

Modular, Concise and Efficient Synthesis of Highly Functionalized 5-Fluoropyridazines by a [2+1]/[3+2]-Cycloaddition Sequence

*Gaël Tran,^a Domingo Gomez Pardo^a, Tomoki Tsuchiya,^b Stefan Hillebrand,^b Jean-Pierre
Vors,^b and Janine Cossy^{*a}*

^a Laboratoire de Chimie Organique, Institute of Chemistry, Biology and Innovation (CBI),
ESPCI ParisTech, UMR 8231, PSL Research University

10 rue Vauquelin, 75231 Paris Cedex 05, France

janine.cossy@espci.fr

^b Bayer S.A.S.-CRLD,

14, impasse Pierre Baizet, CS 99163, 69263 Lyon Cedex 09, France

Supporting Information

Table of Content

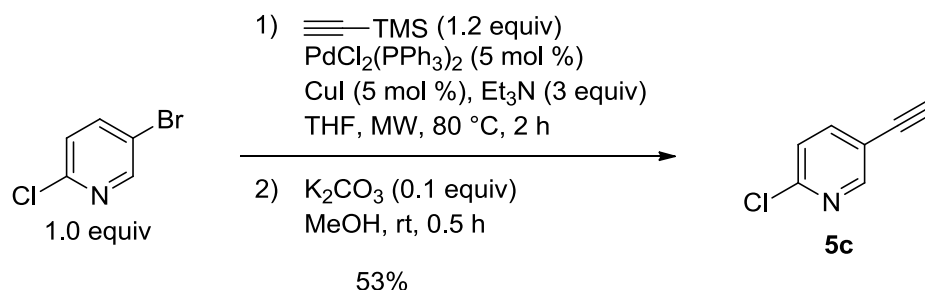
1. General Experimental
2. Experimental Procedures and Spectroscopic Data for Starting Materials **5c**, **5d**, **5e**, **5f**, **5j**, **5l** and **5m**
3. Experimental Procedures and Spectroscopic Data for products **4** and **6**
4. Experimental Procedures and Spectroscopic Data for products **7**, **8** and **9**
3. Experimental Spectra (^1H , ^{13}C)

1. General Experimental

All reactions were carried out under an argon atmosphere unless otherwise specified. Flasks were oven-dried at 120 °C and cooled down under argon prior to use. THF was distilled over sodium/benzophenone. Et₃N, TMEDA, CH₂Cl₂ and diglyme were distilled over CaH₂. NaI and NaF were dried at 120 °C for 24 h and cooled down under vacuum. ZnCl₂ was flame-dried prior to use. Allyl bromide was washed with an aqueous saturated NaHCO₃ solution, then with distilled water, dried over CaCl₂, then fractionally distilled over CaCl₂. Benzoyl chloride was dried and distilled over CaCl₂. Cyclopropylcarboxaldehyde was distilled prior to use. Pyridine, DMF, MeCN and DMSO were bought dry from Aldrich and used as received. All others reagents were used as obtained from Aldrich without further purification unless otherwise specified. Flash column chromatographies were carried out by using silica gel (pore size 60 Å, 230 mesh). TLC were performed on silica gel plate (Merck 60F254) and visualized either with a UV lamp (254 nm) or by treatment with an aqueous potassium permanganate solution (KMnO₄/K₂CO₃/AcOH) and subsequent heating. Melting points (Mp) were recorded using a Wagner & Munz Kofler bench. Infrared (IR) spectra were recorded on a Bruker TENSOR™ 27 (IRFT), wave numbers are indicated in cm⁻¹. ¹H-NMR spectra were recorded on a Bruker Avance 400 at 400 MHz. The chemical shifts δ are reported in ppm relative to tetramethylsilane. Residual CHCl₃ ($\delta_{\text{H}} = 7.26$ ppm) was used as internal reference unless otherwise specified. The multiplicity and shape of signals are designated by the following abbreviations: s singlet, d doublet, t triplet, q quartet, hept heptuplet, m multiplet, br broad. Coupling constants J are reported in Hertz (Hz). ¹³C-NMR Spectra were recorded on a Bruker Avance 400 at 100 MHz. The chemical shifts δ are reported in ppm relative to tetramethylsilane. CDCl₃ ($\delta_{\text{C}} = 77.16$ ppm, triplet) was used as internal reference unless otherwise specified. The multiplicity and shape of signals are designated by the following abbreviations: d doublet, q quartet, m multiplet. Coupling constants J are reported in Hertz (Hz). High resolution mass spectra (HRMS) were realized at the organic spectrochemistry center at the Université Pierre et Marie Curie, Paris (France).

2. Experimental Procedures and Spectroscopic Data for Starting Materials **5c**, **5d**, **5e**, **5f** and **5j**

2-Chloro-5-ethynylpyridine (**5c**)¹



In an oven-dried vial were introduced 5-bromo-2-chloropyridine (1.0 equiv, 1.0 g, 5.2 mmol), CuI (0.05 equiv, 0.05 g, 0.263 mmol) and PdCl₂(PPh₃)₂ (0.05 equiv, 0.183 g, 0.261 mmol). The vial was flushed with argon and THF (13 mL) was added, followed by Et₃N (3.0 equiv, 2.2 mL, 15.8 mmol) and trimethylsilylacetylene (1.2 equiv, 0.90 mL, 6.32 mmol).

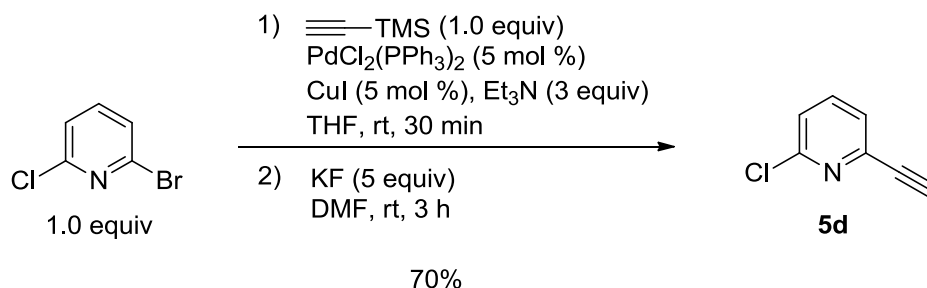
The vial was then sealed with a teflon-lined cap and heated in a Biotage Initiator microwave oven at 80 °C for 2 h. The reaction mixture was cooled down to rt, filtered over a thin bed of silica gel (EtOAc washings), then an aqueous saturated NaHCO₃ solution was added to the filtrate, and the aqueous phase was extracted twice with EtOAc. The combined organic phases were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel with a gradient of eluent (diethyl ether/petroleum ether = 0:100 to 2:98) led to the desired product 2-chloro-5-((trimethylsilyl)ethynyl)pyridine as a white solid (790 mg, 3.77 mmol, 72%). Immediately used in the next step.

To a solution of 2-chloro-5-[2-(trimethylsilyl)ethynyl]pyridine (1.0 equiv, 600 mg, 2.86 mmol) in MeOH (6 mL) was added K₂CO₃ (0.1 equiv, 39 mg, 0.286 mmol) in one portion. The resulting suspension was stirred under air for 30 min. The reaction mixture was then concentrated to *ca.* 1 mL, aqueous saturated NaHCO₃ was added, and the aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (diethyl ether/petroleum ether = 5:95) led to the desired product 2-chloro-5-ethynyl-pyridine **5c** as a white solid (290 mg, 2.11 mmol, 74%). ¹H NMR analysis was consistent with the data reported in the literature.¹

¹ S. Hapuarachchige, G. Montano, C. Ramesh, D. Rodriguez, L. H. Henson, C. C. Williams, S. Kadavakkollu, D. L. Johnson, C. B. Shuster, J. B. Arterburn, *J. Am. Chem. Soc.* **2011**, *133*, 6780–6790.

¹H NMR (400 MHz, CDCl₃): δ 8.49 (d, *J* = 2.3 Hz, 1H), 7.71 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.30 (dd, *J* = 8.3, 0.7 Hz, 1H), 3.26 (s, 1H).

2-Chloro-6-ethynylpyridine (**5d**)



In an oven-dried vial were introduced 2-bromo-6-chloropyridine (1.0 equiv, 1.02 g, 5.30 mmol), CuI (0.05 equiv, 52 mg, 0.273 mmol) and PdCl₂(PPh₃)₂ (0.05 equiv, 187 mg, 0.266 mmol). The vial was flushed with argon and THF (14 mL) was added, followed by Et₃N (3.1 equiv, 2.3 mL, 16.5 mmol) and trimethylsilylacetylene (1.0 equiv, 0.76 mL, 5.34 mmol). The reaction mixture was then stirred at rt for 30 min. The reaction mixture was filtered over a thin bed of silica gel (diethyl ether washings), then aqueous saturated NaHCO₃ was added to the filtrate, and the aqueous phase was extracted twice with diethyl ether. The combined organic phases were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (diethyl ether/petroleum ether = 2:98) led to the desired product 2-chloro-6-[(trimethylsilyl)ethynyl]pyridine as a white solid (1.1 g, 5.24 mmol, 99% yield). Immediately used in the next step.

2-Chloro-6-((trimethylsilyl)ethynyl)pyridine (1.0 equiv, 1.1 g, 5.24 mmol) was dissolved in DMF (10 mL), and KF (5.5 equiv, 1.7 g, 29.3 mmol) was added in one portion. The resulting suspension was stirred under air for 3 h. Water was added, and the aqueous phase was extracted three times with diethyl ether. The combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (diethyl ether/petroleum ether = 5:98) led to the desired product 2-chloro-6-ethynylpyridine **5d** (510 mg, 3.71 mmol, 71%).

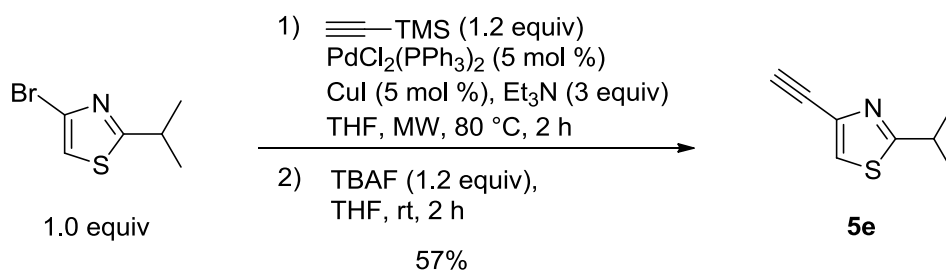
IR (neat): 3275, 3047, 1571, 1552, 1429, 1268, 1164, 1140, 988, 854.

¹H-NMR (CDCl₃, 400 MHz): δ 7.63 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.40 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.32 (ddd, *J* = 8.0, 0.9, 0.2 Hz, 1H), 3.20 (s, 1H).

¹³C-NMR (CDCl₃, 100 MHz): δ 151.4 (C), 142.3 (C), 138.8 (CH), 126.0 (CH), 124.5 (CH), 81.4 (CH), 78.6 (C).

HRMS (ESI+): [M+H]⁺ calculated for C₇H₅ClN: 138.0105. Found: 138.0103.

4-Ethynyl-2-isopropylthiazole (**5e**)



In an oven-dried vial were introduced 4-bromo-2-(propan-2-yl)-1,3-thiazole (1.0 equiv, 500 mg, 2.43 mmol), CuI (0.05 equiv, 23 mg, 0.121 mmol) and PdCl₂(PPh₃)₂ (0.05 equiv, 86 mg, 0.123 mmol). The vial was flushed with argon, and THF was added (6 mL), followed by Et₃N (3.0 equiv, 1 mL, 7.19 mmol) and trimethylsilylacetylene (1.2 equiv, 0.42 mL, 2.95 mmol). The vial was then sealed with a teflon-lined cap and stirred at 80 °C for 2 h in a Biotage Initiator microwave oven. The reaction mixture was filtered over a thin bed of silica gel (EtOAc washings), an aqueous saturated NaHCO₃ solution was added, and the aqueous phase was extracted twice with EtOAc. The combined organic phases were washed with brine, dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (diethyl ether/petroleum ether = 3:97) led to the desired product 2-isopropyl-5-((trimethylsilyl)ethynyl)thiazole as a yellow oil (468 mg, 2.10 mmol, 86%). Used immediately in the next step.

To a solution of 2-isopropyl-5-((trimethylsilyl)ethynyl)thiazole (1.0 equiv, 468 mg, 2.10 mmol) in THF (1 mL) was added a 1.0 M solution of TBAF in THF (1.2 equiv, 2.44 mL, 2.44 mmol), and the resulting solution was stirred at rt for 2 h. Water was added, and the aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 5:95 to 10:90) led to the desired product 4-ethynyl-2-isopropylthiazole **5e** as a pale yellow oil (210 mg, 1.39 mmol, 66%).

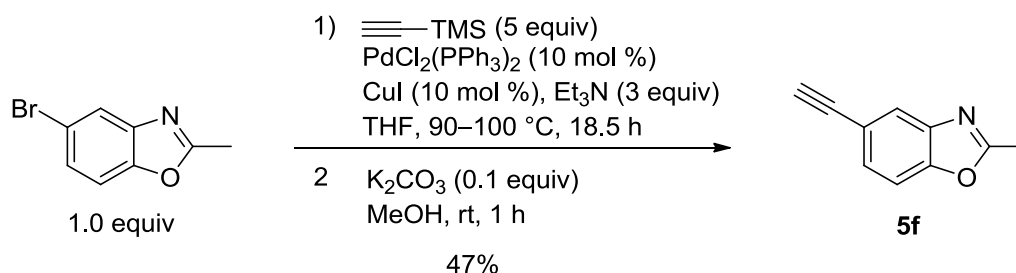
IR (neat): 3293, 3114, 2967, 2929, 1491, 1365, 1306, 1276, 1060, 1013, 875.

¹H-NMR (CDCl₃, 400 MHz): δ 7.38 (s, 1H), 3.30 (hept, J = 6.9 Hz, 1H), 3.09 (s, 1H), 1.40 (d, J = 6.9 Hz, 6H).

¹³C-NMR (CDCl₃, 100 MHz): δ 177.8 (C), 135.7 (C), 122.9 (CH), 78.1 (CH), 77.2 (C), 33.4 (CH), 23.1 (2xCH₃).

HRMS (ESI+): [M+H]⁺ calculated for C₈H₁₀NS: 152.0528. Found: 152.0526.

5-Ethynyl-2-methylbenzo[d]oxazole (**5f**)



In an oven-dried vial were introduced CuI (0.1 equiv, 41 mg, 0.216 mmol) and $\text{PdCl}_2(\text{PPh}_3)_2$ (0.1 equiv, 151 mg, 0.216 mmol). The vial was flushed with argon, and dry THF (5.5 mL) was added, followed by 5-bromo-2-methyl-1,3-benzoxazole (1.0 equiv, 0.31 mL, 2.17 mmol), and Et_3N (3.0 equiv, 0.92 mL, 6.62 mmol). This suspension was stirred at rt for 15 min, then trimethylsilylacetylene was added (2.9 equiv, 0.9 mL, 6.32 mmol). The solution immediately turned to deep red. The vial was then sealed with a teflon-lined cap and stirred at 90 °C in a pre-equilibrated oil bath. After 1 h, supplementary amounts of trimethylsilylacetylene were added (1.0 equiv, 0.3 mL, 2.11 mmol), followed by the same amount 1.5 h later. The resulting reaction mixture was stirred at 100 °C for 16 h. The reaction mixture was allowed to cool down and filtered over a short bed of silica (EtOAc washings) and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 10:90) led to the desired product 2-methyl-5-((trimethylsilyl)ethynyl)benzo[d]oxazole as a yellow oil.

This oil was then dissolved in MeOH (4 mL) and K_2CO_3 (0.1 equiv., 30 mg, 0.217 mmol) was added. The resulting suspension was stirred at rt under air for 1 h, toluene was added, and the mixture was concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 10:90) led to the desired product 5-ethynyl-2-methylbenzo[d]oxazole **5f** (160 mg, 1.02 mmol, 47% overall yield).

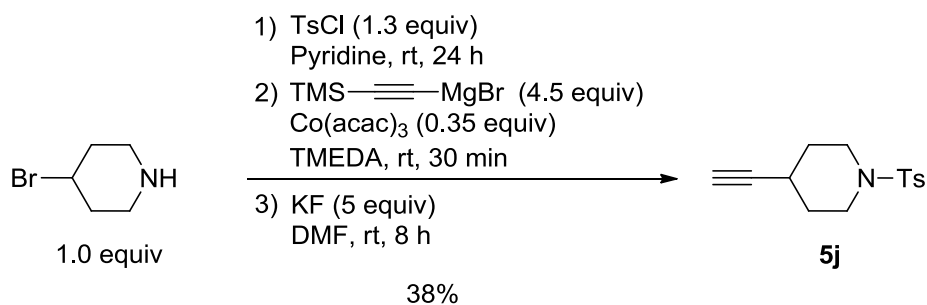
IR (neat): 3205, 1623, 1574, 1467, 1427, 1380, 1261, 1181, 918, 881.

¹H-NMR (CDCl₃, 400 MHz): δ 7.79 (m, 1H), 7.47–7.39 (m, 2H), 3.06 (s, 1H), 2.64 (s, 3H).

¹³C-NMR (CDCl₃, 100 MHz): 164.9 (C), 151.1 (C), 141.6 (C), 128.9 (CH), 123.4 (CH), 118.1 (C), 110.3 (CH), 83.4 (CH), 76.4 (C), 14.5 (CH₃).

HRMS (ESI⁺): [M+H]⁺ calculated for C₁₀H₈NO: 158,0600. Found: 158,0599.

4-Ethynyl-1-tosylpiperidine (**5j**)²



To 4-bromopiperidine hydrobromide (1.0 equiv, 2.08 g, 8.49 mmol) and tosyl chloride (1.3 equiv, 2.15 g, 11.3 mmol) was added pyridine (18 mL). The resulting suspension was stirred under argon for 24 h. CH₂Cl₂ and aqueous 1M HCl were added, the aqueous phase was extracted 3 times with CH₂Cl₂. The combined organic phases were washed with 1M HCl, then brine, dried over Na₂SO₄ and concentrated *in vacuo* to give a yellow solid which was recrystallized from CH₂Cl₂/petroleum ether. Dried *in vacuo* at 40 °C to give 4-bromo-1-[(4-methylphenyl)sulfonyl]piperidine as white crystals (2.41 g, 7.57 mmol, 89%).

To a 1.0 M solution of isopropylmagnesium bromide (4.5 equiv, 24 mL, 24 mmol) in THF was added neat trimethylsilylacetylene (4.5 equiv, 3.4 mL, 24 mmol). The resulting solution was stirred at rt for 3 h. The solvent was then evaporated *in vacuo*, and the resulting solid was suspended in dry TMEDA (12 mL). Co(acac)₃ (0.35 equiv, 0.671 g, 1.88 mmol) was suspended in dry TMEDA (10 mL) under argon, and stirred at rt for 3 min. Solid 4-bromo-1-[(4-methylphenyl)sulfonyl]piperidine (1.0 equiv, 1.7 g, 5.34 mmol) was then added in one portion, quickly followed by addition of the suspension of the Grignard. The resulting green suspension was stirred at rt for 30 min (strong exothermic reaction after 15 min, with a sudden evolution of the color from green to brown). The reaction mixture was poured on aqueous NH₄Cl and Et₂O, and was then filtered over Celite. The aqueous phase was extracted three times with Et₂O, the combined organic phases were dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 10:90), followed by trituration with petroleum ether led to a 12:78 mixture of the E₂ elimination product, 1-tosyl-1,2,3,6-tetrahydropyridine, and the desired 1-tosyl-4-((trimethylsilyl)ethynyl)piperidine product (1.20 g)

² H. Ohmiya, H. Yorimitsu, K. Oshima, *Org Lett.* **2006**, *8*, 3093–3096.

This solid was then suspended in 10 mL of DMF, followed by KF (5 equiv, 1.55 g, 26.7 mmol), and the resulting suspension was stirred under air at rt for 8 h. Water was added, the aqueous phase was extracted three times with EtOAc, the combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/pentane = 15:85) led to two fractions: the first fraction was constituted of the E₂ elimination product 1-tosyl-1,2,3,6-tetrahydropyridine and of the desired product **5j** (540 mg), and the second fraction was constituted by pure **5j** (310 mg). The 4-ethynyl-1-tosylpiperidine **5j** contained in the first fraction could be recrystallized specifically from Et₂O/petroleum ether after germination using a crystal of pure 4-ethynyl-1-tosylpiperidine, to lead to 610 mg of 4-ethynyl-1-tosylpiperidine **5j** (2.32 mmol, 43% yield from 4-bromo-1-[(4-methylphenyl)sulfonyl]piperidine).

Mp (°C): 103–104.

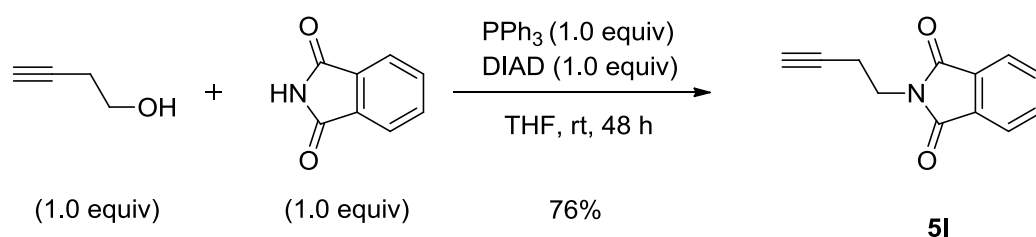
IR (neat): 3292, 2920, 1598, 1443, 1341, 1247, 1160, 1093, 1040, 921.

¹H-NMR (CDCl₃, 400 MHz): δ 7.66–7.59 (m, 2H), 7.36–7.29 (m, 2H), 3.33–3.25 (m, 2H), 2.86–2.78 (m, 2H), 2.43 (s, 3H), 2.02 (d, *J* = 2.4 Hz, 1H), 1.93–1.85 (m, 2H), 1.77–1.68 (m, 2H).

¹³C-NMR (CDCl₃, 100 MHz): 143.6 (C), 133.3 (C), 129.8 (2xCH), 127.7 (2xCH), 85.6 (C), 70.2 (CH), 44.4 (2xCH₂), 30.7 (2xCH₂), 25.9 (CH), 21.7 (CH₃).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₄H₁₇NO₂SN_a: 286.0872. Found: 286.0875.

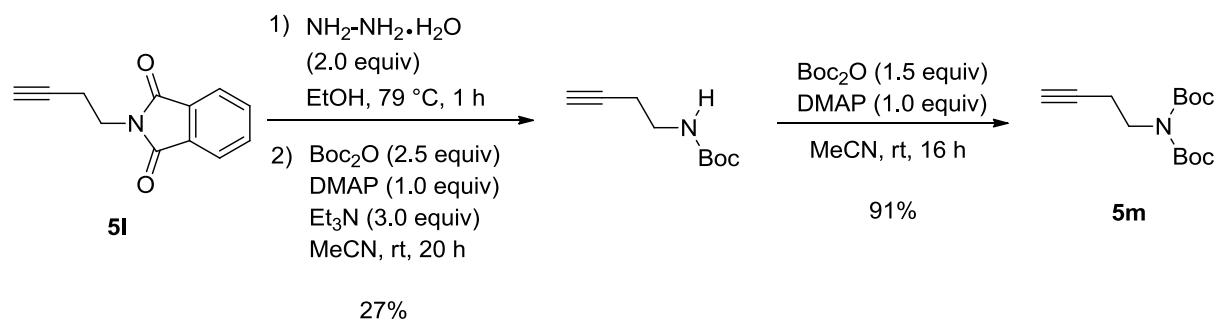
N-Homopropargyl phthalimide (**5I**)³



In an oven-dried flask were weighted PPh₃ (1.0 equiv, 5.23 g, 19.9 mmol) and phthalimide (1.0 equiv, 2.94 g, 20 mmol). The flask was flushed with argon, then dry THF (100 mL) was added, followed by the addition of 3-butyn-1-ol (1.0 equiv, 1.4 g, 1.51 mL, 19.9 mmol) and neat diisopropyl azodicarboxylate (1.0 equiv, 4 mL, 20.2 mmol). The resulting solution was stirred at rt for 48 h. After concentration *in vacuo*, purification by flash column chromatography on silica gel (CH₂Cl₂/petroleum ether = 50:50) led to the desired product *N*-homopropargyl phthalimide **5I** as a white solid (3.01 g, 15.11 mmol, 76% yield). ¹H NMR analysis was consistent with the data reported in the literature.³

¹H NMR (400 MHz, CDCl₃) δ 7.89 – 7.82 (m, 2H), 7.76 – 7.70 (m, 2H), 3.89 (t, *J* = 7.1 Hz, 2H), 2.62 (td, *J* = 7.1, 2.7 Hz, 2H), 1.96 (t, *J* = 2.7 Hz, 1H).

N,N-Bis[(*tert*-butoxy)carbonyl]-*N*-(but-3-yn-1-yl)carbamate (**5m**)



To a solution of *N*-homopropargyl phthalimide **5I** (1 equiv, 2.5 g, 12.5 mmol) in absolute ethanol (60 mL) was added hydrazine hydrate (2.0 equiv, 1.2 mL, 24.7 mmol). The resulting solution was refluxed for 1 h. The resulting suspension was poured onto 15 mL of 1N HCl, and filtered over a fritted glass. The filtrate was concentrated *in vacuo*, triturated with water, and the supernatant was concentrated *in vacuo* to give a yellow sticky solid (2.70 g).

This solid was suspended in MeCN (7 mL), and Boc₂O (2.5 eq., 6.7 g, 30.7 mmol) was added, followed by Et₃N (3.0 equiv, 5.1 mL, 36.7 mmol) and DMAP (1.0 equiv, 1.5 g, 12.3 mmol).

³ S. Iyer, L. S. Liebeskind, *J. Am. Chem. Soc.* **1987**, *109*, 2759–2770.

The resulting suspension was stirred at rt for 20 h. An aqueous saturated solution of NaHCO₃ was added, followed by ethyl acetate. The aqueous phase was extracted twice with ethyl acetate. The combined organic phases were washed once with an aqueous 0.5M HCl solution, twice with water, once with brine, dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 20:80) led to the monoprotected product *tert*-butyl *N*-(but-3-yn-1-yl)carbamate as a pale, colorless oil (560 mg, 3.31 mmol, 27% yield from **5l**).

This oil was dissolved in MeCN (1.8 mL), Boc₂O (1.5 equiv, 1.03 g, 4.7 mmol) was added, followed by DMAP (1.0 eq., 0.38 g, 3.12 mmol). The resulting solution was stirred at rt for 16 h. After concentration *in vacuo*, purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 20:80) led to the desired product *N,N*-Bis[(*tert*-butoxy)carbonyl]-*N*-(but-3-yn-1-yl)carbamate (**5m**) as a white solid (770 mg, 2.86 mmol, 91% yield).

Mp (°C): 61–63.

IR (neat): 3261, 3004, 2983, 1740, 1705, 1442, 1365, 1283, 1146, 1106.

¹H-NMR (CDCl₃, 400 MHz): δ 3.76 (t, *J* = 7.3 Hz, 2H), 2.47 (td, *J* = 7.3, 2.7 Hz, 2H), 1.95 (t, *J* = 2.7 Hz, 1H), 1.50 (s, 18H).

¹³C-NMR (CDCl₃, 100 MHz): δ 152.4 (2xC), 82.7 (2xC), 81.2 (C), 69.8 (CH), 44.9 (CH₂), 28.2 (6xCH₃), 18.9 (CH₂).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₄H₂₃NO₄Na: 292,1519. Found: 292,1520.

3. Experimental Procedures and Spectroscopic Data for products **4** and **6**

Procedure A: TMS-CF₃ as the :CF₂ source.

In an oven-dried vial were introduced NaI (2.2 equiv) and the alkyne if it is a solid or if the density is not known (1.0 equiv). The vial was then flushed with argon, and THF (*c* = 0.375 M) was added through the septum, followed by the alkyne (1.0 equiv) if it is a liquid, and neat TMS-CF₃ (2.0–4.0 equiv). The vial was then sealed with a teflon-lined cap and immersed in a pre-heated oil bath at 110 °C. Vigorous stirring was then applied for 2 h, and completion of the reaction was assessed by TLC or GC/MS. If necessary, supplementary amounts of TMS-CF₃ were added until complete consumption of the alkyne.

The reaction mixture was allowed to cool down to rt, filtered over a frit glass in an oven-dried flask under argon (dry THF washings), the filtrate was concentrated *in vacuo*, and the residue dissolved in DMF (*c* = 0.5 M). To this solution were added Et₃N (1.5 equiv), followed by a 87% w/w solution of the diazo ester in CH₂Cl₂ (5.0 equiv). The resulting solution was stirred in the dark, at rt, under argon, until complete consumption of the *gem*-difluorocyclopropene, as assessed by TLC or GC/MS. Unless otherwise specified, the reaction mixture was then directly purified by column chromatography over silica gel without previous aqueous work-up or concentration.

NOTES: 1) When monitoring the formation/consumption of the *gem*-difluorocyclopropene, the TLC plates should be neutralized with Et₃N, otherwise streaking might occur. 2) Acidic work-up should be avoided as it can lead to partial hydrolysis of the fluoropyridazine. 3) On a large scale, elimination of the DMF and the excess of diazo ester can be accomplished by *in vacuo* concentration without any impact on the final yields.

Procedure B: TFDA as the :CF₂ source.

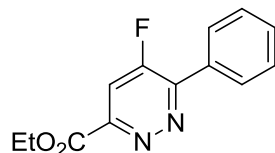
In an oven-dried flask were introduced NaF (0.1 equiv) and the alkyne if it is a solid (1.0 equiv). The vial was then flushed with argon, and diglyme (*c* = 0.5 M) was added through the septum, followed by the alkyne (1.0 equiv) if it is a liquid. The reaction mixture was then heated in a pre-equilibrated oil bath at 120 °C, and neat TFDA (3.0 equiv) was added dropwise over 1 h using a syringe pump. At the end of the addition, the reaction mixture was stirred for 15 min, and completion of the reaction was assessed by TLC or GC/MS. If

necessary, supplementary amounts of TFDA were added until complete consumption of the alkyne.

The reaction mixture was then allowed to cool down to rt, the acidic gases were flushed out the flask using an argon flow, and Et₃N (1.5 equiv) was added, followed by a 87% w/w solution of the diazo ester in CH₂Cl₂ (5.0 equiv). The resulting solution was stirred in the dark, at rt, under argon, until complete consumption of the *gem*-difluorocyclopropene, as assessed by TLC or GC/MS. Unless otherwise specified, the reaction mixture was then directly purified by column chromatography over silica gel without previous aqueous work-up or concentration.

NOTE: TFDA of good quality is necessary for the success of the reaction sequence. If the TFDA has not been used or stored using good laboratory practices, it will result in its hydrolysis, thus generating HF. While it is not problematic for the *gem*-difluorocyclopropene formation, HF will quench Et₃N or the diazo ester in the following steps, thus resulting in complex reaction mixtures. If in doubt, the use of supplementary amounts of Et₃N is recommended.

Ethyl 5-fluoro-6-phenylpyridazine-3-carboxylate (**4aa**)



Prepared according to procedure **A** from phenylacetylene (2.2 mL, 20 mmol). After the addition of the diazo ester, 53 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. The reaction mixture was concentrated in vacuo, and purification by flash column chromatography on silica gel (EtOAc/petroleum ether = 20:80) followed by pentane trituration led to the desired product **4aa** as a pale yellow solid (3.78 g, 15.35 mmol, 77%).

Mp (°C): 64–65.

IR (neat): 3079, 2983, 1717, 1588, 1402, 1381, 1247, 1096, 1011, 968.

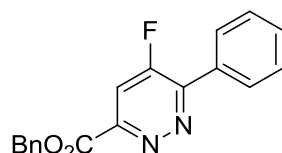
¹H-NMR (CDCl₃, 400 MHz): δ 8.17–8.11 (m, 2H), 7.98 (d, *J* = 11.3 Hz, 1H), 7.64–7.50 (m, 3H), 4.58 (q, *J* = 7.1 Hz, 2H), 1.51 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.3 (C), 160.7 (C, d, *J* = 280 Hz), 153.0 (C, d, *J* = 5 Hz), 152.3 (C, d, *J* = 3 Hz), 131.5 (C, d, *J* = 5 Hz), 131.3 (CH), 129.6 (2xCH, d, *J* = 5 Hz), 129.0 (2xCH), 115.1 (CH, d, *J* = 17 Hz), 63.1 (CH₂), 14.4 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 77 (24), 104 (100), 174 (94), 202 (23), 246 ($M^{+\bullet}$, 4).

HRMS (ESI+): $[M+Na]^+$ calculated for $C_{13}H_{11}FN_2O_2Na$: 269.0697. Found: 269.0697.

Benzyl 5-fluoro-6-phenylpyridazine-3-carboxylate (**4ab**)



Prepared according to procedure **A** from phenylacetylene (0.330 mL, 3.0 mmol). After the addition of the diazo ester, 63 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (EtOAc/petroleum ether = 10:90 to 15:85) followed by pentane trituration led to the desired product **4ab** as a pale yellow solid (630 mg, 2.04 mmol, 68%).

Mp ($^{\circ}C$): 100–101.

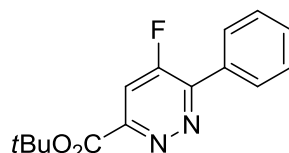
IR (neat): 3067, 2940, 1710, 1587, 1455, 1404, 1366, 1319, 1247, 1103, 970, 779, 688.

1H -NMR ($CDCl_3$, 400 MHz): δ 8.18–8.07 (m, 2H), 7.97 (d, J = 11.2 Hz, 1H), 7.62–7.49 (m, 5H), 7.44–7.32 (m, 3H), 5.54 (s, 2H).

^{13}C -NMR ($CDCl_3$, 100 MHz): δ 163.1 (C, d, J = 3 Hz), 160.7 (C, d, J = 280 Hz), 153.0 (C, d, J = 5 Hz), 152.1 (C, d, J = 3 Hz), 135.0 (C), 131.5 (C, d, J = 5 Hz), 131.3 (CH), 129.6 (2xCH d, J = 5 Hz), 129.0 (2xCH), 128.84 (3xCH), 128.80 (2xCH), 115.2 (CH, d, J = 17 Hz), 68.5 (CH_2).

HRMS (ESI+): $[M+Na]^+$ calculated for $C_{18}H_{13}FN_2O_2Na$: 331.0853. Found: 331.0853.

Tert-butyl 5-fluoro-6-phenylpyridazine-3-carboxylate (**4ac**)



Prepared according to procedure **A** from phenylacetylene (0.110 mL, 1.0 mmol). After the addition of the diazo ester, 47 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et_2O /petroleum ether = 15:85 to 20:80) led to the desired product **4ac** as a yellow solid (160 mg, 0.58 mmol, 58%).

Mp (°C): 210 (degradation).

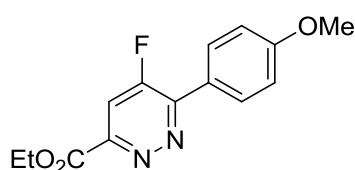
IR (neat): 3073, 2981, 1712, 1590, 1453, 1393, 1369, 1323, 1253, 1158, 1108, 972.

¹H-NMR (Acetone-*d*₆, 400 MHz): δ 8.12–8.06 (m, 3H), 7.65–7.59 (m, 3H), 1.67 (s, 9H).

¹³C-NMR (Acetone-*d*₆, 100 MHz): δ 162.8 (C, d, J = 3 Hz), 161.6 (C, d, J = 277 Hz), 154.6 (C, d, J = 3 Hz), 153.2 (C, d, J = 5 Hz), 132.9 (C, d, J = 5 Hz), 131.7 (CH), 130.1 (2xCH, d, J = 5 Hz), 129.7 (2xCH₂), 115.5 (CH, d, J = 17 Hz), 83.8 (C), 28.2 (3xCH₃).

HRMS (ESI+): [M+H]⁺ calculated for C₁₅H₁₆FN₂O₂: 275.1190. Found: 275.1193.

Ethyl 5-fluoro-6-(4-methoxyphenyl)pyridazine-3-carboxylate (**4b**)



Prepared according to procedure **A** from (4-methoxyphenyl)acetylene (0.120 mL, 0.925 mmol). After the addition of the diazo ester, 85 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 10:90 to 40:60) led to the desired product **4b** as a pale yellow solid (135 mg, 0.489 mmol, 53%).

Mp (°C): 120–121.

IR (neat): 3064, 2983, 2916, 1720, 1609, 1579, 1514, 1386, 1317, 1250, 1184, 1102, 1027, 968.

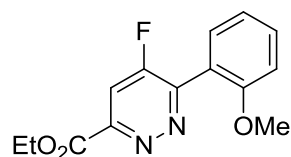
¹H-NMR (CDCl₃, 400 MHz): δ 8.11 (d, J = 8.4 Hz, 2H), 7.88 (d, J = 11.7 Hz, 1H), 7.01 (d, J = 8.9 Hz, 2H), 4.52 (q, J = 7.1 Hz, 2H), 3.85 (s, 3H), 1.45 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.3 (C, d, J = 3 Hz), 162.0 (C), 160.3 (C, d, J = 279 Hz), 152.2 (C, d, J = 4 Hz), 151.5 (C, d, J = 3 Hz), 131.1 (2xCH, d, J = 6 Hz), 123.9 (C, d, J = 5 Hz), 114.8 (CH, d, J = 17 Hz), 114.4 (2xCH), 62.8 (CH₂), 55.4 (CH₃), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) 77 (19), 92 (14), 107 (15), 134 (100), 189 (83), 204 (98), 276 (M⁺, 34).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₄H₁₃FN₂O₃Na: 299.0802. Found: 299.0800.

Ethyl 5-fluoro-6-(2-methoxyphenyl)pyridazine-3-carboxylate (**4c**)



Prepared according to procedure **A** from 1-ethynyl-2-methoxybenzene (132 mg, 1.0 mmol). After the addition of the diazo ester, 85 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 10:90 to 40:60) followed by recrystallization from petroleum ether led to the desired product **4c** as a pale yellow solid (130 mg, 0.471 mmol, 47%).

Mp (°C): 103–105.

IR (neat): 3072, 2988, 1726, 1605, 1495, 1409, 1386, 1267, 1099, 1026, 970, 917.

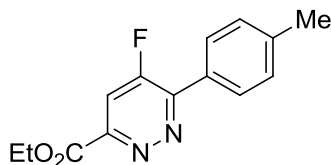
¹H-NMR (CDCl₃, 400 MHz): δ 7.91 (d, J = 9.6 Hz, 1H), 7.59 (dd, J = 7.5, 1.7 Hz, 1H), 7.51 (ddd, J = 8.3, 7.5, 1.7 Hz, 1H), 7.13 (td_{app}, J = 7.5, 0.9 Hz, 1H), 7.03 (broad d, J = 8.3 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 3.82 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.5 (C, d, J = 3 Hz), 160.9 (C, d, J = 279 Hz), 157.6 (C), 153.4 (C, d, J = 10 Hz), 152.7 (C, d, J = 4 Hz), 132.3 (CH), 131.5 (CH), 121.3 (C, d, J = 4 Hz), 121.2 (CH), 114.0 (CH, d, J = 17 Hz), 111.2 (CH), 63.0 (CH₂), 55.8 (CH₃), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 77 (25), 104 (30), 203 (100), 247 (8), 257 (10), 276 (M⁺, 15).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₄H₁₃FN₂O₃Na: 299.0802. Found: 299.0800.

Ethyl 5-fluoro-6-(*p*-tolyl)pyridazine-3-carboxylate (**4d**)



Prepared according to procedure **A** from 4-ethynyltoluene (0.125 mL, 0.986 mmol). After the addition of the diazo ester, 60 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 15:85 to 30:70) led to the desired product **4d** as a pale yellow solid (220 mg, 0.845 mmol, 86%).

Mp (°C): 79–80.

IR (neat): 3077, 2984, 1739, 1578, 1542, 1373, 1237, 1183, 1140, 1098, 1011, 906.

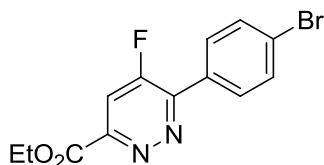
¹H-NMR (CDCl₃, 400 MHz): δ 8.02 (br, d, J = 6.9 Hz, 2H), 7.92 (d, J = 11.5 Hz, 1H), 7.33 (d, J = 8.0 Hz, 2H), 4.54 (q, J = 7.1 Hz, 2H), 2.42 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.3 (C, d, J = 3 Hz), 160.5 (C, d, J = 280 Hz), 152.8 (C, d, J = 5 Hz), 151.9 (C, d, J = 3 Hz), 141.7 (C), 129.7 (2xCH), 129.4 (2xCH, d, J = 6 Hz), 128.7 (C, d, J = 5 Hz), 114.9 (CH, d, J = 17 Hz), 62.9 (CH₂), 21.6 (CH₃), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 65 (18), 91 (17), 118 (100), 133 (22), 216 (21), 260 (M⁺, 10).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₄H₁₃FN₂O₂Na: 283.0853. Found: 283.0852.

Ethyl 6-(4-bromophenyl)-5-fluoropyridazine-3-carboxylate (**4f**)



Prepared according to procedure **A** from 1-bromo-4-ethynylbenzene (182 mg, 1.0 mmol). After the addition of the diazo ester, 26 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 10:90 to 25:75) led to the desired product **4f** as a pale yellow solid (235 mg, 0.723 mmol, 72%).

Mp (°C): 100–102.

IR (neat): 3066, 2977, 2935, 1715, 1583, 1423, 1372, 1305, 1244, 1102, 1003, 958.

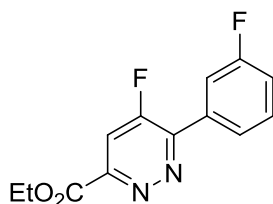
¹H-NMR (CDCl₃, 400 MHz): δ 8.03–7.97 (m, 2H), 7.95 (d, J = 11.4 Hz, 1H), 7.69–7.61 (m, 2H), 4.54 (q, J = 7.1 Hz, 2H), 1.47 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.1 (C, d, J = 3 Hz), 160.6 (C, d, J = 280 Hz), 152.5 (C, d, J = 3 Hz), 151.8 (C, d, J = 5 Hz), 132.3 (2xCH), 130.9 (2xCH, d, J = 6 Hz), 130.3 (C, d, J = 5 Hz), 126.2 (C), 115.1 (CH, d, J = 17 Hz), 63.1 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 71 (25), 75 (27), 102 (13), 144 (24), 73 (100), 182 (51), 184 (50), 252 (62), 254 (63), 280 (16), 282 (15), 324 (M⁺, 6), 326 (M⁺, 6).

HRMS (ESI+): [M+Na]⁺ calculated for: C₁₃H₁₀BrFN₂O₂Na: 346.9802 and 348.9781. Found: 346.9805 and 348.9781.

Ethyl 5-fluoro-6-(3-fluorophenyl)pyridazine-3-carboxylate (4g)



Prepared according to procedure **A** from 1-ethynyl-3-fluorobenzene (0.116 mL, 1.0 mmol). After the addition of the diazo ester, 22 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 10:90 to 30:70) led to the desired product **4g** as a pale yellow solid (145 mg, 0.549 mmol, 55%).

Mp (°C): 66–68.

IR (neat): 3087, 2981, 1723, 1585, 1402, 1377, 1281, 1179, 1099, 1022, 970.

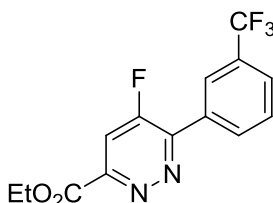
¹H-NMR (CDCl₃, 400 MHz): δ 7.97 (d, *J* = 11.4 Hz, 1H), 7.91 (m, 1H), 7.85 (m, 1H), 7.50 (td, *J* = 8.2, 5.9 Hz, 1H), 7.23 (tdd_{app}, *J* = 8.2, 2.6, 1.0 Hz, 1H), 4.54 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.1 (C, d, *J* = 3 Hz), 162.9 (C, d, *J* = 247 Hz), 160.7 (C, d, *J* = 280 Hz), 152.6 (C, d, *J* = 4 Hz), 151.6 (C, dd, *J* = 5, 3 Hz), 133.4 (C, dd, *J* = 8, 5 Hz), 130.6 (CH, d, *J* = 8 Hz), 125.2 (CH, dd, *J* = 6, 3 Hz), 118.2 (CH, d, *J* = 21 Hz), 116.4 (CH, dd, *J* = 24, 5 Hz), 115.2 (CH, d, *J* = 17 Hz), 63.1 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 71 (22), 95 (20), 122 (96), 192 (100), 220 (24), 264 (M⁺, 3).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₃H₁₀F₂N₂O₂Na: 287.0603. Found: 287.0604.

Ethyl 5-fluoro-6-(3-(trifluoromethyl)phenyl)pyridazine-3-carboxylate (4h)



Prepared according to procedure **A** from 1-ethynyl-3-(trifluoromethyl)benzene (170 mg, 1.0 mmol). After the addition of the diazo ester, 6 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography

on silica gel with a gradient of eluent (Et₂O/petroleum ether = 10:90 to 30:70) led to the desired product **4g** as a pale yellow solid (105 mg, 0.334 mmol, 33%).

Prepared according to procedure **B** from 1-ethynyl-3-(trifluoromethyl)benzene (170 mg, 1.0 mmol). After the addition of the diazo ester, 19 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel (CH₂Cl₂) led to the desired product **4g** as a pale yellow solid (190 mg, 0.605 mmol, 60%).

Mp (°C): 112–114.

IR (neat): 3082, 2997, 1719, 1591, 1414, 1320, 1249, 1156, 1078, 1033, 972, 901.

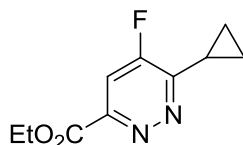
¹H-NMR (CDCl₃, 400 MHz): δ 8.41 (s, 1H), 8.33 (d, *J* = 7.9 Hz, 1H), 8.02 (d, *J* = 11.3 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.69 (t, *J* = 7.9 Hz, 1H), 4.57 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.0 (C, d, *J* = 3 Hz), 160.8 (C, d, *J* = 281 Hz), 152.9 (C, d, *J* = 4 Hz), 151.5 (C, d, *J* = 5 Hz), 132.7 (CH, dd_{app}, *J* = 5, 1 Hz), 132.3 (C, d, *J* = 5 Hz), 131.6 (C, q, *J* = 33 Hz), 129.64 (CH), 127.8 (CH, q, *J* = 4 Hz), 126.3 (CH, m), 123.9 (C, q, *J* = 272 Hz), 115.3 (CH, d, *J* = 17 Hz), 63.2 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 71 (41), 145 (17), 172 (100), 222 (31), 242 (84), 270 (17), 295 (5), 314 (M⁺, 1).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₄H₁₀F₄N₂O₂Na: 337.0571. Found: 337.0568.

Ethyl 6-cyclopropyl-5-fluoropyridazine-3-carboxylate (**4i**)



Prepared according to procedure **A** from cyclopropylacetylene (0.150 mL, 1.77 mmol). However, due to the high volatility of the intermediate **2i**, the mixture was not concentrated in vacuo before the diazo ester addition. Instead, the reaction mixture was decanted and transferred in an oven-dried flask, followed by addition of the diazo ester and of Et₃N. After the addition of the diazo ester, 5 days were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 15:85 to 30:70) led to the desired product **4i** as a pale yellow oil (110 mg, 0.523 mmol, 30%).

IR (neat): 3078, 2984, 2932, 1750, 1720, 1594, 1548, 1412, 1351, 1272, 1243, 1091, 1014, 967.

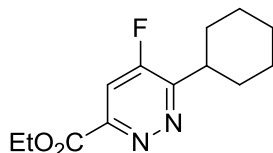
¹H-NMR (CDCl₃, 400 MHz): δ 7.75 (d, J = 9.9 Hz, 1H), 4.50 (q, J = 7.1 Hz, 2H), 2.47–2.38 (m, 1H), 1.52–1.40 (m, 5H), 1.29–1.23 (m, 2H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.6 (C, d, J = 3 Hz), 161.0 (C, d, J = 275 Hz), 158.8 (C, d, J = 9 Hz), 151.0 (C, d, J = 3 Hz), 112.5 (CH, d, J = 15 Hz), 62.8 (CH₂), 14.31 (CH₃), 11.96 (2xCH₂), 9.70 (CH).

MS (EI, 70 eV): m/z (relative intensity) = 68 (35), 83 (19), 138 (100), 166 (28), 181 (25), 210 (M⁺, 3).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₀H₁₁FN₂O₂Na: 233.0697. Found: 233.0694.

Ethyl 6-cyclohexyl-5-fluoropyridazine-3-carboxylate (**4j**)



Prepared according to procedure **A** from cyclohexylacetylene (0.130 mL, 1.0 mmol). However, due to the high volatility of the intermediate **2j**, the mixture was not concentrated in vacuo before the diazo ester addition. Instead, the reaction mixture was decanted and transferred in an oven-dried flask, followed by addition of the diazo ester and of Et₃N. After the addition of the diazo ester, 20 days were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Alternatively, heating the reaction mixture at 80 °C in a sealed vial led to a significantly shorter reaction time of 19 h, without any impact on the yield. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 20:80 to 30:70) led to the desired product **4j** as a pale yellow oil (125 mg, 0.496 mmol, 50%).

IR (neat): 2932, 2856, 1753, 1723, 1546, 1451, 1413, 1268, 1241, 1082, 1018, 967.

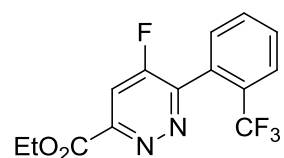
¹H-NMR (CDCl₃, 400 MHz): δ 7.77 (d, J = 10.1 Hz, 1H), 4.50 (q, J = 7.1 Hz, 2H), 3.21 (m, 1H), 2.01–1.66 (m, 7H), 1.48–1.26 (m, 6H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.5 (C), 160.8 (C, d, J = 9 Hz), 160.5 (C, d, J = 277 Hz), 152.2 (C, d, J = 2 Hz), 113.5 (CH, d, J = 16 Hz), 62.8 (CH₂), 39.2 (CH), 31.0 (2xCH₂), 26.3 (2xCH₂), 25.81 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 67 (9), 83 (7), 97 (10), 169 (31), 179 (38), 184 (84), 197 (100), 211 (16), 237 (10), 252 ($M^{+\bullet}$, 5).

HRMS (ESI+): $[M+Na]^+$ calculated for $C_{13}H_{17}FN_2O_2Na$: 275.1166. Found: 275.1165.

Ethyl 5-fluoro-6-(2-(trifluoromethyl)phenyl)pyridazine-3-carboxylate (**4k**)



Prepared according to procedure **B** from 1-ethynyl-2-(trifluoromethyl)benzene (182 mg, 1.07 mmol). After the addition of the diazo ester, 14 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent ($Et_2O/CH_2Cl_2 = 0:100$ to $2:98$, then repurified with Et_2O /petroleum ether = $50:50$) led to the desired product **4k** as a pale yellow oil (250 mg, 0.796 mmol, 74%).

IR (neat): 3073, 2986, 1750, 1725, 1545, 1408, 1314, 1263, 1243, 1169, 1129, 1095, 1067, 962.

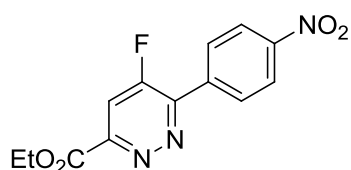
1H -NMR ($CDCl_3$, 400 MHz): δ 8.00 (d, $J = 9.1$ Hz, 1H), 7.85 (m, 1H), 7.75–7.65 (m, 2H), 7.49 (m, 1H), 4.58 (q, $J = 7.1$ Hz, 2H), 1.50 (t, $J = 7.1$ Hz, 3H).

^{13}C -NMR ($CDCl_3$, 100 MHz): δ 163.1 (C, d, $J = 3$ Hz), 160.3 (C, d, $J = 279$ Hz), 154.2 (C, d, $J = 10$ Hz), 153.7 (C, d, $J = 3$ Hz), 132.1 (CH), 131.5 (CH), 130.6 (CH), 129.8 (C, m), 129.7 (C, q, $J = 31$ Hz), 127.1 (CH, q, $J = 5$ Hz), 123.7 (C, q, $J = 274$ Hz), 114.2 (CH, d, $J = 16$ Hz), 63.3 (CH_2), 14.3 (CH_3).

MS (EI, 70 eV): m/z (relative intensity) = 71 (23), 152 (34), 172 (100), 222 (78), 242 (80), 270 (14), 314 ($M^{+\bullet}$, 1).

HRMS (ESI+): $[M+Na]^+$ calculated for $C_{14}H_{10}F_4N_2O_2Na$: 337.0571. Found: 337.0568.

Ethyl 5-fluoro-6-(4-nitrophenyl)pyridazine-3-carboxylate (**4l**)



Prepared according to procedure **B** from 1-ethynyl-4-nitrobenzene (147 mg, 1.0 mmol). After the addition of the diazo ester, 3 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Partial crystallization of the product occurred during the reaction, so small amounts of CH₂Cl₂ were added to the reaction mixture before purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/CH₂Cl₂ = 0:100 to 2:98), which led to the desired product **4l** as a pale yellow solid (210 mg, 0.721 mmol, 72%).

Mp (°C): 158–159.

IR (neat): 3106, 2993, 1746, 1598, 1517, 1350, 1235, 1200, 1093, 1008, 853.

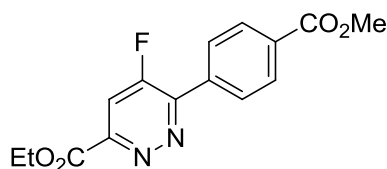
¹H-NMR (CDCl₃, 400 MHz): δ 8.39 (d, *J* = 9.0 Hz, 2H), 8.33 (d, *J* = 9.0 Hz, 2H), 8.05 (d, *J* = 11.2 Hz, 1H), 4.57 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 162.8 (C), 161.0 (C, d, *J* = 282 Hz), 153.3 (C, d, *J* = 3 Hz), 150.8 (C, d, *J* = 4 Hz), 149.3 (C), 137.3 (C, d, *J* = 4 Hz), 130.5 (2xCH, d, *J* = 5 Hz), 124.1 (2xCH), 115.5 (CH, d, *J* = 17 Hz), 63.3 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 71 (63), 76 (27), 149 (77), 172 (16), 202 (59), 219 (100), 247 (21), 291 (M⁺, 2).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₃H₁₀FN₃O₄Na: 314.0548. Found: 314.0547.

Ethyl 5-fluoro-6-(4-(methoxycarbonyl)phenyl)pyridazine-3-carboxylate (**4m**)



Prepared according to procedure **B** from methyl 4-ethynylbenzoate (160 mg, 1.0 mmol). Supplementary amounts of TFDA (2.0 equiv, 0.4 mL) were necessary to reach complete consumption of the alkyne. After the addition of the diazo ester, 19 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/CH₂Cl₂ = 0:100 to 3:97, then repurified with Et₂O/petroleum ether = 40:60) led to the desired product **4m** as a yellow solid (180 mg, 0.592 mmol, 59% overall yield).

Mp (°C): 105–108.

IR (neat): 3084, 2999, 2953, 1715, 1591, 1394, 1379, 1276, 1239, 1110, 1092, 1007, 959.

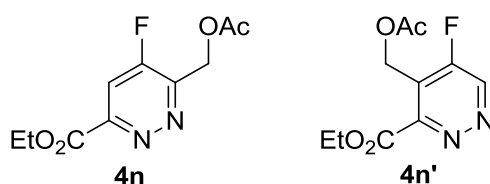
¹H-NMR (CDCl₃, 400 MHz): δ 8.23–8.21 (m, 4H), 8.02 (d, *J* = 11.2 Hz, 1H), 4.58 (q, *J* = 7.1 Hz, 2H), 3.97 (s, 3H), 1.51 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 166.4 (C), 163.0 (C, d, J = 3 Hz), 160.9 (C, d, J = 281 Hz), 152.7 (C, d, J = 4 Hz), 151.9 (C, d, J = 5 Hz), 135.5 (C, d, J = 5 Hz), 132.3 (C), 130.0 (2xCH), 129.4 (2xCH, d, J = 5 Hz), 115.2 (CH, d, J = 17 Hz), 63.1 (CH₂), 52.5 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 71 (19), 162 (96), 173 (32), 200 (66), 217 (13), 232 (100), 260 (27), 273 (12), 304 (M⁺, 3).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₅H₁₃FN₂O₄Na: 327.0752. Found: 327.0749.

Ethyl 6-(acetoxymethyl)-5-fluoropyridazine-3-carboxylate (4n) + ethyl 4-(acetoxymethyl)-5-fluoropyridazine-3-carboxylate (4n')



Prepared according to procedure **B** from propargyl acetate (0.10 mL, 1.0 mmol). After the addition of the diazo ester, 24 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/CH₂Cl₂ = 5:95 to 10:90) led to a mixture of **4n** and **4n'** in a 10:1 ratio in favor of **4n** (65 mg, 0.268 mmol, 27% combined yield). For clarity purposes, only the NMR spectral data for the major regioisomer **4n** are described.

