Supplementary Information

Synthesis, biological activities, and evaluation molecular docking-dynamics studies of new phenylisoxazole quinoxalin-2-amine hybrids as potential α-amylase and α-glucosidase inhibitors

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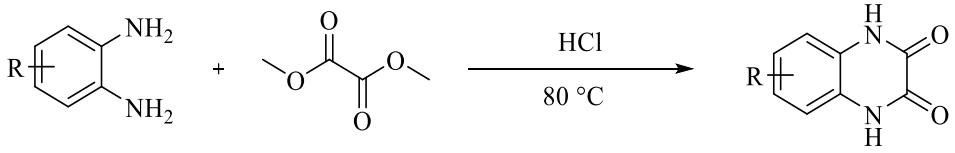
Content

1. General Information

All chemicals and materials purchased from Sigma Aldrich Co. and Merck Chemical Co. and used without purification. DMF and DCM solvents were dried over 4 Å molecular sieves. The purification of synthesised compounds *via* column chromatography were perform using Merck silica gel (0.040-0.063 mm), while the thin-layer chromatography (TLC) was performed using silica-coated aluminium sheets (silica gel 60 F_{254}) and the chromatograms were visualized under UV 254–366 nm Fourier-transform Infrared (FTIR) spectra were obtained using a PerkinElmer 2000 FTIR Spectrum spectrometer (Perkin Elmer,Waltham, MA, USA). The Nuclear magnetic resonance (NMR) spectra were obtained using Bruker Advance 500 (500 MHz for ^{1}H-NMR, 125 MHz for ^{13}C-NMR) spectrometer system and the data was analysed using Topspin 4.1.4 software (Bruker Bioscience, Billerica, MA, USA). The chemical shifts were internally calibrated using the residual DMSO peak (^{1}H: 2.50 ppm, ^{13}C: 39.5 ppm), the $CDCl_3$ peak (^{1}H: 7.26 ppm, ^{13}C: 77.0 ppm) or the or the tetramethylsilane (TMS) signal at 0.00 ppm for both ^{1}H and ^{13}C-NMR. The high-resolution mass spectroscopy (HRMS) was recorded by Waters Xevo QTOF MS (Milford, Massachusetts, United States), and reported in *m/z*. The synthesis method for the intermediates, as well as the NMR, FTIR and HRSM spectra of all synthesised compounds are presented in Supplementary Information.

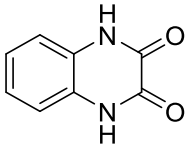
2. Synthesis of quinoxaline-2,3-dione derivatives (1a-e)



1a-e

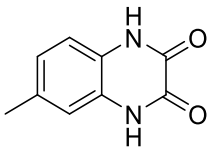
General procedure A. The synthesis of **1a-e** was done in accordance with the procedure reported by J. Lin et al., where substituted 1,2-diaminobenzene (1.00 equiv.) and dimethyl oxalate (1.00 equiv.) was refluxed together in the presence of 4M of HCl at 80 °C. The reaction was monitored using TLC and upon completion, the reaction was cooled to room temperature The precipitate was filtered, washed with distilled water, and dried under fume hood to afford compounds **1a-e**.

1,4-dihydroquinoxaline-2,3-diaone (1a)



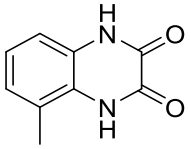
Following general procedure A with o-phenylenediamine (10.4 g, 0.1 mol) and dimethyl oxalate (11.8 g, 0.1 mol) in 4M HCl (58 mL), **1a** was obtained as white solid (15.43 g, 95%). Mp: > 290˚C; $R_f \approx 0.2$, [UV-active, EtOAc/Hexane 30%]; **IR** (cm^{-1}): 3467 (w, N-H), 3045 (m, aromatic C-H), 1667 (s, C=O), 1246 (m, C-N); **^{1}H-NMR** (500 MHz, DMSO-d_6) ***δ***, ppm: 11.94 (s, 2H), 7.08-7.15 (m, 4H); **^{13}C-NMR (**125 MHz, DMSO-d_6) ***δ***, ppm: 155.6, 126.1, 123.5, 115.6.

6-methyl-1,4-dihydroquinoxaline-2,3-diaone (1b)



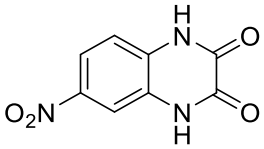
Following general procedure A with 4-methylbenzene-1,2-diamine (1.22 g, 10.0 mmol) and dimethyl oxalate (1.18 g, 10.0 mmol) in 4M HCl (4.0 mL), **1b** was obtained as greyish brown solid (1.53 g, 87% yield). Mp: > 290˚C; $R_f \approx 0.3$, [UV-active, EtOAc/Hexane 30%]; **IR** (cm^{-1}) 3059 (w, N−H), 3059 (aromatic C–H), 2948 (w, Csp3-H), 1681 (s, C=O), 1382 (m, C–N), 807 (m, C=C); **^{1}H NMR** (500 MHz, $CDCl_3$) δ 11.86 (s,1H), 11.84 (s, 1H), 7.01 (d, *J*= 8.0 Hz, 1H), 6.89-6.92 (m, 2H), 2.27 (s, 3H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 155.8, 155.5, 132.8, 125.9, 124.3, 123.8, 115.6, 115.4, 21.0.

5-methyl-1,4-dihydroquinoxaline-2,3-diaone (1c)



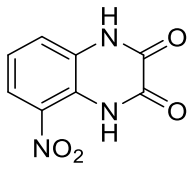
Following general procedure A with 3-methylbenzene-1,2-diamine (1.22 g, 10.0 mmol) and dimethyl oxalate (1.18 g, 10.0 mmol) in 4M HCl (4.0 mL), **1c** was obtained as dark grey solid (1.62 g, 92% yield). Mp: > 290˚C; $R_f \approx 0.8$, [UV-active, EtOAc/Hexane 70%]; **IR υ (cm^{-1}):** 3052 (w, N-H), 3052 (aromatic C-H), 2948 (Csp^3-H), 1690 (s, C=O), 1391 (m, C-N); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 11.95 (s, 1H), 11.20 (s, 1H), 6.94-7.01 (m, 3H), 2.33 (s, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 160.9, 160.1, 130.8, 129.9, 129.2, 129.1, 128.1, 118.4, 22.4.

6-nitro-1,4-dihydroquinoxaline-2,3-diaone (1d)



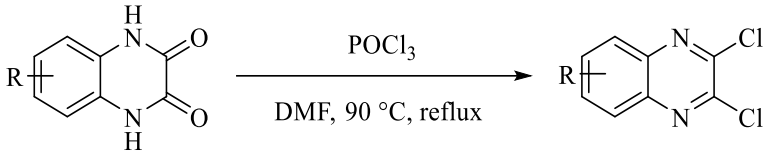
Following general procedure A with 4-nitrobenzene-1,2-diamine (0.94 g, 5.0 mmol) and dimethyl oxalate (0.60 g, 5.0 mmol) in 4M HCl (3.0 mL), **1d** was obtained as dark brown solid (1.62 g, 92% yield). Mp: > 290˚C; $R_f \approx 0.7$, [UV-active, EtOAc/Hexane 30%]; **IR υ (cm^{-1}):** 3539 (w, N-H), 3059 (m, aromatic C-H), 1685 (s, C=O), 1512 (m, NO_2), 1335 (m, C-N); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 12.39 (s, 1H) 12.18 (s, 1H), 7.98 (dd, *J*= 8.8, 2.5 Hz, 1H), 7.95 (d, *J*= 2.5 Hz, 1H), 7.25 (d, *J*= 8.8 Hz, 1H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 155.6, 155.2, 142.6, 132.1, 126.6, 119.1, 116.0, 110.8.

5-nitroquinoxaline-2,3(1H,4H)-dione (1e)



Following general procedure A with 3-nitrobenzene-1,2-diamine (0.31 g, 2.5 mmol) and dimethyl oxalate (0.30 g, 2.5 mmol) in 4M HCl (3.0 mL), **1e** was obtained as a yellow solid (0.31 g, 60% yield). Mp: > 290˚C; $R_f \approx 0.8$, [UV-active, EtOAc/Hexane 70%]; **IR υ (cm^{-1}):** 3325 (w, N-H), 3073 (w, aromatic C-H), 1696 (s, C=O), 1518 (m, NO_2), 1243 (m, C-N); **^{1}H NMR (500 MHz, DMSO-d_6) δ**: 12.35 (s, 1H), 11.92 (s, 1H), 7.91 (d, *J*= 8.0 Hz, 1H), 7.50 (d, *J*= 8.0 Hz, 1H) 7.30 (t, *J*= 8.0 Hz, 1H). **^{13}C NMR (125 MHz, DMSO-d_6) δ**: 154.57, 153.92, 134.50, 128.21, 122.81, 121.27, 121.17, 119.48.

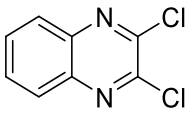
3. Synthesis of 2,3-dichloroquinoxaline derivatives (2a-e)



1a-e **2a-e**

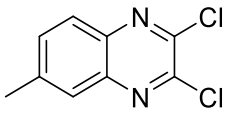
General procedure B. Synthesis of compounds **2a-e** is done following the procedure reported by J. Lin et al., in which respective compounds **1** (1.00 equiv.) is refluxed at 90 °C with phosphoryl chloride (8.00 equiv.) in DMF under inert N_2 atmosphere. The reaction is monitored with TLC and upon completion, the reaction mixture was cooled to room temperature and poured into iced water. The obtained solid was filtered, washed with distilled water, and recrystallized with DCM to afford compounds **2a-e**.

2,3-dichloroquinoxaline (2a)



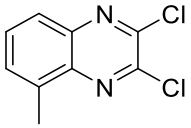
Following general procedure B, with **1a** (0.41 g, 2.5 mmol) and $POCl_3$ (1.9 mL, 20.0 mmol), **2a** was obtained as dark brown solid (0.44 g, 88% yield). Mp: 150-154 ºC; $R_f \approx 0.8$, [UV-active, EtOAc/Hexane 10%]; **IR υ (cm^{-1}):** 3042 (m, aromatic C-H), 1557 (m, C=N), 1268 (m, C-N), 988 (-Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) δ**: 8.09-8.11 (m, 2H), 7.94-7.96 (m, 2H); **^{13}C-NMR (125 MHz, $CDCl_3$) δ**: 149.9, 145.3, 137.0, 133.2.

2,3-dichloro-6-methylquinoxaline (2b)



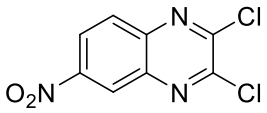
Following general procedure B, with **1b** (0.44 g, 2.5 mmol) and $POCl_3$ (1.9 mL, 20.0 mmol), **2b** was obtained as light brown solid (0.43 g, 81% yield). Mp: 113-114 ºC; $R_f \approx 0.8$, [UV-active, EtOAc/Hexane 10%]; **IR υ (cm^{-1}):** 3031 (w, aromatic C-H), 2918 (w, –CH_3), 1618 (w, C=N), 1252 (m, C–N), 992 (s, C–Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 7.98 (d, *J*= 8.6 Hz, 1H), 7.87 (s, 1H), 7.80 (dd, *J*= 8.6, 1.9 Hz), 2.57 (s, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 144.9, 144.0, 143.0, 140.6, 139.0, 134.3, 127.9, 127.1, 21.8.

2,3,6-trichloroquinoxaline (2c)



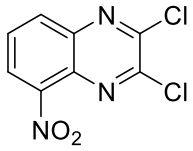
Following general procedure B, with **1c** (0.44 g, 2.5 mmol) and $POCl_3$ (1.9 mL, 20.0 mmol), **2c** was obtained as dark grey solid (0.43 g, 81% yield). Mp: 88-90 ºC; $R_f \approx 0.8$, [UV-active, EtOAc/Hexane 10%]; **IR υ (cm^{-1}):** 3042 (m, aromatic C-H), 1557 (m, C=N), 1268 (m, C-N), 988 (C-Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 7.93 (d, *J*= 8.2 Hz, 1H), 7.81-7.86 (m, 2H), 2.69 (s, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 149.6, 148.7, 145.6, 144.5, 141.6, 136.8, 130.9, 22.0.

2,3-dichloro-6-nitroquinoxaline (2d)



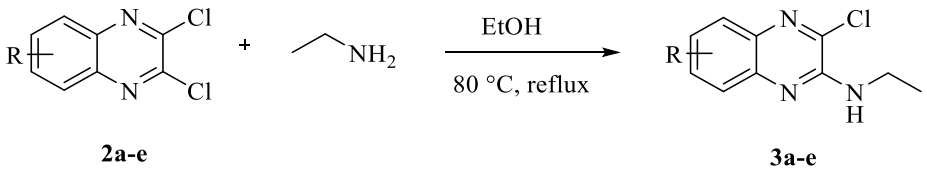
Following general procedure B, with **1d** (0.44 g, 2.5 mmol) and $POCl_3$ (1.9 mL, 20.0 mmol), **2d** was obtained as dark grey solid (0.43 g, 81% yield). Mp: 149-151 ºC; $R_f \approx 0.8$, [UV-active, EtOAc/Hexane 10%]; **IR υ (cm^{-1}):** 3052 (m, aromatic C-H), 1567 (m, C=N), 1524 (s, NO_2), 1273 (m, C-N), 740 (m, C-Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 8.92 (s, 1H), 8.62 (d, *J*= 9.1 Hz, 1H), 8.33 (d, *J*= 9.1, 1H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 155.6, 148.7, 148.0, 143.0, 139.5, 130.3, 125.4, 124.3;

2,3-dichloro-5-nitroquinoxaline (2e)



The compound was prepared according to the **General procedure B** with **1e** (0.21 g, 1.0 mmol) and $POCl_3$ (1.20 g, 8.0 mmol), **2e** is obtained as a yellowish-green solid form (0.22 g, 95% yield). Mp: 152-154 ºC; $R_f \approx 0.8$, [UV-active, EtOAc/Hexane 10%]; **IR υ (cm^{-1})**: 3030 (m, aromatic C-H), 1738 (m, C=N), 1522 (s, NO_2), 1179 (m, C-N), 763 (m, C-Cl); **^{1}H NMR (500 MHz, DMSO-d6) δ:** 8.50 (dd, *J*= 8.0, 1.3 Hz, 1H), 8.38 (dd, *J*= 8.0, 1.3 Hz, 1H), 8.00 (t, *J*= 8.0 Hz, 1H); **^{13}C NMR (125 MHz, DMSO-d6) δ**: 147.5, 147.1, 145.4, 139.9, 132.5, 131.6, 130.8, 125.9.

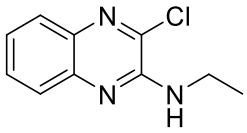
4. Synthesis of 3-chloro-*N*-ethylquinoxalin-2-amine derivatives (3a-e)



2a-e **3a-e**

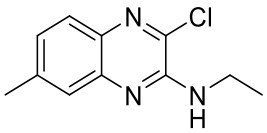
General procedure C. The synthesis of compounds **3a-e** is underwent based on the procedure reported by Keivanloo et al., where respective compound **2** (1.00 equiv.) is reacted with ethylamine (2.00 equiv.) in ethanol and refluxed at 80 °C. The reaction is monitored with TLC and upon completion, the reaction mixture is cooled to room temperature. The solvent is evaporated and the remaining solid is purified via gravitational column chromatography to afford compounds **3a-e**.

3-chloro-*N*-ethylquinoxalin-2-amine (3a)



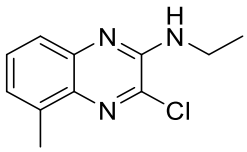
Following general procedure C with **2a** (1.0 g, 5.0 mmol) and ethylamine (0.6 mL, 10.0 mmol), **3a** is obtained as yellowish-white solid (0.96 g, 92% yield). Mp: 72-73 ºC; $R_f \approx 0.6$, [UV-active, EtOAc/Hexane 60%]; **IR υ (cm^{-1}):** 3420 (m, N-H), 2964 (m, aromatic C-H), 2916 (w, Csp3-H), 1510 (m, C=N), 1038 (m, C-N), 752 (C-Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) δ**: 7.72 (d, *J*= 8.0 Hz, 1H), 7.65 (d, *J*= 8.0 Hz, 1H), 7.51 (t, *J*= 8.0 Hz, 1H), 7.31 (t, *J*= 8.0 Hz, 1H), 5.45 (s, 1H), 3.54-3.59 (m, 2H), 1.29 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) δ**: 148.0, 141.5, 137.9, 136.3, 130.1, 127.9, 126.0, 124.9, 36.4, 14.5.

3-chloro-*N*-ethyl-7-methylquinoxalin-2-amine (3b)



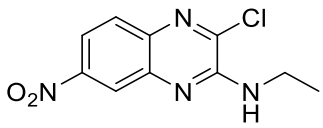
Following general procedure C with **2b** (0.75 g, 3.5 mmol) and ethylamine (0.6 mL, 7.0 mmol), **3b** is obtained as an off-white solid (0.71 g, 92% yield). Mp: 74−76 ºC; $R_f \approx 0.6$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3426 (m, N–H), 2970 (w, –CH_3), 2908 (w, aromatic C-H) 2872 (w, Csp_3-H), 1548 (s, C=N), 1040 (s, C–N), 814 (s, C–Cl); **^{1}H NMR (500 MHz, $CDCl_3$) δ:** 7.66 (d, *J*= 8.4 Hz, 1H), 7.51 (s, 1H), 7.21 (dd, *J*= 8.4, 1.8 Hz, 1H), 5.46 (s, 1H), 3.59-3.65 (m, 2H), 2.50 (s, 3H), 1.34 (t, *J*= 7.5 Hz, 3H); **^{13}C NMR (125 MHz, $CDCl_3$) δ:** 148.1, 141.4, 140.5, 134.6, 132.0, 127.4, 126.9, 125.3, 36.4, 21.8, 14.6.

3-chloro-*N*-ethyl-5-methylquinoxalin-2-amine (3c)



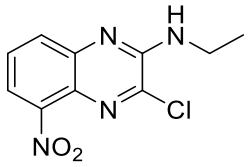
Following general procedure C with **2c** (0.53 g, 2.5 mmol) and ethylamine (0.4 mL, 5.0 mmol), **3d** is obtained as yellowish sticky solid (0.47 g, 85% yield). $R_f \approx 0.6$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1})**: 3433 (m, N-H), 2973 (w, aromatic C-H), 2921 (w, Csp_2-H), 2873 (w, Csp_3-H), 1580 (m, C=N), 1067 (m, C-N), 757 (m, C-Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 7.42-7.56 (m, 2H), 7.22 (d, *J*= 7.2 Hz, 1H), 5.47 (s, 1H), 3.60-3.67 (m, 2H), 2.66 (s, 3H), 1.35 (t, *J*= 7.4 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 147.8, 141.6, 136.6, 136.3, 129.7, 125.4, 124.5, 123.8, 36.4, 17.2, 14.6.

3-chloro-*N*-ethyl-7-nitroquinoxalin-2-amine (3d)



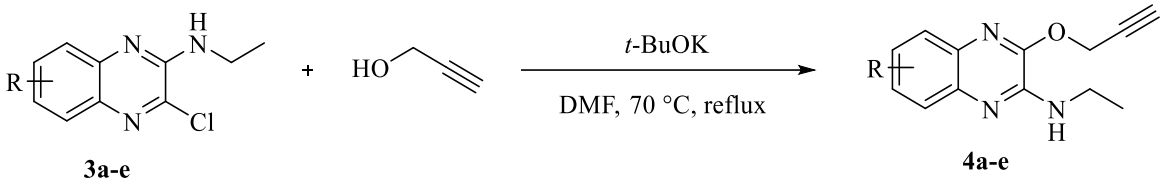
Following general procedure C with **2d** (0.61 g, 2.5 mmol) and ethylamine (0.3 mL, 5.0 mmol), **3d** is obtained as a yellow solid (0.62 g, 98% yield). Mp: 120-123 ºC; $R_f \approx 0.5$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1})**: 3388 (m, NH), 2917 (w, aromatic C-H), 2840 (w, Csp_3-H), 1562 (s, C=N), 1508 (s, NO_2), 1063 (m, C-N), 744 (m, C-Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 8.63 (d, *J*= 2.5 Hz, 1H), 8.31 (dd, *J*= 9.2, 2.5 Hz, 1H), 7.69 (d, *J*= 9.2 Hz, 1H), 5.85 (s, 1H), 3.59-3.64 (m, 2H), 1.21 (t, *J*= 7.3 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 149.3, 145.5, 144.0, 140.4, 134.7, 126.7, 124.4, 124.2, 36.7, 14.3.

3-chloro-*N*-ethyl-5-nitroquinoxalin-2-amine (3e)



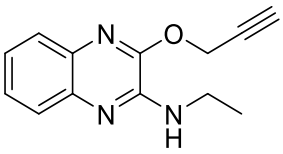
Following general procedure C with **2d** (0.15 g, 0.6 mmol) and ethylamine (0.06 mL, 1.2 mmol), **3d** is obtained as a yellow solid (0.11 g, 68% yield). Mp: 113-116 ºC; $R_f \approx 0.5$, [UV-active, EtOAc/Hexane 90%]; **IR** (cm^{-1}): 3385 (m, NH), 3051 (w, aromatic C-H), 2974 (w, Csp_3-H), 1740 (m, C=N), 1517 (s, NO_2), 1084 (m, C-N), 742 (m, C-Cl); **^{1}H NMR (500MHz, $CDCl_3$) δ**: 8.00 (t, *J*= 8.0 Hz, 2H), 7.40 (t, *J*= 8.0 Hz, 1H), 5.88 (s, 1H), 3.62-3.67 (m, 2H), 1.35 (t, *J*= 7.2, 3H); **^{13}C NMR (125 MHz, $CDCl_3$) δ:** 148.7, 144.7, 139.5, 136.6, 134.2, 132.6, 124.9, 112.8, 36.8, 14.1.

5. General procedure for the synthesis of *N*-ethyl-3-(prop-2-yn-1-yloxy)quinoxalin-2-amine derivatives (4a-e)



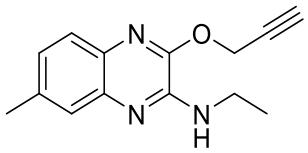
General procedure D. The synthesis of compounds **4a-e** was done in accordance to the procedure reported by Keivanloo et al. with slight modifications. Respective compounds **3** (1.0 equiv.) was reacted with propargyl alcohol (1.1 equiv.) in the presence of catalyst potassium tert-butoxide in DMF at 70 ^{o}C in inert N_2 atmosphere. The reaction is monitored with TLC and upon completion, the reaction mixture is cooled to room temperature and the solvent is evaporated. The crude solid obtained is purified via gravitational column chromatography to obtained products **4a-e**.

***N*-ethyl-3-(prop-2-yn-1-yloxy)quinoxalin-2-amine (4a)**



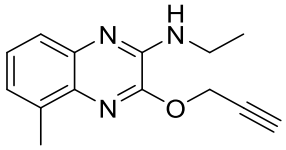
Following general procedure D with **3a** (62.3 mg, 0.3 mmol), propargyl alcohol (0.02 mL, 0.32 mmol) and *t*-BuOK (48.0 mg, 0.43 mmol), **4a** is obtained as an off-white solid (30.3 mg, 88% yield). Mp: 96-100 ^{o}C; $R_f \approx 0.6$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3449 (m, N-H), 3259 (m, C≡CH), 2967 (m, aromatic C-H), 2911 (w, Csp_3-H), 1522 (s, C=N), 1443 (m, C-N), 1196 (s, C-O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 7.63-7.66 (m, 2H), 7.39-7.43 (m, 1H), 7.28-7.31 (m, 1H), 5.42 (s, 1H), 5.15 (d, *J*= 2.4 Hz, 2H), 3.59-3.65 (m, 2H), 2.54 (t, *J*= 2.4 Hz, 1H), 1.33 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 146.9, 144.4, 139.5, 134.6, 126.9, 126.5, 125.4, 124.0, 78.3, 75.3, 54.0, 35.6, 14.6; **HRMS (+ESI) [M+H]$^{+}$**: 228.1136, $C_{13}H_{14}N_3O$, requires 228.1143

***N*-ethyl-7-methyl-3-(prop-2-yn-1-yloxy)quinoxalin-2-amine (4b)**



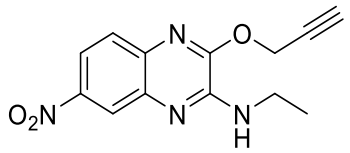
Following general procedure D with **3b** (0.44 g, 2.0 mmol), propargyl alcohol (0.02 mL, 2.1 mmol) and *t*-BuOK (0.25 g, 2.2 mmol), **4b** is obtained as an off-white solid (30.3 mg, 88% yield). Mp: 137-141 ºC; $R_f \approx 0.6$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3437 (w, N-H), 3247 (w, C≡CH), 2975 (w, aromatic C-H), 2924 (w, Csp_2-H), 2872 (w, Csp_3-H), 1510 (s, C=N), 1309 (s, C-N), 1204 (m, C-O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 7.45 (d, *J*= 8.2 Hz, 1H,), 7.39 (s, 1H), 7.06 (dd, *J*= 8.2, 2.0 Hz, 1H,), 5.32 (s, 1H) 5.06 (s, *J*= 2.5 Hz 2H), 3.52-3.57 (m, 2H), 2.46 (t, *J*= 2.5 Hz, 1H), 2.38 (s, 3H), 1.25 (t, *J*= 7.3 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 144.4, 139.4 , 136.8, 132.5, 128.5, 126.0, 125.7, 125.1, 78.4, 75.1, 53.9, 35.6, 21.5, 14.7; **HRMS (+ESI) [M+H]$^+$:** 242.1290, $C_{14}H_{16}N_3O$ requires 242.1293.

***N*-ethyl-5-methyl-3-(prop-2-yn-1-yloxy)quinoxalin-2-amine (4c)**



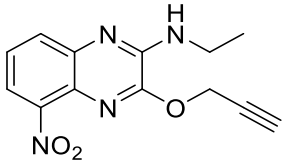
Following general procedure D with **3c** (0.25 g, 1.1 mmol), propargyl alcohol (0.08 mL, 1.2 mmol) and *t*-BuOK (0.14 g, 1.3 mmol), **4c** is obtained as yellowish sticky solid (0.1 g, 37% yield). $R_f \approx 0.7$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3440 (m, N-H), 3293 (m, C≡CH), 2970 (w, aromatic C-H), 2927 (w, Csp_2-H), 2873 (w, Csp_3-H), 1520 (s, C=N), 1295 (m, C-N), 1201 (s, C-O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 7.50 (d, *J*= 7.4 Hz, 1H), 7.28 (d, *J*= 7.4 Hz, 1H), 7.20 (t, *J*= 7.4 Hz, 1H), 5.40 (s, 1H), 5.15 (s, *J*= 2.5 Hz, 2H), 3.61-3.67 (m, 2H), 2.62 (s, 3H), 2.54 (t, *J*= 2.4 Hz, 1H), 1.34 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 146.6, 143.4, 138.2, 134.4, 133.7, 127.3, 124.2, 123.6, 78.4, 75.1, 53.8, 35.7, 17.4, 14.5; **HRMS (+ESI) [M+H]$^+$:** 242.1290, $C_{14}H_{16}N_3O$ requires 242.1290.

***N*-ethyl-7-nitro-3-(prop-2-yn-1-yloxy)quinoxalin-2-amine (4d)**



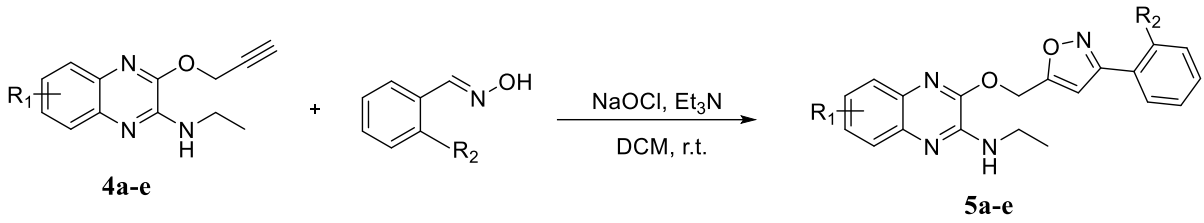
Following general procedure D with **3d** (88.4 mg, 0.35 mmol), propargyl alcohol (0.02 mL, 0.36 mmol) and *t*-BuOK (46.0 mg, 2.20 mmol), **4d** is obtained as a yellow solid (39.0 mg, 41% yield). Mp: 148-151 ºC; $R_f \approx 0.4$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3367 (m, N–H), 3294 (m, C≡C), 2923 (m, aromatic C-H), 2847 (m, Csp_3-H), 1543 (m, C=N), 1523 (m, NO_2), 1293 (s, C–N), 1203 (m, C–O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 8.50 (d, *J*= 2.6 Hz, 1H), 8.17 (dd, *J*= 9.0, 2.6 Hz, 1H), 7.60 (d, *J*= 9.0 Hz, 1H), 5.75 (s, 1H), 5.11 (d, *J*= 2.4 Hz, 2H), 3.58-3.63 (m, 2H), 2.51 (t, *J*= 2.4 Hz, 1H), 1.29 (t, *J*= 7.3 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 147.0, 144.8, 143.3, 142.5, 132.5, 124.7, 121.8, 120.5, 76.5, 74.8, 53.6, 34.8, 13.4; **HRMS (+ESI) [M+H]$^+$:** 273.0984, $C_{13}H_{13}N_4O_3$ requires 273.0987.

