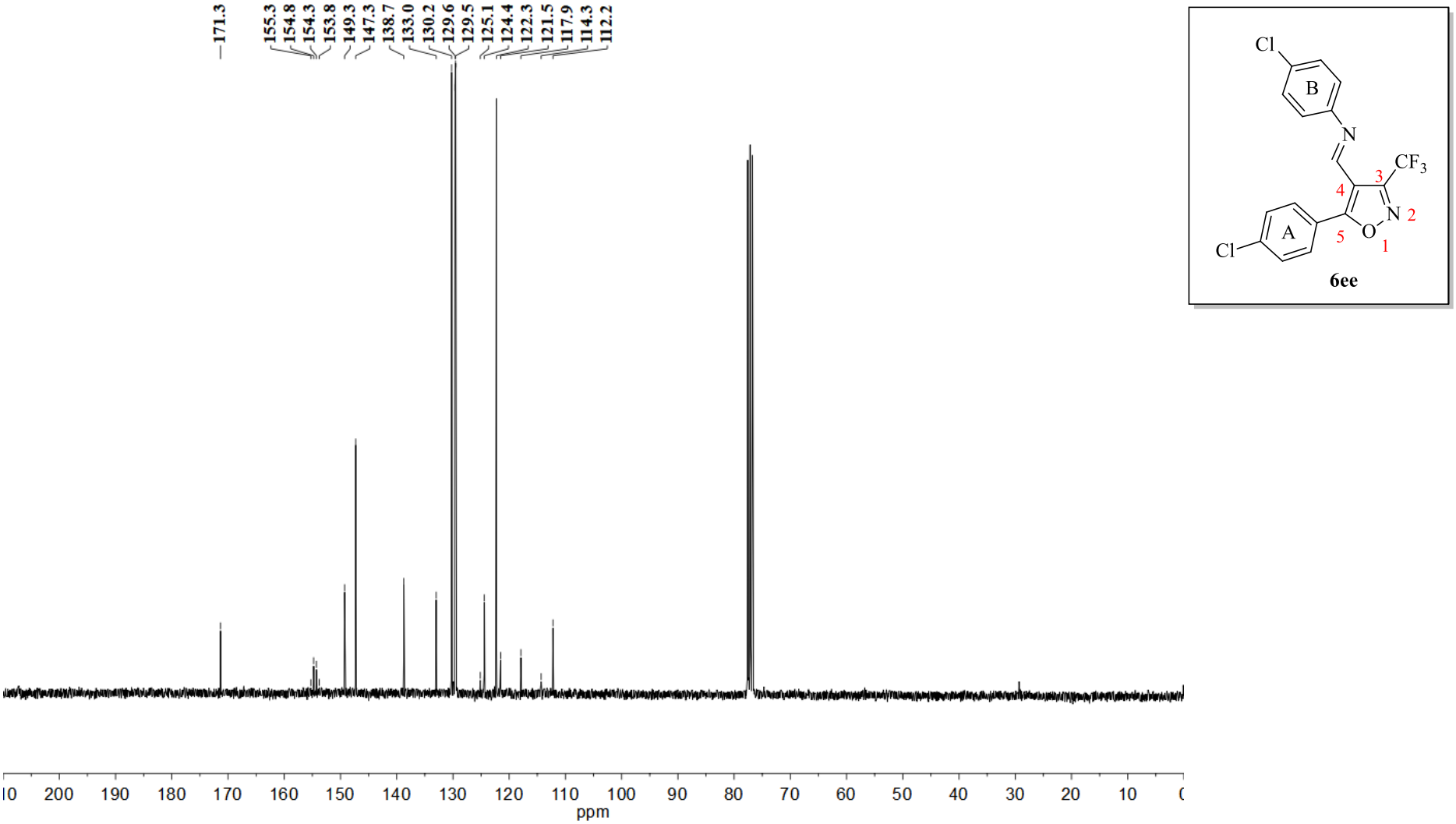


Figure S169 – ^{13}C NMR spectrum of compound **6ee** in $CDCl_3$ at 75.45 MHz.

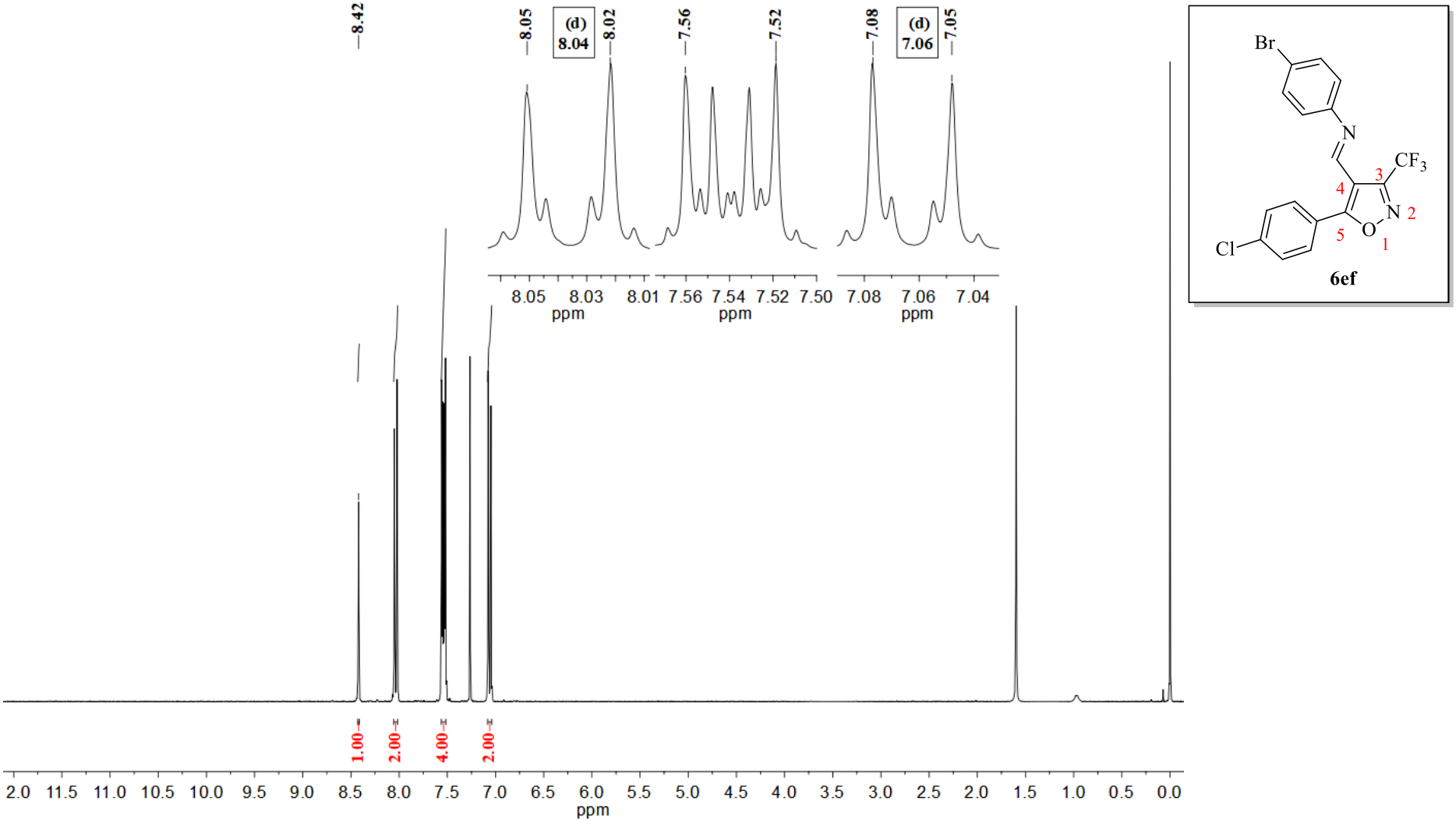


Figure S170 – ^{1}H NMR spectrum of compound **6ef** in $CDCl_3$ at 300.06 MHz.

