

Programmed synthesis of triarylnitroimidazoles via sequential cross-coupling reactions

Gaurav Raina,^{ab} Prakash Kannaboina,^{ab} Nagaraju Mupparapu,^{ab} Sushil Raina,^a Qazi Naveed Ahmed,^{ab*} and Parthasarathi Das^{c*}

^aMedicinal Chemistry Division, CSIR-Indian Institute of Integrative Medicine (IIIM), Jammu-180001 India.

^bAcademy of Scientific and Innovative Research (AcSIR), Uttar Pradesh-201002, India.

^cDepartment of Applied Chemistry, Indian Institute of Technology (ISM), Dhanbad- 826004, India.

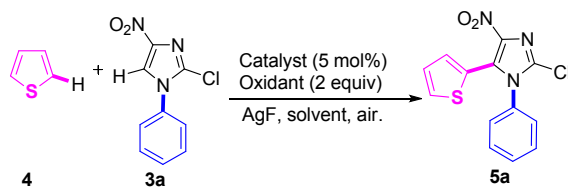
*E-mail: partha@iiitism.ac.in

*Email: naqazi@iiim.ac.in

Table of contents

	Table S1: Optimization of reaction conditions	P2
	Table S2: Optimization of reaction conditions	P2
	The ¹ H, ¹³ C and ¹⁹ F NMR spectra of products	P3-P59
	Compound 3a-3o	P3-P19
	Compound 4f-4g	P20-P22
	Compound 5a-5n	P23-P38
	Compound 6a-6h	P39-P48
	Compound 7a-7h	P49-P58

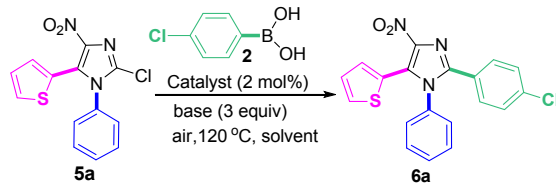
Table S1: Optimization of reaction conditions^a:



entry	catalyst	AgF	temp (°C)	solvent	yield ^b (%)
1	Pd(OAc) ₂	1	120	DMF	33
2	Pd(OAc) ₂	2	120	DMF	46
3^c	Pd(OAc) ₂	2	120	DMF	37

^aReaction Conditions: **3a** (0.179 mmol), **4** (0.215 mmol), Pd(OAc)₂ (5 mol%), Cu(OAc)₂·H₂O (0.358 mmol), AgF in 1.5 mL solvent, 16 h, air. ^bIsolated yields of **5a**. ^cWhen reaction was carried out for 40 h.

Table S2: Optimization of reaction conditions^a:

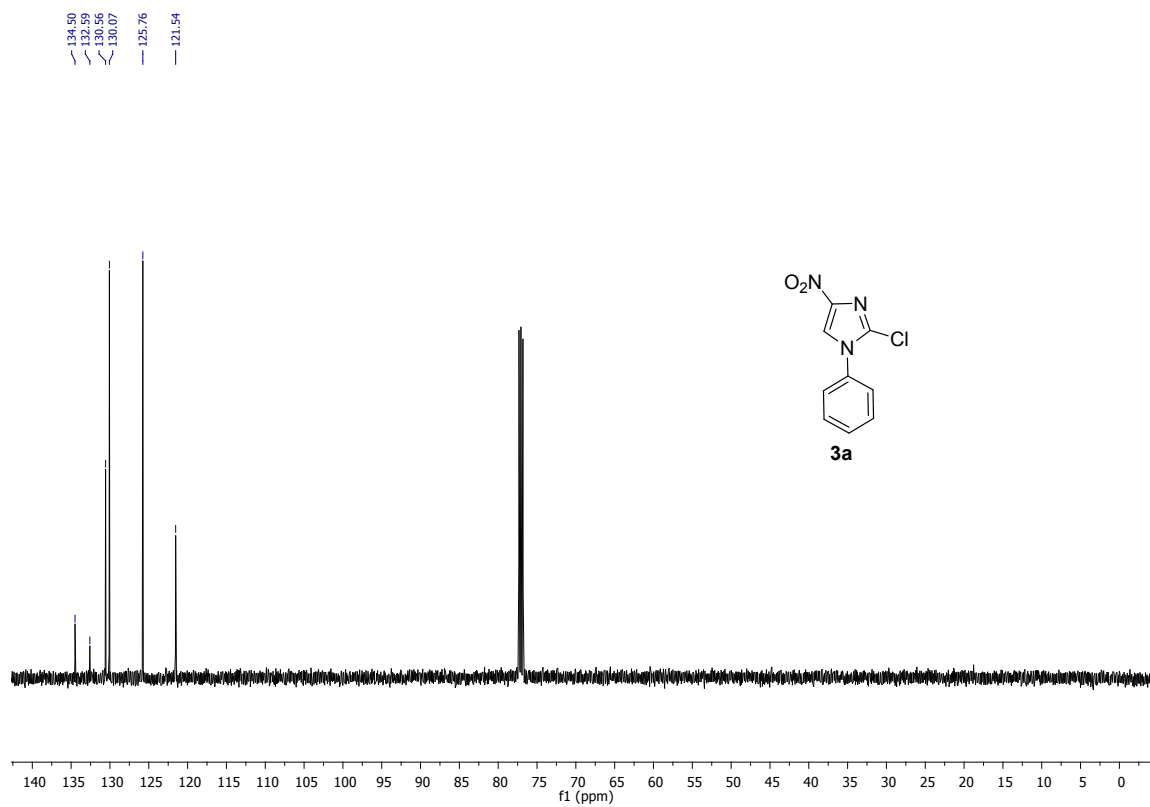
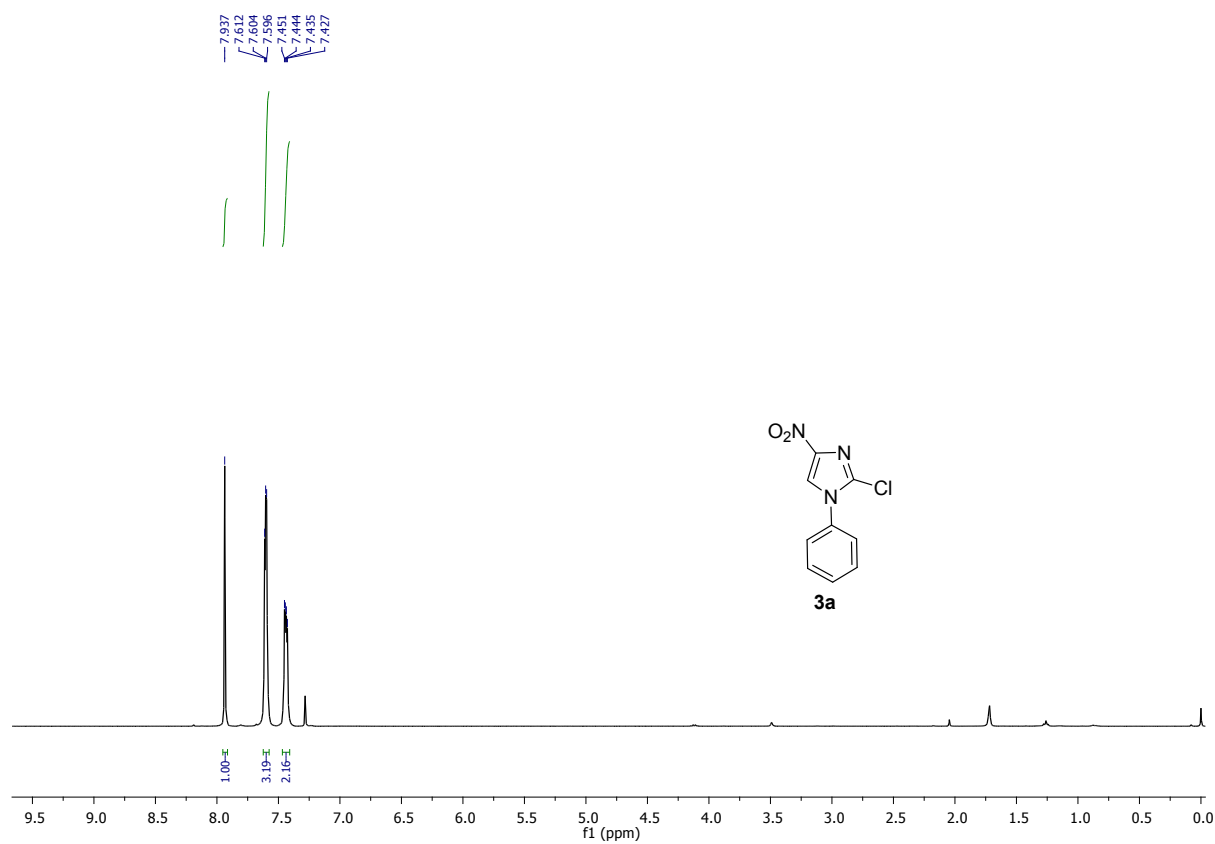


entry	catalyst	base	temp (°C)	solvent	yield ^b (%)
1	NiCl ₂ (PPh ₃) ₂	K ₃ PO ₄	120	dioxane	43
2^c	NiCl ₂ (PPh ₃) ₂	K ₃ PO ₄	120	dioxane	47
3^d	NiCl ₂ (PPh ₃) ₂	K ₃ PO ₄	120	dioxane	31

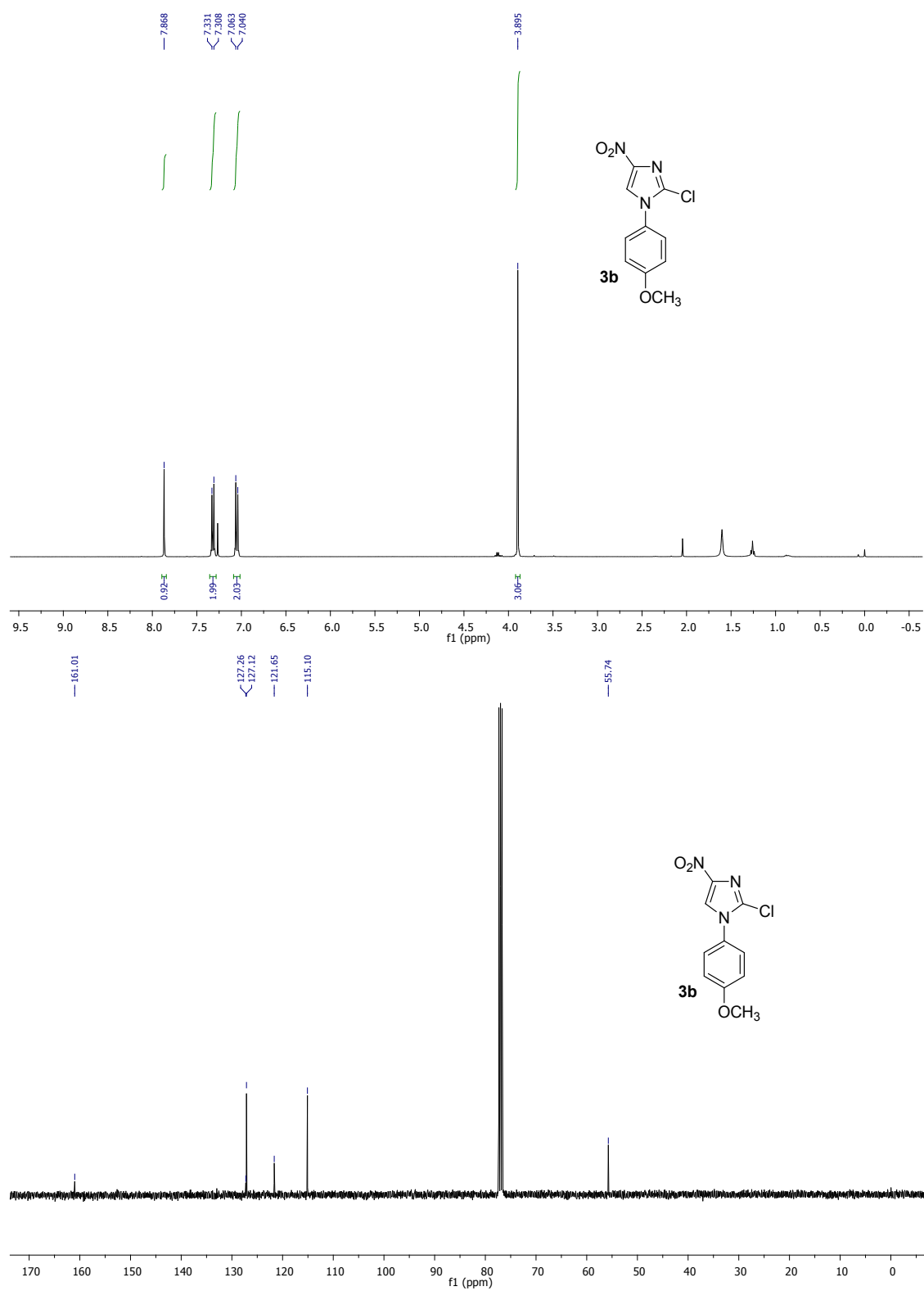
^aReaction conditions: **5a** (0.131 mmol), **2** (0.157 mmol), catalyst (2 mol%), K₃PO₄ (0.393 mmol) in 1 mL dioxane at 120 °C for 18 h, air. ^bIsolated yields of **6a**. ^cWhen 4 mol% of catalyst was used.

^dWhen reaction was carried out for 30 h.

