

## Supporting Information

### Sustainable and fast synthesis of functionalized quinoxalines promoted by natural deep eutectic solvents (NADESs)

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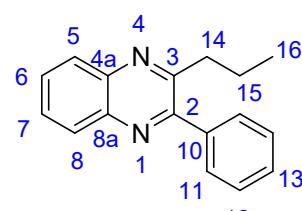
#### General Remarks

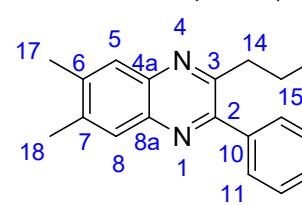
<sup>1</sup>H NMR analyses were recorded at 400 MHz on a Varian Mercury Plus 400. <sup>13</sup>C NMR analyses were recorded at 100 MHz. IR spectra were recorded with a PerkinElmer FTIR spectrometer Spectrum Two UATR. Microanalyses were performed with a CHNS-O analyzer Model EA 1108 from Fisons Instruments. GS-MS analyses were obtained on a Hewlett-Packard GC/MS 6890N that works with the EI technique (70 eV). Diketones **1** were synthesized according to reported literature procedure.<sup>1</sup> 4,5-Dibromobenzene-1,2-diamine was prepared by following the procedure reported by Chen *et al.*<sup>2</sup>

#### General procedure for the synthesis of quinoxaline derivatives **3a-q**.

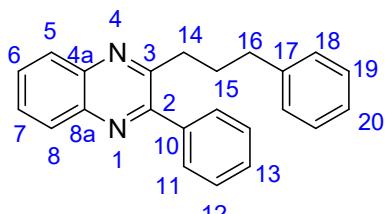
A suspension of the proper diketone **1** (0.3 mmol) in  $\text{CHCl}_3/\text{H}_2\text{O}$  (1:3.33, 30  $\mu\text{L}$ ) and diamine **2** (0.3 mmol) was stirred for 5 minutes at room temperature. Then, the reaction was extracted with  $\text{EtOAc}$  (3 x 1 mL), the combined organic layer dried over  $\text{Na}_2\text{SO}_4$ , filtered and the solvent removed under reduced pressure to give the product **3**.

#### Spectroscopic data of compounds **3a-q**.

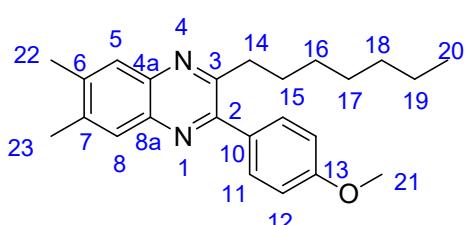
  
**Compound 3a.** Yield 95%, 71 mg. Orange oil. IR ( $\text{cm}^{-1}$ , neat): 699, 760, 1006, 1331, 1481, 1561, 2871, 2931, 2961, 3060. <sup>1</sup>H-NMR ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 0.91 (t,  $J = 7.4\text{Hz}$ , 3H, - $\text{CH}_3$ ), 1.74-1.79 (m, 2H, - $\text{CH}_2\text{-CH}_3$ ), 3.00-3.04 (m, 2H, Ar- $\text{CH}_2$ ), 7.47-7.54 (m, 3H, H13+H12), 7.59-7.62 (m, 2H, H6+H7), 7.69-7.76 (m, 2H, H2H11)), 8.07-8.12 (m, 2H, H5+H8). <sup>13</sup>C-NMR ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 14.3 (C16), 22.6 (C15), 38.2 (C14), 128.7 (C11), 128.8 (C7), 129.0 (C6), 129.41 (C13), 129.43 (C12), 129.9 (C8), 130.27 (C5), 139.4 (C10), 140.9 (C8a), 141.6 (C4a), 155.3 (C2), 156.3 (C3). GC-MS (70eV): *m/z*: 248 ([M<sup>+</sup>], 18), 232 (12), 219 (100), 205 (6), 77 (14). Anal. Calcd. for  $\text{C}_{17}\text{H}_{16}\text{N}_2$  (248.13) C, 82.22; H, 6.49; N, 11.28. Found: C, 82.26; H, 6.52; N, 11.31.

  
**Compound 3b.** Yield 94%, 78mg. Orange oil. IR ( $\text{cm}^{-1}$ , neat): 703, 767, 868, 1002, 1333, 1450, 1482, 2872, 2929, 2961, 3030, 3058. <sup>1</sup>H-NMR ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 0.89 (t,  $J = 7.4\text{Hz}$ , 3H, - $\text{CH}_3$ ), 1.71-1.76 (m, 2H, - $\text{CH}_2\text{-CH}_3$ ), 2.47 (s, 3H, Ar- $\text{CH}_3$ ), 2.49 (s, 3H, Ar- $\text{CH}_3$ ), 2.96-3.00 (m, 2H, Ar- $\text{CH}_2$ ), 7.46-7.52 (m, 3H, H13+H12), 7.57-7.59 (m, 2H, H11), 7.83 (m, 2H, H5+H8). <sup>13</sup>C-NMR ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 14.3 (C16), 20.5 (C17), 20.6 (C18), 22.7 (C15), 38.0 (C14), 127.7 (C11), 128.4 (C8), 128.7 (C5), 128.8 (C13), 129.1 (C12), 130.4 (C10), 139.6 (C8a), 139.9 (C4a), 140.3 (C7), 140.4 (C6), 154.3 (C2), 155.1 (C3). GC-MS (70eV): *m/z*: 276 ([M<sup>+</sup>], 19), 275 (24),

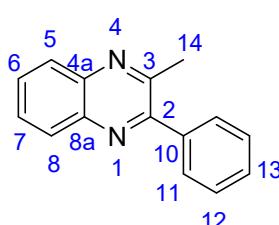
261 (9), 247 (100), 233 (5), 77 (9). Anal. Calcd. for  $C_{19}H_{20}N_2$  (276.16) C, 82.57; H, 7.29; N, 10.14. Found: 82.62; H, 7.33; N, 10.17.



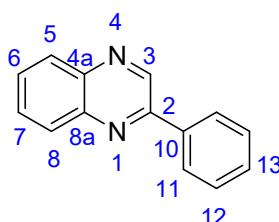
**Compound 3c.** Yield 94%, 91mg. Orange solid, m.p. = 106–108°C. IR ( $\text{cm}^{-1}$ , neat): 695, 767, 1006, 1107, 1220, 1317, 1450, 2856, 2917, 2957, 3022, 3054.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 2.04–2.12 (m, 2H,  $\text{CH}_2-\underline{\text{CH}_2}-\text{CH}_2$ ), 2.63 (t,  $J$  = 7.7Hz, 2H, Ar- $\underline{\text{CH}_2}-\text{CH}_2$ ), 3.09 (m, 2H, - $\text{CH}_2-\underline{\text{CH}_2}-\text{Ph}$ ), 7.08 (d,  $J$  = 7.7Hz, 2H, H18), 7.14–7.17 (m, 1H, H20), 7.21–7.26 (m, 2H, H19), 7.48–7.50 (m, 3H, H13+H12), 7.55–7.57 (m, 2H, H6+H7), 7.70–7.77 (m, 2H, H11), 8.08–8.13 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 30.57 (C15), 35.7 (C14), 35.8 (C16), 126.0 (C20), 128.5 (C11), 128.6 (C18), 128.7 (C19), 128.8 (C13), 129.0 (C12), 129.1 (C7), 129.4 (C6), 129.5 (C8), 130.0 (C5), 139.1 (C10), 140.9 (C17), 141.6 (C8a), 142.0 (C4a), 155.2 (C2), 156.0 (C3). GC-MS (70eV):  $m/z$ : 323 (1), 219 (100), 77 (6). Anal. Calcd. for  $C_{23}H_{20}N_2$  (324.16) C, 85.15; H 6.21; N, 8.63. Found: C, 85.20; H 6.24; N, 8.66.



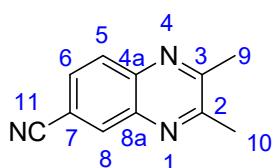
**Compound 3d.** Yield 90%, 98mg. Brown solid, m.p. = 47–50°C. IR ( $\text{cm}^{-1}$ , neat): 404, 578, 619, 828, 872, 1001, 1173, 1253 (C-O), 1335, 1465, 1513, 2847, 2915, 2948, 2965.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 0.86 (t,  $J$  = 7.0, 3H, - $\text{CH}_3$ ), 1.20–1.31 (m, 8H, -( $\text{CH}_2$ )<sub>4</sub>-), 1.71–1.74 (m, 2H, Ar- $\text{CH}_2-\underline{\text{CH}_2}-$ ), 2.48 (s, 3H, Ar- $\text{CH}_3$ ), 2.50 (s, 3H, Ar- $\text{CH}_3$ ), 3.02–3.04 (m, 2H, Ar- $\underline{\text{CH}_2}-\text{CH}_2$ ), 3.89 (s, 3H, O- $\text{CH}_3$ ), 7.04 (d,  $J$  = 8.5Hz, 2H, H12), 7.56–7.57 (d,  $J$  = 8.5Hz, 2H, H11), 7.84 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 14.0 (C20), 20.2 (C22), 20.3 (C23), 22.6 (C19), 28.9 (C18), 29.1 (C17), 29.4 (C16), 31.6 (C15), 36.0 (C14), 55.3 (C21), 113.9 (C12), 127.5 (C8), 128.1 (C5), 130.3 (C11), 131.9 (C10), 139.4 (C8a), 139.7 (C4a), 139.8 (C7), 140.1 (C6), 153.7 (C2), 155.3 (C3), 160.0 (C13). GC-MS (70eV):  $m/z$ : 362 ([M $^+$ ], 5), 333 (2), 305 (2), 278 (100), 247 (26), 77 (5). Anal. Calcd. for  $C_{24}H_{30}N_2O$  (362.23) C, 79.52; H, 8.34; N, 7.73. Found: C, 79.48; H, 8.31; N, 7.70.



**Compound 3e.** Yield 91%, 60mg. orange oil. IR ( $\text{cm}^{-1}$ , neat): 437, 576, 698, 759, 1005, 1191, 1342, 1444, 1482, 2853, 2925, 2959, 3059.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 2.81 (s, 3H, - $\text{CH}_3$ ), 7.52–7.55 (m, 3H, H13+H12), 7.67–7.69 (m, 2H, H6+H7), 7.74–7.77 (m, 2H, H11), 8.08–8.15 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 24.3 (C14), 128.3 (C11), 128.5 (C7), 128.9 (C6), 129.0 (C13), 129.2 (C8), 129.3 (C5), 129.7 (C12), 139.1 (C10), 141.0 (C8a), 141.2 (C4a), 152.5 (C2), 154.9 (C3). GC-MS (70eV):  $m/z$ : 220 ([M $^+$ ], 63), 219 (100), 205 (4), 77 (12). Anal. Calcd. for  $C_{15}H_{12}N_2$  (220.10) C, 81.79; H, 5.49; N, 12.72. Found: C, 81.84; H, 5.52; N, 12.75.

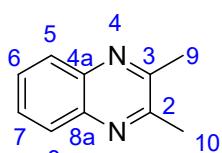


**Compound 3f.** Yield 93%, 57mg. white solid, m.p. = 60–62°C. IR ( $\text{cm}^{-1}$ , neat): 408, 552, 686, 766, 956, 1028, 1048, 1313, 1488, 1547, 3061.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 7.54–7.60 (m, 3H, H13+H12), 7.76–7.80 (m, 2H, H6+H7), 8.14–8.19 (m, 2H, H11), 8.22 (d,  $J$  = 7.3Hz, 2H, H5+H8), 9.35 (s, 1H, H3).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 127.5 (C11), 129.1 (C13), 129.5 (C6+C7), 129.6 (C12), 130.1 (C8), 130.2 (C5), 136.8 (C10), 141.6 (C8a), 142.3 (C4a), 143.3 (C2), 151.8 (C3). GC-MS (70eV):  $m/z$ : 206 ([M $^+$ ], 100), 179 (54), 76 (27). Anal. Calcd. for  $C_{14}H_{10}N_2$  (206.04) C, 81.53; H, 4.89; N, 13.58. Found: C, 81.49; H, 4.86; N, 13.55.

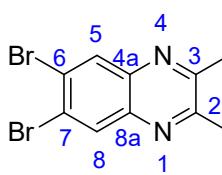


**Compound 3g.** Yield 92%, 50mg. orange oil. IR ( $\text{cm}^{-1}$ , neat): 418, 612, 731, 846, 907, 1165, 1328, 1372, 1397, 1625, 2224 (C≡N), 2922.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 2.78 (s, 3H, Ar- $\text{CH}_3$ ), 2.79 (s, 3H, Ar- $\text{CH}_3$ ), 7.81–7.83 (m, 1H, H6), 8.07 (m, 1H, H5), 8.35 (d,

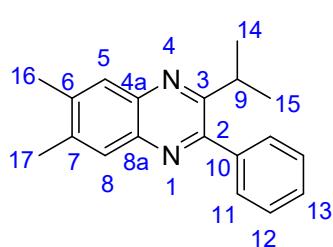
$J = 1.7\text{Hz}$ , 1H, H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 23.2 (C10), 23.4 (C9), 112.2 (C7), 118.2 (C11), 129.8 (C6), 129.9 (C5), 134.3 (C8), 140.2 (C8a), 142.6 (C4a), 155.9 (C2), 156.72 (C3). GC-MS (70eV):  $m/z$ : 183 ([M $^+$ ], 61), 142 (100), 102 (16). ). Anal. Calcd. for  $\text{C}_{11}\text{H}_9\text{N}_3$  (183.08) C, 72.11; H, 4.95; N, 22.94. Found: C, 72.16; H, 4.98; N, 22.97.



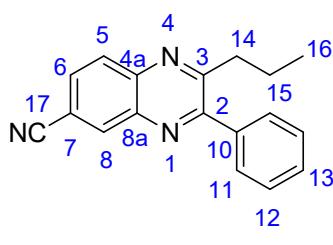
Compound **3h**. Yield 96%, 45mg. dark orange solid, m.p. 69-72°C. IR ( $\text{cm}^{-1}$ , neat): 745, 761, 1023, 1272, 1400, 1450, 2850, 2921, 3063.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 2.75 (s, 6H, Ar-CH $_3$ ), 7.67-7.69 (m, 2H, H6+H7), 7.99-8.01 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 23.1 (C9+C10), 128.3 (C5+C8), 128.8 (C6+C7), 141.0 (C4a+C8a), 153.5 (C2+C3). GC-MS (70eV):  $m/z$ : 158 ([M $^+$ ], 84), 117 (100), 76 (26). Anal. Calcd. for  $\text{C}_{10}\text{H}_{10}\text{N}_2$  (158.08) C, 75.92; H, 6.37; N, 17.71. Found: C, 75.96; H, 6.40; N, 17.68.



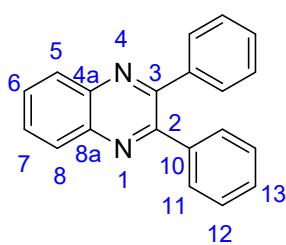
Compound **3i**. Yield 91%, 85mg. orange solid, m.p. = 168-170°C. IR ( $\text{cm}^{-1}$ , neat): 430, 739, 872, 1165, 1317, 1394, 1456, 2850, 2918.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 2.73 (s, 6H, Ar-CH $_3$ ), 8.30 (s, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 23.2 (C9+C10), 125.0 (C6+C7), 132.5 (C5+C8), 140.4 (C4a+C8a), 155.0 (C2+C3). GC-MS (70eV):  $m/z$ : 316 ([M $^+$ ], 100), 275 (73), 234 (25), 155 (15), 74 (23). Anal. Calcd. for  $\text{C}_{10}\text{H}_8\text{Br}_2\text{N}_2$  (313.90) C, 38.01; H, 2.55; N, 8.87. Found: C, 38.06; H, 2.58; N, 8.84.



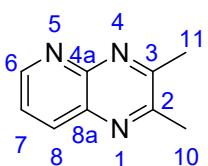
Compound **3j**. Yield 93%, 77mg. Brown solid, m.p. = 78-82°C. IR ( $\text{cm}^{-1}$ , neat): 410, 611, 699, 871, 1002, 1084, 1211, 1322, 1446, 1483, 2869, 2929, 2966.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 1.32 (s, 3H, -CH-CH $_3$ ), 1.34 (s, 3H, -CH-CH $_3$ ), 2.50 (s, 3H, Ar-CH $_3$ ), 2.51 (s, 3H, Ar-CH $_3$ ), 3.46-3.52 (m, 1H, -CH-), 7.49-7.54 (m, 3H, H13+H12), 7.58-7.60 (m, 2H, H11), 7.88 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 20.2 (C16), 20.3 (C17), 22.3 (C14+C15), 31.8 (C9), 127.8 (C11), 128.1 (C13), 128.4 (C7), 128.5 (C6), 128.9 (C12), 139.4 (C10), 139.5 (C8), 139.6 (C5), 139.9 (C8a), 140.7 (C4a), 153.6 (C2), 159.7 (C3). GC-MS (70eV):  $m/z$ : 276 ([M $^+$ ], 84), 275 (100), 261 (33.), 247 (21), 233 (10), 77 (12). Anal. Calcd. for  $\text{C}_{19}\text{H}_{20}\text{N}_2$  (276.16) C, 82.57; H, 7.26; N, 10.14. Found: C, 82.61; H, 7.29; N, 10.17.



Compound **3k + 3k'** (**mixtures of regioisomers**). Yield 92%, 75mg. Brown oil. IR ( $\text{cm}^{-1}$ , neat): 687, 768, 1003, 2228 (C≡N), 2944, 3015.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 0.92 (t,  $J = 7.4\text{Hz}$ , 3H, -CH $_3$ ), 1.76-1.82 (m, 2H, -CH $_2$ -CH $_2$ -CH $_3$ ), 3.03-3.07 (m, 2H, -CH $_2$ -CH $_2$ -CH $_3$ ), 7.53-7.56 (m, 3H, H12+H13), 7.60-7.62 (m, 2H, H11), 7.85-7.89 (m, 1H, H5), 8.15-8.19 (m, 1H, H6), 8.45-8.46 (m, 1H, H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 10.3 (C16), 18.1 (C15), 18.2, 34.4 (C14), 34.5, 108.8 (C7), 109.2, 114.5 (C17), 124.9 (C13), 125.0 (C11), 125.1, 125.7 (C12), 125.8, 126.3 (C6), 126.5, 126.7 (C5), 127.0, 130.9 (C8), 131.4, 134.4 (C8a), 134.5, 138.5 (C4a), 139.1, 153.3 (C2), 153.9, 154.7 (C3), 155.6. GC-MS (70eV):  $m/z$ : 248 ([M $^+$ ], 12), 258 (16), 244 (100), 230 (6), 77 (8). Anal. Calcd. for  $\text{C}_{18}\text{H}_{15}\text{N}_3$  (273.12) C, 79.10; H, 5.53; N, 15.37. Found: 79.15; H, 5.50; N, 15.33.

