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Nucleophilic substitution of hydrogen–the Boger reaction sequence as an approach towards 8-(pyridine-2-yl)coumarins

Ramil F. Fatykhov, Maria I. Savchuk, Ekaterina S. Starnovskaya, Maria V. Bobkina, Dmitry S. Kopchuk, Emiliya V. Nosova, Grigory V. Zyryanov, Igor A. Khalymbadzha, Oleg N. Chupakhin, Valery N. Charushin and Viktor G. Kartsev

General. All common reagents and solvents were used as purchased. NMR spectra were acquired on a Bruker Avance-400 spectrometer, 298 K, digital resolution ± 0.01 ppm, using TMS as internal standard. Mass-spectra were recorded on MicrOTOF-Q II (Bruker Daltonics), electrospray as a method of ionization. Microanalyses (C, H, N) were performed using a Perkin–Elmer 2400 elemental analyzer.

5,7-Dihydroxy-4-methylcoumarin[S1], 5,7-dihydroxy-4-phenylcoumarin and 3-benzyl-5,7-dihydroxy-4-methylcoumarin[S2], 3,6-diphenyl-1,2,4-triazine[S3] were synthesized as described in literature.

*General method for the synthesis of coumarins **1a-c***

A mixture of the corresponding 5,7-dihydroxycoumarin (4 mmol), acetone (50 ml), dimethyl sulfate (10 mmol) and dry K_2CO_3 (1.1 g, 8 mmol) was stirred at reflux for 8 h and then poured into 10% aqueous solution of NH_3. The precipitate formed was filtered off and dried yielding pure products. Data for compounds **1a**[S4], **1b**[S5] and **1c**[S6] were close to reported previously.

*General method for the synthesis of σ^H-adducts **2***

To a solution of the corresponding coumarin **1a-c** (1 mmol) and 3,6-diphenyl-1,2,4-triazine (233 mg, 1 mmol) in CH_2Cl_2 (7 ml), MsOH (195 μl, 3 mmol) was added. The reaction mixture was left at room temperature for 24 h. The mixture was diluted with CH_2Cl_2 (10 ml), basified with saturated solution of Na_2CO_3, the organic layer was separated, and the solvent was removed under reduced pressure. Adduct **2a** was purified by recrystallization (benzene). Adducts **2b,c** were used in the next step without additional purification.

8-(3,6-Diphenyl-2,5-dihydro-1,2,4-triazin-5-yl)-5,7-dimethoxy-4-methyl-2*H*-chromen-2-one (2a). M.p. 238-240 °C. Yield 372 mg (0.82 mmol, 82%). ^{1}H NMR, δ, ppm (DMSO-d_6): 2.43 (s, 3H, Me), 3.86 (s, 3H, OMe), 3.93 (s, 3H, OMe), 5.99 (s, 1H, H-3), 6.40 (s, 1H, H-5 (triazine)), 6.58 (s, 1H, H-6), 7.20–7.30 (m, 3H, Ph), 7.36–7.46 (m, 3H, Ph), 7.61–7.63

(m, 2H, Ph), 7.80–7.82 (m, 2H, Ph); ^{13}C NMR, δ, ppm (DMSO-d_6): 23.8, 45.8, 56.2, 56.4, 92.6, 103.6, 110.5, 111.3, 124.9, 126.2, 128.2, 128.7, 130.2, 133.2, 135.9, 139.4, 149.4, 153.4, 154.4, 158.6, 159.0, 160.7; Found, %: C 71.45, H 5.15, N 9.18. **$C_{27}H_{21}N_3O_4$.** Calculated, %: C 71.51, H 5.11, N 9.27.

*General method for the synthesis of triazines **3***

The corresponding adduct **2** was dissolved in 1,2-dichloroethane (10 ml), DDQ (1.5 mmol) was added, and the mixture was refluxed for 6 h. $DDQH_2$ was filtered off, the solvent was evaporated under reduced pressure, and the residue was recrystallized (MeOH).

8-(3,6-Diphenyl-1,2,4-triazin-5-yl)-5,7-dimethoxy-4-methyl-2*H*-chromen-2-one (3a). M.p. 228-230 °C. Yield 176 mg (0.39 mmol, 77%). ^{1}H NMR, δ, ppm (DMSO-d_6): 2.51 (d, *J*=0.9 Hz, 3H, Me), 3.67 (s, 3H, OMe), 3.97 (s, 3H, OMe), 6.01 (d, *J*=0.9 Hz, 1H, H-3), 6.65 (s, 1H, H-6), 7.34–7.50 (m, 5H, Ph), 7.59–7.66 (m, 3H, Ph), 8.46–7.48 (m, 2H, Ph); ^{13}C NMR, δ, ppm (DMSO-d_6): 23.7, 56.4, 56.6, 92.6, 103.8, 105.6, 111.0, 127.8, 127.9, 128.3, 129.2, 129.6, 131.8, 134.2, 134.9, 152.2, 153.0, 154.1, 158.3, 158.5, 159.7, 160.6, 161.4; Found, %: C 71.71, H 4.82, N 9.18. **$C_{27}H_{21}N_3O_4$.** Calculated, %: C 71.83, H 4.69, N 9.31.

8-(3,6-Diphenyl-1,2,4-triazin-5-yl)-5,7-dimethoxy-4-phenyl-2*H*-chromen-2-one (3b). M.p. 261-263 ºC. Yield 185 mg (0.36 mmol, 72% (over 2 steps)). ^{1}H NMR, δ, ppm (DMSO-d_6): 3.50 (s, 3H, OMe), 3.63 (s, 3H, OMe), 5.95 (s, 1H, H-3), 6.59 (s, 1H, H-6), 7.32–7.34 (m, 2H, Ph), 7.41–7.43 (m, 6H, Ph), 7.52–7.54 (m, 2H, Ph), 7.60–7.67 (m, 3H, Ph), 8.49–8.51 (m, 2H, Ph); ^{13}C NMR, δ, ppm (DMSO-d_6): 56.1, 56.5, 93.0, 102.5, 105.8, 112.4, 127.0, 127.4, 127.8, 127.9, 128.1, 128.4, 129.2, 129.6, 131.9, 134.3, 134.9, 139.1, 152.0, 153.2, 154.9, 158.3, 158.5, 159.7, 160.2, 161.4; Found, %: C 74.71, H 4.66, N 8.01. **$C_{32}H_{23}N_3O_4$.** Calculated, %: C 74.84, H 4.51, N 8.18.

3-Benzyl-8-(3,6-diphenyl-1,2,4-triazin-5-yl)-5,7-dimethoxy-4-methyl-2*H*-chromen-2-one (3c). M.p. 178-180 ºC. Yield 200 mg (0.37 mmol, 74% (over 2 steps)). ^{1}H NMR, δ, ppm (DMSO-d_6): 2.49 (s, 3H, Me), 3.69 (s, 3H, OMe), 3.86–3.88 (m, 2H, Ph-C$\underline{H}_2$), 3.96 (s, 3H, OMe), 6.67 (s, 1H, H-6), 7.09–7.11 (m, 2H, Ph), 7.16–7.18 (m, 1H, Ph), 7.24–7.26 (m, 2H, Ph), 7.33–7.48 (m, 5H, Ph), 7.58–7.68 (m, 3H, Ph), 8.47 (m, 2H, Ph); ^{13}C NMR, δ, ppm (DMSO-d_6): 19.7, 31.7, 56.4, 56.6, 92.9, 104.3, 105.3, 120.3, 126.0, 127.7, 127.8, 127.9, 128.3, 128.4, 129.2, 129.5, 131.8, 134.3, 134.9, 139.0, 149.5, 151.4, 152.2, 158.3, 159.1, 159.8, 160.5, 161.4; Found, %: C 74.71, H 4.66, N 8.01. **$C_{34}H_{27}N_3O_4$.** Calculated, %: C 75.40, H 5.03, N 7.76.

*General method for the synthesis of pyridines **4a-c***

A mixture of the corresponding triazine **3a-c** (0.3 mmol), 2,5-norbornadiene (325 μl, 3.2 mmol) and 1,2-dichlorobenzene (25 ml) was stirred in autoclave under argon atmosphere at 215 °C for 20 h. The solvent was removed under reduced pressure, the residue was purified by flash chromatography (chloroform as eluent).

8-(3,6-Diphenylpyridin-2-yl)-5,7-dimethoxy-4-methyl-2*H*-chromen-2-one (4a). Yield 108 mg (0.24 mmol, 80%). M.p. 209-211 ºC. ^{1}H NMR, δ, ppm ($CDCl_3$): 2.38 (s, 3H, Me), 3.52 (s, 3H, OMe), 3.73 (s, 3H, OMe), 5.76 (s, 1H, H-3), 6.11 (s, 1H, H-6), 7.05–7.14 (m, 5H, Ph), 7.26–7.27 (m, 1H, Ph), 7.32–7.34 (m, 2H, Ph), 7.65 and 7.68 (both d, 1H, ^3J = 8.0 Hz, H-3,4 (py)), 7.90–7.92 (m, 2H, Ph). ^{13}C NMR, δ, ppm ($CDCl_3$): 24.4, 55.7, 55.8, 91.1, 104.6, 111.5, 111.6, 119.9, 127.1, 127.4, 127.7, 128.4, 128.5, 128.6, 137.5, 138.0, 139.6, 139.7, 150.3, 153.9, 154.2, 156.5, 159.2, 160.2, 160.7. **ESI-MS**, *m/z*: found 450.17, calculated 450.17 $[M+H]^+$. Found, %: C 77.33, H 4.97, N 3.44. **$C_{29}H_{23}NO_4$.** Calculated, %: C 77.49, H 5.16, N 3.12.

