Supporting Information

PhenoFluor: Practical Synthesis, New Formulation and Deoxyfluorination of Heteroaromatics

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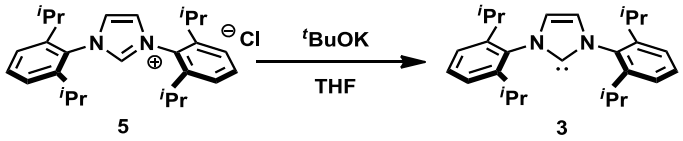
Materials and Methods

All air- and moisture-insensitive reactions were carried out under an ambient atmosphere, magnetically stirred, and monitored by thin layer chromatography (TLC) using EMD TLC plates pre-coated with 250 μm thickness silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. Flash chromatography was performed on Dynamic Adsorbents Silica Gel 40–63 μm particle size using a forced flow of eluent at 0.3–0.5 bar pressure.[1] All air- and moisture-sensitive manipulations were performed using oven-dried glassware, including standard Schlenk and glovebox techniques under an atmosphere of nitrogen. Benzene-d_6, toluene, dioxane and THF were distilled from deep purple sodium benzophenone ketyl. Methylene chloride-d_2 was dried over CaH_2 and vacuum-distilled. Acetonitrile was dried over P_2O_5 and vacuum-distilled. CsF was ground finely and dried at 200 ºC under dynamic vacuum (10^{-4} Torr) before use. Chloroform-d_1 and all other chemicals were used as received. All deuterated solvents were purchased from Cambridge Isotope Laboratories. Dimethyl terephthalate (99.99%, standard for quantitative NMR) was purchased from Sigma-Aldrich. NMR spectra were recorded on either a Varian Unity/Inova 600 spectrometer operating at 600 MHz for ^{1}H acquisitions, a Varian Unity/Inova 500 spectrometer operating at 500 MHz and 125 MHz for ^{1}H and ^{13}C acquisitions, respectively, or a Varian Mercury 400 spectrometer operating at 375 MHz for ^{19}F acquisitions. Chemical shifts were referenced to the residual proton solvent peaks (^{1}H: $CDCl_3$, δ 7.26; C_6D_6, δ 7.16; CD_2Cl_2, δ 5.32; $(CD_3)_2SO$, δ 2.50), solvent ^{13}C signals ($CDCl_3$, δ 77.16; C_6D_6, δ 128.06; CD_2Cl_2, δ 53.84; $(CD_3)_2SO$, δ 39.52).[2] Signals are listed in ppm, and multiplicity identified as s = singlet, br = broad, d = doublet, t = triplet, q = quartet, quin = quintet, sep = septet, m = multiplet; coupling constants in Hz; integration. High resolution mass spectra were obtained using an Agilent 6210 TOF LC/MS or a Bruker Maxis Impact LC-q-TOF. Differential scanning calorimetry (DSC) experiment was measured using a DSC Q200 V24.10 Build122 (TA instruments). Concentration under reduced pressure was performed by rotary evaporation at 25–30 ºC at appropriate pressure. Purified compounds were further dried under high vacuum (0.01–0.05 Torr). Yields refer to purified and spectroscopically pure compounds.

Experimental Data

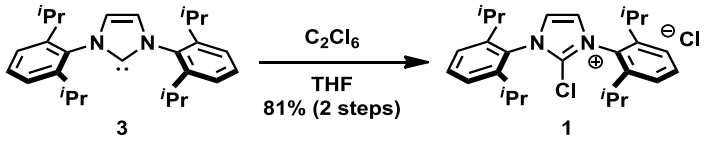
Synthesis of PhenoFluor

_N_,_N_'-1,3-Bis(2,6-diisopropylphenyl)imidazol-2-ylidene (3)



In an N_2-filled glovebox, *N*,*N*'-1,3-bis(2,6-diisopropylphenyl)imidazolium chloride[3] (**5**) (50.0 g, 118 mmol, 1.00 equiv) and t-BuOK (14.0 g, 125 mmol, 1.06 equiv) were placed in a round-bottom flask. THF (240 mL) was added and the flask was capped with a rubber septum, then removed from the glovebox. The mixture was stirred for 3.5 hours at 23 ºC, then the solvent was evaporated *in vacuo*. The residue was dissolved in toluene (450 mL) with gentle heating (50–60 ºC) and the hot solution was filtered through a pad of Celite eluting with toluene (50 mL). The filtrate was concentrated *in vacuo* to afford 39.1 g of the title compound as an off-white solid. The material **3** was used in the next step without any further purification.

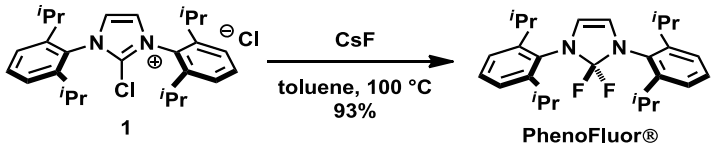
_N_,_N_'-1,3-Bis(2,6-diisopropylphenyl)-2-chloroimidazolium chloride (1)



To a mixture of *N*,*N*'-1,3-bis(2,6-diisopropylphenyl)imidazol-2ylidene (**3**) (39.1 g) in THF (240 mL) was added 1,1,1,2,2,2-hexachloroethane (26.2 g, 111 mmol) at –45 ºC. The mixture was warmed to 23 ºC and stirred for 20 hours. The reaction mixture was filtered, then the filter cake was washed with THF (3 × 100 mL) and toluene (2 × 100 mL) to afford 44.0 g of the title compound as a white solid (81% yield from **5**).

NMR Spectroscopy: ^{1}H NMR (600 MHz, CD_2Cl_2, 23 ºC, δ): 8.87 (s, 2H), 7.67 (t, J = 7.8 Hz, 2H), 7.45 (d, J = 7.8 Hz, 4H), 2.36 (m, 4H), 1.32 (d, J = 7.0 Hz, 12H), 1.22 (d, J = 7.0 Hz, 12H). ^{13}C NMR (125 MHz, CD_2Cl_2, 23 ºC, δ): 145.5, 133.9, 133.1, 128.9, 128.4, 125.6, 29.7, 24.4, 23.5. HRMS-FIA(m/z) calcd for $C_{27}H_{36}ClN_2$ $[M–Cl]^+$, 423.2562; found, 423.2565.

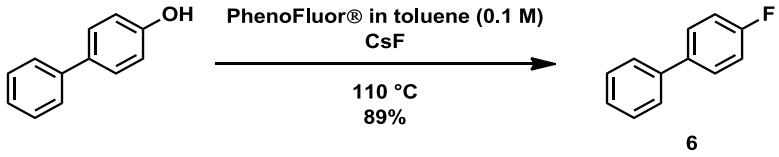
***N*,*N*'-1,3-Bis(2,6-diisopropylphenyl)-2,2-difluoroimidazolidene (PhenoFluor)**



N,*N*'-1,3-Bis(2,6-diisopropylphenyl)-2-chloroimidazolium chloride (**1**) was finely ground using a mortar and dried at 80 ºC under vacuum for 24 hours. CsF was finely ground using a mortar in a glovebox, then removed from the glovebox and dried at 200 ºC under vacuum for 24 hours, prior to use. In a glovebox, *N*,*N*'-1,3-bis(2,6-diisopropylphenyl)-2-chloroimidazolium chloride (**1**) (25.0 g, 54.4 mmol, 1.00 equiv) and CsF (82.6 g, 544 mmol, 10.0 equiv) were placed in a pressure flask. Toluene (181 mL) was added and the flask was sealed, then removed from the glovebox. The flask was sonicated until the mixture appeared creamy (1 hour), then stirred vigorously at 100 ºC for 96 hours. Completion of the reaction was judged by visual inspection: when stirring was stopped, chloroimidazolium salt was floating in the reaction mixture, while cesium salts dropped onto the bottom quickly. When no more chloroimidazolium salt was observed, the mixture was cooled to 23 ºC. The flask was brought into a glovebox and the mixture was filtered through a pad of Celite eluting with toluene (40 mL). The filtrate was concentrated and dried *in vacuo* (approximately 6–8 hours). The residual solid was ground, washed with MeCN (3 × 15 mL) and dried on frit to afford 21.6 g (98% purity: determined by quantitative NMR study with dimethyl terephthalate (99.99%)) of the title compound as an off-white solid (93% yield). PhenoFluor should be stored in an inert gas atmosphere.

NMR Spectroscopy: ^{1}H NMR (600 MHz, C_6D_6, 23 ºC, δ): 7.22 (t, J = 8.2 Hz, 2H), 7.12 (d, J = 8.2 Hz, 4H), 5.71 (s, 2H), 3.61 (m, 4H), 1.36 (d, J = 7.0 Hz, 12H), 1.18 (d, J = 7.0 Hz, 12H). ^{13}C NMR (125 MHz, C_6D_6, 23 ºC, δ): 150.9, 131.6, 129.9, 126.4 (t, J = 247.0 Hz), 124.5, 112.8, 28.9, 25.6, 24.2. ^{19}F NMR (375 MHz, C_6D_6, 23 ºC, δ): –34.0. HRMS-FIA(m/z) calcd for $C_{27}H_{36}FN_2$ $[M–F]^+$, 407.2857; found, 407.2857.

Deoxyfluorination with PhenoFluor solution (0.100 M in toluene)



In a glovebox, PhenoFluor (1.28 g, 3.00 mmol) was dissolved in toluene (30.0 mL) and the solution was transferred into a sure seal bottle.

Under air, 4-phenylphenol (50.0 mg, 0.294 mmol. 1.00 equiv) and previously-dried CsF (134 mg, 0.881 mmol, 3.00 equiv) were placed in a vial. The vial was evacuated and back-filled with N_2 gas (3 times). A solution of PhenoFluor in toluene (0.100 M, 3.52 mL, 0.352 mmol, 1.20 equiv)

was added *via* syringe. The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 3 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:19 (v/v)) to afford 44.9 mg of 4-fluorobiphenyl (**6**) as a colorless solid (89% yield).

R_f = 0.68 (Et_2O/hexanes 1:19 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.60–7.55 (m, 4H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.38 (t, *J* = 7.3 Hz, 1H), 7.16 (t, *J* = 8.8 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 162.6 (d, *J* = 246.1 Hz), 140.4, 137.5, 129.0, 128.8 (d, *J* = 7.6 Hz), 127.4, 127.2, 115.7 (d, *J* = 21.9 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –115.8.

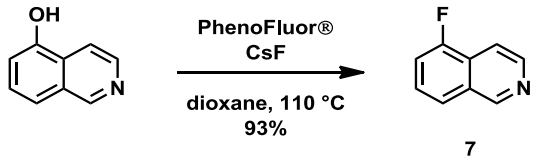
Deoxyfluorination of Heteroaromatics

General Procedure

PhenoFluor is moisture sensitive, and should be appropriately stored in an inert gas atmosphere. CsF was finely ground using a mortar in a glovebox, then removed from the glovebox and dried at 200 ºC under vacuum for 24 hours, prior to use. Reaction solvents and reagents must be dried for optimal results.

In a glovebox, a heteroaromatic compound (0.500 mmol. 1.00 equiv), CsF (228 mg, 1.50 mmol, 3.00 equiv) and PhenoFluor (256–320 mg, 1.20–1.50 mmol, 1.20–1.50 equiv) were placed in a vial. Toluene or dioxane (5.0 mL) was added. The vial was sealed and removed from the glovebox. The mixture was stirred at 23 ºC for 30 min and subsequently heated at 110 ºC for 24 hours. The mixture was cooled to 23 ºC, then filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo* and the residue was purified by flash silica gel column chromatography to afford the fluorinated compound.

5-Fluoroisoquinoline (7)



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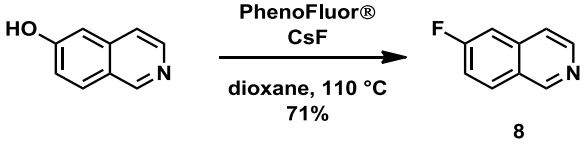
To a mixture of isoquinolin-5-ol (100 mg, 0.689 mmol. 1.00 equiv), CsF (314 mg, 2.07 mmol, 3.00 equiv) and PhenoFluor (427 mg, 1.00 mmol, 1.45 equiv) was added dioxane (6.9 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:9 (v/v)) to afford 94.1 mg of the title compound as an off-white solid (93% yield).

R_f = 0.09 (Et_2O/hexanes 1:9 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, $CDCl_3$, 23 ºC, δ):

9.28 (s, 1H), 8.60 (d, *J* = 5.9 Hz, 1H), 7.88 (d, *J* = 5.9 Hz, 1H), 7.77 (d, *J* = 8.3 Hz, 1H), 7.54 (m, 1H), 7.36 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 157.6 (d, *J* = 254.2 Hz), 152.1 (d, *J* = 2.7 Hz), 143.6, 129.7 (d, *J* = 4.2 Hz), 127.3 (d, *J* = 7.4 Hz), 126.5 (d, *J* = 18.1 Hz), 123.5 (d, *J* = 4.4 Hz), 114.0 (d, *J* = 19.0 Hz), 113.5. ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –123.2. HRMS-FIA(m/z) calcd for C_9H_7FN $[M+H]^+$, 148.0557; found, 148.0563.

6-Fluoroisoquinoline (8)

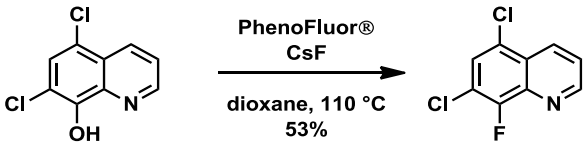


8

To a mixture of isoquinolin-6-ol (100 mg, 0.689 mmol. 1.00 equiv), CsF (314 mg, 2.07 mmol, 3.00 equiv) and PhenoFluor (427 mg, 1.00 mmol, 1.45 equiv) was added dioxane (6.9 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:19, 1:9, 1:4 (v/v)) to afford 73.0 mg of the title compound as a colorless solid (71% yield).

R_f = 0.06 (Et_2O/hexanes 1:9 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, C_6D_6, 23 ºC, δ): 9.01 (s, 1H), 8.46 (d, *J* = 5.7 Hz, 1H), 7.13 (dd, *J* = 8.9, 5.6 Hz, 1H), 6.94 (d, *J* = 5.7 Hz, 1H), 6.88 (dd, *J* = 9.5, 2.3 Hz, 1H), 6.80 (ddd, *J* = 8.8, 8.8, 2.4 Hz, 1H). ^{13}C NMR (125 MHz, C_6D_6, 23 ºC, δ) 163.2 (d, *J* = 251.5 Hz), 152.5, 144.5, 137.2 (d, *J* = 11.0 Hz), 130.8 (d, *J* = 9.2 Hz), 126.1, 119.9 (d, *J* = 5.5 Hz), 117.4 (d, *J* = 25.6 Hz), 107.9 (d, *J* = 21.1 Hz). ^{19}F NMR (375 MHz, C_6D_6, 23 ºC, δ): –107.9. HRMS-FIA(m/z) calcd for C_9H_7FN $[M+H]^+$, 148.0557; found, 148.0566.

5,7-Dichloro-8-fluoroisoquinoline (9)



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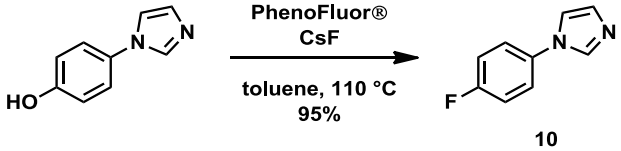
To a mixture of 5,7-dichloroquinolin-8-ol (100 mg, 0.467 mmol. 1.00 equiv), CsF (213 mg, 1.40 mmol, 3.00 equiv) and PhenoFluor (299 mg, 0.701 mmol, 1.50 equiv) was added dioxane (4.7 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:19 (v/v)) to afford 53.5 mg of the title compound as a colorless solid (53% yield).

R_f = 0.29 (Et_2O/hexanes 1:9 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, C_6D_6, 23 ºC, δ):

8.50 (dd, *J* = 4.1, 1.5 Hz, 1H), 7.84 (ddd, *J* = 8.6, 1.5, 1.5 Hz, 1H), 7.01 (d, *J* = 6.0 Hz, 1H), 6.57 (dd, *J* = 8.6, 4.1 Hz, 1H). ^{13}C NMR (125 MHz, C_6D_6, 23 ºC, δ): 153.7 (d, *J* = 262.3 Hz), 151.7, 139.6 (d, *J* = 12.4 Hz), 132.2 (d, *J* = 2.9 Hz), 127.3, 126.1, 122.5 (d, *J* = 3.8 Hz), 121.8 (d, *J* = 2.8 Hz), 117.7 (d, *J* = 23.8 Hz). ^{19}F NMR (375 MHz, C_6D_6, 23 ºC, δ): –125.2. HRMS-FIA(m/z) calcd for $C_9H_5Cl_2FN$ $[M+H]^+$, 215.9778; found, 215.9785.

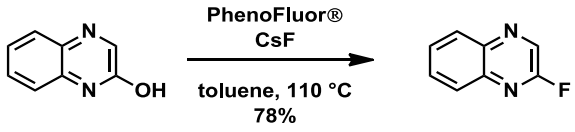
1-(4-Fluorophenyl)imidazole (10)



To a mixture of 4-(1-imidazolyl)phenol (100 mg, 0.624 mmol. 1.00 equiv), CsF (284 mg, 1.87 mmol, 3.00 equiv) and PhenoFluor (320 mg, 0.750 mmol, 1.20 equiv) was added toluene (6.2 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (EtOAc/CH_2Cl_2 1:19; 1:4; 100:0 (v/v)) to afford 96.0 mg of the title compound as a yellow oil (95% yield).

R_f = 0.39 (MeOH/EtOAc 1:19 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.75 (br s, 1H), 7.33 (m, 2H), 7.21-7.11 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 161.7 (d, *J* = 247.4 Hz), 135.8, 133.7 (d, *J* = 2.9 Hz), 130.6, 123.5 (d, *J* = 8.6 Hz, 2C), 118.6, 116.8 (d, *J* = 23.0 Hz, 2C). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –113.6. HRMS-FIA(m/z) calcd for $C_9H_8FN_2$ $[M+H]^+$, 163.0666; found, 163.0664.

2-Fluoroquinoxaline (11)

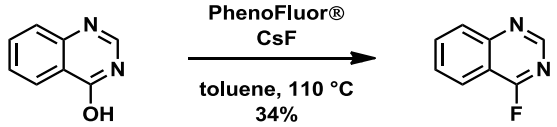


To a mixture of quinoxalin-2-ol (100 mg, 0.684 mmol. 1.00 equiv), CsF (312 mg, 2.05 mmol, 3.00 equiv) and PhenoFluor (521 mg, 1.03 mmol, 1.50 equiv) was added toluene (6.8 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes/Et_3N 10:187:3 (v/v/v)) to afford 79.1 mg of the title compound as a pale yellow oil (78% yield).

R_f = 0.25 (Et_2O/hexanes 1:9 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, $CDCl_3$, 23 ºC, δ):

8.68 (d, *J* = 8.3 Hz, 1H), 8.14 (d, *J* = 8.3 Hz, 1H), 7.95 (d, *J* = 7.8 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.74 (d, *J* = 8.3 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 156.6 (d, *J* = 257.5 Hz), 141.4 (d, *J* = 1.9 Hz), 139.6 (d, *J* = 11.4 Hz), 136.4, 136.1, 131.5, 129.3 (d, *J* = 3.8 Hz), 128.3 (d, *J* = 1.9 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –74.4. HRMS-FIA(m/z) calcd for $C_8H_6FN_2$ $[M+H]^+$, 149.0510; found, 149.0496.

4-Fluoroquinazoline (12)



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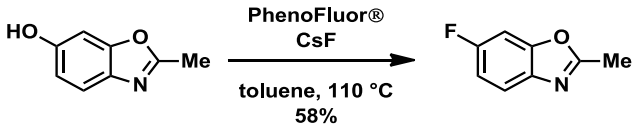
To a mixture of 4-hydroxyquinazoline (73.0 mg, 0.499 mmol. 1.00 equiv), CsF (228 mg, 1.50 mmol, 3.01 equiv) and PhenoFluor (256 mg, 0.600 mmol, 1.20 equiv) was added toluene (5.0 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:9 (v/v)) to afford 25.0 mg of the title compound as a colorless solid (34% yield).

R_f = 0.20 (Et_2O/hexanes 1:4 (v/v)). NMR Spectroscopy: ^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.95 (d, *J* = 1.5 Hz, 1H), 8.16 (d, *J* = 8.3 Hz, 1H), 8.11 (d, *J* = 7.8 Hz, 1H), 8.00 (dt, *J* = 8.3, 1.5 Hz, 1H), 7.73 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 167.2 (d, *J* = 263.2 Hz), 154.1 (d, *J* = 15.3 Hz), 153.7 (d, *J* = 5.7 Hz), 135.3, 128.8, 128.3 (d, *J* = 4.8 Hz), 122.8, 114.7 (d, *J* = 25.8 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –64.1. HRMS-FIA(m/z) calcd for $C_8H_6FN_2$ $[M+H]^+$, 149.0510; found, 149.0506.