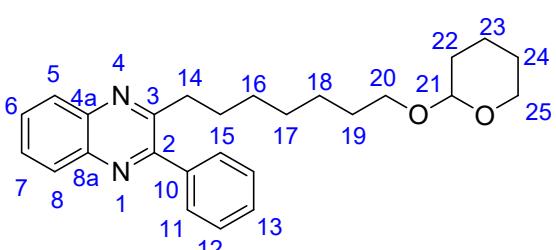


Compound **3l**. Yield 94%, 79mg. yellow oil. IR ( $\text{cm}^{-1}$ , neat): 541, 597, 920, 977, 1057, 1221, 1283, 1442, 1478, 3034, 3059.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 7.32-7.37 (m, 6H, C12+C13), 7.52-7.54 (m, 4H, C11)), 7.76-7.79 (m, 2H, C6+C7), 8.18-8.20 (m, 2H, C5+C8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 128.2 (C11), 128.8 (C13), 129.2 (C12), 129.8 (C5+C8), 129.9 (C6+C7), 139.0 (C10), 141.2 (C4a+C8a), 153.4 (C2+C3). GC-MS (70eV):  $m/z$ : 282 ([M $^+$ ], 100), 205 (4), 179 (34), 76 (17). Anal. Calcd. for  $\text{C}_{20}\text{H}_{14}\text{N}_2$  (282.11) C, 85.08; H, 5.00; N, 9.92. Found: C, 85.03; H, 4.96; N, 9.89.



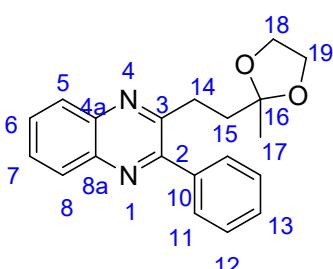
**Compound 3m.** Yield 90%, 43mg. brown solid, m.p. = 114-117°C. IR ( $\text{cm}^{-1}$ , neat): 496, 603, 796, 829, 994, 1105, 1128, 1228, 1395, 1560, 2917, 2994.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 2.76 (s, 3H, - $\text{CH}_3$ ), 2.80 (s, 3H, , - $\text{CH}_3$ ), 7.62-7.65 (m, 1H, H7), 8.35-8.37 (m, 1H, H8), 9.06-9.07 (m, 1H, H6).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 22.9, 23.4, 124.4, 135.8, 137.5, 149.9, 152.4, 155.2, 157.5. GC-MS (70eV):  $m/z$ : 159 ([M $^+$ ], 100), 118 (94), 77 (25). Anal. Calcd.

for  $\text{C}_9\text{H}_9\text{N}_3$  (159.08) C, 67.90; H, 5.70; N, 26.40. Found: C, 67.94; H, 5.72; N, 26.43.

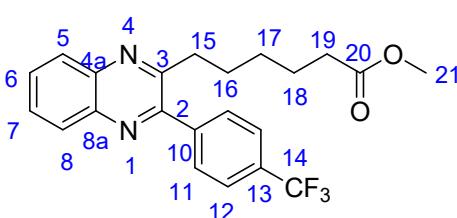


**Compound 3n.** Yield 95%, 134mg. orange oil. IR ( $\text{cm}^{-1}$ , neat): 610, 699, 730, 762, 906, 1022, 1076, 1119, 1134 (C-O), 1351, 1443, 1481, 2855, 2932, 3060.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 1.25-1.34 (m 6H, H16-H18), 1.50-1.61 (m, 6H, H15+H19+1H23+1H24), 1.69-1.75 (m, 3H, 1H22+1H23+1H24), 1.80-1.84 (m, 1H, 1H22), 3.03-3.07 (m, 2H, H14), 3.34-3.38 (m 1H, 1H20), 3.49-3.53 (m, 1H, 1H20),

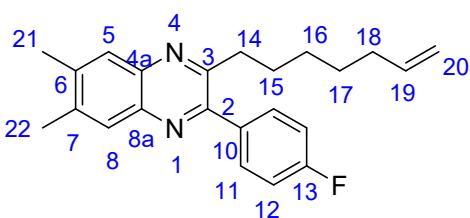
3.68-3.73 (m, 1H, 1H25), 3.85-3.89 (m, 1H, 1H25), 4.57-4.58 (m, 1H, H21), 7.50-7.55 (m, 3H, H13+H12), 7.60-7.63 (m, 2H, H6+H7), 7.71-7.77 (m, 2H, H11), 8.10-8.14 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 19.6 (C23), 25.5 (C24), 26.0 (C15), 28.9 (C16), 29.0 (C18), 29.3 (C17), 29.6 (C19), 30.7 (C22), 35.9 (C14), 62.2 (C20), 67.6 (C25), 98.8 (C21), 128.3 (C11), 128.4 (C13), 128.5 (C17), 128.8 (C5), 129.1 (C8), 129.2 (C12), 129.6 (C6), 139.1 (C10), 140.7 (C8a), 141.4 (C4a), 155.0 (C2), 156.3 (C3). GC-MS (70eV):  $m/z$ : 404 ([M $^+$ ], 2), 320 (12), 220 (100). Anal. Calcd. for  $\text{C}_{26}\text{H}_{32}\text{N}_2\text{O}_2$  (404.24) C, 77.19; H, 7.97; N, 6.92. Found: C, 77.24; H, 8.00; N, 6.95.



**Compound 3o.** Yield 92%, 88mg. Brown solid, m.p. = 67-69°C. IR ( $\text{cm}^{-1}$ , neat): 475, 587, 697, 764, 1014, 1033, 1060, 1267 (C-O), 1371, 1432, 2886, 2943, 2977, 3059.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 1.30 (s, 3H, - $\text{C-CH}_3$ ), 2.12-2.15 (m, 2H, - $\text{CH}_2\text{-CH}_2\text{-C-}$ ), 3.17-3.20 (m, 2H, - $\text{CH}_2\text{-CH}_2\text{-C-}$ ), 3.76-3.77 (m, 2H, 1H18+1H19), 3.86-3.88 (m, 2H, 1H18+1H19), 7.50-7.55 (m, 3H, H12+H13), 7.64-7.66 (m, 2H, H6+H7), 7.72-7.75 (m, 2H, H11), 8.09-8.13 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 23.8 (C14), 31.0 (C17), 37.2 (C15), 64.6 (C18+C19), 109.6 (C16), 116.8 (C11), 120.3 (C13), 128.5 (C7), 128.9 (C5), 129.1 (C8), 129.2 (C12), 129.6 (C&), 139.0 (C10), 140.7 (C8a), 141.3 (C4a), 155.0 (C2), 155.6 (C3). GC-MS (70eV):  $m/z$ : 305 (5), 277 (28), 260 (8), 234 (29), 218 (21), 87 (100). Anal. Calcd. for  $\text{C}_{20}\text{H}_{20}\text{N}_2\text{O}_2$  (320.15) C, 74.98; H, 6.29; N, 8.74. Found: C, 75.02; H, 6.26; N, 8.70.



**Compound 3p.** Yield 93%, 112mg. dark orange oil. IR ( $\text{cm}^{-1}$ , neat): 404, 611, 762, 852, 1004, 1066, 1109, 1165 (C-O), 1320, 1733 (C=O), 2862, 2936.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 1.33-1.40 (m, 2H, H17), 1.60-1.63 (m, 2H, H16), 1.79-1.82 (m, 2H, H18), 2.28 (t,  $J$  = 7.5Hz, 2H, H19), 3.02-3.05 (m, 2H, H15), 3.66 (s, 3H, - $\text{OCH}_3$ ), 7.75-7.83 (m 6H, H6+H7+H11+H12), 8.11-8.13 (m, 2H, H5+H8).  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 24.6 (C16), 28.3 (C17), 28.8 (C18), 33.8 (C19), 35.6 (C15), 51.4 (C21), 116.8 (C14), 120.3 (C12), 125.6 (C11), 128.6 (C7), 129.2 (C8), 129.3 (C5), 129.5 (C6), 130.1 (C13), 134.7 (C10), 140.6 (C8a), 141.7(C4a), 153.4 (C2), 155.3 (C3), 173.9 (C20). GC-MS (70eV):  $m/z$ : 402 ([M $^+$ ], 4), 371 (10), 287 (100), 219 (19). Anal. Calcd. for  $\text{C}_{22}\text{H}_{21}\text{F}_3\text{N}_2\text{O}_2$  (402.15) C, 65.66; H, 5.26; N, 6.96. Found: C, 65.71; H, 5.22; N, 6.99.



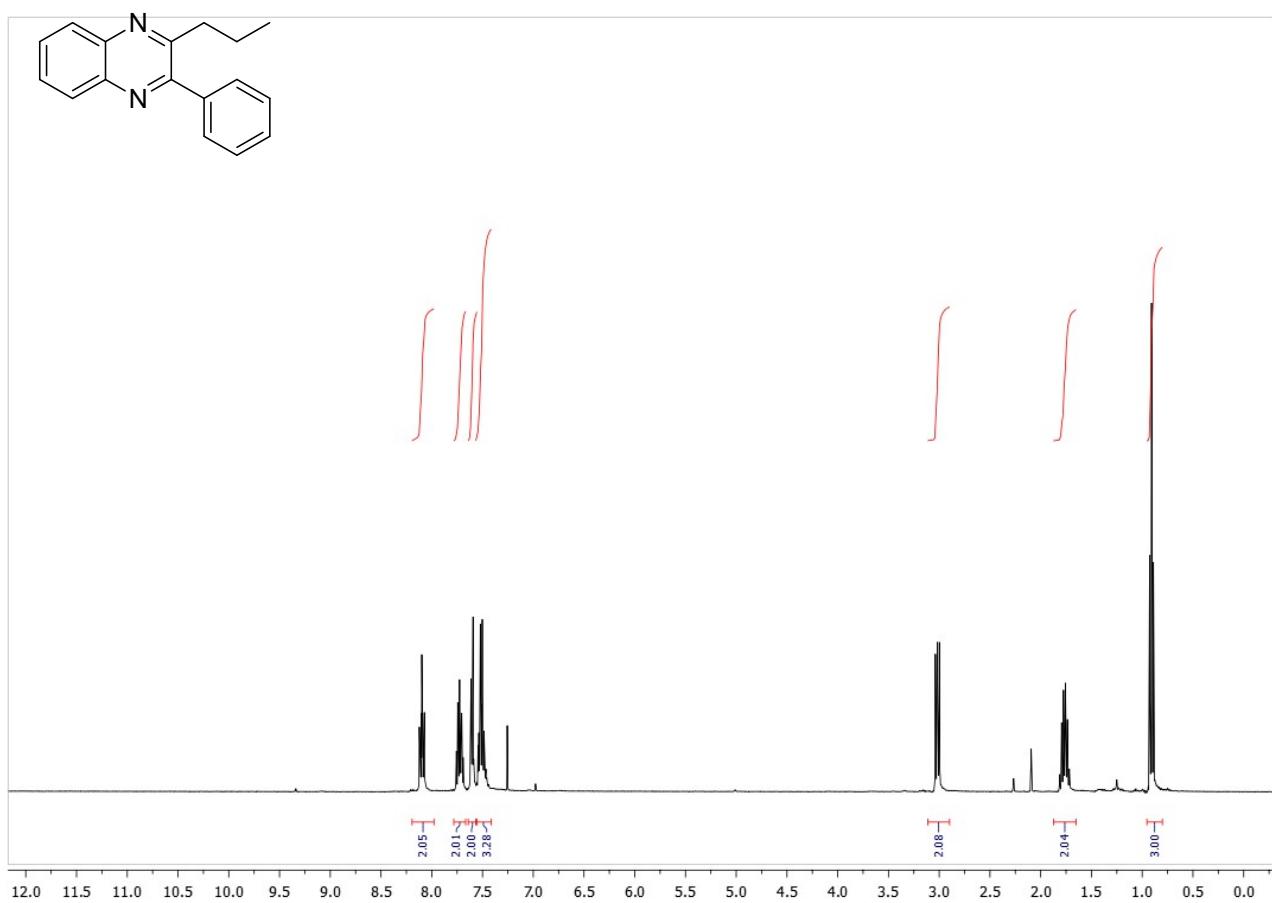
**Compound 3q.** Yield 96%, 100mg. Brown solid, m.p. = 43-45°C. IR ( $\text{cm}^{-1}$ , neat): 418, 532, 572, 839, 870, 909, 1003, 1157, 1223, 1510, 2855, 2925.  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ , 400MHz)  $\delta$ : 1.31-1.36 (m, 4H, H16+H17), 1.72-1.75 (m, 2H, H15), 1.98-2.02 (m, 2H, H18), 2.50 (s, 3H, Ar- $\text{CH}_3$ ), 2.52 (s, 3H, Ar- $\text{CH}_3$ ), 2.99-3.02 (m, 2H Ar- $\text{CH}_2$ -), 4.91-

4.99 (m, 2H, H20), 5.73-5.81 (m, 1H, H19), 7.20-7.24 (m 2H, H12), 7.58-7.61 (m, 2H, H11), 7.85 (bs, 2H, H5+H8).  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ , 100MHz)  $\delta$ : 20.2 ( $\text{CH}_3$ ), 20.3 ( $\text{CH}_3$ ), 28.5 (C15), 28.8 (C17), 28.9 (C16), 33.5 (C18), 35.8 (C14), 114.3 (C12), 114.4 (C12), 115.6 (C20), 127.6 (C8), 128.1 (C5), 130.8 (C11), 130.9 (C10), 138.9(C7), 139.6 (C19), 139.7 (C6), 140.3 (C8a), 140.4 (C4a), 153.0 (C2), 154.9 (C3), 162.0 (C13), 164.0 (C13). GC-MS (70eV):  $m/z$ : 348 ([M $^+$ ], (5)), 307 (6), 279 (23), 265 (100), 77 (6). Anal. Calcd. for  $\text{C}_{23}\text{H}_{25}\text{FN}_2$  (348.20) C, 79.28; H, 7.23; N, 8.04. Found: ) C, 79.33; H, 7.26; N, 8.01.

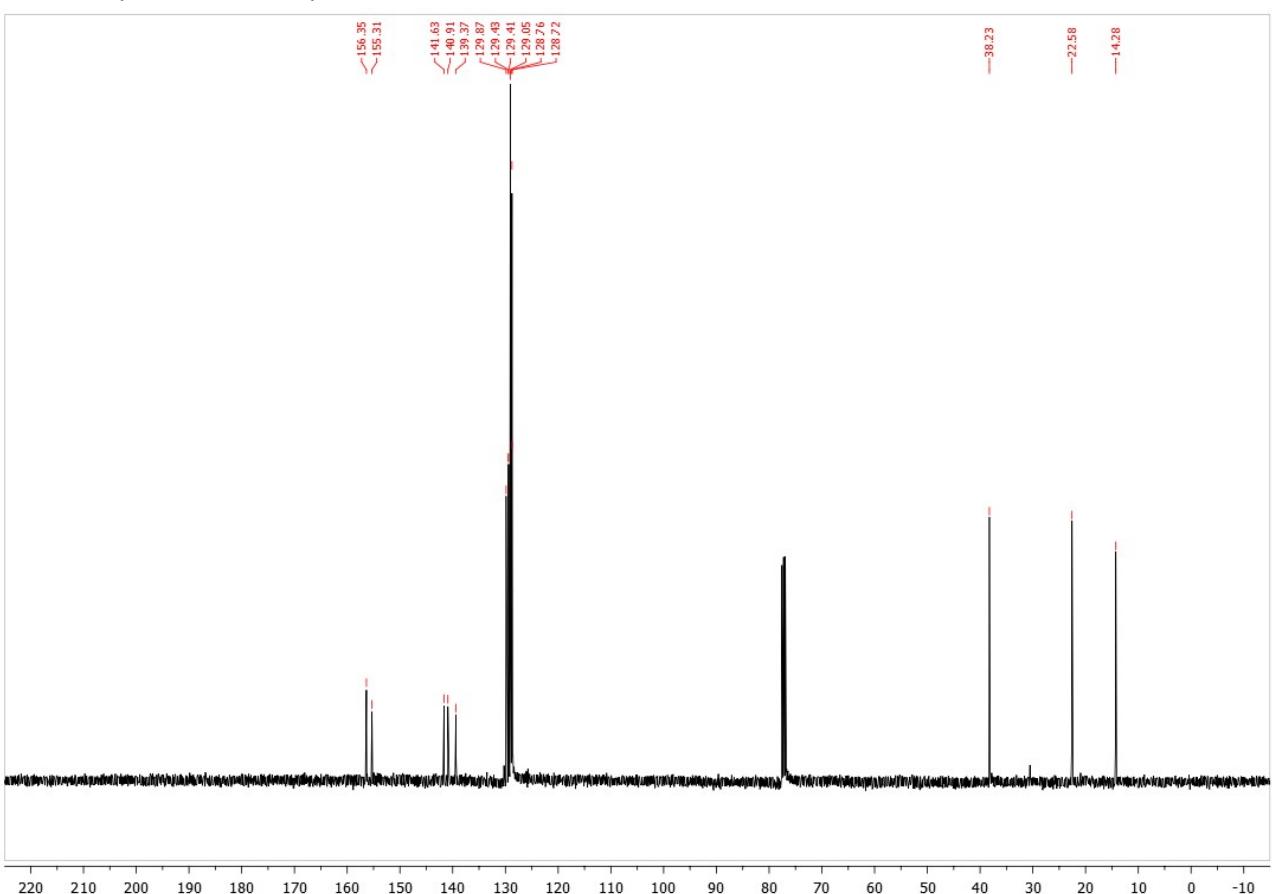
1 A. Palmieri, S. Gabrielli, S. Sampaolesi and R. Ballini, *RCS Adv.*, 2015, **5**, 36652-36655.

