

SUPPORTING INFORMATION

Palladium-Catalyzed Copper(I)-Mediated Cross-Coupling of Arylboronic Acids and 2(1H)-Pyrazinones Facilitated by Microwave Irradiation with Simultaneous Cooling

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General Remarks:

¹H NMR spectra were recorded on a Bruker Avance 300 MHz and 400 MHz instruments, using CDCl₃. The ¹H and ¹³C chemical shifts are reported in ppm relative to tetramethylsilane, using the residual solvent signal as an internal reference. Mass spectra were recorded by using a Kratos MS50TC and a Kratos Mach III data system. The ion source temperature was 150-250 °C as required. High resolution EI-mass spectra were performed with a resolution of 10000. The low resolution spectra were obtained with a HP5989A MS instrument. For thin layer chromatography, analytical TLC plates (Alugram SIL G/UV₂₅₄ and 70-230 mesh silicagel (E.M.Merck)) were used. The Pd(PPh₃)₄, CuTC and boronic acids were purchased from Acros Organics (Janssen Pharmaceutical, Geel) and were used without further purification. All starting pyrazinones were prepared according to a known literature procedure.¹² All the compounds were fully characterised by comparison of their spectral data and melting points. Melting points of the compounds are uncorrected.

Microwave Irradiation Experiments:

All microwave irradiation experiments were carried out in a dedicated CEM-Discover-Coolmate™ monomode microwave apparatus (CEM Corporation P.O. Box 200 Matthews, NC 28106), operating at a frequency of 2.45 GHz with continuous irradiation power from 0 to 300 W. The reactions were carried out in an open 10 mL double walled glass vial which was cooled to 0 °C - 35 °C using a microwave transparent cooling liquid.^{11(b)} The temperature of the cooling liquid was between 10 °C and 15 °C. Irradiation and cooling were started simultaneously, starting with the reaction mixture at rt. The temperature was measured with a fiber-optic device inserted into the reaction vessel (a schematic representation of the set-up can be found at <http://cemsynthesis.com/>).

General Procedure of Liebeskind cross-Coupling of Pyrazinone 1 with Boronic Acids :

- A) Liebeskind Condition:** To a suspension of pyrazinone **1** (0.076 g, 0.21 mmol) in THF (3 mL) were added boronic acid (0.63 mmol, 3 equiv), Pd(PPh₃)₄ (5 mol %) and CuTC (2.0 equiv). The reaction mixture was heated at 65 °C for various time interval (Table 1). After completion of the reaction, the solvent was removed under reduced pressure and the residue was purified by column chromatography [silica gel, *n*-hexane-CH₂Cl₂ (95:5)] to furnish the products 3{1}-3{5}.
- B) Upon microwave irradiation with simultaneous cooling at 0 °C :** To a suspension of pyrazinone **1** (0.076 g, 0.21 mmol) in THF (3 mL) were added boronic acid (0.63 mmol, 3 equiv), Pd(PPh₃)₄ (5 mol %) and CuTC (2.0 equiv). The mixture was irradiated at 35 °C continuously at the maximum power of 300 W for 1 h. After completion of the reaction, the solvent was removed under reduced pressure. The crude product was then absorbed on silica gel and

the residue was purified by column chromatography over silica gel using n-Hexane/ CH₂Cl₂ (95:5) as the eluent, to give the C-3-arylated pyrazinones 3{1}-3{34}.

5-chloro-3-(3-ethoxyphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{1}). It was obtained as a yellow oil in 88 % yield. ¹H NMR (400 MHz, CDCl₃): δ 7.99-7.95 (m, 2H), 7.34-7.25 (m, 3H), 7.14(s, 1H), 7.00-6.98 (m, 1H), 6.89-6.87 (d, 2H, *J*=8.36 Hz), 5.03 (s, 2H), 4.11-4.06 (q, 2H, *J* = 6.9 Hz), 3.76 (s, 3H), 1.42-1.39 (t, 3H, *J* = 6.9 Hz). ¹³C NMR (100 MHz, CDCl₃): 160.13, 158.78, 154.50, 151.9, 136.19, 130.46, 129.18, 126.41, 125.32, 121.93, 117.70, 114.81, 114.72, 63.66, 55.44, 52.45, 14.92. HRMS (EI): calcd for C₂₀H₁₉O₃N₂Cl: 370.1084, found: 370.1071.

5-chloro-3-(3-trifluoromethylphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{2}). It was obtained as a yellow solid m.p. 107-108 °C in 83 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.72 (s, 1H), 8.63-8.60 (m, 1H), 7.71-7.68 (m, 1H), 7.58-7.53 (m, 1H), 7.32-7.30 (d, 2H, *J* = 8.2Hz), 7.23 (s, 1H), 6.93-6.90 (d, 2H, *J* = 9.1 Hz), 5.08 (s, 2H), 3.8 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): 160.18, 154.25, 150.18, 135.50, 132.40, 121.97, 130.35, 129.03, 128.55, 126.98, 126.46, 126.08, 114.72, 114.23, 55.31, 52.49. HRMS (EI): calcd for C₁₉H₁₄O₂N₂ F₃Cl: 394.0696, found: 394.0684.

5-chloro-3-(4-phenoxyphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{3}). It was obtained as a yellow oil in 80 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.43-8.40 (s, 1H), 7.39-7.25 (m, 4H), 7.17-7.01 (m, 6H), 6.92-6.89 (d, 2H, *J* = 9.12 Hz), 5.06 (s, 2H), 3.81 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.19, 159.86, 156.45, 154.59, 151.60, 131.41, 130.49, 129.88, 129.21, 126.66, 126.50, 124.61, 124.07, 119.74, 117.88, 114.78, 55.50, 52.51. HRMS (EI): calcd for C₂₄H₁₉O₃N₂Cl: 418.1084, found: 418.1081.

5-chloro-3-(4-methoxyphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{4}). It was obtained as a yellow solid m.p. 96-97 °C in 90 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.44-8.41 (d, 2H, *J* = 9.1 Hz), 7.30-7.27 (d, 2H, *J* = 8.2 Hz), 7.1 (s, 1H), 6.95-6.88 (m, 4H), 5.03 (s, 2H), 3.84 (s, 3H), 3.79 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 161.78, 160.01, 154.53, 151.60, 131.26, 130.37, 127.75, 126.53, 124.07, 114.62, 113.56, 55.41, 52.36. HRMS (EI): calcd for C₁₉H₁₇O₃N₂Cl: 356.0928, found: 356.0938

5-chloro-3-phenyl-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{5}). It was obtained as a yellow oil in 90 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.36-8.33 (m, 2H), 7.44-7.42 (m, 3H), 7.31-7.28 (d, 2H, *J* = 8.2Hz), 7.16 (s, 1H), 6.91-6.88 (d, 2H, *J* = 9.12 Hz), 5.04 (s, 2H), 3.79 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.10, 154.50, 152.24, 134.94, 130.74, 130.46, 129.37, 128.21, 126.56, 126.35, 125.22, 114.68, 55.41, 52.48. HRMS (EI): calcd for C₁₈H₁₅O₂N₂Cl: 326.0822, found: 326.0817

5-chloro-3-(2-fluorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{6}). It was obtained as a yellow solid m.p. 69-70 °C in 75 % yield. ¹H NMR (400 MHz, CDCl₃): δ 7.64-7.59 (m, 1H), 7.46-7.39 (m, 1H), 7.33-7.31(d, 2H, *J* = 8.22 Hz) 7.23-7.21(m, 2H) 7.18-7.11(m, 1H) 6.92-6.90 (d, 2H, *J* = 8.22 Hz), 5.05 (s, 2H), 3.80 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): 161.89, 160.17, 159.38, 153.91, 152.25, 131.83, 131.75, 131.25, 131.22, 130.64, 130.52, 126.24, 126.17, 126.11, 123.99,

123.96, 123.64, 123.55, 116.15, 115.93, 114.70, 55.33, 52.52. HRMS (EI): calcd for C₁₈H₁₄O₂N₂ClF: 344.0728, found: 344.0734.

5-chloro-3-(3-fluorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{7}). It was obtained as a dark yellow solid 107-108 °C in 76 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.23-8.14 (m, 2H), 7.43-7.36 (m, 1H), 7.33-7.30 (d, 2H, *J* = 8.22 Hz), 7.20-7.14 (m, 2H), 6.92-6.90 (d, 2H, *J* = 8.22 Hz), 5.07 (s, 2H), 3.81 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 164.25, 161.02, 160.22, 154.38, 150.57, 130.55, 129.64, 126.53, 126.17, 125.89, 125.13, 117.82, 117.55, 116.45, 116.15, 114.81, 114.38, 55.50, 52.63. HRMS (EI): calcd for C₁₈H₁₄O₂N₂ClF: 344.0728, found: 344.0732.

5-chloro-3-(2,4-difluorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{8}). It was obtained as a yellow solid m.p. 105-106 °C in 80 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.66-7.62 (m, 1H), 7.32-7.25 (m, 3H), 6.92-6.89 (m, 4H), 5.04 (s, 2H), 3.80 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.22, 154.28, 153.80, 153.61, 151.66, 151.51, 150.42, 150.23, 148.29, 148.22, 131.83, 130.49, 126.47, 126.05, 125.89, 118.80, 118.52, 114.78, 114.35, 55.44, 52.66. HRMS (EI): calcd for C₁₈H₁₃O₂N₂ClF₂: 362.0634, found: 362.0630.

5-chloro-3-(3,4-difluorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{9}). It was obtained as a yellow solid m.p. 80-81 °C in 75 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.40-8.33 (m, 1H), 8.26 (bs, 1H), 7.31-7.28 d, 2H, *J* = 8.22 Hz), 7.21-7.17 (m, 2H), 6.92-6.89 (d, 2H, *J* = 8.22 Hz), 5.06 (s, 2H), 3.80 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.22, 154.28, 153.80, 153.61, 151.66, 151.51, 150.42, 150.23, 148.29, 148.22, 131.83, 130.49, 126.47, 126.05, 125.89, 118.80, 118.52, 114.78, 114.35, 55.44, 52.66. HRMS (EI): calcd for C₁₈H₁₃O₂N₂ClF₂: 362.0634, found: 362.0629.

5-chloro-3-(2-chlorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{10}). It was obtained as a yellow solid m.p. 98-99 °C in 31 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.46-7.33 (m, 3H), 7.30-7.27 (m, 4H), 6.91-6.89 (m, 2H), 5.06 (s, 2H), 3.80 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.13, 154.74, 134.54, 133.69, 133.30, 130.95, 130.83, 130.58, 129.85, 126.81, 126.14, 114.71, 55.41, 52.57. HRMS (EI): calcd for C₁₈H₁₄O₂N₂Cl₂: 360.0432, found: 360.0429.

5-chloro-3-(3-chlorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{11}). It was obtained as a yellow solid m.p. 124-125 °C in 81 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.39-8.36 (d, 2H, *J* = 8.22 Hz), 7.40-7.37 (d, 2H, *J* = 8.22 Hz), 7.30-7.27 (d, 2H, *J* = 8.22 Hz), 7.17 (s, 1H), 6.91-6.88 (d, 2H, *J* = 8.22 Hz), 5.04 (s, 2H), 3.79 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.16, 154.38, 150.72, 136.95, 133.39, 130.77, 130.46, 128.42, 126.53, 126.20, 125.59, 114.74, 55.44, 52.57. HRMS (EI): calcd for C₁₈H₁₄O₂N₂Cl₂: 360.0432, found: 360.0431.

5-chloro-3-(4-chlorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{12}). It was obtained as a yellow solid m.p. 128-129 °C in 73 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.41 (s, 1H), 8.32-8.29 (d, 1H, *J* = 8.22 Hz), 7.39-7.35 (m, 2H), 7.31-7.28 (d, 2H, *J* = 8.22 Hz), 7.20 (s, 1H), 6.91-6.88 (d, 2H, *J* = 8.22 Hz), 5.05 (s, 2H), 3.79 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.16, 154.28, 150.35, 136.52, 134.24, 130.65, 130.46, 129.43, 129.21, 127.48, 126.47, 126.11, 125.99, 114.74, 55.44, 52.60. HRMS (EI): calcd for C₁₈H₁₄O₂N₂Cl₂: 360.0432, found: 360.0428.

5-chloro-3-(3,4-dichlorophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{14}). It was obtained as a yellow solid m.p. 114-115 °C in 89 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.62-8.61 (m, 1H), 8.35-8.31 (m, 1H), 7.51-7.48 (d, 1H, *J* = 8.22 Hz), 7.32-7.29 (d, 2H, *J* = 8.22 Hz), 7.22 (s, 1H), 6.93-6.91 (d, 2H, *J* = 8.22 Hz), 5.07 (s, 2H), 3.81 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.16, 154.28, 150.35, 136.52, 134.24, 130.65, 130.46, 129.43, 129.21, 127.48, 126.47, 126.11, 125.99, 114.74, 55.44, 52.60. HRMS (EI): calcd for C₁₉H₁₅ON₂Cl₃: 394.0043, found: 394.0028.

5-chloro-3-(3-bromophenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{16}). It was obtained as a dark yellow solid m.p. 109-110 °C in 84 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.55 (s, 1H), 8.37-8.34 (d, 1H, *J* = 8.22 Hz), 7.57-7.55 (d, 1H, *J* = 6.39 Hz), 7.31-7.28 (d, 2H, *J* = 8.22 Hz), 7.32-7.25 (m, 3H), 7.20 (s, 1H), 6.92-6.89 (d, 2H, *J* = 8.22 Hz), 5.05 (s, 2H), 3.80 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.19, 154.31, 150.32, 136.77, 133.60, 132.11, 130.49, 129.73, 127.97, 126.56, 126.11, 126.02, 122.39, 114.78, 55.47, 52.66. HRMS (EI): calcd for C₁₈H₁₄O₂N₂ClBr: 403.9927, found: 403.9930.

5-chloro-3-(2-methylphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{17}). It was obtained as a yellow solid m.p. 115-116 °C in 28 % yield. ¹H NMR (400 MHz, CDCl₃): δ 7.46-7.44 (d, 1H, *J* = 7.4 Hz), 7.31-7.29 (m, 3H), 7.25-7.23 (m, 3H), 6.91-6.89 (d, 2H, *J* = 8.7), 5.03 (s, 2H), 3.80 (s, 3H), 2.31 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): 161.27, 157.08, 155.46, 137.20, 134.95, 130.74, 130.55, 129.70, 126.50, 126.17, 125.61, 114.80, 55.46, 52.57, 20.11. HRMS (EI): calcd for C₁₉H₁₇O₂N₂Cl: 340.0978, found: 340.0979.

5-chloro-3-(3-methylphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{18}). It was obtained as a yellow solid m.p. 151-152 °C in 81 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.17-8.15 (bs, 2H), 7.34-7.24 (m, 4H), 7.14 (s, 1H), 6.90-6.87 (m, 2H), 5.02 (s, 2H), 3.78 (s, 3H), 2.39 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.04, 154.47, 152.46, 137.77, 134.88, 131.56, 129.76, 128.06, 126.59, 126.41, 125.10, 114.62, 55.38, 52.39, 21.56. HRMS (EI): calcd for C₁₉H₁₇O₂N₂Cl: 340.0978, found: 340.0980.

5-chloro-3-(4-methylphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{19}). It was obtained as a yellow solid m.p. 108-109 °C in 85 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.31-8.28 (d, 2H, *J* = 8.22 Hz), 7.31-7.28 (d, 2H, *J* = 9.12 Hz), 7.22-7.12 (d, 2H, *J* = 8.22 Hz), 7.13 (s, 1H), 6.91-6.88 (d, 2H, *J* = 9.15 Hz), 5.04 (s, 2H), 3.80 (s, 3H), 2.39 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.13, 154.59, 152.30, 141.22, 132.32, 130.46, 129.40, 129.0, 126.56, 124.71, 114.71, 55.47, 52.45, 21.65. HRMS (EI): calcd for C₁₉H₁₇O₂N₂Cl: 340.0978, found: 340.0979.

5-chloro-3-(3,4-dimethylphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{20}). It was obtained as a yellow solid m.p. 179-180 °C in 80 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.96 (s, 2H), 7.32-7.29 (d, 2H, *J* = 9.15 Hz), 7.14 (s, 1H), 7.09 (s, 1H), 6.91-6.88 (d, 2H, *J* = 9.12 Hz), 5.05 (s, 2H), 3.80 (s, 3H), 2.36 (s, 6H). ¹³C NMR (75 MHz, CDCl₃): 160.10, 154.56, 152.82, 137.68, 134.88, 132.60, 130.43, 127.11, 126.50, 124.89, 114.71, 55.44, 52.42, 21.50. HRMS (EI): calcd for C₂₀H₁₉O₂N₂Cl: 354.1135, found: 354.1133.

5-chloro-3-(4-tert.butylphenyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{21}). It was obtained as a yellow solid m.p. 98-99 °C in 96 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.31-8.28 (d, 2H, *J* = 8.22 Hz), 7.46-7.43 (d, 2H, *J* = 9.13 Hz), 7.30-7.20 (d, 2H, *J* = 8.22 Hz), 7.13 (s, 1H), 6.90-6.87 (d, 2H, *J* = 9.15 Hz), 5.04 (s, 2H), 3.79 (s, 3H), 1.33 (s, 9H). ¹³C NMR (75 MHz, CDCl₃): 160.10, 154.56, 154.16, 152.40, 132.26, 130.43, 129.18, 126.56, 125.22, 124.74, 114.68, 55.44, 52.39, 34.97, 31.25. HRMS (EI): calcd for C₂₂H₂₃O₂N₂Cl: 382.1448, found: 382.1447.