6-Fluoro-2-methylbenzo[*d*]oxazole (13)



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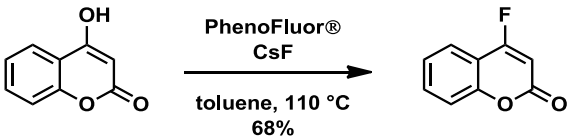
To a mixture of 2-methylbenzo[*d*]oxazol-6-ol (100 mg, 0.670 mmol. 1.00 equiv), CsF (306 mg, 2.01 mmol, 3.00 equiv) and PhenoFluor (429 mg, 1.01 mmol, 1.50 equiv) was added toluene (6.7 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:19 (v/v)) to afford 59.1 mg of the title compound as a yellow oil (58% yield).

R_f = 0.33 (Et_2O/hexanes 1:4 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, C_6D_6, 23 ºC, δ): 7.33 (dd, *J* = 8.7, 4.9 Hz, 1H), 6.86 (dd, *J* = 8.0, 2.1 Hz, 1H), 6.71 (ddd, *J* = 9.2, 9.2, 2.2 Hz, 1H),

1.97 (d, *J* = 0.5 Hz, 3H). ^{13}C NMR (125 MHz, C_6D_6, 23 ºC, δ): 164.1, 160.6 (d, *J* = 242.4 Hz), 151.3 (d, *J* = 14.7 Hz), 138.7, 120.1 (d, *J* = 10.0 Hz), 111.9 (d, *J* = 24.5 Hz), 98.4 (d, *J* = 28.1 Hz), 13.8. ^{19}F NMR (375 MHz, C_6D_6, 23 ºC, δ): –116.8. HRMS-FIA(m/z) calcd for C_8H_7FNO $[M+H]^+$, 152.0506; found, 152.0512.

4-Fluoro-2*H*-chromen-2-one (14)

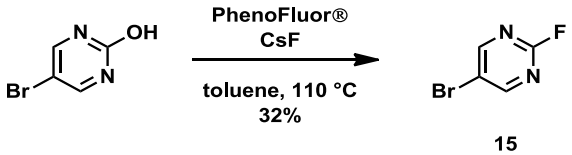


14

To a mixture of 4-hydroxycoumarin (100 mg, 0.617 mmol. 1.00 equiv), CsF (281 mg, 1.85 mmol, 3.00 equiv) and PhenoFluor (395 mg, 0.925 mmol, 1.50 equiv) was added toluene (6.2 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:9 (v/v)) to afford 68.3 mg of the title compound as a colorless solid (68% yield).

R_f = 0.28 (Et_2O/hexanes 1:4 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, $CDCl_3$, 23 ºC, δ): 7.74 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.64 (ddd, *J* = 8.7, 7.4, 1.6 Hz, 1H), 7.40 (d, *J* = 8.5 Hz, 1H), 7.36 (ddd, *J* = 7.8 Hz, 7.8 Hz, 0.9 Hz, 1H), 6.12 (d, *J* = 10.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 169.0 (d, *J* = 264.6 Hz), 161.7 (d, *J* = 21.1 Hz), 153.8 (d, *J* = 9.1 Hz), 133.7, 124.7, 122.3 (d, *J* = 3.6 Hz), 117.1 (d, *J* = 4.3 Hz), 113.6 (d, *J* = 22.0 Hz), 98.1 (d, *J* = 16.9 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –101.8. HRMS-FIA(m/z) calcd for $C_9H_6FO_2$ $[M+H]^+$, 165.0346; found, 165.0352.

5-Bromo-2-fluoropyrimidine (15)



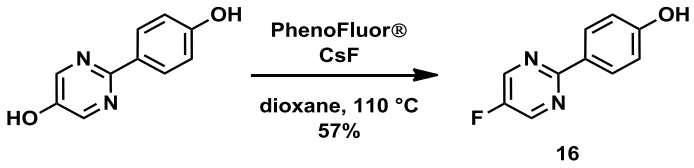
15

To a mixture of 5-bromopyrimidin-2-ol (100 mg, 0.571 mmol. 1.00 equiv), CsF (260 mg, 1.71 mmol, 3.00 equiv) and PhenoFluor (366 mg, 0.857 mmol, 1.50 equiv) was added toluene (5.7 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:9 (v/v)) to afford 31.9 mg of the title compound as a colorless solid (32% yield). The product was highly volatile (yield determined by NMR using an internal standard is 62%).

R_f = 0.31 (Et_2O/hexanes 1:4 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, $CDCl_3$, 23 ºC, δ):

8.68 (s, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 161.8 (d, J = 222.2 Hz), 161.5 (d, J = 12.4 Hz, 2C), 116.8 (d, J = 6.7 Hz). ^{19}F NMR (375 MHz, $CDCl_3$, 23 ºC, δ): –47.6. HRMS-FIA(m/z) calcd for $C_4H_3BrFN_2$ $[M+H]^+$, 176.9458; found, 176.9448.

4-(5-Fluoropyrimidin-2-yl)phenol (16)

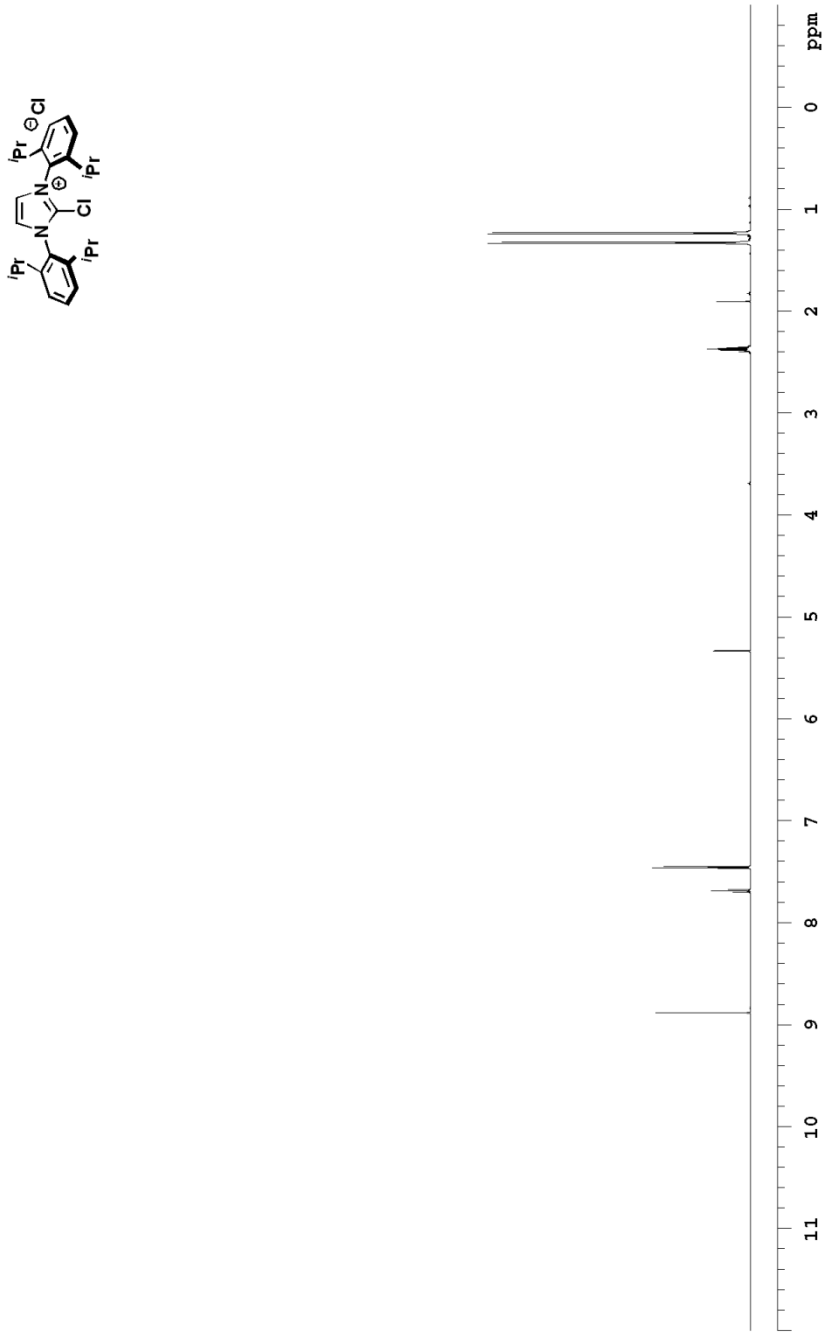


16

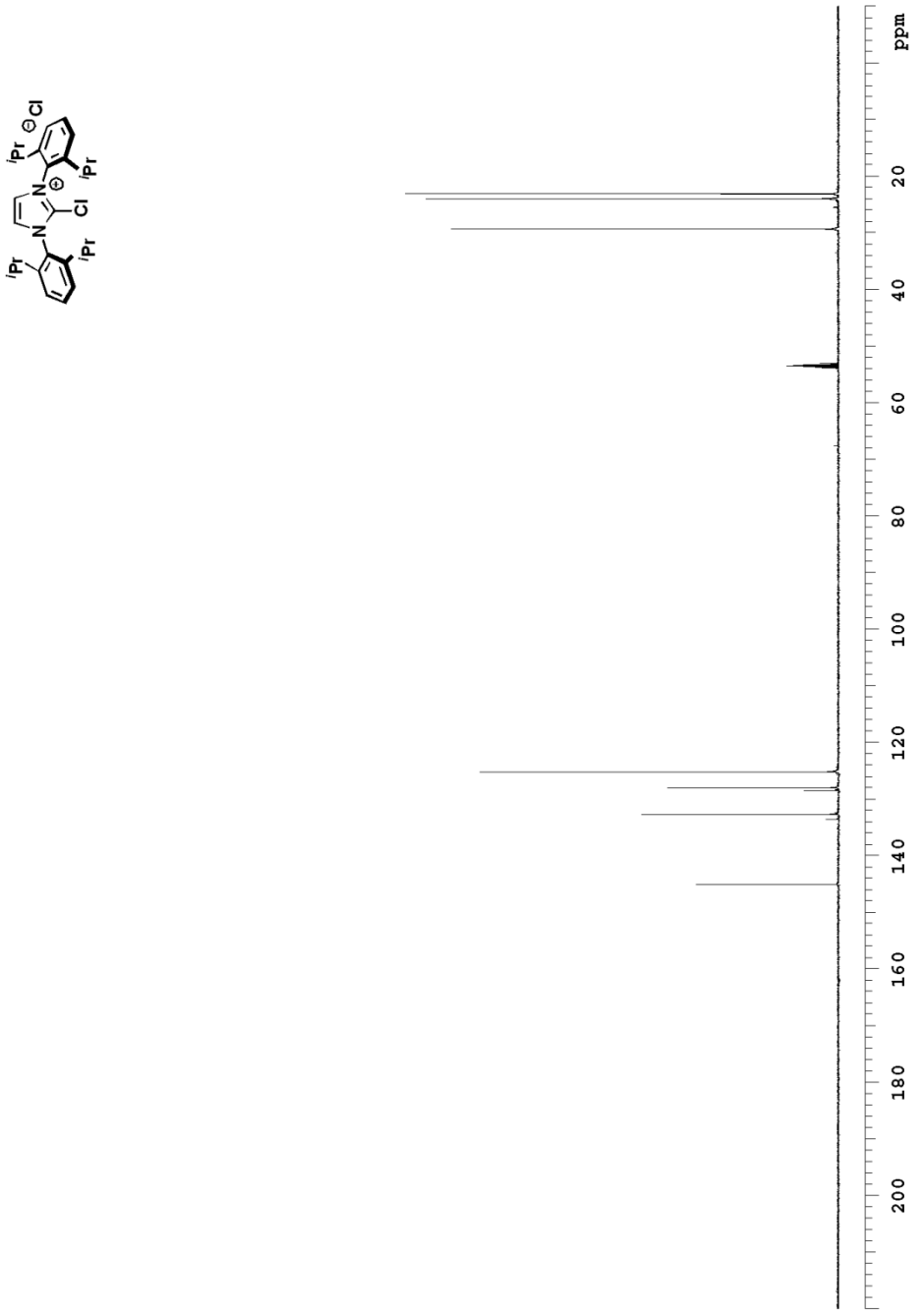
To a mixture of 2-(4-hydroxyphenyl)pyrimidin-5-ol (100 mg, 0.531 mmol. 1.00 equiv), CsF (242 mg, 1.59 mmol, 3.00 equiv) and PhenoFluor (567 mg, 1.33 mmol, 2.50 equiv) was added dioxane (5.7 mL). The mixture was stirred at 23 ºC for 30 min, then at 110 ºC for 24 hours. Once cooled to 23 ºC, the mixture was filtered through a pad of Celite eluting with CH_2Cl_2 (3 × 4 mL). The filtrate was concentrated *in vacuo*, then purified by flash silica gel column chromatography (Et_2O/hexanes 1:19 (v/v)) to afford 57.6 mg of the title compound as a colorless solid (57% yield).

R_f = 0.07 (Et_2O/hexanes 1:19 (v/v)). NMR Spectroscopy: ^{1}H NMR (600 MHz, DMSO-d_6, 23 ºC, δ): 10.08 (br s, 1H), 8.86 (s, 2H), 8.17 (d, J = 8.7 Hz, 2H), 6.90 (d, J = 8.7 Hz, 2H). ^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): 160.2 (d, J = 5.0 Hz), 160.1, 156.1 (d, J = 260.3 Hz), 145.3 (d, J = 20.3 Hz), 145.2 (d, J = 20.4 Hz), 129.4 (2C), 127.3, 115.5 (2C). ^{19}F NMR (375 MHz, DMSO-d_6, 23 ºC, δ): –142.5. HRMS-FIA(m/z) calcd for $C_{10}H_8FN_2O$ $[M+H]^+$, 191.0615; found, 191.0623.