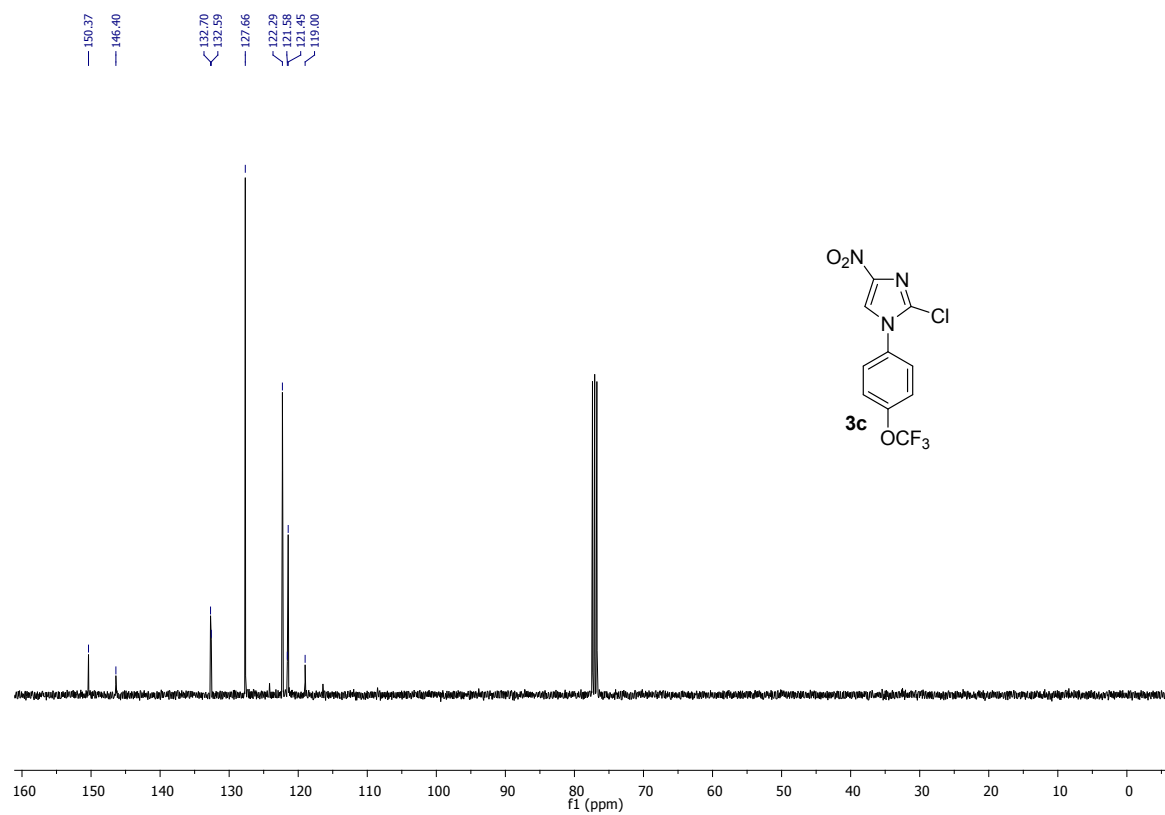
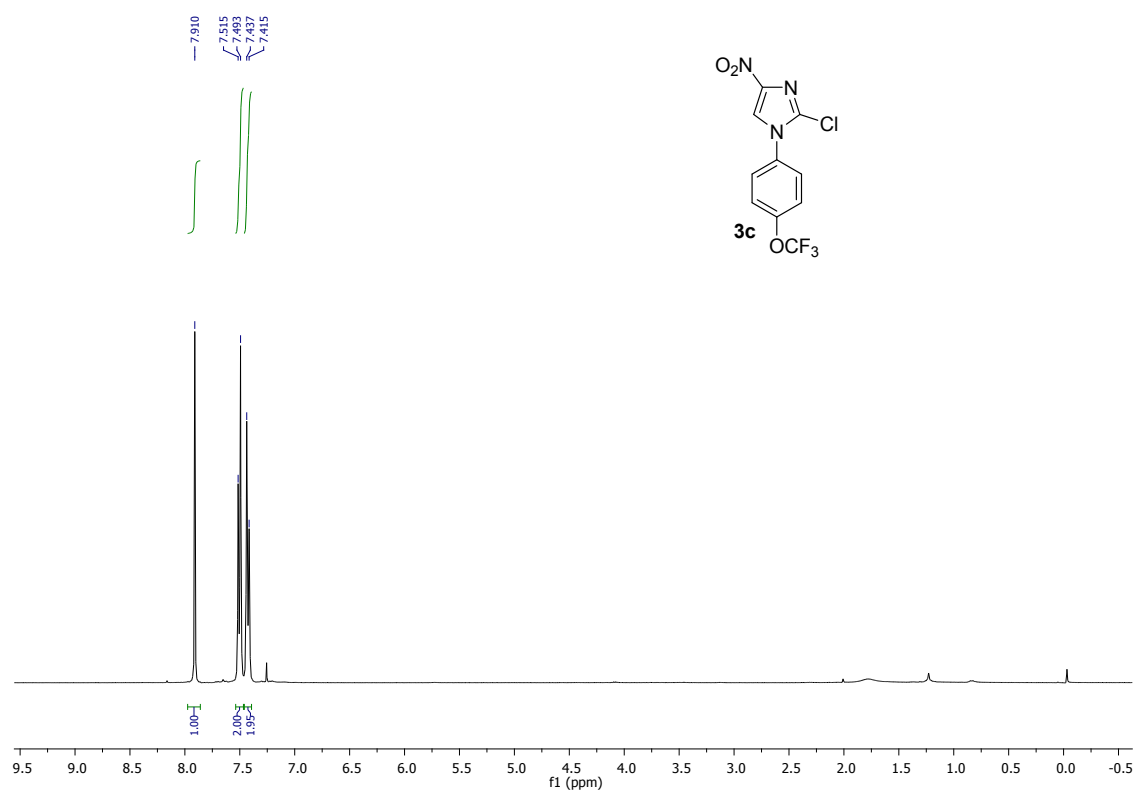
2-Chloro-4-nitro-1-phenyl-1H-imidazole (3a):

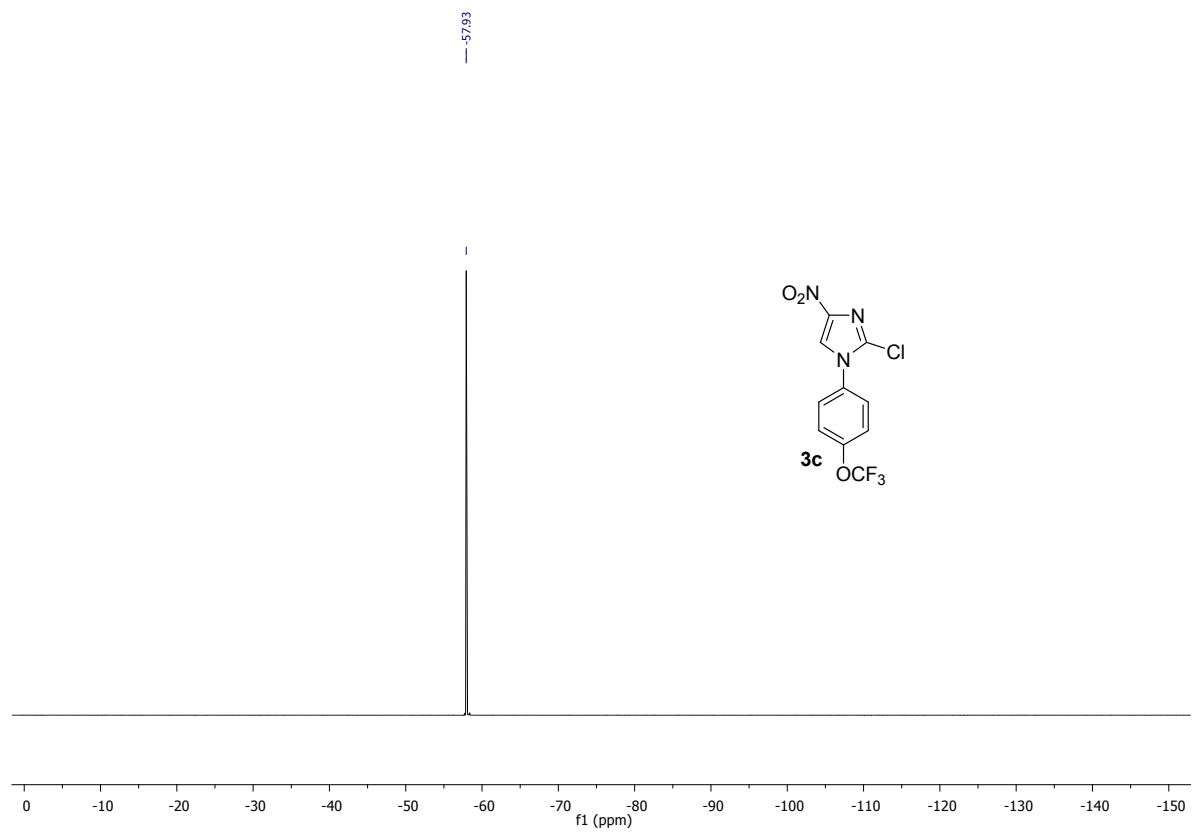


2-Chloro-1-(4-methoxyphenyl)-4-nitro-1H-imidazole (3b):

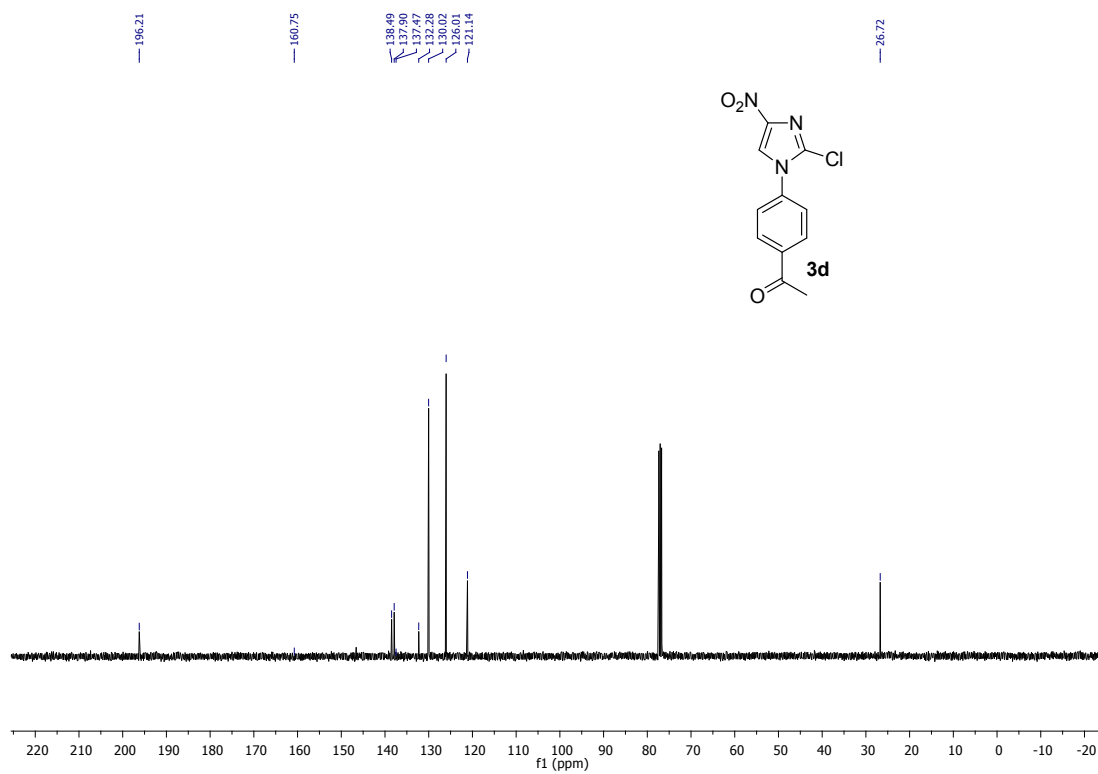
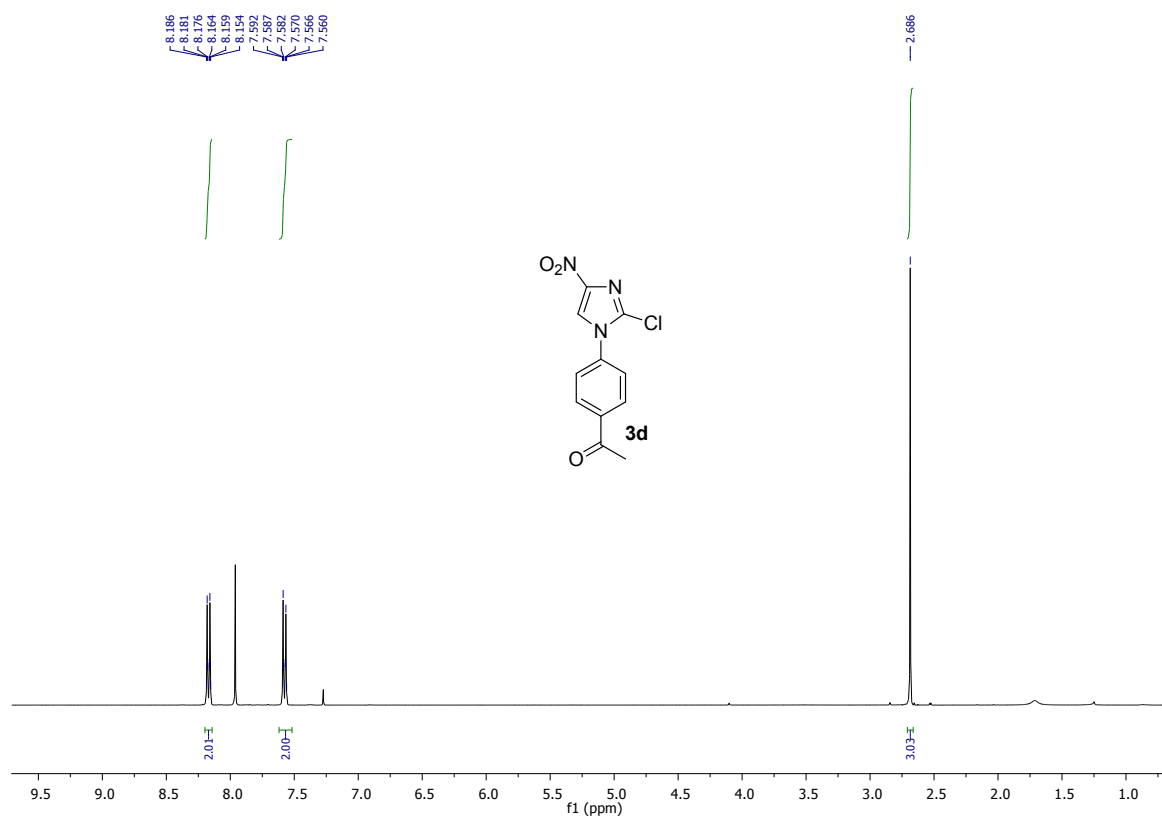


2-Chloro-4-nitro-1-(4-(trifluoromethoxy)phenyl)-1H-imidazole (3c) :