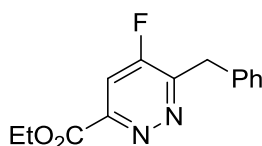
IR (neat): 2985, 1745, 1725, 1598, 1555, 1281, 1223, 1082, 1017, 961, 909, 838.

¹H-NMR (CDCl₃, 400 MHz): δ 7.91 (d, J = 9.7 Hz, 1H), 5.56 (d, J = 1.3 Hz, 2H), 4.56 (q, J = 7.1 Hz, 2H), 2.16 (s, 3H), 1.48 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 170.2 (C), 162.9 (C, d, J = 3 Hz), 161.1 (C, d, J = 280Hz), 154.0 (C, d, J = 3 Hz), 151.2 (C, d, J = 9 Hz), 114.3 (CH, d, J = 15 Hz), 63.2 (CH₂), 60.1 (CH₂, d, J = 1.1 Hz), 20.6 (CH₃), 14.2 (CH₃).

HRMS (ESI+): [M+H]⁺ calculated for C₁₀H₁₂FN₂O₄: 243.0776. Found: 243.0775.

Ethyl 6-benzyl-5-fluoropyridazine-3-carboxylate (4o)



Prepared according to procedure **B** from 3-phenylpropyne (0.25 mL, 2.0 mmol). Intermediate **2o** remained unreacted at rt in the presence of the diazo ester and Et₃N, and heating at 80 °C for 18 h was necessary to reach complete consumption of the *gem*-difluorocyclopropene **2o**. The reaction mixture was concentrated prior to purification by flash column chromatography on silica gel (Et₂O/CH₂Cl₂ = 5:95), which led to the desired product **4o** as a pale yellow oil (75 mg, 0.228 mmol, 14% overall yield).

IR (neat): 3032, 2984, 1750, 1724, 1552, 1414, 1271, 1242, 1225, 1080, 1017, 972.

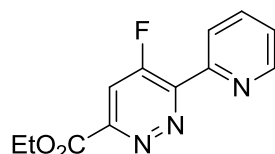
¹H-NMR (CDCl₃, 400 MHz): δ 7.81 (d, *J* = 9.6 Hz, 1H), 7.36–7.32 (m, 2H), 7.31–7.26 (m, 2H), 7.22 (m, 1H), 4.53 (q, *J* = 7.1 Hz, 2H), 4.48 (d, *J* = 2.0 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.4 (C, d, *J* = 3 Hz), 161.0 (C, d, *J* = 277 Hz), 156.4 (C, d, *J* = 10 Hz), 153.0 (C, d, *J* = 3 Hz), 136.2 (C), 129.2 (2xCH), 128.9 (2xCH), 127.3 (CH), 114.1 (CH, d, *J* = 15 Hz), 63.0 (CH₂), 36.8 (CH₂, d, *J* = 2 Hz), 14.3 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 65 (36), 91 (70), 133 (23), 187 (54), 231 (41), 259 (100), 260 (M⁺, 36).

HRMS (ESI+): [M+H]⁺ calculated for C₁₄H₁₄FN₂O₂: 261.1034. Found: 261.1037.

Ethyl 5-fluoro-6-(pyridin-2-yl)pyridazine-3-carboxylate (**6a**)



Prepared according to procedure **A** from 2-ethynylpyridine **5a** (0.10 mL, 1.0 mmol). Supplementary amounts of TMS-CF₃ (1.0 equiv, 0.15 mL, 1.0 mmol), were necessary to reach complete consumption of the alkyne **5a**. After the addition of the diazo ester, 25 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel (EtOAc/CH₂Cl₂ = 30:70) led to the desired product **6a** as a pale yellow solid (45 mg, 0.182 mmol, 18% overall yield).

Mp (°C): 84–86.

IR (neat): 3067, 2977, 2927, 1717, 1588, 1404, 1384, 1299, 1250, 1101, 974.

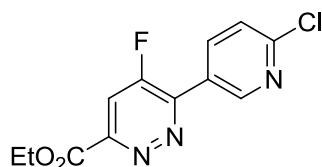
¹H-NMR (CDCl₃, 400 MHz): δ 8.78 (m, 1H), 8.29 (br, d, *J* = 7.8 Hz, 1H), 8.02 (d, *J* = 10.8 Hz, 1H), 7.92 (td, *J* = 7.8, 1.8 Hz, 1H), 7.45 (ddd, *J* = 7.6, 4.8, 1.2 Hz, 1H), 4.55 (q, *J* = 7.1 Hz, 2H), 1.47 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.1 (C, d, J = 3 Hz), 161.3 (C, d, J = 286 Hz), 153.3 (C, d, J = 4 Hz), 152.1 (C, d, J = 3 Hz), 151.7 (C, d, J = 6 Hz), 149.8 (CH), 137.2 (CH), 125.2 (CH), 124.7 (CH), 115.9 (CH, d, J = 16 Hz), 63.1 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 79 (100), 105 (95), 175 (73), 203 (22), 247 (M⁺, 3).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₂H₁₀FN₃O₂Na: 270.0649. Found: 270.0651.

Ethyl 6-(6-chloropyridin-3-yl)-5-fluoropyridazine-3-carboxylate (**6c**)



Prepared according to procedure **A** from 2-chloro-5-ethynylpyridine **5c** (138 mg, 1.0 mmol). Supplementary amounts of TMS-CF₃ (2.0 equiv, 0.30 mL, 2.0 mmol), were necessary to reach complete consumption of the alkyne **5c**. After the addition of the diazo ester, 19 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 20:80 to 50:50) led to the desired product **6c** as a pale yellow solid (151 mg, 0.536 mmol, 54%).

Mp (°C): 120–122.

IR (neat): 3023, 2989, 1727, 1580, 1414, 1344, 1239, 1104, 1004, 956, 863.

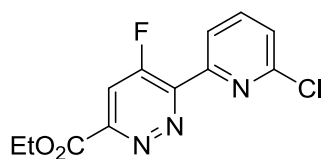
¹H-NMR (CDCl₃, 400 MHz): δ 9.12 (m, 1H), 8.47 (ddd, J = 8.4, 2.5, 1.0 Hz, 1H), 8.02 (d, J = 11.2 Hz, 1H), 7.53 (dd, J = 8.4, 0.7 Hz, 1H), 4.56 (q, J = 7.1 Hz, 2H), 1.48 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 162.9 (C, d, J = 3 Hz), 160.8 (C, d, J = 281 Hz), 154.2 (C), 153.0 (C, d, J = 3 Hz), 150.2 (CH, d, J = 9 Hz), 149.6 (C, d, J = 5 Hz), 139.1 (CH, d, J = 4 Hz), 126.7 (C, d, J = 5 Hz), 124.8 (CH), 115.3 (CH, d, J = 16 Hz), 63.3 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 71 (40), 139 (76), 141 (27), 209 (100), 211 (31), 237 (21), 239 (7), 281 (M⁺, 2).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₂H₉ClFN₃O₂Na: 304.0260. Found: 304.0259.

Ethyl 6-(6-chloropyridin-2-yl)-5-fluoropyridazine-3-carboxylate (**6d**)



Prepared according to procedure **A** from 2-chloro-6-ethynylpyridine **5d** (50 mg, 0.363 mmol). Supplementary amounts of TMS-CF₃ (2.0 equiv, 0.30 mL, 2.0 mmol), were necessary to reach complete consumption of the alkyne **5d**. After the addition of the diazo ester, 16 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 40:60 to 60:40) led to the desired product **6d** as a pale yellow solid (20 mg, 0.071 mmol, 20%).

Prepared according to procedure **B** from 2-chloro-6-ethynylpyridine **5d** (50 mg, 0.363 mmol). After the addition of the diazo ester, 5.5 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 40:60 to 60:40), followed by petroleum ether trituration led to the desired product **6d** as a tan solid (170 mg, 0.604 mmol, 60%).

Mp (°C): 123–124.

IR (neat): 3065, 2991, 2922, 1727, 1584, 1566, 1401, 1375, 1255, 1138, 1107, 1017, 974.

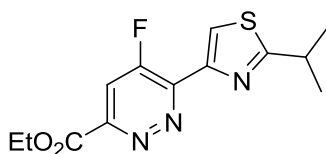
¹H-NMR (CDCl₃, 400 MHz): δ 8.27 (m, 1H), 8.03 (d, J = 10.5 Hz, 1H), 7.91 (t, J = 8.0 Hz, 1H), 7.51 (dd, J = 8.0, 0.9 Hz, 1H), 4.58 (q, J = 7.1 Hz, 2H), 1.50 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.0 (C, d, J = 3 Hz), 161.3 (C, d, J = 287 Hz), 153.6 (C, d, J = 4 Hz), 152.0 (C, d, J = 6 Hz), 151.3 (C), 151.0 (C, d, J = 2 Hz), 139.8 (CH), 126.1 (CH), 123.1 (CH), 116.1 (CH, d, J = 16 Hz), 63.3 (CH₂), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 76 (27), 113 (100), 115 (32), 139 (72), 141, 24), 209 (90), 211 (29), 237 (18), 239 (7), 281 (M⁺, 3), 283 (M⁺, 1).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₂H₉ClFN₃O₂Na: 304.0260. Found: 304.0259.

Ethyl 5-fluoro-6-(2-isopropylthiazol-4-yl)pyridazine-3-carboxylate (**6e**)



Prepared according to procedure **A** from 4-ethynyl-2-isopropylthiazole **5e** (150 mg, 0.992 mmol). Supplementary amounts of TMS-CF₃ (2.0 equiv, 0.30 mL, 2.0 mmol), were necessary to reach complete consumption of the alkyne **5e**. After the addition of the diazo ester, 72 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 20:80 to 50:50), followed by petroleum ether trituration led to the desired product **6e** as a white solid (120 mg, 0.406 mmol, 41%).

Mp (°C): 97–98.

IR (neat): 3099, 2966, 2931, 1718, 1588, 1563, 1478, 1418, 1385, 1323, 1259, 1197, 1095, 1018, 976.

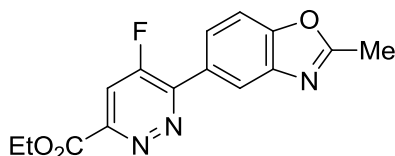
¹H-NMR (CDCl₃, 400 MHz): δ 8.27 (s, 1H), 7.97 (d, *J* = 11.0 Hz, 1H), 4.55 (q, *J* = 7.1 Hz, 2H), 3.46 (hept, *J* = 6.9 Hz, 1H), 1.50–1.44 (m, 9H).

¹³C-NMR (CDCl₃, 100 MHz): δ 179.1 (C), 163.1 (C, d, *J* = 3 Hz), 159.7 (C, d, *J* = 283 Hz), 152.2 (C, d, *J* = 3 Hz), 148.3 (C, d, *J* = 4 Hz), 146.9 (C, d, *J* = 7 Hz), 122.9 (CH, d, *J* = 4 Hz), 115.2 (CH, d, *J* = 16 Hz), 62.9 (CH₂), 33.5 (CH), 23.2 (2xCH₃), 14.2 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 81 (19), 127 (19), 153 (44), 208 (30), 223 (100), 251 (7), 295 (M⁺, 15).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₃H₁₄FN₃O₂SNa: 318.0683. Found: 318.0680.

Ethyl 5-fluoro-6-(2-methylbenzo[d]oxazol-5-yl)pyridazine-3-carboxylate (**6f**)



Prepared according to procedure **A** from 5-ethynyl-2-methylbenzo[d]oxazole **5f** (45 mg, 0.286 mmol). After the addition of the diazo ester, 48 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 30:70 to 100:0) led to the desired product **6f** as a pale yellow solid (66 mg, 0.219 mmol, 77%).

Mp (°C): 138–141.

IR (neat): 3040, 2925, 1719, 1627, 1576, 1400, 1380, 1269, 1246, 1168, 1091, 967, 894.

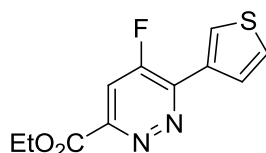
¹H-NMR (CDCl₃, 400 MHz): δ 8.40 (m, 1H), 8.14 (m, 1H), 7.98 (d, *J* = 11.4 Hz, 1H), 7.63 (dd, *J* = 8.6, 0.6 Hz, 1H), 4.56 (q, *J* = 7.1 Hz, 2H), 2.68 (s, 3H), 1.48 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 165.3 (C), 163.2 (C), 160.6 (C, *d*, *J* = 280 Hz), 152.8 (C), 152.7 (C, *d*, *J* = 4 Hz), 152.2 (C, *d*, *J* = 2 Hz), 142.2 (C), 127.8 (C, *d*, *J* = 3 Hz), 126.3 (CH, *d*, *J* = 4 Hz), 121.1 (CH, *d*, *J* = 7 Hz), 115.1 (CH, *d*, *J* = 17 Hz), 110.9 (CH), 63.0 (CH₂), 14.7 (CH₃), 14.3 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 71 (12), 91 (16), 159 (100) 188 (34) 229 (98) 257 (17), 301 (M⁺, 12).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₅H₁₂FN₃O₃Na: 324.0755. Found: 324.0752.

Ethyl 5-fluoro-6-(thiophen-3-yl)pyridazine-3-carboxylate (**6g**)



Prepared according to procedure **B** from 3-ethynylthiophene (108 mg, 1.0 mmol). After the addition of the diazo ester, 72 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel (Et₂O/CH₂Cl₂ = 5:95, then repurified with Et₂O/petroleum ether = 40:60) led to the desired product **6g** as a yellow solid (172 mg, 0.682 mmol, 68%).

Mp (°C): 99–100.

IR (neat): 3104, 3089, 2987, 1741, 1548, 1436, 1344, 1257, 1211, 1099, 1026, 974, 869.

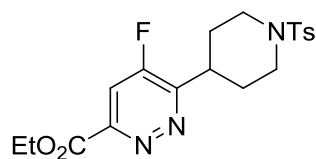
¹H-NMR (CDCl₃, 400 MHz): δ 8.32 (m, 1H), 8.05 (m, 1H), 7.95 (d, *J* = 11.6 Hz, 1H), 7.49 (m, 1H), 4.56 (q, *J* = 7.1 Hz, 2H), 1.49 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.1 (C, *d*, *J* = 3 Hz), 159.6 (d, *J* = 279 Hz), 151.4 (C, *d*, *J* = 3 Hz), 148.6 (C, *d*, *J* = 5 Hz), 132.9 (C, *d*, *J* = 5 Hz), 129.8 (CH, *d*, *J* = 10 Hz), 127.6 (CH, *d*, *J* = 4 Hz), 126.4 (CH, *d*, *J* = 1 Hz), 114.6 (CH, *d*, *J* = 16 Hz), 62.8 (CH₂), 14.2 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 110 (100), 139 (8), 154 (14), 161 (10), 180 (57), 208 (28), 252 (M⁺, 9).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₁H₉FN₂O₂SNa: 275.0261. Found: 275.0261.

Ethyl 5-fluoro-6-(1-tosylpiperidin-4-yl)pyridazine-3-carboxylate (**6j**)



Prepared according to procedure **A** from 4-ethynyl-1-tosylpiperidine **5j** (132 mg, 0.5 mmol). Supplementary amounts of TMS-CF₃ (1.45 mL, 9.7 mmol, 19 equiv), were necessary to reach complete consumption of the alkyne **5j**. The intermediate *gem*-difluorocyclopropene remained unreacted at rt in the presence of the diazo ester and of Et₃N, and heating at 80 °C for 15 h was necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O:petroleum ether = 60:40 to 80:20, then reperfired with diethyl ether/CH₂Cl₂ = 5:95) led to the desired product **6j** as a pale yellow oil (135 mg, 0.331 mmol, 66%).

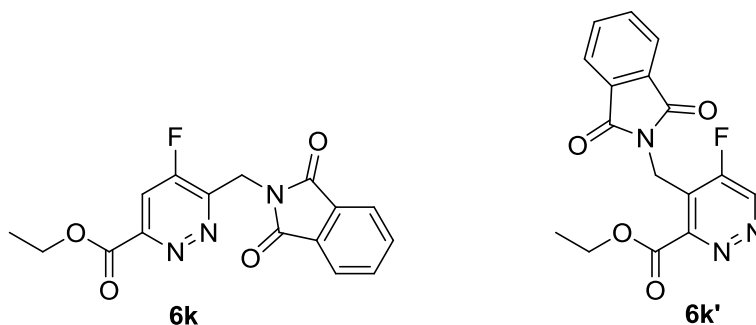
IR (neat): 3066, 2928, 2849, 1747, 1722, 1597, 1546, 1415, 1332, 1269, 1250, 1161, 1082, 1016, 929.

¹H-NMR (CDCl₃, 400 MHz): δ 7.80 (d, J = 10.1 Hz, 1H), 7.69–7.64 (m, 2H), 7.37–7.30 (m, 2H), 4.51 (q, J = 7.1 Hz, 2H), 3.92 (dt, J = 11.8, 2.8 Hz, 2H), 3.16 (tt, J = 11.2, 3.5 Hz, 1H), 2.50 (td, J = 11.8, 2.6 Hz, 2H), 2.44 (s, 3H), 2.28–2.14 (m, 2H), 2.04–1.96 (m, 2H), 1.45 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.3 (C, d, J = 3 Hz), 160.7 (C, d, J = 275 Hz), 158.2 (C, d, J = 9 Hz), 152.8 (C, d, J = 3 Hz), 143.8 (C), 133.2 (C), 129.8 (2xCH), 127.8 (2xCH), 113.8 (CH, d, J = 16Hz), 63.0 (CH₂), 46.2 (2xCH₂), 36.6 (CH, d, J = 2 Hz), 29.3 (2xCH₂), 21.65 (CH₃), 14.3 (CH₃).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₉H₂₂FN₃O₄SNa: 430.1207. Found: 430.1207.

Ethyl 6-((1,3-dioxoisindolin-2-yl)methyl)-5-fluoropyridazine-3-carboxylate (6k) and ethyl 4-((1,3-dioxoisindolin-2-yl)methyl)-5-fluoropyridazine-3-carboxylate (6k')



Prepared according to procedure **B** from *N*-propargylphthalimide **5k** (400 mg, 2.16 mmol). Supplementary amounts of TFDA (3.1 equiv, 1.30 mL) were necessary to reach complete consumption of the alkyne. After the addition of the diazo ester, 20 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 40:60 to 60:40) led to a mixture of **6k** and **6k'** in a 95:5 ratio as a white solid (450 mg, 1.367 mmol, 63% combined yield). For clarity purposes, only the NMR spectral data for the major regioisomer **6k** are described.

Mp (°C): 122–125.

IR (neat): 3475, 3088, 2985, 1773, 1743, 1717, 1591, 1556, 1397, 1269, 1194, 1079, 966, 941.

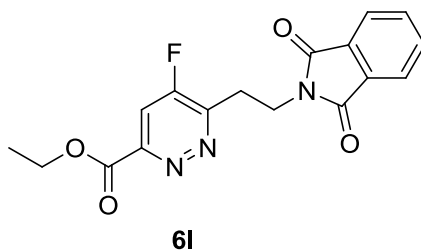
¹H-NMR (CDCl₃, 400 MHz): δ 7.92–7.86 (m, 3H), 7.79–7.72 (m, 2H), 5.33 (d, *J* = 1.1 Hz, 2H), 4.50 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 167.8 (2xC), 162.9 (C, d, *J* = 3 Hz), 160.7 (C, d, *J* = 278 Hz), 153.6 (C, d, *J* = 3.0 Hz), 150.0 (C, d, *J* = 10 Hz), 134.3 (2xCH), 132.2 (2xC), 123.6 (2xCH), 113.8 (CH, d, *J* = 14 Hz), 63.0 (CH₂), 36.3 (CH₂), 14.14 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 50 (23), 76 (53), 104 (46), 117 (15), 133 (14), 160 (64), 161 (100), 212 (12), 257 (62), 285 (M⁺ - CO₂, 6).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₆H₁₂FN₃O₄Na: 352.0704. Found: 352,0699.

Ethyl 6-(2-(1,3-dioxisoindolin-2-yl)ethyl)-5-fluoropyridazine-3-carboxylate (6l)



Prepared according to procedure **B** from *N*-homopropargyl phthalimide **5l** (450 mg, 2.26 mmol). After the addition of the diazo ester, 144 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 60:40 to 100:0), followed by trituration of the resulting beige solid with a 1:1 mixture of Et₂O/pentane led to the desired product **6l** as a white solid (511 mg, 1.488 mmol, 66%).

Mp (°C): 100–104.

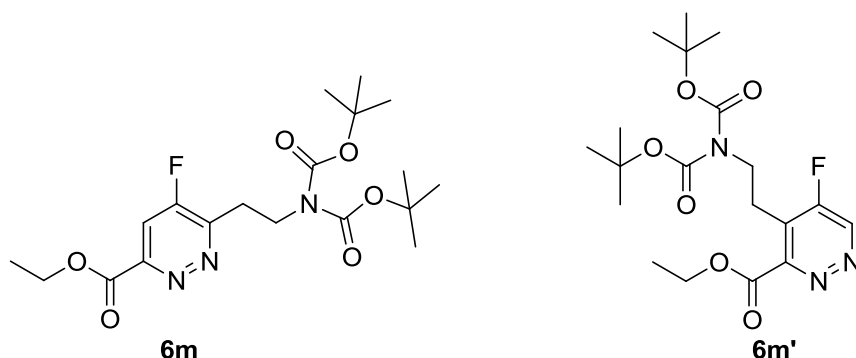
IR (neat): 3457, 3063, 2962, 1764, 1699, 1603, 1547, 1391, 1298, 1260, 1169, 1080, 1001.

¹H-NMR (CDCl₃, 400 MHz): δ 7.85 (d, *J* = 9.7 Hz, 1H), 7.8–7.77 (m, 2H), 7.73–7.68 (m, 2H), 4.53 (q, *J* = 7.1 Hz, 2H), 4.23 (t, *J* = 6.6 Hz, 2H), 3.53 (td, *J* = 6.6, 1.6 Hz, 2H), 1.46 (t, *J* = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 168.0 (2xC), 163.1 (C, d, *J* = 3 Hz), 161.3 (C, d, *J* = 277 Hz), 154.30 (C, d, *J* = 10 Hz), 152.9 (C, d, *J* = 3.0 Hz), 134.1 (2xCH), 131.8 (2xC), 123.4 (2xCH), 113.5 (CH, d, *J* = 15 Hz), 62.9 (CH₂), 35.7 (CH₂), 29.4 (CH₂), 14.2 (CH₃).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₇H₁₄FN₃O₄Na: 366.0861. Found: 366.0860.

Ethyl 6-(2-{bis[(*tert*-butoxy)carbonyl]amino}ethyl)-5-fluoropyridazine-3-carboxylate (6m) and Ethyl 4-(2-{bis[(*tert*-butoxy)carbonyl]amino}ethyl)-5-fluoropyridazine-3-carboxylate (6m')



Prepared according to procedure **B** from *N,N*-Bis[(*tert*-butoxy)carbonyl]-*N*-(but-3-yn-1-yl)carbamate **5m** (400 mg, 1.485 mmol). After the addition of the diazo ester, 160 h were necessary to reach complete consumption of the *gem*-difluorocyclopropene. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 50:50) led to a mixture of the desired products **6m** and **6m'** in a 90:10 ratio in favor of **6m** as a pale yellow oil (451 mg, 1.091 mmol, 73%). For clarity purposes, only the NMR spectral data for the major regioisomer **6m** are described.

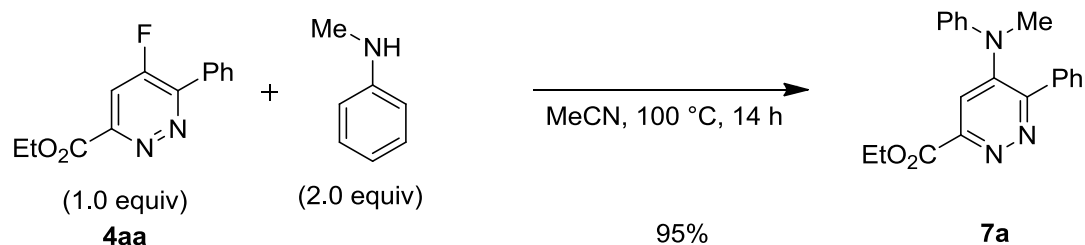
IR (neat): 2982, 2938, 1793, 1751, 1727, 1695, 1553, 1368, 1306, 1230, 1132, 1083, 1020.

¹H-NMR (CDCl₃, 400 MHz): δ 7.81 (d, $J = 9.6$ Hz, 1H), 4.54 (d, $J = 7.1$ Hz, 2H), 4.09 (t, $J = 6.9$ Hz, 2H), 3.43 (td, $J = 7.0, 1.7$ Hz, 2H), 1.46 (t, $J = 7.1$ Hz, 3H), 1.45 (s, 18H). **¹³C-NMR (CDCl₃, 100 MHz):** δ 163.3 (C, d, $J = 3$ Hz), 161.3 (C, d, $J = 276$ Hz), 155.0 (C, d, $J = 10$ Hz), 152.6 (C, d, $J = 3$ Hz), 152.1 (2xC), 113.2 (CH, d, $J = 15$ Hz), 82.7 (CH₂), 62.8 (CH₂), 44.9 (CH₂), 44.4 (CH₂), 29.8 (CH₂, d, $J = 2$ Hz), 28.0 (6xCH₃), 14.2 (CH₃).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₉H₂₈FN₃O₆Na: 436,1854. Found: 436,1854.

4. Experimental Procedures and Spectroscopic Data for products **7**, **8** and **9**

Ethyl 5-(methyl(phenyl)amino)-6-phenylpyridazine-3-carboxylate (**7a**)



In an oven-dried vial, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry MeCN (1.5 mL) was added *N*-methylaniline (2.0 equiv, 44 μ L, 0.405 mmol). The vial was sealed with a teflon-lined cap and heated at 100 °C for 14 h in a pre-equilibrated oil bath. The reaction mixture was allowed to cool down to rt, an aqueous saturated NaHCO₃ solution was added, and the aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (EtOAc/CH₂Cl₂ = 15:85) led to the desired product **7a** as a yellow solid (64 mg, 0.192 mmol, 95%).

Mp (°C): 130–131.

IR (neat): 3063, 2956, 2933, 1746, 1714, 1558, 1492, 1396, 1381, 1263, 1225, 1107, 1006, 846.

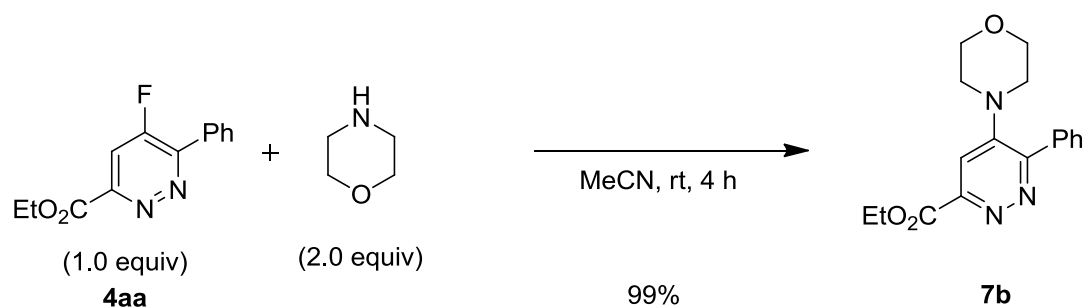
¹H-NMR (CDCl₃, 400 MHz): δ 7.87 (s, 1H), 7.65–7.55 (m, 2H), 7.28–7.23 (m, 3H), 7.17–7.09 (m, 2H), 6.94 (m, 1H), 6.90–6.81 (m, 2H), 4.53 (q, J = 7.1 Hz, 2H), 3.18 (s, 3H), 1.47 (t, J = 7.1 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 164.9 (C), 156.9 (C), 150.2 (C), 147.0 (C), 146.5 (C), 136.7 (C), 129.5 (2xCH), 129.1 (CH), 128.5 (2xCH), 128.2 (2xCH), 124.0 (CH), 121.8 (2xCH), 118.2 (CH), 62.5 (CH₂), 40.9 (CH₃), 14.3 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 77 (88), 89 (51), 116 (47), 131 (46), 143 (52), 157 (81), 180 (25), 207 (10), 246 (13), 261 (100), 333 (M⁺, 350).

HRMS (ESI⁺): [M+H]⁺ calculated for C₂₀H₂₀N₃O₂: 334.1550. Found: 334.1551.

Ethyl 5-(morpholin-4-yl)-6-phenylpyridazine-3-carboxylate (**7b**)



In an oven-dried vial, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry MeCN (0.2 mL) was added neat morpholine (2.0 equiv, 36 μL , 0.409 mmol). The resulting solution was stirred under argon for 4 h, and concentrated in *vacuo*. Purification by flash column chromatography on silica gel (EtOAc/CH₂Cl₂ = 20:80) led to the desired product **7b** as a pale yellow sticky solid (64 mg, 0.192 mmol, 95%).

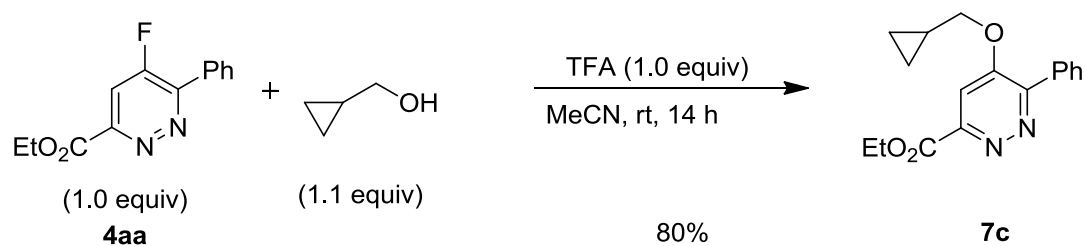
IR (neat): 2963, 2854, 1718, 1564, 1245, 1111, 1009, 982.

¹H-NMR (CDCl₃, 400 MHz): δ 7.91 – 7.86 (m, 2H), 7.56 (s, 1H), 7.50 – 7.36 (m, 3H), 4.49 (q, $J = 7.1$ Hz, 2H), 3.65 (t, $J = 4.7$ Hz, 4H), 3.97 (t, $J = 4.7$ Hz, 4H), 1.44 (t, $J = 7.1$ Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 164.9 (C), 155.3 (C), 150.2 (C), 148.9 (C), 137.2 (C), 129.8 (CH), 128.8 (2xCH), 128.1 (2xCH), 113.9 (CH), 66.0 (2xCH₂), 62.45 (CH₂), 49.32 (2xCH₂), 14.3 (CH₃).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₇H₁₉N₃O₃Na: 336,1319. Found: 336,1316.

Ethyl 5-(cyclopropylmethoxy)-6-phenylpyridazine-3-carboxylate (**7c**)



To a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry MeCN (220 μL) was added neat anhydrous TFA (1.0 equiv, 15 μL , 0.202 mmol), followed by cyclopropyl carbinol (1.1 equiv, 13 μL , 0.231 mmol). The resulting solution was stirred at rt for 80 h. An aqueous saturated NaHCO₃ solution was added, and the aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na₂SO₄, and concentrated in *vacuo*. Purification by flash column chromatography on silica gel (EtOAc/petroleum ether = 20:80) led to the desired product **7c** as a yellow solid (36 mg, 0.121 mmol, 59%).

Mp (°C): 106–108.

IR (neat): 3070, 2989, 2922, 1737, 1559, 1378, 1240, 1107, 1022, 964.

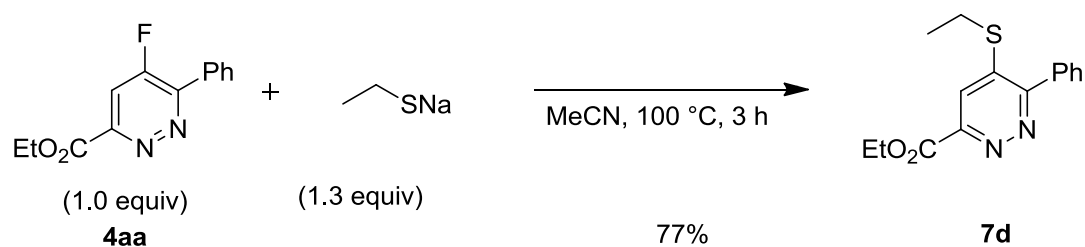
¹H-NMR (CDCl₃, 400 MHz): δ 8.15–8.06 (m, 2H), 7.64 (s, 1H), 7.55–7.41 (m, 2H), 4.54 (q, $J = 7.1$ Hz, 2H), 4.05 (d, $J = 7.0$ Hz, 2H), 1.49 (t, $J = 7.1$ Hz, 3H), 1.33 (m, 1H), 0.82–0.66 (m, 2H), 0.46–0.38 (m, 2H).

¹³C-NMR (CDCl₃, 100 MHz): δ 164.8 (C), 156.3 (C), 154.0 (C), 151.1 (C), 134.0 (C), 130.0 (3xCH), 128.3 (2xCH), 109.2 (CH), 73.7 (CH₂), 62.7 (CH₂), 14.4 (CH₃), 9.7 (CH), 3.6 (2xCH₂).

MS (EI, 70 eV): m/z (relative intensity) = 55 (100), 68 (24), 104 (21), 199 (7), 226 (31), 254 (6), 269 (4), 298 (M⁺, 2).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₇H₁₈N₂O₃Na: 321.1210. Found: 321.1207.

Ethyl 5-(ethylthio)-6-phenylpyridazine-3-carboxylate (**7d**)



In an oven-dried vial, to **4aa** (1.0 equiv, 50 mg, 0.203 mmol) and sodium ethanethiolate (1.3 equiv, 90% w/w, 24 mg, 0.257 mmol) was added dry MeCN (0.2 mL). The vial was sealed with a teflon-lined cap, and the resulting suspension was stirred at 100 °C for 3 h. The reaction mixture was allowed to cool down to rt, an aqueous saturated NaHCO₃ solution was added, and the aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (EtOAc/CH₂Cl₂ = 15:85) led to the desired product **7d** as a white solid (45 mg, 0.156 mmol, 77%).

Mp (°C): 84–86.

IR (neat): 3066, 2961, 2926, 1721, 1548, 1445, 1373, 1334, 1229, 1109, 1003, 897.

¹H-NMR (CDCl₃, 400 MHz): δ 7.96 (s, 1H), 7.77–7.65 (m, 2H), 7.55–7.47 (m, 3H), 4.56 (q, $J = 7.1$ Hz, 2H), 3.01 (q, $J = 7.4$ Hz, 2H), 1.49 (t, $J = 7.1$ Hz, 3H), 1.40 (t, $J = 7.4$ Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 164.6 (C), 160.6 (C), 149.0 (C), 143.4 (C), 135.7 (C), 130.1 (CH), 129.2 (2xCH), 128.5 (2xCH), 122.0 (CH), 62.7 (CH₂), 25.5 (CH₂), 14.4 (CH₃), 12.7 (CH₃).

MS (EI, 70 eV): m/z (relative intensity) = 84 (100), 104 (58), 134 (13), 187 (33), 216 (50), 244 (15), 259 (3), 288 ($M^{+\bullet}$, 5).

HRMS (ESI+): $[M+Na]^+$ calculated for $C_{15}H_{16}N_2O_2SNa$: 311.0825. Found: 311.0822.

Ethyl 5-(nitromethyl)-6-phenylpyridazine-3-carboxylate (**7e**)



In an oven-dried vial, to a solution of **4aa** (1.0 equiv, 110 mg, 0.447 mmol) in dry DMSO (1.1 mL) was added dimethyl malonate (3.0 equiv, 0.15 mL, 1.31 mmol), followed by DBU (3.0 equiv, 200 μ L, 1.34 mmol). The solution immediately turned bright orange. The vial was sealed with a teflon-lined cap and heated at 80 °C for 3 h. The reaction mixture was allowed to cool down to rt, an aqueous saturated NH_4Cl solution was added, acidified to pH~4 with 1N HCl, and the aqueous phase was extracted three times with EtOAc. The combined organic phases were dried over Na_2SO_4 , and concentrated *in vacuo*. Purification by flash column chromatography on silica gel ($Et_2O/CH_2Cl_2 = 5:95$) led to the desired product **7e** as a bright yellow oil (141 mg, 0.394 mmol, 88% yield).

IR (neat): 2956, 1734, 1435, 1396, 1250, 1215, 1122, 1096, 1012..

¹H-NMR (CDCl₃, 400 MHz): δ 8.47 (s, 1H), 7.57–7.55 (m, 5H), 4.97 (s, 1H), 4.58 (q, $J = 7.1$ Hz, 2H), 3.78 (s, 6H), 1.50 (t, $J = 7.1$ Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 166.9 (2xC), 164.1 (C), 163.2 (C), 150.5 (C), 135.3 (C), 131.7 (C), 130.1 (CH), 129.6 (2xCH₂), 129.0 (2xCH₂), 128.9 (CH), 62.8 (CH₂), 53.8 (2xCH₃), 52.9 (CH), 14.4 (CH₃).

HRMS (ESI+): $[M+Na]^+$ calculated for $C_{18}H_{18}N_2O_6Na$: 381,1057. Found: 381,1057.

Ethyl 5-(nitromethyl)-6-phenylpyridazine-3-carboxylate (**7f**)



In an oven-dried vial, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry DMSO (0.6 mL) was added nitromethane (3.0 equiv, 33 μL , 0.606 mmol), followed by DBU (3.0 equiv, 91 μL , 0.609 mmol). The solution immediately turned bright yellow. The vial was sealed with a teflon-lined cap and heated at $80\text{ }^\circ\text{C}$ for 2 h. The reaction mixture was allowed to cool down to rt, an aqueous saturated NH_4Cl solution was added, and the aqueous phase was extracted three times with EtOAc, then four times with CH_2Cl_2 . The combined organic phases were dried over Na_2SO_4 , and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (EtOAc/ CH_2Cl_2 = 20:80) led to the desired product **7f** as a yellow solid (35 mg, 0.122 mmol, 60% yield).

Mp ($^\circ\text{C}$): 152–153.

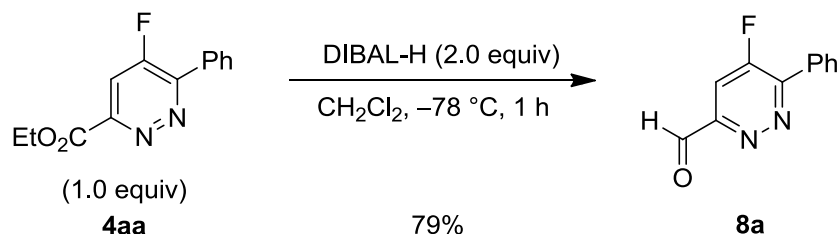
IR (neat): 3068, 2975, 1707, 1551, 1402, 1374, 1307, 1257, 1115, 1013.

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 8.32 (s, 1H), 7.64–7.45 (m, 5H), 5.60 (s, 2H), 4.58 (q, J = 7.1 Hz, 2H), 1.49 (t, J = 7.1 Hz, 3H).

$^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz): δ 163.6 (C), 163.1 (C), 150.8 (C), 134.6 (C), 130.6 (CH), 129.6 (CH), 129.3 (4xCH), 127.7 (C), 75.5 (CH_2), 63.1 (CH_2), 14.4 (CH_3).

HRMS (ESI⁺): $[\text{M}+\text{Na}]^+$ calculated for $\text{C}_{14}\text{H}_{13}\text{N}_3\text{O}_4\text{Na}$: 310.0798. Found: 310.0796.

5-Fluoro-6-phenylpyridazine-3-carbaldehyde (**8a**)



At $-78\text{ }^\circ\text{C}$, to a solution of **4aa** (1.0 equiv, 100 mg, 0.406 mmol) in dry CH_2Cl_2 (4 mL) was added a 1.0 M solution of DIBAL-H (2.0 equiv, 0.80 mL, 0.80 mmol) in CH_2Cl_2 . The resulting solution was stirred at $-78\text{ }^\circ\text{C}$ for 1 h. The reaction mixture was quenched at $-78\text{ }^\circ\text{C}$ with an aqueous saturated NH_4Cl solution, then allowed to warm up to rt and poured onto an aqueous saturated Rochelle salt solution. After stirring for 15 min, the aqueous phase was

extracted three times with CH₂Cl₂, the combined organic phases were dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (diethyl ether/petroleum ether = 40:60) led to the desired product **8a** as a pale yellow solid (65 mg, 0.322 mmol, 79%).

Mp (°C): 89–90.

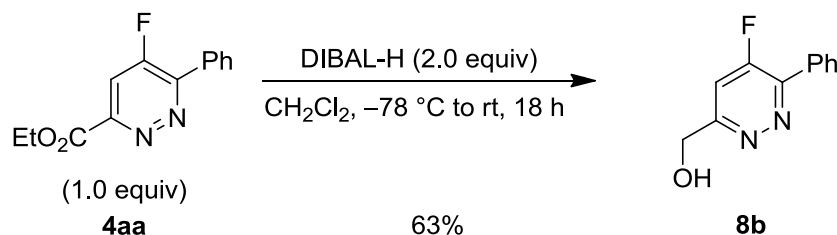
IR (neat): 3064, 2925, 2872, 1707, 1582, 1451, 1407, 1383, 1352, 1205, 1131, 988, 908.

¹H-NMR (CDCl₃, 400 MHz): δ 10.42 (d, *J* = 3 Hz, 1H), 8.16–8.09 (m, 2H), 7.80 (d, *J* = 10.7 Hz, 1H), 7.61–7.54 (m, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 191.0 (CH, d, *J* = 2 Hz), 161.0 (C, d, *J* = 281 Hz), 156.4 (C, d, *J* = 3 Hz), 153.7 (C, d, *J* = 6 Hz), 131.6 (CH), 131.3 (C, d, *J* = 5 Hz), 129.7 (2xCH, d, *J* = 5 Hz), 129.1 (2xCH), 111.3 (CH, d, *J* = 16 Hz).

HRMS (ESI+): [M+H]⁺ calculated for C₁₁H₈FN₂O: 203.0615. Found: 203.0616.

(5-Fluoro-6-phenylpyridazin-3-yl)methanol (**8b**)



At -78 °C, to a solution of **4aa** (100 mg, 0.406 mmol, 1.0 equiv) in dry CH₂Cl₂ (4 mL) was added a 1.0 M solution of DIBAL-H (0.80 mL, 0.80 mmol, 2.0 equiv) in CH₂Cl₂. The resulting solution was stirred at -78 °C for 1 h, allowed to warm up to rt over 1 h, and then stirred at this temperature for 16 h. The reaction mixture was quenched with an aqueous saturated NH₄Cl solution, then poured onto an aqueous saturated Rochelle salt solution. After stirring for 30 min, the aqueous phase was extracted three times with CH₂Cl₂, the combined organic phases were dried over Na₂SO₄ and concentrated *in vacuo*. Purification by flash column chromatography on silica gel with a gradient of eluent (diethyl ether/petroleum ether = 60:40 to 70:30) led to the desired product **8b** as a pale orange oil (52 mg, 0.255 mmol, 63%).

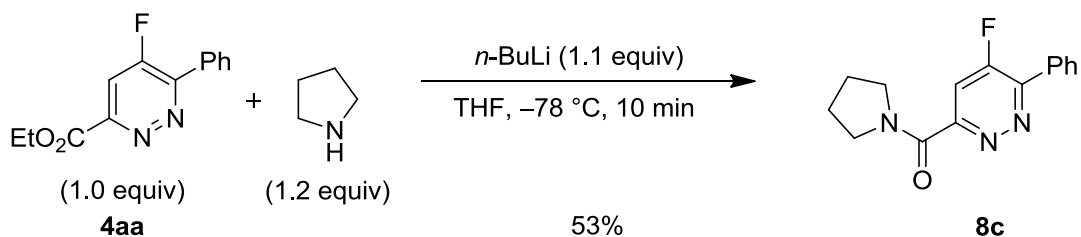
IR (neat): 3421, 3198 (broad), 3021, 1601, 1541, 1421, 1381, 1355, 1320, 1229, 1127, 1080, 1034, 968.

¹H-NMR (CDCl₃, 400 MHz): δ 8.01–7.91 (m, 2H), 7.56–7.47 (m, 3H), 7.44 (d, *J* = 11.4 Hz, 1H), 5.05 (s, 1H), 3.67 (broad, s, 1H).

¹³C-NMR (CDCl₃, 100 MHz): δ 164.1 (C, d, *J* = 4 Hz), 161.1 (C, d, *J* = 279 Hz), 151.1 (C, d, *J* = 7 Hz), 131.9 (C, d, *J* = 4 Hz), 130.5 (CH), 129.1 (2xCH, d, *J* = 5 Hz), 128.9 (2xCH), 111.9 (CH, d, *J* = 15 Hz), 63.2 (CH₂).

HRMS (ESI⁺): [M+H]⁺ calculated for C₁₁H₁₀FN₂O: 205.0772. Found: 205.0773.

(5-Fluoro-6-phenylpyridazin-3-yl)(pyrrolidin-1-yl)methanone (8c)



At 0 °C, to a solution of pyrrolidine (1.2 equiv, 20 μL, 0.244 mmol) in dry THF (0.5 mL) was added a 2.4 M solution of *n*-BuLi (1.1 equiv, 93 μL, 0.223 mmol) in hexanes. The reaction mixture was allowed to warm up to rt and stirred for 10 min, and then added to a -78 °C solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry THF (0.5 mL). The solution instantly turned deep red. The solution was stirred at -78 °C for 10 min, and was then quenched at this temperature with an aqueous saturated NH₄Cl solution. The mixture was then allowed to warm up to rt, and poured onto aqueous saturated NH₄Cl. The aqueous phase was extracted three times with diethyl ether, the combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (EtOAc/petroleum ether = 50:50) led to the desired product **8c** as a pale orange solid (29 mg, 0.107 mmol, 53%).

mp (°C): 140-143.

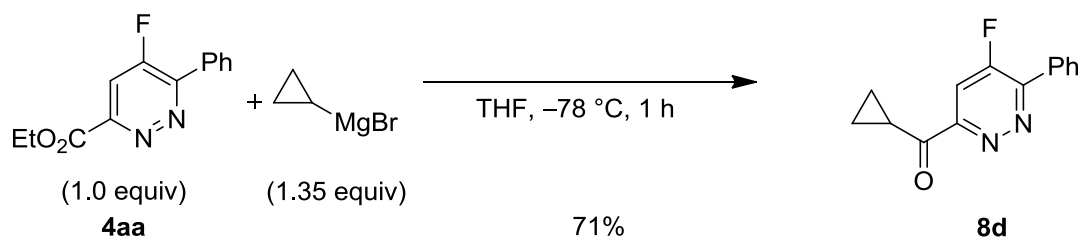
IR (neat): 3054, 2978, 1615, 1589, 1537, 1444, 1401, 1338, 1265, 1186, 1134, 992.

¹H-NMR (CDCl₃, 400 MHz): δ 8.13–8.04 (m, 2H), 7.91 (d, *J* = 11.5 Hz, 1H), 7.58–7.52 (m, 3H), 4.09–4.02 (m, 2H), 3.80–3.71 (m, 2H), 2.06–1.93 (m, 4H).

¹³C-NMR (CDCl₃, 100 MHz): δ 162.5 (C), 161.0 (C, d, *J* = 279 Hz), 157.7 (C, d, *J* = 3 Hz), 131.8 (C, d, *J* = 5 Hz), 131.0 (CH), 129.4 (2xCH, d, *J* = 5 Hz), 129.0 (2xCH), 115.0 (CH, d, *J* = 16 Hz), 49.9 (CH₂), 47.9 (CH₂), 26.9 (CH₂), 24.0 (CH₂).

HRMS (ESI⁺): [M+H]⁺ calculated for C₁₅H₁₅FN₃O: 272.1194. Found: 272.1197.

Cyclopropyl(5-fluoro-6-phenylpyridazin-3-yl)methanone (**8d**)



At $-78\text{ }^{\circ}\text{C}$, in an oven dried vial, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry THF (1 mL) was added a 1.0 M solution of cyclopropylmagnesium bromide (1.35 equiv, 0.275 mL, 0.275 mmol) in 2-methyl-tetrahydrofuran. The solution instantly turned deep red. The solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 1 h, and was then quenched at this temperature with an aqueous saturated NH_4Cl solution. The mixture was then allowed to warm up to rt, and poured onto aqueous saturated NH_4Cl . The aqueous phase was extracted three times with diethyl ether, the combined organic phases were dried over Na_2SO_4 , and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (diethyl ether/petroleum ether = 10:90) led to the desired product **8d** as a pale yellow solid (35 mg, 0.144 mmol, 71%).
Mp ($^{\circ}\text{C}$): 126–128.

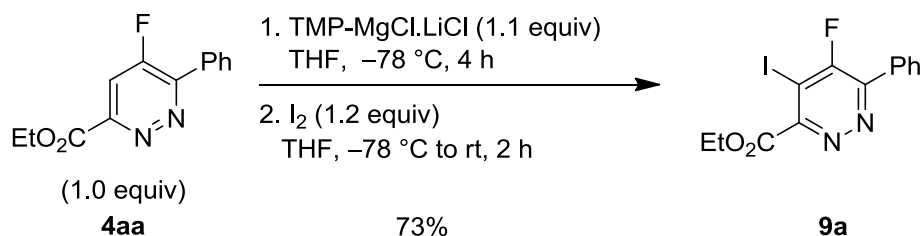
IR (neat): 3062, 2924, 1675, 1583, 1540, 1403, 1205, 1157, 1049, 1019, 927.

$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 8.18–8.07 (m, 2H), 7.89 (d, $J = 11.4$ Hz, 1H), 7.62–7.53 (m, 3H), 3.73 (tt, $J = 7.9, 4.6$ Hz, 1H), 1.41–1.34 (m, 2H), 1.27–1.21 (m, 2H).

$^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz): δ 199.0 (C, d, $J = 1$ Hz), 161.2 (C, d, $J = 280$ Hz), 157.0 (C, d, $J = 3$ Hz), 153.1 (C, d, $J = 6$ Hz), 131.6 (C, d, $J = 5$ Hz), 131.2 (CH), 129.5 (2xCH, d, $J = 5$ Hz), 129.0 (2xCH), 111.9 (CH, d, $J = 16$ Hz), 16.9 (CH), 13.8 (2xCH₂).

HRMS (ESI⁺): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{14}\text{H}_{12}\text{FN}_2\text{O}$: 243.0928. Found: 243.0928.

Ethyl 5-fluoro-4-iodo-6-phenylpyridazine-3-carboxylate (**9a**)



At $-78\text{ }^{\circ}\text{C}$, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry THF (1 mL) was added a 1.0 M solution of TMP-MgCl.LiCl (1.1 equiv, 225 μL , 0.225 mmol) dropwise. The resulting solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 4 h, and a solution of I_2 (1.2 equiv, 61 mg, 0.245 mmol) in THF (0.3 mL) was added dropwise. The resulting solution was allowed to slowly

warm up to rt over 2 h, and then quenched with an aqueous saturated NH₄Cl solution. An aqueous saturated Na₂S₂O₃ solution was added, and the aqueous phase was extracted four times with Et₂O. The combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 15:85) led to the desired product **9a** as a pale yellow solid (55 mg, 0.148 mmol, 73%).

Mp (°C): 92–93.

IR (neat): 3059, 2977, 2931, 1743, 1546, 1441, 1378, 1264, 1184, 1122, 1011, 863.

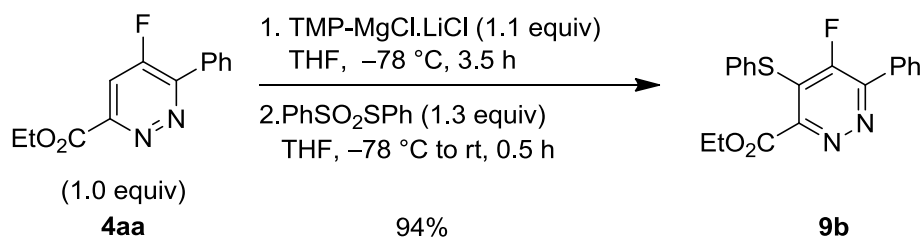
¹H-NMR (CDCl₃, 400 MHz): δ 8.14–7.83 (m, 2H), 7.72–7.36 (m, 3H), 4.56 (q, *J* = 7.2 Hz, 2H), 1.48 (t, *J* = 7.2 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.7 (C, d, *J* = 2 Hz), 160.9 (d, *J* = 275 Hz), 157.0 (C), 151.0 (d, *J* = 10 Hz), 131.3 (CH), 130.8 (C, d, *J* = 5 Hz), 129.6 (2xCH, d, *J* = 5 Hz), 129.0 (2xCH), 88.0 (d, *J* = 22 Hz), 63.3 (CH₂), 14.2 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 77 (39), 104 (99), 144 (27), 173 (100), 300 (67), 328 (26), 372 (M⁺, 4).

HRMS (ESI⁺): [M+Na]⁺ calculated for C₁₃H₁₀FIN₂O₂Na: 394.9663. Found: 394.9665.

Ethyl 5-fluoro-6-phenyl-4-(phenylthio)pyridazine-3-carboxylate (**9b**)



At -78 °C, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry THF (1 mL) was added a 1.0 M solution of TMP-MgCl.LiCl (1.1 equiv, 225 μL, 0.225 mmol) dropwise. The resulting solution was stirred at -78 °C for 3.5 h, and a solution of [(benzenesulfonyl)sulfanyl]benzene (1.3 equiv, 66 mg, 0.264 mmol) in THF (0.5 mL) was added dropwise. The resulting solution was stirred at -78 °C for 30 min, then allowed to warm up to rt over 5 min, and immediately quenched with an aqueous saturated NH₄Cl solution. The aqueous phase was extracted four times with Et₂O, the combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 25:75) led to the desired product **9b** as a pale yellow solid (68 mg, 0.192 mmol, 94%).

Mp (°C): 90–92.

IR (neat): 3054, 3000, 2911, 1718, 1539, 1475, 1388, 1320, 1254, 1222, 1145, 1022, 972.

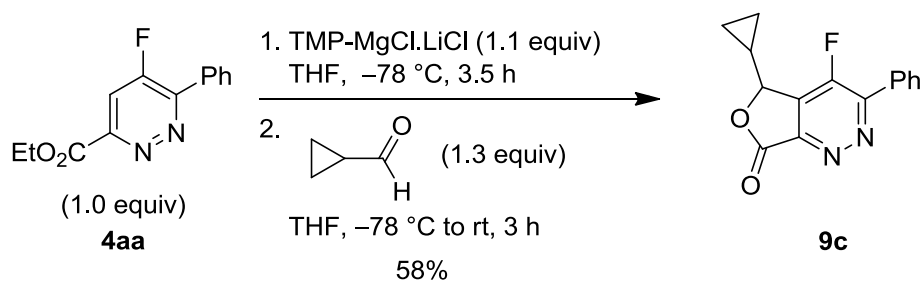
¹H-NMR (CDCl₃, 400 MHz): δ ¹H NMR (400 MHz, CDCl₃) δ 7.96–7.91 (m, 2H), 7.55–7.45 (m, 5H), 7.41–7.28 (m, 3H), 4.44 (q, *J* = 7.2 Hz, 2H), 1.43 (t, *J* = 7.2 Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 163.7 (C, d, *J* = 3 Hz), 159.1 (C, d, *J* = 278 Hz), 153.4 (C), 151.6 (C, d, *J* = 8 Hz), 132.5 (2xCH, d, *J* = 1 Hz), 131.4 (C, d, *J* = 4 Hz), 131.3 (C, d, *J* = 3 Hz), 131.0 (CH), 129.7 (2xCH), 129.5 (2xCH, d, *J* = 5 Hz), 129.1 (CH), 128.9 (2xCH), 127.7 (C, d, *J* = 12 Hz), 63.1 (CH₂), 14.2 (CH₃).

MS (EI, 70 eV): *m/z* (relative intensity) = 77 (34), 109 (15), 252 (9), 281 (100), 310 (40), 354 (M⁺, 16).

HRMS (ESI+): [M+Na]⁺ calculated for C₁₉H₁₅FN₂O₂SNa: 377.0730. Found: 377.0729.

5-Cyclopropyl-4-fluoro-3-phenylfuro[3,4-c]pyridazin-7(5H)-one (**9c**)



At -78 °C, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry THF (1 mL) was added a 1.0 M solution of TMP-MgCl.LiCl (1.1 equiv, 225 μL, 0.225 mmol) dropwise. The resulting solution was stirred at -78 °C for 3.5 h, and neat cyclopropanecarboxaldehyde (1.3 equiv, 20 μL, 0.264 mmol) was then added. The resulting solution was stirred at -78 °C for 1 h, then slowly allowed to warm up to -50 °C over 2 h, then to rt over 5 min, and immediately quenched with an aqueous saturated NH₄Cl solution. The aqueous phase was extracted four times with EtOAc, the combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel with a gradient of eluent (Et₂O/petroleum ether = 30:70 to 60:40) led to the desired product **9c** as a white solid (32 mg, 0.118 mmol, 58%).

Mp (°C): 172–174.

IR (neat): 3076, 2929, 1783, 1614, 1417, 1310, 1225, 1175, 1101, 951, 868.

