Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Copper-Catalyzed Oxidative C–H/C–H Cross-Coupling of Benzamides and Thiophenes

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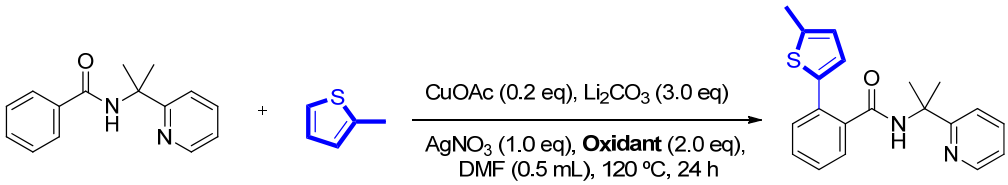
General Information: *N*,*N*-Dimethylformamide was dried by CaH_2, distilled under reduced pressure and stored under nitrogen. The other materials and solvents were purchased from Adamas and other commercial suppliers and used without additional purification. NMR spectra were recorded on a Bruke Avance operating for ^1H NMR at 400 MHz, and ^{13}C NMR at 100 MHz using TMS as internal standard. Chemical shifts were given relative to $CDCl_3$ (7.26 ppm for ^1H NMR, 77.16 ppm for ^{13}C NMR).The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet, br = broad. HRMS for new compounds were recorded on Mass Spectrometry Facilities, Zhejiang University. The substrates benzamides were synthesized from the corresponding carboxylic acids and $PIPNH_2$ according to the literature.[1]

Optimization of Reaction Conditions

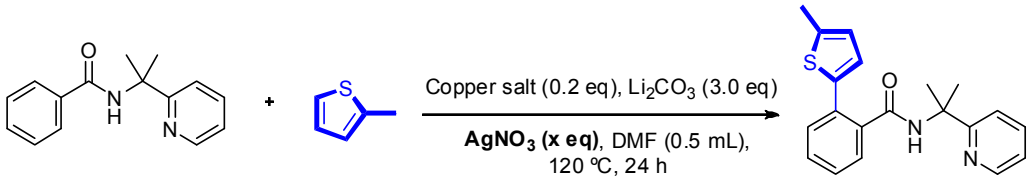
Table S1. Screening of Oxidant



Entry[a]	Oxidant	Yield[b]
1	O_2	trace
2	NMO	trace
3	BQ	N.D
4	BQ/O_2	trace
5	DDQ	N.D
6	$K_2S_2O_8$	N.D
7	$NaIO_3$	trace
8	$NaIO_4$	N.D
9	BPO	N.D

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), $AgNO_3$ (0.15 mmol), Li_2CO_3 (0.45 mmol), solvent (0.5 mL), N_2, 120 °C. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

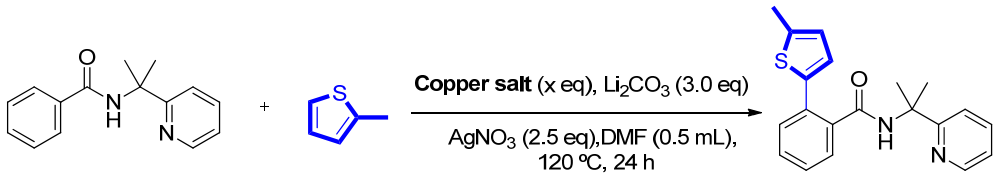
Table S2. Screening of Quantity of Ag salt



Entry[a]	$AgNO_3$	Yield[b]
1	2.0 eq	37 %
2	**2.5 eq**	**43 %**
3	3.0 eq	49 %

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), Li_2CO_3 (0.45 mmol), solvent (0.5 mL), N_2, 120 ºC. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

Table S3. Screening of Quantity of Copper salt



Entry[a]	CuOAc	Yield[b]
1	**0.2 eq**	**43 %**
2	0.5 eq	41 %
3	0.8 eq	36 %
4	1.0 eq	30 %
5	2.0 eq	trace

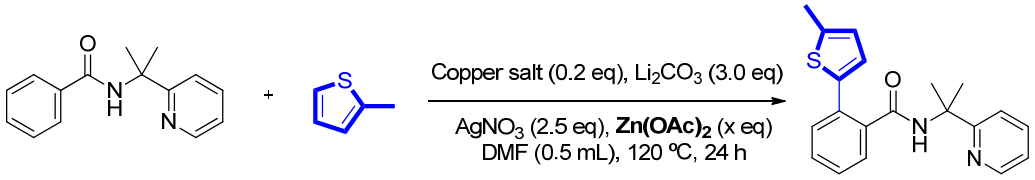
[a] The reactions were carried out **1** (0.15 mmol), 2-methyl-Thiophene (0.45 mmol), Li_2CO_3 (0.45 mmol), $AgNO_3$ (0.375 mmol), solvent (0.5 mL), N_2, 120 ºC. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

Table S4. Screening of Lewis acid

Entry[a]	Lewis acid	Yield[b]
1	**$Zn(OAc)_2$**	**51 %**
2	$ZnCl_2$	30 %
3	$Zn(OTf)_2$	43 %
4	$Cu(OTf)_2$	trace
5	$Fe(OH)_3$	trace
6	$Fe(acac)_3$	N.D
7	$Fe(ClO_4)_3$	trace
8	$Cd(OAc)_2$	trace

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), Li_2CO_3 (0.45 mmol), $AgNO_3$ (0.375 mmol), solvent (0.5 mL), N_2, 120 °C. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

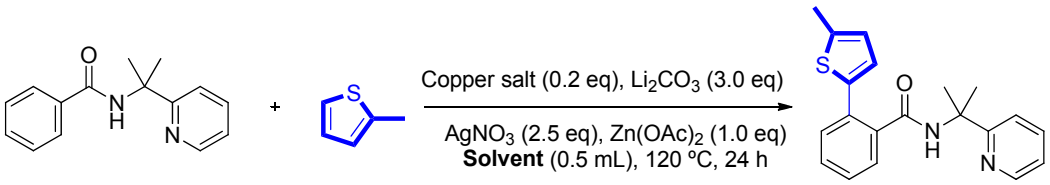
Table S5. Screening of Quantity of $Zn(OAc)_2$



Entry[a]	$Zn(OAc)_2$	Yield[b]
1	0.2 eq	34 %
2	**1.0 eq**	**61 %**
3	2.0 eq	30 %

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), $AgNO_3$ (0.15 mmol), solvent (0.5 mL), N_2, 120 °C. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

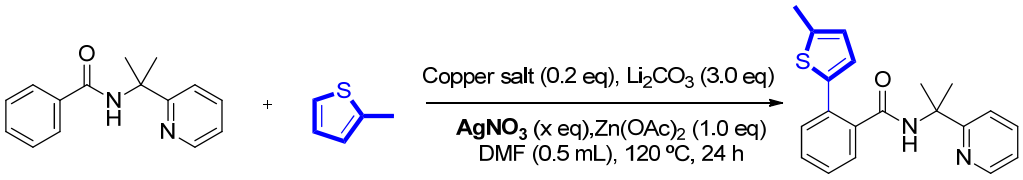
Table S6. Screening of Solvent



Entry[a]	Solvent	Yield[b]
1	DMAC	41%
2	THF	40%
3	DMSO	45%
4	toluene	N.R
5	CH_3CN	trace
6	t-AmOH	48%
7	DCE	trace
8	MeOH	28%
9	EtOH	30%
10	t-AmCN	trace
11	dioxane	48%
12	Actone	N.R

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), $Zn(OAc)_2$ (0.15 mmol), $AgNO_3$ (0.15 mmol), solvent (0.5 mL), N_2, 120 °C. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

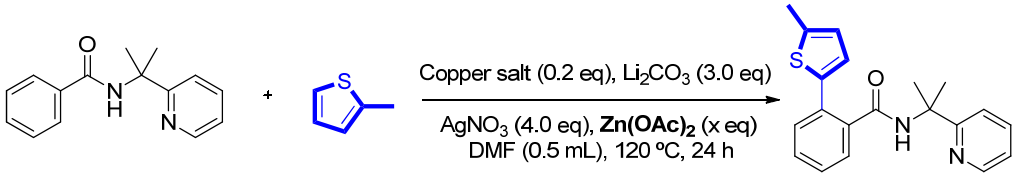
Table S7. Screening of Quantity of Silver



Entry[a]	$AgNO_3$ (x eq)	Yield[b]
1	2.5 eq	61%
2	3.0 eq	66%
3	**4.0 eq**	**75%**

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), $Zn(OAc)_2$ (0.15 mmol), solvent (0.5 mL), N_2, 120 °C. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

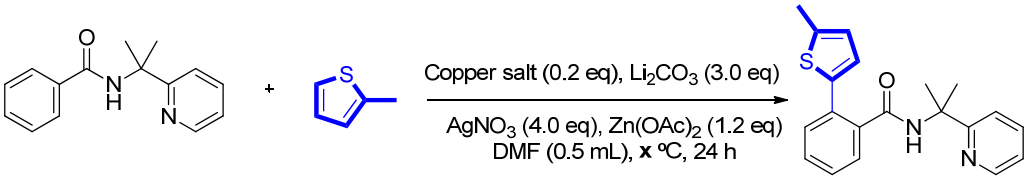
Table S8. Screening of Quantity of $Zn(OAc)_2$



Entry[a]	$Zn(OAc)_2$ (x eq)	Yield[b]
1	0.8 eq	69%
2	1.0 eq	75%
3	**1.2 eq**	**78%**
4	1.5 eq	60%

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), $AgNO_3$ (0.6 mmol), solvent (0.5 mL), N_2, 120 °C. [b] Yield determined by ^1H NMR using CH_2Br_2 as the internal standard.

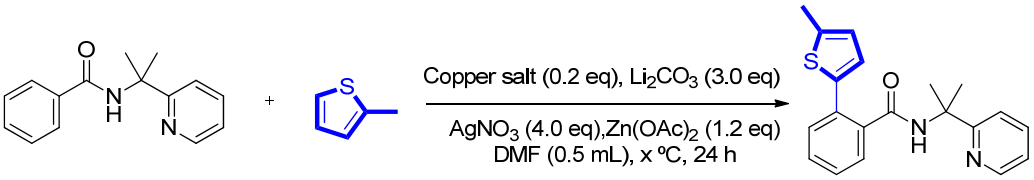
Table S9. Screening of Temperature



Entry[a]	Temperature	Yield[b]
1	100 ºC	68%
2	**120 ºC**	**78%**
3	140 ºC	67%

[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), $Zn(OAc)_2$ (0.18 mmol), $AgNO_3$ (0.6 mmol), solvent (0.5 mL), N_2. [b] Yield determined by 1H NMR using CH_2Br_2 as the internal standard.

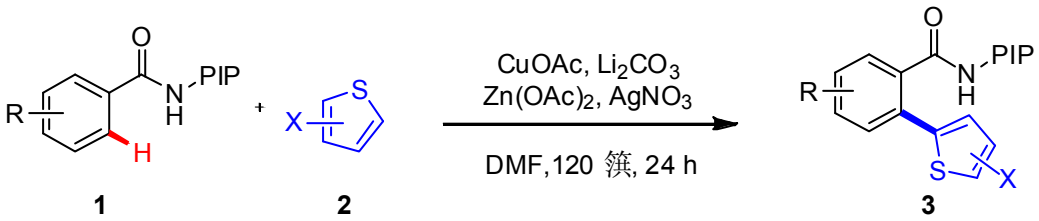
Table S10. Screening of Quantity of Thiophene



Entry[a]	2-methyl-Thiophene	Yield[b]
1	**3.0 eq**	**78%(78%)[c]**
2	2.0 eq	57%
3	1.5 eq	40%

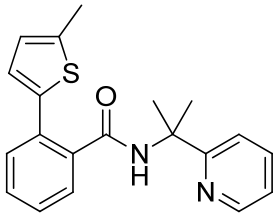
[a] The reactions were carried out **1** (0.15 mmol), CuOAc (0.03 mmol), 2-methyl-Thiophene (0.45 mmol), $Zn(OAc)_2$ (0.18 mmol), $AgNO_3$ (0.6 mmol), solvent (0.5 mL), N_2, 120 ºC. [b] Yield determined by ^{1}H NMR using CH_2Br_2 as the internal standard. [c] Isolated yield in parentheses.

General Procedure for Oxidation C–H/C–H Cross-Coupling



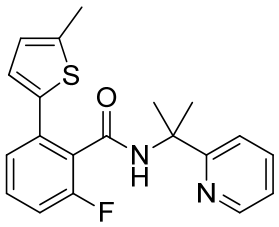
To a 50 mL sealed tube was added substrate (0.15 mmol), CuOAc (3.7 mg, 0.03 mmol), Thiophene (0.45 mmol), Li_2CO_3 (33.3 mg, 0.45 mmol), $Zn(OAc)_2$ (33.0 mg, 0.375 mmol), $AgNO_3$ (101.9 mg, 0.6 mmol) and DMF (0.5 mL). The mixture was then put into pre-heated 120 ^oC oil bath under N_2 for 24 hours. Then the reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane (3×10 mL). The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, the resulting residue was purified by flash chromatography to afford the product.

2-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 3a



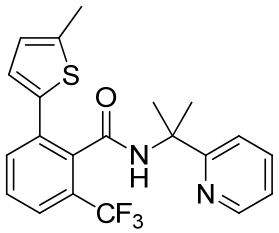
The title compound **3a** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : DCM : EtOAc = 4 : 1 : 1 gave **3a** as a yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, J = 4.8 Hz, 1H), 7.73 (brs, 1H), 7.69 - 7.61 (m, 2H), 7.46 - 7.32 (m, 4H), 7.13 (dd, J = 7.6, 5.2 Hz, 1H), 6.98 (d, J = 3.6 Hz, 1H), 6.64 (d, J = 2.4 Hz, 1H), 2.44 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.62, 164.34, 147.65, 140.67, 139.03, 137.47, 137.00, 132.40, 130.53, 129.57, 128.63, 127.69, 127.18, 125.74, 121.79, 119.42, 57.18, 27.20, 15.37; HRMS (EI-TOF) calcd for $C_{20}H_{20}N_2OS$ (M^+): 336.1296, found: 336.1296.

2-fluoro-6-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 3b



The title compound **3b** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3b** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (d, J = 4.0 Hz, 1H), 7.99 (s, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.40 – 7.27 (m, 3H), 7.18 – 7.11 (m, 2H), 7.04 (t, J = 8.4 Hz, 1H), 6.65 (s, 1H), 2.45 (s, 3H), 1.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.09, 164.07, 159.82 (d, $J_{C\text{-}F}$ = 245.8 Hz), 147.61, 141.01, 137.65 (d, $J_{C\text{-}F}$ = 2.7 Hz), 137.17, 134.56 (d, $J_{C\text{-}F}$ = 4.3 Hz), 130.12 (d, $J_{C\text{-}F}$ = 8.9 Hz), 127.42, 126.01, 125.62 (d, $J_{C\text{-}F}$ = 19.4 Hz), 125.42 (d, $J_{C\text{-}F}$ = 3.0 Hz), 121.95, 119.53, 114.58 (d, $J_{C\text{-}F}$ = 22.0 Hz), 57.53, 27.33, 15.41. HRMS (EI-TOF) calcd for $C_{20}H_{19}FN_2OS$ (M^+): 354.1202, found: 354.1201.

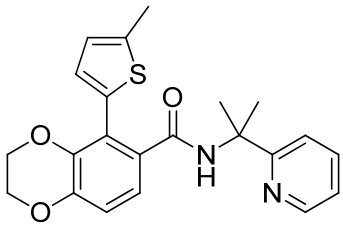
2-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)-6-(trifluoromethyl) benzamide 3c



The title compound **3c** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3c** as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (d, J = 4.4 Hz, 1H), 8.13 (s, 1H), 7.69 – 7.61 (m, 3H), 7.48 (t, J = 8.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.16 – 7.11 (m, 1H), 7.09 (d, J = 3.6 Hz, 1H), 6.63 (d, J = 2.4 Hz, 1H), 2.43 (s, 3H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.46, 164.09, 147.39, 141.11, 137.17, 136.00, 134.36, 134.22, 128.68, 128.31, 128.12 (q, $J_{C\text{-}F}$ = 30.5 Hz), 125.77, 125.30 (q, $J_{C\text{-}F}$ = 5.1 Hz), 123.92 (q, $J_{C\text{-}F}$ = 272.9 Hz), 121.92, 119.51, 57.34, 26.78, 15.34. HRMS (EI-TOF) calcd for

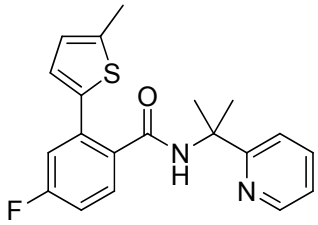
$C_{21}H_{19}F_3N_2OS$ (M^+): 404.1170, found: 404.1174.

5-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)-2,3- dihydrobenzo [b] [1,4]dioxine-6-carboxamide 3d



The title compound **3d** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3d** as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.43 (d, *J* = 4.4 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.29 – 7.21 (m, 3H), 7.12 (dd, *J* = 6.4, 4.8 Hz, 1H), 6.93 – 6.88 (m, 2H), 6.67 (d, *J* = 2.4 Hz, 1H), 4.27 (s, 4H), 2.43 (s, 3H), 1.59 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.57, 164.58, 147.80, 144.91, 141.42, 136.79, 132.94, 132.39, 128.97, 125.28, 121.88, 121.69, 121.64, 119.38, 117.22, 64.69, 64.26, 57.18, 27.21, 15.39. HRMS (EI-TOF) calcd for $C_{22}H_{22}N_2O_3S$ (M^+): 394.1351, found: 394.1352.

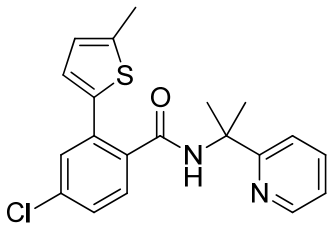
4-fluoro-2-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 3e



The title compound **3e** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3e** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 4.0 Hz, 1H), 7.78 (s, 1H), 7.67 (t, *J* = 7.2 Hz, 1H), 7.61 (dd, *J* = 8.4, 6.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.17 – 7.11 (m, 2H), 7.06 – 6.99 (m, 2H), 6.64 (s, 1H), 2.44 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 164.3, 162.9 (d, $J_{C\text{-}F}$ = 248.0 Hz), 147.6, 141.4, 137.8 (d, $J_{C\text{-}F}$ = 1.8 Hz), 137.1, 134.9 (d, $J_{C\text{-}F}$ = 8.7 Hz), 133.7 (d, $J_{C\text{-}F}$ = 3.2 Hz), 130.9 (d, $J_{C\text{-}F}$ = 8.9 Hz), 127.7, 125.9, 121.9, 119.4, 117.1 (d, $J_{C\text{-}F}$ = 22.2 Hz), 114.5 (d, $J_{C\text{-}F}$ = 21.3 Hz), 57.2, 27.2, 15.4. HRMS (EI-TOF) calcd for $C_{20}H_{19}FN_2OS$ (M^+): 354.1202, found:

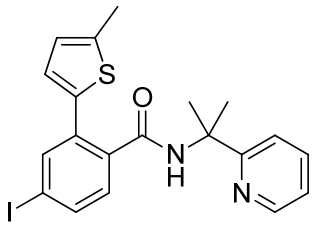
354.1202.

4-chloro-2-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 3f



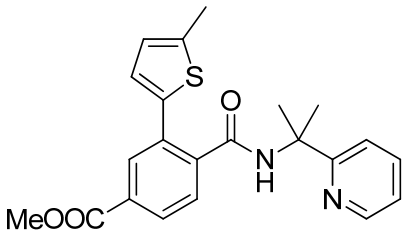
The title compound **3f** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3f** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 4.0 Hz, 1H), 7.84 (s, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.43 (s, 1H), 7.35 – 7.30 (m, 2H), 7.16 – 7.12 (m, 1H), 6.99 (d, *J* = 2.8 Hz, 1H), 6.63 (s, 1H), 2.44 (s, 3H), 1.73 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.62, 164.19, 147.60, 141.46, 137.51, 137.11, 135.85, 135.32, 134.23, 130.28, 130.11, 127.77, 127.67, 125.90, 121.89, 119.43, 57.20, 27.16, 15.40. HRMS (EI-TOF) calcd for $C_{20}H_{19}ClN_2OS$ (M^+): 370.0907, found: 370.0905.

4-iodo-2-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 3g



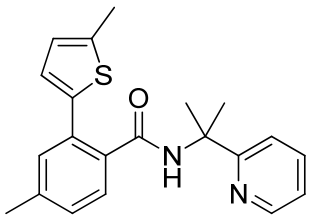
The title compound **3g** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3g** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 4.0 Hz, 1H), 7.85 (s, 1H), 7.80 (d, *J* = 1.6 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.35 – 7.31 (m, 2H), 7.14 (dd, *J* = 6.4, 4.8 Hz, 1H), 6.98 (d, *J* = 3.6 Hz, 1H), 6.63 (d, *J* = 2.4 Hz, 1H), 2.43 (s, 3H), 1.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.76, 164.16, 147.59, 141.46, 139.07, 137.24, 137.10, 136.92, 136.59, 134.38, 130.17, 127.76, 125.87, 121.89, 119.41, 95.50, 57.20, 27.15, 15.40. HRMS (EI-TOF) calcd for $C_{20}H_{19}IN_2OS$ (M^+): 462.0263, found: 462.0267.

methyl 3-(5-methylthiophen-2-yl) - 4 - ((2-(pyridin-2-yl) propan-2-yl)carbamoyl) benzoate 3h



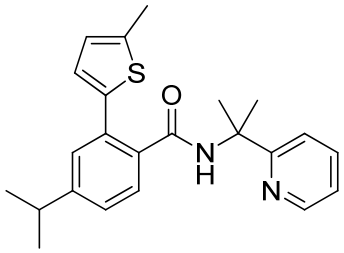
The title compound **3h** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3h** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 4.0 Hz, 1H), 8.12 (s, 1H), 8.00 (d, *J* = 8.0 Hz), 7.92 (s, 1H), 7.70 – 7.64 (m, 2H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.15 (t, *J* = 6.0 Hz, 1H), 7.03 (d, *J* = 2.8 Hz, 1H), 6.64 (d, *J* = 2.4 Hz, 1H), 3.94 (s, 3H), 2.44 (s, 3H), 1.75 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.87, 166.45, 164.11, 147.59, 141.31, 141.27, 137.93, 137.17, 132.76, 131.67, 131.11, 128.78, 128.61, 127.67, 125.89, 121.95, 119.44, 57.28, 52.48, 27.18, 15.42. HRMS (EI-TOF) calcd for $C_{22}H_{22}N_2O_3S$ (M^+): 394.1351, found: 394.1350.

4-methyl-2-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 3i



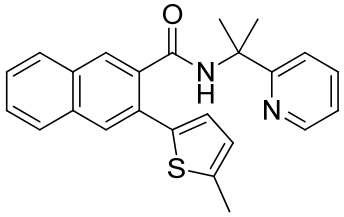
The title compound **3i** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3i** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 3.6 Hz, 1H), 7.68 – 7.60 (m, 2H), 7.54 (d, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.24 (s, 1H), 7.18 – 7.10 (m, 2H), 6.95 (d, *J* = 2.8 Hz, 1H), 6.63 (s, 1H), 2.44 (s, 3H), 2.38 (s, 3H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.56, 164.49, 147.68, 140.53, 139.65, 139.26, 136.93, 134.76, 132.35, 131.23, 128.83, 128.47, 127.14, 125.69, 121.73, 119.43, 57.16, 27.24, 21.34, 15.39. HRMS (EI-TOF) calcd for $C_{21}H_{22}N_2OS$ (M^+): 350.1453, found: 350.1451.

4-isopropyl-2-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamid 3j



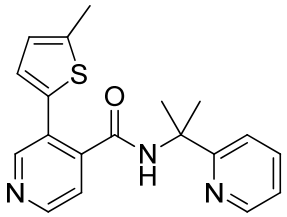
The title compound **3j** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3j** as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 4.4 Hz, 1H), 7.68 – 7.56 (m, 3H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.27 (s, 1H), 7.22 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.12 (dd, *J* = 7.2, 5.2 Hz, 1H), 6.96 (d, *J* = 3.6 Hz, 1H), 6.64 (d, *J* = 2.4 Hz, 1H), 2.97 – 2.90 (m, 1H), 2.45 (s, 3H), 1.71 (s, 6H), 1.27 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.58, 164.50, 150.59, 147.69, 140.52, 139.51, 136.93, 135.10, 132.42, 128.89, 128.82, 127.12, 125.95, 125.69, 121.73, 119.43, 57.19, 34.09, 27.26, 23.94, 15.40. HRMS (EI-TOF) calcd for $C_{23}H_{26}N_2OS$ (M^+): 378.1766, found: 378.1764.

3-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)-2-naphthamide 3k



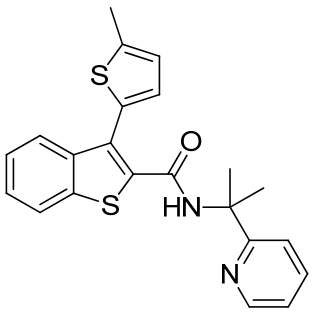
The title compound **3k** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3k** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 4.4 Hz, 1H), 8.12 (s, 1H), 7.92 – 7.82 (m, 4H), 7.68 (t, *J* = 7.2 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.17 – 7.12 (m, 1H), 7.06 (d, *J* = 3.2 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 2.47 (s, 3H), 1.79 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.53, 164.41, 147.71, 140.62, 139.28, 137.05, 135.70, 133.59, 132.19, 130.02, 129.54, 128.52, 128.31, 127.86, 127.50, 127.34, 126.81, 125.88, 121.85, 119.49, 57.31, 27.31, 15.46. HRMS (EI-TOF) calcd for $C_{24}H_{22}N_2OS$ (M^+): 386.1453, found: 386.1456.

3-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)isonicotinamide 3l



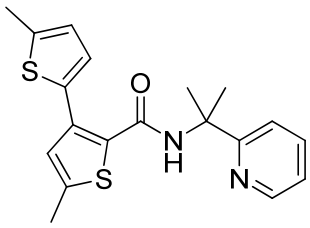
The title compound **3l** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 3 : 1 gave **3l** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (s, 1H), 8.60 (d, *J* = 4.4 Hz, 1H), 8.38 (d, *J* = 4.0 Hz, 1H), 8.15 (s, 1H), 7.70 (t, *J* = 7.2 Hz, 1H), 7.48 (d, *J* = 5.2 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.19 – 7.14 (m, 1H), 7.07 (d, *J* = 2.8 Hz, 1H), 6.69 (s, 1H), 2.46 (s, 3H), 1.77 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.31, 163.81, 150.96, 148.94, 147.53, 143.62, 142.07, 137.28, 134.79, 128.35, 127.69, 126.14, 122.14, 122.06, 119.42, 57.35, 27.16, 15.43. HRMS (EI-TOF) calcd for $C_{19}H_{19}N_3OS$ (M^+): 337.1249, found: 337.1246.

