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Supporting Information

Selective Methylation of Arenes: A Radical C–H Functionalization/ Cross-Coupling Sequence

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SUPPORTING INFORMATION

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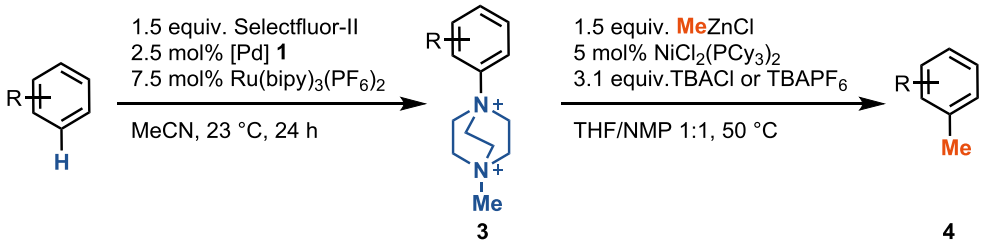
MATERIALS AND METHODS

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 F_{254} plates and visualized by fluorescence quenching under UV light and $KMnO_4$ stain. Flash chromatography was performed on Geduran® Silica Gel 40–63 µm particle size using a forced flow of eluent at 0.3–0.5 bar pressure. All air- and moisture-sensitive manipulations were performed using oven-dried glassware, using standard Schlenk line or dry, nitrogen-filled glovebox techniques. The reactions using a microwave were performed in a Biotage® Initiator+. Anhydrous solvents were obtained from Phoenix Solvent Drying Systems. Acetonitrile and NMP (N-methyl-2-pyrrolidone) were purchased from Sigma-Aldrich® and used as received. All arene substrates were used as received from commercial suppliers, unless otherwise stated. 2,4-Diphenylpyridine[1] and 2,4-diphenylpyrimidine[2] were prepared according to procedures reported in the literature. 1-(Pyridine-2-ylmethyl)pyrrolidine 1-oxide was prepared according to the literature.[3] Selectfluor II was purchased from Sinojie hanson Ltd, and was used as received. The tetra-*n*-butylammonium salt, LiCl and $MgCl_2$ were purchased from commercial suppliers, and dried for 12 h under high vacuum (0.1–0.2 mbar) at 80°C. $Ru(bipy)_3(PF_6)_2$ and $Ni(PCy_3)_2Cl_2$, were purchased from Sigma-Aldrich® and were used as received. MeZnCl 2M in THF and cyclopropylzinc bromide 0.5M in THF were purchased from Acros Organics. Et_2Zn (95%) was purchased from abcr. *n*BuZnCl was prepared according to the literature.[4] All deuterated solvents were purchased from Euriso-Top®. NMR spectra were recorded on a Bruker 500 spectrometer operating at 500 MHz and 125 MHz for ^1H and ^{13}C acquisitions, respectively. Chemical shifts were referenced to the residual proton solvent peaks (^1H: $CDCl_3$, δ 7.26; DMSO-d_6, δ 2.50; CD_3CN, δ 1.94; acteone-d_6, δ 2.05), solvent ^{13}C signals ($CDCl_3$, δ 77.2; DMSO-d_6 δ 40.2; CD_3CN, δ 118.7, 1.4; acteone-d_6, δ 29.84). ^{19}F NMR spectra were referenced using a unified chemical shift scale based on the ^1H resonance of tetramethylsilane (1% v/v solution in the respective solvent).[5] Signals are listed in ppm, and multiplicity identified as s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad; coupling constants in Hz; integration. All HRMS data were recorded on Q Exactive Plus from Thermo. Concentration under reduced pressure was performed by rotary evaporation at 40 °C under appropriate pressure. Purified compounds were further dried under high vacuum (0.1–0.2 mbar). Yields refer to purified and spectroscopically pure compounds, unless otherwise noted.

EXPERIMENTAL DATA

General procedure for the C–H functionalization-methylation sequence



To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 mg, 1.50 mmol, 1.50 equiv), and an arene (1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 x 2 mL). The resulting pure Ar-TEDA **3** was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours.

An oven-dried, argon-filled Schlenk tube was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), Ar-TEDA **3** (0.250 mmol, 1.00 equiv.), and $n Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.) or $n Bu_4N^+PF_6^-$ ($TBAPF_6$) (300 mg, 0.775 mmol, 3.10 equiv.). The Schlenk flask was capped with a rubber septum, then evacuated and back-filled with argon. This evacuation/back-filling process was repeated three times. NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added to the reaction mixture. The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL), with brine (5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel to give the title product.

Note 1: the purification procedure for Ar-TEDAs presented above is general. Combination of Et_3N and $MeCN/CH_2Cl_2$ allowed to purge the remaining TEDA-H^{2+} and/or $TEDA^+$ formed in the course of the reaction (Figure S1). The purging efficiency is comparable when Selectfluor is used instead of Selectfluor II.

Note 2: when the Ar–TEDAs were contaminated with remaining TEDA-H^{2+} and/or $TEDA^+$(), a second purification was performed as described below.

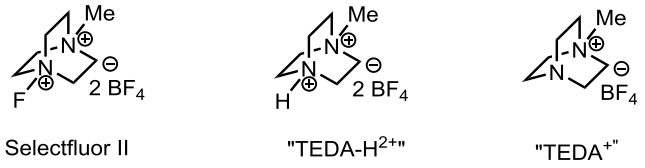


Figure S1. Selectfluor II and side-products after 24 h of reaction

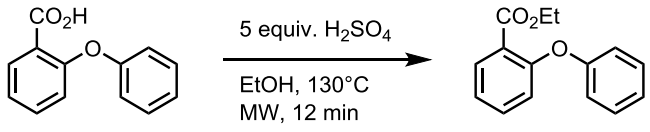
In a 20 mL-vial, acetonitrile (2 mL) was added to the solids, followed by Et_3N (excess, V = 0.3 mL) was added and the resulting mixture was stirred for 2 min at 23 °C. Dichloromethane (10 mL) was then added, and the precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial and methanol (5 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting solid was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours.

Note 3: The Ar–TEDA compounds have been purified and characterized by NMR and HRMS. However, in some cases, due to a low solubility of the isolated compounds in deuterated solvents (Acetone-d_6, DMSO-d_6, CD_3CN), the signal to noise ratio of the recorded ^{13}C-NMR spectra is low.

Note 4: We appreciate that, generally, for practical use, many scientists prefer not to use a glovebox. The transformation, as reported in this general procedure, was carried out conveniently without the use of a glovebox. For simplicity, in our own research, we have opted to execute the transformation for most compounds by using a glovebox. Control experiments showed that yields were within error of measurement if the reaction was carried out using a glovebox or not.

Preparation of starting materials

Ethyl 2-phenoxybenzoate (2c)



2c, 87%

A 10 mL microwave vial equipped with a magnetic stirring bar was charged 2-phenoxybenzoic acid (320 mg, 1.49 mmol, 1.00 equiv.). EtOH (2.5 mL) and concentrated H_2SO_4 (0.40 mL) were then added to the vial. The vial was sealed with a cap and placed in the microwave. The reaction mixture was stirred for 12 minutes at 130 °C under microwave irradiation. After cooling to 23 °C, the pH was adjusted to 7–8 by addition of a saturated aqueous solution of sodium bicarbonate. The solution was then transferred to a separatory funnel, and extracted three times with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (1 × 5 mL), dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **2c** (310 mg, 87%) as a colorless liquid.

R_f = 0.52 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.92 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.47 (ddd, *J* = 8.2, 7.3, 1.8 Hz, 1H), 7.34–7.28 (m, 2H), 7.20 (td, *J* = 7.7, 1.2 Hz, 1H), 7.06 (tt, *J* = 7.3, 1.1 Hz, 1H), 7.02 (dd, *J* = 8.2, 1.2 Hz, 1H), 6.96–6.92 (m, 2H), 4.26 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 165.9, 158.0, 155.8, 133.6, 131.9, 129.8, 124.1, 123.8, 122.9, 121.5, 117.8, 61.2, 14.2.

HRMS-FIA(m/z) calc'd for $C_{15}H_{14}O_3Na^+$ $[M+Na]^+$, 265.0835; found, 265.0837.

N-(Biphenyl-4-sulfonyl)nortropinone (2q)

2q, 66%

A 50 mL round bottom flask was charged with nortropinone hydrochloride (0.808 g, 5.00 mmol, 1.00 equiv.), dichloromethane (25 mL, c = 0.2 M), biphenyl-4-sulfonyl chloride (1.26 g, 5.00 mmol, 1.00 equiv.), triethylamine (2.0 g, 2.8 mL, 20 mmol, 4.0 equiv.) and 4-dimethylamino pyridine (61 mg, 0.50 mmol, 0.10 equiv.). After stirring for 24 hours at 23 ºC, the reaction mixture was diluted with dichloromethane (100 mL) and washed with 0.5 M aqueous HCl (150 mL). The aqueous layer was extracted with dichloromethane (3 × 50 mL), and the combined organic phases were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting residue was purified by column chromatography on silica gel, eluting with dichloromethane/ethyl acetate (90:10 (v/v)) to afford *N*-(biphenyl-4-sulfonyl)nortropinone **2q** (1.12 g, 3.28 mmol, 66%) as a colorless solid.

R_f = 0.40 (ethyl acetate/dichloromethane, 10:90 (v/v)).

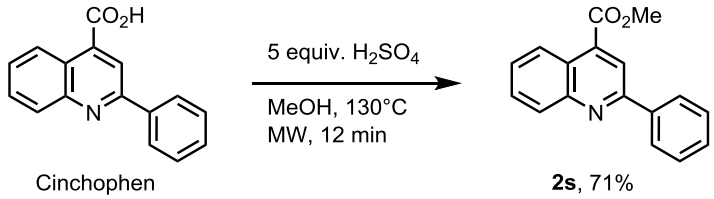
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 °C, δ): 7.97 (m, 2H), 7.73 (m, 2H), 7.61 (m, 2H), 7.48 (m, 2H), 7.43 (m, 1H), 4.55 (m, 2H), 2.82 (dd, *J* = 16.4, 4.5 Hz, 2H), 2.39 (dd, *J* = 17.1, 1.5 Hz, 2H), 1.78 (m, 2H), 1.62 (m, 2H) ppm.

^{13}C NMR (125 MHz, $CDCl_3$, 23 °C, δ): δ 206.9, 146.2, 139.1, 138.4, 129.2, 128.8, 127.943, 127.936, 127.4, 56.2, 50.4, 29.5 ppm.

HRMS-ESI (m/z) calculated for $C_{19}H_{19}SNO_3Na^+$ $[M+Na]^+$, 364.0978; found, 364.0981

.Methyl 2-phenylquinoline-4-carboxylate (2s)



A 20 mL microwave vial equipped with a magnetic stirring bar was charged with Cinchophen (1.99 g, 8.00 mmol, 1.00 equiv.). MeOH (8.3 mL) and concentrated H_2SO_4 (2.0 mL) were then added to the vial. The vial was sealed with a cap and placed in the microwave. The reaction mixture was stirred for 12 minutes at 130 °C under microwave irradiation. After cooling to 23 °C, the pH was adjusted to 7–8 by addition of aqueous solution of sodium hydroxide 1M. The solution was then transferred to a separatory funnel, and extracted three times with EtOAc (1 × 40 mL, 2 × 20 mL). The combined organic layer was washed with brine (1 × 10 mL), dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:9 (v/v) to afford the desired product **2s** (1.50 g, 71%) as a colorless solid.

R_f = 0.43 (EtOAc/pentane 1:9 (v/v)).

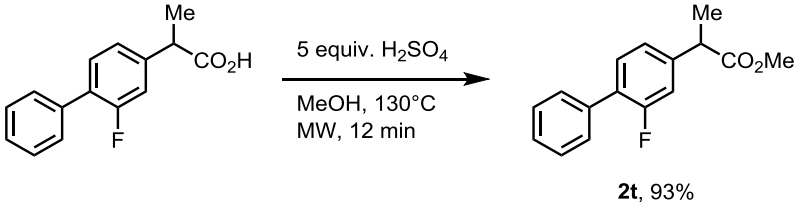
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.75 (dd, *J* = 8.4, 1.3 Hz, 1H), 8.42 (s, 1H), 8.27–8.18 (m, 3H), 7.78 (ddd, *J* = 8.4, 6.9, 1.4 Hz, 1H), 7.64 (ddd, *J* = 8.3, 6.9, 1.3 Hz, 1H), 7.59–7.53 (m, 2H), 7.52–7.47 (m, 1H), 4.08 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 167.0, 156.9, 149.4, 139.0, 135.8, 130.5, 130.1, 129.9, 129.1, 128.0, 127.6, 125.6, 124.1, 120.5, 52.9.

These spectroscopic data correspond to those reported in the literature.[6]

(±)-Flurbiprofen methyl-ester (2t)



A 20 mL microwave vial equipped with a magnetic stirring bar was charged with (±)-Flurbiprofen (1.63 g, 6.67 mmol, 1.00 equiv.). MeOH (7.0 mL) and concentrated H_2SO_4 (1.8 mL) were then added to the vial. The vial was sealed with a cap and placed in the microwave. The reaction mixture was stirred for 12 minutes at 130 °C under microwave irradiation. After cooling to 23 °C, the pH was adjusted to 7–8 by addition of aqueous solution of sodium hydroxide 1M. The solution was then transferred to a separatory funnel, and extracted three times with EtOAc (1 × 40 mL, 2 × 20 mL). The combined organic layer was washed with

brine (1 × 10 mL), dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **2t** (1.68 g, 93%) as a colorless liquid.

R*f* = 0.49 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

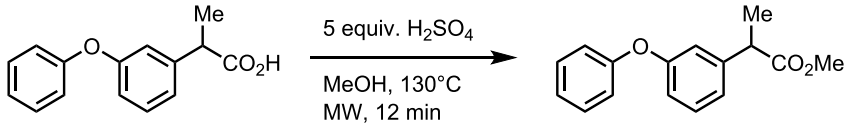
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.56–7.51 (m, 2H), 7.47–7.42 (m, 2H), 7.42–7.32 (m, 2H), 7.19–7.10 (m, 1H), 3.77 (q, *J* = 7.2 Hz, 1H), 3.71 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 174.6, 159.8 (d, *J* = 248 Hz), 141.9 (d, *J* = 7.7 Hz), 135.6, 131.0 (d, *J* = 4.0 Hz), 129.08 (d, *J* = 2.9 Hz), 128.6, 128.0 (d, *J* = 13.6 Hz), 127.8, 123.7 (d, *J* = 3.4 Hz), 115.4 (d, *J* = 24.3 Hz), 52.4, 45.1, 18.6.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –117.6.

These spectroscopic data correspond to those reported in the literature.[7]

(±)-Fenoprofen methyl-ester (2u)



2u, 99%

A 10 mL microwave vial equipped with a magnetic stirring bar was charged with (±)-Fenoprofen (485 mg, 2.00 mmol, 1.00 equiv.). MeOH (2.1 mL) and concentrated H_2SO_4 (0.53 mL) were then added to the vial. The vial was sealed with a cap and placed in the microwave. The reaction mixture was stirred for 12 minutes at 130 °C under microwave irradiation. After cooling to 23 °C, the pH was adjusted to 7–8 by addition of a saturated aqueous solution of sodium bicarbonate. The solution was then transferred to a separatory funnel, and extracted three times with EtOAc (3 × 10 mL). The combined organic layer was washed with brine (1 × 5 mL), dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **2r** (507 mg, 99%) as a colorless liquid.

R*f* = 0.49 (EtOAc/pentane 1:9 (v/v)).

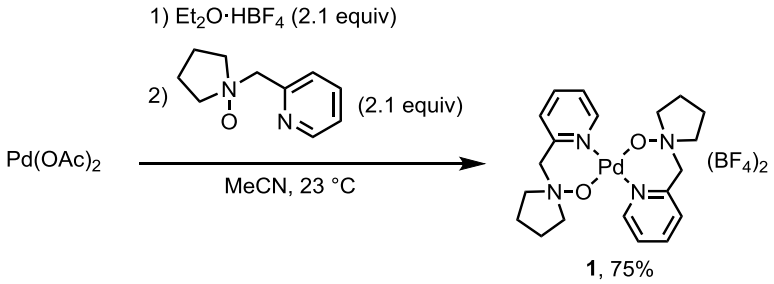
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.38–7.30 (m, 2H), 7.27 (t, *J* = 7.9 Hz, 1H), 7.13–7.08 (m, 1H), 7.06–6.97 (m, 4H), 6.88 (dd, *J* = 8.1, 2.2 Hz, 1H), 3.70 (q, *J* = 7.2 Hz, 1H), 3.67 (s, 3H), 1.49 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 174.8, 157.6, 157.1, 142.6, 130.0, 129.9, 123.5, 122.4, 119.1, 118.3, 117.4, 52.2, 45.4, 18.6.

These spectroscopic data correspond to those reported in the literature.[8]

Procedure for preparation of palladium complex 1[9]



A flame-dried, 250 mL 2-neck flask under nitrogen was charged with $Pd(OAc)_2$ (5.00 g, 22.3 mmol, 1.0 equiv), and the flask was evacuated and refilled with N_2. Through a septum was added dry acetonitrile (50 mL, Aldrich Sure/Seal™), followed by $Et_2O{\cdot}HBF_4$ (6.4 mL, 47 mmol, 2.1 equiv). The resulting suspension was stirred at 23 °C for 30 min, after which 1-(pyridine-2-ylmethyl)pyrrolidine 1-oxide (8.334 g, 46.77 mmol, 2.1 equiv) was added as a solution in dry acetonitrile (40 mL, Aldrich Sure/Seal™). The resulting mixture was stirred for 1 h, after which the reaction mixture was diluted with 100 mL acetonitrile to dissolve the precipitated product, and the resulting solution was filtered through celite, and the filtrate was concentrated by rotary evaporation. The resulting brown solid was triturated with dichloromethane (40 mL) by sonication. The product was collected by filtration on a glass frit, then washed with dichloromethane (40 mL) followed by tetrahydrofuran (40 mL), then allowed to dry on the frit with applied suction to yield 10.61 g of a yellow powder (16.66 mmol, 75%).

NMR Spectroscopy:

^{1}H NMR (600 MHz, DMSO-d_6,, 23 ºC, δ): 8.50 (dd, J = 5.8, 1.2 Hz, 2H), 8.30 (ddd, J = 7.7, 7.7, 1.5 Hz, 2H), 7.86 (ddd, J = 7.5, 5.8, 1.4 Hz, 2H), 7.79 (dd, J = 7.8, 1.2 Hz, 2H), 5.35 (s, 4H), 3.56–3.46 (m, 4H), 3.45–3.36 (m, 4H), 2.26–2.15 (m, 4H), 2.10–1.99 (m, 4H).

^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): 149.2, 148.2, 142.0, 128.2, 126.5, 70.1, 67.2, 21.3.

HRMS-FIA(m/z) calc'd for $C_{20}H_{28}N_4O_2Pd^{2+}$ $[M]^{2+}/2$, 231.0622; found, 231.0632.

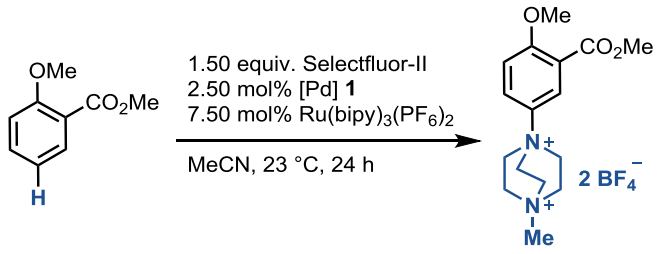
Elemental analysis Calc´d for $C_{20}H_{28}B_2F_8N_4O_2Pd$: C, 37.74; H, 4.43; N, 8.80. Found: C, 37.83; H, 4.14; N, 9.04.

These spectroscopic data correspond to those reported in the literature.[9]

Procedures for C–H TEDAylation of arenes

The isolated Ar–TEDA$^+$ BF_4^- compounds may contain trace PF_6^- anions instead of the BF_4^- anions, as observed by a doublet in the ^{19}F NMR at –72.3 ppm with a coupling constant of J = 707 Hz. The counterion has no dramatic effect on the reaction; we have made no attempt to obtain material free of PF_6^-, and for stoichiometry calculations have assumed the BF_4 to be the sole counteranion.

Methyl 5-TEDA-2-methoxybenzoate (3a)



3a, 89%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 mg, 1.50 mmol, 1.50 equiv), and methyl-2-methoxybenzoate (166 mg, 107 µL, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried undervacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 414 mg of the desired product **3a** as a colorless solid (89%).

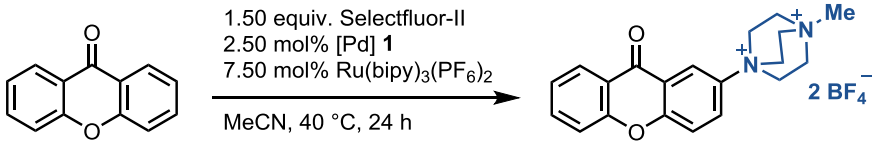
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.36 (d, *J* = 3.5 Hz, 1H), 8.28 (dd, *J* = 9.5, 3.5 Hz, 1H), 7.51 (d, *J* = 9.5 Hz, 1H), 4.94–4.85 (m, 6H), 4.58–4.48 (m, 6H), 4.01 (s, 3H), 3.87 (s, 3H), 3.75 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): 164.9, 158.9, 136.3, 126.0, 123.4, 121.0, 114.2, 56.8, 54.2, 52.8, 52.6, 51.5.

HRMS-ESI (m/z) calc'd for $C_{16}H_{24}N_2O_3BF_4^+$ $[M\text{-}BF_4]^+$, 379.1811; found, 379.1813.

2-TEDA-xanthone (3b)



Xanthone

3b, 79%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and Xanthone (192 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (10 mL, c = 0.10 M) was added via syringe to the

mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 40 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 392 mg of the desired product **3b** as a beige solid (79%).

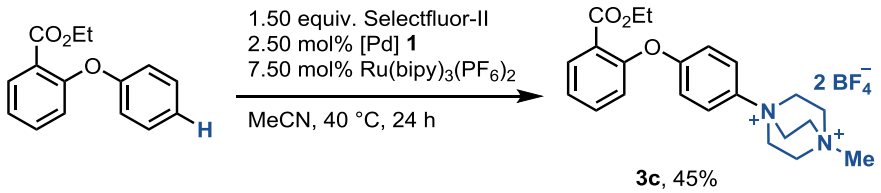
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.84 (d, *J* = 3.4 Hz, 1H), 8.63 (dd, *J* = 9.5, 3.4 Hz, 1H), 8.29 (dd, *J* = 7.9, 1.7 Hz, 1H), 8.04 (d, *J* = 9.5 Hz, 1H), 7.97 (ddd, *J* = 8.7, 7.2, 1.7 Hz, 1H), 7.71 (d, *J* = 8.7 Hz, 1H), 7.60–7.56 (m, 1H), 5.08–5.02 (m, 6H), 4.66–4.60 (m, 6H), 3.80 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): 175.4, 155.7, 155.6, 140.1, 136.6, 127.7, 126.2, 125.3, 121.5, 121.2, 120.8, 119.5, 118.5, 54.3, 52.9, 51.6.

HRMS-ESI (m/z) calc'd for $C_{20}H_{22}N_2O_2BF_4^+$ $[M\text{-}BF_4]^+$, 409.1705; found, 409.1706.

Ethyl 2-(4-TEDAphenoxy)benzoate (3c)



3c, 45%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and ethyl 2-phenoxybenzoate (242 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 40 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 245 mg of the desired product **3c** as a colorless solid (45%).

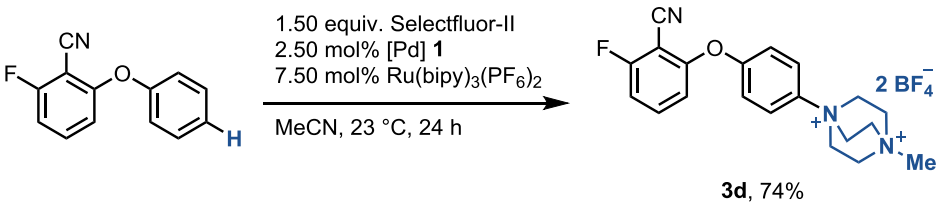
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.10–8.05 (m, 2H), 8.00 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.72 (ddd, *J* = 8.1, 7.4, 1.8 Hz, 1H), 7.45 (td, *J* = 7.6, 1.1 Hz, 1H), 7.26 (dd, *J* = 8.1, 1.1 Hz, 1H), 7.19–7.13 (m, 2H), 4.85–4.79 (m, 6H), 4.52–4.45 (m, 6H), 4.16 (q, *J* = 7.1 Hz, 2H), 3.72 (s, 3H), 1.12 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, CD_3CN, 23 ºC, δ): 176.2, 165.6, 161.5, 154.1, 135.4, 133.0, 127.0, 125.6, 124.1, 123.0, 118.7, 62.0, 55.6, 54.3, 53.6, 14.2.

HRMS-ESI (m/z) calc'd for $C_{22}H_{28}N_2O_3BF_4^+$ $[M\text{-}BF_4]^+$, 455.2124; found, 455.2119.

2-(4-TEDAphenoxy)-6-fluorobenzonitrile (3d)



3d, 74%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 2-Fluoro-6-phenoxybenzonitrile (213 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and transferred to an Erlenmeyer flask. Dichloromethane (25 mL) was added, followed by pentane (50 mL), and the mixture was stirred for 5 min at room temperature. The solids were collected by filtration on a glass frit, washed two times with pentane (2 × 2 mL), then two times with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 379 mg of the desired product **3d** as an orange solid (74%).

NMR Spectroscopy:

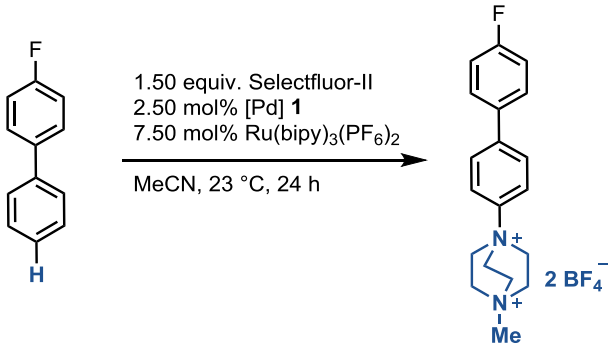
^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.30–8.21 (m, 2H), 7.80 (td, *J* = 8.5, 6.6 Hz, 1H), 7.60–7.52 (m, 2H), 7.29 (td, *J* = 8.7, 0.9 Hz, 1H), 7.03 (dd, *J* = 8.5, 0.9 Hz, 1H), 4.93–4.87 (m, 6H), 4.58–4.50 (m, 4H), 3.76 (s, 3H).

^{13}C NMR (125 MHz, Acetone-d_6, 23 ºC, δ): 164.8 (d, *J* = 257.5 Hz), 159.5 (m), 158.2, 137.3 (d, *J* = 10.5 Hz), 124.2, 121.8, 115.8 (m), 112.7 (d, *J* = 19.7 Hz), 111.3, 56.1, 54.6, 53.4.

^{19}F NMR (470 MHz, Acetone-d_6, 23 ºC, δ): –107.1, –150.7.

HRMS-ESI (m/z) calc'd for $C_{20}H_{22}N_3OBF_5^+$ $[M\text{-}BF_4]^+$, 426.1770; found, 426.1776.

4-TEDA-4'-fluoro-[1,1'-biphenyl] (3e)



3e, 93%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 4-fluoro-1,1'-biphenyl (172 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 439 mg of the desired product **3e** as a colorless solid (93%).

NMR Spectroscopy:

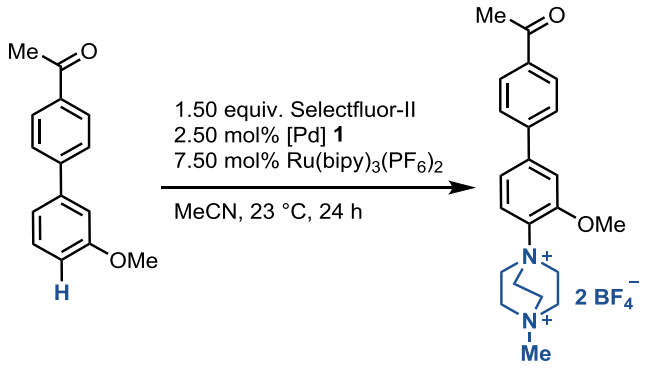
^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.28–8.17 (m, 2H), 8.09–8.01 (m, 2H), 7.90–7.77 (m, 2H), 7.38–7.26 (m, 2H), 5.00–4.87 (m, 6H), 4.63–4.48 (m, 6H), 3.76 (s, 3H).

^{13}C NMR (125 MHz, Acetone-d_6, 23 ºC, δ): 164.1 (d, *J* = 246.5 Hz), 144.47, 143.72, 135.4 (d, *J* = 3.3 Hz), 130.2 (d, *J* = 8.4 Hz), 129.9, 122.13, 116.9 (d, *J* = 21.9 Hz), 55.9, 54.7, 53.4.

^{19}F NMR (470 MHz, CD_3CN, 23 ºC, δ): –115.1, –151.4.

HRMS-ESI (m/z) calc'd for $C_{19}H_{23}N_2BF_5^+$ $[M\text{-}BF_4]^+$, 385.1869; found, 385.1866.

1-(3'-Methoxy-4´-TEDAbiphenyl-4-yl)ethanone (3f)



3f, 67%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 1-(3'-methoxy[1,1'-biphenyl]-4-yl)ethan-1-one (226 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting pure Ar-TEDA was dried undervacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 354 mg of the desired product **3f** as a beige solid (67%).

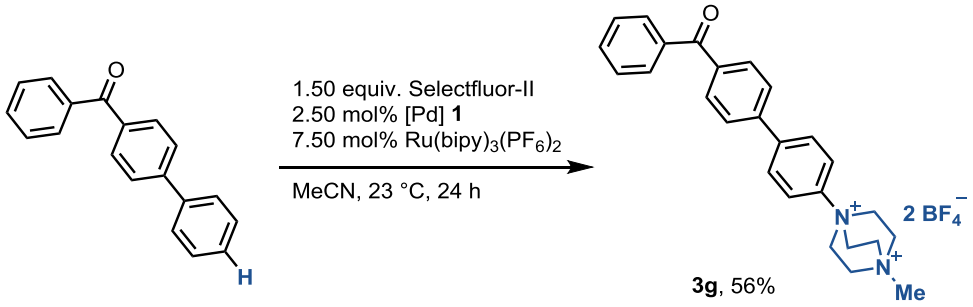
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.16–8.09 (m, 2H), 8.04 (d, *J* = 8.9 Hz, 1H), 7.97–7.90 (m, 2H), 7.82 (d, *J* = 2.1 Hz, 1H), 7.62 (dd, *J* = 8.8, 2.1 Hz, 1H), 5.09–4.95 (m, 6H), 4.60–4.47 (m, 6H), 4.31 (s, 3H), 3.70 (s, 3H).

^{13}C NMR (125 MHz, CD_3CN, 23 ºC, δ): 198.5, 153.2, 145.7, 143.2, 138.3, 129.9, 128.6, 123.2, 123.0, 121.2, 115.00, 57.9, 54.31, 53.8, 27.1.

HRMS-ESI (m/z) calc'd for $C_{22}H_{28}N_2O_2BF_4^+$ $[M\text{-}BF_4]^+$, 439.2174; found, 439.2171.

(4'-TEDA-[1,1'-biphenyl]-4-yl)(phenyl)methanone (3g)



To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 4-benzoylbiphenyl (258 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 310 mg of the desired product **3g** as a colorless solid (56%).

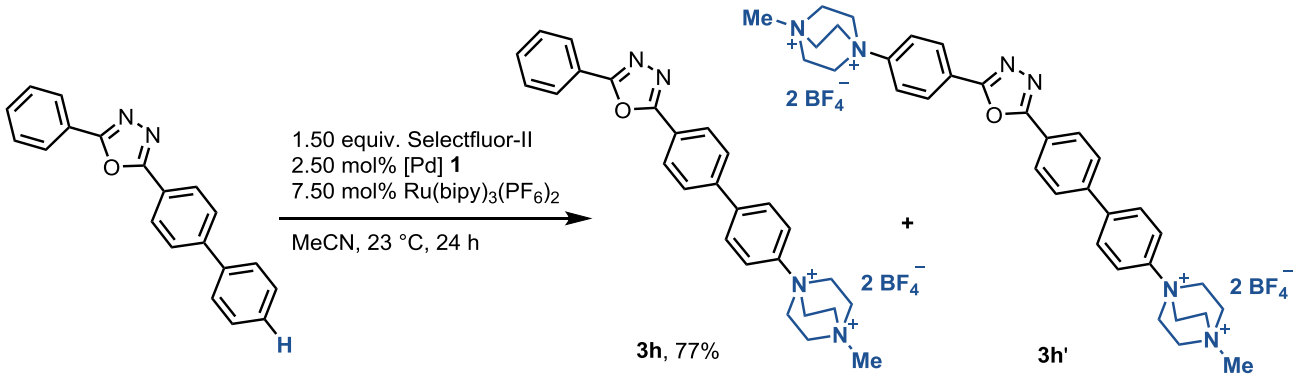
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.31–8.26 (m, 2H), 8.19–8.15 (m, 2H), 7.99–7.96 (m, 2H), 7.95–7.91 (m, 2H), 7.84–7.81 (m, 2H), 7.72–7.68 (m, 1H), 7.63–7.57 (m, 2H), 5.00–4.91 (m, 6H), 4.63–4.45 (m, 6H), 3.78 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): 195.3, 144.2, 141.5, 141.3, 136.9, 136.9, 132.9, 130.5, 129.6, 128.8, 128.7, 127.3, 121.7, 54.1, 52.8, 51.6.

HRMS-ESI (m/z) calc'd for $C_{26}H_{28}N_2OBF_4^+$ $[M\text{-}BF_4]^+$, 471.2225; found, 471.2222.

2-(4'-TEDA-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (3h)



To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 2-(4-biphenylyl)-5-phenyl-1,3,4-oxadiazole (298 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 469 mg of the desired product **3h** as a colorless solid (77%).[a]

[a]: The compound **3h** is isolated as a mixture with the bis-functionnalized arene **3h'**. The ratio **3h**/**3h'** calculated by ^{1}H-NMR is 85:15.

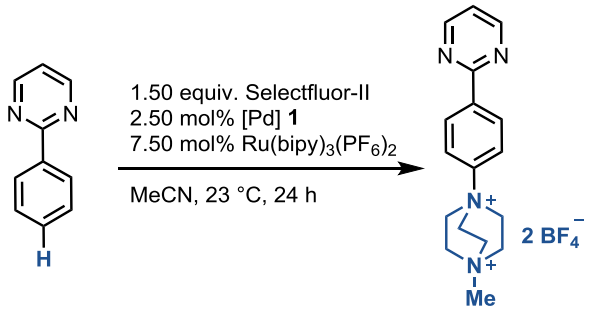
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.34–8.32 (m, 2H), 8.31–8.27 (m, 2H), 8.25–8.17 (m, 4H), 8.07–8.03 (m, 2H), 7.71–7.63 (m, 3H), 5.01–4.92 (m, 6H), 4.63–4.55 (m, 6H), 3.79 (s, 3H).

^{13}C NMR (125 MHz, Acetone-d_6, 23 ºC, δ): 164.8, 164.3, 144.8, 142.2, 141.5, 132.4, 129.7, 129.3, 128.5, 128.5, 127.9, 127.1, 124.2, 122.2, 55.0, 53.7, 52.3.

HRMS-ESI (m/z) calc'd for $C_{27}H_{28}N_4OBF_4^+$ $[M\text{-}BF_4]^+$, 511.2287; found, 511.2286.

2-(4-TEDAphenyl)pyrimidine (3i)



3i, 65%

To a 4 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (8.4 mg, 13 µmol, 2.5 mol%), $Ru(bipy)_3(PF_6)_2$ (34.1 mg, 39.7 µmol, 7.50 mol%), Selectfluor II (254 g, 794 µmol, 1.50 equiv), and 2-phenylpyrimidine (82.7 mg, 529 µmol, 1.00 equiv). Acetonitrile (2.6 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The solvent was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.2 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and MeOH (5 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting solid was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 155 mg of the desired product **3i** as a colorless solid (65%).

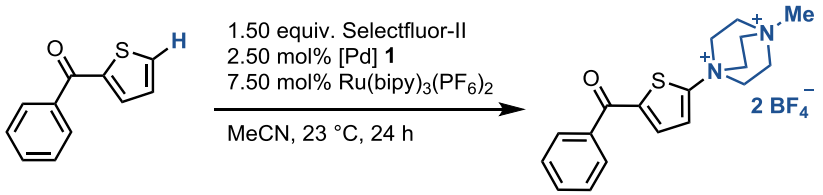
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.96 (d, J = 4.9 Hz, 2H), 8.81–8.70 (m, 2H), 8.37–8.20 (m, 2H), 7.52 (t, J = 4.9 Hz, 1H), 4.98–4.88 (m 6H), 4.62–4.50 (m, 6H), 3.77 (s, 3H).

^{13}C NMR (125 MHz, Acetone-d_6, 23 ºC, δ): 162.9, 158.9, 141.6, 136.7, 131.1, 122.1, 121.8, 56.1, 54.8, 53.5.

HRMS-ESI (m/z) calc'd for $C_{17}H_{22}N_4BF_4^+$ $[M\text{-}BF_4]^+$, 369.1868; found, 369.1870.

(5-TEDAthiophen-2-yl)(phenyl)methanone (3j)



3j, 42%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol,

2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 2-benzoylthiophene (231 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (5 mL) and EtOAc (10 mL) were added to the vial. The precipitate was collected by filtration on a glass frit, washed with EtOAc (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 204 mg of the desired product **3j** as a beige solid (42%).

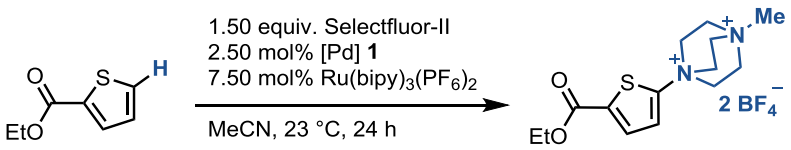
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.00 (d, *J* = 4.4 Hz, 1H), 7.96–7.91 (m, 2H), 7.86 (d, *J* = 4.4 Hz, 1H), 7.78–7.71 (m, 1H), 7.68–7.54 (m, 2H), 5.08–4.97 (m, 6H), 4.61–4.52 (m, 6H), 3.77 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): 186.9, 151.9, 142.2, 135.7, 134.2, 133.6, 129.2, 129.0, 125.0, 56.7, 52.7, 51.7.

HRMS-ESI (m/z) calc'd for $C_{18}H_{22}N_2OSBF_4^+$ $[M\text{-}BF_4]^+$, 401.1476; found, 401.1474.

Ethyl 5-TEDAthiophene-2-carboxylate (3k)



3k, 47%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and ethyl 2-thiophenecarboxylate (156 mg, 135 µL, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (5 mL) and EtOAc (10 mL) were added to the vial. The precipitate was collected by filtration on a glass frit, washed with EtOAc (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting pure Ar-TEDA was dried undervacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 215 mg of the desired product **3k** as a beige solid (47%).

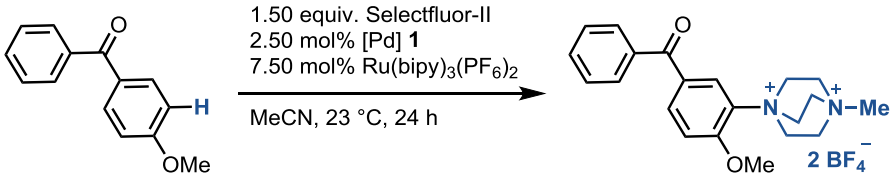
NMR Spectroscopy:

^{1}H NMR (500 MHz, DMSO-d_6, 23 ºC, δ): 7.91 (d, J = 4.1 Hz, 1H), 7.84 (d, J = 4.4 Hz, 1H), 4.65–4.49 (m, 6H), 4.36 (q, J = 7.1 Hz, 2H), 4.12–3.98 (m, 6H), 3.38 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): δ 160.2, 150.2, 132.7, 132.6, 124.8, 62.2, 56.7, 52.7, 51.7, 14.1.

HRMS-ESI (m/z) calc'd for $C_{14}H_{22}N_2O_2S^{2+}$ $[M]^{2+}$/2, 141.0695; found, 141.0696.

(3-TEDA-4-methoxyphenyl)(phenyl)methanone (3l)



3l, 57%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 4-methoxybenzophenone (212 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 294 mg of the desired product **3l** as a beige solid (57%).

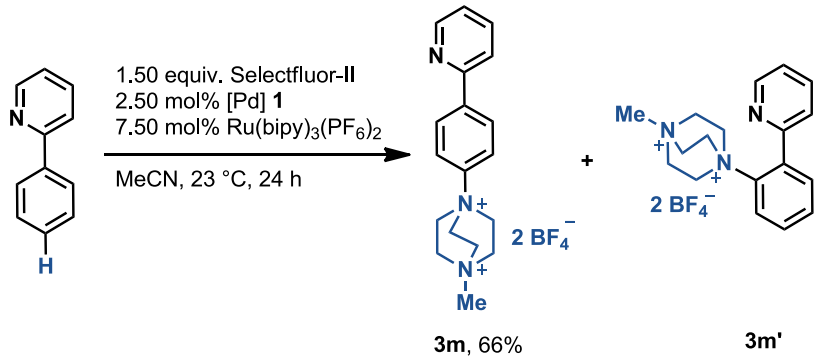
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6), 23 ºC, δ 8.30 (d, J = 1.9 Hz, 1H), 8.12 (dd, J = 8.7, 1.9 Hz, 1H), 7.84–7.79 (m, 2H), 7.72–7.68 (m, 2H), 7.62–7.55 (m, 2H), 5.10–5.02 (m, 6H), 4.58–4.50 (m, 6H), 4.30 (s, 3H), 3.69 (s, 3H).

^{13}C NMR (125 MHz, CD_3CN, 23 ºC, δ): 194.3, 156.0, 137.6, 136.1, 133.9, 131.8, 130.9, 130.9, 130.7, 129.7, 124.6, 116.2, 58.3, 54.3, 54.2, 54.2, 53.8.

HRMS-ESI (m/z) calc'd for $C_{21}H_{26}N_2O_2BF_4^+$ $[M\text{-}BF_4]^+$, 425.2018; found, 425.2019.

2-(4-TEDAphenyl)pyridine (3m)



To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 2-phenylpyridine (155 mg, 143 µL, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 302 mg of the desired product **3m** as a brown solid (66%)[a].

[a]: The compound **3m** is isolated in mixture with the isomer **3m'**. The ratio 3m/3m' calculated by ^{1}H-NMR is 95:5.

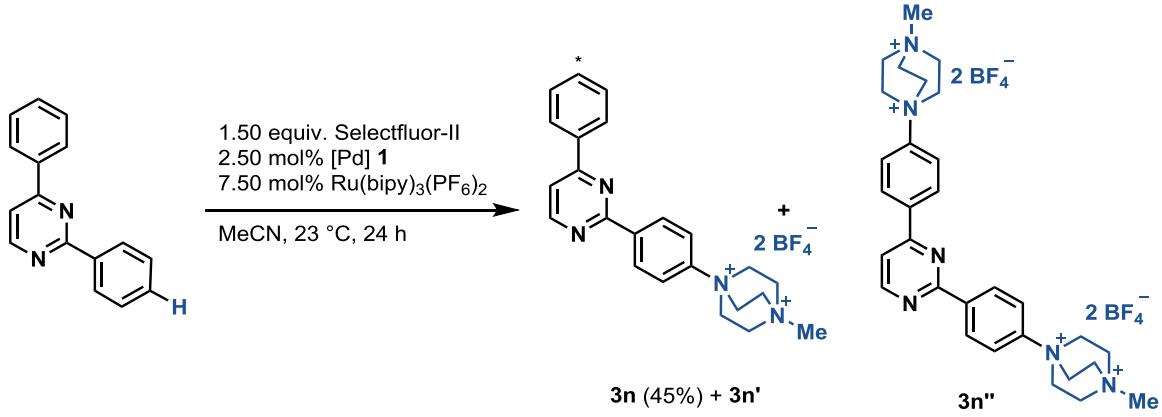
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.74 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H), 8.53–8.43 (m, 2H), 8.29–8.21 (m, 2H), 8.10 (dt, *J* = 8.0, 1.0 Hz, 1H), 8.00–7.91 (m, 1H), 7.44 (ddd, *J* = 7.6, 4.8, 1.1 Hz, 1H), 4.97–4.87 (m, 6H), 4.61–4.52 (m, 6H), 3.77 (s, 3H).

^{13}C NMR (125 MHz, DMSO-d_6, 23 ºC, δ): 154.1, 150.4, 145.1, 141.4, 138.1, 128.7, 124.3, 121.9, 121.52, 54.5, 53.3, 52.1.

HRMS-ESI (m/z) calc'd for $C_{18}H_{23}N_3BF_4^+$ $[M\text{-}BF_4]^+$, 368.1916; found, 368.1912.

2-(4-TEDAphenyl)-4-phenylpyrimidine (3n)



To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 2,4-diphenylpyrimidine (232 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 320 mg of a mixture of isomers as a colorless solid (60%) that contains the major isomer **3n** (45%).[a,a]: the compound **3n** contains about 14 % of the mono-functionnalized 2,4-phenylpyrimidine **3n'** (other isomer) and 11 % of the compound **3n''** (percentages estimated by ^{1}H-NMR). These compounds were not purged before the methylation step.

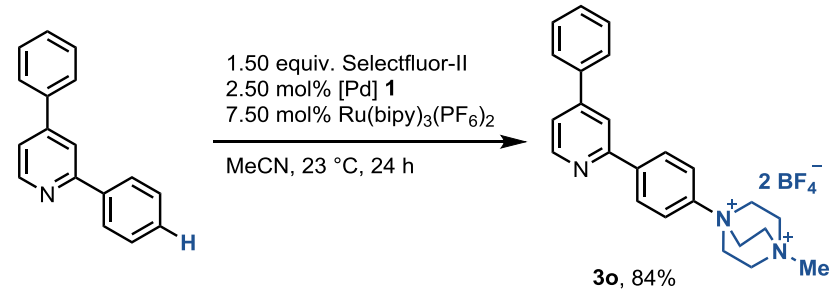
NMR Spectroscopy:

1H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 9.01 (d, *J* = 5.3 Hz, 1H), 8.94–8.88 (m, 2H), 8.40–8.36 (m, 2H), 8.34–8.31 (m, 2H), 8.05 (d, *J* = 5.3 Hz, 1H), 7.63–7.59 (m, 3H), 5.02–4.92 (m, 6H), 4.64–4.53 (m, 6H), 3.78 (s, 3H).

^{13}C NMR (CD_3CN , 23 ºC, δ): 164.7, 162.4, 159.2, 141.7, 136.9, 133.9, 132.0, 131.0, 129.7, 127.8, 121.3, 116.6, 55.2, 54.0, 53.3.

HRMS-ESI (m/z) calc'd for $C_{23}H_{26}N_4^{2+}$ $[M]^{2+}/2$, 179.1073; found, 179.1074.

2-(4-TEDAphenyl)-4-phenylpyridine (3o)



To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and 2,4-diphenylpyridine (231 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 448 mg of the desired product **3o** as a colorless solid (84%).

NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.80 (br d, *J* = 5.1 Hz, 1H), 8.65–8.59 (m, 2H), 8.39–8.37 (m, 1H), 8.30–8.24 (m, 2H), 7.94–7.88 (m, 2H), 7.75 (dd, *J* = 5.1, 1.7 Hz, 1H), 7.62–7.49 (m, 3H), 5.03–4.92 (m, 6H), 4.65–4.55 (m, 6H), 3.79 (s, 3H).

^{13}C NMR (125 MHz, Acetone-d_6, 23 ºC, δ): 155.7, 151.5, 150.4, 145.7, 143.1, 138.8, 130.3, 130.2, 130.1, 128.1, 122.3, 122.0, 119.6, 56.0, 54.8, 53.5.

HRMS-ESI (m/z) calc'd for $C_{24}H_{27}N_3^{2+}$ $[M]^{2+}/2$, 178.6097; found, 178.6098.

N-ethyl-4-nitro-N-(4-TEDAphenyl)benzenesulfonamide (3p)

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and *N*-ethyl-4-nitro-N-phenylbenzenesulfonamide (306 mg, 1.00 mmol, 1.00 equiv.). Acetonitrile (10 mL, c = 0.10 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 40 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 479 mg of the desired product **3p** as a colorless solid (79%).

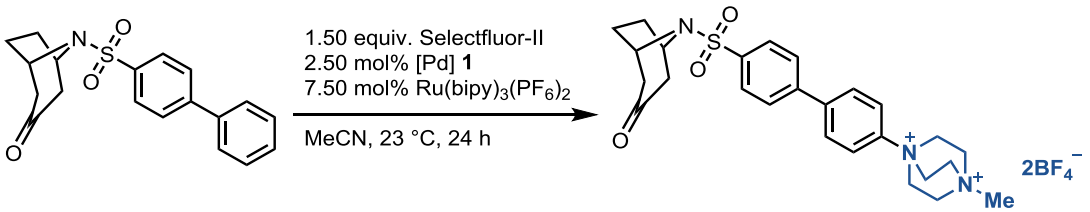
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetonitrile-d_3, 23 ºC, δ): 8.44-8.19 (m, 2H), 7.88-7.65(m, 4H), 7.57-7.36 (m, 2H), 4.35-4.30 (m, 6H), 4.06-4.01 (m, 6H) 3.68 (q, *J* = 7.1 Hz, 2H), 3.37 (s, 3H), 1.06 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, Acetonitrile-d_3, 23 ºC, δ): 151.2, 143.5, 143.3, 141.8, 131.3, 129.5, 125.1, 122.1, 55.2, 53.9, 53.3, 46.2, 13.7.

HRMS-ESI (m/z) calc'd for $C_{21}H_{28}N_4O_4S^+$ $[M\text{-}BF_4]^+$, 432.1820; found, 432.1821.

N-(4-TEDAphenyl-4-sulfonyl)nortropinone (3q)



3q, 81%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 mg, 1.50 mmol, 1.50 equiv), and *N*-(Biphenyl-4-sulfonyl)nortropinone (341 mg, 1.00 mmol, 1.00 equiv.). Acetonitrile (10.0 mL, c = 0.10 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a

glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried undervacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 519 mg of the desired product **3q** as a colorless solid (81%).

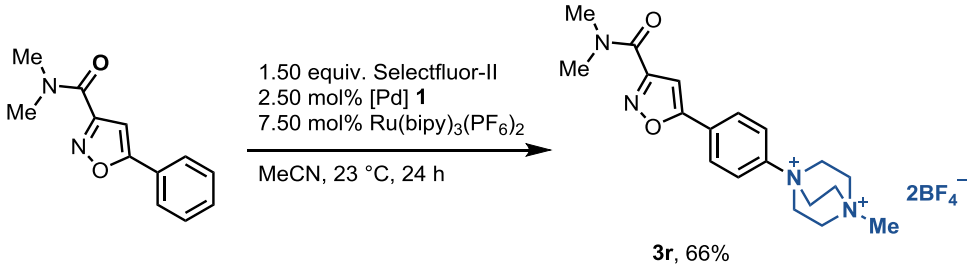
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetonitrile-d_3, 23 ºC, δ): 8.13-7.99 (m, 4H), 7.97-7.86 (m, 4H), 4.60-4.48 (m, 2H), 4.38 (t, *J* = 7.4 Hz, 6H), 4.06 (t, *J* = 7.4 Hz, 6H), 3.40 (s, 3H), 2.77 (dd, *J* = 16.6, 4.6 Hz, 2H), 2.44-2.28 (m, 2H), 1.44-1.15 (m, 2H), 0.91 (dd, *J* = 6.6, 2.5 Hz, 3H).

^{13}C NMR (125 MHz, Acetonitrile-d_3, 23 ºC, δ): 207.0, 144.2, 143.0, 142.8, 140.6, 130.1, 128.9, 128.6, 121.7, 56.9, 55.2, 54.0, 53.3, 50.5, 29.4.

HRMS-ESI (m/z) calc'd for $C_{26}H_{23}N_3O_3S^+$ $[M\text{-}BF_4]^+$, 467.2231; found, 467.2232.

N,*N*-dimethyl-5-(4-TEDAphenyl)isoxazole-3-carboxamide (3r)



3r, 66%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 mg, 1.50 mmol, 1.50 equiv), and *N*,*N*-dimethyl-5-phenylisoxazole-3-carboxamide (216 mg, 1.00 mmol, 1.00 equiv.). Acetonitrile (10.0 mL, c = 0.10 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried undervacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 341 mg of the desired product **3r** as a colorless solid (66%).

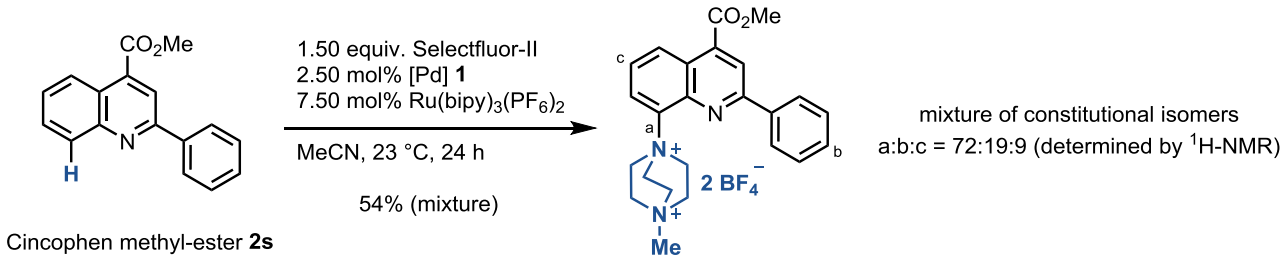
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetonitrile-d_3, 23 ºC, δ): 8.29-8.08 (m, 2H), 8.03-7.78 (m, 2H), 7.09 (s, 1H), 4.38-4.33 (m, 6H), 4.07-4.01 (m, 6H), 3.37 (s, 3H), 3.17 (s, 3H), 3.08 (s, 3H).

^{13}C NMR (125 MHz, Acetonitrile-d_3, 23 ºC, δ): 206.8, 146.0, 138.8, 136.1, 129.8, 127.8, 127.5, 127.1, 56.1, 50.3, 29.4, 21.2, 14.2.

HRMS-ESI (m/z) calc'd for $C_{19}H_{26}N_4O_2^+$ $[M\text{-}BF_4]^+$, 342.2045; found, 342.2045.

Methyl 8-TEDA-2-phenylquinoline-4-carboxylate (3s)



Cincophen methyl-ester **2s**

3s, 40%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and Cincophen methyl-ester (263 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). A second purification was performed to eliminate the remaining impurities (see S10, note 1). The resulting Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 309 mg of a mixture of constitutional isomers as a yellow solid (54%) that contains the major isomer **3s** (40% yield).

Major isomer (**3s**):

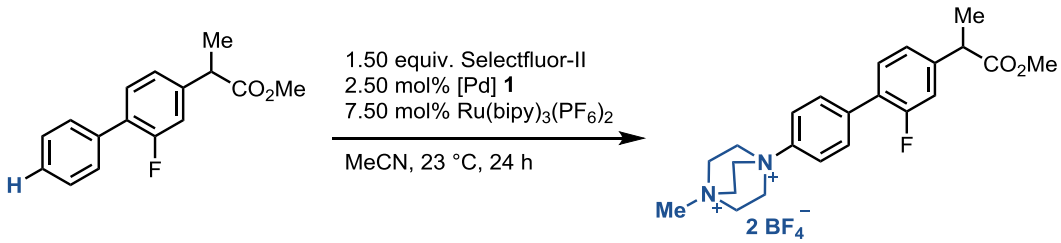
NMR Spectroscopy:

^{1}H NMR (400 MHz, DMSO-d_6, 23 ºC, δ): 8.79 (d, *J* = 8.5 Hz, 1H), 8.71 (s, 1H), 8.39 (d, *J* = 8.2 Hz, 1H), 8.34–8.26 (m, 2H), 7.98 (t, *J* = 8.3 Hz, 1H), 7.72–7.65 (m, 3H), 5.04–4.94 (m, 6H), 4.27–4.18 (m, 6H), 4.06 (s, 3H), 3.43 (s, 4H).

^{13}C NMR (101 MHz, acetone-d_6, 23 ºC, δ) 167.1, 154.5, 149.9, 146.2, 142.2, 137.9, 131.4, 131.2, 130.5, 129.5, 126.4, 125.1, 122.2, 120.4, 56.0, 54.7, 53.4, 53.3.

HRMS-ESI (m/z) calc'd for $C_{24}H_{27}N_3O_2BF_4^+$ $[M\text{-}BF_4]^+$, 476.2127; found, 476.2130.

(±)-Methyl 2-(4'-TEDA-2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (3t)



(±)-Flurbiprofen methyl-ester **2t** **3t**, 75%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and (±)-Flurbiprofen methyl-ester (258 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and transferred to an Erlenmeyer flask. Dichloromethane (30mL) was added, followed by pentane (60 mL), and the mixture was stirred for 5 min at room temperature. The solids were collected by filtration on a glass frit, washed two times with pentane (2 × 2 mL), then two times with diethyl ether (2 × 2 mL). Recrystallizations in methanol afforded the pure Ar-TEDA,[a] subsequently dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 300 mg of the desired product **3t** as a colorless solid (75%).

[a] The recrystallization was performed to purge the remaining $TEDA^{2+}$ and $TEDA\text{-}H^{+}$ side-products (see Figure S1). No other isomer was eliminated during this process, as the reaction is >98% selective to the para-position of the arene (amination monitored by ^{1}H-NMR).