5-chloro-3-(5-methylthiophene)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{23}). It was obtained as a yellow solid m.p. 104-105 °C in 64 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.19-8.17 (d, 1H, *J* = 3.66 Hz), 7.31-7.28 (d, 2H, *J* = 8.22 Hz) 7.03 (s, 1H), 6.92-6.89 (d, 2H, *J* = 8.22 Hz), 6.83-6.81 (d, 1H, *J* = 3.66), 5.07 (s, 2H), 3.81 (s, 3H), 2.54 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.07, 153.16, 147.89, 147.58, 135.98, 132.44, 130.46, 130.40, 126.81, 126.50, 122.69, 114.78, 55.44, 52.24, 15.74. HRMS (EI): calcd for C₁₇H₁₅O₂N₂ClS: 346.0542, found: 346.0540.

5-chloro-3-(1-naphthalene)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{26}). It was obtained as a yellow solid m.p. 173-174 °C in 90 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.93-7.84 (m, 3H), 7.79-7.76 (d, 1H, *J* = 7.29 Hz), 7.54-7.45 (m, 4H), 7.32-7.25 (m, 2H), 6.90-6.87 (d, 2H, *J* = 9.15), 5.01 (s, 2H), 3.78 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.19, 155.78, 154.89, 133.84, 132.44, 131.07, 130.65, 128.64, 128.39, 126.75, 126.32, 126.08, 125.95, 125.22, 124.98, 114.71, 55.44, 52.69. HRMS (EI): calcd for C₂₂H₁₇O₂N₂Cl: 376.0979, found: 376.0977.

5-chloro-3-(2-naphthalene)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{27}). It was obtained as a yellow solid m.p. 156-157 °C in 88 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.38-8.35 (m, 1H) 7.97-7.95 (m, 1H), 7.87-7.81 (m, 3H), 7.52-7.48 (m, 2H), 7.33-7.30 (d, 2H, *J* = 8.22 Hz), 7.17 (s, 1H) 6.92-6.89 (d, 2H, *J* = 9.15 Hz), 5.08 (s, 2H), 3.79 (s, 3H). ¹³C NMR (75 MHz, CDCl₃): 160.16, 154.74, 151.66, 134.48, 133.02, 132.35, 130.68, 130.46, 129.67, 129.46, 127.81, 127.66, 126.75, 126.41, 126.32, 125.71, 125.10, 114.78, 55.47, 52.57. HRMS (EI): calcd for C₂₂H₁₇O₂N₂Cl: 376.0979, found: 376.0979.

5-chloro-3-(2-ethoxycarbonyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{28}). It was obtained as a yellow oil in 26 % yield. ¹H NMR (300 MHz, CDCl₃): δ 7.97-7.95 (d, 1H, *J* = 8.22 Hz), 7.617.52 (m, 3H), 7.32-7.29 (d, 2H *J* = 9.15 Hz), 6.90-6.87 (d, 2H, *J* = 9.12 Hz), 4.98 (s, 2H), 4.23-4.16 (q, 2H, *J* = 6.8 Hz), 3.79 (s, 3H), 1.43-1.38 (t, 3H, *J* = 7.29 Hz). ¹³C NMR (75 MHz, CDCl₃): 166.32, 160.13, 154.38, 150.72, 138.84, 131.86, 130.46, 129.24, 126.56, 126.29, 126.11, 114.71, 61.22, 55.41, 52.60, 14.40. HRMS (EI): calcd for C₂₁H₁₉O₄N₂Cl: 398.1033, found: 398.1028.

5-chloro-3-(4-ethoxycarbonyl)-1-(4-methoxybenzyl)-2(1H)-pyrazinone (3{29}). It was obtained as a yellow solid m.p. 117-118 °C in 90 % yield. ¹H NMR (300 MHz, CDCl₃): δ 8.48-8.45 (d, 2H, *J* = 8.22 Hz), 8.09-8.07 (d, 2H, *J* = 8.22 Hz), 7.32-7.29 (d, 3H, *J* = 9.15 Hz), 6.91-6.88 (d, 2H, *J* = 9.15 Hz), 5.06 (s, 2H), 4.42-4.35 (q, 2H, *J* = 6.8 Hz), 3.79 (s, 3H), 1.22-1.18 (t, 3H, *J* = 7.29 Hz). ¹³C NMR (75 MHz, CDCl₃): 167.05, 160.04, 157.60, 154.80, 135.98, 133.57, 131.47, 130.49,

130.31, 129.73, 129.52, 126.47, 125.47, 114.59, 61.25, 55.41, 52.30, 14.13. HRMS (EI): calcd for $C_{21}H_{19}O_4N_2Cl$: 398.1033, found: 398.1028.

5-chloro-1-(cyclohexyl)-3-(3-ethoxyphenyl)-2(1*H*)-pyrazinone (3{30}). It was obtained as a yellow oil in 90 % yield. 1H NMR (300 MHz, $CDCl_3$): δ 7.97 (s, 2H), 7.35-7.30 (t, 1H, $J=8.22$ Hz), 7.27(s, 1H), 7.00-6.97 (m, 1H), 4.84-4.81 (m, 1H), 4.13-4.06 (q, 2H, $J = 7.32$ Hz), 2.00-1.92 (m, 4H), 1.80-1.76 (m, 1H), 1.54-1.39 (m, 7H), 1.27-1.20 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): 158.76, 154.04, 151.45, 136.43, 129.12, 126.75, 122.39, 121.93, 117.73, 114.78, 63.69, 55.38, 32.25, 25.74, 25.34, 14.95. HRMS (EI): calcd for $C_{18}H_{21}O_2N_2Cl$: 332.1292, found: 332.1300.

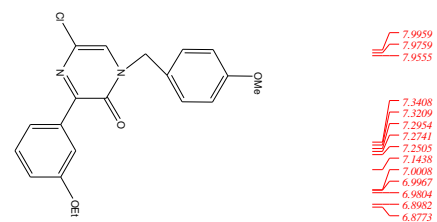
5-chloro-1-(cyclohexylmethyl)-3-(3-ethoxyphenyl)-2(1*H*)-pyrazinone (3{31}). It was obtained as a yellow solid m.p. 79-80 °C in 89 % yield. 1H NMR (300 MHz, $CDCl_3$): δ 7.99-7.97 (m, 2H), 7.35-7.30 (t, 1H, $J = 8.22$ Hz), 7.27(s, 1H), 7.01-6.97 (m, 1H), 4.13-4.061 (q, 2H, $J = 6.42$ Hz), 3.78-3.76 (d, 2H, $J = 7.32$ Hz), 1.91-1.85 (m, 1H), 1.72-1.69 (m, 6H), 1.44-1.39 (t, 4H, $J = 7.29$ Hz), 1.25-1.21 (m, 2H), 1.06-0.99 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): 158.76, 154.56, 151.76, 136.22, 129.12, 126.62, 125.95, 121.90, 117.70, 114.81, 63.66, 56.93, 36.76, 30.64, 26.19, 25.61, 14.92. HRMS (EI): calcd for $C_{19}H_{23}O_2N_2Cl$: 346.1448, found: 346.1450.

5-chloro-3-(3-ethoxyphenyl)-1-(3-phenylpropyl)-2(1*H*)-pyrazinone (3{32}). It was obtained as a yellow oil in 92 % yield. 1H NMR (300 MHz, $CDCl_3$): δ 7.98-7.95 (m, 1H), 7.36-7.18 (m, 7H), 7.12(s, 1H), 7.02-6.98 (m, 1H), 4.14-4.07 (q, 2H, $J = 7.32$ Hz), 3.99-3.94 (t, 2H, $J = 7.29$ Hz), 2.76-2.71 (t, 4H, $J = 7.29$ Hz), 2.21-2.11 (p, 2H, $J = 7.29$ Hz), 1.45-1.40 (t, 2H, $J = 7.29$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 158.76, 154.38, 151.69, 140.15, 136.13, 129.15, 128.73, 128.36, 126.50, 126.29, 126.05, 121.87, 117.73, 114.78, 63.66, 50.41, 32.88, 29.76, 14.92. HRMS (EI): calcd for $C_{21}H_{21}O_2N_2Cl$: 368.1291, found: 368.1288.

1-benzyl-5-chloro-3-(3-ethoxyphenyl)-6-methyl-2(1*H*)-pyrazinone (3{33}). It was obtained as a yellow solid m.p. 135-136 °C in 91 % yield. 1H NMR (300 MHz, $CDCl_3$): δ 8.01-7.99 (m, 2H), 7.36-7.31 (m, 4H), 7.26-7.25 (m, 2H), 6.99-6.97 (d, 1H, $J = 7.29$ Hz), 5.40 (s, 2H), 4.13-4.06 (q, 2H, $J = 7.32$ Hz), 2.44 (s, 3H), 1.44-1.39 (t, 2H, $J = 7.29$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 158.82, 155.47, 148.34, 136.43, 135.09, 134.76, 129.18, 128.09, 126.81, 126.62, 121.66, 119.65, 117.24, 114.62, 63.66, 49.10, 17.21, 14.95. HRMS (EI): calcd for $C_{20}H_{19}O_2N_2Cl$: 354.1135, found: 354.1132.

5-chloro-3-(3-ethoxyphenyl)-1,6-dimethyl-2(1*H*)-pyrazinone (3{34}). It was obtained as a yellow solid m.p. 155-156 °C in 94 % yield. 1H NMR (300 MHz, $CDCl_3$): δ 7.94 (s, 1H), 7.35-7.30 (t, 1H, $J = 8.22$ Hz), 7.26(s, 1H), 6.98-6.96 (d, 1H, $J = 7.29$ Hz), 4.14-4.07 (q, 2H, $J = 7.32$ Hz), 3.64 (s, 3H), 2.5 (s, 3H), 1.45-1.40 (t, 2H, $J = 7.29$ Hz). ^{13}C NMR (75 MHz, $CDCl_3$): 158.73, 155.32, 147.28, 136.43, 135.15, 129.06, 126.11, 121.48, 117.03, 114.41, 63.57, 32.86, 17.39, 14.92. HRMS (EI): calcd for $C_{14}H_{15}O_2N_2Cl$: 278.0822, found: 278.0824.

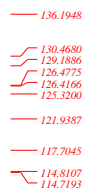
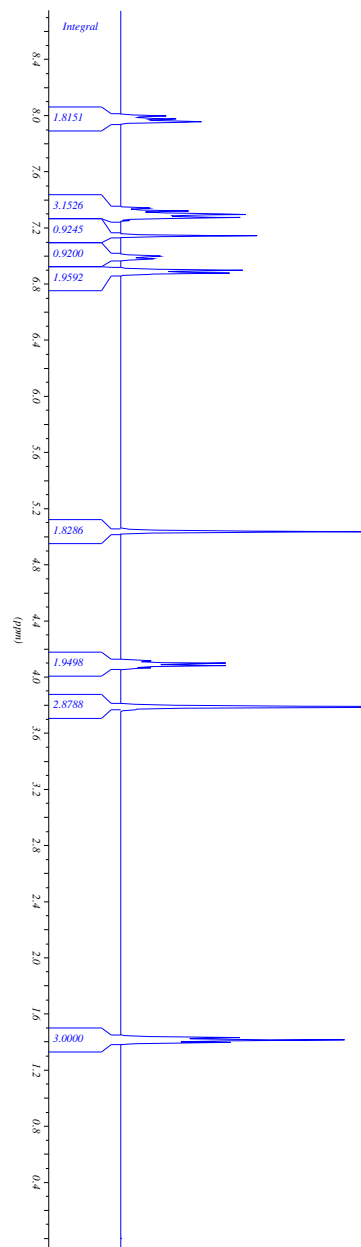
¹H and ¹³C spectra for compound 3 {1}



5.0351



0.0005

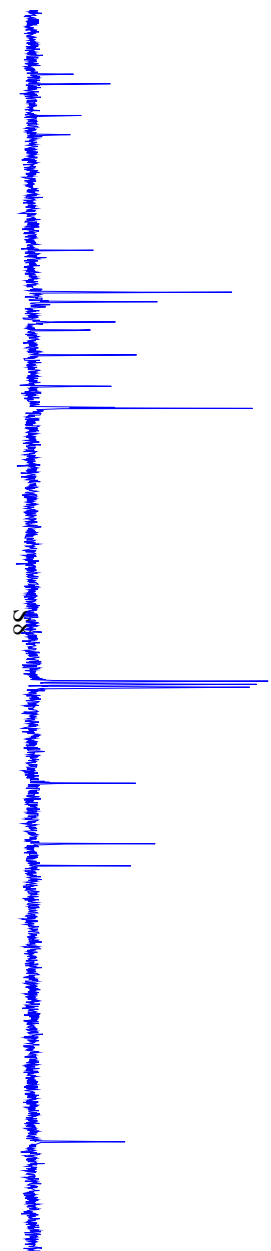
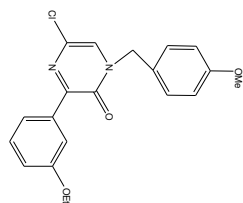


63.6655

55.4408

52.4556

14.9267



¹H and ¹³C spectra for compound 3{2}

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8.6033

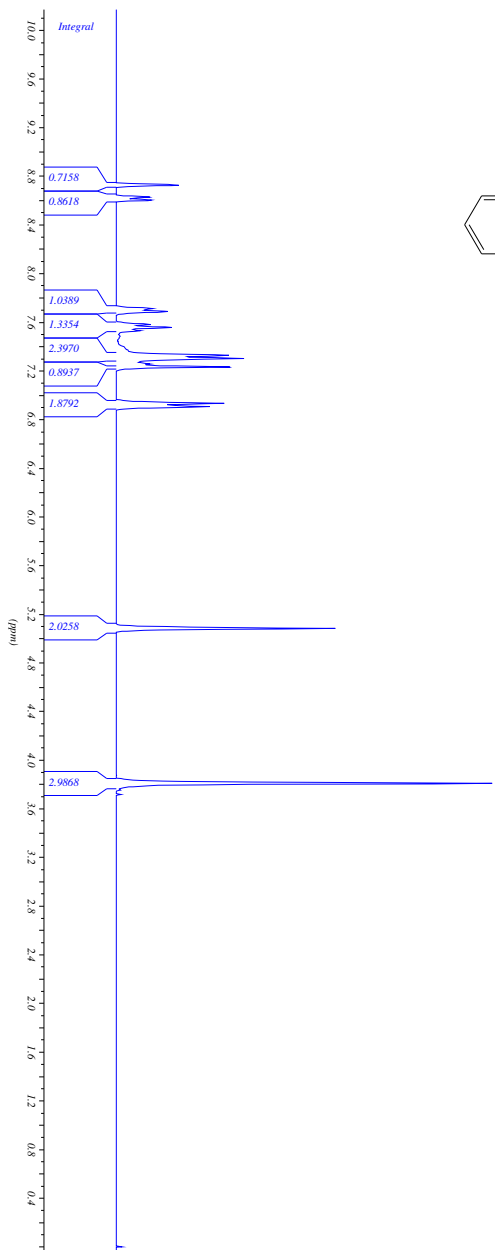
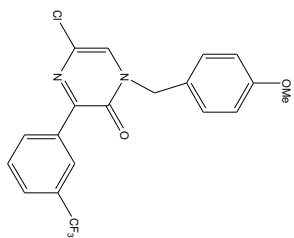
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7.5317

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5.0810

3.8085

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160.3514

154.4140

150.3496

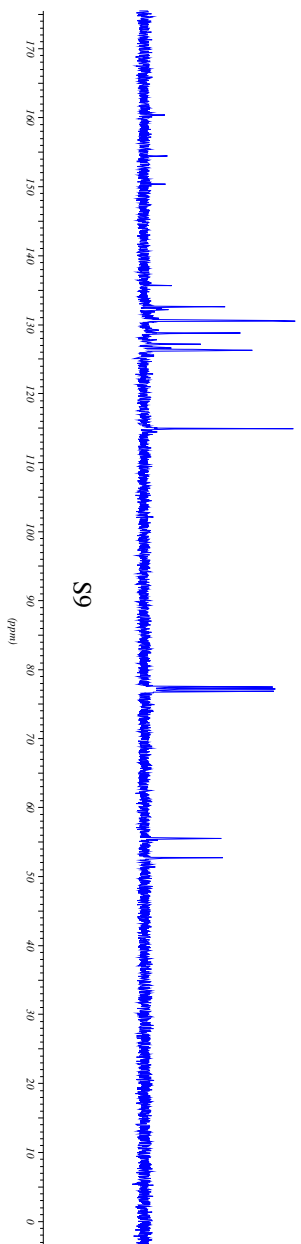
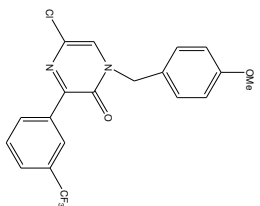
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114.8847