8-(3,6-Diphenylpyridin-2-yl)-5,7-dimethoxy-4-phenyl-2*H*-chromen-2-one (4b). Yield 118 mg (0.23 mmol, 77%). M.p. 215-217 ºC. ^{1}H NMR, δ, ppm ($CDCl_3$): 3.44 (s, 3H, OMe), 3.64 (s, 3H, OMe), 5.96 (s, 1H, H-3), 6.17 (s, 1H, H-6), 7.20–7.31 (m, 7H, Ph), 7.35–7.44 (m, 4H, Ph), 7.47–7.49 (m, 2H, Ph), 7.81 and 7.85 (both d, 1H, ^3J = 8.0 Hz, H-3,4 (py)), 8.04–8.06 (m, 2H, Ph). ^{13}C NMR, δ, ppm ($CDCl_3$): 55.5, 55.8, 91.6, 103.5, 111.9, 112.9, 120.1, 127.1 (2C), 127.4 (2C), 127.8, 127.8, 128.5, 128.6 (2C), 137.5, 138.0, 139.7, 140.1, 150.2, 154.1, 155.3, 156.7, 158.4, 160.5, 160.7. **ESI-MS**, *m/z*: found 512.19, calculated 512.19 $[M+H]^+$. Found, %: C 79.70, H 5.04, N 2.52. **$C_{34}H_{25}NO_4$.** Calculated, %: C 79.83, H 4.93, N 2.74.

3-Benzyl-8-(3,6-diphenylpyridin-2-yl)-5,7-dimethoxy-4-methyl-2*H*-chromen-2-one (4c). Yield 125 mg (0.23 mmol, 78%). M.p. 201-203 ºC. ^{1}H NMR, δ, ppm ($CDCl_3$): 2.37 (s, 3H, Me), 3.53 (s, 3H, OMe), 3.70 (s, 3H, OMe), 3.86 (s, 2H, CH_2), 6.13 (s, 1H, H-6), 7.02–7.18 (m, 10H, Ph), 7.27–7.27 (m, 1H, Ph), 7.32–7.34 (m, 2H, Ph), 7.65 and 7.69 (both d, 1H, ^3J = 8.0 Hz, H-3,4 (py)), 7.91 (m, 2H, Ph). ^{13}C NMR, δ, ppm ($CDCl_3$): 20.0, 32.5, 55.7, 55.9, 91.5, 105.3, 111.3, 119.9, 120.8, 126.0, 127.0, 127.4, 127.7, 128.2, 128.4, 128.6, 128.6, 129.8, 137.6, 138.0, 139.6, 139.7, 139.8, 149.7, 150.5, 152.3, 156.5, 159.0, 159.5, 161.6. **ESI-MS**, *m/z*: found 540.22, calculated 540.22 $[M+H]^+$. Found, %: C 79.82, H 5.24, N 2.78. **$C_{36}H_{29}NO_4$.** Calculated, %: C 80.13, H 5.42, N 2.60.

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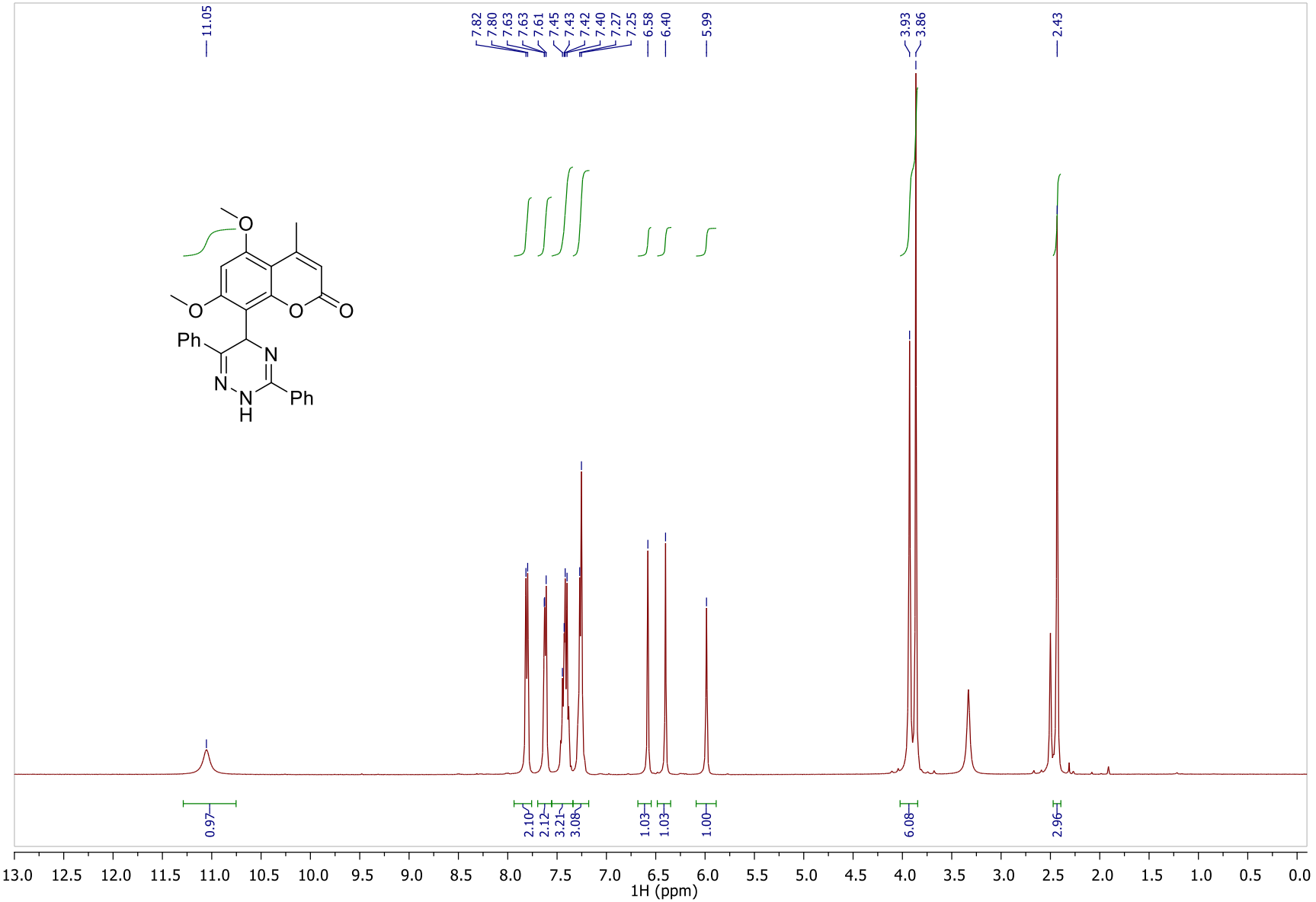

Figure S1. ^{1}H NMR spectrum of **2a** (DMSO-d_6)

