Palladium-Catalyzed Selective Defluorinative Arylation for the Stereospecific Synthesis of β-Fluoroacrylamides

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Supplementary data

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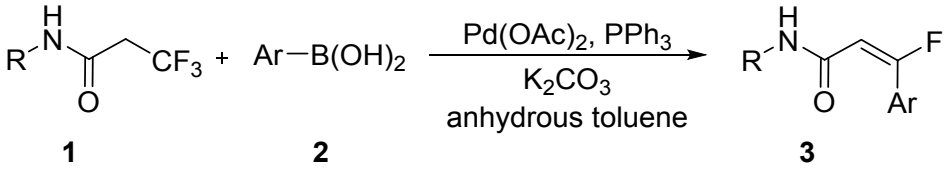
1. General Information.

Chemicals were either purchased or purified by standard techniques. ^{1}H NMR and ^{13}C NMR spectra were measured on 500 or 400 MHz spectrometer (^{1}H: 500 or 400 MHz, ^{13}C: 125 MHz), using DMSO-*d6* as the solvent with tetramethylsilane (TMS) as an internal standard at room temperature. Chemical shifts are given in δ relative to TMS, the coupling constants *J* are given in Hz. High resolution mass spectra were recorded on an ESI-Q-TOF mass spectrometry. All reactions were conducted under nitrogen atmosphere using standard Schlenk techniques. Melting points were measured on X4 melting point apparatus and uncorrected. Column chromatography was performed using EM Silica gel 60 (300-400 mesh).

2. Typical Experimental Procedure for the Synthesis of β-Fluoroacrylamides Derivatives 3a–3x

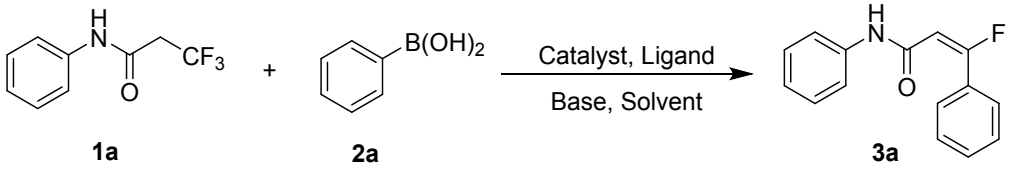


1 **2** **3**

To a flame-dried Schlenk tube with a magnetic stirring bar were charged **1** (0.2 mmol), **2** (0.3 mmol), $Pd(OAc)_2$ (4.5 mg, 0.02 mmol), PPh_3 (10.6 mg, 0.04 mmol), K_2CO_3 (110.4 mg, 0.8 mmol) in anhydrous toluene (2 mL). The mixture was stirred at 60 ^{o}C for 12 hours. After the reaction was completed, the solvent was removed by a rotary evaporator to obtain a residue, which was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired products **3a-3x**.

3. Optimization Details.

Table 1. Optimization of reaction conditions. [a]

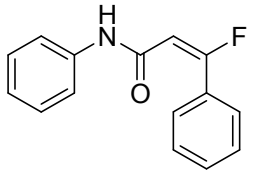


1a **2a** **3a**

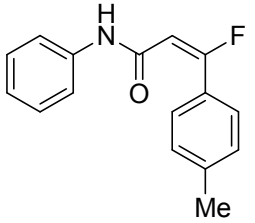
Entry	Catalyst	Ligand	Base	Solvent	Yield (%)
1	CuI	-	K_3PO_4	Toluene	NR
2	$Pd(OAc)_2$	-	K_3PO_4	Toluene	30
3	$Pd(OAc)_2$	PPh_3	K_3PO_4	Toluene	48
4	$Pd(OAc)_2$	X-Phos	K_3PO_4	Toluene	33
5	$Pd(OAc)_2$	PCy_3	K_3PO_4	Toluene	35
6	$Pd(OAc)_2$	PBu_3	K_3PO_4	Toluene	30
7	$Pd(PPh_3)_2Cl_2$	PPh_3	K_3PO_4	Toluene	41
8	$PdCl_2$	PPh_3	K_3PO_4	Toluene	35
9	$Pd(PPh_3)_4$	PPh_3	K_3PO_4	Toluene	36
10	$Pd_2(dba)_3$	PPh_3	K_3PO_4	Toluene	35
11	$Pd(OAc)_2$	PPh_3	Cs_2CO_3	Toluene	40
12	$Pd(OAc)_2$	PPh_3	K_2CO_3	Toluene	65
13	$Pd(OAc)_2$	PPh_3	*t*-BuOK	Toluene	Trace
14	$Pd(OAc)_2$	PPh_3	DBU	Toluene	ND
15	$Pd(OAc)_2$	PPh_3	KOH	Toluene	53
16	$Pd(OAc)_2$	PPh_3	K_2CO_3	MeCN	48
17	$Pd(OAc)_2$	PPh_3	K_2CO_3	DMSO	trace
18	$Pd(OAc)_2$	PPh_3	K_2CO_3	DMF	trace
19	$Pd(OAc)_2$	PPh_3	K_2CO_3	NMP	NR
20	$Pd(OAc)_2$	PPh_3	K_2CO_3	anhydrous Toluene	75
21[b]	$Pd(OAc)_2$	PPh_3	K_2CO_3	anhydrous Toluene	70
22[c]	$Pd(OAc)_2$	PPh_3	K_2CO_3	anhydrous Toluene	91
23[d]	$Pd(OAc)_2$	PPh_3	K_2CO_3	anhydrous Toluene	NR
24[c]	-	PPh_3	K_2CO_3	anhydrous Toluene	ND
25[c]	$Pd(OAc)_2$	PPh_3	-	anhydrous Toluene	ND

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol), catalyst (10 mol%), Liand (20 mol%), base (4.0 equiv.), solvent 2 mL at 80 °C for 12 h, isolated yields. [b] At 100 °C. [c] At 60 °C. [d] At 25 °C.

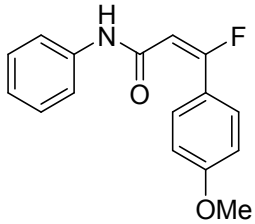
4. Analytical Data for All Compounds



(E)-3-fluoro-N,3-diphenylacrylamide (**3a**): White solid (43.9 mg, 91% yield); m.p.: 111.6-112.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.59 (s, 1H), 7.50-7.43 (m, 5H), 7.34-7.30 (m, 2H), 7.16-7.12 (m, 1H), 6.00 (d, *J* = 20.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.4 (d, *J* = 260.0 Hz), 162.7 (d, *J* = 18.8 Hz), 137.7, 131.2, 130.1, 128.9, 128.7, 128.4, 124.6, 120.1, 104.8 (d, *J* = 28.8 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -83.88; LRMS (EI 70 ev) m/z (%): 241 (M^+, 23), 149 (100), 101 (40), 93 (90), 75 (9), 65 (8). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{12}FNONa^+$: 264.0795; found: 264.0800.

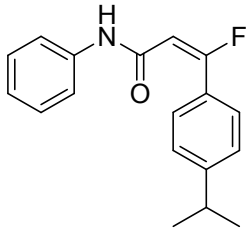


(E)-3-fluoro-N-phenyl-3-(p-tolyl)acrylamide (**3b**): White solid (42.3 mg, 83% yield); m.p.: 162.2-162.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.2 Hz, 2H), 7.37-7.35 (m, 3H), 7.26-7.22 (m, 2H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.05 (s, 1H), 5.87 (d, *J* = 20.0 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6 (d, *J* = 261.3 Hz), 162.7 (d, *J* = 20.0 Hz), 141.8, 137.7, 129.1, 129.0, 128.7, 127.2, 124.5, 120.0, 104.8 (d, *J* = 30.0 Hz), 21.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -83.59; LRMS (EI 70 ev) m/z (%): 255 (M^+, 21), 163 (100), 133 (21), 115 (33), 93 (62), 65 (8). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNONa^+$: 278.0952; found:278.0957.

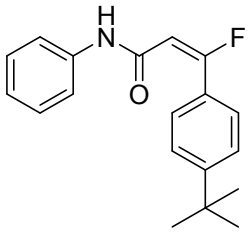


(E)-3-fluoro-3-(4-methoxyphenyl)-N-phenylacrylamide (**3c**): Light-yellow solid (42.3

mg, 78% yield); m.p.: 139.0-139.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.0 Hz, 2H), 7.58 (s, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.34-7.29 (m, 2H), 7.14-7.11(m, 1H), 6.94 (d, *J* = 8.0 Hz, 2H), 5.89 (d, *J* = 20.0 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.7 (d, *J* = 260.0 Hz), 163.0 (d, *J* = 21.3 Hz), 161.8, 137.8, 136.6, 130.5, 124.4, 122.1, 120.0, 113.7, 103.2 (d, *J* = 30.0 Hz), 55.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -82.89; LRMS (EI 70 ev) m/z (%): 271 (M^+, 9), 180 (11), 179 (100), 136 (11), 93 (12). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNO_2Na^+$: 294.0901; found: 294.0911.

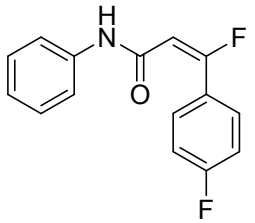


(E)-3-fluoro-3-(4-isopropylphenyl)-N-phenylacrylamide (**3d**): Light-yellow solid (37.3 mg, 66% yield); m.p.: 176.4-179.0°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1H), 7.69 (d, *J* = 10.0 Hz, 2H), 7.62 (d, *J* = 8.0 Hz, 2H), 7.36-7.30 (m, 4H), 7.08 (d, *J* = 14.0 Hz, 1H), 6.24 (d, *J* = 23.2 Hz, 1H), 2.98-2.91 (m, 1H), 1.24 (d, *J* = 2.0 Hz, 3H), 1.22 (d, *J* = 2.0 Hz, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.3 (d, *J* = 253.8 Hz), 161.8 (d, *J* = 21.3 Hz), 151.5, 139.0, 128.7, 128.5, 127.6, 126.0, 123.4, 119.3, 104.5 (d, *J* = 28.8 Hz), 33.4. 23.5; ^{19}F NMR (470 MHz, DMSO-d_6) δ -85.64; LRMS (EI 70 ev) m/z (%): 283 (M^+, 36), 192 (13), 149 (100), 146 (17), 133 (20), 93 (81). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{18}FNONa^+$: 306.1265; found: 306.1262.

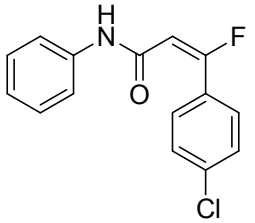


(E)-3-(4-(tert-butyl)phenyl)-3-fluoro-N-phenylacrylamide (**3e**): Light-yellow solid (35.6 mg, 60% yield); m.p.: 215.7-216.2°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.24 (s, 1H), 7.71-7.69 (m, 2H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.34-7.30 (m, 2H), 7.09-7.05 (m, 1H), 6.24 (d, *J* = 24.0 Hz, 1H), 1.31 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 165.2 (d, *J* = 253.8 Hz), 161.8 (d, *J* = 21.3 Hz), 153.7, 139.0,

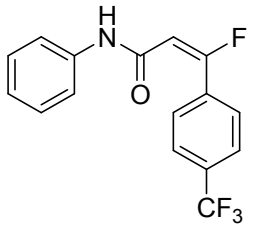
128.7, 127.2, 125.6, 124.8, 123.4, 119.3, 104.6 (d, J = 30.0 Hz), 34.6. 30.8; ^{19}F NMR (470 MHz, DMSO-d_6) δ -85.91; LRMS (EI 70 ev) m/z (%): 297 (M^+, 35), 205 (100), 175 (11), 133 (11), 93 (86), 57 (32). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{19}H_{21}FNO^+$: 298.1602; found:298.1611



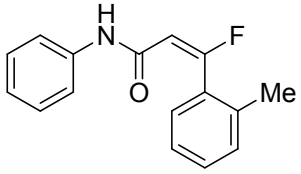
(E)-3-fluoro-3-(4-fluorophenyl)-N-phenylacrylamide (**3f**): White solid (31.1 mg, 60% yield); m.p.: 136.9-139.7°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81-7.78 (m, 2H), 7.54 (s, 1H), 7.47 (d, J = 8.0 Hz, 2H), 7.35-7.30 (m, 2H), , 7.17-7.10 (m, 3H), 5.97 (d, J = 20.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1 (d, J = 215.0 Hz), 164.1 (d, J = 205.0 Hz), 162.4 (d, J = 20.0 Hz), 137.5, 131.1, 129.1, 126.1 (d, J = 23.8 Hz), 124.7, 120.1, 115.6, 104.3 (d, J = 30.0 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -82.58 (s, 1F), -107.48 (s, 1F); LRMS (EI 70 ev) m/z (%): 259 (M^+, 20), 168 (10), 167 (100), 139 (17), 119 (35), 93 (63). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}F_2NO^+$: 260.0881; found: 260.0877.



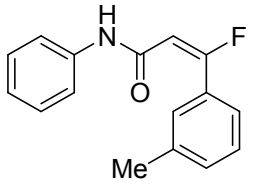
(E)-3-(4-chlorophenyl)-3-fluoro-N-phenylacrylamide (**3g**): White solid (28.3 mg, 51% yield); m.p.: 132.4-133.6°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.29 (s, 1H), 7.78 (d, J = 8.0 Hz, 2H), 7.61-7.55 (m, 4H), 7.35-7.30 (m, 2H), 7.11-7.06 (m, 1H), 6.32 (d, J = 24.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 164.1 (d, J = 256.3 Hz), 161.5 (d, J = 21.3 Hz), 138.8, 135.6, 130.5, 130.4, 128.8, 128.2, 123.6, 119.3, 105.8 (d, J = 28.8 Hz); ^{19}F NMR (470 MHz, DMSO-d_6) δ -85.99; LRMS (EI 70 ev) m/z (%): 275 (M^+, 16), 277 (5), 195 (34), 183 (100), 120 (50), 93 (86). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}FNOCl^+$: 276.0586; found: 276.0592.



(E)-3-fluoro-N-phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (**3h**): Light-yellow solid (40.2 mg, 65% yield); m.p.: 219.2-219.5°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.35 (s, 1H), 7.95 (d, J = 8.0 Hz, 2H), 7.85 (d, J = 8.0 Hz, 2H), 7.61 (d, J = 8.0 Hz, 2H), 7.34-7.31 (m, 2H), 7.10-7.07 (m, 1H), 6.43 (d, J = 24.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.7 (d, J = 255.0 Hz), 161.2 (d, J = 21.3 Hz), 138.7, 130.4 (d, J = 27.5 Hz), 130.7, 129.5, 128.7, 124.9, 123.7, 121.6 (d, J = 266.3 Hz), 119.4, 106.9 (d, J = 27.5 Hz); ^{19}F NMR (470 MHz, DMSO-d_6) δ -61.57 (s, 3F), -86.49 (s, 1F); LRMS (EI 70 ev) m/z (%): 309 (M^+, 18), 218 (10), 217 (100), 169 (49), 120 (19), 93 (69). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{16}H_{12}F_4NO^+$: 310.0850; found: 310.0859.

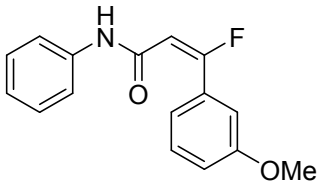


(E)-3-fluoro-N-phenyl-3-(o-tolyl)acrylamide (**3i**): White solid (41.8 mg, 82% yield); m.p.: 95.1-96.0°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53-7.46 (m, 2H), 7.41-7.37 (m, 2H), 7.35-7.26 (m, 5H), 7.12 (s, 1H), 6.11 (d, J = 18.0 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.7 (d, J = 265.0 Hz), 162.2 (d, J = 17.5 Hz), 137.5, 131.2, 130.8, 130.3, 130.1, 130.0, 128.9, 126.1, 124.4, 119.8, 107.2 (d, J = 27.5 Hz), 19.6; ^{19}F NMR (470 MHz, $CDCl_3$) δ -72.73; LRMS (EI 70 ev) m/z (%): 255 (M^+, 9), 164 (11), 163 (93), 133 (29), 115 (57), 65 (11). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNONa^+$: 278.0952; found:278.0942.

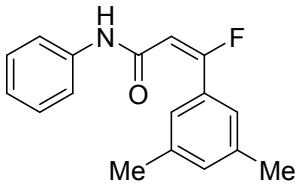


(E)-3-fluoro-N-phenyl-3-(m-tolyl)acrylamide (**3j**): White solid (40.8 mg, 80% yield); m.p.: 146.1-146.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.55-7.52 (m, 2H),

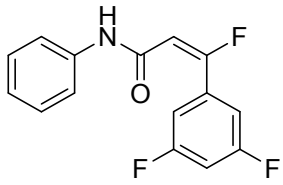
7.42 (d, J = 8.0 Hz, 2H), 7.34-7.29 (m, 4H), 7.15-7.12 (m, 1H), 5.96 (d, J = 20.0 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5 (d, J = 260.0 Hz), 162.8 (d, J = 20.0 Hz), 138.2, 137.7, 132.1, 130.0, 129.8, 128.9, 128.3, 126.0, 124.5, 120.1, 104.8 (d, J = 28.8 Hz), 21.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -83.51; LRMS (EI 70 ev) m/z (%): 255 (M^+, 27), 164 (11), 163 (100), 133 (23), 115 (36), 93 (54). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNONa^+$: 278.0952; found:278.0944.



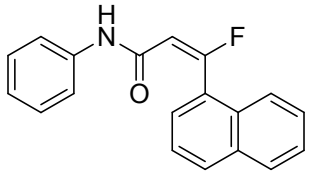
(E)-3-fluoro-3-(3-methoxyphenyl)-N-phenylacrylamide (**3k**): White solid (35.8 mg, 66% yield); m.p.: 103.9-104.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.43 (d, J = 8.0 Hz, 2H), 7.35-7.28 (m, 5H), 7.13-7.03 (m, 2H), 6.00 (d, J = 20.0 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.7 (d, J = 260.0 Hz), 162.6 (d, J = 21.3 Hz), 159.4, 137.6, 131.2, 129.5, 129.0, 124.6, 121.1, 120.0, 117.5, 113.5, 105.1 (d, J = 28.8 Hz), 55.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -84.72; LRMS (EI 70 ev) m/z (%): 271 (M^+, 19), 179 (100), 136 (23), 108 (18), 107 (12), 93 (64). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNO_2Na^+$: 294.0901; found: 294.0894.



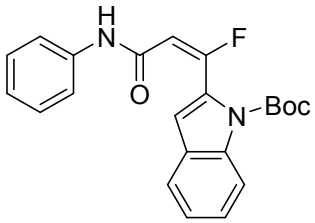
(E)-3-(3,5-dimethylphenyl)-3-fluoro-N-phenylacrylamide (**3l**): White solid (44.7 mg, 83% yield); m.p.: 148.5-149.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.40 (d, J = 8.4 Hz, 2H), 7.31-7.29 (m, 4H), 7.14-7.11 (m, 2H), 5.96 (d, J = 20.4 Hz, 1H), 2.34 (s, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6 (d, J = 262.5 Hz), 162.9 (d, J = 20.0 Hz), 138.2, 137.7, 133.0, 129.9, 129.0, 126.4, 124.5, 120.0, 104.8 (d, J = 28.8 Hz), 21.2; ^{19}F NMR (470 MHz, $CDCl_3$) δ -83.08; LRMS (EI 70 ev) m/z (%): 269 (M^+, 23), 177 (100), 133 (23), 129 (17), 128 (11), 93 (40). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{16}FNONa^+$: 292.1108; found: 292.1118.



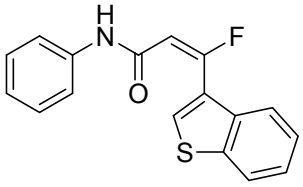
(E)-3-(3,5-difluorophenyl)-3-fluoro-N-phenylacrylamide (**3m**): White solid (19.9 mg, 36% yield); m.p.: 117.2-118.8°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.0 Hz, 2H), 7.40-7.34 (m, 4H), 7.30-7.29 (m, 1H), 7.19-7.16 (m, 1H), 6.96-6.92 (m, 1H), 6.07 (d, *J* = 24.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.6 (d, *J* = 236.3 Hz), 165.2 (d, *J* = 208.8 Hz), 161.5 (d, *J* = 15.0 Hz), 156.3. (d, *J* = 236.3 Hz), 129.2, 120.2, 119.6 (d, *J* = 6.3 Hz), 118.6 (d, *J* = 6.3 Hz), 106.5 (d, *J* = 25.0 Hz), 106.0 (d, *J* = 27.5 Hz), 104.2 (d, *J* = 25.0 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -85.32 (s, 1F), -108.55 (s, 2F); LRMS (EI 70 ev) m/z (%): 277 (M^+, 26), 185 (100), 157 (24), 137 (37), 93 (79), 65 (9). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{11}F_3NO^+$: 278.0787; found: 278.0775.



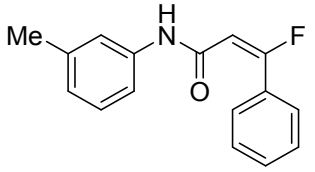
(E)-3-fluoro-3-(naphthalen-1-yl)-N-phenylacrylamide (**3n**): Light-yellow solid (23.9 mg, 41% yield); m.p.: 118.6-119.3°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.27 (s, 1H), 8.10 (d, *J* = 8.0 Hz, 1H), 8.04 (d, *J* = 8.0 Hz, 1H), 7.95-7.94 (m, 1H), 7.72 (d, *J* = 8.0 Hz, 1H) 7.62-7.58 (m, 3H), 7.52 (d, *J* = 8.0 Hz, 2H), 7.28-7.25 (m, 2H), 7.05-7.01 (m, 1H), 6.61 (d, *J* = 20.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 166.5 (d, *J* = 260.0 Hz), 161.1 (d, *J* = 21.3 Hz), 138.9, 132.9, 130.6, 130.5, 130.3, 128.9, 128.7, 128.4, 127.1, 126.3, 125.0, 124.5, 123.4, 119.2, 107.9(d, *J* = 27.5 Hz); ^{19}F NMR (470 MHz, DMSO-d_6) δ -73.15; LRMS (EI 70 ev) m/z (%): 291 (M^+, 25), 199 (100), 110 (62), 151 (26), 93 (19), 65 (21). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{14}FNONa^+$:314.0952; found: 314.0950.



(E)-tert-butyl-2-(1-fluoro-3-oxo-3-(phenylamino)prop-1-en-1-yl)-1H-indole-1-carboxylate (**3o**): White solid (47.1 mg, 62% yield); m.p.: 151.2-152.8°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.22 (s, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.70 (d, J = 7.6 Hz, 1H), 7.57 (d, J = 8.0 Hz, 2H), 7.48-7.44 (m, 1H), 7.34-7.27 (m, 3H), 7.13-7.12 (m, 1H), 7.06-7.03 (m, 1H), 6.38 (d, J = 17.6 Hz, 1H), 1.58 (s, 9H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.1 (d, J = 18.8 Hz), 159.6 (d, J = 255.0 Hz), 148.5, 138.8, 136.0, 128.7, 128.2, 127.9, 126.0, 123.5, 123.2, 121.8, 119.2, 115.0, 114.2 (d, J = 6.3 Hz), 107.9 (d, J = 27.5 Hz), 84.6, 27.3; ^{19}F NMR (470 MHz, DMSO-d_6) δ -79.00; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{22}FN_2O_3^+$:381.1609; found: 381.1600.

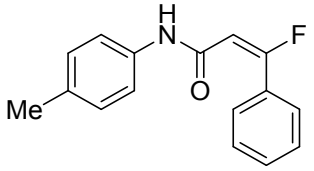


(E)-3-(benzo[b]thiophen-3-yl)-3-fluoro-N-phenylacrylamide (**3p**): White solid (44.6 mg, 75% yield); m.p.: 117.9-118.3°C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.25 (s, 1H), 8.48 (s, 1H), 8.11-8.08 (m, 1H), 7.84 (d, J = 7.2 Hz, 1H), 7.59 (d, J = 8.0 Hz, 2H), 7.49-7.44 (m, 2H), 7.32-7.29 (m, 2H), 7.08-7.04 (m, 1H), 6.48 (d, J = 21.2 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 161.5 (d, J = 253.8 Hz), 161.3 (d, J = 20.0 Hz), 139.0, 138.7, 136.6, 133.5 (d, J = 8.8 Hz), 128.7, 125.7, 124.9, 124.8, 123.5, 123.0, 122.8, 119.3, 107.0 (d, J = 27.5 Hz); ^{19}F NMR (470 MHz, DMSO-d_6) δ -82.33; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{17}H_{13}FNOS^+$:298.0696; found: 298.0693.

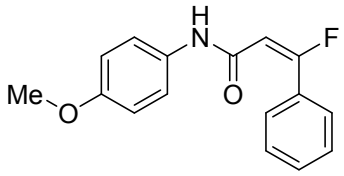


(E)-3-fluoro-3-phenyl-N-(m-tolyl)acrylamide (**3q**): White solid (30.6 mg, 60% yield); m.p.: 106.1-106.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.0 Hz, 2H), 7.52-

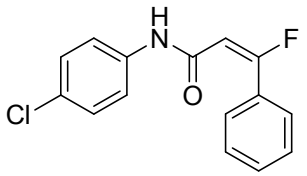
7.43 (m, 3H), 7.35-7.32 (m, 2H), 7.21-7.16 (m, 2H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.00 (d, *J* = 20.0 Hz, 1H), 2.33 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2 (d, *J* = 261.3 Hz), 162.5 (d, *J* = 20.0 Hz), 139.0, 137.5, 131.2, 130.1, 128.8, 128.7, 128.4, 125.4, 120.6, 117.0, 104.9 (d, *J* = 28.8 Hz), 21.4; ^{19}F NMR (470 MHz, $CDCl_3$) δ -84.28; LRMS (EI 70 ev) m/z (%): 255 (M^+, 20), 149 (86), 107 (100), 106 (14), 101 (36), 77 (14). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNONa^+$: 278.0952; found:278.0943.



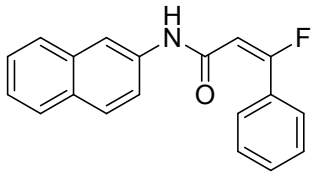
(E)-3-fluoro-3-phenyl-N-(p-tolyl)acrylamide (**3r**): White solid (41.8 mg, 82% yield); m.p.: 122.9-123.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.51-7.44 (m, 4H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.00 (d, *J* = 20.0 Hz, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.1 (d, *J* = 260.0 Hz), 162.5 (d, *J* = 22.5 Hz), 135.0, 134.3, 131.2, 129.9, 129.5, 128.7, 128.4, 120.1, 104.9 (d, *J* = 28.8 Hz), 20.9; ^{19}F NMR (470 MHz, $CDCl_3$) δ -84.66; LRMS (EI 70 ev) m/z (%): 255 (M^+, 17), 149 (64), 107 (100), 106 (22), 101 (30), 75 (6). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNONa^+$: 278.0952; found:278.0941.



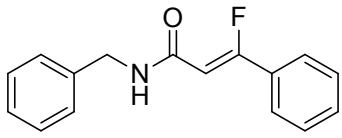
(E)-3-fluoro-N-(4-methoxyphenyl)-3-phenylacrylamide (**3s**): Light-yellow solid (37.9 mg, 70% yield); m.p.: 110.2-110.8°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75-7.74 (m, 2H), 7.49-7.42 (m, 4H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 5.97 (d, *J* = 20.0 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.0 (d, *J* = 260.0 Hz), 162.5 (d, *J* = 21.3 Hz), 156.6, 131.1, 130.7, 130.2, 128.7, 128.3, 121.9, 114.1, 104.8 (d, *J* = 28.8 Hz), 55.5; ^{19}F NMR (470 MHz, $CDCl_3$) δ -84.72; LRMS (EI 70 ev) m/z (%): 271 (M^+, 25), 149 (64), 123 (100), 108 (33), 101 (26), 95 (7). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNO_2Na^+$: 294.0901; found: 294.0901.