2 S. Chen, F. S. Raad, M. Ahmida, B. L. Kaafarani and S. H. Eichhorn, *Org. Lett.* 2013, **15**, 558-561.

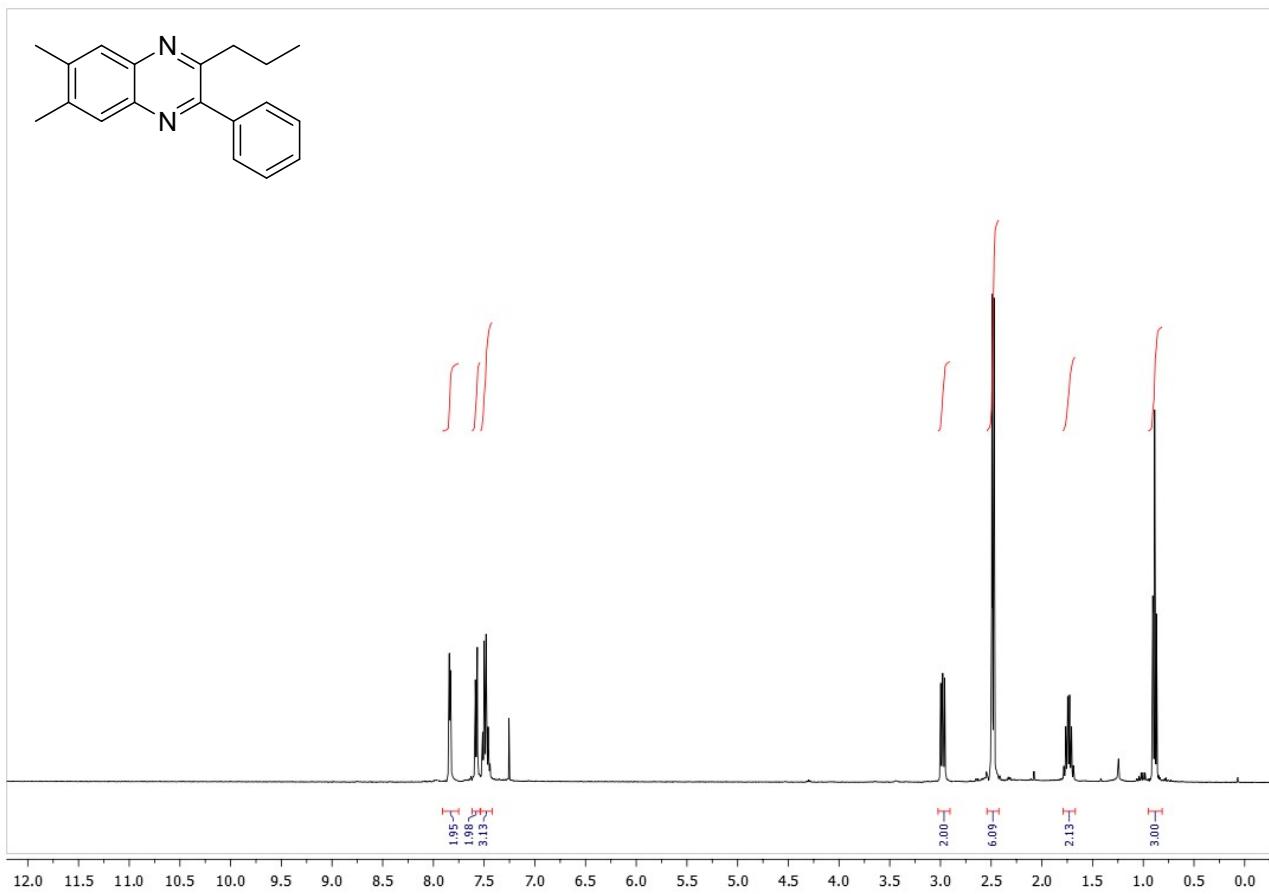
<sup>1</sup>H-NMR spectrum of compound 3a.



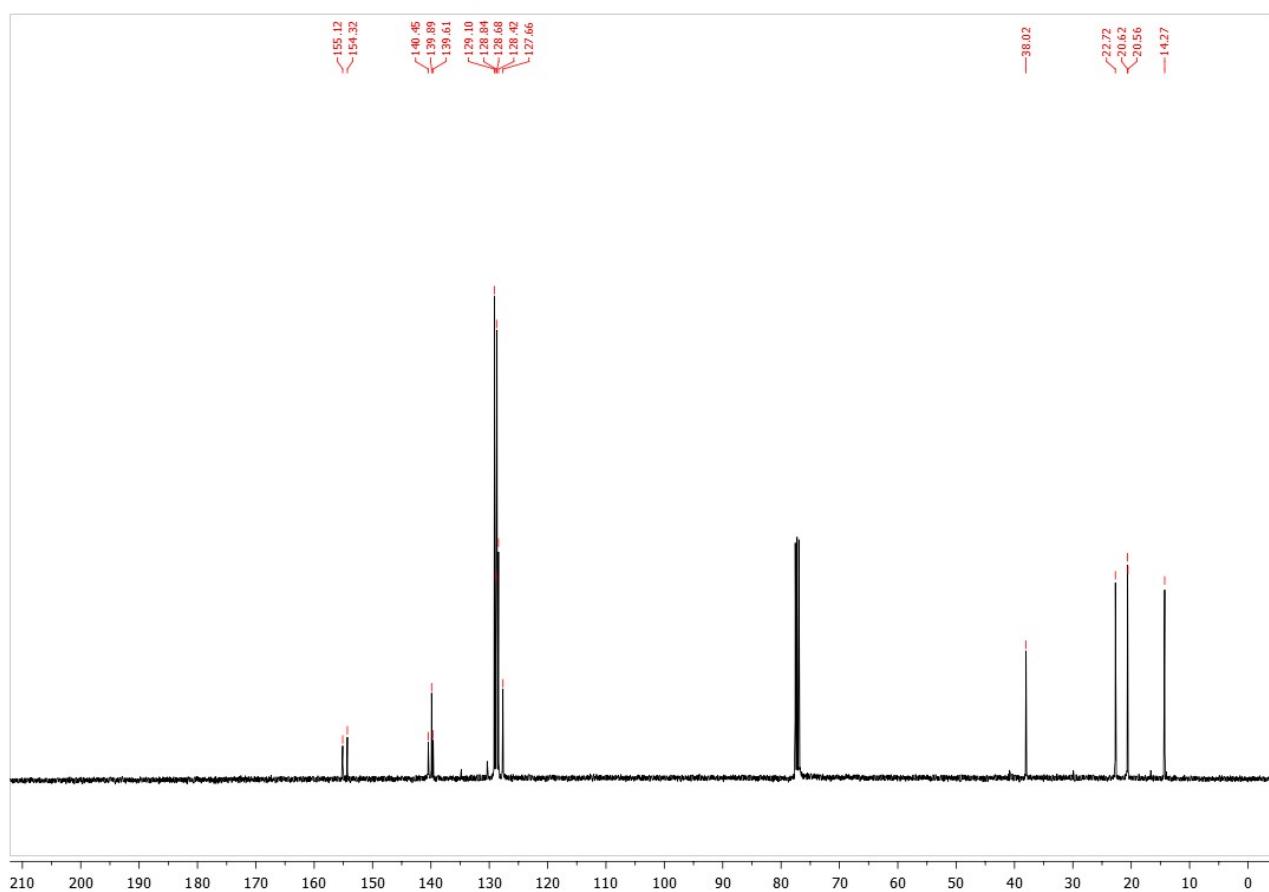
<sup>13</sup>C-NMR spectrum of compound 3a.



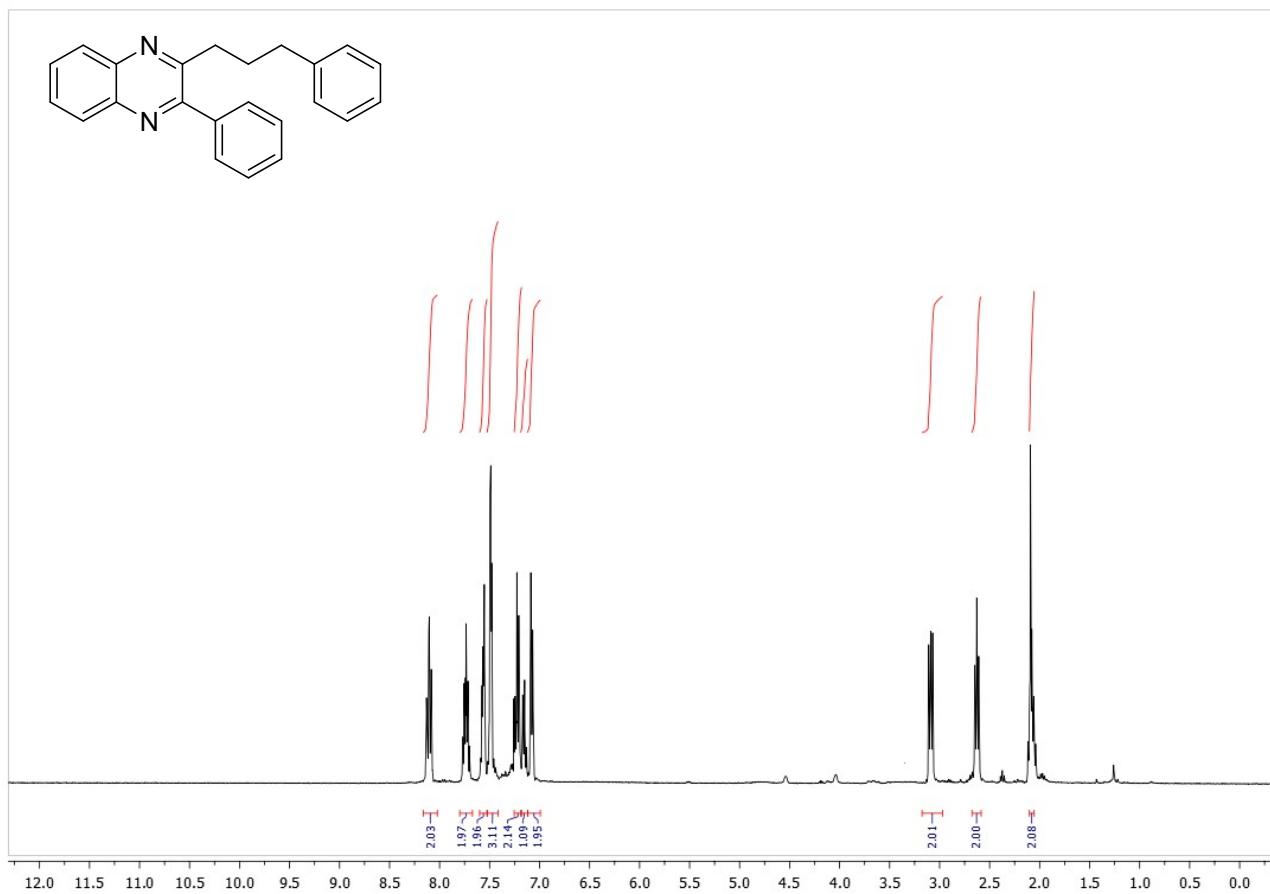
<sup>1</sup>H-NMR spectrum of compound **3b**.



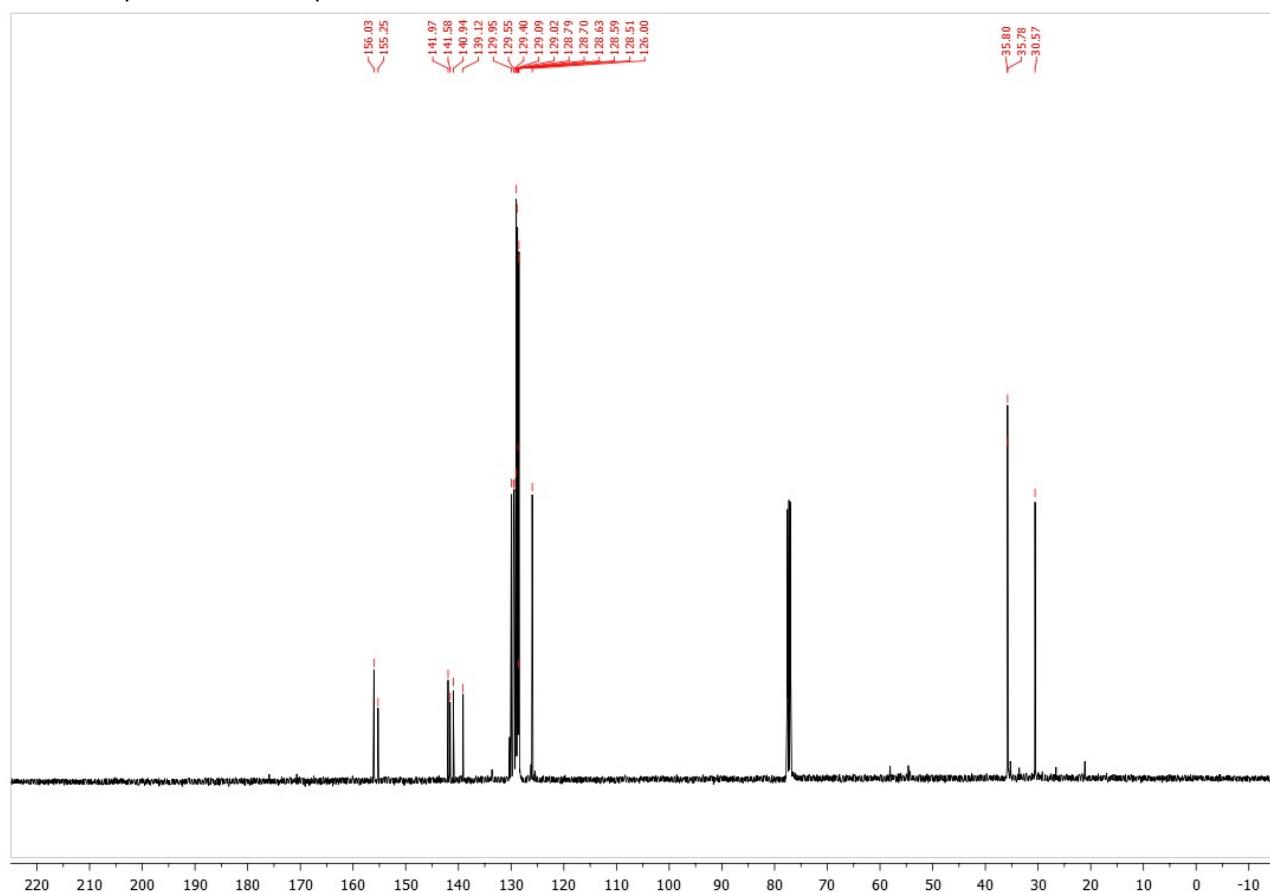
<sup>13</sup>C-NMR spectrum of compound **3b**.



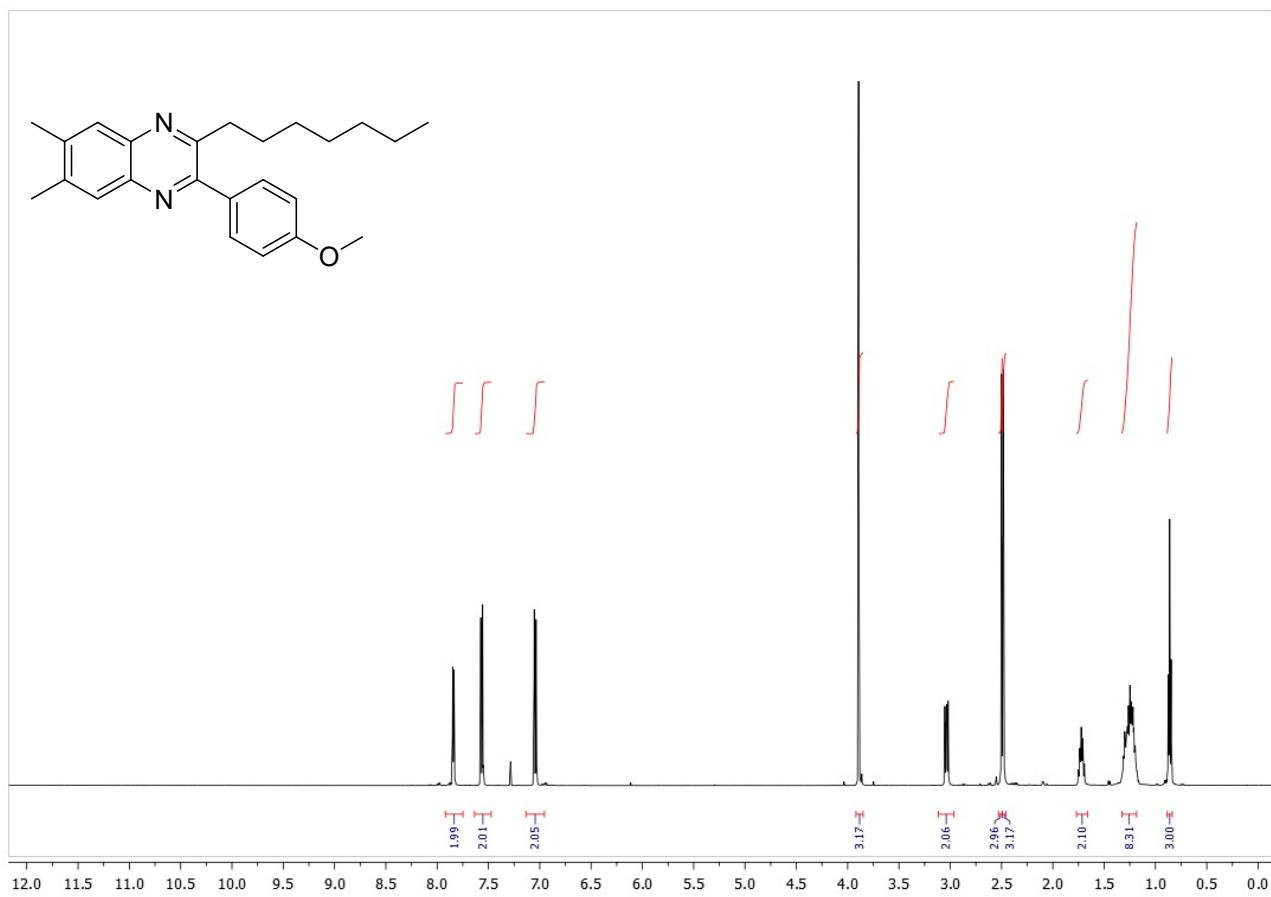
<sup>1</sup>H-NMR spectrum of compound 3c.