***N*-ethyl-5-nitro-3-(prop-2-yn-1-yloxy)quinoxalin-2-amine (4e)**



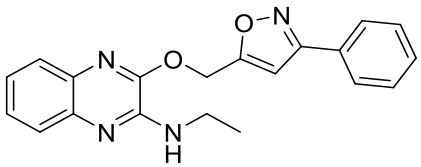
Following general procedure D with **3e** (80.0 mg, 0.31 mmol), propagyl alcohol (0.02 mL, 0.33 mmol) and *t*-BuOK (37.02 mg, 0.33 mmol) in DMF (2 mL), **4e** is afforded as a yellow solid (58.3 mg, 72% yield). Mp: 127-130 ºC; $R_f \approx 0.3$, [UV-active, EtOAc/Hexane 90%]; **IR υ (cm^{-1}):** 3380 (m, N–H), 3265 (m, C≡C), 2924 (m, aromatic C-H), 2854 (m, Csp_3-H), 1728 (m, C=N), 1523 (m, NO_2), 1270 (m, C–O), 1190 (m, C–N); **^{1}H-NMR (500 MHz, $CDCl_3$) δ:** 7.80 (t, *J*= 7.80 Hz, 2H), 7.22 (t, J= 7.80, 1H), 5.77 (s, 1H), 5.15 (d, *J*= 2.5 Hz, 2H), 3.60-3.65 (m, 2H), 2.57 (t, *J*= 2.4 Hz, 1H), 1.32 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) δ**: 147.4, 145.1, 135.6, 132.4, 130.5, 122.0, 121.7, 77.6, 75.7, 54.5, 29.7, 14.3; **HRMS (+ESI) [M+H]$^+$:** 273.0976, $C_{13}H_{13}N_4O_3$ requires 273.0987.

6. Synthesis of *N*-ethyl-3-((3-phenylisoxazol-5-yl)methoxy)quinoxalin-2-amine derivatives (5a-i)



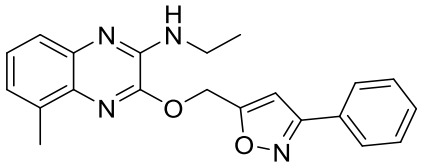
General procedure E. Compounds **5a-i** were synthesised by stirring respective compounds **4** (1.2 eq.) with 6% NaOCl in the presence of Et_3N at 0 ^oC. After 5 mins, benzaldehyde oxime (1.0 eq.) in DCM was added into the mixture and the reaction was stirred for 2 hours. After 2 hours, the reaction was left to stir at room temperature and monitored using TLC. After completion, the mixture was extracted and evaporated, and the crude obtained was purified by gravitational column chromatography to produce final products **5a-i**.

***N*-ethyl-3-((3-phenylisoxazol-5-yl)methoxy)quinoxalin-2-amine (5a)**



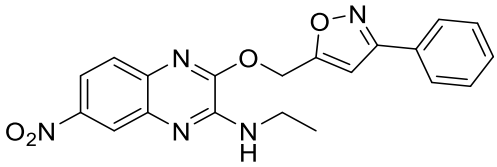
Following general procedure E with **4a** (45.5 mg, 0.2 mmol), 6% NaOCl (0.8 mL), Et_3N (0.02 mL) and benzaldehyde oxime (18.6 mg, 0.15 mmol), **5a** is afforded as sticky pale-yellow solid (33.0 mg, 61% yield). $R_f \approx 0.5$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3431 (m, N-H), 3088 (w, aromatic C-H), 2978 (w, Csp_3-H), 1531 (s, aromatic C=C), 1447 (s, C=N), 1378 (m, C-N), 1195 (s, C-O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 7.80-7.82 (m, 2H), 7.68 (d, *J*= 8.0 Hz, 2H), 7.44-7.47 (m, 4H), 7.31-7.34 (m, 1H), 6.73 (s, 1H), 5.70 (s, 2H), 5.41 (s), 3.58-3.66 (m, 2H), 1.33 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 167.5, 162.7, 146.9, 144.4, 139.6, 134.4, 130.2, 129.0, 129.0, 128.7, 127.1, 126.9, 126.9, 126.4, 125.5, 124.1, 102.8, 58.2, 35.7, 14.7; **HRMS** (+ESI) $[M+H]^+$: 347.1504, $C_{20}H_{19}N_4O_2$, requires 347.1508.

***N*-ethyl-5-methyl-3-((3-phenylisoxazol-5-yl)methoxy)quinoxalin-2-amine (5b)**



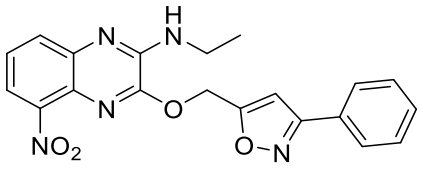
Following general procedure E with **4c** (45.0 mg, 0.18 mmol), 6% NaOCl (0.8 mL), Et_3N (0.02 mL) and benzaldehyde oxime (18.8 mg, 0.15 mmol), **5b** is afforded as sticky pale-yellow liquid (29.4 mg, 53% yield). $R_f \approx 0.5$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3445 (m, N–H), 3062 (w, aromatic C-H), 2963 (w, Csp_2-H), 2826 (w, Csp_3-H), 1529 (s, aromatic C=C), 1476 (m, C=N), 1298 (m, C–N), 1203 (s, C–O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 7.80-7.82 (m, 2H), 7.54 (d, *J*= 7.6 Hz, 1H), 7.45-7.46 (m, 3H), 7.31 (d, *J*= 7.6 Hz, 1H), 7.23 (t, *J*= 7.6 Hz, 1H), 6.76 (s, 1H), 5.73 (s, 2H), 5.44 (s, 1H), 3.65-3.72 (m, 2H), 2.67 (s, 3H), 1.38 (t, *J*= 7.2, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ***: 167.7, 162.7, 146.6, 143.4, 138.3, 134.3, 133.8, 130.2, 128.9, 128.9, 128.7, 127.4, 126.9, 124.2, 123.7, 102.7, 58.0, 35.7, 17.4, 14.5; **HRMS (+ESI) [M+H]$^+$:** 361.1678, $C_{21}H_{21}N_4O_2$, requires 361.1650.

***N*-ethyl-7-nitro-3-((3-phenylisoxazol-5-yl)methoxy)quinoxalin-2-amine (5c)**



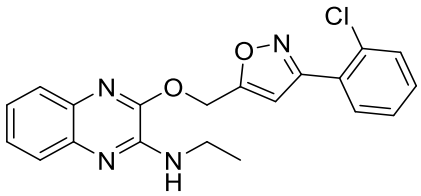
Following general procedure E with **4d** (36.0 mg, 0.15 mmol), 6% NaOCl (0.8 mL), Et_3N (0.02 mL) and benzaldehyde oxime (15.1 mg, 0.12 mmol), **5c** is afforded as a yellow solid (32.3 mg, 66% yield). Mp: 158-163 ºC; $R_f \approx 0.5$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3379 (w, N-H), 3057 (w, aromatic C-H), 2926 (w, Csp_3-H), 1579 (s, aromatic C=C), 1546 (s, NO_2), 1502 (m, C=N), 1327 (m, =C-N), 1201 (s, C-O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 8.57 (d, *J*= 2.5 Hz, 1H), 8.25 (dd, *J*= 9.0, 2.5 Hz, 1H), 7.80-7.82 (m, 2H), 7.68 (d, *J*= 9.0 Hz, 1H), 7.46-7.47 (m, 3H), 6.78 (s, 1H), 5.84 (s, 1H), 5.72 (s, 2H), 3.64-3.69 (m, 2H), 1.35 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 166.5, 162.8, 148.1, 145.8, 144.4, 143.6, 133.4, 130.3, 129.1, 128.5, 127.4, 126.9, 126.3, 125.9, 122.7, 121.7, 103.3, 58.5, 35.9, 14.4; **HRMS (+ESI) [M+H]$^+$:** 392.1357, $C_{20}H_{18}N_5O_4$, requires 392.1359.

***N*-ethyl-5-nitro-3-((3-phenylisoxazol-5-yl)methoxy)quinoxalin-2-amine (5d)**



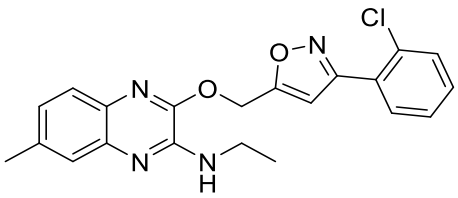
Following general procedure E with **4e** (43.0 mg, 0.16 mmol), 6% NaOCl (0.3 mL), Et_3N (0.02 mL) and benzaldehyde oxime (15.3 mg, 0.18 mmol), **5d** is afforded as a sticky yellow solid (36.3 mg, 76% yield). $R_f \approx 0.3$; [UV-active, EtOAc/Hexane 90%]; **IR υ (cm^{-1}):** 3414 (w, N-H), 3067 (aromatic C-H), 2932 (w, Csp_3-H), 1529 (s, NO_2), 1297 (m, C-N), 1189 (s, C-O); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 7.79-7.84 (m, 4H), 7.45-7.46 (m, 3H), 7.31 (t, *J*= 8.0 Hz, 1H), 6.72 (s, 1H), 5.77 (s, 1H), 5.70 (s, 2H), 3.59-3.62 (m, 2H), 1.30 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 171.3, 166.8, 162.8, 147.6, 145.3, 135.6, 132.7, 130.5, 130.4, 129.1, 128.6, 126.9, 122.3, 122.0, 103.1, 60.5, 58.7, 36.1, 14.4; **HRMS (+ESI) [M+H]$^+$:** 392.1354, $C_{20}H_{18}N_5O_4$, requires 392.1359.

3-((3-(2-chlorophenyl)isoxazol-5-yl)methoxy)-*N*-ethylquinoxalin-2-amine (5e)



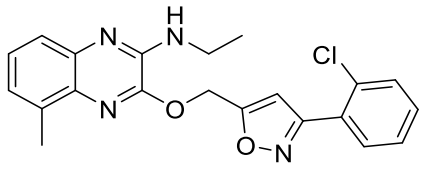
Following general procedure E with **4a** (45.5 mg, 0.2 mmol), 6% NaOCl (0.8 mL), Et_3N (0.02 mL) and 2-chlorobenzaldehyde oxime (23.4 mg, 0.15 mmol), **5e** is afforded as sticky pale-yellow solid (42.9 mg, 73% yield). $R_f \approx 0.6$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3441 (w, N-H), 3064 (w, aromatic C-H), 2974 (w, Csp_3-H), 1531 (s, aromatic C=C), 1442 (m, C=N), 1309 (m, C-N), 1196 (m, C-O), 759 (m, Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 7.74 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.65-7.69 (m, 2H), 7.50 (dd, *J* = 7.5, 1.8 Hz, 1H), 7.30-7.45 (m, 4H), 6.92 (s, 1H), 5.71 (s, 2H), 5.43 (s, 1H), 3.57-3.66 (m, 2H), 1.33 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 166.7, 150.5, 147.6, 146.9, 139.6, 134.4, 132.9, 131.0, 130.5, 130.0, 128.8, 127.9, 127.0, 126.4, 125.4, 124.2, 106.2, 58.2, 35.7, 14.6; **HRMS (+ESI) [M+H]$^+$:** 381.1119, $C_{20}H_{18}ClN_4O_2$, requires 381.1118.

3-((3-(2-chlorophenyl)isoxazol-5-yl)methoxy)-*N*-ethyl-7-methylquinoxalin-2-amine (5f)



Following general procedure E with **4b** (48.3 mg, 0.2 mmol), 6% NaOCl (0.8 mL), Et_3N (0.02 mL) and 2-chlorobenzaldehyde oxime (25.9 mg, 0.15 mmol), **5f** is afforded as sticky pale-yellow liquid (41.6 mg, 63% yield). $R_f \approx 0.7$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3451 (w, N-H), 3056 (aromatic C-H), 2967 (w, Csp_2-H), 2928 (w, Csp_3-H), 1592 (m, aromatic C=C), 1530 (s, C=N), 1317 (m, C-N), 1200 (m, C-O), 763 (m, Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ***: 7.76 (dd, *J* =7.6, 1.7 Hz, 1H, H-5), 7.54-7.57 (m, 1H, H-3″), 7.45-7.50 (m, 2H), 7.34-7.41 (m, 2H, H-7), 7.14 (dd, *J* = 7.5, 1.7 Hz, 1H), 6.91 (s, 1H′), 5.69 (s, 2H), 5.39 (br. s, 1H), 3.58-3.64 (m, 2H), 2.49 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 166.8, 161.3, 146.5, 144.4, 139.5, 137.1, 132.9, 132.4, 131.1, 130.5, 128.7, 128.0, 127.2, 125.9, 125.8, 125.1, 106.2, 58.1, 35.6, 21.5, 14.7 (C-11); **HRMS (+ESI) [M+H]$^+$**: 395.1274, $C_{21}H_{20}ClN_4O_2$, requires 395.1275.

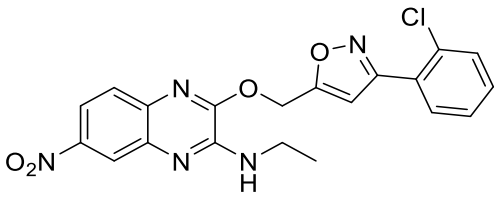
3-((3-(2-chlorophenyl)isoxazol-5-yl)methoxy)-*N*-ethyl-5-methylquinoxalin-2-amine (5g)



Following general procedure E with **4c** (39.3 mg, 0.18 mmol), 6% NaOCl (0.8 mL), Et_3N (0.02 mL) and 2-chlorobenzaldehyde oxime (19.5 mg, 0.13 mmol), **5g** is afforded as sticky pale-yellow liquid (27.0 mg, 55% yield). $R_f \approx 0.6$, [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3445 w, (N-H), 3065 (w, aromatic C-H), 2967 (w, Csp_2-H), 2927 (w, Csp_3-H), 1529 (s, aromatic C=C), 1298 (m, C-N), 1203 (m, C-O), 762 (m, Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 7.73 (dd, *J* = 7.9, 1.8 Hz, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.49 (dd, *J* = 7.9, 1.2 Hz, 1H), 7.34-7.41 (m, 2H, H-8), 7.30 (d, *J* = 7.9 Hz, 1H), 7.21 (t, *J* = 7.6 Hz, 1H), 6.91 (s, 1H, H-4′), 5.70 (s, 2H, H-6′), 5.40 (br. s, 1H, N-H), 3.61-3.66 (m, 2H, H-10), 2.62 (s, 3H), 1.34 (t, *J* = 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 166.9, 161.2, 146.6, 143.3, 138.3, 134.3, 133.8, 132.9, 131.0, 130.5, 128.0, 127.4,

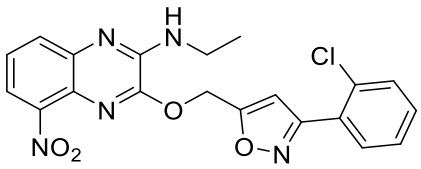
127.2, 124.2, 123.7, 106.1, 58.0, 35.7, 17.4, 14.5; **HRMS (+ESI) [M+H]$^+$:** 395.1279, $C_{21}H_{20}ClN_4O_2$, requires 395.1275.

3-((3-(2-chlorophenyl)isoxazol-5-yl)methoxy)-*N*-ethyl-7-nitroquinoxalin-2-amine (5h)



Following general procedure E with **4d** (34.0 mg, 0.13 mmol), 6% NaOCl (0.8 mL), Et_3N (0.02 mL) and 2-chlorobenzaldehyde oxime (16.2 mg, 0.10 mmol), **5h** is afforded as a sticky yellow solid (37.9 mg, 85% yield). $R_f \approx 0.6$; [UV-active, EtOAc/Hexane 80%]; **IR υ (cm^{-1}):** 3426 (w, N-H), 3065 (w, aromatic C-H), 2924 (m, Csp^3-H), 1544 (aromatic C=C), 1500 (m, C=N), 1459 (m, NO_2), 1325 (m, =C-N), 1080 (m, C-O), 767 (m, Cl); **^{1}H-NMR (500 MHz, $CDCl_3$) *δ*:** 7.80-7.84 (m, 2H), 7.74 (dd, *J*= 7.5, 1.8 Hz, 1H), 7.50 (dd, *J*= 7.5, 1.8 Hz, 1H), 7.34-7.42 (m, 2H), 7.31 (t, *J*= 8.0 Hz, 1H) 6.92 (s, 1H), 5.77 (s, 1H), 5.72 (s, 2H), 3.60-3.66 (m, 2H), 1.32 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (125 MHz, $CDCl_3$) *δ*:** 165.9, 161.3, 147.5, 145.2, 135.5, 132.9, 132.6, 131.2, 131.0, 130.5, 130.4, 129.5, 127.8, 127.2, 122.2, 121.9, 106.4, 58.5, 35.9, 14.3; **HRMS (+ESI) [M+H]$^+$:** 426.0971, $C_{20}H_{17}ClN_5O_4$, requires 426.0969.

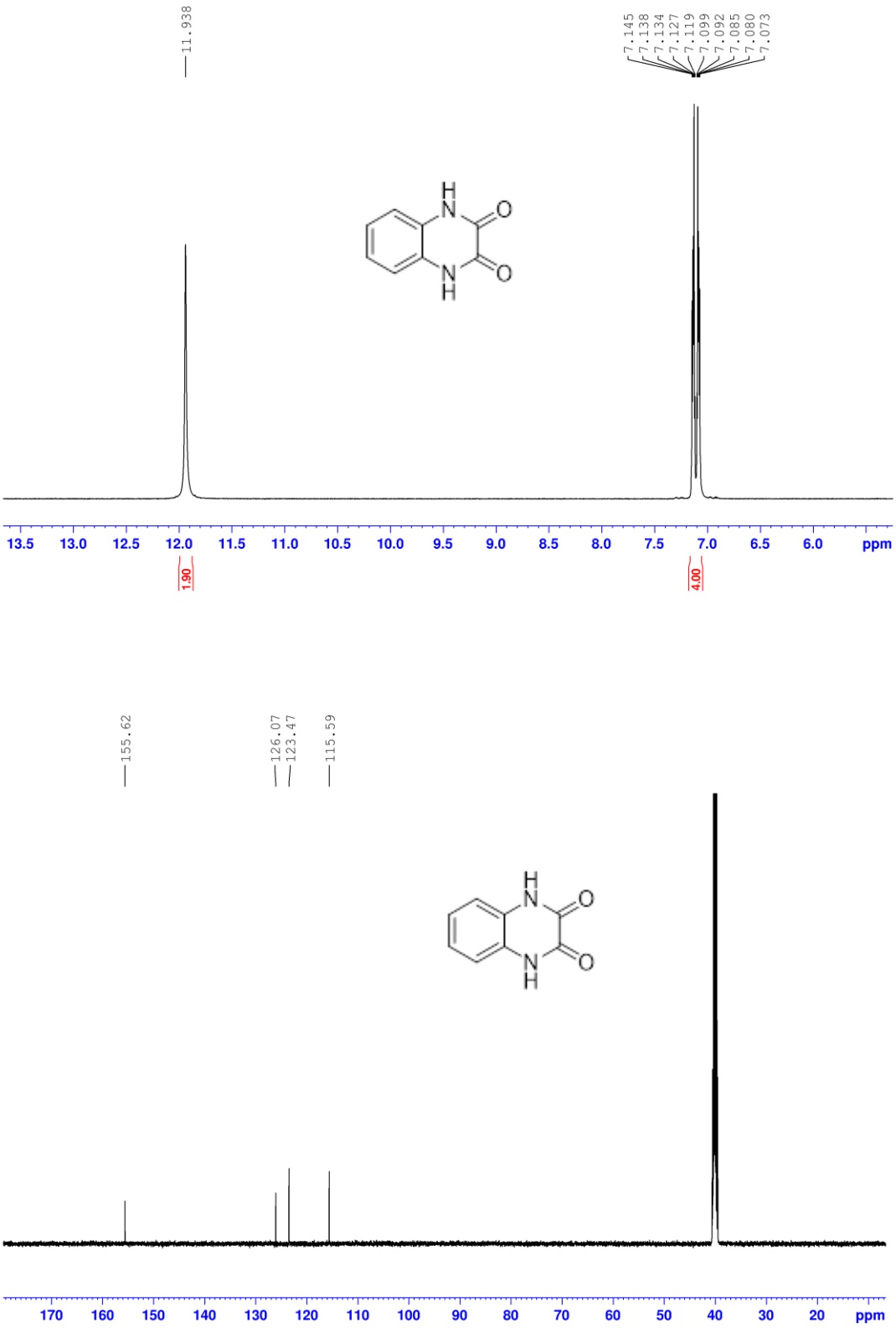
3-((3-(2-chlorophenyl)isoxazol-5-yl)methoxy)-*N*-ethyl-5-nitroquinoxalin-2-amine (5i)



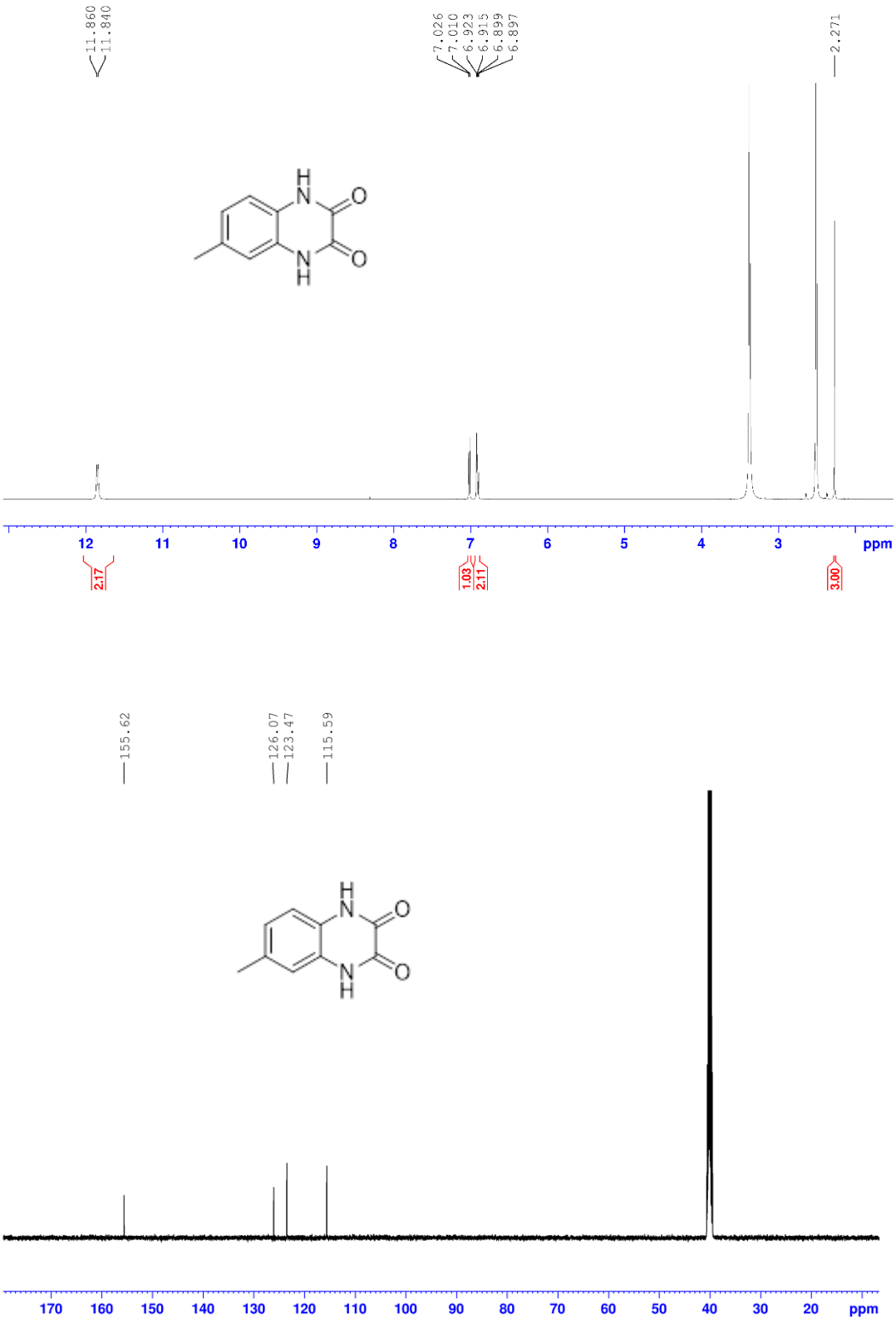
Following general procedure E with **4e** (41.3 mg, 0.14 mmol), 6% NaOCl (0.5 mL), Et_3N (0.02 mL) and 2-chlorobenzaldehyde oxime (30.2 mg, 0.19 mmol), **5i** is afforded as a sticky yellow solid (52.0 mg, 80% yield). Mp: 116-119 °C; $R_f \approx 0.3$; [UV-active, EtOAc/Hexane 90%]; **IR** υ (cm^{-1}): 3327 (w, N-H), 3141 (s, aromatic C-H), 2923(m, Csp_3-H),), 1594 (m, aromatic C=C), 1594 (m, aromatic C=C), 1532 (s, C=N),1532 (m, NO_2), 1224 (m, C-N), 1032 (m, C-O), 767 (m, Cl); **^{1}H-NMR** (500 MHz, $CDCl_3$) ***δ***: 7.80-7.84 (m, 2H), 7.74 (dd, *J*= 7.5, 1.8 Hz, 1H), 7.50 (dd, *J*= 7.5, 1.8 Hz, 1H), 7.34-7.42 (m, 2H), 7.31 (t, *J*= 8.0 Hz, 1H) 6.92 (s, 1H), 5.77 (s, 1H), 5.72 (s, 2H), 3.60-3.66 (m, 2H), 1.32 (t, *J*= 7.2 Hz, 3H); **^{13}C-NMR (**125 MHz, $CDCl_3$) ***δ***: 165.9,

161.3, 147.5, 145.2, 135.5, 132.9, 132.6, 131.2, 131.0, 130.5, 130.4, 129.5, 127.8, 127.2, 122.2, 121.9, 106.4, 58.5, 35.9, 14.3; **HRMS** (+ESI) $[M+H]^+$: 426.0971, $C_{20}H_{17}ClN_5O_4$, requires 426.0969.

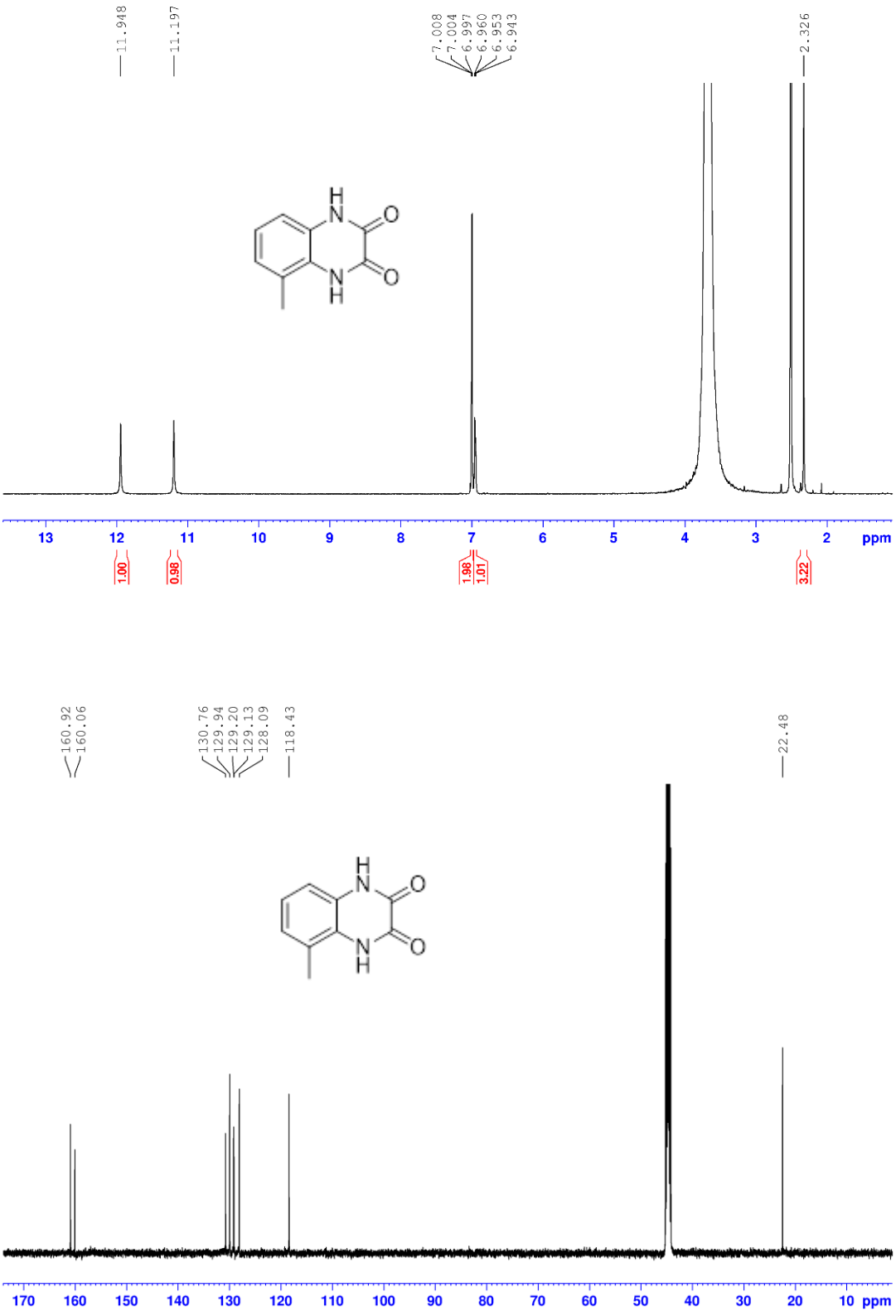
7. ^{1}H-NMR and ^{13}C-NMR Spectra



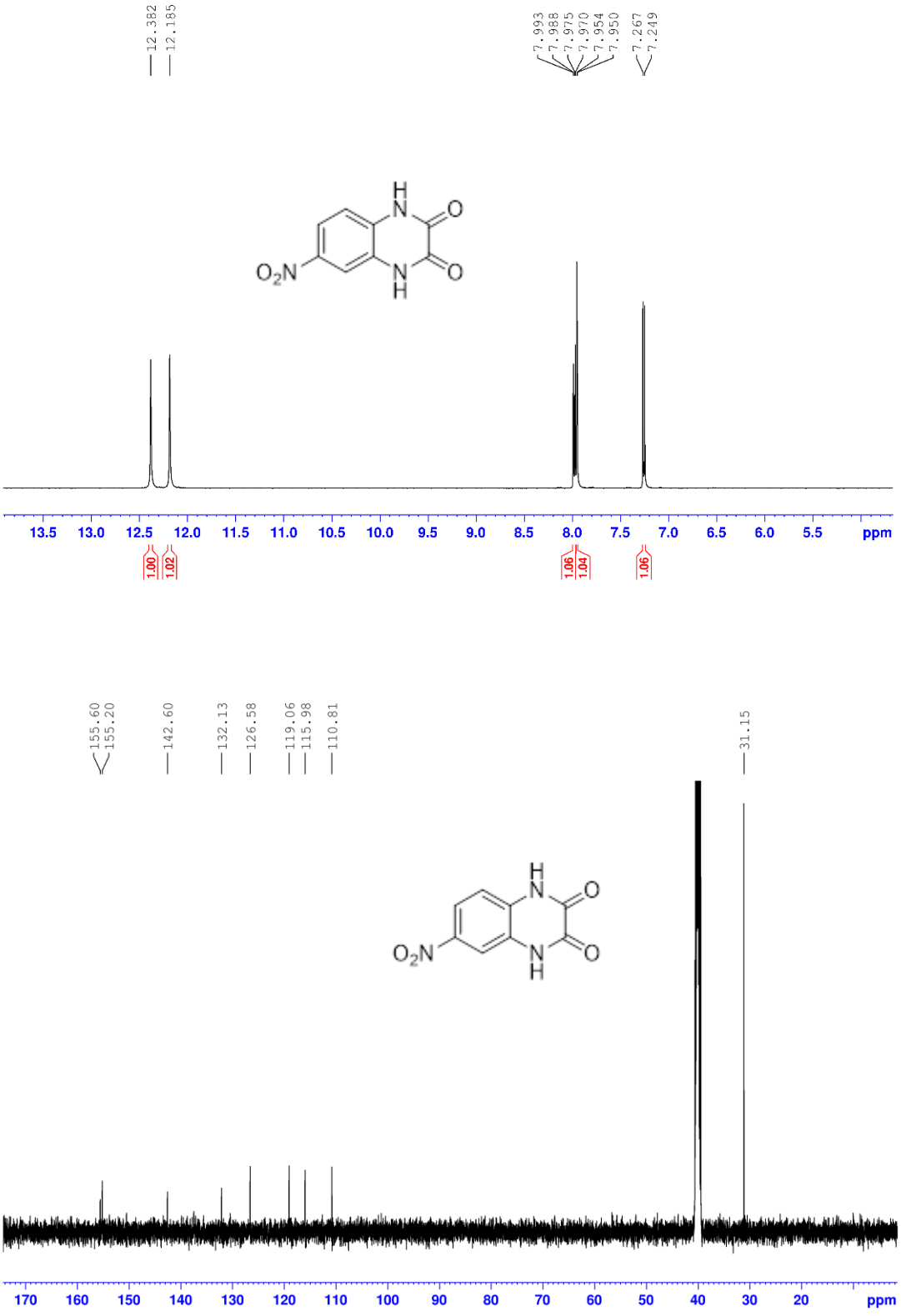
S1: ^{1}H- and ^{13}C-NMR spectra of compound **1a** in DMSO-d_6