3-(5-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzo[b]thiophene-2-carboxamide 3m



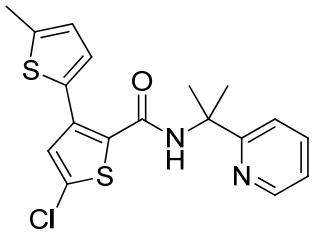
The title compound **3m** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **3m** as a red solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.32 (d, *J* = 4.4 Hz, 1H), 8.11 (s, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.68 – 7.61 (m, 2H), 7.44 – 7.31 (m, 3H), 7.12 (dd, *J* = 6.4, 4.8 Hz, 1H), 7.06 (d, *J* = 3.6 Hz, 1H), 6.87 (d, *J* = 2.4 Hz, 1H), 2.54 (s, 3H), 1.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.27, 161.43, 147.67, 142.64, 141.26, 139.98, 139.27, 136.94, 131.10, 129.84, 129.03, 126.31, 125.99, 124.82, 124.55, 122.55, 121.69, 119.37, 57.73, 27.51, 15.57. HRMS (EI-TOF) calcd for $C_{22}H_{20}N_2OS_2$ (M^+): 392.1017, found: 392.1020.

5,5'-dimethyl-*N*-(2-(pyridin-2-yl)propan-2-yl)-[2,3'-bithiophene]-2'-carboxamide 3n



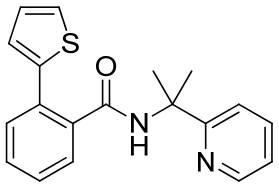
The title compound **3n** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3n** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.31 (d, *J* = 4.4 Hz, 1H), 7.92 (s, 1H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.10 (dd, *J* = 6.4, 4.8 Hz, 1H), 7.03 (d, *J* = 3.2 Hz, 1H), 6.72 (s, 1H), 6.70 (d, *J* = 2.4 Hz, 1H), 2.48 (s, 3H), 2.46 (s, 3H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.47, 161.37, 147.71, 142.41, 141.31, 136.87, 134.50, 134.13, 134.06, 129.98, 128.22, 125.69, 121.62, 119.39, 57.43, 27.64, 15.57, 15.43. HRMS (EI-TOF) calcd for $C_{19}H_{20}N_2OS_2$ (M^+): 356.1017, found: 356.1020.

5'-chloro-5-methyl-*N*-(2-(pyridin-2-yl)propan-2-yl)-[2,3'-bithiophene]-2'-carboxamide 3o



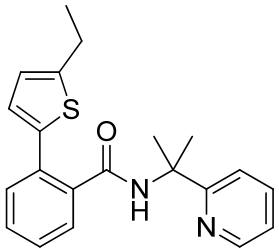
The title compound **3o** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 4 : 1 gave **3o** as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 4.4 Hz, 1H), 8.46 (s, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.11 (dd, *J* = 6.8, 4.8 Hz, 1H), 7.04 (d, *J* = 3.6 Hz, 1H), 6.87 (s, 1H), 6.72 (d, *J* = 2.4 Hz, 1H), 2.49 (s, 3H), 1.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.13, 160.30, 147.57, 142.11, 137.02, 135.99, 133.55, 133.21, 132.55, 130.51, 128.89, 125.87, 121.76, 119.37, 57.57, 27.52, 15.46. HRMS (EI-TOF) calcd for $C_{18}H_{17}ClN_2OS_2$ (M^+): 376.0471, found: 376.0475.

***N*-(2-(pyridin-2-yl)propan-2-yl)-2-(thiophen-2-yl)benzamide 4a**



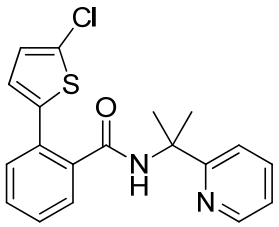
The title compound **4a** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4a** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (d, *J* = 4.0 Hz, 1H), 7.73 (brs, 1H), 7.68 – 7.61 (m, 2H), 7.50 – 7.36 (m, 3H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.27 (d, *J* = 5.2 Hz, 1H), 7.20 (d, *J* = 3.2 Hz, 1H), 7.12 (dd, *J* = 7.2, 5.6 Hz, 1H), 7.01 – 6.96 (m, 1H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.44, 164.26, 147.61, 141.47, 137.85, 137.01, 132.06, 130.77, 129.58, 128.62, 128.05, 127.45, 127.31, 126.02, 121.80, 119.38, 57.13, 27.17; HRMS (EI-TOF) calcd for $C_{19}H_{18}N_2OS$ (M^+): 322.1140, found: 322.1143.

2-(5-ethylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4b



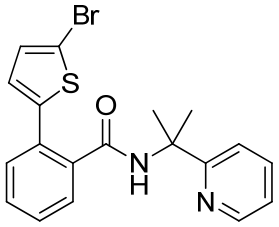
The title compound **4b** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4b** as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (d, *J* = 4.0 Hz, 1H), 7.68 – 7.62 (m, 3H), 7.46 – 7.31 (m, 4H), 7.12 (dd, *J* = 6.4, 4.8 Hz, 1H), 6.99 (d, *J* = 3.2 Hz, 1H), 6.67 (d, *J* = 3.2 Hz, 1H), 2.79 (q, *J* = 7.6 Hz, 2H), 1.72 (s, 6H), 1.24 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.54, 164.42, 148.49, 147.69, 138.69, 137.55, 136.97, 132.53, 130.59, 129.58, 128.72, 127.75, 127.01, 123.87, 121.76, 119.40, 57.20, 27.22, 23.57, 16.10. HRMS (EI-TOF) calcd for $C_{21}H_{22}N_2OS$ (M^+): 350.1453, found: 350.1456.

2-(5-chlorothiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4c



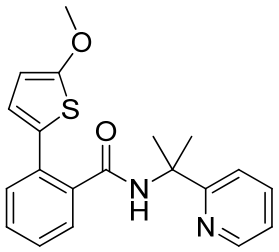
The title compound **4c** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4c** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (dd, *J* = 4.8, 0.8 Hz, 1H), 7.98 (brs, 1H), 7.68 (td, *J* = 8.0, 1.6 Hz, 1H), 7.64 – 7.60 (m, 1H), 7.45 – 7.37 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.15 (ddd, *J* = 7.6, 5.2, 0.8 Hz, 1H), 6.96 (d, *J* = 4.0 Hz, 1H), 6.78 (d, *J* = 4.0 Hz, 1H), 1.76 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.26, 164.10, 147.57, 140.14, 137.81, 137.19, 131.24, 130.50, 130.24, 129.72, 128.65, 128.40, 126.55, 126.53, 121.98, 119.44, 57.16, 27.17; HRMS (EI-TOF) calcd for $C_{19}H_{17}ClN_2OS$ (M^+): 356.0750, found: 356.0751.

5'-bromo-*N*-(2-(pyridin-2-yl)propan-2-yl)-[2,3'-bithiophene]-2'-carboxamide 4d



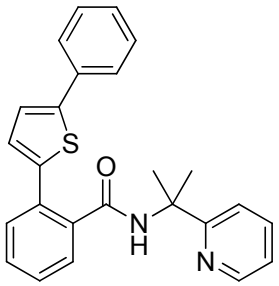
The title compound **4d** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4d** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 4.8 Hz, 1H), 7.96 (brs, 1H), 7.69 (td, *J* = 8.0, 1.6 Hz, 1H), 7.63 (d, *J* = 6.4 Hz, 1H), 7.44 - 7.37 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.16 (dd, *J* = 7.6, 5.2 Hz, 1H), 6.95 (d, *J* = 4.0 Hz, 1H), 6.92 (d, *J* = 3.6 Hz, 1H)，1.75 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.23, 164.12, 147.60, 143.11, 137.80, 137.18, 131.23, 130.51, 130.29, 129.74, 128.67, 128.46, 127.54, 121.97, 119.44, 112.49, 77.48, 77.16, 76.84, 57.18, 27.17; MS (MALDI-TOF) calcd for $C_{17}H_{15}BrN_2OS_2$ ($M+H^+$): 401.032, found:401.032.

2-(5-methoxythiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4e



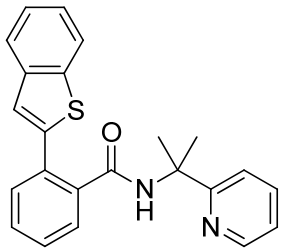
The title compound **4e** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4e** as a brown liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (d, *J* = 4.0 Hz, 1H), 7.82 (s, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 7.2 Hz, 1H), 7.42 – 7.30 (m, 4H), 7.14 (t, *J* = 6.4 Hz, 1H), 6.83 (d, *J* = 3.6 Hz, 1H), 6.10 (d, *J* = 3.6 Hz, 1H), 3.83 (s, 3H), 1.76 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.67, 167.08, 164.33, 147.66, 137.49, 137.03, 132.28, 130.35, 129.59, 128.68, 127.47, 127.31, 124.88, 121.82, 119.42, 104.53, 60.33, 57.17, 27.26. HRMS (EI-TOF) calcd for $C_{20}H_{20}N_2O_2S$ (M^+): 352.1245, found: 352.1242.

2-(5-phenylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4f



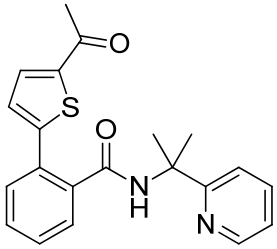
The title compound **4f** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4f** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 4.0 Hz, 1H), 7.87 (brs, 1H), 7.67 - 7.58 (m, 2H), 7.57 - 7.50 (m, 3H), 7.45 - 7.40 (m, 1H), 7.38 - 7.30 (m, 4H), 7.28 - 7.24 (m, 1H), 7.20 - 7.16 (m, 2H), 7.07 (dd, *J* = 6.4, 5.2 Hz, 1H), 1.75 (s, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 168.52, 164.23, 147.63, 145.00, 140.89, 137.67, 137.03, 134.39, 131.95, 130.49, 129.67, 129.00, 128.70, 128.27, 128. 09, 127.61, 125.79, 123.56, 121.83, 119.39, 57.21, 27.21; HRMS (EI-TOF) calcd for $C_{25}H_{22}N_2OS$ (M^+): 398.1453, found: 398.1471.

2-(benzo[b]thiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4g



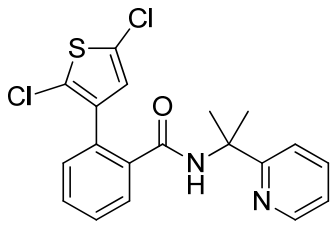
The title compound **4g** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4g** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 4.8 Hz, 1H), 7.86 (brs, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.71 - 7.66(m, 2H), 7.58 - 7.40 (m, 5H), 7.33 - 7.24 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.03 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 1.69 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.37, 164.05, 147.54, 141.62, 140.41, 140.39, 138.03, 136.96, 132.01, 130.82, 129.67, 128.68, 128.56, 124.48, 124.34, 124.01, 123.73, 122.09, 121.76, 119.28, 57.22, 27.13; HRMS (EI-TOF) calcd for $C_{23}H_{20}N_2OS$ (M^+): 372.1296, found: 372.1314.

2-(5-acetylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4h



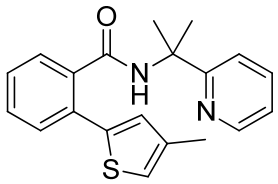
The title compound **4h** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4h** as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 4.0 Hz, 1H), 8.09 (brs, 1H), 7.71 - 7.63 (m, 2H), 7.54 (d, *J* = 3.6 Hz, 1H), 7.50 - 7.44 (m, 3H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.22 (d, *J* = 4.0 Hz, 1H), 7.14 (ddd, *J* = 7.2, 4.8, 0.8 Hz, 1H), 2.49 (s, 3H), 1.76 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.73, 168.13, 164.04, 150.47, 147.54, 144.41, 137.99, 137.24, 132.77, 131.29, 130.57, 129.87, 129.10, 128.64, 128.21, 122.02, 119.43, 57.19, 27.15, 26.76; HRMS (EI-TOF) calcd for $C_{21}H_{20}N_2O_2S$ (M^+): 364.1245, found: 364.1252.

2-(2,5-dichlorothiophen-3-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4i



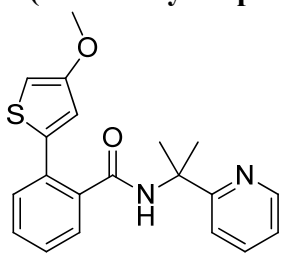
The title compound **4i** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4i** as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.41 (d, *J* = 4.4 Hz, 1H), 8.12 (s, 1H), 7.79 (d, *J* = 7.6 Hz, 1H), 7.69 (t, *J* = 7.6 Hz, 1H), 7.42 – 7.50 (m, 2H), 7.31 – 7.38 (m, 2H), 7.16 (dd, *J* = 6.8, 5.2 Hz), 6.84 (s, 1H), 1.74 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) 167.32, 164.17, 147.45, 138.06, 137.58, 137.28, 130.93, 130.66, 129.92, 129.07, 128.83, 128.47, 126.24, 123.70, 121.96, 119.35, 56.96, 27.07. HRMS (ESI) calcd for $C_{19}H_{17}Cl_2N_2OS$ ($M+H^+$): 391.0433, found: 391.0442.

2-(4-methylthiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4j



The title compound **4j** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4j** as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 4.4 Hz, 1H), 7.71 - 7.61 (m, 3H), 7.48 - 7.31 (m, 4H), 7.13 (dd, *J* = 7.2, 4.8 Hz, 1H), 7.03 (s, 1H), 6.85 (s, 1H), 2.19 (s, 3H), 1.72 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.58, 164.29, 147.65, 141.16, 138.09, 137.66, 137.02, 132.28, 130.47, 129.68, 129.57, 128.57, 127.92 121.81, 121.32 , 119.37, 57.16 , 27.15, 15.81. HRMS (EI-TOF) calcd for $C_{20}H_{20}N_2OS$ (M^+): 336.1296, found: 336.1301.

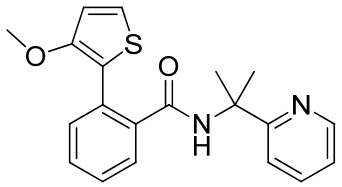
2-(4-methoxythiophen-2-yl)-*N*-(2-(pyridin-2-yl)propan-2-yl)benzamide 4ka



The title compound **4ka** was prepared according to General procedure. A purification

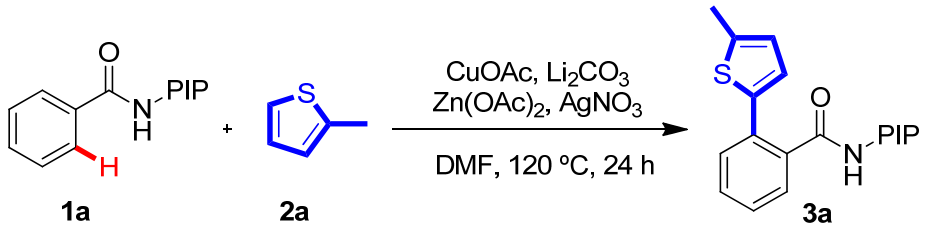
by flash chromatography in petroleum ether : actone = 5 : 1 gave **4ka** as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 4.8 Hz, 1H), 7.81 (s, 1H), 7.70 – 7.61 (m, 2H), 7.47 – 7.32 (m, 4H), 7.14 (dd, *J* = 7.2, 4.8 Hz, 1H), 6.91 (s, 1H), 6.20 (s, 1H), 3.73 (s, 3H), 1.75 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.32, 164.34, 158.32, 147.67, 140.34, 137.67, 137.05, 132.24, 130.31, 129.66, 128.67, 128.28, 121.82, 119.55, 119.42, 97.72, 77.48, 77.16, 76.84, 57.31, 57.23, 27.23. HRMS (EI-TOF) calcd for $C_{20}H_{20}N_2O_2S$ (M^+): 352.1245, found: 352.1242.

2-(3-methoxythiophen-2-yl)-N-(2-(pyridin-2-yl)propan-2-yl)benzamide 4kb



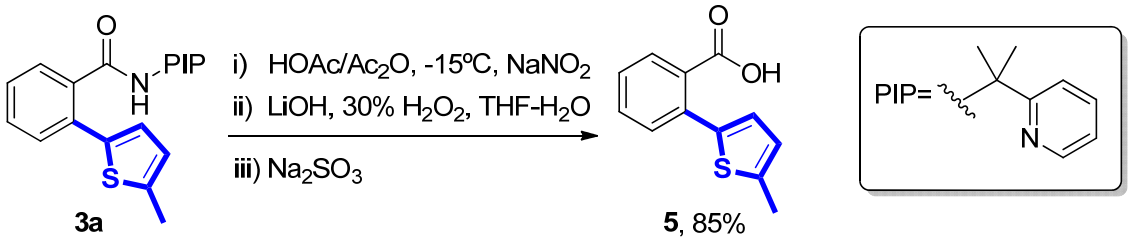
The title compound **4kb** was prepared according to General procedure. A purification by flash chromatography in petroleum ether : actone = 5 : 1 gave **4kb** as a yellow liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 4.0 Hz, 1H), 7.80 – 7.75 (m, 1H), 7.72 (s, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.46 – 7.37 (m, 3H), 7.30 – 7.26 (m, 1H), 7.21 (dd, *J* = 5.6, 1.2 Hz, 1H), 7.13 – 7.09 (m, 1H), 6.81 (dd, *J* = 5.6, 1.2 Hz, 1H), 3.77 (d, *J* = 1.2 Hz, 3H), 1.68 (d, *J* = 1.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.85, 164.64, 154.02, 147.73, 138.50, 136.88, 132.14, 129.75, 129.73, 129.23, 128.22, 123.88, 121.65, 119.38, 117.72, 116.35, 77.48, 77.16, 76.84, 58.76, 57.15, 27.38. HRMS (EI-TOF) calcd for $C_{20}H_{20}N_2O_2S$ (M^+): 352.1245, found: 352.1247.

Gram-Scale Synthesis of 3a



A mixture of **1** (1.08 g, 4.5 mmol), **2a** (1.32 mL, 13.5 mmol), CuOAc (0.111 g, 0.9 mmol), Li_2CO_3 (1.00 g, 13.5 mmol), $Zn(OAc)_2$ (0.90g, 5.4 mmol), $AgNO_3$ (3.06 g, 18.0 mmol) and DMF (15.0 mL) in a 100 mL round-bottom flask equipped with condenser was vigorously stirred at 120 ^oC under N_2 for 24 hours. The reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane (3×100 mL). The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, the resulting residue was purified by flash chromatography (petroleum ether : actone = 4 : 1) to give the desired product 3a (1.08g, 71%).

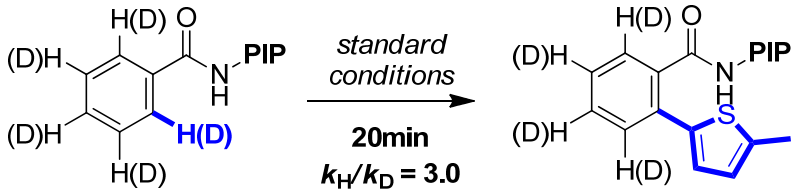
Removal of Directing Group[2]



A solution of substrate 3a (73.6 mg, 0.22 mmol) in a mixture of acetic acid (0.3 mL) and acetic anhydride (1.5 mL) was cooled to -15 ^{o}C and 330 mg of granular sodium nitrite (22 equiv) was added slowly in portions. After being stirred for 48 hours at -15 ^{o}C and the mixture poured into a mixture of ice and water. (Caution! Thenitrosoamide is unstable and the subsequent work-up should be carried out at 0 ^{o}C) The nitrosoamide was extracted with cold ether, and the organic phase was washedwith ice water, with an aqueous solution of sodium carbonate (5%), with ice water and then dried with anhydrous sodium sulfate under ice bath. The solvent wasremoved under reduce pressure under ice bath. The resident was dissolved in THF (4.4 mL)/ H_2O (1.5 mL) and cooled to -15 ^{o}C. Then 30% H_2O_2 (0.5 mL) was addedfollowed by lithium hydroxide monohydrate (92.3 mg, 2.2 mmol). The mixture wasstirred at -15 ^{o}C for 2 hours and at 0 ^{o}C overnight, and then quenched withan aqueous solution of Na_2SO_3. The mixture was basified with 1N NaOH and washed with ethyl acetate. The aqueous phase was acidied with 1M HCl and extracted with ethyl acetate.The organic layer was washed with brine, dried over anhydrous sodium sulfate and concentrated in vacuo. The resulting residue was purified by flash chromatography(petroleum ether : ethyl acetate : acetic acid = 1 : 1 : 0.02). 5 was obtained as a light yellow solid (40.9 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): δ ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86 (d, J = 7.6 Hz, 1H), 7.53 – 7.44 (m, 2H), 7.39 (t, J = 7.6 Hz, 1H), 6.89 (d, J = 3.2 Hz, 1H), 6.72 (d, J = 2.4 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.00, 141.06, 139.24, 135.39, 131.94, 131.67, 130.52, 130.09, 127.58, 126.88, 125.83, 15.48. HRMS (EI-TOF) calcd for $C_{12}H_{10}O_2S$ (M^+): 218.0402, found: 218.0400.

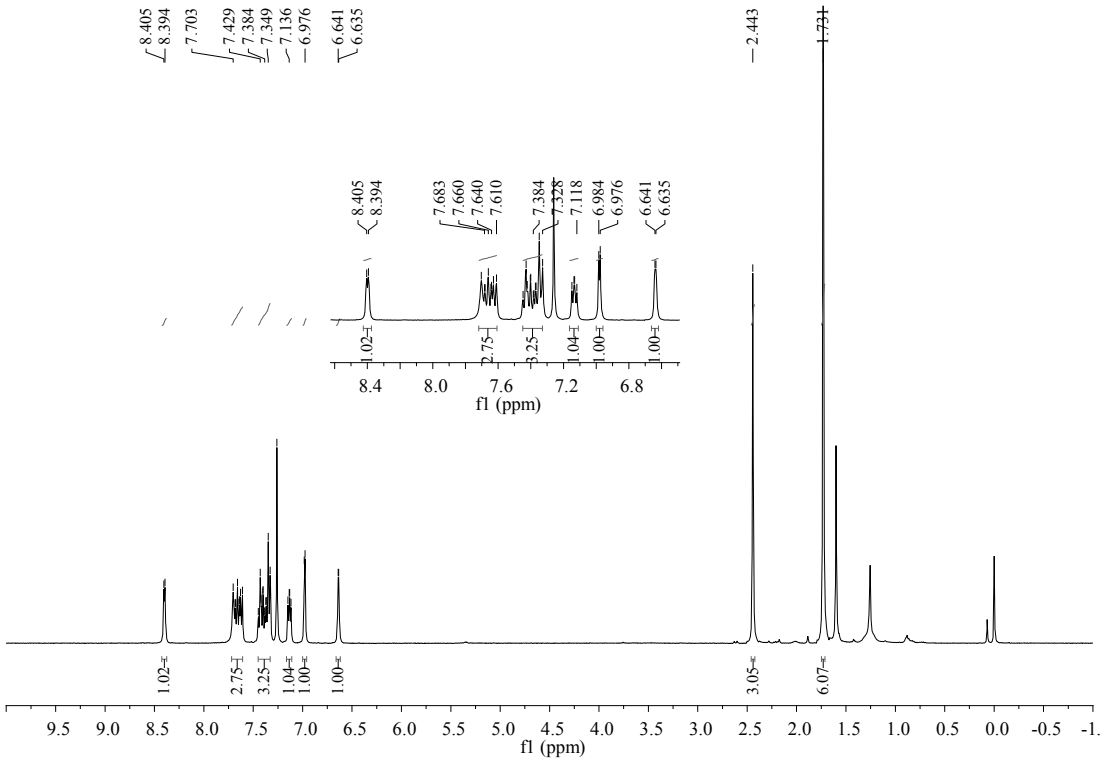
Mechanistic Investigation

Intermolecular Competition KIE.

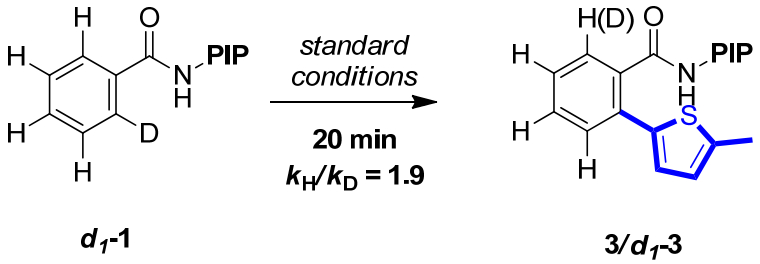


1/d_5-1 **3/d_4-3**

To a 50 mL sealed tube was added **1** (0.075 mmol), **d_5-1** (0.075 mmol), 2-methylthiophene (44 uL, 0.45 mmol) , CuOAc (3.7 mg, 0.03 mmol), $AgNO_3$ (101.9 mg, 0.6 mmol), Li_2CO_3 (33.3 mg, 0.45 mmol), $Zn(OAc)_2$ (33.0 mg, 0.18 mmol) and DMF (0.5 mL). The mixture was then put into pre-heated 120 ^oC oil bath under N_2 for 24 hours. The reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane(3×10 mL). The combined organic phase was dried with anhydrous magnesium sulfate. After concentration, the resulting residue was purified by flash chromatography (petroleum ether : actone = 4 : 1) to give the desired product in 8% yield. The KIE value was calculated k_H/k_D = 3.0.

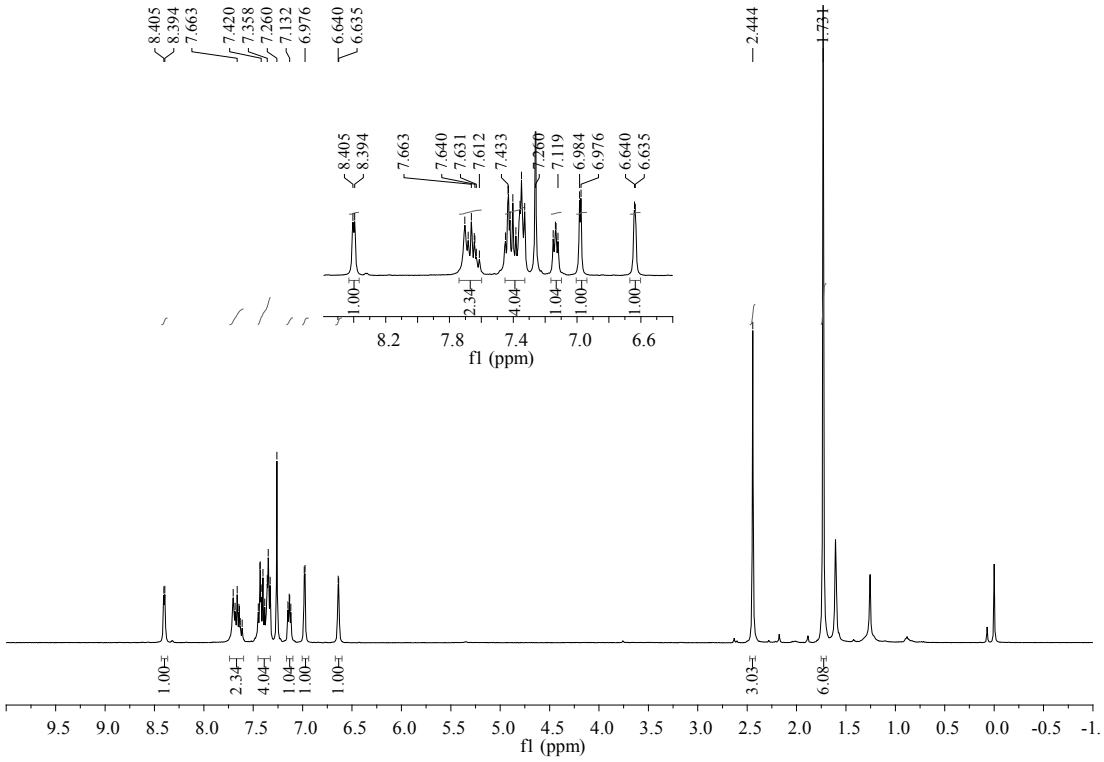


Intramolecular Competition KIE



***d*$_1$-1** **3/*d*$_1$-3**

To a 50mL sealed tube was added **d_1-1** (0.15 mmol), 2-methylthiophene (44 uL, 0.45 mmol) , CuOAc (3.7 mg, 0.03 mmol), $AgNO_3$ (101.9 mg, 0.6 mmol), Li_2CO_3 (33.3 mg, 0.45 mmol), $Zn(OAc)_2$ (33.0 mg, 0.18 mmol) and DMF (0.5 mL). The mixture was then put into pre-heated 100^{o}C oil bath under N_2 for 24 hours. The reaction mixture was cooled to room temperature, diluted with dichloromethane and quenched with saturated sodium sulfide solution. The aqueous phase was extracted with dichloromethane(3×10 mL). The combined organicphase was dried with anhydrous magnesium sulfate. After concentration, the resulting residue was purified by flash chromatography (petroleum ether : actone = 4 : 1) to give the desired product in 10% yield. The KIE value was calculated k_H/k_D = 1.9.