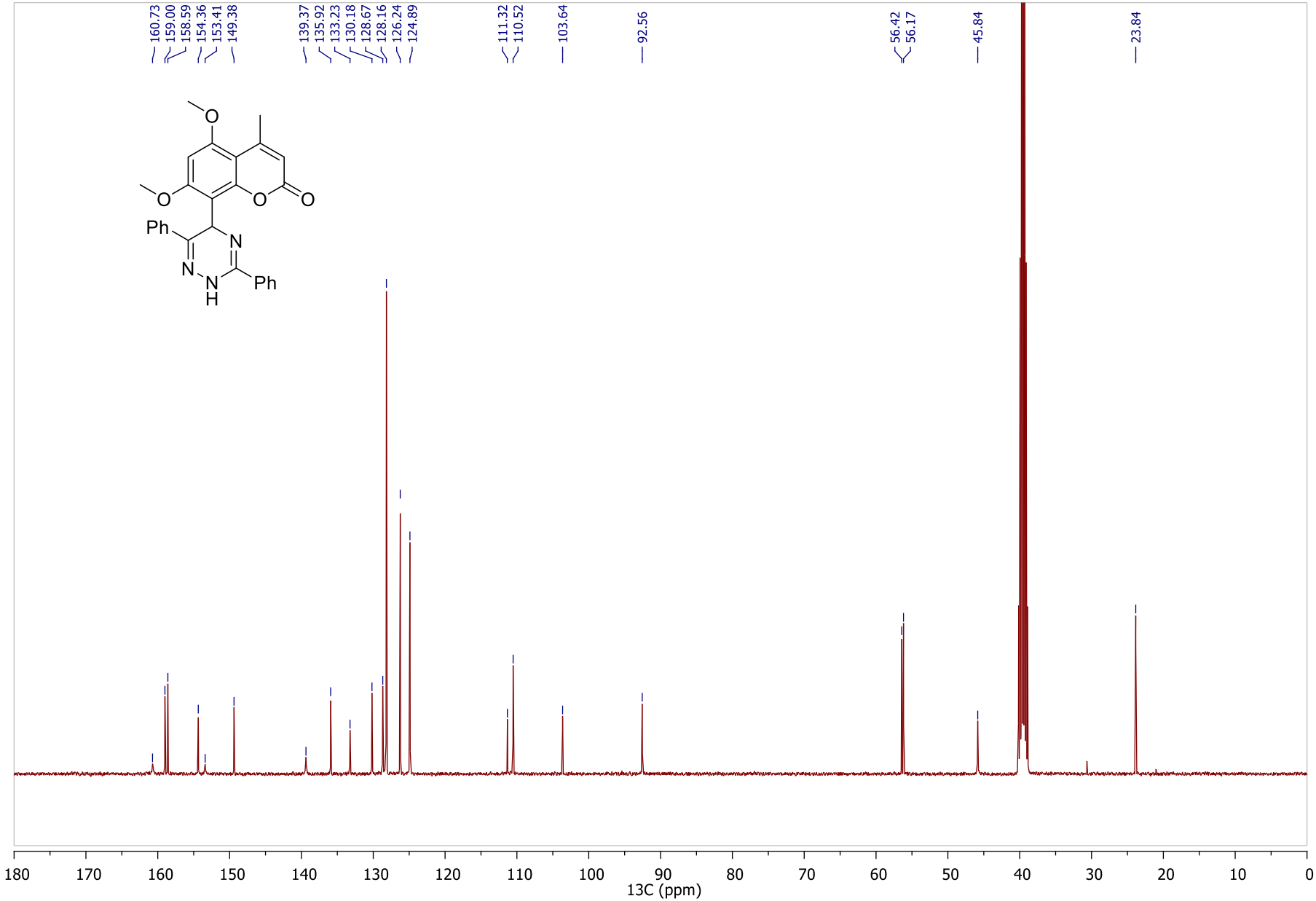

Figure S2. ^{13}C NMR spectrum of **2a** (DMSO-d_6)

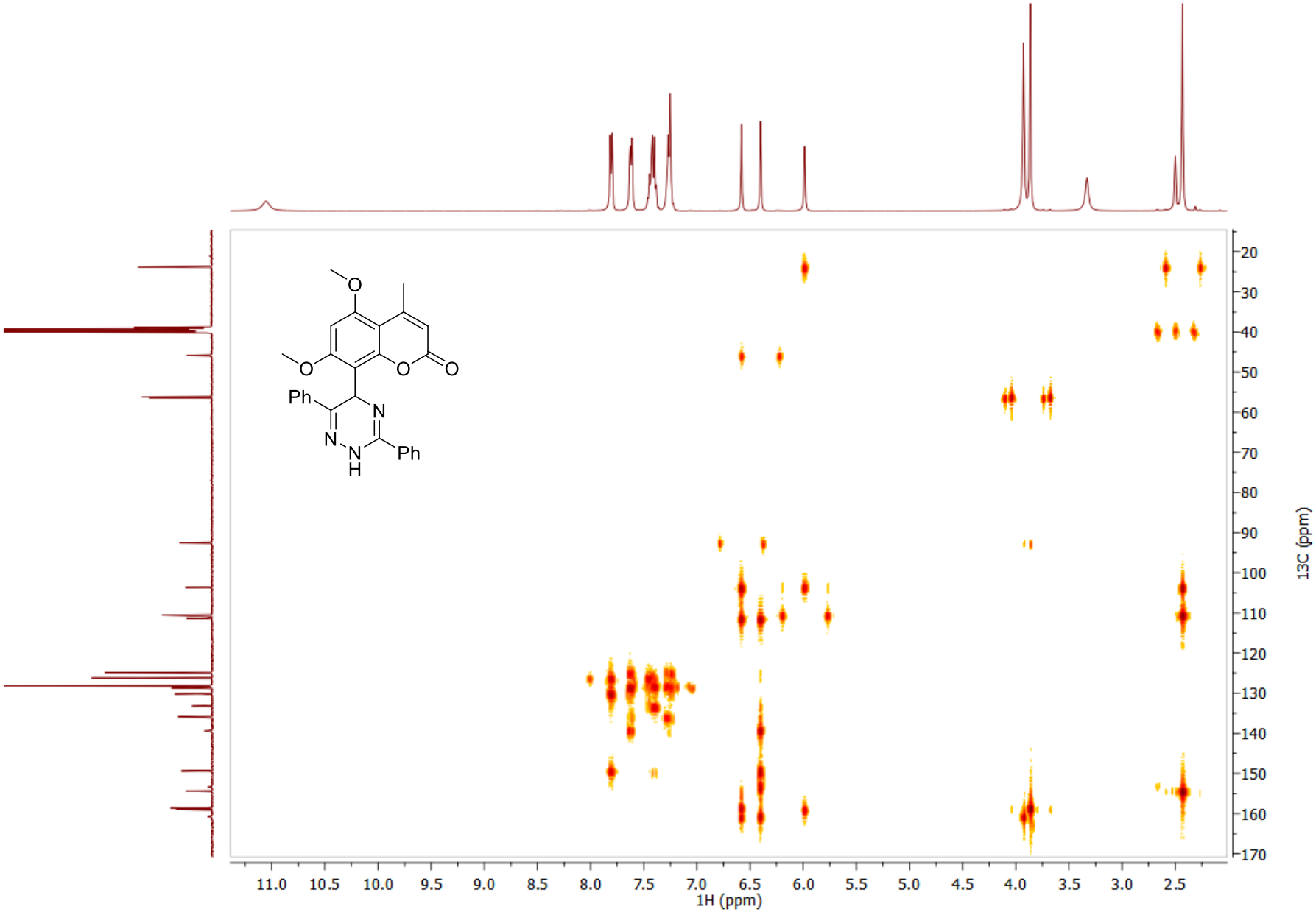

Figure S3. 2D ^{1}H-^{13}C HMBC spectrum of **2a** (DMSO-d_6)

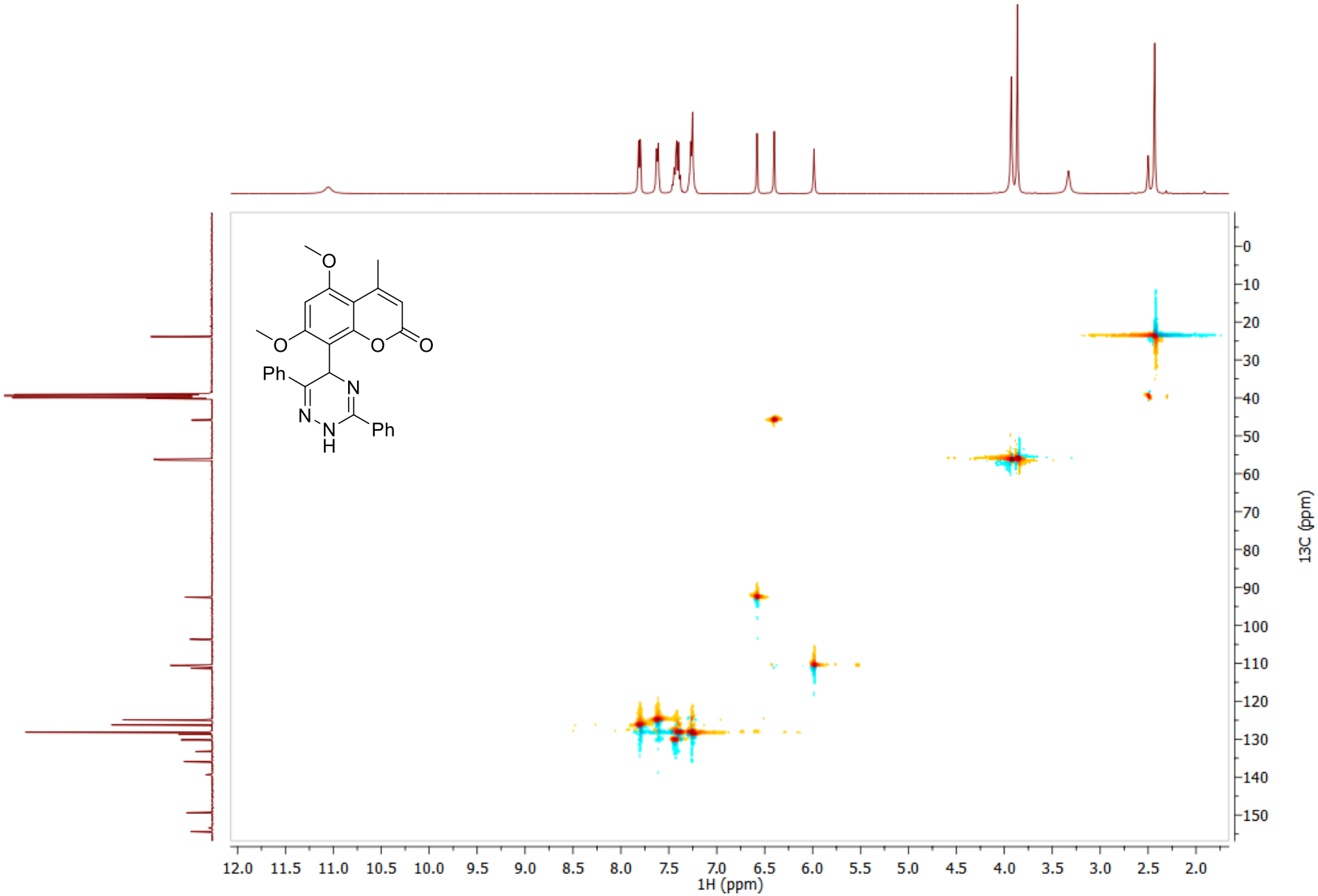

Figure S4. 2D ^{1}H-^{13}C HSQC spectrum of **2a** (DMSO-d_6)