¹H-NMR (CDCl₃, 400 MHz): δ 8.16–8.03 (m, 2H), 7.67–7.48 (m, 3H), 5.11 (dd, *J* = 8.5, 1.0 Hz, 1H), 1.31–1.21 (m, 1H), 0.98–0.67 (m, 4H).

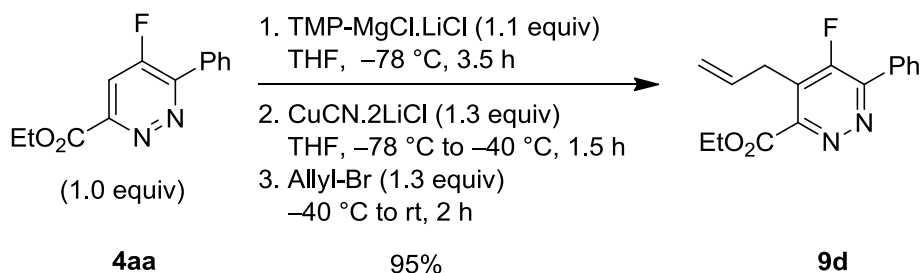
¹³C-NMR (CDCl₃, 100 MHz): δ 164.5 (C, d, *J* = 1 Hz), 155.5 (C, d, *J* = 287 Hz), 152.8 (C, d, *J* = 4 Hz), 150.4 (C, d, *J* = 2 Hz), 132.1 (C, d, *J* = 14 Hz), 131.6 (CH), 131.0 (C, d, *J* = 5 Hz),

129.9 (2xCH, d, $J = 5$ Hz), 129.2 (2xCH), 81.4 (CH, d, $J = 2$ Hz), 13.7 (CH₃), 4.2 (CH₂), 2.9 (CH₂, d, $J = 2$ Hz).

MS (EI, 70 eV): m/z (relative intensity) = 77 (60), 104 (19), 144 (24), 186 (11), 214 (7), 229 (11), 242 (14), 270 (M⁺, 100).

HRMS (ESI+): [M+H]⁺ calculated for C₁₅H₁₂FN₂O₂: 271.0877. Found: 271.0879.

Ethyl 4-allyl-5-fluoro-6-phenylpyridazine-3-carboxylate (**9d**)



At -78 °C, to a solution of **4aa** (1.0 equiv, 50 mg, 0.203 mmol) in dry THF (1 mL) was added a 1.0 M solution of TMP-MgCl.LiCl (1.1 equiv, 225 μ L, 0.225 mmol) dropwise. The resulting solution was stirred at -78 °C for 3.5 h, a 1.0 M solution of CuCN.2LiCl (1.3 equiv, 0.264 mL, 0.264 mmol) in THF was then added dropwise at -78 °C. The resulting solution was stirred at -78 °C for 30 min, then allowed to warm up to -40 °C over 1 h. Neat allyl bromide (1.3 equiv, 23 μ L, 0.264 mmol) was added, the resulting solution was allowed to warm up to rt over 2 h, and then quenched with an aqueous saturated NH₄Cl solution. The aqueous phase was extracted four times with EtOAc, the combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O /petroleum ether = 25:75) led to the desired product **9d** as a pale yellow solid (55 mg, 0.192 mmol, 95%).

Mp (°C): 48–52.

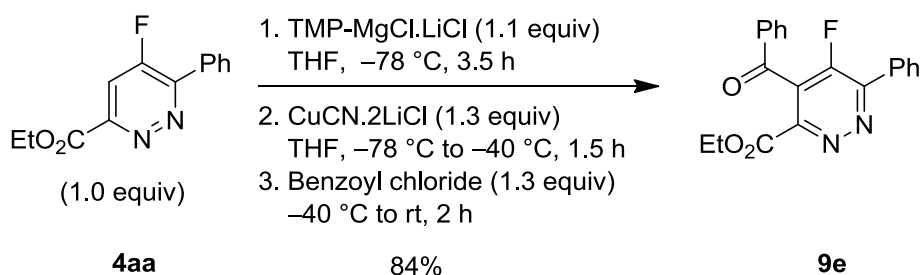
IR (neat): 3064, 2982, 1724, 1639, 1581, 1407, 1258, 1102, 1020, 923.

¹H-NMR (CDCl₃, 400 MHz): δ 8.12–8.05 (m, 2H), 7.58–7.52 (m, 3H), 5.96 (m, 1H), 5.19–5.08 (m, 2H), 4.53 (q, $J = 7.1$ Hz, 2H), 3.80 (dq_{app}, $J = 6.3, 1.5$ Hz, 2H), 1.48 (t, $J = 7.1$ Hz, 3H).

¹³C-NMR (CDCl₃, 100 MHz): δ 164.3 (C, d, $J = 3$ Hz), 159.4 (C, d, $J = 276$ Hz), 152.7 (C), 151.6 (C, d, $J = 8$ Hz), 132.8 (CH), 131.8 (C, d, $J = 5$ Hz), 130.9 (CH), 129.5 (2xCH, d, $J = 5$ Hz), 128.9 (2xCH), 127.7 (C, d, $J = 13$ Hz), 118.2 (CH₂), 62.8 (CH₂), 28.3 (CH₂, d, $J = 4$ Hz), 14.3 (CH₃).

HRMS (ESI+): [M+H]⁺ calculated for C₁₆H₁₆FN₂O₂: 287.1190. Found: 287.1192.

Ethyl 4-benzoyl-5-fluoro-6-phenylpyridazine-3-carboxylate (**9e**)



At $-78\text{ }^{\circ}\text{C}$, to a solution of **4aa** (1.0 equiv, 400 mg, 1.62 mmol) in dry THF (8 mL) was added a 1.0 M solution of TMP-MgCl.LiCl (1.2 equiv, 2 mL, 2.0 mmol) dropwise. The resulting solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 3.5 h, a 1.0 M solution of CuCN.2LiCl (1.3 equiv, 2.1 mL, 2.1 mmol) in THF was then added dropwise at $-78\text{ }^{\circ}\text{C}$, the resulting solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min, then allowed to warm up to $-40\text{ }^{\circ}\text{C}$ over 1 h. Neat benzoyl chloride (1.3 equiv, 0.245 mL, 2.11 mmol) was added, the resulting solution was allowed to warm up to rt over 30 min, stirred at rt for 1 h, and then quenched with an aqueous saturated NH_4Cl solution. The aqueous phase was extracted four times with Et_2O , the combined organic phases were dried over Na_2SO_4 , and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et_2O /petroleum ether = 35:65) led to the desired product **9e** as a pale yellow solid (480 mg, 1.37 mmol, 84%).

Mp ($^{\circ}\text{C}$): 140–141.

IR (neat): 3069, 2976, 1715, 1682, 1597, 1453, 1393, 1316, 1284, 1260, 1220, 1026, 958.

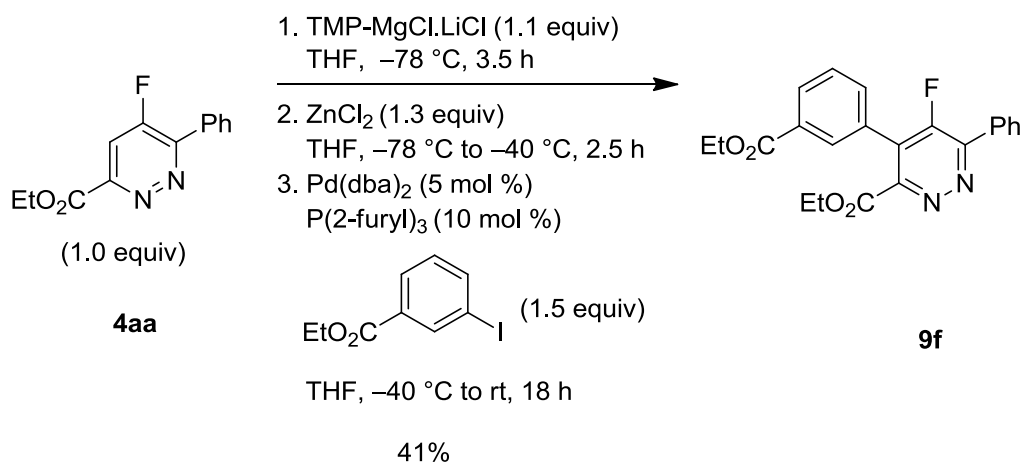
$^1\text{H-NMR}$ (CDCl_3 , 400 MHz): δ 8.18–8.10 (m, 2H), 7.85–7.80 (m, 2H), 7.67 (m, 1H), 7.60–7.49 (m, 5H), 4.39 (q, $J = 7.2\text{ Hz}$, 2H), 1.30 (t, $J = 7.1\text{ Hz}$, 3H).

$^{13}\text{C-NMR}$ (CDCl_3 , 100 MHz): δ 188.2 (C, d, $J = 2\text{ Hz}$), 162.7 (C, d, $J = 3\text{ Hz}$), 157.1 (C, d, $J = 279\text{ Hz}$), 152.9 (C, d, $J = 6\text{ Hz}$), 149.2 (C), 135.8 (C), 134.9 (CH), 131.7 (CH), 131.0 (C, d, $J = 5\text{ Hz}$), 129.7 (2xCH, d, $J = 6\text{ Hz}$), 129.3 (2xCH), 129.2 (4xCH), 128.2 (C, d, $J = 16\text{ Hz}$), 63.4 (CH_2), 14.0 (CH_3).

MS (EI, 70 eV): m/z (relative intensity) = 51 (20), 77 (100), 105 (97), 250 (12), 277 (34), 306 ($\text{M-CH}_2\text{CHOH}^+$, 41).

HRMS (ESI+): $[\text{M}+\text{H}]^+$ calculated for $\text{C}_{20}\text{H}_{16}\text{FN}_2\text{O}_3$: 351.1139. Found: 351.1139.

Ethyl 4-(3-(ethoxycarbonyl)phenyl)-5-fluoro-6-phenylpyridazine-3-carboxylate (**9f**)



At -78 °C, to a solution of **4aa** (1.0 equiv, 100 mg, 0.203 mmol) in dry THF (2 mL) was added a 1.0 M solution of TMP-MgCl.LiCl (1.2 equiv, 0.5 mL, 0.5 mmol) dropwise. The resulting solution was stirred at -78 °C for 3.5 h, a 1.0 M solution of ZnCl₂ (1.3 equiv, 0.53 mL, 0.530 mmol) in THF was then added dropwise at -78 °C, the resulting solution was stirred at -78 °C for 30 min, then allowed to warm up to -40 °C over 2 h. A solution of Pd(dba)₂ (0.05 equiv, 12 mg, 0.0209 mmol) and tri(2-furyl)phosphine (0.1 equiv, 9.5 mg, 0.0409 mmol) in THF (1 mL) was then added dropwise at -40 °C, followed by neat ethyl 3-iodobenzoate (1.5 equiv, 100 μL, 0.601 mmol). The resulting solution was allowed to warm up to rt over 1 h, stirred for 17 h, and then quenched with an aqueous saturated NH₄Cl solution. The aqueous phase was extracted four times with EtOAc, the combined organic phases were dried over Na₂SO₄, and concentrated *in vacuo*. Purification by flash column chromatography on silica gel (Et₂O/petroleum ether = 30:70) led to the desired product **9f** as a pale yellow oil (65 mg, 0.165 mmol, 41% yield).

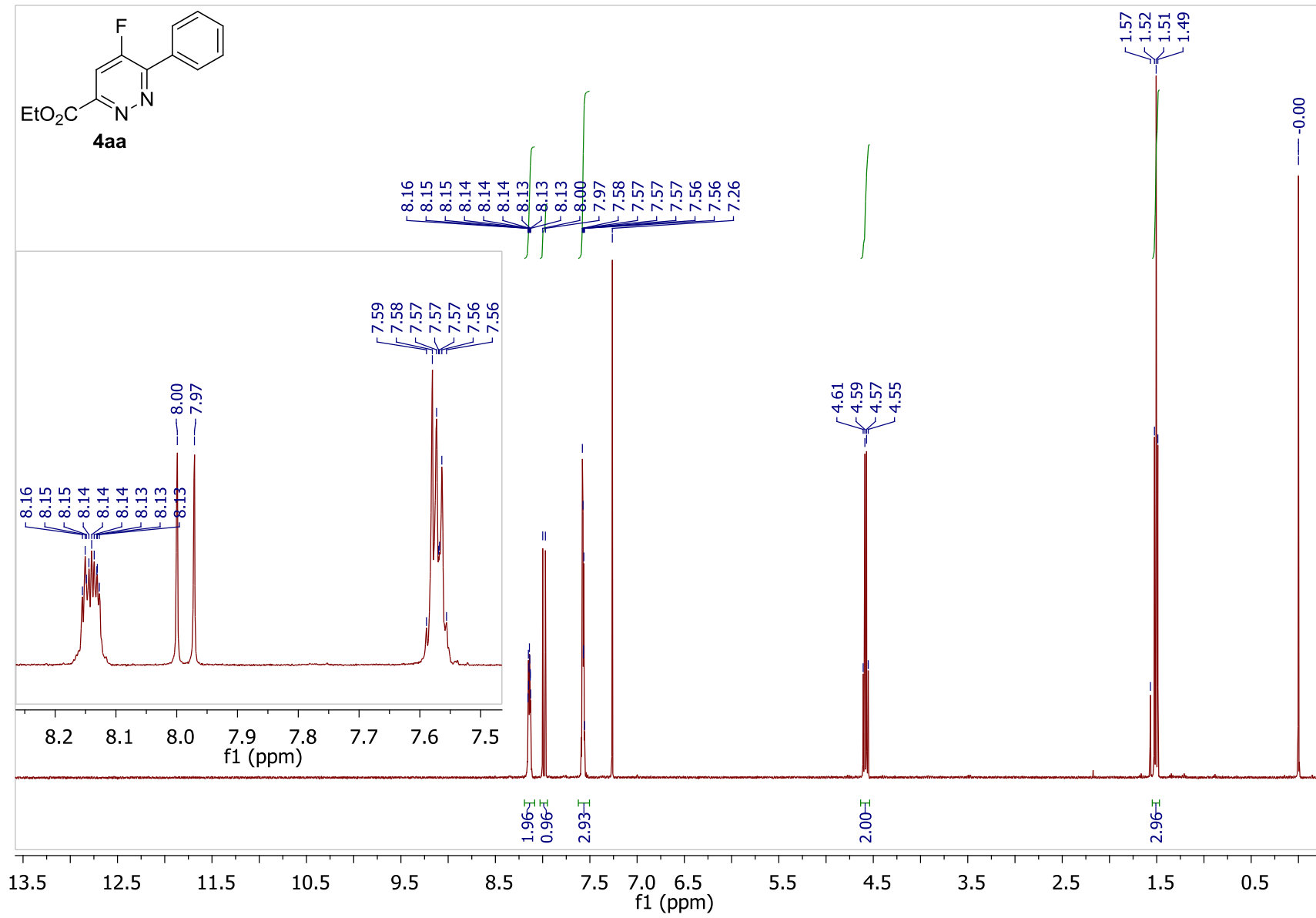
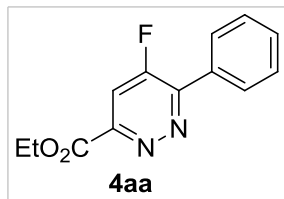
IR (neat): 3063, 2981, 1718, 1579, 1401, 1299, 1249, 1176, 1112, 1023.

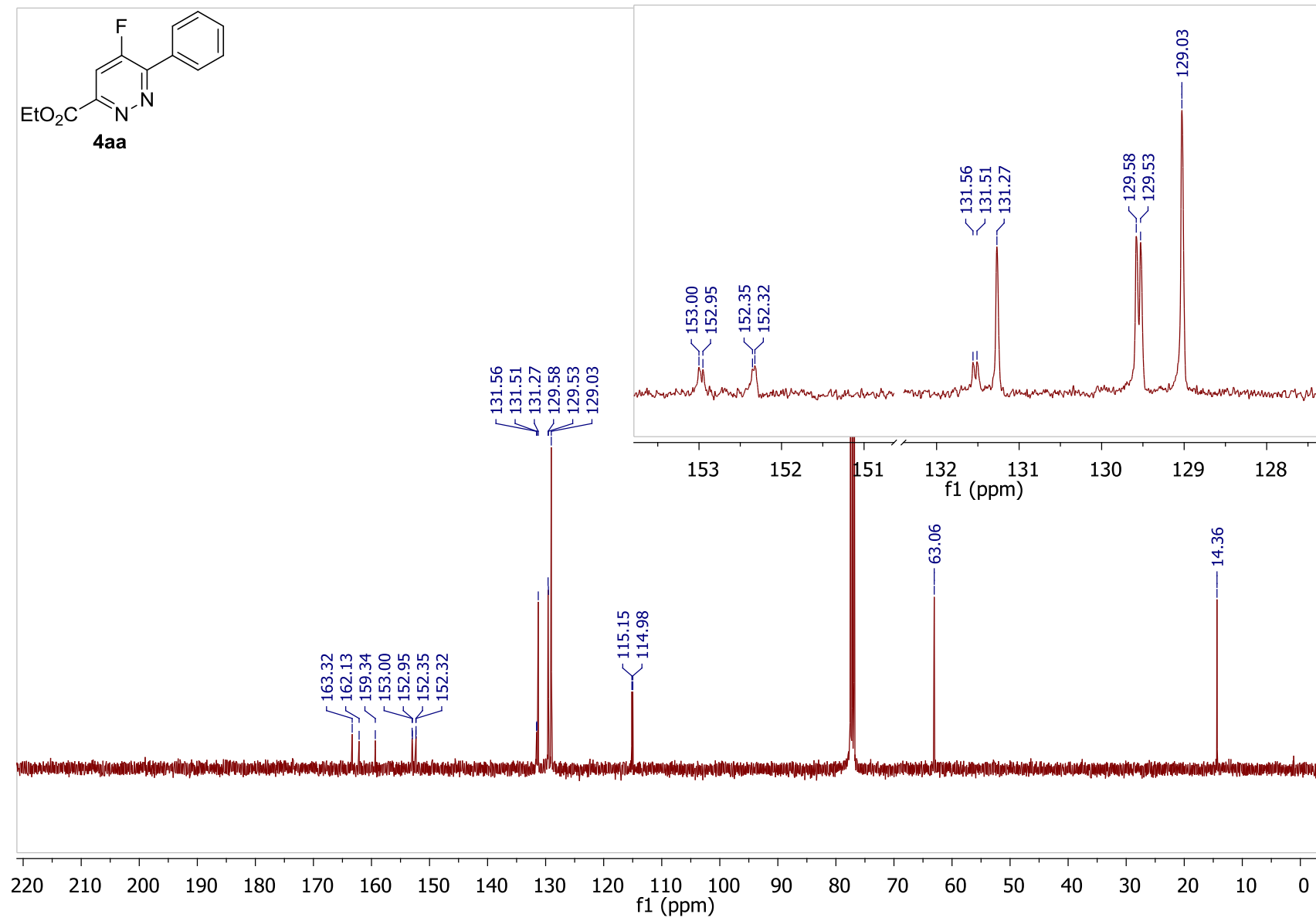
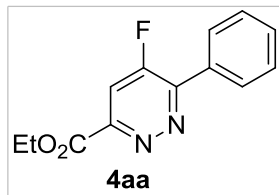
¹H-NMR (CDCl₃, 400 MHz): δ 8.20 (m, 1H), 8.13–8.08 (m, 3H), 7.63–7.59 (m, 2H), 7.59–7.54 (m, 3H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.40 (t, *J* = 7.1 Hz, 3H), 1.21 (t, *J* = 7.1 Hz, 3H).

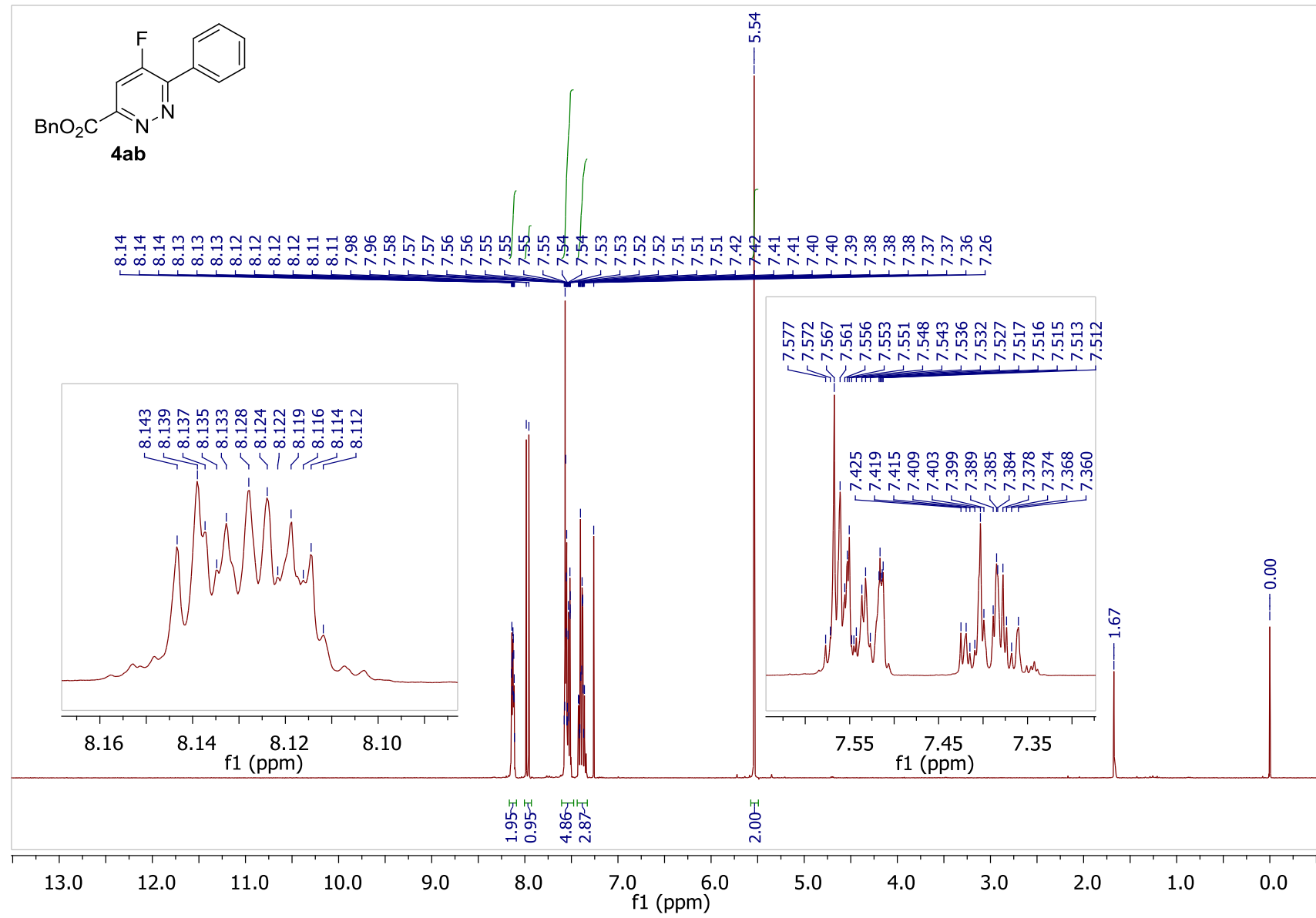
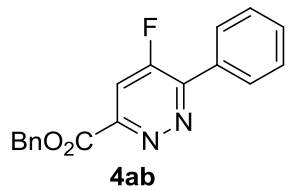
¹³C-NMR (CDCl₃, 100 MHz): δ 165.8 (C), 163.9 (C, d, *J* = 3 Hz), 157.5 (C, d, *J* = 278 Hz), 153.0 (C), 152.4 (C, d, *J* = 8 Hz), 133.4 (CH), 131.6 (C, d, *J* = 5 Hz), 131.3 (C), 131.1 (CH), 131.0 (CH), 130.3 (CH, d, *J* = 1 Hz), 129.6 (2xCH, d, *J* = 5 Hz), 129.02 (2xCH), 129.00 (CH), 128.83 (C), 127.0 (C, d, *J* = 12 Hz), 62.8 (CH₂), 61.6 (CH₂), 14.4 (CH₃), 14.0 (CH₃).

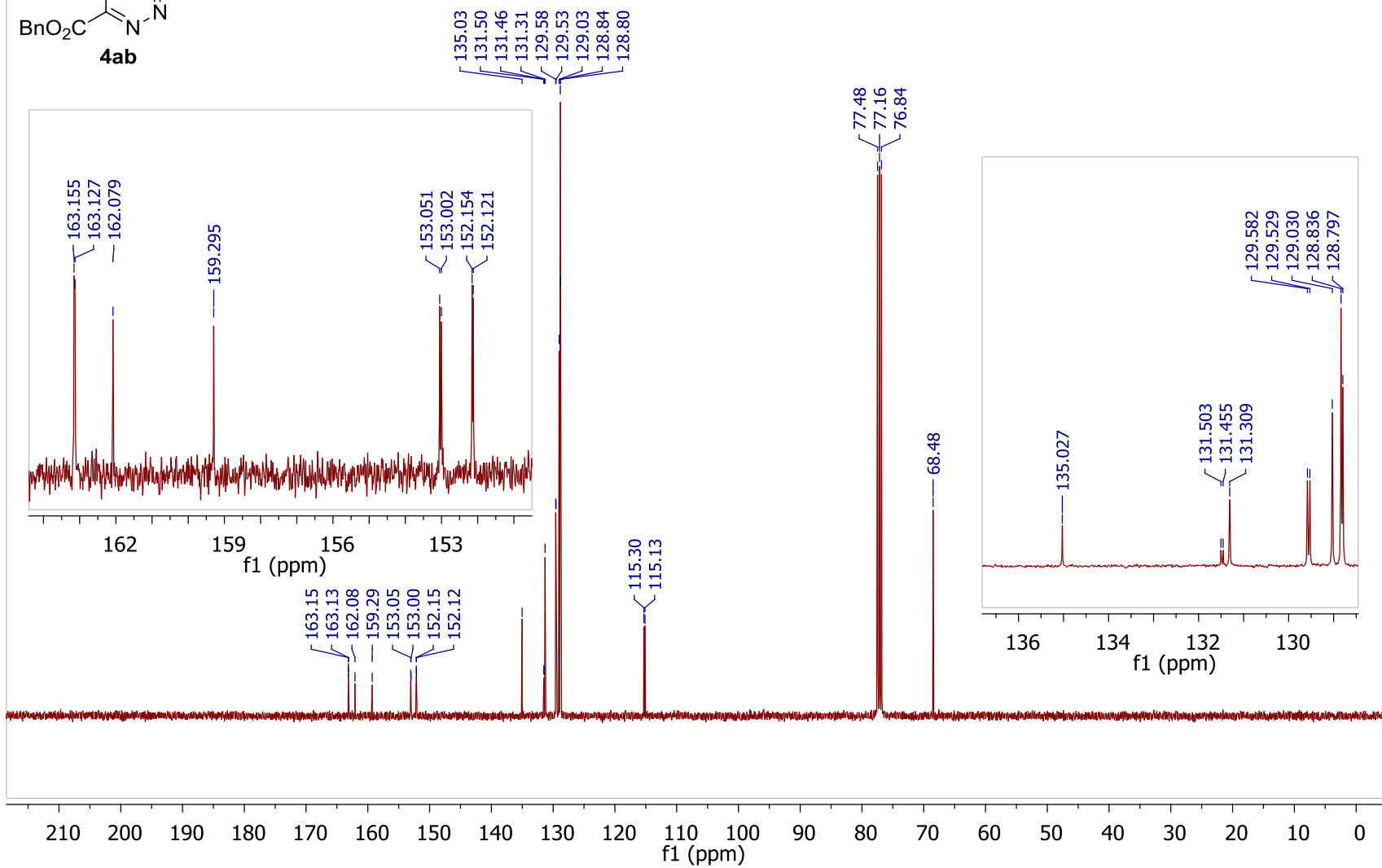
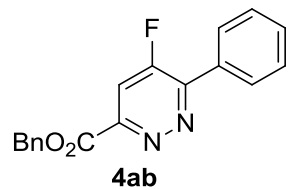
HRMS (ESI⁺): [M+Na]⁺ calculated for C₂₂H₁₉FN₂O₄Na: 417.1221. Found: 417.1219.

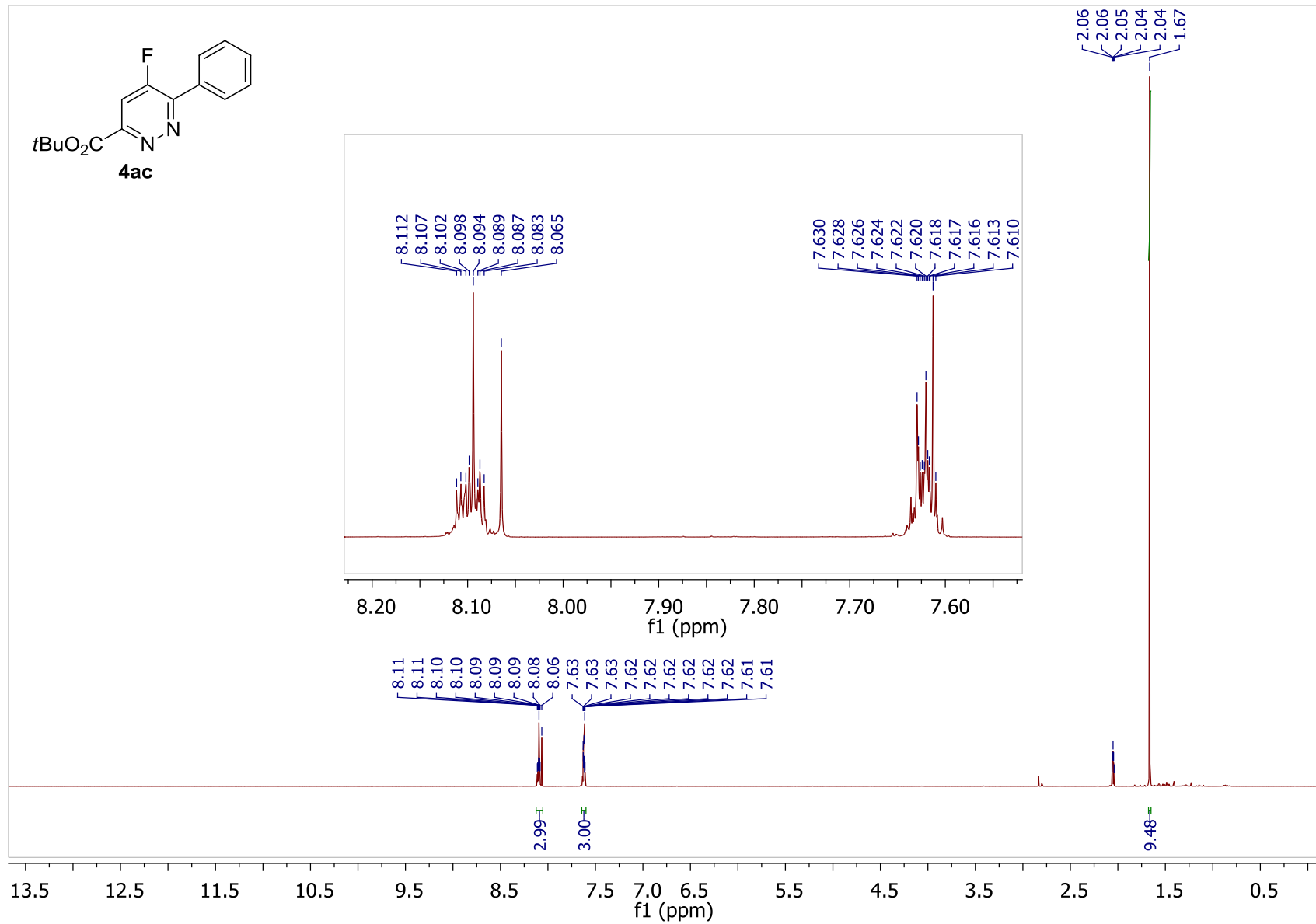
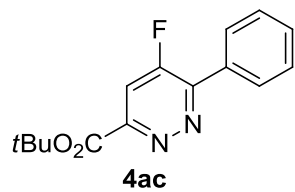
2. Experimental Spectra

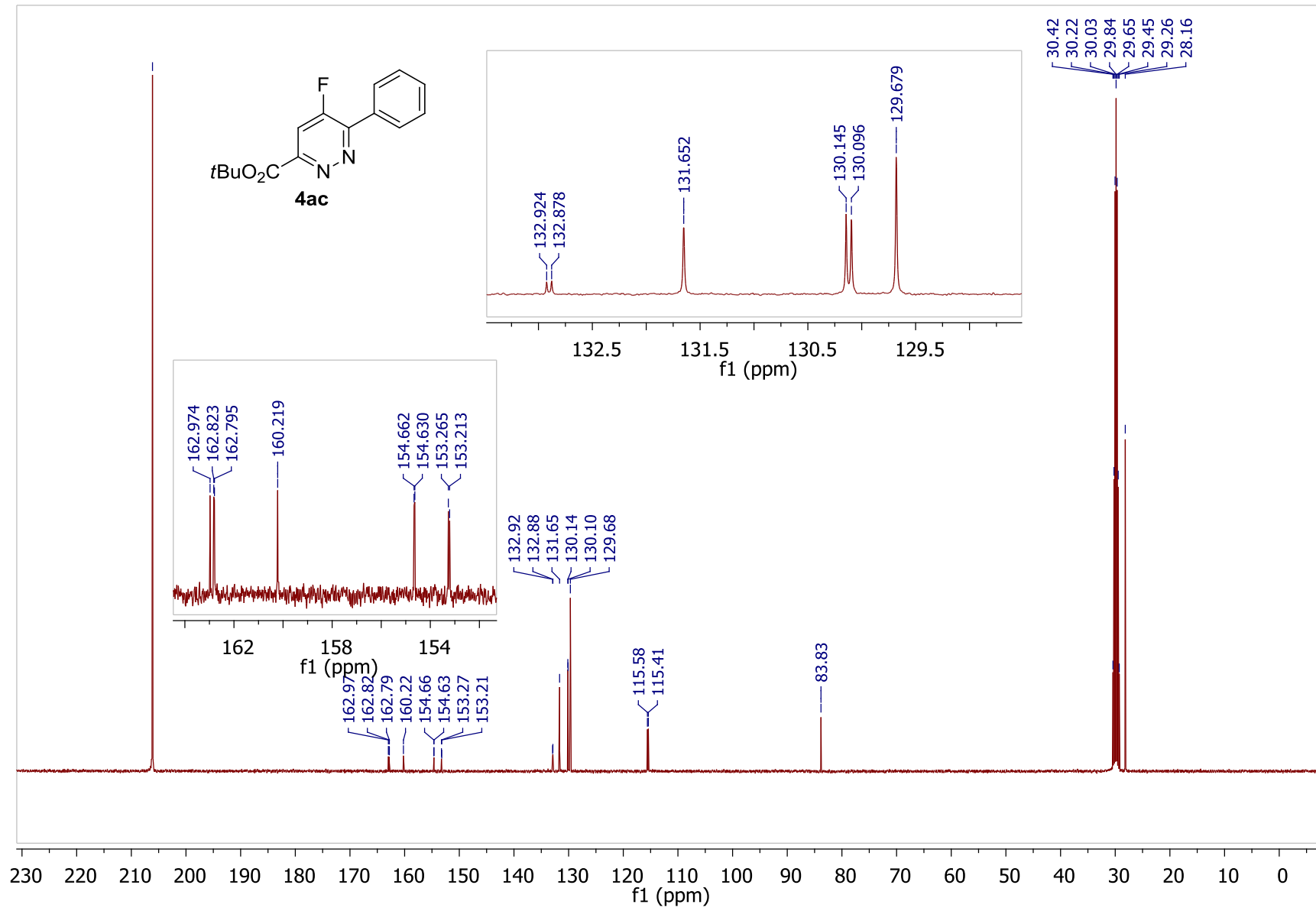


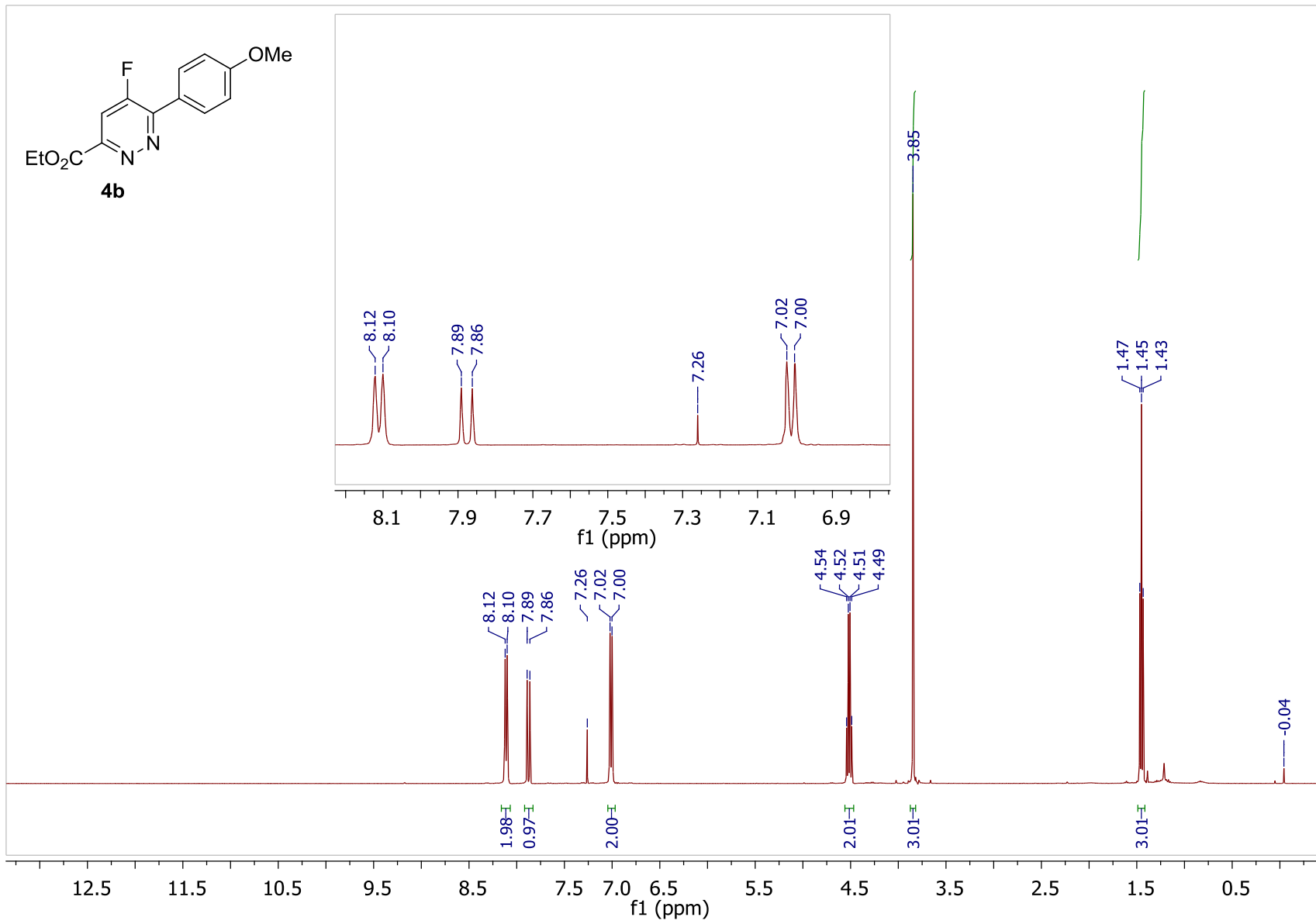
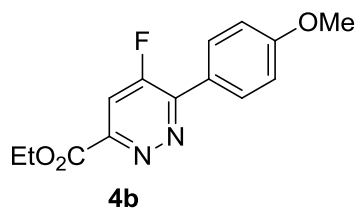


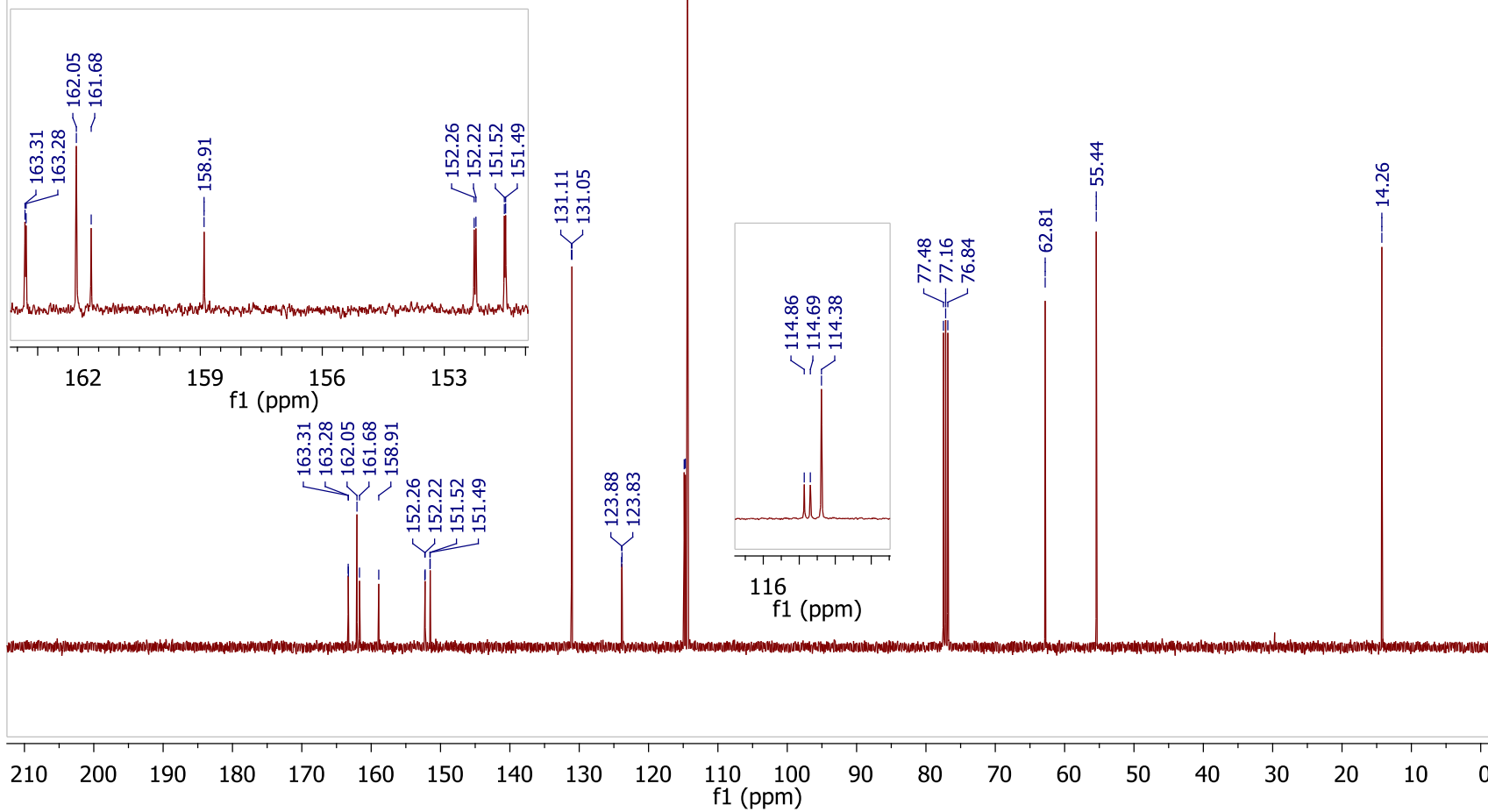
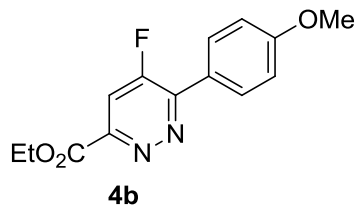


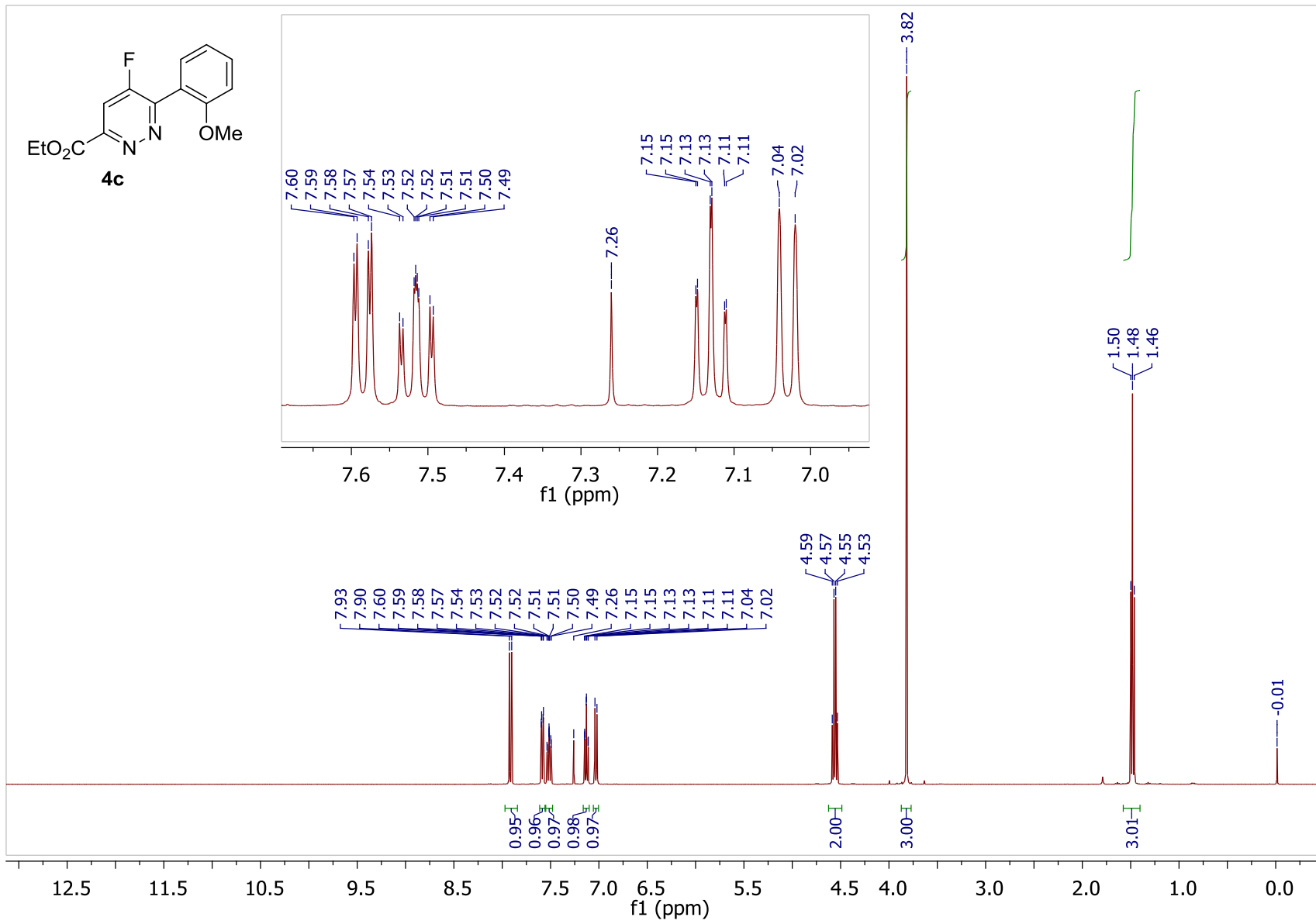
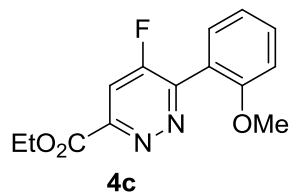


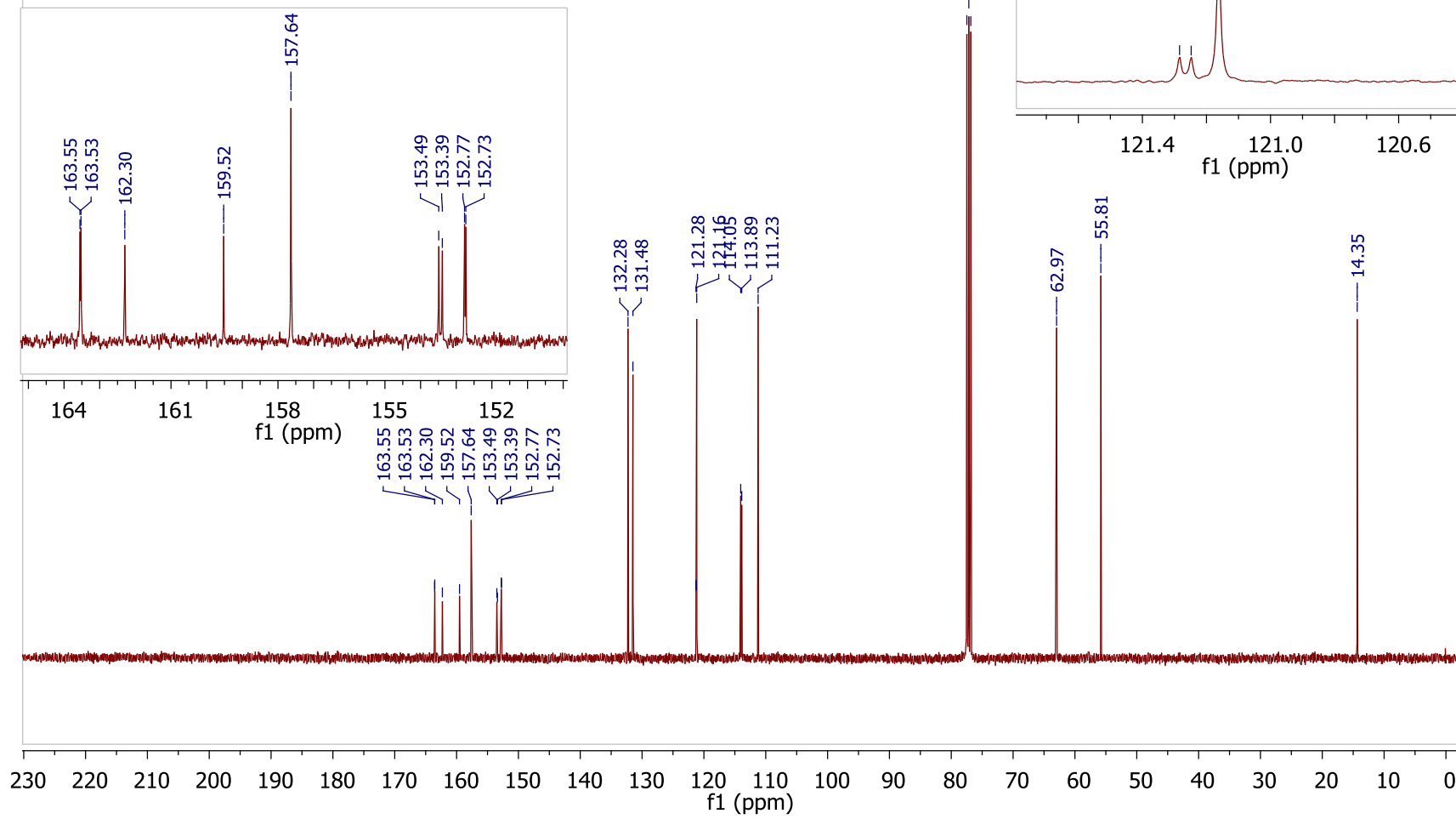
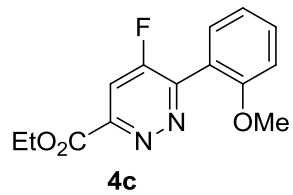


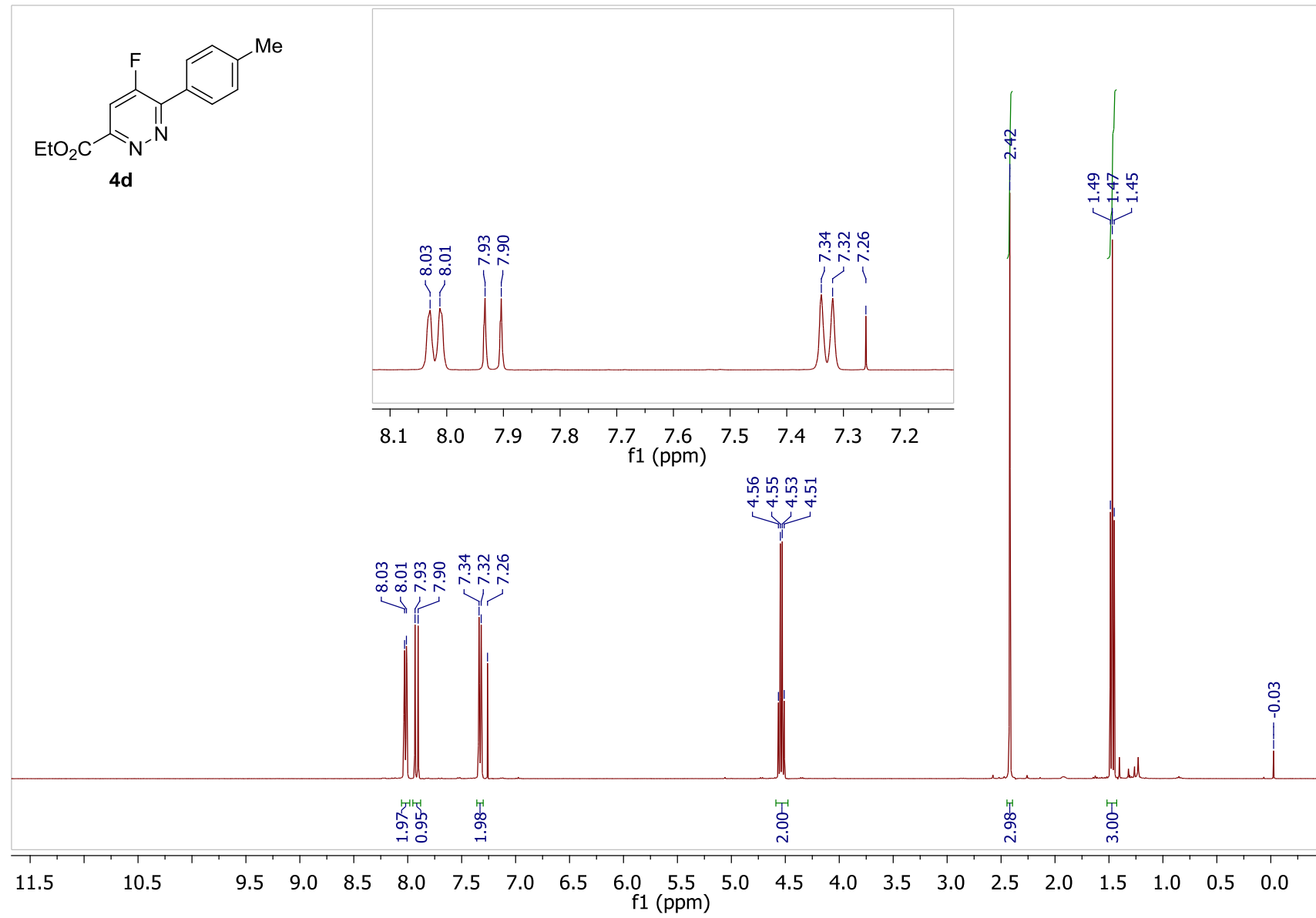
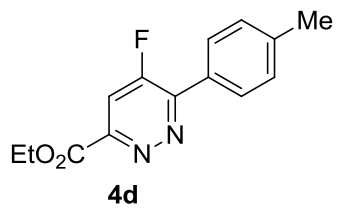