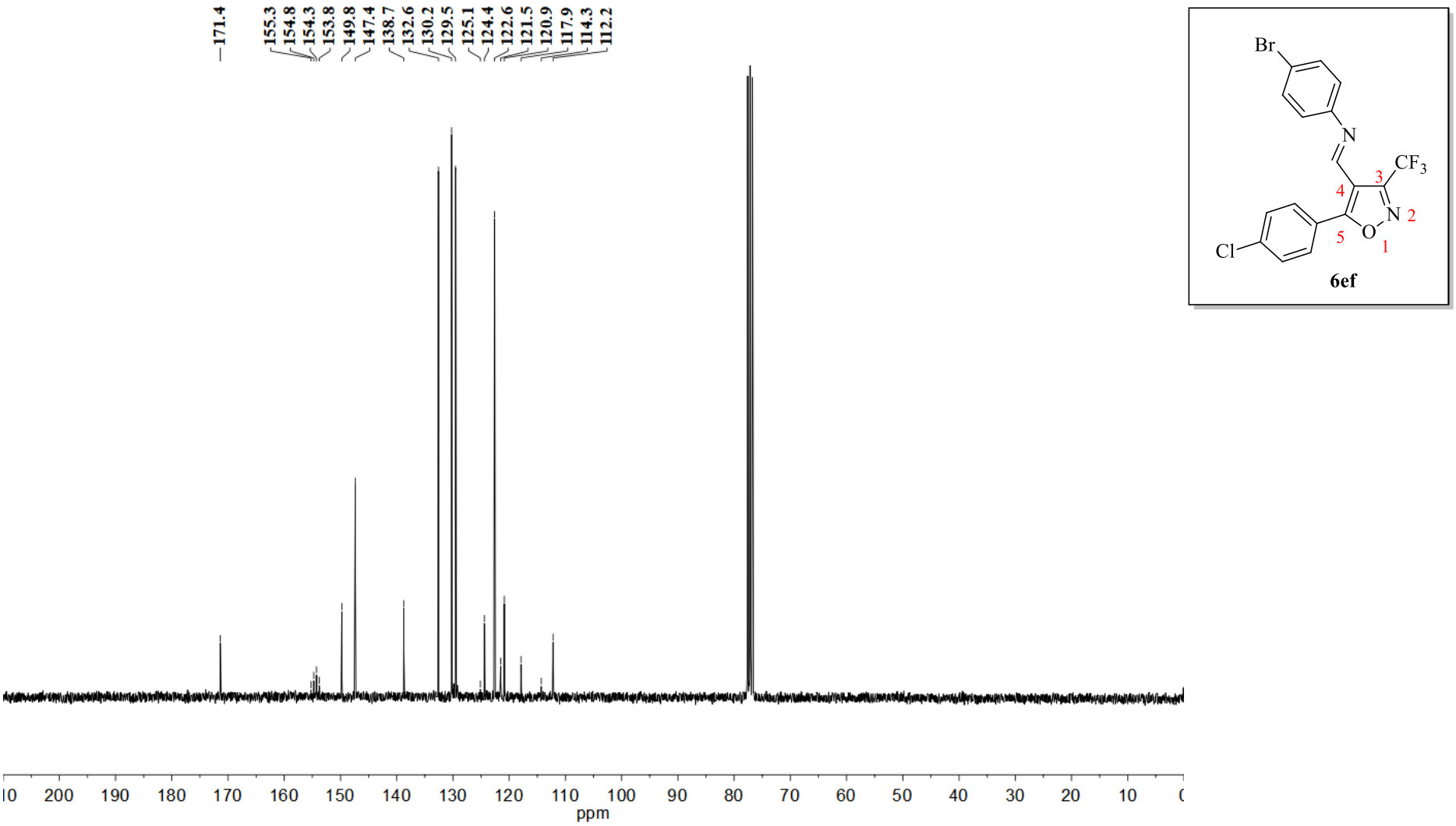


Figure S171 – ^{13}C NMR spectrum of compound **6ef** in $CDCl_3$ at 75.45 MHz.

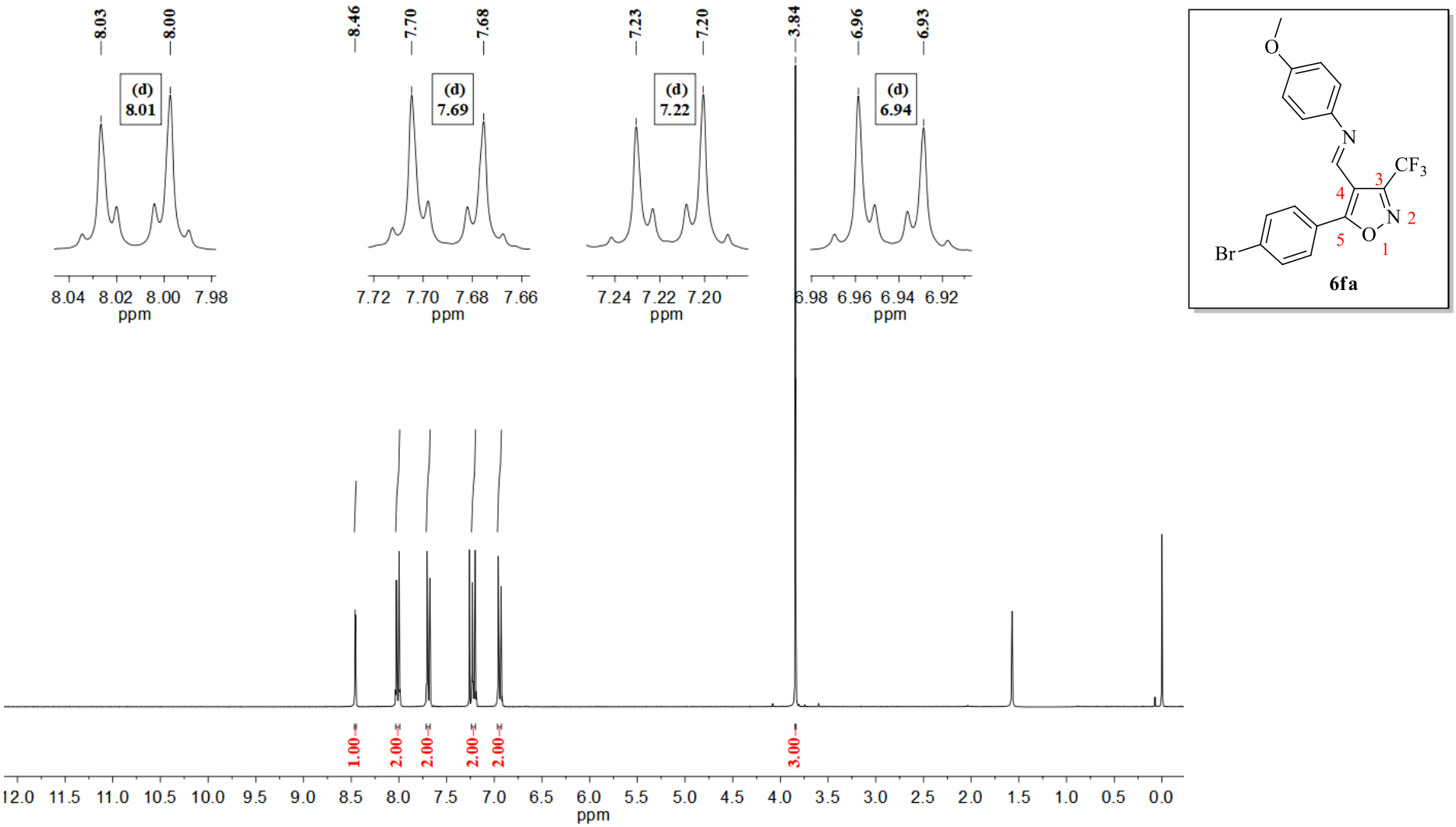


Figure S172 – ^{1}H NMR spectrum of compound **6fa** in $CDCl_3$ at 300.06 MHz.