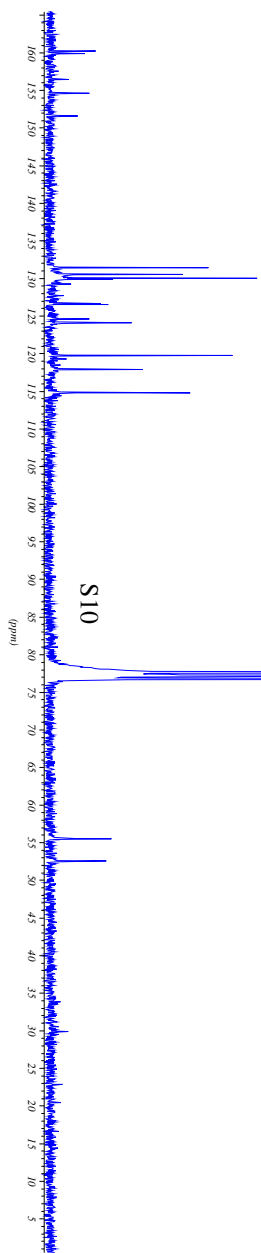
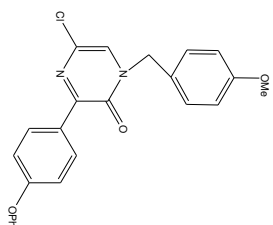
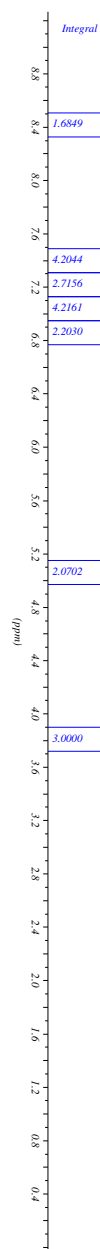
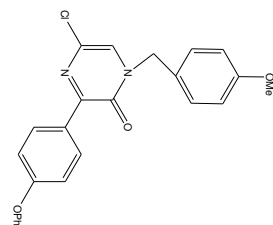
77.4785
77.1600
76.8491

55.4731

52.6522



¹H and ¹³C spectra for compound 3 {3}



¹H and ¹³C spectra for compound 3 (4)

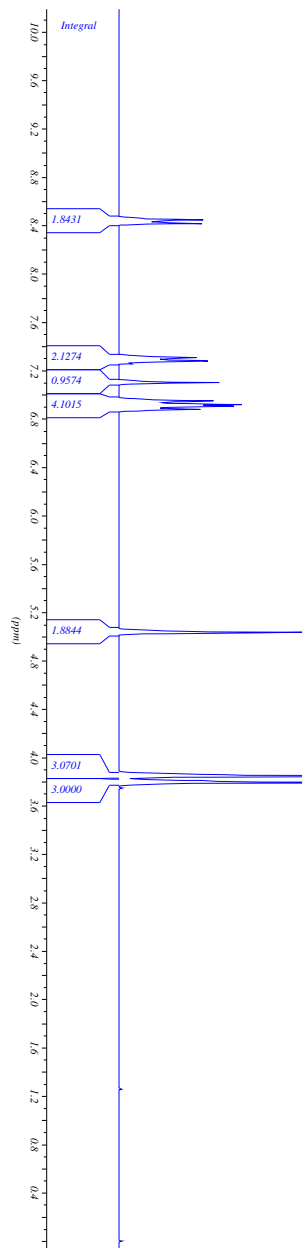
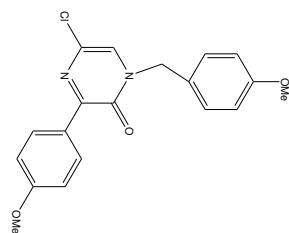
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7.3064
7.2790
7.1025
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6.9076
6.8802

5.0253

3.8481
3.7933

-0.0000

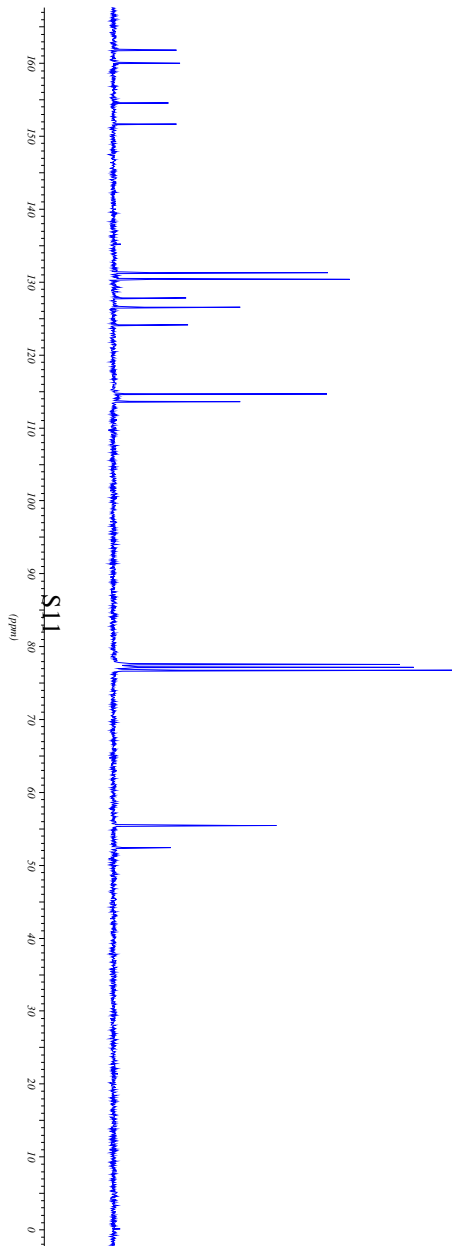
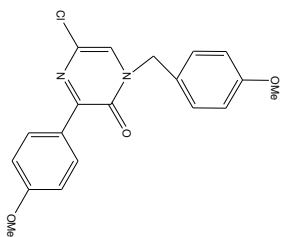


161.7826
160.0158
154.5327
151.6084

131.2600
130.3766
127.7569
126.5384
124.0710

77.5560
77.1600
76.7335

55.4104
52.3642



¹H and ¹³C spectra for compound 3{5}

8.3659
8.3506
8.3385

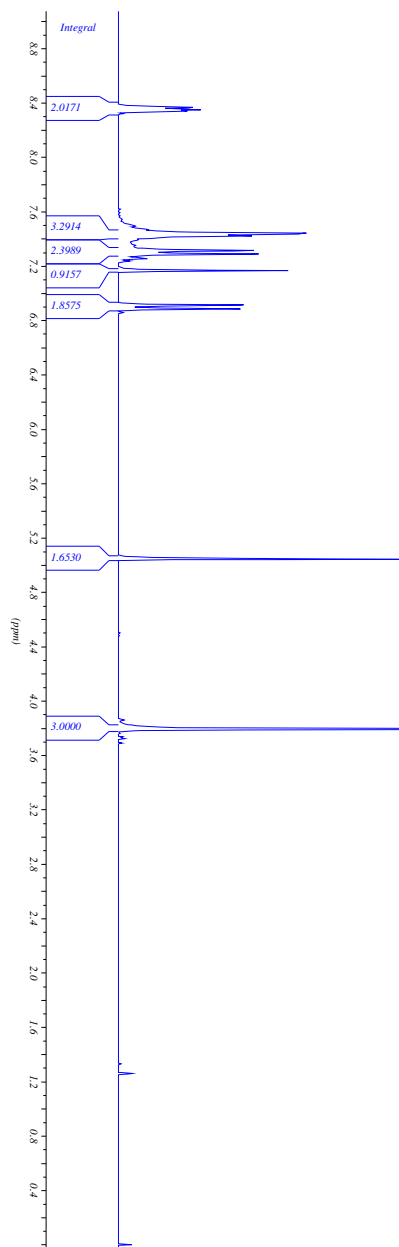
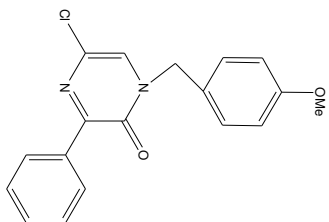
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7.2882
7.1664

6.9137
6.8833

5.0445

3.7933

-0.0000



160.1072

154.5023

152.2481

134.9459

131.2600

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130.4680

128.5794

128.2138

126.5689

126.3537

125.2286

114.6888

114.2928

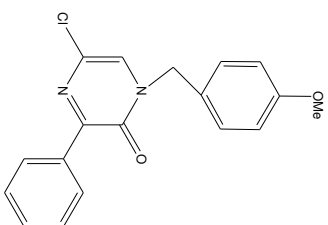
77.5865

77.1600

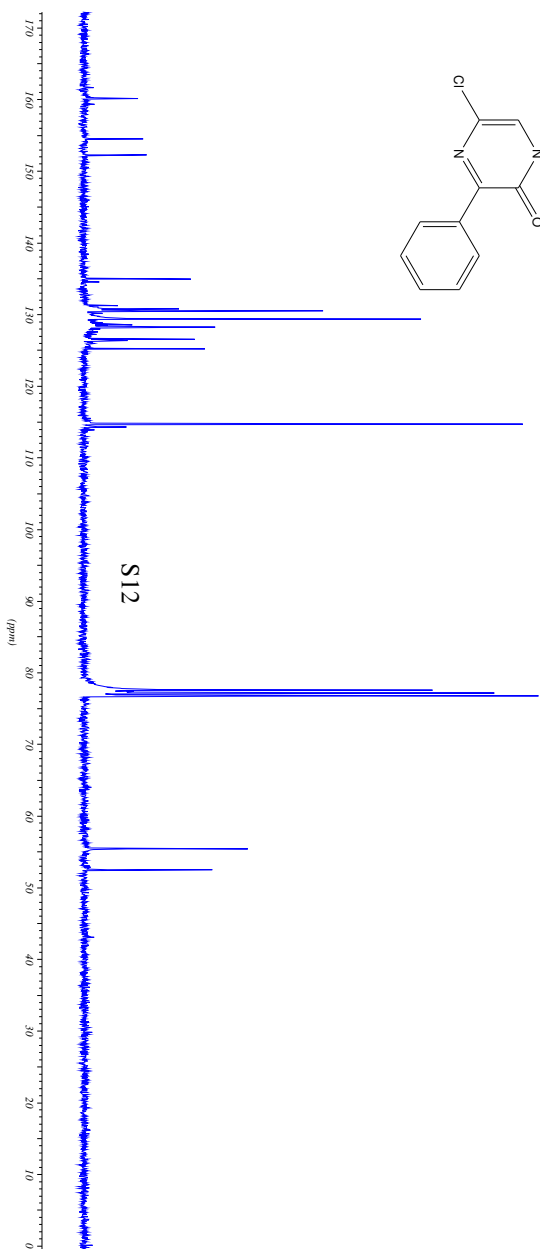
76.7335

55.4104

52.4860



S12



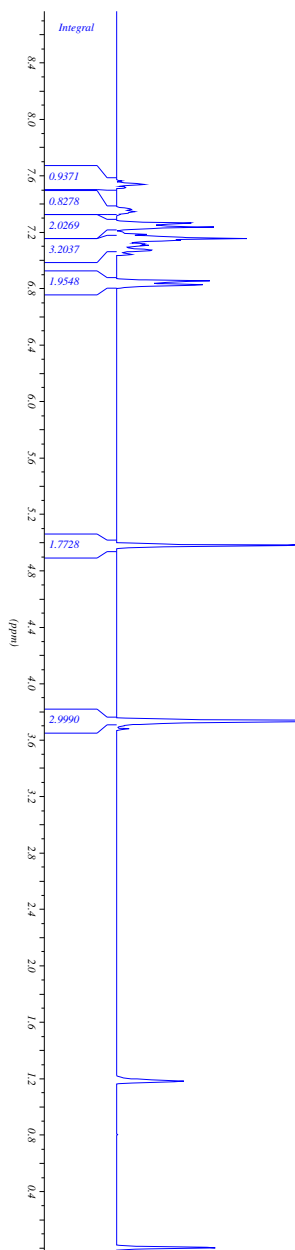
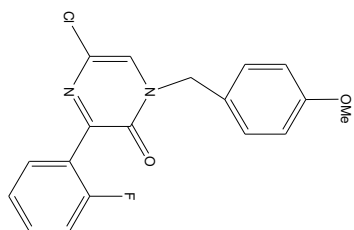
¹H and ¹³C spectra for compound 3{6}

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7.1055
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6.8254

4.9806

3.7354

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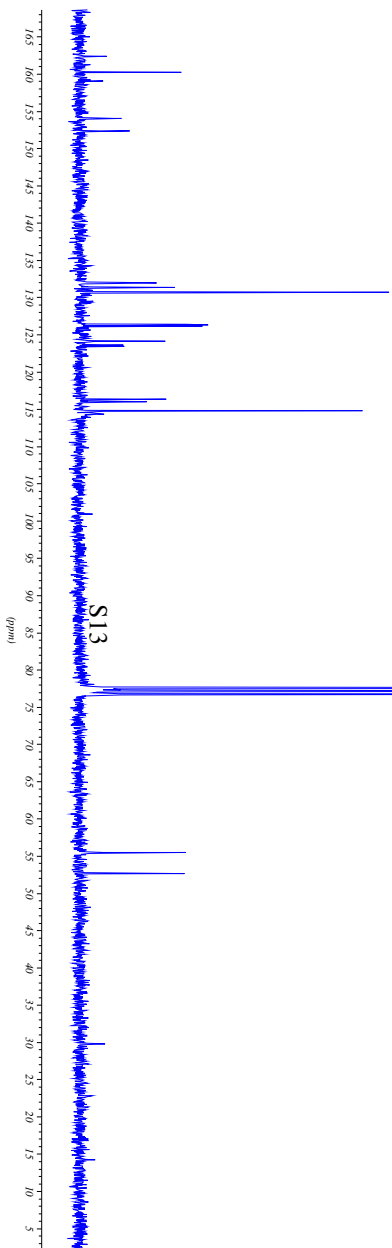
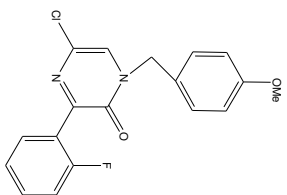


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159.0411
154.0149
152.3395

132.0215
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126.1120
124.1624
124.1015
123.6141
123.4513
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116.0291
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77.5865
77.1600
76.7335

55.4713
52.6688



¹H and ¹³C spectra for compound 3 {7}

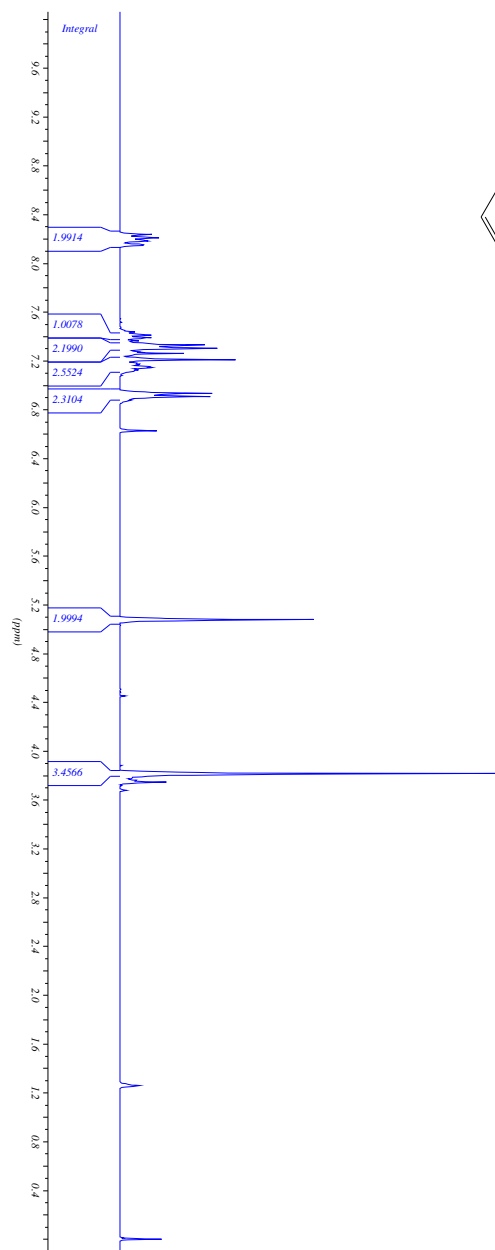
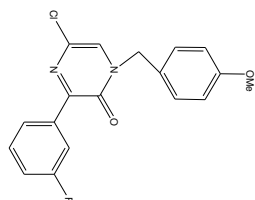
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7.2090
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6.9076

5.0780

3.8146

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164.2500
161.0211
160.2291

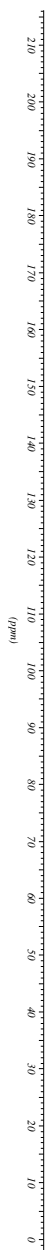
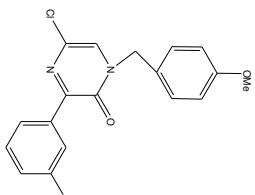
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136.8954
130.5594
129.6455
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125.8987
125.1372