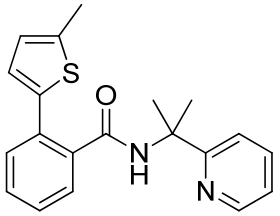


References:

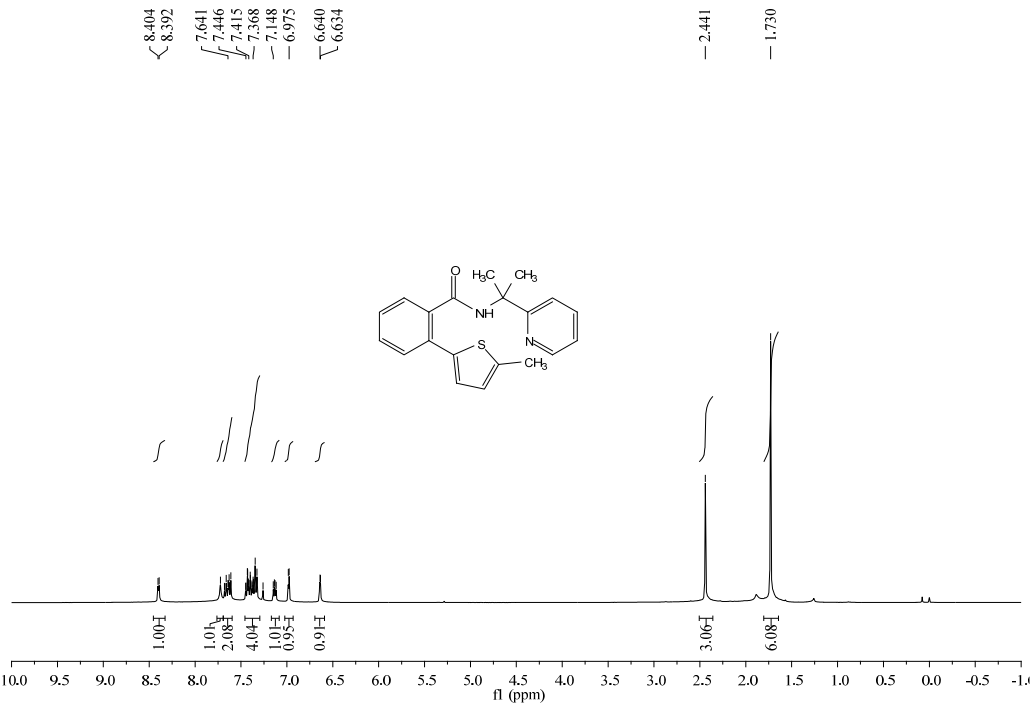
1. X. Li, Y.-H. Liu, W.-J. Gu, B. Li, F.-J. Chen and B.-F. Shi, *Org. Lett.*, 2014, **16**, 3904.

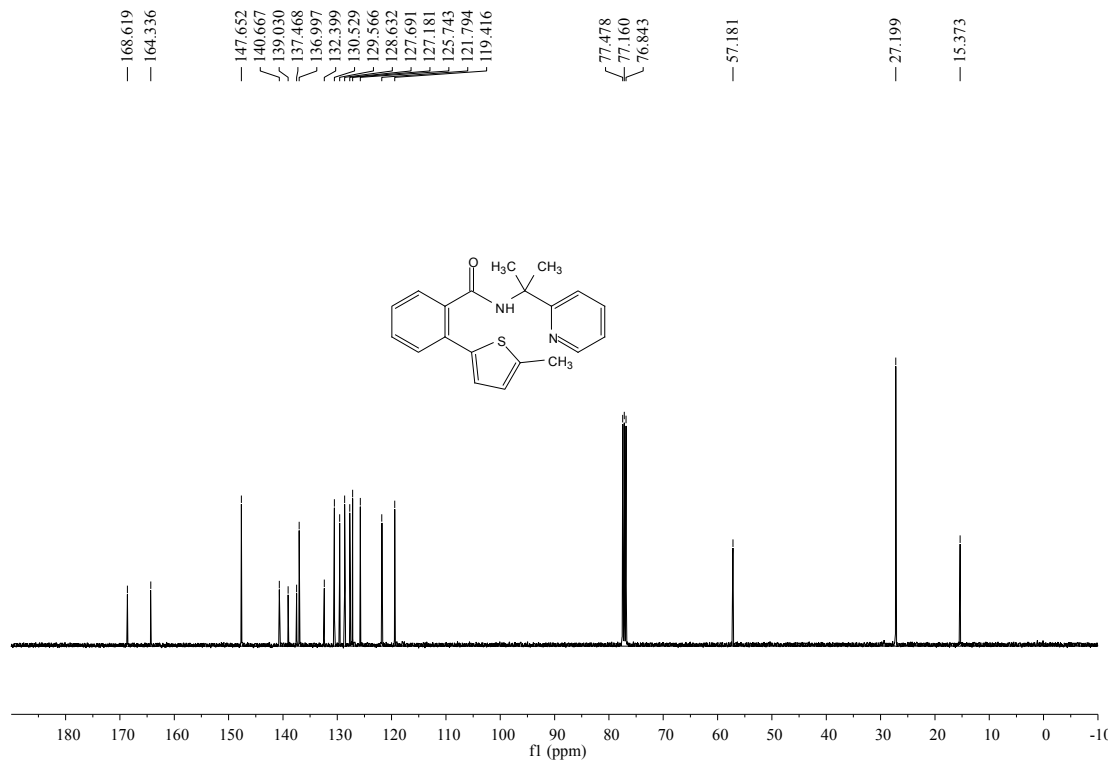
2. F.-J. Chen, G. Liao, X. Li, J. Wu and B.-F. Shi, *Org. Lett.*, 2014, **16**, 5644.

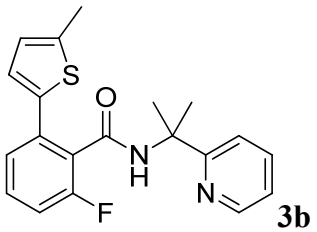
NMR Spectra:



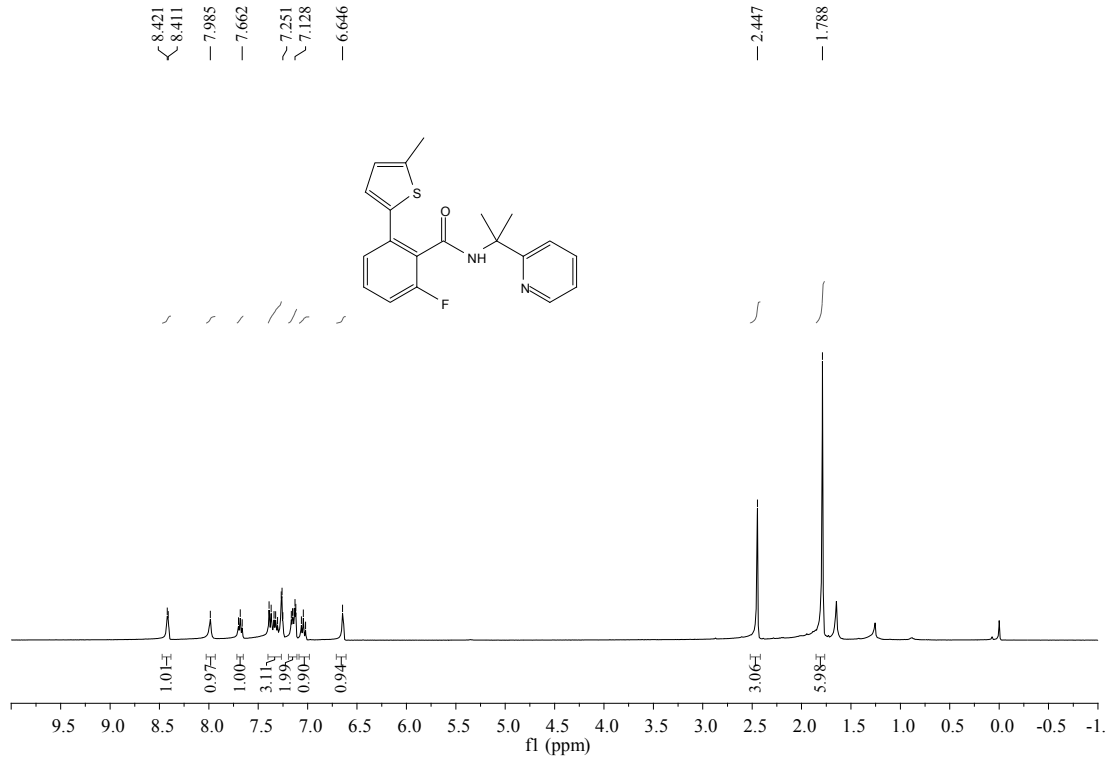
3a







3b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7.662
7.251
7.128
6.646
2.447
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1.01
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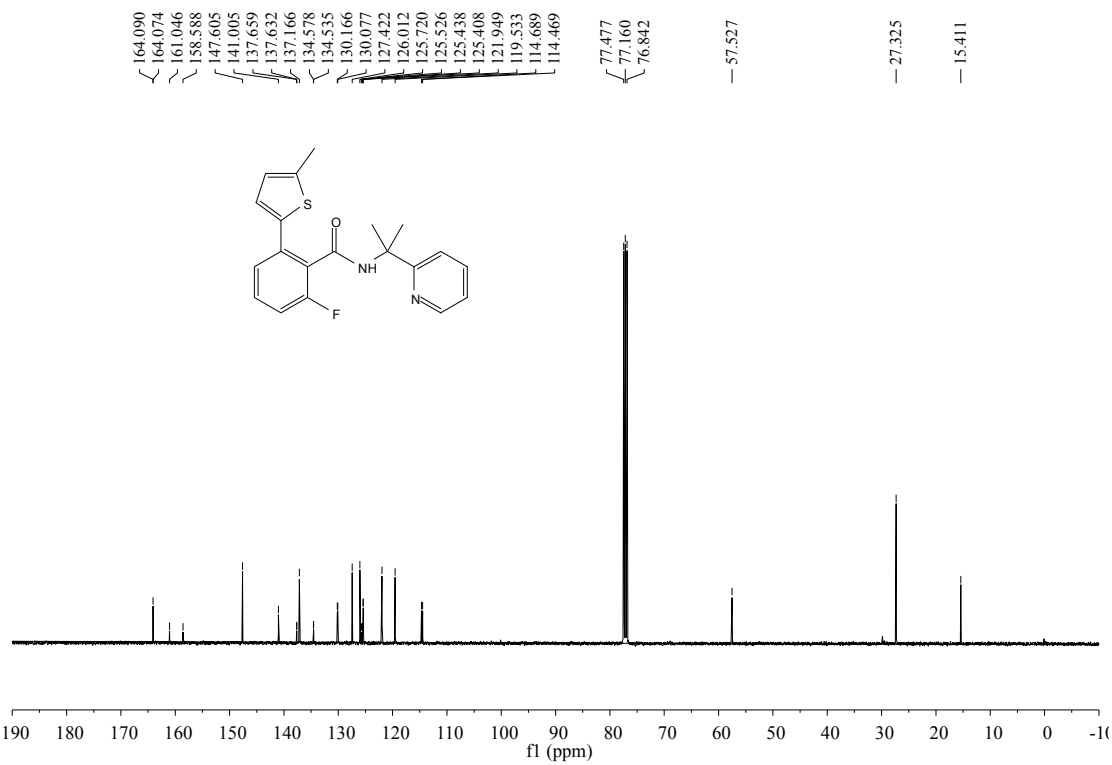
1.00
3.11
1.99
0.90
0.94
3.06
5.98
fl (ppm)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158.588
147.605
141.005
137.659
137.632
137.166
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134.535
130.166
130.077
127.422
126.012
125.720
125.526
125.438
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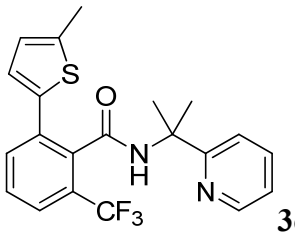
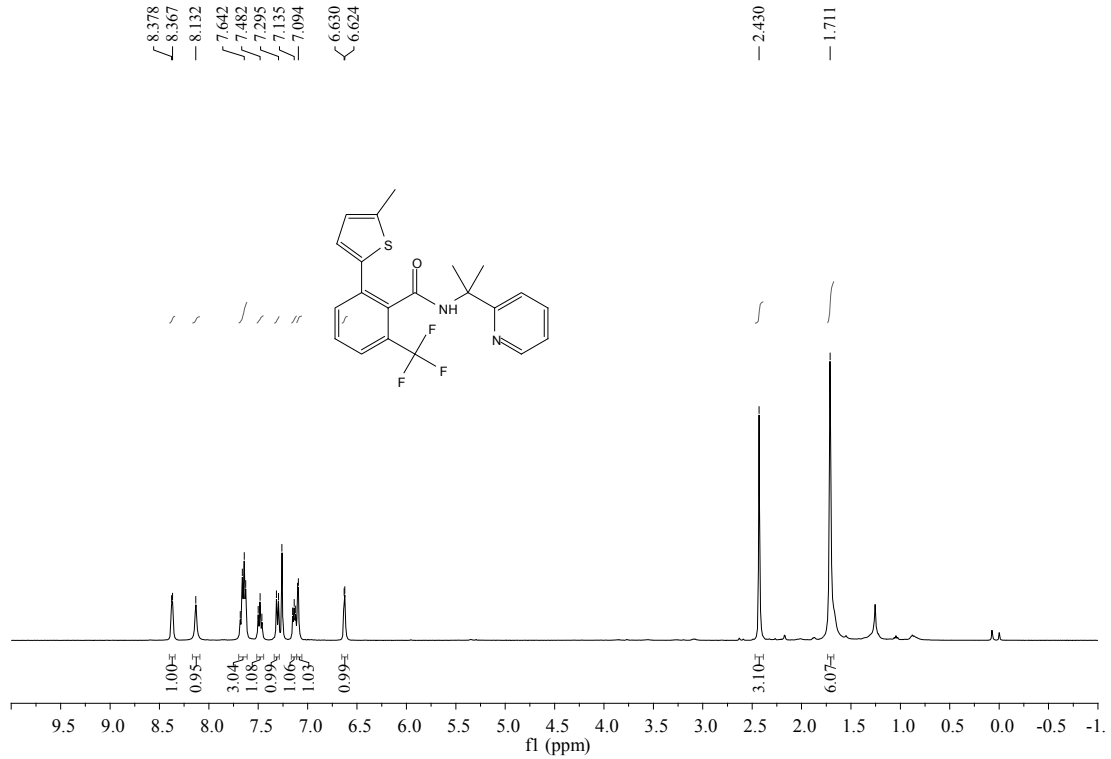
27.325
15.411
fl (ppm)



3c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7.295
7.135
7.094
6.630
6.624
2.430
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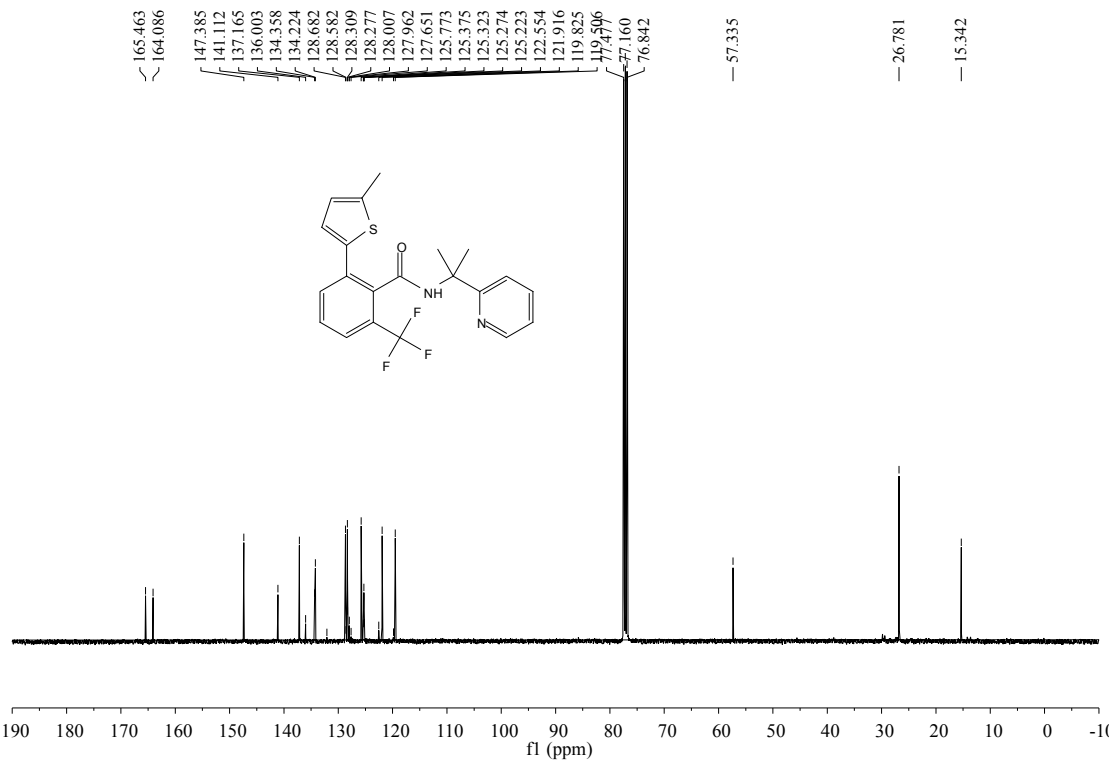
1.00
0.95
3.04
1.08
0.99
1.06
1.03
0.99
3.10
6.07
fl (ppm)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164.086
147.385
141.112
137.165
136.003
134.358
134.224
128.682
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128.309
128.277
128.007
127.962
127.651
125.773
125.375
125.323
125.274
125.223
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119.825
119.506
77.477
77.160
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57.335
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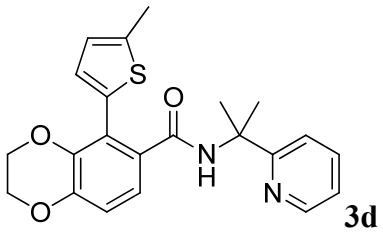
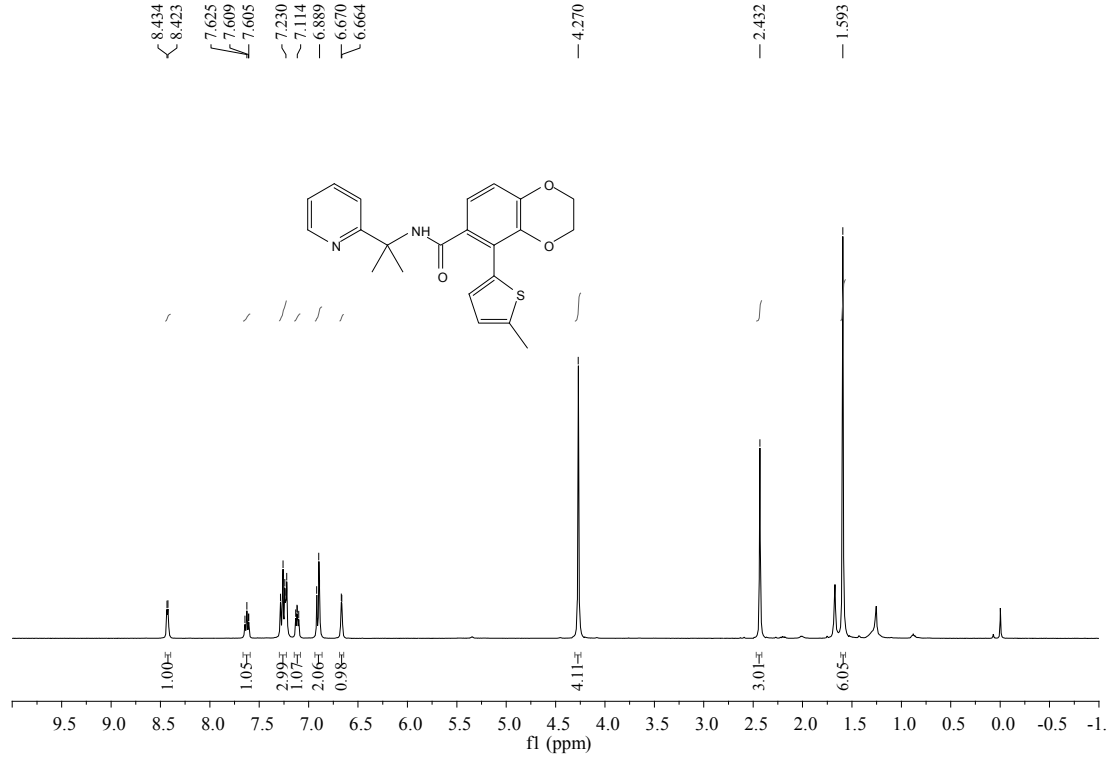
15.342
fl (ppm)



3d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7.605
7.230
7.114
6.889
6.670
6.664
4.270
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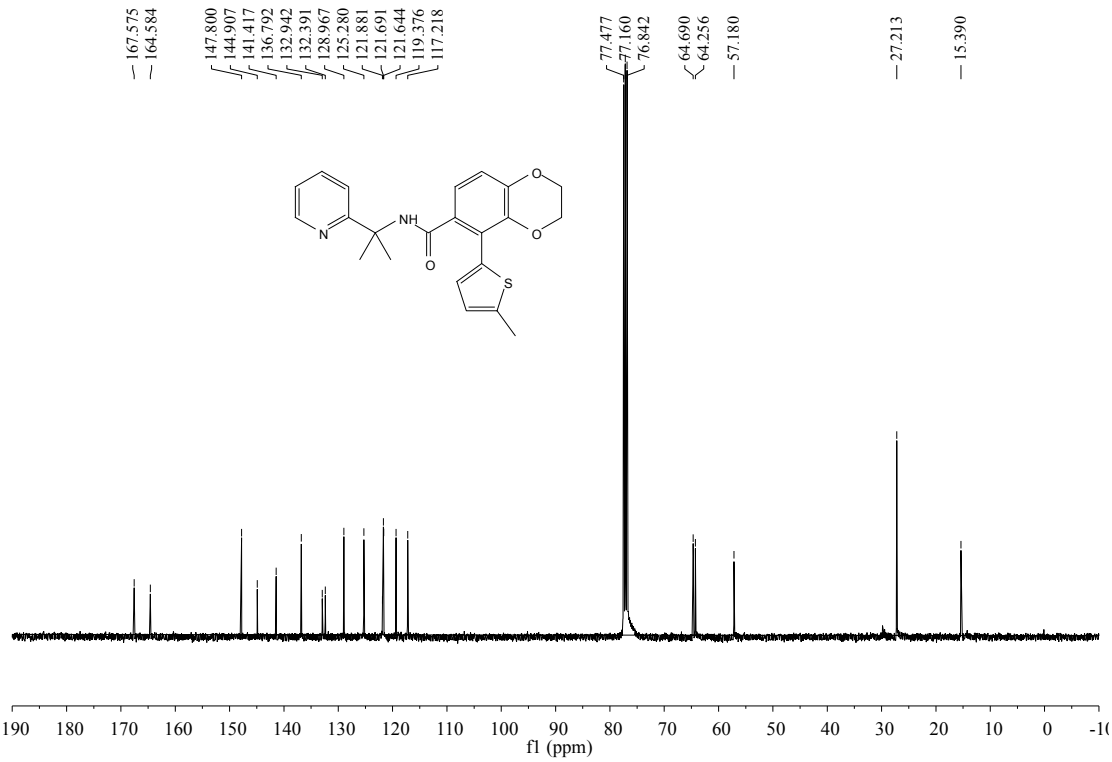
1.593
1.00
1.05
2.99
1.07
2.06
0.98
4.11
3.01
6.05
f1 (ppm)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147.800
144.907
141.417
136.792
132.942
132.391
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121.691
121.644
119.376
117.218
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77.160
76.842
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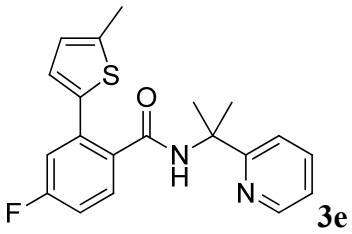
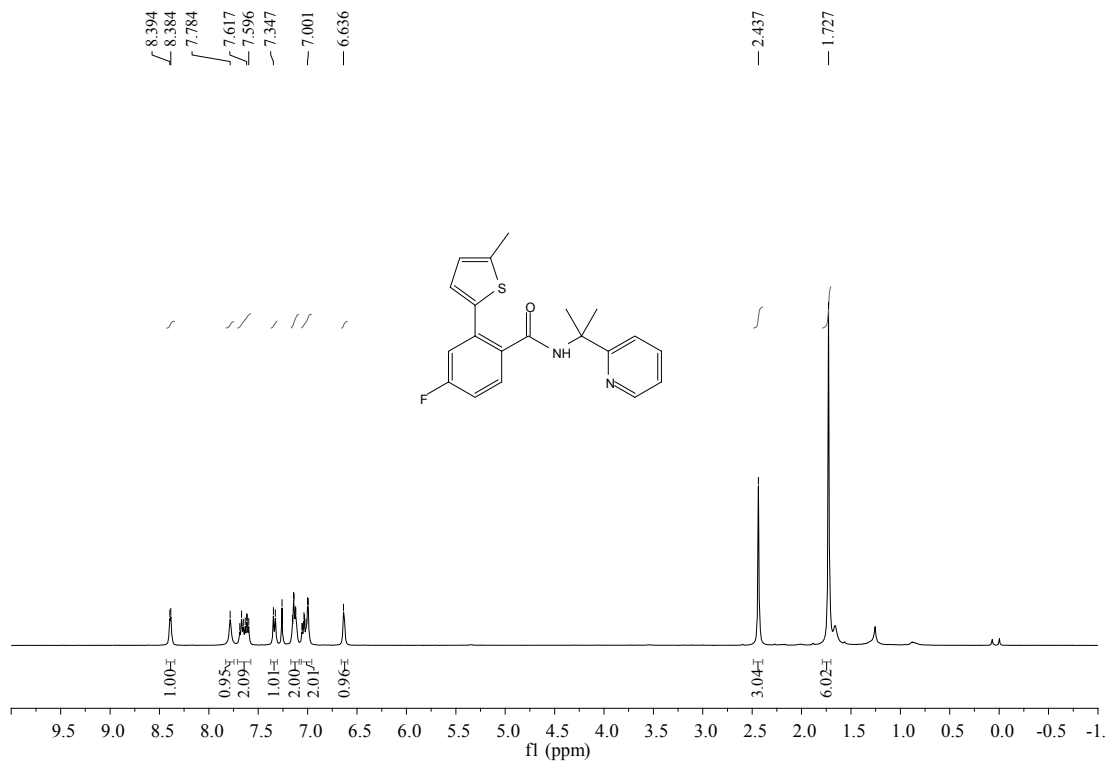
57.180
27.213
15.390
f1 (ppm)