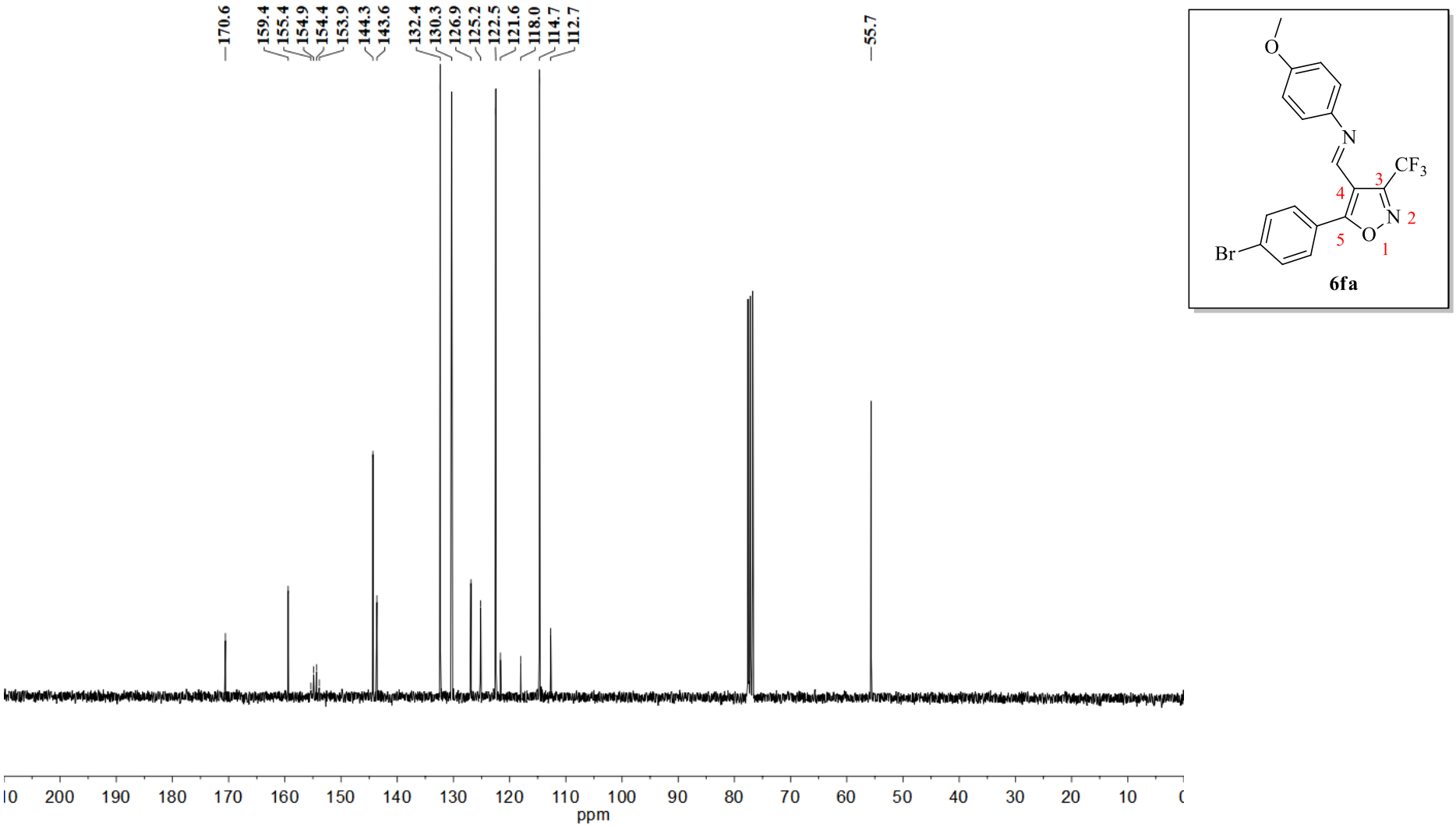


Figure S173 – ^{13}C NMR spectrum of compound **6fa** in $CDCl_3$ at 75.45 MHz.