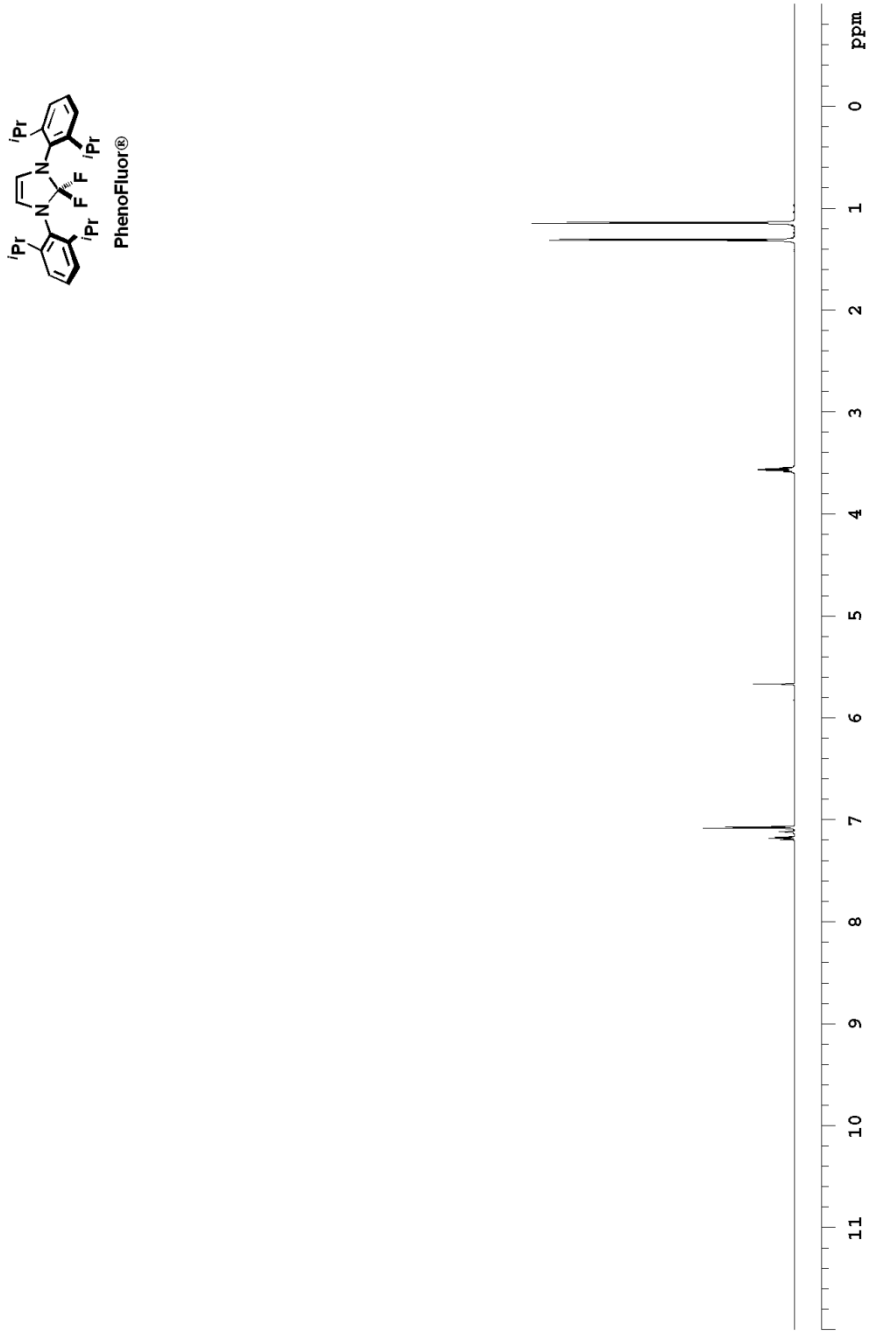
Spectroscopic Data



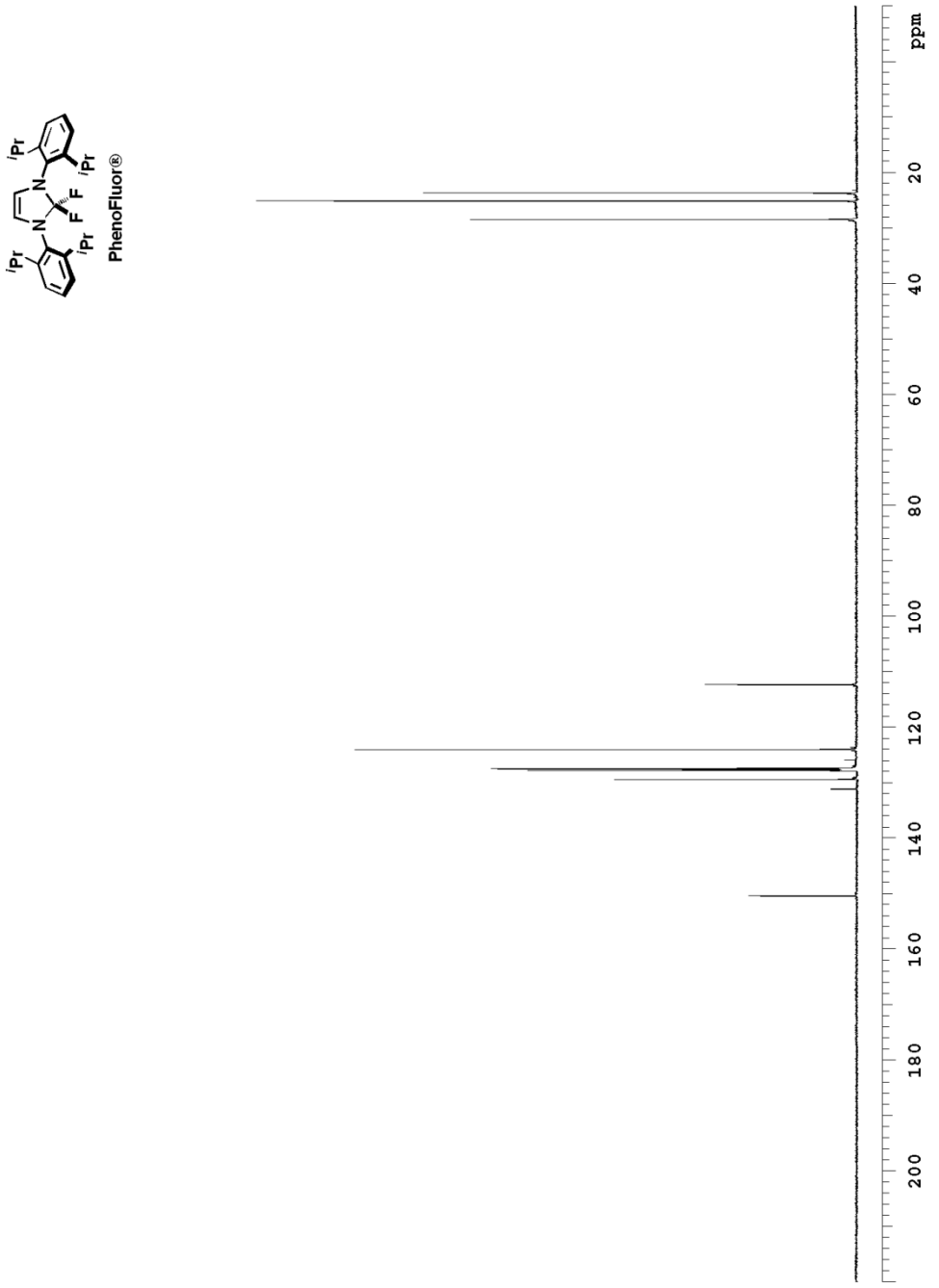
^{1}H NMR (CD_2Cl_2, 23 ºC) of **1**



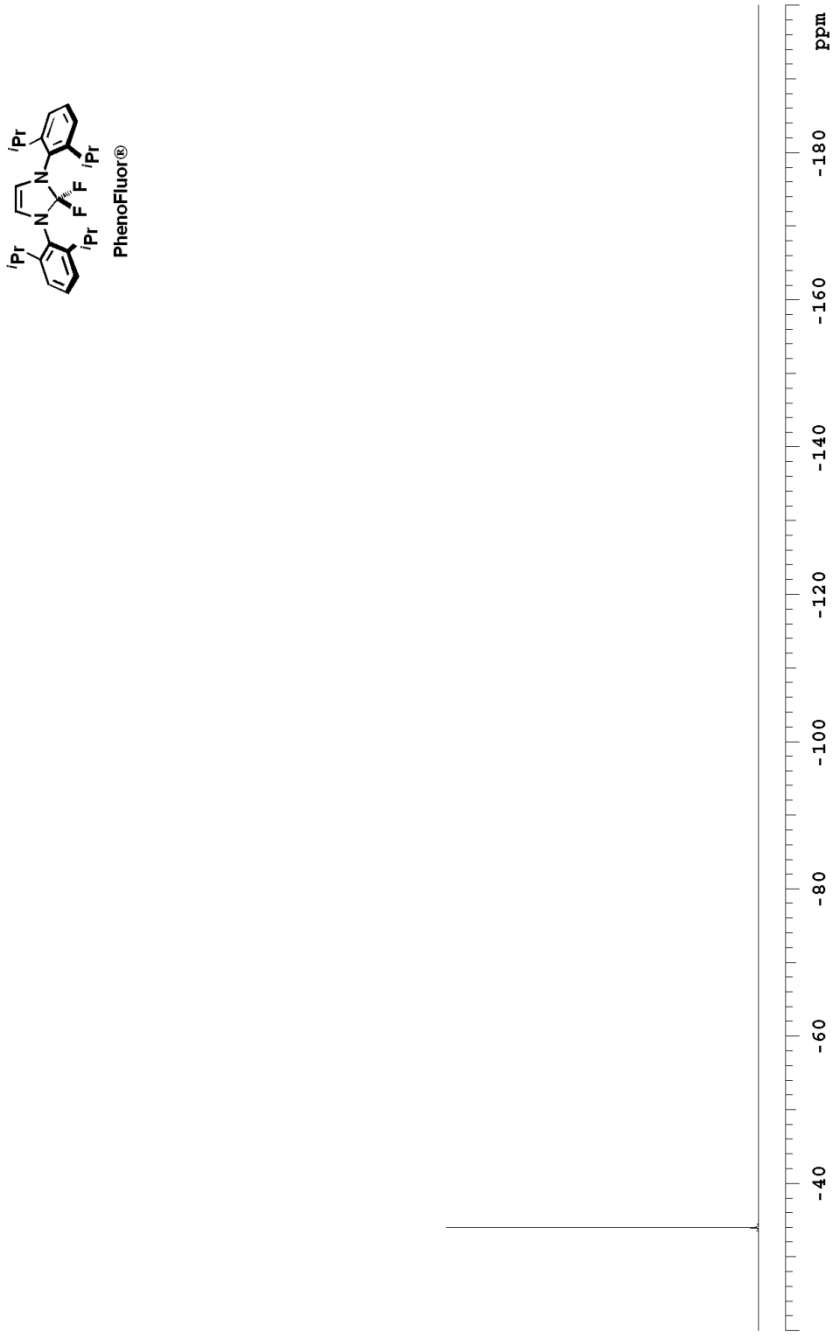
^{13}C NMR (CD_2Cl_2, 23 ºC) of **1**



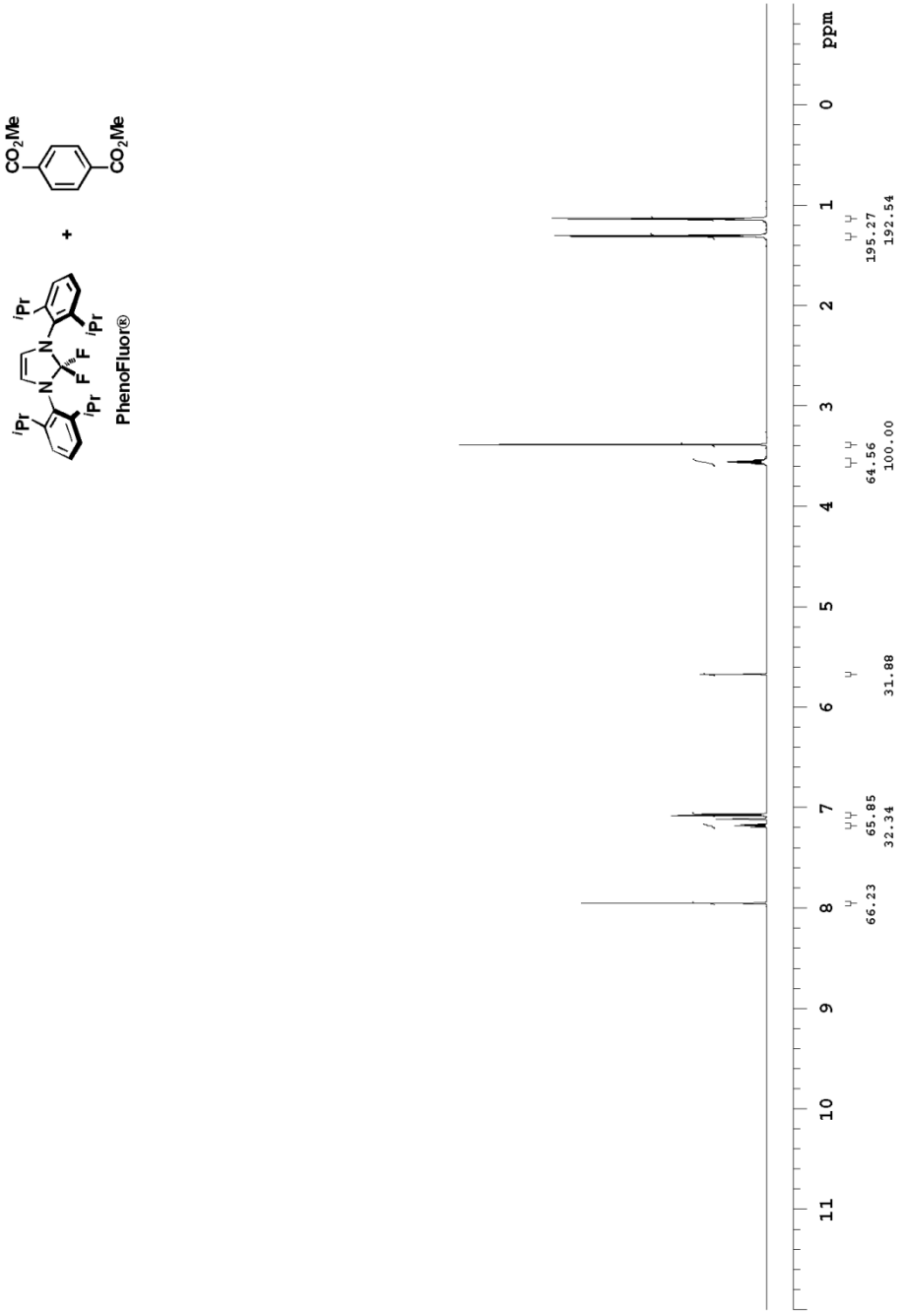
^{1}H NMR (C_6D_6, 23 ºC) of **PhenoFluor**



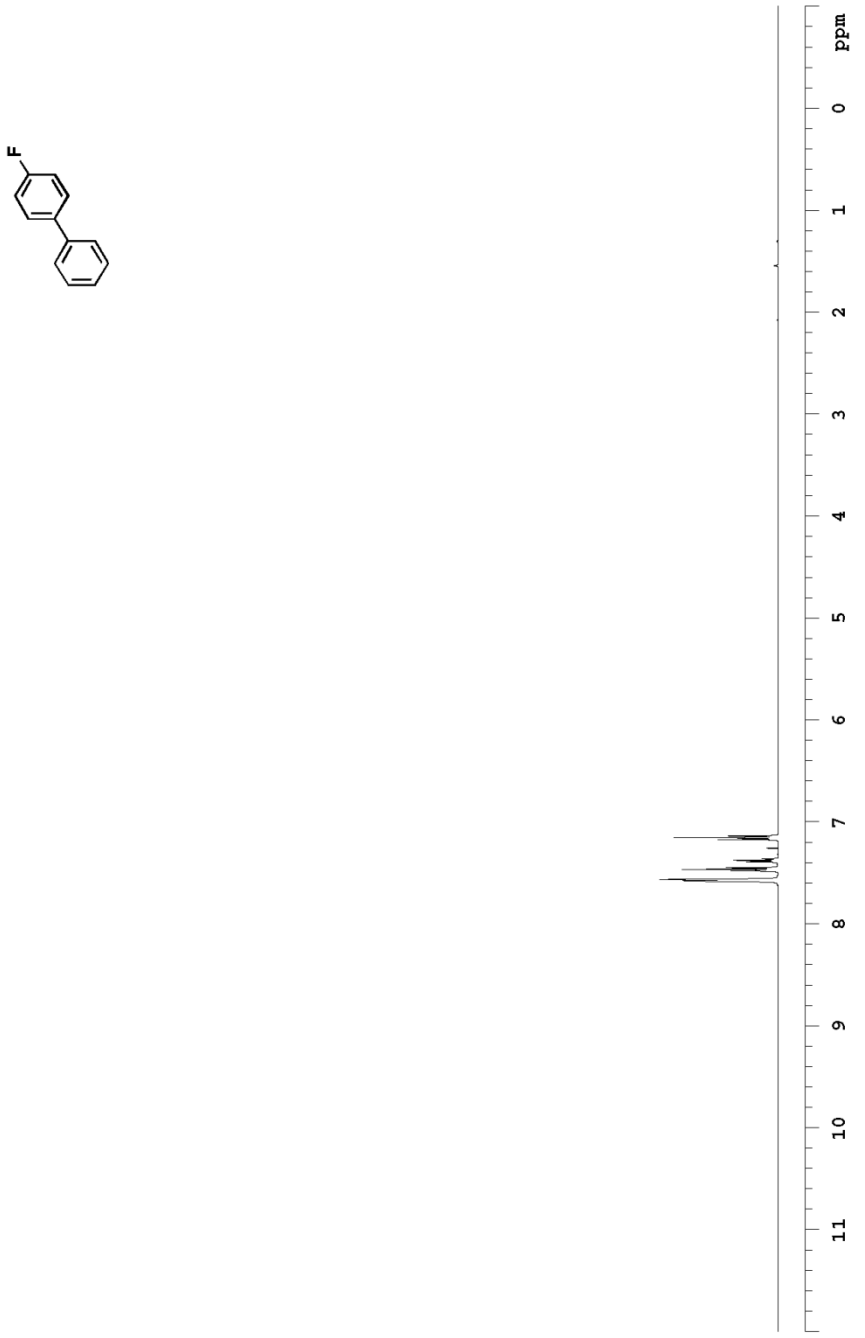
^{13}C NMR (C_6D_6, 23 ºC) of **PhenoFluor**



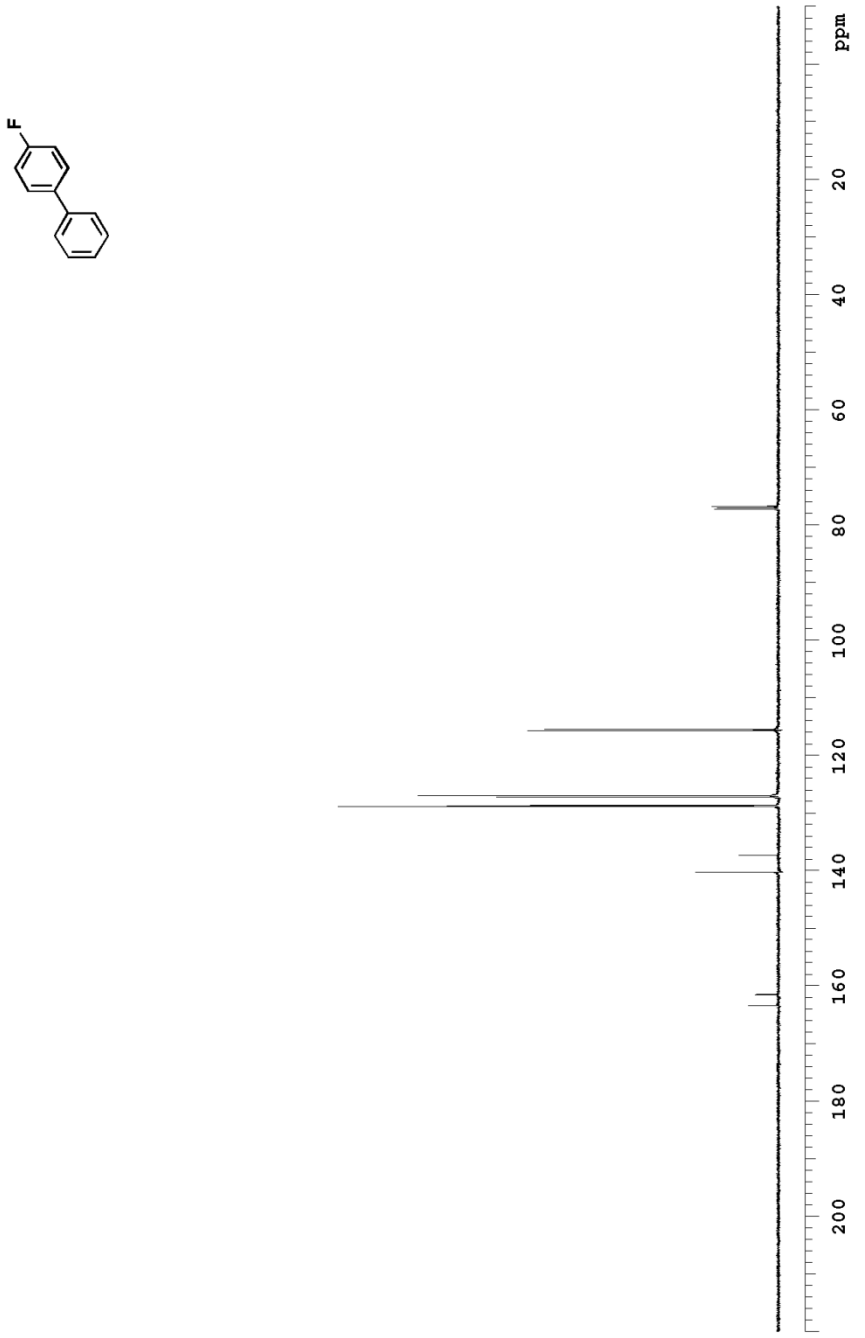
^{19}F NMR (C_6D_6, 23 ºC) of **PhenoFluor**



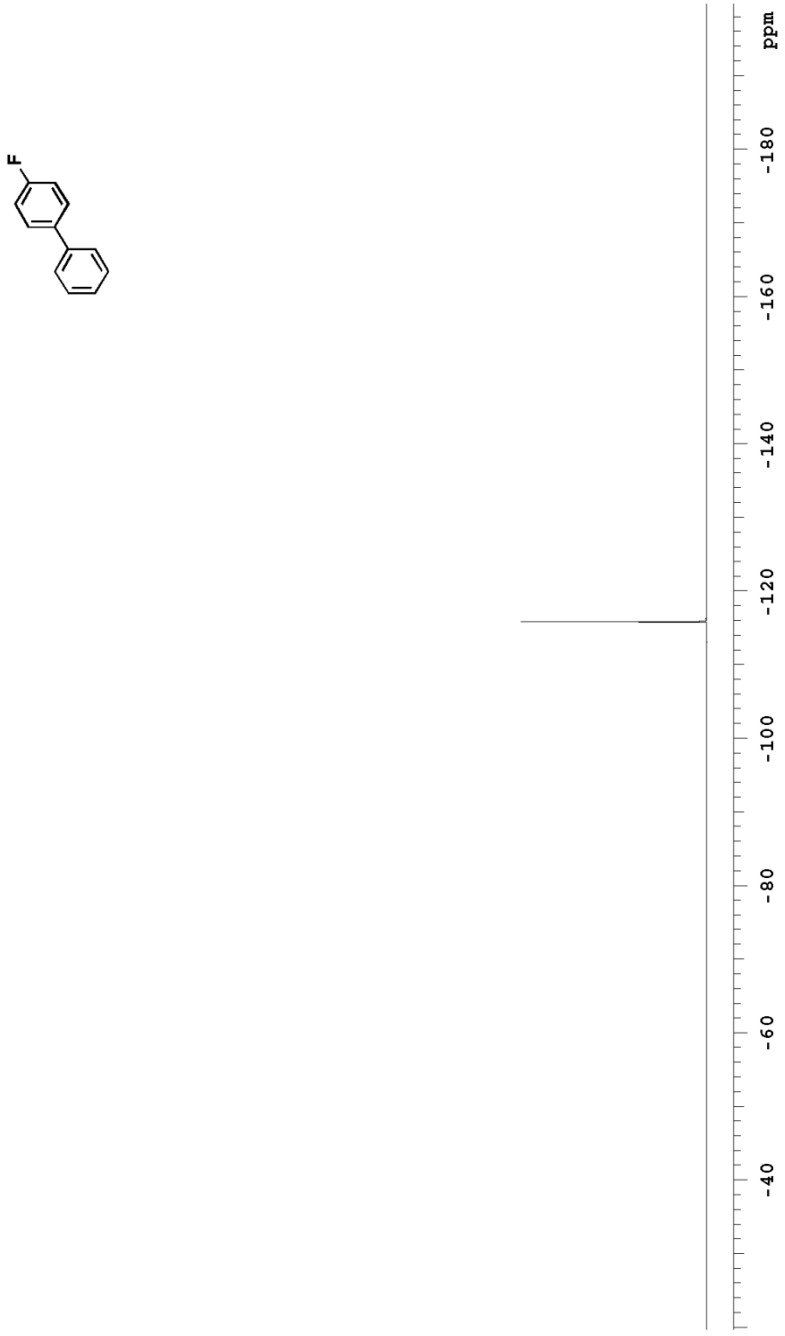
^{1}H NMR (C_6D_6, 23 ºC) of **PhenoFluor** (23.7 mg) + dimethyl terephthalate (10.9 mg)



