Catalyst-Controlled Chemodivergent C–H Functionalization of 2-Pyridylthiophenes with Allylic Alcohols

Guibin Wan,[‡] Qiang Zhang,[‡] Ying Liu, Haowei Zeng, Taoyuan Liang, Shuangliang Zhao* and Zhuan Zhang*

School of Chemistry and Chemical Engineering, Guangxi University, Nanning, Guangxi 530004, P. R. China

Email: szhao@gxu.edu.cn; zhuan.zhang@gxu.edu.cn

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1. General information

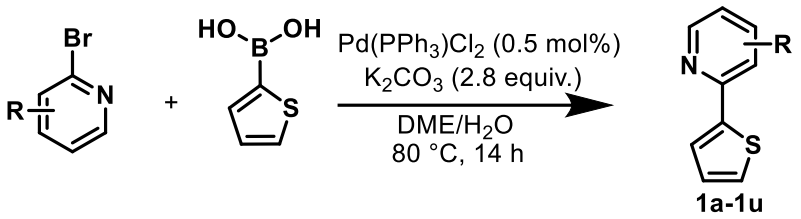
All the reagents were purchased from Bide Pharmatech Ltd. and Energy Chemical. All solvents were purchased from Greagent (Shanghai Titansci incorporated company) and used without further purification. Unless otherwise stated, all reactions were carried out in oven-dried glassware under air atmosphere. All heating reactions were heated by metal sand bath (WATTCAS, LAB-500).

^{1}H-NMR spectra were obtained on Bruker-600. NMR spectra for all the samples were recorded in deuterochloroform ($CDCl_3$). Chemical shifts (δ) were reported in parts per million relative to residual chloroform (7.28 ppm for ^{1}H; 77.23 ppm for ^{13}C), constants were reported in Hertz. ^{1}H NMR assignment abbreviations were the following: singlet (s), doublet (d), triplet (t), quartet (q), doublet of doublets (dd), doublet of triplets (dt), triplet of doublets (td), triplet of triplets (tt) and multiplet (m). ^{13}C NMR spectra were recorded at 151 MHz on the same spectrometer and reported in ppm. All spectra were processed using the MestReNova program.

High-resolution mass spectra (HRMS) were recorded on a mass spectrometer (Thermo fisher Q Exactive HRMS) using electrospray ionization-time of flight (ESI-TOF) reflection experiments.

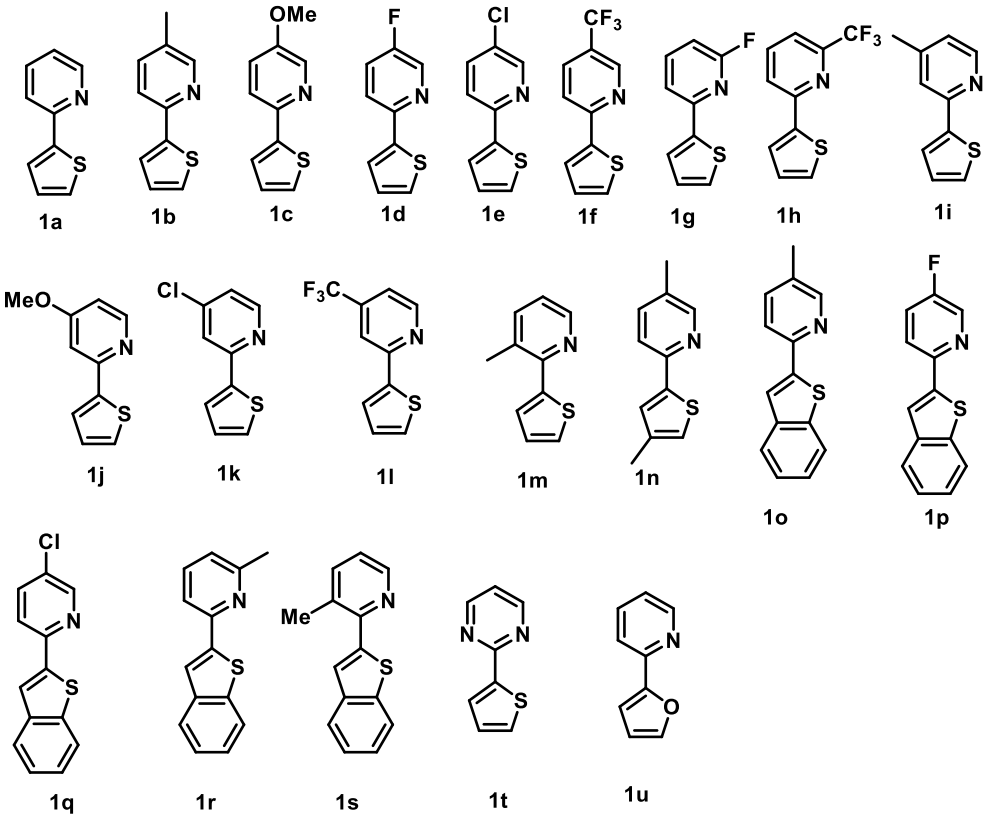
2. Experimental procedure

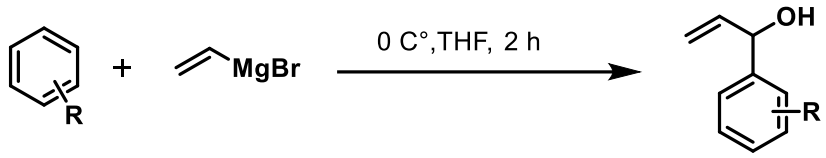
2.1 Procedure for the synthesis of starting materials



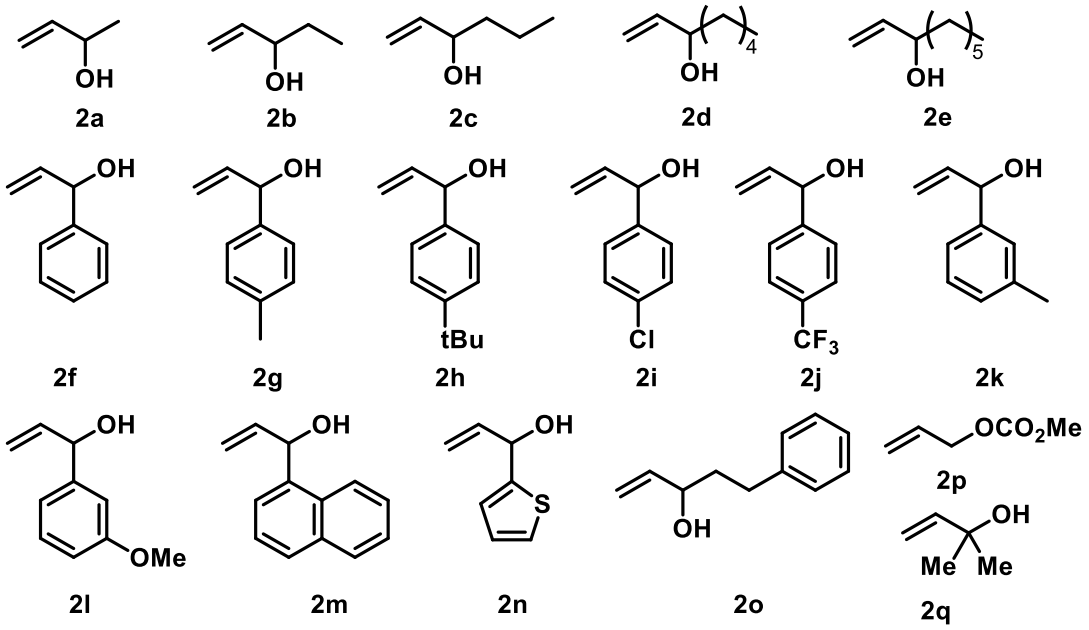
1a-1u

Synthesis of substrates 1a-1u[1]: To a solution of boronic acid derivatives (1.2 mmol, 1.2 equiv.), K_2CO_3 (2.8 mmol, 2.8 equiv.) and $[Pd(PPh_3)_2Cl_2]$ (3.5 mg, 0.5 mol%) in DME (30 mL) and H_2O (14 mL) was added substituted 2-bromopyridine derivatives (1.0 mmol, 1.0 equiv.). The reaction mixture was stirred at 80 °C for 14 h. Then the reaction mixture was quenched with water (10 mL) and extracted with EtOAc (3 x 20 mL). The combined organic phases were washed with brine (25 mL), dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate = 30:1) to get the desired products.





Synthesis of substrates 2f-2o[2]: In a flame-dried 100 mL round-bottomed flask equipped with a stir bar, benzaldehyde (2.0 mL, 19.8 mmol) was dissolved in THF (40 mL), and the mixture was cooled to 0°C in an ice bath; vinylmagnesium bromide (1.6 M in Et_2O, 14.85 mL, 23.75 mmol) was then added to the mixture at 0 °C, and the reaction mixture was stirred at this temperature for 2 h. After this period, the reaction was quenched by the addition of 40 mL of 2 M HCl, and the mixture was extracted three times with Et_2O. The combined organic extracts were washed with water and brine, dried over $MgSO_4$, filtered, and concentrated to afford the products. Substrates **2a-2e** and **2p** are commercially available.



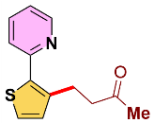
2.2 Rh(III)-catalyzed C3-alkylation of 2-pyridylthiophenes

General Procedure A: To a 15 mL oven dried Schlenk tube, $Cu(OAc)_2$ (0.6 mmol, 2 equiv.), $AgSbF_6$ (0.06 mmol, 20 mol%), 2-pyridylthiophene derivatives **1** (0.3 mmol, 1 equiv.), $[Cp^*RhCl_2]_2$ (4.6 mg, 0.0075 mmol, 2.5 mol%), allylic alcohols **2** (0.6 mmol, 2 equiv.), and DCE (2 mL) were successively added. The reaction mixture was stirred at 120 °C (metal sand bath temperature) for 10 hours under Ar. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired alkylated products **3**.

2.3 Co(III)-catalyzed C3-allylation of 2-pyridylthiophenes

General Procedure B: To a 15 mL oven dried Schlenk tube, $AgSbF_6$ (0.06 mmol, 20 mol%), **1** (0.3 mmol, 1 equiv.), $[Cp^*Co(CO)I_2]_2$ (0.015 mmol, 5 mol%), **2** (0.6 mmol, 2 equiv.), AgOAc (0.15 mmol, 0.5 equiv.) and DCE (2 mL) were successively added. The reaction mixture was stirred at 120 °C (metal sand bath temperature) for 10 hours under air. After cooling the reaction at

120 °C temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired allylated products **4**.

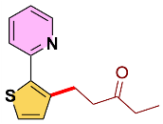


4-(2-(Pyridin-2-yl)thiophen-3-yl)butan-2-one (3aa) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3aa** (57.5 mg, 83%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (d, *J* = 4.8 Hz, 1H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 5.1 Hz, 1H), 7.17 – 7.13 (m, 1H), 6.95 (d, *J* = 5.1 Hz, 1H), 3.22 – 3.16 (m, 2H), 2.84 – 2.78 (m, 2H), 2.14 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.3, 153.4, 149.7, 139.2, 138.0, 136.7, 130.7, 125.8, 122.0, 121.6, 44.4, 30.1, 23.8.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{14}NOS$ 232.0536; Found 232.0561.

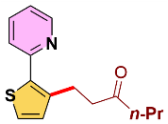


1-(2-Pyridin-2-yl)thiophen-3-yl)pentan-3-one (3ab) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and pent-1-en-3-one (50.4 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ab** (57.3 mg, 78%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 (d, *J* = 4.3 Hz, 1H), 7.72 (t, *J* = 7.7 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 5.1 Hz, 1H), 7.21 – 7.16 (m, 1H), 6.97 (d, *J* = 5.1 Hz, 1H), 3.25 – 3.19 (m, 2H), 2.84 – 2.78 (m, 2H), 2.44 (q, *J* = 7.3 Hz, 2H), 1.07 (t, *J* = 7.3 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 211.0, 153.4, 149.7, 139.4, 136.7, 130.7, 125.8, 122.0, 121.6, 43.0, 36.1, 23.9, 7.9.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NOS$ 246.0947; Found 246.0945.

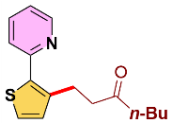


1-(2-(Pyridin-2-yl)thiophen-3-yl)hexan-3-one (3ac) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and hex-1-en-3-one (58.8 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ac** (62.2 mg, 80%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.4 Hz, 1H), 7.73 – 7.68 (m, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 5.1 Hz, 1H), 7.16 (dd, *J* = 7.4, 5.7 Hz, 1H), 6.96 (d, *J* = 5.1 Hz, 1H), 3.24 – 3.18 (m, 2H), 2.82 – 2.77 (m, 2H), 2.39 (t, *J* = 7.3 Hz, 2H), 1.60 (dt, *J* = 14.8, 7.4 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 210.6, 153.4, 149.6, 139.4, 138.0, 136.6, 130.7, 125.7, 121.9, 121.6, 44.9, 43.3, 23.8, 17.4, 13.8.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{18}NOS$ 260.1103; Found 260.1099.



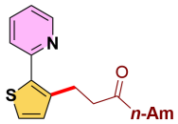
1-(2-(Pyridin-2-yl)thiophen-3-yl)heptan-3-one (3ad) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and hept-1-en-3-ol (58.8 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ad** (62.0 mg,

76%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.8 Hz, 1H), 7.72 – 7.67 (m, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.28 (d, *J* = 5.1 Hz, 1H), 7.16 (dd, *J* = 8.5, 4.8 Hz, 1H), 6.96 (d, *J* = 5.1 Hz, 1H), 3.24 – 3.16 (m, 2H), 2.83 – 2.77 (m, 2H), 2.40 (t, *J* = 7.5 Hz, 2H), 1.55 (p, *J* = 7.5 Hz, 2H), 1.32 – 1.27 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 210.7, 153.3, 149.6, 139.3, 137.9, 136.6, 130.7, 125.7, 121.9, 121.5, 43.3, 42.7, 26.0, 23.8, 22.4, 13.9.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{20}NOS$ 274.1260; Found 274.1254.

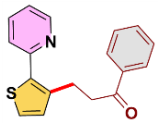


1-(2-(Pyridin-2-yl)thiophen-3-yl)octan-3-one (3ae) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and oct-1-en-3-ol (76.8 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ae** (65.4 mg, 76%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, J = 4.8 Hz, 1H), 7.69 (t, J = 8.6 Hz, 1H), 7.54 (d, J = 7.9 Hz, 1H), 7.28 (d, J = 5.2 Hz, 1H), 7.19 – 7.13 (m, 1H), 6.96 (d, J = 5.1 Hz, 1H), 3.26 – 3.16 (m, 2H), 2.85 – 2.75 (m, 2H), 2.39 (t, J = 7.5 Hz, 2H), 1.57 (p, J = 7.5 Hz, 2H), 1.30 (q, J = 7.5, 6.9 Hz, 2H), 1.25 (d, J = 7.3 Hz, 2H), 0.88 (t, J = 7.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 210.7, 153.3, 149.6, 139.3, 137.9, 136.6, 130.7, 125.7, 121.9, 121.5, 43.3, 42.9, 31.4, 23.8, 23.6, 22.5, 14.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{22}NOS$ 288.1416; Found 288.1412.

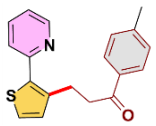


1-Phenyl-3-(2-(pyridin-2-yl)thiophen-3-yl)propan-1-one (3af) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-phenylprop-2-en-1-one (79.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3af** (59.8 mg, 68%) as a brown oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.4 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.56 (dd, *J* = 14.1, 7.6 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.30 (d, *J* = 5.1 Hz, 1H), 7.18 – 7.13 (m, 1H), 7.03 (d, *J* = 5.1 Hz, 1H), 3.37 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 199.7, 153.4, 149.7, 139.6, 138.1, 136.9, 136.7, 133.2, 130.9, 128.7, 128.3, 125.8, 122.0, 121.6, 39.7, 24.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{16}NOS$ 294.0947; Found 294.0942.

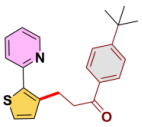


3-(2-(Pyridin-2-yl)thiophen-3-yl)-1-(p-tolyl)propan-1-one (3ag) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(*p*-tolyl)prop-2-en-1-one (87.6 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ag** (61.7 mg, 67%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.91 (d, *J* = 7.4 Hz, 2H), 7.72 (s, 1H), 7.60 (s, 1H), 7.34 – 7.15 (m, 4H), 7.04 (s, 1H), 3.37 (m, 4H), 2.43 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 199.4, 153.4, 149.7, 144.0, 139.6, 138.1, 136.7, 134.5, 130.9, 129.4, 128.4, 125.8, 122.1, 121.7, 39.5, 24.5, 21.8.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NOS$ 308.1103; Found 308.1100.

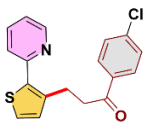


1-(4-(*tert*-Butyl)phenyl)-3-(2-(pyridin-2-yl)thiophen-3-yl)propan-1-one (3ah) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(4-(*tert*-butyl)phenyl)prop-2-en-1-one (112.8 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ah** (64.9 mg, 62%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, *J* = 4.5 Hz, 1H), 7.93 (d, *J* = 8.5 Hz, 2H), 7.69 (t, *J* = 8.6 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 5.1 Hz, 1H), 7.16 (dd, *J* = 7.1, 5.1 Hz, 1H), 7.03 (d, *J* = 5.1 Hz, 1H), 3.36 (m, 4H), 1.34 (s, 9H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 199.3, 156.9, 153.4, 149.7, 139.6, 138.1, 136.7, 134.4, 130.9, 128.2, 125.8, 125.6, 122.0, 121.6, 39.5, 35.2, 31.2, 24.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{24}NOS$ 350.1573; Found 350.1570.

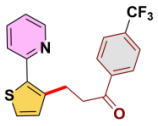


1-(4-Chlorophenyl)-3-(2-(pyridin-2-yl)thiophen-3-yl)propan-1-one (3ai) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(4-chlorophenyl)prop-2-en-1-one (99.6 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ai** (69.6 mg, 71%) as a brown solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.69 (t, *J* = 7.5 Hz, 1H), 7.55 (d, *J* = 7.6 Hz, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 5.0 Hz, 1H), 7.16 (s, 1H), 7.01 (d, *J* = 5.0 Hz, 1H), 3.41 – 3.27 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 198.5, 153.3, 149.6, 139.5, 139.3, 138.0, 136.6, 135.1, 130.9, 129.6, 128.9, 125.7, 122.0, 121.6, 39.6, 24.4.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{15}ClNOS$ 328.0557; Found 328.0550.



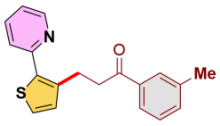
3-(2-(Pyridin-2-yl)thiophen-3-yl)-1-(4-(trifluoromethyl)phenyl)propan-1-one (3aj) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(4-(trifluoromethyl)phenyl)prop-2-en-1-one (120.0 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3aj** (80.1 mg, 74%) as a yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.08 (d, *J* = 6.9 Hz, 2H), 7.70 (d, *J* = 7.2 Hz, 3H), 7.55 (s, 1H), 7.29 (s, 1H), 7.16 (s, 1H), 7.01 (s, 1H), 3.39 (m, 4H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 198.9, 153.4, 149.6, 139.6, 139.3, 138.0, 136.8, 134.5, 134.3, 131.0, 128.6, 125.7 (q, *J* = 4.9 Hz), 124.6, 122.8, 122.2, 121.7, 40.1, 24.4.

^{19}F NMR (565 MHz, $CDCl_3$) δ -63.07 (s).

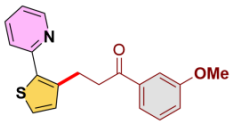
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}F_3NOS$ 362.0820; Found 362.0814.



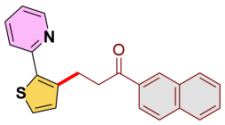
3-(2-(Pyridin-2-yl)thiophen-3-yl)-1-(*m*-tolyl)propan-1-one (3ak) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(*m*-tolyl)prop-2-en-1-one (87.6 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ak** (64.5 mg, 70%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.78 (s, 2H), 7.69 (s, 1H), 7.57 (s, 1H), 7.33 (dt, *J* = 23.2, 6.5 Hz, 3H), 7.16 (s, 1H), 7.03 (d, *J* = 4.4 Hz, 1H), 3.36 (m, 4H), 2.39 (s, 3H).

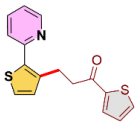
^{13}C NMR (151 MHz, $CDCl_3$) δ 199.8, 153.4, 149.6, 139.5, 138.4, 136.9, 136.7, 133.9, 130.9, 128.7, 128.5, 125.8, 125.4, 122.1, 121.7, 39.6, 24.4, 21.4.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NOS$ 308.1103; Found 308.1100.



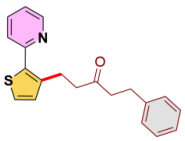
1-(3-Methoxyphenyl)-3-(2-(pyridin-2-yl)thiophen-3-yl)propan-1-one (3al) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(3-methoxyphenyl)prop-2-en-1-one (97.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3al** (69.7 mg, 72%) as a yellow oil.
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.71 (s, 1H), 7.56 (d, *J* = 31.7 Hz, 3H), 7.34 (d, *J* = 13.4 Hz, 2H), 7.26 – 6.97 (m, 3H), 3.85 (s, 3H), 3.37 (m, 4H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 199.5, 159.9, 153.4, 149.7, 139.5, 138.3, 138.0, 136.7, 130.9, 129.6, 125.8, 122.1, 121.7, 120.9, 119.6, 112.5, 55.5, 39.7, 24.5.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NO_2S$ 324.1052; Found 324.1049.



1-(Naphthalen-2-yl)-3-(2-(pyridin-2-yl)thiophen-3-yl)propan-1-one (3am) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(naphthalen-2-yl)prop-2-en-1-one (109.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3am** (63.8 mg, 62%) as a yellow solid.
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.47 (s, 1H), 8.06 (d, *J* = 10.2 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.87 (t, *J* = 9.0 Hz, 2H), 7.69 (t, *J* = 7.7 Hz, 1H), 7.59 (t, *J* = 6.9 Hz, 2H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.32 (d, *J* = 5.1 Hz, 1H), 7.18 – 7.13 (m, 1H), 7.07 (d, *J* = 5.1 Hz, 1H), 3.53 – 3.49 (m, 2H), 3.47 – 3.42 (m, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 199.7, 153.5, 149.7, 139.6, 138.2, 136.7, 135.7, 134.2, 132.6, 131.0, 130.0, 129.7, 128.55, 128.53, 127.9, 126.9, 125.9, 124.0, 122.1, 121.7, 39.7, 24.6.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{18}NOS$ 344.1103; Found 344.1100.



3-(2-(Pyridin-2-yl)thiophen-3-yl)-1-(thiophen-2-yl)propan-1-one (3an) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(thiophen-2-yl)prop-2-en-1-one (82.8 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3an** (53.8 mg, 60%) as a yellow oil.
^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.08 (d, *J* = 3.9 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.55 (d, *J* = 6.1 Hz, 2H), 7.29 (dd, *J* = 5.1, 1.9 Hz, 2H), 7.17 (s, 1H), 7.01 (d, *J* = 5.1 Hz, 1H), 3.39 – 3.33 (m, 2H), 3.30 – 3.24 (m, 2H).
^{13}C NMR (151 MHz, $CDCl_3$) δ 194.1, 153.4, 149.6, 142.3, 139.5, 138.1, 136.7, 132.3, 131.0, 127.1, 126.4, 125.8, 122.1, 121.7, 40.9, 24.5.
HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{14}NOS_2$ 300.0511; Found 300.0507.



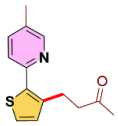
1-Phenyl-5-(2-(pyridin-2-yl)thiophen-3-yl)pentan-3-one (3ao) Following the general procedure **A** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 5-phenylpent-1-en-3-one (96.0 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to

afford **3ao** (75.1 mg, 78%) as a brown oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (s, 1H), 7.71 – 7.67 (m, 1H), 7.52 (d, *J* = 7.9 Hz, 1H), 7.30 – 7.25 (m, 3H), 7.21 – 7.13 (m, 4H), 6.93 (d, *J* = 5.1 Hz, 1H), 3.23 – 3.18 (m, 2H), 2.90 (t, *J* = 7.6 Hz, 2H), 2.81 – 2.76 (m, 2H), 2.73 (t, *J* = 7.6 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 209.4, 153.3, 149.6, 141.1, 139.2, 138.0, 136.6, 130.7, 128.6, 128.4, 126.2, 125.7, 121.9, 121.6, 44.4, 43.6, 29.8, 23.8.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{20}NOS$ 322.1260; Found 322.1257.

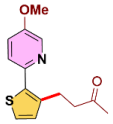


4-(2-(5-Methylpyridin-2-yl)thiophen-3-yl)butan-2-one (3ba) Following the general procedure **A** using 5-methyl-2-(thiophen-2-yl)pyridine (52.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ba** (64.7 mg, 88%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.24 (d, *J* = 5.1 Hz, 1H), 6.93 (d, *J* = 5.1 Hz, 1H), 3.16 (t, *J* = 7.7 Hz, 2H), 2.79 (t, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 2.13 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.4, 150.7, 150.1, 138.6, 138.1, 137.2, 131.2, 130.5, 125.2, 121.6, 44.4, 30.0, 23.7, 18.3.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NOS$ 246.0947; Found 246.0944.

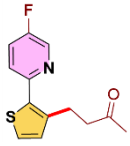


4-(2-(5-Methoxypyridin-2-yl)thiophen-3-yl)butan-2-one (3ca) Following the general procedure **A** using 5-methoxy-2-(thiophen-2-yl)pyridine (57.3 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ca** (69.7 mg, 89%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.31 (s, 1H), 7.44 (d, *J* = 8.7 Hz, 1H), 7.22 – 7.19 (m, 2H), 6.91 (d, *J* = 5.1 Hz, 1H), 3.86 (s, 3H), 3.16 – 3.10 (m, 2H), 2.82 – 2.77 (m, 2H), 2.12 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.4, 154.3, 146.0, 137.85, 137.76, 137.2, 130.3, 124.7, 122.5, 121.1, 55.7, 44.4, 30.0, 23.6.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NO_2S$ 262.0896; Found 262.0891.



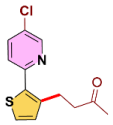
4-(2-(5-Fluoropyridin-2-yl)thiophen-3-yl)butan-2-one (3da) Following the general procedure **A** using 5-fluoro-2-(thiophen-2-yl)pyridine (53.7 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3da** (67.2 mg, 90%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.51 (dd, *J* = 8.7, 4.2 Hz, 1H), 7.40 (td, *J* = 8.4, 2.9 Hz, 1H), 7.25 (d, *J* = 5.1 Hz, 1H), 6.93 (d, *J* = 5.1 Hz, 1H), 3.17 – 3.11 (m, 2H), 2.83 – 2.77 (m, 2H), 2.12 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.1, 158.9, 157.2, 149.71, 149.69, 139.2, 137.8, 137.6, 136.7, 130.6, 125.6, 123.6, 123.4, 123.0, 122.9, 44.3, 30.0, 23.6.

^{19}F NMR (565 MHz, $CDCl_3$) δ -129.38 (s).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{13}FNOS$ 250.0696; Found 250.0693.

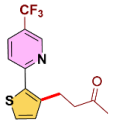


4-(2-(5-Chloropyridin-2-yl)thiophen-3-yl)butan-2-one (3ea) Following the general procedure **A** using 5-chloro-2-(thiophen-2-yl)pyridine (58.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ea** (71.5 mg, 90%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.66 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.49 (d, *J* = 8.5 Hz, 1H), 7.29 (d, *J* = 5.1 Hz, 1H), 6.96 (d, *J* = 5.1 Hz, 1H), 3.20 – 3.16 (m, 2H), 2.81 (t, *J* = 7.7 Hz, 2H), 2.15 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.1, 151.5, 148.3, 139.9, 136.5, 136.3, 130.9, 129.8, 126.0, 122.5, 44.2, 30.0, 23.7.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{13}ClNOS$ 266.0400; Found 266.0398.



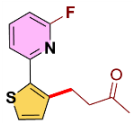
4-(2-(5-(Trifluoromethyl)pyridin-2-yl)thiophen-3-yl)butan-2-one (3fa) Following the general procedure **A** using 2-(thiophen-2-yl)-5-(trifluoromethyl)pyridine (68.7 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3fa** (76.2 mg, 85%) as a light yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.91 (d, *J* = 8.4 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.35 (d, *J* = 5.1 Hz, 1H), 6.99 (d, *J* = 5.1 Hz, 1H), 3.26 – 3.20 (m, 2H), 2.83 (t, *J* = 7.6 Hz, 2H), 2.15 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.0, 156.7, 146.53, 146.50, 146.47, 146.4, 141.6, 136.3, 133.9 (q, *J* = 3.4 Hz) 133.8, 131.4, 127.2, 124.7, 124.0, 123.8, 122.9, 121.1, 44.2, 30.1, 24.0.

^{19}F NMR (565 MHz, $CDCl_3$) δ -62.27 (s).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{13}F_3NOS$ 300.0664; Found 300.0658.



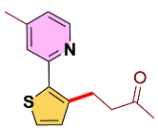
4-(2-(6-Fluoropyridin-2-yl)thiophen-3-yl)butan-2-one (3ga) Following the general procedure **A** using 2-fluoro-6-(thiophen-2-yl)pyridine (53.7 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ga** (52.3 mg, 70%) as a light yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (q, *J* = 8.1 Hz, 1H), 7.40 (dd, *J* = 7.6, 2.4 Hz, 1H), 7.27 (d, *J* = 5.1 Hz, 1H), 6.95 (d, *J* = 5.1 Hz, 1H), 6.78 (dd, *J* = 8.1, 3.0 Hz, 1H), 3.24 – 3.19 (m, 2H), 2.87 – 2.82 (m, 2H), 2.17 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.5, 163.7, 162.1, 152.1, 152.0, 141.7, 141.6, 140.9, 135.8, 131.3, 126.2, 118.93, 118.90, 107.2, 106.9, 44.3, 30.0, 24.1.

^{19}F NMR (565 MHz, $CDCl_3$) δ -66.25 (s).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{13}FNOS$ 250.0696; Found 250.0693.



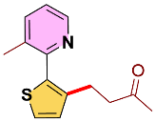
4-(2-(4-Methylpyridin-2-yl)thiophen-3-yl)butan-2-one (3ia) Following the general procedure **A** using 4-methyl-2-(thiophen-2-yl)pyridine (52.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ia** (58.8 mg, 80%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.44 (d, *J* = 5.0 Hz, 1H), 7.32 (s, 1H), 7.23 (d, *J* = 5.1 Hz, 1H), 6.96

(d, *J* = 4.9 Hz, 1H), 6.92 (d, *J* = 5.1 Hz, 1H), 3.20 – 3.15 (m, 2H), 2.81 – 2.76 (m, 2H), 2.35 (s, 3H), 2.11 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.3, 153.2, 149.3, 147.7, 139.0, 137.9, 130.5, 125.4, 122.9, 122.7, 44.4, 30.0, 23.7, 21.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NOS$ 246.0947; Found 246.0944.

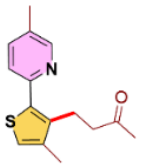


4-(2-(3-Methylpyridin-2-yl)thiophen-3-yl)butan-2-one (3ma) Following the general procedure **A** using 3-methyl-2-(thiophen-2-yl)pyridine (52.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ma** (59.5 mg, 81%) as a yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.46 (d, *J* = 3.9 Hz, 1H), 7.54 (d, *J* = 7.1 Hz, 1H), 7.27 (d, *J* = 5.1 Hz, 1H), 7.16 (dd, *J* = 7.7, 4.8 Hz, 1H), 6.91 (d, *J* = 5.1 Hz, 1H), 2.68 (dd, *J* = 8.2, 6.3 Hz, 2H), 2.63 (dd, *J* = 8.9, 6.3 Hz, 2H), 2.22 (s, 3H), 2.02 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.0, 152.5, 147.0, 138.8, 138.2, 136.2, 133.5, 128.2, 125.1, 122.9, 44.3, 29.9, 22.8, 19.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NOS$ 246.0947; Found 246.0943.

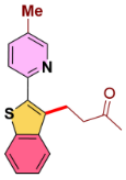


4-(4-Methyl-2-(5-methylpyridin-2-yl)thiophen-3-yl)butan-2-one (3na) Following the general procedure **A** using 5-methyl-2-(4-methylthiophen-2-yl)pyridine (56.7 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3na** (58.3 mg, 75%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.43 (s, 1H), 7.48 (d, *J* = 9.8 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 6.93 (s, 1H), 3.13 – 3.09 (m, 2H), 2.74 – 2.70 (m, 2H), 2.34 (s, 3H), 2.21 (s, 3H), 2.15 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.7, 151.2, 150.0, 138.7, 138.4, 138.3, 137.2, 131.1, 121.6, 121.2, 43.8, 30.0, 22.2, 18.3, 15.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{18}NOS$ 260.1103; Found 260.1101.

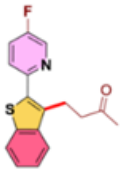


4-(2-(5-Methylpyridin-2-yl)benzo[*b*]thiophen-3-yl)butan-2-one (3oa) Following the general procedure **A** using 2-(benzo[*b*]thiophen-2-yl)-5-methylpyridine (67.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3oa** (62.0 mg, 70%) as a yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.74 (d, *J* = 7.8 Hz, 1H), 7.54 (d, *J* = 7.9 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.41 – 7.33 (m, 2H), 3.49 – 3.41 (m, 2H), 2.92 – 2.85 (m, 2H), 2.36 (s, 3H), 2.17 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.4, 150.7, 150.2, 140.6, 139.3, 138.2, 137.2, 132.9, 132.0, 125.0, 124.4, 122.5, 122.2, 43.6, 30.0, 21.5, 18.3.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{18}NOS$ 296.1103; Found 296.1101.



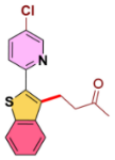
4-(2-(5-Fluoropyridin-2-yl)benzo[*b*]thiophen-3-yl)butan-2-one (3pa) Following the general procedure **A** using 2-(benzo[*b*]thiophen-2-yl)-5-fluoropyridine (68.7 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3pa** (77.1 mg, 86%) as a yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.54 (d, *J* = 2.6 Hz, 1H), 7.83 (d, *J* = 7.7 Hz, 1H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.60 (dd, *J* = 8.6, 4.1 Hz, 1H), 7.45 (td, *J* = 8.4, 2.8 Hz, 1H), 7.38 (dt, *J* = 18.8, 7.0 Hz, 2H), 3.45 – 3.39 (m, 2H), 2.89 – 2.85 (m, 2H), 2.18 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.2, 159.2, 157.5, 149.72, 149.70, 140.5, 139.2, 138.1, 137.9, 136.5, 133.7, 125.3, 124.5, 124.0, 123.6, 123.5, 122.5, 122.4, 43.5, 30.0, 21.4.

^{19}F NMR (565 MHz, $CDCl_3$) δ -128.08 (s).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}FNOS$ 300.0852; Found 300.0850.

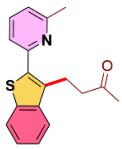


4-(2-(5-Chloropyridin-2-yl)benzo[*b*]thiophen-3-yl)butan-2-one (3qa) Following the general procedure **A** using 2-(benzo[*b*]thiophen-2-yl)-5-chloropyridine (73.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3qa** (84.1 mg, 89%) as a yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (d, *J* = 2.4 Hz, 1H), 7.84 (d, *J* = 7.2 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.71 (dd, *J* = 8.5, 2.5 Hz, 1H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.43 – 7.35 (m, 1H), 3.47 – 3.41 (m, 2H), 2.90 – 2.84 (m, 2H), 2.18 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.2, 151.6, 148.6, 140.6, 139.4, 136.50, 136.46, 134.5, 130.6, 125.5, 124.6, 123.7, 122.6, 122.5, 43.5, 30.1, 21.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{15}ClNOS$ 316.0557; Found 316.0553.

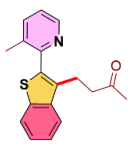


4-(2-(6-Methylpyridin-2-yl)benzo[*b*]thiophen-3-yl)butan-2-one (3ra) Following the general procedure **A** using 2-(benzo[*b*]thiophen-2-yl)-6-methylpyridine (67.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3ra** (69.0 mg, 78%) as a yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (d, *J* = 7.7 Hz, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 7.61 (t, *J* = 7.7 Hz, 1H), 7.40 (dd, *J* = 12.8, 7.6 Hz, 2H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.07 (d, *J* = 7.7 Hz, 1H), 3.49 – 3.43 (m, 2H), 2.95 – 2.90 (m, 2H), 2.59 (s, 3H), 2.18 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.4, 158.5, 152.7, 140.7, 139.3, 138.0, 136.9, 133.6, 125.1, 124.4, 122.5, 122.2, 121.8, 120.1, 43.7, 30.0, 24.7, 21.6.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{18}NOS$ 296.1103; Found 296.1101.



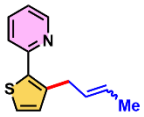
4-(2-(3-Methylpyridin-2-yl)benzo[*b*]thiophen-3-yl)butan-2-one (3sa) Following the general procedure **A** using 2-(benzo[*b*]thiophen-2-yl)-3-methylpyridine (67.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **3sa** (66.3 mg, 75%) as a yellow solid.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.53 (d, *J* = 5.8 Hz, 1H), 7.85 (d, *J* = 7.8 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.60 (d, *J* = 7.7 Hz, 1H), 7.42 – 7.39 (m, 1H), 7.38 – 7.34 (m, 1H), 7.24 (dd, *J* = 7.8, 4.8 Hz,

1H), 2.97 – 2.92 (m, 2H), 2.76 – 2.71 (m, 2H), 2.27 (s, 3H), 2.04 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.0, 152.5, 147.1, 140.0, 139.1, 138.3, 136.9, 133.6, 133.0, 124.6, 124.3, 123.4, 122.6, 122.0, 43.4, 29.8, 21.0, 19.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{18}NOS$ 296.1103; Found 296.1101.

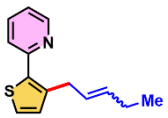


2-(3-(But-2-en-1-yl)thiophen-2-yl)pyridine (4aa) Following the general procedure **B** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4aa** (58.0 mg, 90%) as a light yellow oil in the E: Z ratio of 1.44/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 – 8.61 (m, 1H), 7.71 – 7.67 (m, 1H), 7.54 – 7.51 (m, 1H), 7.30 (t, *J* = 4.9 Hz, 1H), 7.18 – 7.14 (m, 1H), 6.99 – 6.95 (m, 1H), 5.68 – 5.45 (m, 2H), 3.70 – 3.51 (m, 2H), 1.73 – 1.67 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.4, 153.2, 149.6, 138.9, 138.4, 138.3, 137.9, 136.4, 131.0, 130.7, 129.0, 128.5, 126.6, 125.8, 125.0, 122.0, 121.8, 121.5, 32.7, 27.4, 17.9, 13.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{14}NS$ 216.0769; Found 216.0773.

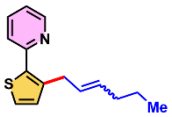


2-(3-(Pent-2-en-1-yl)thiophen-2-yl)pyridine (4ab) Following the general procedure **B** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and pent-1-en-3-ol (51.6 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ab** (56.3 mg, 82%) as a light yellow oil in the E: Z ratio of 1.47/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.64 – 8.61 (m, 1H), 7.70 – 7.66 (m, 1H), 7.55 – 7.50 (m, 1H), 7.32 – 7.28 (m, 1H), 7.17 – 7.13 (m, 1H), 6.99 – 6.95 (m, 1H), 5.65 – 5.47 (m, 2H), 3.69 – 3.56 (m, 2H), 2.18 – 1.99 (m, 2H), 1.02 – 0.95 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 153.4, 149.73, 149.71, 139.0, 138.5, 138.4, 138.0, 136.5, 133.9, 132.8, 131.1, 130.8, 127.0, 126.9, 125.88, 125.86, 122.1, 121.9, 121.6, 32.8, 27.7, 25.7, 20.8, 14.3, 13.9.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NS$ 230.0925; Found 230.0997.

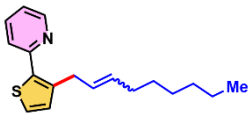


2-(3-(Hex-2-en-1-yl)thiophen-2-yl)pyridine (4ac) Following the general procedure **B** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and hex-1-en-3-ol (60 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ac** (46.6 mg, 64%) as a light yellow oil in the E: Z ratio of 1.66/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.65 – 8.61 (m, 1H), 7.72 – 7.67 (m, 1H), 7.56 – 7.52 (m, 1H), 7.33 – 7.29 (m, 1H), 7.19 – 7.13 (m, 1H), 7.00 – 6.95 (m, 1H), 5.67 – 5.45 (m, 2H), 3.69 – 3.57 (m, 2H), 2.15 – 1.97 (m, 2H), 1.45 – 1.33 (m, 2H), 0.94 – 0.85 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 153.4, 149.7, 139.1, 138.5, 138.4, 138.0, 136.5, 132.3, 131.1, 131.0, 130.8, 128.0, 127.7, 125.89, 125.86, 122.1, 121.9, 121.6, 34.7, 32.9, 29.6, 27.8, 22.9, 22.7, 14.0, 13.8.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{18}NS$ 244.1082; Found 244.1154.

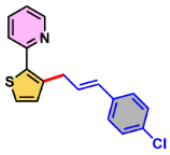


2-(3-(Hex-2-en-1-yl)thiophen-2-yl)pyridine (4ad) Following the general procedure **B** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and non-1-en-3-ol (85.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ad** (41.4 mg, 51%) as a light yellow oil in the E: Z ratio of 1.32/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 – 8.61 (m, 1H), 7.71 – 7.67 (m, 1H), 7.56 – 7.51 (m, 1H), 7.30 (dd, J = 6.4, 5.1 Hz, 1H), 7.18 – 7.14 (m, 1H), 6.97 (dd, J = 7.5, 5.1 Hz, 1H), 5.65 – 5.46 (m, 2H), 3.68 – 3.57 (m, 2H), 2.19 – 1.97 (m, 2H), 1.43 – 1.20 (m, 8H), 0.90 – 0.85 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 153.4, 149.8, 149.7, 139.1, 138.5, 138.5, 138.0, 136.5, 132.6, 131.3, 131.2, 130.8, 127.8, 127.5, 125.9, 125.9, 122.2, 121.9, 121.6, 32.9, 32.6, 31.7, 31.5, 29.4, 29.3, 27.8, 27.5, 22.72, 22.66, 14.2.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{24}NS$ 286.1551; Found 285.1556.

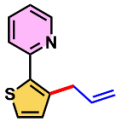


***(E)*-2-(3-(3-(4-chlorophenyl)allyl)thiophen-2-yl)pyridine (4ai)** Following the general procedure **B** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and 1-(4-chlorophenyl)but-3-en-2-ol (109.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ai** (49.4 mg, 53%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 – 8.51 (m, 1H), 7.69 – 7.65 (m, 1H), 7.63 – 7.57 (m, 1H), 7.46 (d, J = 3.7 Hz, 1H), 7.30 – 7.27 (m, 4H), 7.14 – 7.10 (m, 1H), 6.89 – 6.84 (m, 1H), 6.52 – 6.46 (m, 1H), 6.39 – 6.34 (m, 1H), 3.74 (dt, J = 6.9, 1.2 Hz, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 145.5, 136.7, 135.6, 132.9, 130.6, 128.7, 128.4, 127.5, 126.0, 124.7, 33.7, 29.7.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for$C_{18}H_{15}ClNS$ 312.0535; Found 312.0542.

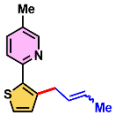


2-(3-Allylthiophen-2-yl)pyridine (4ap) Following the general procedure **B** using 2-(thiophen-2-yl)pyridine (48.3 mg, 0.3 mmol) and Allyl methyl carbonate (69.6 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ap** (54.9 mg,91%) as a light yellow oil.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 – 8.61 (m, 1H), 7.71 – 7.67 (m, 1H), 7.54 – 7.50 (m, 1H), 7.34 – 7.30 (m, 1H), 7.18 – 7.13 (m, 1H), 6.99 – 6.94 (m, 1H), 6.09 – 5.99 (m, 1H), 5.15 – 5.01 (m, 2H), 3.70 – 3.59 (m, 2H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.3, 149.7, 138.7, 137.4, 136.633, 136.60, 131.1, 126.0, 121.9, 121.6, 116.2, 33.9.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{12}NS$ 202.0612; Found 202.0661.

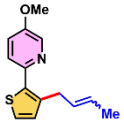


2-(3-(But-2-en-1-yl)thiophen-2-yl)-5-methylpyridine (4ba) Following the general procedure **B** using 5-methyl-2-(thiophen-2-yl)pyridine (52.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ba** (61.8 mg,90%) as a light yellow oil in the E: Z ratio of 1.73/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.48 – 8.45 (m, 1H), 7.52 – 7.48 (m, 1H), 7.43 – 7.40 (m, 1H), 7.28 – 7.26 (m, 1H), 6.95 (dd, J = 8.6, 5.1 Hz, 1H), 5.68 – 5.46 (m, 2H), 3.67 – 3.53 (m, 2H), 2.34 (d, J = 2.5 Hz, 3H), 1.72 – 1.67 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 150.7, 150.6, 150.02, 150.00, 138.32, 138.25, 138.0, 137.8, 137.0, 136.9, 131.0, 130.9, 130.5, 129.2, 128.6, 126.5, 125.2, 124.8, 121.6, 121.4, 32.6, 27.3, 18.2, 17.9, 13.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NS$ 230.0925; Found 230.0977.

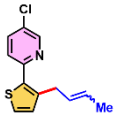


2-(3-(But-2-en-1-yl)thiophen-2-yl)-5-methoxypyridine (4ca) Following the general procedure **B** using 4-methoxy-2-(thiophen-2-yl)pyridine (57.3 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ca** (58.8 mg,80%) as a light yellow oil in the E: Z ratio of 1.23/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.35 (dd, J = 4.6, 3.0 Hz, 1H), 7.45 (dd, J = 8.7, 3.8 Hz, 1H), 7.32 – 7.17 (m, 2H), 6.94 (dd, J = 8.6, 5.1 Hz, 1H), 5.73 – 5.45 (m, 2H), 3.88 (d, J = 2.1 Hz, 3H), 3.67 – 3.41 (m, 2H), 1.76 – 1.65 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 154.20, 154.18, 146.1, 146.0, 138.0, 137.7, 137.6, 137.12, 137.10, 137.0, 130.8, 130.4, 129.2, 128.7, 126.5, 124.8, 124.7, 122.5, 122.3, 120.96, 120.95, 55.7, 32.5, 27.2, 17.9, 13.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NOS$ 246.0874; Found 246.0974.

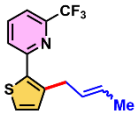


2-(3-(But-2-en-1-yl)thiophen-2-yl)-5-chloropyridine (4ea) Following the general procedure **B** using 5-chloro-2-(thiophen-2-yl)pyridine (58.2 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ea** (38.8 mg,52%) as a light yellow oil in the E: Z ratio of 1.61/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.57 (dd, *J* = 5.3, 2.5 Hz, 1H), 7.66 (dq, J = 8.5, 2.1 Hz, 1H), 7.46 (dd, J = 8.5, 3.7 Hz, 1H), 7.31 (d, J = 5.1 Hz, 1H), 6.96 (dd, J = 10.1, 5.1 Hz, 1H), 5.69 – 5.43 (m, 2H), 3.68 – 3.51 (m, 2H), 1.72 – 1.65 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 151.6, 151.4, 148.4, 139.5, 138.9, 137.0, 136.6, 136.2, 136.1, 131.2, 130.9, 129.7, 128.8, 128.2, 126.8, 126.12, 126.08, 125.2, 122.5, 122.3, 32.7, 27.4, 17.9, 13.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{13}ClNS$ 250.0379; Found 250.0451.



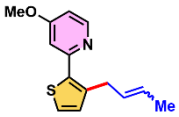
2-(3-(But-2-en-1-yl)thiophen-2-yl)-6-(trifluoromethyl)pyridine (4ha) Following the general procedure **B** using 2-(thiophen-2-yl)-6-(trifluoromethyl)pyridine (68.7 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ha** (39.9 mg,47%) as a light yellow oil in the E: Z ratio of 2.06/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.92 (d, J = 2.6 Hz, 1H), 7.96 – 7.92 (m, 1H), 7.61 – 7.57 (m, 1H), 7.36 – 7.33 (m, 1H), 7.19 (t, J = 5.4 Hz, 1H), 5.71 – 5.54 (m, 2H), 3.95 – 3.80 (m, 2H), 1.74 – 1.67 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 148.7, 142.1, 141.1, 137.88, 137.87, 128.6, 127.7, 126.2, 126.0, 125.7, 124.6, 120.9, 117.8 (q, *J* = 3.0 Hz)114.4, 39.5, 33.7, 21.7, 17.9.