NMR Spectroscopy:

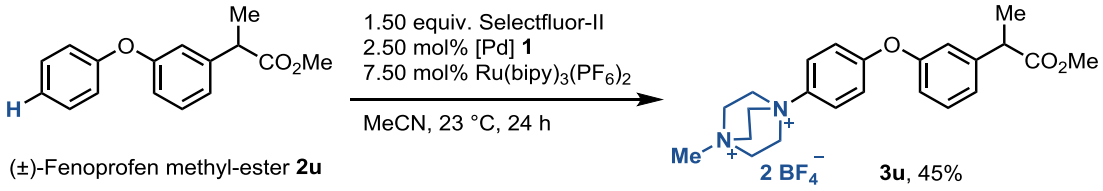
^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.27–8.21 (m, 2H), 8.01–7.91 (m, 2H), 7.59 (t, *J* = 8.1 Hz, 1H), 7.35–7.24 (m, 2H), 5.01–4.88 (m, 6H), 4.63–4.50 (m, 6H), 3.91 (q, *J* = 7.2 Hz, 1H), 3.76 (s, 3H), 3.67 (s, 3H), 1.50 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, CD_3CN, 23 ºC, δ): 175.0, 160.4 (d, *J* = 247.7 Hz), 145.4 (d, *J* = 8.0 Hz), 143.9, 139.7, 132.2 (d, *J* = 3.4 Hz), 131.8 (d, *J* = 3.3 Hz), 125.6 (d, *J* = 13.3 Hz), 125.3 (d, *J* = 3.3 Hz), 121.49, 116.3 (d, *J* = 23.5 Hz), 55.50, 54.32, 53.61, 52.69, 45.46, 18.70.

^{19}F NMR (470 MHz, CD_3CN,, 23 ºC, δ): –119.3, –151.4.

HRMS-ESI (m/z) calc'd for $C_{23}H_{29}N_4O_2F^{2+}$ $[M]^{2+}/2$, 192.1101; found, 192.1101.

(±)-Methyl 2-(3-(4-TEDAphenoxy)phenyl)propanoate (3u)



(±)-Fenoprofen methyl-ester **2u** **3u**, 45%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and (±)-Fenoprofen methyl-ester (256 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and transferred to an Erlenmeyer flask. Dichloromethane (50 mL) was added, followed by pentane (100 mL), and the mixture was stirred for 5 min at room temperature. The solids were collected by filtration on a glass frit, washed two times with pentane (2 × 2 mL), then two times with diethyl ether (2 × 2 mL). Recrystallizations in methanol afforded the pure Ar-TEDA,[a] subsequently dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 251 mg of the desired product **3u** as a colorless solid (45%).

[a] The recrystallization was performed to purge the remaining $TEDA^{2+}$ and $TEDA\text{-}H^{+}$ side-products (see Figure S1). No other isomer was eliminated during this process, as the reaction is >98% selective to the para-position of the arene (amination monitored by ^{1}H-NMR).

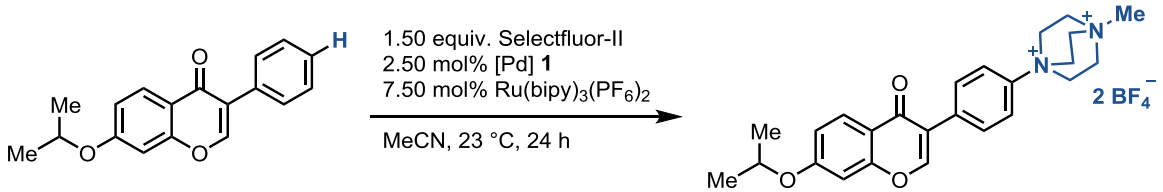
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.17–8.07 (m, 2H), 7.44 (t, *J* = 8.0 Hz, 1H), 7.31–7.25 (m, 2H), 7.24–7.20 (m, 1H), 7.11 (t, *J* = 2.3 Hz, 1H), 7.02 (dd, *J* = 8.0, 2.3 Hz, 1H), 5.93–4.79 (m, 6H), 4.58–4.44 (m, 6H), 3.83 (q, *J* = 7.2 Hz, 1H), 3.74 (s, 3H), 3.63 (s, 3H), 1.45 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, CD_3CN, 23 ºC, δ): 175.2, 160.6, 156.2, 144.7, 131.5, 125.3, 123.2, 120.1, 120.1, 119.5, 55.6, 54.3, 53.6, 52.6, 45.7, 18.8.

HRMS-ESI (m/z) calc'd for $C_{23}H_{30}N_4O_3^{2+}$ $[M]^{2+}/2$, 191.1123; found, 191.1123.

3-(4-TEDAphenyl)-7-isopropoxy-4H-chromen-4-one (3v)



Ipriflavone **3v**, 42%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv),

and Ipriflavone (280 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (5.0 mL, c = 0.20 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 23 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and transferred to an Erlenmeyer flask. Dichloromethane (25 mL) was added, followed by pentane (50 mL), and the mixture was stirred for 5 min at room temperature. The solids were collected by filtration on a glass frit, washed two times with pentane (2 × 2 mL), then two times with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL). The resulting pure Ar-TEDA was dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 244 mg of the desired product **3v** as a colorless solid (42%).

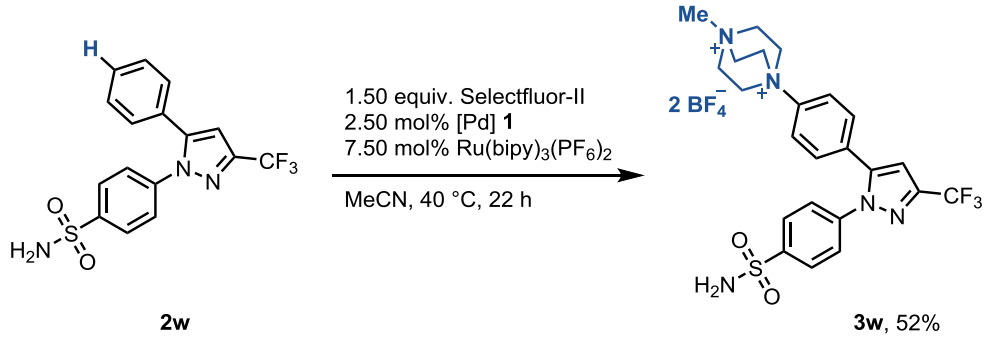
NMR Spectroscopy:

^{1}H NMR (500 MHz, Acetone-d_6, 23 ºC, δ): 8.50 (s, 1H), 8.21–8.15 (m, 2H), 8.14–8.09 (m, 1H), 8.06–8.01 (m, 2H), 7.13–7.04 (m, 2H), 4.91 (m, 6H), 4.94–4.87 (d, *J* = 6.0 Hz, 1H), 4.58–4.51 (m, 6H), 3.76 (s, 3H), 2.82 (s, 3H), 1.39 (d, *J* = 6.0 Hz, 6H).

^{13}C NMR (125 MHz, Acetone-d_6, 23 ºC, δ): 175.1, 163.9, 159.0, 155.7, 144.7, 137.0, 132.1, 128.3, 123.2, 121.4, 118.8, 116.9, 102.8, 71.8, 56.1, 54.8, 53.5, 22.1.

HRMS-ESI (m/z) calc'd for $C_{25}H_{30}N_2O_3BF_4^+$ $[M\text{-}BF_4]^+$, 493.2280; found, 493.2283.

4-(5-(4-TEDAphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (3w)



2w **3w**, 52%

To a 50 mL-round bottomed flask equipped with a magnetic stirring bar were added palladium complex **1** (43.3 mg, 68.1 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (176 mg, 204 µmol, 7.50 mol%), Selectfluor II (1.31 g, 4.08 mmol, 1.5 equiv), and **2t** (1.00 g, 2.72 mmol, 1.00 equiv). Acetonitrile (11 mL, [**2t**] = 0.25 M) was added via syringe to the mixture, the flask was capped with a rubber septum and the reaction mixture was stirred at 40 °C for 22 h. Et_3N (excess, V = 0.8 mL) was added dropwise to the flask at room temperature. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (70 mL) was added to the flask. After being stirred for 5 min, the precipitate was collected by filtration on a glass frit. The residue remaining in the reaction flask was dissolved in acetonitrile (10 mL), dichloromethane (50 mL) was then added to the flask, and the resulting precipitate was collected by filtration on the glass frit. The solids were washed with

dichloromethane (2 × 15 mL), affording a resin containing the Ar-TEDA, TEDA-H^{2+} and $TEDA^{+}$ (see figure S1). A purification by prep-HPLC (YMC-Pack Triart C18 (30x150 mm: 5 µm), MeOH/H_2O = 40:60 (v/v), injection volume V_{inj} = 400 µL (m = 40 mg), flow rate = 30.0 mL/min, 35 °C, retention time; 3.3 min) afforded a solid, which was subsequently stirred in Et_2O for 30 min, filtered on a glass frit and dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 954 mg of the desired product **3w** as an orange solid (52%). The resonance of the $–CF_3$ substituent could not be clearly identified in the ^{13}C NMR, but the corresponding ^{19}F NMR resonance was identified.

NMR Spectroscopy:

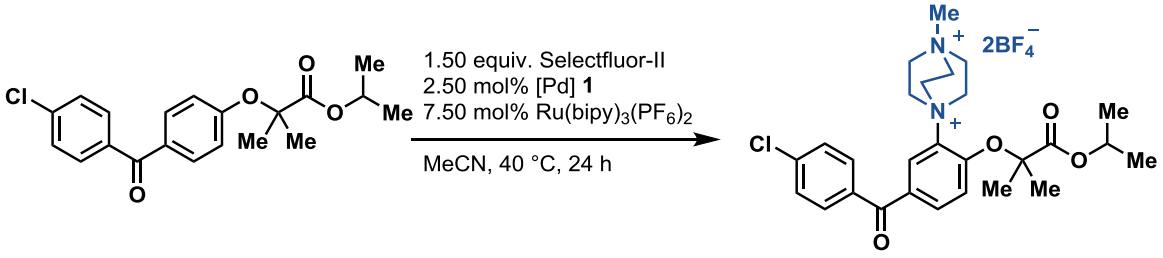
^{1}H NMR (500 MHz, CD_3CN, 23 ºC, δ): 7.97–7.88 (m, 2H), 7.81–7.75 (m, 2H), 7.64–7.59 (m, 2H), 7.54–7.47 (m, 2H), 7.11 (s, 1H), 5.79 (br s, 2H), 4.34–4.27 (m, 6H), 4.05–3.97 (m, 6H), 3.36 (s, 3H).

^{13}C NMR (125 MHz, CD_3CN, 23 ºC, δ): 145.0, 144.4, 144.1, 143.8, 142.4, 133.1, 132.4, 55.6, 54.3, 53.7.

^{19}F NMR (470 MHz, CD_3CN, 23 ºC, δ): –62.9, –151.3.

HRMS-ESI (m/z) calc'd for $C_{23}H_{26}N_5O_2SF_3^{2+}$ $[M]^{2+}/2$, 246.5874; found, 246.5875.

Isopropyl 2-(4-(4-chlorobenzoyl)-2-TEDAphenoxy)-2-methylpropanoate (3x)



3x, 61%

To a 20 mL-vial equipped with a magnetic stirring bar were added palladium complex **1** (15.9 mg, 25.5 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (64.5 mg, 75.0 µmol, 7.50 mol%), Selectfluor II (480 g, 1.50 mmol, 1.50 equiv), and Fenofibrate (361 mg, 1.00 mmol, 1.00 equiv). Acetonitrile (10 mL, c = 0.10 M) was added via syringe to the mixture, the vial was sealed with a Teflon cap, and the reaction mixture was stirred at 40 °C for 24 h. The mixture was concentrated *in vacuo* to half of its original volume, and Et_3N (excess, V = 0.3 mL) was added to the vial. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (18 mL) was added to the vial. The precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 2 mL), then with diethyl ether (2 × 2 mL). The remaining solid was transferred to a glass vial, and methanol (10 mL) was added. The vial was sealed with a Teflon cap and the resulting mixture was stirred at 70 °C for 1 h. After cooling to 23 °C, the solids were collected by filtration on a glass frit, washed with methanol (2 × 2 mL), then with diethyl ether (2 × 2 mL), affording a resin. A purification by prep-HPLC (YMC-Pack Triart C18 (30x150 mm: 5 µm), MeOH/H_2O = 70:30 (v/v), injection volume V_{inj} = 400 µL (m = 40 mg), flow rate = 42.5 mL/min, 35 °C, retention time; 3.1 min) afforded a solid, which was subsequently stirred in Et_2O for 30 min, filtered on a glass frit and dried under vacuum (P < 0.1 mbar) at 70 °C for 3 hours to afford 403 mg of the desired product **3x** as an orange solid (61%).

NMR Spectroscopy:

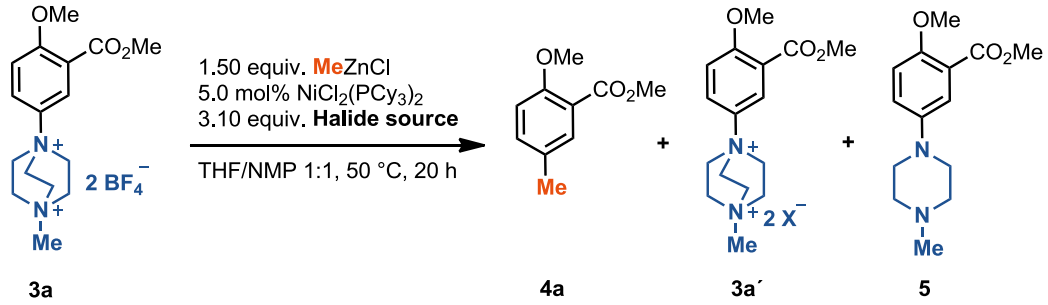
^{1}H NMR (500 MHz, Acetonitrile-d_6, 23 ºC, δ): 8.04 (d, *J* = 1.9 Hz, 1H), 7.94 (dd, *J* = 8.8, 1.8 Hz, 1H), 7.82-7.65 (m, 2H), 7.63-7.48 (m, 2H), 7.14 (d, *J* = 8.7 Hz, 1H), 5.01 (p, *J* = 6.2 Hz, 1H), 4.56 (t, *J* = 7.2 Hz, 6H), 4.08 (t, *J* = 7.2 Hz, 6H), 3.35 (s, 3H), 1.88 (s, 6H), 1.15 (d, *J* = 6.2 Hz, 6H).

^{13}C NMR (125 MHz, Acetonitrile-d_6, 23 ºC, δ): 192.6, 171.1, 152.0, 135.6, 134.9, 131.9, 131.2, 130.9, 129.3, 124.7, 118.2, 84.2, 70.9, 53.6, 53.5, 53.1, 25.2, 21.0.

HRMS-ESI (m/z) calc'd for $C_{27}H_{25}N_2O_4Cl^+$ $[M\text{-}BF_4]^+$, 486.2274; found, 486.2277.

Optimization of the Negishi cross-coupling

Optimization of the halide source



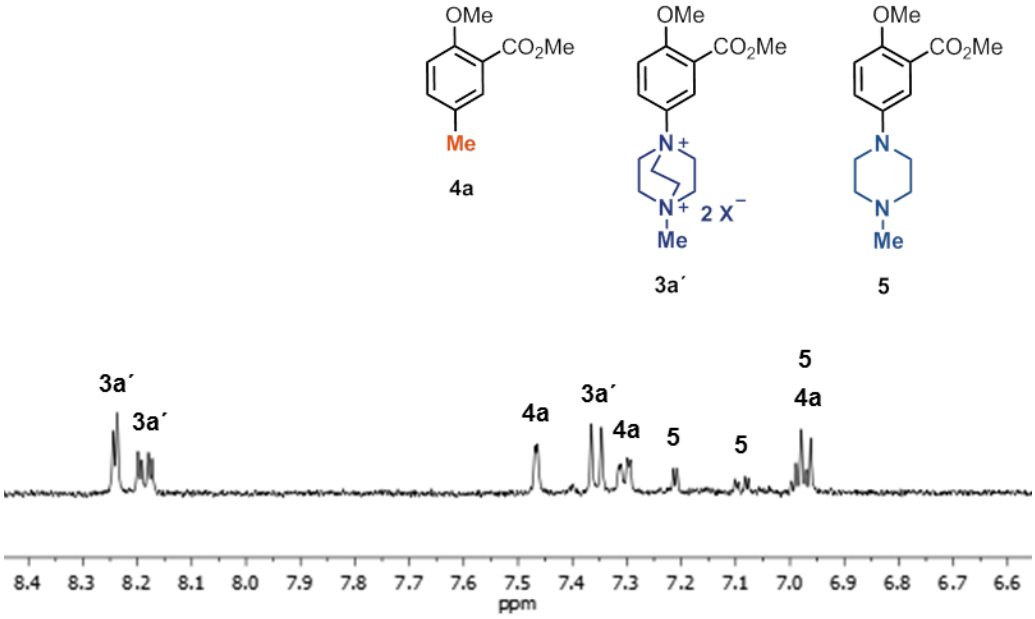
3a **4a** **3a´** **5**

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (1.7 mg, 2.5 µmol, 5.0 mol%), **3a** (23.3 mg, 50.0 µmol, 1.00 equiv.), and the halide source (155 µmol, 3.10 equiv.). NMP (0.15 mL), THF (0.15 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.15 mL, 0.15 mmol, 1.50 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 48 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, followed by acetonitrile (0.5 mL), and DCM (10 µmol) via syringe. The closed vial was sonicated for 1 minute, and an aliquot of the resulting mixture was taken with a pipette, transferred to an NMR tube and the pipette was rinced with CD_3CN.

Halide source	**4a** Yield [%][a]	**3a´** Yield [%][a]	**5** Yield [%][a]
-	8	90	<1
TBAI	9	52	17
TBABr	33	43	10
TBACl	**71**	**8**	**<1**

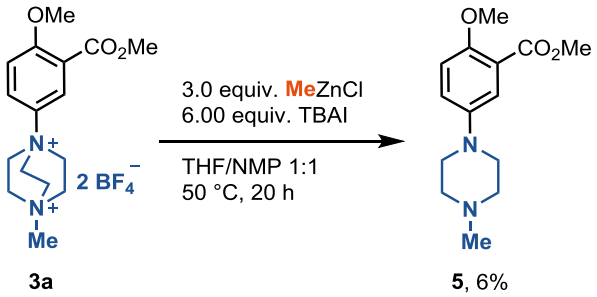
$TBAPF_6$	14	85	<1
$MgCl_2$	<1	23	<1
LiCl	<5	18	<1

[a]Yield determined by ^{1}H NMR spectroscopy; the resonance at 8.24 ppm (**3a´**, aromatic C–H), the resonance at 7.47 ppm (**4a**, aromatic C–H), and the resonance at 7.21 ppm (**5**, aromatic C–H) were compared to the resonance at 5.48 ppm (DCM).



Representation of ^{1}H resonances of 4a, 3a´, and 5 (halide source = TBABr)

Characterization of methyl 2-methoxy-5-(4-methylpiperazin-1-yl)benzoate 5



A 4 mL vial was charged with **3a** (55.0 mg, 120 µmol, 1.00 equiv.), and tetra-*n*-butylammonium iodide (266 mg, 720 µmol, 6.00 equiv.). NMP (0.55 mL) a solution of MeZnCl in THF (c = 1.0 M, 0.45 mL, 0.35 mmol, 3.0 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and placed on a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were

removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL), with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with DCM/MeOH 95:5 (v/v) to afford the desired product **5** (4 mg, 6%) as a colorless liquid.

R*f* = 0.20 (DCM/MeOH 95:5 (v/v)).

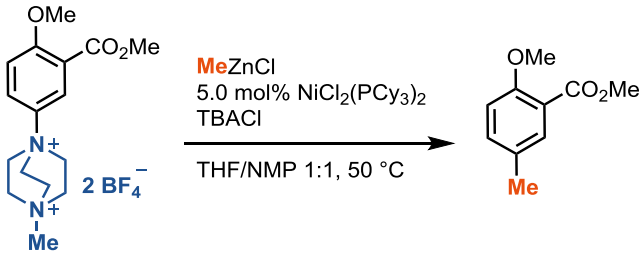
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.38 (d, *J* = 3.2 Hz, 1H), 7.07 (dd, *J* = 9.0, 3.2 Hz, 1H), 6.91 (d, *J* = 9.0 Hz, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 3.18–3.11 (m, 4H), 2.64–2.55 (m, 4H), 2.35 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$,, 23 ºC, δ): 167.0, 153.3, 145.2, 122.1, 120.5, 119.9, 113.6, 56.7, 55.3, 52.2, 50.2, 46.3.

HRMS-ESI (m/z) calc'd for $C_{14}H_{21}N_2O_3^+$ $[M+H]^+$, 265.1549; found, 265.1547.

Optimization of the MeZnCl/TBACl ratio



3a **4a**

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (1.7 mg, 2.5 µmol, 5.0 mol%), **3a** (23.3 mg, 50.0 µmol, 1.00 equiv.), and $n$$Bu_4N^+Cl^-$ (TBACl) (various equiv.). NMP (0.15 mL), THF (amount needed to obtain c = 0.17 M), and a solution of 1.0 M MeZnCl in THF (various equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 48 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, followed by acetonitrile (0.5 mL), and DCM (10 µmol) via syringe. The closed vial was sonicated for 1 minute, and an aliquot of the resulting mixture was taken with a pipette, transferred to a NMR tube and the pipette was rinced with CD_3CN.

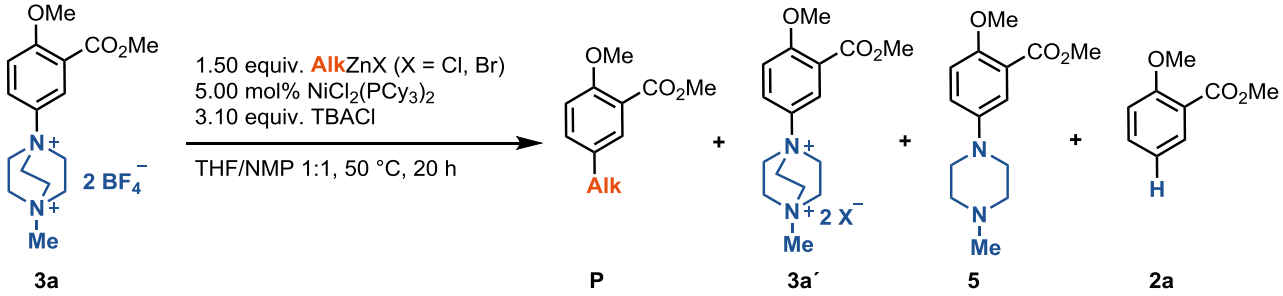
Equiv MeZnCl	Equiv TBACl	**4a** Yield [%][a]	**3a** Yield [%][a]
1.5	0.75	21	77
1.5	1.6	20	35
1.5	**3.1**	**71**	**8**

1.5	4.5	32	<1
3	1.6	18	29
3	3.2	15	14
3	6.1	68	<1

[a] Yield determined by ^{1}H NMR spectroscopy; the resonance at 8.24 ppm (**3a**, aromatic C–H) and the resonance at 7.47 ppm (**4a**, aromatic C–H) were compared to the resonance at 5.48 ppm (DCM).

The experiments on the ratio MeZnCl/TBACl revealed that excess of TBACl was required to obtain high yield of the arene **4a**. With a 1:1 ratio or lower, less than 30% yield was obtained. Starting material accounted for the remainder of the mass balance.

Cross-coupling with other alkyl sources

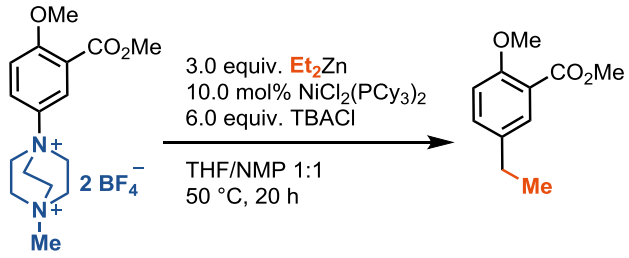


Alkyl source	**P** Yield [%][a]	**3a´** Yield [%][a]	**5**Yield [%][a]	**2a** Yield [%][a]
MeMgCl	**4a**, <1	77	<1	<1
Me$_2$Zn	**4a**, 40	<1	10	<1
MeZnCl	**4a**, 71	8	<1	<1
Et$_2$Zn	**5a**, 22	22	<1	18
***n*Bu**ZnCl	<1	<5	<1	21
CyclopropylZnBr	**6a**, 24	n.d.[b]	<1	<1
BnZnBr	**7a**, <1	<5	<1	<1

***t*BuZnCl**[c]	**8a**, <1	<5	<1	<1
AdamantylZnCl[d]	**9a**, <1	<5	<1	<1

[a] ^{1}H-NMR yield. measured by comparing the integration of the aromatic protons of the product or substrate with the signal of DCM. [b] n.d.: not detected. [c] Prepared by transmetalation of commercially available *t*BuMgCl with $ZnCl_2$. [d] Prepared by LiCl-mediated magnesium insertion in the presence of zinc chloride in adamantly bromide.

Characterization of the ethylated arene 4a´



3a **4a´**, 8%

A 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (17.2 mg, 25.0 µmol, 5.00 mol%), **3a** (117 mg, 250 µmol, 1.00 equiv.), and tetra-*n*-butylammonium chloride (417 mg, 1.50 mmol, 6.00 equiv.). NMP (0.75 mL), THF (0.67 mL), and Et_2Zn (76.8 µL, 92.5 mg, 750 µmol, 3.00 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and placed on a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL), with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with DCM/MeOH 95:5 (v/v) to afford the desired product **4a´** (4 mg, 8%) as a colorless liquid.

R_f = 0.27 (DCM/MeOH 95:5 (v/v)).

NMR Spectroscopy:

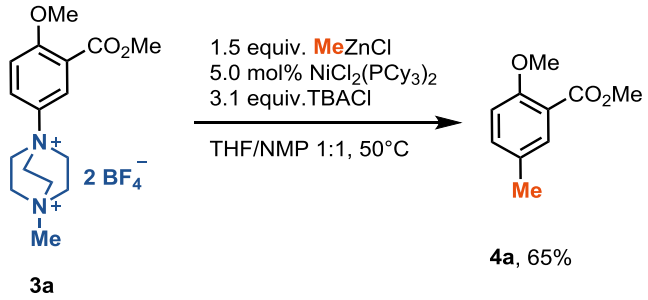
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.62 (d, *J* = 2.5 Hz, 1H), 7.29 (dd, *J* = 8.5, 2.5 Hz, 1H), 6.90 (dd, *J* = 8.5 Hz, 1H), 3.89 (s, 3H), 3.88 (s, 3H), 2.61 (q, *J* = 7.6 Hz, 2H), 1.22 (t, *J* = 7.6 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$,, 23 ºC, δ): 167.1, 157.4, 136.1, 133.0, 131.0, 119.9, 112.3, 56.3, 52.1, 27.9, 15.8.

HRMS-ESI (m/z) calc'd for $C_{11}H_{15}O_3^+$ $[M+H]^+$, 195.1016; found, 195.1016.

Procedures for the methylation of Ar-TEDA

Methyl 2-methoxy-5-methylbenzoate (4a)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3a** (117 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$Cl$^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.), NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4a** (28 mg, 62%) as a colorless liquid.

R$_f$ = 0.27 (EtOAc/pentane 1:9 (v/v)).

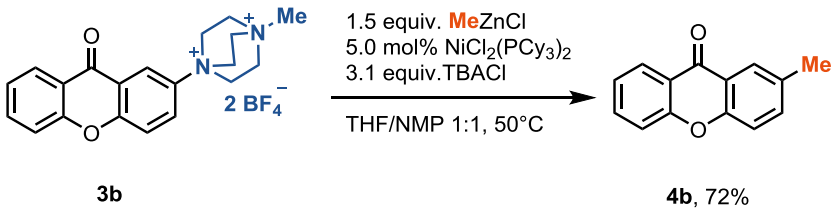
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.61–7.58 (m, 1H), 7.57–7.23 (m, 1H), 6.87 (d, *J* = 8.5 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 2.29 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 167.0, 157.2, 134.1, 132.1, 129.6, 119.8, 112.2, 56.2, 52.1, 20.4.

HRMS-EI (m/z) calc'd for $C_{10}H_{12}O_3^+$ $[M]^+$, 180.0781; found, 180.0783.

2-Methyl-9*H*-xanthen-9-one (4b)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3b** (124 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$Cl$^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.)

were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4b** (38 mg, 72%) as a colorless solid.

R*f* = 0.46 (EtOAc/pentane 1:9 (v/v)).

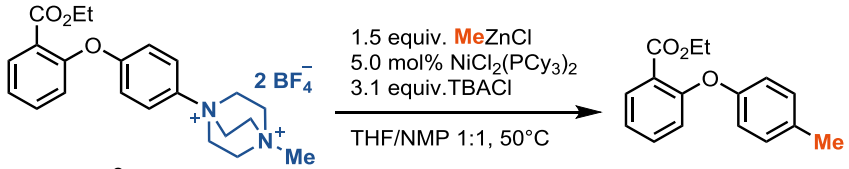
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.24–8.20 (m, 1H), 8.00 (br s, 1H), 7.61–7.56 (m, 1H), 7.42–7.38 (m, 1H), 7.35 (br d, *J* = 8.4 Hz, 1H), 7.28–7.21 (m, 2H), 2.35 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 177.4, 156.3, 154.5, 136.2, 134.7, 133.8, 126.8, 126.1, 123.8, 121.9, 121.6, 118.1, 117.8, 21.0.

HRMS-ESI (m/z) calc'd for $C_{14}H_{11}O_2^+$ $[M+H]^+$, 211.0753; found, 211.0754.

Ethyl 2-(p-tolyloxy)benzoate (4c)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3c** (136 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4c** (55 mg, 85%) as a colorless oil.

R*f* = 0.58 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

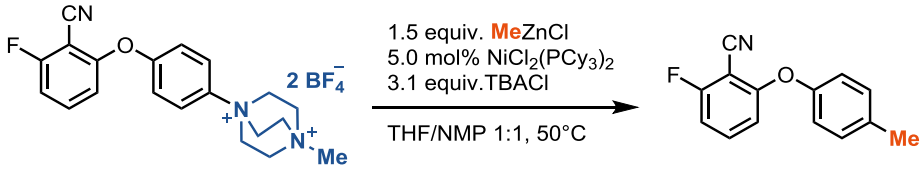
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.89 (dd, *J* = 7.7, 1.8 Hz, 1H), 7.43 (ddd, *J* = 8.3, 7.4, 1.8 Hz, 1H),

7.16 (td, *J* = 7.7, 1.1 Hz, 1H), 7.13 – 7.09 (m, 2H), 6.96 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.88–6.84 (m, 2H), 4.28 (q, *J* = 7.2 Hz, 2H), 2.32 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 166.0, 156.5, 155.5, 133.5, 132.6, 131.8, 130.3, 123.7, 123.3, 120.7, 118.2, 61.2, 20.8, 14.3.

HRMS-ESI (m/z) calc'd for $C_{16}H_{17}O_3^+$ $[M+H]^+$, 257.1172; found, 257.1174.

2-Fluoro-6-(p-tolyloxy)benzonitrile (4d)



3d **4d**, 45%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3d** (128 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **4d** (26 mg, 45%) as a colorless solid.

R_f = 0.45 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

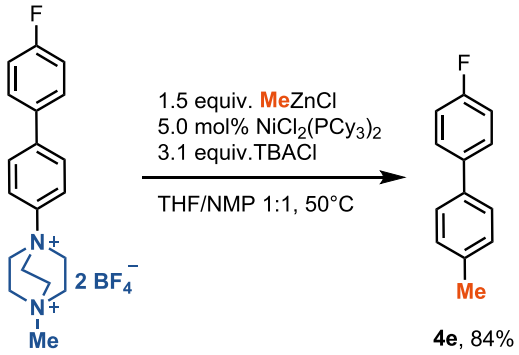
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.39 (td, *J* = 8.5, 6.5 Hz, 1H), 7.24–7.20 (m, 2H), 7.02–6.97 (m, 2H), 6.85 (td, *J* = 8.4, 0.8 Hz, 1H), 6.59–6.55 (m, 1H), 2.37 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 164.2 (d, *J* = 259.3 Hz), 161.7 (d, *J* = 4.3 Hz), 152.2, 135.6, 134.9 (d, *J* = 10.7 Hz), 130.9, 120.5, 111.5 (d, *J* = 3.8 Hz), 111.4, 109.4 (d, *J* = 19.7 Hz), 20.98.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –105.0.

HRMS-ESI (m/z) calc'd for $C_{14}H_{10}ONFNa^+$ $[M+Na]^+$, 250.0638; found, 250.0639.

4-Fluoro-4'-methyl-1,1'-biphenyl (4e)



3e **4e**, 84%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3e** (118 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:100 (v/v) to afford the desired product **4e** (39 mg, 84%) as a colorless solid.

R_f = 0.84 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

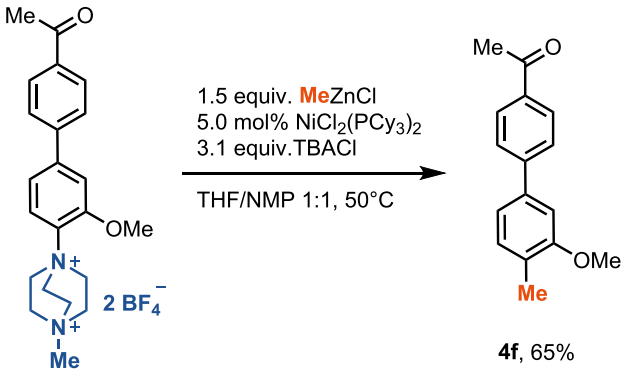
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.58–7.53 (m, 2H), 7.50–7.45 (m, 2H), 7.30–7.25 (m, 1H), 7.17–7.11 (m, 2H), 2.43 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 162.4 (d, *J* = 245.8 Hz), 137.5, 137.4 (d, *J* = 3.1 Hz), 137.2, 129.7, 128.6 (d, *J* = 8.1 Hz), 127.0, 115.7 (d, *J* = 21.3 Hz), 21.2.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –116.2.

HRMS-EI (m/z) calc'd for $C_{13}H_{11}F^+$ $[M]^+$, 186.0839; found, 186.0841.

1-(3'-Methoxy-4´-methylbiphenyl-4-yl)ethanone (4f)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3f** (132 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered, and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4f** (39 mg, 65%) as a colorless solid.

R_f = 0.3 (EtOAc/pentane 1:9 (v/v)).

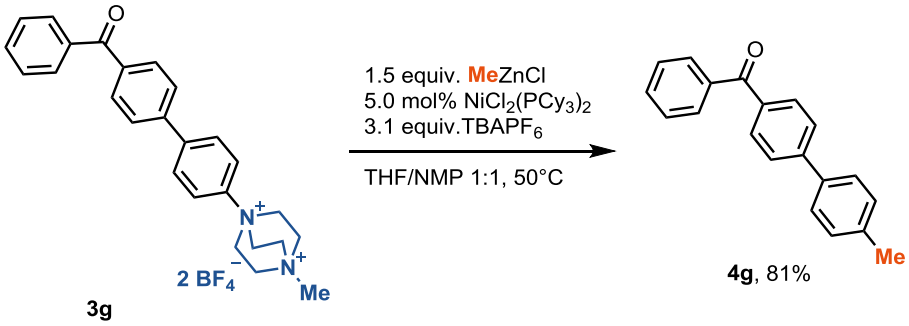
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.06–7.99 (m, 2H), 7.70–7.66 (m, 2H), 7.23 (br d, *J* = 7.6 Hz, 1H), 7.13 (dd, *J* = 7.6, 1.7 Hz, 1H), 7.07 (br d, *J* = 1.7 Hz, 1H), 3.92 (s, 3H), 2.64 (s, 3H), 2.28 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 197.9, 158.3, 146.2, 139.0, 135.8, 131.2, 129.0, 127.2, 127.2, 119.4, 109.0, 55.5, 26.8, 16.2.

HRMS-ESI (m/z) calc'd for $C_{16}H_{16}O_2Na^+$ $[M+Na]^+$, 263.1042; found, 263.1044.

(4'-Methyl-[1,1'-biphenyl]-4-yl)(phenyl)methanone (4g)



3g **4g**, 81%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3g** (140 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+PF_6^-$ ($TBAPF_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4g** (55 mg, 81%) as a colorless solid.

R_f = 0.49 (EtOAc/pentane 1:9 (v/v)).

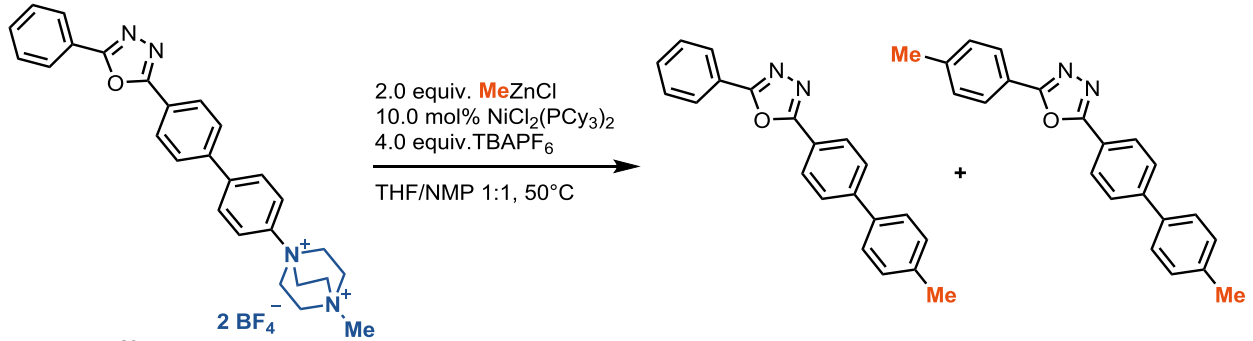
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.91–7.86 (m, 2H), 7.86–7.82 (m, 2H), 7.72–7.67 (m, 2H), 7.62–7.58 (m, 1H), 7.57–7.54 (m, 2H), 7.53–7.48 (m, 2H), 7.31–7.28 (m, 2H), 2.42 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 196.5, 145.3, 138.3, 137.98, 137.2, 136.1, 132.5, 130.9, 130.1, 129.9, 128.4, 127.3, 126.9, 21.3.

HRMS-ESI (m/z) calc'd for $C_{20}H_{17}O^+$ $[M+H]^+$, 273.1274; found, 273.1275.

2-(4'-Methyl-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (4h)



3h **4h**, 54% **4h´**, 5%

In an anhydrous, nitrogen-filled glovebox, a 4 mL-vial was charged with $Ni(PCy_3)_2Cl_2$ (17.2 mg, 25.0 µmol, 10.0 mol%), **3h** (150 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+PF_6^-$ ($TBAPF_6$) (387 mg, 1.00 mmol, 4.00 equiv.). NMP (0.75 mL), THF (0.25 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.50 mL, 0.50 mmol, 2.0 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford a mixture of products **4h** and **4h´** (48 mg) in a 88:12 ratio (determined by ^{1}H-NMR). Further purification by prep-HPLC (YMC-Pack Triart C18 (30x150 mm: 5 µm), MeCN/H_2O = 90:10 (v/v), injection volume V_{inj} = 600 µL (m = 6 mg), flow rate = 42.5 mL/min, 35 °C, retention time; 4.45 min (**4h**), 5.22 min (**4h´**) provided the title compound **4h** (40 mg, 54%) and **4h´** (4 mg, 5%).

The following data was obtained for the mixture:

R_f = 0.28 (EtOAc/pentane 1:9 (v/v)).

The following data were obtained for the pure products:

2-(4'-Methyl-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (**4h**)

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.22–8.19 (m, 2H), 8.18–8.14 (m, 2H), 7.78–7.73 (m, 2H), 7.60–7.53 (m, 5H), 7.30 (d, *J* = 7.8 Hz, 1H), 2.42 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 164.7, 164.6, 144.5, 138.3, 137.0, 131.8, 129.8, 129.2, 127.5, 127.5, 127.1, 127.0, 124.1, 122.4, 21.3.

HRMS-EI (m/z) calc'd for $C_{21}H_{16}N_2O^+$ $[M]^+$, 312.1257; found, 312.1259.

2-(4'-methyl-[1,1'-biphenyl]-4-yl)-5-(p-tolyl)-1,3,4-oxadiazole (**4h´**)

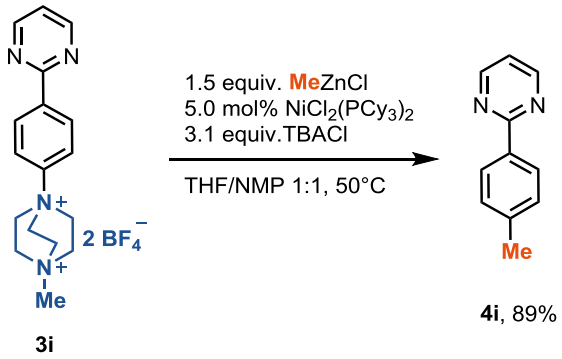
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.25–8.14 (m, 2H), 8.09–8.01 (m, 2H), 7.78–7.72 (m, 2H), 7.59–7.55 (m, 2H), 7.37–7.33 (m, 2H), 7.31–7.28 (m, 2H), 2.45 (s, 1H), 2.42 (s, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 164.7, 164.3, 144.3, 142.3, 138.2, 137.0, 129.8, 129.7, 127.5, 127.3, 127.0, 126.9, 122.5, 121.2, 21.7, 21.2.

HRMS-ESI (m/z) calc'd for $C_{22}H_{18}N_2ONa^+$ $[M+Na]^+$, 349.1311; found, 349.1312.

2-(p-Tolyl)pyrimidine (4i)



3i **4i**, 89%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3i** (114 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$Cl$^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4i** (38 mg, 89%) as a beige solid

R$_f$ = 0.3 (EtOAc/pentane 1:9 (v/v)).

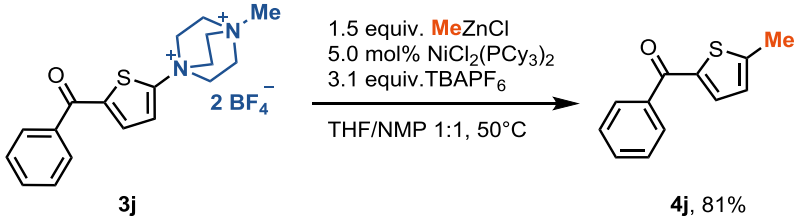
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.77 (d, J = 4.8 Hz, 2H), 8.36–8.32 (m, 2H), 7.32–7.28 (m, 2H), 7.12 (t, J = 4.8 Hz, 1H), 2.42 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 164.9, 157.3, 141.1, 135.0, 129.5, 128.2, 118.9, 21.6.

HRMS-EI (m/z) calc'd for $C_{11}H_{10}N_2^+$ $[M]^+$, 170.0838; found, 170.0838.

5-Methylthiophen-2-yl)(phenyl)methanone (4j)



3j **4j**, 81%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3j** (122 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$PF$_6^-$ (TBAPF$_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.)

were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **4j** (41 mg, 81%) as a colorless liquid.

R*f* = 0.5 (EtOAc/pentane 1:9 (v/v)).

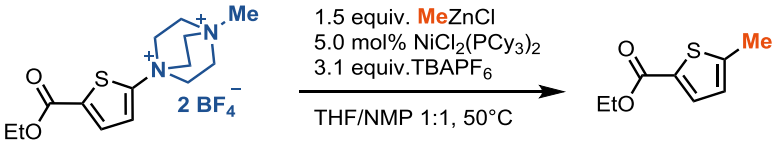
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.85–7.80 (m, 2H), 7.58–7.54 (m, 1H), 7.50–7.44 (m, 3H), 6.84–6.81 (m, 1H), 2.57 (br d, *J* = 1.0 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 188.0, 150.5, 141.6, 138.4, 135.8, 132.1, 129.1, 128.4, 126.8, 16.2.

HRMS-EI (m/z) calc'd for $C_{12}H_{10}OS^+$ $[M]^+$, 202.0447; found, 202.0449.

(5-Methylthiophen-2-yl)(phenyl)methanone (4k)



3k **4k**, 63%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3k** (114 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+PF_6^-$ ($TBAPF_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **4k** (27 mg, 63%) as a colorless liquid.

R*f* = 0.68 (EtOAc/pentane 1:9 (v/v)).

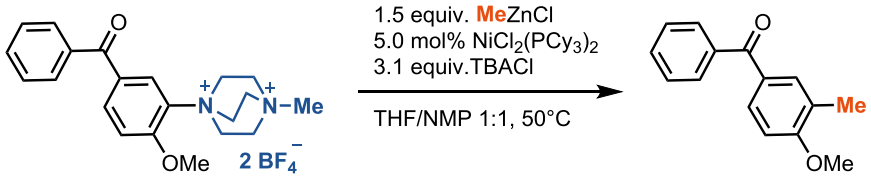
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.60 (d, *J* = 3.7 Hz, 1H), 6.75 (dq, *J* = 3.7, 1.1 Hz, 1H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.51 (d, *J* = 1.1 Hz, 3H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 162.4, 147.7, 133.8, 131.5, 126.4, 61.0, 15.9, 14.5.

HRMS-ESI (m/z) calc'd for $C_{12}H_{10}O_2SNa^+$ $[M+Na]^+$, 193.0294; found, 193.0293.

(4-Methoxy-3-methylphenyl)(phenyl)methanone (4l)



3l **4l**, 79%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3l** (132 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4l** (45 mg, 79%) as a colorless oil.

R_f = 0.35 (EtOAc/pentane 1:9 (v/v)).

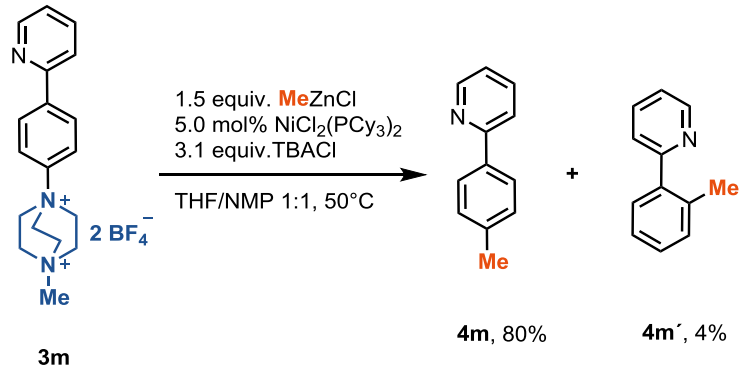
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.78–7.73 (m, 2H), 7.70–7.66 (m, 2H), 7.59–7.53 (m, 1H), 7.49–7.44 (m, 2H), 6.86 (d, *J* = 8.3 Hz, 1H), 3.90 (s, 3H), 2.25 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 195.9, 161.6, 138.6, 132.8, 131.8, 130.7, 129.8, 129.7, 128.2, 126.8, 109.1, 55.6, 16.3.

HRMS-ESI (m/z) calc'd for $C_{15}H_{15}O_2^+$ $[M+H]^+$, 227.1066; found, 227.1066.

2-(*p*-Tolyl)pyridine (4m)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3m** (114 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford a mixture of products **4m** and **4m´** (39 mg) in a 94:6 ratio. Further purification by prep-HPLC (YMC-Pack Triart C18 (30x150 mm: 5 µm), MeOH/H_2O (0.1% trifluoroacetic acid) = 40:60 (v/v), injection volume V_{inj} = 500 µL (m = 10 mg), flow rate = 42.5 mL/min, 35 °C, retention time; 4.08 min (**4m´**), 4.82 min (**4m**)) provided the title compound **4m** (34 mg, 80%) and **4m´** (2 mg, 4%) as a colorless liquids.

The following data was obtained for the mixture:

R_f = 0.44 (EtOAc/pentane 1:9 (v/v)).

The following data were obtained for the pure products:

2-(p-tolyl)pyridine (**4m**):

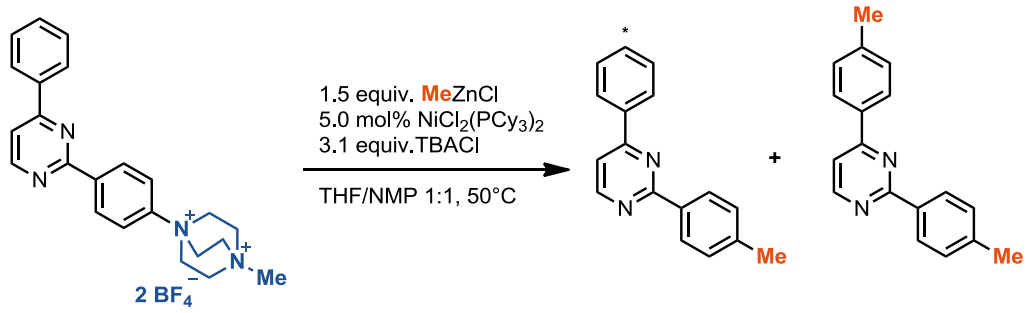
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.70–8.66 (m, 1H), 7.93–7.88 (m, 2H), 7.74–7.68 (m, 2H), 7.31–7.27 (m, 2H), 7.19 (ddd, *J* = 6.3, 4.8, 2.2 Hz, 1H), 2.41 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 157.6, 149.7, 139.0, 136.8, 136.7, 129.6, 126.9, 121.9, 120.3, 21.4.

HRMS-EI (m/z) calc'd for $C_{12}H_{11}N^+$ $[M]^+$, 169.0886; found, 169.0886.

4-Phenyl-2-(*p*-tolyl)pyrimidine (4n)



3n **4n**, 86%[a] **4n"**, 4%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3n** (133 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford a mixture of products **4n** and **4n''** (60 mg) in a 97:3 ratio (determined by ^{1}H-NMR). Further purification by prep-HPLC (YMC-Pack Triart C18 (30x150 mm: 5 µm), MeCN/H_2O = 90:10 (v/v), injection volume V_{inj} = 600 µL (m = 6 mg), flow rate = 42.5 mL/min, 35 °C, retention time; 4.34 min (**4n**), 5.20 min (**4n´'**)) provided the title compounds **4n** (53 mg, 86%)[a] and **4n´** (3 mg, 4%) as a colorless liquids.

[a]: the compound **4n** contains 5% of the mono-methylated 2,4-phenylpyridine 4n' (other isomer, measured by ^{1}H-NMR).

The following data was obtained for the mixture:

R_f = 0.43 (EtOAc/pentane 1:9 (v/v)).

The following data were obtained for the pure products:

4-Phenyl-2-(p-tolyl)pyrimidine (**4n**)

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.82 (d, *J* = 5.3 Hz, 1H), 8.50–8.46 (m, 2H), 8.26–8.22 (m, 2H), 7.58 (d, *J* = 5.3 Hz, 1H), 7.56–7.49 (m, 3H), 7.36–7.30 (m, 2H), 2.45 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 164.8, 163.9, 157.9, 141.1, 137.2, 135.3, 131.0, 129.4, 129.0, 128.4, 127.3, 114.4, 21.7.

HRMS-EI (m/z) calc'd for $C_{17}H_{14}N_2^+$ $[M]^+$, 246.1151; found, 246.1153.

2,4-di-*p*-tolylpyrimidine (**4n''**)

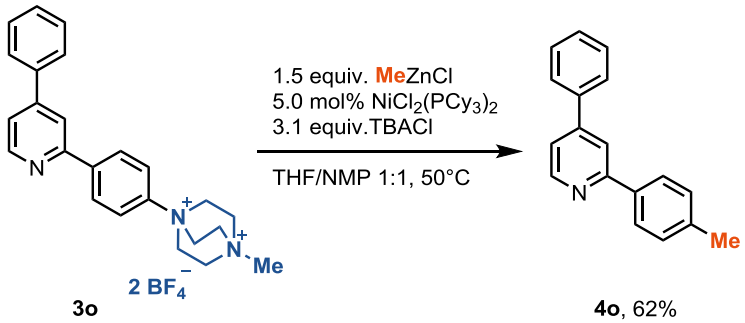
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.79 (d, *J* = 5.3 Hz, 1H), 8.49–8.43 (m, 2H), 8.17–8.08 (m, 2H), 7.55 (d, *J* = 5.3 Hz, 1H), 7.36–7.30 (m, 4H), 2.45 (s, 3H), 2.44 (s, 3H).

^{13}C NMR (151 MHz, $CDCl_3$, 23 ºC, δ): 164.7, 163.9, 157.8, 141.4, 141.0, 135.4, 134.4, 129.8, 129.4, 128.4, 127.3, 114.1, 21.7, 21.6.

HRMS-ESI (m/z) calc'd for $C_{18}H_{17}N_2^+$ $[M+H]^+$, 261.1386; found, 261.1388.

4-Phenyl-2-(*p*-tolyl)pyridine (4o)



3o **4o**, 62%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3o** (133 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4o** (32 mg, 62%) as a pale yellow liquid.

R_f = 0.36 (EtOAc/pentane 1:9 (v/v)).

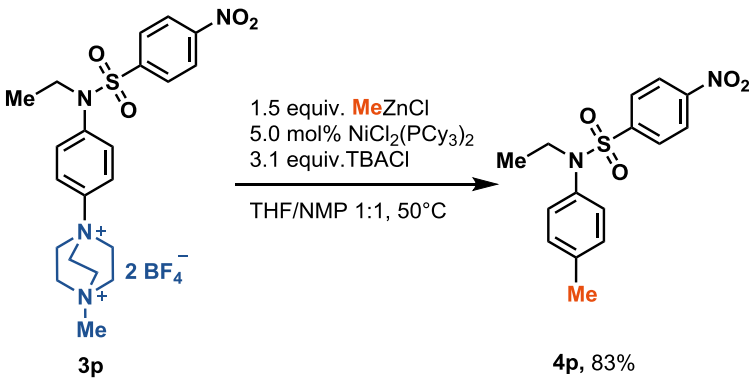
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.72 (dd, *J* = 5.2, 0.8 Hz, 1H), 7.99–7.93 (m, 2H), 7.91 (dd, *J* = 1.7, 0.8 Hz, 1H), 7.73–7.68 (m, 2H), 7.55–7.49 (m, 2H), 7.49–7.44 (m, 1H), 7.42 (dd, *J* = 5.2, 1.7 Hz, 1H), 7.34–7.29 (m, 2H), 2.43 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 158.2, 150.2, 149.4, 139.2, 138.8, 136.9, 129.7, 129.3, 129.1, 127.2, 127.0, 120.1, 118.6, 21.4.

HRMS-EI (m/z) calc'd for $C_{18}H_{15}N^+$ $[M]^+$, 243.1203; found, 245.1199.

N-ethyl-4-nitro-*N*-(*p*-tolyl)benzenesulfonamide (4p)



3p **4p,** 83%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3p** (152 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **4p** (66.4 mg, 83%) as a colorless solid.

R_f = 0.61 (EtOAc/pentane 1:9 (v/v)).

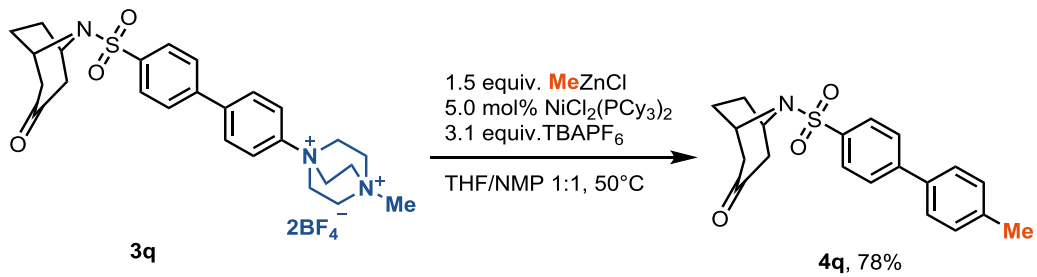
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.33-8.22 (m, 2H), 7.95-7.69 (m, 2H), 7.16–7.05 (m, 2H), 6.96–6.77 (m, 2H), 3.63 (q, *J* = 7.1 Hz, 2H), 2.36 (s, 3H), 1.11 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 149.9, 144.4, 138.6, 135.1, 130.0, 128.7, 128.6, 124.0, 46.1, 21.1, 14.1.

HRMS-EI (m/z) calc'd for $C_{15}H_{16}N_2O_4SNa^+$ $[M+Na]^+$, 343.0723; found, 343.0723.

8-((4'-methyl-[1,1'-biphenyl]-4-yl)sulfonyl)-8-azabicyclo[3.2.1]octan-3-one (4q)



3q **4q**, 78%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3q** (160 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+PF_6^-$ ($TBAPF_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **4q** (69 mg, 81%) as a colorless liquid.

R*f* = 0.5 (EtOAc/pentane 1:9 (v/v)).

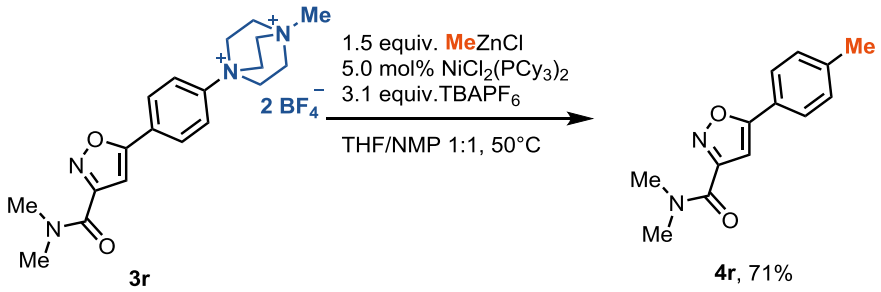
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.04-7.89 (m, 2H), 7.81-7.64 (m, 2H), 7.63–7.45 (m, 2H), 7.36–7.27 (m, 2H), 4.55 (tt, *J* = 4.7, 2.3 Hz, 2H), 2.93-2.72 (m, 2H), 2.41 (s, 3H), 2.40 (d, *J* = 6.3 Hz, 2H), 2.37 (d, *J* = 1.7 Hz, 2H), 1.86-1.72 (m, 2H) , 1.62 (t, *J* = 7.3 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 188.0, 150.5, 141.6, 138.4, 135.8, 132.1, 129.1, 128.4, 126.8, 16.2.