(E)-N-(4-chlorophenyl)-3-fluoro-3-phenylacrylamide (**3t**): Light-yellow solid (44.8 mg, 81% yield); m.p.: 135.3-136.1°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73(d, *J* = 8.0 Hz, 2H), 7.52-7.43 (m, 4H), 7.37(d, *J* = 8.0 Hz, 2H), 7.26(d, *J* = 8.0 Hz, 2H), 5.95 (d, *J* = 20.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.8 (d, *J* = 263.8 Hz), 162.6 (d, *J* = 21.3 Hz), 136.2, 131.4, 129.8, 129.6, 129.0, 128.7, 128.4, 121.2, 104.5 (d, *J* = 30.0 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -82.46; LRMS (EI 70 ev) m/z (%): 277 (M^+, 4), 275 (13), 150 (10), 149 (100), 129 (24), 101 (33). HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{15}H_{12}FNOCl^+$: 276.0586; found: 276.0579.

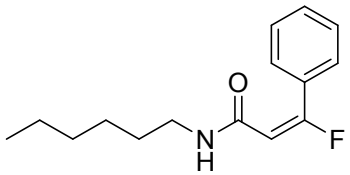


(E)-3-fluoro-N-(naphthalen-2-yl)-3-phenylacrylamide (**3u**): Light-yellow solid (45.3 mg, 78% yield); m.p.: 115.5-117.6°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.80-7.77 (m, 5H), 7.55-7.42 (m, 6H), 7.34-7.31 (m, 1H), 6.07 (d, *J* = 20.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.3 (d, *J* = 243.8 Hz), 162.6 (d, *J* = 17.5 Hz), 140.4, 135.0, 133.8, 131.3, 130.7, 128.8, 128.7, 128.4, 127.7, 127.6, 126.6, 125.2, 119.7, 116.8, 104.8 (d, *J* = 31.3 Hz); ^{19}F NMR (470 MHz, $CDCl_3$) δ -83.45; LRMS (EI 70 ev) m/z (%): 291 (M^+, 13), 207 (14), 149 (43), 144 (12), 143 (100), 101 (17). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{14}FNONa^+$:314.0952; found: 314.0961.

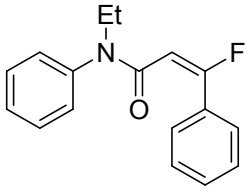


(E)-N-benzyl-3-fluoro-3-phenylacrylamide (**3v**): Clear oil (20.4 mg, 40% yield); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.73 (s, 1H), 7.69 (d, *J* = 8.0 Hz, 2H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.45-7.41 (m, 2H), 7.36-7.32 (m, 2H), 7.26 (d, *J* = 8.0 Hz, 3H), 6.14 (d, *J* = 24.0 Hz, 1H), 4.33 (d, *J* = 4.0 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.7 (d, *J*

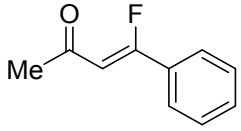
= 252.5 Hz), 163.1 (d, J = 20.0 Hz), 139.0, 130.6, 130.2, 130.0, 128.3, 127.9, 127.4, 126.9, 104.7(d, J = 27.5 Hz), 42.2; ^{19}F NMR (470 MHz, DMSO-d_6) δ -89.05; LRMS (EI 70 ev) m/z (%): 255 (M^+, 54), 149 (100), 122 (13), 106 (39), 101 (31), 91 (14). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{14}FNONa^+$: 278.0952; found: 278.0957.



(E)-3-fluoro-N-hexyl-3-phenylacrylamide (**3w**): Clear oil (13.4 mg, 27% yield); ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.20 (s, 1H), 7.70 (d, J = 8.0 Hz, 2H), 7.51-7.43 (m, 3H), 6.06 (d, J = 24.0 Hz, 1H), 3.11-3.06 (m, 2H), 1.44-1.37 (m, 2H), 1.30-1.24 (m, 6H), 0.89-0.85 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 163.1 (d, J = 251.3 Hz), 163.0 (d, J = 20.0 Hz), 130.4, 130.3, 128.2, 127.9, 105.0 (d, J = 27.5 Hz), 38.6, 30.9, 28.8, 26.1, 22.0, 13.8; ^{19}F NMR (470 MHz, DMSO-d_6) δ -88.11; LRMS (EI 70 ev) m/z (%): 249 (M^+, 4), 179 (16), 164 (12), 150 (12), 149 (100), 101 (18). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{15}H_{20}FNONa^+$: 272.1421; found: 272.1430



(E)-N-ethyl-3-fluoro-N,3-diphenylacrylamide (**3x**): Pale yellow oil (25.8 mg, 48% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.0 Hz, 2H), 7.48-7.36 (m, 6H), 7.08 (d, J = 8.0 Hz, 2H), 5.69 (d, J = 20.0 Hz, 1H), 3.85 (q, J = 8.4 Hz, 2H), 1.19 (t, J = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.4 (d, J = 255.0 Hz), 164.3 (d, J = 20.0 Hz), 141.9, 130.8, 130.5, 129.4, 128.3, 128.0, 127.9, 127.7, 103.8 (d, J = 30.0 Hz), 44.0, 13.0; ^{19}F NMR (470 MHz, $CDCl_3$) δ -88.82; LRMS (EI 70 ev) m/z (%): 269 (M^+, 10), 149 (100), 121 (76), 106 (40), 101 (37), 77 (17). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{17}H_{16}FNONa^+$: 292.1108; found: 292.1104.

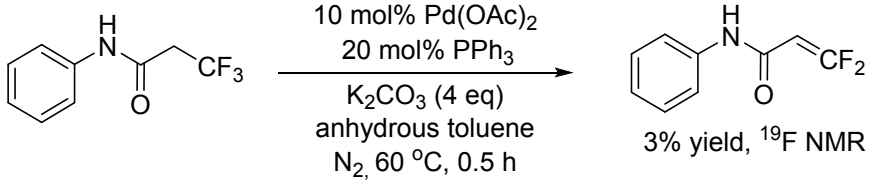


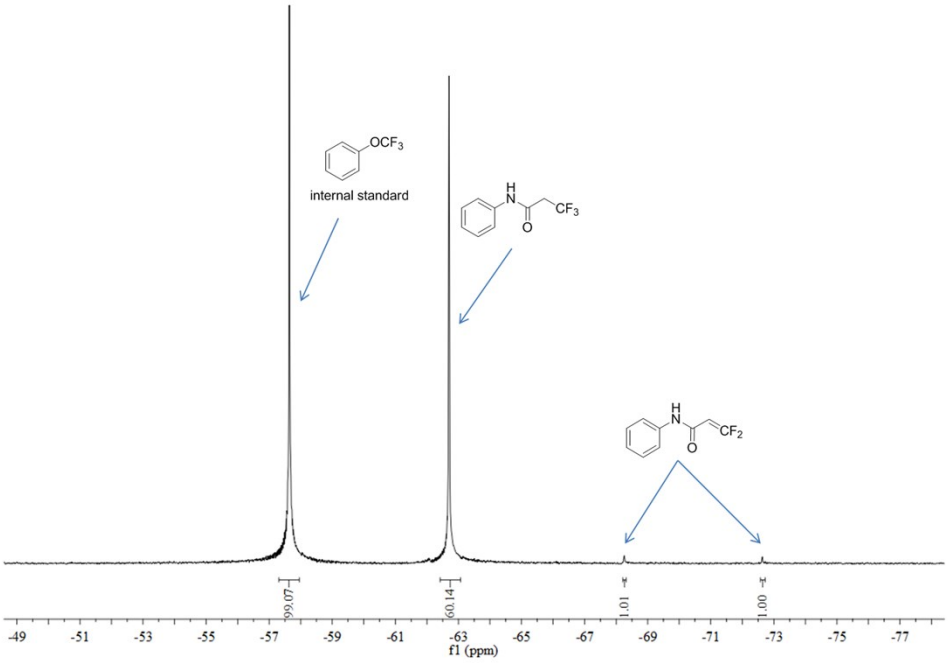
(Z)-4-fluoro-4-phenylbut-3-en-2-one (**3y**)[1]: pale yellow oil (19.7 mg, 60% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ7.69-7.66 (m, 2H), 7.52-7.46 (m, 3H), 6.10 (d, J = 40.0 Hz, 1H), 2.53 (d, J = 4.0 Hz, 3H).

Reference

[1] T. J. O'Connor, F. D. Toste, Gold-Catalyzed Hydrofluorination of Electron-Deficient Alkynes: Stereoselective Synthesis of β-Fluoro Michael Acceptors. *ACS Catalysis*, **2018**, *8*, 5947-5951.

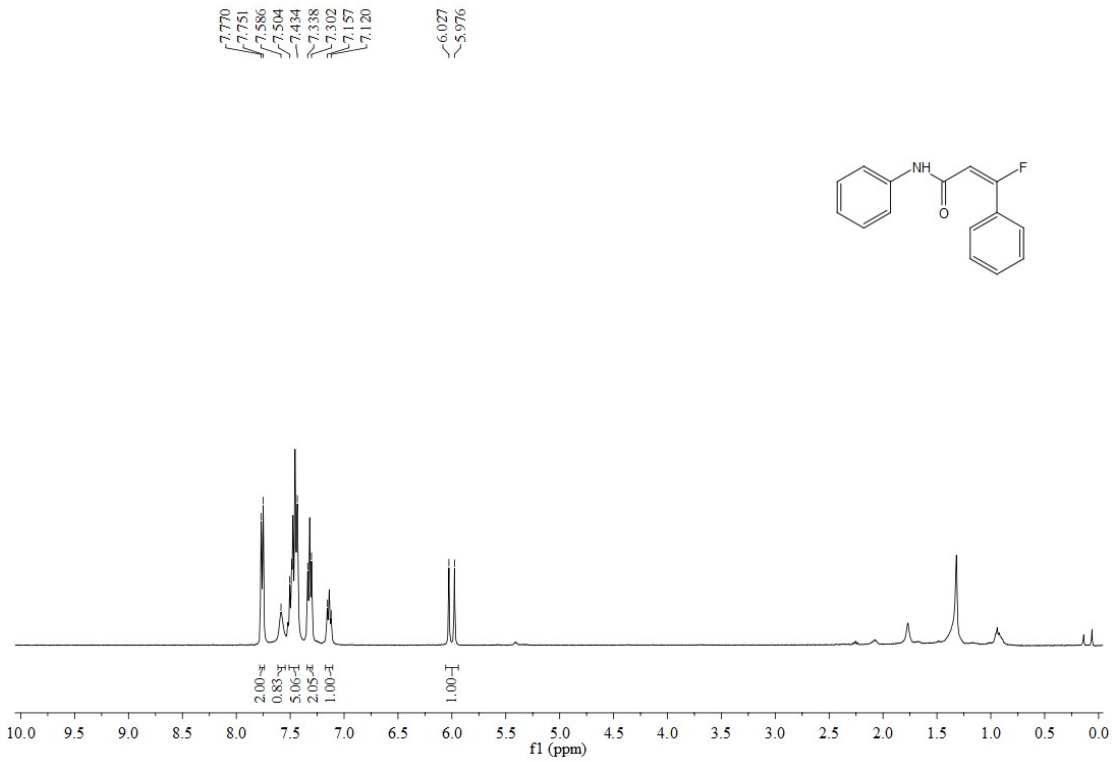
5. ^{19}F NMR of *gem*-Difluoroalkenes Intermediate



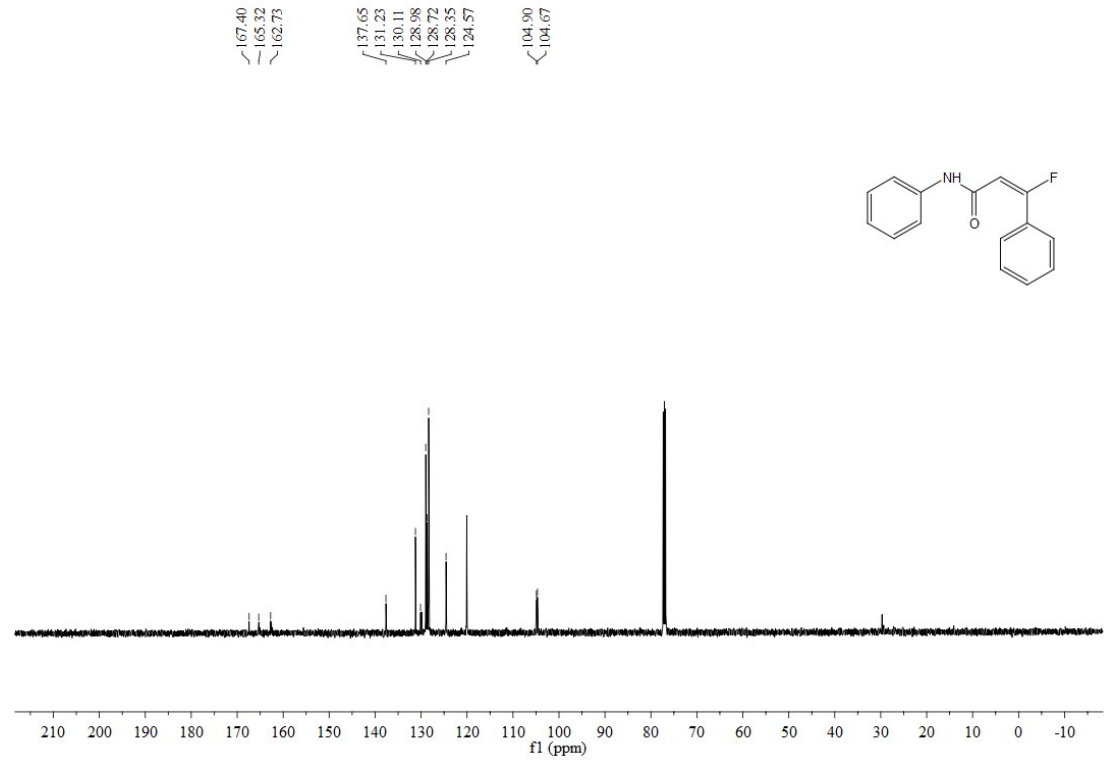


6. NMR Spectra for All Compounds

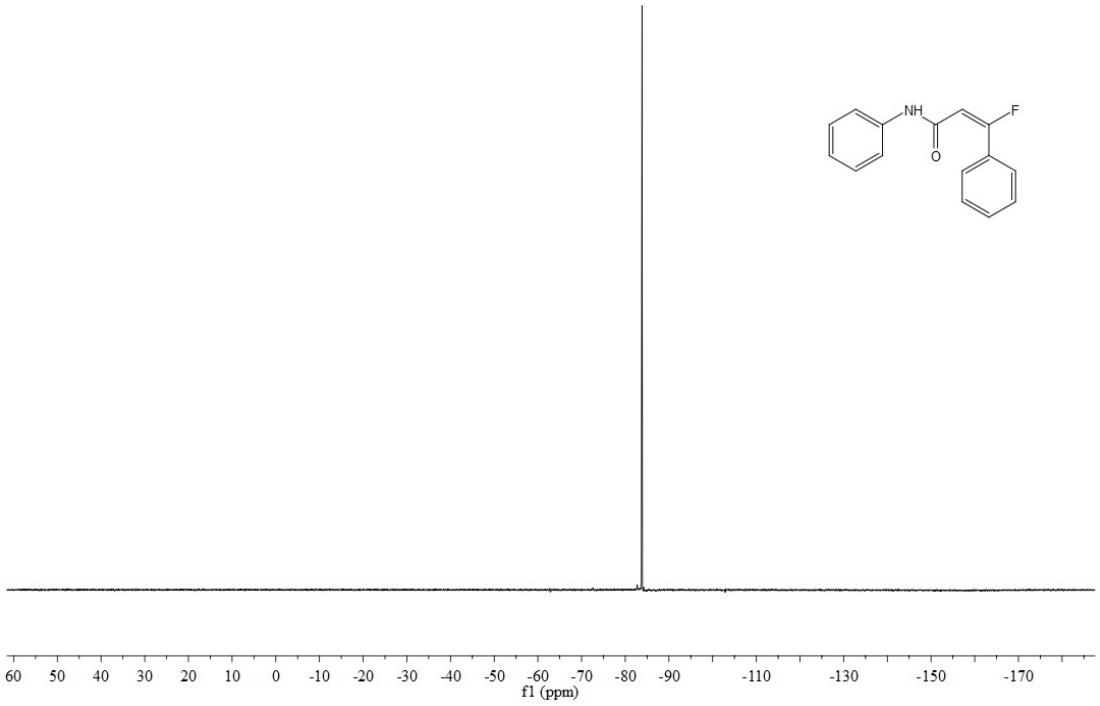
^{1}H NMR: (*E*)-3-fluoro-*N*,*3*-diphenylacrylamide (3a)



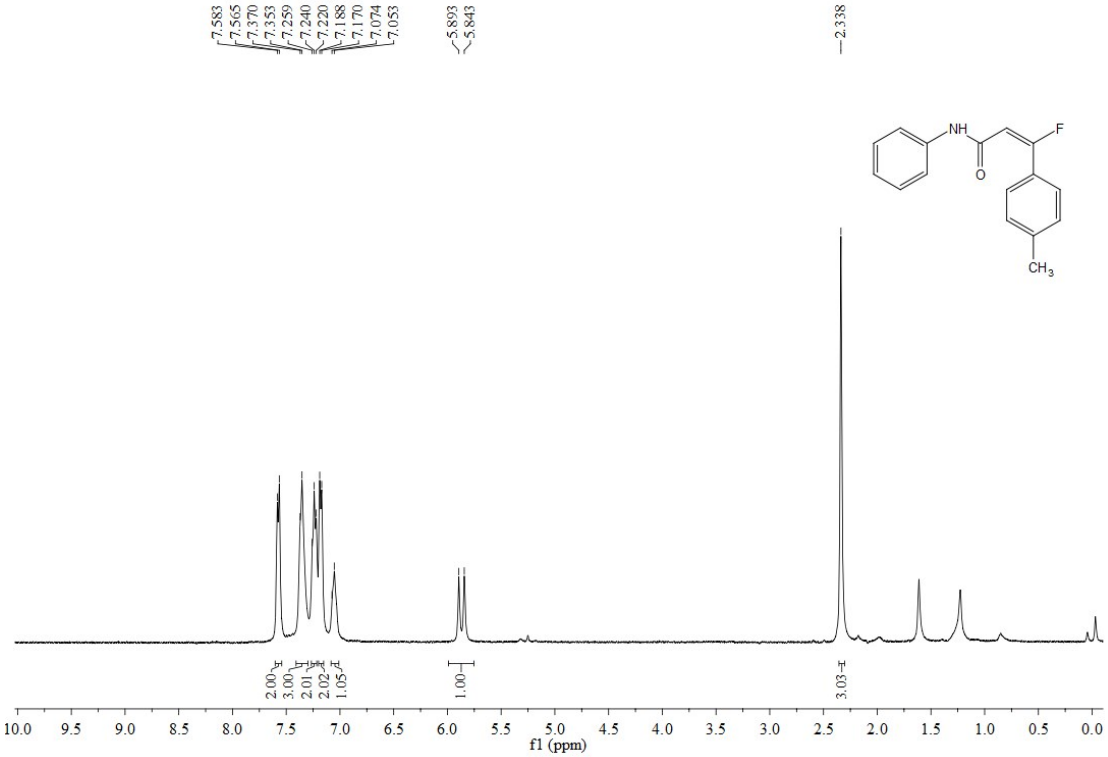
^{13}C NMR: (*E*)-3-fluoro-*N*,*3*-diphenylacrylamide (3a)



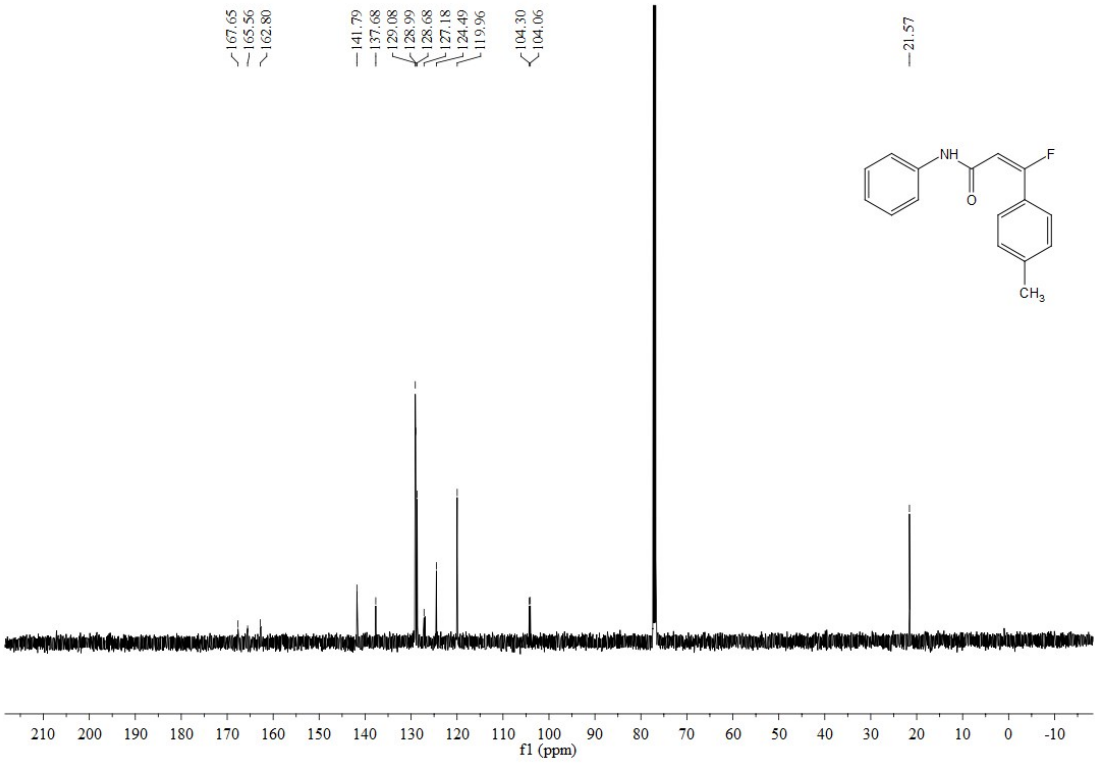
^{19}F NMR: (*E*)-3-fluoro-*N*,*3*-diphenylacrylamide (3a)



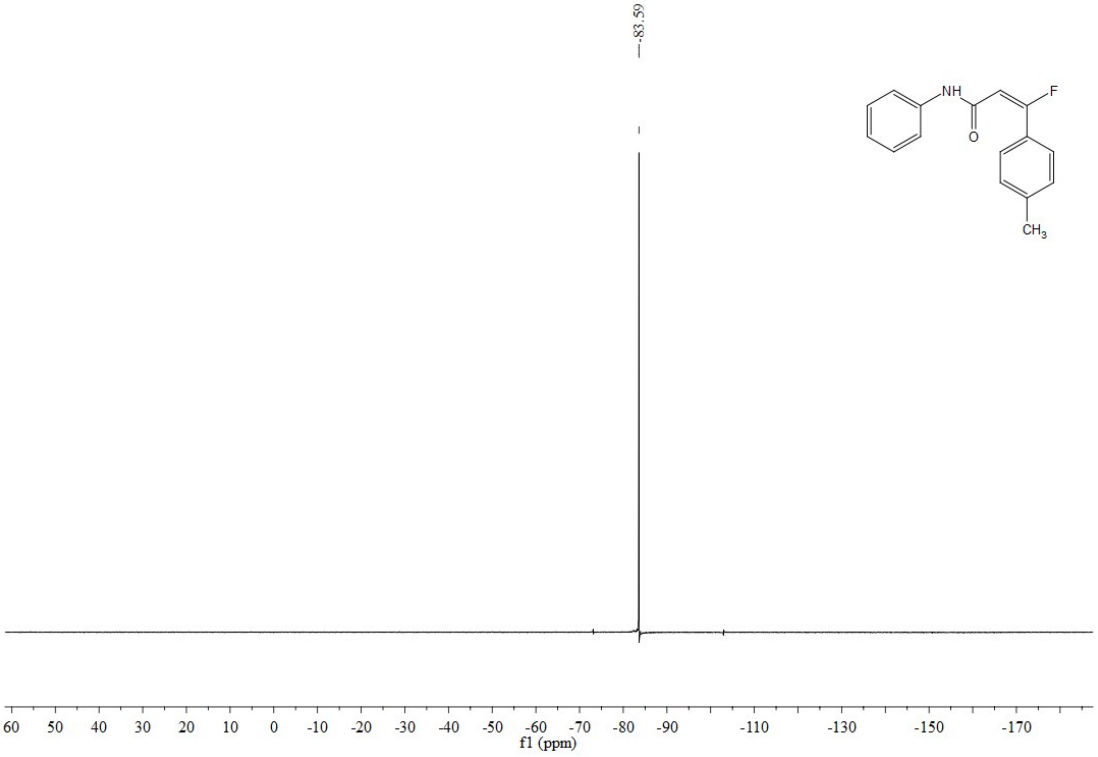
^{1}H NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*p*-tolyl)acrylamide (3b)



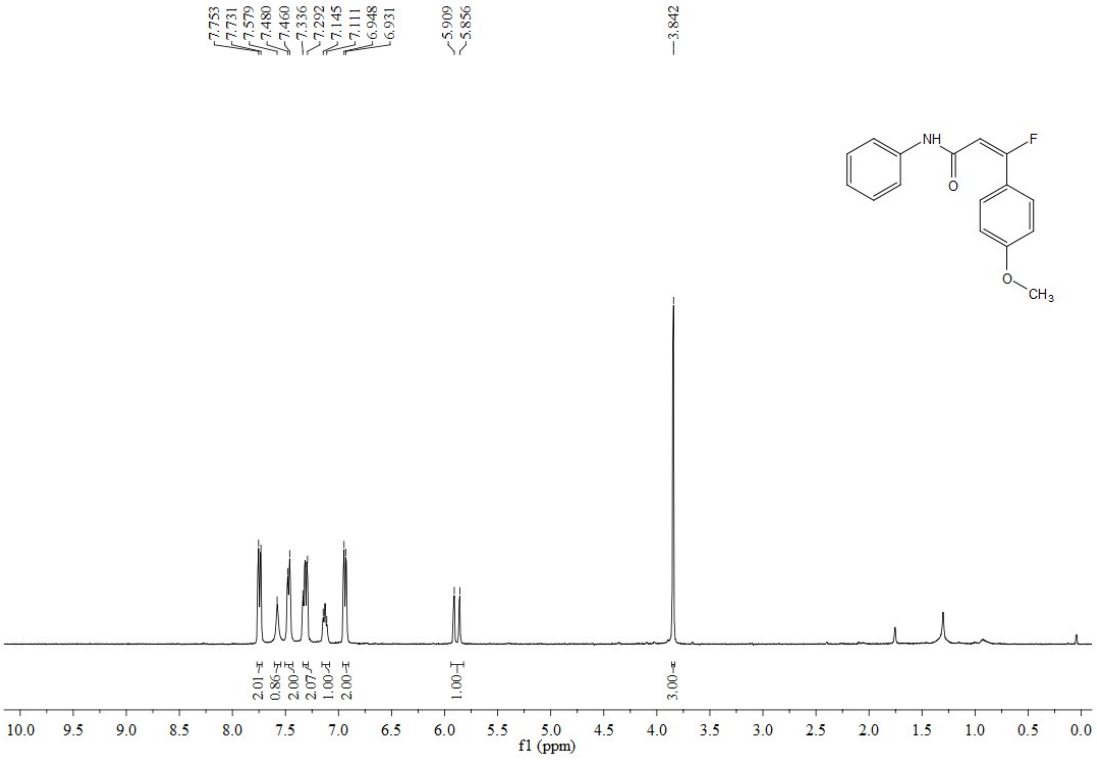
^{13}CNMR: (*E*)-3-fluoro-*N*-phenyl-3-(*p*-tolyl)acrylamide (3b)