^{19}F NMR (565 MHz, $CDCl_3$) δ -68.3 (s).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{13}F_3NS$ 284.0643; Found 284.1457.

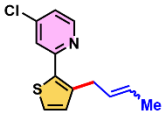


2-(3-(But-2-en-1-yl)thiophen-2-yl)-4-methoxypyridine (4ja) Following the general procedure **B** using 4-methoxy-2-(thiophen-2-yl)pyridine (57.3 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ja** (58.8 mg,80%) as a light yellow oil in the E: Z ratio of 1.38/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.47 – 8.44 (m, 1H), 7.31 – 7.28 (m, 1H), 7.09 – 7.04 (m, 1H), 6.97 – 6.94 (m, 1H), 6.73 – 6.70 (m, 1H), 5.73 – 5.45 (m, 2H), 3.87 (d, J = 3.8 Hz, 3H), 3.68 – 3.54 (m, 2H), 1.74 – 1.68 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 166.2, 154.8, 154.7, 151.0, 150.9, 138.9, 138.5, 138.3, 138.1, 131.1, 130.8, 129.2, 128.7, 126.8, 125.9, 125.8, 125.2, 110.3, 108.6, 108.1, 107.9, 107.6, 55.3, 32.8, 27.6, 18.0, 13.1.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{16}NOS$ 246.0874; Found 246.0974.

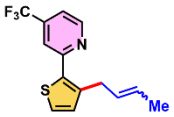


2-(3-(But-2-en-1-yl)thiophen-2-yl)-4-chloropyridine (4ka) Following the general procedure **B** using 4-chloro-2-(thiophen-2-yl)pyridine (58.2 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ka** (58.2 mg,78%) as a light yellow oil in the E: Z ratio of 1.62/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.55 – 8.48 (m, 1H), 7.61 – 7.50 (m, 1H), 7.36 – 7.30 (m, 1H), 7.19 – 7.14 (m, 1H), 7.05 – 6.95 (m, 1H), 5.67 – 5.48 (m, 2H), 3.68 – 3.55 (m, 2H), 1.75 – 1.68 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 154.7, 154.6, 150.3, 144.3, 139.9, 139.4, 136.9, 136.7, 131.2, 131.0, 128.7, 128.1, 127.0, 126.61, 126.58, 125.2, 121.9, 121.8, 121.6, 32.8, 27.6, 17.9, 13.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{13}ClNS$ 250.0379; Found 250.0451.



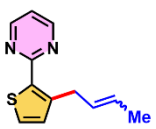
2-(3-(But-2-en-1-yl)thiophen-2-yl)-4-(trifluoromethyl)pyridine (4la) Following the general procedure **B** using 2-(thiophen-2-yl)-4-(trifluoromethyl)pyridine (68.7 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4la** (72.1 mg, 85%) as a light yellow oil in the E: Z ratio of 1.62/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 – 8.77 (m, 1H), 7.78 – 7.71 (m, 1H), 7.36 (t, J = 4.8 Hz, 2H), 7.04 – 6.97 (m, 1H), 5.68 – 5.47 (m, 2H), 3.70 – 3.57 (m, 2H), 1.75 – 1.67 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 154.8, 154.61, 150.59, 150.6, 140.5, 140.0, 137.1, 136.7, 131.6, 131.4, 128.6, 128.1, 127.3, 127.1, 127.0, 125.6, 122.1, 117.3 (q, *J* = 3.8 Hz) 33.0, 27.7, 18.0, 13.1.

^{19}F NMR (565 MHz, CDCl3) δ -64.9 (s).

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{13}F_3NS$ 284.0643; Found 284.1457.

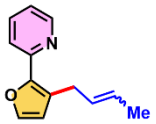


2-(3-(But-2-en-1-yl)thiophen-2-yl)pyrimidine (4ta) Following the general procedure **B** using 2-(thiophen-2-yl)pyrimidine (48.6 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ta** (27.2 mg, 42%) as a light yellow oil in the E: Z ratio of 2.27/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 – 8.69 (m, 2H), 7.35 (s, 1H), 7.08 – 7.03 (m, 1H), 7.00 (t, J = 5.4 Hz, 1H), 5.72 – 5.52 (m, 2H), 4.07 – 3.92 (m, 2H), 1.81 – 1.64 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 162.9, 156.9, 144.3, 131.8, 131.6, 129.7, 128.8, 128.2, 128.1, 126.2, 124.7, 117.8, 33.4, 28.0, 18.1, 13.1.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}N_2S$ 217.0721; Found 217.0793.



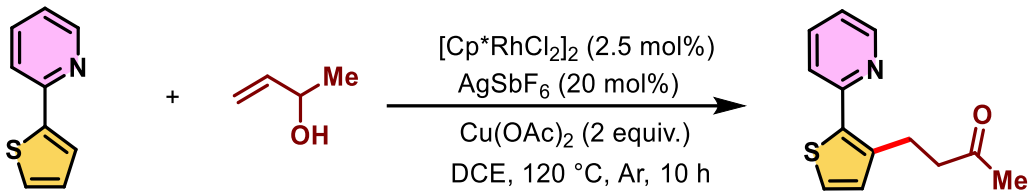
2-(3-(But-2-en-1-yl)furan-2-yl)pyridine (4ua) Following the general procedure **B** using 2-(furan-2-yl)pyridine (43.5 mg, 0.3 mmol) and but-3-en-2-ol (43.2 mg, 0.6 mmol), the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 30:1) to afford **4ua** (22.1 mg, 37%) as a light yellow oil in the E: Z ratio of 0.77/1.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.67 – 8.59 (m, 1H), 7.75 – 7.67 (m, 1H), 7.57 – 7.49 (m, 1H), 7.38 – 7.29 (m, 1H), 7.22 – 7.14 (m, 1H), 7.05 – 6.93 (m, 1H), 5.71 – 5.37 (m, 2H), 3.73 – 3.53 (m, 2H), 1.74 – 1.67 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.4, 153.2, 149.6, 138.9, 138.4, 138.3, 137.9, 136.4, 131.0, 130.7, 129.0, 128.5, 126.6, 125.8, 125.0, 122.0, 121.8, 121.5, 32.7, 27.4, 17.9, 13.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{14}NO$ 200.0997; Found 200.0120.

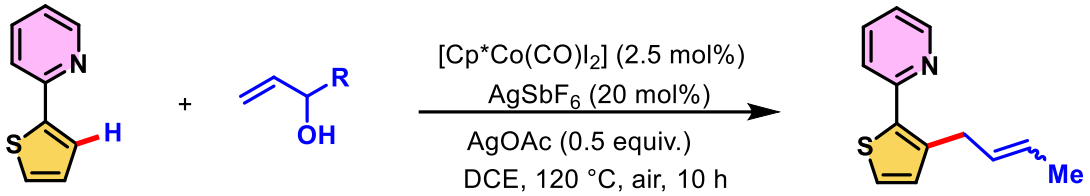
2.4 Rh(III)-catalyzed C3-alkylation: reaction on 3 mmol scale



1a **2a** **3aa**

To a 100 mL oven dried Schlenk tube, **1a** (3 mmol, 1 equiv.), $[Cp^*RhCl_2]_2$ (0.075 mmol, 2.5 mol%), but-3-en-2-ol **2a** (6 mmol, 2 equiv.), $AgSbF_6$ (0.6 mmol, 20 mol%) and DCE (30 mL) were successively added. The reaction mixture was stirred at 120 °C (metal sand bath temperature) for 10 hours under Ar. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography (petroleum ether/ethyl acetate = 30:1) to afford the desired alkylated product **3aa** (0.51 g, 75%).

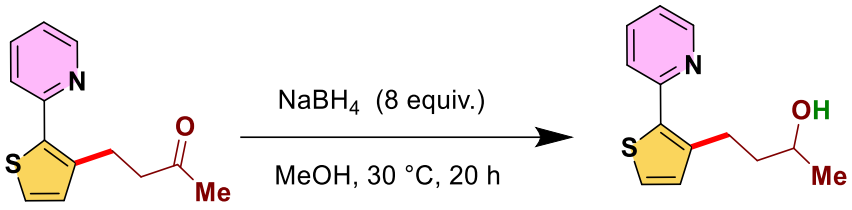
2.5 Co(III)-catalyzed C3-allylation: reaction on 3 mmol scale



1a **2a** **4aa**

To a 100 mL oven dried Schlenk tube, **1a** (3 mmol, 1 equiv.), $[Cp^*Co(CO)I_2]_2$ (0.15 mmol, 5 mol%), but-3-en-2-ol **2a** (6 mmol, 2 equiv.), $AgSbF_6$ (0.6 mmol, 20 mol%), AgOAc (1.5mmol, 0.5equiv.)and DCE (30 mL) were successively added. The reaction mixture was stirred at 120°C (metal sand bath temperature) for 10 hours under air. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography (petroleum ether/ethyl acetate = 30:1) to afford the desired allylated product **4aa** (0.52 g, 81%).

2.6 Preparation and characterization of products 5, 6, 7, 8,9



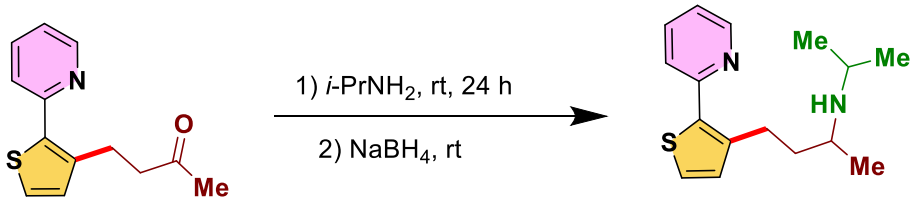
3aa **5,** 62%

4-(2-(Pyridin-2-yl)thiophen-3-yl)butan-2-one (**3aa**) (92.4 mg, 0.4 mmol) were dissolved in MeOH (4 mL). $NaBH_4$ (121.0 mg, 3.2 mmol, 8 equiv.) was added in portions with stirring under cooling for 1 h. Then the reaction mixture was stirred for another 20 h at 30 °C. After the removal of the solvents, the residue was absorbed to small amounts of silica. The purification was performed by flash column chromatography on silica gel to afford the product **5** (57.8 mg) in 62% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (d, J = 5.8 Hz, 1H), 7.73 – 7.69 (m, 1H), 7.52 (d, J = 8.0 Hz, 1H), 7.30 (d, J = 5.1 Hz, 1H), 7.19 (dd, J = 8.5, 5.0 Hz, 1H), 6.97 (d, J = 5.1 Hz, 1H), 3.71 – 3.61 (m, 1H), 3.41 – 3.34 (m, 1H), 2.75 – 2.69 (m, 1H), 1.89 – 1.80 (m, 1H), 1.80 – 1.70 (m, 1H), 1.16 (d, J = 6.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.1, 148.6, 140.8, 137.6, 136.5, 130.7, 125.9, 123.8, 121.9, 64.3, 39.7, 24.8, 23.0.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{13}H_{16}NOS$ 234.0874; Found 234.0876.



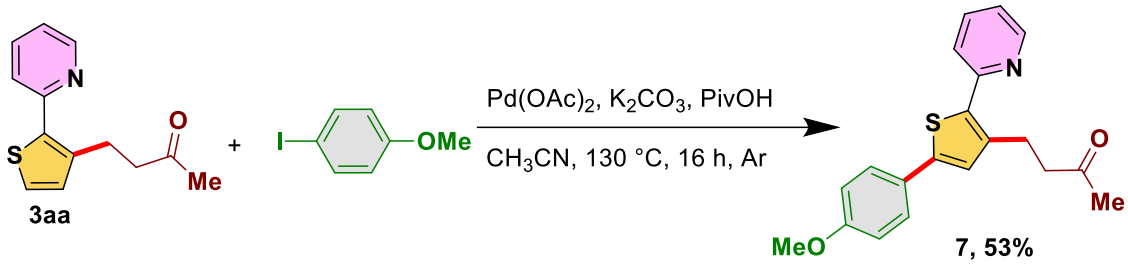
3aa **6, 58%**

4-(2-(pyridin-2-yl)thiophen-3-yl)butan-2-one (**3aa**) (92.4 mg, 0.4 mmol), isopropylamine (70.8 mg, 0.8 mmol) were dissolved in MeOH (4 mL). $NaBH_4$ (121.0 mg, 3.2 mmol, 8 equiv.), the reaction mixture was stirred for 24 h at room temperature, then the reaction mixture was added in portions with stirring under cooling for 1 h. Then the reaction mixture was stirred for another 20 h at 30 °C. After the removal of the solvents, the residue was absorbed to small amounts of silica. The purification was performed by flash column chromatography on silica gel to afford the product **6** (63.5 mg) in 58% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (d, *J* = 5.5 Hz, 1H), 7.71 – 7.66 (m, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.29 (d, *J* = 5.1 Hz, 1H), 7.16 (dd, *J* = 7.0, 4.4 Hz, 1H), 6.98 (d, *J* = 5.1 Hz, 1H), 3.02 (dd, J = 14.0, 9.9 Hz, 1H), 2.96 – 2.89 (m, 2H), 2.79 (p, *J* = 6.4 Hz, 1H), 1.88 – 1.81 (m, 1H), 1.69 (ddd, J = 13.6, 10.0, 6.6 Hz, 1H), 1.09 (d, *J* = 6.3 Hz, 3H), 1.06 (d, *J* = 6.3 Hz, 3H), 0.95 (d, *J* = 6.2 Hz, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 153.5, 149.6, 140.5, 137.5, 136.7, 130.6, 125.8, 122.3, 121.6, 49.6, 45.5, 37.6, 25.8, 23.5, 22.6, 20.6.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{23}N_2S$ 275.1504; Found 275.1507.

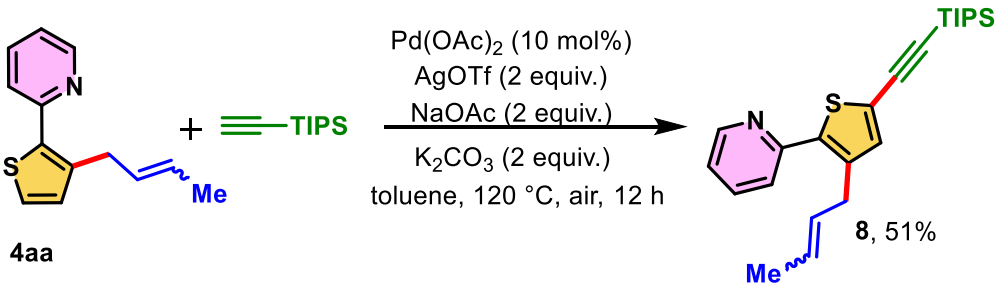


To a 15 mL oven dried Schlenk tube, K_2CO_3 (82.9 mg, 0.6 mmol, 2 equiv.), **3aa** (69.3 mg, 0.3 mmol, 1 equiv.), $Pd(OAc)_2$ (3.4 mg, 0.015 mmol, 5 mol%), PivOH (9.2 mg, 0.09 mmol, 0.3 equiv.), 1-iodo-4-methoxybenzene (104.9 mg, 0.45 mmol) and CH_3CN (2 mL) were successively added. The reaction mixture was stirred at 130 °C (metal sand bath temperature) for 16 hours under argon. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired product **7** (63.7 mg) in 63% yield.

^{1}H NMR (600 MHz, $CDCl_3$) δ 8.63 (d, J = 4.8 Hz, 1H), 7.73 – 7.69 (m, 1H), 7.60 – 7.54 (m, 3H), 7.17 – 7.14 (m, 1H), 7.08 (s, 1H), 6.93 (d, J = 8.7 Hz, 2H), 3.84 (s, 3H), 3.25 – 3.20 (m, 2H), 2.91 – 2.85 (m, 2H), 2.18 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 208.3, 159.6, 153.3, 149.7, 144.0, 140.3, 136.7, 136.3, 127.0, 126.9, 125.8, 121.5, 121.4, 114.4, 55.4, 44.3, 30.1, 24.1.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{20}NO_2S$ 338.1137; Found 338.1139.

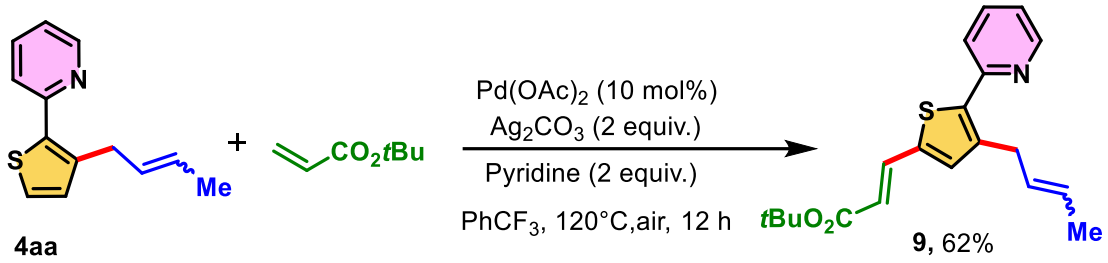


To a 15 mL oven dried Schlenk tube, K_2CO_3 (82.9 mg, 0.6 mmol, 2 equiv.), **4aa** (69.3 mg, 0.3 mmol, 1 equiv.), $Pd(OAc)_2$ (6.8 mg, 0.03 mmol, 10 mol%), NaOAc (49.2 mg, 0.6mmol, 2.0 equiv.), AgOTf (256.9 mg, 0.6mmol, 2.0 equiv.), ethynyltriisopropylsilane (109.2 mg, 0.6 mmol) and toluene (2 mL) were successively added. The reaction mixture was stirred at 120 °C (metal sand bath temperature) for 12 hours under air. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired product **8** (60.4 mg, 51%) as a light yellow oil in the E: Z ratio of 1.65/1.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.63 – 8.59 (m, 1H), 7.70 – 7.67 (m, 1H), 7.51 – 7.49 (m, 1H), 7.18 – 7.15 (m, 1H), 7.07 (d, J = 7.3 Hz, 1H), 5.66 – 5.47 (m, 2H), 3.63 – 3.50 (m, 2H), 1.72 – 1.68 (m, 3H), 1.12 (s, 21H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 149.8, 149.8, 139.7, 138.8, 138.3, 136.6, 136.2, 135.9, 128.6, 128.1, 127.2, 125.5, 123.6, 121.9, 121.7, 99.8, 99.7, 96.8, 32.8, 27.5, 18.8, 18.1, 13.1, 11.5.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{34}NSSi$ 396.2103; Found 396.2175.



4aa **9**, 62%

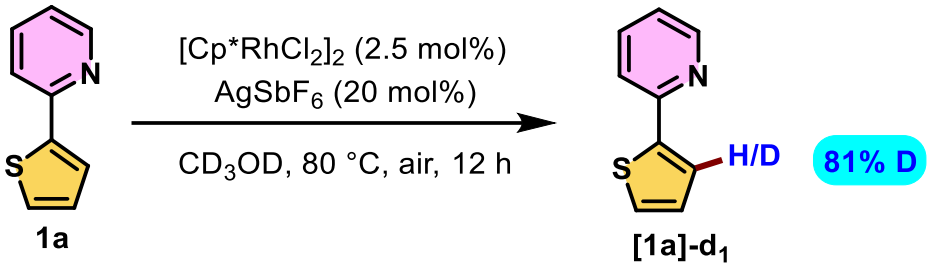
To a 15 mL oven dried Schlenk tube, Ag_2CO_3 (165.3 mg, 0.6 mmol, 2 equiv.), **4aa** (69.3 mg, 0.3 mmol, 1 equiv.), $Pd(OAc)_2$ (6.8 mg, 0.03 mmol, 10 mol%), pyridine (47.4 mg, 0.6mmol, 2.0 equiv.), *tert*-butyl acrylate (76.8 mg, 0.6 mmol) and $PhCF_3$ (2 mL) were successively added. The reaction mixture was stirred at 120 °C (metal sand bath temperature) for 12 hours under air. After cooling the reaction at room temperature and concentration, the crude mixture was purified by silica column chromatography to afford the desired product **9** (63.4mg, 62%) as a light yellow oil in the E: Z ratio of 2.18/1.

^{1}H NMR (600 MHz, Chloroform-*d*) δ 8.65 – 8.62 (m, 1H), 7.72 – 7.69 (m, 1H), 7.55 – 7.51 (m, 1H), 7.19 (dddd, J = 6.0, 4.9, 3.0, 1.4 Hz, 1H), 7.13 – 7.09 (m, 1H), 6.26 (dd, J = 15.7, 3.1 Hz, 1H), 5.65 – 5.47 (m, 2H), 4.19 (t, J = 6.7 Hz, 2H), 3.64 – 3.51 (m, 2H), 1.72 – 1.65 (m, 6H), 1.45 – 1.40 (m, 2H), 0.98 – 0.94 (m, 3H).

^{13}C NMR (151 MHz, $CDCl_3$) δ 167.1, 152.5, 149.9, 141.2, 140.9, 139.9, 139.4, 139.0, 137.1, 136.7, 135.0, 134.6, 128.5, 127.9, 127.4, 125.8, 122.20, 122.18, 122.0, 117.4, 64.6, 32.8, 30.9, 27.6, 19.3, 18.1, 13.9, 13.1.

HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{24}NO_2S$ 342.1450; Found 342.1462.

2.7 H/D exchange experiment.



2-(Thiophen-2-yl)pyridine **1a** (48.3 mg, 0.3 mmol), $[Cp^*RhCl_2]_2$ (3.8 mg, 0.06 mmol), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (119.8 mg, 0.6 mmol), CD_3OD (0.2 mL) and DCE (2 mL) were charged into a Schlenk tube. The mixture was then stirred at 120 °C under Ar for 2 h. Then, the reaction mixture was cooled to room temperature and filtered through a plug of celite. The organic phase was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 10:1) to afford **[1a]-d_1-1**. Upon analyzing the ^{1}H NMR spectra as shown in **Figure S1**, the estimated deuterium incorporation at the C3-position of the thiophen ring was 81%.

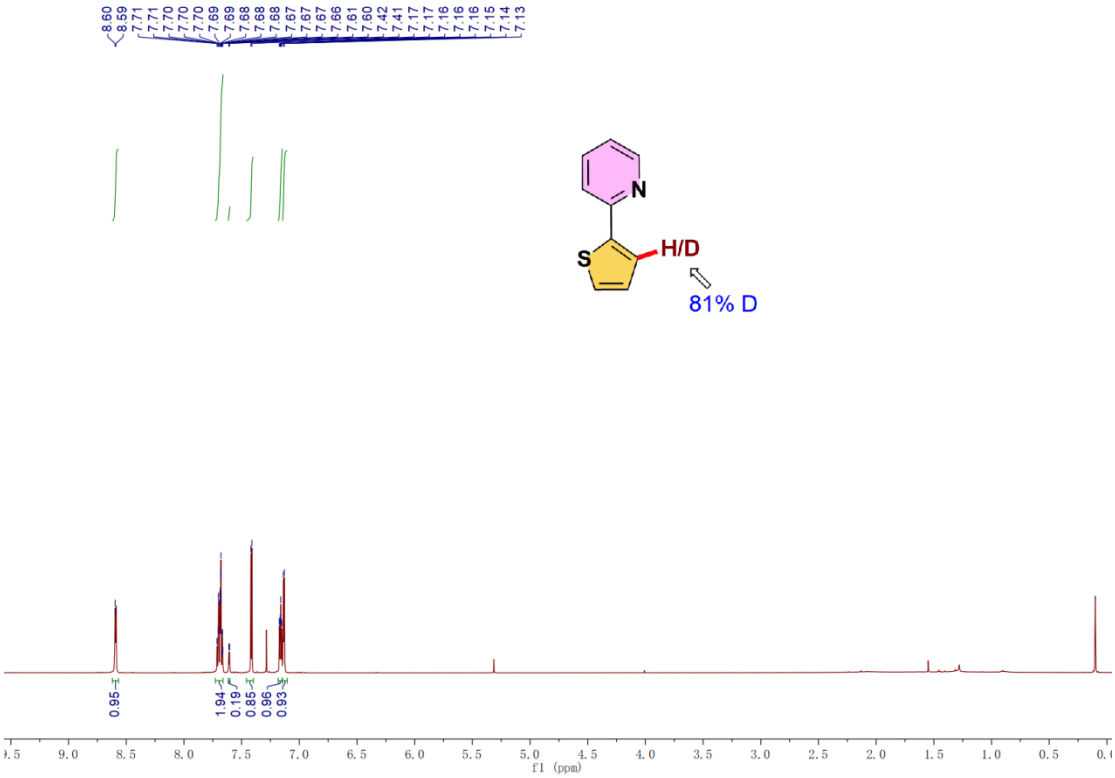
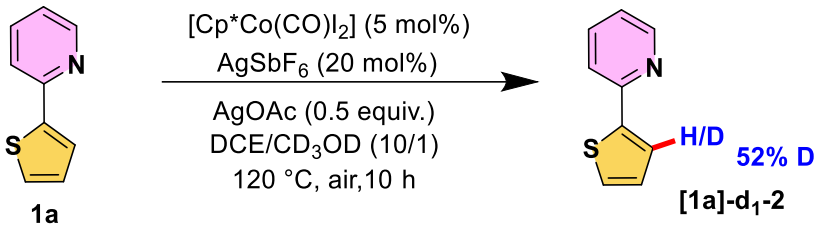


Figure S1. The ^{1}H NMR spectra of **[1a]-d_1-1**



2-(thiophen-2-yl)pyridine **1a** (48.3 mg, 0.3 mmol), $[Cp^*(CO)I_2]_2$ (7.1 mg, 0.015 mmol), $AgSbF_6$ (20 mol%), AgOAc (24.9 mg, 0.6 mmol), CD_3OD (0.2 mL) and DCE (2 mL) were charged into a Schlenk tube. The mixture was then stirred at 120 °C under air for 10 h. Then, the reaction mixture was cooled to room temperature and filtered through a plug of celite. The organic phase was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 10:1) to afford **[1a]-d_1-2**. Upon analyzing the ^{1}H NMR spectra as shown in **Figure S2**, the estimated deuterium incorporation at the C3-position of the thiophen ring was 52%.

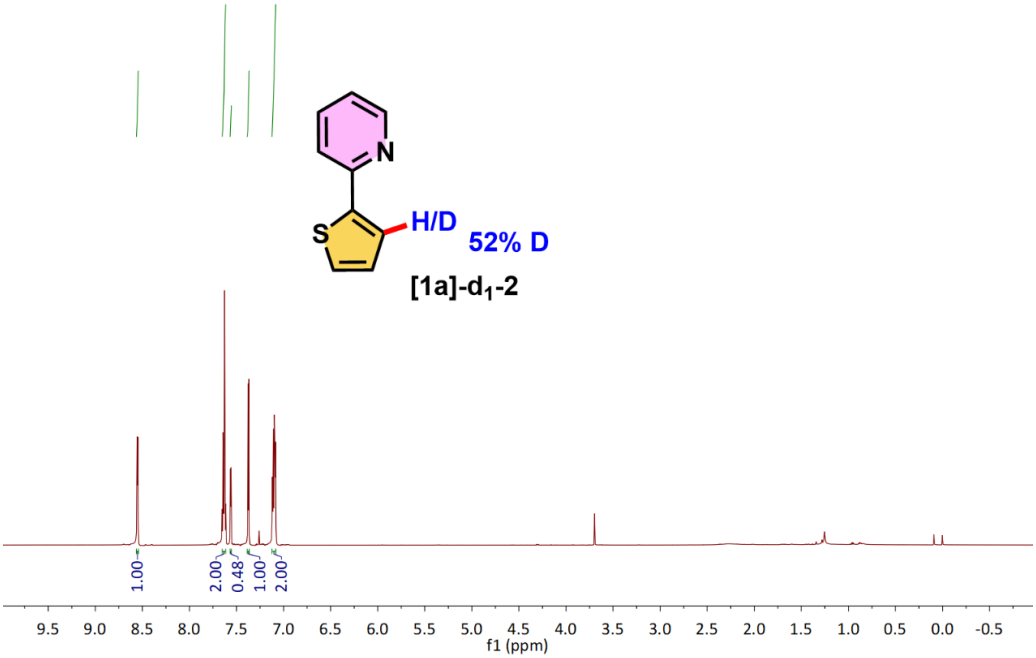
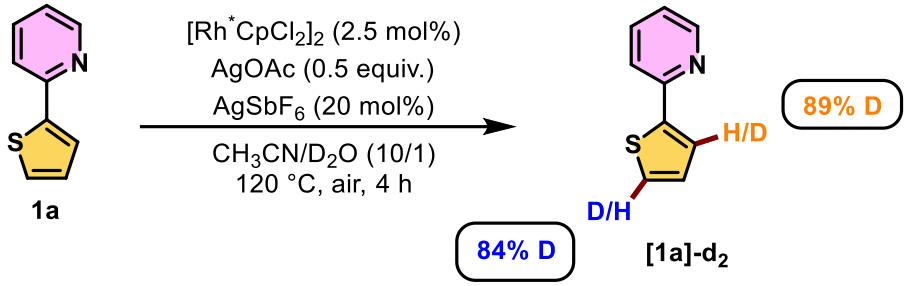


Figure S2. The ^{1}H NMR spectra of **1a-d_1-2**

2.8 KIE determination



Modified procedure for the synthesis of [1a]-d_2 of 2-pyridylthiophene[3]: To a 15 mL oven dried Schlenk tube, 2-(thiophen-2-yl)pyridine **1a** (32.2 mg, 0.2 mmol, 1 equiv.), AgOAc (68.8 mg, 0.4 mmol, 2 equiv.), $AgSbF_6$ (13.7 mg, 0.04 mmol, 20 mol%), $[Rh^*CpCl_2]_2$ (3.1 mg, 0.005 mmol, 2.5 mol%), D_2O (0.15 mL) and CH_3CN (1.5 mL) were successively added. The mixture was then stirred at 120 °C for 4 h. Then, the reaction mixture was cooled to room temperature and filtered through a plug of celite. The organic phase was concentrated under reduced pressure, and the residue was purified by silica gel chromatography (petroleum ether/ethyl acetate = 20:1) to afford **[1a]-d_2**. Upon analyzing the ^{1}H NMR spectra as shown in **Figure S3**, the estimated deuterium incorporation at the C3-position of the thiophene ring was 89% and at the C5-position was 84%.

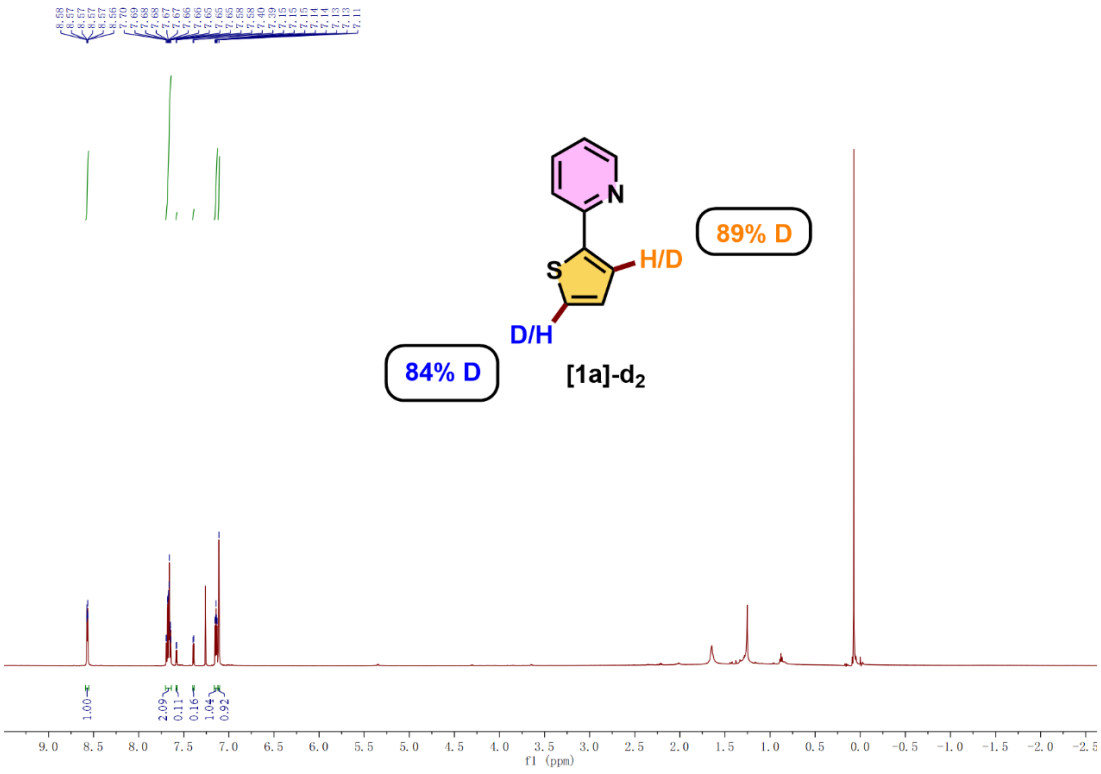


Figure S3. The ^{1}H NMR spectra of **[1a]-d_2**

To a 15 mL oven dried Schlenk tube, **1a** (0.15 mmol), **[1a]-d₂** (0.15 mmol), $[Cp^*RhCl_2]_2$ (3.8 mg, 0.006 mmol, 2.5 mol%), $AgSbF_6$ (20 mol%), $Cu(OAc)_2$ (0.6 mmol, 2 equiv.), **2a** (0.3 mmol, 2 equiv.), and DCE (2 mL) were successively added. The reaction mixture was stirred at 120 °C (metal sand bath temperature) for 10 hours under Ar. After cooling the reaction at room temperature and concentration, the crude mixture was purified over a column of silica gel (petroleum ether/ethyl acetate = 30:1) to afford the mixture of products **3aa** and **[3aa]-d₁** as yellow solid. By analyzing the ^{1}H NMR of the mixture **3aa** and **[3aa]-d₁** as shown in **Figure S4**, the ratio of **3aa** and **[3aa]-d₁** was determined to be 0.52:0.48. Accordingly, the intermolecular **KIE** (k_H/k_D) = 0.52/1.00-0.52 = 1.08.

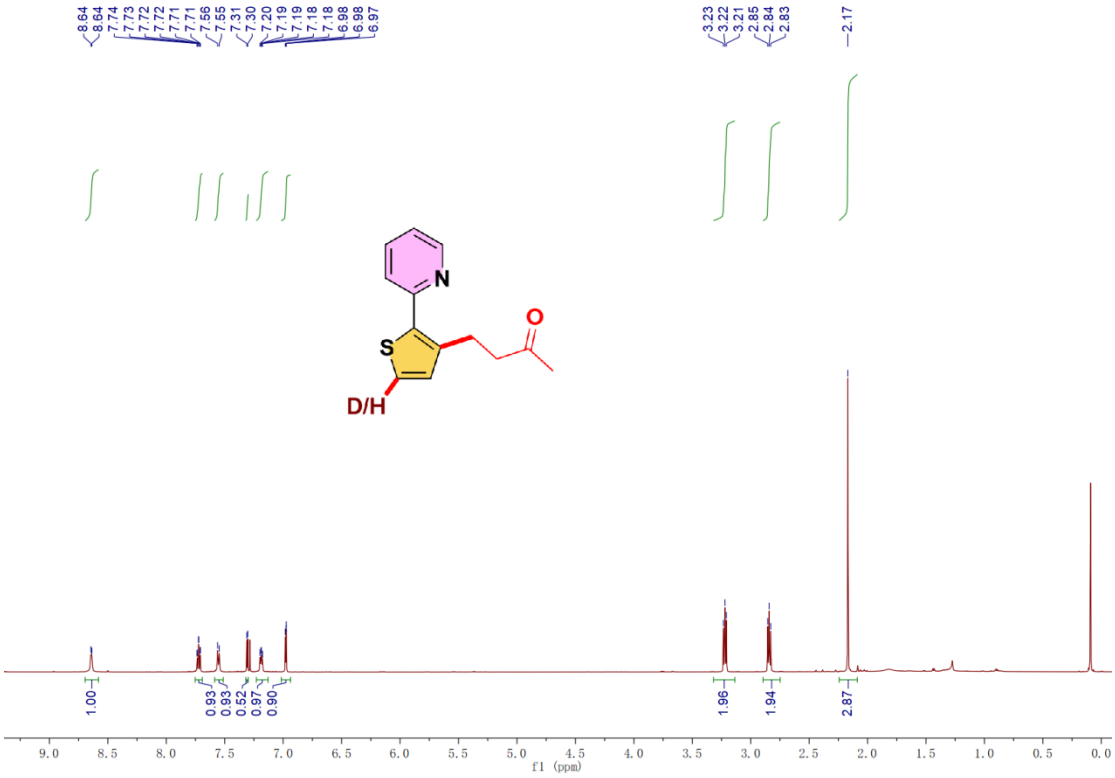
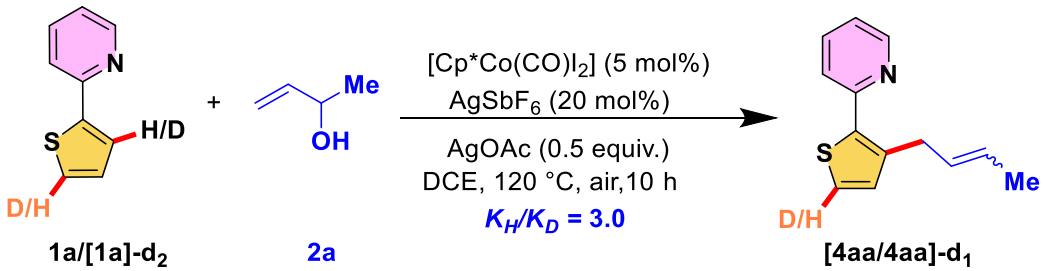


Figure S4. The ^{1}H NMR spectra of **3aa/[3aa]-d₁**



1a/[1a]-d₂ **2a** **[4aa/4aa]-d₁**

To a 15 mL oven dried Schlenk tube, **1a** (0.15 mmol), **[1a]-d₂** (0.15 mmol), $[Cp^*(CO)I_2]_2$ (3.5 mg, 0.075mmol), $AgSbF_6$ (20 mol%), AgOAc (24.9 mg, 0.6 mmol), **2a** (0.3 mmol, 2 equiv.), and DCE (2 mL) were successively added. The reaction mixture was stirred at 120 °C (metal sand bath temperature) for 10 hours under Ar. After cooling the reaction at room temperature and concentration, the crude mixture was purified over a column of silica gel (petroleum ether/ethyl acetate = 30:1) to afford the mixture of products **4aa** and **[4aa]-d₁** as yellow solid.

By analyzing the ^{1}H NMR of the mixture **4aa** and **[4aa]-d$_1$** as shown in **Figure S5**, the ratio of **4aa** and **[4aa]-d$_1$** was determined to be 0.75:0.25. Accordingly, the intermolecular **KIE** (k_H/k_D) = 0.75/1.00-0.75 = 3.0.

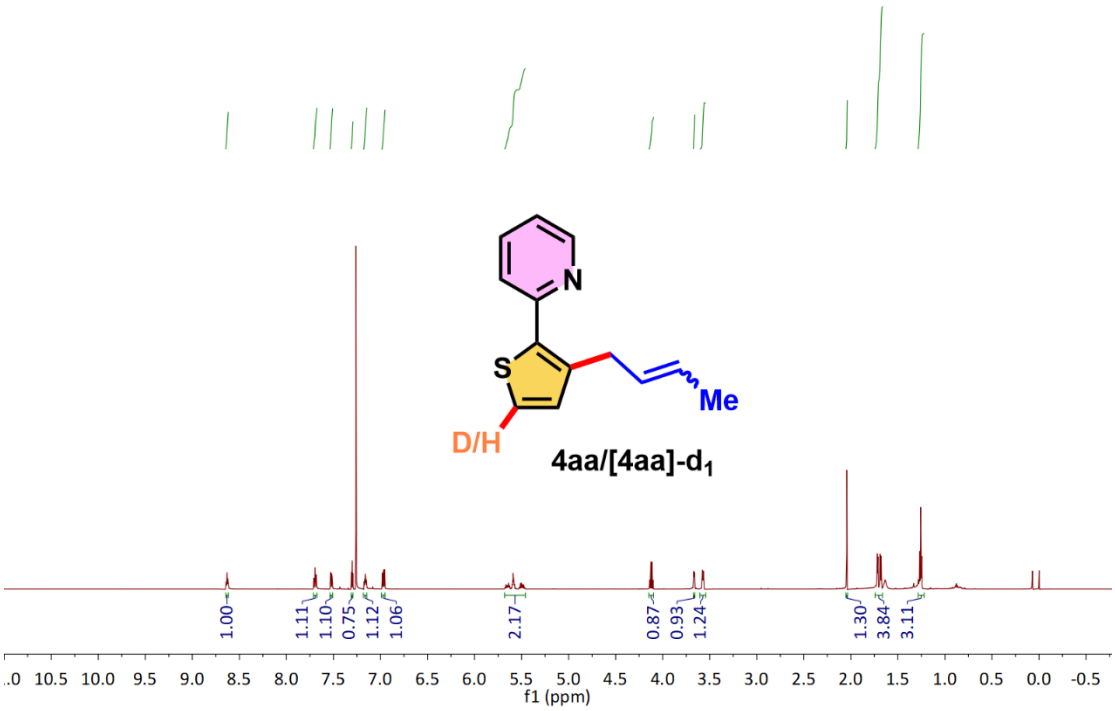


Figure S5. The ^{1}H NMR spectra of **4aa/[4aa]-d$_1$**

3. Crystallographic description

White block-like single crystals of **3ra** were grown by layering a dichlormethane solution with hexane at ambient temperature. X-Ray diffraction data of one these crystals were collected on a R-AXIS SPIDER diffractometer. The measurements were performed with Mo-Kα radiation (λ = 0.71073 Å). Data were collected at 298(2) K, using the *ω*- and *φ*- scans to a maximum θ value of 28.327°. The data were refined by full-matrix least-squares techniques on F^2 with SHELXL-2018/3. And the structures were solved by direct methods SHELXL-2018/3. All the non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included at geometrically idealized positions. And an ORTEP representation of the structure is shown below.

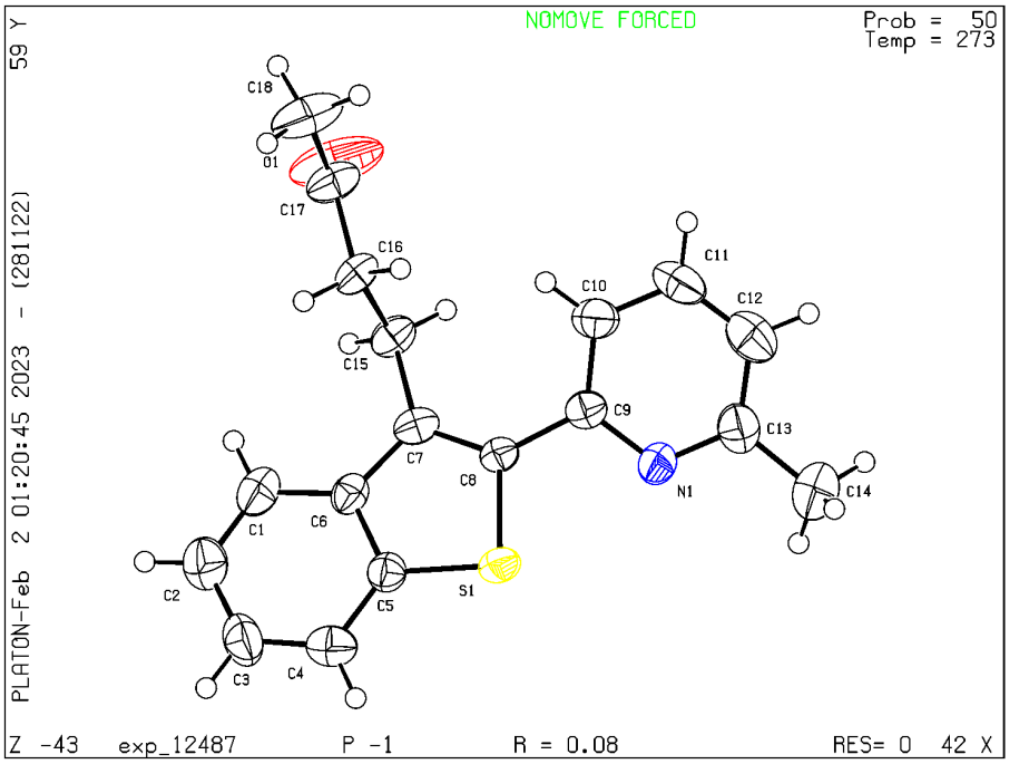


Figure S5. ORTEP diagram of **3ra** with the thermal ellipsoids set at 50% probability.

Table 1 Crystal data and structure refinement for 3ra.

Identification code	3ra
Empirical formula	$C_{18}H_{17}NOS$
Formula weight	295.38
Temperature/K	273
Crystal system	triclinic
Space group	P-1
a/Å	8.9181(9)
b/Å	9.3908(10)
c/Å	10.8301(12)
α/°	113.868(10)
β/°	100.187(9)

γ/°	104.576(9)
Volume/Å^3	761.90(15)
Z	2
ρ_{calc}g/cm^3	1.288
μ/mm^{-1}	0.210
F(000)	312.0
Crystal size/mm^3	0.3 × 0.2 × 0.1
Radiation	? (λ = 0.71073)
2Θ range for data collection/°	7.292 to 58.608
Index ranges	-11 ≤ h ≤ 12, -12 ≤ k ≤ 12, -9 ≤ l ≤ 13
Reflections collected	6169
Independent reflections	3466 [R_{int} = 0.0601, R_{sigma} = 0.1109]
Data/restraints/parameters	3466/0/193
Goodness-of-fit on F^2	1.001
Final R indexes [I>=2σ (I)]	R_1 = 0.0837, wR_2 = 0.2136
Final R indexes [all data]	R_1 = 0.1286, wR_2 = 0.2843
Largest diff. peak/hole / e Å^{-3}	0.71/-1.19

Table 2 Fractional Atomic Coordinates (×10^4) and Equivalent Isotropic Displacement Parameters (Å^2×10^3) for 3ra. U_{eq} is defined as 1/3 of the trace of the orthogonalised U_{IJ} tensor.

Atom	*x*	*y*	*z*	U(eq)
S1	1744.4(9)	2124.9(10)	4328.2(10)	39.5(4)
N1	2234(3)	2372(4)	1845(3)	41.1(8)
C7	2170(3)	5278(4)	5326(4)	36.0(8)
C6	1643(3)	4783(4)	6321(4)	35.6(8)
C9	2837(4)	3886(4)	2990(4)	34.6(8)
C8	2291(3)	3984(4)	4214(4)	32.0(7)
C5	1407(4)	3100(4)	5909(4)	36.7(8)
C15	2513(4)	7015(4)	5539(4)	39.3(9)
C16	4208(4)	8190(4)	6574(4)	40.4(9)
C4	914(4)	2388(5)	6766(5)	49.3(10)
O1	3704(4)	10428(4)	6337(5)	108.4(18)
C10	3998(4)	5222(5)	3035(4)	47.1(10)
C17	4657(4)	9951(4)	6827(5)	50.8(11)
C13	2734(5)	2160(6)	716(5)	50.8(10)
C1	1330(4)	5718(5)	7563(4)	50.9(10)
C3	664(5)	3360(6)	7981(4)	55.8(11)
C11	4525(5)	4989(6)	1875(5)	57.2(12)
C12	3882(5)	3471(6)	703(5)	61.0(12)
C2	847(5)	5022(6)	8388(5)	62.0(12)
C18	6379(5)	11097(5)	7700(6)	80.2(17)
C14	2037(7)	446(7)	-530(6)	84.0(16)

Table 3 Anisotropic Displacement Parameters ($Å^2×10^3$) for 3ra. The Anisotropic displacement factor exponent takes the form: $-2π^2[h^2a^{*2}U_{11}+2hka*b*U_{12}+…]$.

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
S1	45.1(5)	27.0(5)	45.7(7)	16.4(4)	16.7(4)	11.8(4)
N1	50.0(16)	34.6(15)	37.2(18)	14.0(14)	15.3(13)	16.4(13)
C7	28.4(14)	30.8(16)	45(2)	17.3(16)	4.8(13)	9.5(12)
C6	30.8(14)	33.1(17)	33.6(19)	9.2(15)	7.3(12)	10.3(12)
C9	34.4(14)	33.5(17)	38(2)	18.9(16)	8.2(13)	14.1(12)
C8	33.1(14)	27.1(15)	34.3(19)	14.4(14)	8.5(12)	10.1(12)
C5	33.0(15)	35.9(17)	36(2)	13.9(16)	10.9(13)	10.5(12)
C15	38.5(16)	31.1(17)	44(2)	15.0(16)	5.4(14)	16.0(13)
C16	41.0(16)	27.1(16)	43(2)	9.2(16)	7.3(14)	13.1(13)
C4	43.4(18)	46(2)	57(3)	28(2)	11.1(17)	9.7(16)
O1	77(2)	48.9(19)	180(5)	60(3)	-10(2)	16.6(17)
C10	47.1(19)	43(2)	47(2)	24.4(19)	9.9(16)	8.0(15)
C17	47.6(19)	29.9(18)	67(3)	18.5(19)	11.6(18)	14.3(15)
C13	59(2)	56(2)	44(2)	25(2)	20.4(17)	26.3(18)
C1	50(2)	42(2)	47(3)	10.0(19)	13.0(17)	17.6(17)
C3	60(2)	69(3)	37(2)	24(2)	19.1(18)	19(2)
C11	52(2)	69(3)	60(3)	45(3)	19.3(19)	11(2)
C12	64(2)	77(3)	58(3)	44(3)	23(2)	26(2)
C2	66(2)	62(3)	56(3)	22(2)	29(2)	24(2)
C18	57(2)	37(2)	117(5)	25(3)	8(3)	3.6(19)
C14	114(4)	62(3)	65(4)	17(3)	40(3)	28(3)

Table 4 Bond Lengths for 3ra.

