Supporting Information

Photoredox/copper cocatalyzed domino cyclization of oxime esters with TMSCN: access to antifungal active tetrasubstituted pyrazines

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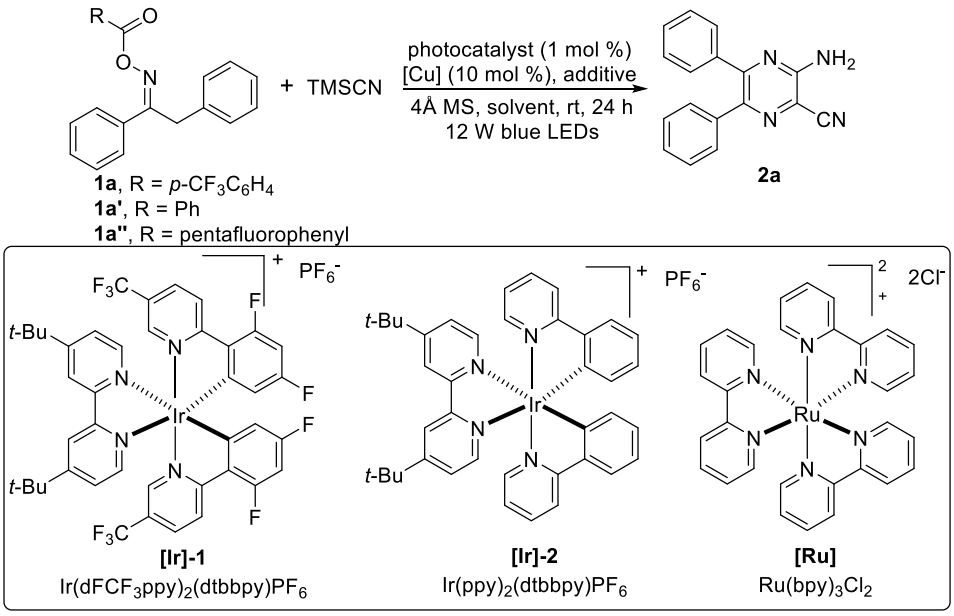
1. General information.

All commercially available reagents were used without further purification. Column chromatography was performed on silica gel (200-300 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker 400 MHz and 500 MHz NMR spectrometers. Chemical shifts (δ) were reported in ppm, and coupling constants (J) were given in Hertz (Hz). Data were reported as s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, hept = heptet, m = multiplet. High-resolution mass spectra (HRMS) were recorded on an AB SCIEX Triple TOF 5600+ mass spectrometer. Melting points were uncorrected. Substrate**s 1a–1t** and **1ai** were prepared according to the literature procedure.[1] Oxime ester substrates **1u–1aa** were synthesized following the literature methods.[2] Substrates **1ab-1ah** were prepared following the literature methods.[3] Substrates **1aj** was prepared following the literature methods.[4] Substrates **1ak** was prepared following the literature methods.[5] Substrates **1al** was prepared following the literature methods.[6] Compound **13** was prepared following the reported methods.[7]

2. Optimization of reaction conditions

Table S1. Optimization of reaction conditions[a]



Entry	**CN** source	Photocatalyst	[Cu]	Additive	Solvent	Yield (%)[b]
1	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	–	DMSO	49
2	TMSCN	**[Ir]-1**	$Cu(OTf)_2$	–	DMSO	0
3	TMSCN	**[Ir]-2**	$Cu(OTf)_2$	–	DMSO	0
4	TMSCN	$Ru(bpy)_3Cl_2$	$Cu(OTf)_2$	–	DMSO	0
5	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	Et_3N	DMSO	28
6	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	AcOH	DMSO	68
7	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	TFA	DMSO	34
8	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	citric acid	DMSO	50
9	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	NH_4Cl	DMSO	55
10	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	NH_4F	DMSO	30
11	**TMSCN**	**$Ir(ppy)_3$**	**$Cu(OTf)_2$**	**$Et_3N \cdot HCl$**	**DMSO**	**85**
12	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N \cdot HBr$	DMSO	73
13	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Py \cdot HCl$	DMSO	68
14	TMSCN	$Ir(ppy)_3$	$CuCl_2$	$Et_3N \cdot HCl$	DMSO	70
15	TMSCN	$Ir(ppy)_3$	$CuBr_2$	$Et_3N \cdot HCl$	DMSO	73
16	TMSCN	$Ir(ppy)_3$	$Cu(OAc)_2$	$Et_3N \cdot HCl$	DMSO	64
17	TMSCN	$Ir(ppy)_3$	$Cu(acac)_2$	$Et_3N \cdot HCl$	DMSO	59
18	TMSCN	$Ir(ppy)_3$	$CuSO_4$	$Et_3N \cdot HCl$	DMSO	65
19	TMSCN	$Ir(ppy)_3$	$Cu(NO_3)_2$	$Et_3N \cdot HCl$	DMSO	73
20	TMSCN	$Ir(ppy)_3$	CuCl	$Et_3N \cdot HCl$	DMSO	58
21	TMSCN	$Ir(ppy)_3$	CuBr	$Et_3N \cdot HCl$	DMSO	65
22	TMSCN	$Ir(ppy)_3$	CuI	$Et_3N \cdot HCl$	DMSO	58
23	TMSCN	$Ir(ppy)_3$	CuOAc	$Et_3N \cdot HCl$	DMSO	53
24	TMSCN	$Ir(ppy)_3$	CuOTf	$Et_3N \cdot HCl$	DMSO	63
25	TMSCN	$Ir(ppy)_3$	$Cu(MeCN)_4PF_6$	$Et_3N \cdot HCl$	DMSO	65
26	TMSCN	$Ir(ppy)_3$	$CuBr \cdot SMe_2$	$Et_3N \cdot HCl$	DMSO	60
27	TMSCN	$Ir(ppy)_3$	CuTC	$Et_3N \cdot HCl$	DMSO	54
28	TMSCN	$Ir(ppy)_3$	CuSCN	$Et_3N \cdot HCl$	DMSO	71
29	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N \cdot HCl$	DMF	62

30	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMA	58
31	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	MeCN	38
32	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	THF	0
33	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	EtOAc	0
34	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DCE	0
35	$Zn(CN)_2$	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	0
36	$K_3[Fe(CN)_6]$	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	0
37[c]	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	64
38[d]	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	0
39[e]	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	48
40[f]	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	77
41[g]	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	65
42[h]	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	52
43	TMSCN	–	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	0
44	TMSCN	$Ir(ppy)_3$	–	$Et_3N·HCl$	DMSO	0
45[i]	TMSCN	$Ir(ppy)_3$	$Cu(OTf)_2$	$Et_3N·HCl$	DMSO	0

[a]All reactions were carried out with **1a** (76.6 mg, 0.20 mmol), TMSCN (59.4 mg, 0.60 mmol, 3.0 equiv.), photocatalyst (0.0020 mmol), copper catalyst (0.020 mmol), additive (0.40 mmol, 2.0 equiv.), and 4Å MS (200 mg) in solvent (2.0 mL) at room temperature under N_2 for 24 h under irradiation with a 12 W blue LED lamp unless otherwise stated. [b]Isolated yield based on **1a**. [c]Without 4Å MS. [d]**1a′** (R = Ph) was used instead of **1a**. [e]**1a″** (R = pentafluorophenyl) was used instead of **1a**. [f]$Et_3N·HCl$ (1.5 equiv.) was used. [g]$Et_3N·HCl$ (1.0 equiv.) was used. [h]$Et_3N·HCl$ (0.50 equiv.) was used. [i]The reaction was conducted in the dark. TMSCN = trimethylsilyl cyanide. TFA = trifluoroacetic acid. Py = pyridine. $Cu(acac)_2$ = cupric acetylacetonate. CuTC = copper(I) thiophene-2-carboxylate. DCE = 1,2-dichloroethane.

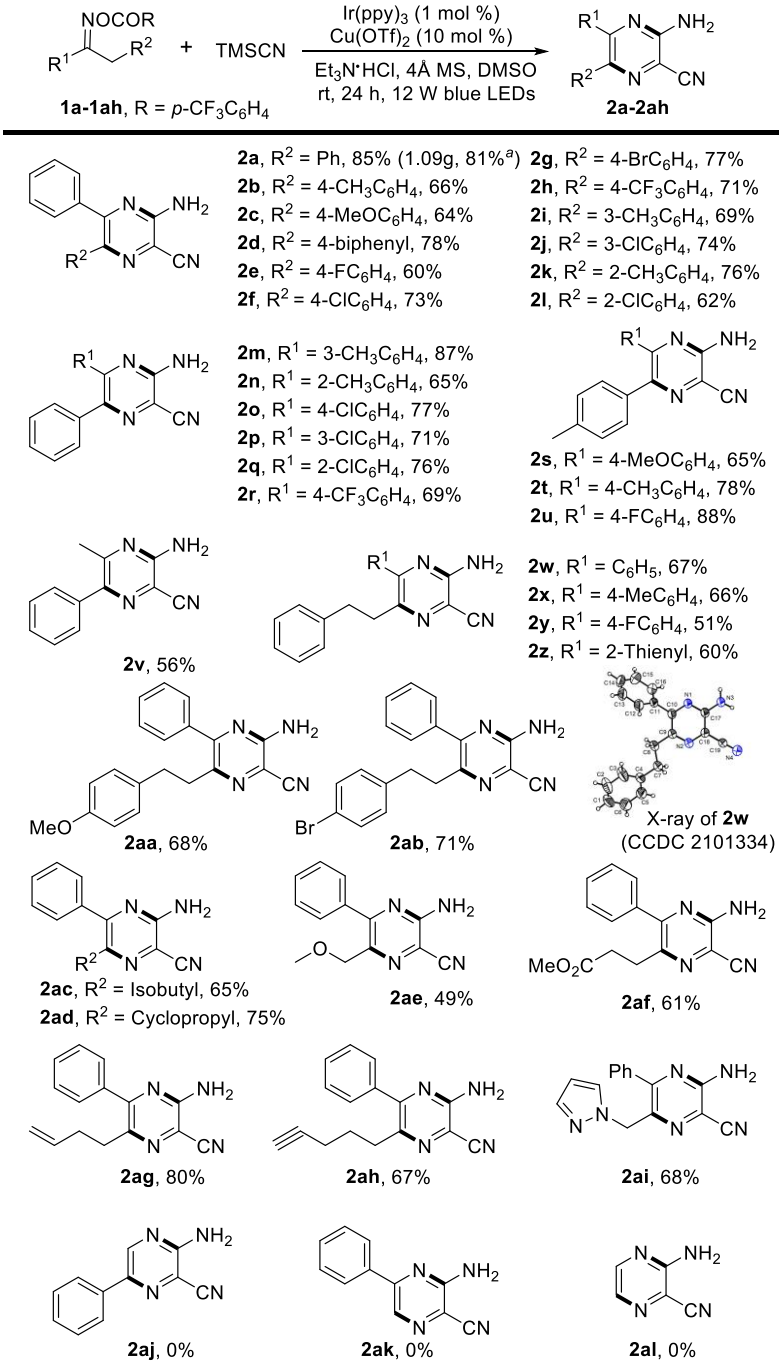
We started our investigation with oxime ester **1a** and TMSCN as model substrates to optimize various reaction parameters (Table S1). To our delight, the desired pyrazine product **2a** was obtained in 49% yield by the treatment of **1a** (0.20 mmol) with TMSCN (0.60 mmol), $Ir(ppy)_3$ (1 mol%), $Cu(OTf)_2$ (10 mol%), and 4Å MS (200 mg) in DMSO (2.0 mL) under irradiation with a 12 W blue LED lamp at room temperature for 24 h (Table S1, entry 1). Other photocatalysts such as $Ir(dFCF_3ppy)_2(dtbbpy)PF_6$ (**Ir-1**), $Ir(ppy)_2(dtbbpy)PF_6$ (**Ir-2**), and $Ru(bpy)_3Cl_2$ gave no product formation (Table S1, entries 2-4). It was found that basic and acidic

additives had a significant effect on the yield of product **2a**. Basic Et_3N resulted in a lower yield of 28% (Table S1, entry 5 *vs* entry 1). Next, various acidic additives, including AcOH, TFA, citric acid, NH_4Cl, NH_4F, $Et_3N \cdot HCl$, $Et_3N \cdot HBr$, and $Py \cdot HCl$ were examined (Table S1, entries 6-13). Among the acidic additives tested, $Et_3N \cdot HCl$ was found to be the best for this transformation, giving product **2a** in 85% yield (Table S1, entry 11). The catalytic efficiency of different copper salts was also checked. Among the examined Cu salts (Table S1, entry 11 and entries 14-28), $Cu(OTf)_2$ gave the highest product yield of 85% (Table S1, entry 11). The screening of solvents showed that DMSO was superior to other solvents such as DMF, DMA, MeCN, THF, EtOAc, and DCE (Table S1, entries 29-34). Other CN sources such as $Zn(CN)_2$ and $K_3[Fe(CN)_6]$ resulted in no product formation (Table S1, entries 35 and 36). This reaction could still proceed without the addition of 4Å MS, albeit in a lower yield of 64% (Table S1, entry 37). The effect of acyloxy leaving groups of oxime esters on the reactivity and the product yield was also investigated. It was found that oxime esters **1a′** (R = Ph) and **1a′′** (R = pentafluorophenyl) gave inferior results than that of **1a** (R = *p*-$CF_3C_6H_4$) (Table S1, entries 38 and 39). Decreasing the amount of $Et_3N \cdot HCl$ from 2.0 equiv. to 1.5 equiv., 1.0 equiv., or 0.50 equiv. resulted in diminished yields (Table S1, entries 40-42), which showed enough amounts of the acidic $Et_3N \cdot HCl$ would more efficiently facilitate the protodemetalation of intermediate **G** (depicted in Scheme 5) and the product formation. No product was observed in the absence of $Ir(ppy)_3$, $Cu(OTf)_2$, or light source (Table S1, entries 43-45).

3. General procedure for the synthesis of pyrazines

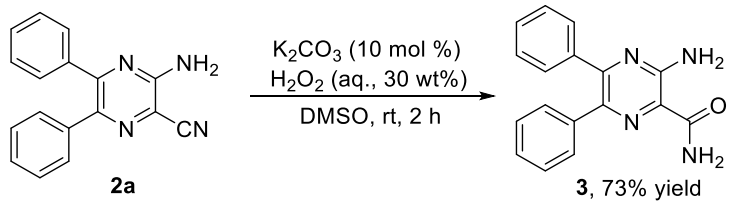
General procedure for the synthesis of pyrazines 2 from oxime esters and TMSCN (Scheme 2). To a reaction tube equipped with a magnetic stir bar were added oxime ester **1** (0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Ir(ppy)_3$ (1.3 mg, 0.0020 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), $Et_3N \cdot HCl$ (55.2 mg, 0.40 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^oC under nitrogen atmosphere

for 24 h. After that, the mixture was diluted with water (15 mL) and extracted with EtOAc (15 mL×3). The combined organic layers were washed with saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1 ~ 10:1) to give product **2**.



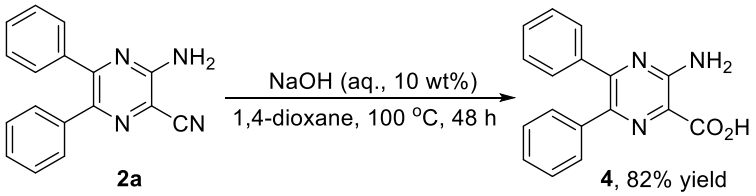
4. Further transformations of product 2a (Scheme 3)

The procedure for the synthesis of compound 3 from 2a.



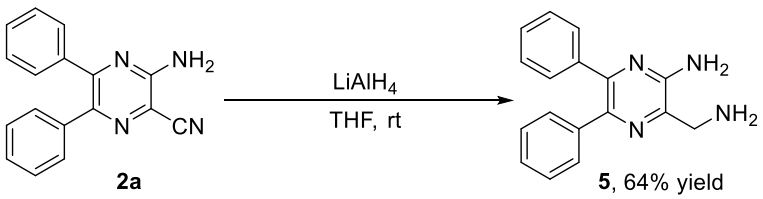
To a reaction tube equipped with a magnetic stir bar were added **2a** (54.5 mg, 0.20 mmol), K_2CO_3 (2.8 mg, 0.020 mmol), and DMSO (2.0 mL). After stirring at room temperature for 0.5 h, H_2O_2 (2.0 mL, 30 wt% in water) was added. The reaction mixture was then allowed to stir at room temperature for 2 h, quenched with H_2O (15.0 mL), and extracted with EtOAc (15 mL×3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5:1) to give compound **3** (42.4 mg, 73%) as a yellow solid.

The procedure for the synthesis of compound 4 from 2a.



To a reaction tube equipped with a magnetic stir bar were added **2a** (54.5 mg, 0.20 mmol), NaOH aqueous solution (3.0 mL, 10 wt%), and 1,4-dioxane (3.0 mL). The reaction mixture was stirred at 100 ^oC under nitrogen atmosphere for 48 h, cooled to room temperature, and concentrated under reduced pressure. The residue was diluted with 3 M HCl (15 mL) and extracted with EtOAc (15 mL×3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 1:1) to give compound **4** (47.8 mg, 82%) as a yellow solid.

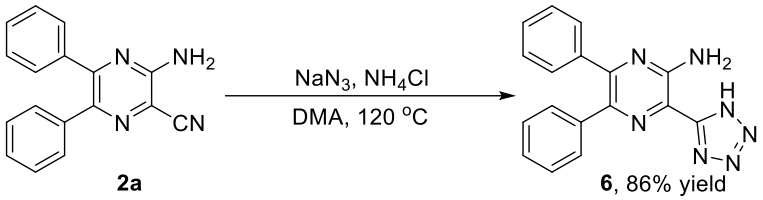
The procedure for the synthesis of compound 5 from 2a.



To a reaction tube equipped with a stirring bar, and $LiAlH_4$ (1.0 mL, 1.0 M in THF).

The solution of **2a** (54.5 mg, 0.20 mmol) in THF (1.0 mL) was added dropwise to the suspension at 0 ℃. The reaction mixture was stirred under room temperature for 24 h. The mixture was cooled to 0 ℃, then H_2O (36 mg, 0.20 mmol), NaOH (2M, aq, 1.0 equiv) and H_2O (180 mg, 1.0 mmol) were added dropwise successively, and stirred 1 h. Then the mixture was diluted with H_2O (15 mL) and extracted with EtOAc (15 mL×3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: dichloromethane/methanol = 20:1) to give compound **5** (35.6 mg, 64%) as a yellow solid.

The procedure for the synthesis of compound 6 from 2a.

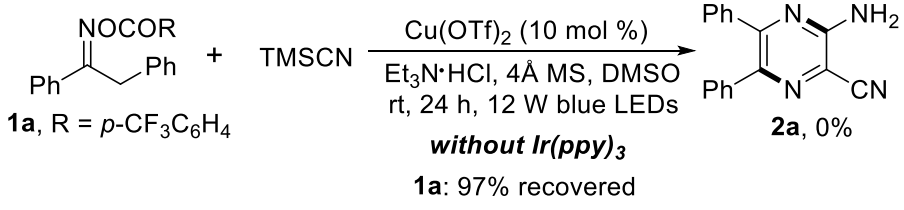


To a reaction tube equipped with a magnetic stir bar were added **2a** (54.5 mg, 0.20 mmol), NH_4Cl (21.8 mg, 0.40 mmol), NaN_3 (26.0 mg, 0.40 mmol), and DMA (2.0 mL). The reaction mixture was stirred at 120 °C for 12 h and cooled to rt. The residue was dissolved in 10 mL water, neutralized with 10% HCl and extracted with EtOAc (15 mL×3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 1:1) to give compound **6** (54.5 mg, 86%) as a yellow solid.

5. Mechanistic studies

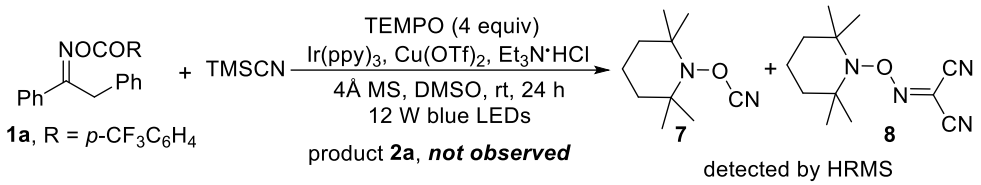
5.1 Control experiments

The experiment in the absence of $Ir(ppy)_3$ (Scheme 4a)

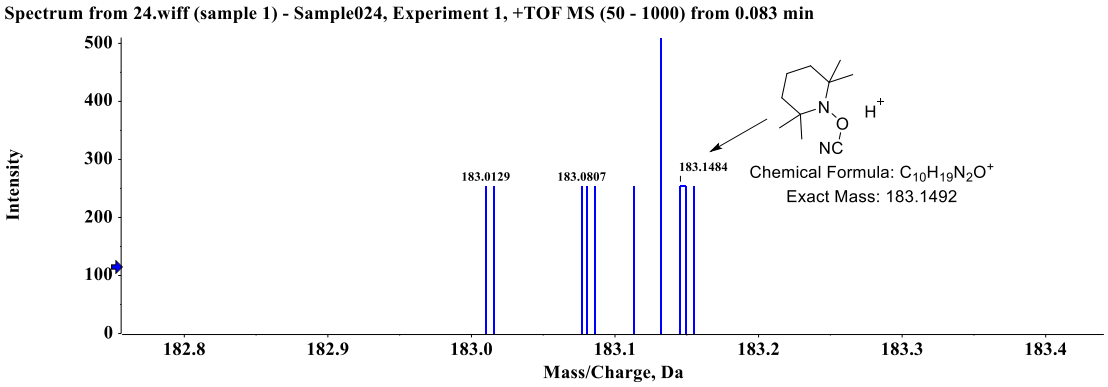


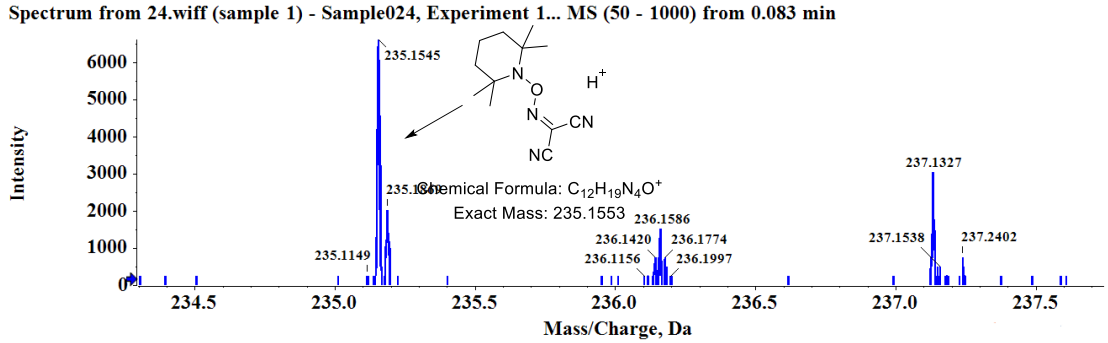
To a reaction tube equipped with a magnetic stir bar were added oxime ester **1a** (76.6 mg, 0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), $Et_3N \cdot HCl$ (55.2 mg, 0.40 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^oC under nitrogen atmosphere for 24 h. Thin-layer chromatography (TLC) indicated that the oxime ester **1a** was kept intact, and the formation of product **2a** was not observed. After that, the mixture was diluted with water (15 mL) and extracted with EtOAc (15 mL×3). The combined organic layers were washed with saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1) to afford the recovered oxime ester **1a** (74.5 mg, 97% recovered). Such results are not contradictory with previous reports about copper-mediated/catalyzed N-O bond cleavage reactions of oxime esters, which need to be conducted under heating conditions.

The experiment of the addition of radical scavenger TEMPO (Scheme 4b)

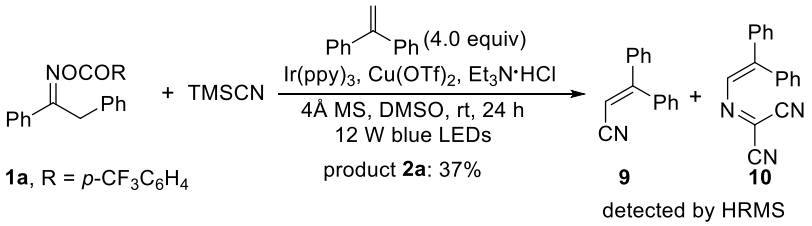


To a reaction tube equipped with a magnetic stir bar were added oxime ester **1a** (76.6 mg, 0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Ir(ppy)_3$ (1.3 mg, 0.0020 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), $Et_3N \cdot HCl$ (55.2 mg, 0.40 mmol), TEMPO (125.0 mg, 0.80 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^oC under nitrogen atmosphere for 24 h. Thin-layer chromatography (TLC) analysis indicated that the formation of product **2a** was not observed. After that, a trace amount of the crude reaction mixture was subjected to the HRMS analysis.



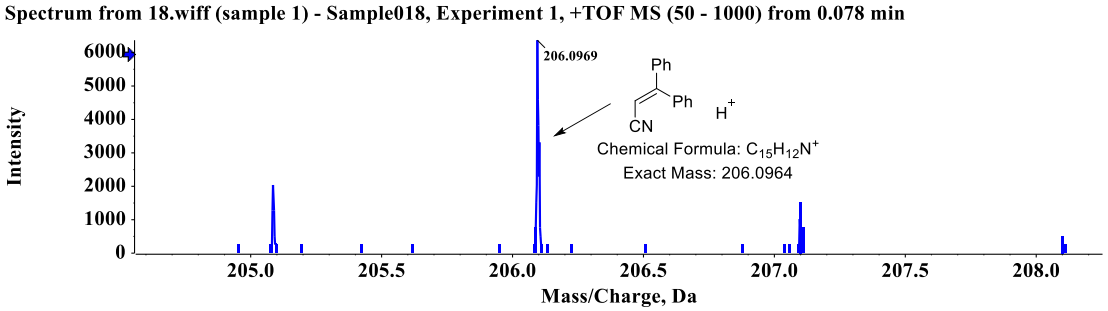


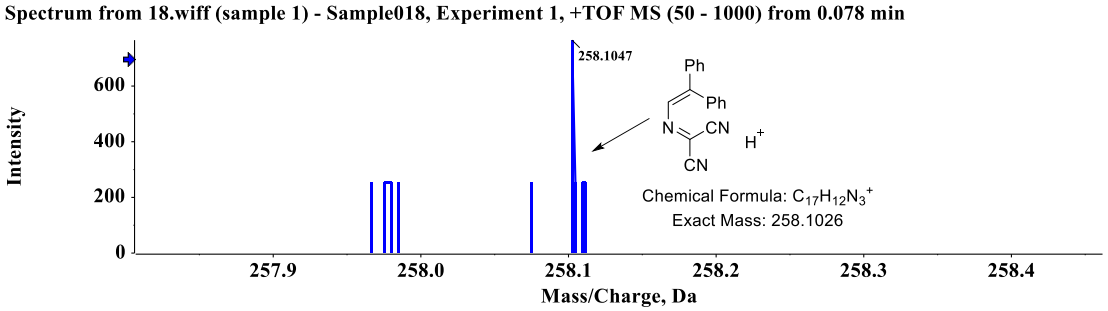
The experiment of the addition of radical scavenger 1,1-diphenylethylene (Scheme 4b)



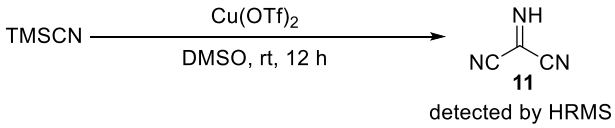
To a reaction tube equipped with a magnetic stir bar were added oxime ester **1a** (76.6 mg, 0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Ir(ppy)_3$ (1.3 mg, 0.0020 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), $Et_3N·HCl$ (55.2 mg, 0.40 mmol), 1,1-diphenylethylene (144.2 mg, 0.80 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^{o}C under nitrogen atmosphere for 24 h. After that, a trace amount of the crude reaction mixture was subjected to the HRMS analysis. Afterwards, the mixture was diluted with water (15 mL) and extracted with EtOAc (15 mL×3). The combined organic layers were washed with saturated aqueous $NaHCO_3$, brine, dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was

purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 100:1) to give product **2a** (20.1 mg, 37%) as a white solid.

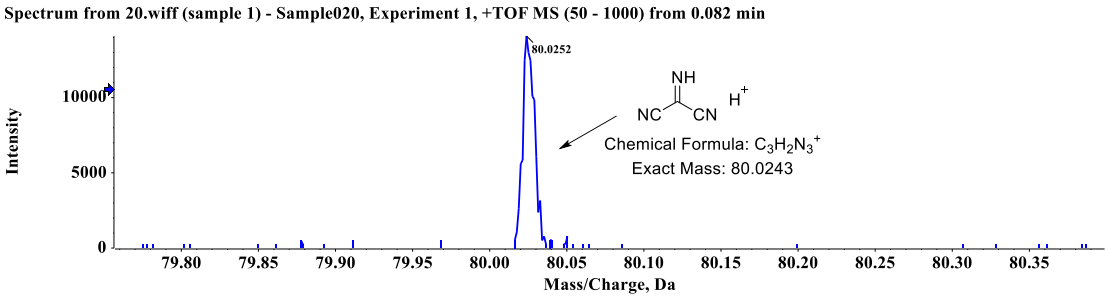




Intermediates trapping experiments (Scheme 4c)

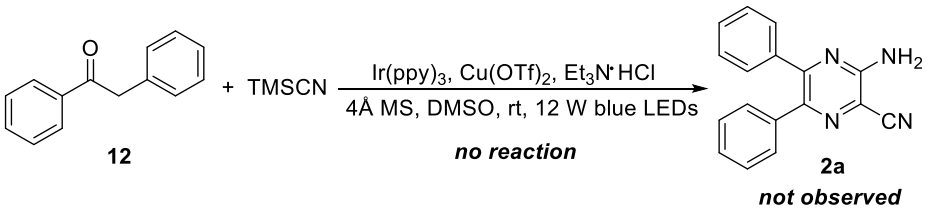


To a reaction tube equipped with a magnetic stir bar were added TMSCN (59.5 mg, 0.60 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), and anhydrous DMSO (2.0 mL). The reaction mixture was stirred at 25 ^{o}C under nitrogen atmosphere for 12 h. After that, a trace amount of the crude reaction mixture was subjected to the HRMS analysis, which indicated that the intermediate **11**could be formed *in situ*.



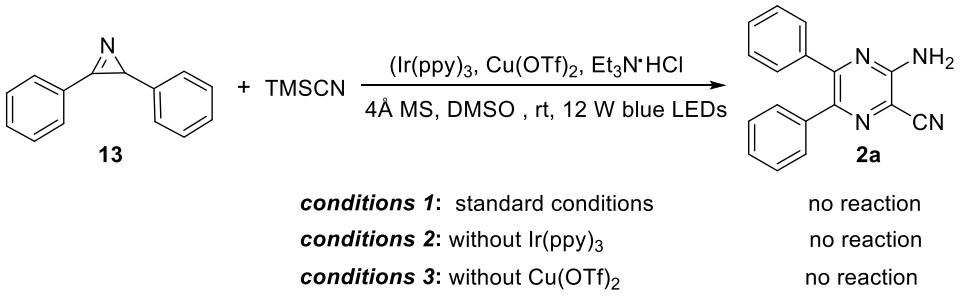
The possible reaction between 2-phenylacetophenone (12) and TMSCN (Scheme

4d)



To a reaction tube equipped with a magnetic stir bar were added **12** (38.6 mg, 0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Ir(ppy)_3$ (1.3 mg, 0.0020 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), $Et_3N \cdot HCl$ (55.2 mg, 0.40 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^oC under nitrogen atmosphere for 24 h. Thin-layer chromatography (TLC) analysis indicated that no reaction took place and the formation of product **2a** was not observed. The results suggested that 2-phenylacetophenone (**12**) was not likely to be the intermediate in the transformation of oxime ester **1a** to the pyrazine product **2a**.

The possible reaction between 2,3-diphenyl-2*H*-azirine (13) and TMSCN (Scheme 4f)



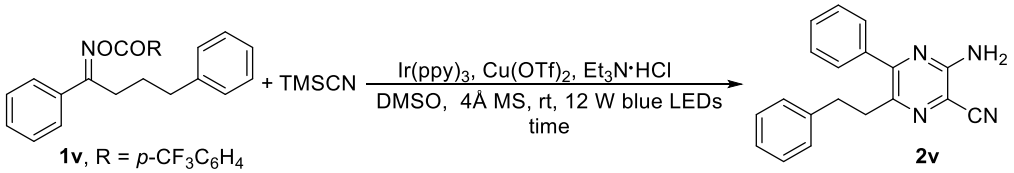
***Reaction conditions 1 (standard conditions)*:** To a reaction tube equipped with a magnetic stir bar were added azirine **13** (38.6 mg, 0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Ir(ppy)_3$ (1.3 mg, 0.0020 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), $Et_3N \cdot HCl$ (55.2 mg, 0.40 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^oC under nitrogen atmosphere for 24 h. Thin-layer chromatography (TLC) analysis indicated that the formation of product **2a** was not observed.

***Reaction conditions 2 (without $Ir(ppy)_3$)*:** To a reaction tube equipped with a magnetic stir bar were added azirine **13** (38.6 mg, 0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Cu(OTf)_2$ (7.24 mg, 0.020 mmol), $Et_3N·HCl$ (55.2 mg, 0.40 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^oC under nitrogen atmosphere for 24 h. Thin-layer chromatography (TLC) analysis indicated that the formation of product **2a** was not observed.

***Reaction conditions 3 (without $Cu(OTf)_2$)*:** To a reaction tube equipped with a magnetic stir bar were added azirine **13** (38.6 mg, 0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Ir(ppy)_3$ (1.3 mg, 0.0020 mmol), $Et_3N·HCl$ (55.2 mg, 0.40 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was irradiated with a 12 W blue LED lamp and stirred at 25 ^oC under nitrogen atmosphere for 24 h. Thin-layer chromatography (TLC) analysis indicated that the formation of product **2a** was not observed. The results suggested that the azirine was not likely to be the intermediate to the formation of the pyrazine product.

5.2 Light On/Off experiments

To a reaction tube equipped with a magnetic stir bar were added oxime ester **1a** (0.20 mmol), TMSCN (59.5 mg, 0.60 mmol), $Ir(ppy)_3$ (1.3 mg, 0.0020 mmol), $Cu(OTf)_2$ (7.24 mg, 0.02 mmol), $Et_3N·HCl$ (55.2 mg, 0.40 mmol), 4Å MS (200 mg), and anhydrous DMSO (2.0 mL). The reaction mixture was stirred at 25 ℃ under nitrogen atmosphere with the light turned on and off at intervals and the yields were determined by ^1H NMR with 1,2-dibromoethane as the internal standard. The light on/off profile over time illustrated that the product generation could only be observed under blue light irradiation. The results indicated that the radical chain reaction might not be involved in the mechanism.



1v, R = *p*-$CF_3C_6H_4$ **2v**

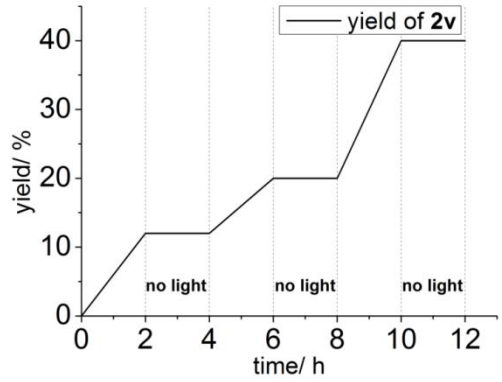
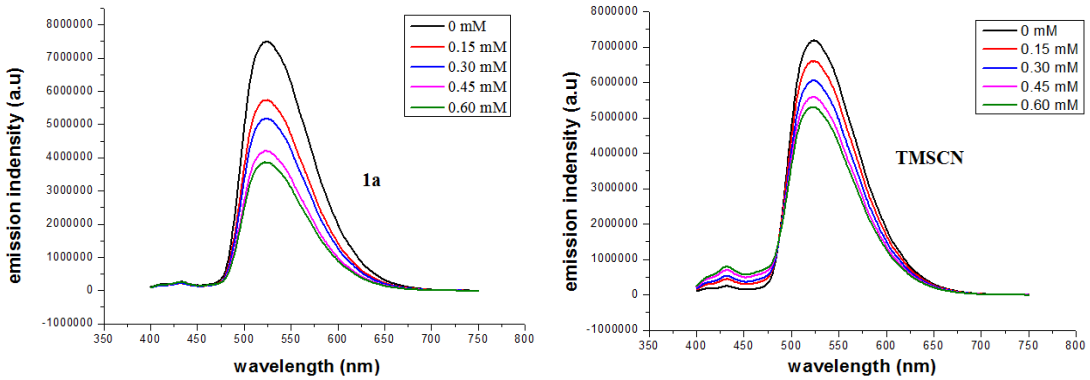


Figure S1 Light on-off experiments

5.3 Fluorescence quenching experiments

The luminescence quenching experiment was taken using a FluoroMax-4 Spectrophotometer. The experiments were carried out with the 3 x 10^{-5} mol/L of $Ir(ppy)_3$ in DMSO at 25 ^{o}C under nitrogen atmosphere. The concentrations of quencher (**1a**, TMSCN, $Et_3N \cdot HCl$, $Cu(OTf)_2$) in DMSO were 0.15 mmol/L, 0.3 mmol/L, 0.45 mmol/L, 0.6 mmol/L. The excitation wavelength was 384 nm and the emission intensity was collected at 523 nm. The ratio of I_0/I was plotted as a function of the quencher concentration (I_0 = emission intensity of the photocatalyst in isolation at the specified wavelength; I = observed emission intensity of the photocatalyst with added quencher). The Stern-Volmer plots exhibited that the **1a** was a much better quencher than TMSCN, $Cu(OTf)_2$ or $Et_3N \cdot HCl$, indicating that the reaction was likely initiated from oxidative quenching of the excited Ir(III) photocatalyst.



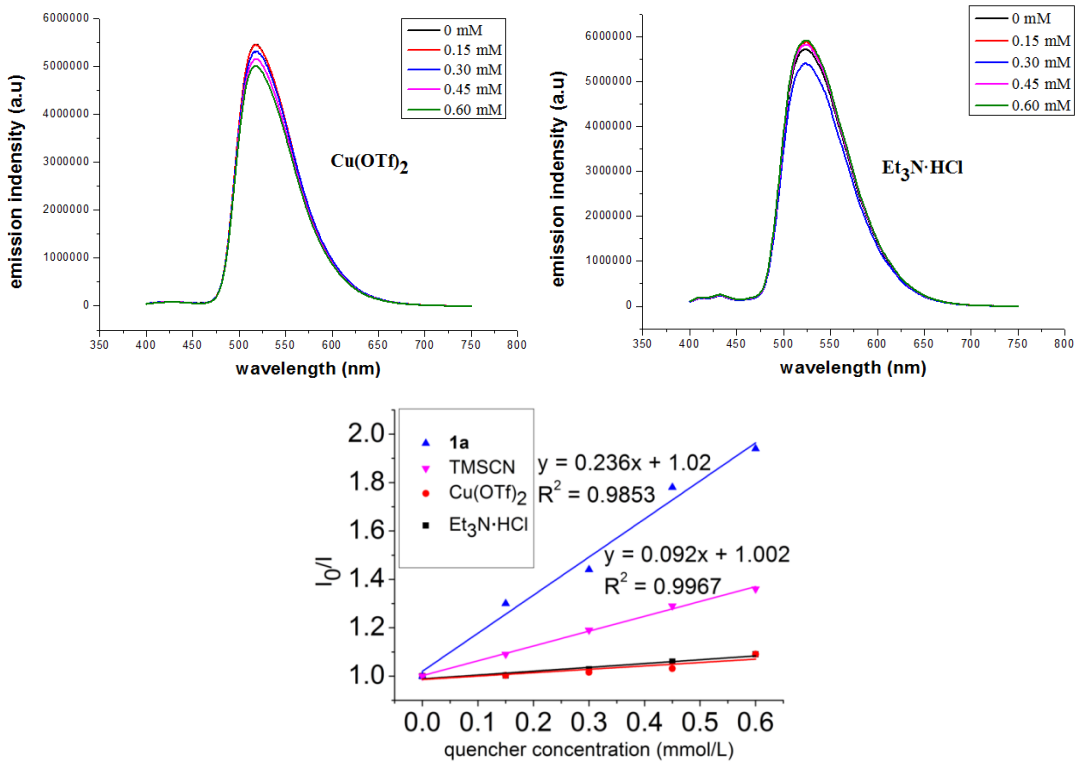


Figure S2. $Ir(ppy)_3$ Emission Quenching by **1a**, TMSCN, $Et_3N \cdot HCl$, and $Cu(OTf)_2$

5.4 Cyclic voltammetry experiments

Cyclic Voltammetry was performed on a CHI 660E electrochemical analyzer. The CV measurement of the sample (0.001 M) was carried out in 0.10 M of Bu_4NPF_6/MeCN at a scan rate of 50 mV/s with the protection of N_2, using a glassy carbon as the working electrode, a Pt wire as the counter electrode, and Ag/AgCl (3.5 M KCl) as the reference electrode.

Reductive potential of substrate

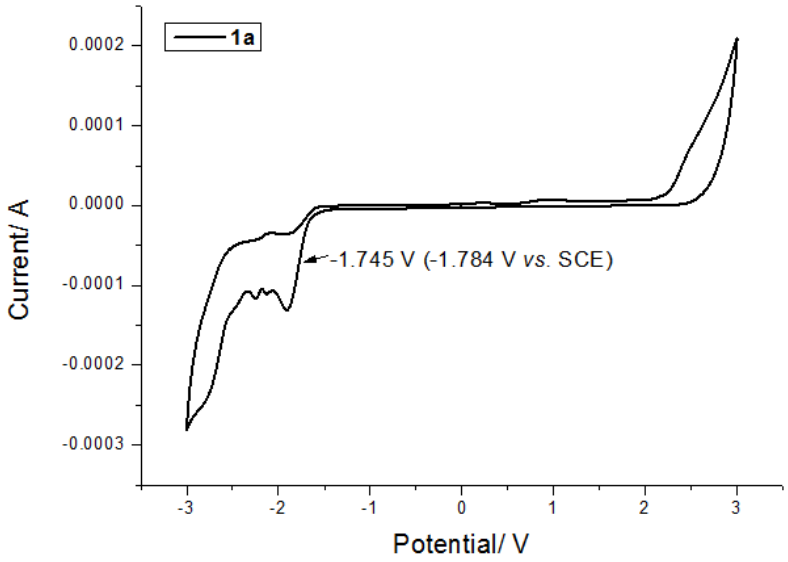


Figure S3. Cyclic voltammogram of 1a

$E_{1/2}^{Red}$ (**1a**) = -1.78 V *vs.* SCE

Reductive potential of $Cu(OTf)_2$

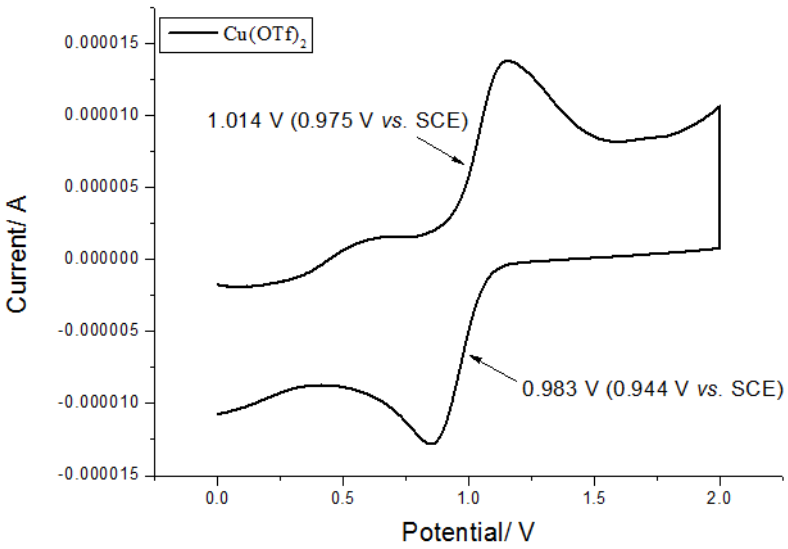
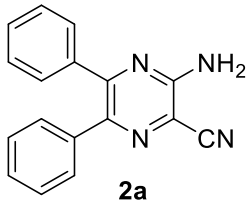


Figure S4. Cyclic voltammogram of $Cu(OTf)_2$

$E_{1/2}^{Red}$ ($Cu(OTf)_2$) = 0.94 V *vs.* SCE

6. Characterization data

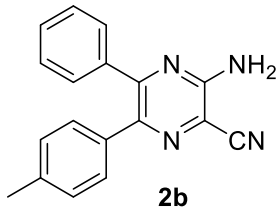
3-Amino-5,6-diphenylpyrazine-2-carbonitrile（2a）



2a

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (0.20 mmol scale, 46.2 mg, 85%; 5.0 mmol scale, 1.09 g, 81%); mp 166-167 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 6.9 Hz, 2H), 7.36 (d, J = 7.0 Hz, 1H), 7.34 – 7.23 (m, 7H), 5.35 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 154.0, 144.5, 137.32, 137.28, 129.7, 129.6, 129.3, 128.4, 128.30, 128.26, 115.5, 110.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{13}N_4$ 273.1135, found 273.1138.