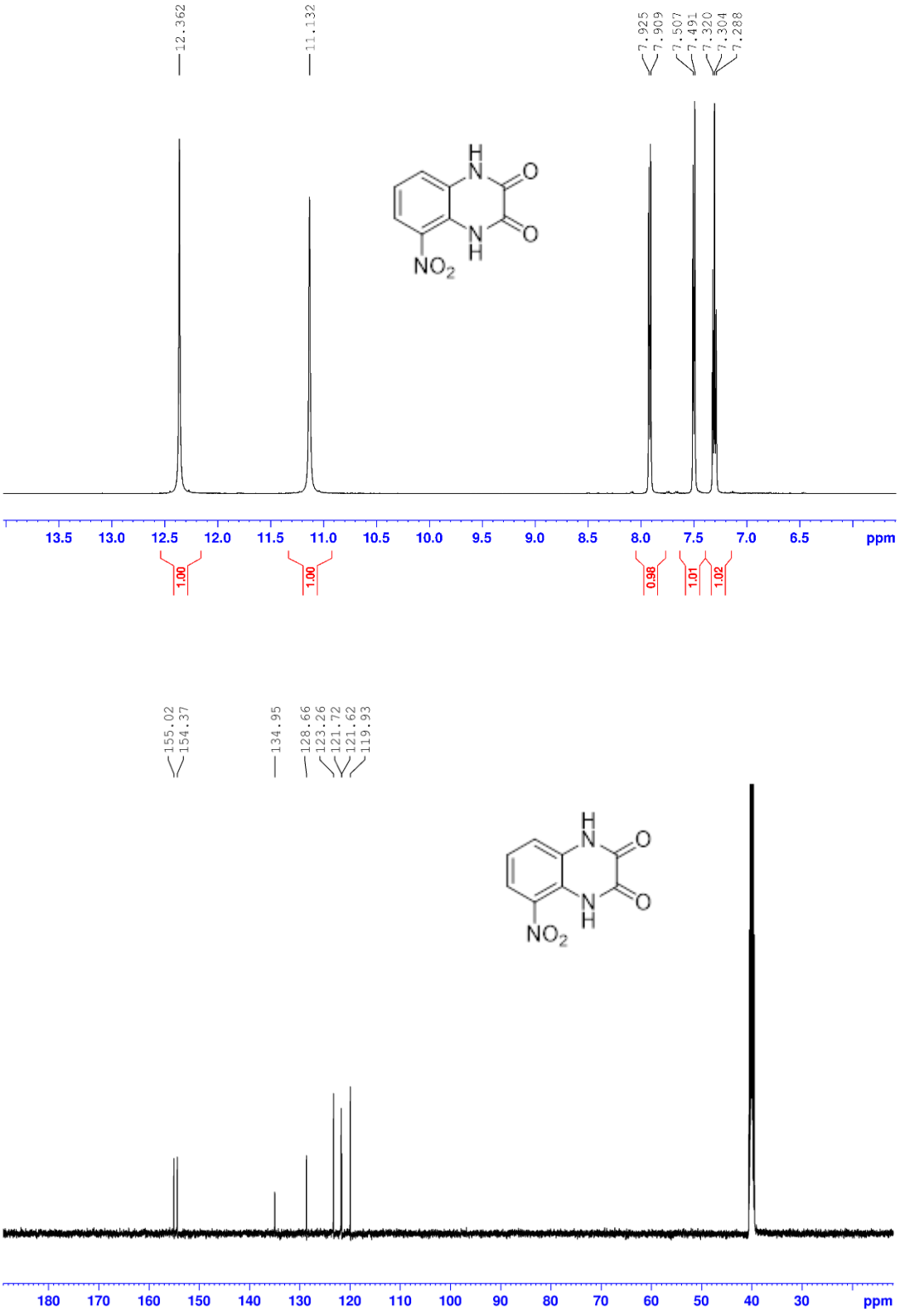
S2: ^{1}H- and ^{13}C-NMR spectra of compound **1b** in DMSO-d_6.



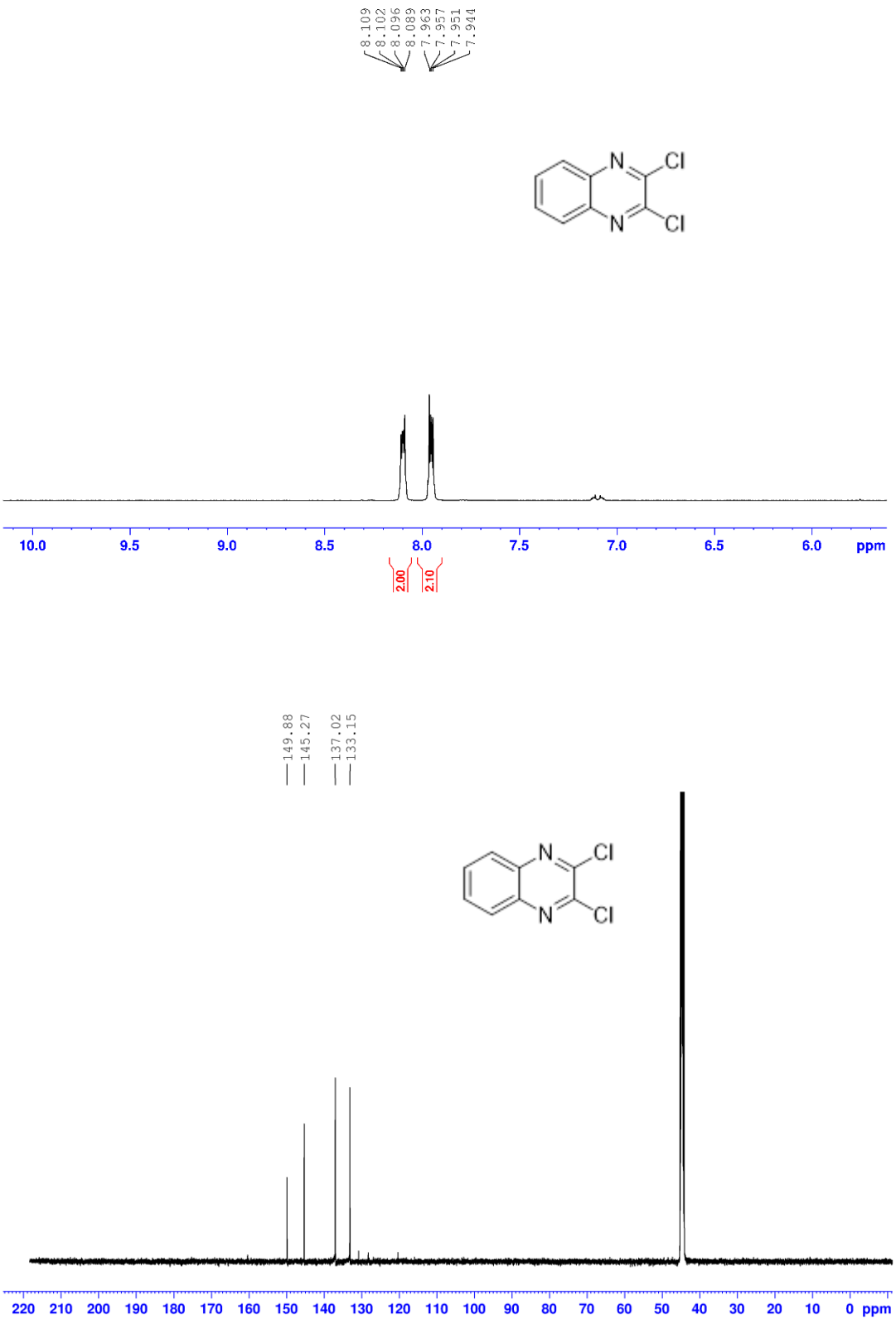
S3: ^{1}H- and ^{13}C-NMR spectra of compound **1c** in DMSO-d_6.



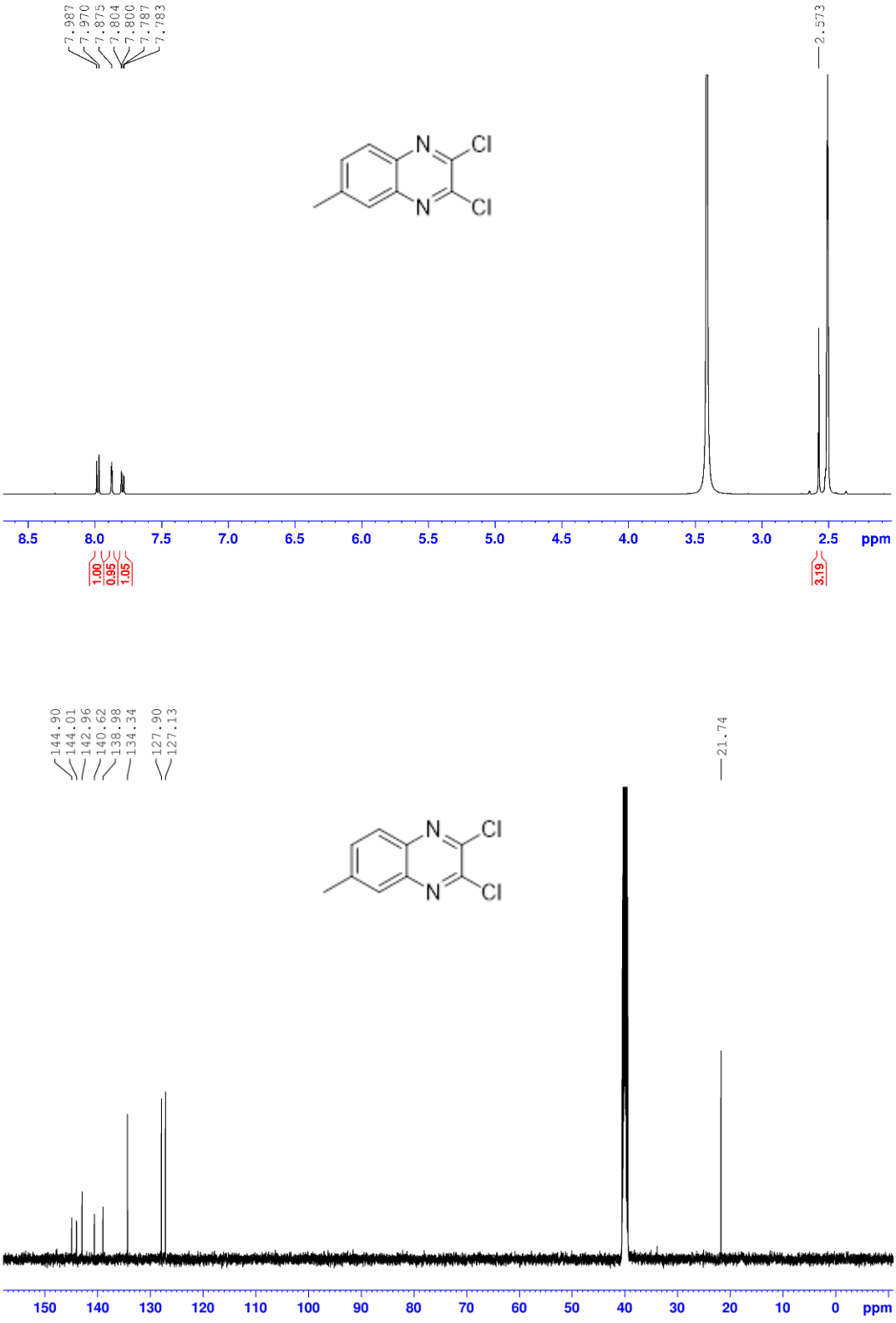
S4: ^{1}H- and ^{13}C-NMR spectra of compound **1d** in DMSO-d_6.



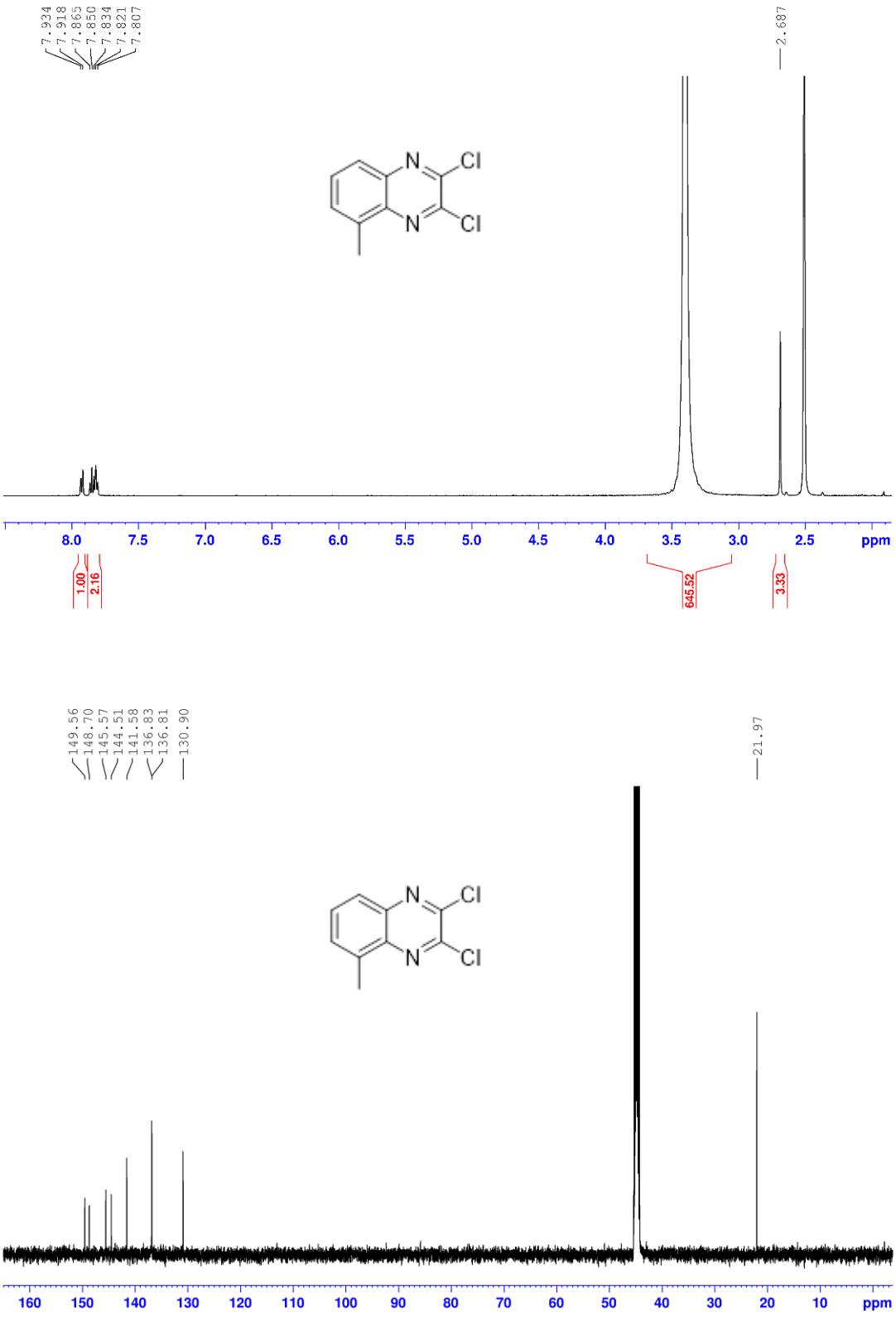
S5: ^{1}H- and ^{13}C-NMR spectra of compound **1e** in DMSO-d_6.



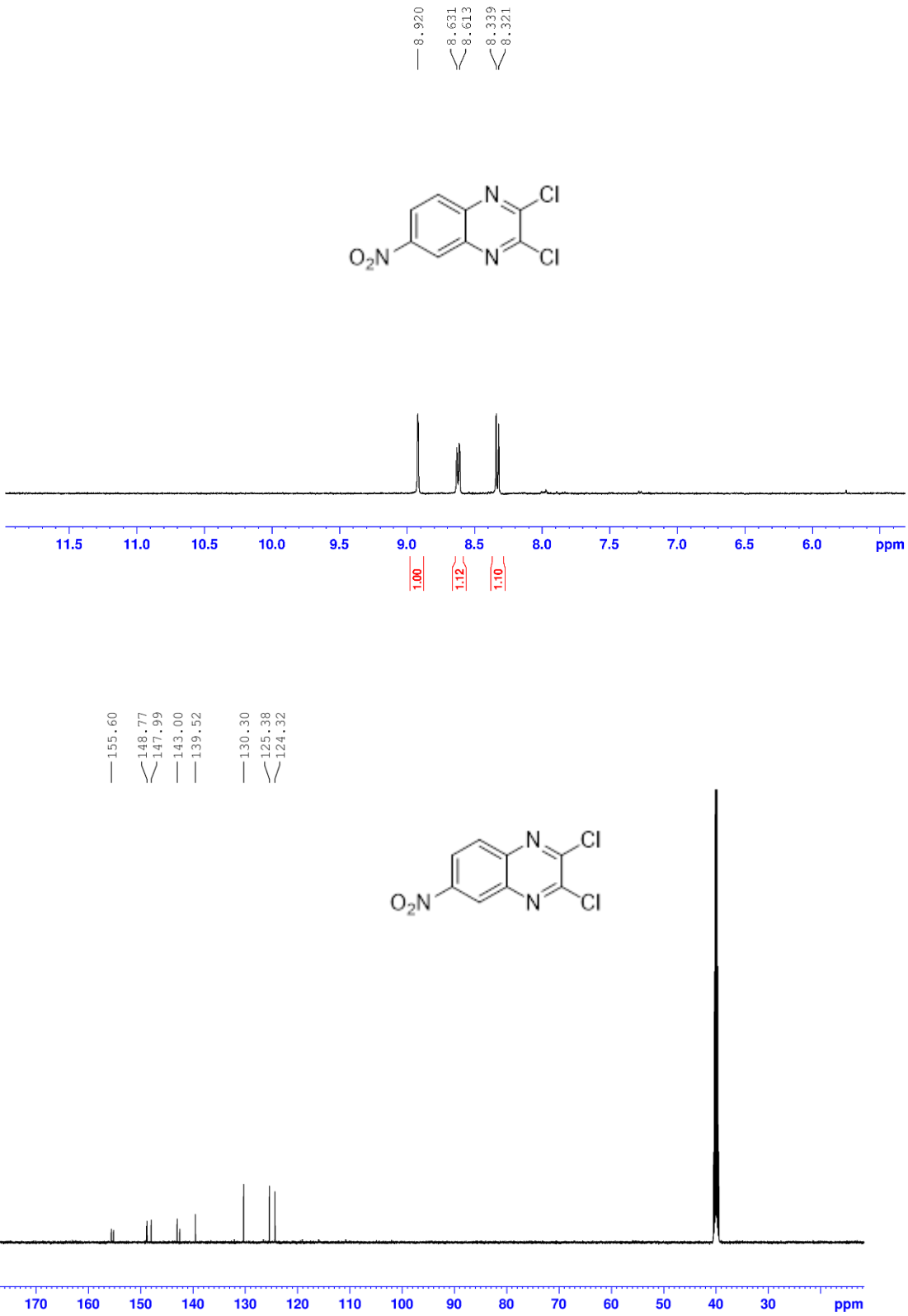
S6: ^{1}H- and ^{13}C-NMR spectra of compound **2a** in DMSO-d_6.



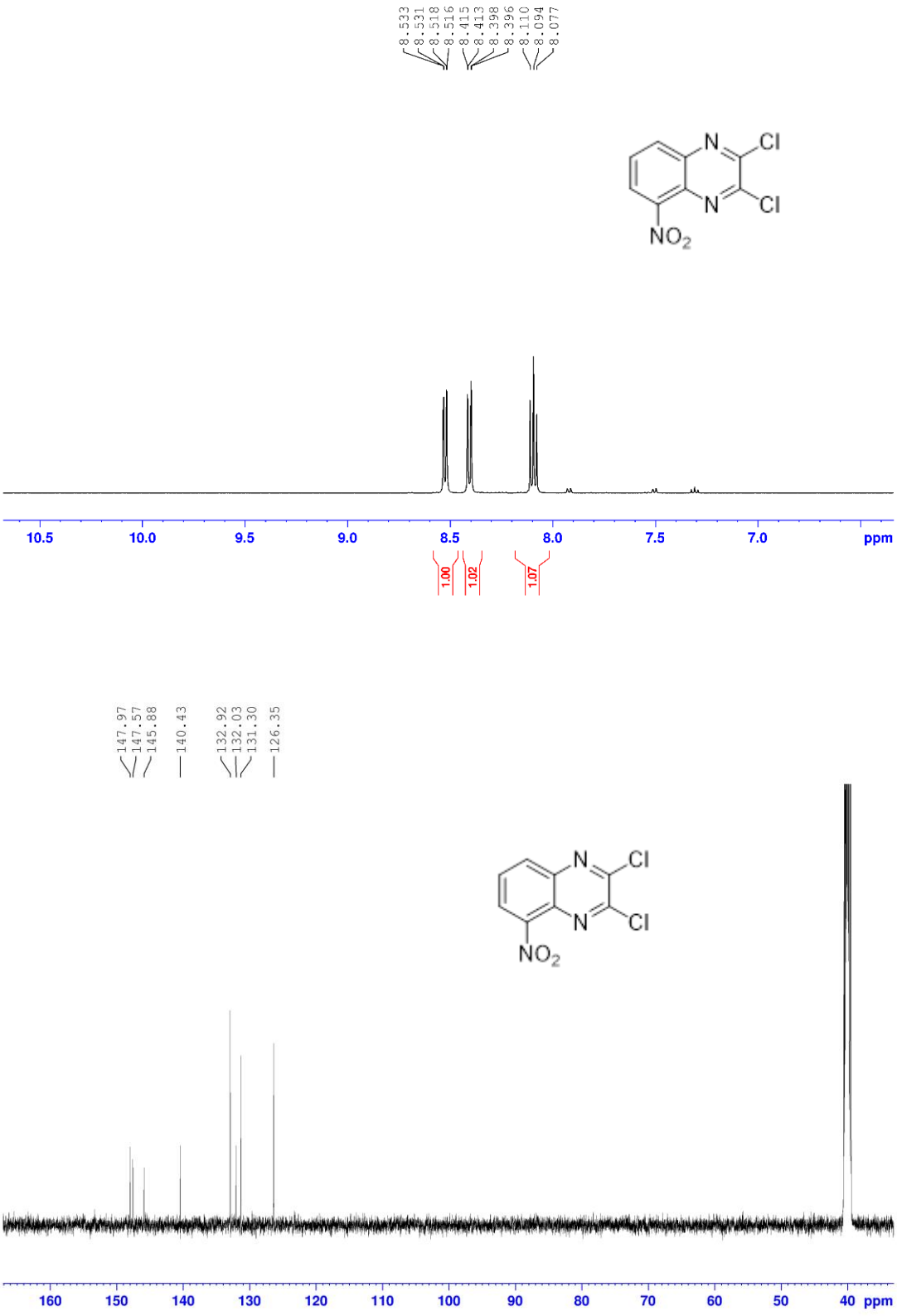
S7: ^{1}H- and ^{13}C-NMR spectra of compound **2b** in DMSO-d_6.



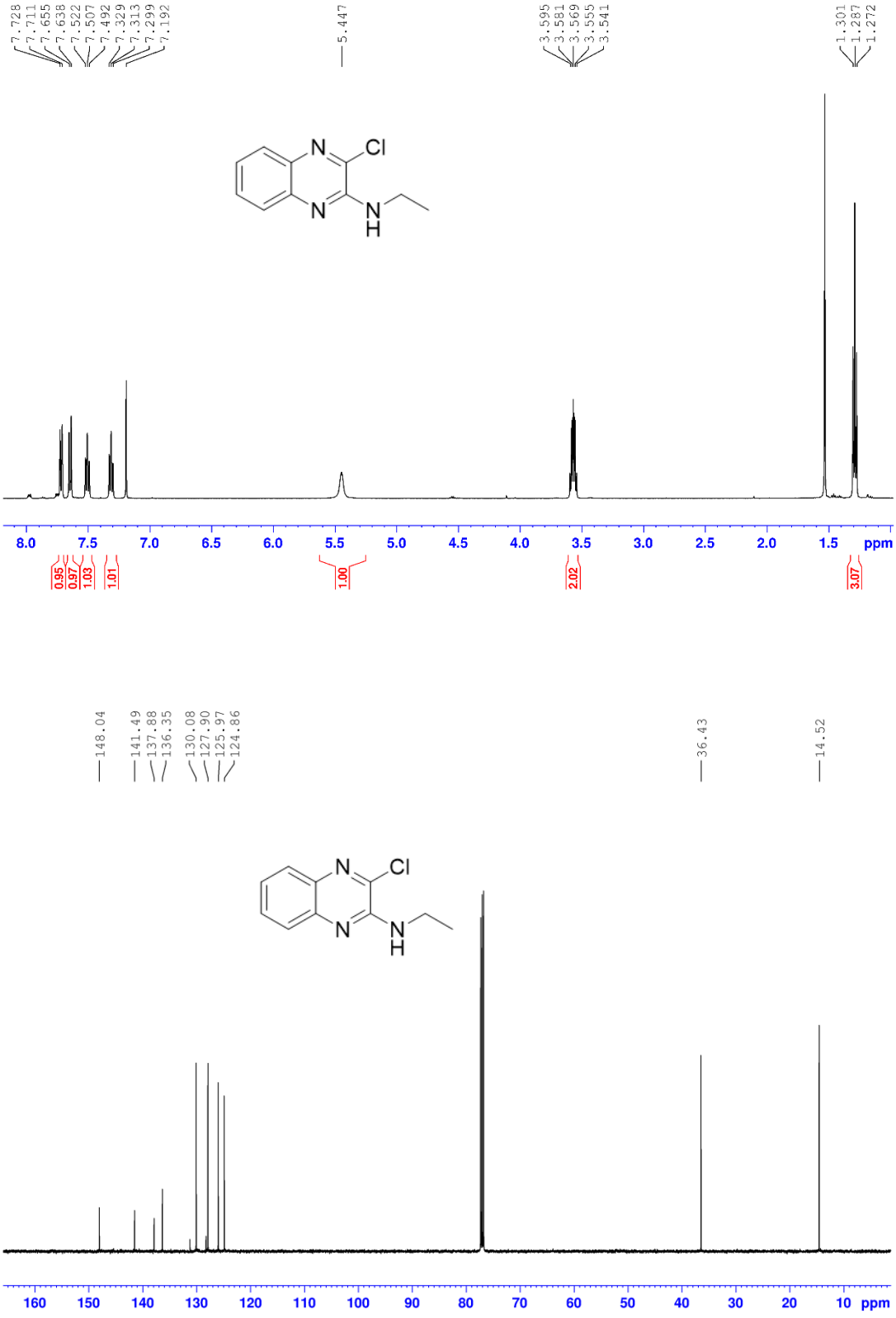
S8: ^{1}H- and ^{13}C-NMR spectra of compound **2c** in DMSO-d_6.