117.8264
117.5522
116.4556
116.1510
114.8107
114.3842

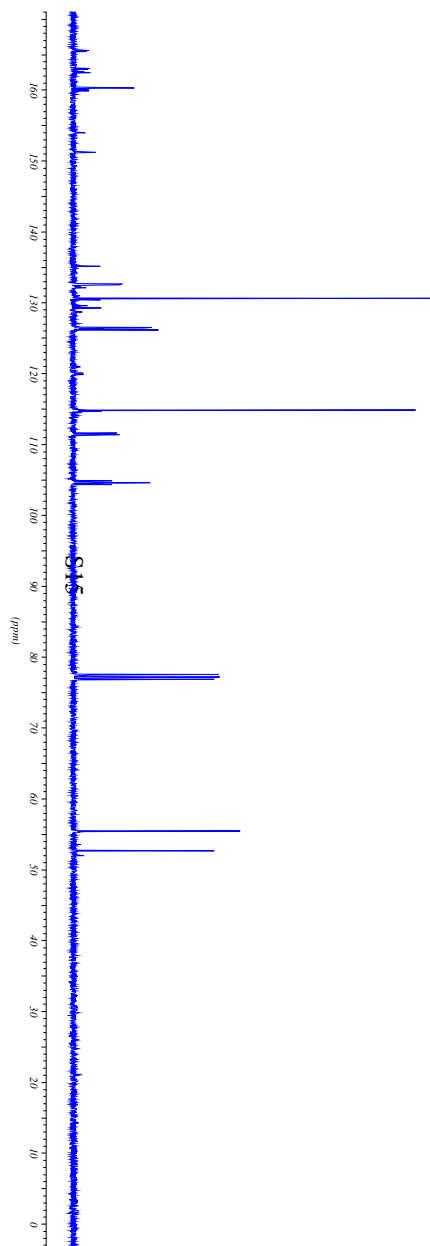
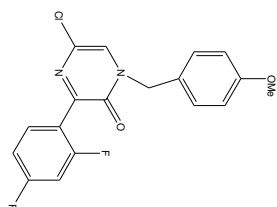
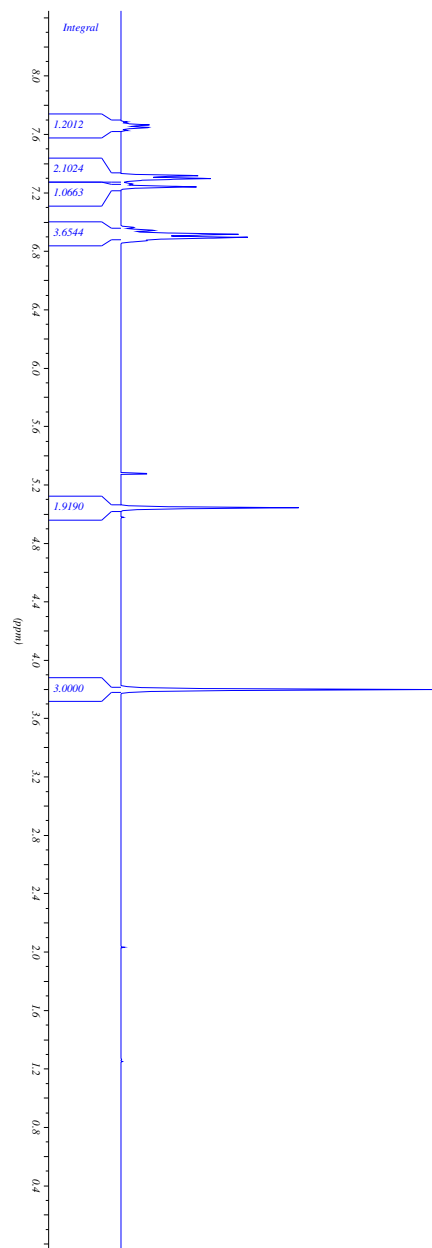
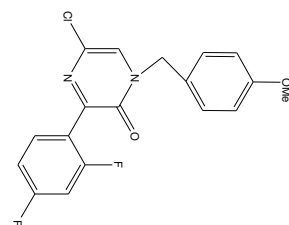
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76.7335

55.5017
52.6383

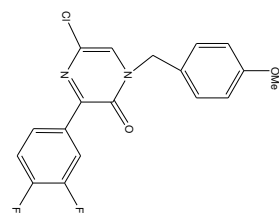


S14

¹H and ¹³C spectra for compound 3{8}



¹H and ¹³C spectra for compound 3{9}



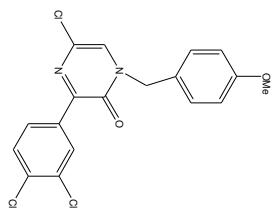
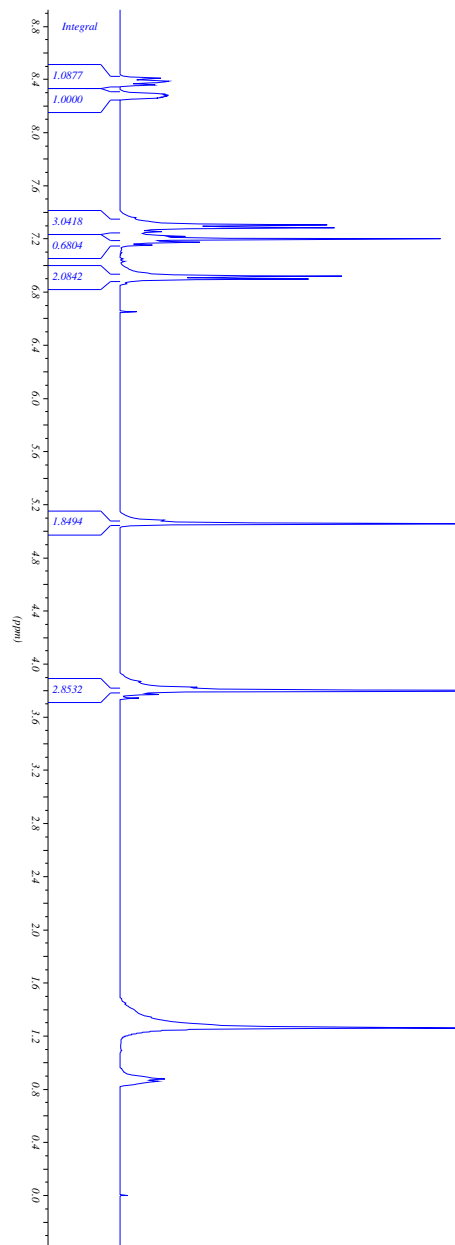
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8.2674

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7.2541
7.2192
7.1983
7.1738
7.1520
6.9168
6.8955

5.0546

3.7989

-0.0005



160.2291
159.9549
154.2890
153.8016
153.6189
151.6693
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148.4099
148.2272

131.9301
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131.7778
130.4984

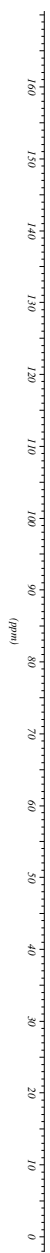
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125.8987

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116.8516
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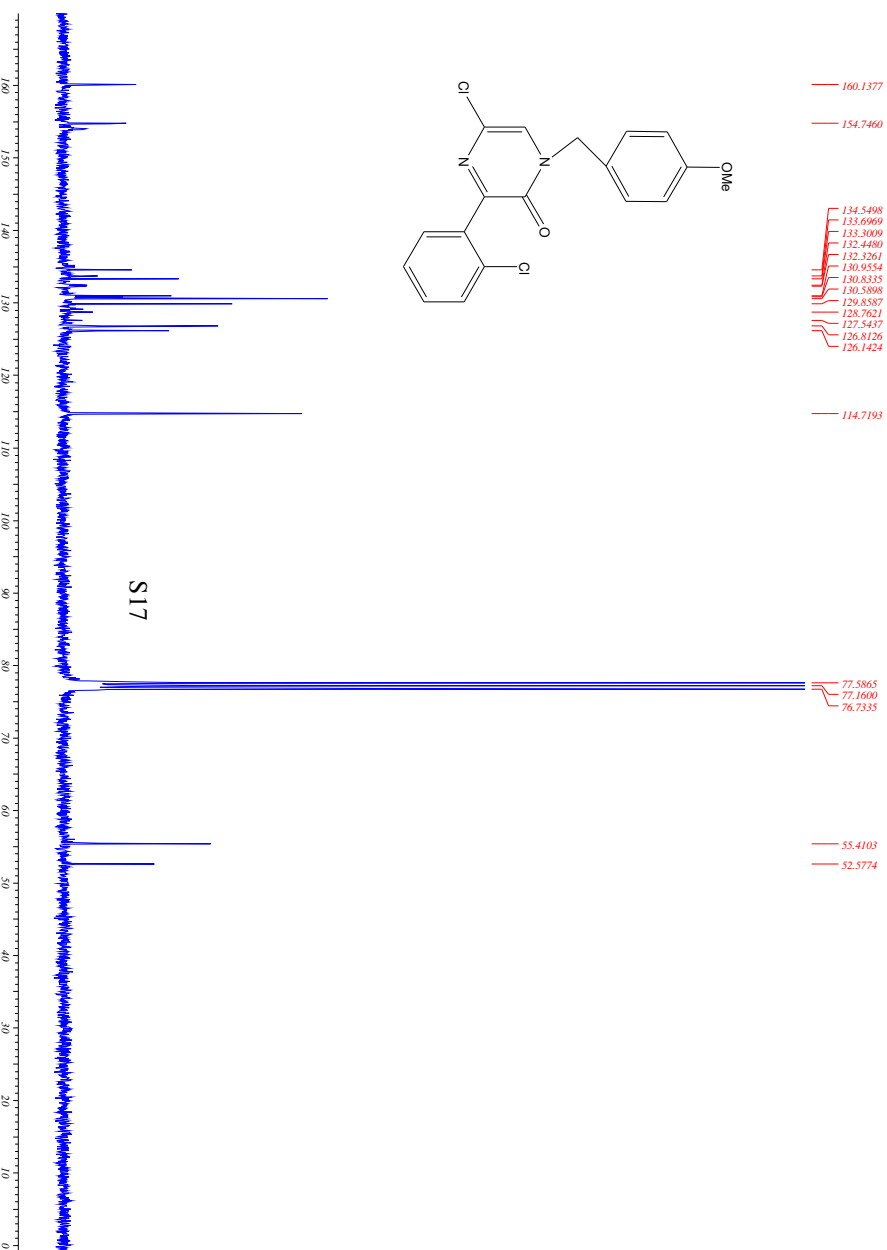
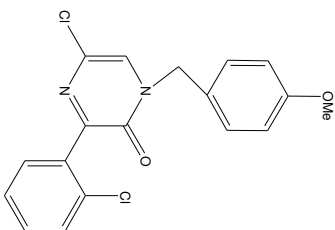
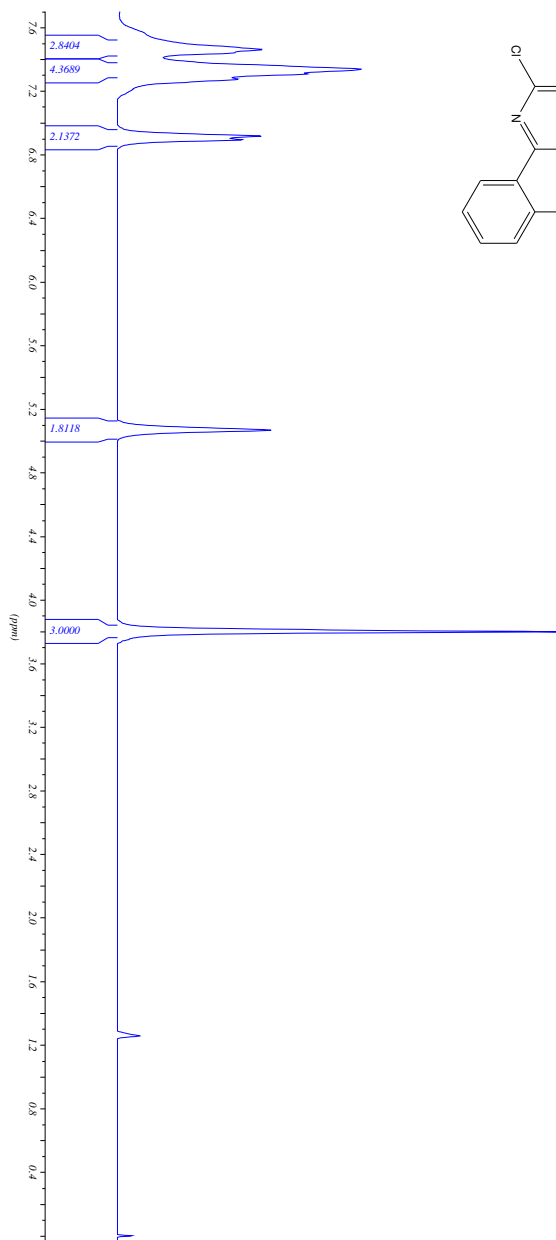
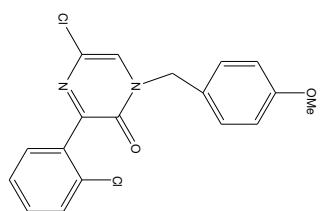
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76.7335

55.4408
52.6688

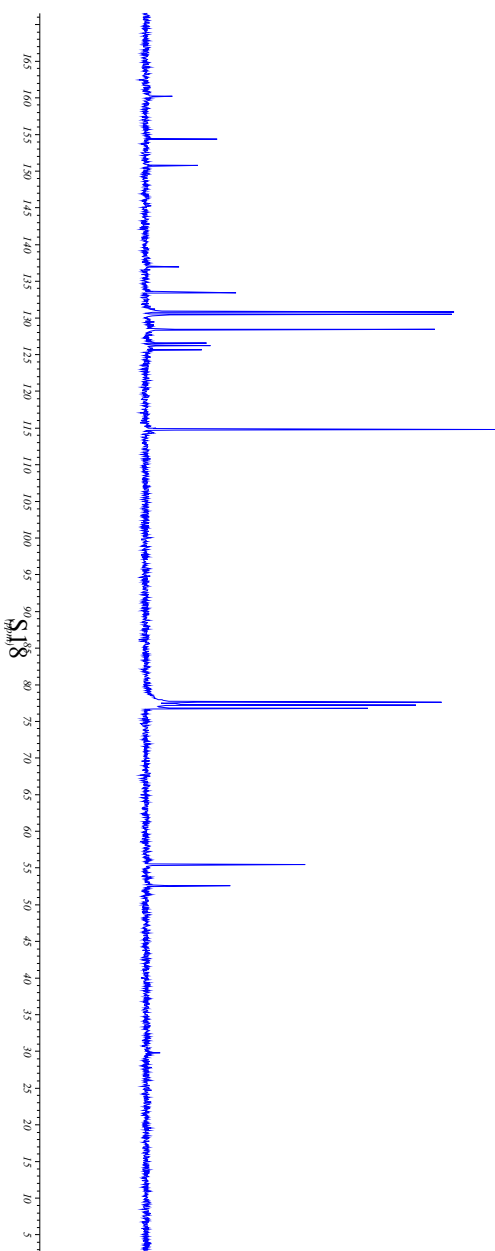
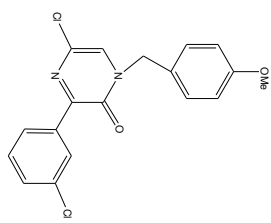
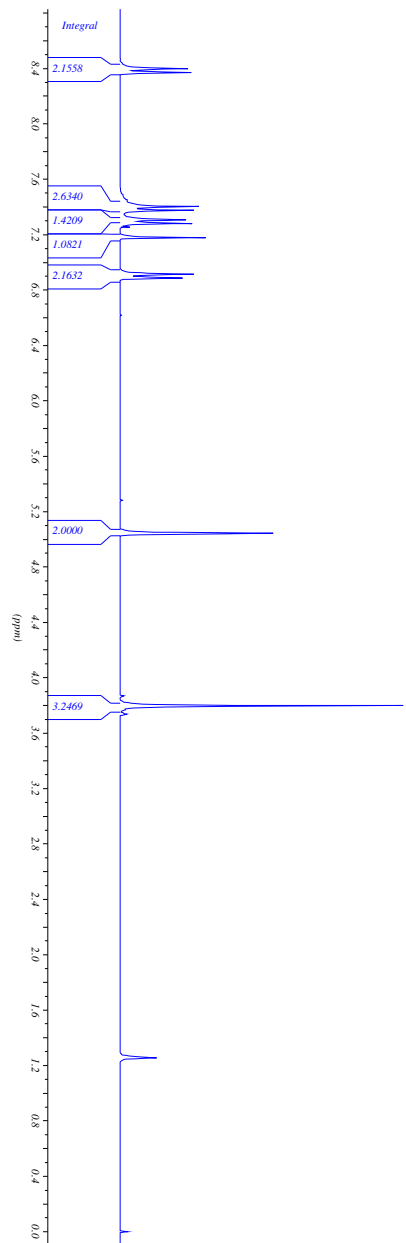
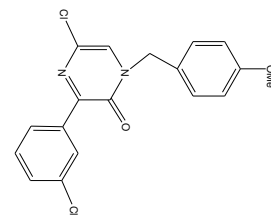
S16



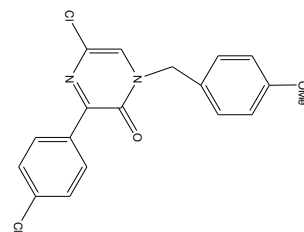
¹H and ¹³C spectra for compound 3 {10}



¹H and ¹³C spectra for compound 3 {11}



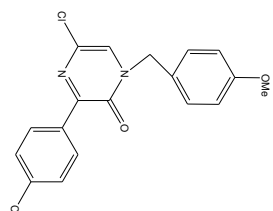
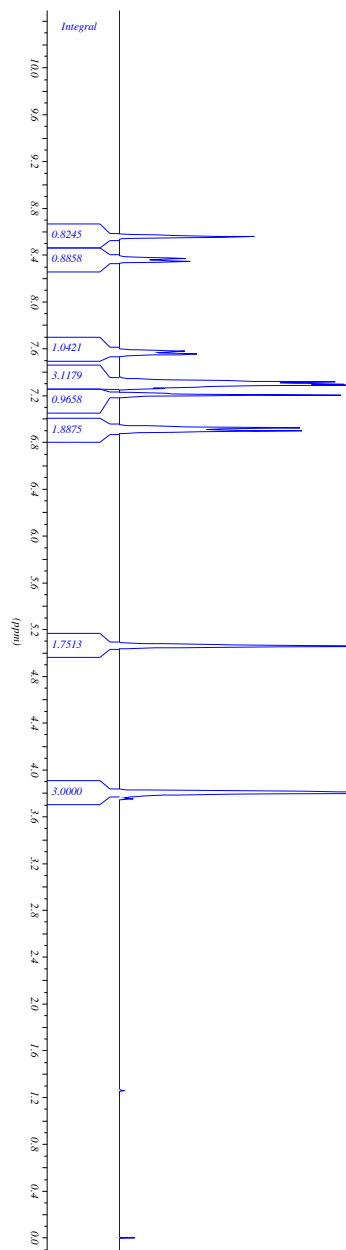
¹H and ¹³C spectra for compound 3 {12}