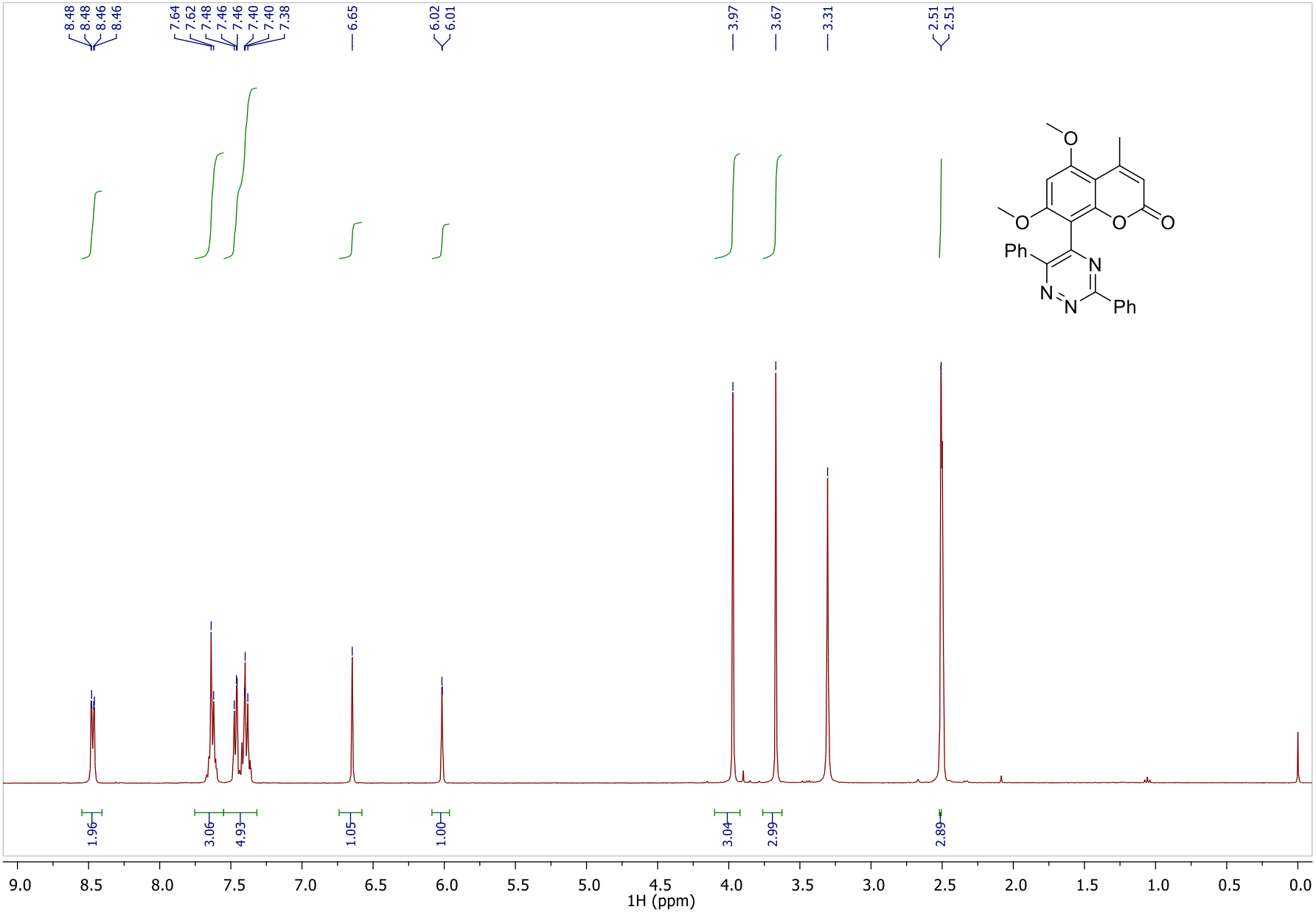

Figure S5. ^{1}H NMR spectrum of **3a** (DMSO-d_6)

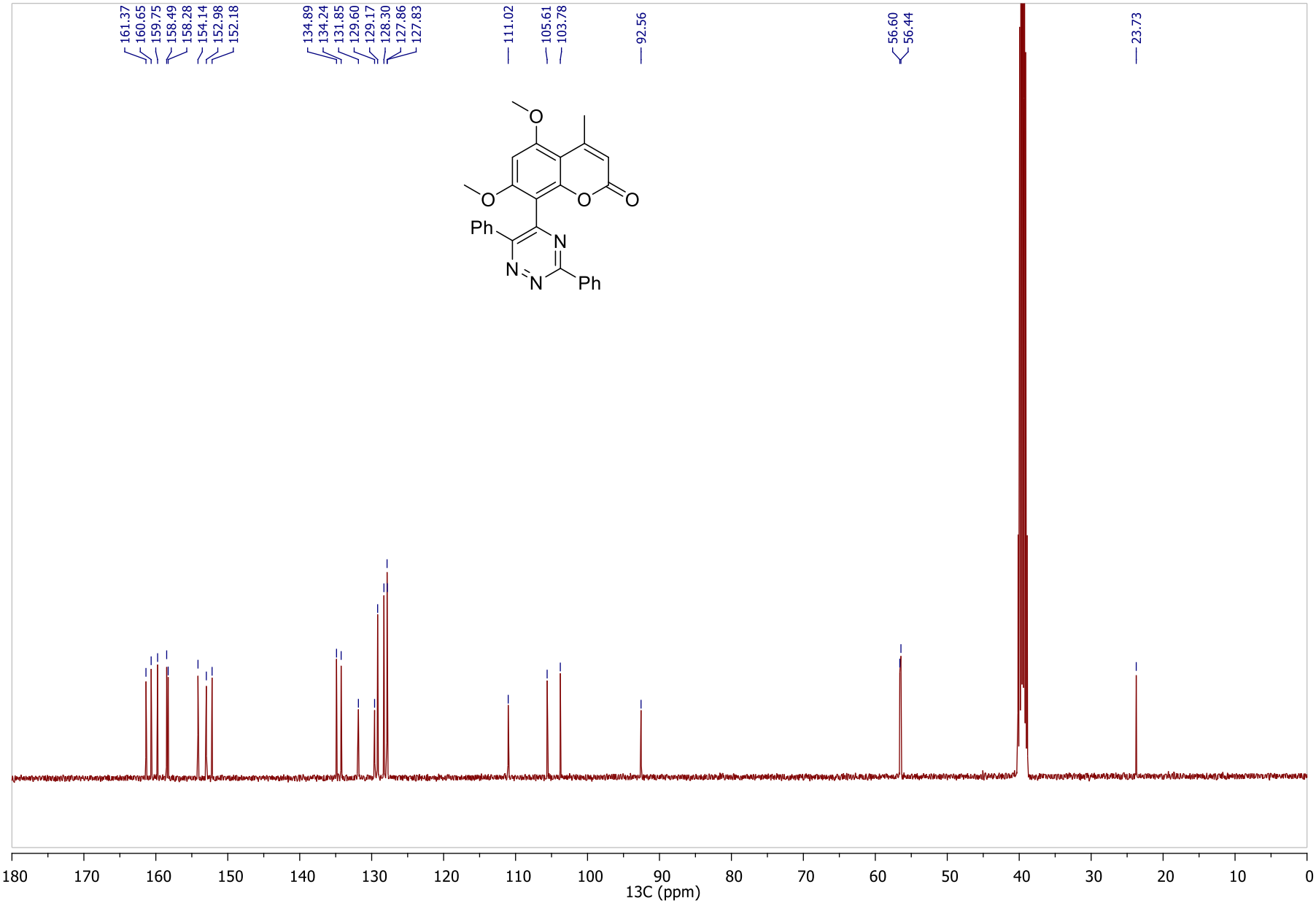

Figure S6. ^{13}C NMR spectrum of **3a** (DMSO-d_6)