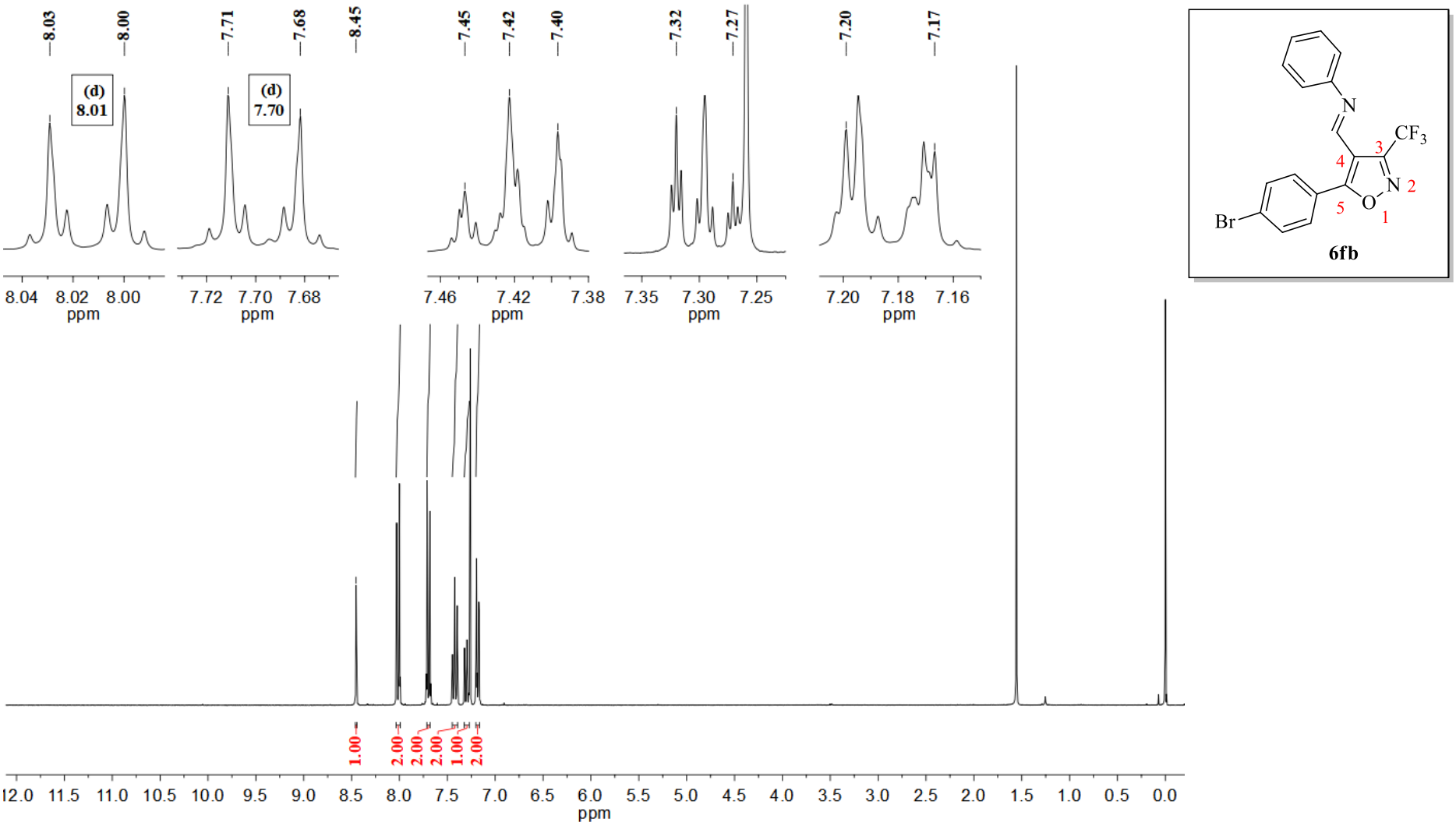


Figure S174 – ^{1}H NMR spectrum of compound **6fb** in $CDCl_3$ at 300.06 MHz.

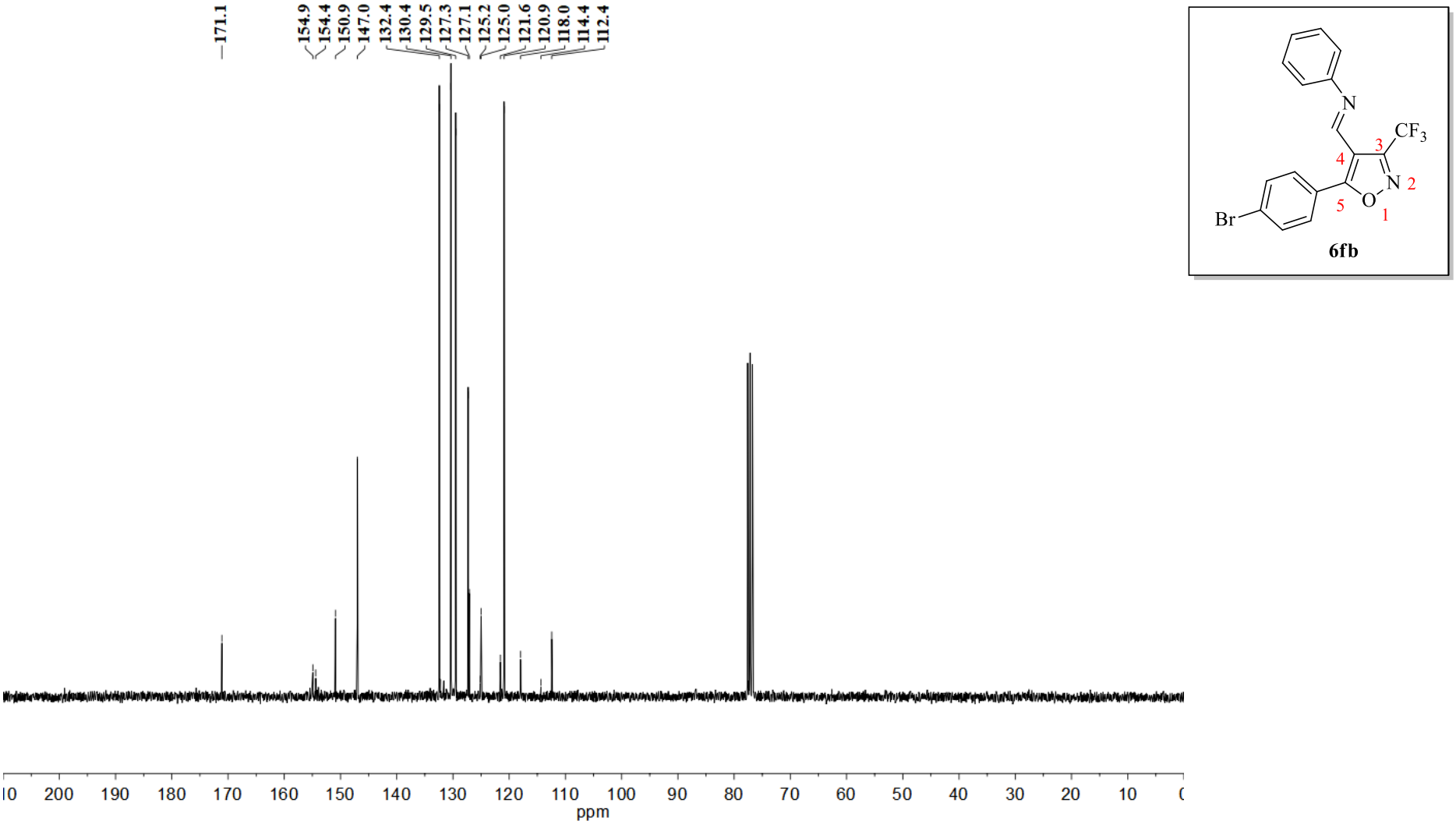


Figure S175 – ^{13}C NMR spectrum of compound **6fb** in $CDCl_3$ at 75.45 MHz.