S
O
N
H
N
F

3e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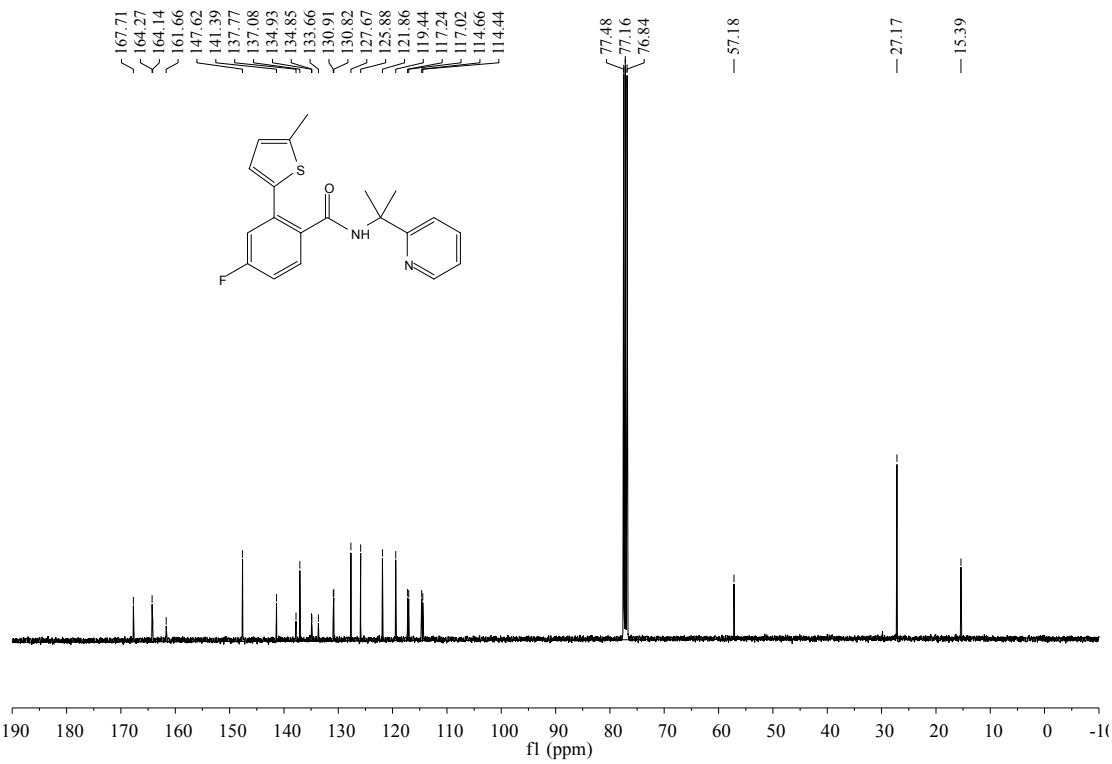
2.09
1.01
2.00
2.01
0.96
3.04
6.02
f1 (ppm)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137.08
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134.85
133.66
130.91
130.82
127.67
125.88
121.86
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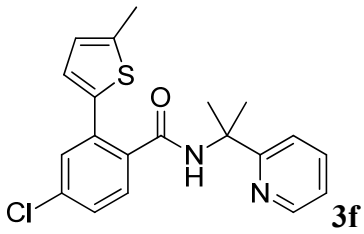
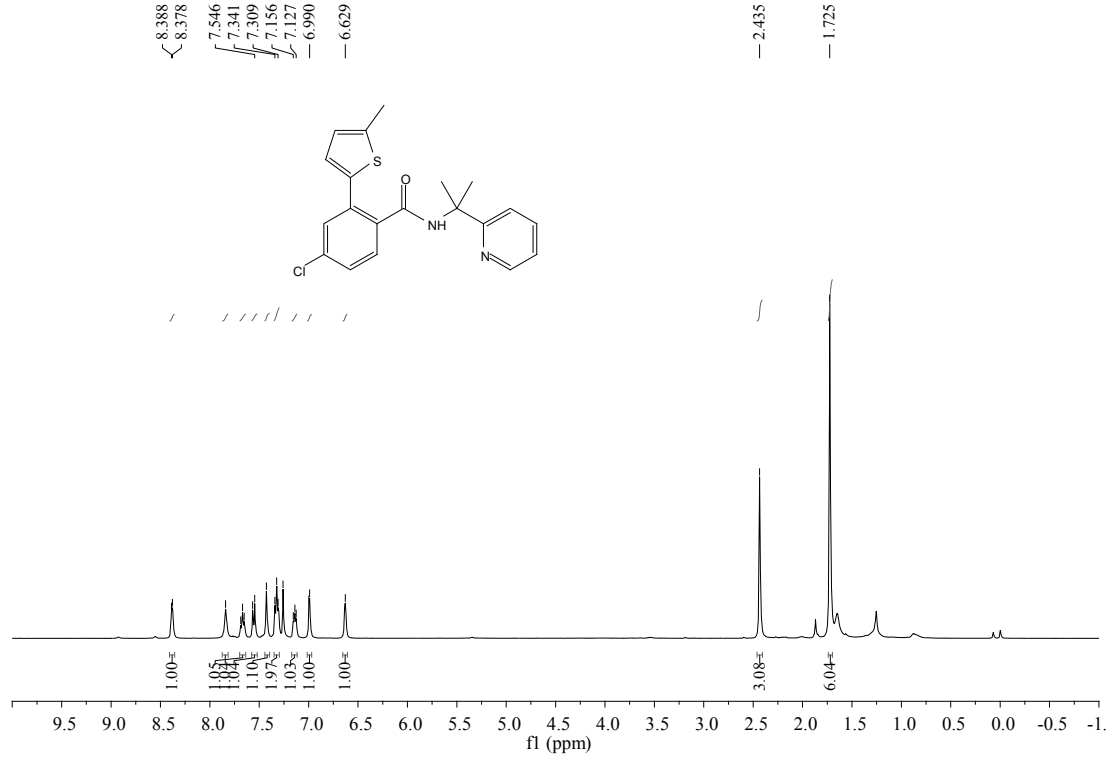
76.84
57.18
27.17
15.39
f1 (ppm)


S
O
N
H
N
Cl

3f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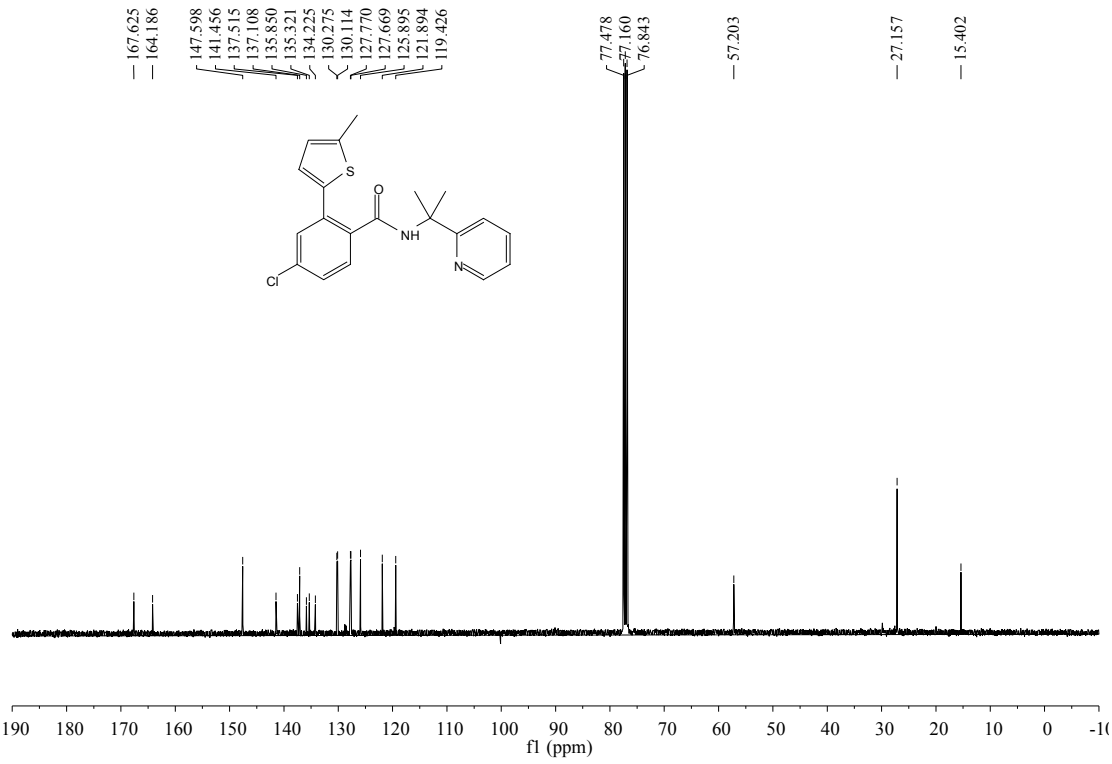
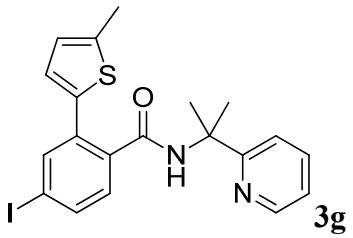
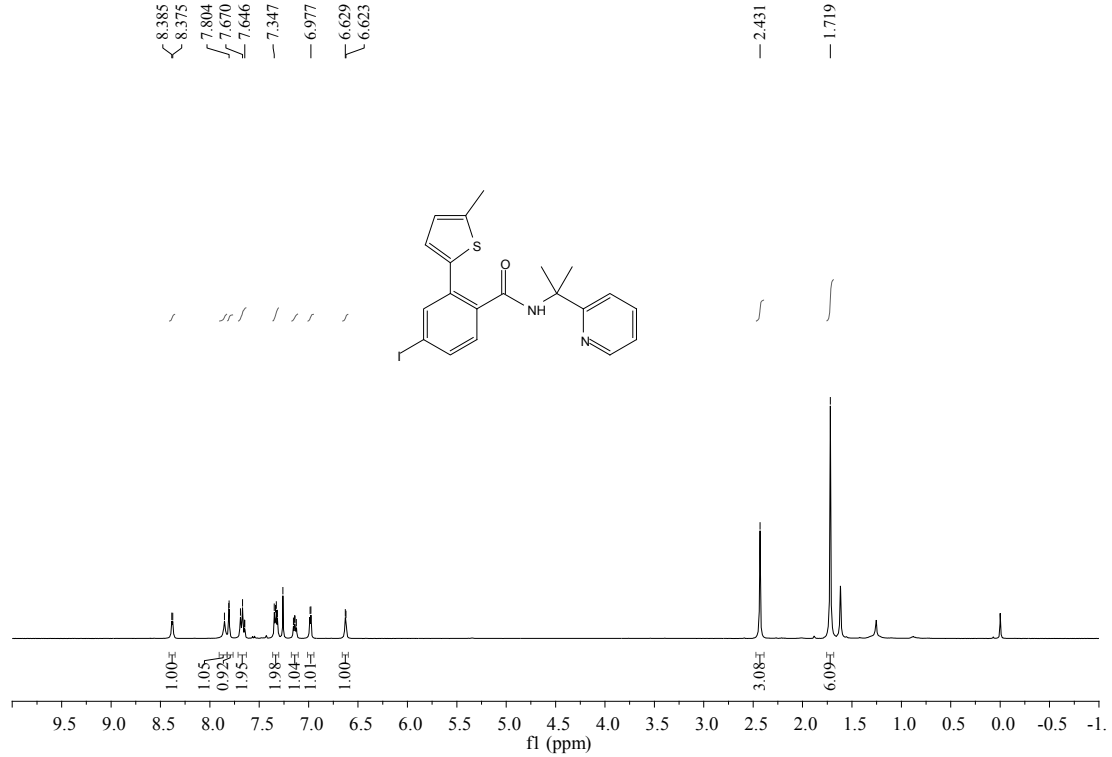
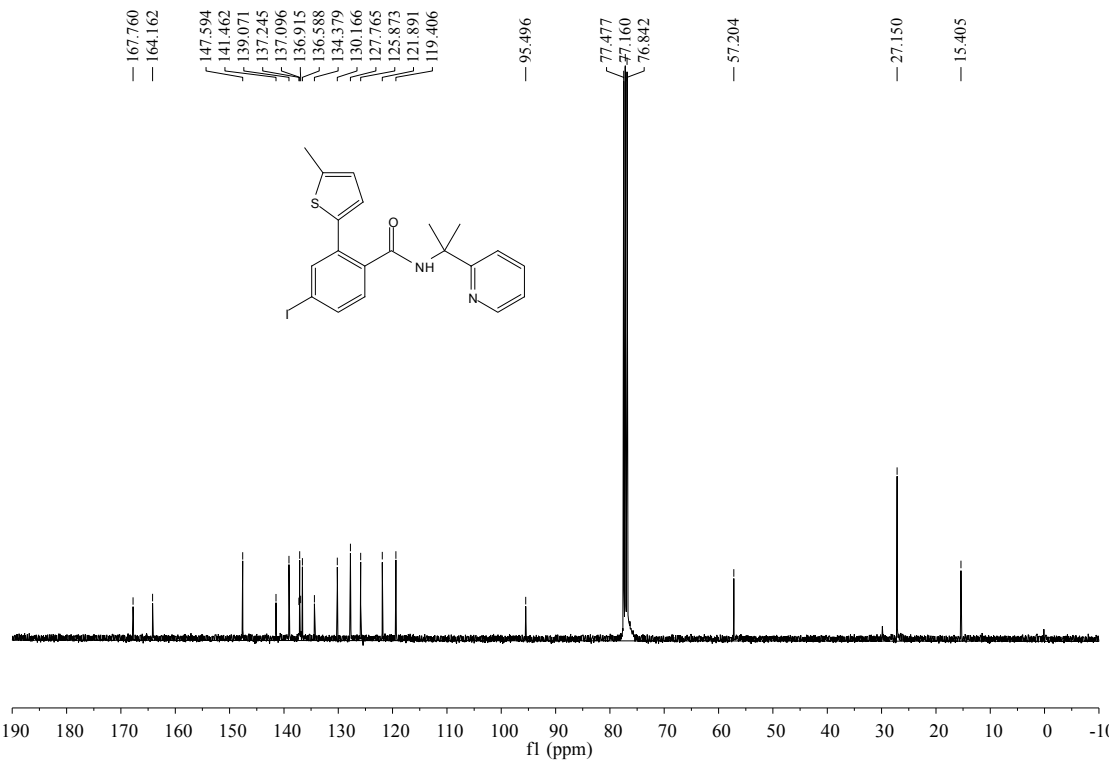
1.725
1.00
1.85
1.84
1.10
1.97
1.03
1.00
1.00
3.08
6.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

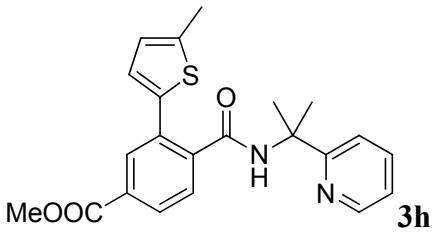

167.625
164.186
147.598
141.456
137.515
137.108
135.850
135.321
134.225
130.275
130.114
127.770
127.669
125.895
121.894
119.426
77.478
77.160
76.843
57.203
27.157
15.402
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


S
O
N
H
N
I

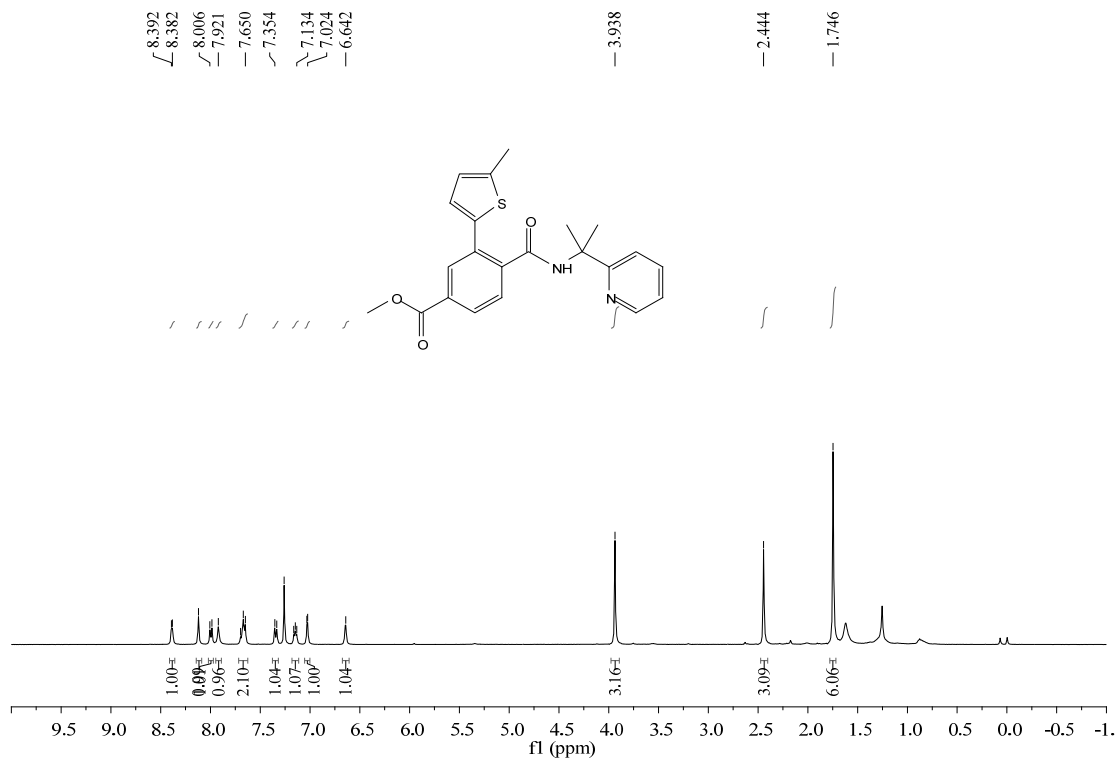
3g

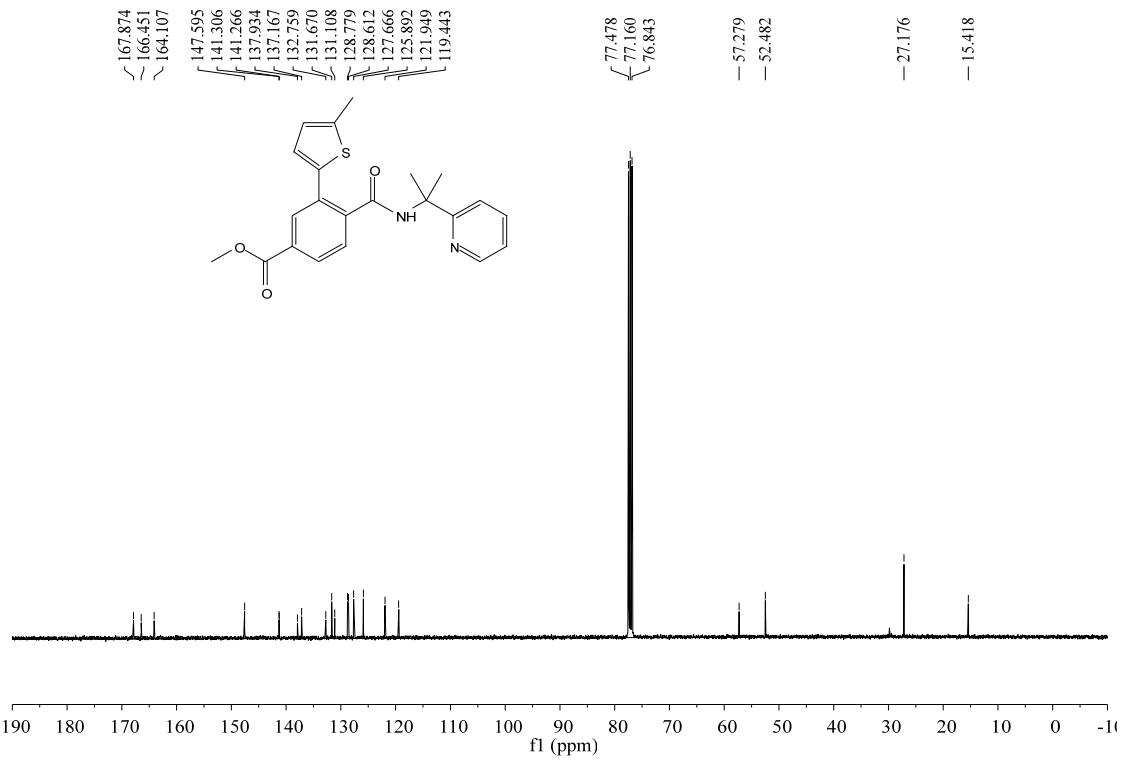

8.385
8.375
7.804
7.670
7.646
7.347
6.977
6.629
6.623
2.431
1.719
S
O
NH
N
I
1.00
1.05
0.92
1.95
1.98
1.04
1.01
1.00
3.08
6.09
fl (ppm)

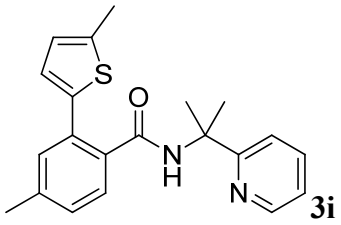

167.760
164.162
147.594
141.462
139.071
137.245
137.096
136.915
136.588
134.379
130.166
127.765
125.873
121.891
119.406
95.496
77.477
77.160
76.842
57.204
27.150
15.405
S
O
NH
N
I
fl (ppm)


MeOOC
S
O
N
H
N

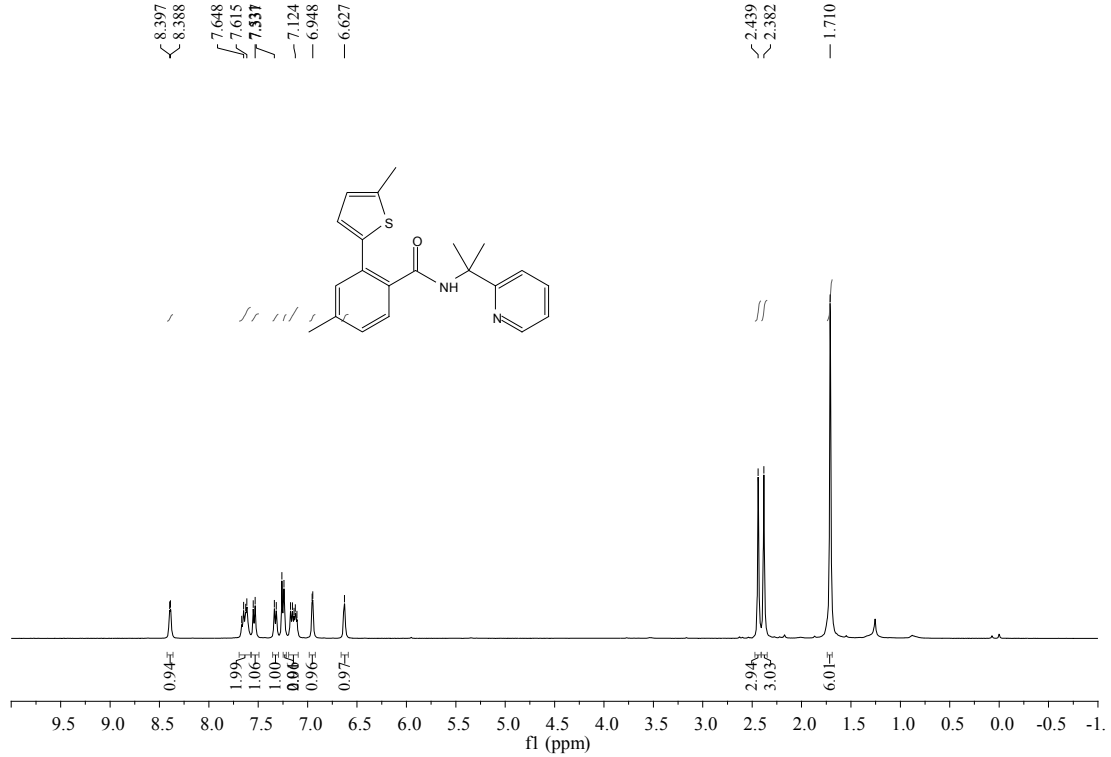
3h

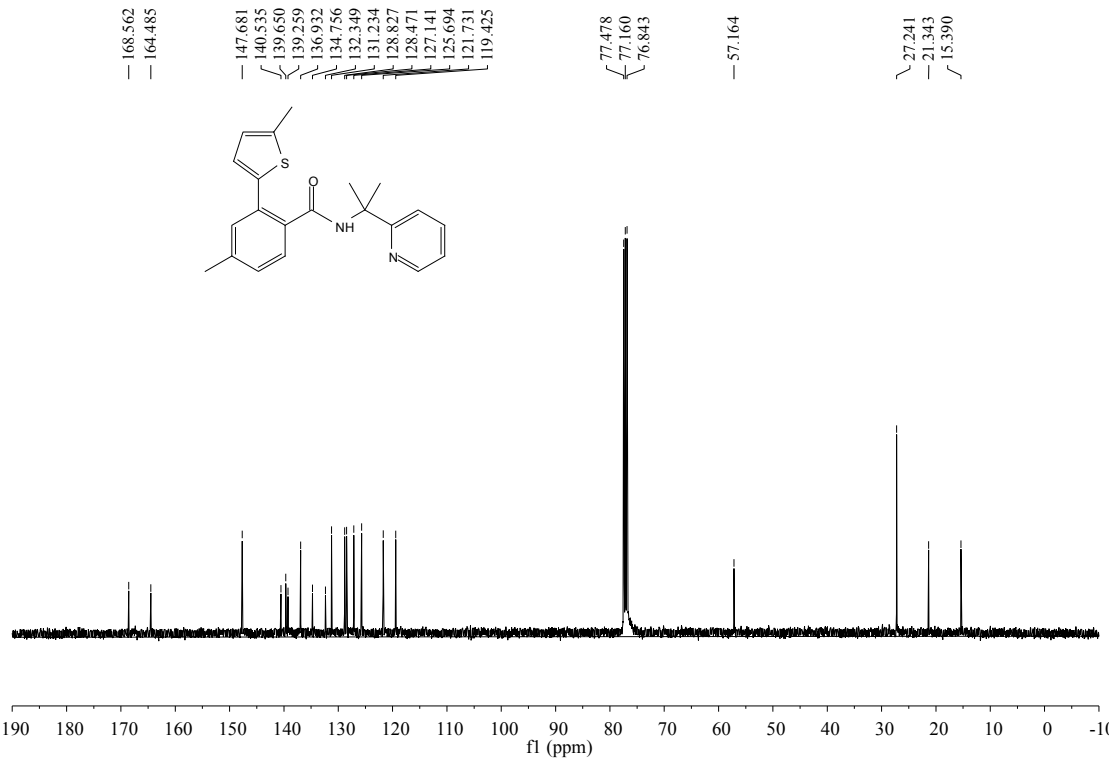

8.392
8.382
8.006
7.921
7.650
7.354
7.134
7.024
6.642
3.938
2.444
1.746
1.00
0.99
0.96
2.10
1.04
1.07
1.00
1.04
3.16
3.09
6.06
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)