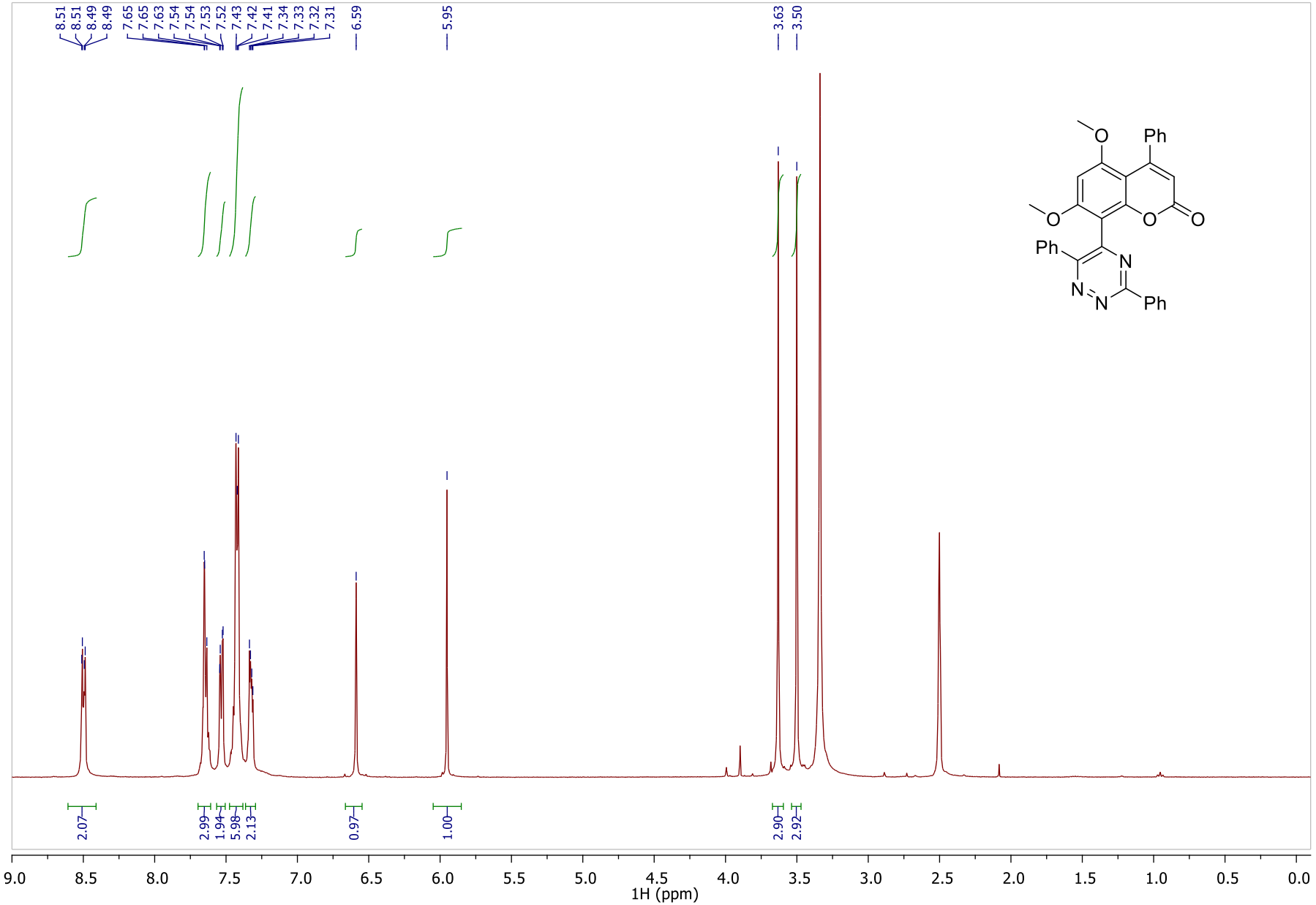

Figure S7. ^{1}H NMR spectrum of **3b** (DMSO-d_6)

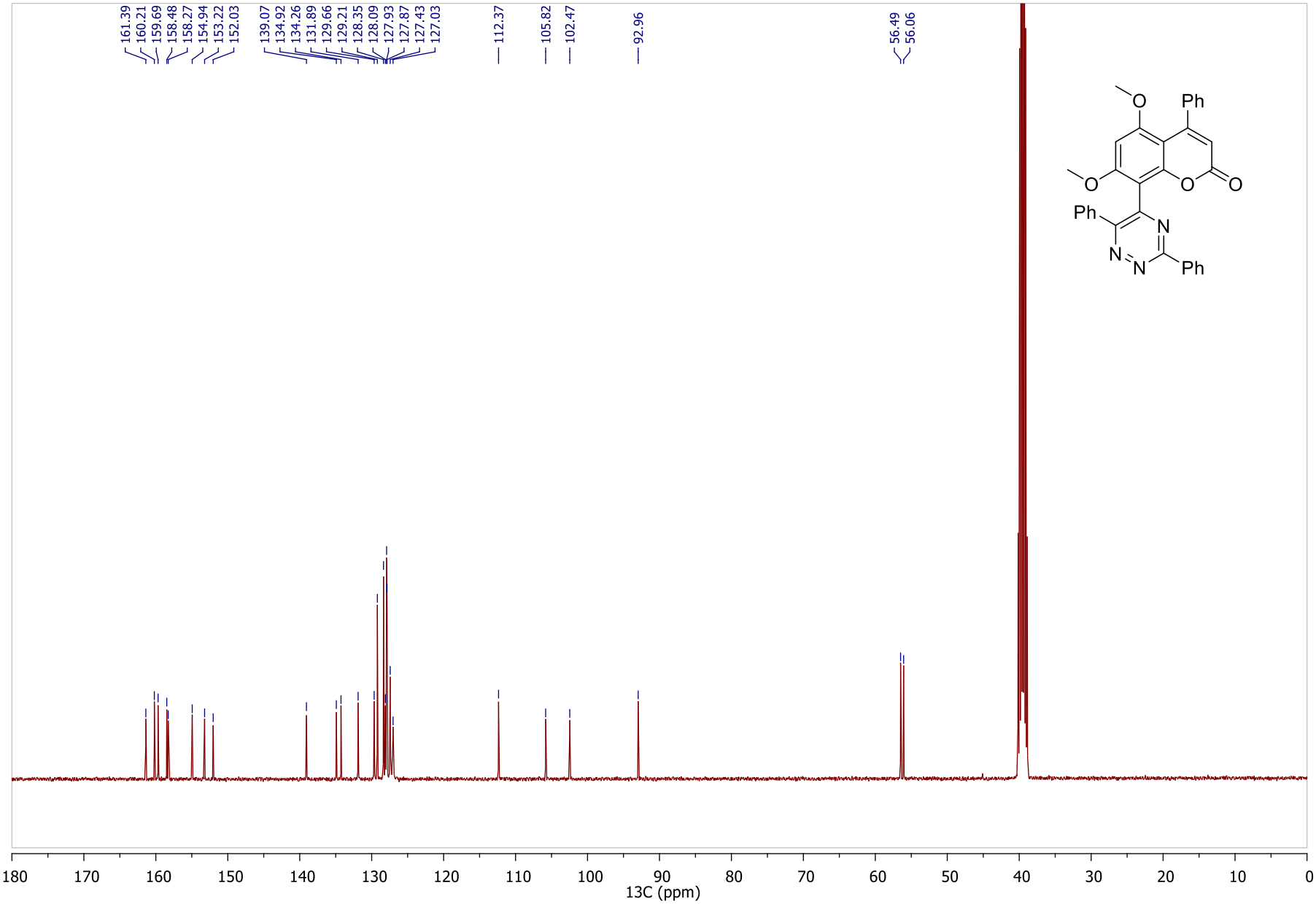

Figure S8. ^{13}C NMR spectrum of **3b** (DMSO-d_6)

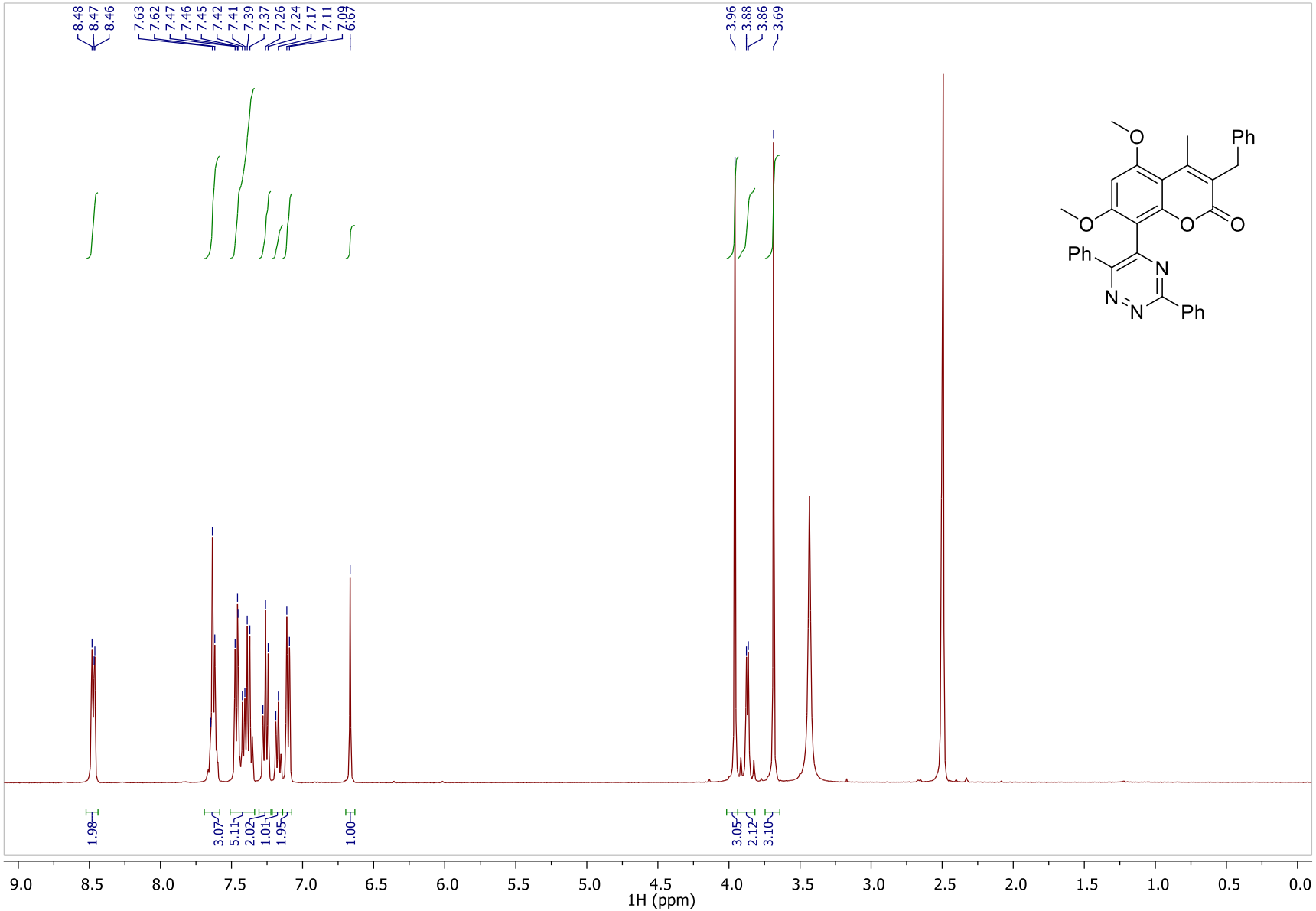

Figure S9. ^{1}H NMR spectrum of **3c** (DMSO-d_6)

