Electronic Supplementary Information

Microwave-assisted Palladium catalysed C-H acylation with aldehydes. Synthesis and diversification of 3-acylthiophenes

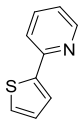
Carlos Santiago,[a] Xabier Jiménez-Aberasturi,[a] Eztizen Leicea,[a] Marta G. Lete,[b] Nuria Sotomayor,*[a] and Esther Lete*[a]

[a]Departamento de Química Orgánica e Inorgánica, Facultad de Ciencia y Tecnología, Universidad del País Vasco / Euskal Herriko Unibertsitatea UPV/EHU, Apdo. 644. 48080 Bilbao, Spain.
[b]CIC bioGUNE, Bizkaia Technology Park, Building 801A, Derio 48170, Spain

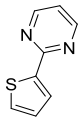
(+) 34946012576. Phone: Fax: (+) 34946012748. E-mail: esther.lete@ehu.eus; nuria.sotomayor@ehu.eus

Table of content

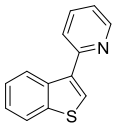
1. Synthesis of 1a,b and 5a,b, 7, 9, 11



2-(Thiophen-2-yl)pyridine (1a)[1]. Under argon atmosphere, a mixture of pyridin-2-yl 4-methylbenzenesulfonate (1556.7 mg, 6.2 mmol), 2-thienyl boronic acid (879.8 mg, 7.5 mmol), XPhos (71.5 mg, 0.15 mmol), $Pd(OAc)_2$ (26.4 mg, 0.12 mmol) in dry *n*-butanol was stirred for 15 min at room temperature. Then, a solution of NaOH (421.6 mg) in degassed H_2O (8.4 mL) was added to initiate the Suzuki reaction. The mixture was stirred at room temperature for 45 min. The mixture was passed through a short plug of silica gel with ethyl acetate, the solvent was removed under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc 7/3) leading to **1a** as light brown solid (994.9 mg, >99 %), whose data were coincidental to those reported:[1] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.07–7.14 (m, 2H), 7.38 (dd, J = 5.1, 1.2 Hz, 1H), 7.56 (dd, J = 3.7, 1.2 Hz, 1H), 7.66–7.59 (m, 2H), 8.56 (dt, J = 4.9, 1.4 Hz, 1H ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 118.8, 121.9, 124.6, 127.6, 128.1, 136.7, 144.9, 149.5, 152.6 ppm.



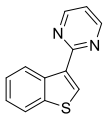
2-(Thiophen-2-yl)pyrimidine 1b.[2] Under argon atmosphere, a mixture of 2-chloropyrimidine (229.1 mg, 2 mmol), 2-thiophene boronic acid (353.9 mg, 3 mmol), K_3PO_4 (849.1 mg, 4 mmol), $Pd_2(dba)_3$ (18.1 mg, 0.04 mmol) and XPhos (38.1 mg, 0.16 mmol) in *tert*-amyl alcohol (4 mL) was heated to 100 °C for 5 h. The mixture was passed through a short plug of silica gel with ethyl acetate, solvent was removed under vacuum and the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc 8/2) affording **1b** as white solid (325.3 mg, 67%), whose data were coincidental to those reported:[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.00 (t, J = 4.9 Hz, 1H), 7.10 (dd, J = 5.0, 3.7 Hz, 1H), 7.44 (dd, J = 5.0, 1.2 Hz, 1H), 7.98 (dd, J = 3.7, 1.2 Hz, 1H), 8.62 (d, J = 4.9 Hz, 2H,) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 118.5, 128.3, 129.0, 129.9, 143.2, 157.2, 161.5 ppm.



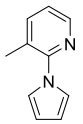
2-(Benzo[*b*]thiophen-3-yl)pyridine (5a).[3] Under argon atmosphere, benzo[*b*]thien-3-ylboronic acid (640.9 mg, 3.6 mmol), *n*-butanol (4.5 mL) and 2-bromopyridine (0.29 mL, 3

[1] J. Yang, S. Liu, J-F. Zheng, J. Zhou, *Eur. J. Org. Chem.,* 2012, 6248.
[2] K. Billingsley, S. L. Buchwald, *J. Am. Chem. Soc.,* 2007, **129**, 3358.
[3] B. Qu, H. P. R. Mangunuru, S. Tcyrulnikov.; D. Rivalti, O. V. Zatolochnaya, D. Kurouski, S. Radomkit, S. Biswas, S. Karyakarte, K. R. Fandrick, J. D. Sieber, S. Rodriguez, J.-N. Desrosiers, N. Haddad, K. McKellop, S. Pennino, H. Lee, N. K. Yee, J. J. Song, M. C. Kozlowski, C. H. Senanayake, *Org. Lett*., 2018, **20**, 1333.

mmol). The mixture was purged with argon for 30 min; then degassed sodium hydroxide aqueous solution (1.5 mL, 4 M) was slowly added. To this mixture add $Pd(OAc)_2$ (13.5 mg, 0.06 mmol) and tri-*tert*-butylphosphonium tetrafluoroborate (21.8 mg, 0.075 mmol). The resulting reaction mixture was stirred for 6 h at room temperature. Then, reaction was stopped with addition of water (10 mL) and extracted with ethyl acetate (3 x 15 mL), dried over sodium sulphate, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, petroleum ether/EtOAc 9/1) affording **5a** as colourless oil (466.4 mg, 74 %), whose data are coincidental to those reported:[3] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (ddd, *J* = 7.4, 4.7, 1.3 Hz, 1H), 7.38–7.51 (m, 2H), 7.71 (dt, *J* = 7.9, 1.2 Hz, 1H), 7.76–7.85 (m, 2H), 7.91–7.98 (m, 1H), 8.42–8.52 (m, 1H), 8.78 (d, *J* = 4.7 Hz, 1H,) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 122.0, 122.6, 122.7, 124.1, 124.6, 124.7, 126.4, 136.6, 136.7, 137.3, 140.9, 149.7, 154.7 ppm.



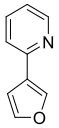
2-(Benzo[b]thiophen-3-yl)pyrimidine (5b). Following the previous procedure, Benzo[*b*]thien-3-ylboronic acid (640.9 mg, 3.6 mmol), was treated with *n*-butanol (4.5 mL), 2-chloropyrimidine (342.6 mg, 3 mmol), degassed sodium hydroxide aqueous solution (1.5 mL, 4 M), $Pd(OAc)_2$ (13.5 mg, 0.06 mmol) and tri-*tert*-butylphosphonium tetrafluoroborate (21.8 mg, 0.075 mmol). After 6 h at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **5b** as red solid (107.9 mg, 17 %), whose data are coincidental to those reported:[4] mp: 80-82 °C (Lit:[4] 86 ºC); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (t, *J* = 4.9 Hz, 1H), 7.44 (ddd, *J* = 8.1, 7.0, 1.3 Hz, 1H), 7.55 (ddd, *J* = 8.2, 7.0, 1.1 Hz, 1H), 7.94 (dt, *J* = 8.1, 1.1 Hz, 1H), 8.65 (s, 1H), 8.79 (d, *J* = 4.9 Hz, 2H), 9.18 (d, *J* = 8.2 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 118.6, 122.7, 124.7, 124.9, 125.8, 132.1, 134.7, 137.1, 141.1, 156.9, 162.6 ppm; HRMS (ESI-TOF): calcd. for $C_{12}H_9N_2S$ [MH^+]: 213.0481; found: 213.0491.



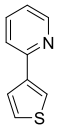
3-Methyl-2-(1*H*-pyrrol-1-yl)pyridine (7).[5] A mixture of pyrrole (0.42 mL, 6 mmol), 2-bromo-3-methyl pyridine (0.86 mL, 7.2 mmol), and KOH (841.6 mg, 15 mmol) in DMSO (8 mL) was stirred at 120 °C for 18 h. The mixture was cooled to room temperature, was diluted with EtOAc (25 mL) and washed with H_2O (2 × 25 mL). The aqueous phase was extracted with EtOAc (2 × 20 mL), the combined organic phase was dried over Na_2SO_4 and the solvent was evaporated under reduced pressure. Then, the crude product was purified by column chromatography (silica gel, petroleum ether/EtOAc 8/2) to give **7**

[4] C. Zhu, T. Pinkert, S. Greβies, F. Glorius, *ACS Catal.,* 2018, **8**, 10036.
[5] C. Santiago, I. Rubio, N. Sotomayor, E. Lete, *Eur. J. Org. Chem.,* 2020, 4284.

as an orange solid, (888 mg, 94%), whose data are coincidental to those reported:[5] ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.27 (s, 3H), 6.31 (s, 2H), 7.05-6.97 (m, 1H), 7.12 (s, 2H), 7.48 (d, J = 7.6 Hz, 1H), 8.27 (d, J = 4.8 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 18.8, 109.6, 121.0, 121.9, 125.6, 140.8, 146.5, 151.6 ppm.



2-(Furan-3-yl)pyridine (9).[6] 3-Furanylboronic acid (805.6 mg, 7.2 mmol), K_2CO_3 (2321.9 mg, 16.8 mmol.) and [$Pd(PPh_3)_2Cl_2$] (21.1 mg, 0.03 mmol) were dissolved in DME (18 mL) and H_2O (6.6 mL). Then, 2-bromopyridine (0.57 mL, 6 mmol) was added, and the mixture was stirred at 80 °C for 18 h. The reaction mixture was extracted with DCM (3 x 20 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. Purification by flash chromatography (petroleum ether/EtOAc = 20:1 to 10:1) afforded **11** (717,5 mg, 82%) as yellow oil whose data are coincidental with those reported:[6] ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83 (dd, J = 1.9, 0.9 Hz, 1H), 7.00 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 7.31 (dt, J = 7.9, 1.1 Hz, 1H), 7.41 (t, J = 1.7 Hz, 1H), 7.50 (td, J = 7.8, 1.9 Hz, 1H), 7.98 (dd, J = 1.8, 0.9 Hz, 1H), 8.50 (ddd, J = 4.9, 1.9, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 108.6, 120.0, 121.6, 127.1, 136.5, 141.2, 143.8, 149.5, 151.7 ppm.

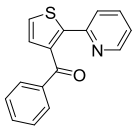


2-(Thiophen-3-yl)pyridine (11).[6] 3-thienylboronic acid (921.3 mg, 7.2 mmol), K_2CO_3 (2321.9 mg, 16.8 mmol.) and [$Pd(PPh_3)_2Cl_2$] (21.1 mg, 0.03 mmol) were dissolved in DME (18 mL) and H_2O (6.6 mL). Then, 2-bromopyridine (0.57 mL, 6 mmol) was added the mixture was stirred at 80 °C for 18 h. The reaction mixture was quenched with DCM (30 mL) and washed (3 x 20 mL). The combined organic layers were washed with brine (25 mL), dried over Na_2SO_4 and the solvent was removed under reduced pressure. Purification by flash chromatography (petroleum ether/EtOAc = 15:1 to 9:1) afforded **9** (490.0 mg, 51%), whose data are coincidental to those reported:[6] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (ddd, J = 7.3, 4.9, 1.3 Hz, 1H), 7.39 (dd, J = 5.1, 3.0 Hz, 1H), 7.60 (dt, J = 8.0, 1.2 Hz, 1H), 7.64–7.73 (m, 2H), 7.91 (dd, J = 3.0, 1.3 Hz, 1H), 8.63 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 120.3, 121.9, 123.5 , 126.2, 126.4, 136.8, 142.2, 149.6, 153.5 ppm.

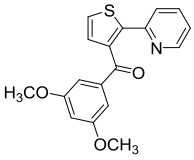
[6] J. Pospech, A. Tlili, A. Spannenberg, H. Neumann, M. Beller, *Chem. Eur. J.,* 2014, **20**, 3135.

2. Microwave-assisted acylation reactions of 1a,b with aldehydes. General procedure. Synthesis of ketones 3,4, 6, 8, 10, 12

Under argon atmosphere, a sealable reaction tube (10 mL, 1.3 × 9 cm) equipped with a stirring bar was charged with **1a,b**, **5a,b 7**, **9** or **11** (0.5 mmol), $Pd(OAc)_2$ (0.05 mmol), PivOH (0.38 mmol) and the corresponding aldehyde **2a-x** (1 mmol). After, DCE was added (1.5 mL), and the mixture was stirred for 2 min until solids were dissolved. Then, TBHP (5.5 M in decane, 2 mmol) was added; the reaction tube was sealed and heated under microwave irradiation at 80 °C for 15-30 min. After cooling to room temperature, the solvent was evaporated under vacuum and the residue was purified by column chromatography affording **3a-v, 4a-x**, **6a,b**, **8, 10**, or **12**.



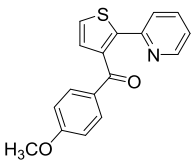
Phenyl[2-(pyridin-2-yl)thiophen-3-yl]methanone (3a). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), benzaldehyde **2a** (0.10 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 15 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3a** as a white solid(110.9 mg, 84%), whose data are coincidental to those reported:[7] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 (ddd, J = 7.4, 4.9, 1.2 Hz, 1H), 7.22 (d, J = 5.2 Hz, 1H), 7.29– 7.40 (m, 3H), 7.41 – 7.51 (m, 3H), 7.77 – 7.85 (m, 2H), 8.46 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 122.4 122.5, 126.6, 128.4, 129.8, 129.9, 133.1, 136.3, 137.6, 137.8, 145.8, 149.4, 151.3, 193.7 ppm.



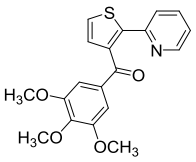
(3,5-Dimethoxyphenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanone (3b). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 3,5-dimethoxybenzaldehyde **2b** (166.1 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3b** as a yellow oil (140.7 mg, 86%): IR (ATR): 3060, 2942, 1743, 1658 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.73 (s, 6H), 6.57 (t, J = 2.3 Hz, 1H), 6.97 (d, J = 2.3 Hz, 2H), 7.07 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 7.22 (d, J = 5.2 Hz, 1H), 7.37 (dt, J = 8.0, 1.1 Hz, 1H), 7.41 (d, J = 5.2 Hz, 1H), 7.49 (ddd, J = 8.0, 7.5, 1.8 Hz, 1H), 8.48 (ddd, J = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.5, 105.9, 107.6, 122.4, 122.5, 126.5,129.9,

[7] Y. Wu, Q. Zhang, F. Yang, *Chem. Commun*., 2013, **49**, 6837.

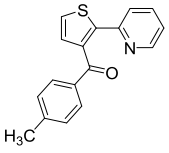
136.4, 137.7, 139.4, 145.8, 149.4, 151.4, 160.6, 193.2 ppm; MS (ESI): *m/z* (rel intensity): 327 (MH^+, 100), 296 (1), 274 (1); HRMS (ESI-TOF): calcd. for $C_{18}H_{16}NO_3S$ [MH^+]: 326.0845; found: 326.0865.



(4-Methoxyphenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanone (3c). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-methoxybenzaldehyde **2c** (0.12 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 20 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3c** as a white solid (70.2 mg, 48%): mp: 112-114 °C; IR (ATR): 3006, 2967, 2839, 1651 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H), 6.82–6.85 (m, 2H), 7.07 (ddd, *J* = 7.4, 4.9, 1.2 Hz, 1H), 7.18 (d, *J* = 5.2 Hz, 1H), 7.36 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.42 (d, *J* = 5.2 Hz, 1H), 7.47 (ddd, *J* = 8.1, 7.4, 1.8 Hz, 1H), 7.76–7.88 (m, 2H), 8.49 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* 55.5, 113.7, 122.2, 122.3, 126.7, 129.7, 130.3, 132.3, 136.4, 138.1, 144.9, 149.4, 151.4, 163.8, 192.7 ppm; MS (ESI): *m/z* (rel intensity): 297 (MH^+, 15), 296 (100), 188 (6). HRMS (ESI-TOF): calcd. for $C_{17}H_{14}NO_2S$ [MH^+]: 296.0745; found: 296.0750.

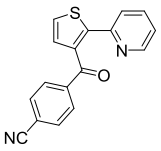


[2-(Pyridin-2-yl)thiophen-3-yl](3,4,5-trimethoxyphenyl)methanone (3d). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.1mmol), PivOH (38.8 mg, 0.38 mmol), 3,4,5-trimethoxybenzaldehyde **2d** (196.2 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3d** as a white solid (135.3 mg; 78%). mp: 142–144 °C; IR (ATR): 16478 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) *δ* 3.76 (s, 6H), 3.86 (s, 3H), 7.03– 7.14 (m, 3H), 7.25 (d, *J* = 5.2 Hz, 1H), 7.31 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.40–7.54 (m, 2H), 8.50 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* 56.2, 60.9, 107.5, 122.5, 122.8, 126.7, 130.0, 132.4, 136.3, 137.5, 142.6, 145.8, 149.5, 151.5, 152.9, 192.3 ppm; MS (EI): *m/z* (rel intensity): 355 (M^+, 88), 326 (100), 280 (29), 188 (51). HRMS (ESI-TOF): calcd. for $C_{19}H_{18}NO_4S$ [MH^+]: 356.0957; found: 356.0962.

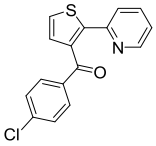


[2-(Pyridin-2-yl)thiophen-3-yl](*p*-tolyl)methanone (3e). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-methylbenzaldehyde **2e** (0.12 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3e** as a white solid (117.6 mg, 84%): mp: 103-105 °C; IR (ATR):

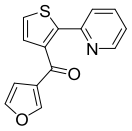
3013, 2970, 1736, 1658 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.37 (s, 3H), 7.08 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.20 (d, *J* = 5.2 Hz, 1H), 7.36–7.41 (m, 1H), 7.43 (d, *J* = 5.2 Hz, 1H), 7.48 (td, *J* = 7.7, 1.8 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 2H), 8.50 (dt, *J* = 4.8, 1.3 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.7, 122.3, 122.4, 126.6, 129.1, 129.8, 130.1, 135.0, 136.3, 138.1, 144.2, 145.4, 149.4, 151.4, 193.6 ppm; MS (ESI): *m/z* (rel intensity): 280 (MH^+, 100), 188 (1); HRMS (ESI-TOF): calcd. for $C_{17}H_{14}NOS$ [MH^+]: 280.0796; found: 280.0802.



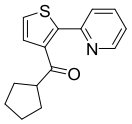
4-[2-(Pyridin-2-yl)thiophene-3-carbonyl]benzonitrile (3f). Following the general procedure, **1a** (80.6 mg, 1 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-formylbenzonitrile **2f** (131.1 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 15 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3f** as a white solid (85.5 mg, 59%). mp: 100-102 °C; IR (ATR): 2228, 1669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.04 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.24 (d, *J* = 5.2 Hz, 1H), 7.39 – 7.30 (m, 1H), 7.44 (d, *J* = 5.2 Hz, 1H), 7.50 (td, *J* = 7.7, 1.8 Hz, 1H), 7.58 (d, *J* = 8.5 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 8.31 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 115.7, 118.0, 122.4, 122.7,126.9, 129.7, 132.1, 136.5, 137.1, 141.2, 146.1, 149.3, 150.7, 191.9 ppm; MS (EI): *m/z* (rel intensity): 290 (11, M^+), 261 (100), 188 (21), 102 (13); HRMS (ESI-TOF): calcd. for$C_{17}H_{11}N_2OS$ [MH^+]: 291.0592; found: 291.0598.



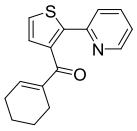
(4-Chlorophenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanone (3g). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-chlorobenzaldehyde **2g** (140.6 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3g** as a light yellow solid (118.1 mg, 79%). mp: 77–79 °C. IR (ATR): 3052, 2988, 1736, 1655 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 7.07 (ddd, *J* = 7.5, 4.9, 1.1 Hz, 1H), 7.21 (d, *J* = 5.2 Hz, 1H), 7.27–7.33 (m, 2H), 7.35 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.43 (d, *J* = 5.2 Hz, 1H), 7.49 (td, *J* = 7.7, 1.8 Hz, 1H), 7.71–7.78 (m, 2H), 8.44 (ddd, *J* = 4.9, 1.7, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 122.4, 122.5, 126.8, 128.7, 129.7, 131.1, 136.0, 136.4, 137.5, 139.4, 145.7, 149.4, 151.1, 192.5 ppm; MS (ESI): *m/z* (rel intensity): 302 (37, MH^+ + 2), 300(100, MH^+); HRMS (ESI-TOF): calcd. for $C_{16}H_{11}ClNOS$ [MH^+]: 300.0250; found: 300.0258.



Furan-3-yl[2-(pyridin-2-yl)thiophen-3-yl]methanone (3h) Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), PivOH (38.8 mg, 0.38 mmol), furan-3-carbaldehyde **2h** (0.09 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3h** as an orange solid (65.7 mg, 51%). mp: 73-76 °C;IR (ATR): 3123, 3006, 2981, 1732, 1648 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.82 (dd, *J* = 1.9, 0.8 Hz, 1H), 7.15 (ddd, *J* = 7.4, 4.9, 1.2 Hz, 1H), 7.27 (d, *J* = 5.2 Hz, 1H), 7.39 (dd, *J* = 1.9, 1.4 Hz, 1H), 7.42 (d, *J* = 5.2 Hz, 1H), 7.48 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.58 (ddd, *J* = 8.0, 7.4, 1.8 Hz, 1H), 7.71 (dd, *J* = 1.5, 0.8 Hz, 1H), 8.55 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 109.3, 122.6, 122.7, 126.9, 128.2, 129.4, 136.5, 138.4, 144.2, 145.7, 149.5, 149.8, 151.3, 186.7 ppm; MS (ESI): *m/z* (rel intensity): 256 (MH^+, 100), 188 (2); HRMS (ESI-TOF): calcd. for $C_{14}H_{10}NO_2S$ [MH^+]: 256.0432; found: 256.0433.

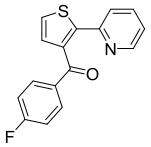


Cyclopentyl[2-(pyridin-2-yl)thiophen-3-yl]methanone (3i). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.1mmol), PivOH (38.8 mg, 0.75 mmol), cyclopentanecarbaldehyde **2i** (0.11 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 20 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3i** as an orange solid (58.6 mg, 45%): mp: 78-80 ºC; IR (ATR): 3052, 2952, 2868, 1680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.40–1.95 (m, 8H), 3.10–3.32 (m, 1H), 7.13 (ddd, *J* = 7.3, 4.9, 1.3 Hz, 1H), 7.21 (d, *J* = 5.3 Hz, 1H), 7.26 (d, *J* = 5.3 Hz, 1H), 7.54 (dt, *J* = 8.0, 1.2 Hz, 1H), 7.57–7.64 (m, 1H), 8.52 (ddd, *J* = 4.9, 1.7, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.2, 29.9, 50.9, 122.7, 123.1, 126.3, 128.9, 136.4, 139.1, 146.3, 149.3, 151.9, 202.8 ppm; MS (ESI): *m/z* (rel intensity): 258 (MH^+, 100), 240 (2); HRMS (ESI-TOF): calcd. for $C_{15}H_{16}NOS$ [MH^+]: 258.0953; found: 258.0960.

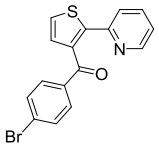


Cyclohex-1-en-1-yl[2-(pyridin-2-yl)thiophen-3-yl]methanone (3j). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.1mmol), PivOH (38.8 mg, 0.75 mmol), cyclohex-1-ene-1-carbaldehyde **2j** (0.11 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3j** as an orange solid (97.6 mg, 72%): mp: 113-116 °C; IR (ATR): 2939, 1627 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.45–1.57 (m, 2H), 1.56 – 1.67 (m, 2H), 1.94–2.06 (m, 2H), 2.32–2.43 (m, 2H), 6.55 (dt, *J* = 4.0, 2.2 Hz, 1H), 7.10 (d, *J* = 5.1 Hz, 1H), 7.14 (ddd, *J* = 7.6, 4.9, 1.1 Hz, 1H), 7.39–7.28 (m, 2H), 7.61 (td, *J* = 7.8, 1.8 Hz, 1H), 8.55 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5

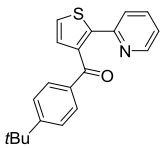
MHz, $CDCl_3$): δ 21.5, 21.8, 23.3, 26.2, 122.0, 122.2, 126.4, 129.4, 136.4, 138.6, 140.1, 143.8, 145.5, 149.4, 151.8, 195.8 ppm; MS (EI): *m/z* (rel intensity): 269 (18, M^+), 241 (37), 212 (100), 188 (64); HRMS (ESI-TOF): calcd. for $C_{16}H_{16}NOS$ [MH^+]: 270.0953; found: 270.0959.



(4-Fluorophenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanone (3k). Following the general procedure, **1a** (80.6 mg, 1 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-fluorobenzaldehyde **2k** (0.11 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3k** as an yellow solid (117.7 mg, 83%) whose data are coincidental to those reported:[6] ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.97–7.05 (m, 2H), 7.09 (ddd, *J* = 7.9, 4.8, 1.2 Hz, 1H), 7.23 (d, *J* = 5.2 Hz, 1H), 7.36 (d, *J* = 7.9 Hz, 1H), 7.45 (d, *J* = 5.2 Hz, 1H), 7.50 (td, *J* = 7.9, 1.8 Hz, 1H), 7.79–7.90 (m, 2H), 8.47 (dt, *J* = 4.8, 1.2 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 115.5 (d, *J* = 22.0 Hz) , 122.4, 122.5, 126.8, 129.7, 132.4 (d, *J* = 9.5 Hz), 134.1 (d, *J* = 2.9 Hz), 136.4, 137.6, 145.5, 149.4, 151.1, 165.6 (d, *J* = 252.6 Hz), 192.2 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -104.94 – -104.84 (m).

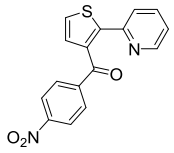


(4-Bromophenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanone (3l). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-bromobenzaldehyde **2l** (185.0 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3l** as a light brown solid (130.6 mg, 76%): mp: 101-103 °C; IR (ATR): 3109, 3006, 1743, 1658 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.22 (d, *J* = 5.2 Hz, 1H), 7.37 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.41–7.55 (m, 4H), 7.60–7.72 (m, 2H), 8.45 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 122.4, 122.5, 126.8, 128.2, 129.7, 131.2, 131.7, 136.4, 136.5, 137.4, 145.7, 149.4, 151.1, 192.6 ppm; MS (ESI): *m/z* (rel intensity): 345 (MH^++2, 100), 343 (MH^+, 97); HRMS (ESI-TOF): calcd. for $C_{16}H_{11}BrNOS$ [MH^+]: 343.9745; found: 343.9745.

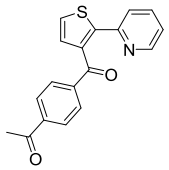


[4-(*tert*-Butyl)phenyl][2-(pyridin-2-yl)thiophen-3-yl]methanone (3m). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-(*tert*-butyl)benzaldehyde **2m** (162.2 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 20 min at 80 °C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3m** as a yellow oil (117.9 mg, 73%): IR

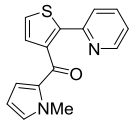
(ATR): 3056, 2960, 2903, 2868, 1654 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.30 (s, 9H), 7.06 (ddd, *J* = 7.3, 4.9, 1.3 Hz, 1H), 7.20 (d, *J* = 5.2 Hz, 1H), 7.33–7.43 (m, 4H), 7.47 (td, *J* = 7.7, 1.8 Hz, 1H), 7.71–7.84 (m, 2H), 8.50 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 31.1, 35.1, 122.3, 122.4, 125.4, 126.5, 129.8, 130.0, 134.9, 136.3, 138.1, 145.6, 149.4, 151.4, 157.1, 193.5 ppm; MS (ESI): *m/z* (rel intensity): 322 (MH^+, 100), 318 (1); HRMS (ESI-TOF): calcd. for $C_{20}H_{20}NOS$ [MH^+]: 322.1266; found: 322.1275.



(4-Nitrophenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanone (3n). Following the general procedure, **1a** (80.6 mg, 1 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-nitrobenzaldehyde **2n** (151.1 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3n** as an orange solid (24.6 mg, 16%): mp: 132-115 °C; IR (ATR): 3006, 2988, 1669, 1527 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.07 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.30 (d, *J* = 5.1 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.49 (d, *J* = 5.2 Hz, 1H), 7.55 (td, *J* = 7.7, 1.8 Hz, 1H), 7.88–7.97 (m, 2H), 8.09–8.21 (m, 2H), 8.34 (dt, *J* = 4.7, 1.4 Hz, 1H) ppm;^{13}C NMR (75.5 MHz, $CDCl_3$): δ 122.4, 122.7, 123.4, 126.9, 129.7, 130.2, 136.6, 137.2, 142.9, 146.1, 149.3, 149.8, 150.7, 191.7 ppm; MS (ESI): *m/z* (rel intensity): 311 (MH^+, 100), 274(1); HRMS (ESI-TOF): calcd. for $C_{16}H_{11}N_2O_3S$ [MH^+]: 311.0490; found: 311.0500.

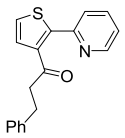


1-{4-[2-(Pyridin-2-yl)thiophene-3-carbonyl]phenyl}ethan-1-one (3o). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (16.8 mg, 0.075 mmol), PivOH (38.8 mg, 0.38 mmol), 4-acetylbenzaldehyde **2o** (148.1 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 20 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3o** as grey solid (81.5 mg, 53%): mp: 78-80 °C; IR (ATR): 3101, 3006, 1682, 1658 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.58 (s, 3H), 7.04 (ddd, *J* = 7.5, 4.9, 1.2 Hz, 1H), 7.24 (d, *J* = 5.2 Hz, 1H), 7.37 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.42–7.54 (m, 2H), 7.80–7.93 (m, 4H), 8.38 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H,) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.7, 122.4, 122.5, 126.7, 128.1, 129.7, 129.8, 136.4, 137.5, 139.8, 141.1, 146.0, 149.4, 151.0, 192.8, 197.5 ppm; MS (ESI): *m/z* (rel intensity): 308 (MH^+, 100); HRMS (ESI-TOF): calcd. for $C_{18}H_{14}NO_2S$ [MH^+]: 308.0745; found: 308.0754.

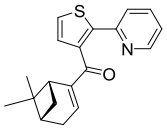


(1-Methylpyrrol-3-yl)[2-(pyridin-2-yl)thiophen-3-yl]methanone (3p). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 1-methyl-1*H*-pyrrole-3-carbaldehyde **2p** (0.11 mL, 1 mmol) and TBHP

(5.5 M in decane, 0.36 mL, 2 mmol). After 20 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **3p** as an amber oil (99.6 mg, 74%): IR (ATR): 3102, 3056, 2946, 1712, 1622 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 4.05 (s, 3H), 6.01 (dd, *J* = 4.1, 2.4 Hz, 1H), 6.58 (dd, *J* = 4.1, 1.8 Hz, 1H), 6.85–6.87 (m, 1H), 7.09 (ddd, *J* = 6.7, 4.9, 1.7 Hz, 1H), 7.22 (d, *J* = 5.2 Hz, 1H), 7.36 (d, *J* = 5.2 Hz, 1H), 7.58–7.47 (m, 2H), 8.54 (ddd, *J* = 4.9, 1.6, 1.1 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 37.5, 108.5, 122.1, 122.2, 123.5, 126.1, 130.0, 131.4, 132.0, 136.4, 139.1, 144.5, 149.4, 151.8, 183.1 ppm; MS (ESI): *m/z* (rel intensity): 269 (MH^+, 47), 189 (9), 188 (100); HRMS (ESI-TOF): calcd. for $C_{15}H_{13}N_2OS$ [MH^+]: 269.0749; found: 269.0751.

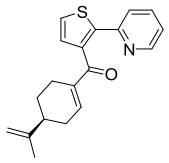


3-Phenyl-1-[2-(pyridin-2-yl)thiophen-3-yl]propan-1-one (3q). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05mmol), PivOH (38.8 mg, 0.38 mmol), hydrocinnamaldehyde **2q** (0.12 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3q** as an yellow oil (94.5 mg, 64%): IR (ATR): 3003, 2984, 1682 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.97–3.16 (m, 4H), 7.13–7.36 (m, 8H), 7.58 (d, *J* = 7.8 Hz, 1H), 7.65 (td, *J* = 7.7, 1.8 Hz, 1H), 8.60 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 30.3, 44.5, 122.9, 123.4, 126.1, 126.4, 128.5, 128.8, 136.5, 138.7, 141.0, 146.8, 149.4, 151.8, 198.4 ppm; MS (ESI): *m/z* (rel intensity): 294 (MH^+, 100), 278(2), 239(2), 178 (7); HRMS (ESI-TOF): calcd. for $C_{18}H_{16}NOS$ [MH^+]: 294.0953; found: 294.0961.

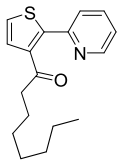


[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl][2-(pyridin-2-yl)thiophen-3-yl]methanone (3r). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), (1*R*)-(−)-myrtenal **2r** (0.15 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3r** as an white solid (91.5 mg, 59%): mp: 83-86 °C; IR (ATR): 2981, 2939, 2882, 1739, 1640 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.70 (s, 3H) , 0.93 (d, *J* = 9.1 Hz, 1H), 1.35 (s, 3H), 1.97–2.12 (m, 1H), 2.28–2.30 (m, 2H), 2.46 (dt, *J* = 9.1, 5.7 Hz, 1H), 3.10 (td, *J* = 5.7, 1.6 Hz, 1H), 6.40 (dt, *J* = 3.3, 1.8 Hz, 1H), 7.04–7.19 (m, 2H), 7.31–7.40 (m, 2H), 7.52–7.64 (m, 1H), 8.55 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.9, 25.8, 31.0, 32.7, 37.6, 39.9, 40.3, 122.1, 122.2, 126.5, 129.4, 136.5, 138.3, 142.7, 143.6, 149.5, 150.0, 151.7, 193.3 ppm; MS (ESI): *m/z*

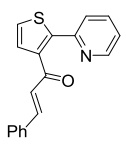
(rel intensity): 310 (MH^+, 100), 299 (<1), 292 (<1); HRMS (ESI-TOF): calcd. for $C_{19}H_{20}NOS$ [MH^+]: 310.1266; found: 310.1267.



(*S*)-[4-(Prop-1-en-2-yl)cyclohex-1-en-1-yl][2-(pyridin-2-yl)thiophen-3-yl]methanone (3s). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), (*S*)-(−)-perillaldehyde **2s** (0.16 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3s** as a yellow oil (101.9 mg, 66%): IR (ATR): 3073, 3049, 2974, 2931, 1739, 1633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (dtd, *J* = 13.2, 10.9, 5.4 Hz, 1H), 1.61 (t, *J* = 1.0 Hz, 3H), 1.76– 1.93 (m, 2H), 1.94– 2.14 (m, 2H), 2.16–2.33 (m, 1H), 2.52-2.68 (m, 1H), 4.52 (dt, *J* = 1.6, 1.0 Hz, 1H), 4.63 (t, J = 1.6 Hz, 1H), 6.48 (tq, J = 3.5, 2.1, 1.6 Hz, 1H), 7.02 (d, *J* = 5.2 Hz, 1H), 7.07 (ddd, J = 7.5, 4.9, 1.1 Hz, 1H), 7.18–7.36 (m, 2H), 7.54 (td, *J* = 7.8, 1.8 Hz, 1H), 8.48 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.7, 23.6, 26.7, 31.4, 40.0, 109.3, 121.9, 122.2, 126.4, 129.4, 136.4, 138.6, 139.9, 143.8, 144.6, 148.5, 149.5, 151.8, 195.5 ppm; MS (ESI): *m/z* (rel intensity): 310 (MH^+, 100), 292 (1), 188 (<1); HRMS (ESI-TOF): calcd. for $C_{19}H_{20}NOS$ [MH^+]: 310.1266; found: 310.1272.

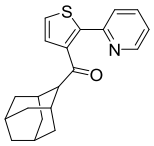


1-[2-(Pyridin-2-yl)thiophen-3-yl]octan-1-one (3t). Following the general procedure, **1a** (322.4 mg, 2 mmol) was treated with $Pd(OAc)_2$ (45.0 mg, 0.2 mmol), PivOH (153.0 mg, 1.50 mmol), octanal **2t** (0.64 mL, 4 mmol) and TBHP (5.5 M in decane, 1.44 mL, 8 mmol). After 15 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3t** as a yellow oil (335.7 mg, 58 %): IR (ATR): 3052, 2960, 2854.13, 1736, 1683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.78–0.91 (m, 3H), 1.19–1.28 (m, 8H), 1.64 (quint., *J* = 7.3 Hz, 2H), 2.71 (t, *J* = 7.3 Hz, 2H), 7.20-7.25 (m, 1H), 7.28–7.36 (m, 2H), 7.57–7.78 (m, 2H), 8.60 (d, *J* = 4.7 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 14.1, 22.6, 24.3, 29.1, 29.2, 31.7, 42.8, 122.9,123.5, 126.3,128.9, 136.6, 138.9, 146.4, 149.2, 151.8, 199.6 ppm; MS (ESI): *m/z* (rel intensity): 288 (MH^+, 100), 260 (<1), 178 (<1); HRMS (ESI-TOF): calcd. for $C_{17}H_{22}NOS$ [MH^+]: 288.1422; found: 288.1426.

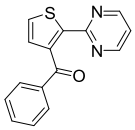


(*E*)-3-Phenyl-1-[2-(pyridin-2-yl)thiophen-3-yl]prop-2-en-1-one (3u). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (16.9 mg, 0.075mmol), PivOH (38.8 mg, 0.38 mmol), *trans*-cinnamaldehyde **2u** (0.12 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column

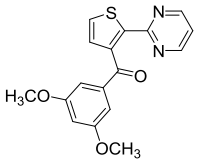
chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **3u** as an orange oil (33.5 mg, 23%): IR (ATR): 3087, 3056, 2984, 1729, 1658, 1633 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.86 (d, J = 16.0 Hz, 1H), 7.11 (ddd, J = 6.8, 4.9, 1.5 Hz, 1H), 7.20–7.37 (m, 7H), 7.42–7.61 (m, 3H), 8.54 (d, J = 4.7 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 122.8, 123.4, 126.5, 126.7, 128.4, 128.9, 129.5, 130.6, 134.6, 136.5, 139.0, 144.9, 146.3, 149.6, 151.7, 190.5 ppm; MS (ESI): *m/z* (rel intensity): 292 (MH^+, 100), 188 (7); HRMS (ESI-TOF): calcd. for $C_{18}H_{14}NOS$ [MH^+]: 292.0796; found: 292.0801.



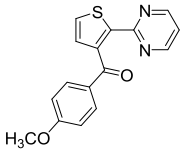
(Adamantan-1-yl)[2-(pyridin-2-yl)thiophen-3-yl)]methanone (3v). Following the general procedure, **1a** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.1mmol), PivOH (38.8 mg, 0.75 mmol), adamantane-1-carbaldehyde **2v** (164.3 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 15 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 10/1) afforded **3v** as a white solid (36.9 mg, 23%): mp: 126-128°C ; IR (ATR): 2903, 2850, 1746, 1683 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.56–1.77 (m, 6H), 1.90 (d, J = 3.0 Hz, 6H), 1.98–2.03 (m, 3H), 6.96 (d, J = 5.1 Hz, 1H), 7.16 (ddd, J = 7.7, 4.8, 1.1 Hz, 1H), 7.37 (d, J = 5.1 Hz, 1H), 7.43–7.51 (m, 1H), 7.66 (td, J = 7.7, 1.8 Hz, 1H), 8.56 (dt, J = 4.8, 1.4 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 28.0, 36.5, 38.5, 47.5, 120.7, 122.2, 126.3, 127.1, 136.7, 139.4, 140.2, 149.3, 151.7, 212.2 ppm; MS (ESI): *m/z* (rel intensity): 324 (MH^+, 100), 318 (<1), 200 (<1).); HRMS (ESI-TOF): calcd. for $C_{20}H_{22}NOS$ [MH^+]: 324.1422; found: 324.1430.



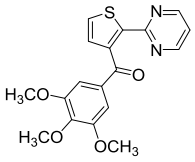
Phenyl[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4a). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), benzaldehyde **2a** (0.10 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **4a** as a white solid (97.7 mg, 74%): mp: 143-144 °C; IR (ATR): 3098, 3041, 1739, 1669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.84 (t, J = 4.9 Hz, 1H), 7.07 (d, J = 5.1 Hz, 1H), 7.22–7.30 (m, 2H), 7.34–7.42 (m, 1H), 7.43 (d, J = 5.1 Hz, 1H), 7.70–7.78 (m, 2H), 8.36 (d, J = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 118.5, 128.3, 129.0, 129.3, 129.4, 132.9, 137.7, 140.9, 141.9, 156.8, 160.5, 194.7 ppm; MS (ESI): *m/z* (rel intensity): 267 (MH^+, 100), 227 (2), 149 (1); HRMS (ESI-TOF): calcd. for $C_{15}H_{11}N_2OS$ [MH^+]: 267.0592; found: 267.0605.



(3,5-Dimethoxyphenyl)[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4b). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.75 mmol), 3,5-dimethoxybenzaldehyde **2b** (166.2 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 35 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **4b** as a white solid (150.8 mg, 92%): mp: 125-126 °C; IR (ATR): 3091, 3005, 2941, 2835, 1669, 1594 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.77 (s, 6H), 6.60 (t, J = 2.3 Hz, 1H), 6.93– 7.04 (m, 3H), 7.16 (d, J = 5.1 Hz, 1H), 7.52 (d, J = 5.1 Hz, 1H), 8.51 (d, J = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.5, 105.4, 107.2, 118.5, 128.9, 129.3, 139.7, 140.9, 141.7, 156.8, 160.5, 160.6, 194.2 ppm; MS (ESI): *m/z* (rel intensity): 327 (MH^+, 100), 296 (1), 274 (1); HRMS (ESI-TOF): calcd. for $C_{17}H_{15}N_2O_3S$ [MH^+]: 327.0803; found: 327.0806.

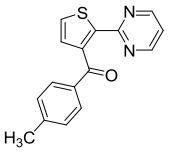


(4-Methoxyphenyl)[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4c). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-methoxybenzaldehyde **2c** (0.12 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **4c** as a white solid (94.5 mg, 64%): mp: 159.161 °C; IR (ATR): 3094, 3034, 2963, 2840, 1661 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.81 (s, 3H), 6.77–6.88 (m, 2H), 6.95 (t, J = 4.9 Hz, 1H), 7.13 (d, J = 5.1 Hz, 1H), 7.51 (d, J = 5.1 Hz, 1H), 7.73–7.88 (m, 2H), 8.48 (d, J = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.4, 113.6, 118.4, 128.9, 129.2, 130.8, 131.7, 140.4, 142.2, 156.9, 160.6, 163.4, 193.4 ppm;; MS (ESI): *m/z* (rel intensity): 297 (MH^+, 100), 190 (2), 189 (30); HRMS (ESI-TOF): calcd. for $C_{16}H_{13}N_2O_2S$ [MH^+]: 297.0698; found: 297.0701.

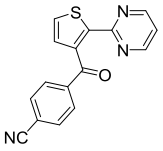


[2-(Pyrimidin-2-yl)thiophen-3-yl](3,4,5-trimethoxyphenyl)methanone (4d). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 3,4,5-trimethoxybenzaldehyde **2d** (196.2 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtO_2 7/3) afforded **4d** as a yellow solid (140.0 mg, 79%): mp: 161-163 °C; IR (ATR): 1659 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.76 (s, 6H), 3.87 (s, 3H), 6.98 (t, J = 4.9 Hz, 1H), 7.10 (s, 2H), 7.17 (d, J = 5.1 Hz, 1H), 7.53 (d, J = 5.1 Hz, 1H), 8.51 (d, J = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 56.2, 60.9, 106.9, 118.5, 129.0, 129.2, 132.9, 141.1,

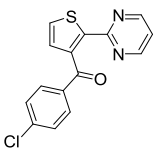
141.5, 142.4, 152.9, 156.9, 160.6, 193.2 ppm; MS (EI): *m/z* (rel intensity): 356 (M^+, 100), 327 (52) 189 (54); HRMS (ESI-TOF): calcd. for $C_{18}H_{17}N_2O_4S$ [MH^+]: 357.0909; found: 357.0909.



[2-(Pyrimidin-2-yl)thiophen-3-yl](*p*-tolyl)methanone (4e). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-methylbenzaldehyde **2e** (0.12 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtO_2 8/2) afforded **4e** as a white solid (115.4 mg, 82%): mp: 153-155 °C; IR (ATR): 3045, 2977, 2924, 1665 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.36 (s, 3H), 6.95 (t, J = 4.9 Hz, 1H), 7.19–7.12 (m, 3H), 7.52 (d, J = 5.1 Hz, 1H), 7.69–7.82 (m, 2H), 8.47 (d, J = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.7, 118.4, 128.9, 129.1, 129.3, 129.5, 135.2, 140.6, 142.2, 143.7, 156.9, 160.5, 194.4 ppm; MS (ESI): *m/z* (rel intensity): 281 (MH^+, 100), 189 (3); HRMS (ESI-TOF): calcd. for $C_{16}H_{13}N_2OS$ [MH^+]: 281.0749; found: 281.0762.

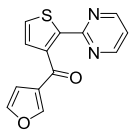


4-[2-(Pyrimidin-2-yl)thiophene-3-carbonyl]benzonitrile (4f). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-formylbenzonitrile **2f** (131.1 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **4f** as an amber solid (120.6 mg, 83%): mp: 164-166°C; IR (ATR): 2227, 1672 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.96 (t, J = 4.9 Hz, 1H), 7.19 (d, J = 5.1 Hz, 1H), 7.56 (d, J = 5.1 Hz, 1H), 7.60 – 7.70 (m, 2H,), 7.82 – 7.92 (m, 2H), 8.41 (d, J = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 115.7, 118.1, 118.7, 128.9, 129.3, 130.0, 132.2, 140.5, 141.1, 141.7, 156.8, 160.0, 192.9 ppm; MS (ESI): *m/z* (rel intensity): 292 (MH^+, 100), 259 (1), 246 (1); HRMS (ESI-TOF): calcd. for $C_{16}H_{10}N_3OS$ [MH^+]: 292.0545; found: 292.0556.

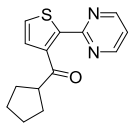


(4-Chlorophenyl)[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4g). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-chlorobenzaldehyde **2g** (140.6 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80 °C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **4g** as a light-yellow solid (119.7 mg, 80 %): mp: 155-158 °C; IR (ATR): 1661 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.99 (t, J = 4.9 Hz, 1H), 7.18 (d, J = 5.1 Hz, 1H), 7.30–

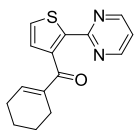
7.40 (m, 2H), 7.56 (d, *J* = 5.1 Hz, 1H), 7.74–7.85 (m, 2H), 8.49 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* 118.5, 128.6, 128.8, 129.6, 130.6, 136.2, 139.2, 141.3, 156.9, 160.6, 163.5, 193.4 ppm; MS (EI): *m/z* (rel intensity): 302 (M^++ 2, 18) 300 (M^+, 43), 271 (100), 189 (51), 135 (25), 111 (41), 75 (29); HRMS (ESI-TOF):calcd. for $C_{15}H_{10}ClN_2OS$ [MH^+]: 301.0202; found: 301.0204.



Furan-3-yl[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4h). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), furan-3-carbaldehyde **2h** (0.09 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **4h** as a light-brown solid (61.6 mg, 48%): mp: 1117-119°C; IR (ATR): 3123, 3045, 1661, 1563 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.89–6.80 (m, 1H), 7.04 (t, *J* = 4.9 Hz, 1H), 7.19 (d, *J* = 5.1 Hz, 1H), 7.40 (t, *J* = 1.7 Hz, 1H), 7.50 (d, *J* = 5.1 Hz, 1H), 7.60–7.67 (m, 1H), 8.58 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* 109.0, 118.6, 128.7, 128.9, 129.2, 141.1, 142.3, 144.2, 149.1, 157.0, 160.6, 187.9 ppm; MS (ESI): *m/z* (rel intensity): 257 (MH^+, 100), 189 (11); HRMS (ESI-TOF): calcd. for $C_{13}H_9N_2O_2S$ [MH^+]: 257.0385; found: 257.0388.

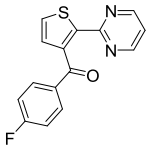


Cyclopentyl[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4i) Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), cyclopentanecarbaldehyde **2i** (0.11 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 20 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **4i** as a yellow oil (65,3 mg, 51%): IR (ATR): 2952, 2868, 1690 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 1.46–1.62 (m, 2H), 1.66–1.89 (m, 4H), 1.89–2.05 (m, 2H), 3.36 (quint, *J* = 7.9 Hz, 1H), 7.06 (d, *J* = 5.1 Hz, 1H), 7.11 (t, *J* = 4.9 Hz, 1H), 7.43 (d, *J* = 5.1 Hz, 1H), 8.67 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): *δ* 26.2, 29.8, 52.6, 118.6,128.0, 129.2, 139.6, 144.9, 157.0, 160.8, 207.2 ppm; MS (ESI): *m/z* (rel intensity): 259 (MH^+, 100), 241 (7); HRMS (ESI-TOF): calcd. for $C_{14}H_{15}N_2OS$ [MH^+]: 259.0905; found: 259.0911.

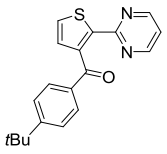


Cyclohex-1-en-1-yl[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4j). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), cyclohex-1-ene-1-carbaldehyde **2j** (0.11 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **4j** as a brown solid (85.9 mg, 64%): mp: 129-132°C; IR (ATR): 3034,

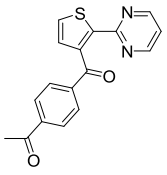
2935, 2860, 1650, 1637 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.50–1.60 (m, 2H), 1.59–1.73 (m, 2H), 1.92–2.13 (m, 2H), 2.43–2.54 (m, 2H), 6.32–6.46 (m, 1H), 6.97–7.11 (m, 2H ·), 7.44 (d, *J* = 5.1 Hz, 1H), 8.61 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.7, 21.9, 23.3, 26.0, 118.4, 128.8, 128.9, 140.1, 141.0, 142.6, 142.8, 156.8, 160.7, 196.3 ppm; MS (ESI): *m/z* (rel intensity): 271 (MH^+, 100), 253 (4); HRMS (ESI-TOF): calcd. for $C_{15}H_{15}N_2OS$ [MH^+]: 271.0905; found: 271.0912.



(4-Fluorophenyl)[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4k). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-fluorobenzaldehyde **2k** (0.11 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **4k** as a light-brown solid (112.7 mg, 79%): mp: 120-122°C; IR (ATR): 3045, 2988, 1739, 1669 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.97 (t, *J* = 4.9 Hz, 1H), 6.99–7.07 (m, 2H), 7.16 (d, *J* = 5.1 Hz, 1H), 7.53 (d, *J* = 5.1 Hz, 1H), 7.81–7.90 (m, 2H), 8.46 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 115.4 (d, *J* = 21.9 Hz), 118.5, 128.8, 129.5, 131.9 (d, *J* = 9.0 Hz), 134.3 (d, *J* = 3.3 Hz), 140.9, 141.5, 156.9, 160.4, 165.6 (d, *J* = 255.0 Hz), 193.1 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -105.49 (tt, *J* = 8.6, 5.4 Hz) ppm; MS (ESI): *m/z* (rel intensity): 250 (MH^+, 100), 105 (1); HRMS (ESI-TOF): calcd. for $C_{15}H_{10}FN_2OS$ [MH^+]: 285.0498; found: 285.0504.

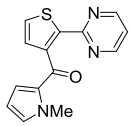


4-(*tert*-Butyl)phenyl][2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4m). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-*tert*-butylbenzaldehyde **2m** (0.17 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **4m** as a brown solid (126.7 mg, 79%): mp: 150-152 °C; IR (ATR): 3037, 2963, 2867, 1665, 1601 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.31 (s, 9H) , 6.96 (t, *J* = 4.9 Hz, 1H), 7.14 (d, *J* = 5.1 Hz, 1H), 7.39 (d, *J* = 8.5 Hz, 2H), 7.52 (d, *J* = 5.1 Hz, 1H), 7.727–7.872 (m, 2H), 8.49 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 31.1, 35.1, 118.4, 125.3, 128.9, 129.2, 129.4, 135.0, 140.6, 142.2, 156.7, 156.9, 160.6, 194.4 ppm; MS (ESI): *m/z* (rel intensity): 323 (MH^+, 100), 189 (1); HRMS (ESI-TOF): calcd. for $C_{19}H_{19}N_2OS$ [MH^+]: 323.1218; found: 323.1224.

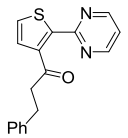


1-{4-[2-(Pyrimidin-2-yl)thiophene-3-carbonyl]phenyl}ethan-1-one (4o). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 4-acetylbenzaldehyde **2o** (148.1 mg, 1

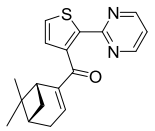
mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2 to 6:4) afforded **4o** as a yellow solid (70.3 mg, 46%): mp: 108-110 °C; IR (ATR): 3098, 3013, 1679 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.59 (s, 3H), 6.95 (t, *J* = 4.9 Hz, 1H), 7.20 (d, *J* = 5.1 Hz, 1H), 7.56 (d, *J* = 5.1 Hz, 1H), 7.84–8.04 (m, 4H), 8.43 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 26.9, 118.6, 128.2, 128.9, 129.3, 129.7, 139.8, 141.2, 141.2, 141.4, 156.8, 160.2, 193.9, 197.6 ppm; MS (ESI): *m/z* (rel intensity): 309 (MH^+, 100), 246 (1), 207 (1); HRMS (ESI-TOF): calcd. for $C_{17}H_{13}N_2O_2S$ [MH^+]: 309.0698; found: 309.0704.