Atom	Atom	Length/Å	Atom	Atom	Length/Å
S1	C8	1.752(3)	C15	C16	1.523(4)
S1	C5	1.706(4)	C16	C17	1.494(5)
N1	C9	1.342(4)	C4	C3	1.360(6)
N1	C13	1.331(5)	O1	C17	1.196(5)
C7	C6	1.440(5)	C10	C11	1.373(6)
C7	C8	1.367(5)	C17	C18	1.497(5)
C7	C15	1.492(5)	C13	C12	1.396(6)
C6	C5	1.403(5)	C13	C14	1.496(7)
C6	C1	1.400(5)	C1	C2	1.370(6)
C9	C8	1.467(5)	C3	C2	1.395(7)
C9	C10	1.388(4)	C11	C12	1.356(7)
C5	C4	1.414(5)			

Table 5 Bond Angles for 3ra.

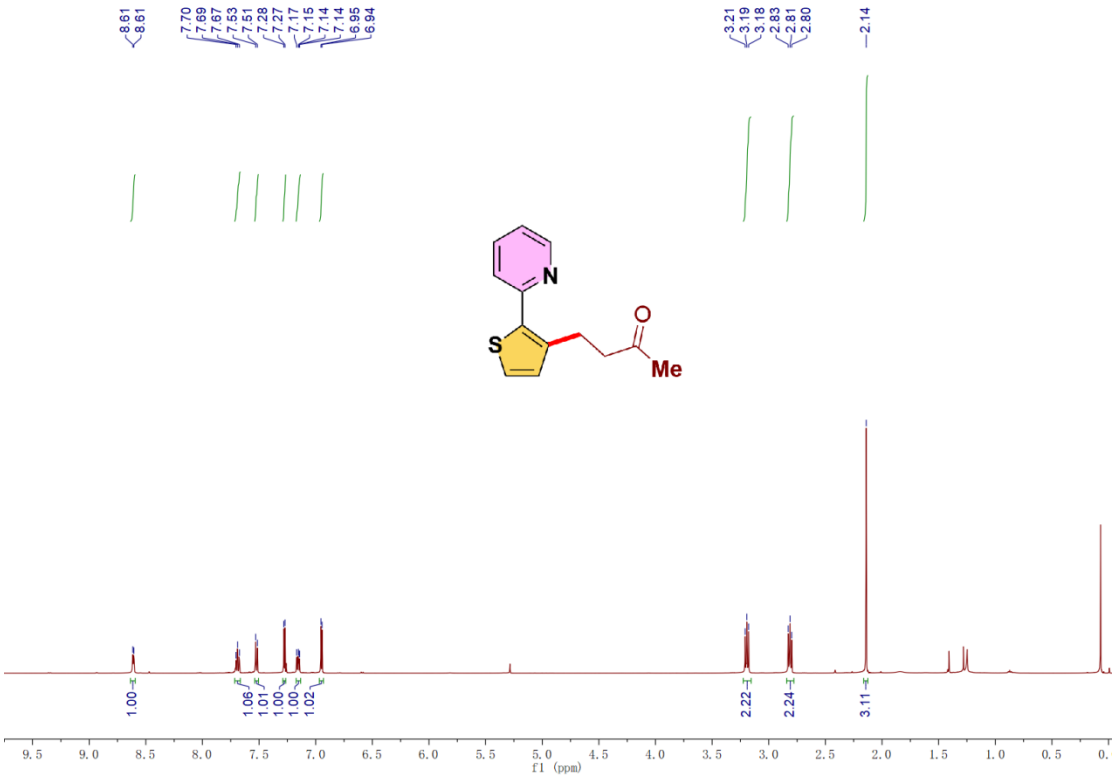
Atom	Atom	Atom	Angle/˚	Atom	Atom	Atom	Angle/˚
C5	S1	C8	91.11(17)	C4	C5	S1	127.3(3)
C13	N1	C9	119.2(3)	C7	C15	C16	111.9(3)
C6	C7	C15	121.8(3)	C17	C16	C15	115.3(3)
C8	C7	C6	111.8(3)	C3	C4	C5	118.8(4)
C8	C7	C15	126.4(3)	C11	C10	C9	119.1(4)
C5	C6	C7	111.8(3)	C16	C17	C18	116.9(3)
C1	C6	C7	129.4(3)	O1	C17	C16	122.1(3)
C1	C6	C5	118.8(4)	O1	C17	C18	121.0(4)
N1	C9	C8	115.5(3)	N1	C13	C12	121.5(4)
N1	C9	C10	121.4(3)	N1	C13	C14	117.2(4)
C10	C9	C8	122.9(3)	C12	C13	C14	121.3(4)
C7	C8	S1	112.7(3)	C2	C1	C6	120.8(4)
C7	C8	C9	132.1(3)	C4	C3	C2	122.0(4)
C9	C8	S1	115.2(3)	C12	C11	C10	119.4(4)
C6	C5	S1	112.6(3)	C11	C12	C13	119.4(4)
C6	C5	C4	120.1(4)	C1	C2	C3	119.5(5)

Table 6 Hydrogen Atom Coordinates (Å×10^4) and Isotropic Displacement Parameters (Å^2×10^3) for 3ra.

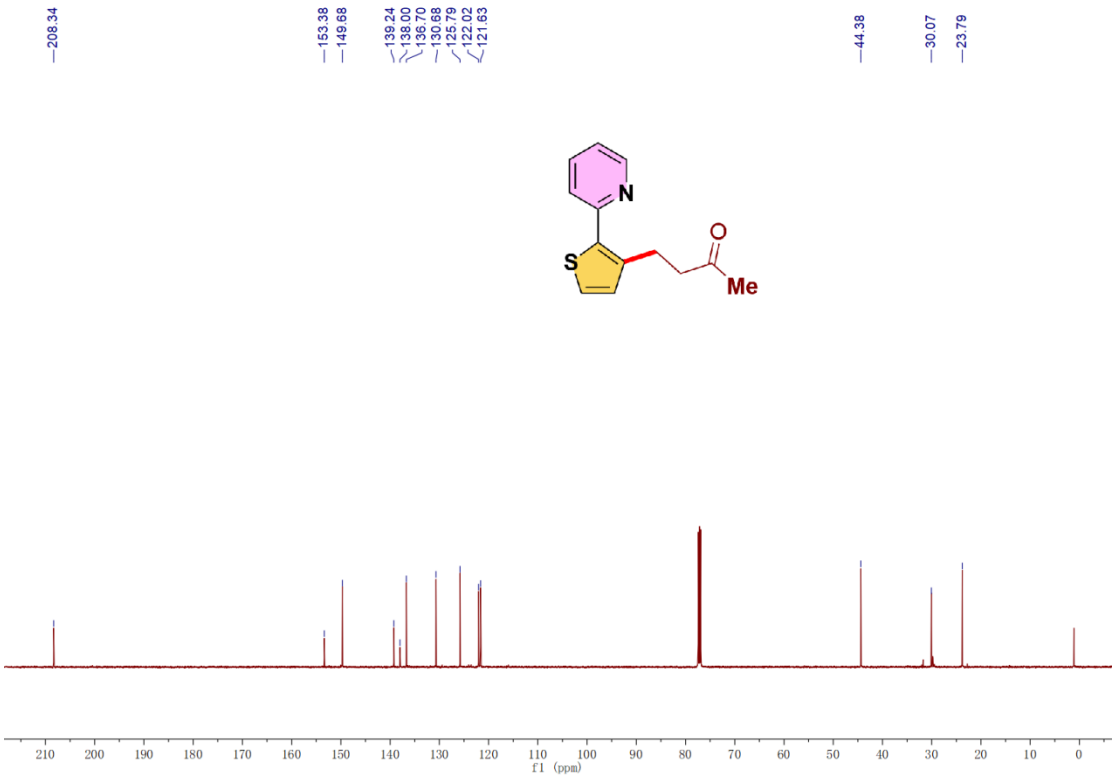
Atom	*x*	*y*	*z*	U(eq)
H15A	1702.42	7423.82	5900.45	47
H15B	2422.55	7007.4	4630.49	47
H16A	4281.92	8191.49	7479.36	48
H16B	5005.32	7751.18	6216.22	48
H4	764.04	1276.29	6502.97	59
H10	4413.54	6260.93	3840.64	57
H1	1449.93	6824.83	7831.62	61
H3	360.89	2903.1	8557.19	67
H11	5315.48	5864.94	1892.48	69
H12	4201.88	3304.74	-100.7	73
H2	643.85	5652.09	9213.08	74
H18A	6703.87	10930.87	8510.52	120
H18B	6450.4	12232.47	8016.18	120
H18C	7087.41	10861.71	7133.77	120
H14A	2756.99	-146.38	-467.78	126
H14B	1918.31	528.84	-1394.75	126
H14C	988.9	-142.33	-527.62	126

4. NMR charts

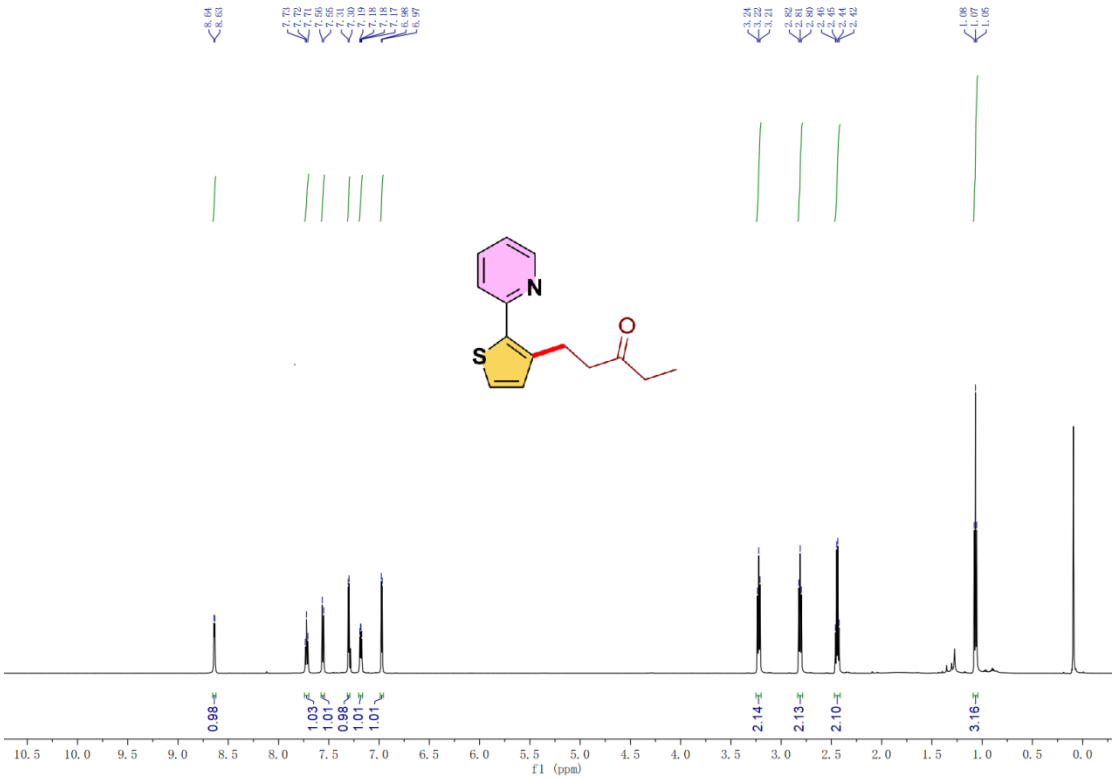
3aa | ^{1}H NMR ($CDCl_3$, 600 MHz)



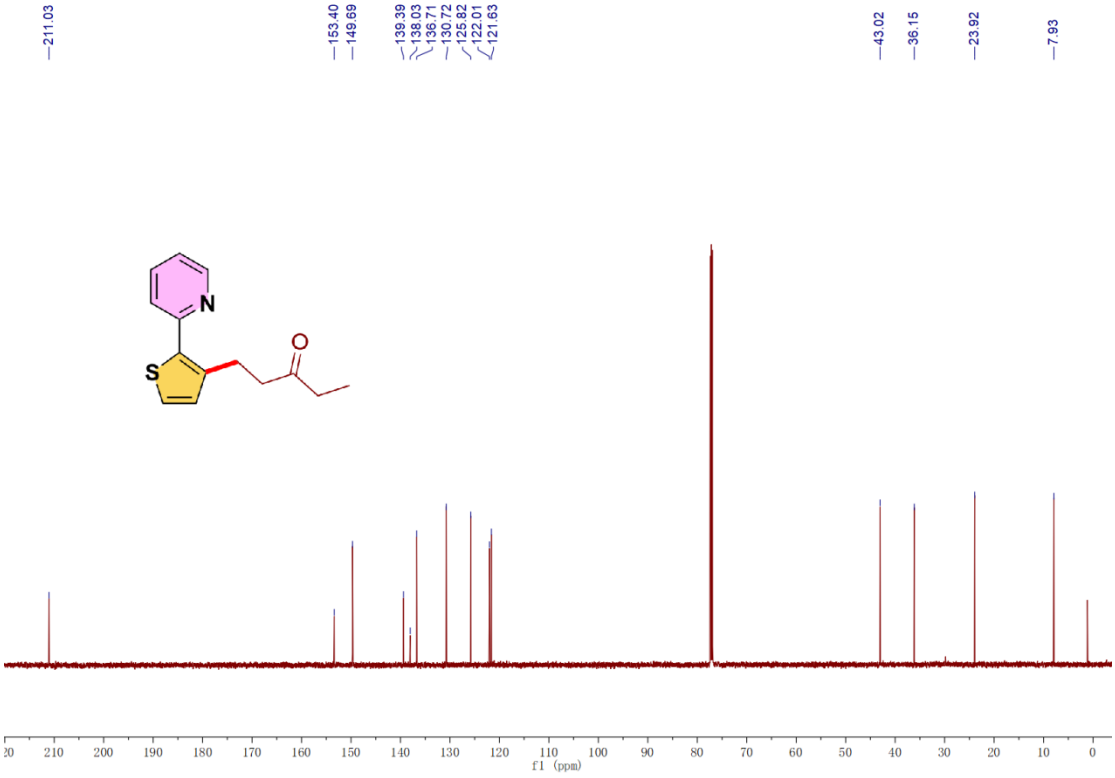
3aa | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



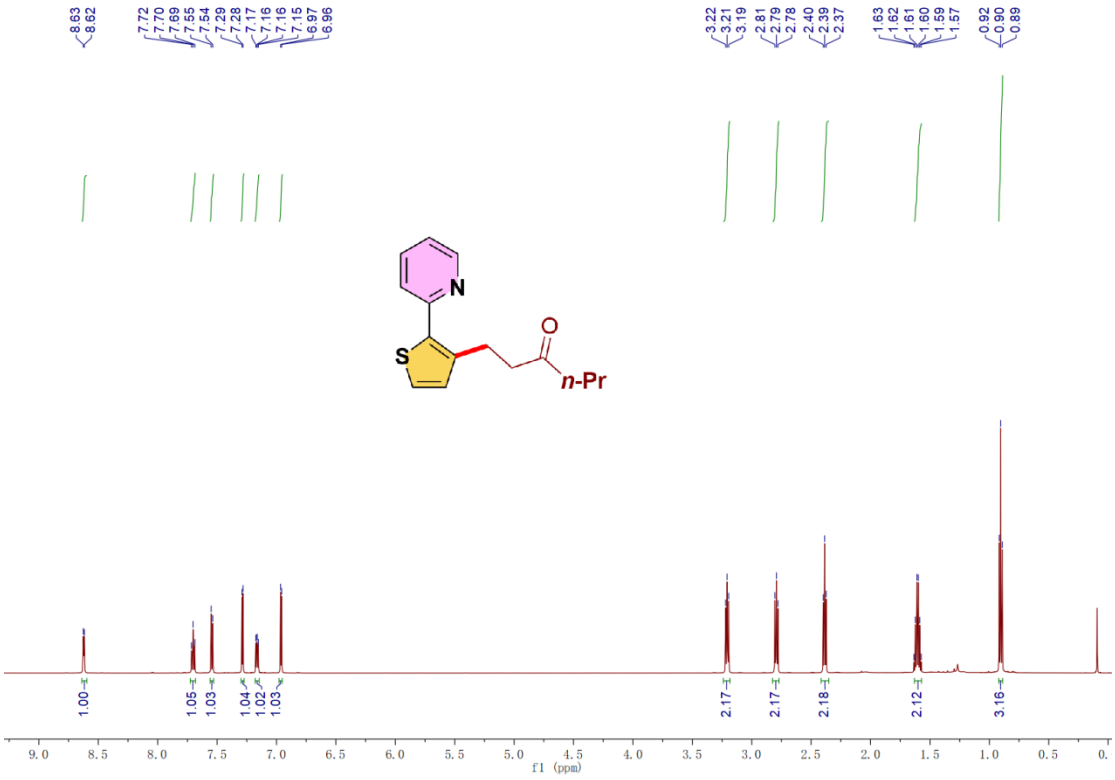
3ab | ^{1}H NMR ($CDCl_3$, 600 MHz)



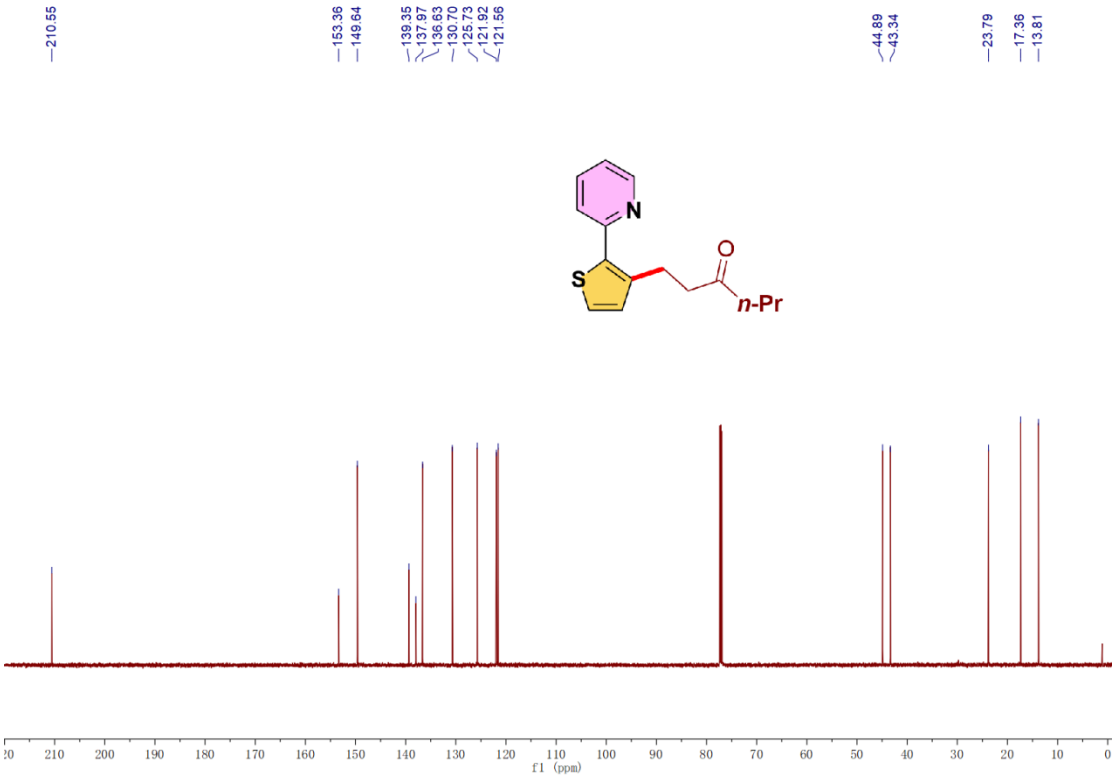
3ab | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



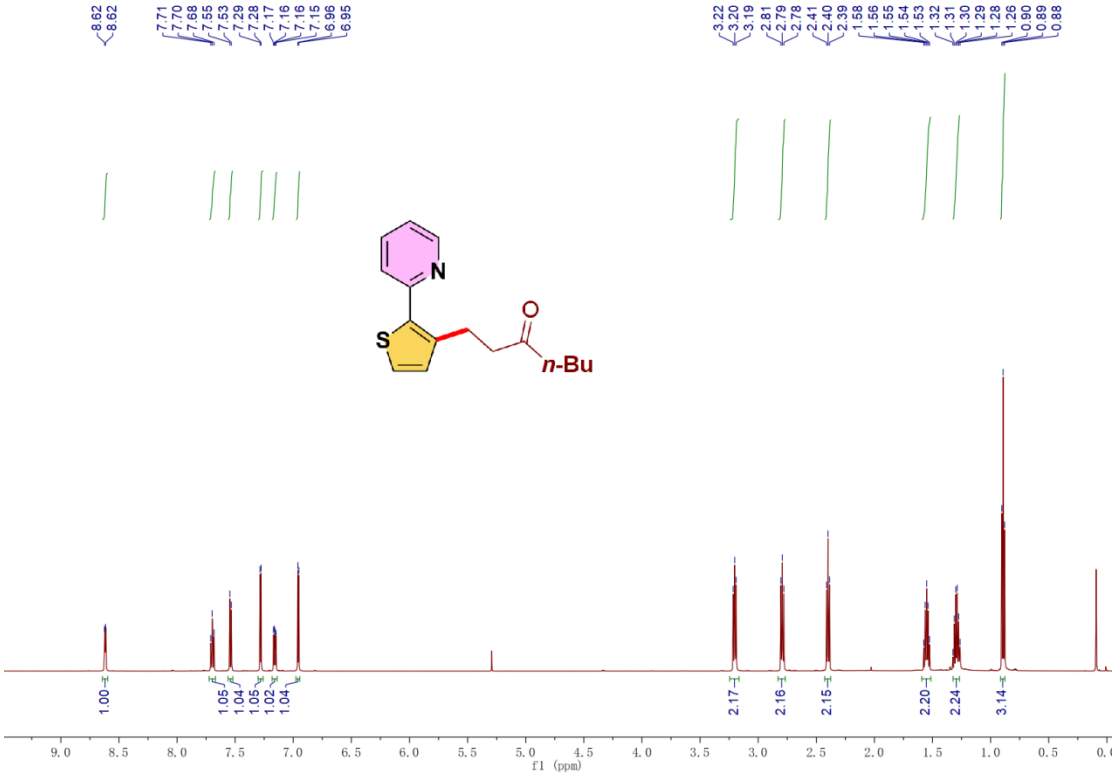
3ac | ^{1}H NMR ($CDCl_3$, 600 MHz)



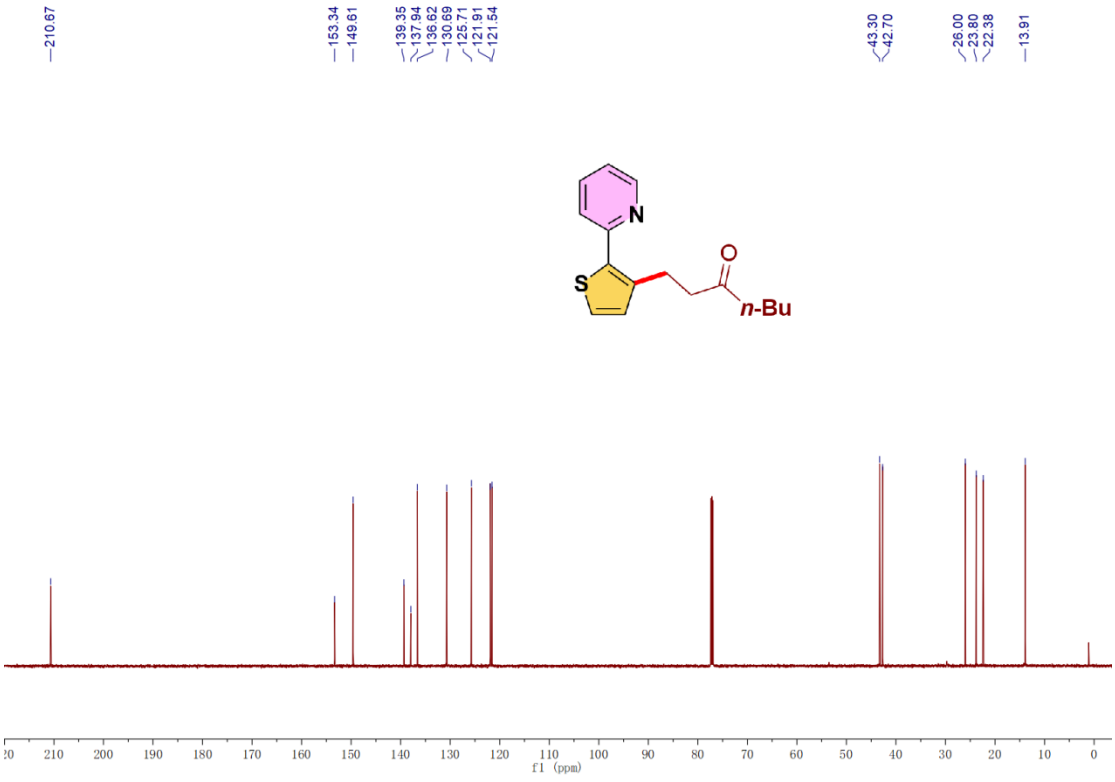
3ac | ^{13}C{^{1}H} NMR ($CDCl_3$, 151 MHz)



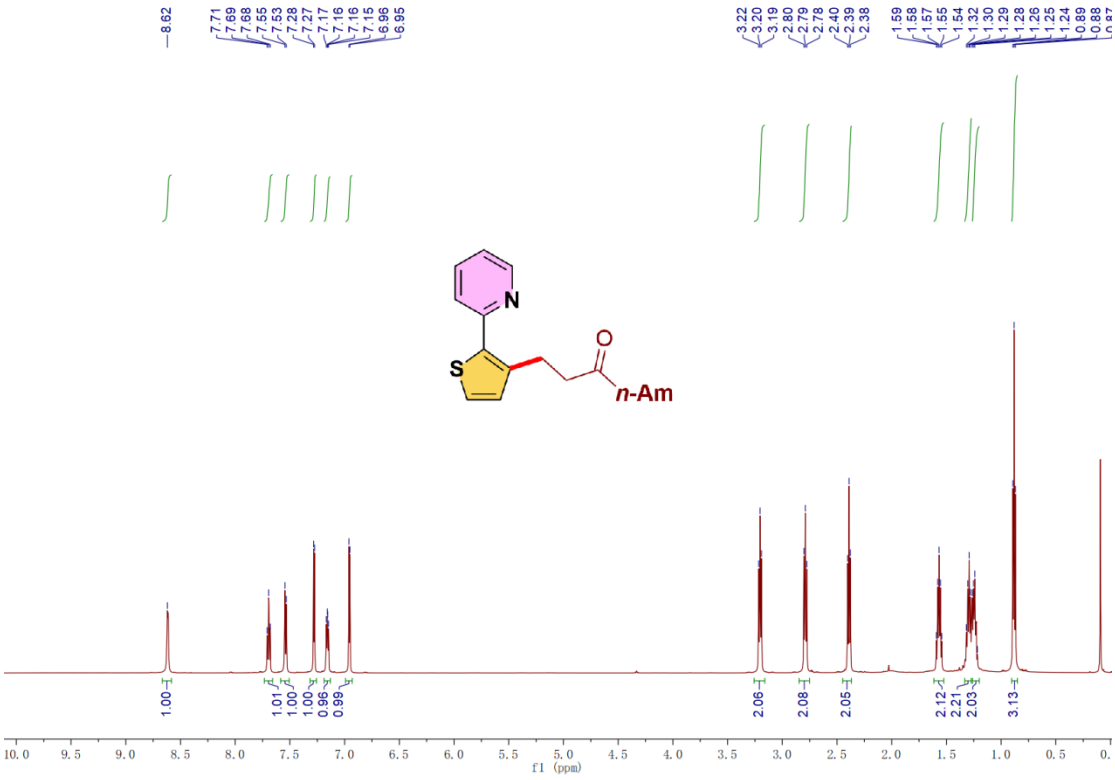
3ad| ^{1}H NMR ($CDCl_3$, 600 MHz)



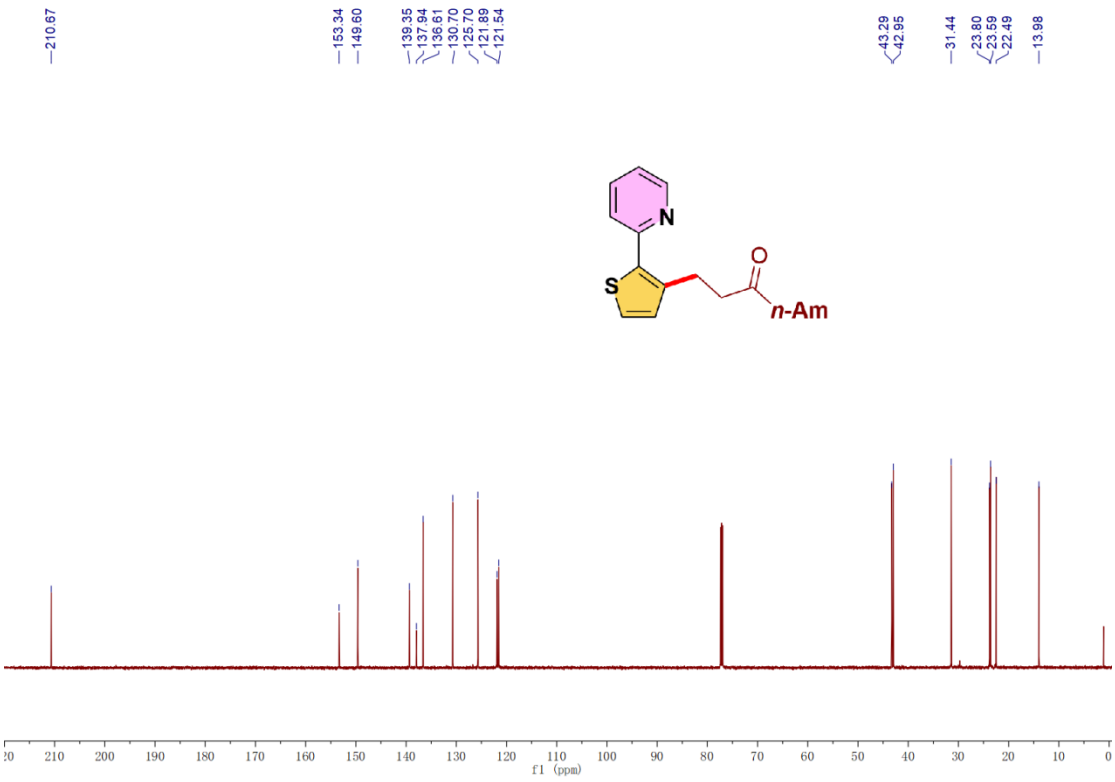
3ad | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



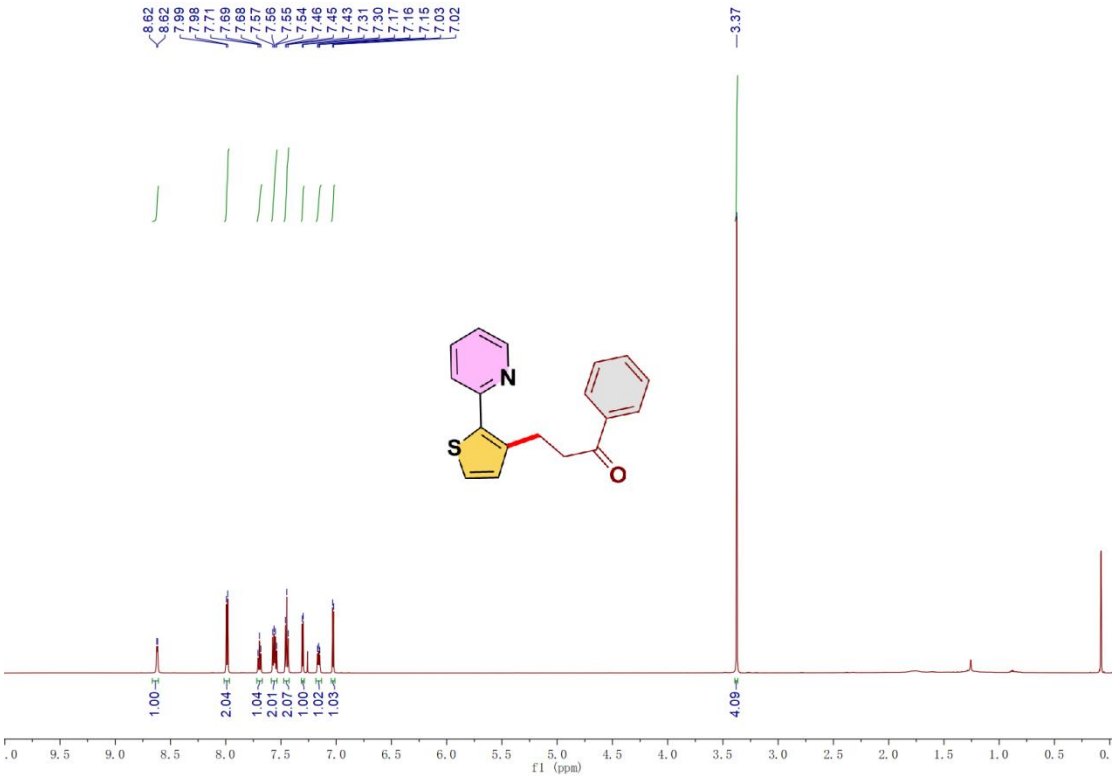
3ae | ^{1}H NMR ($CDCl_3$, 600 MHz)



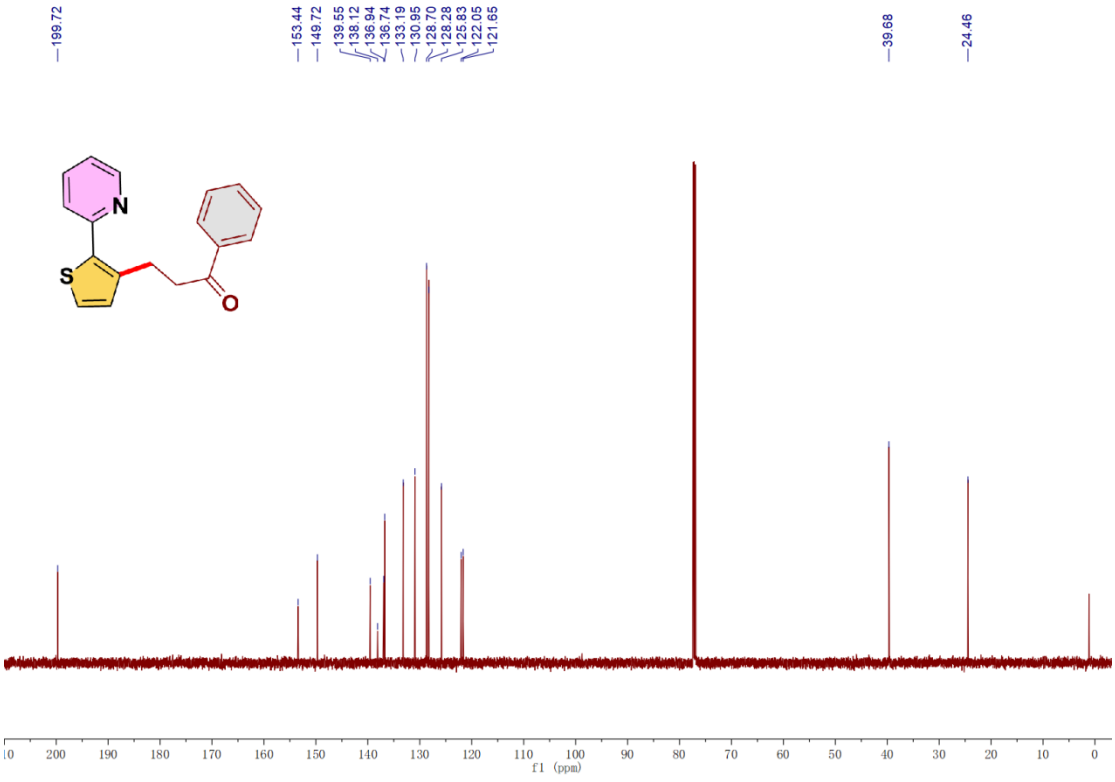
3ae | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



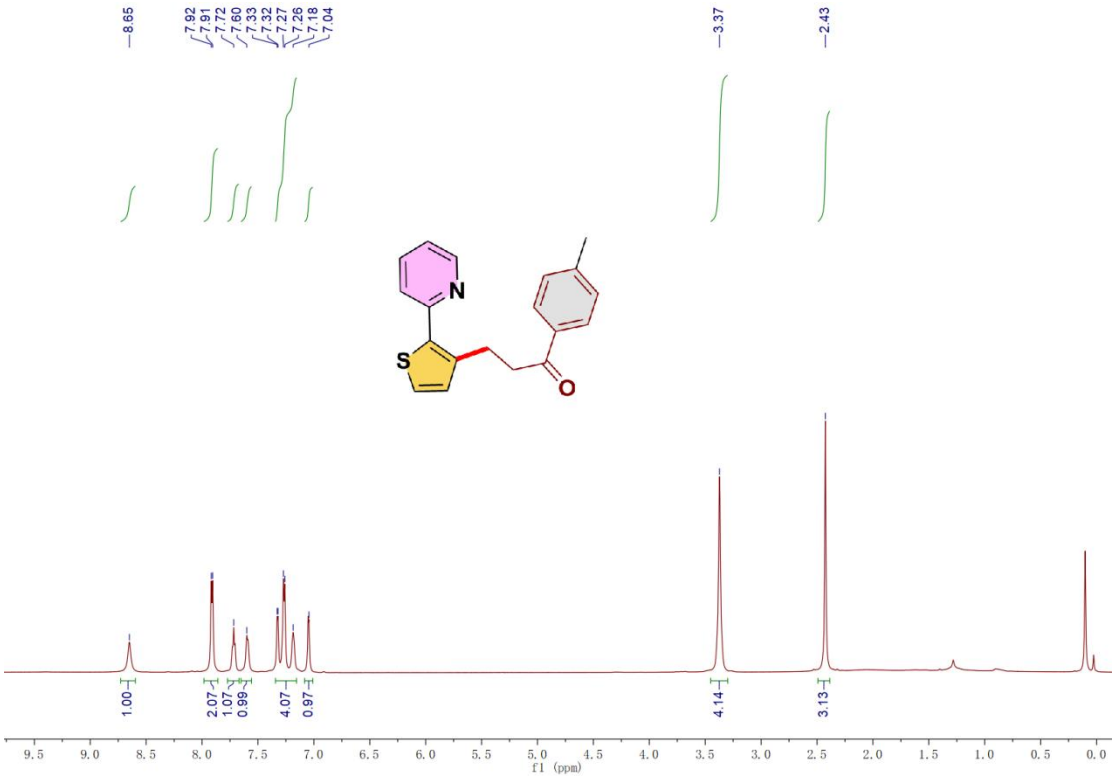
3af | ^{1}H NMR ($CDCl_3$, 600 MHz)



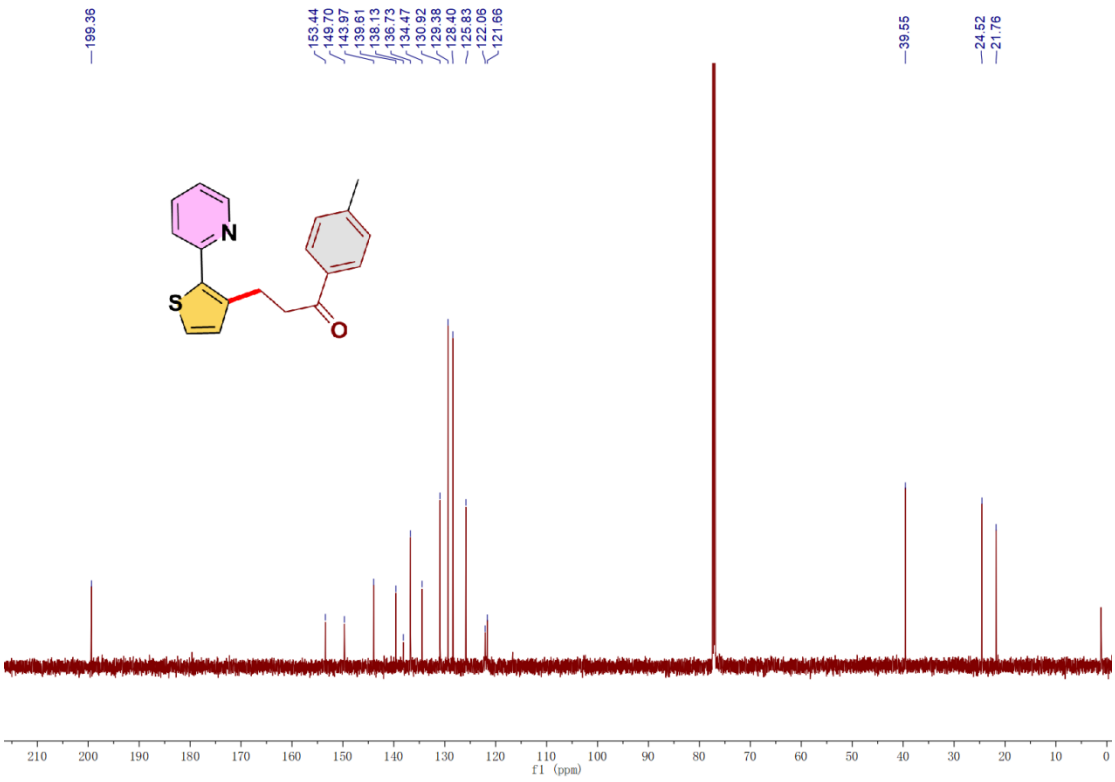
3af | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



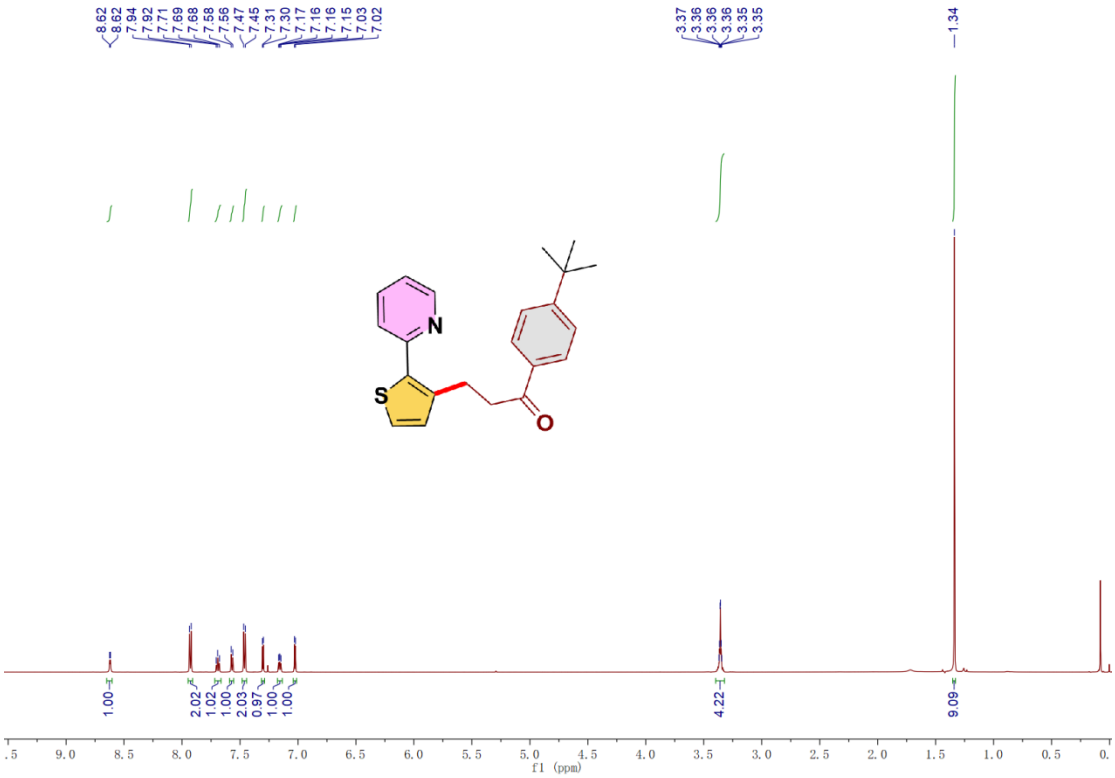
3ag | ^{1}H NMR ($CDCl_3$, 600 MHz)



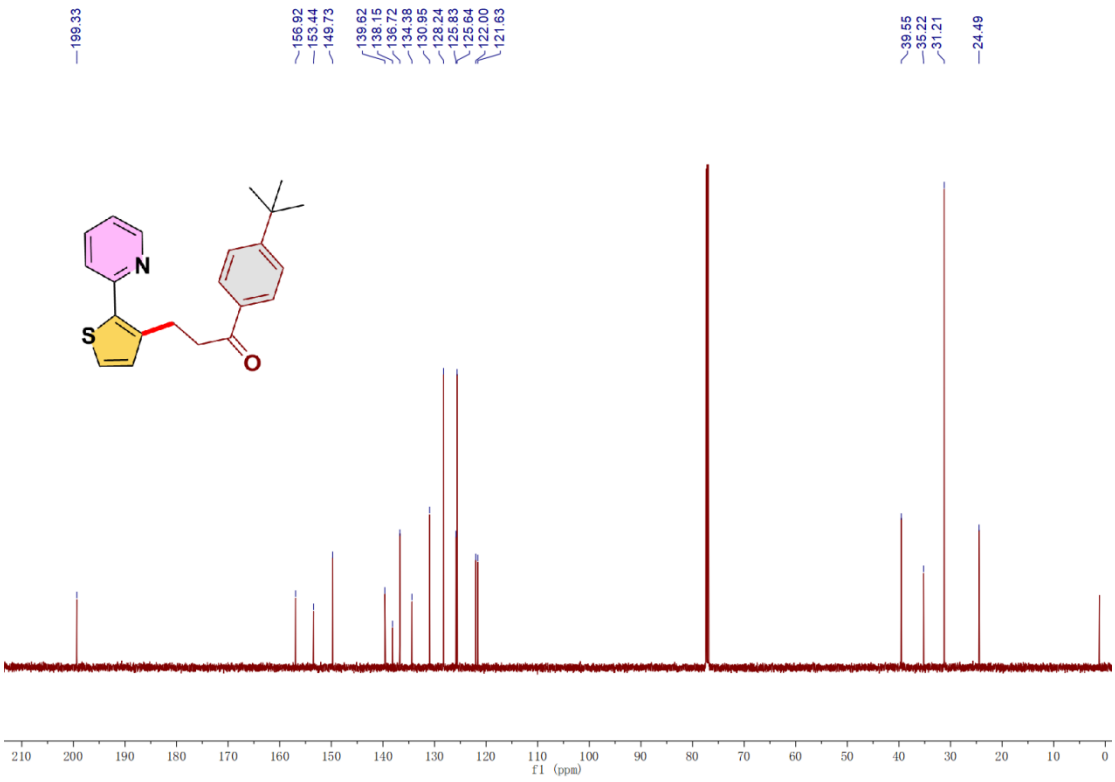
3ag | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