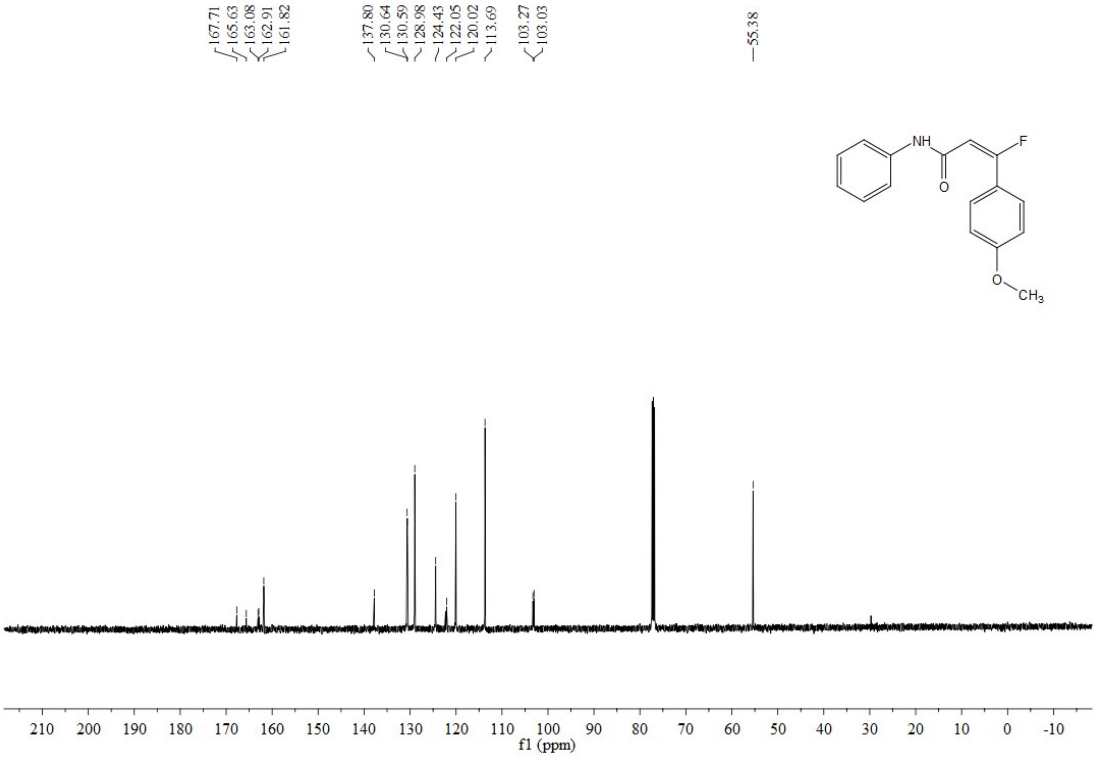
^{19}F NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*p*-tolyl)acrylamide (3b)



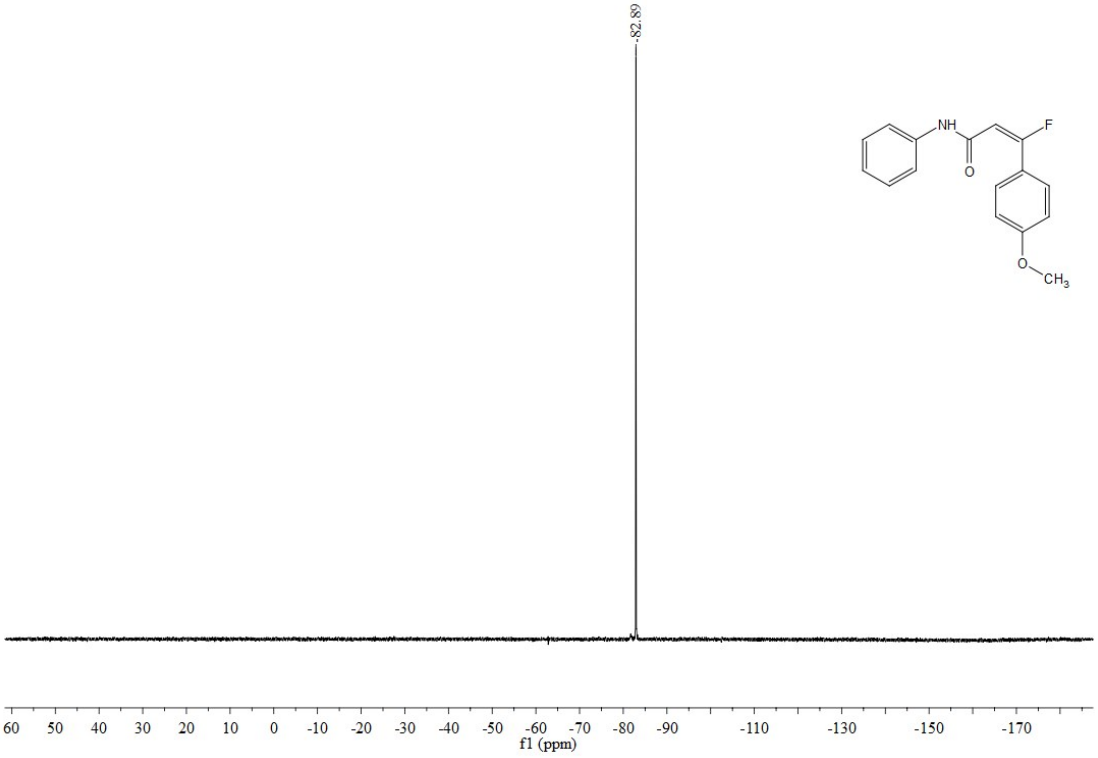
^{1}H NMR: (*E*)-3-fluoro-3-(4-methoxyphenyl)-*N*-phenylacrylamide (3c)



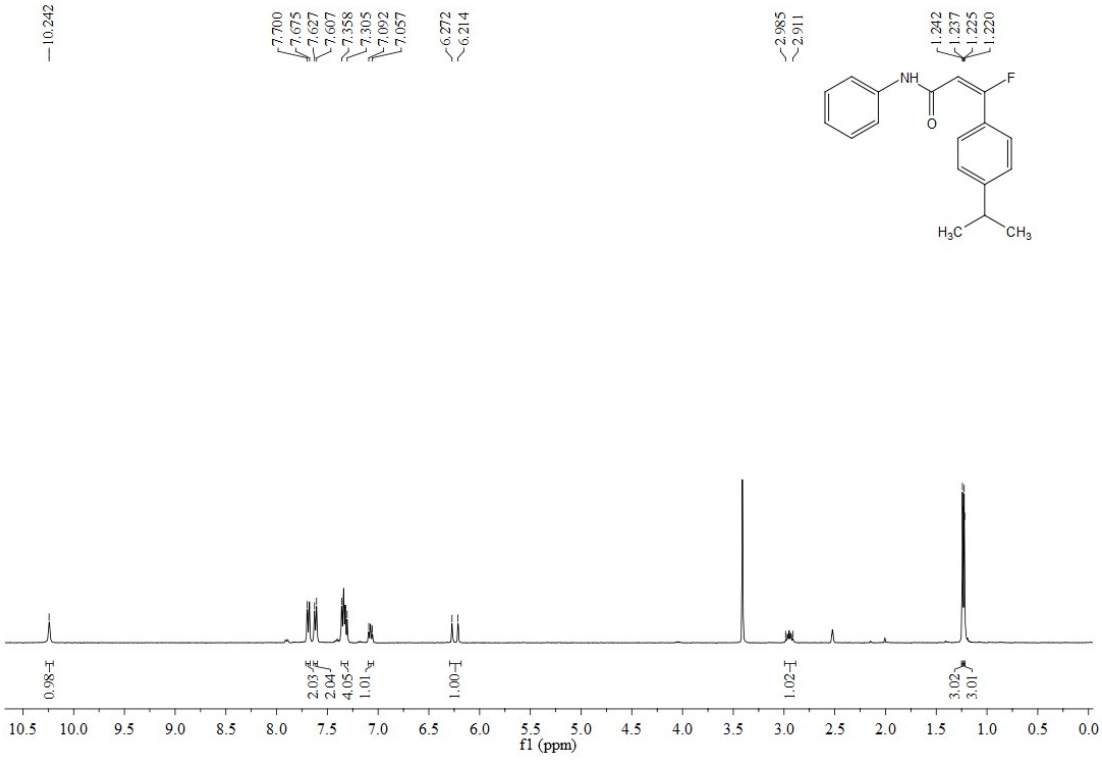
^{13}C NMR: (*E*)-3-fluoro-3-(4-methoxyphenyl)-*N*-phenylacrylamide (3c)



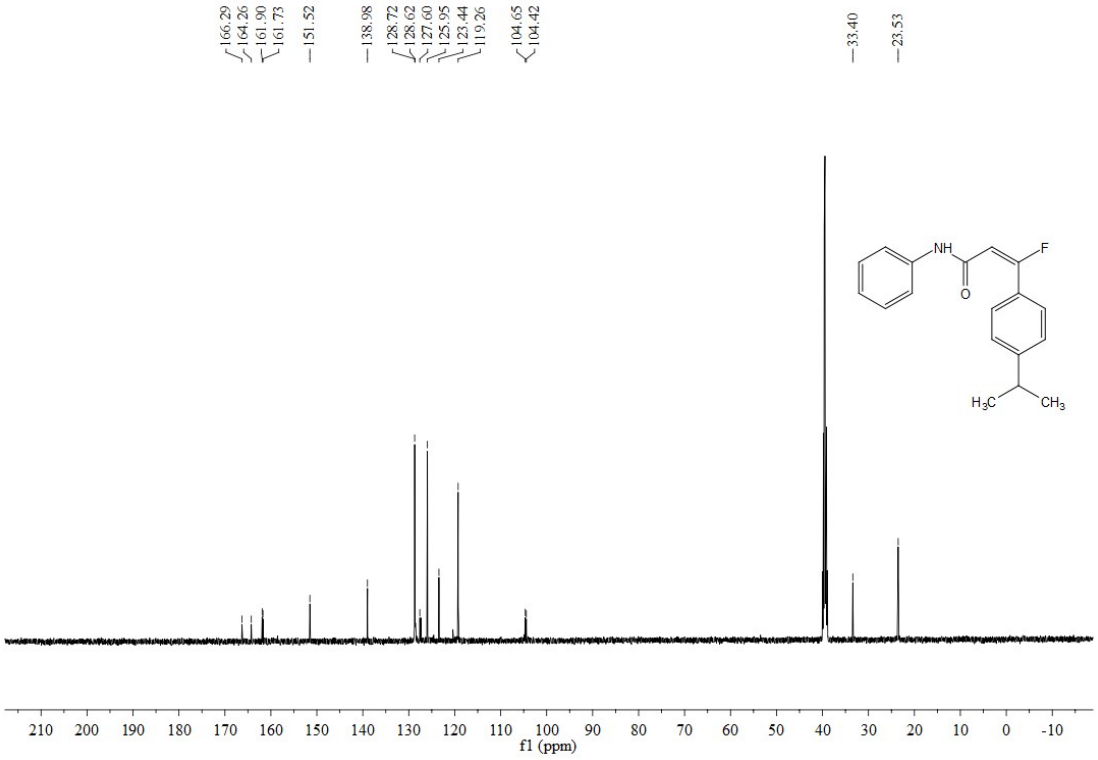
^{19}F NMR: (*E*)-3-fluoro-3-(4-methoxyphenyl)-*N*-phenylacrylamide (3c)



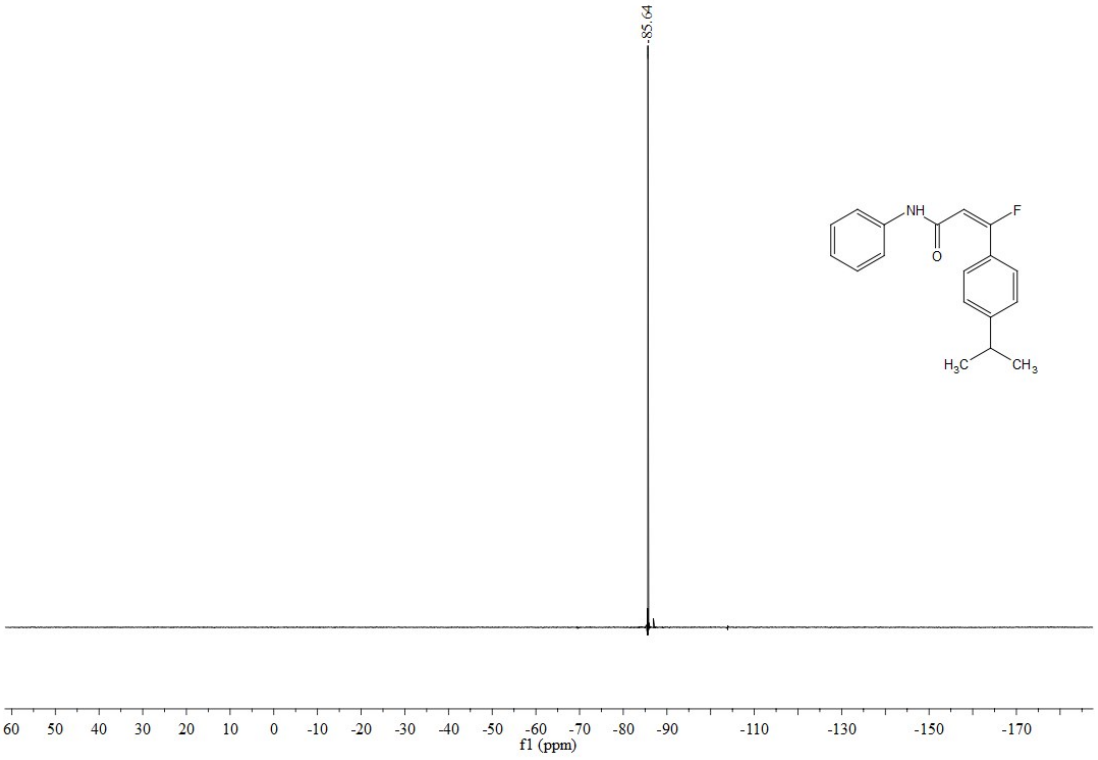
^{1}H NMR: (*E*)-3-fluoro-3-(4-isopropylphenyl)-*N*-phenylacrylamide (3d)



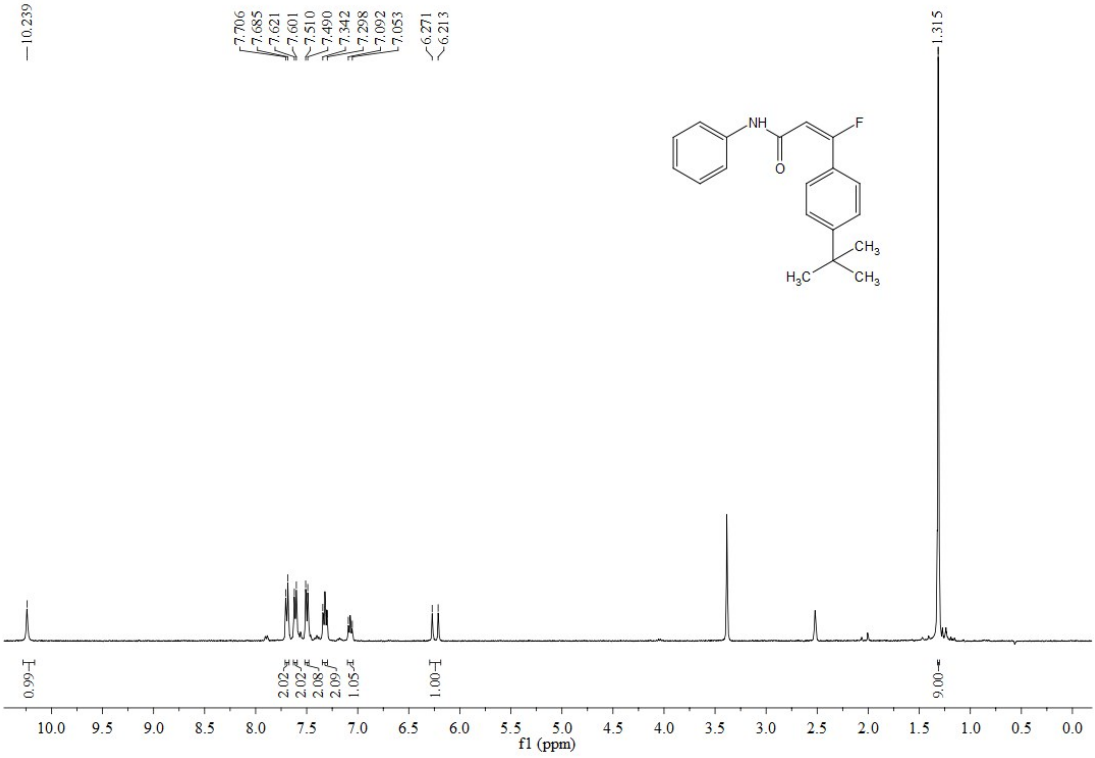
^{13}C NMR: (*E*)-3-fluoro-3-(4-isopropylphenyl)-*N*-phenylacrylamide (3d)



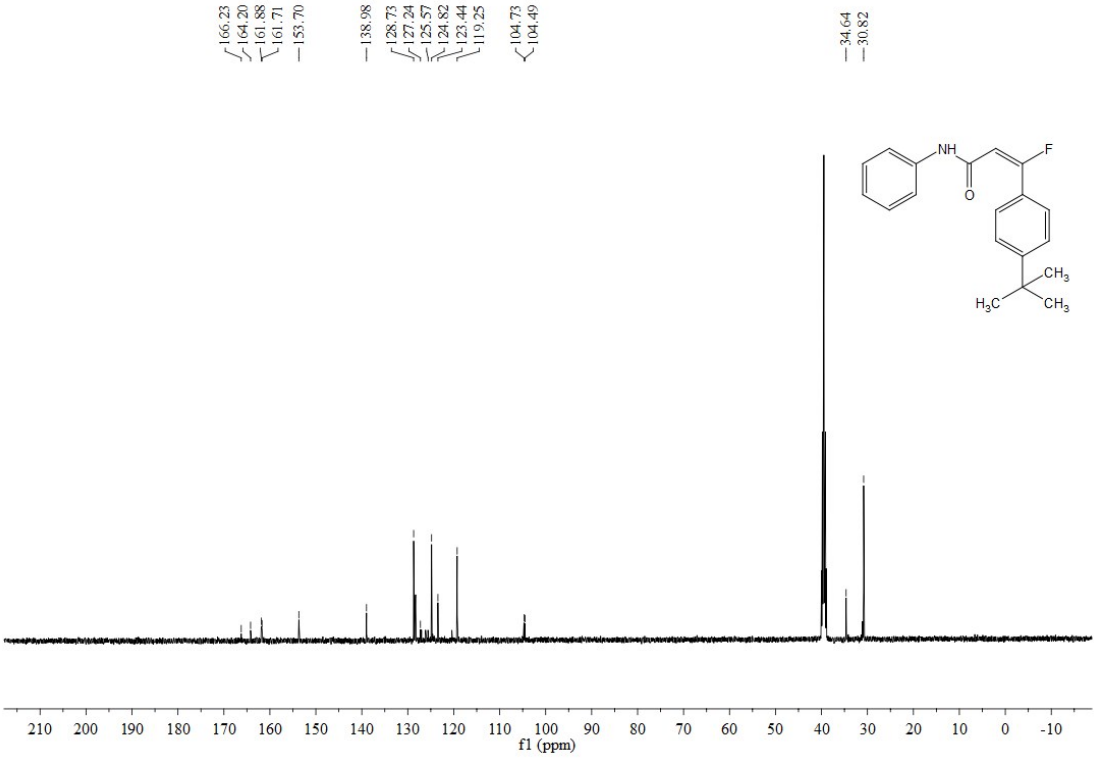
^{19}F NMR: (*E*)-3-fluoro-3-(4-isopropylphenyl)-*N*-phenylacrylamide (3d)



^{1}H NMR: (*E*)-3-(4-(*tert*-butyl)phenyl)-3-fluoro-*N*-phenylacrylamide (3e)

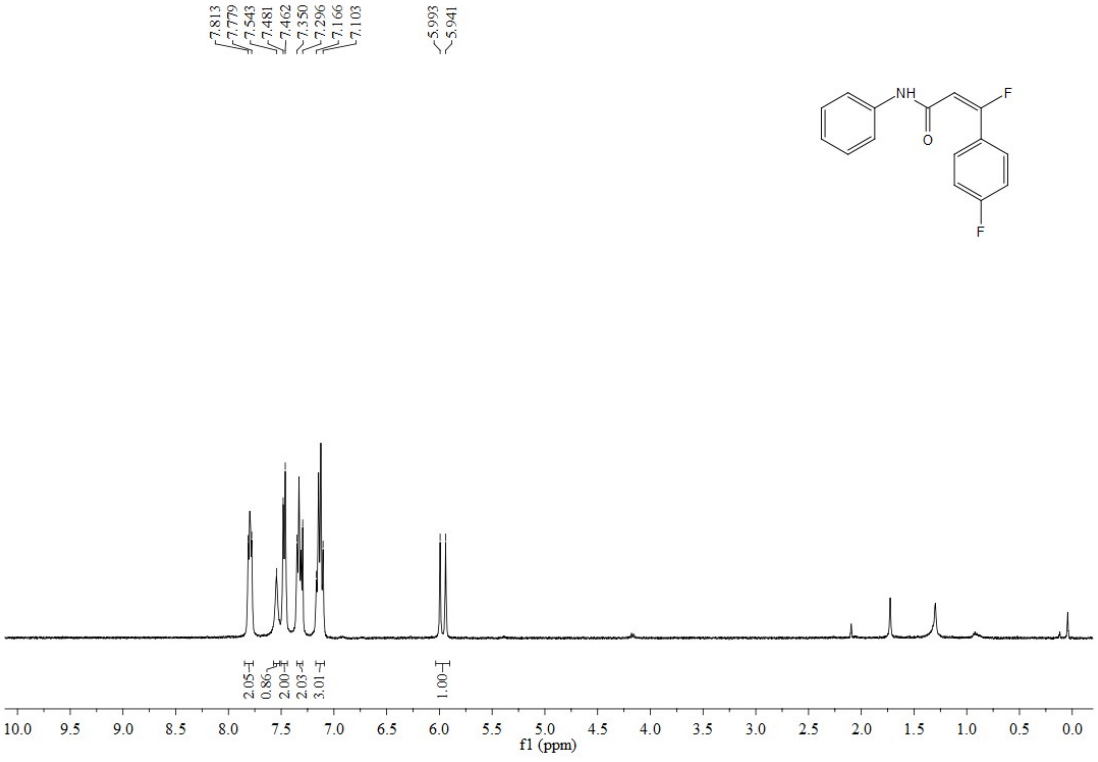


^{13}C NMR: (*E*)-3-(4-(*tert*-butyl)phenyl)-3-fluoro-*N*-phenylacrylamide (3e)

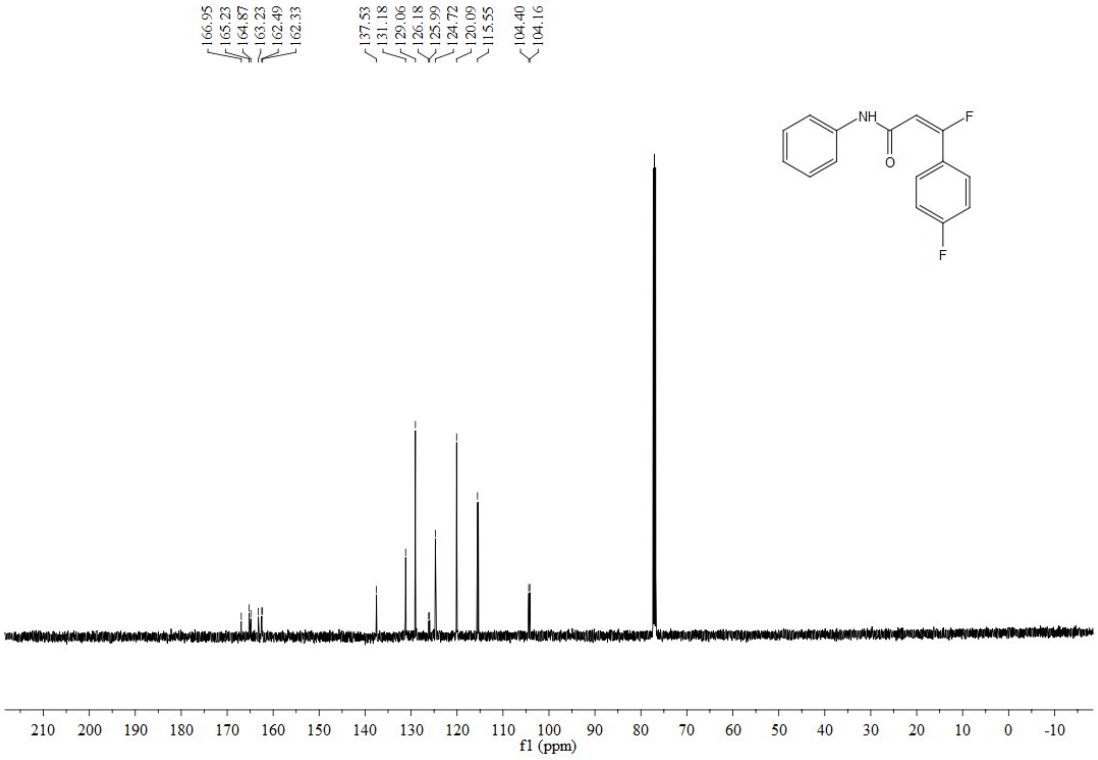


^{19}F NMR: (*E*)-3-(4-(*tert*-butyl)phenyl)-3-fluoro-*N*-phenylacrylamide (3e)

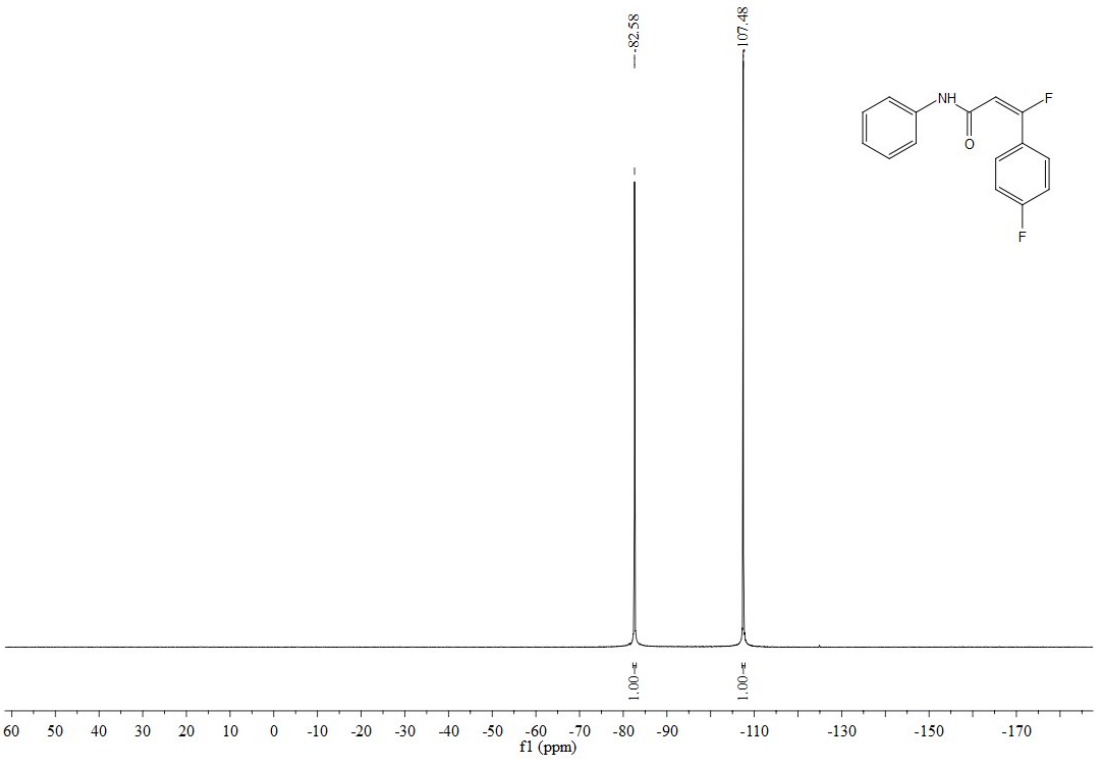
^{1}H NMR: (*E*)-3-fluoro-3-(4-fluorophenyl)-*N*-phenylacrylamide (3f)