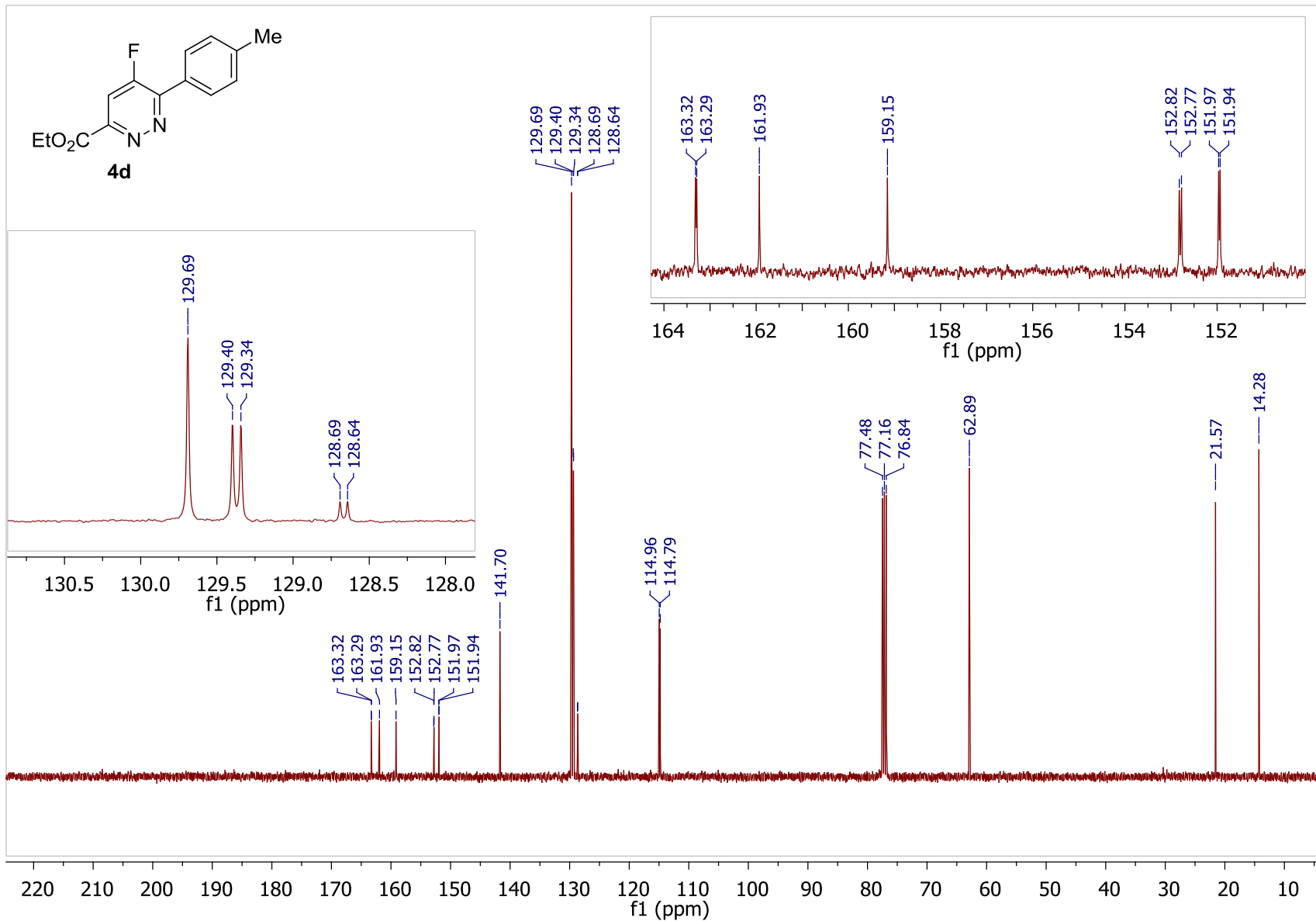
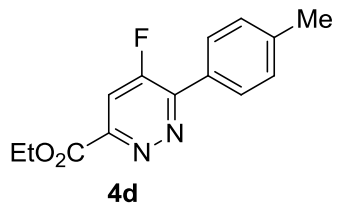


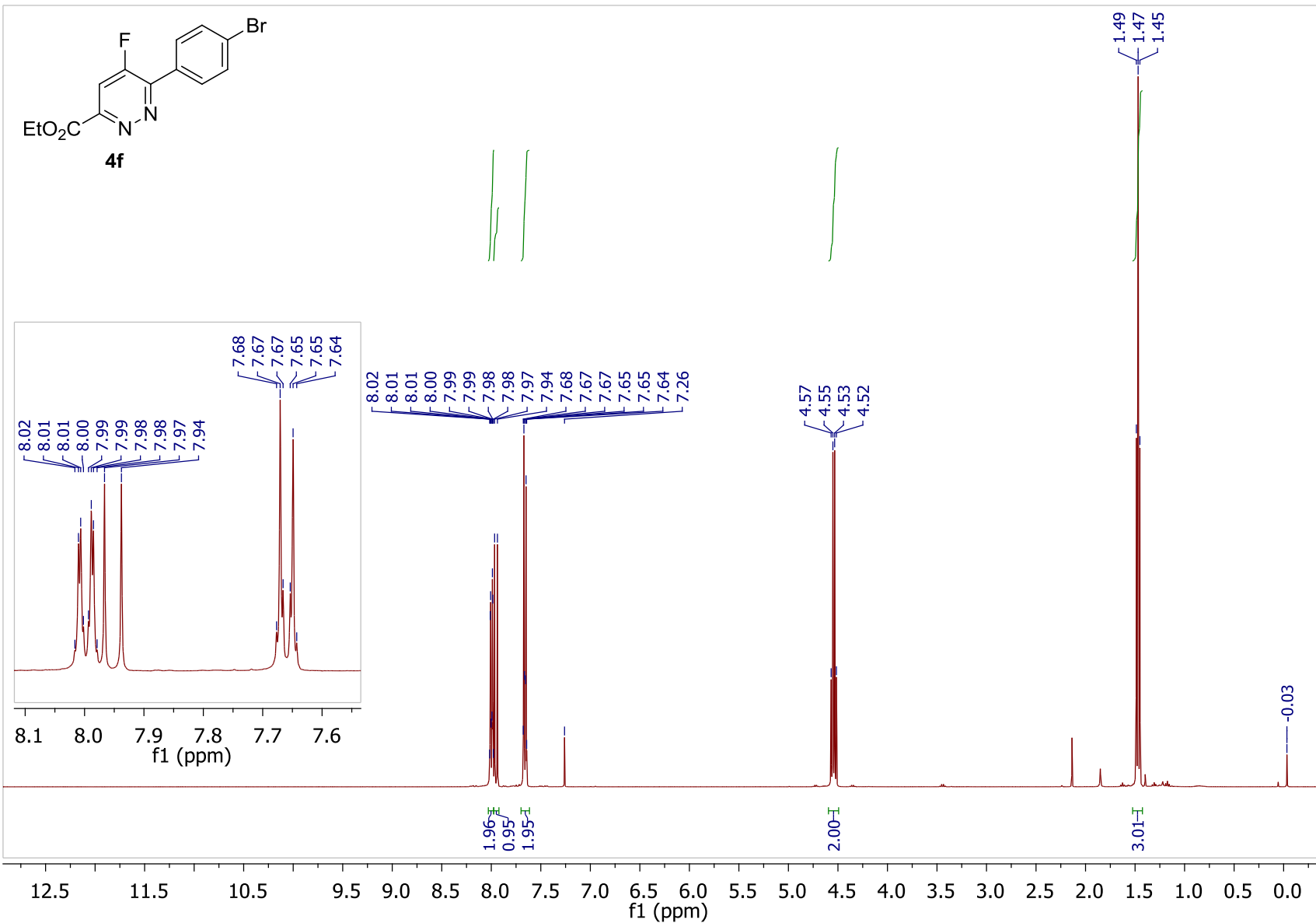
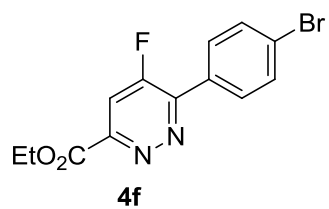


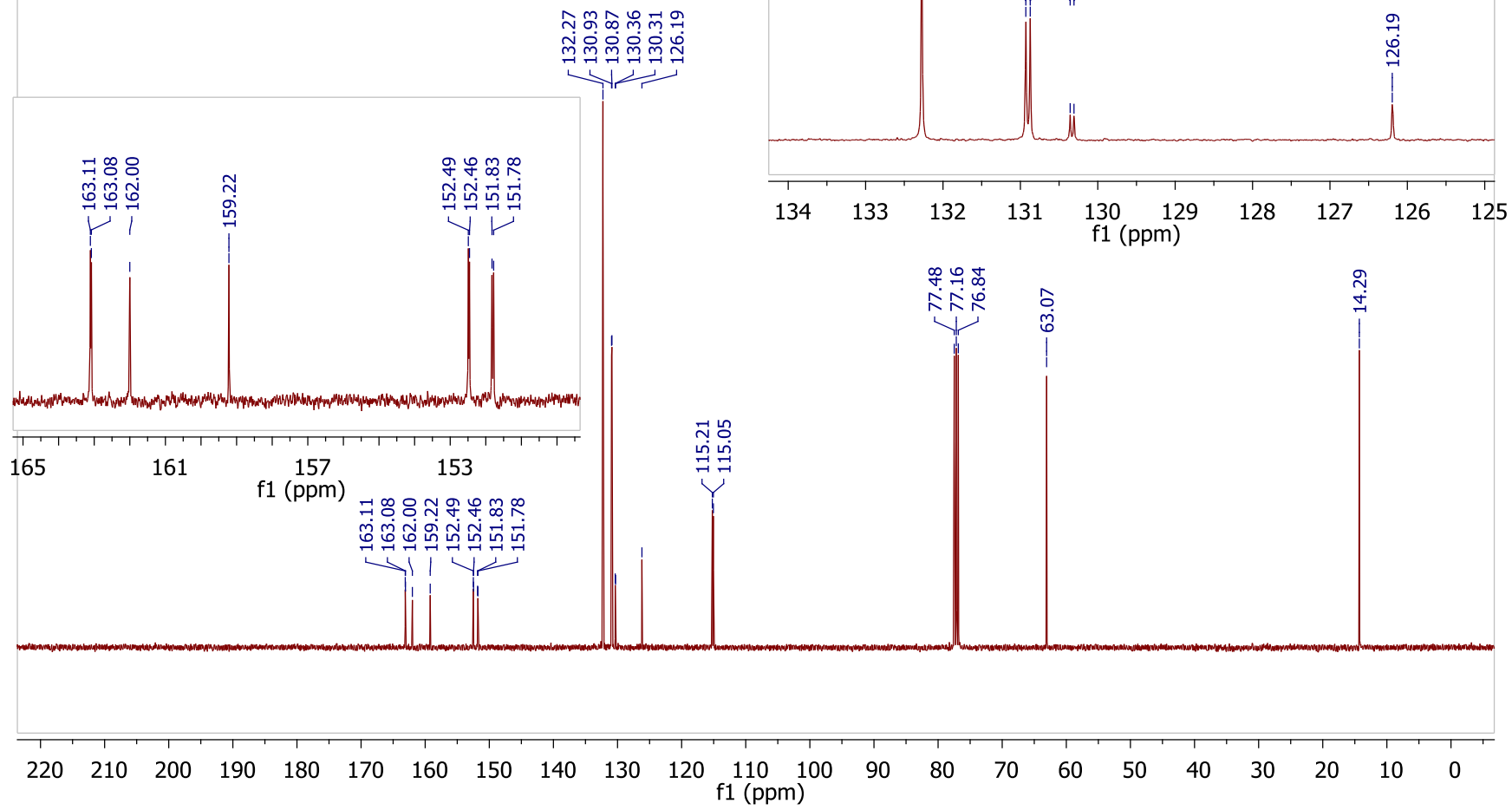
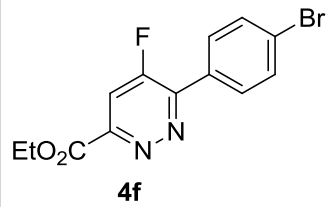


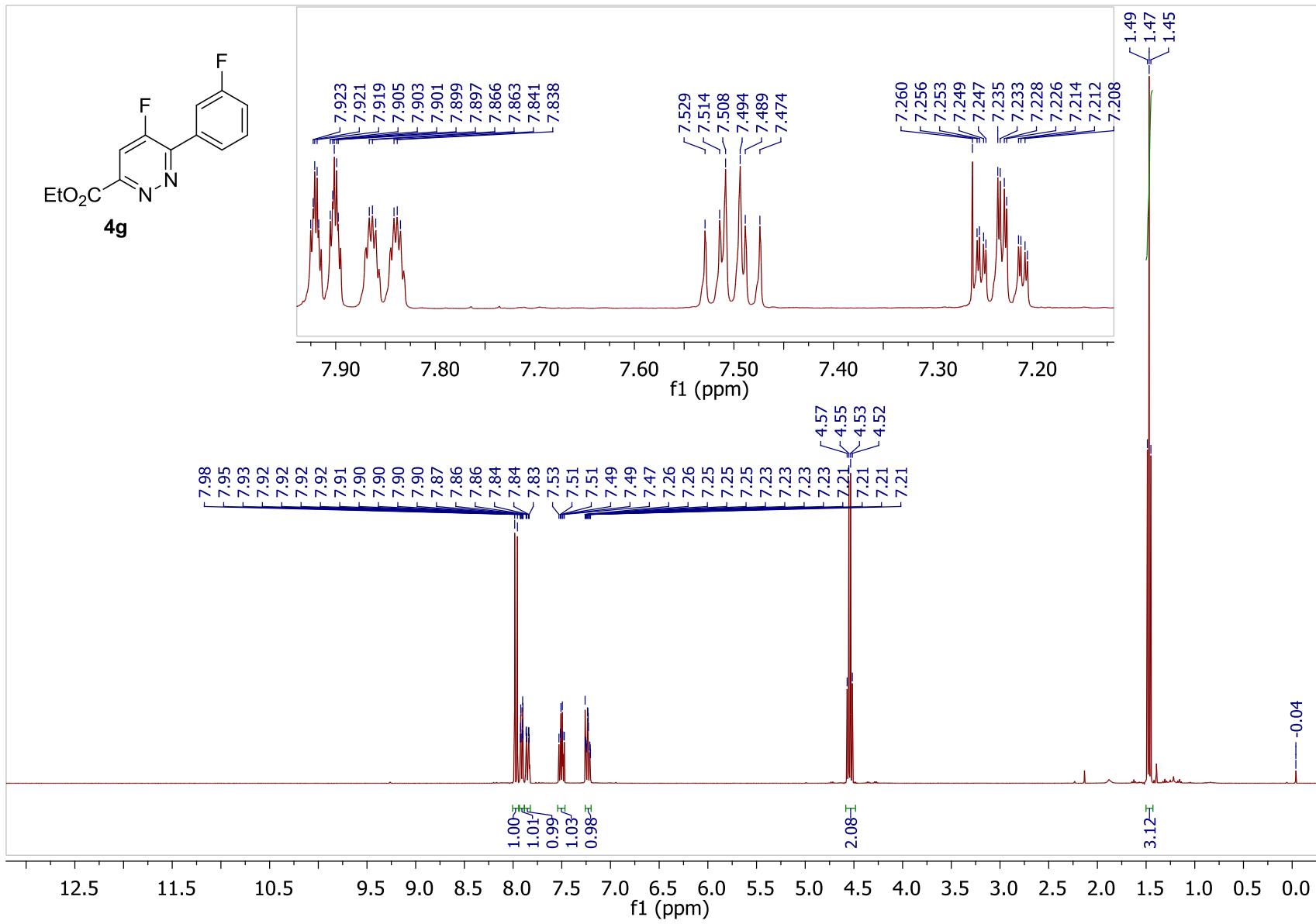
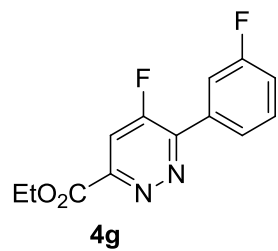


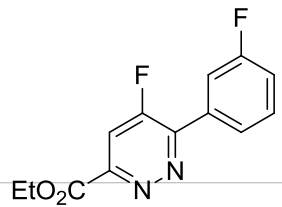




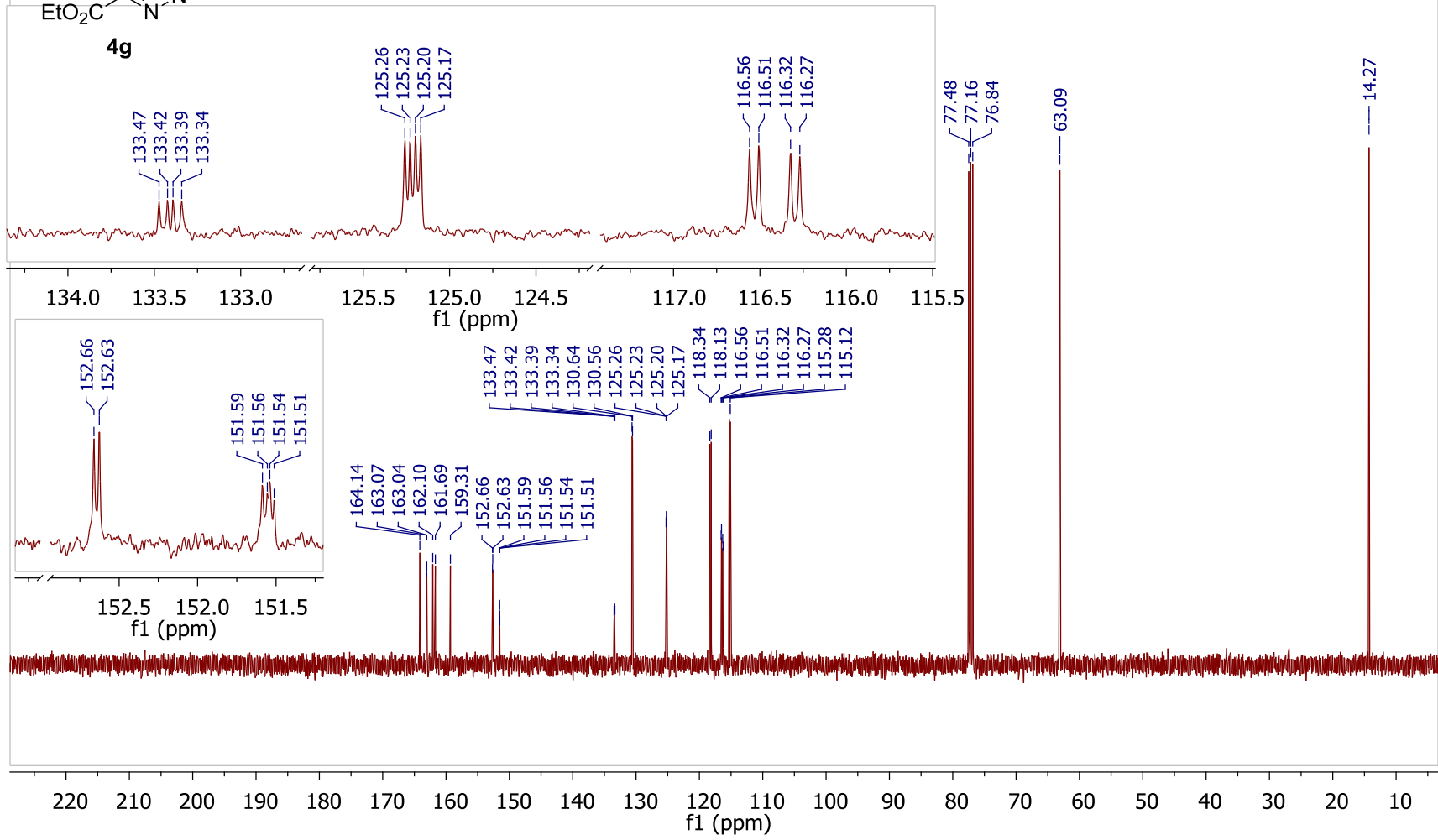


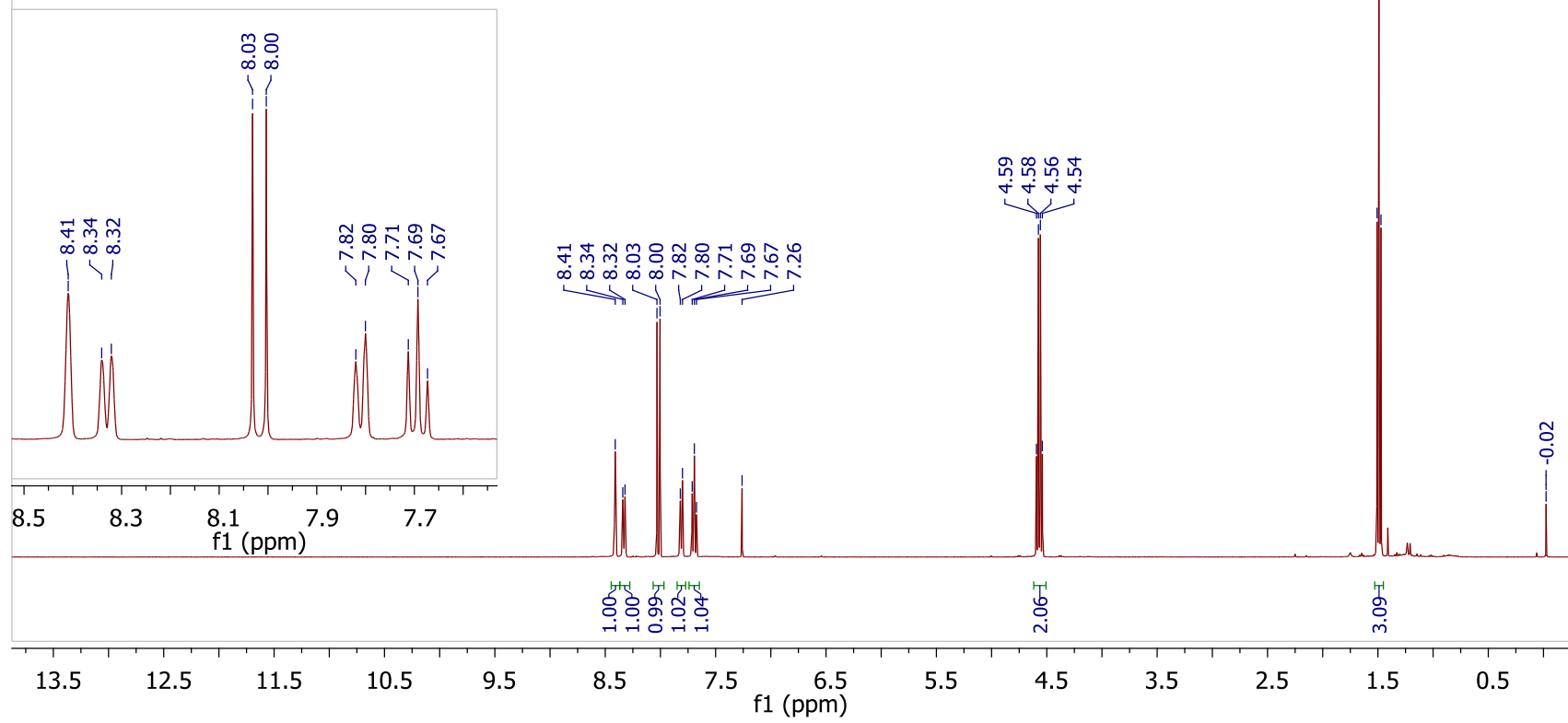
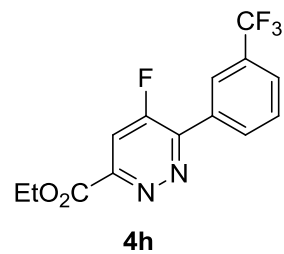


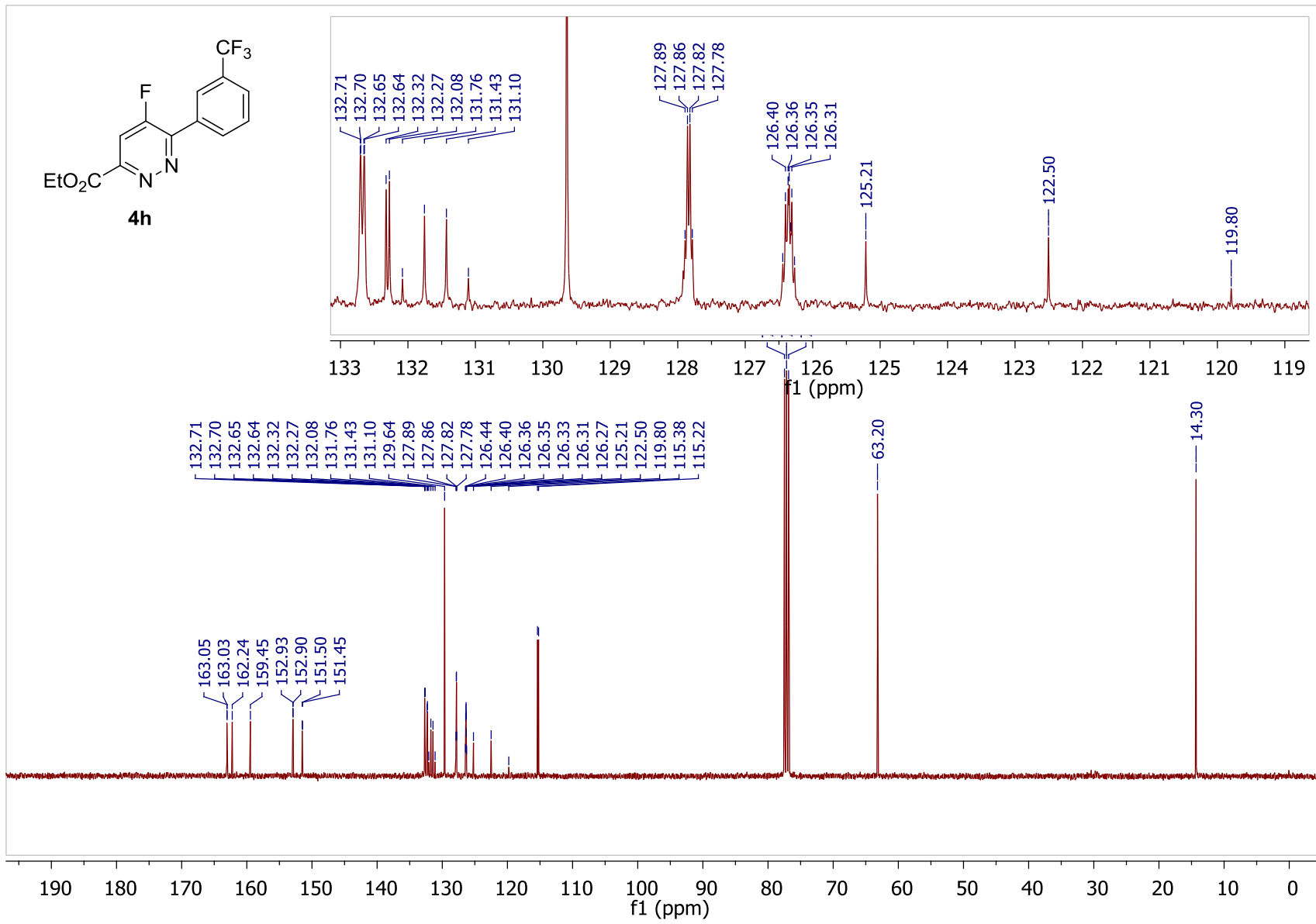
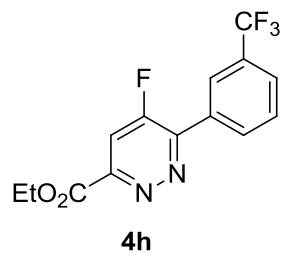


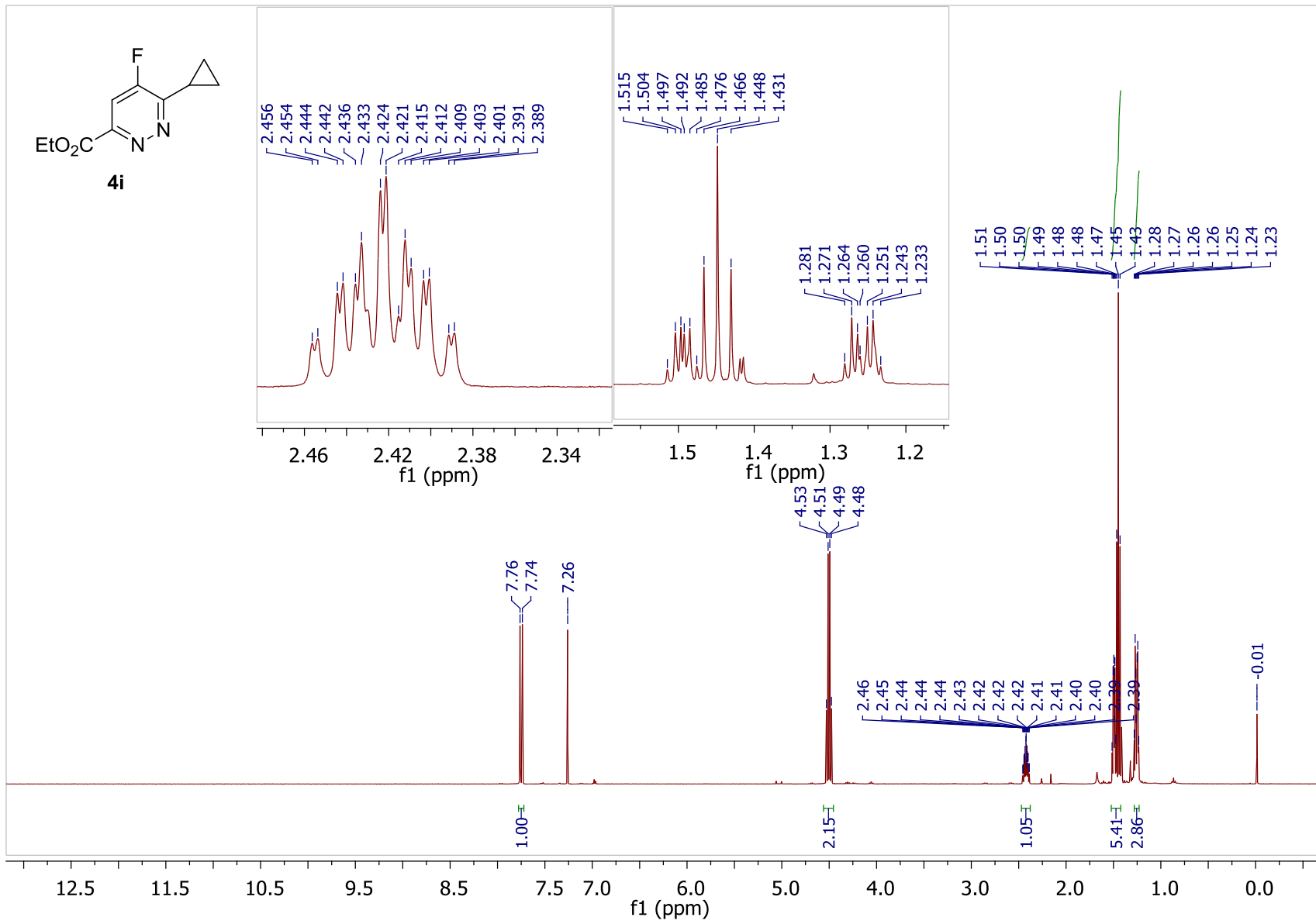
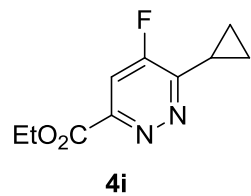


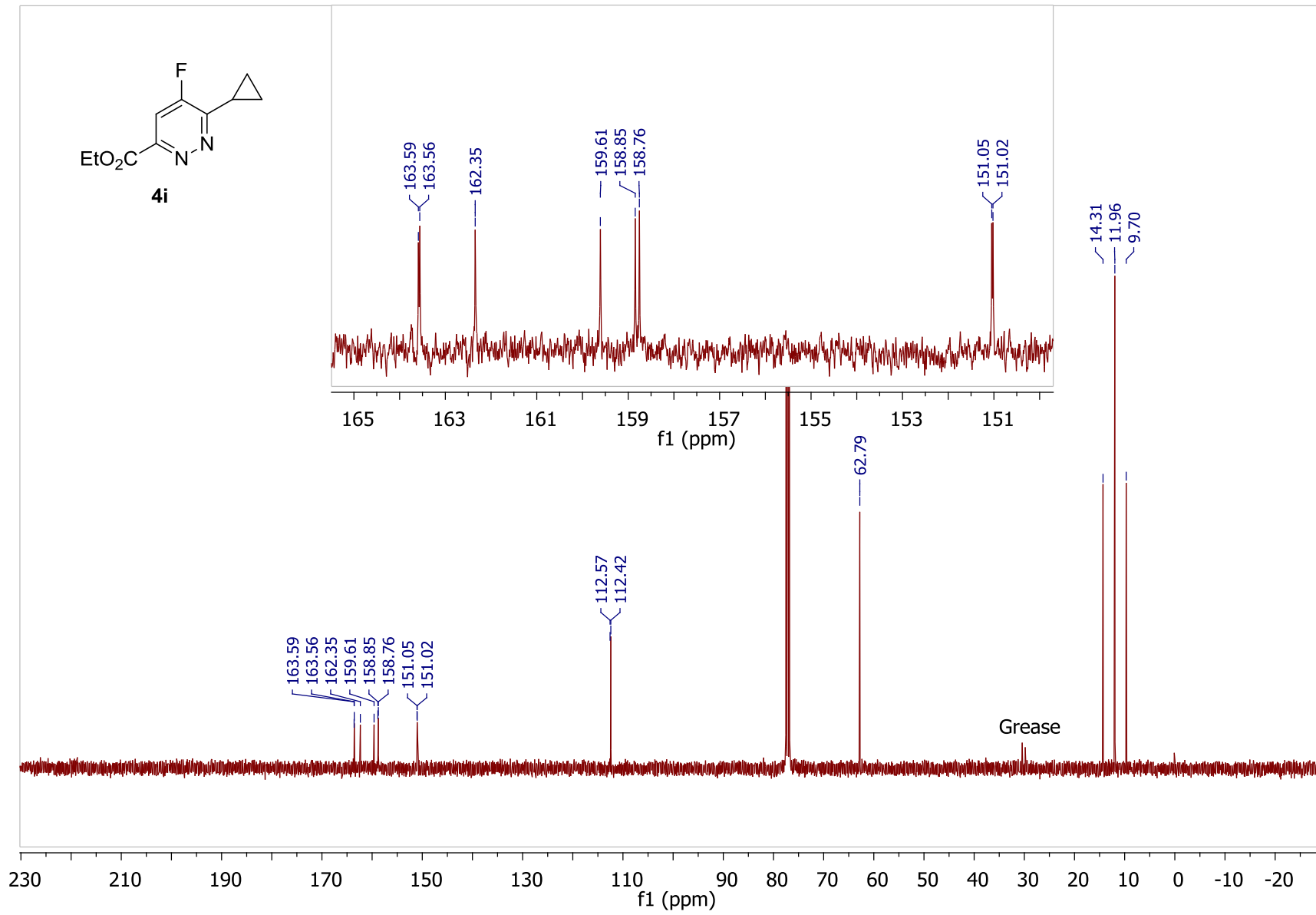
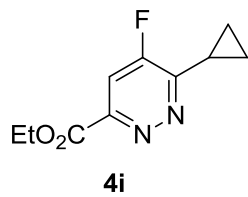
4g

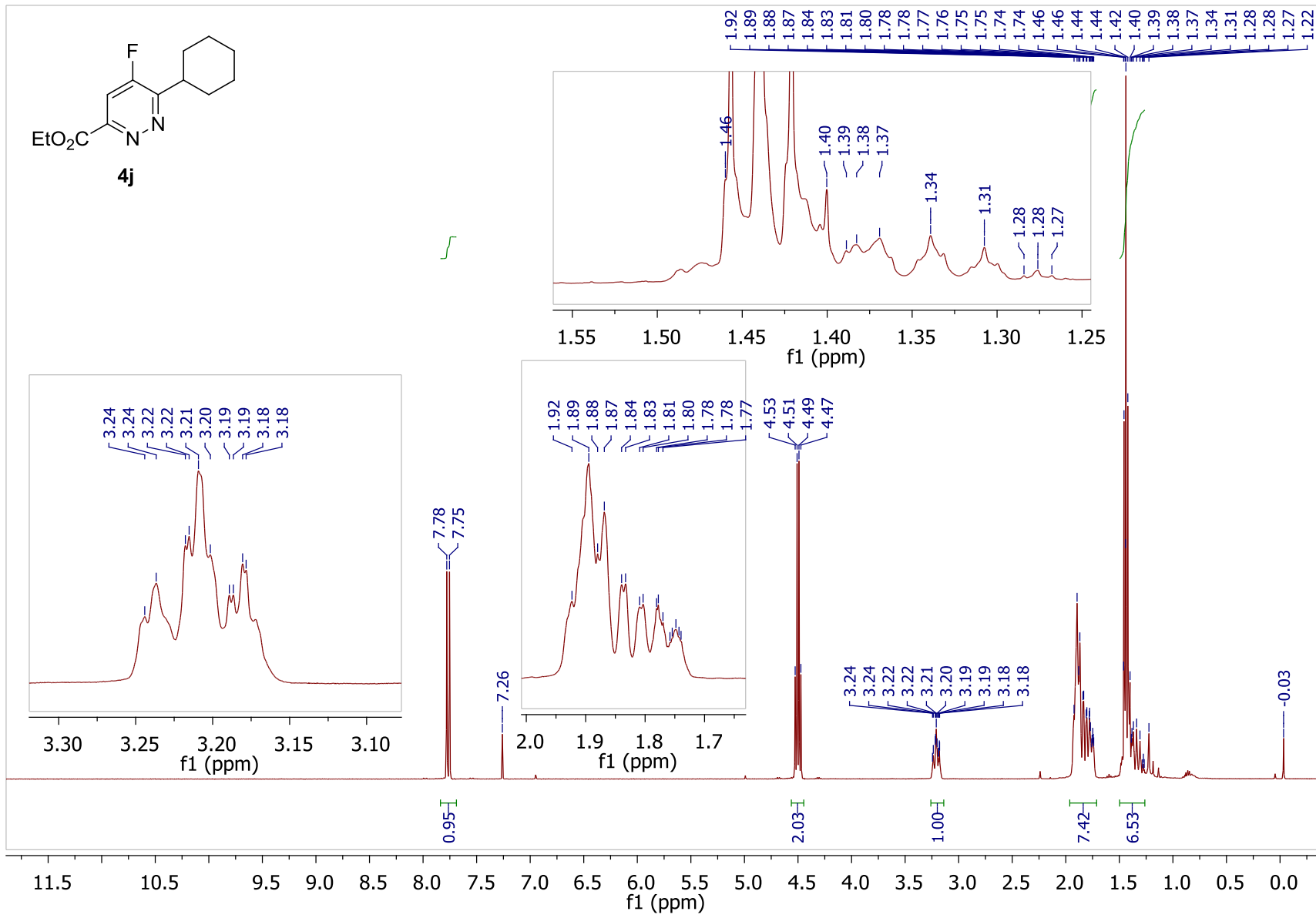
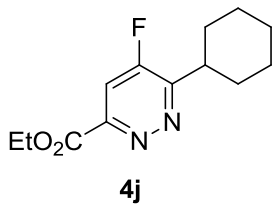


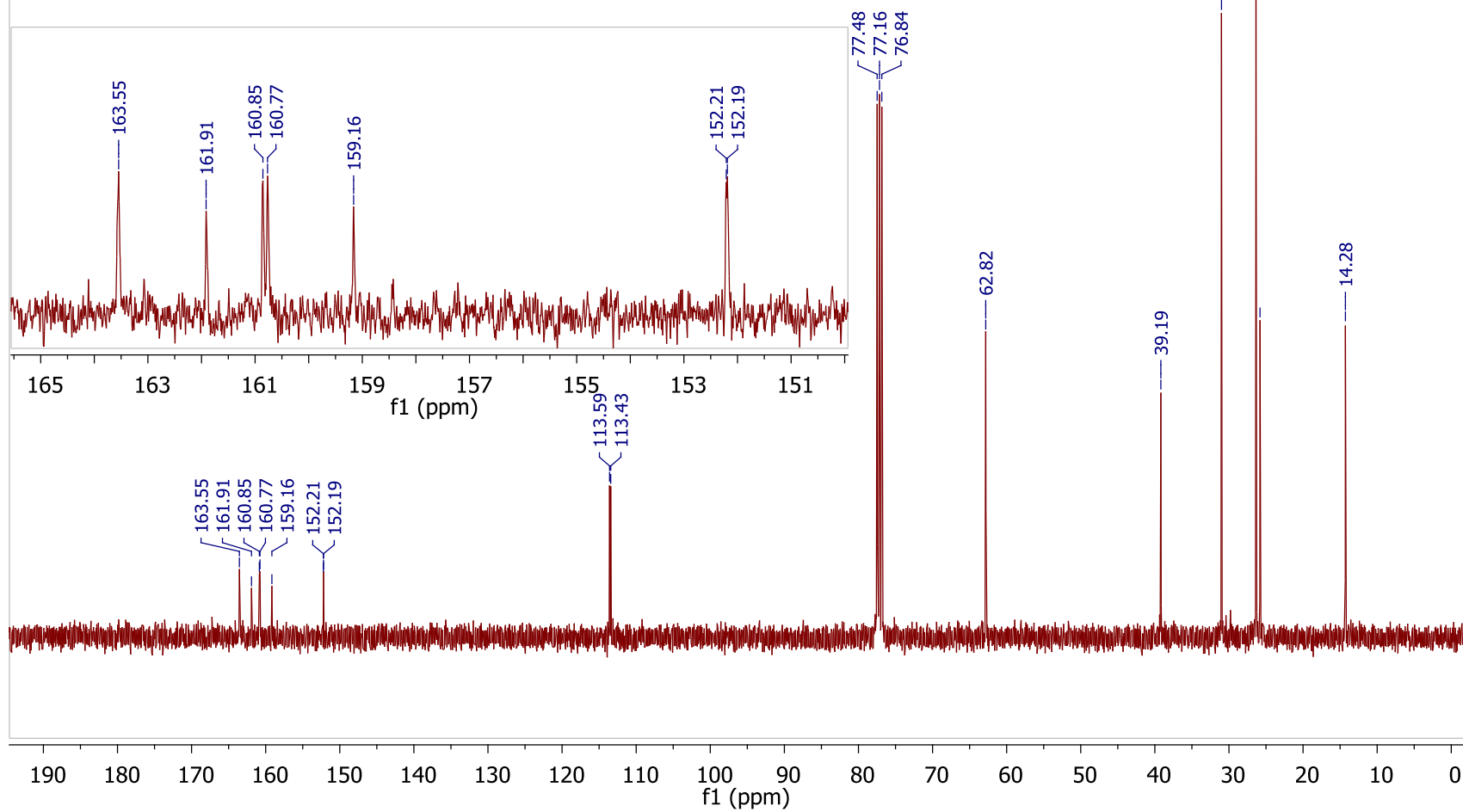
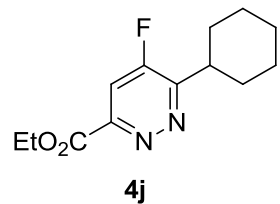


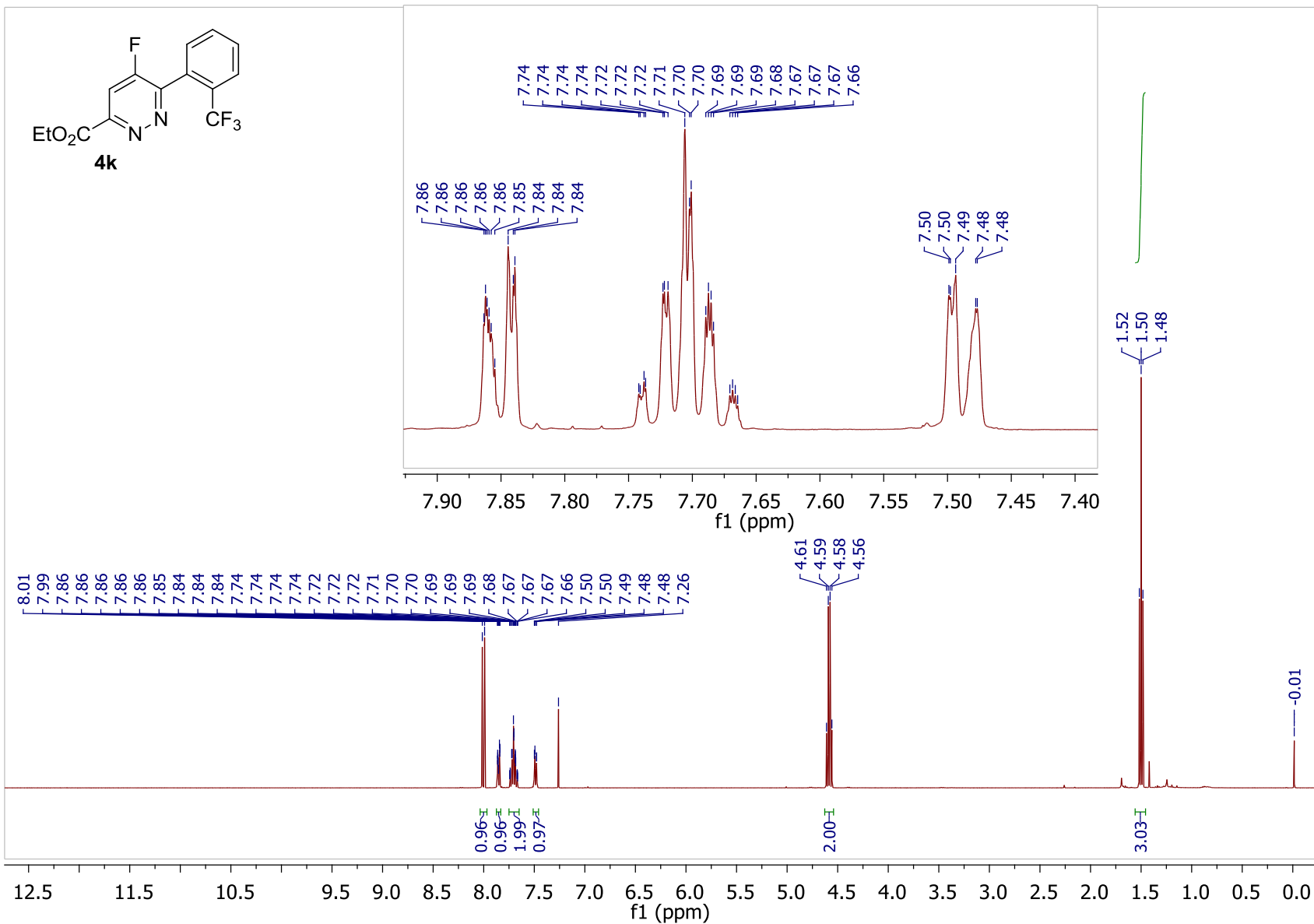
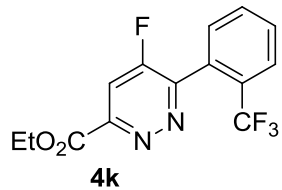


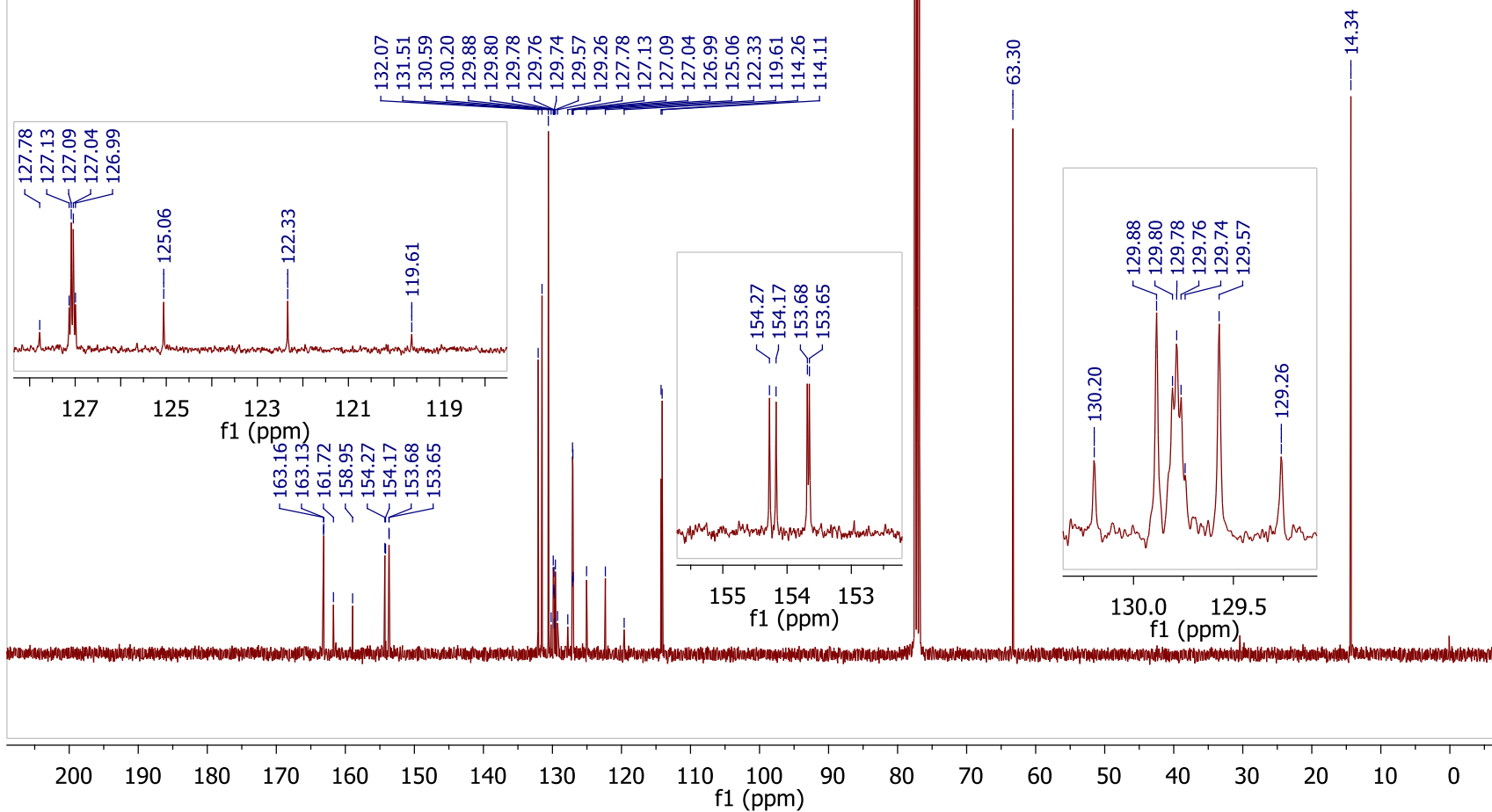
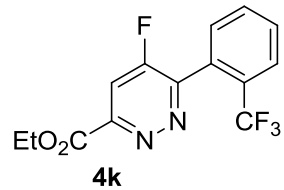


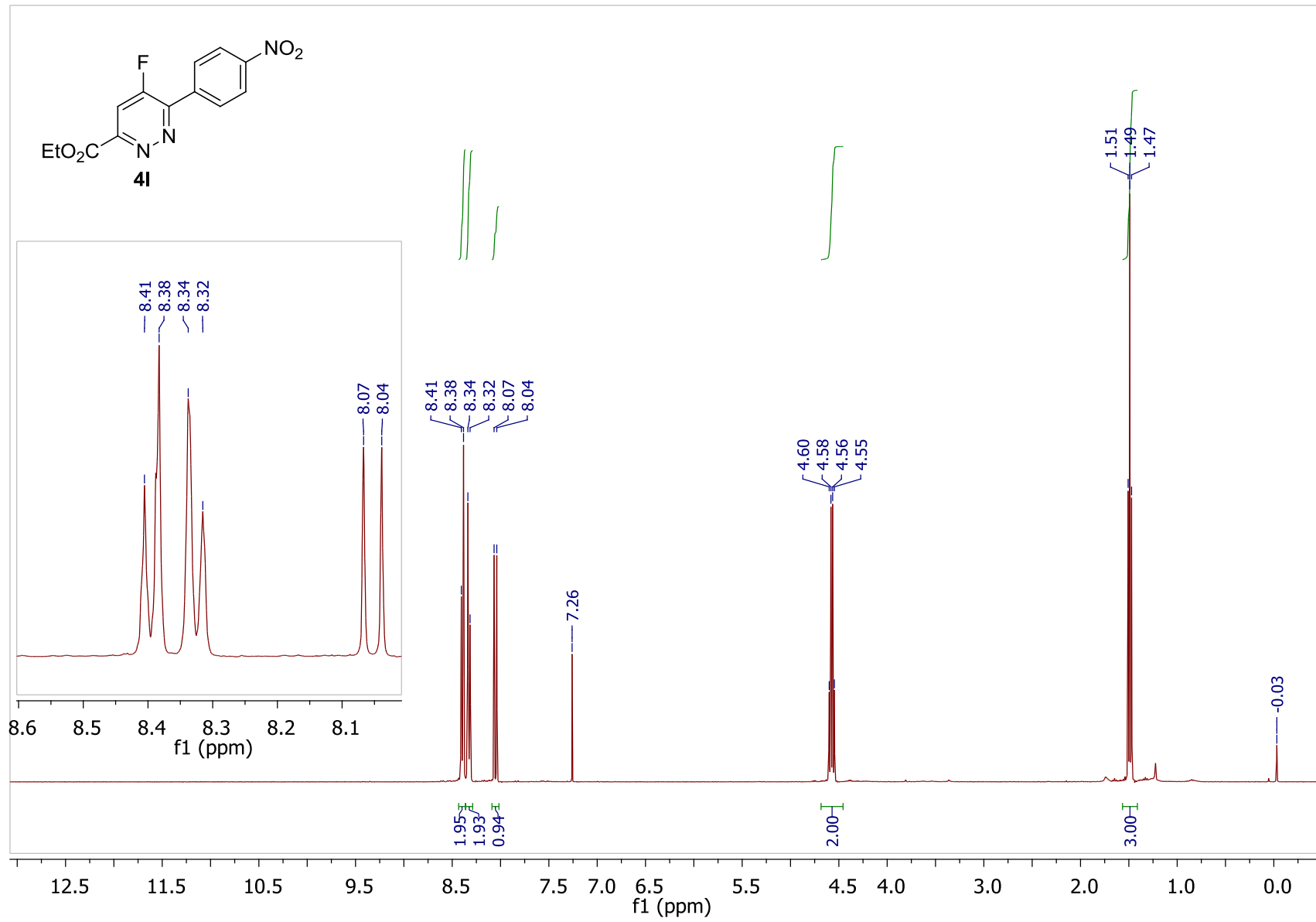
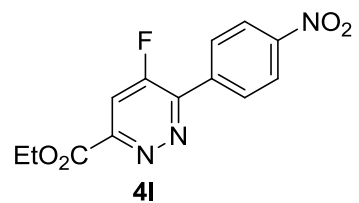


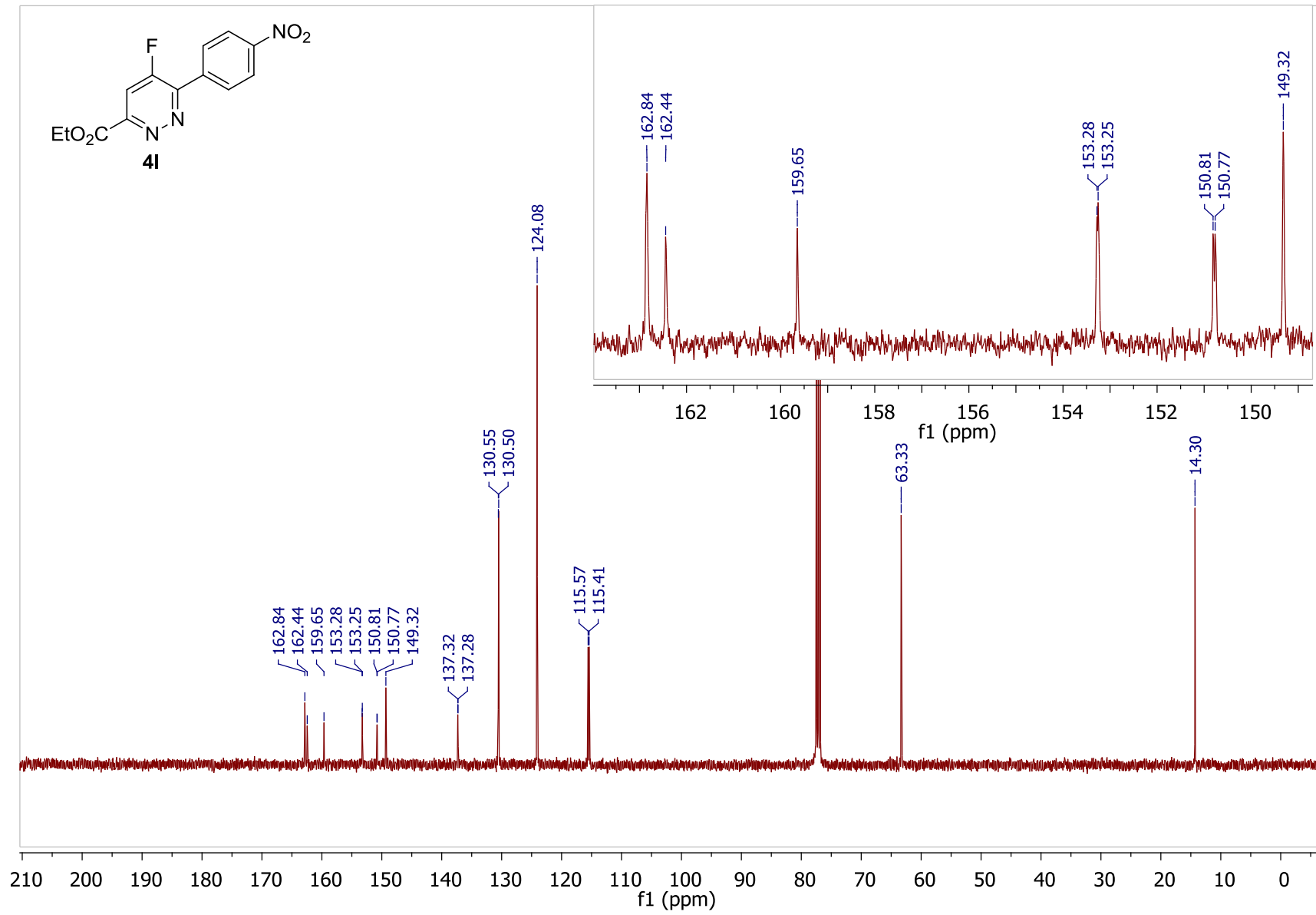
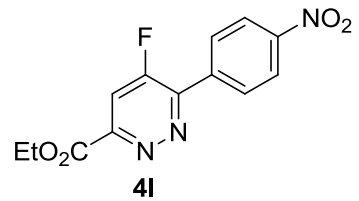