5.0567

3.8054

0.0000



160.1681

154.2890

150.3595

136.5299

134.2452

130.6508

130.4680

129.4323

129.2191

127.4827

126.4775

126.1120

125.9901

114.7497

77.5560

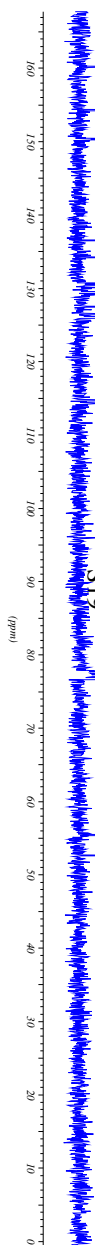
77.1600

76.7335

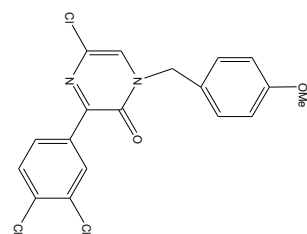
55.4408

52.6079

S19



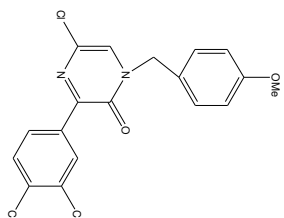
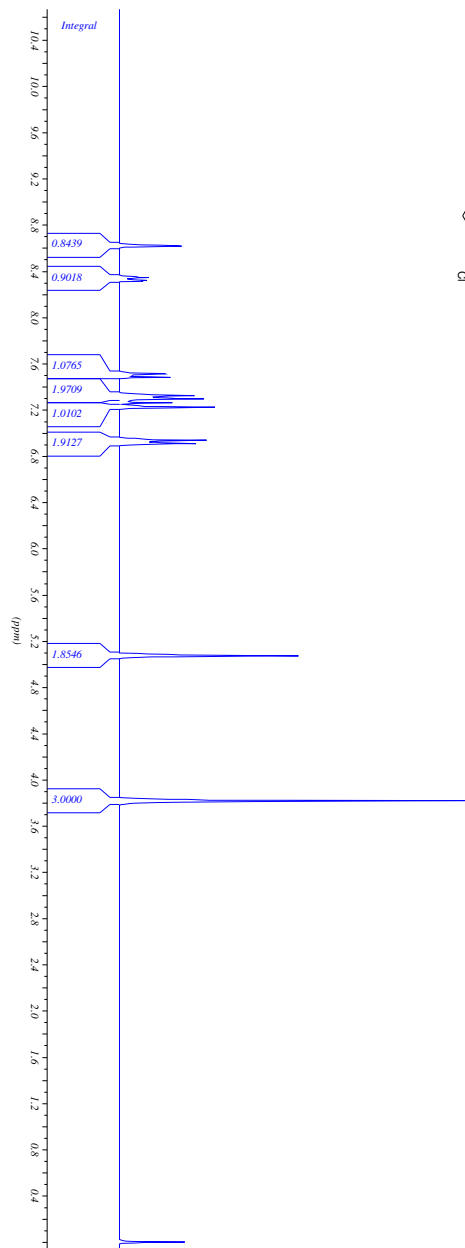
¹H and ¹³C spectra for compound 3 {14}



5.0749

3.8176

-0.0000



¹³C NMR peaks (ppm):

- 160.2900
- 154.2890
- 149.2933

¹³C NMR peaks (ppm):

- 135.0068
- 134.7326
- 132.6003
- 131.1381
- 130.5289
- 130.1938
- 128.5794
- 126.5689
- 126.2033
- 126.0206

114.8411

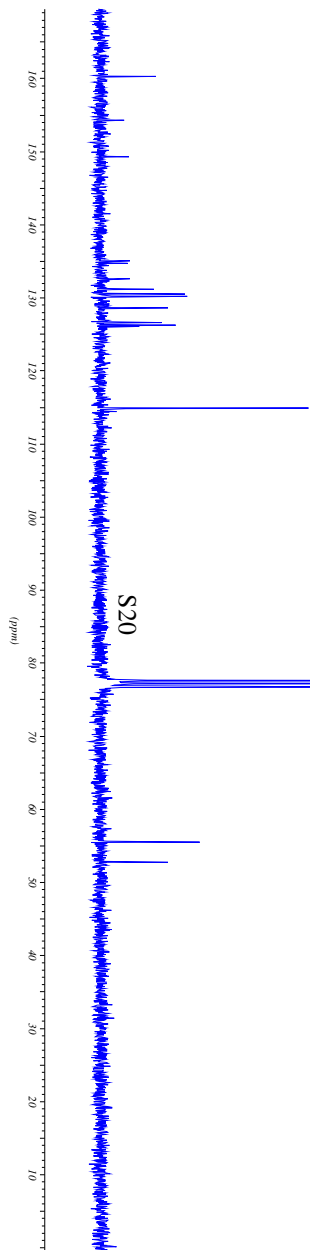
77.5865

77.1600

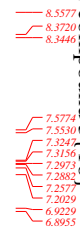
76.7335

55.5017

52.7297



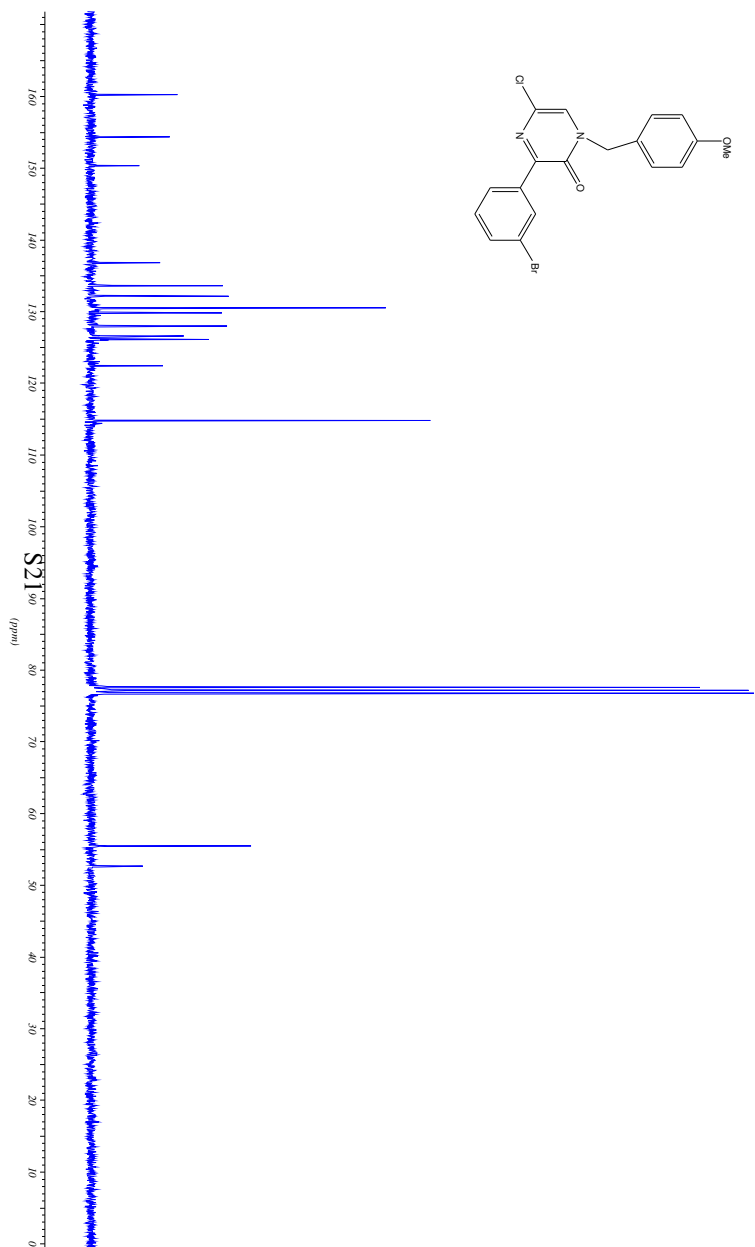
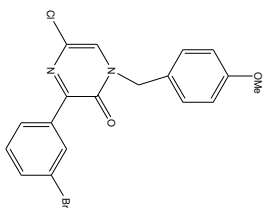
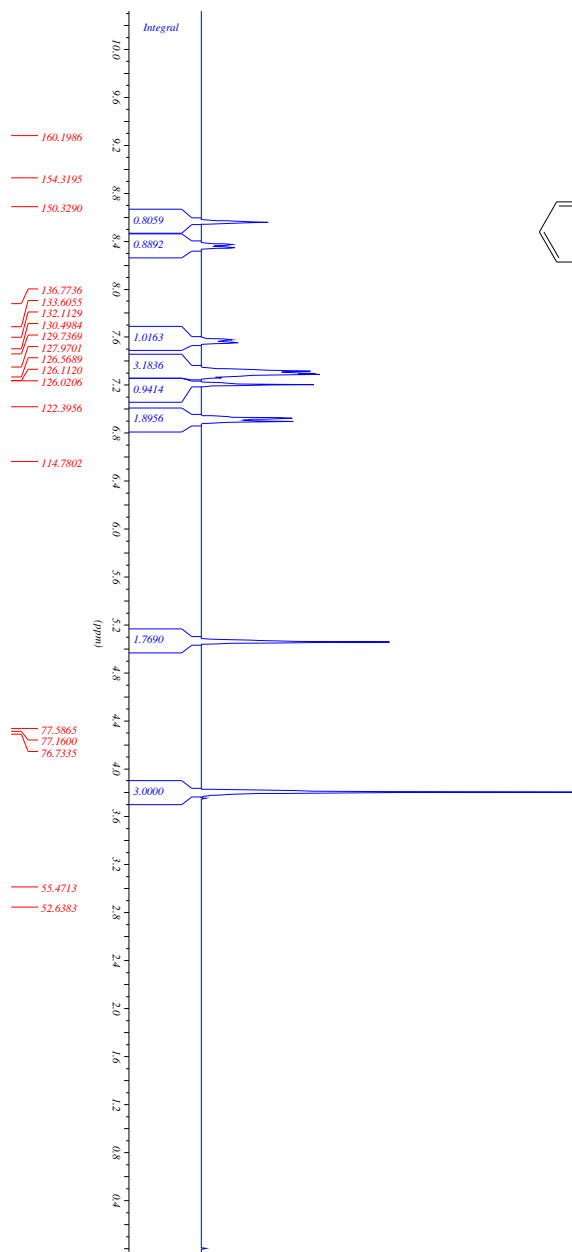
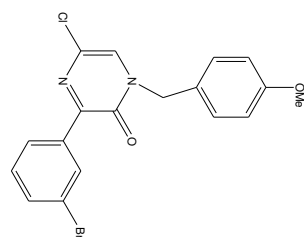
¹H and ¹³C spectra for compound 3 (16)



5.0567

3.8054

0.0000



¹H and ¹³C spectra for compound 3{17}

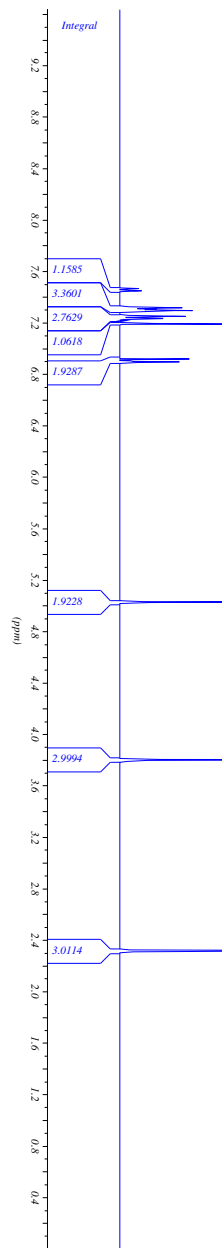
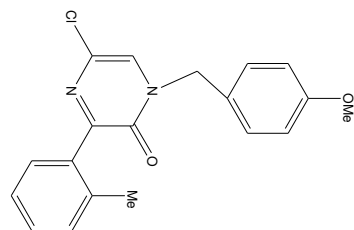
7.4657
7.4471
7.4173
7.3127
7.3063
7.2963
7.2909
7.2509
7.2332
7.1924
6.9173
6.8955

5.0296

3.8030

2.3185

0.0005



160.2756
157.0832
154.4671

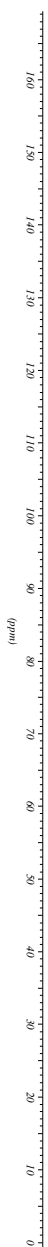
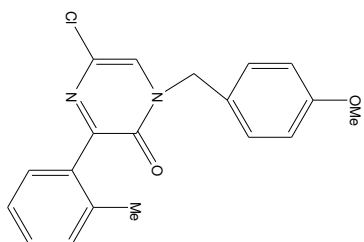
137.2010
134.9565
130.7404
130.5584
129.7016
126.5016
126.1755
125.6144

114.8088

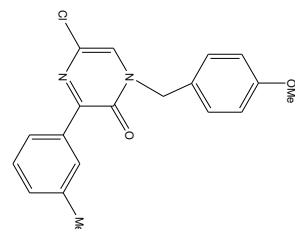
77.4785
77.1600
76.8415

55.4655
52.5764

20.1143



¹H and ¹³C spectra for compound 3 {18}



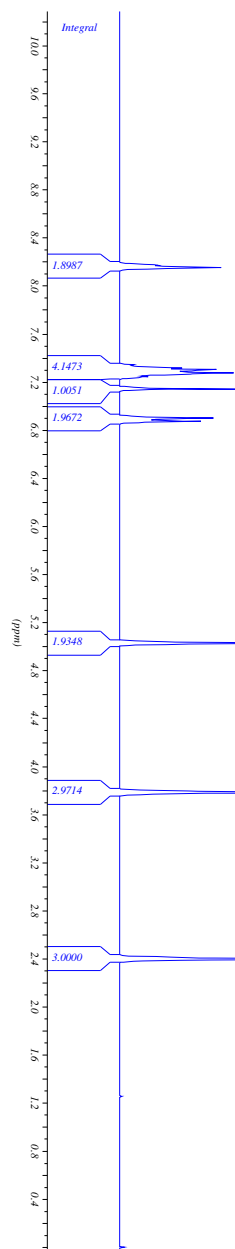
8.1710
8.1528
7.3430
7.3156
7.3034
7.2973
7.2760
7.2669
7.2455
7.1420
6.9015
6.8711

5.0262

3.7841

2.3989

0.0000



160.0463
154.4718
152.4613

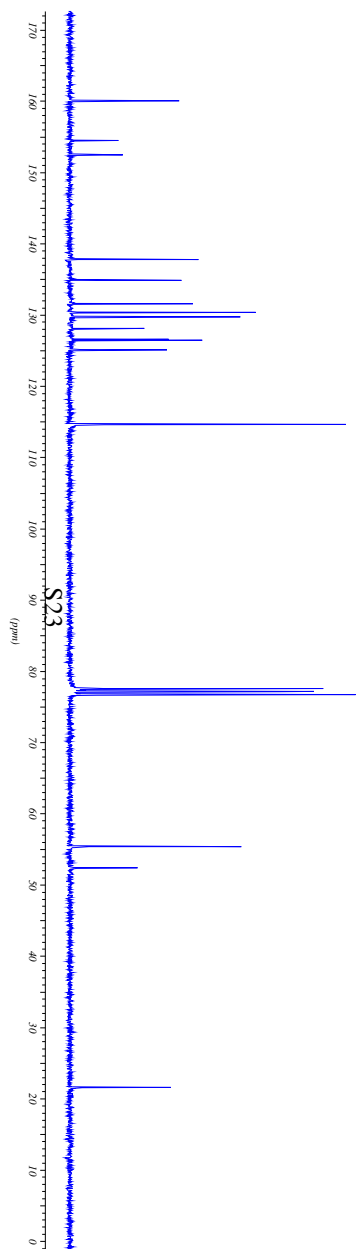
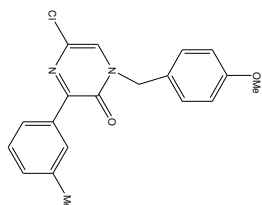
137.7788
134.8849
131.5646
130.3766
129.7674
128.0615
126.5903
126.4166
125.1067

