

Supporting Information

Synthesis of Pyrrolo[1,2-*a*]quinoxalines via Copper or Iron-Catalyzed Aerobic Oxidative Carboamination of sp³C-H Bonds

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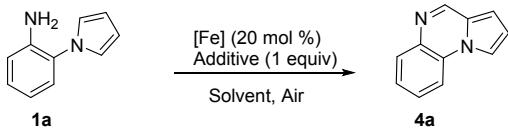
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General Information

¹H and ¹³C NMR spectra were recorded on BRUKER DRX-400 spectrometer. IR spectra were obtained with an infrared spectrometer on either potassium bromide pellets or liquid films between two potassium bromide pellets. HRMS was carried out on a high-resolution mass spectrometer (LCMS-IT-TOF). TLC was performed using commercially available 100–400 mesh silica gel plates (GF₂₅₄). Unless otherwise stated, all reagents and solvents were purchased from commercial suppliers and used without further purification.

Optimization of Reaction Conditions for Products 4^a

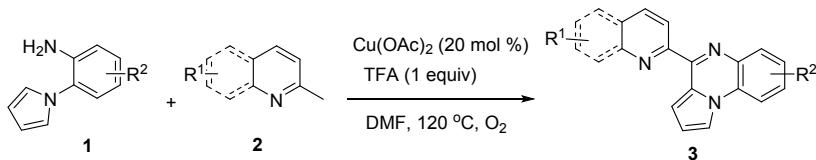


Entry	[Fe]	Additive	Solvent	Yield (%)
1	FeBr ₂	AcOH	DMSO	46
2	FeCl ₃	AcOH	DMSO	34
3	Fe(NO ₃) ₃	AcOH	DMSO	61
4	Fe(0)	AcOH	DMSO	82
5	Fe(OAc) ₂	AcOH	DMSO	37
6	Fe(0)	TfOH	DMSO	42
7	Fe(0)	TsOH	DMSO	17
8	Fe(0)	TFA	DMSO	58
9 ^b	Fe(0)	AcOH	DMSO	58
10 ^c	Fe(0)	AcOH	DMSO	71
11 ^d	Fe(0)	AcOH	DMSO	80
12 ^e	Fe(0)	AcOH	DMSO	n.d.

^a Reactions were performed with **2a** (0.3 mmol), [Fe] (20 mol %), Additive (0.3 mmol) in solvent (3.0 mL) under air atmosphere at 100 °C for 12 h. Isolated yield. n.d. = not determined. ^b The reaction temperature was 80 °C. ^c The reaction temperature was 120 °C. ^d The reaction was under O₂. ^e The reaction was under N₂ atmosphere.

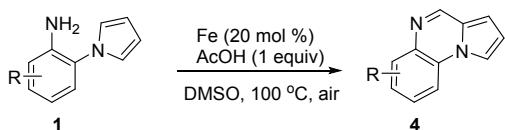
Initially, we treated 2-(1*H*-pyrrol-1-yl)aniline (**1a**) with FeBr₂ (20 mol %) and HOAc (0.3 mmol) in DMSO at 100 °C for 12 h, the product pyrrolo[1,2-*a*]quinoxaline **4a** was formed in 46% yield (entry 1). Afterwards, different Fe catalysts were investigated and Fe(0) was confirmed as the best choice (entries 2-5). Furthermore, acid screening indicated that HOAc was the best. Other acids, such as TfOH, TsOH, and TFA resulted in low yields (entries 6-8). When we reduced or increased the reaction temperature, the yields decreased (entries 9-10). Finally, when we carried out the reaction under the O₂ atmosphere, the yield did not increase (entry 11). And no product was detected under N₂ atmosphere (entry 12). Thus, the optimized reaction system for this Fe-catalyzed cyclization reaction was: **1a** (0.3 mmol), Fe(0) (0.06 mmol), HOAc (0.3 mmol), and DMSO (3 mL) at 100 °C under air for 12 h.

Experimental Section for Products 3



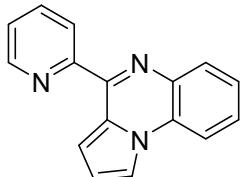
General procedure for products **3**: the 2-(1*H*-pyrrol-1-yl)aniline **1** (0.3 mmol), 2-methylpyridine/quinoline **2** (0.6 mmol), Cu(OAc)₂ (20 mol %), TFA (0.3 mmol), DMF (3 mL) were added to a 25 mL tube with magnetic stirrer bar. The reaction mixture was stirred at 120°C (oil bath temperature) with a O₂ balloon which was attached to the reaction tube for 12 h. After the reaction was finished (monitored by TLC), the mixture was cooled to room temperature, quenched with solution of NaHCO₃ (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄ and the solvent was removed under vacuum. The crude product was purified by column chromatography (EtOAc/hexanes) on silica gel.

Experimental Section for Products 4



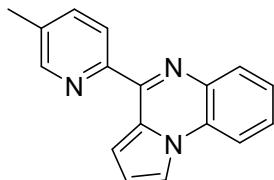
General procedure for products **4**: the 2-(1*H*-pyrrol-1-yl)aniline **1** (0.3 mmol), Fe(0) (20 mol %), HOAc (0.3 mmol), DMSO (3 mL) were added to a 25 mL tube with magnetic stirrer bar. The reaction mixture was exposed to the air and stirred at 100°C (oil bath temperature) for 12 h. After the reaction was finished (monitored by TLC), the mixture was cooled to room temperature, quenched with solution of NaHCO₃ (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over anhydrous MgSO₄ and the solvent was removed under vacuum. The crude product was purified by column chromatography (EtOAc/hexanes) on silica gel.

Characterization Data for All Products



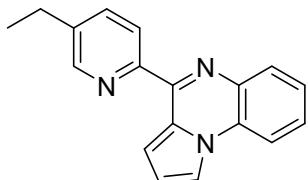
4-(pyridin-2-yl)pyrrolo[1,2-a]quinoxaline (3a)¹

Green solid (57.3 mg, 78%); m.p. = 103–104 °C. ¹H NMR (400 MHz, DMSO) δ 8.83 – 8.81 (m, 1H), 8.56 (dd, *J* = 2.7, 1.3 Hz, 1H), 8.50 – 8.47 (m, 1H), 8.34 (dd, *J* = 8.3, 1.1 Hz, 1H), 8.06 – 7.98 (m, 2H), 7.84 (dd, *J* = 4.0, 1.3 Hz, 1H), 7.67 – 7.51 (m, 3H), 7.03 – 7.00 (m, 1H). ¹³C NMR (100 MHz, DMSO) δ 156.0, 150.3, 149.2, 137.4, 135.2, 130.2, 128.9, 127.6, 125.9, 125.2, 124.0, 123.3, 116.5, 115.1, 114.8, 111.4. IR (KBr) ν (cm⁻¹): 3092, 2922, 1607, 1458, 1336, 1031, 745.



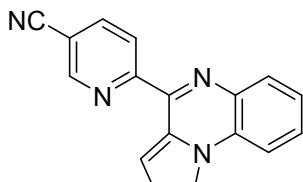
4-(5-methylpyridin-2-yl)pyrrolo[1,2-a]quinoxaline (3b)

Yellow solid (52.8 mg, 68%); m.p. = 95–96 °C. ¹H NMR (400 MHz, DMSO) δ 8.65 (dd, *J* = 1.4, 0.7 Hz, 1H), 8.55 (dd, *J* = 2.7, 1.3 Hz, 1H), 8.40 (d, *J* = 8.1 Hz, 1H), 8.34 (dd, *J* = 8.3, 1.1 Hz, 1H), 7.99 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.87 – 7.83 (m, 2H), 7.66 – 7.62 (m, 1H), 7.55 – 7.50 (m, 1H), 7.00 (dd, *J* = 4.0, 2.7 Hz, 1H), 2.43 (s, 3H). ¹³C NMR (100 MHz, DMSO) δ 153.5, 150.4, 149.4, 137.7, 135.3, 134.9, 130.1, 128.7, 127.6, 125.8, 124.0, 122.8, 116.4, 115.1, 114.7, 111.4, 18.4. IR (KBr) ν (cm⁻¹): 2919, 2853, 1468, 1422, 1358, 1029, 751, 713. HRMS-ESI (m/z): calcd for C₁₇H₁₄N₃, [M+H]⁺: 260.1182; found, 260.1177.