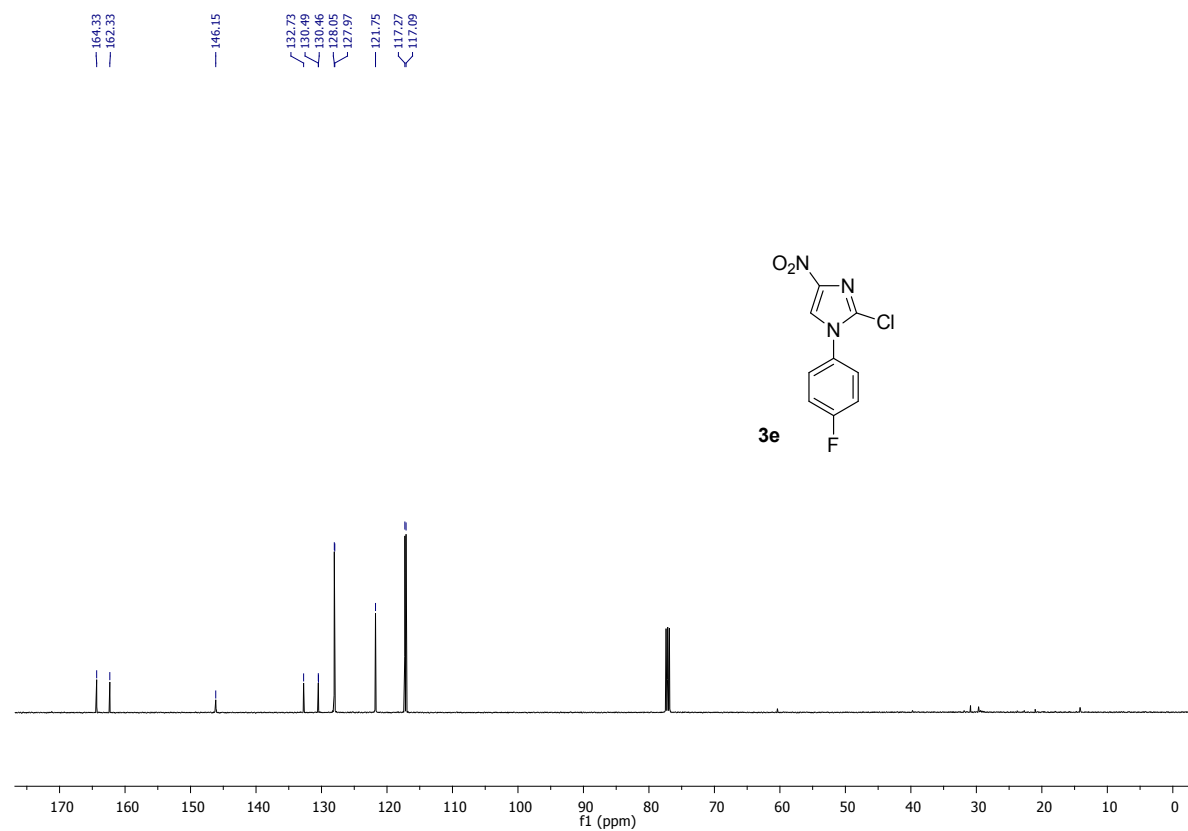
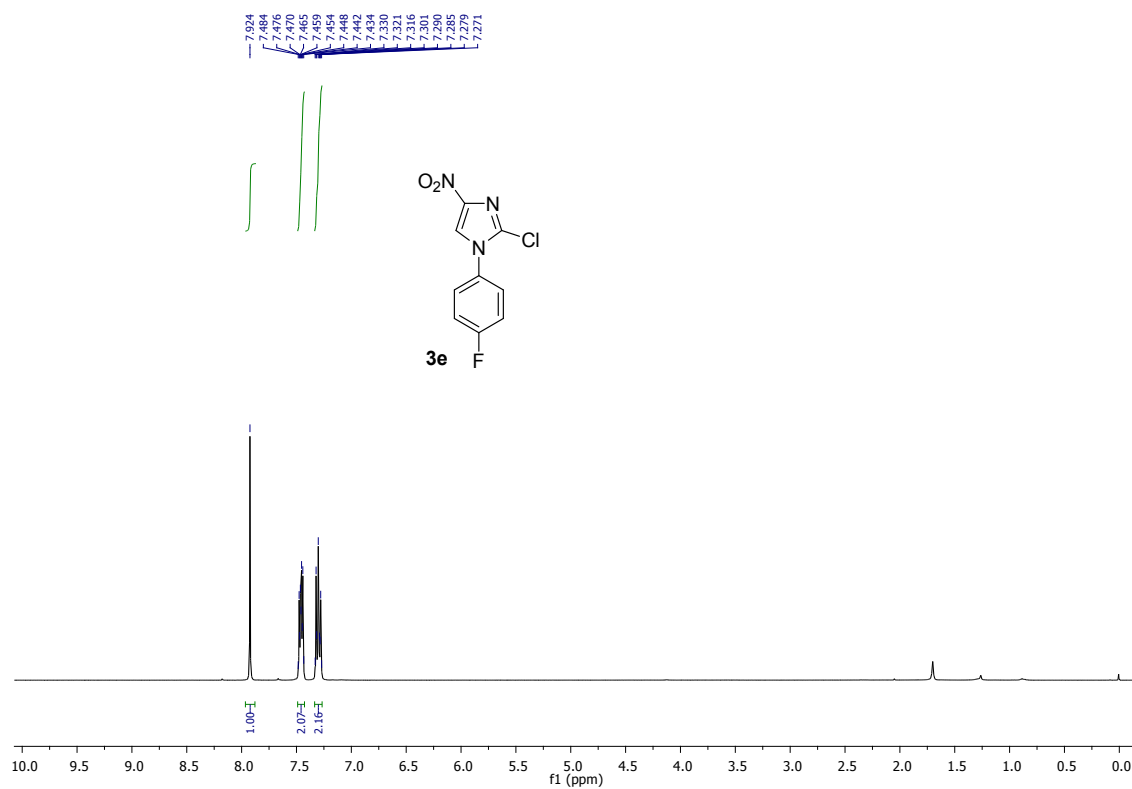


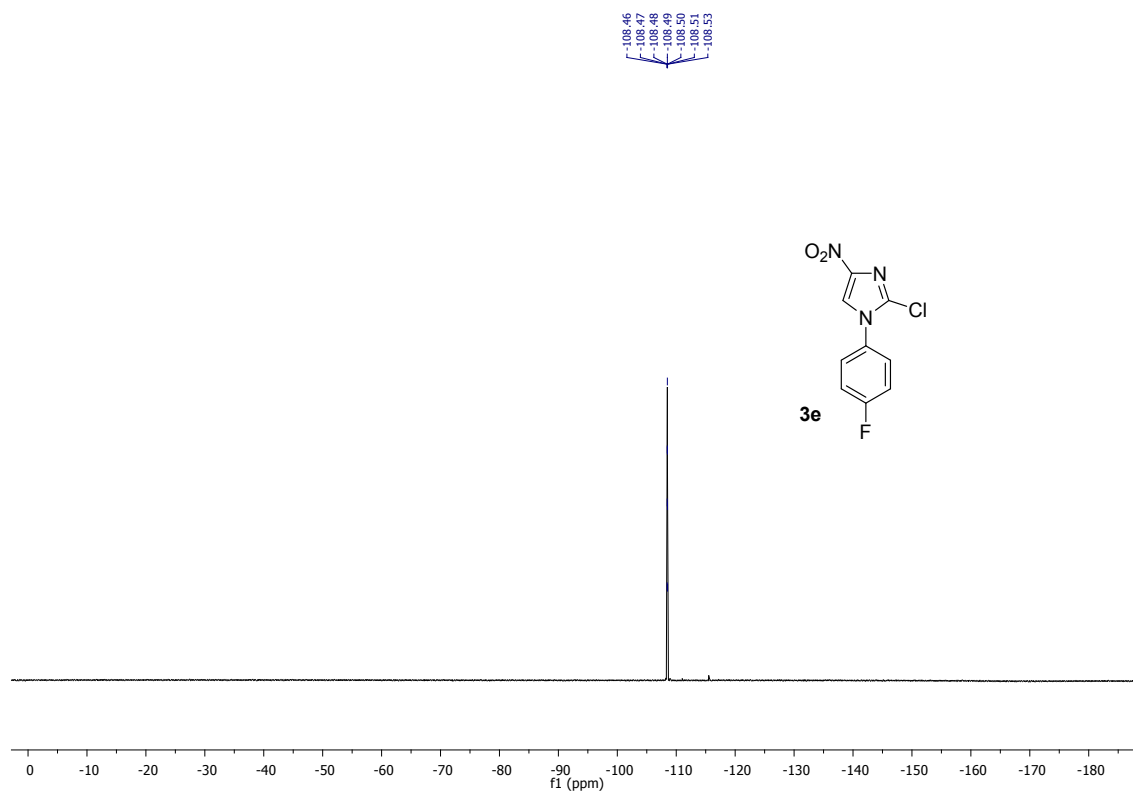


1-(4-(2-Chloro-4-nitro-1H-imidazol-1-yl)phenyl)ethan-1-one (3d):

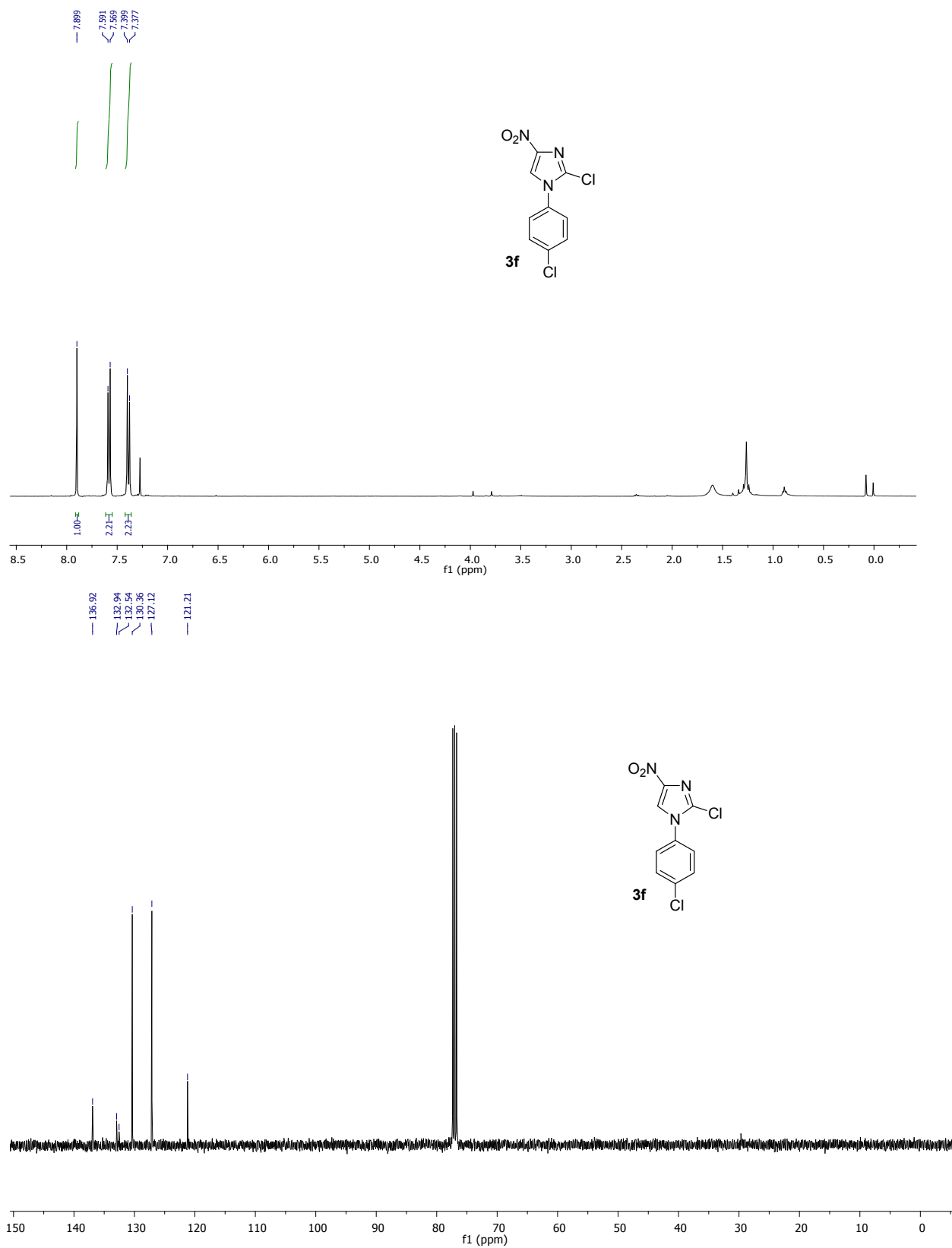


2-Chloro-1-(4-fluorophenyl)-4-nitro-1H-imidazole (3e):

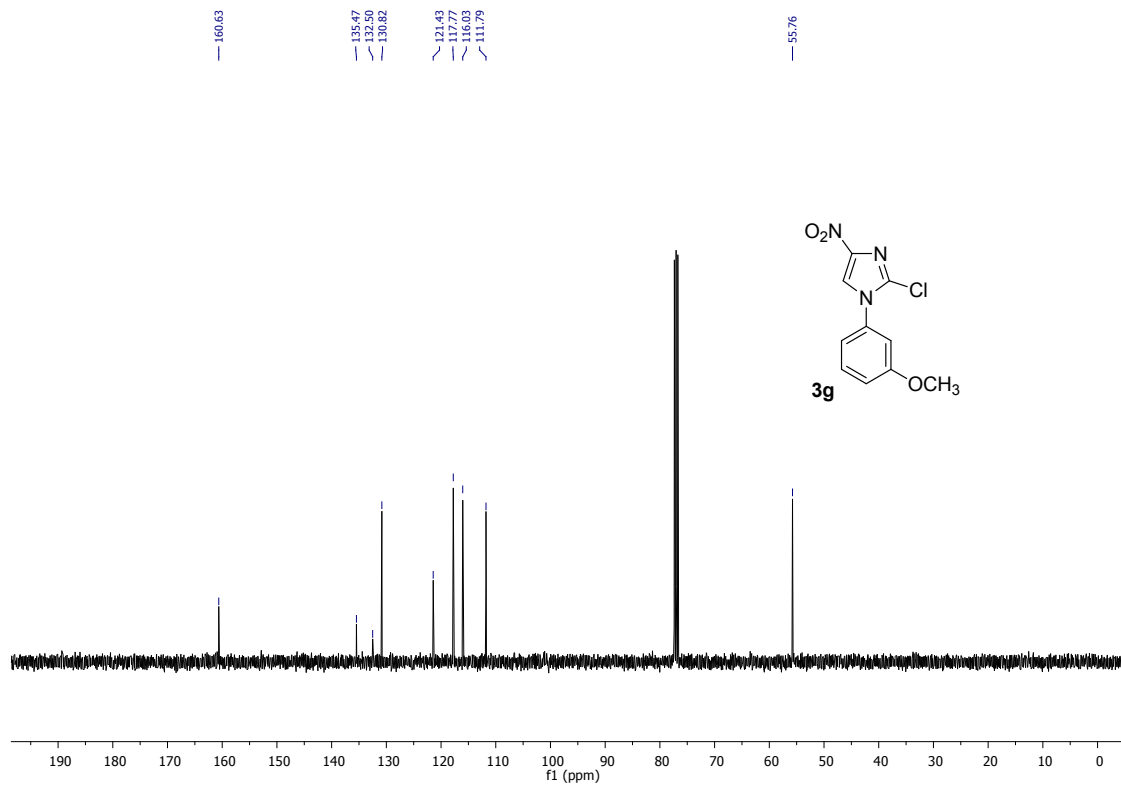
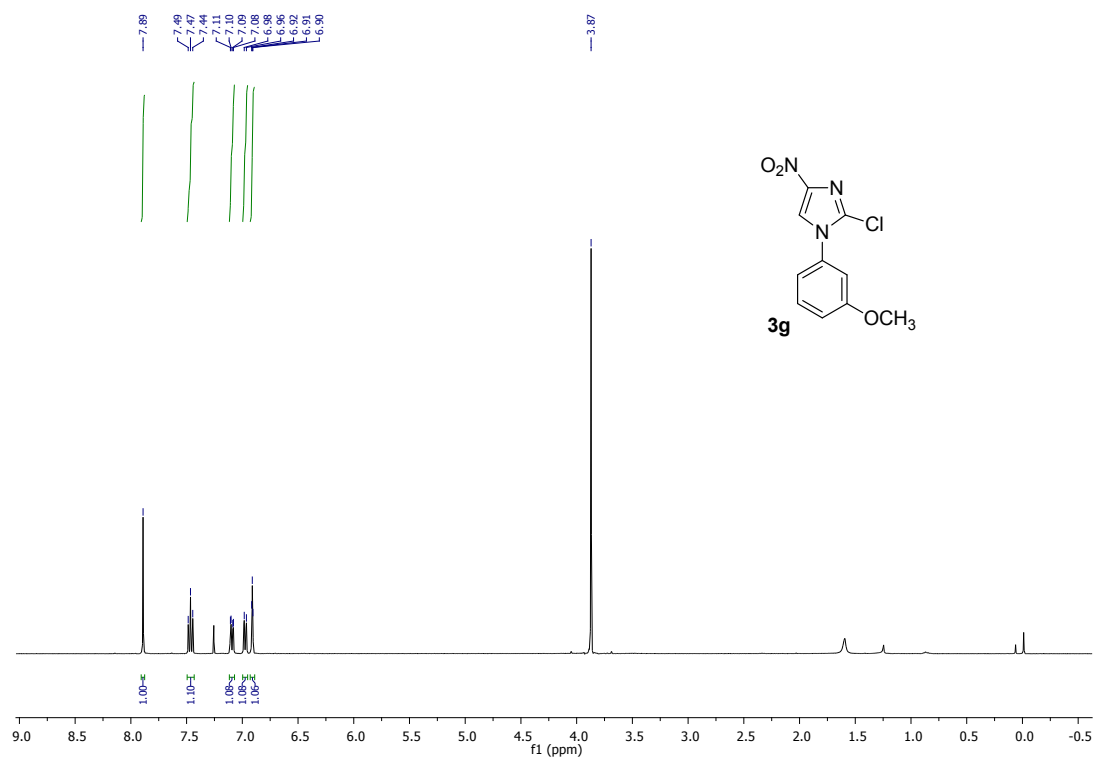