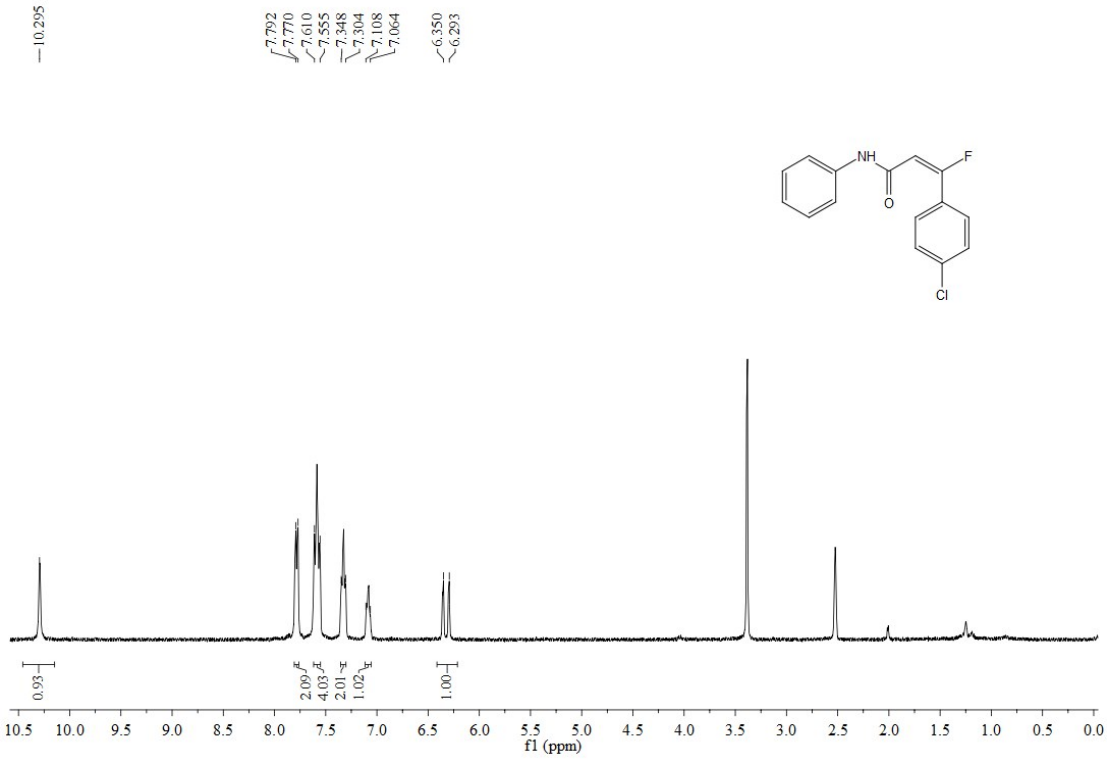
^{13}C NMR: (*E*)-3-fluoro-3-(4-fluorophenyl)-*N*-phenylacrylamide (3f)



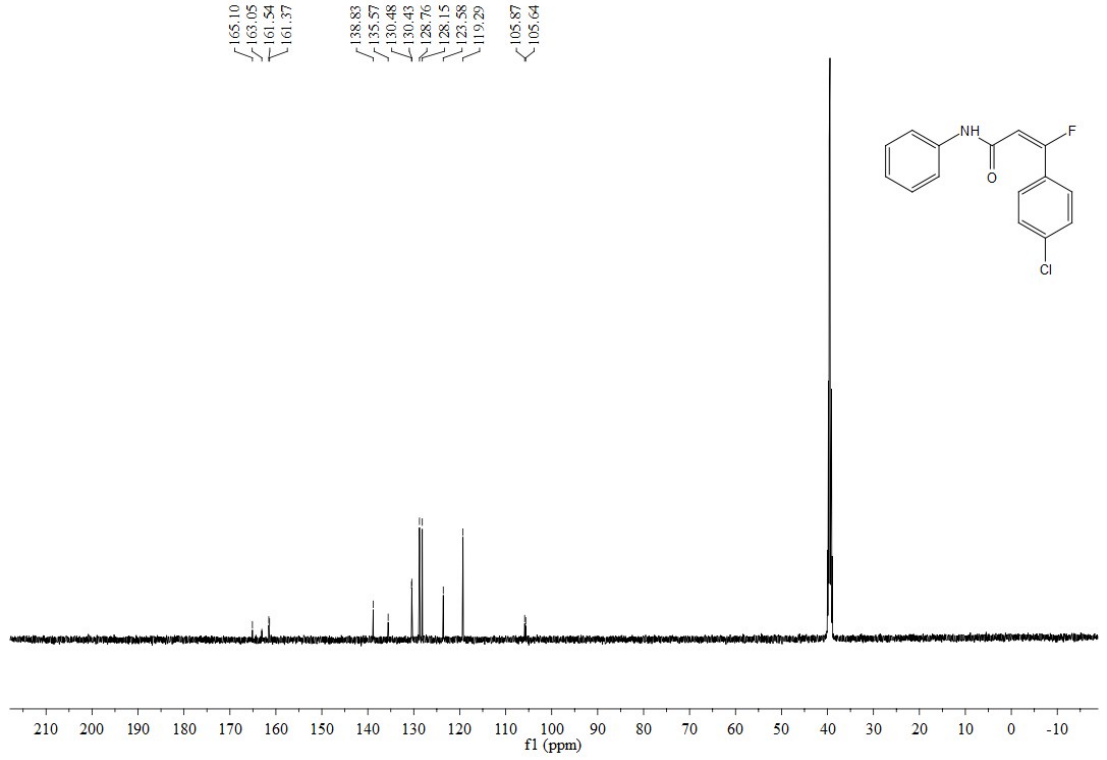
^{19}F NMR: (*E*)-3-fluoro-3-(4-fluorophenyl)-*N*-phenylacrylamide (3f)



^{1}H NMR: (*E*)-3-(4-chlorophenyl)-3-fluoro-*N*-phenylacrylamide (3g)

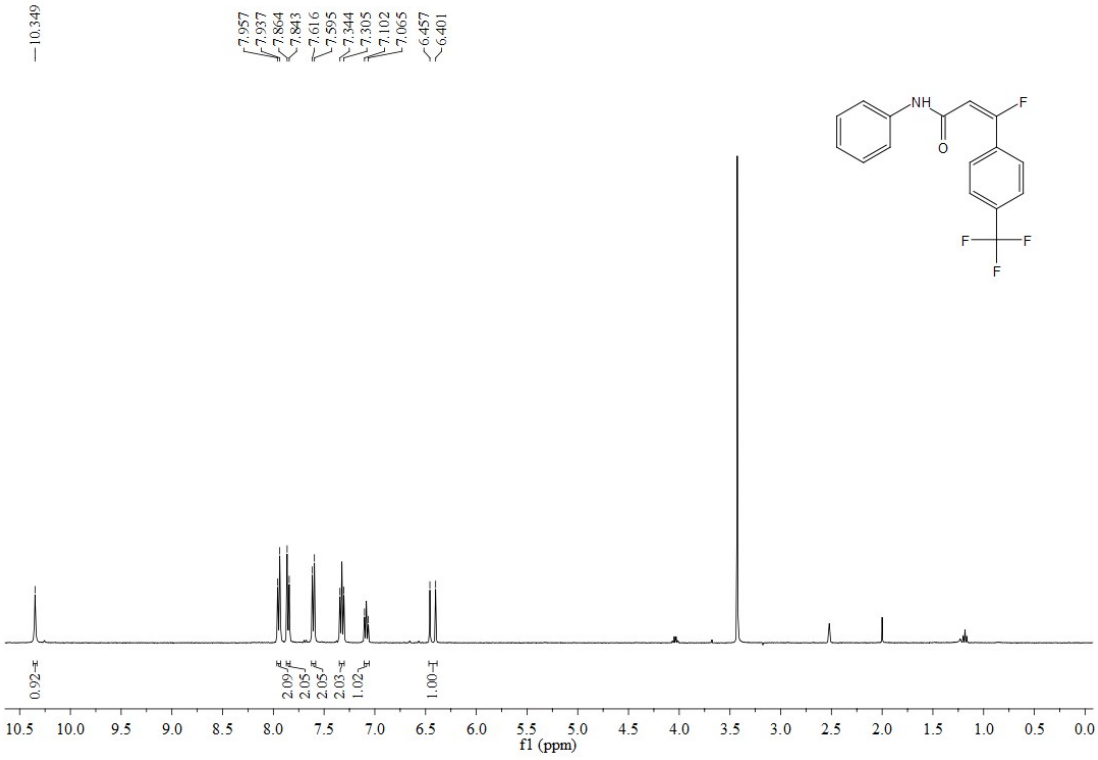


^{13}C NMR: (*E*)-3-(4-chlorophenyl)-3-fluoro-*N*-phenylacrylamide (3g)

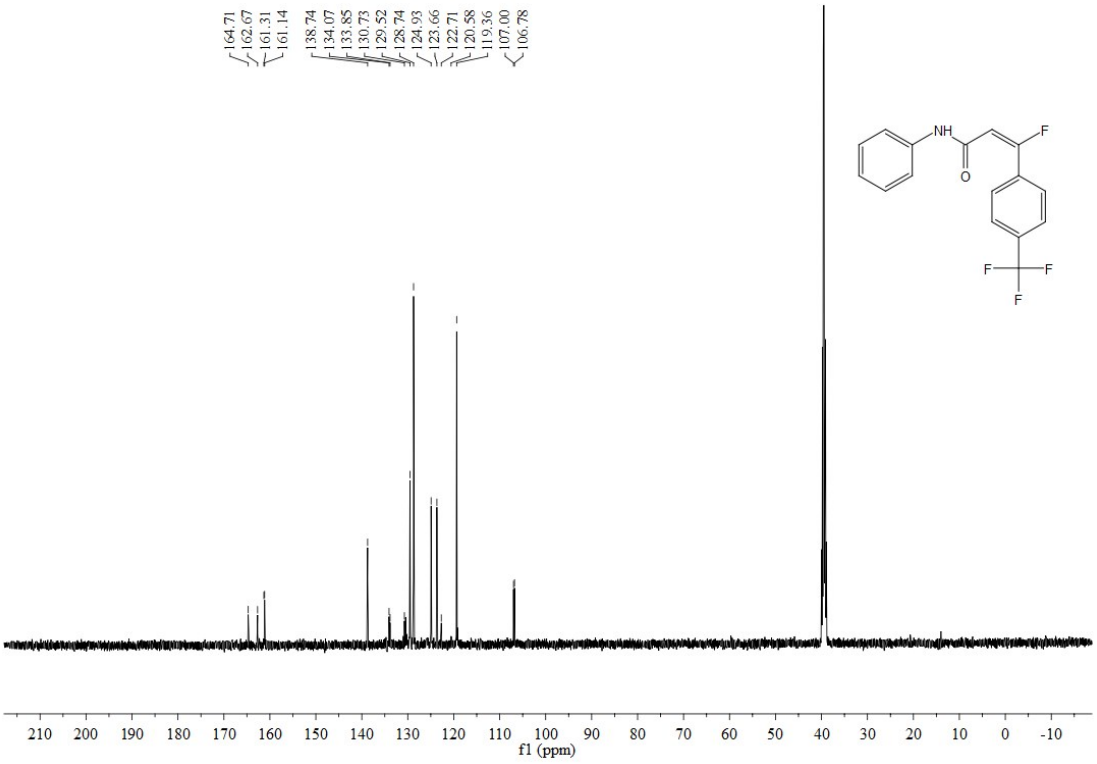


^{19}F NMR: (*E*)-3-(4-chlorophenyl)-3-fluoro-*N*-phenylacrylamide (3g)

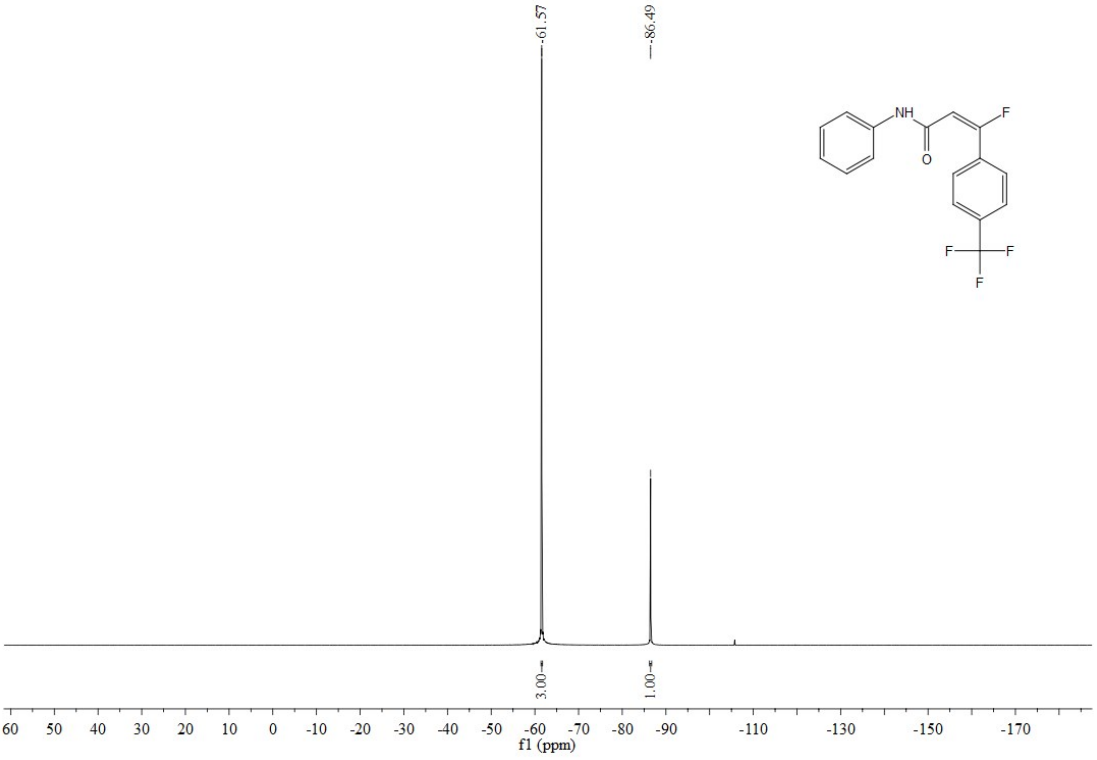
^{1}H NMR: (*E*)-3-fluoro-*N*-phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (3h)



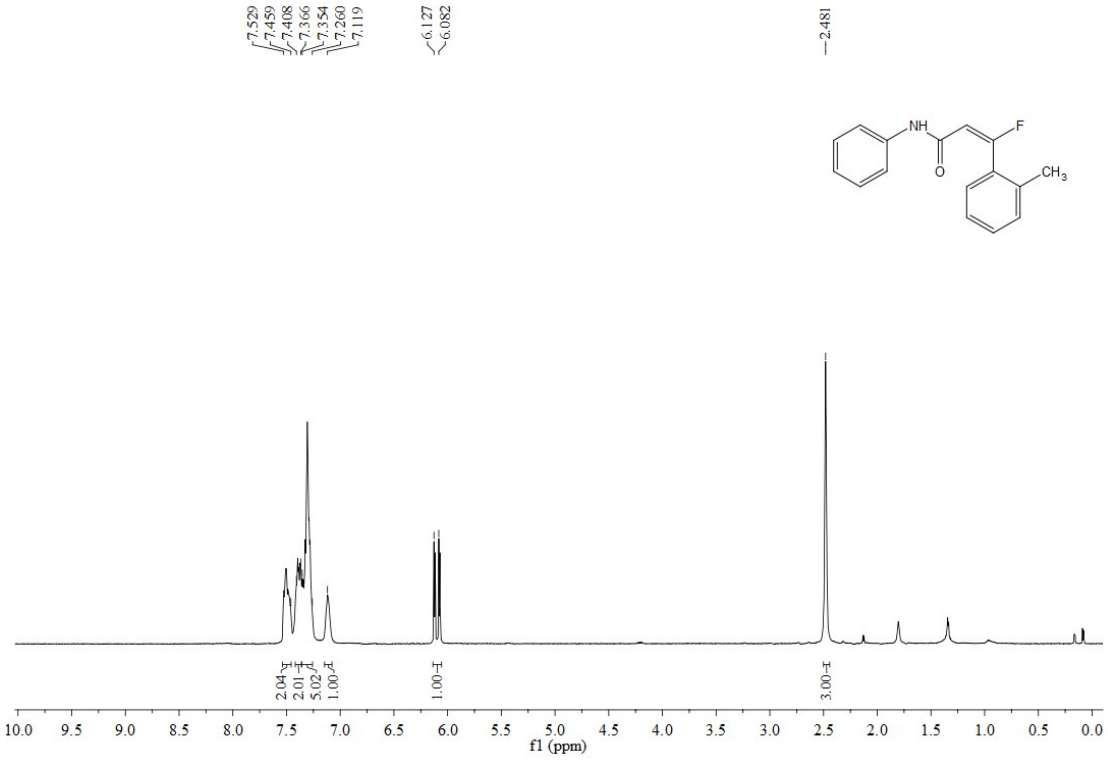
^{13}C NMR: (*E*)-3-fluoro-*N*-phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (3h)



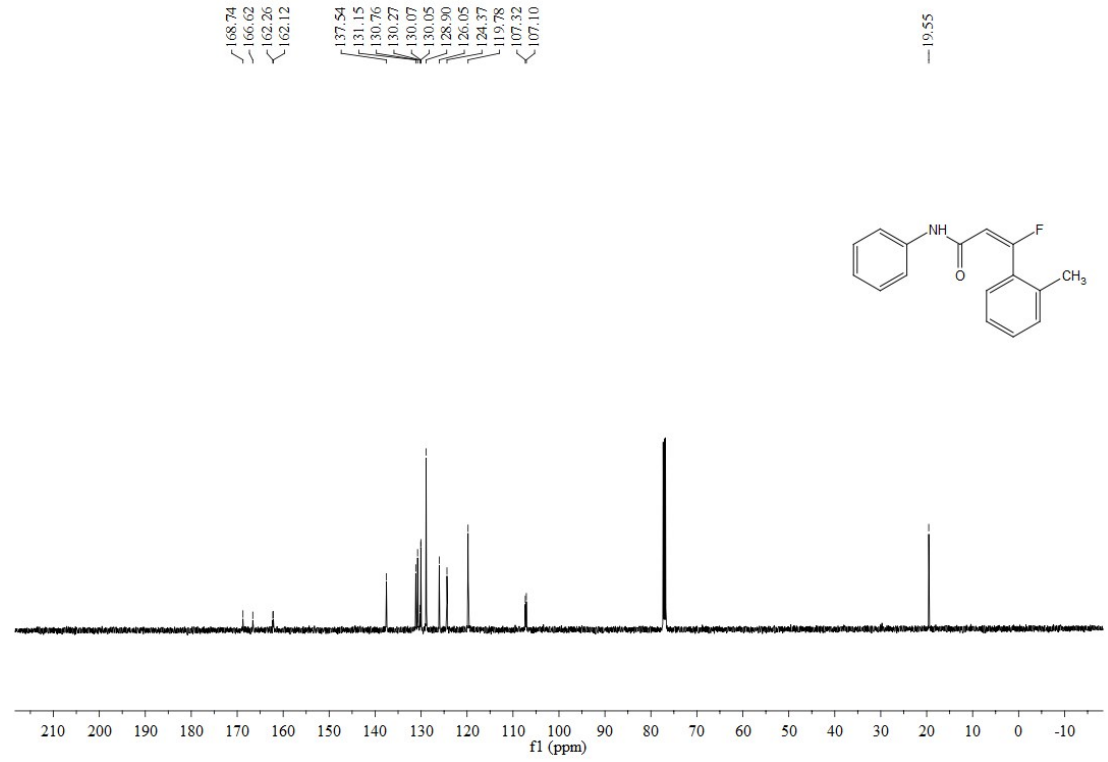
^{19}F NMR: (*E*)-3-fluoro-*N*-phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (3h)



^{1}H NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*o*-tolyl)acrylamide (3i)

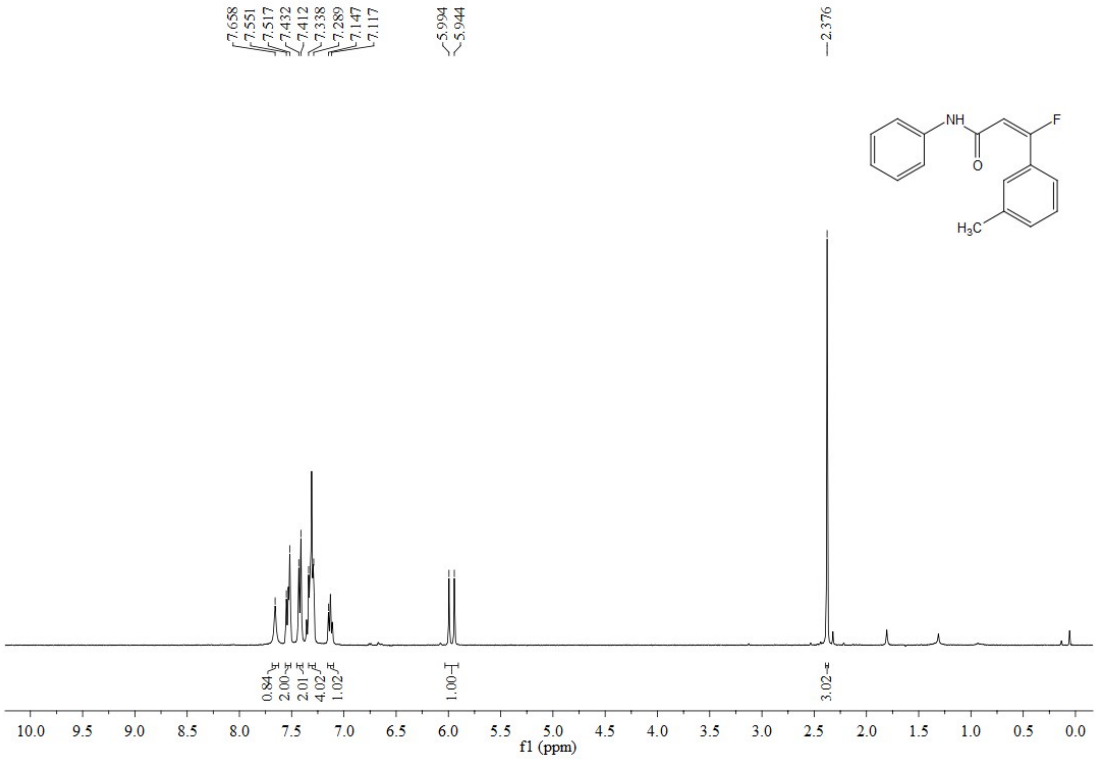


^{13}C NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*o*-tolyl)acrylamide (3i)

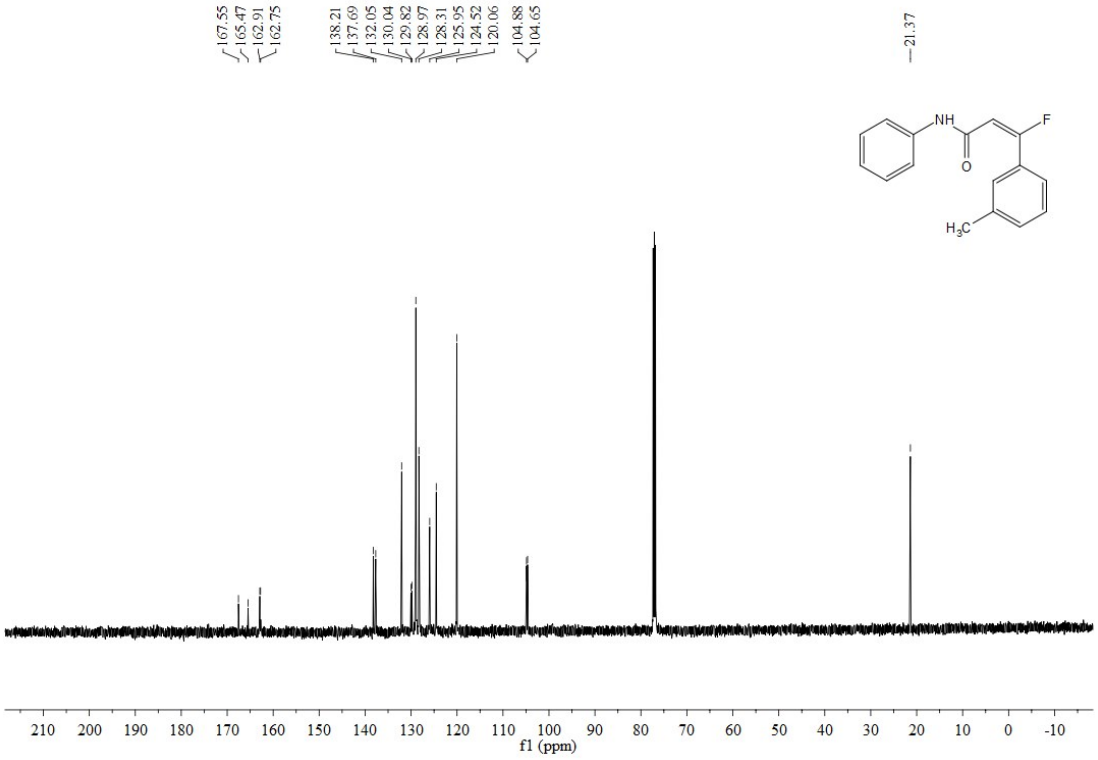


^{19}F NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*o*-tolyl)acrylamide (3i)

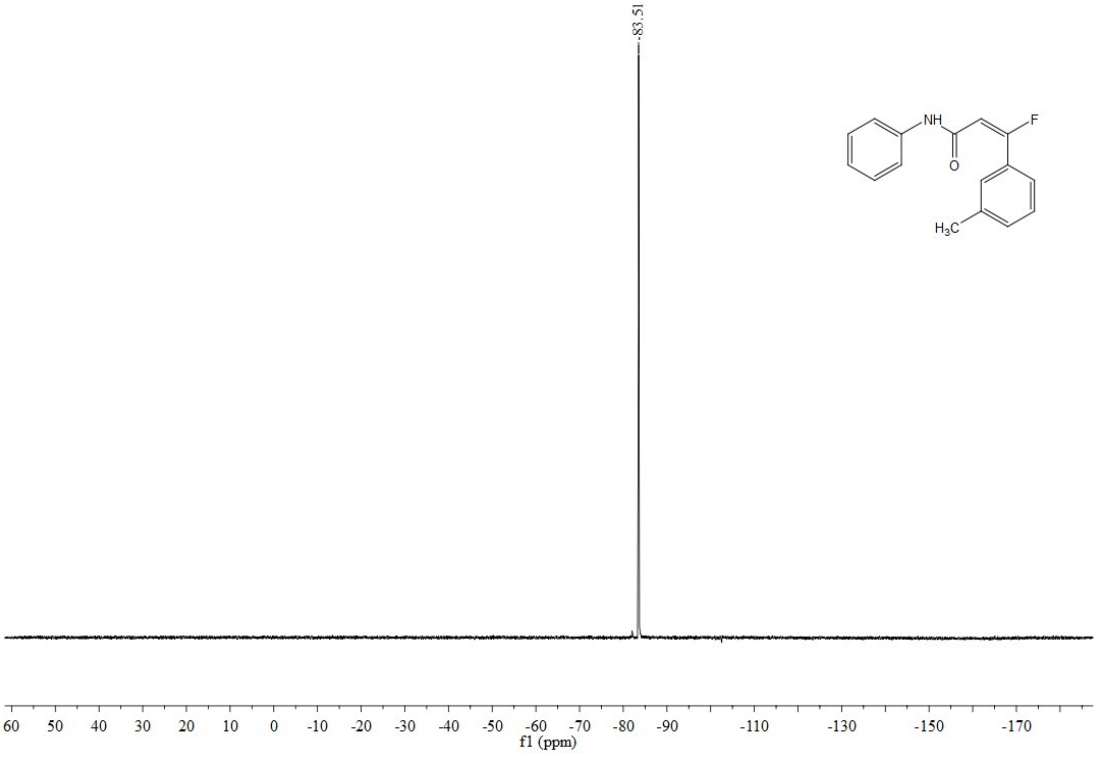
^{1}H NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*m*-tolyl)acrylamide (3j)