4-(5-ethylpyridin-2-yl)pyrrolo[1,2-a]quinoxaline (3c)

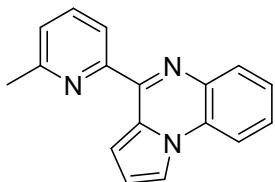
Green solid (53.2 mg, 65%); m.p. = 89–90 °C. ¹H NMR (400 MHz, DMSO) δ 8.67 (s, 1H), 8.55 (d, *J* = 1.1 Hz, 1H), 8.42 (d, *J* = 8.1 Hz, 1H), 8.34 (d, *J* = 8.2 Hz, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.90 – 7.84 (m, 2H), 7.63 (t, *J* = 7.7 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.03 – 6.99 (m, 1H), 2.74 (q, *J* = 7.6 Hz, 2H), 1.27 (t, *J* = 7.6 Hz, 3H). ¹³C NMR (100 MHz, DMSO) δ 153.7, 150.3, 148.7, 140.7, 136.5, 135.3, 130.1, 128.7, 127.6, 125.8, 124.0, 123.0, 116.4, 115.1, 114.7, 111.4, 25.7, 15.6. IR (KBr) ν (cm⁻¹): 2964, 2924, 1469, 1428, 1361, 1031, 754, 713. HRMS-ESI (m/z): calcd for C₁₈H₁₆N₃, [M+H]⁺: 274.1339; found, 274.1334.



6-(pyrrolo[1,2-a]quinoxalin-4-yl)nicotinonitrile (3d)

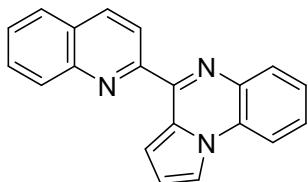
Yellow solid (42.1 mg, 52%); m.p. = 201–202 °C. ¹H NMR (400 MHz, DMSO) δ 9.26 (s, 1H), 8.66 (d, *J* = 8.3 Hz, 1H), 8.61 (s, 1H), 8.52 (d, *J* = 8.4 Hz, 1H), 8.38 (d, *J* = 8.3 Hz, 1H), 8.03 (d, *J* = 8.0 Hz, 1H), 7.84 (d, *J* = 4.0 Hz, 1H), 7.70 (t,

J = 7.7 Hz, 1H), 7.57 (t, *J* = 7.6 Hz, 1H), 7.05 (d, *J* = 2.6 Hz, 1H). ^{13}C NMR (100 MHz, DMSO) δ 158.6, 152.3, 148.6, 141.1, 135.0, 130.5, 129.7, 127.7, 126.1, 123.7, 123.1, 117.5, 117.0, 115.3, 115.1, 111.3, 109.9. IR (KBr) ν (cm $^{-1}$): 2913, 2852, 1589, 1425, 1379, 1017, 753, 716. HRMS-ESI (m/z): calcd for C₁₇H₁₁N₄, [M+H] $^+$: 271.0978; found, 271.0978.



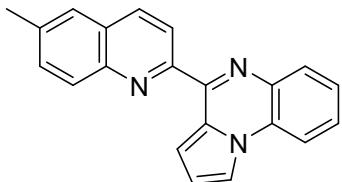
4-(6-methylpyridin-2-yl)pyrrolo[1,2-a]quinoxaline (3e)

Green solid (49.0 mg, 63%); m.p. = 125–126 °C. ^1H NMR (400 MHz, DMSO) δ 8.53 (s, 1H), 8.30 (dd, *J* = 15.2, 8.0 Hz, 2H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.90 (dd, *J* = 13.4, 5.8 Hz, 2H), 7.62 (t, *J* = 7.7 Hz, 1H), 7.51 (t, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 2.2 Hz, 1H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 157.2, 155.0, 150.0, 137.2, 134.9, 129.8, 128.4, 127.3, 125.4, 124.1, 123.7, 120.0, 116.0, 114.7, 114.4, 111.2, 24.2. IR (KBr) ν (cm $^{-1}$): 2921, 1574, 1461, 1414, 1034, 812, 751. HRMS-ESI (m/z): calcd for C₁₇H₁₄N₃, [M+H] $^+$: 260.1182; found, 260.1183.



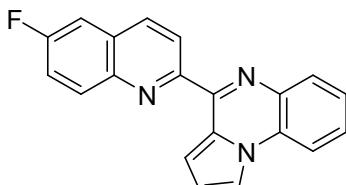
4-(quinolin-2-yl)pyrrolo[1,2-a]quinoxaline (3f)

Yellow solid (75.2 mg, 85%); m.p. = 186–187 °C. ^1H NMR (400 MHz, CDCl₃) δ 8.65 (d, *J* = 8.6 Hz, 1H), 8.31 (dd, *J* = 8.4, 4.6 Hz, 2H), 8.12 (dd, *J* = 10.5, 5.9 Hz, 2H), 8.02 (s, 1H), 7.89 (d, *J* = 8.1 Hz, 2H), 7.78 (t, *J* = 7.6 Hz, 1H), 7.63 – 7.44 (m, 3H), 7.04 – 6.99 (m, 1H). ^{13}C NMR (100 MHz, CDCl₃) δ 156.1, 150.8, 147.5, 136.3, 135.7, 130.5, 130.1, 129.5, 128.2, 128.2, 127.7, 127.6, 127.2, 125.1, 124.7, 120.6, 114.6, 114.3, 113.7, 111.2. IR (KBr) ν (cm $^{-1}$): 2923, 1593, 1412, 1365, 1027, 838, 754. HRMS-ESI (m/z): calcd for C₂₀H₁₄N₃, [M+H] $^+$: 296.1182; found, 296.1177.



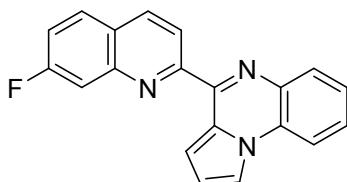
4-(6-methylquinolin-2-yl)pyrrolo[1,2-a]quinoxaline (3g)

Green solid (66.7 mg, 72%); m.p. = 180–181 °C. ^1H NMR (400 MHz, CDCl₃) δ 8.61 (d, *J* = 8.6 Hz, 1H), 8.23 (d, *J* = 8.6 Hz, 1H), 8.20 – 8.10 (m, 3H), 8.03 (s, 1H), 7.90 (d, *J* = 8.1 Hz, 1H), 7.67 – 7.45 (m, 4H), 7.01 (s, 1H), 2.58 (s, 3H). ^{13}C NMR (100 MHz, CDCl₃) δ 155.2, 150.9, 146.1, 137.4, 135.7, 135.4, 131.9, 130.3, 129.8, 128.3, 128.1, 127.7, 126.5, 125.1, 124.7, 120.7, 114.7, 114.5, 113.7, 111.6, 21.7. IR (KBr) ν (cm $^{-1}$): 2919, 1593, 1473, 1422, 1365, 1028, 832, 752. HRMS-ESI (m/z): calcd for C₂₁H₁₆N₃, [M+H] $^+$: 310.1339; found, 310.1331.