HRMS-EI (m/z) calc'd for $C_{20}H2_1NO_3SNa^+$ $[M+Na]^+$, 378.1134; found, 378.1134.

N,*N*-dimethyl-5-(*p*-tolyl)isoxazole-3-carboxamide (4r)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3r** (122 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+PF_6^-$ ($TBAPF_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column

chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **4r** (41 mg, 81%) as a colorless liquid.

R*f* = 0.5 (EtOAc/pentane 1:9 (v/v)).

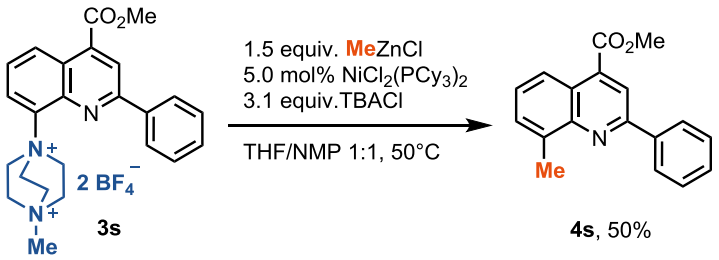
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.73–7.64 (m, 2H), 7.36-7.27 (m, 2H), 6.77 (s, 1H), 3.33 (s, 3H), 3.15 (s, 3H), 2.41 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 170.3, 161.1, 159.4, 141.0, 129.8, 125.9, 124.1, 100.1, 38.8, 36.0, 21.5.

HRMS-EI (m/z) calc'd for $C_{13}H_{14}N_2O_2Na^+$ $[M+Na]^+$, 253.0947; found, 253.0947.

Methyl 8-methyl-2-phenylquinoline-4-carboxylate (4s)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), Ar-TEDAs mixture (141 mg, 0.250 mmol, 1.00 equiv.) including **3s** (72 mol%), and $n$$Bu_4N^+Cl^-$ (215.4 mg, 0.77 mmol, 3.10 equiv). NMP (0.75 mL), THF (0.375 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.375 mL, 0.37 mmol, 1.5 equiv.) were then added to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23°C, the reaction was quenched by addition of MeOH (0.1 mL), the volatiles but the NMP were evaporated on a rotary evaporator, and the resulting mixture dissolved in MTBE (20 mL). Transferred to a separatory funnel, the organic layer was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with MTBE/pentane 2:98 (v/v) to afford the desired product **4s** (34 mg, 68%) as a colorless solid.

R*f* = 0.54 (EtOAc/pentane 1:9 (v/v)).

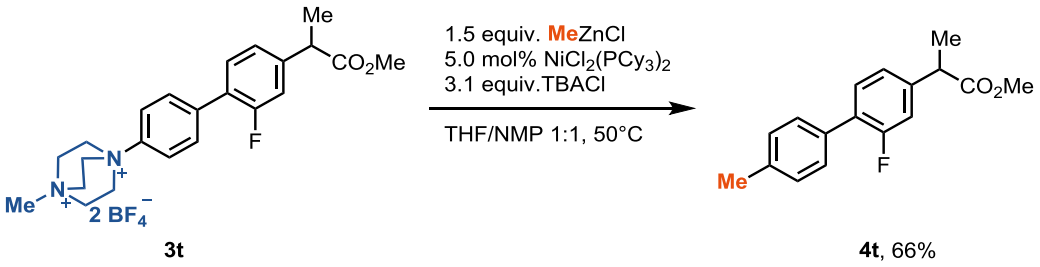
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.58–8.52 (br d, *J* = 8.6 Hz, 1H), 8.40 (s, 1H), 8.32–8.26 (m, 2H), 7.63–7.59 (m, 1H), 7.58–7.46 (m, 4H), 4.07 (s, 3H), 2.92 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 167.3, 154.8, 148.2, 139.1, 138.2, 136.0, 130.1, 129.7, 129.0, 127.6, 127.5, 124.0, 123.3, 119.5, 52.8, 18.6.

HRMS-ESI (m/z) calc'd for $C_{18}H_{16}N_2O^+$ $[M+H]^+$, 278.1175; found, 278.1176.

(±)-4´-Methyl-flurbiprofen methyl-ester (4t)



3t **4t**, 66%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3t** (140 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$Cl$^-$ (215.4 mg, 0.77 mmol, 3.10 equiv). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:100 (v/v) to afford the desired product **4t** (45 mg, 66%) as a colorless liquid.

R$_f$ = 0.52 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

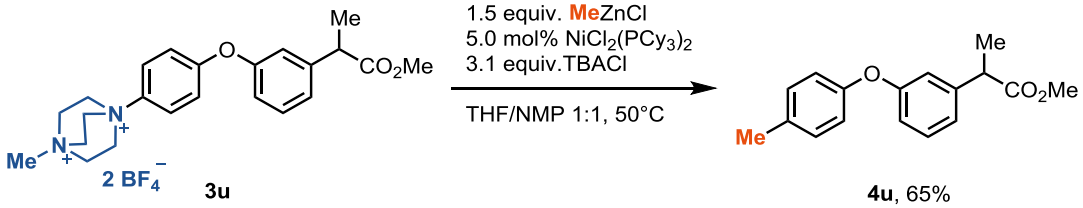
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.46–7.41 (m, 2H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.27–7.23 (m, 2H), 7.17–7.09 (m, 2H), 3.76 (q, *J* = 7.2 Hz, 1H), 3.70 (s, 3H), 2.40 (s, 3H), 1.54 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 174.6, 159.9 (d, *J* = 249.3 Hz), 141.6 (d, *J* = 8.0 Hz),137.6, 132.7, 130.8 (d, *J* = 4.4 Hz), 129.3, 128.9 (d, *J* = 3.2 Hz), 128.0 (d, *J* = 14.0 Hz), 123.6 (d, *J* = 3.5 Hz), 115.33 (d, *J* = 23.8 Hz), 52.4, 45.1, 21.3, 18.6.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –117.6.

HRMS-EI (m/z) calc'd for $C_{17}H_{17}O_2F^+$ $[M]^+$, 272.1207; found, 272.1205.

(±)-Methyl 2-(3-(*p*-tolyloxy)phenyl)propanoate (4u)



3u **4u**, 65%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3u** (139 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$Cl$^-$ (215.4 mg, 0.77 mmol, 3.10 equiv). NMP (0.75

mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **4u** (44 mg, 65%) as a colorless liquid.

R*f* = 0.54 (EtOAc/pentane 1:9 (v/v)).

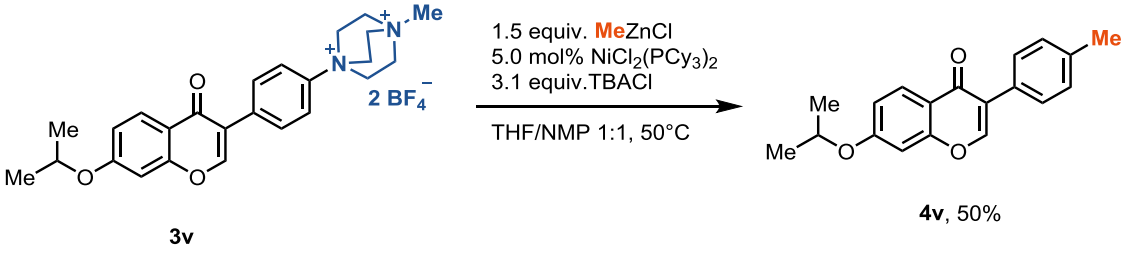
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.31–7.27 (m, 1H), 7.20–7.13 (m, 2H), 7.05–7.01 (m, 1H), 6.99–6.97 (m, 1H), 6.97–6.91 (m, 2H), 6.87 (ddd, *J* = 8.2, 2.5, 1.0 Hz, 1H), 3.72 (q, *J* = 7.2 Hz, 1H), 3.69 (s, 3H), 2.37 (s, 3H), 1.51 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 174.8, 158.1, 154.6, 142.5, 133.2, 130.4, 129.9, 122.0, 119.3, 117.7, 116.9, 52.2, 45.4, 20.9, 18.7.

HRMS-EI (m/z) calc'd for $C_{17}H_{18}O_3^+$ $[M]^+$, 270.1250; found, 270.1252.

7-Isopropoxy-3-(p-tolyl)-4H-chromen-4-one (4v)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3v** (145 mg, 0.250 mmol, 1.00 equiv) and $n$$Bu_4N^+Cl^-$ (215.4 mg, 0.77 mmol, 3.10 equiv). NMP (0.75 mL), THF (0.37 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.37 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL)and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:9 (v/v) to afford the desired product **4v** (37 mg, 50%) as a colorless solid.

R*f* = 0.31 (EtOAc/pentane 1:9 (v/v)).

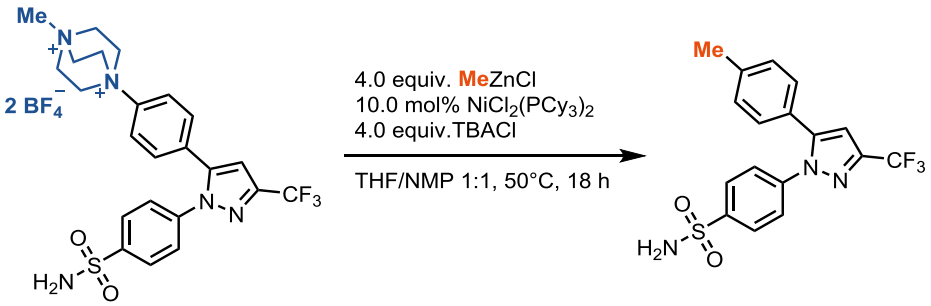
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.20 (dd, *J* = 9.0, 1.1 Hz, 1H), 7.92 (d, *J* = 1.1 Hz, 1H), 7.49–7.43 (m, 2H), 7.29–7.21 (m, 2H), 6.95 (ddd, *J* = 9.0, 2.4, 1.0 Hz, 1H), 6.86–6.81 (m, 1H), 4.67 (hept, *J* = 6.0, 1H), 2.39 (s, 3H), 1.43–1.39 (m, 6H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 175.9, 162.5, 158.1, 152.4, 138.0, 129.3, 129.2, 129.0, 128.0, 125.3, 118.3, 115.6, 101.7, 70.9, 22.0, 21.4.

HRMS-ESI (m/z) calc'd for $C_{19}H_{19}O_3^+$ $[M+H]^+$, 295.1329; found, 295.1328.

Celecoxib (4w)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial (vial n°1) was charged with nBu$_4$N$^+$Cl$^-$ (277.9 mg, 1.00 mmol, 4.00 equiv), then NMP (0.50 mL) and a solution of MeZnCl in THF (c = 1.0 M, 0.50 mL, 0.50 mmol, 2.0 equiv.) were successively added to the vial. The resulting mixture was stirred at 23 °C for 15 min. A second 4 mL vial (vial n°2) was charged with $Ni(PCy_3)_2Cl_2$ (17.2 mg, 25.0 µmol, 10.0 mol%) and **3w** (167 mg, 0.250 mmol, 1.00 equiv). A solution of MeZnCl in THF (c = 1.0 M, 0.50 mL, 0.50 mmol, 2.0 equiv.) and NMP (0.50 mL) were then added to the vial. The resulting solution was stirred at 23 °C for 10 min, before being transferred to the vial n°1 using a pipette. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 18 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture was diluted with water (10 mL). The aqueous layer was extracted with MTBE (3 × 20 mL), and the combined organic layers were washed with water (2 × 10 mL) andwith brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The crude material was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:4 (v/v) to afford the desired product **4w** (58 mg, 61%) as a colorless solid.

R*f* = 0.14 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

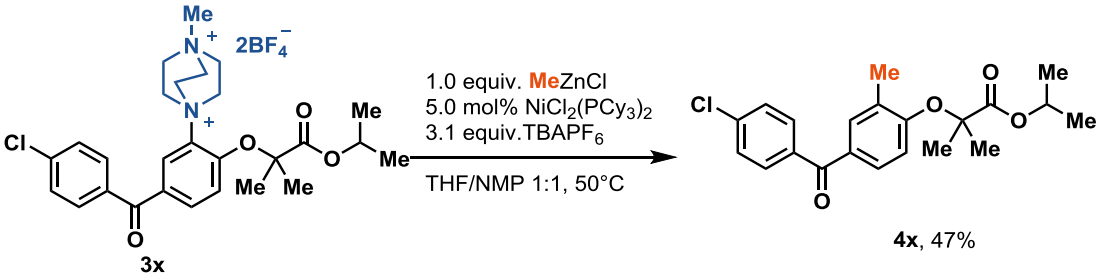
^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.96–7.87 (m, 2H), 7.51–7.44 (m, 2H), 7.21–7.16 (m, 2H), 7.14–7.08 (m, 2H), 6.74 (s, 1H), 4.95 (br s, 2H), 2.38 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 145.4, 144.3 (q, *J* = 38.4 Hz), 142.7, 141.4, 140.0, 129.9, 128.9, 127.7, 125.8, 125.6, 121.2 (d, *J* = 269.3 Hz), 106.5, 21.5.

^{19}F NMR (470 MHz, $CDCl_3$, 23 ºC, δ): –62.5.

HRMS-ESI (m/z) calc'd for $C_{17}H_{15}N_3O_2SF_3^+$ $[M+H]^+$, 382.0831; found, 382.0382.

Isopropyl 2-(4-(4-chlorobenzoyl)-2-methylphenoxy)-2-methylpropanoate (4x)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3x** (165 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+PF_6^-$ ($TBAPF_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), THF (0.50 mL), and a solution of MeZnCl in THF (c = 1.0 M, 0.25 mL, 0.25 mmol, 1.0 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 5:95 (v/v) to afford the desired product **4x** (44 mg, 47%) as a colorless solid.

R_f = 0.64 (EtOAc/pentane 1:9 (v/v)).

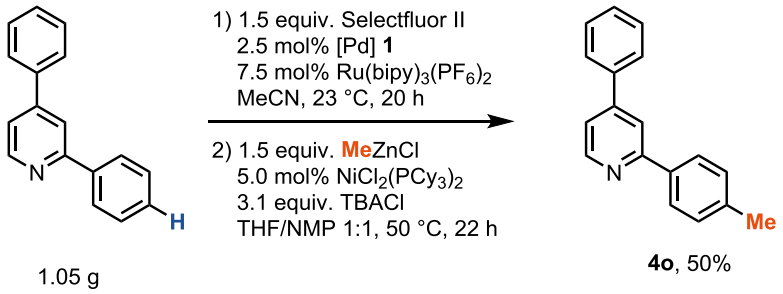
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.71–7.68 (m, 2H), 7.65 (dd, *J* = 2.3, 0.9 Hz, 1H), 7.51 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.46–7.42 (m, 2H), 6.65 (d, *J* = 8.6 Hz, 1H), 5.08 (p , *J* = 6.3 Hz, 1H), 2.27 (s, 3H), 1.66 (s, 6H), 1.20 (d, *J* = 6.3 Hz, 6H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 194.5, 173.2, 158.1, 138.2, 136.6, 133.0, 131.2, 129.8, 129.3, 129.0, 128.5, 114.1, 79.4, 69.2, 25.5, 21.5, 16.8.

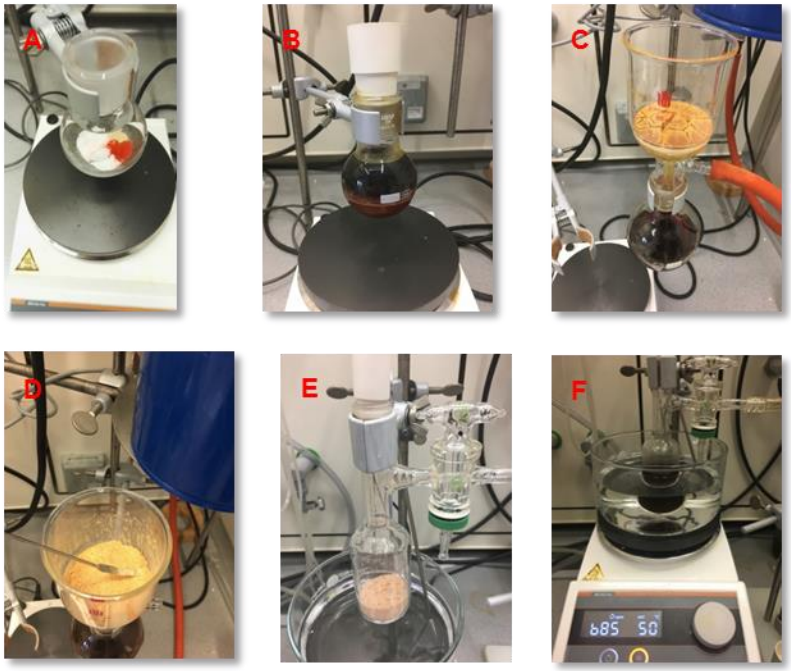
HRMS-ESI (m/z) calc'd for $C_{21}H_{23}O_4ClNa^+$ $[M+Na]^+$, 397.1177; found, 397.1178.

Gram-scale methylation of 2,4-diphenylpyridine



To a 100 mL-round bottomed flask equipped with a magnetic stirring bar were added palladium complex **1** (72.2 mg, 113 µmol, 2.50 mol%), $Ru(bipy)_3(PF_6)_2$ (293 mg, 340 µmol, 7.50 mol%), Selectfluor II (2.18 g, 6.81 mmol, 1.5 equiv), and a solution of 2,4-diphenylpyridine (1.05 g, 4.54 mmol, 1.00 equiv) in MeCN (10 mL). Additionnal acetonitrile (13 mL) was added via syringe to the mixture, the flask was capped with a rubber septum and the reaction mixture was stirred at 23 °C for 20 h. Et_3N (excess, V = 1.5 mL) was added dropwise to the flask at room temperature. The resulting mixture was stirred for 2 min at 23 °C, and dichloromethane (75 mL) was added to the flask. After being stirred for 5 min, the precipitate was collected by filtration on a glass frit, washed with dichloromethane (2 × 15 mL), then with diethyl ether (2 × 15 mL). The resulting Ar-TEDA was dried under vacuum (P < 0.1 mbar) at room temperature for 1 hour. In an oven-dried argon-filled Schlenck flask was charged with $Ni(PCy_3)_2Cl_2$ (157 mg, 227 µmol, 5.44 mol%), **3o** (2.27 g, 4.17 mmol, 1.00 equiv.), and $n Bu_4N^+Cl^-$ (TBACl) (3.91 g, 14.1 mmol, 3.38 equiv.). The Schlenk flask was capped with a rubber septum, then evacuated and back-filled with argon. This evacuation/back-filling process was repeated three times. NMP (13.6 mL), THF (6.80 mL), and a solution of MeZnCl in THF (c = 1.0 M, 6.81 mL, 6.81 mmol, 1.63 equiv.) were then added successively to the reaction mixture. The Schlenck was moved to a preheated oil bath (50 °C) and the reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (120 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 50 mL) and with brine (1 × 50 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:100 (v/v) to afford the desired product **4o** (562 mg, 50% over two steps) as a pale yellow liquid.

Figure S2. Photographic guide of the gram-scale methylation of arene



A: solid reagents introduced under air in a flask before addition of the arene and MeCN

B: TEDAylation reaction after 24 h, stopped by addition of Et_3N and dichloromethane

C: filtration of the reaction mixture over a frit size F

D: Ar-TEDA compound after two washings with Et_2O

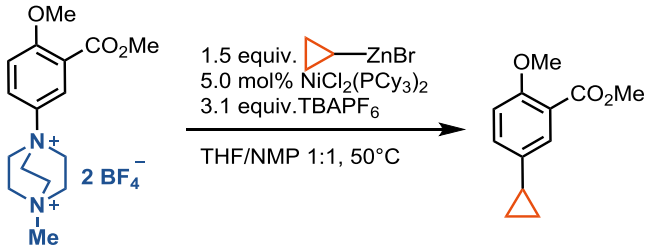
E: solid reagents introduced in the Schlenk flask under argon before addition of MeZnCl solution and solvents

F: Negishi coupling performed at 50° C for 20 h under argon

G: work-up of the cross-coupling before purification by flash chromatography on silica gel

Procedures for the cyclopropylation of Ar-TEDAs

Methyl 5-cyclopropyl-2-methoxybenzoate (6a)



3a **6a**, 21%

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3a** (116 mg, 0.250 mmol, 1.00 equiv.), and $n$$Bu_4N^+Cl^-$ (TBACl) (215 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), and a solution of cyclopropylzinc bromide in THF (c = 0.5 M, 0.75 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **6a** (11 mg, 21%) as a colorless oil.

R_f = 0.52 (EtOAc/pentane 1:9 (v/v)).

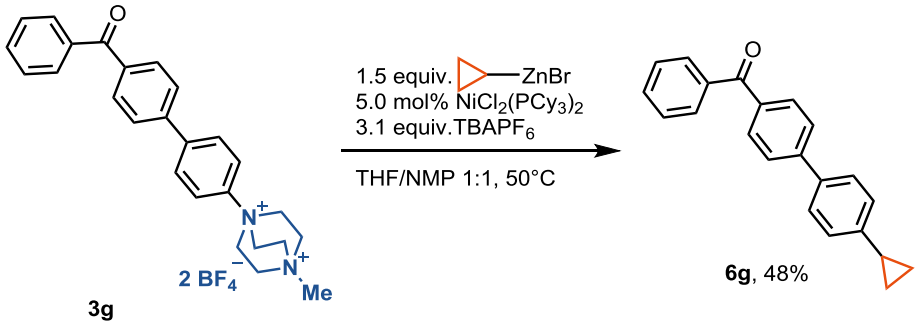
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.51 (d, *J* = 2.5 Hz, 1H), 7.19 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 1.86 (tt, *J* = 8.4, 5.1 Hz, 1H), 0.96–0.89 (m, 2H), 0.69–0.59 (m, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ):167.0, 157.3, 135.7, 131.2, 129.2, 119.9, 112.3, 56.3, 52.2, 14.6, 8.7.

HRMS-ESI (m/z) calc'd for $C_{12}H_{14}O_3^+$ $[M+Na]^+$, 229.0835; found, 229. 0835.

(4'-Cyclopropyl-[1,1'-biphenyl]-4-yl)(phenyl)methanone (6g)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3g** (139 mg, 0.250 mmol, 1.00 equiv.), and $n Bu_4N^+PF_6^-$ ($TBAPF_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), and a solution of cyclopropylzinc bromide in THF (c = 0.5 M, 0.75 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **6g** (36 mg, 48%) as a colorless solid.

R_f = 0.52 (EtOAc/pentane 1:9 (v/v)).

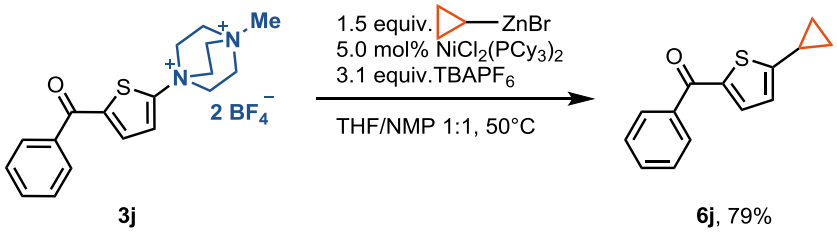
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.91–7.86 (m, 2H), 7.87–7.82 (m, 2H), 7.70–7.66 (m, 2H), 7.63–7.58 (m, 1H), 7.58–7.54 (m, 2H), 7.53–7.48 (m, 2H), 7.21–7.17 (m, 1H), 1.96 (tt, *J* = 8.4, 4.9 Hz, 1H), 1.08–0.99 (m, 2H), 0.76 (dt, *J* = 6.7, 4.9 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 196.5, 145.2, 144.6, 138.0, 137.1, 136.0, 132.4, 130.9, 130.9, 130.1, 128.4, 127.3, 126.8, 126.3, 15.4, 9.7.

HRMS-ESI (m/z) calc'd for $C_{22}H_{19}O^+$ $[M+H]^+$, 299.1430; found, 299.1432.

(5-Cyclopropylthiophen-2-yl)(phenyl)methanone (6j)



In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with $Ni(PCy_3)_2Cl_2$ (8.6 mg, 12 µmol, 5.0

mol%), **3j** (122 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$PF$_6^-$ (TBAPF$_6$) (300 mg, 0.775 mmol, 3.10 equiv.). NMP (0.75 mL), and a solution of cyclopropylzinc bromide in THF (c = 0.5 M, 0.75 mL, 0.37 mmol, 1.5 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **6j** (45 mg, 79%) as a pale yellow liquid.

R$_f$ = 0.41 (EtOAc/pentane 1:9 (v/v)).

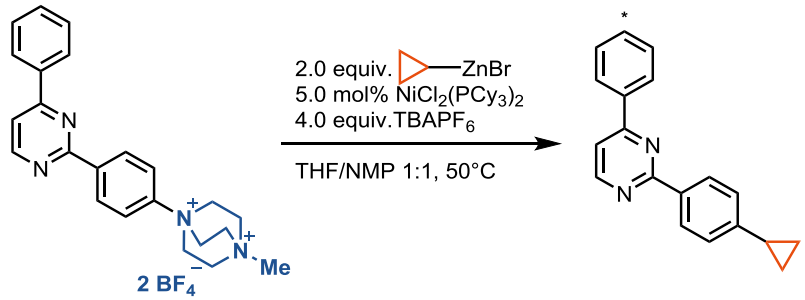
NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 7.86–7.79 (m, 2H), 7.59–7.54 (m, 1H), 7.50–7.45 (m, 2H), 7.44 (d, *J* = 3.8 Hz, 1H), 6.81 (dd, *J* = 3.8, 0.6 Hz, 1H), 2.23–2.12 (m, 1H), 1.20–1.08 (m, 2H), 0.86 (dt, *J* = 6.8, 4.8 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 187.9, 160.1, 139.8, 138.4, 135.7, 132.0, 129.1, 128.5, 123.8, 12.5, 11.7.

HRMS-ESI (m/z) calc'd for $C_{14}H_{12}OSNa^+$ $[M+Na]^+$, 251.0501; found, 251.0500.

2-(4-Cyclopropylphenyl)-4-phenylpyrimidine (6n)



3n **6n**, 79%[a]

In an anhydrous, nitrogen-filled glovebox, a 4 mL vial was charged with Ni(PCy$_3$)$_2$Cl$_2$ (8.6 mg, 12 µmol, 5.0 mol%), **3n** (133 mg, 0.250 mmol, 1.00 equiv.), and nBu$_4$N$^+$PF$_6^-$ (TBAPF$_6$) (387 mg, 1.00 mmol, 4.00 equiv.). NMP (0.75 mL), and a solution of cyclopropylzinc bromide in THF (c = 0.5 M, 1.0 mL, 0.50 mmol, 2.0 equiv.) were then added successively to the reaction mixture. The vial was sealed with a Teflon cap and moved from the glovebox to a preheated metal heating block (50 °C). The reaction mixture was then stirred at 50 °C for 20 hours. After cooling to 23 °C, MeOH (0.1 mL) was added to the mixture, the volatiles except the NMP were removed *in vacuo*, and the resulting mixture dissolved in MTBE (20 mL). The solution was then transferred to a separatory funnel and was washed with water (4 × 10 mL) and with brine (1 × 5 mL), then dried over Na_2SO_4, filtered and concentrated to dryness. The residue was purified by flash column chromatography on silica gel eluting with EtOAc/pentane 1:99 (v/v) to afford the desired product **6n** (58 mg,

79%)[a] as a colorless oil.

[a]: the compound **6n** contains 5% of the mono-cyclopropylated 2,4-phenylpyridine (other isomer, measured by ^{1}H-NMR).

R_f = 0.38 (EtOAc/pentane 1:9 (v/v)).

NMR Spectroscopy:

^{1}H NMR (500 MHz, $CDCl_3$, 23 ºC, δ): 8.81 (d, *J* = 5.3 Hz, 1H), 8.53–8.44 (m, 2H), 8.25–8.20 (m, 2H), 7.57 (d, *J* = 5.2 Hz, 1H), 7.55–7.51 (m, 3H), 7.24–7.18 (m, 2H), 1.98 (tt, *J* = 8.4, 4.9 Hz, 1H), 1.09–1.01 (m, 2H), 0.80 (dt, *J* = 6.6, 4.9 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$, 23 ºC, δ): 164.8, 163.9, 157.9, 147.4, 137.3, 135.3, 131.0, 129.1, 128.4, 127.3, 125.8, 114.3, 15.7, 10.0.

HRMS-ESI (m/z) calc'd for $C_{19}H_{17}N_2^+$ $[M+H]^+$, 273.1386; found, 273.1384.

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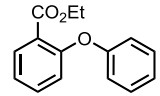
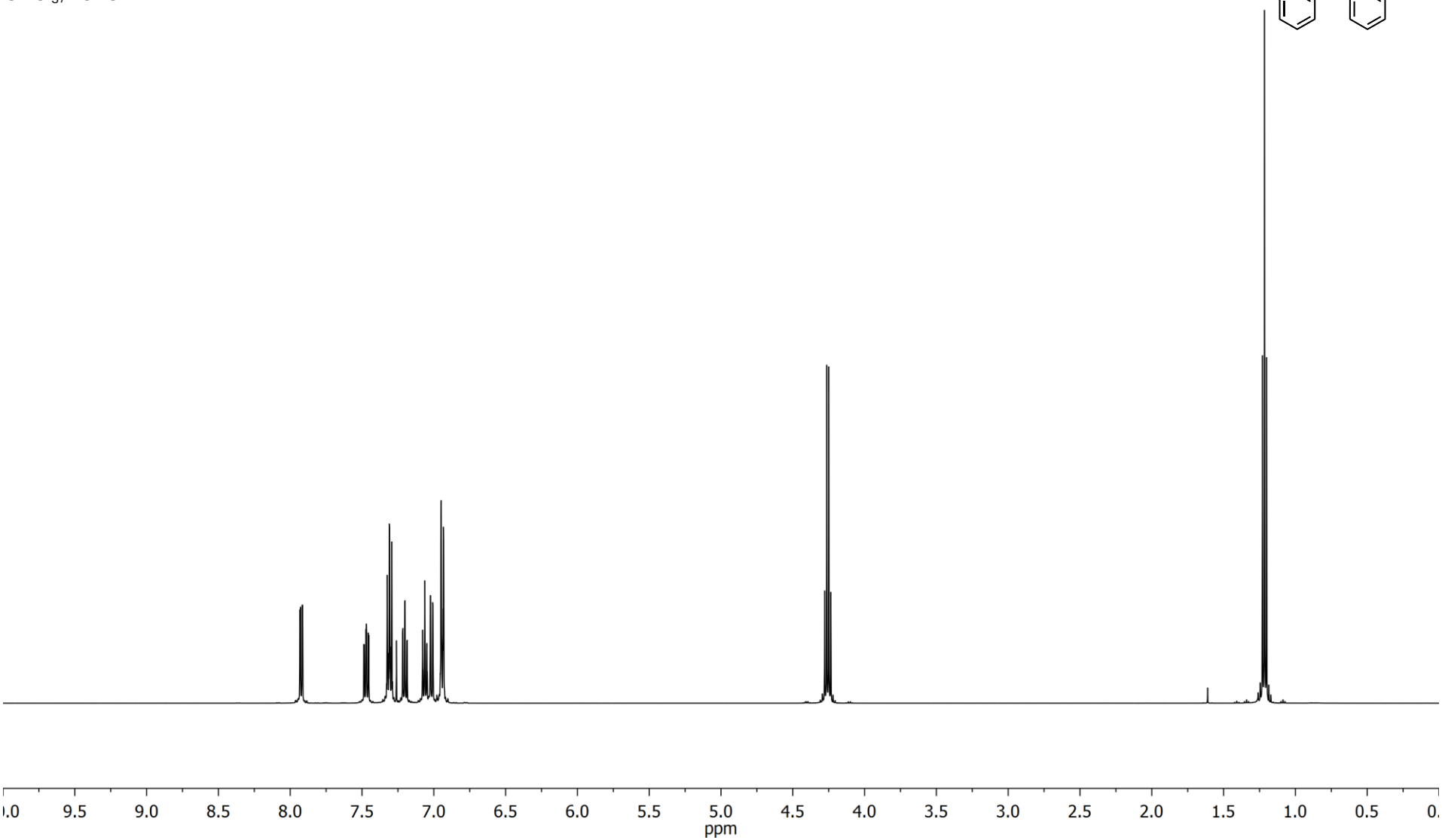
SPECTROSCOPIC DATA

^{1}H NMR of ethyl 2-phenoxybenzoate (2c)

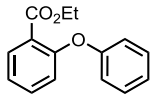
$CDCl_3$, 23 ºC

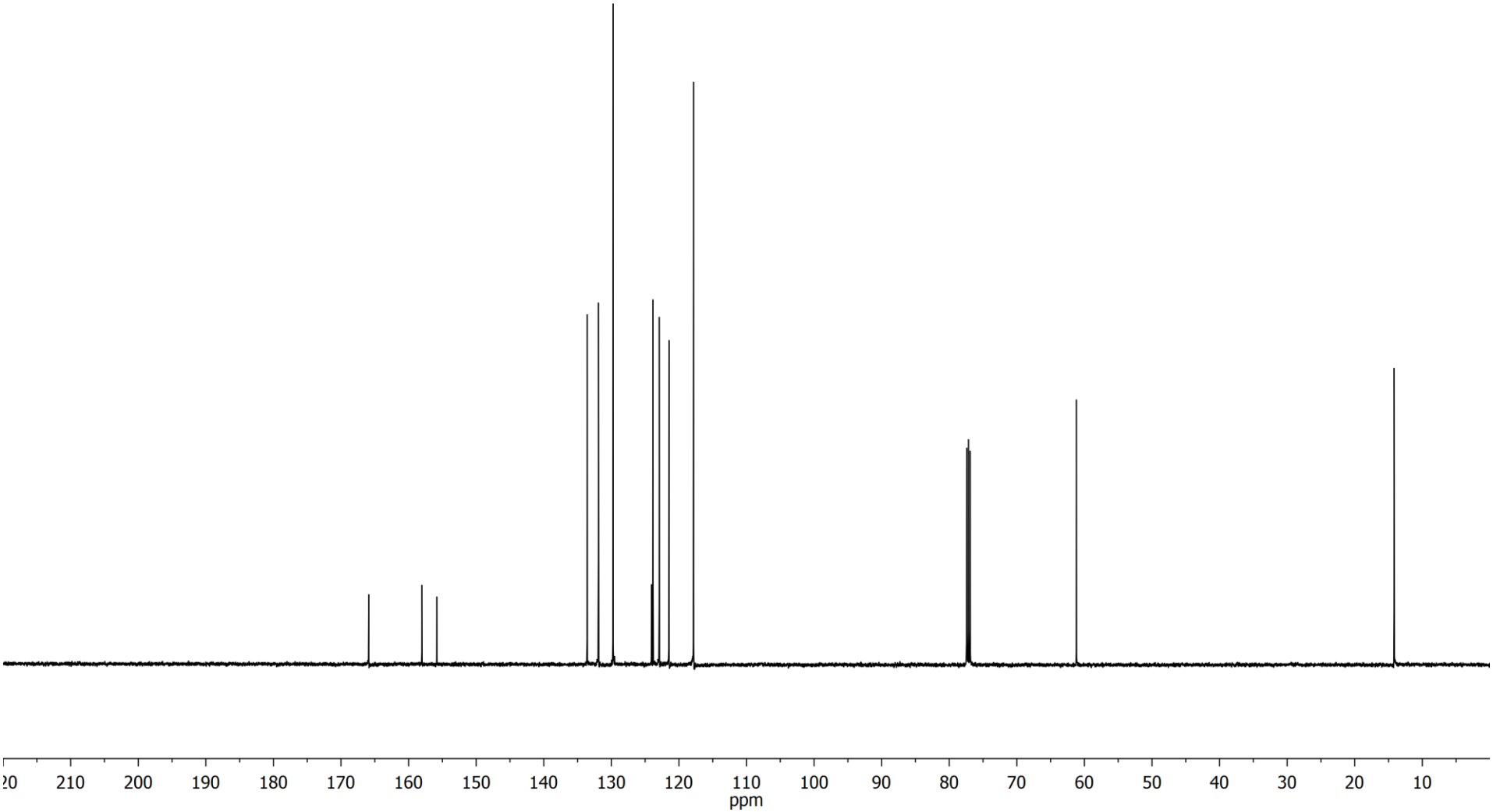




^{13}C NMR of ethyl 2-phenoxybenzoate (2c)

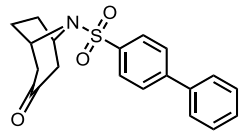
$CDCl_3$, 23 ºC

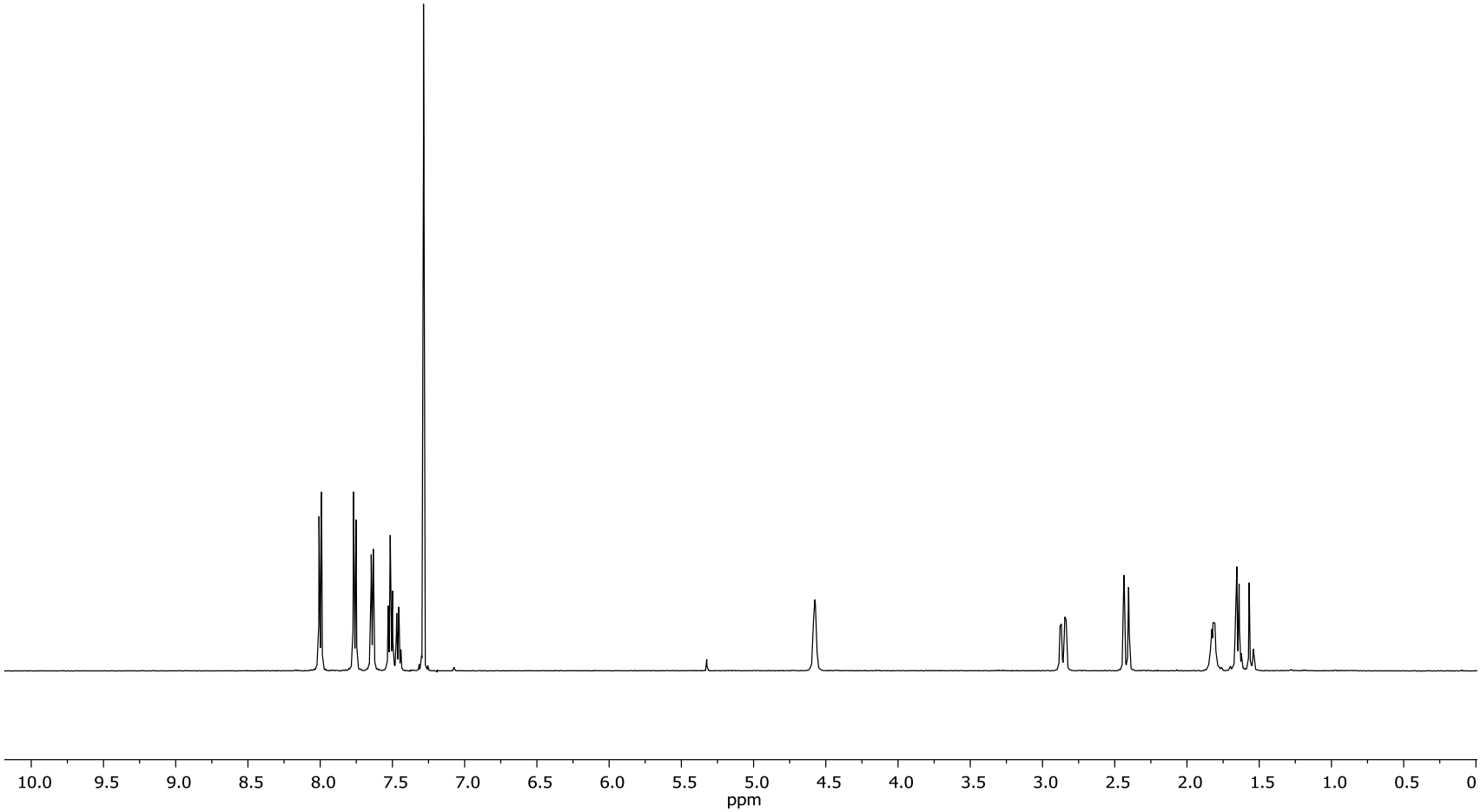




^{1}H NMR of *N*-(biphenyl-4-sulfonyl)nortropinone (2q)

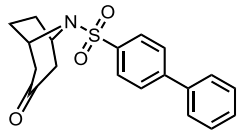
$CDCl_3$, 23 ^{o}C

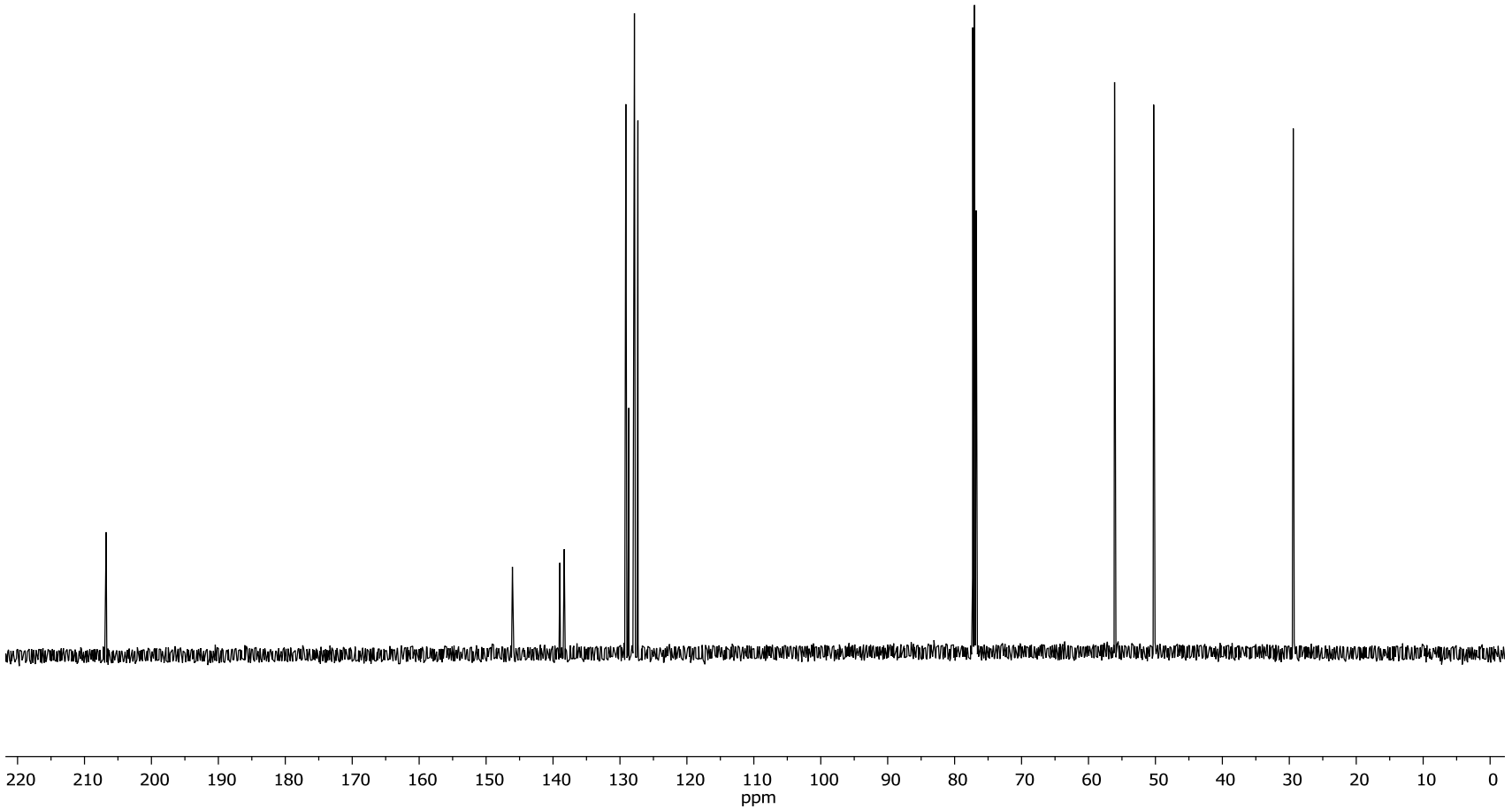




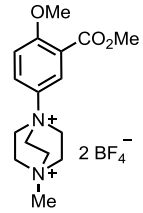
^{13}C NMR of *N*-(biphenyl-4-sulfonyl)nortropinone (2q)

$CDCl_3$, 23 ^{o}C

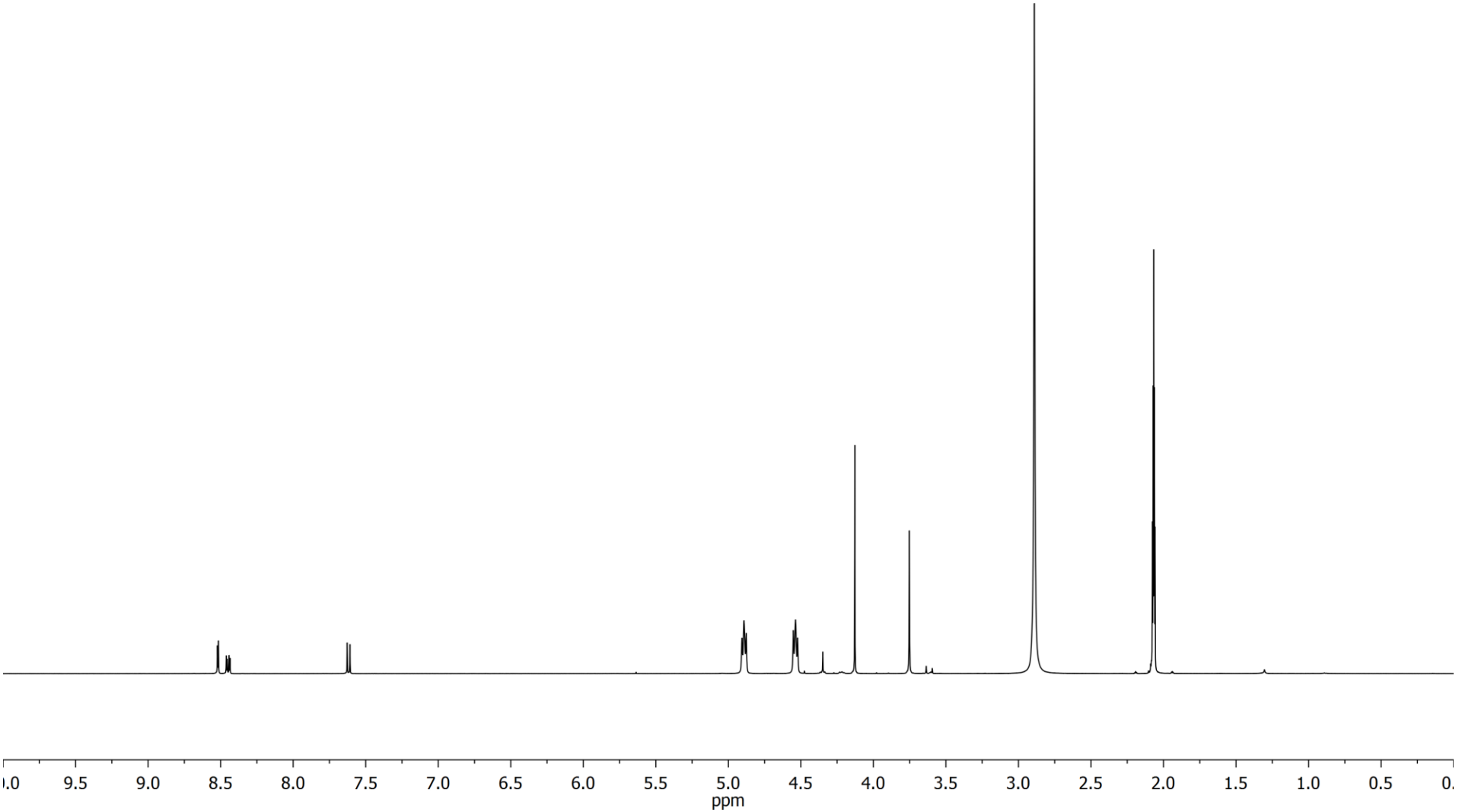




^{1}H NMR of methyl 5-TEDA-2-methoxybenzoate (3a)

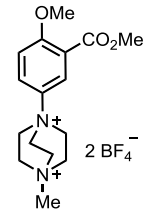


Acetone-d_6, 23 ºC



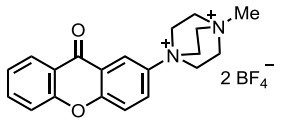
^{13}C NMR of methyl 5-TEDA-2-methoxybenzoate (3a)

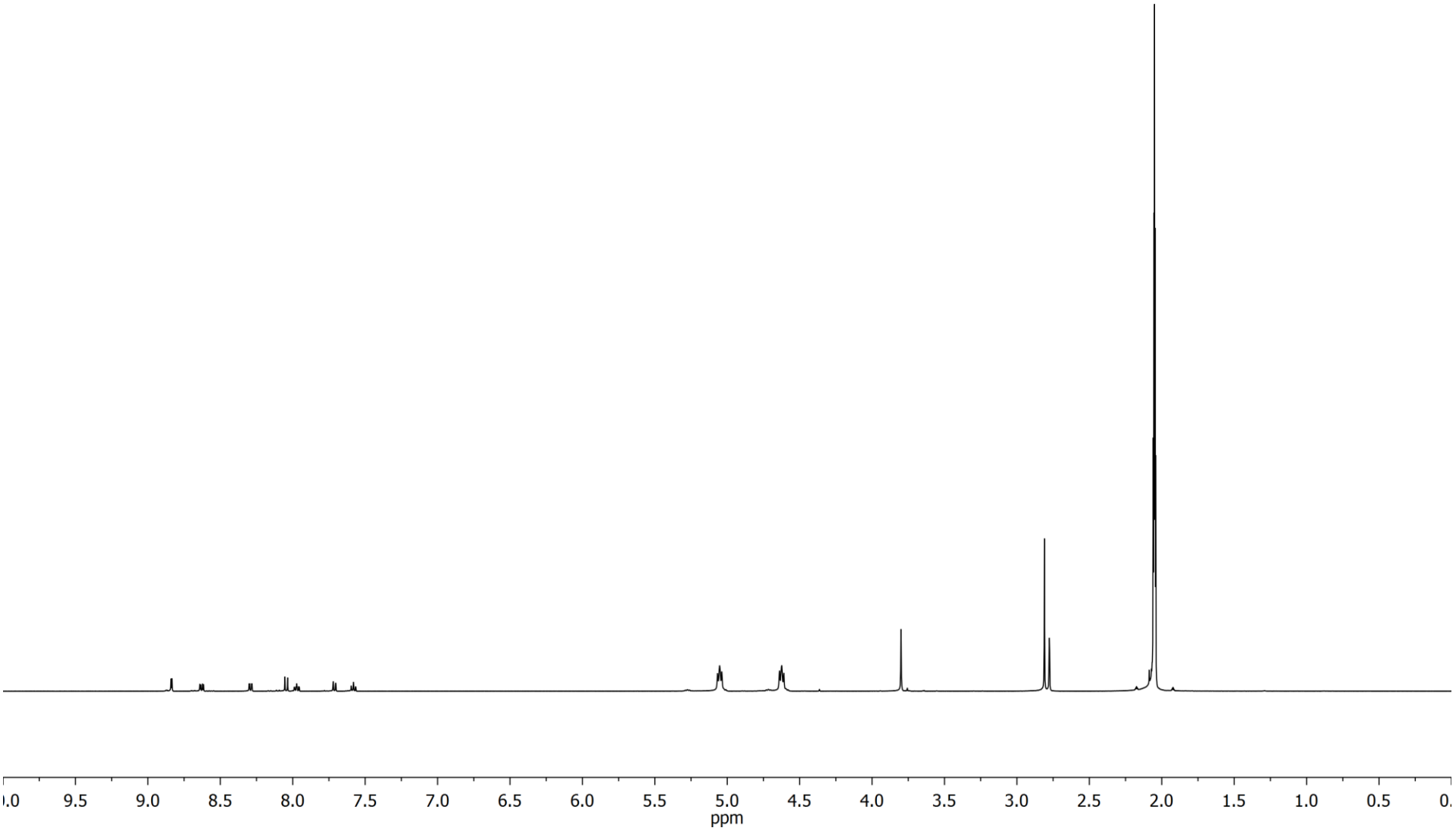
DMSO-d_6, 23 ºC



^{1}H NMR of 2-TEDA-xanthone (3b)

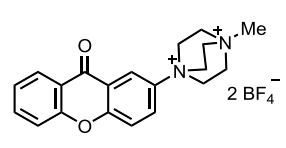
Acetone-d_6, 23 ºC





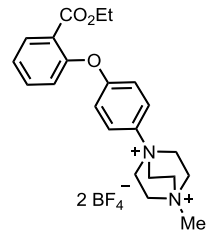
^{13}C NMR of 2-TEDA-xanthone (3b)

DMSO-d_6, 23 ºC



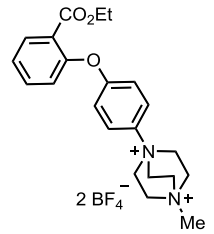
^{1}H NMR of ethyl 2-(4-TEDAphenoxy)benzoate (3c)

Acetone-d_6, 23 ºC



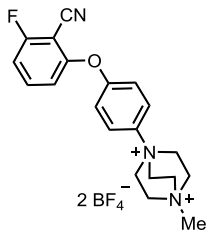
^{13}C NMR of ethyl 2-(4-TEDAphenoxy)benzoate (3c)

CD_3CN, 23 ºC



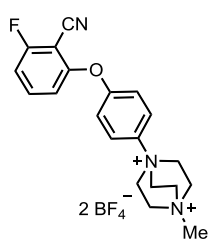
^{1}H NMR of 2-(4-TEDAphenoxy)-6-fluorobenzonitrile (3d)

Acetone-d_6, 23 ºC

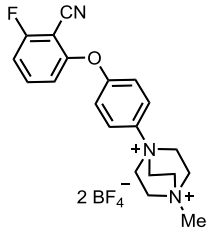


^{13}C NMR of 2-(4-TEDAphenoxy)-6-fluorobenzonitrile (3d)

Acetone-d_6, 23 ºC



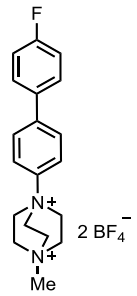
^{19}F NMR of 2-(4-TEDAphenoxy)-6-fluorobenzonitrile (3d)

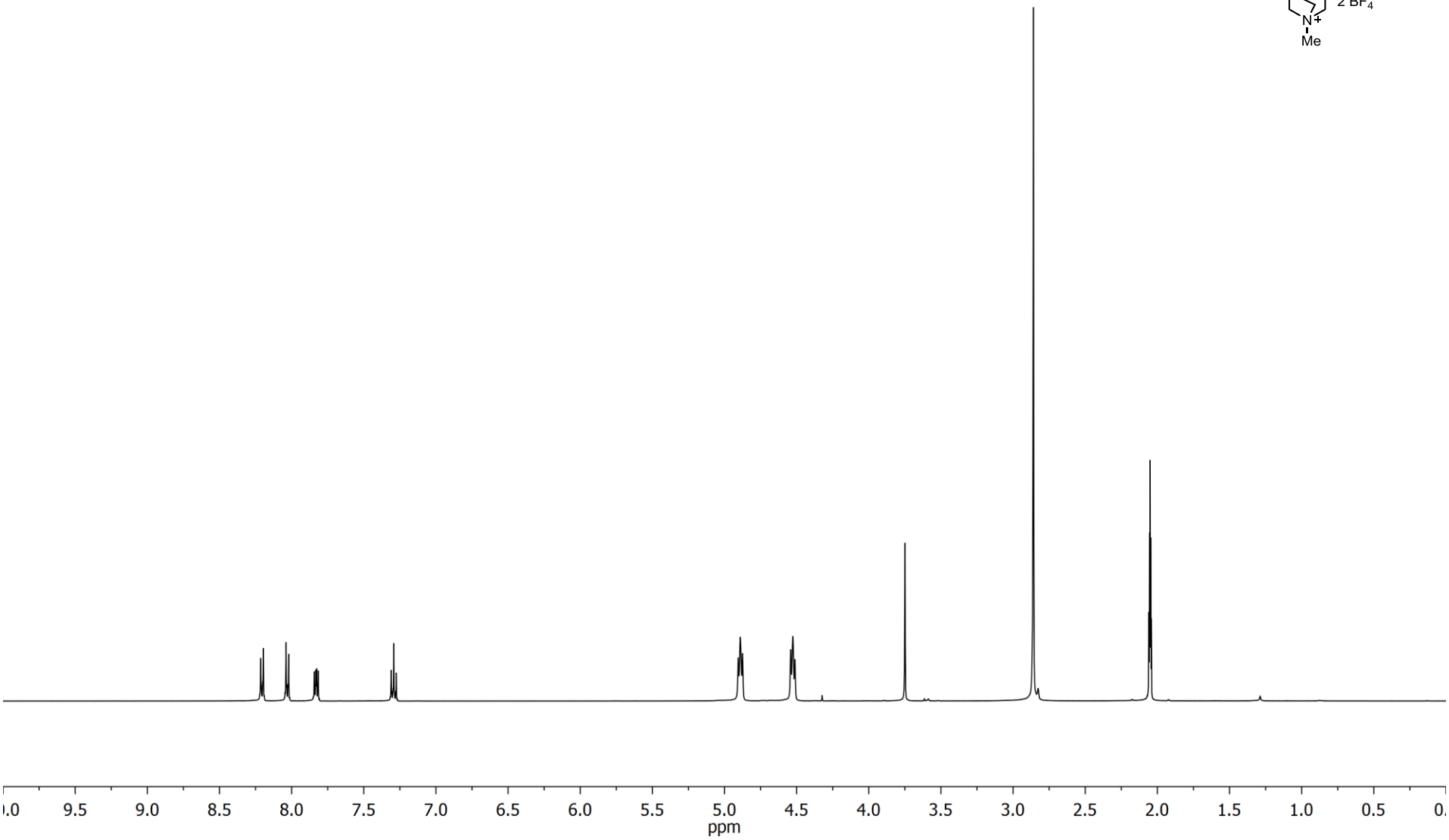


Acetone-d_6, 23 ºC

^{1}H NMR of 4-TEDA-4'-fluoro-[1,1'-biphenyl] (3e)