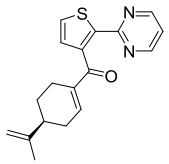
(1-Methyl-1*H*-pyrrol-2-yl)[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4p). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 1-methyl-1*H*-pyrrole-2-carbaldehyde **2p** (0.11 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **4p** as a light-grey solid (84.2 mg, 63%): mp: 104-106°C; IR (ATR): 3098, 2984, 2949, 1629 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.10 (s, 3H), 5.98 (dd, *J* = 4.1, 2.3 Hz, 1H), 6.42 (dd, *J* = 4.1, 1.7 Hz, 1H), 6.84 (t, *J* = 2.3 Hz, 1H), 6.98 (t, *J* = 4.9 Hz, 1H), 7.20 (d, *J* = 5.1 Hz, 1H), 7.45 (d, *J* = 5.1 Hz, 1H), 8.56 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 37.3, 108.1, 118.3, 121.9, 128.5, 129.3, 131.2, 131.9, 140.6, 143.0, 156.9, 160.9, 183.8 ppm; MS (ESI): *m/z* (rel intensity): 270 (MH^+, 13), 190 (8), 189 (100); HRMS (ESI-TOF): calcd. for $C_{14}H_{12}N_3OS$ [MH^+]: 270.0701; found: 270.0703.



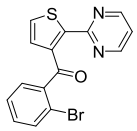
3-Phenyl-1-[2-(pyrimidin-2-yl)thiophen-3-yl]propan-1-one (4q). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), hydrocinnamaldehyde **2q** (0.12 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 35 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **4q** as a white solid (70.8 mg, 48%): mp: 69-71°C; IR (ATR): 3023, 1697cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.43–2.69 (m, 4H), 7.05 (d, *J* = 5.1 Hz, 1H), 7.10 (t, *J* = 4.9 Hz, 1H), 7.17–7.33 (m, 5H), 7.43 (d, *J* = 5.1 Hz, 1H), 8.60 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 30.3, 45.5, 118.7, 126.0, 127.9, 128.5, 128.6, 129.5, 139.9, 141.3, 144.2, 157.1, 160.7, 203.2 ppm; MS (ESI): *m/z* (rel intensity): 295 (MH^+, 100), 293 (2), 279 (1), 277 (1), 229 (3), 179 (4), 103 (1); HRMS (ESI-TOF): calcd. for $C_{17}H_{15}N_2OS$ [MH^+]: 295.0905; found: 295.0910.



[(1*R*,5*S*)-6,6-Dimethylbicyclo[3.1.1]hept-2-en-2-yl][2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4r). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), (1*R*)-(−)-myrtenal **2r** (0.15 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **4r** as a white solid (84.2 mg, 54%): mp. 123-125°C; IR (ATR): 2984, 2878, 1650, 1616 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.80 (s, 3H), 1.05 (d, *J* = 9.0 Hz, 1H), 1.39 (s, 3H), 2.09–2.15 (m, 1H), 2.31–2.37 (m, 2H), 2.52 (dt, *J* = 9.0, 5.7 Hz, 1H), 3.21 (td, *J* = 5.7, 1.7 Hz, 1H), 6.29 (dt, *J* = 3.4, 1.7 Hz, 1H), 6.97–7.24 (m, 2H), 7.46 (d, *J* = 5.1 Hz, 1H), 8.61 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 21.1, 25.9, 31.2, 32.5, 37.7, 39.7, 40.5, 118.3, 128.9, 128.9, 139.8, 140.5, 142.6, 150.6, 156.9, 160.8, 193.8 ppm; MS (ESI): *m/z* (rel intensity): 311 (MH^+, 100), 309 (2), 189 (1); HRMS (ESI-TOF): calcd. for $C_{18}H_{19}N_2OS$ [MH^+]: 311.1218; found: 311.1223.

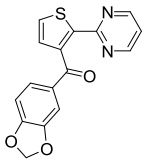


(*S*)-[4-(Prop-1-en-2-yl)cyclohex-1-en-1-yl][2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4s). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), (*S*)-(−)-perillaldehyde **2s** (0.16 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1) afforded **4s** as a white solid (61.4 mg, 40%): mp: 147-150°C; IR (ATR): 3009, 2931, 1654, 1637, cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.38–1.56 (m, 1H), 1.71 (s, 3H), 1.87–2.28 (m, 4H), 2.31–2.51 (m, 1H), 2.65–2.82 (m, 1H), 4.60–4.67 (m, 1H), 4.71 (t, *J* = 1.6 Hz, 1H), 6.49–6.38 (m, 1H), 6.94–7.13 (m, 2H), 7.46 (d, *J* = 5.1 Hz, 1H), 8.63 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 20.8, 23.5, 26.9, 31.3, 40.2, 109.2, 118.4, 128.8, 128.9, 140.1, 140.7, 141.9, 142.7, 148.7, 156.9,160.7, 196.0 ppm; MS (ESI): *m/z* (rel intensity): 311 (MH^+, 100), 309 (9), 293 (2), 189 (2); HRMS (ESI-TOF): calcd. for $C_{18}H_{19}N_2OS$ [MH^+]: 311.1218; found: 311.1220.

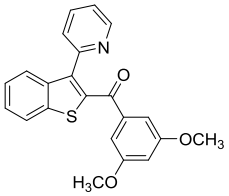


(2-Bromophenyl)[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4w). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 2-bromobenzaldehyde **2w** (183.0 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 25 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **4w** as a light-brown solid (130.6 mg, 76%): mp: 102-105°C; IR (ATR): 3034, 1675 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.95 (t, *J* = 4.9 Hz, 1H), 7.09–7.20 (m, 2H), 7.32–7.42 (m, 2H), 7.50 (d, *J* = 5.1 Hz, 1H), 7.56–7.61 (m, 1H), 8.51 (d, *J* = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 118.6,

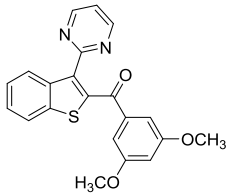
121.8, 126.5, 128.8, 130.2, 131.0, 131.8, 134.1, 139.8, 141.8, 143.0, 156.7, 160.1, 192.5 ppm; MS (ESI): *m/z* (rel intensity): 347 (MH^+ +2, 100), 345 (MH^+, 97), 274 (1), 265 (1), 189 (1); HRMS (ESI-TOF): calcd. for $C_{15}H_{10}BrN_2OS$ [MH^+]: 344.9697; found: 344.9704.



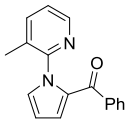
Benzo[*d*][1,3]dioxol-5-yl[2-(pyrimidin-2-yl)thiophen-3-yl]methanone (4x). Following the general procedure, **1b** (81.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), piperonal **2x** (150.1 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **4x** as a white solid (119.2 mg, 77%); mp: 178-181 °C; IR (ATR): 3048, 2907, 1658, 1605 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.02 (s, 2H), 6.72 (d, J = 8.1 Hz, 1H), 6.99 (t, J = 4.9 Hz, 1H), 7.14 (d, J = 5.1 Hz, 1H), 7.32 (dd, J = 8.1, 1.7 Hz, 1H), 7.44 (d, J = 1.7 Hz, 1H), 7.52 (d, J = 5.1 Hz, 1H), 8.52 (d, J = 4.9 Hz, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 101.8, 107.7, 108.6, 118.4, 126.4, 128.9, 129.3, 132.7, 140.5, 142.0, 148.1, 151.8, 156.9, 160.5, 193.0 ppm; MS (ESI): *m/z* (rel intensity): 311 (MH^+, 100), 189 (12); HRMS (ESI-TOF): calcd. for $C_{16}H_{11}N_2O_3S$ [MH^+]: 311.0490; found: 311.0496.



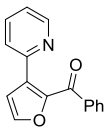
(3,5-Dimethoxyphenyl)[3-(pyridin-2-yl)benzo[*b*]thiophen-2-yl]methanone (6a). Following the general procedure, **5a** (105.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (16.8 mg, 0.075mmol), PivOH (38.8 mg, 0.38 mmol), 3,5-dimethoxybenzaldehyde **2b** (166.2 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 40 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **6a** as an orange solid (106.9 mg, 57%) mp: 94-96 °C;IR (ATR): 3056, 3009, 2960, 2836, 1640, 1591 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.71 (s, 6H), 6.45 (t, J = 2.3 Hz, 1H), 6.84 (d, J = 2.3 Hz, 2H), 7.15 (ddd, J = 7.6, 4.9, 1.2 Hz, 1H), 7.24–7.33 (m, 1H), 7.46 (ddd, J = 8.3, 7.0, 1.4 Hz, 1H), 7.47–7.59 (m, 2H), 7.94-8.00 (m, 2H), 8.64 (ddd, J = 4.9, 1.8, 0.9 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.5, 105.8, 107.2, 122.5, 122.6, 125.3, 125.4, 125.9, 127.0, 135.9, 138.7, 139.5, 139.5, 140.1, 140.8, 149.6, 153.5, 160.2, 190.6 ppm; MS (ESI): *m/z* (rel intensity): 376 (MH^+, 100), 226 (1); HRMS (ESI-TOF): calcd. for $C_{22}H_{18}NO_3S$ [MH^+]: 376.1007; found: 376.1011.



(3,5-Dimethoxyphenyl)[3-(pyrimidin-2-yl)benzo[*b*]thiophen-2-yl]methanone (6b). Following the general procedure, **5b** (106.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), 3,5-dimethoxybenzaldehyde **2b** (166.1 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 40 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **6b** as a light-yellow solid (20.4 mg, 15%); mp: 158-160 °C; IR (ATR): 2938, 1650, 1594 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.72 (s, 6H), 6.51 (t, J = 2.3 Hz, 1H), 6.93 (d, J = 2.3 Hz, 2H), 7.06 (t, J = 4.9 Hz, 1H), 7.47–7.58 (m, 2H), 7.89– 8.03 (m, 1H), 8.56–8.74 (m, 3H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.6, 105.7, 106.8, 118.8,122.5, 125.5, 125.8, 126.4, 135.9, 137.4, 139.8, 140.2, 143.2, 156.6, 160.5, 162.0, 190.8 ppm; MS (ESI): *m/z* (rel intensity): 377 (MH^+, 100), 295 (1); HRMS (ESI-TOF): calcd. for $C_{21}H_{17}N_2O_3S$ [MH^+]: 377.0960; found: 377.0962.

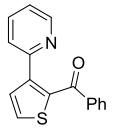


[1-(3-methylpyridin-2-yl)-1*H*-pyrrol-2-yl](phenyl)methanone (8). Following the general procedure, **7** (79.1 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), benzaldehyde **2a** (106 mg, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **8** as a yellow oil (63 mg, 48%), whose data are coincidental to those reported:[5] ^1H NMR (300 MHz, $CDCl_3$) δ 2.10 (s, 3H), 6.37 (dd, J = 3.9, 2.6 Hz, 1H), 6.90 (dd, J = 3.9, 1.6 Hz, 1H), 7.10 (dd, J = 2.6, 1.6, 1H), 7.20-7.25 (m, 1H), 7.40 (dd, J = 8.2, 6.6 Hz, 2H), 7.43-7.54 (m, 1H), 7.56-7.64 (m, 1H), 7.79-7.91 (m, 2H), 8.33-8.38 (m, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 17.3, 109.8, 122.2, 123.7, 128.2, 129.4, 129.6, 130.0, 131.7, 131.9, 138.7, 139.4, 146.4, 152.4, 184.6 ppm.



Phenyl[3-(pyridin-2-yl)furan-2-yl]methanone (10). Following the general procedure, **9** (72.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), benzaldehyde **2a** (0.10 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 15 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **10** as a yellow oil (32,3 mg, 26%): IR (ATR): 3006, 2926, 1644 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.12 (d, J = 1.8 Hz, 1H), 7.23 (ddd, J = 7.5, 4.9, 1.2 Hz, 1H), 7.40–746 (m, 2H), 7.48–7.59 (m, 1H), 7.62–7.75 (m, 2H), 7.85–7.99 (m, 3H), 8.65 (ddd, J = 4.8, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 114.5, 122.9, 125.0, 128.2,

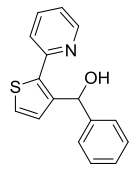
129.7, 132.6, 134.7, 136.1, 137.7, 144.9, 147.8, 149.4, 150.9, 184.4 ppm; MS (ESI): *m/z* (rel intensity): 250 (MH^+, 100), 237 (1), 105 (1); HRMS (ESI-TOF): calcd. for $C_{16}H_{12}NO_2$ [MH^+]: 250.0868; found: 250.0880.



Phenyl[3-(pyridin-2-yl)thiophen-2-yl]methanone (12). Following the general procedure, **11** (80.6 mg, 0.5 mmol) was treated with $Pd(OAc)_2$ (11.2 mg, 0.05 mmol), PivOH (38.8 mg, 0.38 mmol), benzaldehyde **2a** (0,10 mL, 1 mmol) and TBHP (5.5 M in decane, 0.36 mL, 2 mmol). After 30 min at 80°C, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **12** as a yellow oil (48,1 mg, 36%): IR (ATR): 3051, 3012, 1641 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.01 (ddd, *J* = 7.6, 4.9, 1.2 Hz, 1H), 7.16–7.26 (m, 3H), 7.32–7.39 (m, 1H), 7.43 (td, *J* = 7.7, 1.8 Hz, 1H), 7.48 (d, *J* = 5.1 Hz, 1H), 7.57–7.72 (m, 3H), 8.41 (ddd, *J* = 4.9, 1.8, 1.0 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$) δ 122.1, 124.2, 127.9,129.5, 129.6, 129.9, 132.3, 135.8, 137.9, 138.9, 145.1, 149.3, 153.4, 190.2 ppm. MS (ESI): *m/z* (rel intensity): 266 (MH^+, 100), 235 (3), 137 (3) ; HRMS (ESI-TOF): calcd. for $C_{16}H_{12}NOS$ [MH^+]: 266.0646; found: 266.0640.

3. Diversification of ketones 3. Synthesis of 13-18

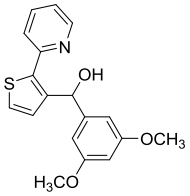
Carbonyl group reduction. General procedure. A solution of corresponding ketone **3a-q** (1 mmol) in methanol (6 mL) was cooled at 0°C. Then, sodium borohydride (2 mmol) was added portion wise. The mixture was stirred for 1.5-3h at room temperature. The reaction mixture was quenched with saturated NH_4Cl solution, extracted with EtOAc (3 × 15mL) dried over anhydrous Na_2SO_4, concentrated under reduced pressure. The residue was purified by column chromatography affording corresponding alcohols **13a-q**.



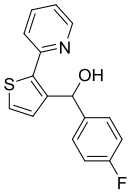
Phenyl[2-(pyridin-2-yl)thiophen-3-yl]methanol (13a). Following the general procedure, **3a** (79.6 mg, 0.3 mmol) was treated with $NaBH_4$ (22.7 mg, 0.6 mmol). After 1.5 h at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **13a** as a colourless oil whose data are coincidental to those reported[8] (66.7 mg, 83%): IR (ATR): 3314, 3059, 2984, 1587 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.04 (s, 1H), 6.73 (d, *J* = 5.2 Hz, 1H), 7.17–7.37 (m, 5H), 7.43–7.49 (m, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.69–7.78 (m, 2H), 8.58 (d, *J* = 4.9

[8] C. Wang, B. Zhou, Y. Hu, *Angew.Chem. Int.Ed.,* 2015, **54**,13659.

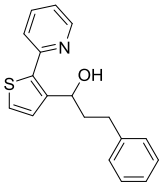
Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): 70.3, 121.8, 122.7, 125.1, 126.5, 126.9, 128.0, 131.1, 137.7, 138.1, 143.3, 146.0, 148.2, 152.6 ppm; MS (ES^+): *m/z* (rel intensity): 290 (MNa^+, 3), 250 (100), 157 (1); HRMS (ESI-TOF): calcd. for $C_{16}H_{13}NNaOS$ [MNa^+]: 290.0616; found: 290.0617.



(3,5-Dimethoxyphenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanol (13b). Following the general procedure, **3b** (97.6 mg, 0.3 mmol) was treated with $NaBH_4$ (22.7 mg, 0.6 mmol). After 1.5 h at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **13b** as a yellow oil (90.5 mg, 92%): IR (ATR): 3300 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.76 (s, 6H), 5.94 (s, 1H), 6.36 (t, *J* = 2.2 Hz, 1H), 6.63 (d, *J* = 2.2 Hz, 2H), 6.76 (d, *J* = 5.2 Hz, 1H), 7.17–7.24 (m, 2H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.74 (td, *J* = 7.9, 1.7 Hz, 1H), 8.58 (d, *J* = 4.3 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.3, 70.3, 99.3, 104.5, 121.9, 122.8, 125.1, 131.1,137.8, 138.0, 145.8, 145.8, 148.2, 152.6, 160.6 ppm; MS (ESI): *m/z* (rel intensity): 311 (19), 310 (100); HRMS (ESI-TOF): calcd. for $C_{18}H_{17}NNaO_3S$ [MNa^+]: 350.0827; found: 350.0824.



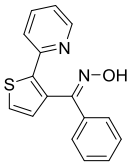
(4-Fluorophenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanol (13k). Following the general procedure, **3k** (85.0 mg, 0.3 mmol) was treated with $NaBH_4$ (22.7 mg, 0.6 mmol). After 1.5 h at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **13k** as a yellow oil (63.7 mg, 74%): IR (ATR): 3275 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.99 (s, 1H), 6.71 (d, *J* = 5.2 Hz, 1H), 6.96–7.06 (m, 2H), 7.15–7.27 (m, 2H), 7.41 (dd, *J* = 8.4, 5.6 Hz, 2H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.70–7.84 (m, 2H), 8.57 (d, *J* = 4.3 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 69.8, 114.8 (d, *J* = 21.0 Hz), 121.9, 122.7, 125.2, 128.0 (d, *J* = 7.7 Hz), 130.9, 137.8, 138.1, 139.1 (d, J = 3.0 Hz), 145.8, 148.2, 152.5, 162.0 (d, *J* = 245 Hz) ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -116.20 (tt, *J* = 8.9, 4.4 Hz) ppm; MS (EI): *m/z* (rel intensity): 269 (15), 268 (100); HRMS (ESI-TOF): calcd. for $C_{16}H_{12}FNNaOS$ [MNa^+]: 308.0521; found: 308.0525.



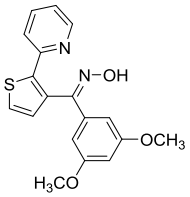
3-Phenyl-1-[2-(pyridin-2-yl)thiophen-3-yl]propan-1-ol (13q). Following the general procedure, **3q** (88.0 mg, 0.3 mmol) was treated with $NaBH_4$ (22.7 mg, 0.6 mmol). After 1.5 h at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **13q** as a colourless oil (73.5 mg, 83 %): IR (ATR): 3388 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.04–2.39 (m, 2H), 2.99–2.67 (m, 2H), 4.86 (dd, *J* = 8.7, 5.4 Hz, 1H), 7.13 (d, *J* = 5.1 Hz, 1H), 7.17–7.36 (m, 7H), 7.63 (d, *J* = 7.9 Hz, 1H), 7.75 (td, *J* = 7.9, 1.8 Hz, 1H), 8.60 (d, *J* = 4.9 Hz,

1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 32.9, 38.3, 68.5, 121.8, 122.7, 125.6, 125.7, 128.3, 128.5, 129.7, 137.7, 137.8, 142.3, 145.9, 148.3, 152.9 ppm; MS (EI): *m/z* (rel intensity): 279(16), 278 (100); HRMS (ESI-TOF): calcd. for $C_{18}H_{17}NNaOS$ [MNa^+]: 318.0929; found: 318.0938.

Oxime formation. General procedure. To a solution of NH_2OH-HCl (2 mmol) and corresponding ketone **3a,b** (1 mmol) in EtOH (5 mL), a solution of NaOAc (1 mmol.) in H_2O (2 mL) was added and the mixture was refluxed for 5h. The mixture was cooled down to rt, the solvent was removed under vacuum and the residue was dissolved in H_2O and extracted with Et_2O (3 × 15 mL). The organic extract was dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography afforded oximes **14a,b**.



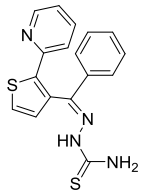
(*E*)-Phenyl[2-(pyridin-2-yl)thiophen-3-yl]methanone oxime (14a). Following the general procedure, **3a** (106.1 mg, 0.4 mmol) was treated with NH_2OH-HCl (55.9 mg, 0.8 mmol). After 5 h under reflux, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded oxime **14a** as a white solid (83.6 mg, 77%): mp: 156-158 °C; IR (ATR): 3006, 1587 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03–7.13 (m, 2H), 7.24–7.34 (m, 3H), 7.46–7.57 (m, 5H), 8.56 (d, *J* = 4.8 Hz, 1H), 9.50 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 120.4, 122.2, 127.0, 127.2, 128.5, 129.5, 129.8, 129.8, 134.7, 136.8, 142.6, 149.3, 151.7, 155.0 ppm; MS (ESI): *m/z* (rel intensity): 281 (MH^+, 78), 264 (14), 263 (100); HRMS (ESI-TOF): calcd. for $C_{16}H_{13}N_2OS$ [MH^+]: 281.0749; found: 281.0752.



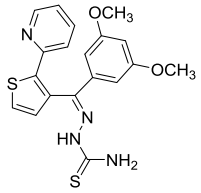
(*E*)-(3,5-Dimethoxyphenyl)[2-(pyridin-2-yl)thiophen-3-yl]methanone oxime (14b). Following the general procedure, **3b** (130.2 mg, 0.4 mmol) was treated with NH_2OH-HCl (55.9 mg, 0.8 mmol). After 5 h under reflux, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded oxime **14b** as an orange solid (101.0 mg, 74%): mp: 145-147 °C; IR (ATR): 3006, 1587 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.72 (s, 6H), 6.45 (t, *J* = 2.2 Hz, 1H), 6.72 (d, *J* = 2.2 Hz, 2H), 7.00 (d, *J* = 5.1 Hz, 1H), 7.08–7.12 (m, 1H), 7.48–7.53 (m, 3H), 8.56 (d, *J* = 4.8 Hz, 1H), 8.96 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.4, 102.0, 105.3, 120.3, 122.2, 127.1, 129.5, 129.6, 136.7, 136.8, 142.5, 149.3, 151.8, 155.0, 160.7 ppm; MS (ESI): *m/z* (rel intensity): 341 (MH^+, 100), 324 (10), 323 (63); HRMS (ESI-TOF): calcd. for $C_{18}H_{16}N_2NaO_3S$ [MNa^+]: 363.0779; found: 363.0780.

Synthesis of thiosemicarbazones 15. General procedure. Thiosemicarbazide (1 mmol) was added to a solution of corresponding ketone **3** (1 mmol) in EtOH (25 mL). 4Å molecular sieve and 3 drops of conc. HCl were added and the mixture was stirred and under reflux for 24 hours. The mixture was cooled down to

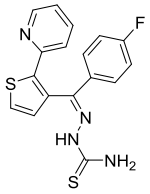
rt, filtered under vacuum and the solvent was removed under reduced pressure. The residue was purified by column chromatography affording corresponding thiosemicarbazones **15**.



(*Z*)-2-(Phenyl[2-(pyridin-2-yl)thiophen-3-yl)methylene]hydrazine-1-carbothioamide (15a). Following the general procedure, **3a** (212.3 mg, 0.8 mmol) was reacted with thiosemicarbazide (72.9 mg, 0.8 mmol). After 24 h under reflux, purification by column chromatography (silica gel, petroleum ether/EtOAc 6/4) afforded **15a** as a white solid (229.2 mg, 85%): mp: 185-188 °C; IR (ATR): 3427, 3331, 3253 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.92 (d, J = 5.1 Hz, 1H), 7.04 (dd, J = 7.0, 4.8 Hz, 1H), 7.20 (s, 1H), 7.24–7.33 (m, 4H), 7.41–7.52 (m, 2H), 7.57 (m, 3H), 8.48 (d, J = 4.8 Hz, 1H), 8.76 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 119.8, 122.9, 127.3, 127.5, 128.7, 128.9, 129.4, 130.4, 135.4, 137.1, 144.4, 147.5, 149.7, 150.4, 178.8 ppm; MS (EI): *m/z* (rel intensity): 339 (MH^+, 55), 322 (100), 264 (3); HRMS (ESI-TOF): calcd. for $C_{17}H_{15}N_4S_2$ [MH^+]: 339.0738; found: 339.0739.

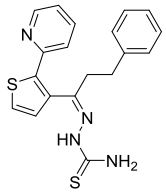


(*Z*)-2-{(3,5-Dimethoxyphenyl)[2-(pyridin-2-yl)thiophen-3-yl]methylene}hydrazine-1-carbothioamide (15b). Following the general procedure, **3b** (260.3 mg, 0.8 mmol) was reacted with thiosemicarbazide (72.9 mg, 0.8 mmol). After 24 h under reflux, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **15b** as a white solid (257.8 mg, 81%): mp: 206-208 °C; IR (ATR): 3388, 3310, 3261 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 6H), 6.40–6.58 (m, 2H), 6.74 (d, J = 2.3 Hz, 2H), 6.96 (d, J = 5.1 Hz, 1H), 7.13 (ddd, J = 7.5, 4.8, 1.0 Hz, 1H), 7.29–7.33 (m, 1H), 7.40 (s, 1H), 7.54 (td, J = 7.8, 1.8 Hz, 1H), 7.62 (d, J = 5.1 Hz, 1H), 8.63–8.49 (m, 1H), 8.74 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, DMSO-d^6): δ 55.5, 102.0, 105.7, 119.8, 122.9, 127.3, 128.9, 129.3, 137.0,137.4, 144.5, 147.4, 149.8, 150.5, 160.9, 179.1 ppm; MS (ESI): *m/z* (rel intensity): 399 (MH^+, 100), 384 (4), 382 (53); HRMS (ESI-TOF): calcd. for $C_{19}H_{19}N_4O_2S_2$ [MH^+]: 399.0949; found: 399.0950. [The stereochemistry of **15b** was determined by 2D-experiments (NOESY)]



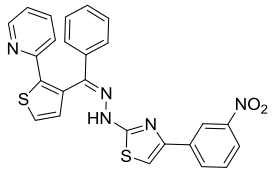
(*Z*)-2-{(4-Fluorophenyl)[2-(pyridin-2-yl)thiophen-3-yl]methylene}hydrazine-1-carbothioamide (15k). Following the general procedure, **3k** (226.6 mg, 0.8 mmol) was reacted with thiosemicarbazide (73.0 mg, 0.80 mmol). After 24 h under reflux, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **15k** as a yellow solid (213.7 mg, 75%): mp: 190-192°C; IR (ATR): 3487, 3423, 3328, 3261, 3147, 3056, 2988, 1584

cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.83 (s, 1H); 6.93–7.03 (m, 3H), 7.11 (ddd, J = 7.6, 4.9, 1.0 Hz, 1H), 7.24–7.32 (m, 1H), 7.43 (s, 1H), 7.50–7.59 (m, 3H), 7.63 (d, J = 5.1 Hz, 1H), 8.51 (dt, J = 4.8, 1.3 Hz, 1H), 8.75 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 115.8 (d, J = 21.9 Hz), 119.9, 122.9, 127.3, 128.7, 129.3 (d, J = 8.5 Hz), 129.5, 131.7 (d, J = 3.3 Hz), 137.0, 144.5, 146.7, 149.8, 150.3, 164.2 (d, J = 251.8 Hz), 178.9 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -109.66 – -109.56 (m) ppm; MS (ESI): *m/z* (rel intensity): 357 (MH^+,59), 340 (100), 284 (2), 282 (2), 281 (2), 274 (1); HRMS (ESI-TOF): calcd. for $C_{17}H_{14}FN_4S_2$ [MH^+]: 357.0644; found: 357.0649.



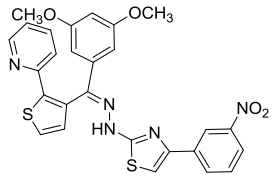
(*Z*)-2-{3-Phenyl-1-[2-(pyridin-2-yl)thiophen-3-yl]propylidene}hydrazine-1-carbothioamide (15q). Following the general procedure, **3q** (196.3 mg, 0.67 mmol) was reacted with thiosemicarbazide (61.1 mg, 0.67 mmol). After 24 h under reflux, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **15q** as a light-brown solid (170.2 mg, 69%): mp: 190-191°C; IR (ATR): 3388, 3267, 3168 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.82–2.97 (m, 4H), 6.31 (s, 1H), 6.89 (d, J = 5.2 Hz, 1H), 7.11–7.35 (m, 8H), 7.53 (d, J = 5.2 Hz, 1H), 7.64 (td, J = 7.8, 1.6 Hz, 1H), 8.44–8.73 (m, 2H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 32.2, 38.8, 120.3, 122.8, 126.2, 127.7, 128.3, 128.5, 128.8, 130.0, 137.1, 140.7, 142.6, 149.8, 150.7, 151.4, 178.9 ppm; MS (EI): *m/z* (rel intensity): 367 (MH^+, 88), 350 (100), 351 (17); HRMS (ESI-TOF): calcd. for $C_{19}H_{19}N_4S_2$ [MH^+]: 367.1051; found: 367.1055.

Synthesis of thiazoles 16. General procedure. A solution of 2-bromo-3′-nitroacetophenone (2 mmol) and corresponding thiosemicarbazone **15** (1 mmol) in EtOH (30 mL) was stirred at room temperature for 24h. Then, the solvent was removed under vacuum, the residue was dissolved in dichloromethane and the resulting solution was washed with water (2 × 15mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. Purification by column chromatography afforded thiazoles **16**.

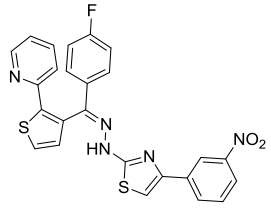


(*Z*)-4-(3-nitrophenyl)-2-{{2-{phenyl[2-(pyridin-2-yl)thiophen-3-yl]methylene}hydrazineyl}}thiazole (16a). Following the general procedure, **15a** (101.5 mg, 0.3 mmol) was treated 2-bromo-3′-nitroacetophenone (146.4 mg, 0.6 mmol). After 24 hours at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1 to 6:4) afforded **16a** as an orange solid (123.8 mg, 85%): mp: 206-208°C; IR (ATR): 3006, 2992, 2971, 1739, 1552 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (d, J

= 5.2 Hz, 1H), 7.06–7.13 (m, 2H), 7.33–7.42 (m, 4H), 7.51 (t, *J* = 7.8 Hz, 2H), 7.62–7.74 (m, 3H), 8.05 (dt, *J* = 7.8, 1.4 Hz, 1H), 8.10 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1H), 8.61–8.52 (m, 2H), 8.88 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 106.2, 119.5, 120.7, 122.2, 122.7, 126.7, 128.1, 128.7, 129.0, 129.3, 129.5, 129.6, 131.5, 135.8, 136.3, 137.1, 144.1, 145.7, 148.6, 149.2, 149.6, 150.7, 168.4 ppm; MS (ESI): *m/z* (rel intensity): 484 (MH^+, 100), 249 (<1); HRMS (ESI-TOF): calcd. for $C_{25}H_{18}N_5O_2S_2$ [MH^+]: 484.0902; found: 484.0903.

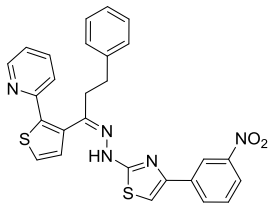


(*Z*)-2-{{2-{(3,5-Dimethoxyphenyl)[2-(pyridin-2-yl)thiophen-3-yl]methylene}hydrazineyl}}-4-(3-nitrophenyl)thiazole (16b). Following the general procedure, **15b** (119.5 mg, 0.3 mmol) was treated 2-bromo-3´-nitroacetophenone (146.4 mg, 0.6 mmol). After 24 hours at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 7/3) afforded **16b** as an orange solid (127.9 mg, 78%): mp: 192-195 °C; IR (ATR): 3006 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.80 (s, 6H), 6.48 (s, 1H), 6.86 (d, *J* = 2.1 Hz, 2H), 6.97 (d, *J* = 5.1 Hz, 1H), 7.05–7.14 (m, 2H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.44 –7.54 (m, 2H), 7.62 (d, *J* = 5.1 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 8.08 (dd, *J* = 8.4, 1.6 Hz, 1H), 8.55–8.58 (m, 2H), 8.90 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 55.4, 101.5, 105.0, 106.1, 119.5, 120.7, 122.2, 122.8, 127.9, 129.1, 129.3, 129.5, 131.6, 136.3, 137.2, 137.8, 144.1, 145.4, 148.6, 149.3, 149.7, 150.7, 160.9, 168.2 ppm; MS (ESI): *m/z* (rel intensity): 545 (25), 544 (MH^+, 100); HRMS (ESI-TOF): calcd. for $C_{27}H_{22}N_5O_4S_2$ [MH^+]: 544.1113; found: 544.1117.

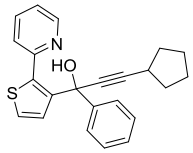


(*Z*)-2-{{2-{(4-Fluorophenyl)[2-(pyridin-2-yl)thiophen-3-yl]methylene}hydrazineyl}}-4-(3-nitrophenyl)thiazole (16k). Following the general procedure, **15k** (106.9 mg, 0.3 mmol) was treated 2-bromo-3´-nitroacetophenone (146.4 mg, 0.6 mmol). After 24 hours at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **10k** as a dark-orange solid (130.6 mg, 87%): mp: 203-206; IR (ATR): 3310, 3113, 3052, 2992, 1605, 1555 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.94 (d, *J* = 5.2 Hz, 1H), 6.98–7.13 (m, 4H), 7.36 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.41–7.52 (m, 2H,), 7.55–7.70 (m, 3H), 7.95–8.08 (m, 2H), 8.42–8.61 (m, 2H), 9.05 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 106.1, 115.70 (d, *J* = 21.9 Hz), 119.5, 120.7, 122.1, 122.8, 127.9, 128.5, 128.6, 128.8, 129.4 (d, *J* = 4.7 Hz), 131.5, 132.0 (d, *J* = 3.2 Hz), 136.2, 137.1, 144.1, 144.8, 148.6, 149.2, 149.7, 150.6, 163.6 (d, *J* = 250.3 Hz), 168.3 ppm; ^{19}F NMR (282.4 MHz, $CDCl_3$) δ -111.06 (tt, *J* = 8.8, 4.3 Hz) ppm; MS

(ES$^+$): *m/z* (rel intensity): 502 (MH$^+$, 100), 472 (1), 320 (<1), 267 (<1), 228 (<1); HRMS (ESI-TOF): calcd. for $C_{25}H_{17}FN_5O_2S_2$ [MH$^+$]: 502.0808; found: 502.0799.

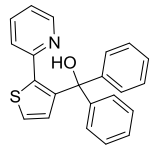


(*Z*)-4-(3-Nitrophenyl)-2-{{2-{3-phenyl-1-[2-(pyridin-2-yl)thiophen-3-yl]propylidene}hydrazineyl}}thiazole (16q). Following the general procedure, **15q** (110.0 mg, 0.3 mmol) was treated 2-bromo-3´-nitroacetophenone (146.4 mg, 0.6 mmol). After 24 hours at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 9/1 to 9:1) afforded **16q** as a brown solid (109.2 mg, 71 %): mp: 69-72°C; IR (ATR): 3314 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.94 (t, *J* = 7.5 Hz, 2H), 3.04 (t, J = 7.5 Hz, 2H), 6.92 (d, *J* = 5.1 Hz, 1H), 7.03 (s, 1H), 7.16 (dd, *J* = 7.4, 4.9 Hz, 1H), 7.22–7.33 (m, 6H), 7.48–7.56 (m, 2H)*, 7.52 (d, d, *J* = 5.1 Hz, 1H)* 8.04–8.10 (m, 2H), 8.53–8.59 (m, 2H), 8.73 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 32.0, 38.8, 105.6, 119.8, 120.7, 122.1, 122.7, 126.1, 127.8, 128.4, 128.7, 128.9, 129.5, 130.7, 131.5, 136.4, 137.1, 141.1, 142.4, 148.6, 149.0, 149.7, 150.8, 168.8 ppm; MS (ESI): *m/z* (rel intensity): 513 (28), 512 (MH$^+$, 100); HRMS (ESI-TOF): calcd. for $C_{27}H_{22}N_5O_2S_2$ [MH$^+$]: 512.1215; found: 512.1224. (* partially overlapped signals).

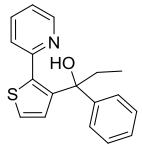


3-Cyclopentyl-1-phenyl-1-[2-(pyridin-2-yl)thiophen-3-yl]prop-2-yn-1-ol (17a). Under Argon atmosphere, a well-stirred solution of cyclopentylacetylene (0.11 mL mmol, 0.99 mmol) in anhydrous THF (6 mL) was cooled down to –78 °C. Then, *n*-BuLi (1.6 M solution in hexanes, 1.09 mmol) was added dropwise and the solution was stirred at –78 °C for 2.5 h. Then, a solution of **3a** (238.8 mg, 0.9 mmol) in anhydrous THF (3 mL) was added dropwise at –78 °C. The mixture was allowed to reach slowly room temperature and stirred for an additional 2 h. The reaction was quenched with a saturated NH_4Cl solution (20 mL) and the mixture was extracted with EtOAc (2 × 15 mL). The organic layers were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (silica gel, petroleum ether/EtOAc 9/1) to afford **17a** as a white solid (199.9 mg, 62%): mp: 112-114 °C; IR (ATR): 3087, 3052, 2960, 2868, 2231, 1587, 1474 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22–1.62 (m, 6H), 1.62 –1.78 (m, 2H), 2.51 (quint, *J* = 7.3 Hz, 1H), 6.73 (d, *J* = 5.2 Hz, 1H), 7.06–7.38 (m, 5H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.65–7.74 (m, 3H), 8.54 (dd, *J* = 5.1, 1.8 Hz, 1H), 9.58 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 24.9, 24.9, 30.1, 33.6, 33.6, 70.8, 83.5, 89.4, 122.0, 123.1, 124.1, 126.5, 127.2, 127.7, 131.5, 137.5, 137.8, 145.5, 147.3, 148.2, 152.7 ppm; MS (ESI): *m/z* (rel intensity): 382 (MNa$^+$,

3), 343 (18), 342 (100), 308 (1); HRMS (ESI-TOF): calcd. for $C_{23}H_{21}NNaOS$ [MNa^+]: 382.1242; found: 382.1244.

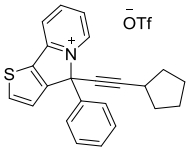


Diphenyl[2-(pyridin-2-yl)thiophen-3-yl]methanol (17b). Under Argon atmosphere, phenylmagnesium bromide (1 M in THF, 1.13 mmol) was added dropwise to a solution of **3a** (199.0 mg, 0.75 mmol) in dry THF (2.3 mL) at 0 °C. The solution was allowed to reach room temperature and stirred for 5 hours. The reaction was quenched with a saturated NH_4Cl solution (20 mL) and extracted with EtOAc (2 × 15 mL). The organic layers were dried over Na_2SO_4, filtered and concentrated. The crude product was purified by column chromatography (silica gel, petroleum ether/EtOAc 8/2) to afford **17b** as a white solid (192.1 mg, 75%): mp: 160-163 °C; IR (ATR): 3084, 3056, 2840, 1587 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 6.38 (d, J = 5.2 Hz, 1H), 6.99 (ddd, J = 6.8, 5.0, 1.6 Hz, 1H), 7.12–7.29 (m, 7H,), 7.34–7.44 (m, 4H), 7.51–7.65 (m, 2H), 8.26 (dd, J = 5.0, 1.4 Hz, 1H), 9.78 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 78.7, 121.5, 123.0, 123.8, 126.6, 127.4, 127.5, 133.3, 137.6, 137.8, 147.1, 147.9, 150.0, 152.5 ppm; MS (ESI): *m/z* (rel intensity): 366 (MNa^+, 2), 326 (100), 320 (1), 318 (1); HRMS (ESI-TOF): calcd. for $C_{22}H_{17}NNaOS$ [MNa^+]: 366.0929; found: 366.0939.

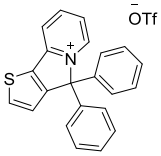


1-Phenyl-1-[2-(pyridin-2-yl)thiophen-3-yl]propan-1-ol (17c). Following the previous procedure, **3a** (199.0 mg, 0.75 mmol) was treated with an ethylmagnesium bromide solution (1 M in THF, 1.13 mmol). After 5 h at room temperature, purification by column chromatography (silica gel, petroleum ether/EtOAc 8/2) afforded **17c** as a white solid (88.2 mg, 40%): mp = 67-69 °C; IR (ATR): 3056, 3016, 2974, 2935, 2871, 1591 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ, 0.93 (t, J = 7.3 Hz, 3H), 2.10–2.26 (m, 1H), 2.29–2.48 (m, 1H), 6.94–7.14 (m, 4H), 7.22–7.31 (m, 2H), 7.29–7.39 (m, 2H), 7.41 (dt, J = 8.1, 1.1 Hz, 1H), 7.55 (td, J = 8.0, 1.8 Hz, 1H), 8.41 (ddd, J = 5.0, 1.9, 1.0 Hz, 1H), 9.09 (s, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 8.5, 36.6, 75.9, 121.5, 123.1, 124.6, 125.8, 126.1, 126.9, 130.1, 137.5, 137.9, 147.0, 147.6, 149.9, 152.6 ppm; MS (ESI): *m/z* (rel intensity): 296 (MH^+, 1), 278 (100); HRMS (ESI-TOF): calcd. for $C_{18}H_{18}NOS$ [MH^+]: 296.1104; found: 296.1118.

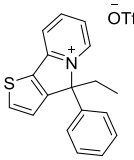
Synthesis of 4*H*-thieno[2,3-*a*]indolizin-5-ium salts 18. General procedure. Under argon atmosphere, trifluoromethanesulfonic acid (0.25 mmol) was added to a solution of corresponding tertiary alcohol **17** (0.25 mmol) in dry toluene/MeOH (10:1, v/v, 2.53 mL). The mixture was stirred at 80 °C for 3h. The reaction mixture was filtered through a Celite pad washing with MeOH. The filtrate was concentrated, and the crude product was purified using column chromatography on silica gel to obtain **18a-c.**



4-(Cyclopentylethynyl)-4-phenyl-*4H*-thieno[2,3-*a*]indolizin-5-ium trifluoromethanesulfonate (18a). Following the general procedure, **17a** (89.9 mg, 0.25 mmol) was treated with trifluoromethanesulfonic acid (22 µL, 0.25 mmol). After 3 h at 80°C, purification by column chromatography (silica gel, DCM/MeOH 25/1) afforded **18a** as a white solid (107.3 mg, 87%): mp: 172-174°C; IR (ATR): 3081, , 2971, 2871, 2238, 1739, 1623 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 1.55–1.86 (m, 6H), 1.95–2.12 (m, 2H), 2.78–3.06 (m, 1H), 7.28 (d, *J* = 5.0 Hz, 1H), 7.44–7.57 (m, 5H), 7.84 (ddd, *J* = 7.6, 6.4, 1.3 Hz, 1H), 8.24 (d, *J* = 5.0 Hz, 1H), 8.42 (dt, *J* = 8.3, 1.0 Hz, 1H), 8.63 (td, *J* = 7.9, 1.2 Hz, 1H), 9.02 (dt, *J* = 6.4, 1.1 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, CD_3OD): δ 24.7, 29.8, 33.0, 71.4, 76.3, 97.7, 120.4, 120.5 (q, *J* = 317.5 Hz), 121.1, 124.3, 126.3, 129.6, 130.7, 132.0, 134.4, 140.5, 141.0, 147.6, 148.7, 155.6 ppm; MS (ESI): *m/z* (rel intensity): 342 (M^+, 100); HRMS (ESI-TOF): calcd. for $C_{23}H_{20}NS$ [M^+]: 342.1311; found: 342.1324.



4,4-Diphenyl-4*H*-thieno[2,3-*a*]indolizin-5-ium trifluoromethanesulfonate (18b). Following the general procedure, **17b** (85.9 mg, 0.25 mmol) was treated with trifluoromethanesulfonic acid (22 µL, 0.25 mmol). After 3 h at 80°C, purification by column chromatography (silica gel, DCM/MeOH 25/1) afforded **18b** as a light-brown solid (92.7 mg, 78%): mp: 164-167°C; IR (ATR): 3084, 3009, 2988, 1739,1627 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 7.14–7.30 (m, 4H), 7.43 (d, *J* = 5.0 Hz, 1H), 7.42–7.52 (m, 6H), 7.81– 7.92 (m, 1H), 8.21 (d, *J* = 5.0 Hz, 1H), 8.48 (d, *J* = 8.3 Hz, 1H),8.57–8.71 (m, 1H), 9.08 (d, *J* = 6.4 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, CD_3OD): δ 86.5, 120.5 (q, *J* = 317.7 Hz), 120.7, 122.2, 123.6, 127.4, 129.6, 130.0, 131.3, 137.0, 140.7, 141.7, 147.2, 149.6, 158.2 ppm; MS (ESI): *m/z* (rel intensity): 326 (M^+, 100), 209 (1); HRMS (ESI-TOF): calcd. for $C_{22}H_{16}NS$ [M^+]: 326.1003; found: 326.1006

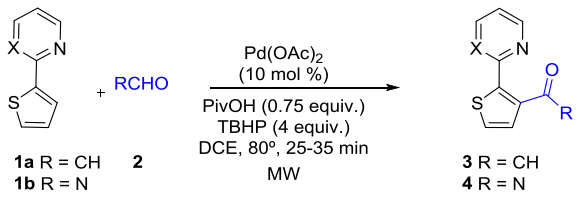


4-Ethyl-4-phenyl-4*H*-thieno[2,3-*a*]indolizin-5-ium trifluoromethanesulfonate (18c). Following the general procedure, **17c** (51.0 mg, 0.17 mmol) was treated with trifluoromethanesulfonic acid (15 µL, 0.17 mmol). After 3 h at 80°C, purification by column chromatography (silica gel, DCM/MeOH 20/1) afforded **18c** as a colourless oil (21.9 mg, 30%). IR (ATR): 3081, 3009, 2984, 1627, 1496 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.62 (t, *J* = 7.2 Hz, 3H), 2.88 (dq, *J* = 14.5, 7.2 Hz, 1H), 3.03 (dq, *J* = 14.5, 7.2 Hz, 1H), 7.15 (d, *J* = 4.9 Hz, 1H), 7.30–7.37 (m, 2H), 7.39–7.44 (m, 3H), 7.85 (ddd, *J* = 7.6, 6.3, 1.3 Hz, 1H), 8.04 (d, *J* = 4.9 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 8.43–8.59 (m, 1H), 9.02 (d, *J* = 6.3 Hz, 1H) ppm; ^{13}C NMR (75.5 MHz, $CDCl_3$): δ 7.8, 30.6, 84.2, 119.8, 120.7 (q, *J* = 319.8 Hz),

121.9, 124.5, 126.7, 130.1, 130.8, 132.4, 134.4, 139.8, 141.2, 146.6, 148.7, 156.9 ppm; MS (ESI): *m/z* (rel intensity): 278 (M^+, 100), 215 (1); HRMS (ESI-TOF): calcd. for $C_{18}H_{16}NS$ [M^+]: 278.1003; found: 278.1007.

4. Additional assays on substrates 1a,b with selected aldehydes 2 at different reaction times.

In addition to the results depicted in Tables 4 and 5 for the acylation of **1a,b**, different reaction times under MW irradiation were tested to try to improve the obtained yields of **3,4**. The results are summarized in Figure S1. The best yield obtained for each compound is included in Tables 4 and 5. As can be seen, the extension of the reaction time can lead to lower isolated yields of **3,4** due to the formation of decomposition products.



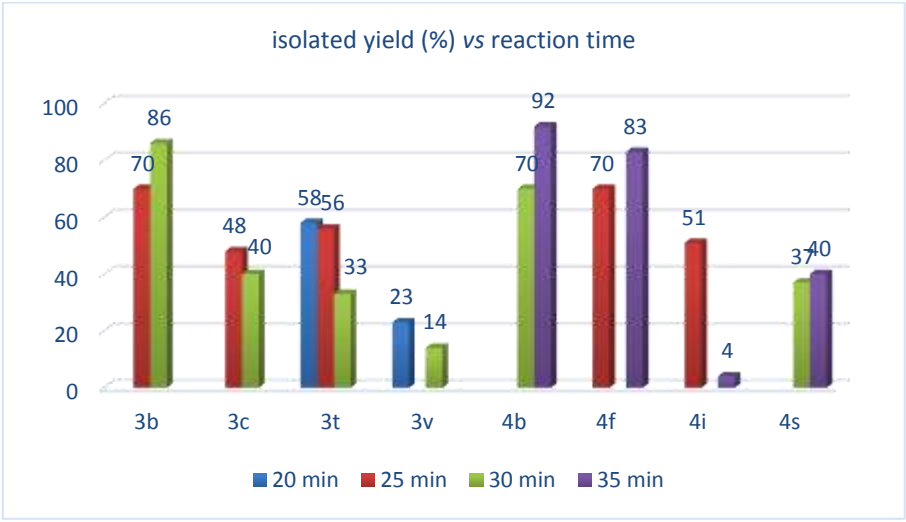


Figure S1. Additional essays on substrates **1a,b** with selected aldehydes **2** at different reaction times

5. X-ray diffraction data for 18a

The structure of one of the thieno[2,3-*a*]indolizin-5-ium trifluoromethanesulfonates (**18a**) was unambiguously confirmed by single-crystal X-ray analysis. **18a** was recrystallized from ethanol. **CCDC2107402** contains the supplementary crystallographic data for this structure.

Intensity data were collected on an Agilent Technologies Super-Nova diffractometer, which was equipped with monochromated Mo kα radiation (λ= 0.71073 Å) and Eos CCD detector. Measurement was carried out at 150.01(10) K with the help of an Oxford Cryostream 700 PLUS temperature device. Data frames were processed (united cell determination, analytical absorption correction with face indexing, intensity data integration and correction for Lorentz and polarization effects) using the Crysalis software package.[9] The structure was solved using SHELXT[10] and refined by full-matrix least-squares with SHELXL-97.[11] Final geometrical calculations were carried out with Mercury[12] and PLATON[13] as integrated in WinGX.[14]

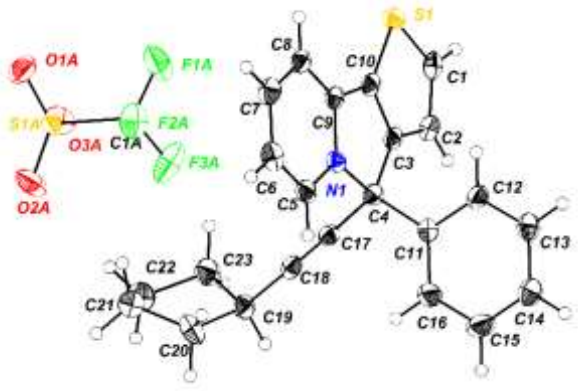


Figure S2. ORTEP plot of compound **18a** with thermal ellipsoids at the 50% probability level with the atomic nomenclature used

Crystal Data for $C_{25}H_{23}F_3NO_{3.5}S_2$ (*M* =514.56 g/mol): triclinic, space group P-1 (no. 2), *a* = 9.1139(10) Å, *b* = 11.7059(12) Å, *c* = 12.6851(14) Å, *α* = 109.356(9)°, *β* = 100.318(9)°, *γ* = 106.611(9)°, *V* = 1166.1(2) Å^3, *Z* = 2, *T* = 150.01(10) K, μ(MoKα) = 0.284 mm^{-1}, *Dcalc* = 1.466 g/cm^3, 7751 reflections measured (3.57° ≤ 2Θ ≤ 52.996°), 4588 unique (R_{int} = 0.0547, R_{sigma} = 0.1218) which were used in all calculations. The final R_1 was 0.0679 (I > 2σ(I)) and wR_2 was 0.1502 (all data).

[9] CrysAlisPro, Agilent Technologies,Version 1.171.37.31 (release 14-01-2014 CrysAlis171 .NET)(compiled Jan 14 2014,18:38:05)
[10] G. M. Sheldrick, *Acta Cryst*., 2015, **A71**, 3.
[11] G. M. Sheldrick, *Acta Cryst*., 2008, **A64**, 112.
[12] C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek, P. A. Wood, *J. Appl. Cryst*., 2008, **41**, 466.
[13] (a) A. L. Spek*, PLATON, A Multipurpose Crystallographic Tool*, Utrecht University: Utrecht, The Netherlands; 2010. (b) A. L. Spek*, J. Appl. Cryst.,* 2003, **36**, 7.
[14] L. J. Farrugia*, J. Appl. Cryst.,* 1999, **32**, 837.