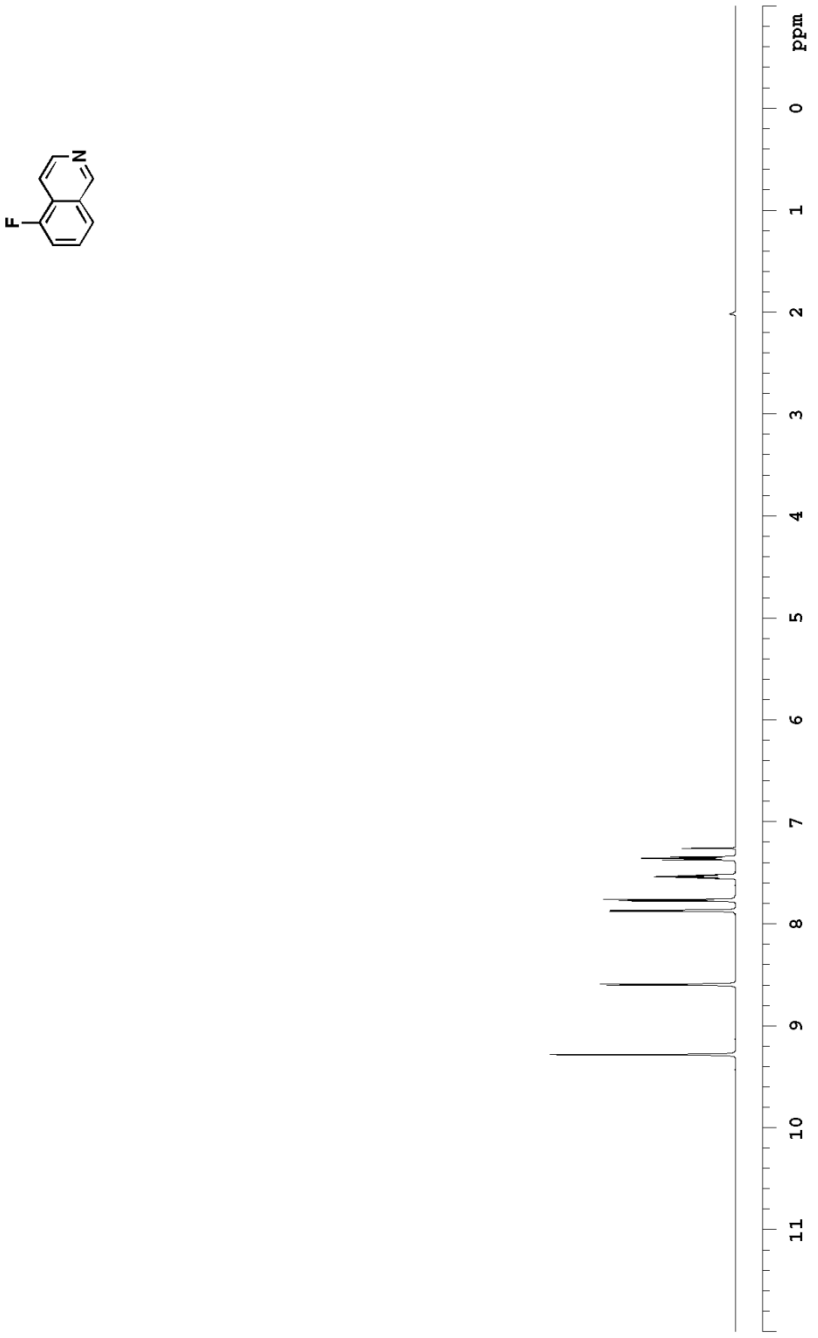
^{1}H NMR ($CDCl_3$, 23 ºC) of **6**



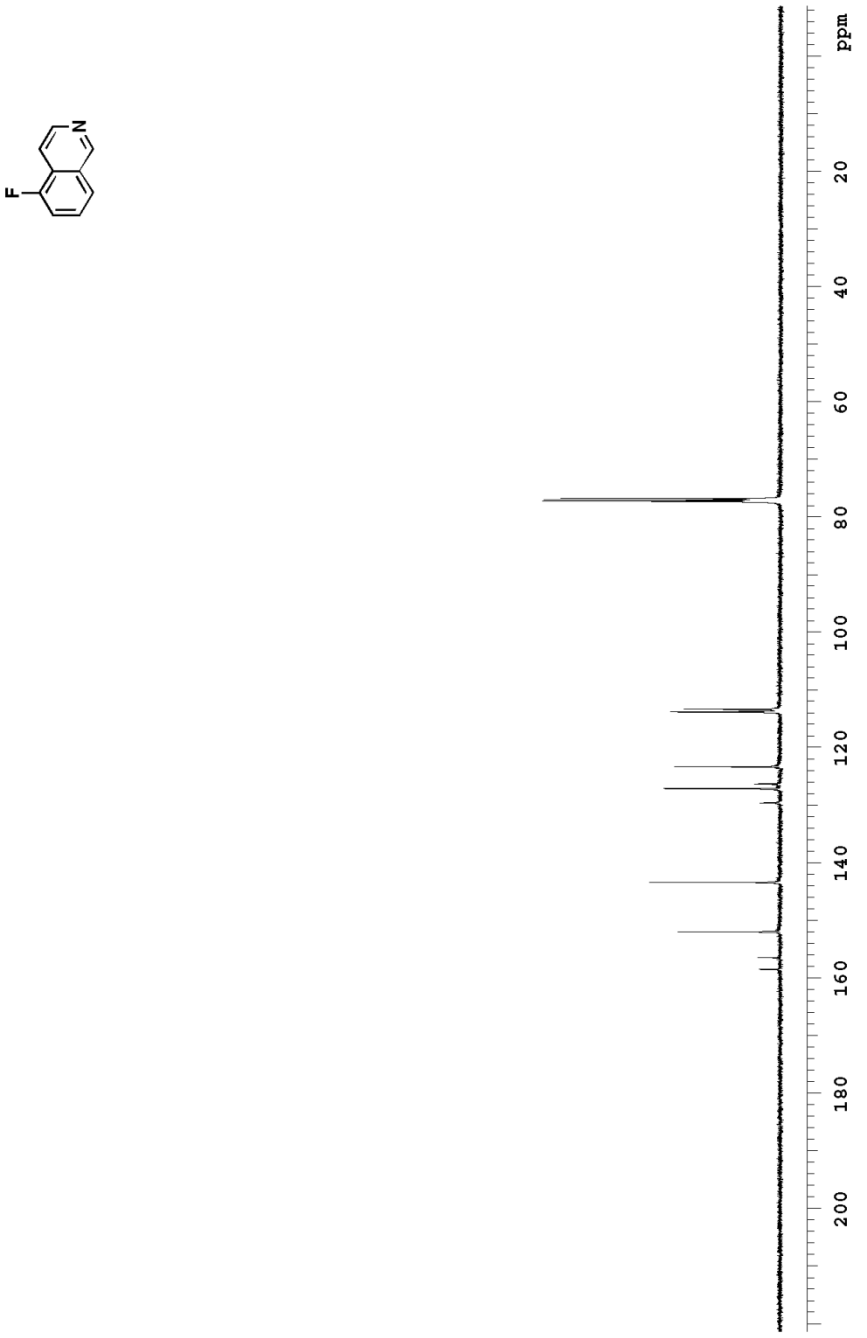
^{13}C NMR ($CDCl_3$, 23 ºC) of **6**



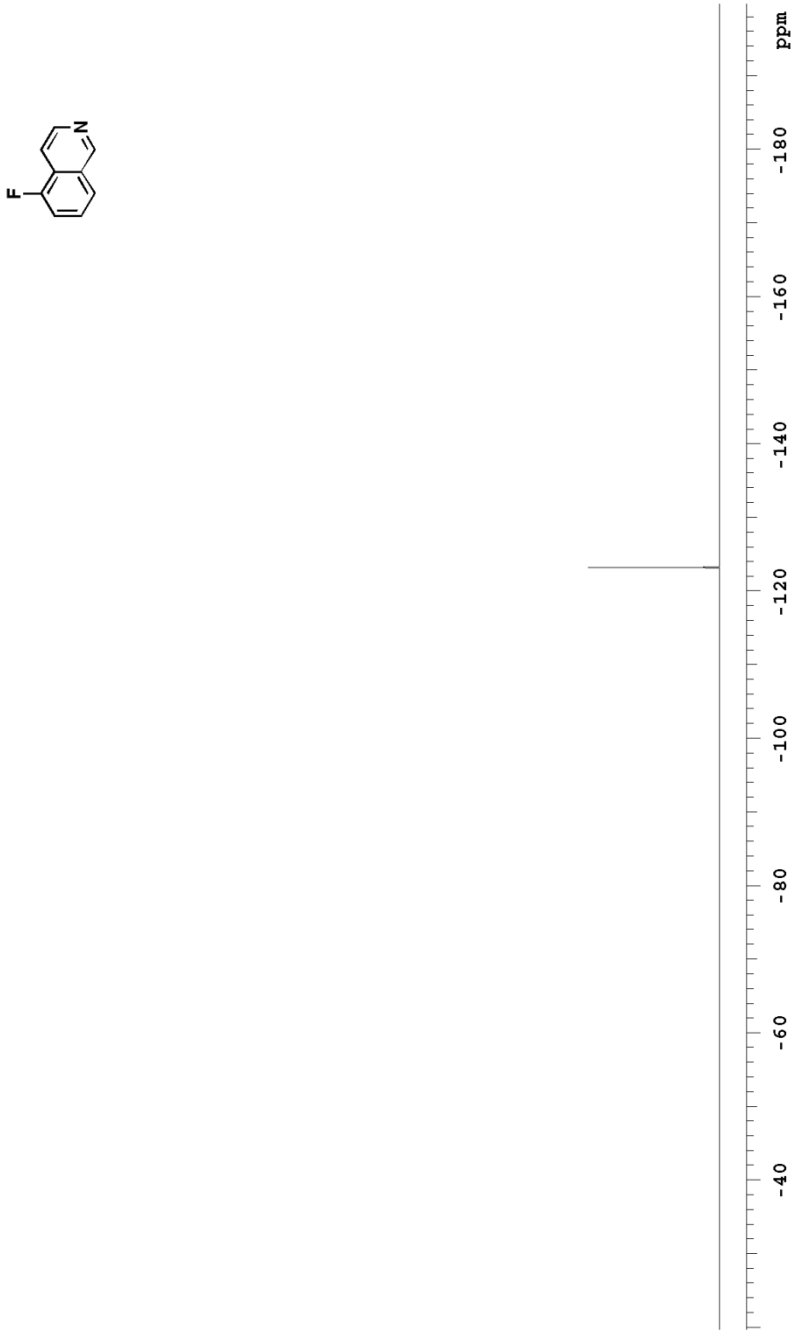
^{19}F NMR ($CDCl_3$, 23 ºC) of **6**



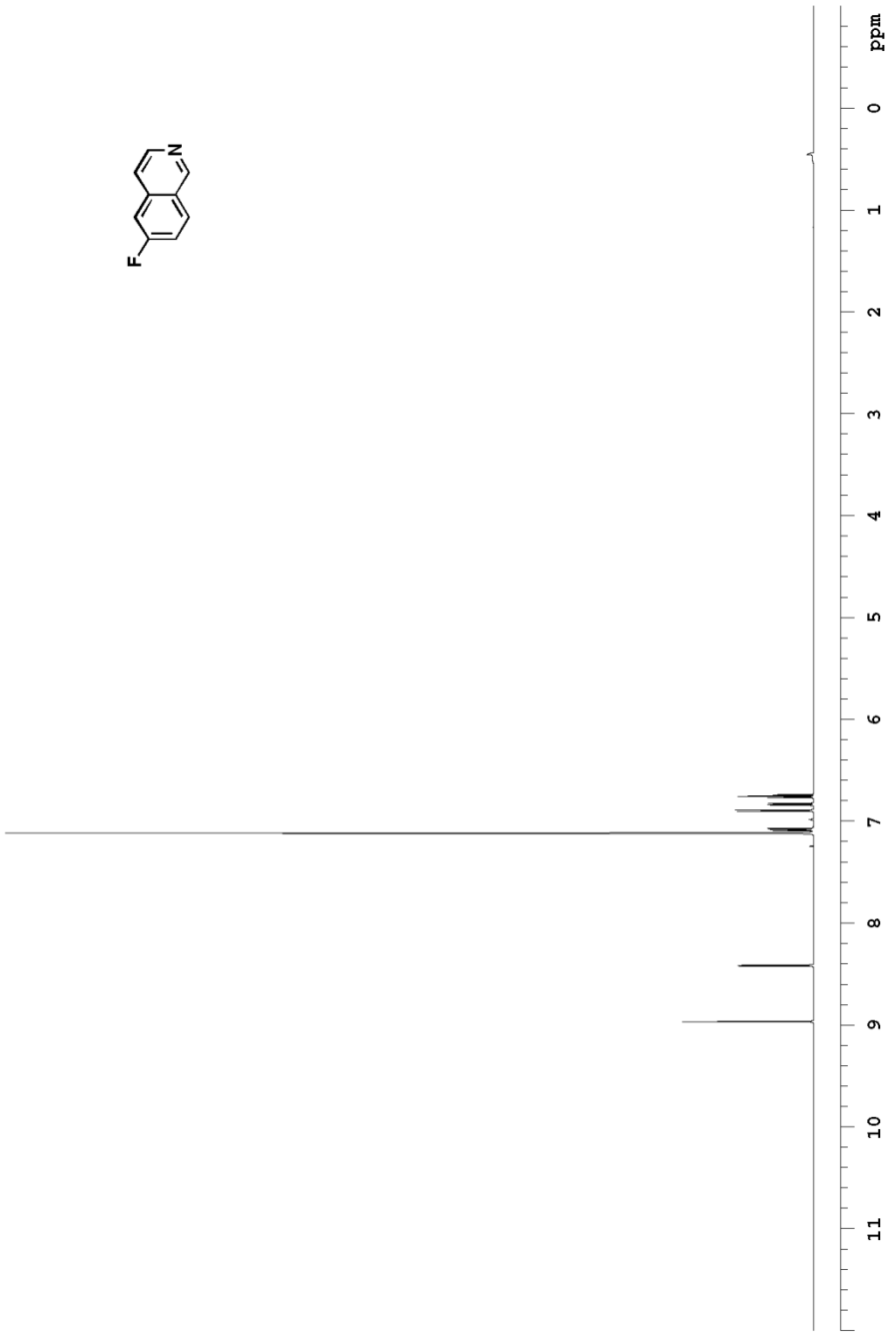
^{1}H NMR ($CDCl_3$, 23 ºC) of **7**



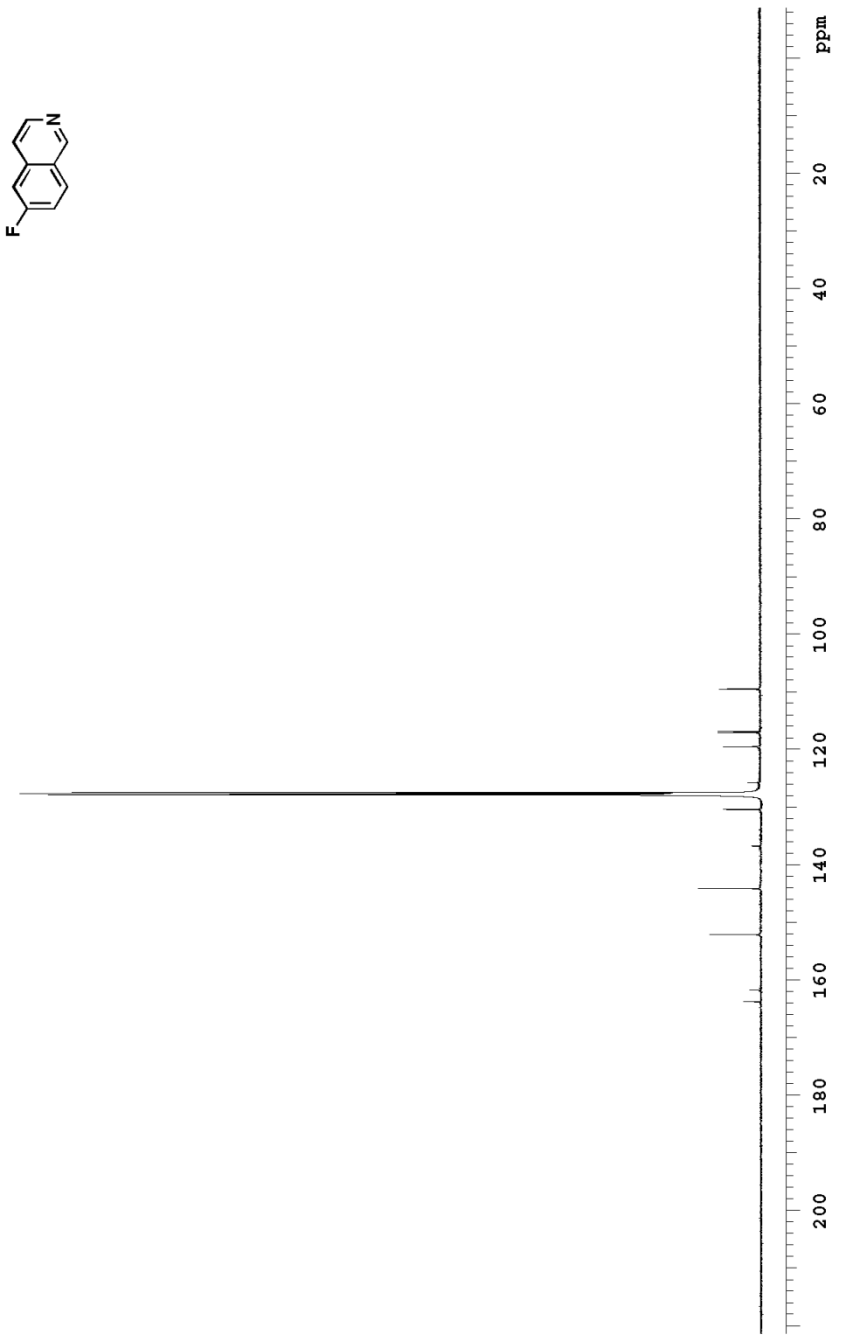
^{13}C NMR ($CDCl_3$, 23 ºC) of **7**



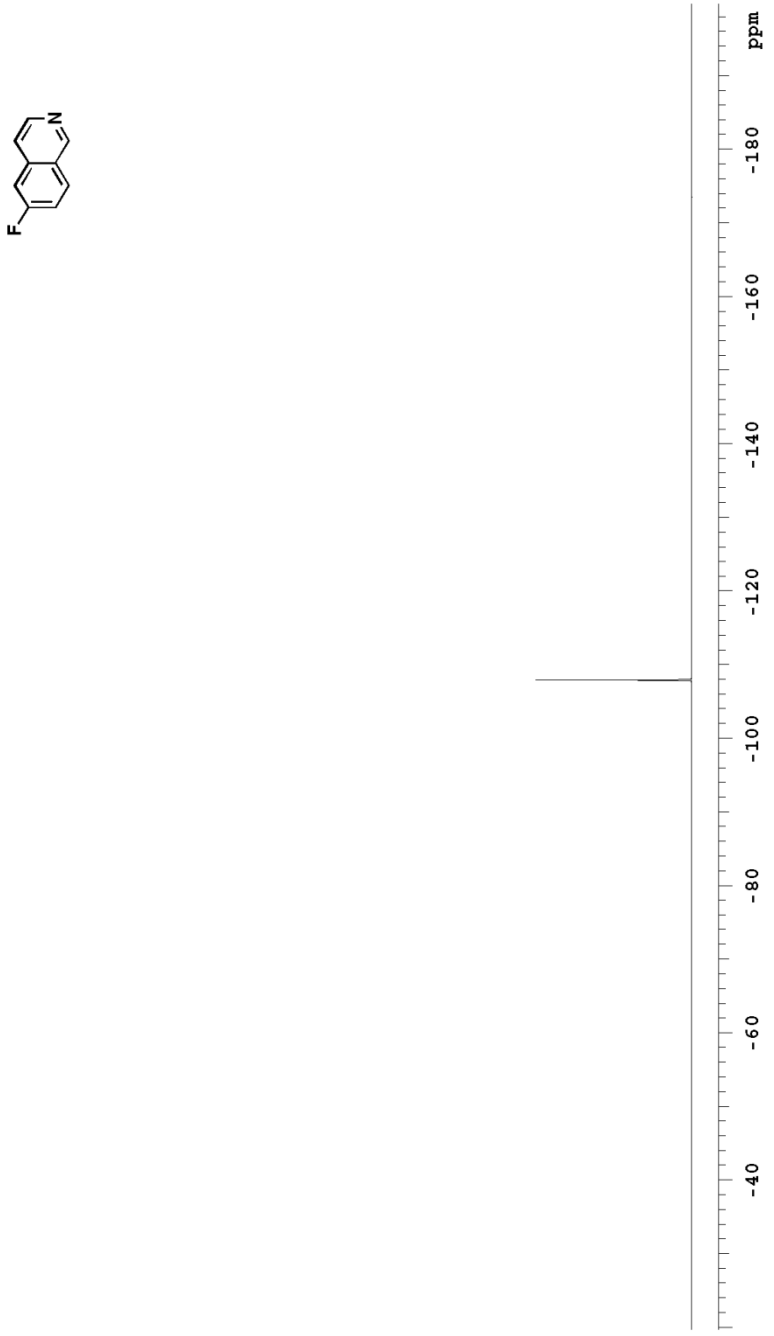
^{19}F NMR ($CDCl_3$, 23 ºC) of **7**



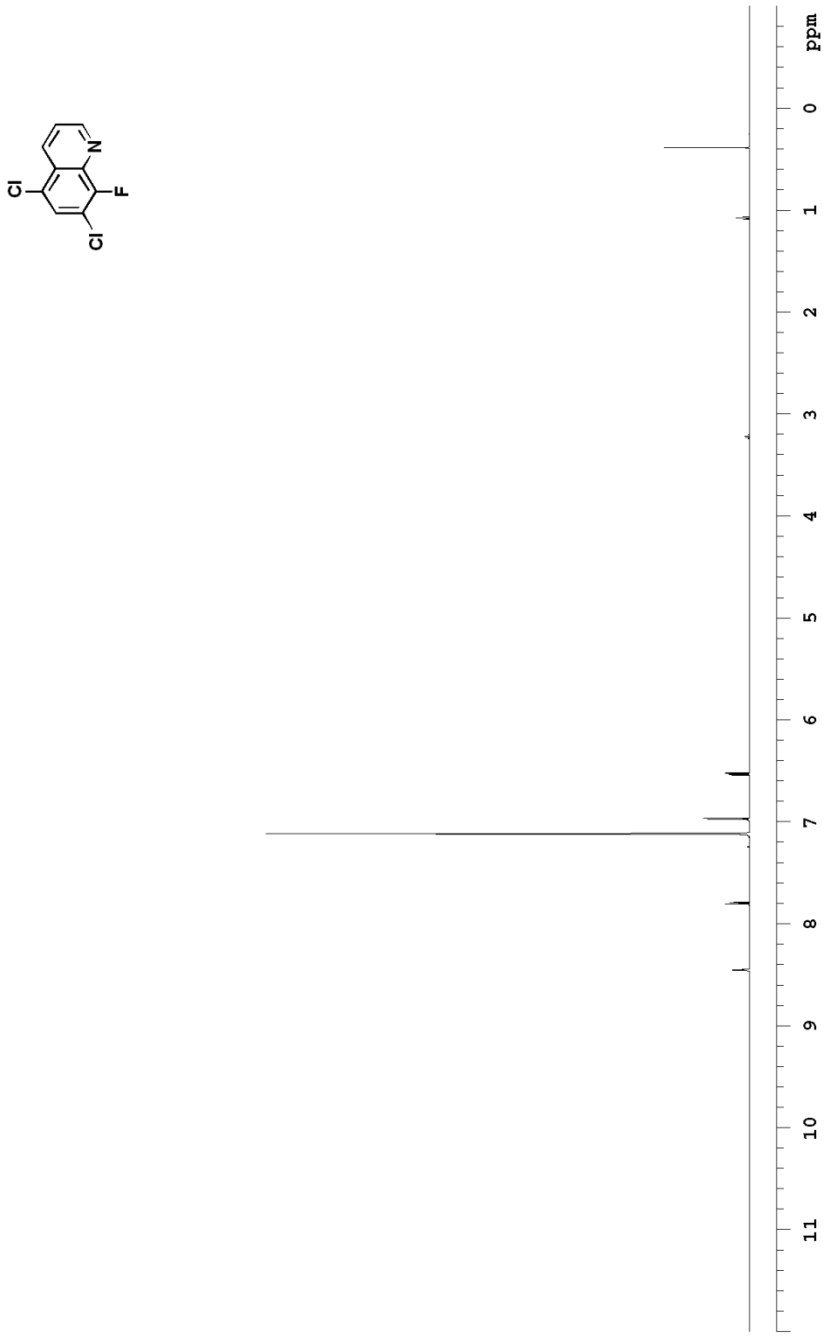