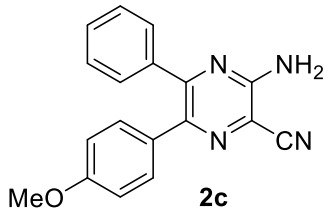
3-Amino-5-phenyl-6-(p-tolyl)pyrazine-2-carbonitrile（2b）



2b

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (37.8 mg, 66%); mp 212-213 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.40 (m, 2H), 7.39 – 7.35 (m, 1H), 7.33 – 7.29 (m, 2H), 7.22 (d, J = 8.1 Hz, 2H), 7.07 (d, J = 7.9 Hz, 2H), 5.29 (s, 2H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 153.8, 144.6, 138.3, 137.5, 134.4, 129.6, 129.5, 129.2, 129.0, 128.3, 115.6, 110.6, 21.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1291, found 287.1285.

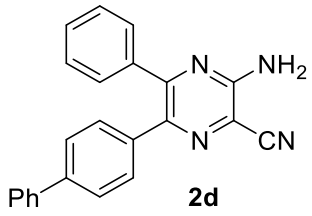
3-Amino-6-(4-methoxyphenyl)-5-phenylpyrazine-2-carbonitrile（2c）



2c

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1), yellow solid (38.6 mg, 64%); mp 204-205 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.38 – 7.35 (m, 1H), 7.34 – 7.29 (m, 2H), 7.28 – 7.23 (m, 2H), 6.80 (d, J = 8.8 Hz, 2H), 5.27 (s, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7, 154.2, 153.7, 144.3, 137.6, 130.6, 129.7, 129.6, 129.5, 128.3, 115.6, 113.7, 110.5, 55.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_4O$ 303.1240, found 303.1246.

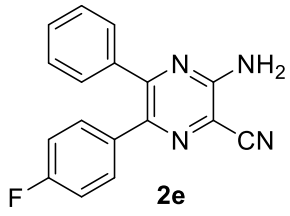
6-([1,1'-Biphenyl]-4-yl)-3-amino-5-phenylpyrazine-2-carbonitrile（2d）



2d

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 15:1), yellow solid (54.3 mg, 78%); mp 218-219 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 7.3 Hz, 2H), 7.52 (d, J = 8.3 Hz, 2H), 7.50 – 7.37 (m, 6H), 7.40 – 7.29 (m, 4H), 5.33 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 153.9, 144.1, 141.0, 140.3, 137.4, 136.2, 129.74, 129.71, 129.6, 128.8, 128.4, 127.6, 127.0, 126.9, 115.5, 110.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{23}H_{17}N_4$ 349.1448, found 349.1458.

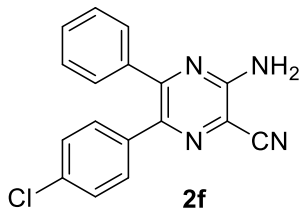
3-Amino-6-(4-fluorophenyl)-5-phenylpyrazine-2-carbonitrile（2e）



2e

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (34.8 mg, 60%); mp 161-162 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.36 (m, 3H), 7.36 – 7.27 (m, 4H), 6.96 (t, J = 8.5 Hz, 2H), 5.36 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (d, J = 248.7 Hz), 154.4, 154.0, 143.3, 137.2, 133.3 (d, J = 3.3 Hz), 131.2 (d, J = 8.3 Hz), 129.8, 129.5, 128.4, 115.4, 115.3 (d, J = 21.6 Hz), 110.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}FN_4$ 291.1041, found 291.1042.

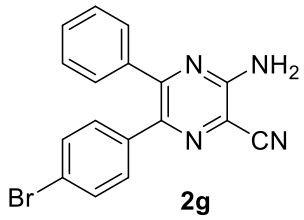
3-Amino-6-(4-chlorophenyl)-5-phenylpyrazine-2-carbonitrile（2f）



2f

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (44.7 mg, 73%); mp 195-196 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 – 7.37 (m, 3H), 7.36 – 7.31 (m, 2H), 7.28 – 7.21 (m, 4H), 5.38 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 154.0, 143.1, 137.1, 135.7, 134.5, 130.6, 129.9, 129.5, 128.5, 115.4, 110.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}ClN_4$ 307.0745, found 307.0755.

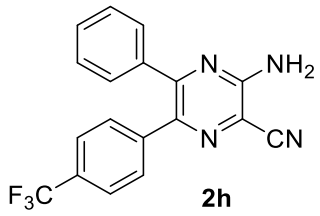
3-Amino-6-(4-bromophenyl)-5-phenylpyrazine-2-carbonitrile（2g）



2g

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (54.1 mg, 77%); mp 174-175 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.38 (m, 5H), 7.36 – 7.30 (m, 2H), 7.21 (d, J = 8.2 Hz, 2H), 5.36 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 154.0, 143.1, 137.1, 136.2, 131.4, 130.9, 129.9, 129.5, 128.5, 122.8, 115.3, 110.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}BrN_4$ 351.0240, found 351.0251.

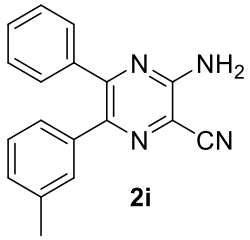
3-Amino-5-phenyl-6-(4-(trifluoromethyl)phenyl)pyrazine-2-carbonitrile（2h）



2h

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), white solid (48.2 mg, 71%); mp 192-193 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 8.2 Hz, 2H), 7.45 – 7.37 (m, 3H), 7.37 – 7.30 (m, 2H), 5.44 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 154.2, 142.6, 140.8, 136.8, 130.2 (q, J = 32.4 Hz), 130.0, 129.6, 129.5, 128.6, 125.2 (q, J = 3.8 Hz), 123.9 (q, J = 270.5 Hz), 115.2, 110.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{12}F_3N_4$ 341.1009, found 341.1013.

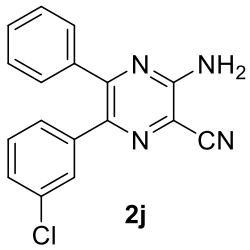
3-Amino-5-phenyl-6-(m-tolyl)pyrazine-2-carbonitrile（2i）



2i

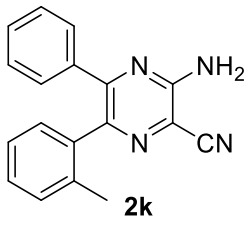
Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (39.5 mg, 69%); mp 148-150 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.39 (m, 2H), 7.38 – 7.34 (m, 1H), 7.33 – 7.28 (m, 2H), 7.24 (s, 1H), 7.16 – 7.07 (m, 2H), 7.04 – 6.98 (m, 1H), 5.34 (s, 2H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 153.9, 144.6, 138.1, 137.4, 137.2, 129.9, 129.62, 129.56, 129.1, 128.2, 128.0, 126.5, 115.5, 110.5, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1291, found 287.1299.

3-Amino-6-(3-chlorophenyl)-5-phenylpyrazine-2-carbonitrile（2j）



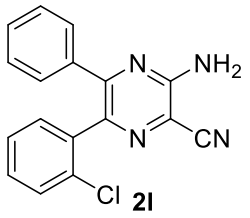
Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (45.3 mg, 74%); mp 157-158 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.37 (m, 4H), 7.37 – 7.30 (m, 2H), 7.27 (d, J = 7.4 Hz, 1H), 7.16 (t, J = 7.7 Hz, 1H), 7.11 (d, J = 8.1 Hz, 1H), 5.40 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 154.1, 142.8, 139.0, 136.9, 134.3, 130.0, 129.5, 129.33, 129.30, 128.5, 127.5, 115.3, 110.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}ClN_4$ 307.0745, found 307.0756.

3-Amino-5-phenyl-6-(o-tolyl)pyrazine-2-carbonitrile（2k）



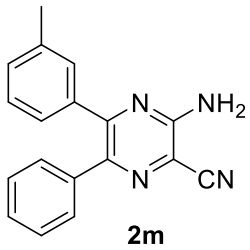
Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (43.5 mg, 76%); mp 147-148 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.34 (m, 2H), 7.33 – 7.29 (m, 1H), 7.27 – 7.20 (m, 3H), 7.19 – 7.11 (m, 3H), 5.39 (s, 2H), 1.97 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 154.4, 144.6, 137.1, 136.8, 136.1, 130.5, 130.1, 129.7, 129.3, 128.7, 128.1, 126.0, 115.5, 110.4, 19.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1291, found 287.1282.

3-Amino-6-(2-chlorophenyl)-5-phenylpyrazine-2-carbonitrile（2l）



Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (38.0 mg, 62%); mp 161-162 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.33 (m, 4H), 7.32 – 7.29 (m, 3H), 7.27 – 7.22 (m, 2H), 5.45 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.3, 154.7, 142.3, 136.74, 136.69, 133.2, 131.6, 130.0, 129.8, 129.1, 128.1, 127.1, 115.3, 110.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}ClN_4$ 307.0745, found 307.0756.

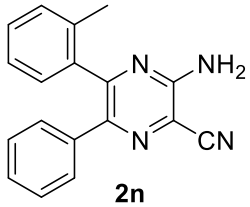
3-Amino-6-phenyl-5-(m-tolyl)pyrazine-2-carbonitrile（2m）



2m

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (49.8 mg, 87%); mp 145-146 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (dd, J = 7.5, 2.1 Hz, 2H), 7.31 – 7.23 (m, 4H), 7.20 – 7.14 (m, 2H), 7.13 – 7.08 (m, 1H), 5.39 (s, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 154.0, 144.4, 138.1, 137.3, 137.2, 130.4, 130.1, 129.3, 128.3, 128.2, 128.0, 126.7, 115.5, 110.5, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1291, found 287.1285.

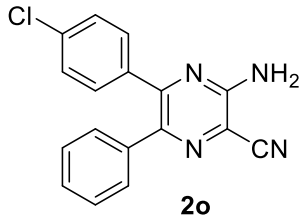
3-Amino-6-phenyl-5-(o-tolyl)pyrazine-2-carbonitrile（2n）



2n

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (37.2 mg, 65%); mp 143-144 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.17 (m, 8H), 7.15 (d, J = 7.6 Hz, 1H), 5.40 (s, 2H), 1.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 153.9, 144.7, 137.4, 136.7, 135.5, 130.7, 129.3, 128.7, 128.3, 128.1, 126.1, 115.4, 111.4, 19.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{15}N_4$ 287.1291, found 287.1283.

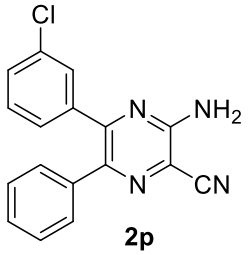
3-Amino-5-(4-chlorophenyl)-6-phenylpyrazine-2-carbonitrile（2o）



2o

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (47.2 mg, 77%); mp 145-147 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.34 (m, 2H), 7.34 – 7.24 (m, 7H), 5.34 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 153.1, 144.3, 137.0, 136.0, 135.7, 131.0, 129.3, 128.6, 128.4, 115.4, 110.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}ClN_4$ 307.0745, found 307.0742.

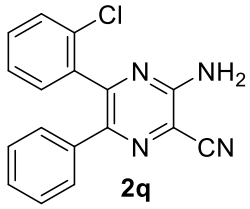
3-Amino-5-(3-chlorophenyl)-6-phenylpyrazine-2-carbonitrile（2p）



2p

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (43.5 mg, 71%); mp 187-188 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (s, 1H), 7.37 – 7.23 (m, 6H), 7.22 – 7.14 (m, 2H), 5.32 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 152.8, 144.4, 139.1, 136.8, 134.5, 129.72, 129.67, 129.4, 129.3, 128.7, 128.4, 127.9, 115.3, 111.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}ClN_4$ 307.0745, found 307.0752.

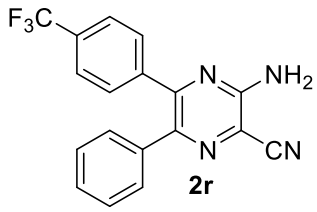
3-Amino-5-(2-chlorophenyl)-6-phenylpyrazine-2-carbonitrile（2q）



2q

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (46.6 mg, 76%); mp 184-185 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.33 (m, 2H), 7.33 – 7.29 (m, 3H), 7.28 (d, J = 2.0 Hz, 1H), 7.27 – 7.19 (m, 3H), 5.42 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 153.0, 145.0, 136.9, 136.5, 132.4, 130.8, 130.5, 130.0, 128.7, 128.4, 128.1, 127.0, 115.2, 112.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{12}ClN_4$ 307.0745, found 307.0754.

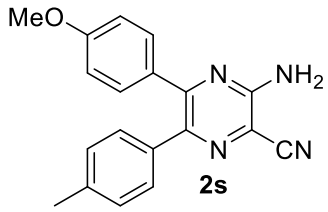
3-Amino-6-phenyl-5-(4-(trifluoromethyl)phenyl)pyrazine-2-carbonitrile（2r）



2r

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1), yellow solid (47.1 mg, 69%); mp 201-202 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.59 – 7.51 (m, 4H), 7.36 – 7.27 (m, 5H), 5.42 (s, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0, 152.7, 144.4, 140.8, 136.7, 131.3 (q, J = 32.8 Hz), 130.0, 129.3, 128.7, 128.5, 125.2 (q, J = 3.7 Hz), 123.7 (q, J = 272.2 Hz), 115.2, 111.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{12}F_3N_4$ 341.1009, found 341.1007.

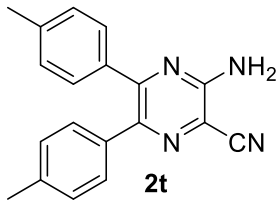
3-Amino-5-(4-methoxyphenyl)-6-(p-tolyl)pyrazine-2-carbonitrile（2s）



2s

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1), yellow solid (41.1 mg, 65%); mp 213-214 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 7.9 Hz, 2H), 7.09 (d, J = 7.9 Hz, 2H), 6.81 (d, J = 8.7 Hz, 2H), 5.29 (s, 2H), 3.81 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 153.9, 153.8, 144.3, 138.2, 134.8, 131.3, 129.7, 129.1, 129.0, 115.8, 113.7, 109.8, 55.3, 21.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_4O$ 317.1397, found 317.1392.

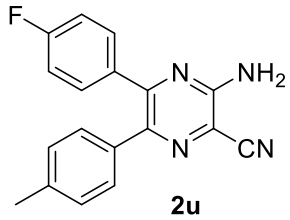
3-Amino-5,6-di-p-tolylpyrazine-2-carbonitrile（2t）



2t

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (46.8 mg, 78%); mp 166-167 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 8.2 Hz, 2H), 7.26 – 7.20 (m, 2H), 7.14 – 7.04 (m, 4H), 5.31 (s, 2H), 2.36 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 153.9, 144.4, 139.9, 138.2, 134.61, 134.56, 129.5, 129.1, 128.98, 128.95, 115.7, 110.1, 21.4, 21.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_4$ 301.1448, found 301.1452.

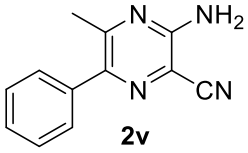
3-Amino-5-(4-fluorophenyl)-6-(p-tolyl)pyrazine-2-carbonitrile（2u）



2u

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (53.5 mg, 88%); mp 174-175 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.38 (m, 2H), 7.21 (d, J = 7.8 Hz, 2H), 7.09 (d, J = 7.8 Hz, 2H), 6.99 (t, J = 8.6 Hz, 2H), 5.31 (s, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.5 (d, J = 250.9 Hz), 153.8, 153.1, 144.4, 138.5, 134.3, 133.5 (d, J = 3.4 Hz), 131.7 (d, J = 8.0 Hz), 129.11, 129.09, 115.5, 115.4 (d, J = 21.7 Hz), 110.6, 21.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{18}H_{14}FN_4$ 305.1197, found 305.1189.

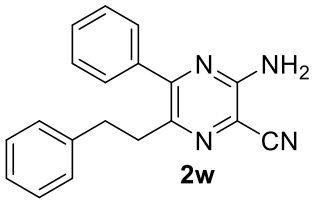
3-Amino-5-methyl-6-phenylpyrazine-2-carbonitrile（2v）



2v

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (23.5 mg, 56%); mp 117-118 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.40 (m, 5H), 5.19 (s, 2H), 2.53 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 154.1, 145.6, 137.2, 128.8, 128.6, 128.5, 115.5, 109.9, 23.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{12}H_{11}N_4$ 211.0978, found 211.0983.

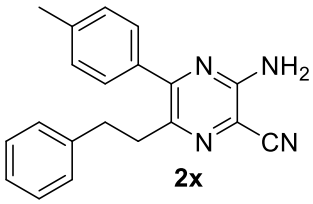
3-Amino-6-phenethyl-5-phenylpyrazine-2-carbonitrile（2w）



2w

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (40.2 mg, 67%); mp 121-122 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.40 (m, 3H), 7.40 – 7.34 (m, 2H), 7.25 – 7.19 (m, 2H), 7.18 – 7.13 (m, 1H), 7.03 (dd, J = 6.7, 1.6 Hz, 2H), 5.15 (s, 2H), 3.11 – 3.02 (m, 2H), 2.94 (dd, J = 9.2, 5.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 153.8, 145.2, 141.0, 137.2, 129.5, 128.50, 128.47, 128.39, 128.36, 126.0, 115.7, 110.9, 35.5, 34.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{17}N_4$ 301.1448, found 301.1451.

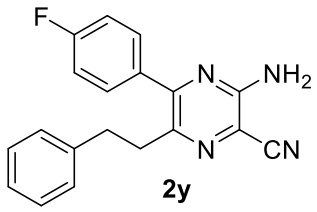
3-Amino-6-phenethyl-5-(p-tolyl)pyrazine-2-carbonitrile（2x）



2x

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (41.5 mg, 66%); mp 123-124 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 – 7.19 (m, 6H), 7.18 – 7.13 (m, 1H), 7.05 (d, J = 6.9 Hz, 2H), 5.19 (s, 2H), 3.06 (dd, J = 9.4, 5.5 Hz, 2H), 2.95 (dd, J = 9.3, 5.5 Hz, 2H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 153.8, 145.2, 141.1, 139.7, 134.3, 129.2, 128.5, 128.4, 128.3, 126.0, 115.8, 110.5, 35.6, 34.8, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{19}N_4$ 315.1604, found 315.1609.

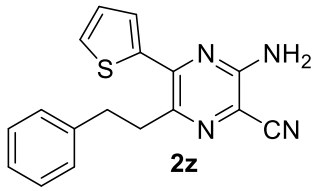
3-Amino-5-(4-fluorophenyl)-6-phenethylpyrazine-2-carbonitrile（2y）



2y

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (32.4 mg, 51%); mp 120-121 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 2H), 7.25 – 7.20 (m, 2H), 7.18 (d, J = 7.0 Hz, 1H), 7.16 – 7.09 (m, 2H), 7.02 (d, J = 7.0 Hz, 2H), 5.20 (s, 2H), 3.10 – 3.01 (m, 2H), 3.00 – 2.92 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, J = 250.2 Hz), 154.8, 153.8, 145.0, 140.8, 133.3 (d, J = 3.3 Hz), 130.6 (d, J = 8.4 Hz), 128.40, 128.38, 126.1, 115.60 (d, J = 21.7 Hz), 115.56, 111.0, 35.5, 34.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{16}FN_4$ 319.1354, found 319.1361.

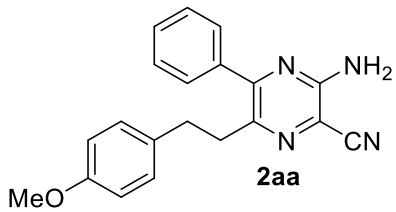
3-Amino-6-phenethyl-5-(thiophen-2-yl)pyrazine-2-carbonitrile（2z）



2z

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 15:1), yellow solid (36.7 mg, 60%); mp 125-126 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 3.8 Hz, 1H), 7.55 (d, J = 5.1 Hz, 1H), 7.35 – 7.26 (m, 2H), 7.28 – 7.17 (m, 3H), 7.18 – 7.11 (m, 1H), 5.11 (s, 2H), 3.35 – 3.26 (m, 2H), 3.13 – 3.06 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 148.1, 143.2, 141.2, 141.1, 130.8, 129.6, 128.50, 128.45, 128.4, 126.2, 115.8, 109.5, 36.6, 33.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{15}N_4S$ 307.1012, found 307.1007.

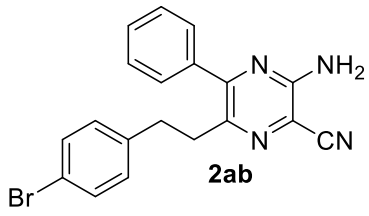
3-Amino-6-(4-methoxyphenethyl)-5-phenylpyrazine-2-carbonitrile（2aa）



2aa

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1), yellow solid (44.9 mg, 68%); mp 142-144 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.42 (m, 3H), 7.40 – 7.34 (m, 2H), 6.94 (d, J = 8.6 Hz, 2H), 6.76 (d, J = 8.6 Hz, 2H), 5.24 (s, 2H), 3.76 (s, 3H), 3.03 (dd, J = 9.6, 6.4 Hz, 2H), 2.88 (dd, J = 9.6, 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 155.8, 153.8, 145.2, 137.2, 133.0, 129.4, 129.3, 128.47, 128.46, 115.7, 113.7, 110.9, 55.2, 35.8, 34.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{20}H_{19}N_4O$ 331.1553, found 331.1558.

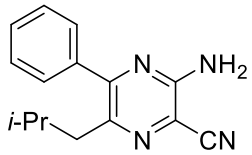
3-Amino-6-(4-bromophenethyl)-5-phenylpyrazine-2-carbonitrile（2ab）



2ab

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (53.8 mg, 71%); mp 132-133 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 – 7.41 (m, 3H), 7.38 – 7.33 (m, 2H), 7.31 (d, J = 8.2 Hz, 2H), 6.87 (d, J = 8.2 Hz, 2H), 5.23 (s, 2H), 3.04 (dd, J = 9.2, 6.4 Hz, 2H), 2.89 (dd, J = 9.2, 6.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.9, 153.8, 144.6, 139.9, 137.1, 131.4, 130.1, 129.5, 128.52, 128.45, 119.8, 115.6, 110.9, 35.2, 34.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{19}H_{16}BrN_4$ 379.0553, found 379.0564.

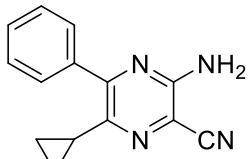
3-Amino-6-isobutyl-5-phenylpyrazine-2-carbonitrile（2ac）



2ac

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (32.8 mg, 65%); mp 131-132 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.40 (s, 5H), 5.14 (s, 2H), 2.66 (d, J = 7.2 Hz, 2H), 2.06 – 1.94 (m, 1H), 0.78 (d, J = 6.8 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.1, 153.6, 145.9, 137.7, 129.4, 128.7, 128.5, 115.7, 110.9, 42.3, 28.4, 22.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{17}N_4$ 253.1448, found 253.1452.

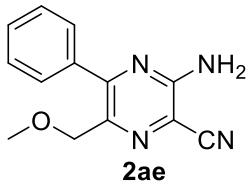
3-Amino-6-cyclopropyl-5-phenylpyrazine-2-carbonitrile（2ad）



2ad

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (35.4 mg, 75%); mp 124-125 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 – 7.66 (m, 2H), 7.54 – 7.45 (m, 3H), 5.11 (s, 2H), 2.12 – 2.04 (m, 1H), 1.11 – 1.05 (m, 2H), 0.94 – 0.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 153.3, 146.8, 137.2, 129.6, 129.2, 128.4, 115.9, 110.5, 13.8, 10.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{14}H_{13}N_4$ 237.1135, found 237.1141.

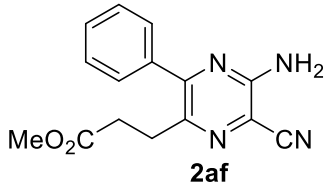
3-Amino-6-(methoxymethyl)-5-phenylpyrazine-2-carbonitrile（2-2ae）



2ae

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (23.5 mg, 49%); mp 133-134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.70 (m, 2H), 7.58 – 7.45 (m, 3H), 5.34 (s, 2H), 4.39 (s, 2H), 3.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 154.7, 141.0, 136.6, 130.1, 129.0, 128.5, 115.3, 110.9, 72.4, 58.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{13}H_{13}N_4O$ 241.1084, found 241.1089.

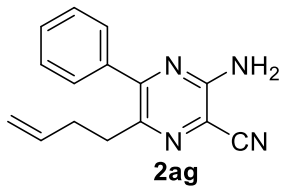
Methyl 3-(5-amino-6-cyano-3-phenylpyrazin-2-yl)propanoate（2af）



2af

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 15:1), yellow solid (34.4 mg, 61%); mp 136-137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.45 (m, 5H), 5.22 (s, 2H), 3.65 (s, 3H), 3.08 (t, J = 7.1 Hz, 2H), 2.74 (t, J = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 155.8, 154.0, 143.7, 137.0, 129.7, 128.63, 128.59, 115.6, 110.4, 51.7, 31.6, 28.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}N_4O_2$ 283.1190, found 283.1186.

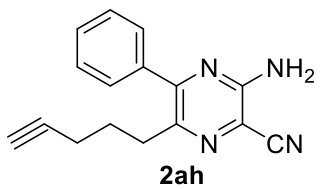
3-Amino-6-(but-3-en-1-yl)-5-phenylpyrazine-2-carbonitrile（2ag）



2ag

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (39.9 mg, 80%); mp 121-122 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (s, 5H), 5.78 – 5.66 (m, 1H), 5.35 (s, 2H), 5.02 – 4.83 (m, 2H), 3.04 – 2.69 (m, 2H), 2.51 – 2.29 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 153.8, 145.2, 137.2, 137.1, 129.5, 128.54, 128.50, 115.6, 115.3, 110.9, 32.9, 32.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{15}N_4$ 251.1291, found 251.1295.

3-Amino-6-(pent-4-yn-1-yl)-5-phenylpyrazine-2-carbonitrile（2ah）

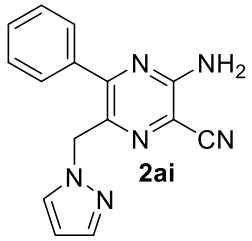


2ah

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1), yellow solid (35.1 mg, 67%); mp 117-118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ

7.56 – 7.44 (m, 5H), 5.19 (s, 2H), 2.88 (t, *J* = 7.7 Hz, 2H), 2.24 – 2.12 (m, 2H), 1.94 – 1.84 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 153.8, 145.2, 137.2, 129.6, 128.6, 128.5, 115.6, 110.8, 83.6, 68.8, 32.5, 27.4, 17.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{16}H_{15}N_4$ 263.1291, found 263.1297.

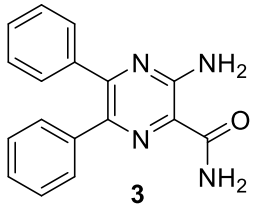
6-((1*H*-Pyrazol-1-yl)methyl)-3-amino-5-phenylpyrazine-2-carbonitrile（2ai）



2ai

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 10:1), yellow solid (37.6 mg, 68%); mp 194-195 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 6.7, 2.9 Hz, 2H), 7.55 – 7.47 (m, 4H), 7.42 (d, *J* = 2.3 Hz, 1H), 6.23 (t, *J* = 2.1 Hz, 1H), 5.35 (s, 4H, overlap). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 154.6, 139.8, 139.5, 136.2, 131.1, 130.1, 128.9, 128.8, 115.1, 111.4, 105.8, 53.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}N_6$ 277.1196, found 277.1192.

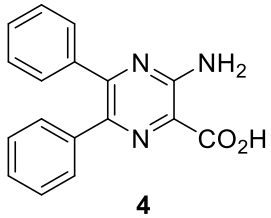
3-Amino-5,6-diphenylpyrazine-2-carboxamide（3）



3

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 5:1), yellow solid (42.4 mg, 73%); mp 200-202 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.07 (s, 1H), 7.69 (s, 3H, overlap), 7.42 – 7.28 (m, 7H), 7.28 – 7.21 (m, 3H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 154.0, 153.5, 139.1, 138.9, 138.7, 129.9, 129.8, 129.2, 128.5, 128.3, 127.8, 123.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{15}N_4O$ 291.1240, found 291.1239.

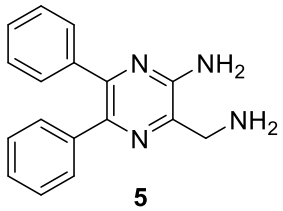
3-Amino-5,6-diphenylpyrazine-2-carboxylic acid（4）



4

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl = 1:1), yellow solid (47.8 mg, 82%); mp 190-191 ^{o}C; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.86 (s, 1H), 7.50 (s, 2H), 7.40 – 7.23 (m, 10H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.3, 154.8, 154.4, 140.4, 138.8, 138.6, 129.9, 129.8, 129.4, 128.5, 128.4, 127.9, 121.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{14}N_3O_2$ 292.1081, found 292.1088.

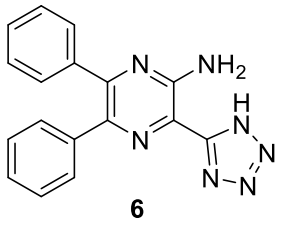
3-(Aminomethyl)-5,6-diphenylpyrazin-2-amine（5）



5

Purified by column chromatography on silica gel (eluent: MeOH/DCM = 1:20), yellow solid (35.6 mg, 64%); mp 177-178 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.40 – 7.35 (m, 3H), 7.33 – 7.29 (m, 5H), 7.28 – 7.22 (m, 4H), 6.74 (s, 2H), 4.09 (s, 2H). ^{13}C NMR (126 MHz, DMSO-D_6) δ 151.3, 148.9, 139.4, 139.3, 138.5, 133.0, 129.92, 129.89, 128.7, 128.5, 128.4, 127.6, 45.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for C17H17N4 277.1448, found 277.1445.

5,6-Diphenyl-3-(1H-tetrazol-5-yl)pyrazin-2-amine（6）



6

Purified by column chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 1:1), yellow solid (54.5 mg, 86%); mp 198-199 ^{o}C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.63 (s, 2H), 7.44 – 7.41 (m, 2H), 7.41 – 7.38 (m, 2H), 7.38 – 7.35 (m, 1H), 7.35 – 7.32 (m, 2H), 7.32 – 7.28 (m, 3H). ^{13}C NMR (126 MHz, DMSO-D_6) δ 154.0, 153.1, 151.6, 140.8, 138.8, 138.7, 130.02, 130.00, 129.4, 128.6, 128.5, 128.2, 119.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{17}H_{14}N_7$ 316.1305, found 316.1300.

7. Biological Assays

The antifungal activities of pyrazine products **2** were tested against six phytopathogenic fungi (*Rhizoctorzia solani*, *Gibberella zeae*, *Alternaria solani*, *Botrytis cinerea*, *Colletotrichun orbiculare*, *Alternaria alternate*) at the concentration of 50 μg/mL using mycelia growth inhibitory rate methods on PDA, with Boscalid used as the positive control (**Table S2**). The compounds were dissolved in 10 mL DMF to generate a 50 μg/mL stock solution. The EC_{50} values of compounds possessing good activity (inhibitory rate >60%) were further evaluated using different concentration by diluting the above solution (**Table S3**). DMF served as the negative control.

Table S2. Antifungal activity of pyrazines derivatives (inhibitory rate, %)[a, b]

Compound	inhibitory rate η (%)[c]					
	RHI	GIB	ALT	BOT	COL	ALA
Boscalid	95.8	35.5	57.3	36.9	7.9	90.9
2a	45.3	40.0	15.6	49.3	59.6	32.0
2b	—	23.2	4.4	15.3	45.7	—
2c	—	24.6	3.8	—	20.0	—
2d	9.0	26.0	6.2	2.1	14.5	—
2e	59.0	43.1	13.6	58.6	**89.4**	33.9
2f	6.3	23.0	7.4	14.2	**77.1**	13.8
2g	30.2	25.1	5.3	17.2	**100.0**	18.5
2h	35.4	20.4	6.2	5.5	29.6	0.3
2i	53.8	40.0	19.8	54.4	**60.6**	49.0
2j	50.0	28.3	20.6	12.1	**68.8**	30.9
2k	51.6	50.8	26.3	36.7	35.5	34.4
2l	52.0	52.2	30.4	48.8	46.1	39.4
2m	12.2	25.1	—	10.8	15.1	—
2n	53.4	35.8	14.5	15.6	38.4	36.9
2o	**66.2**	46.1	53.1	**88.9**	8.3	—
2p	—	25.3	3.2	**79.4**	23.4	—
2q	45.7	38.6	23.8	30.9	42.9	36.4
2r	30.1	22.6	10.2	8.7	33.6	—
2s	—	23.9	3.8	31.2	35.8	22.3
2t	—	29.3	8.6	53.7	44.7	11.6
2u	—	24.8	17.1	19.1	**61.6**	10.2
2v	12.2	24.1	10.0	5.0	9.1	0.8
2w	45.9	32.6	5.9	20.9	28.6	20.4
2x	0	18.5	3.2	7.1	22.9	6.3
2y	9.5	23.9	7.4	10.0	28.8	30.6
2z	—	22.7	4.1	6.3	13.8	5.5
2aa	10.4	29.7	9.4	8.2	8.6	5.8
2ab	—	15.2	3.2	5.8	8.6	—
2ac	57.2	37.5	12.7	**90.8**	**95.1**	28.9
2ad	**77.5**	52.2	34.8	**73.6**	**93.0**	43.8
2ae	—	9.4	—	32.7	8.3	12.4
2af	8.3	21.5	—	10.3	5.5	2.8
2ag	54.5	51.1	26.3	**91.8**	**100.0**	9.9
2ah	19.6	34.7	3.8	**97.6**	**100.0**	9.1
2ai	2.7	12.2	—	3.7	1.0	—

[a]RHI: *Rhizoctorzia solani*; GIB: *Gibberella zeae*; ALT: *Alternaria solani*; BOT: *Botrytis cinerea*; COL: *Colletotrichun orbiculare;* ALA: *Alternaria alternate*. [b]All the data was the average value of three replications

Table S3. EC_{50} determination of pyrazines derivatives[a, b]

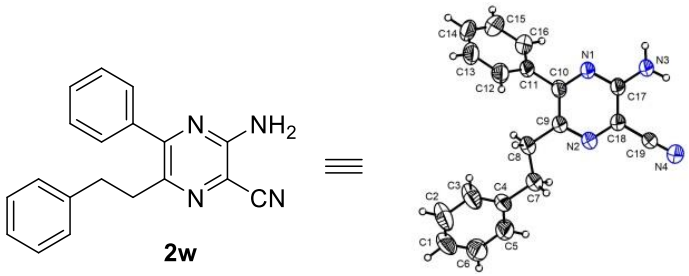
pathogen	compound	toxic regression	R	EC_{50} (μg/mL)	95 % confidence interval
RHI	**2p**	Y=0.6103x+4.4029	0.9618	9.5171	6.8587-13.2057
	2ad	Y=2.3245x+2.2381	0.8706	15.4245	8.1251-29.2815
	Boscalid	Y=0.7616X+5.0446	0.9912	0.8739	0.7467-1.0227
BOT	**2p**	Y=1.5693x+3.4075	0.9878	10.3464	8.6588-12.3628
	2q	Y=1.3104x+3.1421	0.8636	26.1676	11.6314-58.8704
	2ac	Y=2.0027x+2.7246	0.9772	13.6824	10.7417-17.4283
	2ad	Y=1.4353x+2.9888	0.9408	25.1919	15.4108-41.1809
	2ag	Y=1.2699x+4.1755	0.9962	4.4591	3.8722-5.1349
	2ah	Y=1.8200x+4.0383	0.9828	3.3761	2.6499-4.3012
	Boscalid	Y=1.3068x+5.3296	0.9870	0.5595	0.4429-0.7068
COL	**2e**	Y=2.0577x+2.8770	0.9947	10.7571	9.5808-12.0779
	2f	Y=0.5993x+4.8172	0.8545	2.0189	0.7177-5.6789
	2g	Y=0.5432x+5.1354	0.8817	0.5633	0.1620-1.9587
	2i	Y=1.3159x+3.3746	0.9507	17.1874	11.7493-25.1426
	2j	Y=1.7896x+2.6226	0.9868	21.3022	17.3103-26.2146
	2u	Y=1.7821x+4.4551	0.9588	2.0220	1.4679-2.7854
	2ac	Y=3.5404x+2.3609	0.9946	5.5645	4.9466-6.2595
	2ad	Y=2.3648x+2.5810	0.9546	10.5421	7.4199-14.9779
	2ag	Y=2.7287x+4.2592	0.8968	1.8685	0.8436-4.1386
	2ah	Y=2.7542x+4.5182	0.9579	1.4960	0.9434-2.3723
	Boscalid	Y=2.9242+1.351X	0.9673	34.393	18.9576-62.3960

[a]RHI: *Rhizoctorzia solani*; BOT: *Botrytis cinerea*; COL: *Colletotrichun orbiculare*.

[b]The EC_{50} value was the average value of three replications.

8. X-ray structure of product 2w

X-ray structure of 2w with thermal ellipsoids shown at the 50% probability level (CCDC 2101334)



Crystal data and structure refinement for product 2w

Identification code	**2w**	
Empirical formula	$C_{19}H_{16}N_4$	
Formula weight	300.36	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 6.3310(9) Å	α = 80.485(4) °.
	b = 9.7410(13) Å	β = 88.980(5) °.
	c = 13.1586(19) Å	γ = 82.009(5) °.
Volume	792.55(19) $Å^3$	
Z	2	
Density (calculated)	1.259 Mg/m^3	
Absorption coefficient	0.077 mm^{-1}	
F(000)	316	
Crystal size	0.200 x 0.180 x 0.050 mm^3	
Theta range for data collection	2.437 to 24.999 °.	

Index ranges	-7<=h<=7, -11<=k<=11, -15<=l<=15
Reflections collected	10488
Independent reflections	2766 [R(int) = 0.0368]
Completeness to theta = 24.999 °	98.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6905
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2766 / 0 / 208
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0499, wR2 = 0.1184
R indices (all data)	R1 = 0.0886, wR2 = 0.1374
Extinction coefficient	n/a
Largest diff. peak and hole	0.153 and -0.148 e.$Å^{-3}$

9. References

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(5) H. Yuan, M. Wang, Z. Xu and H. Gao, *Adv. Synth. Catal*., 2019, **361**, 4386.