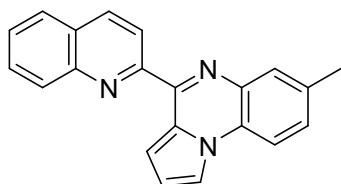
4-(6-fluoroquinolin-2-yl)pyrrolo[1,2-a]quinoxaline (3h)

Green solid (54.5 mg, 58%); m.p. = 225–226 °C. ^1H NMR (400 MHz, CDCl₃) δ 8.70 (d, *J* = 8.7 Hz, 1H), 8.28 (dd, *J* = 8.8, 4.5 Hz, 2H), 8.17 (d, *J* = 7.9 Hz, 1H), 8.11 (d, *J* = 3.8 Hz, 1H), 8.06 (s, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.62 – 7.45 (m, 4H), 7.06 – 7.00 (m, 1H). ^{13}C NMR (100 MHz, CDCl₃) δ 161.0 (d, *J* = 249 Hz), 155.0, 150.3, 144.6, 135.8 (d, *J* = 5.4 Hz), 132.6 (d, *J* = 9.2 Hz), 130.2, 129.1 (d, *J* = 10 Hz), 128.4, 127.7, 125.3, 124.5, 121.5, 120.0, 119.8, 114.9, 114.8, 113.7, 111.9, 110.7 (d, *J* = 21.6 Hz). IR (KBr) ν (cm $^{-1}$): 2918, 2850, 1641, 1006, 827, 752. HRMS-ESI (m/z): calcd for C₂₀H₁₃FN₃, [M+H] $^+$: 314.1088; found, 314.1087.



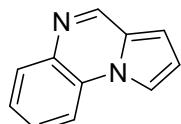
4-(7-fluoroquinolin-2-yl)pyrrolo[1,2-a]quinoxaline (3i)

Green solid (50.7 mg, 54%), m.p. = 190–192 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.63 (d, *J* = 8.6 Hz, 1H), 8.30 (d, *J* = 8.6 Hz, 1H), 8.12 (t, *J* = 9.2 Hz, 1H), 8.09 (d, *J* = 3.8 Hz, 1H), 8.04 (s, 1H), 7.93 – 7.83 (m, 3H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.39 (td, *J* = 8.7, 2.4 Hz, 1H), 7.05 – 7.01 (m, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 163.1 (d, *J* = 245 Hz), 156.7, 150.4, 148.4 (d, *J* = 13 Hz), 136.2, 135.3, 130.3, 129.5 (d, *J* = 10 Hz), 128.4, 127.7, 125.3, 125.2, 124.5, 120.1 (d, *J* = 2.5 Hz), 117.8 (d, *J* = 25.3 Hz), 114.8, 114.6, 113.7, 113.6 (d, *J* = 21 Hz), 111.59. IR (KBr) ν (cm⁻¹): 2923, 2852, 1593, 1510, 1419, 1366, 856, 753. HRMS-ESI (m/z): calcd for C₂₀H₁₃FN₃, [M+H]⁺: 314.1088; found, 314.1083.



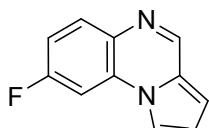
7-methyl-4-(quinolin-2-yl)pyrrolo[1,2-a]quinoxaline (3j)

Yellow solid (62.1 mg, 67%); m.p. = 180–181 °C. ¹H NMR (400 MHz, DMSO) δ 8.68 (d, *J* = 8.7 Hz, 1H), 8.55 (dd, *J* = 6.9, 5.4 Hz, 2H), 8.27 (dd, *J* = 8.4, 3.1 Hz, 2H), 8.18 (dd, *J* = 4.0, 1.2 Hz, 1H), 8.09 (d, *J* = 8.1 Hz, 1H), 7.88 (dt, *J* = 8.2, 2.9 Hz, 2H), 7.74 – 7.68 (m, 1H), 7.50 (dd, *J* = 8.4, 1.4 Hz, 1H), 7.05 (dd, *J* = 3.9, 2.7 Hz, 1H). ¹³C NMR (100 MHz, DMSO) δ 155.9, 149.8, 147.3, 137.0, 135.3, 135.2, 130.5, 130.3, 130.0, 128.3, 128.1, 125.7, 123.9, 120.4, 116.3, 114.9, 114.8, 111.6, 21.0. IR (KBr) ν (cm⁻¹): 2922, 1592, 1419, 1426, 1334, 1278, 1032, 810, 735. HRMS-ESI (m/z): calcd for C₂₁H₁₆N₃, [M+H]⁺: 310.1339; found, 310.1331.



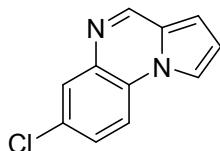
pyrrolo[1,2-a]quinoxaline (4a)²

Yellow solid (41.3 mg, 82%); m.p. = 126–127 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.81 (s, 1H), 7.97 (d, *J* = 8.0 Hz, 1H), 7.92 (s, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.52 (t, *J* = 7.7 Hz, 1H), 7.44 (t, *J* = 7.6 Hz, 1H), 6.94 – 6.85 (m, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 145.6, 135.5, 129.9, 128.0, 127.8, 126.4, 125.2, 114.3, 1141, 113.8, 107.6. IR (KBr) ν (cm⁻¹): 2922, 1607, 1458, 1337, 1031, 745.



8-fluoropyrrolo[1,2-a]quinoxaline (4b)²

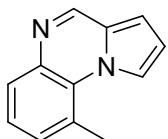
Yellow solid (40.7 mg, 73%); m.p. = 143–144 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.76 (s, 1H), 7.93 (dd, *J* = 8.9, 5.8 Hz, 1H), 7.79 (d, *J* = 1.8 Hz, 1H), 7.51 (dd, *J* = 9.2, 2.7 Hz, 1H), 7.19 – 7.13 (m, 1H), 6.89 (d, *J* = 1.9 Hz, 2H). ¹³C NMR (100 MHz, CDCl₃) δ 161.5 (d, *J* = 247 Hz), 144.9, 132.3, 131.9 (d, *J* = 9.7 Hz), 128.7 (d, *J* = 10.9 Hz), 126.0, 114.5, 114.3, 113.1 (d, *J* = 23.1 Hz), 107.5, 100.6 (d, *J* = 27 Hz). IR (KBr) ν (cm⁻¹): 3093, 2922, 1616, 1553, 1466, 1340, 1179, 1026, 874, 822, 739.



7-chloropyrrolo[1,2-a]quinoxaline (4c)²

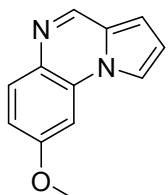
Yellow solid (39.4 mg, 65%); m.p. = 135–136 °C. ¹H NMR (400 MHz, CDCl₃) δ 8.78 (s, 1H), 7.92 (d, *J* = 2.3 Hz, 1H), 7.89 – 7.85 (m, 1H), 7.75 (d, *J* = 8.8 Hz, 1H), 7.45 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.92 – 6.88 (m, 2H). ¹³C NMR (100 MHz,

CDCl_3) δ 146.6, 136.6, 130.3, 129.4, 127.8, 126.6, 126.3, 114.9, 114.6, 114.4, 108.1. IR (KBr) ν (cm^{-1}): 2923, 1587, 1474, 1332, 814, 746.



9-methylpyrrolo[1,2-a]quinoxaline (4d)

Yellow solid (41.0 mg, 75%); m.p. = 119–120 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.77 (s, 1H), 8.32 (d, J = 2.7 Hz, 1H), 7.84 (dd, J = 6.7, 2.9 Hz, 1H), 7.37 – 7.31 (m, 2H), 6.93 (dd, J = 4.1, 1.2 Hz, 1H), 6.87 (dd, J = 4.0, 2.8 Hz, 1H), 2.95 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 145.4, 137.3, 131.2, 128.3, 127.7, 125.7, 124.7, 120.1, 113.4, 107.1, 23.9. IR (KBr) ν (cm^{-1}): 2923, 1603, 1460, 1328, 1261, 1092, 1031, 784, 715. HRMS-ESI (m/z): calcd for $\text{C}_{12}\text{H}_{11}\text{N}_2$, $[\text{M}+\text{H}]^+$: 183.0917; found, 183.0918.