6. Copies of ^{1}H ,^{13}C, and ^{19}F NMR spectra

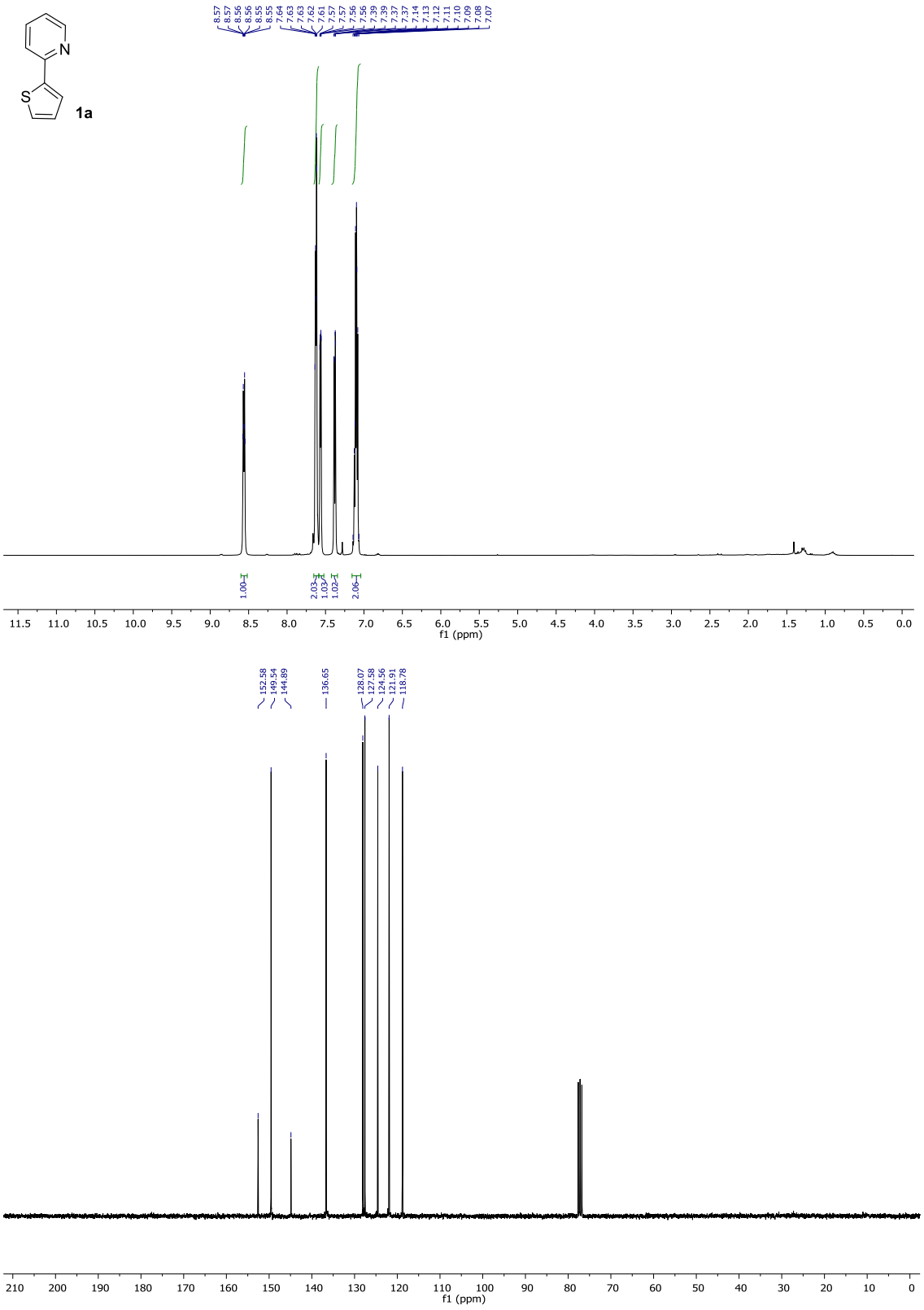


Figure S3. ^{1}H NMR and ^{13}C NMR spectra of **1a**

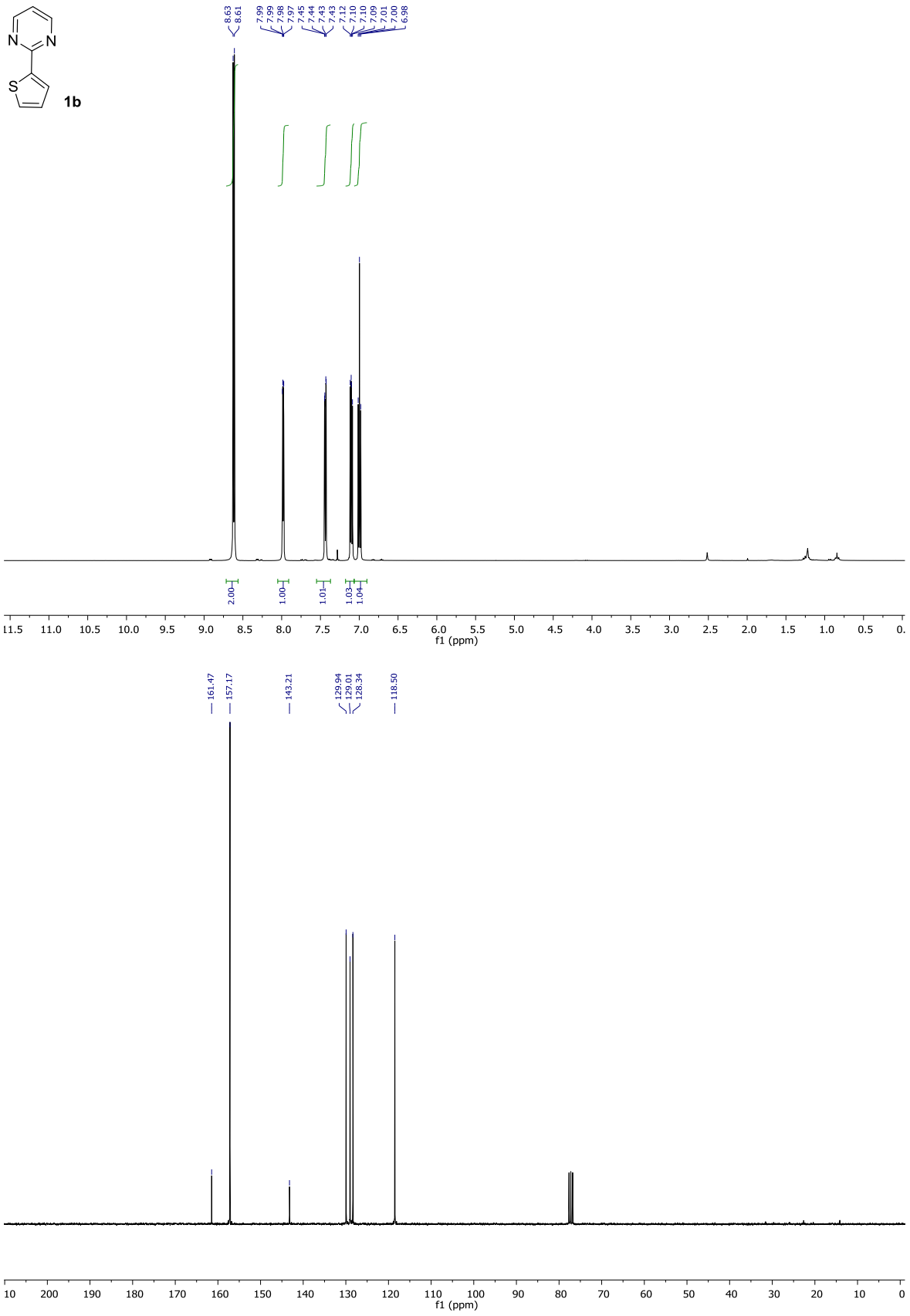


Figure S4. ^{1}H NMR and ^{13}C NMR spectra of **1b**

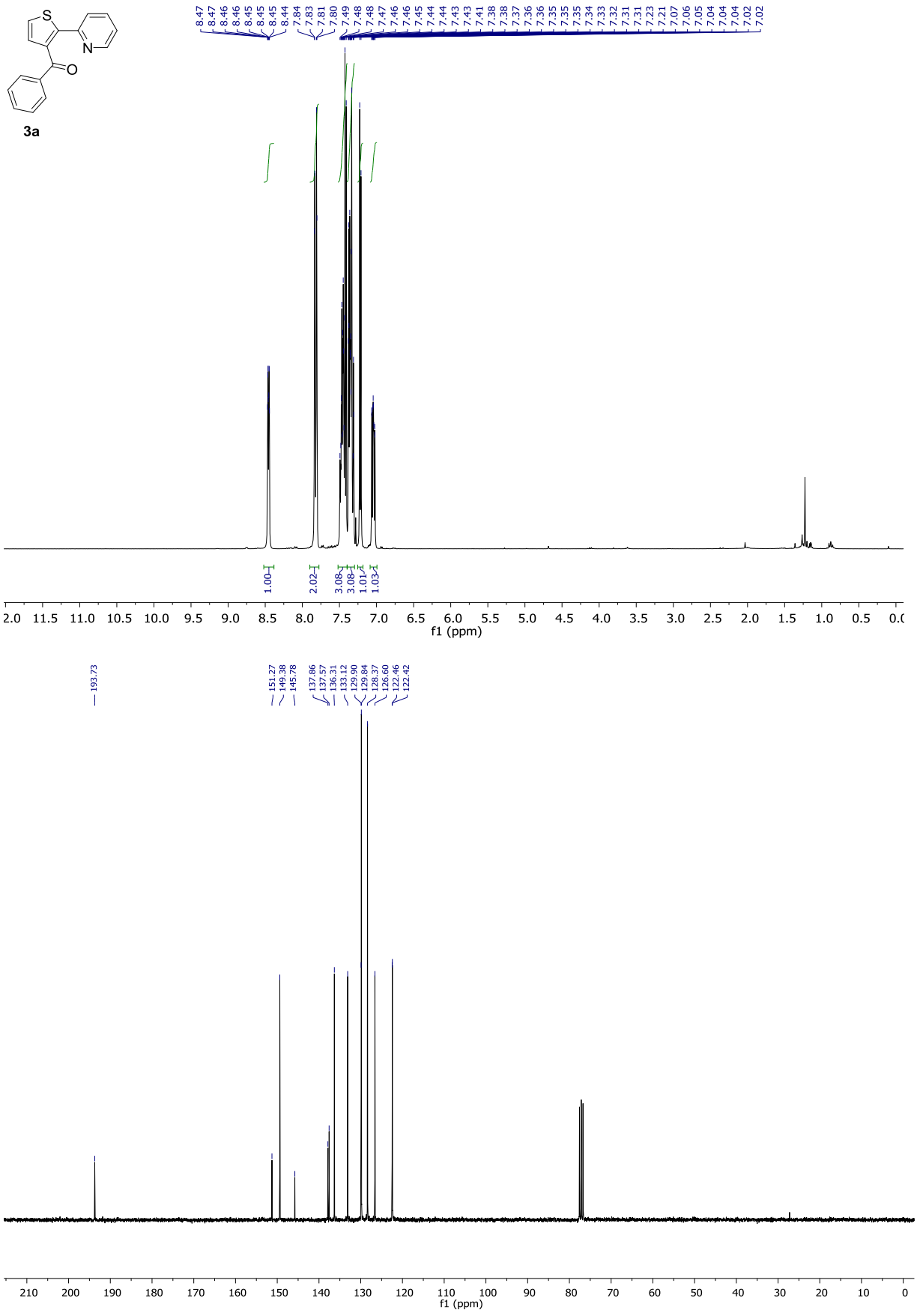
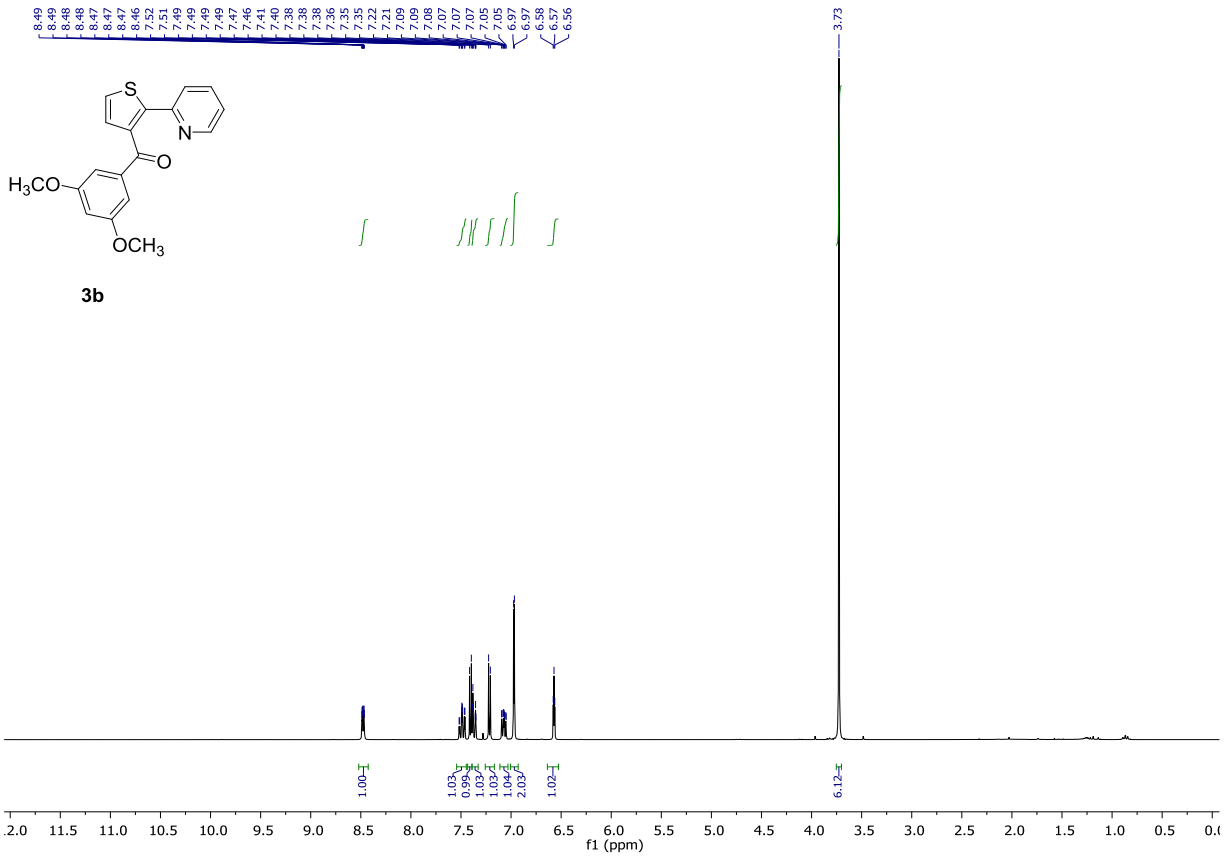