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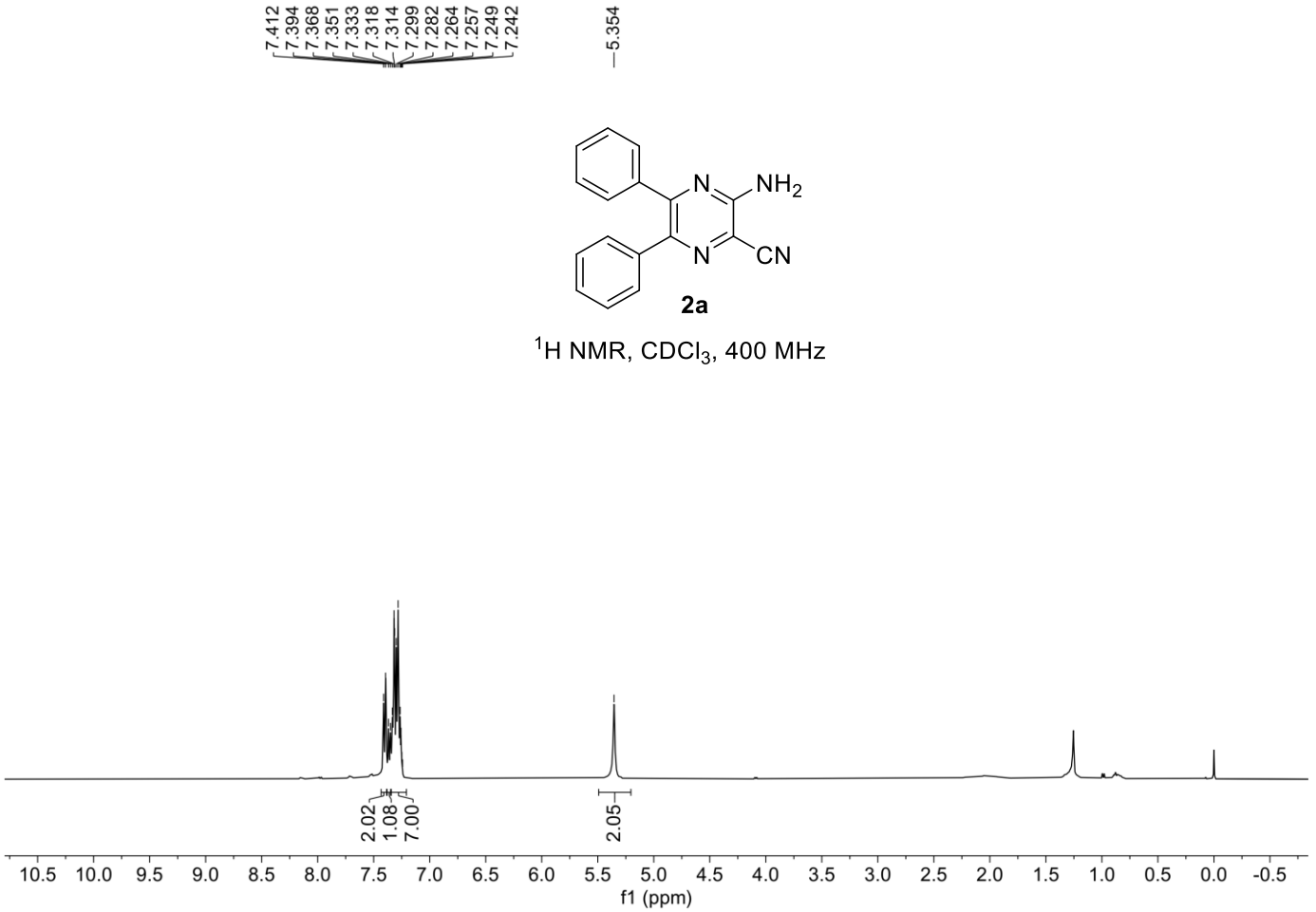
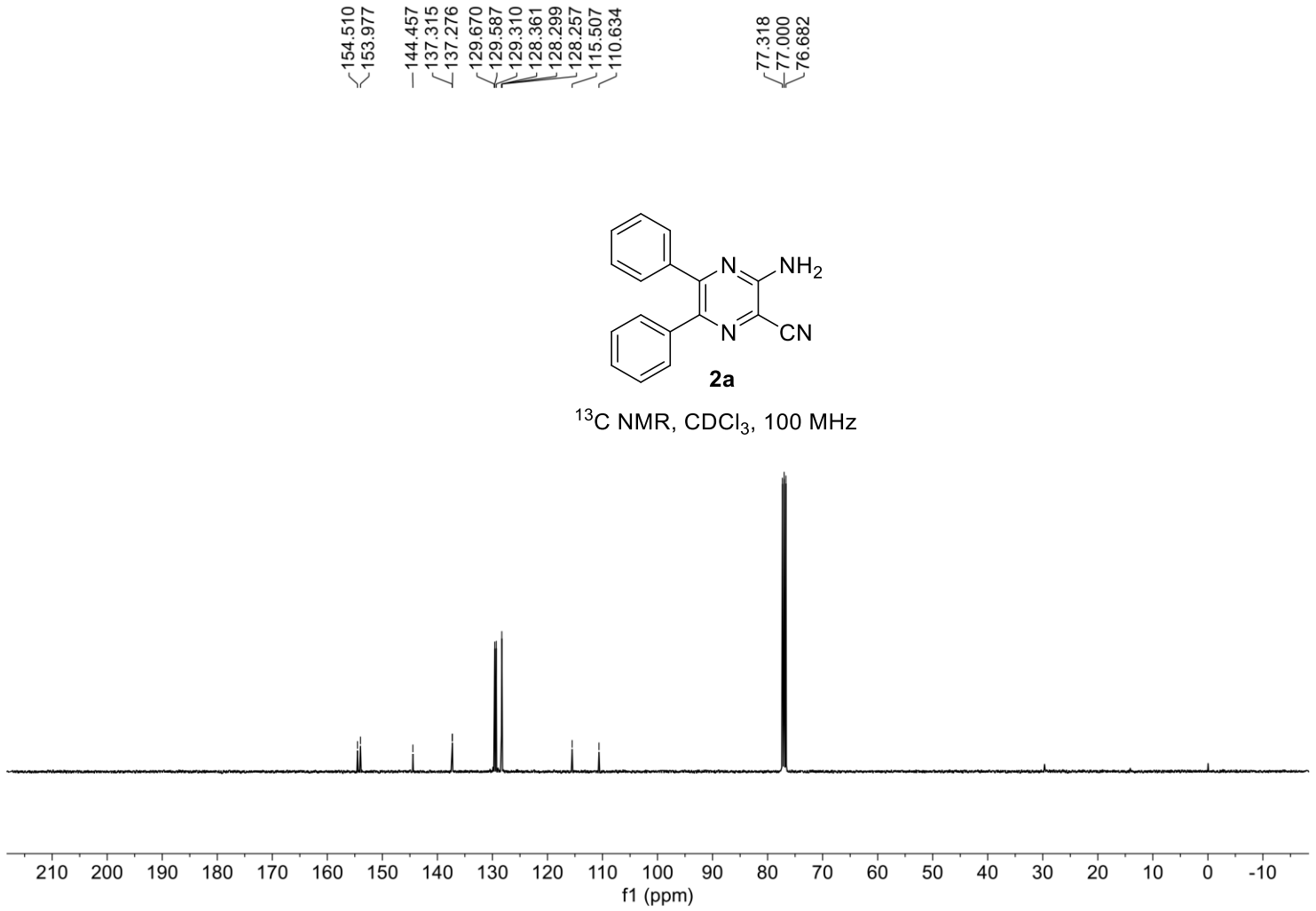
10. NMR spectra

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137.315
137.276
129.670
129.587
129.310
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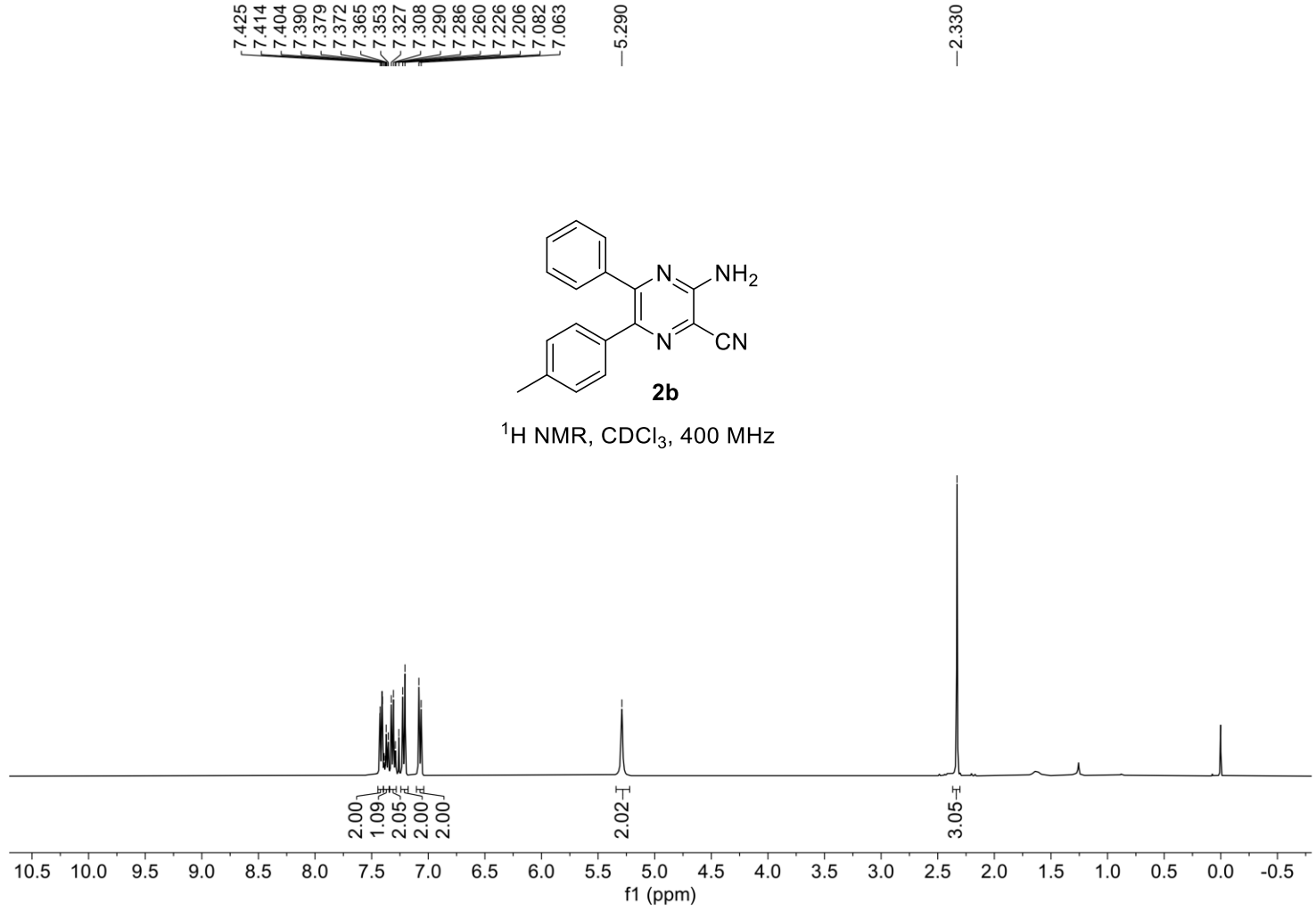
128.299
128.257
115.507
110.634
77.318
77.000
76.682
N
NH2
N
CN
2a
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.379
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7.353
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7.290
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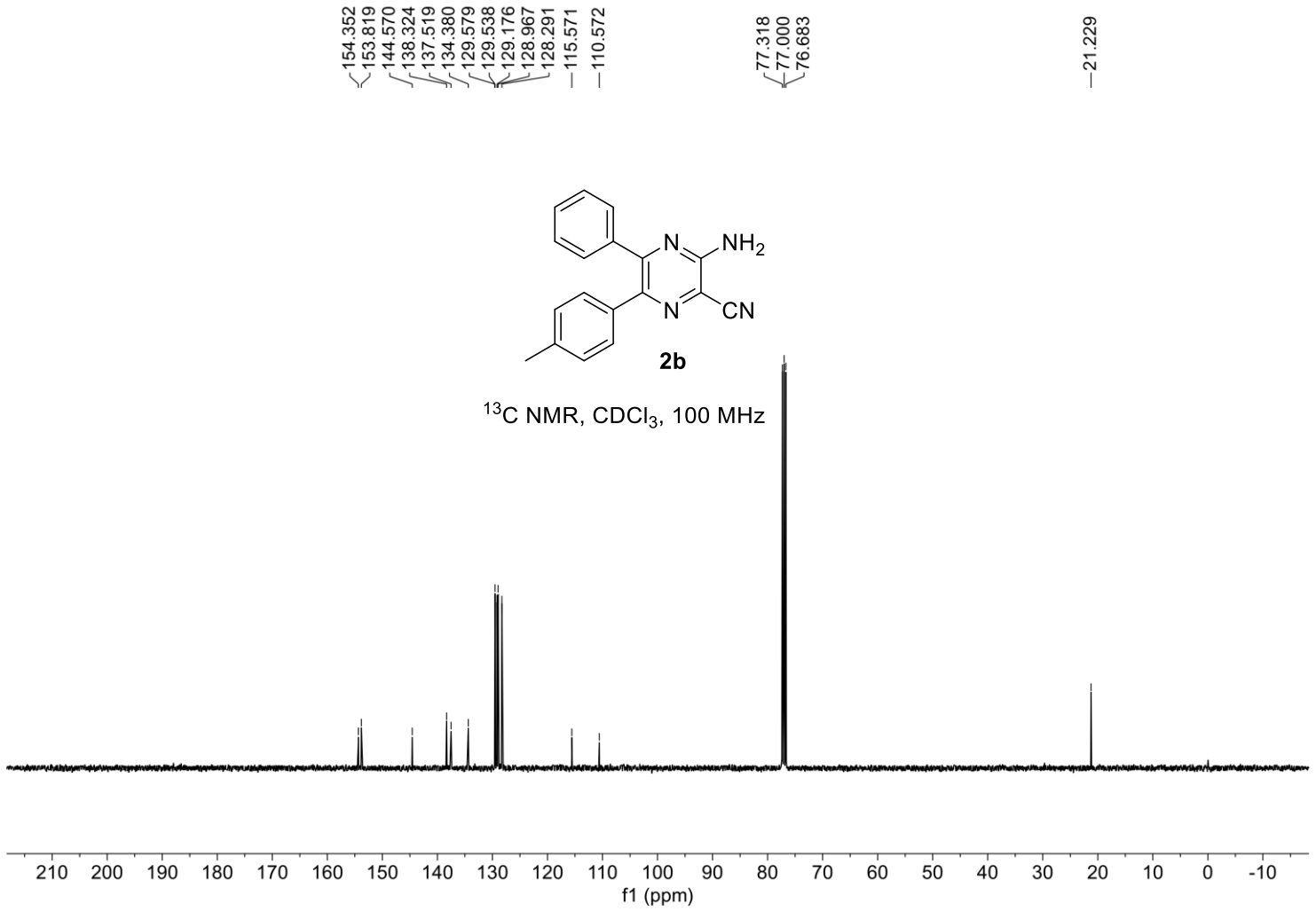
7.260
7.226
7.206
7.082
7.063
5.290
2.330
N
NH2
N
CN
2b
1H NMR, CDCl3, 400 MHz
2.00
1.09
2.05
2.00
2.00
2.02
3.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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77.318
77.000
76.683
21.229
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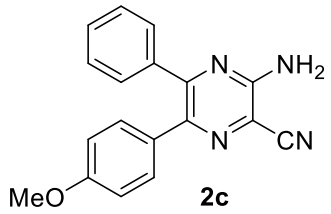
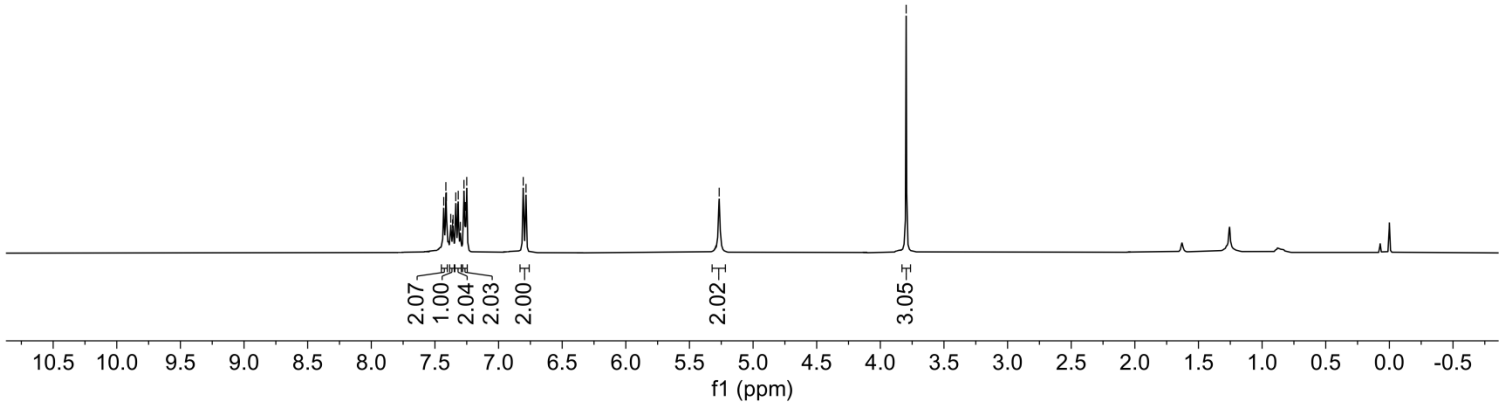
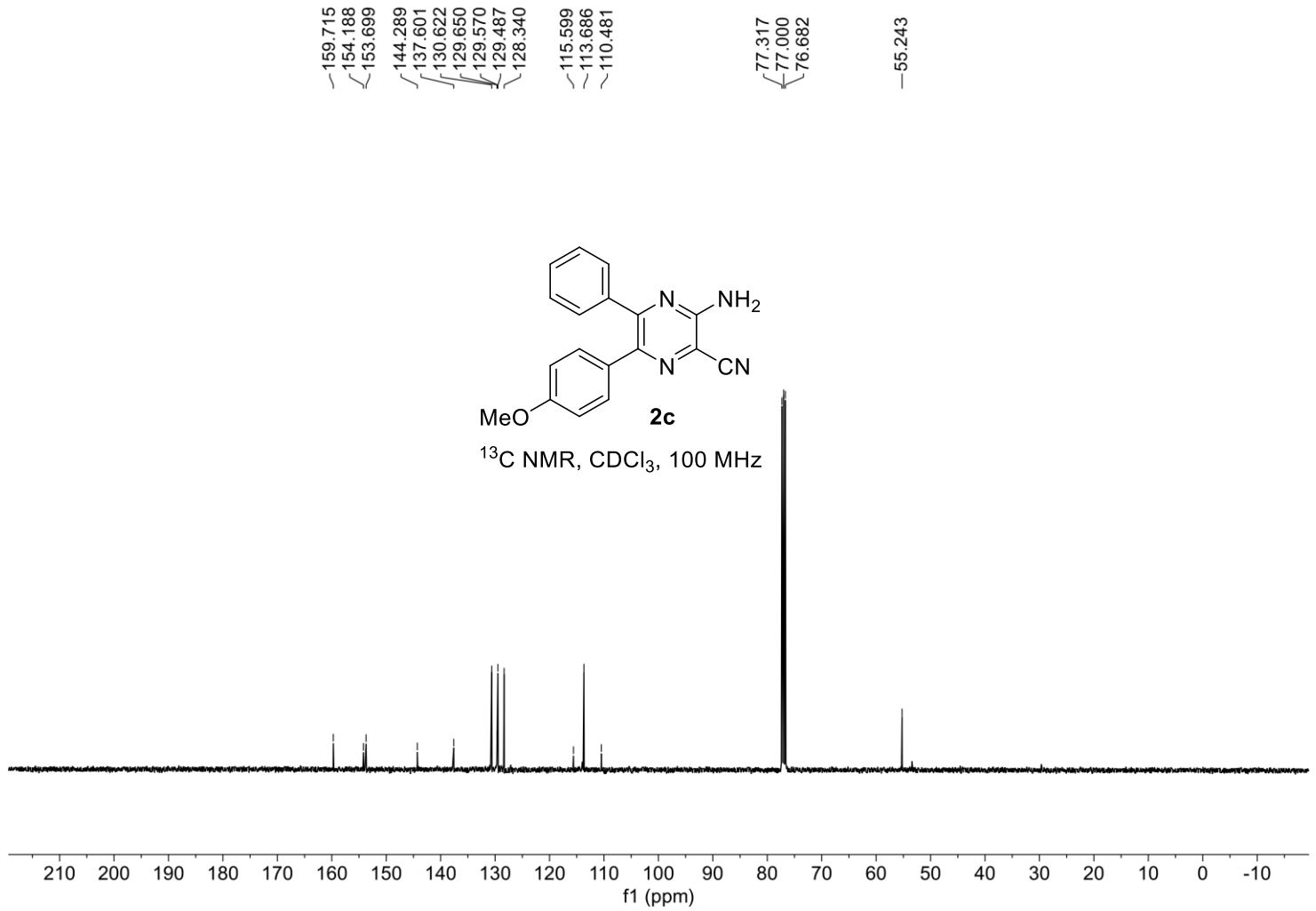
2b
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



2c

^{1}H NMR, $CDCl_3$, 400 MHz

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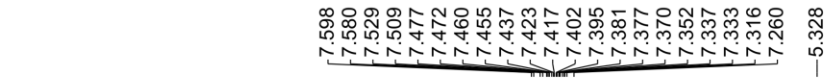
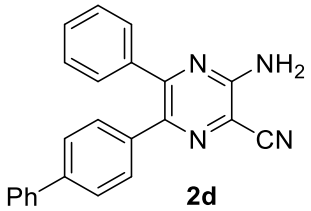
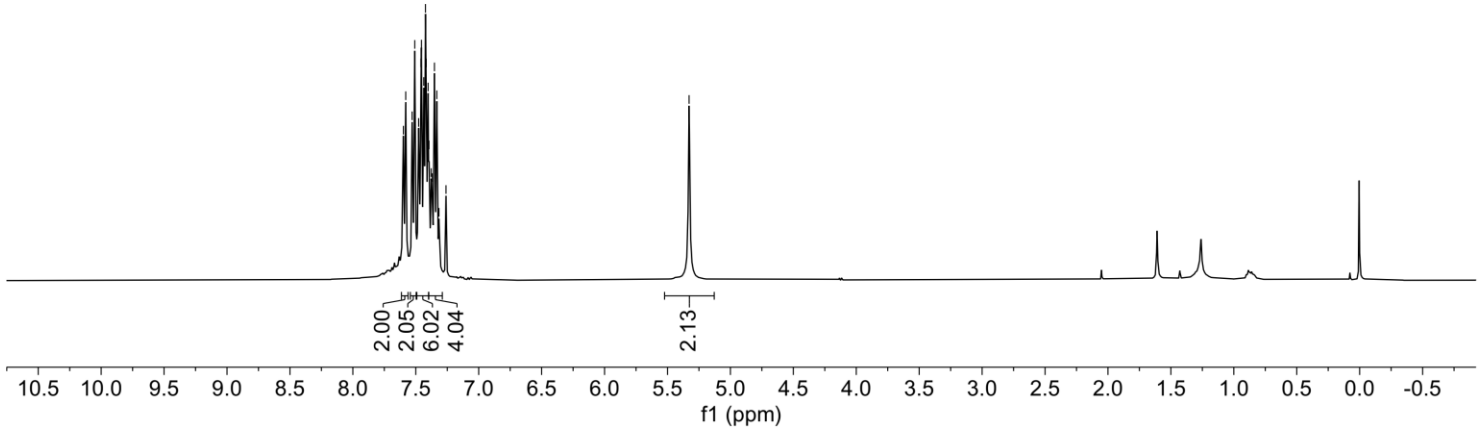
110.481
77.317
77.000
76.682
55.243
N
NH2
N
CN
MeO
2c
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

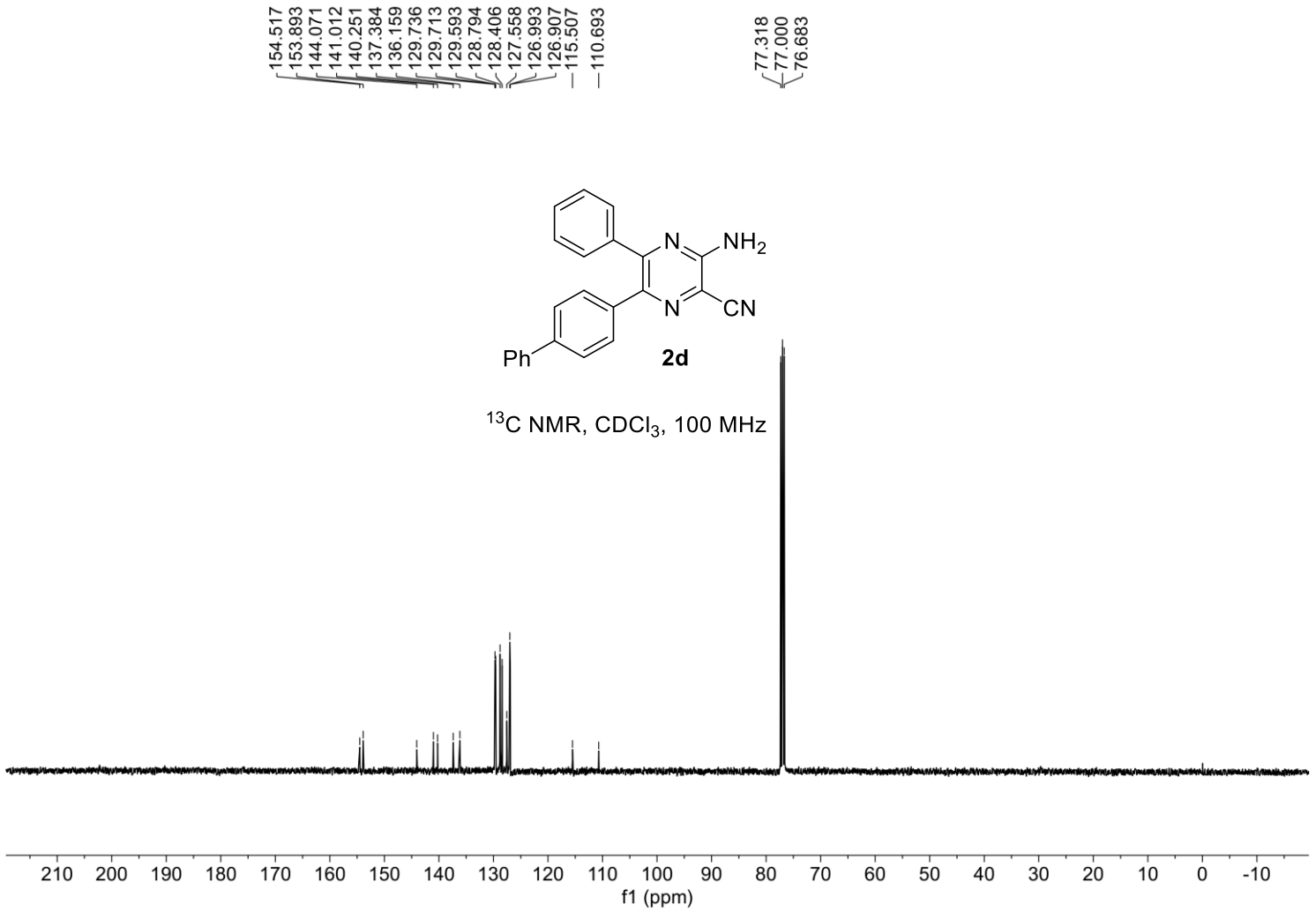


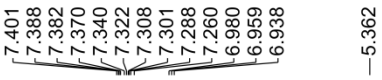


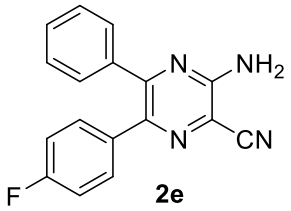
2d

^{1}H NMR, $CDCl_3$, 400 MHz



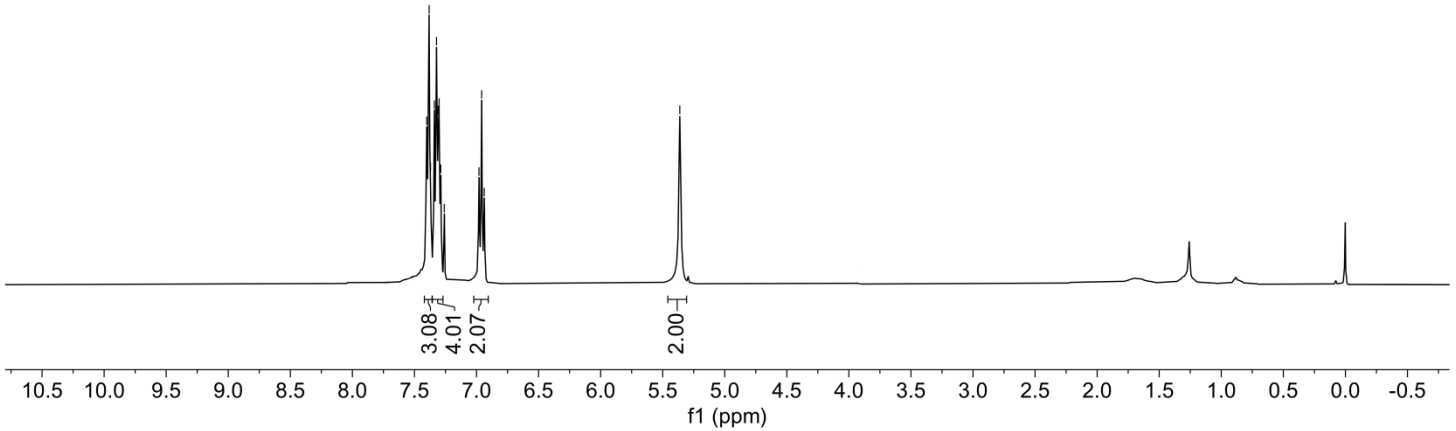

154.517
153.893
144.071
141.012
140.251
137.384
136.159
129.736
129.713
129.593
128.794
128.406
127.558
126.993
126.907
115.507
110.693
77.318
77.000
76.683
N
NH2
N
CN
Ph
2d
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

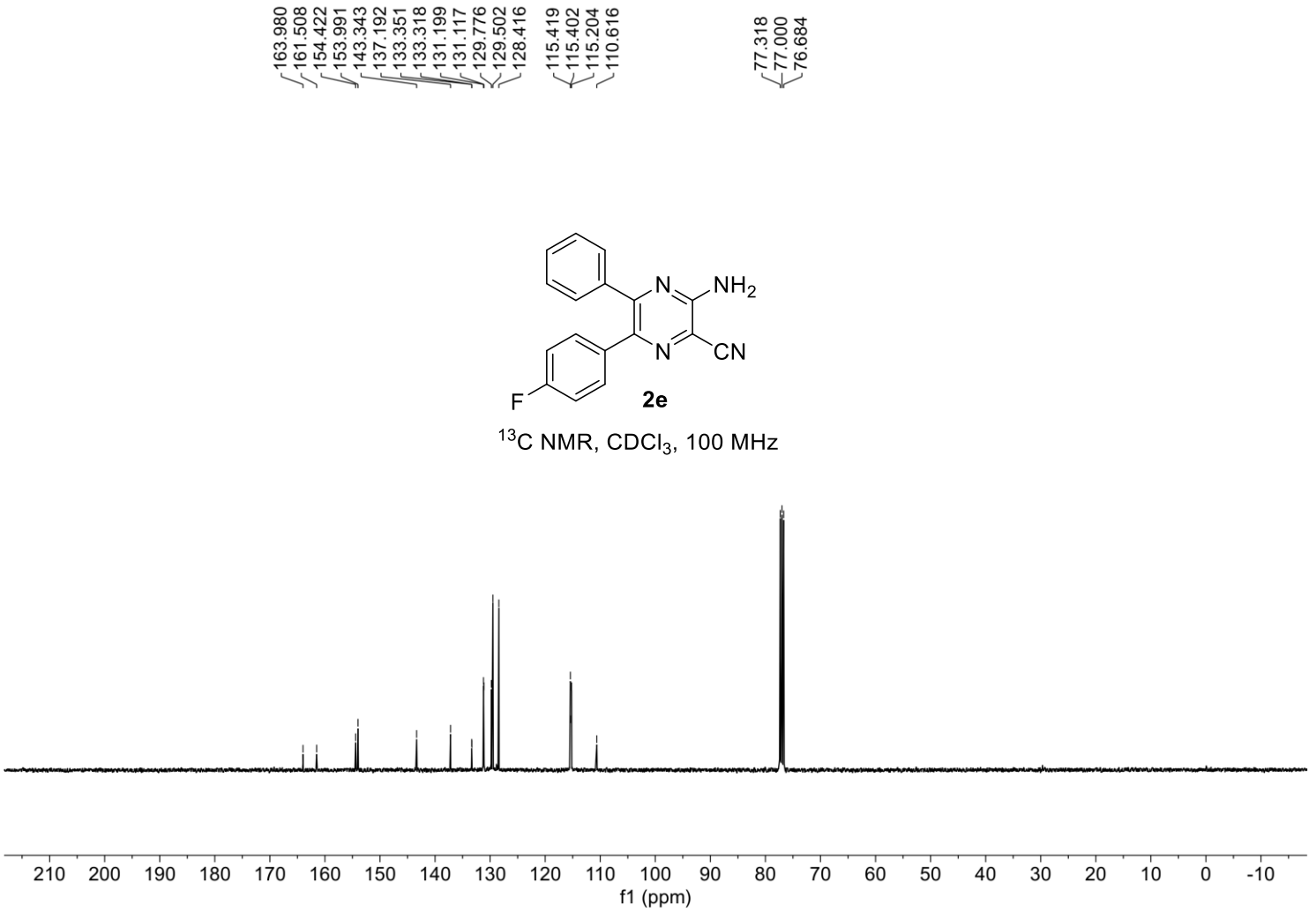


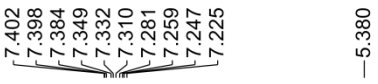


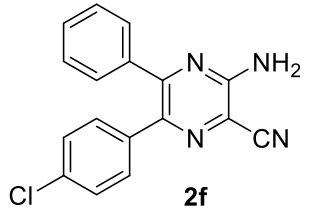
2e

^{1}H NMR, $CDCl_3$, 400 MHz



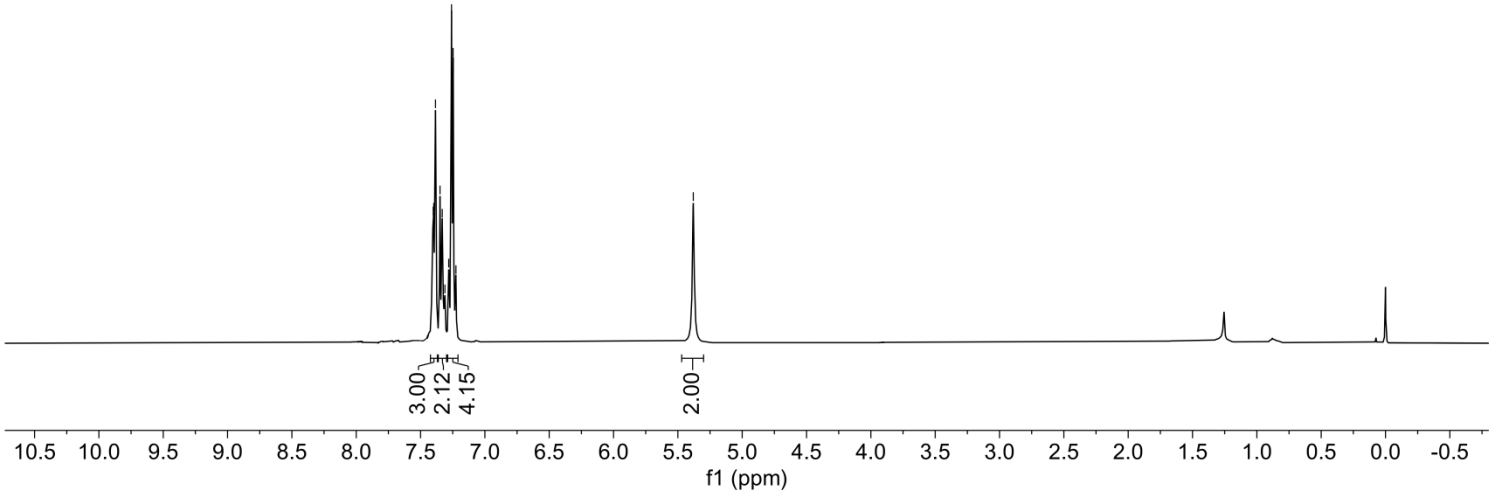

163.980
161.508
154.422
153.991
143.343
137.192
133.351
133.318
131.199
131.117
129.776
129.502
128.416
115.419
115.402
115.204
110.616
77.318
77.000
76.684
N
NH2
N
CN
F
2e
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

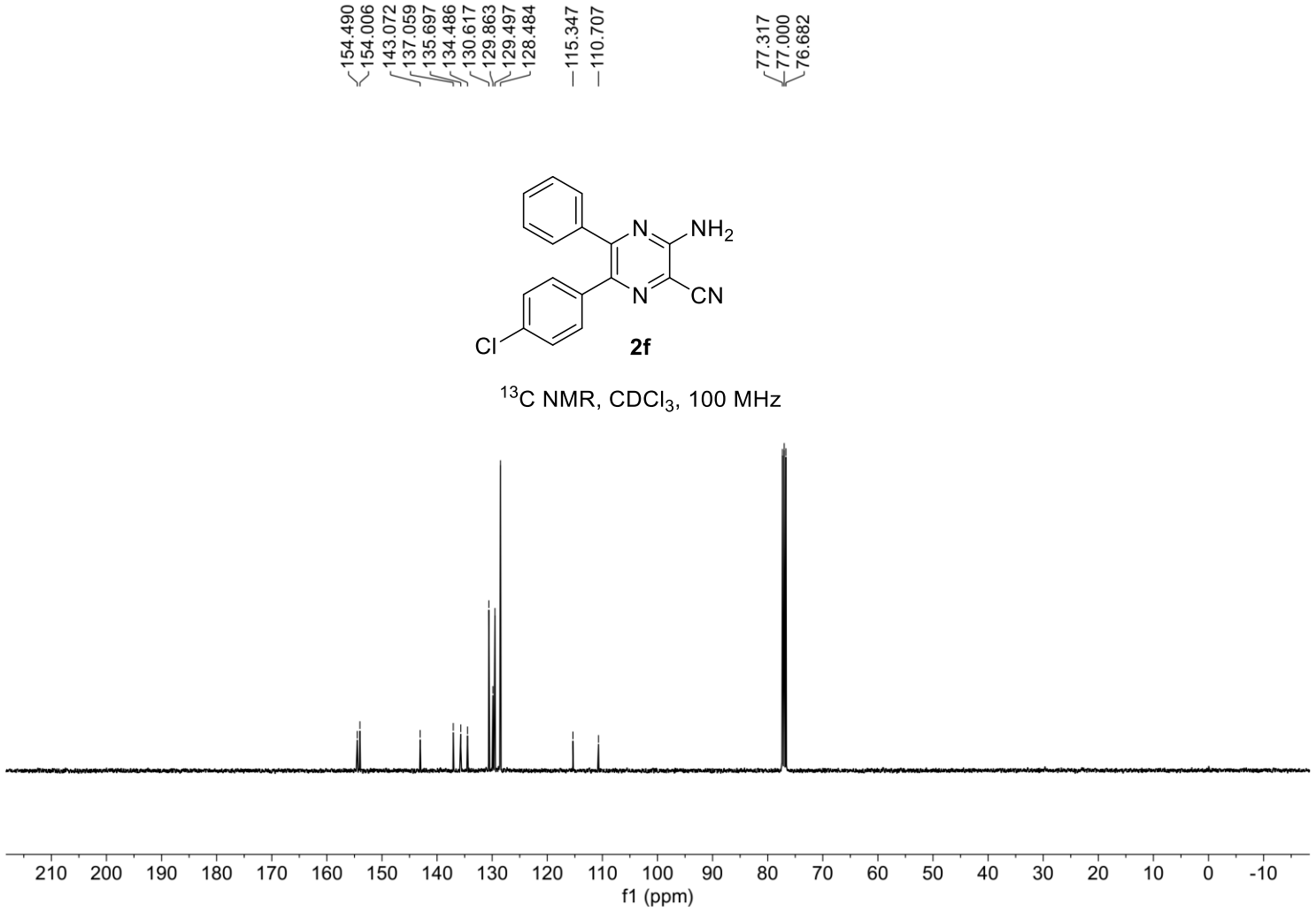


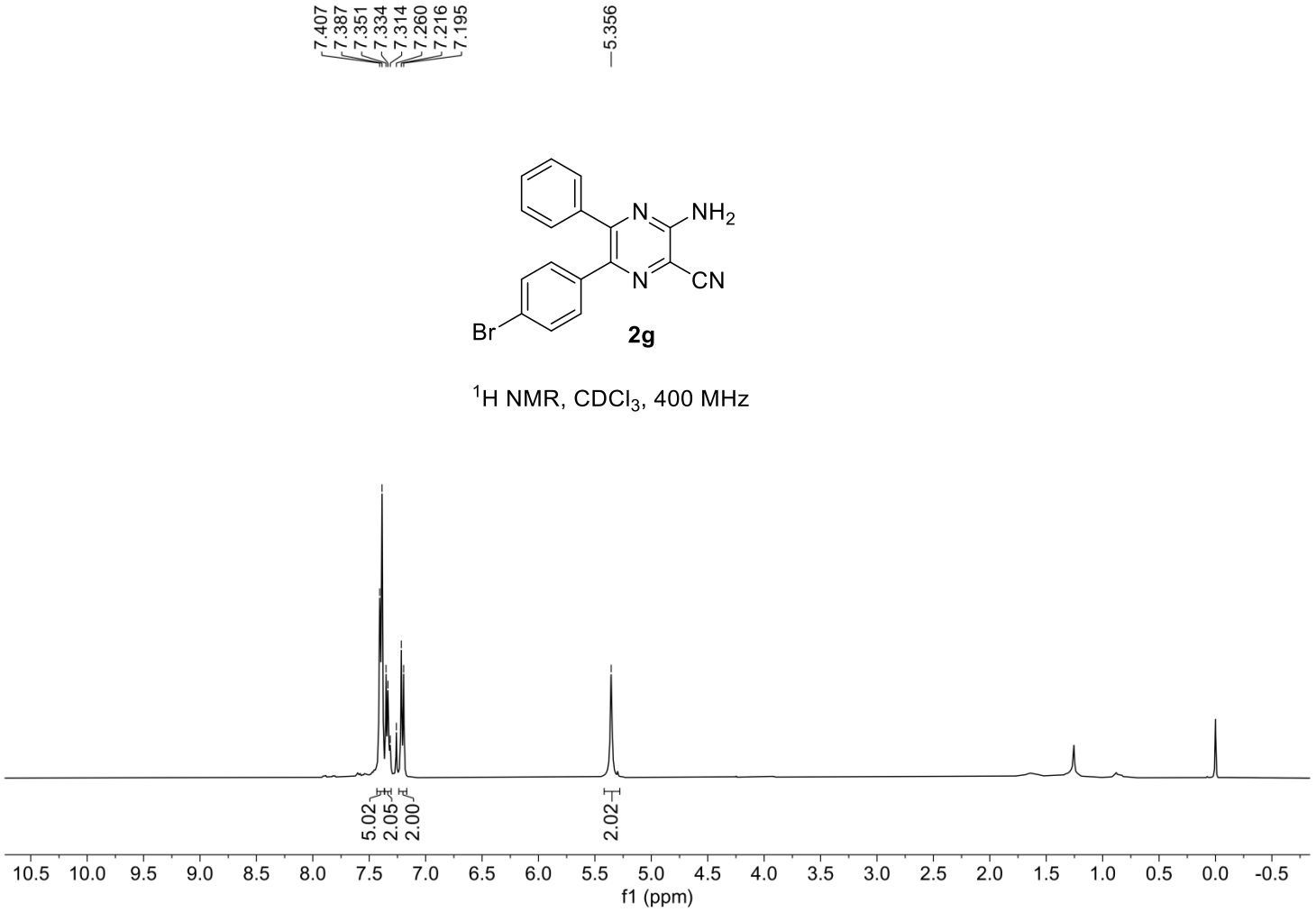


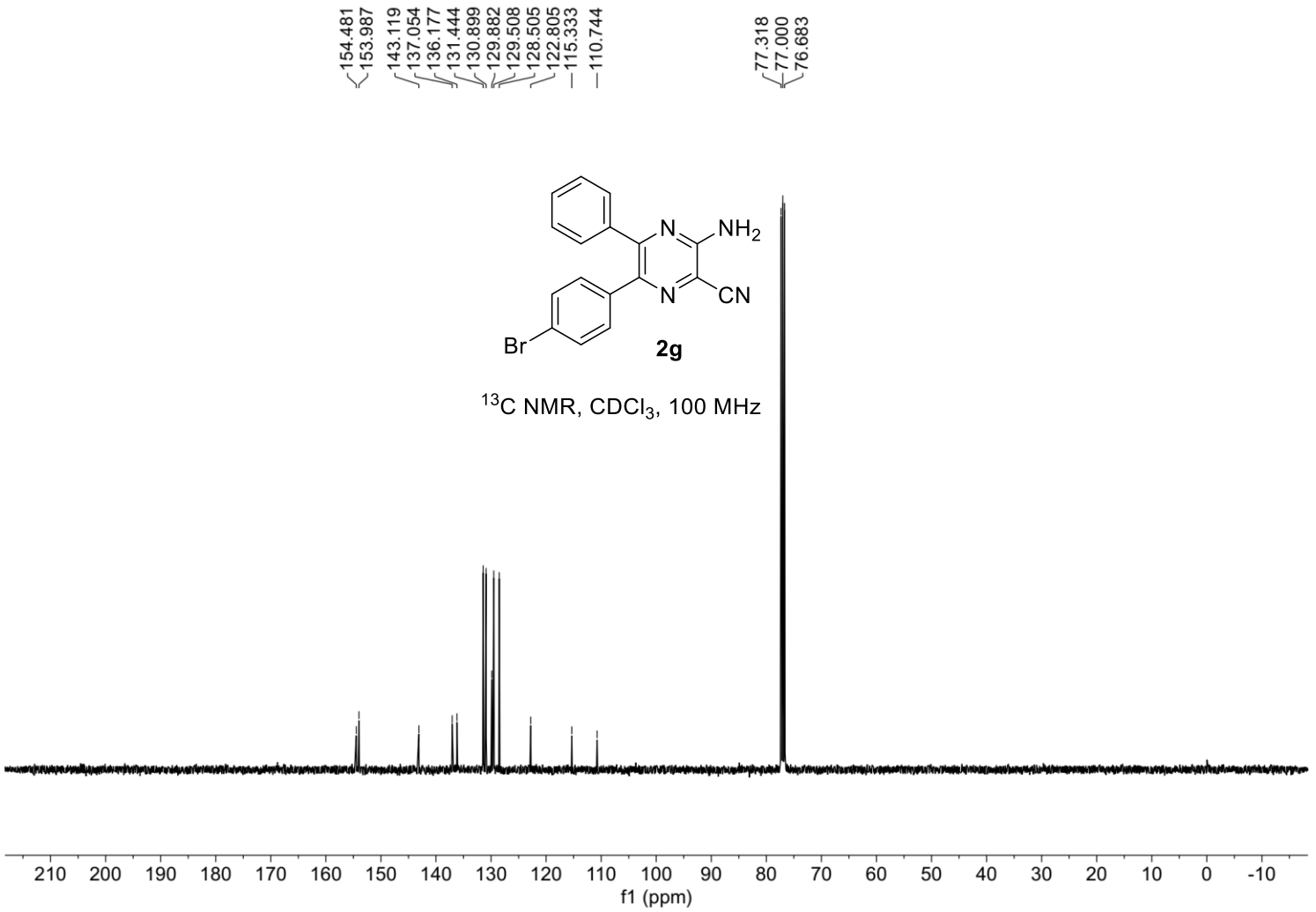
2f

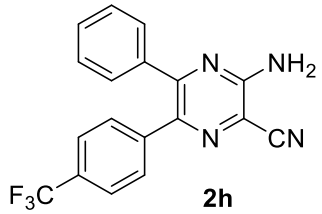
^{1}H NMR, $CDCl_3$, 400 MHz




154.490
154.006
143.072
137.059
135.697
134.486
130.617
129.863
129.497
128.484
115.347
110.707
77.317
77.000
76.682
N
NH2
N
CN
Cl
2f
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