^{1}H NMR (C_6D_6, 23 ºC) of **8**



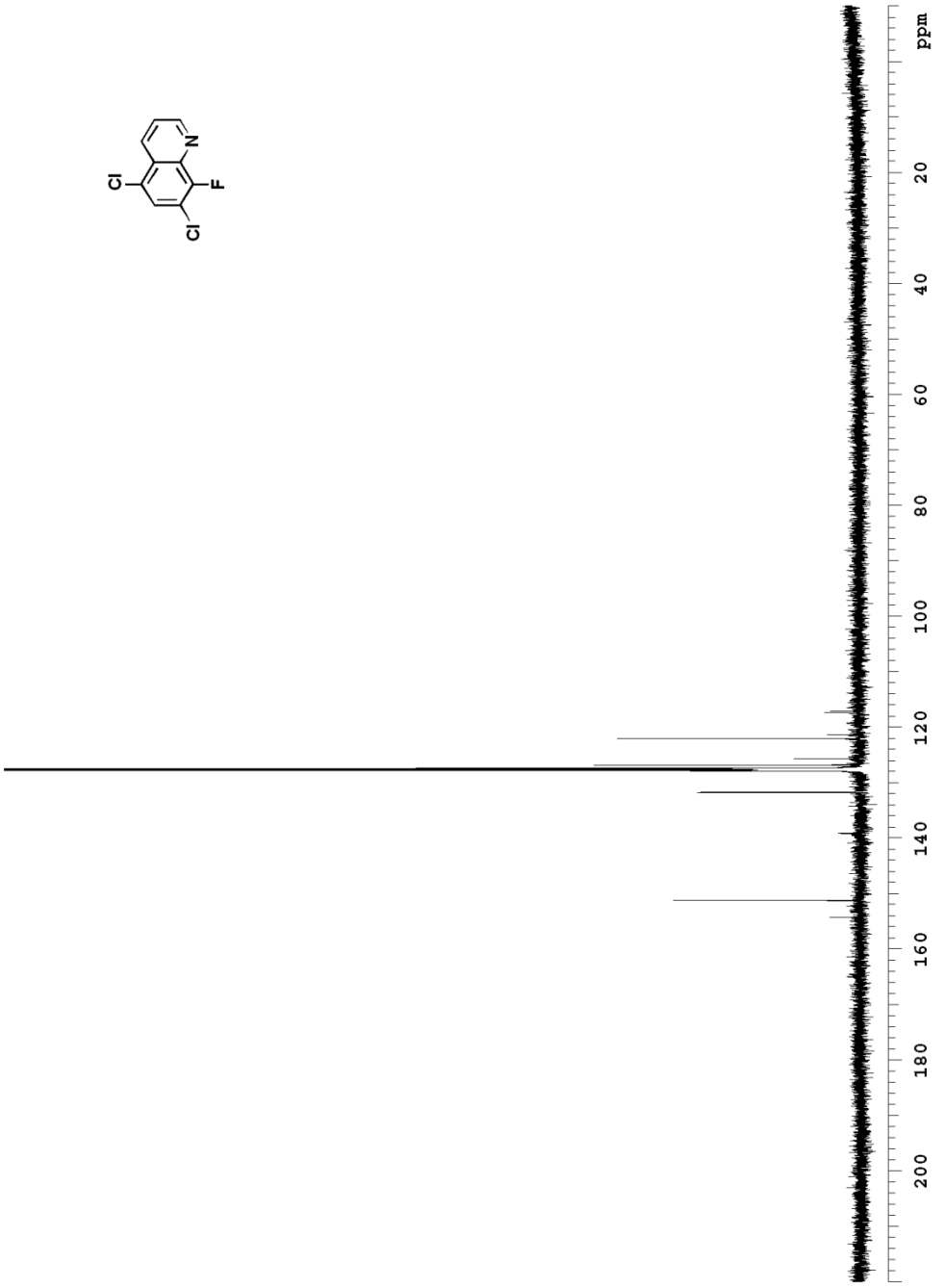
^{13}C NMR (C_6D_6, 23 ºC) of **8**



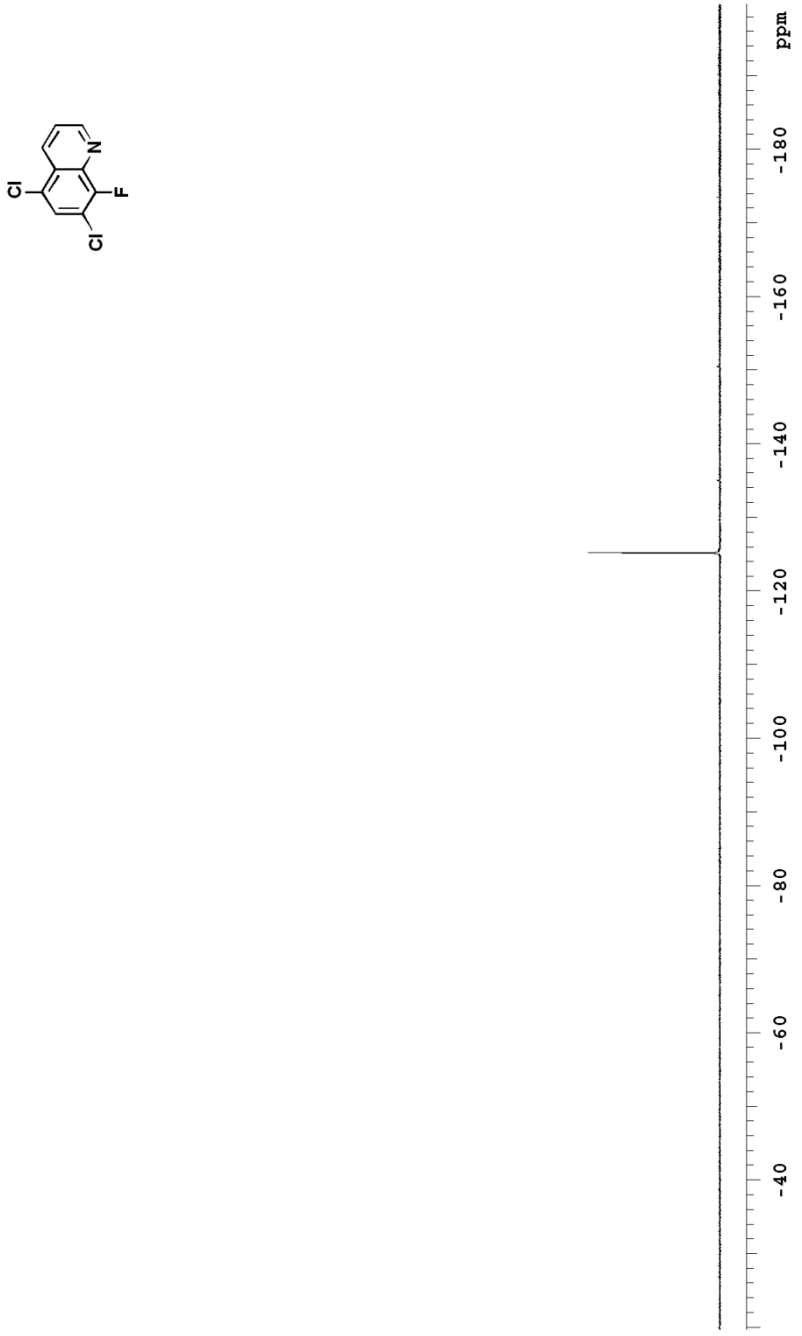
^{19}F NMR (C_6D_6, 23 ºC) of **8**



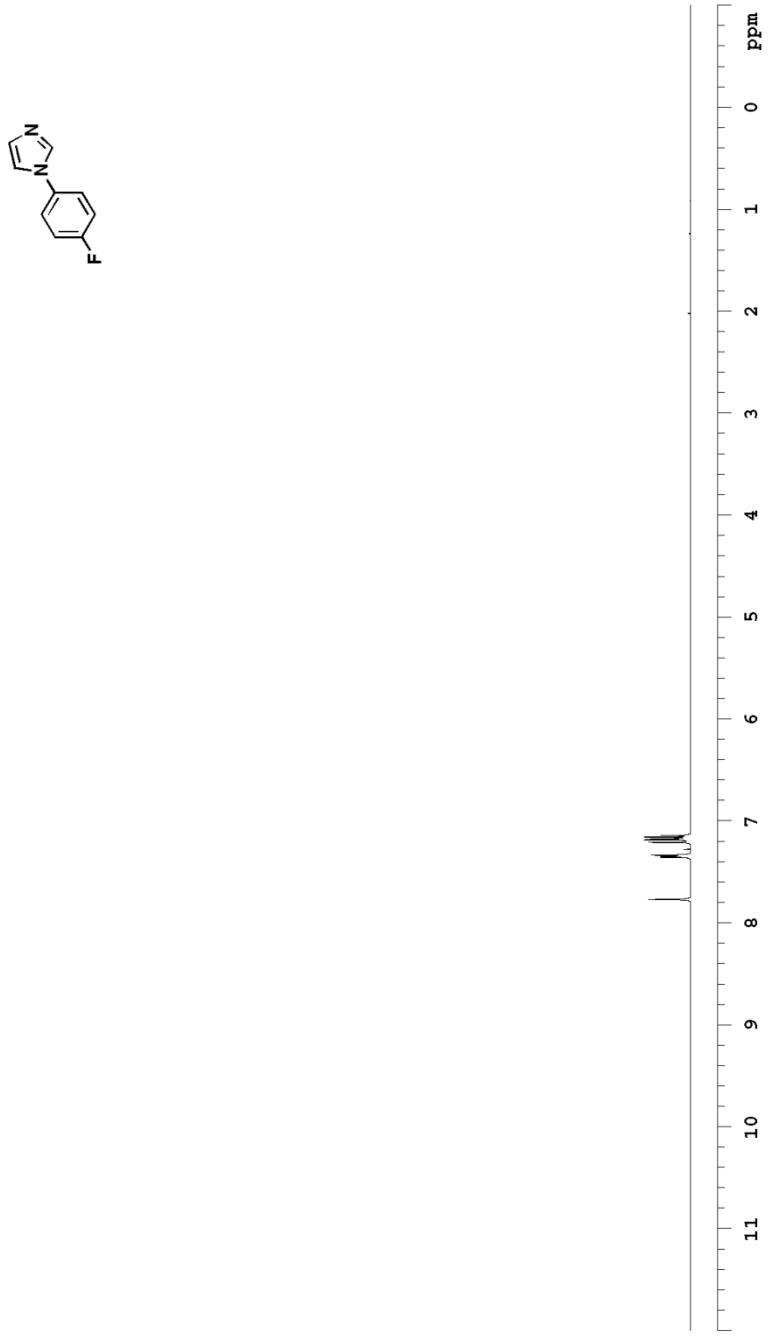
^{1}H NMR (C_6D_6, 23 ºC) of **9**



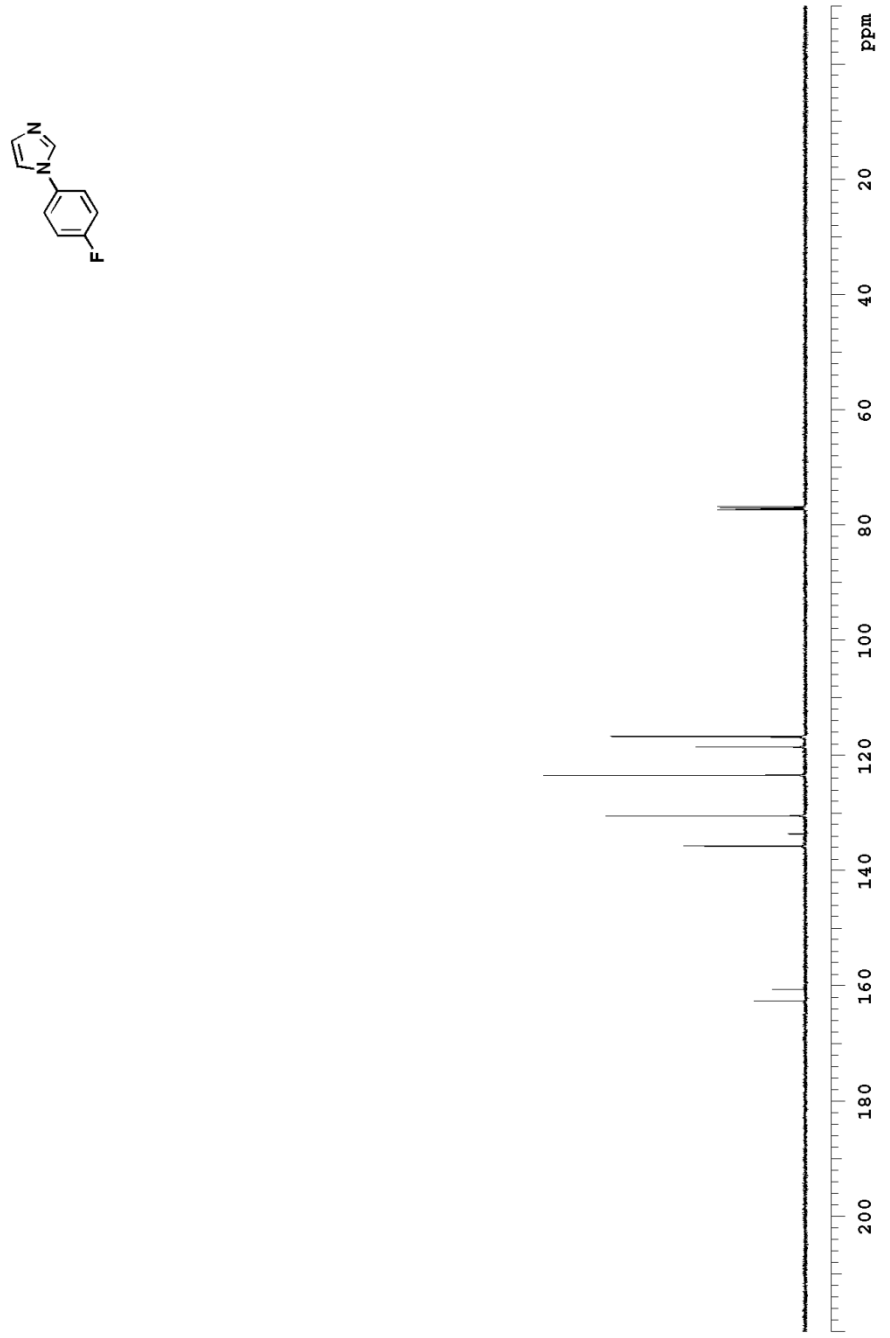
^{13}C NMR (C_6D_6, 23 ºC) of **9**



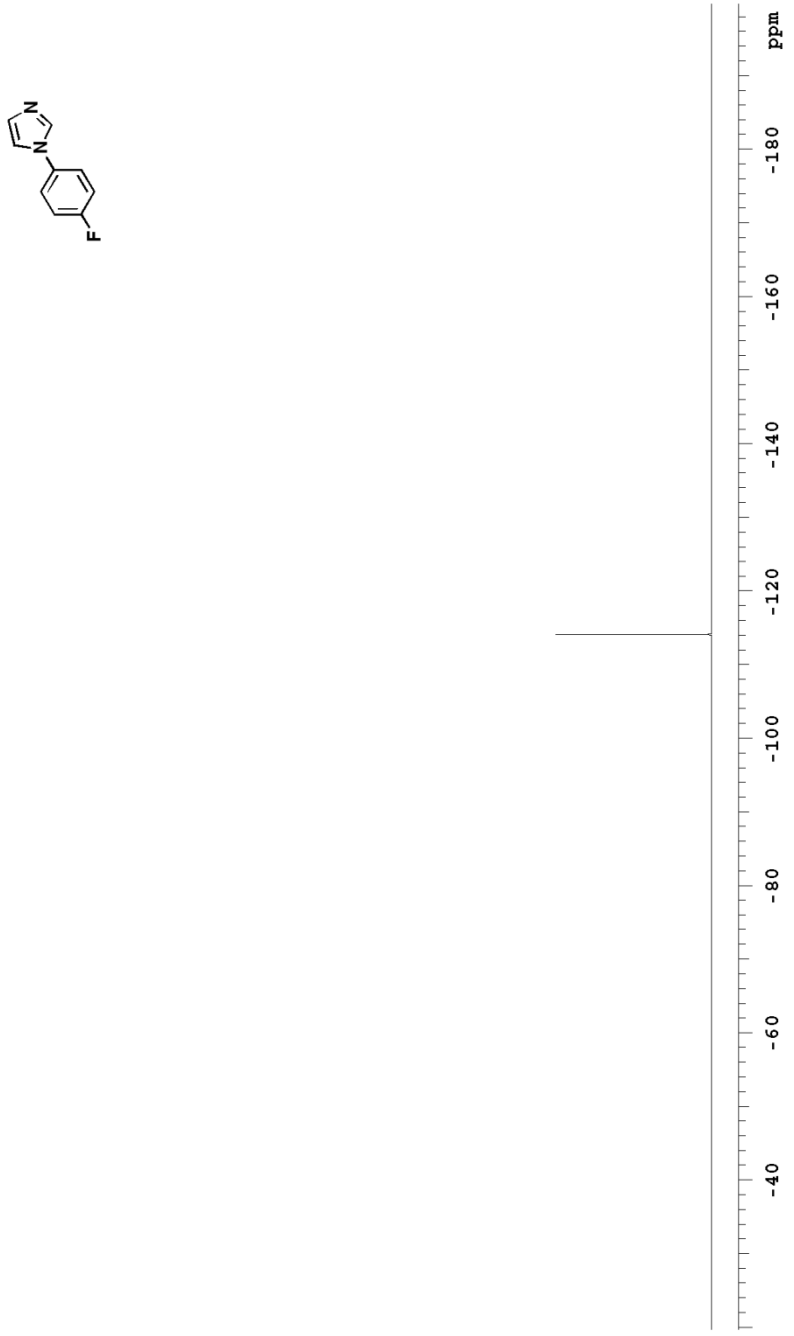
^{19}F NMR (C_6D_6, 23 ºC) of **9**



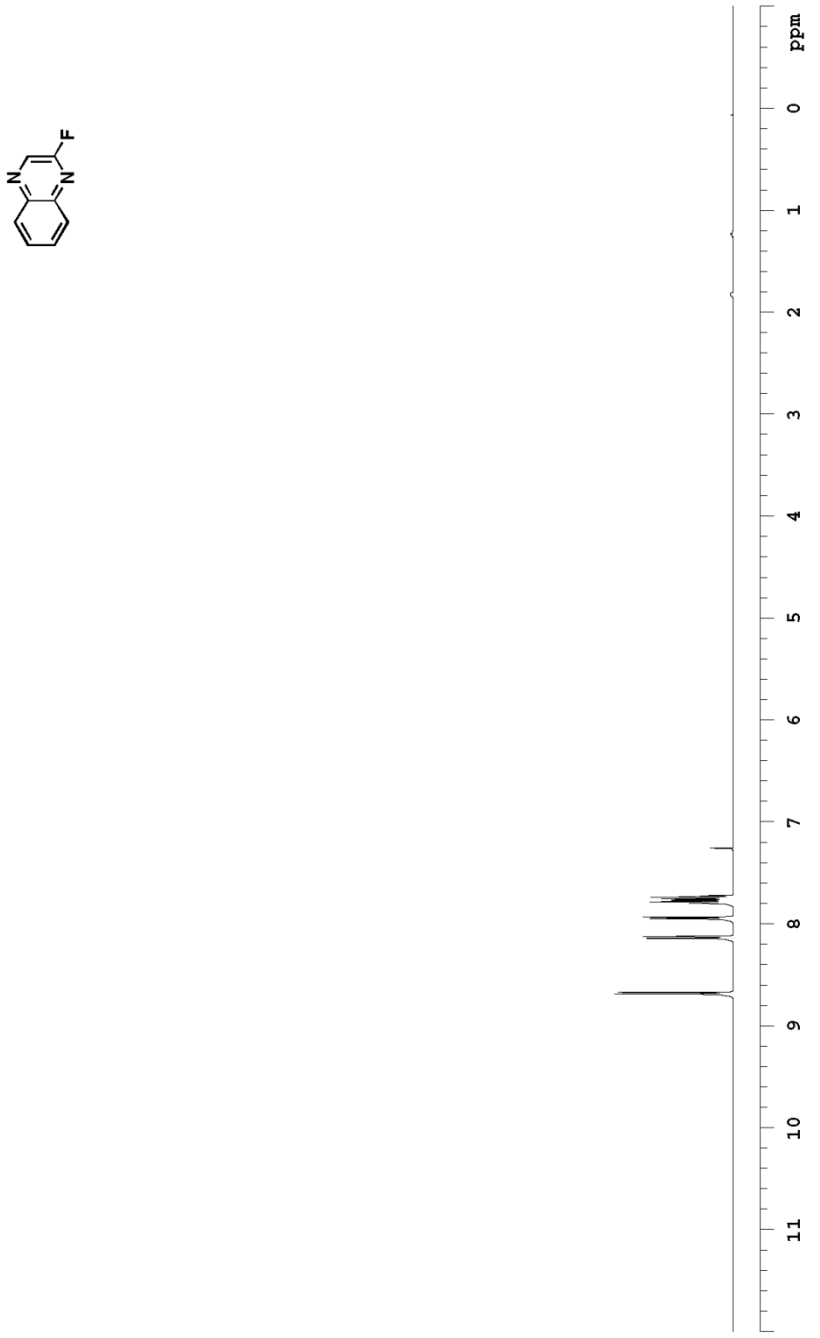
^{1}H NMR ($CDCl_3$, 23 ºC) of **10**