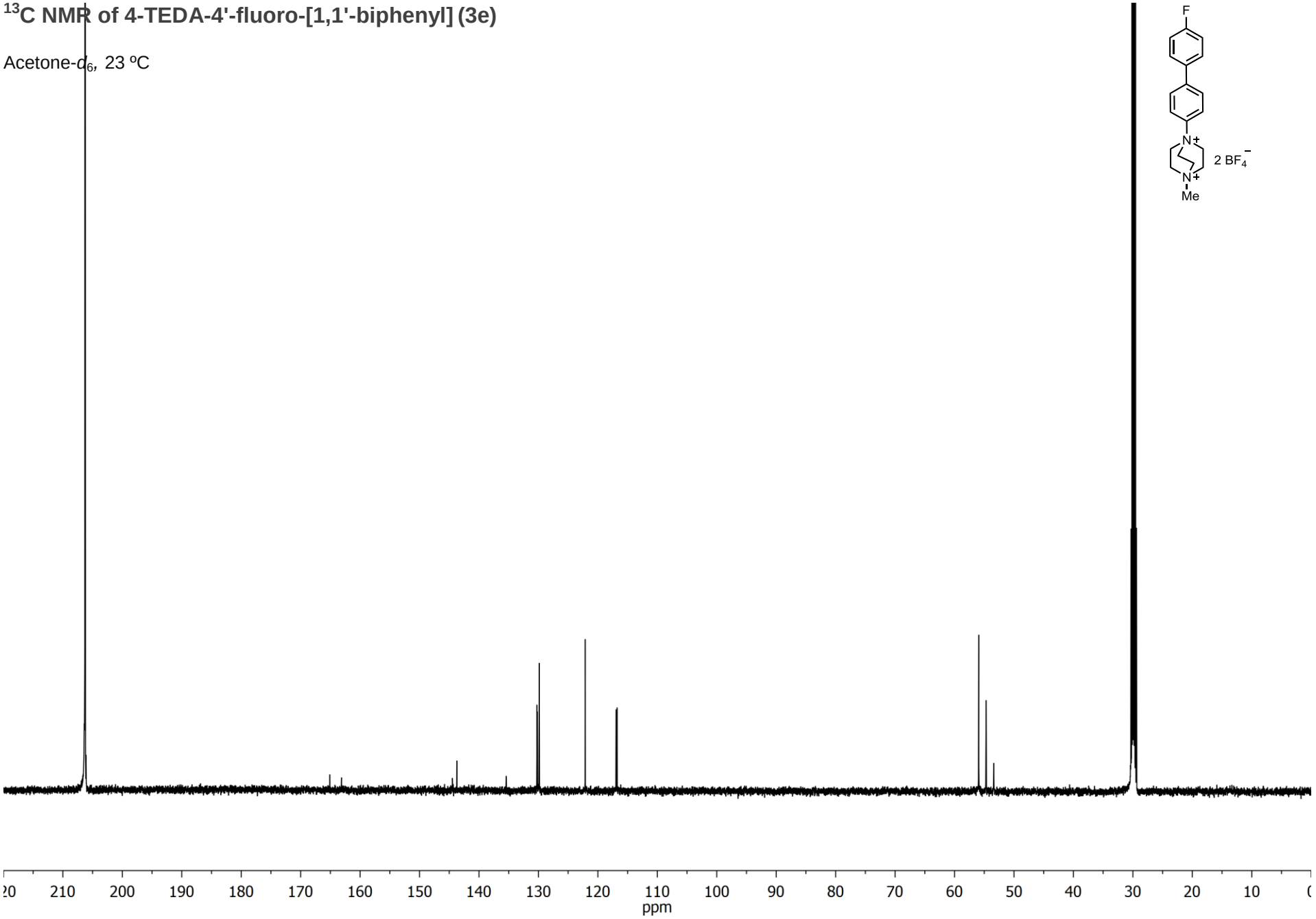
Acetone-d_6, 23 ºC





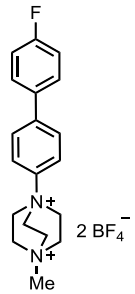
^{13}C NMR of 4-TEDA-4'-fluoro-[1,1'-biphenyl] (3e)

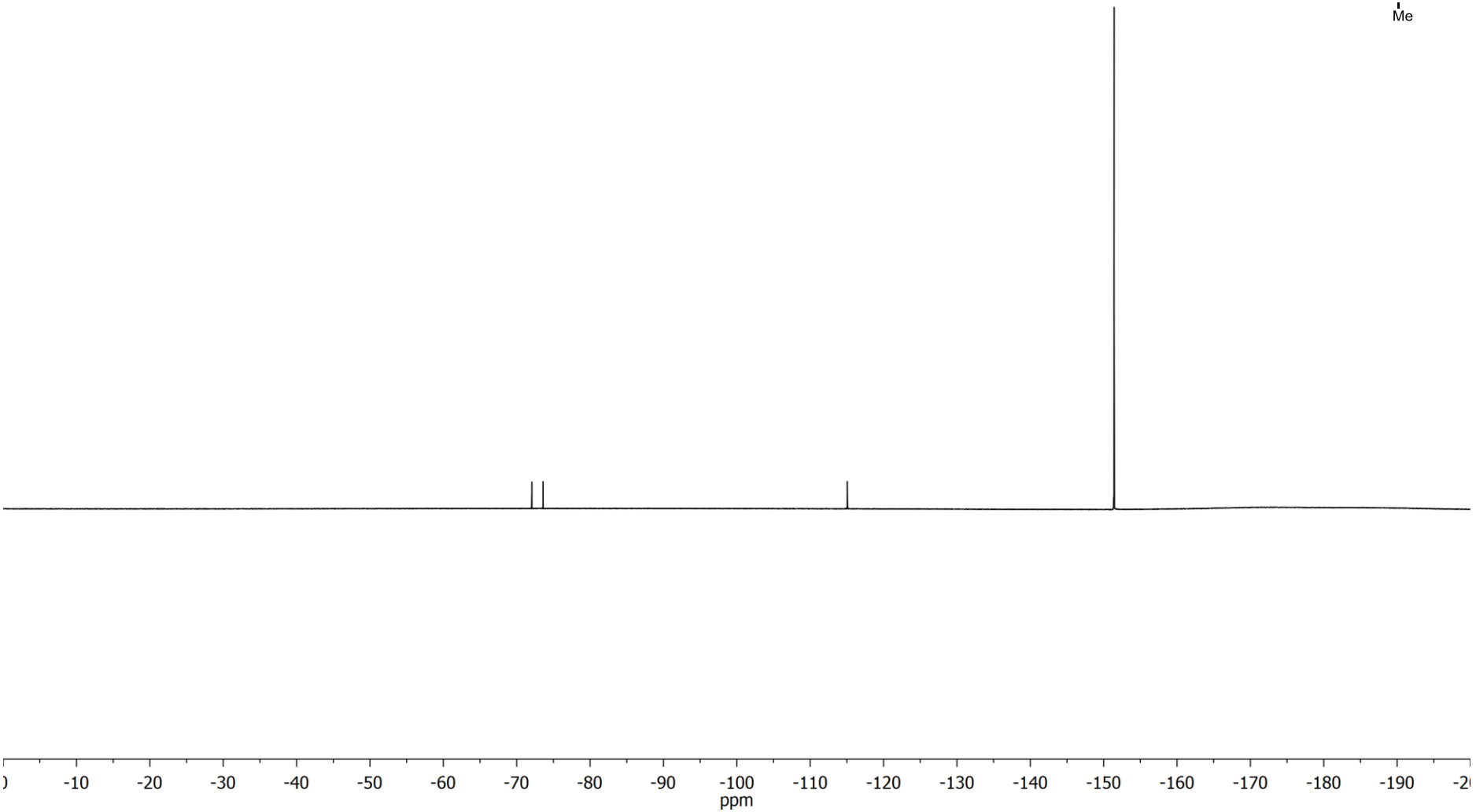
Acetone-d_6, 23 ºC



^{19}F NMR of 4-TEDA-4'-fluoro-[1,1'-biphenyl] (3e)

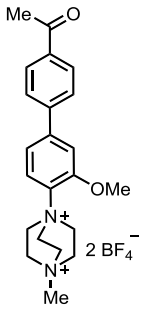
CD_3CN, 23 ºC





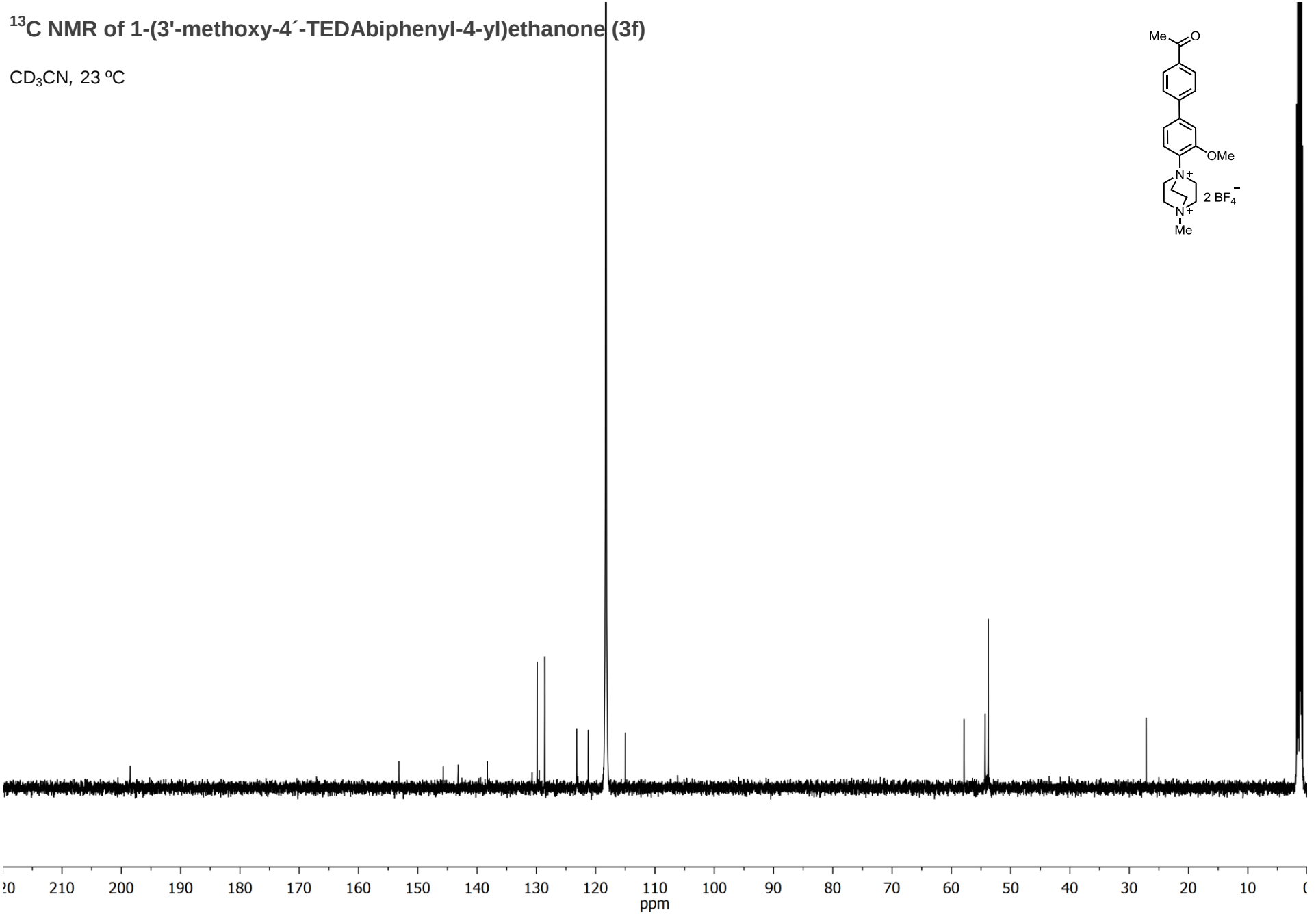
^{1}H NMR of 1-(3'-methoxy-4´-TEDAbiphenyl-4-yl)ethanone (3f)

Acetone-d_6, 23 ºC



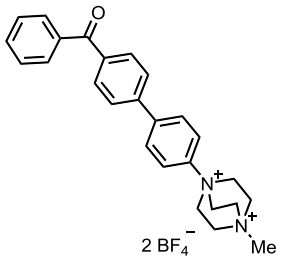
^{13}C NMR of 1-(3'-methoxy-4´-TEDAbiphenyl-4-yl)ethanone (3f)

CD_3CN, 23 ºC



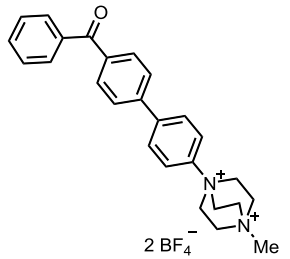
^{1}H NMR of (4'-TEDA-[1,1'-biphenyl]-4-yl)(phenyl)methanone (3g)

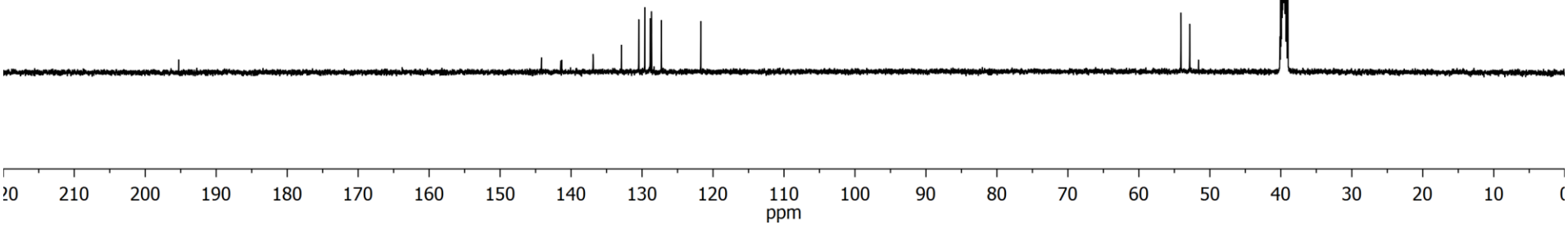
Acetone-d_6, 23 ºC



^{13}C NMR of (4'-TEDA-[1,1'-biphenyl]-4-yl)(phenyl)methanone (3g)

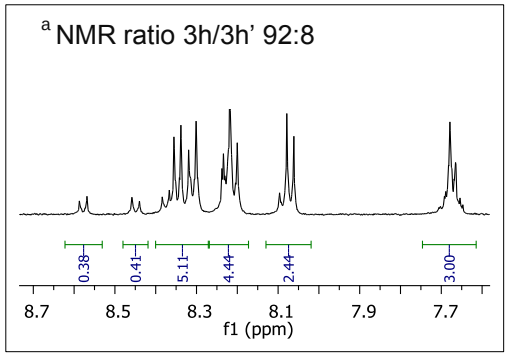
DMSO-d_6, 23 ºC

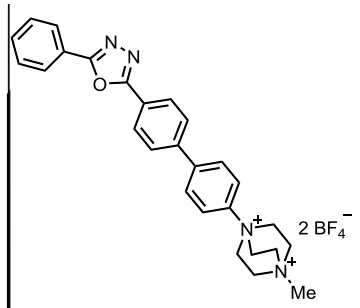




^{1}H NMR of 2-(4'-TEDA-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (3h) (containing 5% of 3h')[a]

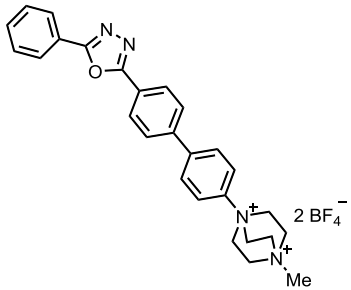
Acetone-d_6, 23 ºC





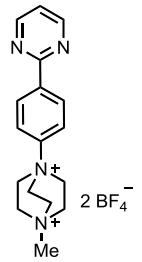
^{13}C NMR of 2-(4'-TEDA-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (3h)

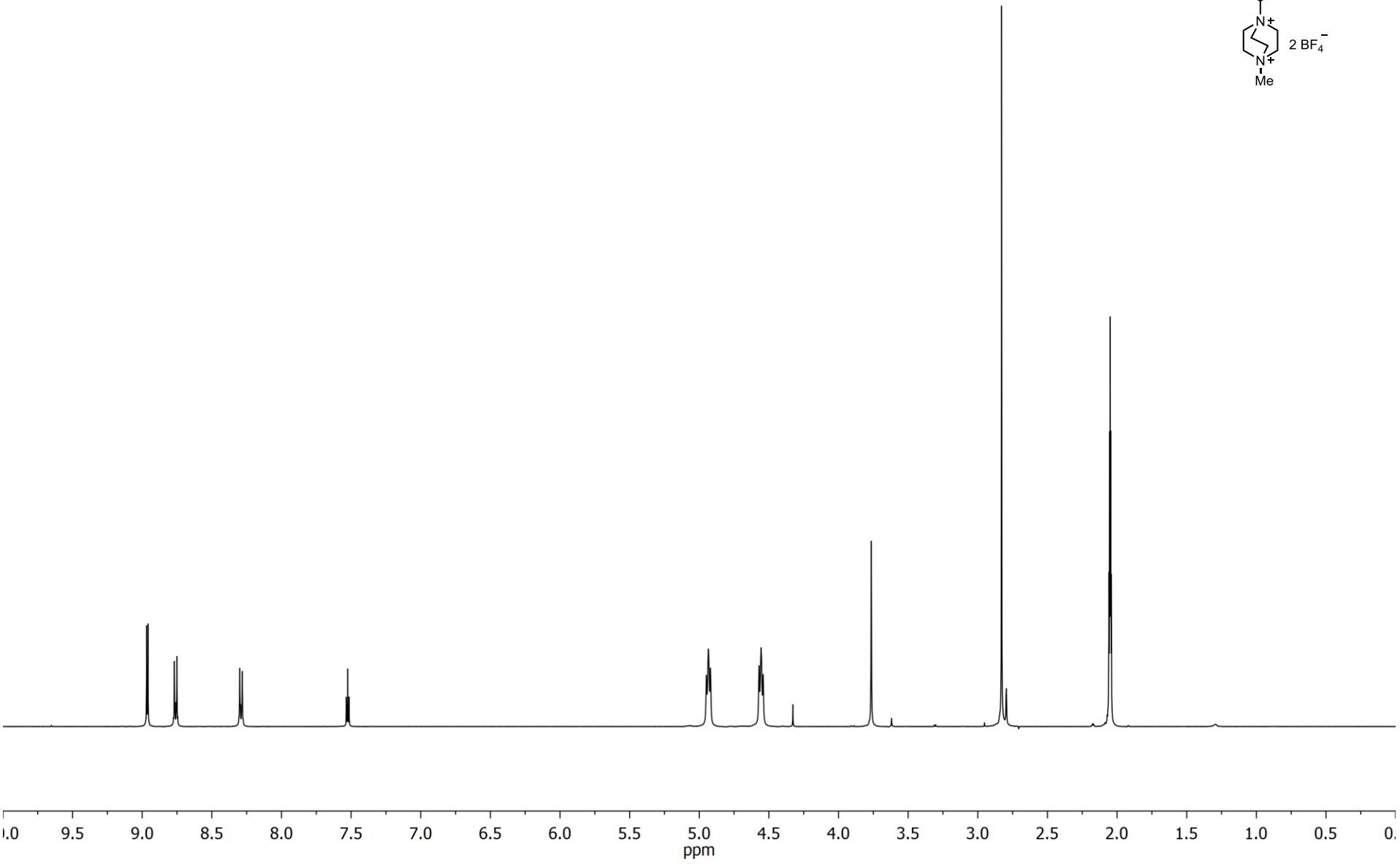
Acetone-d_6, 23 ºC (DMSO-d_6 was added to improve solubility)



^{1}H NMR of 2-(4-TEDAphenyl)pyrimidine (3i)

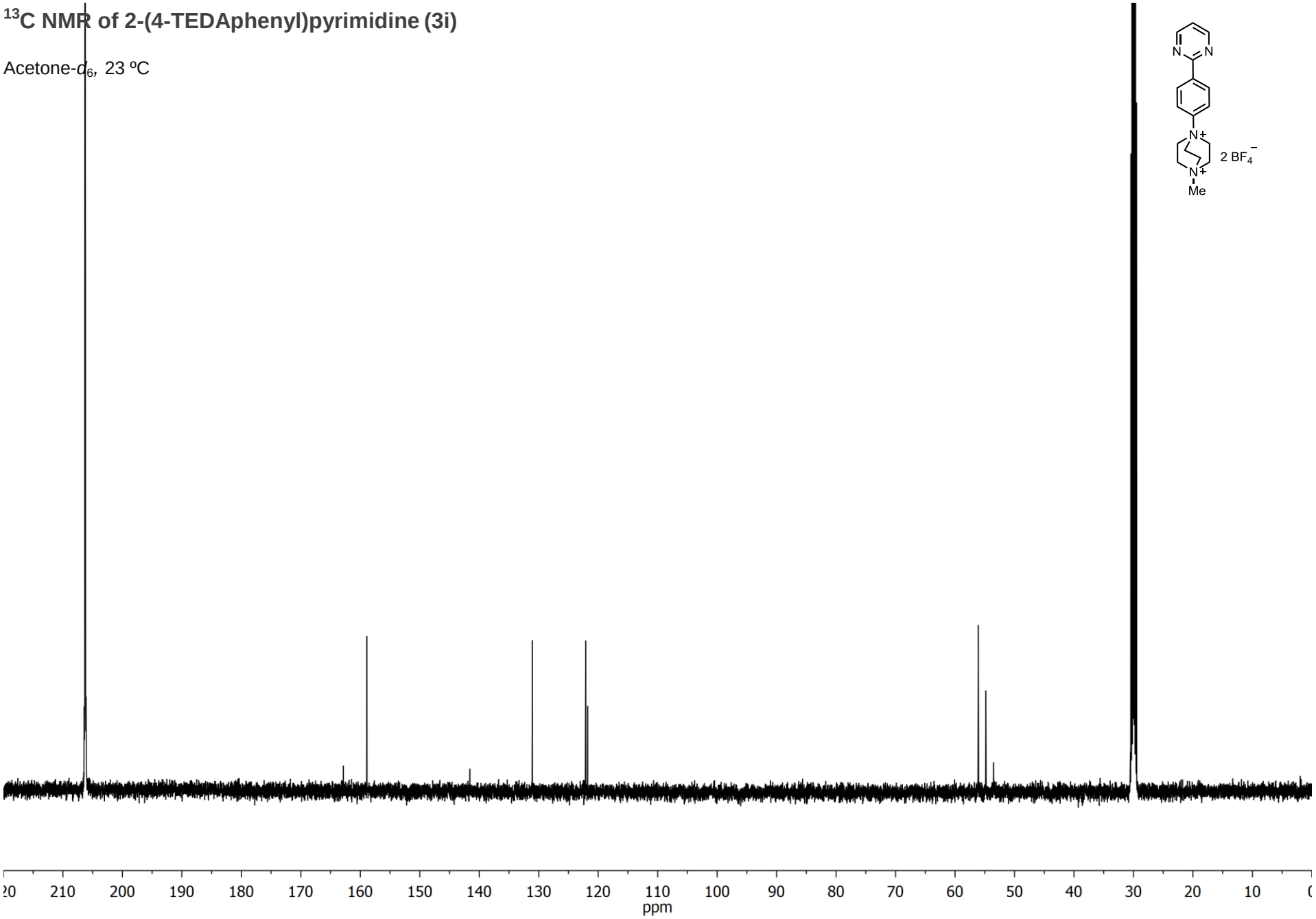
Acetone-d_6, 23 ºC





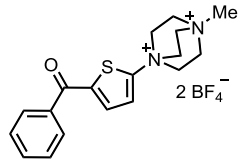
^{13}C NMR of 2-(4-TEDAphenyl)pyrimidine (3i)

Acetone-d_6, 23 ºC



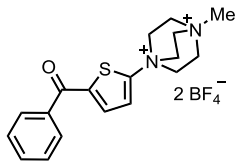
^{1}H NMR of (5-TEDAthiophen-2-yl)(phenyl)methanone (3j)

Acetone-d_6, 23 ºC



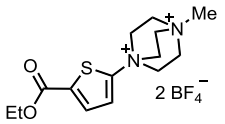
^{13}C NMR of (5-TEDAthiophen-2-yl)(phenyl)methanone (3j)

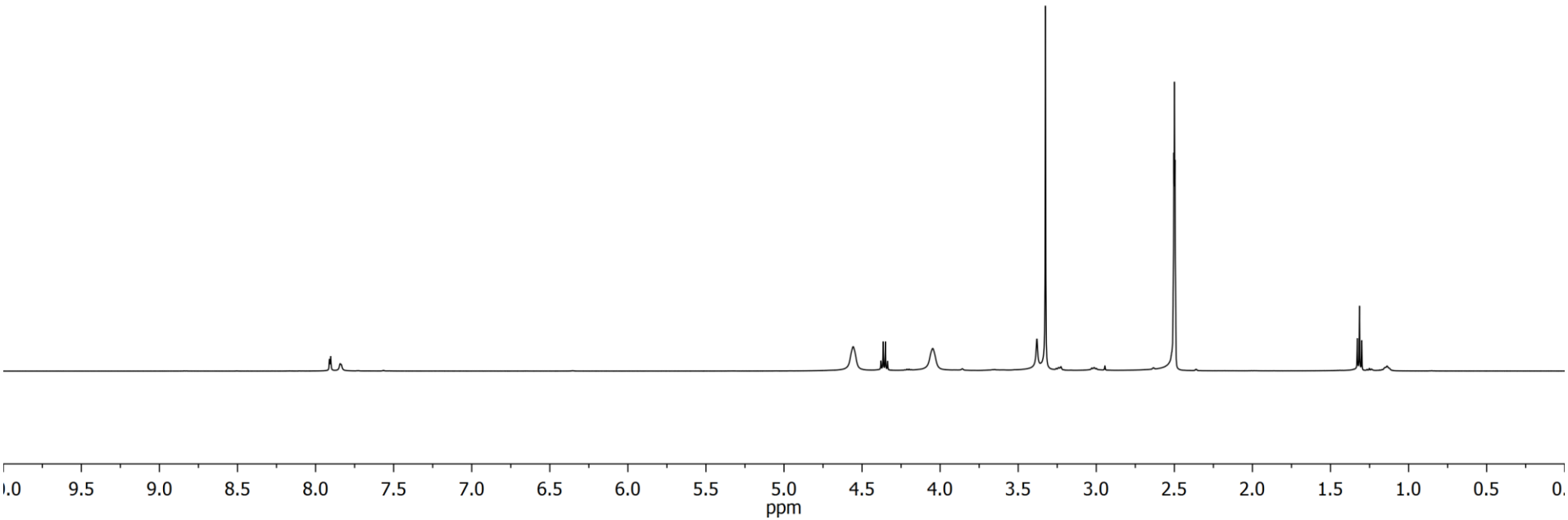
DMSO-d_6, 23 ºC



^{1}H NMR of ethyl 5-TEDAthiophene-2-carboxylate (3k)

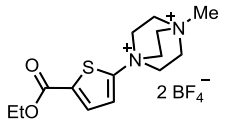
DMSO-d_6, 23 ºC





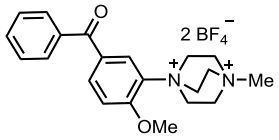
^{13}C NMR of ethyl 5-TEDAthiophene-2-carboxylate (3k)

DMSO-d_6, 23 ºC



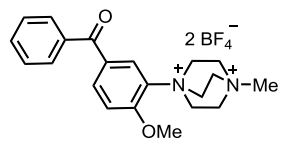
^{1}H NMR of (3-TEDA-4-methoxyphenyl)(phenyl)methanone (3l)

Acetone-d_6, 23 ºC



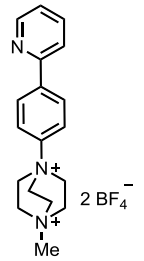
^{13}C NMR of (3-TEDA-4-methoxyphenyl)(phenyl)methanone (3l)

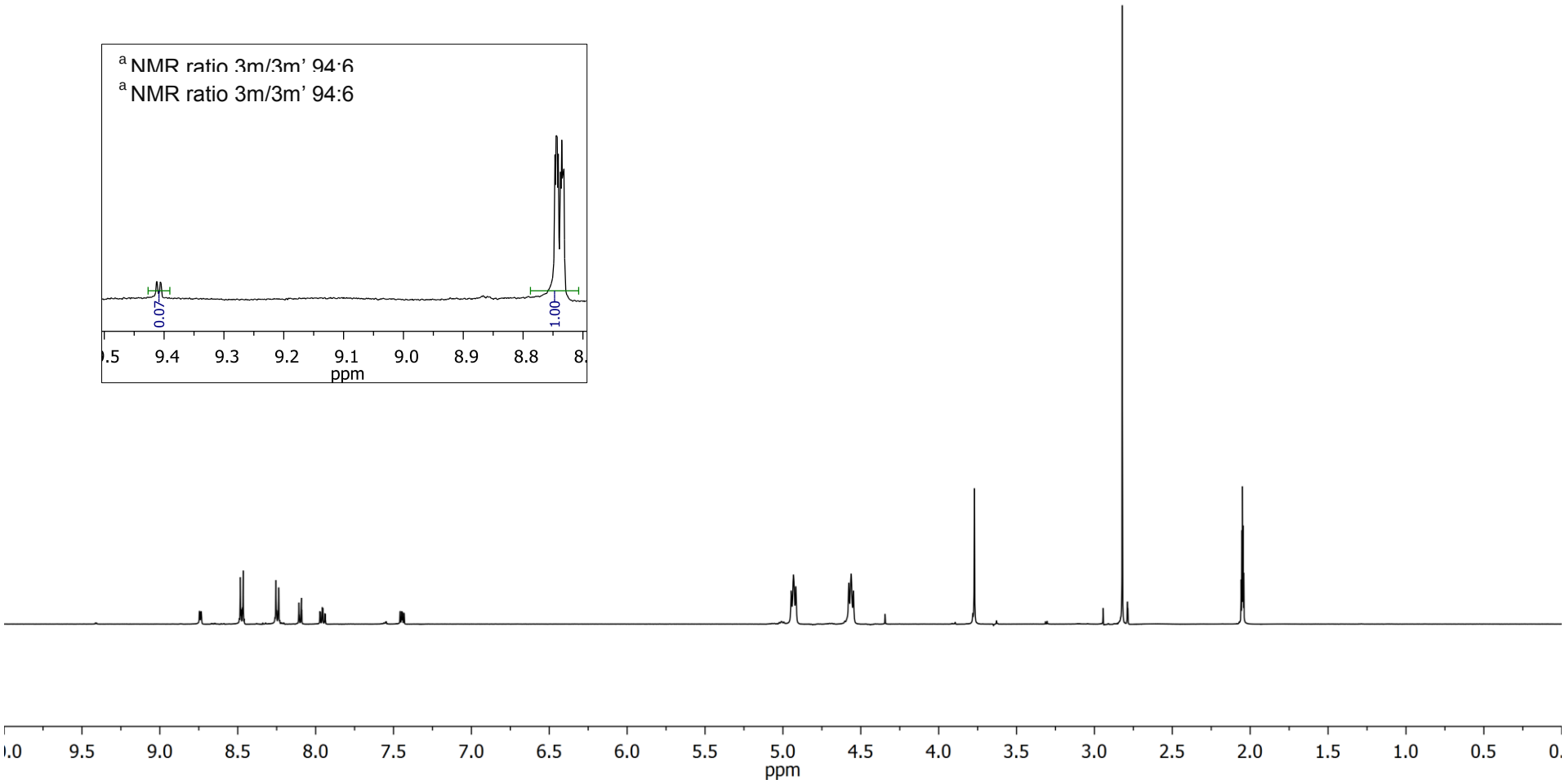
CD_3CN, 23 ºC



^{1}H NMR of 2-(4-TEDAphenyl)pyridine (3m) (containing 5% of 3m')[a]

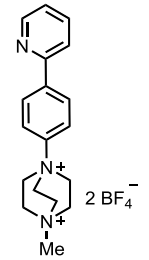
Acetone-d_6, 23 ºC





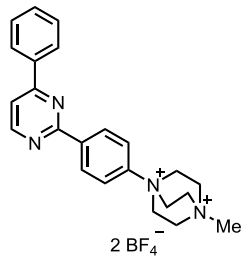
^{13}C NMR of 2-(4-TEDAphenyl)pyridine (3m)

DMSO-d_6, 23 ºC

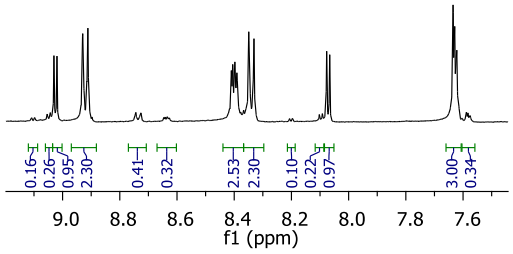


^{1}H NMR of 2-(4-TEDAphenyl)-4-phenylpyrimidine (3n) (containing ≈ 14% of 3n' and 11% of 3n'')[a]

Acetone-d_6, 23 ºC

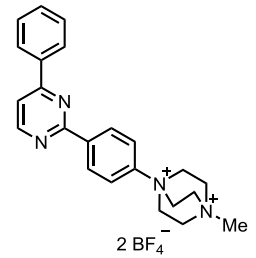


[a] NMR ratio 3n/3n'/3n'' 75:14:11



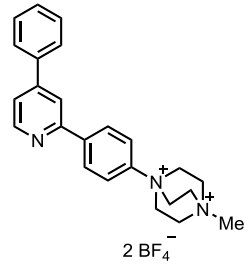
^{13}C NMR of 2-(4-TEDAphenyl)-4-phenylpyrimidine (3n)

CD_3CN, 23 ºC



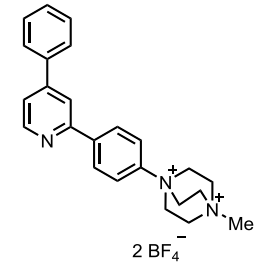
^{1}H NMR of 2-(4-TEDAphenyl)-4-phenylpyridine (3o)

Acetone-d_6, 23 ºC



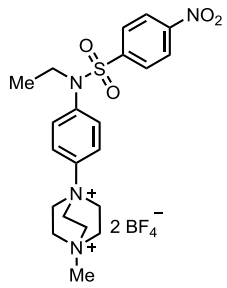
^{13}C NMR of 2-(4-TEDAphenyl)-4-phenylpyridine (3o)

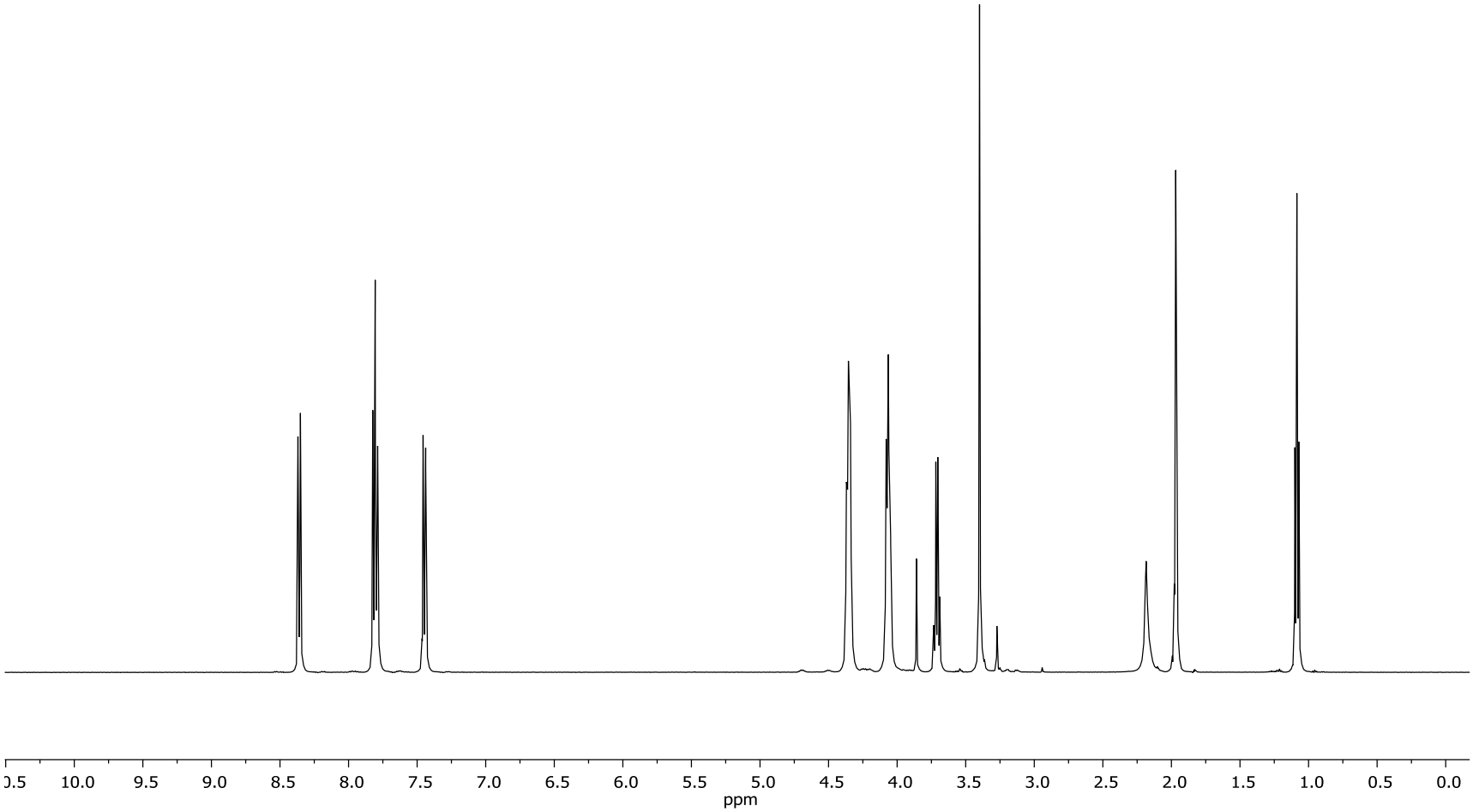
Acetone-d_6, 23 ºC



^{1}H NMR of *N*-ethyl-4-nitro-*N*-(4-TEDAphenyl)benzenesulfonamide (3p)

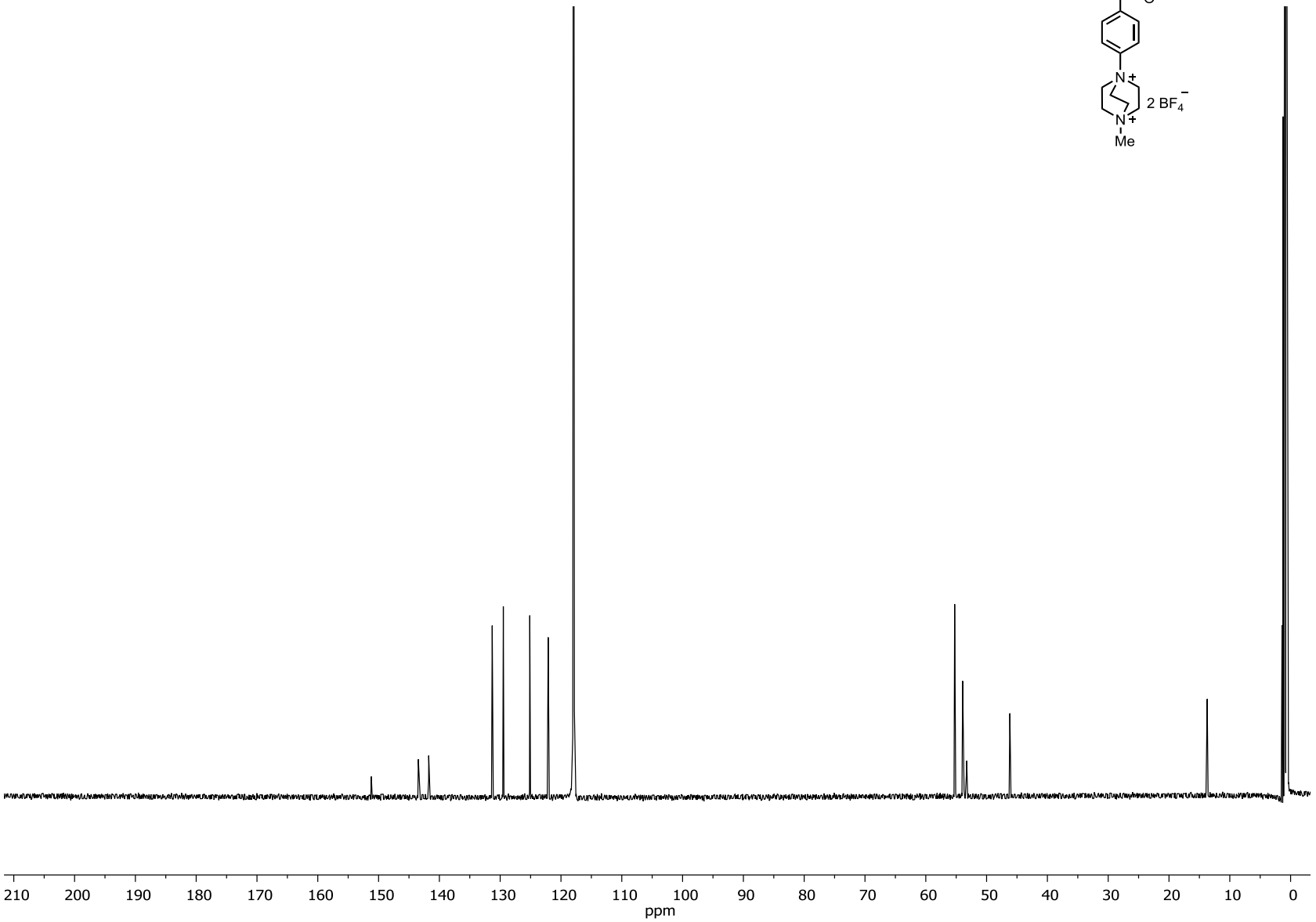
CD_3CN, 23 ^oC





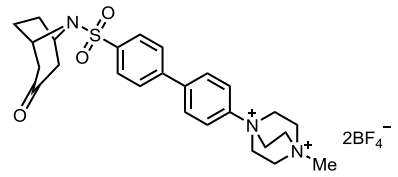
^{13}C NMR of *N*-ethyl-4-nitro-*N*-(4-TEDAphenyl)benzenesulfonamide (3p)

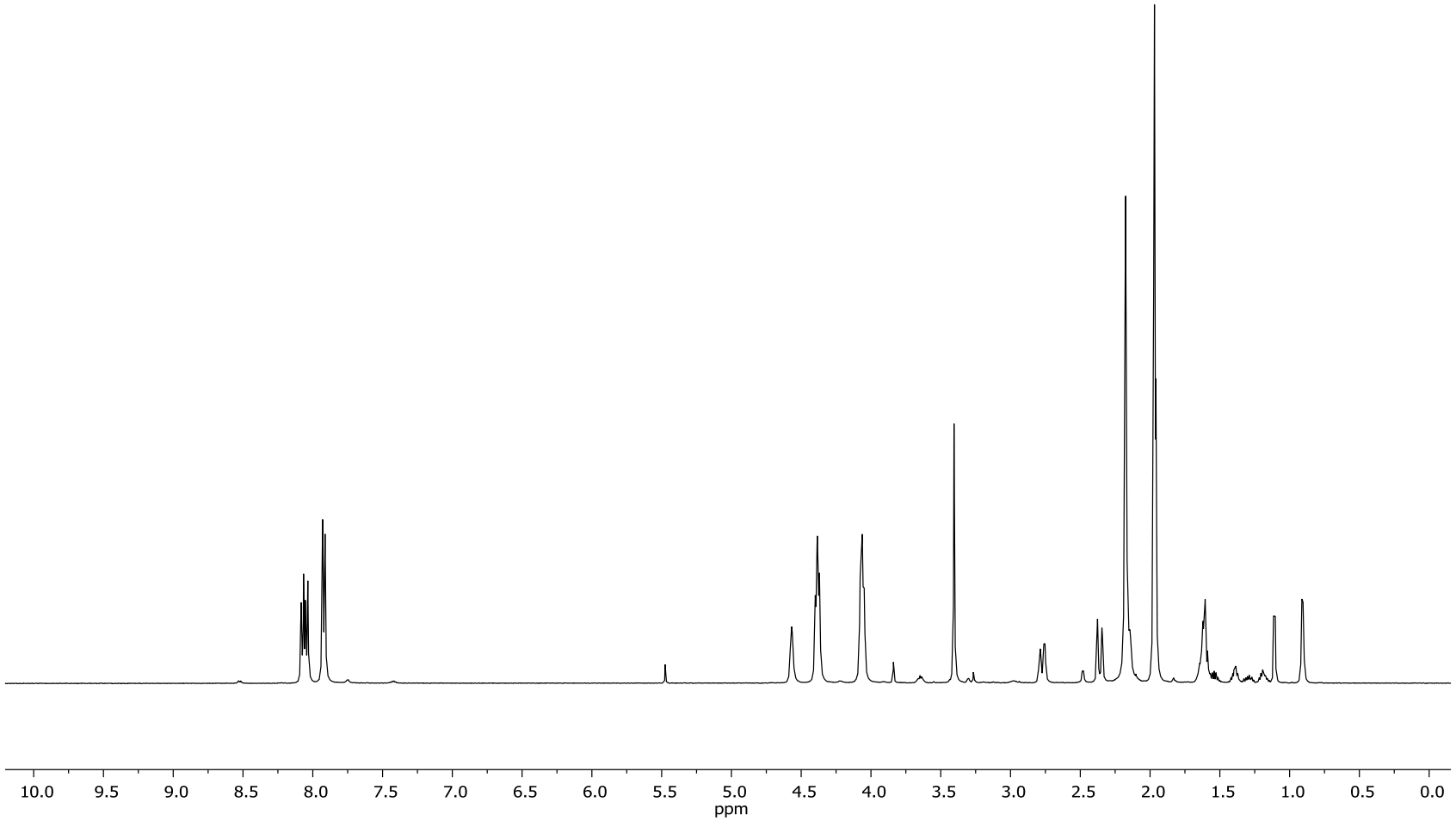
CD_3CN, 23 °C



^{1}H NMR of *N*-(4-TEDAphenyl-4-sulfonyl)nortropinone (3q)

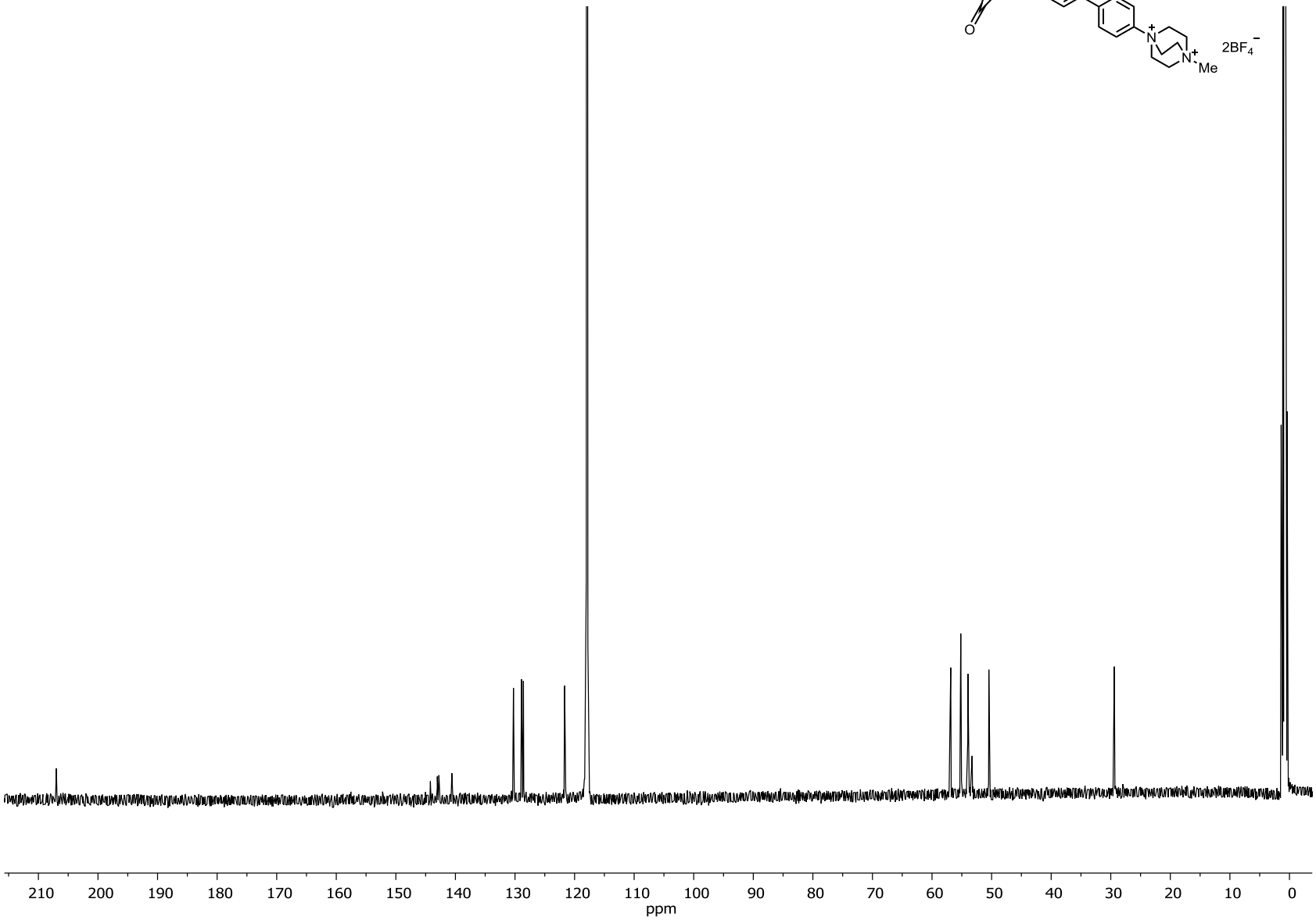
CD_3CN, 23 °C





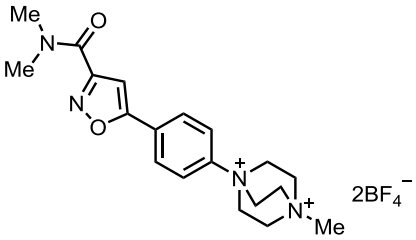
^{13}C NMR of *N*-(4-TEDAphenyl-4-sulfonyl)nortropinone (3q)

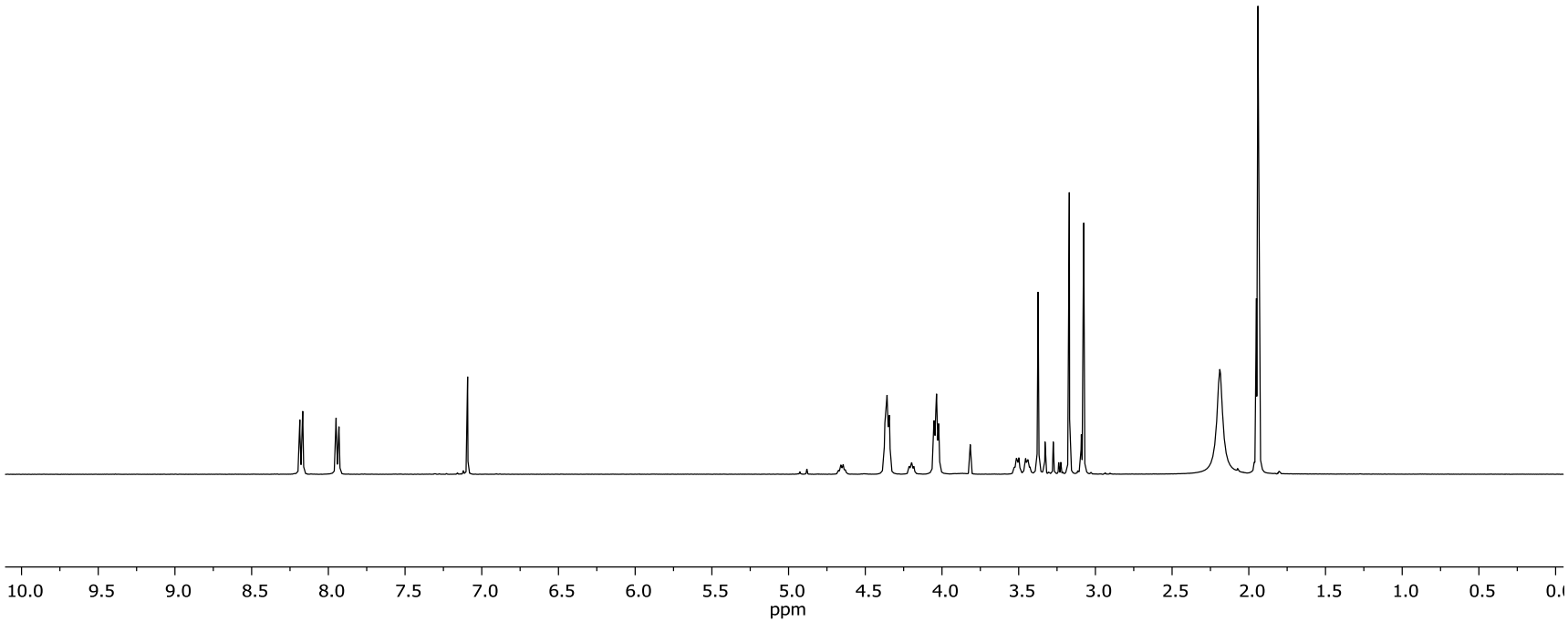
CD_3CN, 23 °C



^{1}H NMR of *N*,*N*-dimethyl-5-(4-TEDAphenyl)isoxazole-3-carboxamide (3r)

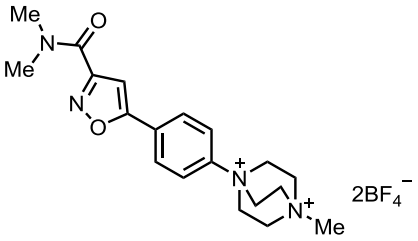
CD_3CN, 23 °C

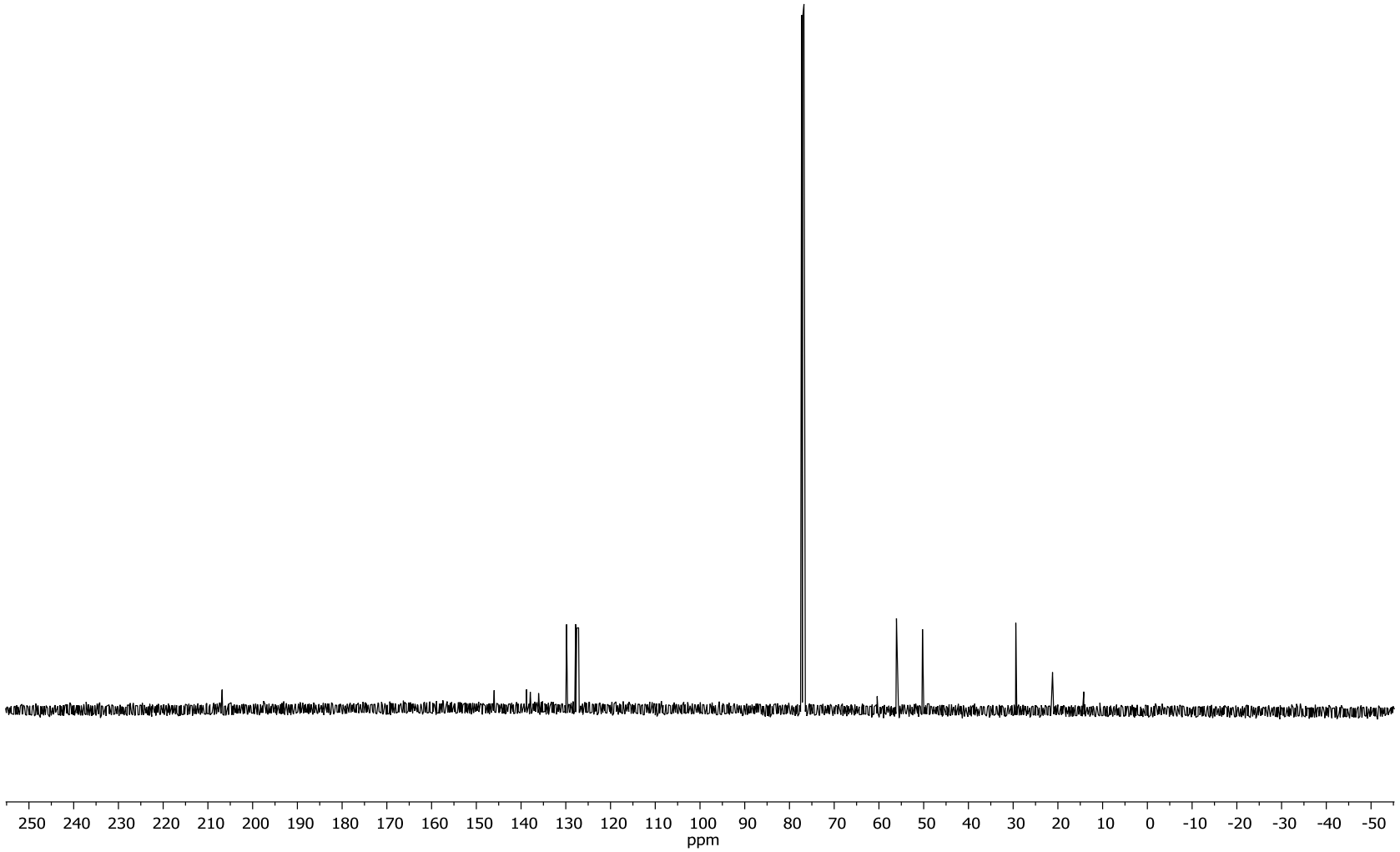




^{13}C NMR of *N*,*N*-dimethyl-5-(4-TEDAphenyl)isoxazole-3-carboxamide (3r)