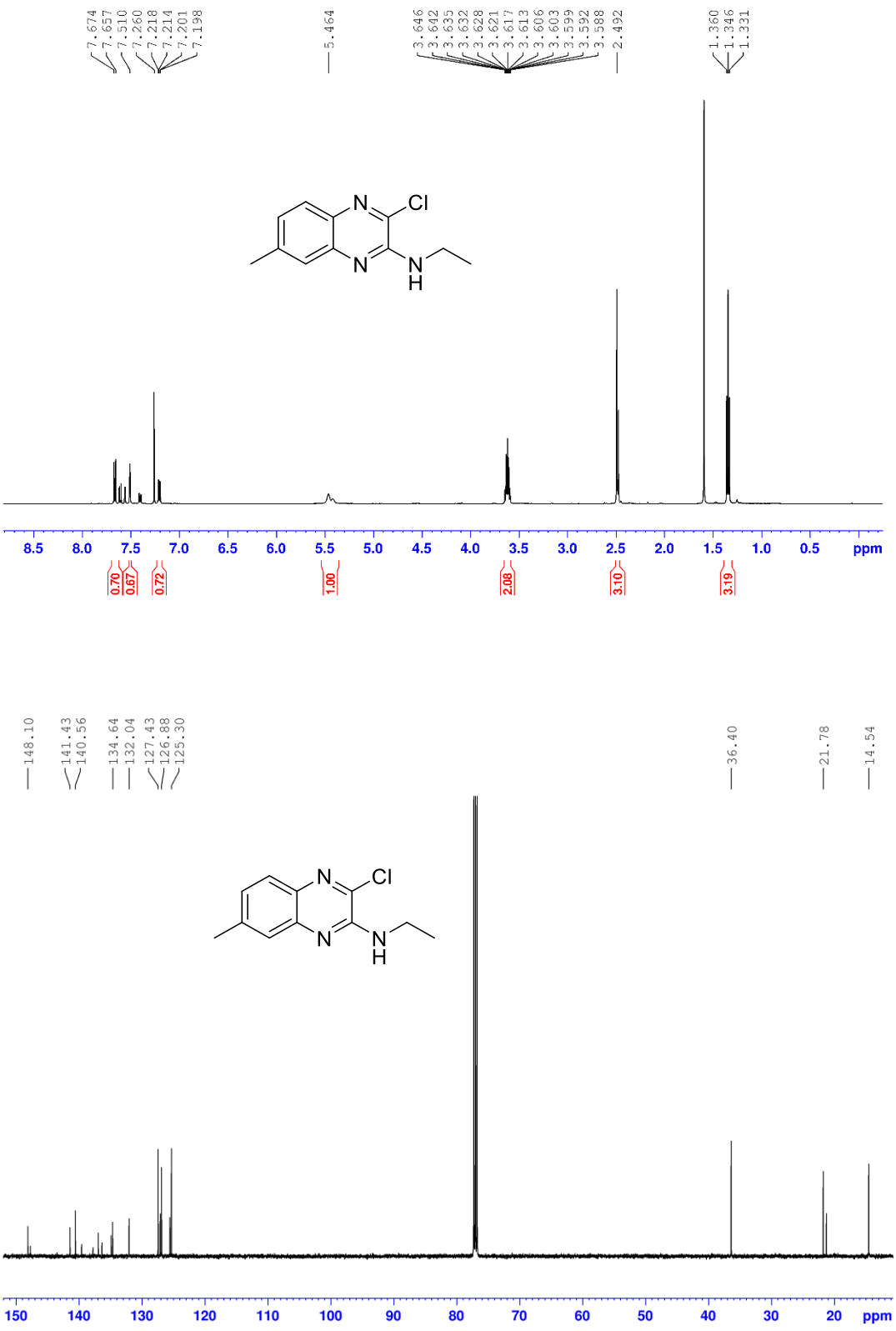
S9: ^{1}H- and ^{13}C-NMR spectra of compound **2d** in DMSO-d$_6$.



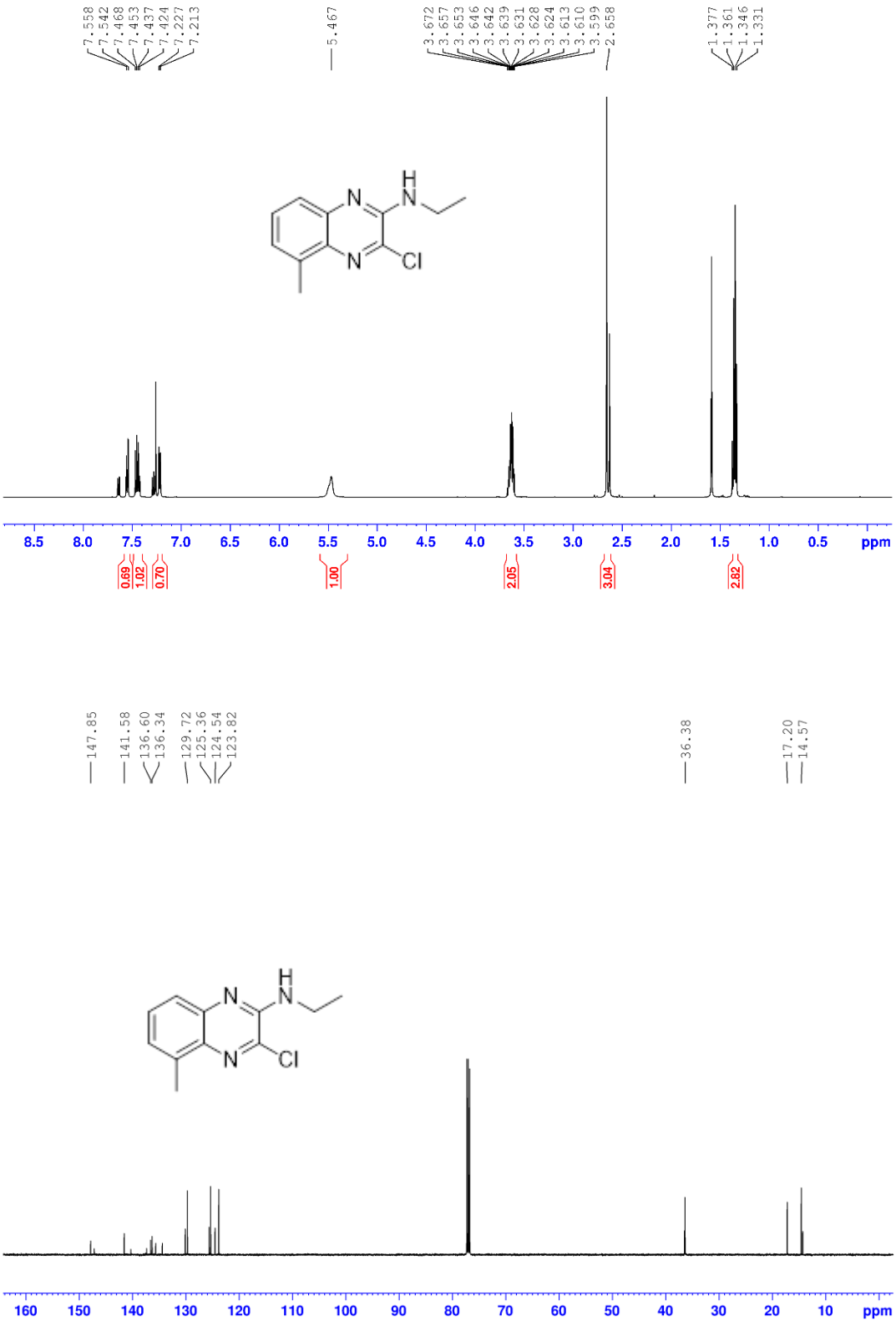
S10: ^{1}H- and ^{13}C-NMR spectra of compound **2e** in DMSO-d_6.



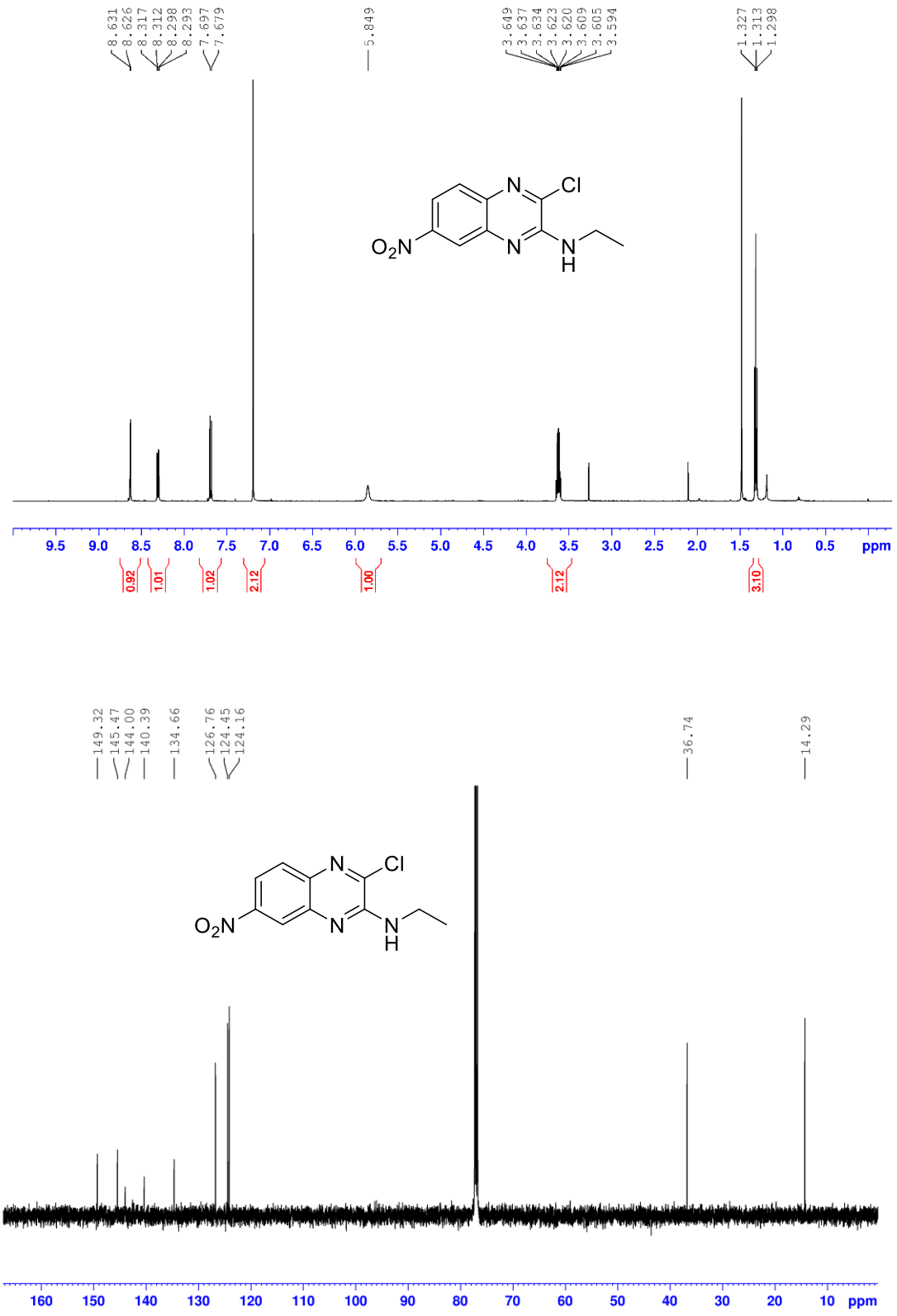
S11: ^{1}H- and ^{13}C-NMR spectra of compound **3a** in $CDCl_3$.



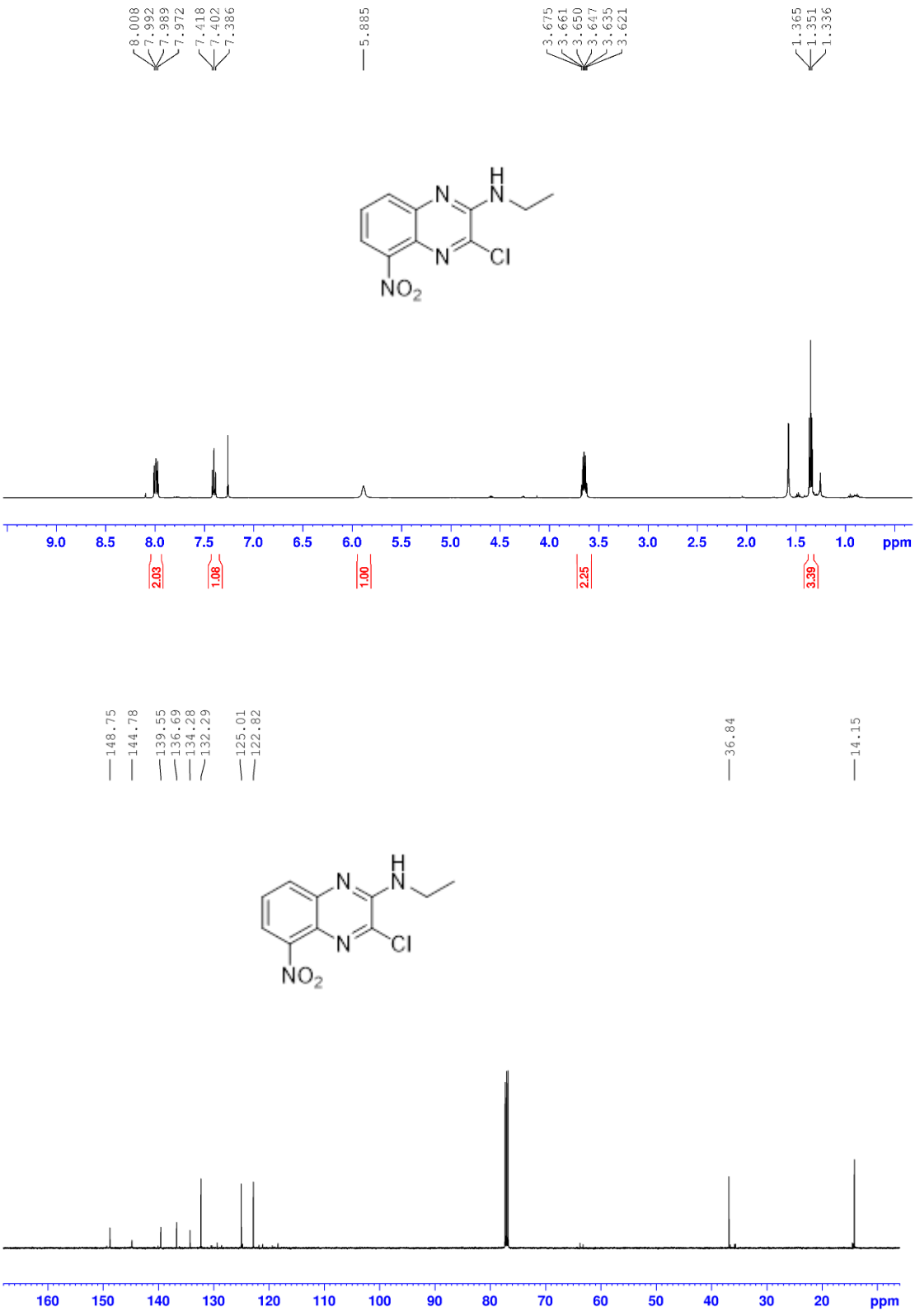
S12: ^{1}H- and ^{13}C-NMR spectra of compound **3b** in $CDCl_3$.



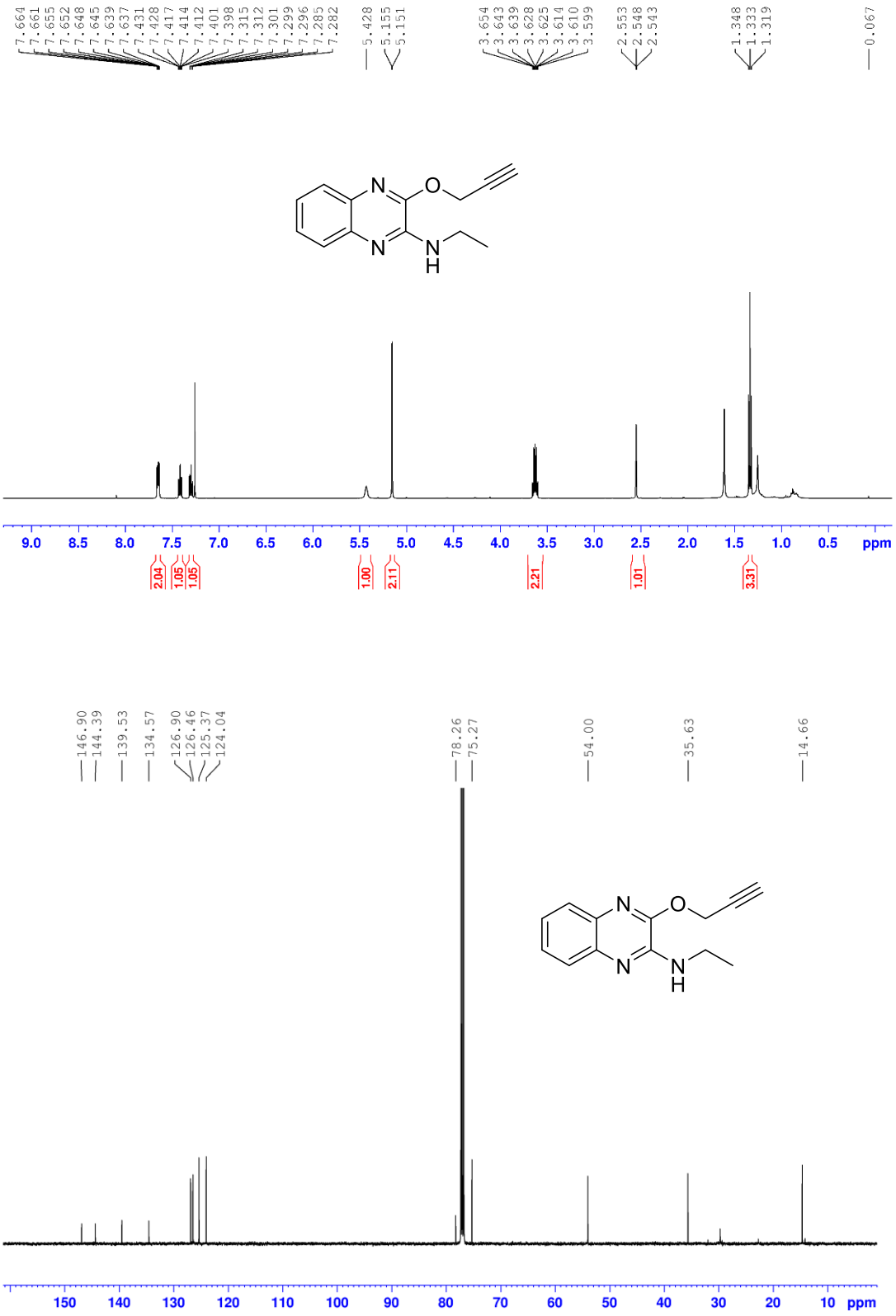
S13: ^{1}H- and ^{13}C-NMR spectra of compound **3c** in $CDCl_3$.



S14: ^{1}H- and ^{13}C-NMR spectra of compound **3d** in $CDCl_3$.

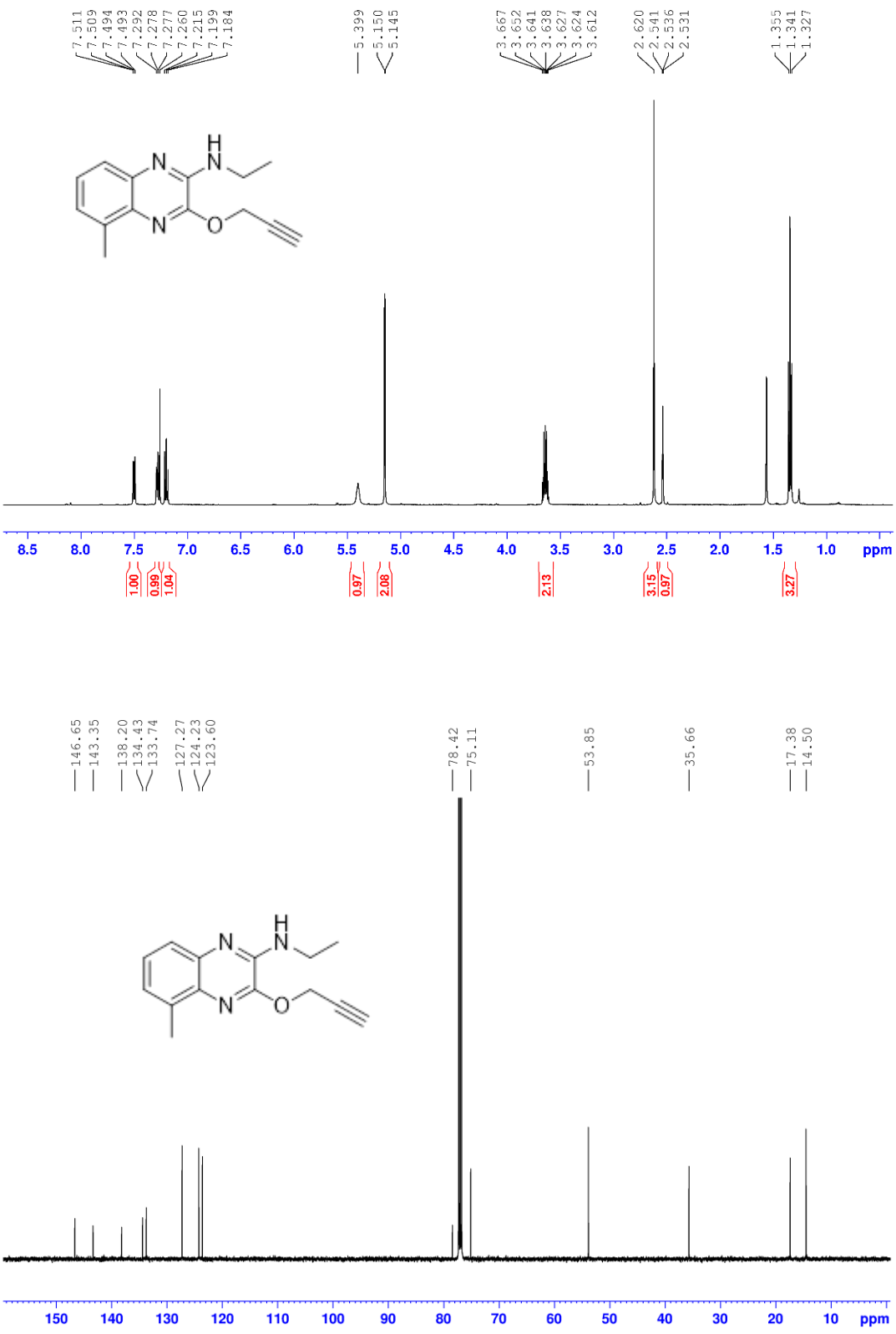


S15: ^{1}H- and ^{13}C-NMR spectra of compound **3e** in $CDCl_3$.

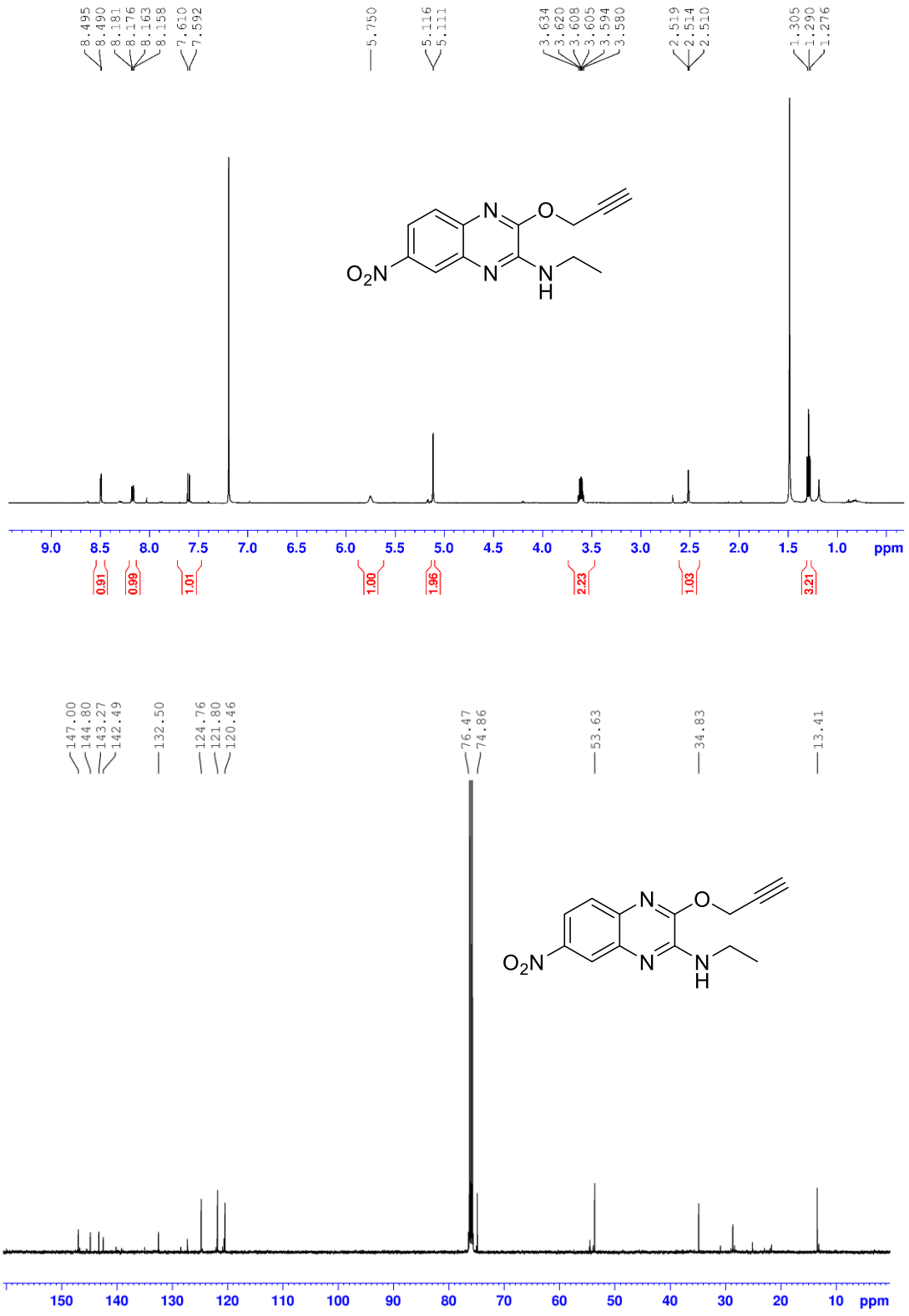


S16: ^{1}H- and ^{13}C-NMR spectra of compound **4a** in $CDCl_3$.

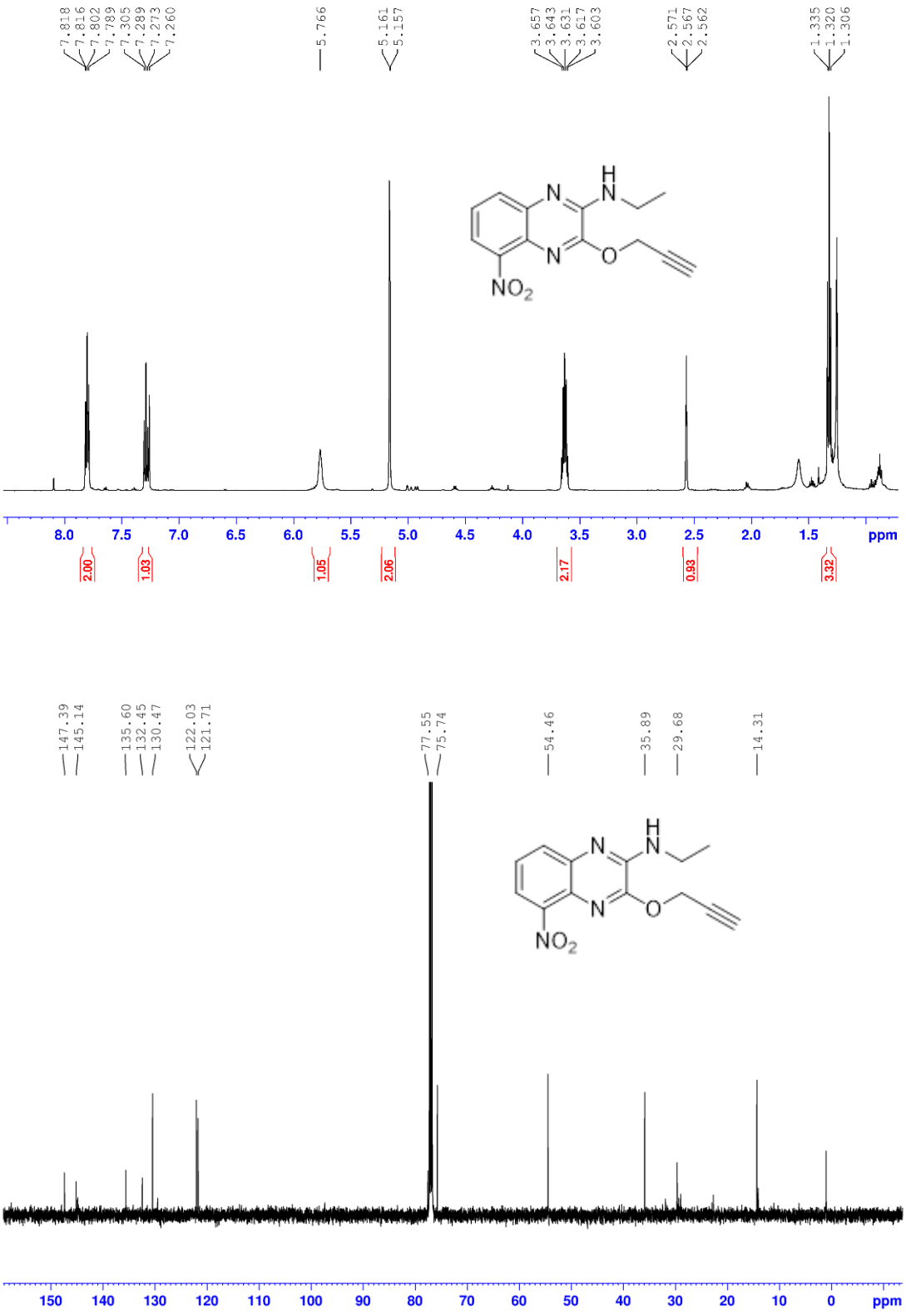
S17: ^{1}H- and ^{13}C-NMR spectra of compound **4b** in $CDCl_3$.