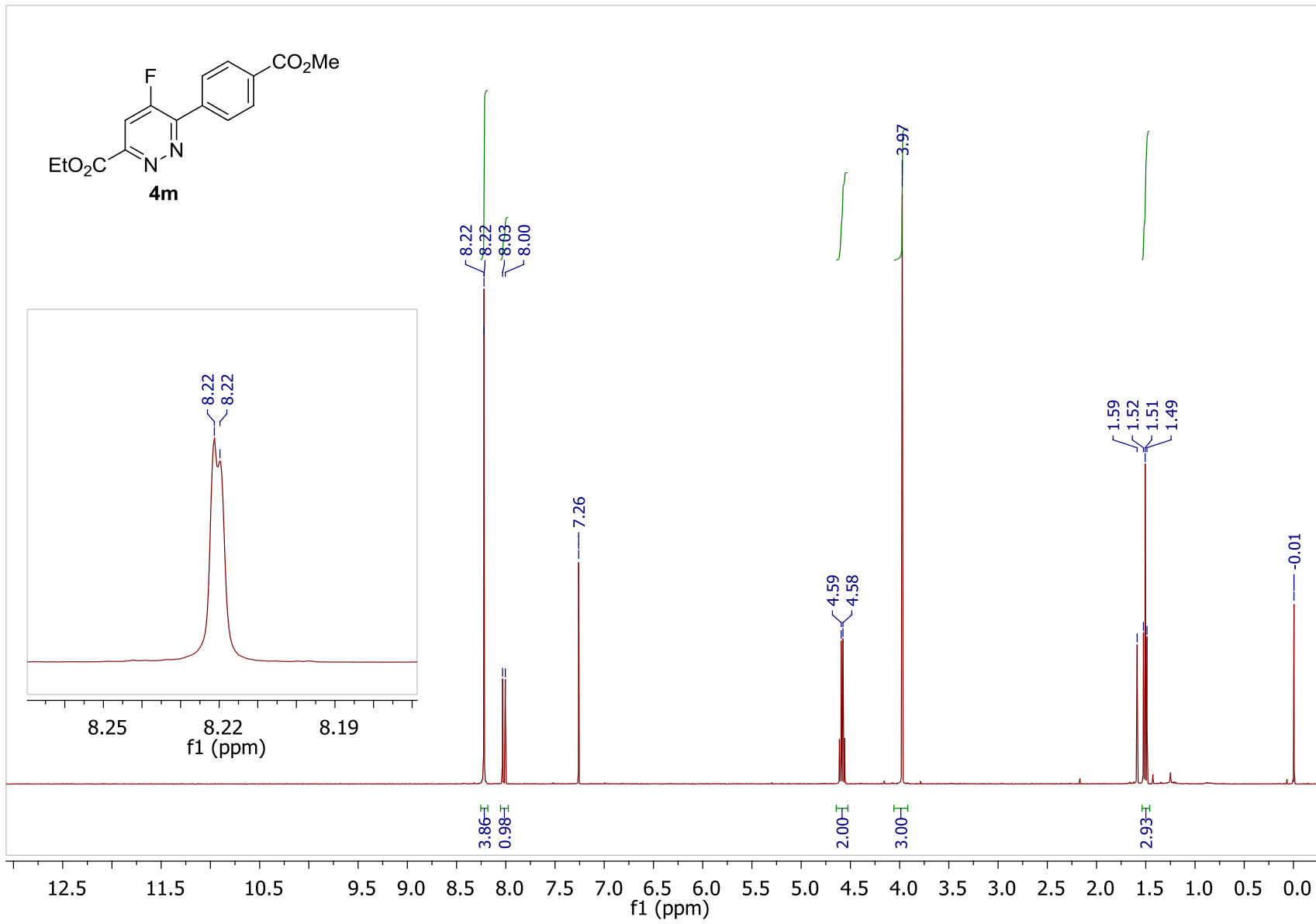
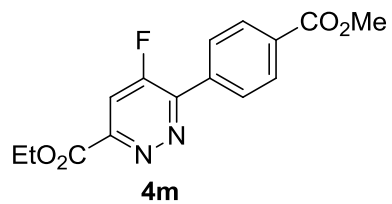


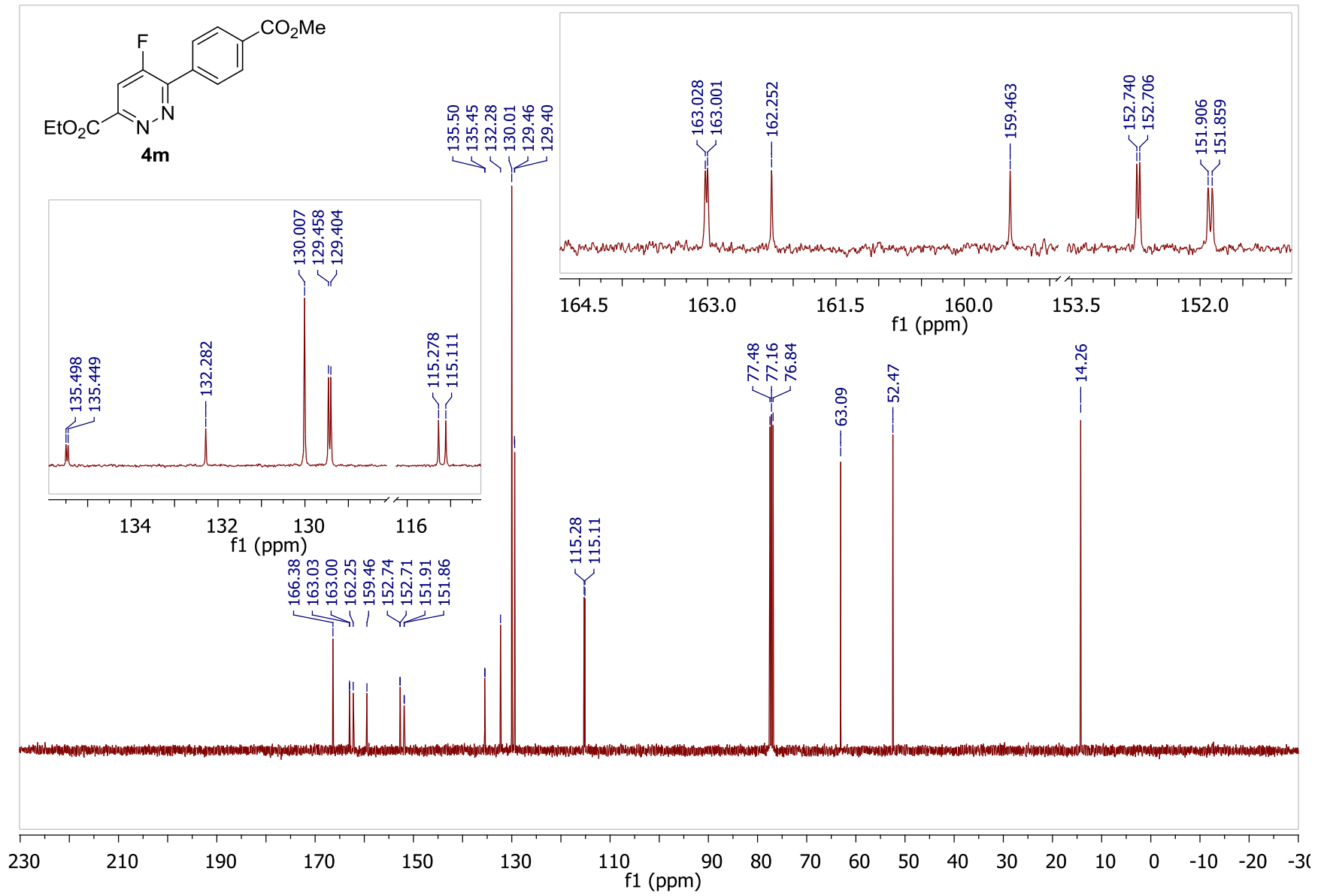
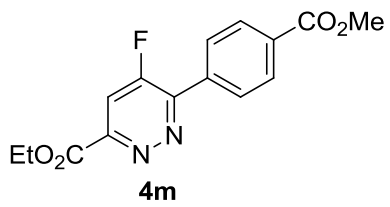


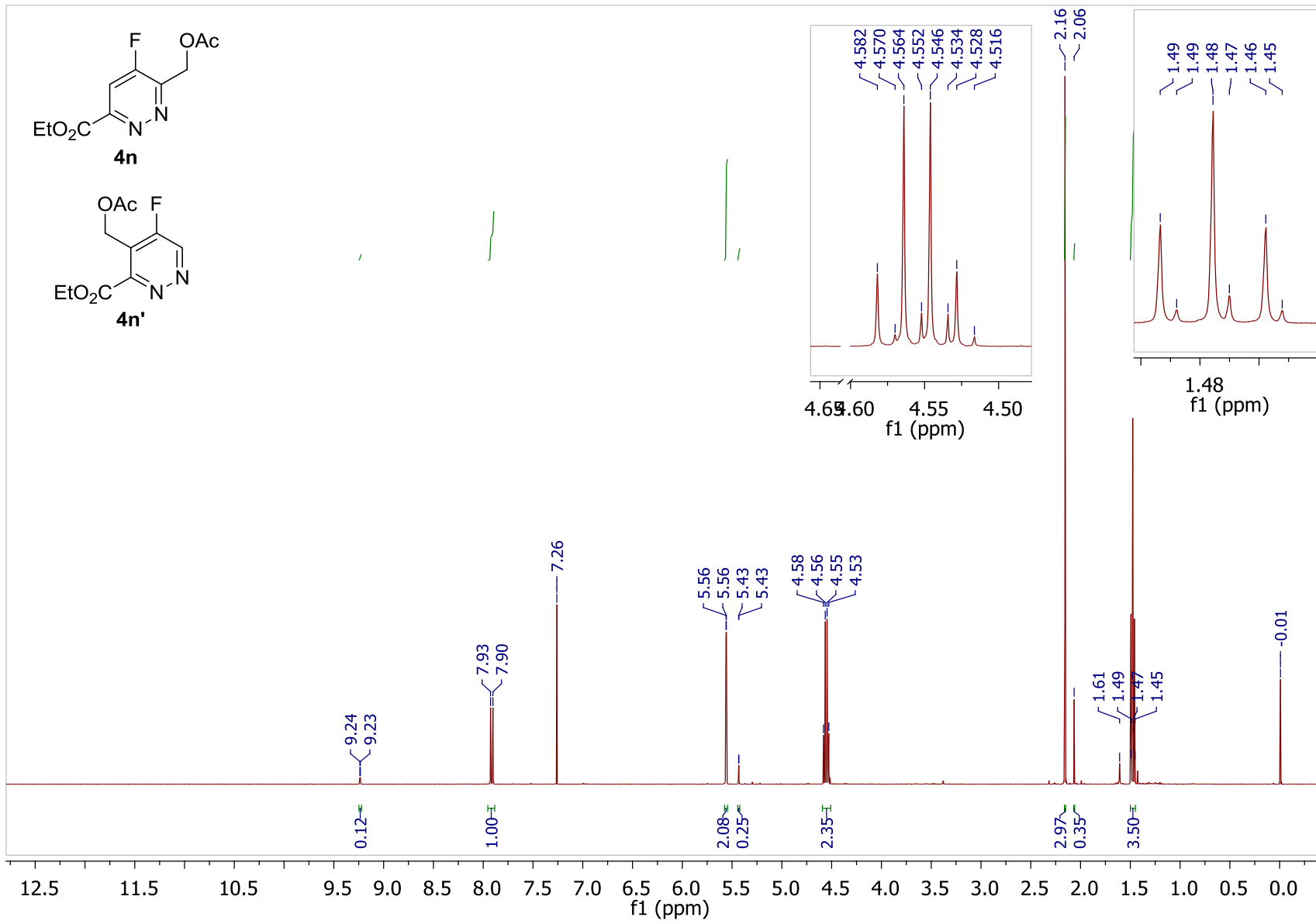


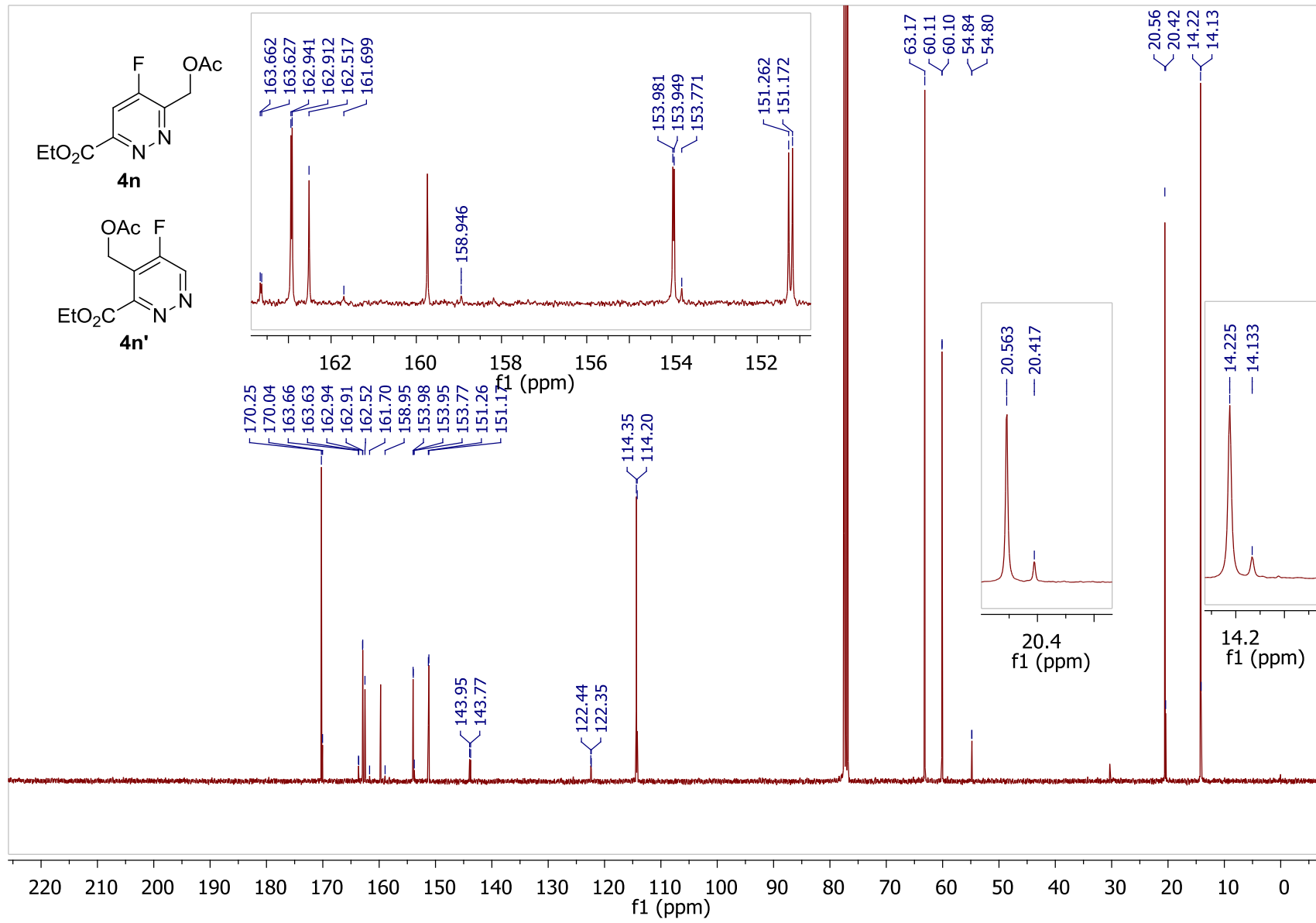


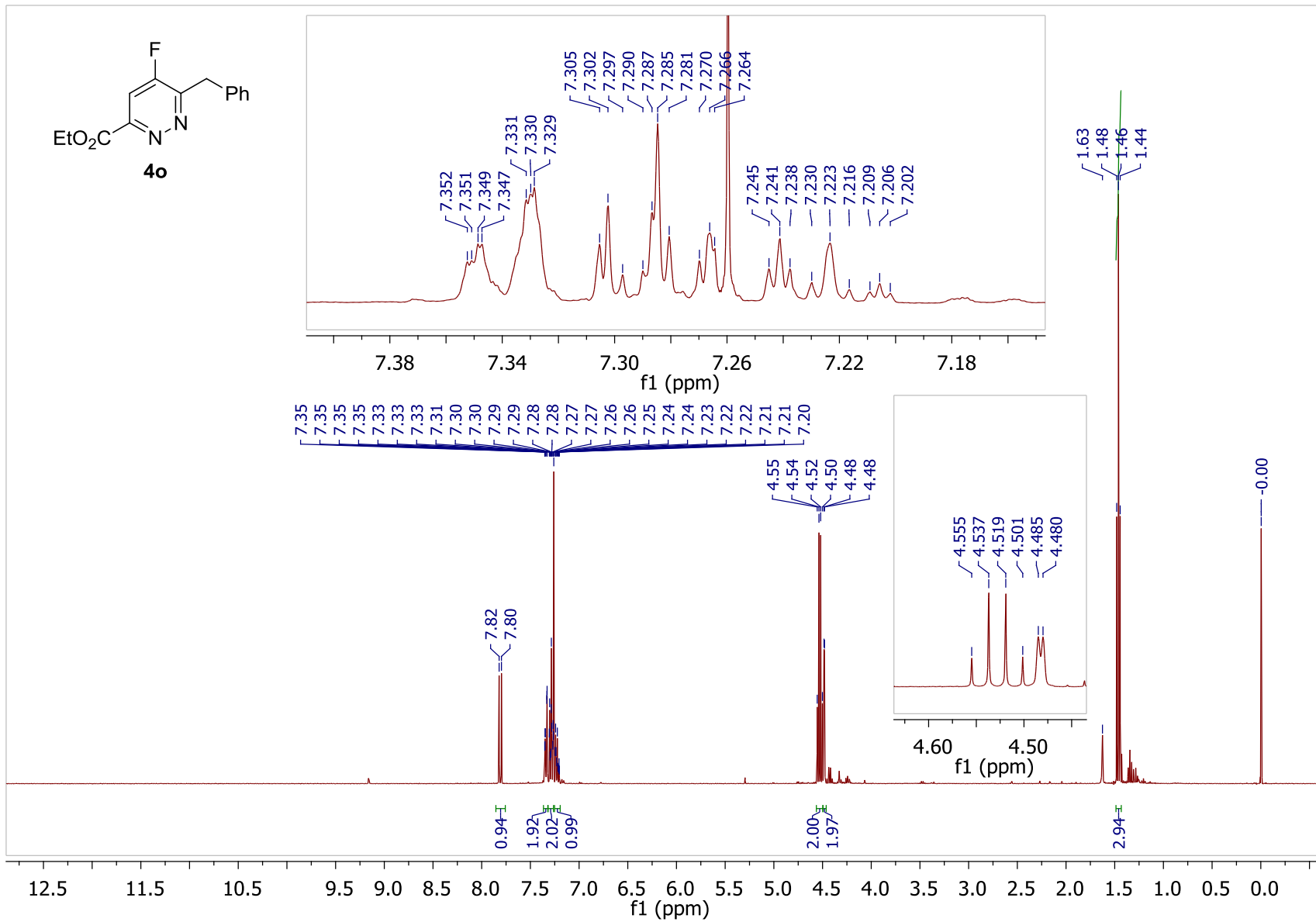
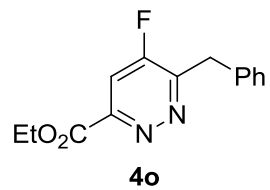


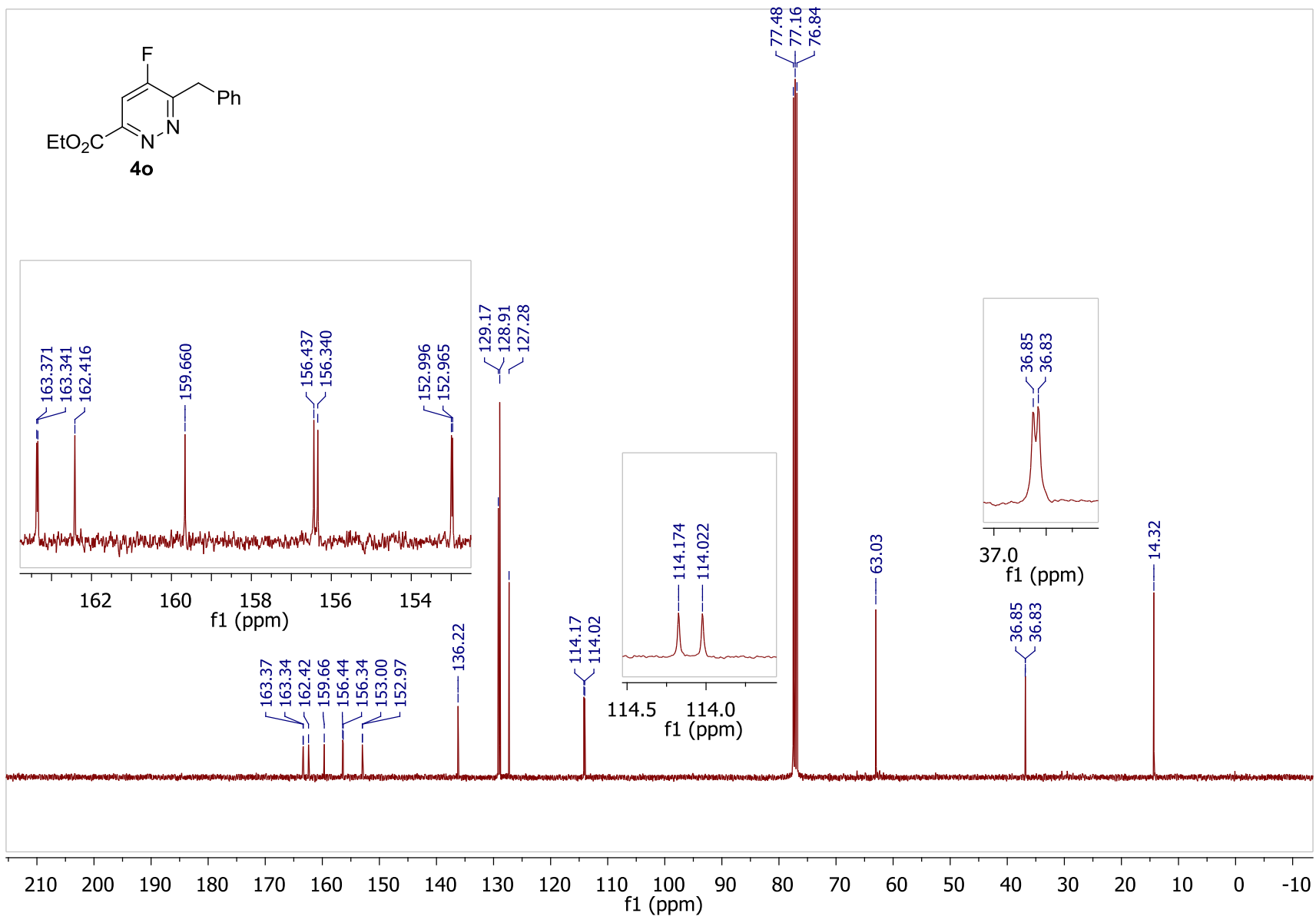
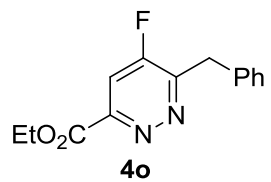


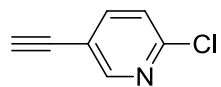




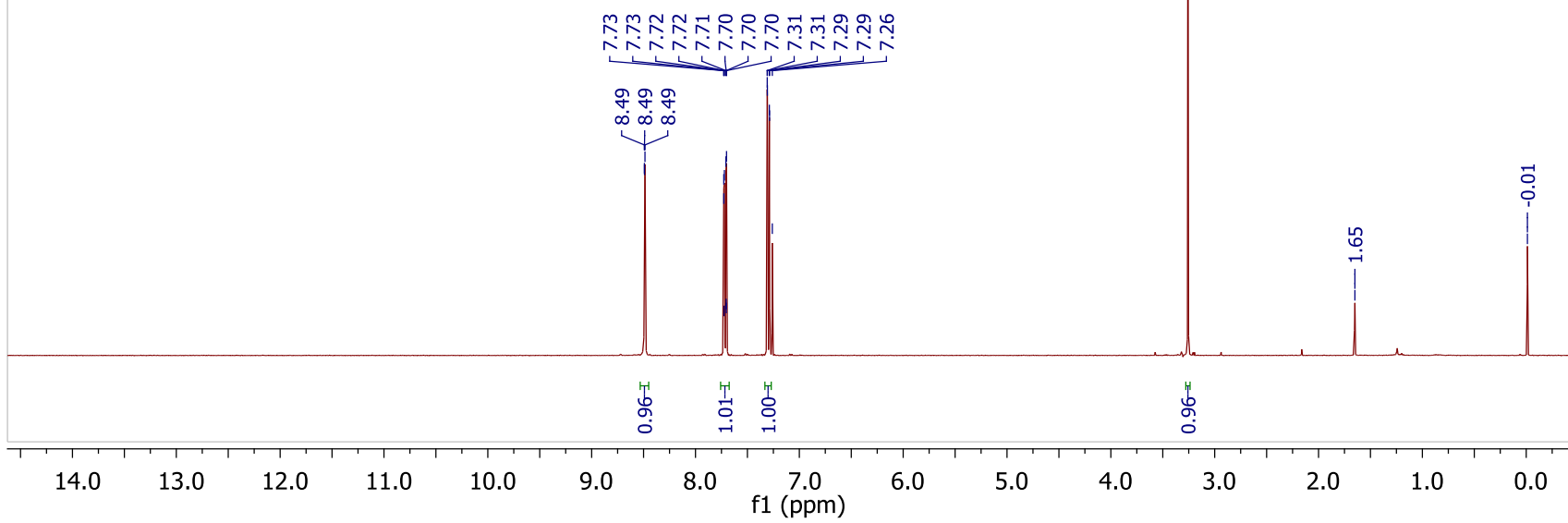
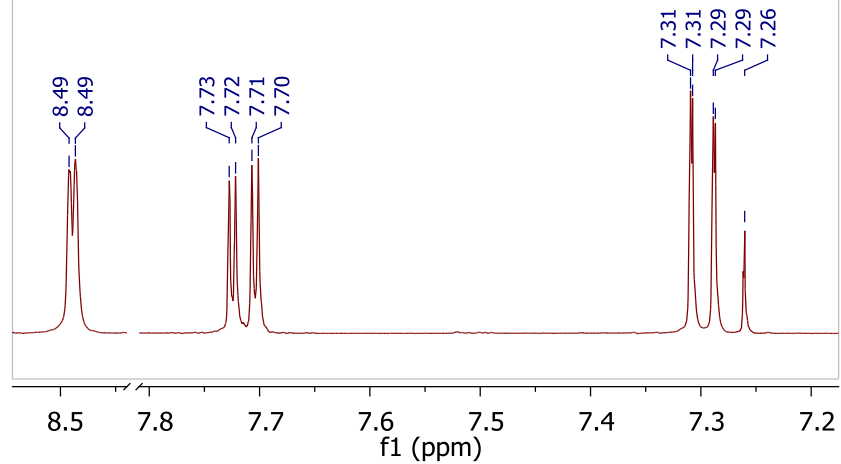


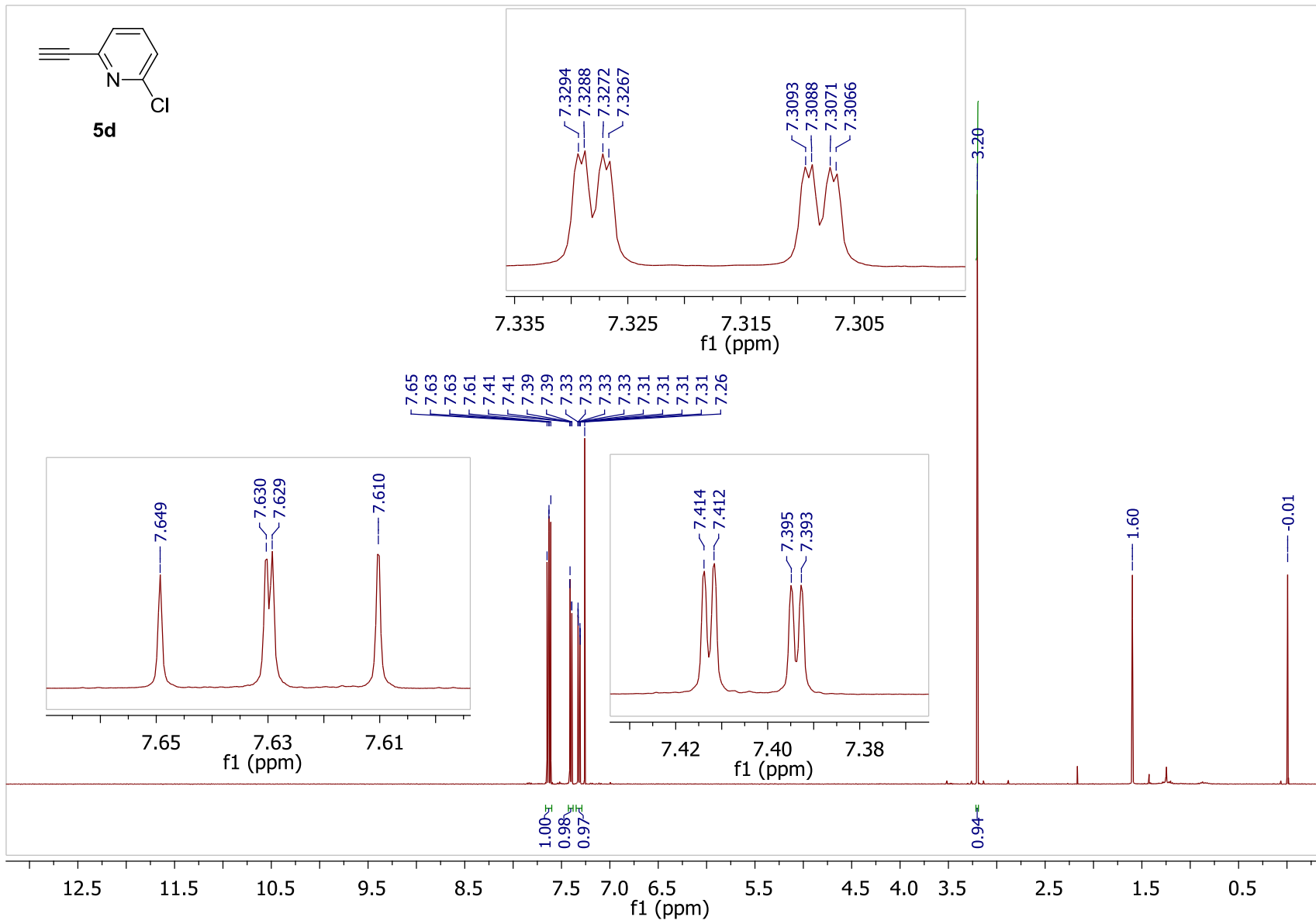
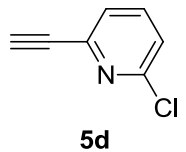


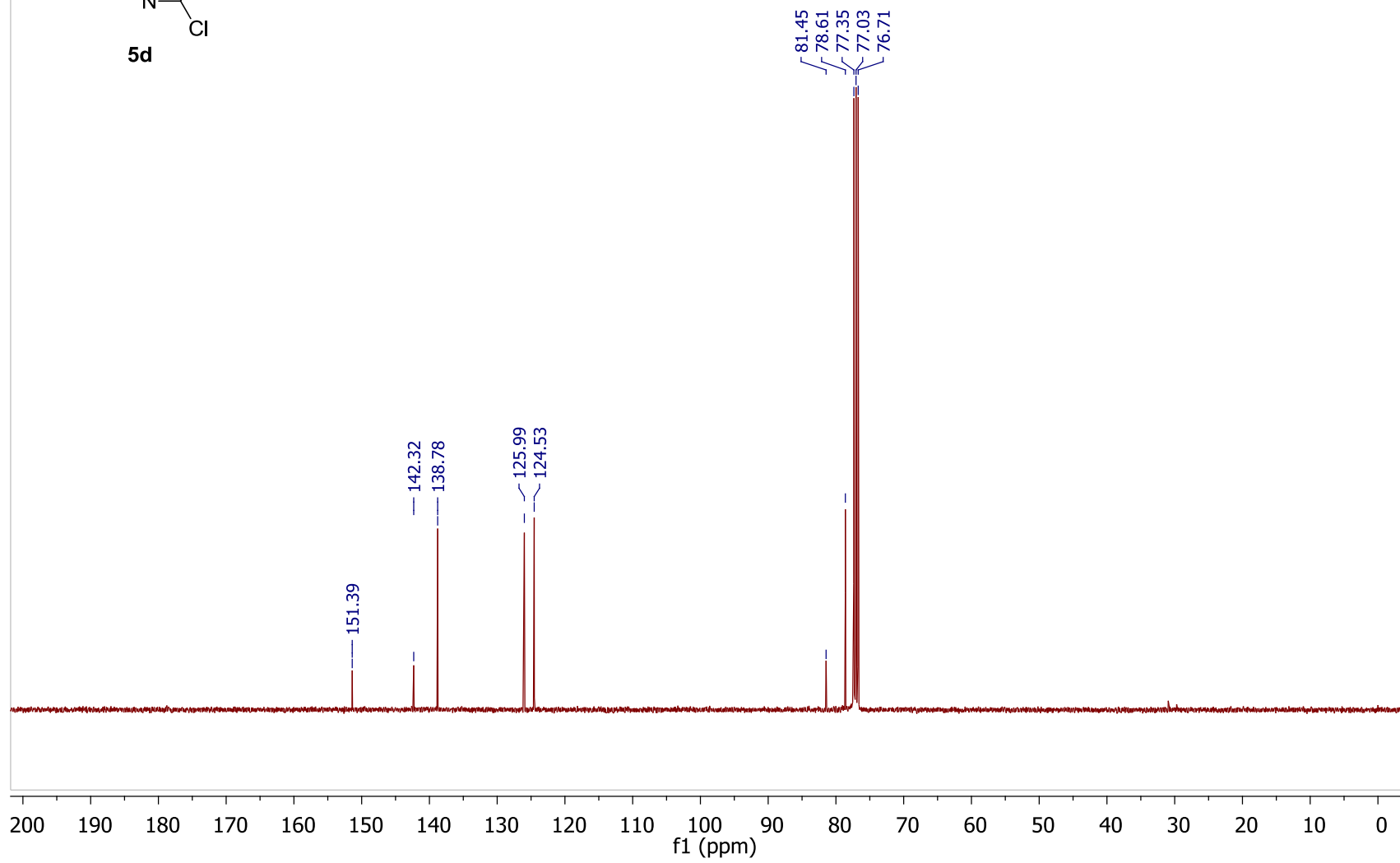
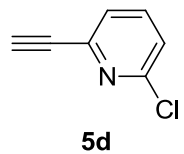


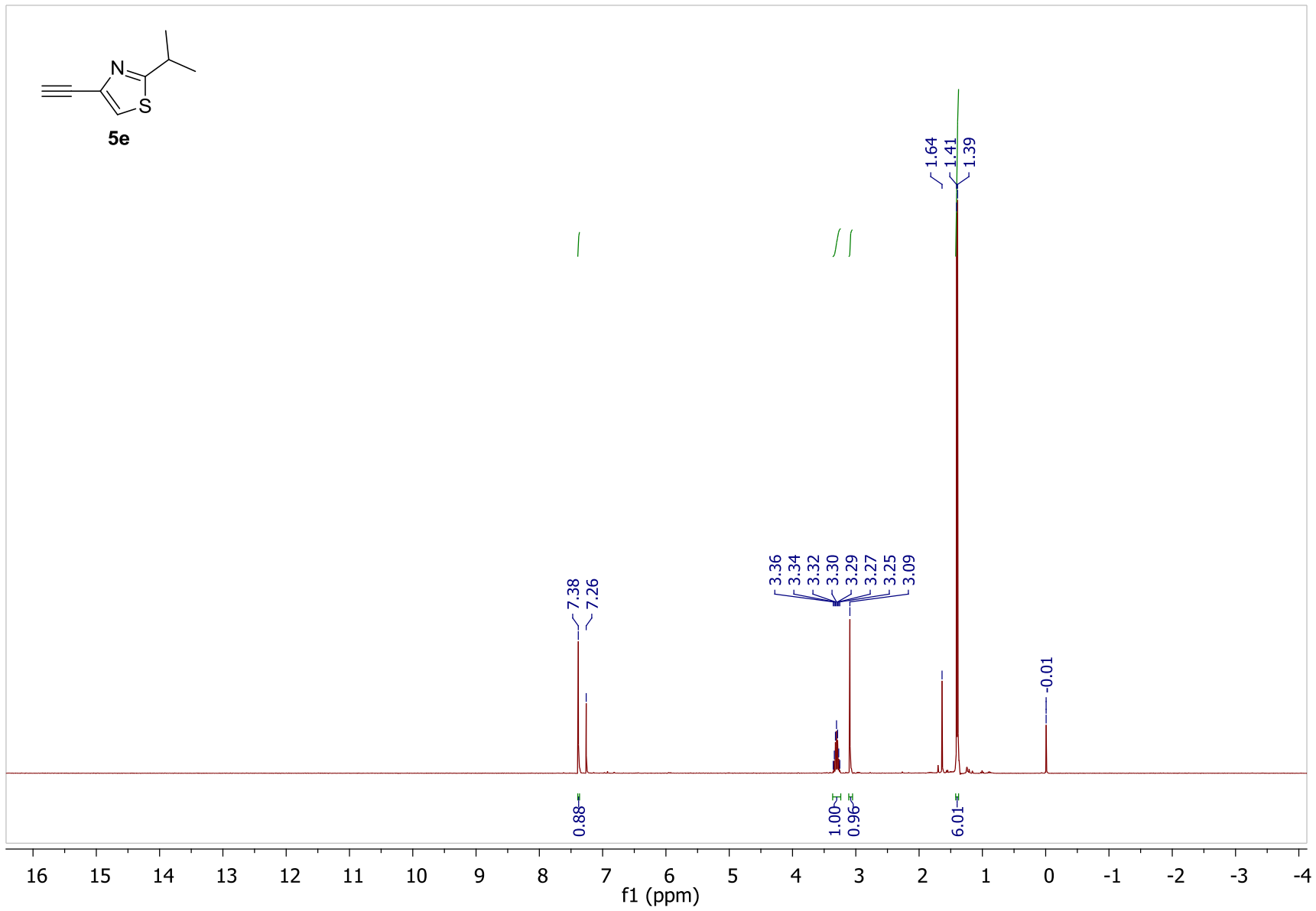
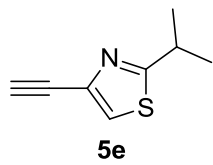


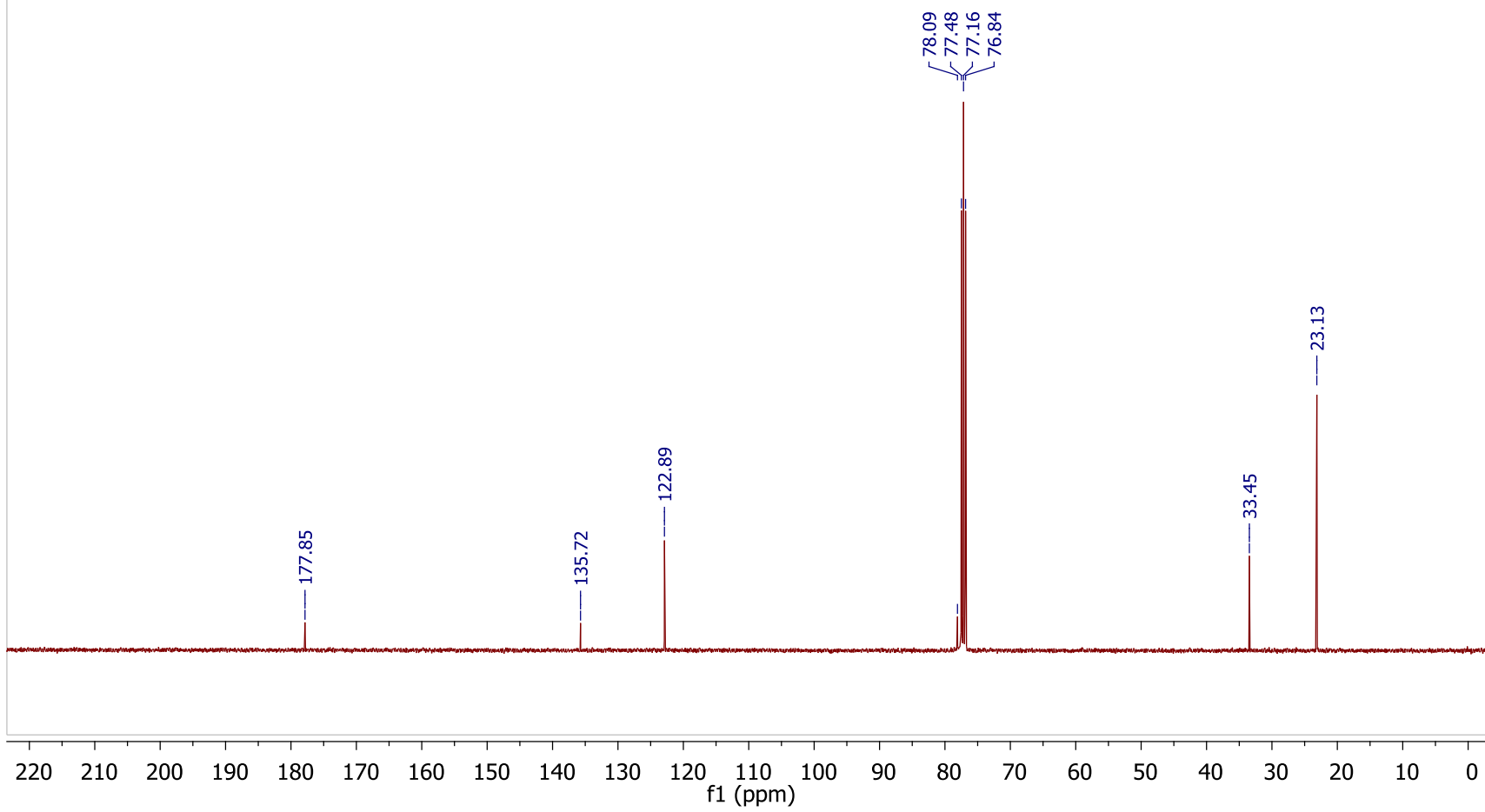
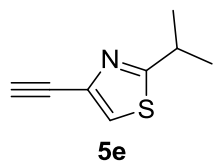
5c

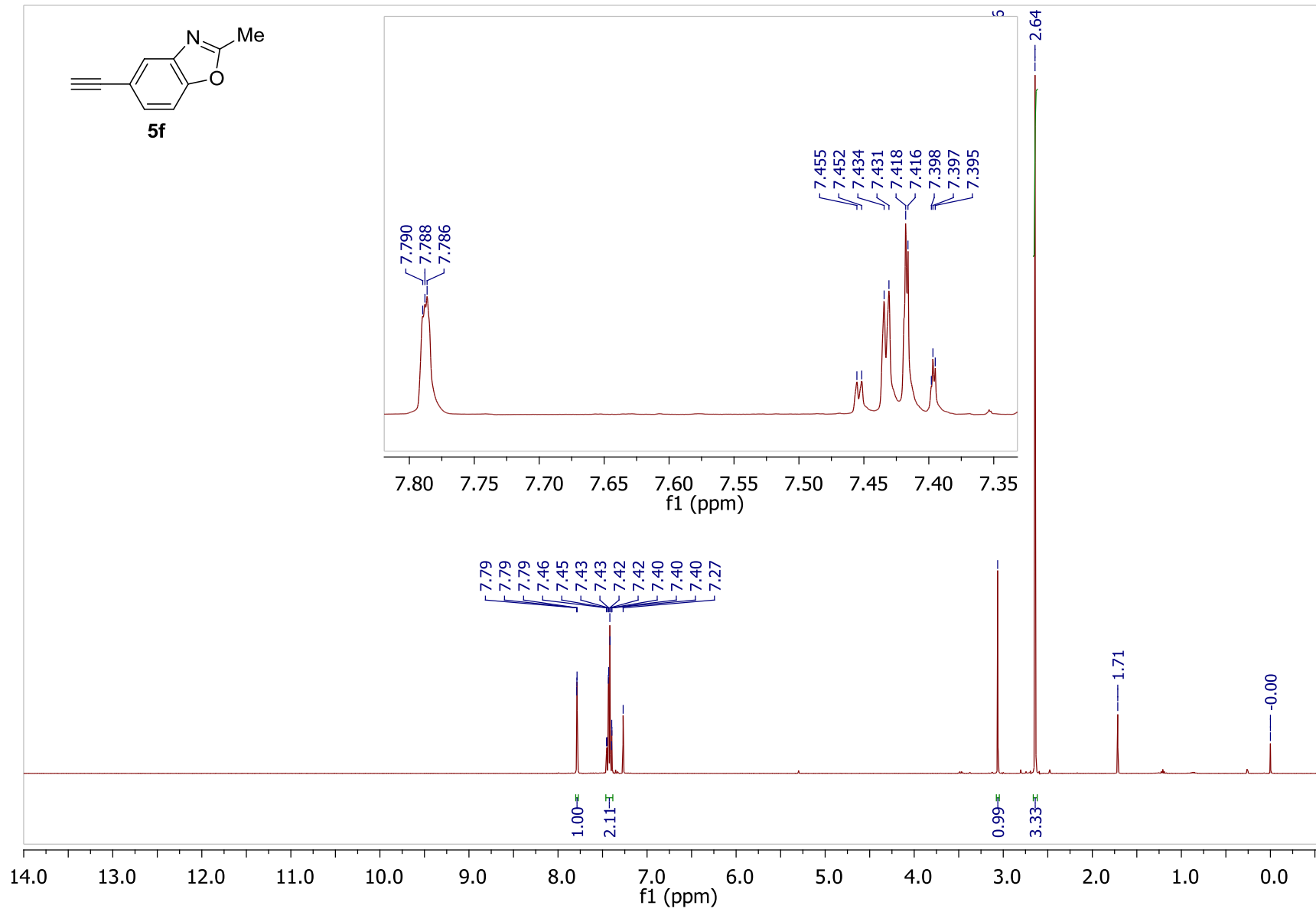
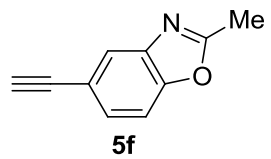


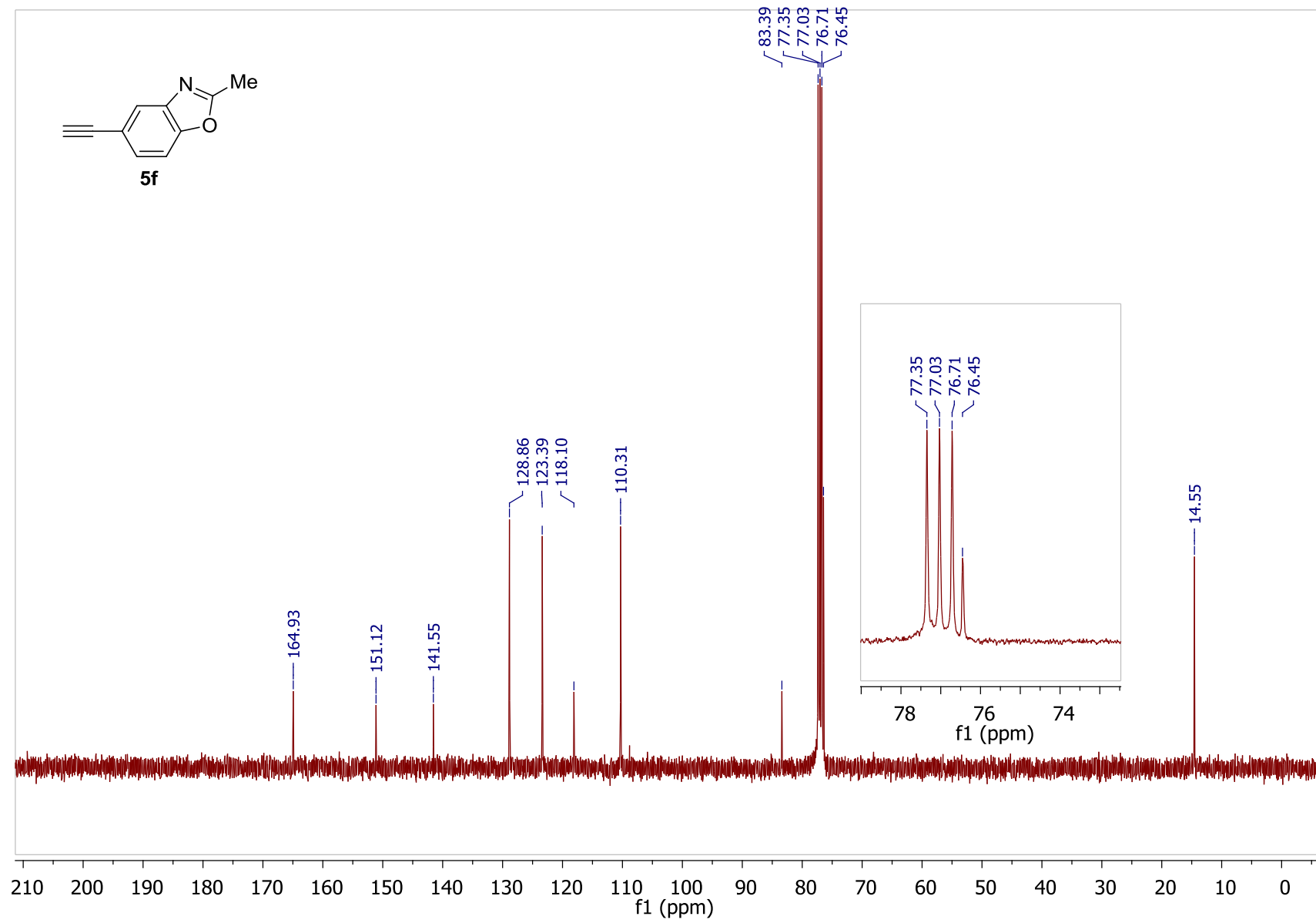
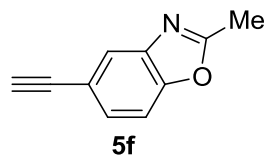


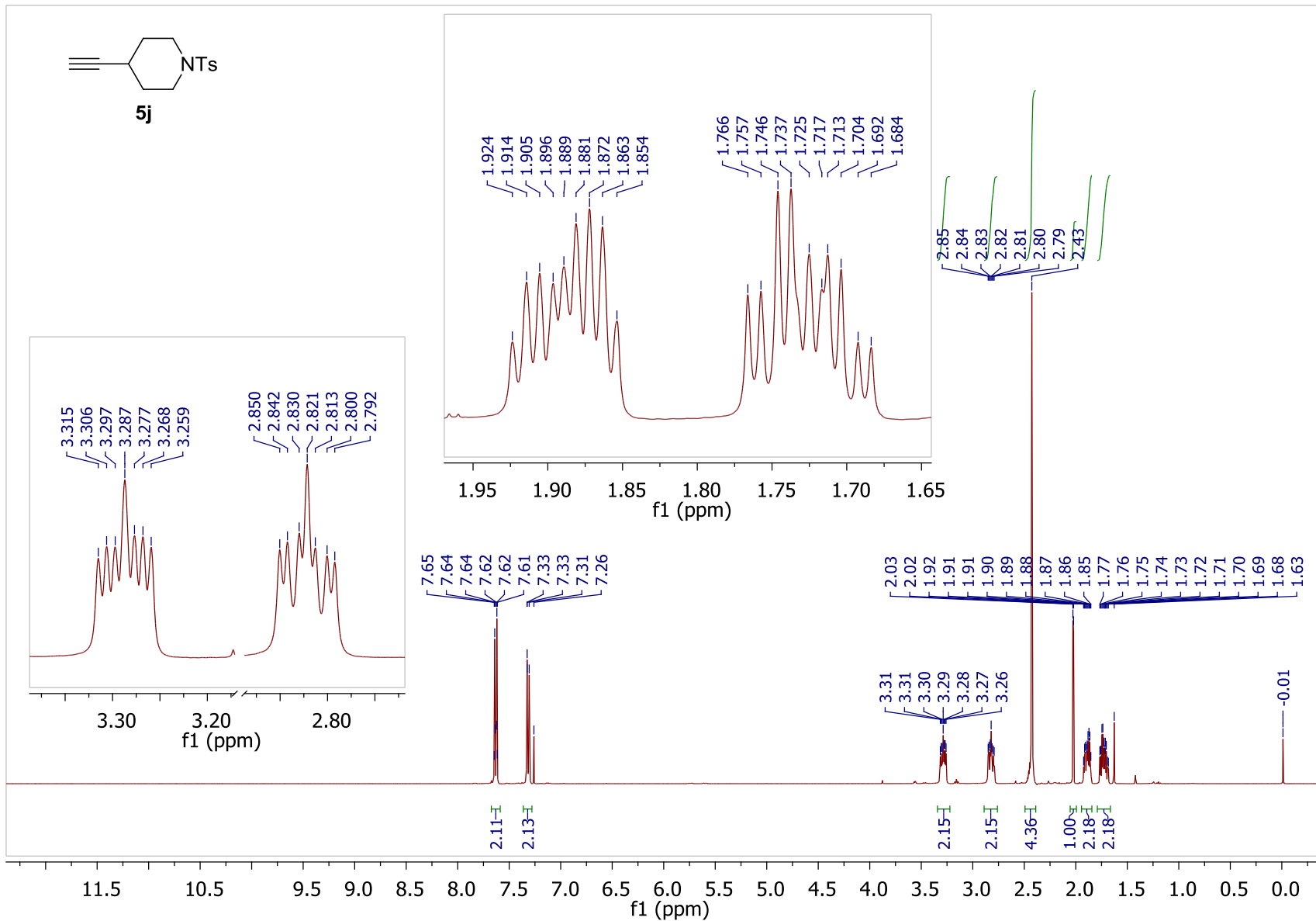
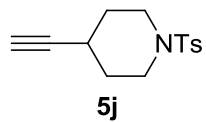


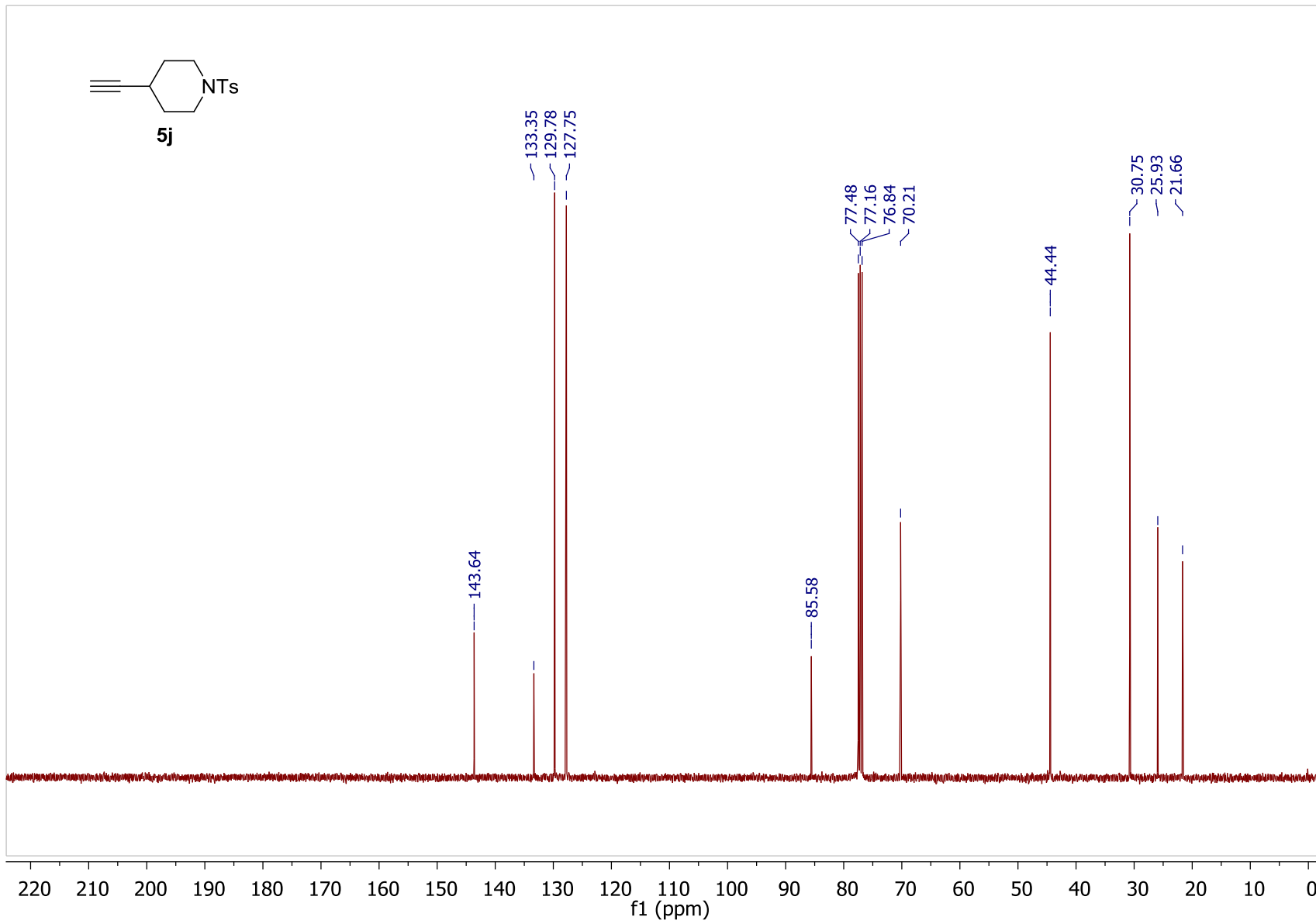
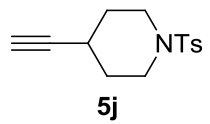