8-methoxypyrrrolo[1,2-a]quinoxaline (4e)²

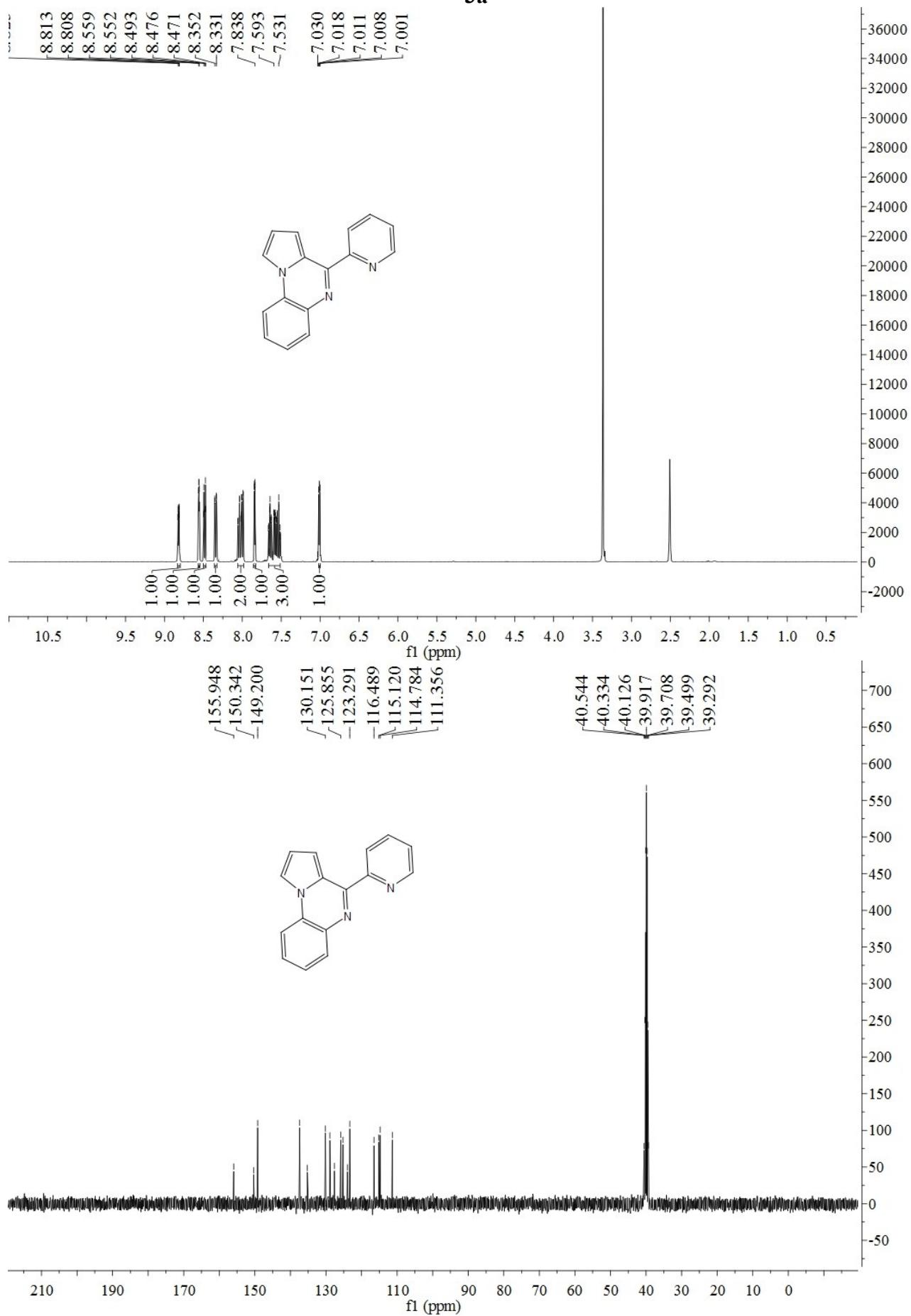
Yellow solid (26.7 mg, 45%); m.p. = 120–121 °C. ^1H NMR (400 MHz, CDCl_3) δ 8.70 (s, 1H), 7.89 (d, J = 8.9 Hz, 1H), 7.82 (s, 1H), 7.26 (s, 1H), 7.04 (dd, J = 8.9, 2.6 Hz, 1H), 6.91 – 6.85 (m, 2H), 3.96 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3) δ 159.3, 143.1, 131.2, 130.0, 128.7, 126.4, 114.1, 113.8, 112.8, 106.9, 97.6, 56.2. IR (KBr) ν (cm^{-1}): 2921, 1620, 1549, 1462, 1346, 1232, 1087, 1026, 804, 734.

References

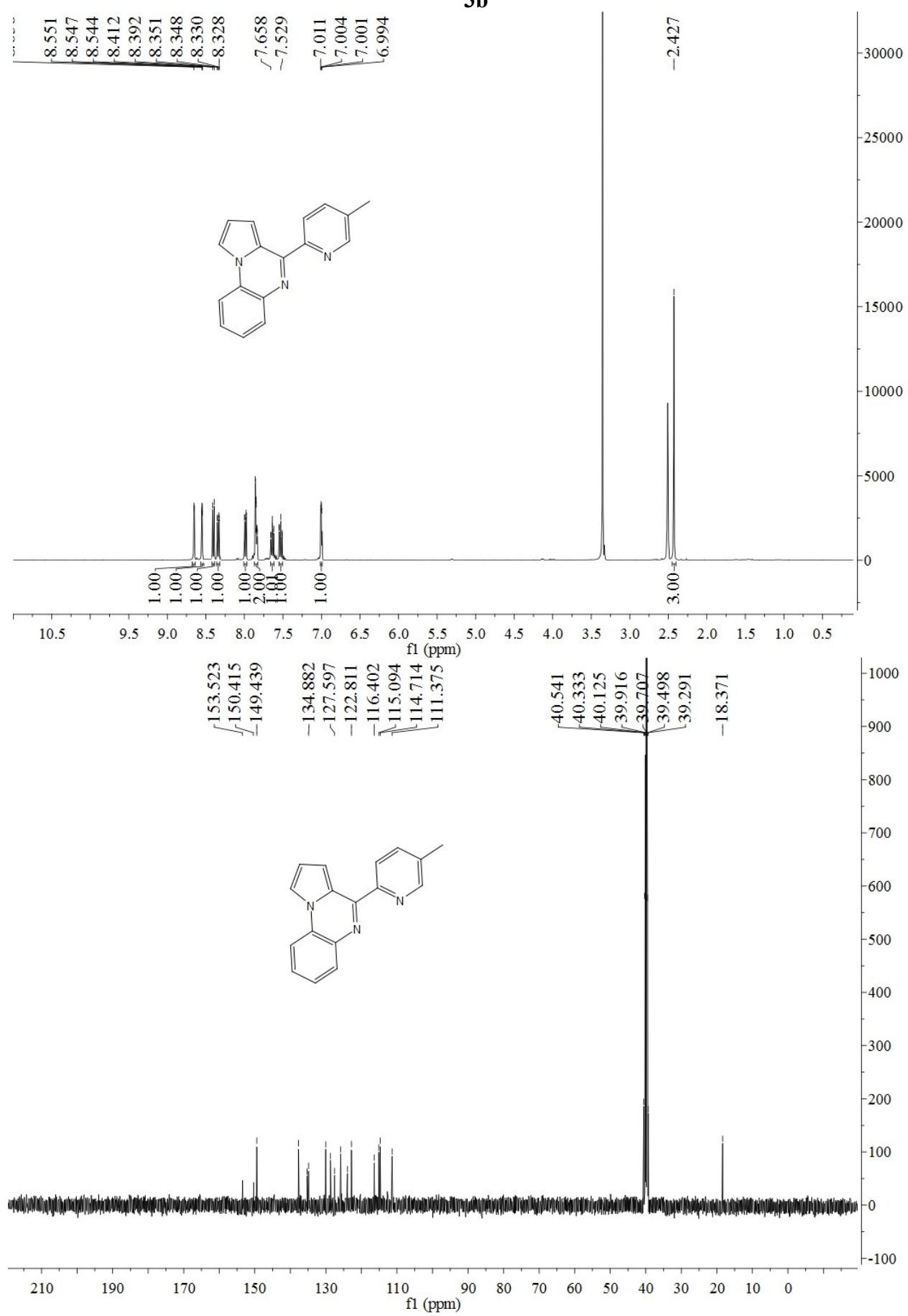
1. A. Preetam and M. Nath, *RSC Adv.*, 2015, **5**, 21843.
2. C. Xie, Z. Zhang, D. Li, J. Gong, X. Han, X. Liu and C. Ma, *J. Org. Chem.*, 2017, **82**, 3491.