114.6279

77.5560
77.1600
76.7335

55.3799
52.3946

21.5674



¹H and ¹³C spectra for compound 3 {19}

8.3111
8.2837

7.3186
7.2882
7.2516
7.2242
7.1299

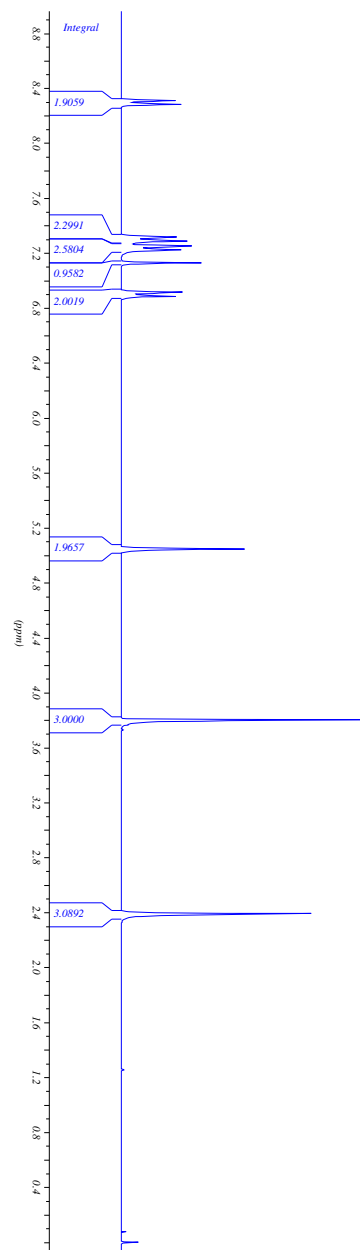
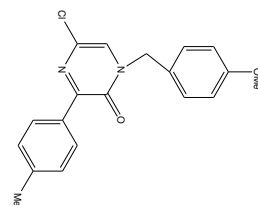
6.9168
6.8863

5.0475

3.8024

2.3929

-0.0000



160.1377

154.5937

152.3090

141.2210

132.3261

130.4680

129.4018

129.0058

126.5689

124.7107

114.7193

77.5865

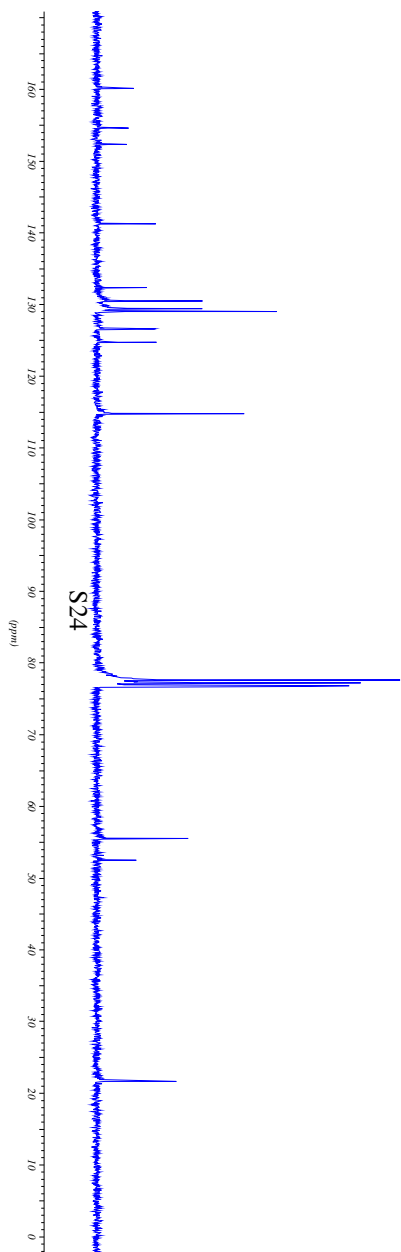
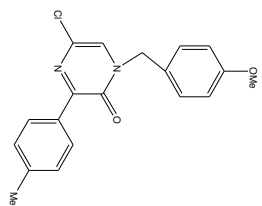
77.1600

76.7640

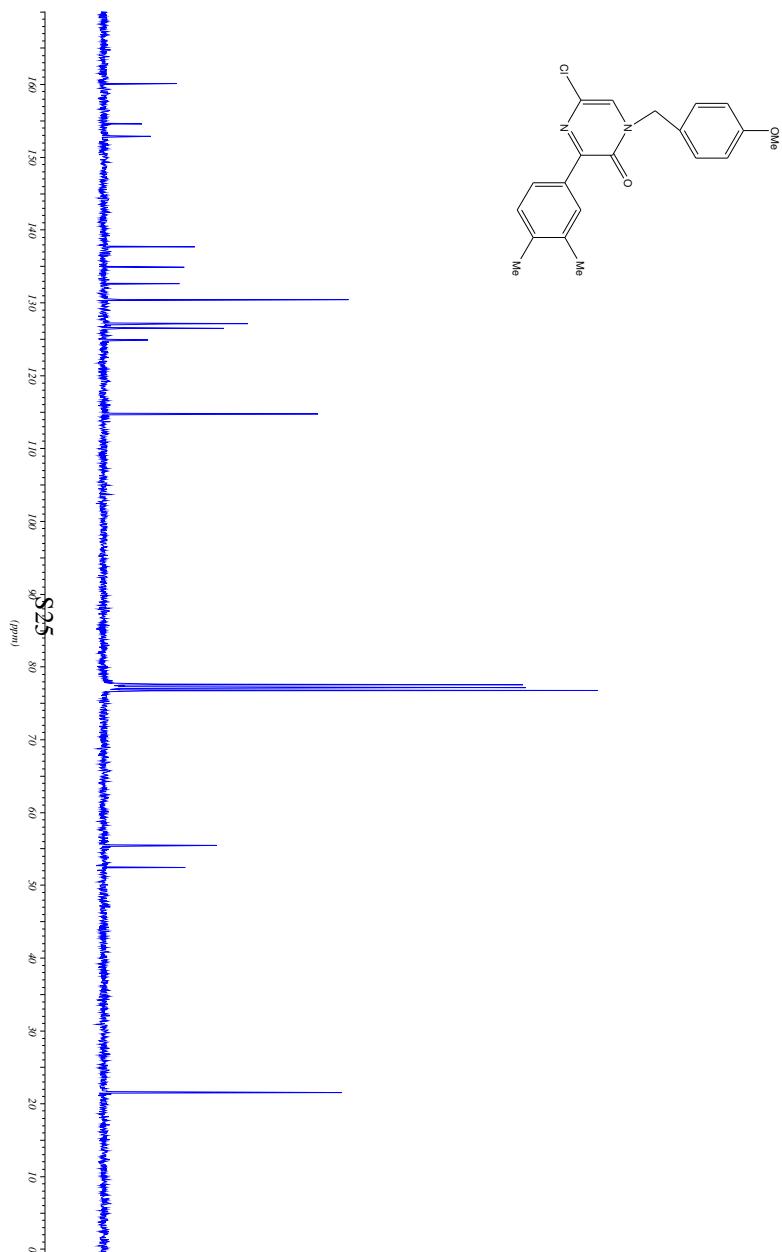
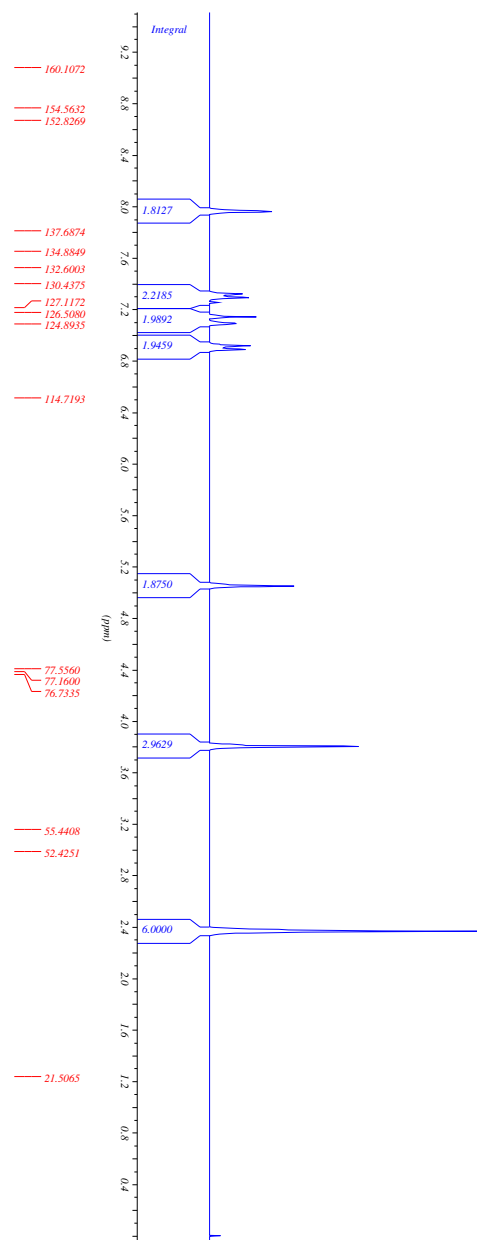
55.4713

52.4556

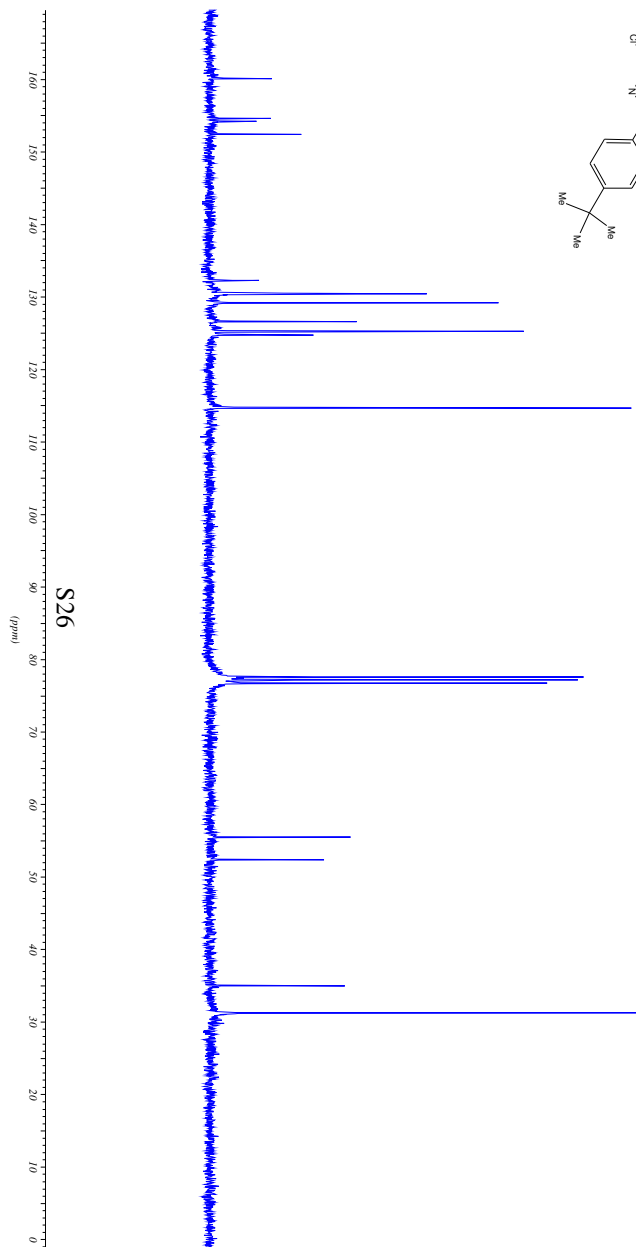
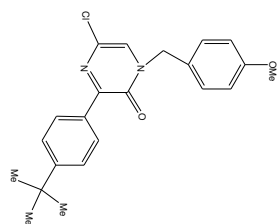
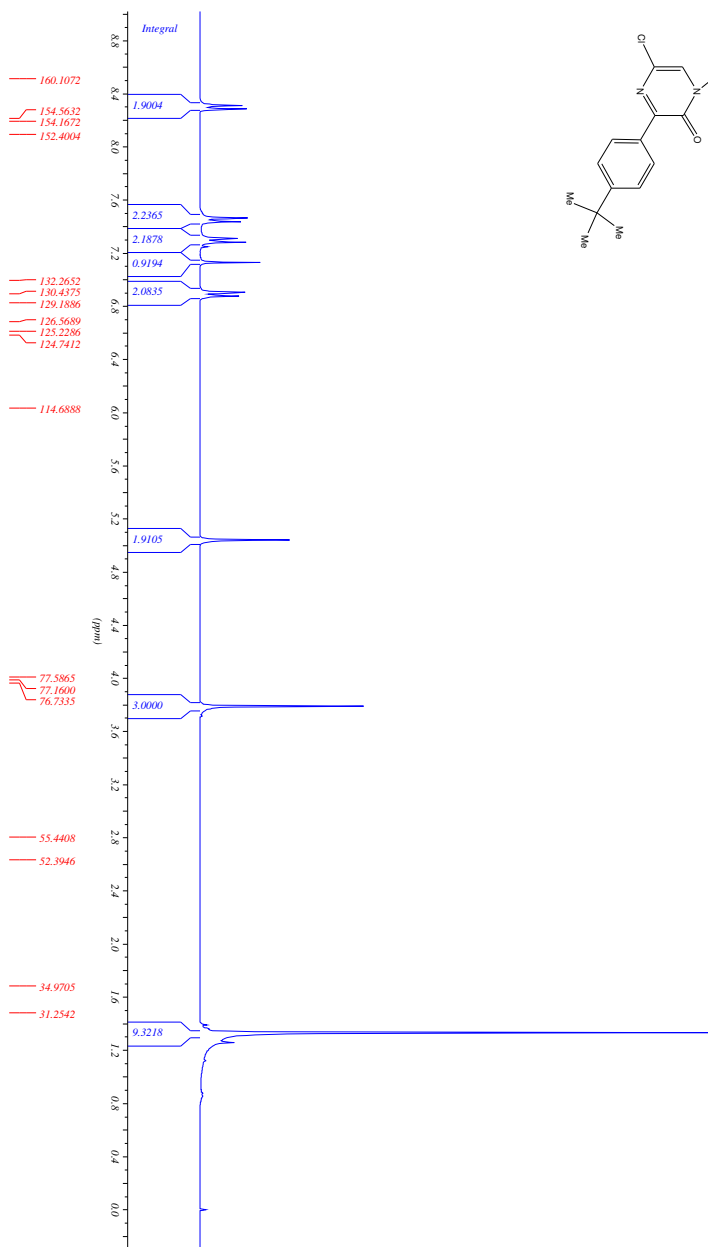
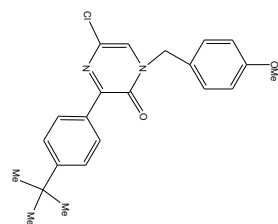
21.6588



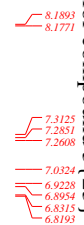
¹H and ¹³C spectra for compound 3 {20}



¹H and ¹³C spectra for compound 3{21}



¹H and ¹³C spectra for compound 3 {23}

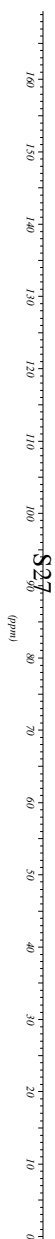
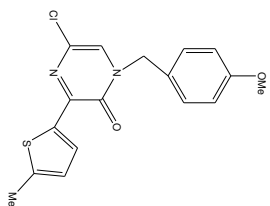
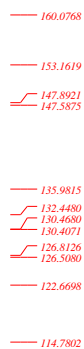
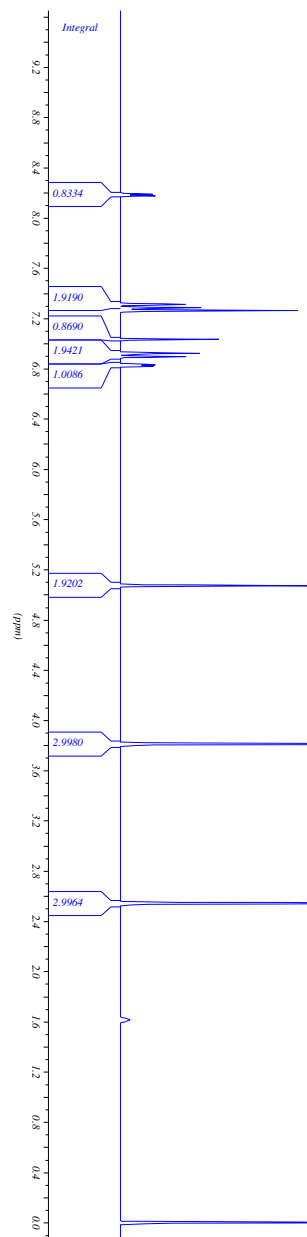
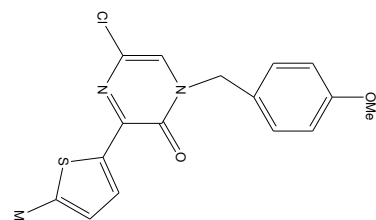