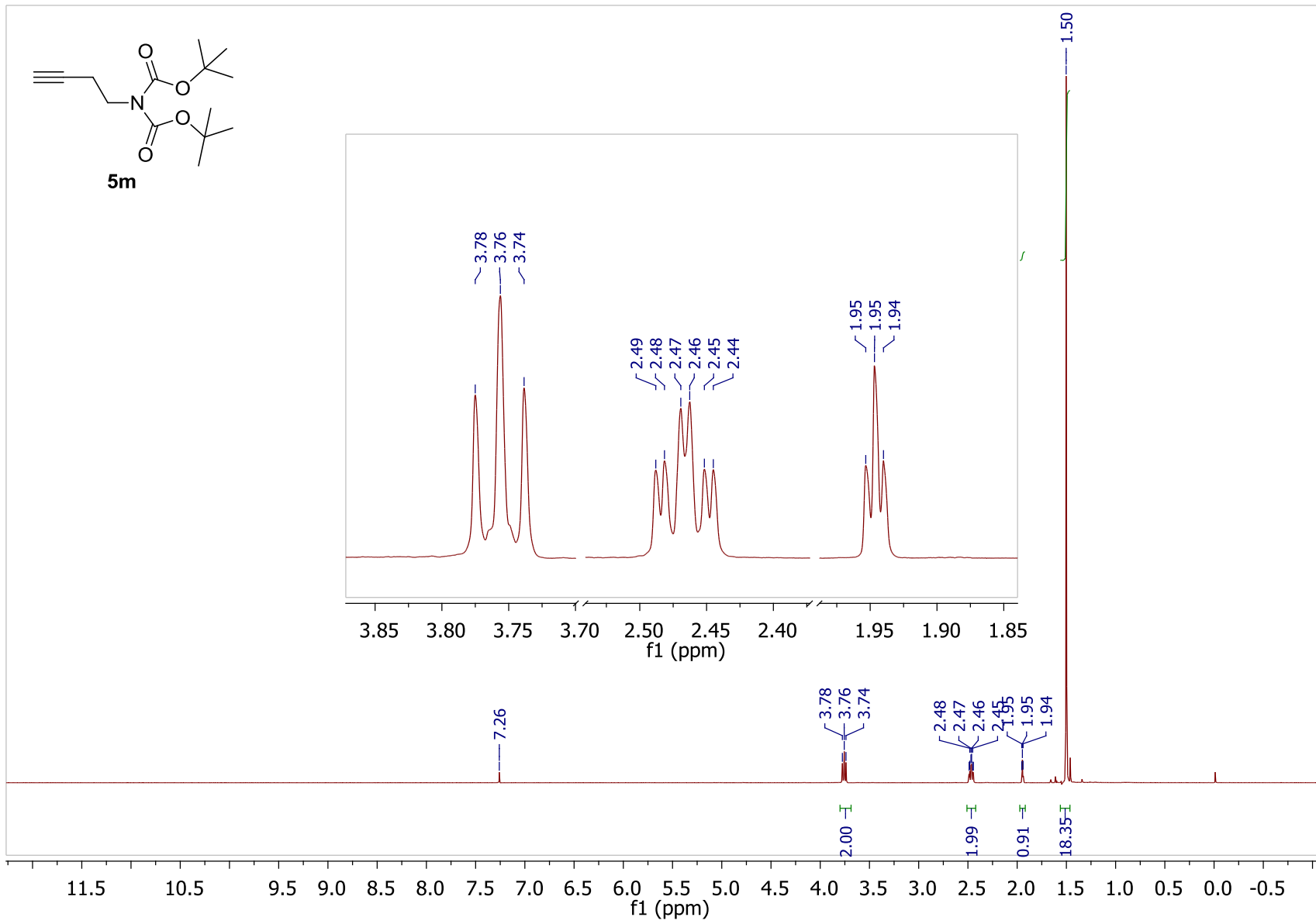
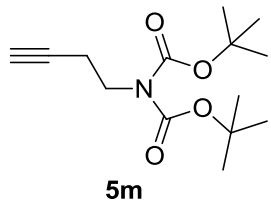


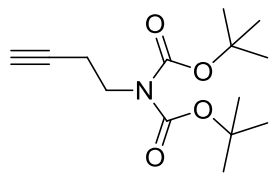




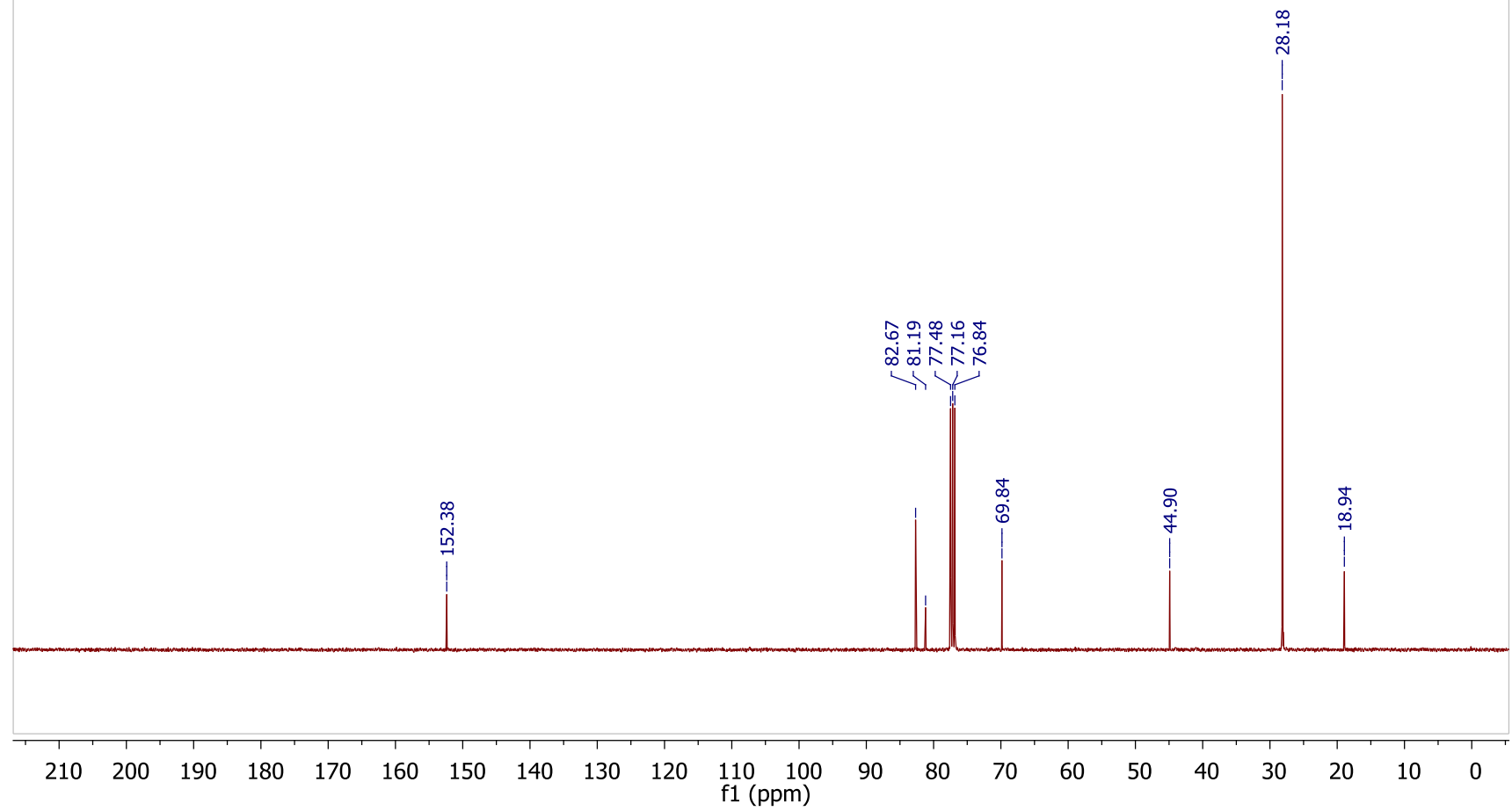


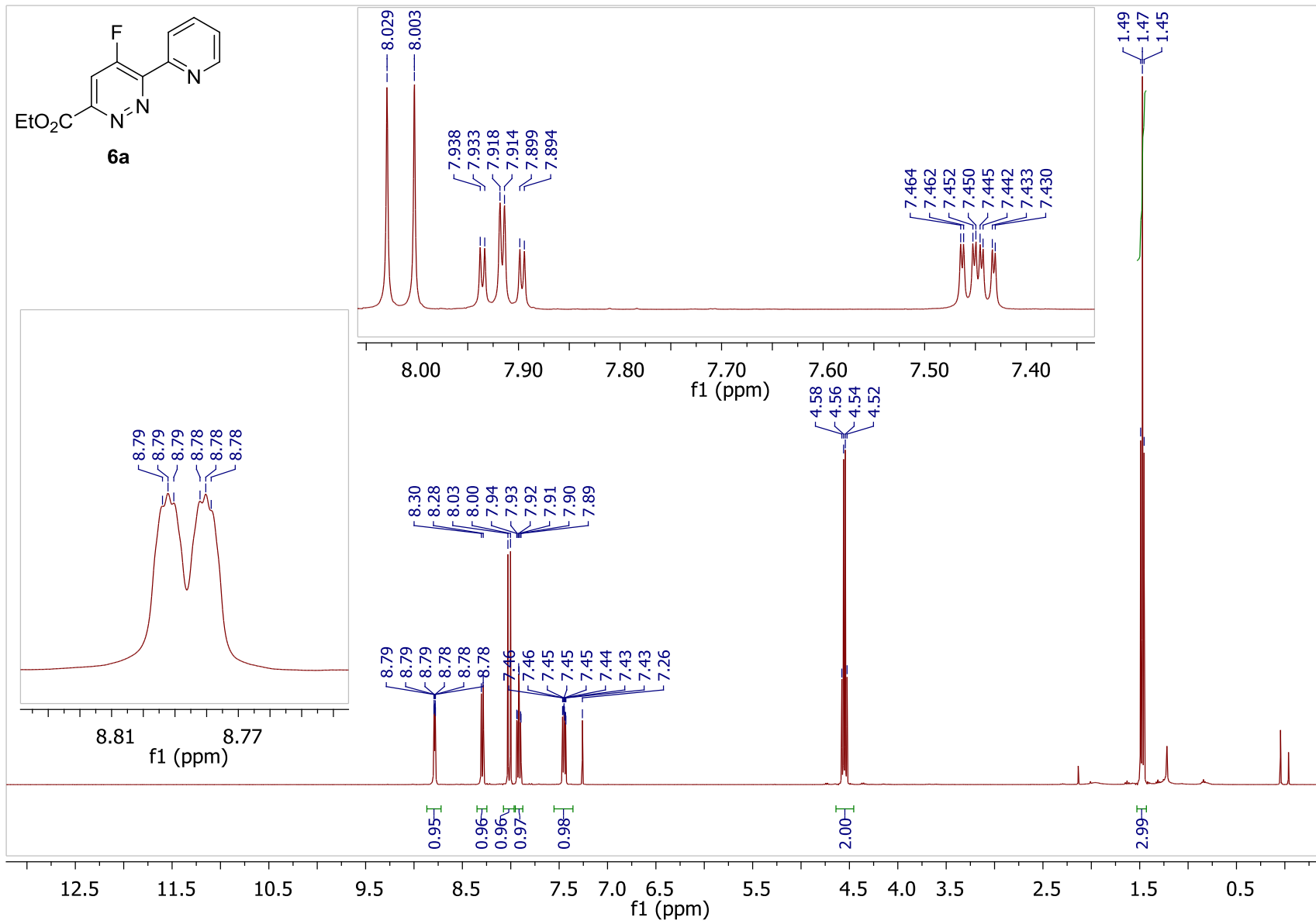
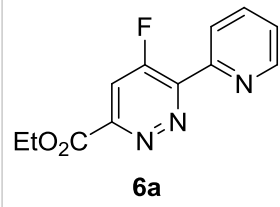


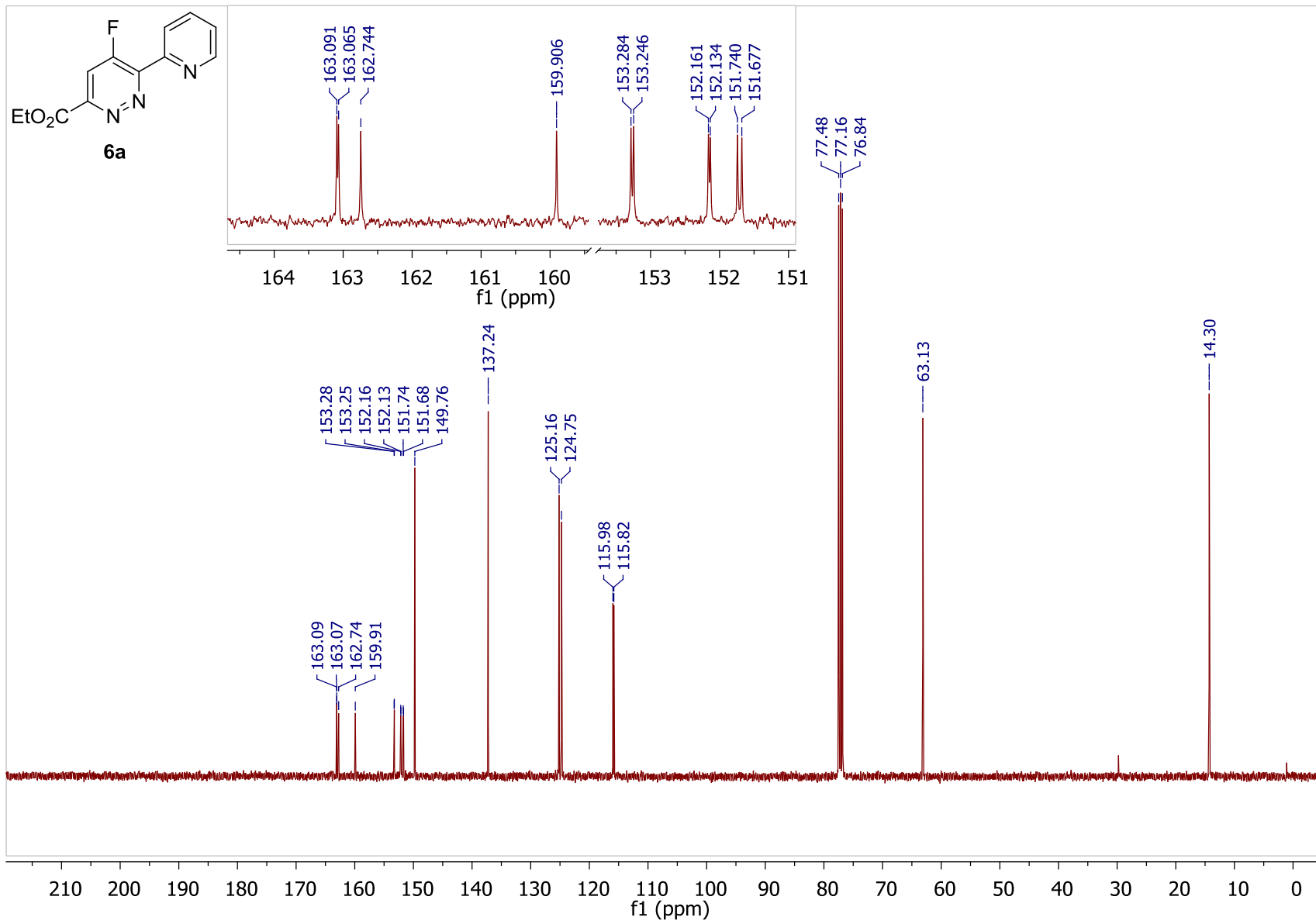


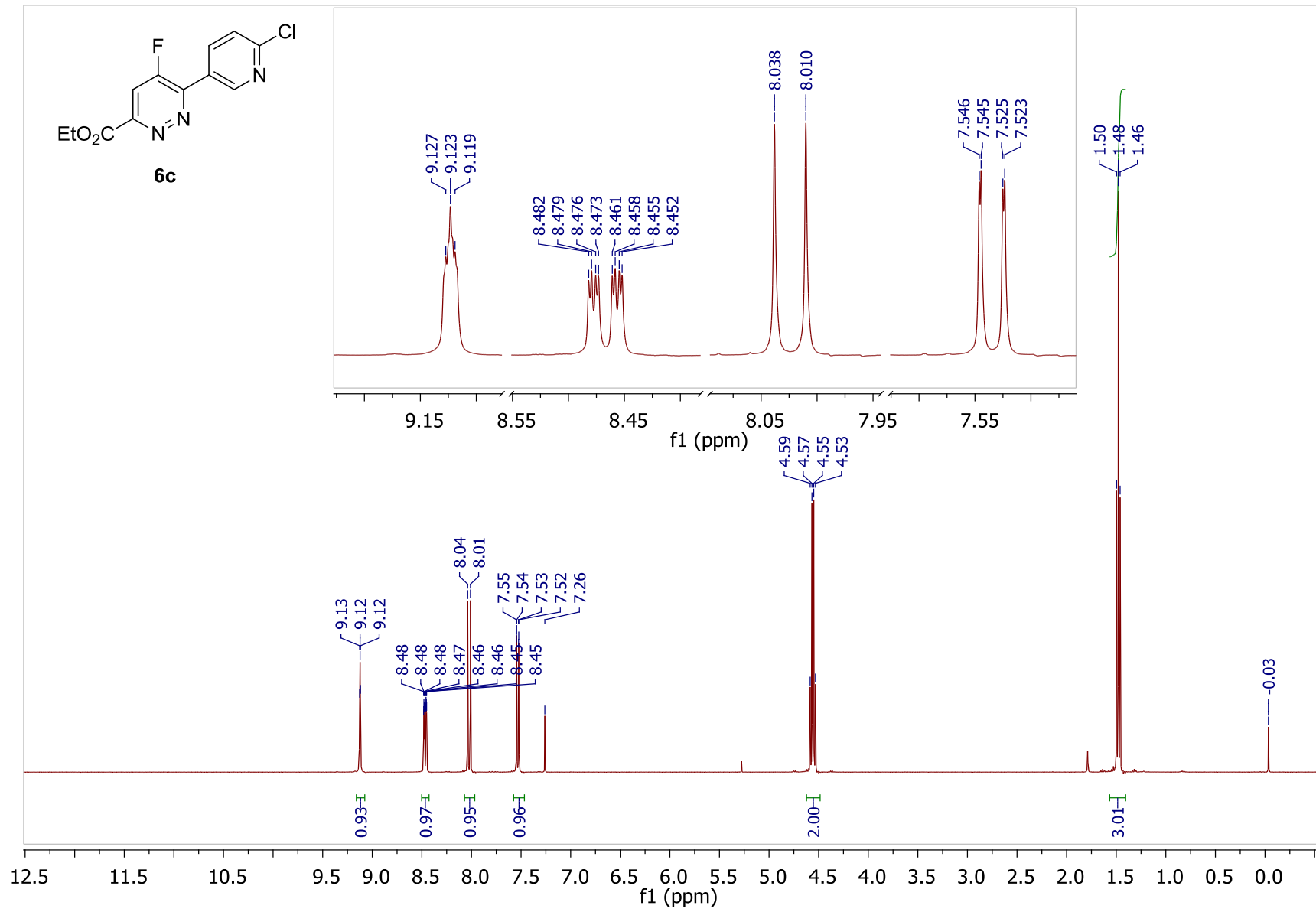
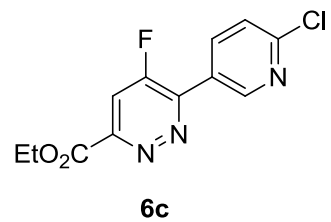


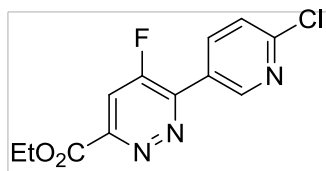
5m



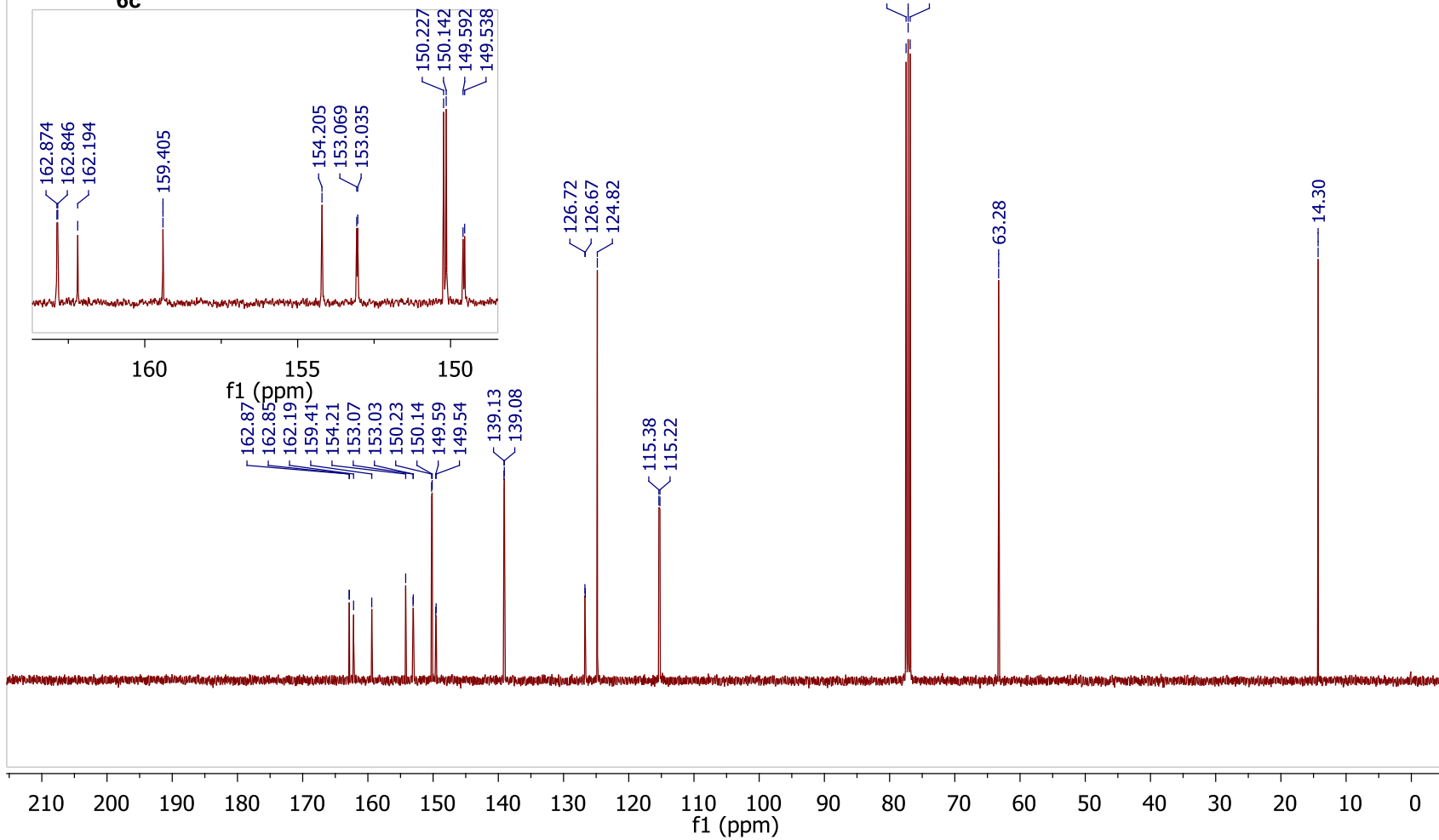


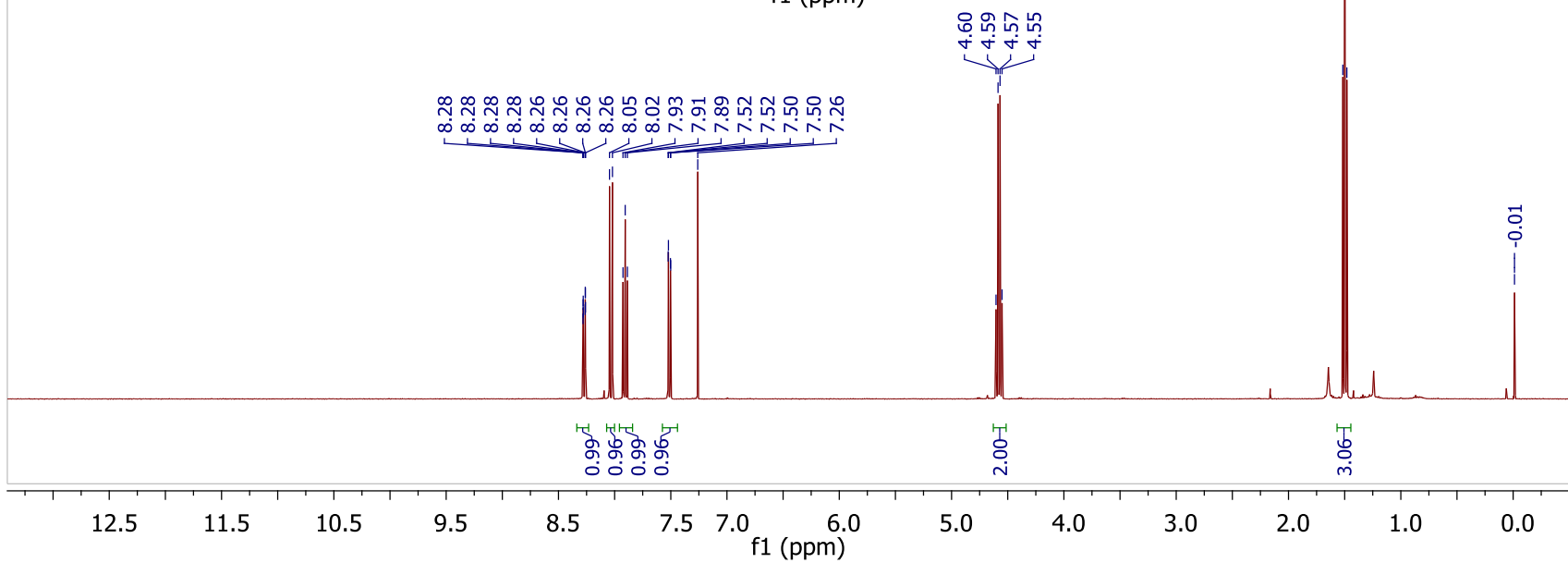
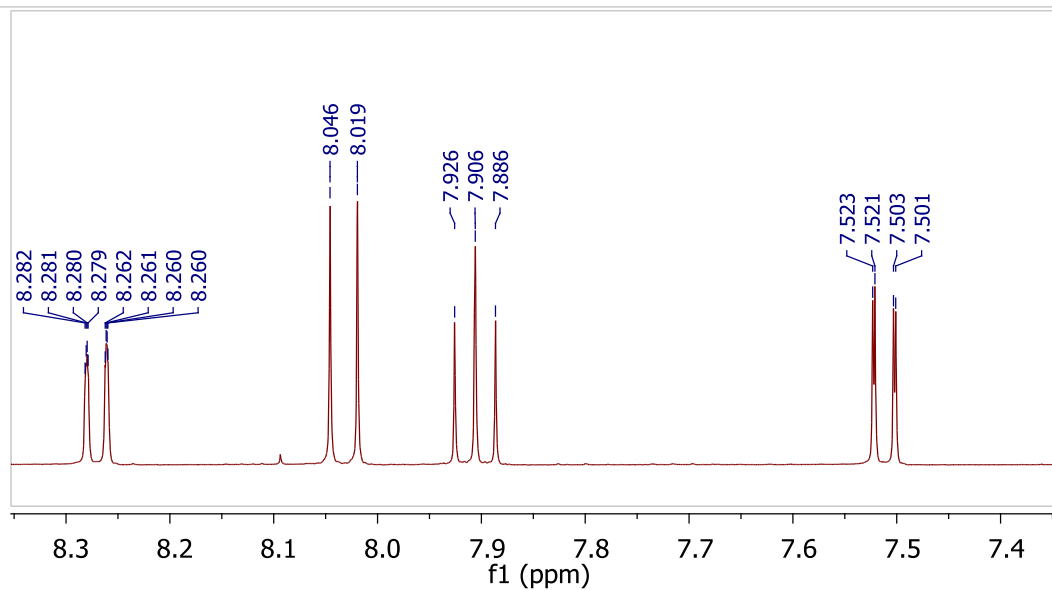
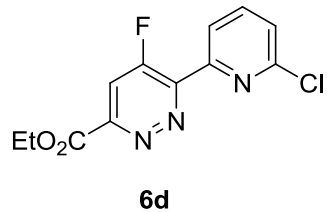


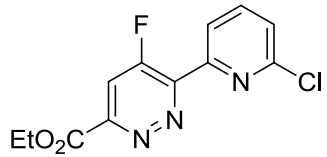




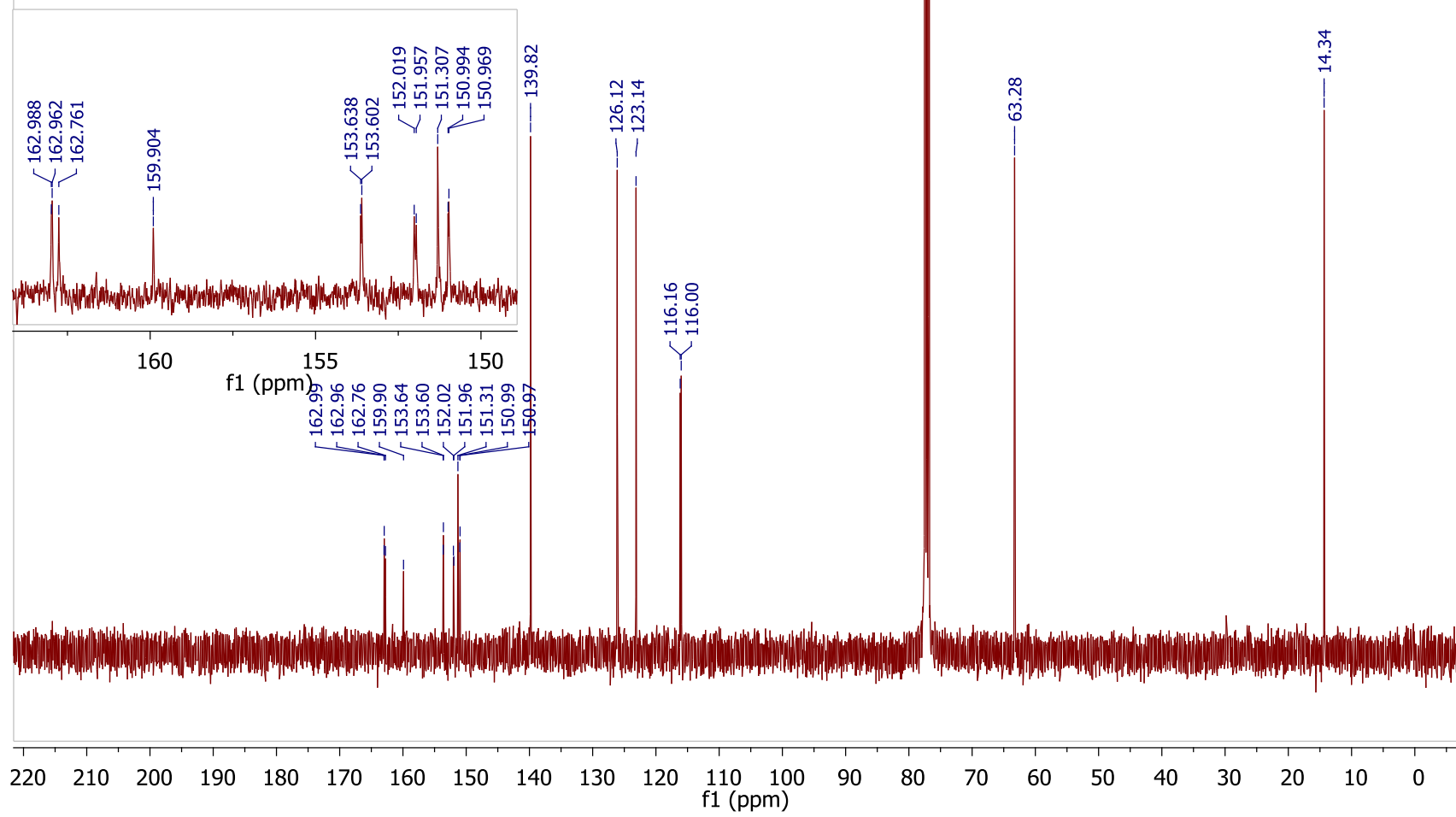
6c

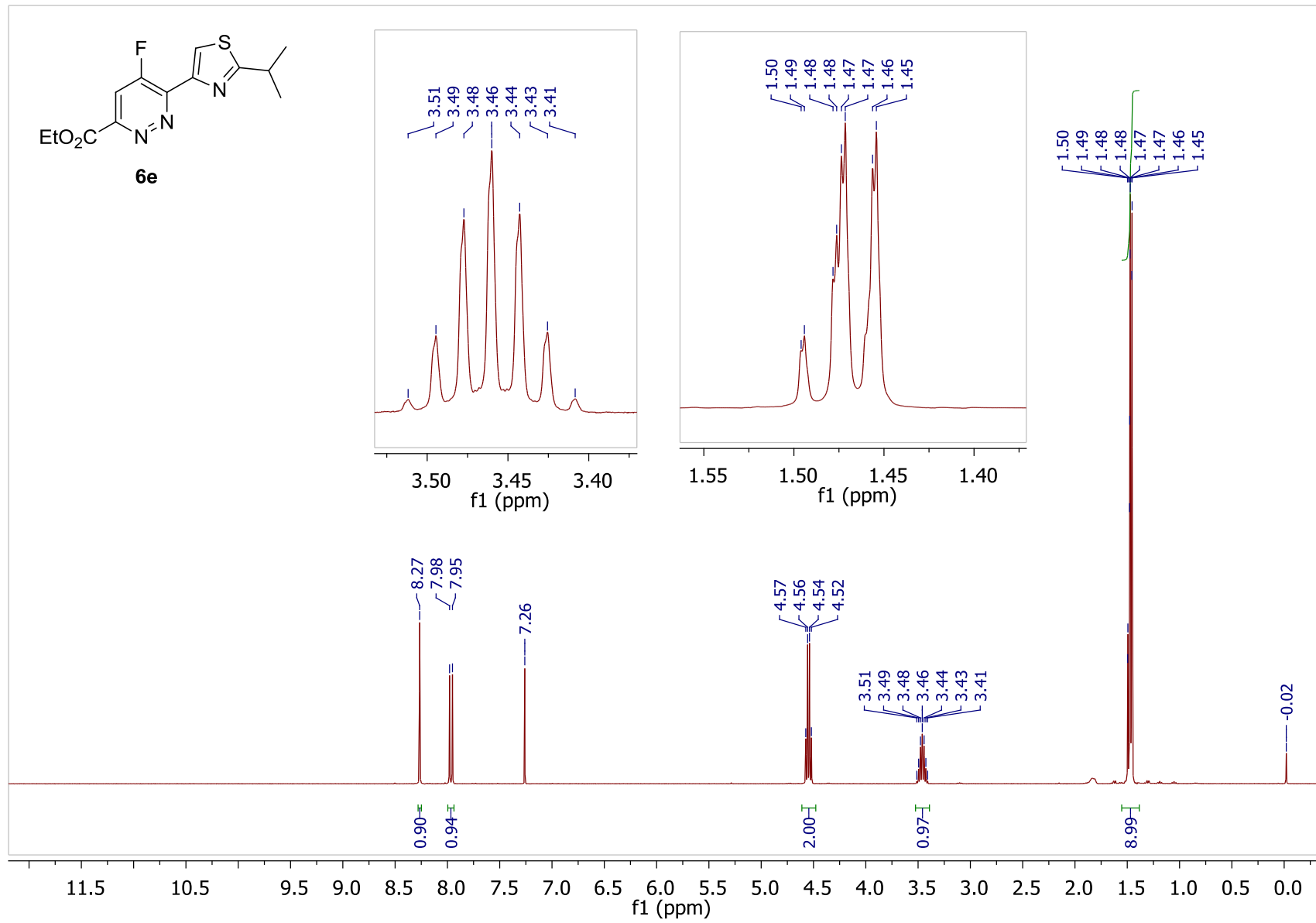
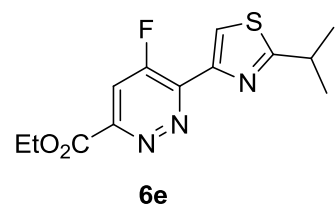


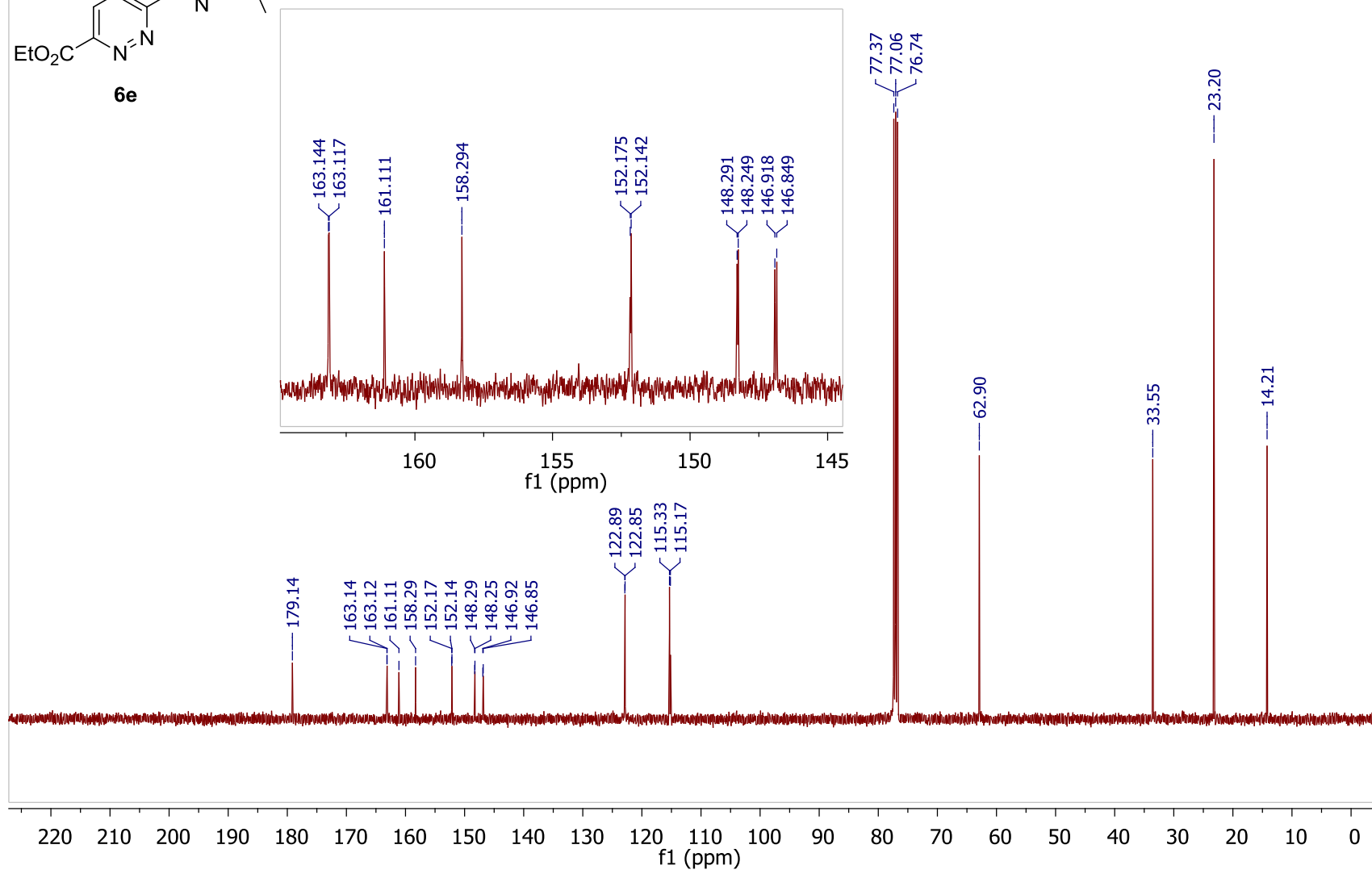
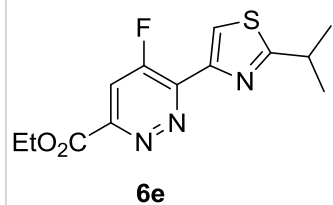


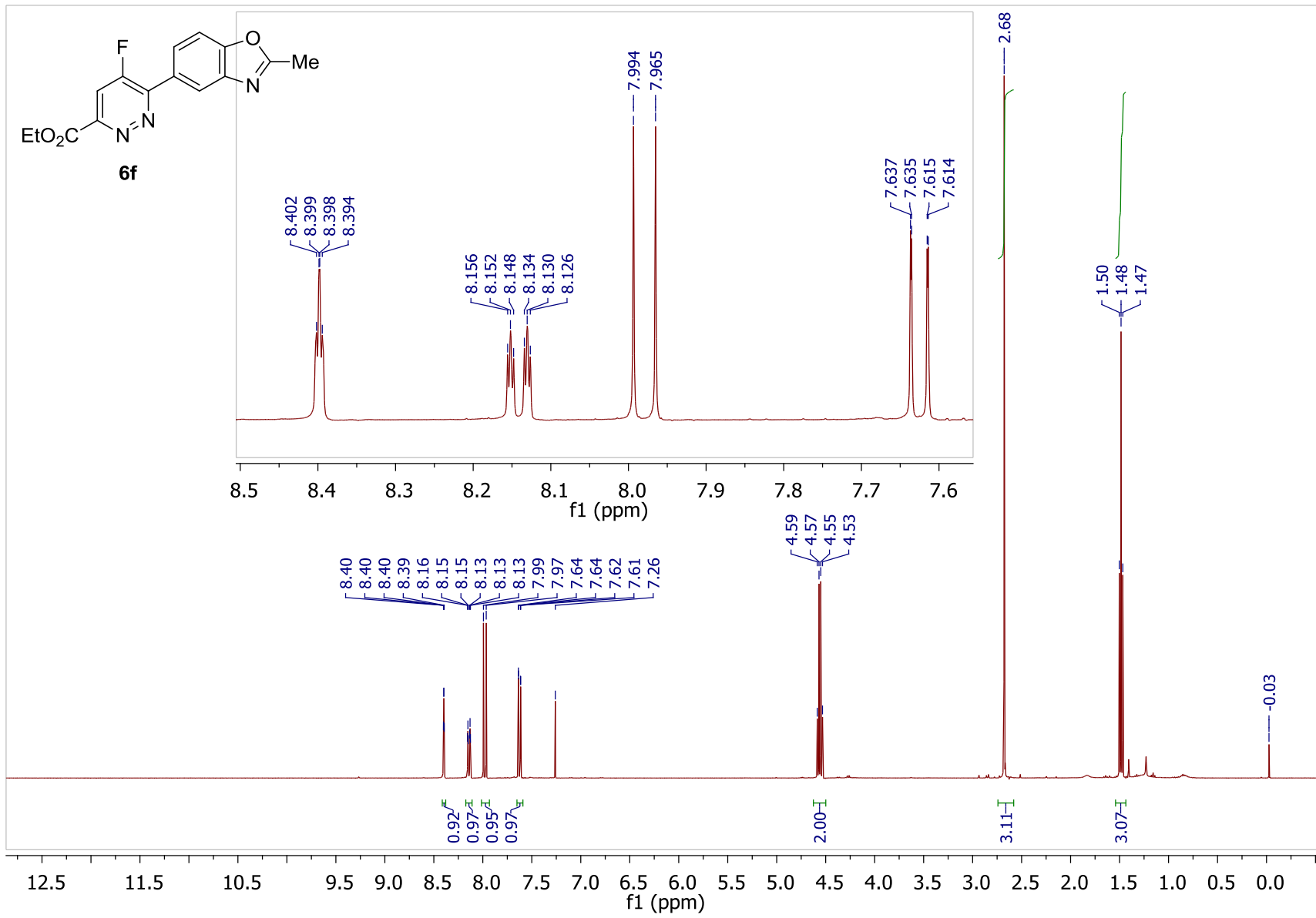
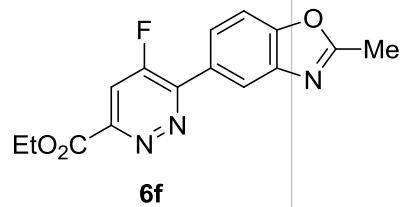


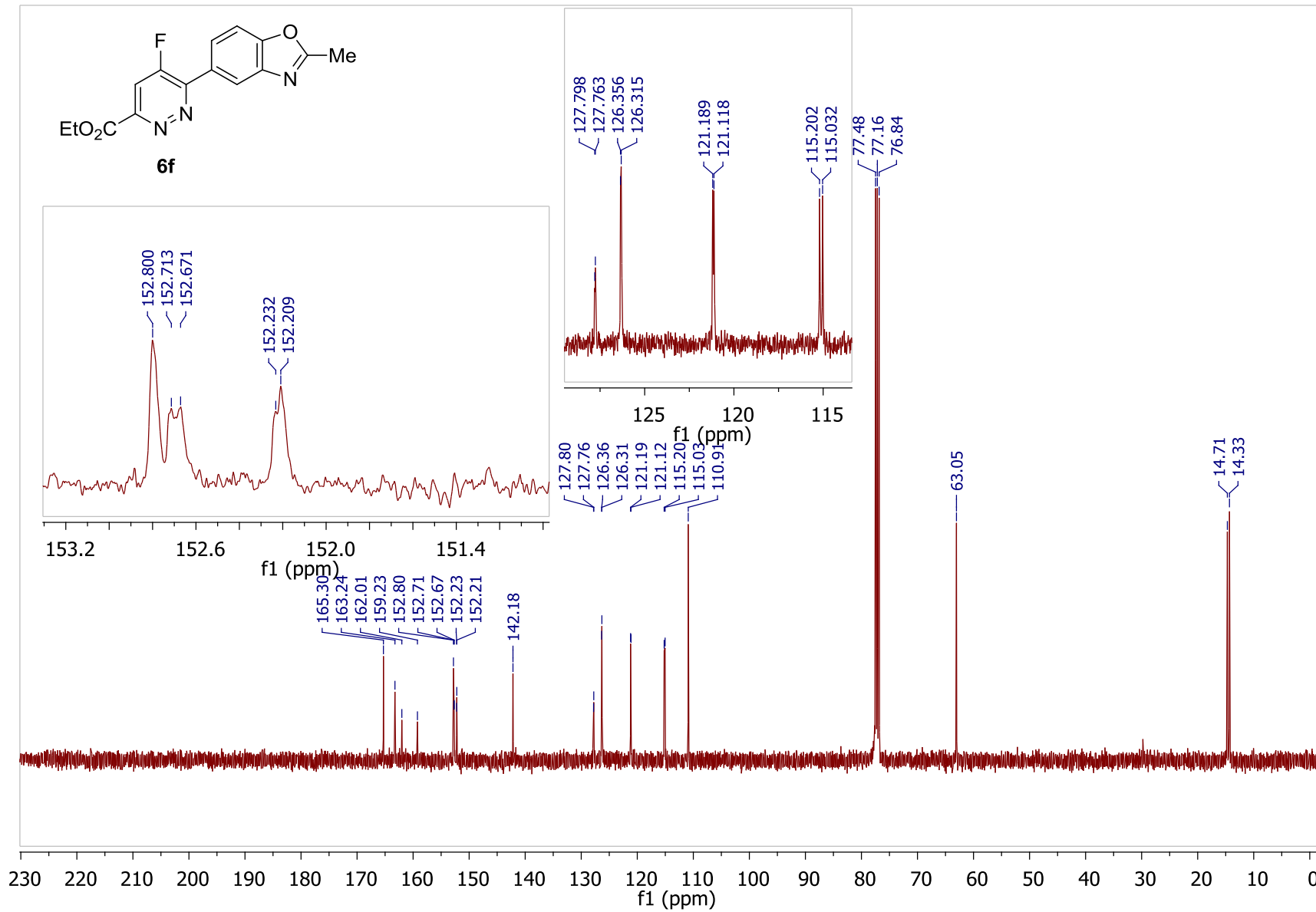
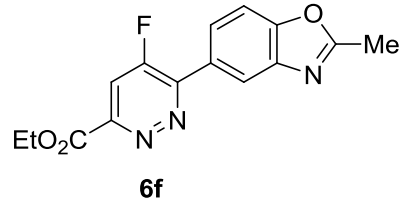
6d

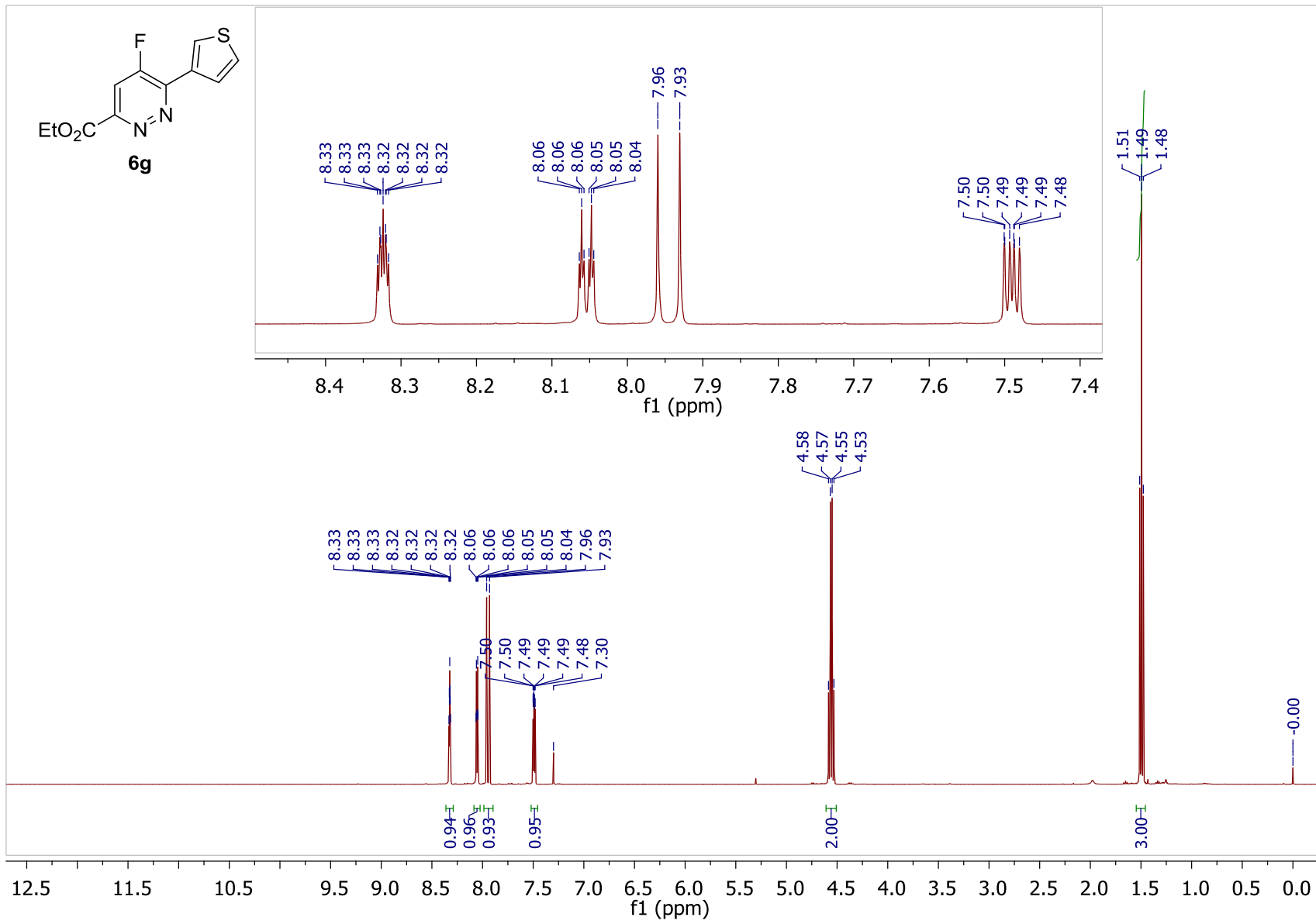
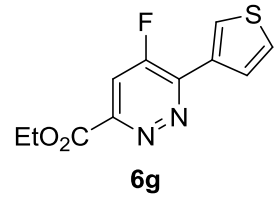


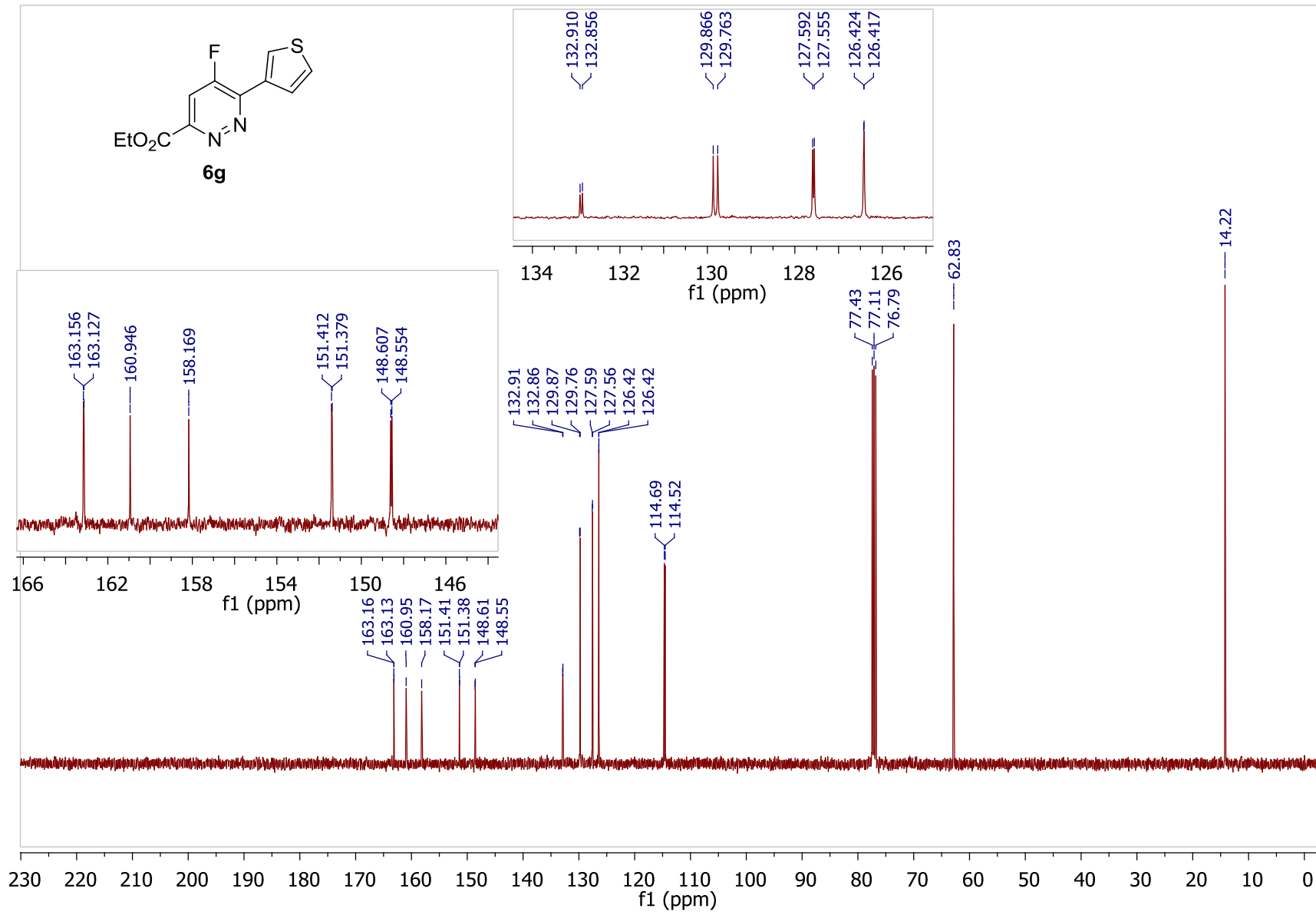
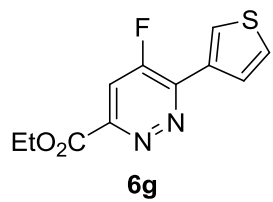