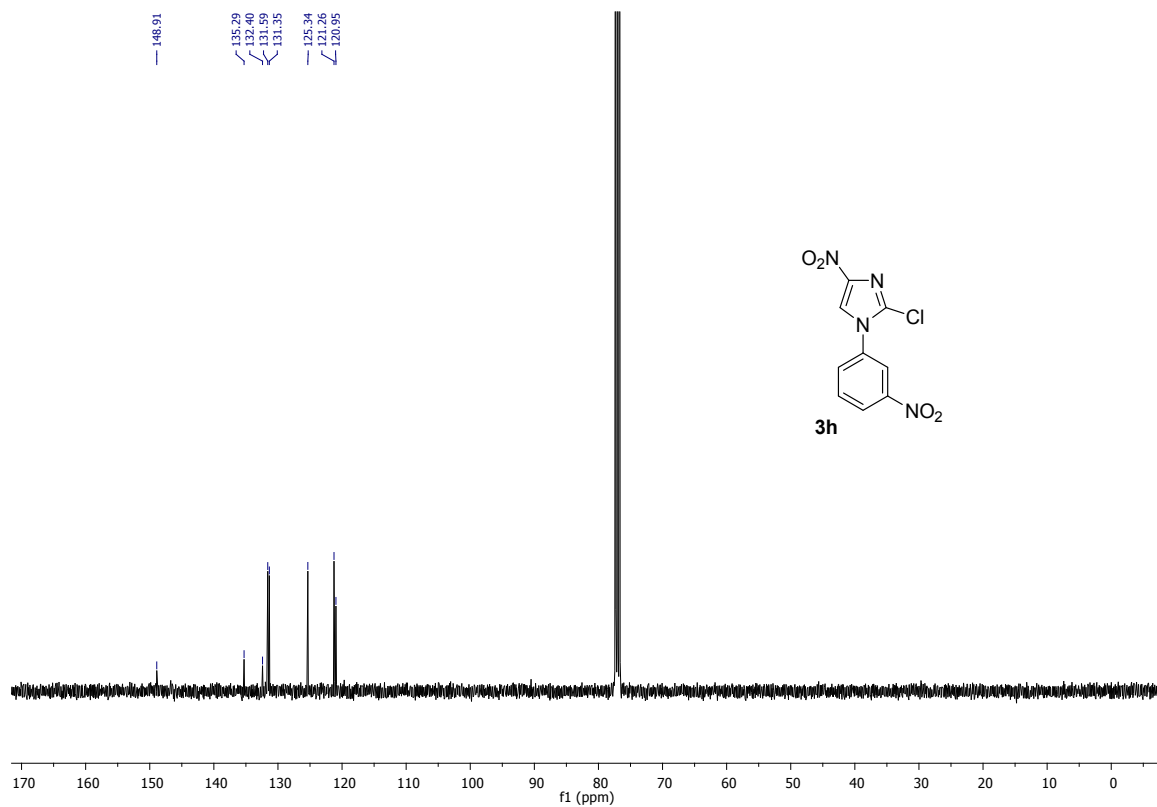
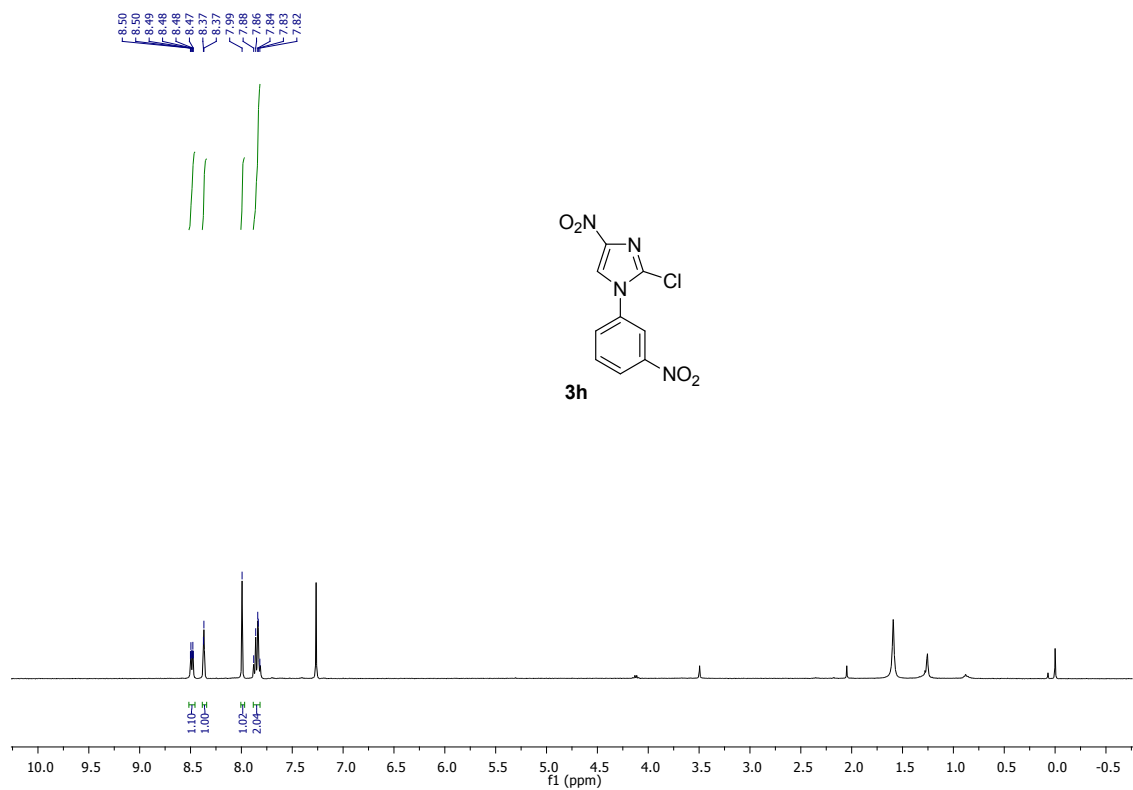
2-Chloro-1-(4-chlorophenyl)-4-nitro-1H-imidazole (3f) :



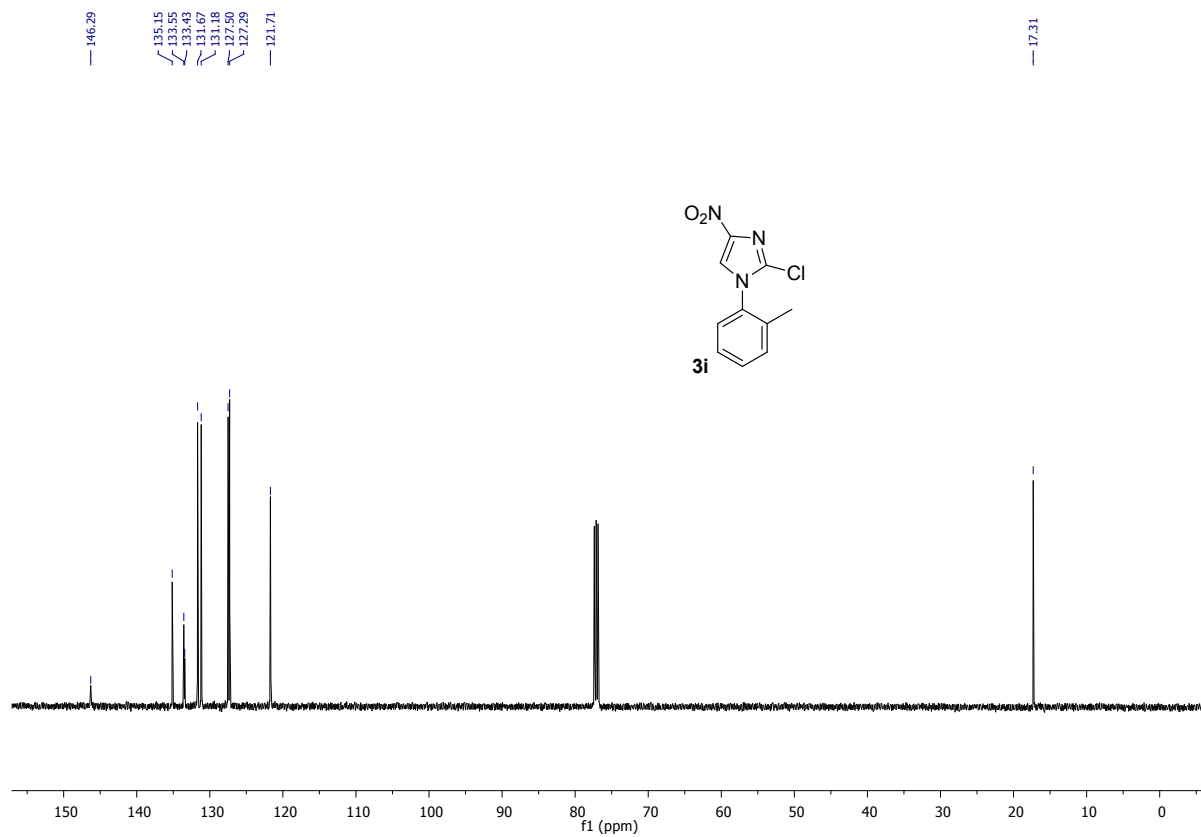
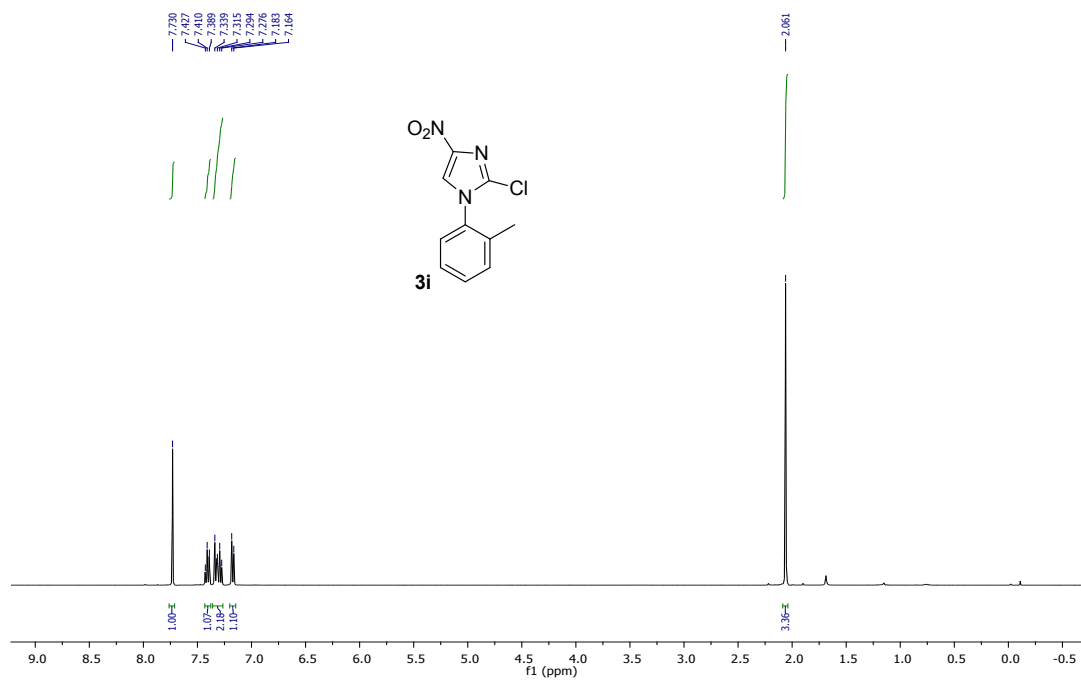
2-Chloro-1-(3-methoxyphenyl)-4-nitro-1H-imidazole (3g):



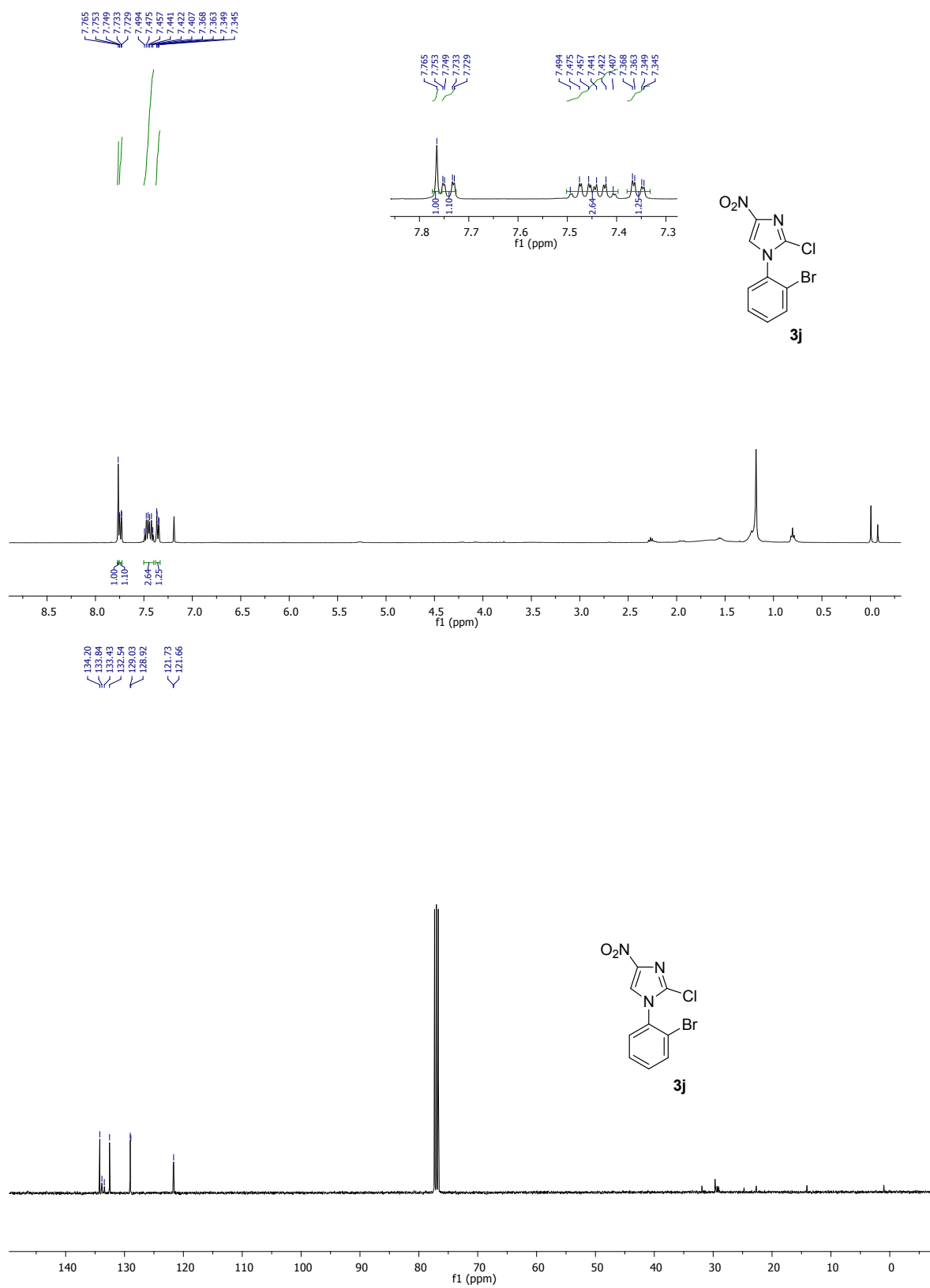
2-Chloro-4-nitro-1-(3-nitrophenyl)-1H-imidazole (3h):