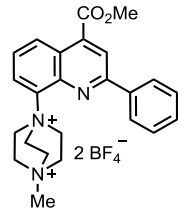
CD_3CN, 23 °C





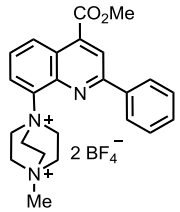
^{1}H NMR of methyl 8-TEDA-2-phenylquinoline-4-carboxylate (3s) (in mixture with 2 constituional isomers - 72:19:9 ratio)

DMSO-d_6, 23 ºC



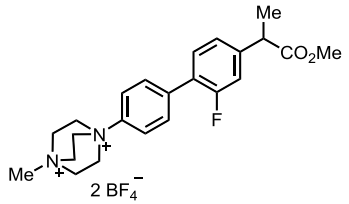
^{13}C NMR of methyl 8-TEDA-2-phenylquinoline-4-carboxylate (3s) (in mixture with 2 constitutional isomers - 72:19:9 ratio)

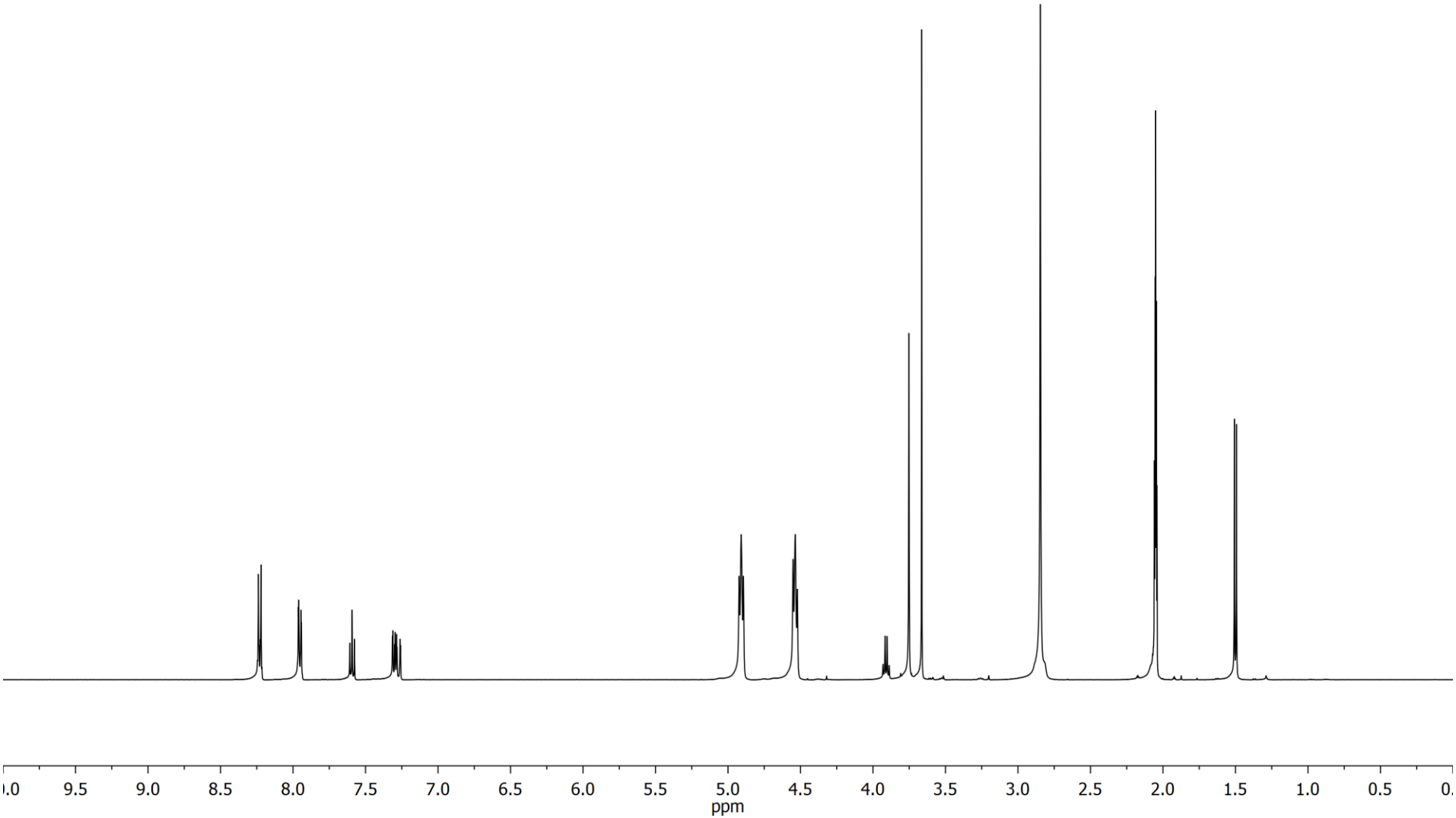
Acetone-d_6, 23 ºC



^{1}H NMR of (±)-methyl 2-(4'-TEDA-2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (3t)

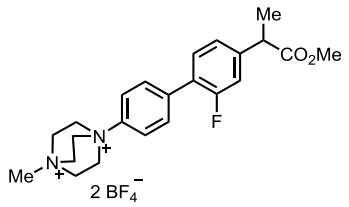
Acetone-d_6, 23 ºC





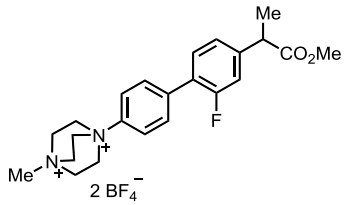
^{13}C NMR of (±)-methyl 2-(4'-TEDA-2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (3t)

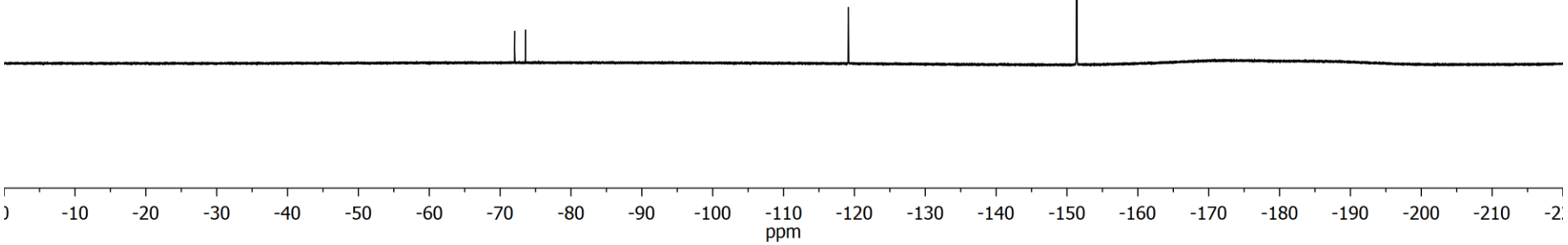
CD_3CN, 23 ºC



^{19}F NMR of (±)-methyl 2-(4'-TEDA-2-fluoro-[1,1'-biphenyl]-4-yl)propanoate (3t)

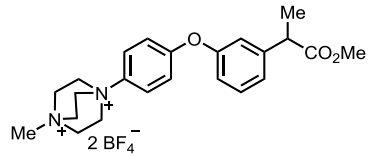
CD_3CN, 23 ºC





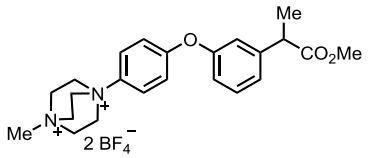
^{1}H NMR of (±)-methyl 2-(3-(4-TEDAphenoxy)phenyl)propanoate (3u)

Acetone-d_6, 23 ºC



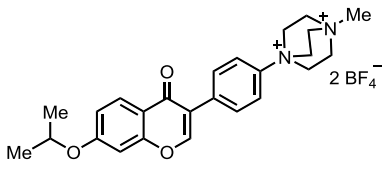
^{13}C NMR of (±)-methyl 2-(3-(4-TEDAphenoxy)phenyl)propanoate (3u)

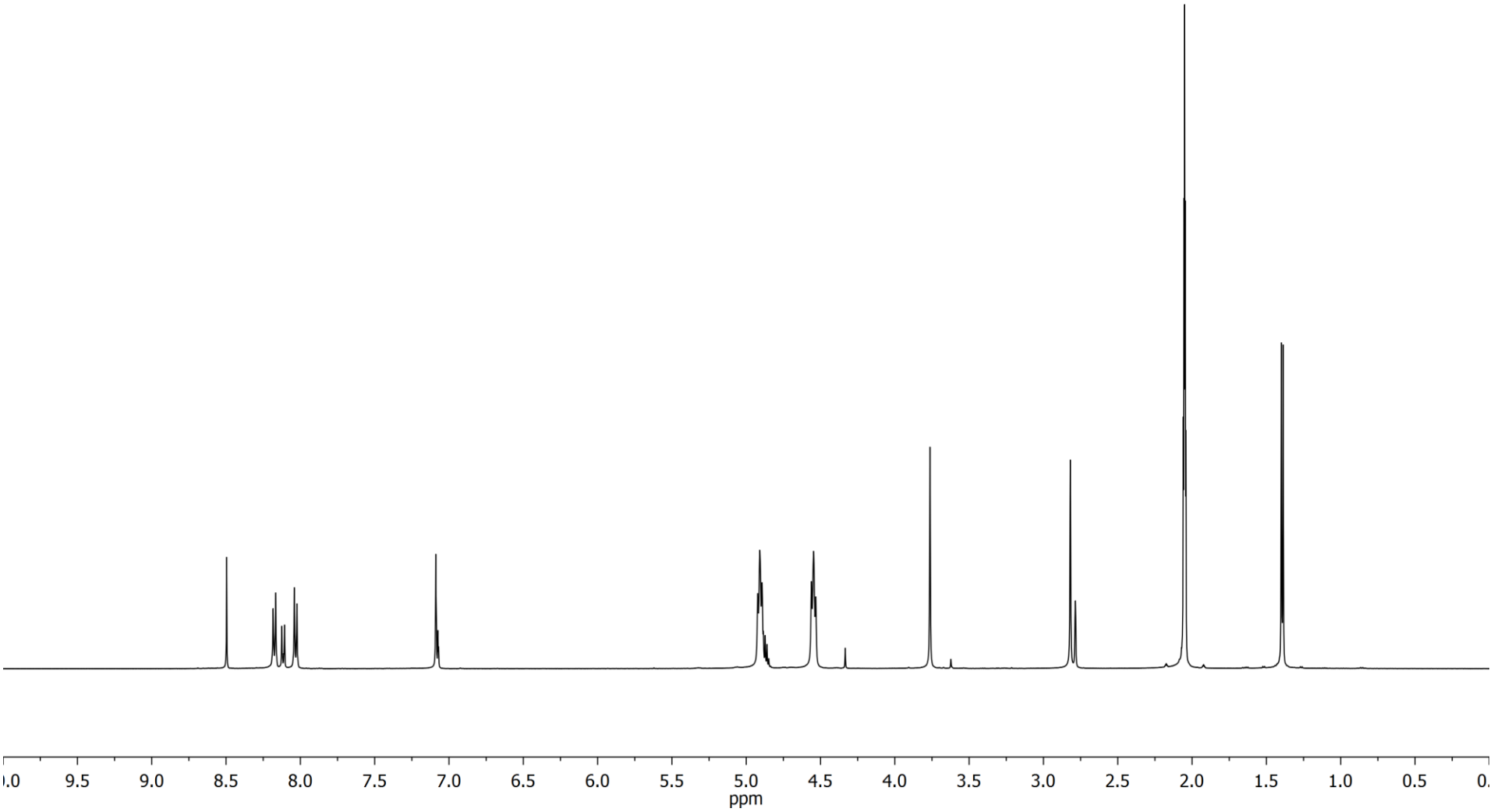
CD_3CN, 23 ºC



^{1}H NMR of 3-(4-TEDAphenyl)-7-isopropoxy-4H-chromen-4-one (3v)

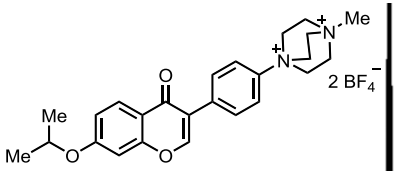
Acetone-d_6, 23 ºC





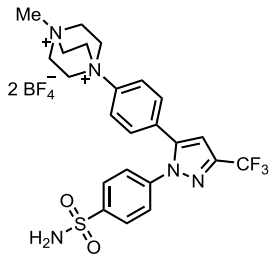
^{13}C NMR of 3-(4-TEDAphenyl)-7-isopropoxy-4H-chromen-4-one (3v)

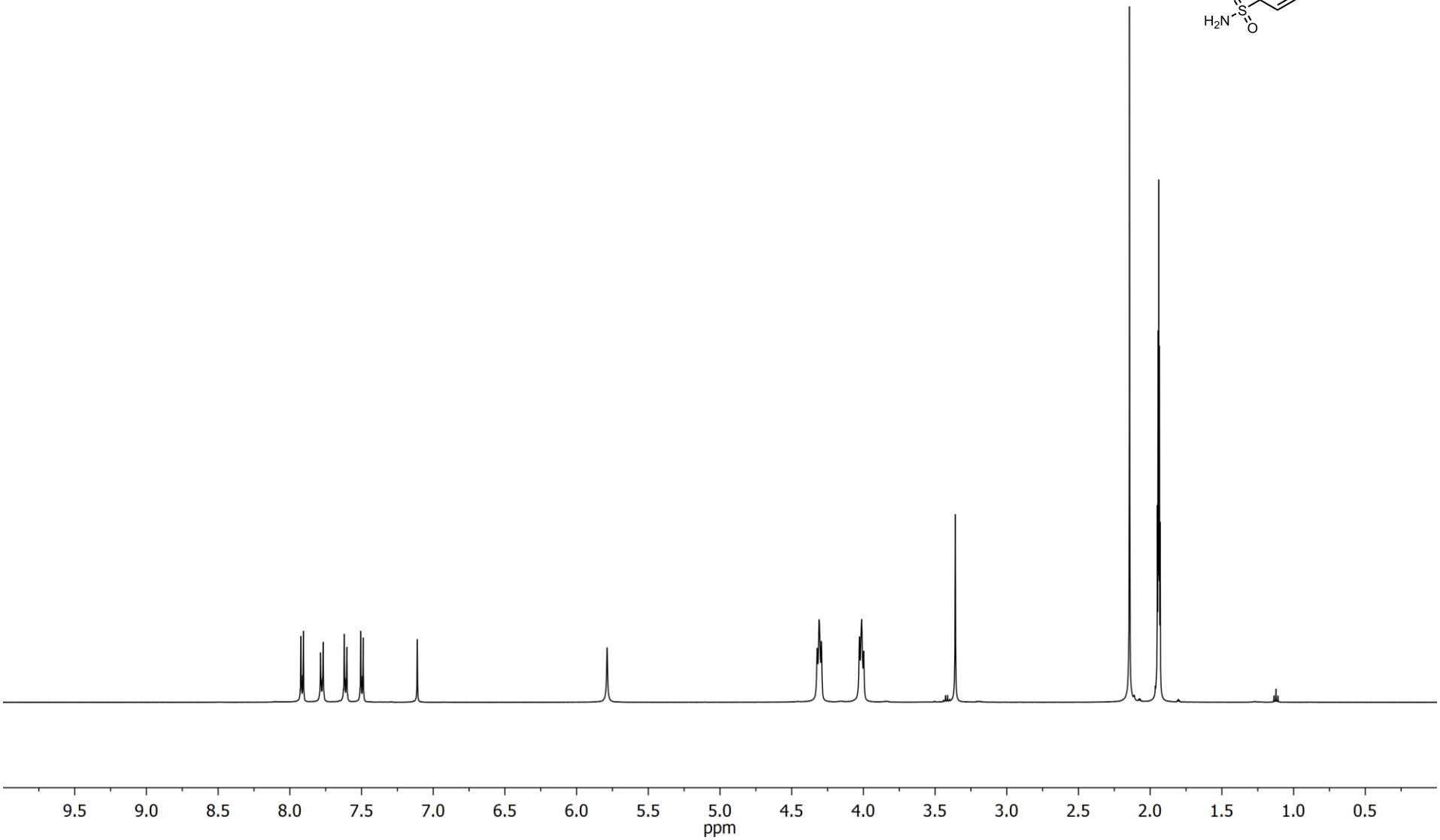
Acetone-d_6, 23 ºC



^{1}H NMR of 4-(5-(4-TEDAphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (3w)

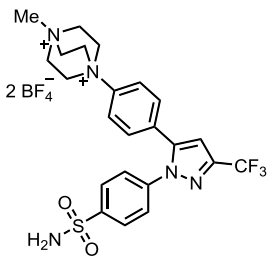
CD_3CN, 23 ºC





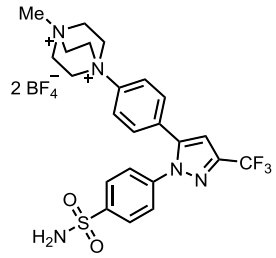
^{13}C NMR of 4-(5-(4-TEDAphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (3w)

CD_3CN, 23 ºC



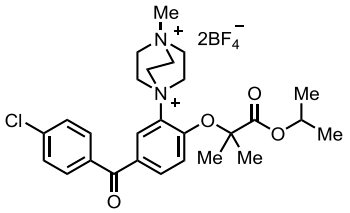
^{19}F NMR of 4-(5-(4-TEDAphenyl)-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzenesulfonamide (3w)

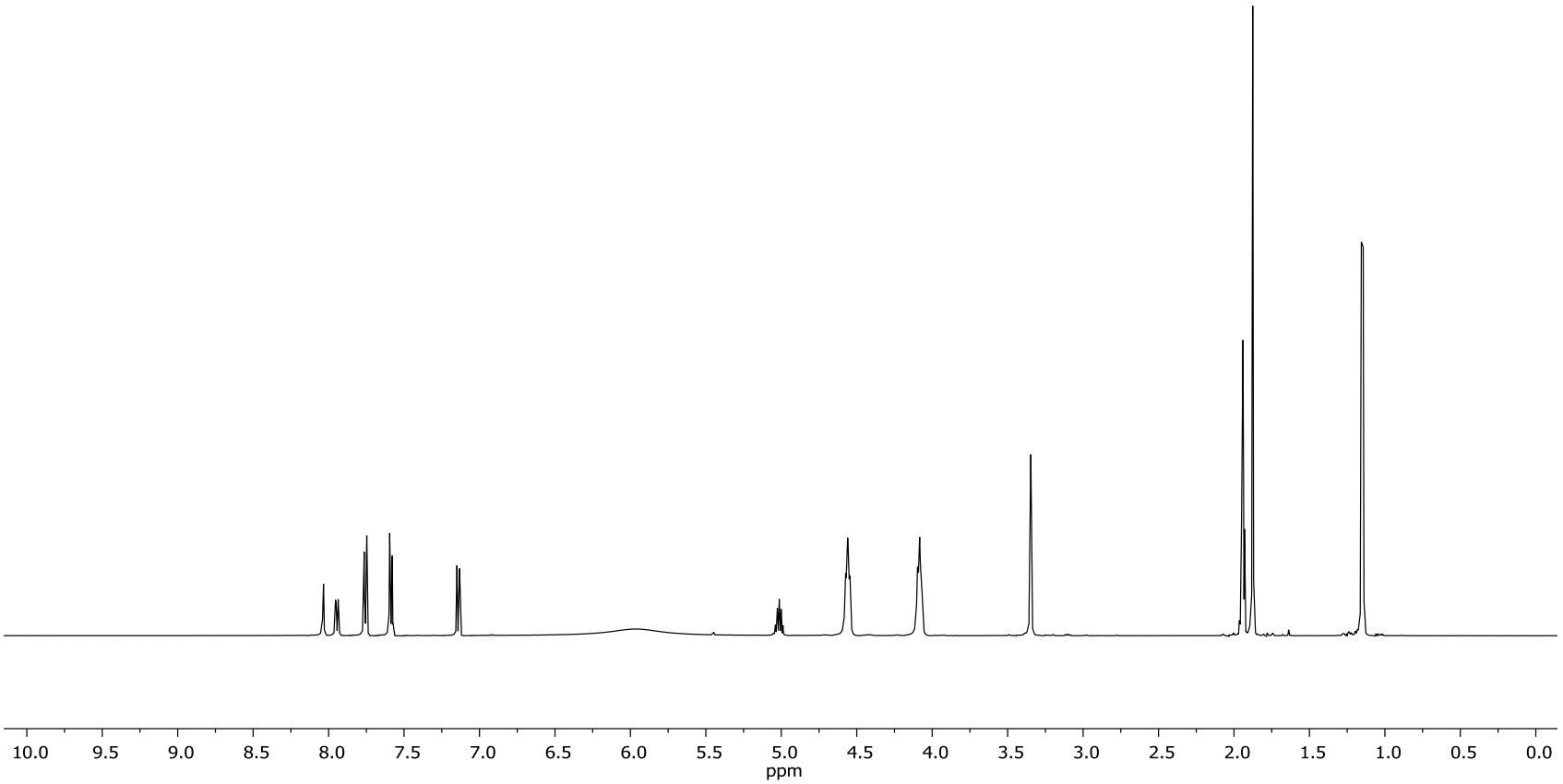
CD_3CN, 23 ºC



^{1}H NMR of isopropyl 2-(4-(4-chlorobenzoyl)-2-TEDAphenoxy)-2-methylpropanoate (3x)

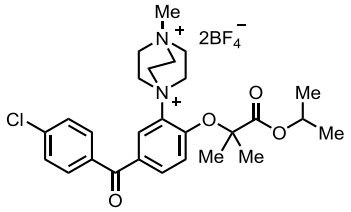
CD_3CN, 23 ^oC



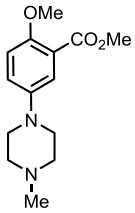


^{13}C NMR of isopropyl 2-(4-(4-chlorobenzoyl)-2-TEDAphenoxy)-2-methylpropanoate (3x)

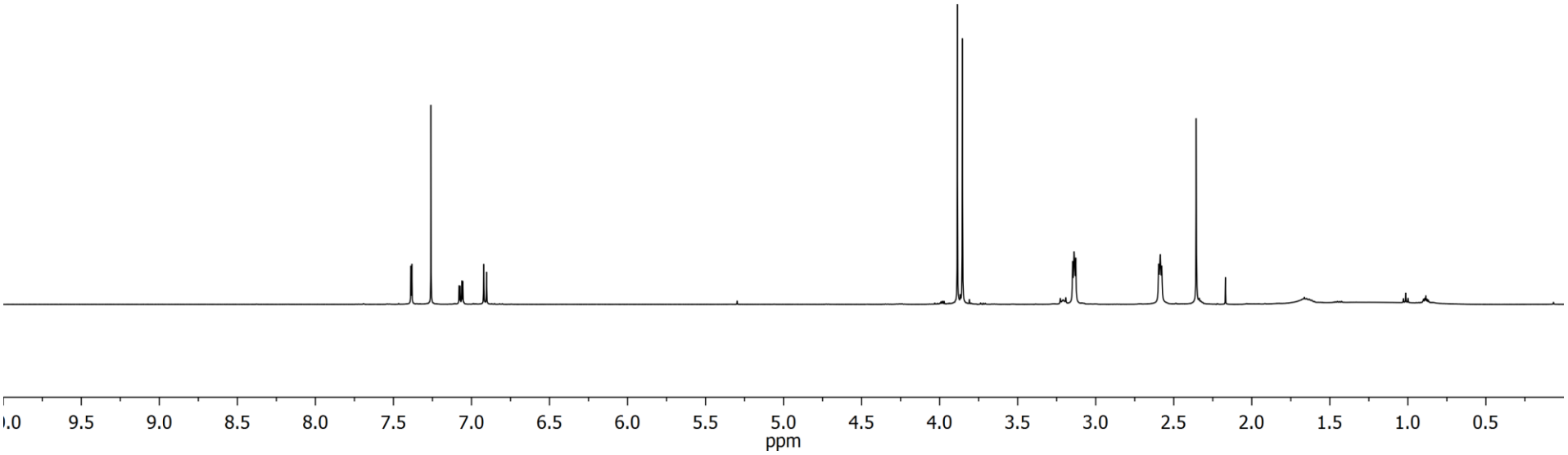
CD_3CN, 23 ^{o}C



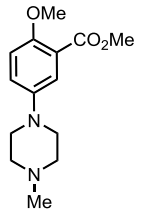
^{1}H NMR of methyl 2-methoxy-5-(4-methylpiperazin-1-yl)benzoate (5)



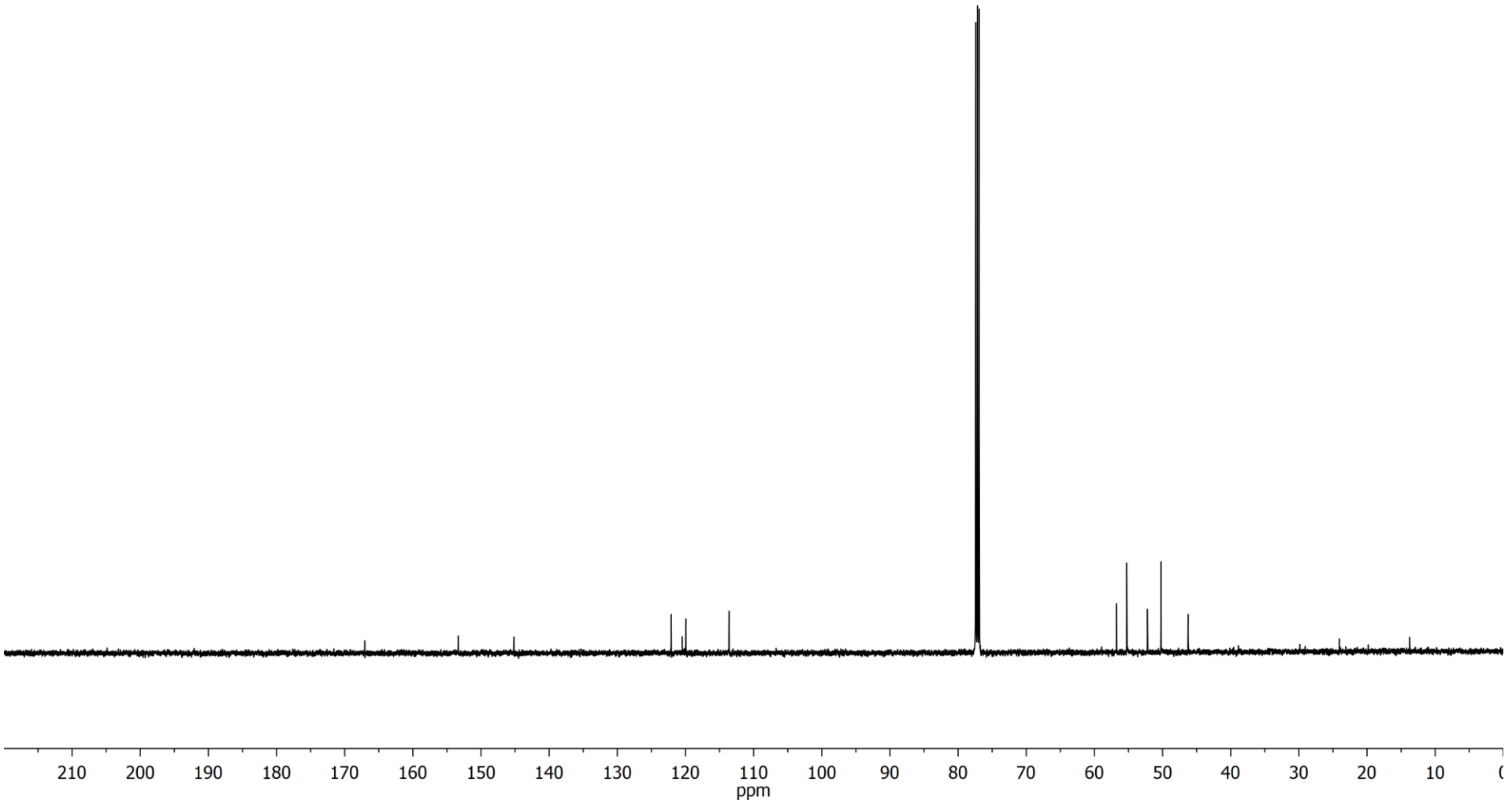
$CDCl_3$, 23 ºC



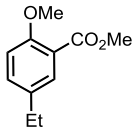
^{13}C NMR of methyl 2-methoxy-5-(4-methylpiperazin-1-yl)benzoate (5)



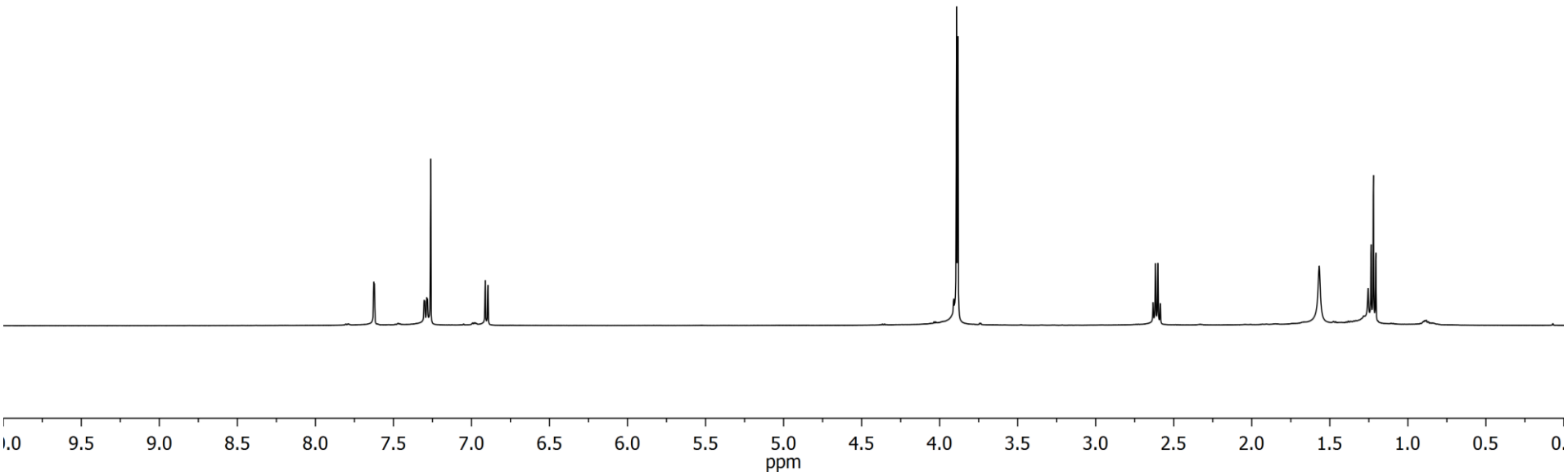
$CDCl_3$, 23 ºC



^{1}H NMR of methyl 2-methoxy-5-ethylbenzoate (4a´)

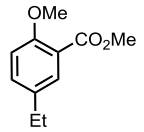


$CDCl_3$, 23 ºC

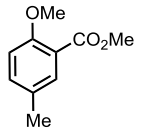


^{13}C NMR of methyl 2-methoxy-5-ethylbenzoate (4a´)

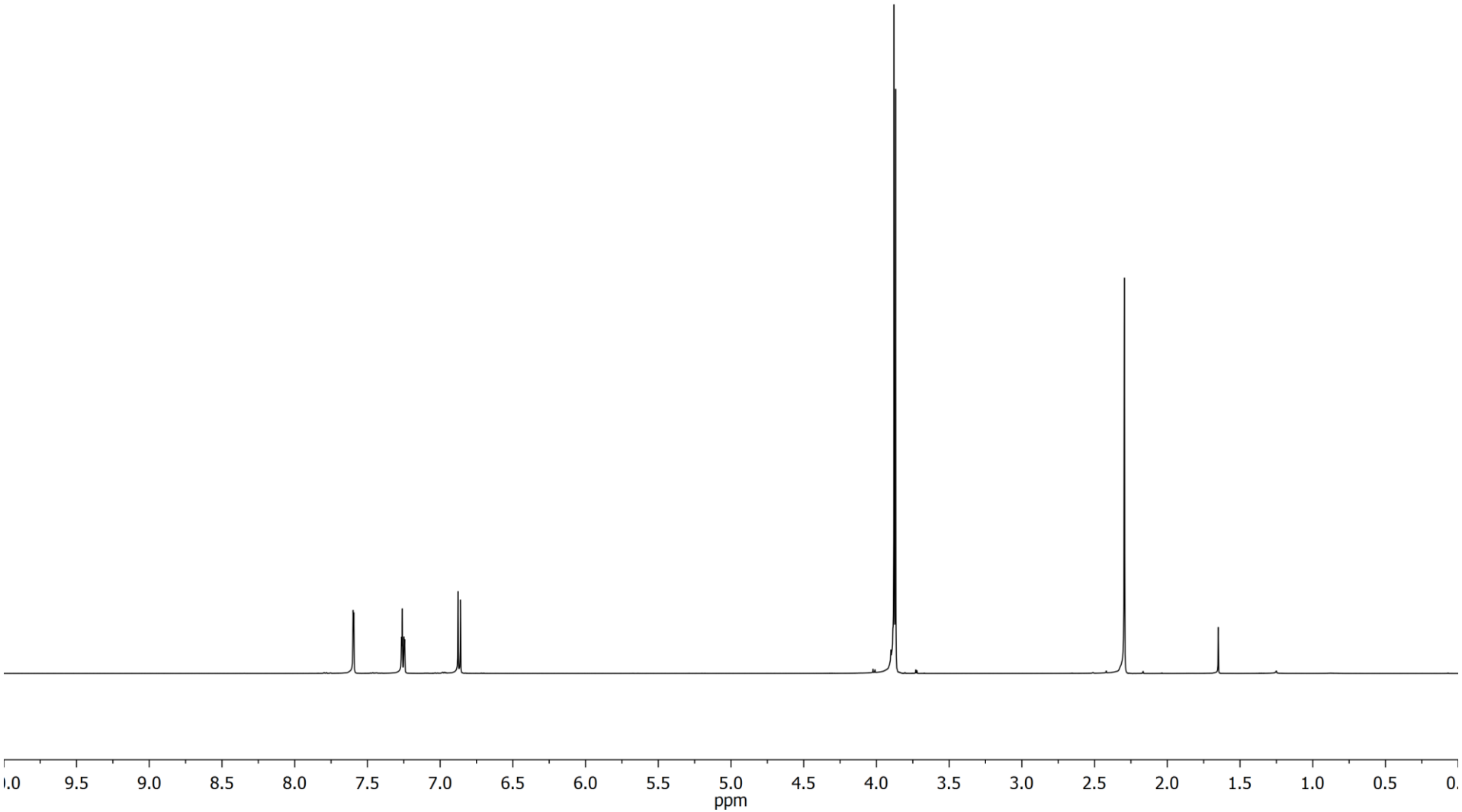
$CDCl_3$, 23 ºC



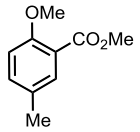
^{1}H NMR of methyl 2-methoxy-5-methylbenzoate (4a)



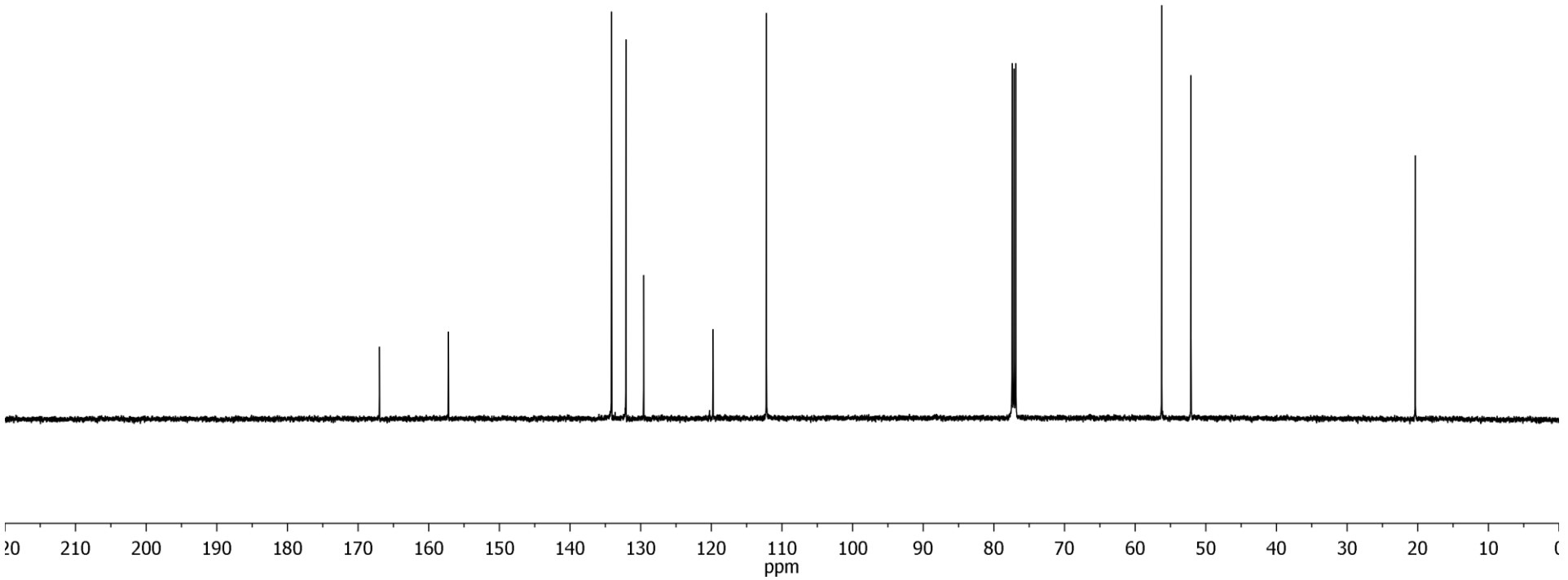
$CDCl_3$, 23 ºC



^{13}C NMR of methyl 2-methoxy-5-methylbenzoate (4a)

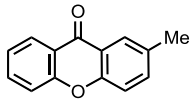


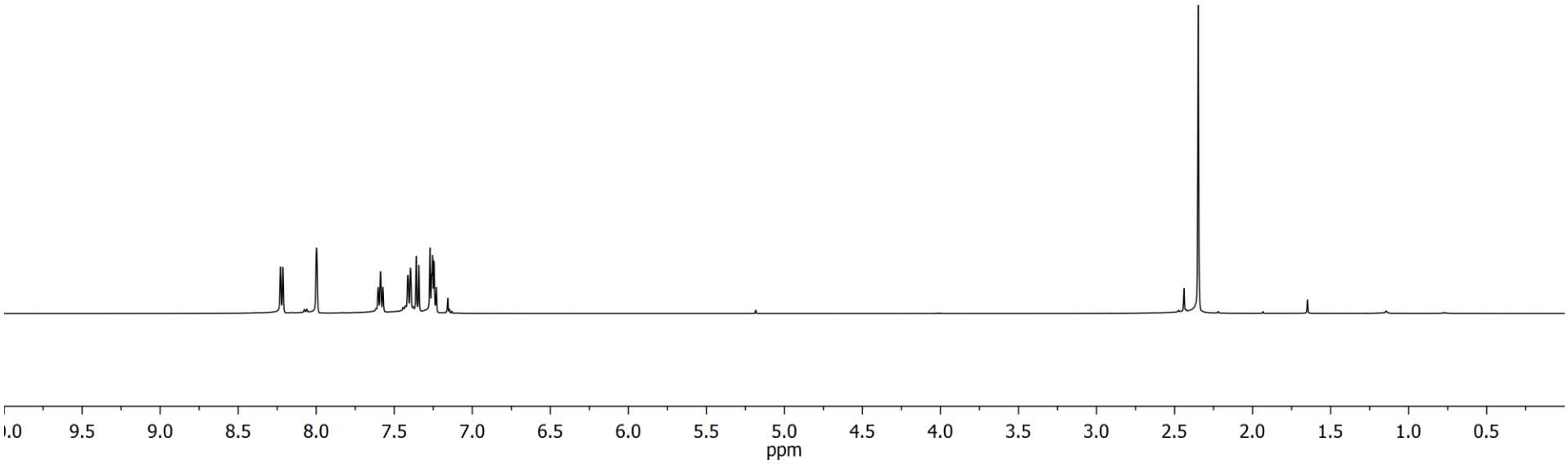
$CDCl_3$, 23 ºC



^{1}H NMR of 2-methyl-9H-xanthen-9-one (4b)

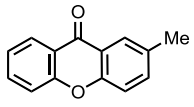
$CDCl_3$, 23 ºC





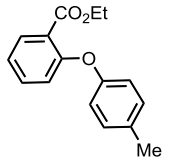
^{13}C NMR of 2-methyl-9H-xanthen-9-one (4b)

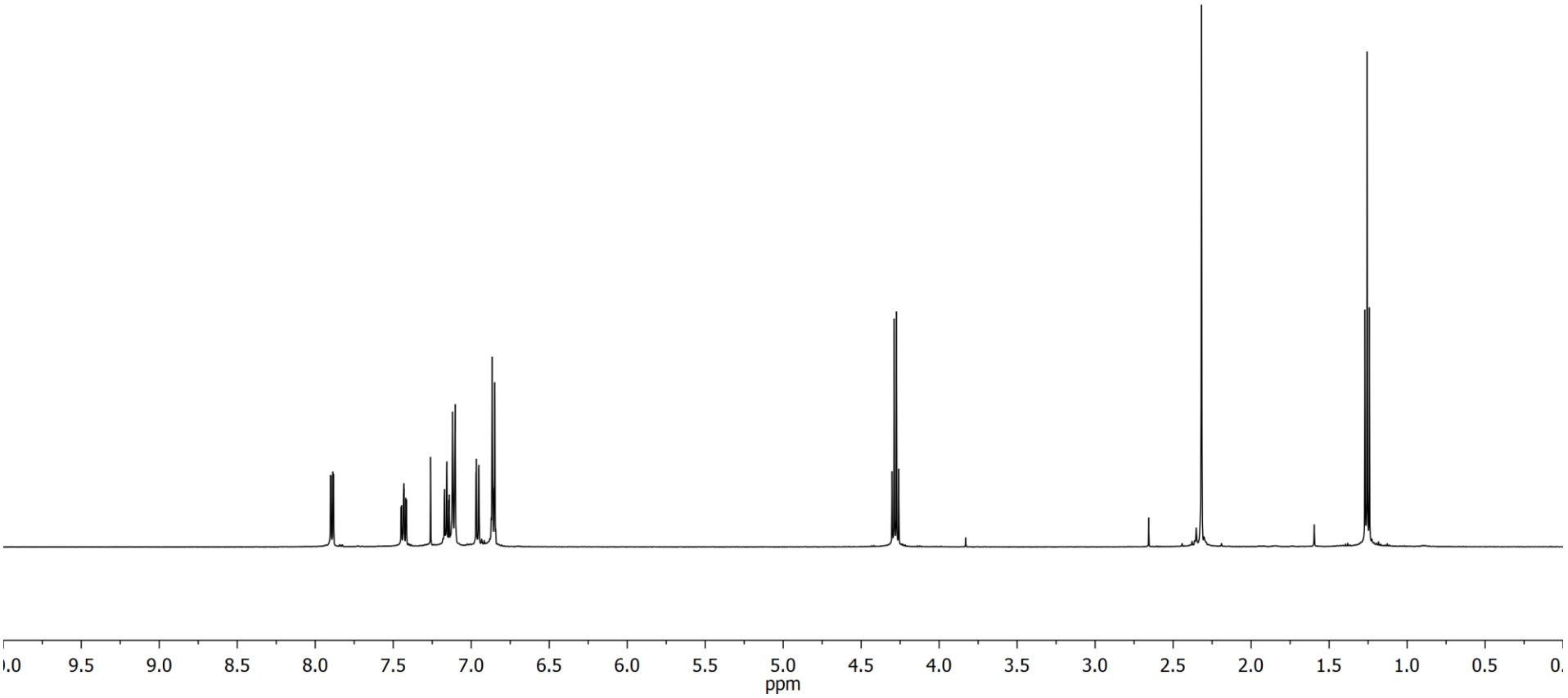
$CDCl_3$, 23 ºC



^{1}H NMR of ethyl 2-(p-tolyloxy)benzoate (4c)

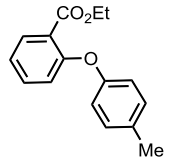
$CDCl_3$, 23 ºC

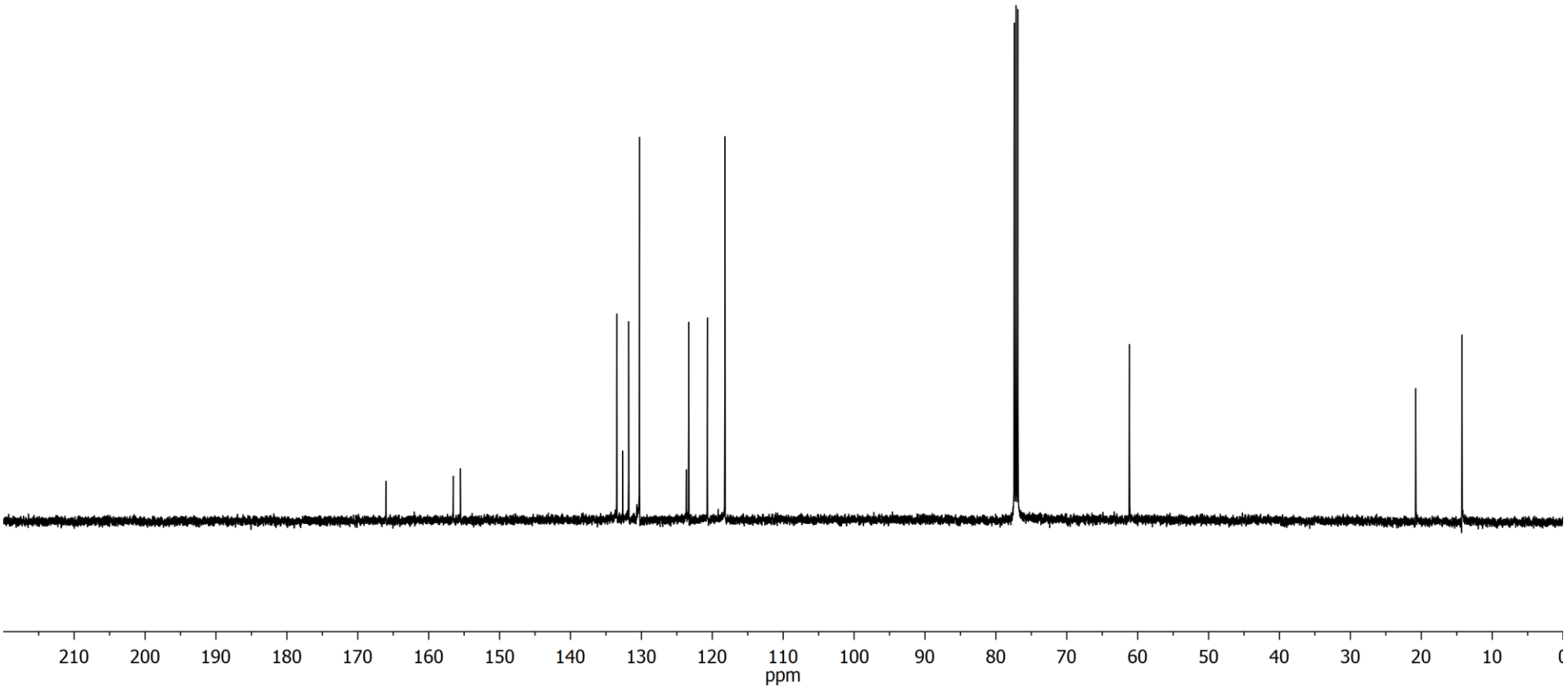




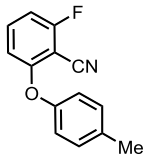
^{13}C NMR of ethyl 2-(p-tolyloxy)benzoate (4c)

$CDCl_3$, 23 ºC

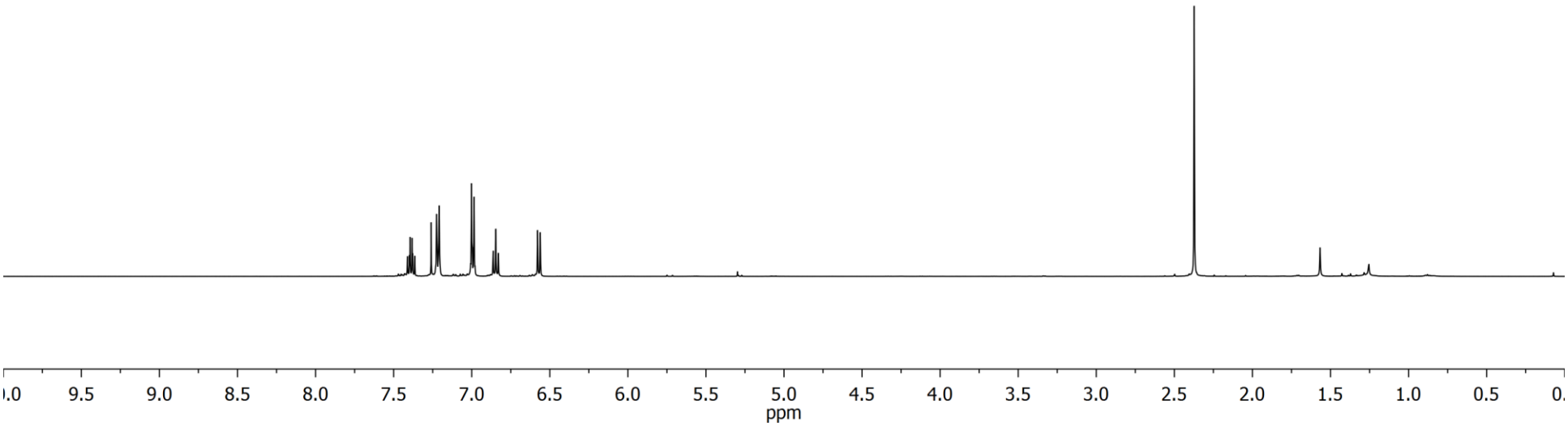




^{1}H NMR of 2-fluoro-6-(p-tolyloxy)benzonitrile (4d)

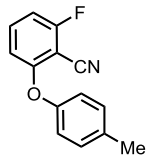


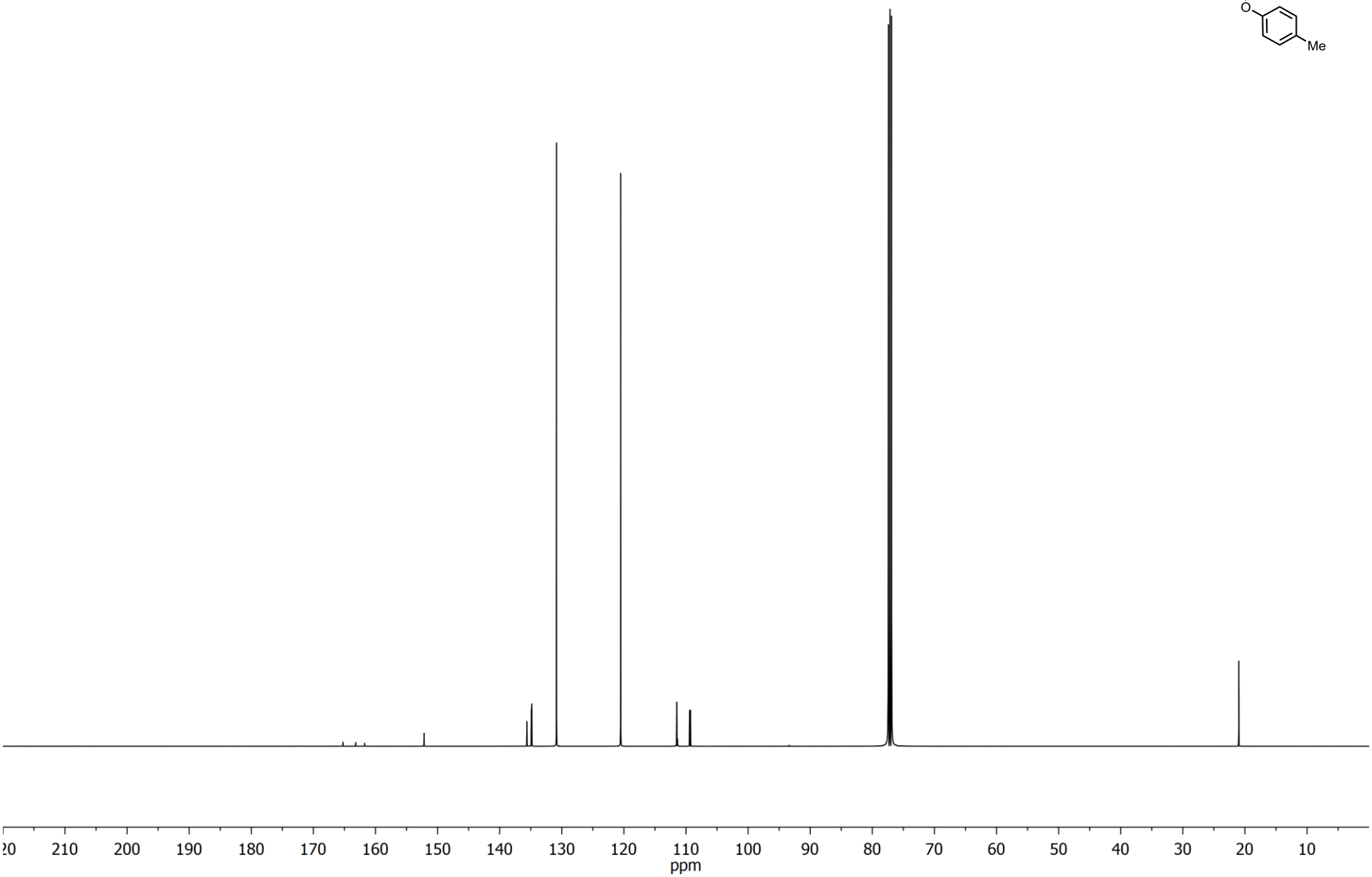
$CDCl_3$, 23 ºC



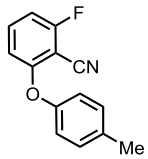
^{13}C NMR of 2-fluoro-6-(p-tolyloxy)benzonitrile (4d)

$CDCl_3$, 23 ºC

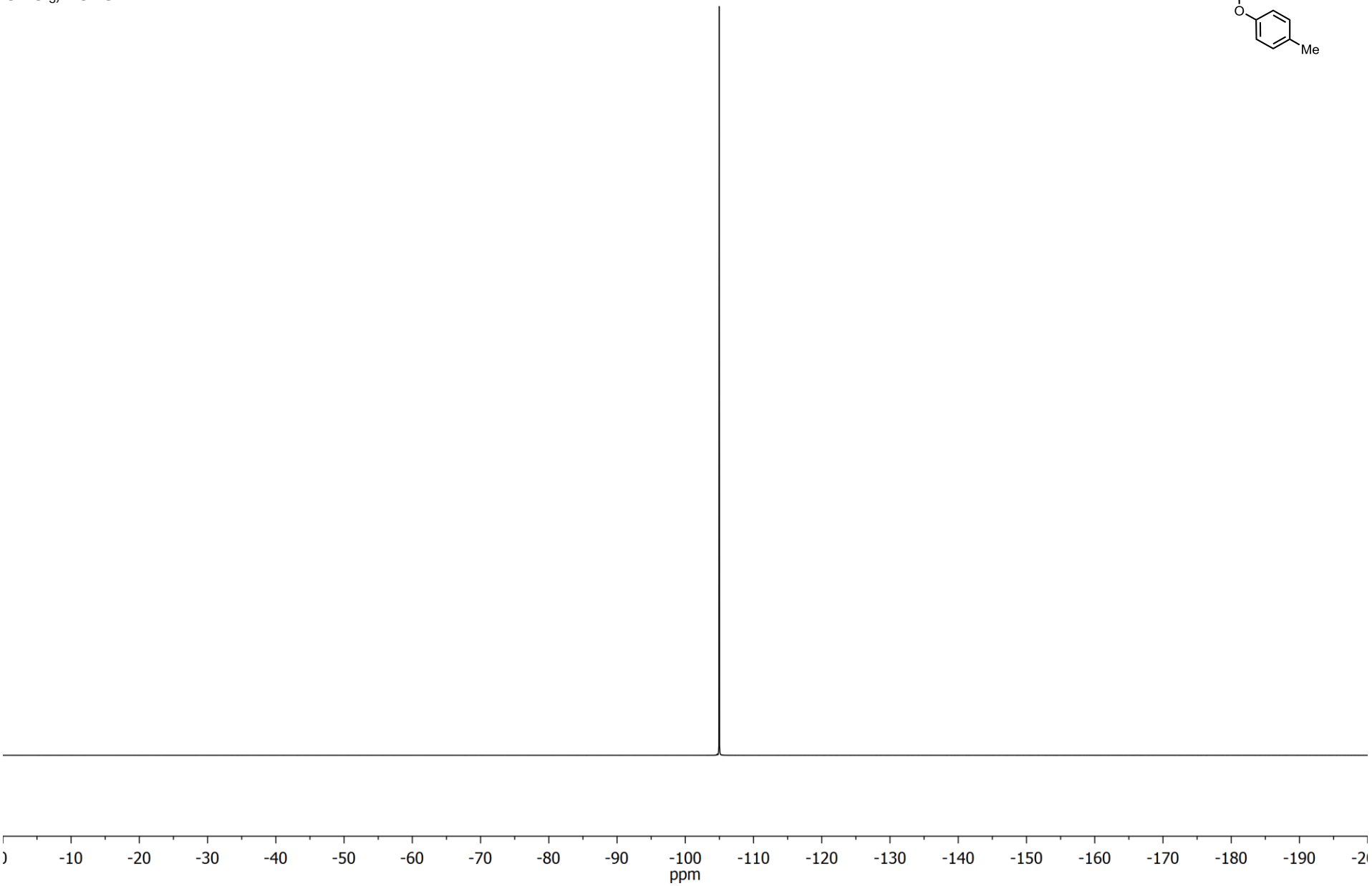




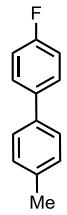
^{19}F NMR of 2-fluoro-6-(p-tolyloxy)benzonitrile (4d)