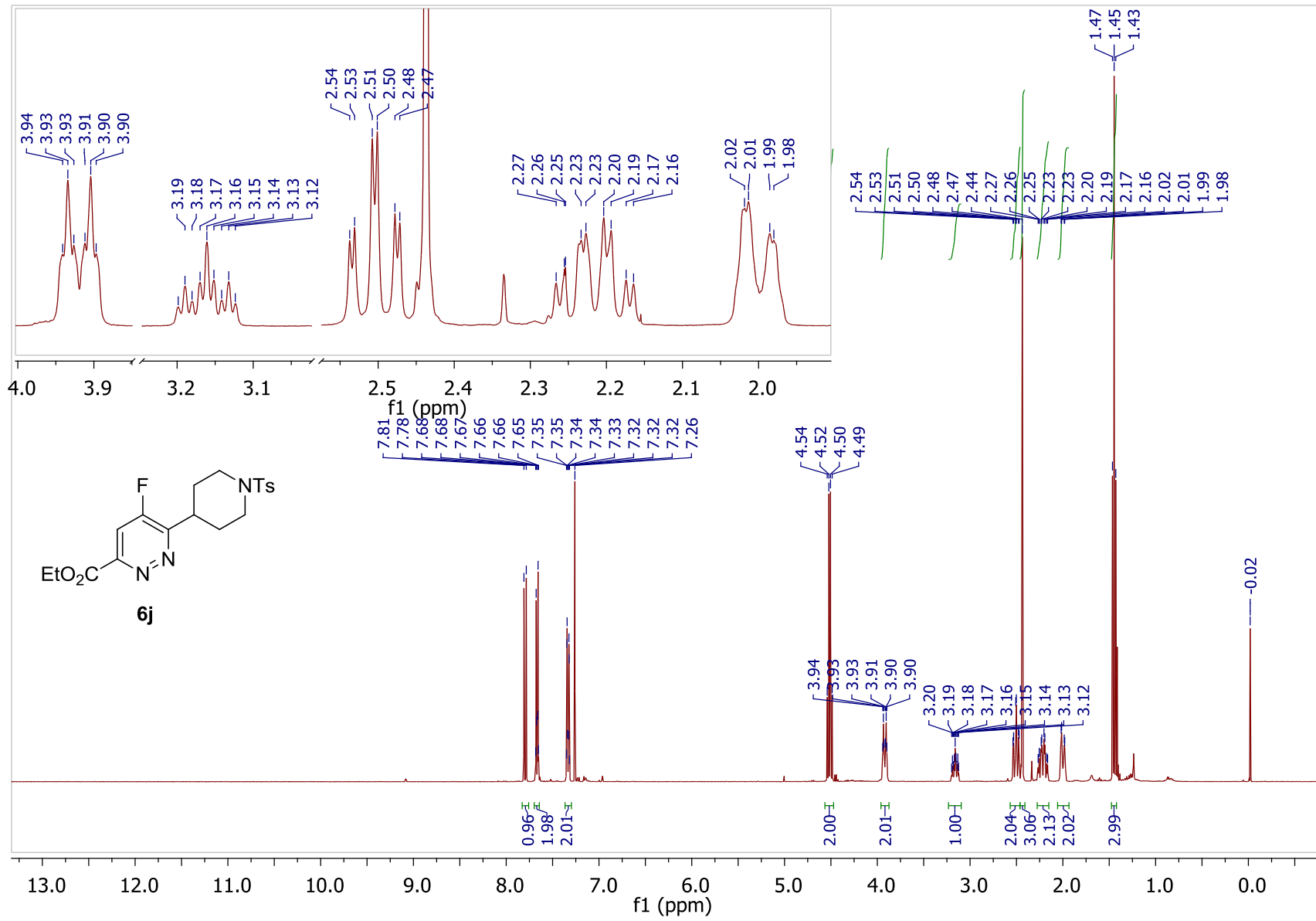


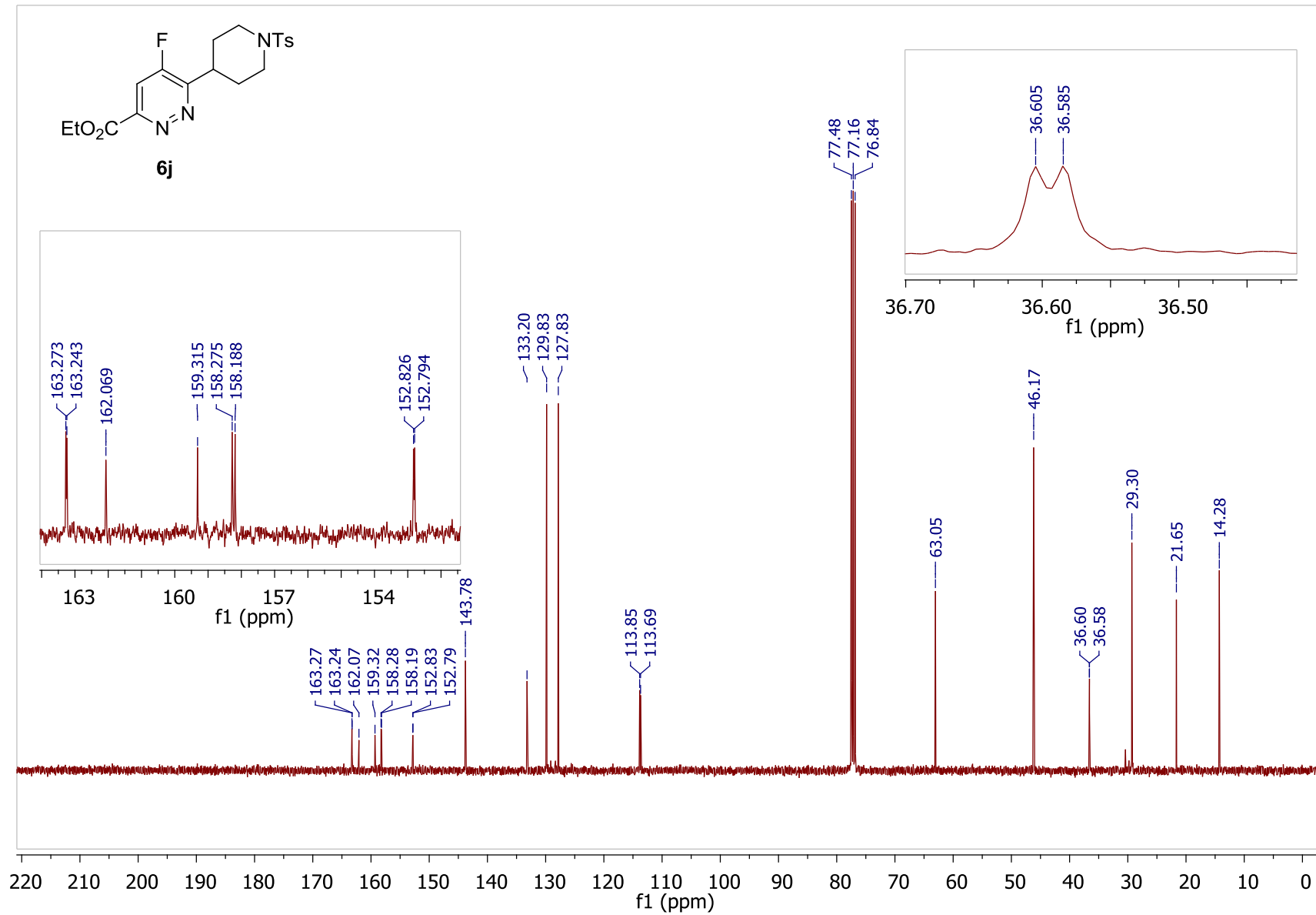
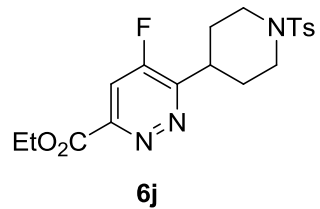


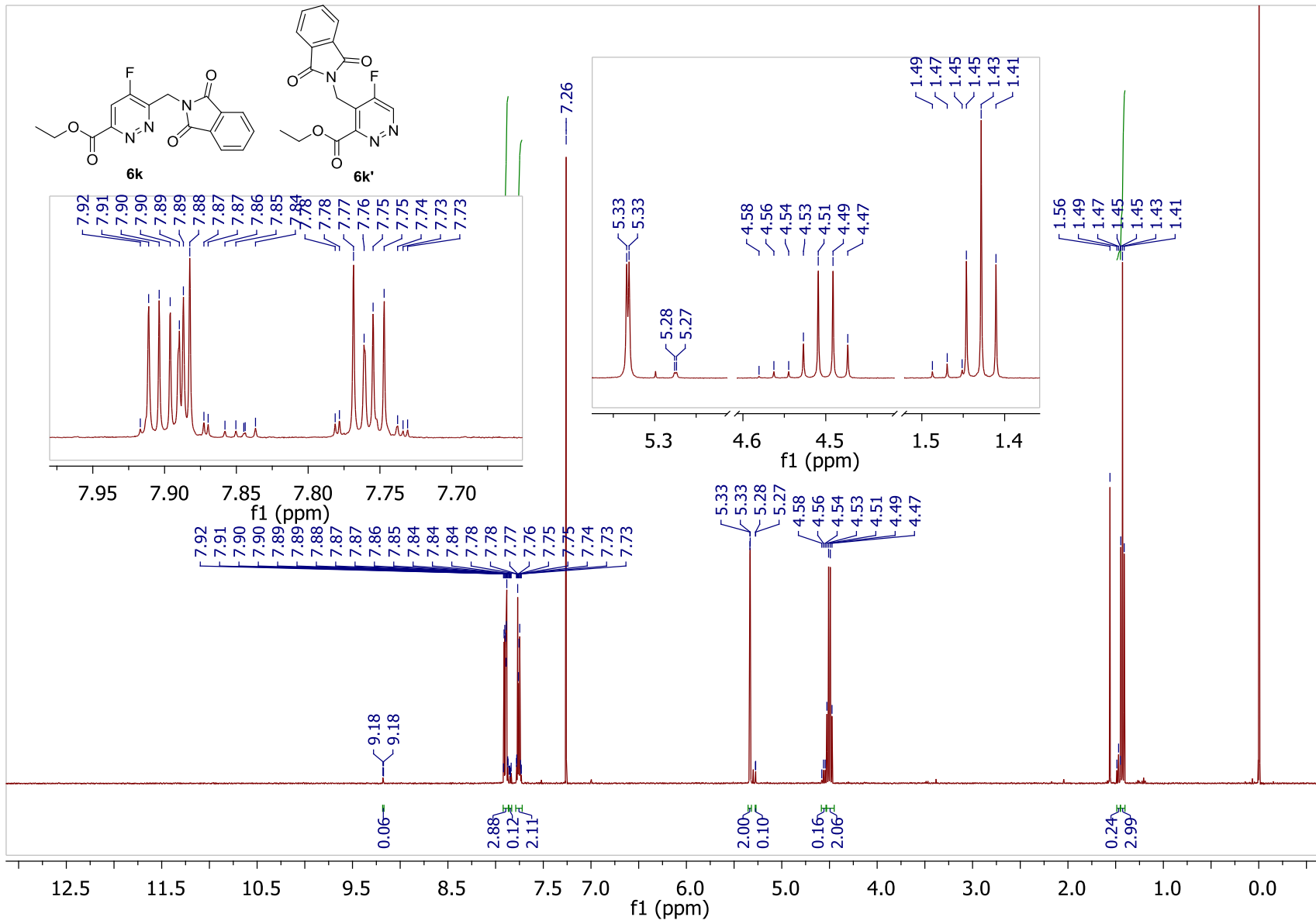


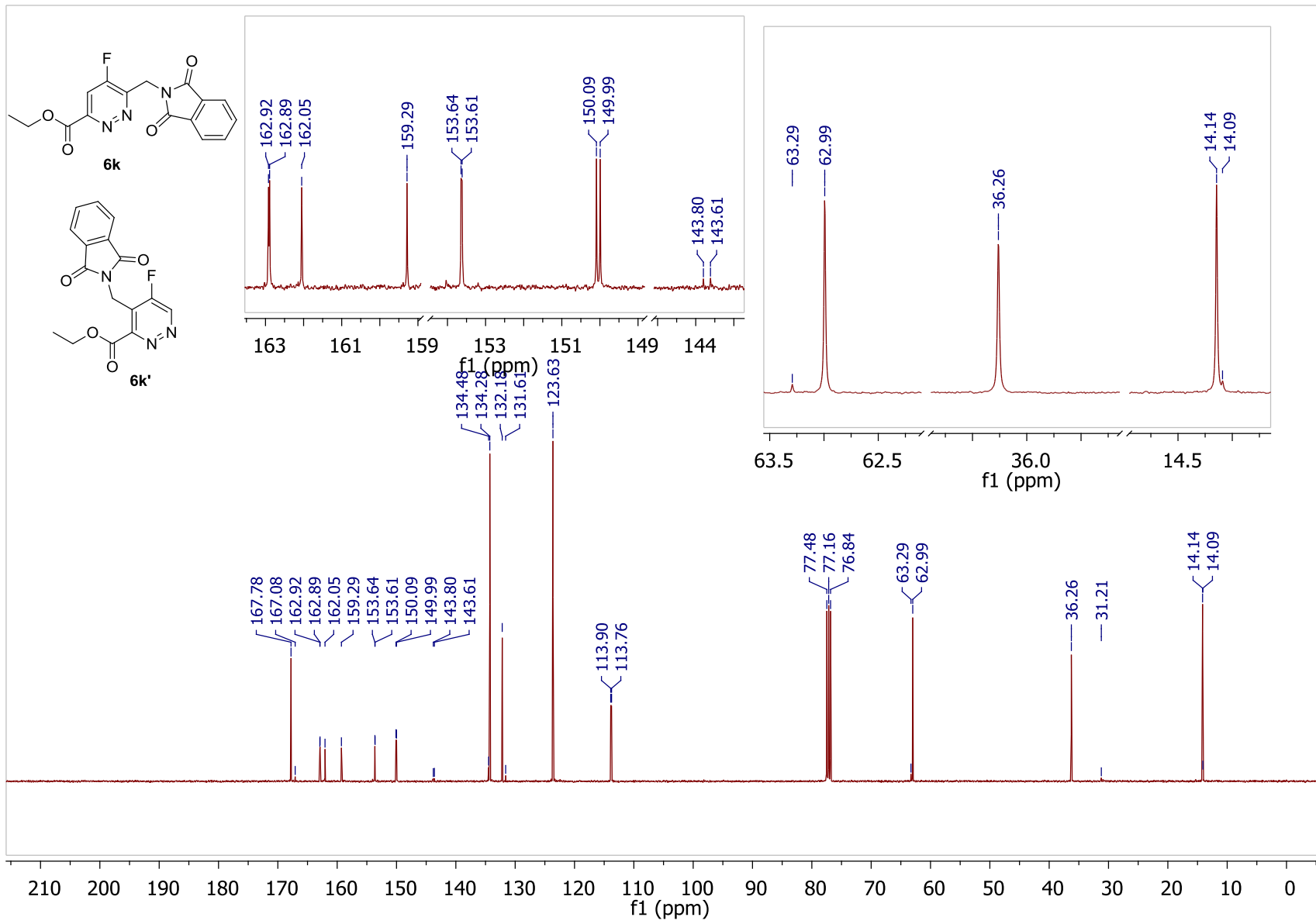


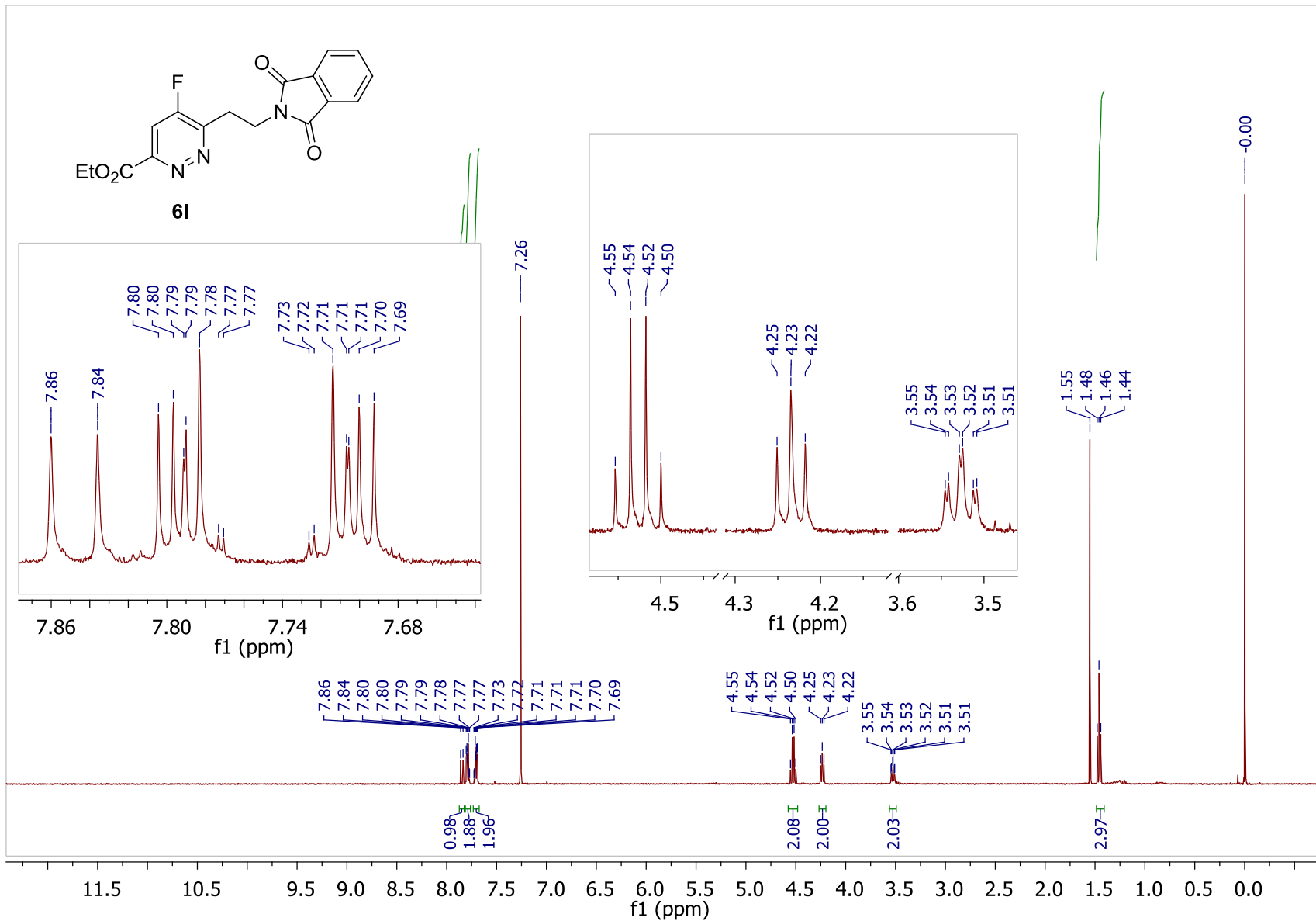
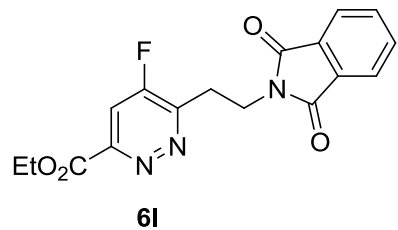


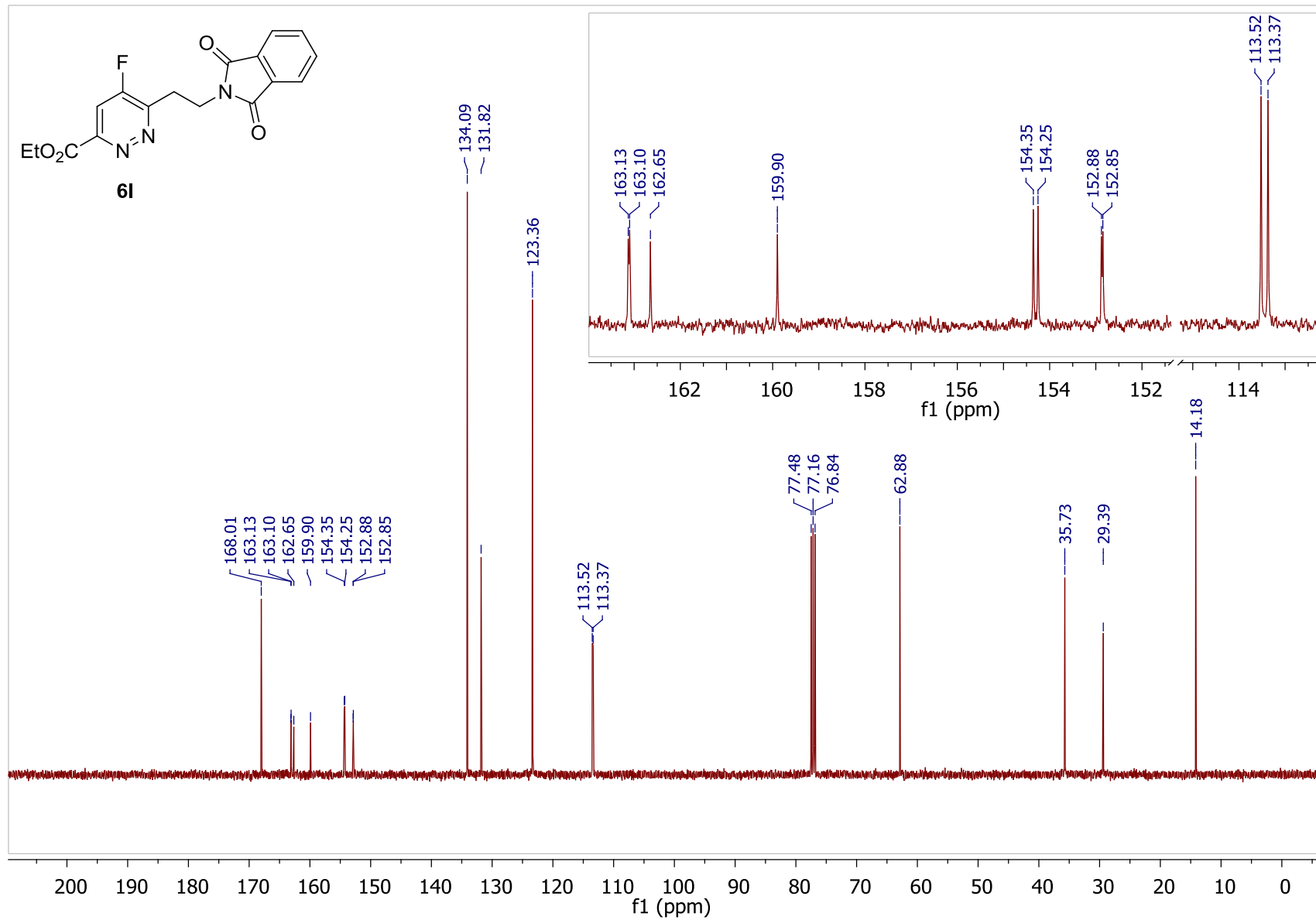
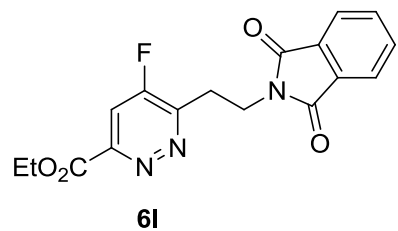


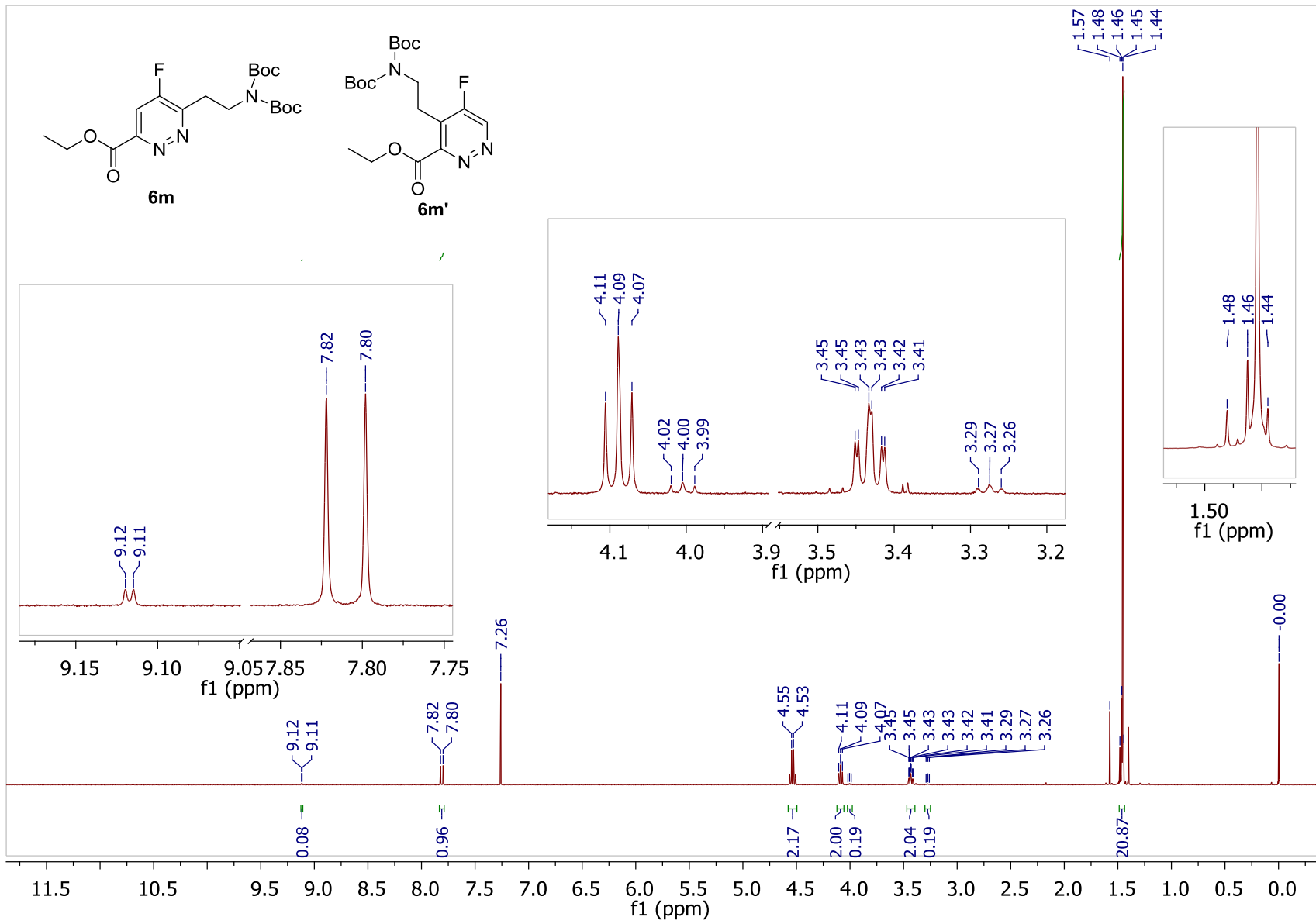


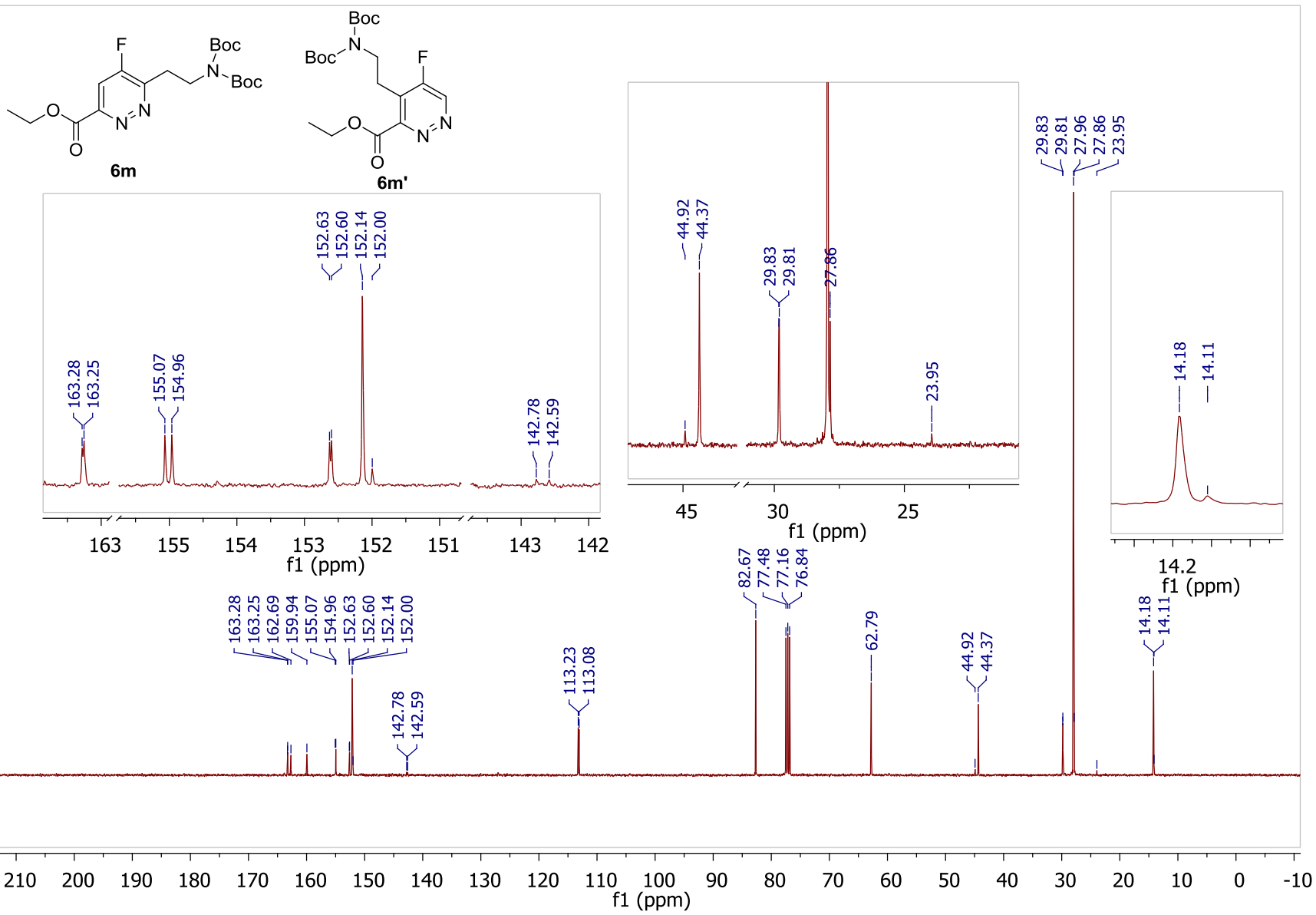


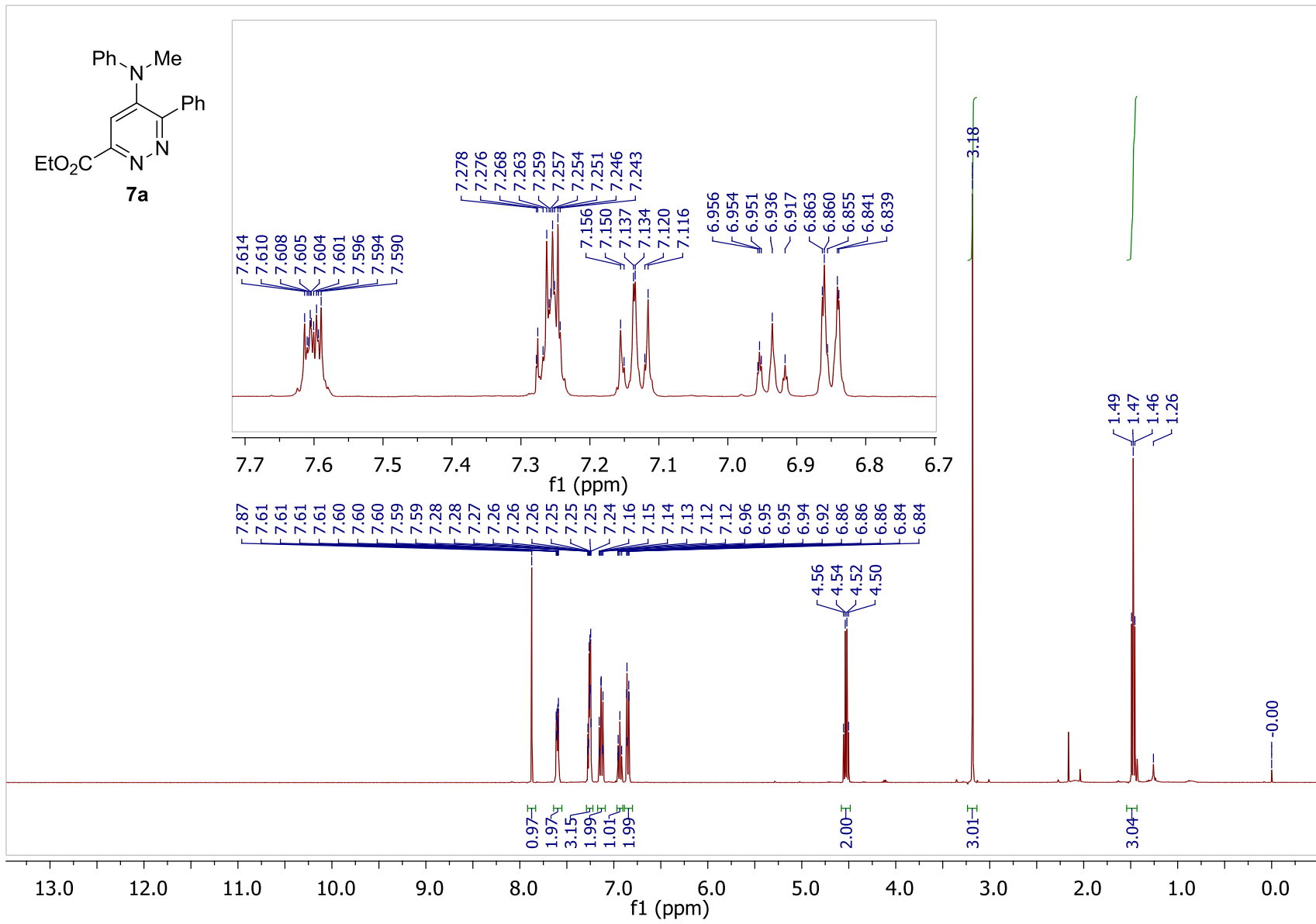
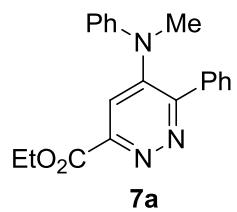


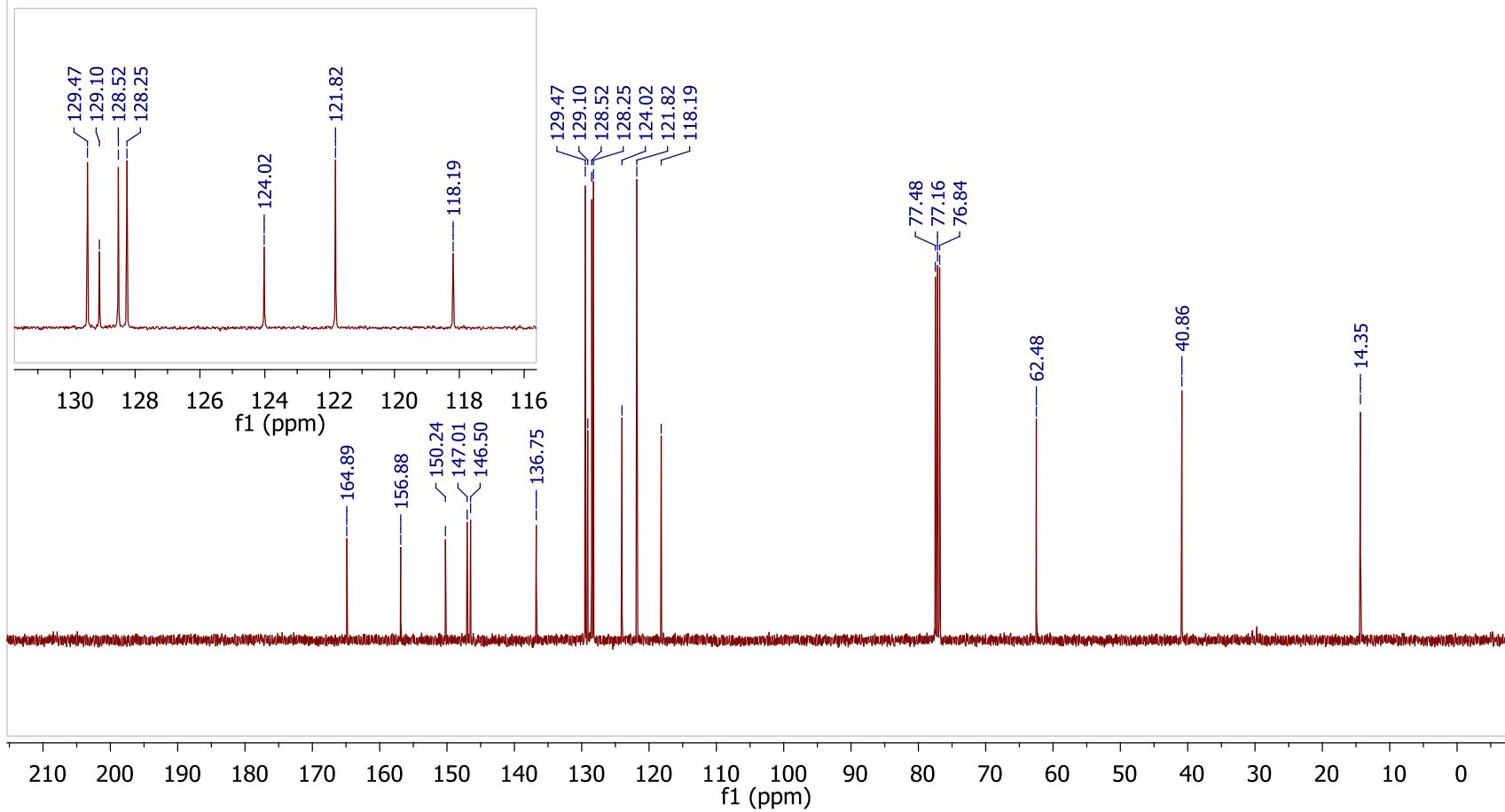
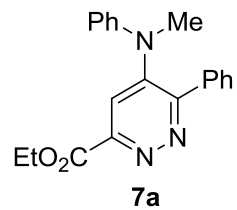


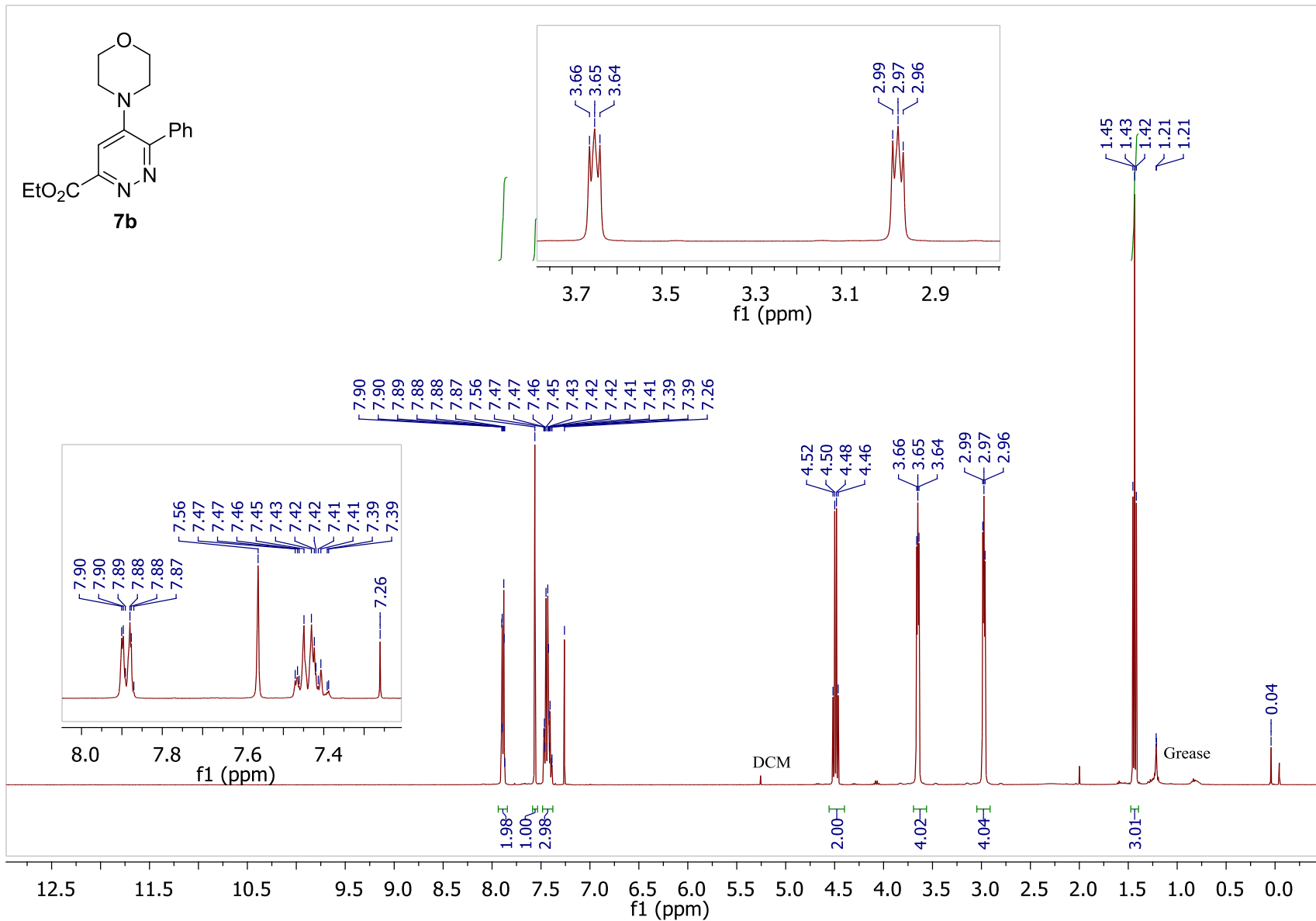
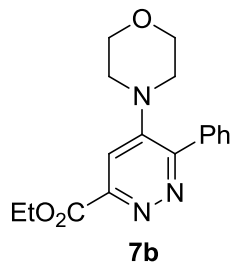


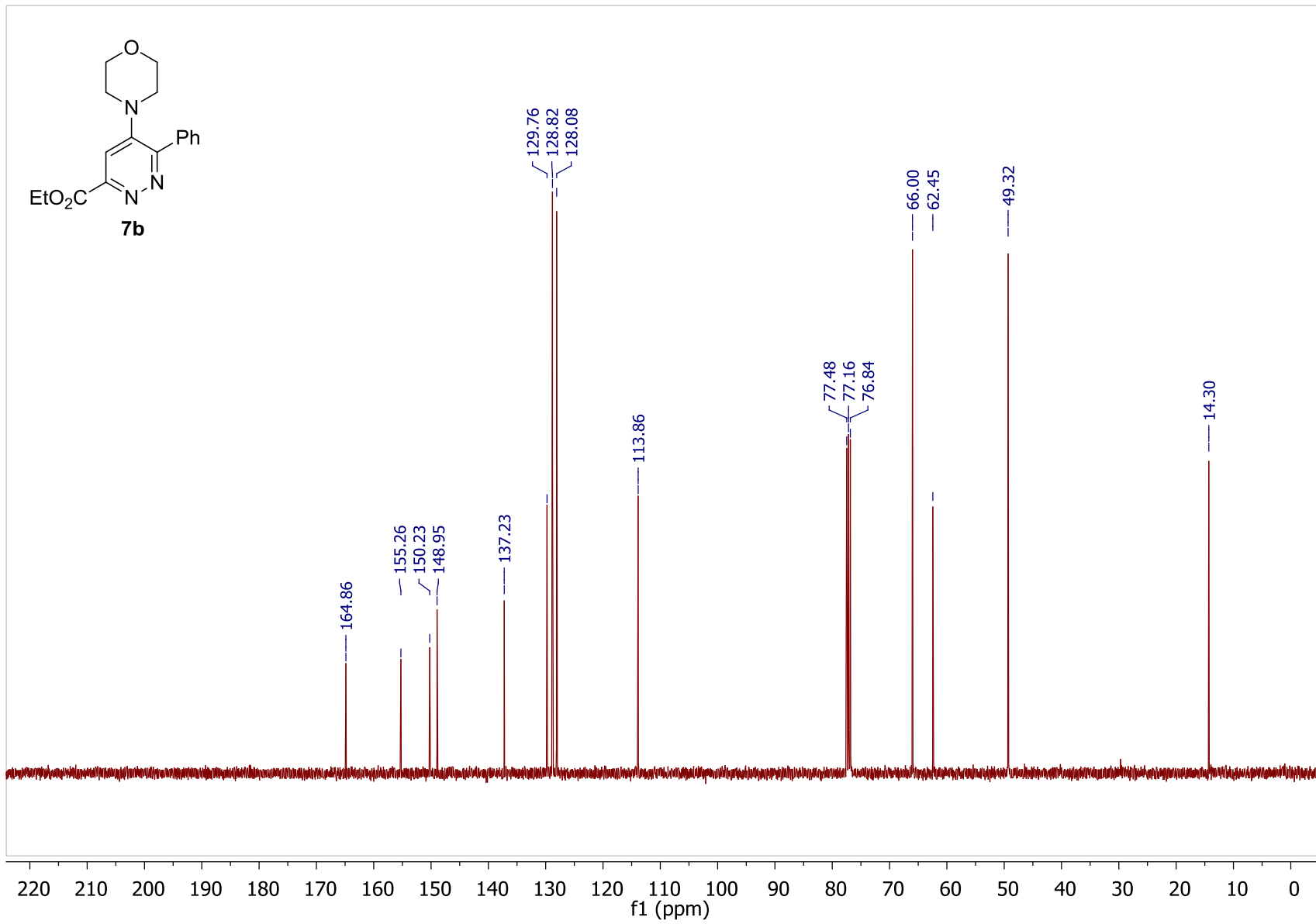
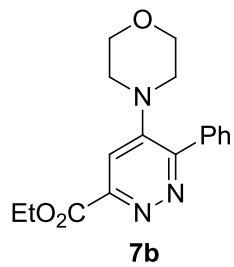


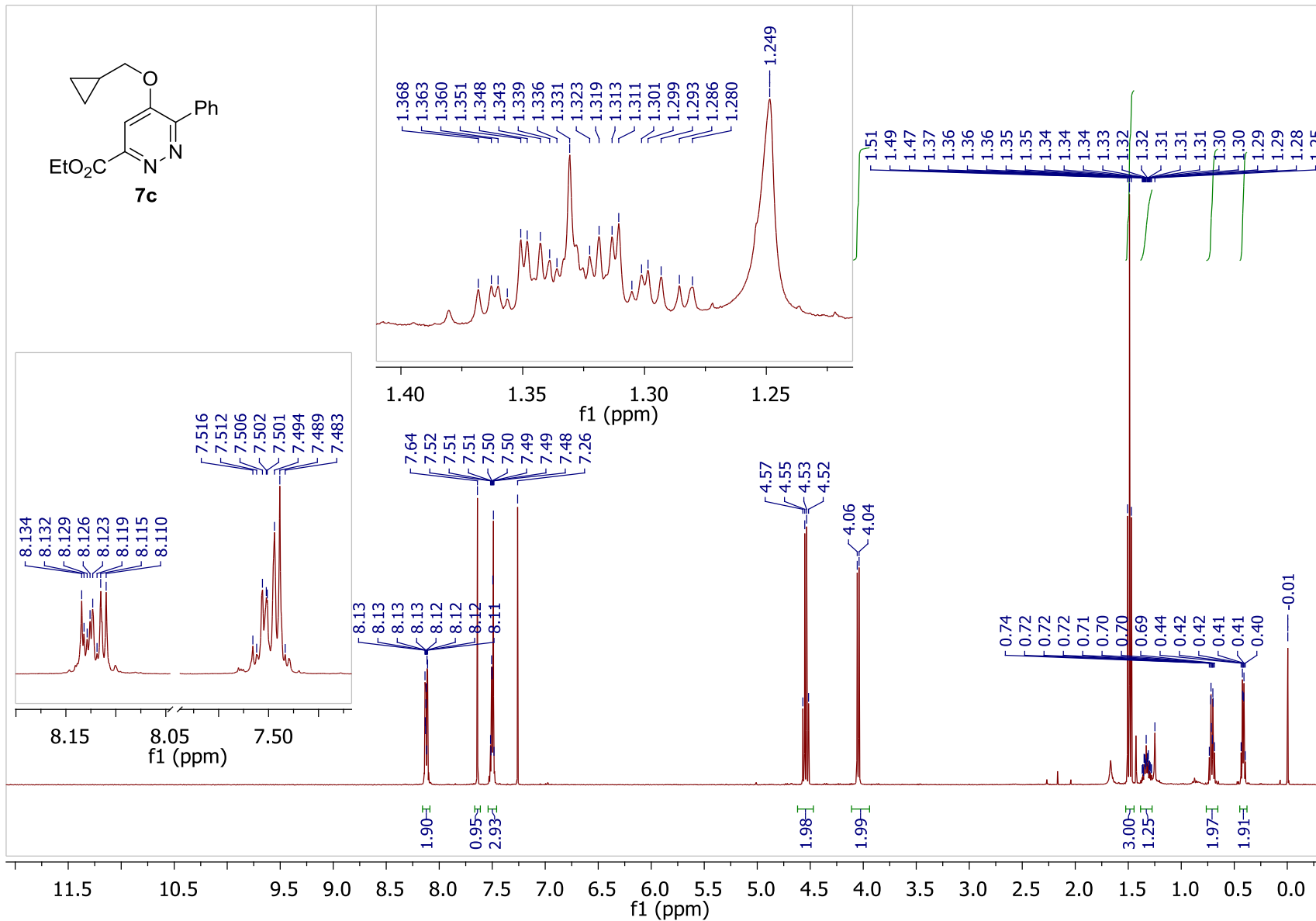
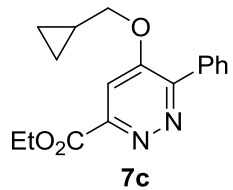


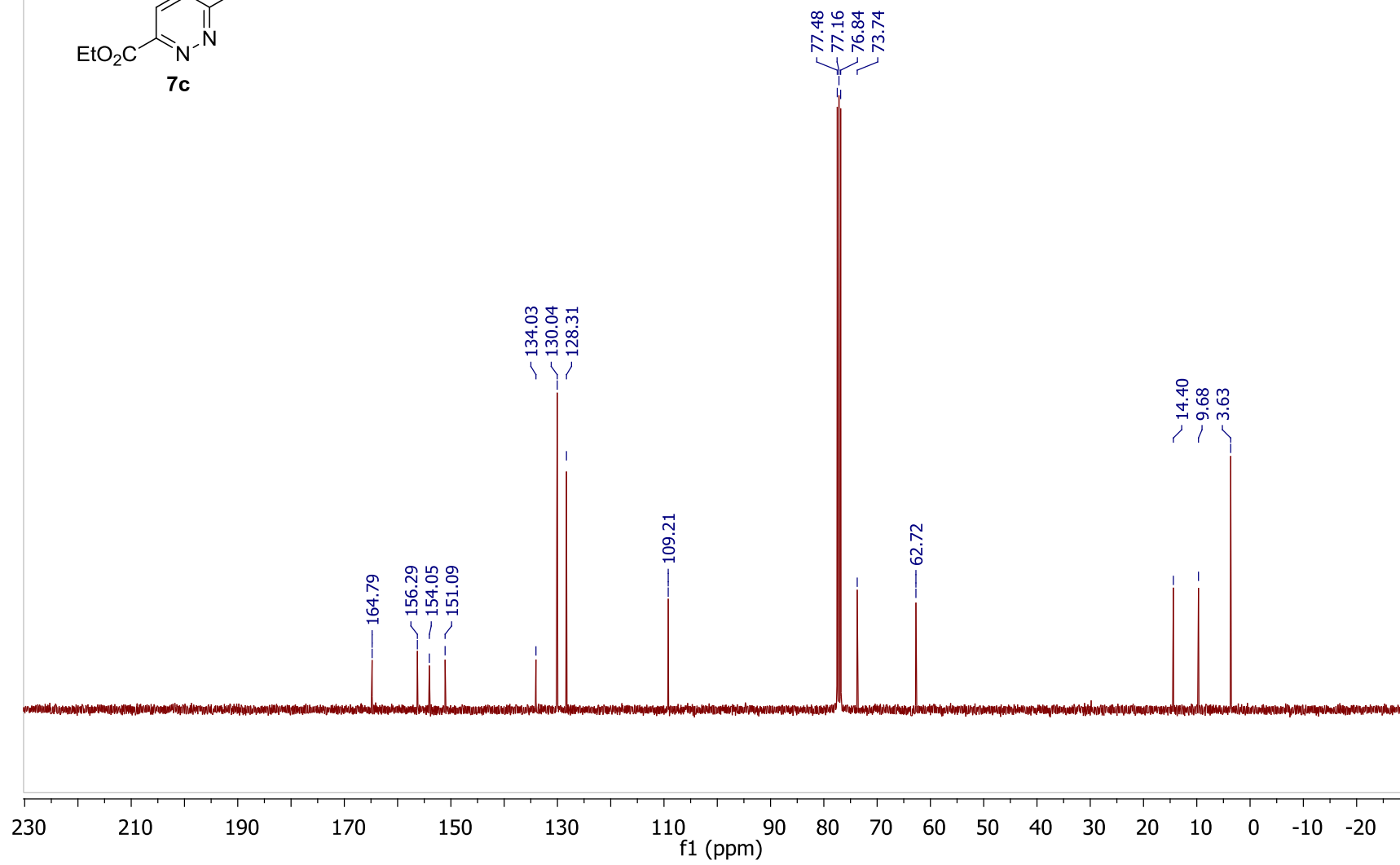
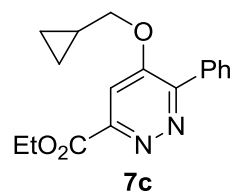