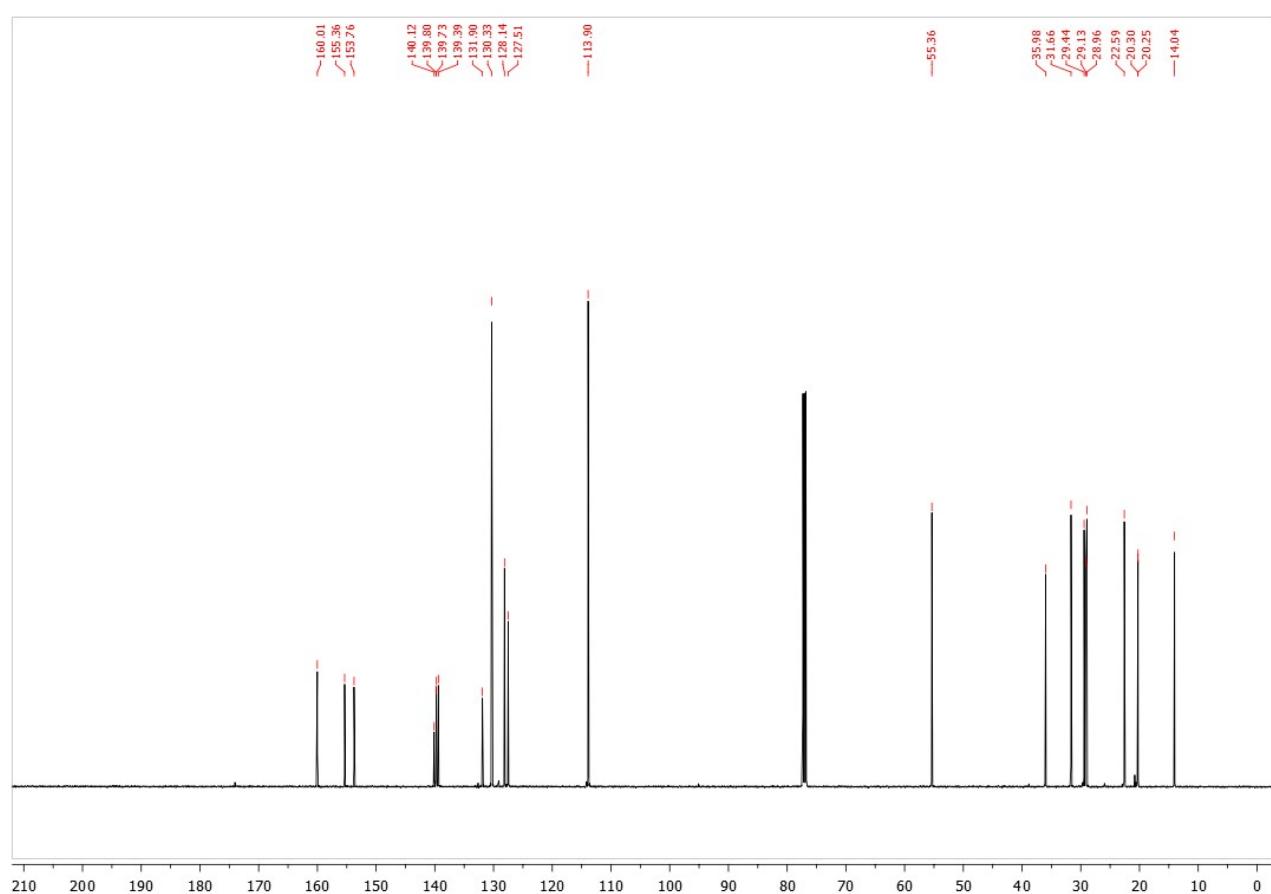
<sup>13</sup>C-NMR spectrum of compound 3c.



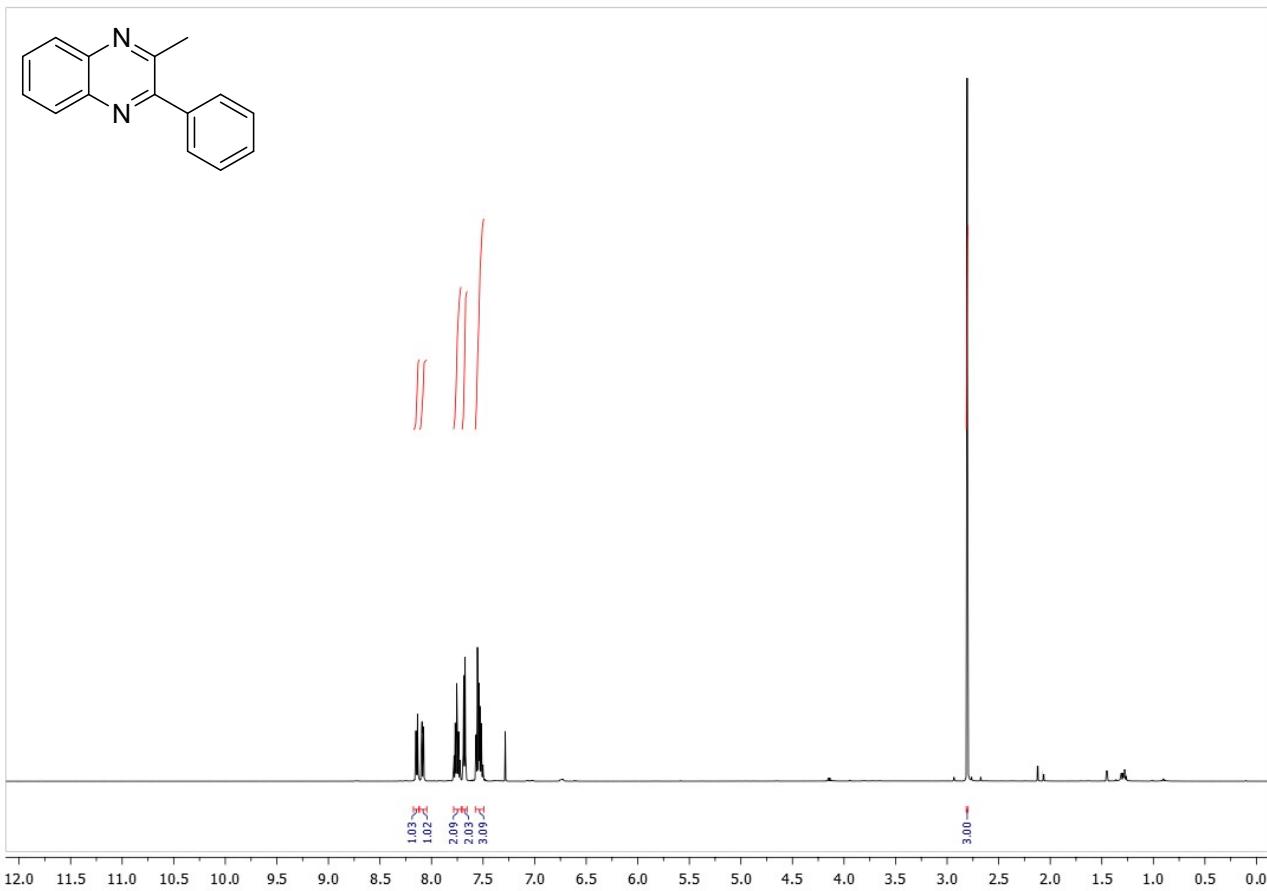
<sup>1</sup>H-NMR spectrum of compound 3d.



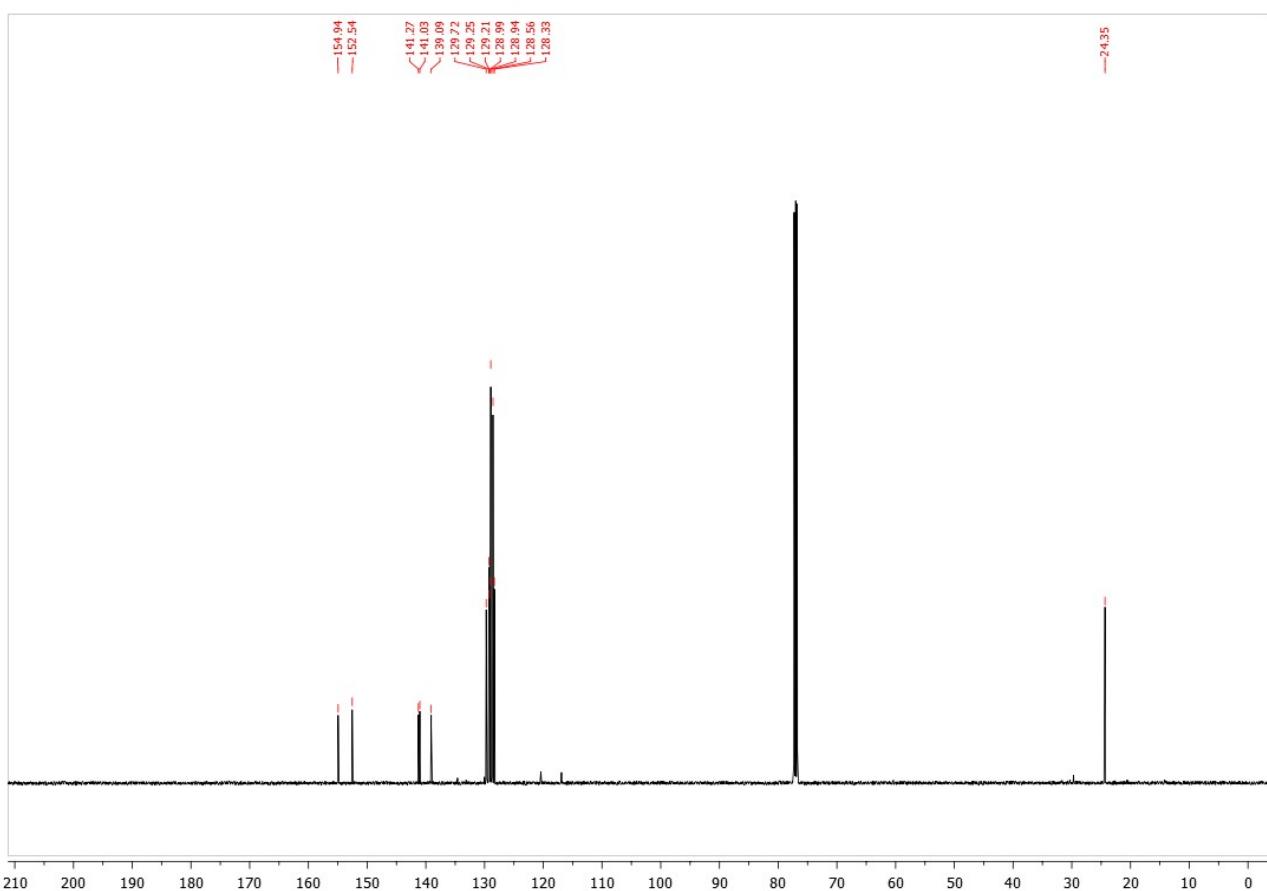
<sup>13</sup>C-NMR spectrum of compound 3d.



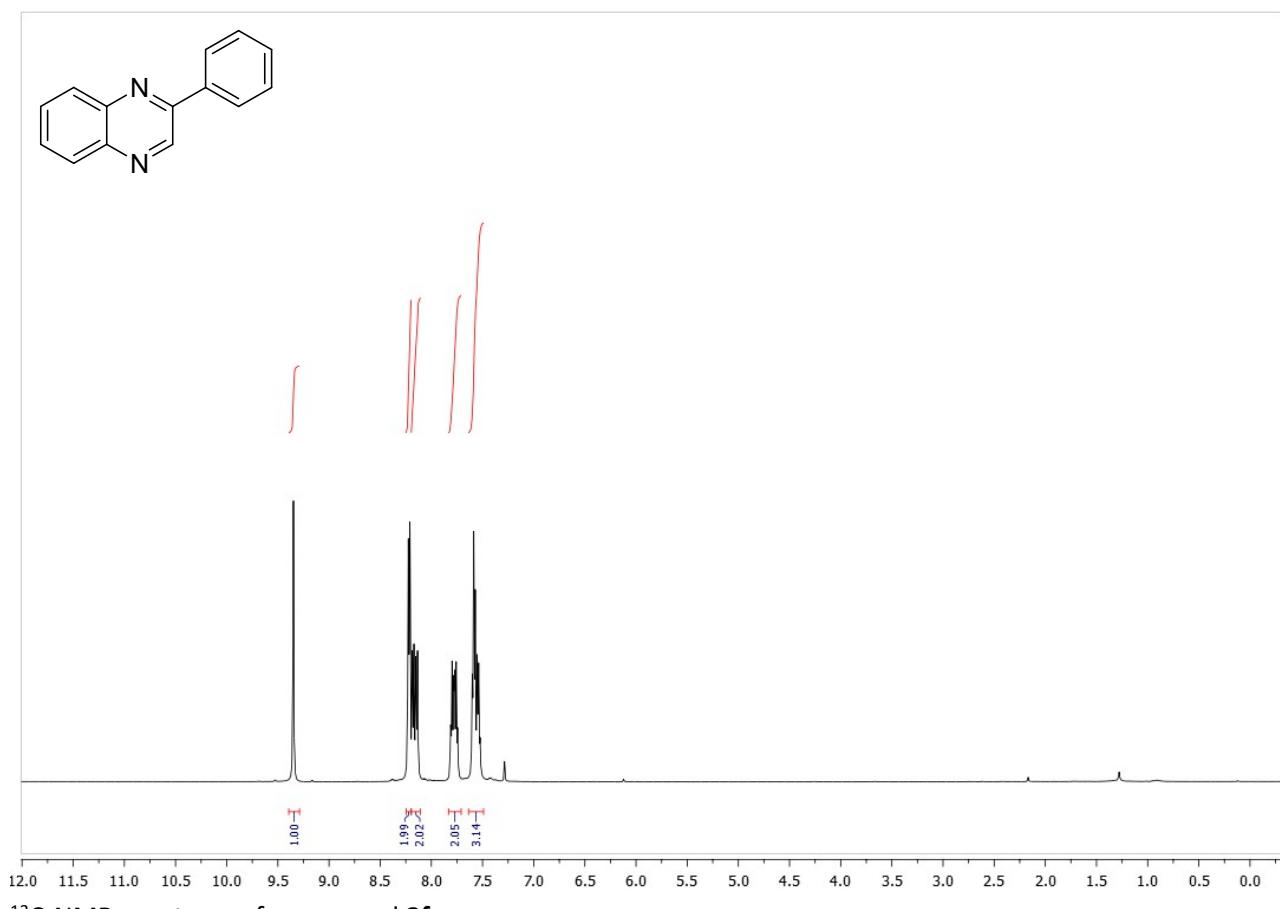
### <sup>1</sup>H-NMR spectrum of compound 3e



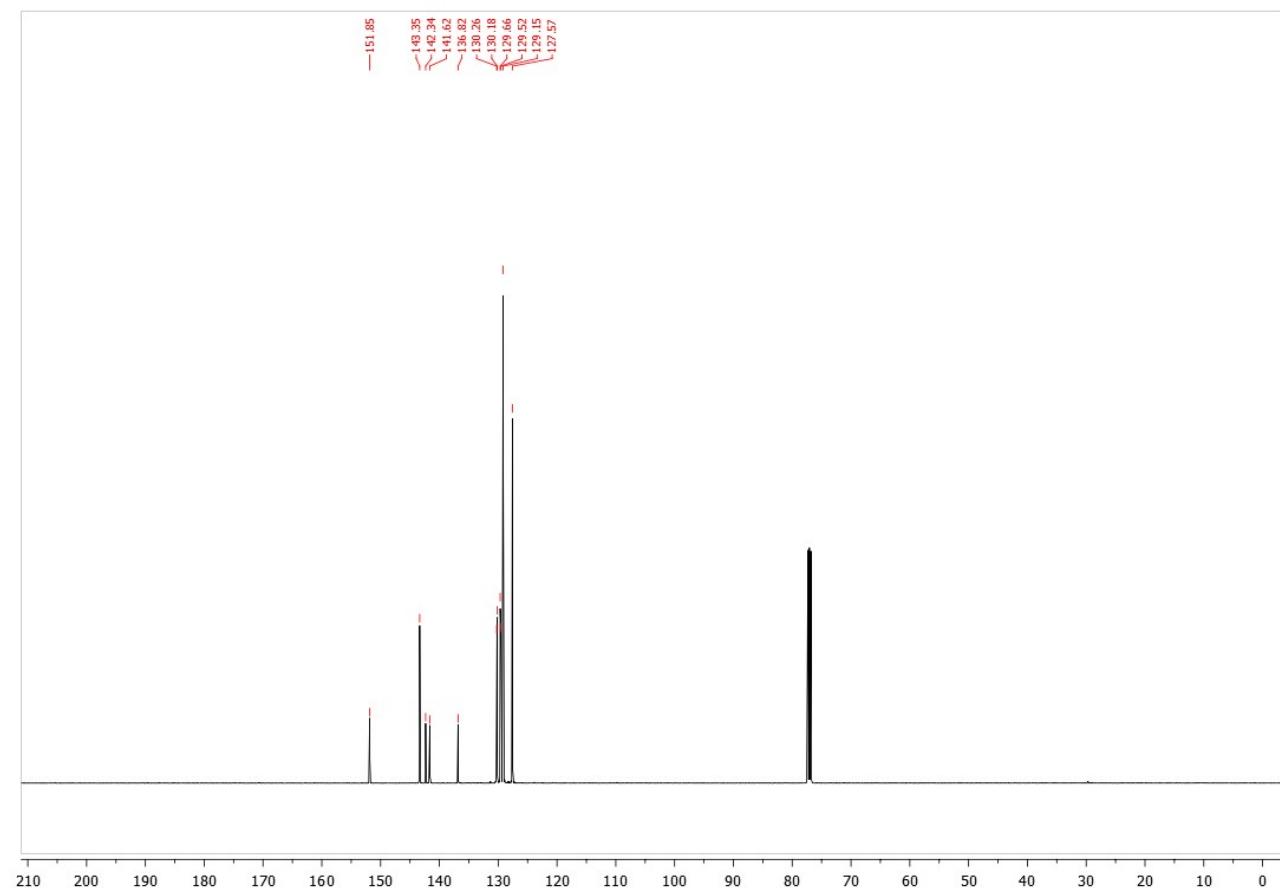
<sup>13</sup>C-NMR spectrum of compound **3e**.