NMR Spectra for All Compounds

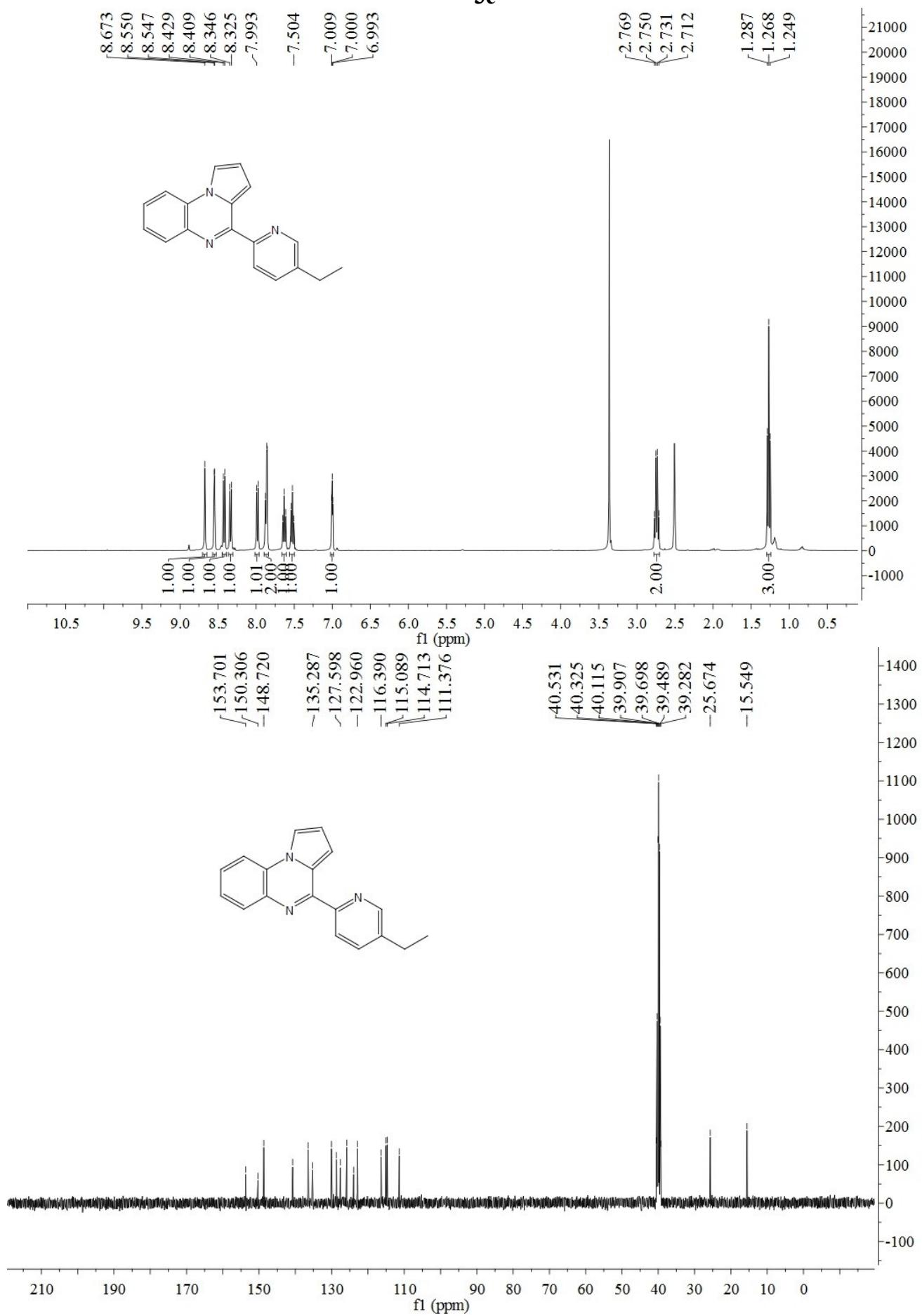
3a



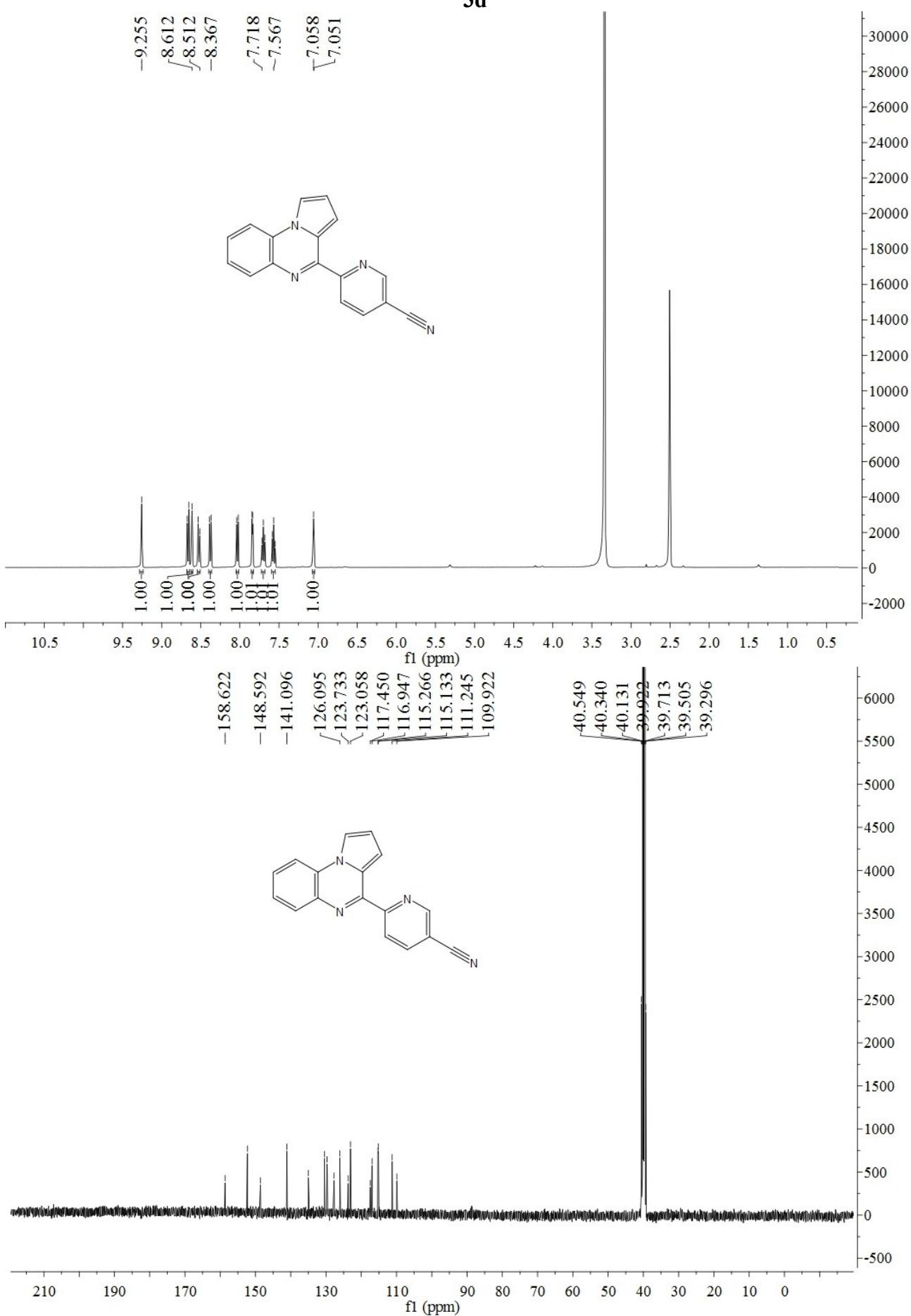
3b