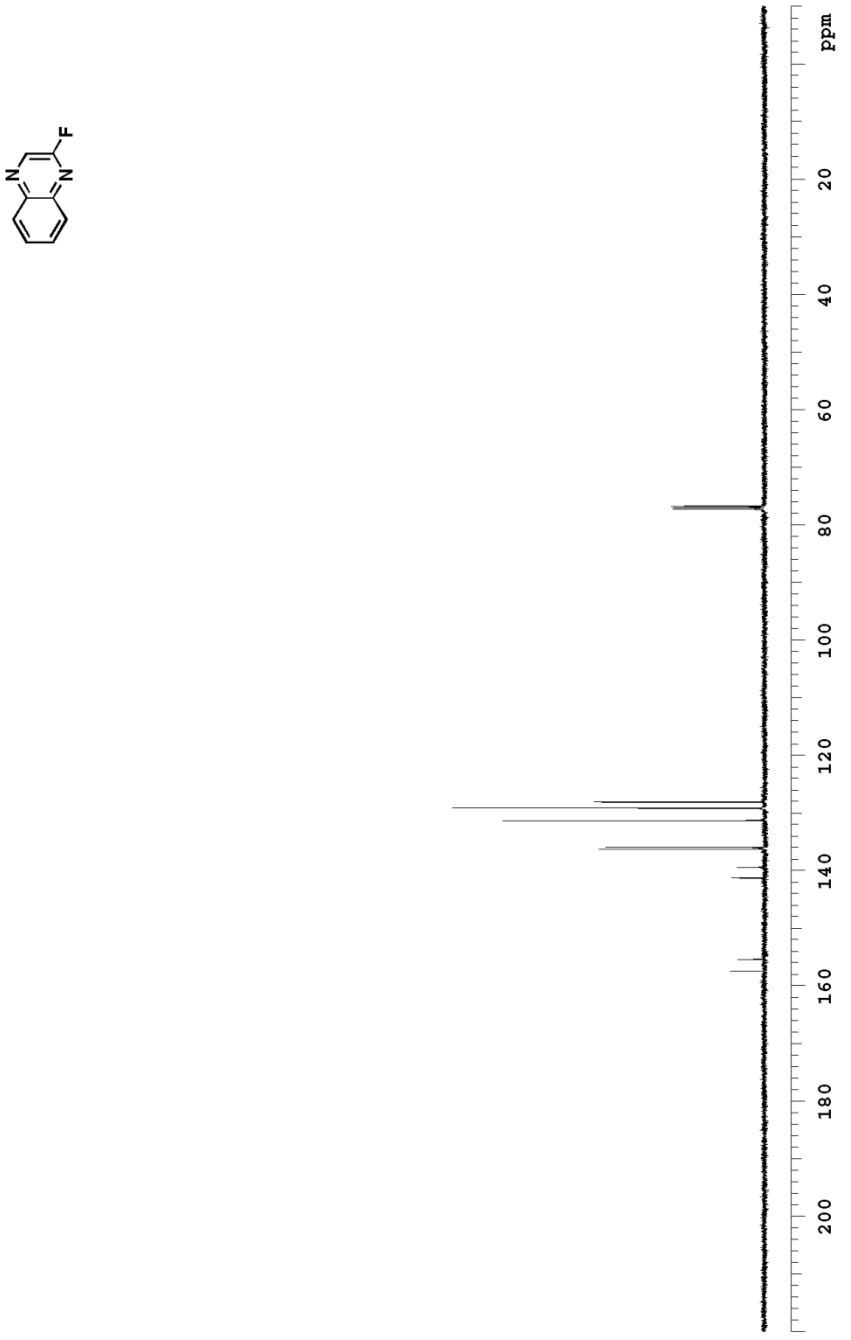
^{13}C NMR ($CDCl_3$, 23 ºC) of **10**



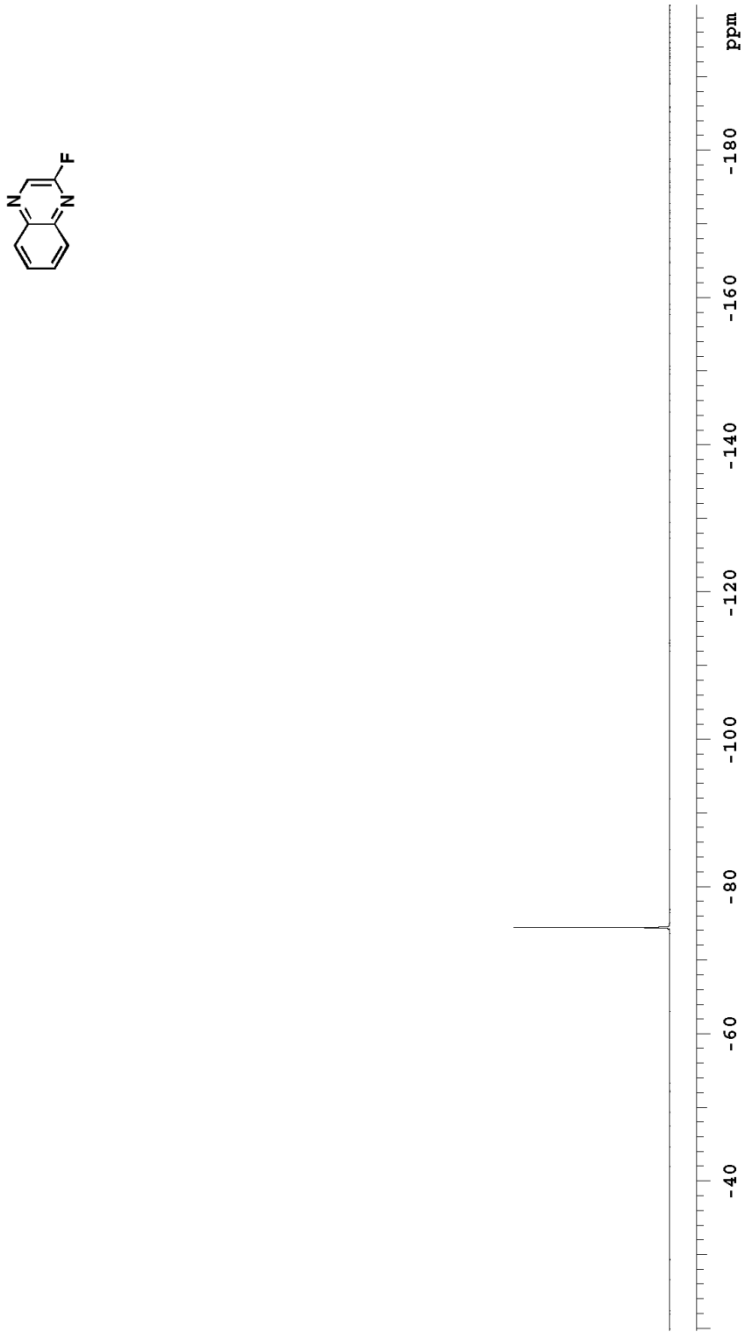
^{19}F NMR ($CDCl_3$, 23 ºC) of **10**



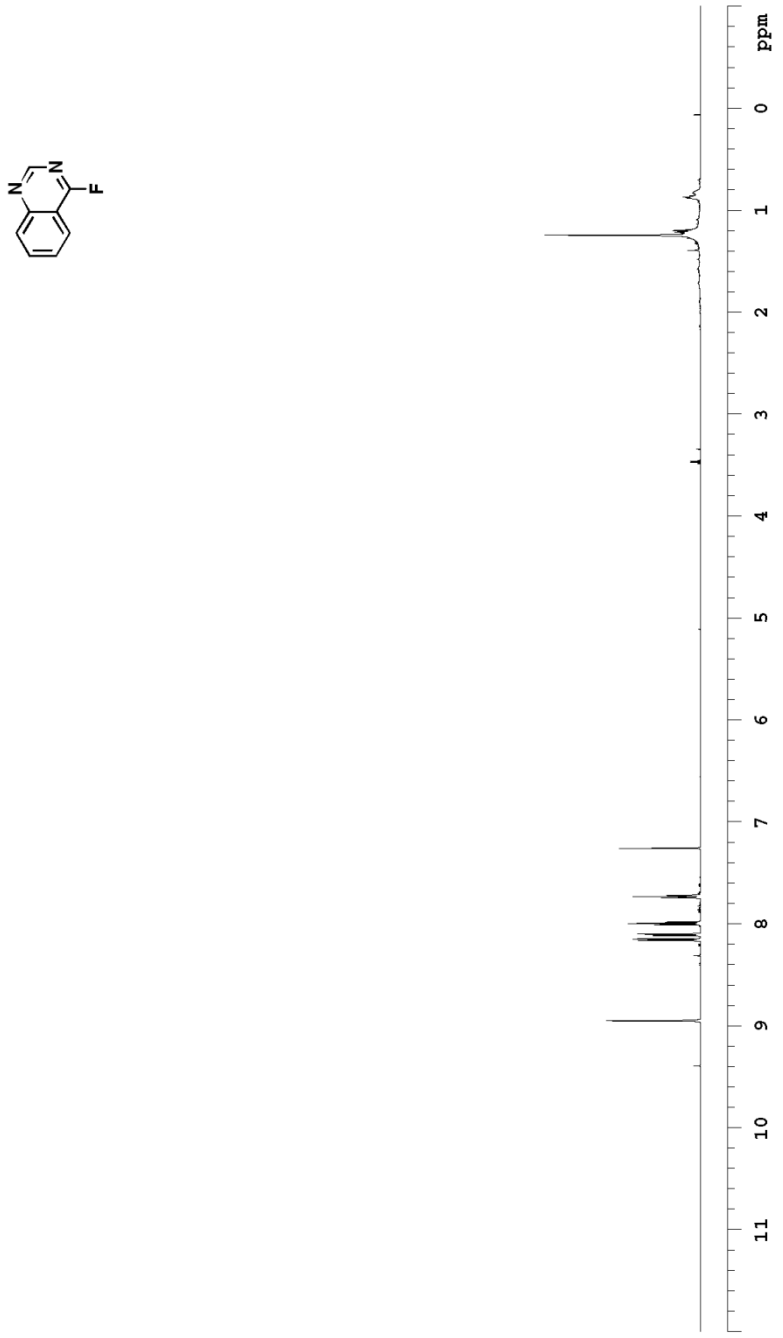
^{1}H NMR ($CDCl_3$, 23 ºC) of **11**



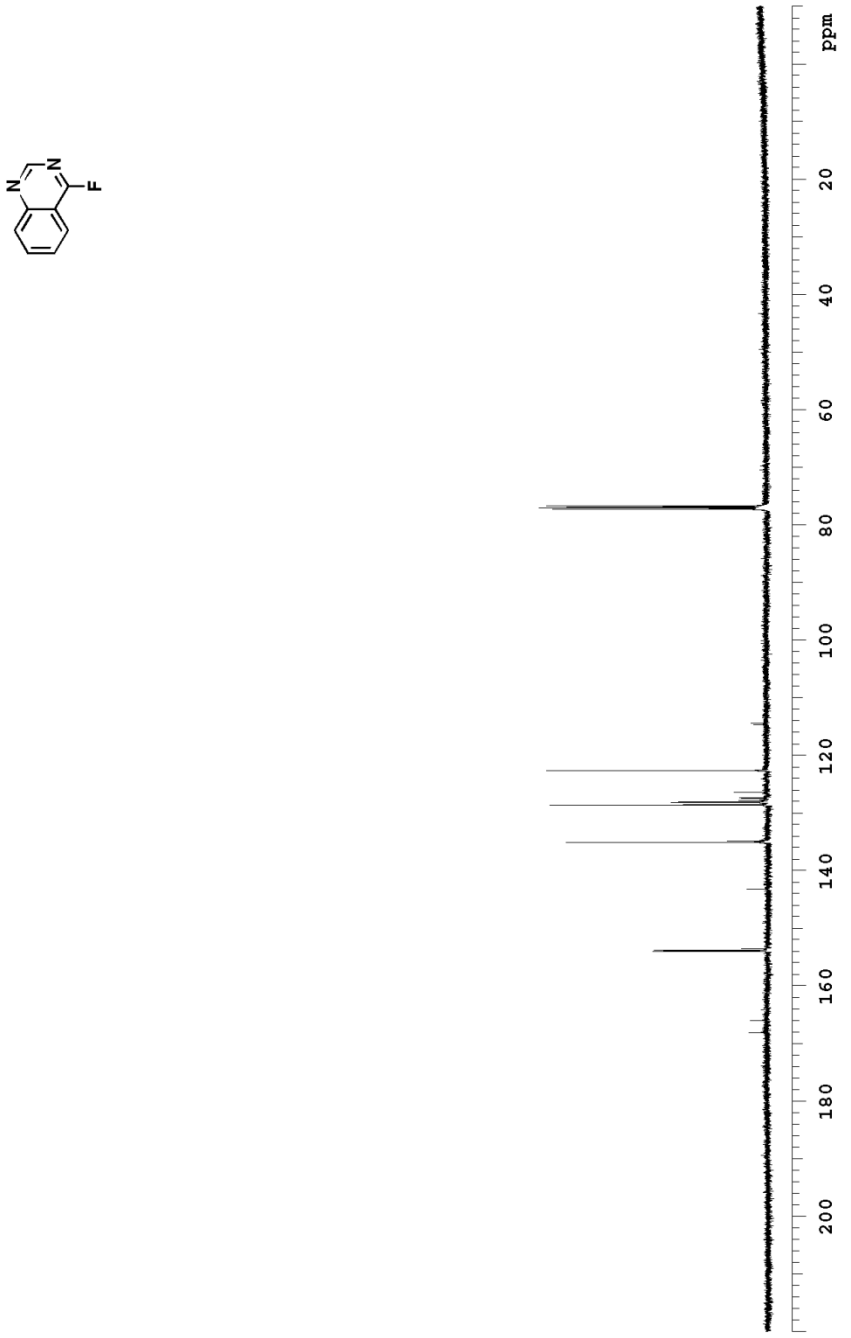
^{13}C NMR ($CDCl_3$, 23 ºC) of **11**



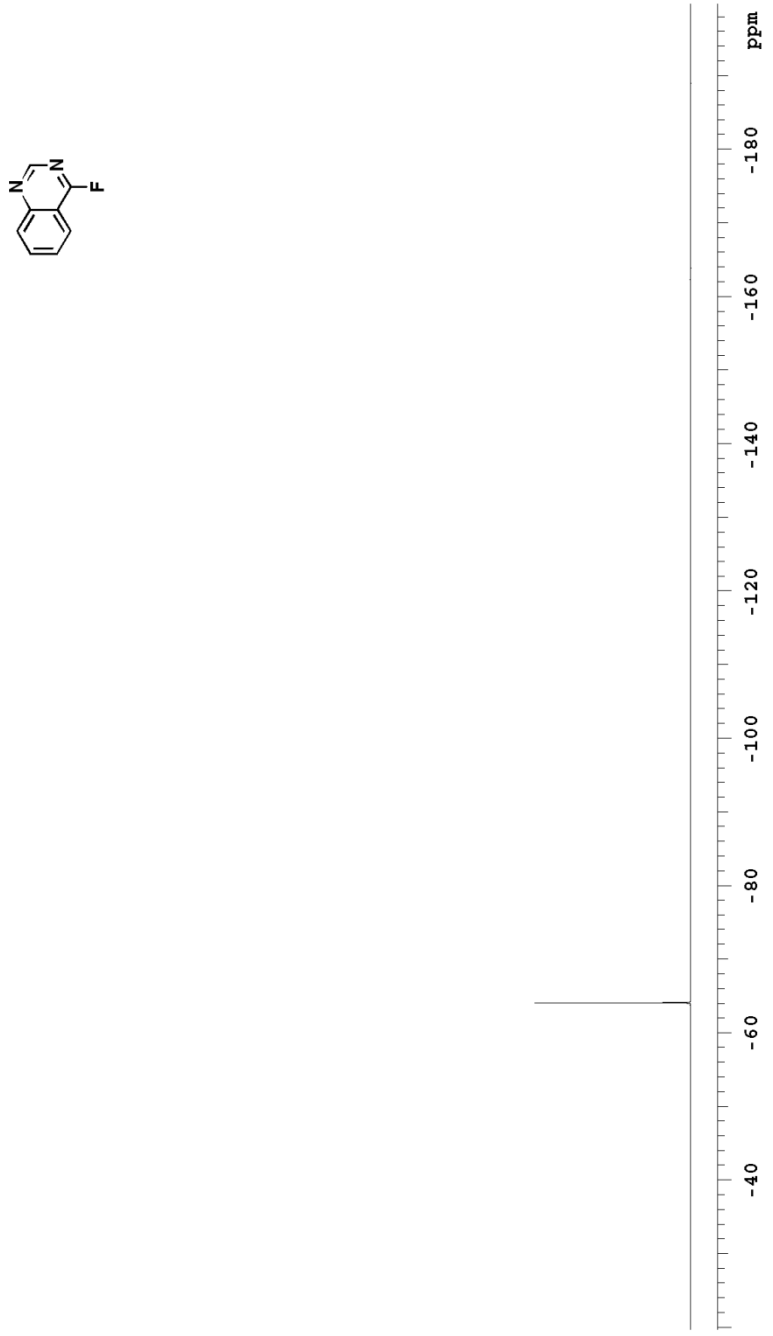
^{19}F NMR ($CDCl_3$, 23 ºC) of **11**



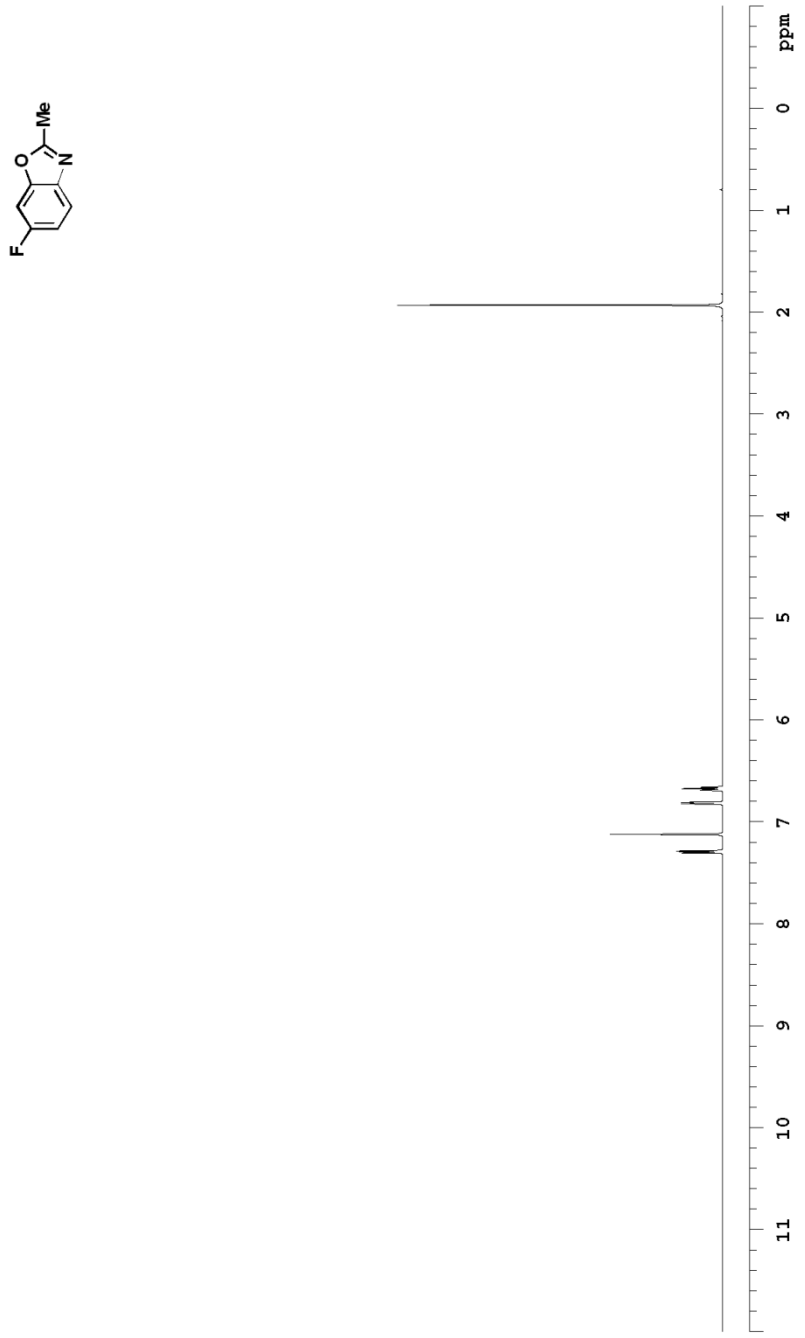
^{1}H NMR ($CDCl_3$, 23 ºC) of **12**



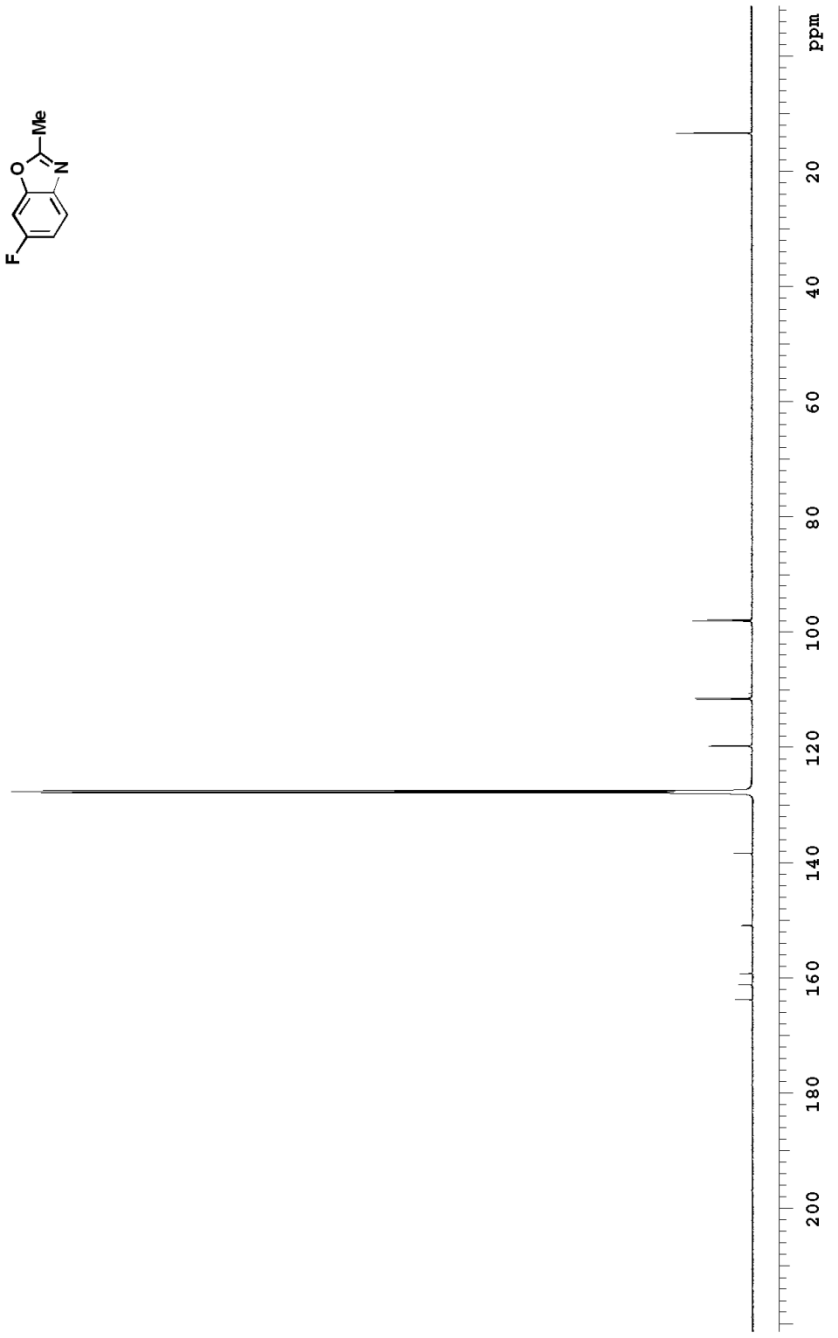