Figure S5. ^{1}H NMR and ^{13}C NMR spectra of **3a**



3b

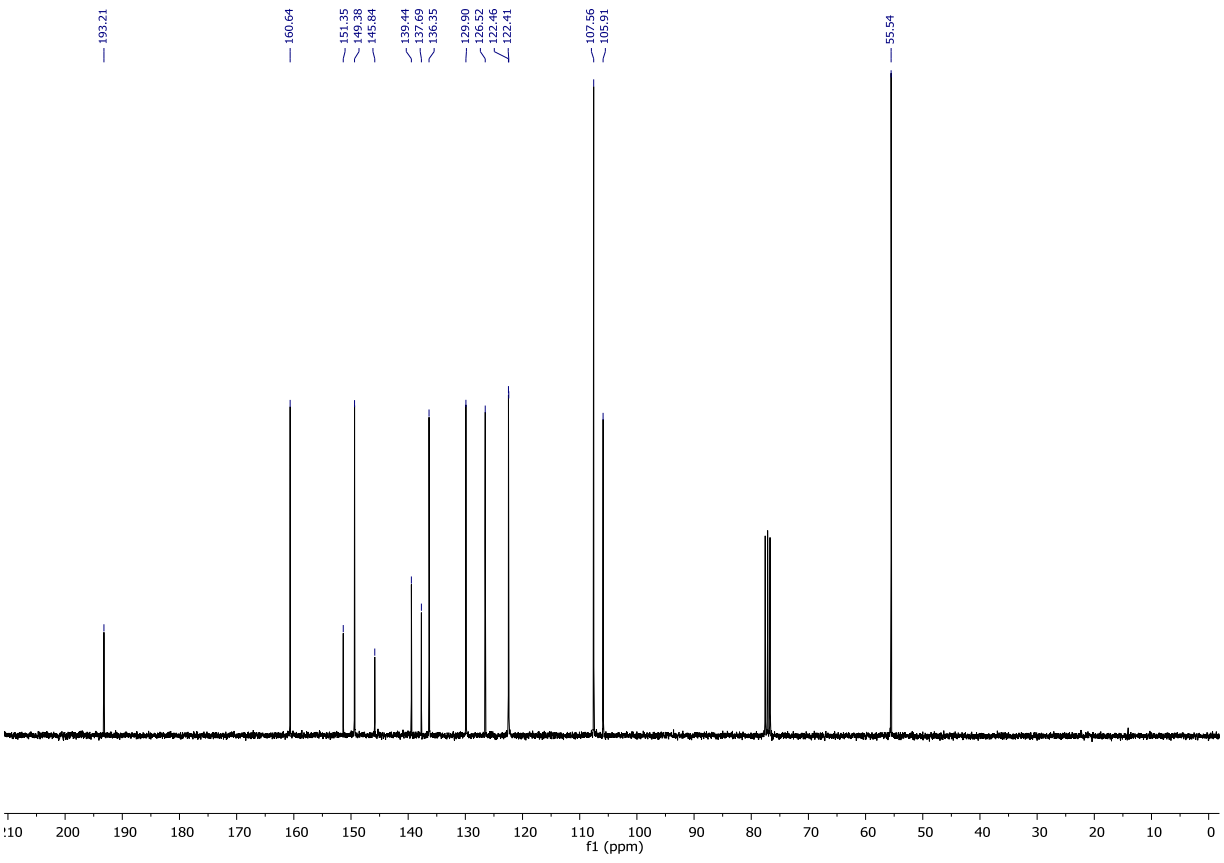


Figure S6. ^{1}H NMR and ^{13}C NMR spectra of **3b**

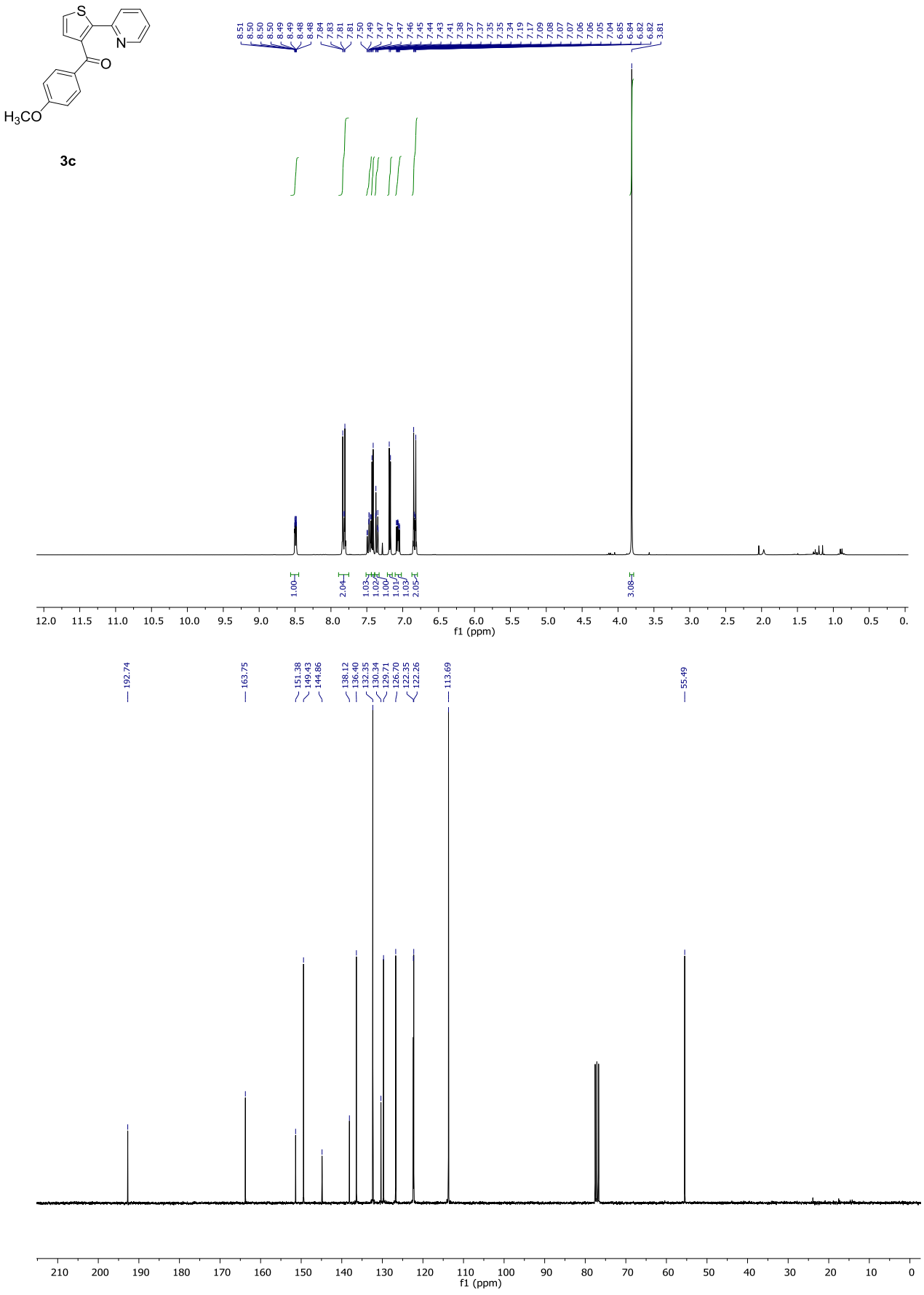


Figure S7. ^{1}H NMR and ^{13}C NMR spectra of **3c**

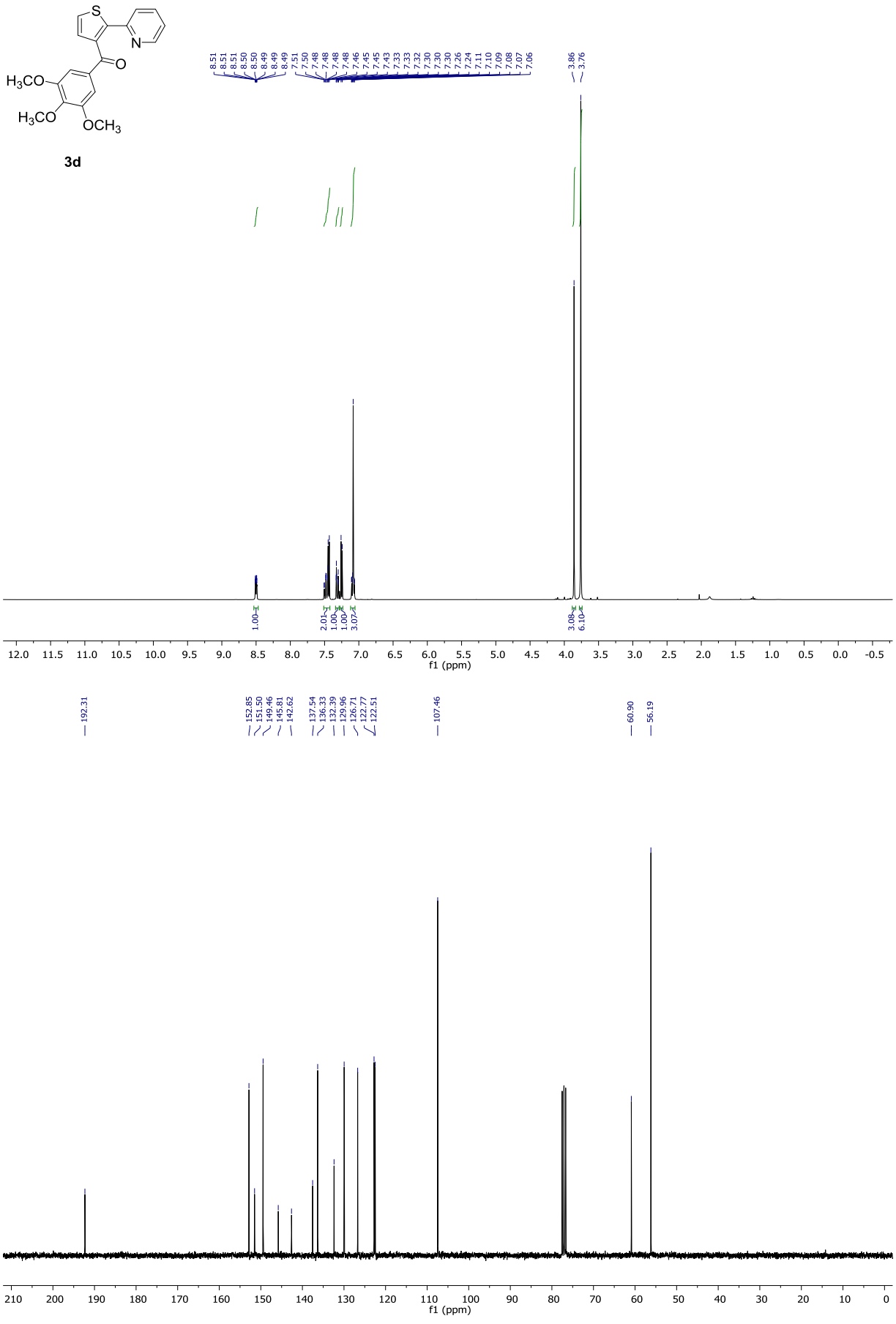


Figure S8. ^{1}H NMR and ^{13}C NMR spectra of **3d**

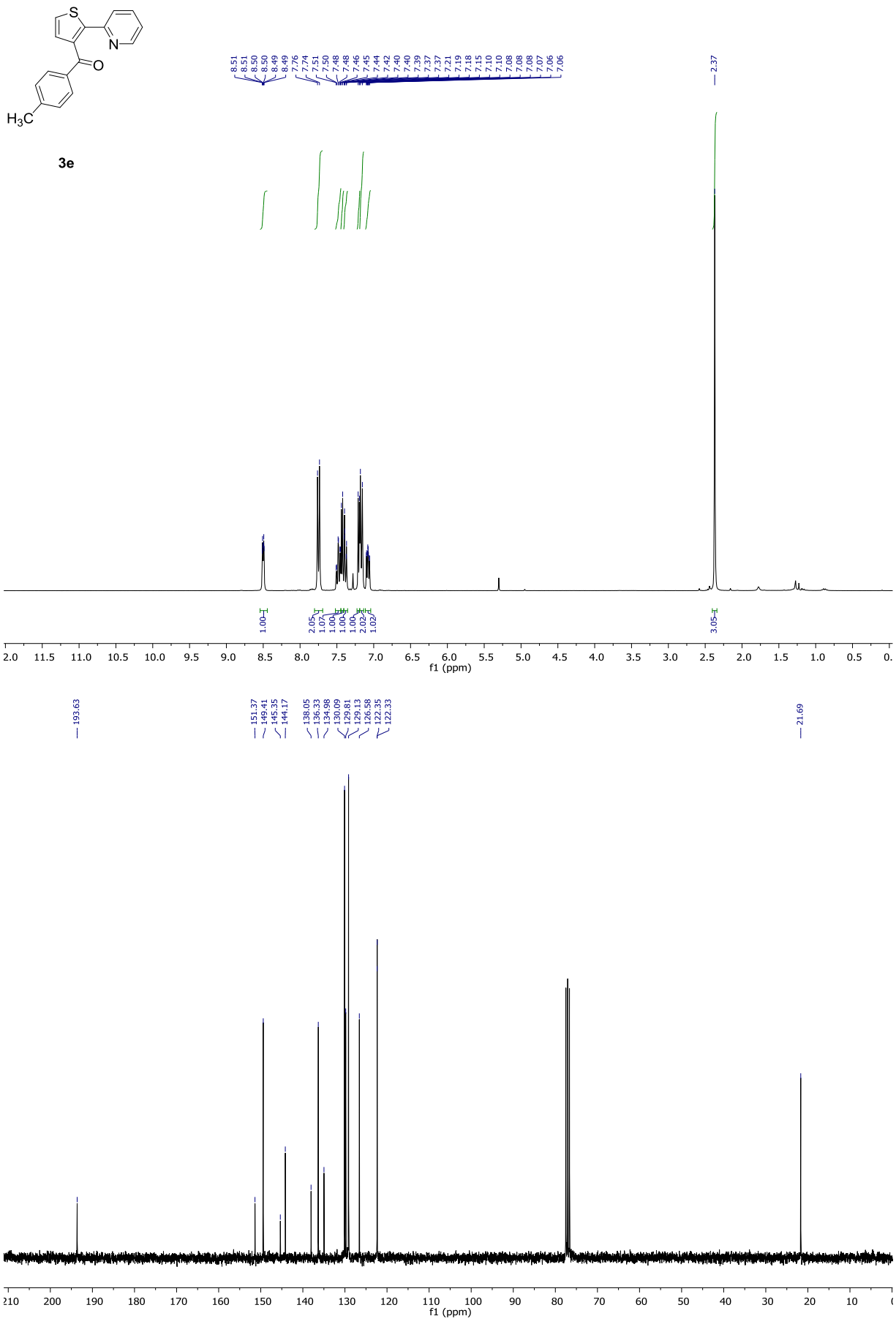


Figure S9. ^{1}H NMR and ^{13}C NMR spectra of **3e**

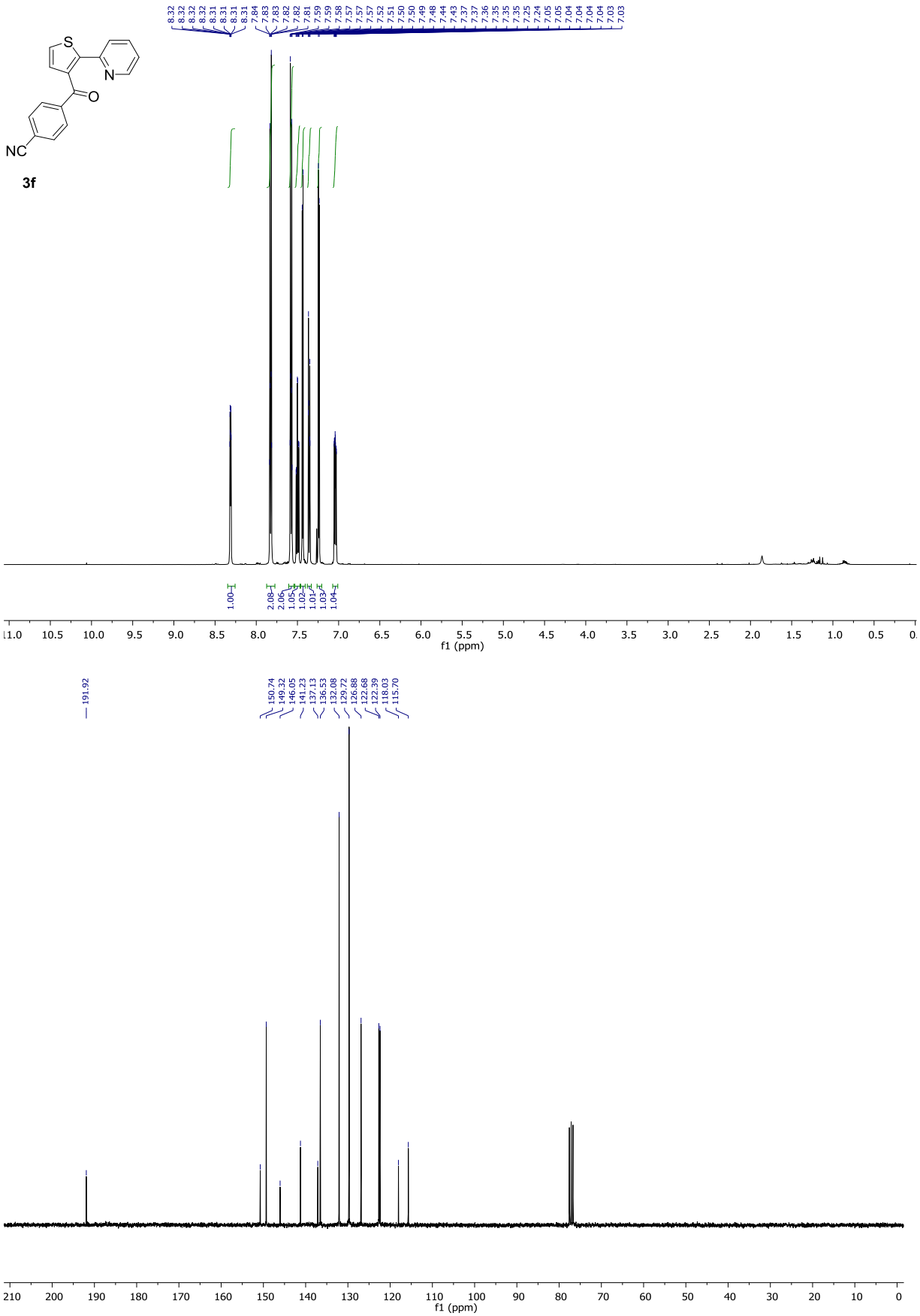


Figure S10. ^{1}H NMR and ^{13}C NMR spectra of **3f**

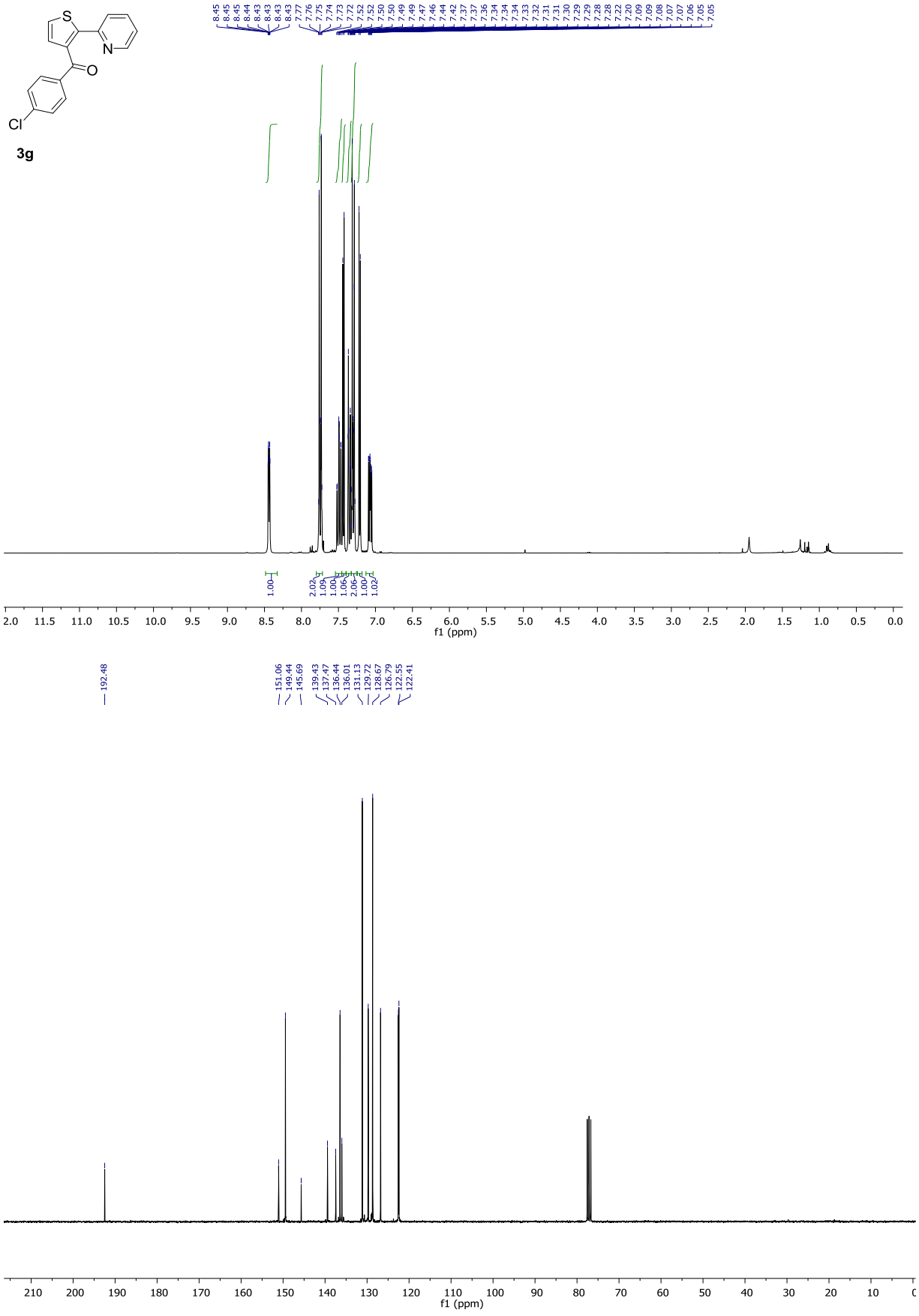


Figure S11. ^{1}H NMR and ^{13}C NMR spectra of **3g**

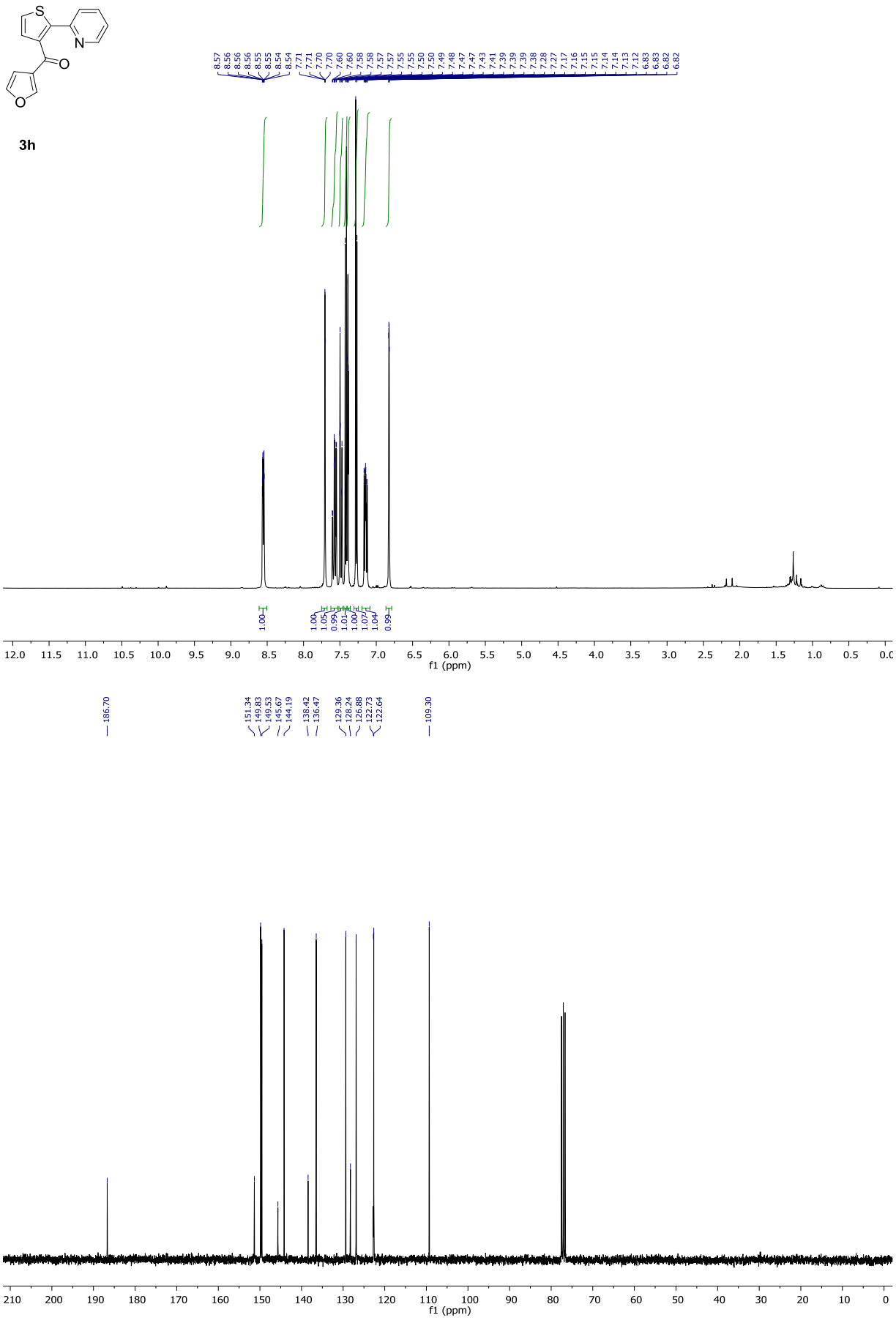


Figure S12. ^{1}H NMR and ^{13}C NMR spectra of **3h**

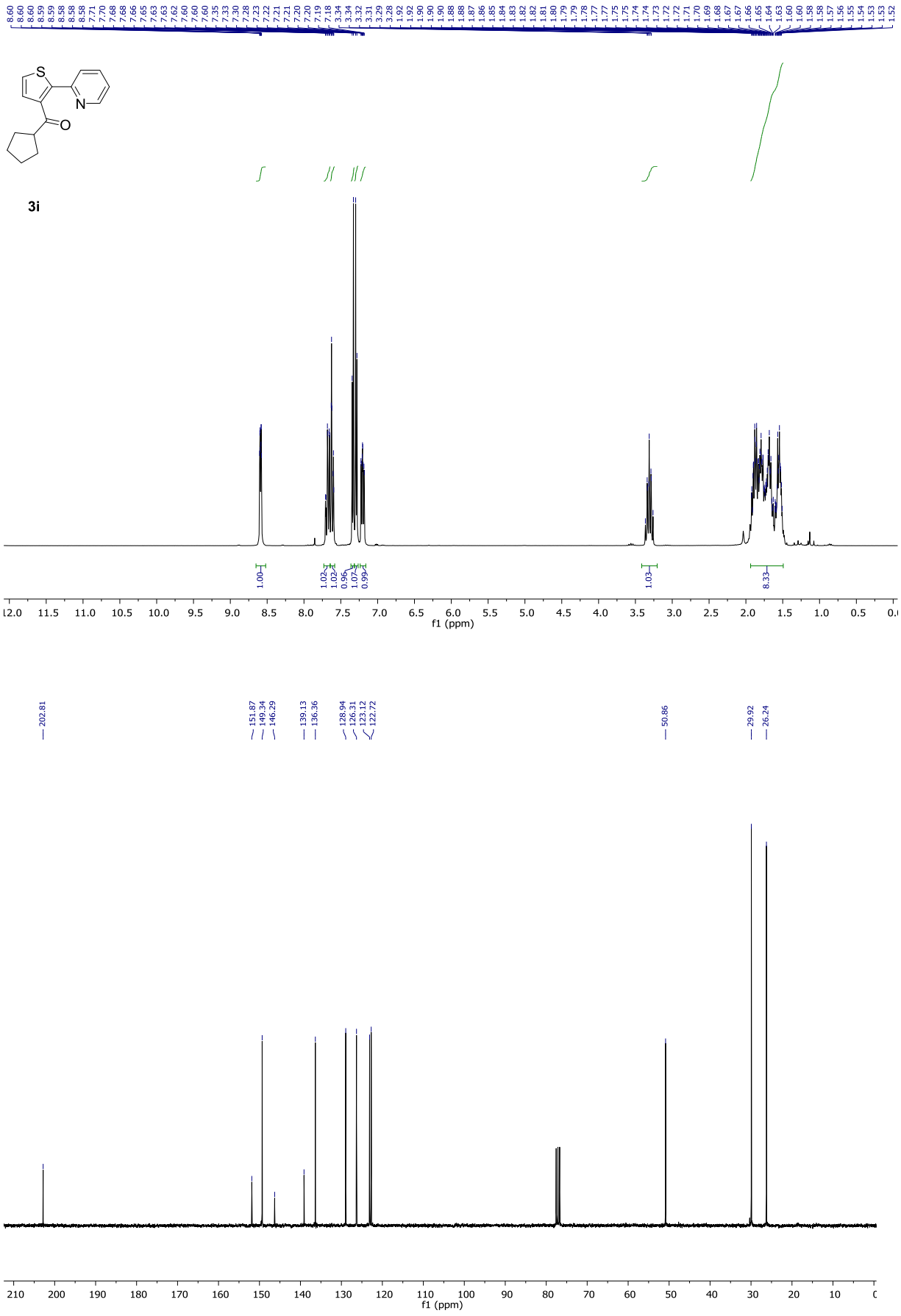


Figure S13. ^{1}H NMR and ^{13}C NMR spectra of **3i**

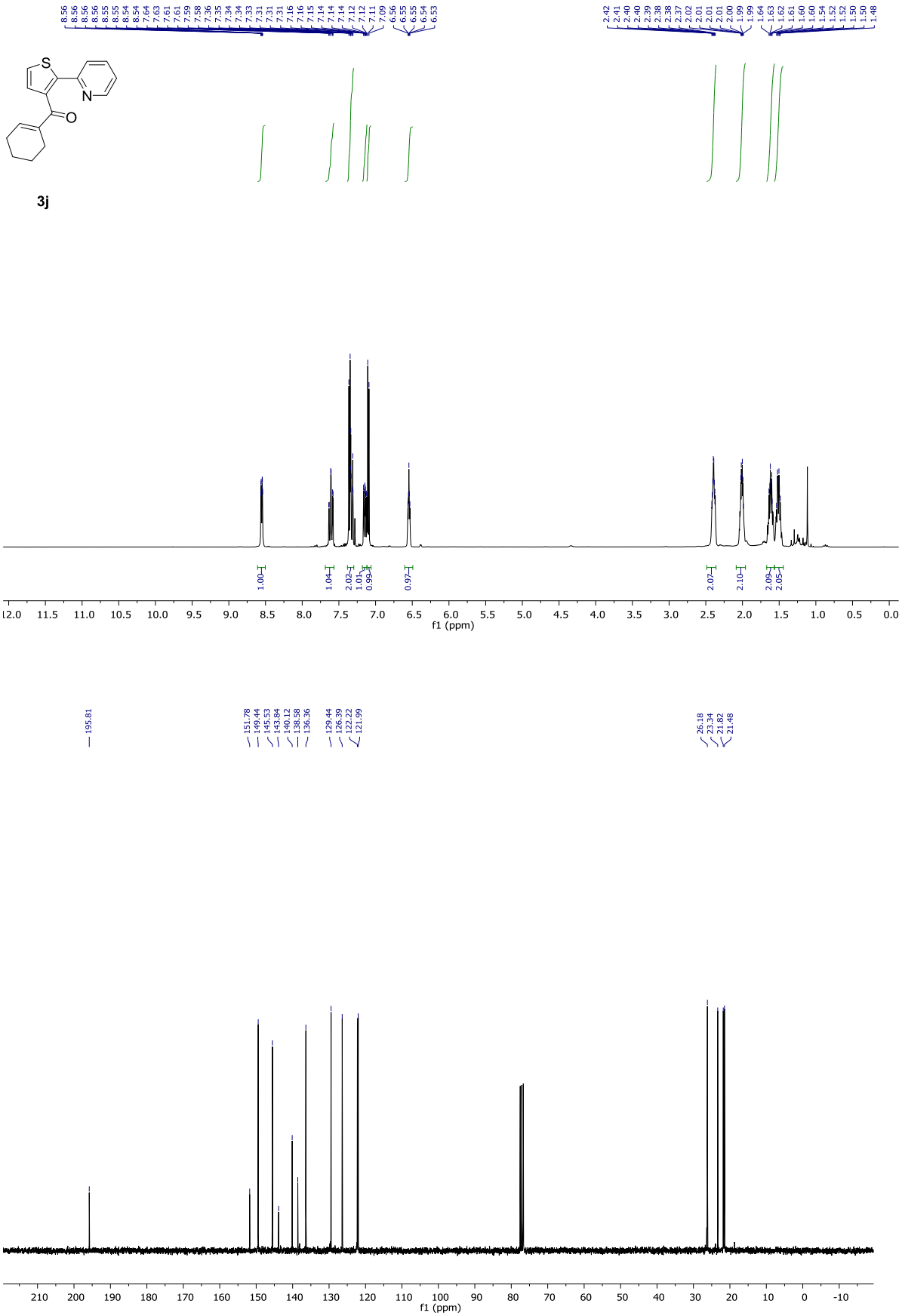


Figure S14. ^{1}H NMR and ^{13}C NMR spectra of **3j**

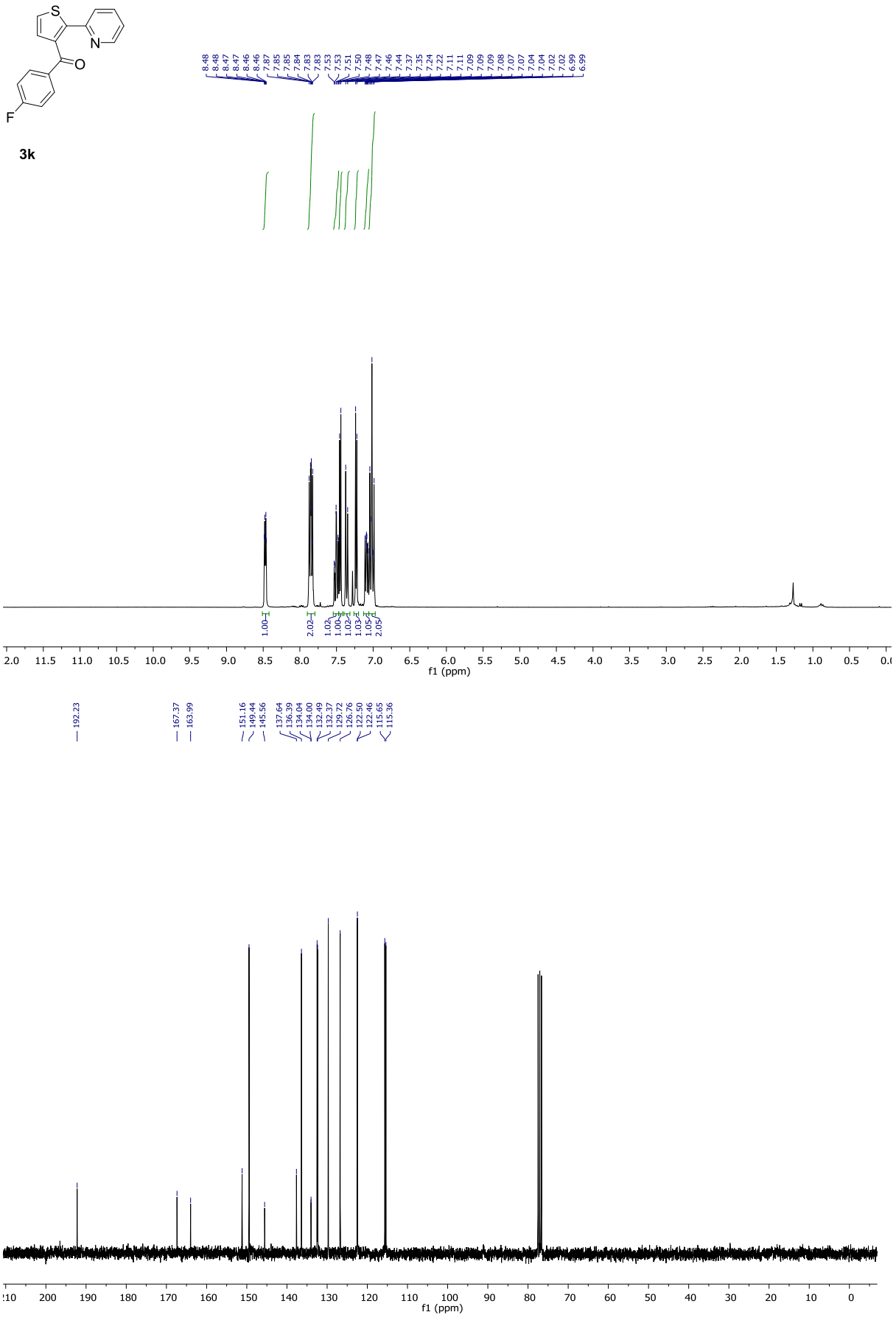


Figure S15. ^{1}H NMR and ^{13}C NMR spectra of **3k**

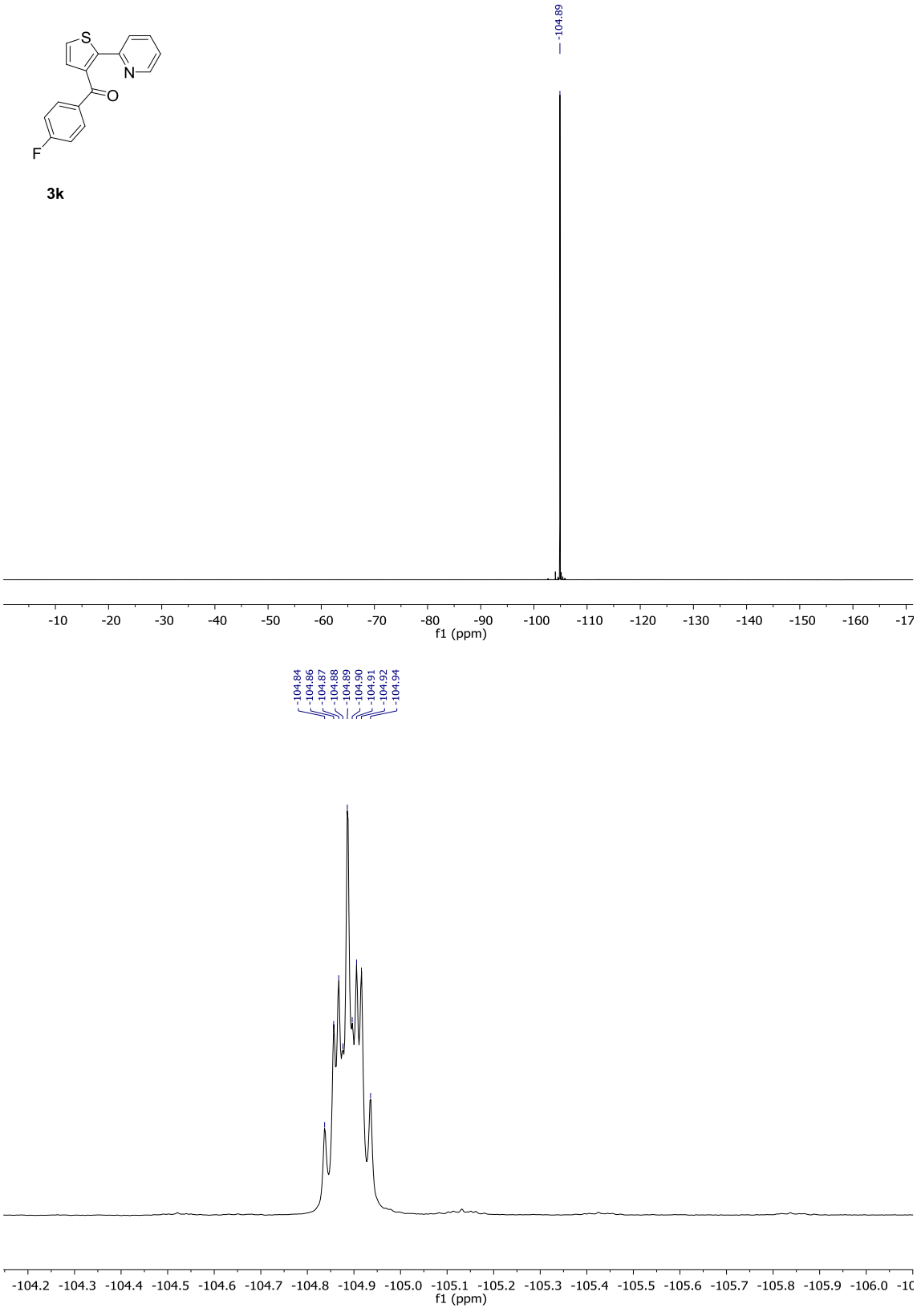


Figure S16. ^{19}F NMR (^{1}H-decoupled and coupled) spectra of **3k**

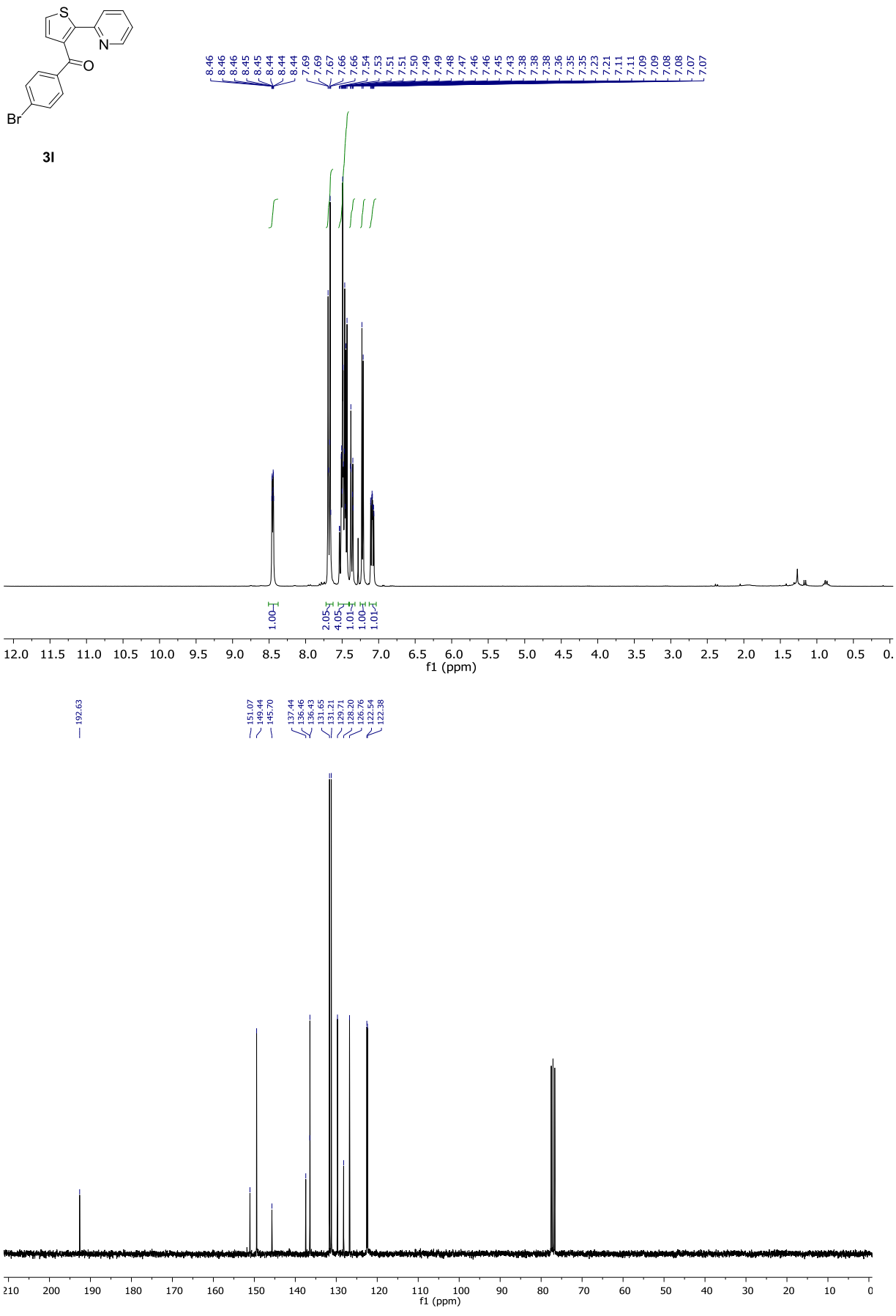


Figure S17. ^{1}H NMR and ^{13}C NMR spectra of **3l**

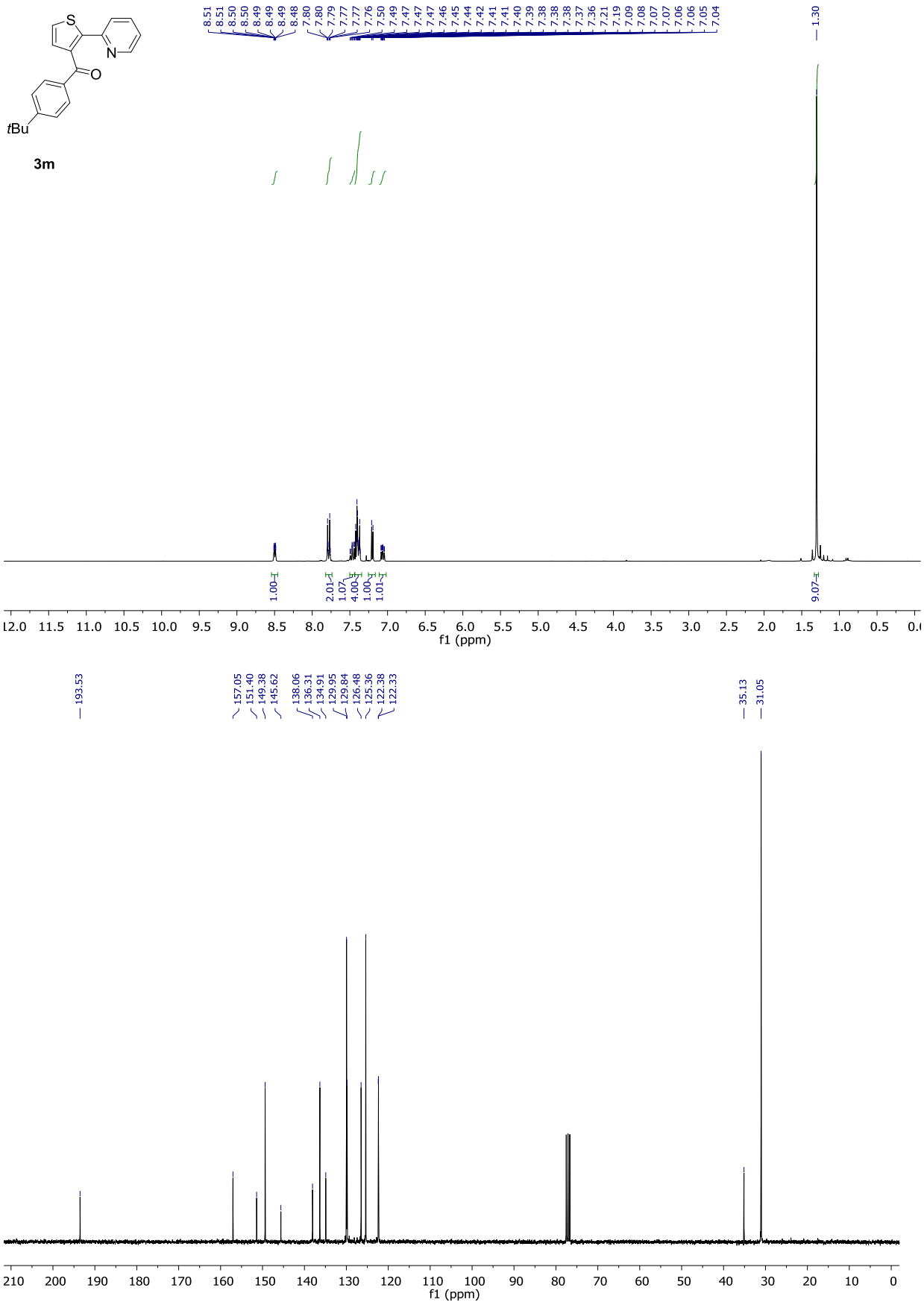


Figure S18. ^{1}H NMR and ^{13}C NMR spectra of **3m**

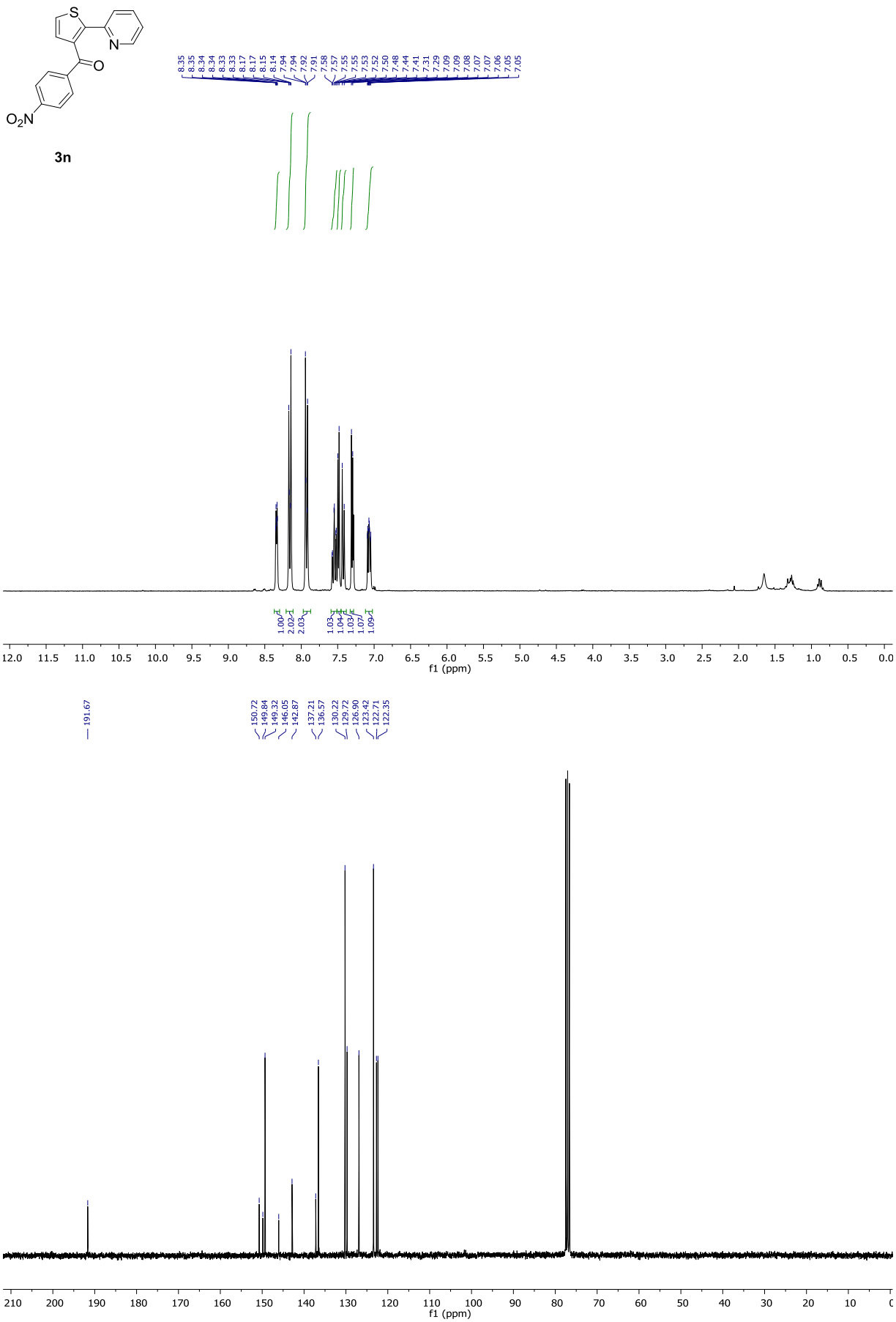


Figure S19. ^{1}H NMR and ^{13}C NMR spectra of **3n**

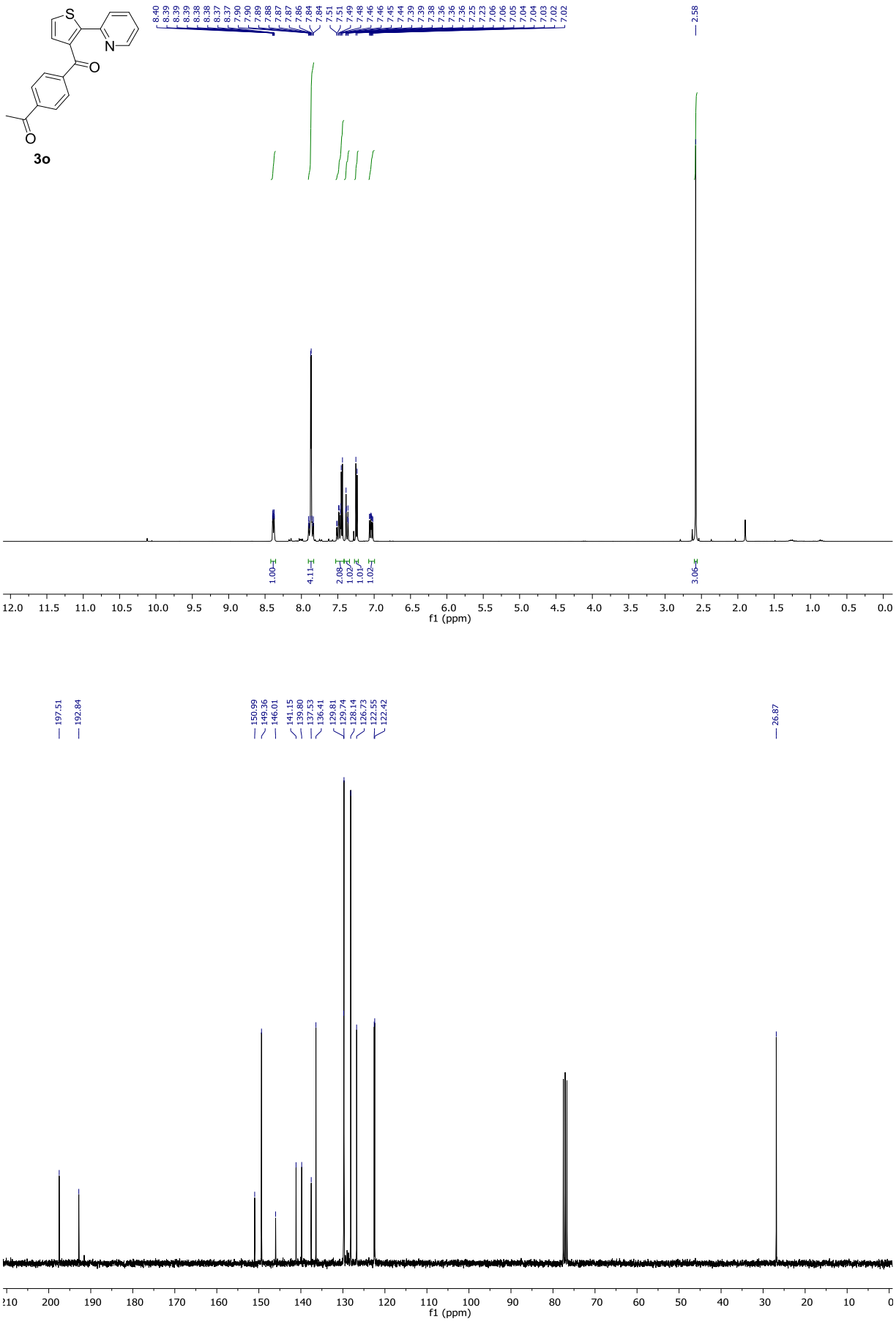
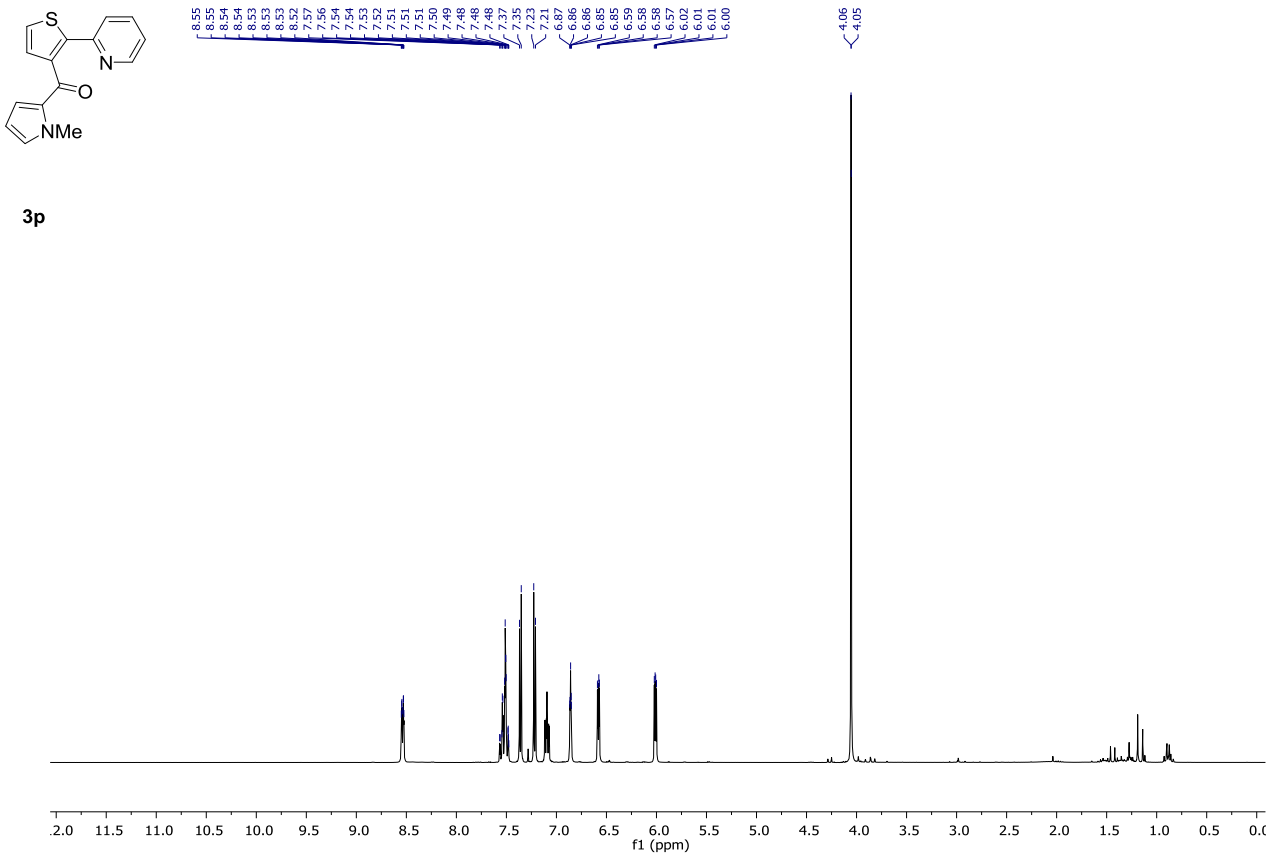


Figure S20. ^{1}H NMR and ^{13}C NMR spectra of **3o**



3p

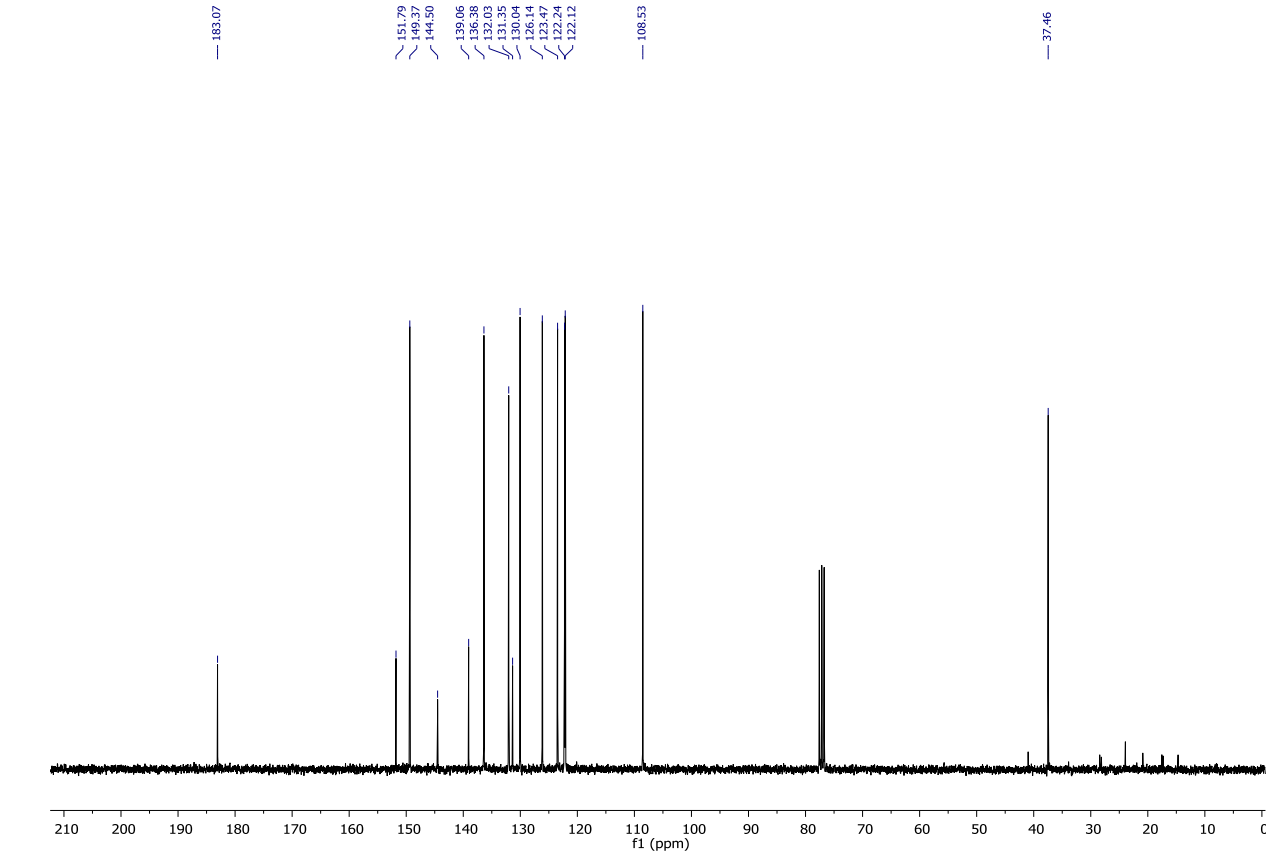
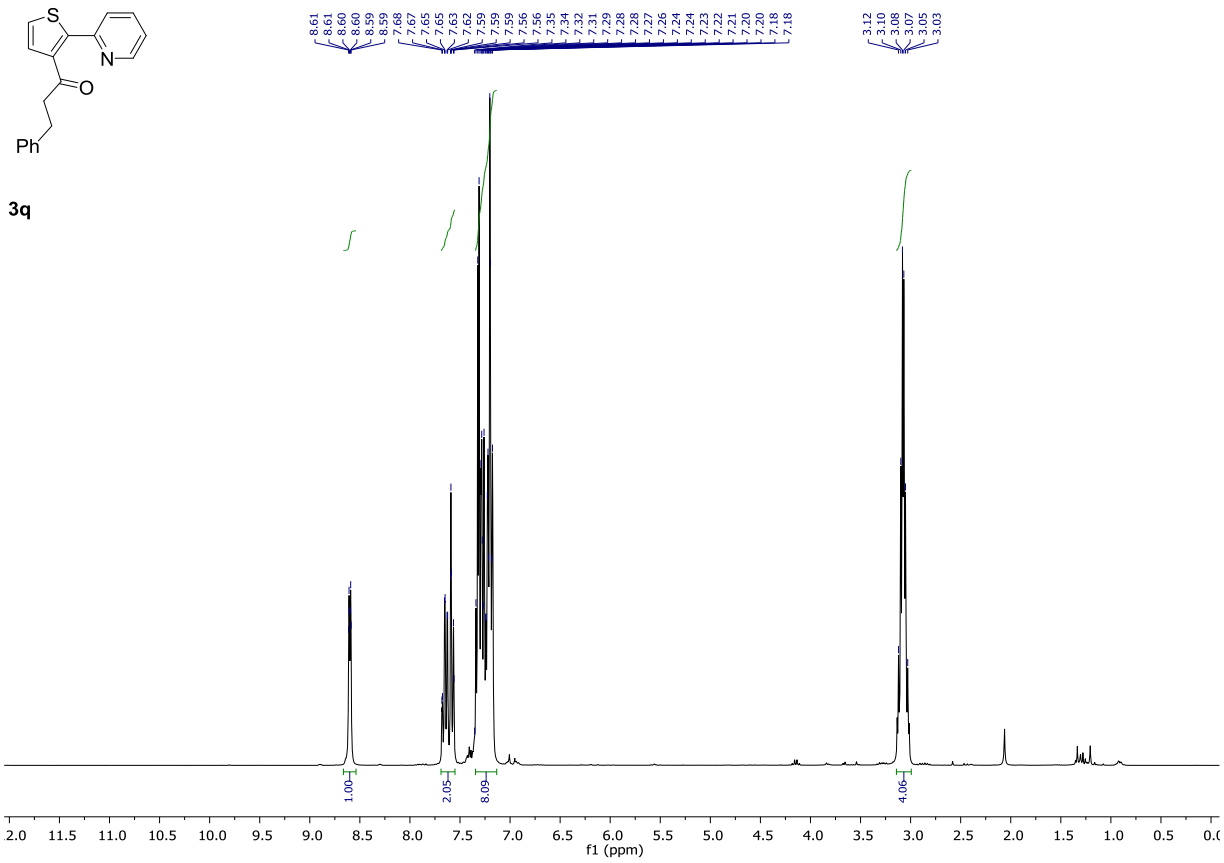