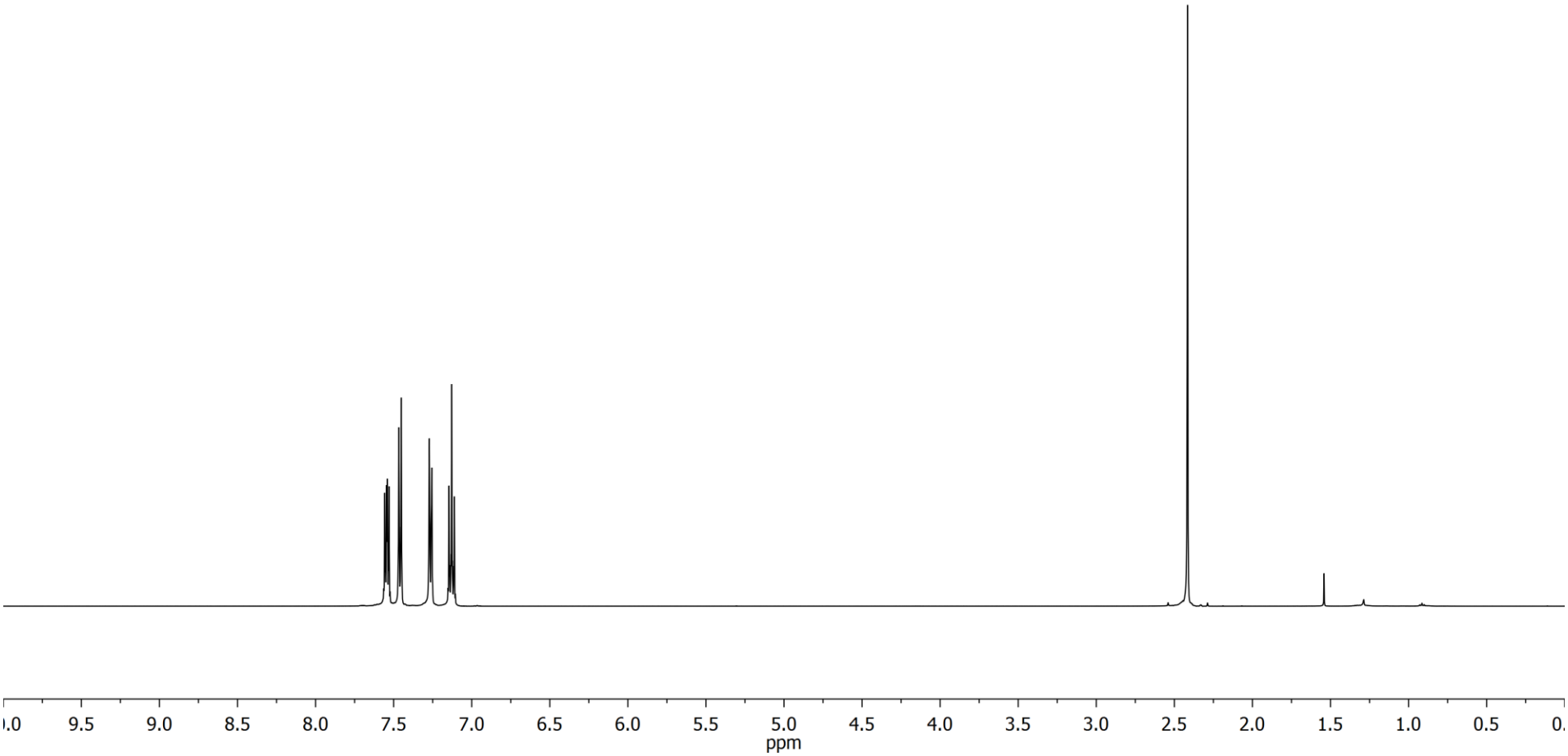
$CDCl_3$, 23 ºC



^{1}H NMR of 4-fluoro-4'-methyl-1,1'-biphenyl (4e)

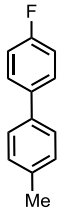


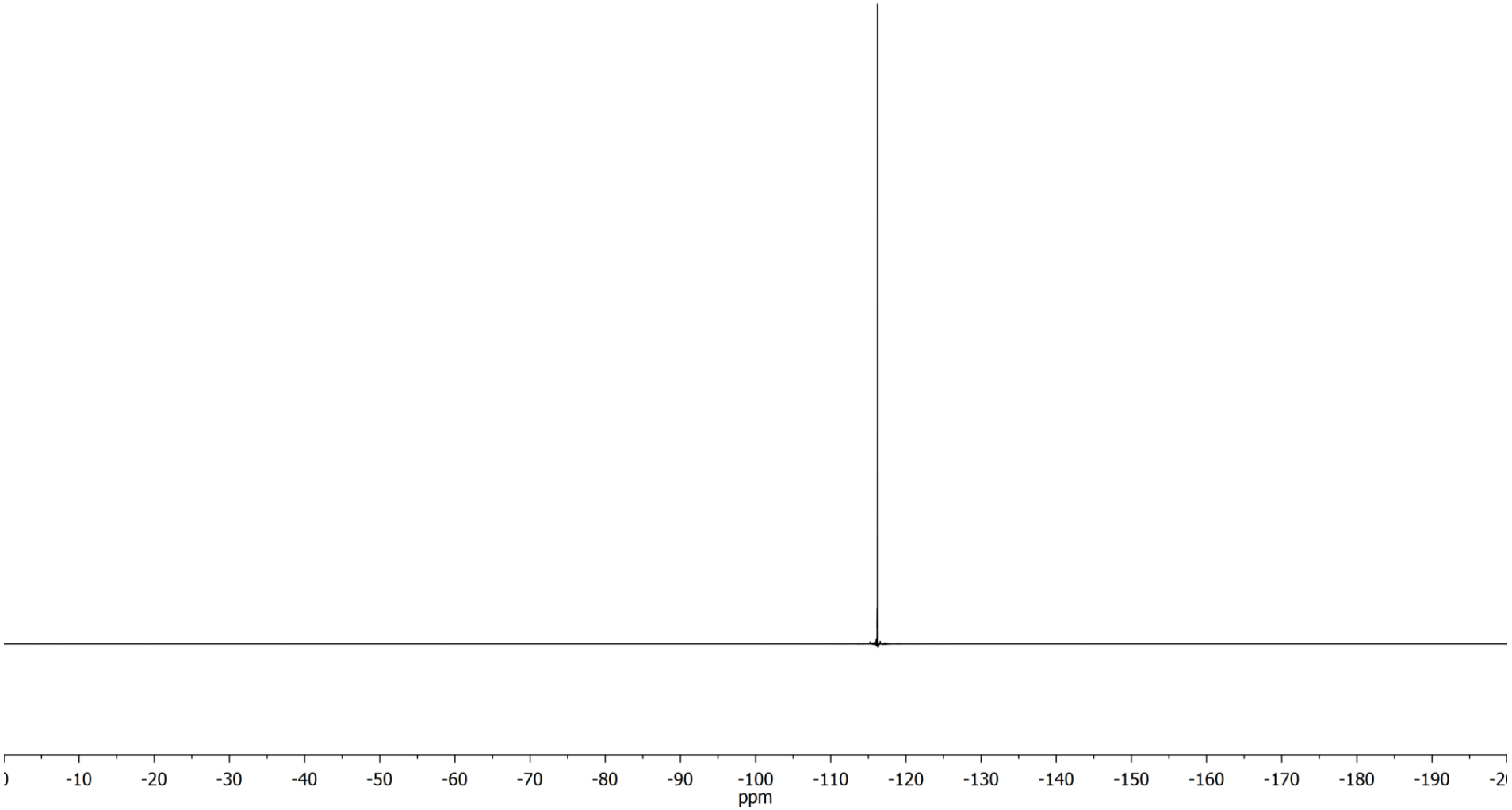
$CDCl_3$, 23 ºC



^{19}F NMR of 4-fluoro-4'-methyl-1,1'-biphenyl (4e)

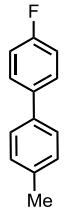
$CDCl_3$, 23 ºC

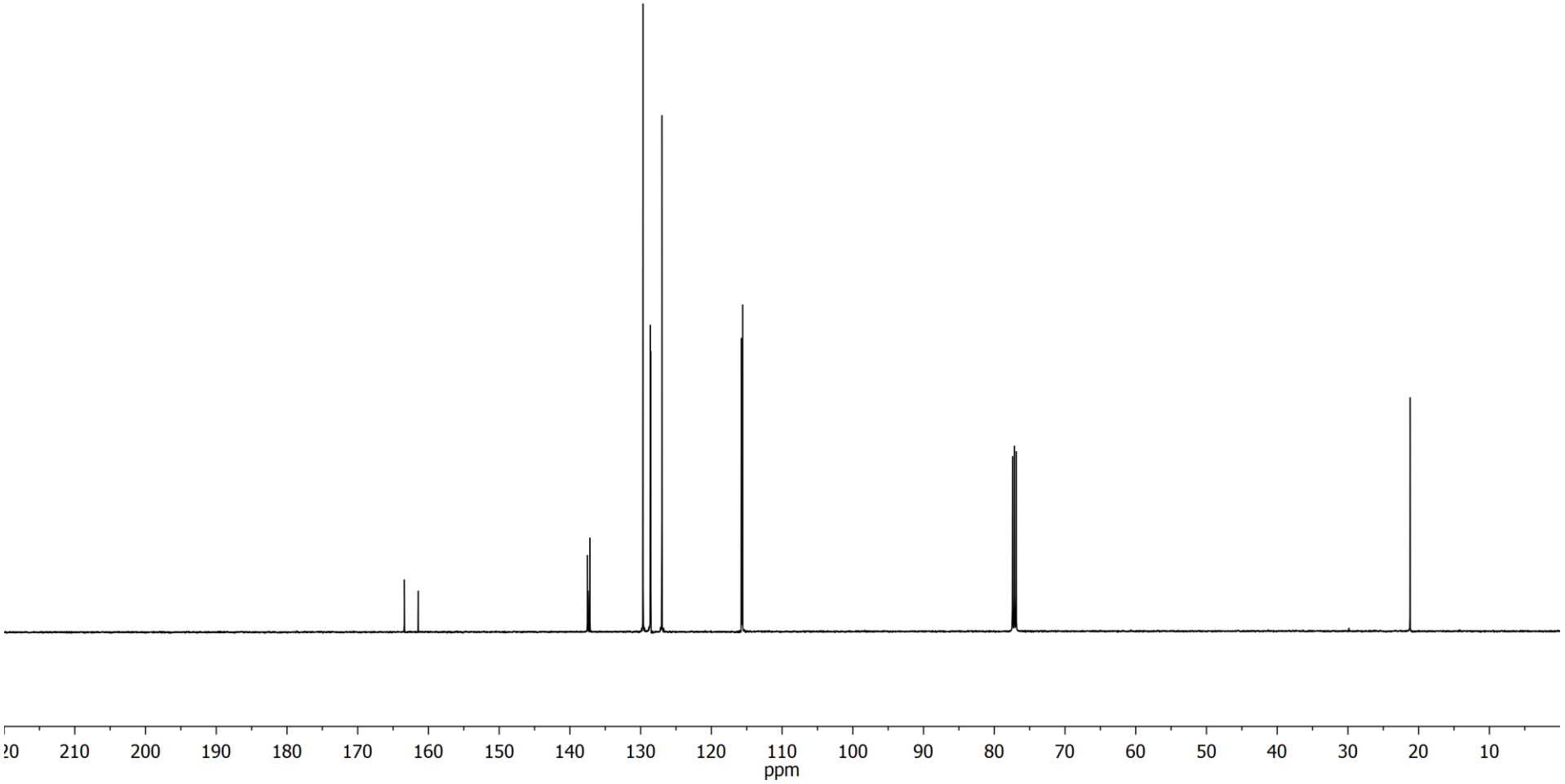




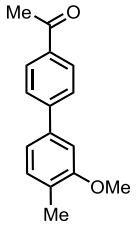
^{13}C NMR of 4-fluoro-4'-methyl-1,1'-biphenyl (4e)

$CDCl_3$, 23 ºC

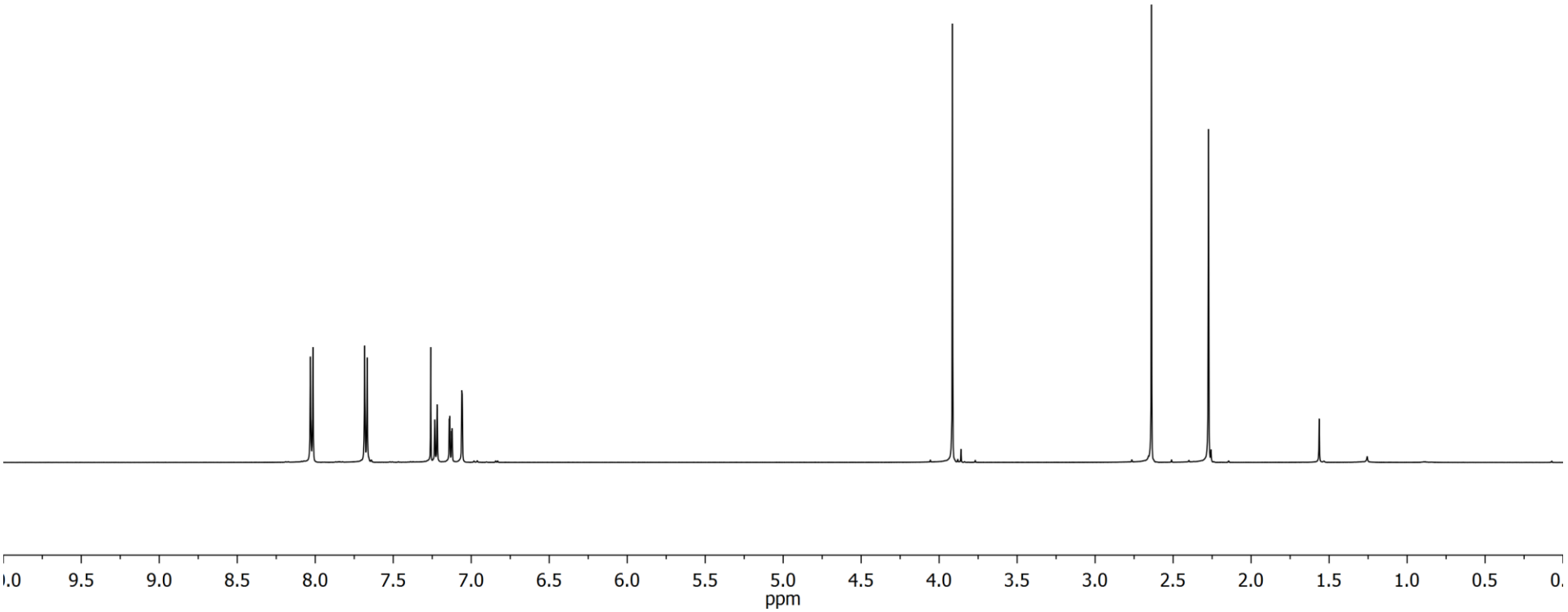




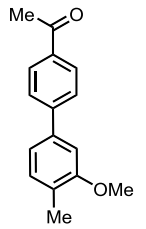
^{1}H NMR of 1-(3'-methoxy-4'-methyl-[1,1'-biphenyl]-4-yl)ethan-1-one (4f)



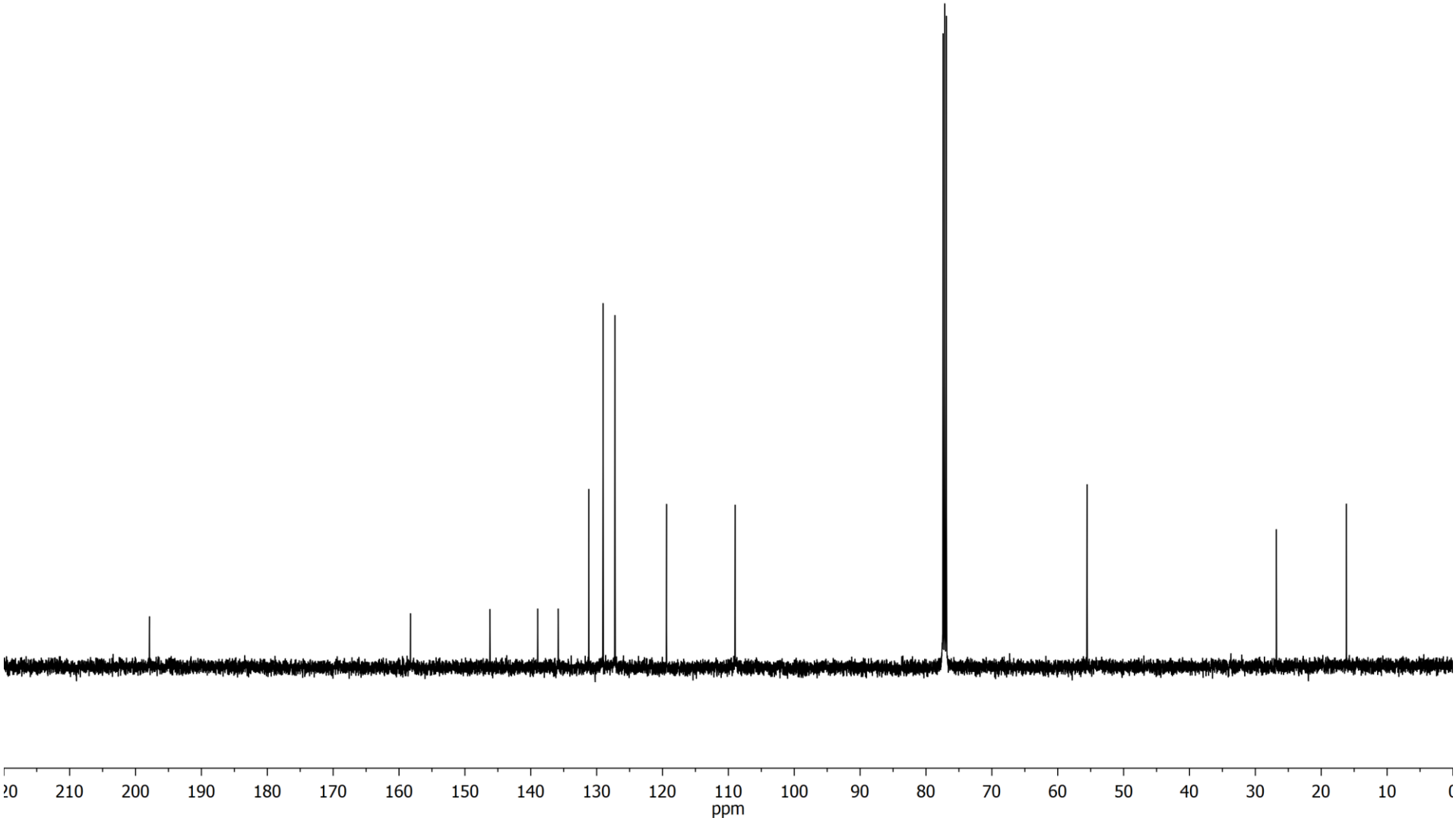
$CDCl_3$, 23 ºC



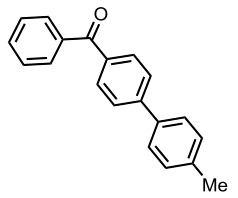
^{13}C NMR of 1-(3'-methoxy-4'-methyl-[1,1'-biphenyl]-4-yl)ethan-1-one (4f)



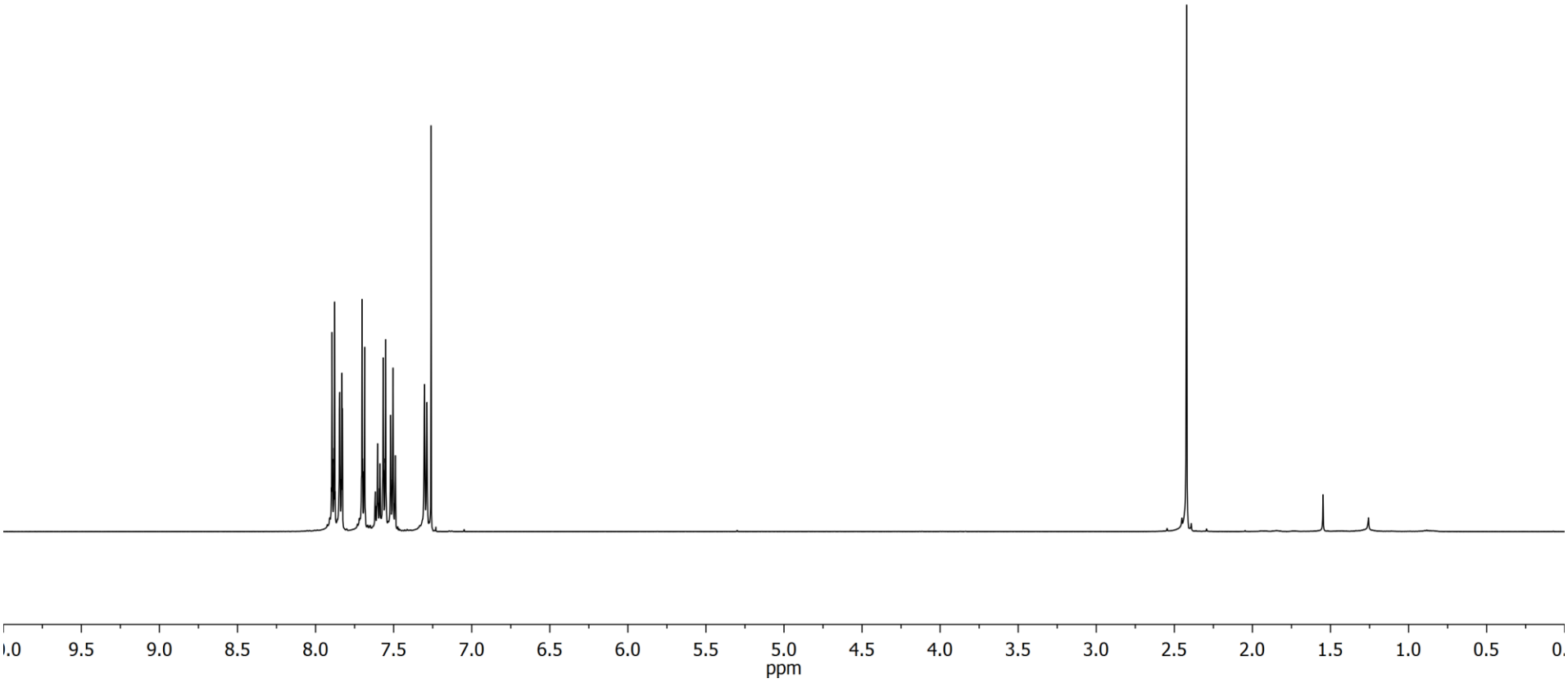
$CDCl_3$, 23 ºC



^{1}H NMR of 2-(4'-methyl-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (4g)

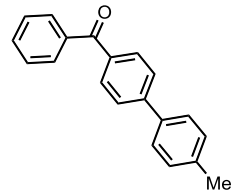


$CDCl_3$, 23 ºC

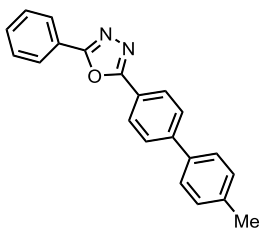


^{13}C NMR of 2-(4'-methyl-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (4g)

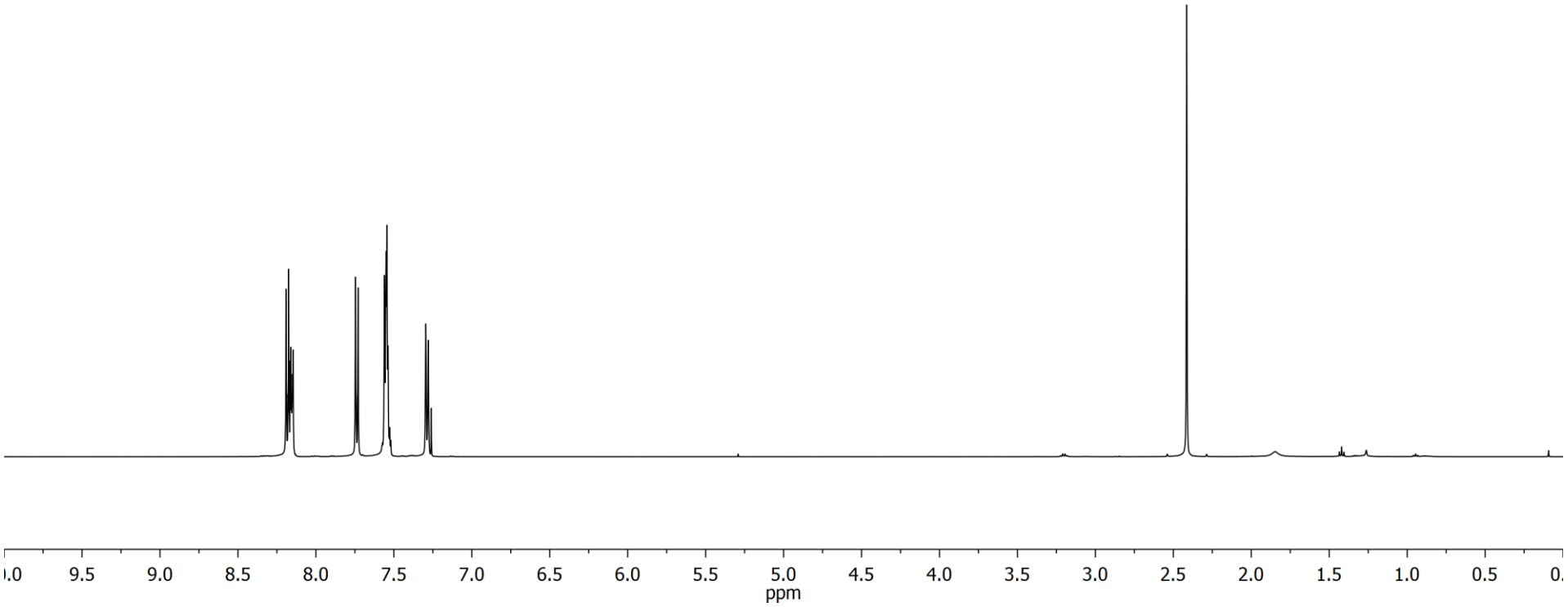
$CDCl_3$, 23 ºC



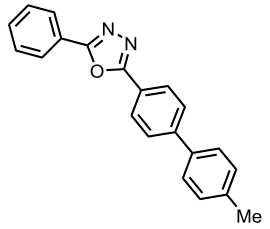
^{1}H NMR of 2-(4'-methyl-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (4h)



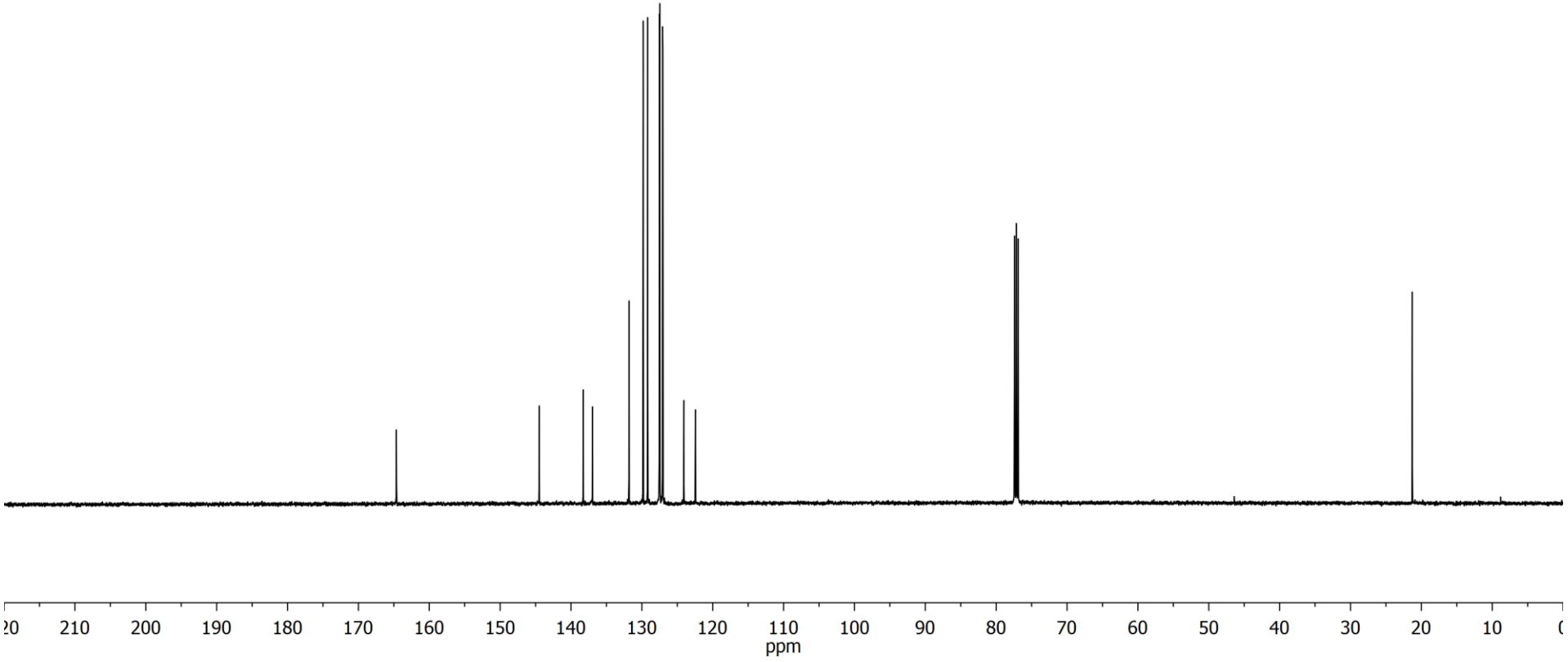
$CDCl_3$, 23 ºC



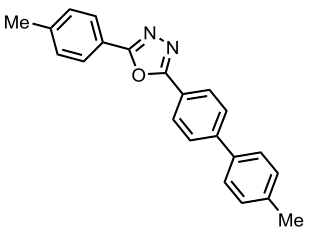
^{13}C NMR of 2-(4'-methyl-[1,1'-biphenyl]-4-yl)-5-phenyl-1,3,4-oxadiazole (4h)



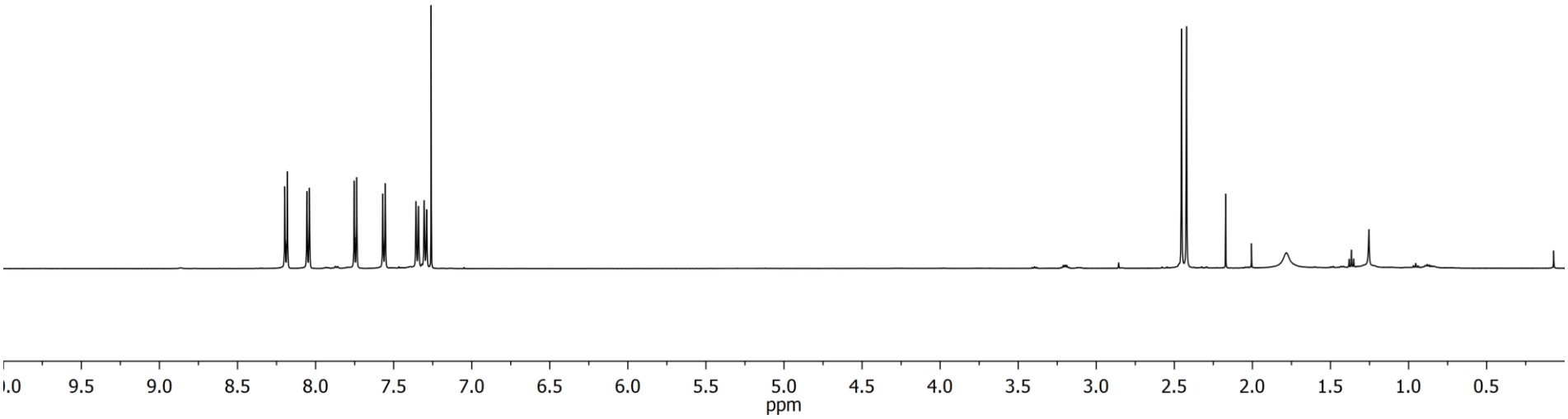
$CDCl_3$, 23 ºC



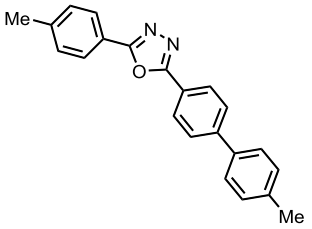
^{1}H NMR of 2-(4'-methyl-[1,1'-biphenyl]-4-yl)-5-(p-tolyl)-1,3,4-oxadiazole (4h´)



$CDCl_3$, 23 ºC



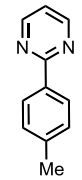
^{13}C NMR of 2-(4'-methyl-[1,1'-biphenyl]-4-yl)-5-(p-tolyl)-1,3,4-oxadiazole (4h´)

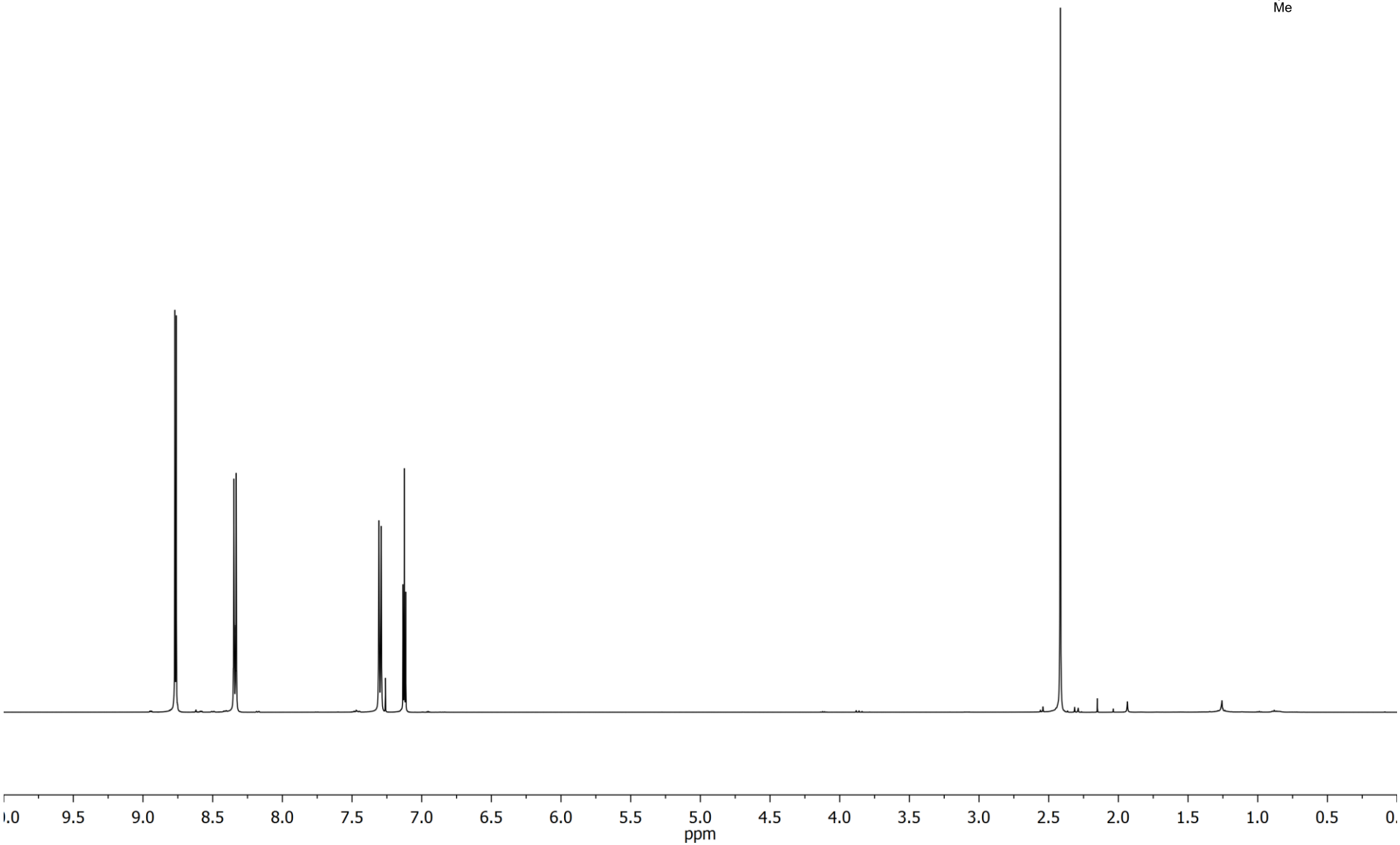


$CDCl_3$, 23 ºC

^{1}H NMR of 2-(*p*-tolyl)pyrimidine (4i)

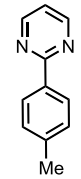
$CDCl_3$, 23 ºC

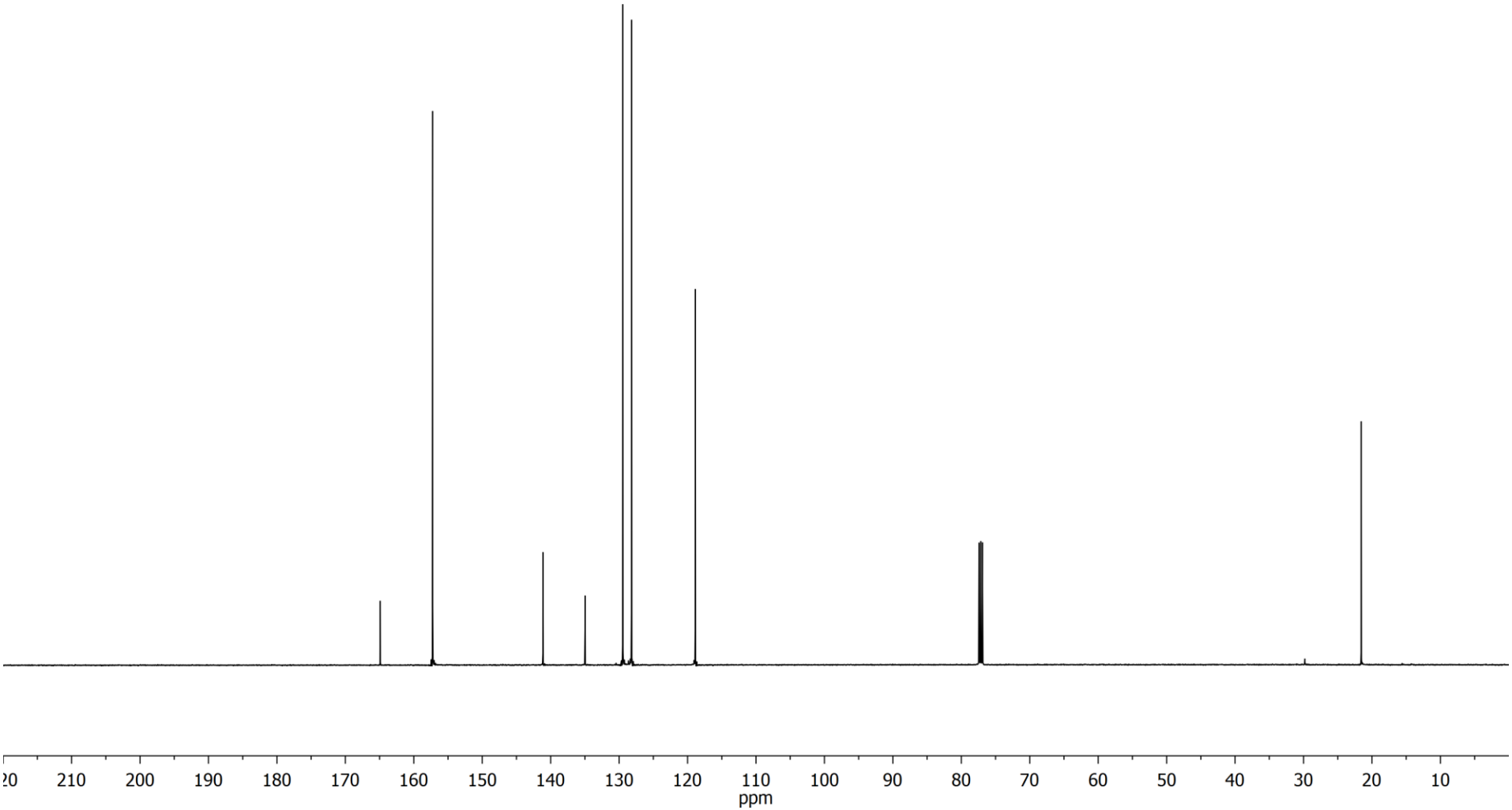




^{13}C NMR of 2-(*p*-tolyl)pyrimidine (4i)

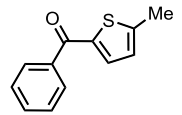
$CDCl_3$, 23 ºC

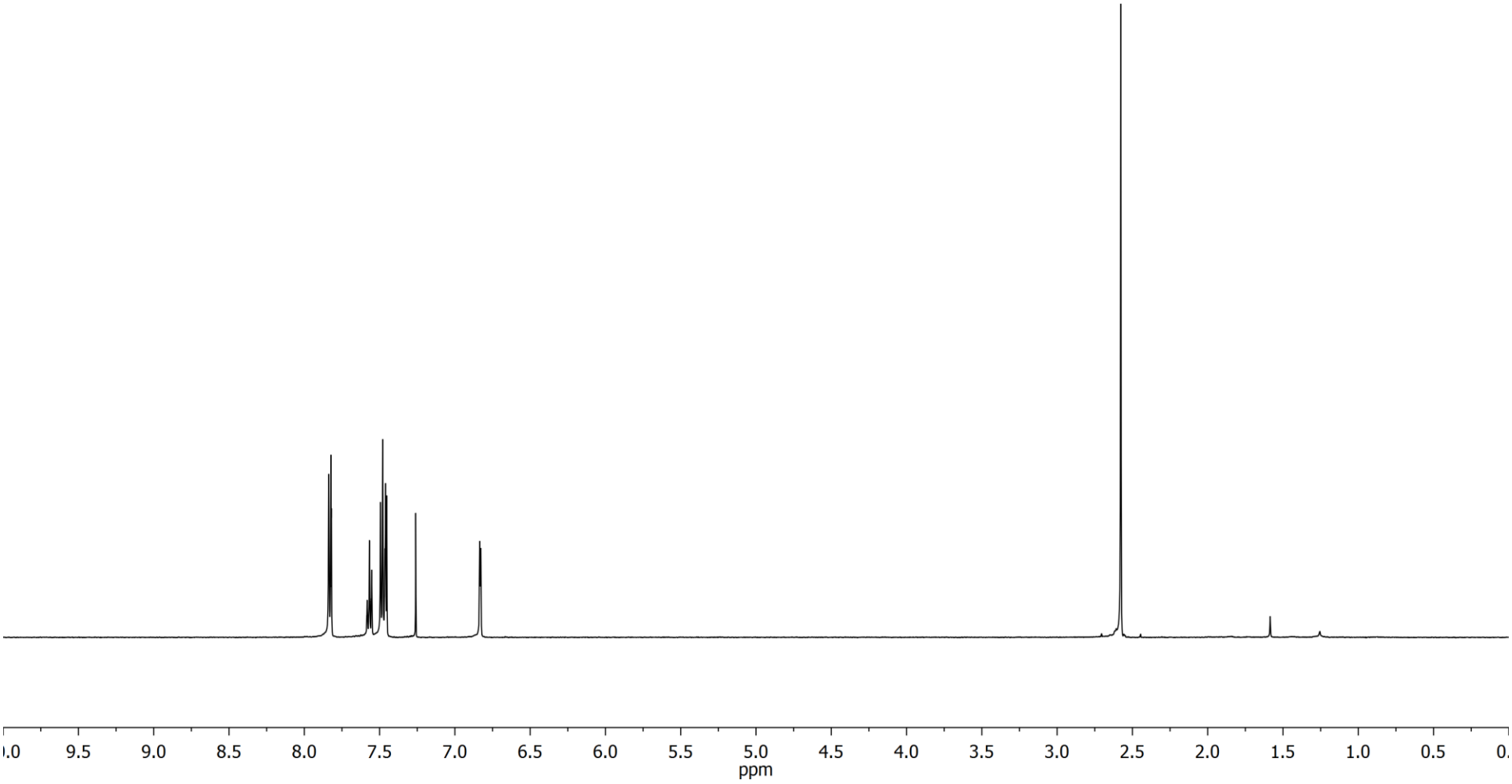




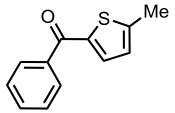
^{1}H NMR of (5-methylthiophen-2-yl)(phenyl)methanone (4j)

$CDCl_3$, 23 ºC

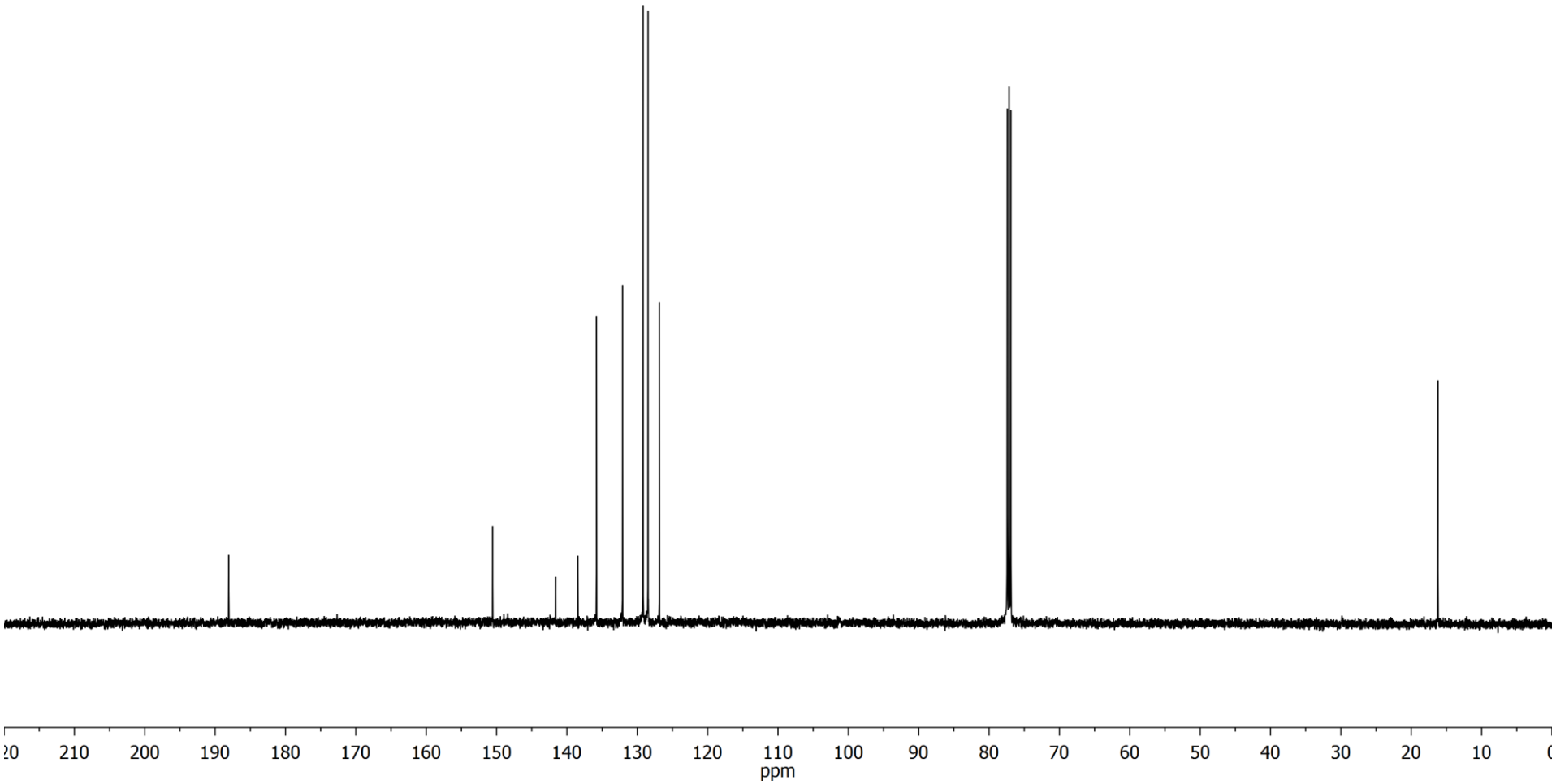




^{13}C NMR of (5-methylthiophen-2-yl)(phenyl)methanone (4j)

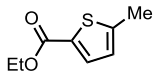


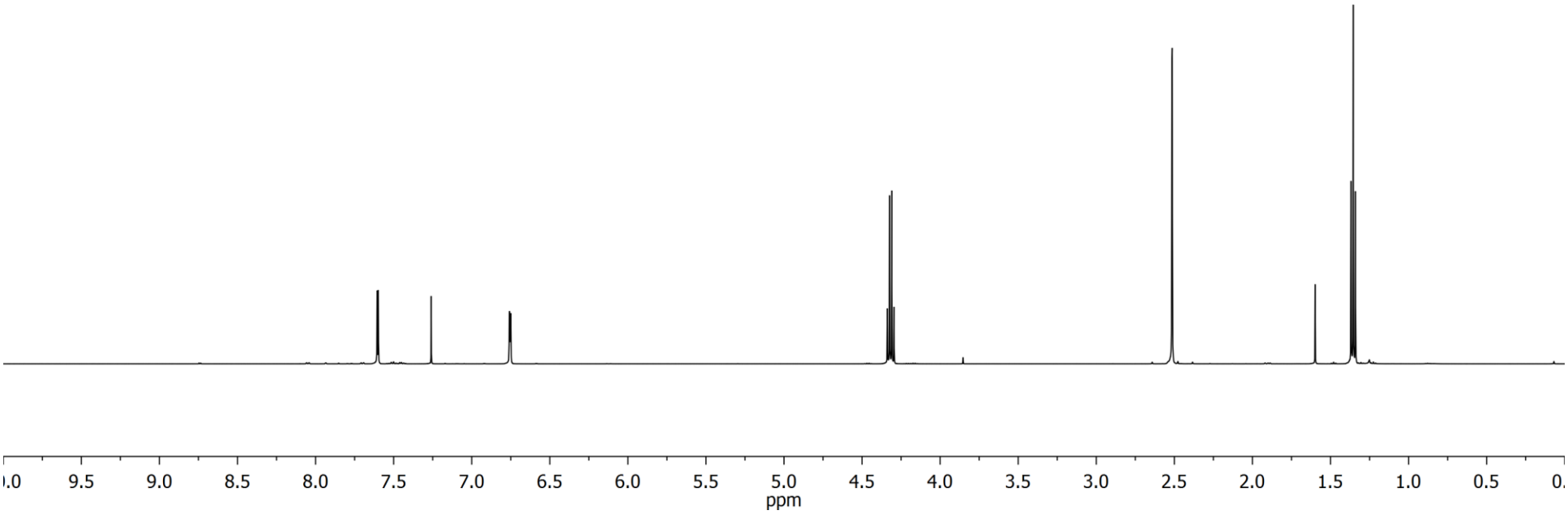
$CDCl_3$, 23 ºC



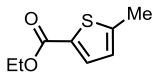
^{1}H NMR of ethyl 5-methylthiophene-2-carboxylate (4k)

$CDCl_3$, 23 ºC

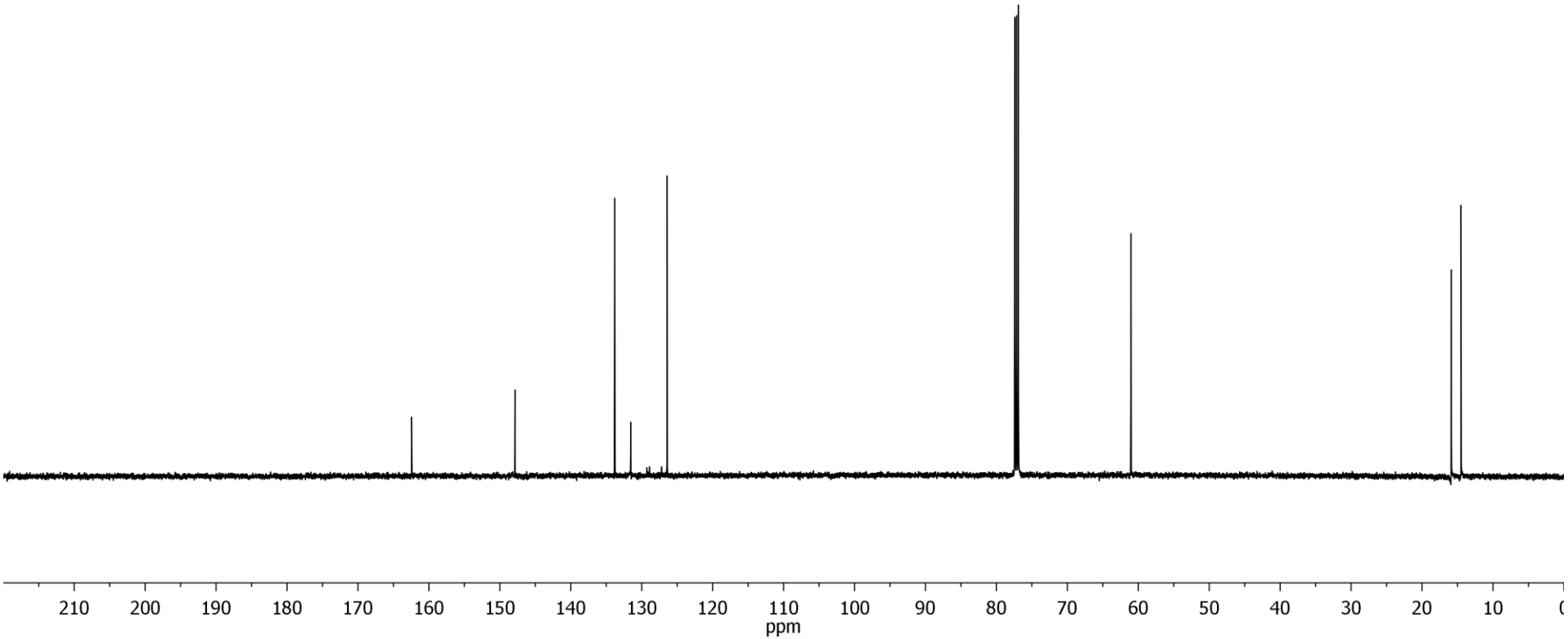




^{13}C NMR of ethyl 5-methylthiophene-2-carboxylate (4k)

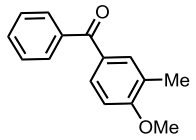


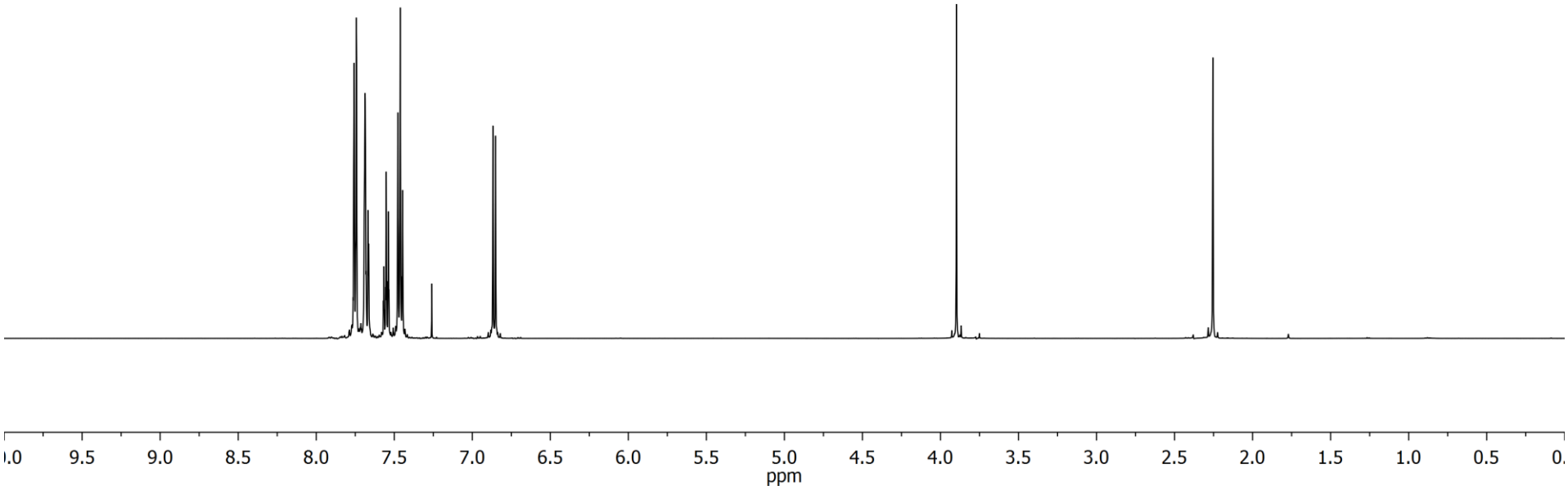
$CDCl_3$, 23 ºC



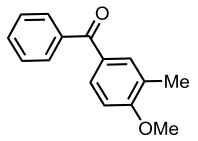
^{1}H NMR of (4-methoxy-3-methylphenyl)(phenyl)methanone (4l)