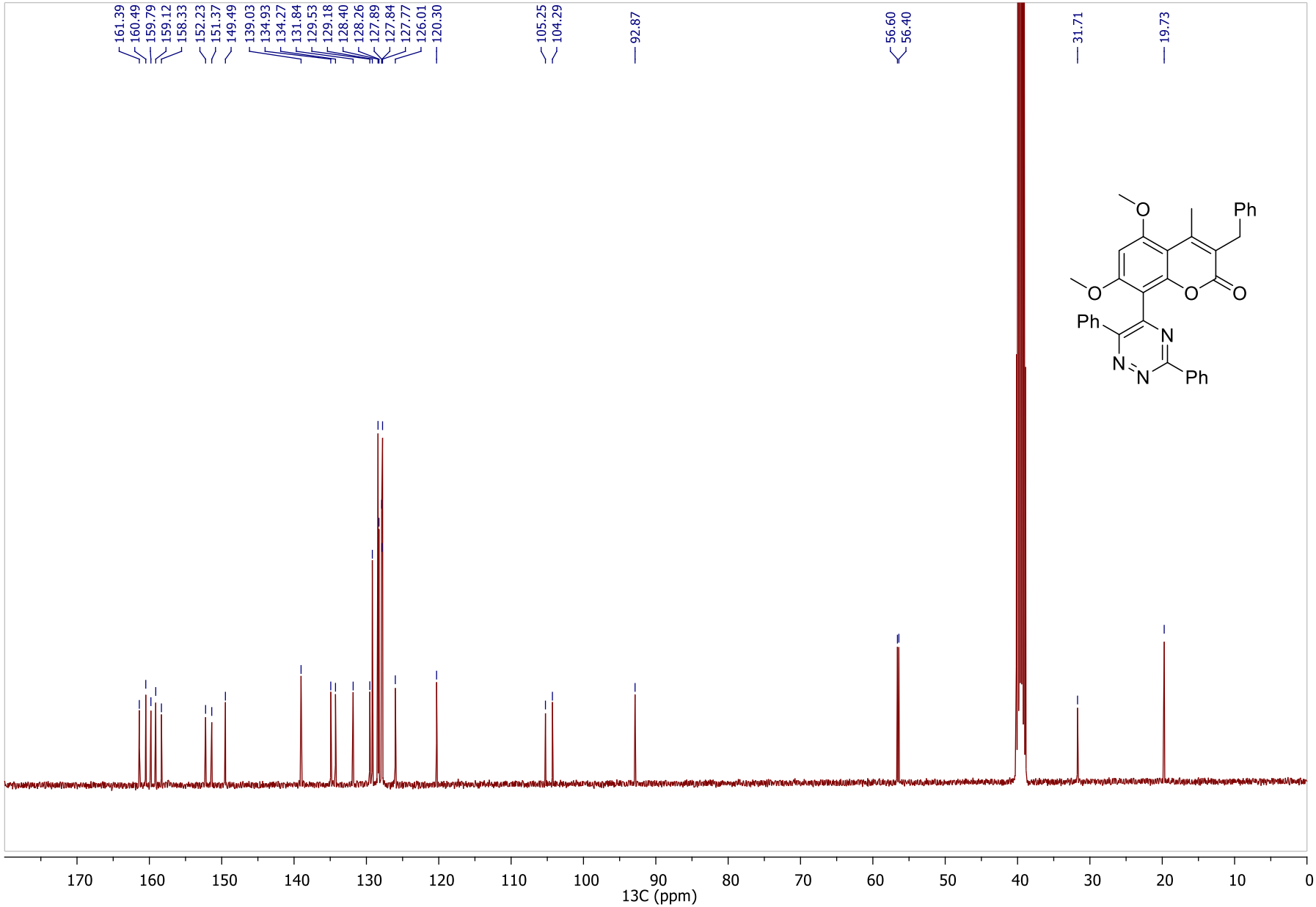

Figure S10. ^{13}C NMR spectrum of **3c** (DMSO-d_6)

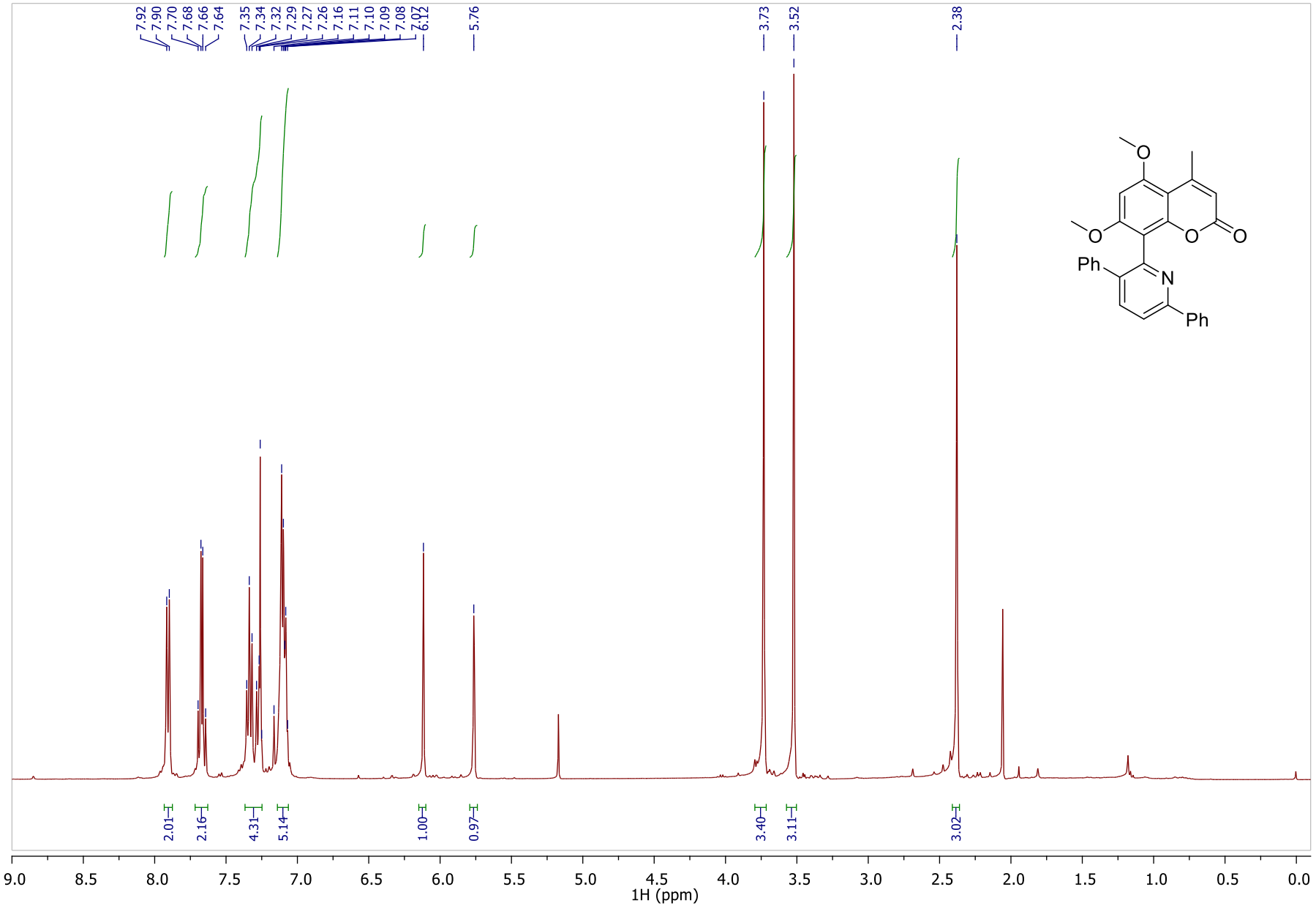

Figure S11. ^{1}H NMR spectrum of **4a** ($CDCl_3$)