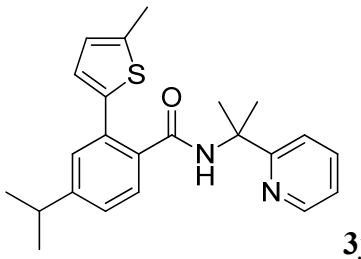

167.874
166.451
164.107
147.595
141.306
141.266
137.934
137.167
132.759
131.670
131.108
128.779
128.612
127.666
125.892
121.949
119.443
77.478
77.160
76.843
57.279
52.482
27.176
15.418
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)



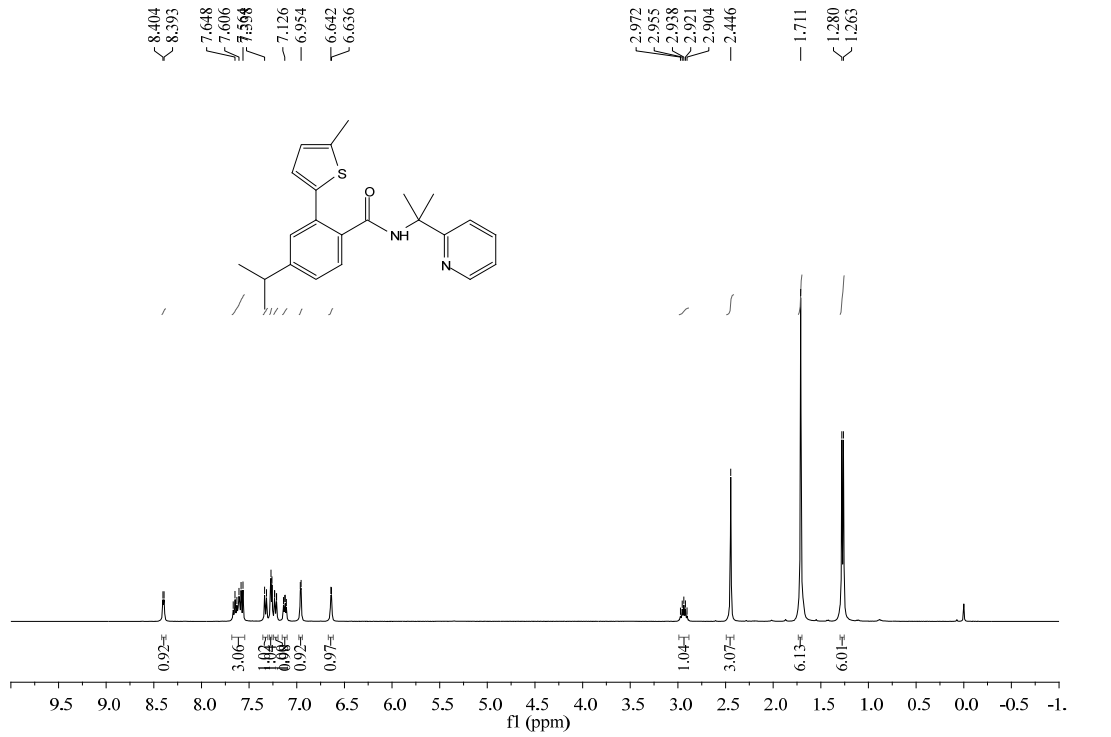
3i

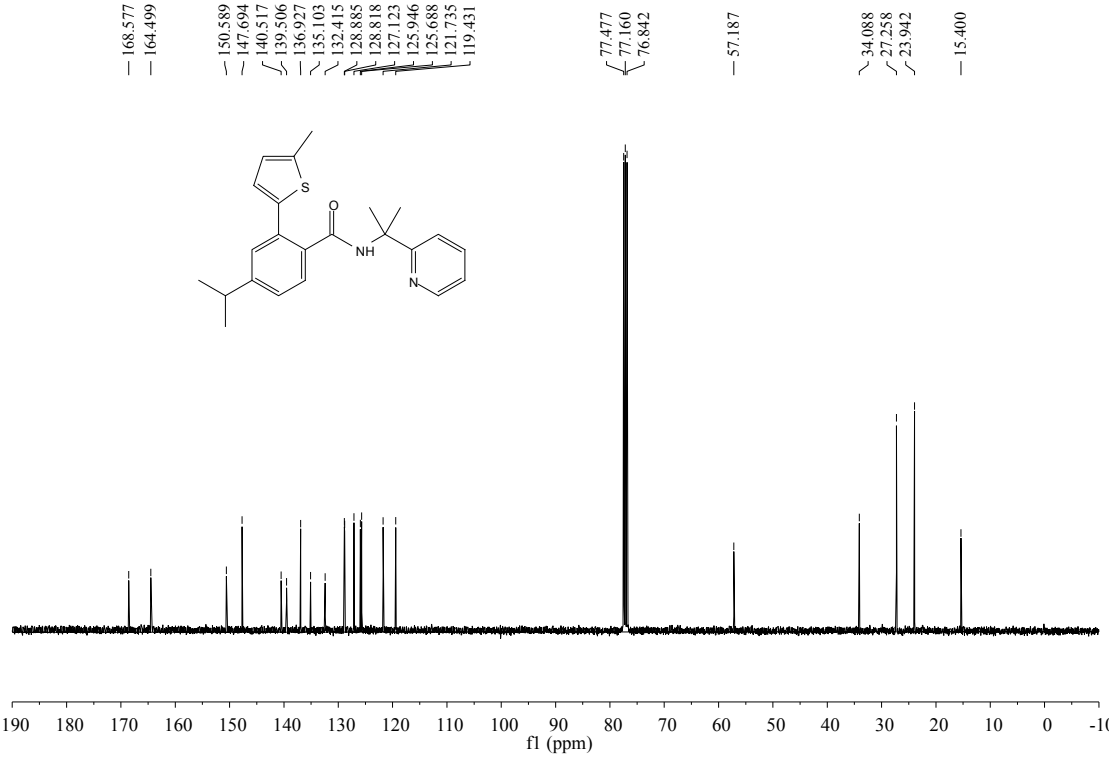

8.397
8.388
7.648
7.615
7.331
7.124
6.948
6.627
2.439
2.382
1.710
0.94
1.99
1.06
1.00
0.96
0.97
2.94
3.03
6.01
fl (ppm)


168.562
164.485
147.681
140.535
139.650
139.259
136.932
134.756
132.349
131.234
128.827
128.471
127.141
125.694
121.731
119.425
77.478
77.160
76.843
57.164
27.241
21.343
15.390
fl (ppm)



3j


8.404
8.393
7.648
7.606
7.126
6.954
6.642
6.636
2.972
2.955
2.938
2.921
2.904
2.446
1.711
1.280
1.263
0.92
3.06
0.92
0.97
1.04
3.07
6.13
6.01
fl (ppm)


168.577
164.499
150.589
147.694
140.517
139.506
136.927
135.103
132.415
128.885
128.818
127.123
125.946
125.688
121.735
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77.160
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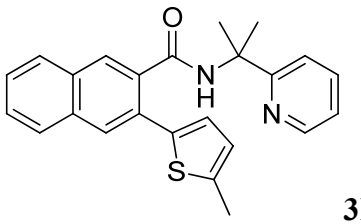
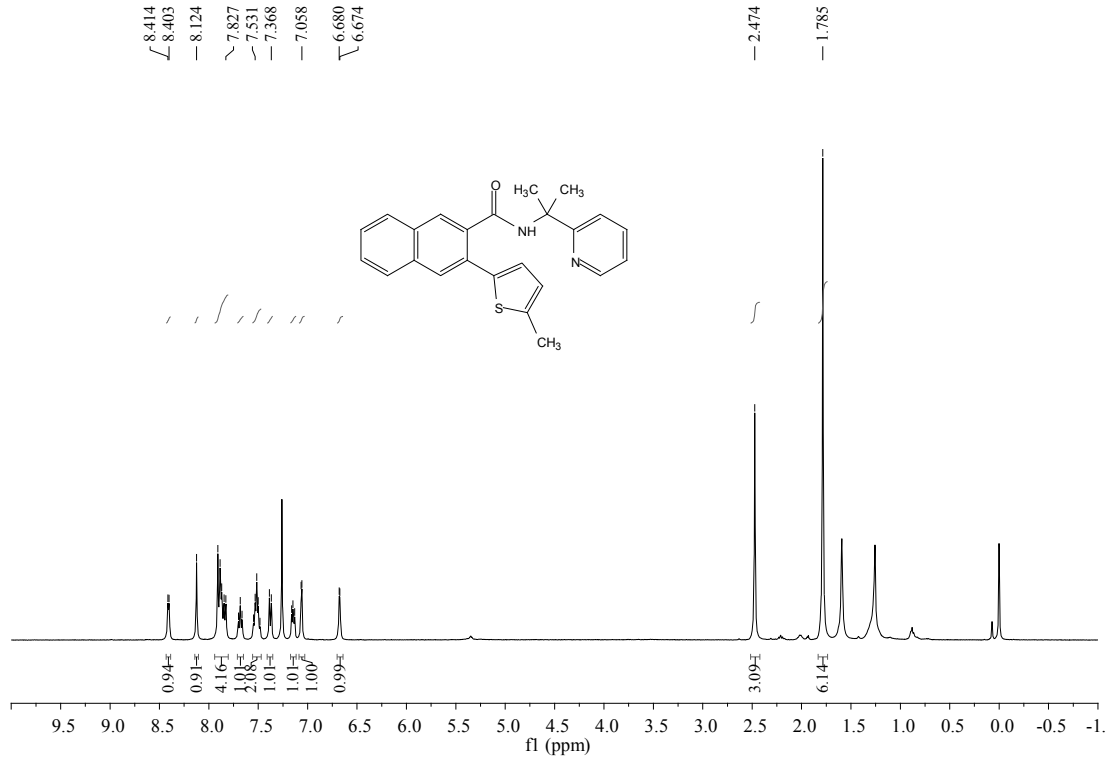
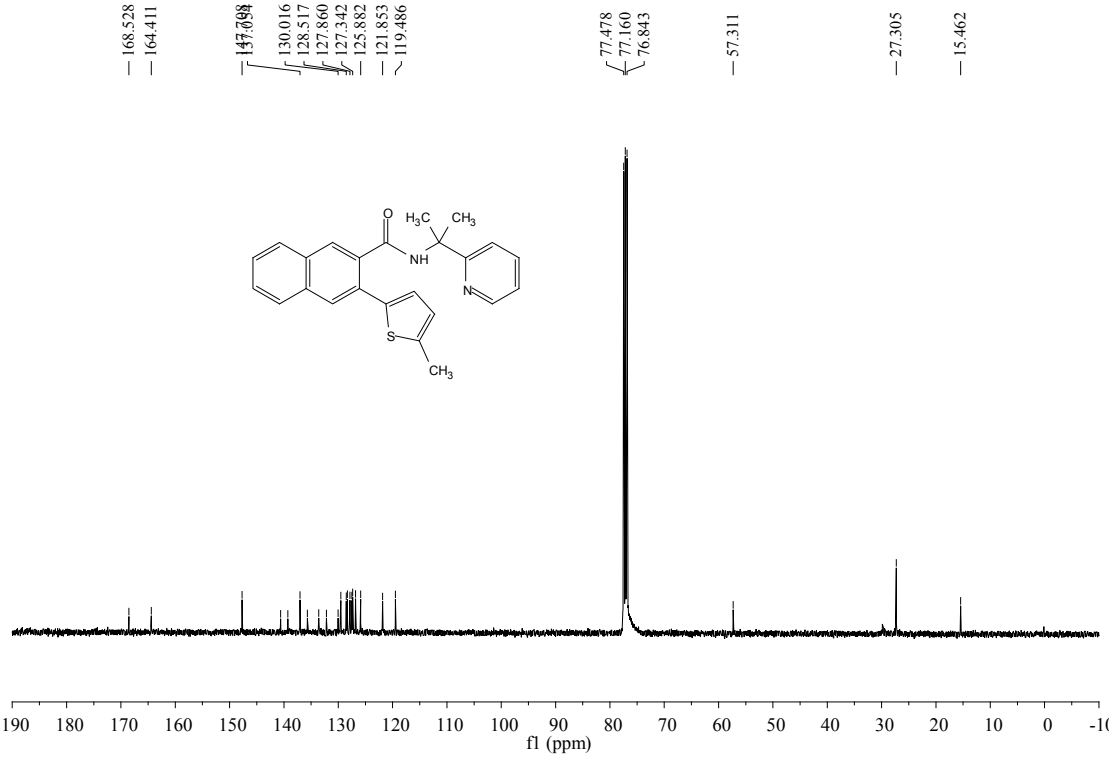
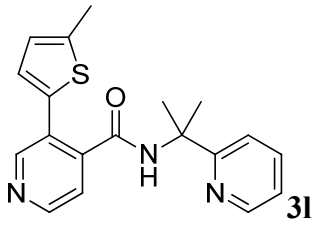
57.187
34.088
27.258
23.942
15.400
fl (ppm)



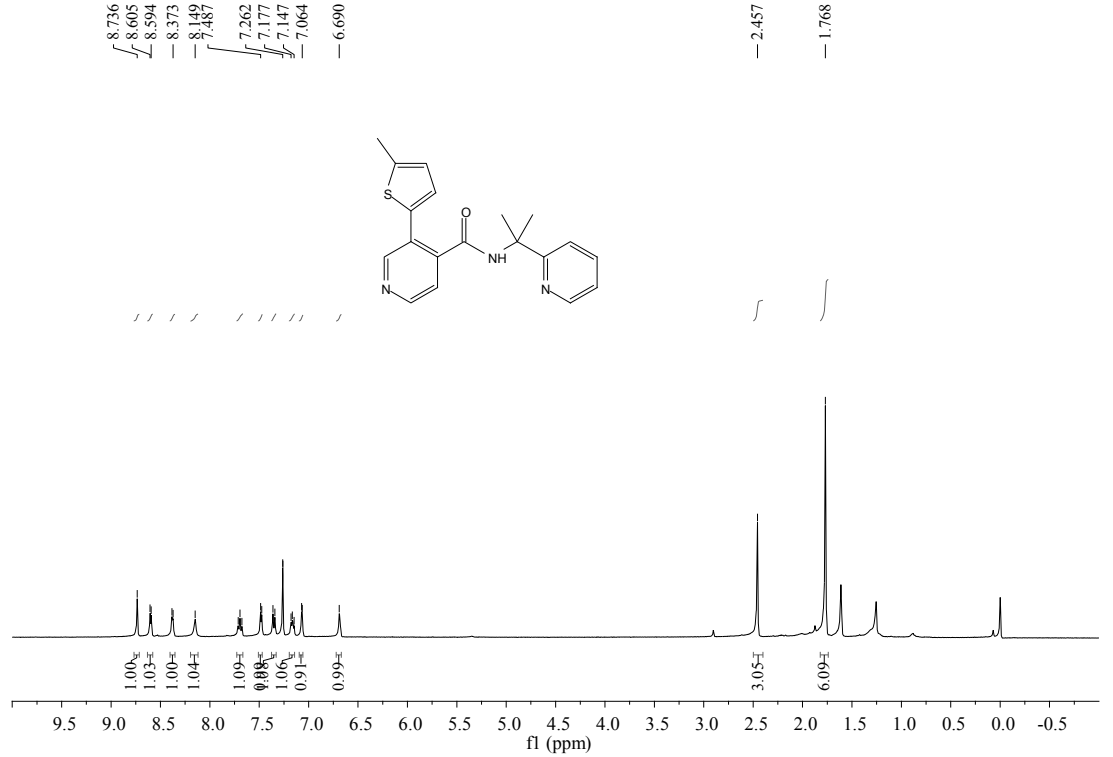
3k

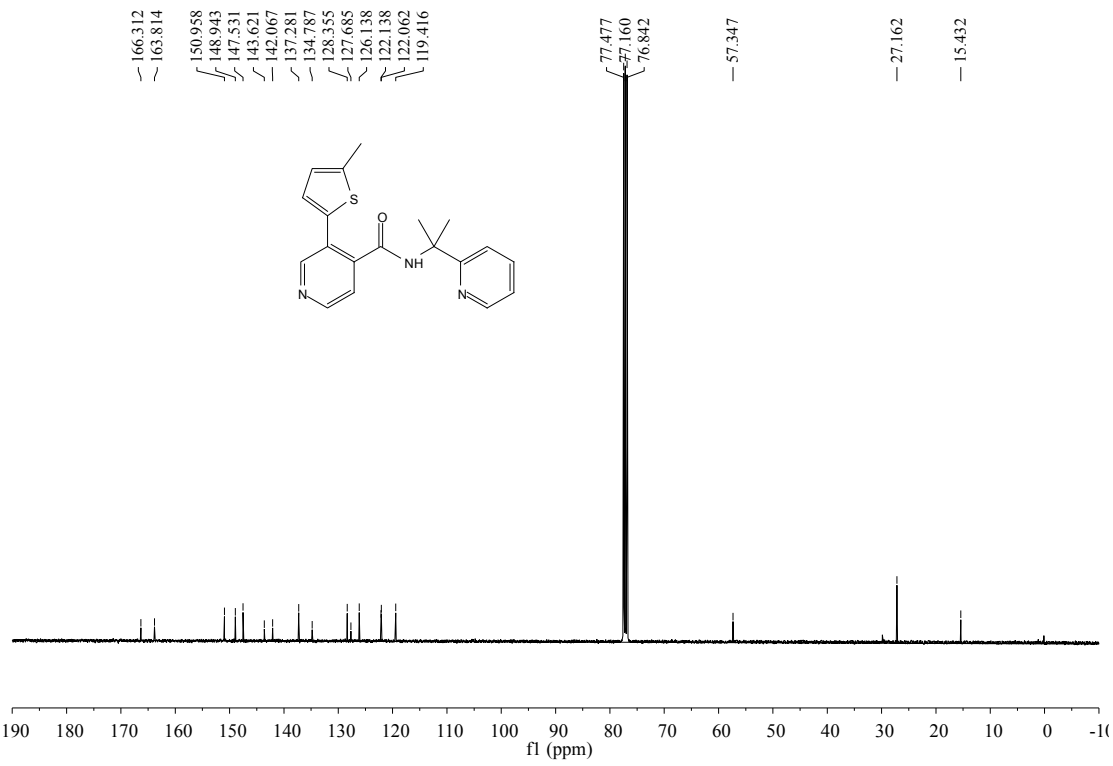

8.414
8.403
8.124
7.827
7.531
7.368
7.058
6.680
6.674
2.474
1.785
0.94
0.91
4.16
2.08
1.01
1.00
0.99
3.09
6.14
fl (ppm)

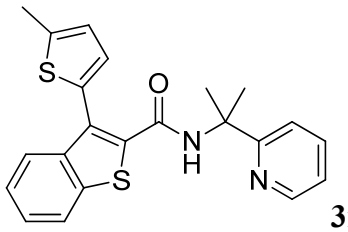

168.528
164.411
147.708
147.098
130.016
128.517
127.860
127.342
125.882
121.853
119.486
77.478
77.160
76.843
57.311
27.305
15.462
fl (ppm)


S
O
N
H
N
N

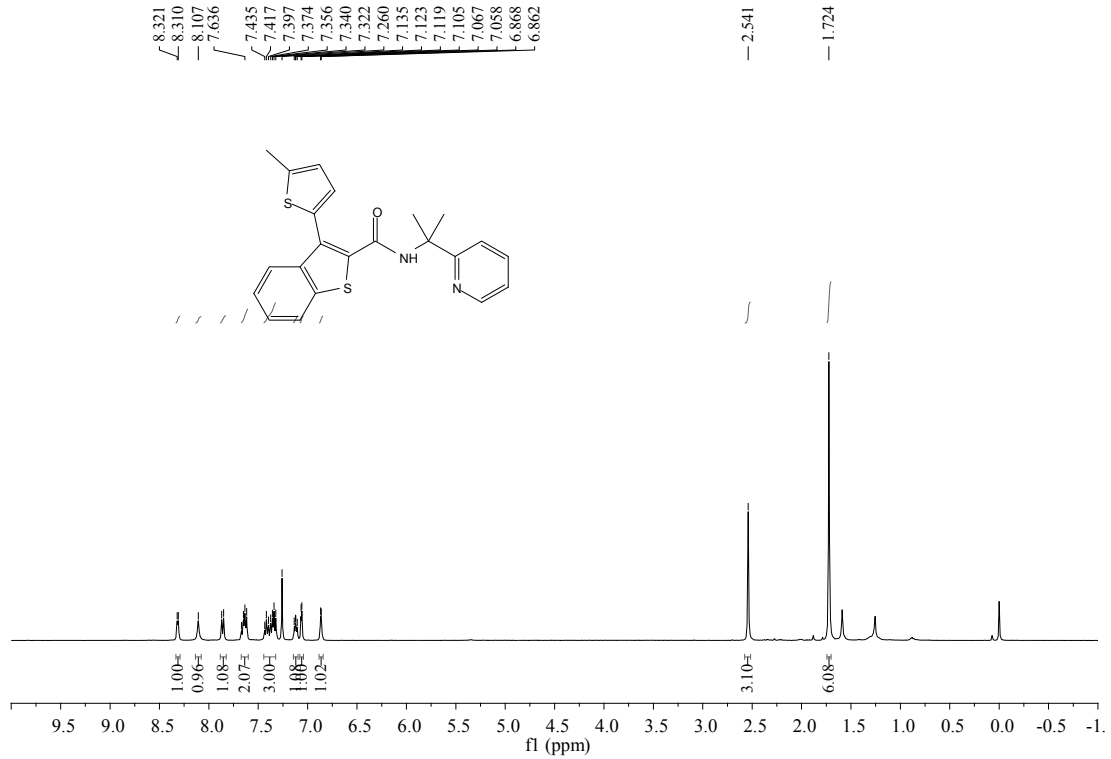
3l

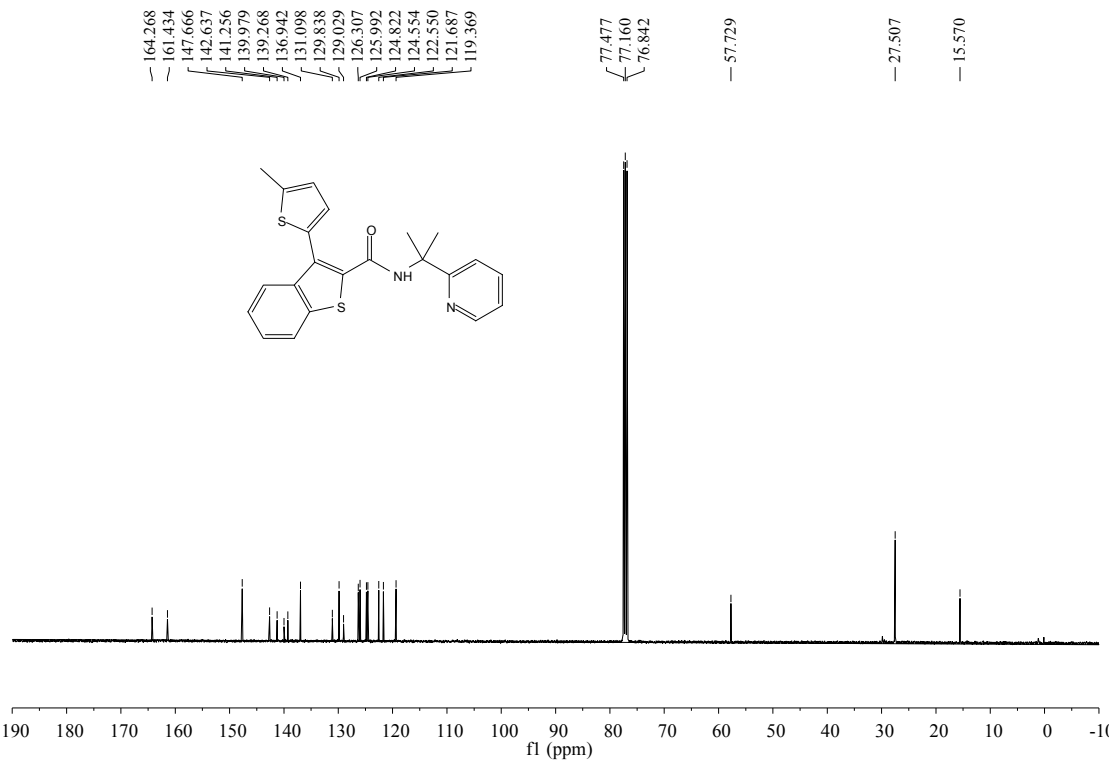

8.736
8.605
8.594
8.373
8.149
7.487
7.262
7.177
7.147
7.064
6.690
2.457
1.768
1.00
1.03
1.00
1.04
1.09
1.08
1.06
0.91
0.99
3.05
6.09
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

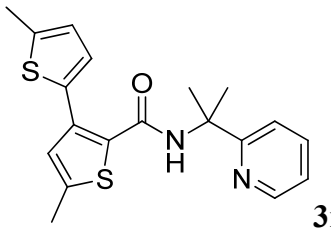

166.312
163.814
150.958
148.943
147.531
143.621
142.067
137.281
134.787
128.355
127.685
126.138
122.138
122.062
119.416
77.477
77.160
76.842
57.347
27.162
15.432
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)