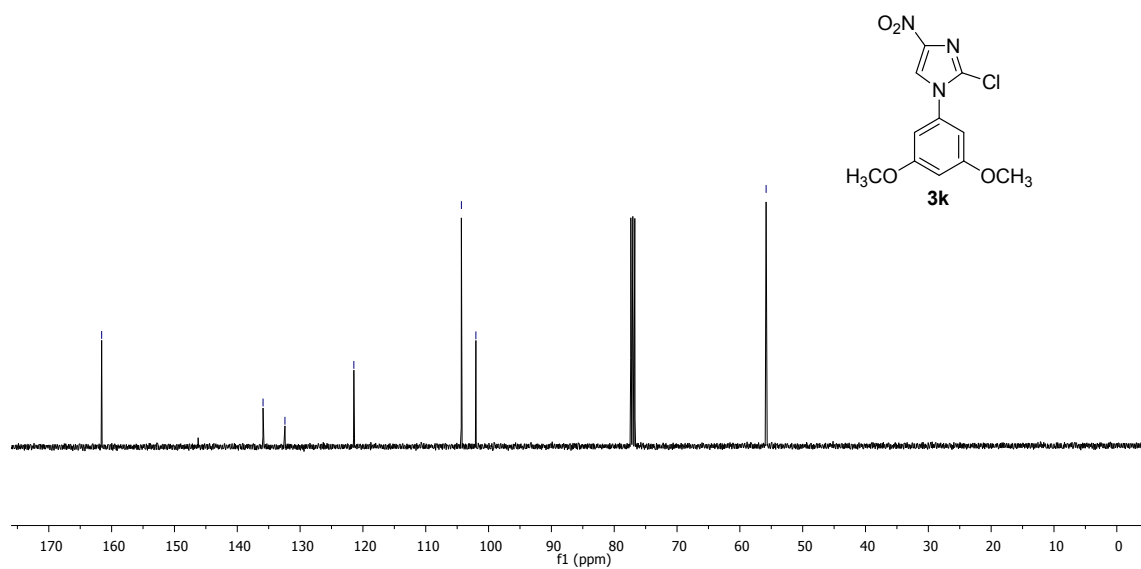
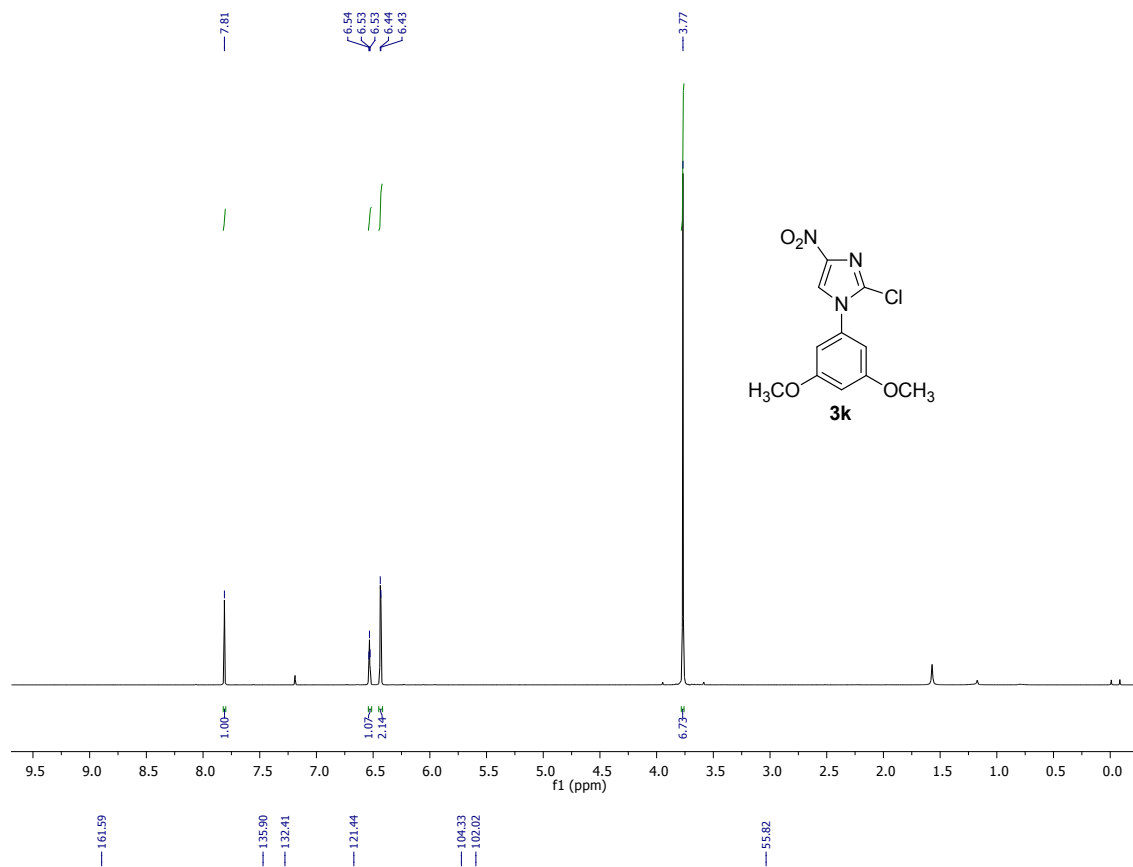
2-Chloro-4-nitro-1-(*o*-tolyl)-1*H*-imidazole (3i):



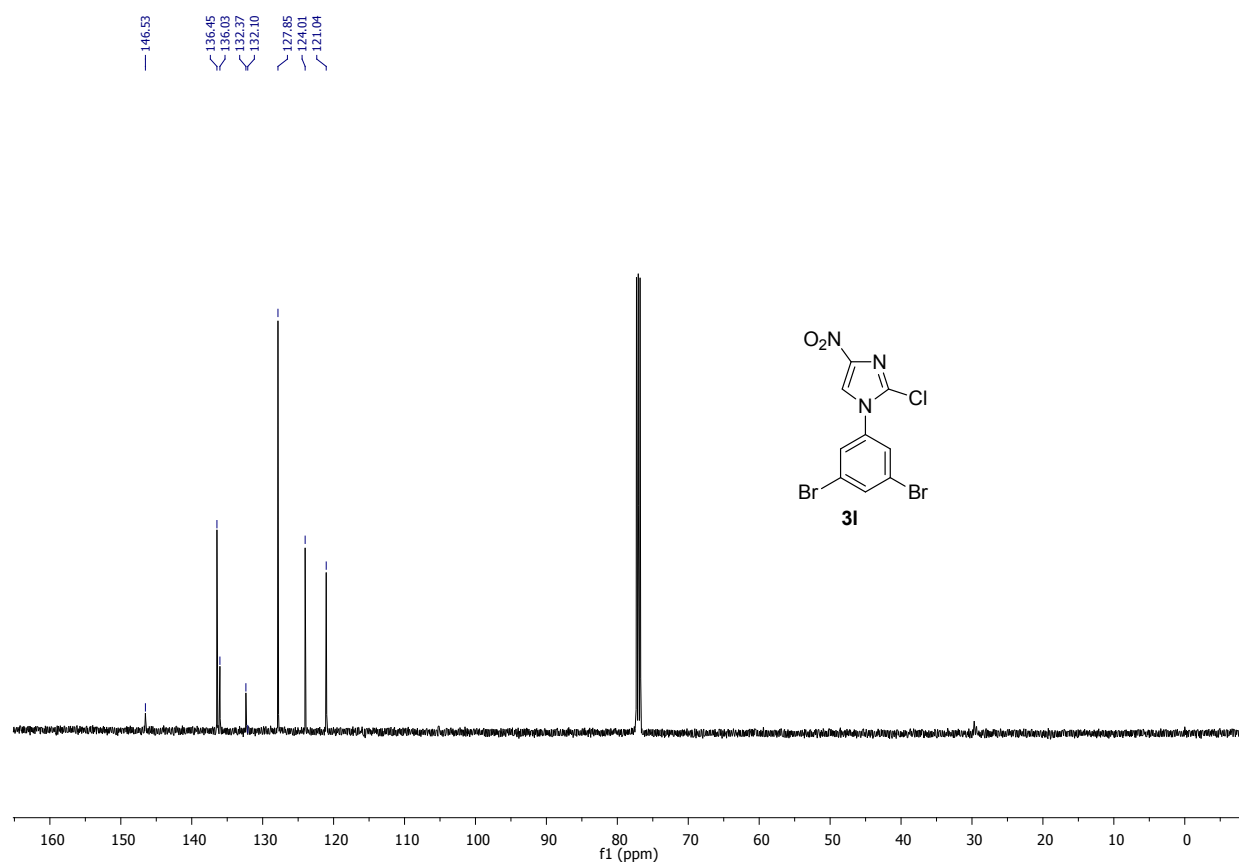
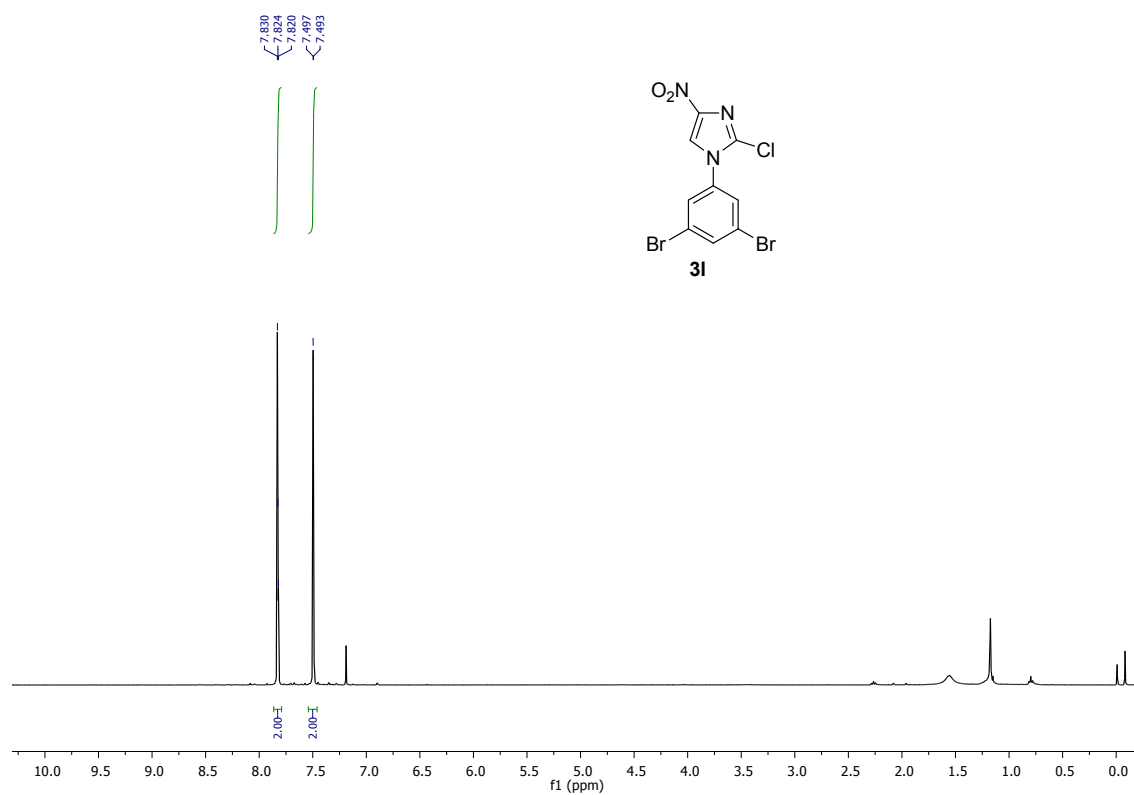
1-(2-Bromophenyl)-2-chloro-4-nitro-1*H*-imidazole (3j):