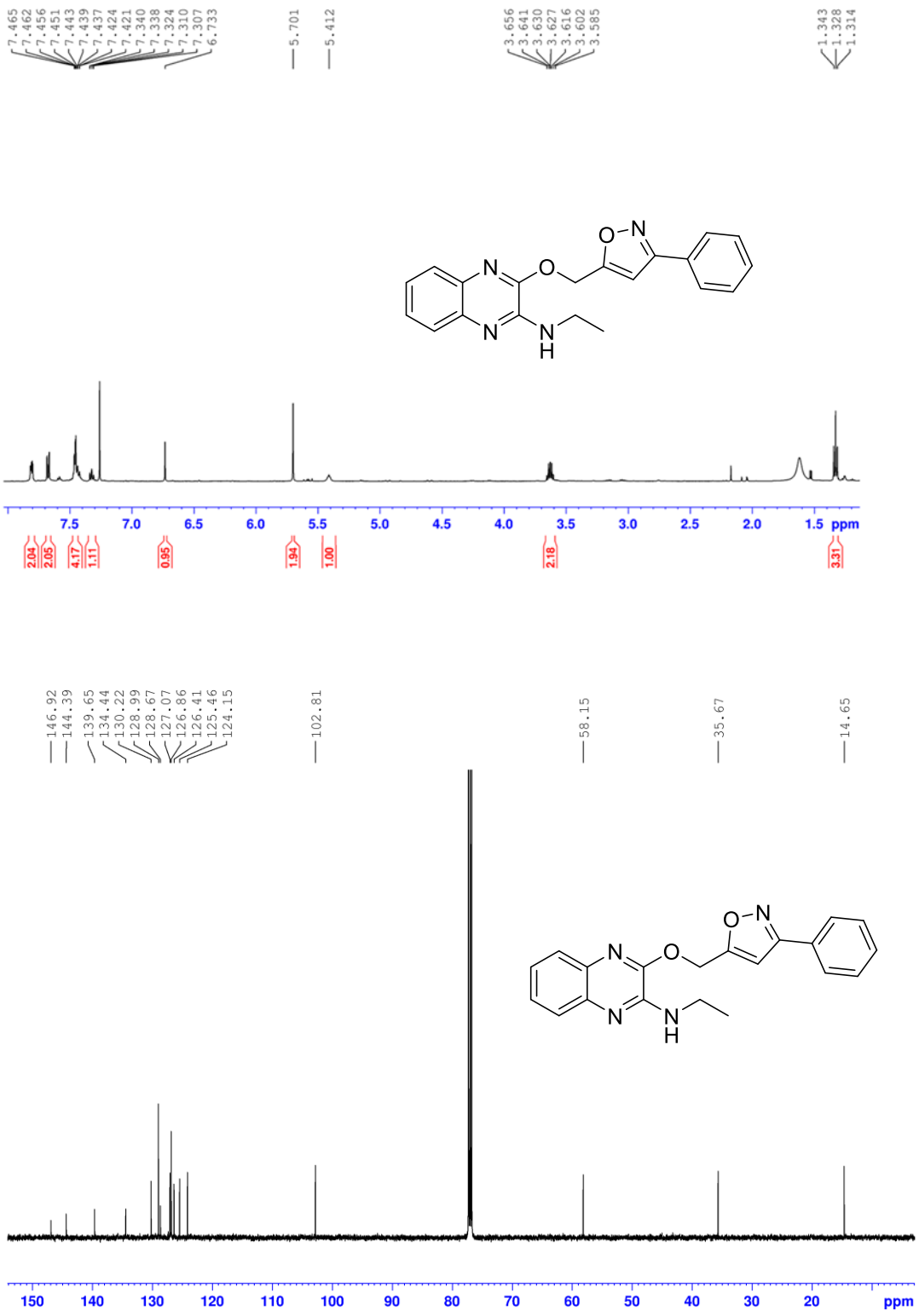
S18: ^{1}H- and ^{13}C-NMR spectra of compound **4c** in $CDCl_3$.



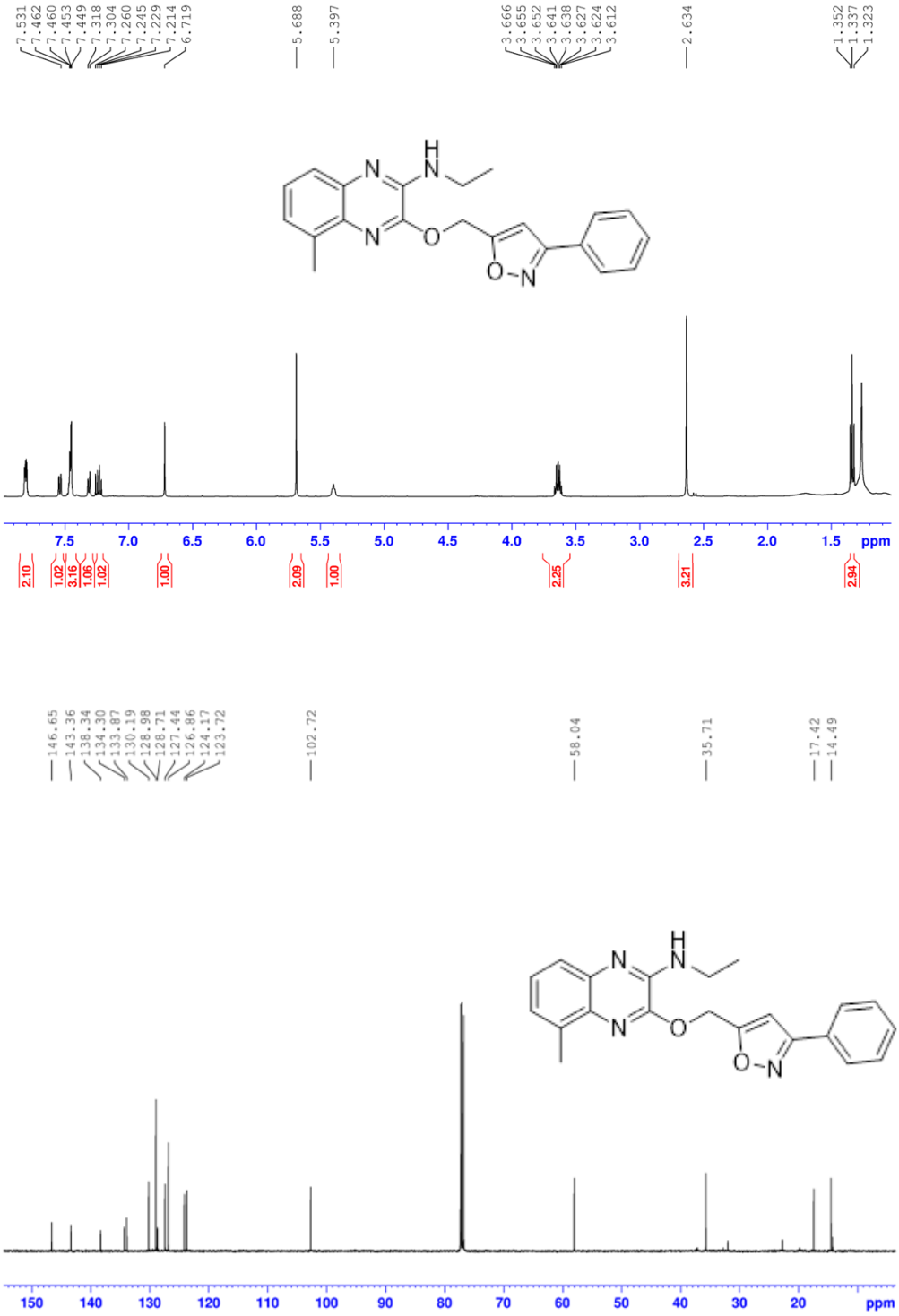
S19: ^{1}H- and ^{13}C-NMR spectra of compound **4d** in $CDCl_3$.



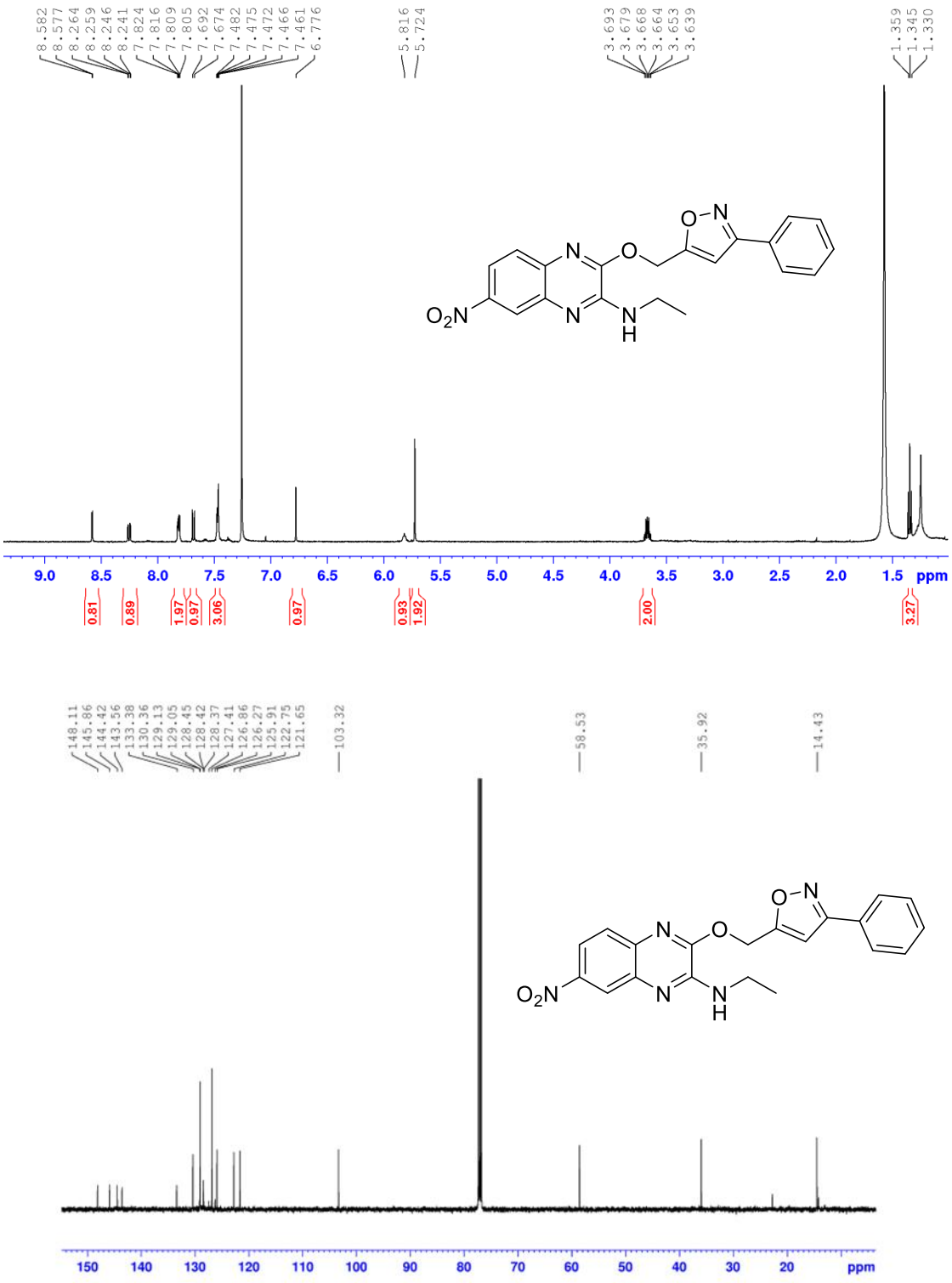
S20: ^{1}H- and ^{13}C-NMR spectra of compound **4e** in $CDCl_3$.



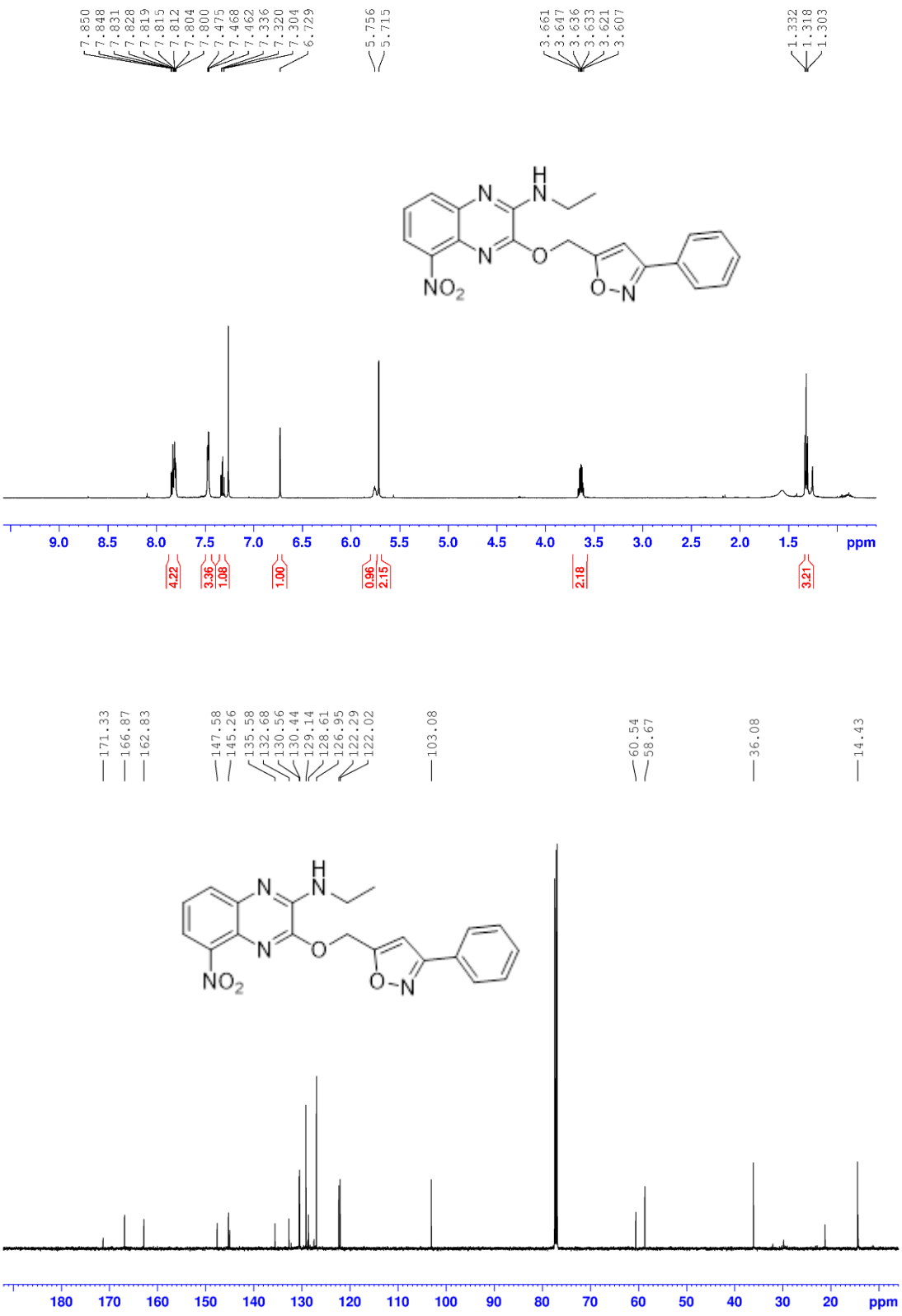
S21: ^{1}H- and ^{13}C-NMR spectra of compound **5a** in $CDCl_3$.



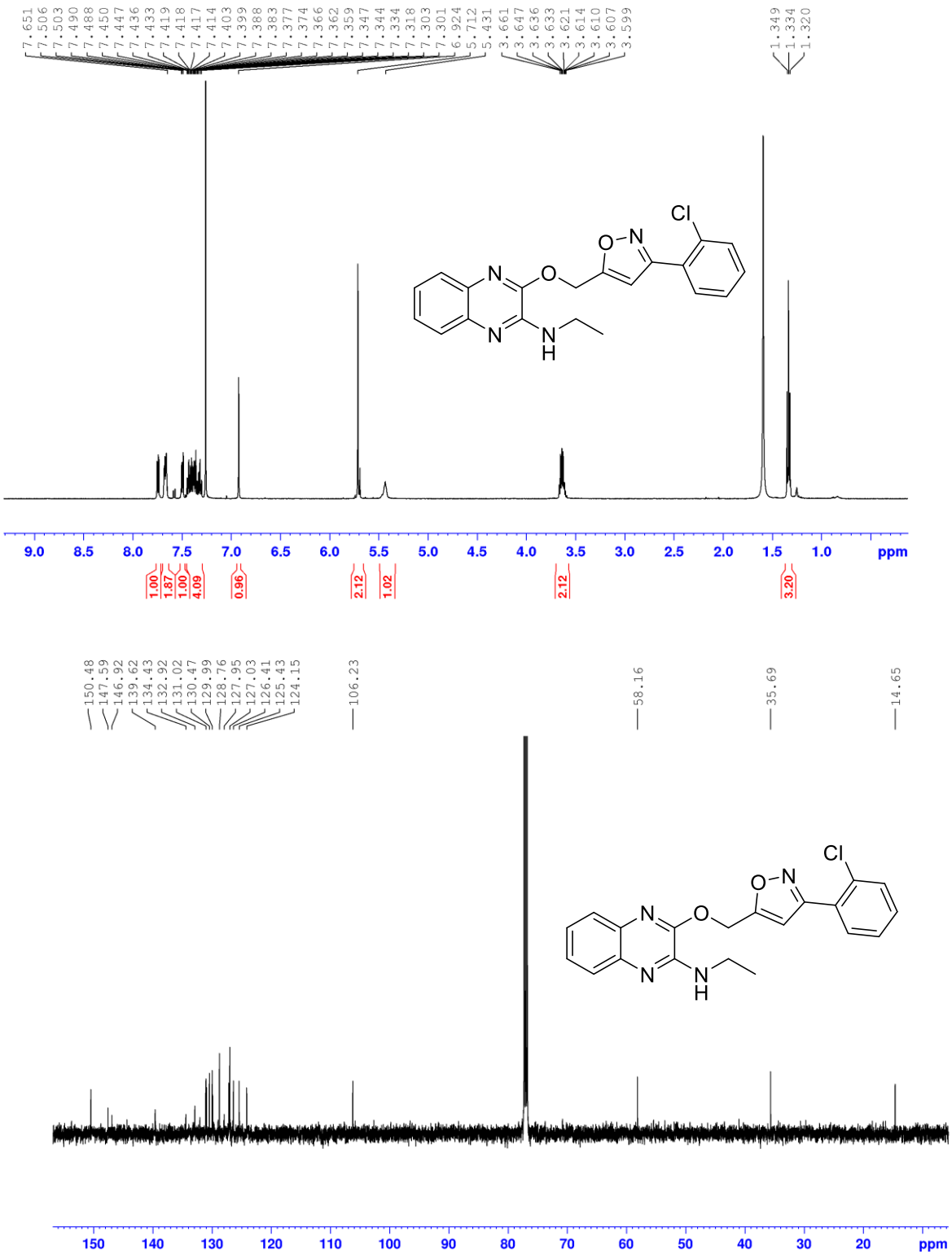
S22: ^{1}H- and ^{13}C-NMR spectra of compound **5b** in $CDCl_3$.



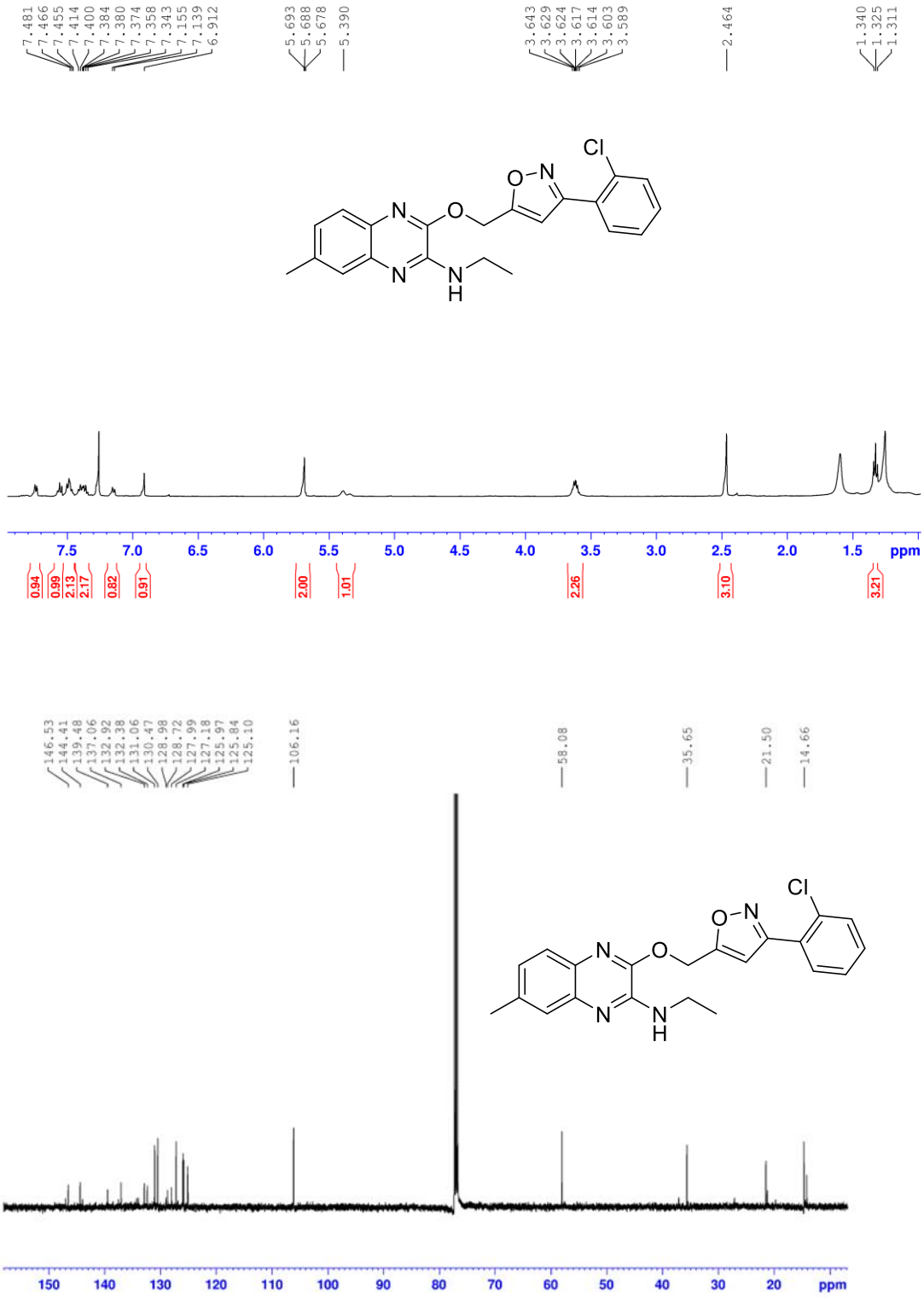
S23: ^{1}H- and ^{13}C-NMR spectra of compound **5c** in $CDCl_3$.



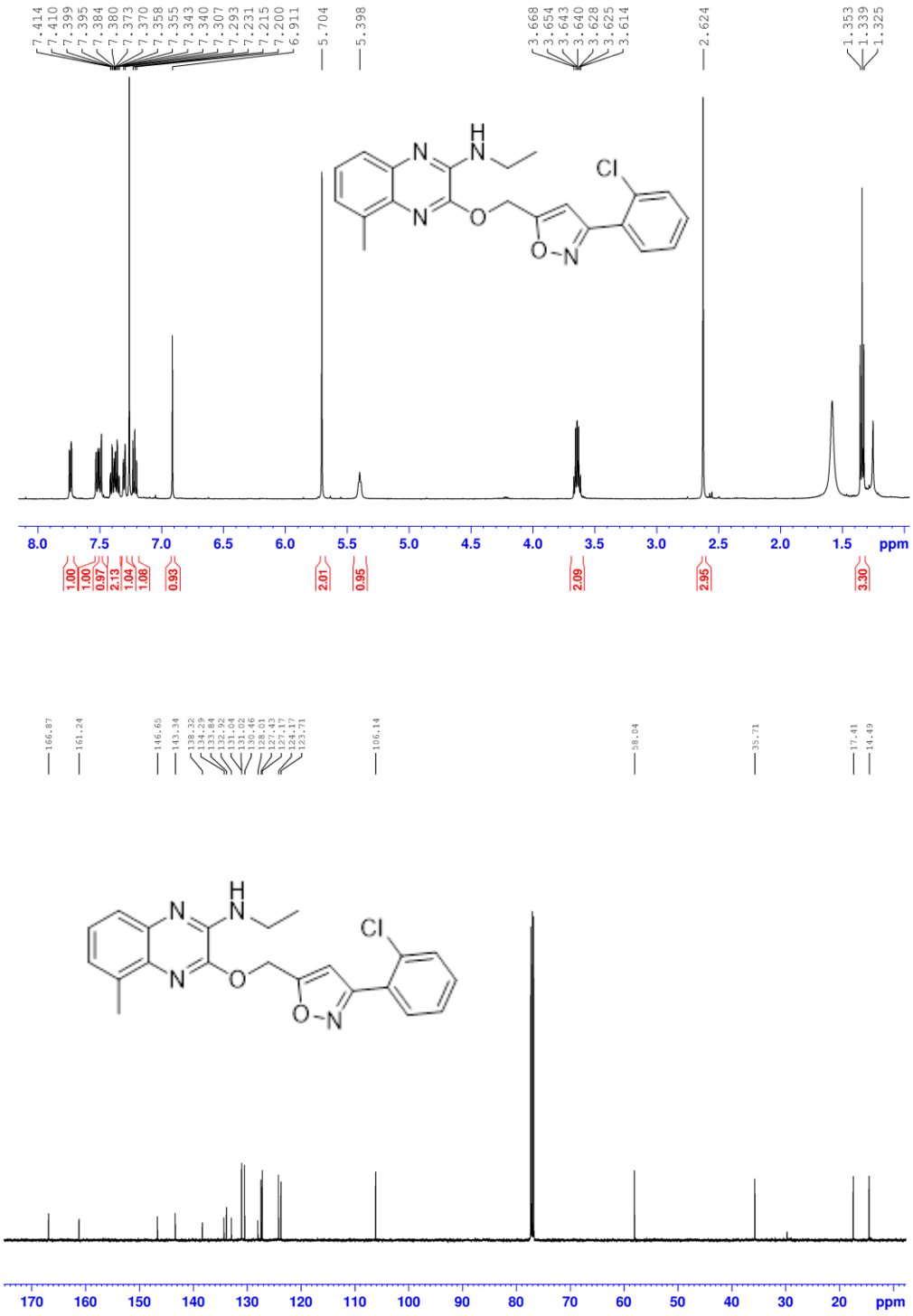
S24: ^{1}H- and ^{13}C-NMR spectra of compound **5d** in $CDCl_3$.



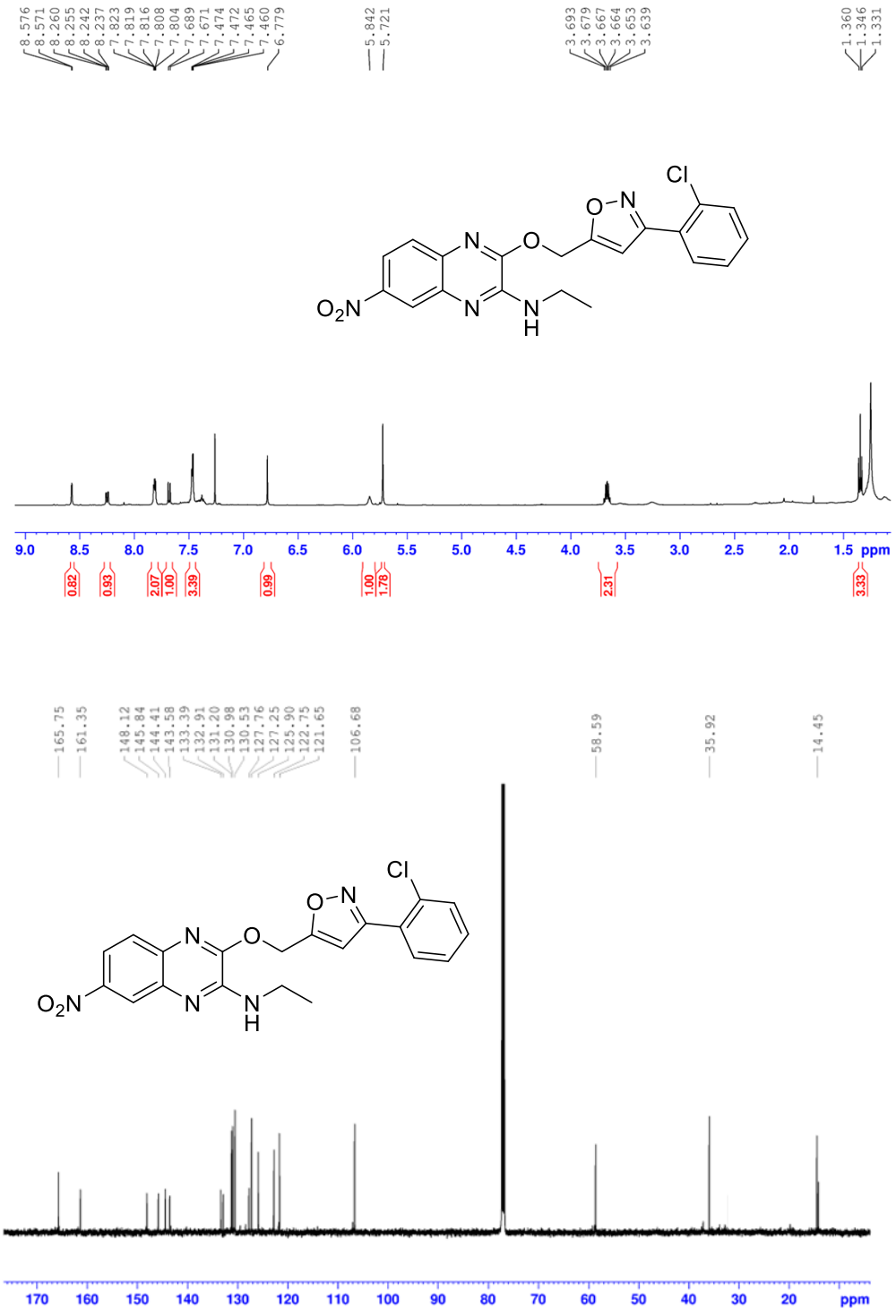
S25: ^{1}H- and ^{13}C-NMR spectra of compound **5e** in $CDCl_3$.