^{13}C NMR ($CDCl_3$, 23 ºC) of **12**



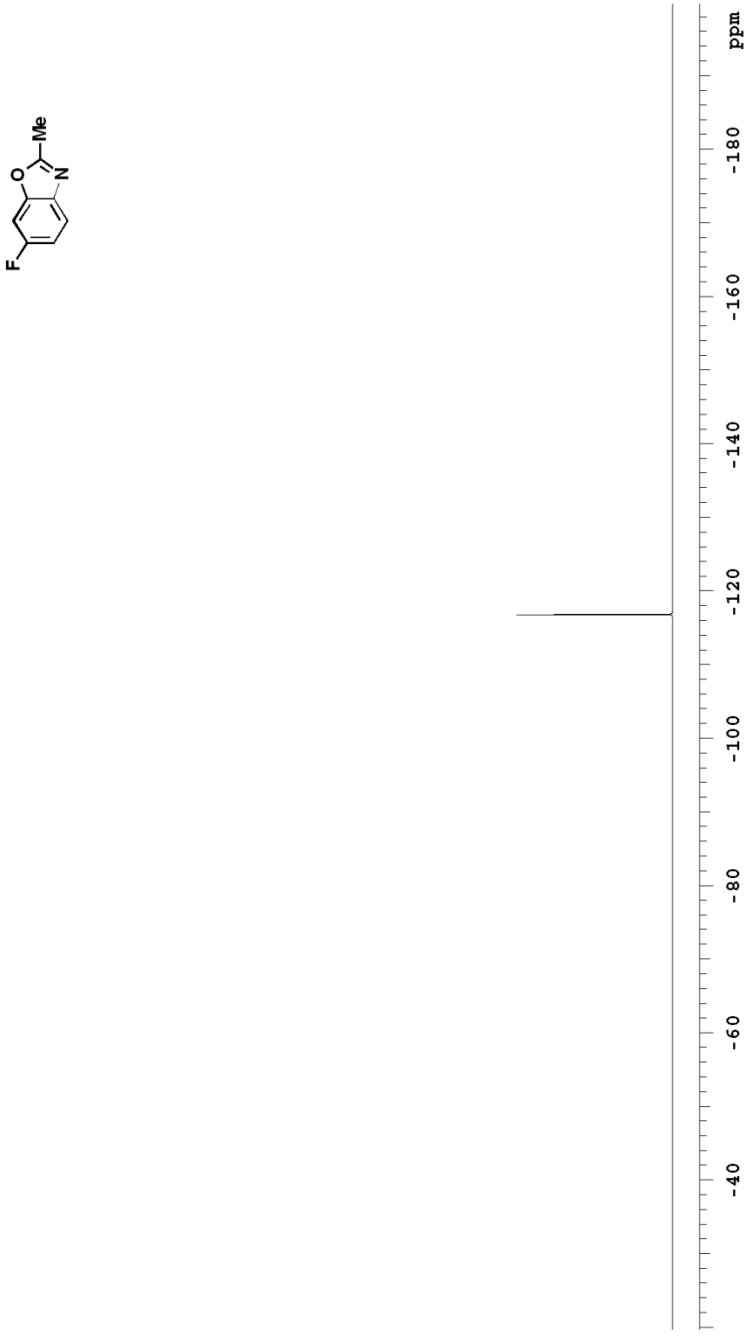
^{19}F NMR ($CDCl_3$, 23 ºC) of **12**



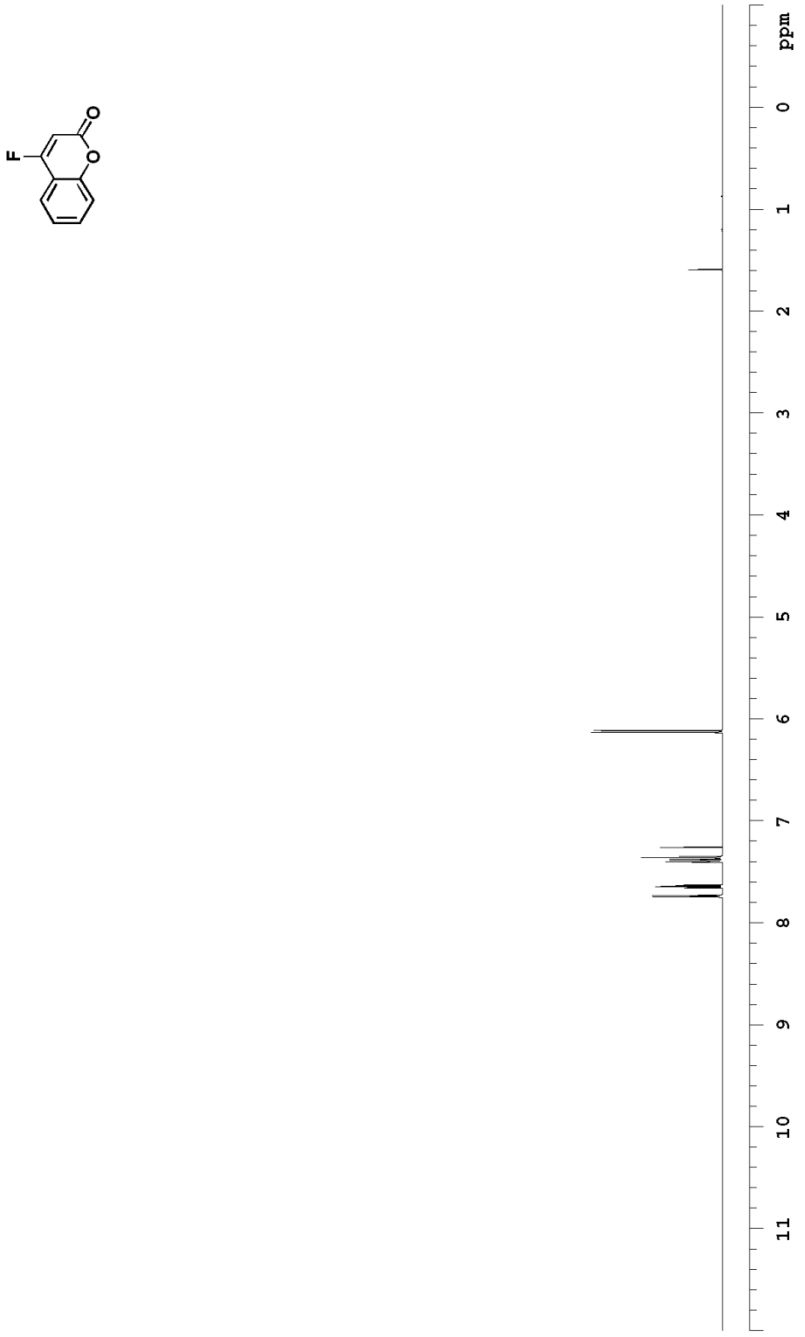
^{1}H NMR (C_6D_6, 23 ºC) of **13**



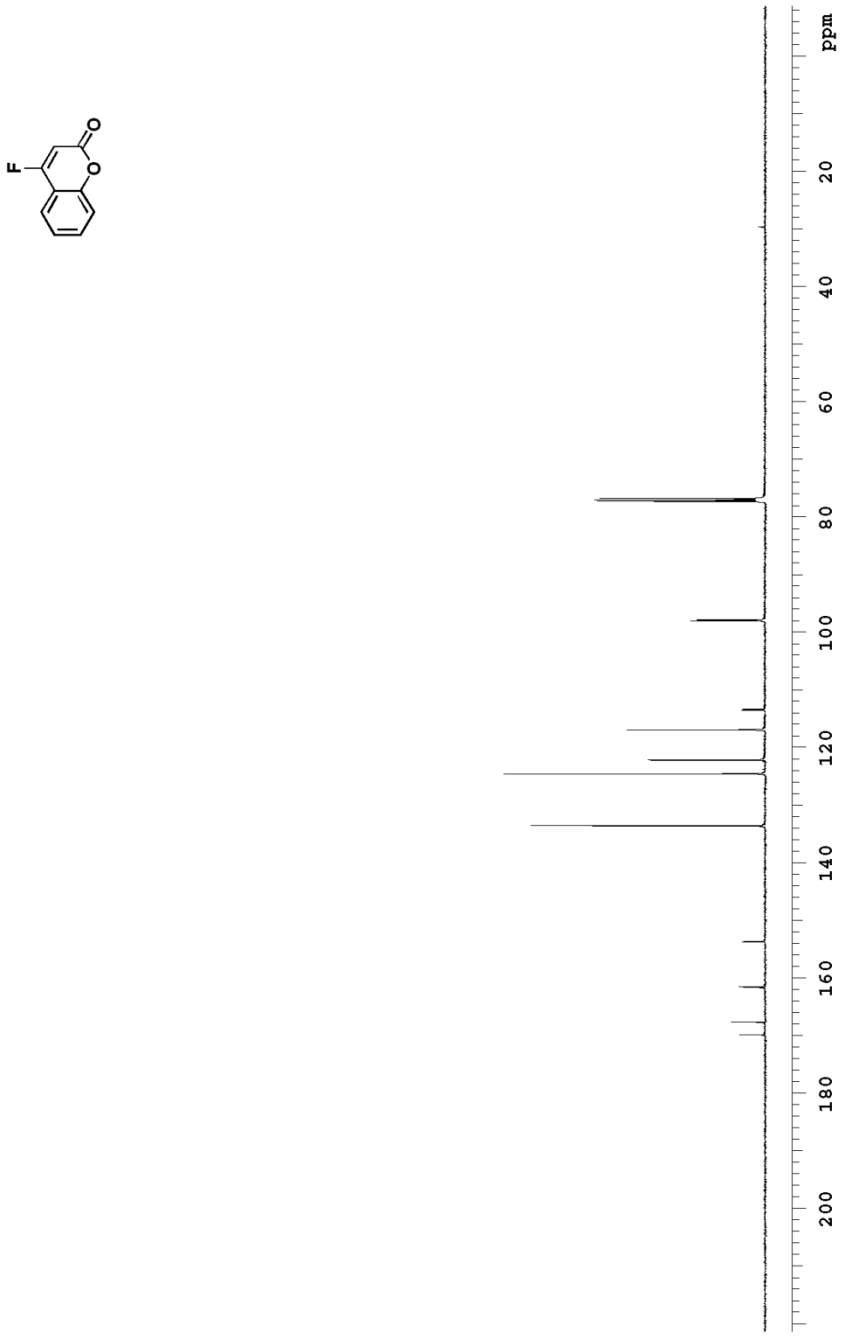
^{13}C NMR (C_6D_6, 23 ºC) of **13**



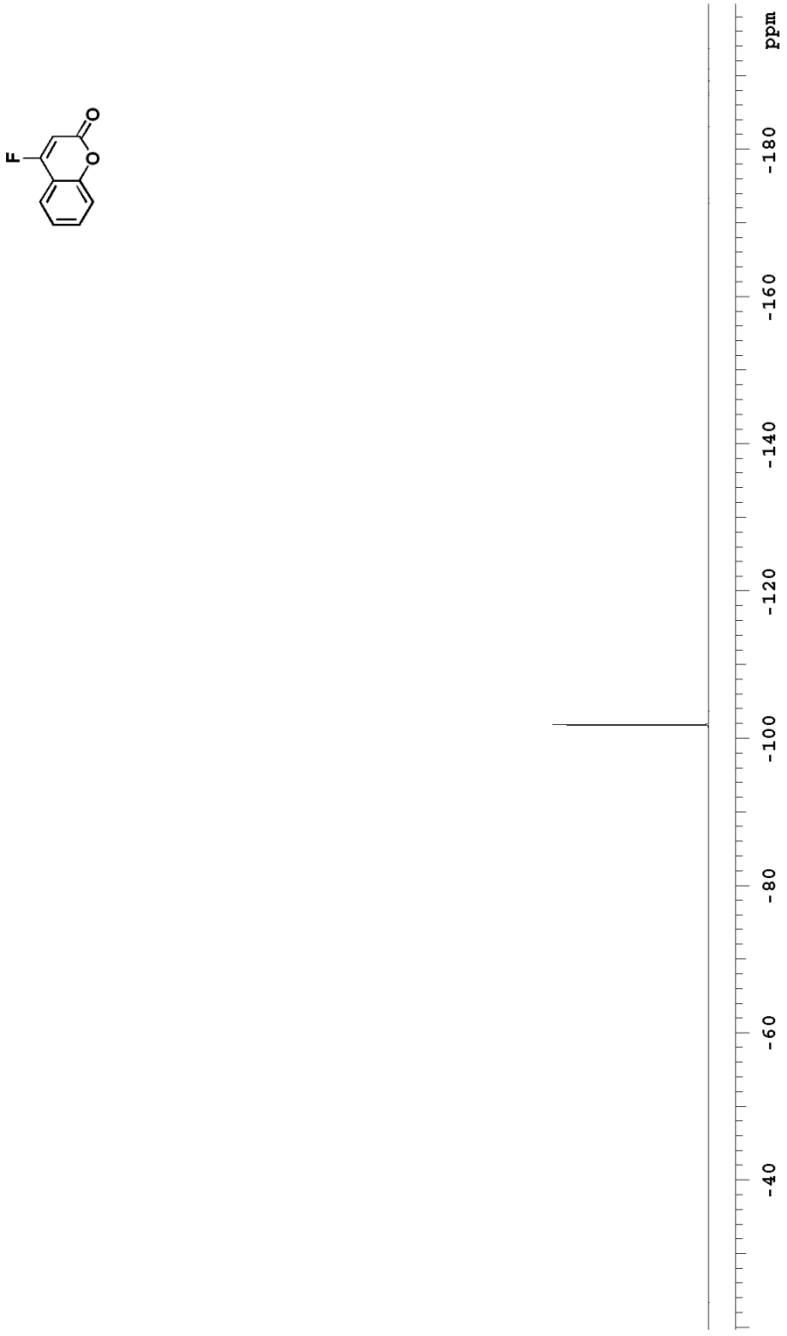
^{19}F NMR (C_6D_6, 23 ºC) of **13**



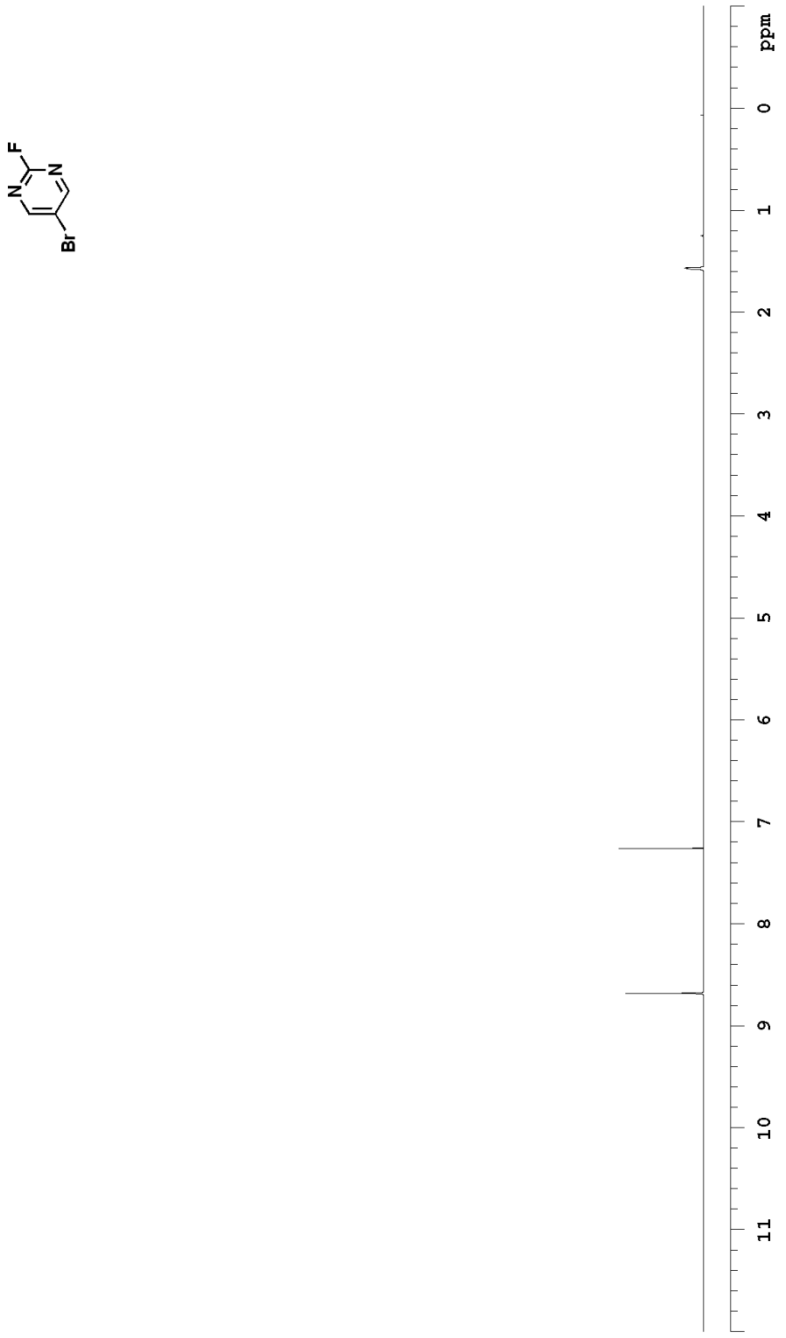
^{1}H NMR ($CDCl_3$, 23 ºC) of **14**



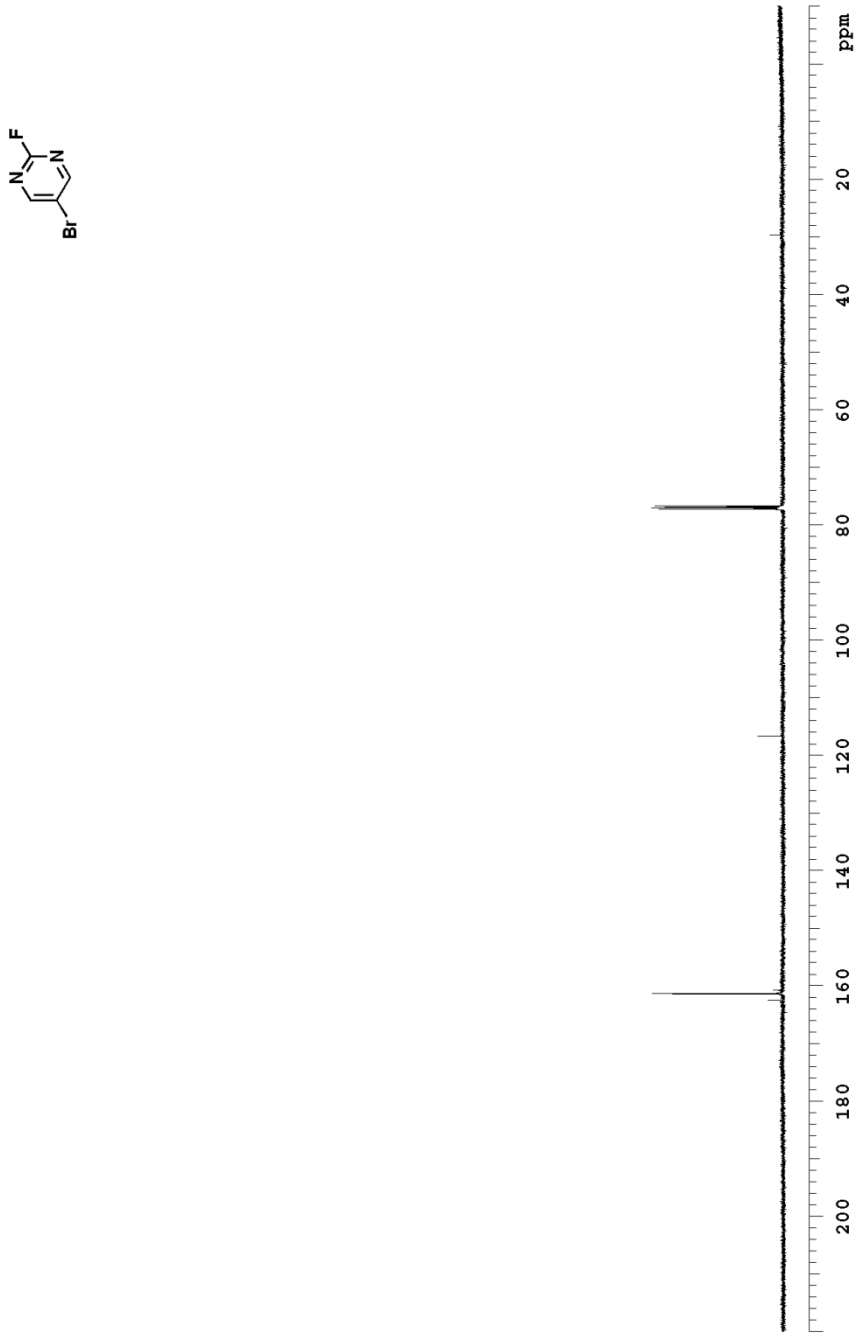
^{13}C NMR ($CDCl_3$, 23 ºC) of **14**