5.0719

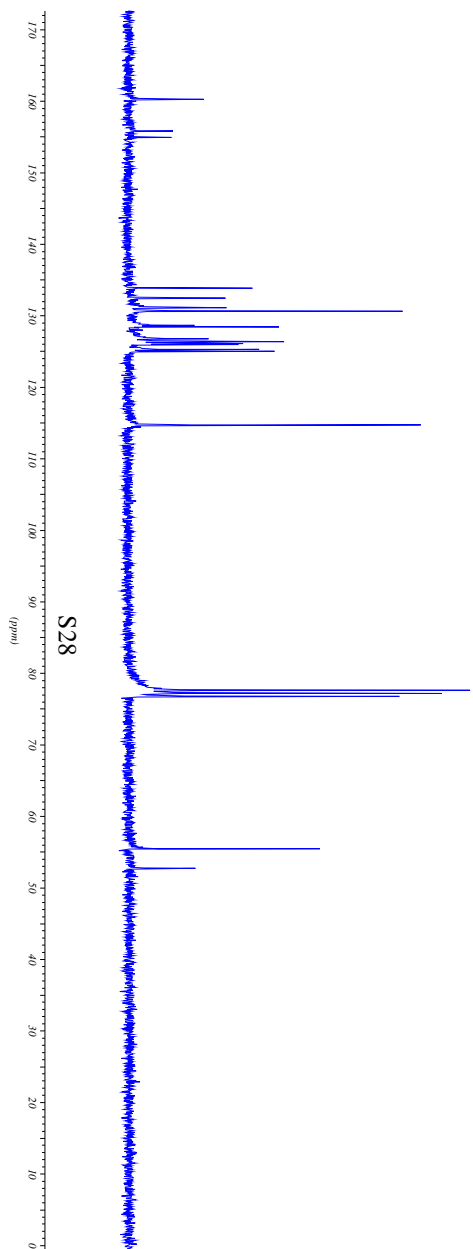
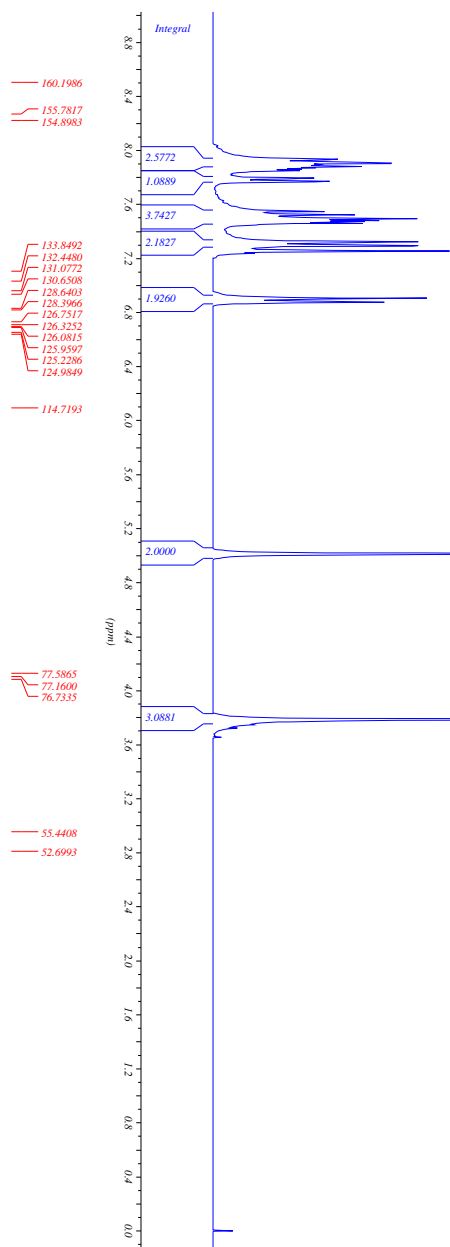
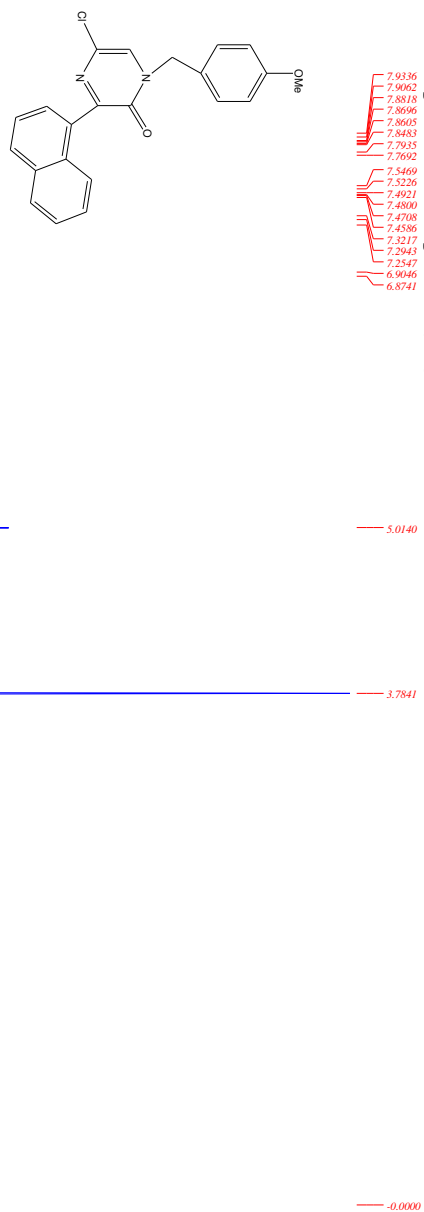
3.8115

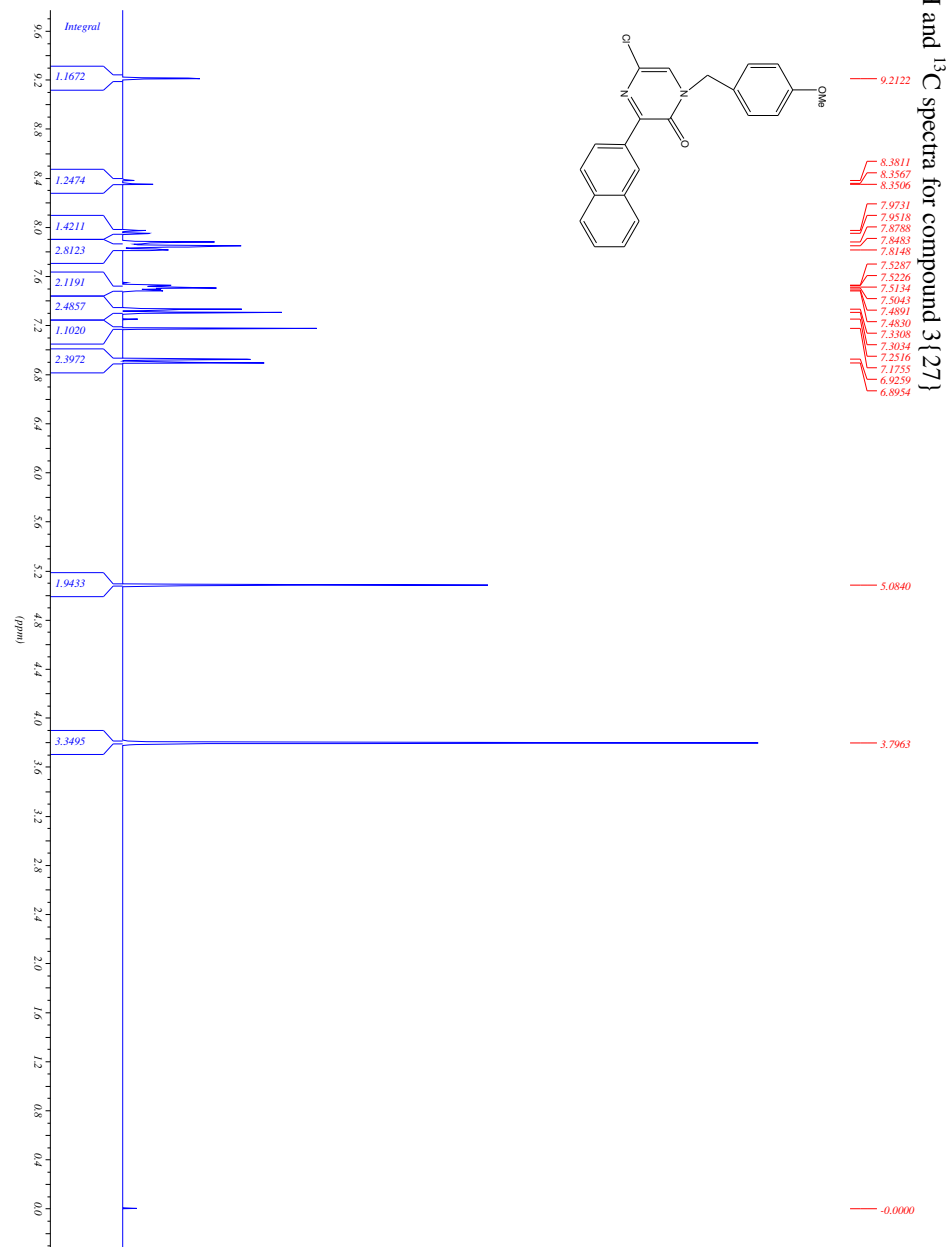
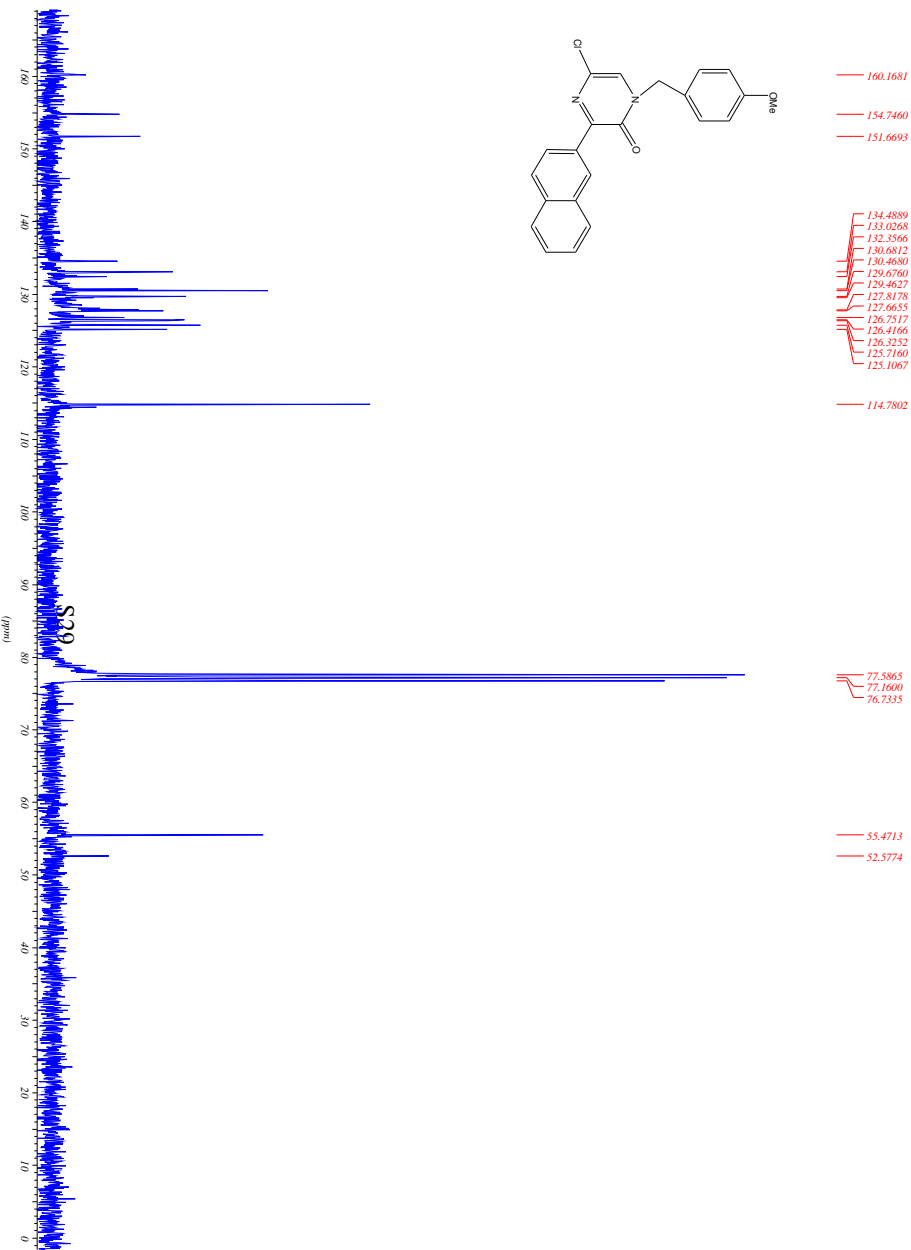
2.5420

-0.0000

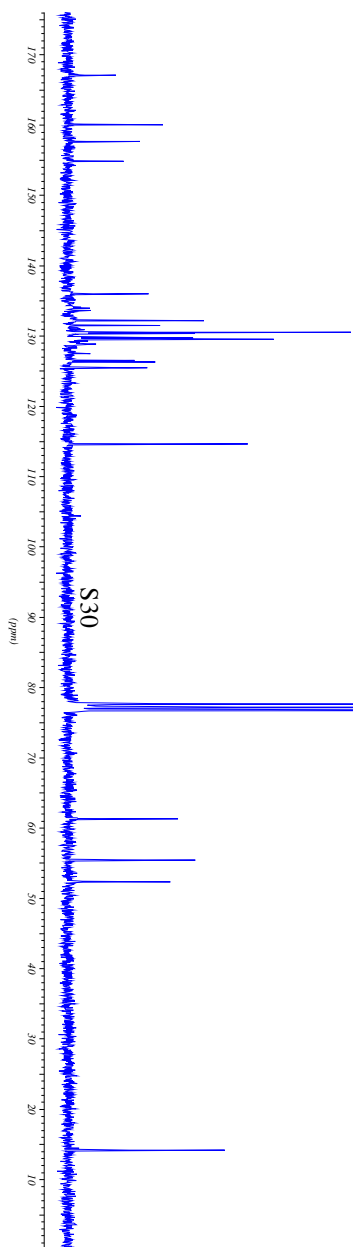
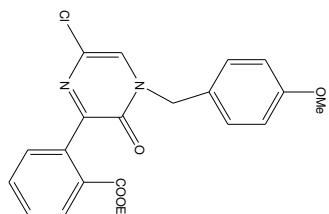
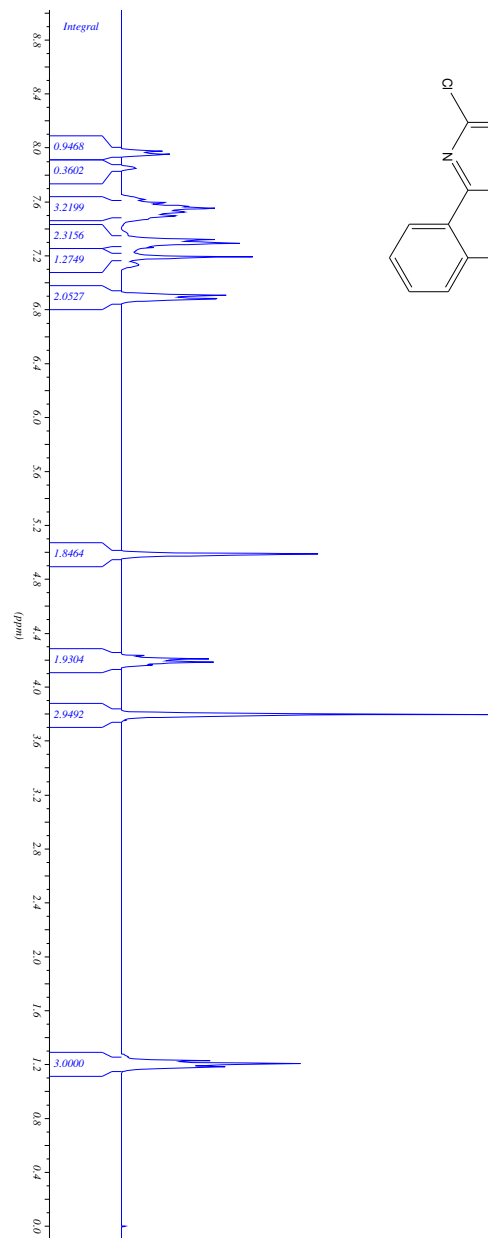
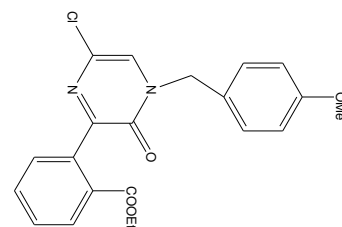


¹H and ¹³C spectra for compound 3 {26}

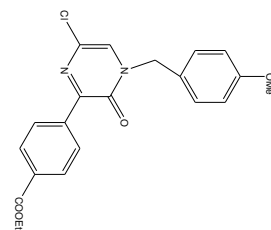




¹H and ¹³C spectra for compound 3 {28}



¹H and ¹³C spectra for compound 3 {29}



8.4816
8.4542

8.0980
8.0706

7.3217
7.2912
7.2425

6.9168
6.8863

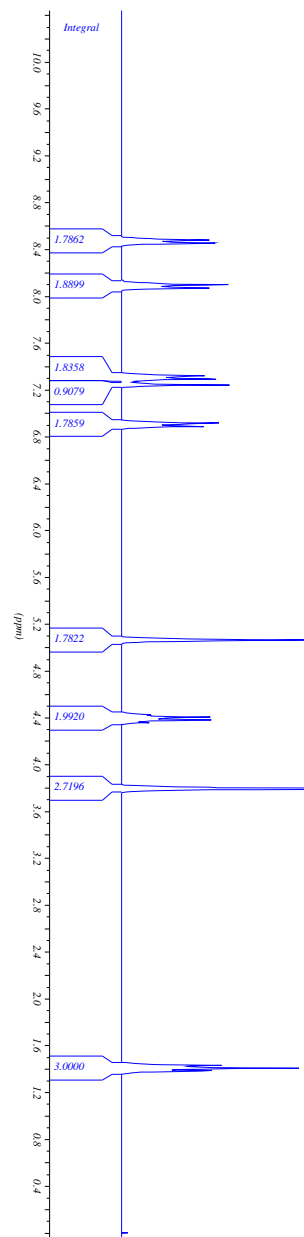
5.0627

4.4265
4.4052
4.3808
4.3565

3.7933

1.4308
1.4065
1.3852

0.0000



166.3214

160.1377

154.3804

150.7250

138.8450

131.8692

130.4680

129.2495

126.5059

126.2947

126.1120

114.7193

77.5865

77.1600

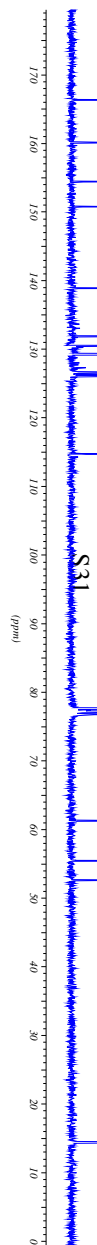
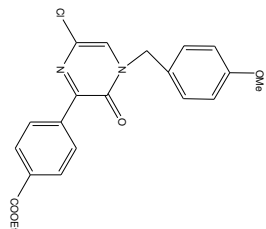
76.7640