$CDCl_3$, 23 ºC

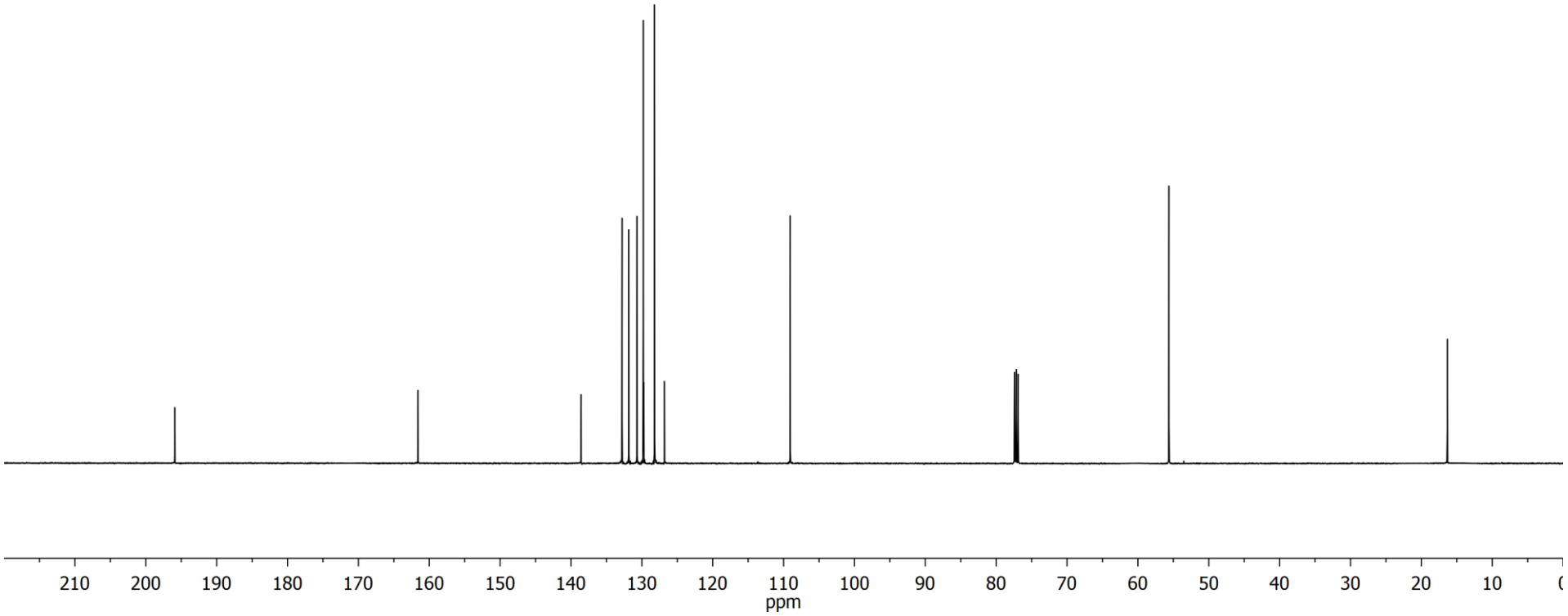




^{13}C NMR of (4-methoxy-3-methylphenyl)(phenyl)methanone (4l)

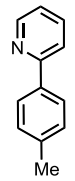


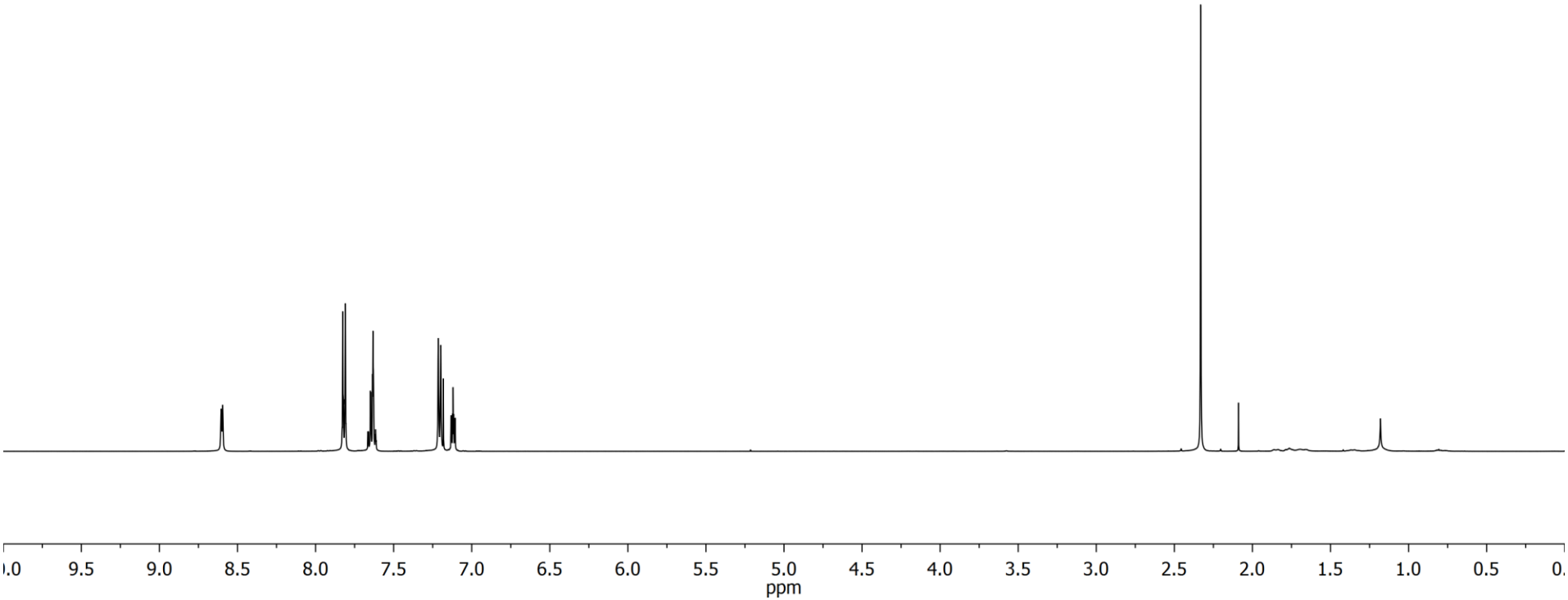
$CDCl_3$, 23 ºC



^{1}H NMR of 2-(*p*-tolyl)pyridine (4m)

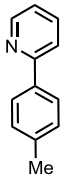
$CDCl_3$, 23 ºC

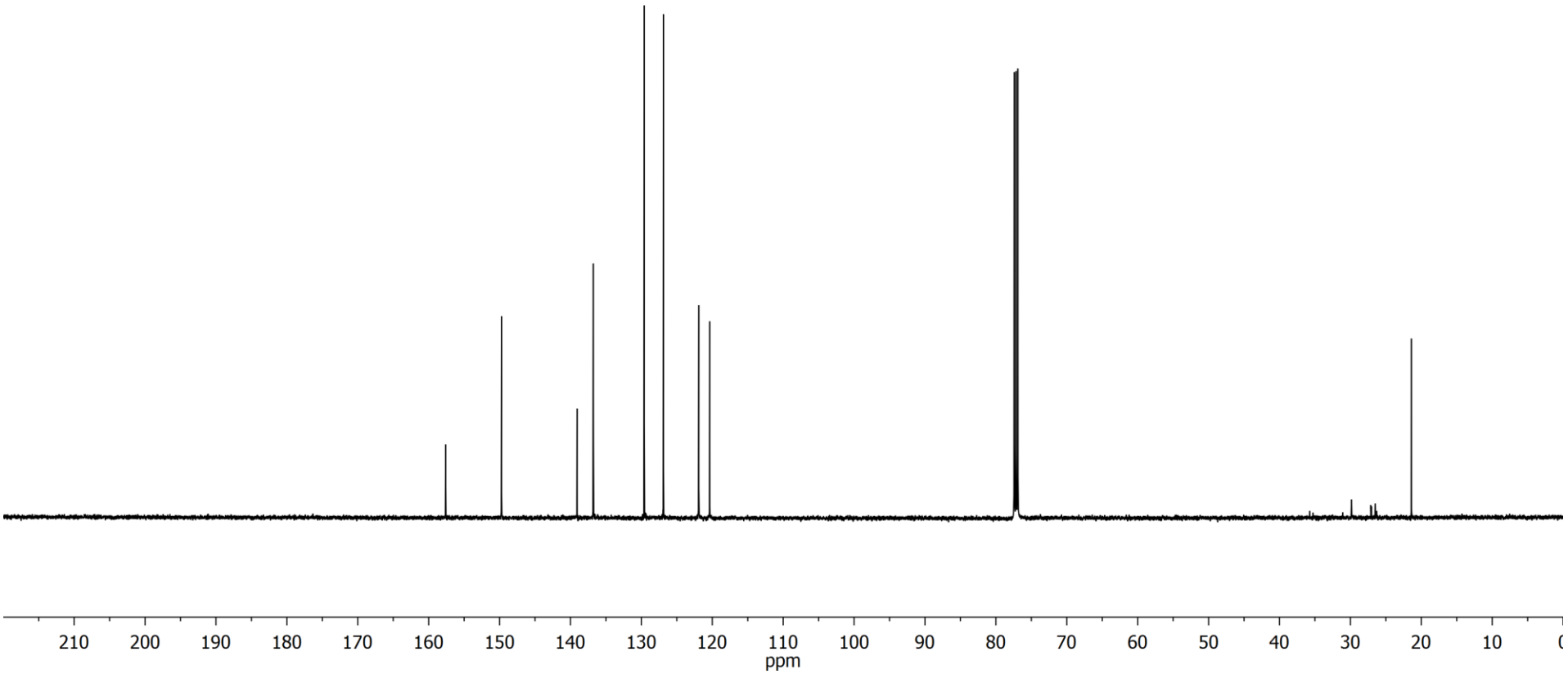




^{13}C NMR of 2-(*p*-tolyl)pyridine (4m)

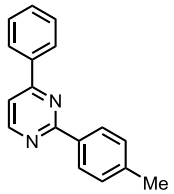
$CDCl_3$, 23 ºC

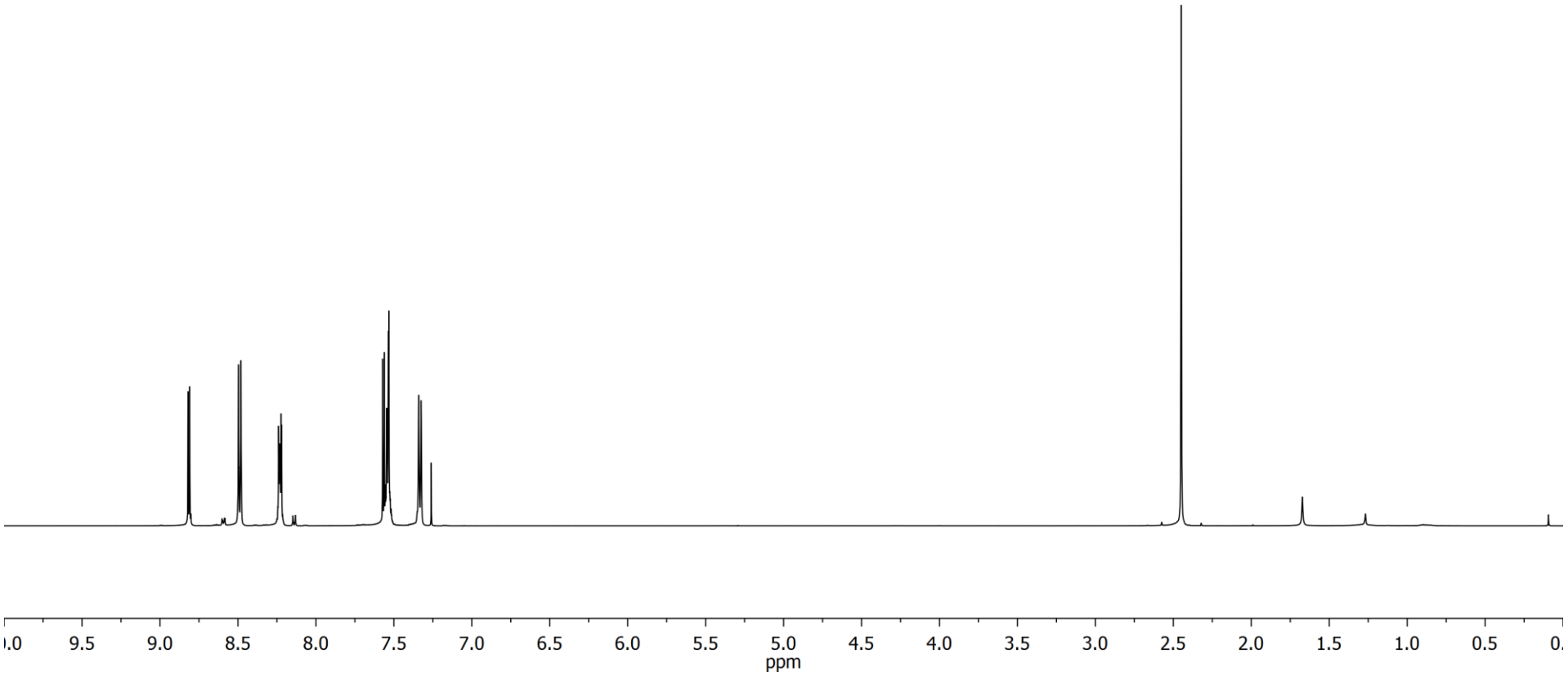




^{1}H NMR of 4-phenyl-2-(*p*-tolyl)pyrimidine (4n)

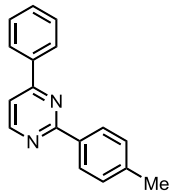
$CDCl_3$, 23 ºC

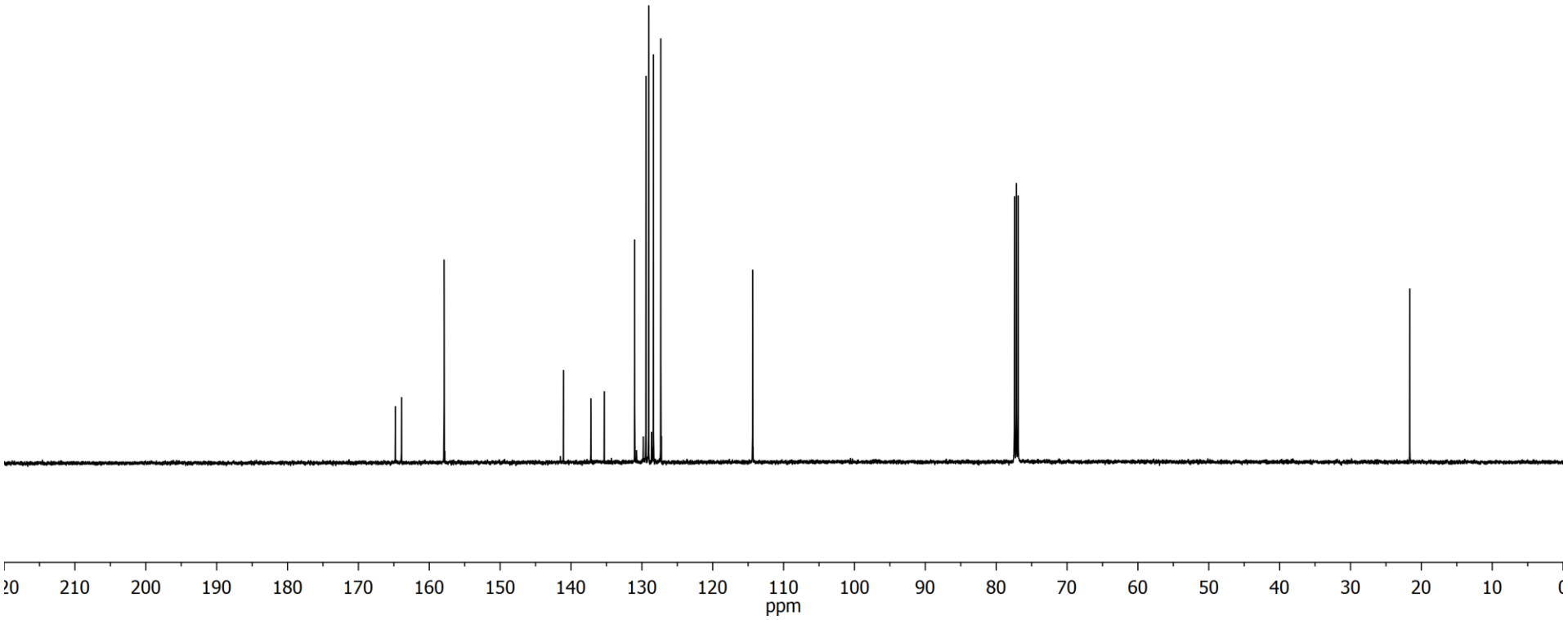




^{13}C NMR of 4-phenyl-2-(*p*-tolyl)pyrimidine (4n)

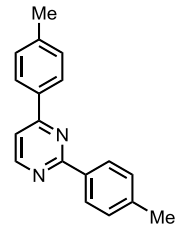
$CDCl_3$, 23 ºC





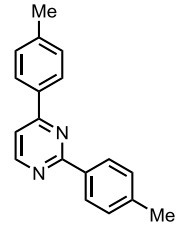
^{1}H NMR of 2,4-di-*p*-tolylpyrimidine (4n'')

$CDCl_3$, 23 ºC



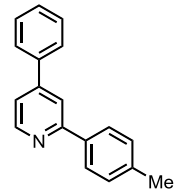
^{13}C NMR of 2,4-di-*p*-tolylpyrimidine (4n'')

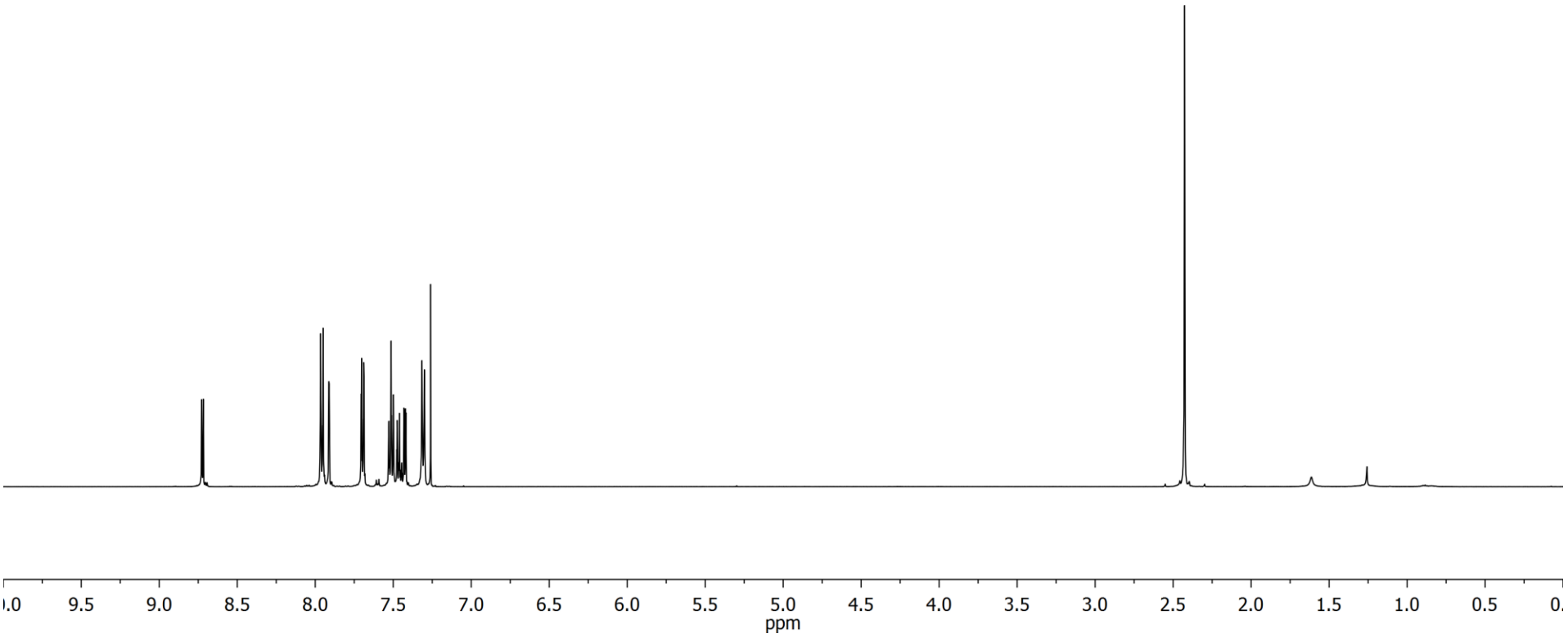
$CDCl_3$, 23 ºC



^{1}H NMR of 4-phenyl-2-(*p*-tolyl)pyridine (4o)

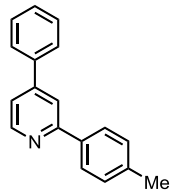
$CDCl_3$, 23 ºC

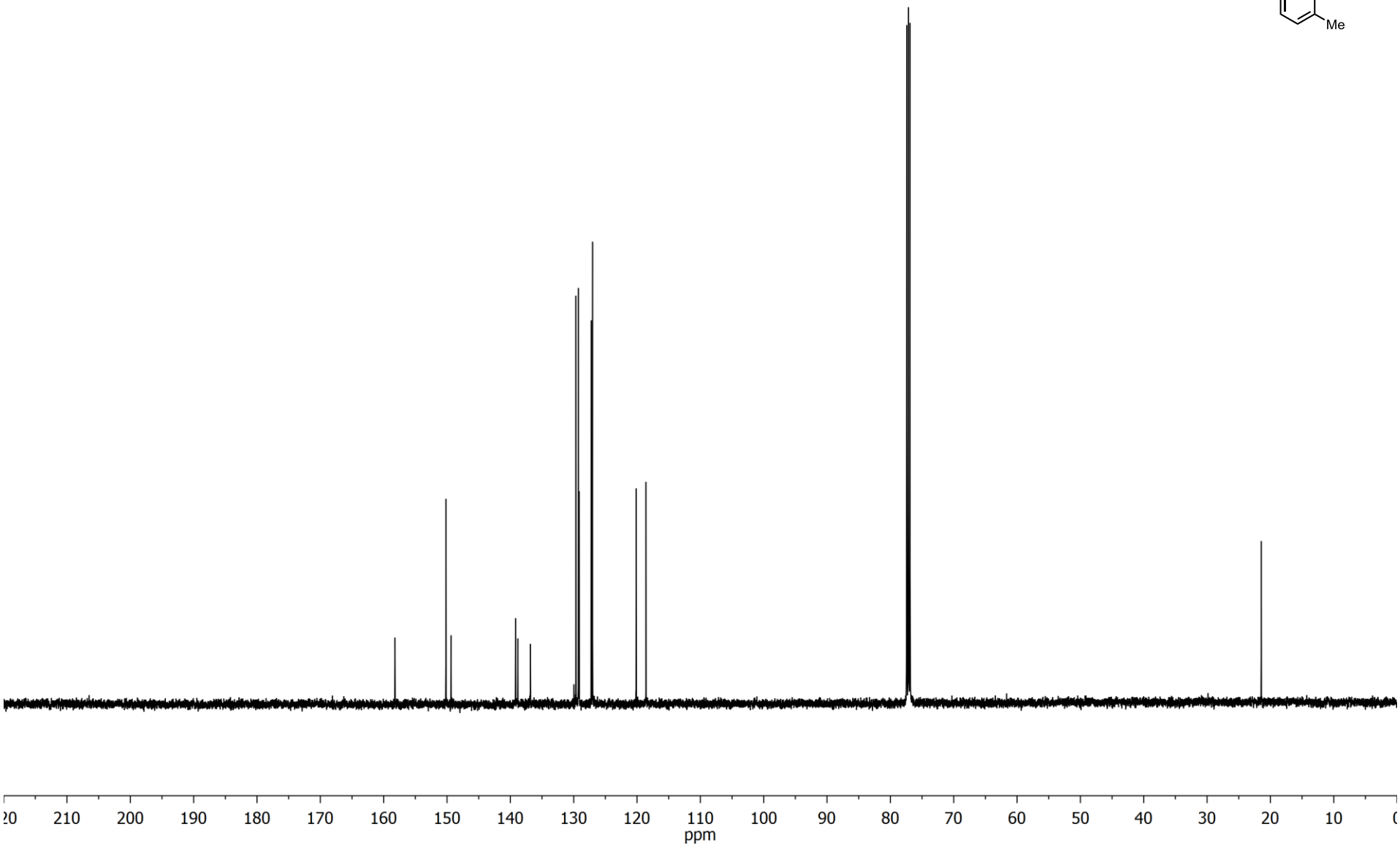




^{13}C NMR of 4-phenyl-2-(*p*-tolyl)pyridine (4o)

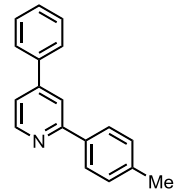
$CDCl_3$, 23 °

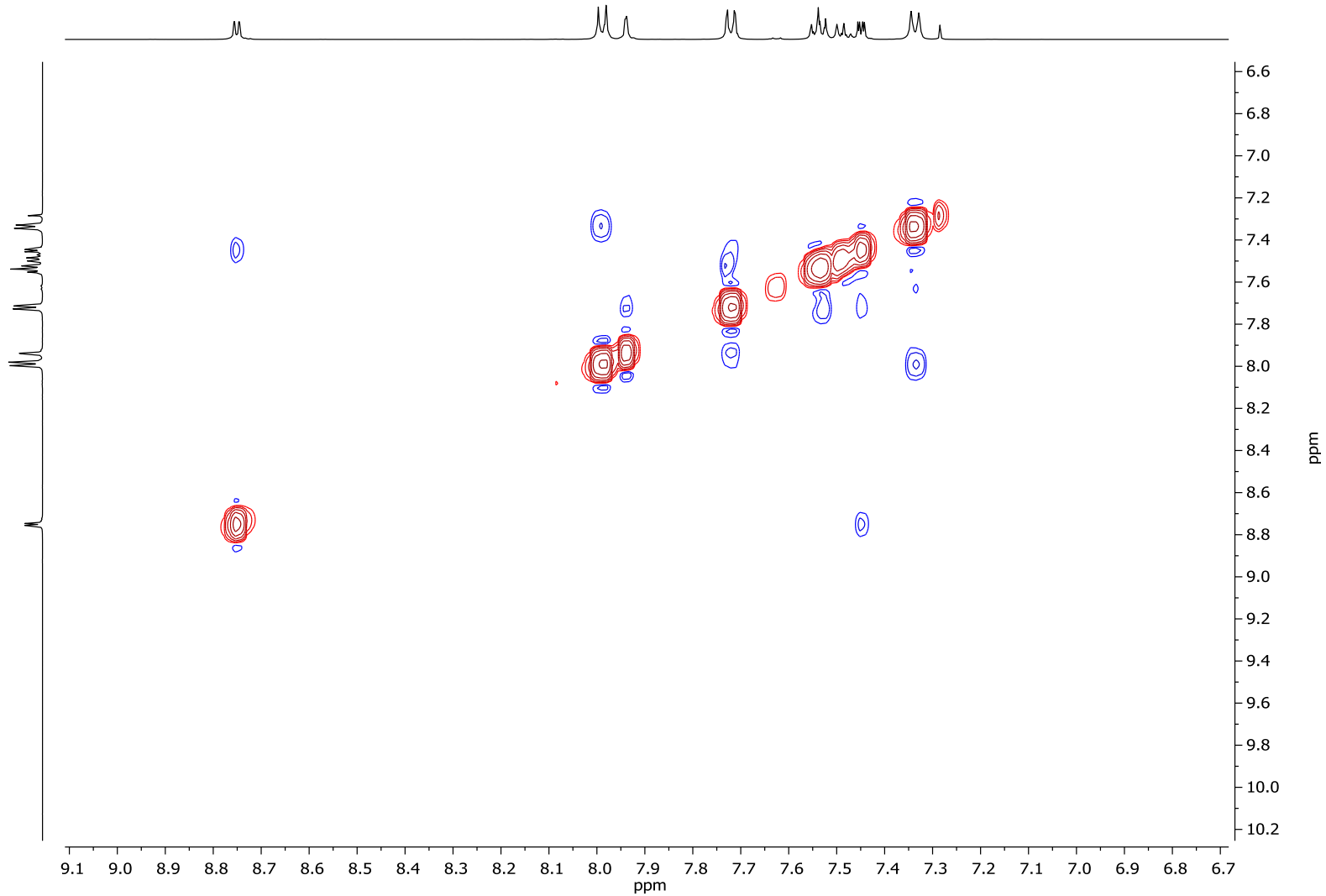




NOESY spectrum of 4-phenyl-2-(*p*-tolyl)pyridine (4o)

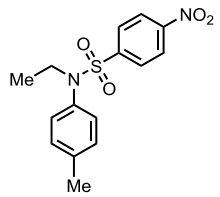
$CDCl_3$, 23 ºC

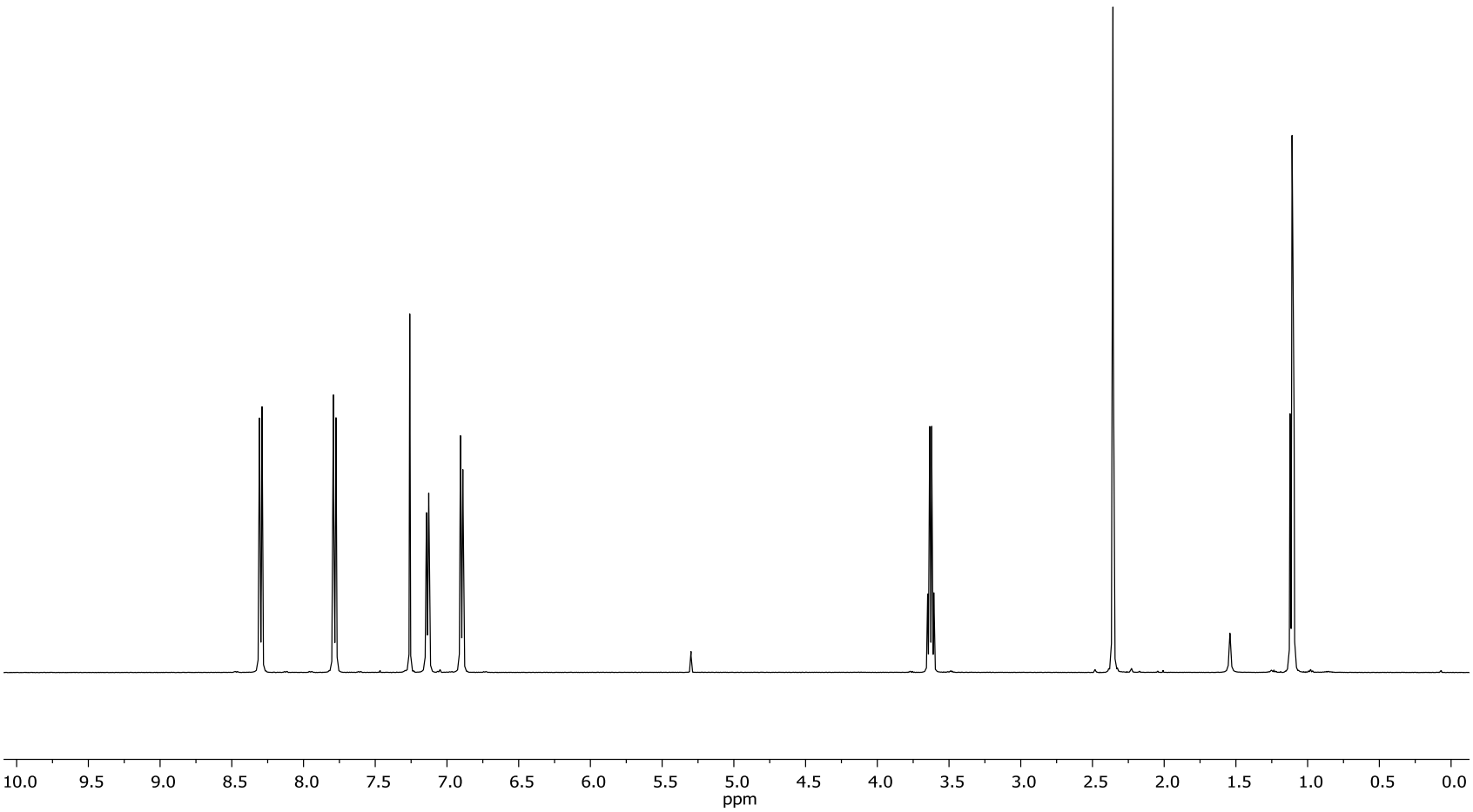




^{1}H NMR of *N*-ethyl-4-nitro-*N*-(*p*-tolyl)benzenesulfonamide (4p)

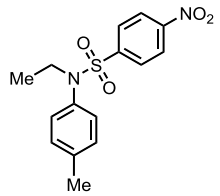
$CDCl_3$, 23 ºC

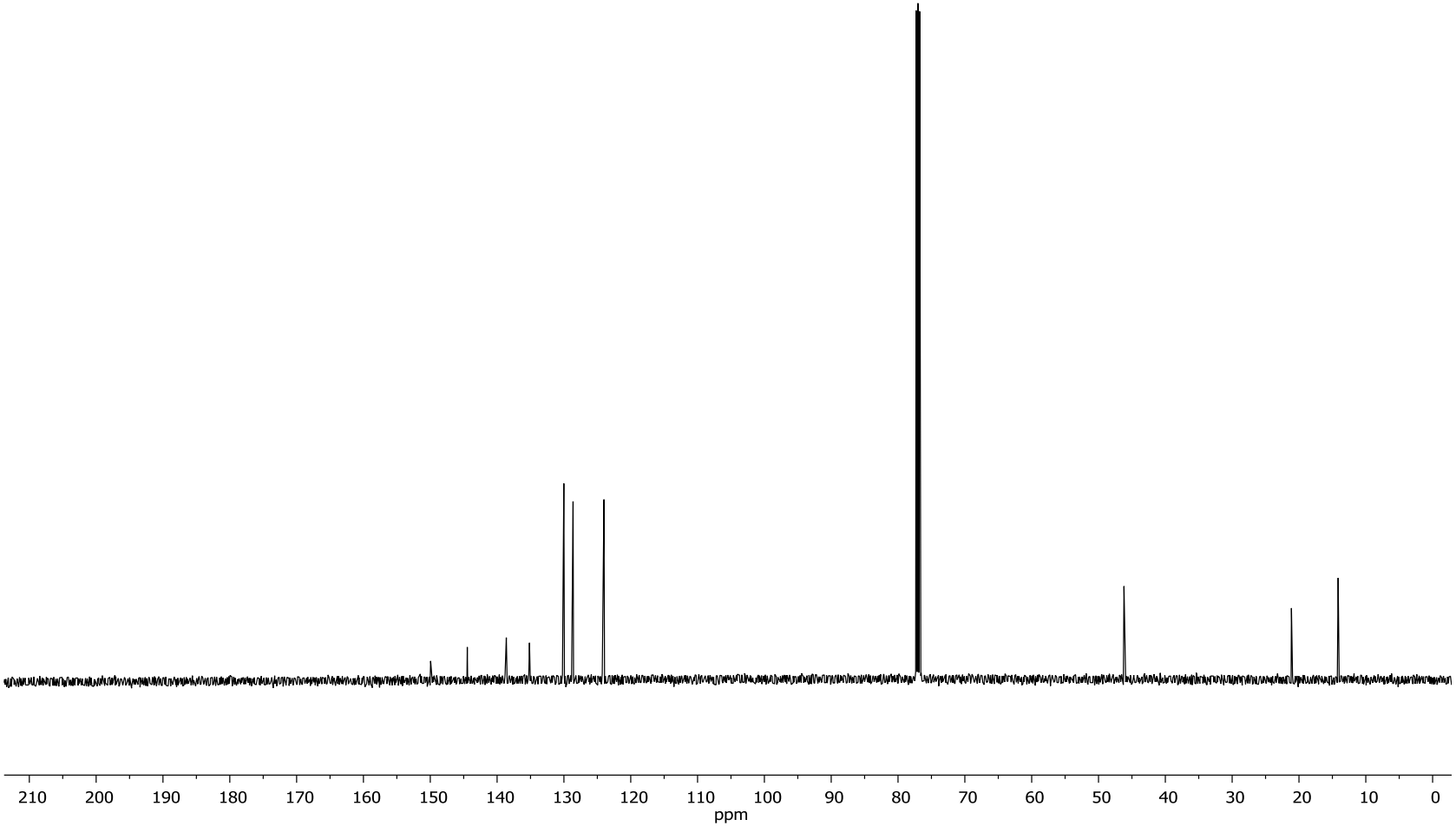




^{13}C NMR of *N*-ethyl-4-nitro-*N*-(*p*-tolyl)benzenesulfonamide (4p)

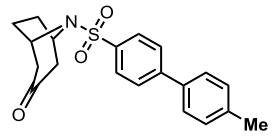
$CDCl_3$, 23 ºC

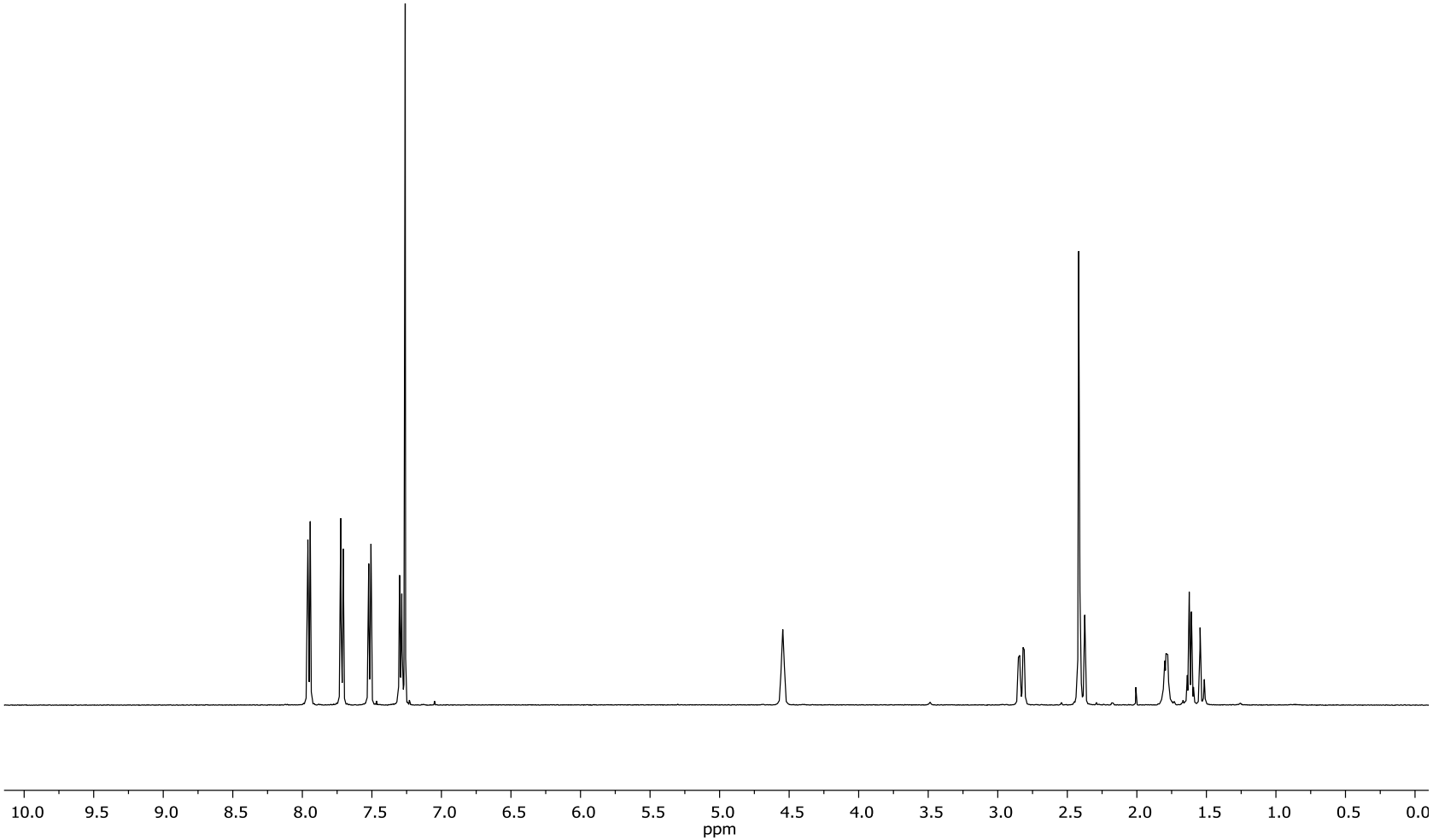




^{1}H NMR of 8-((4'-methyl-[1,1'-biphenyl]-4-yl)sulfonyl)-8-azabicyclo[3.2.1]octan-3-one (4q)

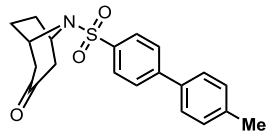
$CDCl_3$, 23 ^oC

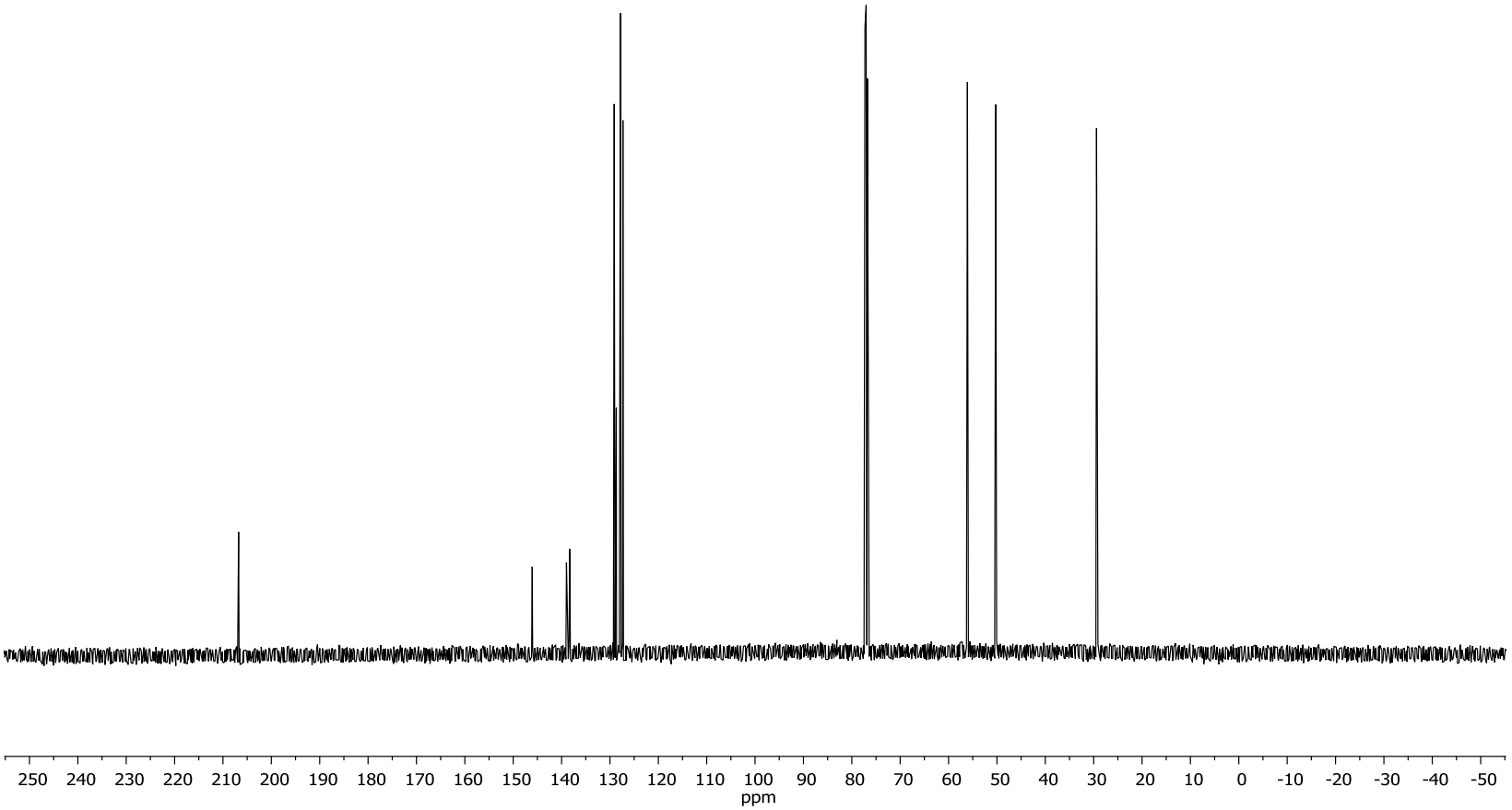




^{13}C NMR of 8-((4'-methyl-[1,1'-biphenyl]-4-yl)sulfonyl)-8-azabicyclo[3.2.1]octan-3-one (4q)

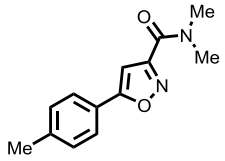
$CDCl_3$, 23 ^{o}C

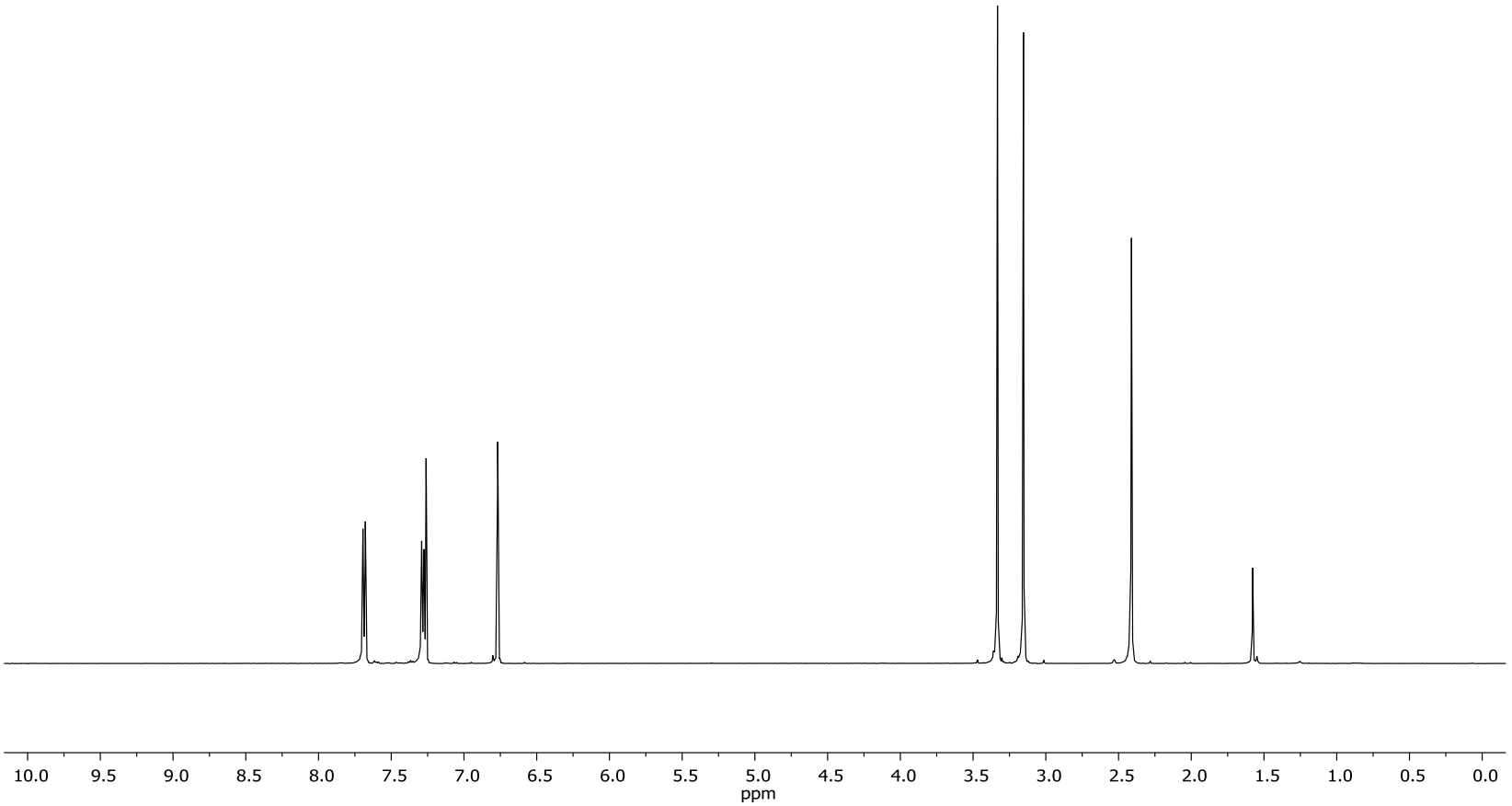




^{1}H NMR of *N*,*N*-dimethyl-5-(*p*-tolyl)isoxazole-3-carboxamide (4r)

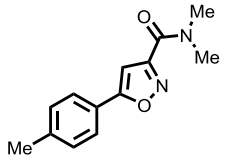
$CDCl_3$, 23 ^{o}C

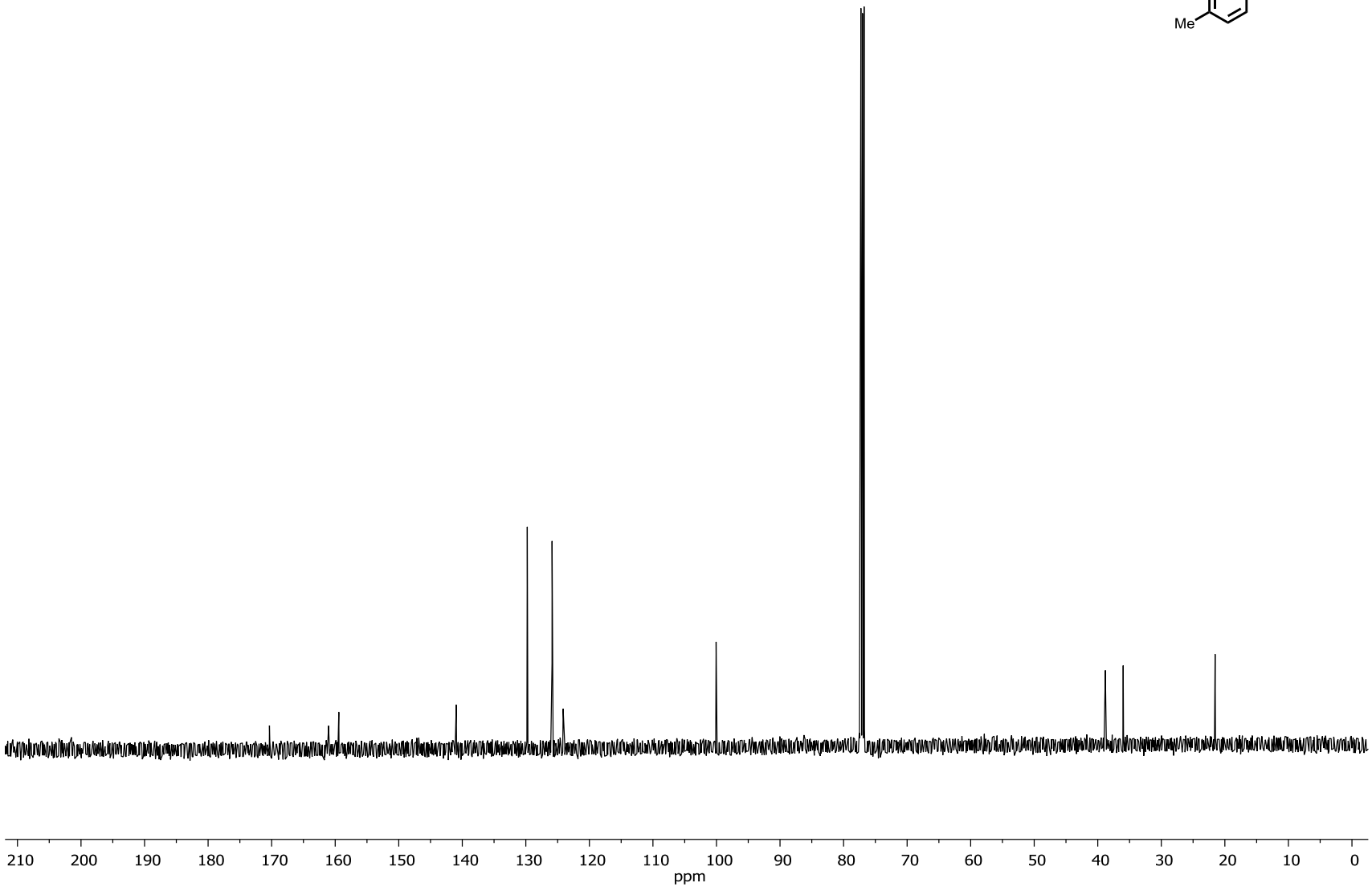




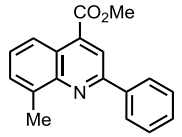
^{13}C NMR of *N*,*N*-dimethyl-5-(*p*-tolyl)isoxazole-3-carboxamide (4r)

$CDCl_3$, 23 ^{o}C

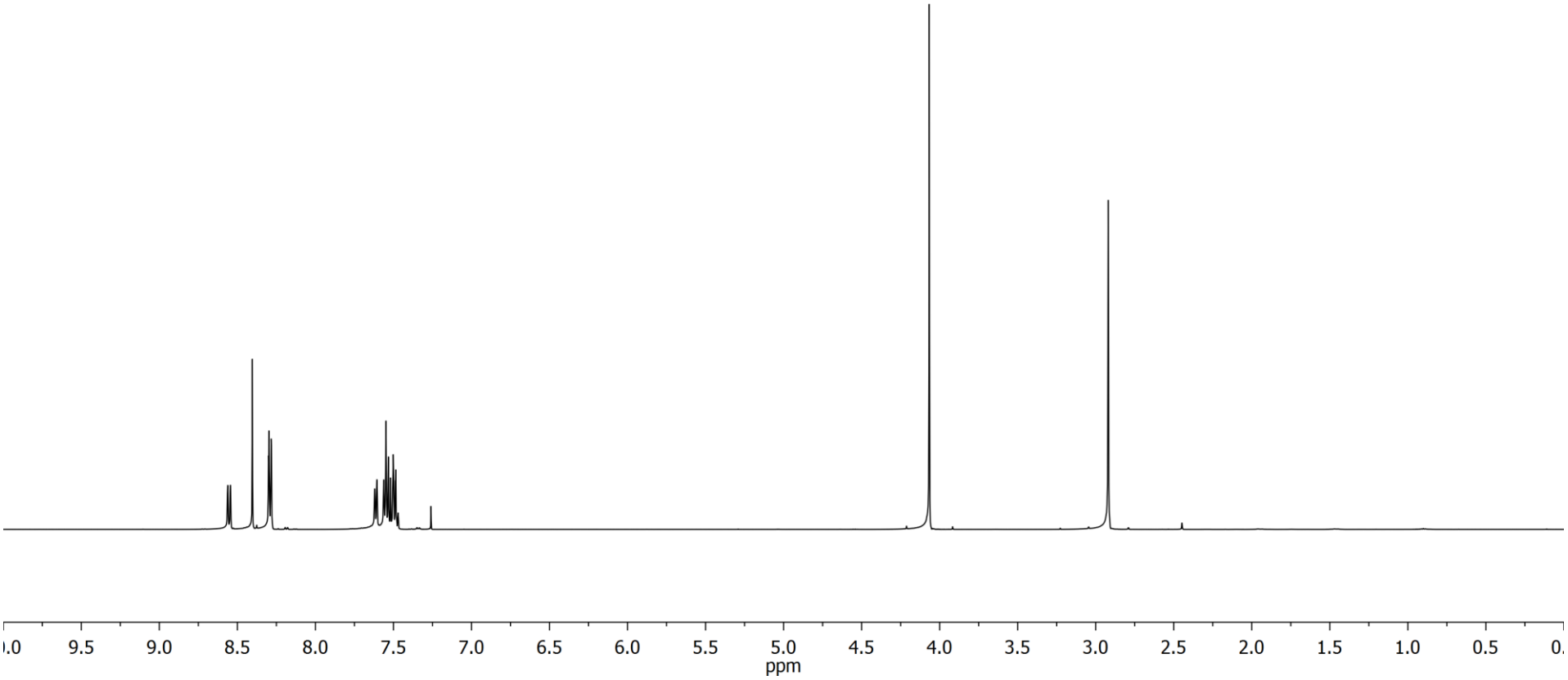




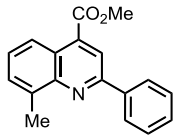
^{1}H NMR of methyl 8-methyl-2-phenylquinoline-4-carboxylate (4s)