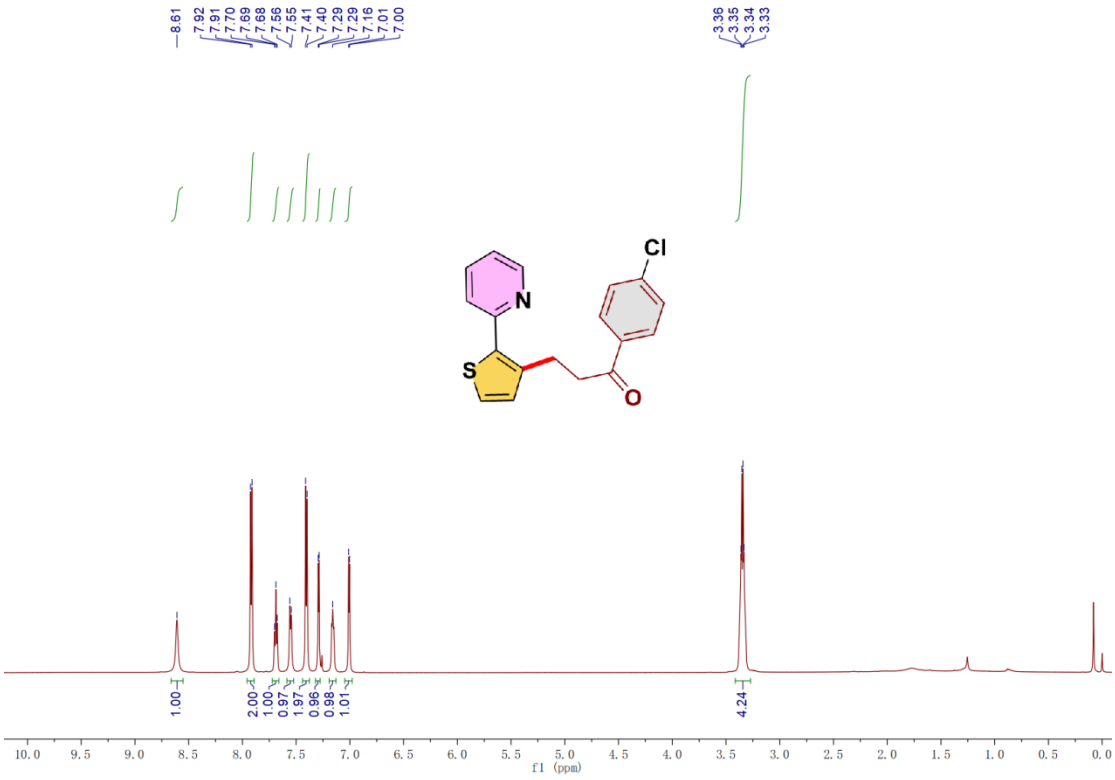
3ah | ^{1}H NMR ($CDCl_3$, 600 MHz)



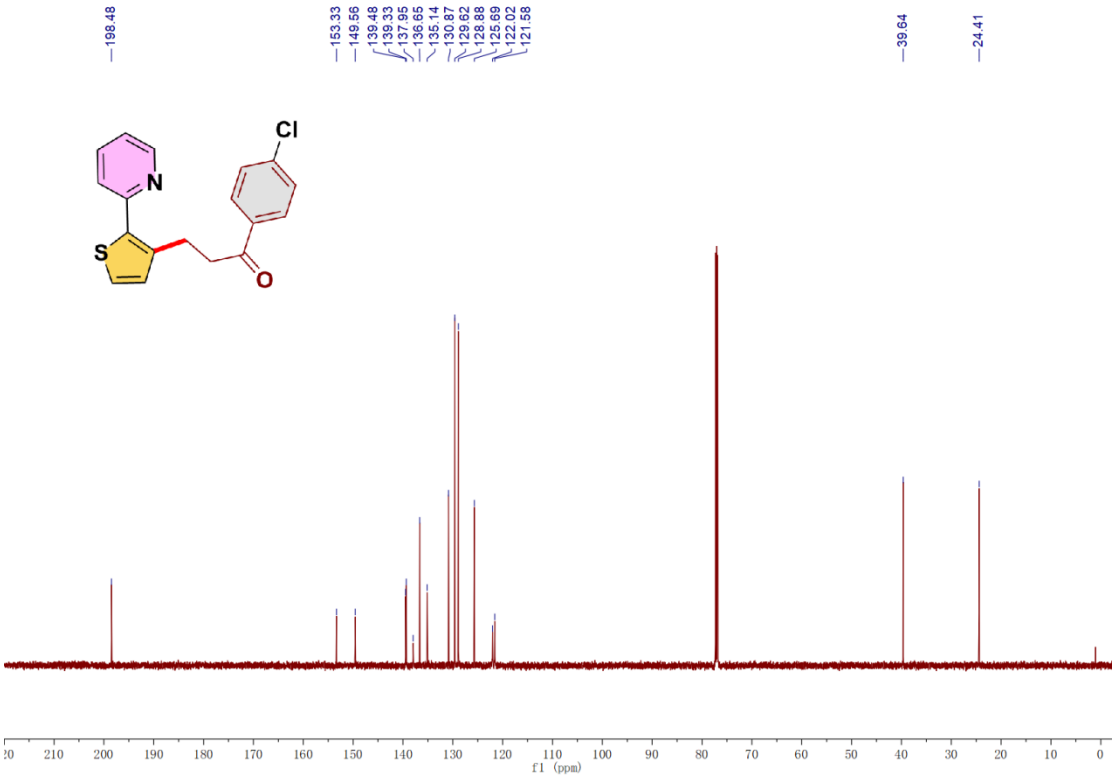
3ah | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



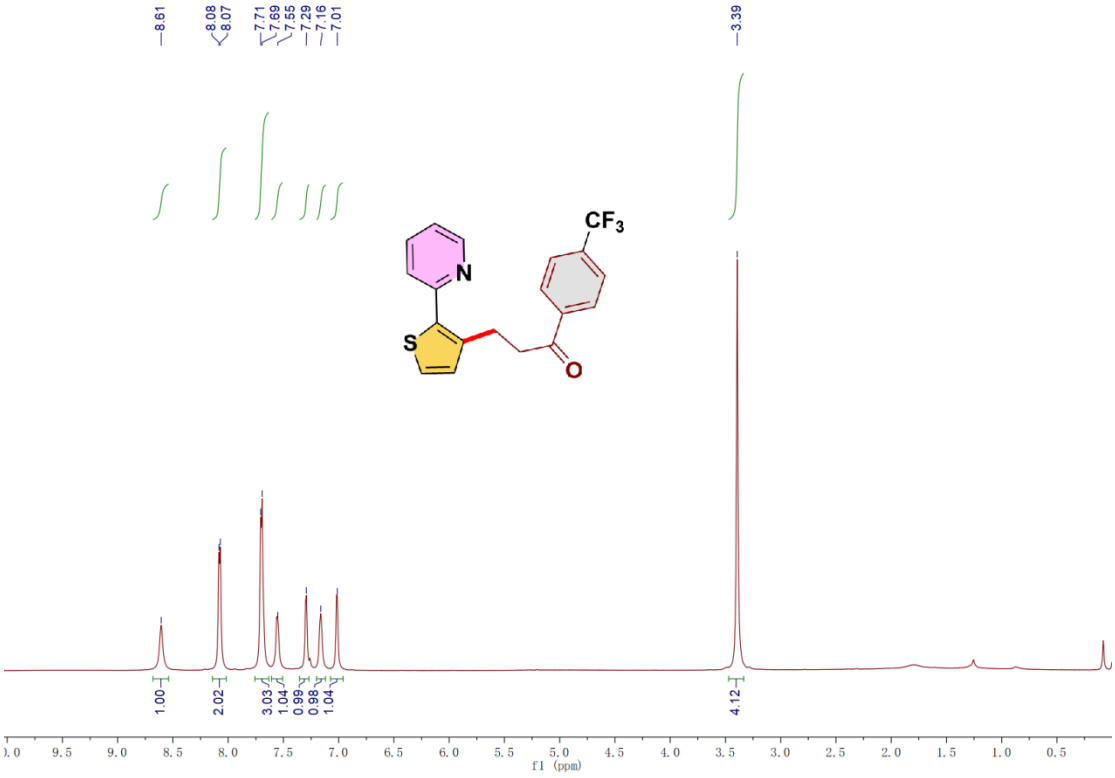
3ai | ^{1}H NMR ($CDCl_3$, 600 MHz)



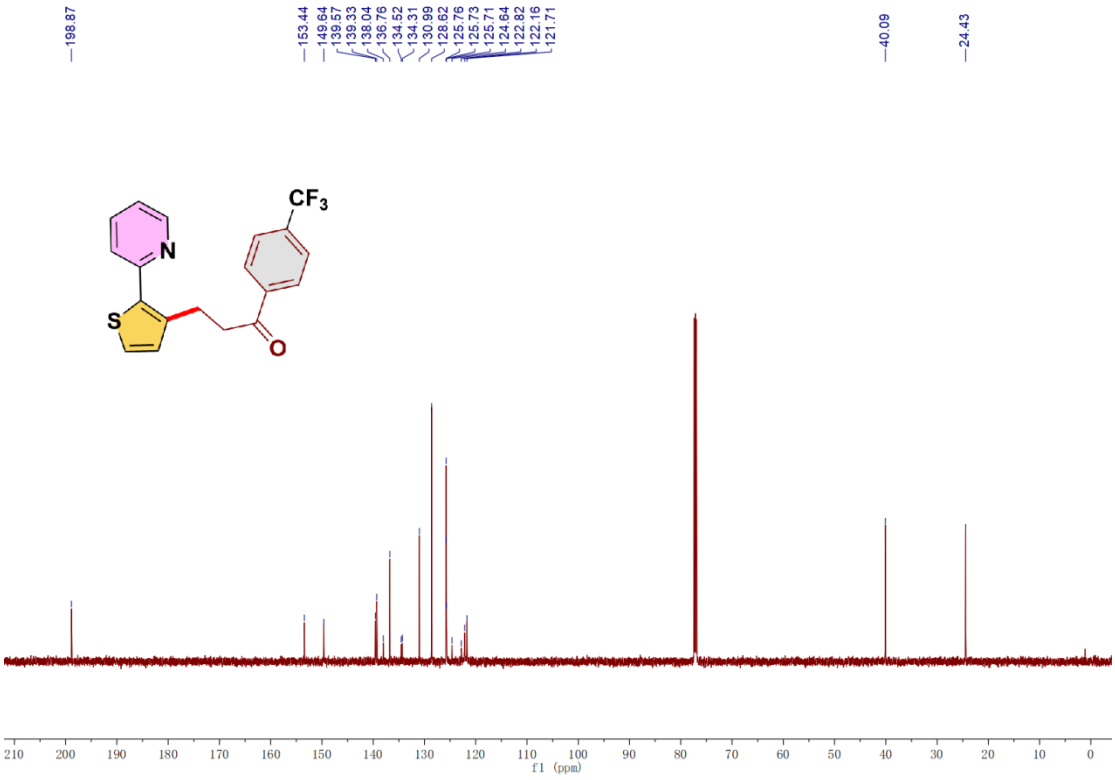
3ai | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



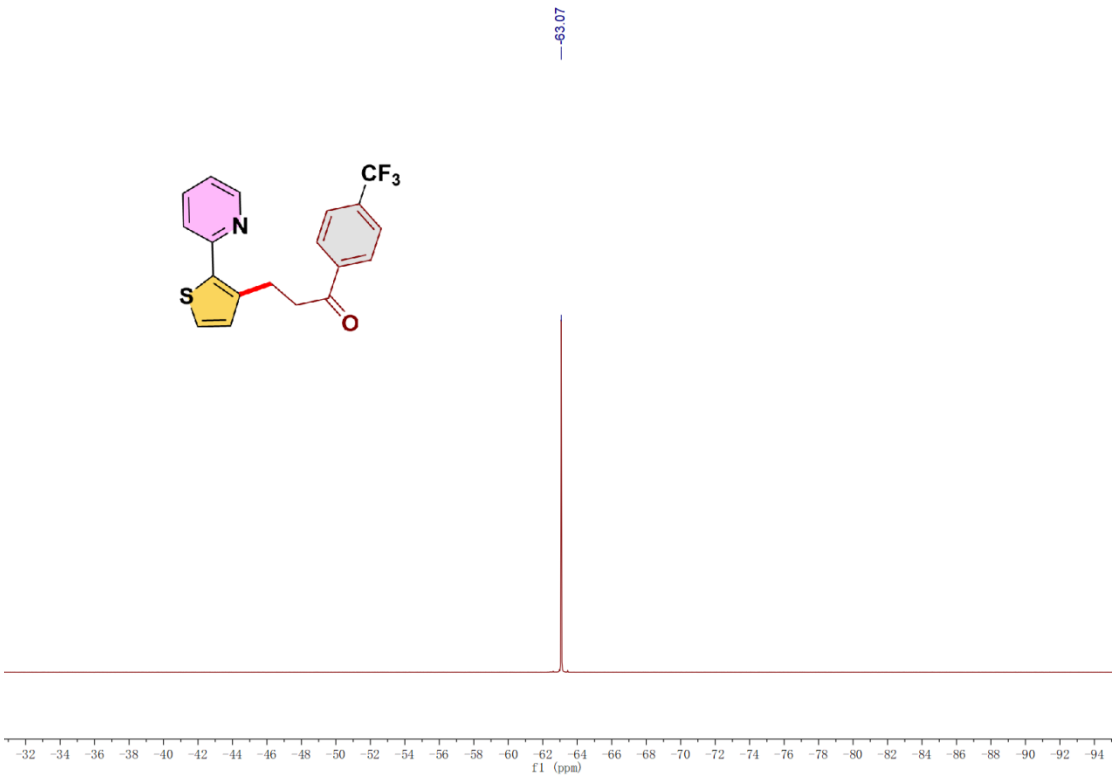
3aj | ^{1}H NMR ($CDCl_3$, 600 MHz)



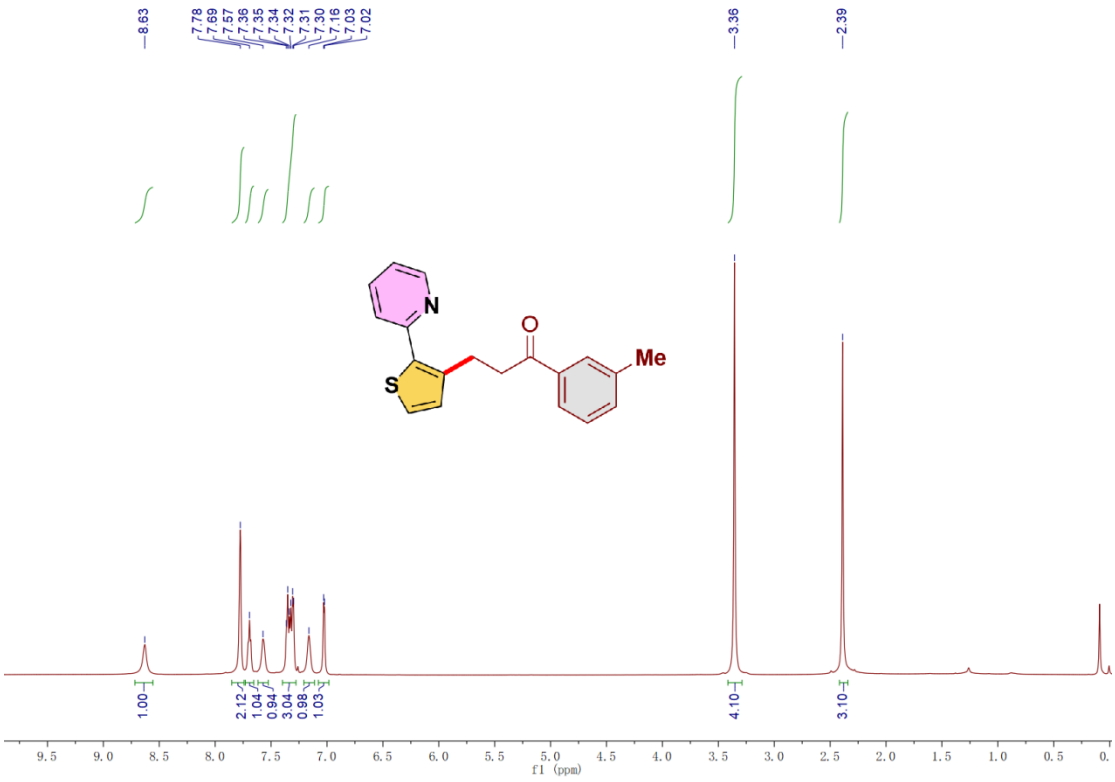
3aj | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



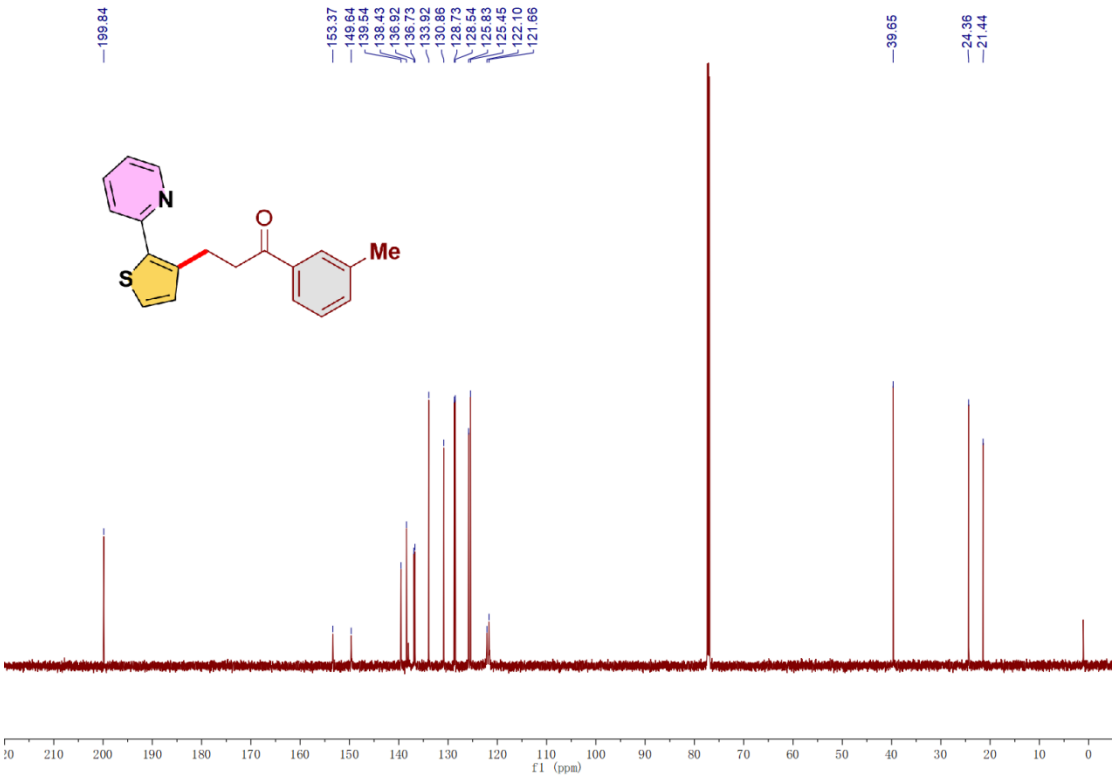
3aj | $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 565 MHz)



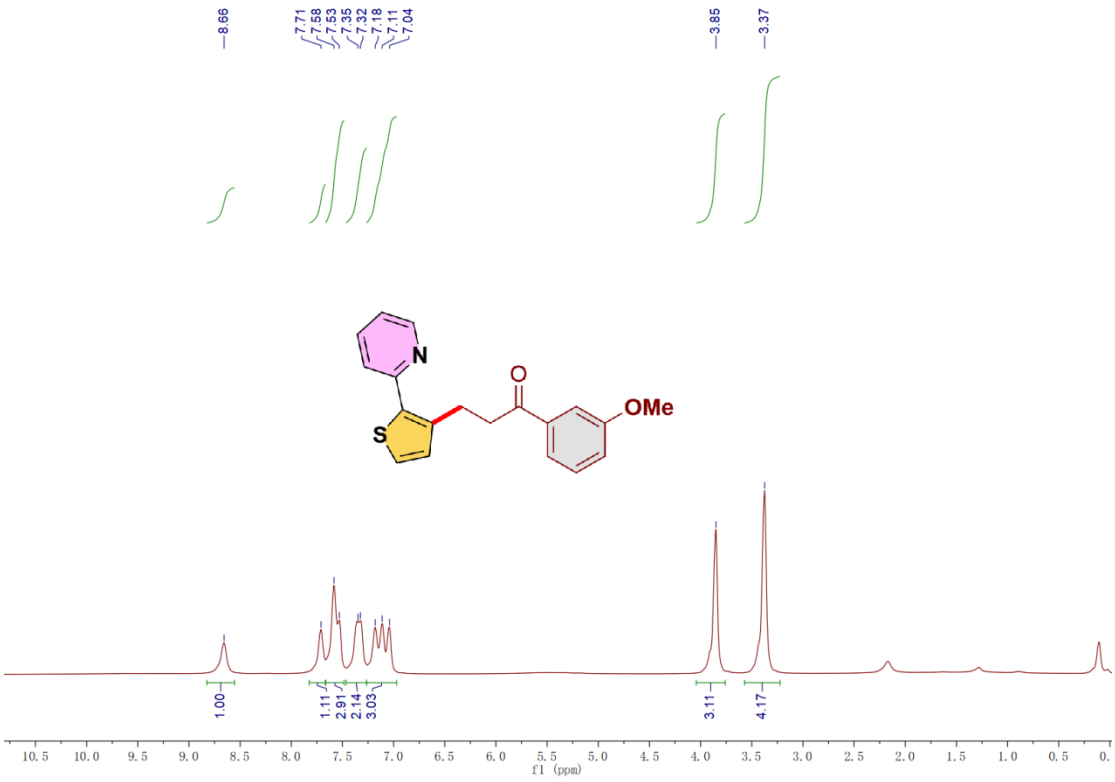
3ak | ^{1}H NMR ($CDCl_3$, 600 MHz)



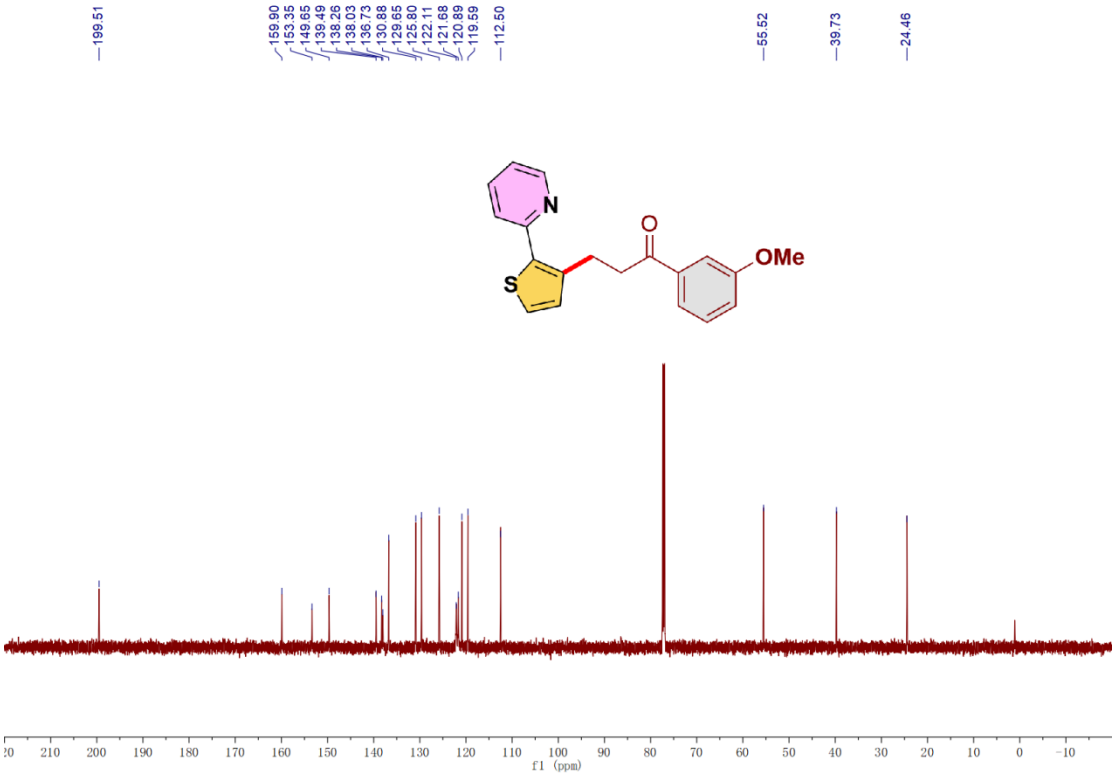
3ak | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



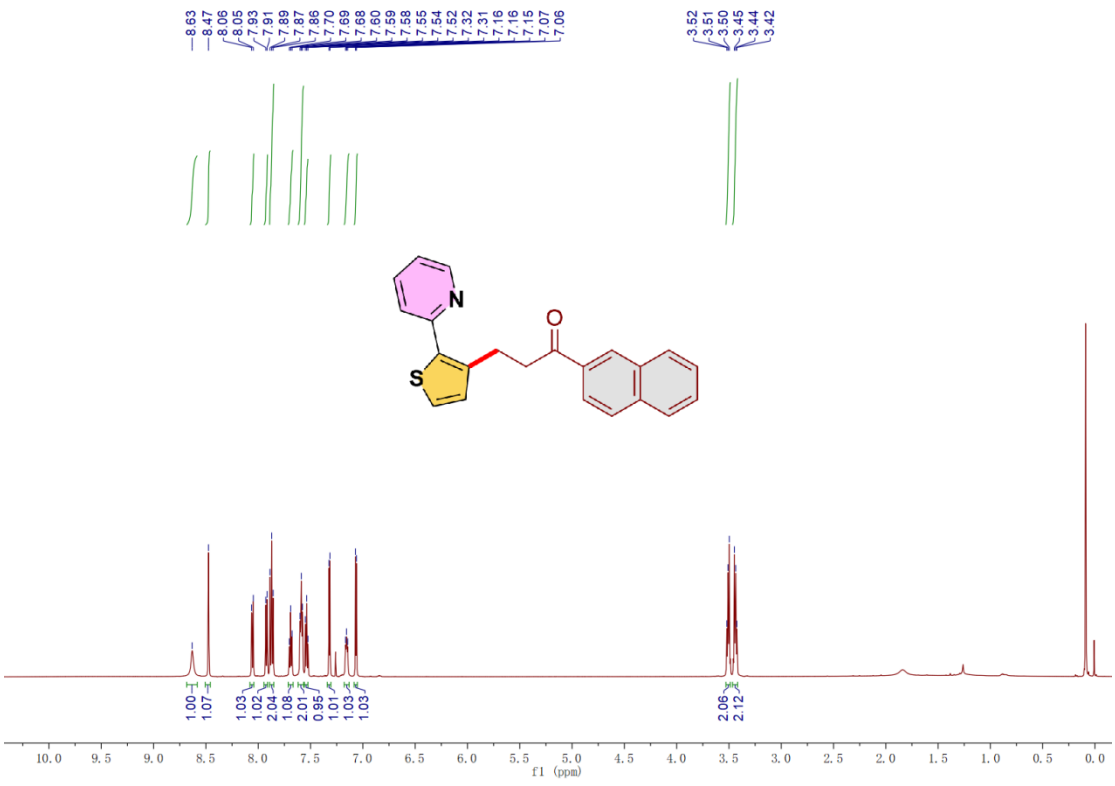
3al | ^{1}H NMR ($CDCl_3$, 600 MHz)



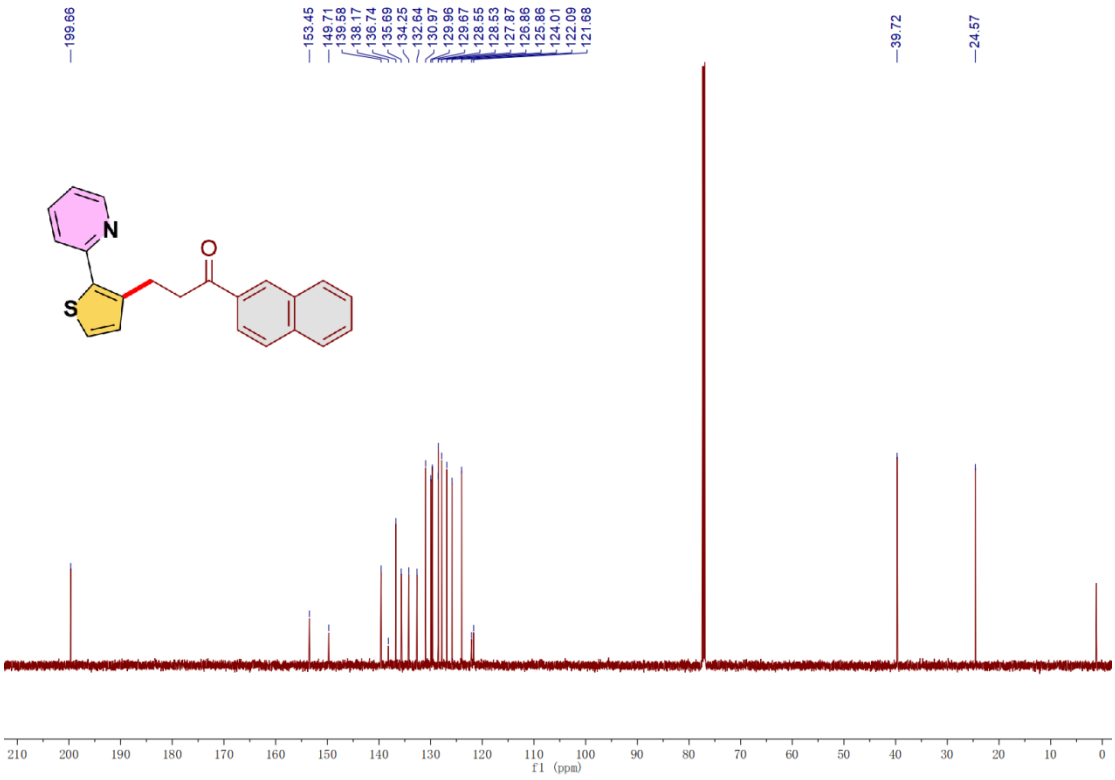
3al | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



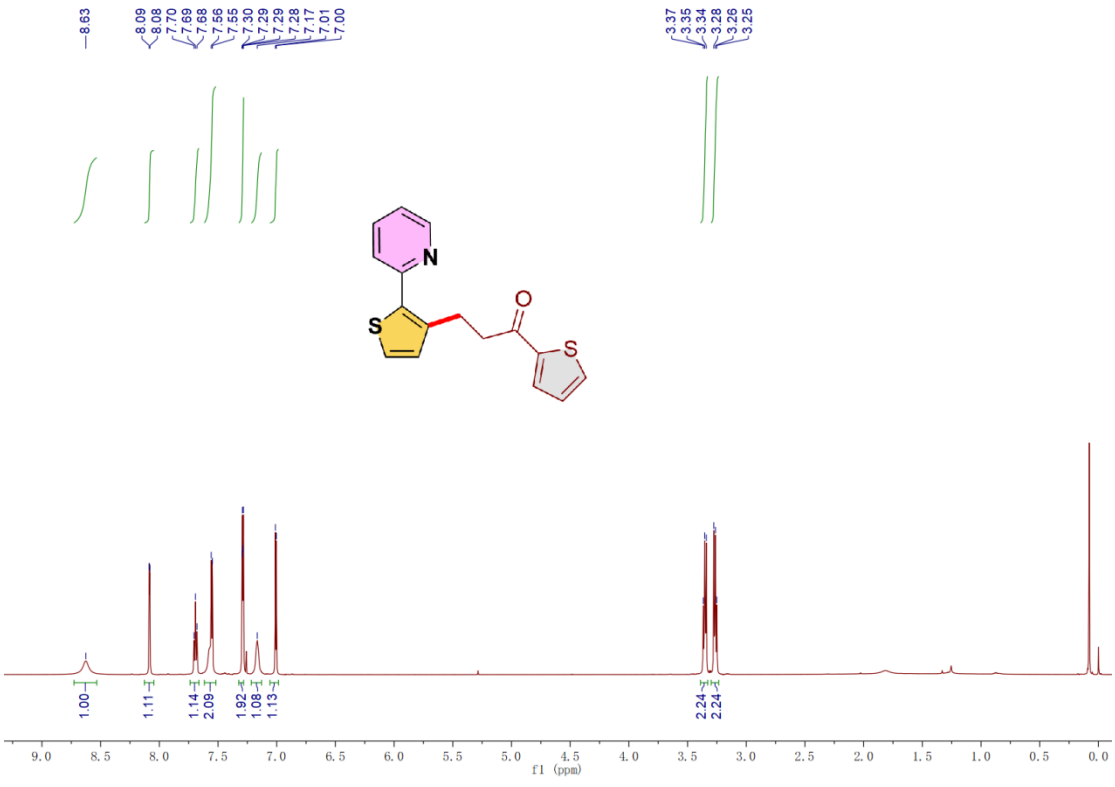
3am | ^{1}H NMR ($CDCl_3$, 600 MHz)



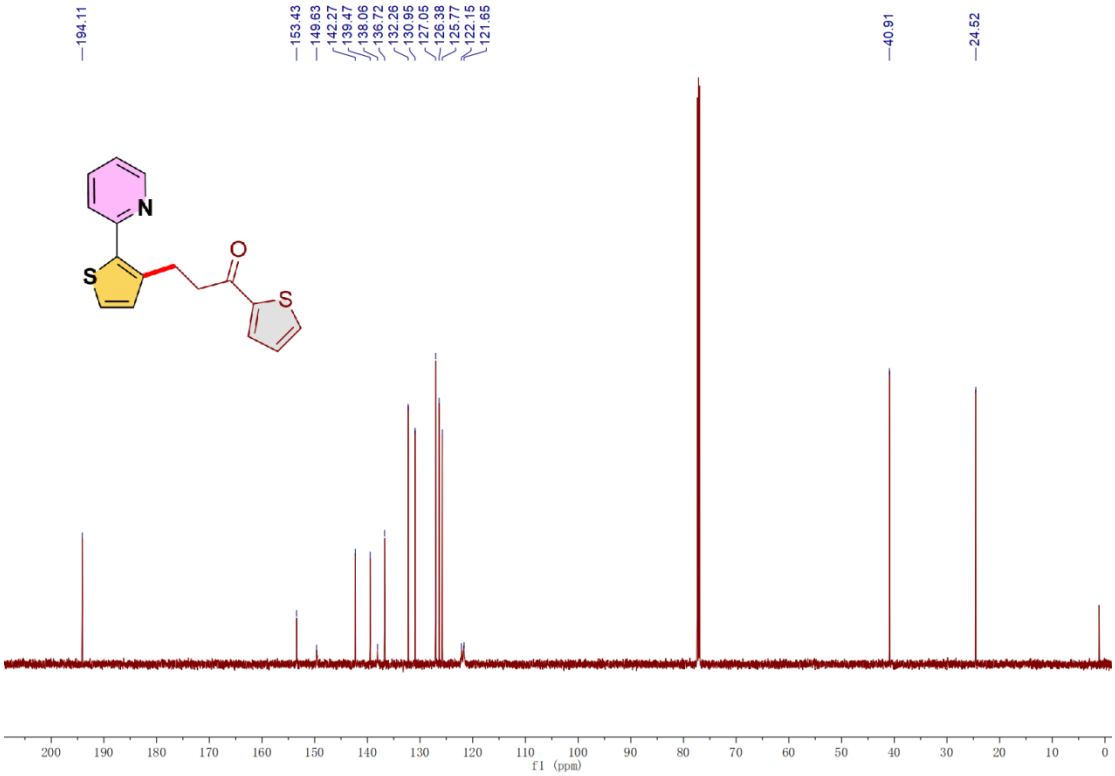
3am | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



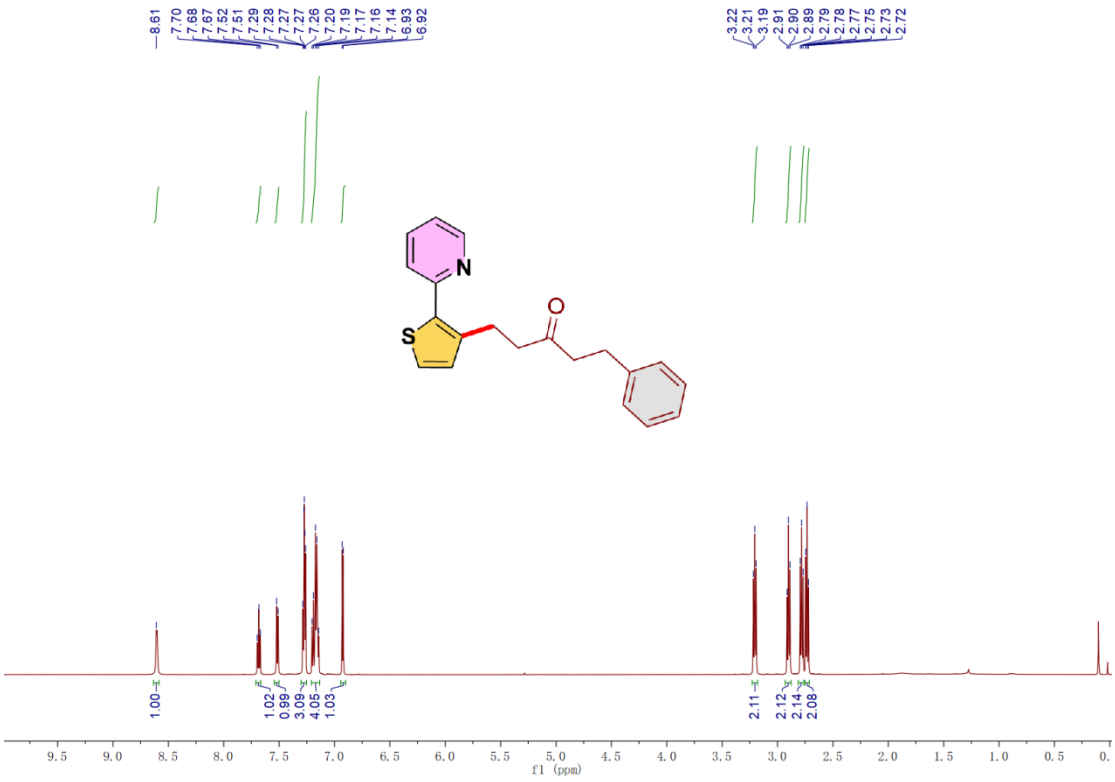
3an | ^{1}H NMR ($CDCl_3$, 600 MHz)



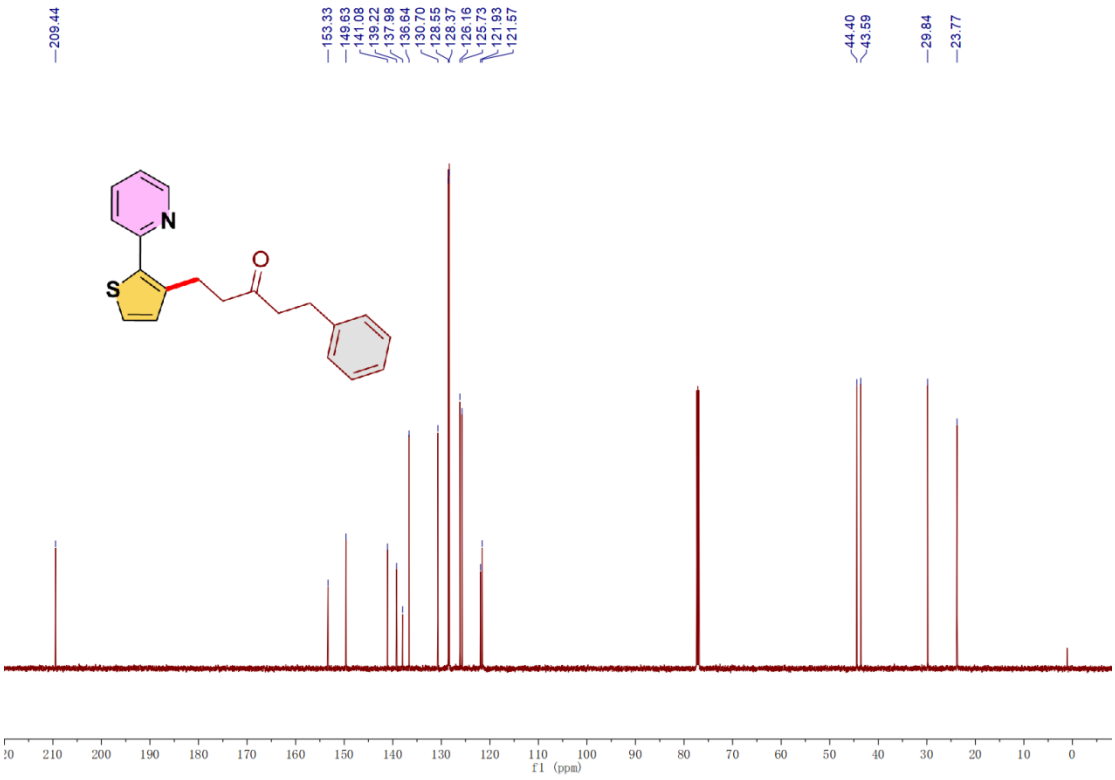
3an | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



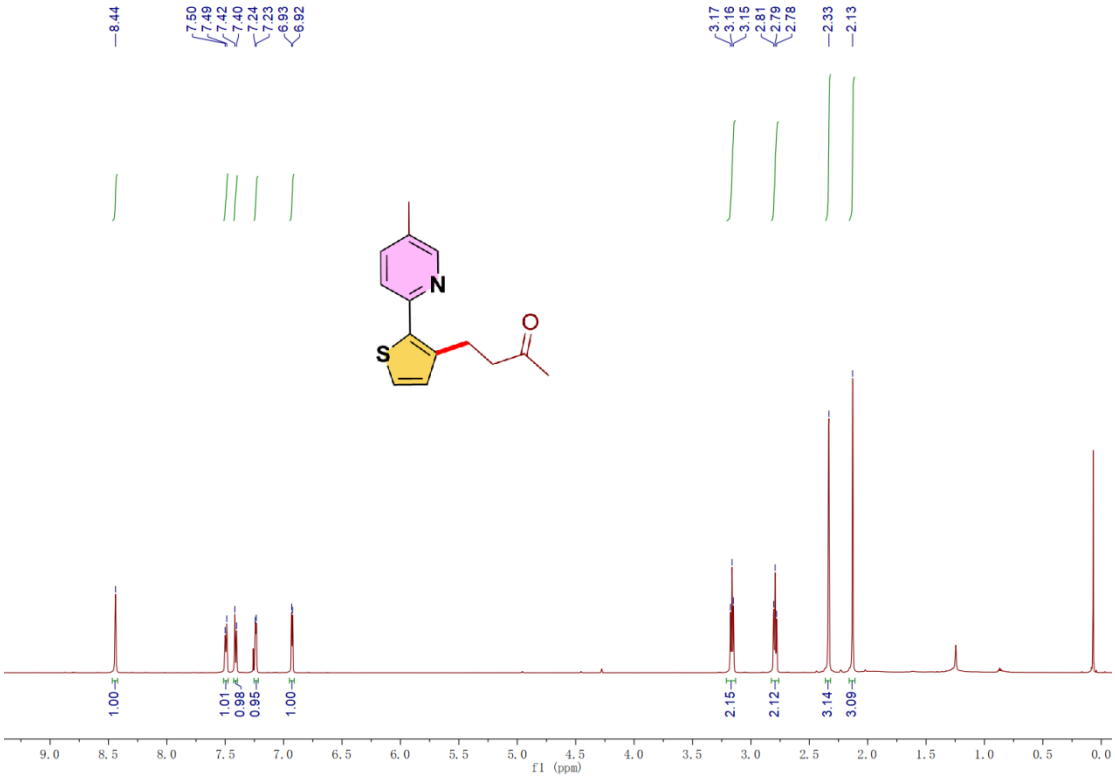
3ao | ^{1}H NMR ($CDCl_3$, 600 MHz)



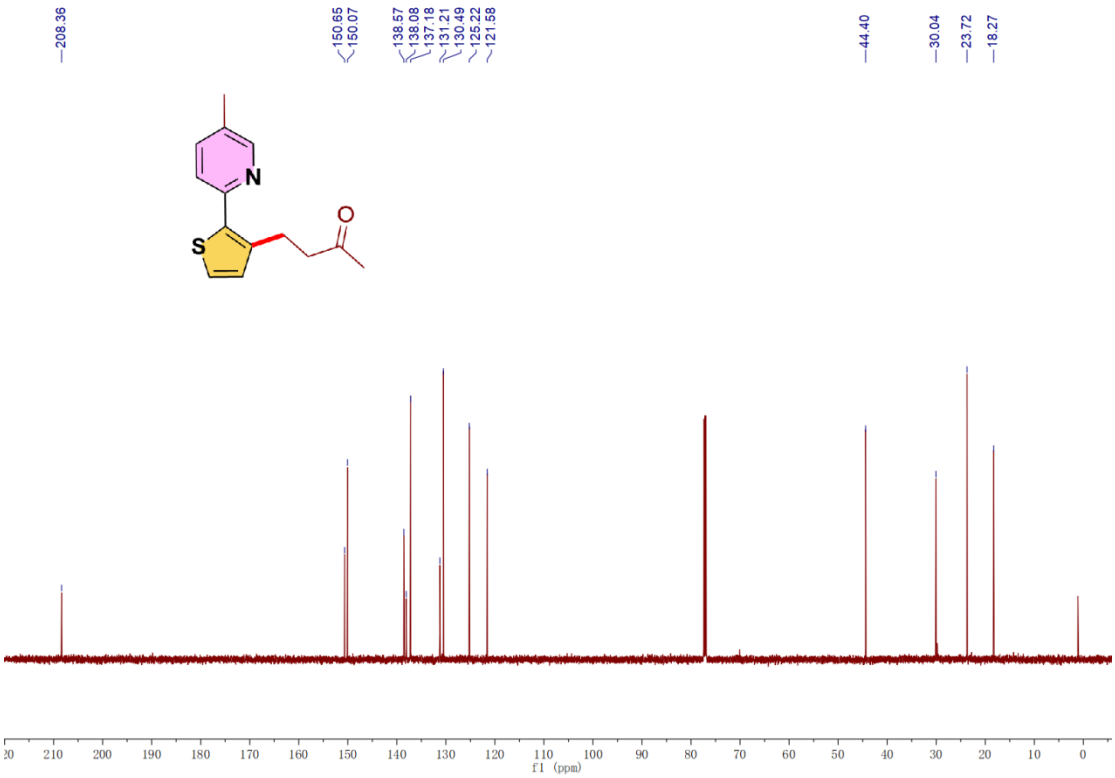
3ao | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



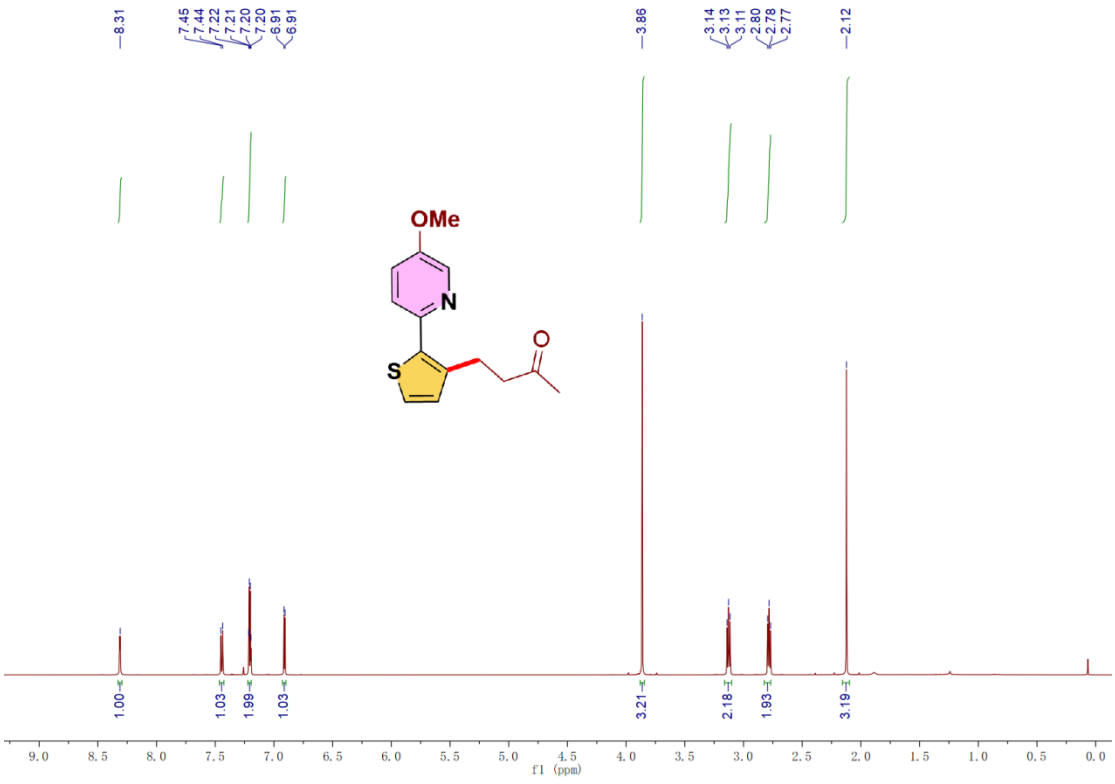
3ba | ^{1}H NMR ($CDCl_3$, 600 MHz)