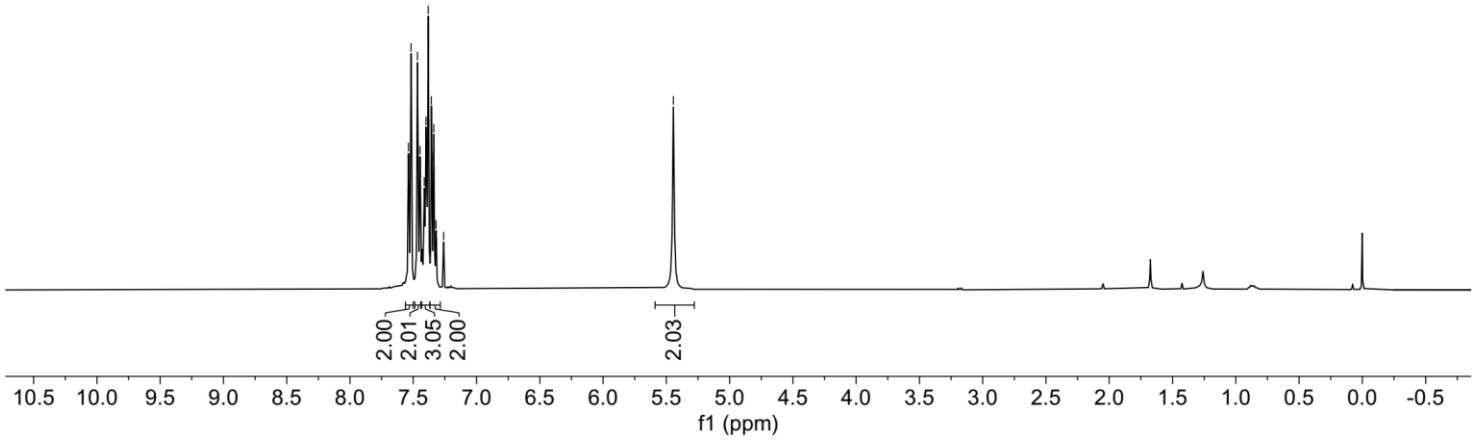

7.407
7.387
7.351
7.334
7.314
7.260
7.216
7.195
5.356
N
NH2
N
CN
Br
2g
1H NMR, CDCl3, 400 MHz
5.02
2.05
2.00
2.02
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

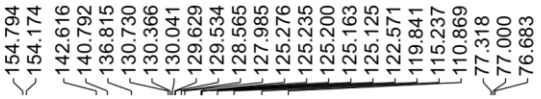

154.481
153.987
143.119
137.054
136.177
131.444
130.899
129.882
129.508
128.505
122.805
115.333
110.744
77.318
77.000
76.683
N
NH2
N
CN
Br
2g
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

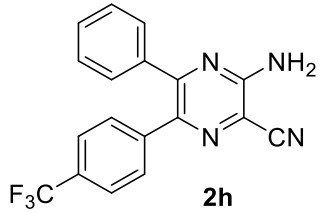


2h

^{1}H NMR, $CDCl_3$, 400 MHz

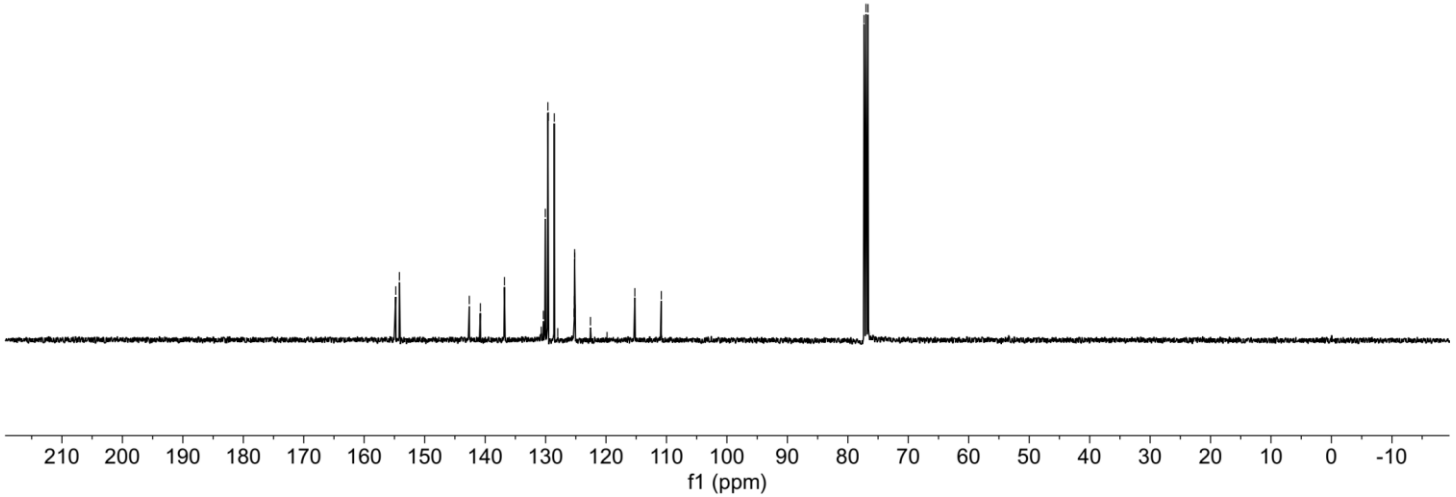


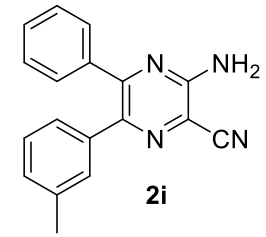




2h

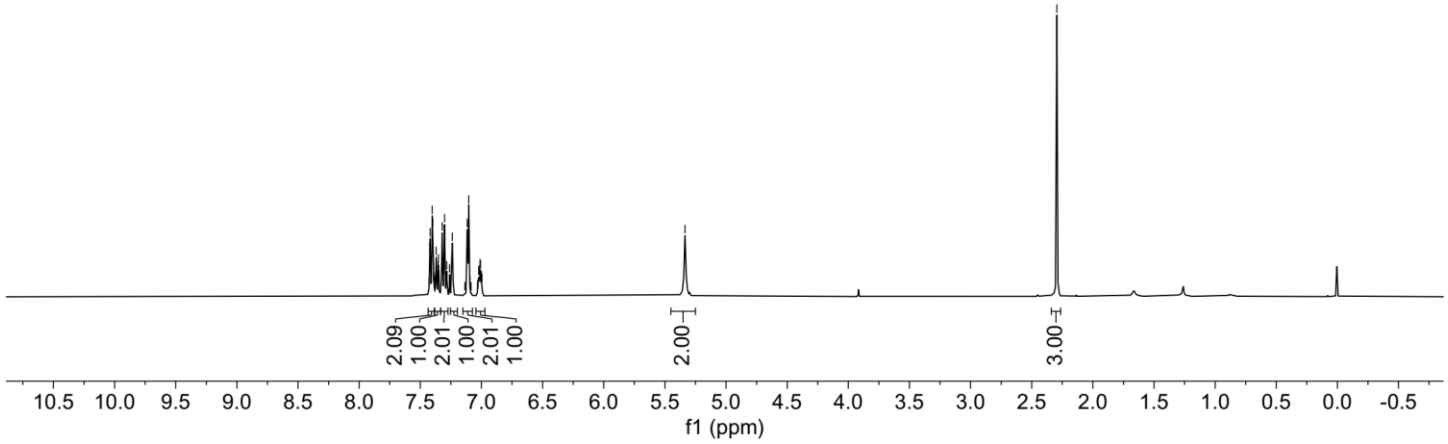
^{13}C NMR, $CDCl_3$, 100 MHz

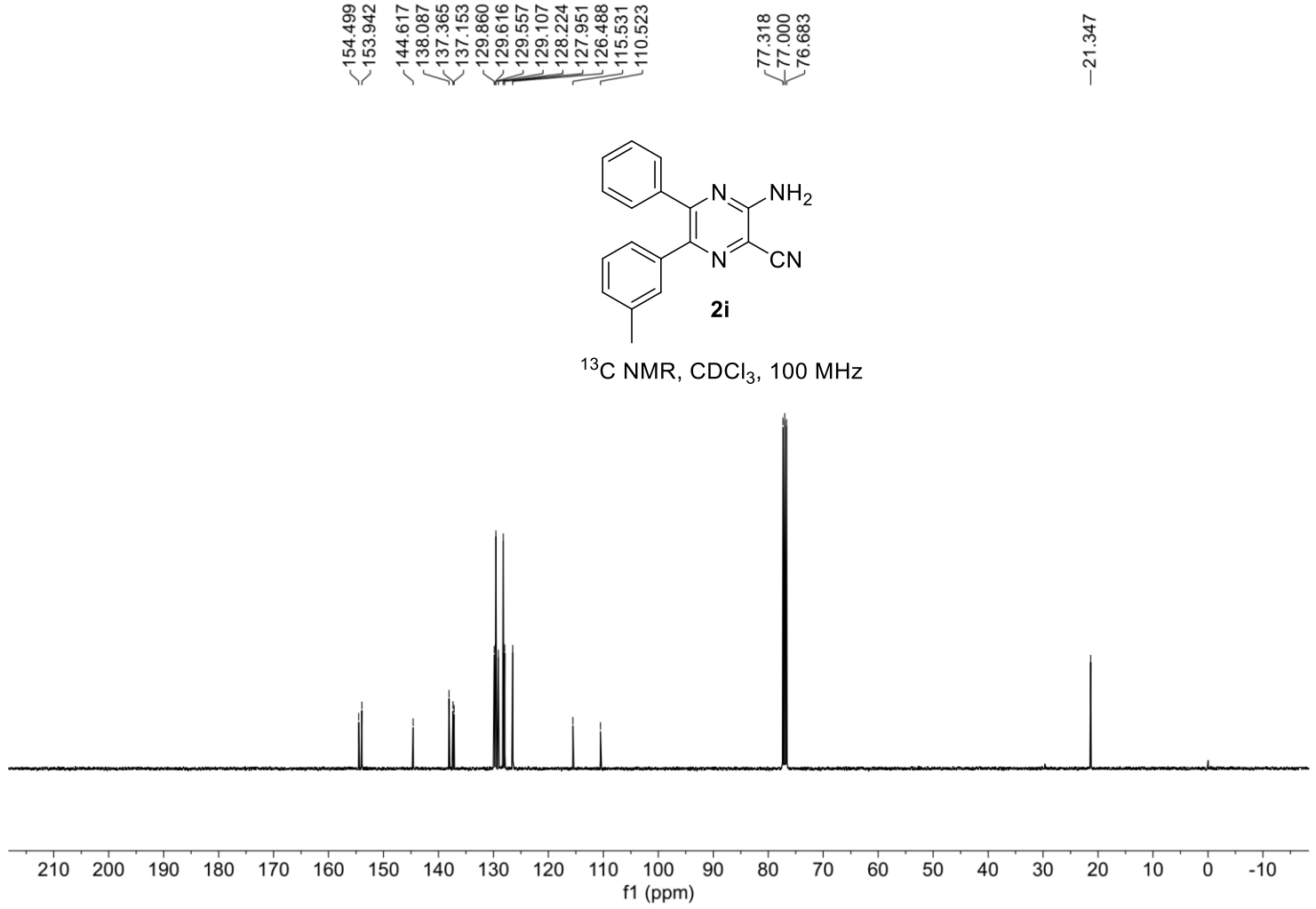


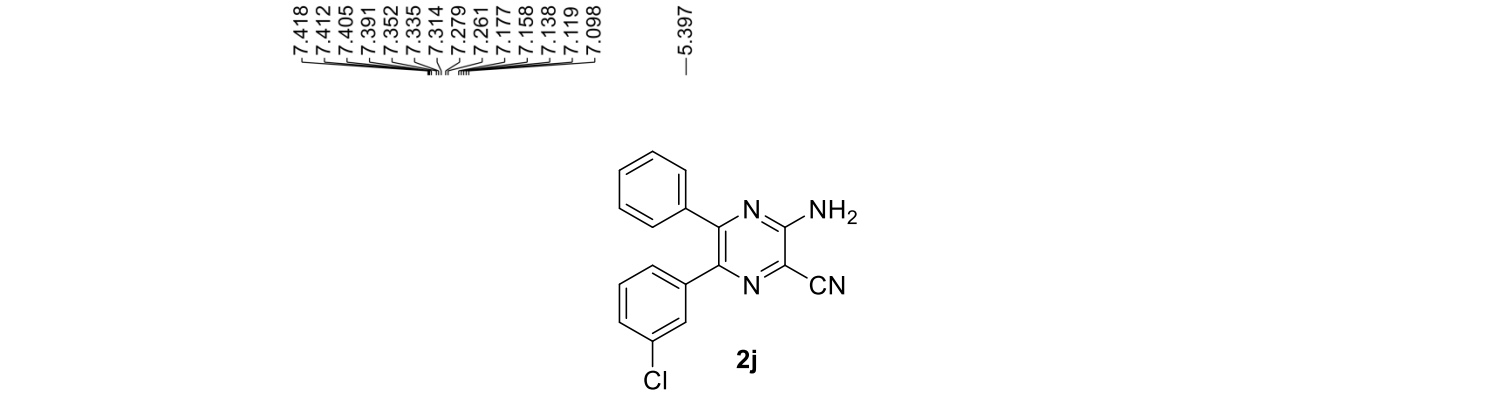


2i

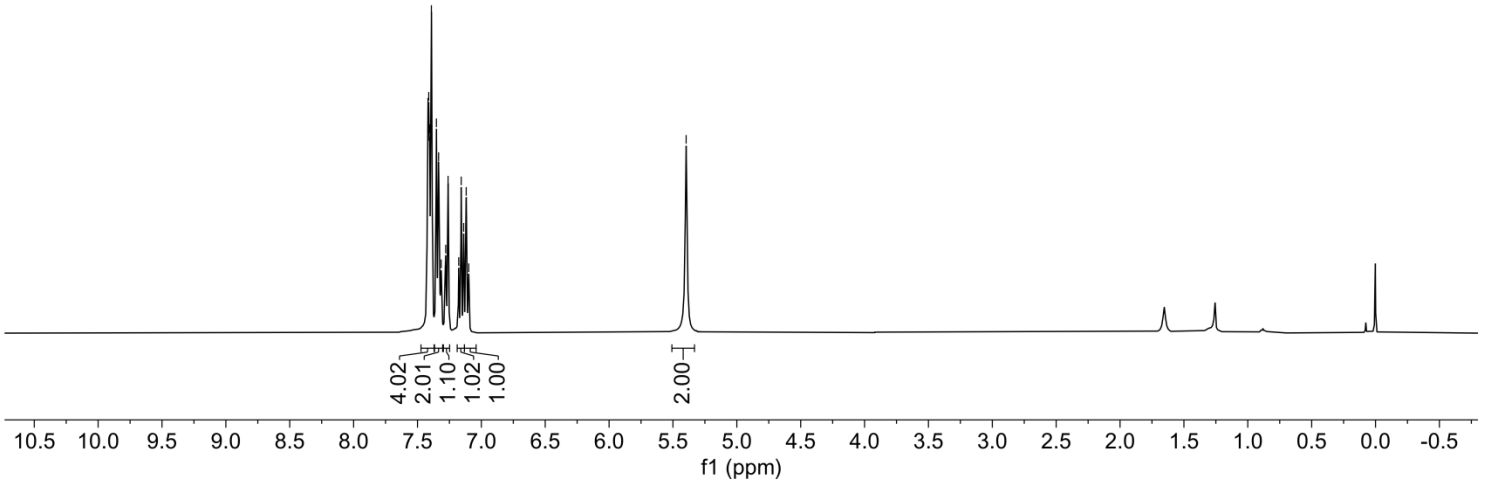
^{1}H NMR, $CDCl_3$, 400 MHz

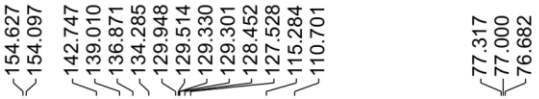


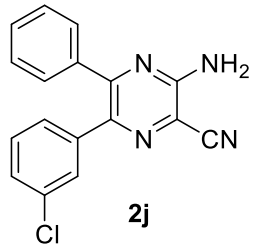

154.499
153.942
144.617
138.087
137.365
137.153
129.860
129.616
129.557
129.107
128.224
127.951
126.488
115.531
110.523
77.318
77.000
76.683
21.347
N
NH2
N
CN
2i
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



^{1}H NMR, $CDCl_3$, 400 MHz

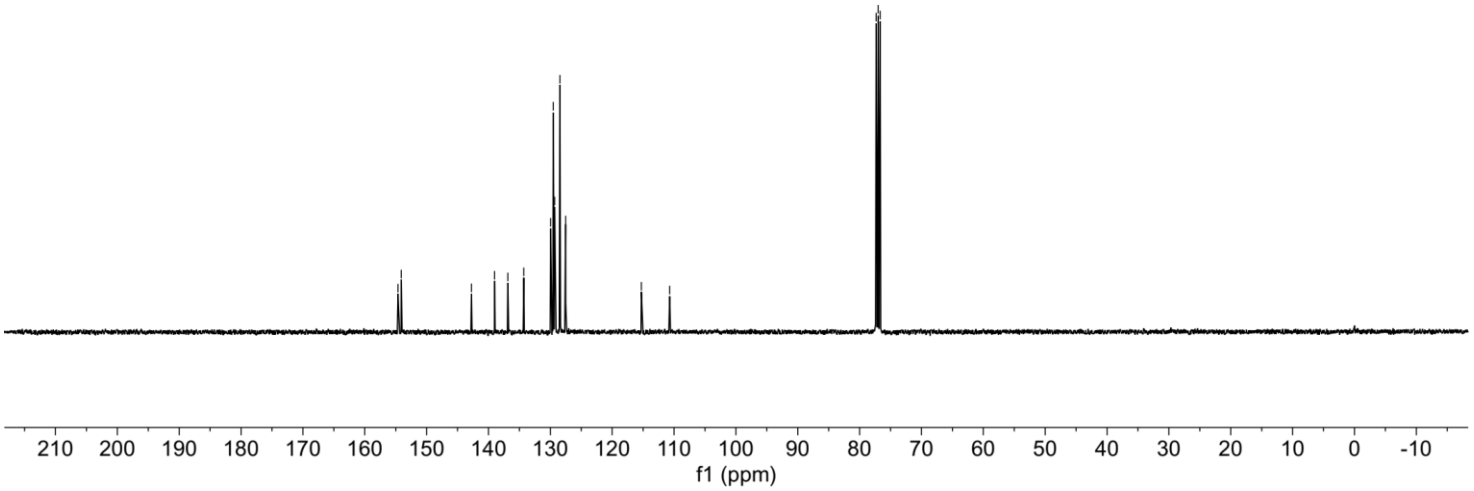


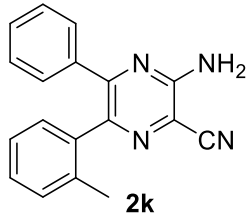




2j

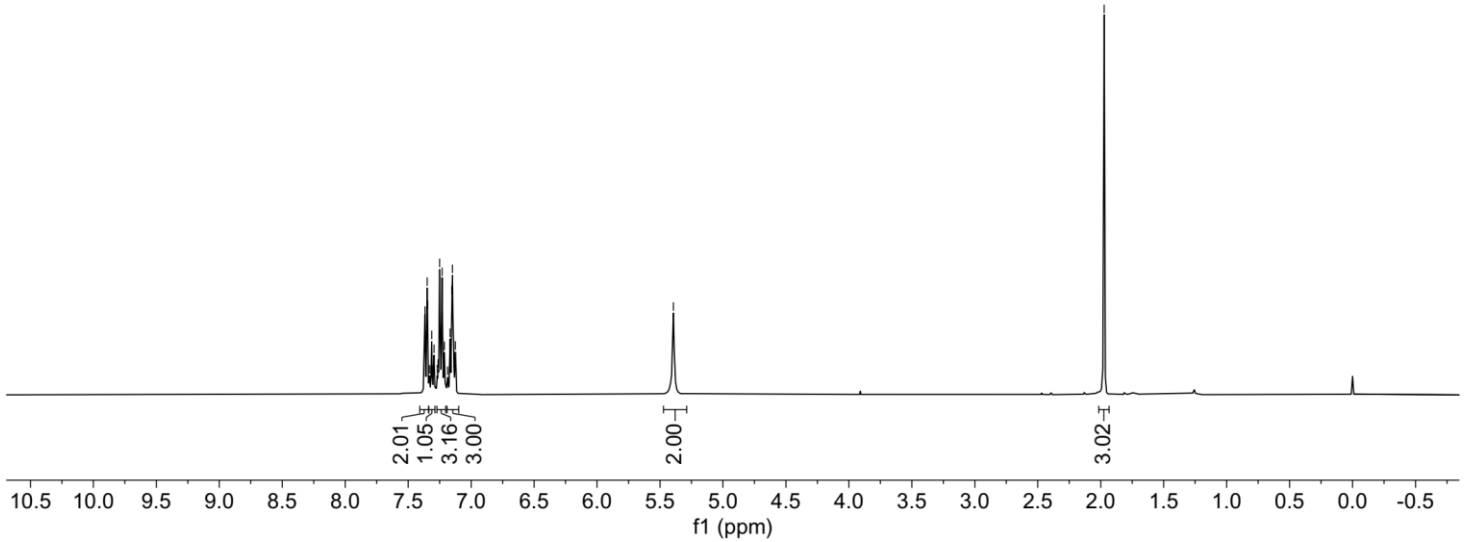
^{13}C NMR, $CDCl_3$, 100 MHz

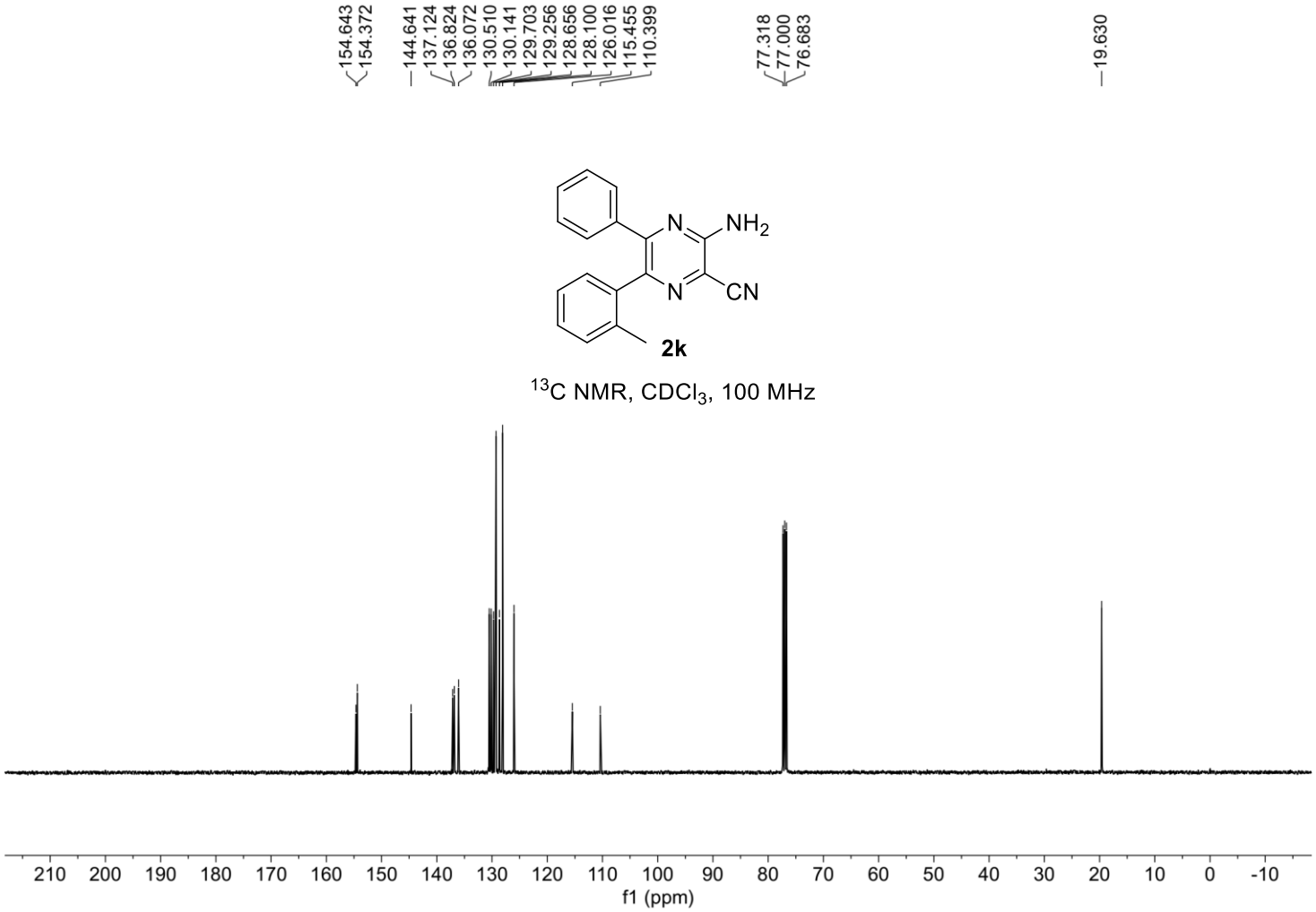


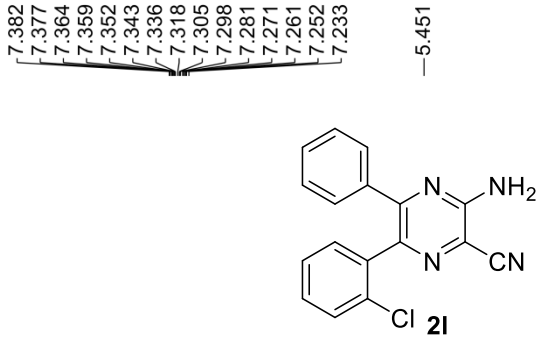


2k

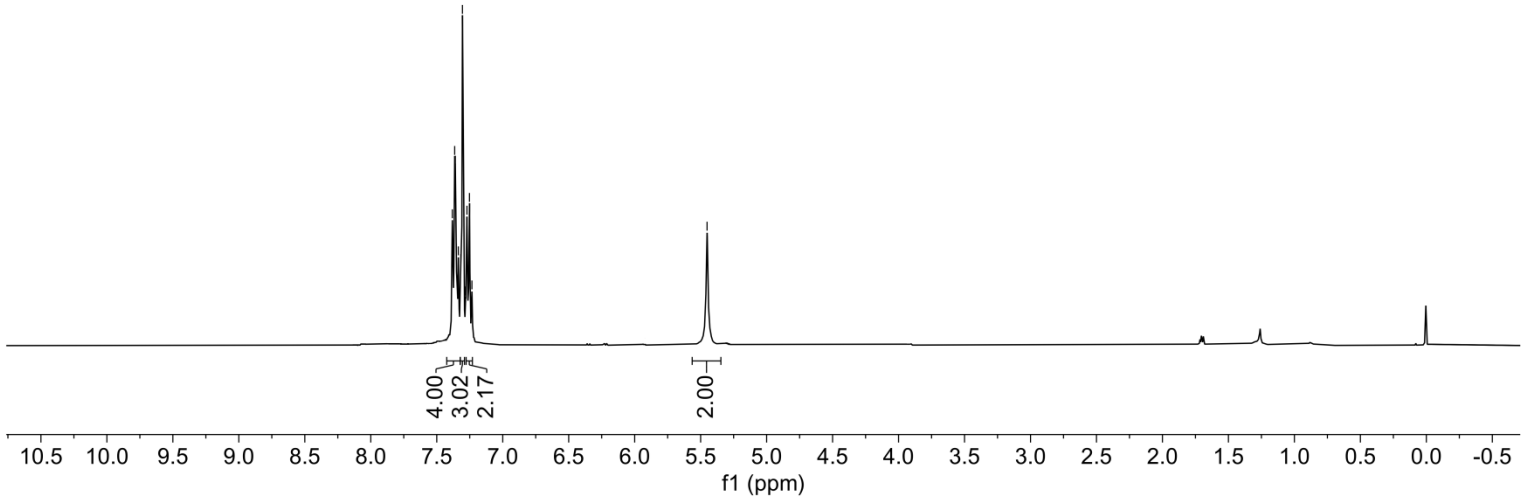
^{1}H NMR, $CDCl_3$, 400 MHz

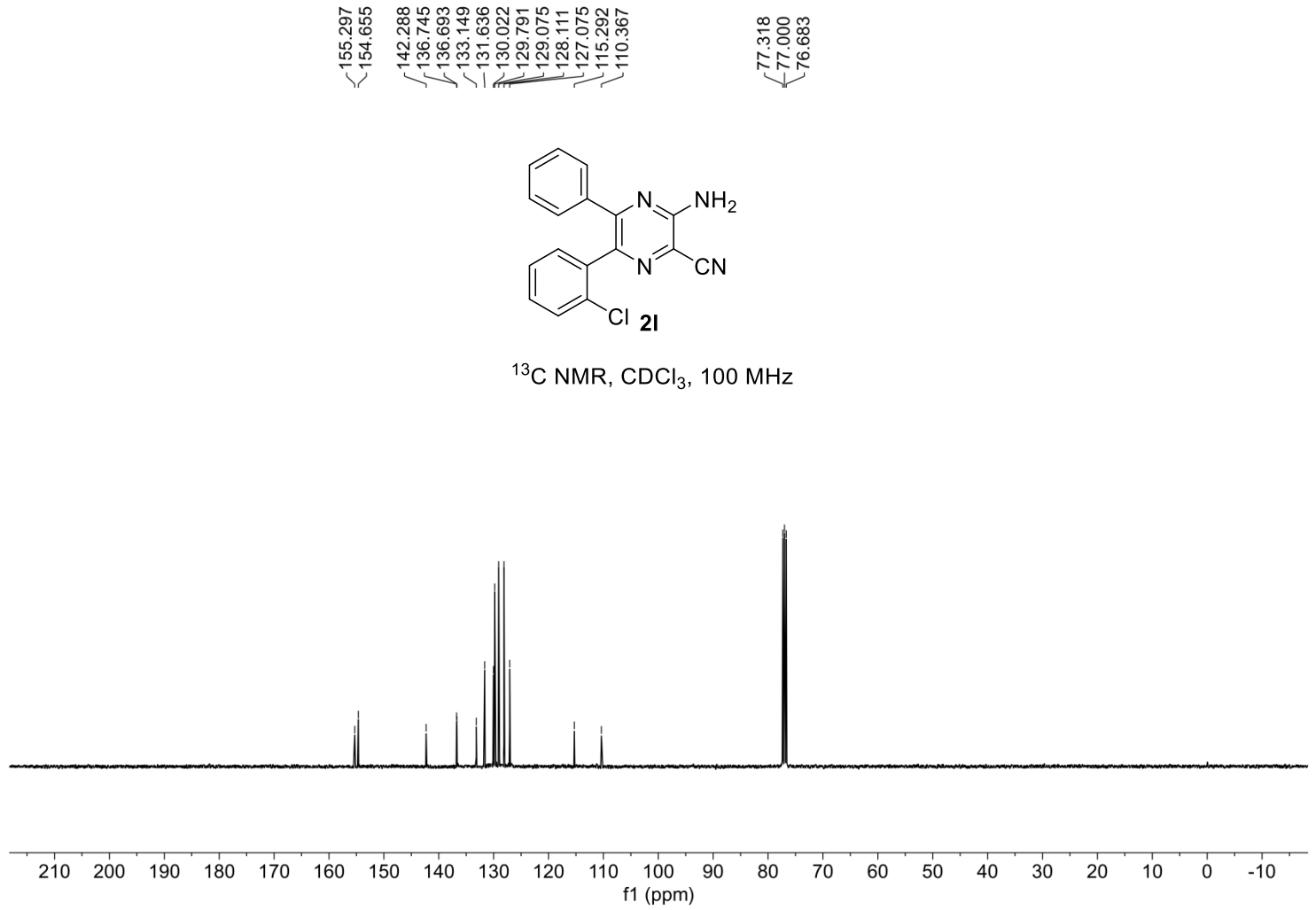



154.643
154.372
144.641
137.124
136.824
136.072
130.510
130.141
129.703
129.256
128.656
128.100
126.016
115.455
110.399
77.318
77.000
76.683
19.630
N
NH2
N
CN
2k
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



^{1}H NMR, $CDCl_3$, 400 MHz

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136.693
133.149
131.636
130.022
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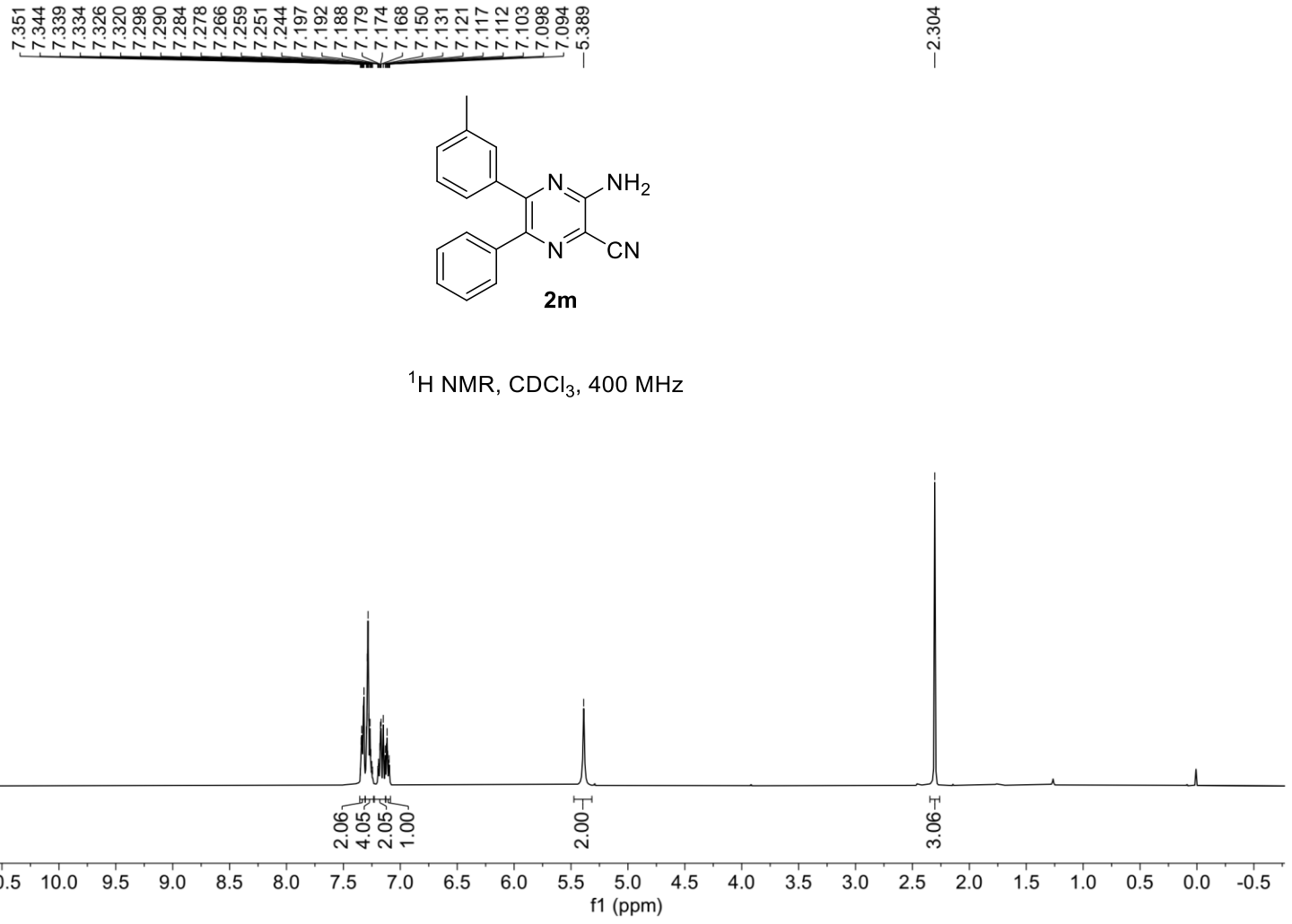
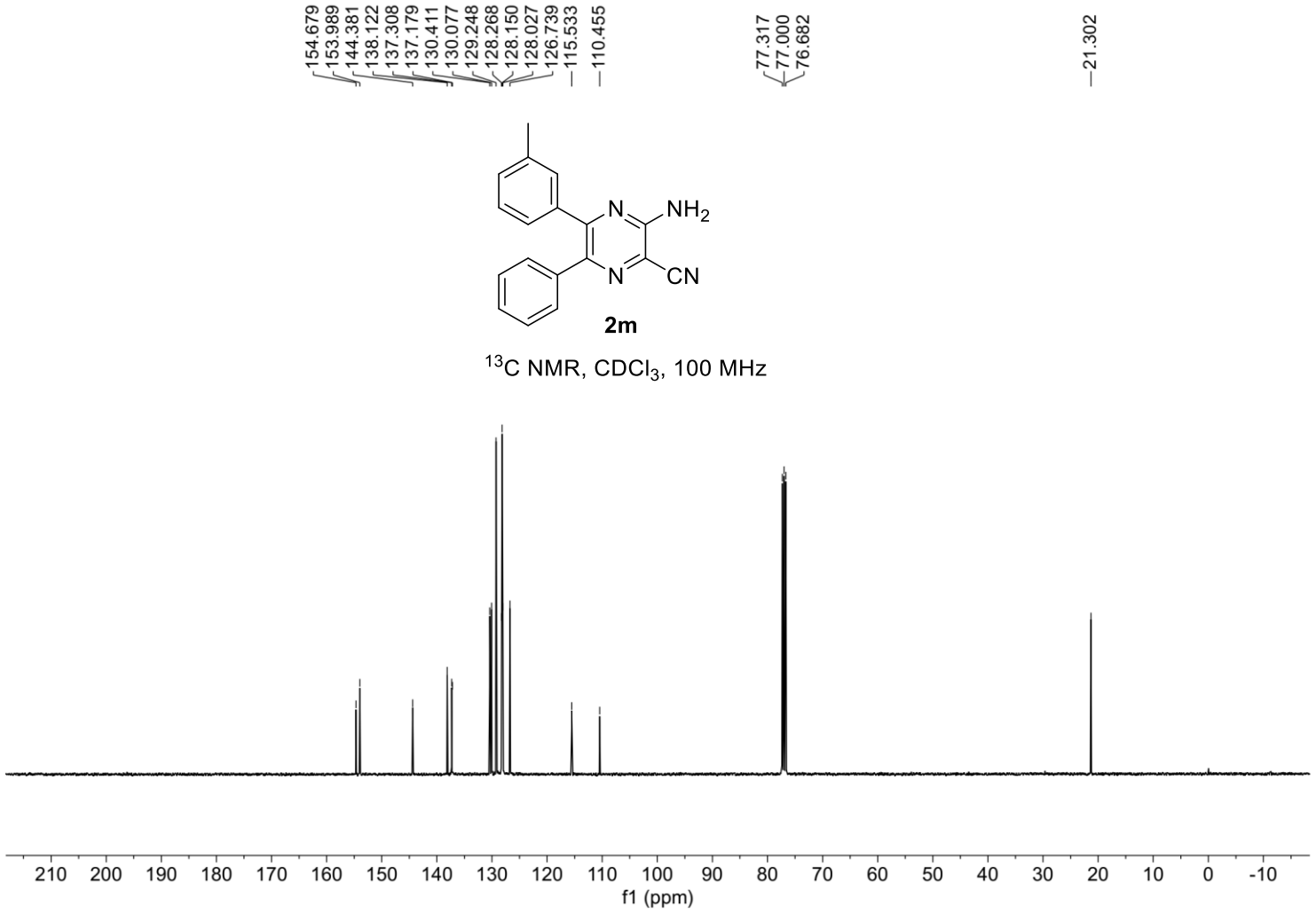
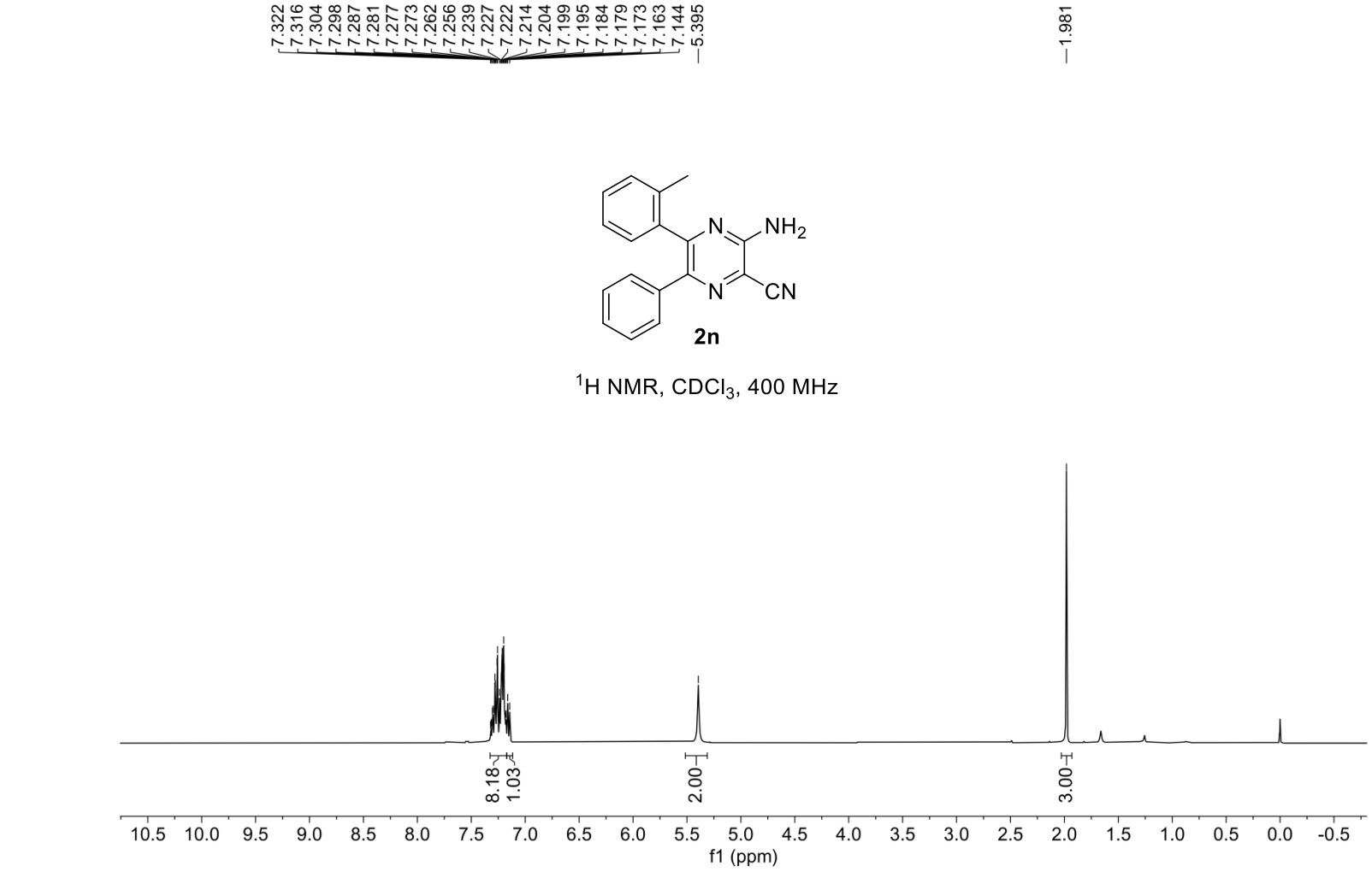
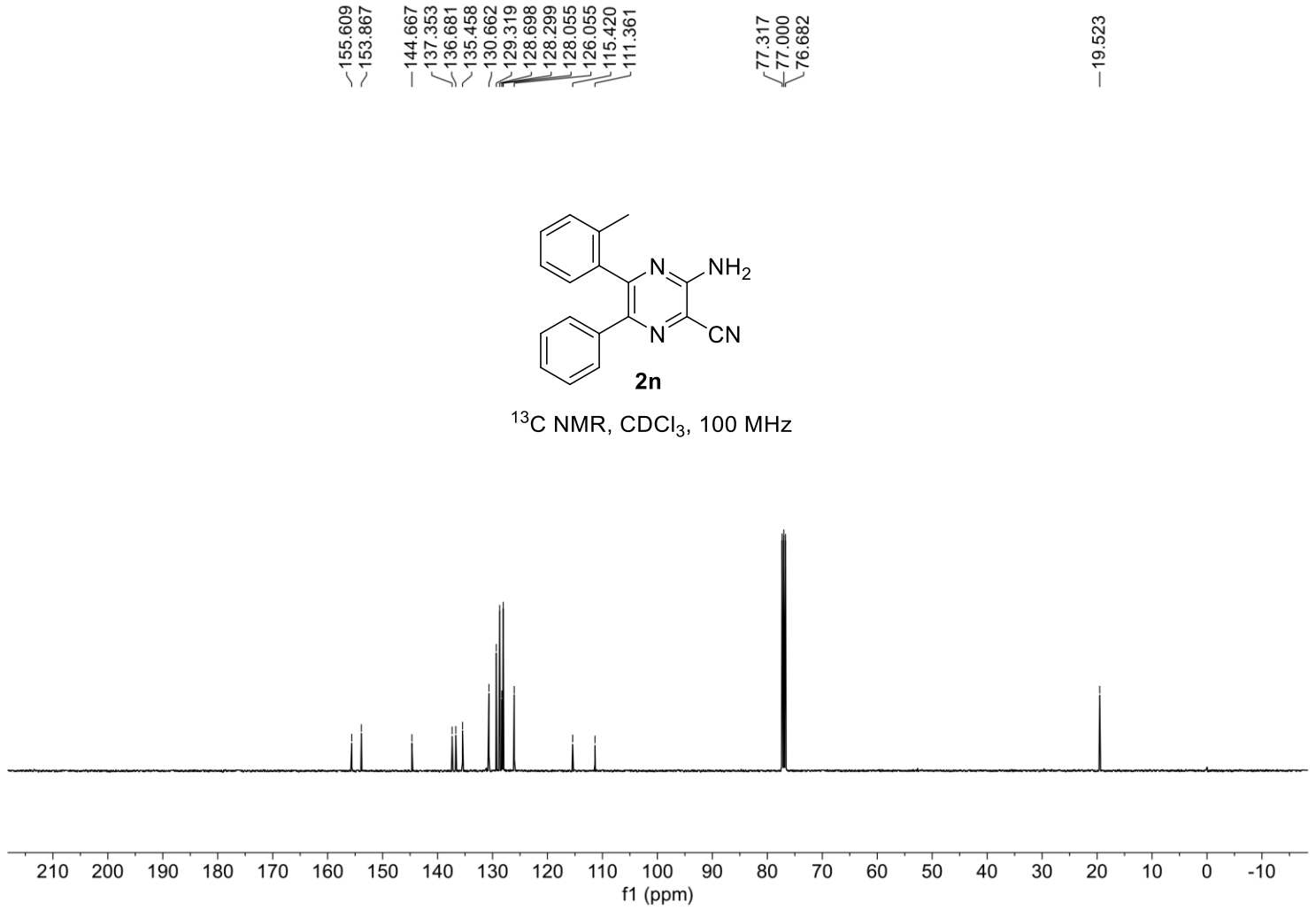
129.075
128.111
127.075
115.292
110.367
77.318
77.000
76.683
N
NH2
N
CN
Cl
2l
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