Figure S21. ^{1}H NMR and ^{13}C NMR spectra of **3p**



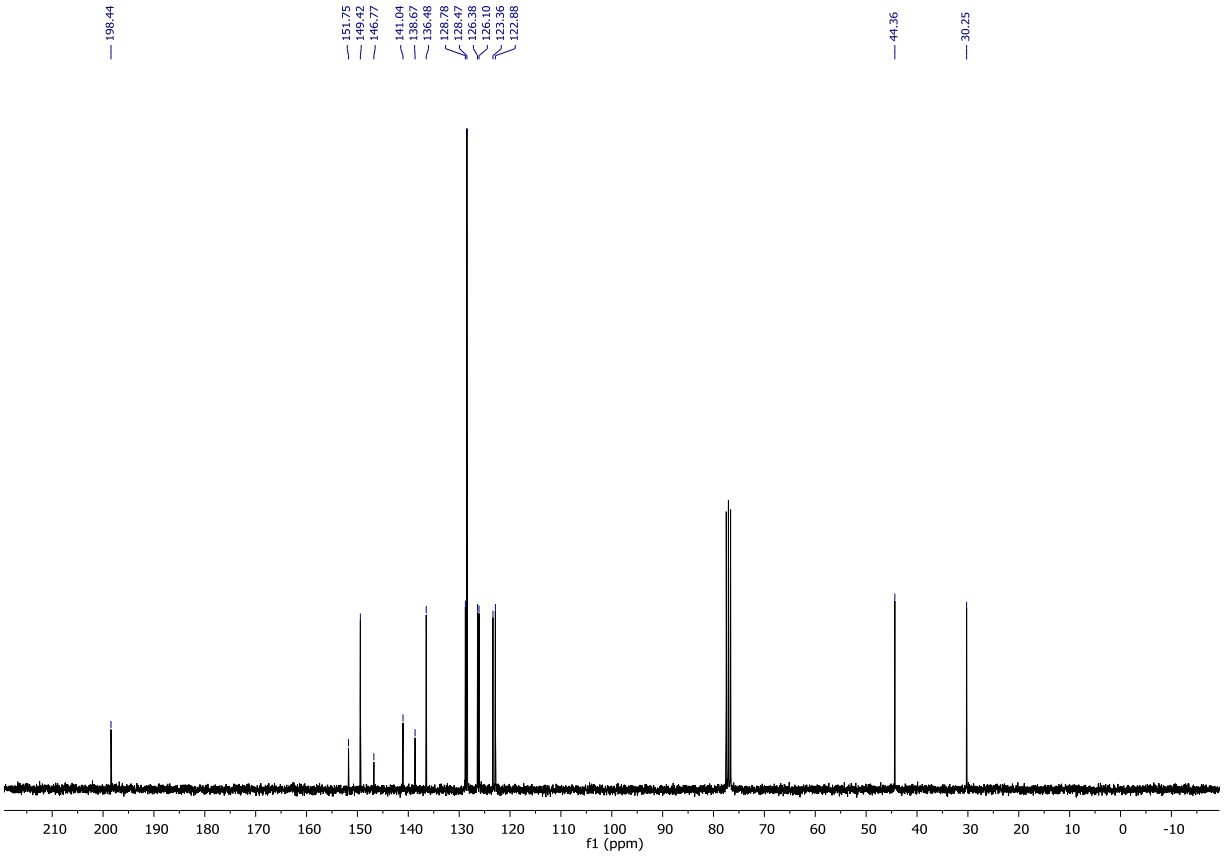


Figure S22. ^{1}H NMR and ^{13}C NMR spectra of **3q**

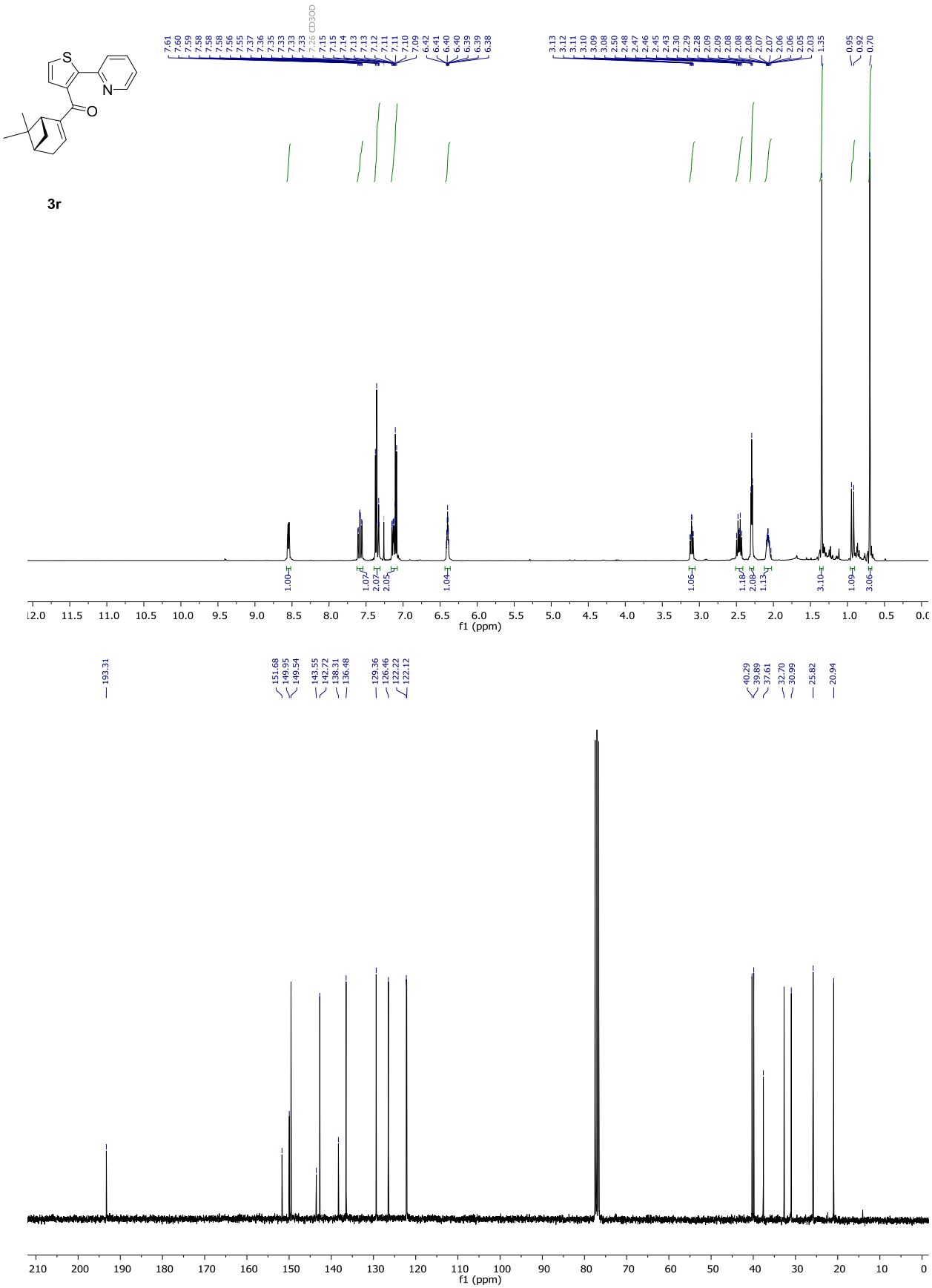


Figure S23. ^{1}H NMR and ^{13}C NMR spectra of **3r**

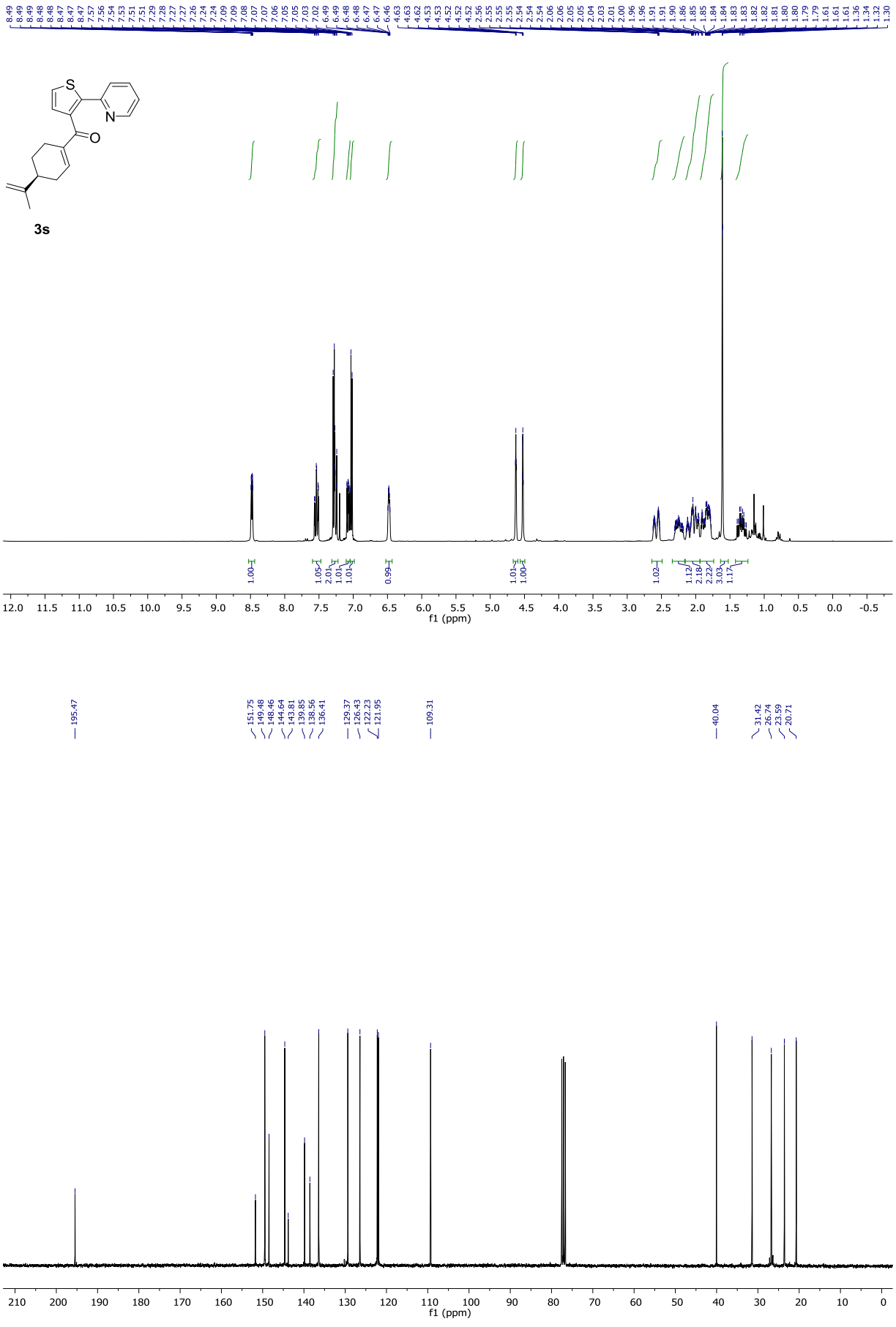


Figure S24. ^{1}H NMR and ^{13}C NMR spectra of **3s**

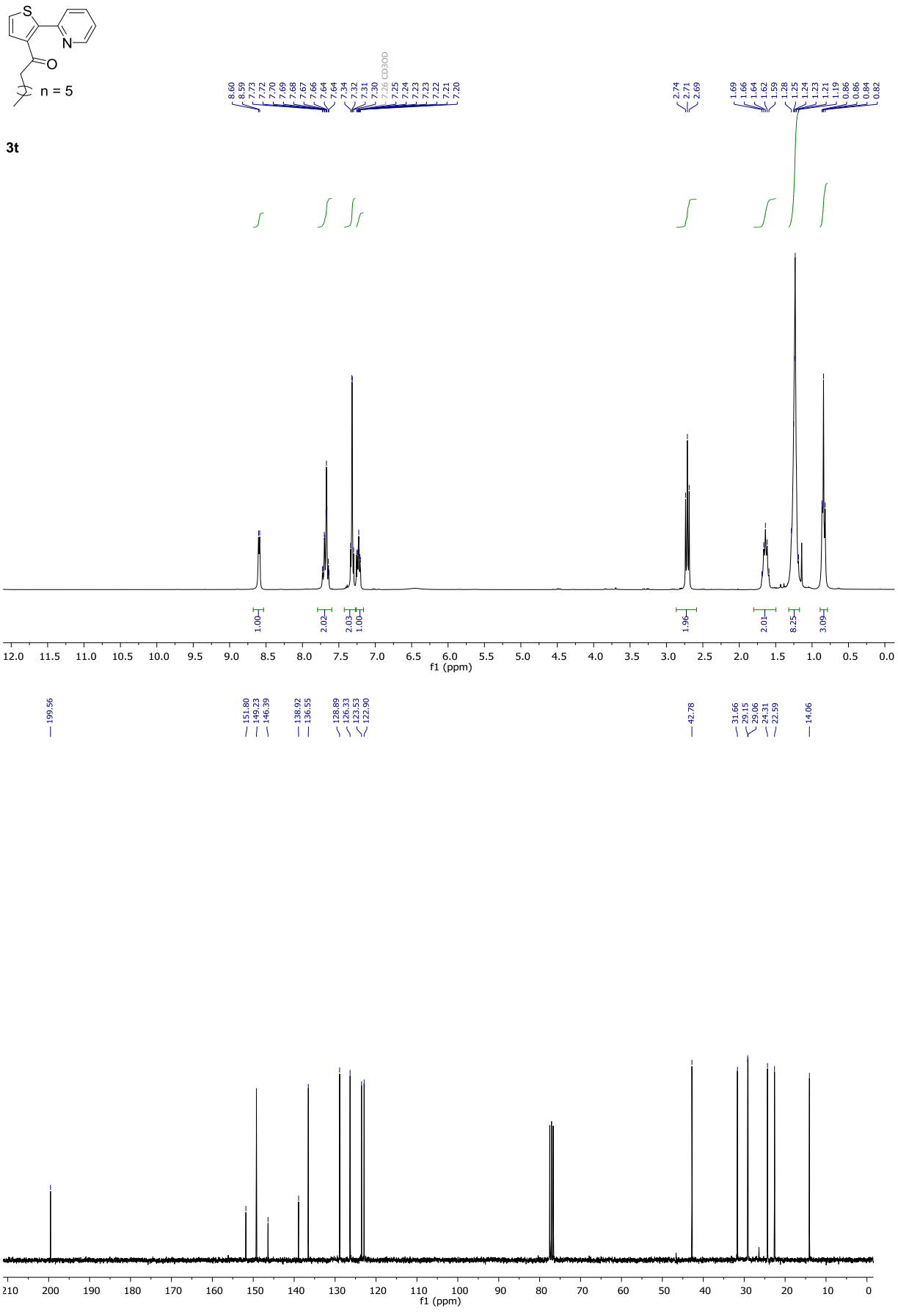


Figure S25. ^{1}H NMR and ^{13}C NMR spectra of **3t**

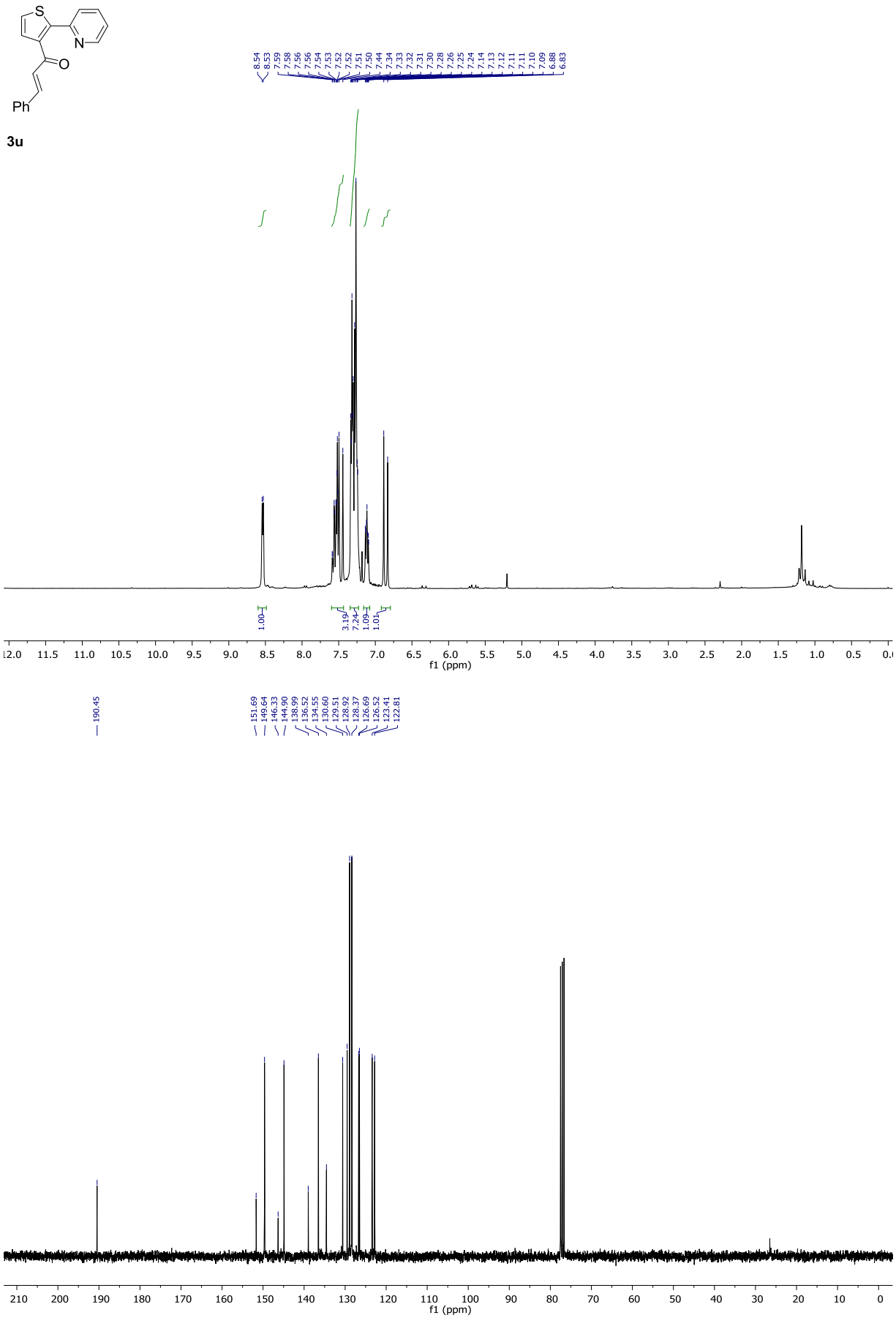


Figure S26. ^{1}H NMR and ^{13}C NMR spectra of **3u**

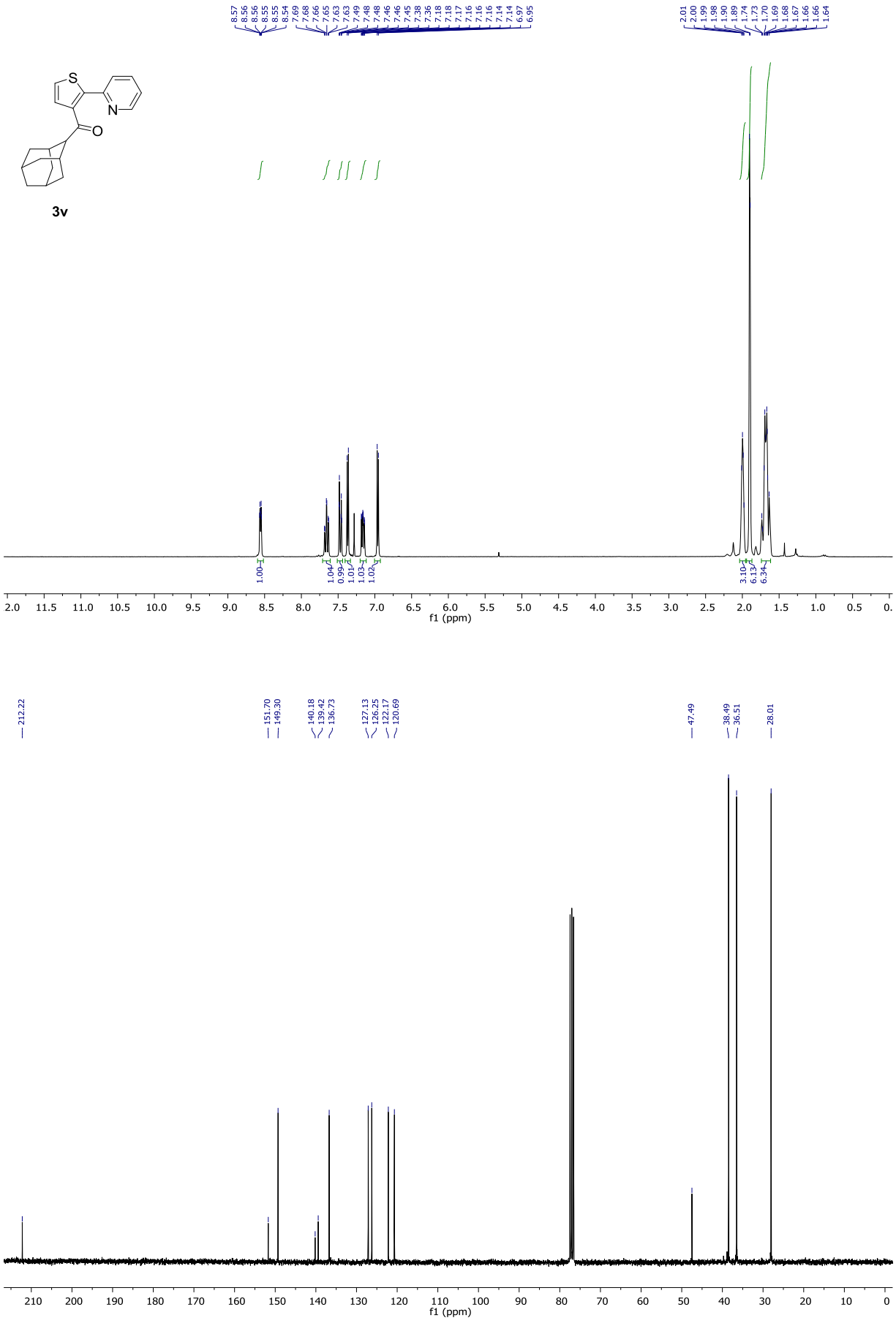


Figure S27. ^{1}H NMR and ^{13}C NMR spectra of **3v**

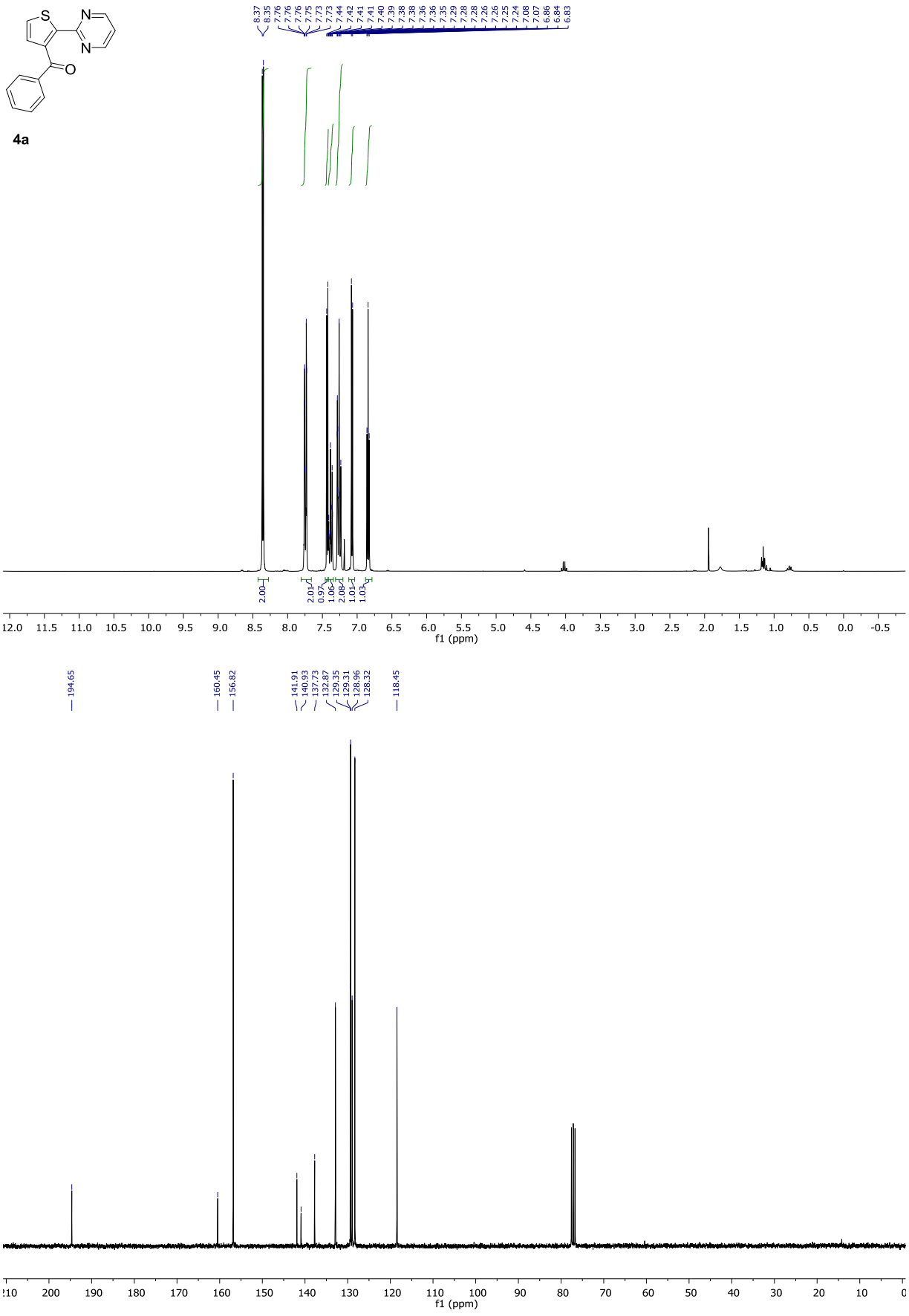


Figure S28. ^{1}H NMR and ^{13}C NMR spectra of **4a**

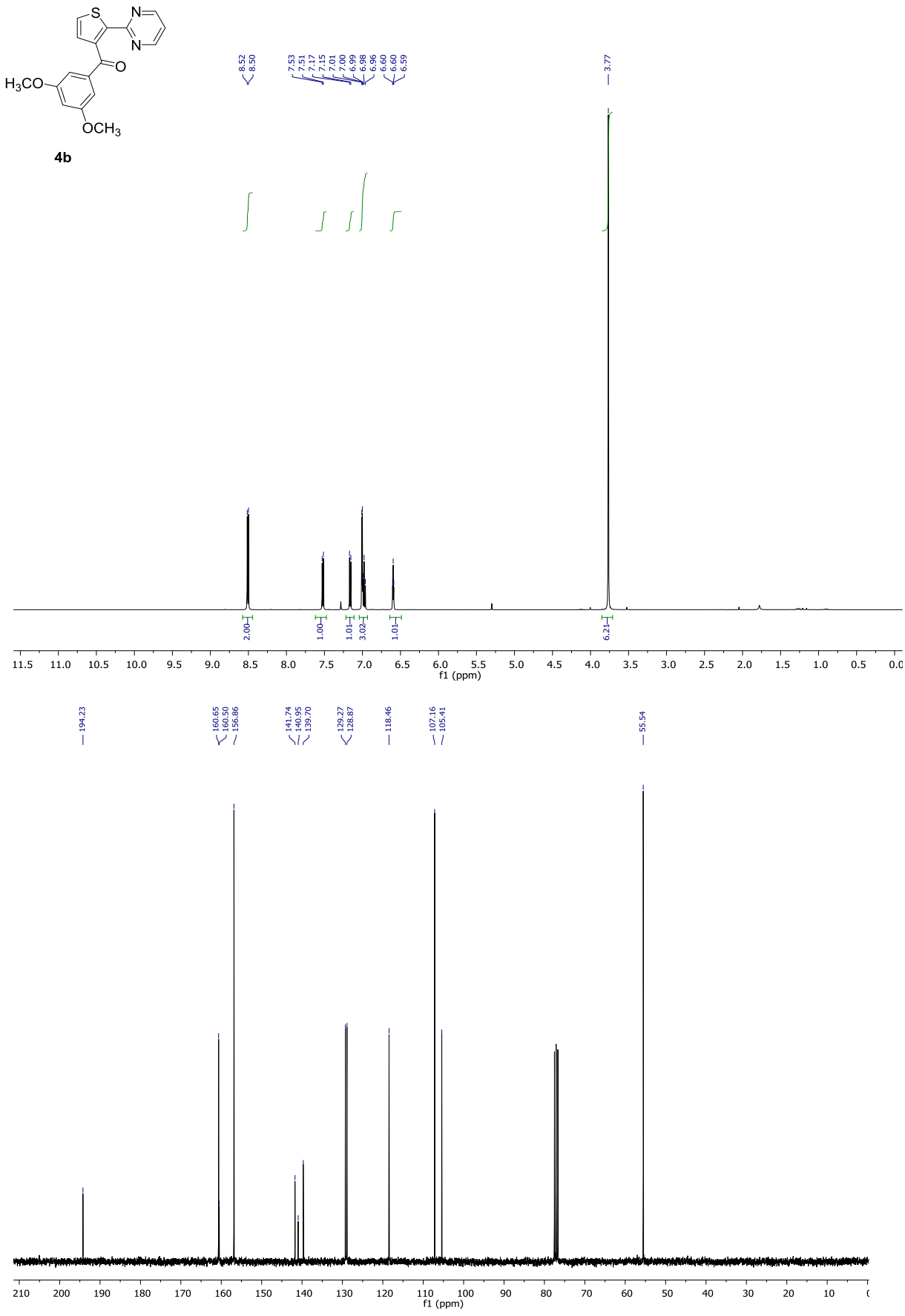


Figure S29. ^{1}H NMR and ^{13}C NMR spectra of **4b**

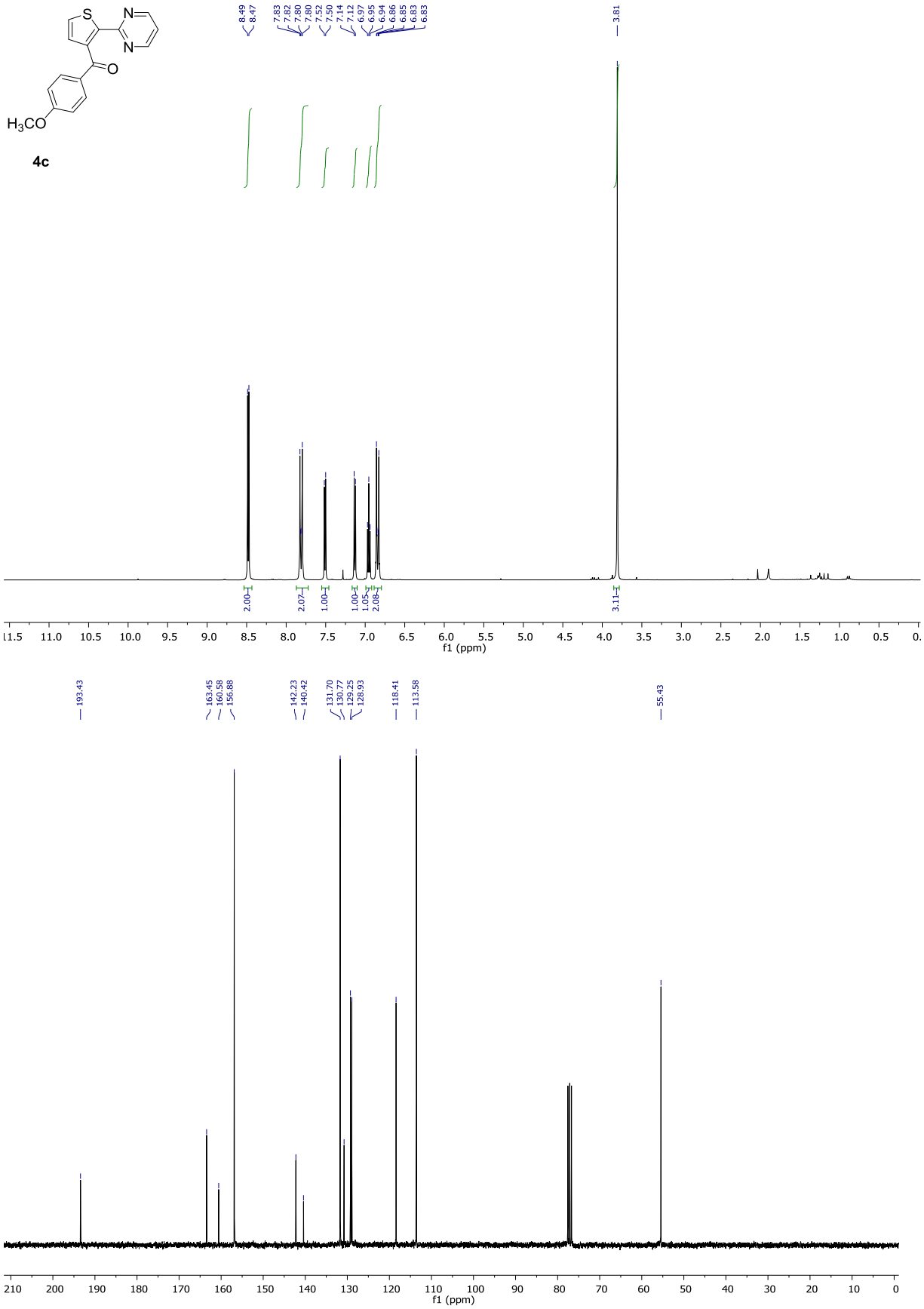


Figure S30. ^{1}H NMR and ^{13}C NMR spectra of **4c**

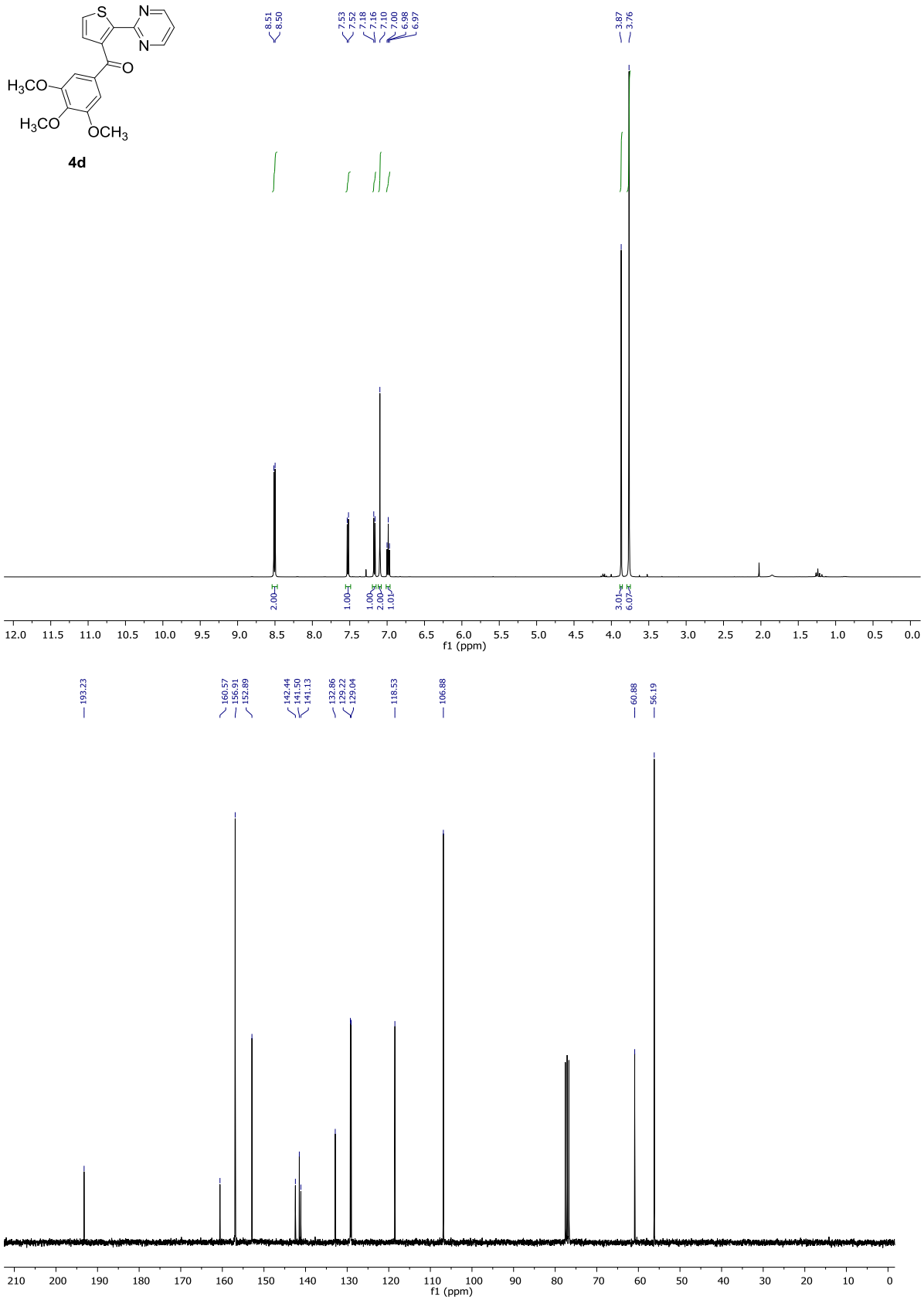


Figure S31. ^{1}H NMR and ^{13}C NMR spectra of **4d**

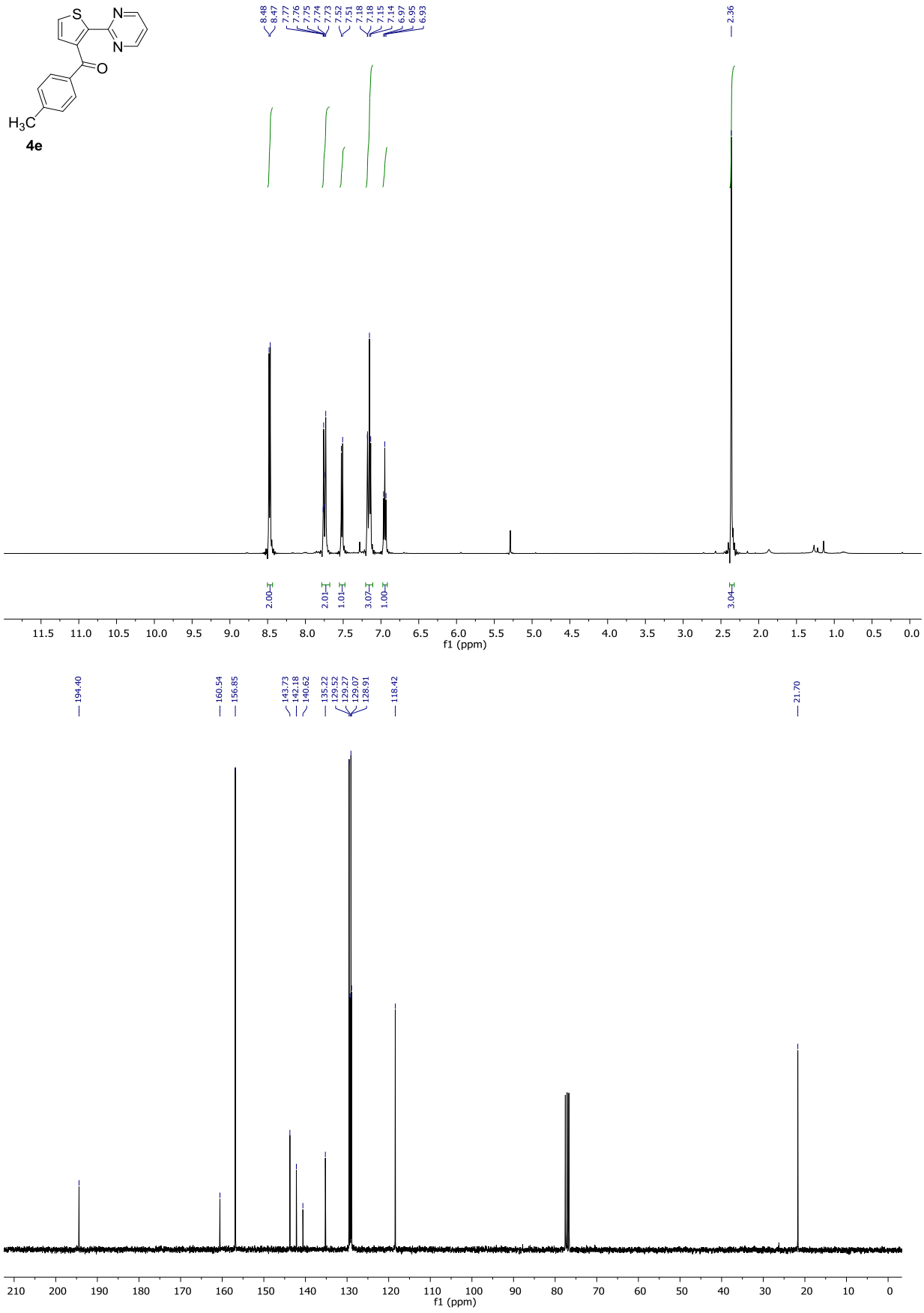


Figure S32. ^{1}H NMR and ^{13}C NMR spectra of **4e**

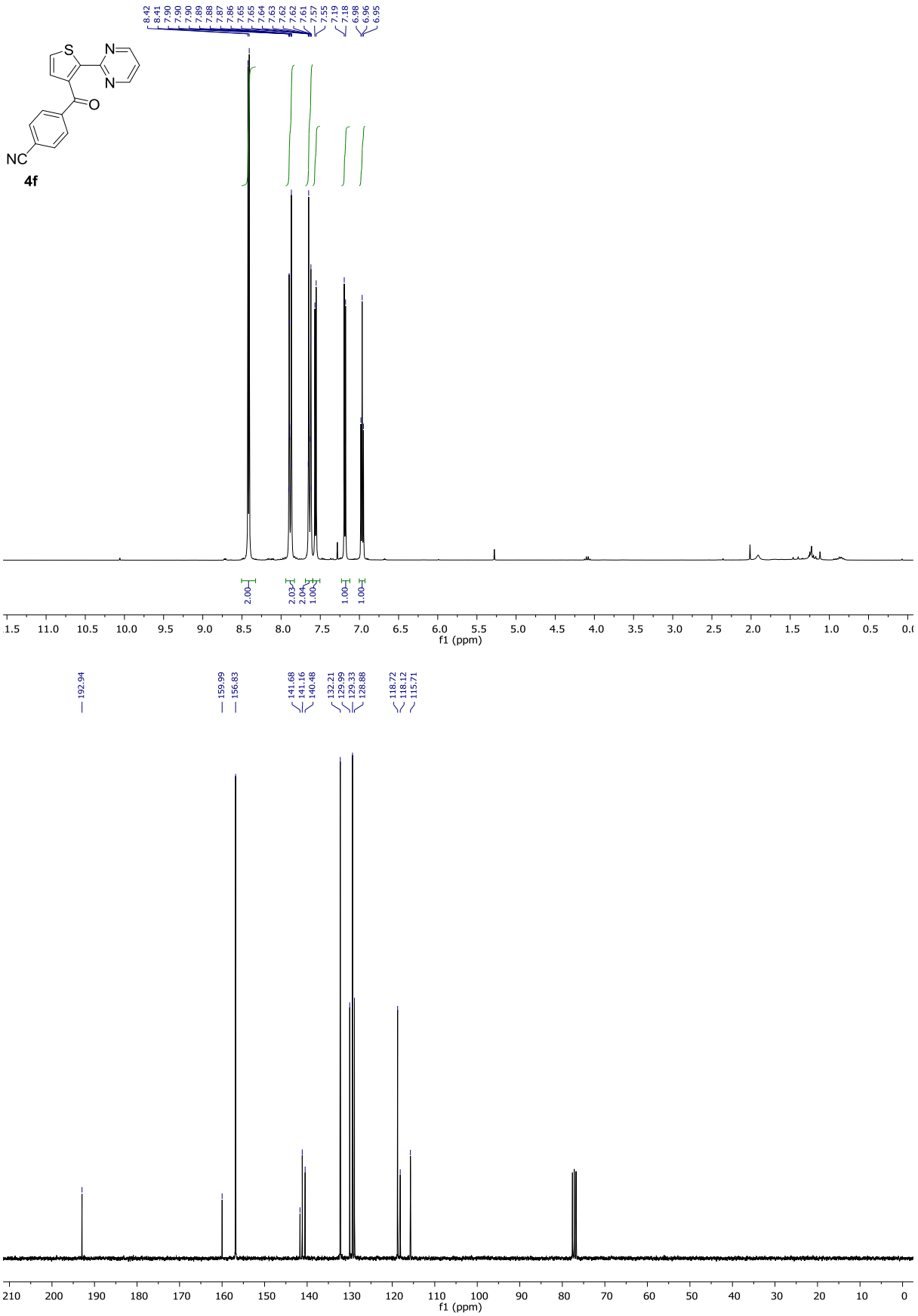


Figure S33. ^{1}H NMR and ^{13}C NMR spectra of **4f**

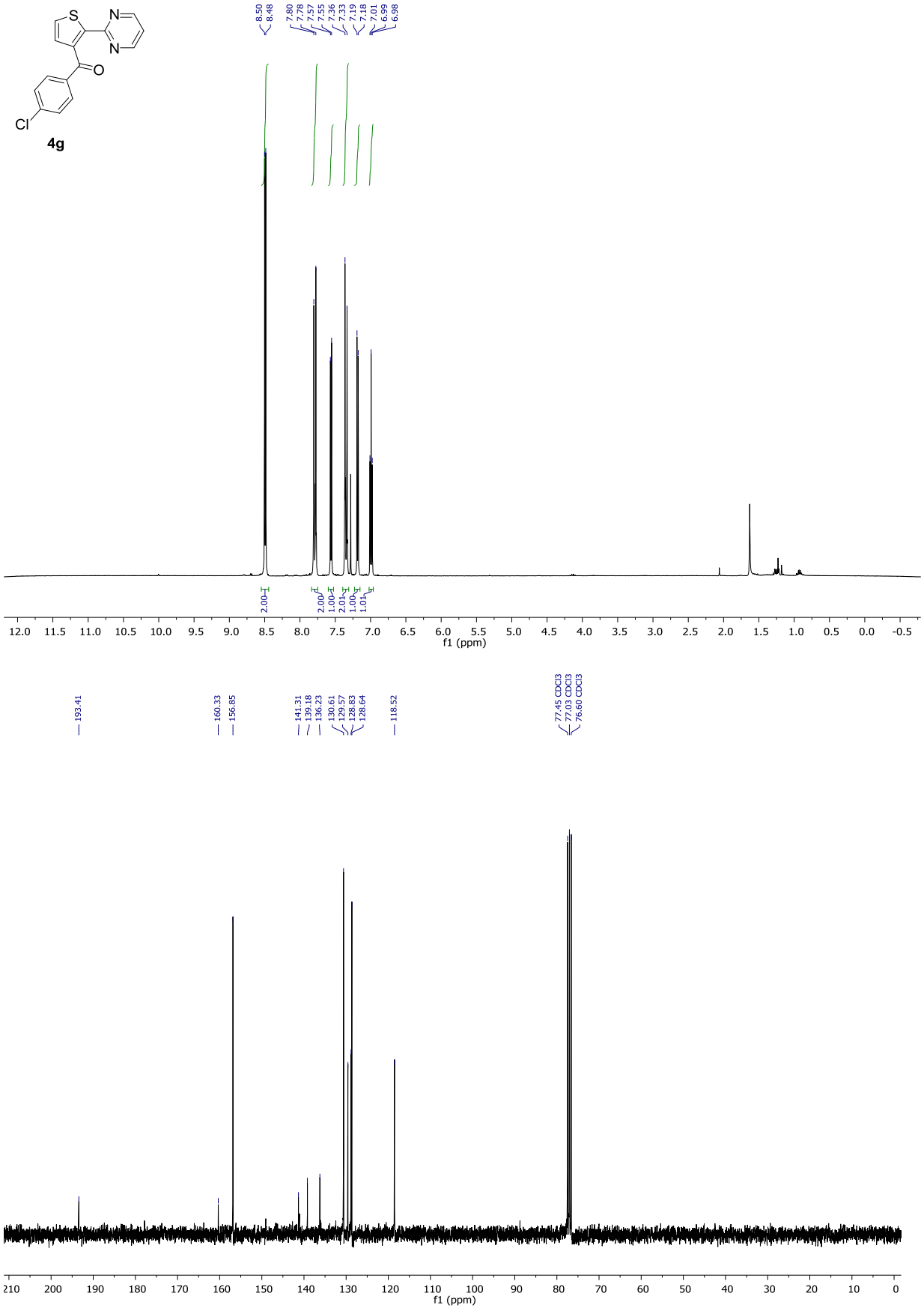


Figure S34. ^{1}H NMR and ^{13}C NMR spectra of **4g**

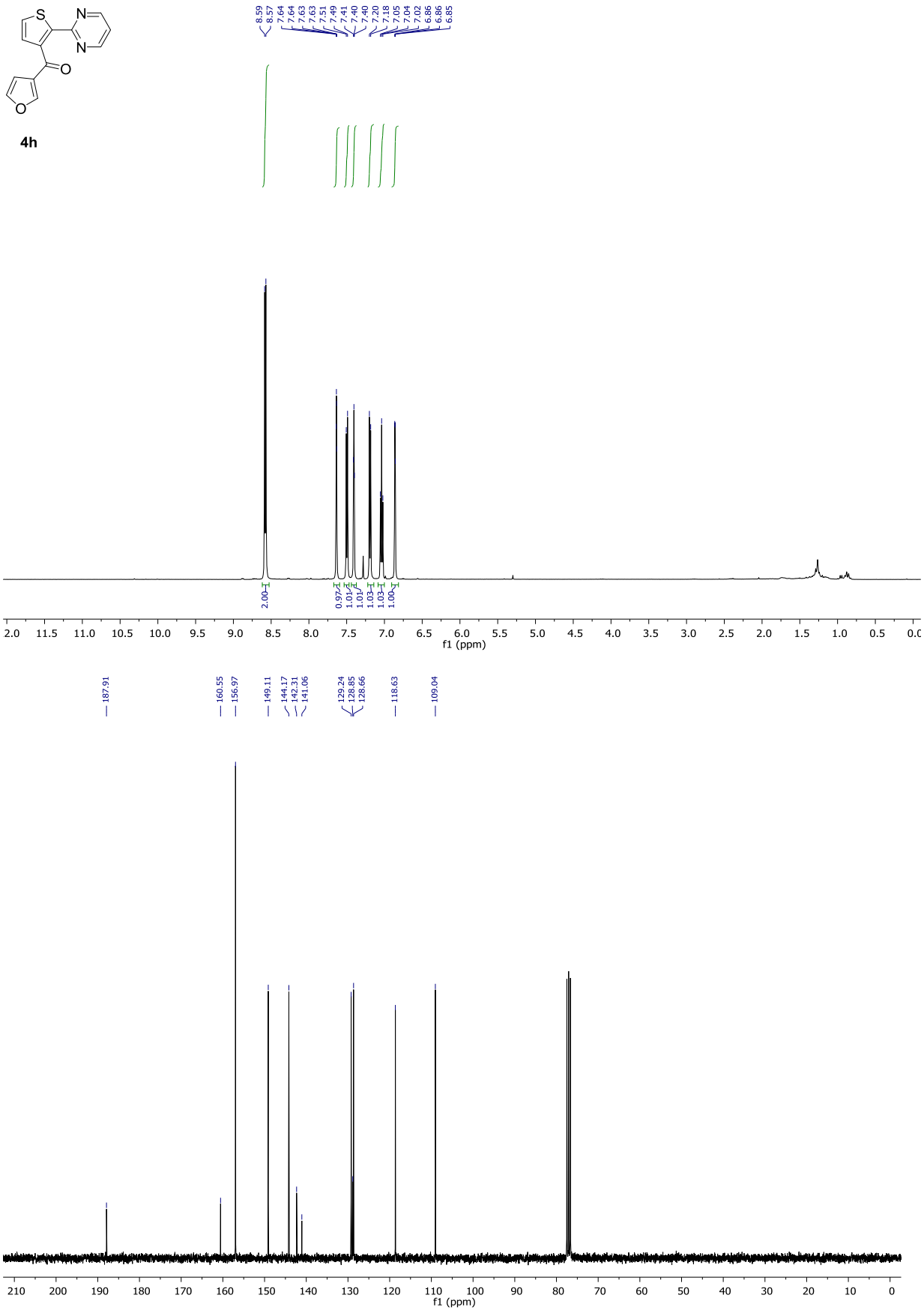


Figure S35. ^{1}H NMR and ^{13}C NMR spectra of **4h**

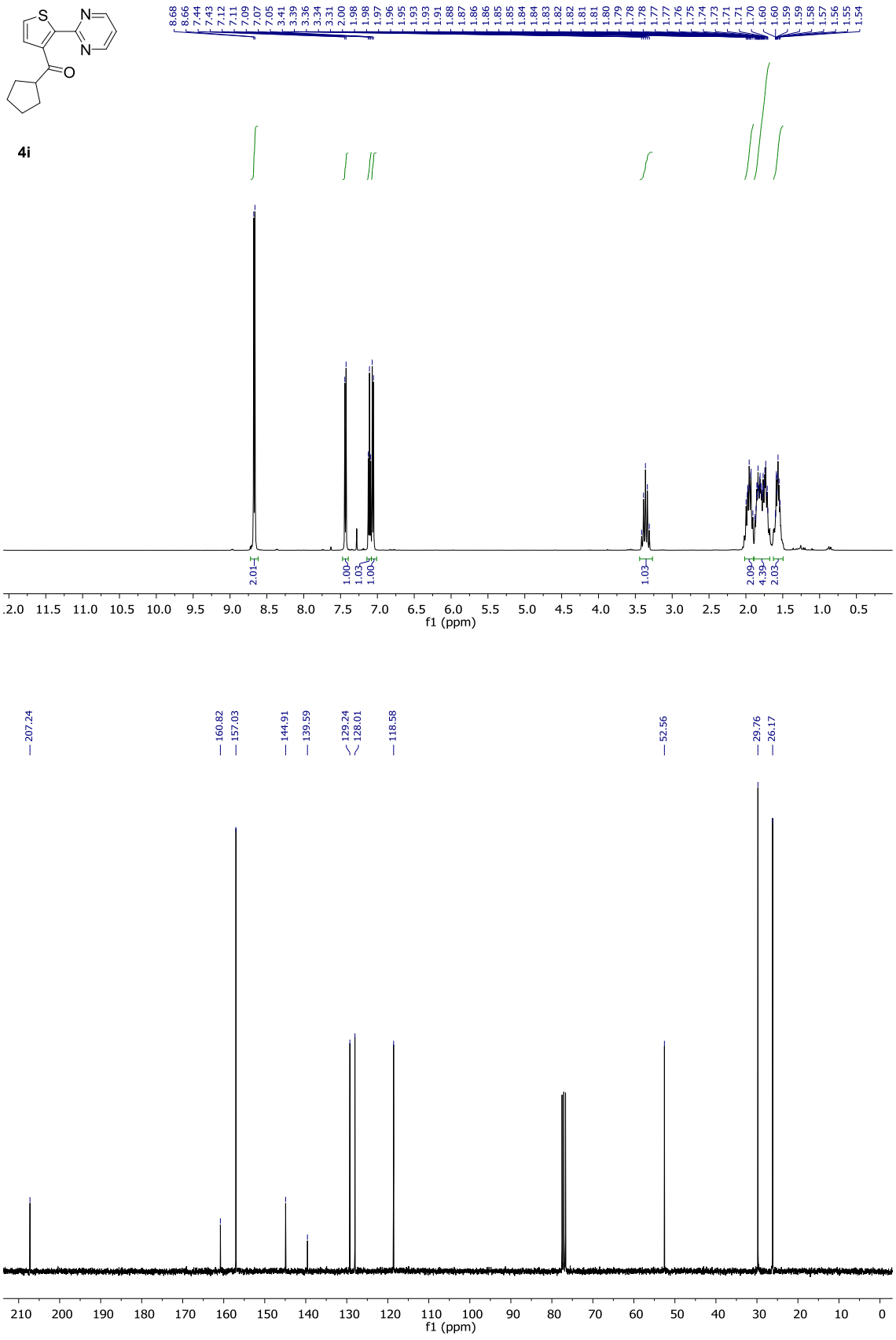


Figure S36. ^{1}H NMR and ^{13}C NMR spectra of **4i**

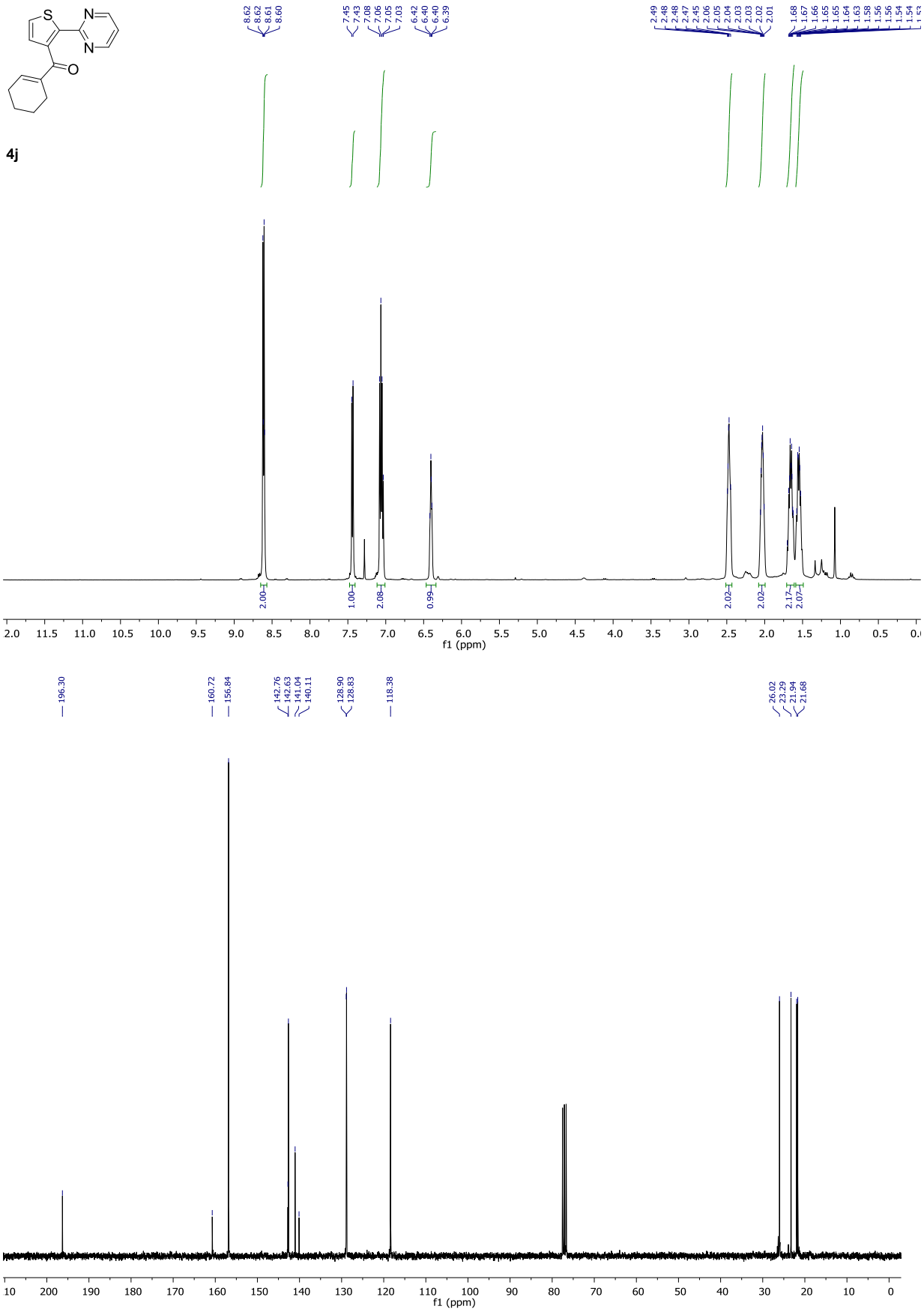