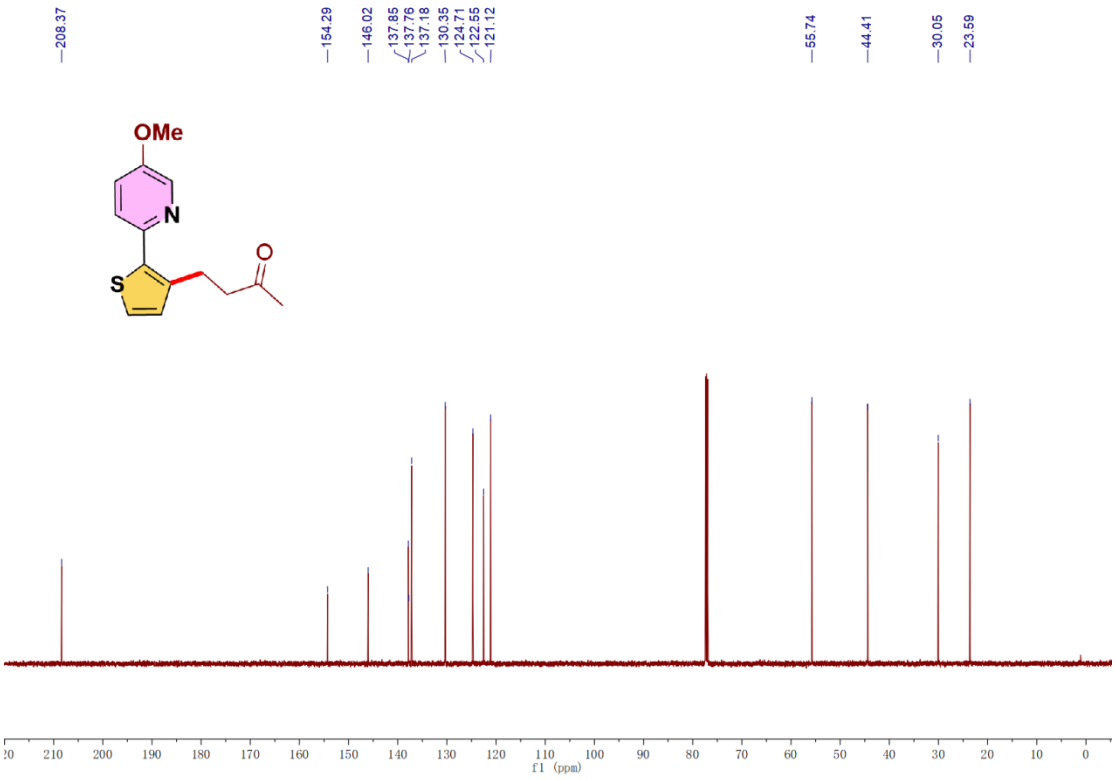
3ba | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



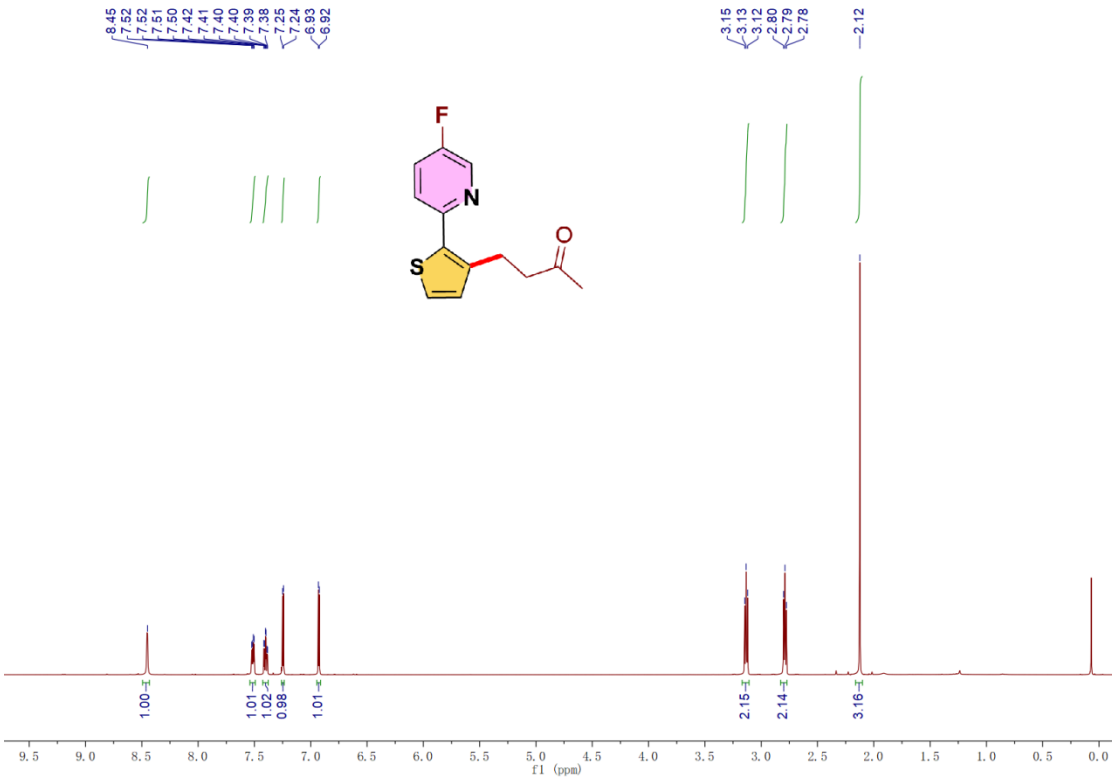
3ca | ^{1}H NMR ($CDCl_3$, 600 MHz)



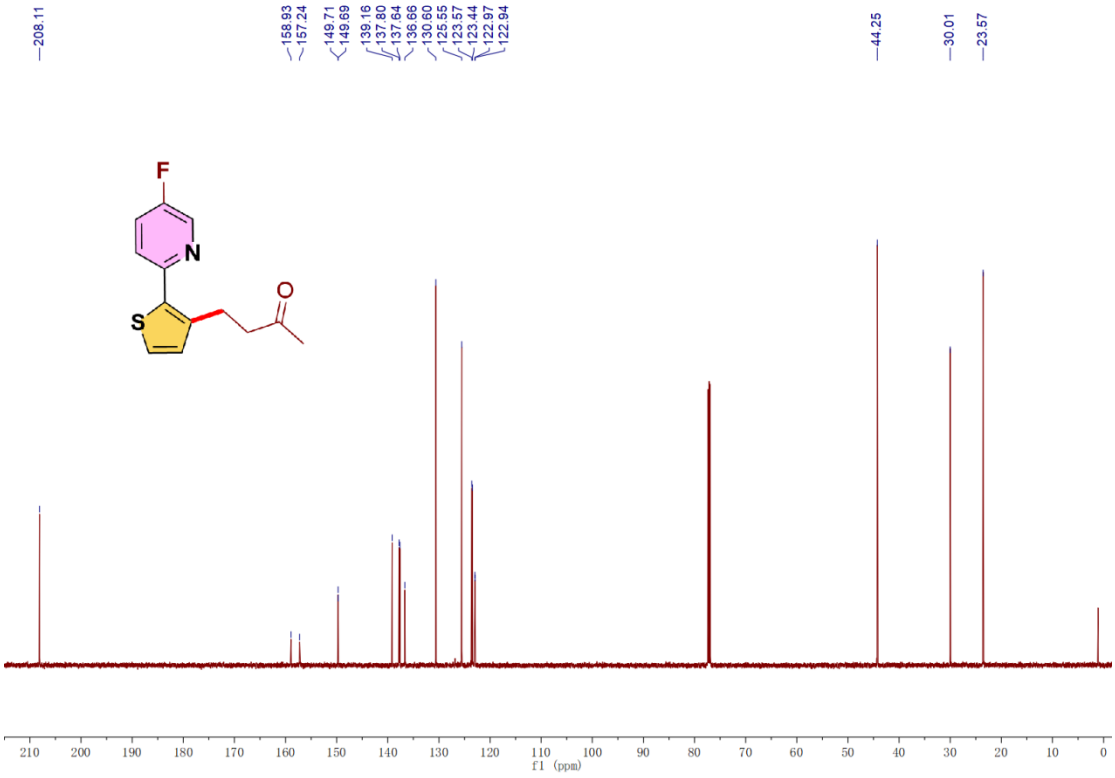
3ca | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



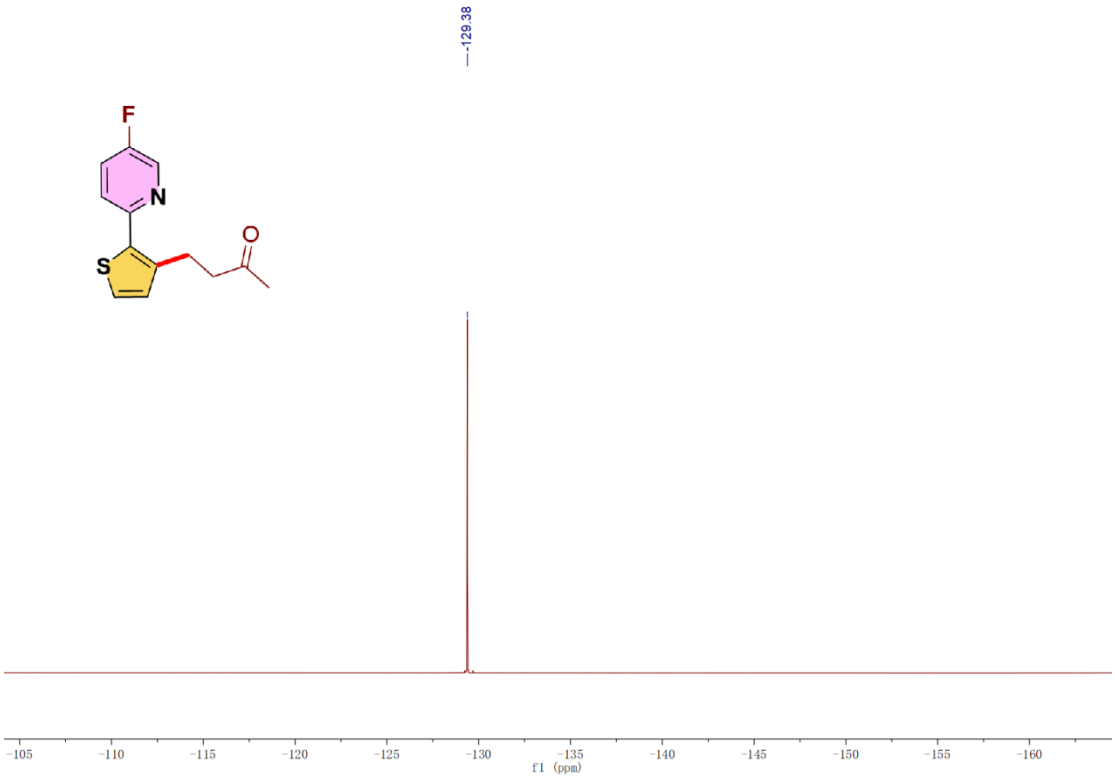
3da | ^{1}H NMR ($CDCl_3$, 600 MHz)



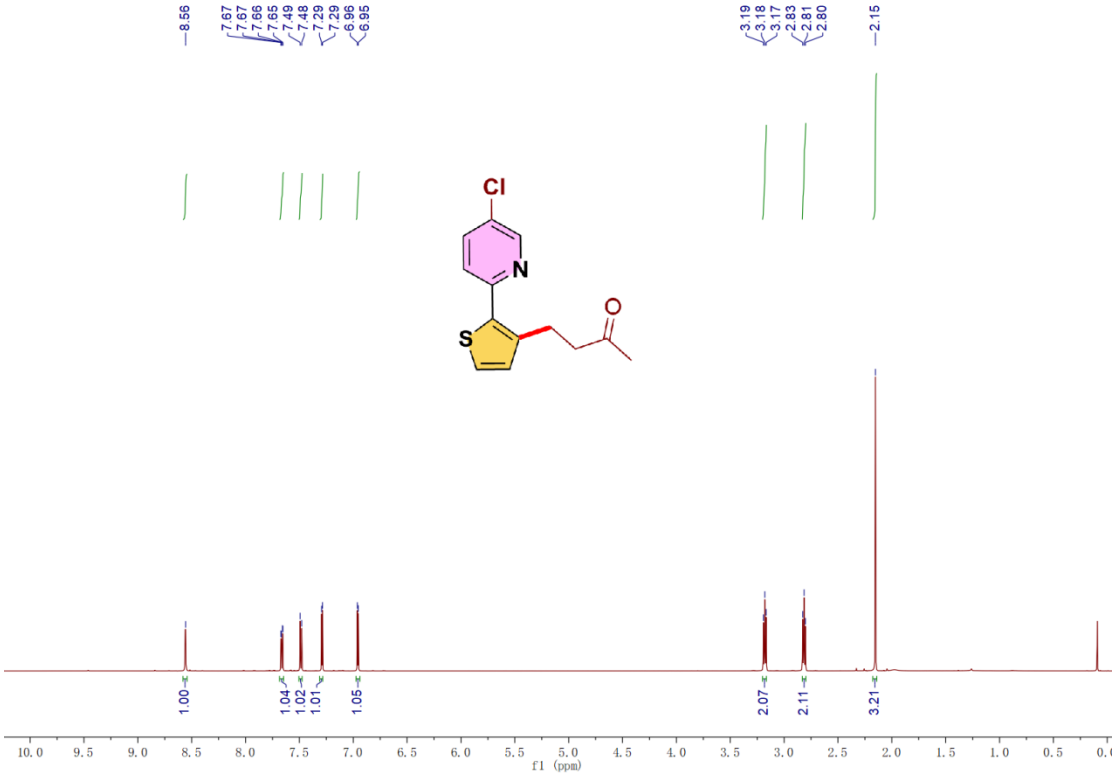
3da | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



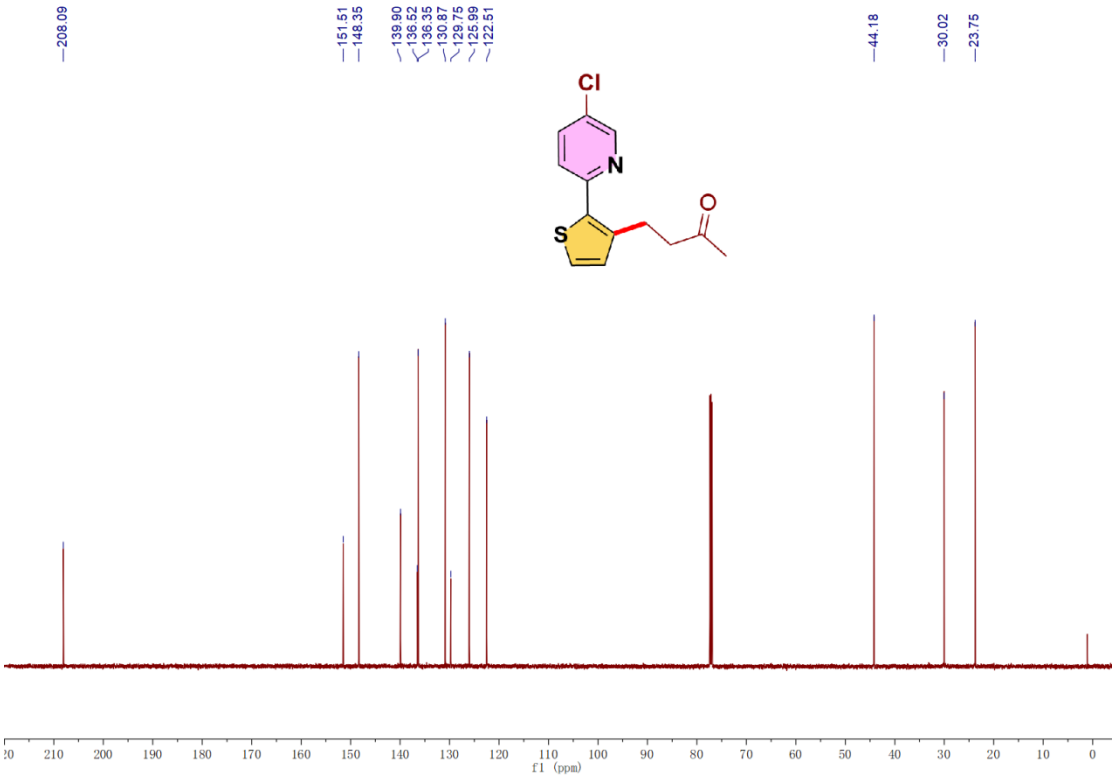
3da | $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 565 MHz)



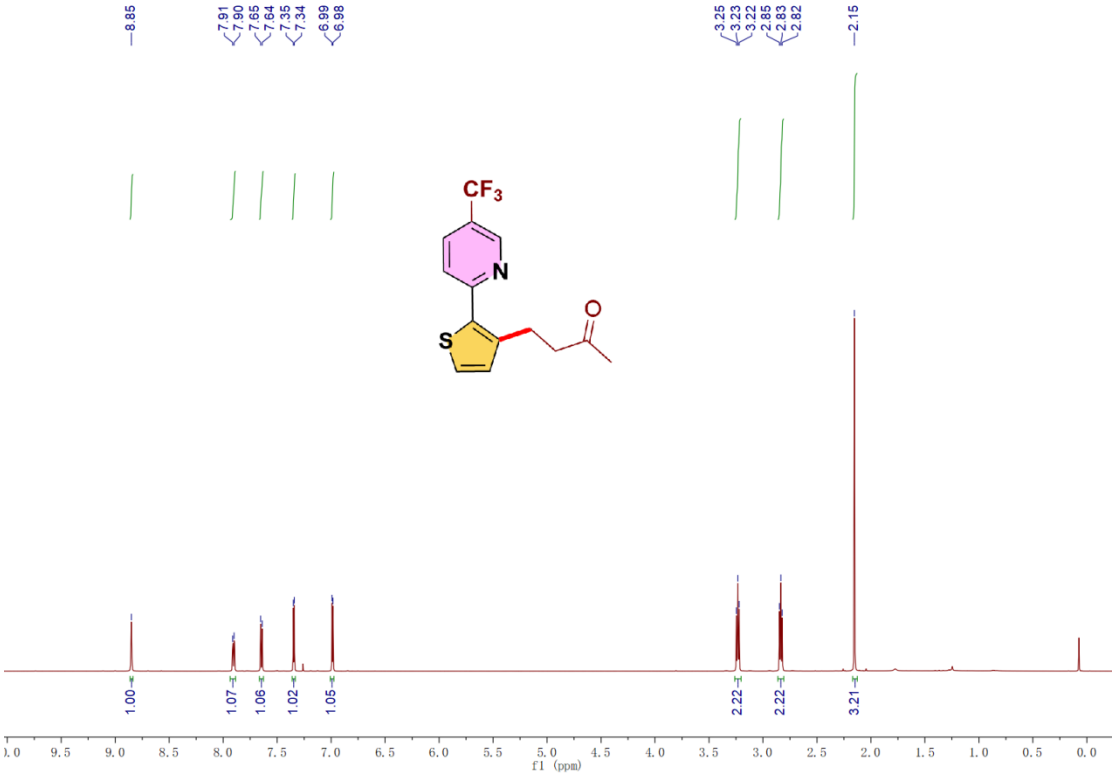
3ea | ^{1}H NMR ($CDCl_3$, 600 MHz)



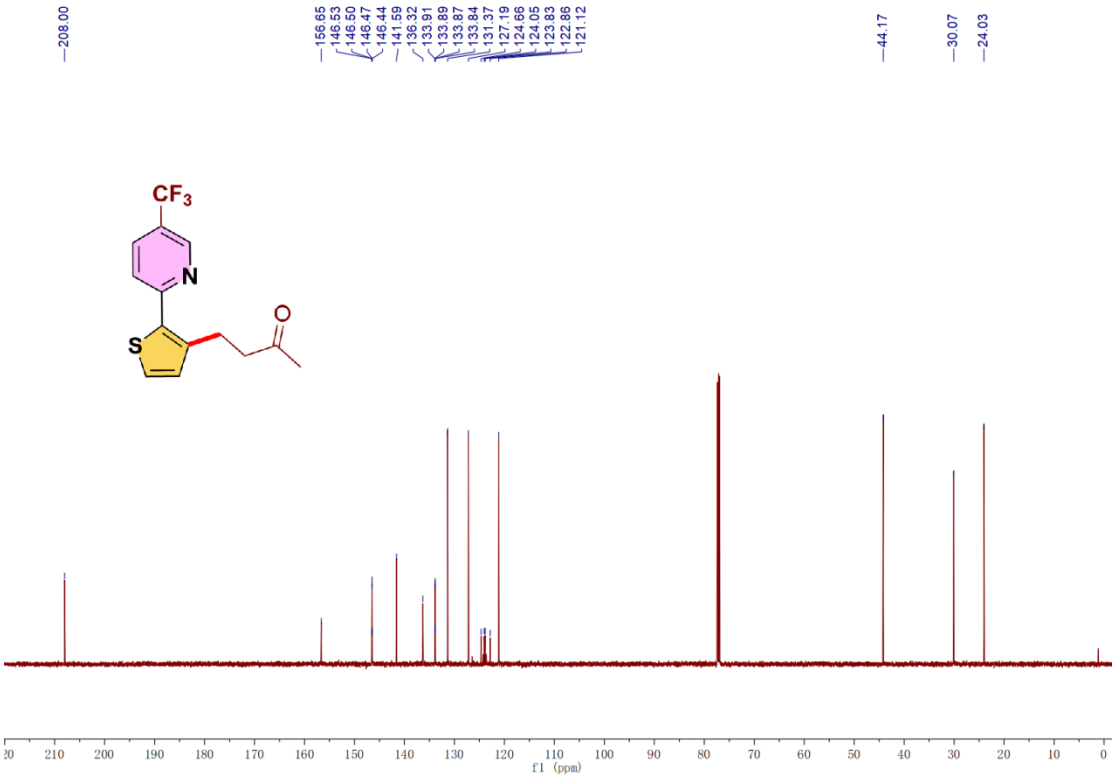
3ea | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



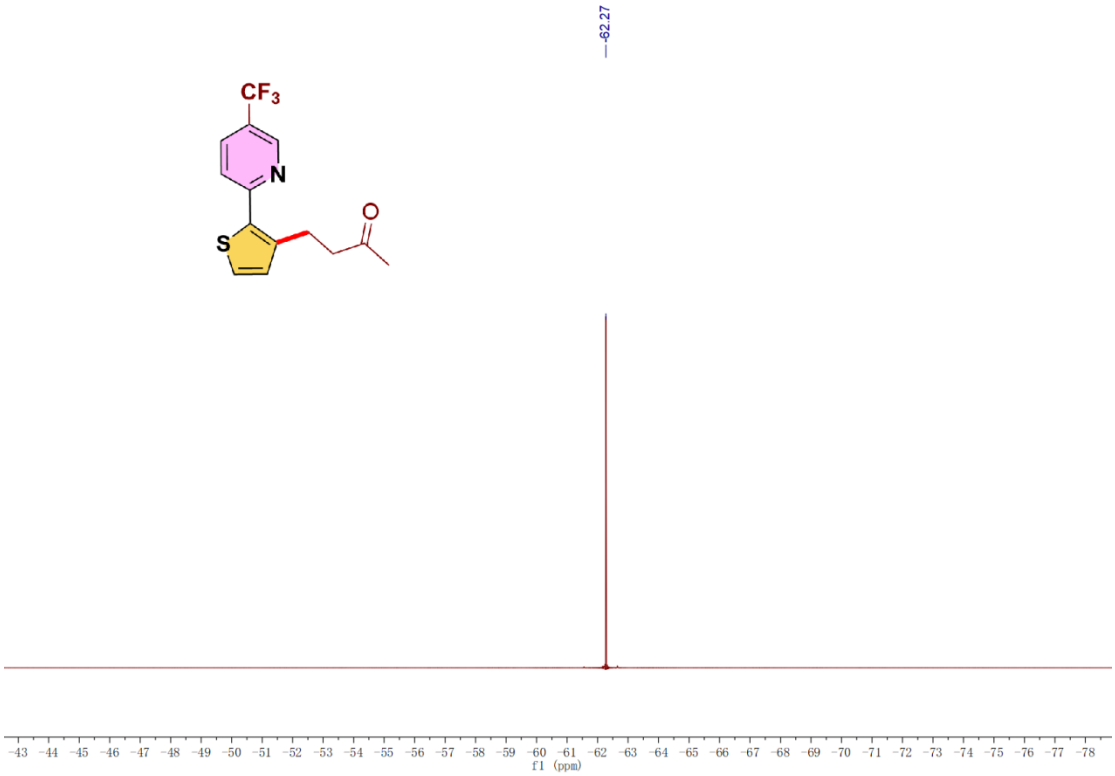
3fa | ^{1}H NMR ($CDCl_3$, 600 MHz)



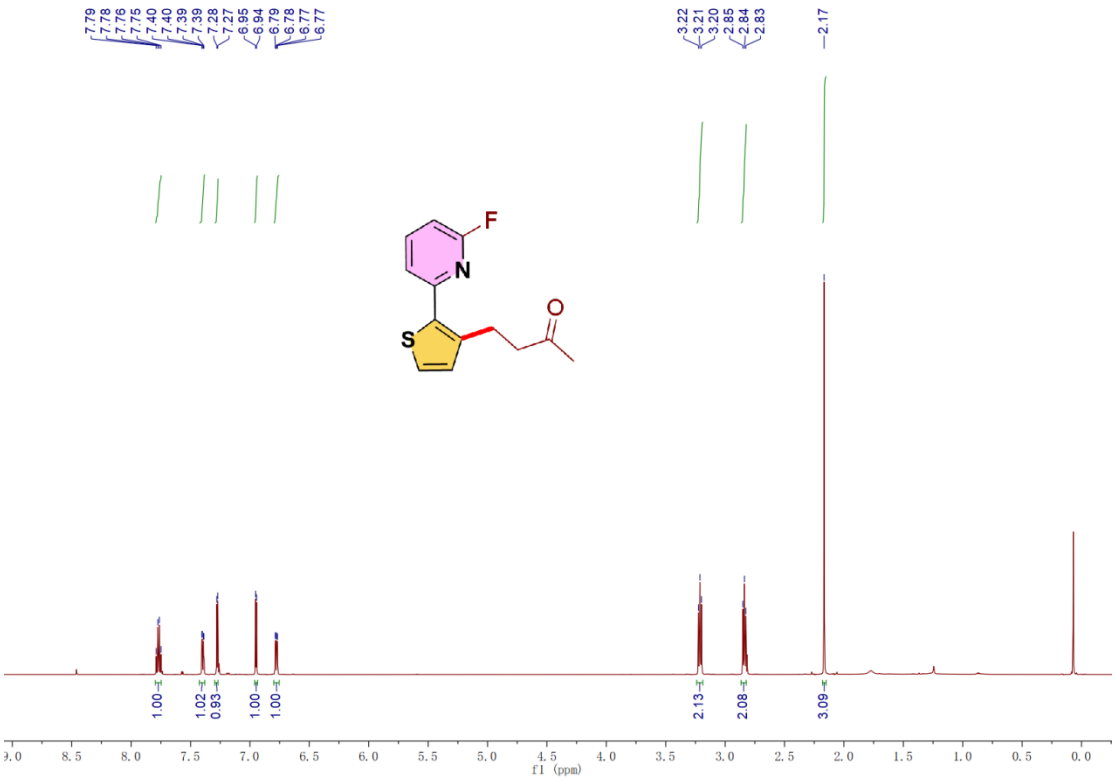
3fa | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



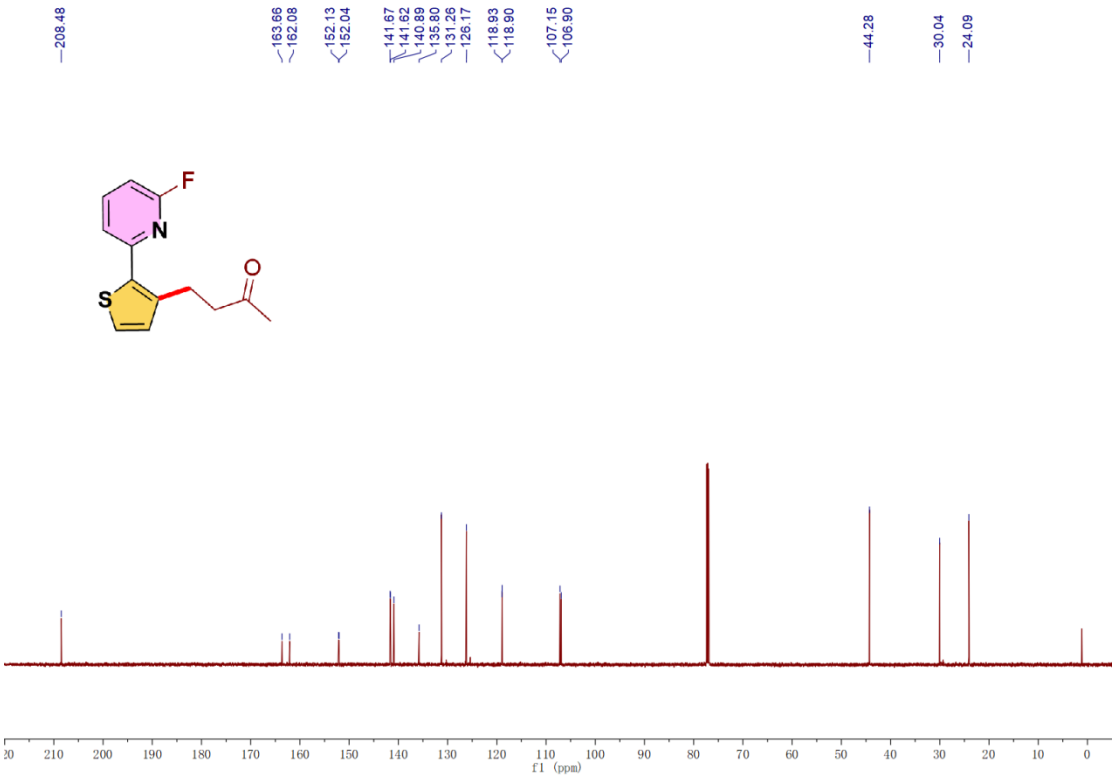
3fa | $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 565 MHz)



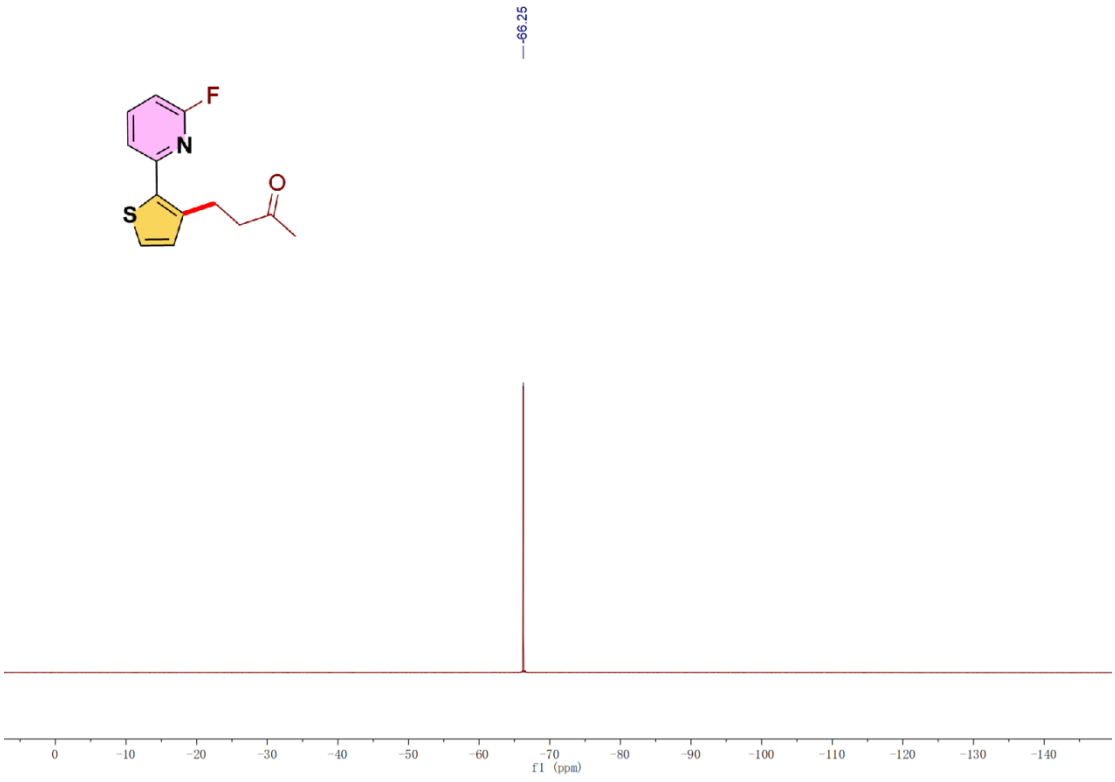
3ga | ^{1}H NMR ($CDCl_3$, 600 MHz)



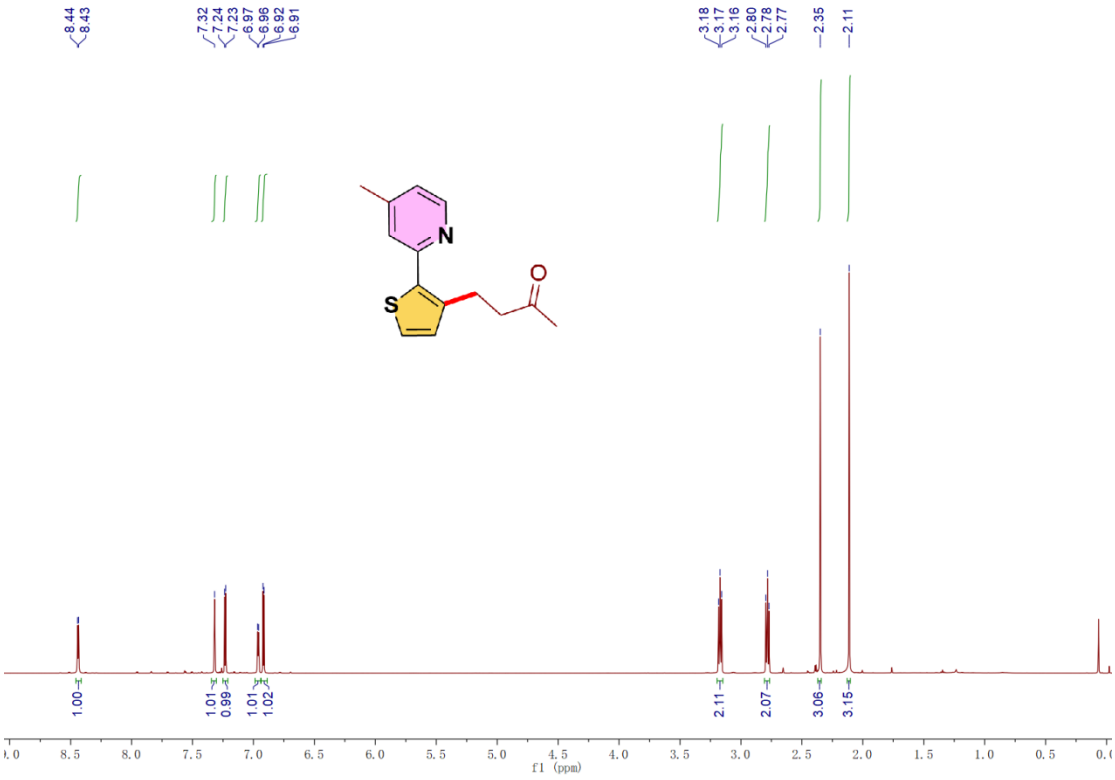
3ga | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



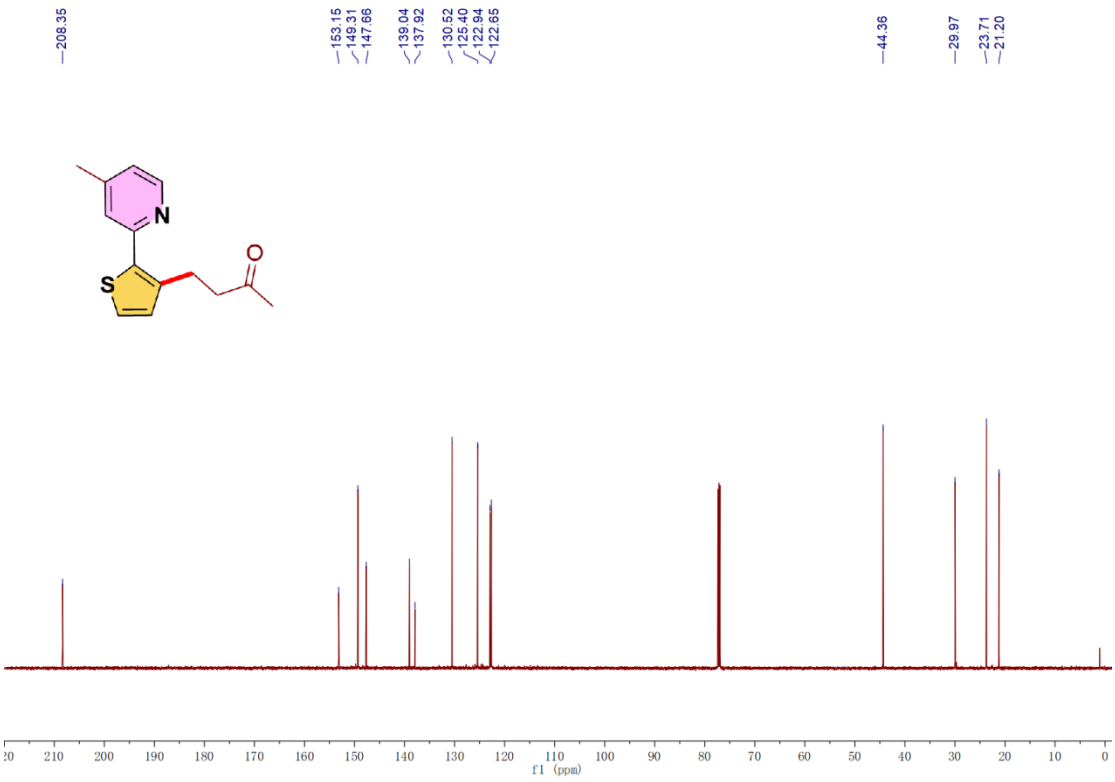
3ga | $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 565 MHz)



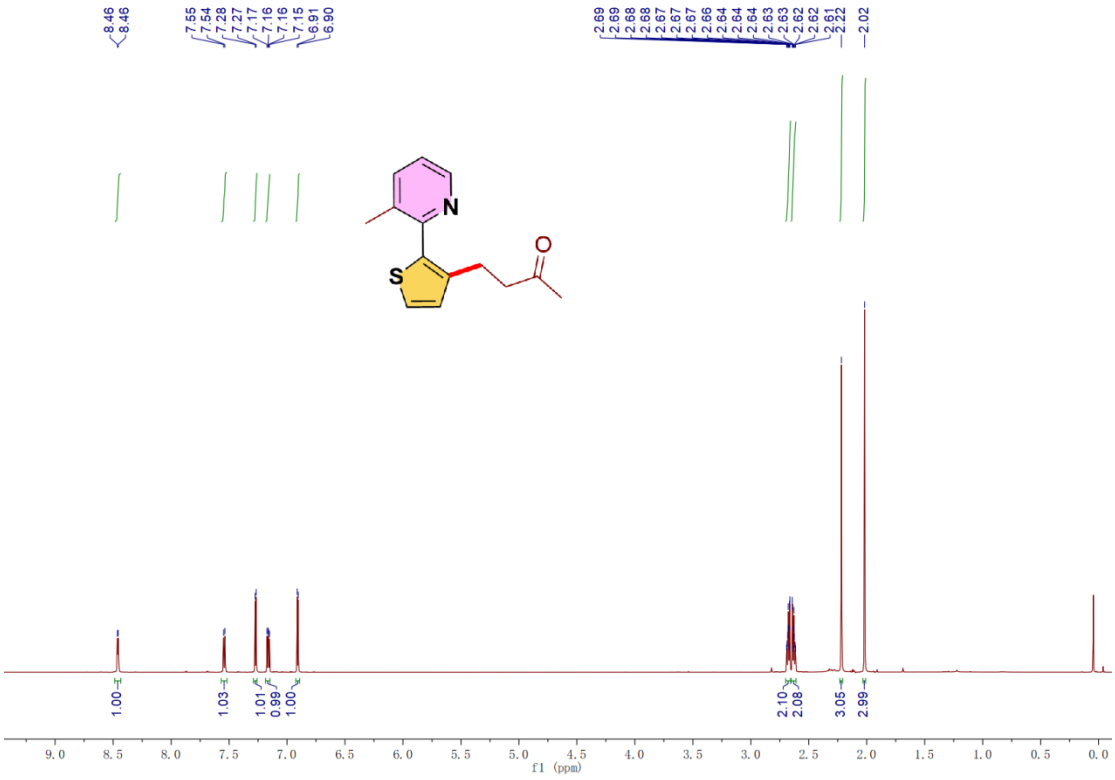
3ia | ^{1}H NMR ($CDCl_3$, 600 MHz)



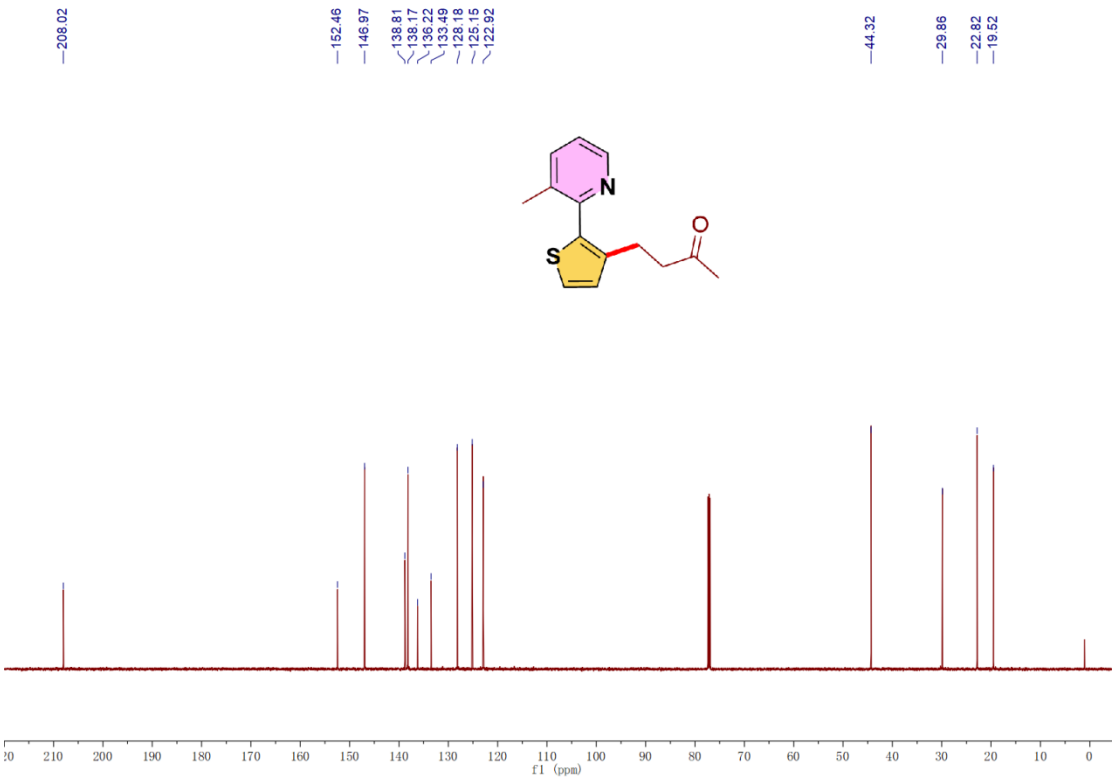
3ia | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



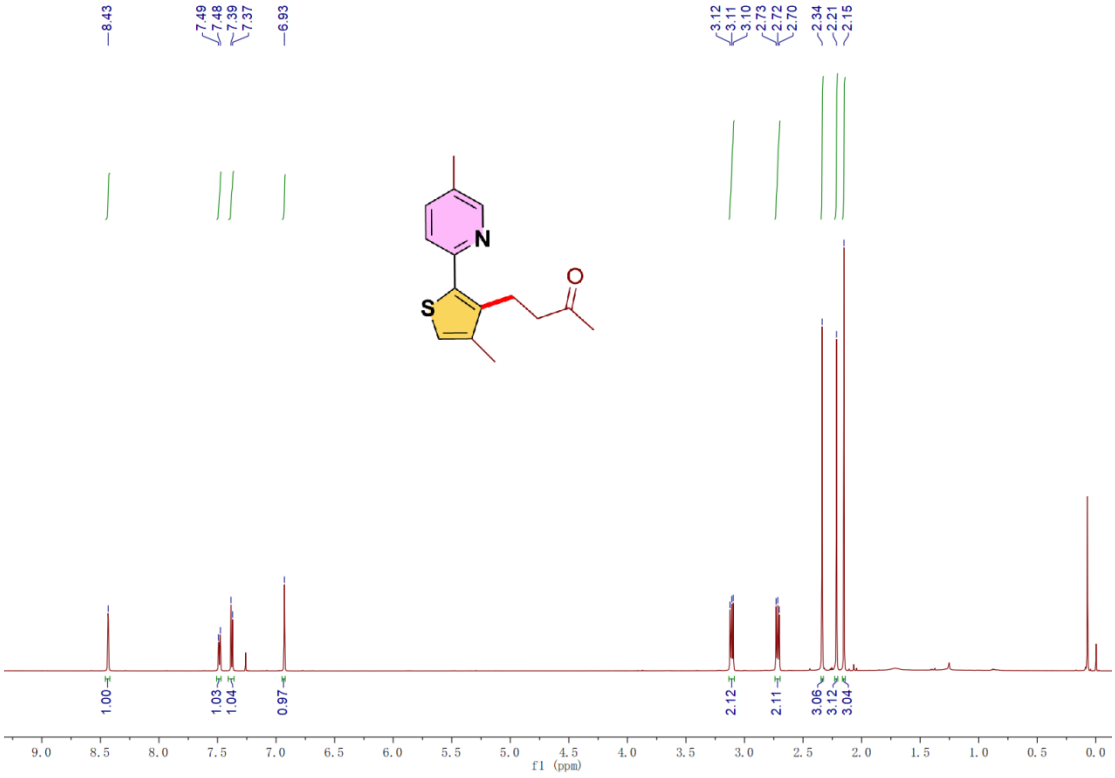
3ma | ^{1}H NMR ($CDCl_3$, 600 MHz)



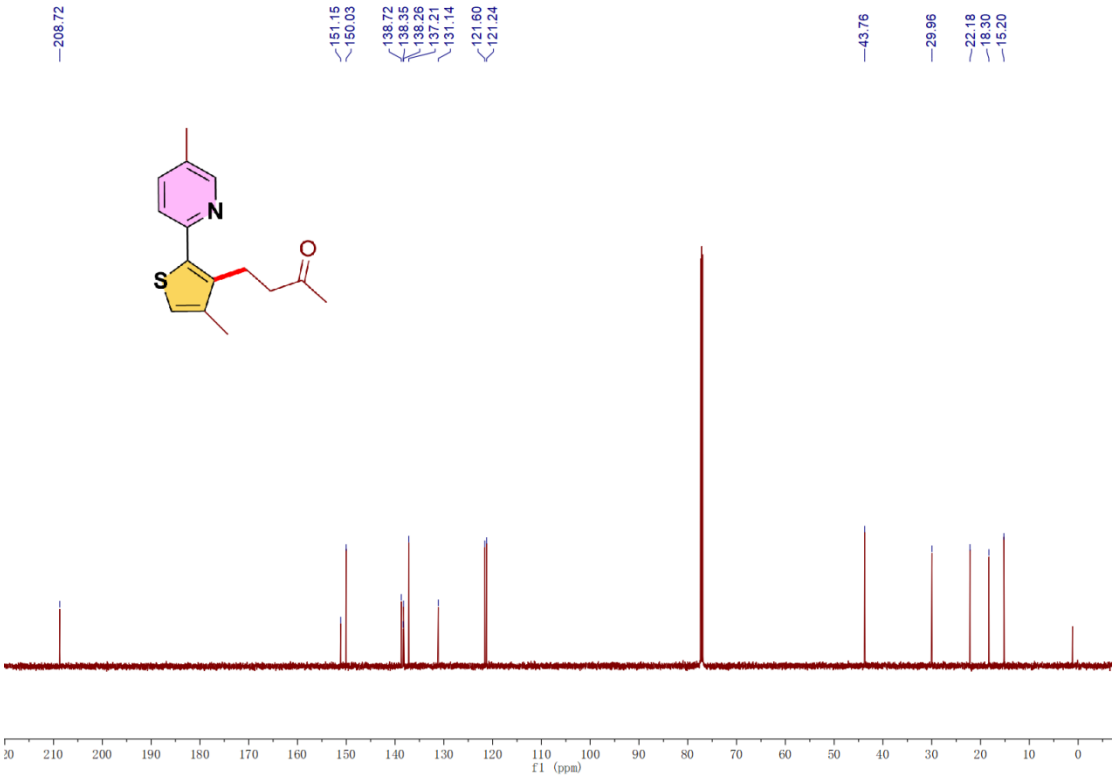
3ma | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