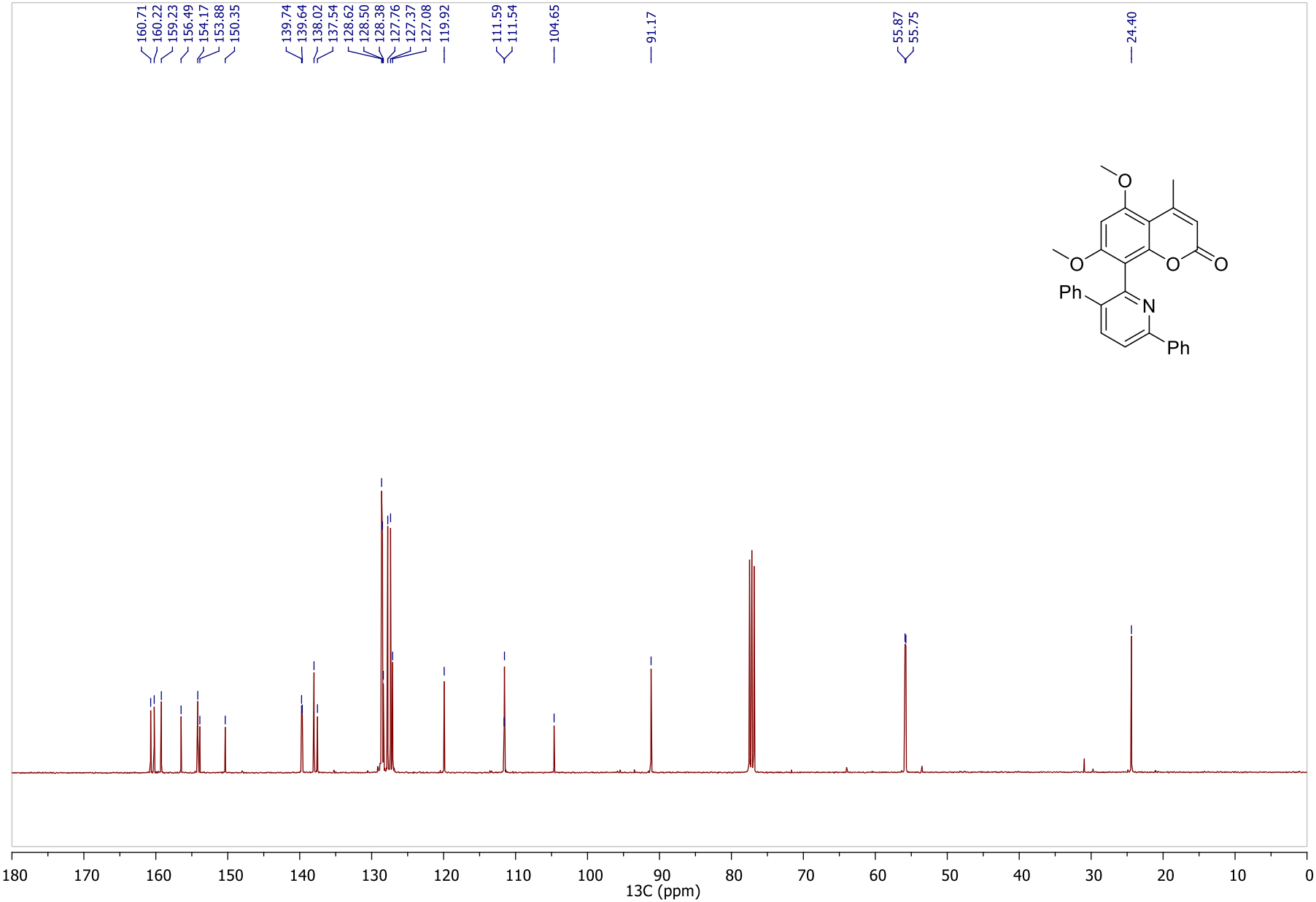

Figure S12. ^{13}C NMR spectrum of **4a** ($CDCl_3$)

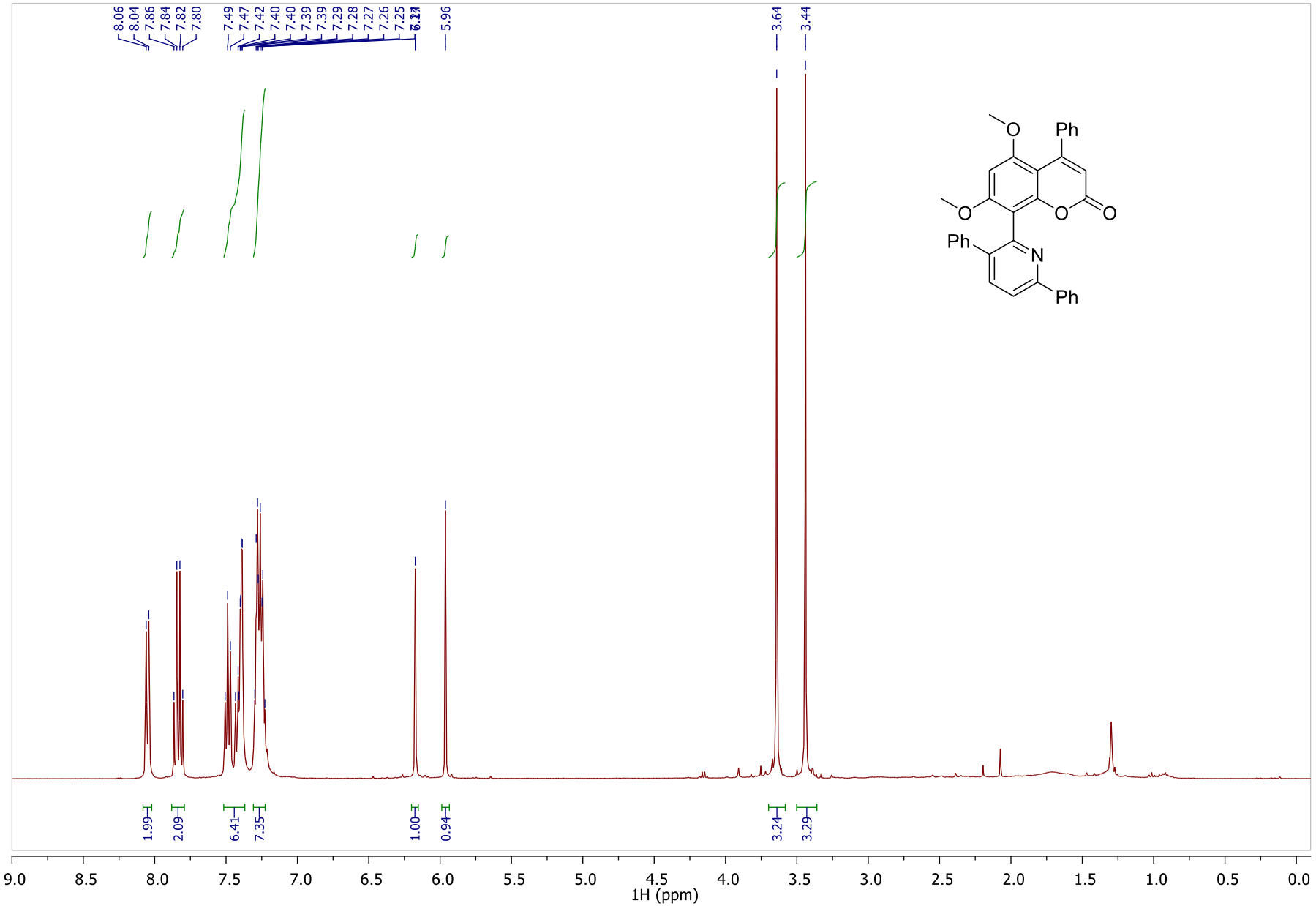

Figure S13. ^{1}H NMR spectrum of **4b** ($CDCl_3$)