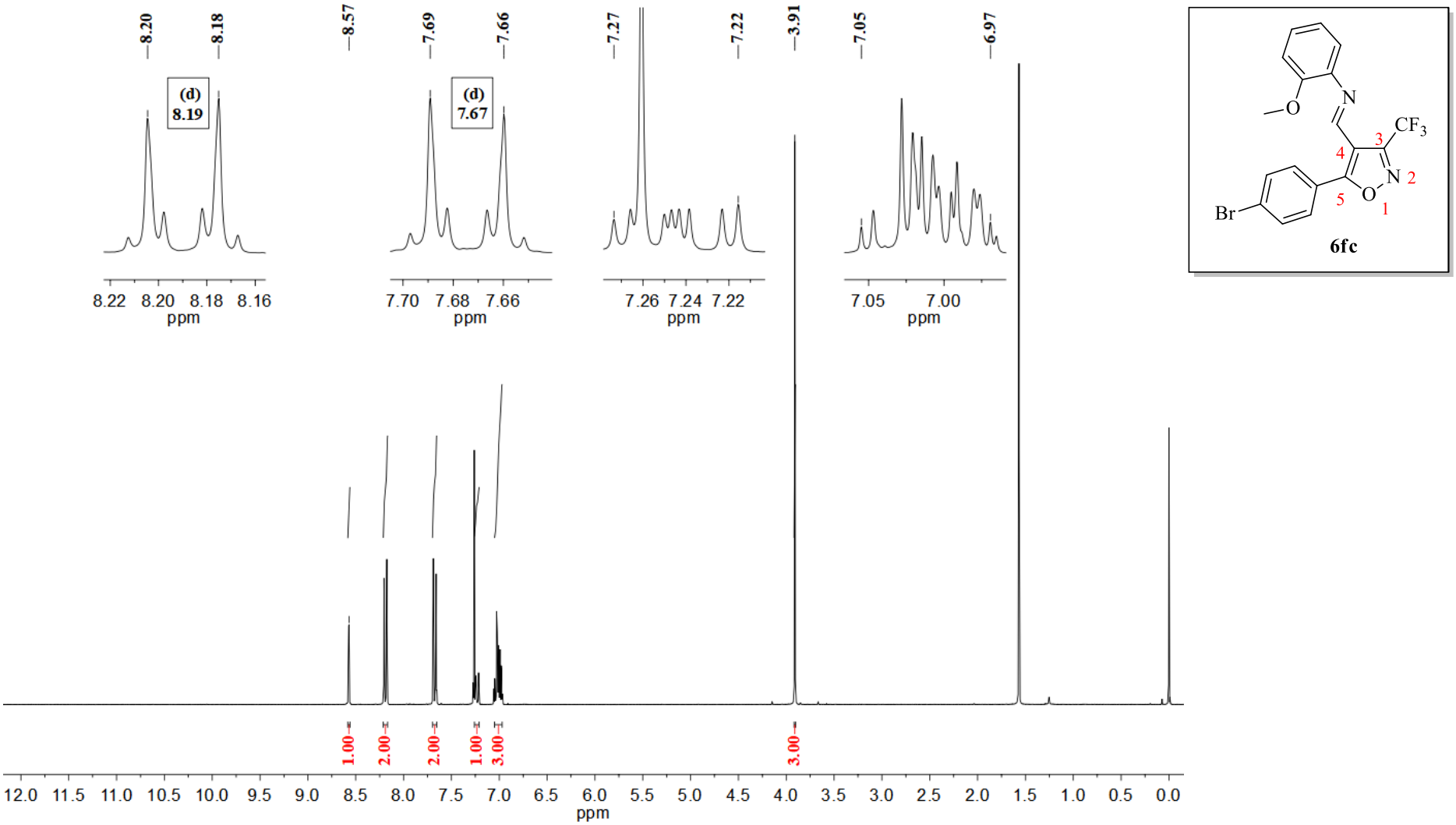


Figure S176 – ^{1}H NMR spectrum of compound **6fc** in $CDCl_3$ at 300.06 MHz.

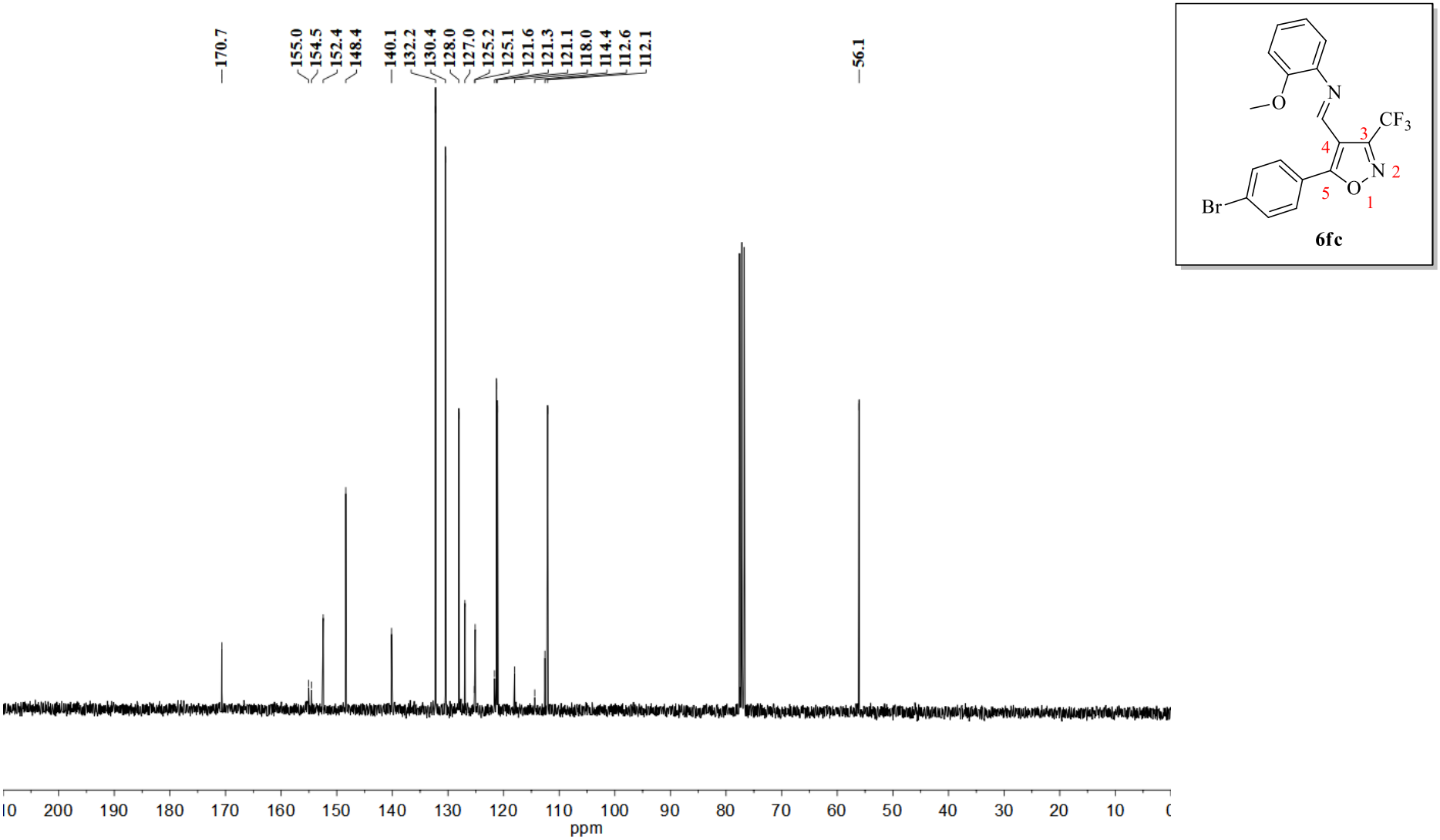


Figure S177 – ^{13}C NMR spectrum of compound **6fc** in $CDCl_3$ at 75.45 MHz.