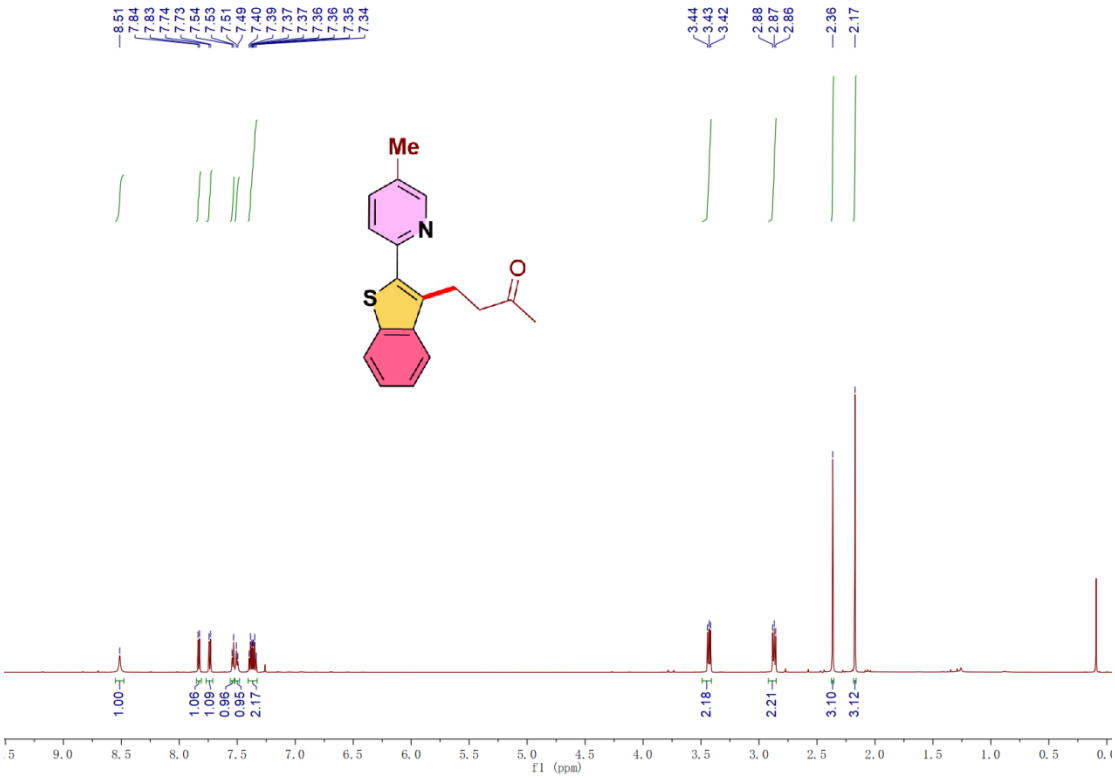
3na | ^{1}H NMR ($CDCl_3$, 600 MHz)



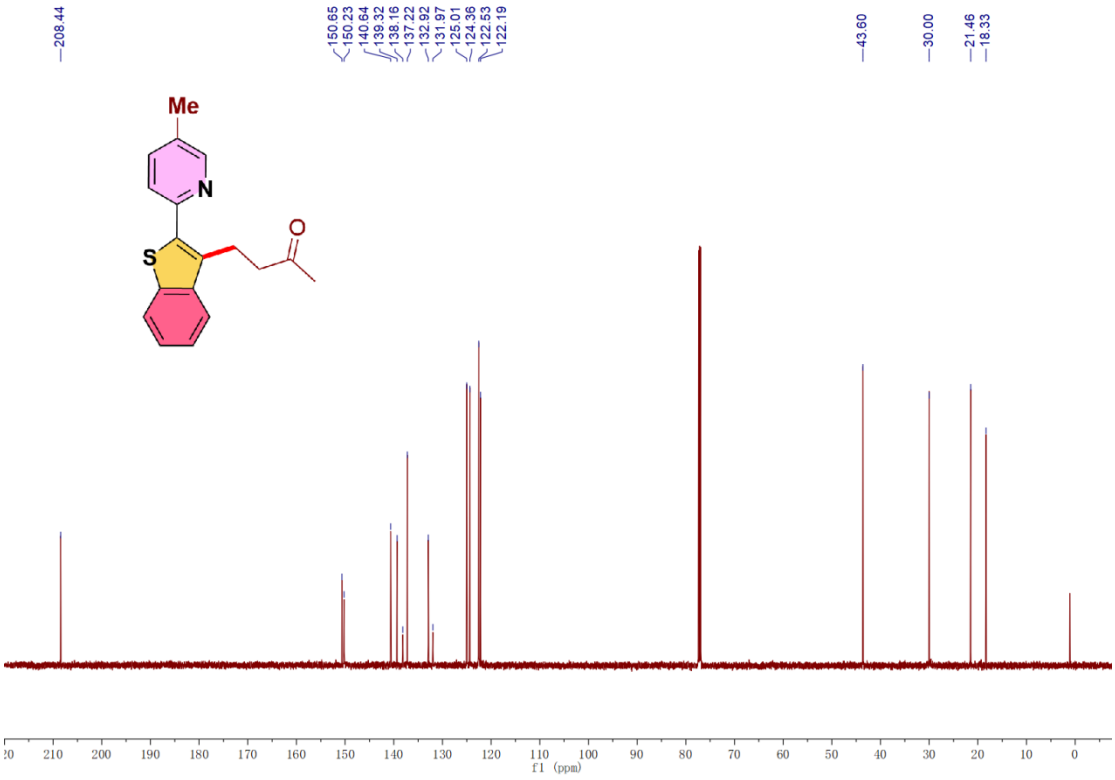
3na | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



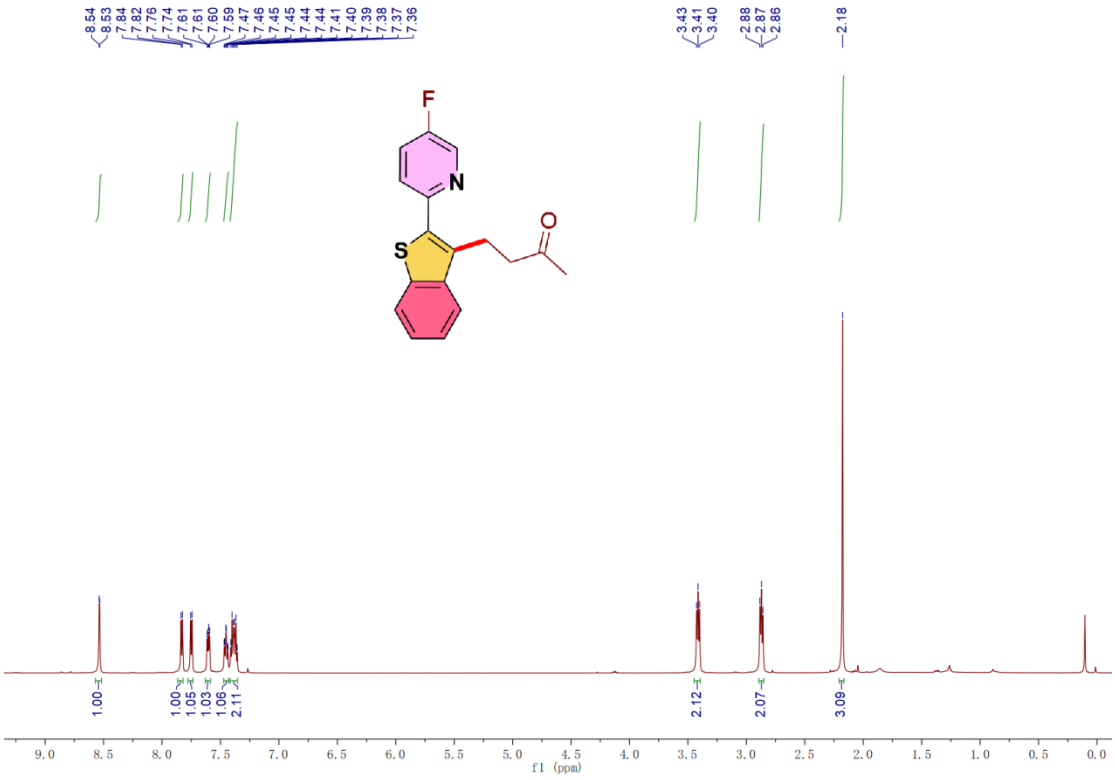
3oa | ^{1}H NMR ($CDCl_3$, 600 MHz)



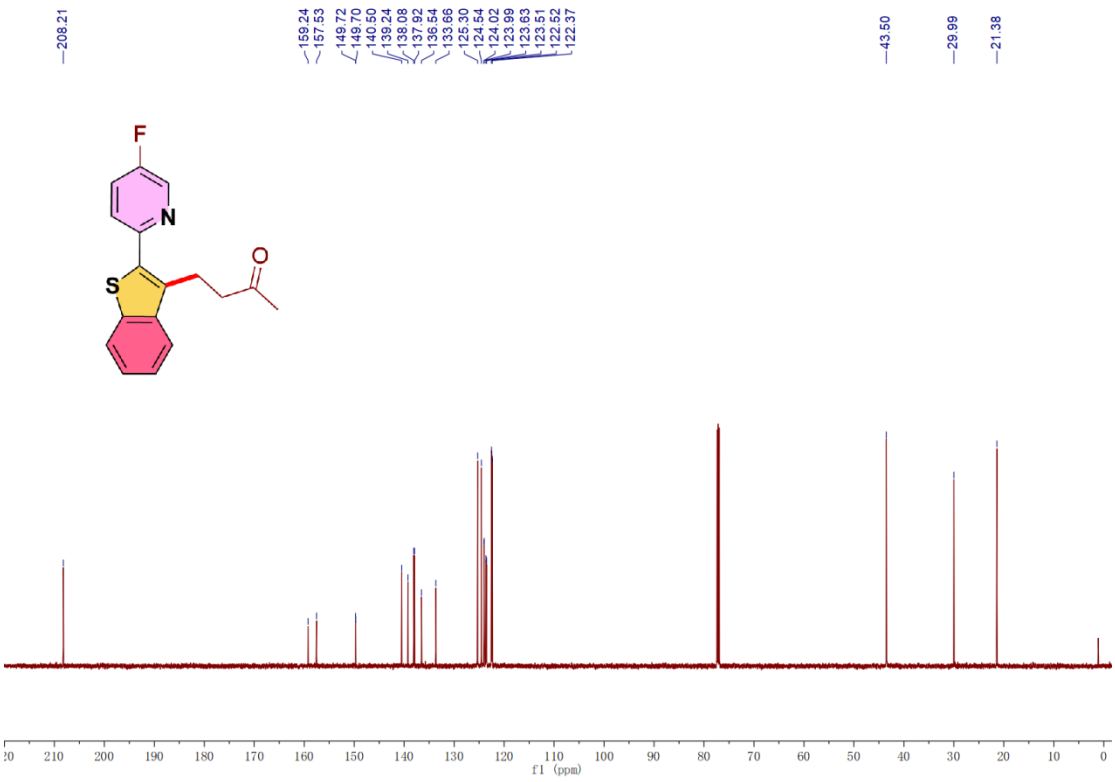
3oa | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



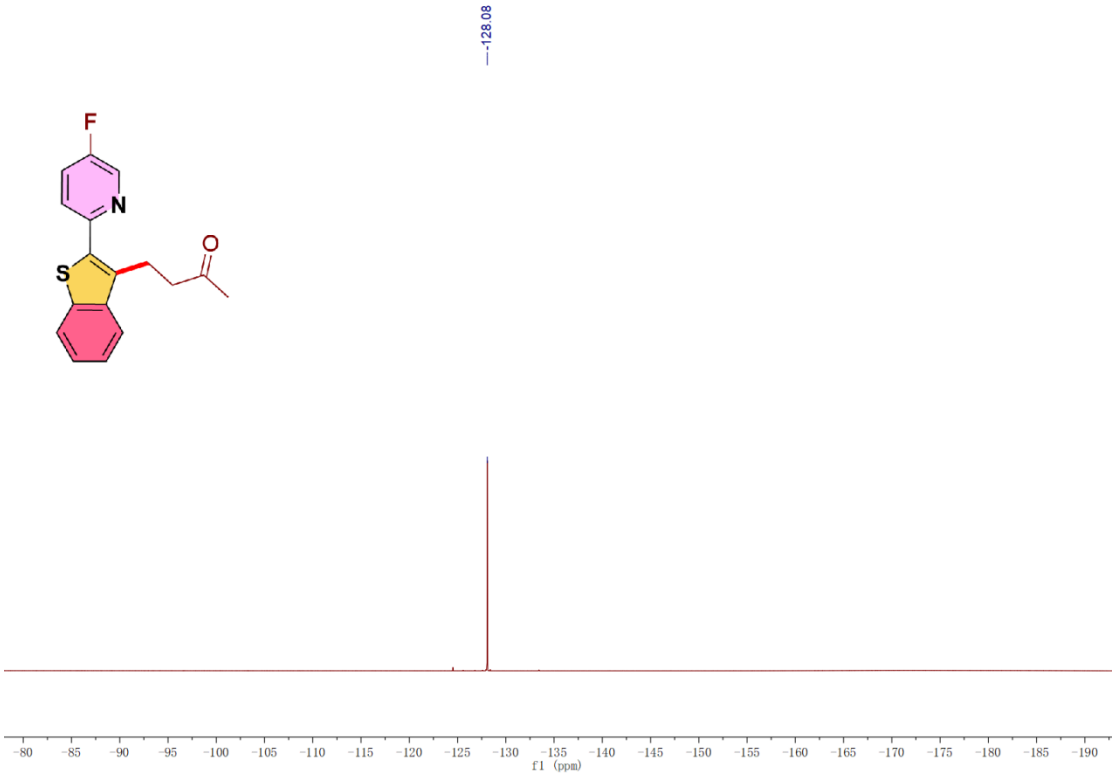
3pa | ^{1}H NMR ($CDCl_3$, 600 MHz)



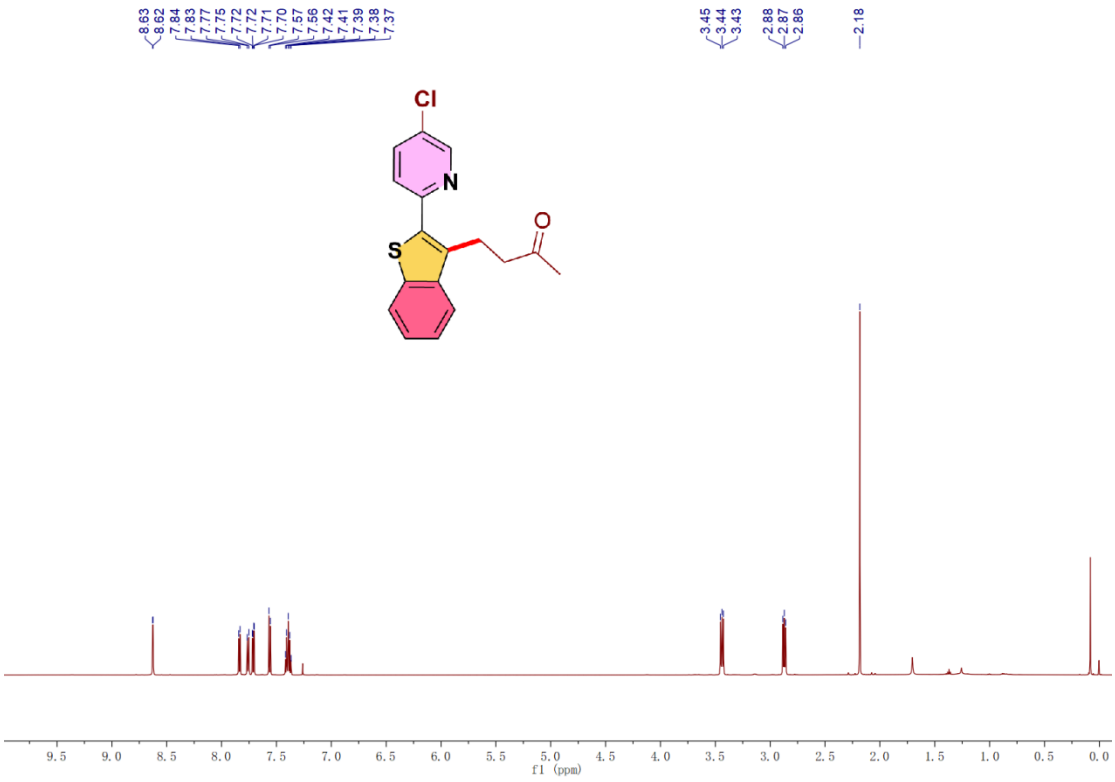
3pa | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



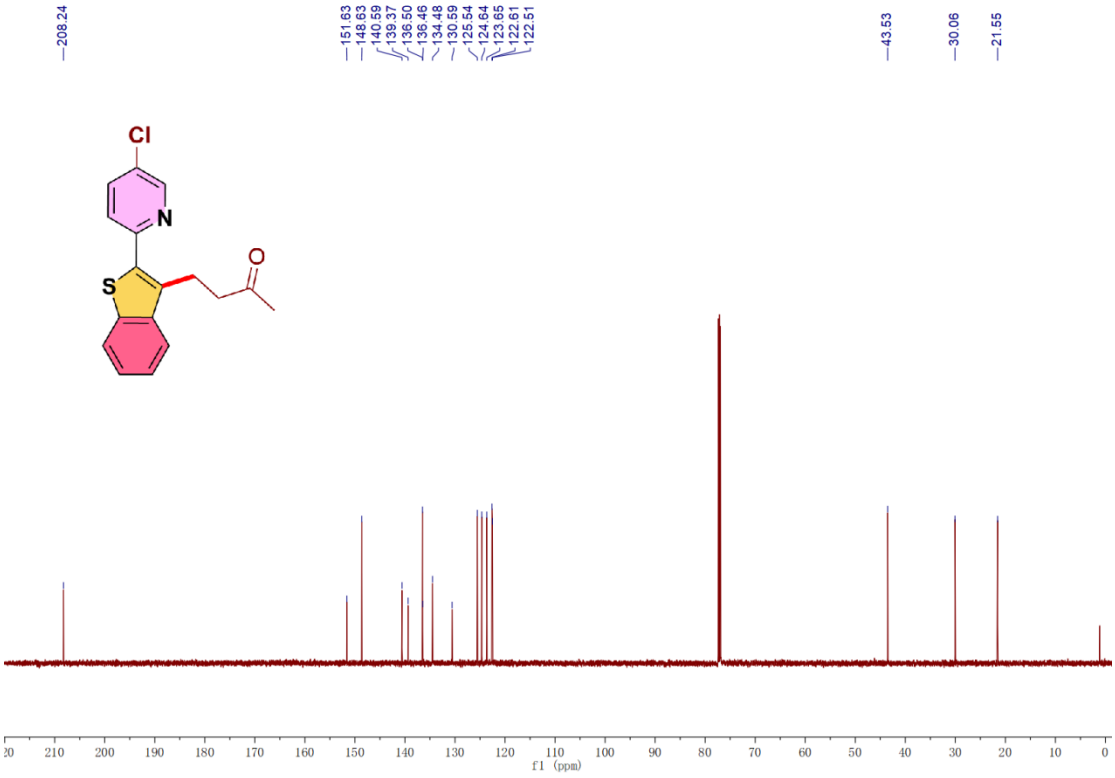
3pa | $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 565 MHz)



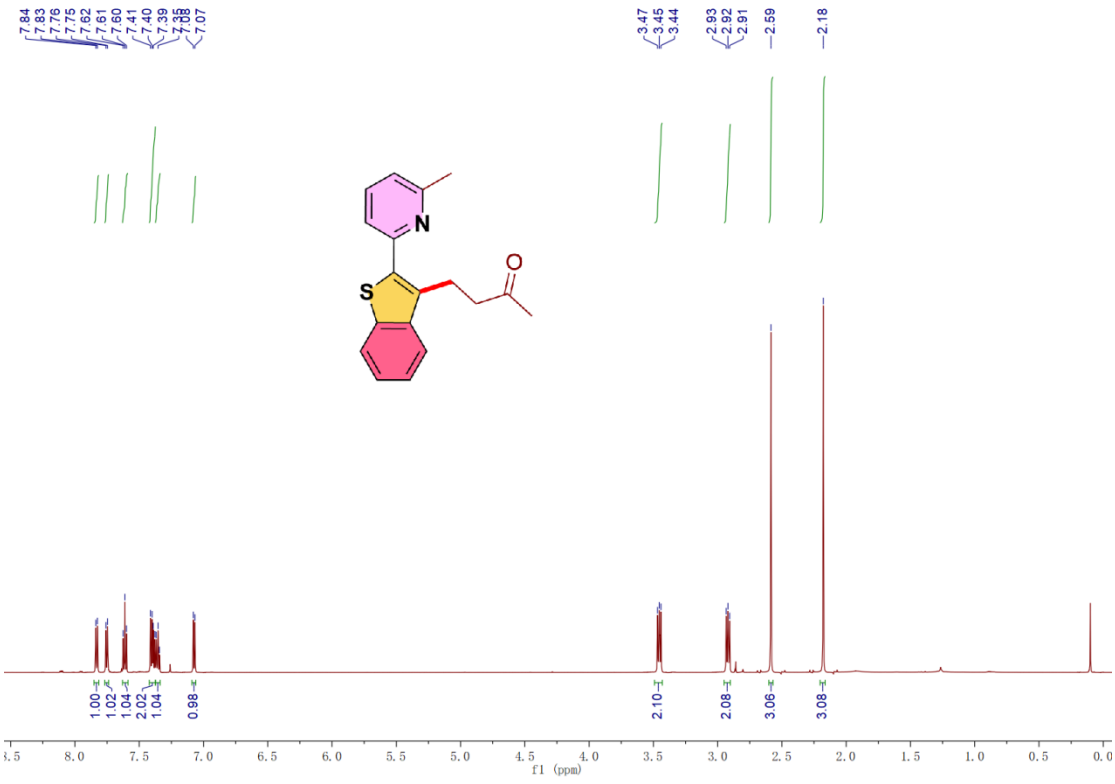
3qa | ^{1}H NMR ($CDCl_3$, 600 MHz)



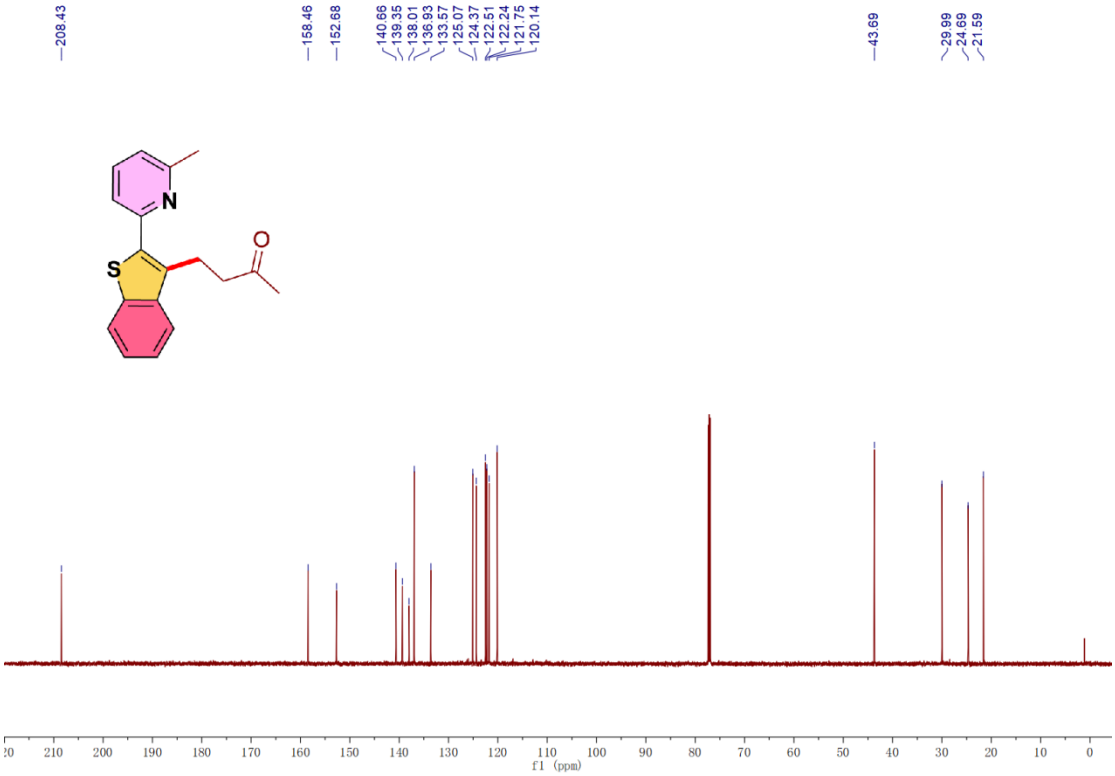
3qa | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



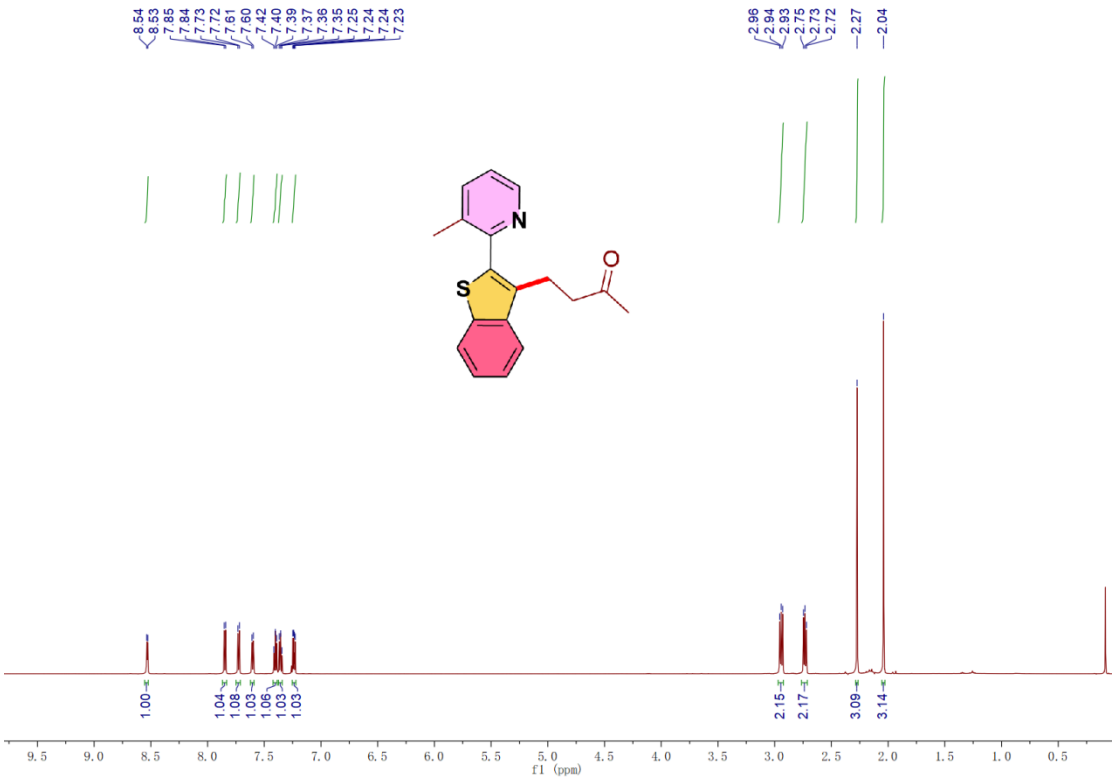
3ra | ^{1}H NMR ($CDCl_3$, 600 MHz)



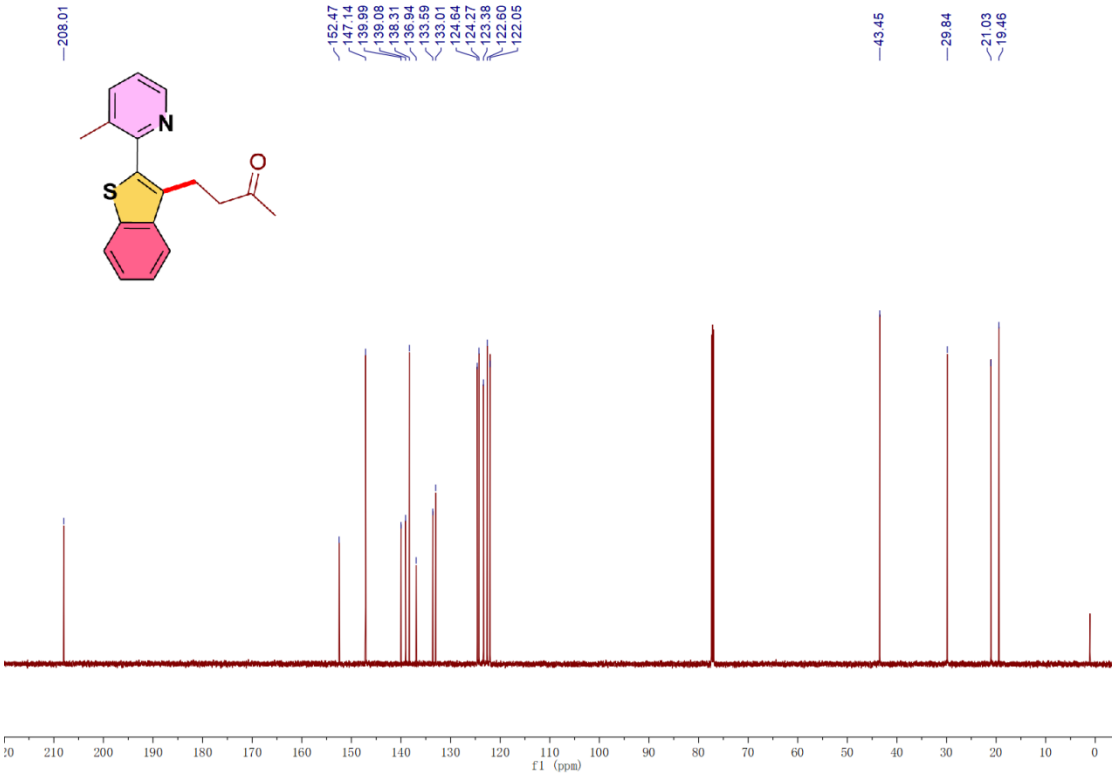
3ra | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



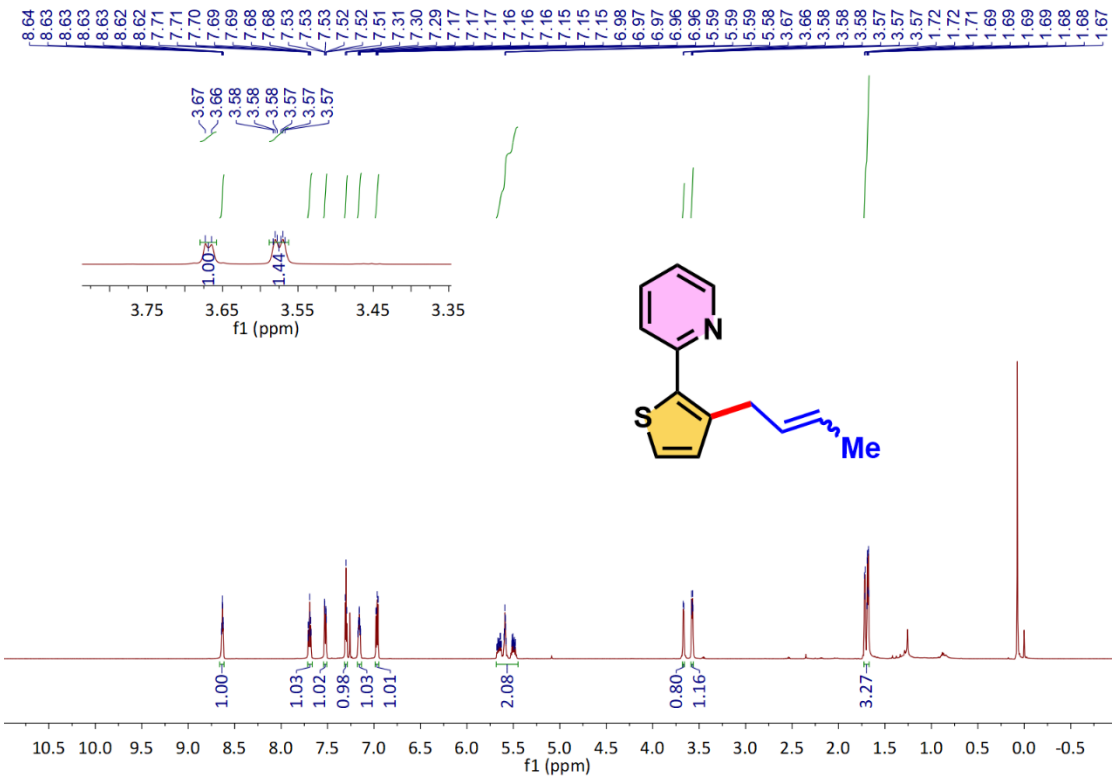
3sa | ^{1}H NMR ($CDCl_3$, 600 MHz)



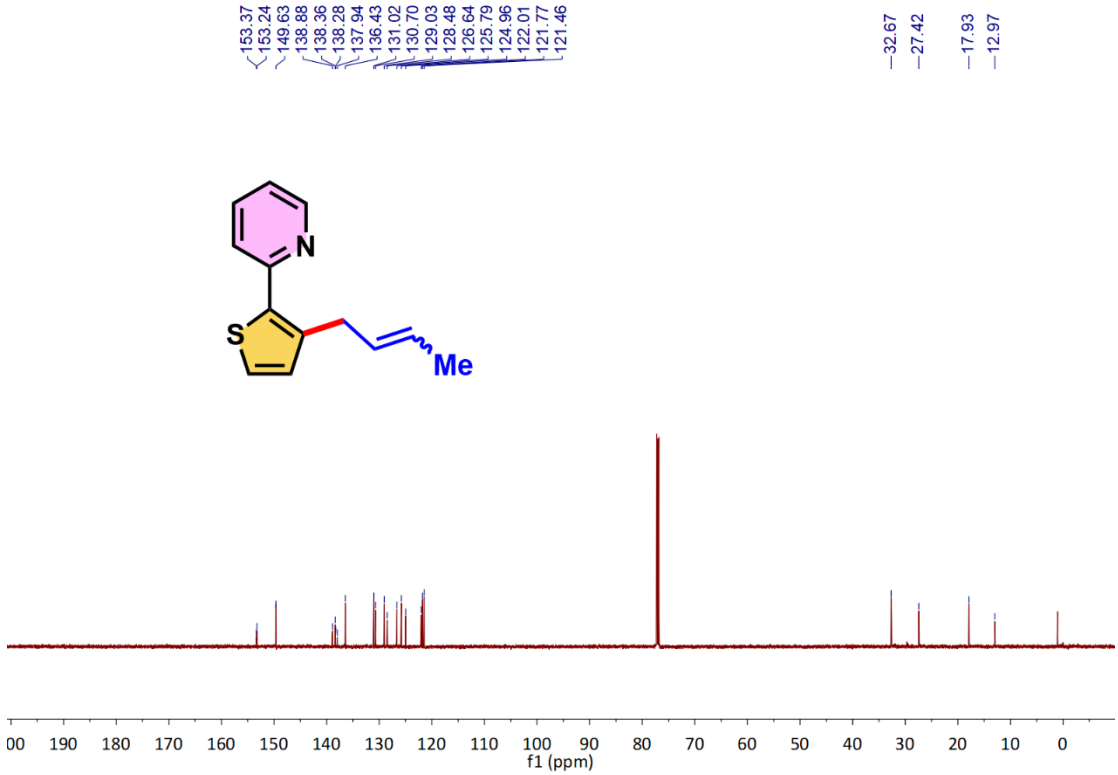
3sa | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



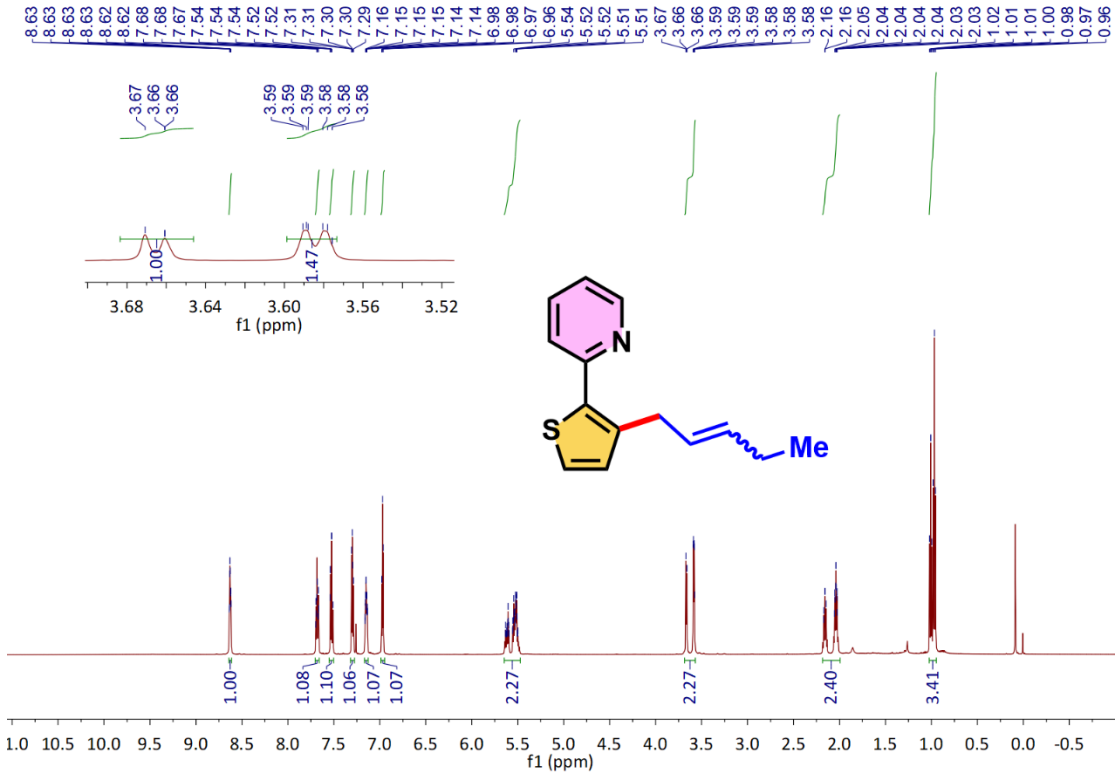
4aa | ^{1}H NMR ($CDCl_3$, 600 MHz)



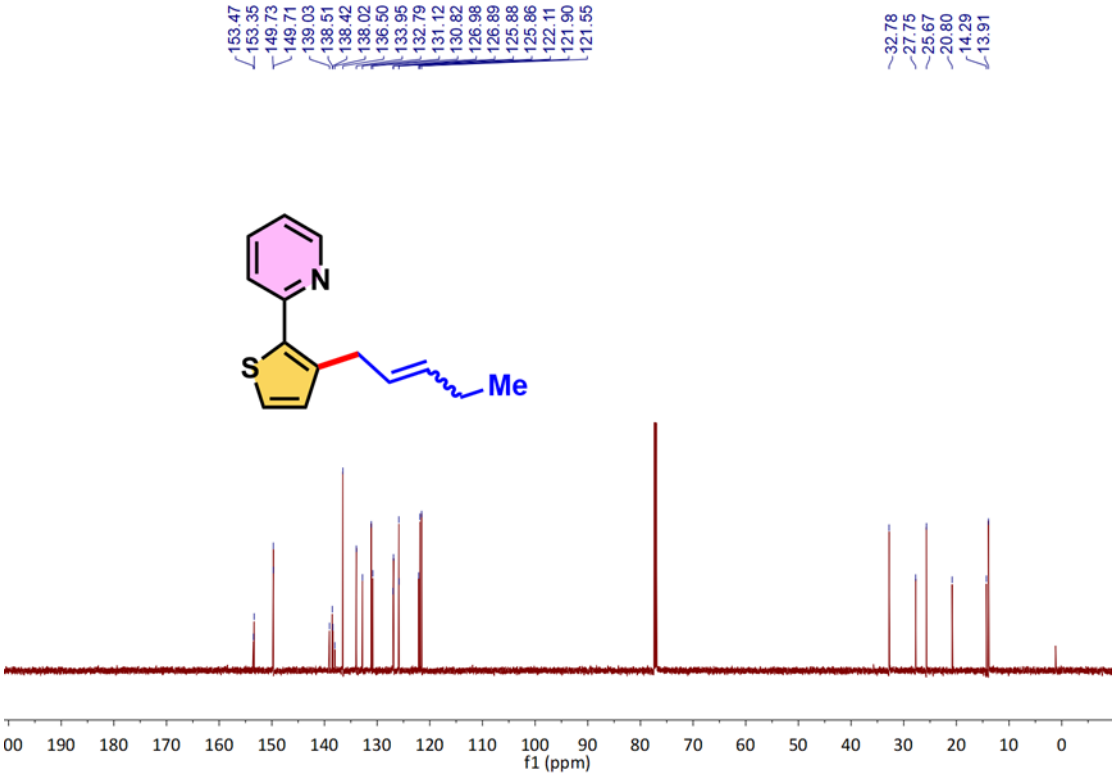
4aa | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



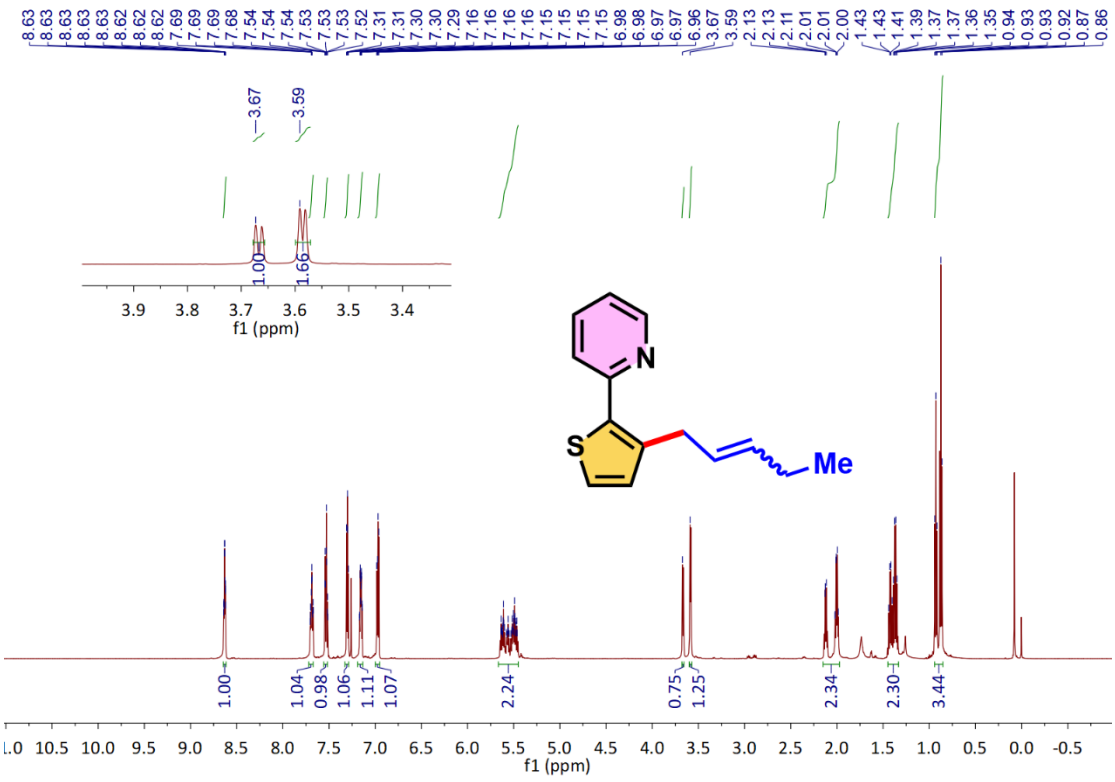
4ab | ^{1}H NMR ($CDCl_3$, 600 MHz)



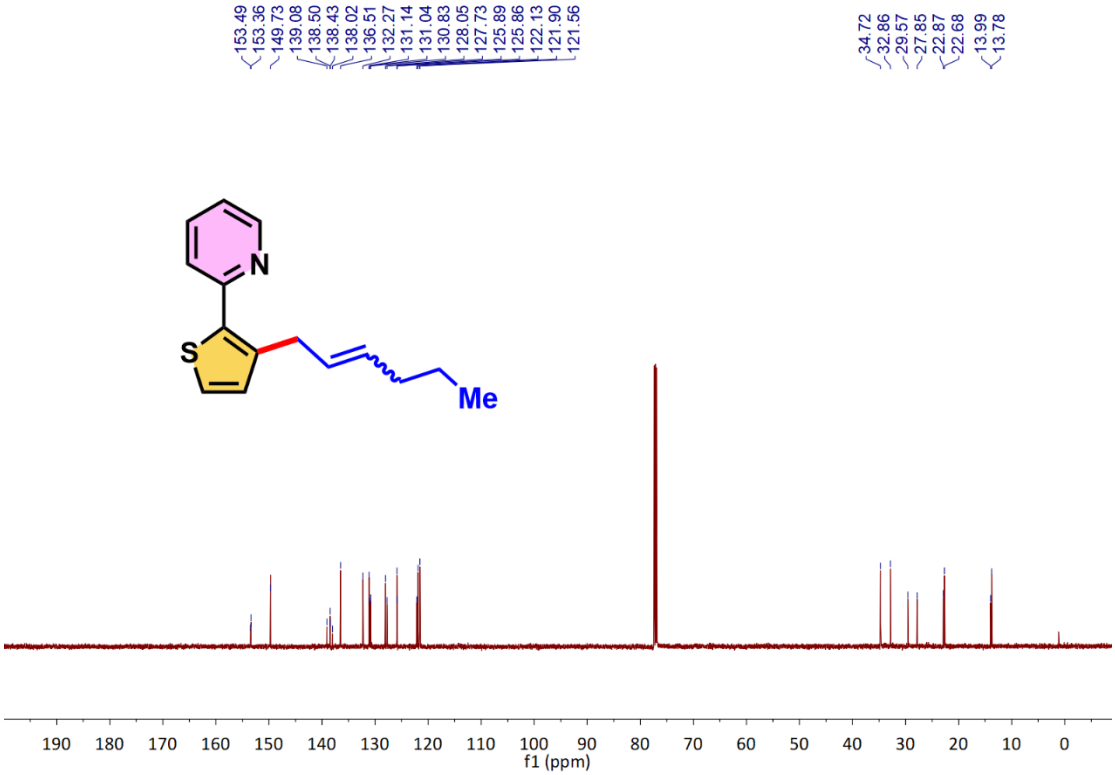
4ab | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



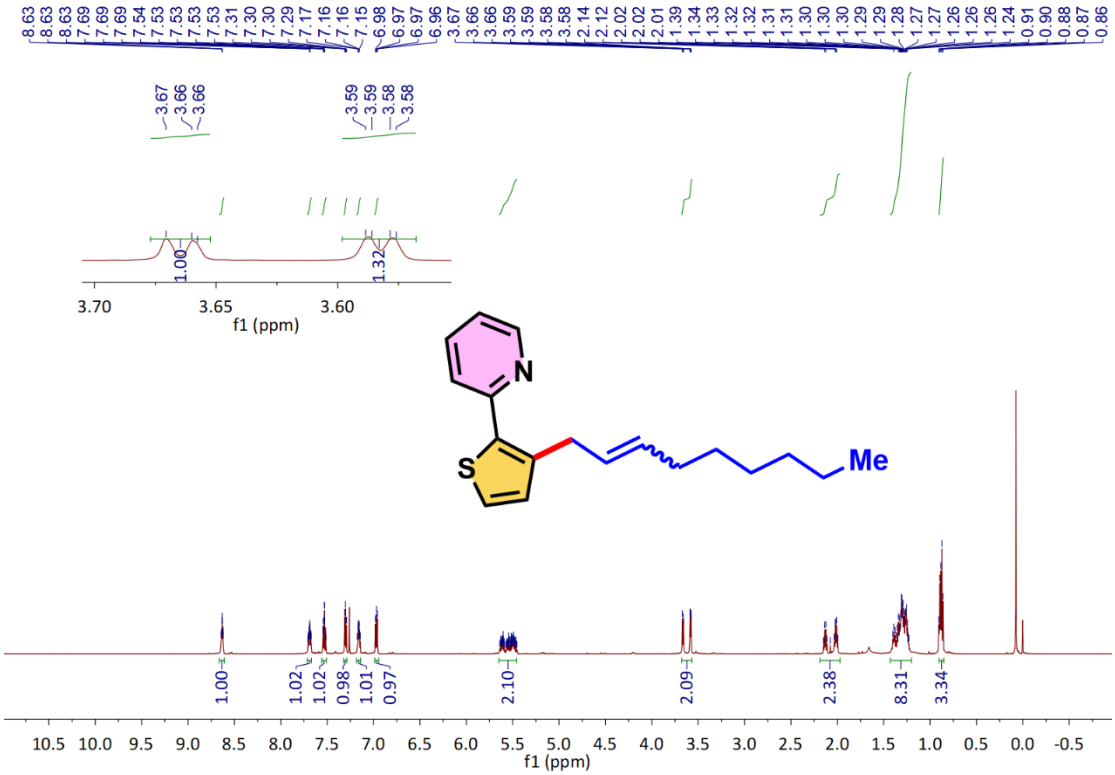
4ac | ^{1}H NMR ($CDCl_3$, 600 MHz)