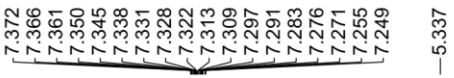


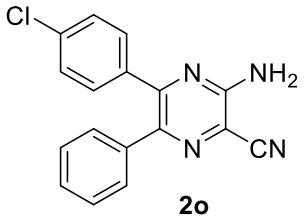
^{1}H NMR, $CDCl_3$, 400 MHz


154.679
153.989
144.381
138.122
137.308
137.179
130.411
130.077
129.248
128.268
128.150
128.027
126.739
115.533
110.455
77.317
77.000
76.682
21.302
N
NH2
N
CN
2m
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.322
7.316
7.304
7.298
7.287
7.281
7.277
7.273
7.262
7.256
7.239
7.227
7.222
7.214
7.204
7.199
7.195
7.184
7.179
7.173
7.163
7.144
5.395
1.981
N
NH2
N
CN
2n
1H NMR, CDCl3, 400 MHz
8.18
1.03
2.00
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

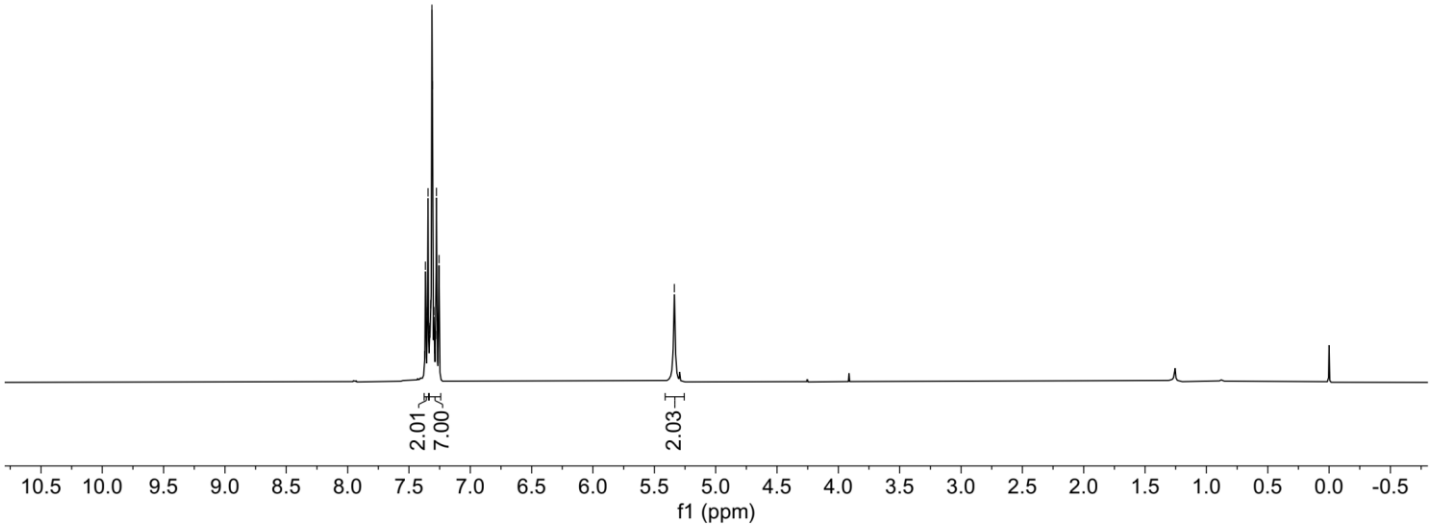

155.609
153.867
144.667
137.353
136.681
135.458
130.662
129.319
128.698
128.299
128.055
126.055
115.420
111.361
77.317
77.000
76.682
19.523
N
NH2
N
CN
2n
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

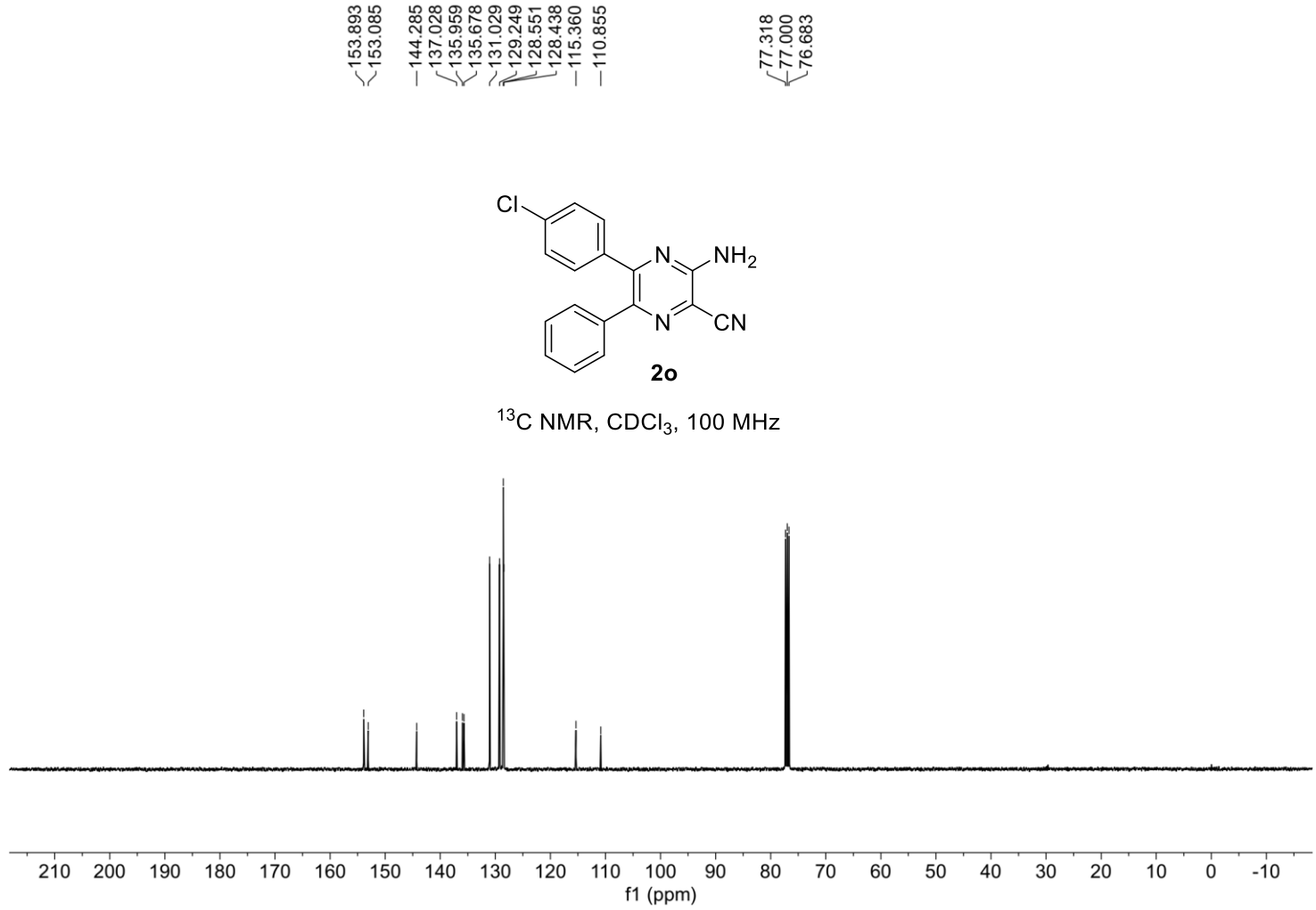


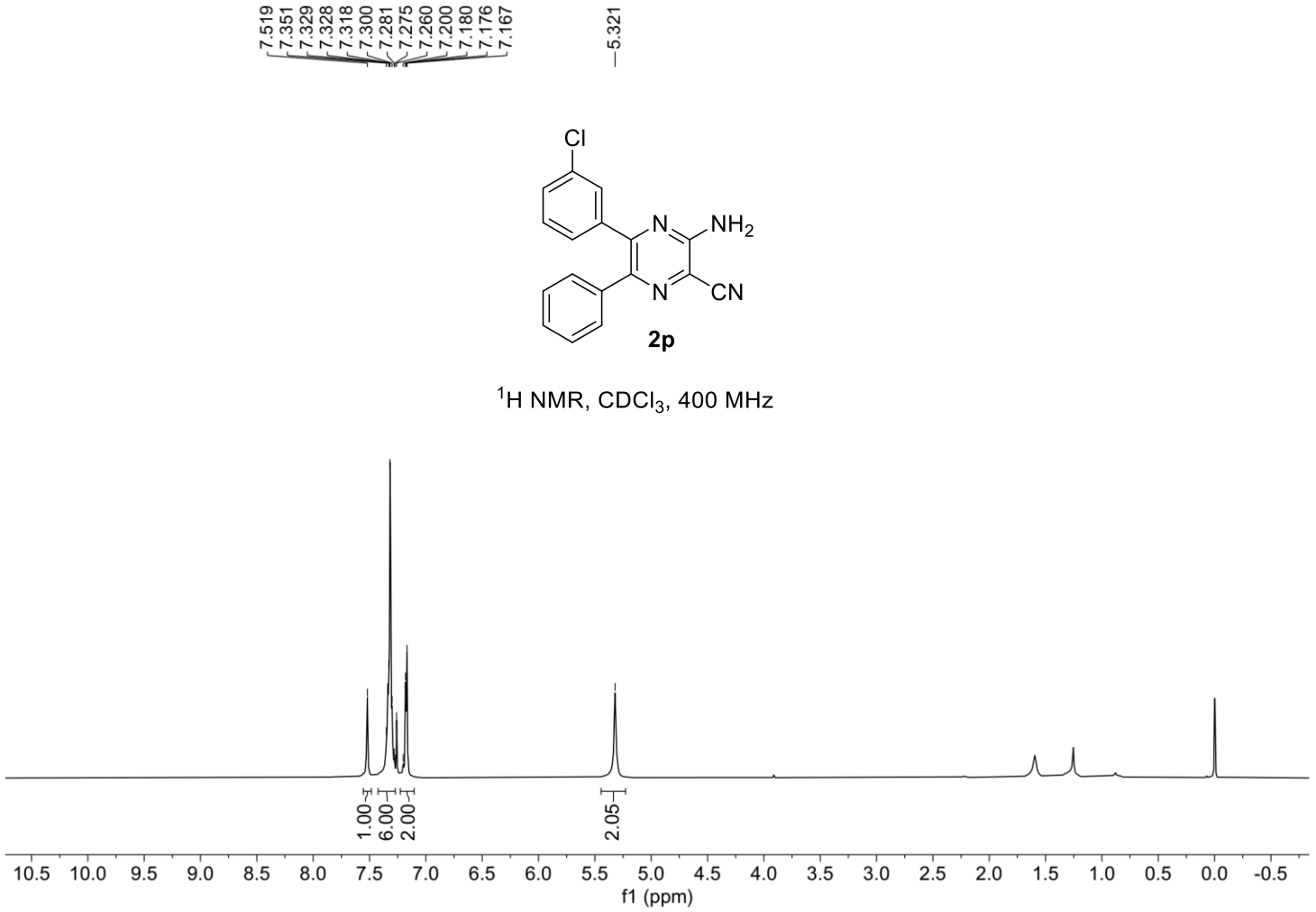


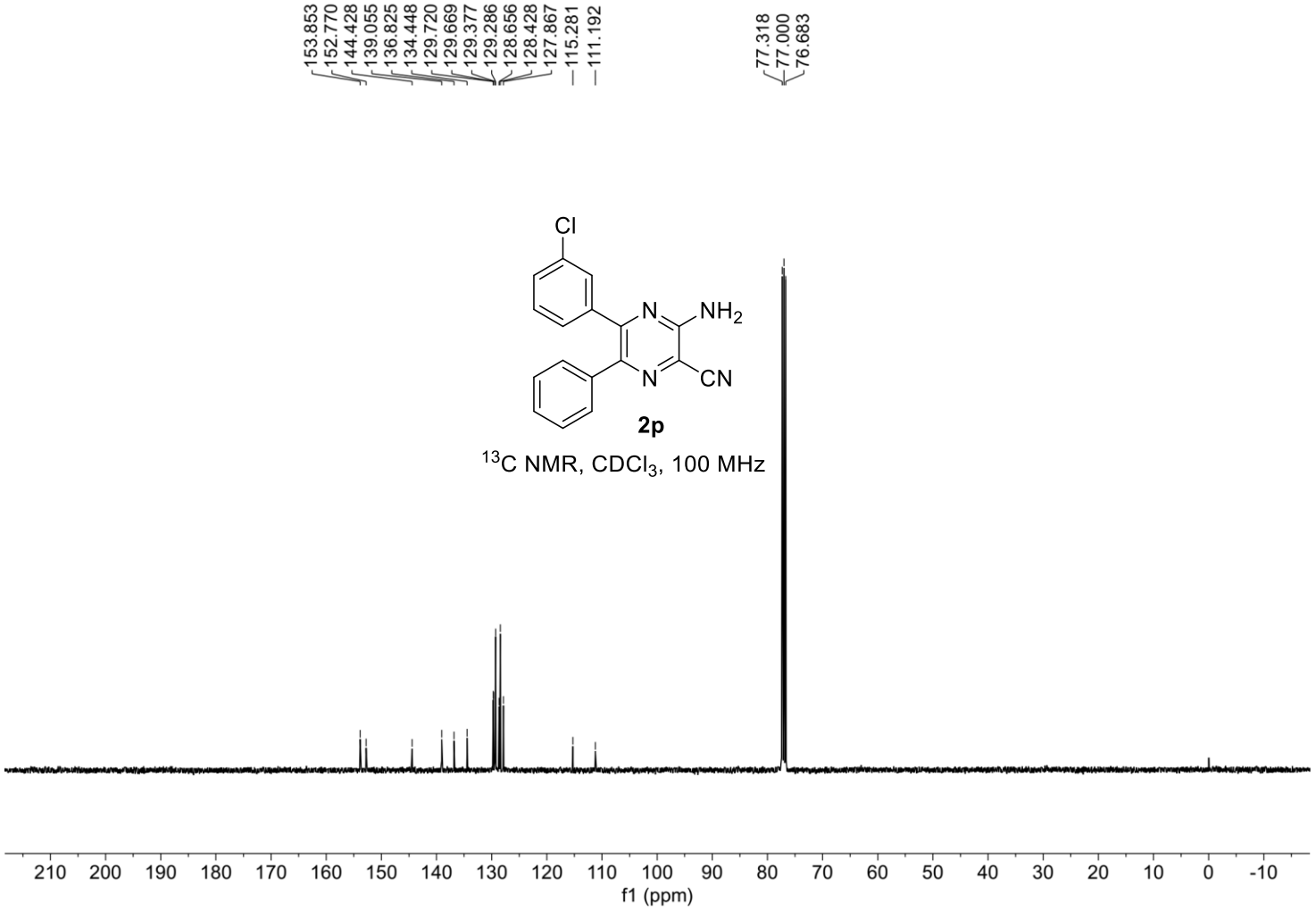
2o

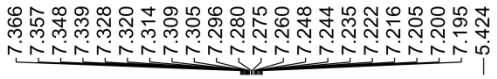
^{1}H NMR, $CDCl_3$, 400 MHz

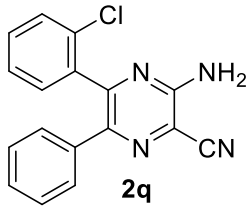



153.893
153.085
144.285
137.028
135.959
135.678
131.029
129.249
128.551
128.438
115.360
110.855
77.318
77.000
76.683
Cl
N
NH2
N
CN
2o
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.519
7.351
7.329
7.328
7.318
7.300
7.281
7.275
7.260
7.200
7.180
7.176
7.167
5.321
Cl
N
NH2
N
CN
2p
1H NMR, CDCl3, 400 MHz
1.00
6.00
2.00
2.05
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

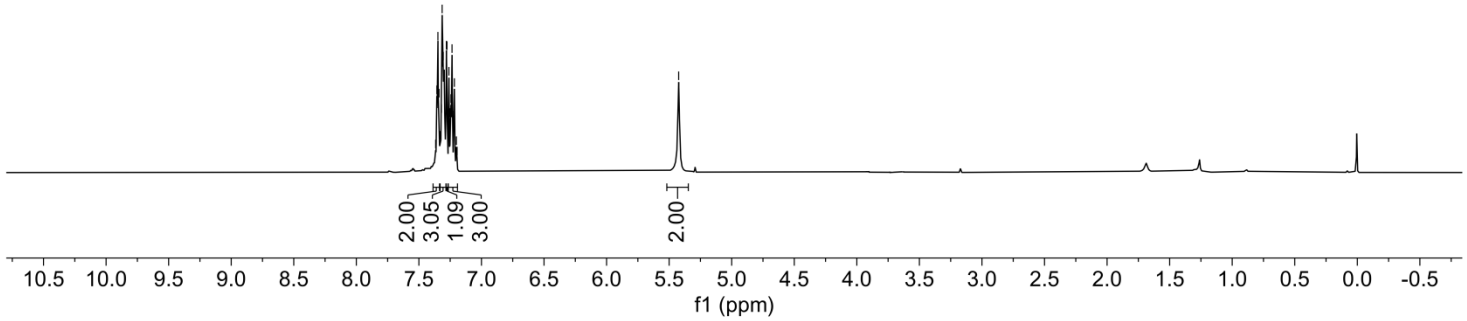

153.853
152.770
144.428
139.055
136.825
134.448
129.720
129.669
129.377
129.286
128.656
128.428
127.867
115.281
111.192
77.318
77.000
76.683
Cl
N
NH2
N
CN
2p
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

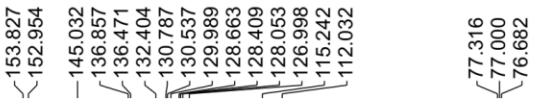


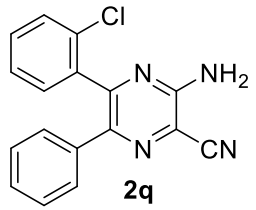


2q

^{1}H NMR, $CDCl_3$, 400 MHz

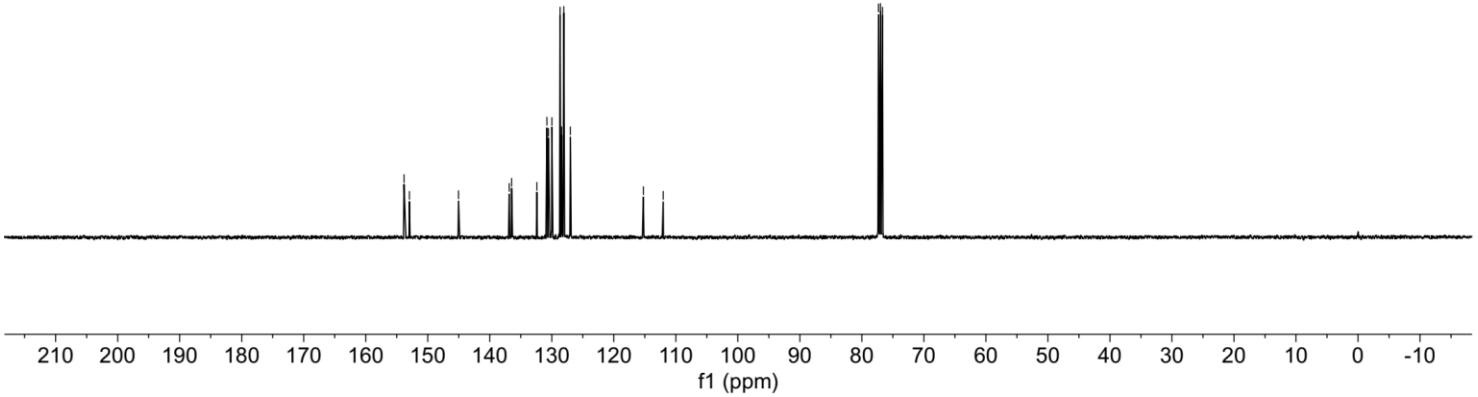


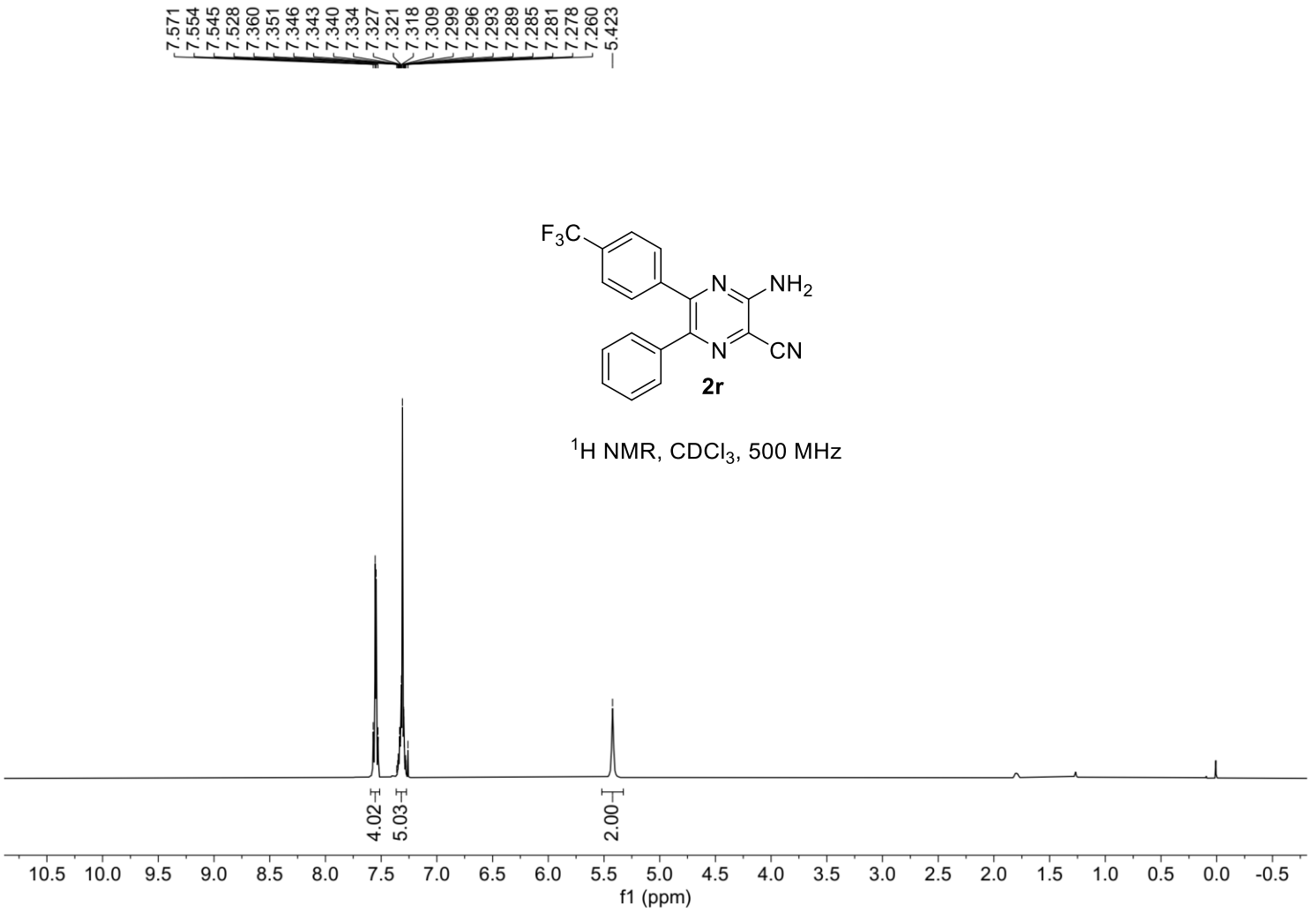


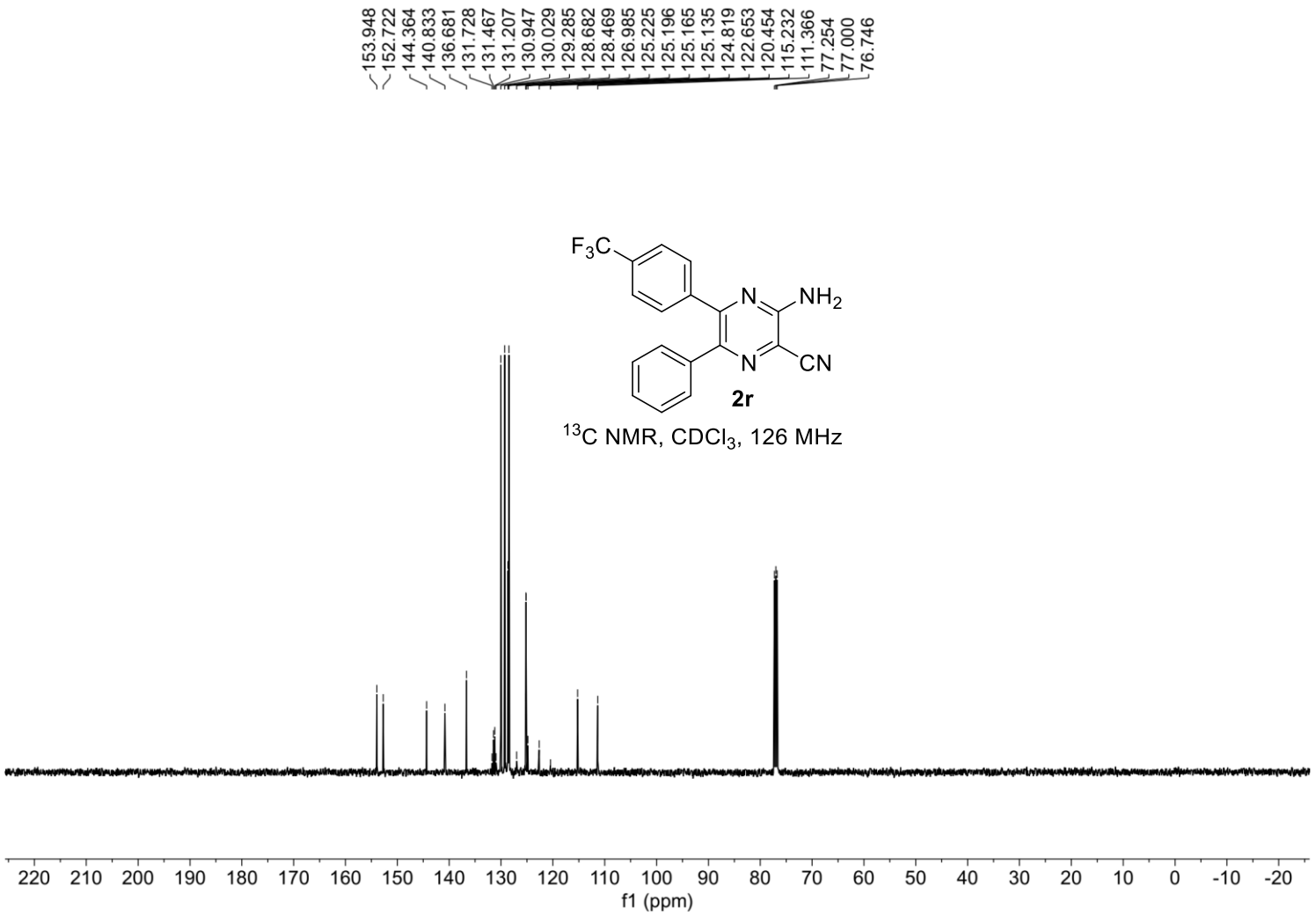


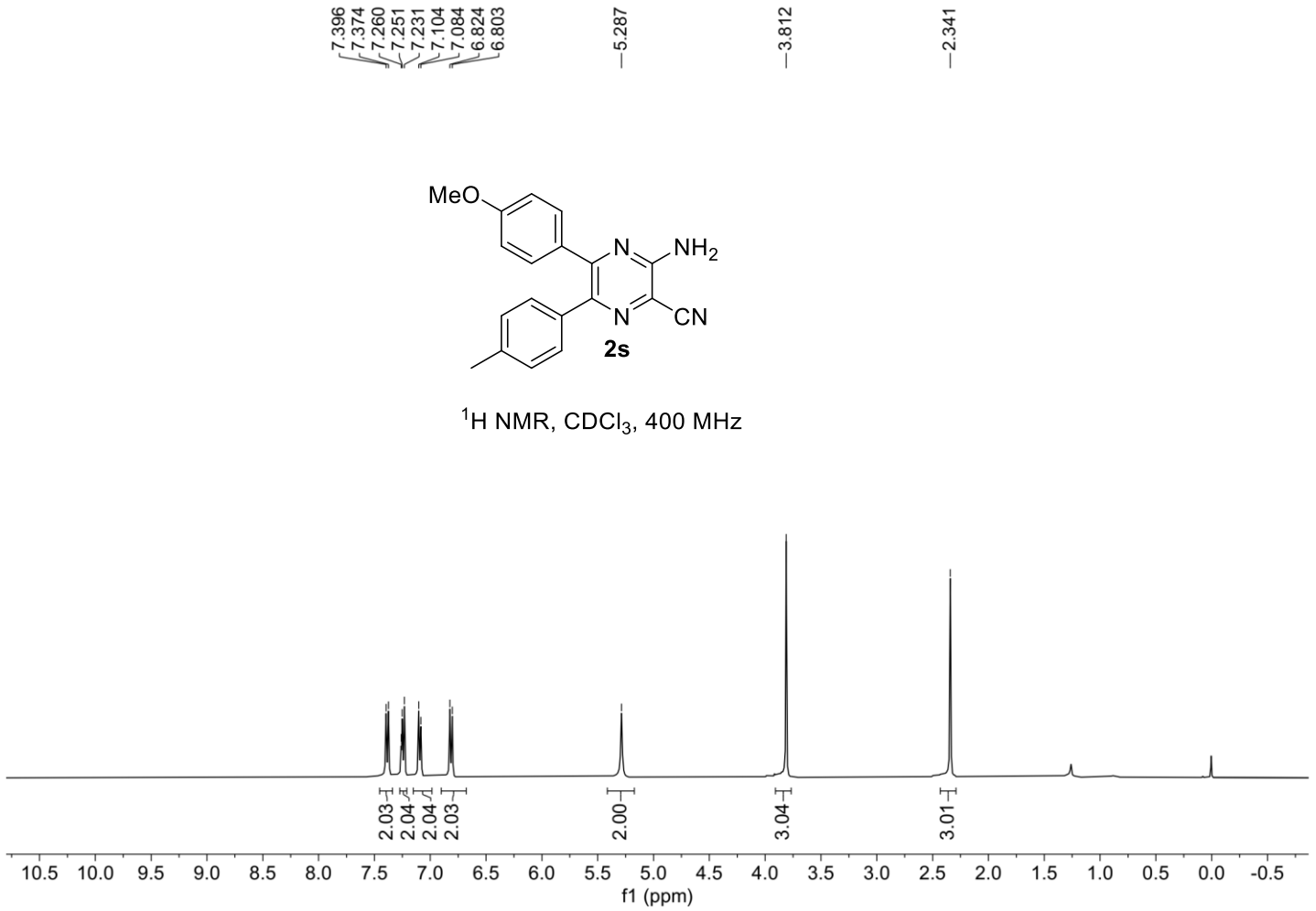
2q

^{13}C NMR, $CDCl_3$, 100 MHz

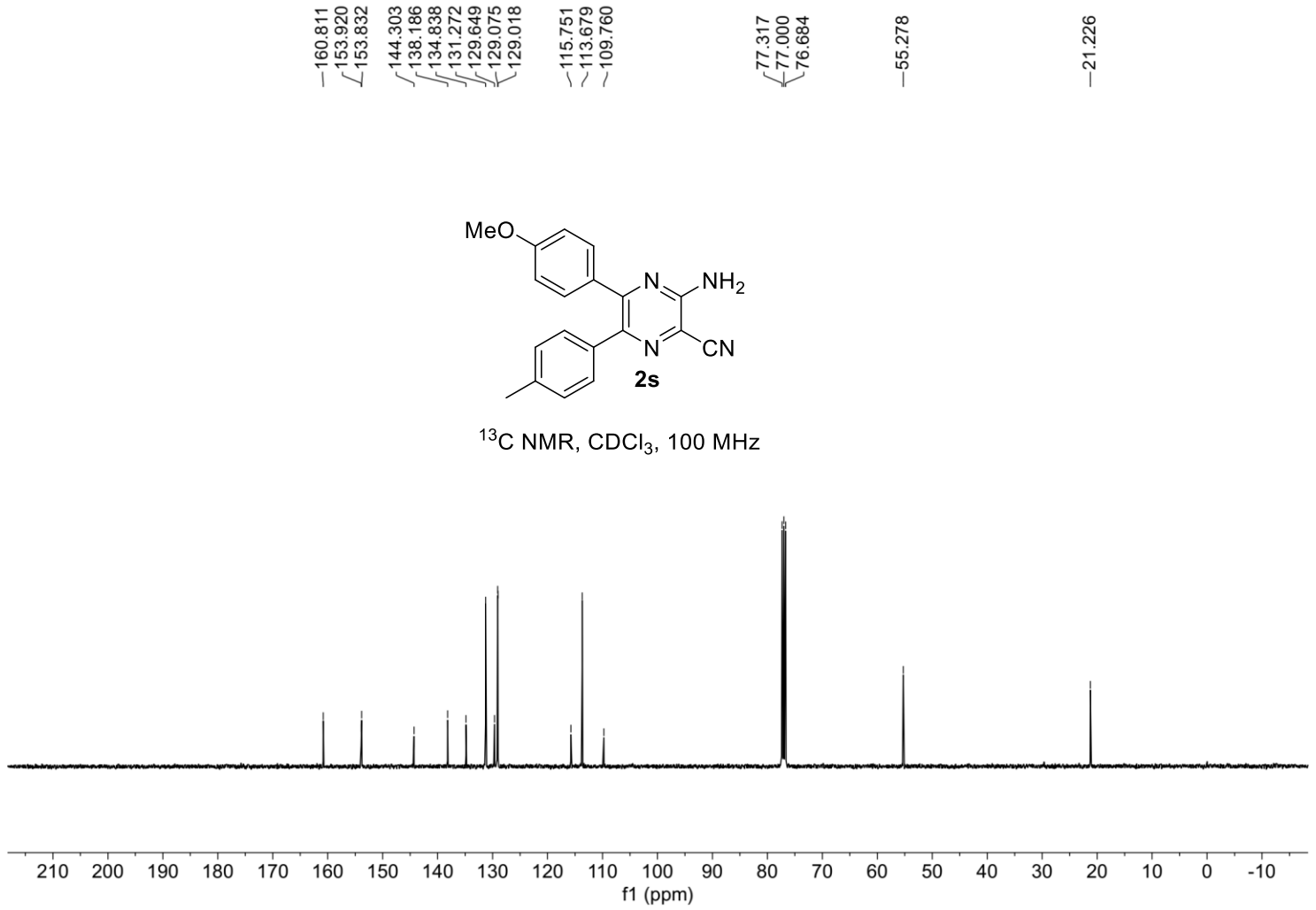


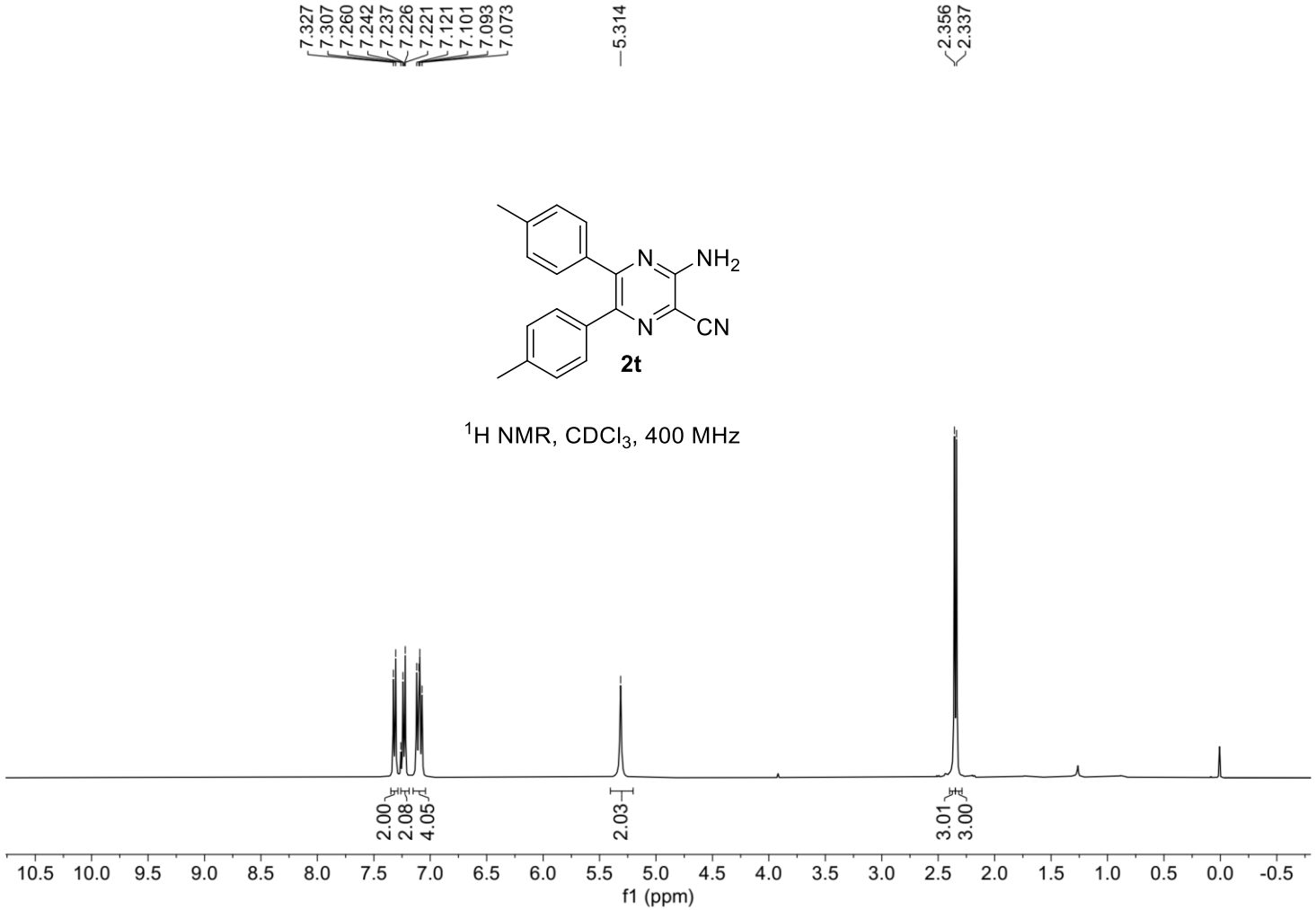

7.571
7.554
7.545
7.528
7.360
7.351
7.346
7.343
7.340
7.334
7.327
7.321
7.318
7.309
7.299
7.296
7.293
7.289
7.285
7.281
7.278
7.260
5.423
F3C
N
NH2
N
CN
2r
1H NMR, CDCl3, 500 MHz
4.02
5.03
2.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