Figure S37. ^{1}H NMR and ^{13}C NMR spectra of **4j**

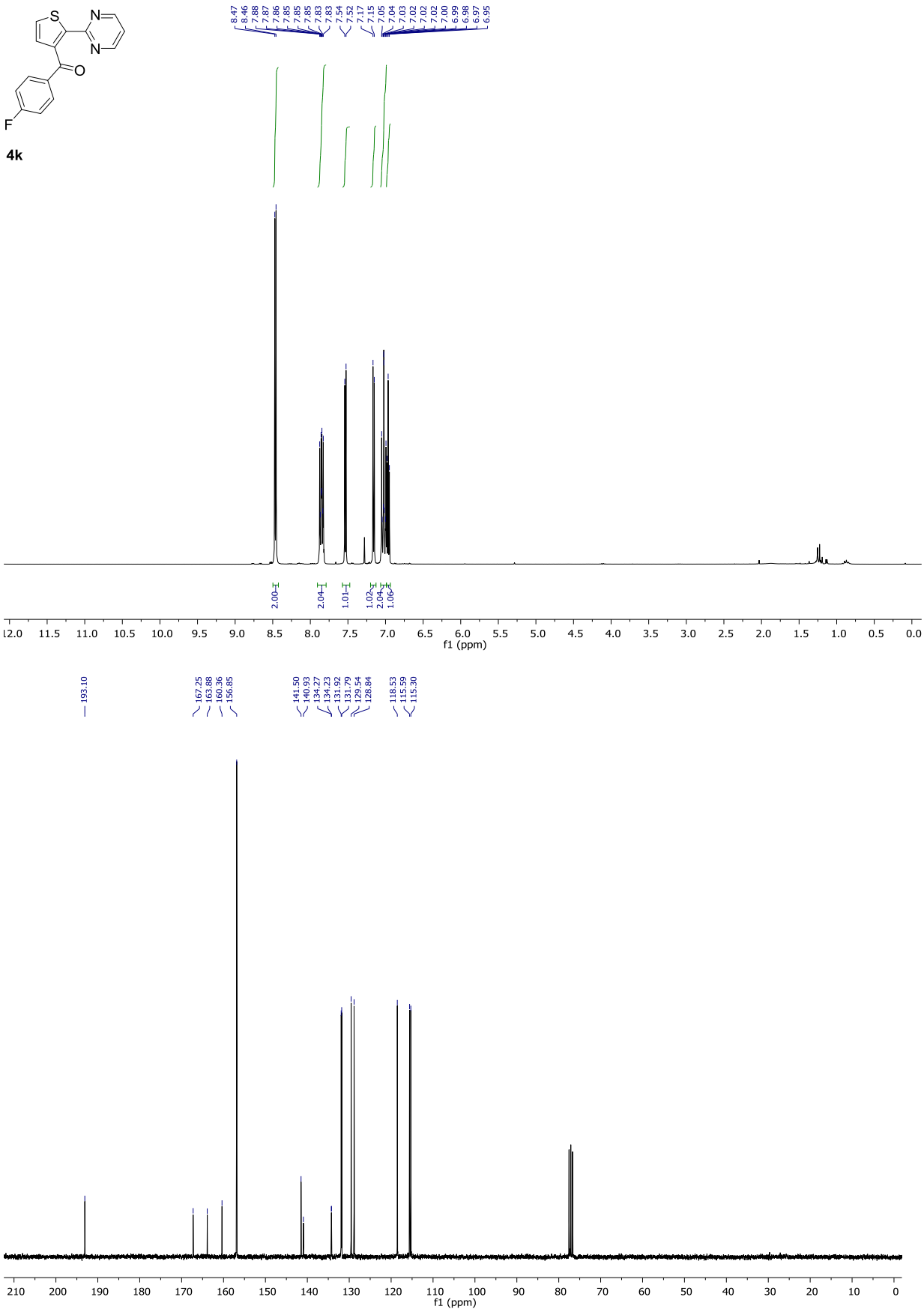


Figure S38. ^{1}H NMR and ^{13}C NMR spectra of **4k**

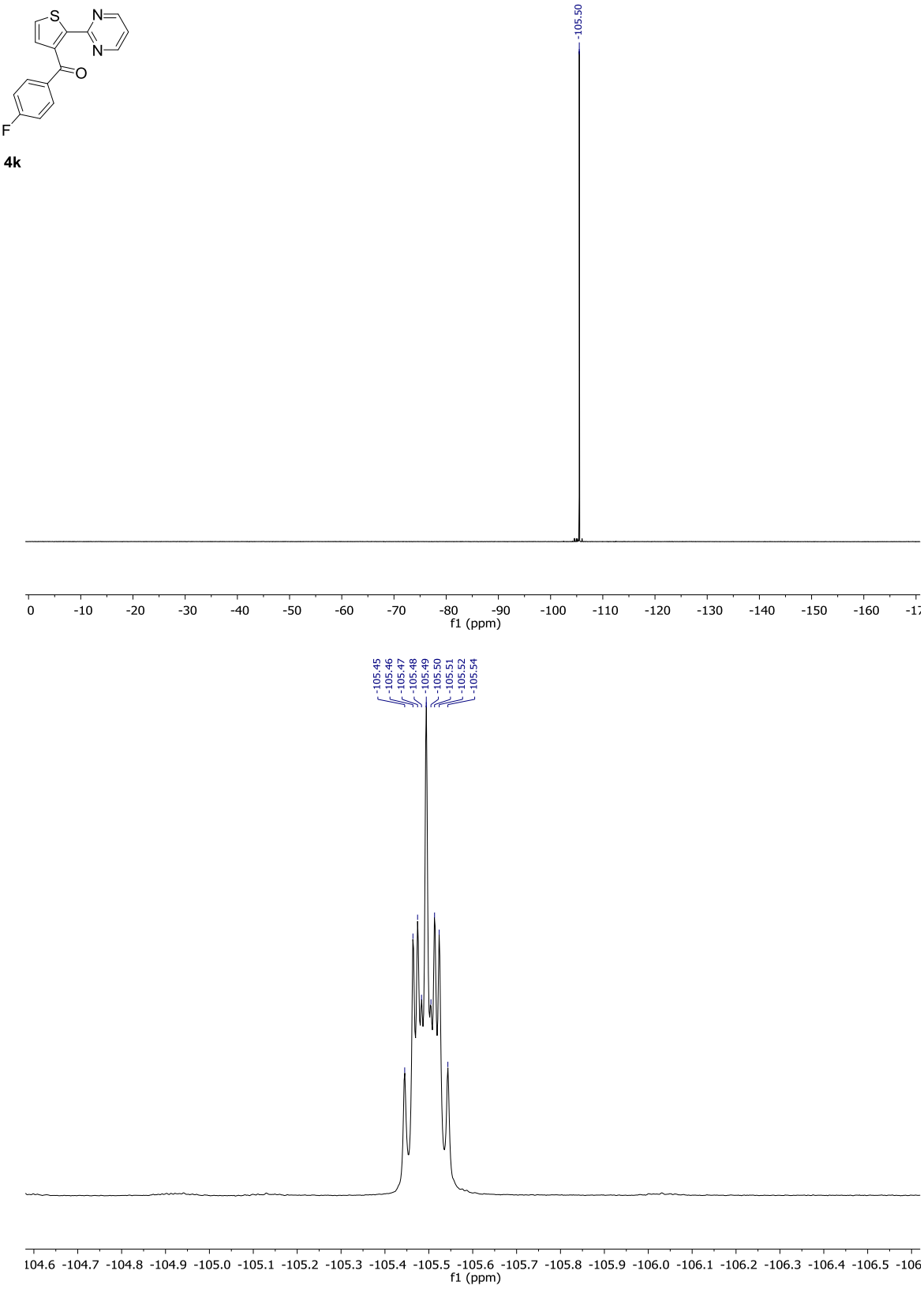


Figure S39. ^{19}F NMR (^{1}H-decoupled and coupled) spectra of **4k**

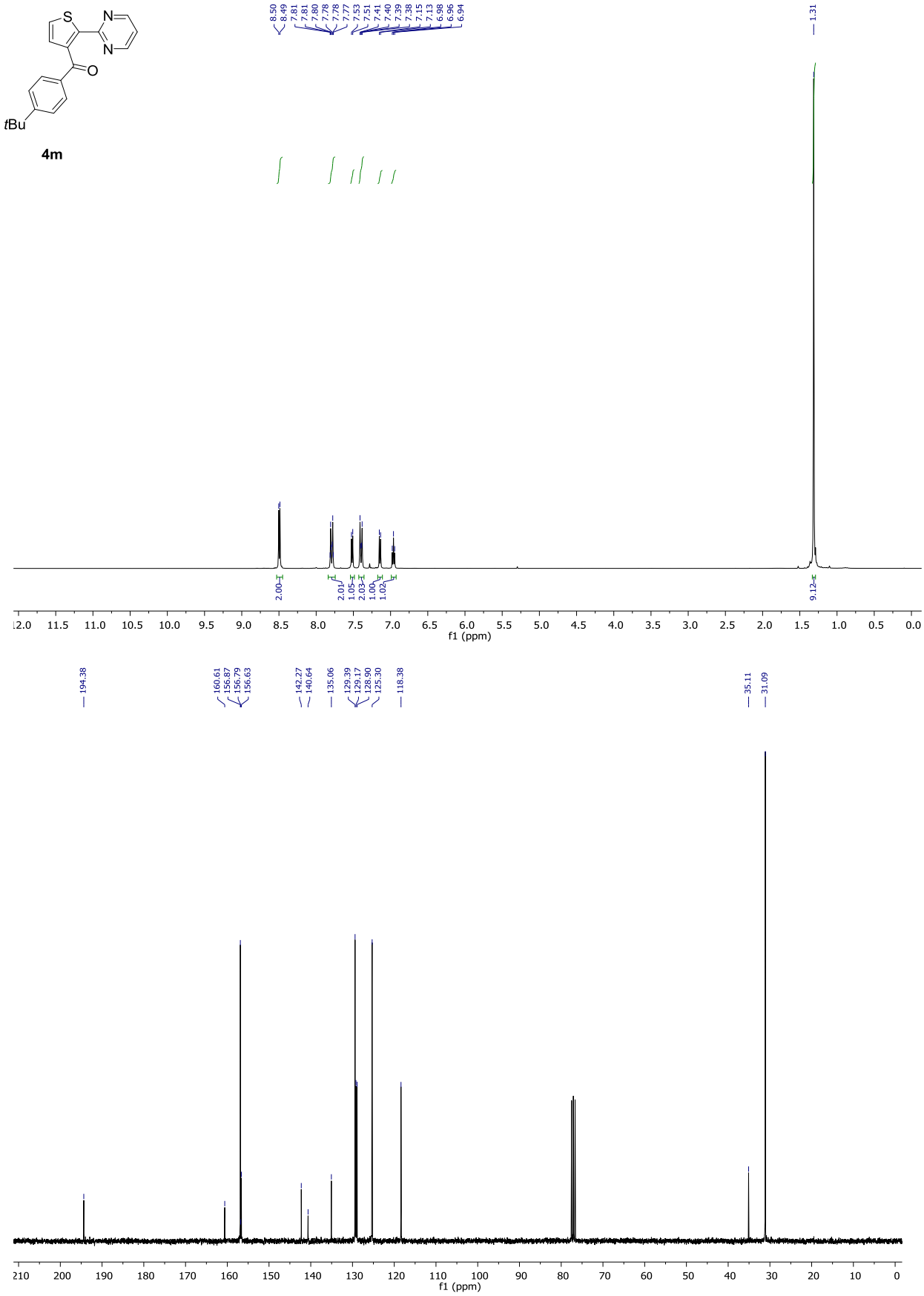


Figure S40. ^{1}H NMR and ^{13}C NMR spectra of **4m**

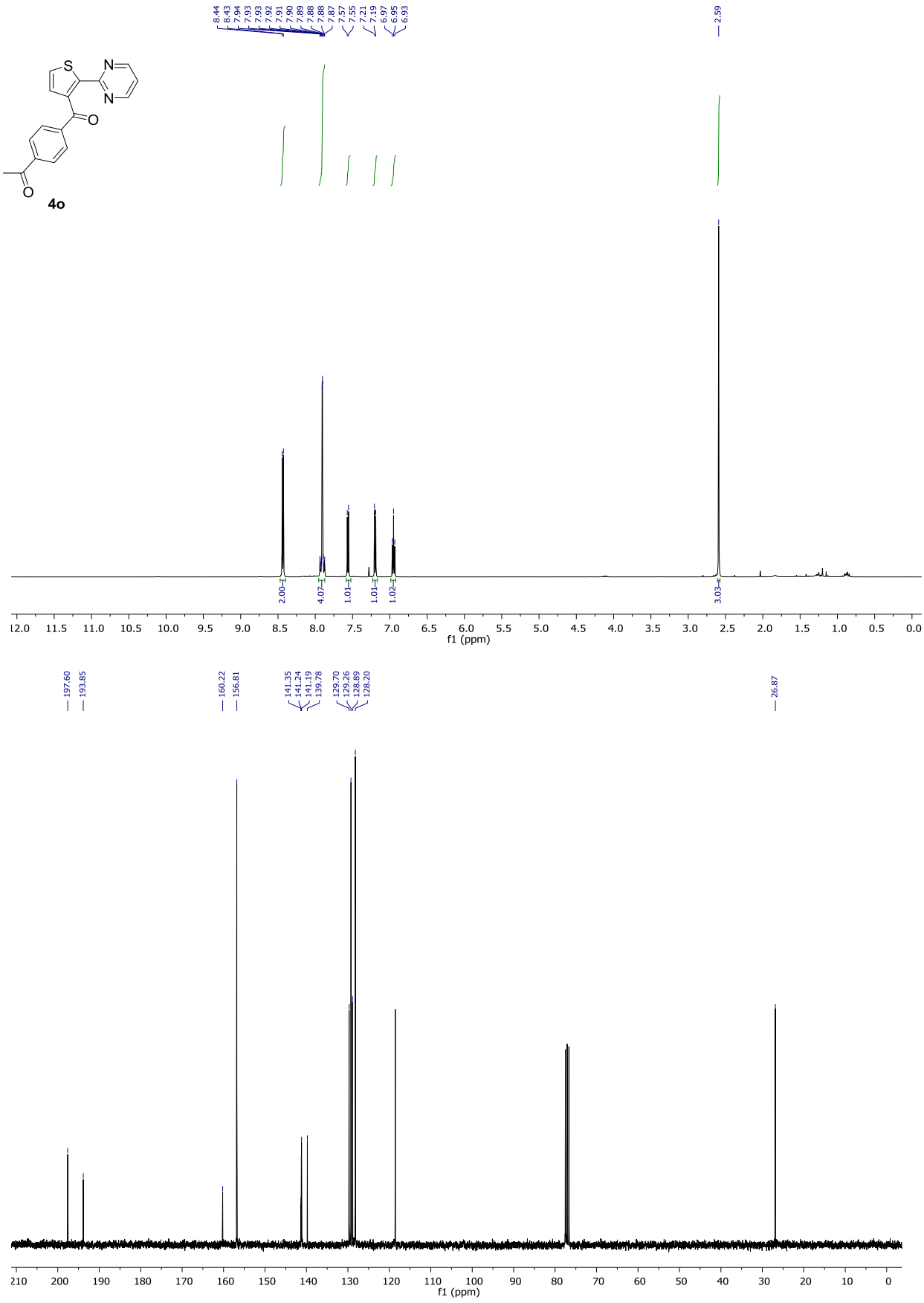


Figure S41. ^{1}H NMR and ^{13}C NMR spectra of **4o**

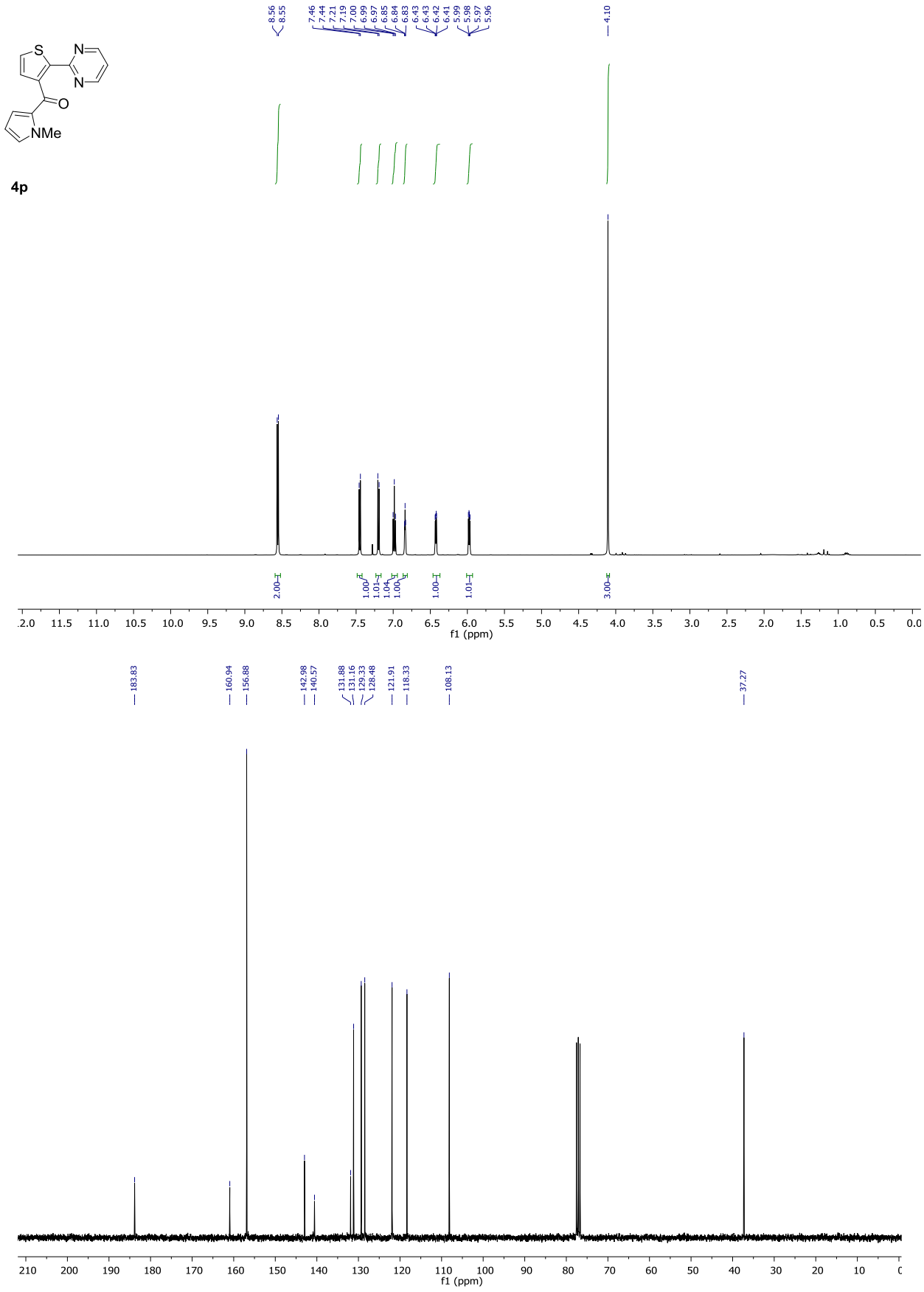


Figure S42. ^{1}H NMR and ^{13}C NMR spectra of **4p**

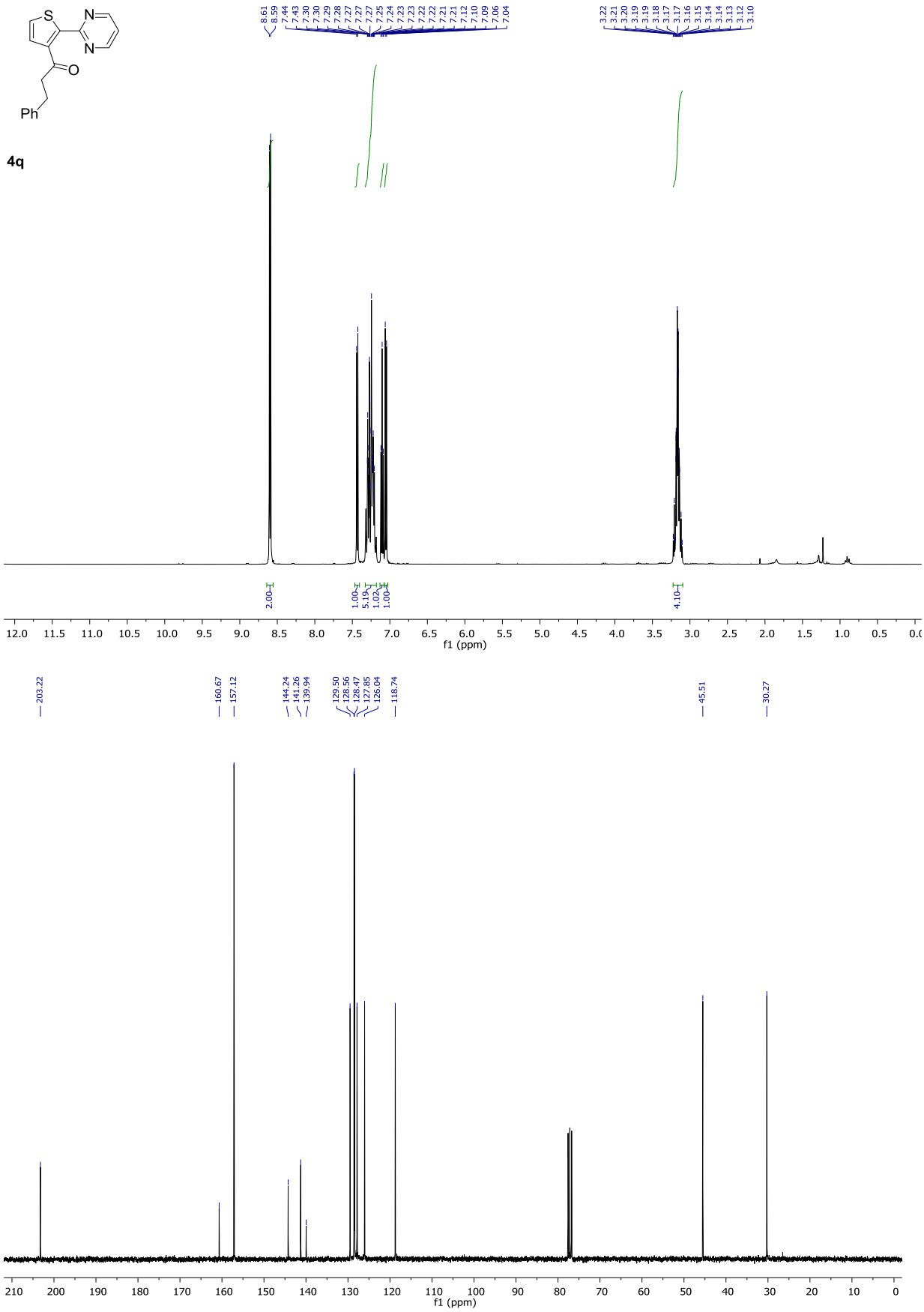


Figure S43. ^{1}H NMR and ^{13}C NMR spectra of **4q**

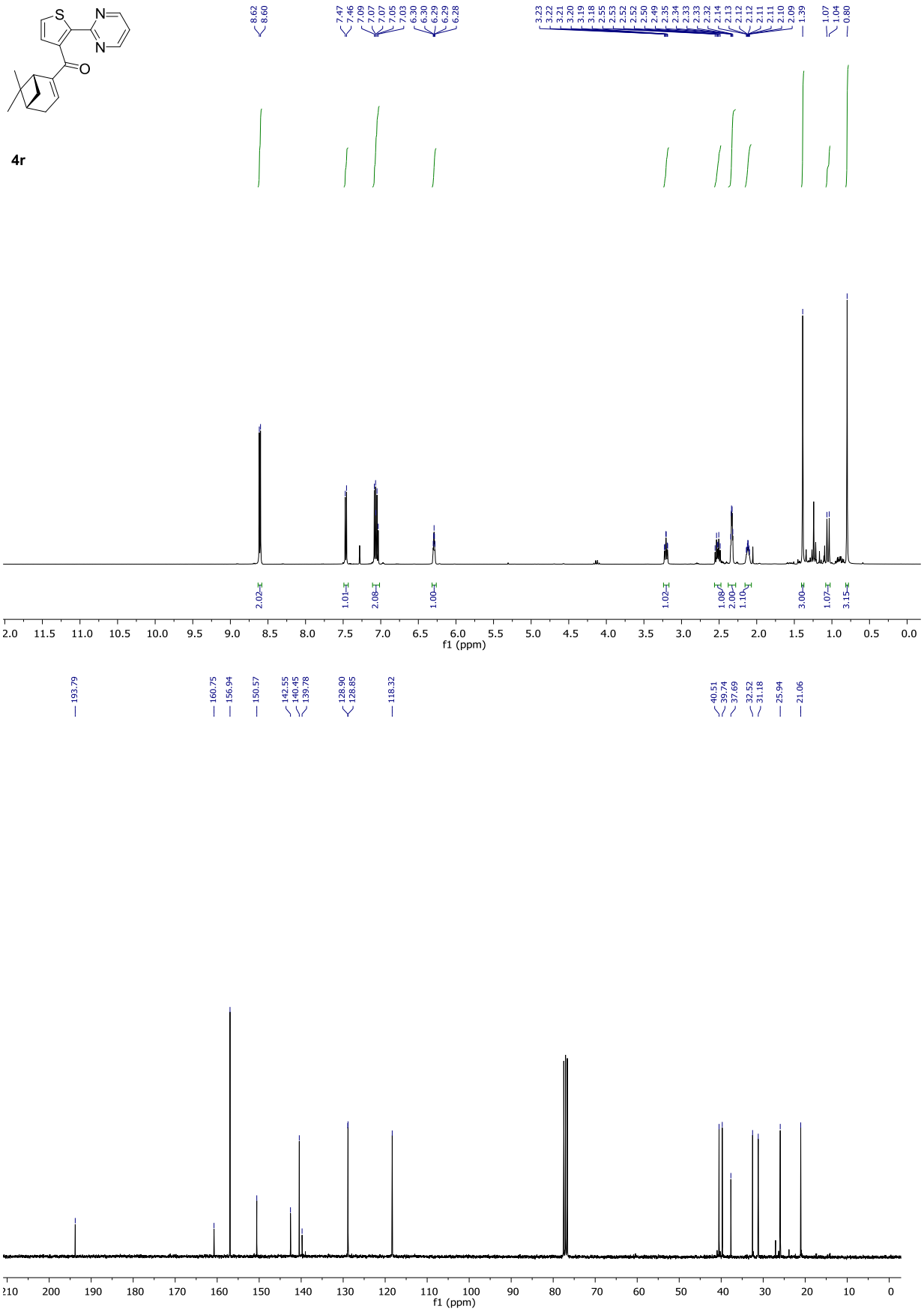


Figure S44. ^{1}H NMR and ^{13}C NMR spectra of **4r**

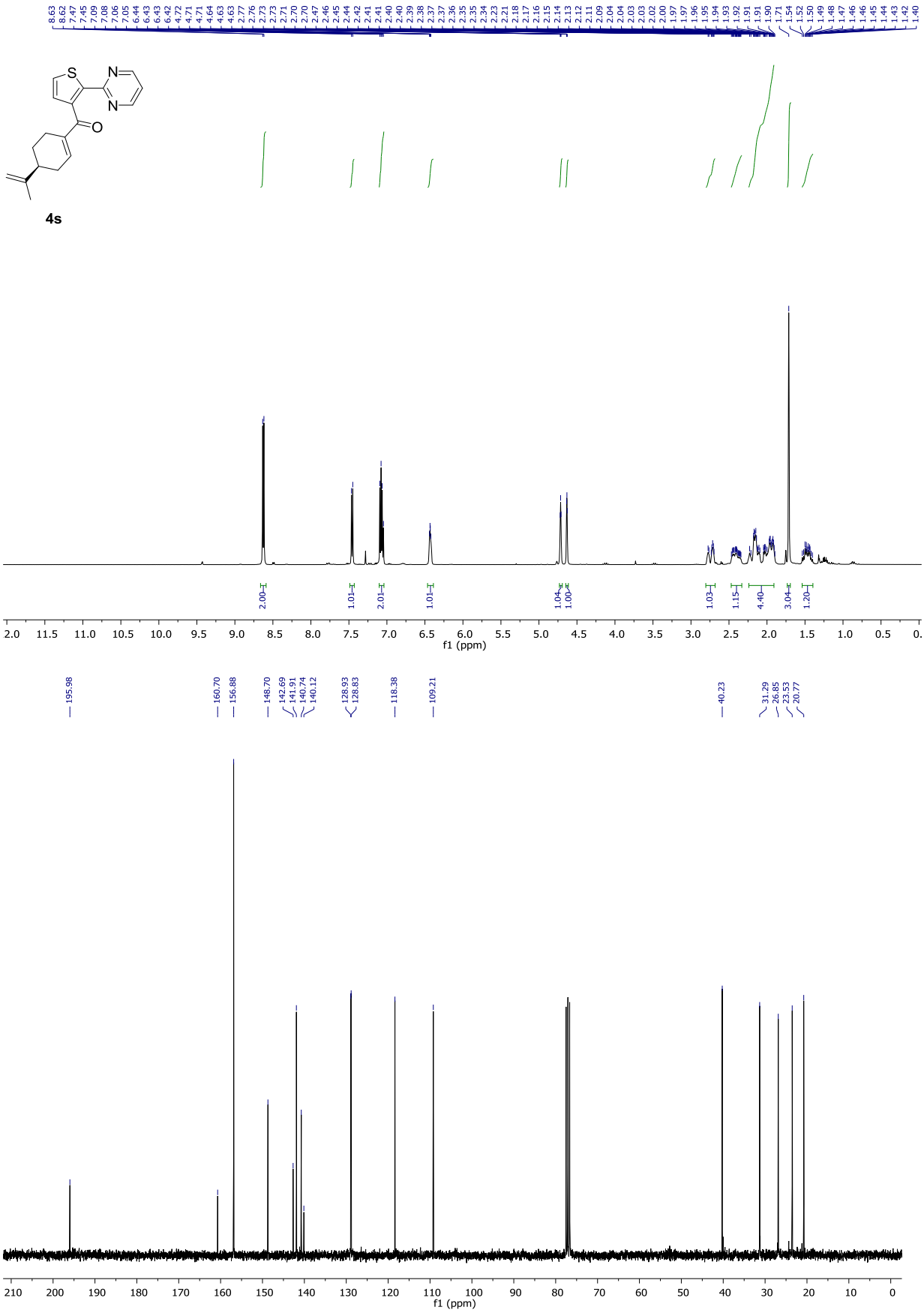


Figure S45. ^{1}H NMR and ^{13}C NMR spectra of **4s**

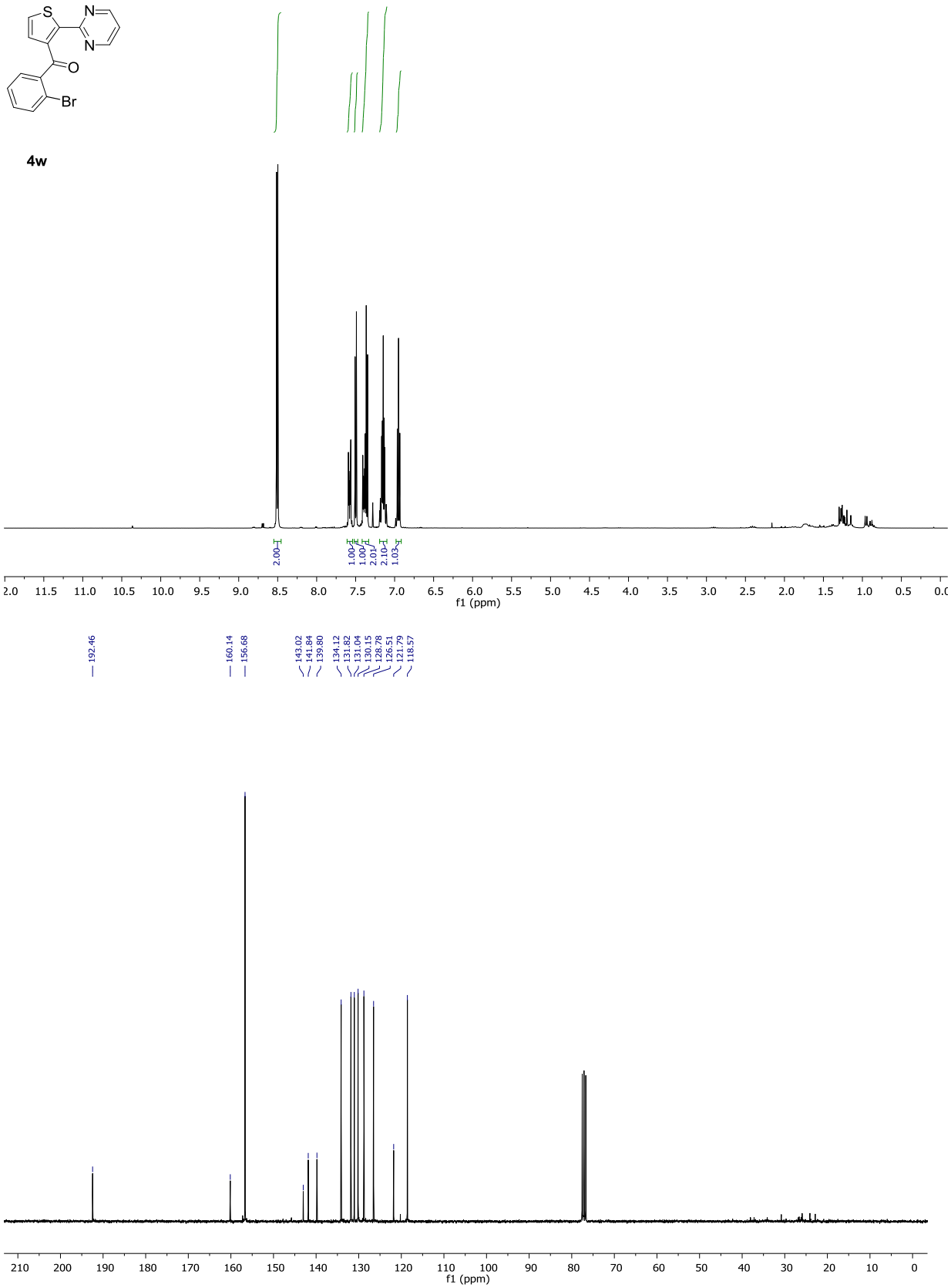


Figure S46. ^{1}H NMR and ^{13}C NMR spectra of **4w**

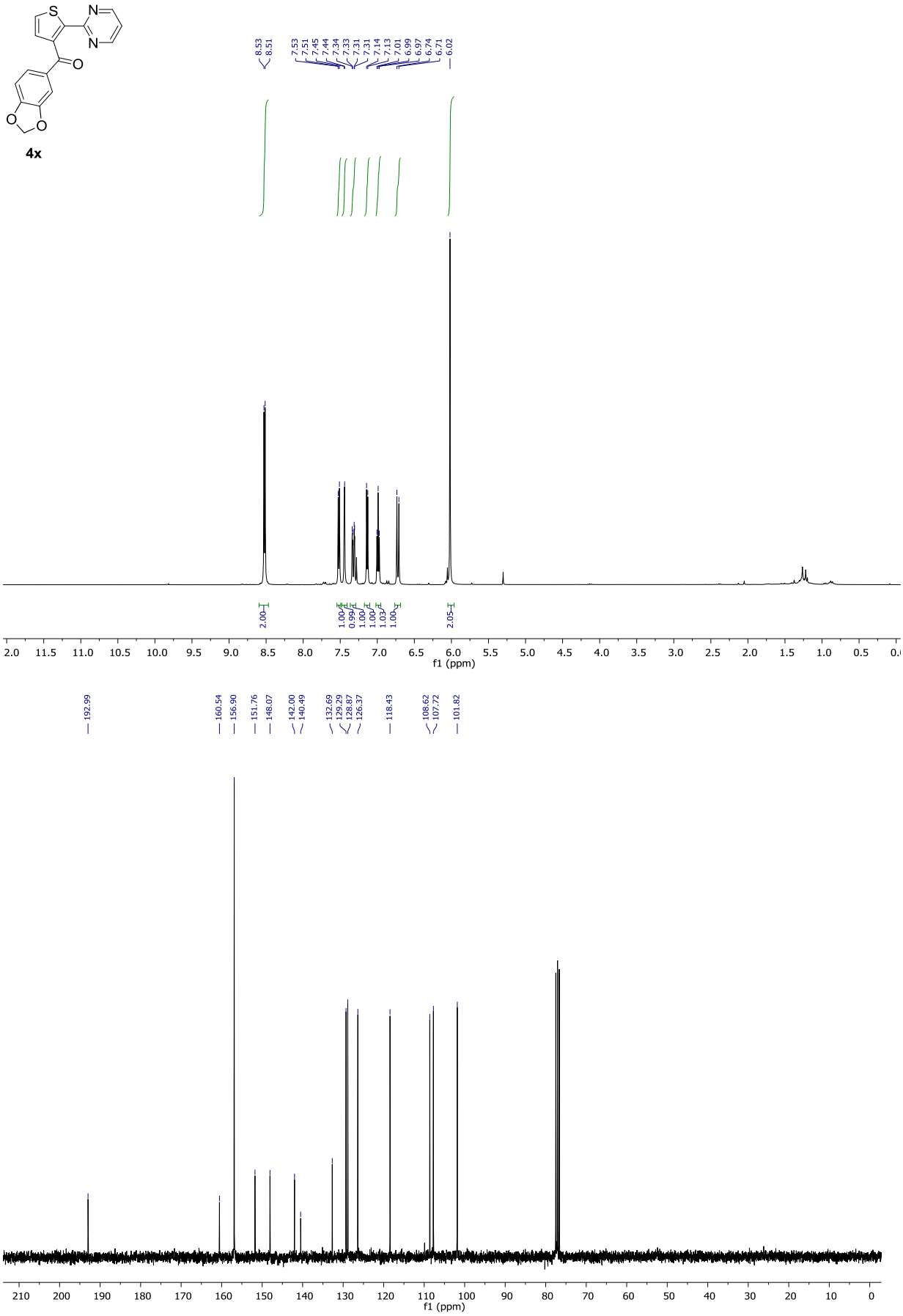


Figure S47. ^{1}H NMR and ^{13}C NMR spectra of **4x**

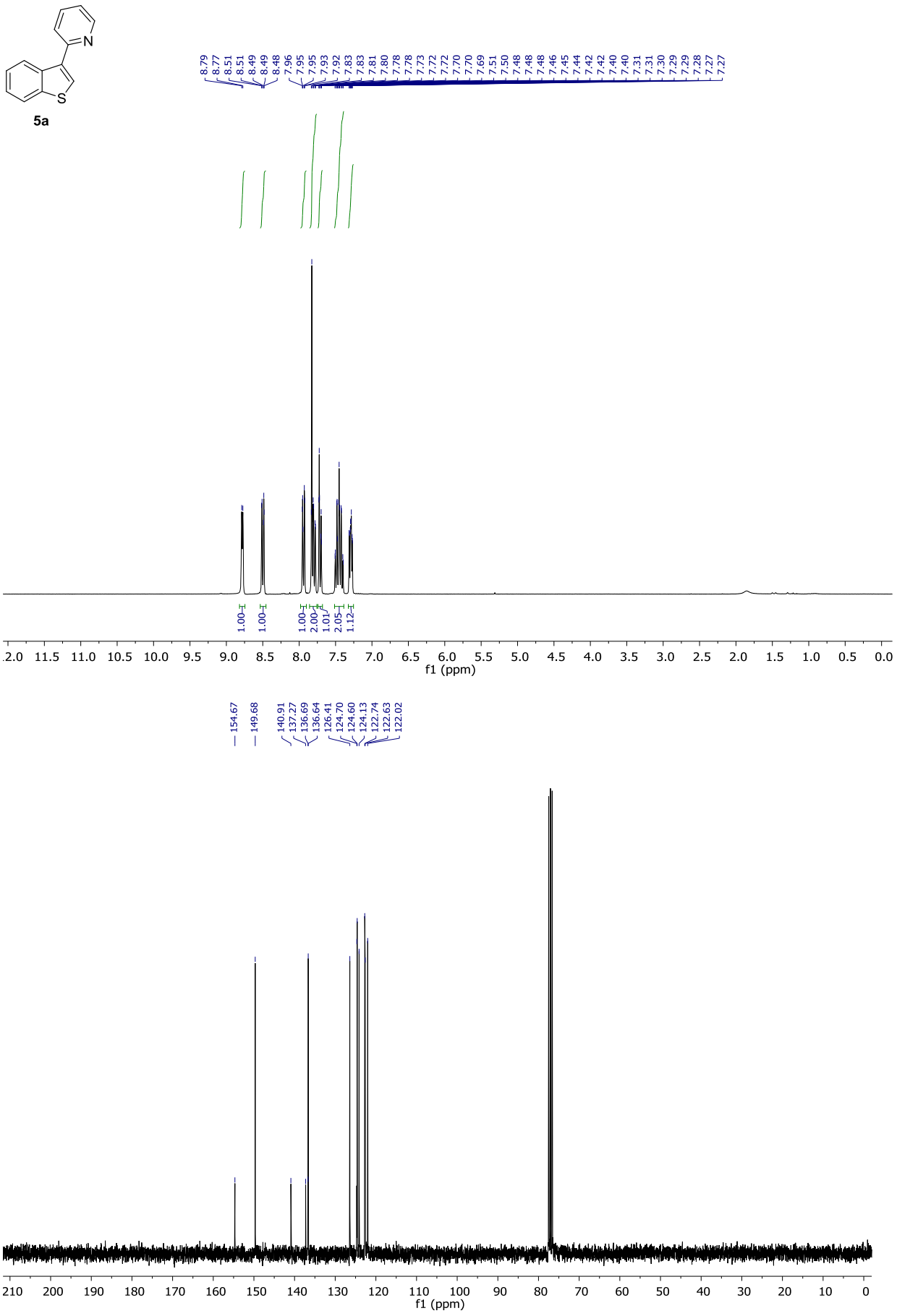


Figure S48. ^{1}H NMR and ^{13}C NMR spectra of **5a**

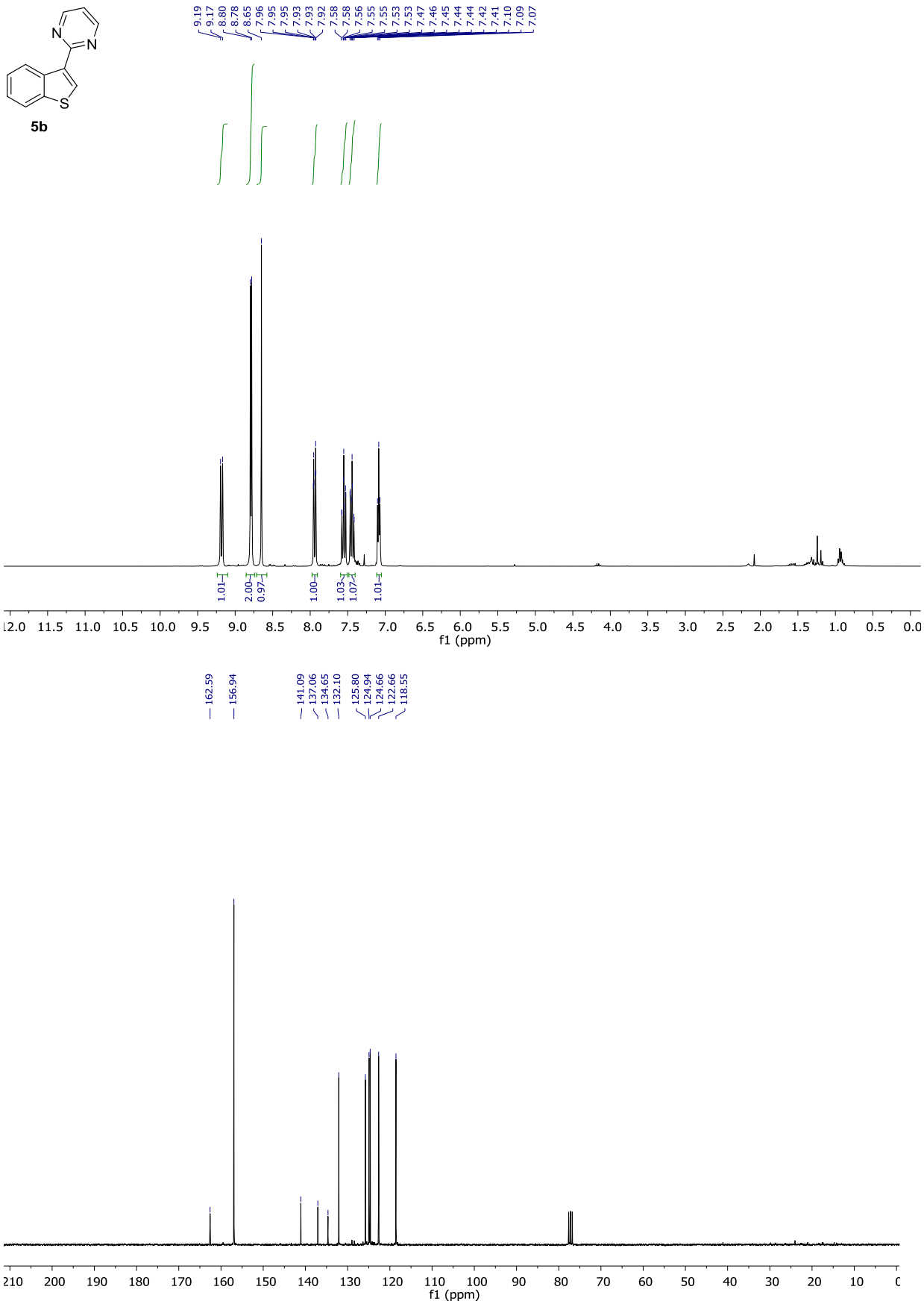


Figure S49. ^{1}H NMR and ^{13}C NMR spectra of **5b**

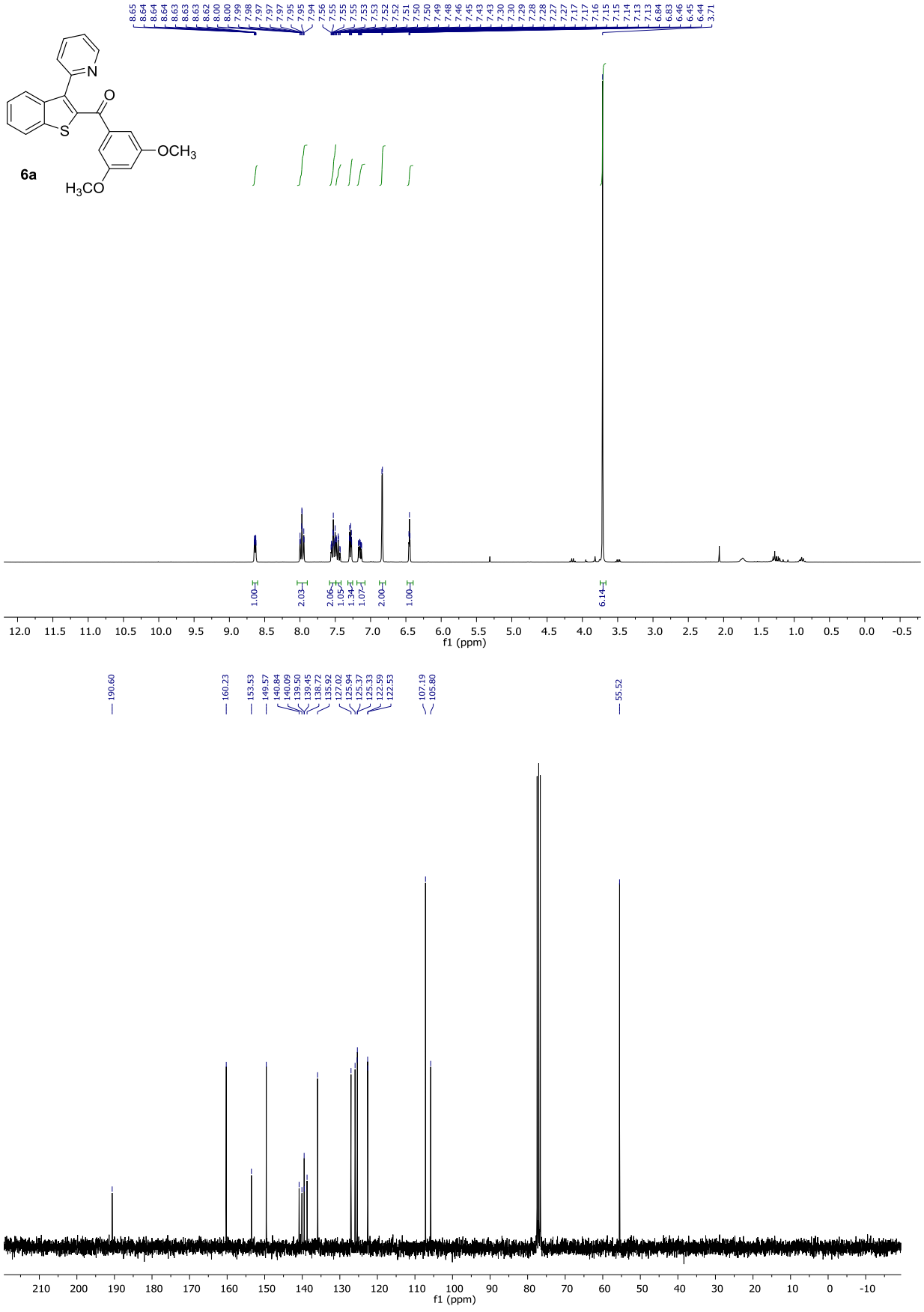


Figure S50. ^{1}H NMR and ^{13}C NMR spectra of **6a**

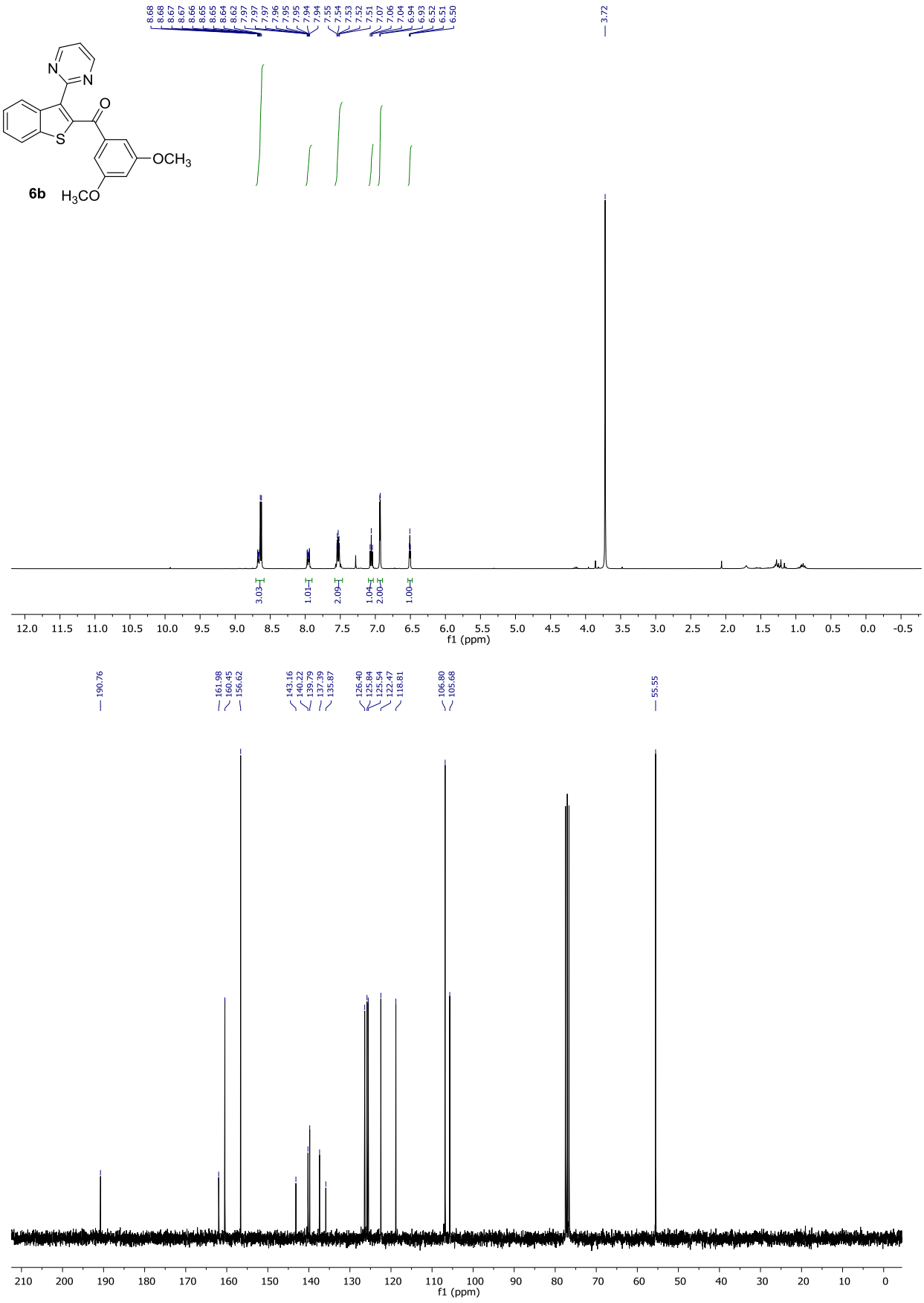


Figure S51. ^{1}H NMR and ^{13}C NMR spectra of **6b**

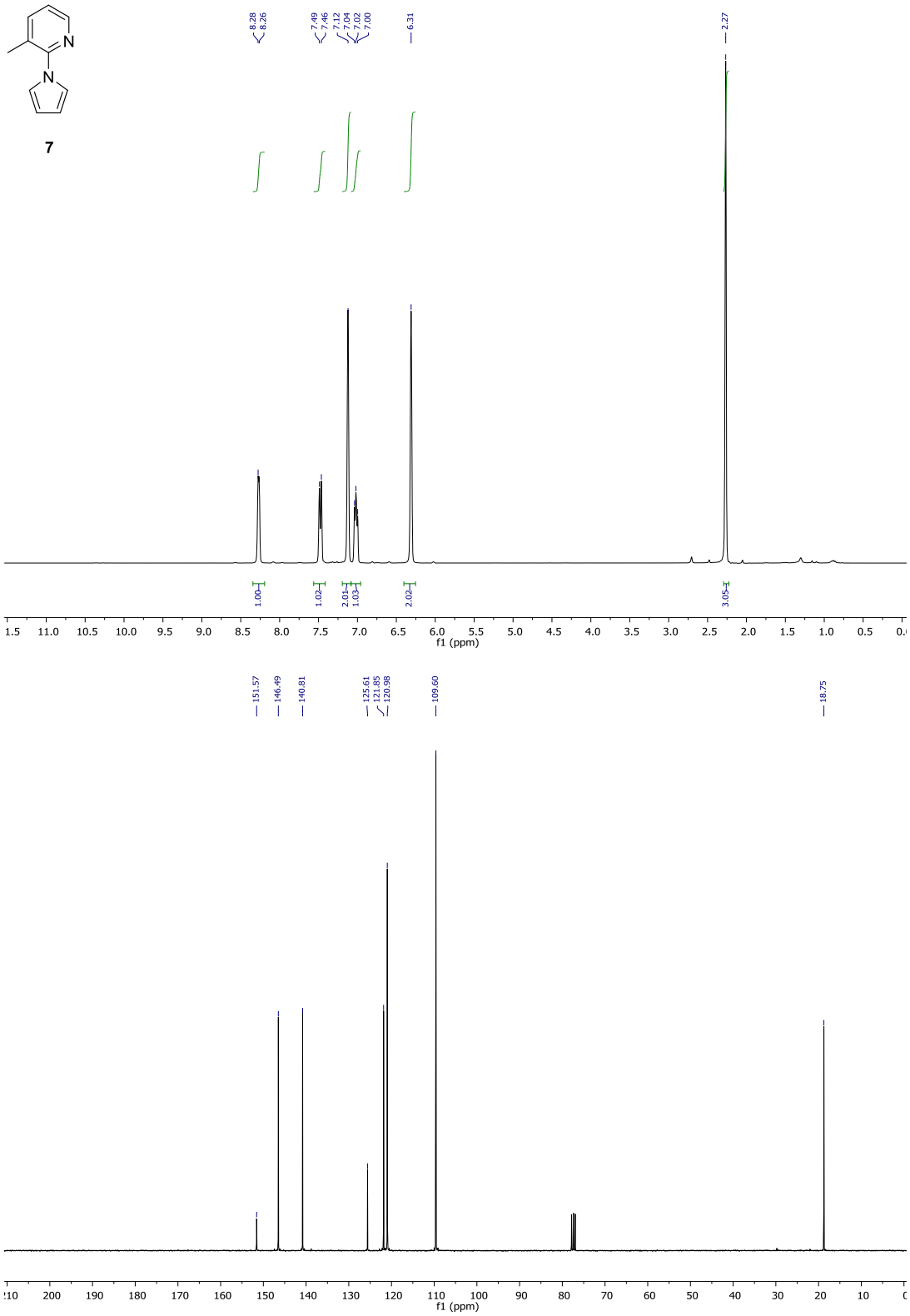
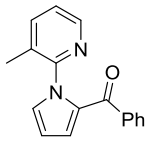
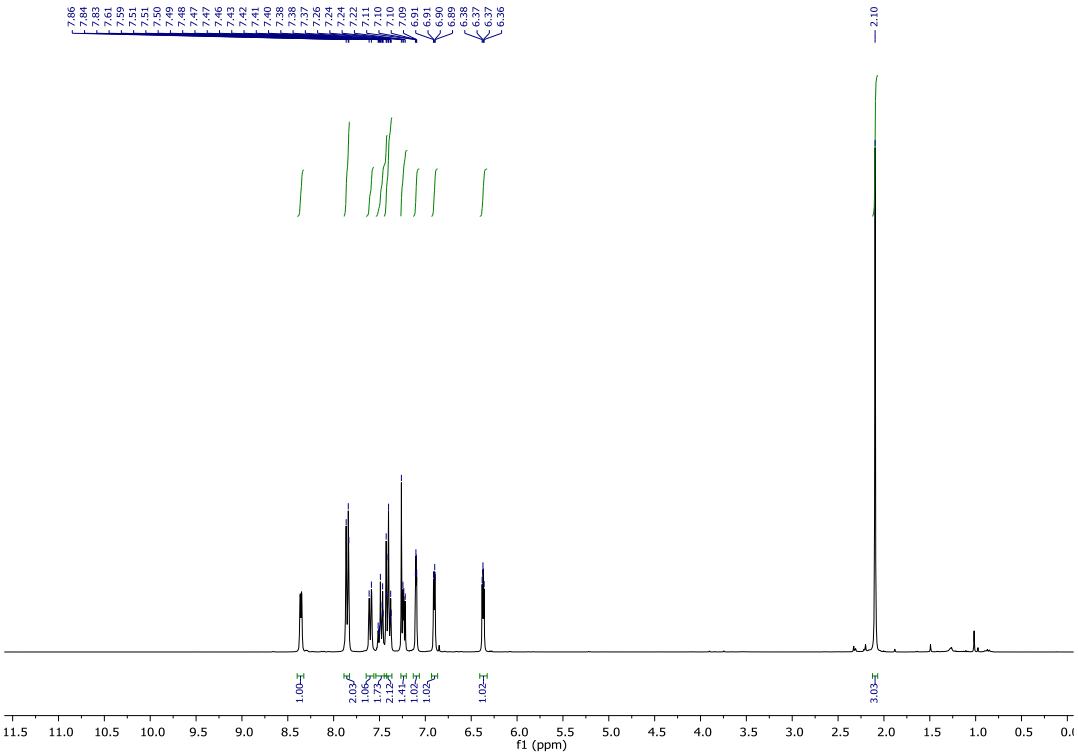