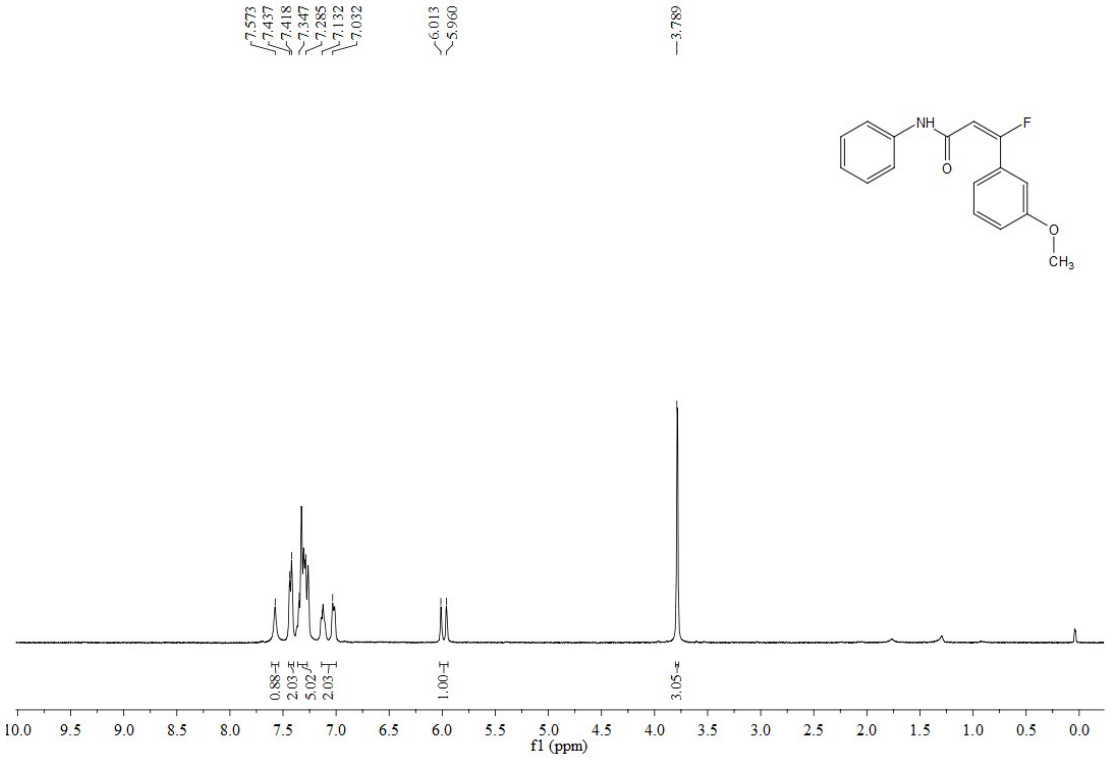
^{13}C NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*m*-tolyl)acrylamide (3j)



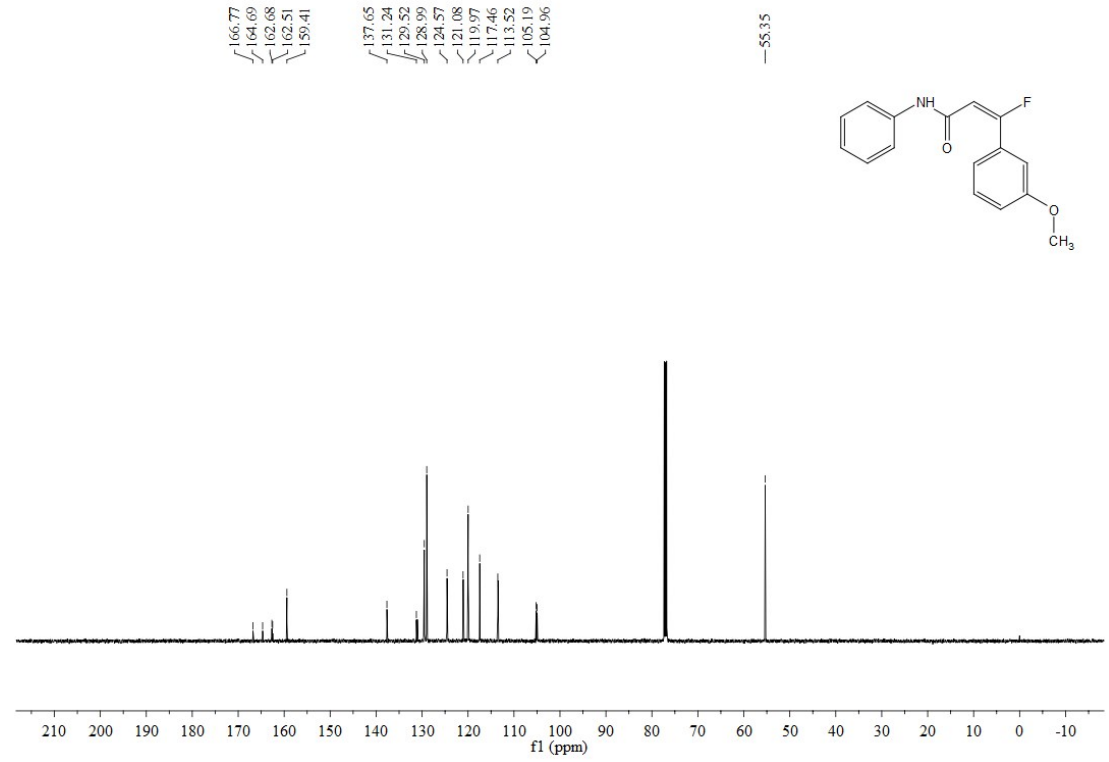
^{19}F NMR: (*E*)-3-fluoro-*N*-phenyl-3-(*m*-tolyl)acrylamide (3j)



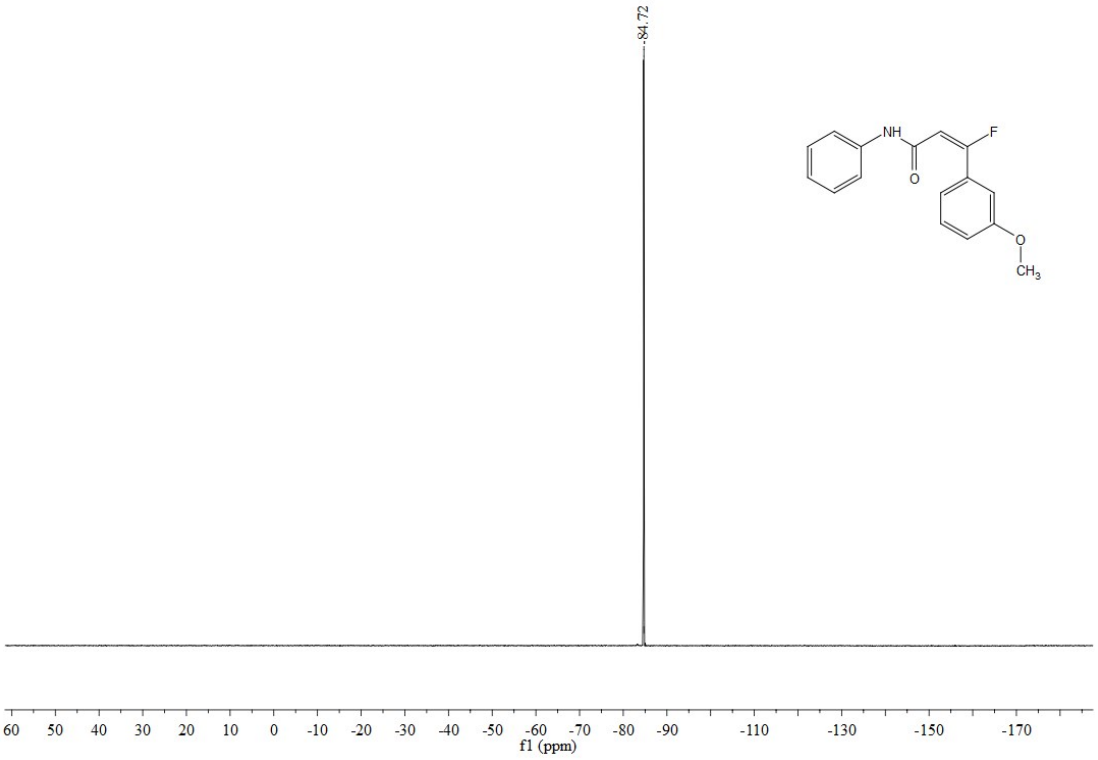
^{1}H NMR: (*E*)-3-fluoro-3-(3-methoxyphenyl)-*N*-phenylacrylamide (3k)



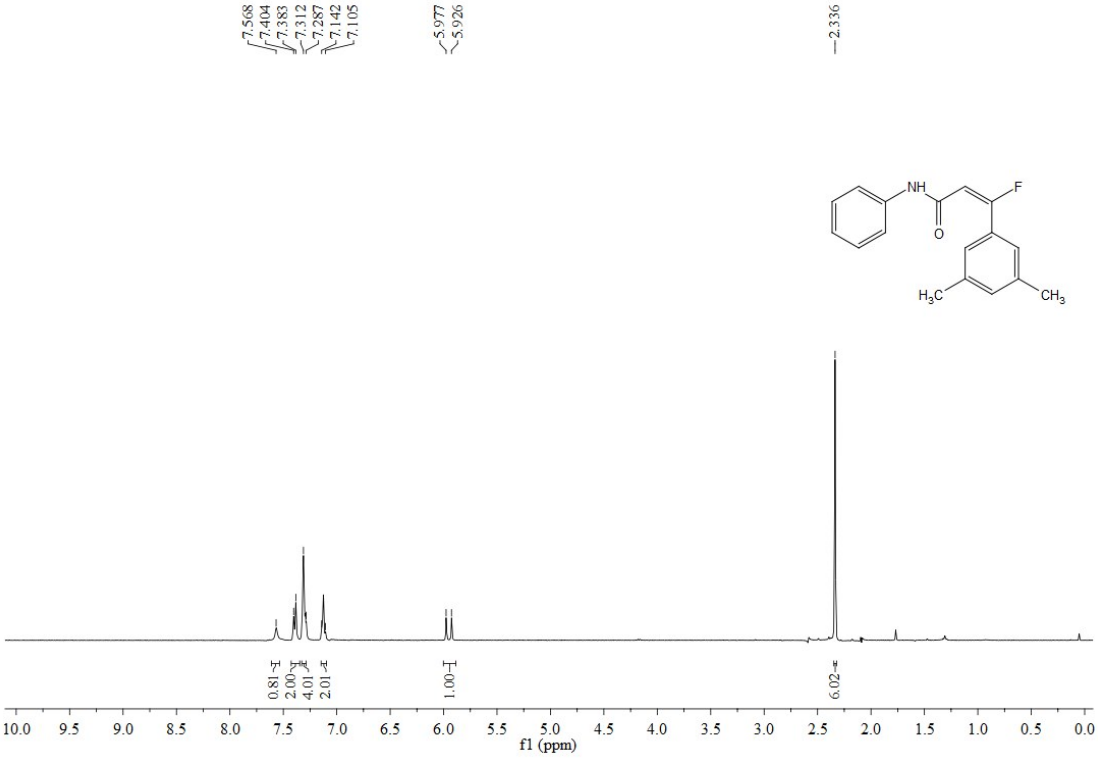
^{13}C NMR: (*E*)-3-fluoro-3-(3-methoxyphenyl)-*N*-phenylacrylamide (3k)



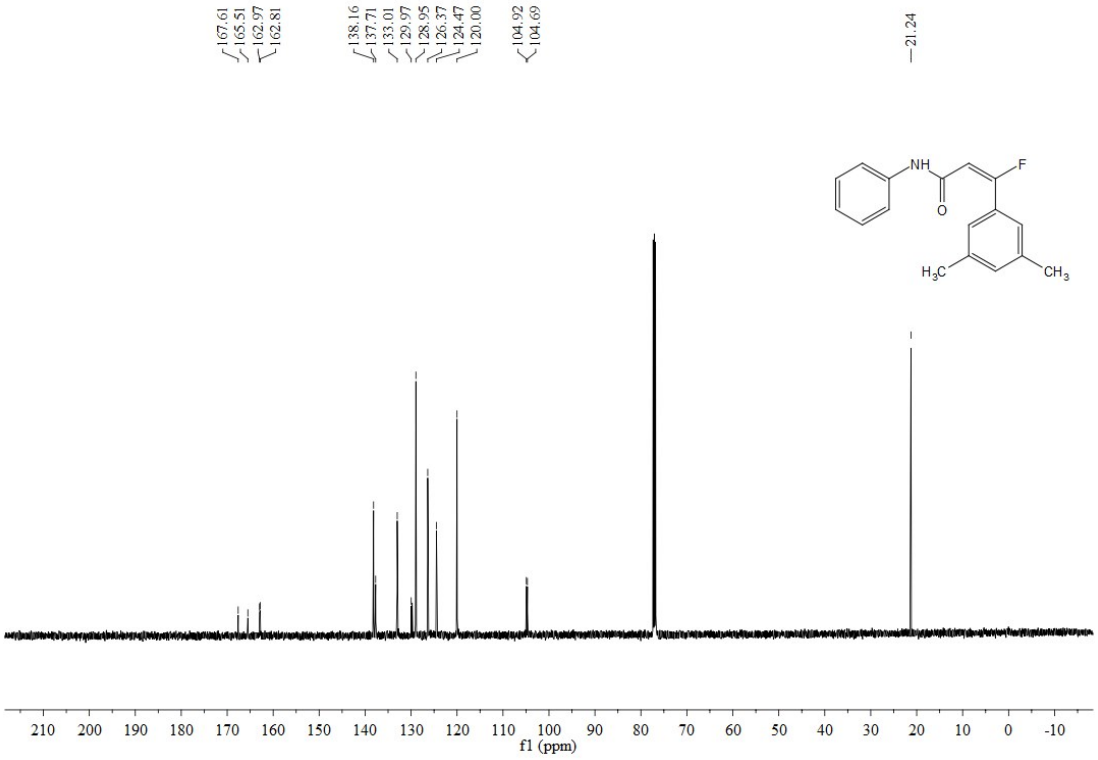
^{19}F NMR: (*E*)-3-fluoro-3-(3-methoxyphenyl)-*N*-phenylacrylamide (3k)



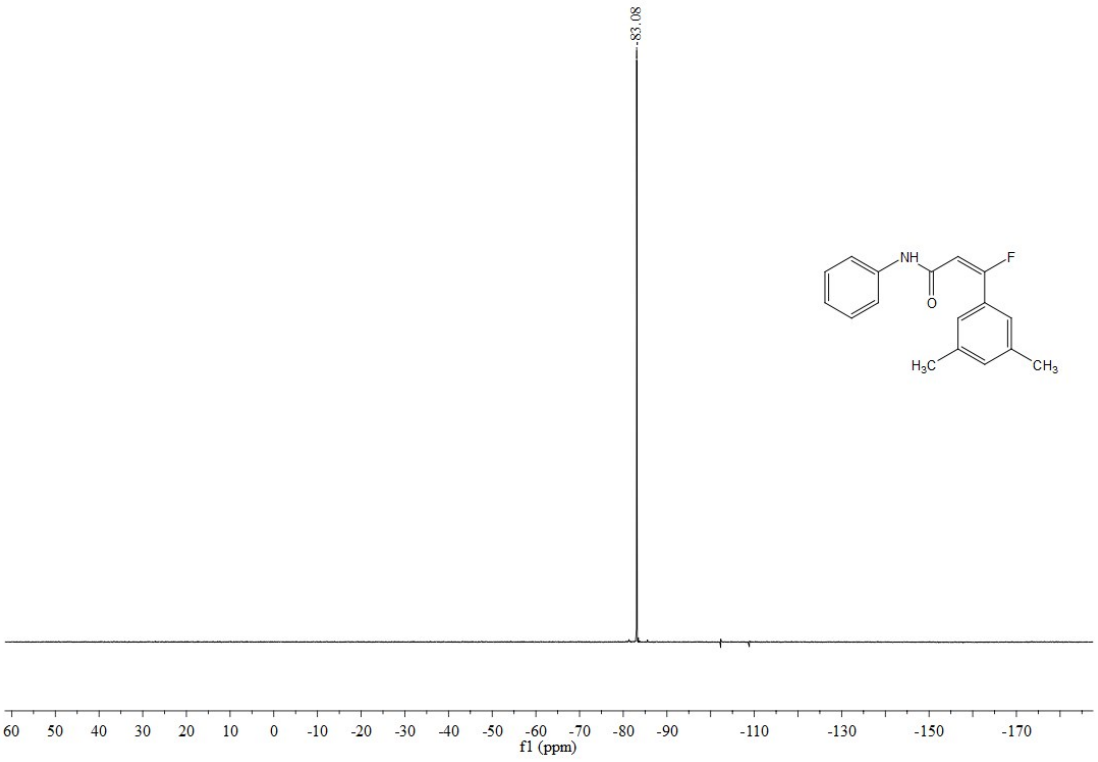
^{1}H NMR: (*E*)-3-(3,5-dimethylphenyl)-3-fluoro-*N*-phenylacrylamide (3l)



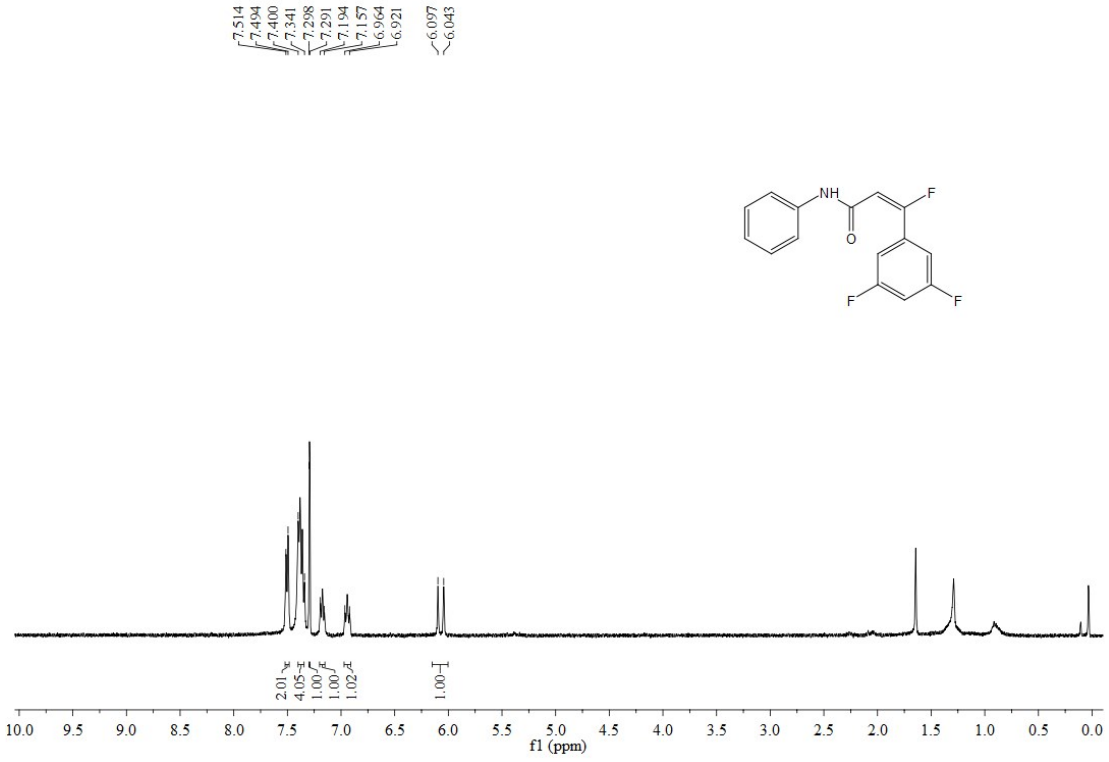
^{13}C NMR: (*E*)-3-(3,5-dimethylphenyl)-3-fluoro-*N*-phenylacrylamide (3l)



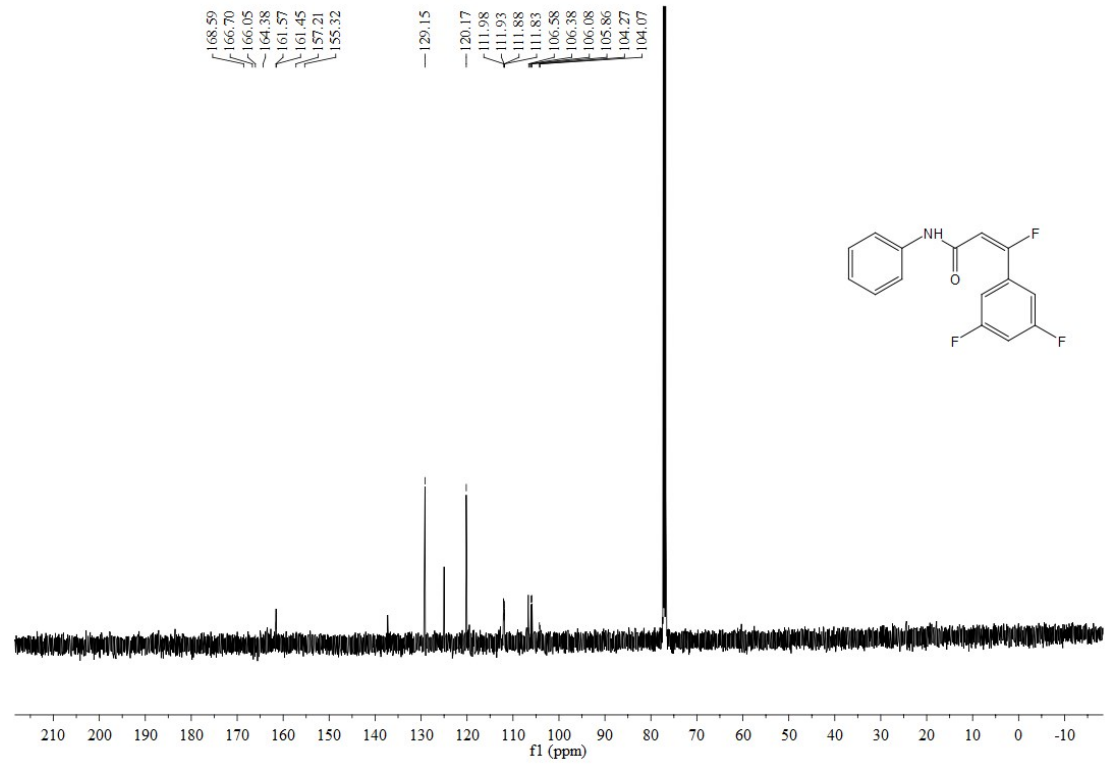
^{19}F NMR: (*E*)-3-(3,5-dimethylphenyl)-3-fluoro-*N*-phenylacrylamide (3l)



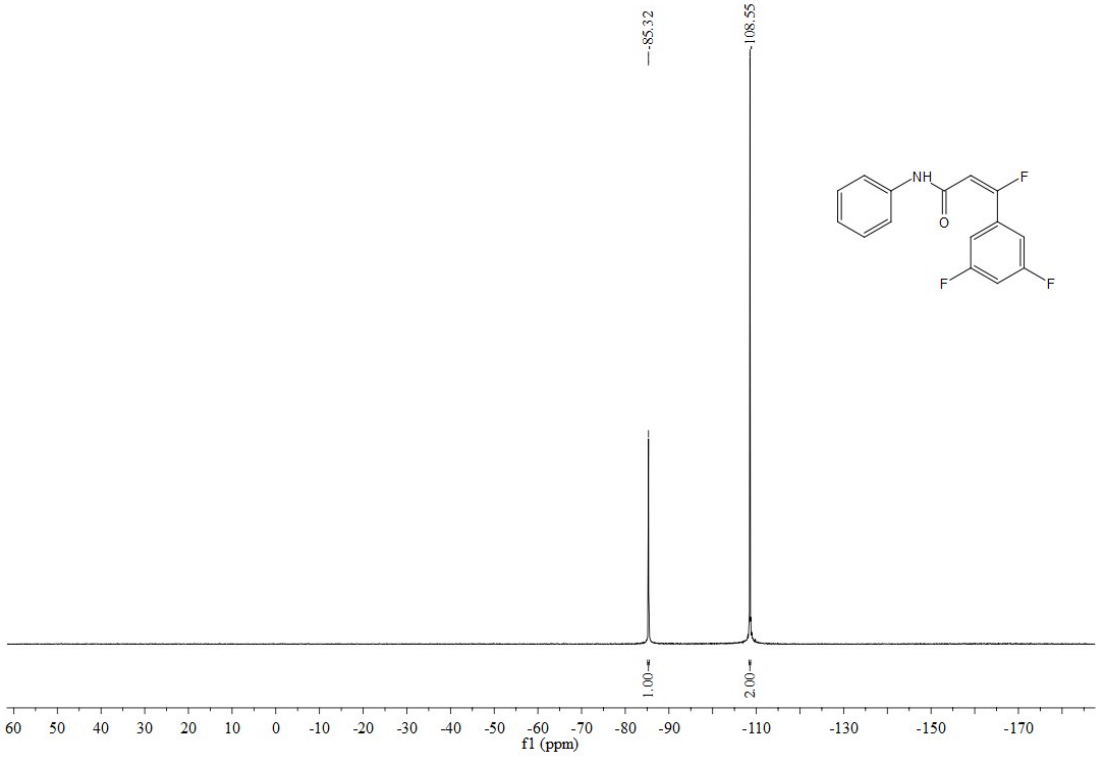
^{1}H NMR: (*E*)-3-(3,5-difluorophenyl)-3-fluoro-*N*-phenylacrylamide (3m)



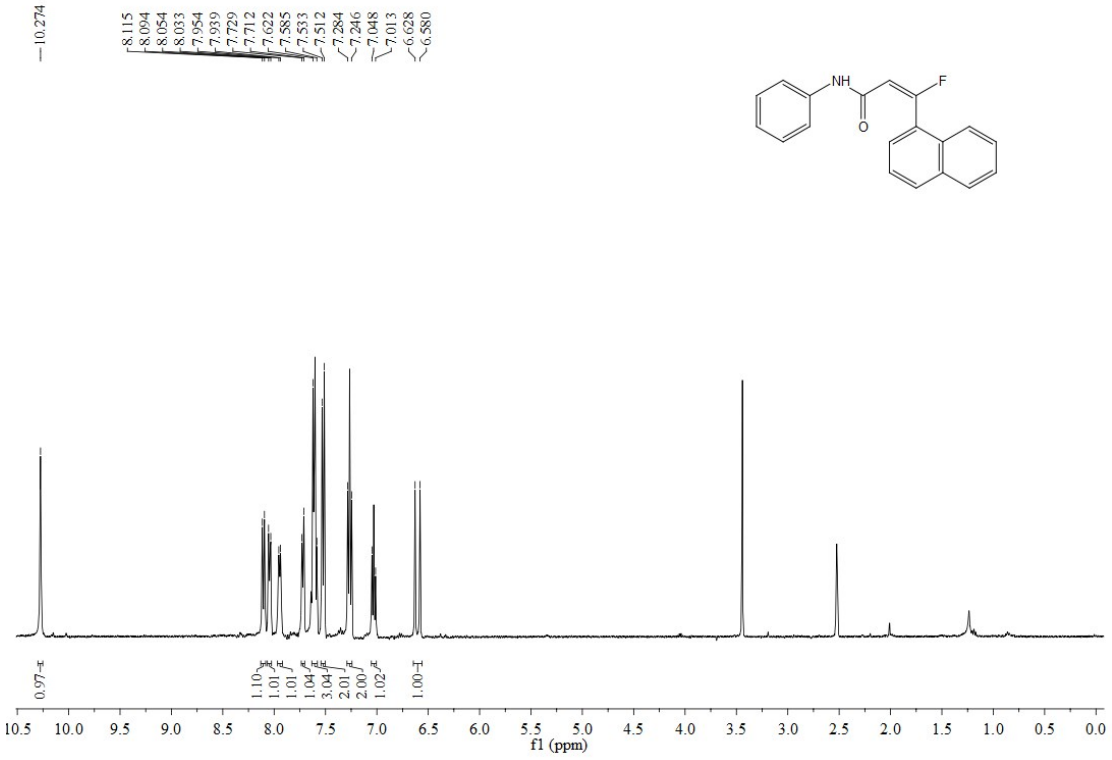
^{13}C NMR: (*E*)-3-(3,5-difluorophenyl)-3-fluoro-*N*-phenylacrylamide (3m)