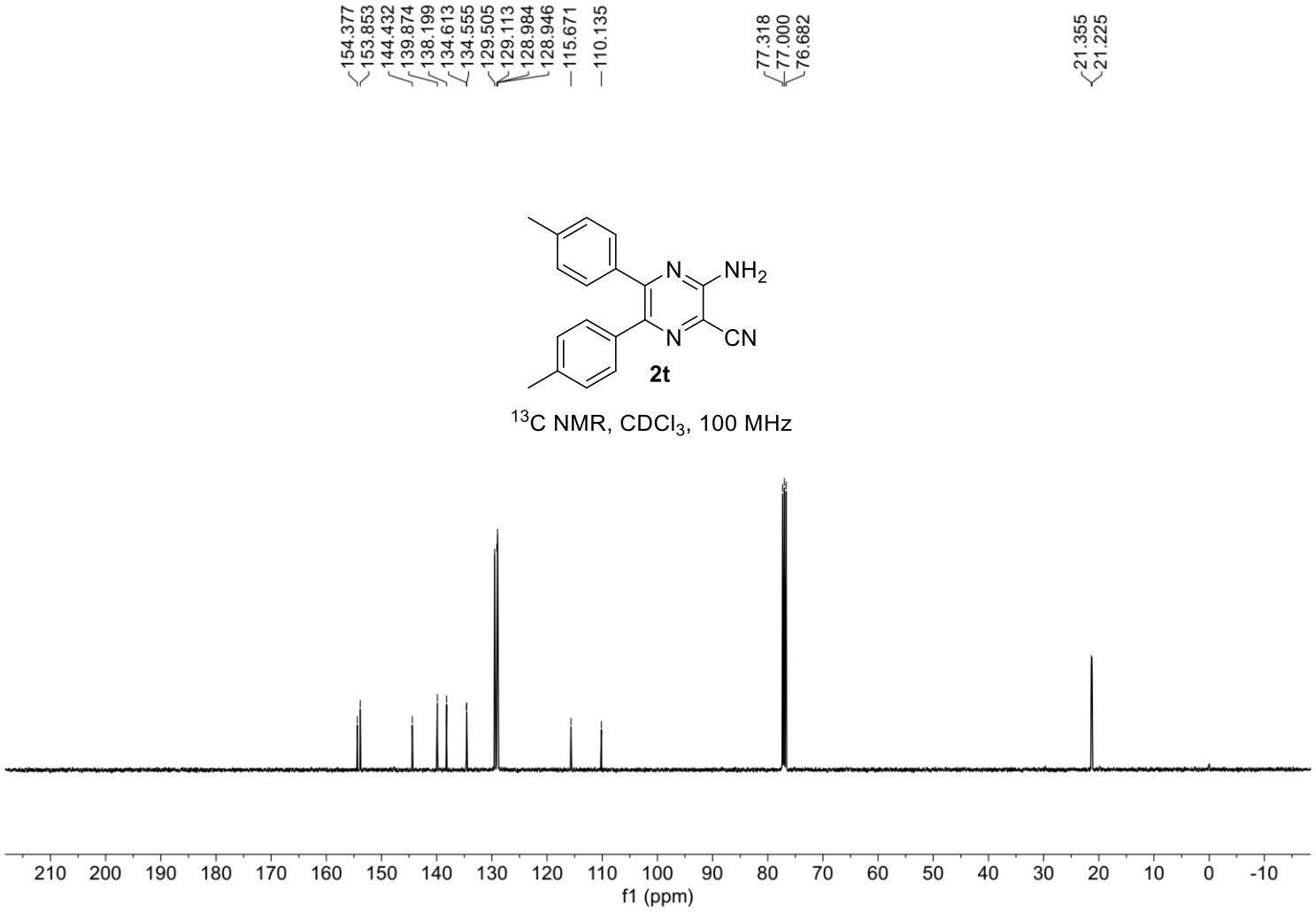

153.948
152.722
144.364
140.833
136.681
131.728
131.467
131.207
130.947
130.029
129.285
128.682
128.469
126.985
125.225
125.196
125.165
125.135
124.819
122.653
120.454
115.232
111.366
77.254
77.000
76.746
F3C
N
NH2
N
CN
2r
13C NMR, CDCl3, 126 MHz
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

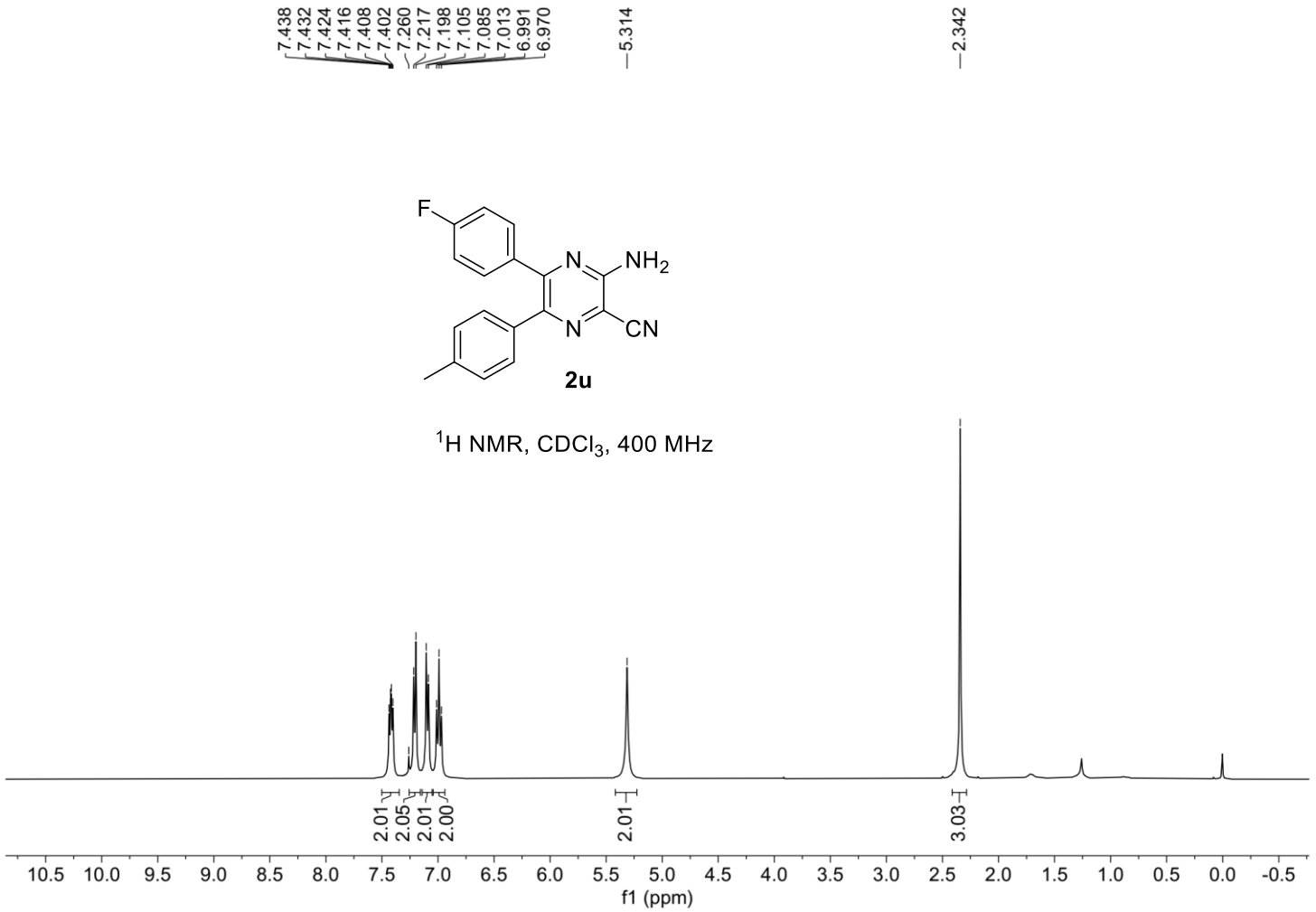


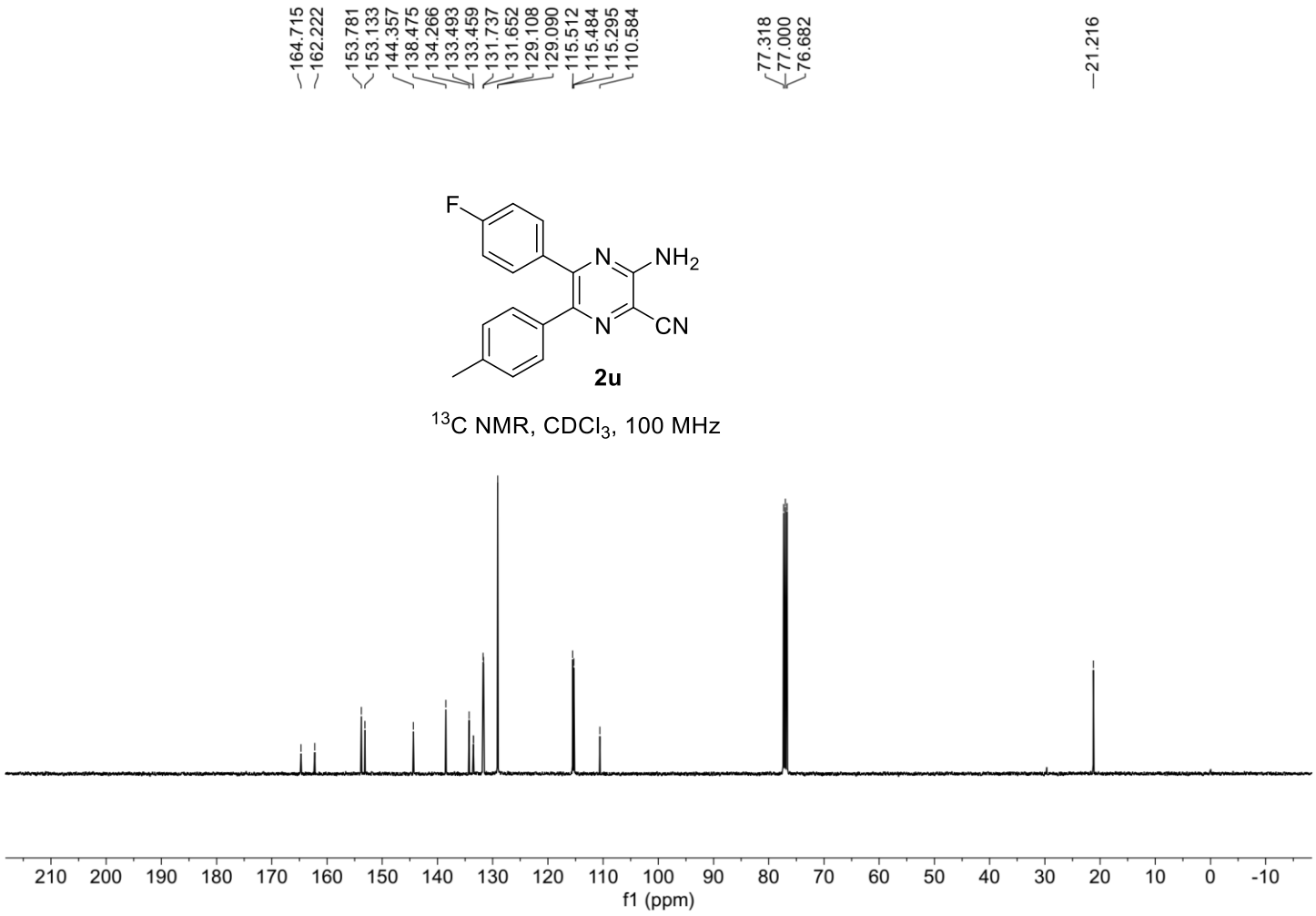
^{1}H NMR, $CDCl_3$, 400 MHz

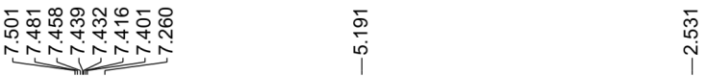

160.811
153.920
153.832
144.303
138.186
134.838
131.272
129.649
129.075
129.018
115.751
113.679
109.760
77.317
77.000
76.684
55.278
21.226
MeO
N
NH2
N
CN
2s
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

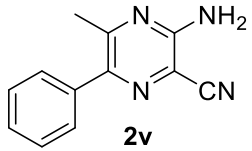

7.327
7.307
7.260
7.242
7.237
7.226
7.221
7.121
7.101
7.093
7.073
5.314
2.356
2.337
N
NH2
N
CN
2t
1H NMR, CDCl3, 400 MHz
2.00
2.08
4.05
2.03
3.01
3.00
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


154.377
153.853
144.432
139.874
138.199
134.613
134.555
129.505
129.113
128.984
128.946
115.671
110.135
77.318
77.000
76.682
21.355
21.225
N
NH2
N
CN
2t
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


7.438
7.432
7.424
7.416
7.408
7.402
7.260
7.217
7.198
7.105
7.085
7.013
6.991
6.970
5.314
2.342
F
N
NH2
N
CN
2u
1H NMR, CDCl3, 400 MHz
2.01
2.05
2.01
2.00
2.01
3.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

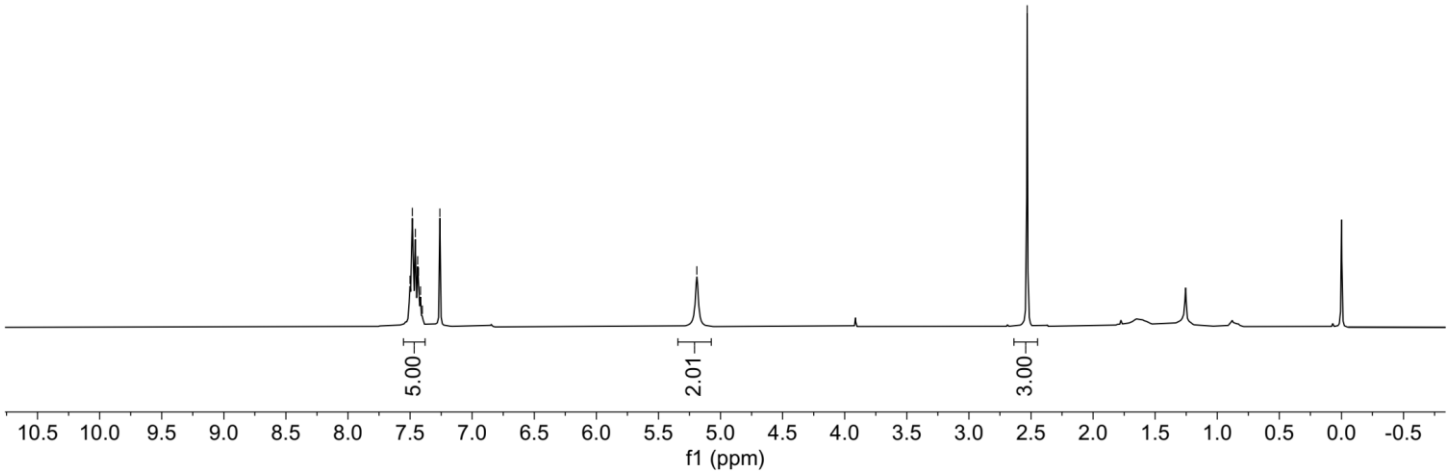

164.715
162.222
153.781
153.133
144.357
138.475
134.266
133.493
133.459
131.737
131.652
129.108
129.090
115.512
115.484
115.295
110.584
77.318
77.000
76.682
21.216
F
N
NH2
N
CN
2u
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

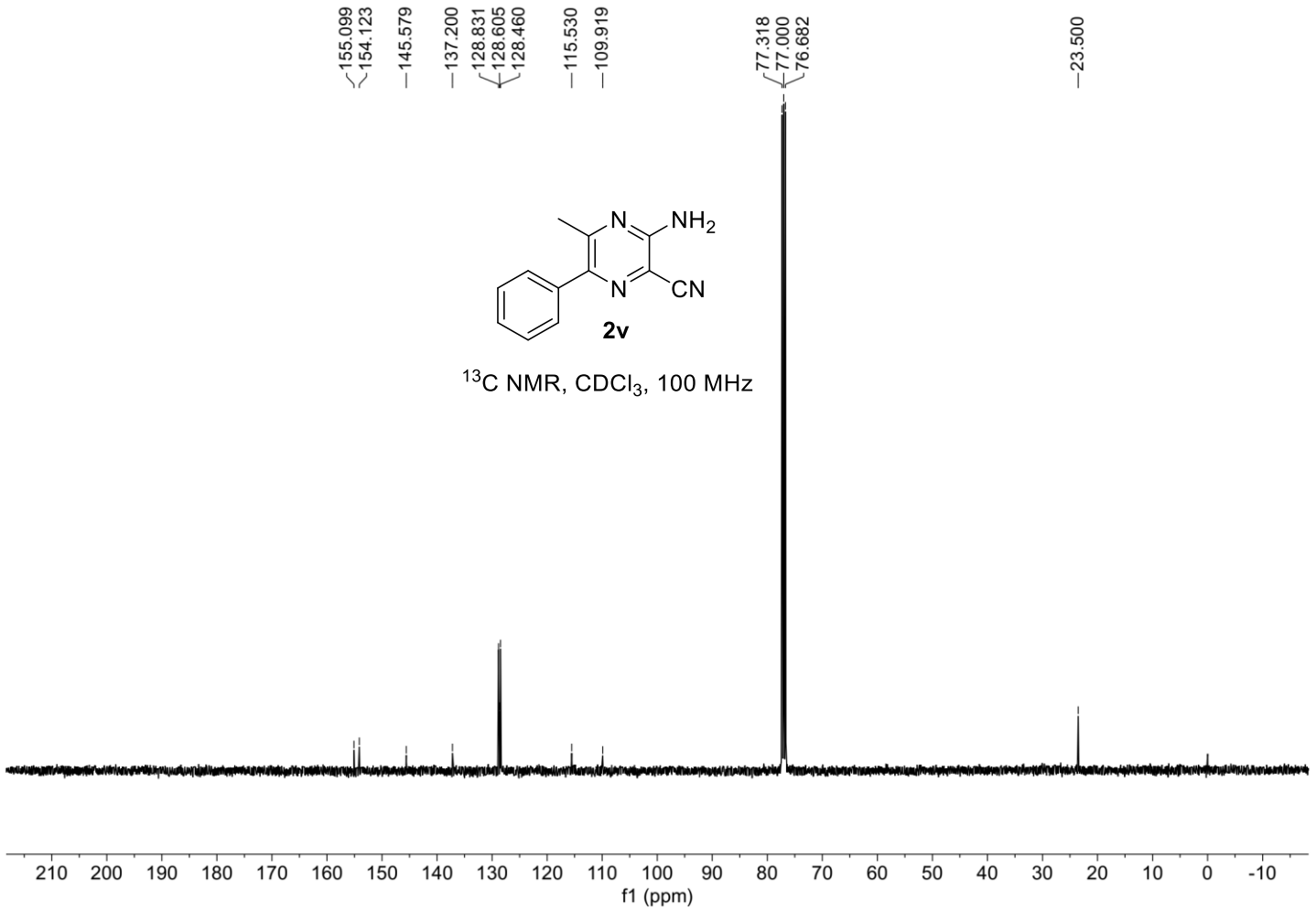


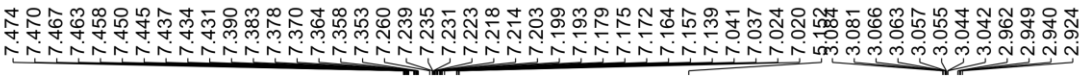


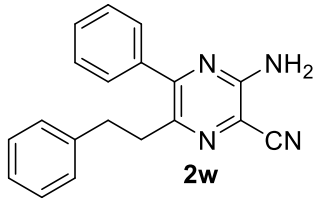
2v

^{1}H NMR, $CDCl_3$, 400 MHz



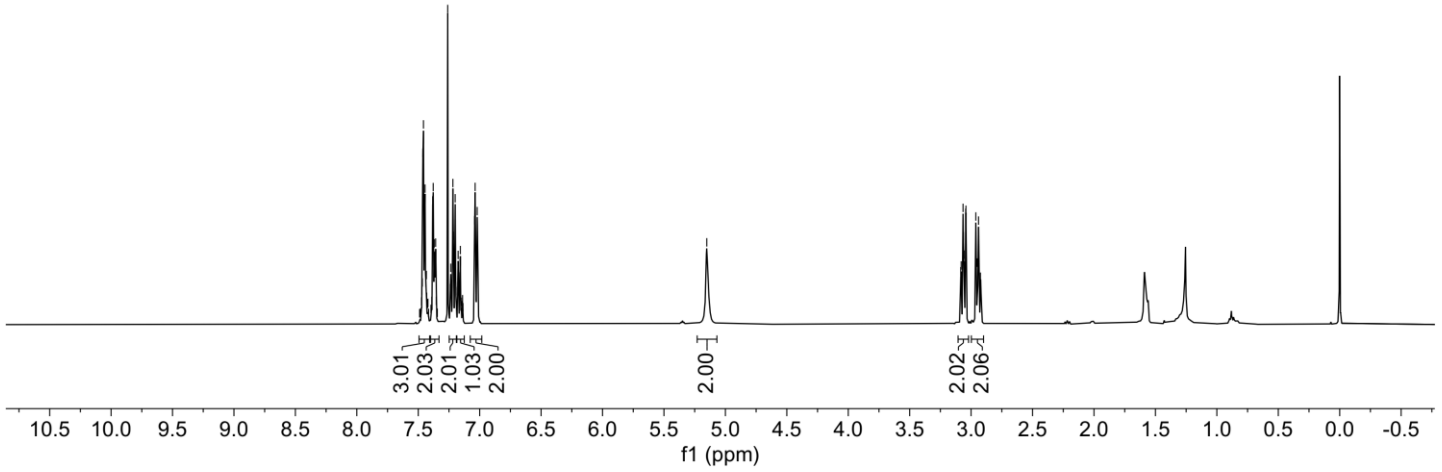

155.099
154.123
145.579
137.200
128.831
128.605
128.460
115.530
109.919
77.318
77.000
76.682
23.500
N
NH2
N
CN
2v
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

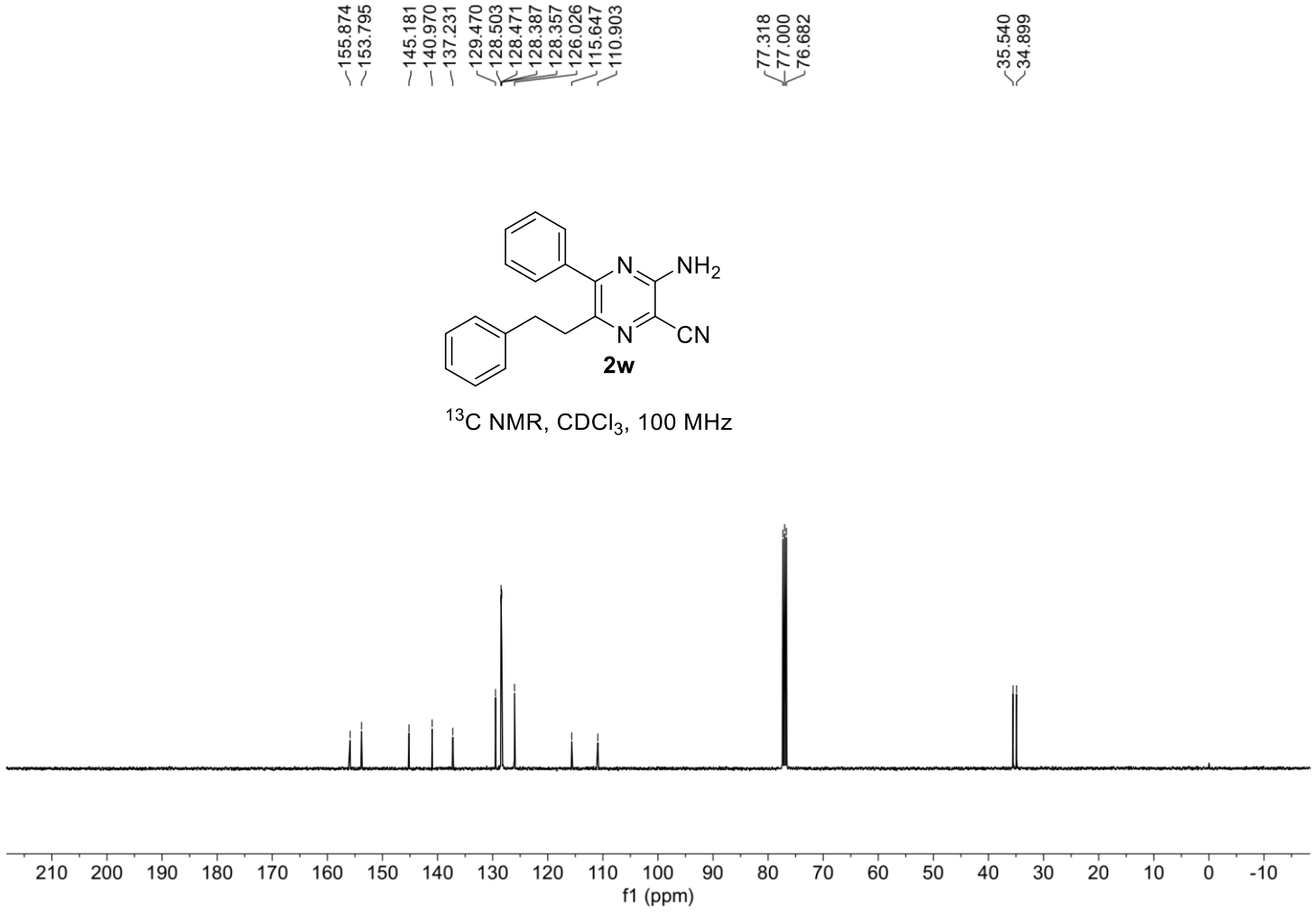


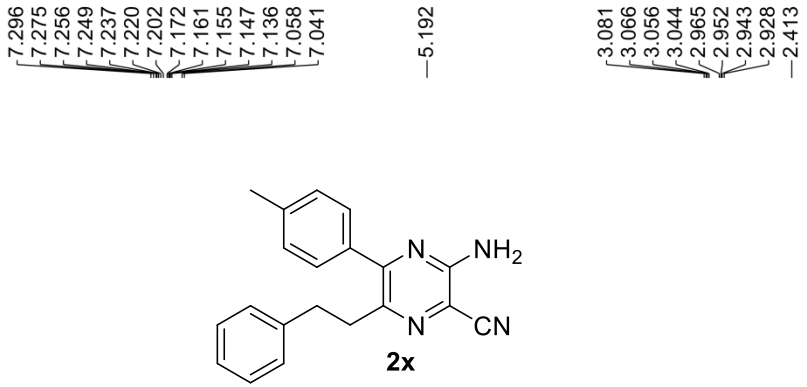


2w

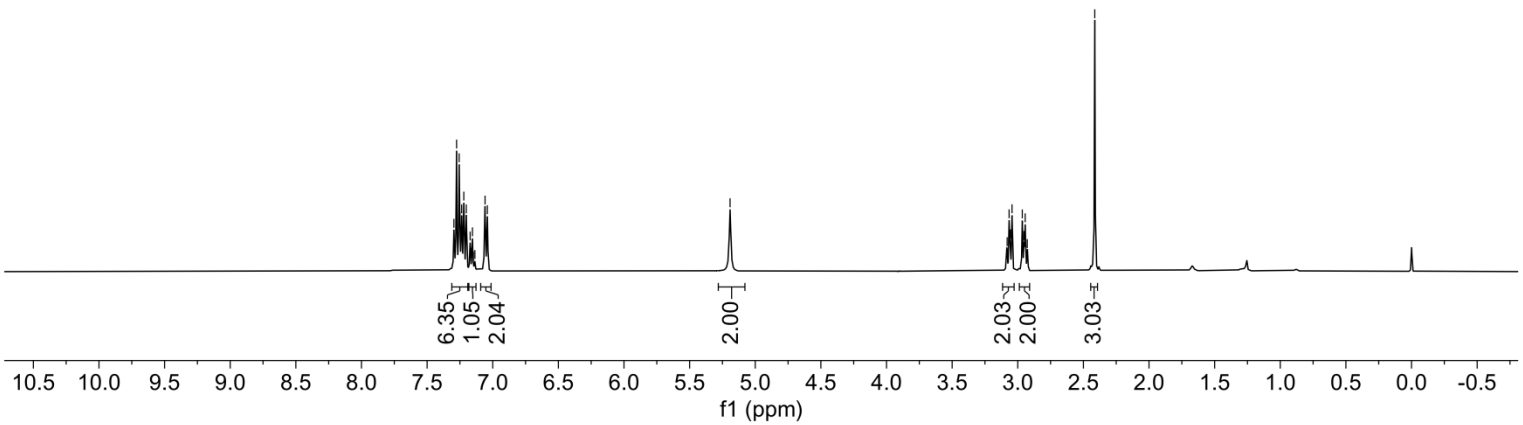
^{1}H NMR, $CDCl_3$, 400 MHz

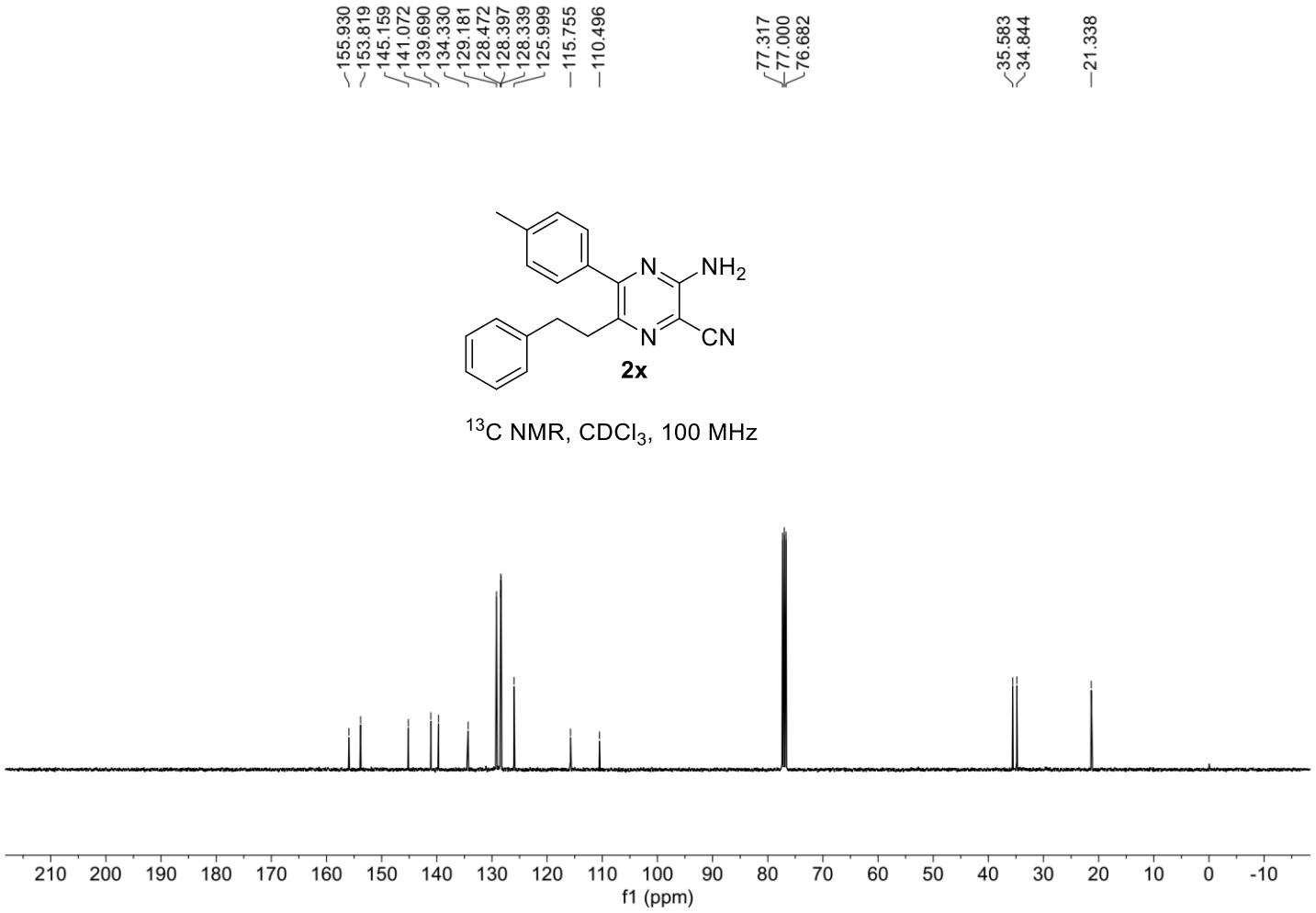


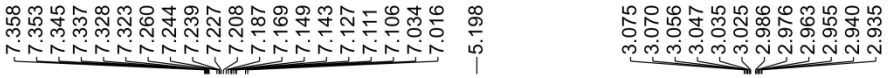

155.874
153.795
145.181
140.970
137.231
129.470
128.503
128.471
128.387
128.357
126.026
115.647
110.903
77.318
77.000
76.682
35.540
34.899
N
NH2
N
CN
2w
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

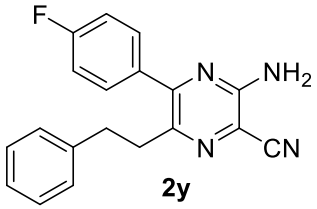


^{1}H NMR, $CDCl_3$, 400 MHz



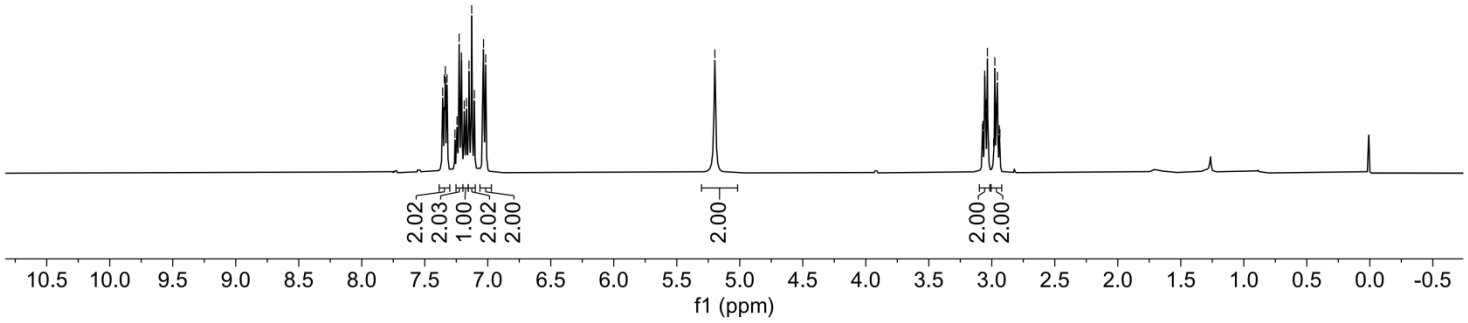

155.930
153.819
145.159
141.072
139.690
134.330
129.181
128.472
128.397
128.339
125.999
115.755
110.496
77.317
77.000
76.682
35.583
34.844
21.338
N
NH2
N
CN
2x
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

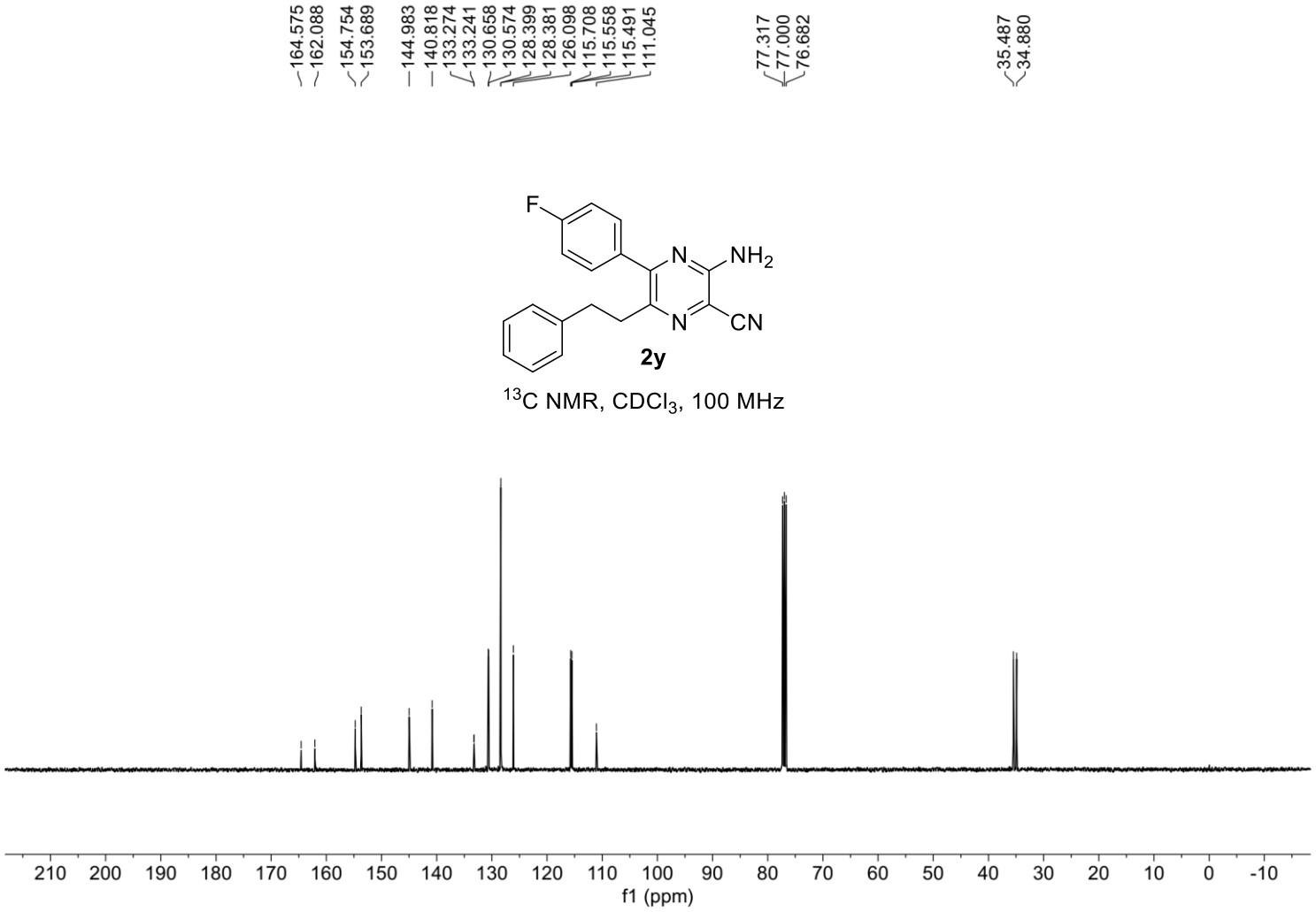


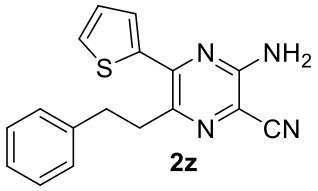


2y

^{1}H NMR, $CDCl_3$, 400 MHz

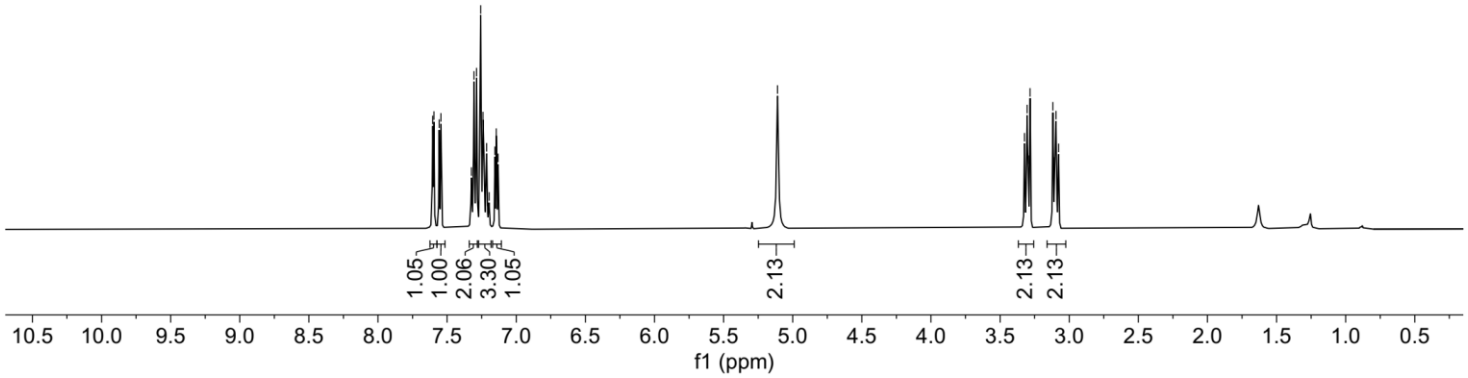


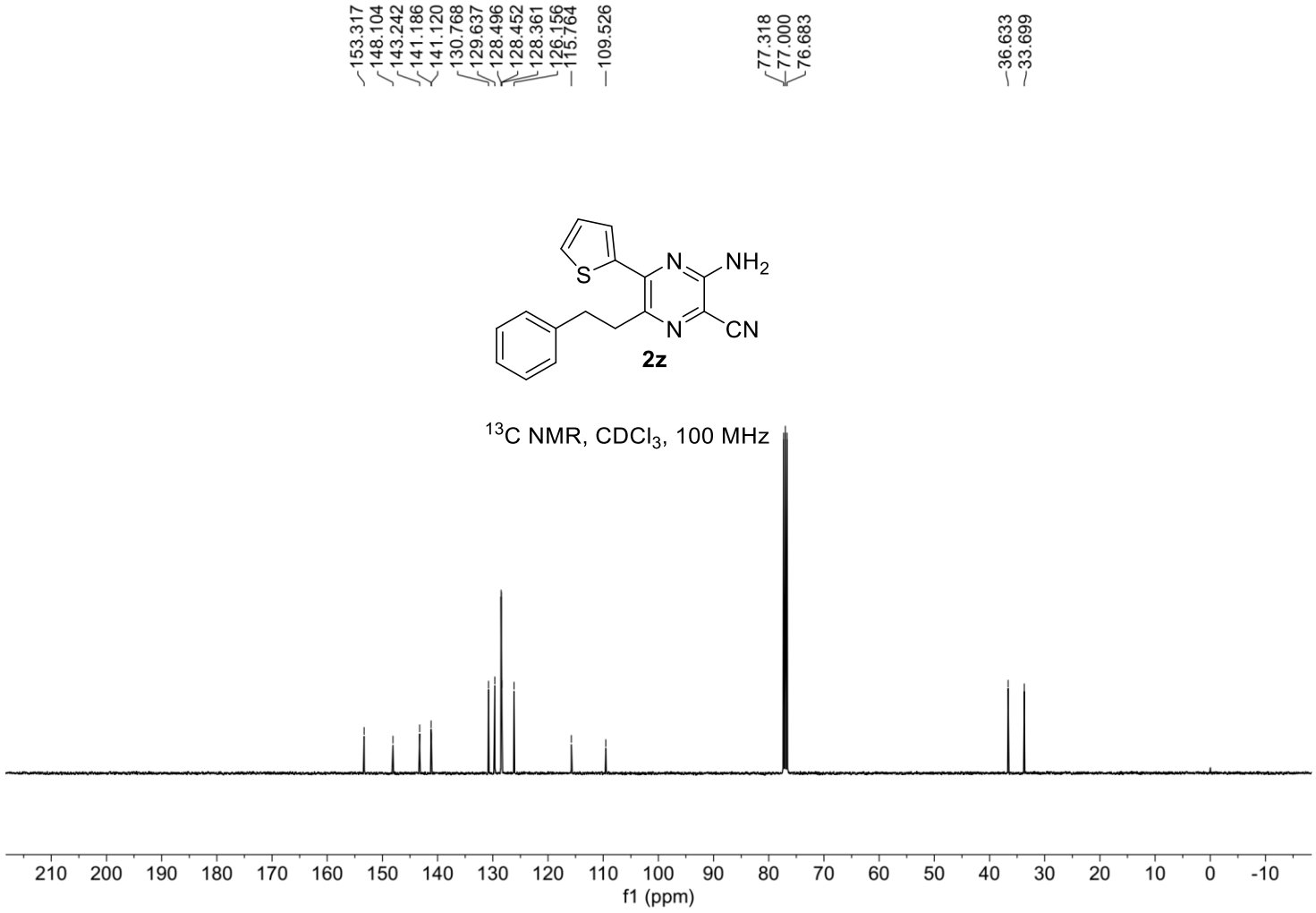

164.575
162.088
154.754
153.689
144.983
140.818
133.274
133.241
130.658
130.574
128.399
128.381
126.098
115.708
115.558
115.491
111.045
77.317
77.000
76.682
35.487
34.880
F
N
NH2
N
CN
2y
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