Figure S52. ^{1}H NMR and ^{13}C NMR spectra of **7**



8



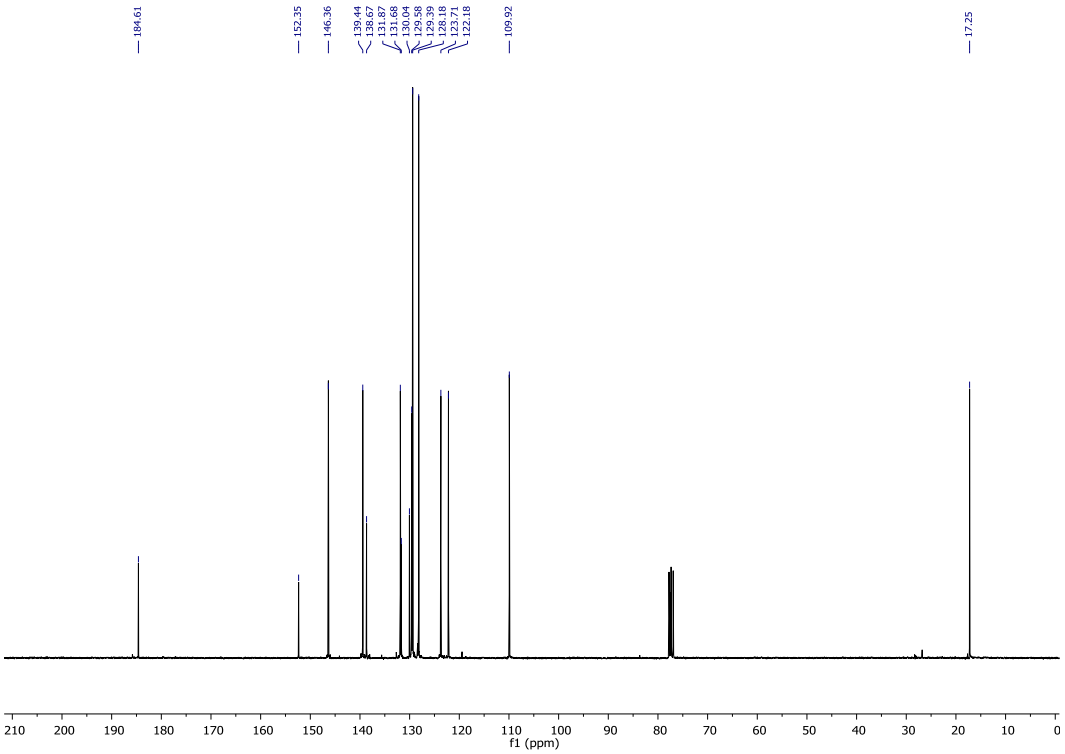


Figure S53. ^{1}H NMR and ^{13}C NMR spectra of **8**

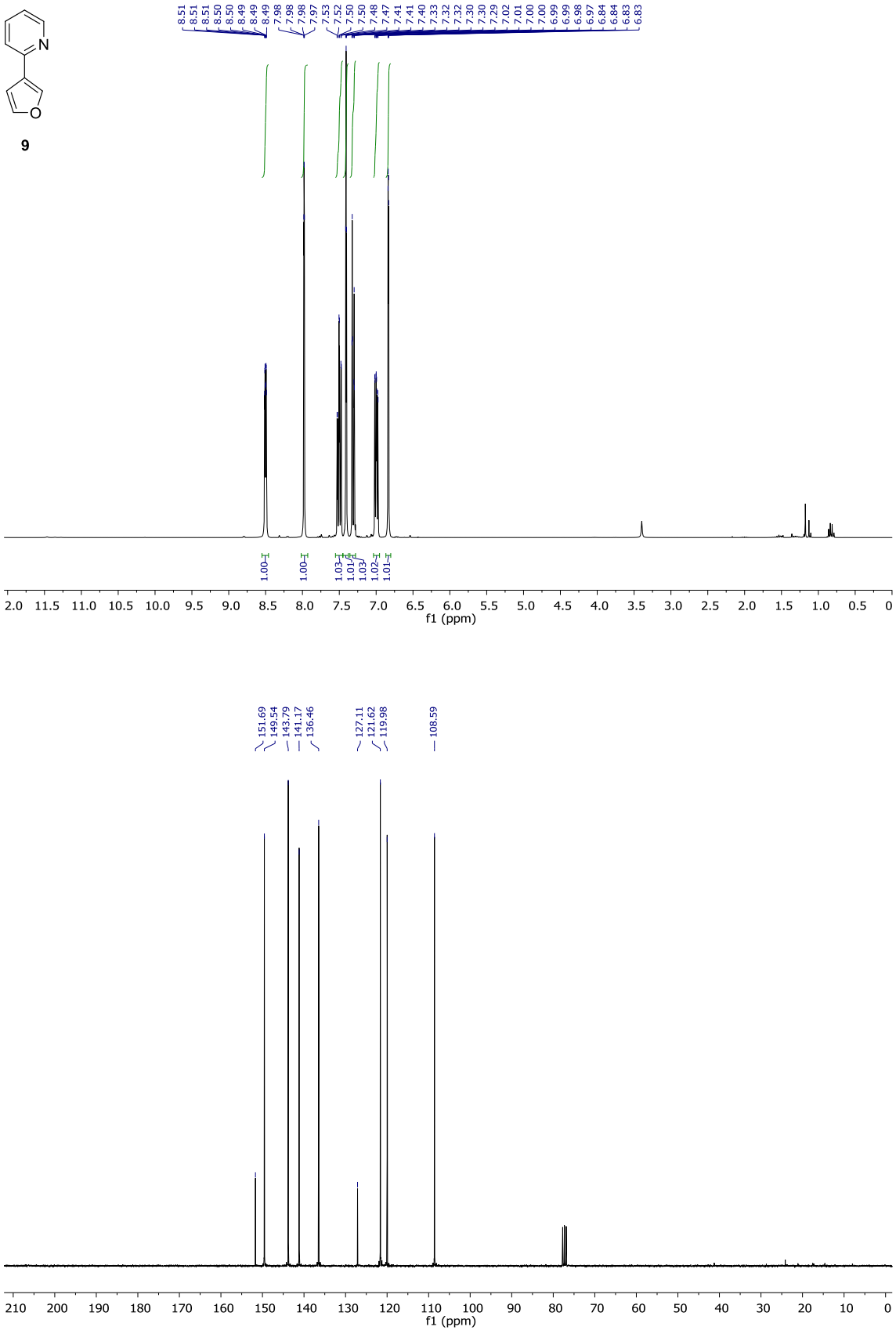


Figure S54. ^{1}H NMR and ^{13}C NMR spectra of **9**

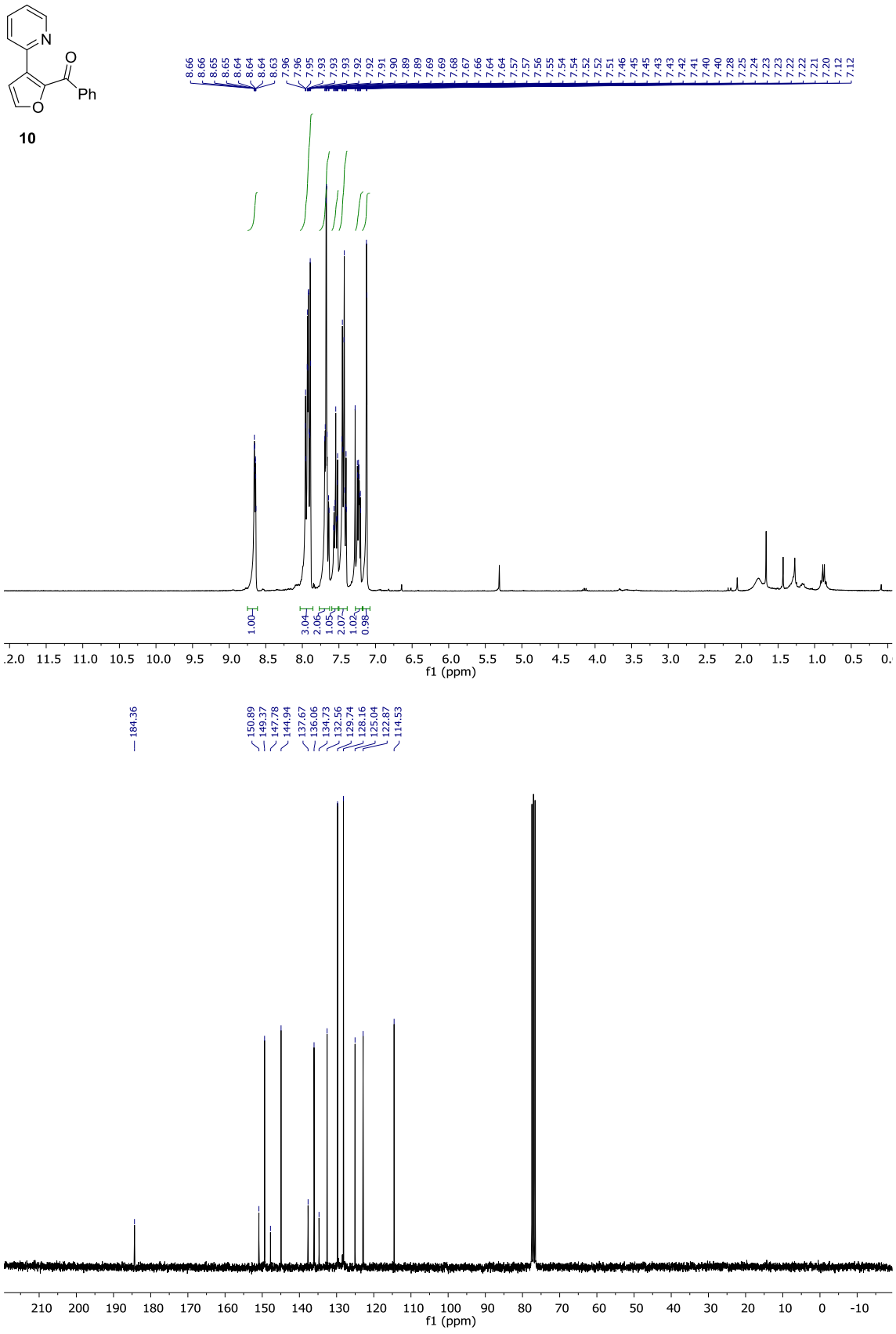


Figure S55. ^{1}H NMR and ^{13}C NMR spectra of **10**

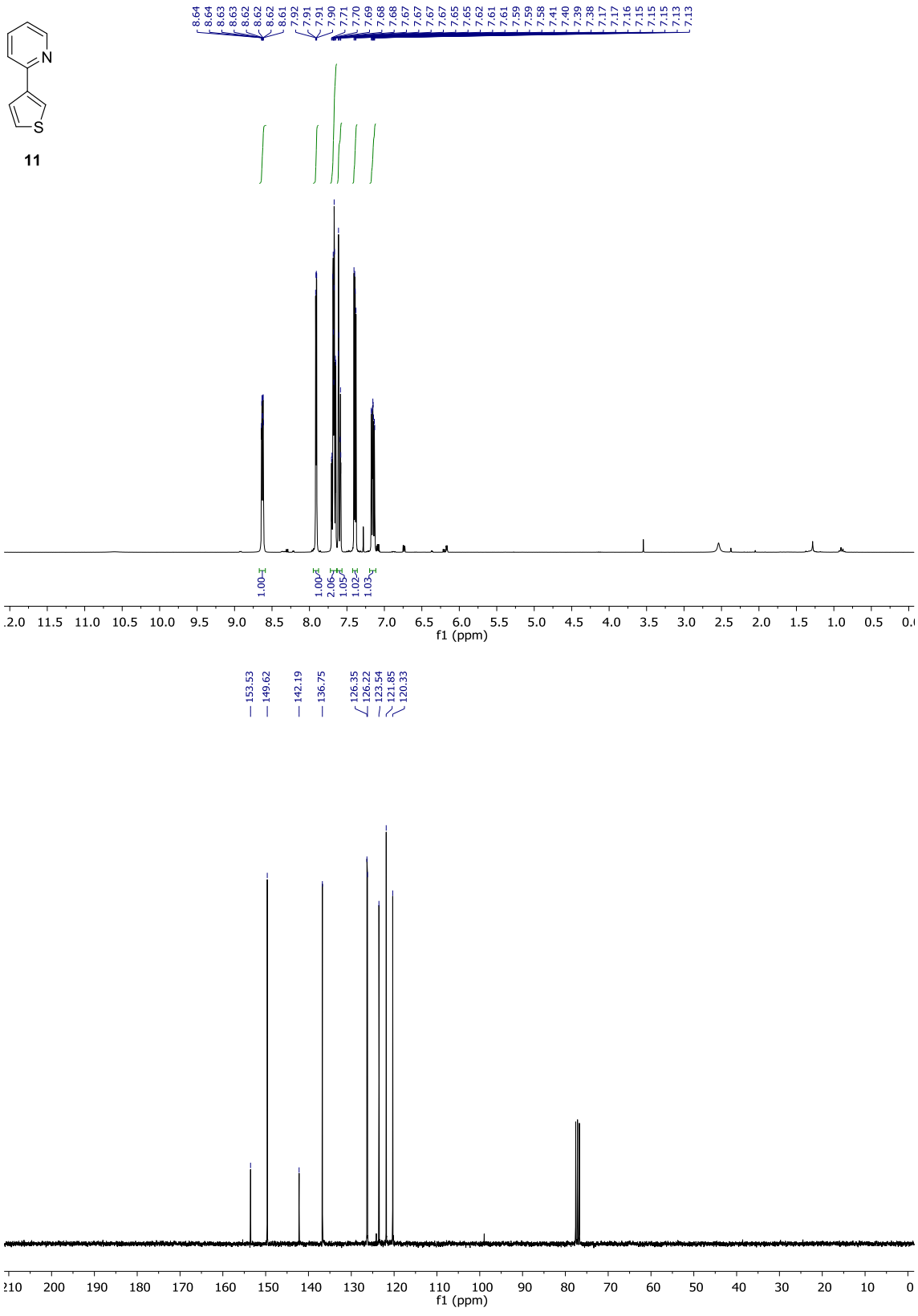


Figure S56. ^{1}H NMR and ^{13}C NMR spectra of **11**

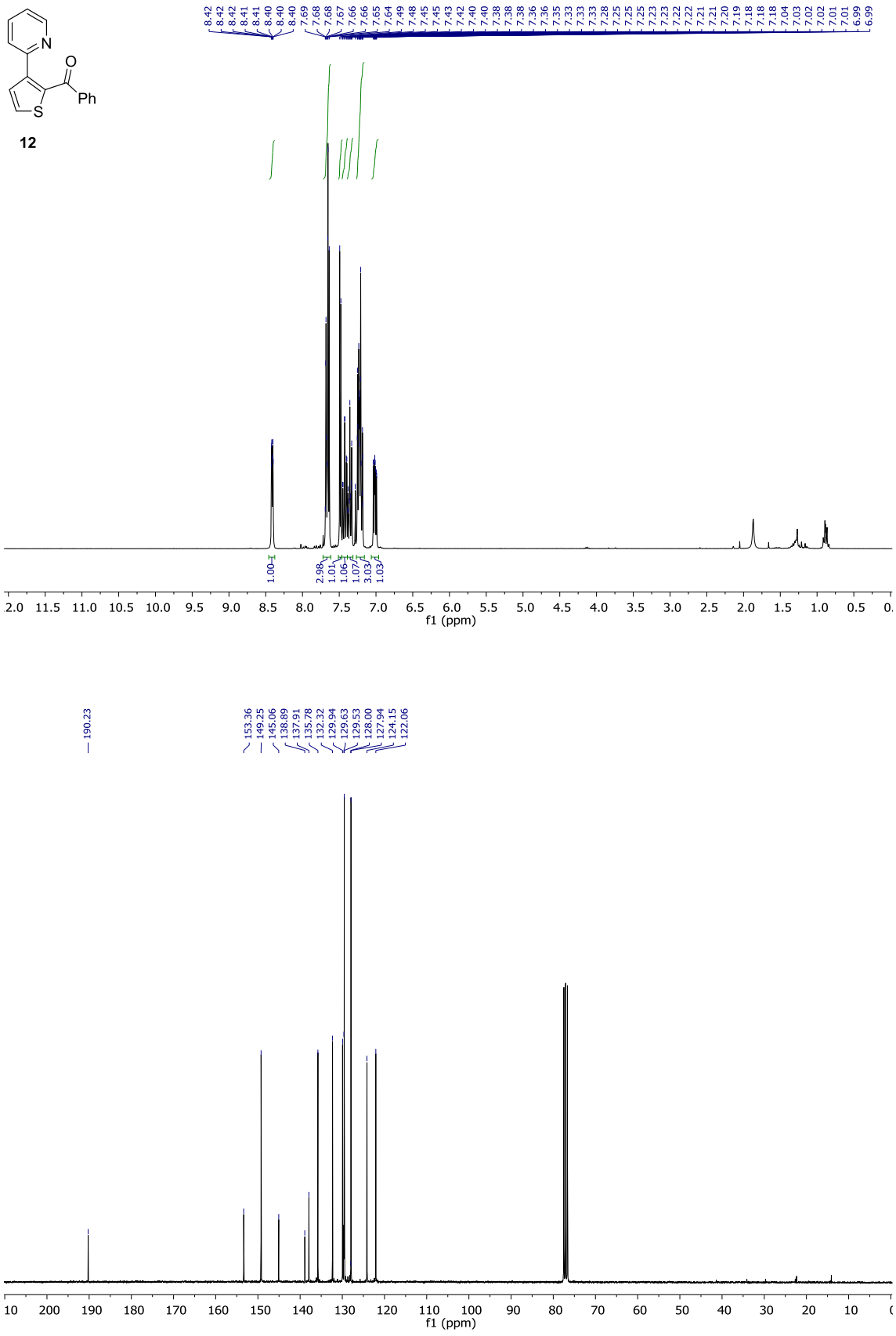


Figure S57. ^{1}H NMR and ^{13}C NMR spectra of **12**

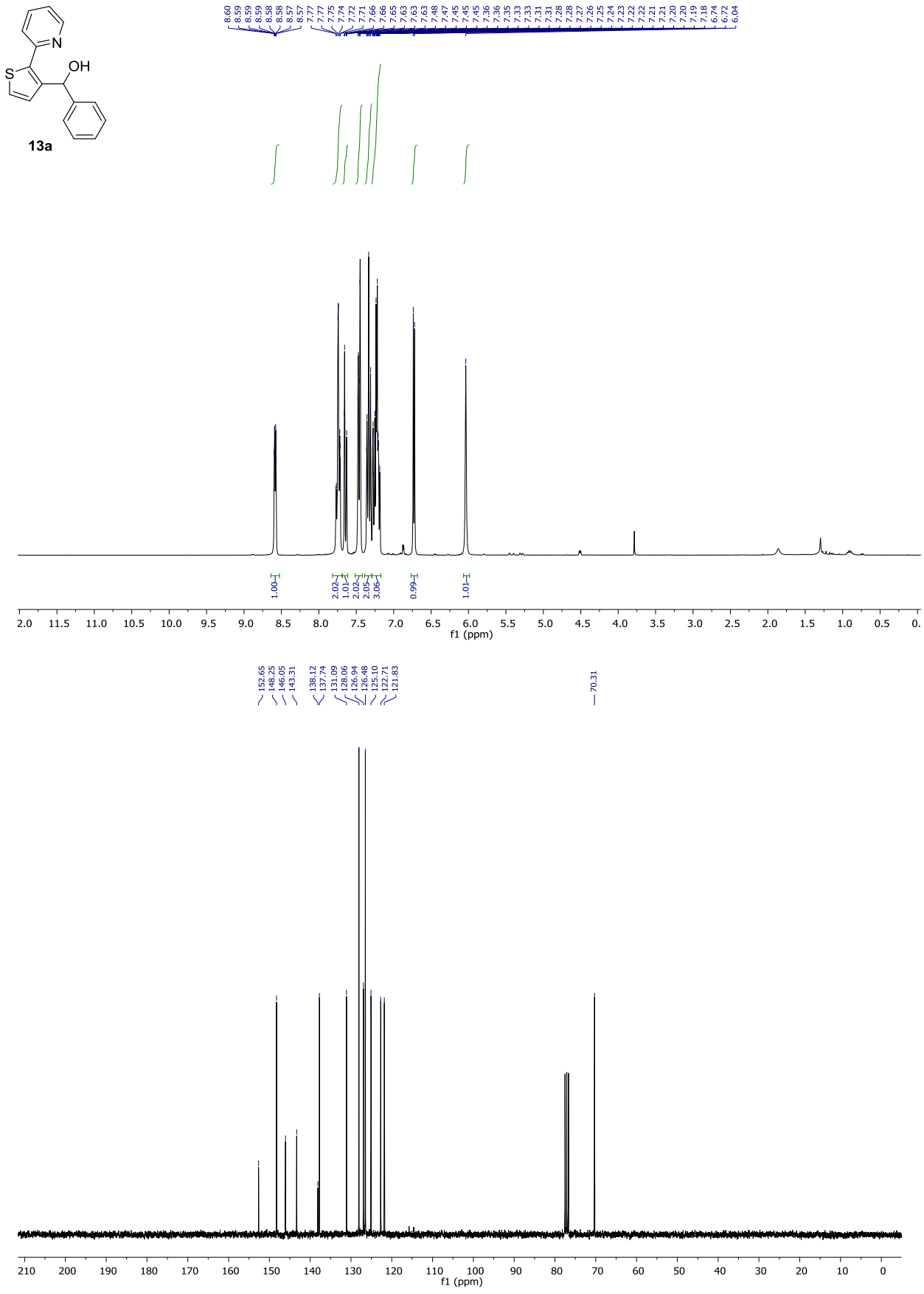


Figure S58. ^{1}H NMR and ^{13}C NMR spectra of **13a**

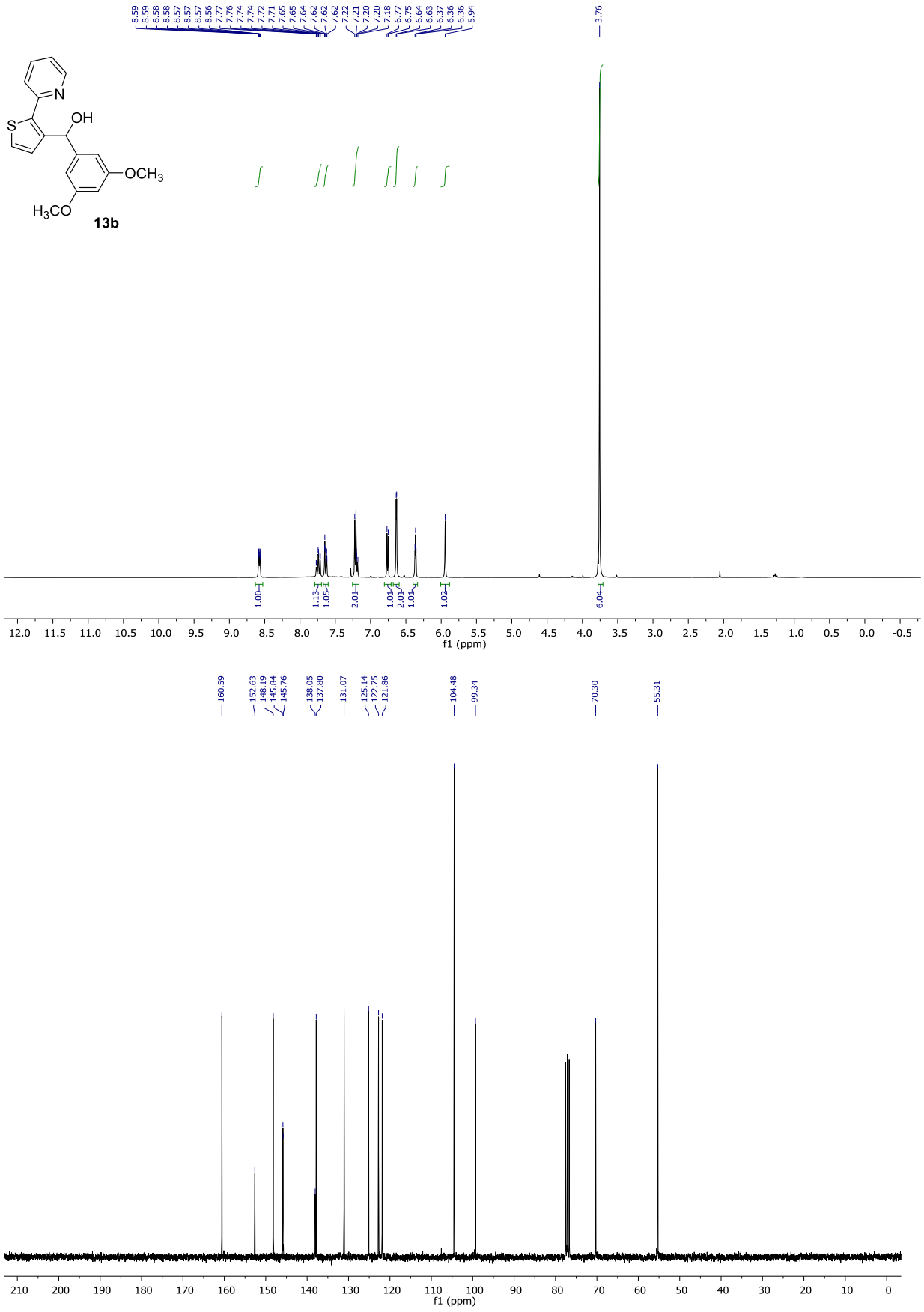


Figure S59. ^{1}H NMR and ^{13}C NMR spectra of **13b**

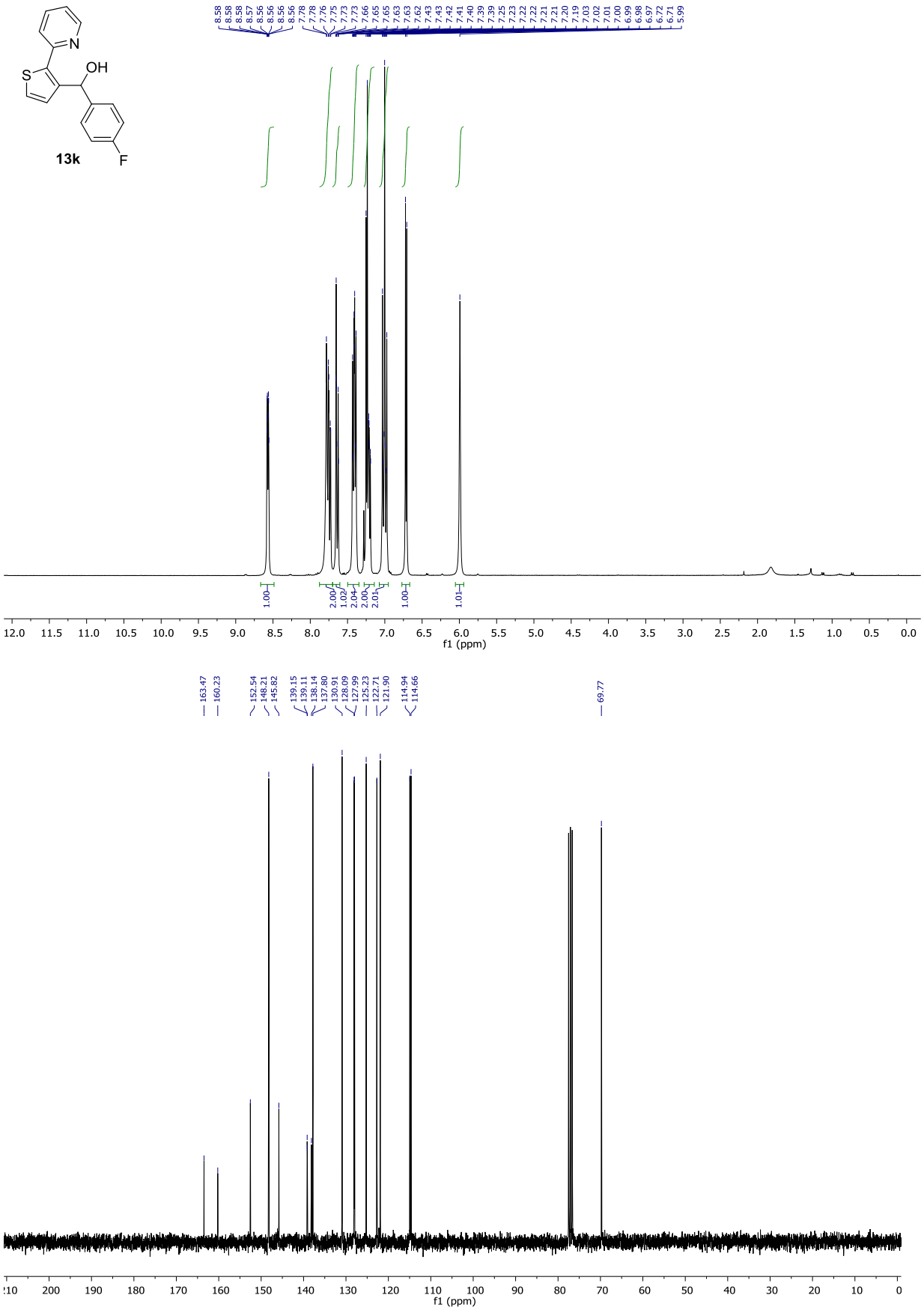


Figure S60. ^{1}H NMR and ^{13}C NMR spectra of **13k**

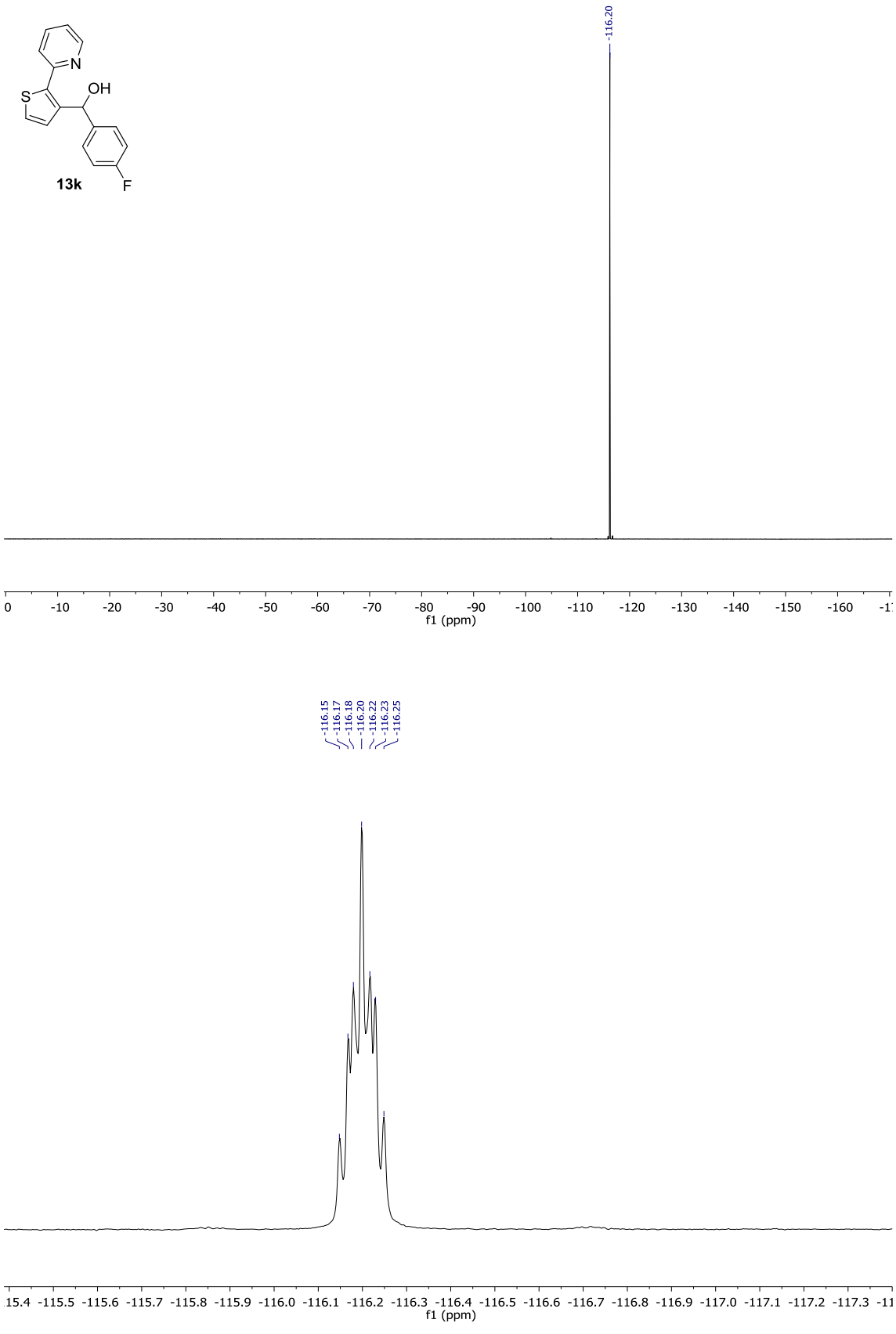


Figure S61. ^{19}F NMR (^{1}H-decoupled and coupled) spectra of **13k**

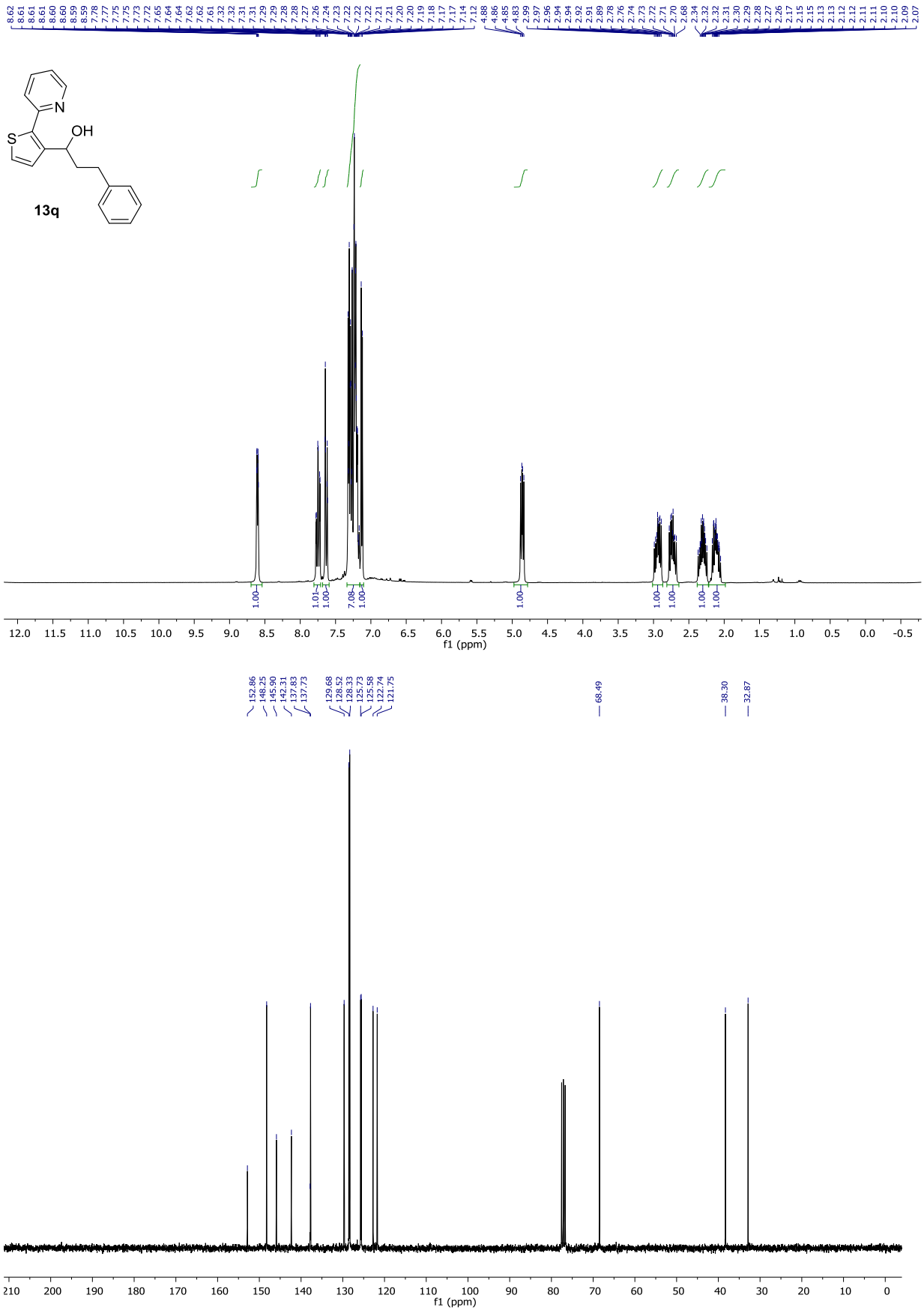


Figure S62. ^{1}H NMR and ^{13}C NMR spectra of **13q**

.