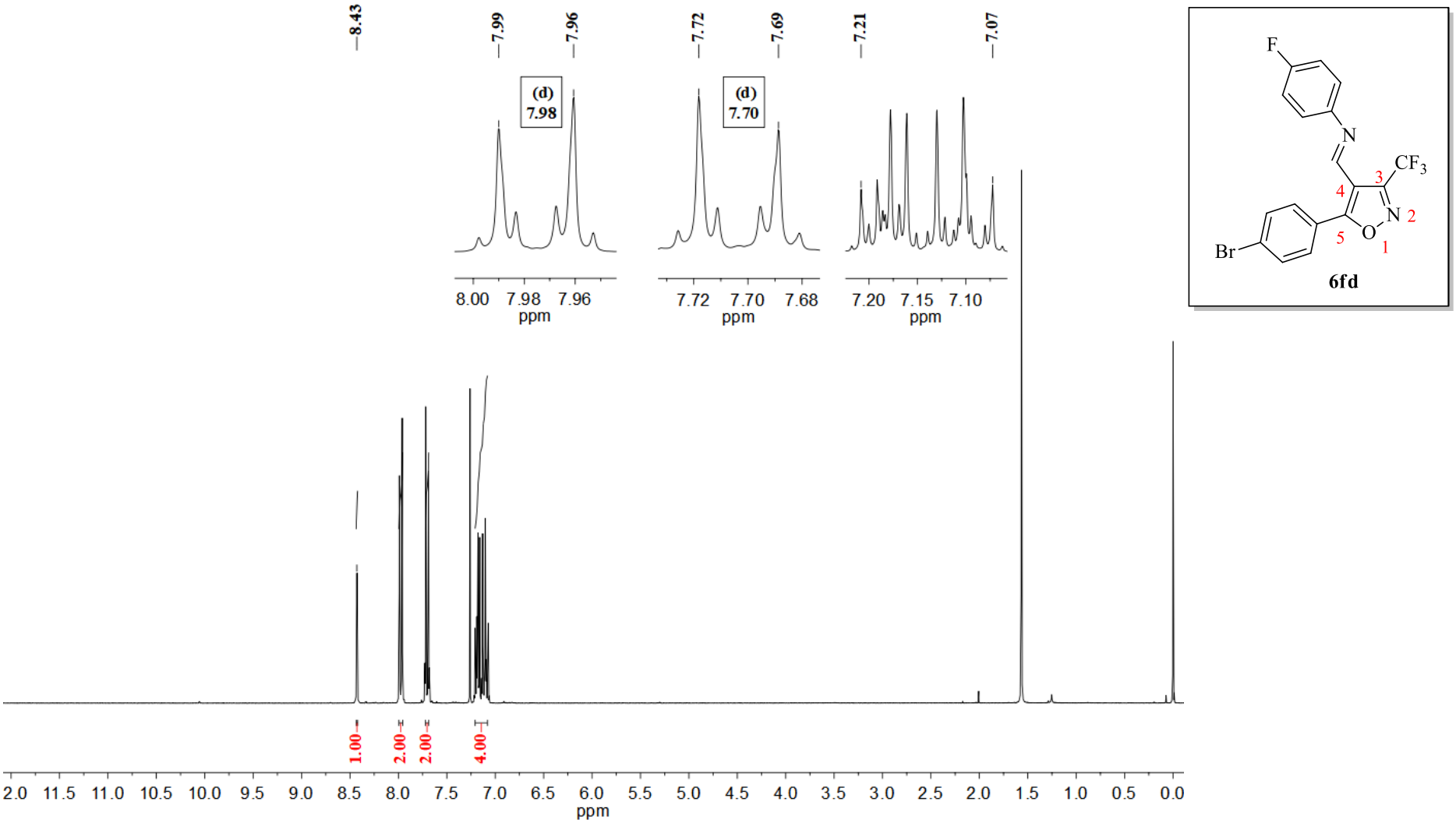


Figure S178 – ^{1}H NMR spectrum of compound **6fd** in $CDCl_3$ at 300.06 MHz.

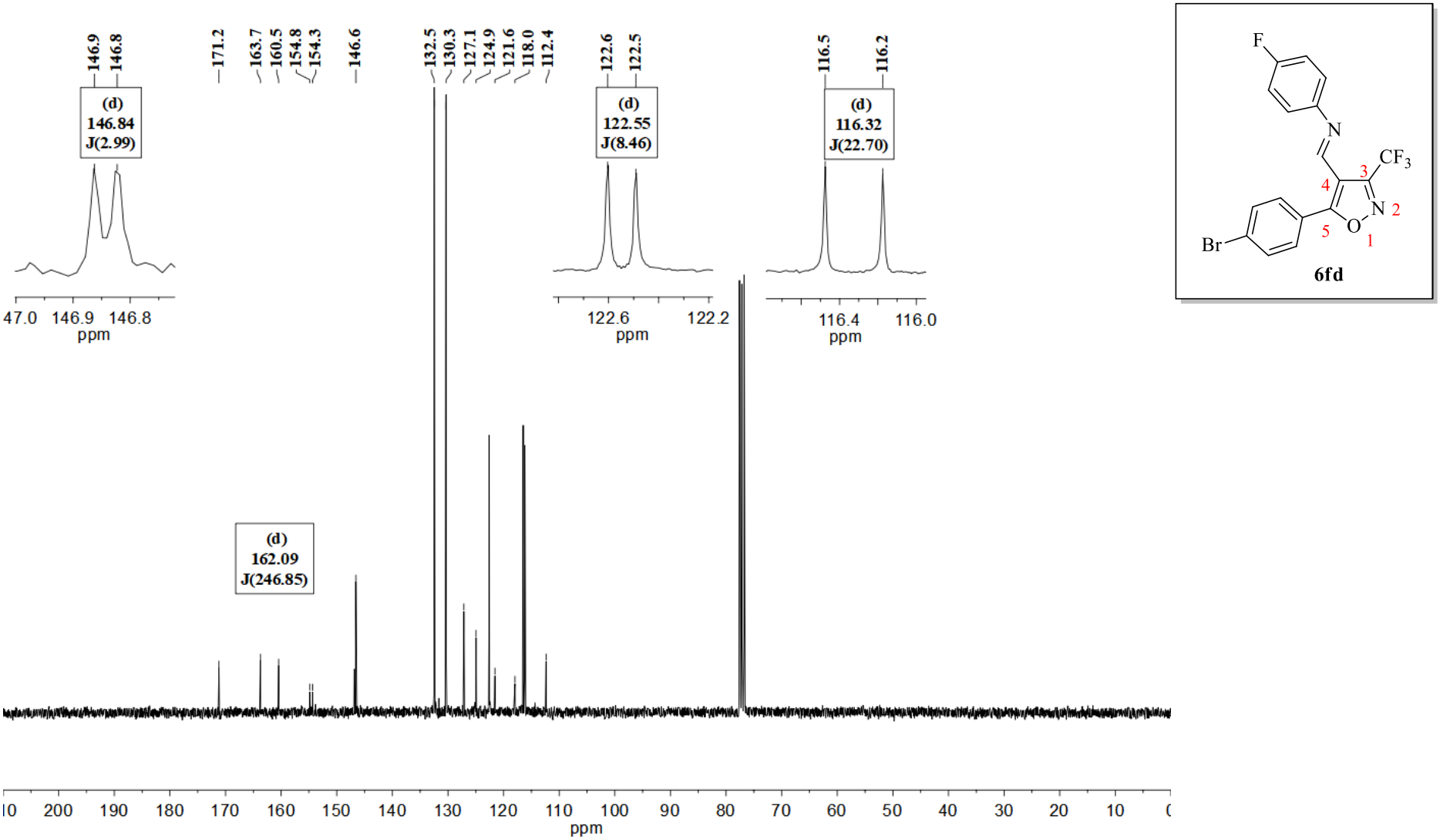


Figure S179 – ^{13}C NMR spectrum of compound **6fd** in $CDCl_3$ at 75.45 MHz.