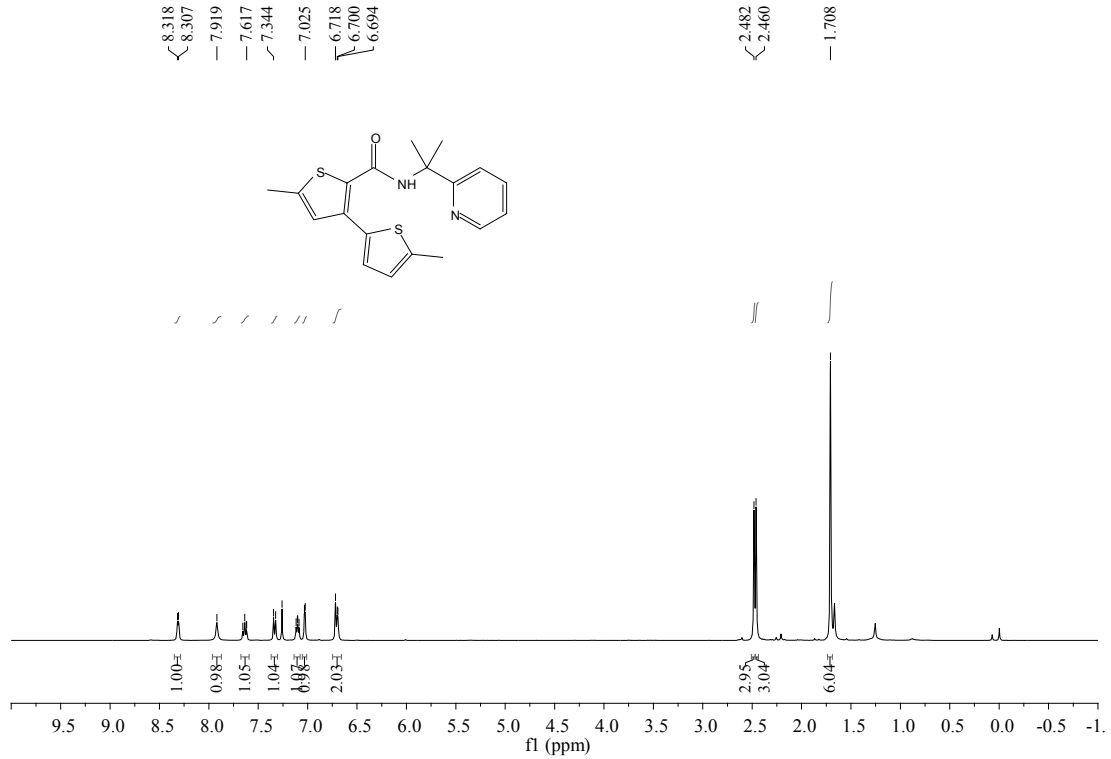
3m

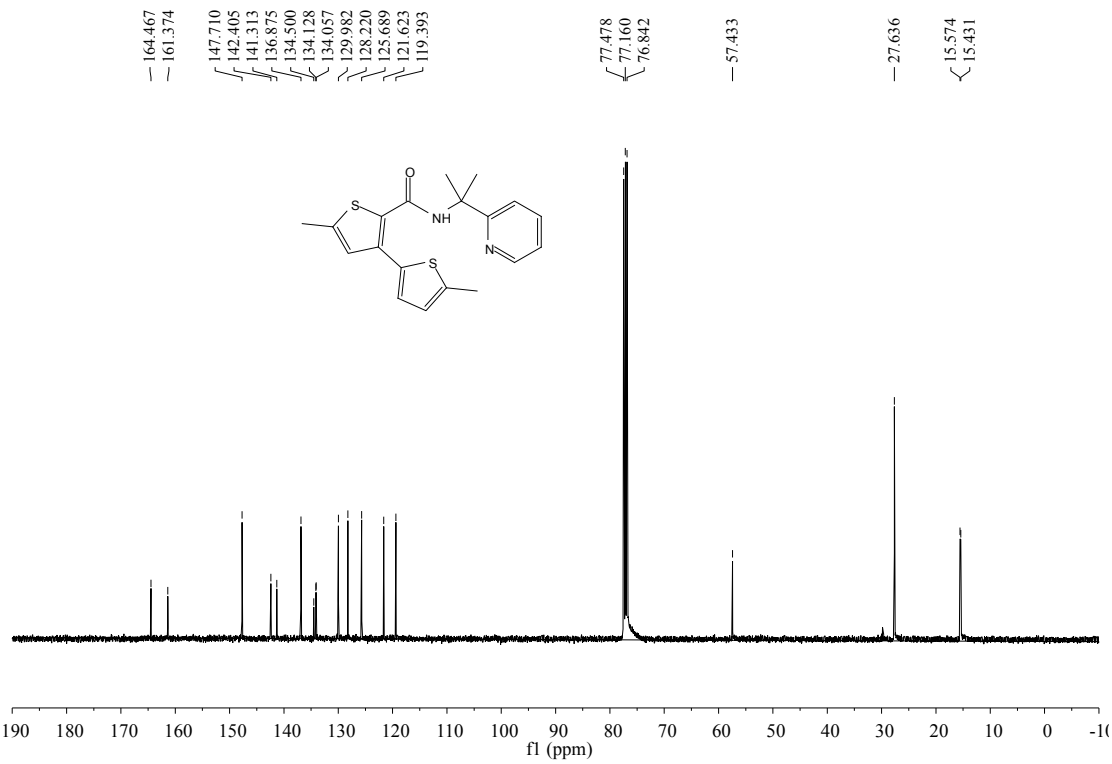

8.321
8.310
8.107
7.636
7.435
7.417
7.397
7.374
7.356
7.340
7.322
7.260
7.135
7.123
7.119
7.105
7.067
7.058
6.868
6.862
2.541
1.724
1.00
0.96
1.08
2.07
3.00
1.08
1.02
3.10
6.08
fl (ppm)

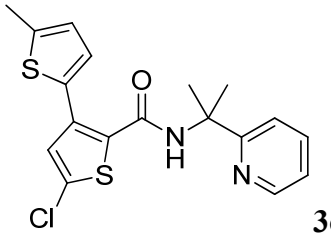

164.268
161.434
147.666
142.637
141.256
139.979
139.268
136.942
131.098
129.838
129.029
126.307
125.992
124.822
124.554
122.550
121.687
119.369
77.477
77.160
76.842
57.729
27.507
15.570
fl (ppm)



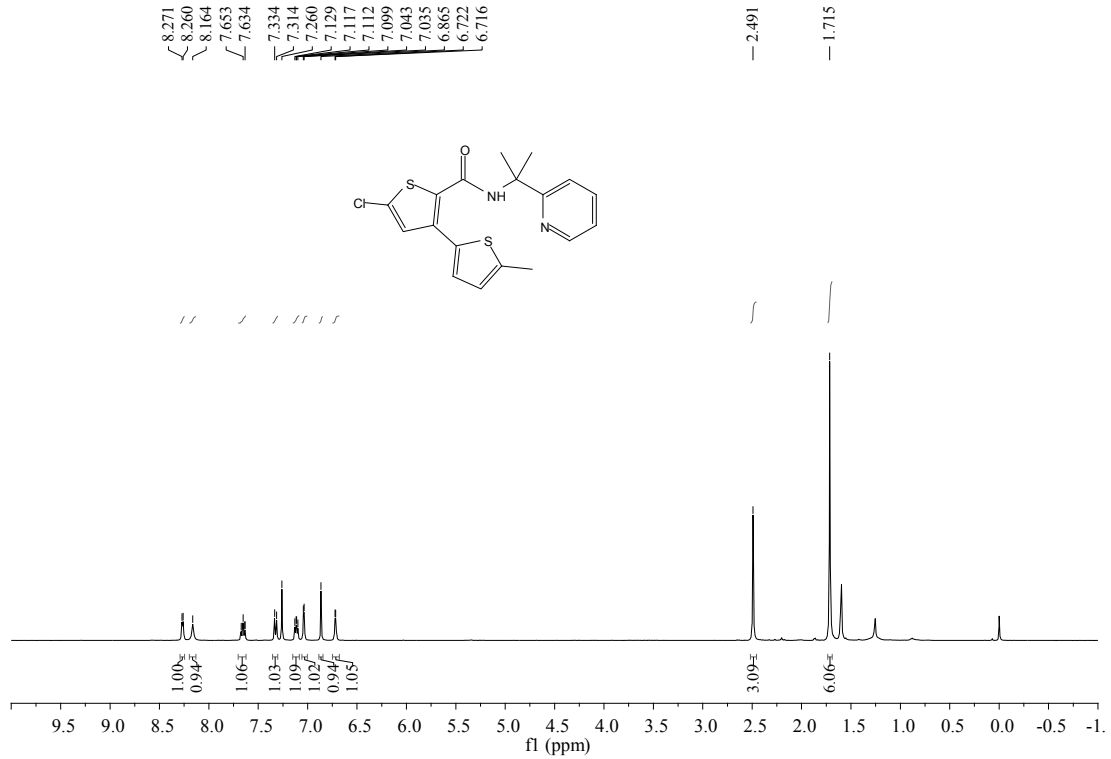
3n

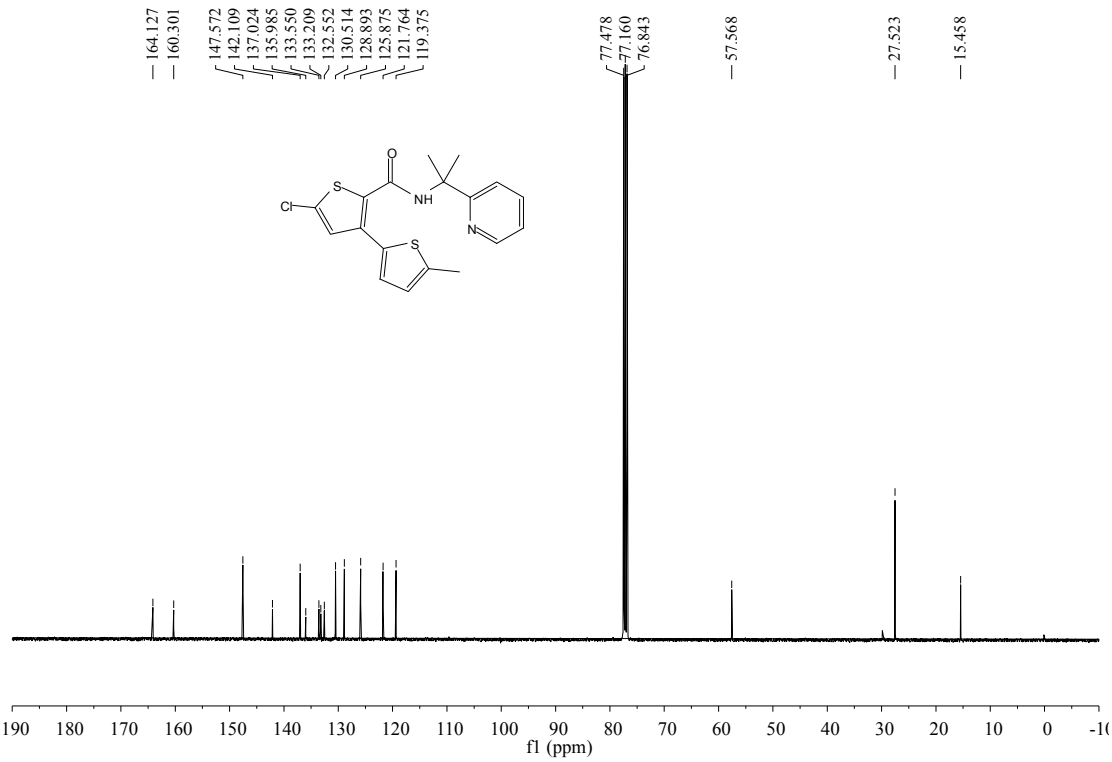

8.318
8.307
7.919
7.617
7.344
7.025
6.718
6.700
6.694
2.482
2.460
1.708
1.00
0.98
1.05
1.04
1.07
0.98
2.03
2.95
3.04
6.04
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.
f1 (ppm)


164.467
161.374
147.710
142.405
141.313
136.875
134.500
134.128
134.057
129.982
128.220
125.689
121.623
119.393
77.478
77.160
76.842
57.433
27.636
15.574
15.431
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1(
f1 (ppm)



3o


8.271
8.260
8.164
7.653
7.634
7.334
7.314
7.260
7.129
7.117
7.112
7.099
7.043
7.035
6.865
6.722
6.716
2.491
1.715
1.00
0.94
1.06
1.03
1.09
1.02
0.94
1.05
3.09
6.06
fl (ppm)


164.127
160.301
147.572
142.109
137.024
135.985
133.550
133.209
132.552
130.514
128.893
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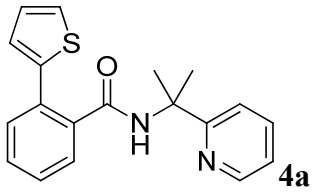
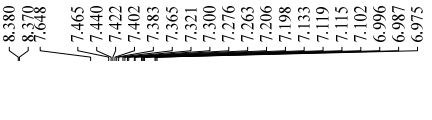
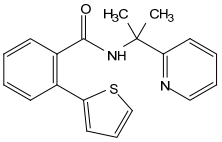
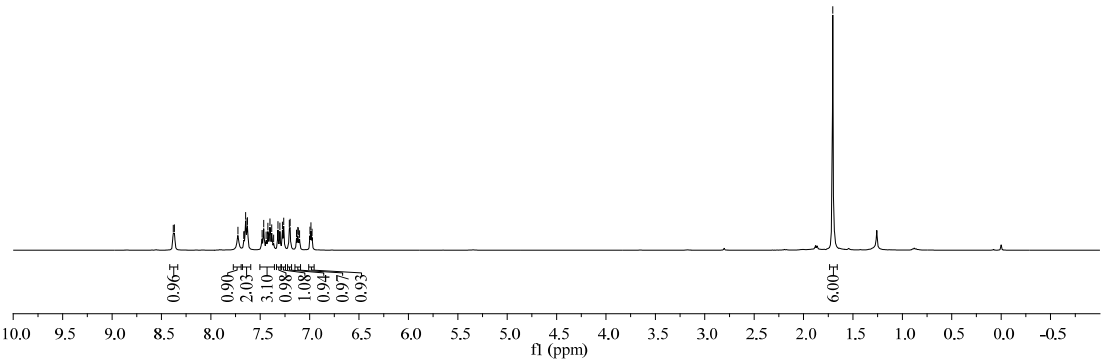
121.764
119.375
77.478
77.160
76.843
57.568
27.523
15.458
fl (ppm)

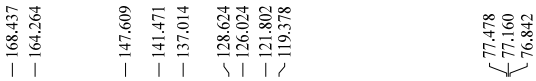


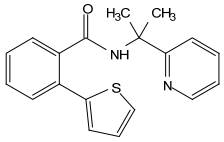
4a

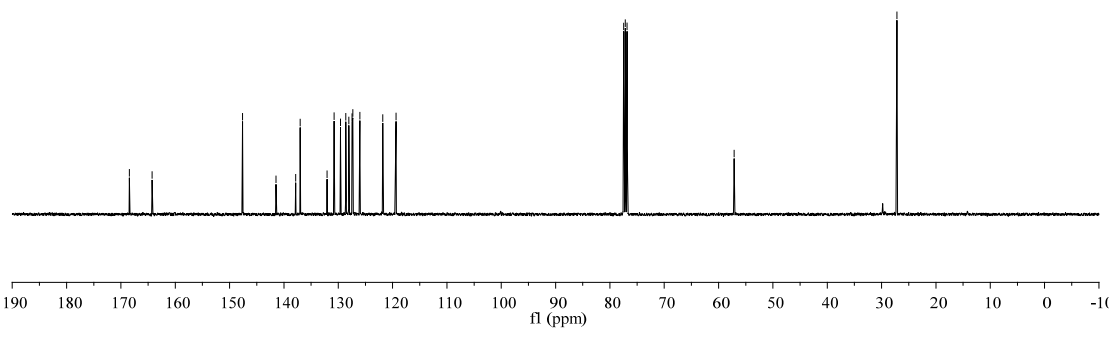

8.380
8.370
7.648
7.465
7.440
7.422
7.402
7.383
7.365
7.321
7.300
7.276
7.263
7.206
7.198
7.133
7.119
7.115
7.102
6.996
6.987
6.975
1.705

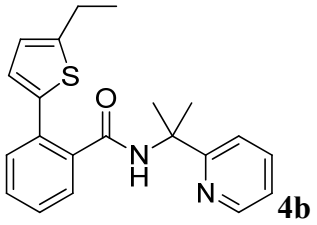



0.96
0.90
2.03
3.10
0.98
1.08
0.94
0.97
0.93
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

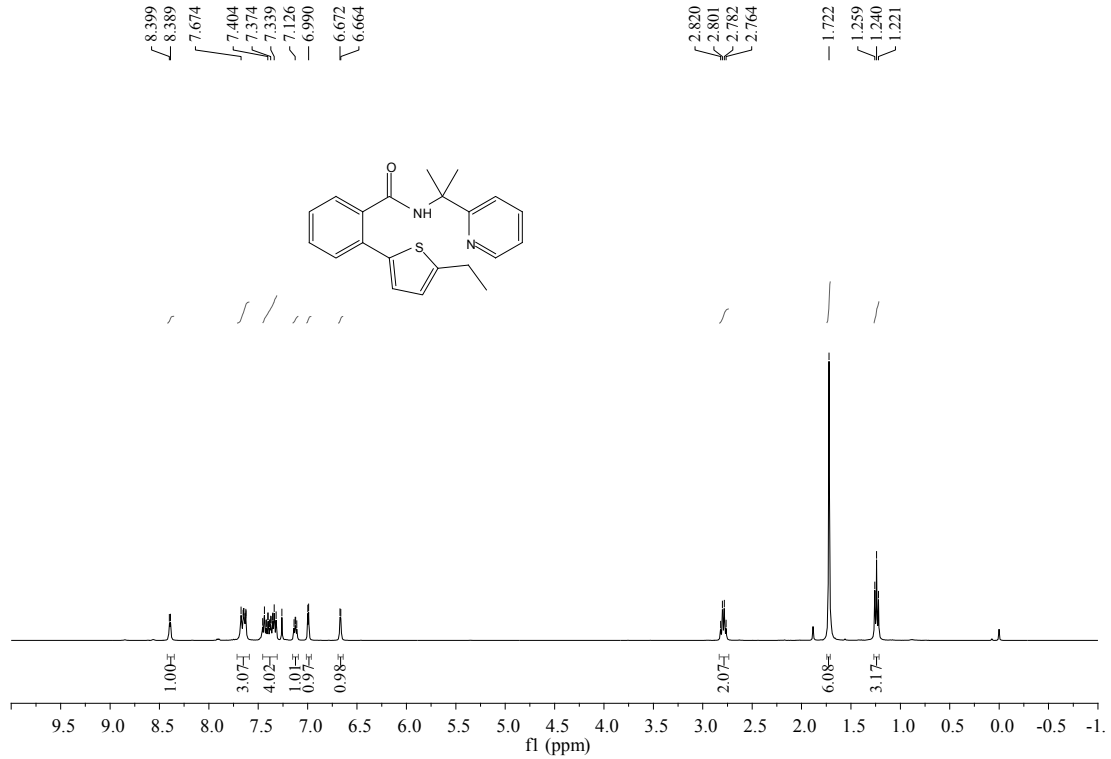

168.437
164.264
147.609
141.471
137.014
128.624
126.024
121.802
119.378
77.478
77.160
76.842
57.129
27.171

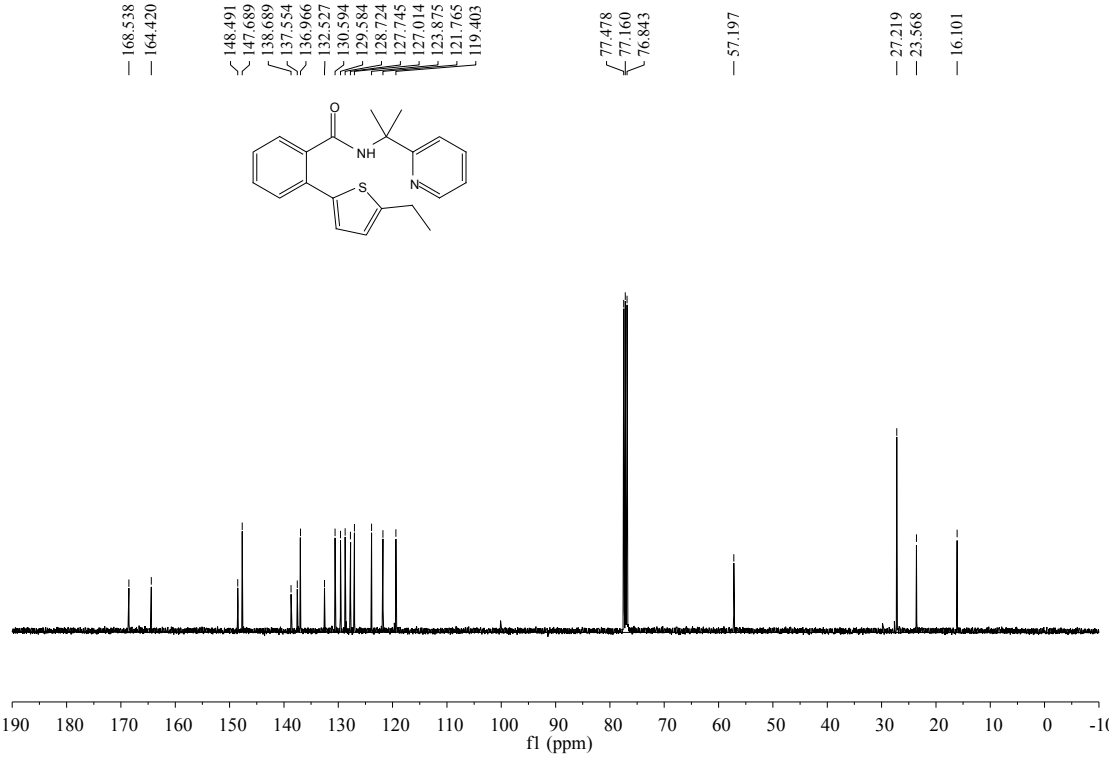


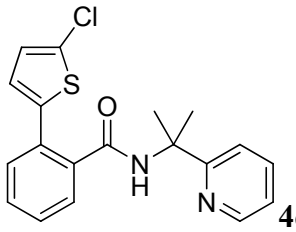

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)



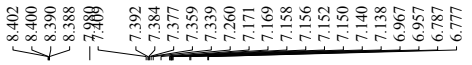
4b

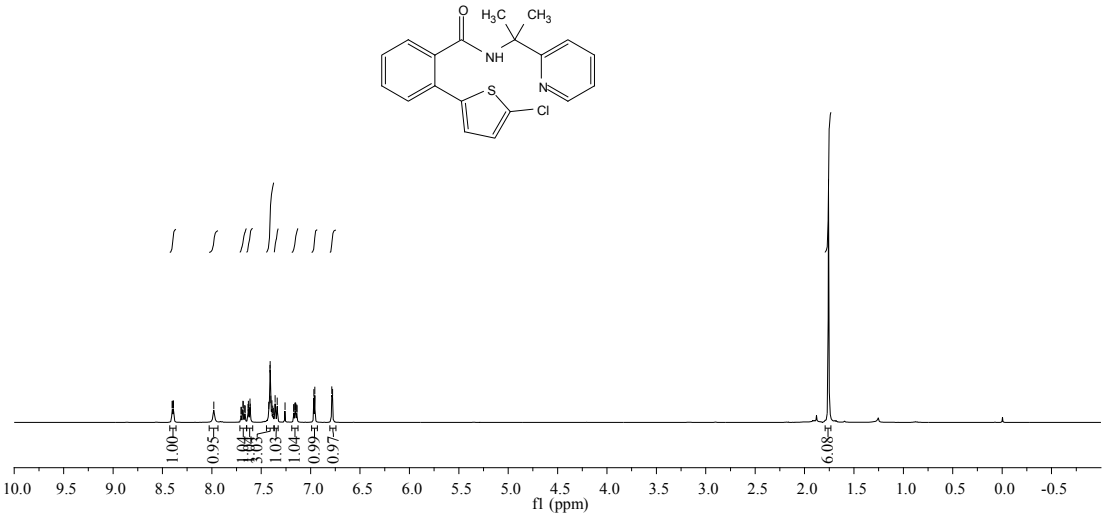

8.399
8.389
7.674
7.404
7.374
7.339
7.126
6.990
6.672
6.664
2.820
2.801
2.782
2.764
1.722
1.259
1.240
1.221
1.00
3.07
4.02
1.01
0.97
0.98
2.07
6.08
3.17
fl (ppm)

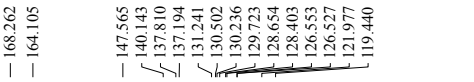

168.538
164.420
148.491
147.689
138.689
137.554
136.966
132.527
130.594
129.584
128.724
127.745
127.014
123.875
121.765
119.403
77.478
77.160
76.843
57.197
27.219
23.568
16.101
fl (ppm)

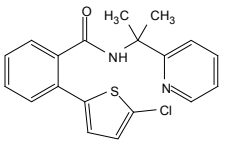

Cl
S
O
N
H
N

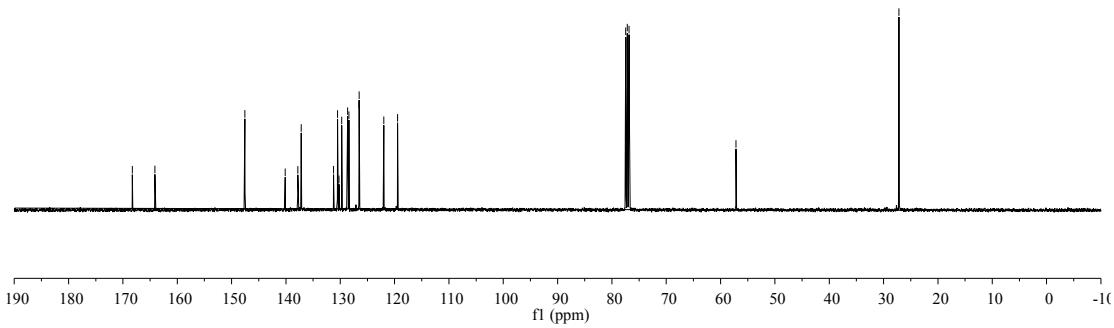
4c

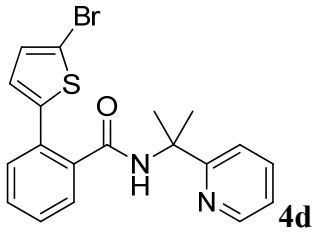

8.402
8.400
8.390
8.388
7.392
7.384
7.377
7.359
7.339
7.260
7.171
7.169
7.158
7.156
7.152
7.150
7.140
7.138
6.967
6.957
6.787
6.777
1.757


O
H3C
CH3
NH
S
Cl
N
1.00
0.95
1.03
1.04
0.99
0.97
6.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

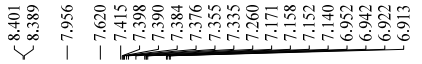

168.262
164.105
147.565
140.143
137.810
137.194
131.241
130.502
130.236
129.723
128.654
128.403
126.553
126.527
121.977
119.440
77.478
77.160
76.843
57.163
27.166


O
H3C
CH3
NH
S
Cl
N


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
S
O
N
H
N

4d


8.401
8.389
7.956
7.620
7.415
7.398
7.390
7.384
7.376
7.355
7.335
7.260
7.171
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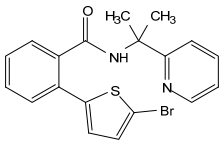
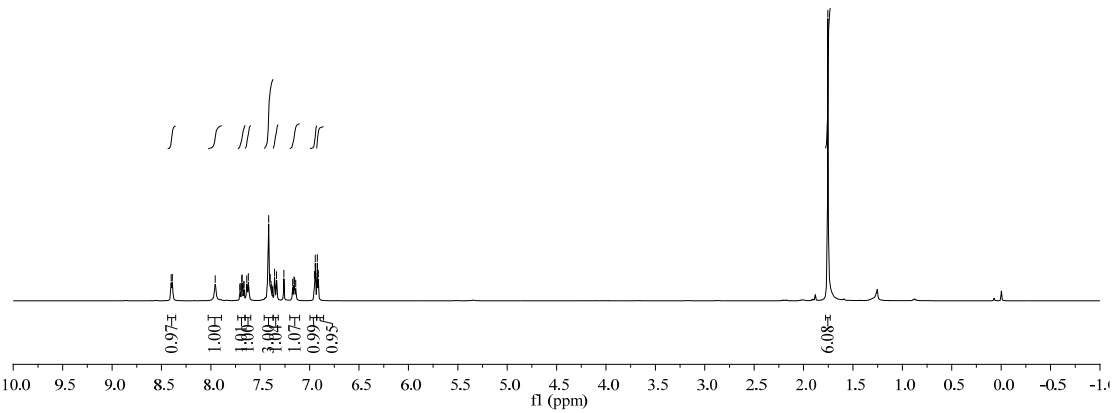
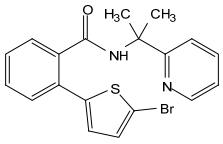
7.152
7.140
6.952
6.942
6.922
6.913
1.754