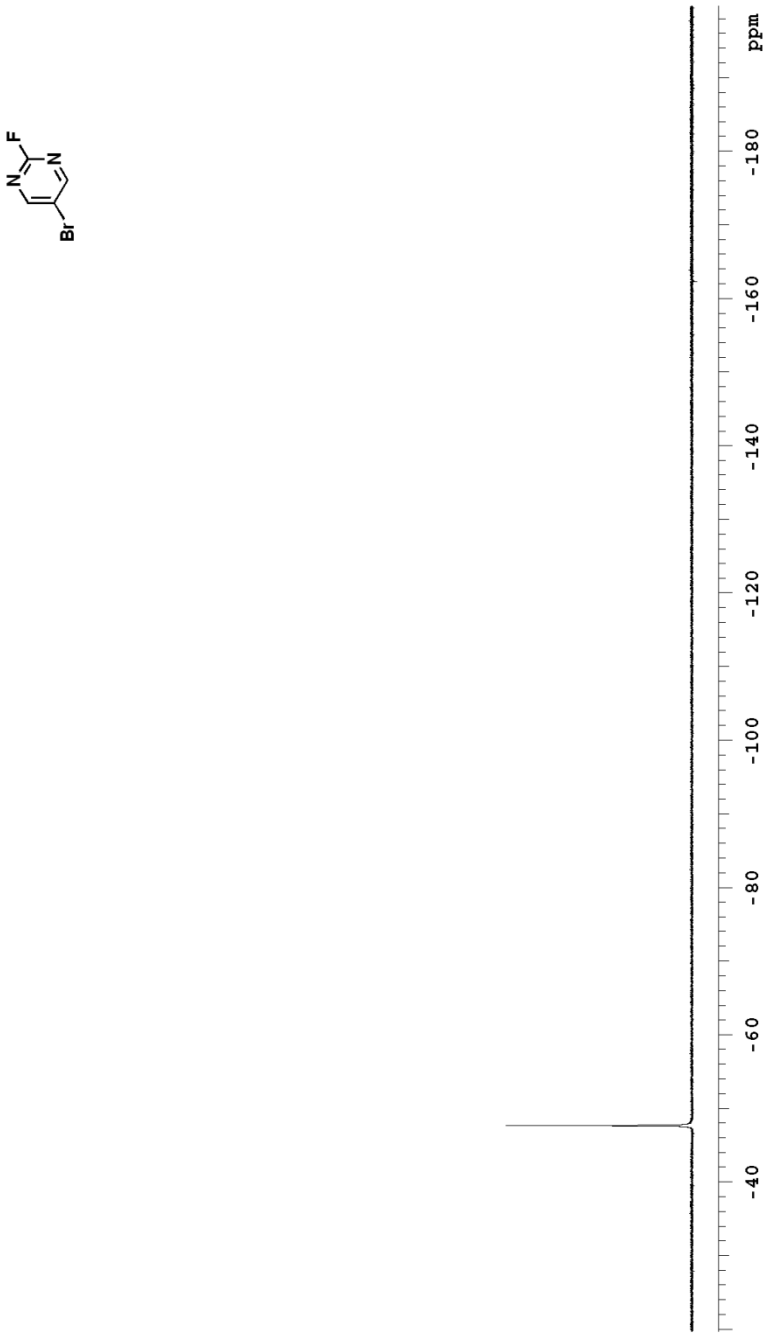
^{19}F NMR ($CDCl_3$, 23 ºC) of **14**



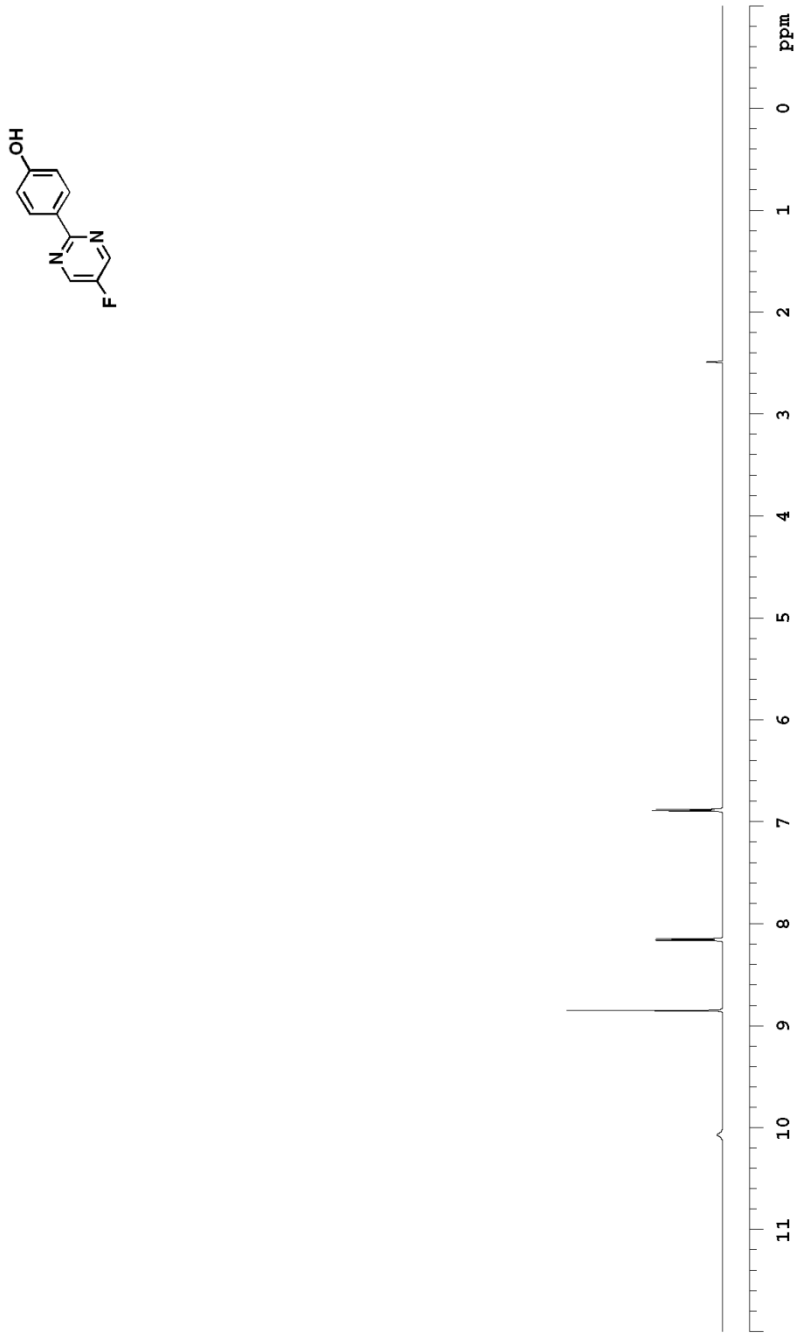
^{1}H NMR ($CDCl_3$, 23 ºC) of **15**



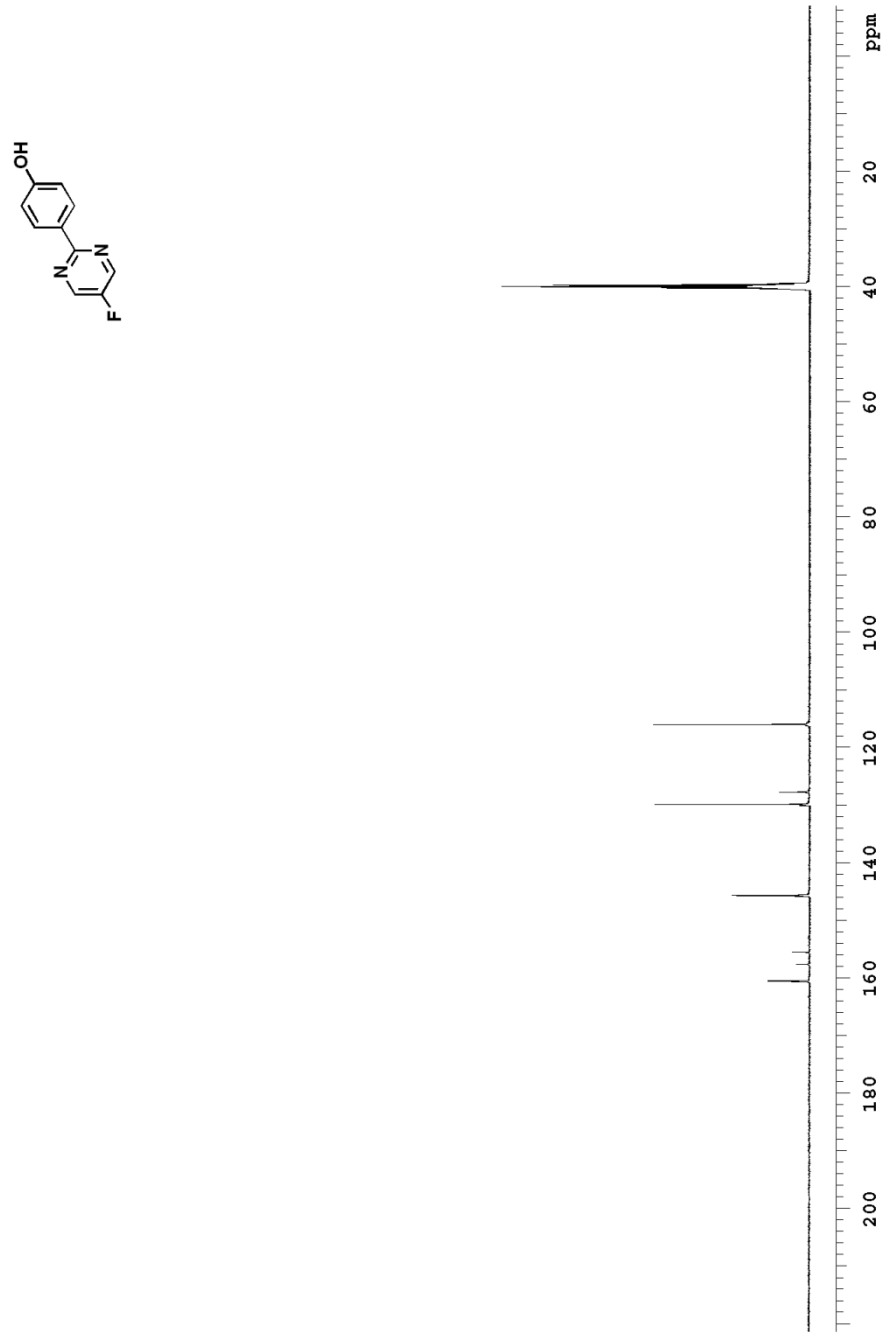
^{13}C NMR ($CDCl_3$, 23 ºC) of **15**



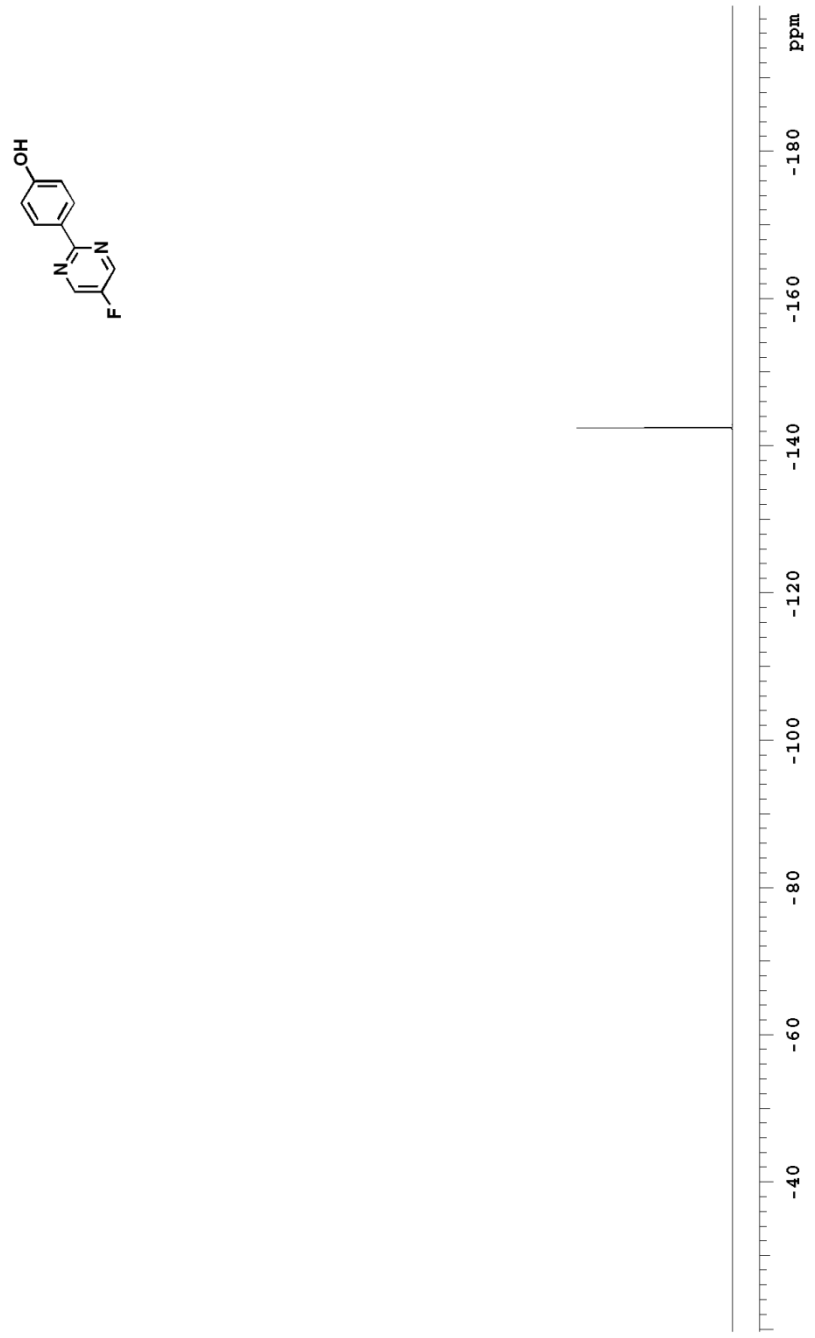
^{19}F NMR ($CDCl_3$, 23 ºC) of **15**



^{1}H NMR (DMSO-d_6, 23 ºC) of **16**



^{13}C NMR (DMSO-d_6, 23 ºC) of **16**



^{19}F NMR (DMSO-d_6, 23 ºC) of **16**

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