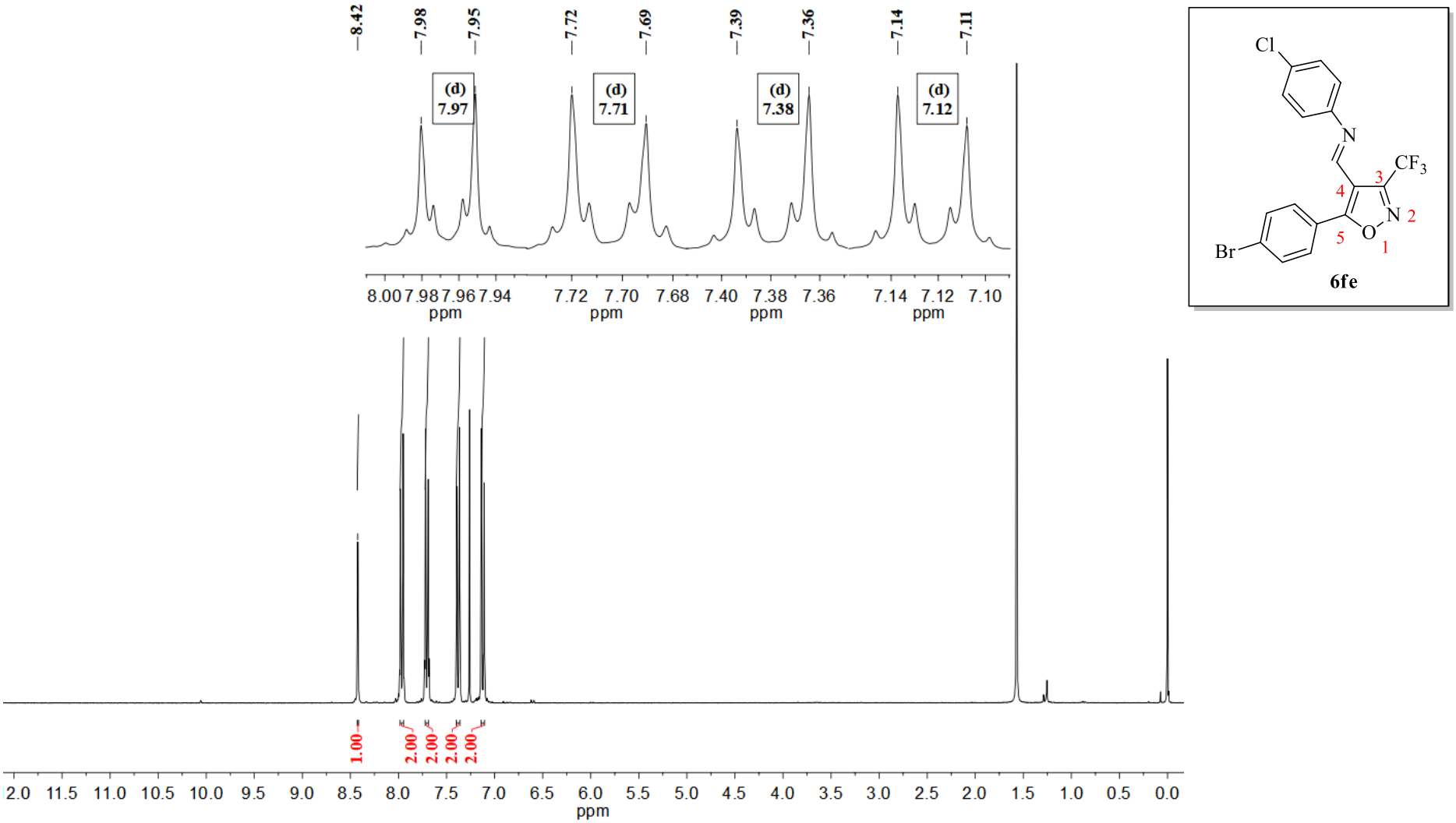
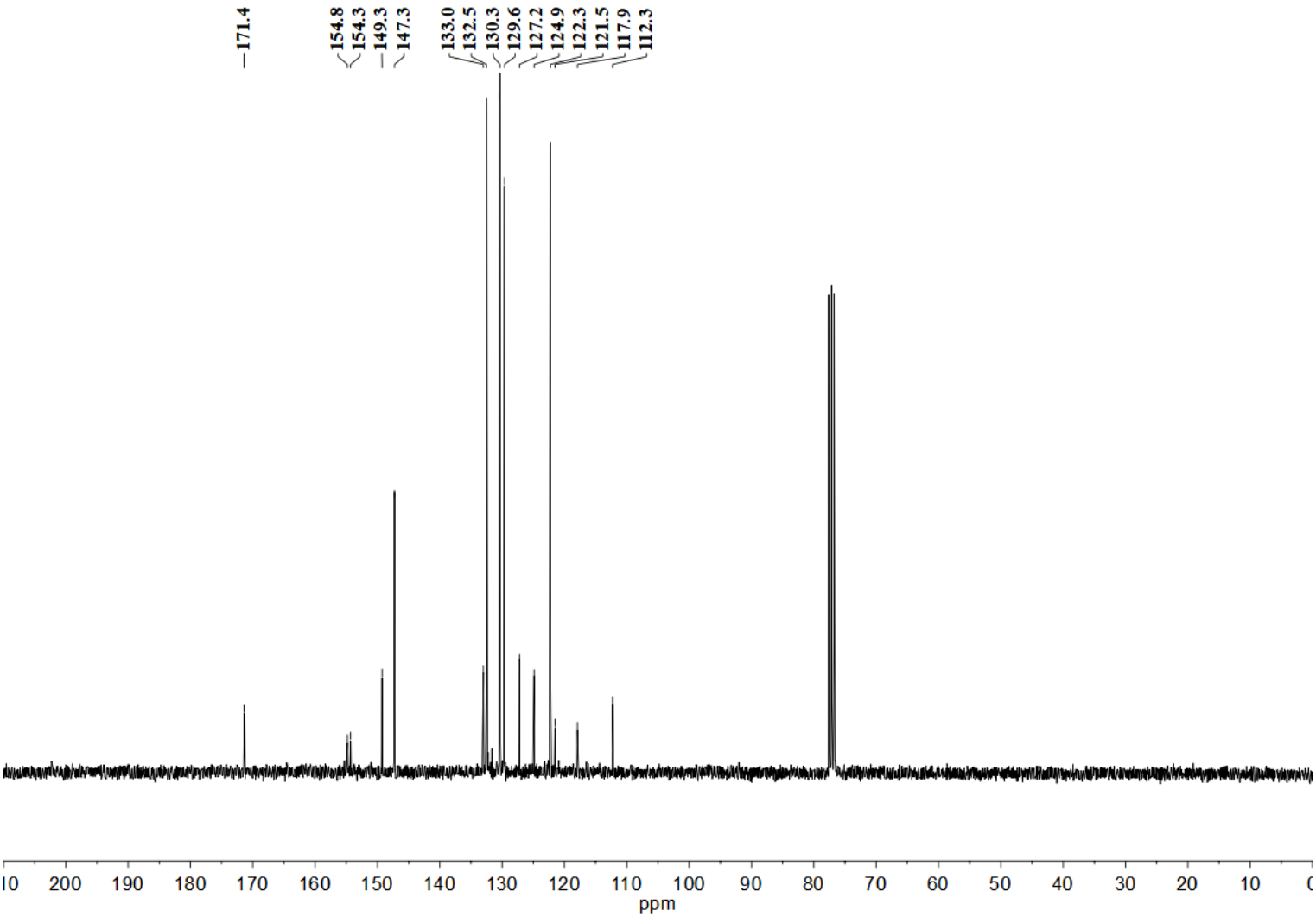


Figure S180 – ^{1}H NMR spectrum of compound **6fe** in $CDCl_3$ at 300.06 MHz.



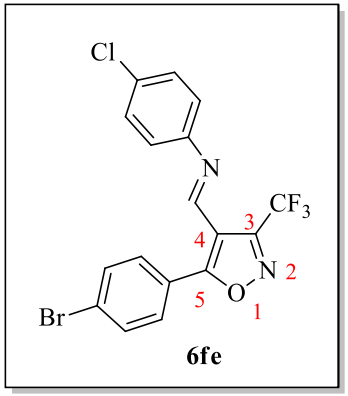


Figure S181 – ^{13}C NMR spectrum of compound **6fe** in $CDCl_3$ at 75.45 MHz.