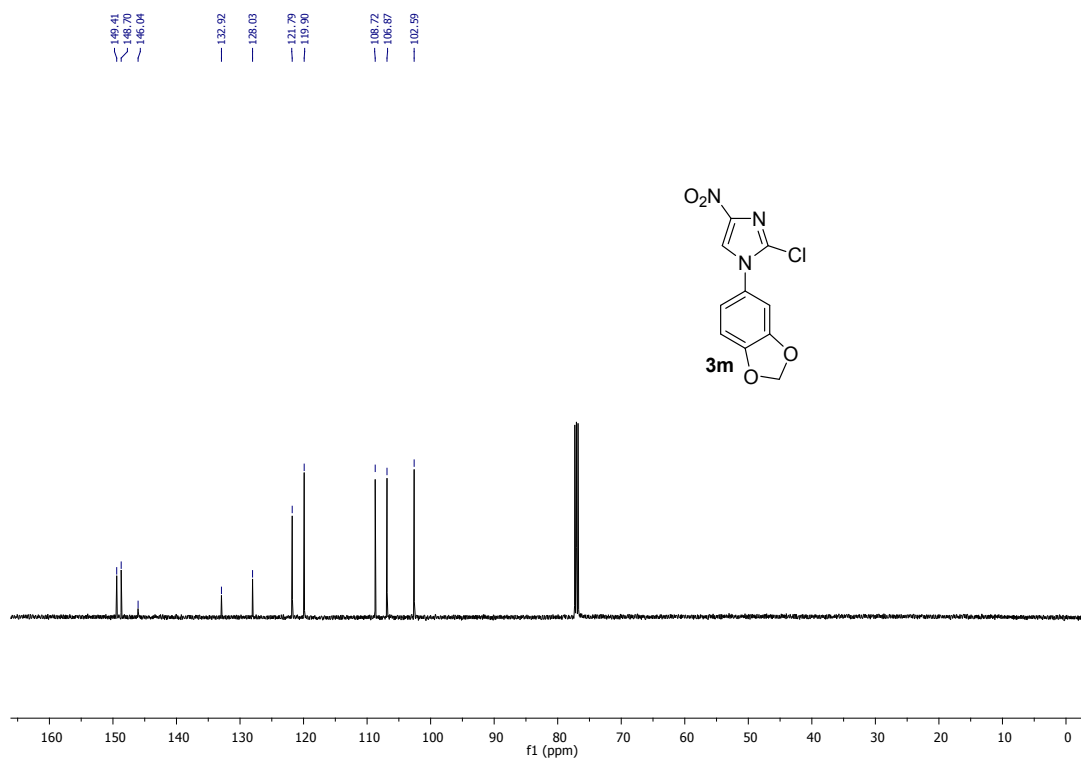
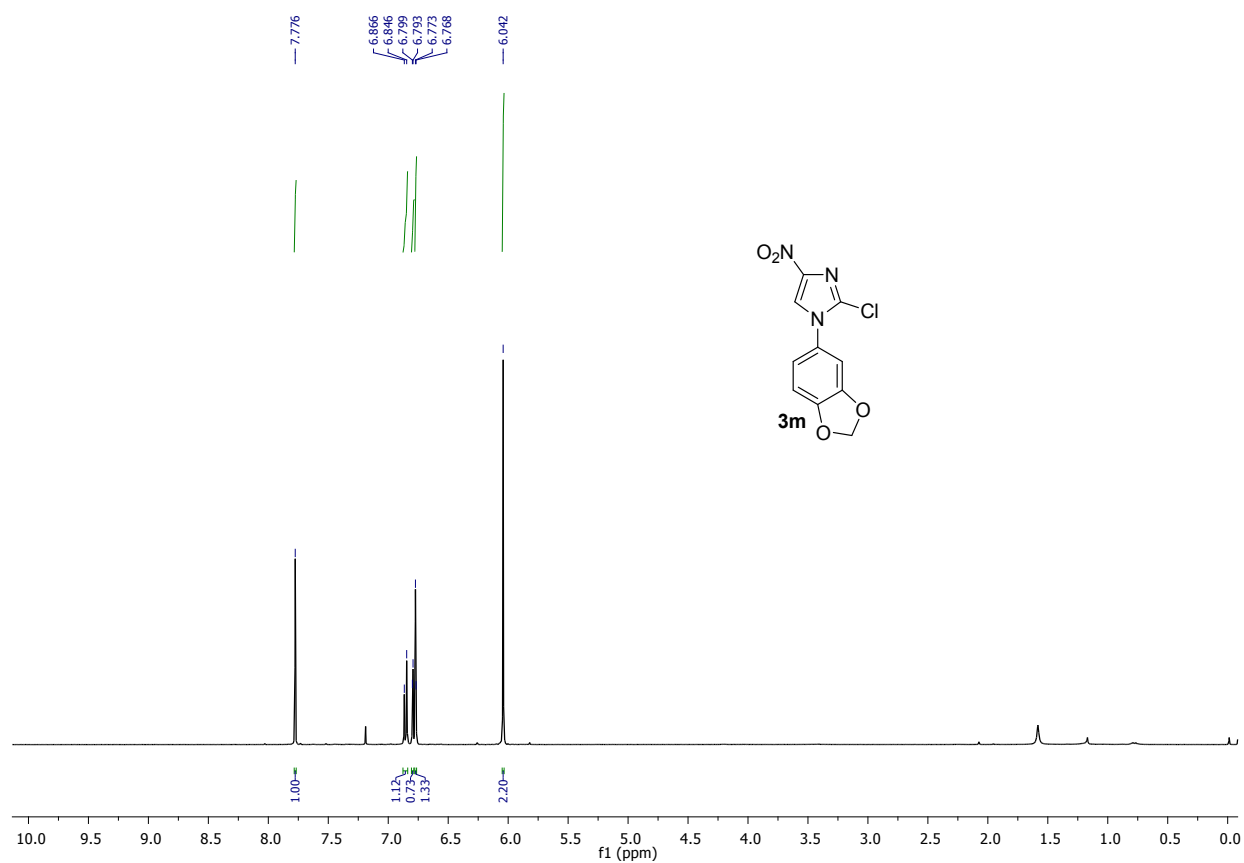
2-Chloro-1-(3,5-dimethoxyphenyl)-4-nitro-1H-imidazole (3k):



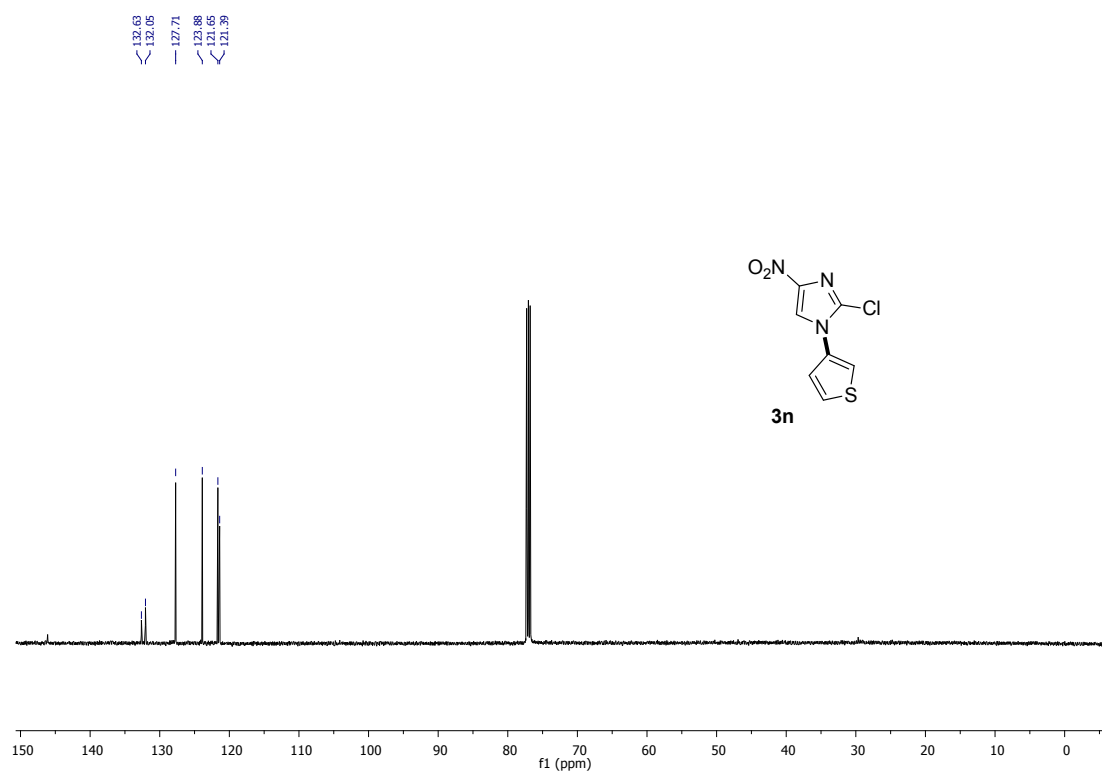
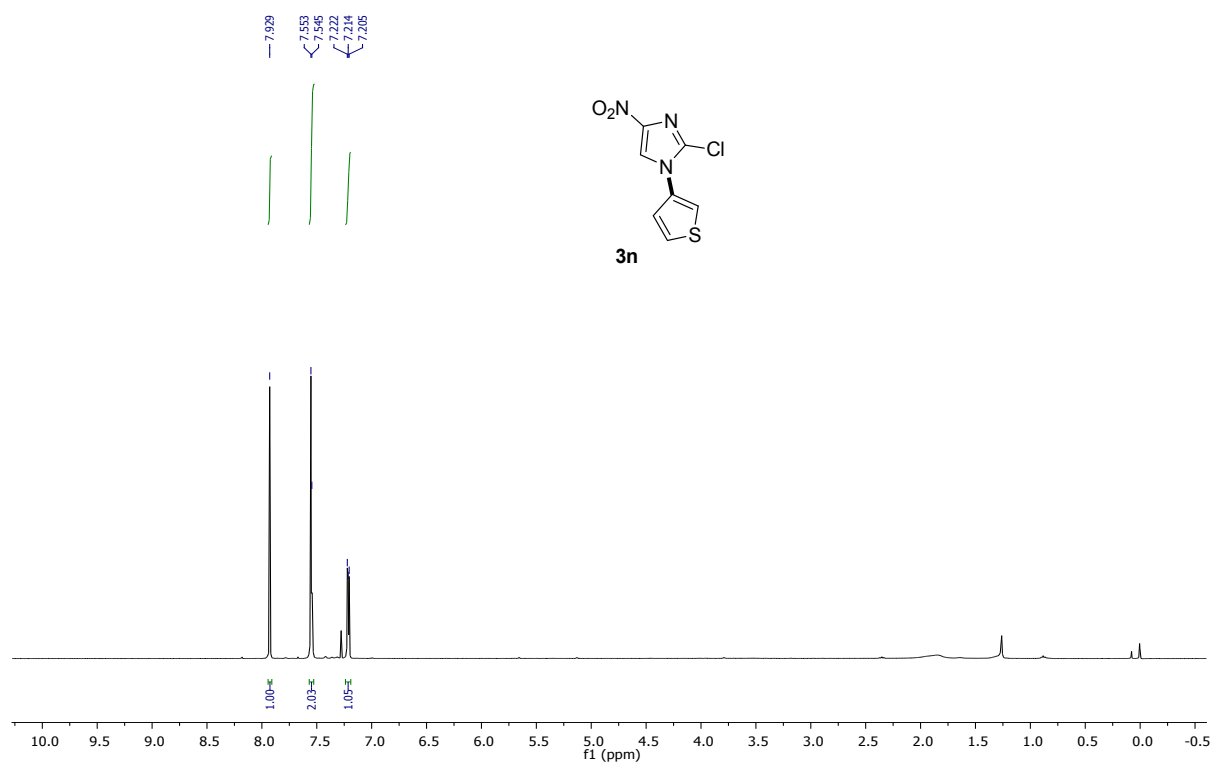
2-Chloro-1-(3,5-dibromophenyl)-4-nitro-1H-imidazole (3I):



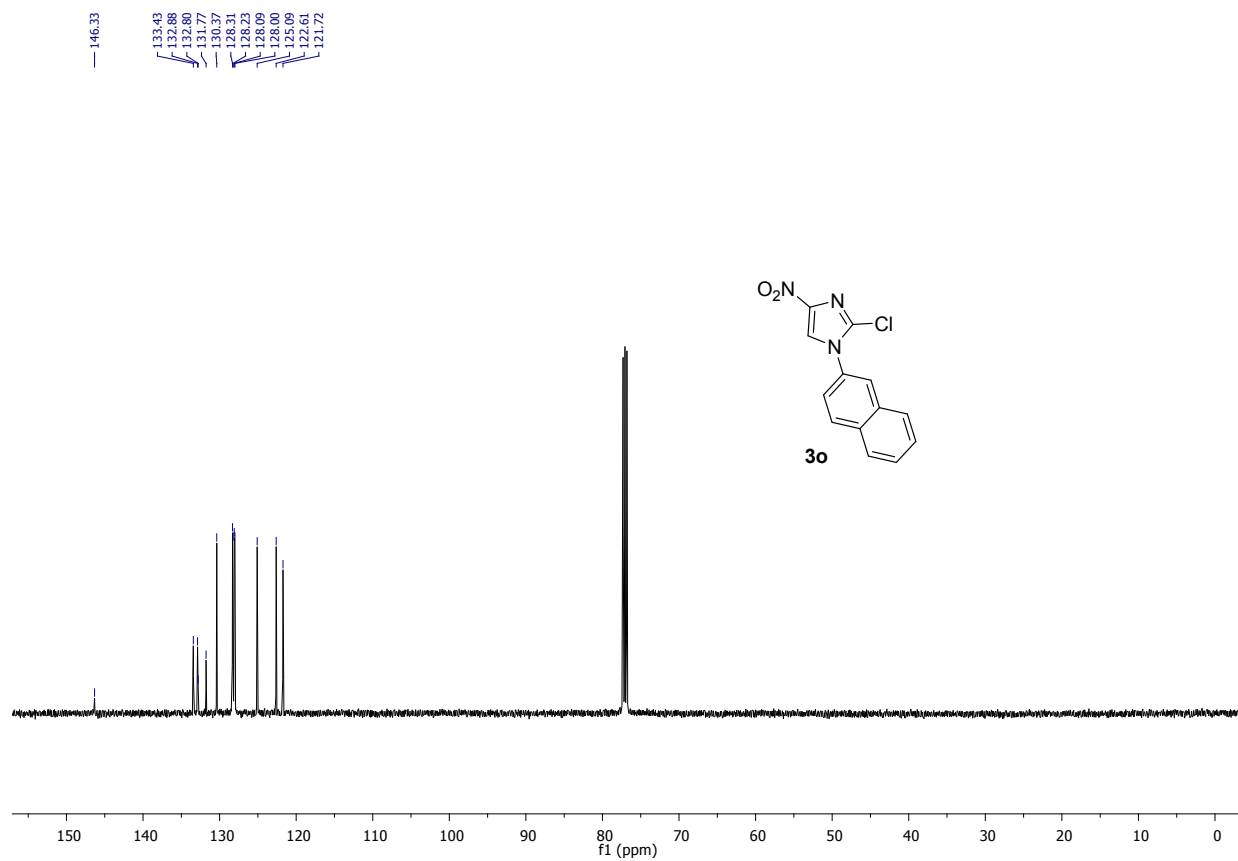
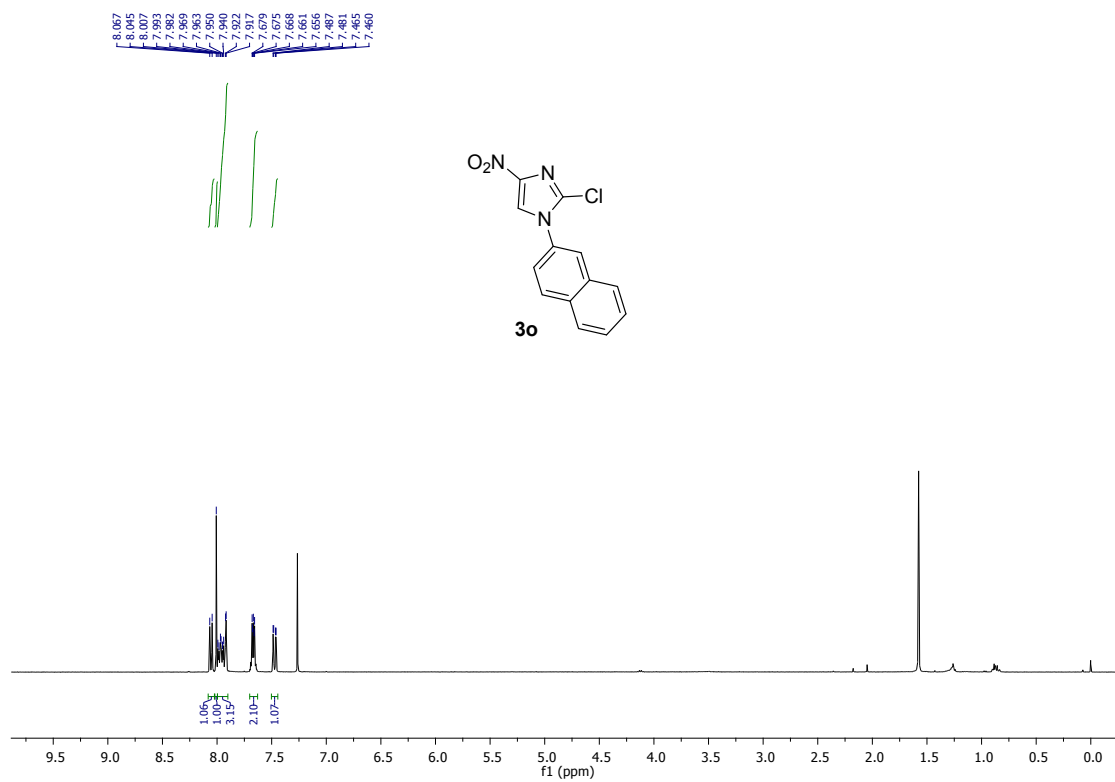
1-(Benzo[d][1,3]dioxol-5-yl)-2-chloro-4-nitro-1*H*-imidazole (3m) :