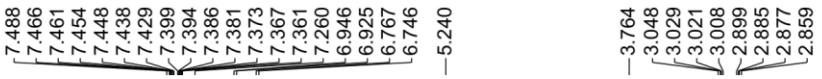


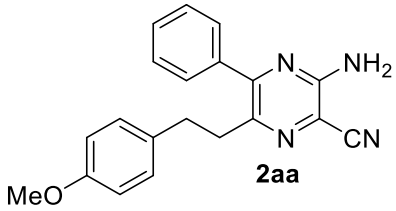
2z

^{1}H NMR, $CDCl_3$, 400 MHz



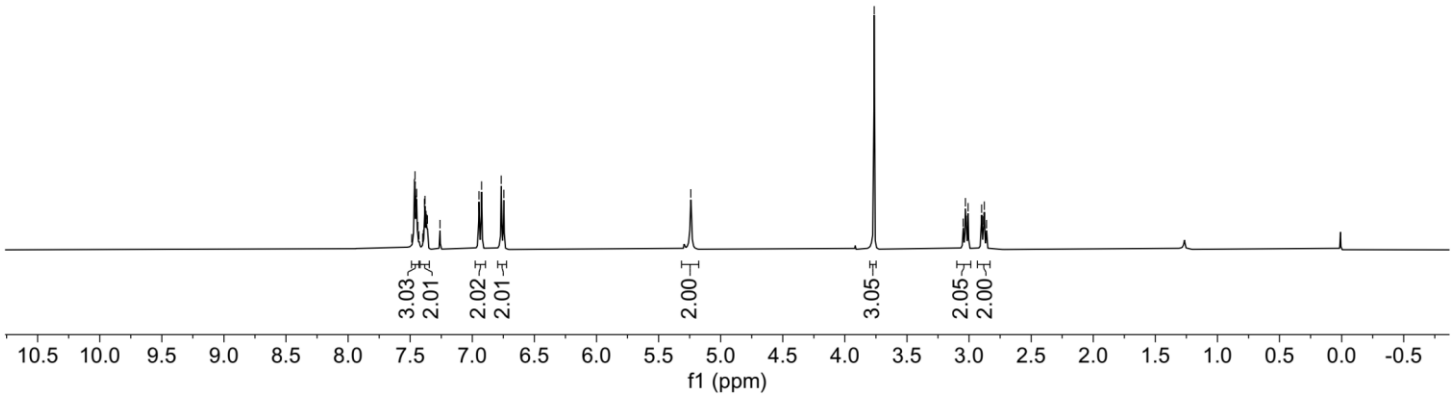

153.317
148.104
143.242
141.186
141.120
130.768
129.637
128.496
128.452
128.361
126.156
115.764
109.526
77.318
77.000
76.683
36.633
33.699
S
N
NH2
N
CN
2z
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

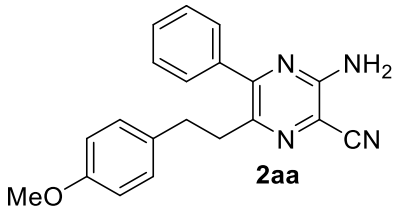




2aa

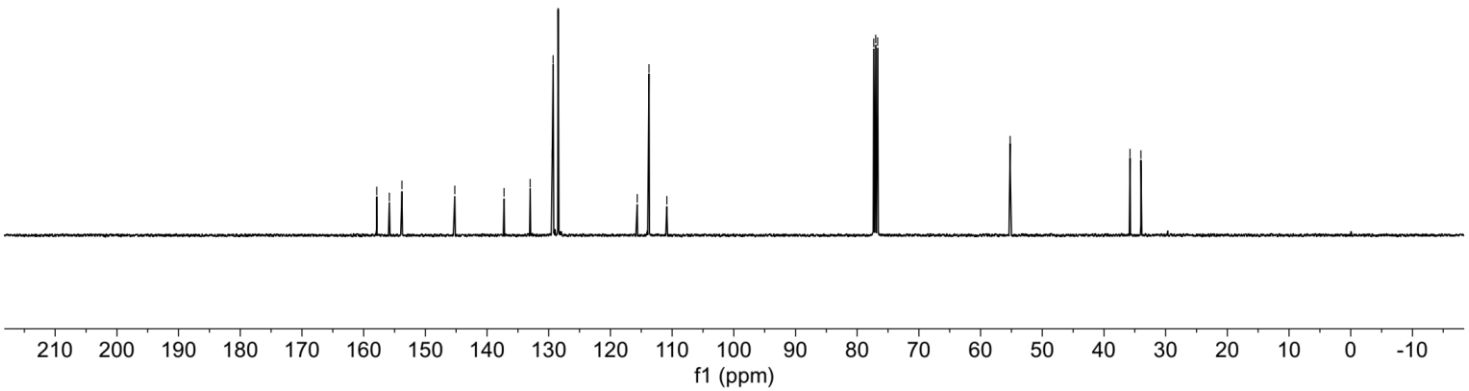
^{1}H NMR, $CDCl_3$, 400 MHz

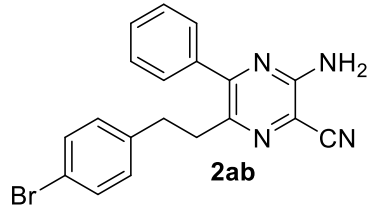




2aa

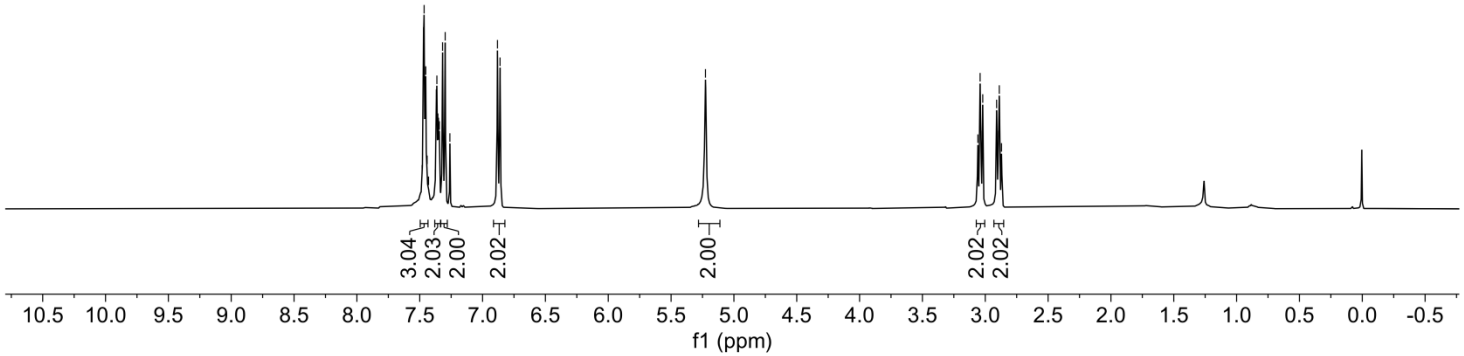
^{13}C NMR, $CDCl_3$, 100 MHz

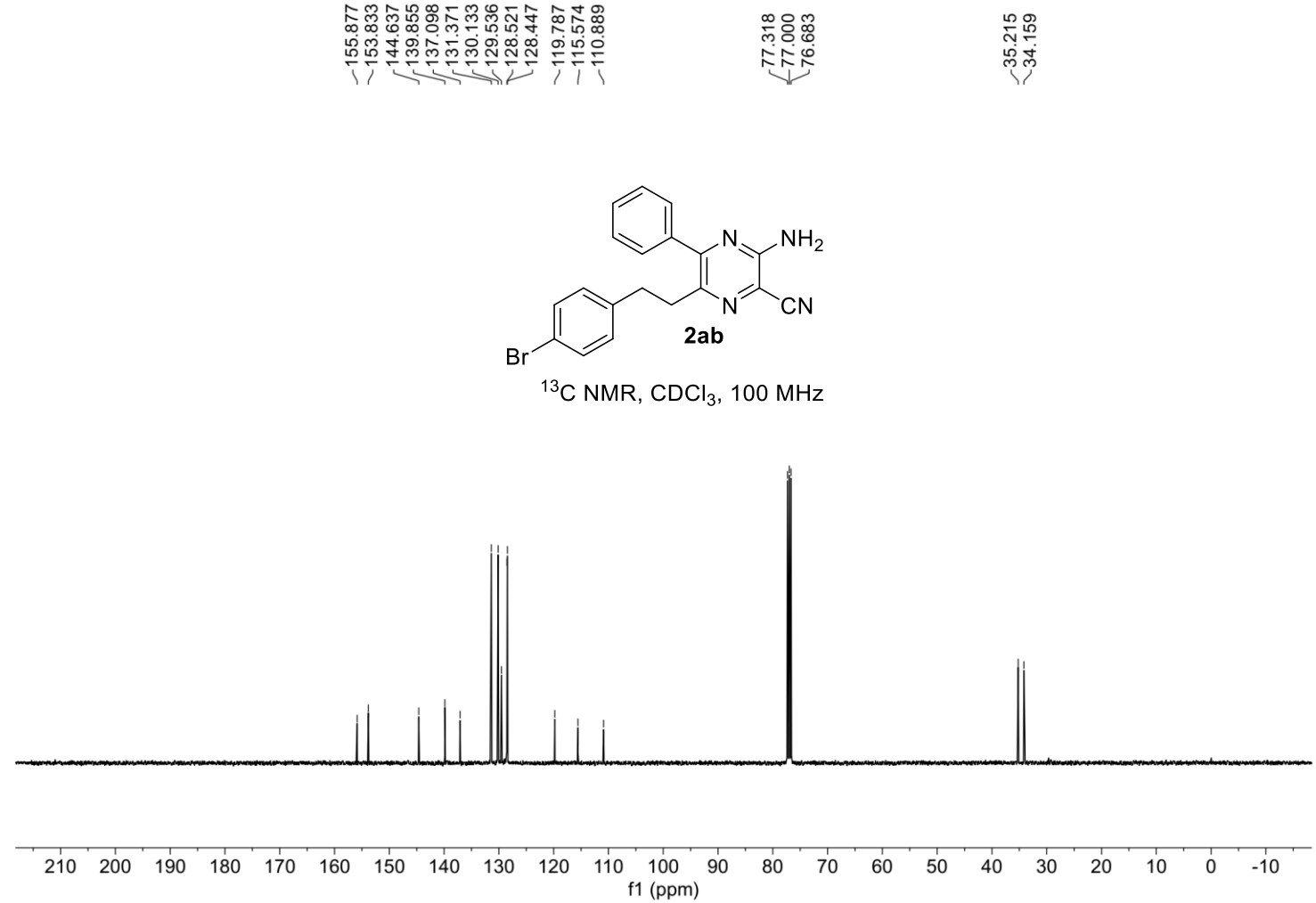


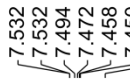


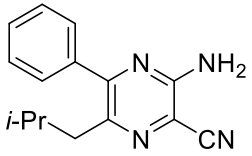
2ab

^{1}H NMR, $CDCl_3$, 400 MHz



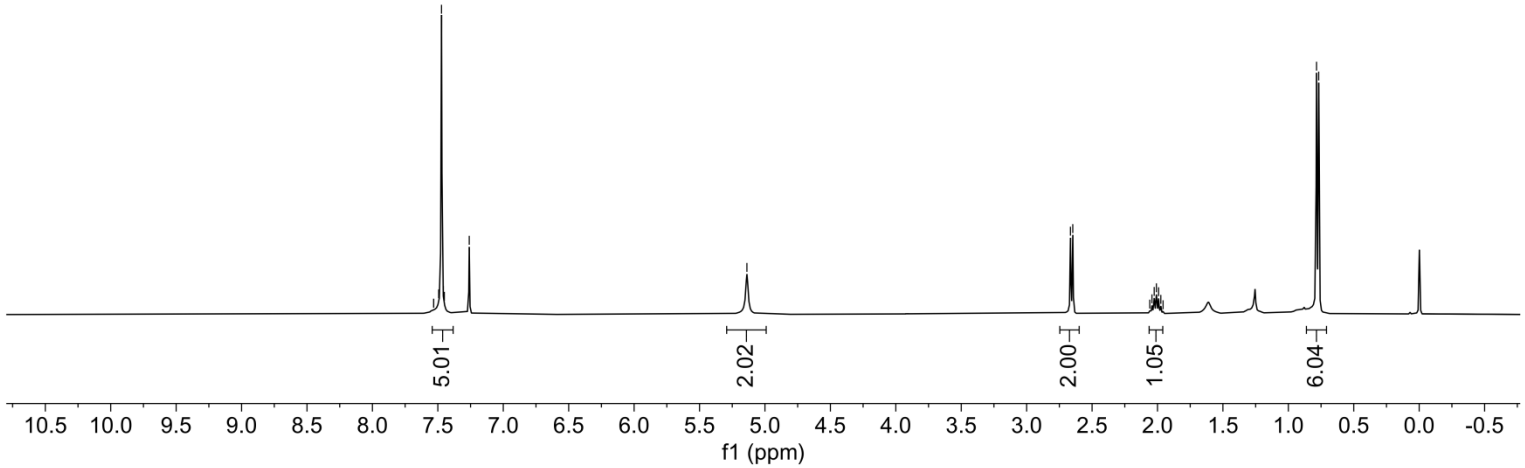

155.877
153.833
144.637
139.855
137.098
131.371
130.133
129.536
128.521
128.447
119.787
115.574
110.889
77.318
77.000
76.683
35.215
34.159
N
NH2
N
CN
Br
2ab
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

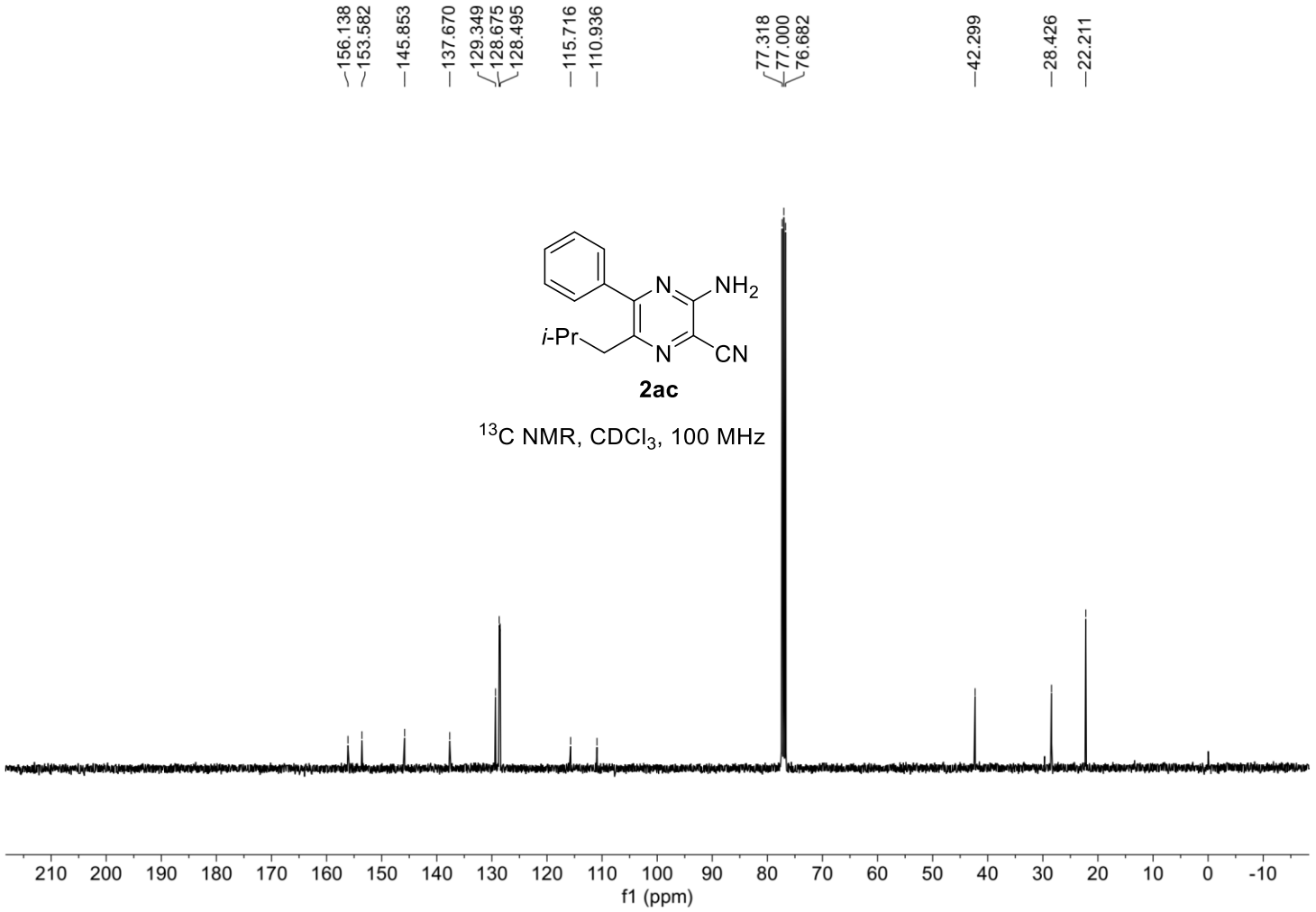


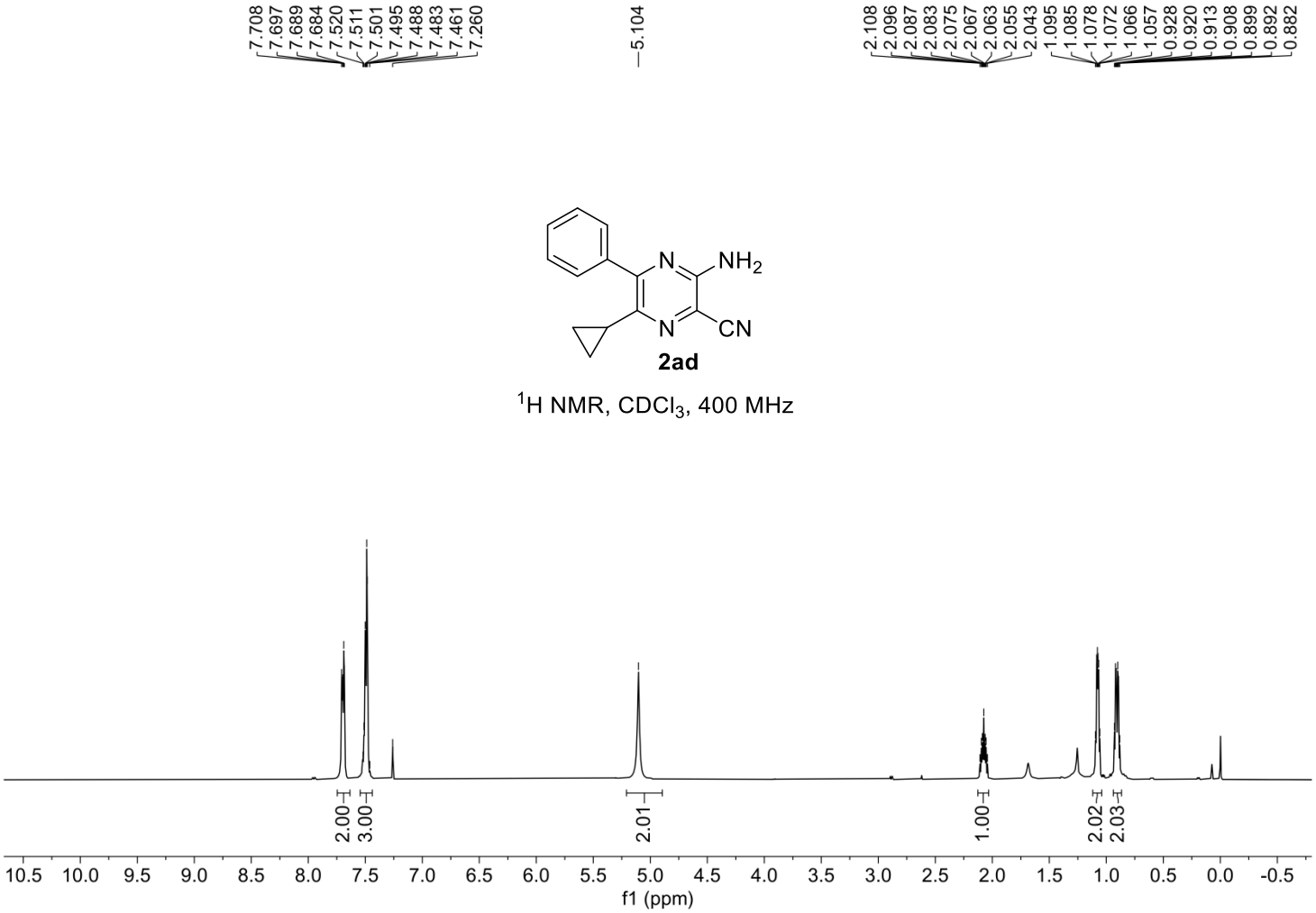


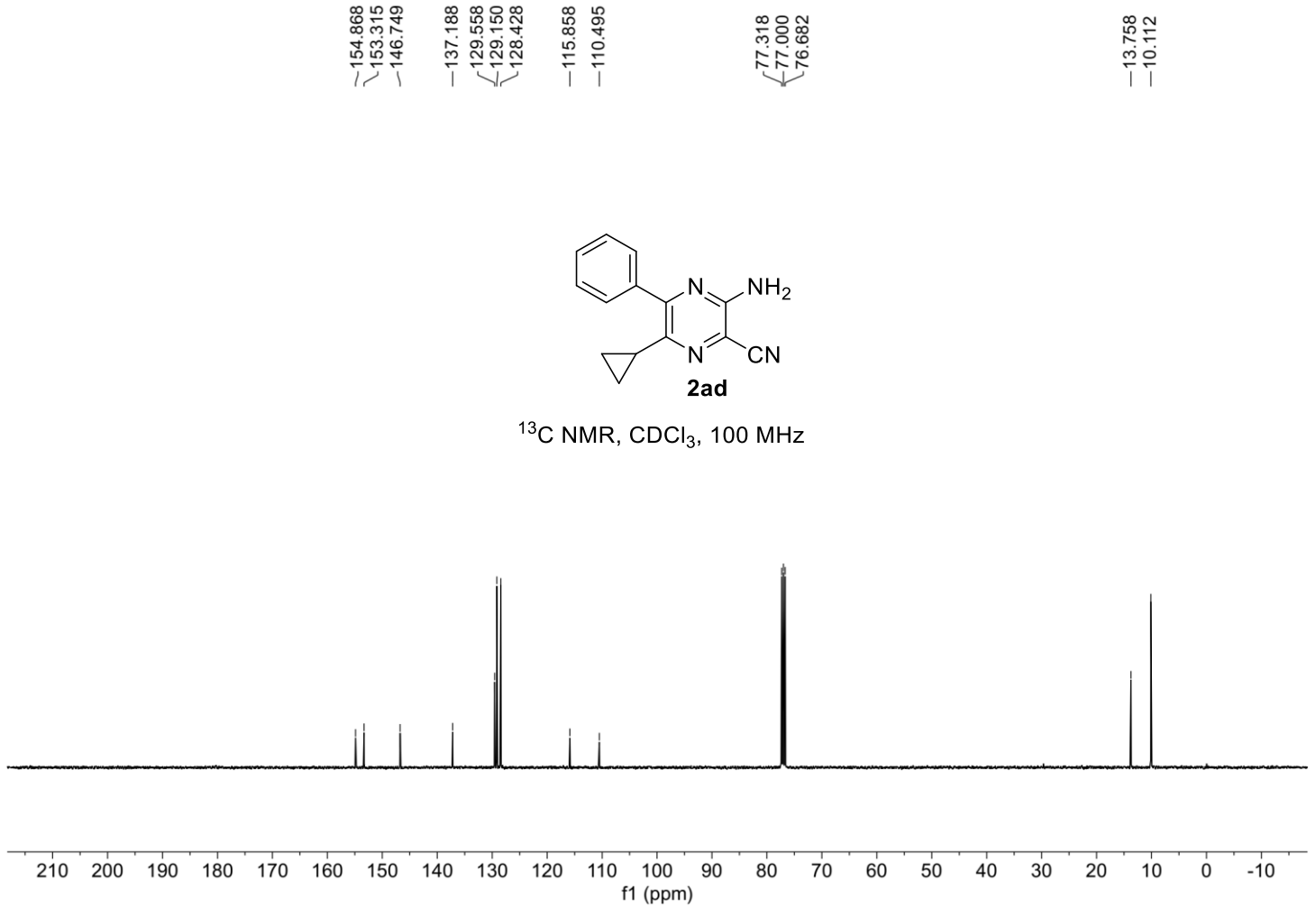
2ac

^{1}H NMR, $CDCl_3$, 400 MHz



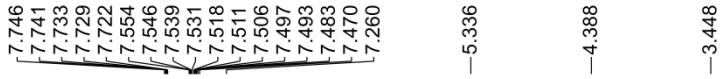

156.138
153.582
145.853
137.670
129.349
128.675
128.495
115.716
110.936
77.318
77.000
76.682
42.299
28.426
22.211
N
NH2
i-Pr
N
CN
2ac
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

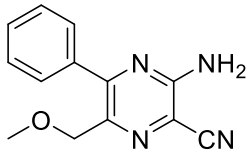

7.708
7.697
7.689
7.684
7.520
7.511
7.501
7.495
7.488
7.483
7.461
7.260
5.104
2.108
2.096
2.087
2.083
2.075
2.067
2.063
2.055
2.043
1.095
1.085
1.078
1.072
1.066
1.057
0.928
0.920
0.913
0.908
0.899
0.892
0.882
N
NH2
N
CN
2ad
1H NMR, CDCl3, 400 MHz
2.00
3.00
2.01
1.00
2.02
2.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)



2ad

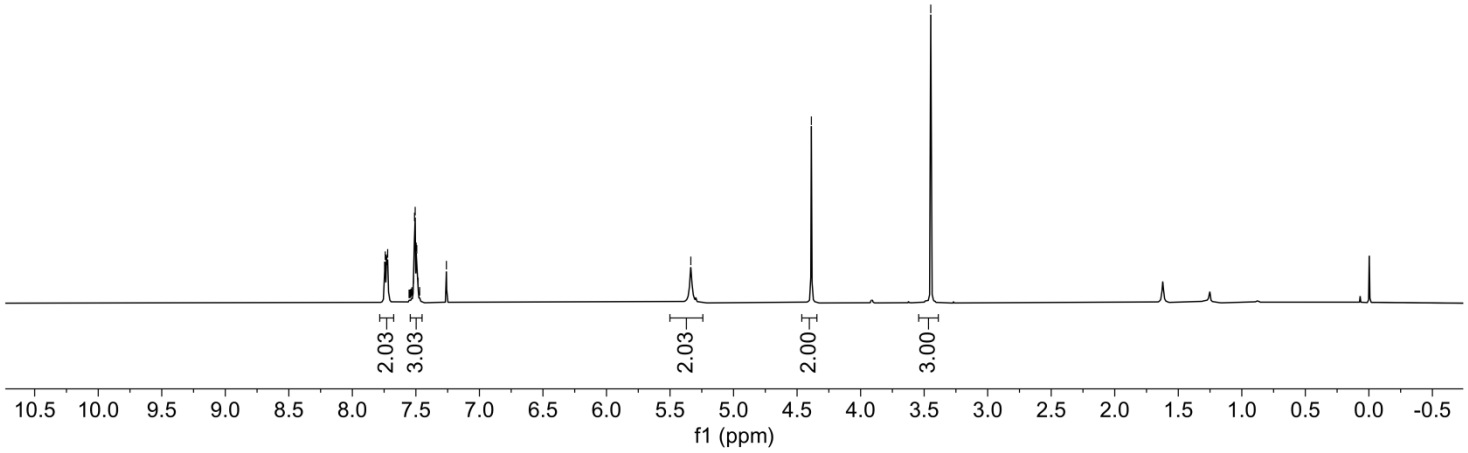
^{13}C NMR, $CDCl_3$, 100 MHz

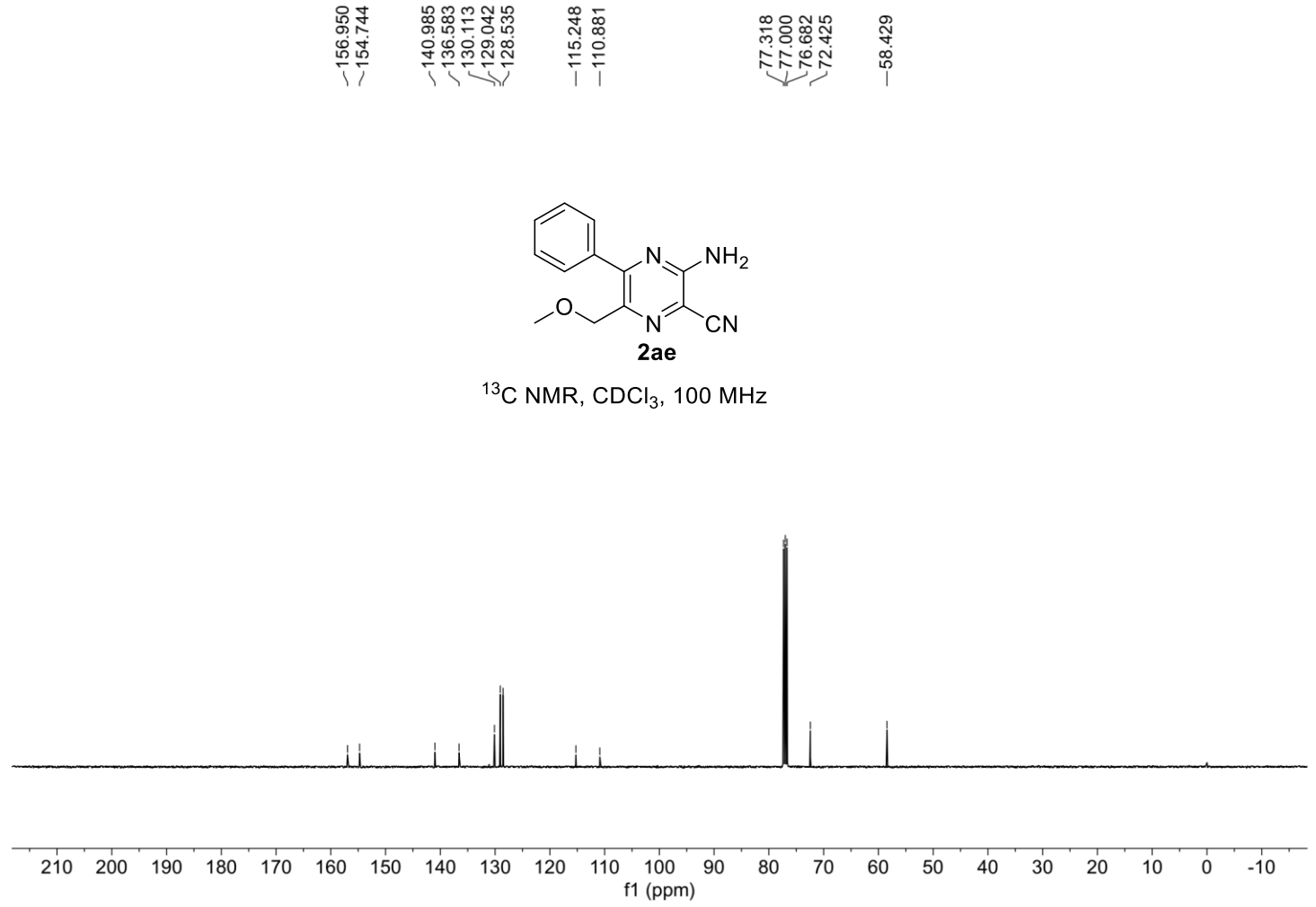


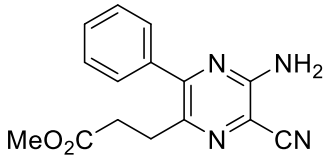


2ae

^{1}H NMR, $CDCl_3$, 400 MHz

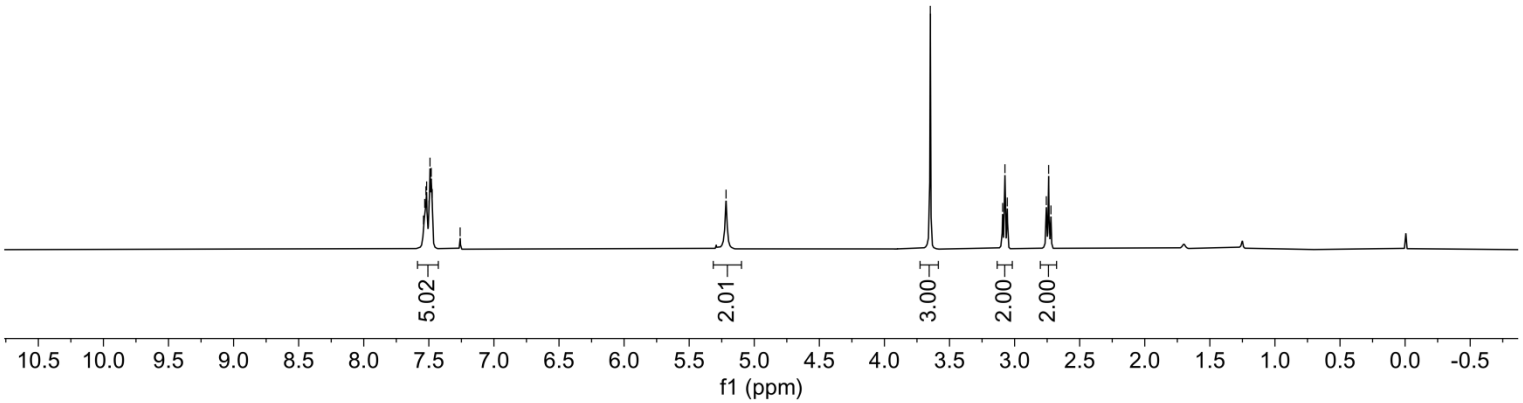


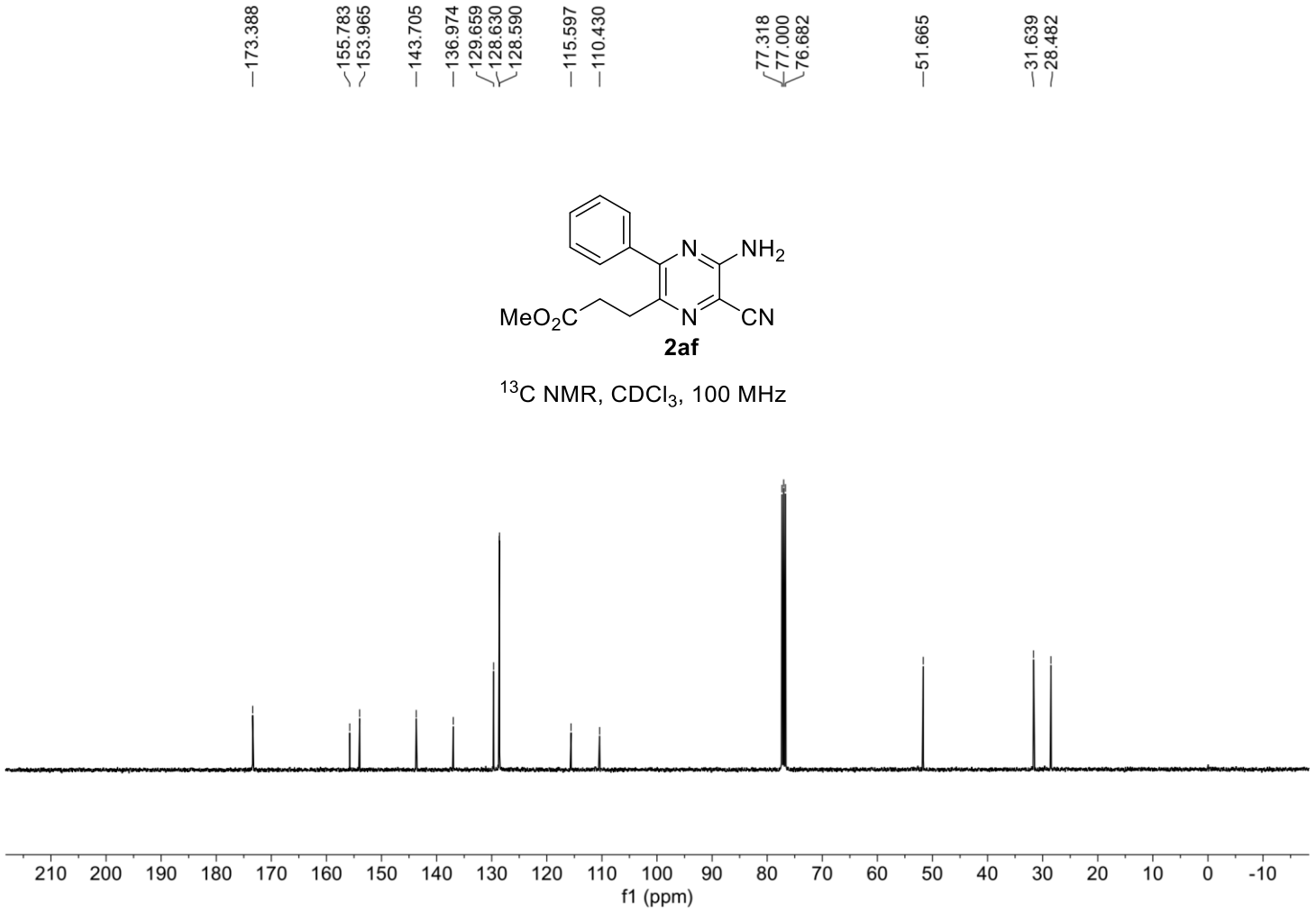

156.950
154.744
140.985
136.583
130.113
129.042
128.535
115.248
110.881
77.318
77.000
76.682
72.425
58.429
N
NH2
O
N
CN
2ae
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

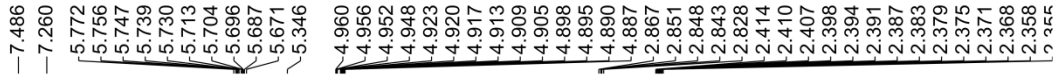


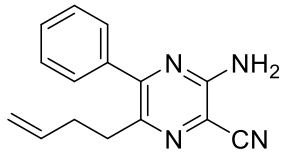
2af

^{1}H NMR, $CDCl_3$, 400 MHz



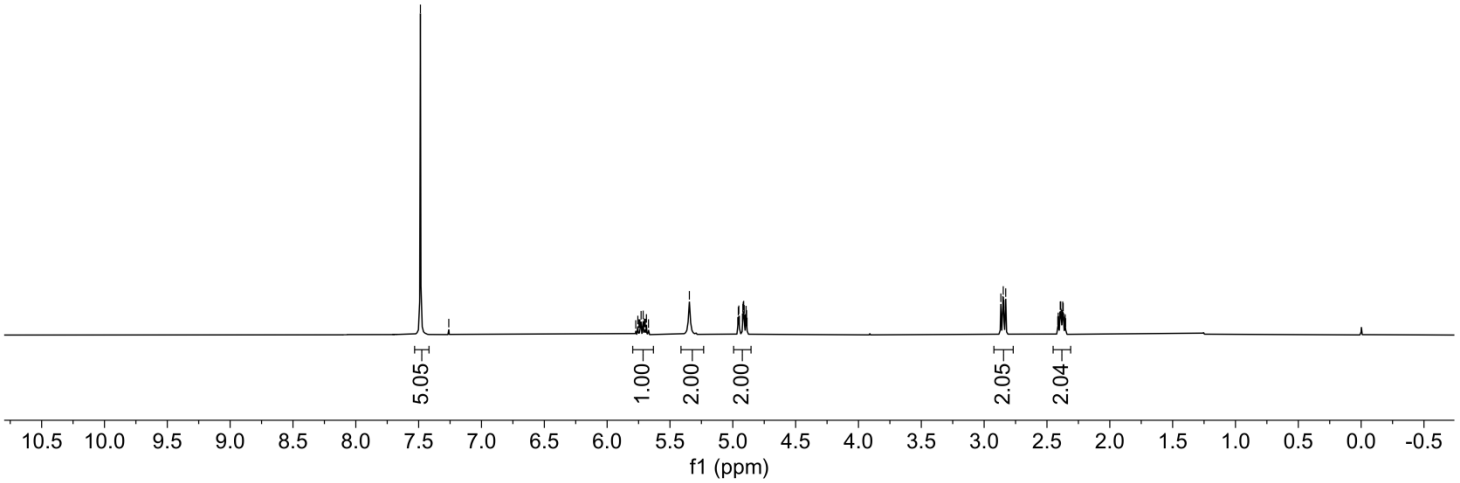

173.388
155.783
153.965
143.705
136.974
129.659
128.630
128.590
115.597
110.430
77.318
77.000
76.682
51.665
31.639
28.482
N
NH2
MeO2C
N
CN
2af
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