61.2285

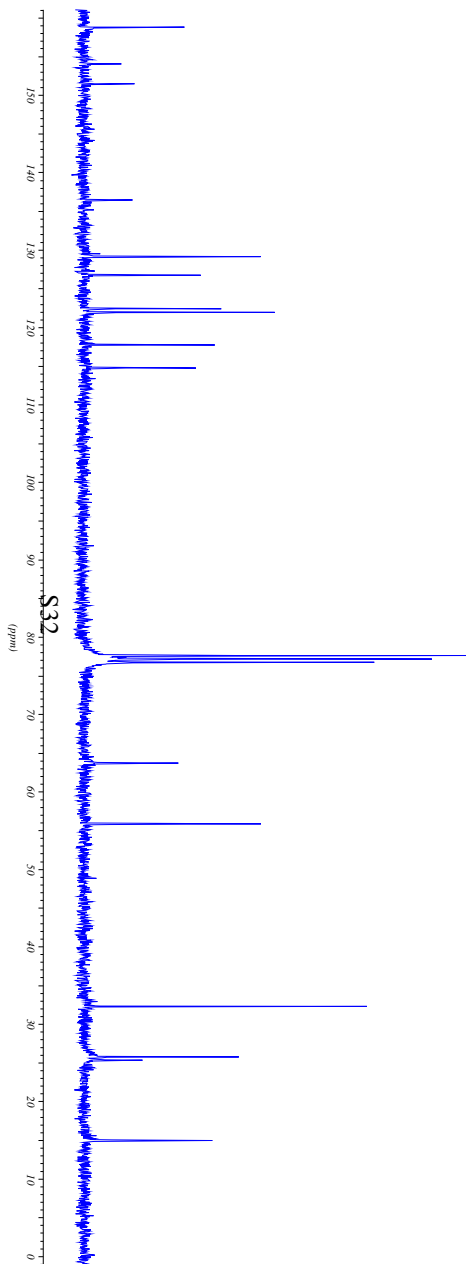
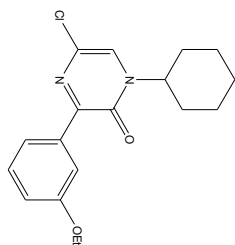
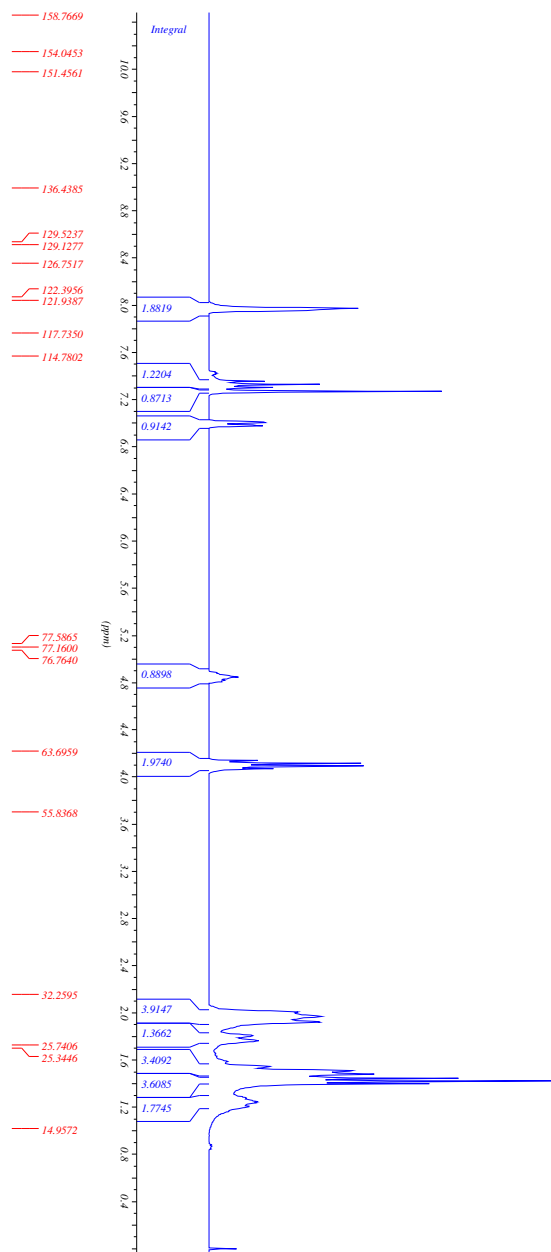
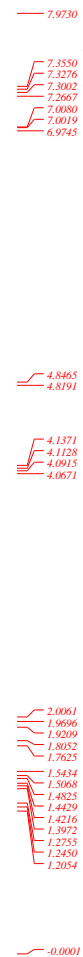
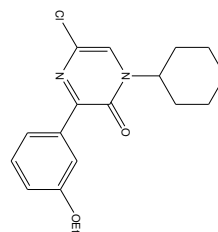
55.4104

52.6079

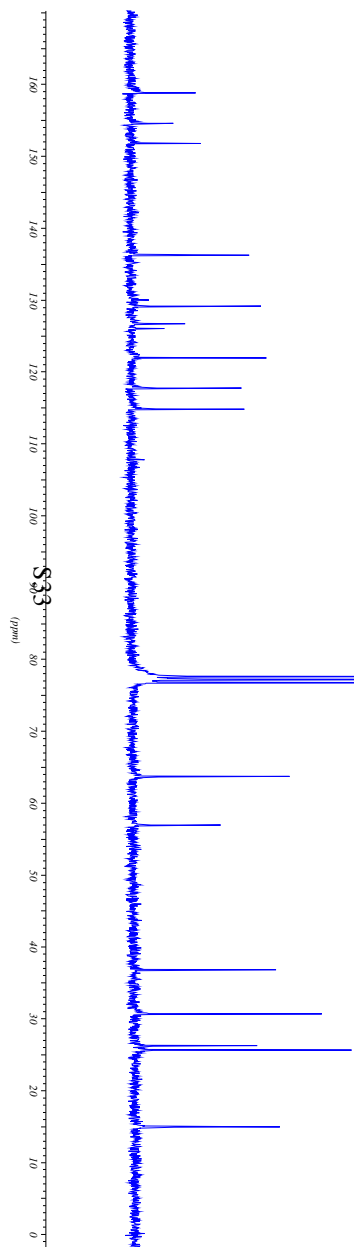
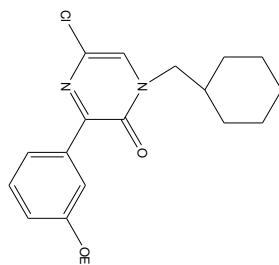
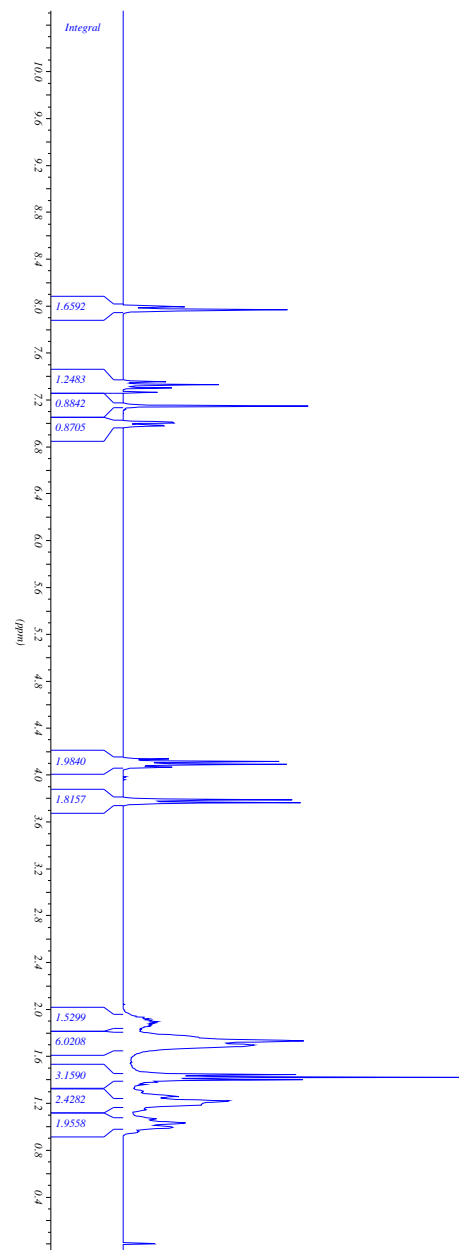
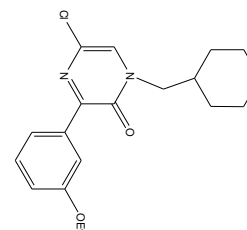
14.4089



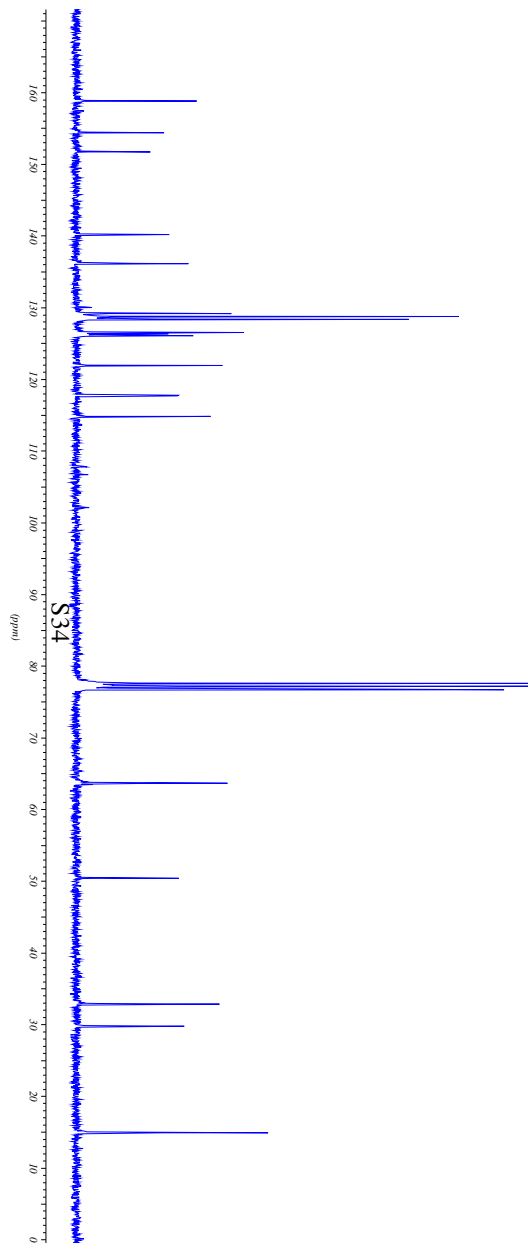
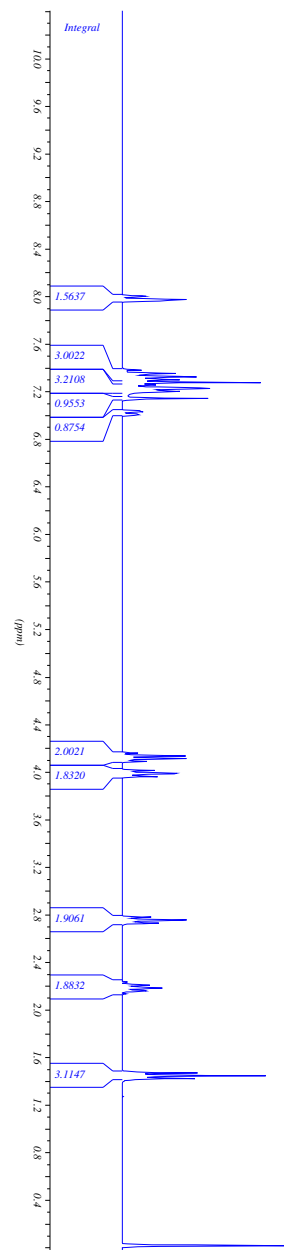
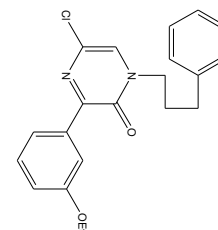
¹H and ¹³C spectra for compound 3 {30}



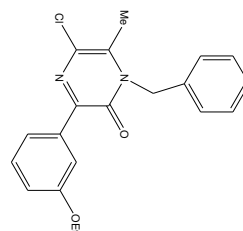
¹H and ¹³C spectra for compound 3{31}



¹H and ¹³C spectra for compound 3 {32}



¹H and ¹³C spectra for compound 3 {33}



8.0158
7.9945
7.3612
7.3399
7.3156
7.2608
7.2547
7.2060
7.1847
6.9990
6.9716

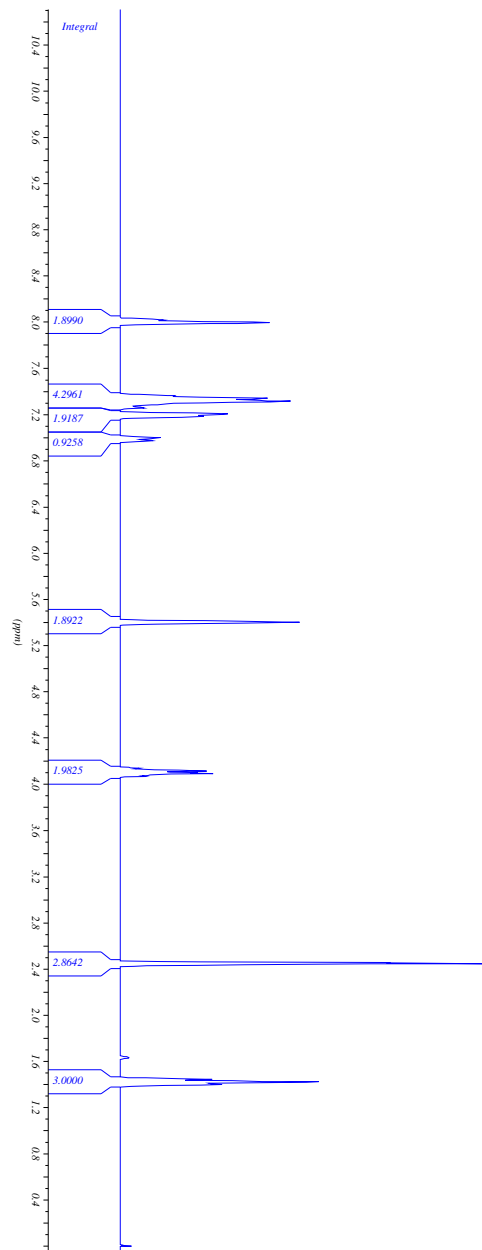
5.4007

4.1373
4.1129
4.0916
4.0672

2.4446

1.4430
1.4217
1.3974

-0.0000



1.58.8278
1.55.4770

1.48.3490

1.36.4385
1.35.0982
1.34.7631

1.29.1886
1.28.0920
1.26.8126
1.26.6298

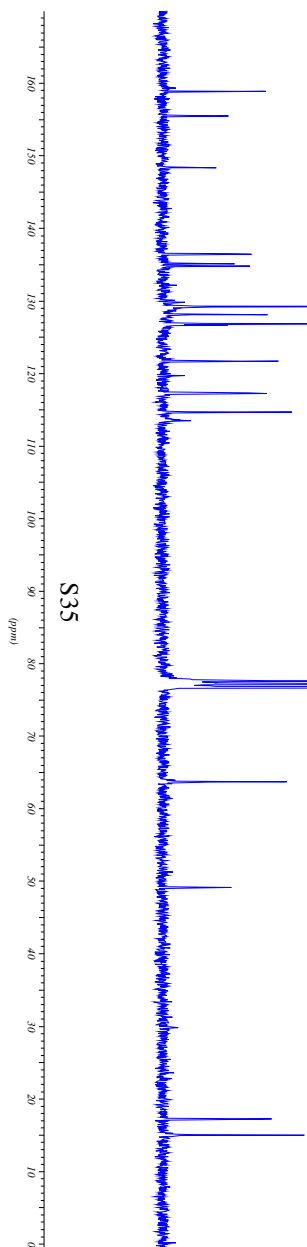
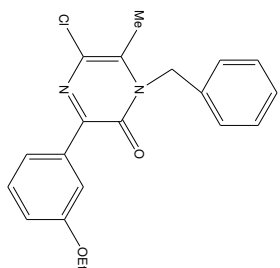
1.21.6645
1.19.6541
1.17.2476
1.14.6279
1.13.4703

77.5865
77.1600
76.7335

63.6655

49.1048

17.2114
14.9572



¹H and ¹³C spectra for compound 3 (34)