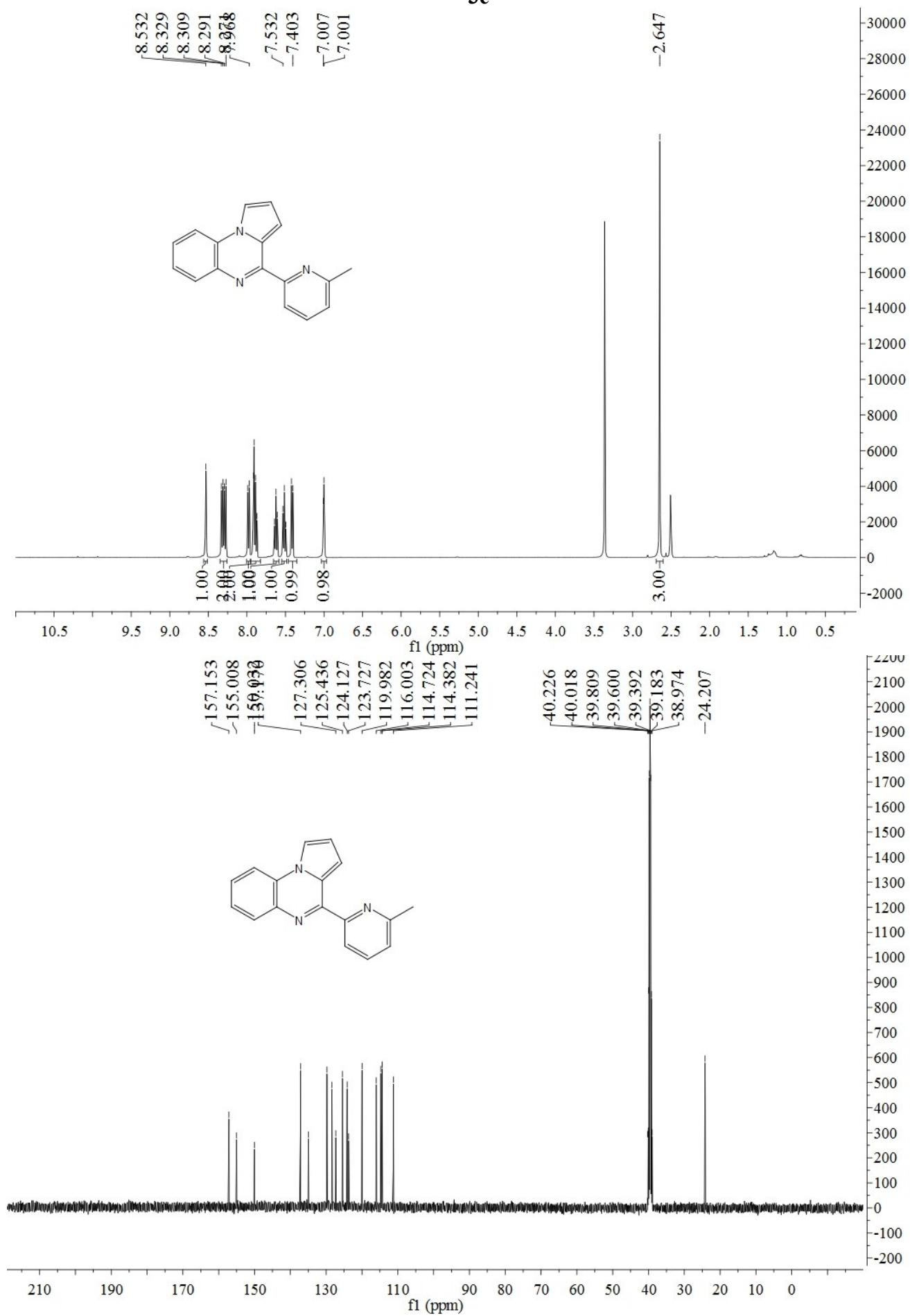
3c



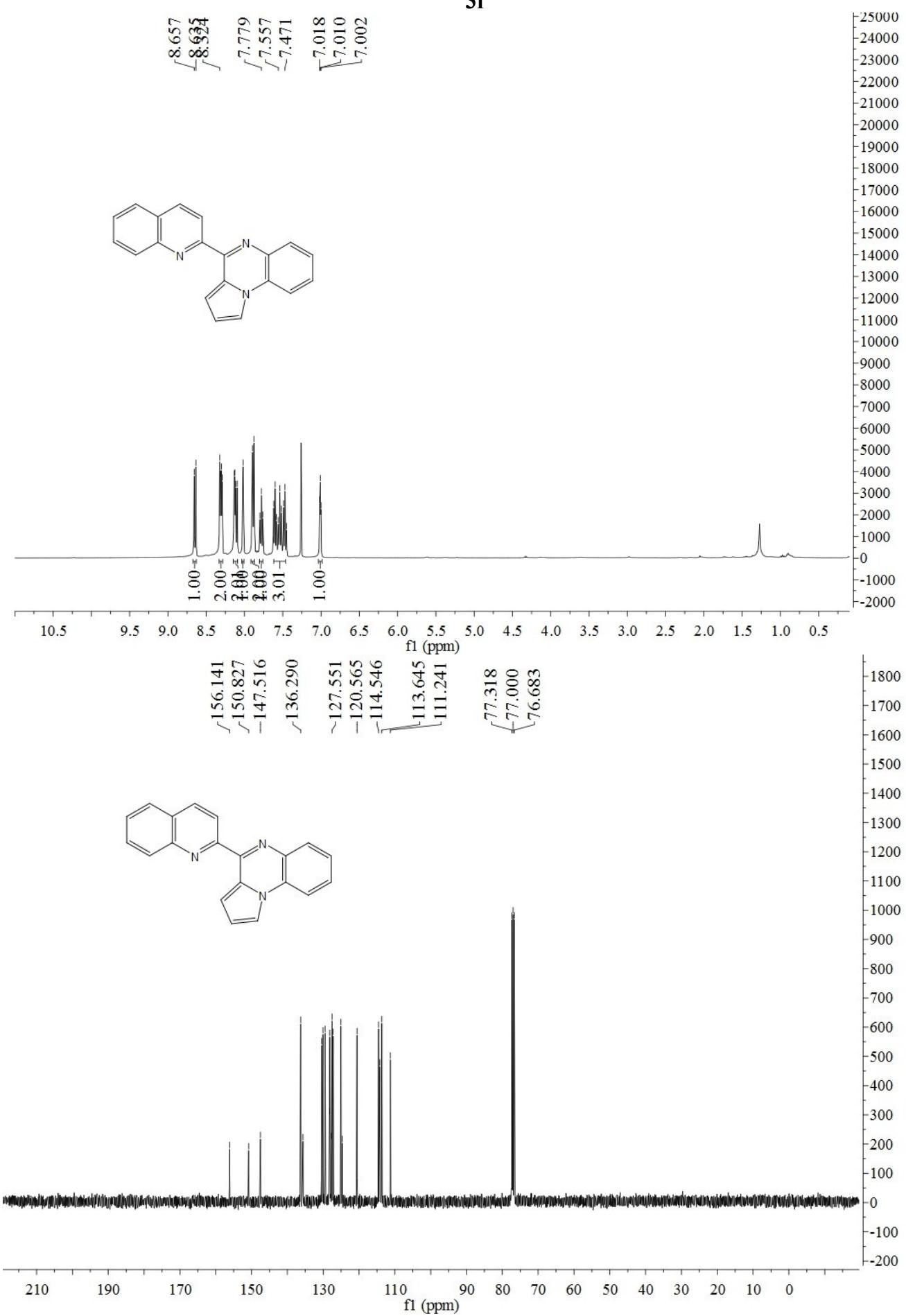
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