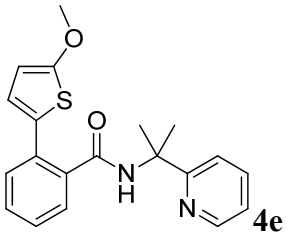

O
H3C
CH3
NH
N
S
Br


0.97
1.00
6.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

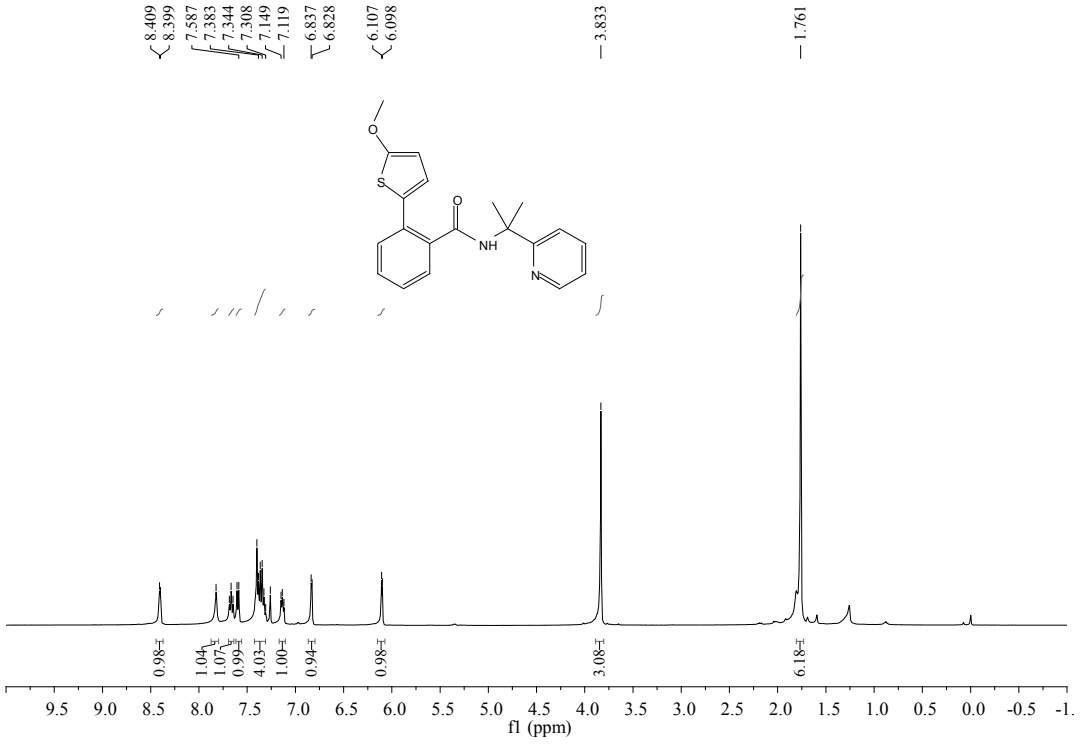

168.230
164.124
147.602
143.110
137.796
137.184
131.230
130.513
130.293
129.736
128.671
128.462
127.538
121.975
119.436
112.493
77.478
77.160
76.843
57.183
27.171

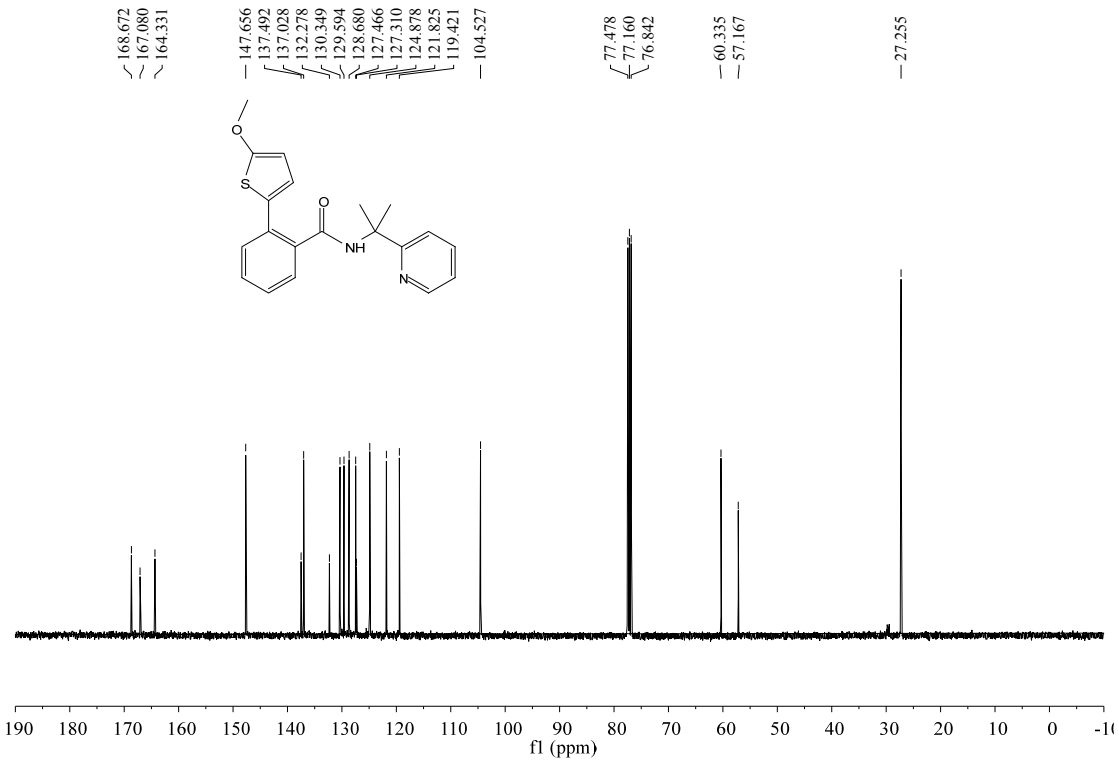

O
H3C
CH3
NH
N
S
Br

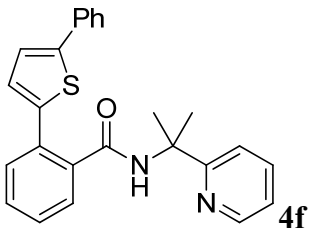
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



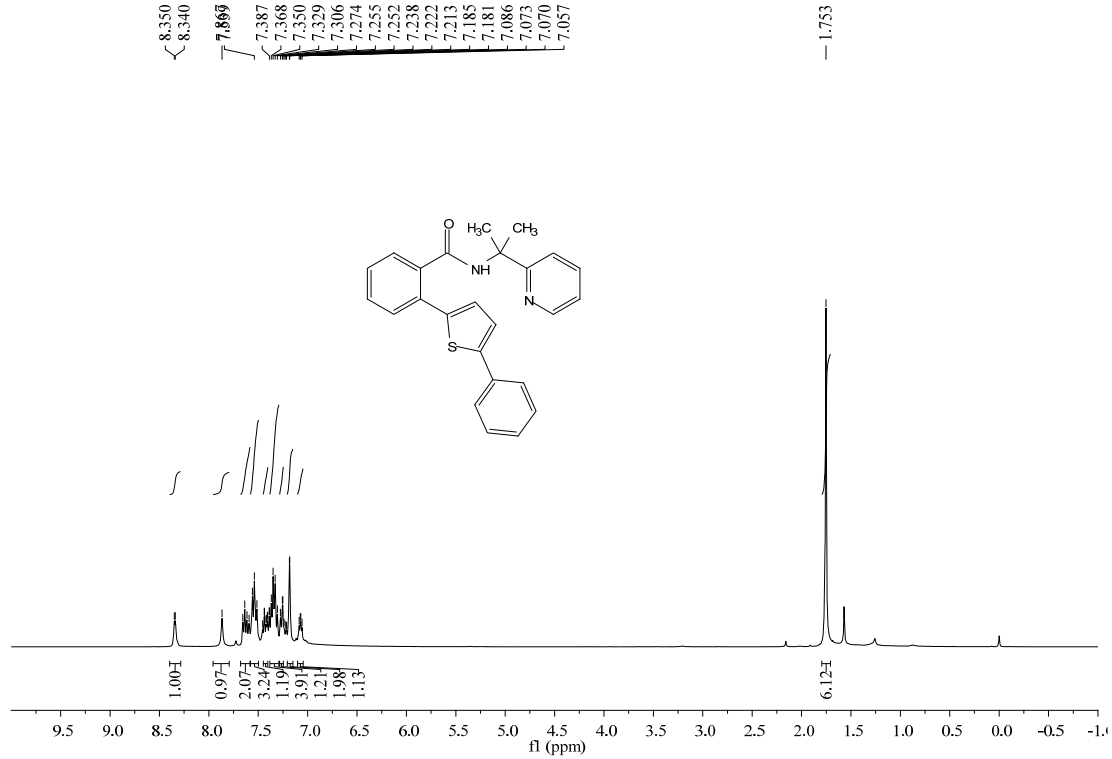
4e

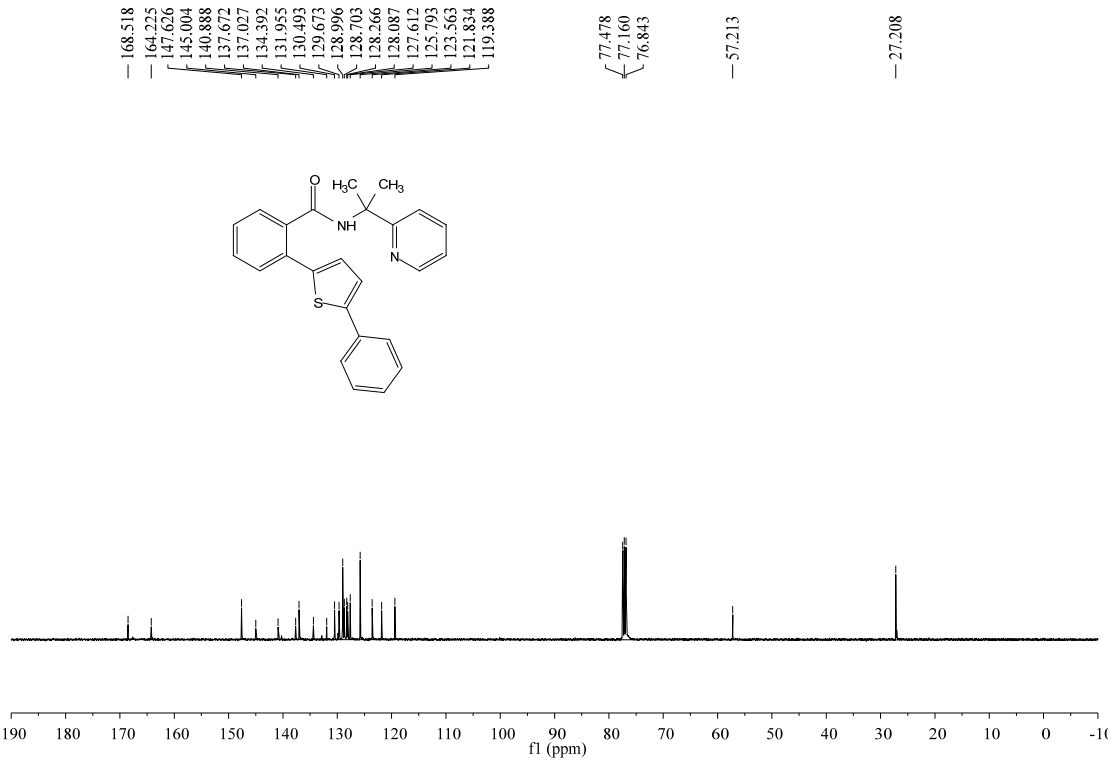

8.409
8.399
7.587
7.383
7.344
7.308
7.149
7.119
6.837
6.828
6.107
6.098
3.833
1.761
0.98
1.04
1.07
0.99
4.03
1.00
0.94
0.98
3.08
6.18
fl (ppm)

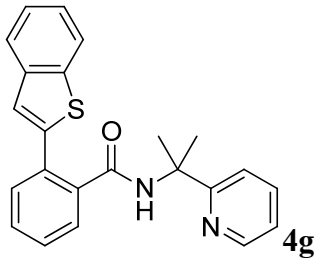

168.672
167.080
164.331
147.656
137.492
137.028
132.278
130.349
129.594
128.680
127.466
127.310
124.878
121.825
119.421
104.527
77.478
77.160
76.842
60.335
57.167
27.255
fl (ppm)


Ph
S
O
N
H
N

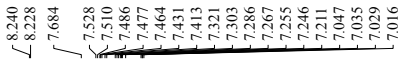
4f

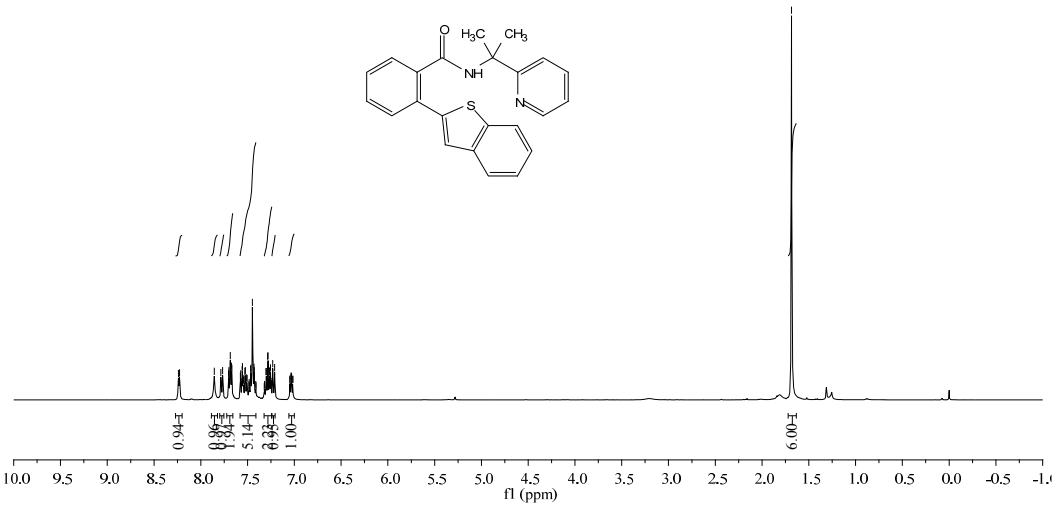

8.350
8.340
7.387
7.368
7.350
7.329
7.306
7.274
7.255
7.252
7.238
7.222
7.213
7.185
7.181
7.086
7.073
7.070
7.057
1.753
O
H3C
CH3
NH
N
S
1.00
0.97
2.07
3.24
1.19
3.91
1.21
1.98
1.13
6.12
fl (ppm)

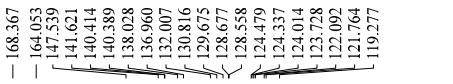

168.518
164.225
147.626
145.004
140.888
137.672
137.027
134.392
131.955
130.493
129.673
128.996
128.703
128.266
128.087
127.612
125.793
123.563
121.834
119.388
77.478
77.160
76.843
57.213
27.208
O
H3C
CH3
NH
N
S
fl (ppm)

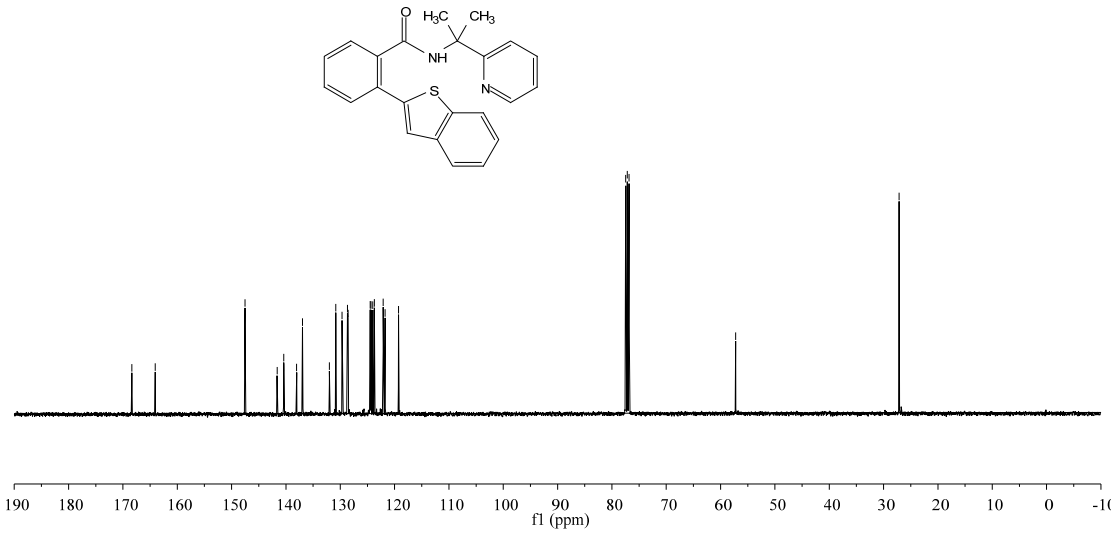


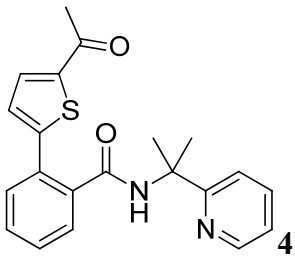
4g


8.240
8.228
7.684
7.528
7.510
7.486
7.477
7.464
7.431
7.413
7.321
7.303
7.286
7.267
7.255
7.246
7.211
7.047
7.035
7.029
7.016
1.685

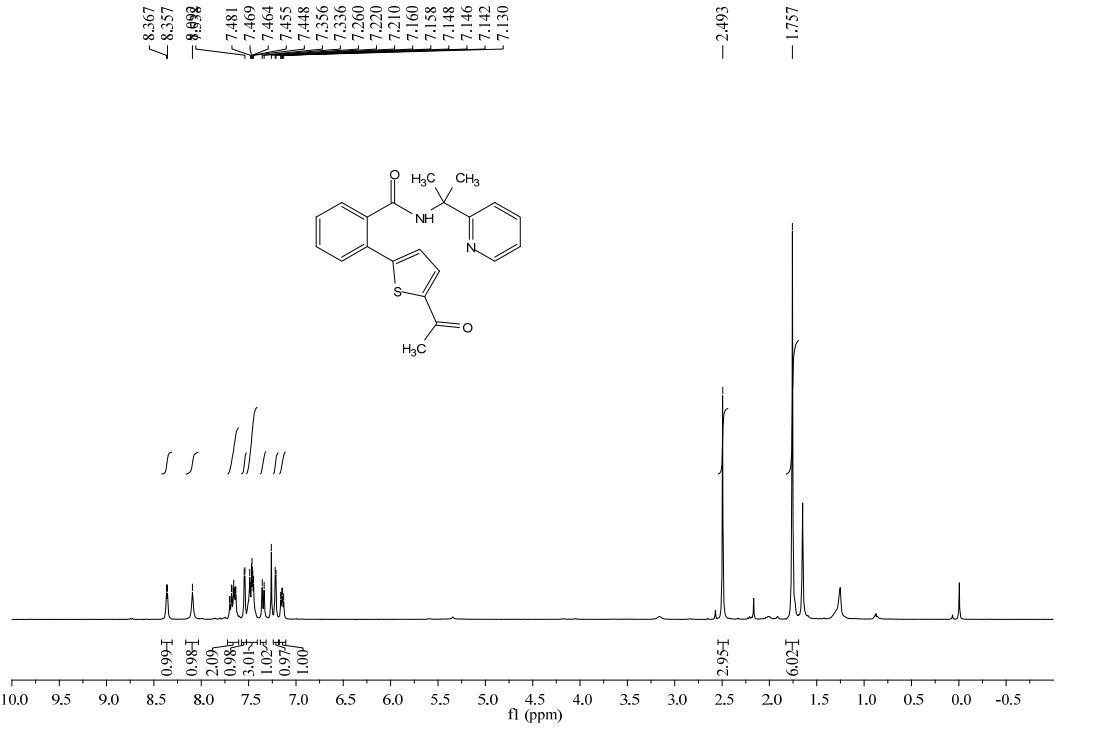

0.94
0.96
1.94
5.14
2.33
1.00
6.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

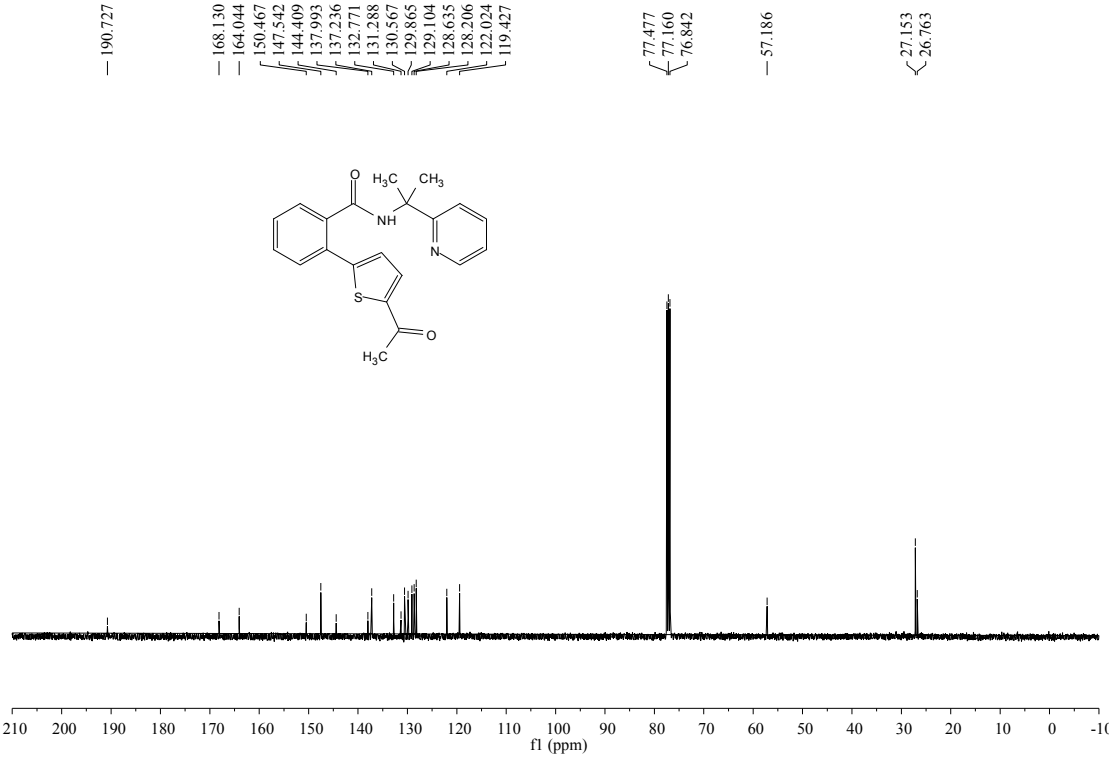

168.367
164.053
147.539
141.621
140.414
140.389
138.028
136.960
132.007
130.816
129.675
128.677
128.558
124.479
124.337
124.014
123.728
122.092
121.764
119.277
77.478
77.160
76.843
57.222
27.132

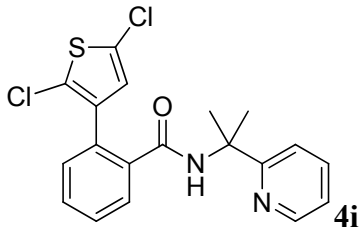

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)



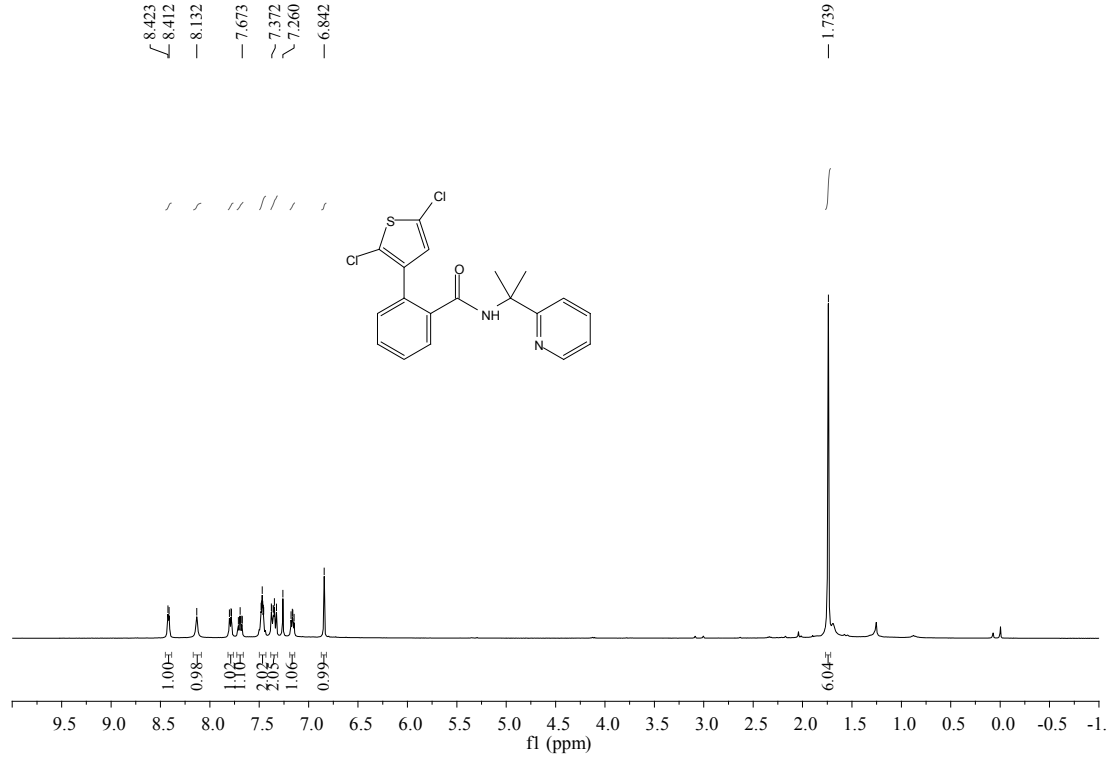
4h

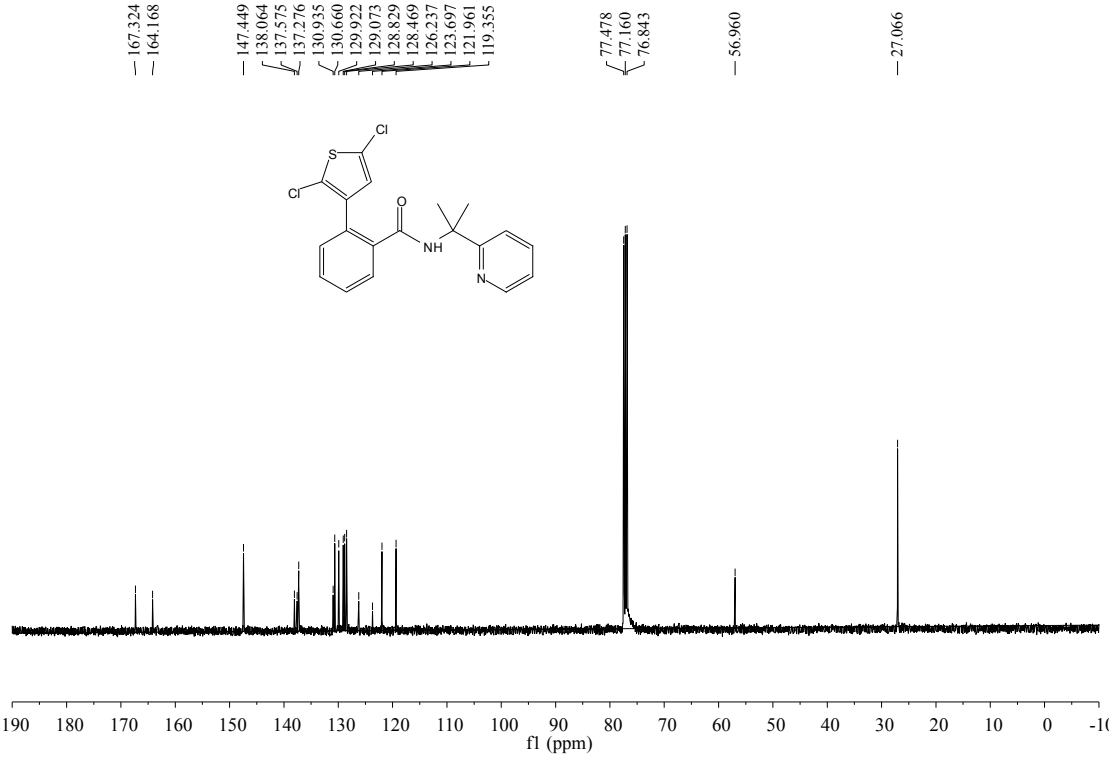

8.367
8.357
7.481
7.469
7.464
7.455
7.448
7.356
7.336
7.260
7.220
7.210
7.160
7.158
7.148
7.146
7.142
7.130
2.493
1.757
0.99
0.98
2.09
0.98
3.01
1.02
0.97
1.00
2.95
6.02
fl (ppm)