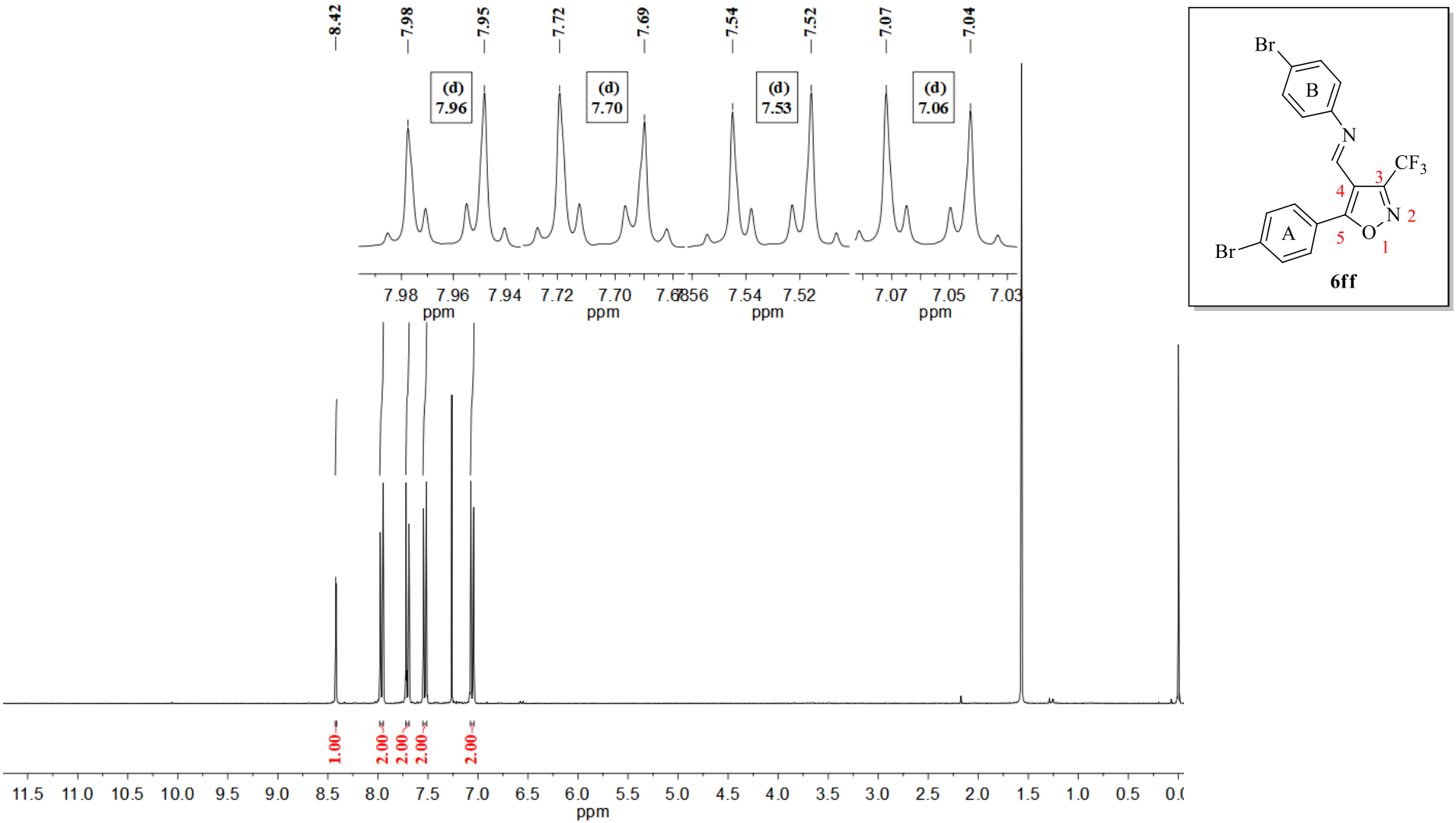
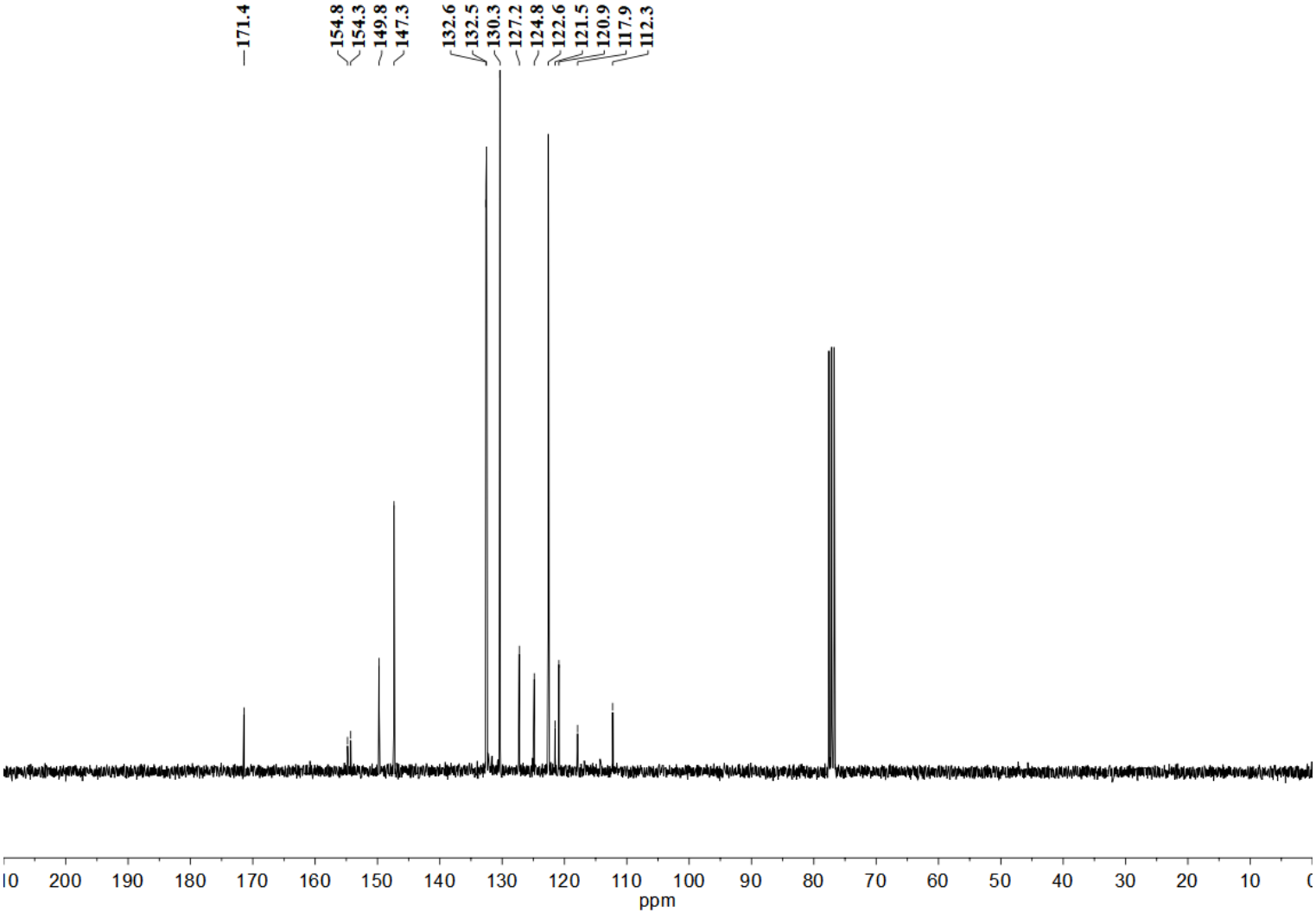


Figure S182 – ^{1}H NMR spectrum of compound **6ff** in $CDCl_3$ at 300.06 MHz.



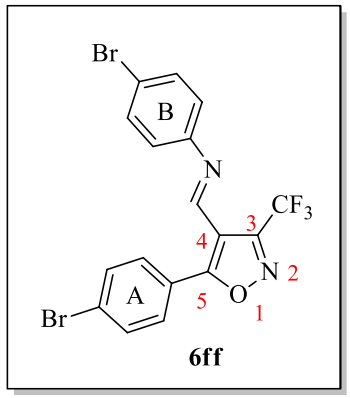


Figure S183 – ^{13}C NMR spectrum of compound **6ff** in $CDCl_3$ at 75.45 MHz.

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