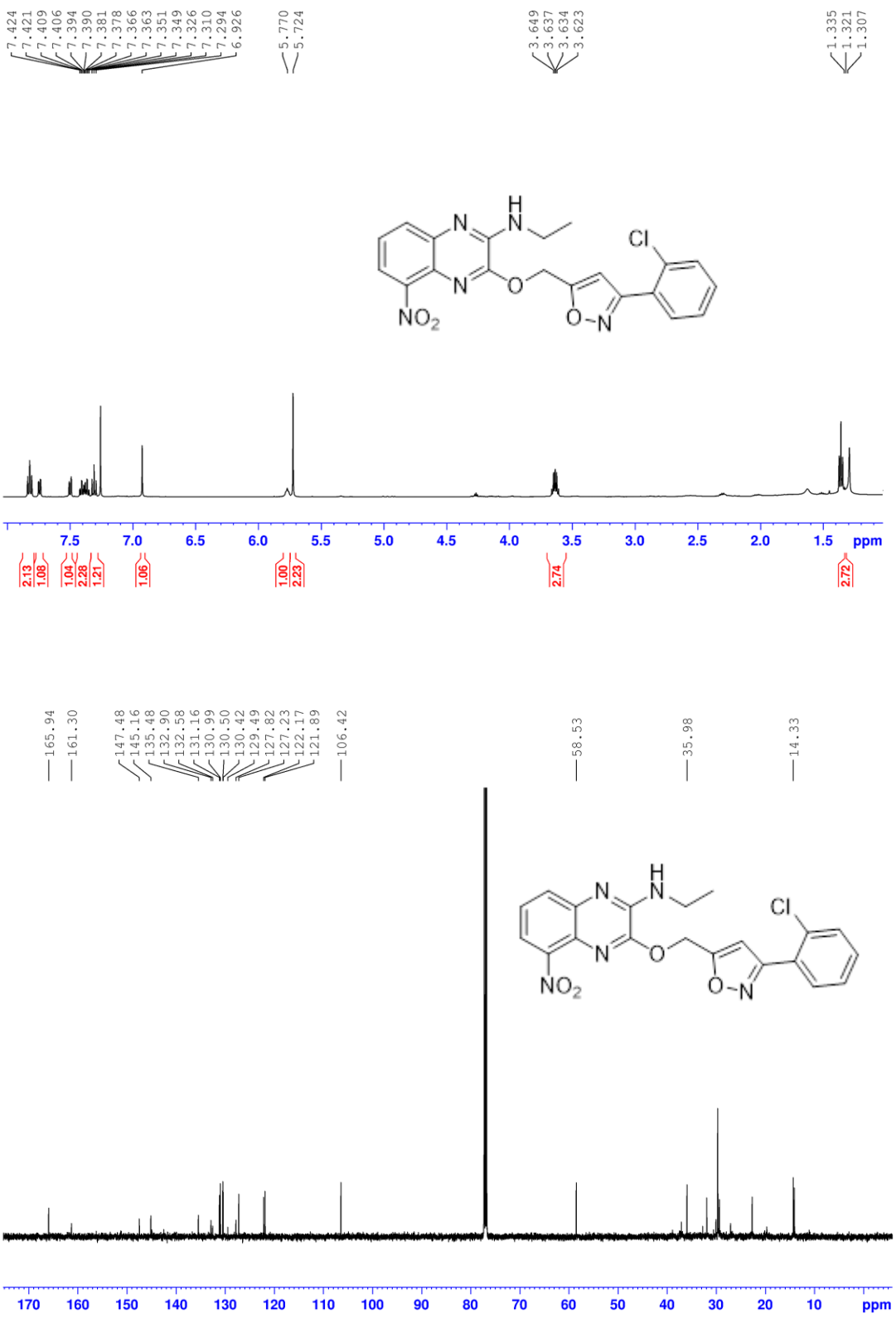
S26: ^{1}H- and ^{13}C-NMR spectra of compound **5f** in $CDCl_3$.



S27: ^{1}H- and ^{13}C-NMR spectra of compound **5g** in $CDCl_3$.

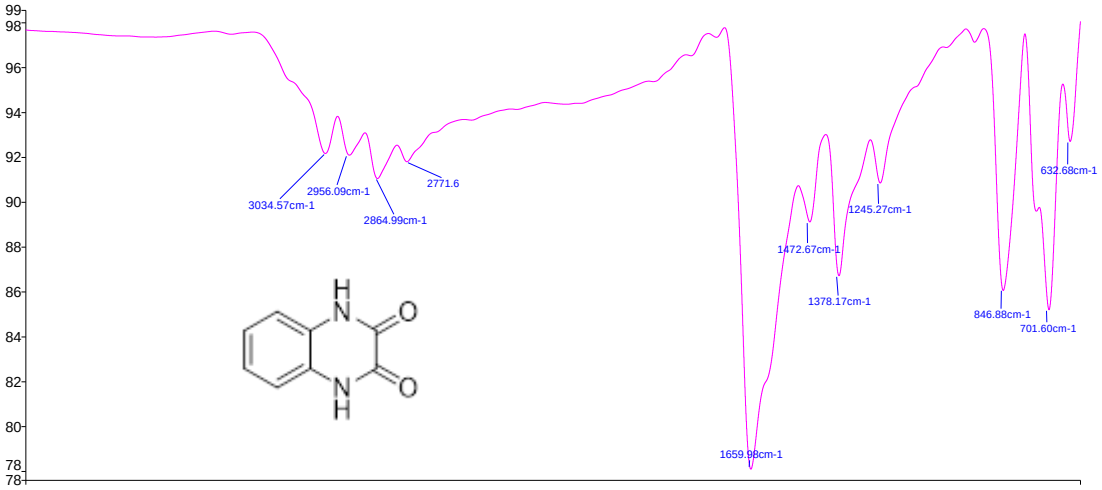


S28: ^{1}H- and ^{13}C-NMR spectra of compound **5h** in $CDCl_3$.

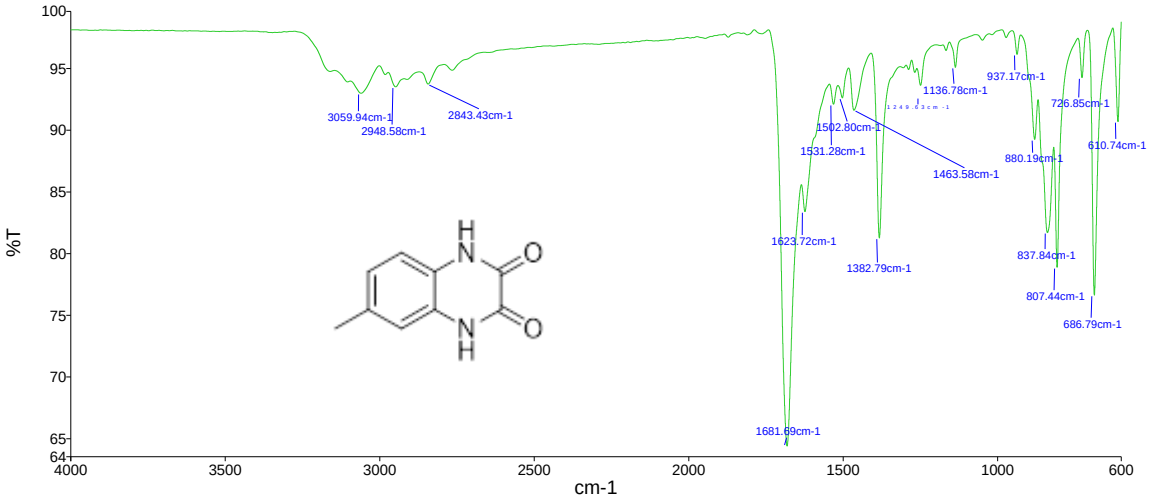


S29: ^{1}H- and ^{13}C-NMR spectra of compound **5i** in $CDCl_3$.

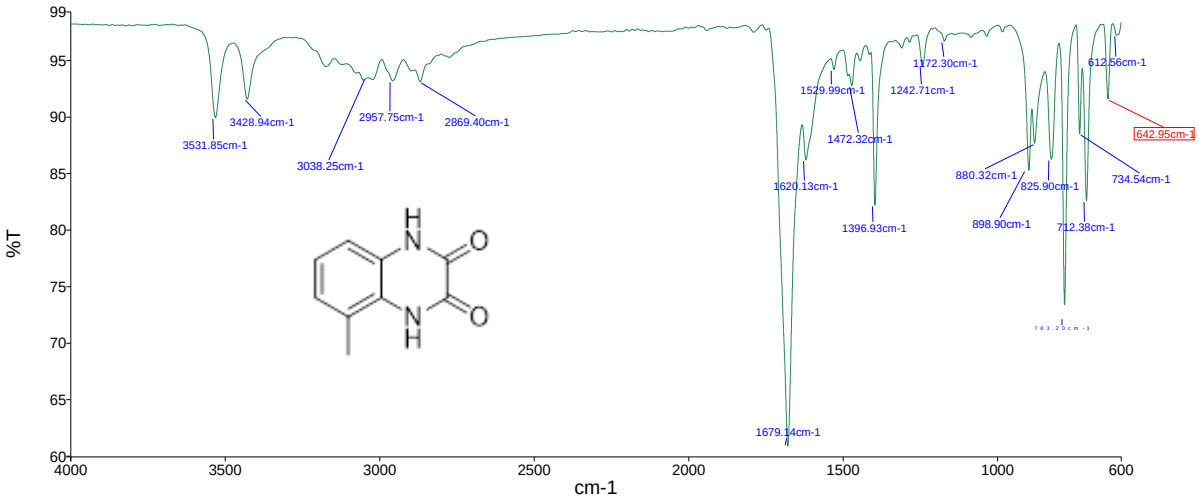
8. IR Spectra



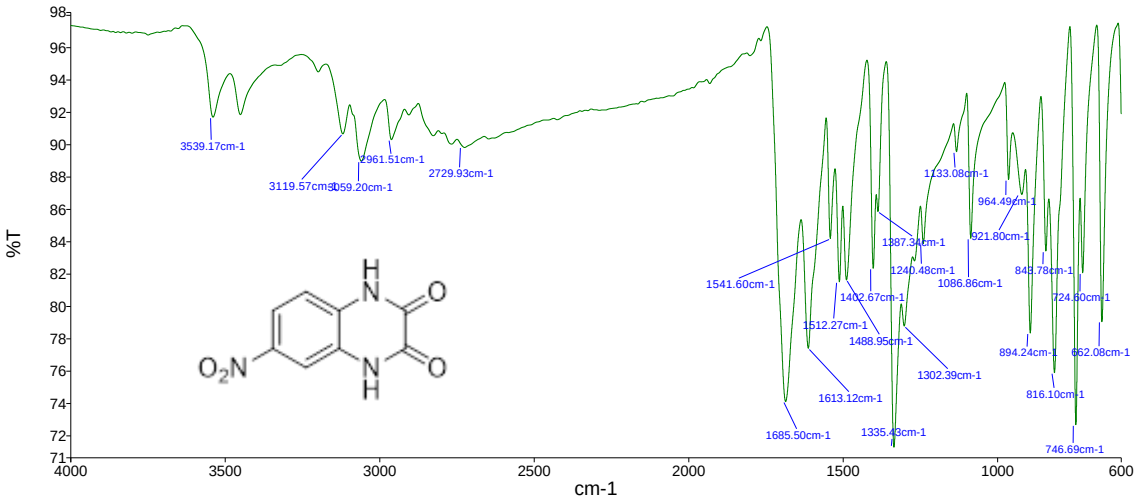
S30: ATR-FTIR spectrum of compound **1a**



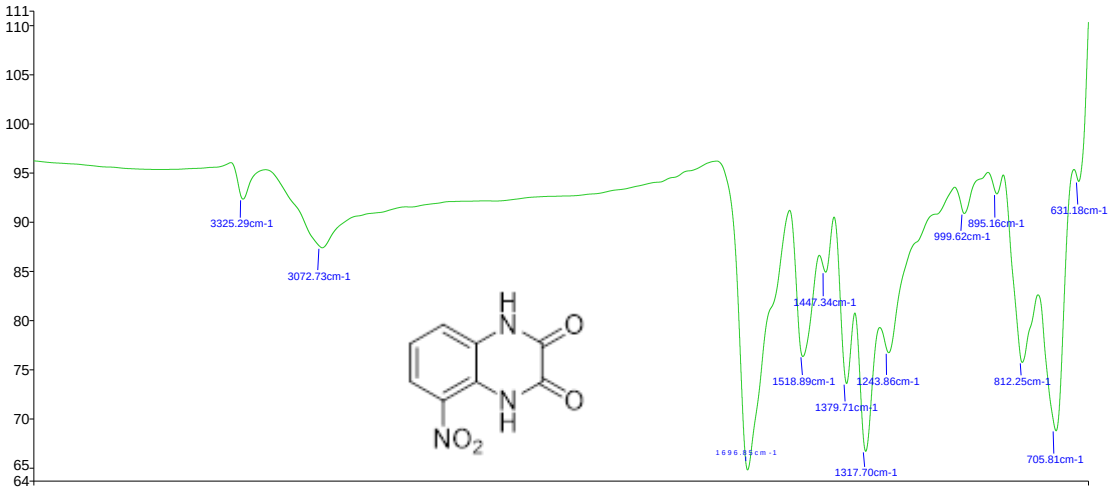
S31: ATR-FTIR spectrum of compound **1b**



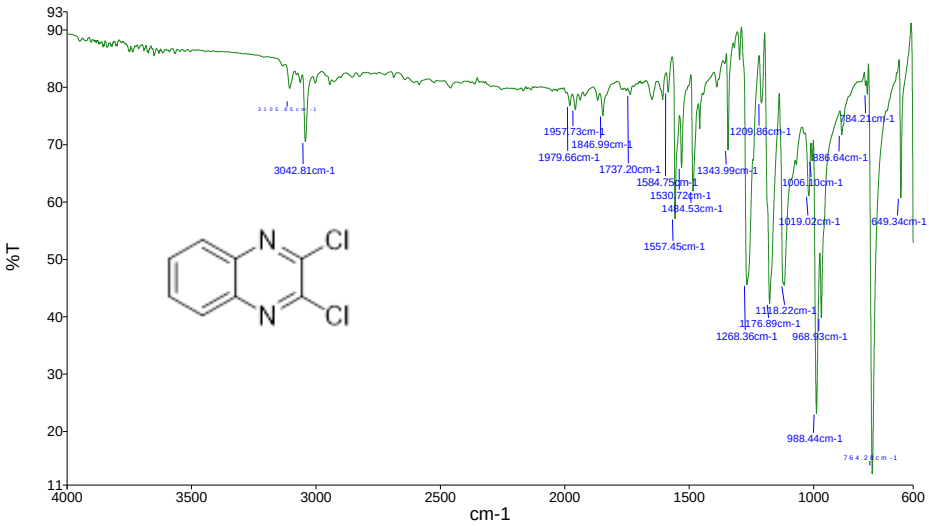
S32: ATR-FTIR spectrum of compound **1c**



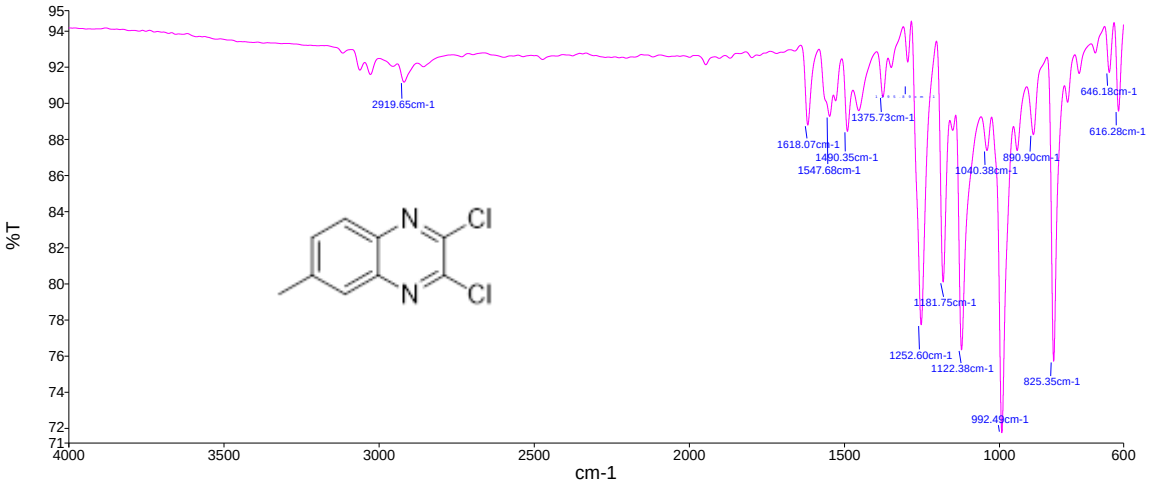
S33: ATR-FTIR spectrum of compound **1d**



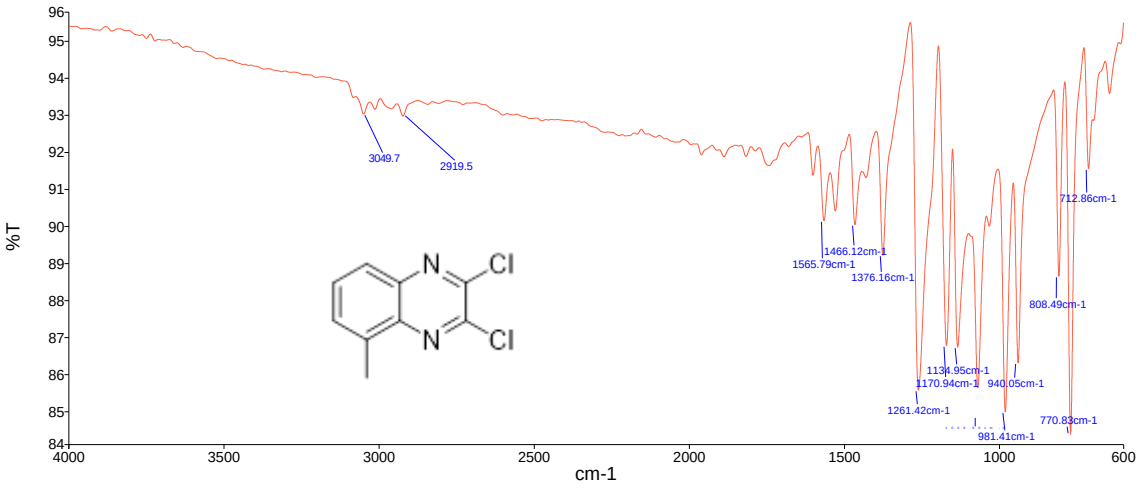
S34: ATR-FTIR spectrum of compound **1e**



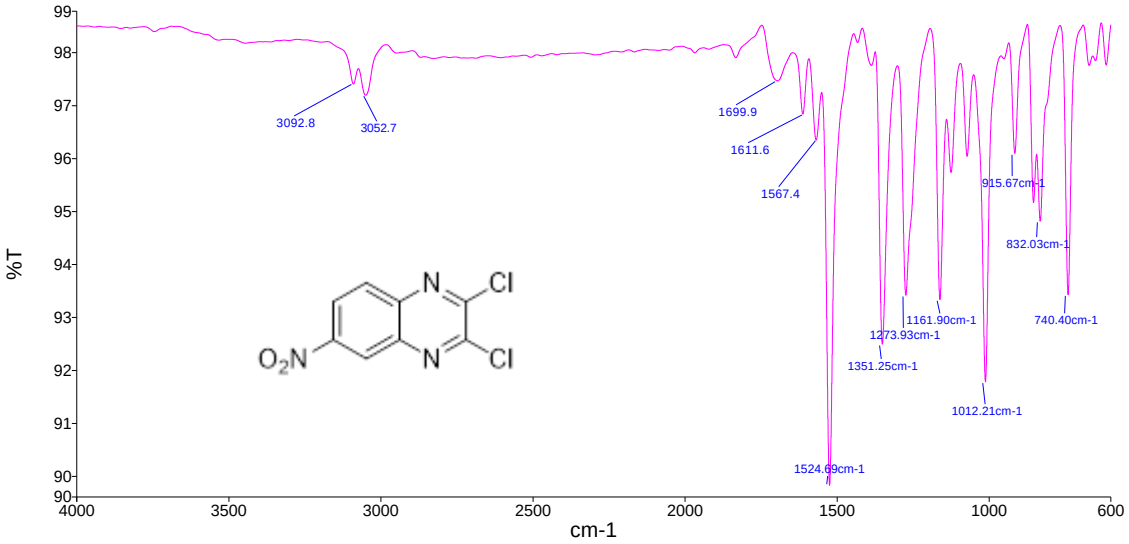
S35: ATR-FTIR spectrum of compound **2a**



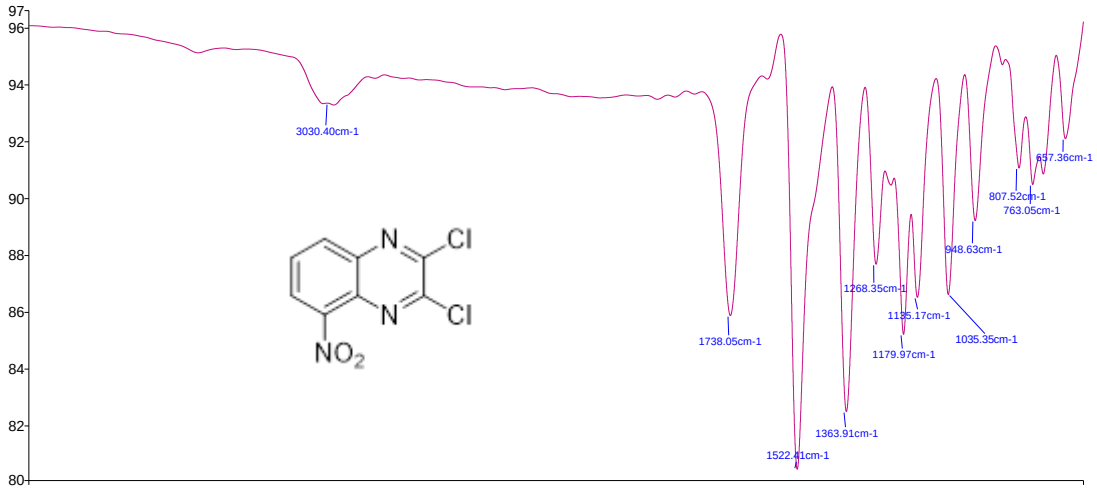
S36: ATR-FTIR spectrum of compound **2b**



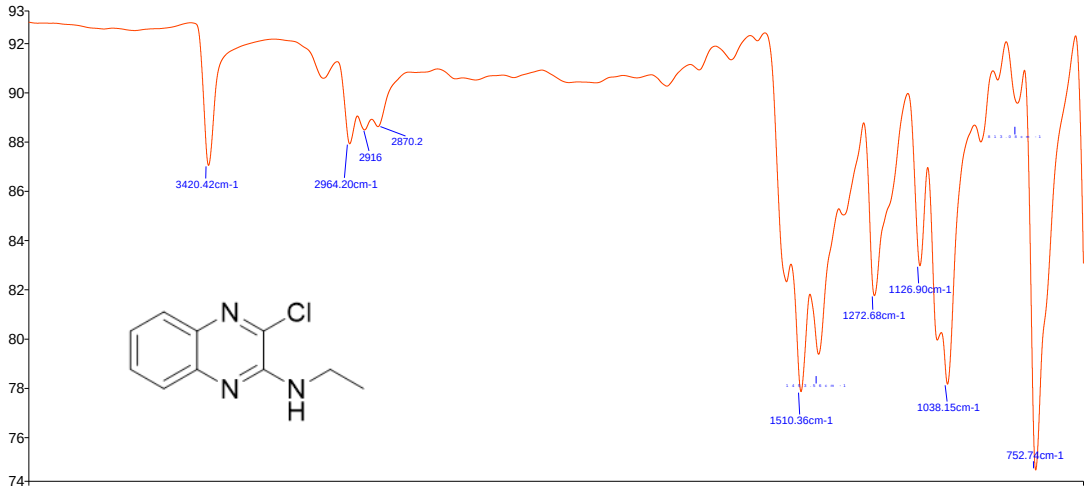
S37: ATR-FTIR spectrum of compound **2c**



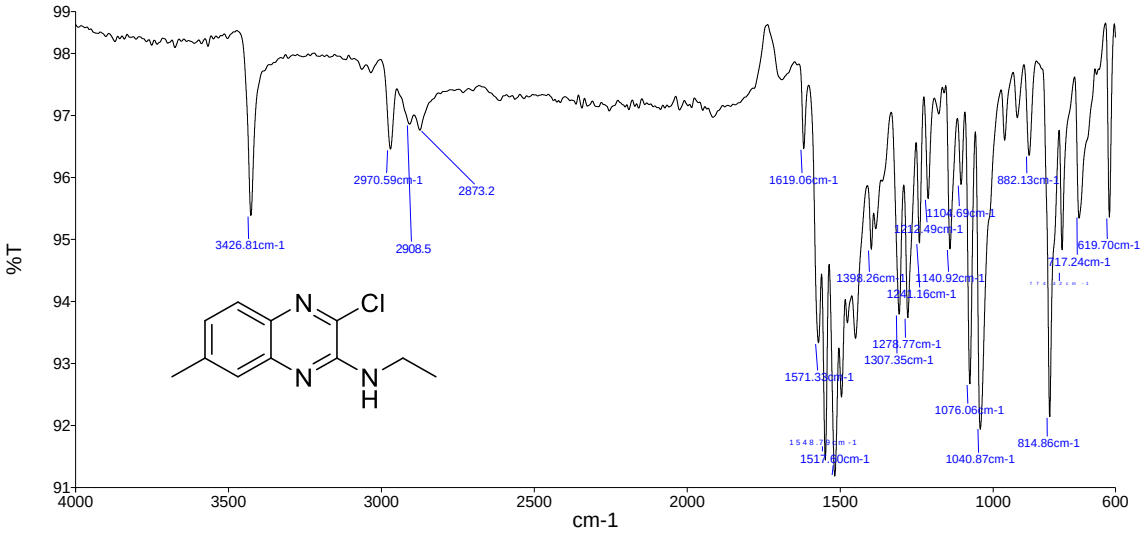
S38: ATR-FTIR spectrum of compound **2d**



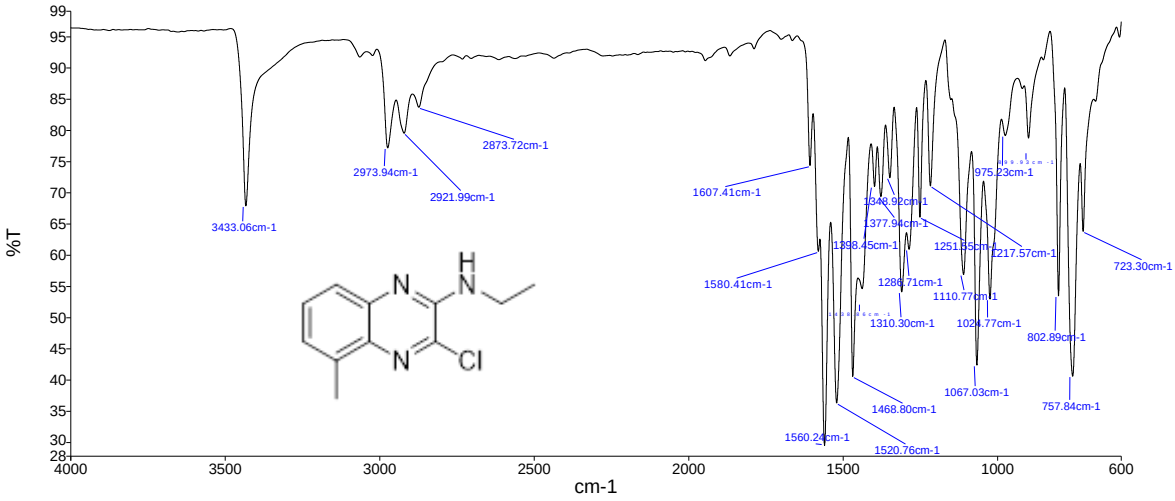
S39: ATR-FTIR spectrum of compound **2e**



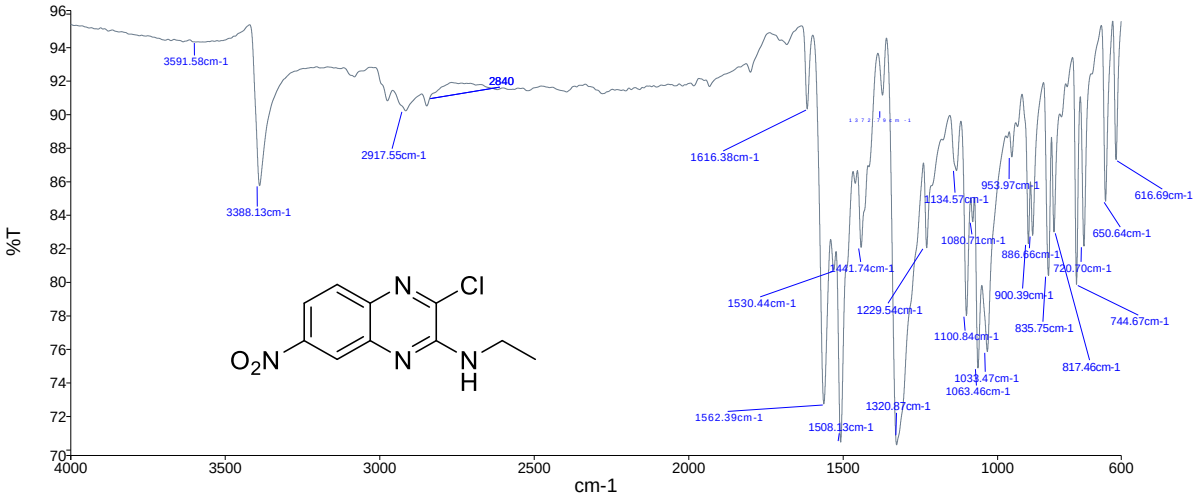
S40: ATR-FTIR spectrum of compound **3a**