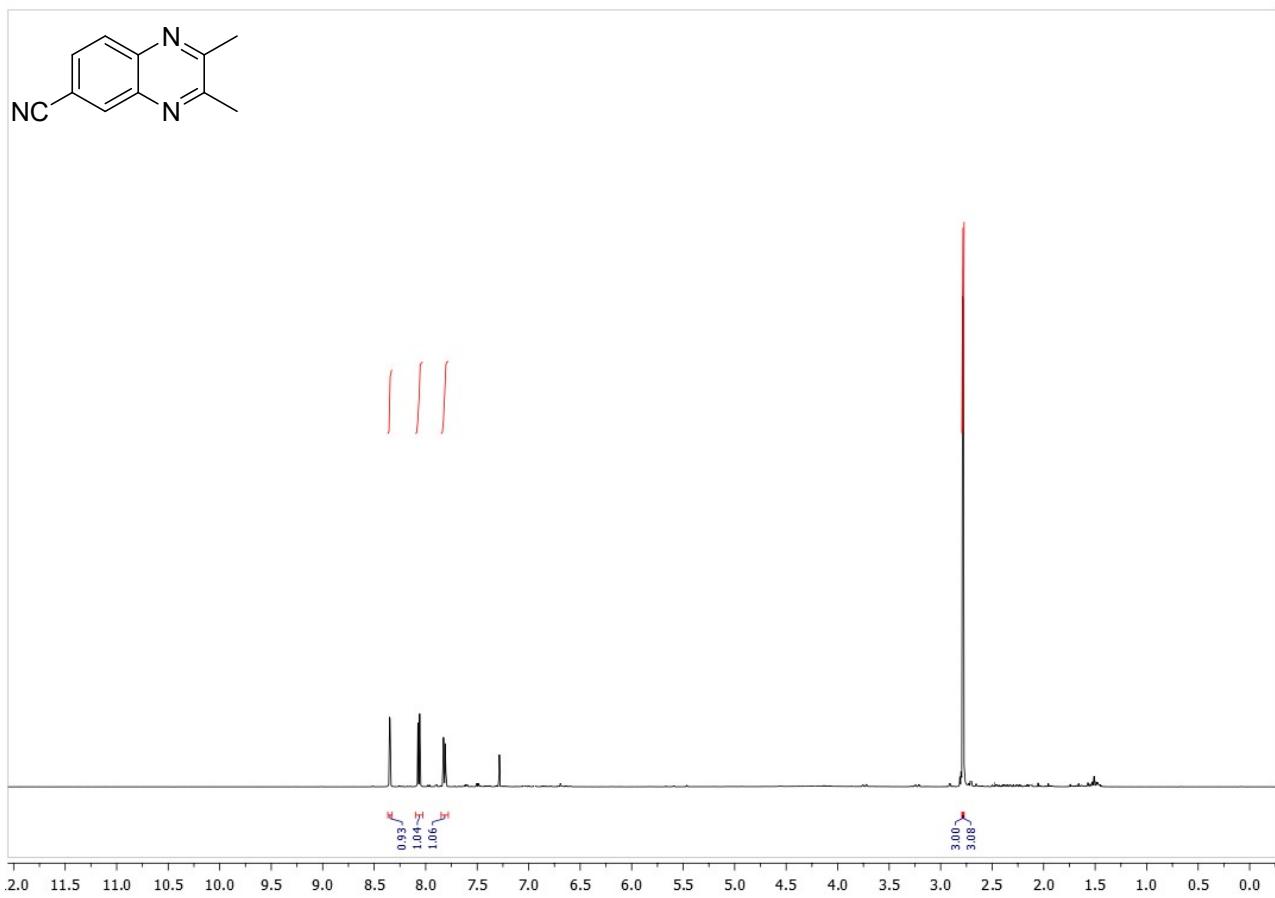
<sup>1</sup>H-NMR spectrum of compound **3f**



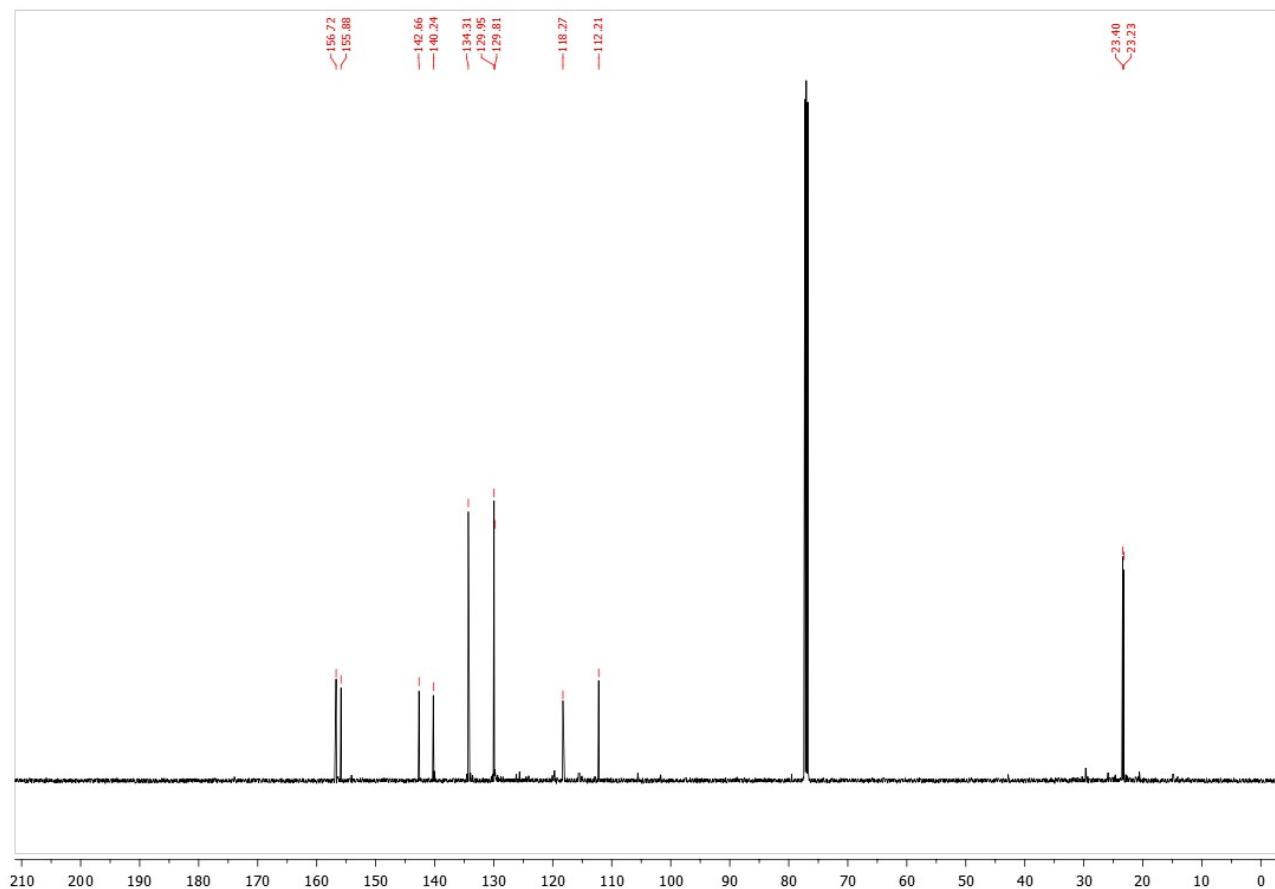
<sup>13</sup>C-NMR spectrum of compound **3f**.



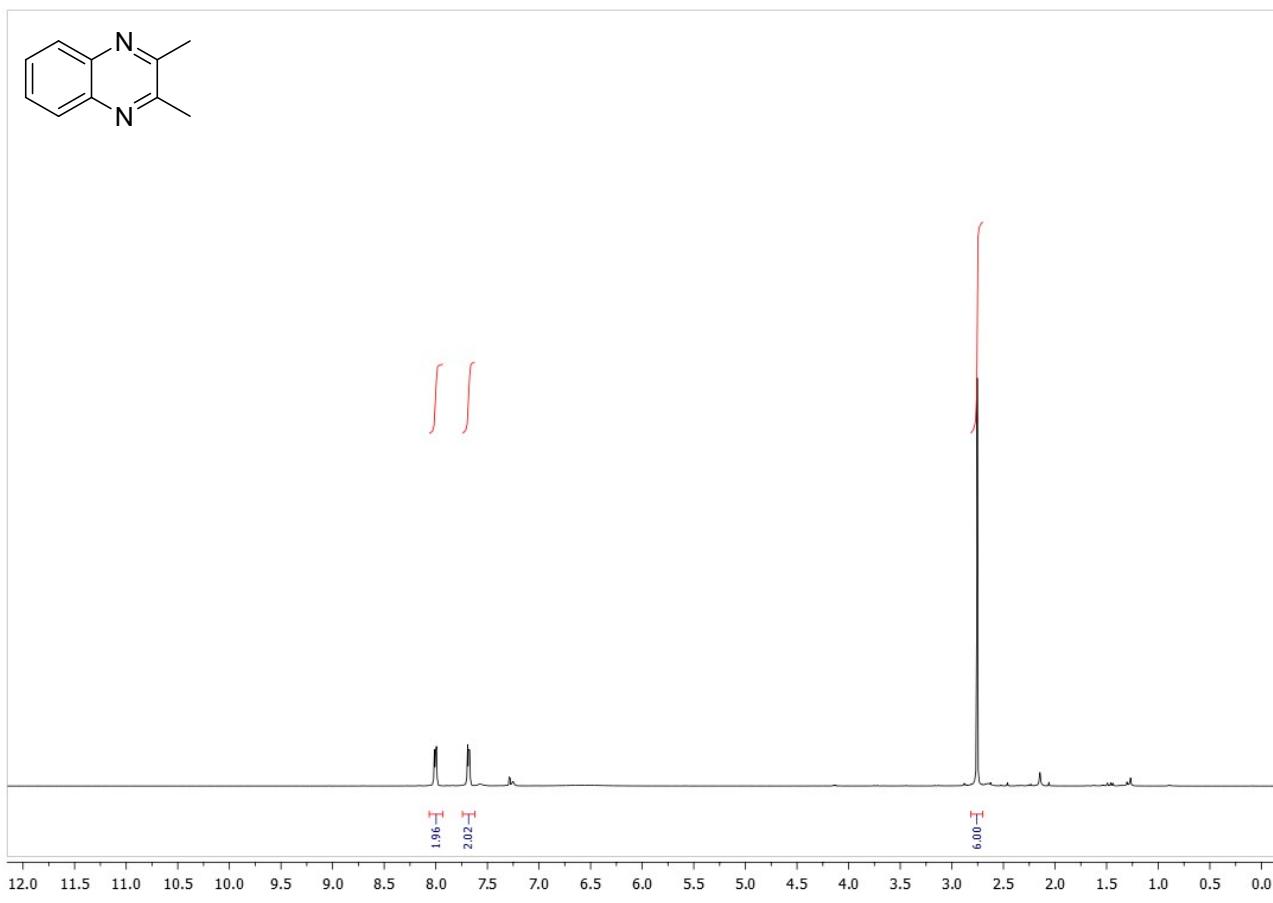
<sup>1</sup>H-NMR spectrum of compound **3g**



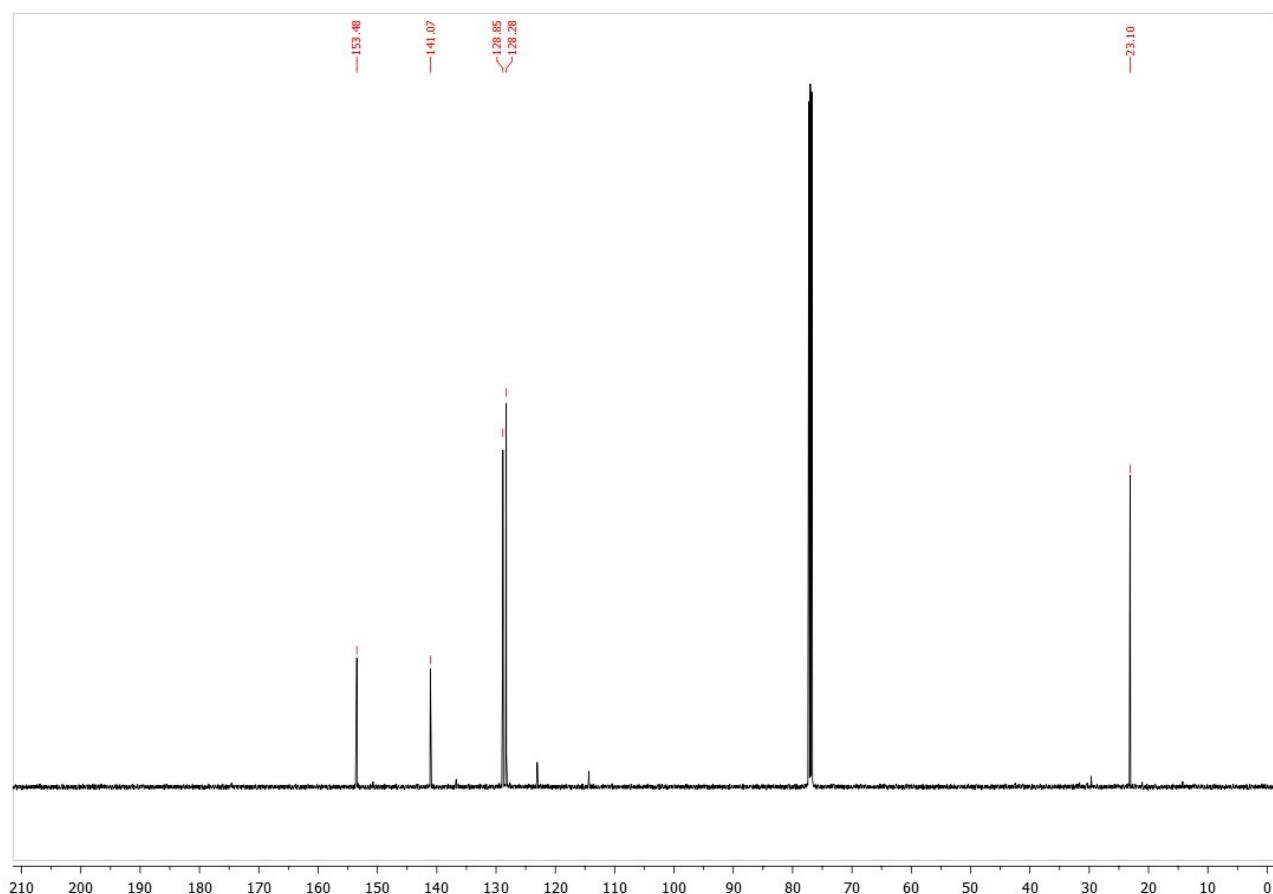
<sup>13</sup>C-NMR spectrum of compound **3g**.



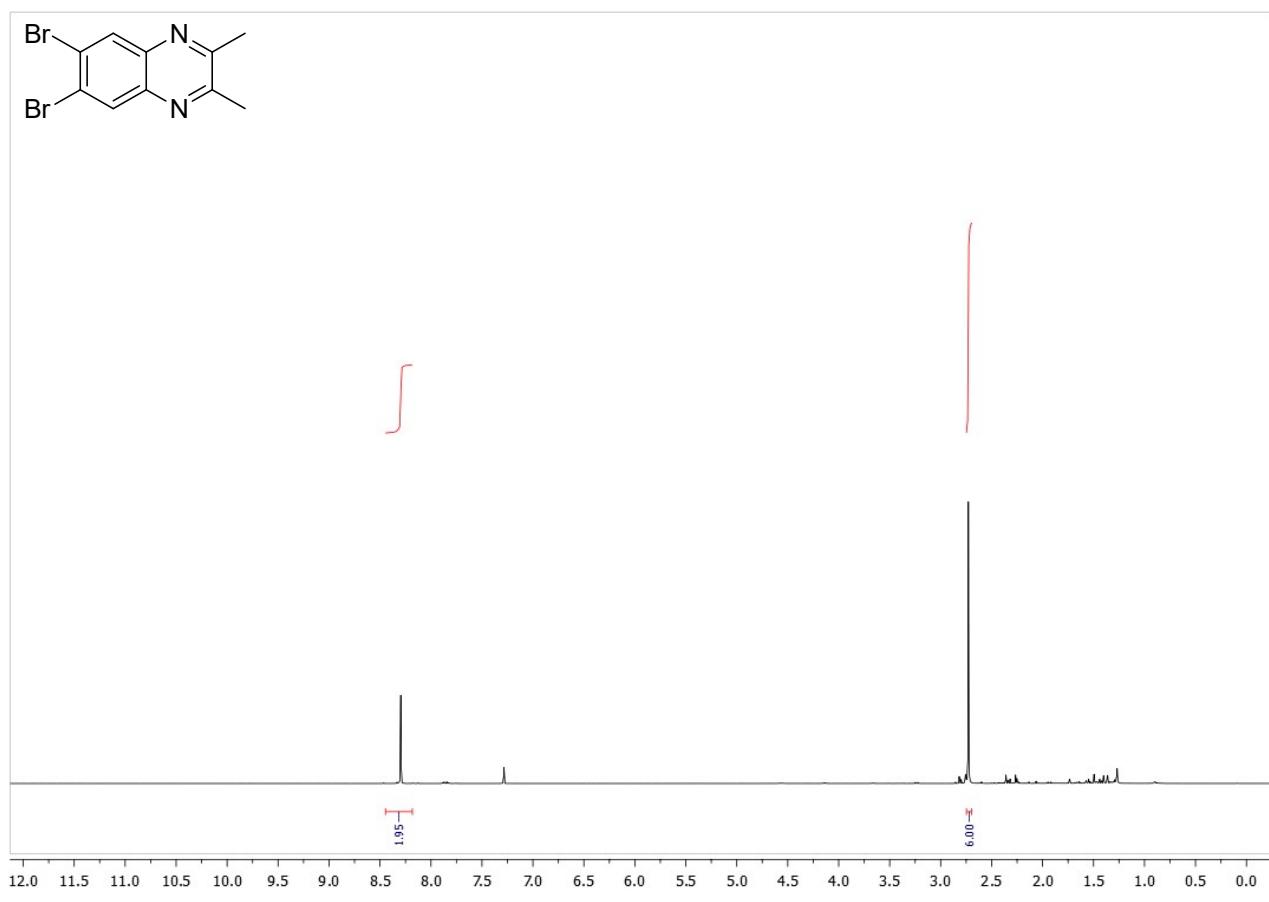
<sup>1</sup>H-NMR spectrum of compound **3h**.



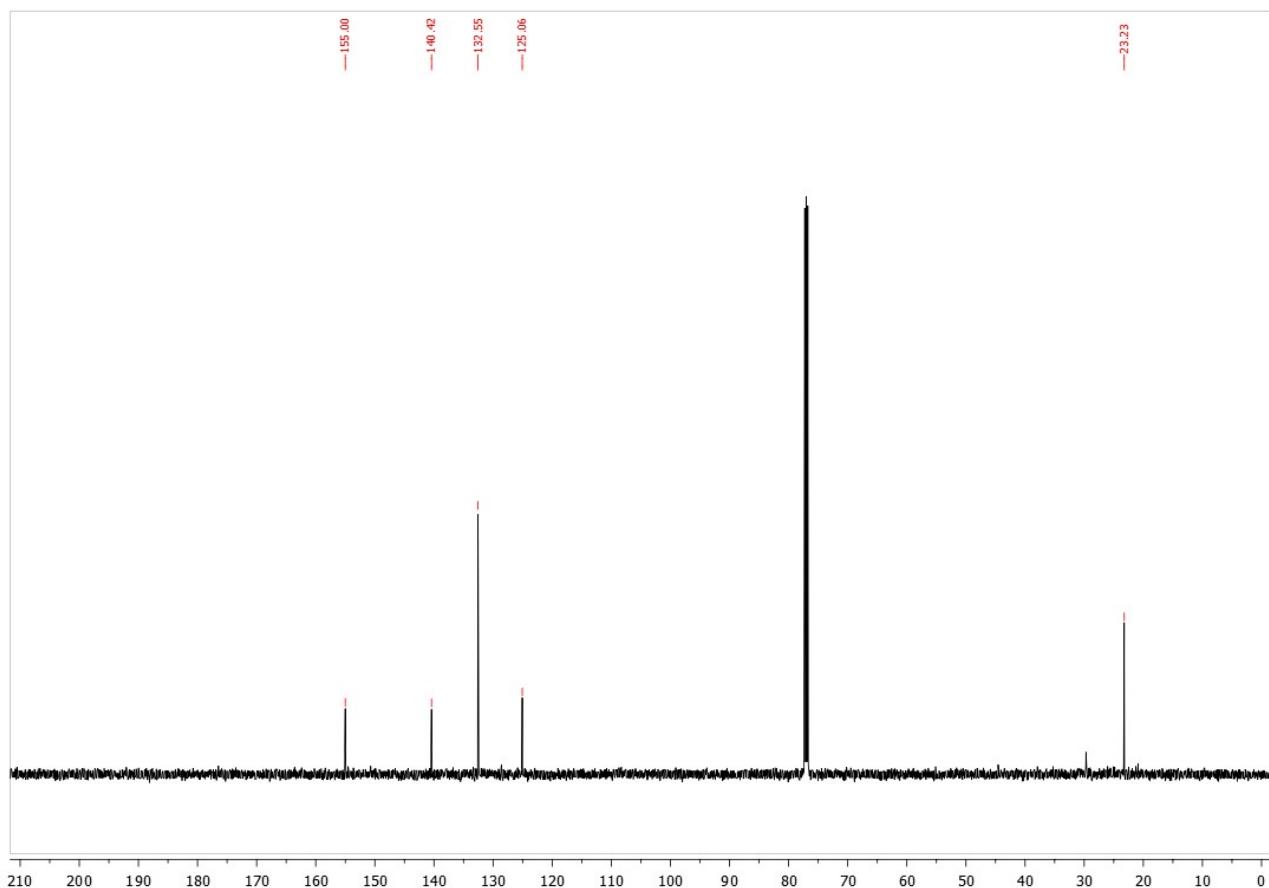
<sup>13</sup>C-NMR spectrum of compound **3h**.