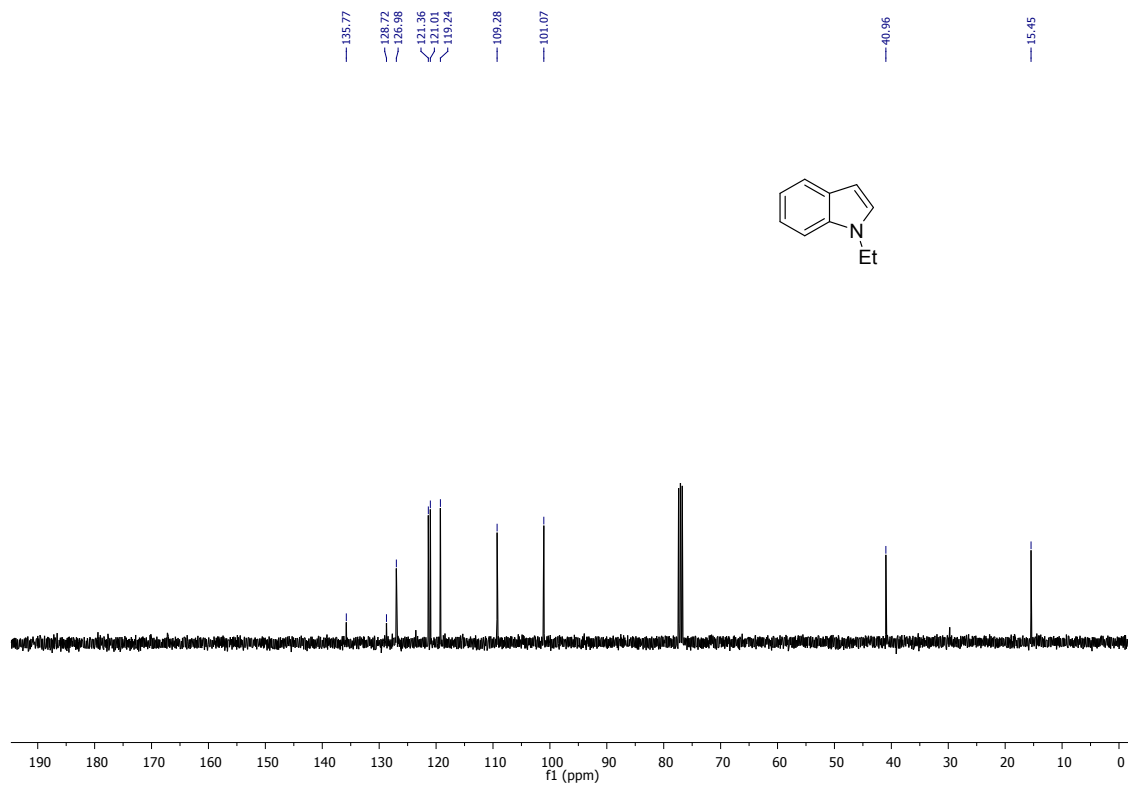
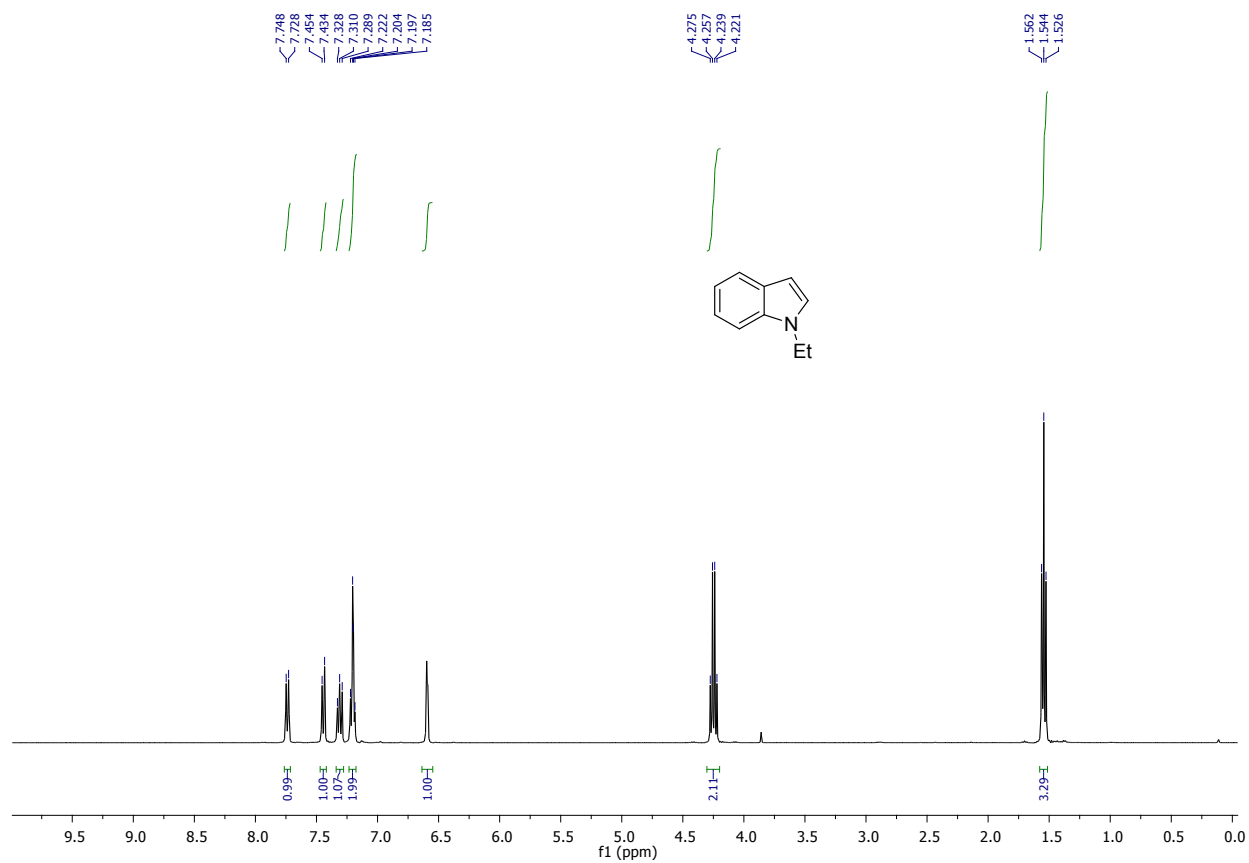
2-Chloro-4-nitro-1-(thiophen-3-yl)-1H-imidazole (3n):

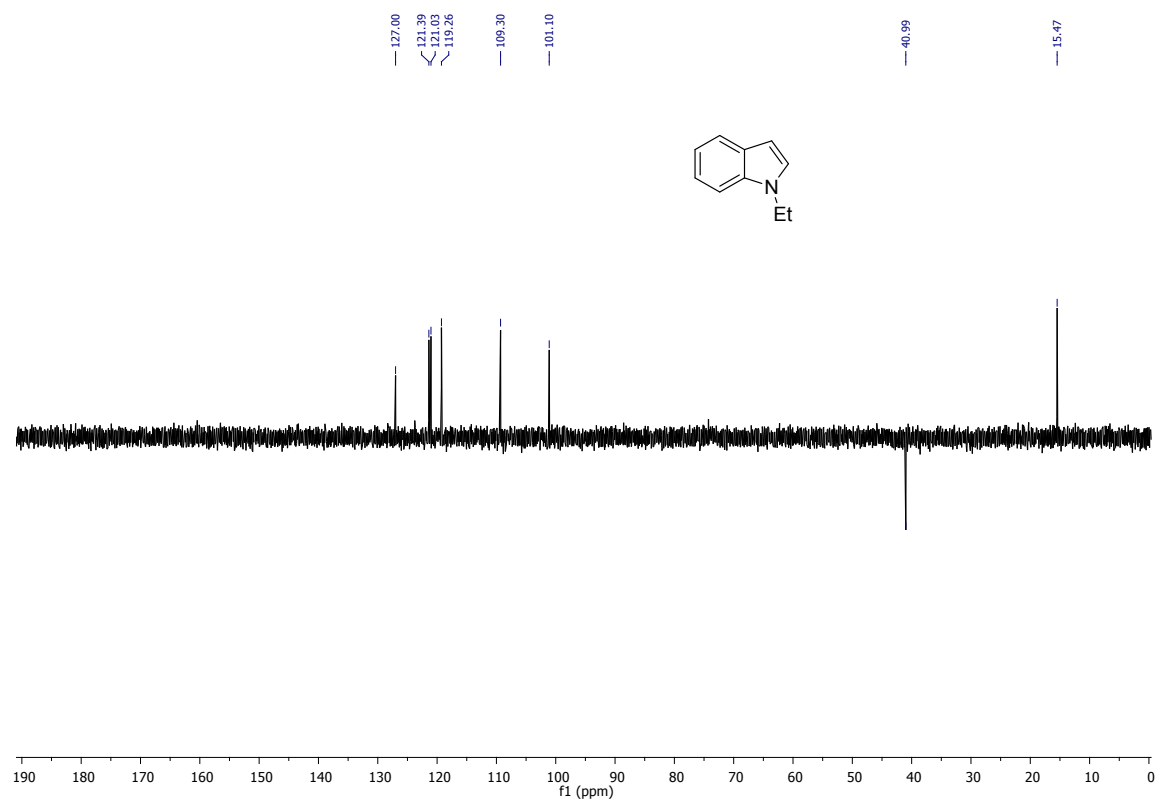


2-Chloro-1-(naphthalen-2-yl)-4-nitro-1*H*-imidazole (3o):

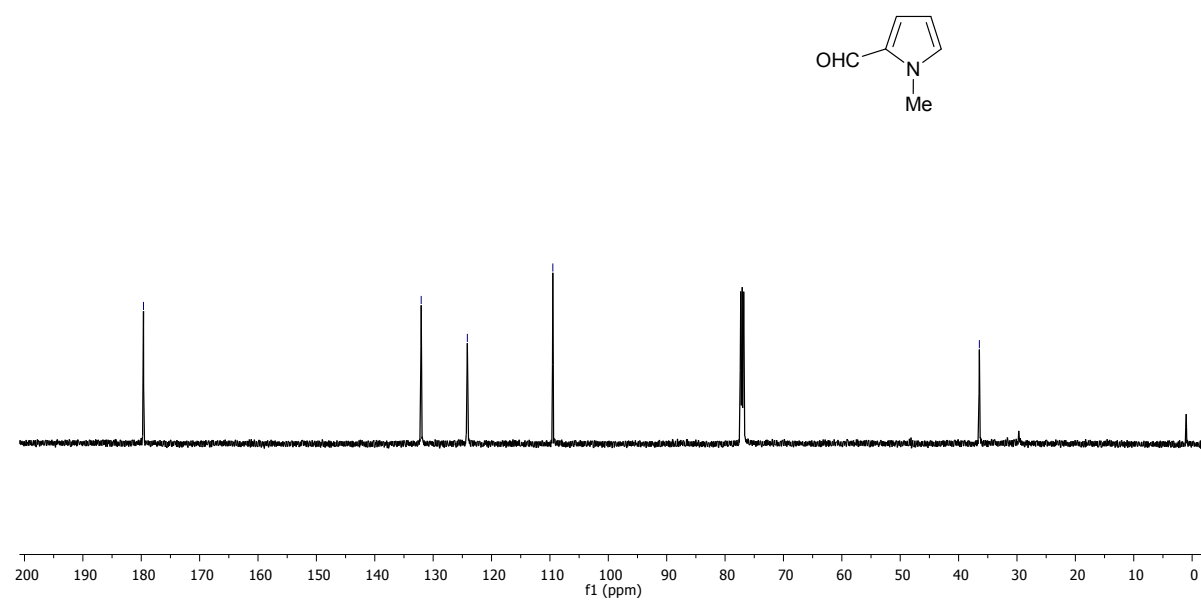
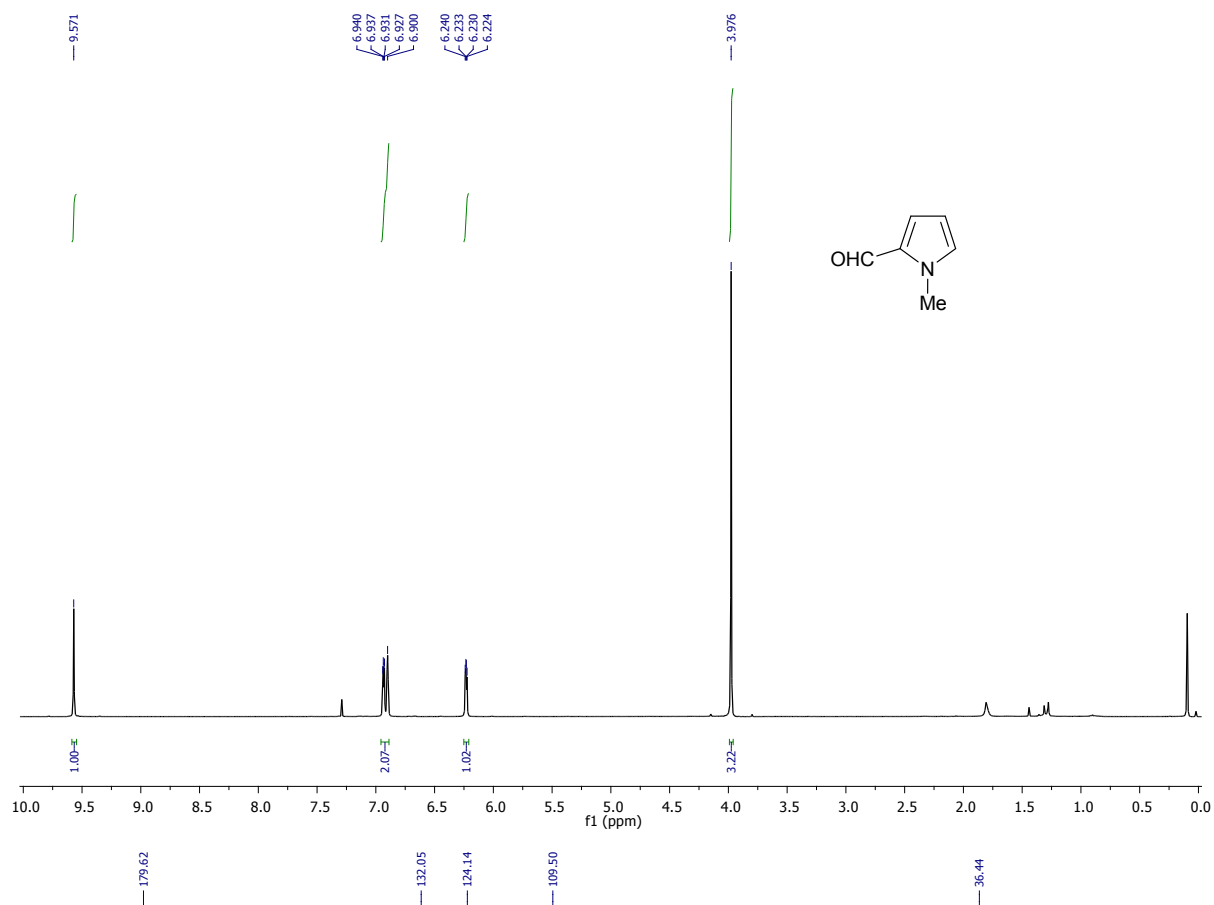