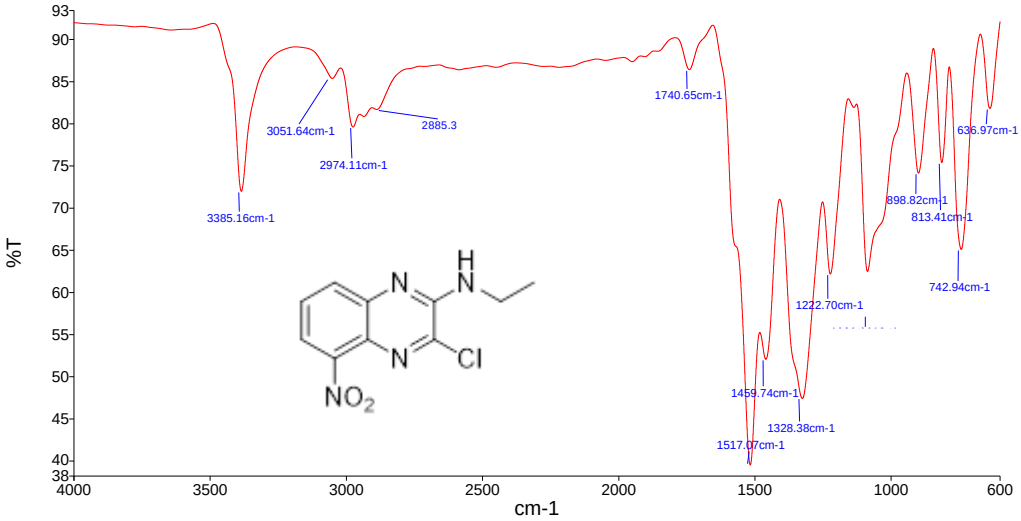
S41: ATR-FTIR spectrum of compound **3b**



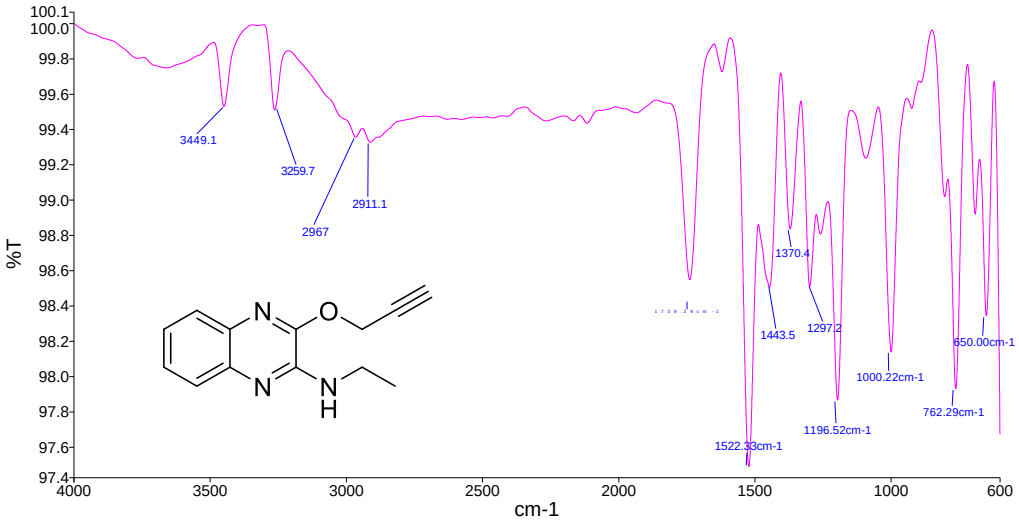
S42: ATR-FTIR spectrum of compound **3c**



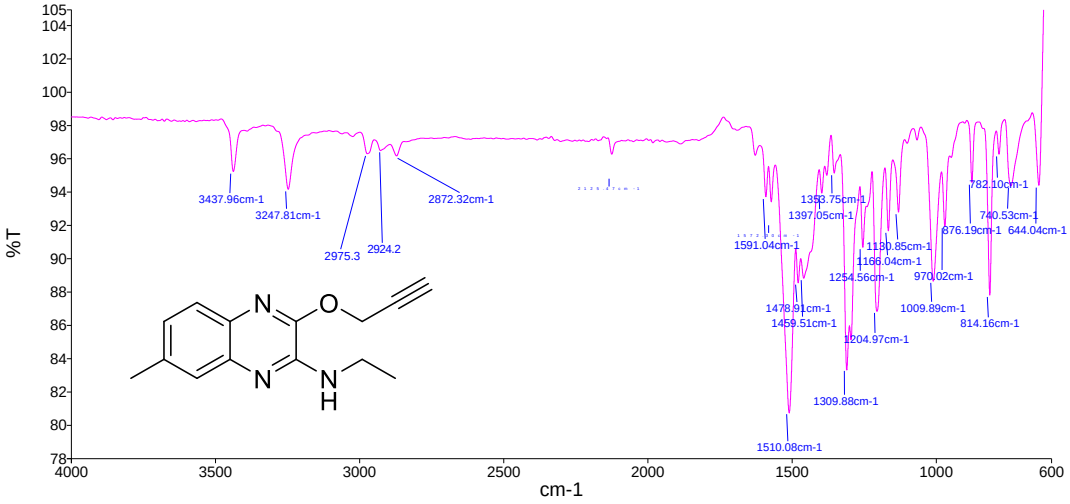
S43: ATR-FTIR spectrum of compound **3d**



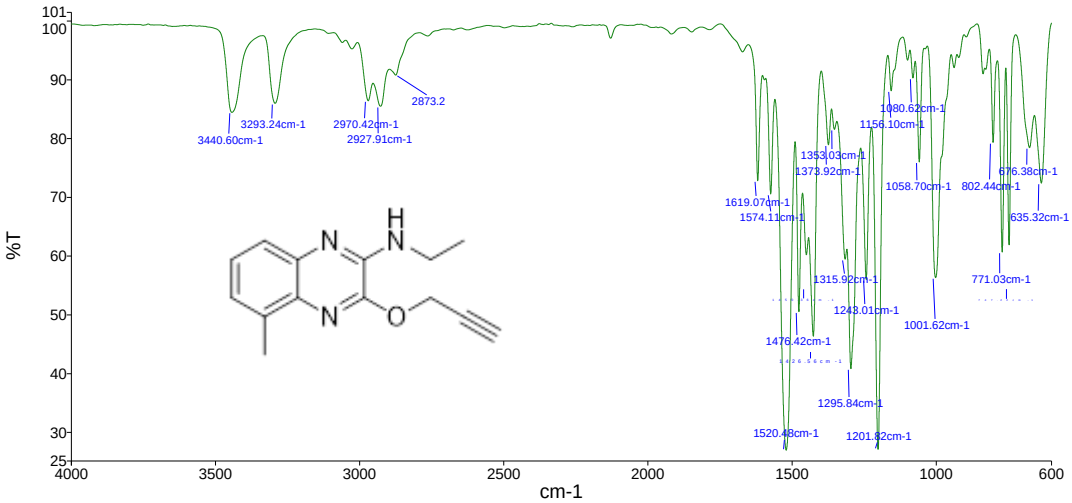
S44: ATR-FTIR spectrum of compound **3e**



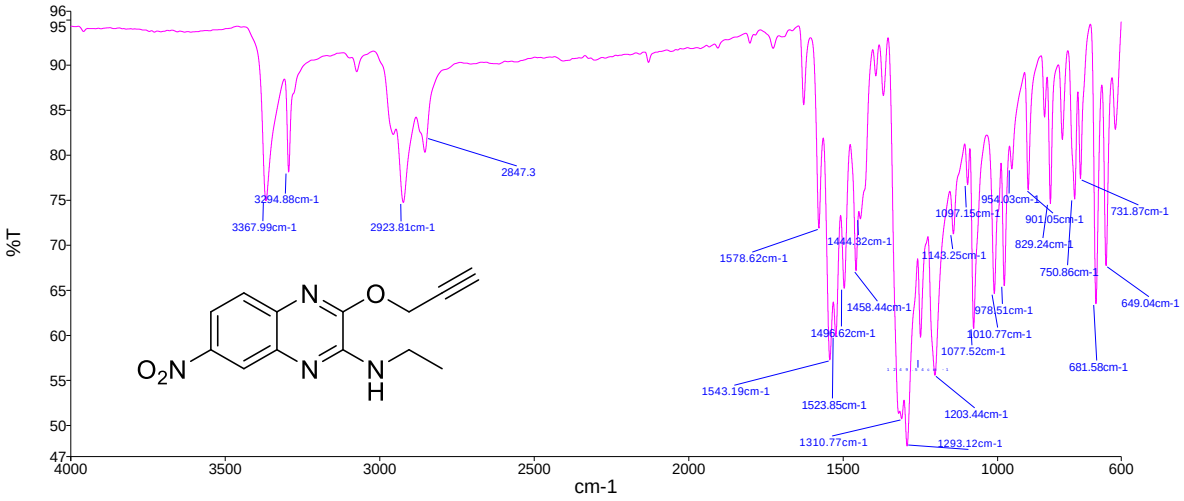
S45: ATR-FTIR spectrum of compound **4a**



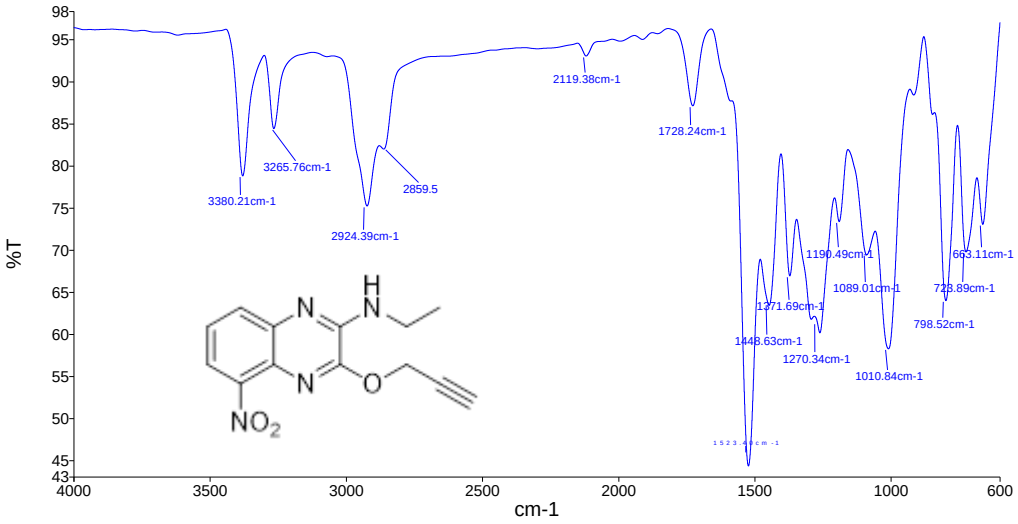
S46: ATR-FTIR spectrum of compound **4b**



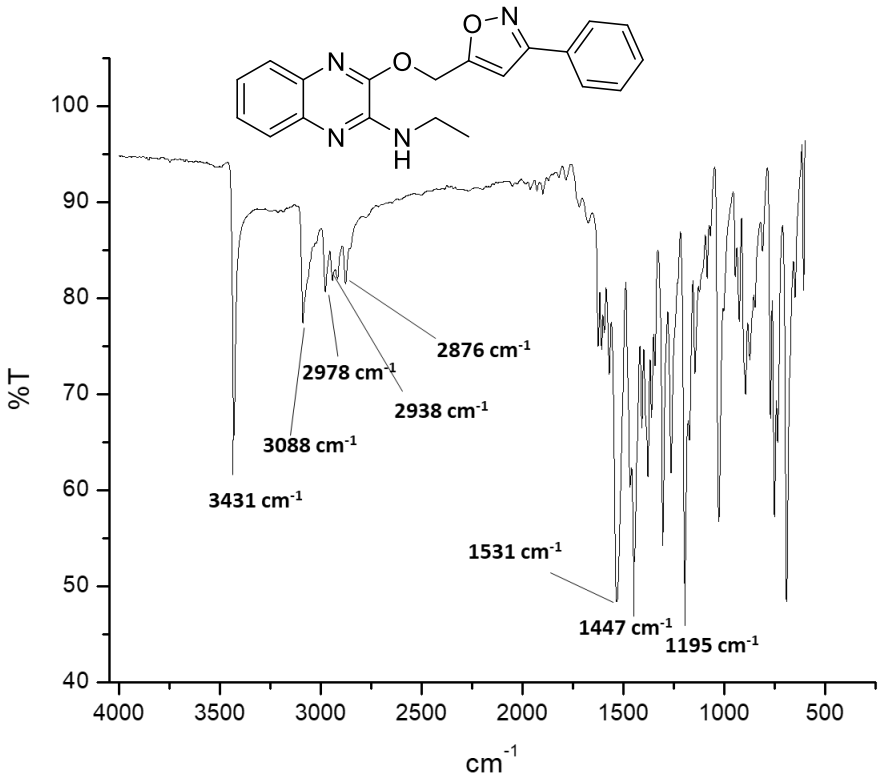
S47: ATR-FTIR spectrum of compound **4c**



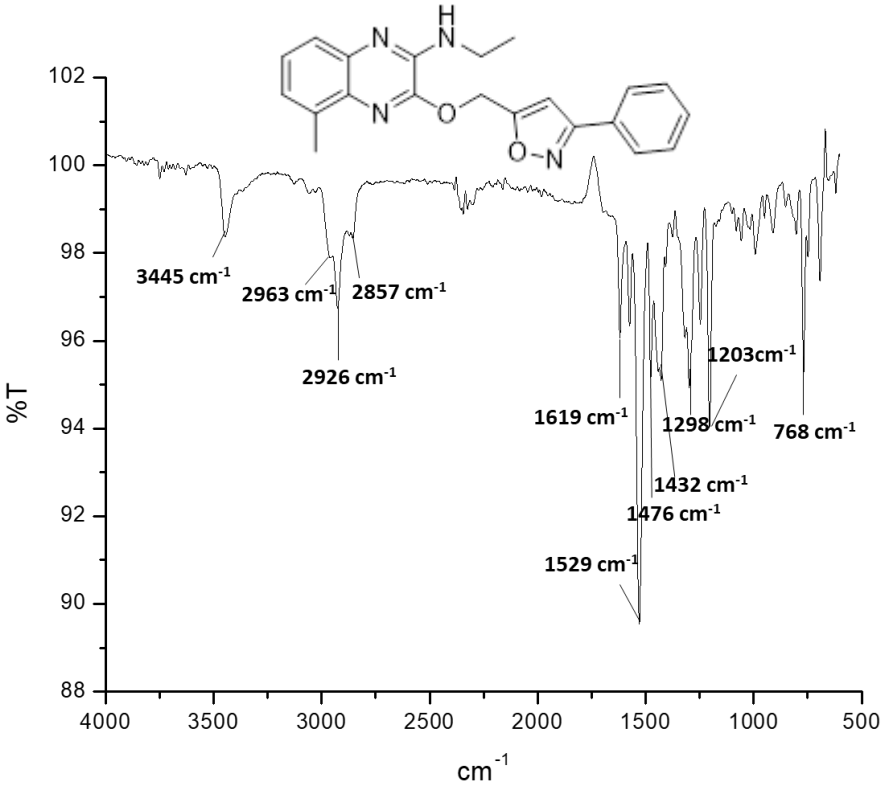
S48: ATR-FTIR spectrum of compound **4d**



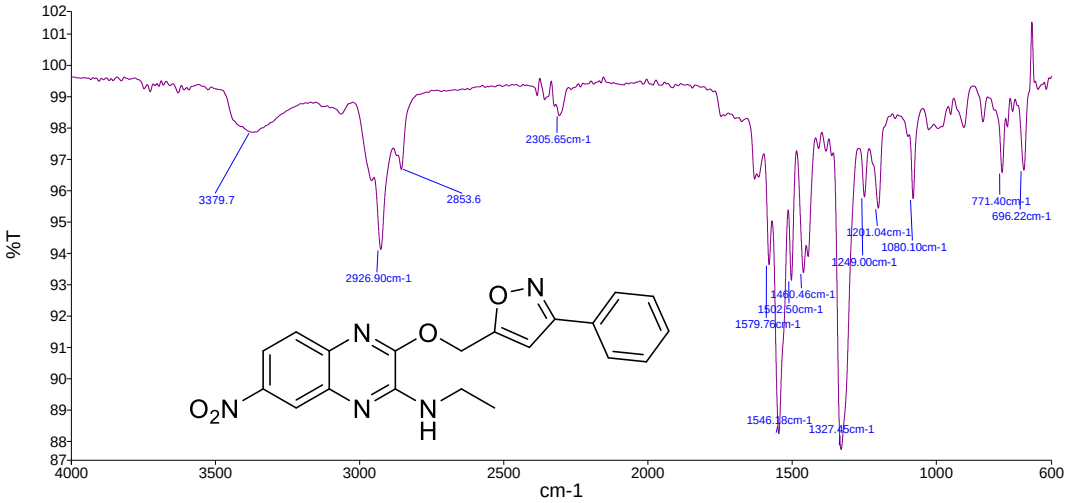
S49: ATR-FTIR spectrum of compound **4e**



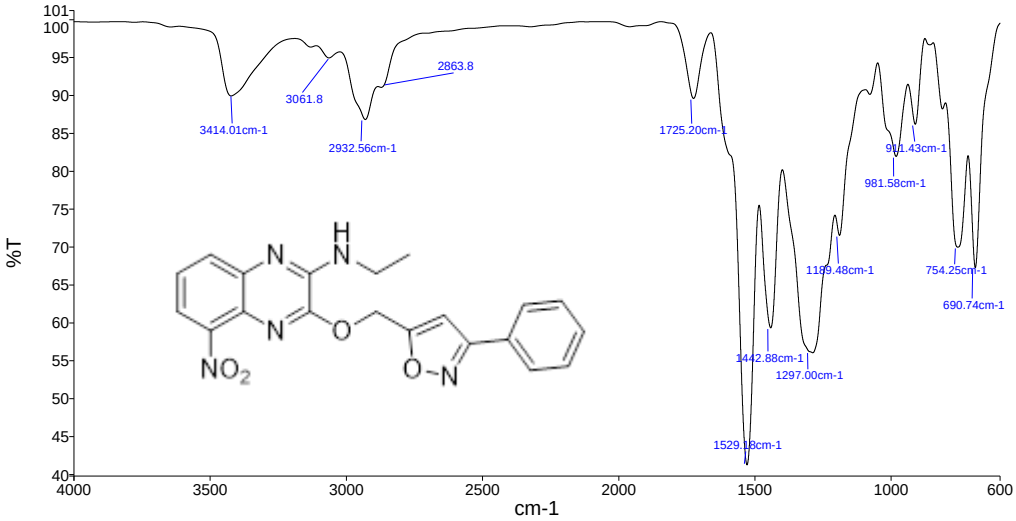
S50: ATR-FTIR spectrum of compound **5a**



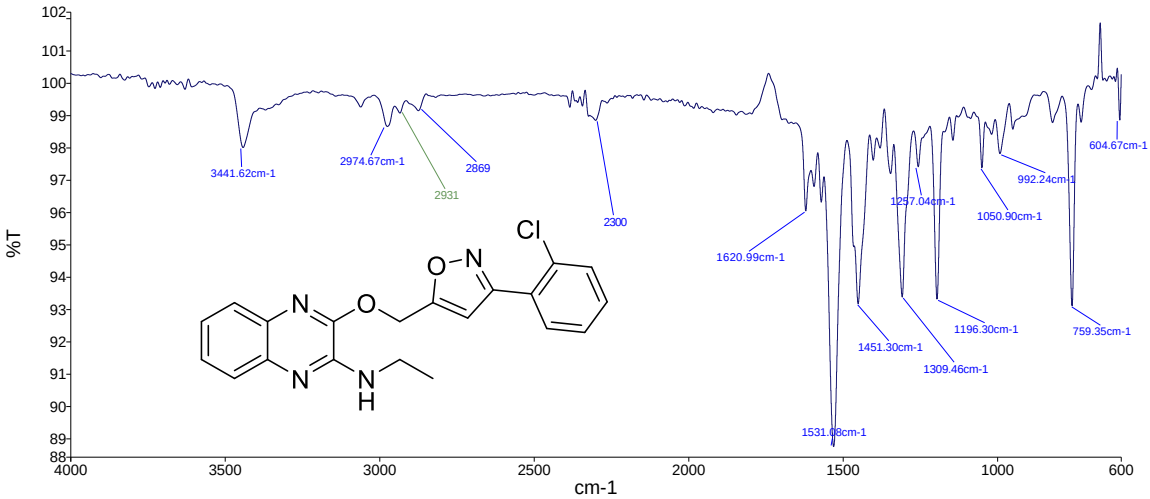
S51: ATR-FTIR spectrum of compound **5b**



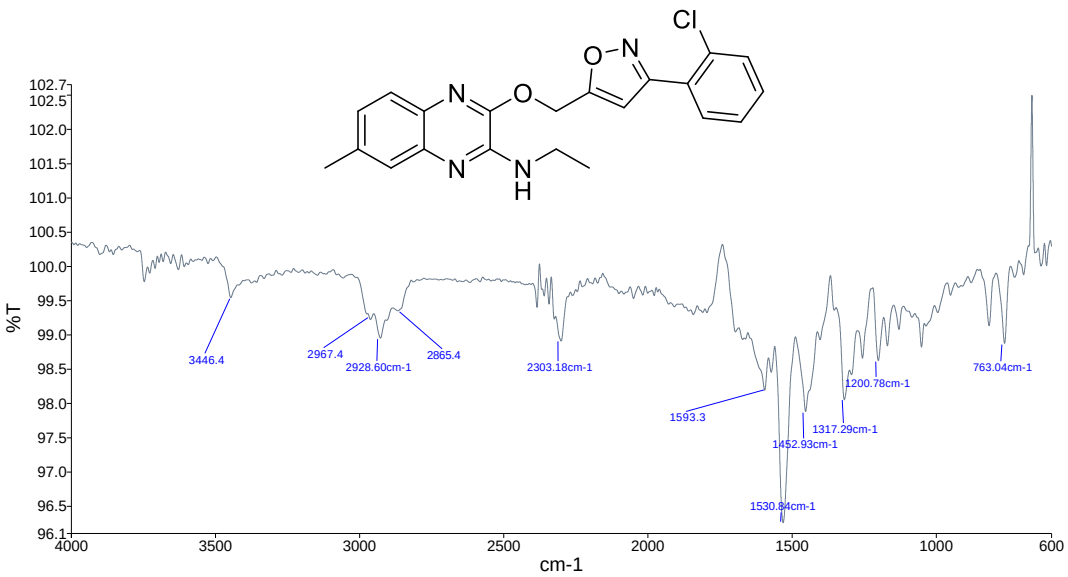
S52: ATR-FTIR spectrum of compound **5c**



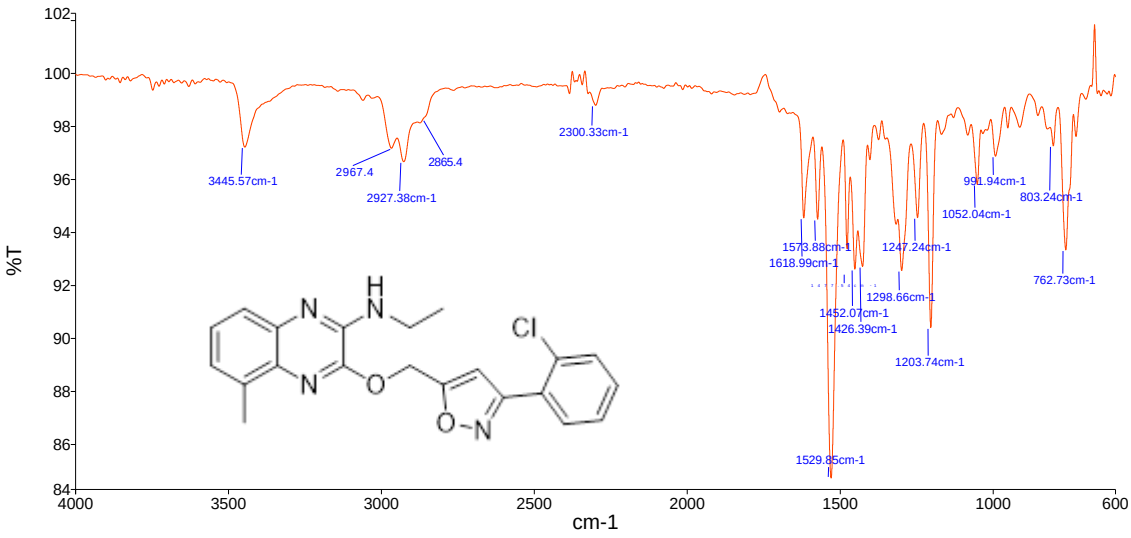
S53: ATR-FTIR spectrum of compound **5d**



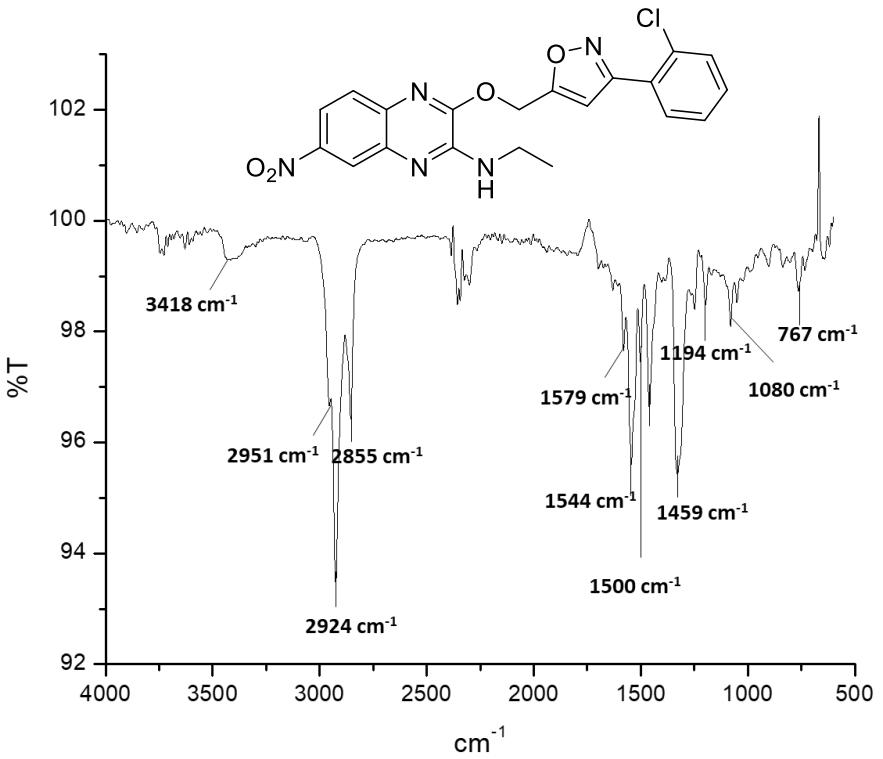
S54: ATR-FTIR spectrum of compound **5e**



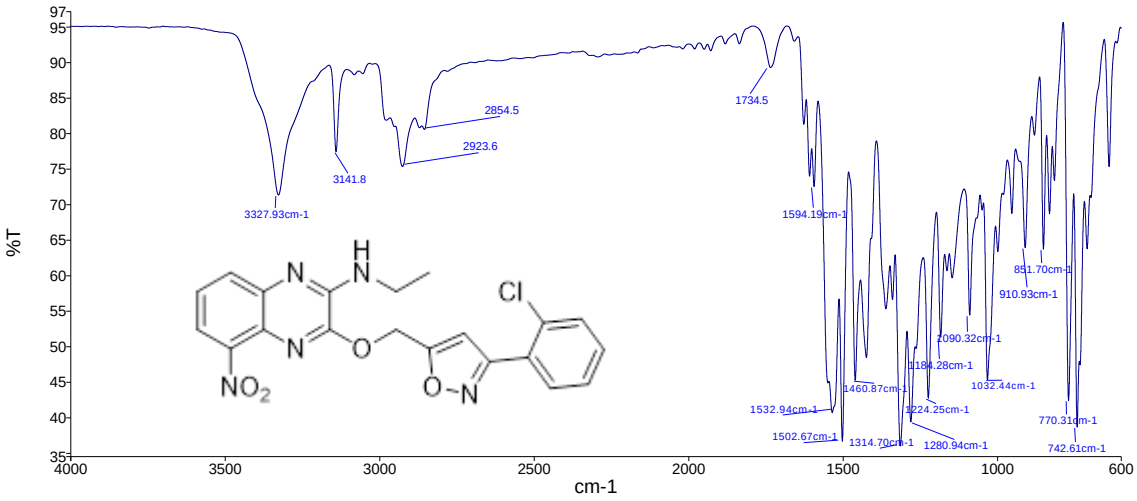
S55: ATR-FTIR spectrum of compound **5f**