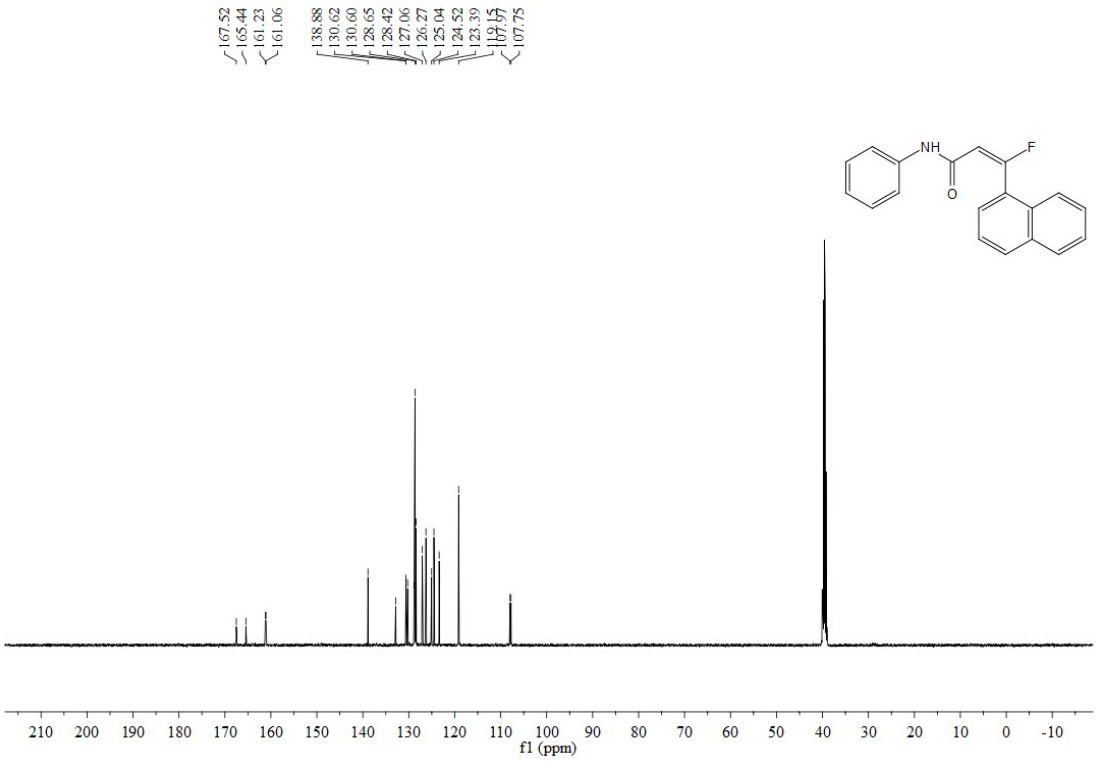
^{19}F NMR: (*E*)-3-(3,5-difluorophenyl)-3-fluoro-*N*-phenylacrylamide (3m)



^{1}H NMR: (*E*)-3-fluoro-3-(naphthalen-1-yl)-*N*-phenylacrylamide (3n)

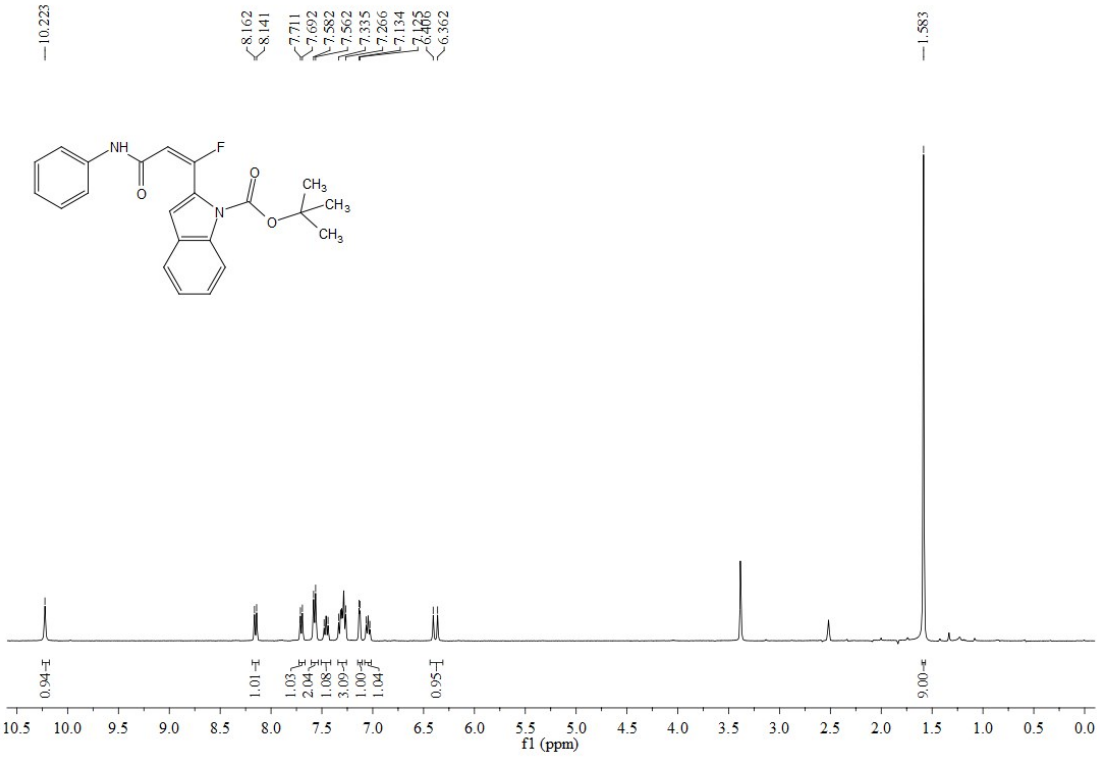


^{13}C NMR: (*E*)-3-fluoro-3-(naphthalen-1-yl)-*N*-phenylacrylamide (3n)

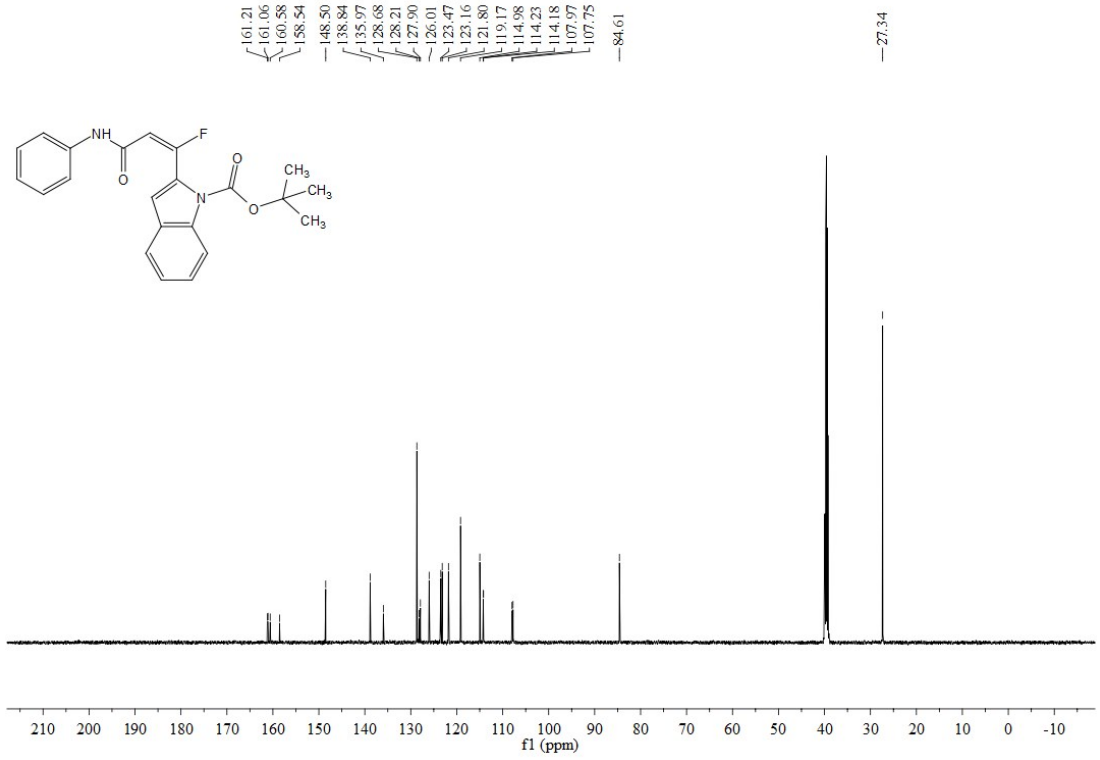


^{19}F NMR: (*E*)-3-fluoro-3-(naphthalen-1-yl)-*N*-phenylacrylamide (3n)

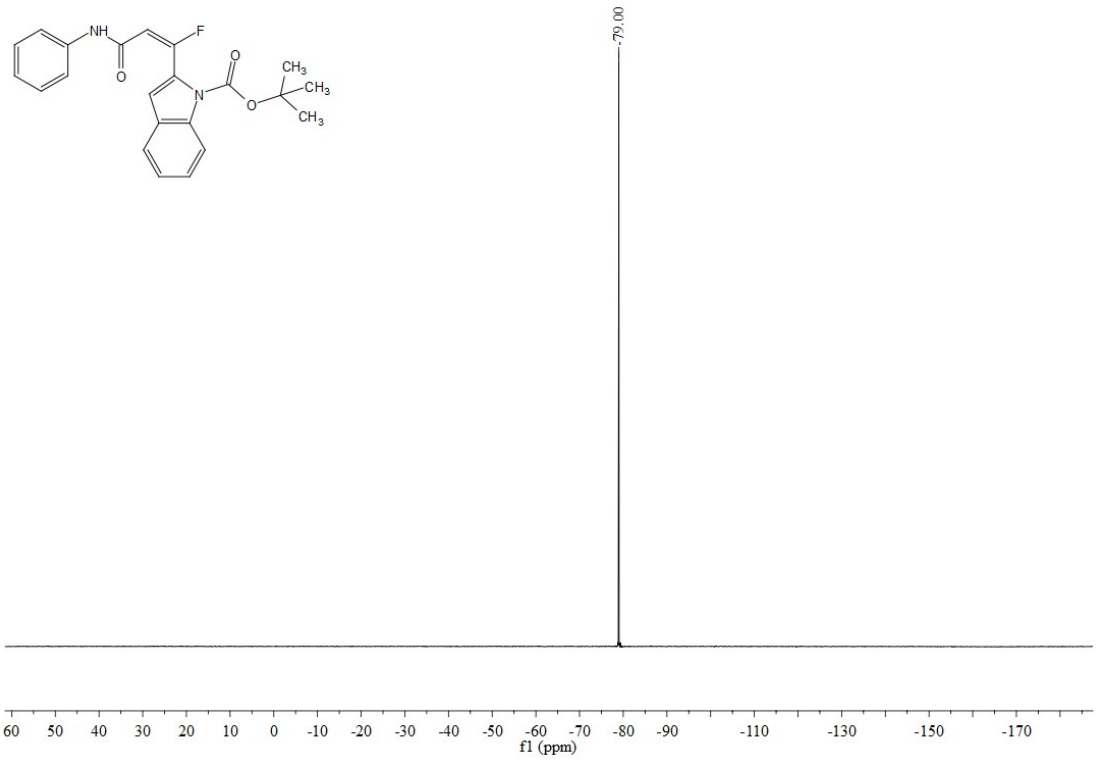
^{1}H NMR: (*E*)-*tert*-butyl 2-(1-fluoro-3-oxo-3-(phenylamino)prop-1-en-1-yl)-1*H*-indole-1-carboxylate (3o)



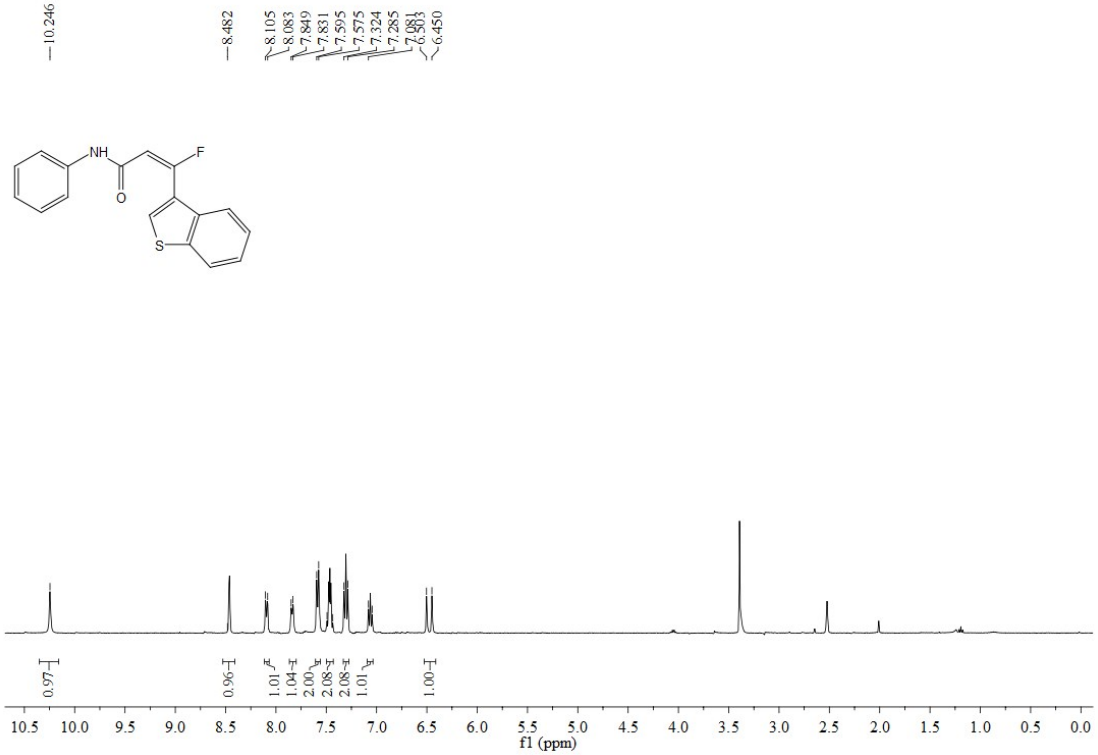
^{13}C NMR: (*E*)-*tert*-butyl 2-(1-fluoro-3-oxo-3-(phenylamino)prop-1-en-1-yl)-1*H*-indole-1-carboxylate (3o)



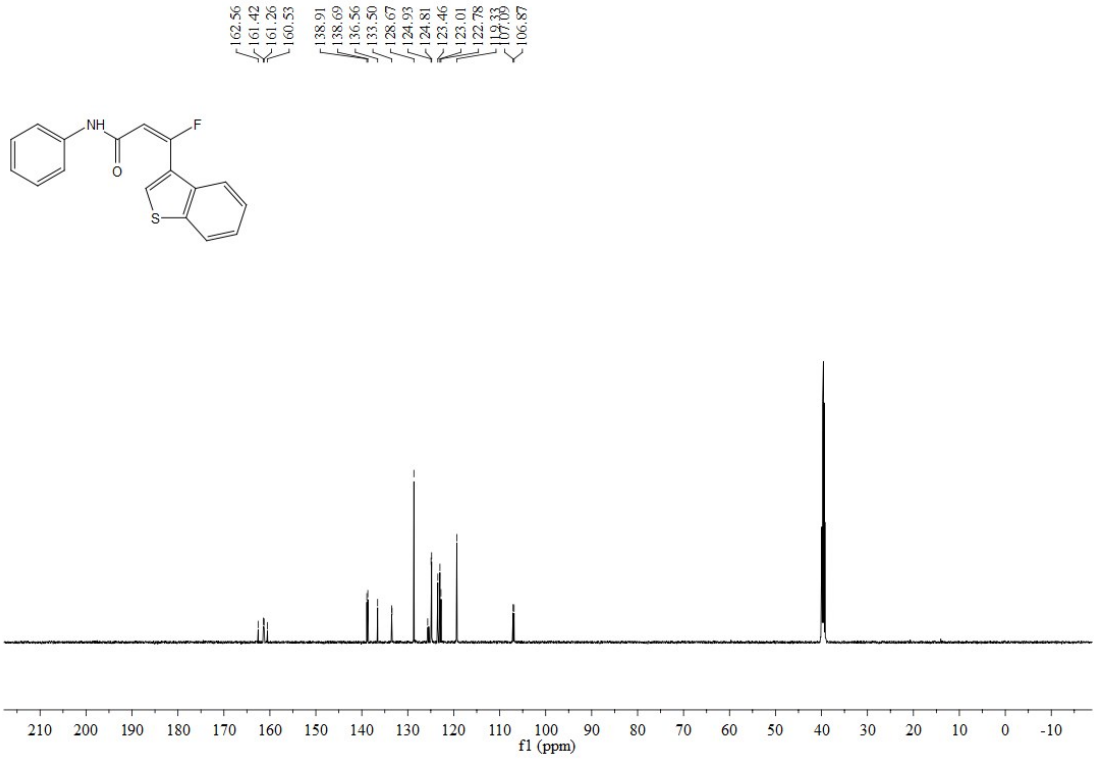
^{19}F NMR: (*E*)-*tert*-butyl 2-(1-fluoro-3-oxo-3-(phenylamino)prop-1-en-1-yl)-1*H*-indole-1-carboxylate (3o)



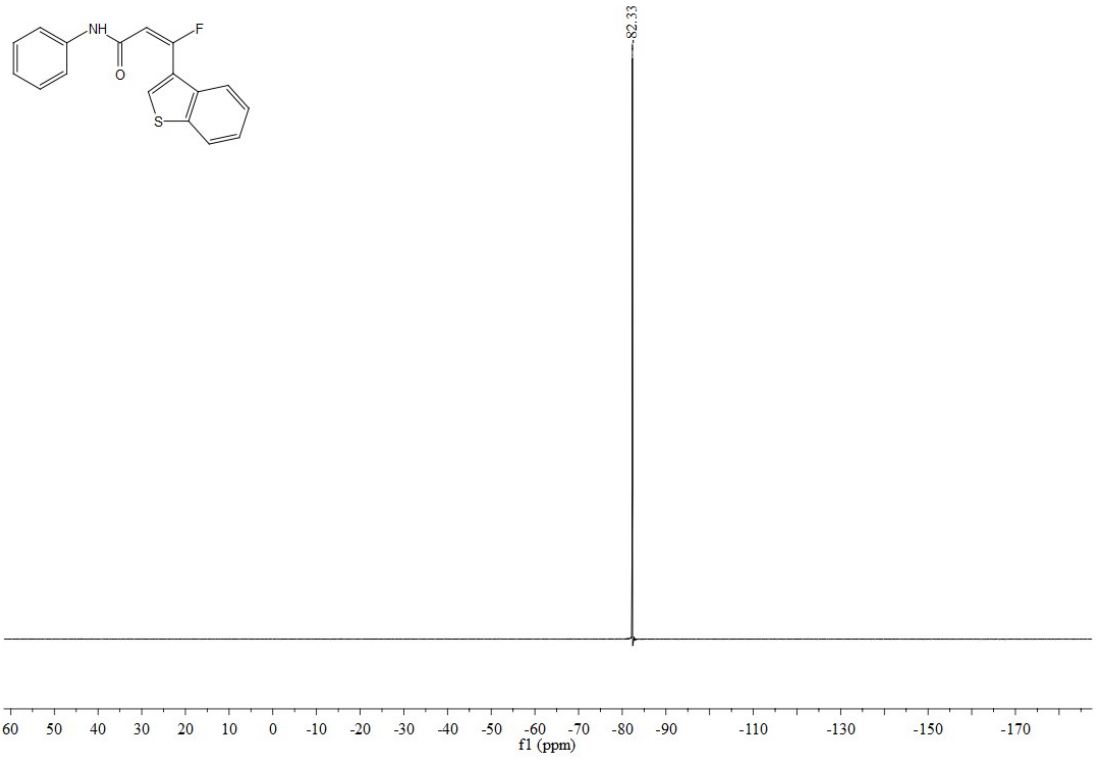
^{1}H NMR: (*E*)-3-(benzo[*b*]thiophen-3-yl)-3-fluoro-*N*-phenylacrylamide (3p)



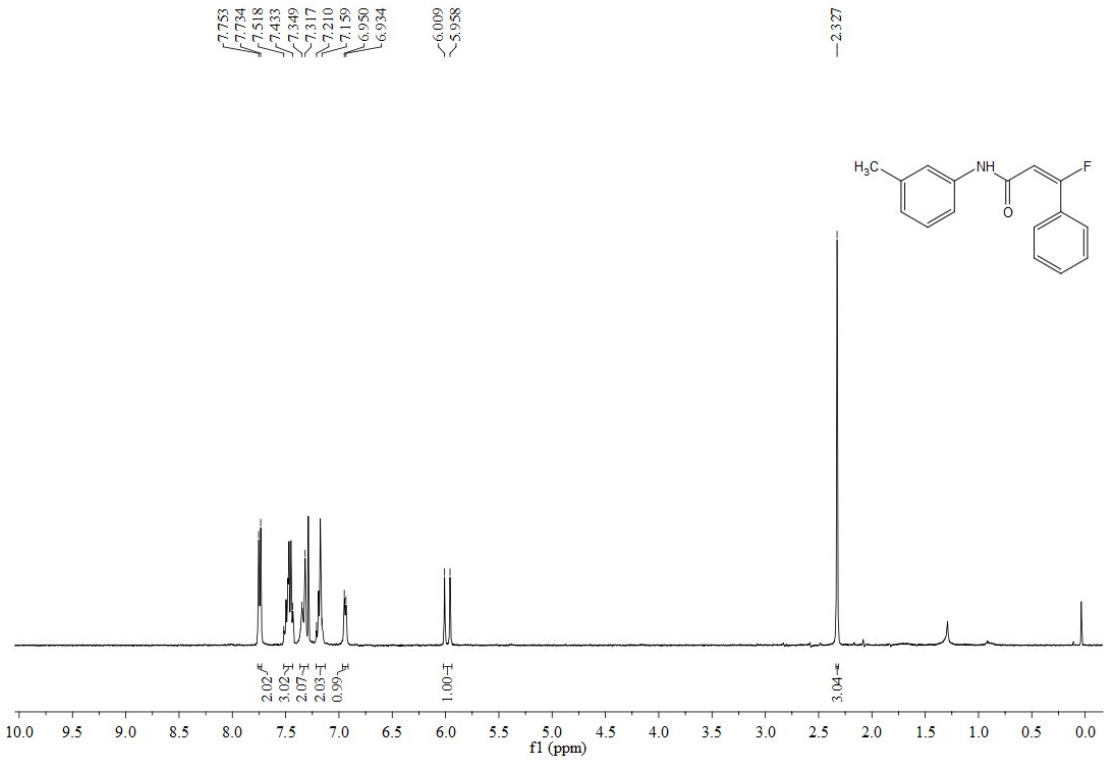
^{13}C NMR: (*E*)-3-(benzo[*b*]thiophen-3-yl)-3-fluoro-*N*-phenylacrylamide (3p)



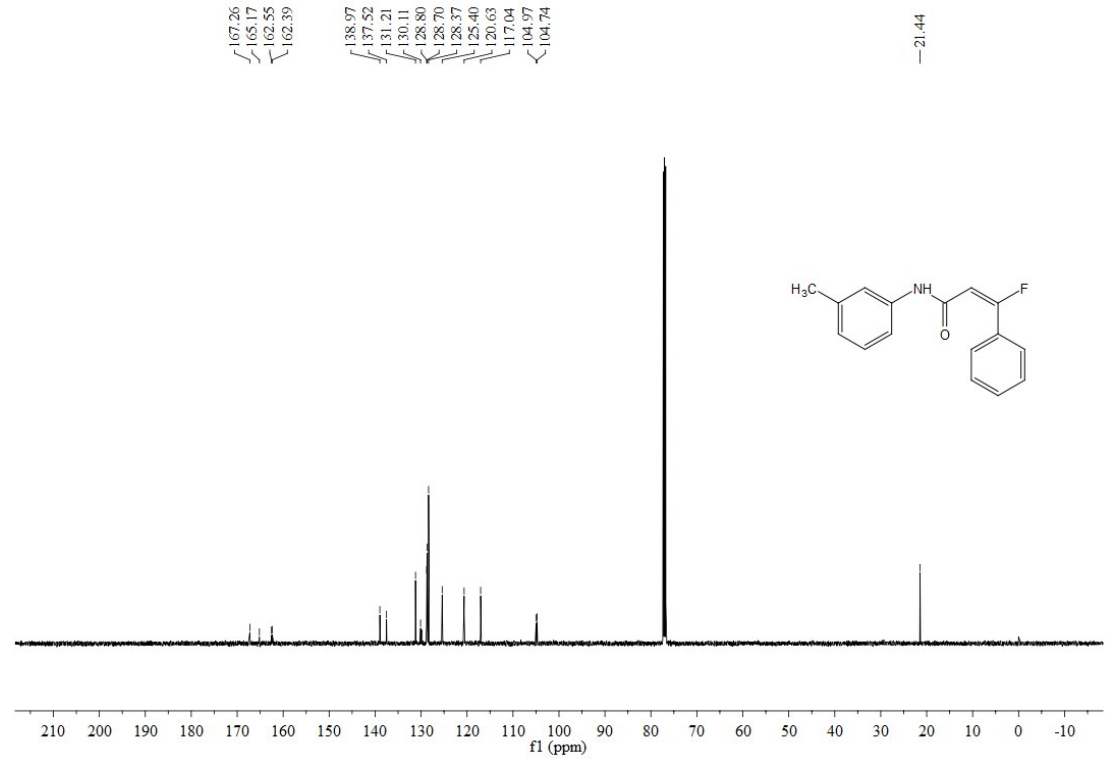
^{19}F NMR: (*E*)-3-(benzo[*b*]thiophen-3-yl)-3-fluoro-*N*-phenylacrylamide (3p)



^{1}H NMR: (*E*)-3-fluoro-3-phenyl-*N*-(*m*-tolyl)acrylamide (3q)

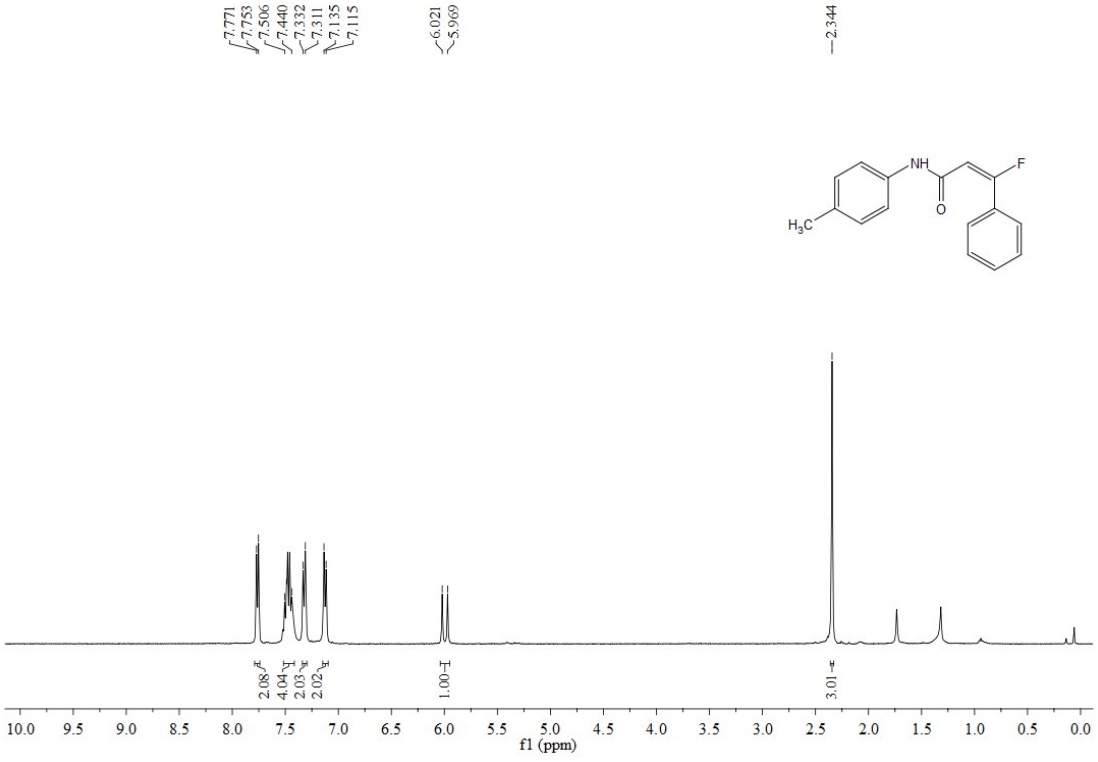


^{13}C NMR: (*E*)-3-fluoro-3-phenyl-*N*-(*m*-tolyl)acrylamide (3q)