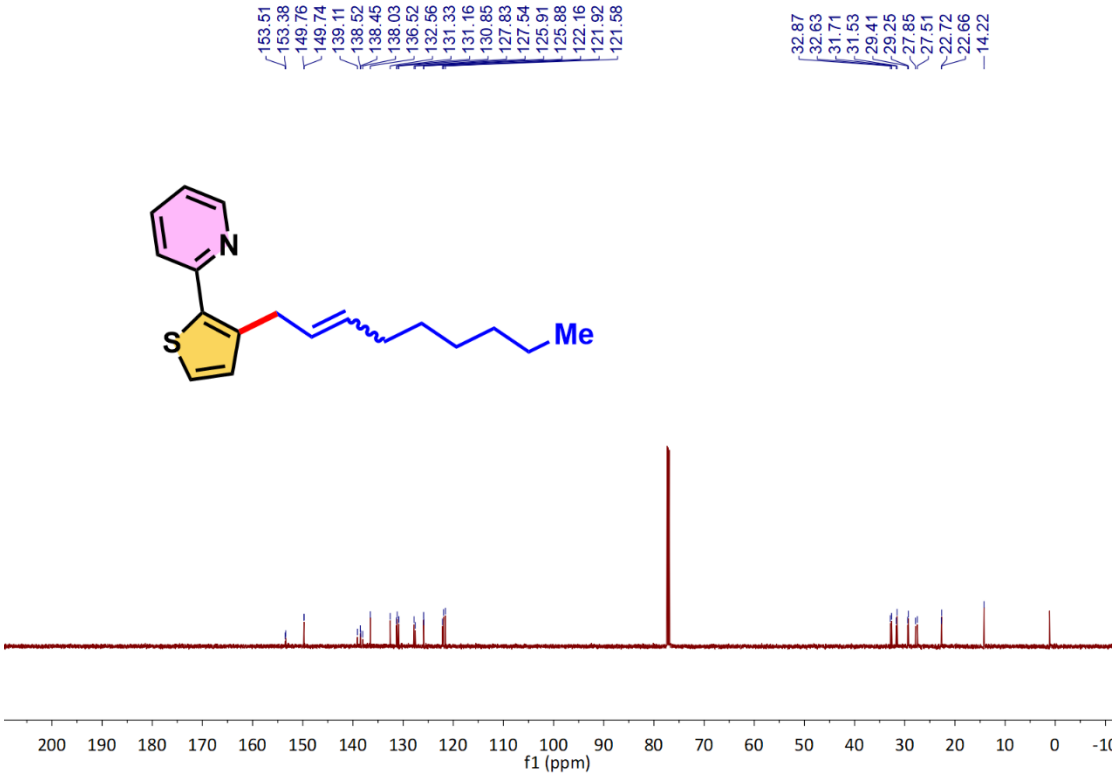
4ac | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



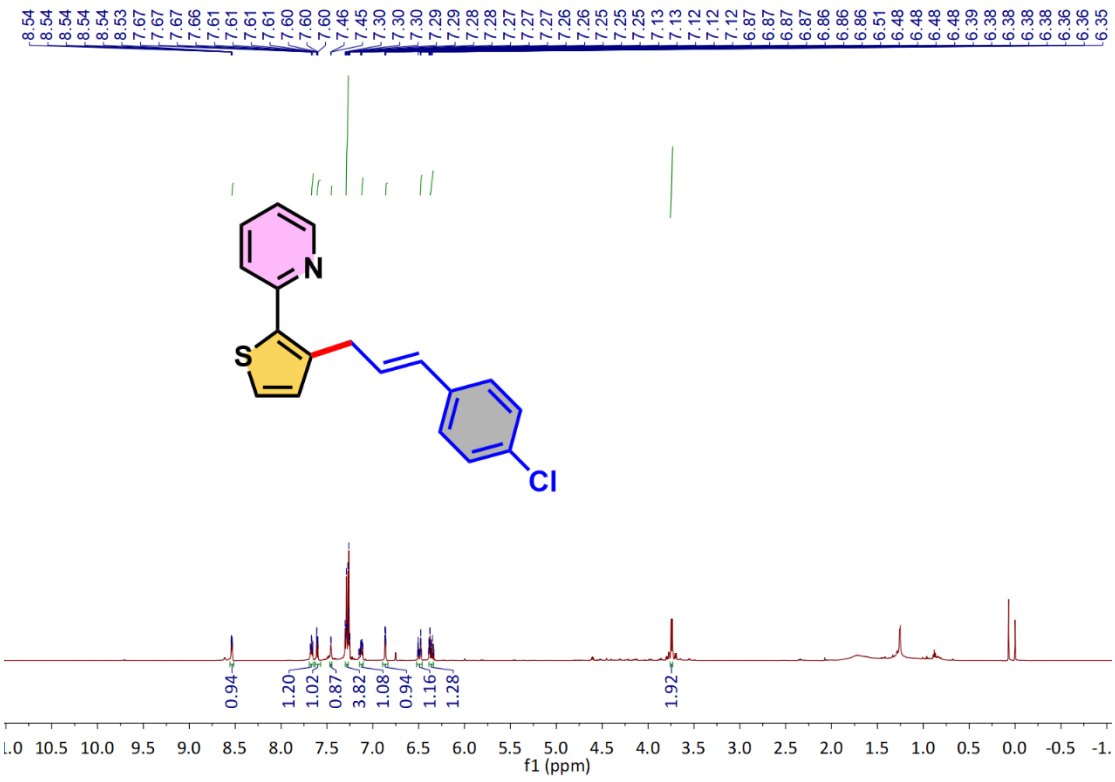
4ad | ^{1}H NMR ($CDCl_3$, 600 MHz)



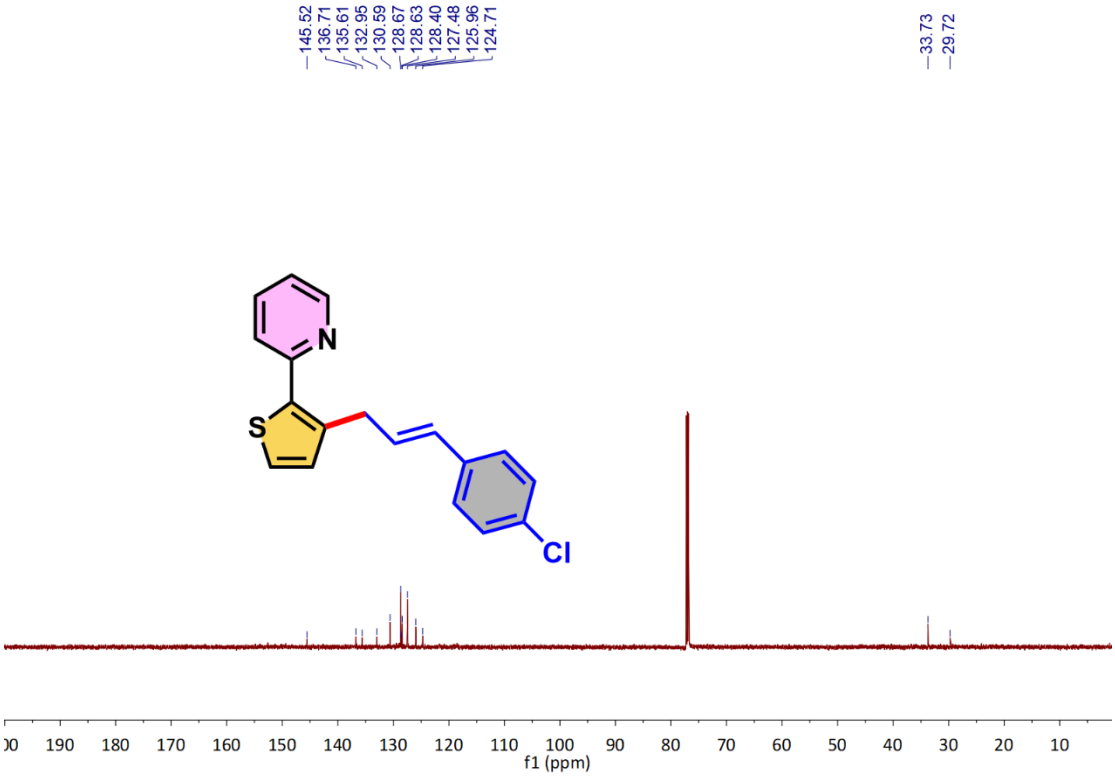
4ad | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



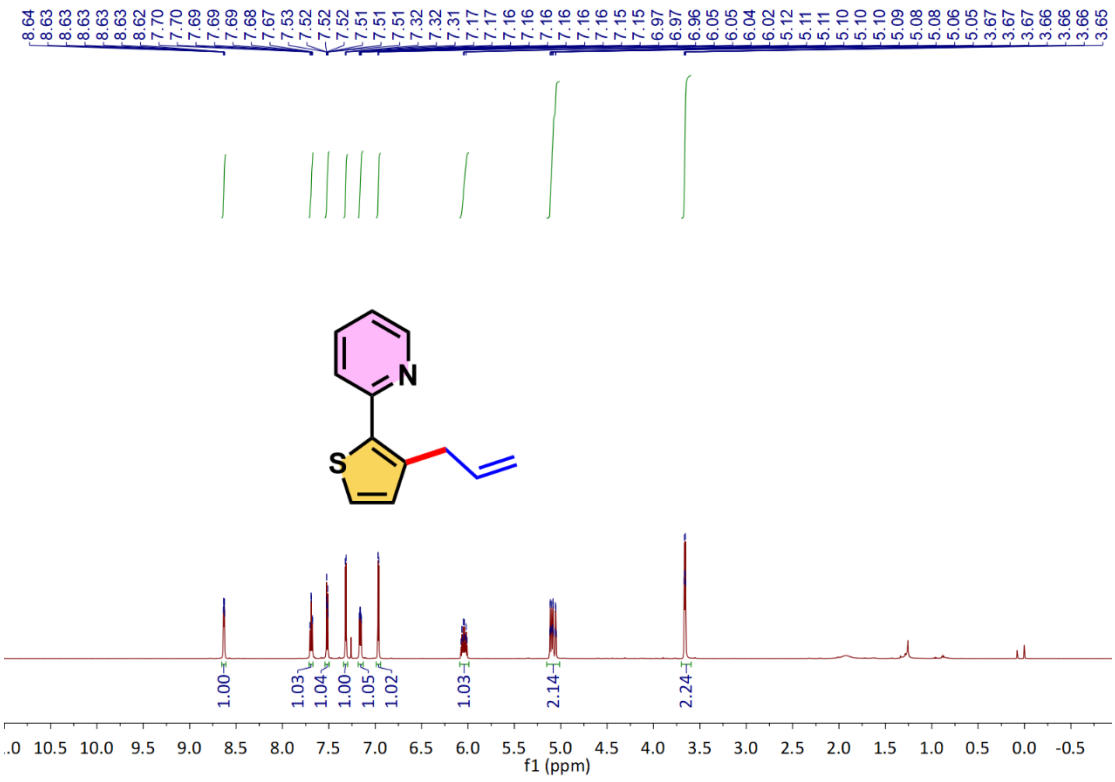
4ai | ^{1}H NMR ($CDCl_3$, 600 MHz)



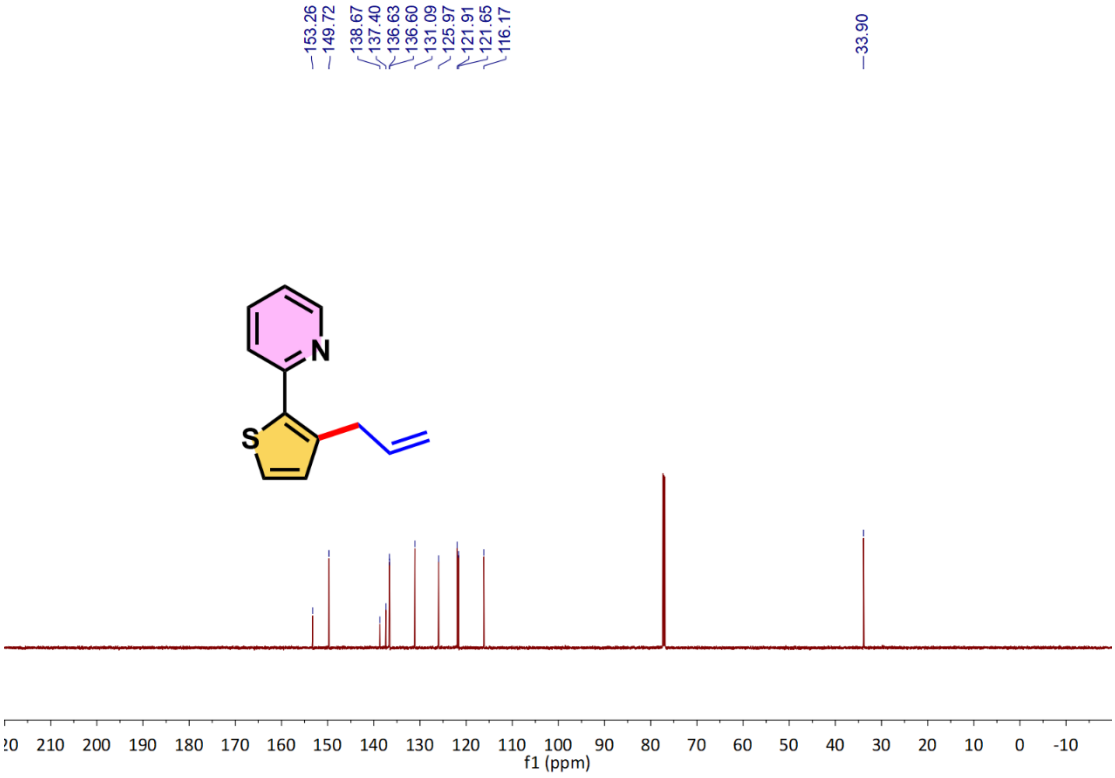
4ai | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



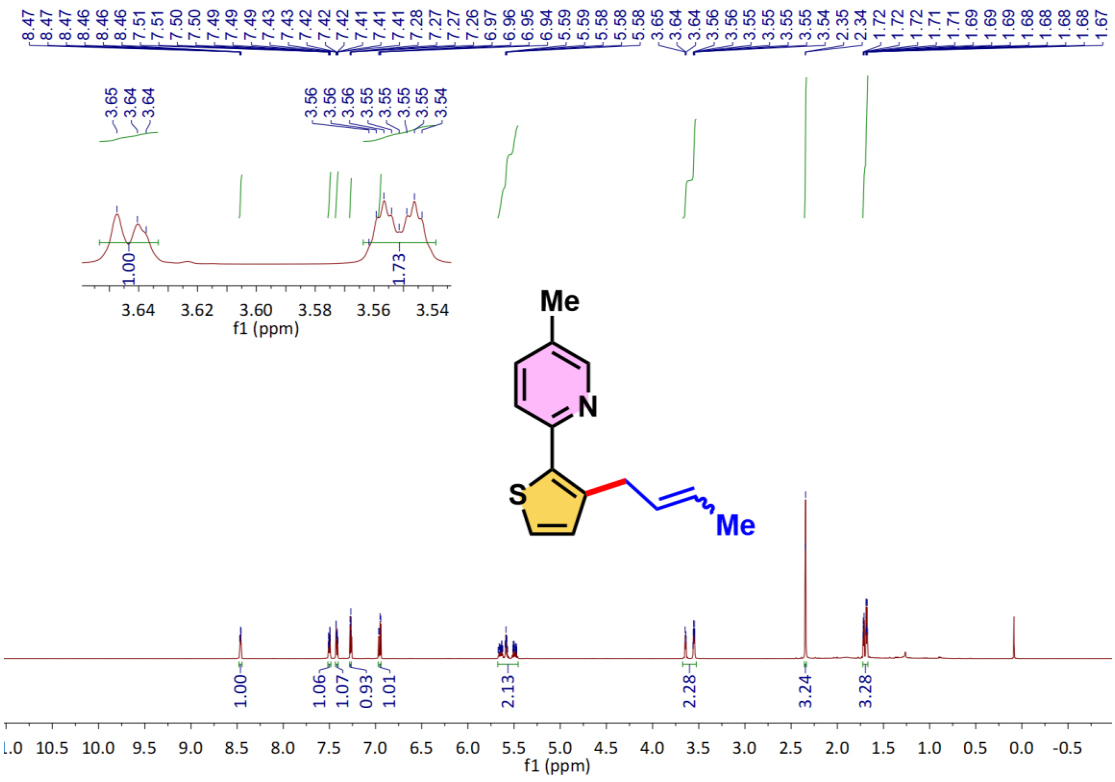
4ap | ^{1}H NMR ($CDCl_3$, 600 MHz)



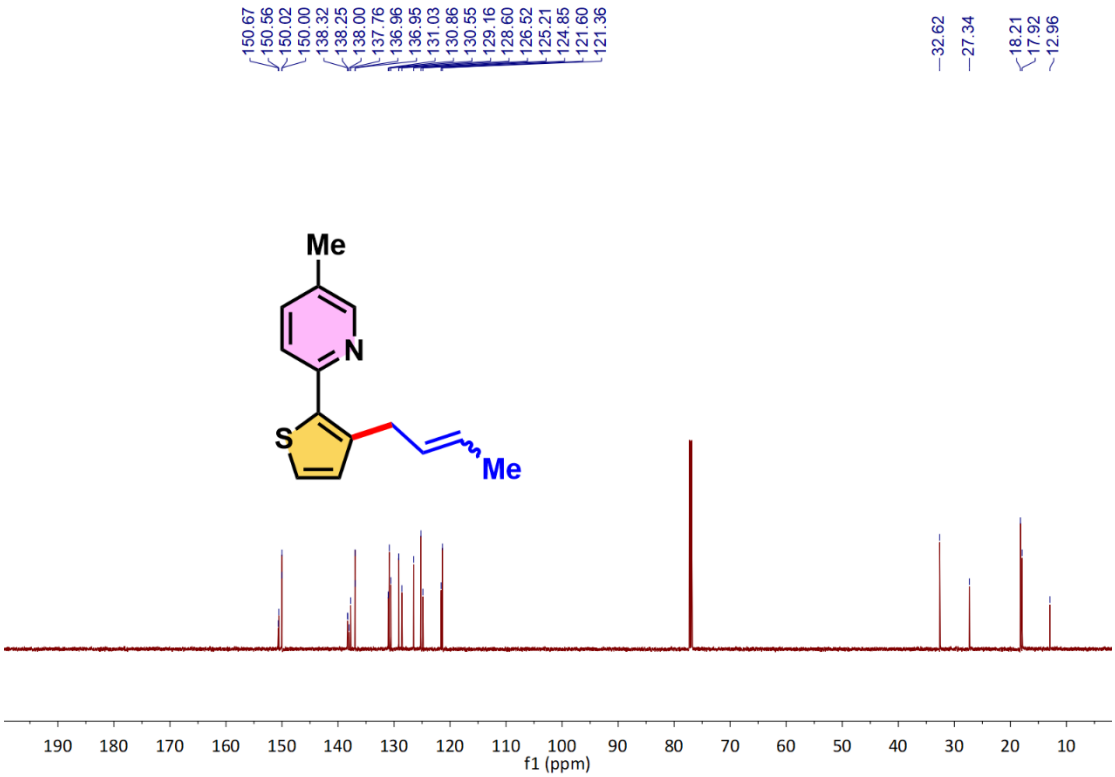
4ap | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



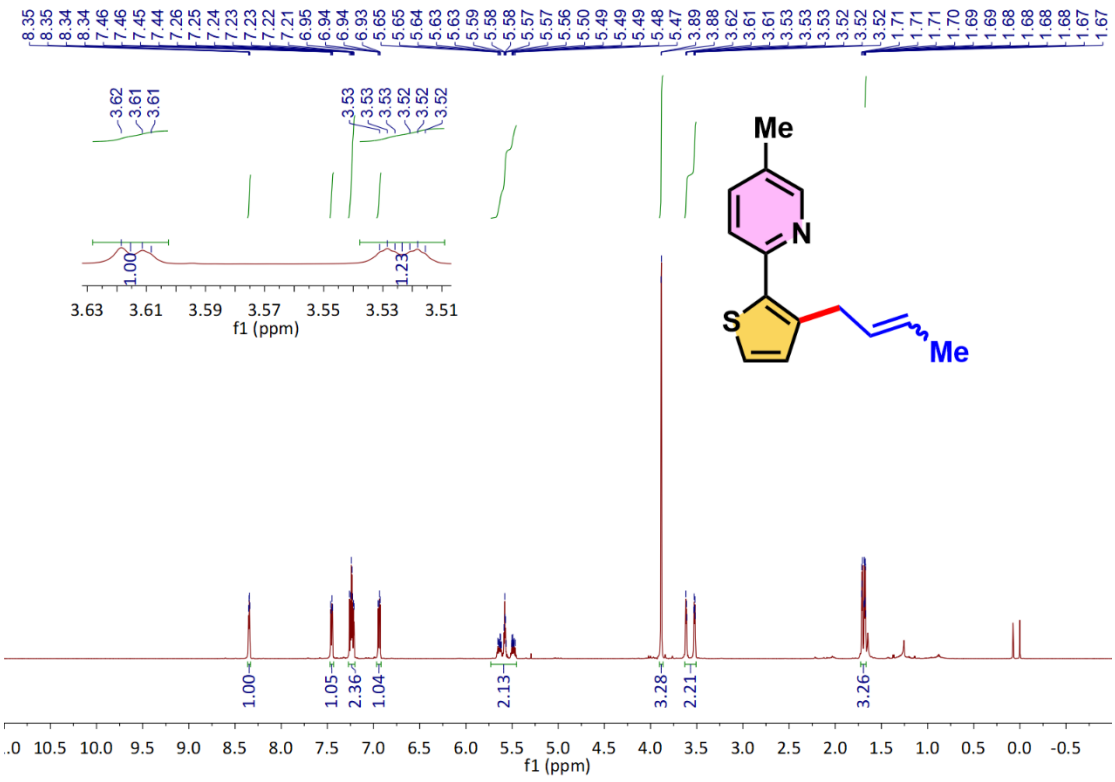
4ba | ^{1}H NMR ($CDCl_3$, 600 MHz)



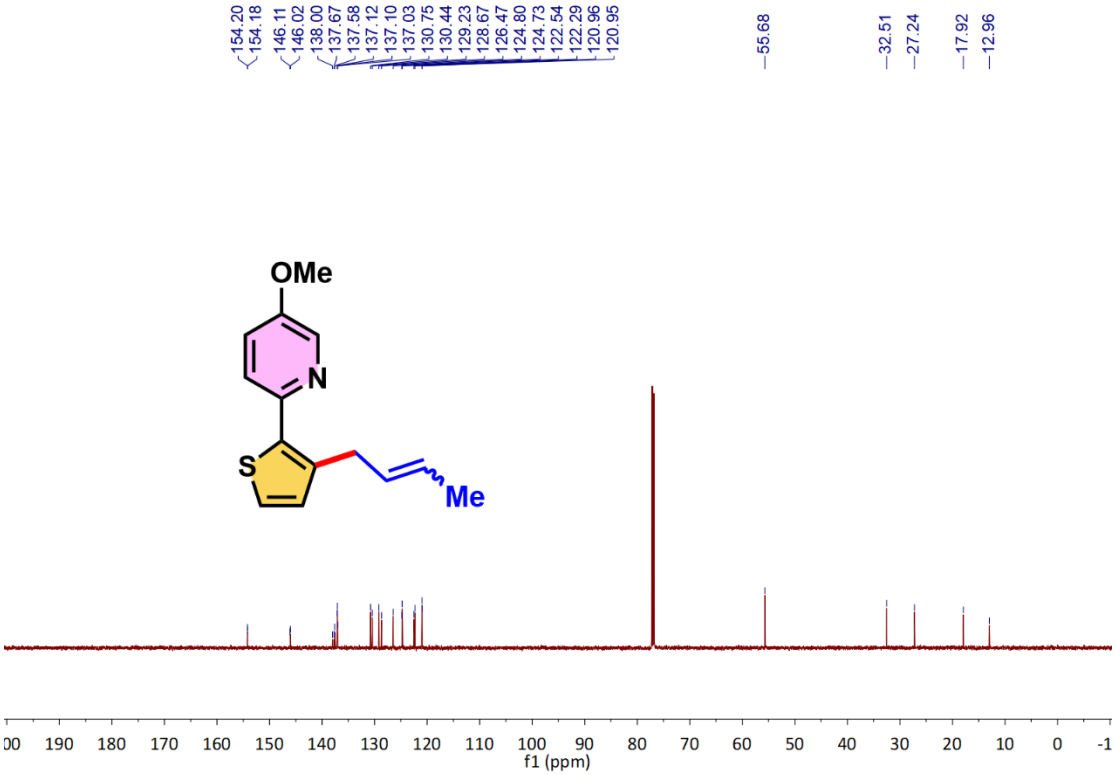
4ba | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



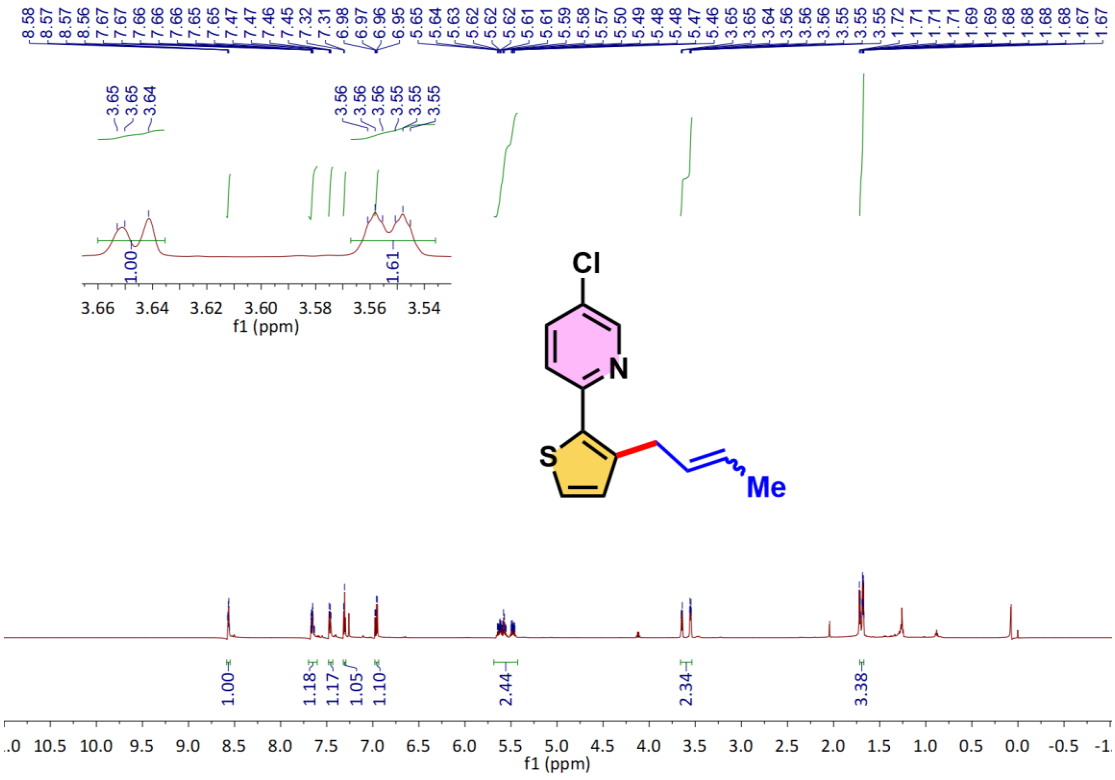
4ca | ^{1}H NMR ($CDCl_3$, 600 MHz)



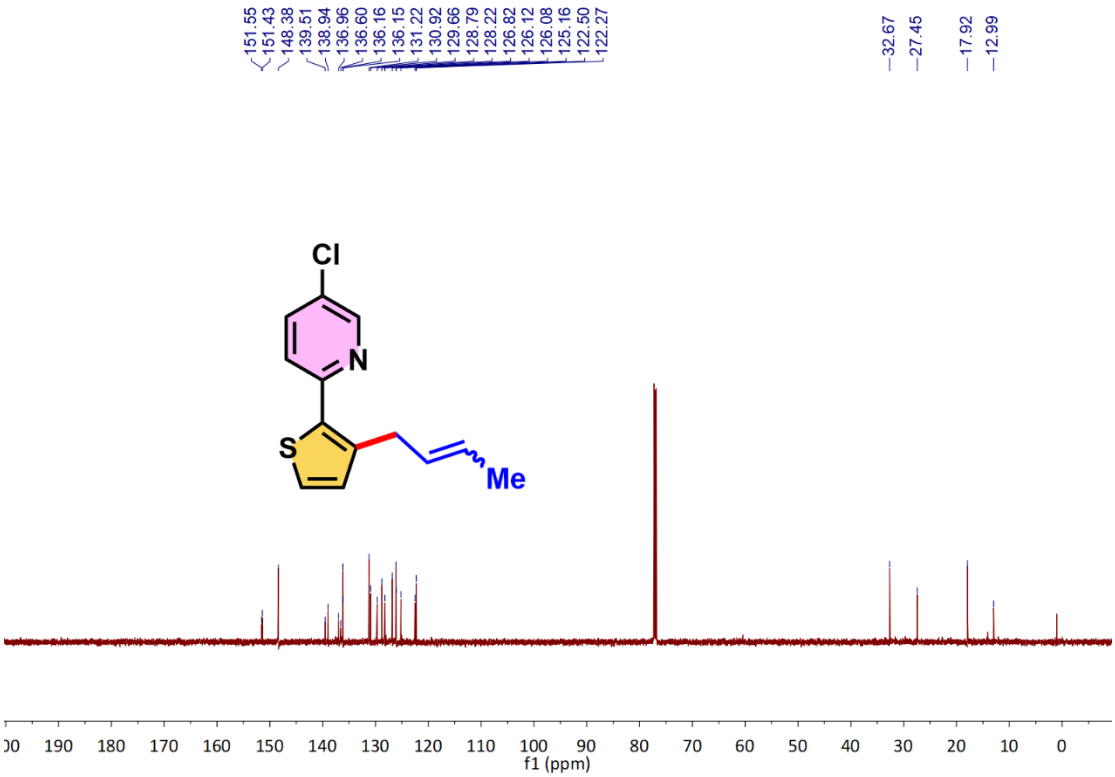
4ca | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



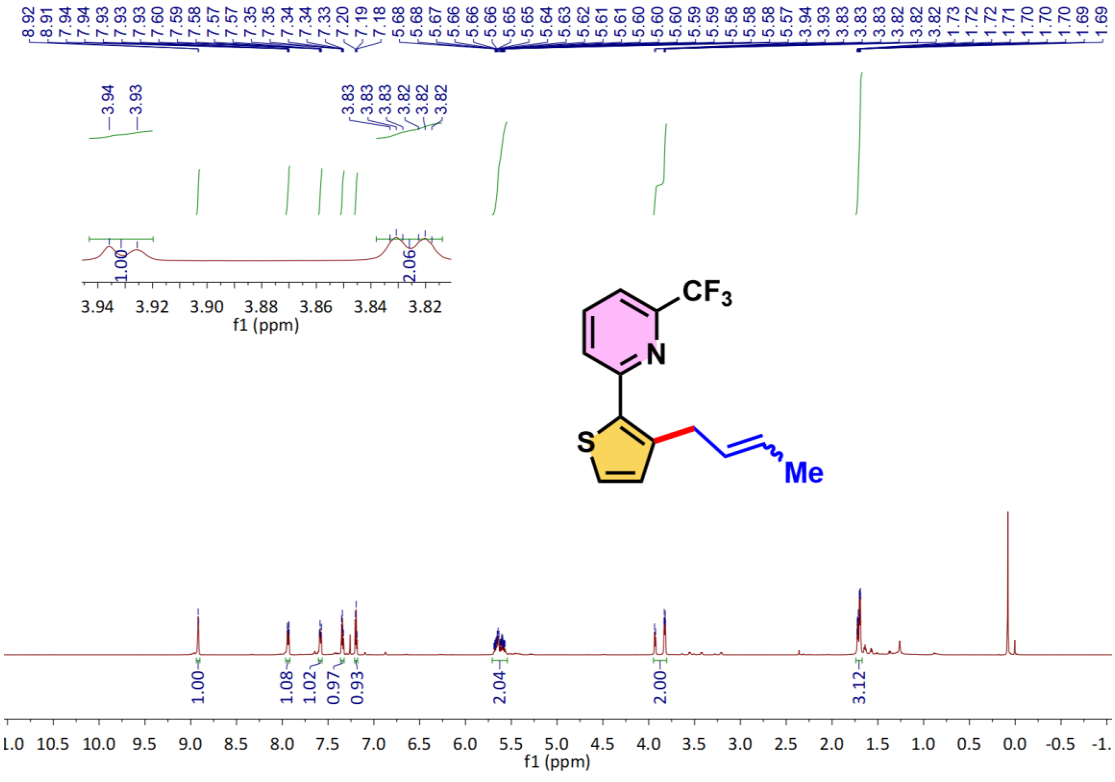
4ea | ^{1}H NMR ($CDCl_3$, 600 MHz)



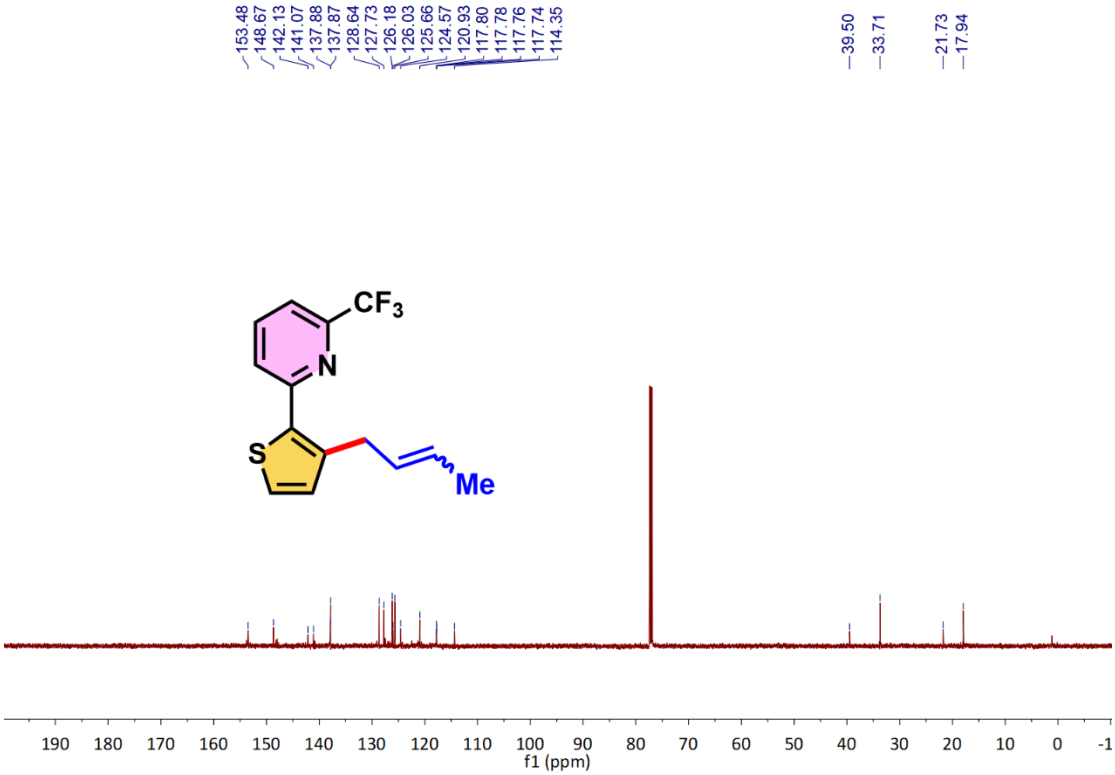
4ea | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



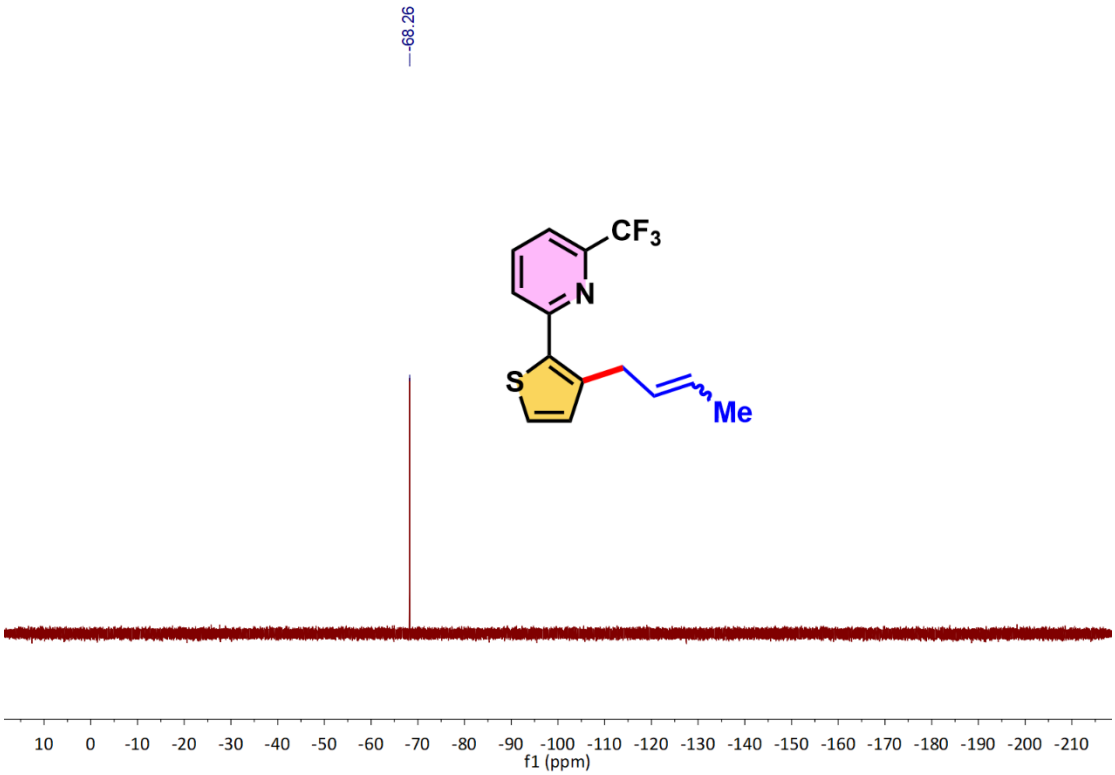
4ha | ^{1}H NMR ($CDCl_3$, 600 MHz)



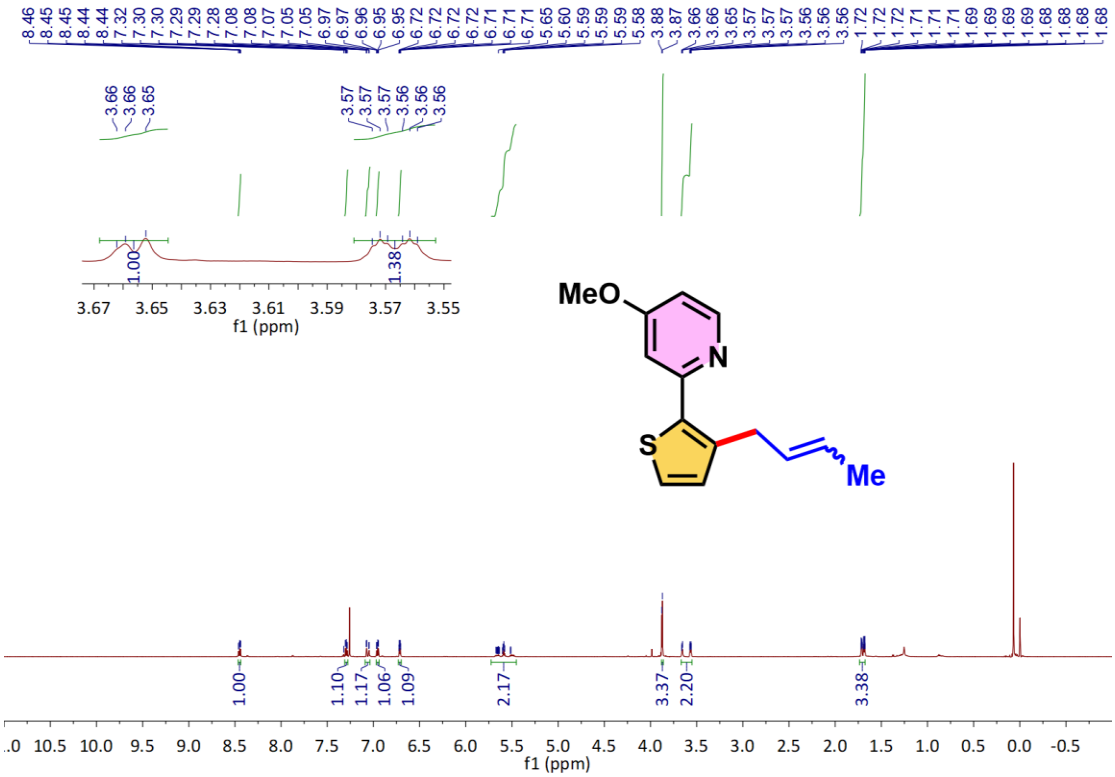
4ha | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



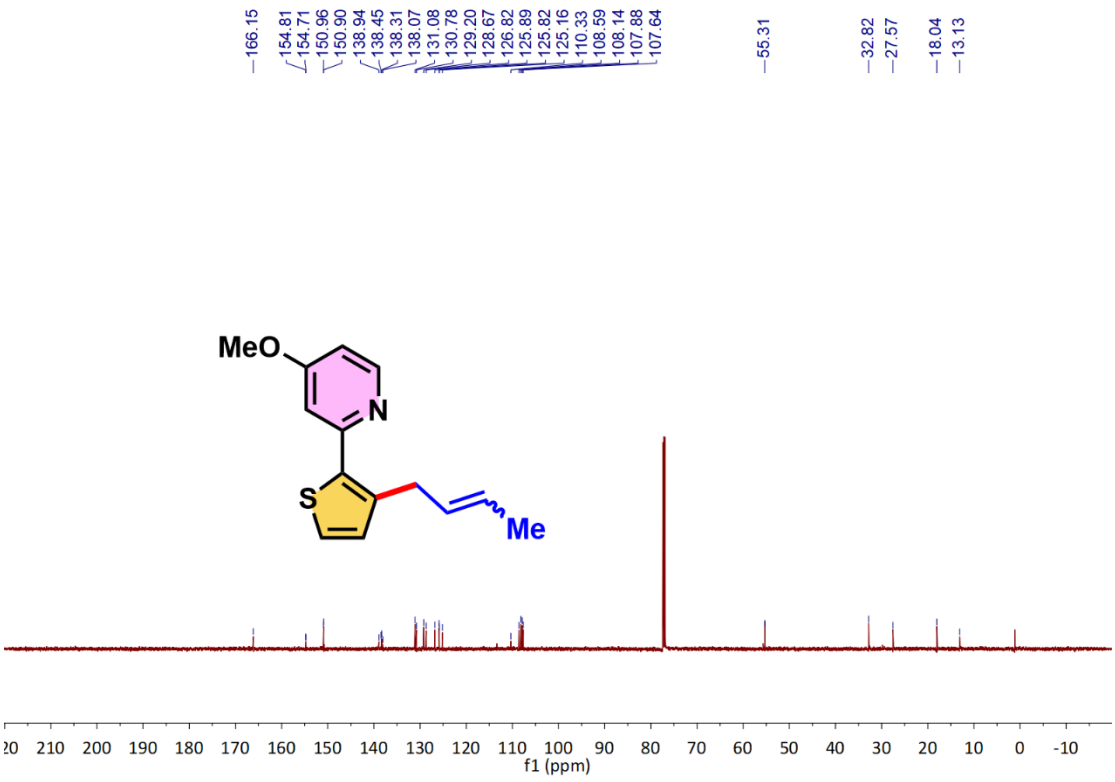
4ha | $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 565 MHz)



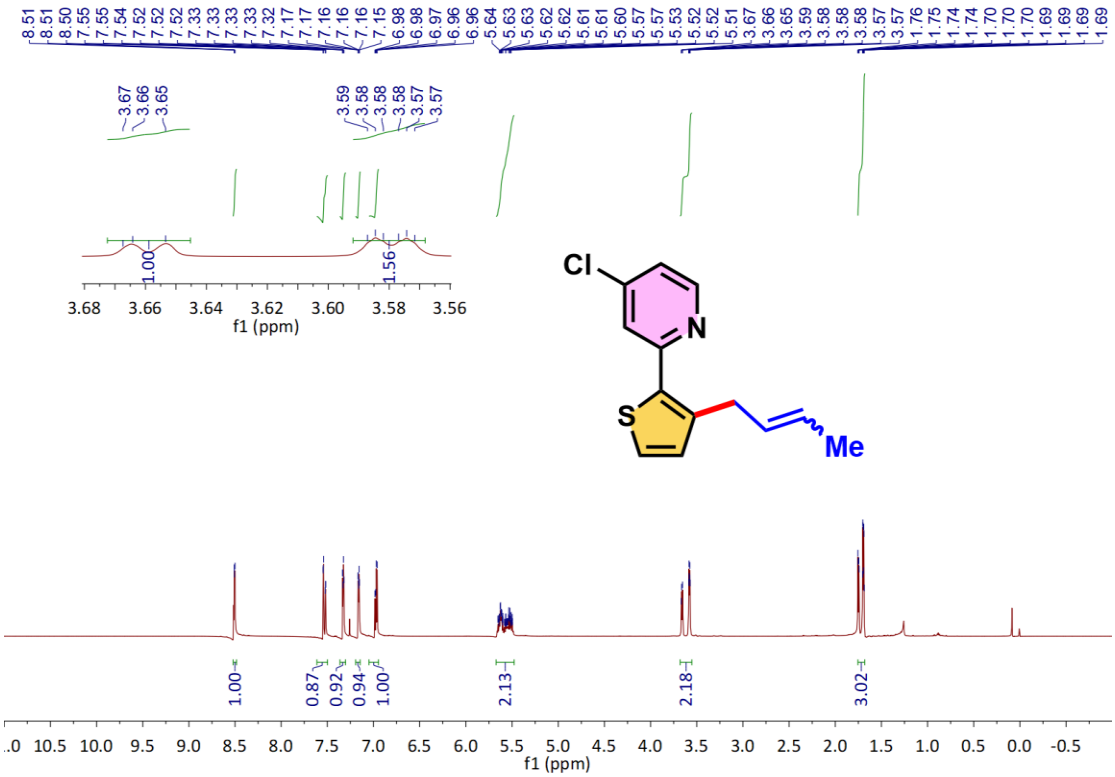
4ja | ^{1}H NMR ($CDCl_3$, 600 MHz)



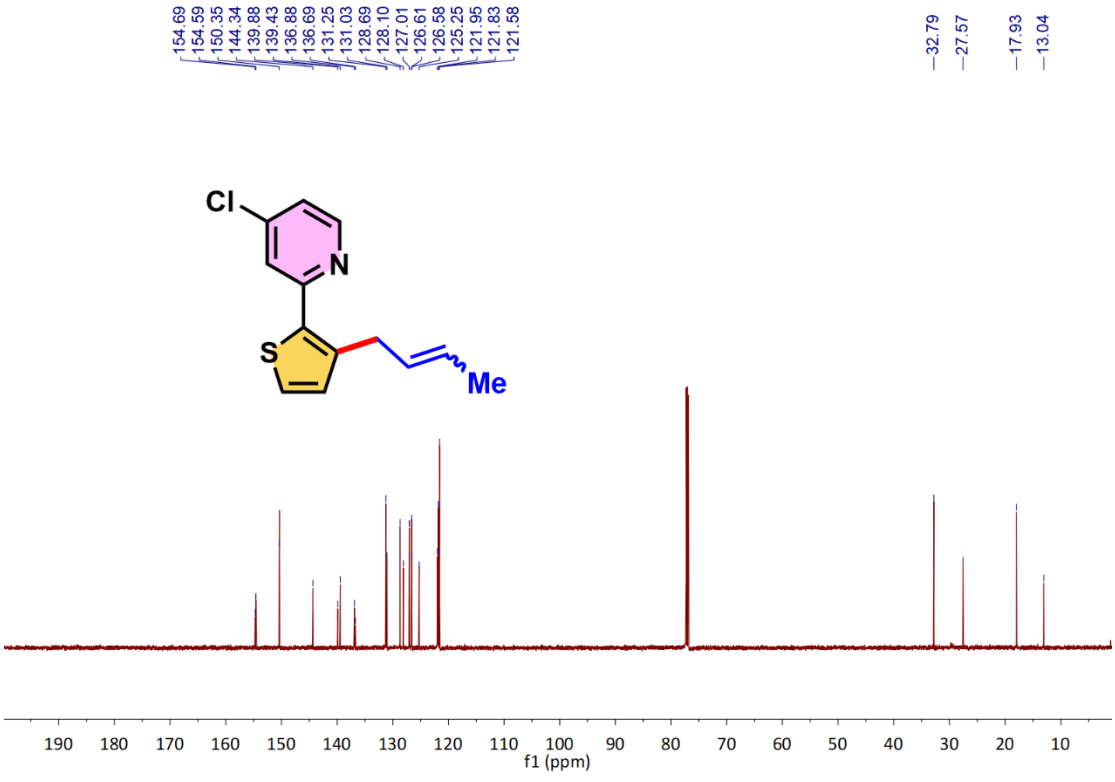
4ja | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