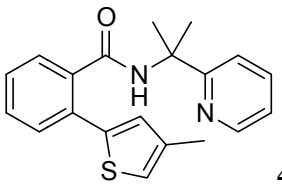

190.727
168.130
164.044
150.467
147.542
144.409
137.993
137.236
132.771
131.288
130.567
129.865
129.104
128.635
128.206
122.024
119.427
77.477
77.160
76.842
57.186
27.153
26.763
fl (ppm)


Cl
S
Cl
O
N
H
N

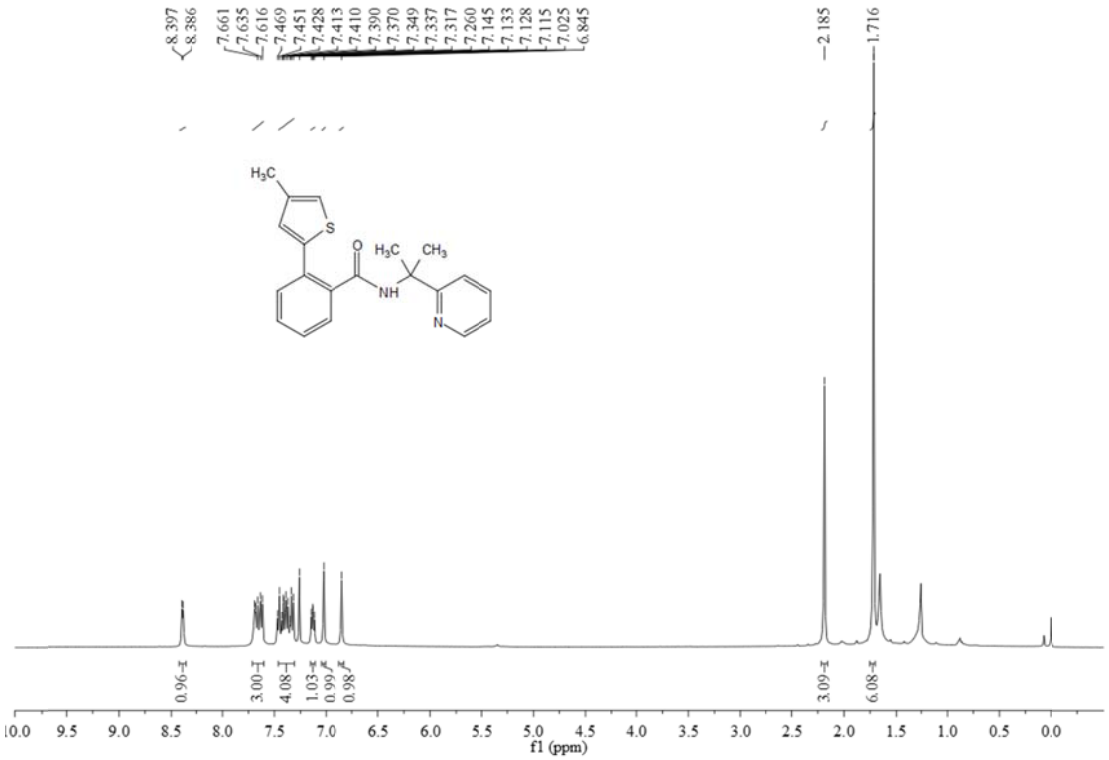
4i

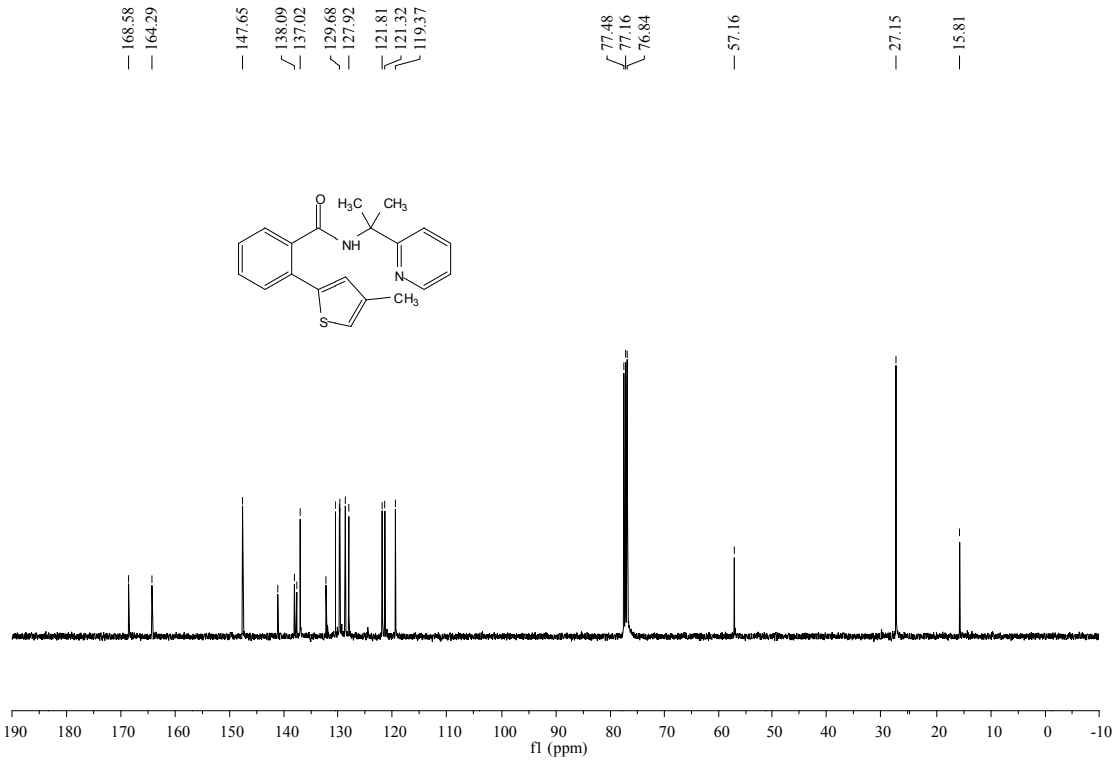

8.423
8.412
8.132
7.673
7.372
7.260
6.842
1.739
1.00
0.98
1.02
1.10
2.02
2.05
1.06
0.99
6.04
fl (ppm)

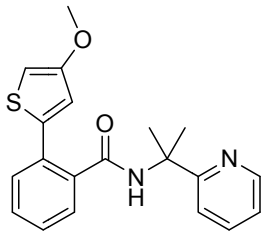

167.324
164.168
147.449
138.064
137.575
137.276
130.935
130.660
129.922
129.073
128.829
128.469
126.237
123.697
121.961
119.355
77.478
77.160
76.843
56.960
27.066
fl (ppm)



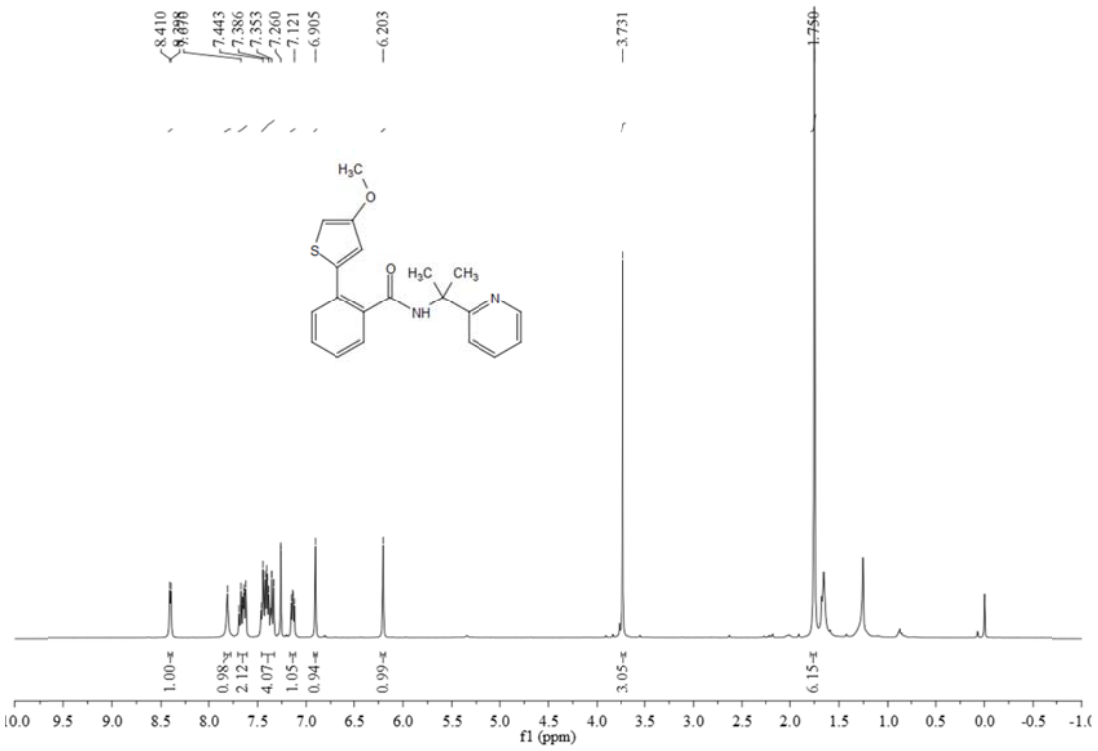
4j

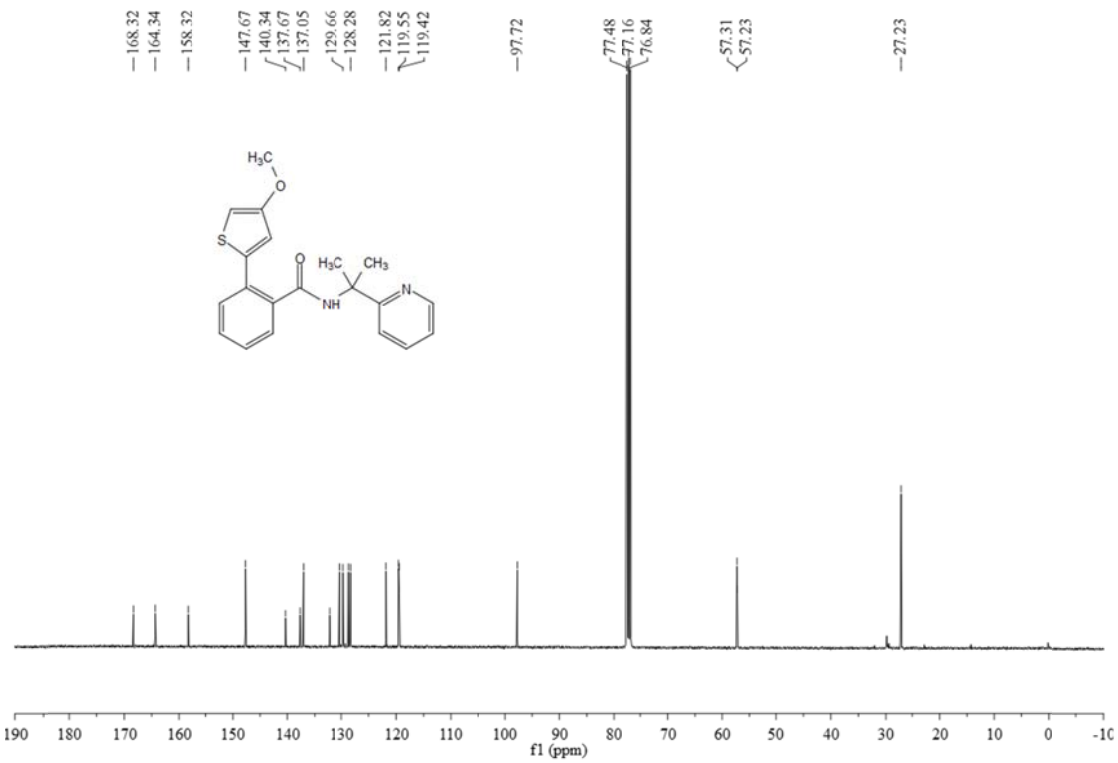

8.397
8.386
7.661
7.635
7.616
7.469
7.451
7.428
7.413
7.410
7.390
7.370
7.349
7.337
7.317
7.260
7.145
7.133
7.128
7.115
7.025
6.845
2.185
1.716
0.96
3.00
4.08
1.03
0.99
0.98
3.09
6.08
f1 (ppm)

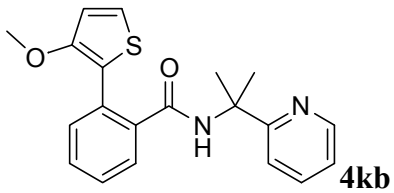

168.58
164.29
147.65
138.09
137.02
129.68
127.92
121.81
121.32
119.37
77.48
77.16
76.84
57.16
27.15
15.81
f1 (ppm)



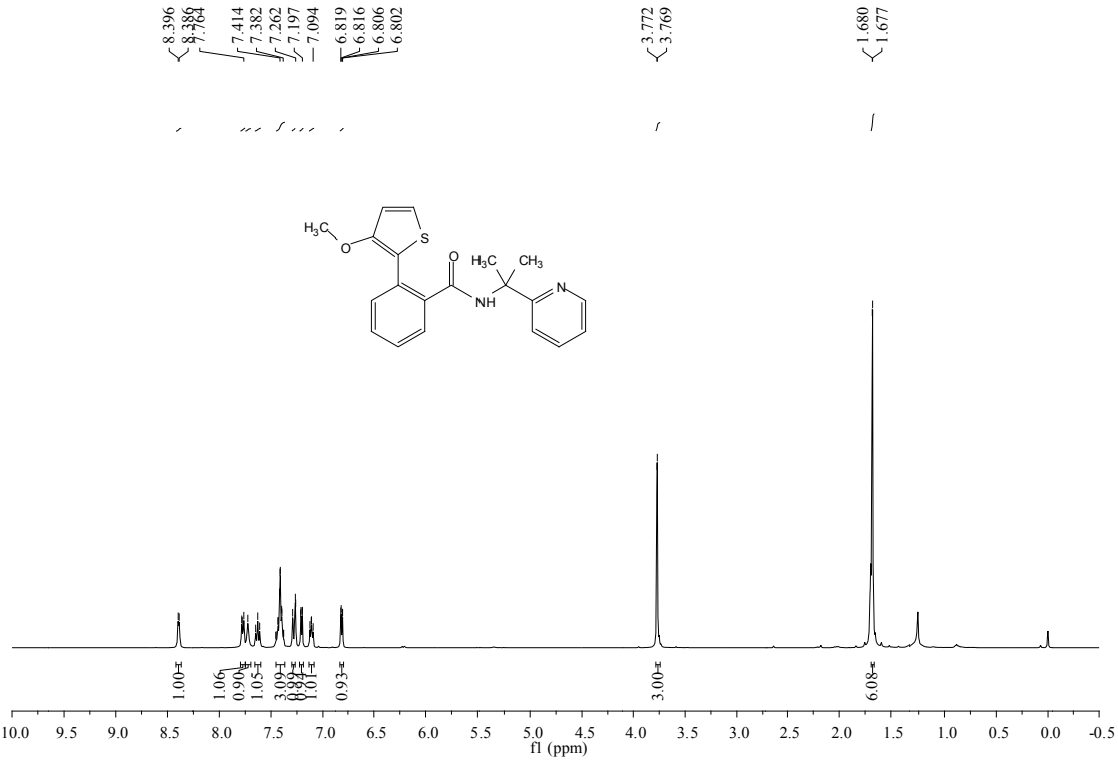
4ka


8.410
7.443
7.386
7.353
7.260
7.121
6.905
6.203
3.731
1.750
1.00
0.98
2.12
4.07
1.05
0.94
0.99
3.05
6.15
f1 (ppm)


168.32
164.34
158.32
147.67
140.34
137.67
137.05
129.66
128.28
121.82
119.55
119.42
97.72
77.48
77.16
76.84
57.31
57.23
27.23
f1 (ppm)



4kb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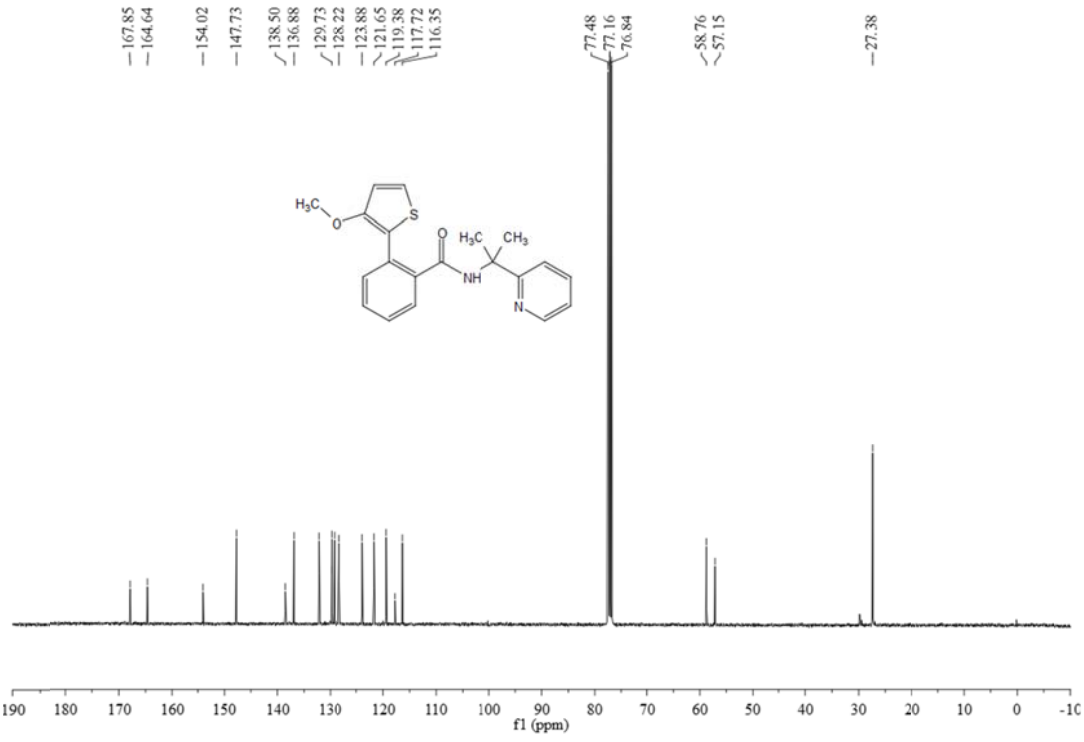
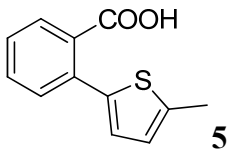
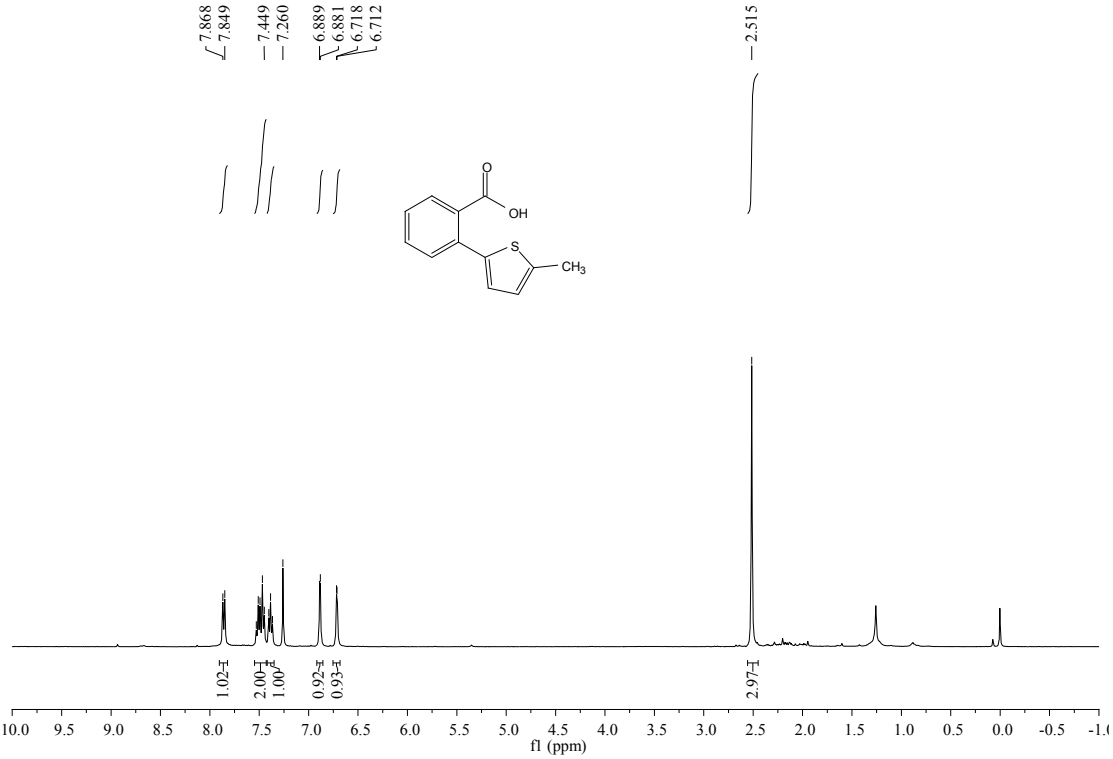
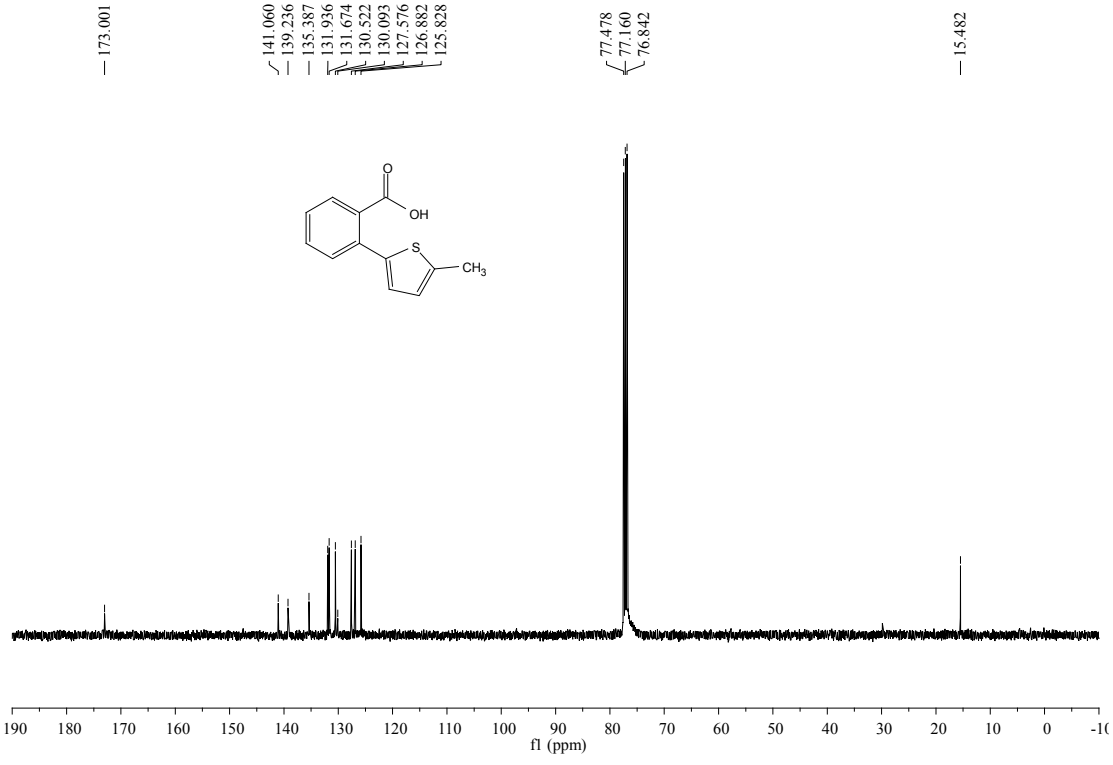
8.386
8.384
7.764
7.414
7.382
7.262
7.197
7.094
6.819
6.816
6.806
6.802
3.772
3.769
1.680
1.677
1.00
1.06
0.90
1.05
3.09
3.04
0.94
1.01
0.93
3.00
6.08
fl (ppm)


167.85
164.64
154.02
147.73
138.50
136.88
129.73
128.22
123.88
121.65
119.38
117.72
116.35
77.48
77.16
76.84
58.76
57.15
27.38
fl (ppm)


COOH
S

5


7.868
7.849
7.449
7.260
6.889
6.881
6.718
6.712
2.515
O
OH
S
CH3
1.02
2.00
1.00
0.92
0.93
2.97
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


173.001
141.060
139.236
135.387
131.936
131.674
130.522
130.093
127.576
126.882
125.828
77.478
77.160
76.842
15.482
O
OH
S
CH3
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)