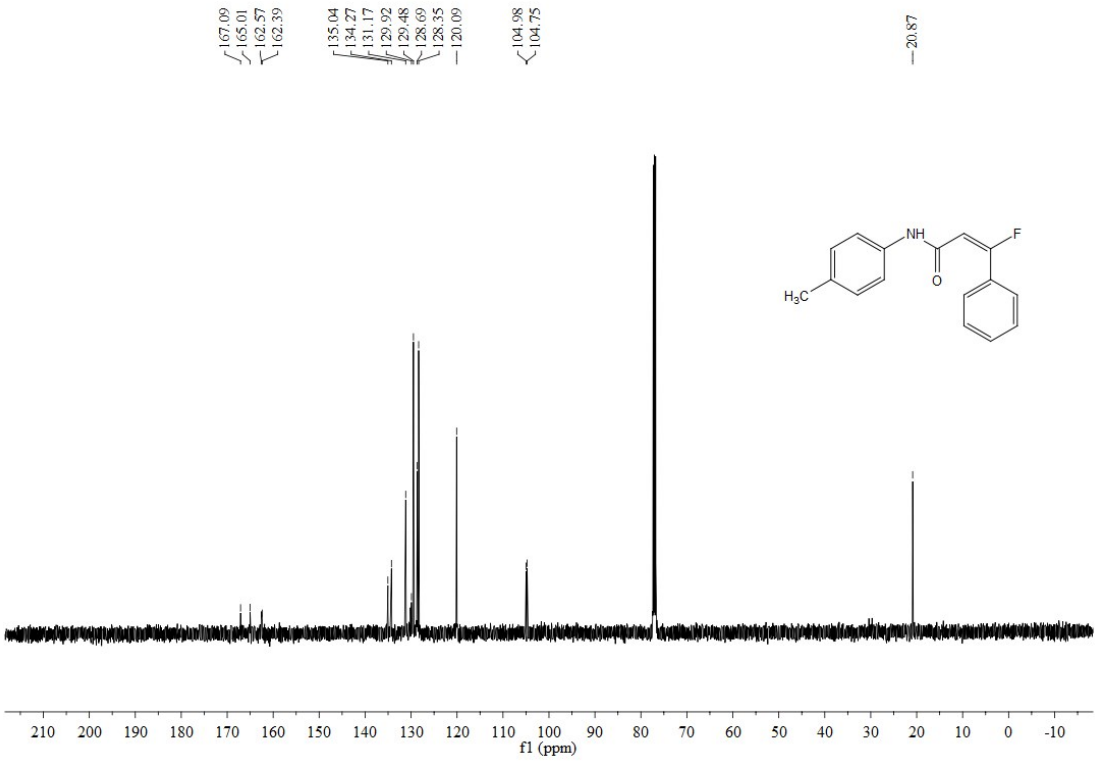


^{19}F NMR: (*E*)-3-fluoro-3-phenyl-*N*-(*m*-tolyl)acrylamide (3q)

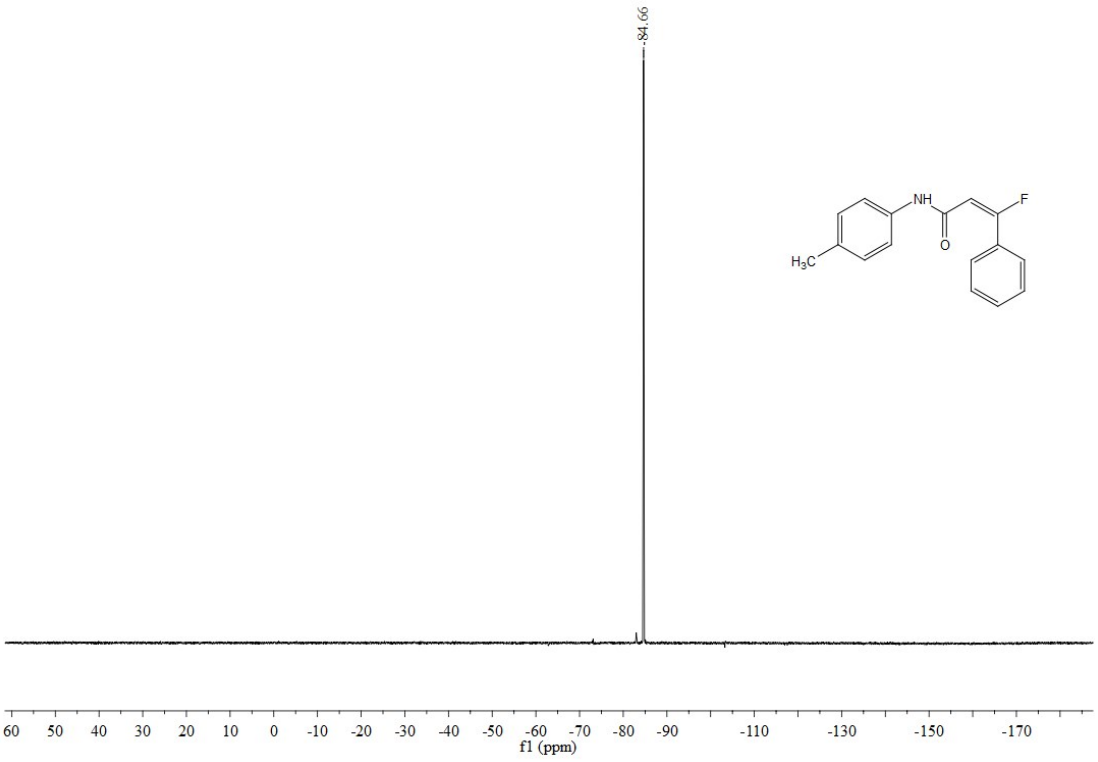
^{1}H NMR: (*E*)-3-fluoro-3-phenyl-*N*-(*p*-tolyl)acrylamide (3r)



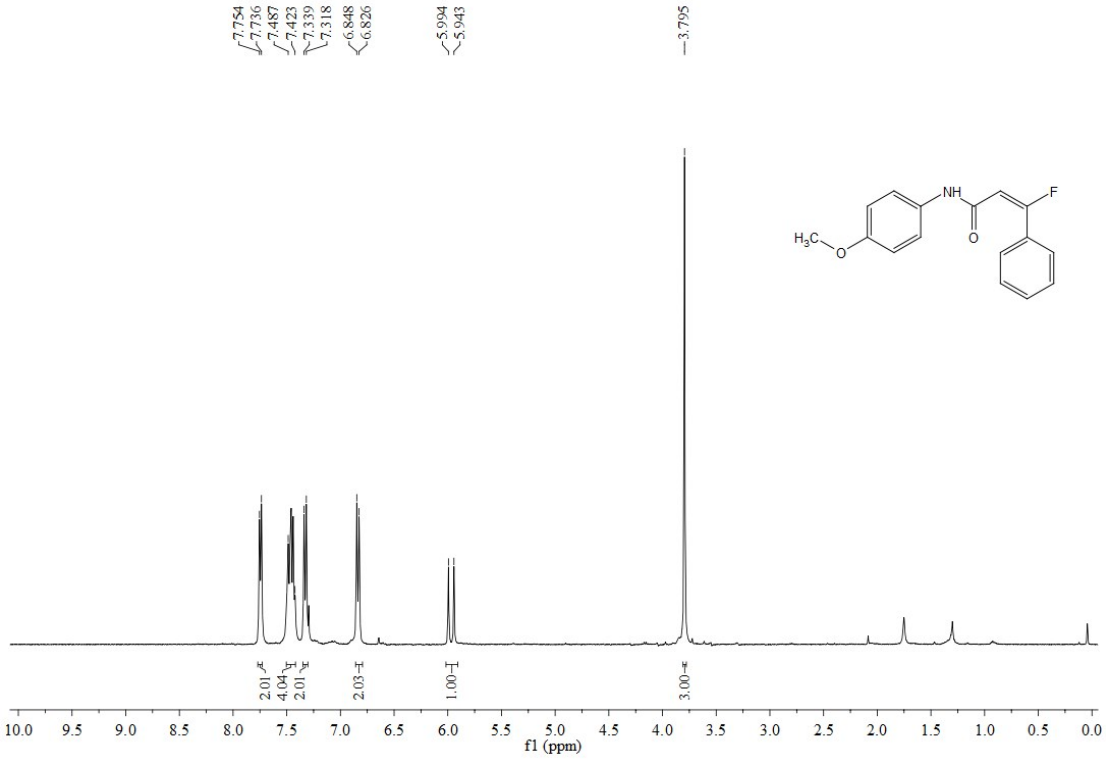
^{13}C NMR: (*E*)-3-fluoro-3-phenyl-*N*-(*p*-tolyl)acrylamide (3r)



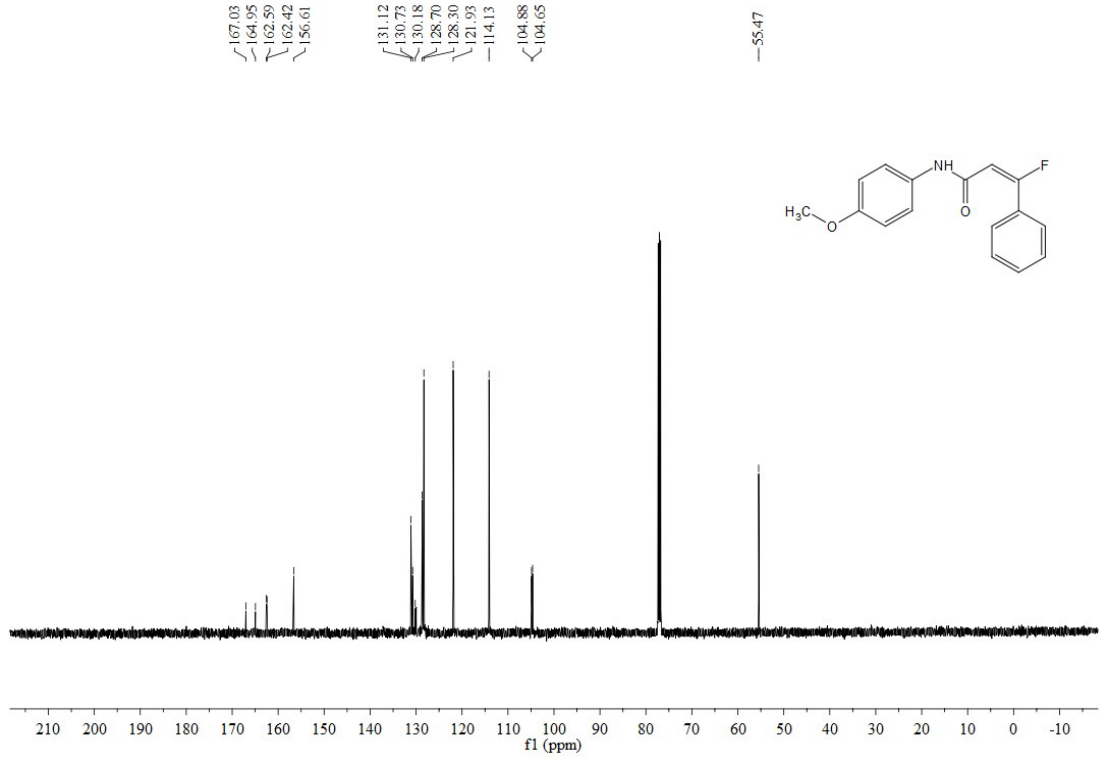
^{19}F NMR: (*E*)-3-fluoro-3-phenyl-*N*-(*p*-tolyl)acrylamide (3r)



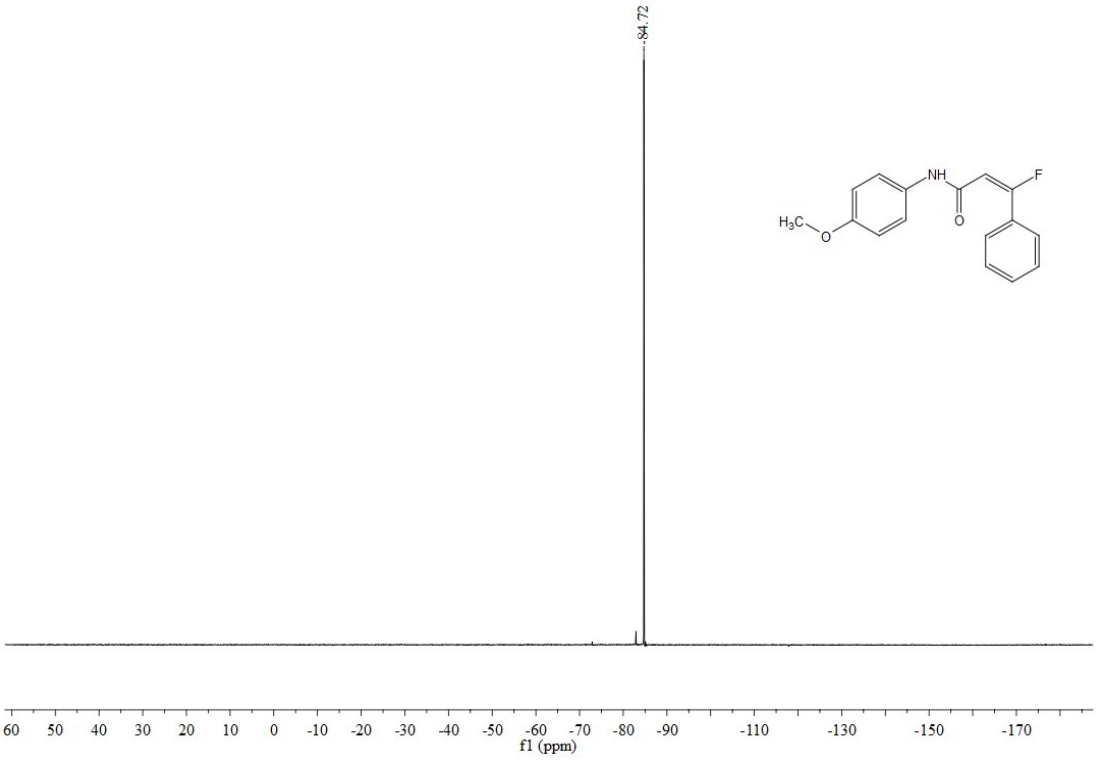
^{1}H NMR: (*E*)-3-fluoro-*N*-(4-methoxyphenyl)-3-phenylacrylamide (3s)



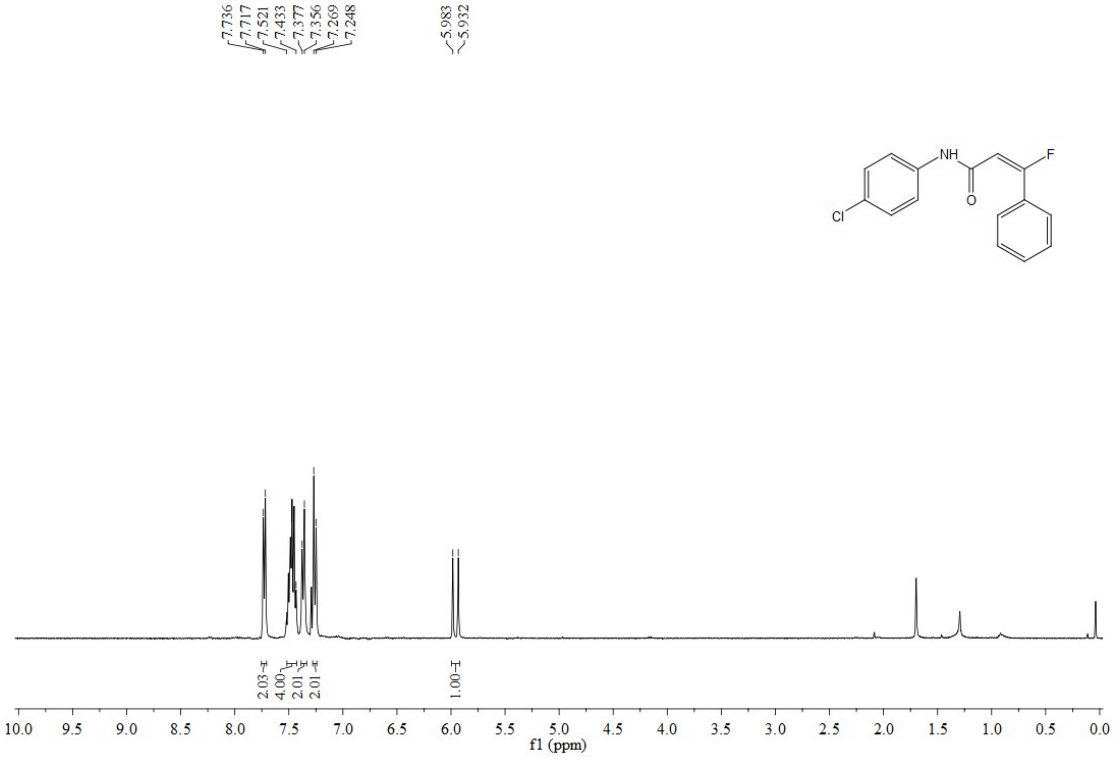
^{13}C NMR: (*E*)-3-fluoro-*N*-(4-methoxyphenyl)-3-phenylacrylamide (3s)



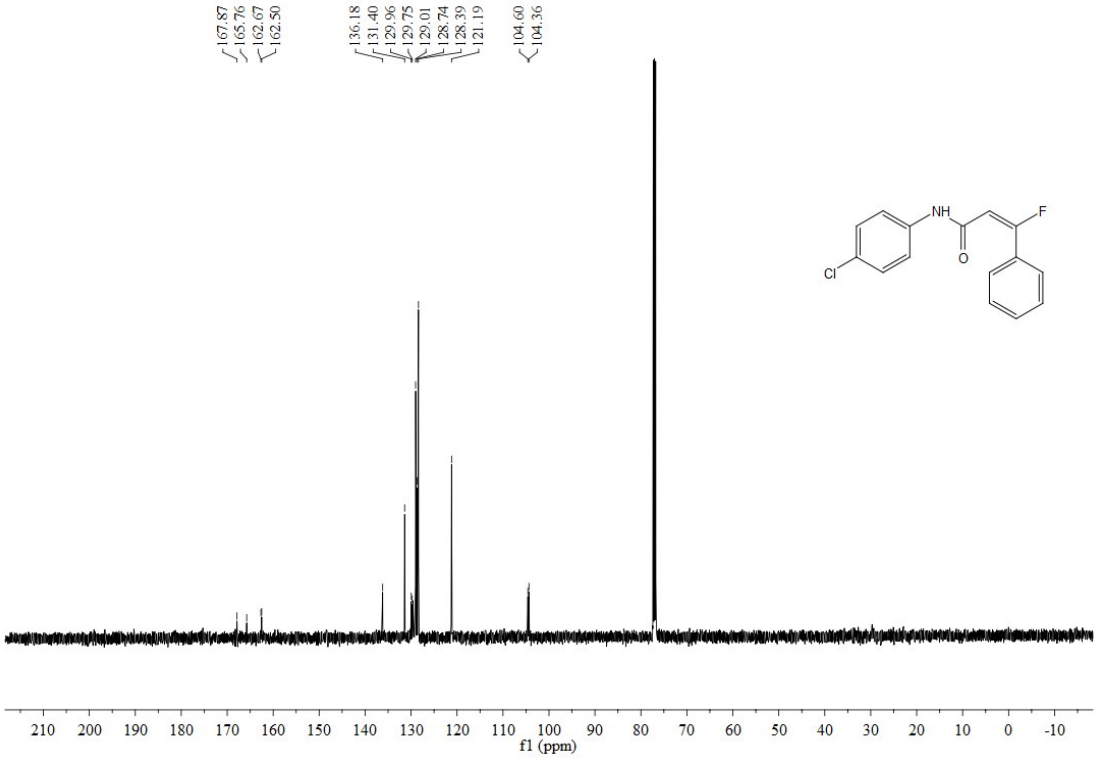
^{19}F NMR: (*E*)-3-fluoro-*N*-(4-methoxyphenyl)-3-phenylacrylamide (3s)



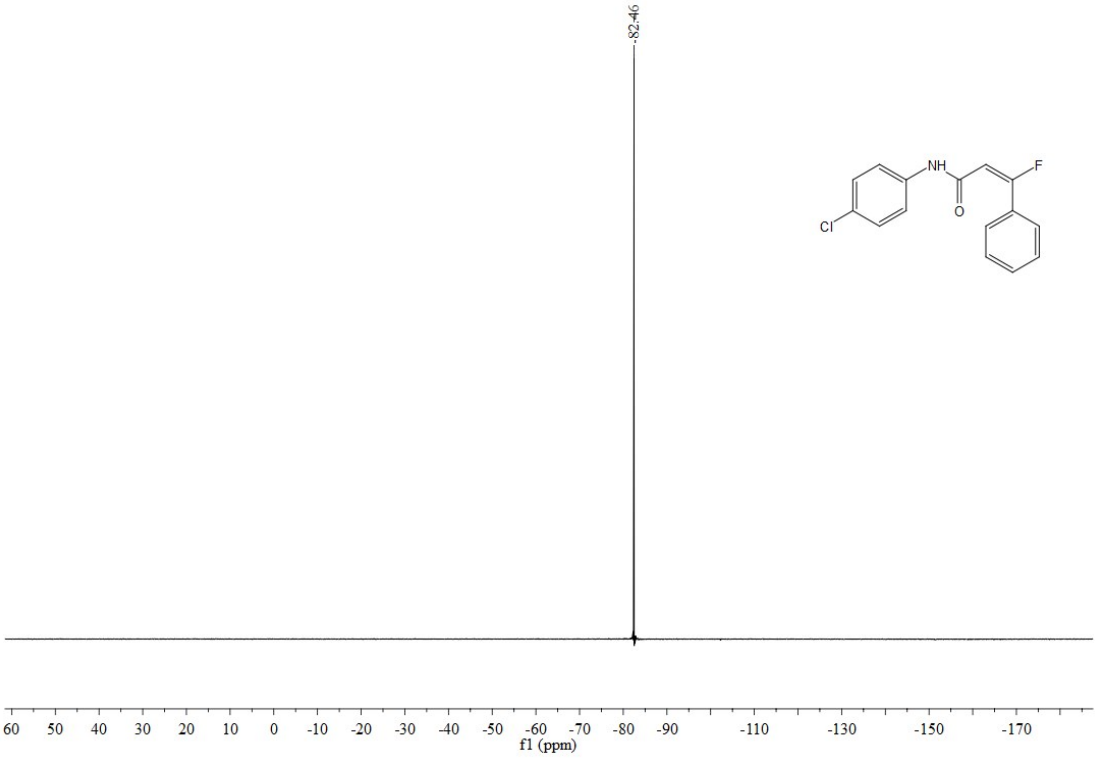
^{1}H NMR: (*E*)-*N*-(4-chlorophenyl)-3-fluoro-3-phenylacrylamide (3t)



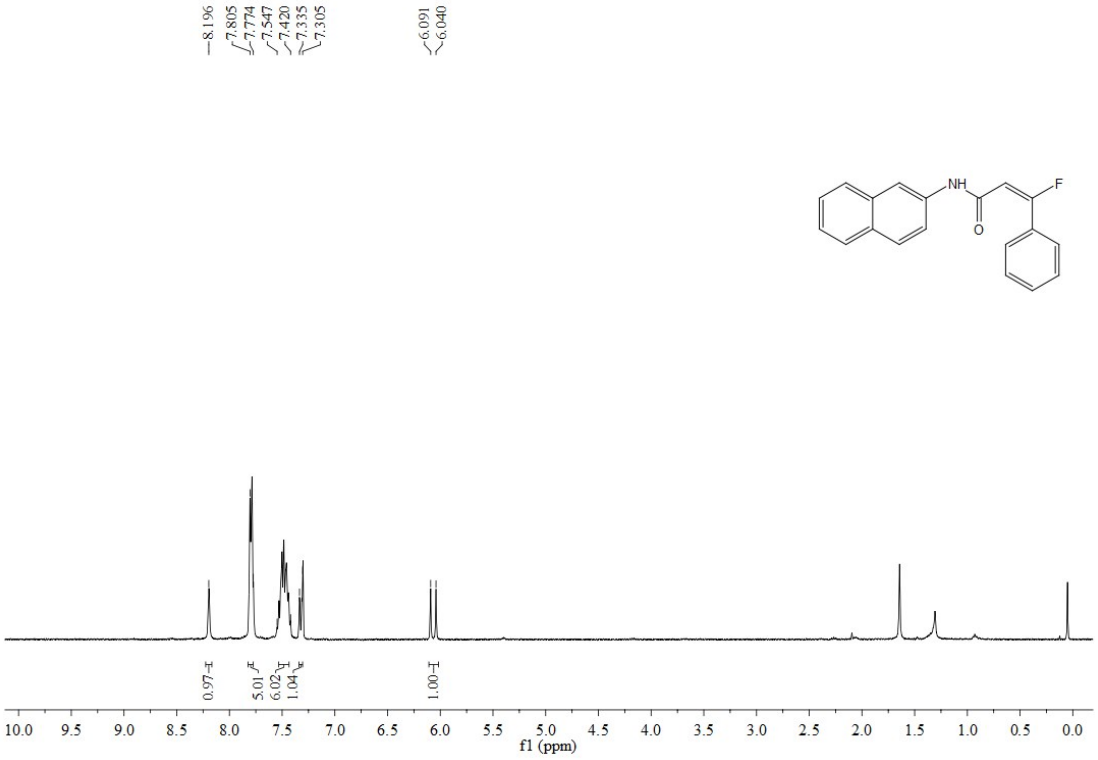
^{13}C NMR: (*E*)-*N*-(4-chlorophenyl)-3-fluoro-3-phenylacrylamide (3t)



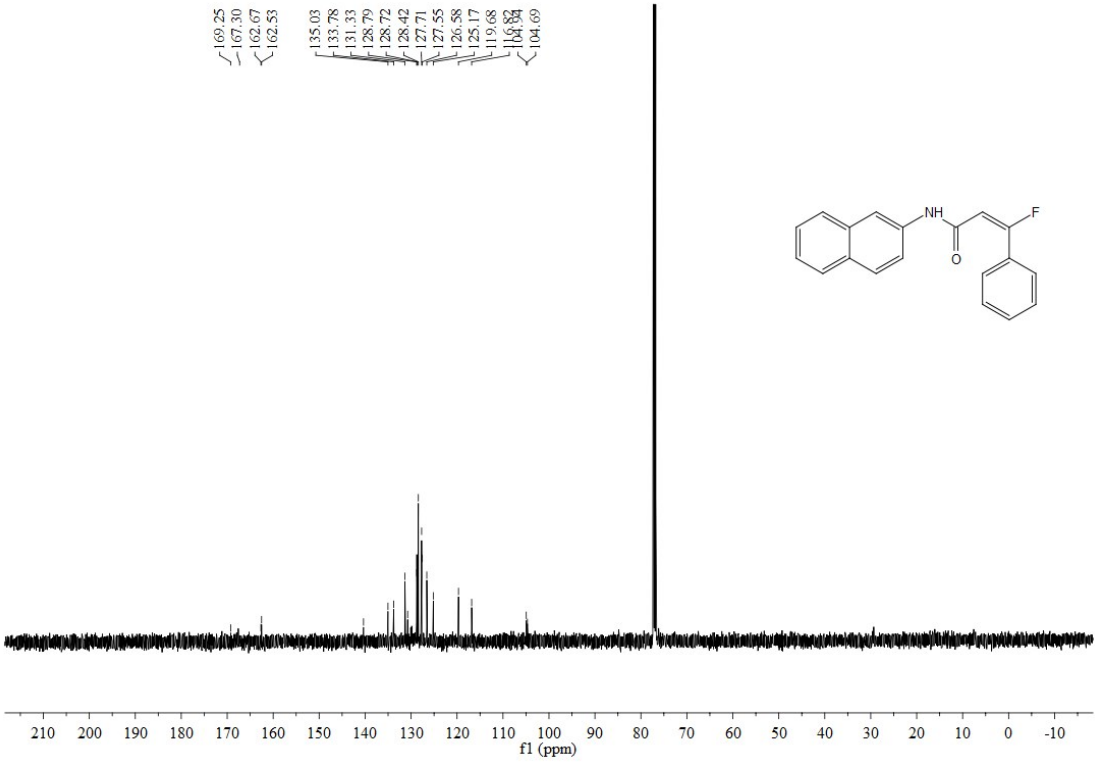
^{19}F NMR: (*E*)-*N*-(4-chlorophenyl)-3-fluoro-3-phenylacrylamide (3t)