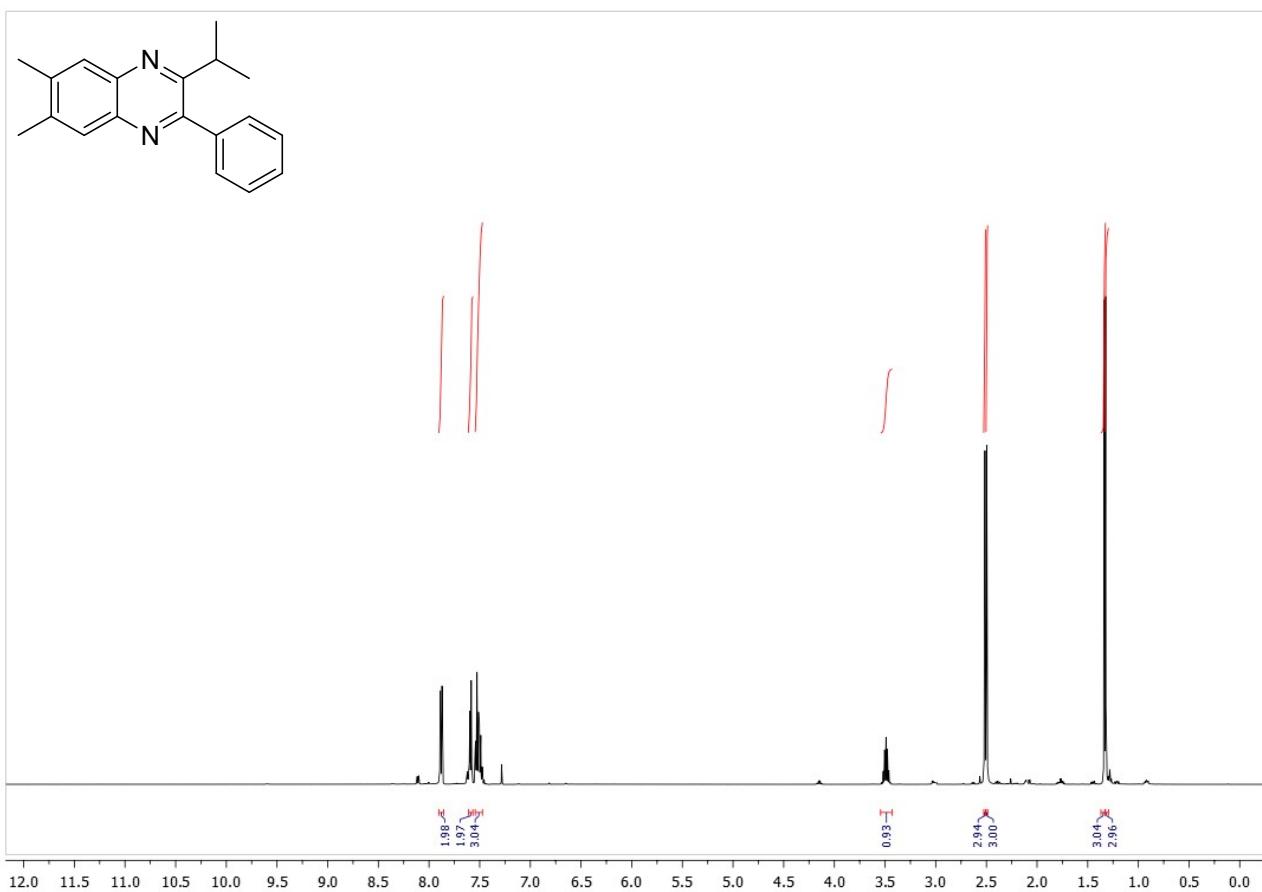
<sup>1</sup>H-NMR spectrum of compound **3i**



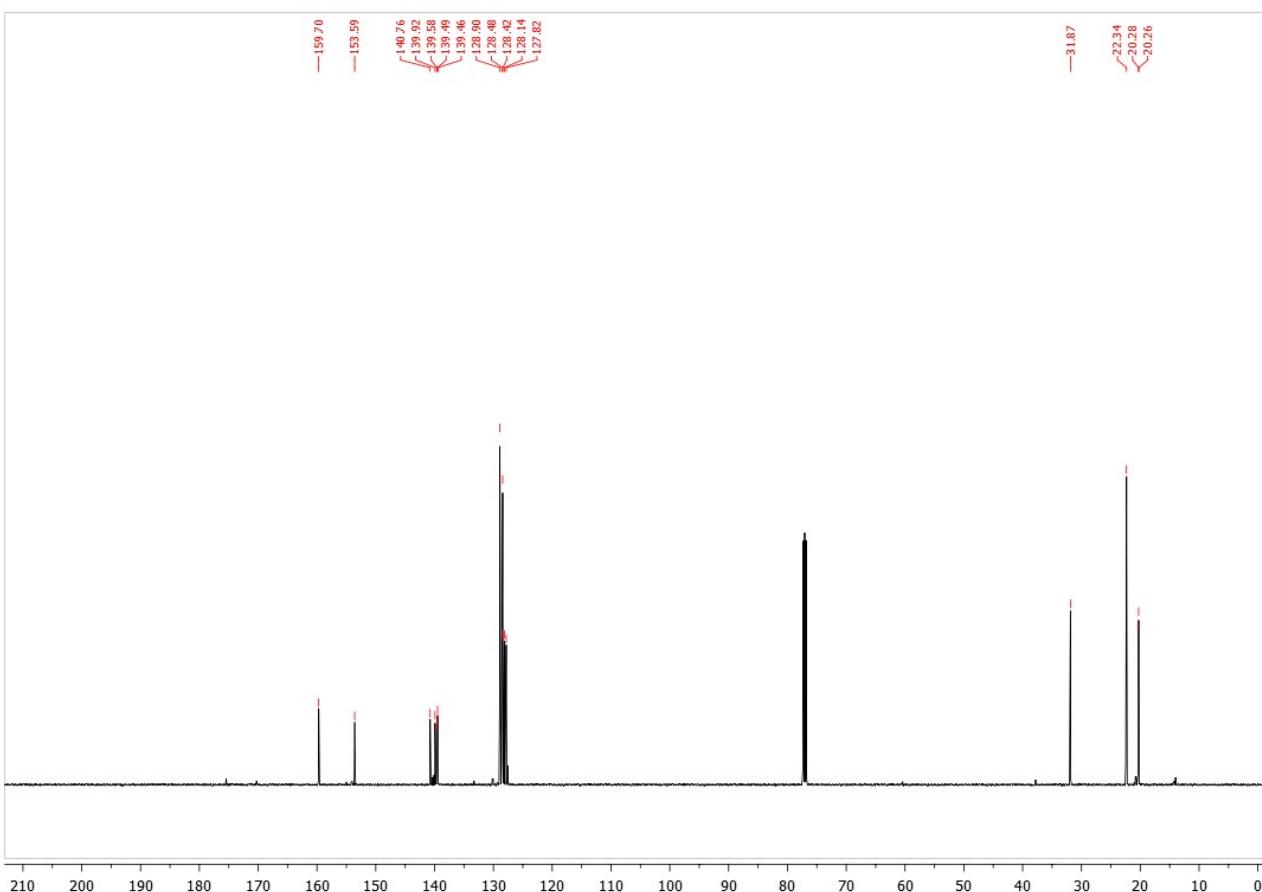
<sup>13</sup>C-NMR spectrum of compound **3i**.



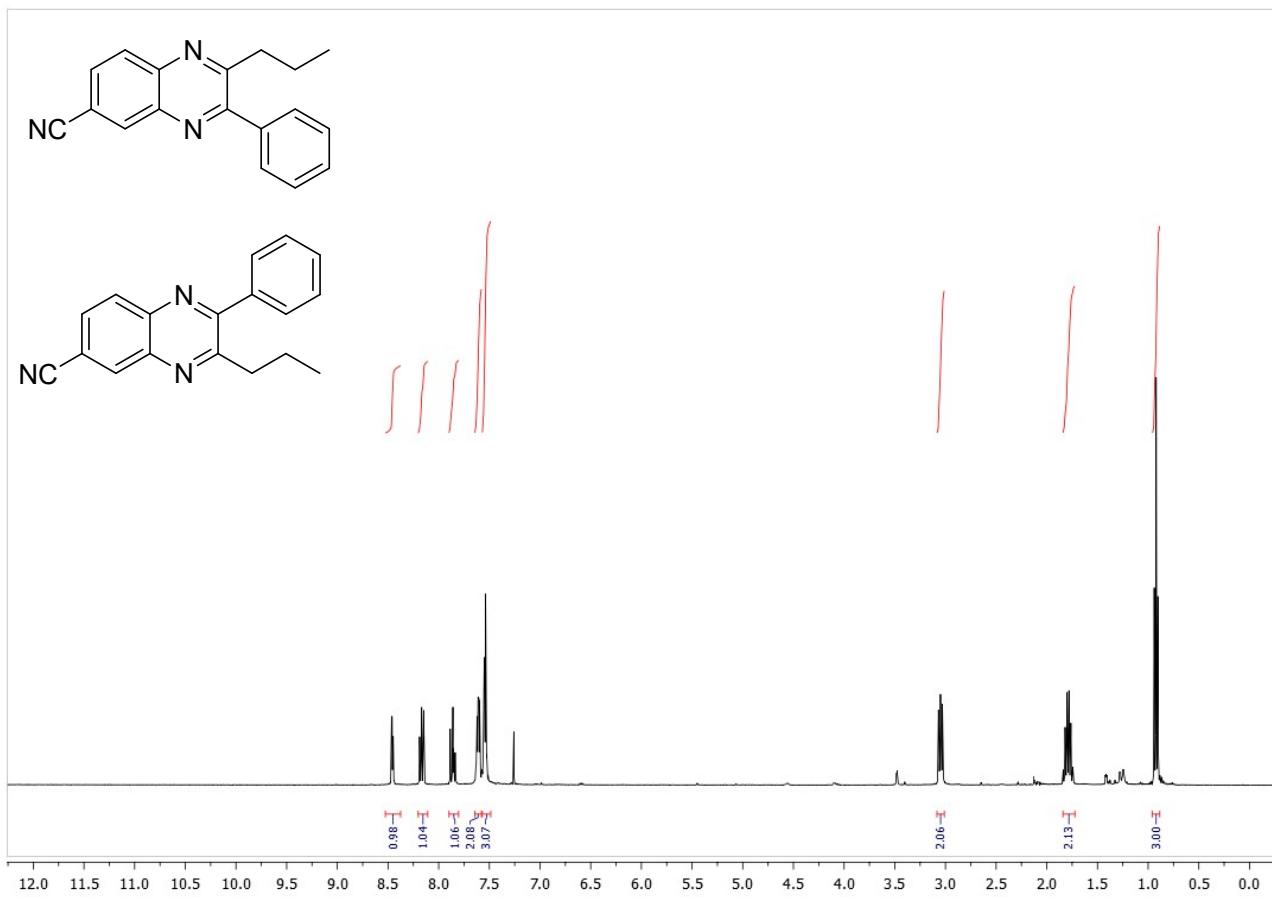
<sup>1</sup>H-NMR spectrum of compound 3j.



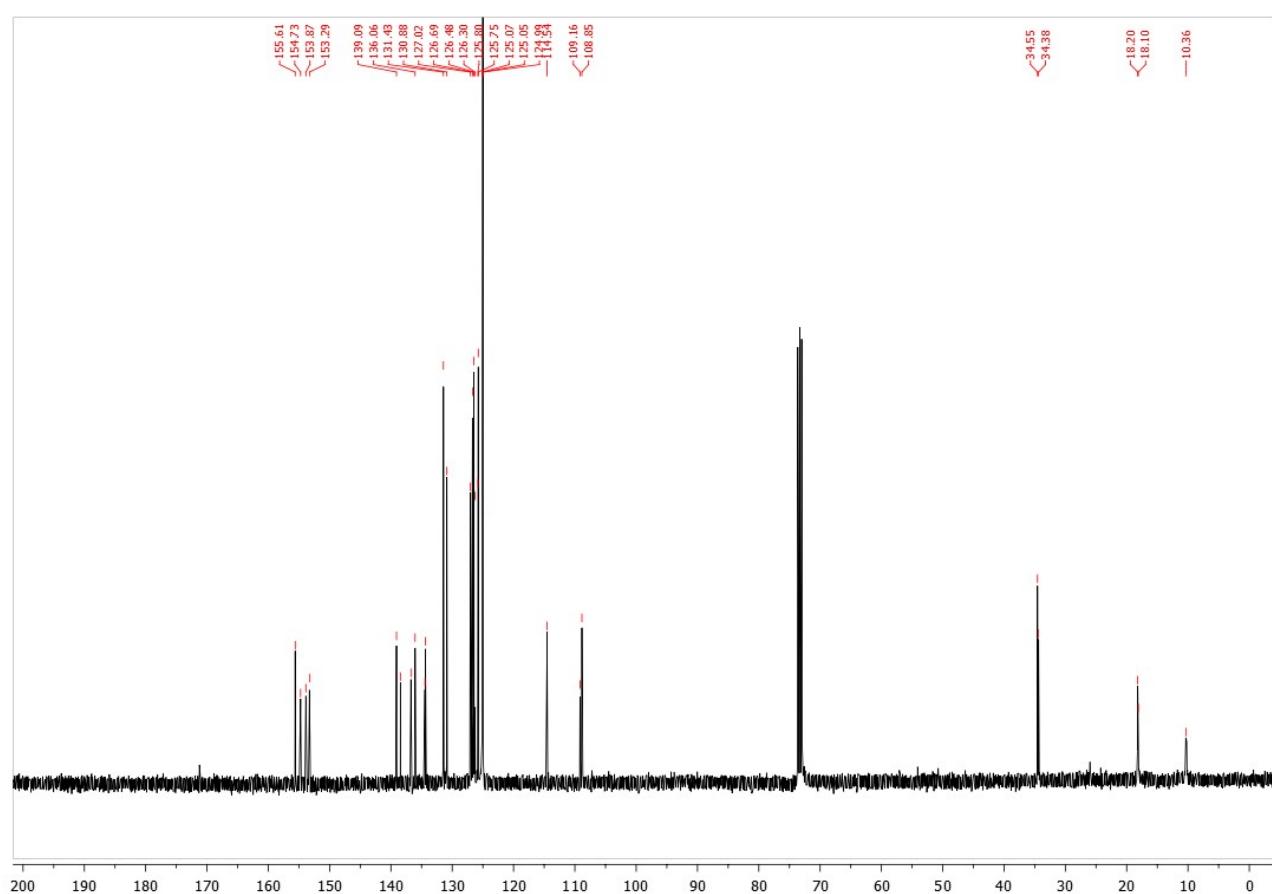
<sup>13</sup>C-NMR spectrum of compound 3j.



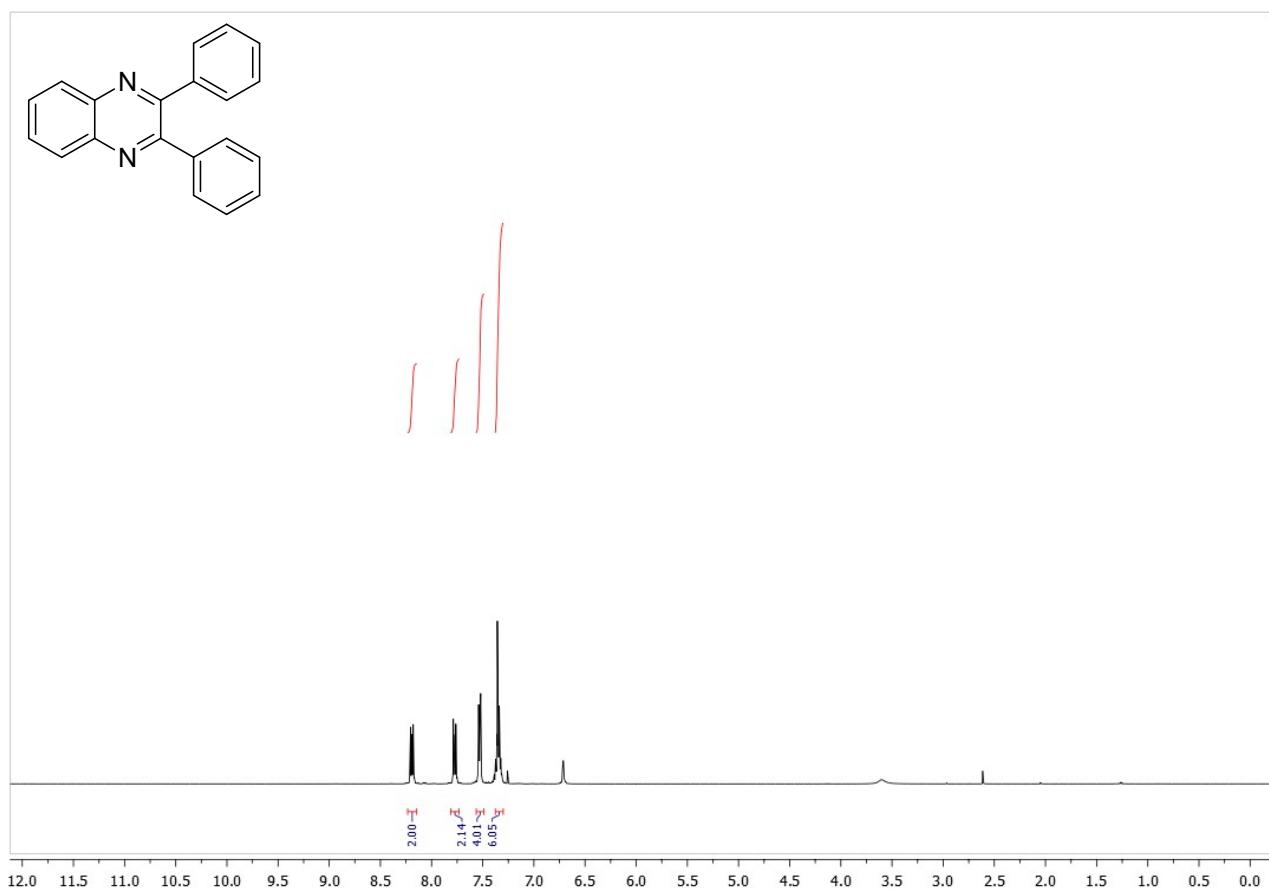
<sup>1</sup>H-NMR spectrum of compound **3k + 3k'**.