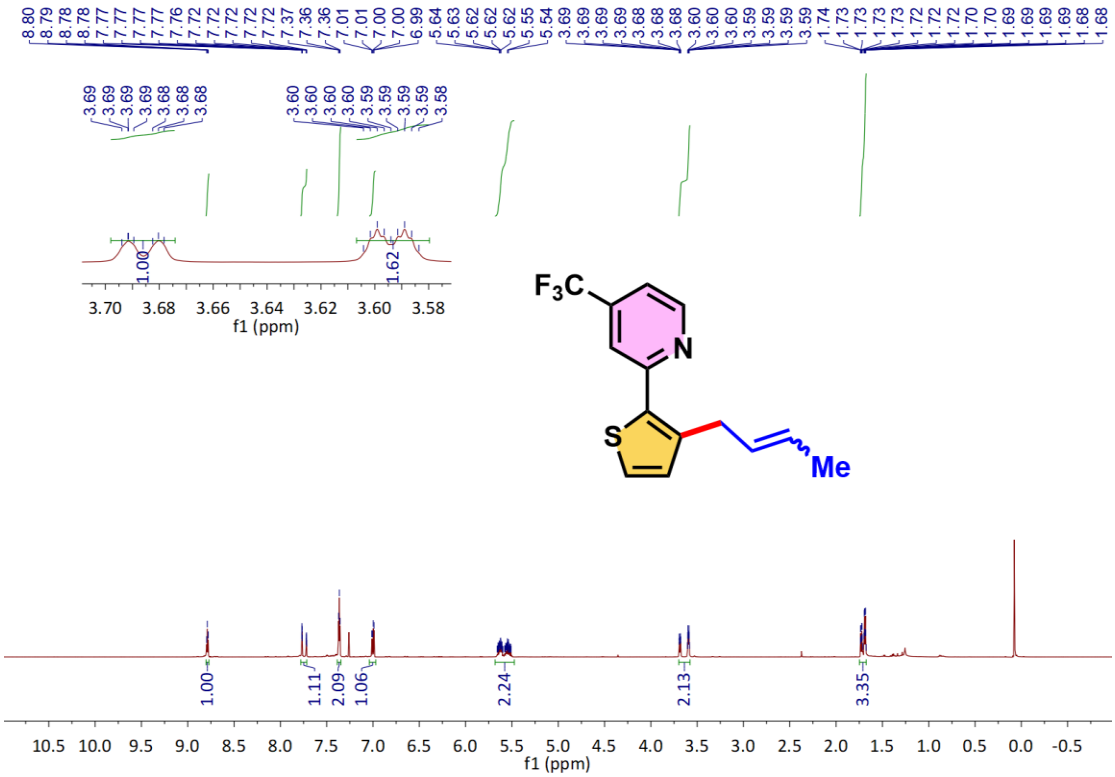
4ka | ^{1}H NMR ($CDCl_3$, 600 MHz)



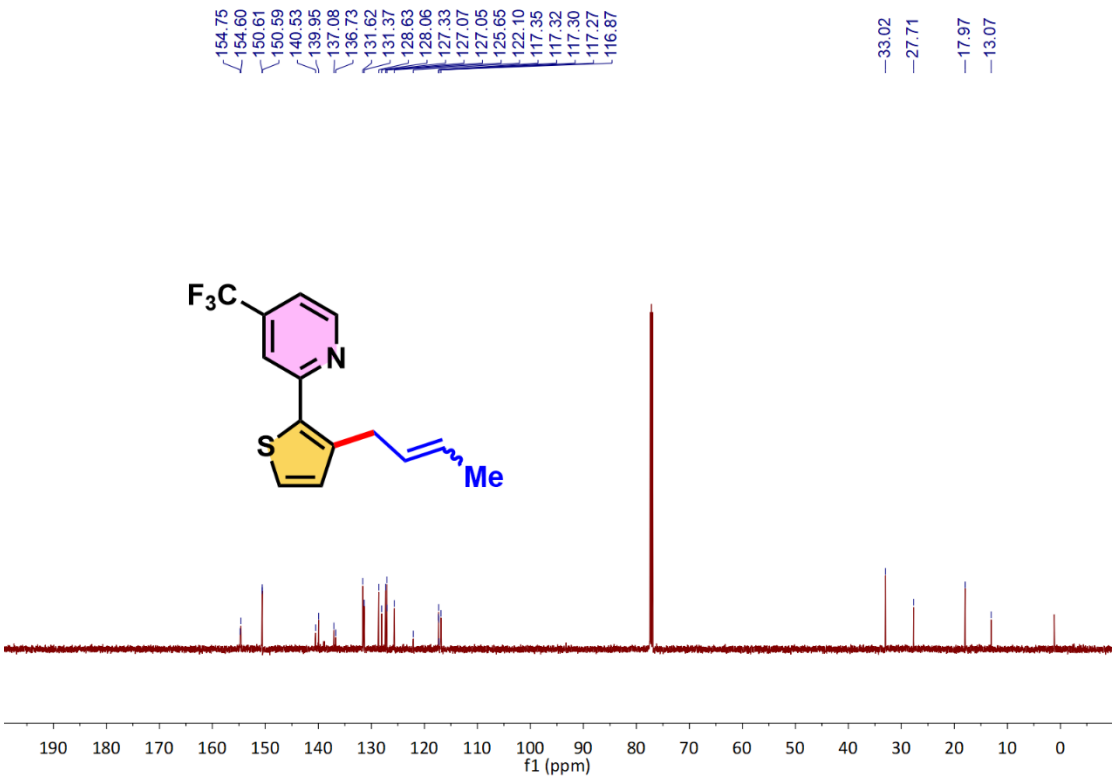
4ka | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



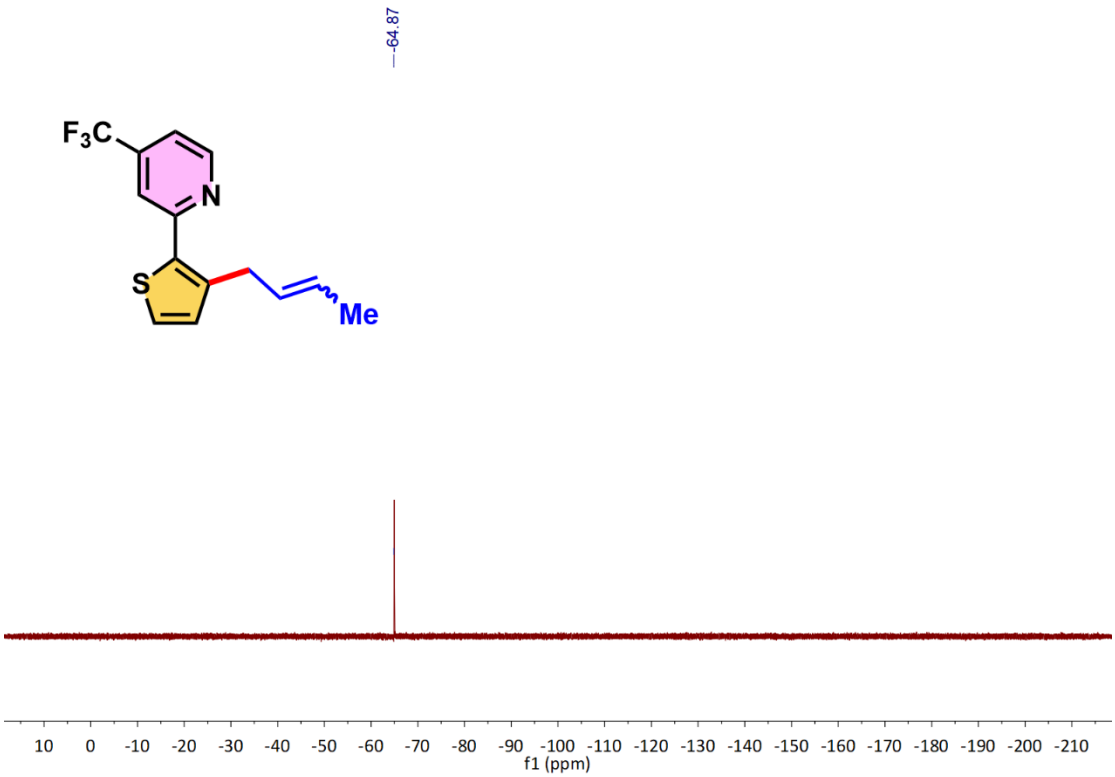
4la | ^{1}H NMR ($CDCl_3$, 600 MHz)



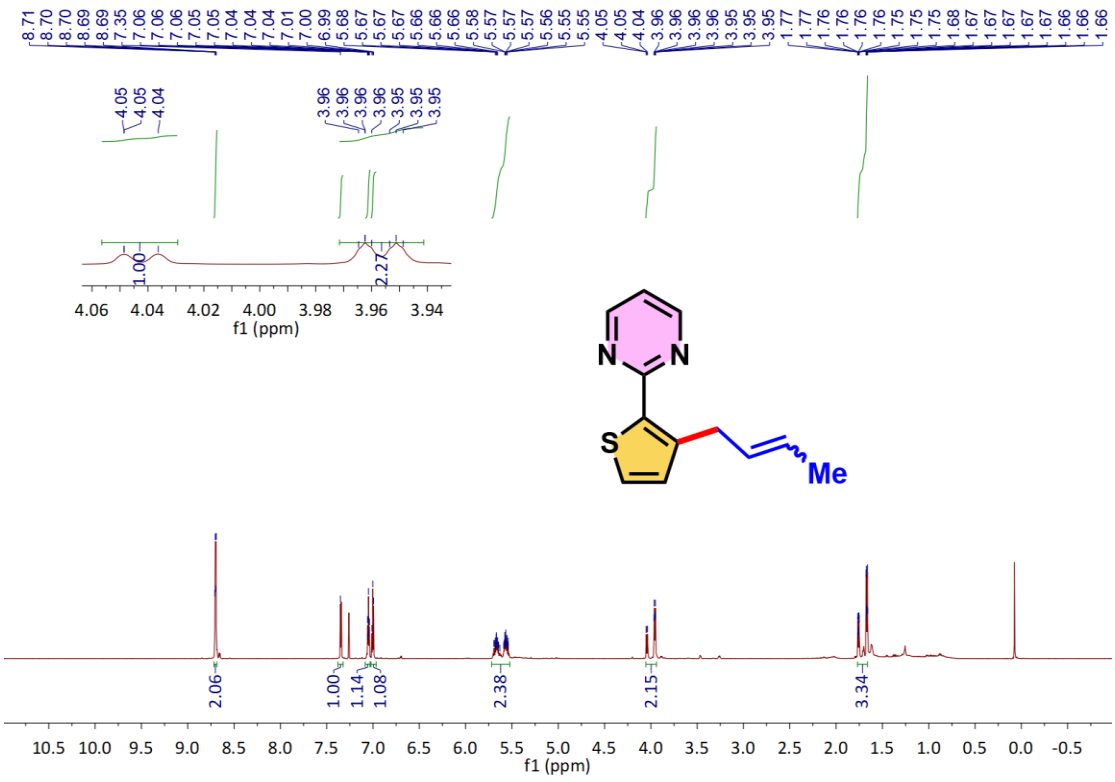
4la | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



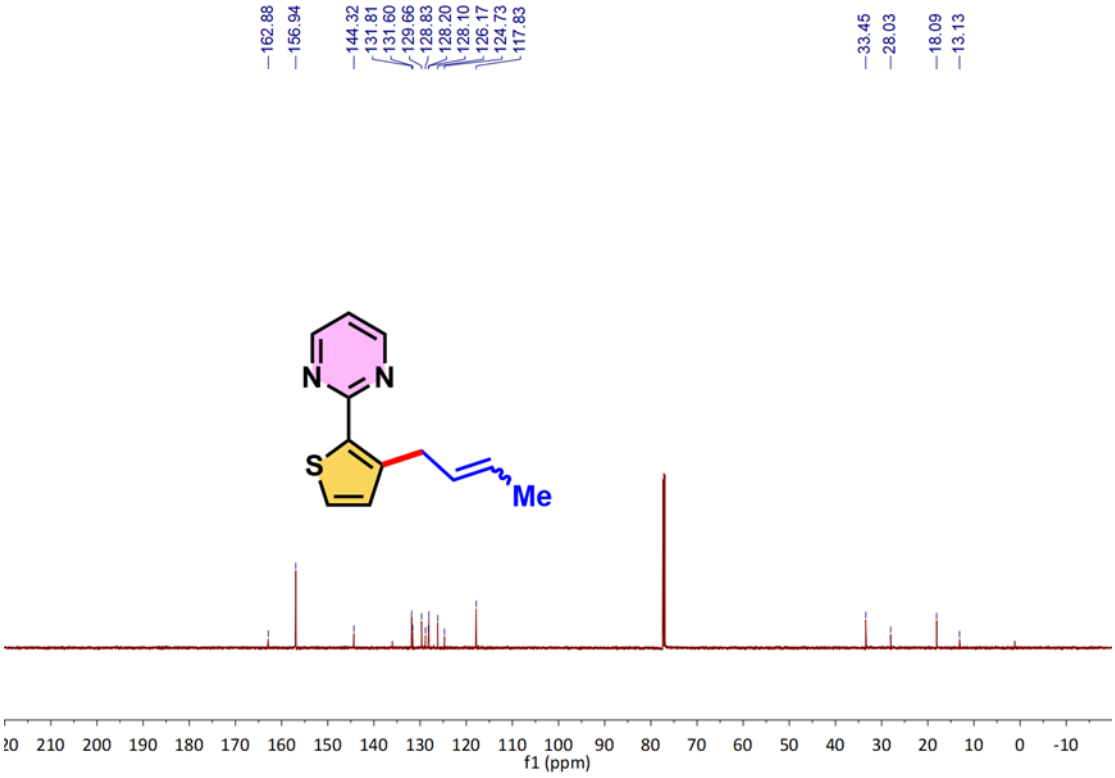
4la | $^{19}F\{^{1}H\}$ NMR ($CDCl_3$, 565 MHz)



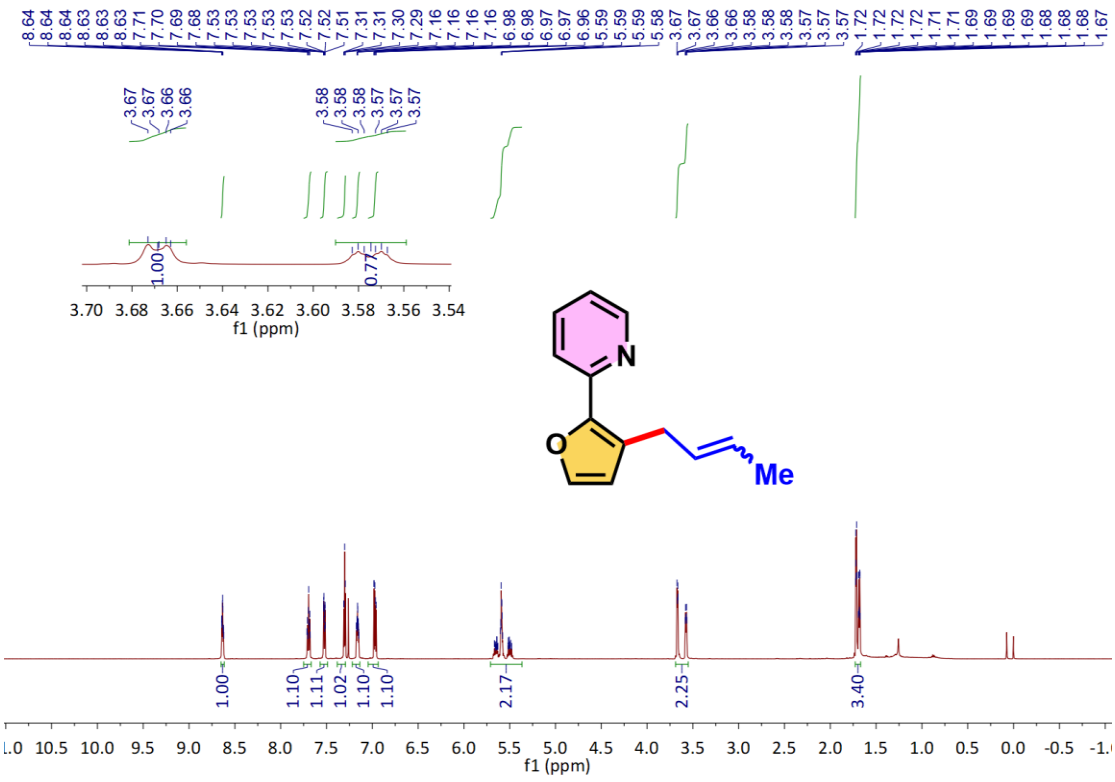
4ta | ^{1}H NMR ($CDCl_3$, 600 MHz)



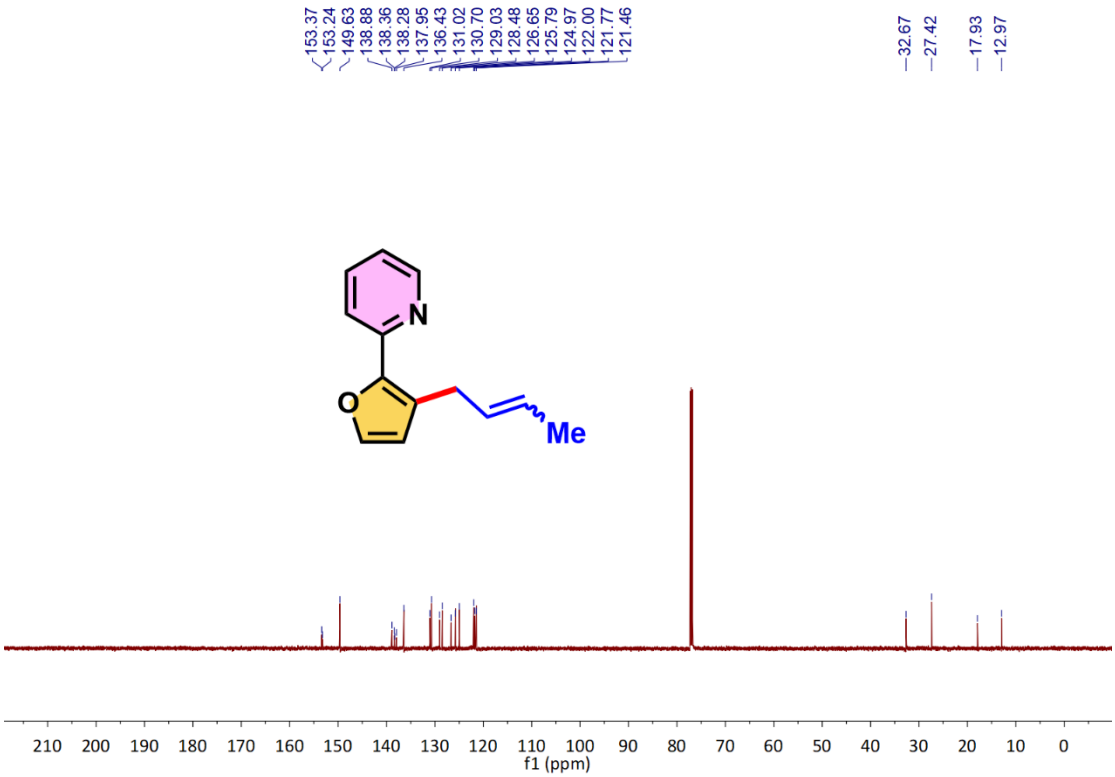
4ta | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



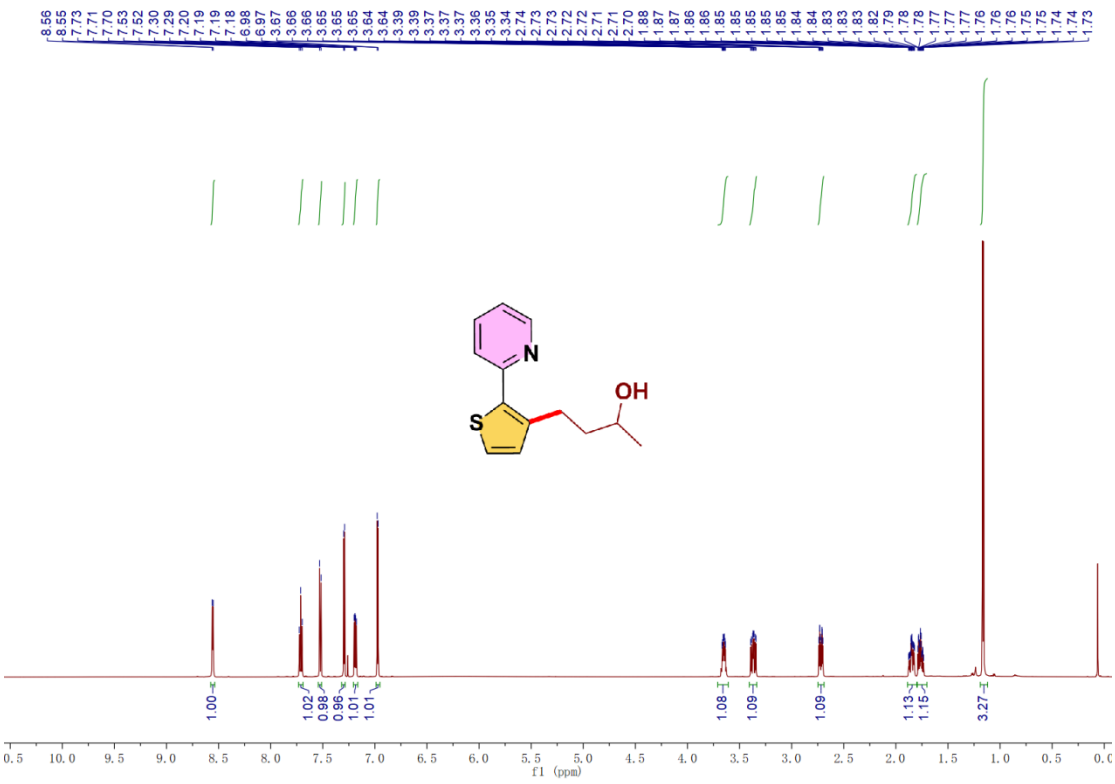
4ua | ^{1}H NMR ($CDCl_3$, 600 MHz)



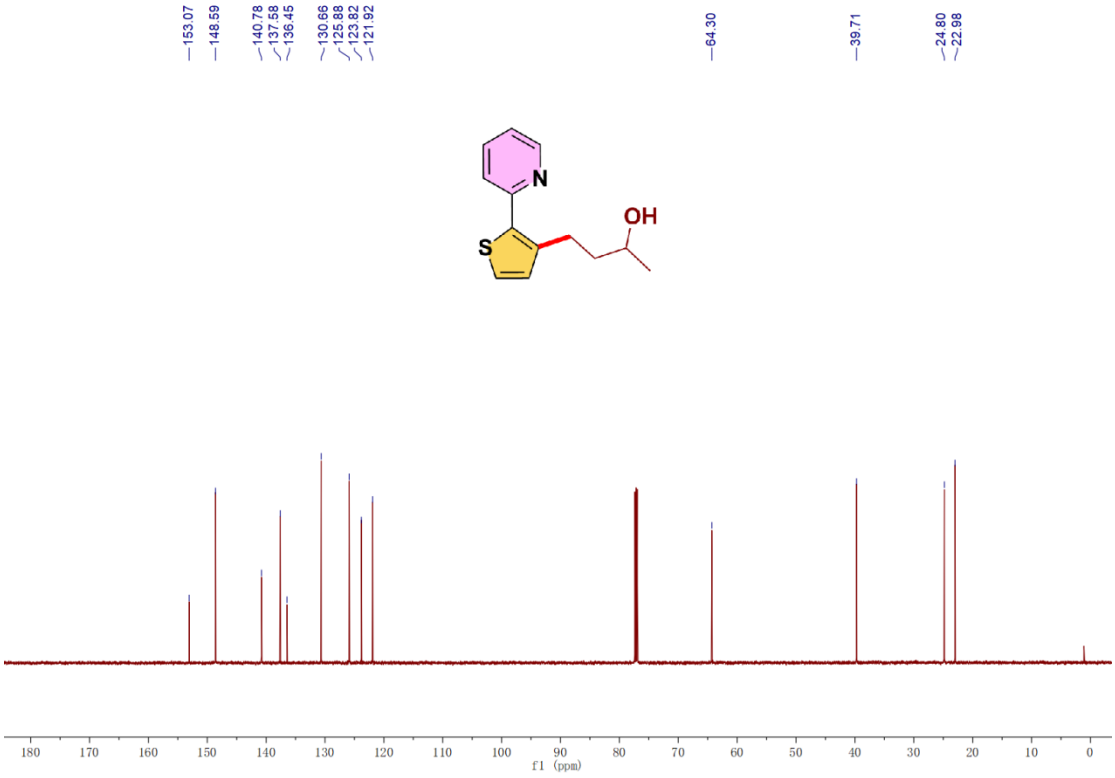
4ua | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



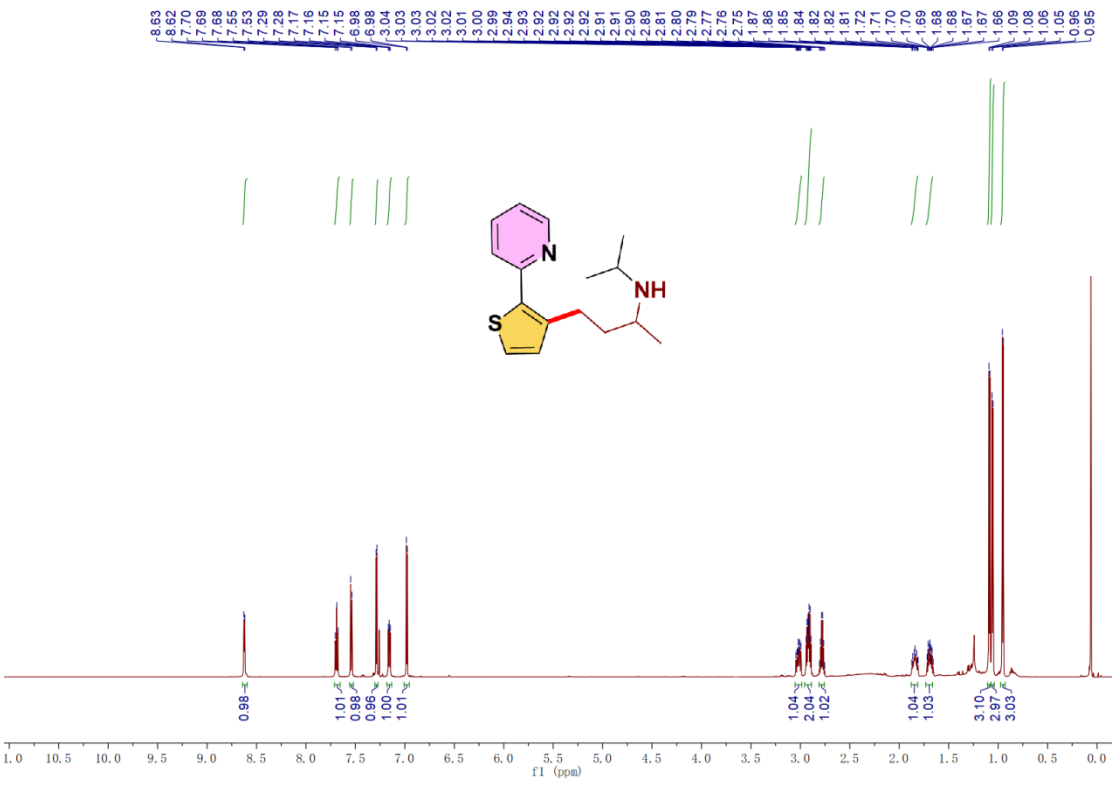
5 | ^{1}H NMR ($CDCl_3$, 600 MHz)



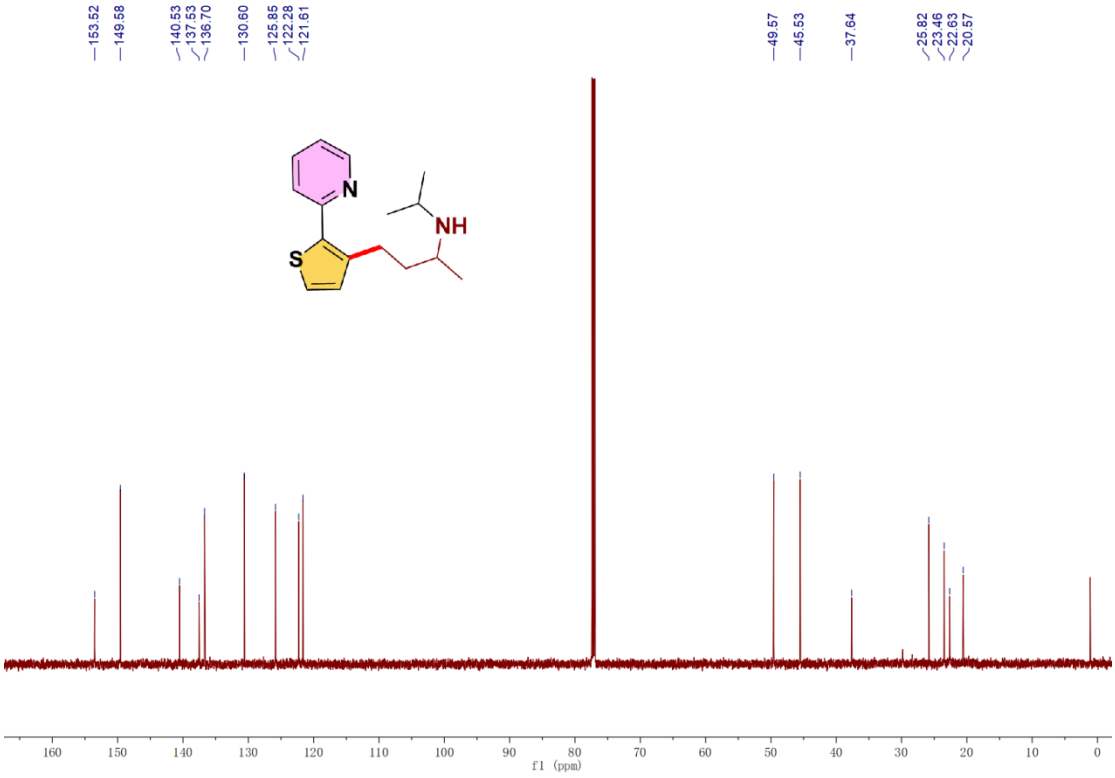
5 | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



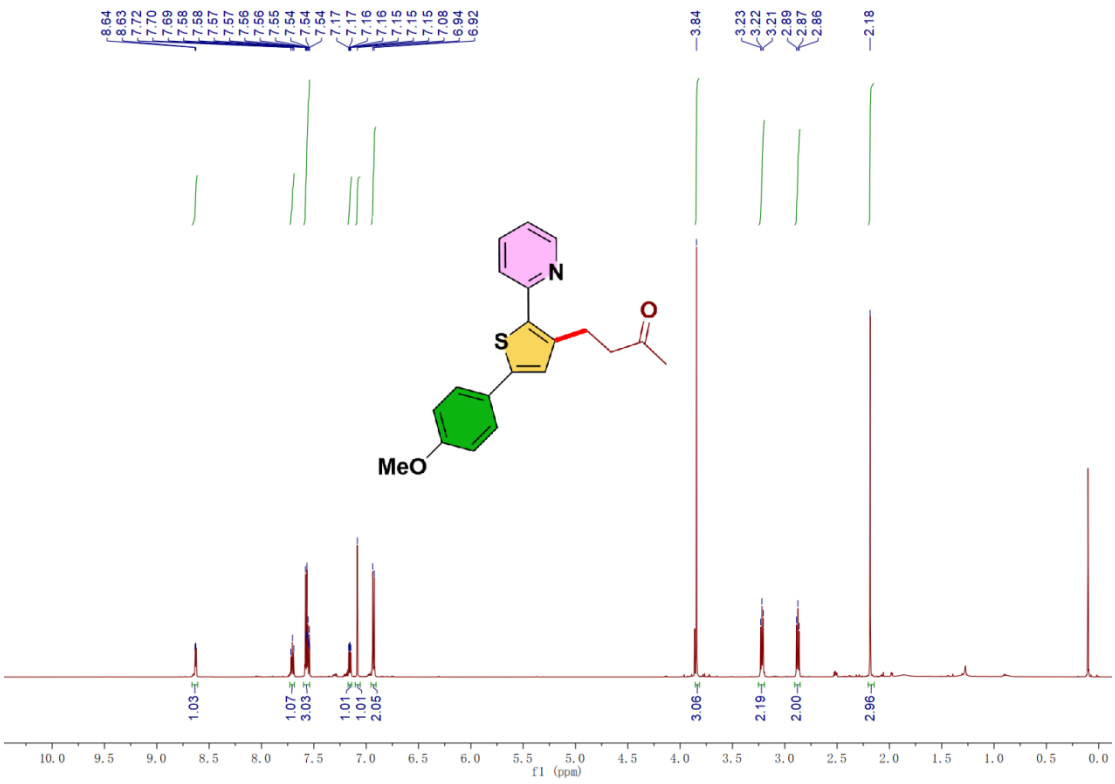
6 | ^{1}H NMR ($CDCl_3$, 600 MHz)



6 | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)

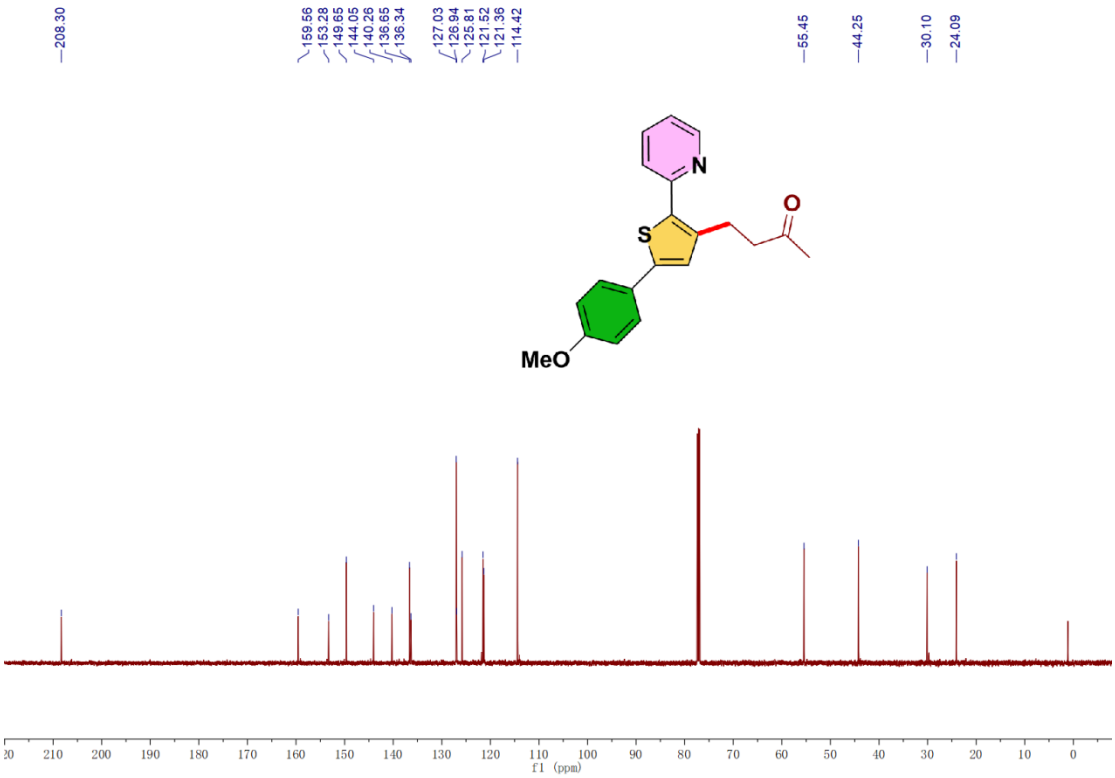


7 | ^{1}H NMR ($CDCl_3$, 600 MHz)

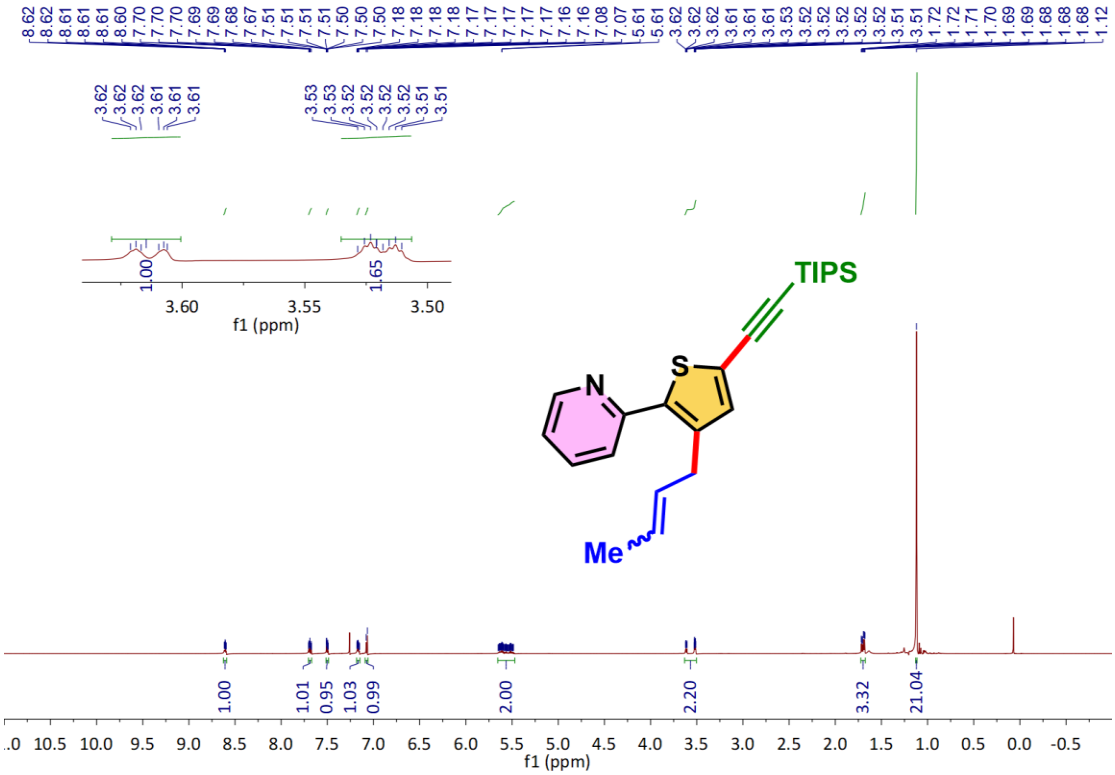


7 | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)

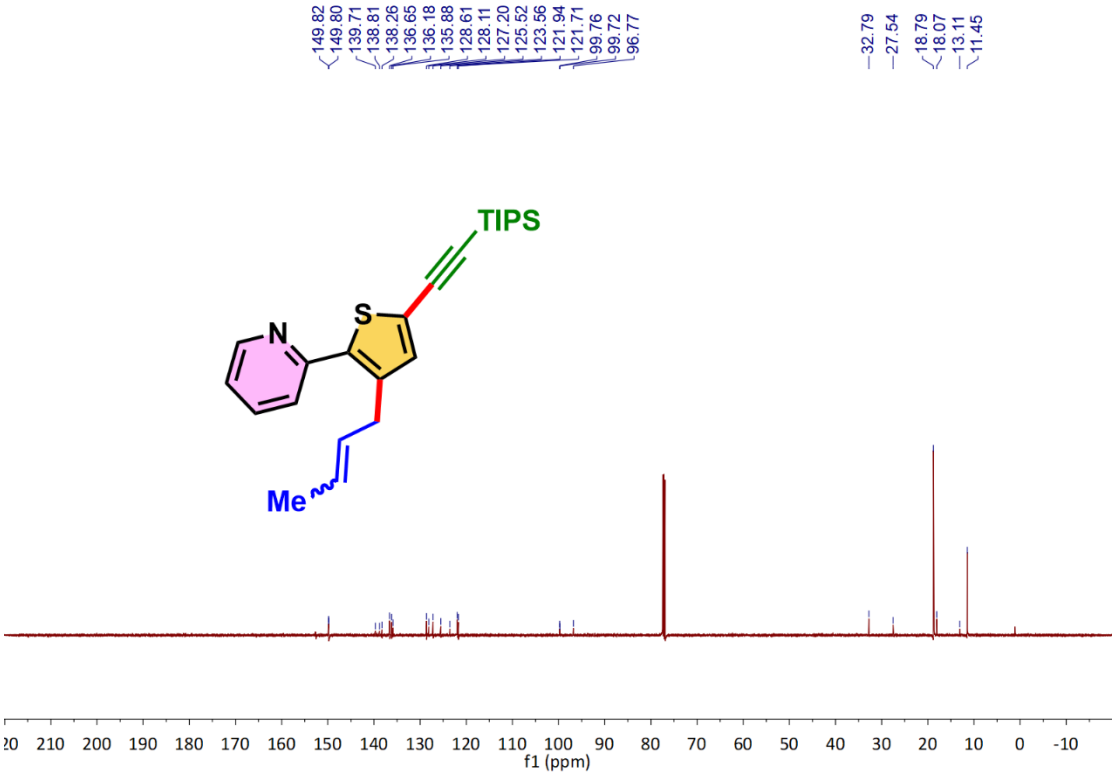
)



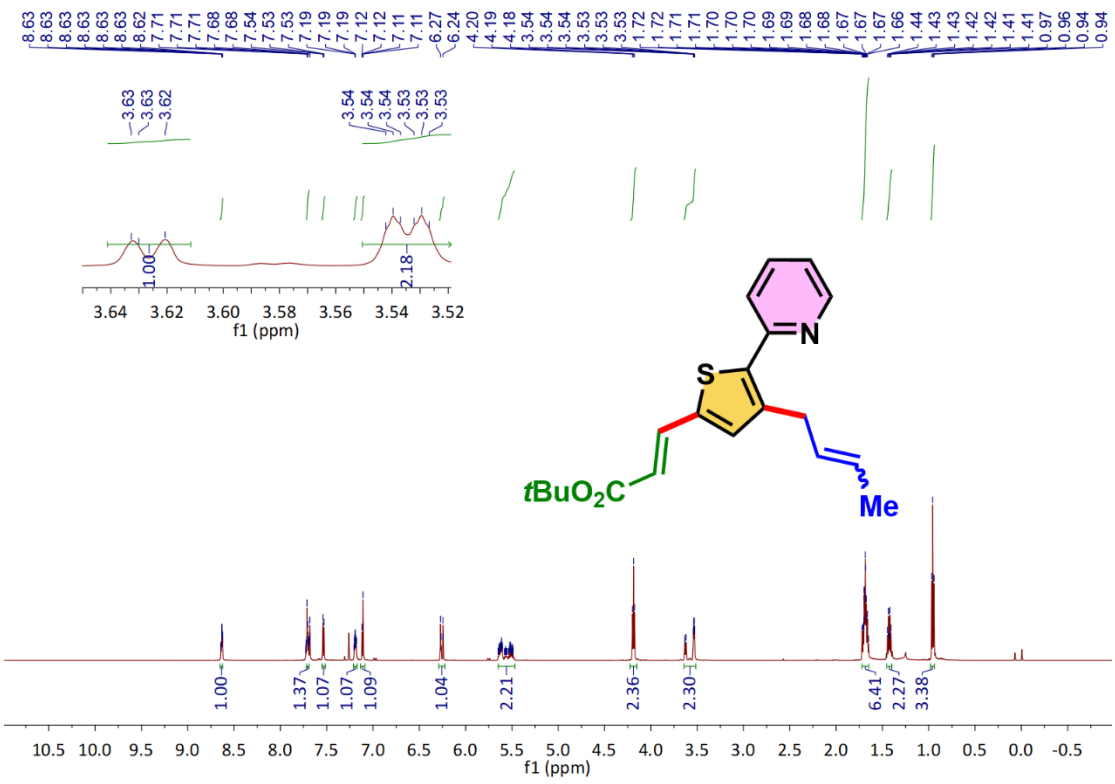
8 | ^{1}H NMR ($CDCl_3$, 600 MHz)



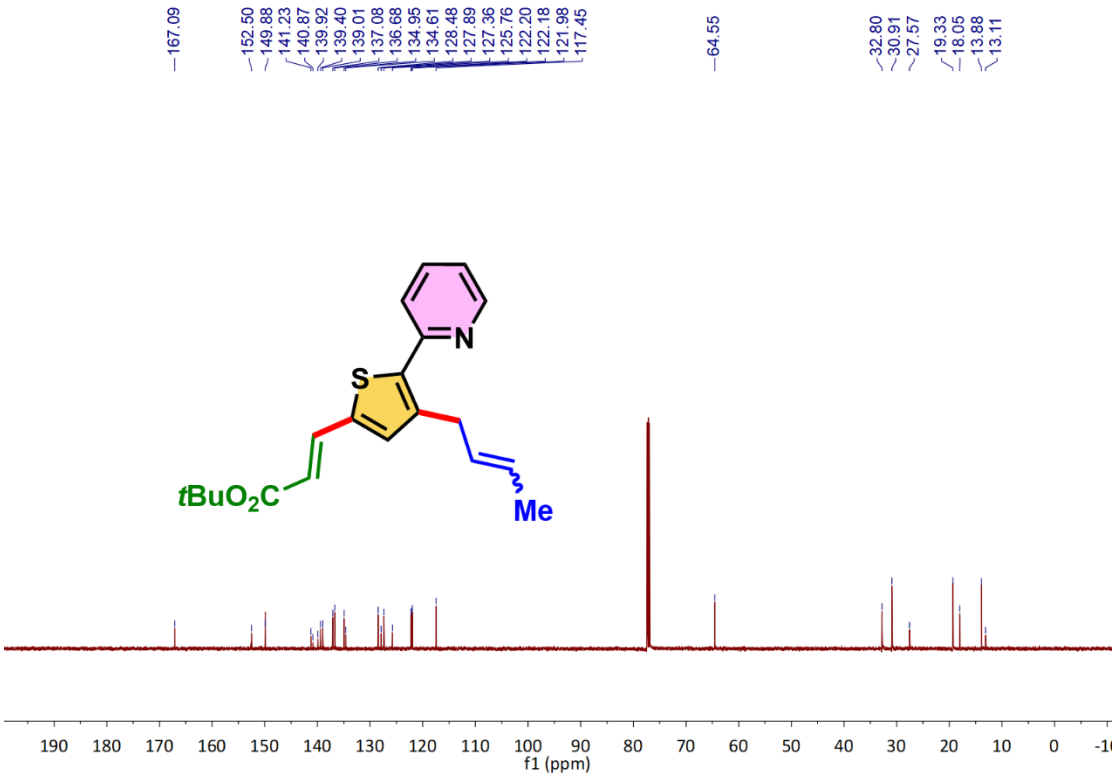
8 | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



9 | ^{1}H NMR ($CDCl_3$, 600 MHz)



9 | $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 151 MHz)



5. References

1. Gao, D.; Wang, F.; Liu, X. Y.; Feng, K. R.; Zhao, J. Y.; Wang, Y. H.; Yang, X. D.; Tian, P.; Lin, G. Q. Synthesis of Decahydrocyclobuta [cd] indene Skeletons: Rhodium(III)–Catalyzed Hydroarylation and Relay Thiophene–Promoted Intramolecular [2+ 2] Cycloaddition. *Adv. Synth. Catal.* **2020,** *362*, 4384-4390.
2. Hwang, Y.; Baek, S. B.; Kim, D. and Chang, S. Chain Walking as a Strategy for Iridium-Catalyzed Migratory Amidation of Alkenyl Alcohols to Access α-Amino Ketones. *J. Am. Chem. Soc.* **2022**, *144*, 4277-4285.
3. Gui, Y.; Zhao, Y.; Li, X.; Liang, T.; Zhao, S.; Zhang, Z. Catalyst–Controlled Regiodivergent C–H Alkynylation of 2–Pyridylthiophenes. Adv. Synth. Catal. 2025, 367, e202400856.