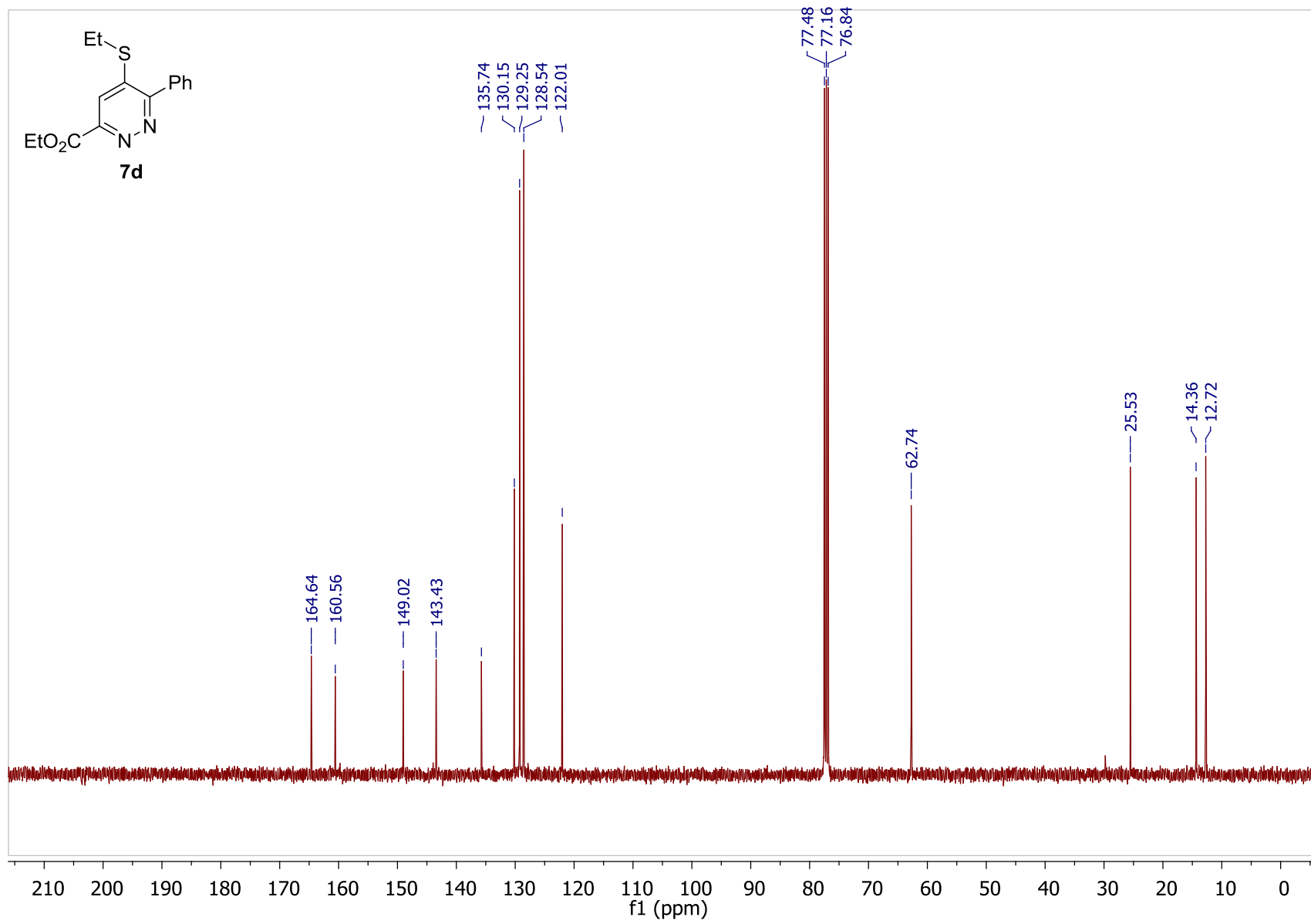
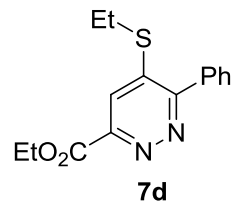


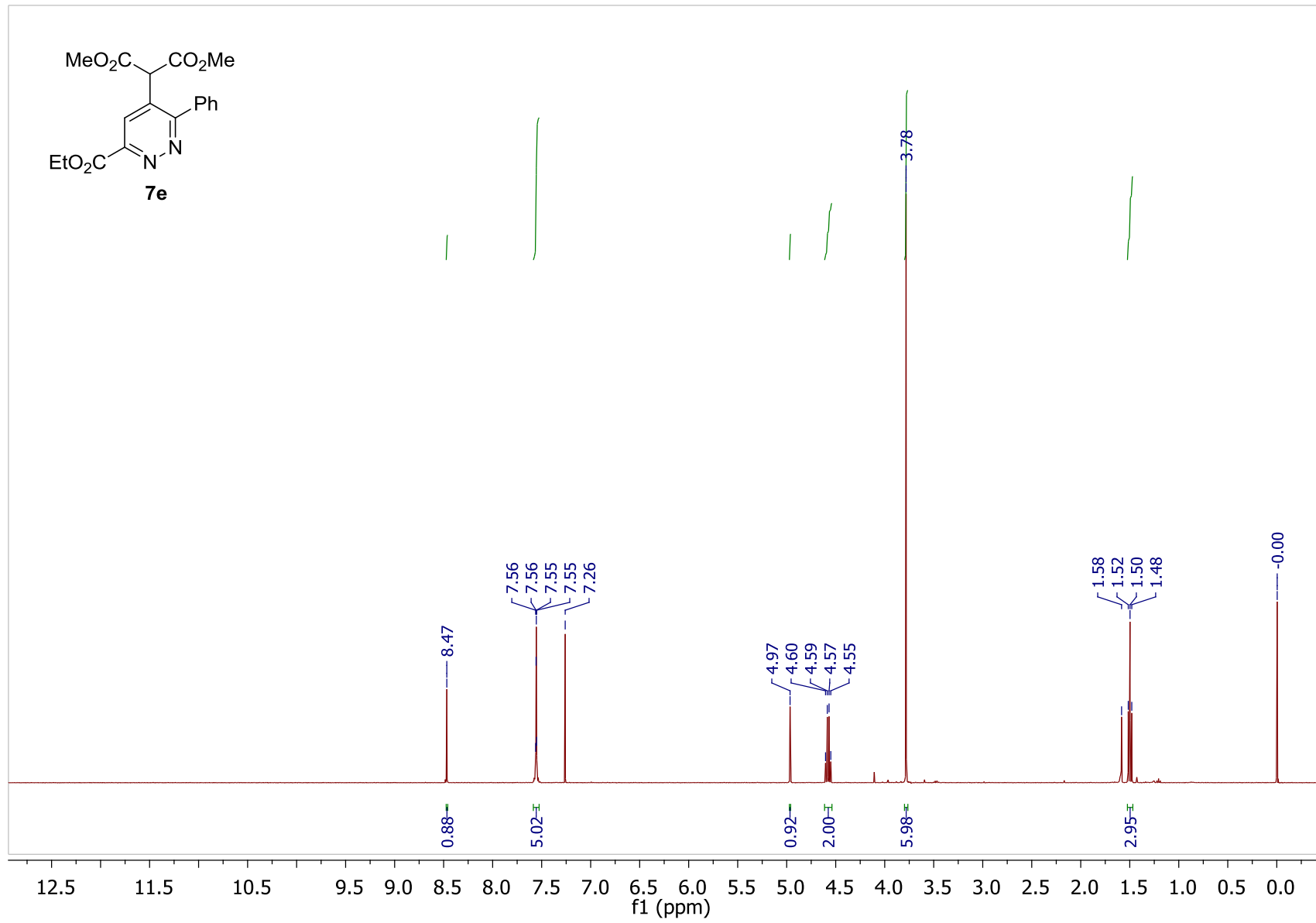
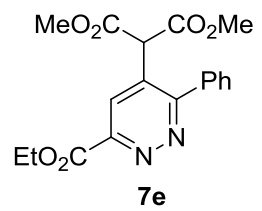


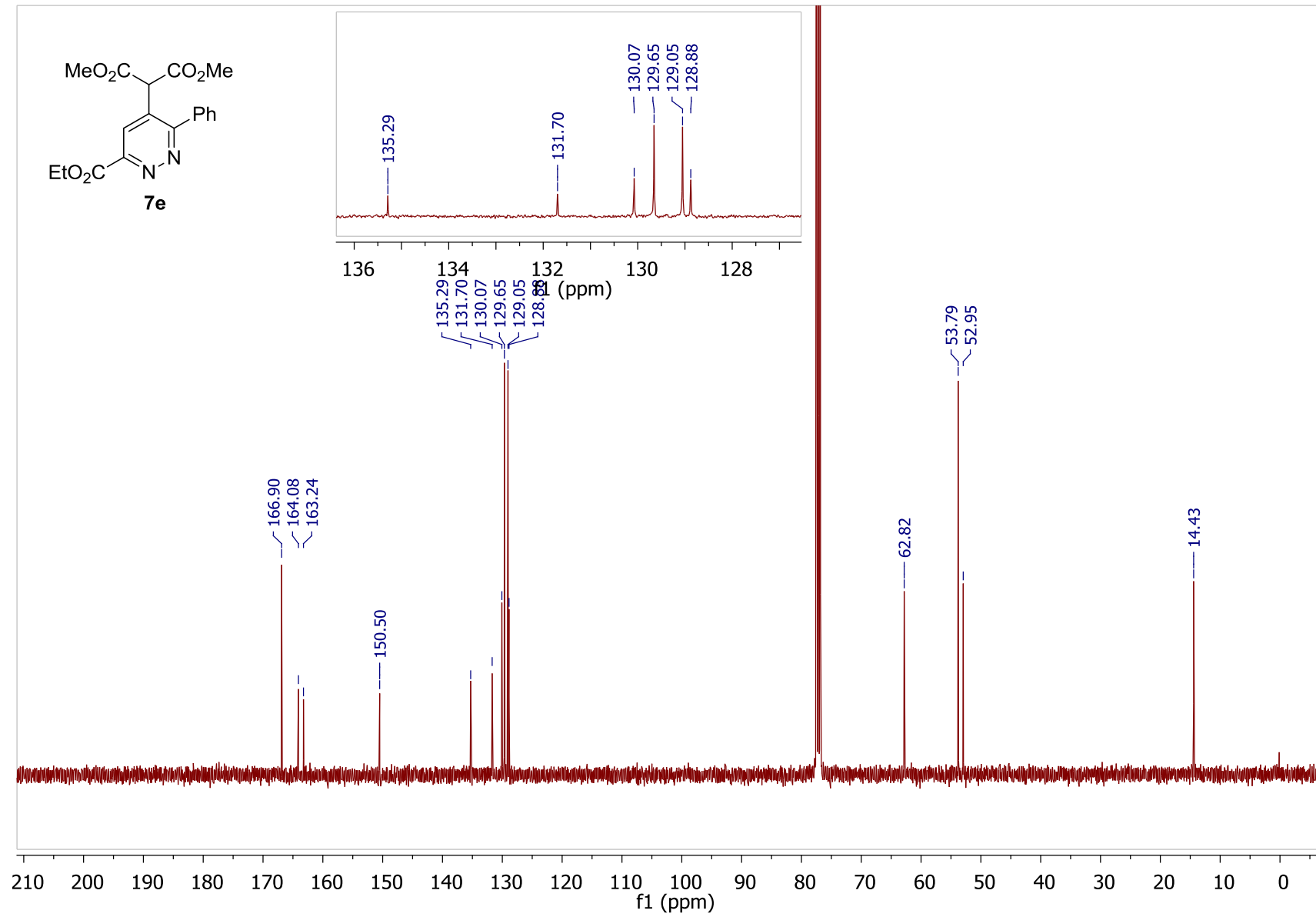
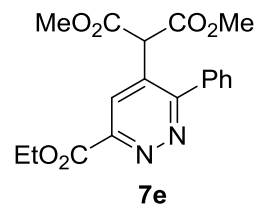


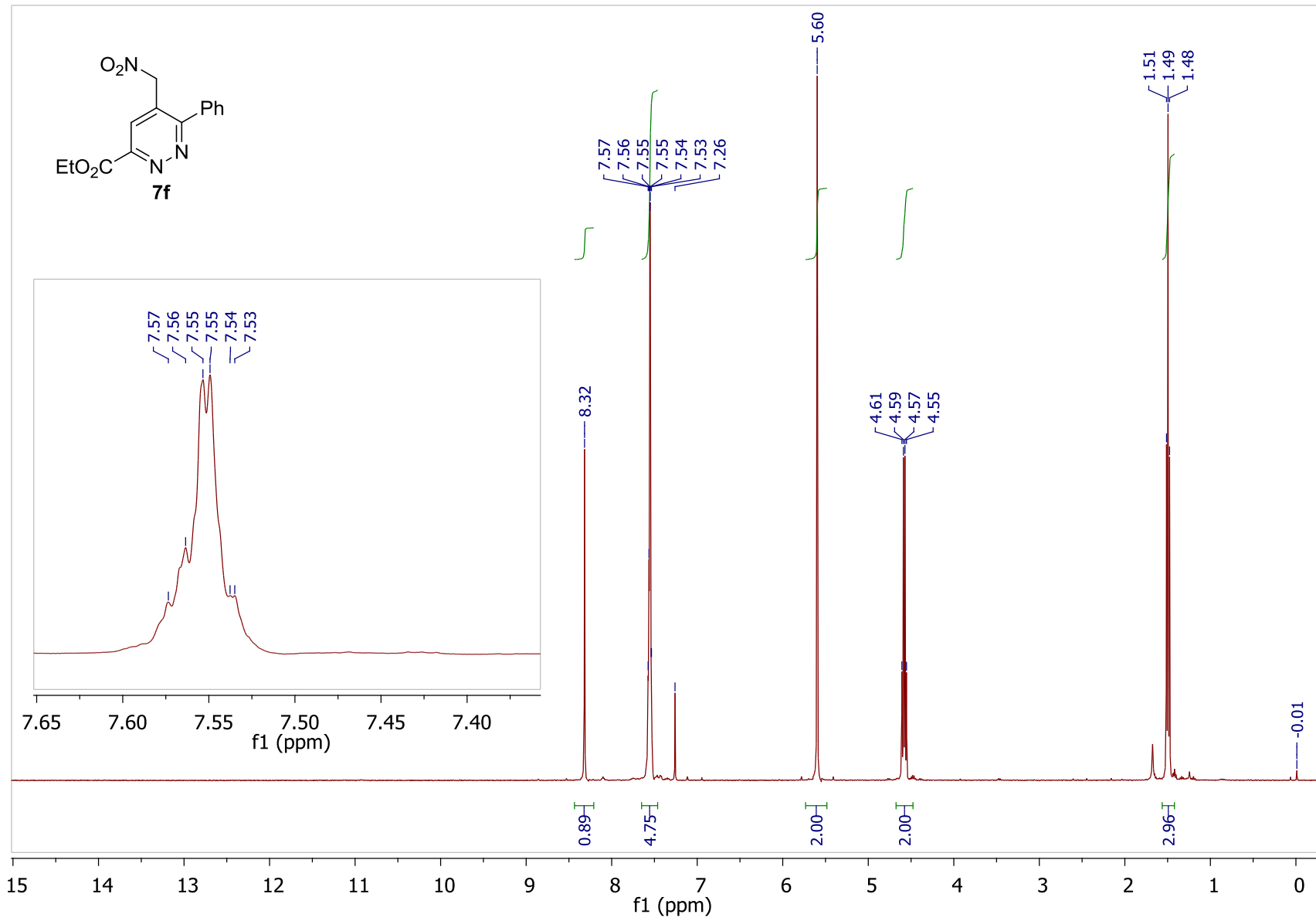


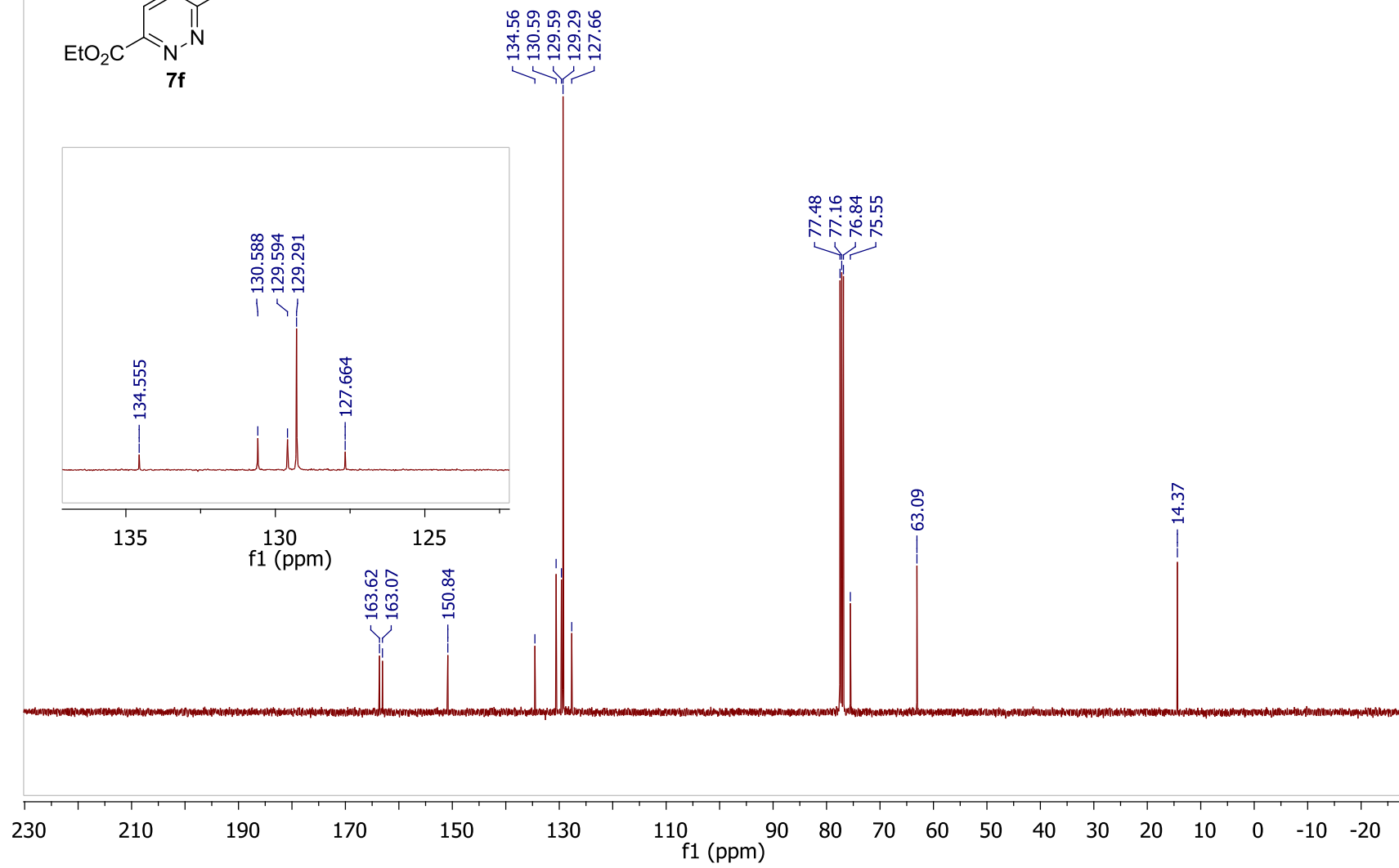
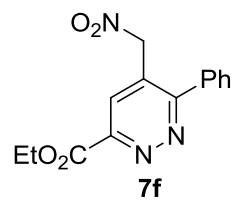


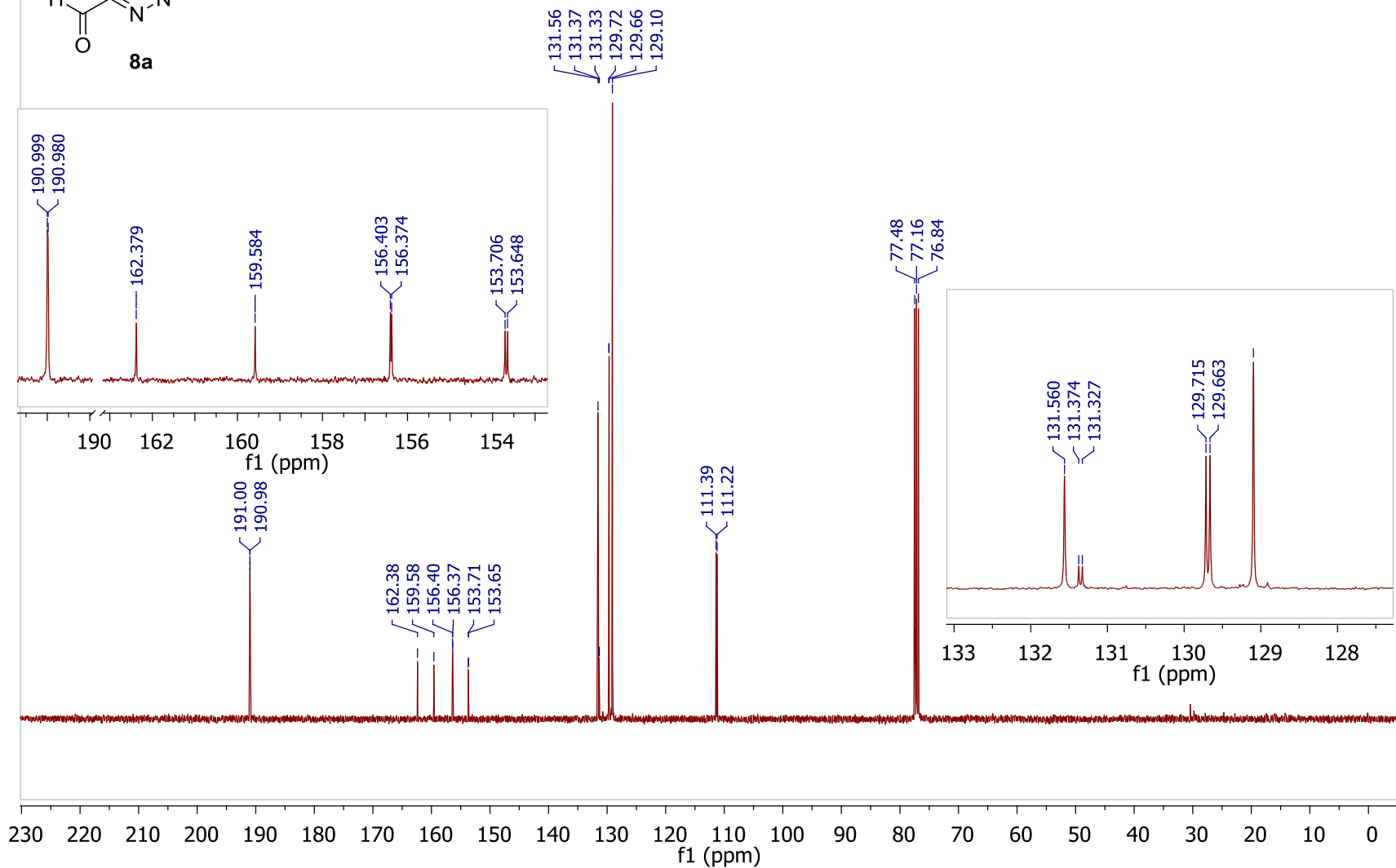
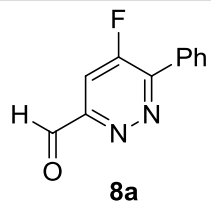


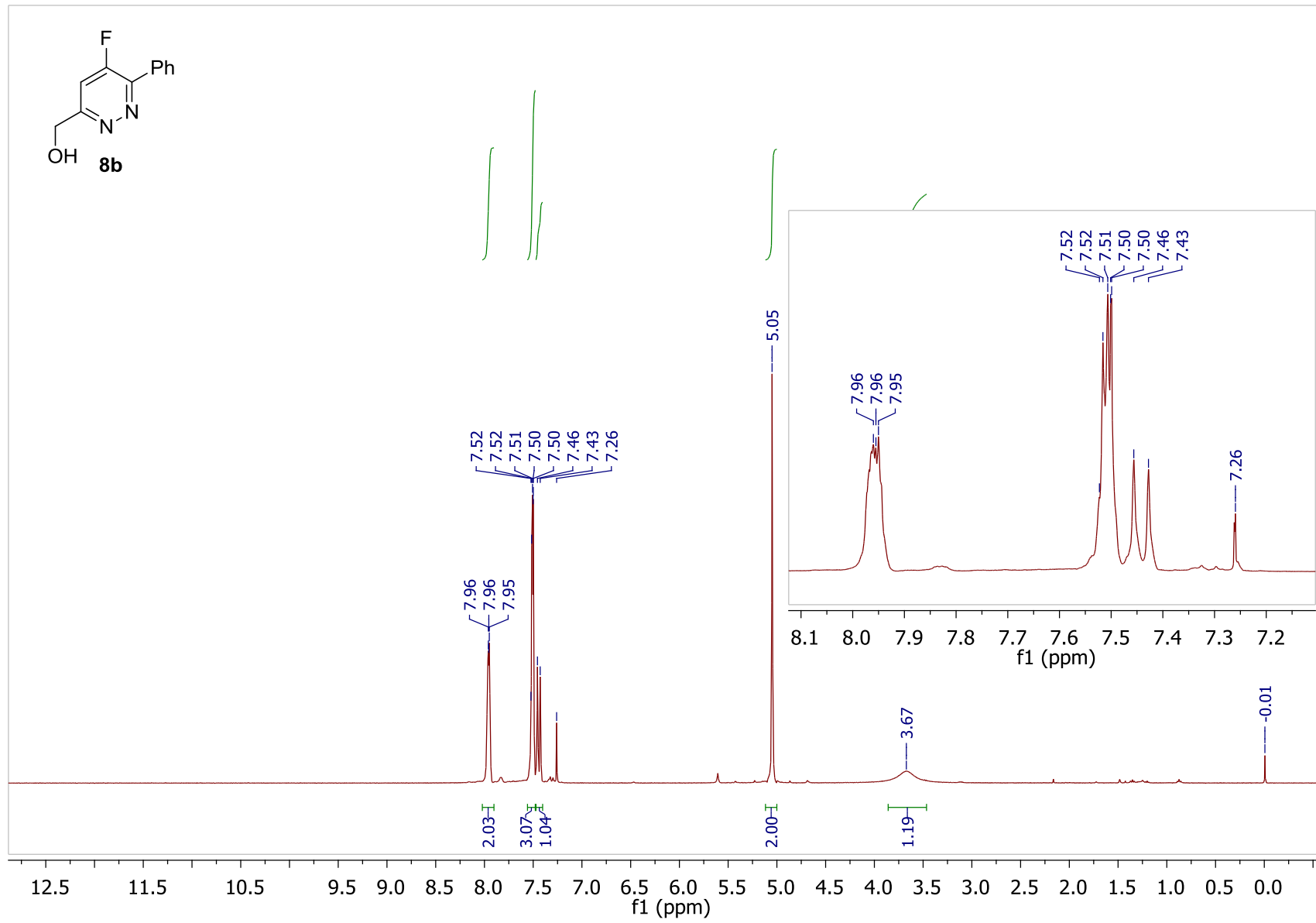
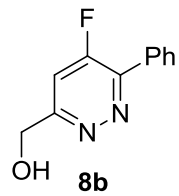


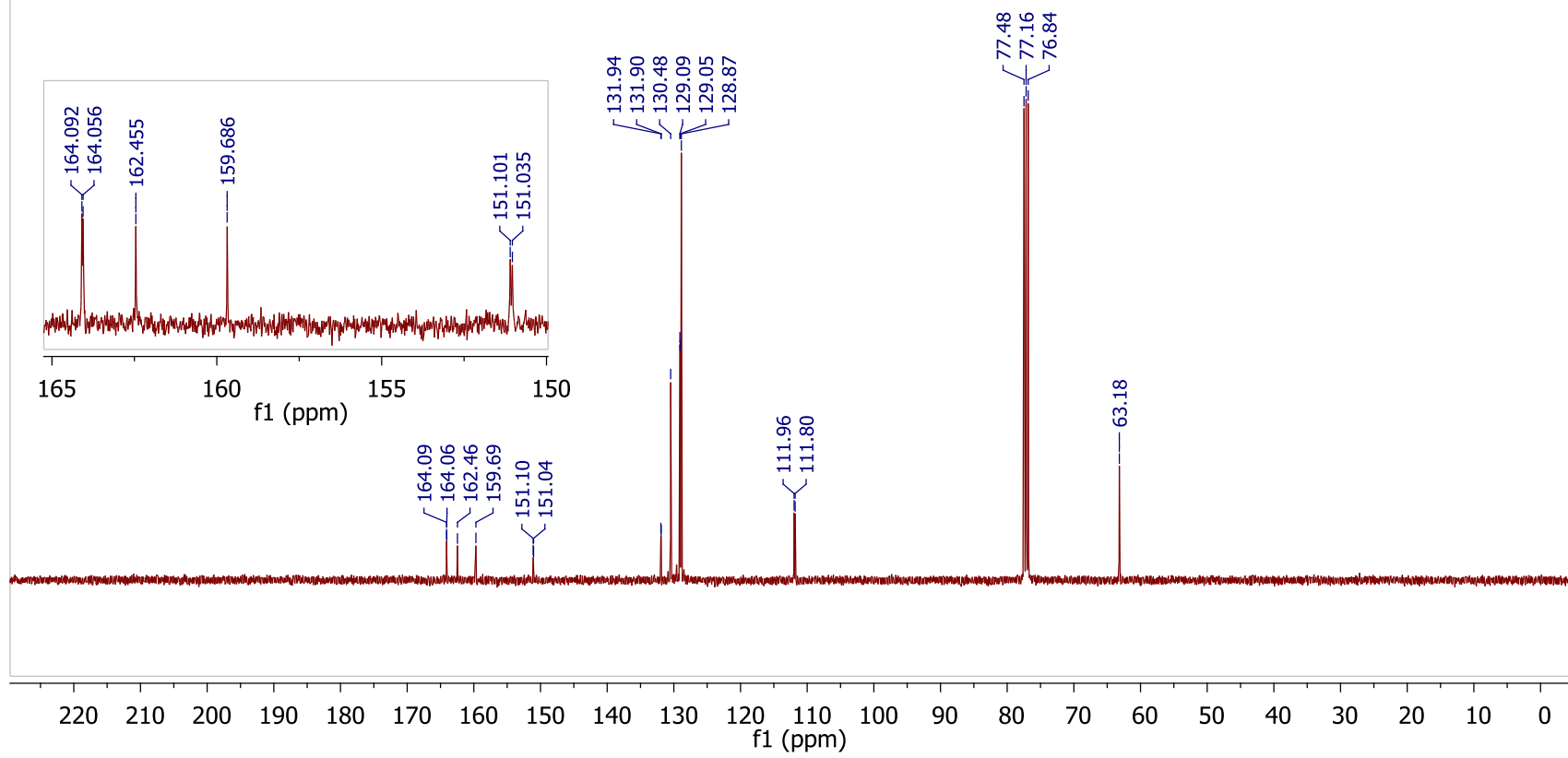
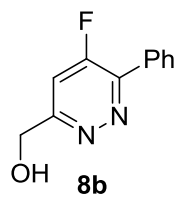


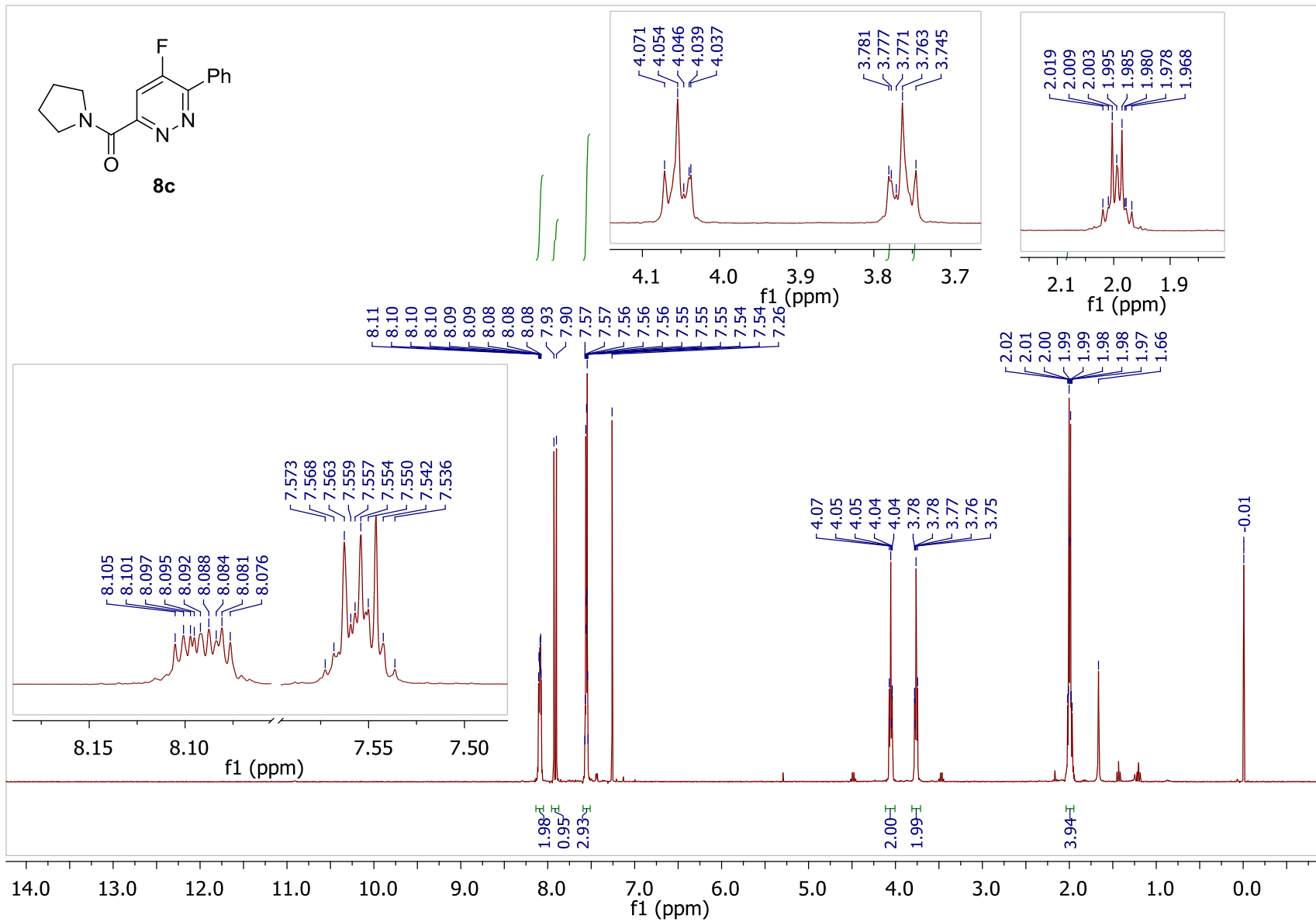
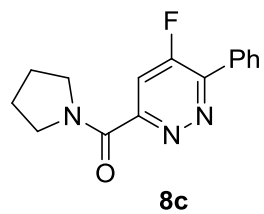


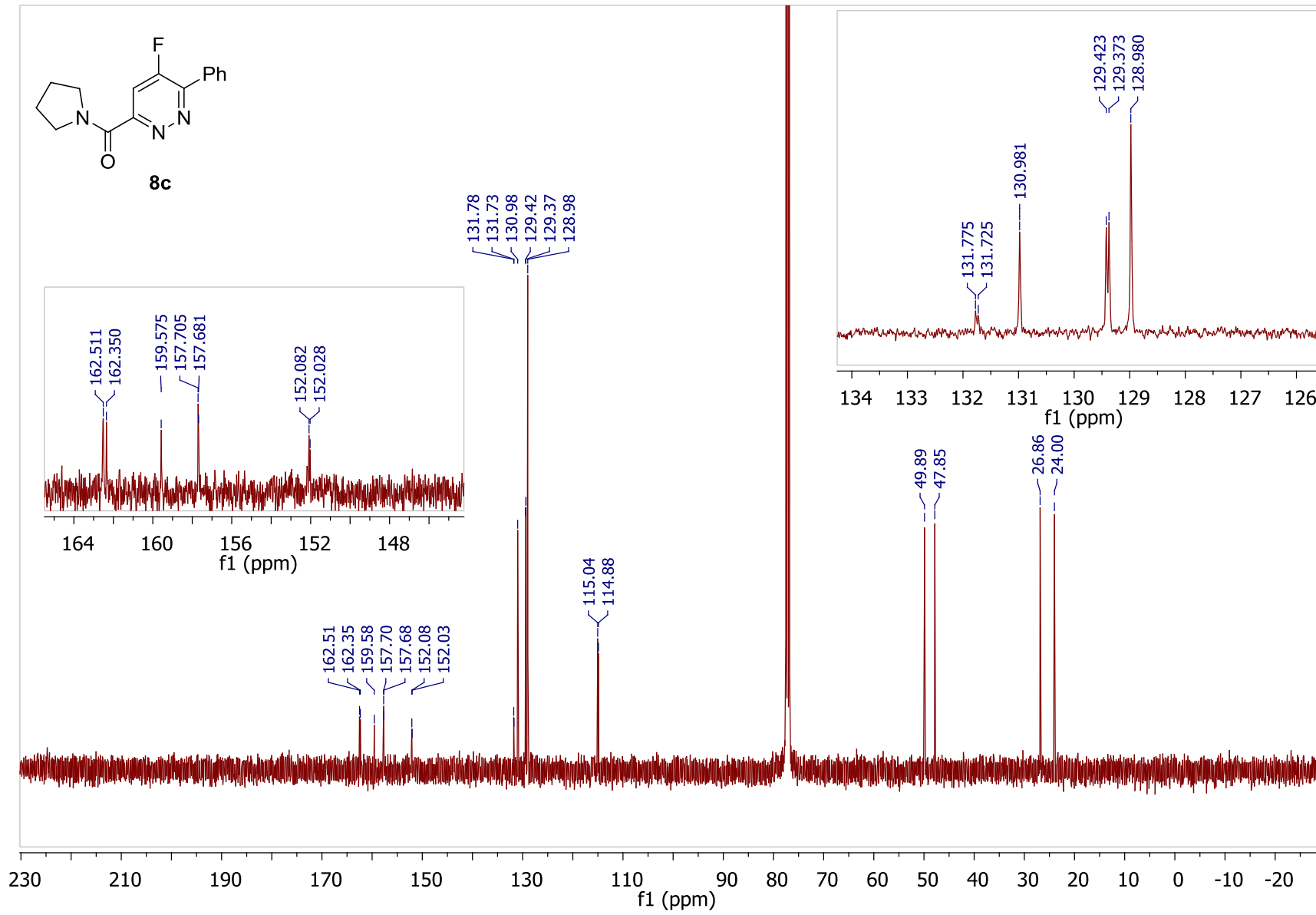
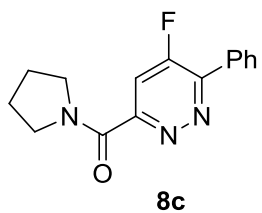


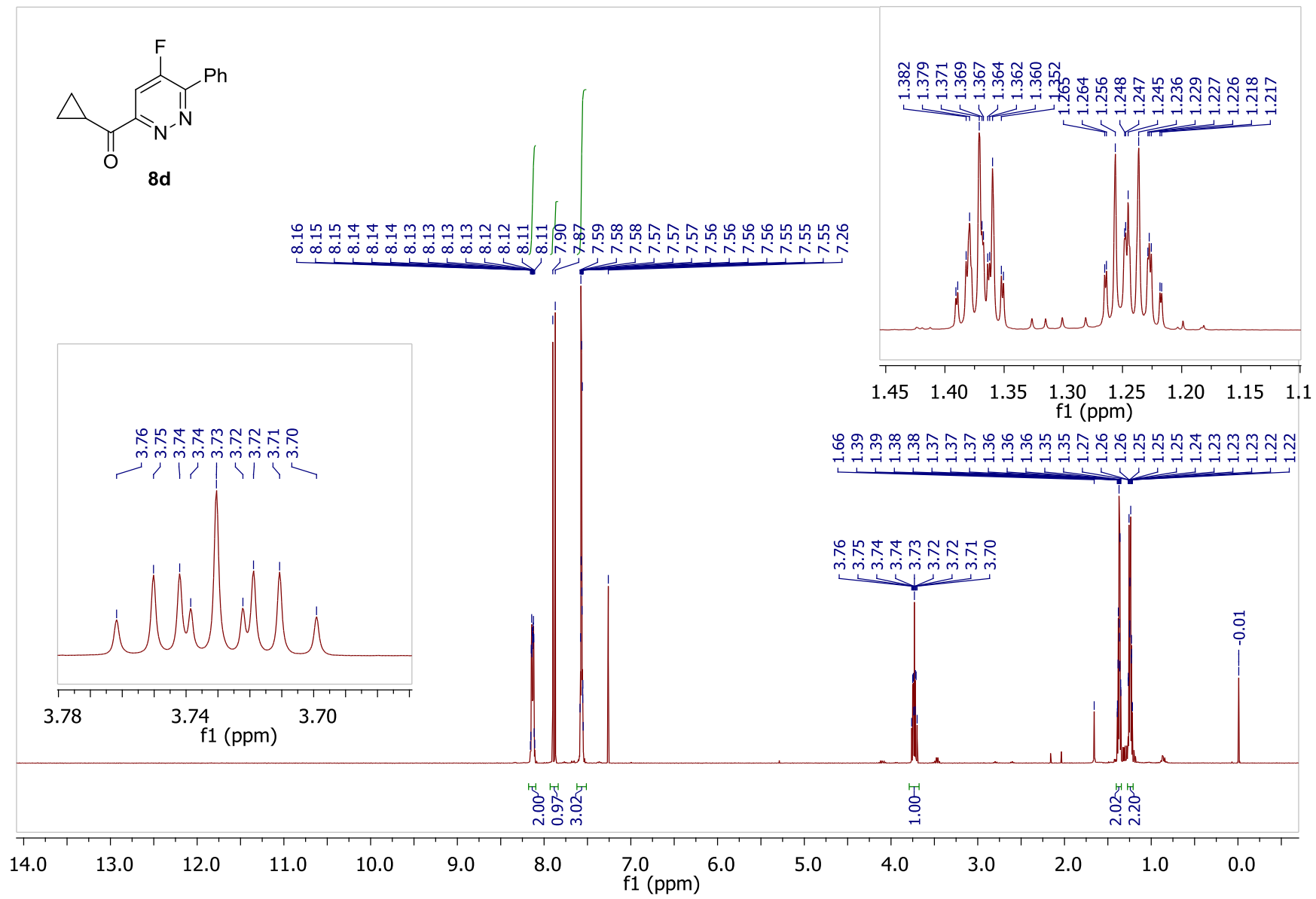
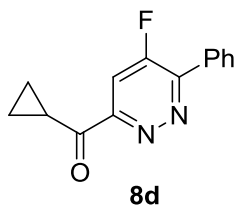


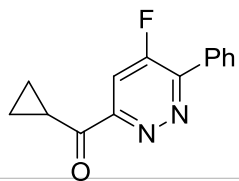




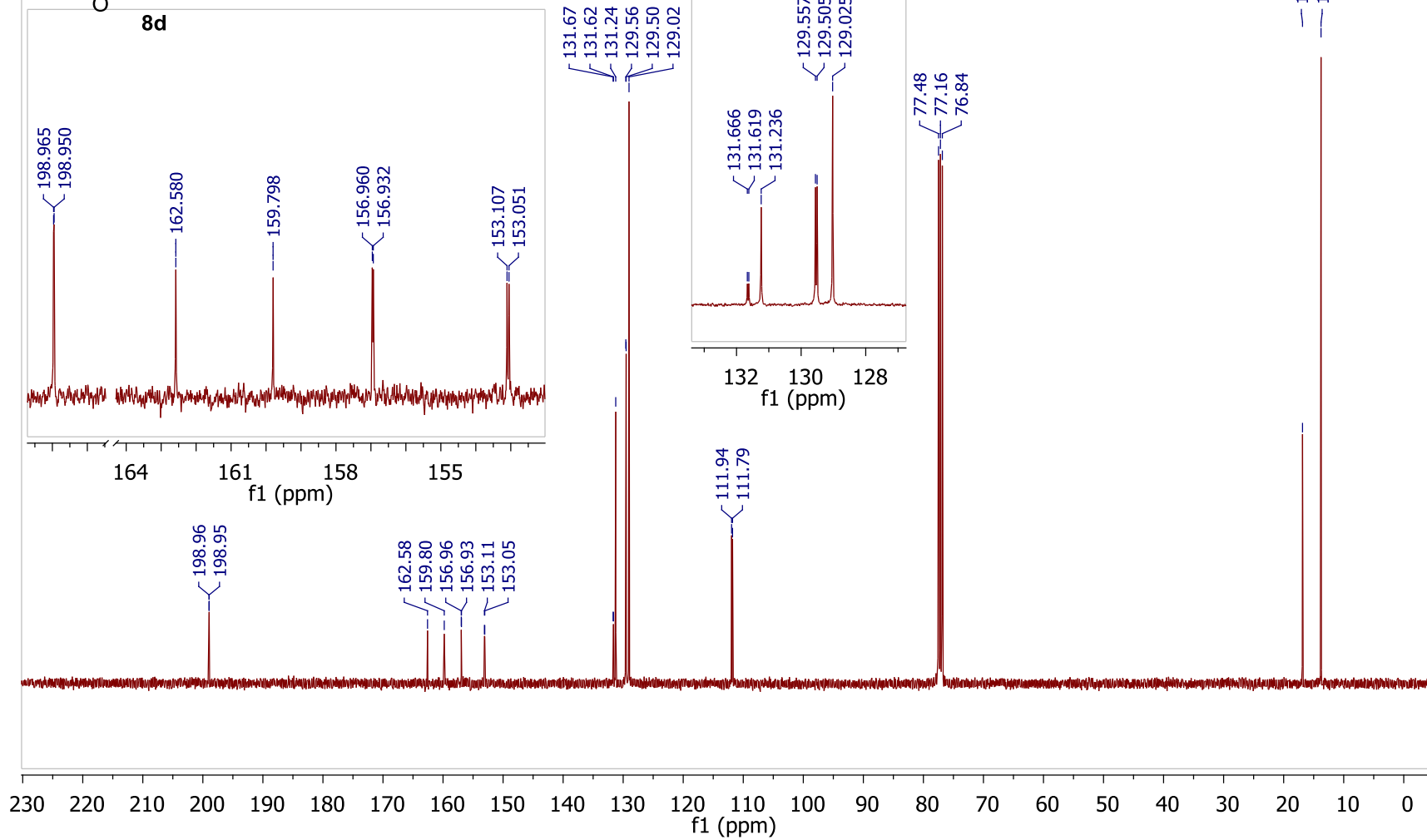


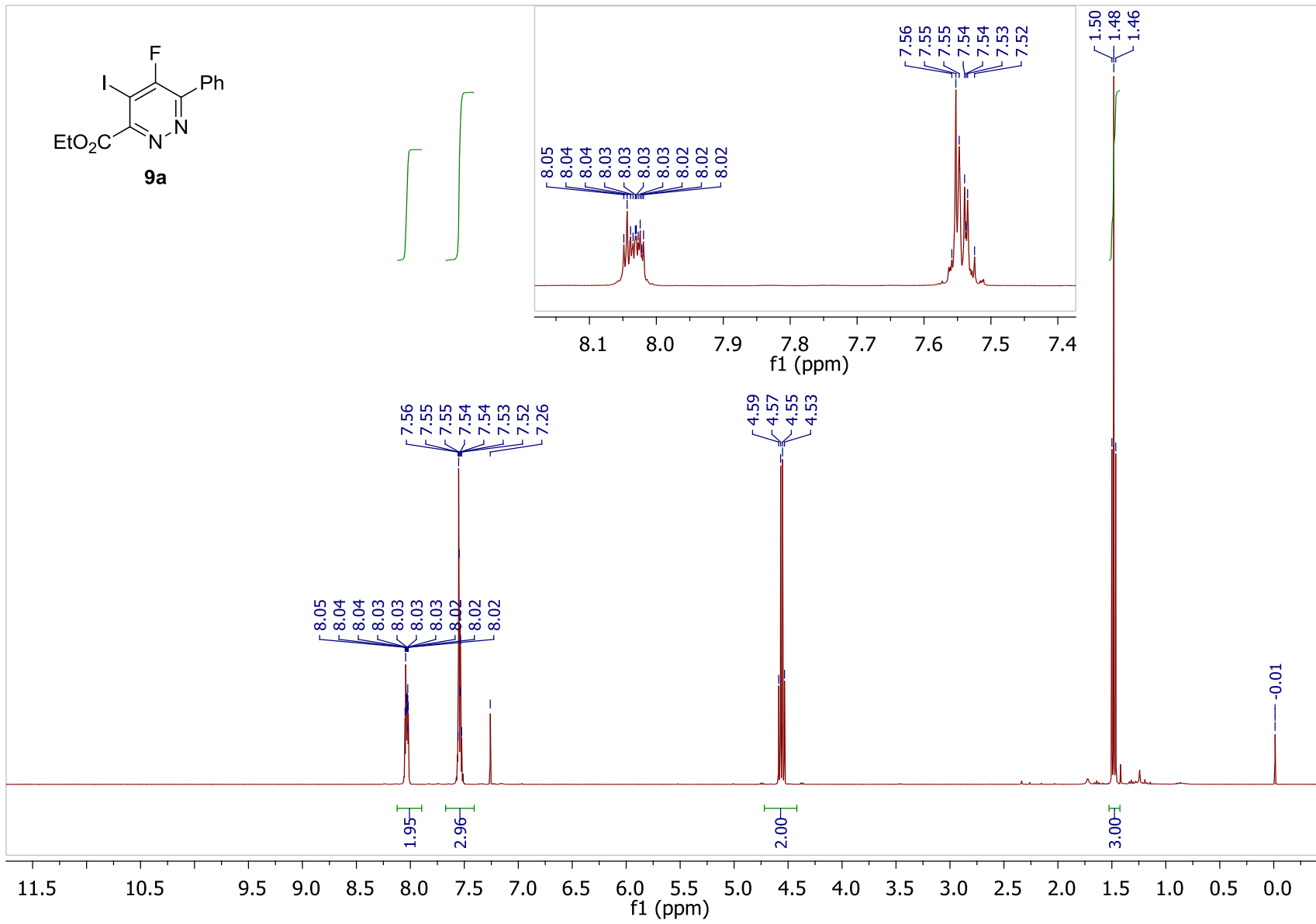
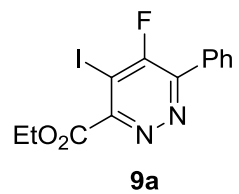


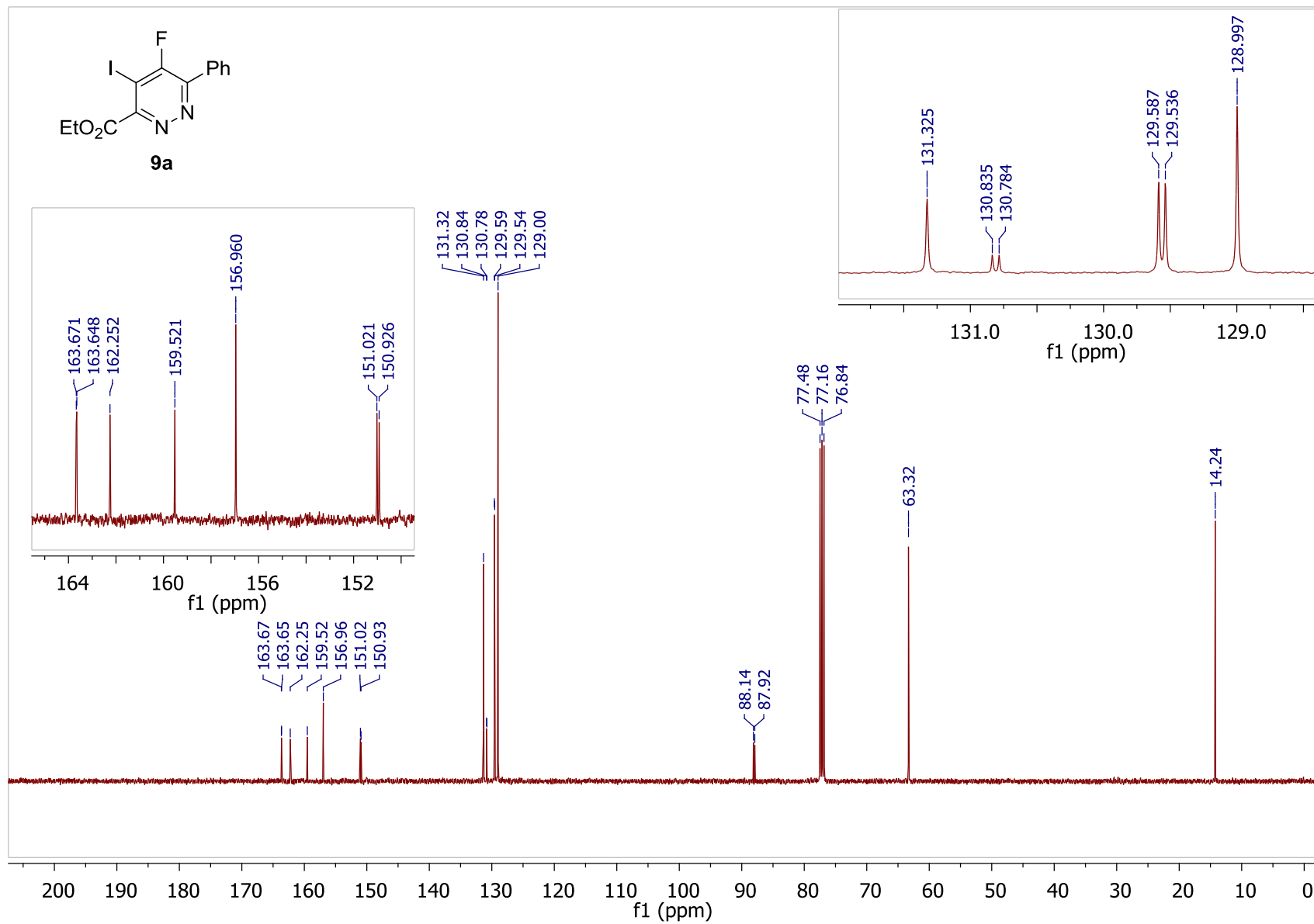
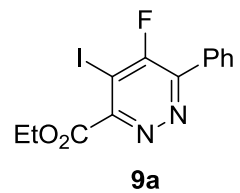


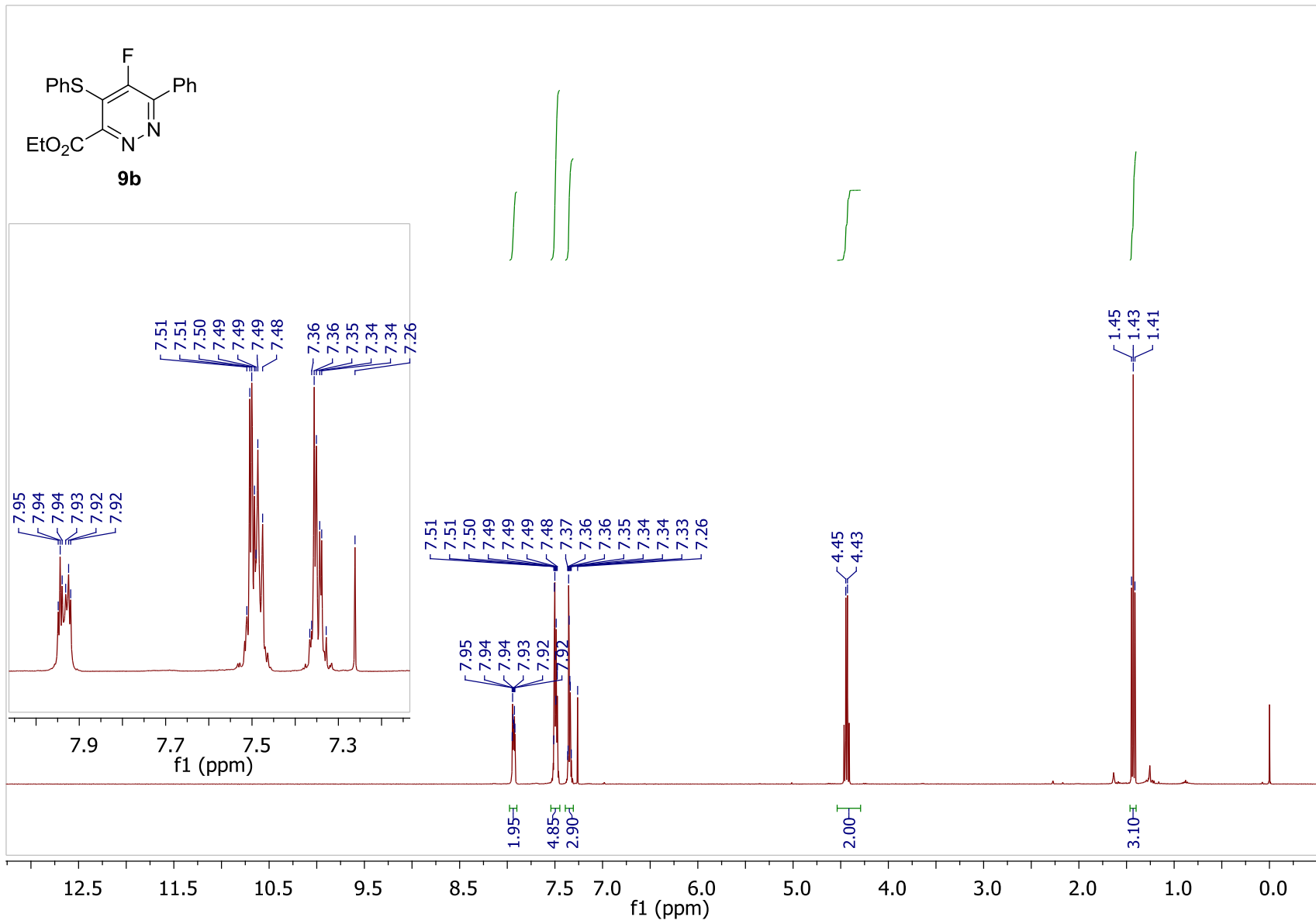


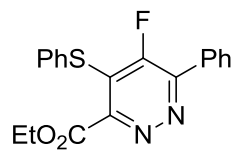
8d











9b