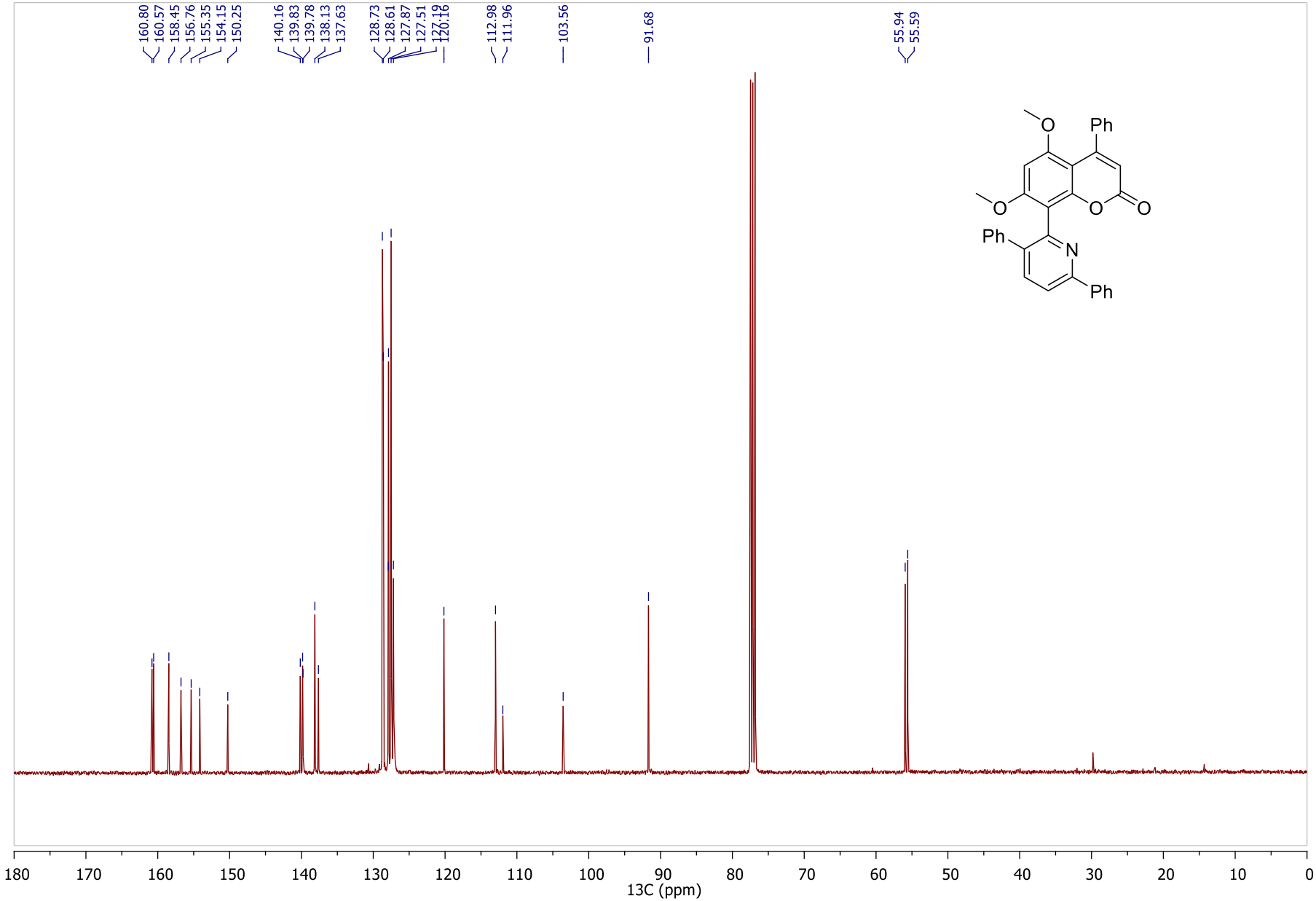

Figure S14. ^{13}C NMR spectrum of **4b** ($CDCl_3$)

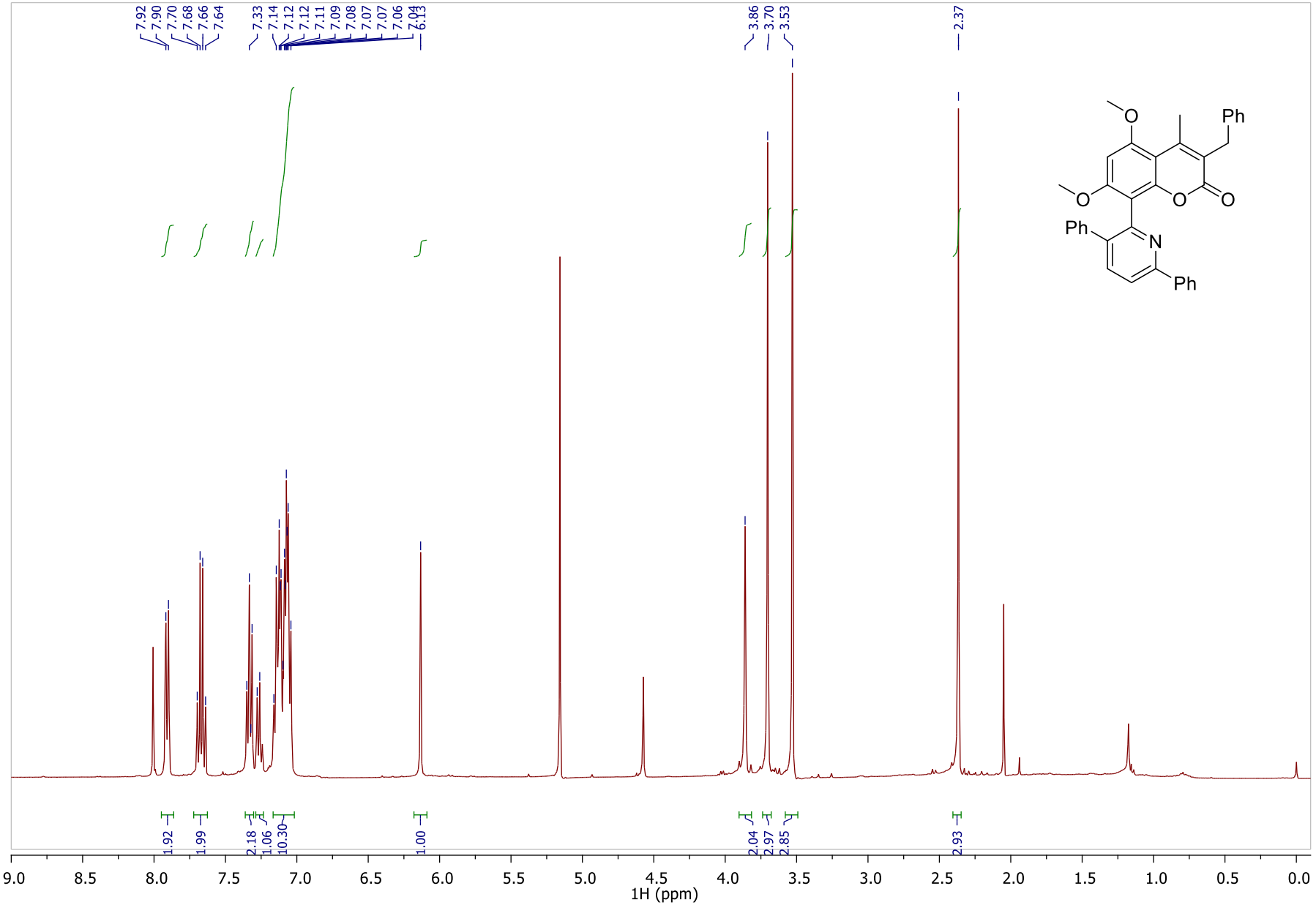

Figure S15. ^{1}H NMR spectrum of **4c** ($CDCl_3$)

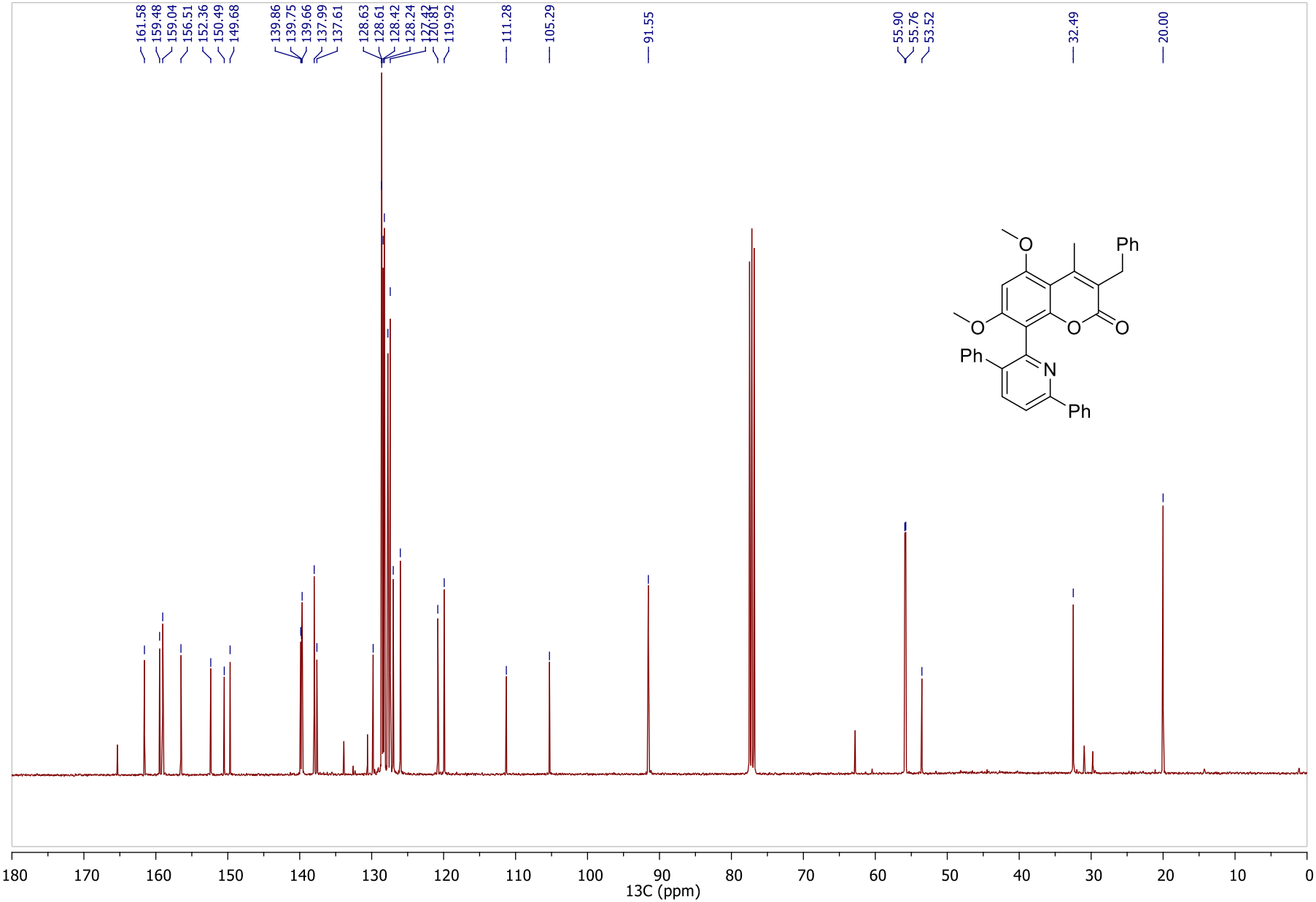

Figure S16. ^{13}C NMR spectrum of **4c** ($CDCl_3$)