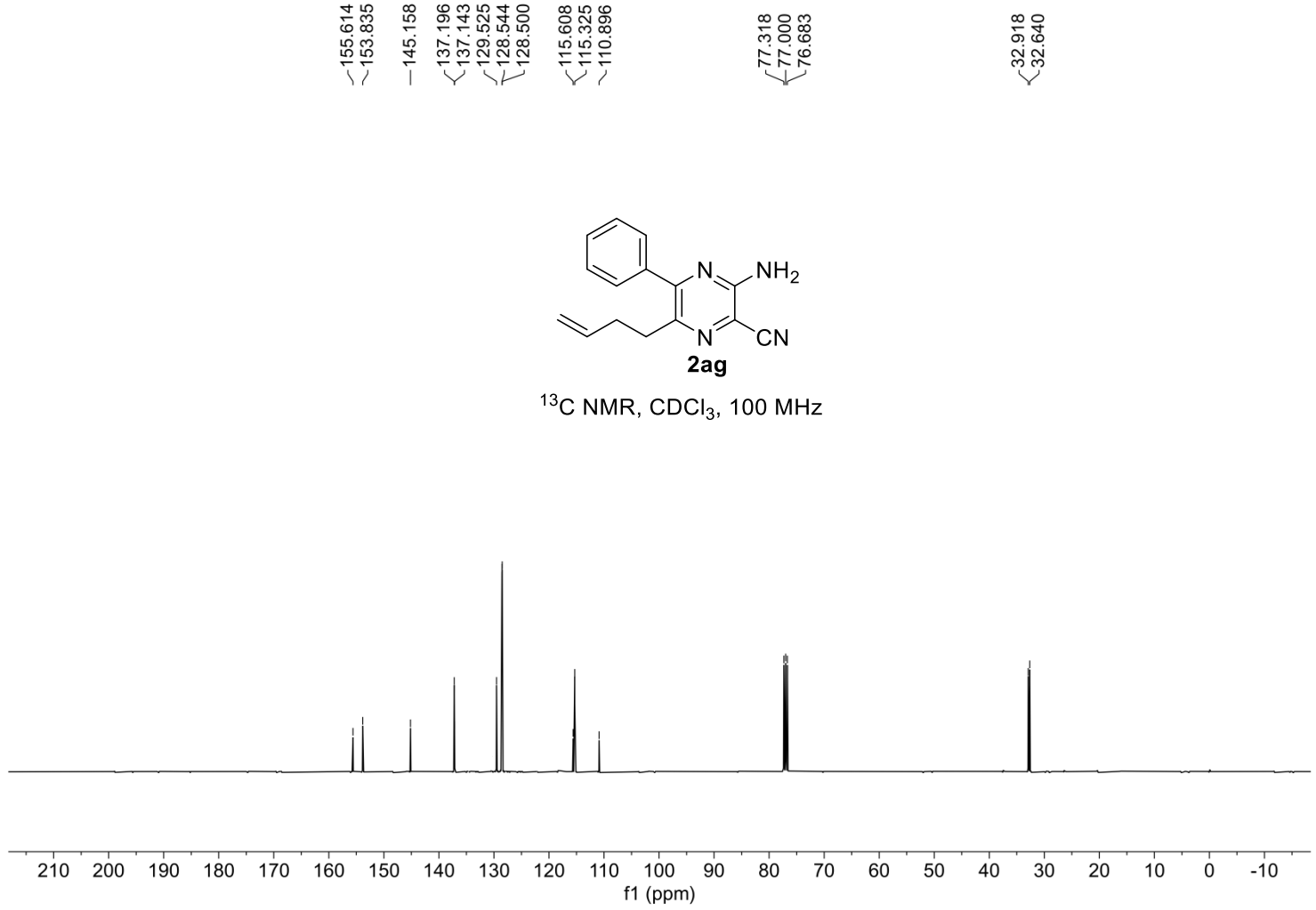


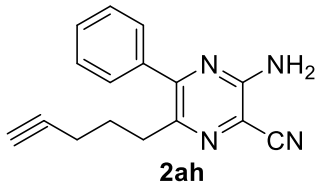


2ag

^{1}H NMR, $CDCl_3$, 400 MHz

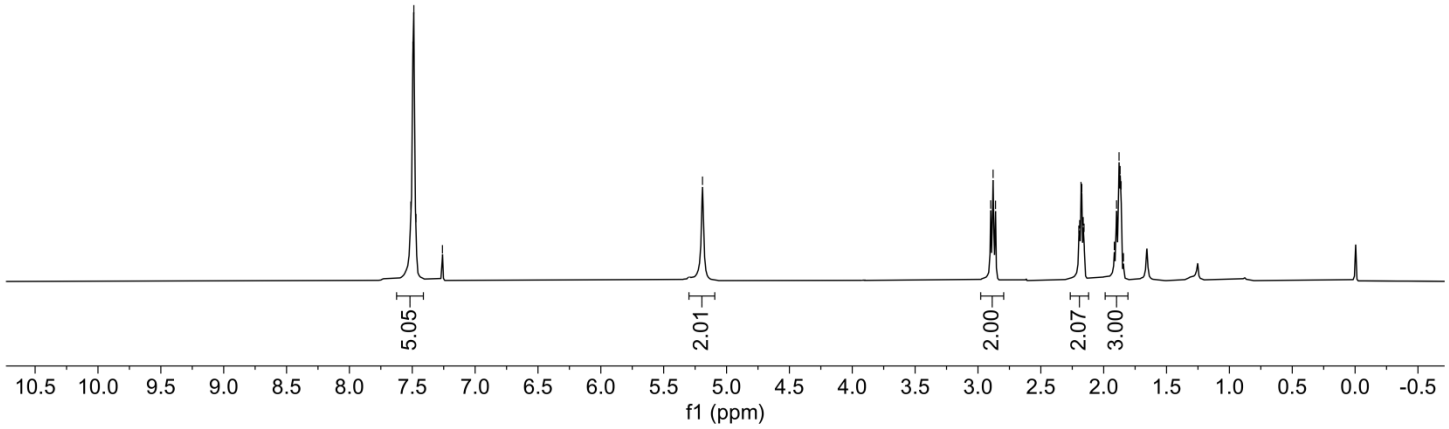


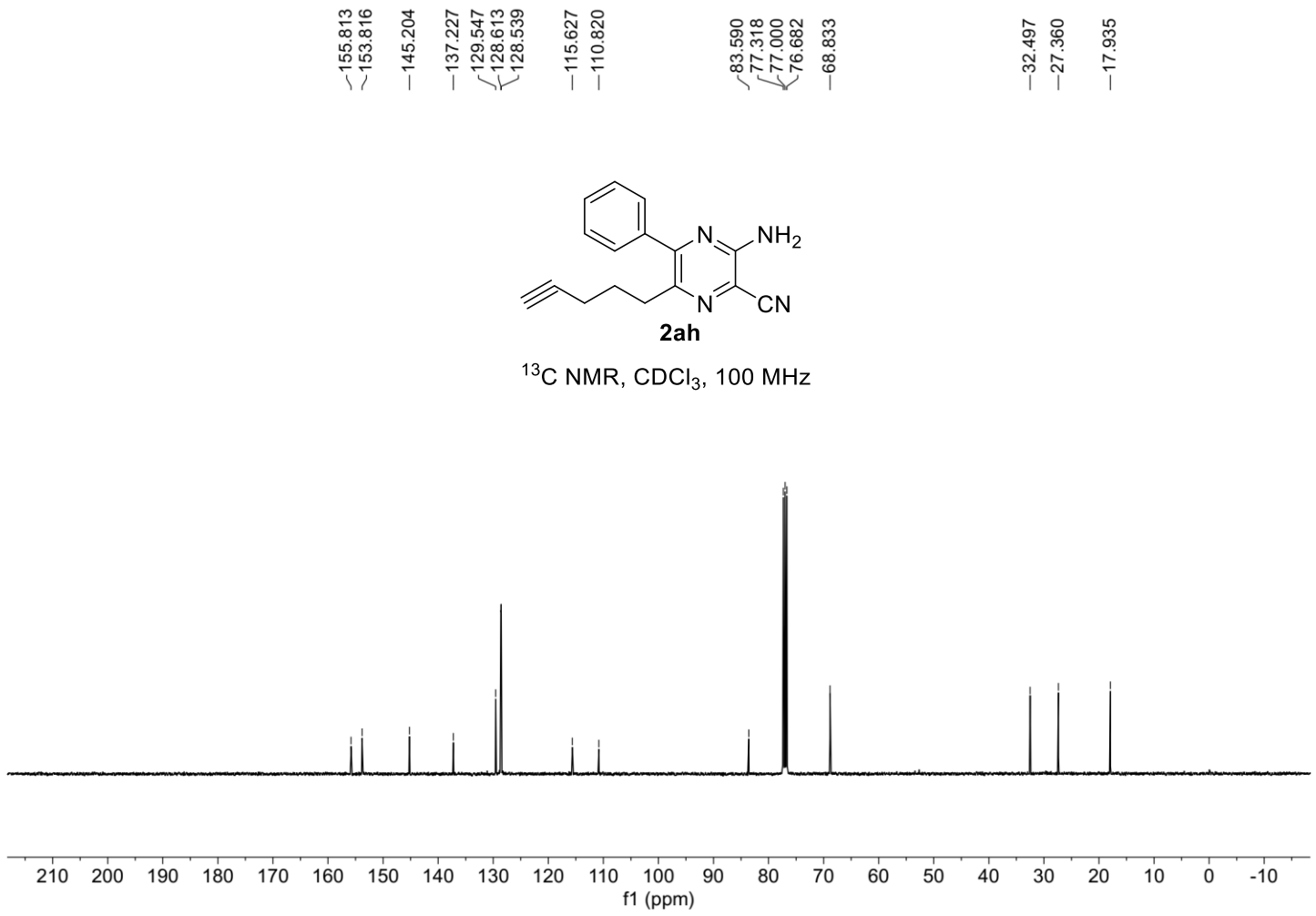

155.614
153.835
145.158
137.196
137.143
129.525
128.544
128.500
115.608
115.325
110.896
77.318
77.000
76.683
32.918
32.640
N
NH2
N
CN
2ag
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

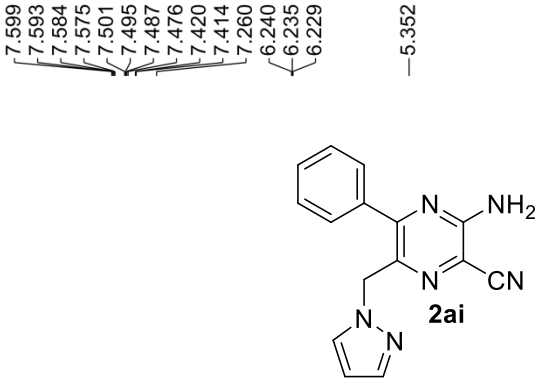


2ah

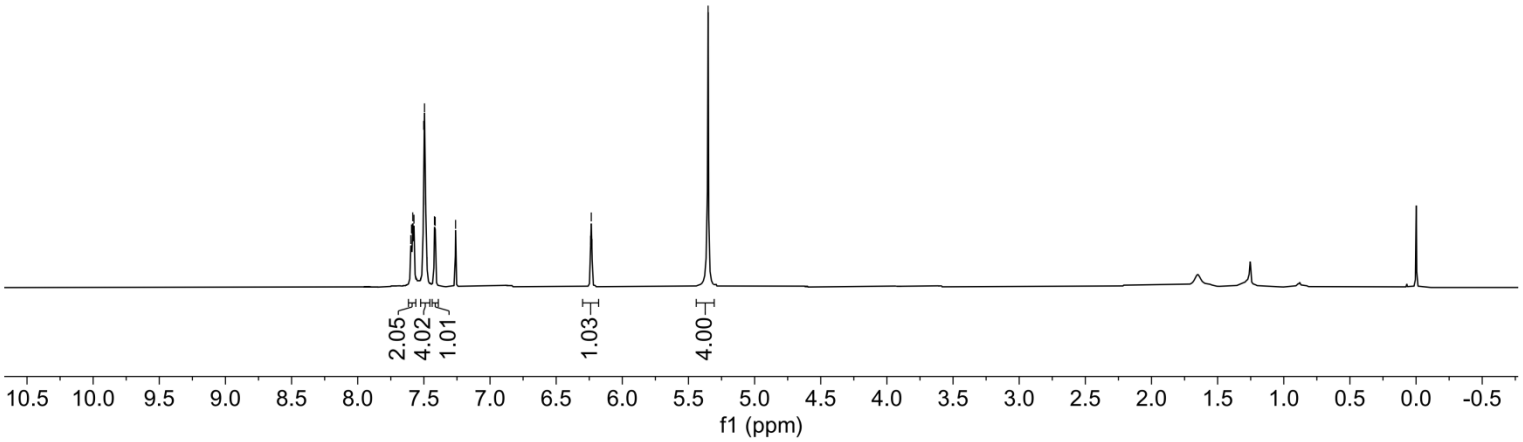
^{1}H NMR, $CDCl_3$, 400 MHz

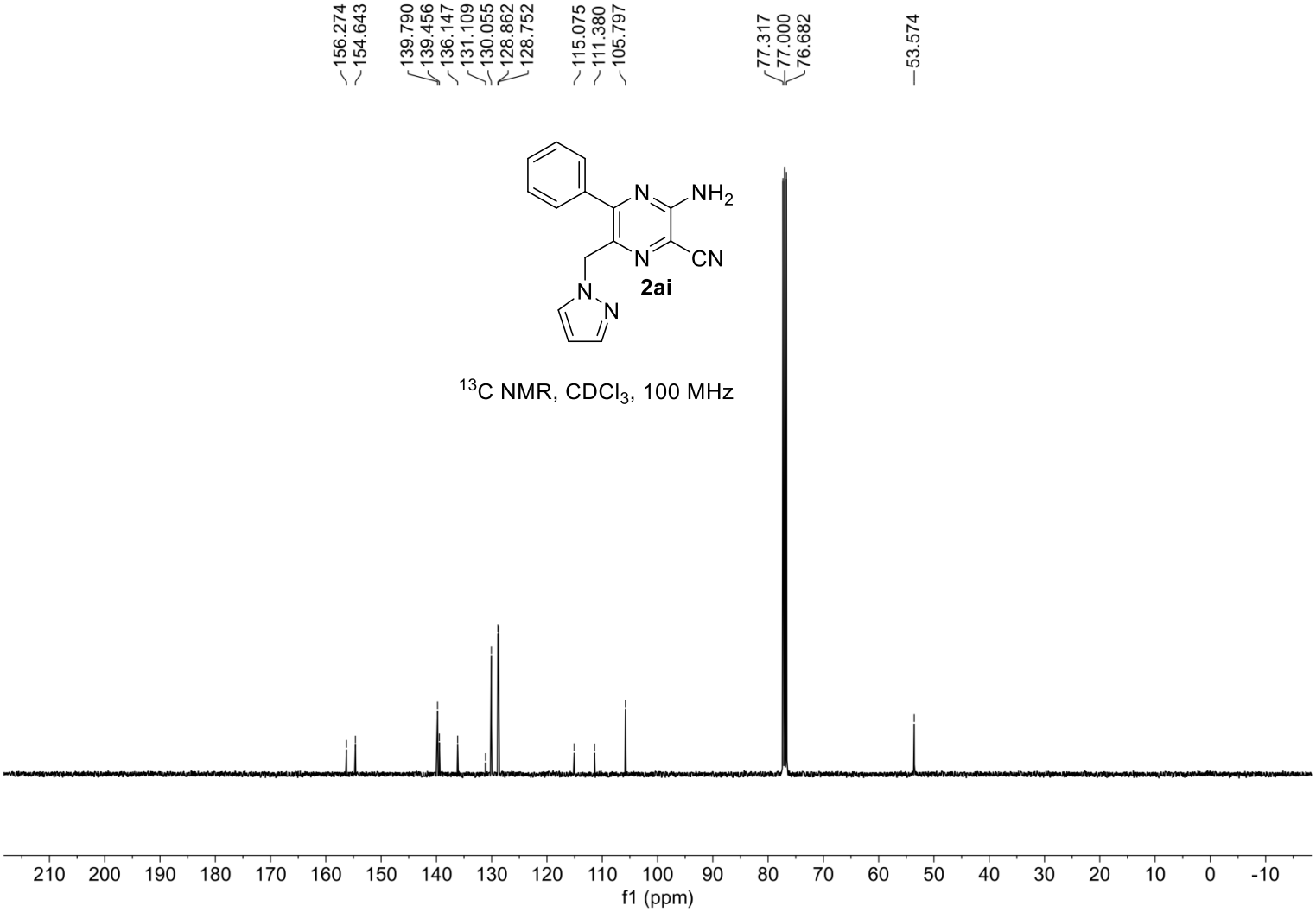


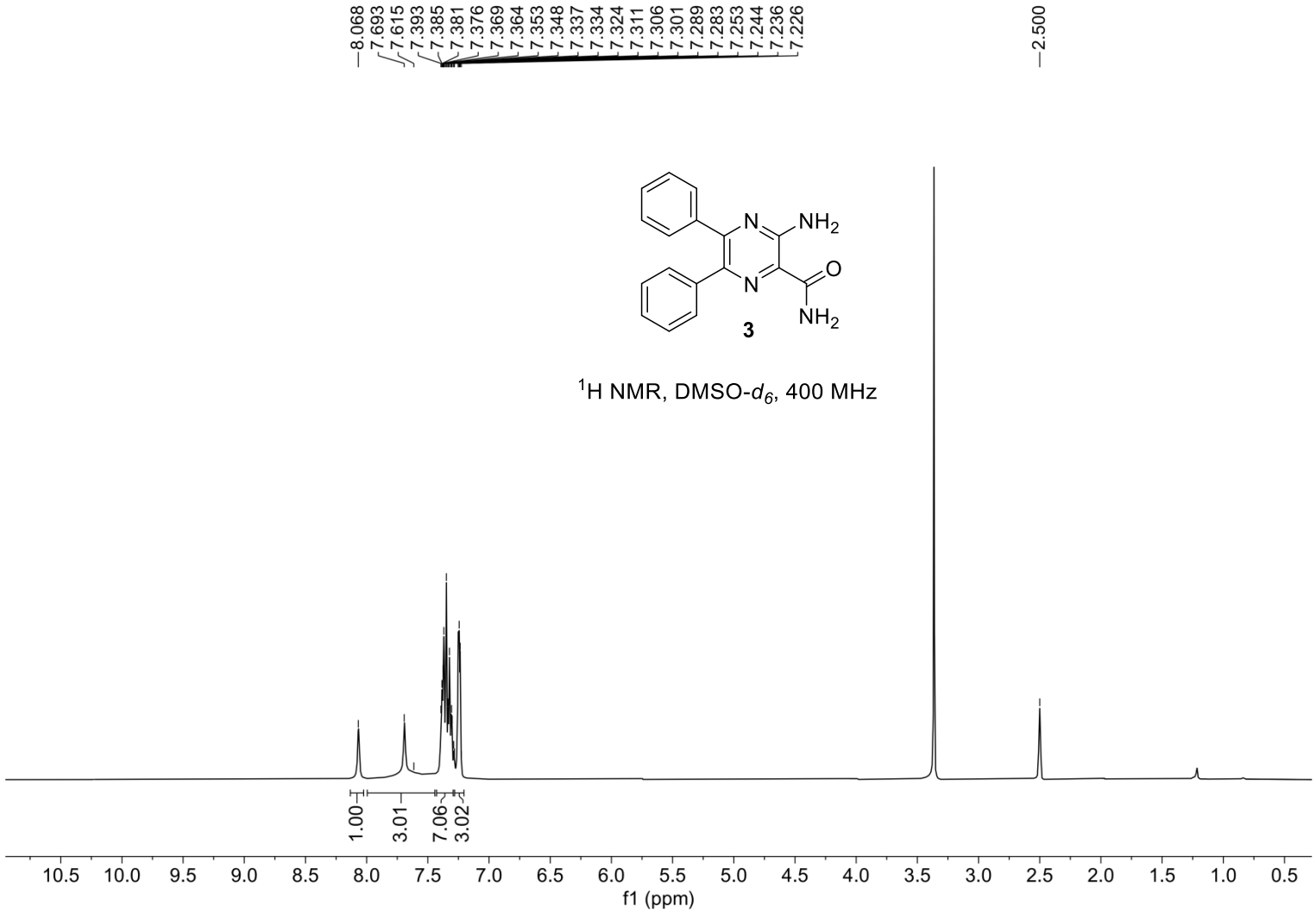

155.813
153.816
145.204
137.227
129.547
128.613
128.539
115.627
110.820
83.590
77.318
77.000
76.682
68.833
32.497
27.360
17.935
N
NH2
N
CN
2ah
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

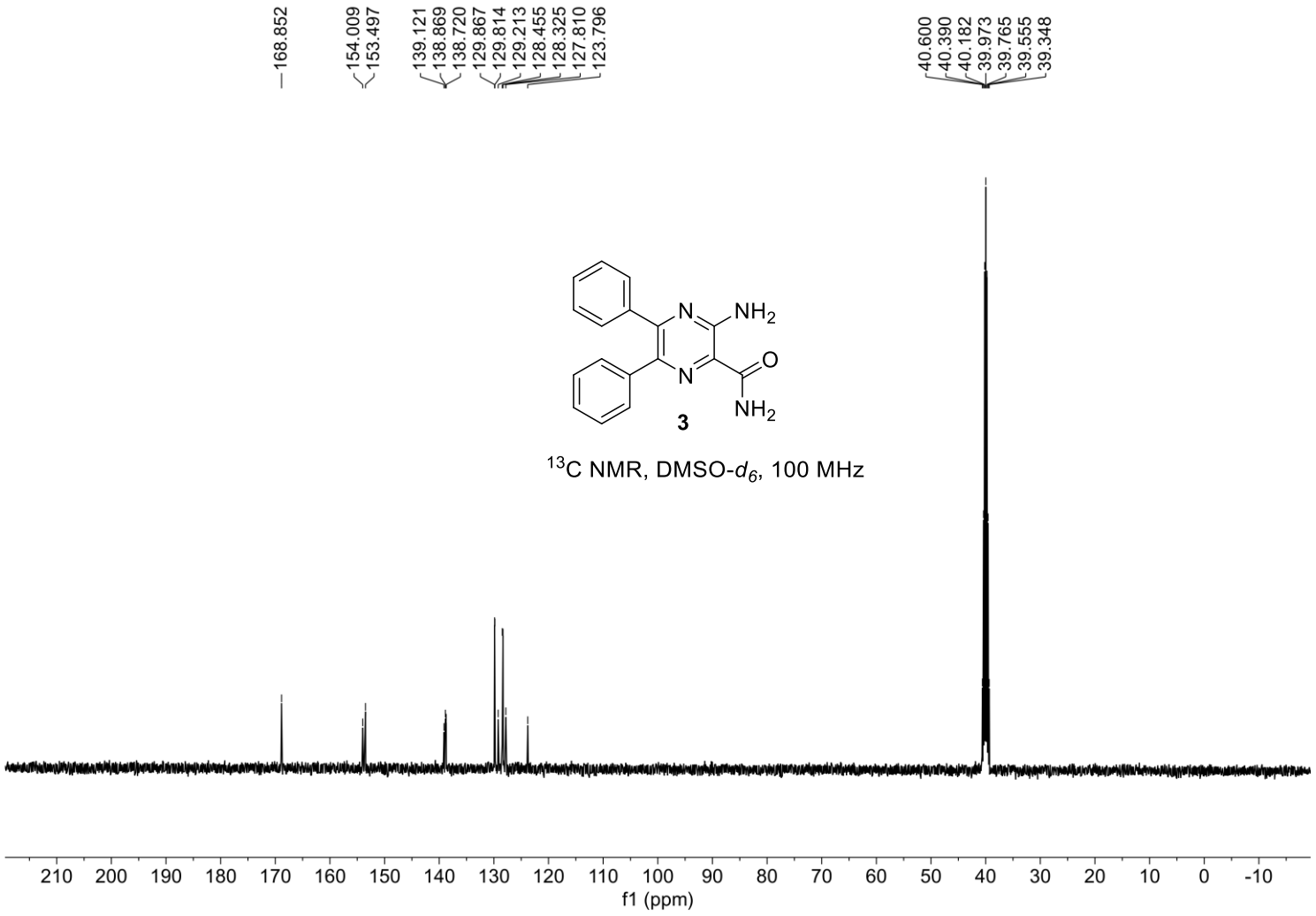


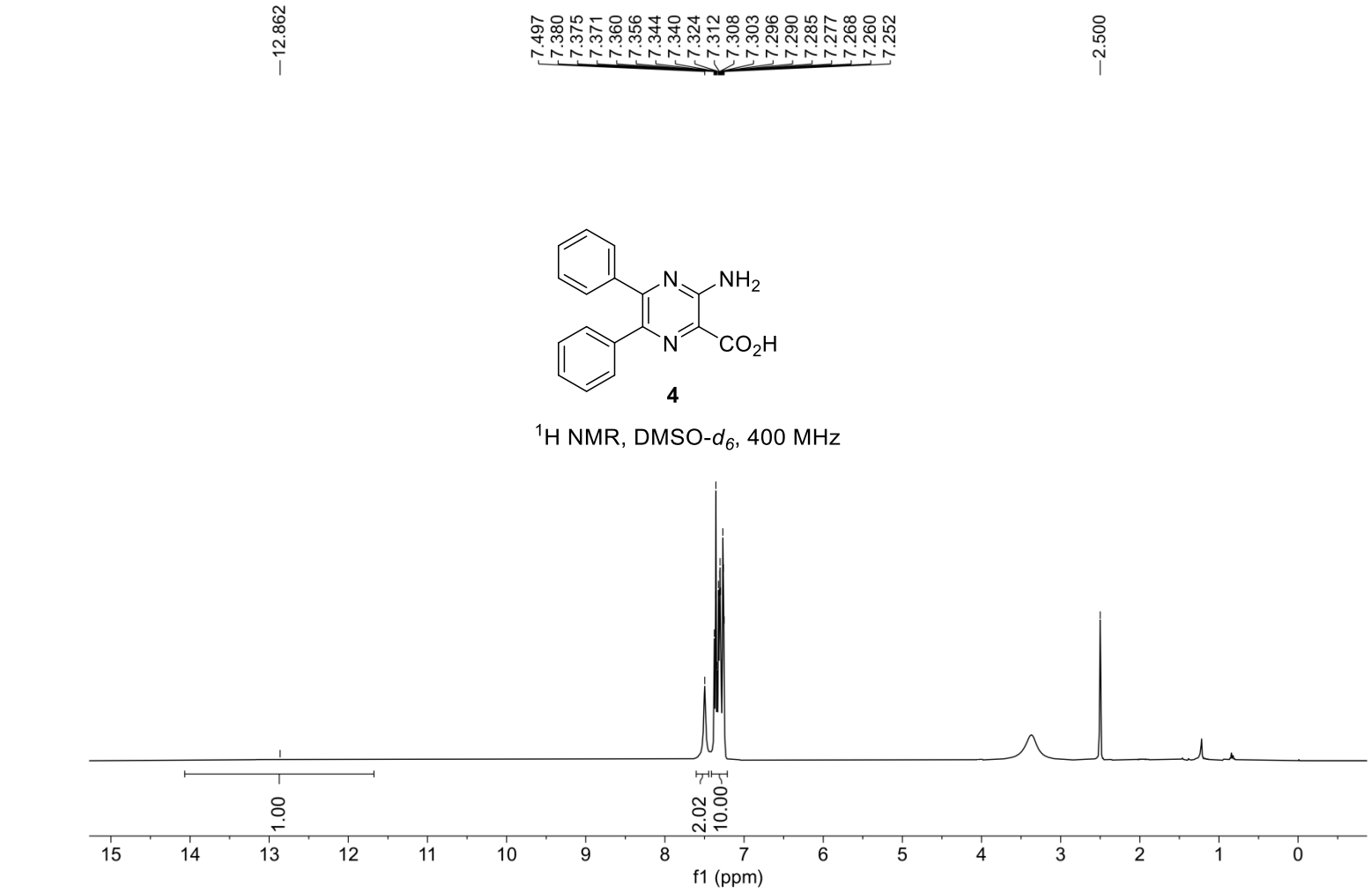
^{1}H NMR, $CDCl_3$, 400 MHz

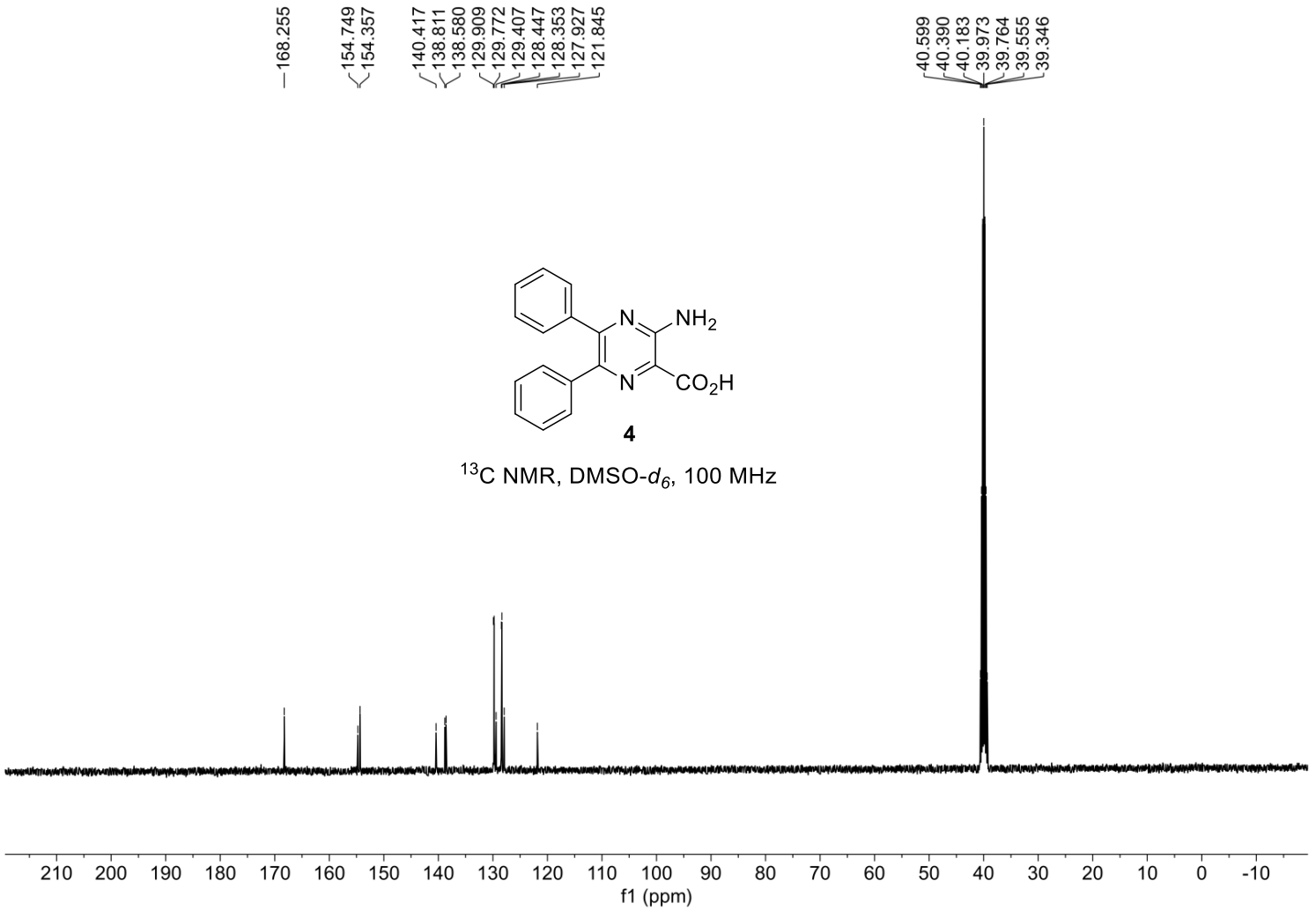


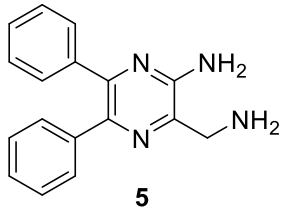

156.274
154.643
139.790
139.456
136.147
131.109
130.055
128.862
128.752
115.075
111.380
105.797
77.317
77.000
76.682
53.574
NH2
CN
2ai
13C NMR, CDCl3, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


8.068
7.693
7.615
7.393
7.385
7.381
7.376
7.369
7.364
7.353
7.348
7.337
7.334
7.324
7.311
7.306
7.301
7.289
7.283
7.253
7.244
7.236
7.226
2.500
N
NH2
O
N
NH2
3
1H NMR, DMSO-d6, 400 MHz
1.00
3.01
7.06
3.02
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


168.852
154.009
153.497
139.121
138.869
138.720
129.867
129.814
129.213
128.455
128.325
127.810
123.796
40.600
40.390
40.182
39.973
39.765
39.555
39.348
N
NH2
O
N
NH2
3
13C NMR, DMSO-d6, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

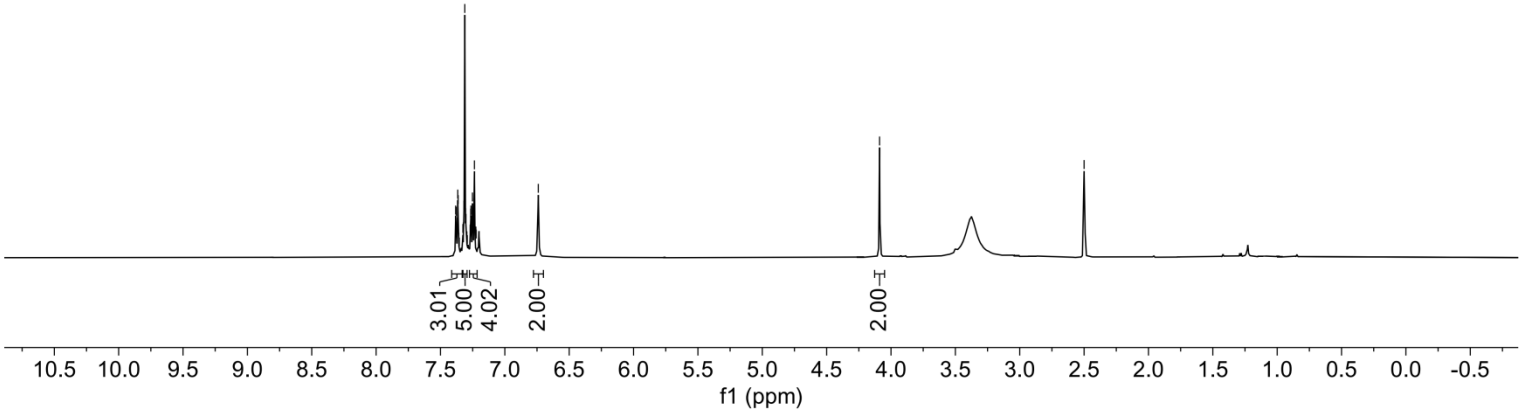

12.862
7.497
7.380
7.375
7.371
7.360
7.356
7.344
7.340
7.324
7.312
7.308
7.303
7.296
7.290
7.285
7.277
7.268
7.260
7.252
2.500
N
NH2
N
CO2H
4
1H NMR, DMSO-d6, 400 MHz
1.00
2.02
10.00
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
f1 (ppm)

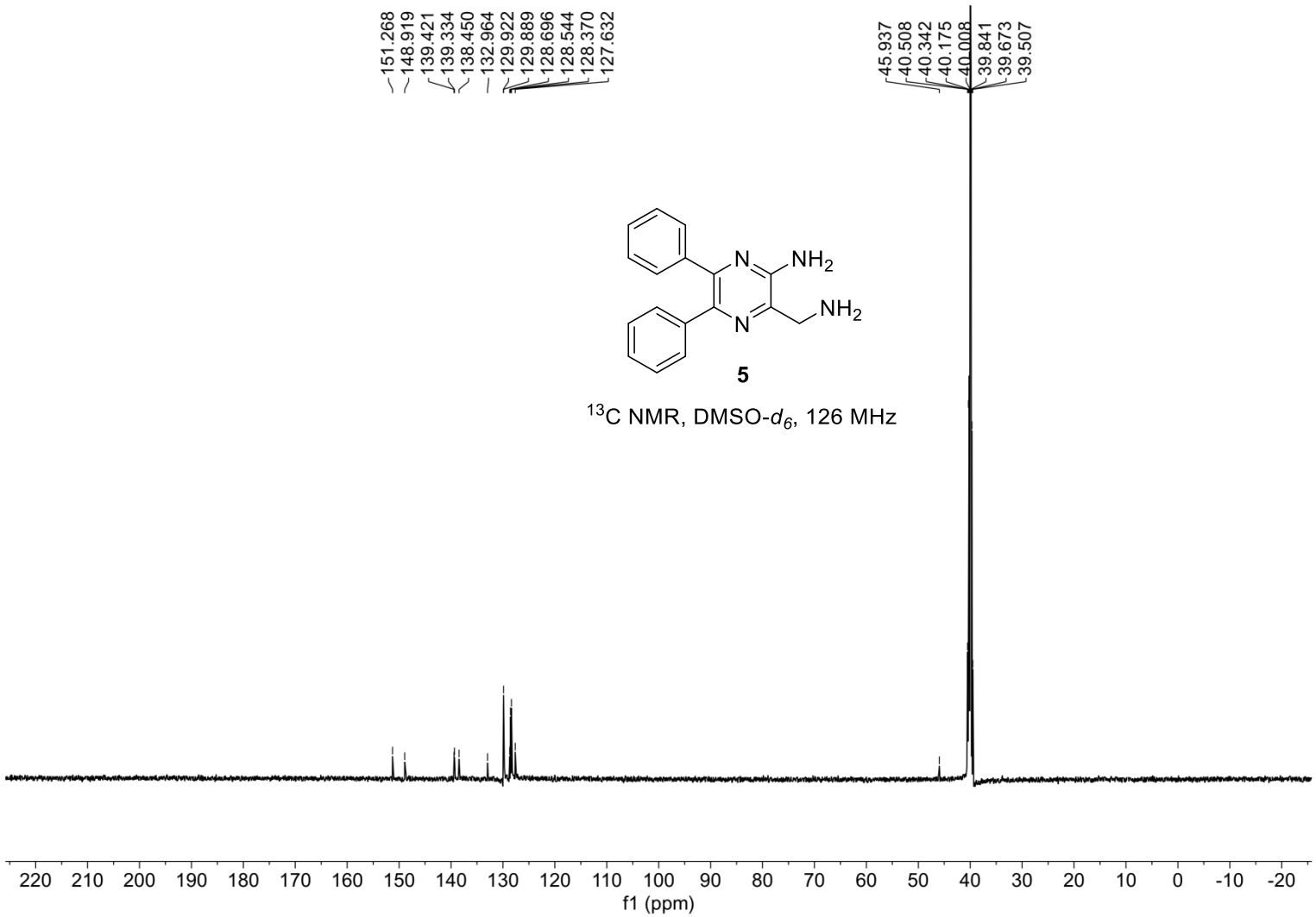

168.255
154.749
154.357
140.417
138.811
138.580
129.909
129.772
129.407
128.447
128.353
127.927
121.845
40.599
40.390
40.183
39.973
39.764
39.555
39.346
N
NH2
N
CO2H
4
13C NMR, DMSO-d6, 100 MHz
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

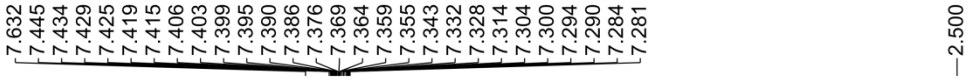


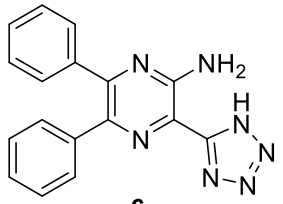
5

^{1}H NMR, DMSO-d_6, 500 MHz



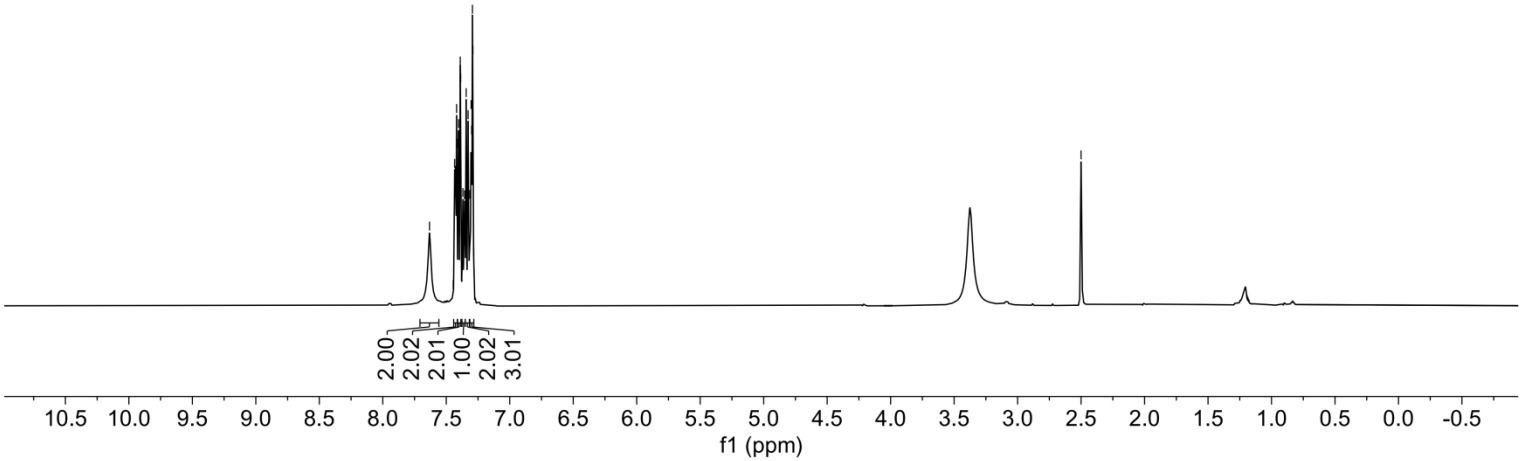

151.268
148.919
139.421
139.334
138.450
132.964
129.922
129.889
128.696
128.544
128.370
127.632
45.937
40.508
40.342
40.175
40.008
39.841
39.673
39.507
N
NH2
NH2
N
5
13C NMR, DMSO-d6, 126 MHz
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)

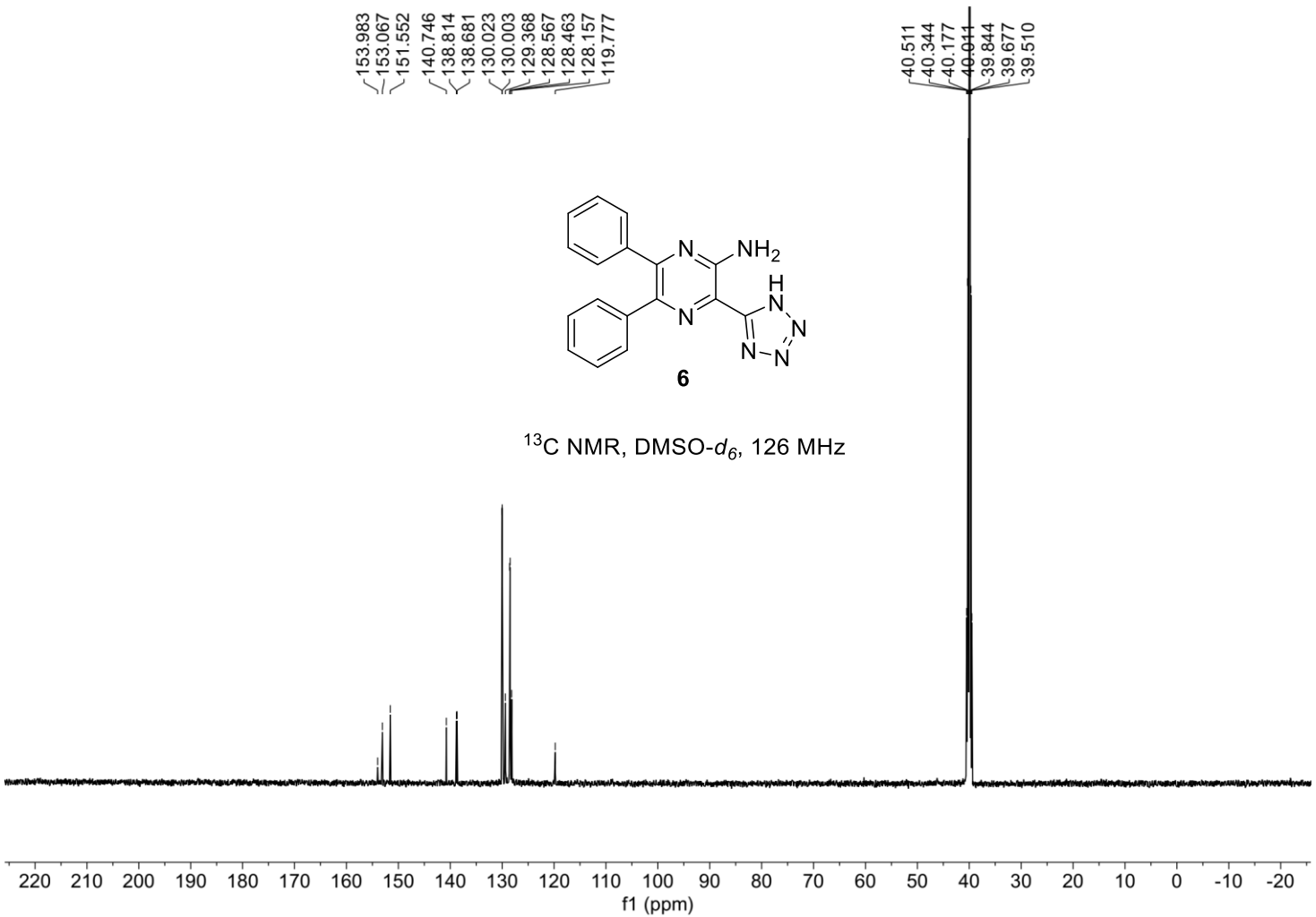




6

^{1}H NMR, DMSO-d_6, 500 MHz




153.983
153.067
151.552
140.746
138.814
138.681
130.023
130.003
129.368
128.567
128.463
128.157
119.777
40.511
40.344
40.177
40.011
39.844
39.677
39.510
NH2
H
N
N
N
N
N
6
13C NMR, DMSO-d6, 126 MHz
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20
f1 (ppm)