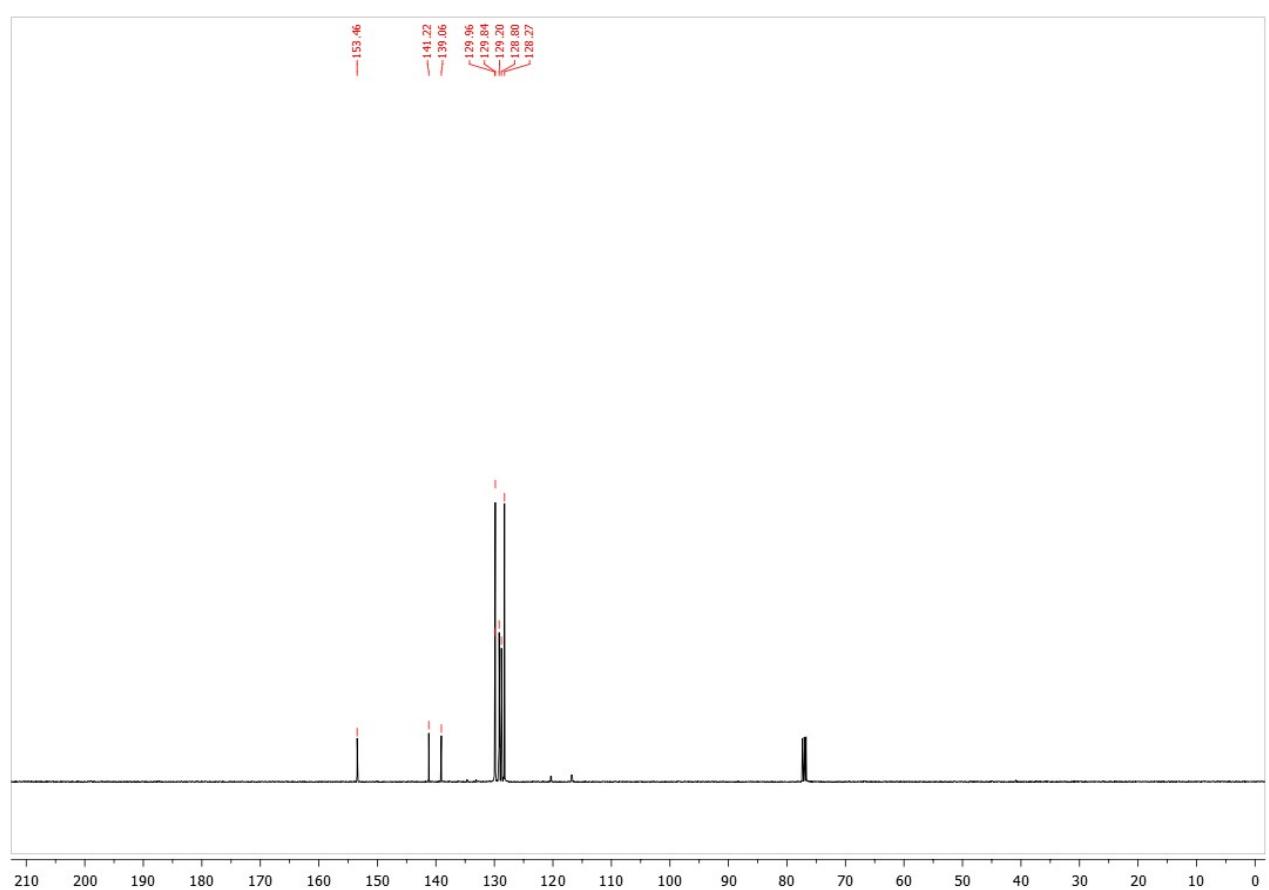
<sup>13</sup>C-NMR spectrum of compound **3k + 3k'**.



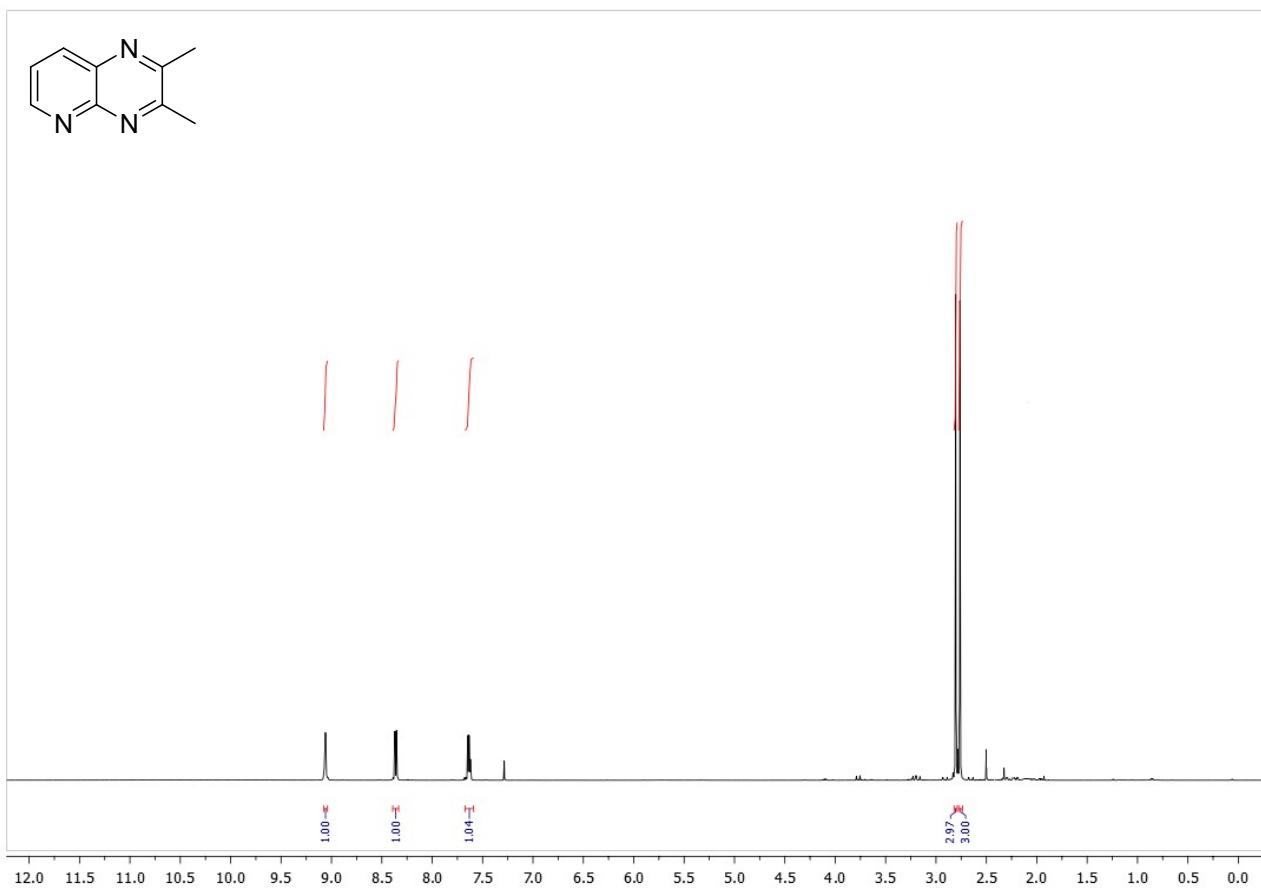
<sup>1</sup>H-NMR spectrum of compound 3I



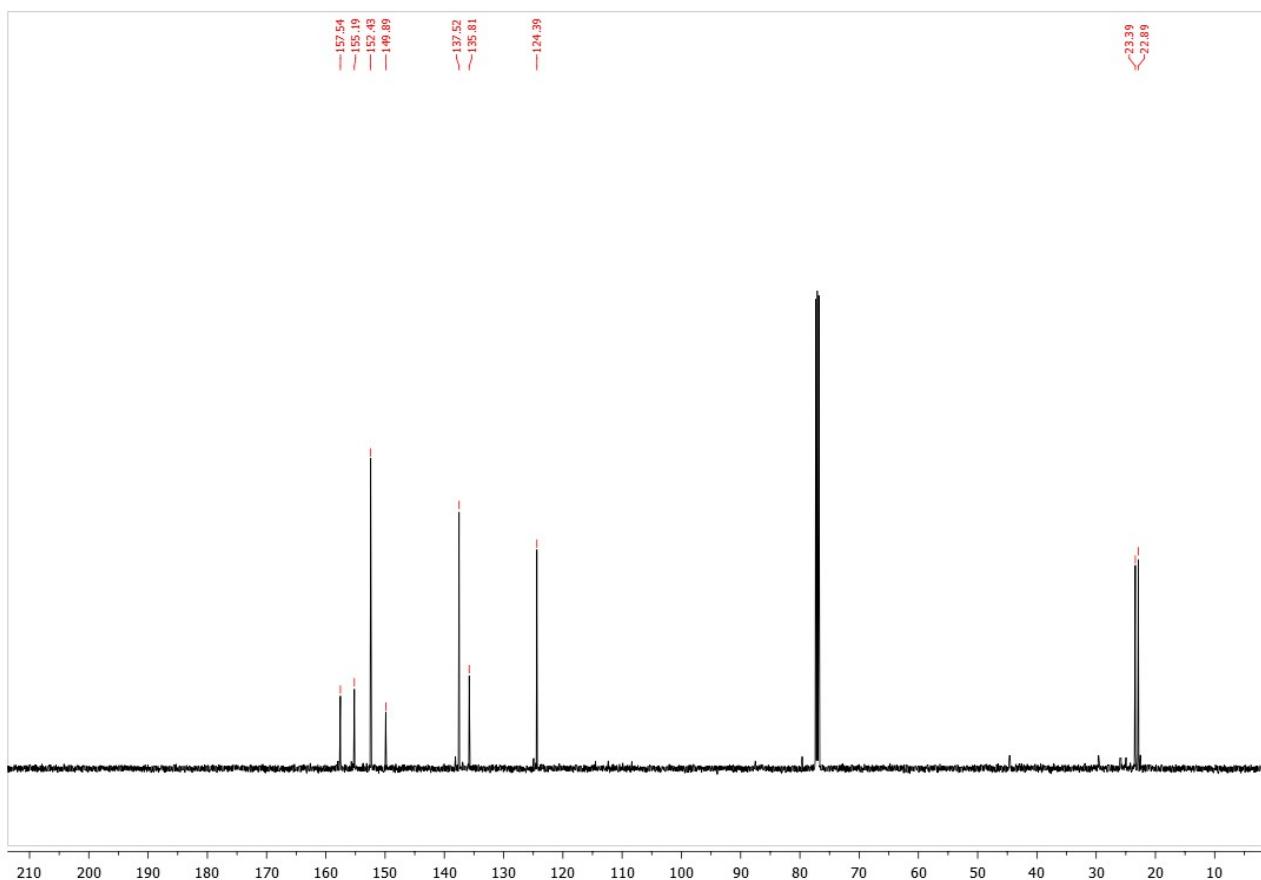
<sup>13</sup>C-NMR spectrum of compound 3I.



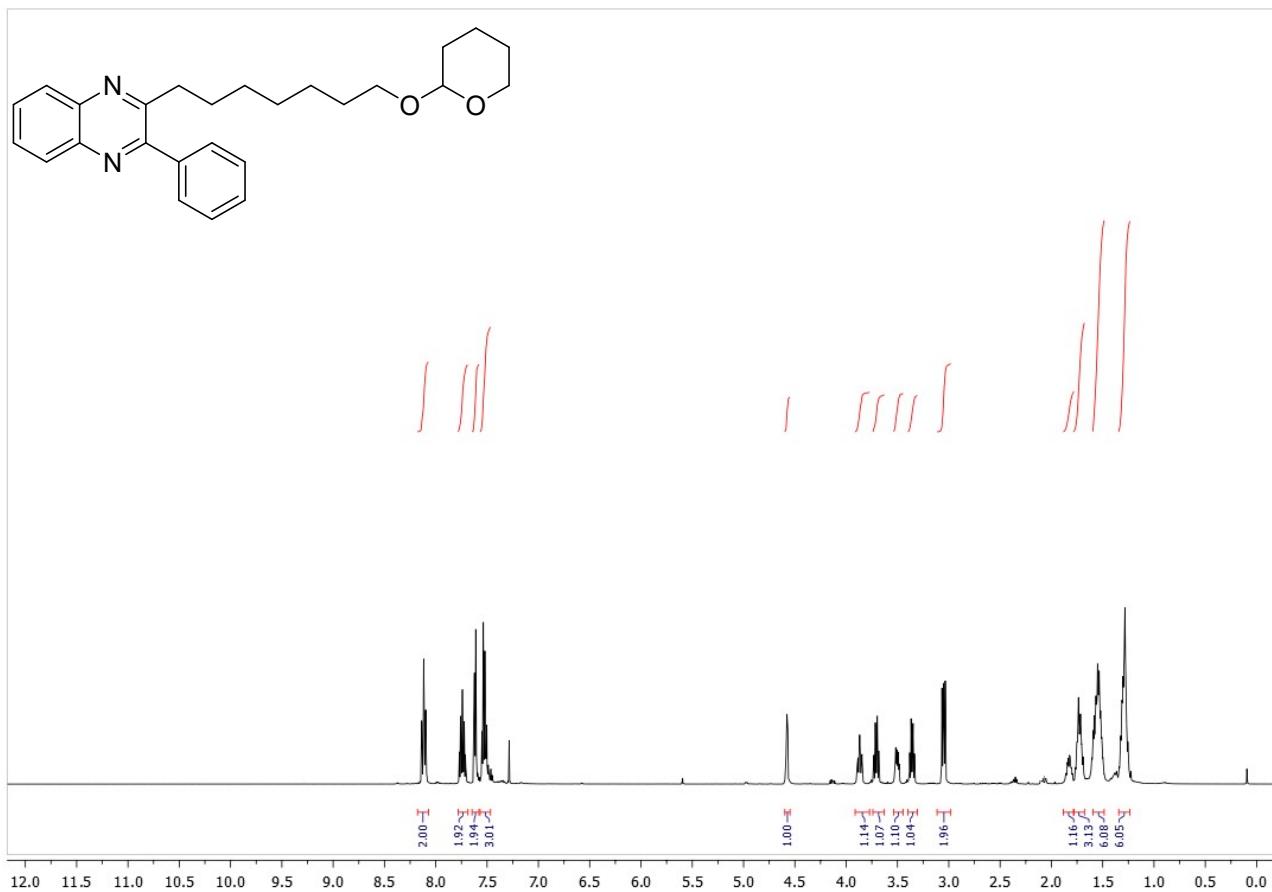
<sup>1</sup>H-NMR spectrum of compound **3m**



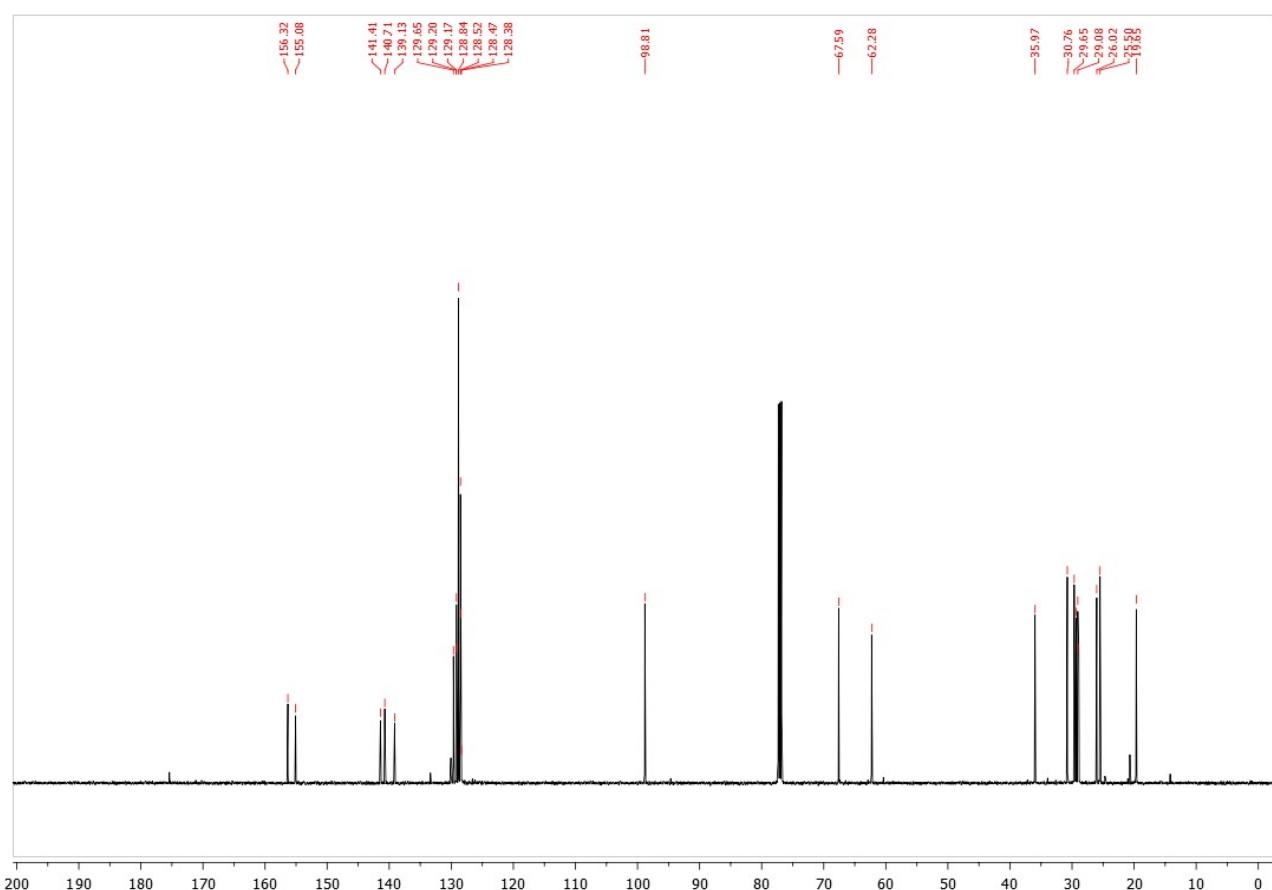
<sup>13</sup>C-NMR spectrum of compound **3m**.