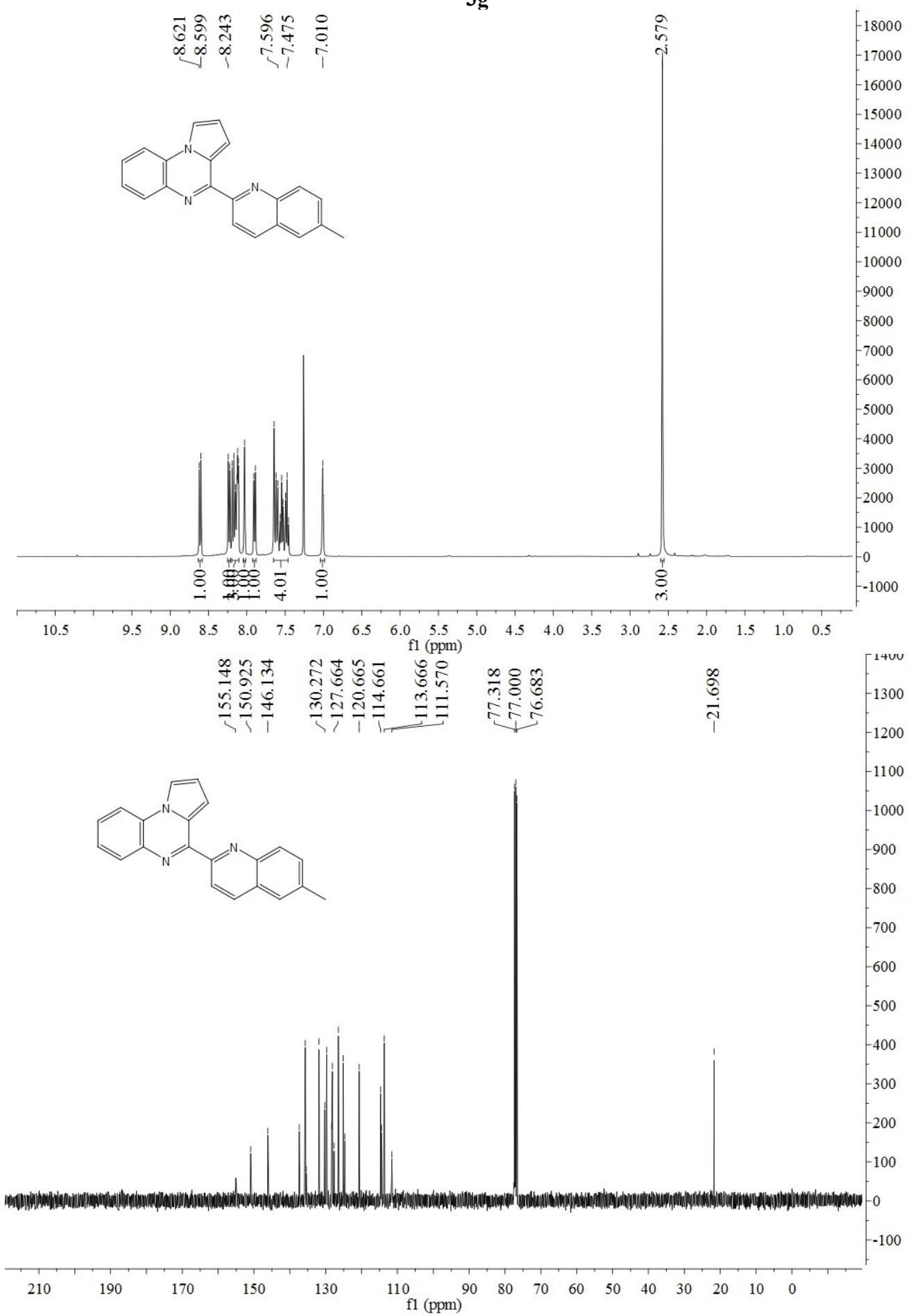
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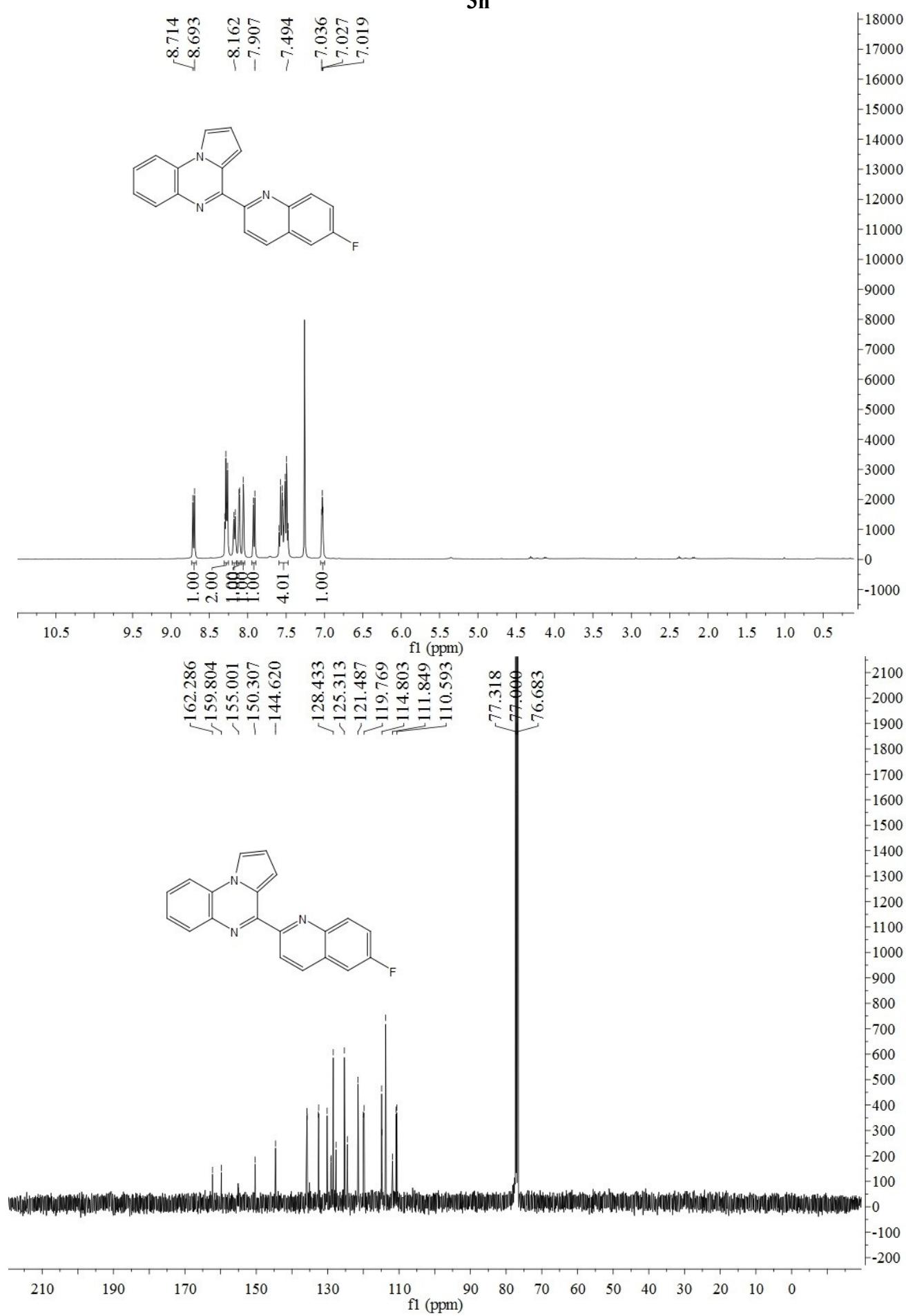
3f