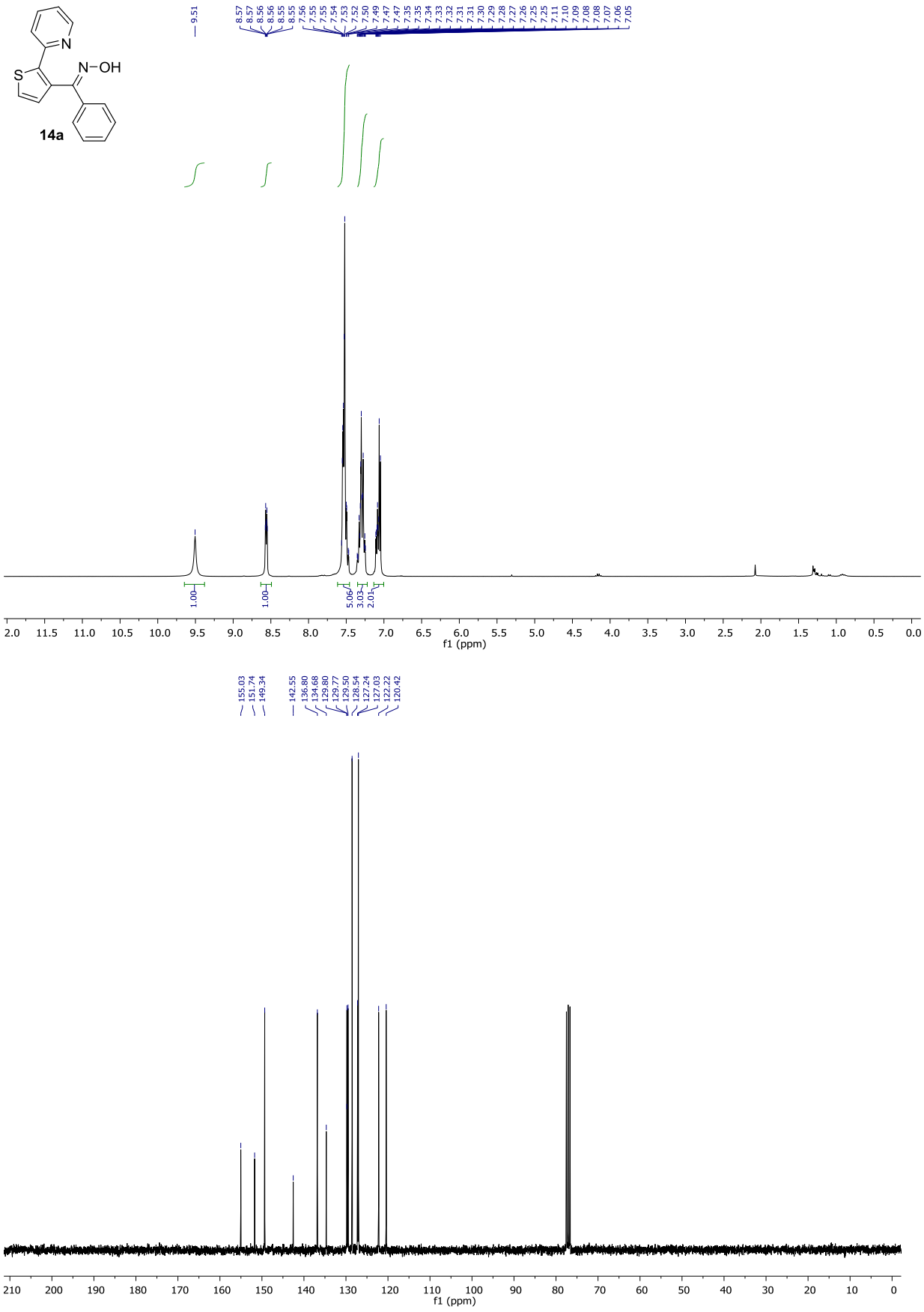


Figure S63. ^{1}H NMR and ^{13}C NMR spectra of **14a**

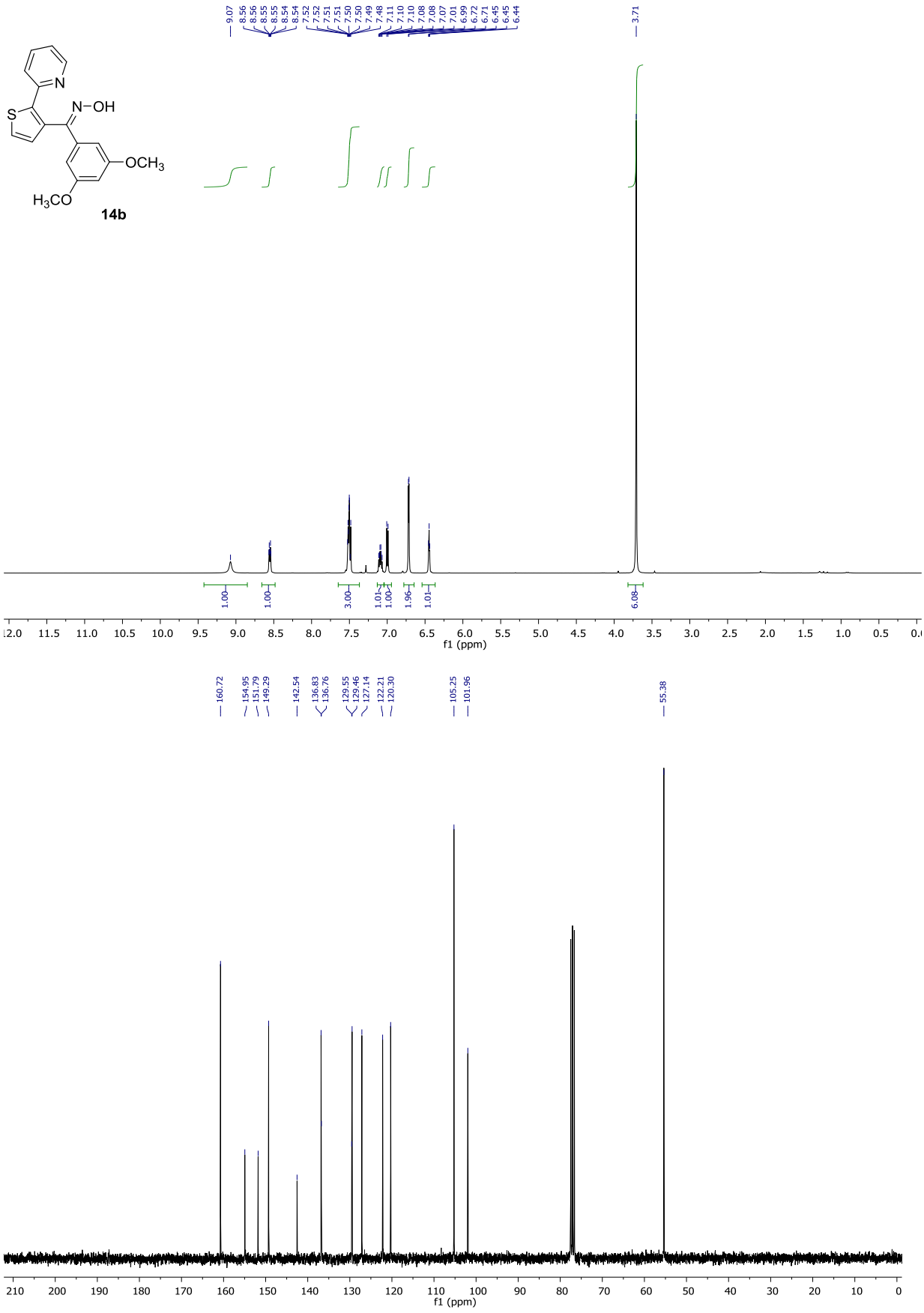


Figure S64. ^{1}H NMR and ^{13}C NMR spectra of **14b**

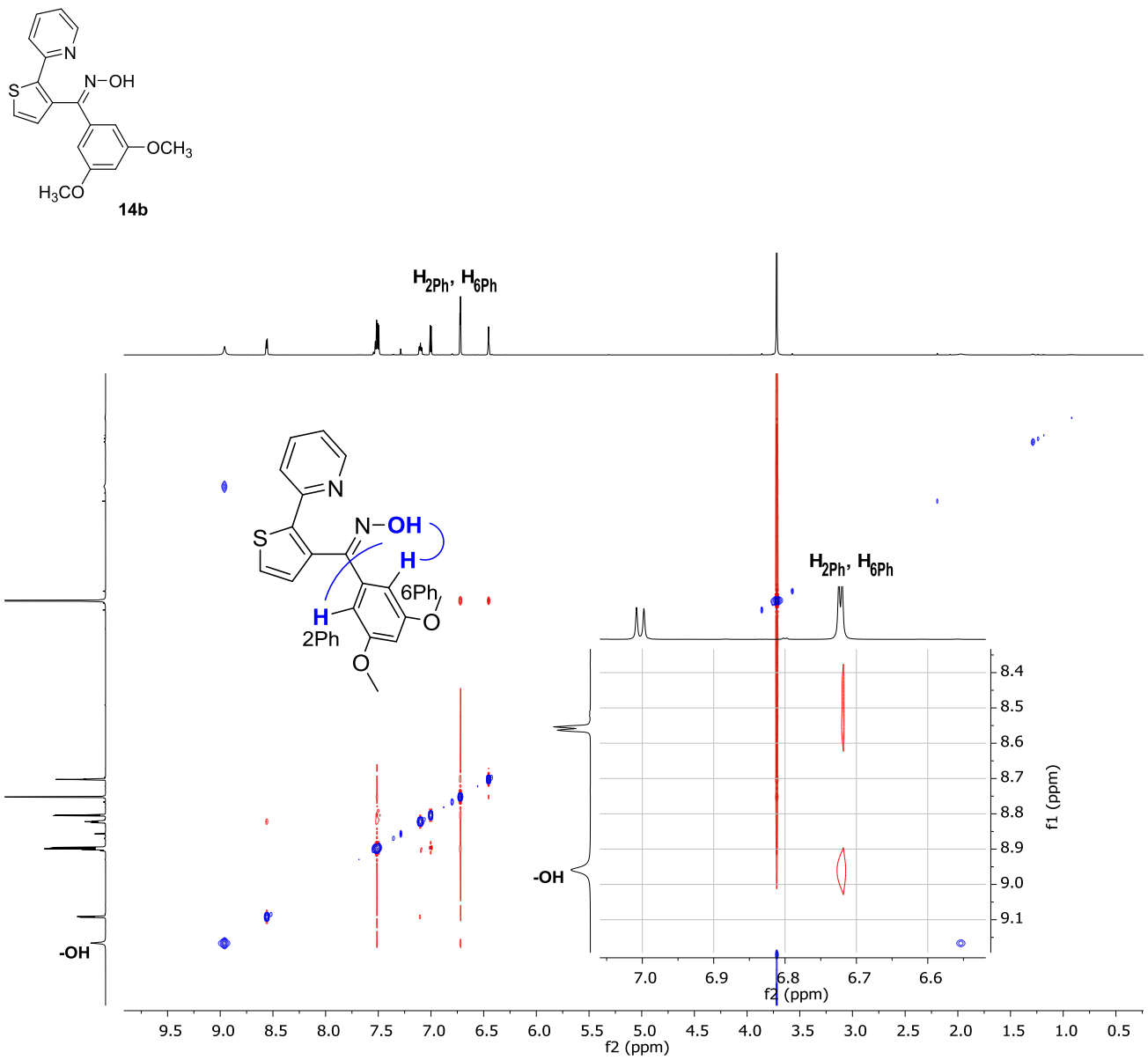


Figure S65. NOESY experiment for **14b**

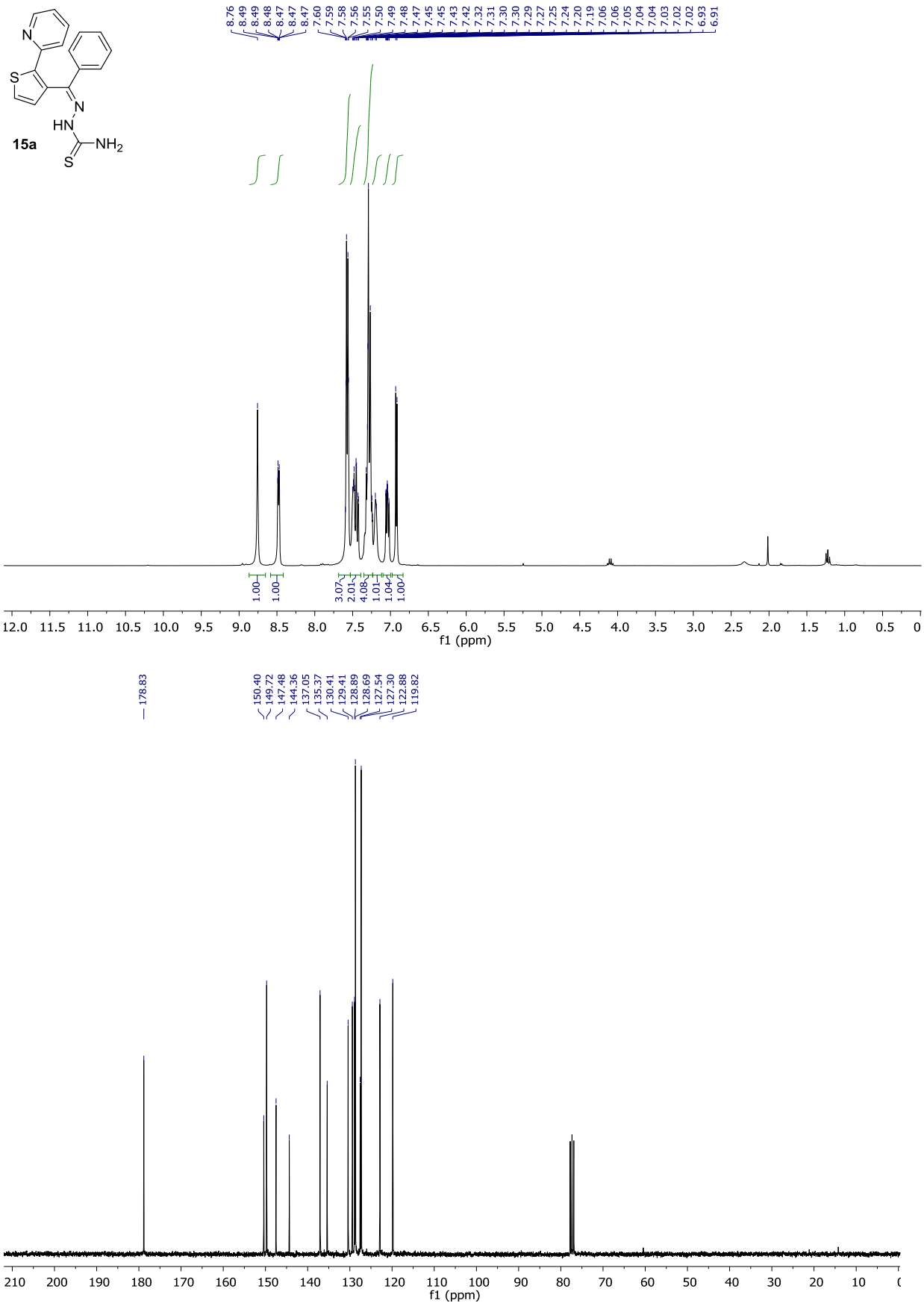


Figure S66. ^{1}H NMR and ^{13}C NMR spectra of **15a**

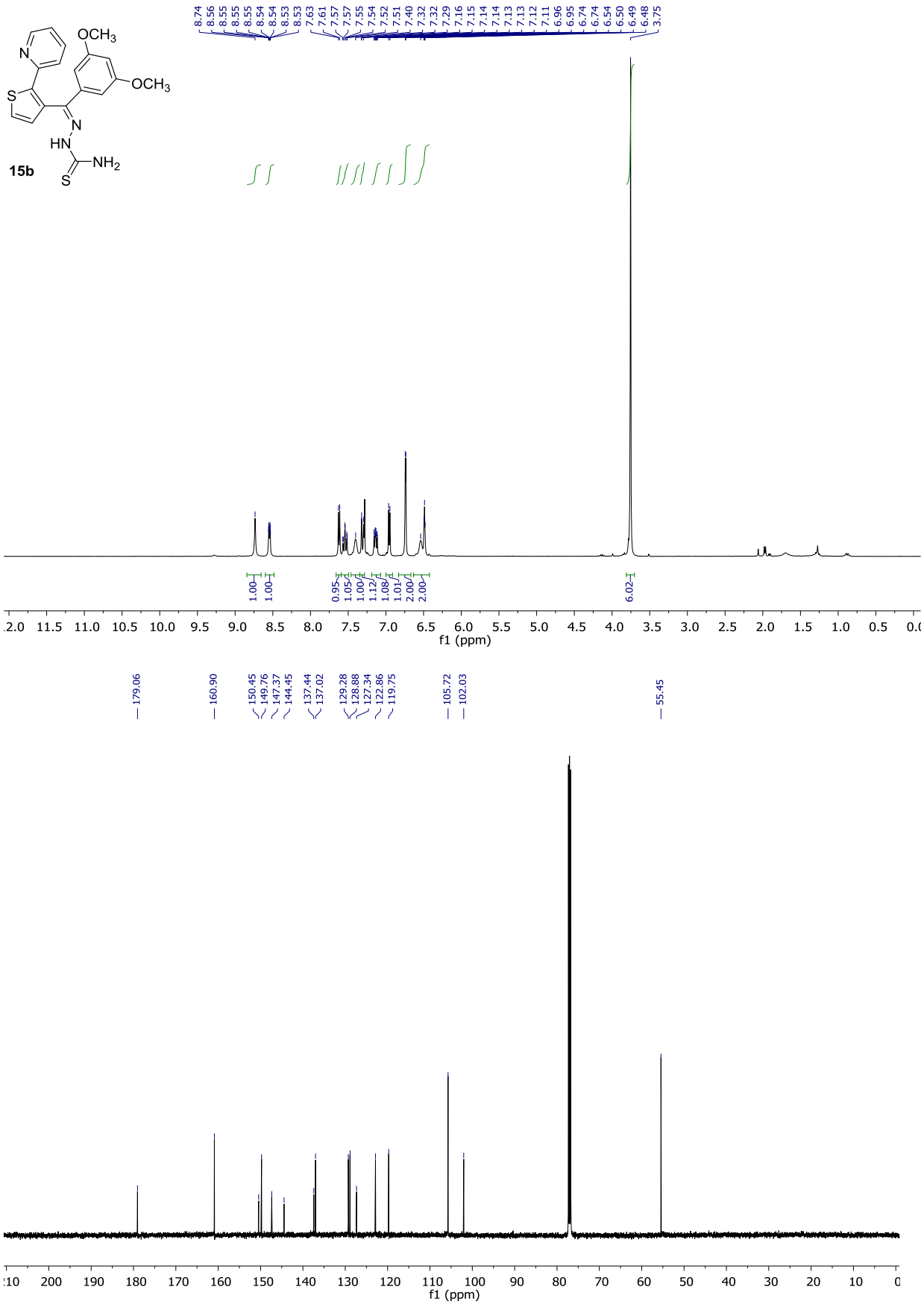


Figure S67. ^{1}H NMR and ^{13}C NMR spectra of **15b**

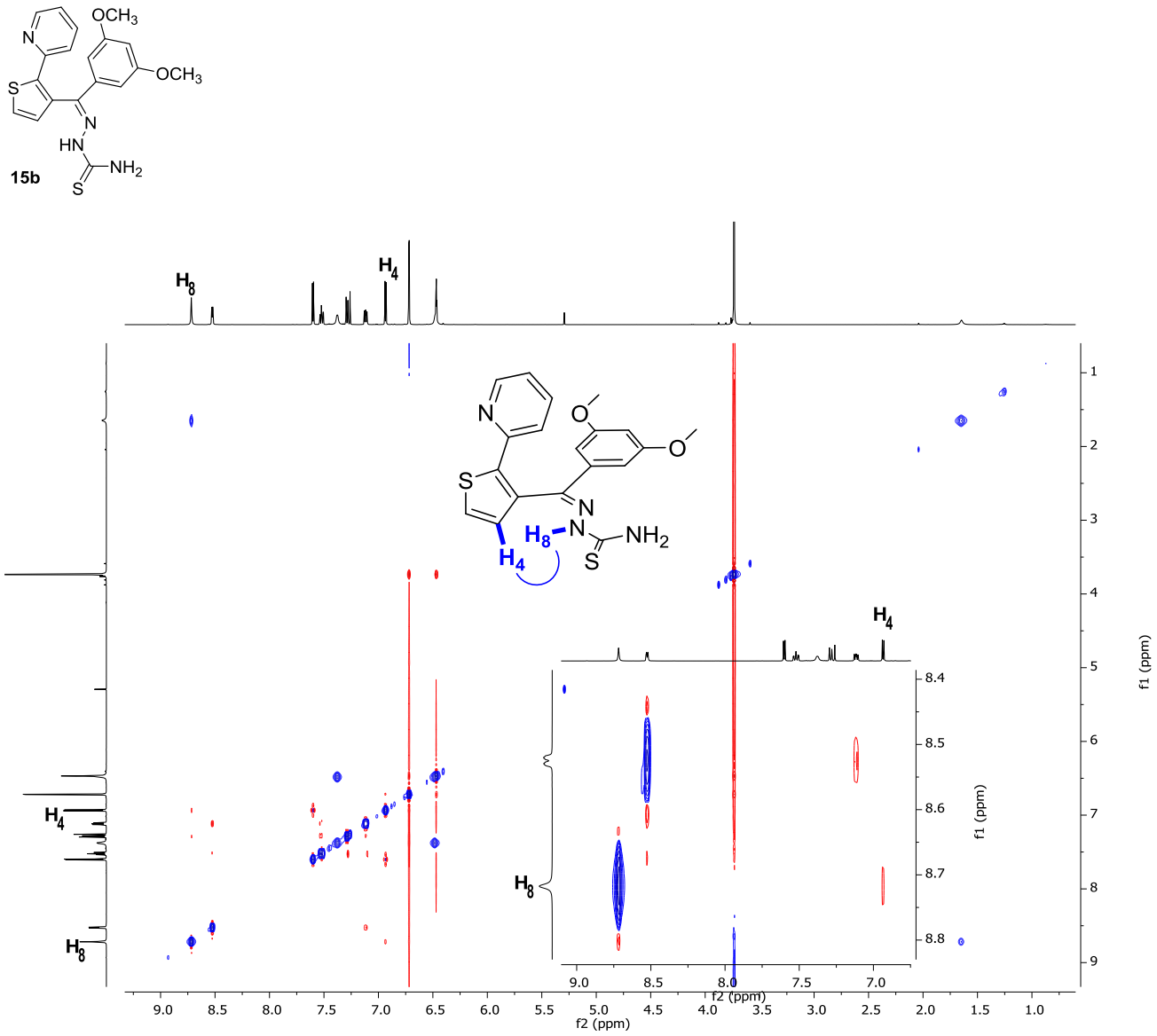


Figure S68. NOESY experiment for **15b**

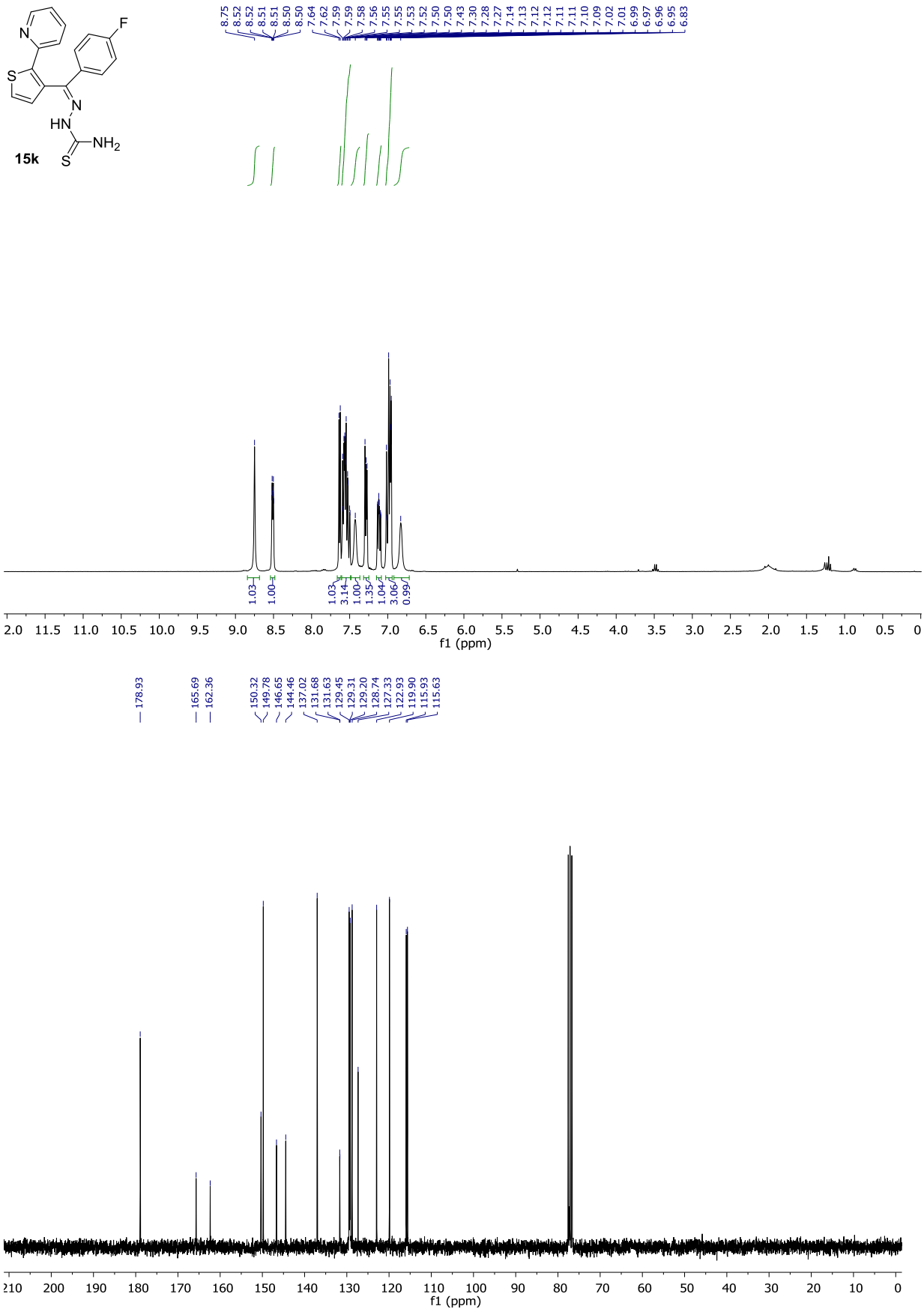


Figure S69. ^{1}H NMR and ^{13}C NMR spectra of **15k**

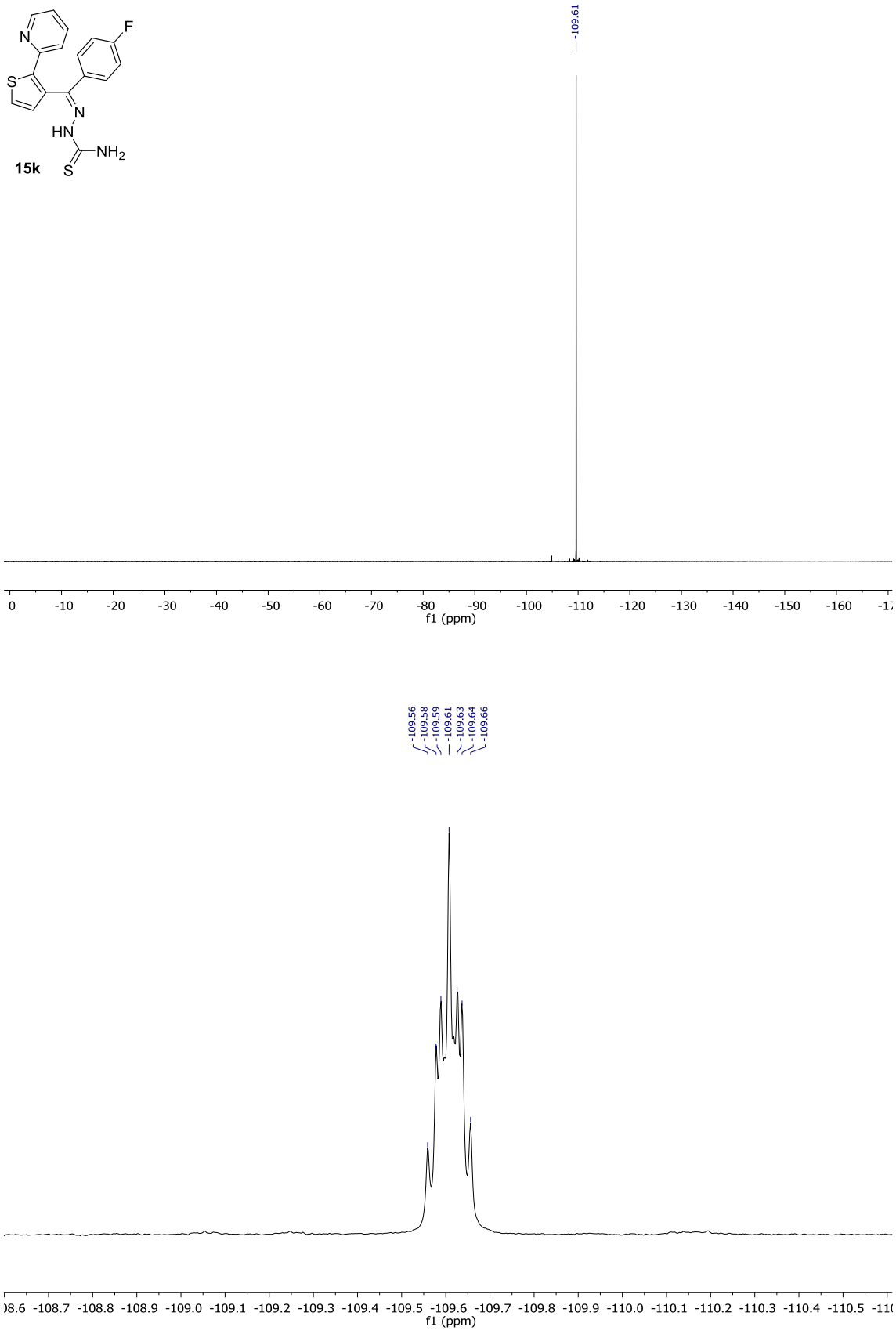


Figure S70. ^{19}F NMR (^{1}H-decoupled and coupled) spectra of **15k**

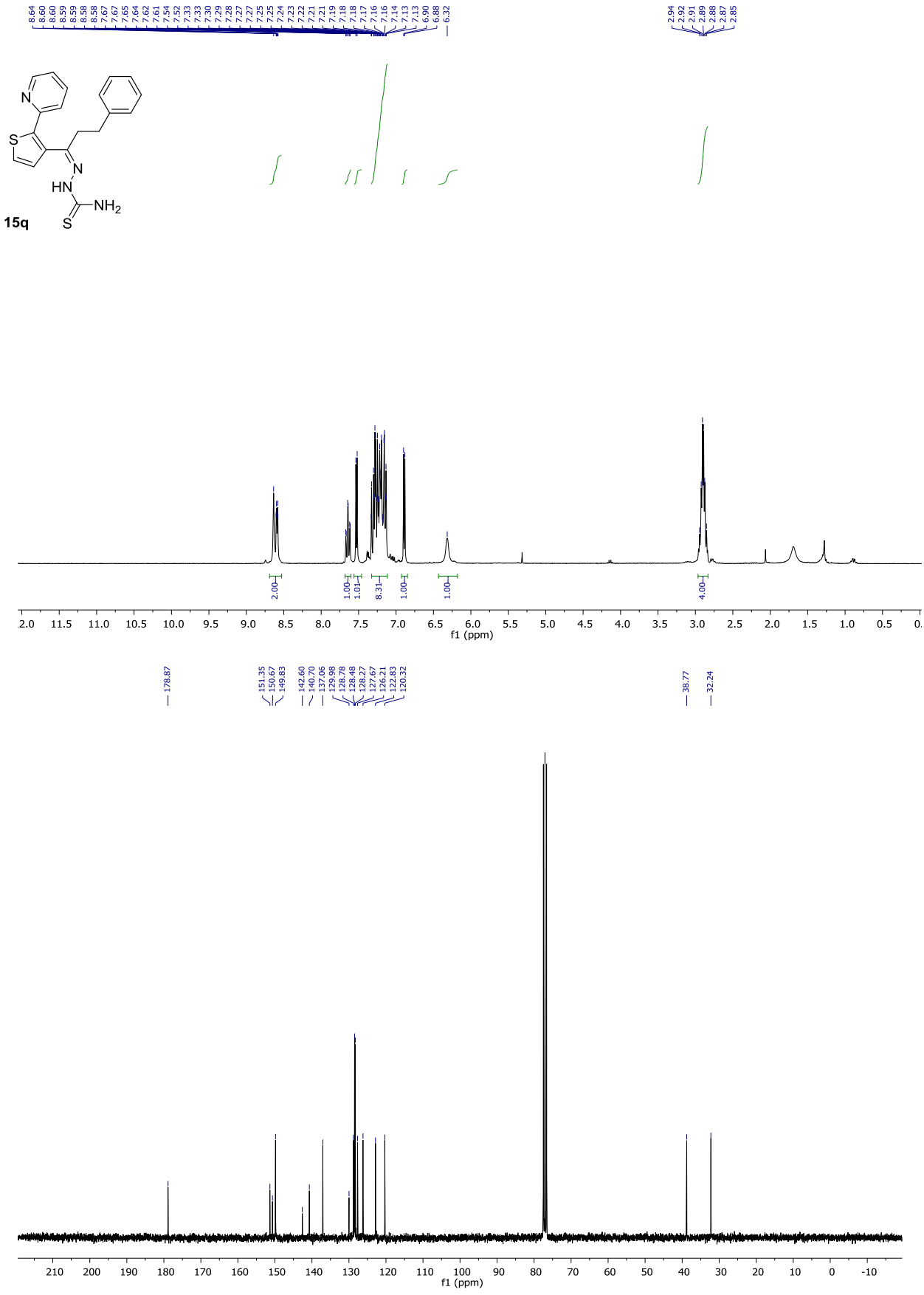


Figure S71. ^{1}H NMR and ^{13}C NMR spectra of **15q**

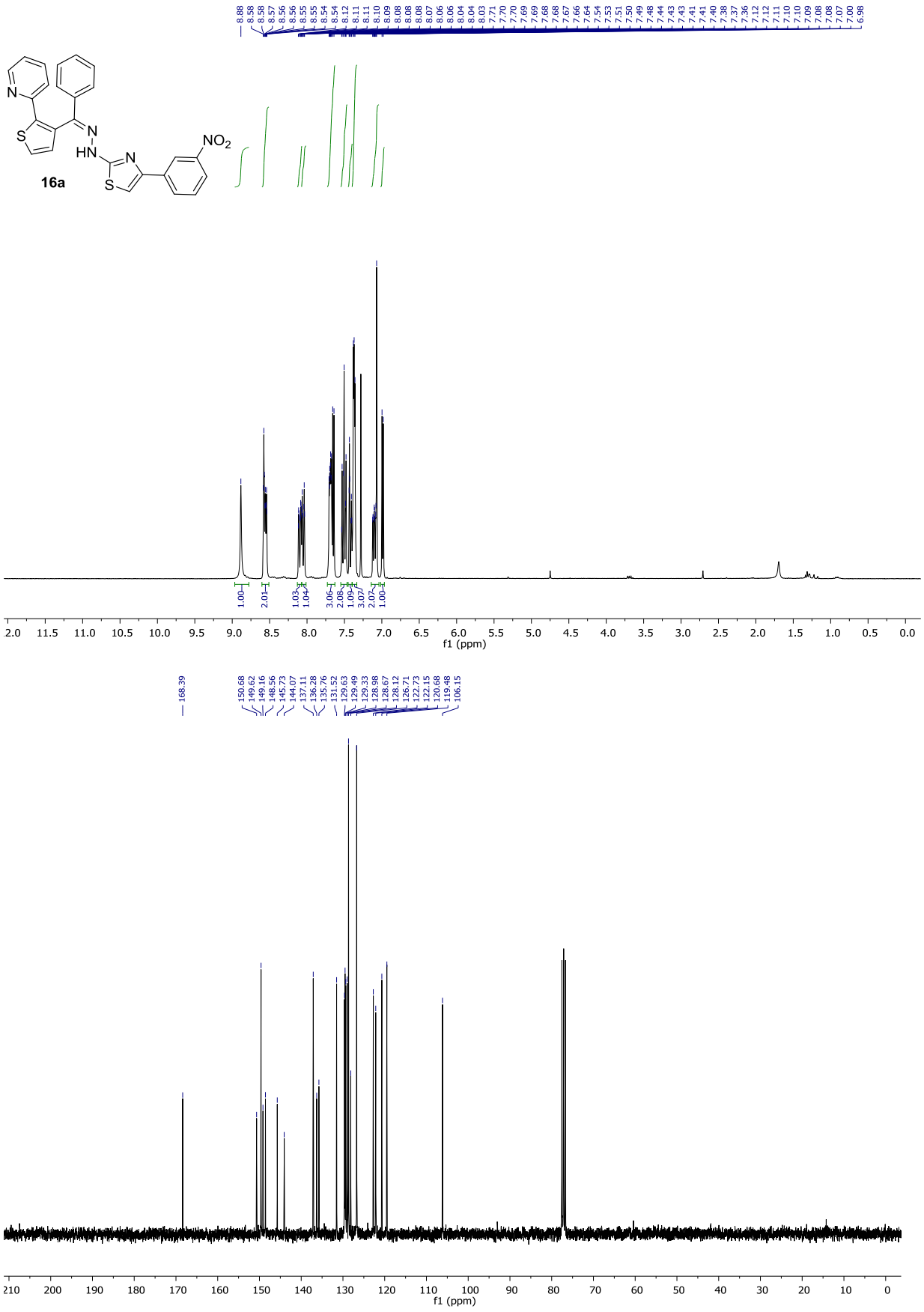


Figure S72. ^{1}H NMR and ^{13}C NMR spectra of **16a**

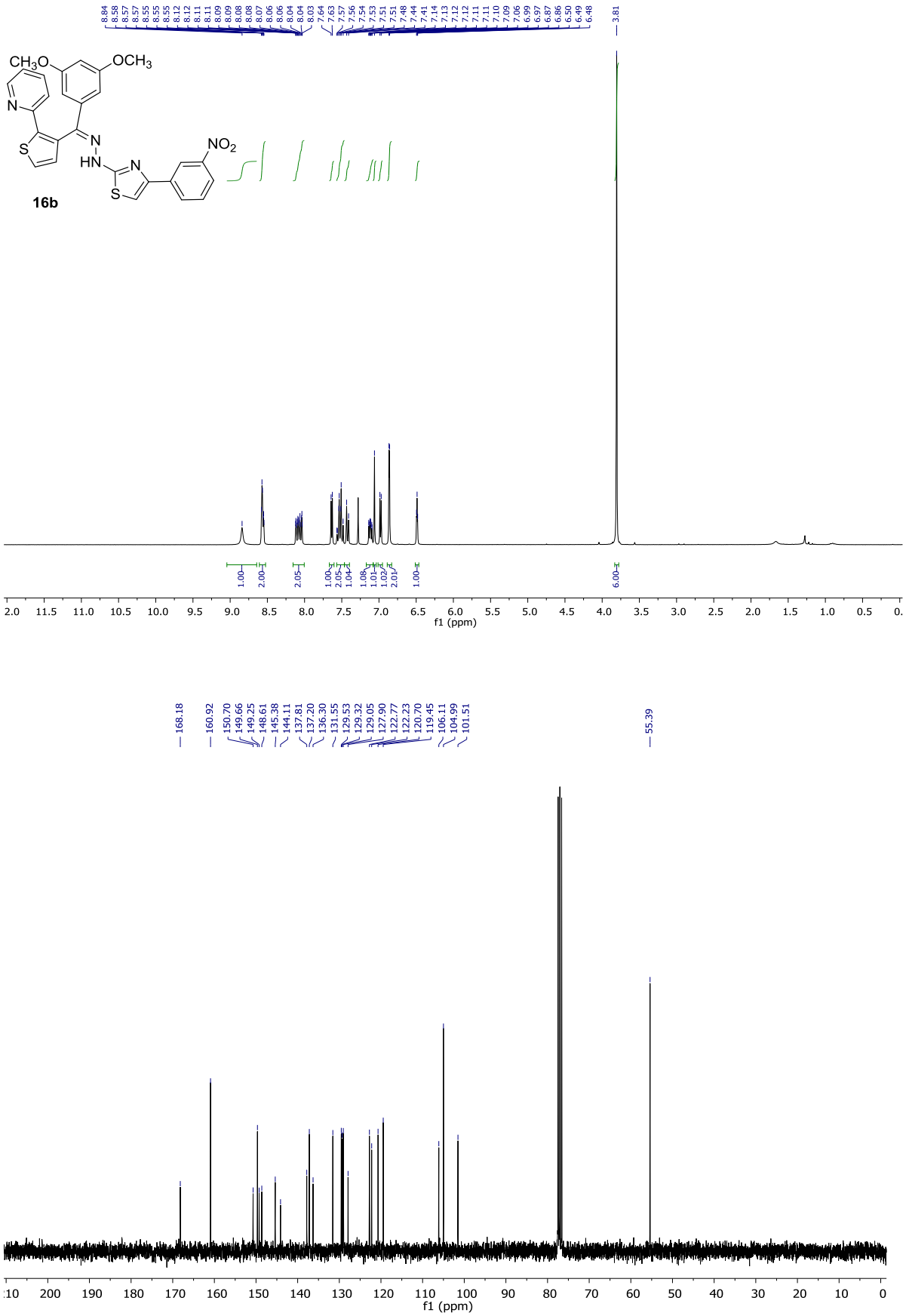
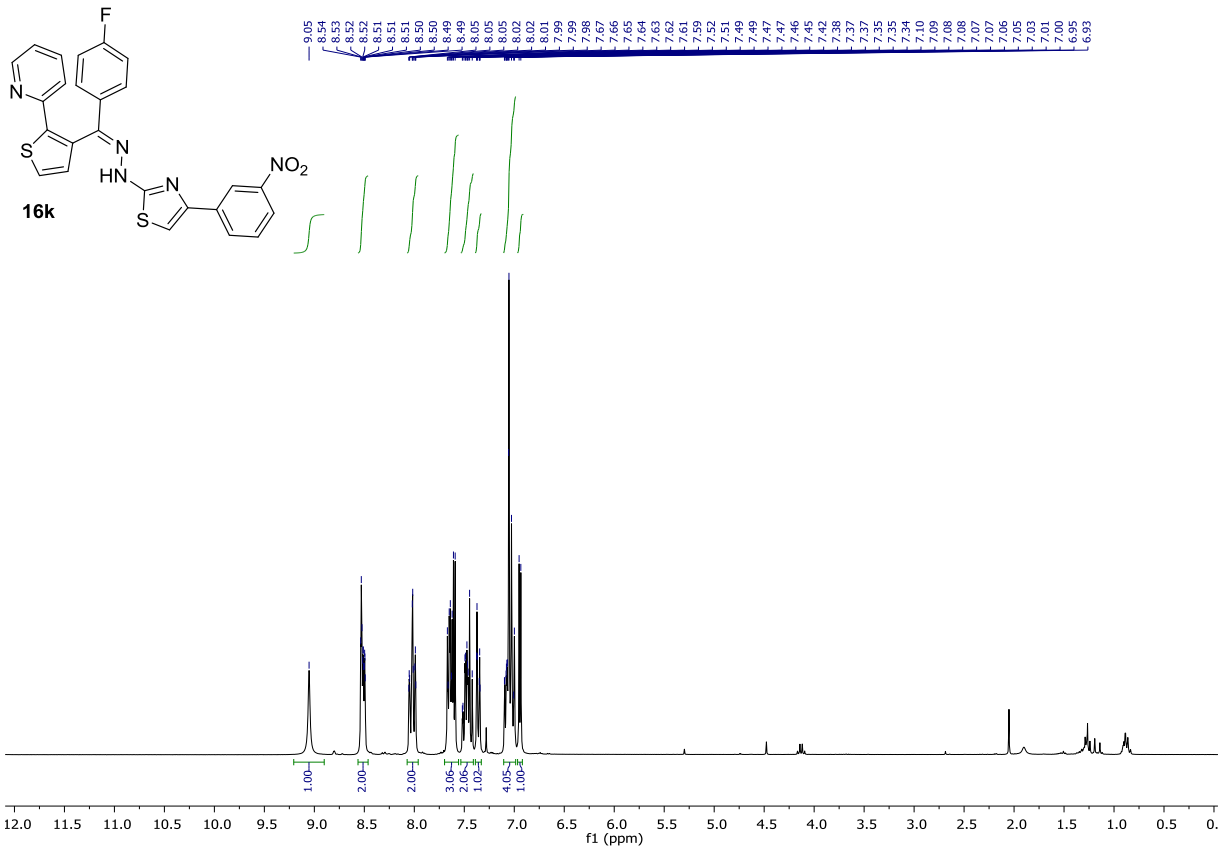


Figure S73. ^{1}H NMR and ^{13}C NMR spectra of **16b**



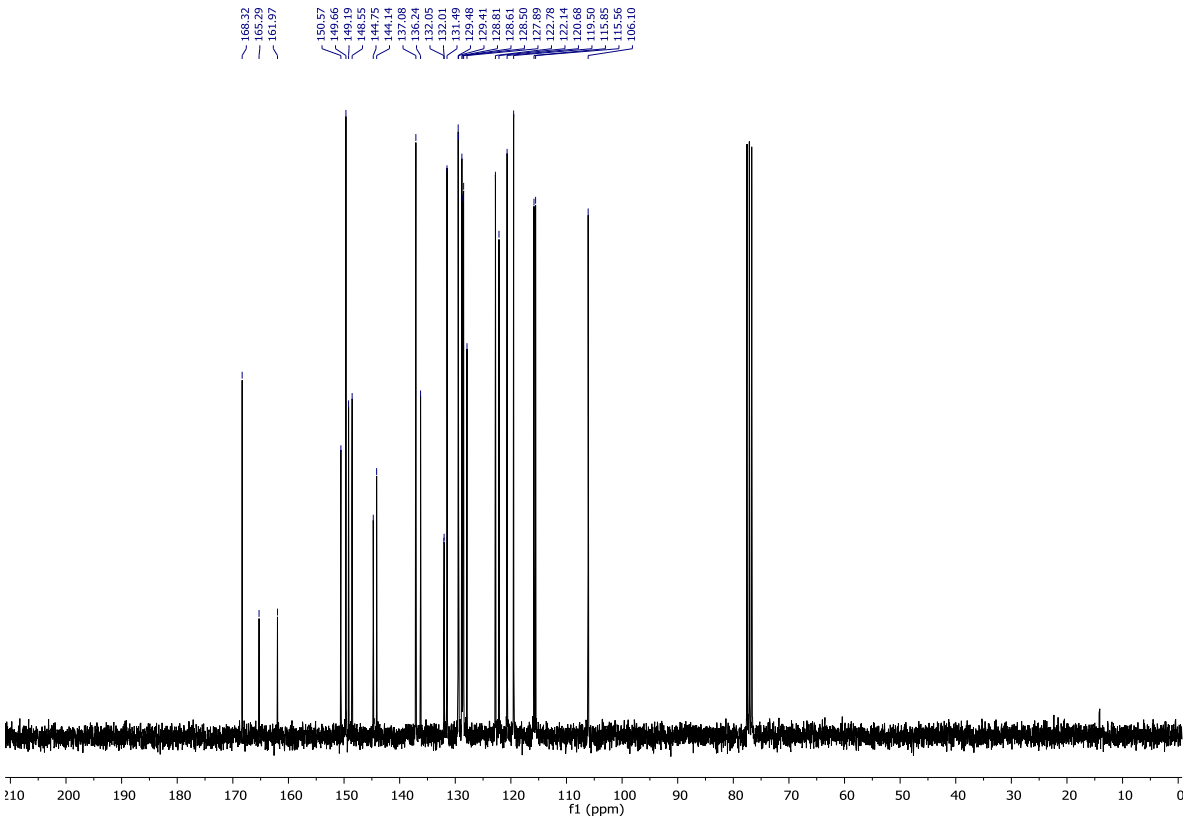


Figure S74. ^{1}H NMR and ^{13}C NMR spectra of **16k**

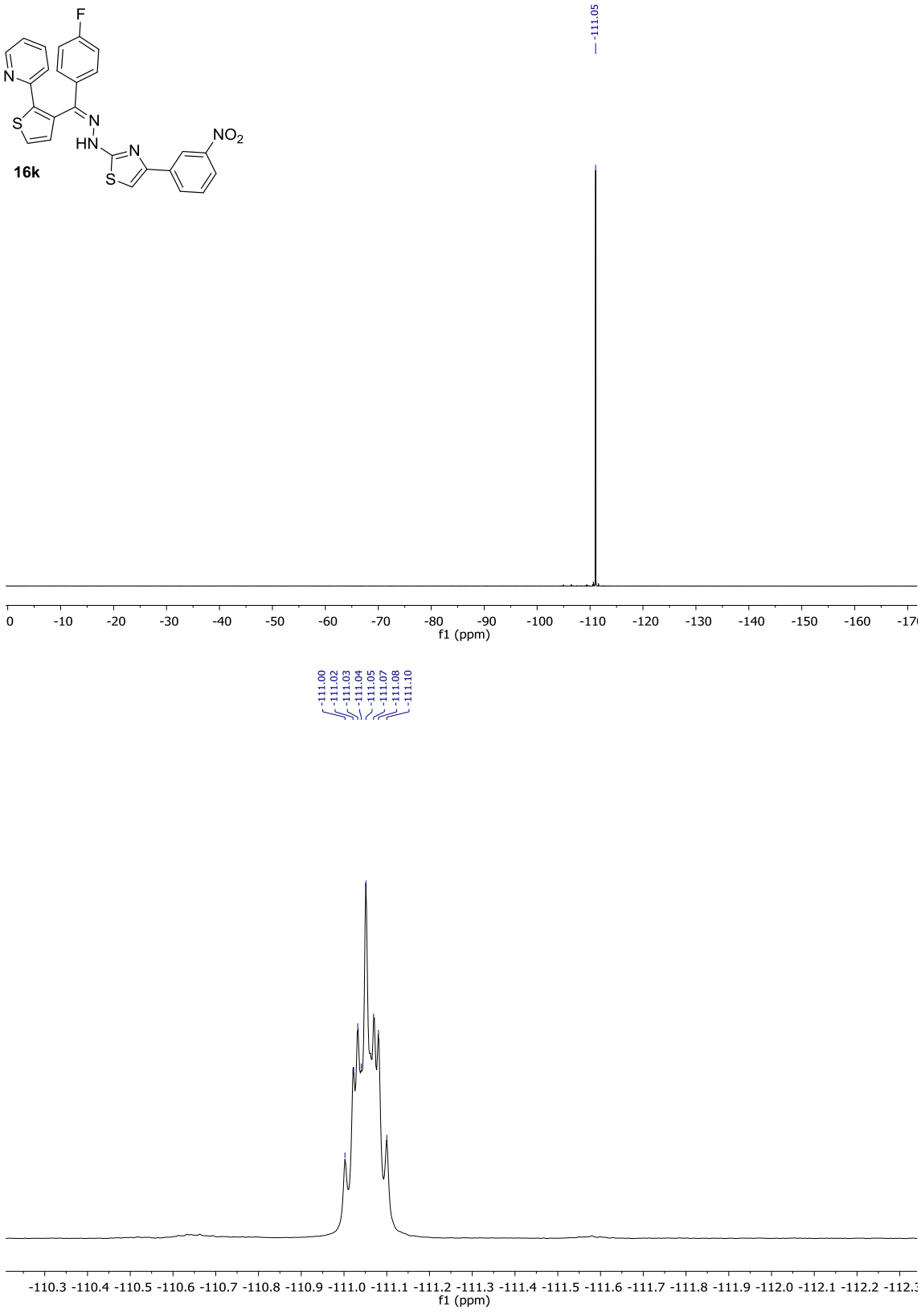


Figure S75. ^{19}F NMR (^{1}H-decoupled and coupled) spectra of **16k**

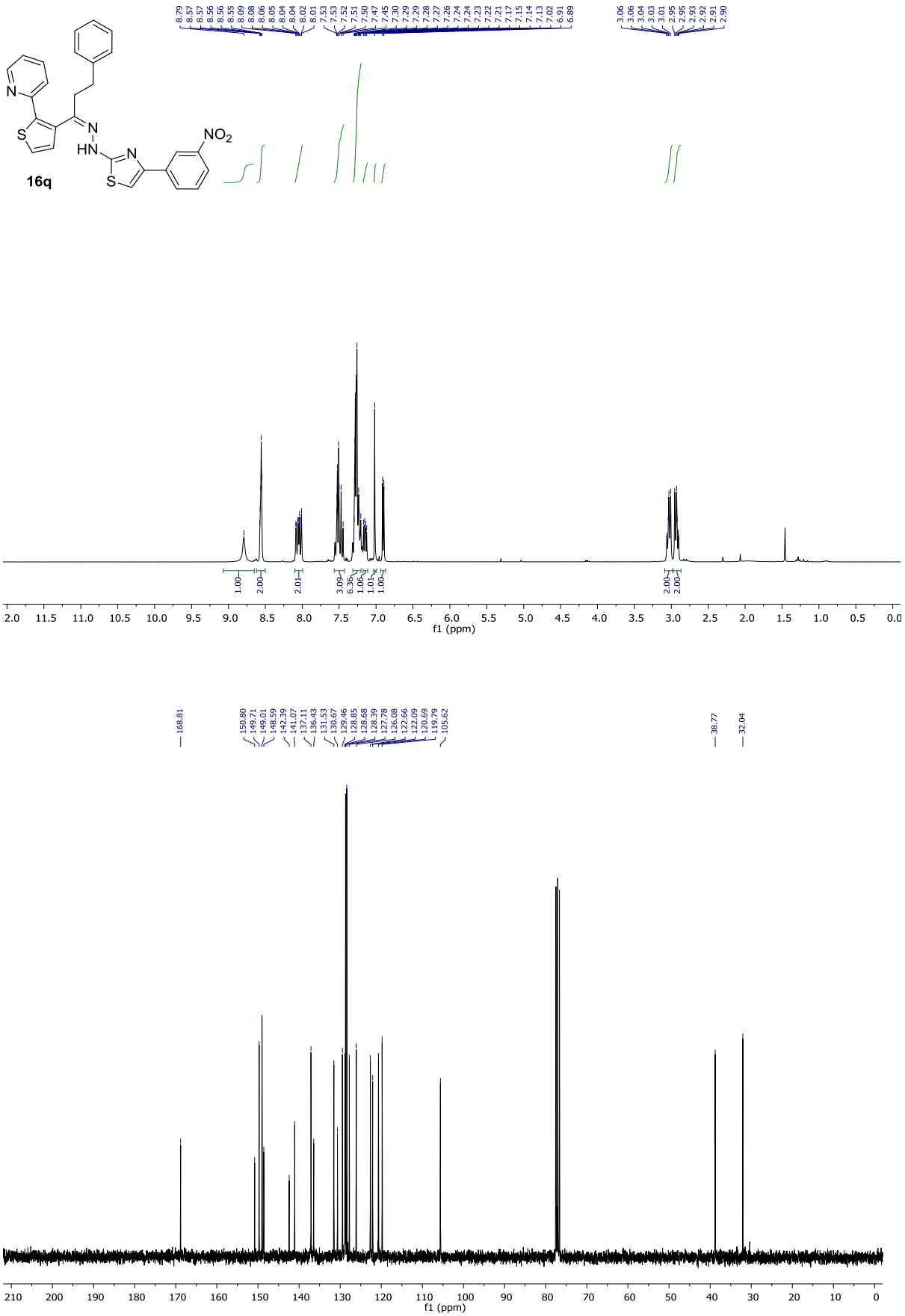


Figure S76. ^{1}H NMR and ^{13}C NMR spectra of **16q**

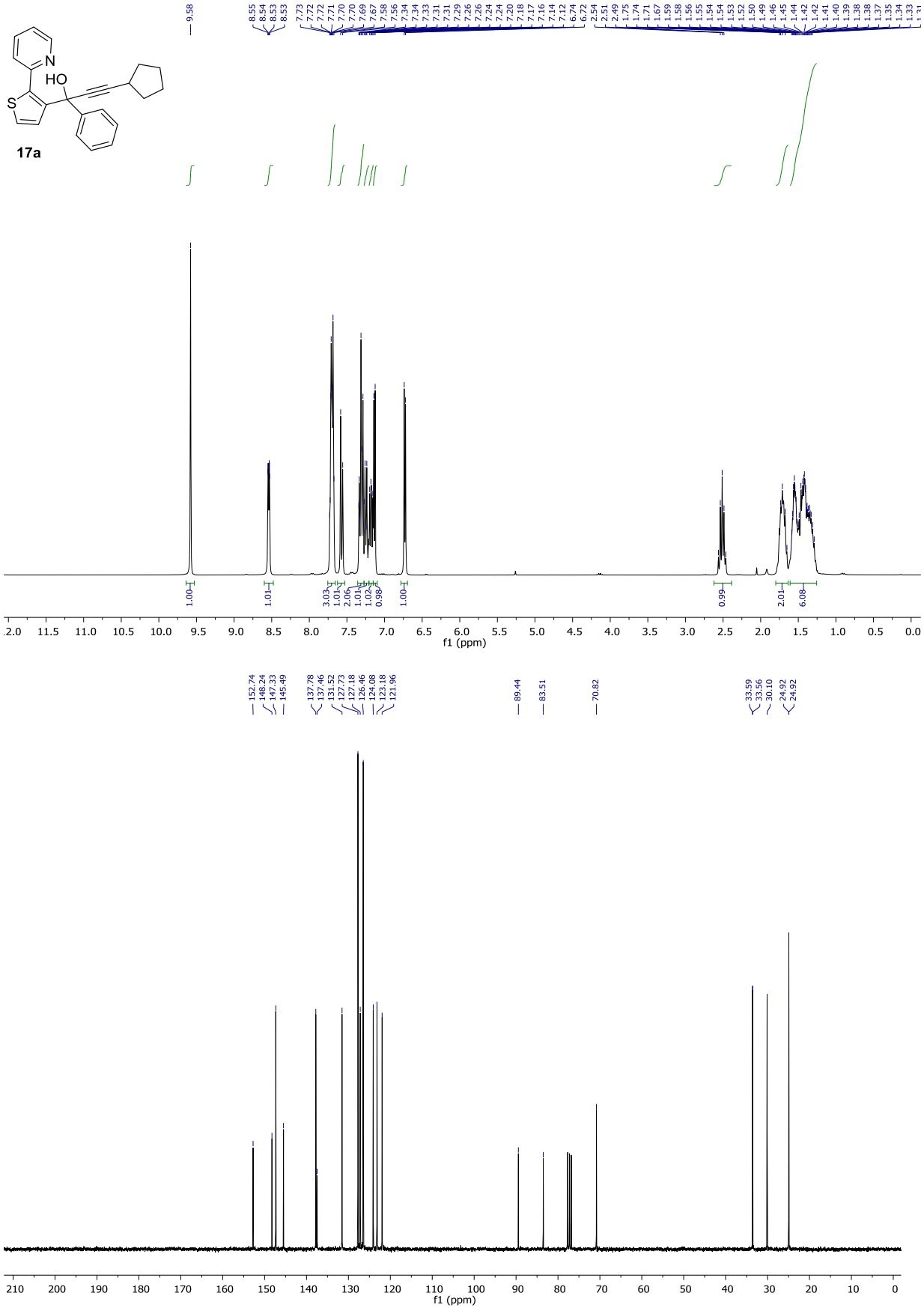


Figure S77. ^{1}H NMR and ^{13}C NMR spectra of **17a**

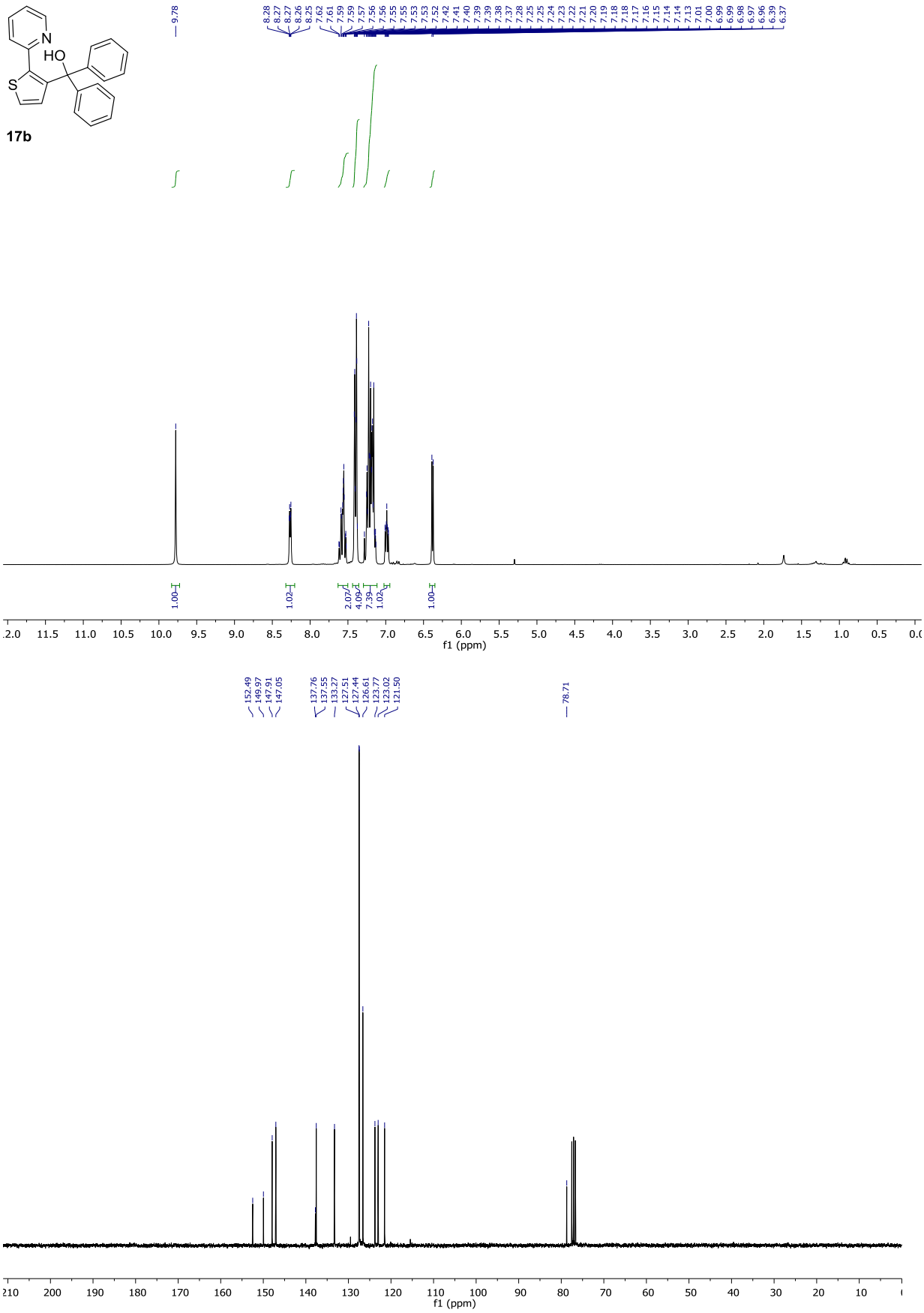


Figure S78. ^{1}H NMR and ^{13}C NMR spectra of **17b**

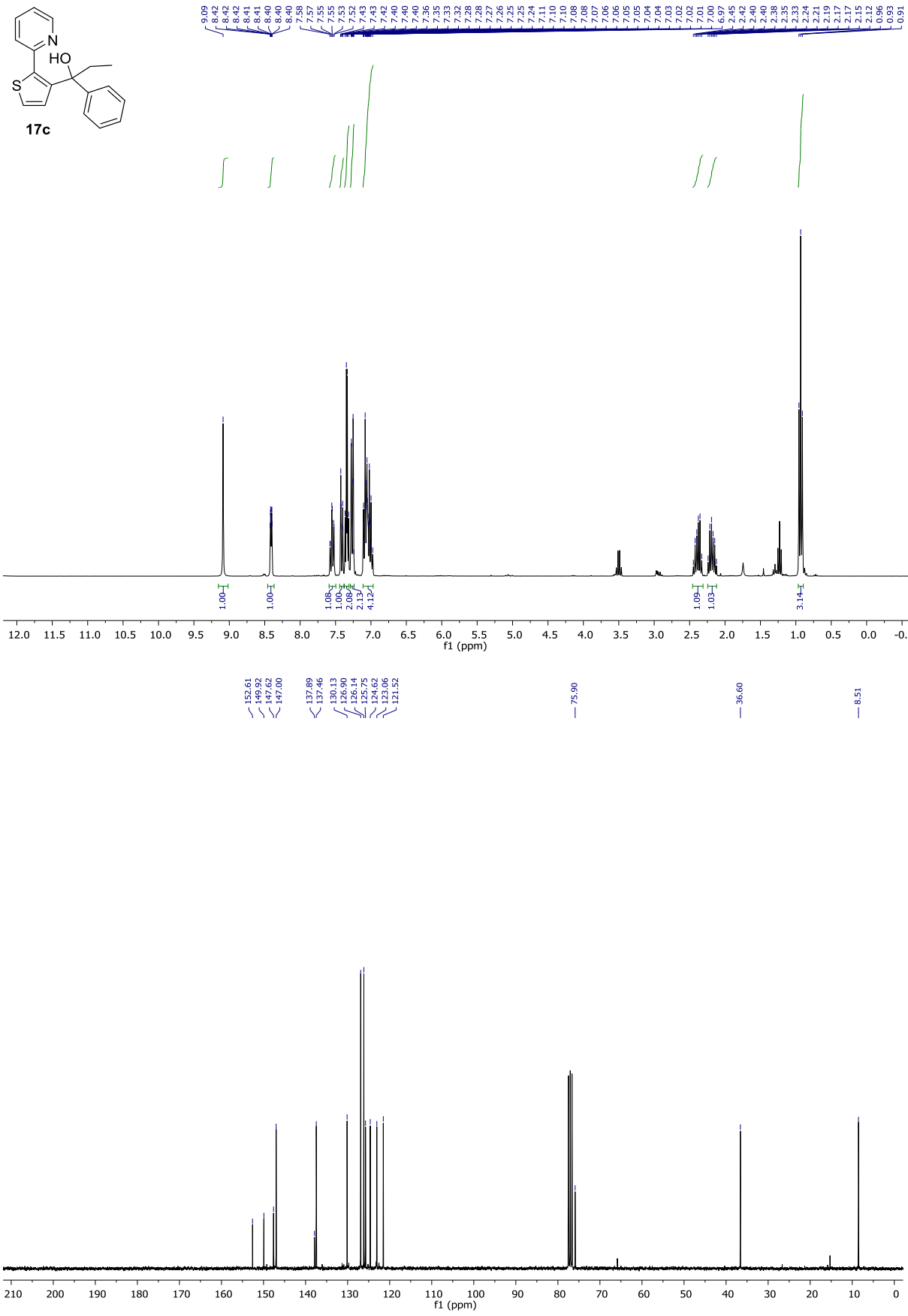


Figure S79. ^{1}H NMR and ^{13}C NMR spectra of **17c**

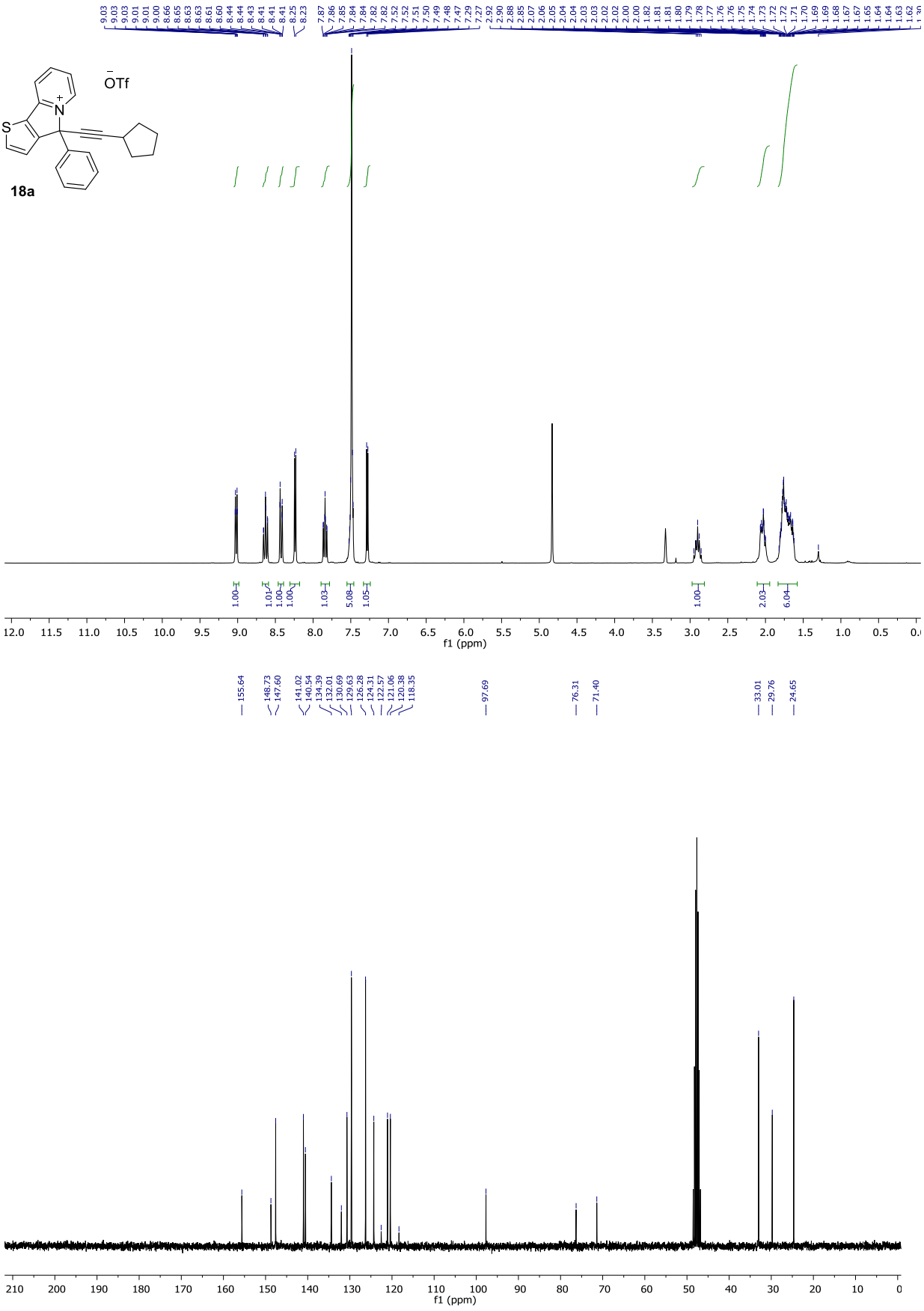


Figure S78. ^{1}H NMR and ^{13}C NMR spectra of **18a**

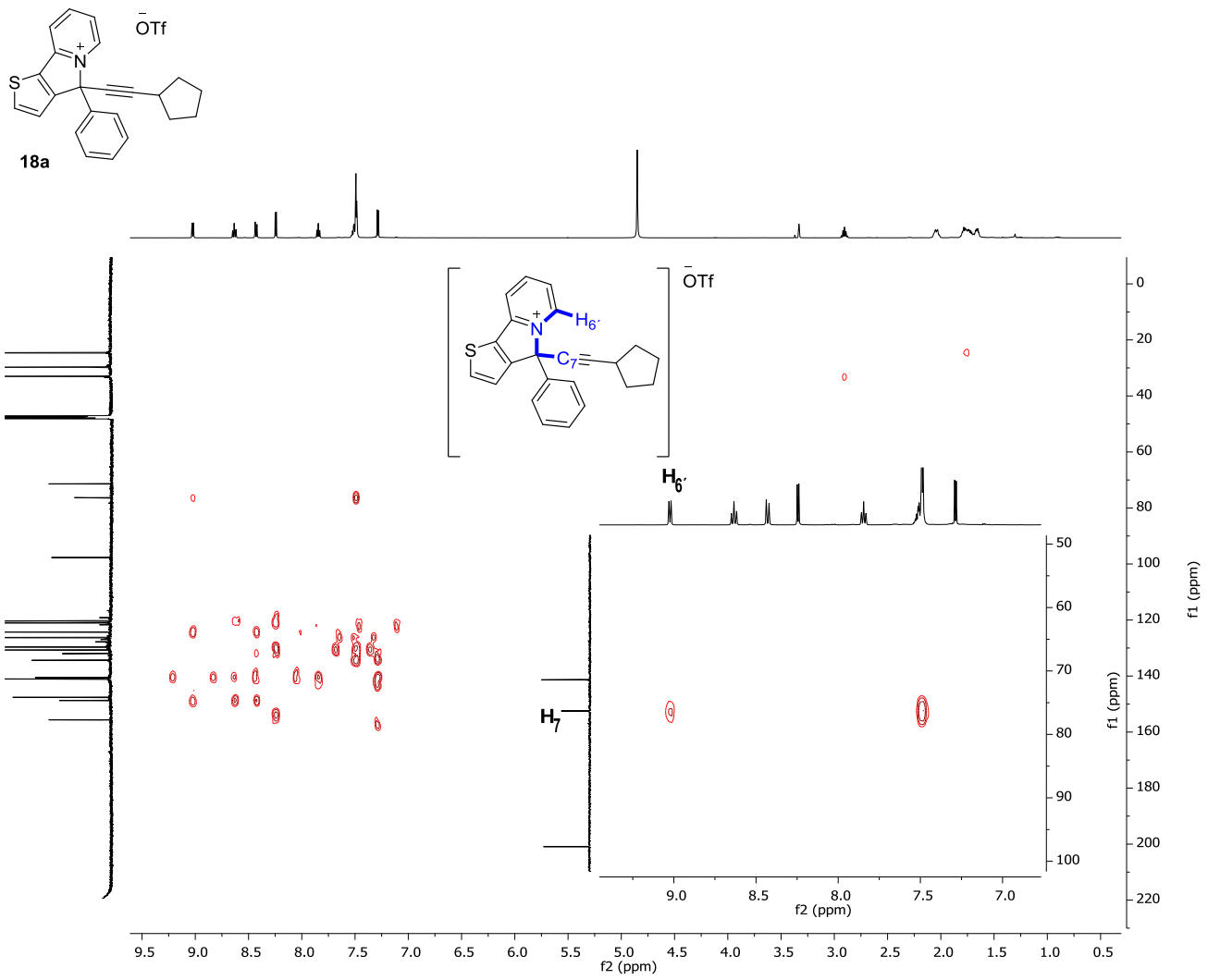


Figure S79. HMBC experiment for **18a**

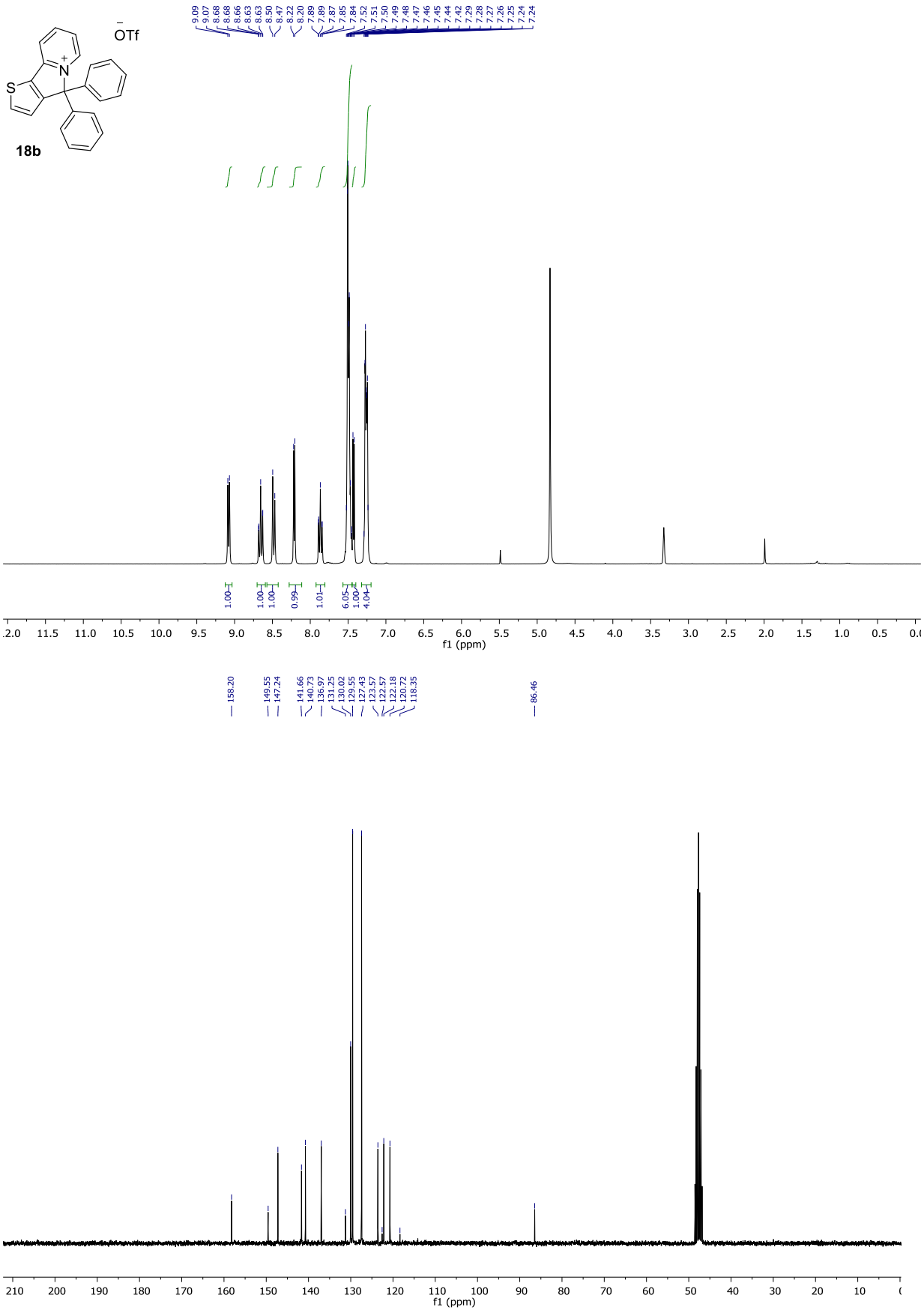


Figure S80. ^{1}H NMR and ^{13}C NMR spectra of **18b**

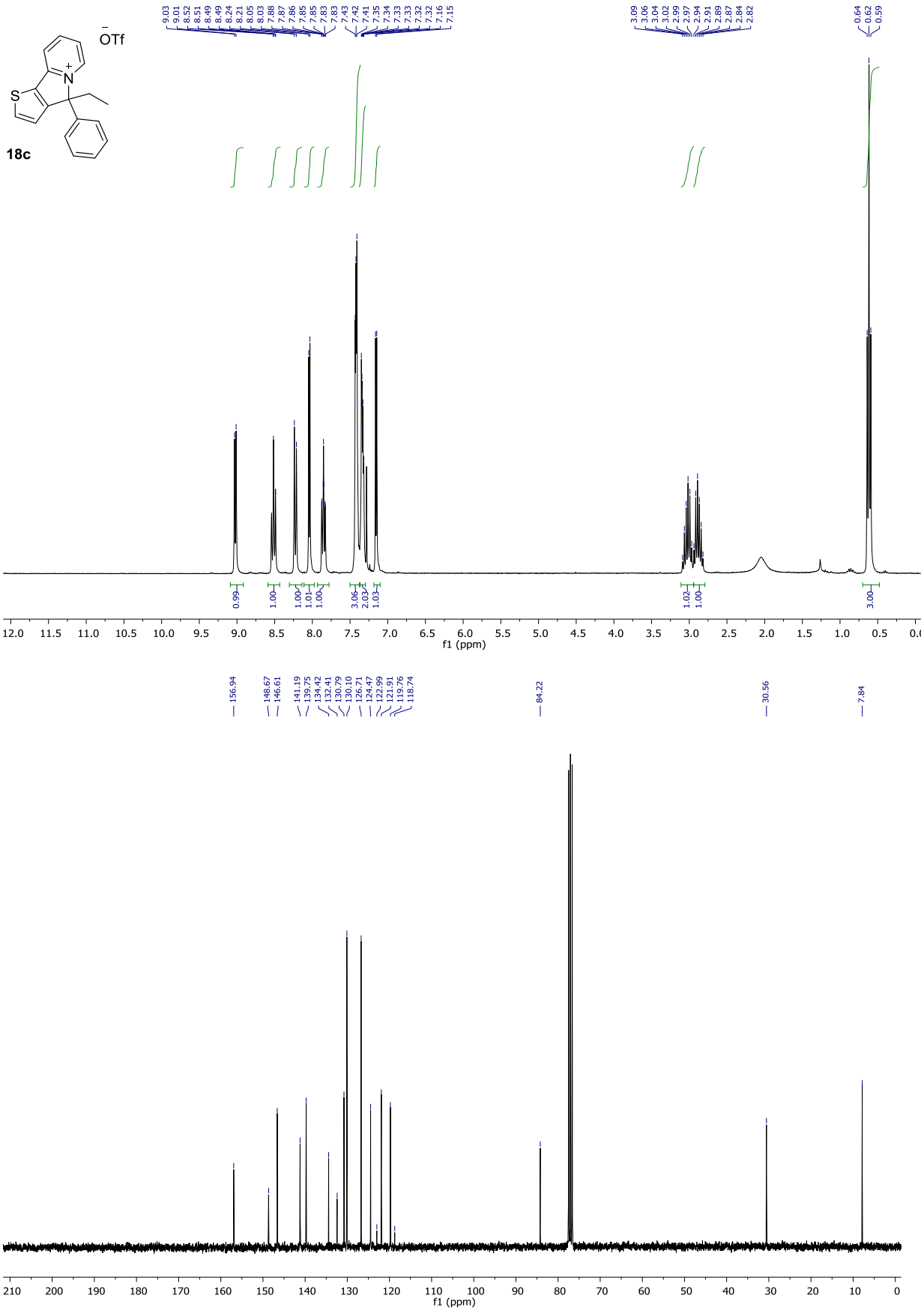


Figure S81. ^{1}H NMR and ^{13}C NMR spectra of **18c**