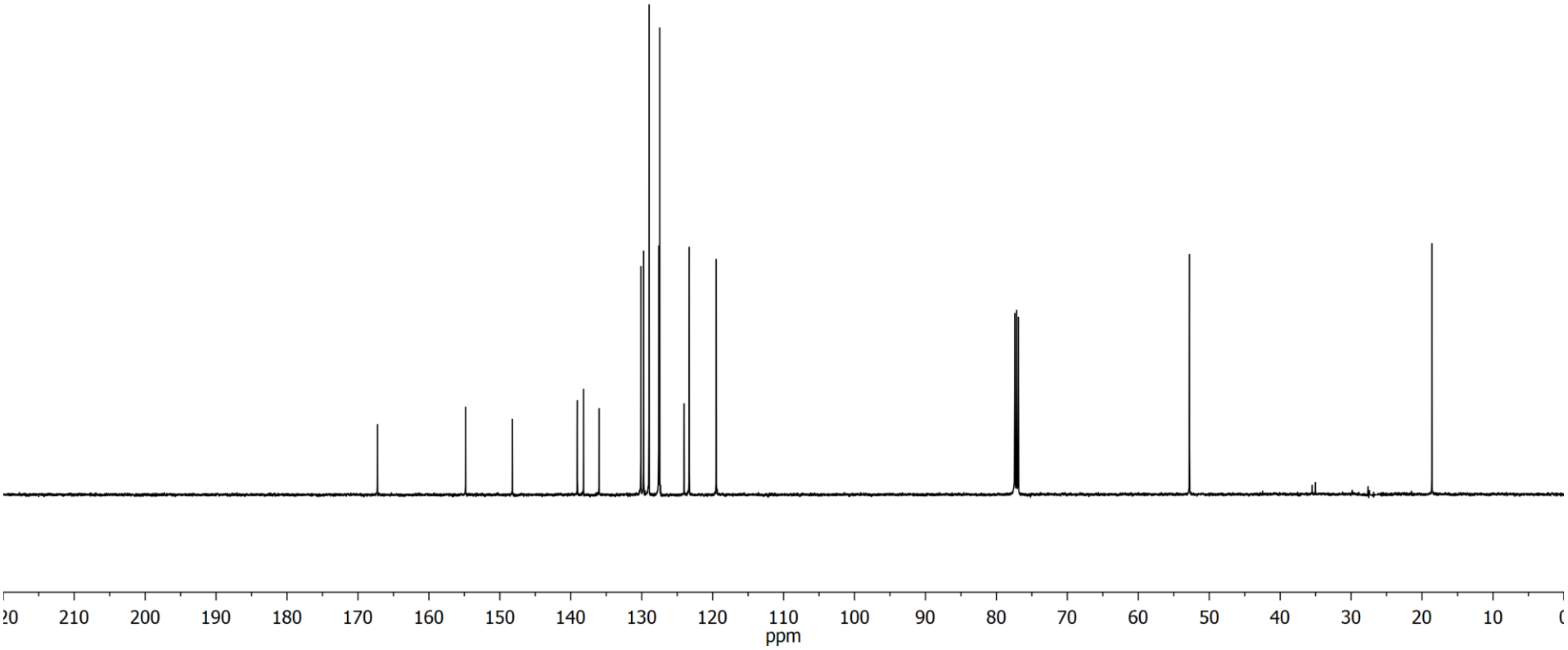
$CDCl_3$, 23 ºC



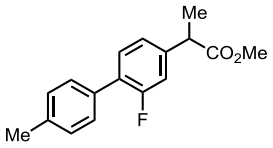
^{13}C NMR of methyl 8-methyl-2-phenylquinoline-4-carboxylate (4s)



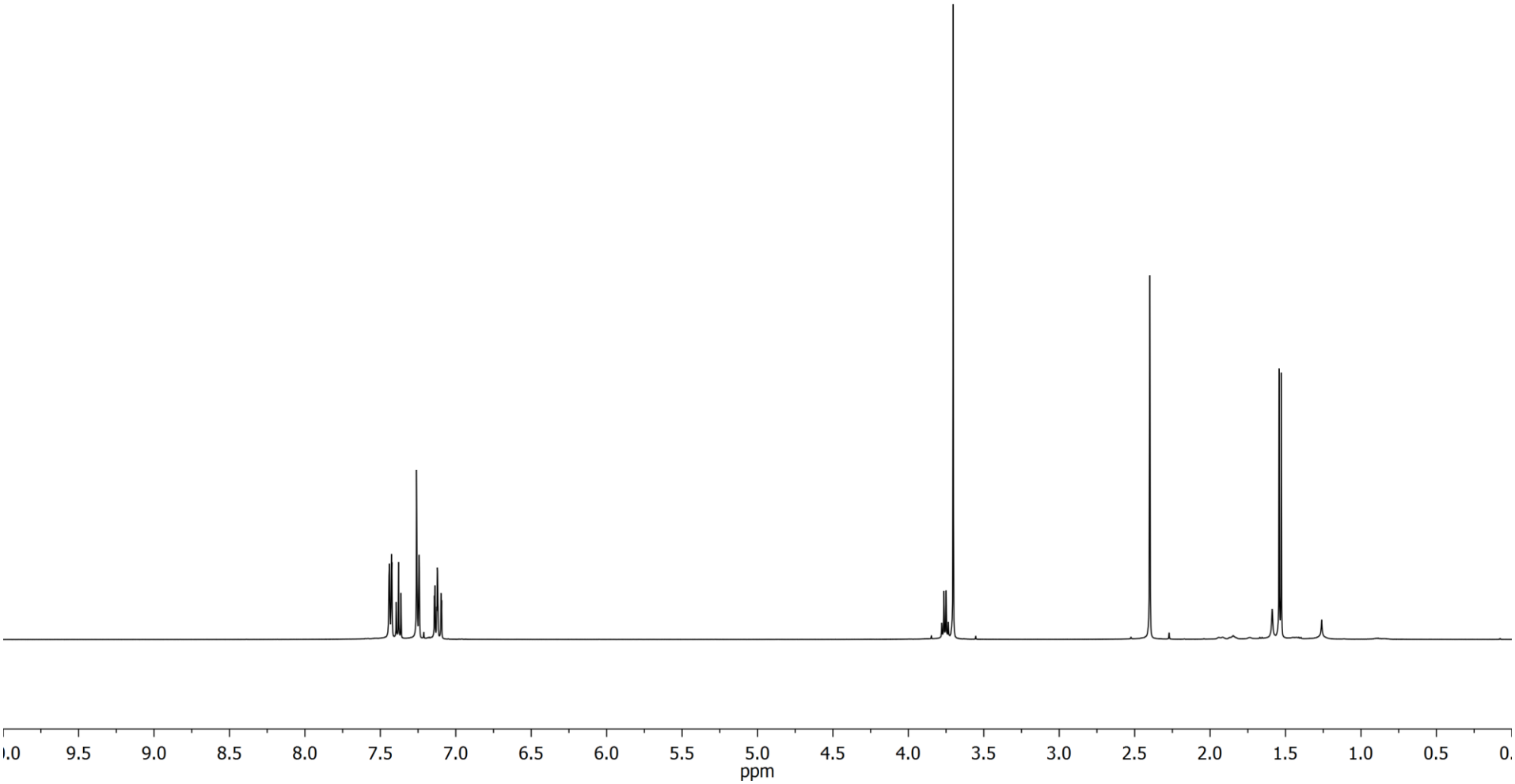
$CDCl_3$, 23 ºC



^{1}H NMR of (±)-methyl 2-(2-fluoro-4'-methyl-[1,1'-biphenyl]-4-yl)propanoate (4t)

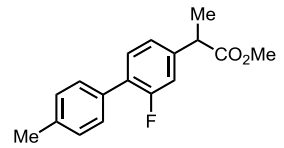


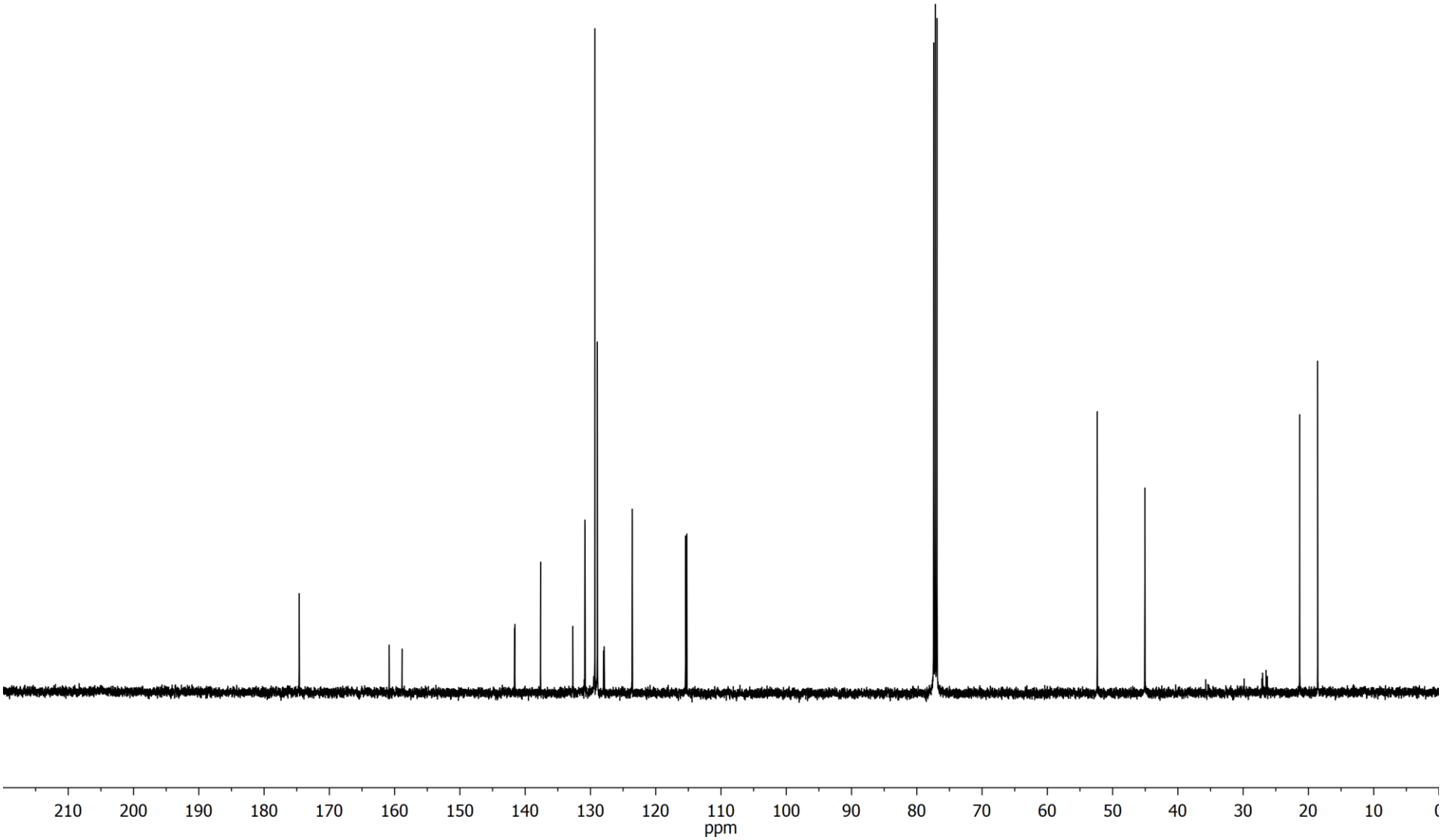
$CDCl_3$, 23 ºC



^{13}C NMR of (±)-methyl 2-(2-fluoro-4'-methyl-[1,1'-biphenyl]-4-yl)propanoate (4t)

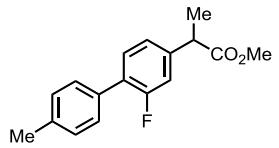
$CDCl_3$, 23 ºC





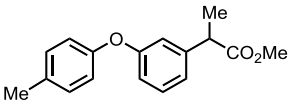
^{19}F NMR of (±)-methyl 2-(2-fluoro-4'-methyl-[1,1'-biphenyl]-4-yl)propanoate (4t)

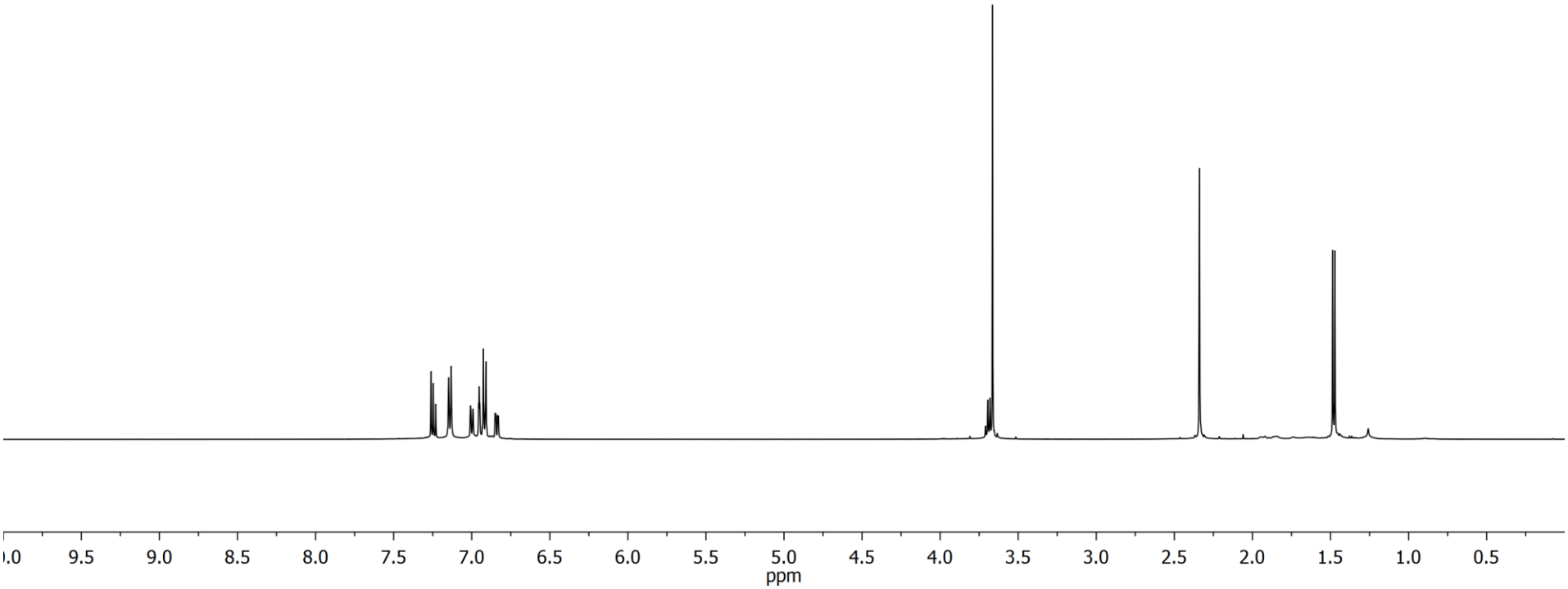
$CDCl_3$, 23 ºC



^{1}H NMR of (±)-methyl 2-(3-(p-tolyloxy)phenyl)propanoate (4u)

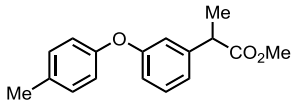
$CDCl_3$, 23 ºC

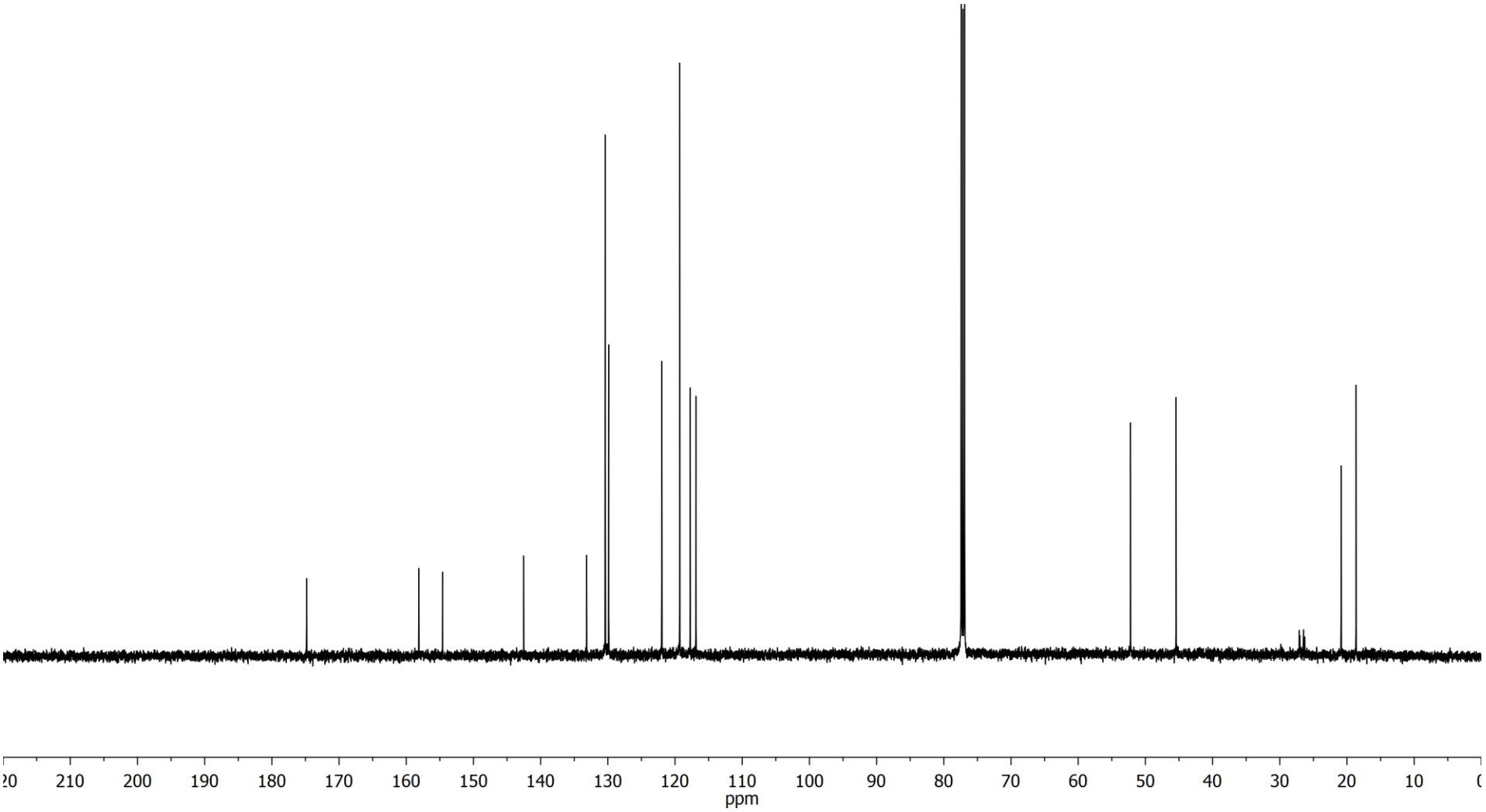




^{13}C NMR of (±)-methyl 2-(3-(p-tolyloxy)phenyl)propanoate (4u)

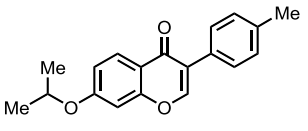
$CDCl_3$, 23 ºC

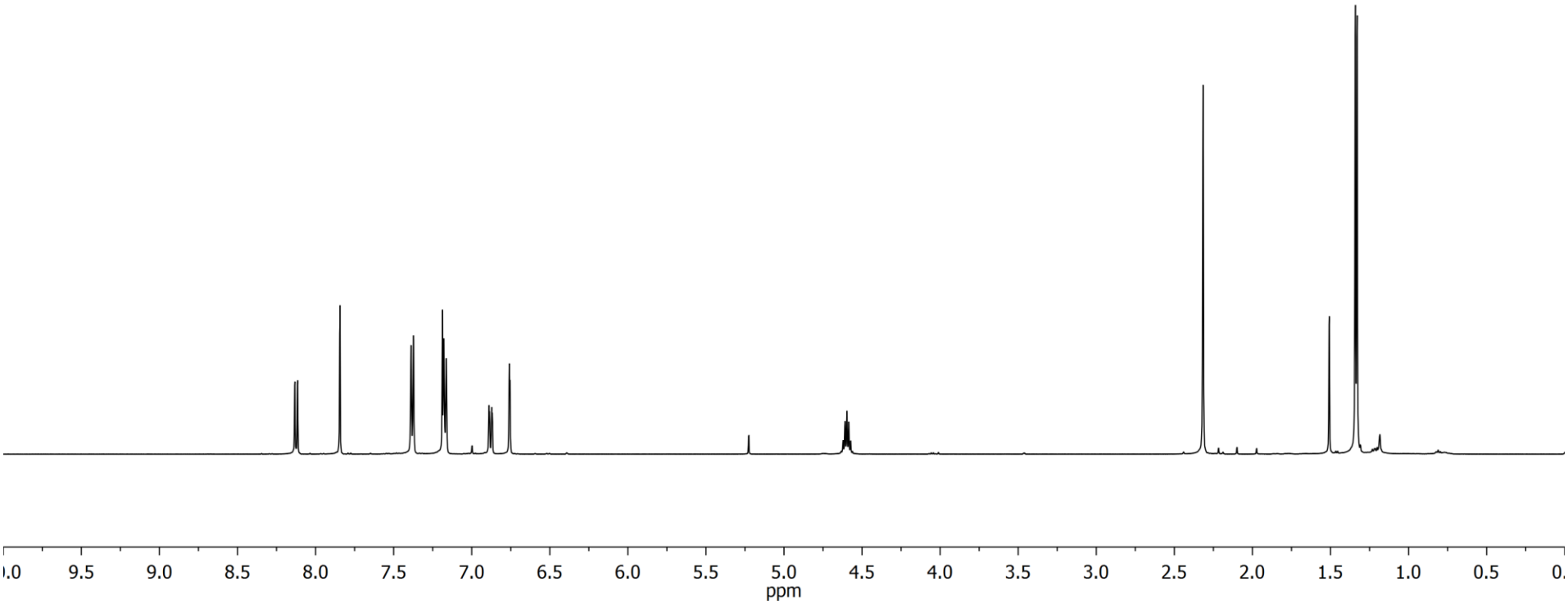




^{1}H NMR of 7-isopropoxy-3-(*p*-tolyl)-4H-chromen-4-one (4v)

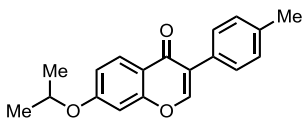
$CDCl_3$, 23 ºC

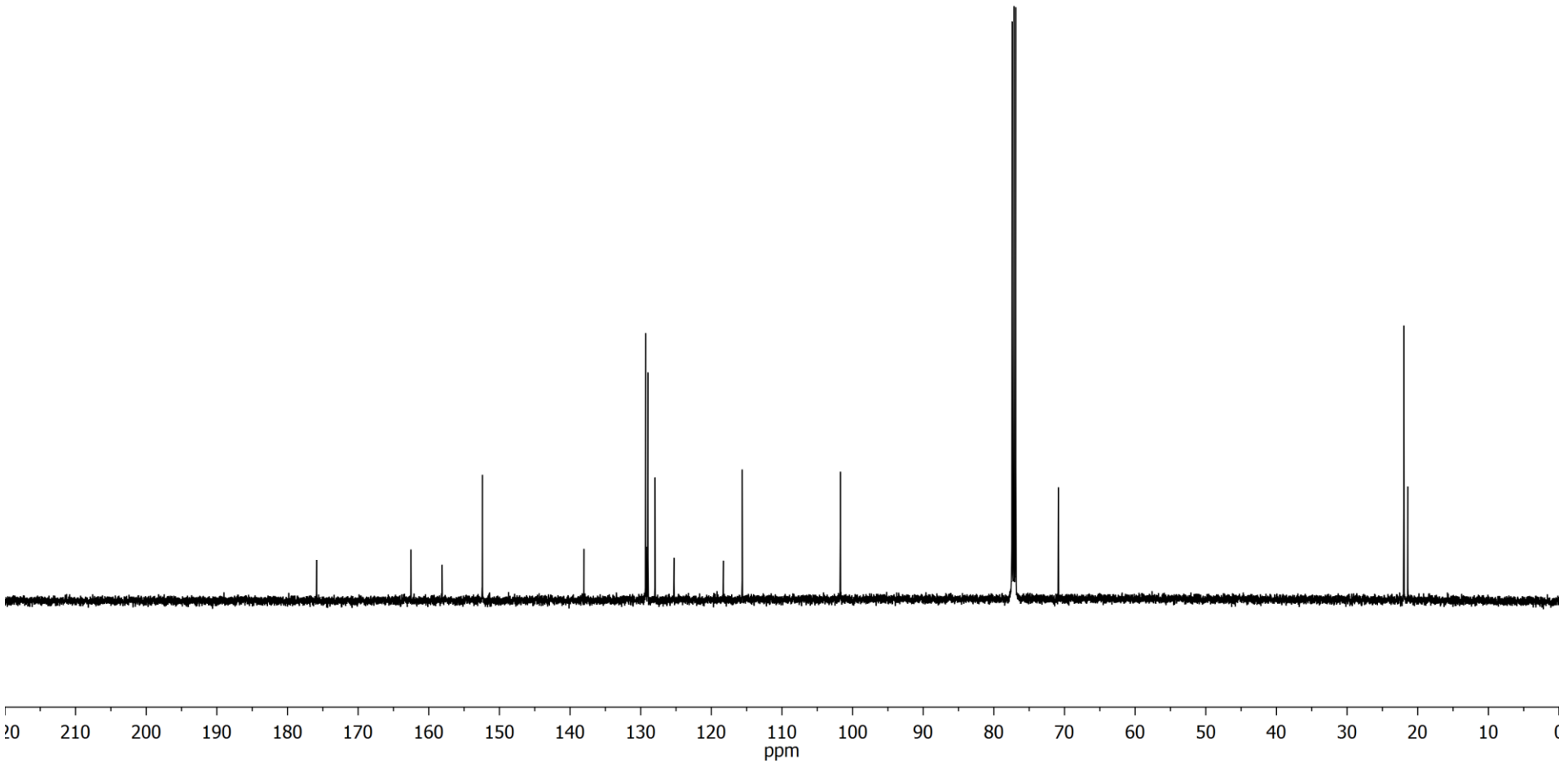




^{13}C NMR of 7-isopropoxy-3-(*p*-tolyl)-4H-chromen-4-one (4v)

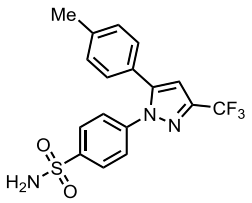
$CDCl_3$, 23 ºC

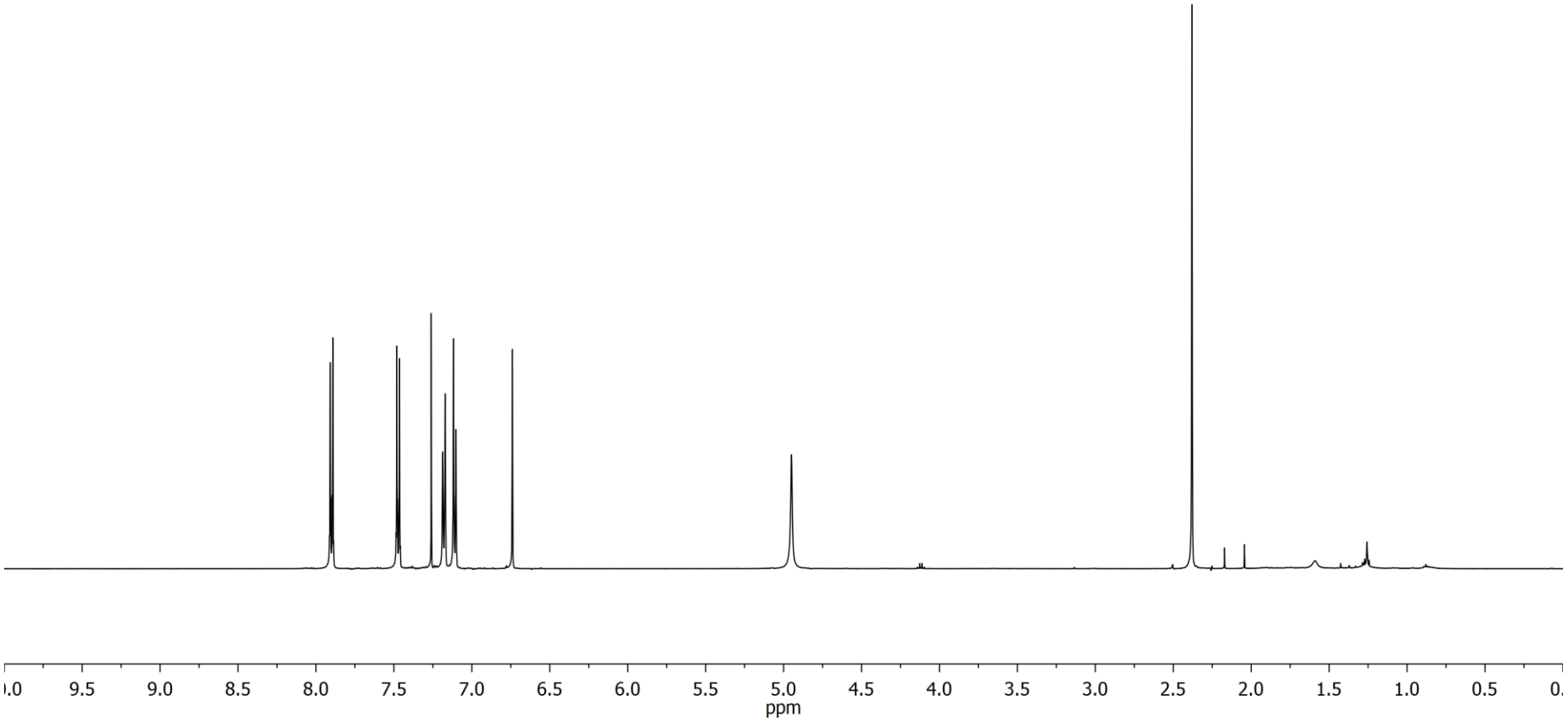




^{1}H NMR of celecoxib (4w)

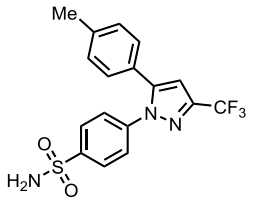
$CDCl_3$, 23 ºC





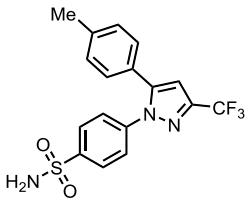
^{13}C NMR of celecoxib (4w)

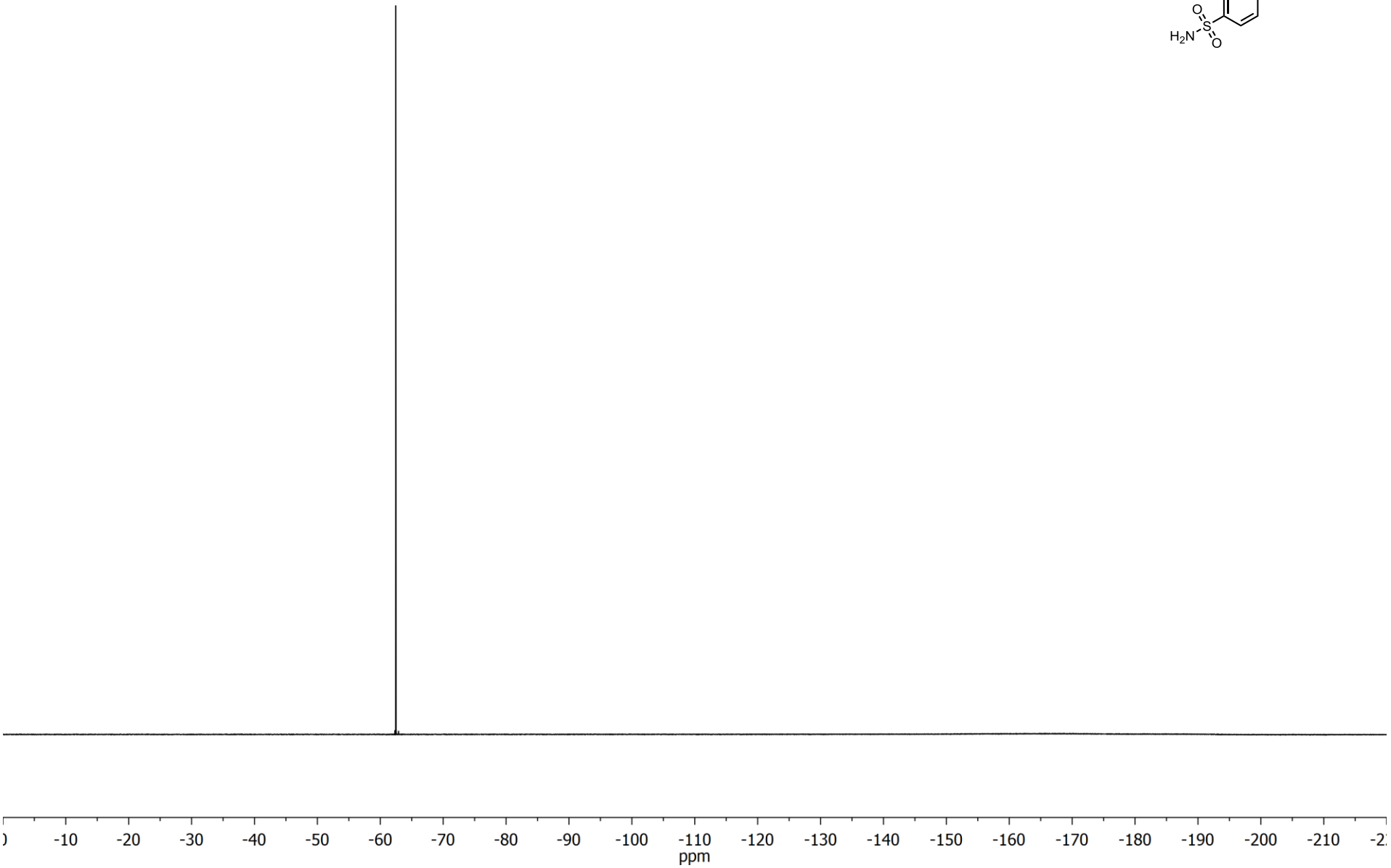
$CDCl_3$, 23 ºC



^{19}F NMR of celecoxib (4w)

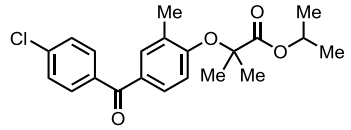
$CDCl_3$, 23 ºC

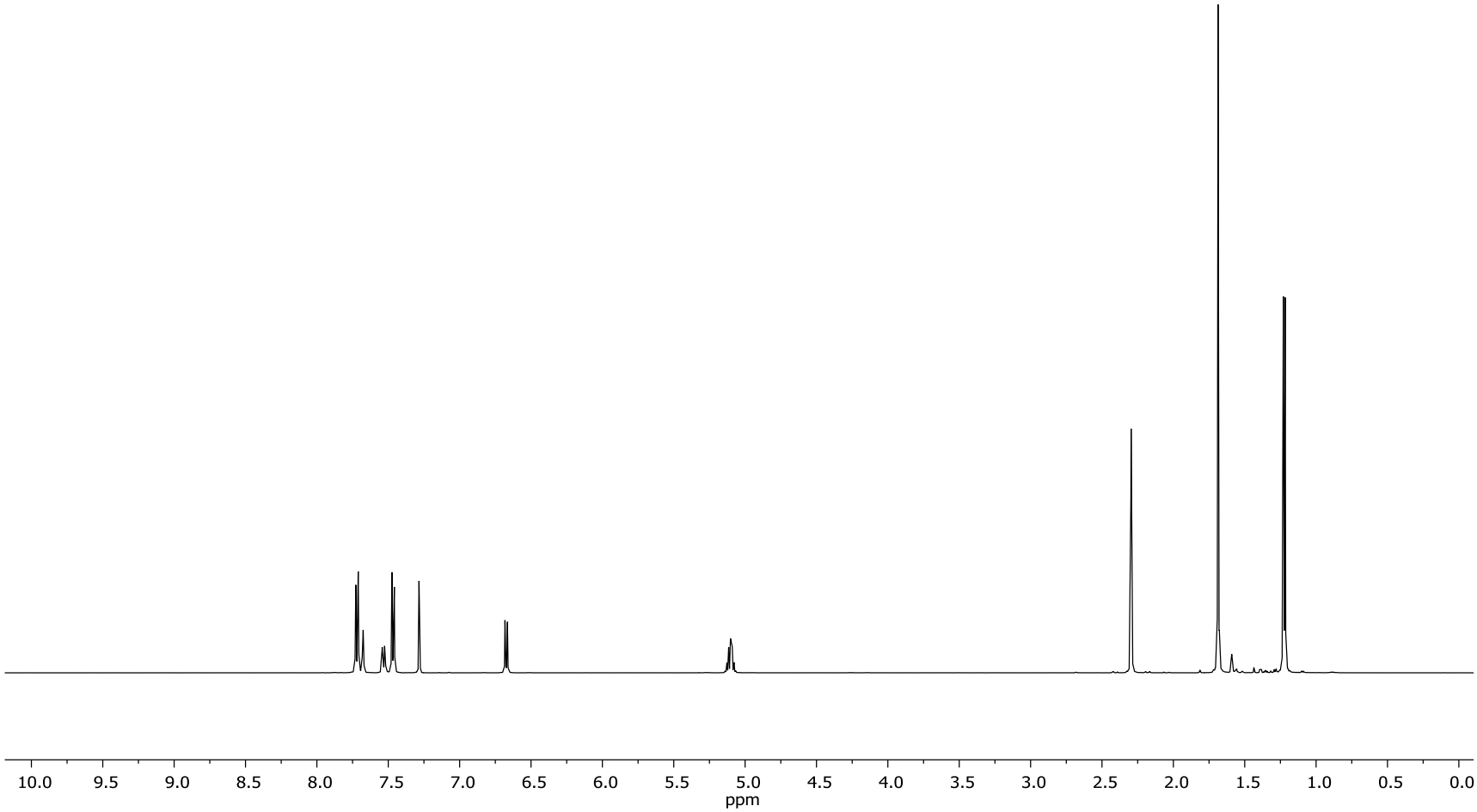




^{1}H NMR of ethyl 5-methylthiophene-2-carboxylate (4x)

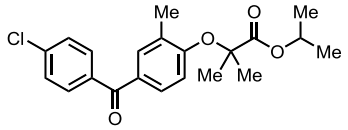
$CDCl_3$, 23 ºC

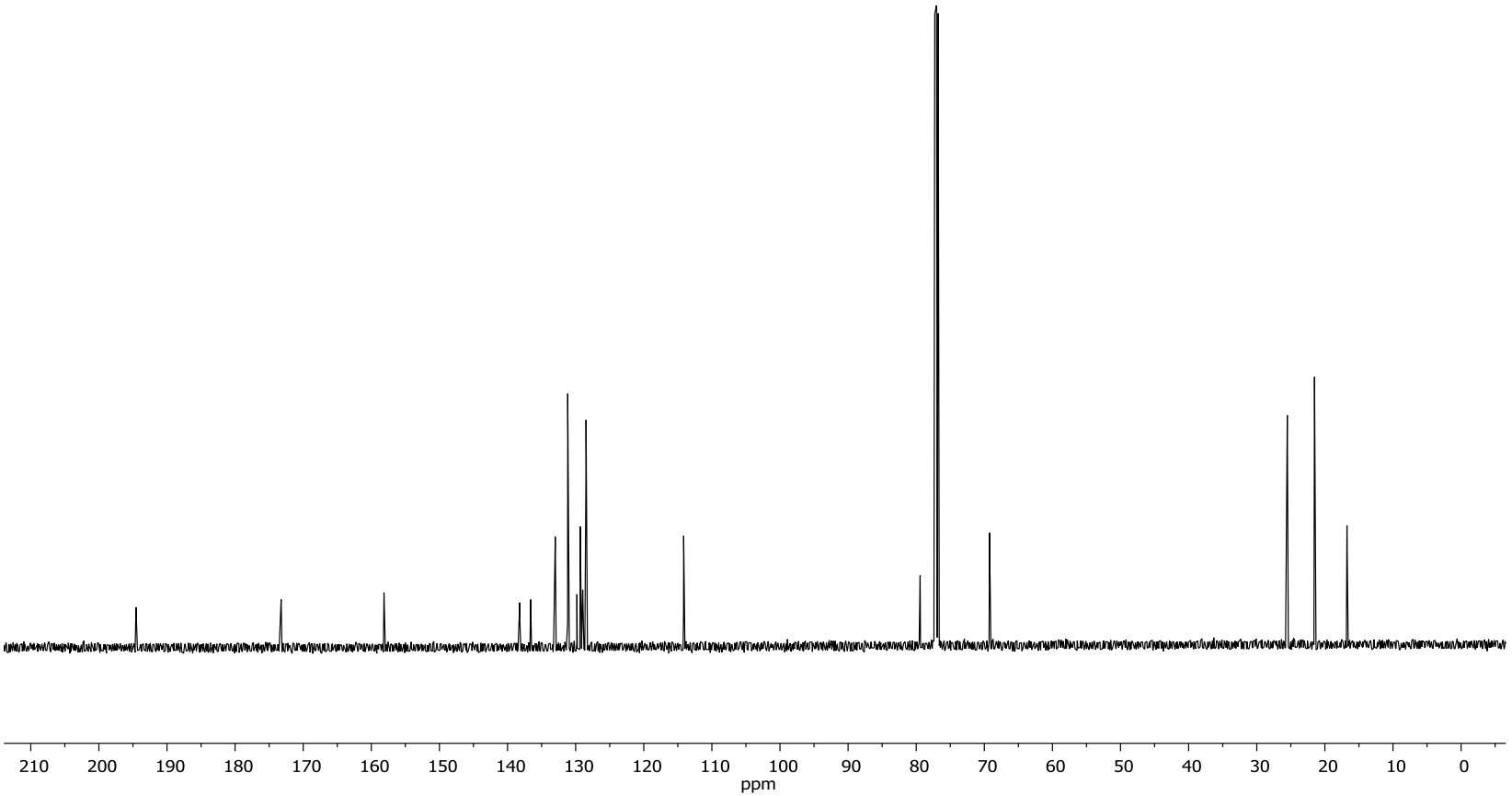




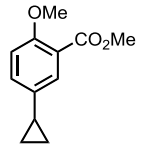
^{13}C NMR of ethyl 5-methylthiophene-2-carboxylate (4x)

$CDCl_3$, 23 ºC

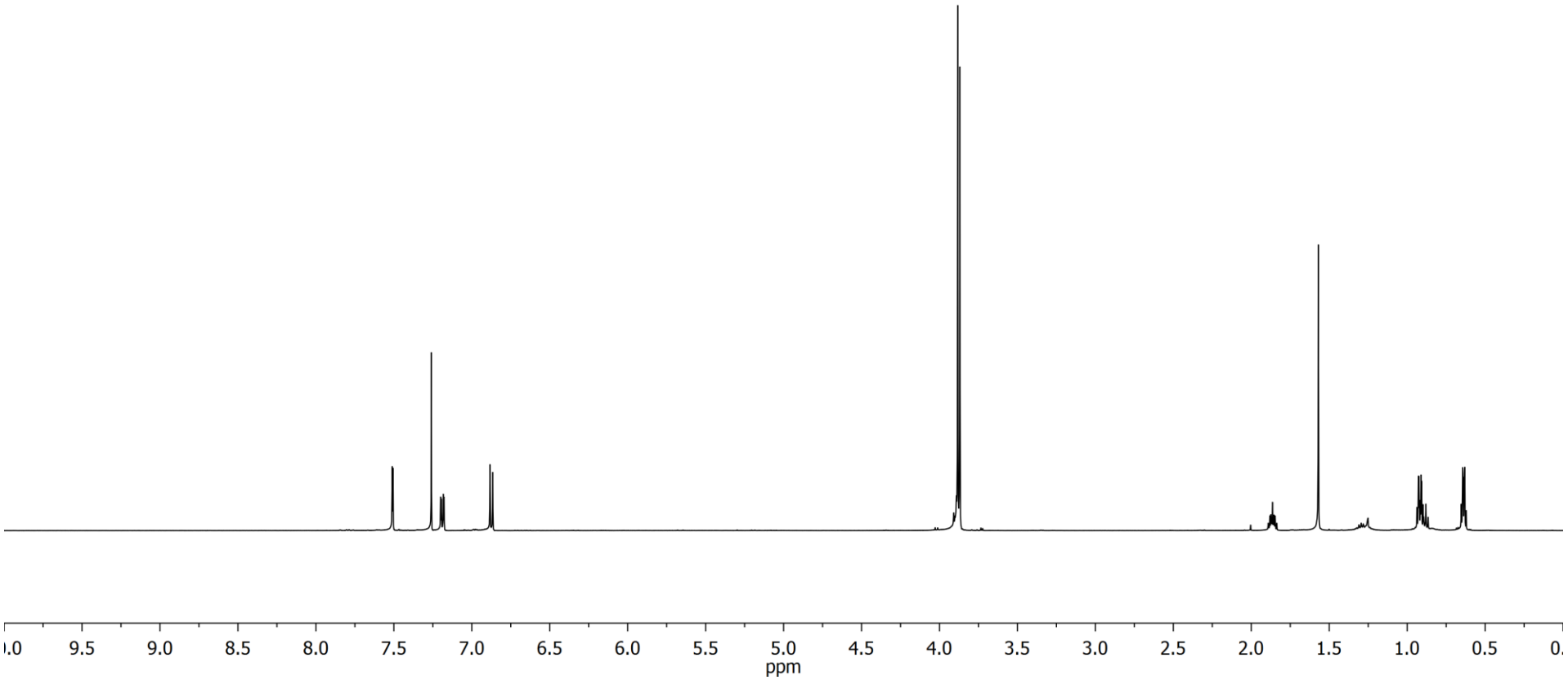




^{1}H NMR of methyl 5-cyclopropyl-2-methoxybenzoate (6a)

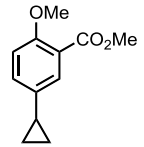


$CDCl_3$, 23 ºC



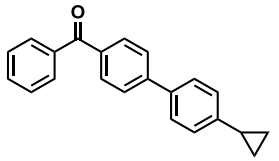
^{13}C NMR of methyl 5-cyclopropyl-2-methoxybenzoate (6a)

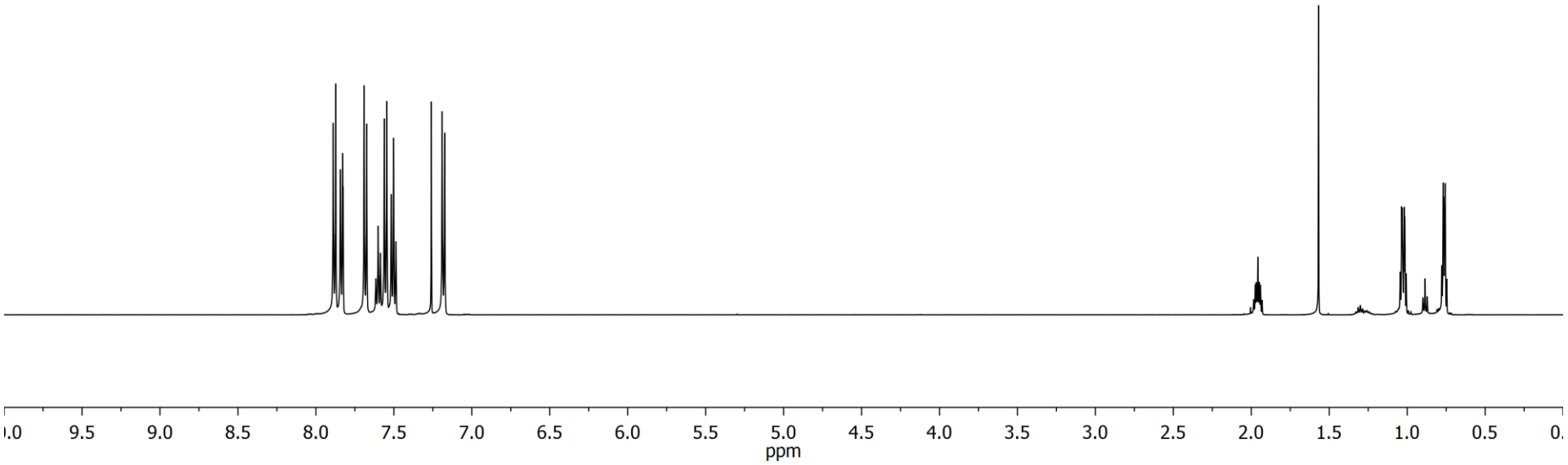
$CDCl_3$, 23 ºC



^{1}H NMR of (4'-cyclopropyl-[1,1'-biphenyl]-4-yl)(phenyl)methanone (6g)

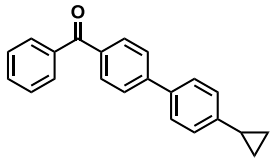
$CDCl_3$, 23 ºC





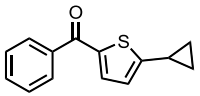
^{13}C NMR of (4'-cyclopropyl-[1,1'-biphenyl]-4-yl)(phenyl)methanone (6g)

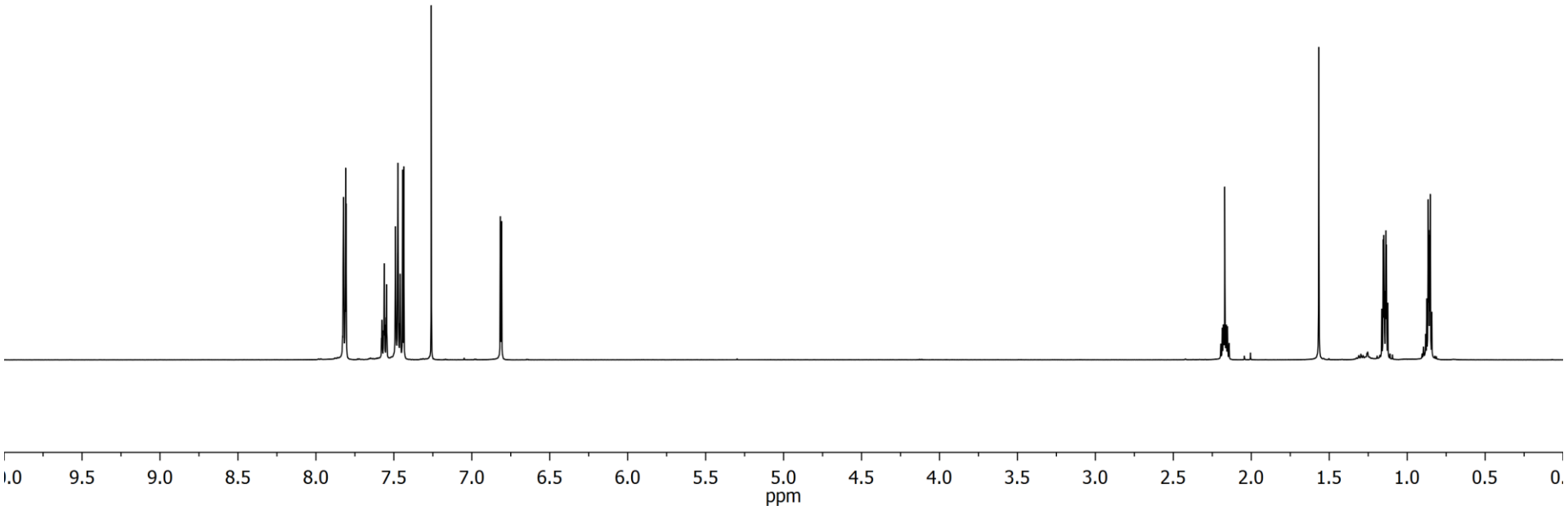
$CDCl_3$, 23 ºC



^{1}H NMR of (5-cyclopropylthiophen-2-yl)(phenyl)methanone (6j)

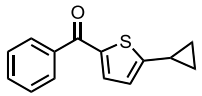
$CDCl_3$, 23 ºC

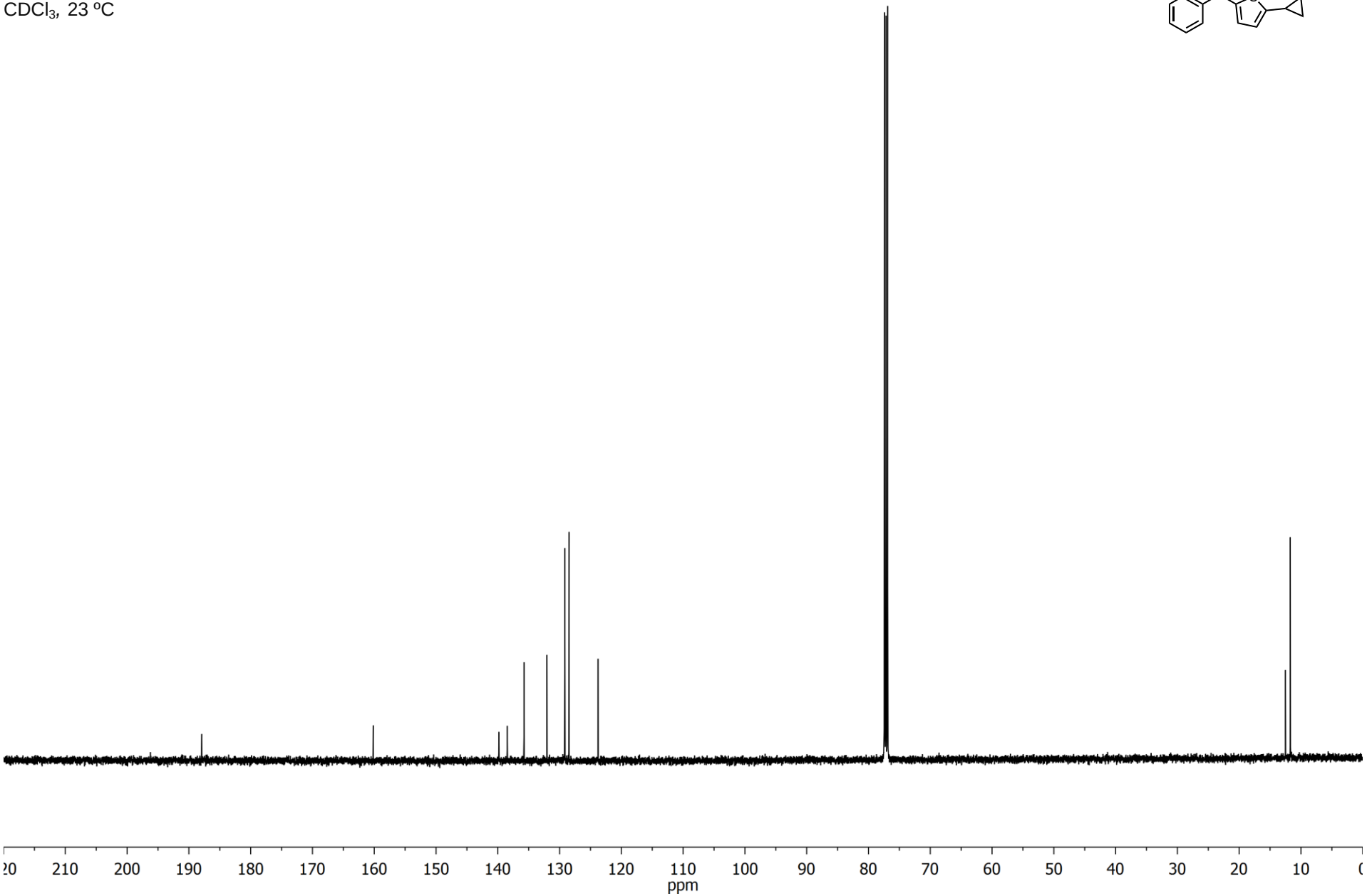




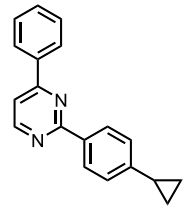
^{13}C NMR of (5-cyclopropylthiophen-2-yl)(phenyl)methanone (6j)

$CDCl_3$, 23 ºC

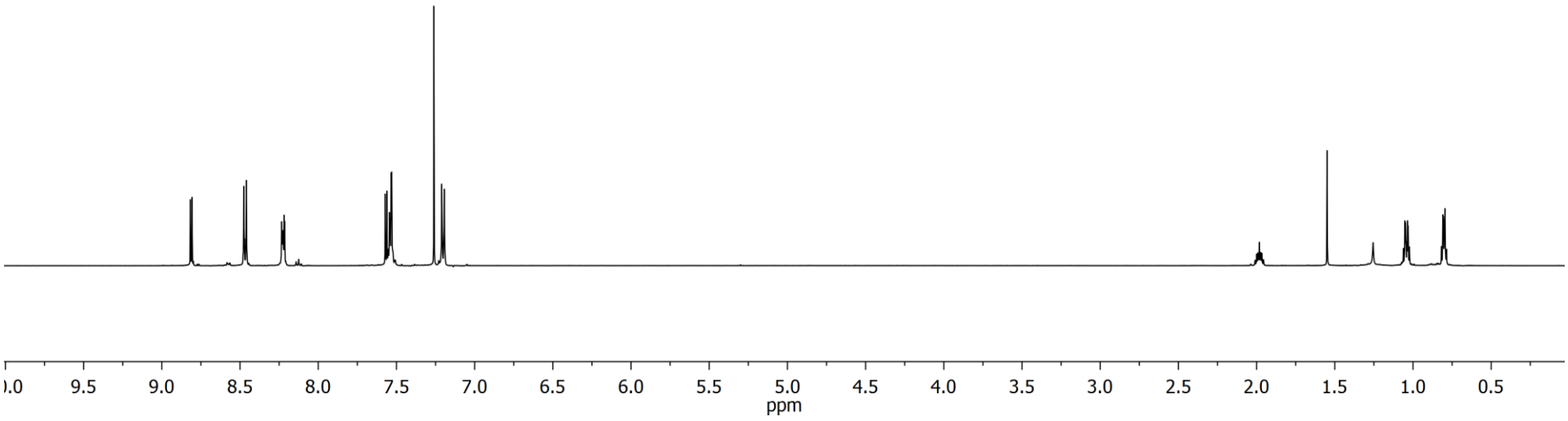




^{1}H NMR of 2-(4-cyclopropylphenyl)-4-phenylpyrimidine (6n)



$CDCl_3$, 23 ºC



^{13}C NMR of 2-(4-cyclopropylphenyl)-4-phenylpyrimidine (6n)

$CDCl_3$, 23 ºC