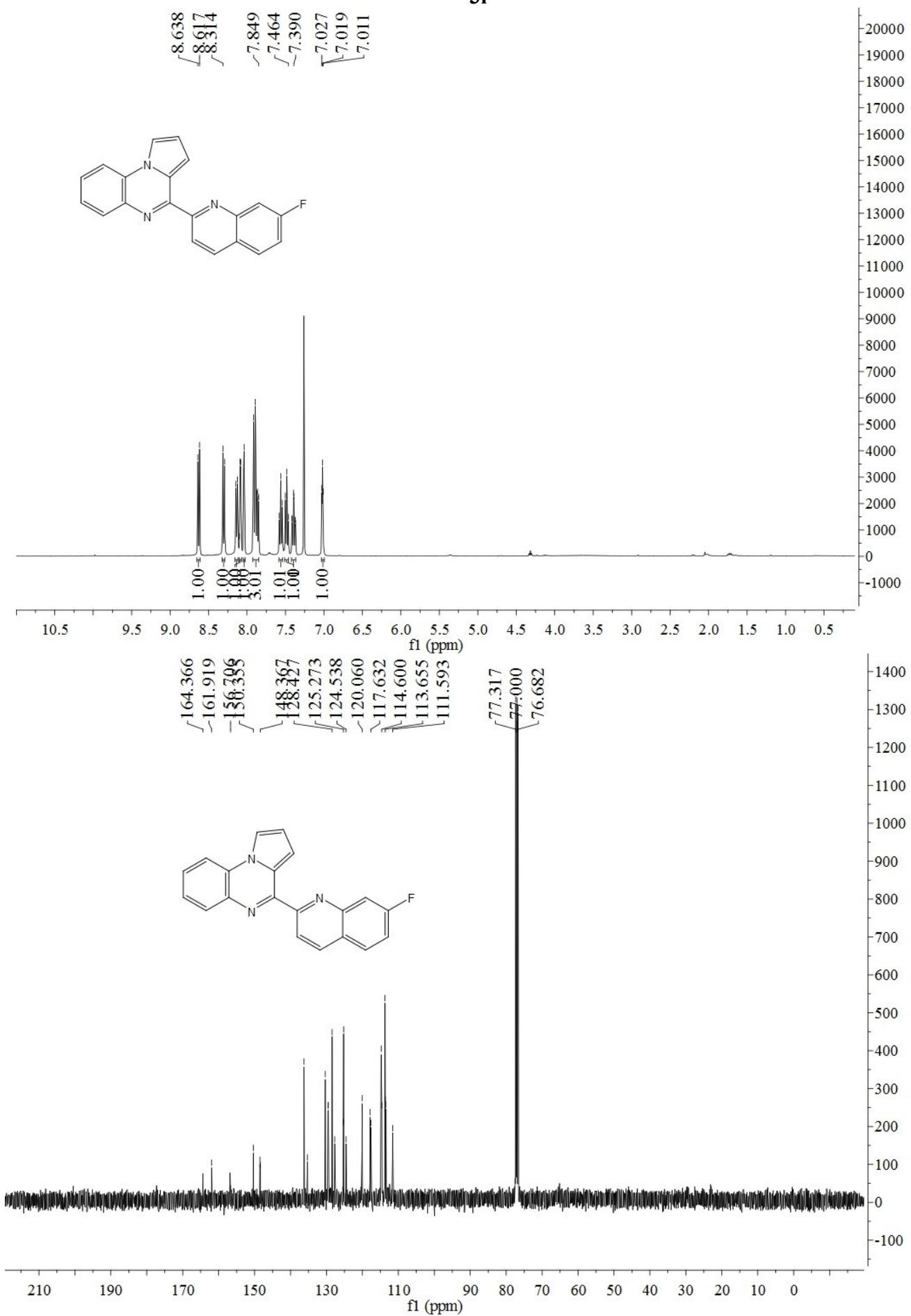
3g

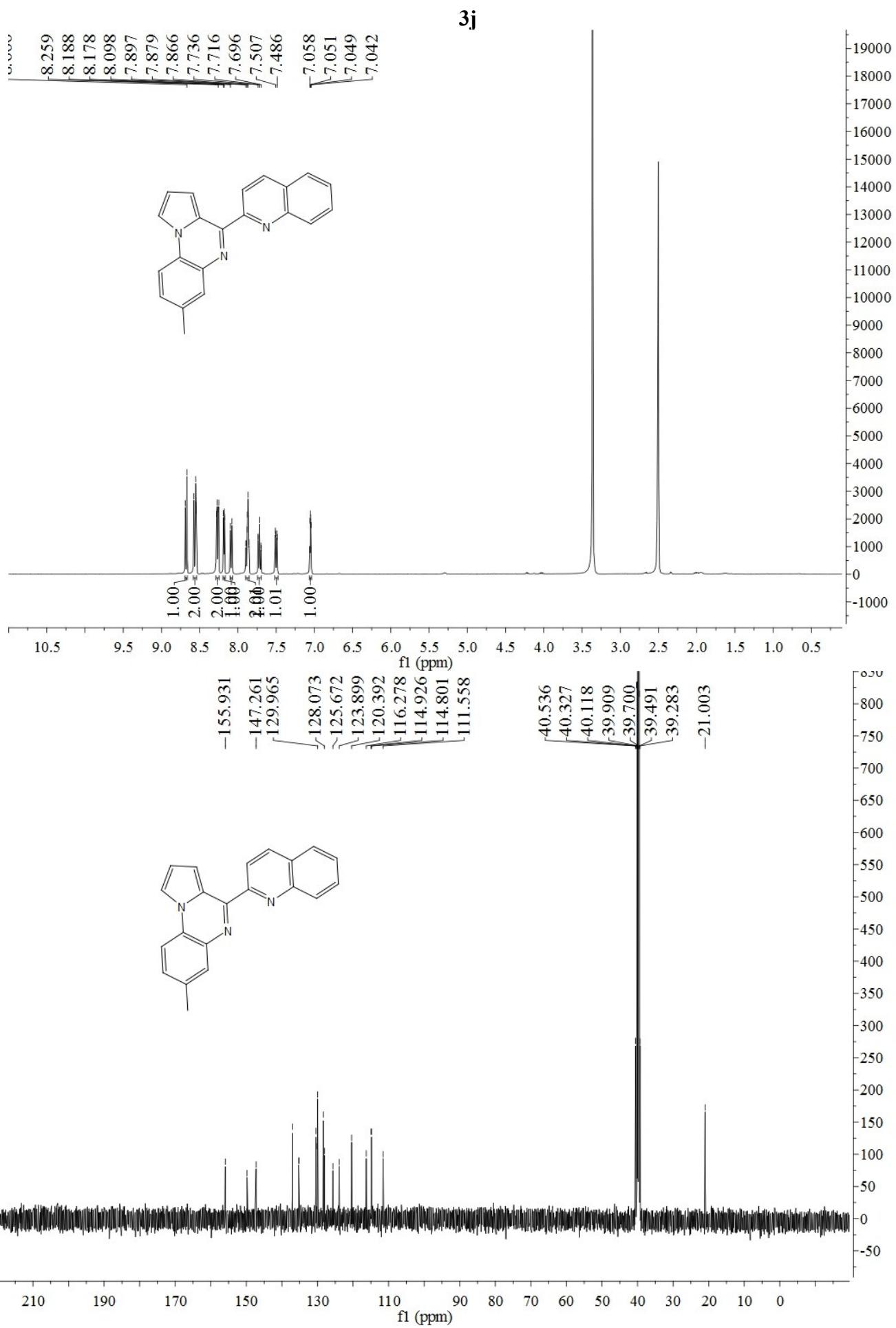


3h



3i





4a