S56: ATR-FTIR spectrum of compound **5g**

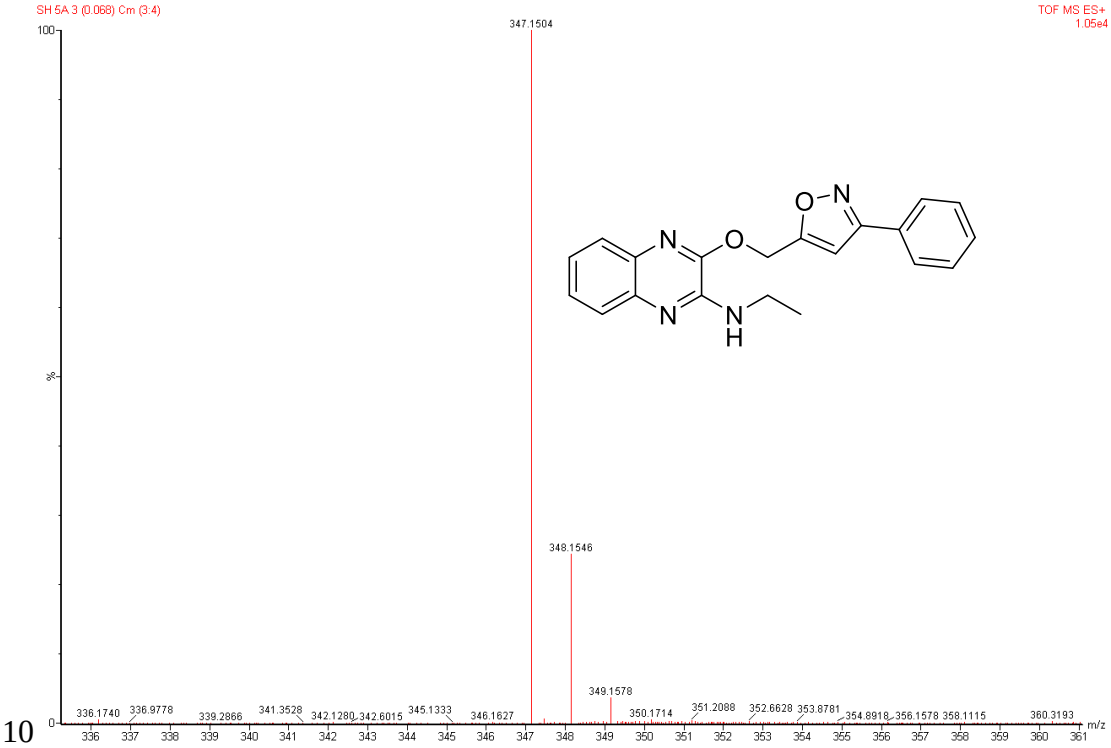


S57: ATR-FTIR spectrum of compound **5h**

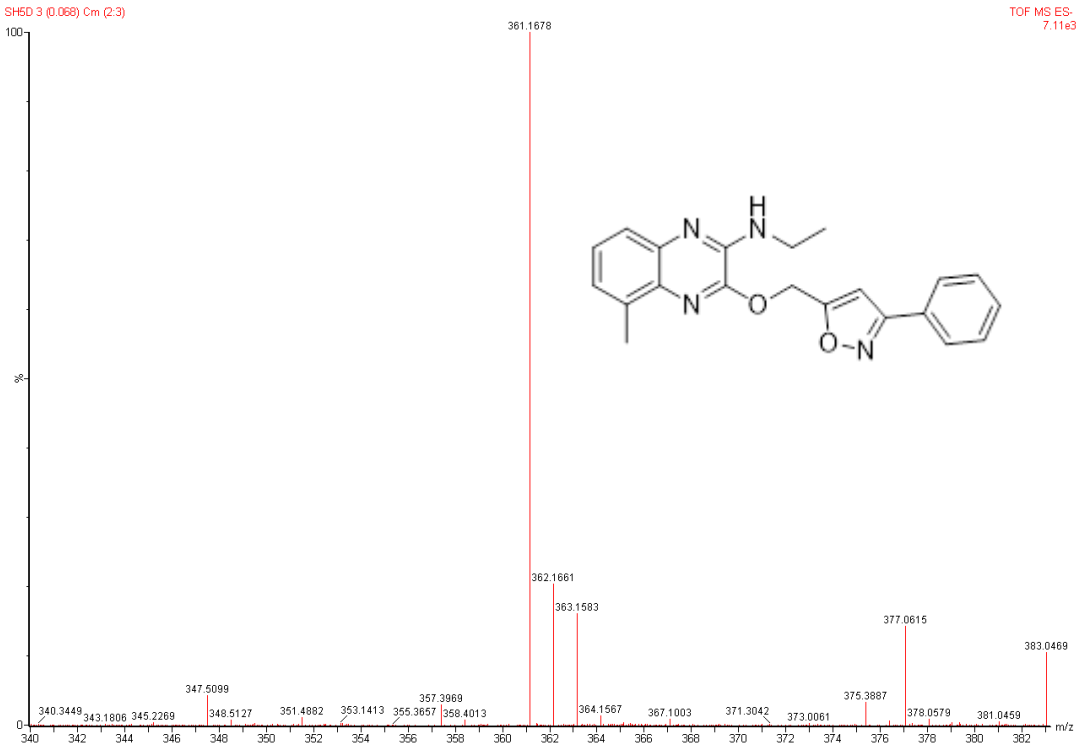


S58: ATR-FTIR spectrum of compound **5i**

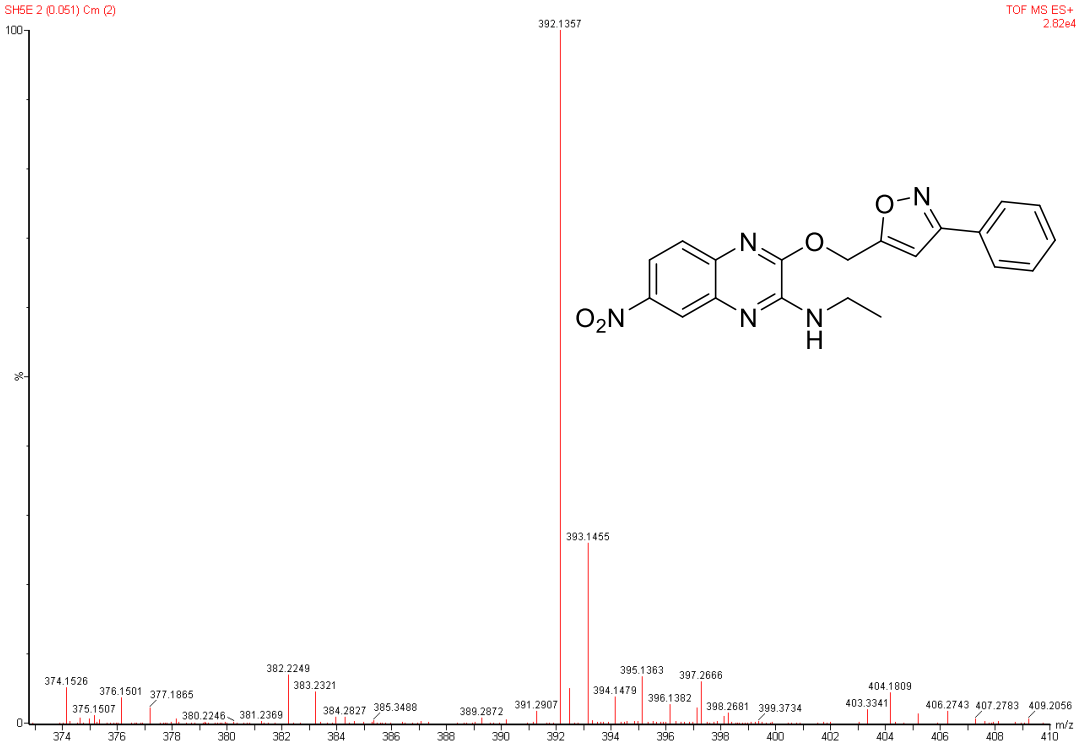
9. HRMS Spectra



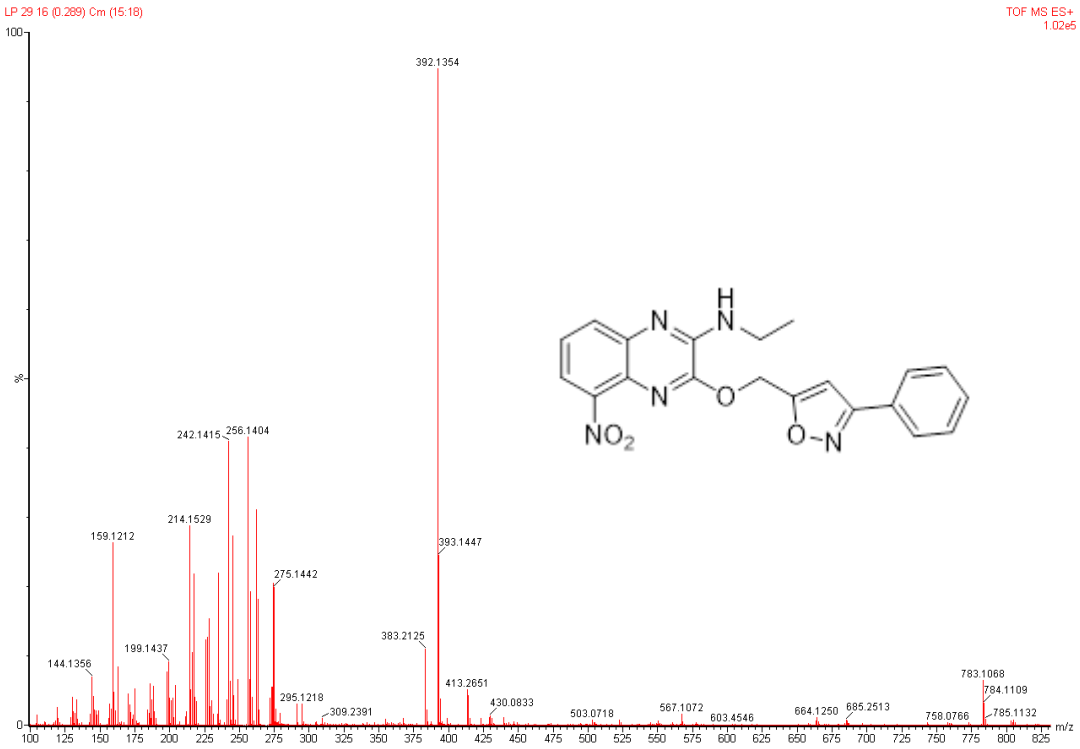
S59: HRMS spectrum of compound **5a**.



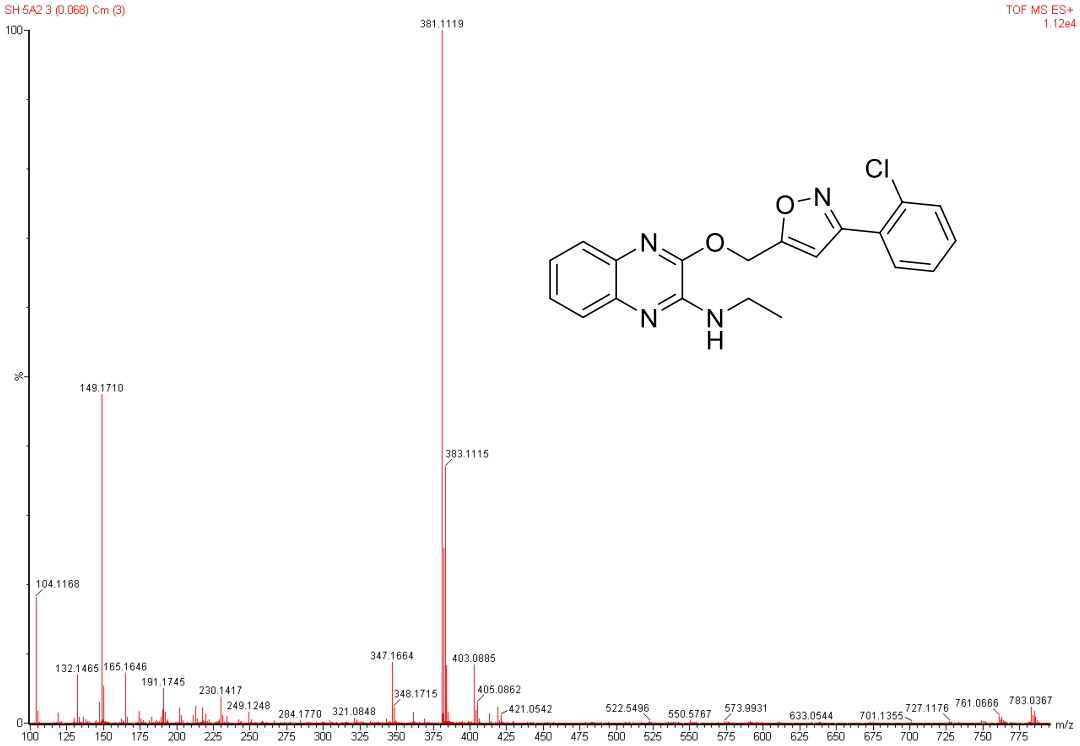
S60: HRMS spectrum of compound **5b**.



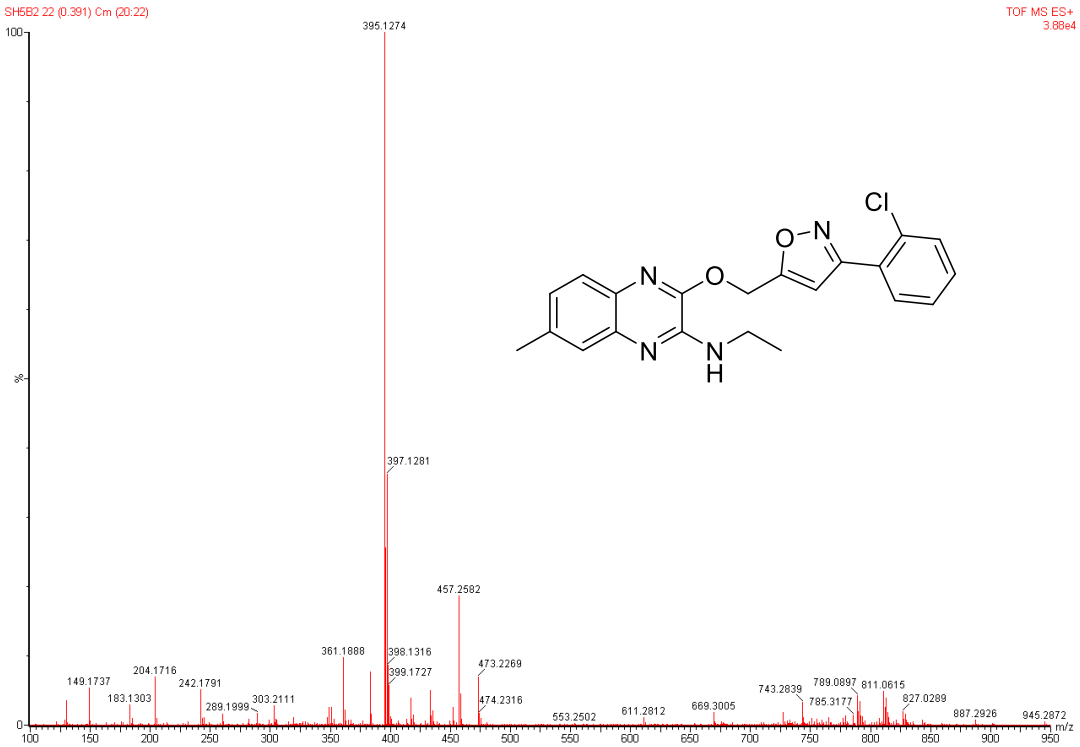
S61: HRMS spectrum of compound **5c**.



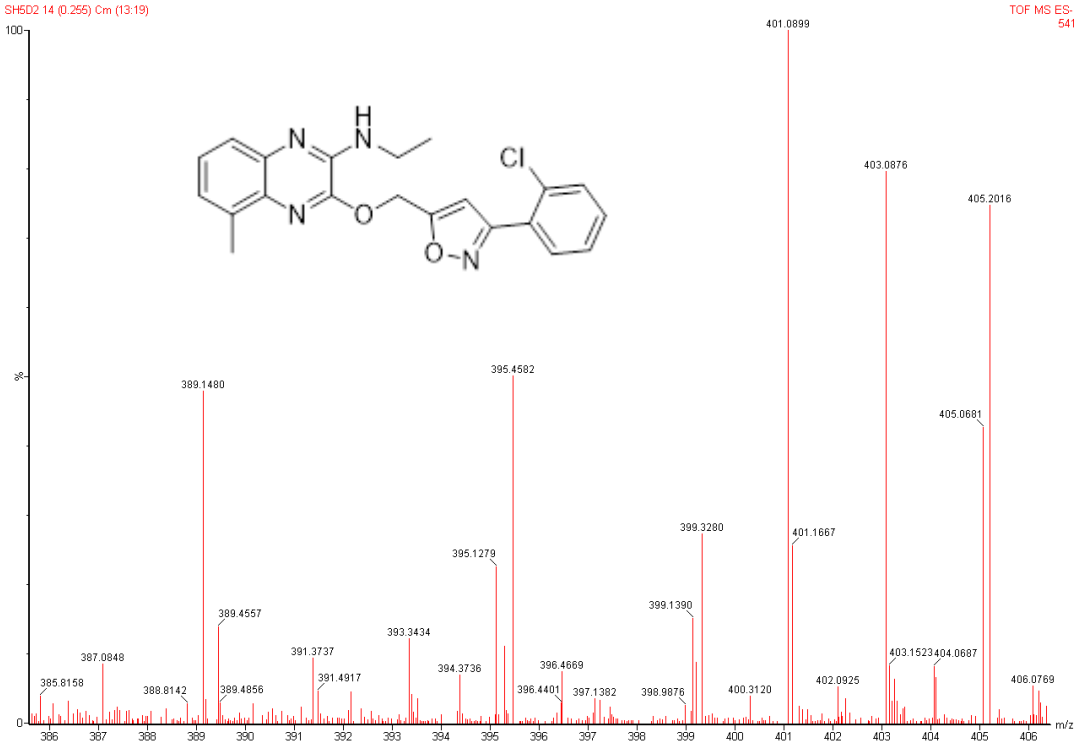
S62: HRMS spectrum of compound **5d**.



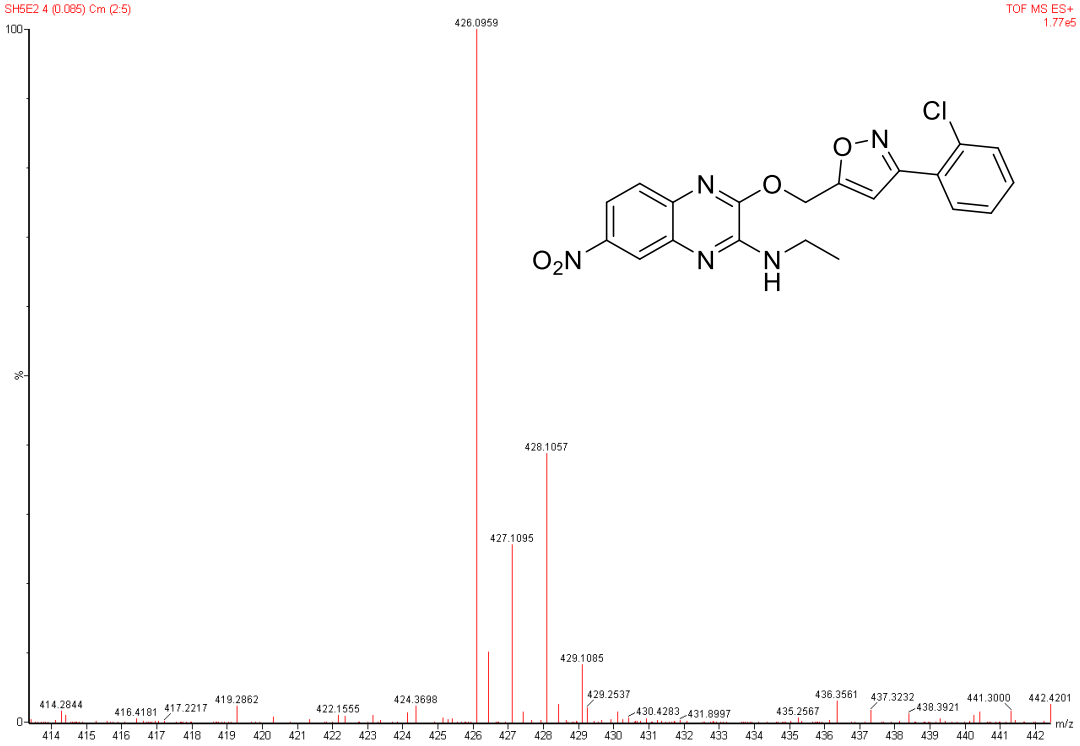
S63: HRMS spectrum of compound **5e**.



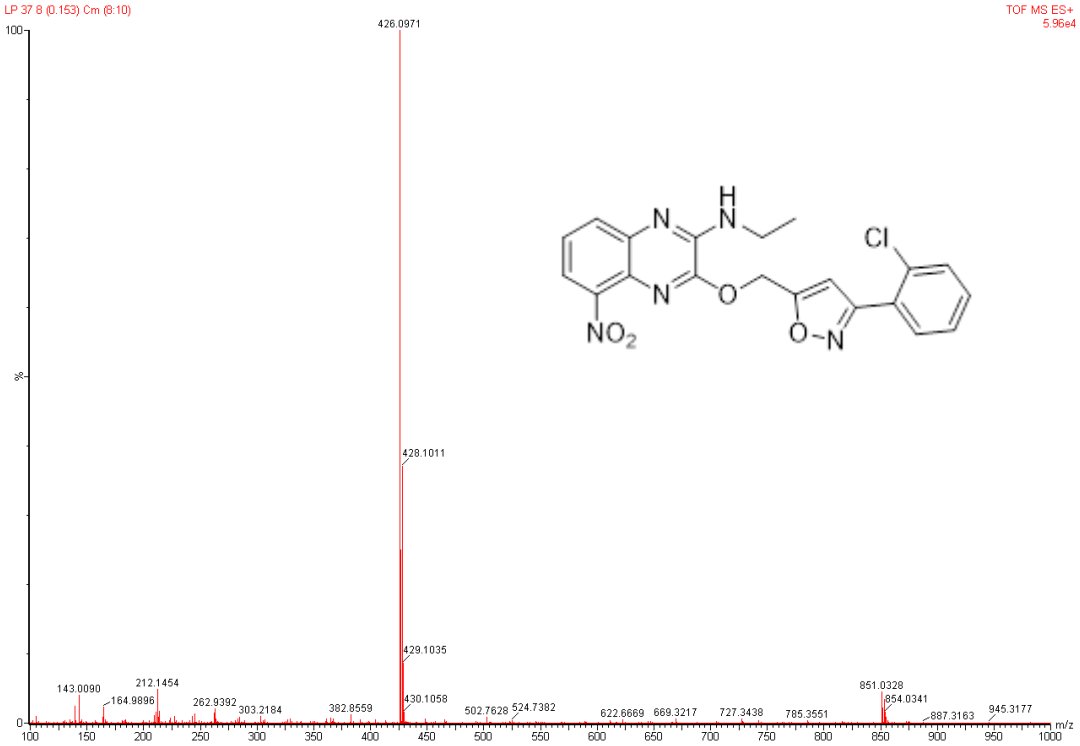
S64: HRMS spectrum of compound **5f**.



S65: HRMS spectrum of compound **5g**.

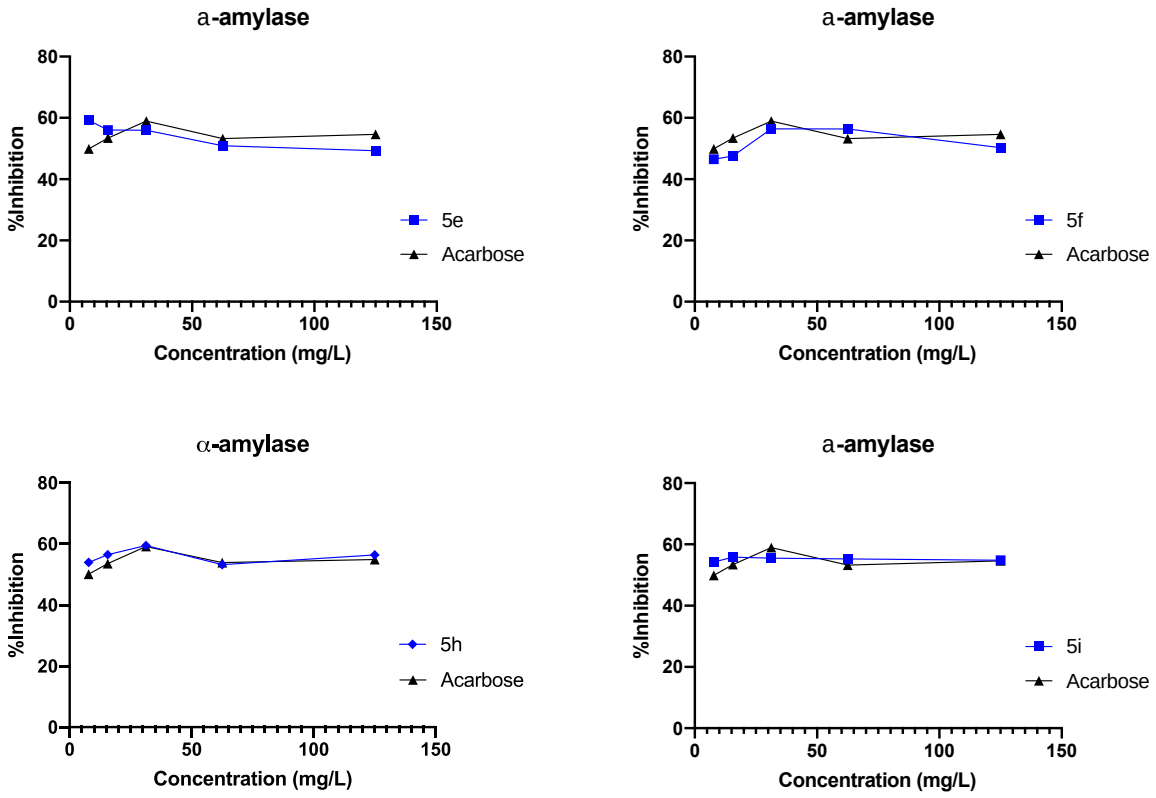


S66: HRMS spectrum of compound **5h**.



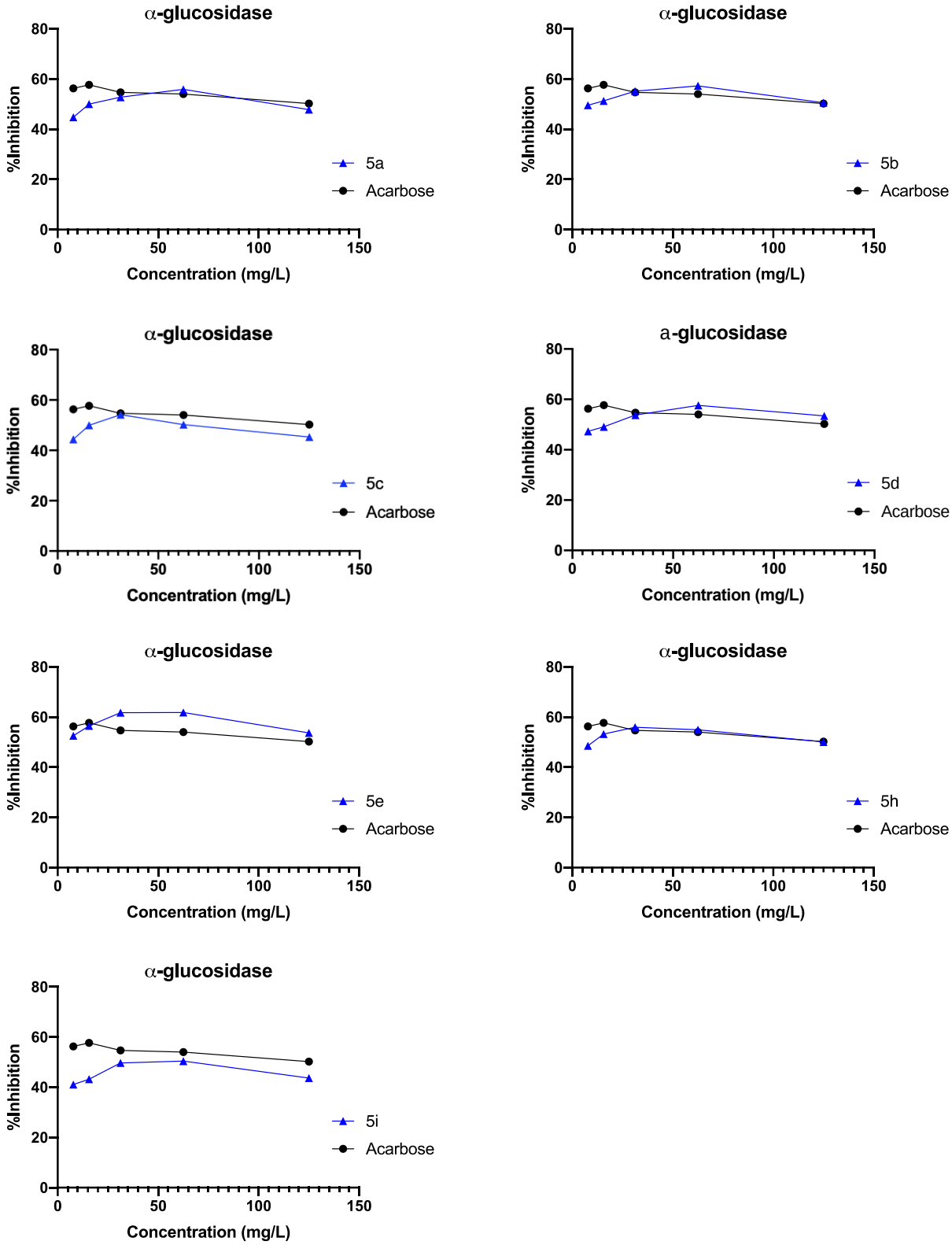
S67: HRMS spectrum of compound **5i**.

10. Graph of α-amylase inhibitory activity



S68 Inhibitory activity graphs of selected compounds **5e-f**, **5h-i** against α-amylase compared to acarbose.

11. Graph of α-Glucosidase inhibitory activity



S69: Inhibitory activity graphs of selected compounds **5a-e**, **5h-i** against α-glucosidase compared to acarbose.