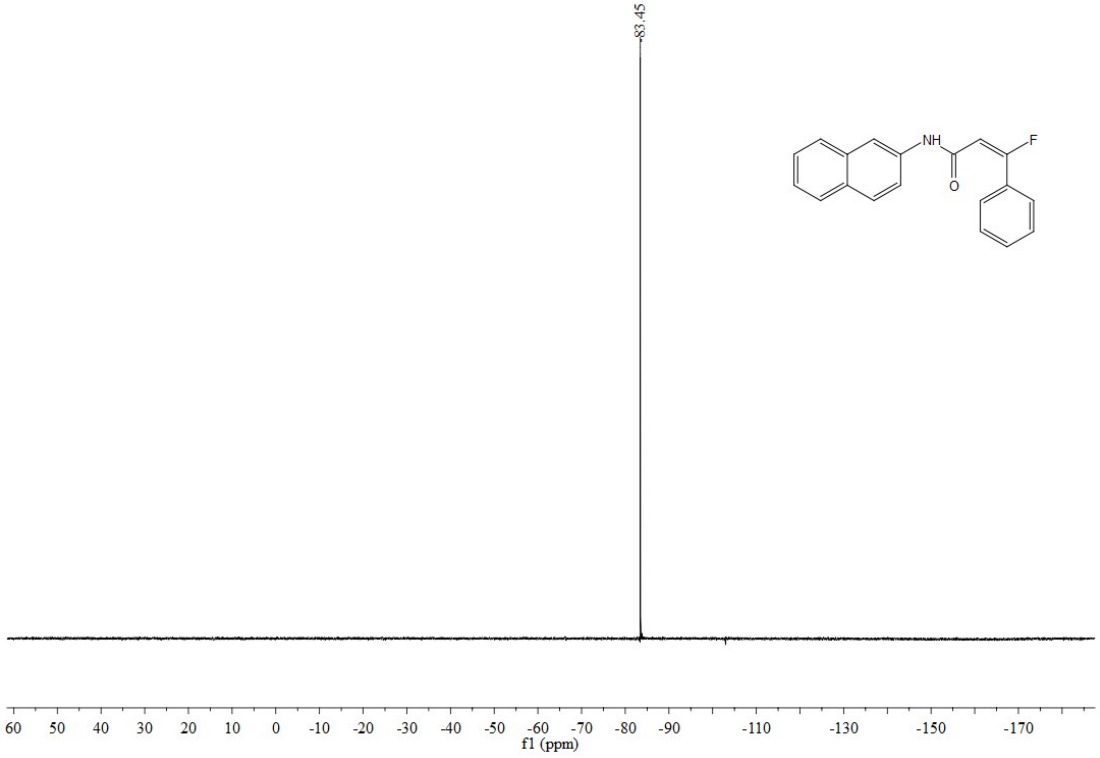
^{1}H NMR: (*E*)-3-fluoro-*N*-(naphthalen-2-yl)-3-phenylacrylamide (3u)



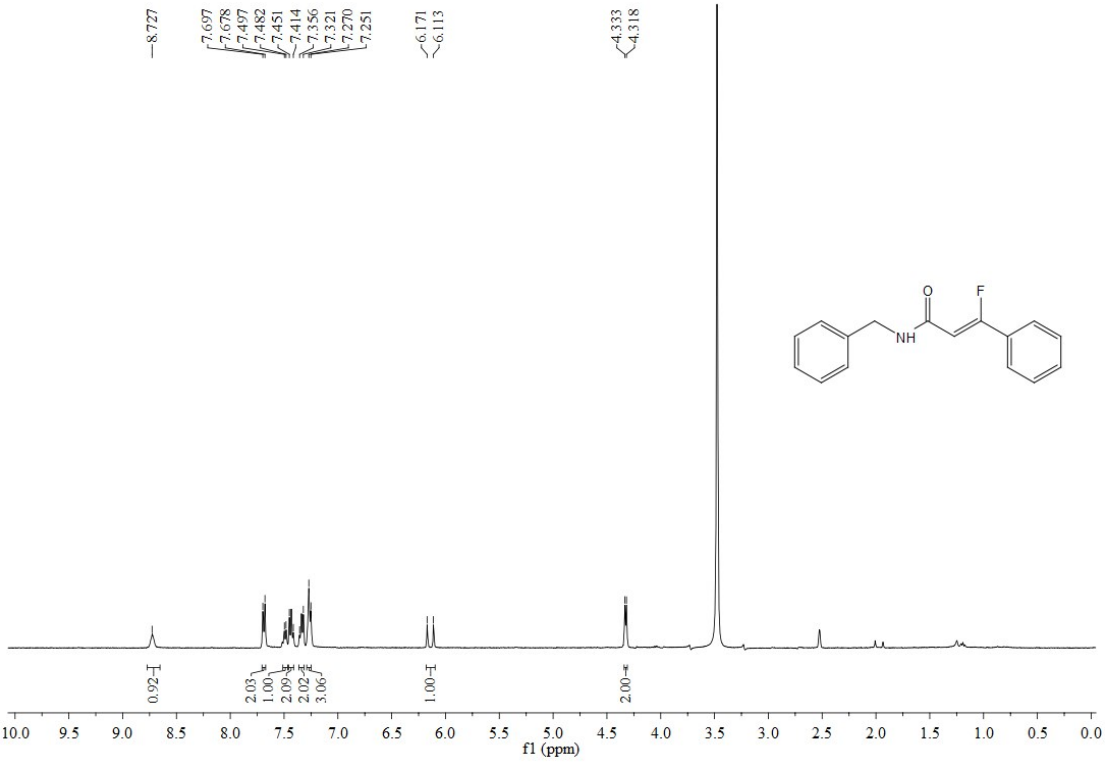
^{13}C NMR: (*E*)-3-fluoro-*N*-(naphthalen-2-yl)-3-phenylacrylamide (3u)



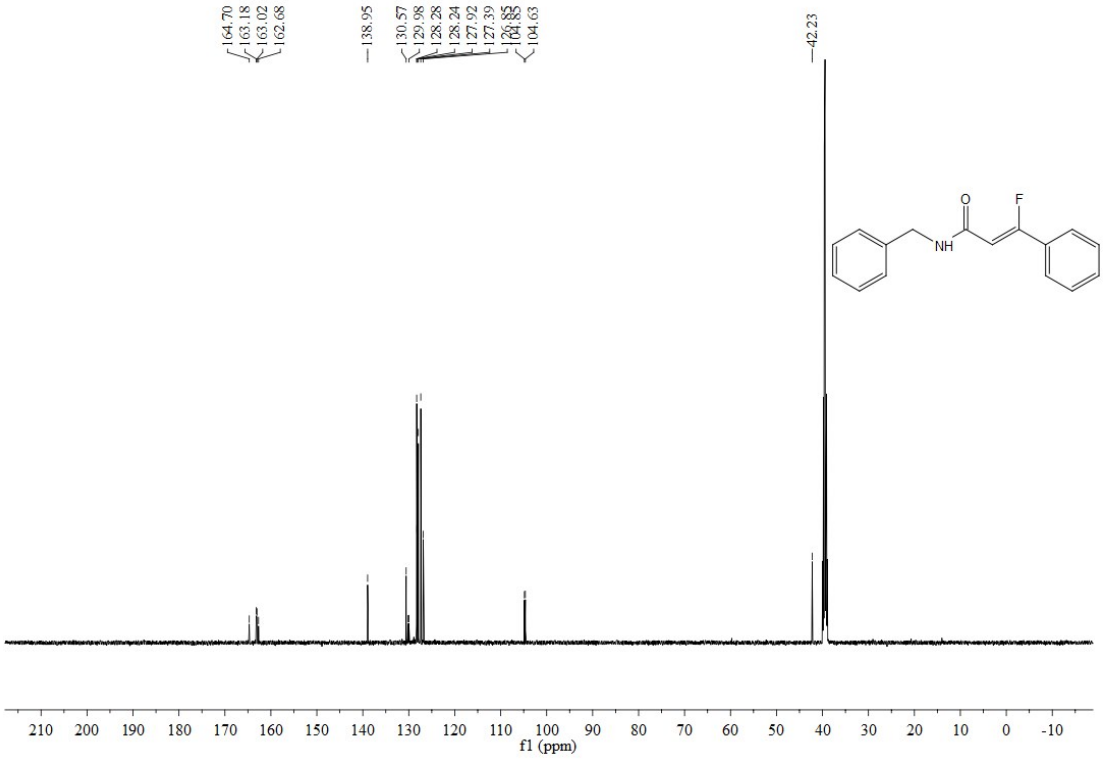
^{19}F NMR: (*E*)-3-fluoro-*N*-(naphthalen-2-yl)-3-phenylacrylamide (3u)



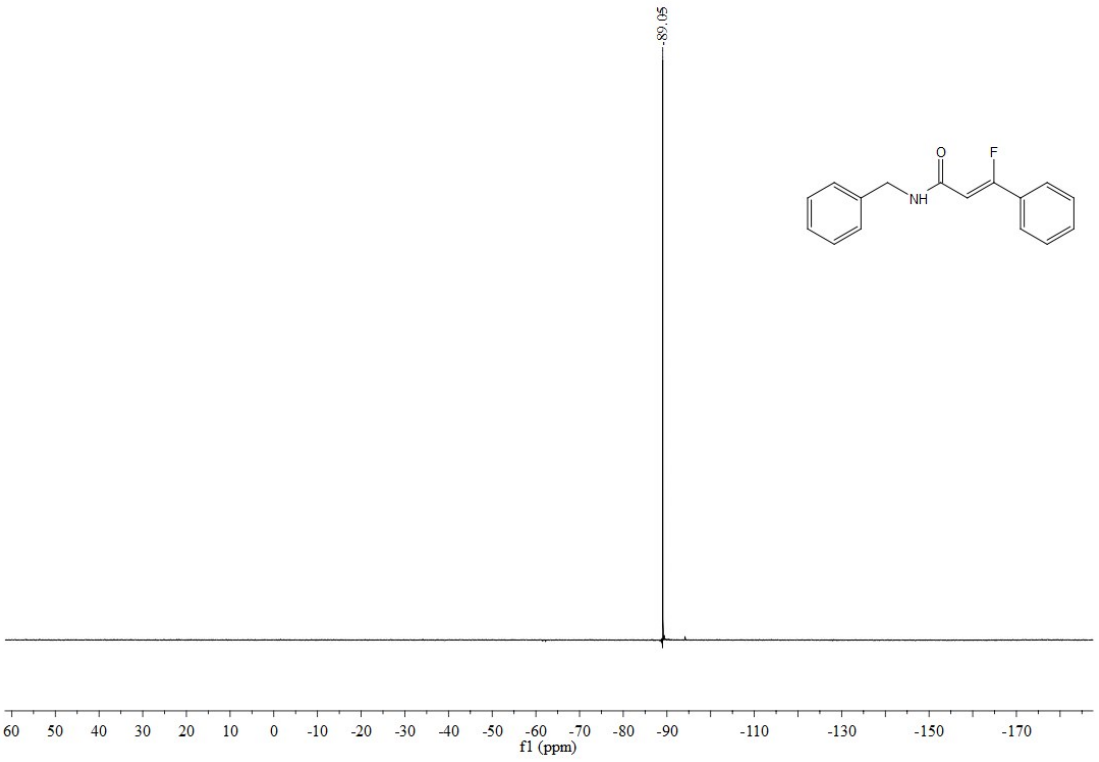
^{1}H NMR: (*E*)-*N*-benzyl-3-fluoro-3-phenylacrylamide (3v)



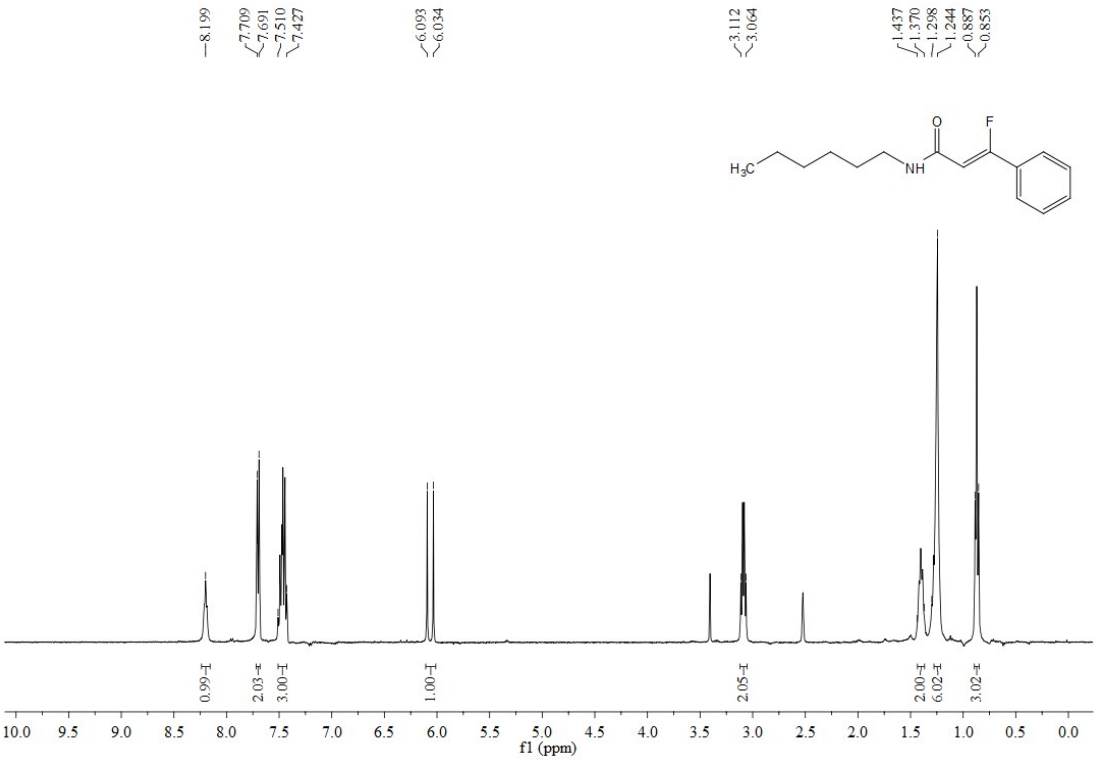
^{13}C NMR: (*E*)-*N*-benzyl-3-fluoro-3-phenylacrylamide (3v)



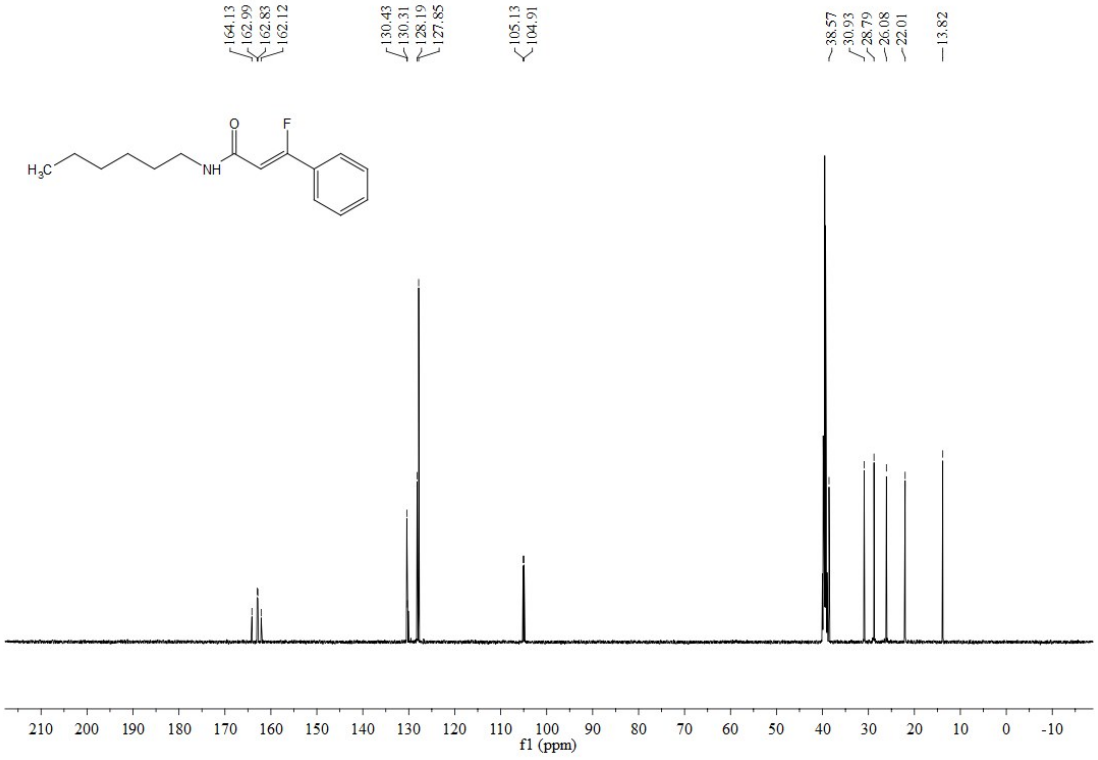
^{19}F NMR: (*E*)-*N*-benzyl-3-fluoro-3-phenylacrylamide (3v)



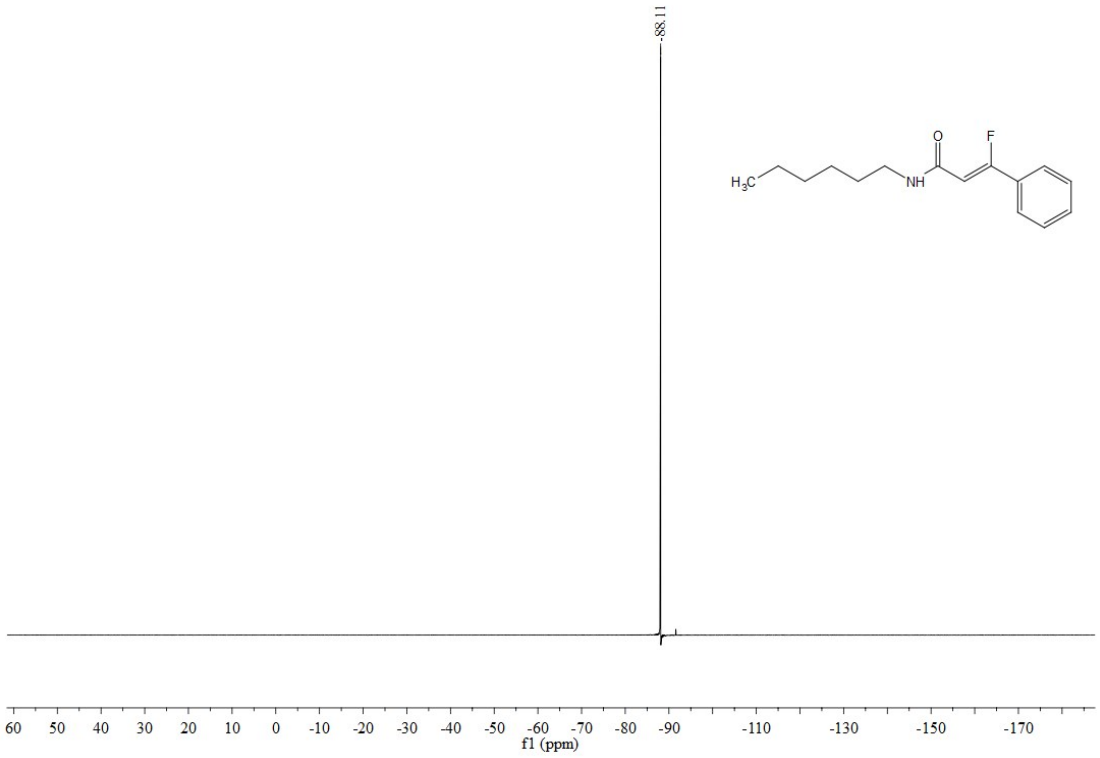
^{1}H NMR: (*E*)-3-fluoro-*N*-hexyl-3-phenylacrylamide (3w)



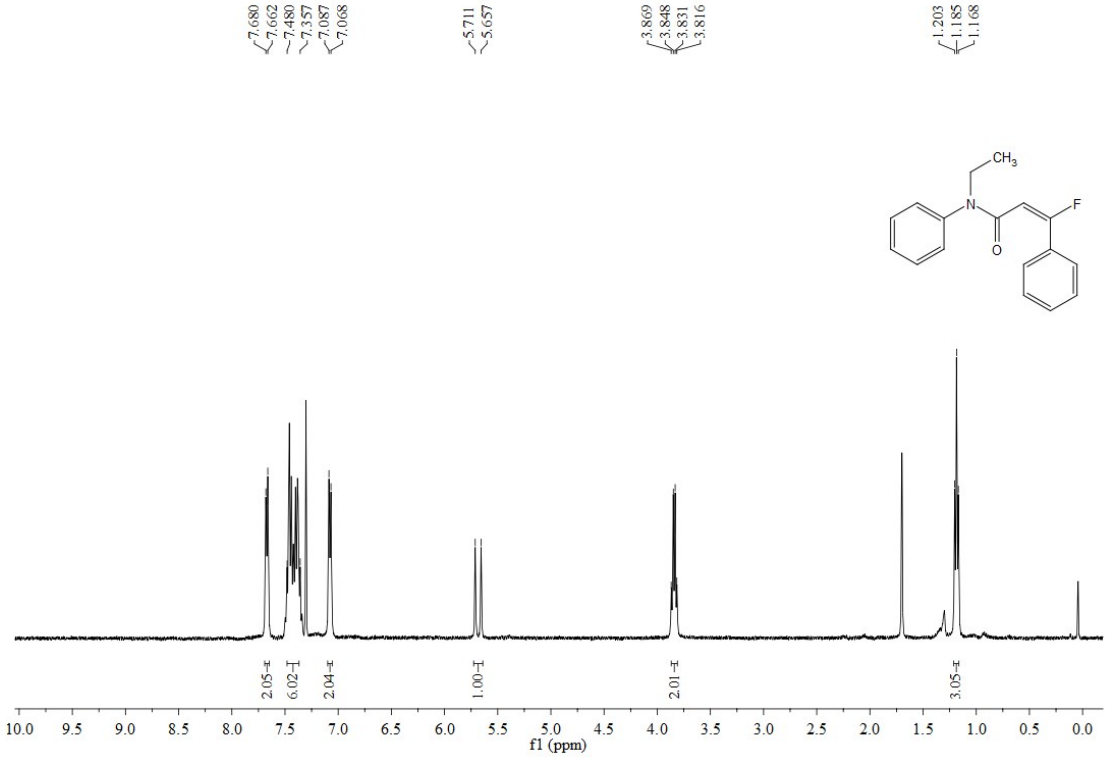
^{13}C NMR: (*E*)-3-fluoro-*N*-hexyl-3-phenylacrylamide (3w)



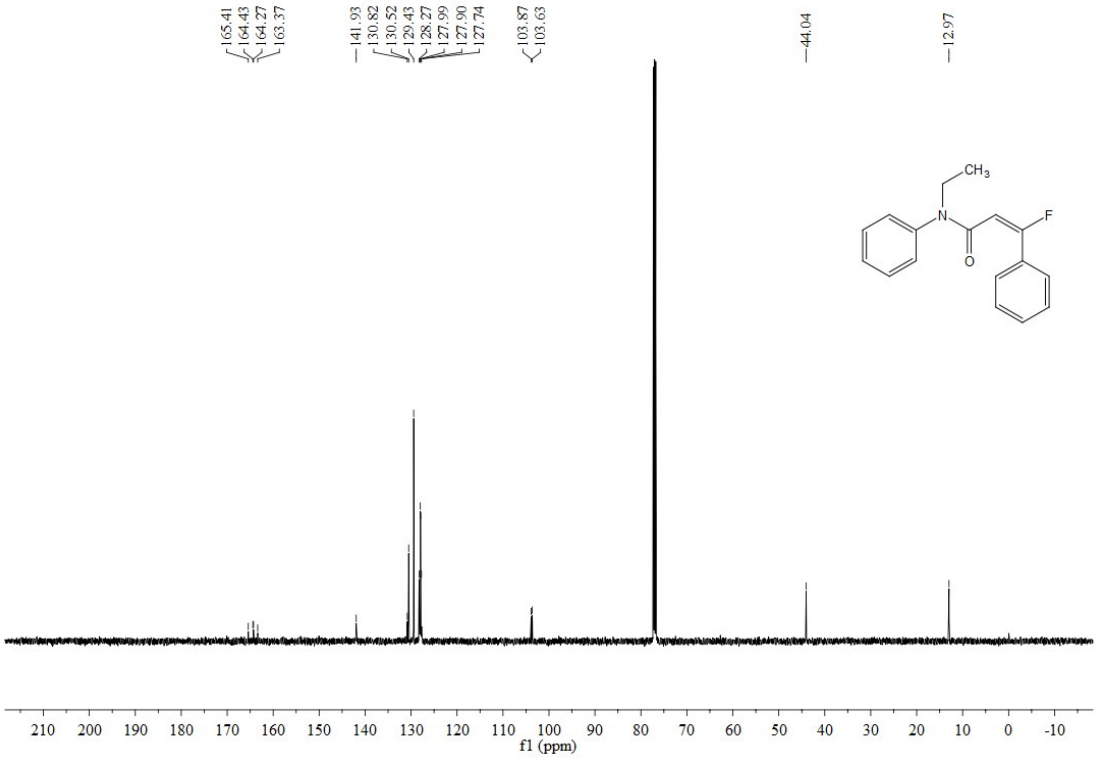
^{19}F NMR: (*E*)-3-fluoro-*N*-hexyl-3-phenylacrylamide (3w)



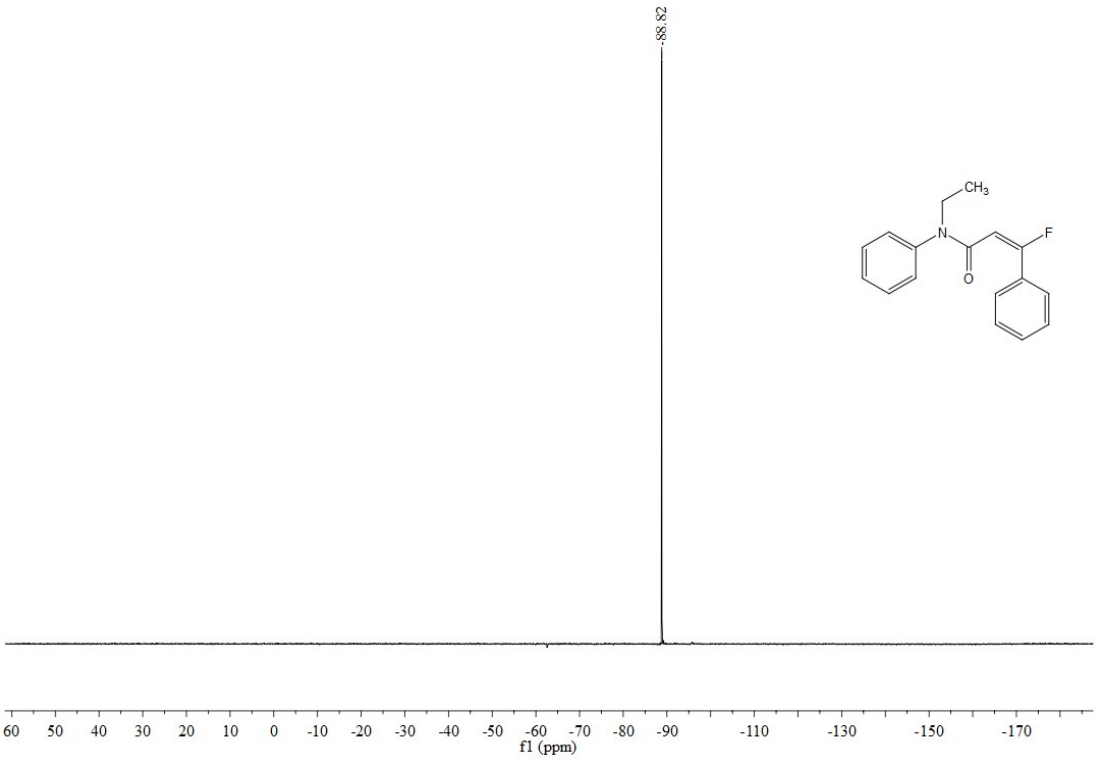
^{1}H NMR: (*E*)-*N*-ethyl-3-fluoro-*N,3*-diphenylacrylamide (3x)



^{13}C NMR: (*E*)-*N*-ethyl-3-fluoro-*N,3*-diphenylacrylamide (3x)



^{19}F NMR: (*E*)-*N*-ethyl-3-fluoro-*N,3*-diphenylacrylamide (3x)



^{1}H NMR: (*Z*)-4-fluoro-4-phenylbut-3-en-2-one (3y)