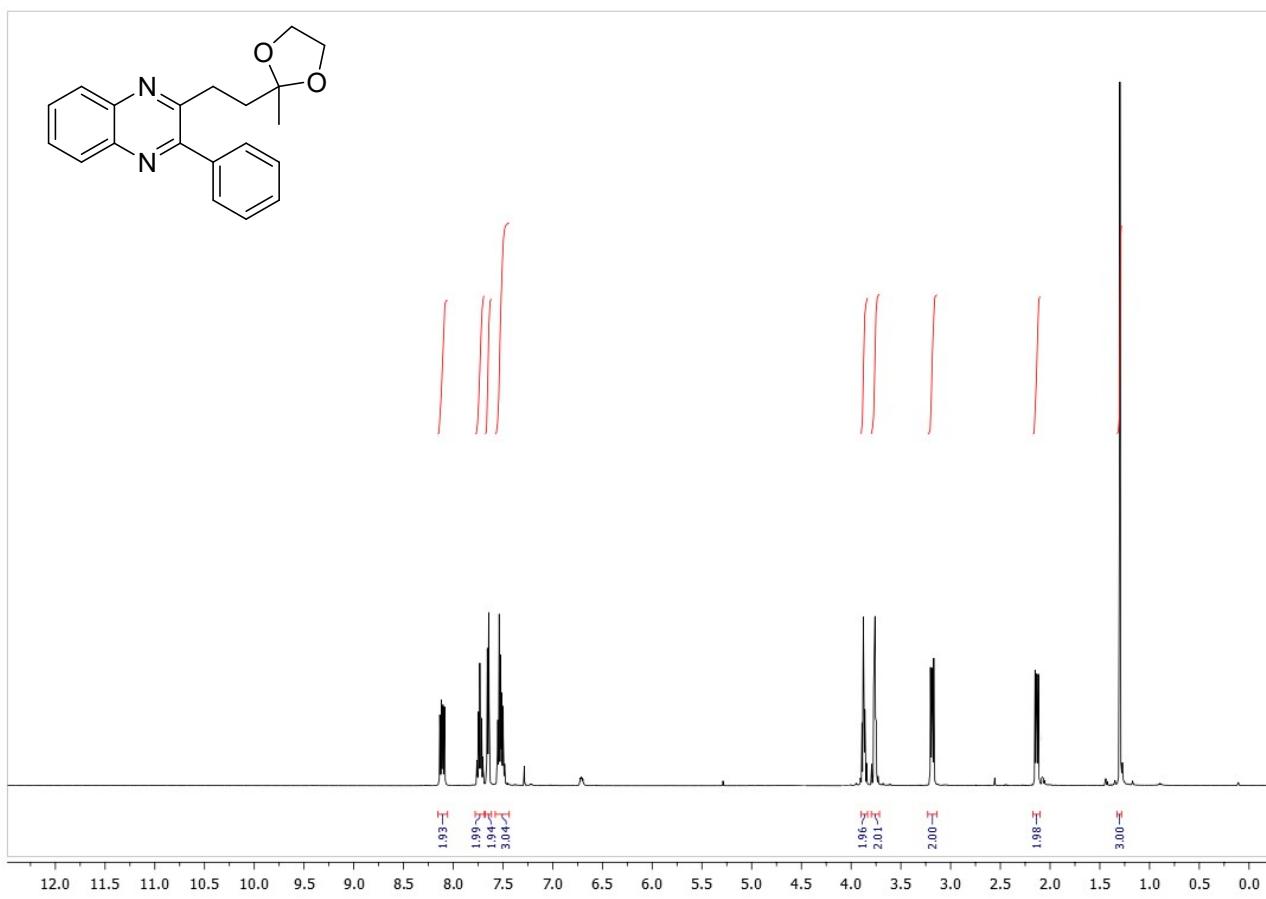
<sup>1</sup>H-NMR spectrum of compound 3n



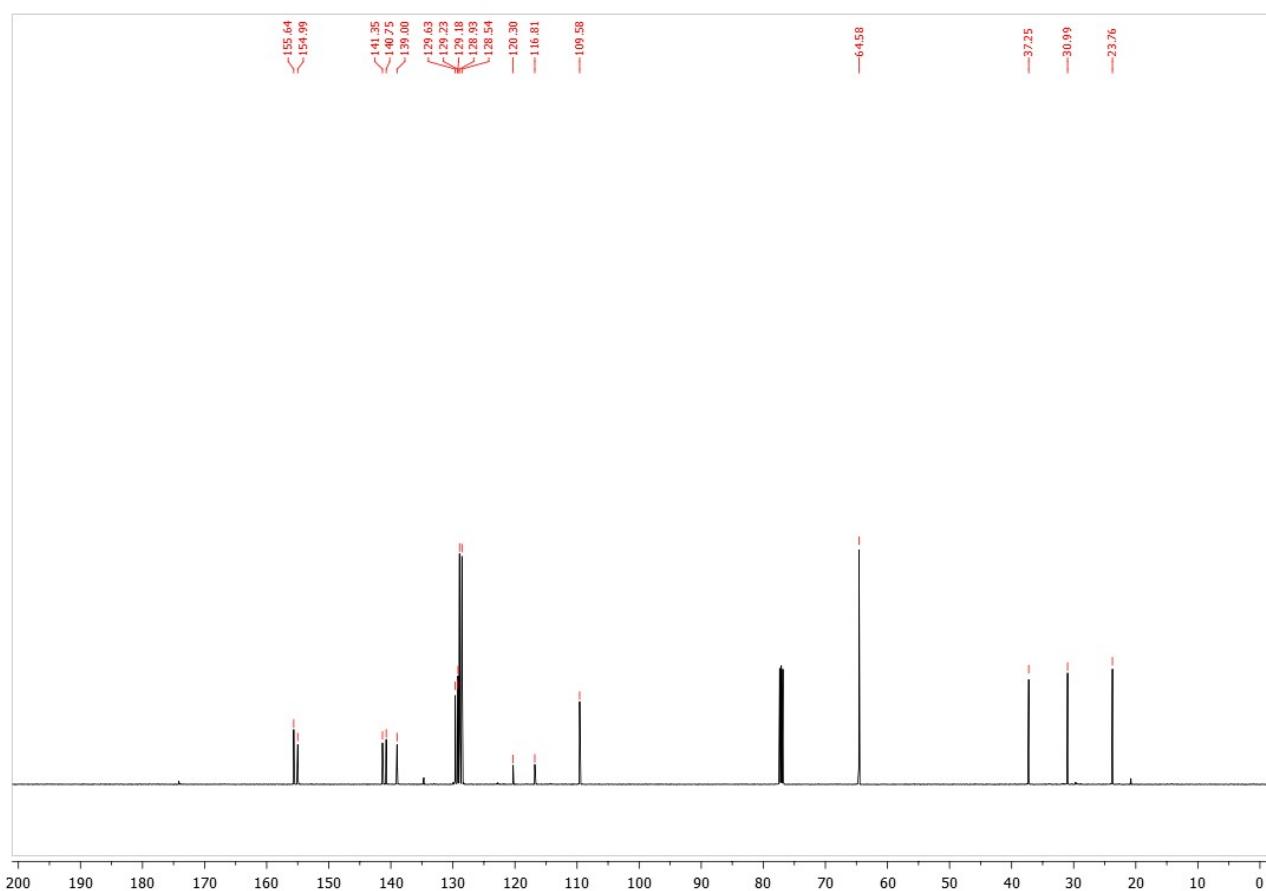
<sup>13</sup>C-NMR spectrum of compound 3n.



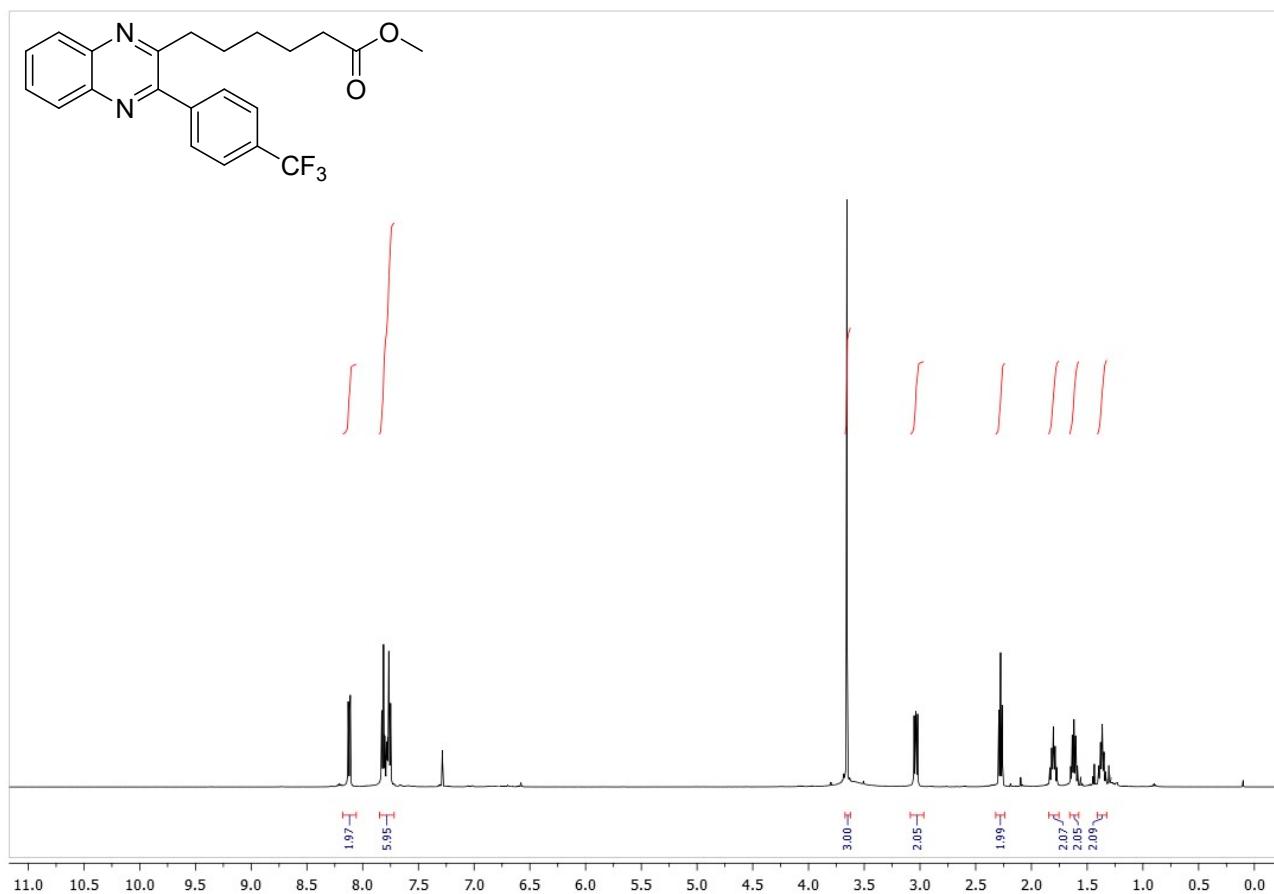
<sup>1</sup>H-NMR spectrum of compound 3o.



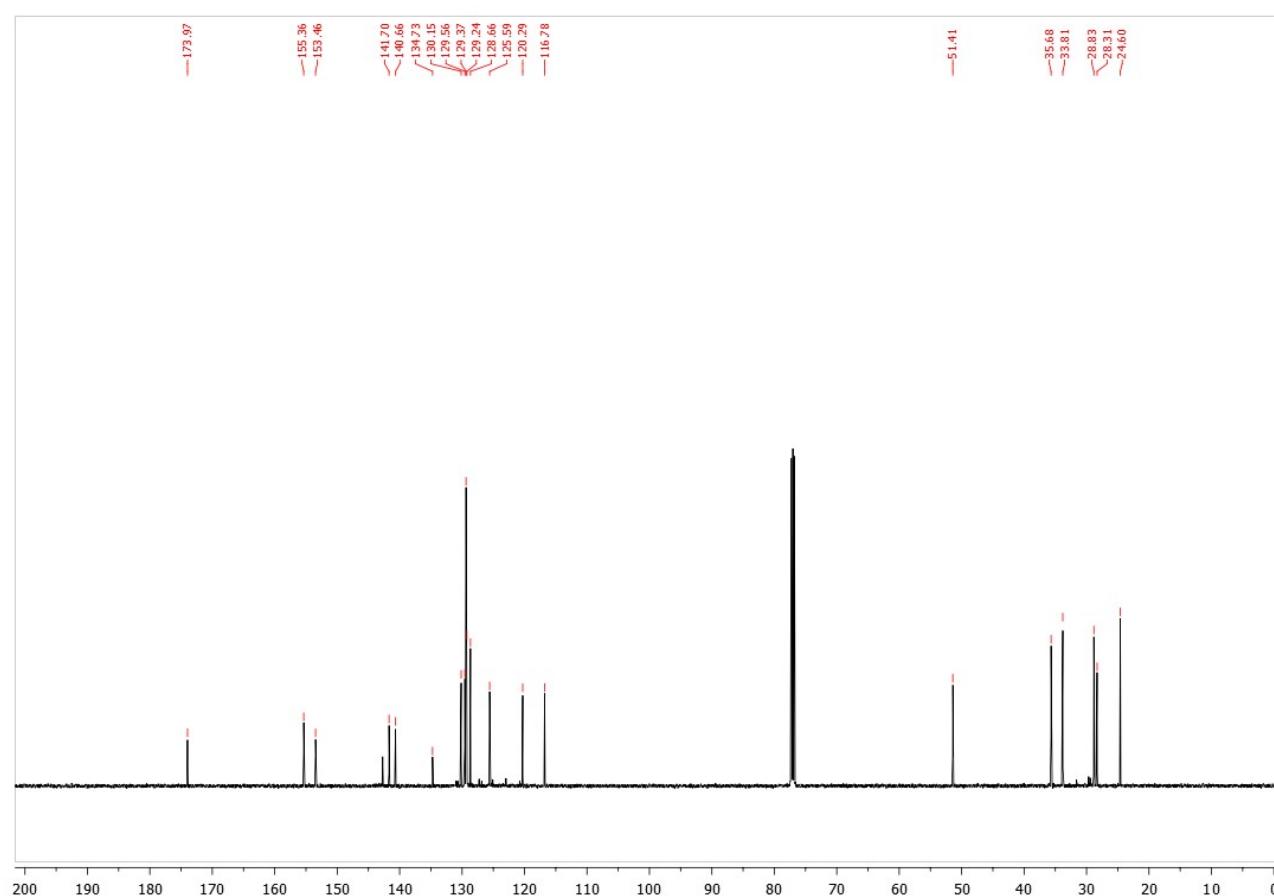
<sup>13</sup>C-NMR spectrum of compound 3o.



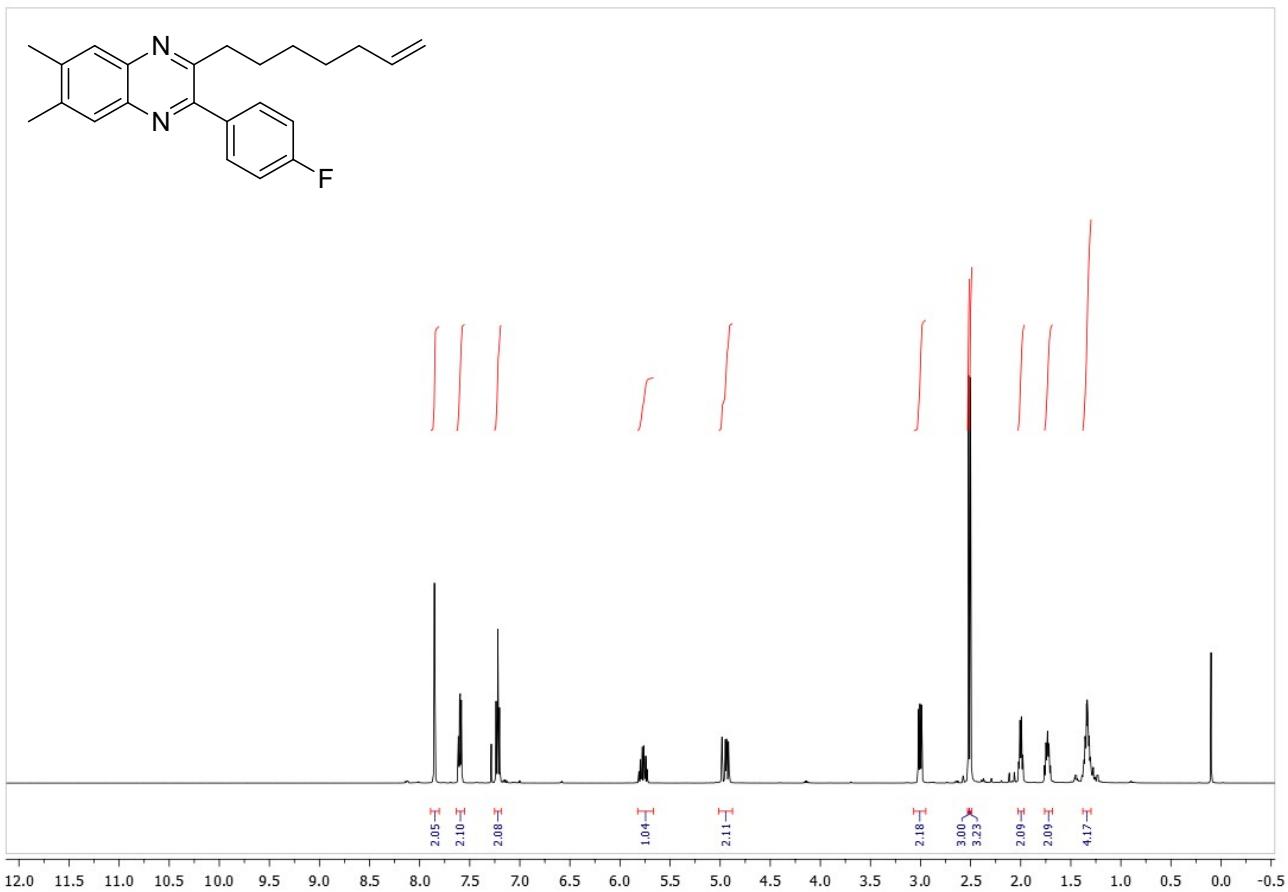
<sup>1</sup>H-NMR spectrum of compound **3p**.



<sup>13</sup>C-NMR spectrum of compound **3p**.



### <sup>1</sup>H-NMR spectrum of compound 3q.



### <sup>13</sup>C-NMR spectrum of compound 3q.