1-Ethyl-1*H*-indole (4f) :

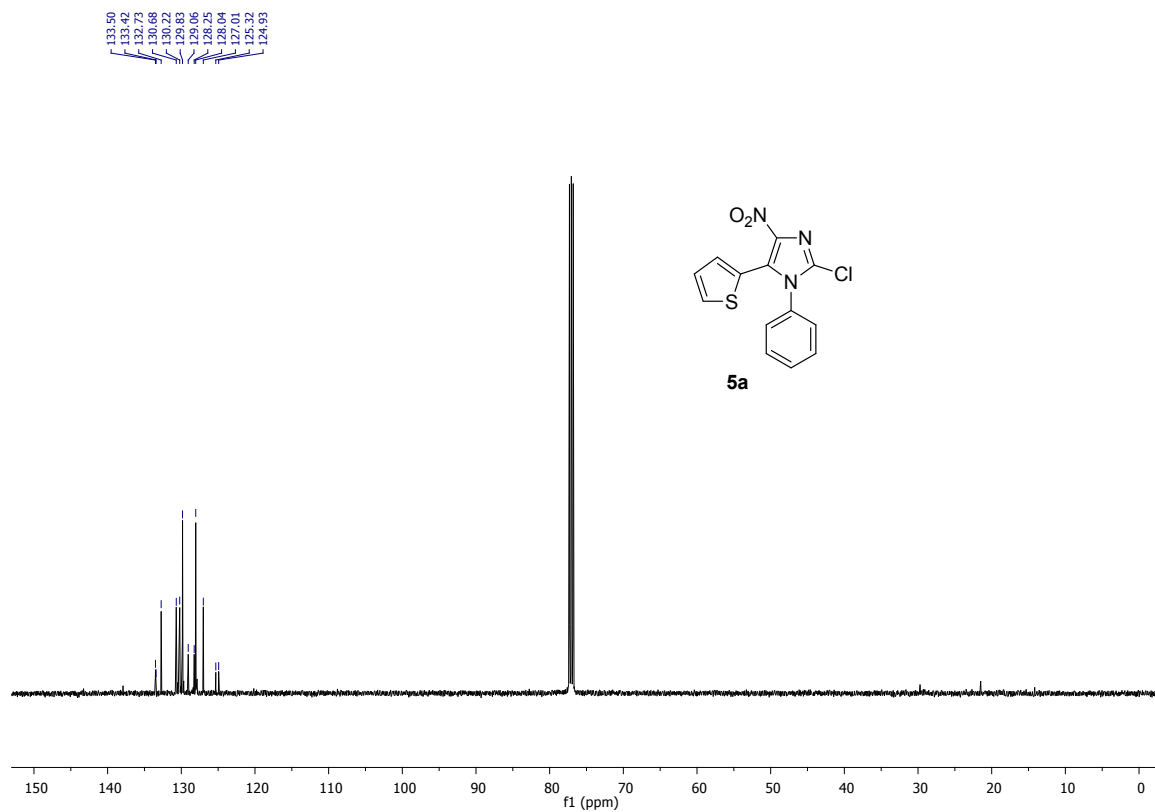
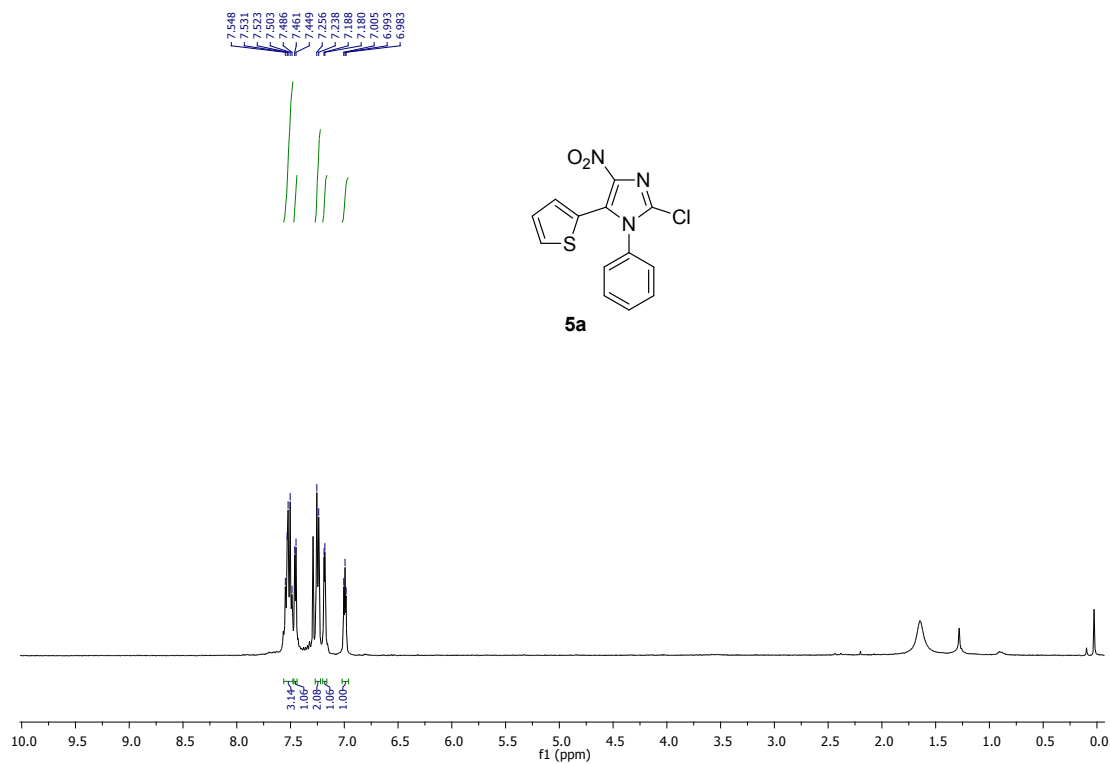




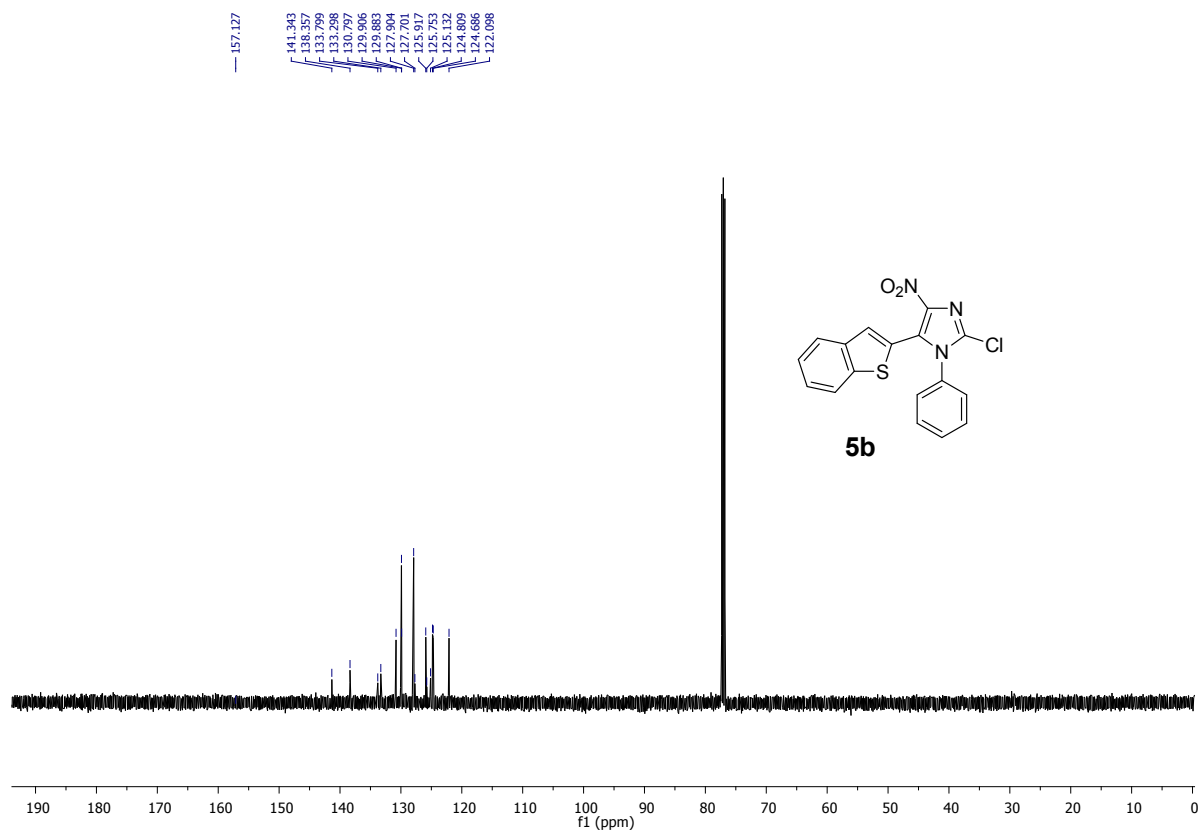
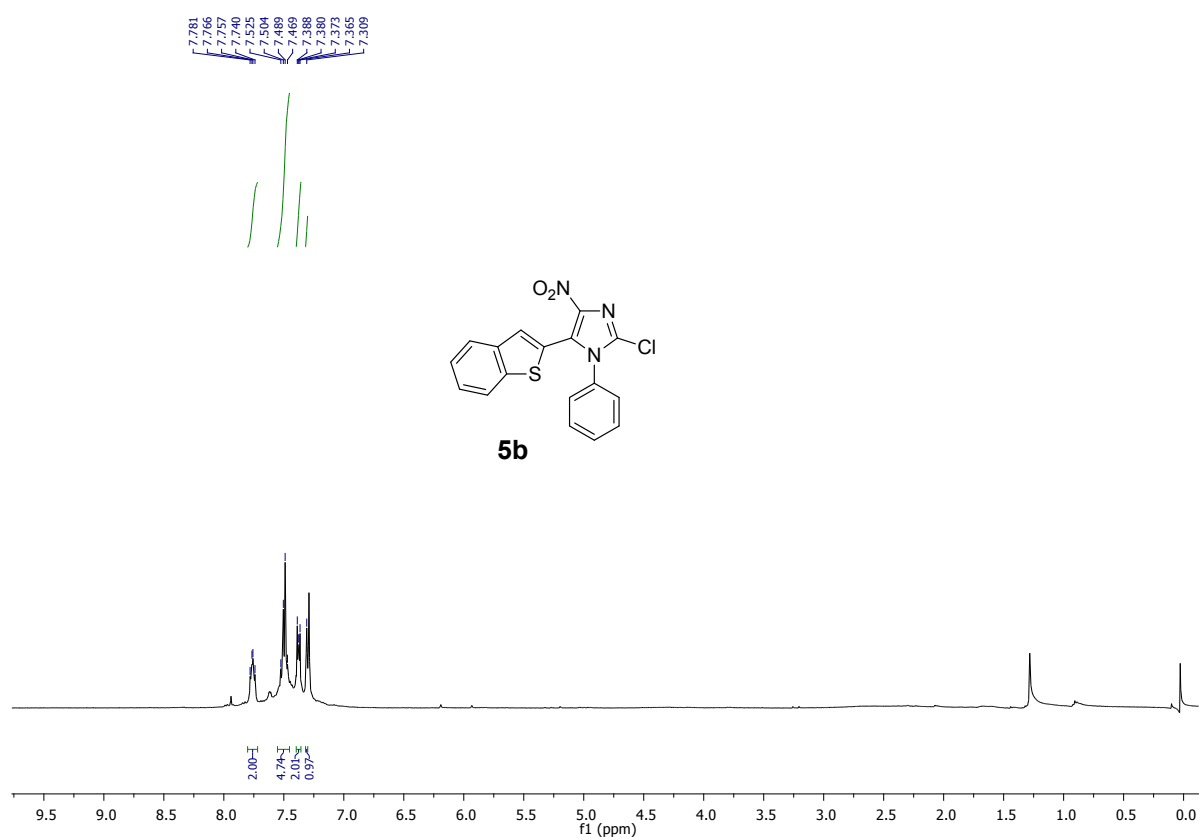
1-Methyl-1*H*-pyrrole-2-carbaldehyde (4g) :



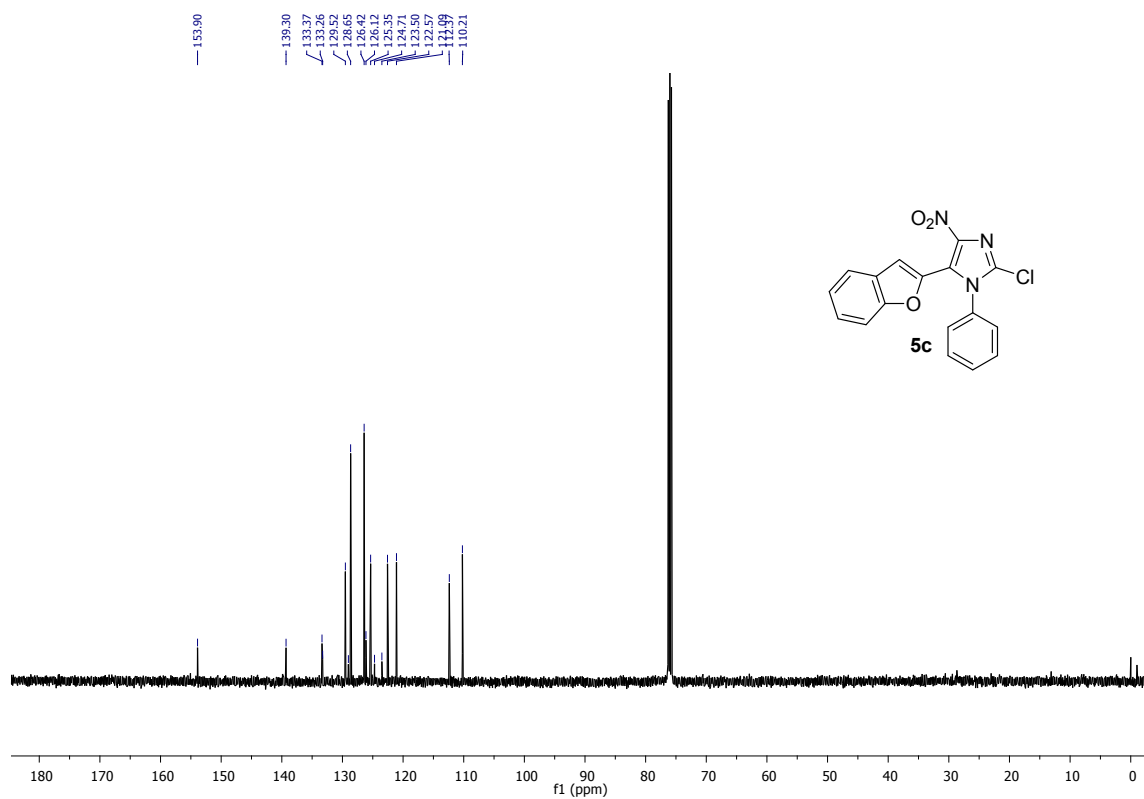
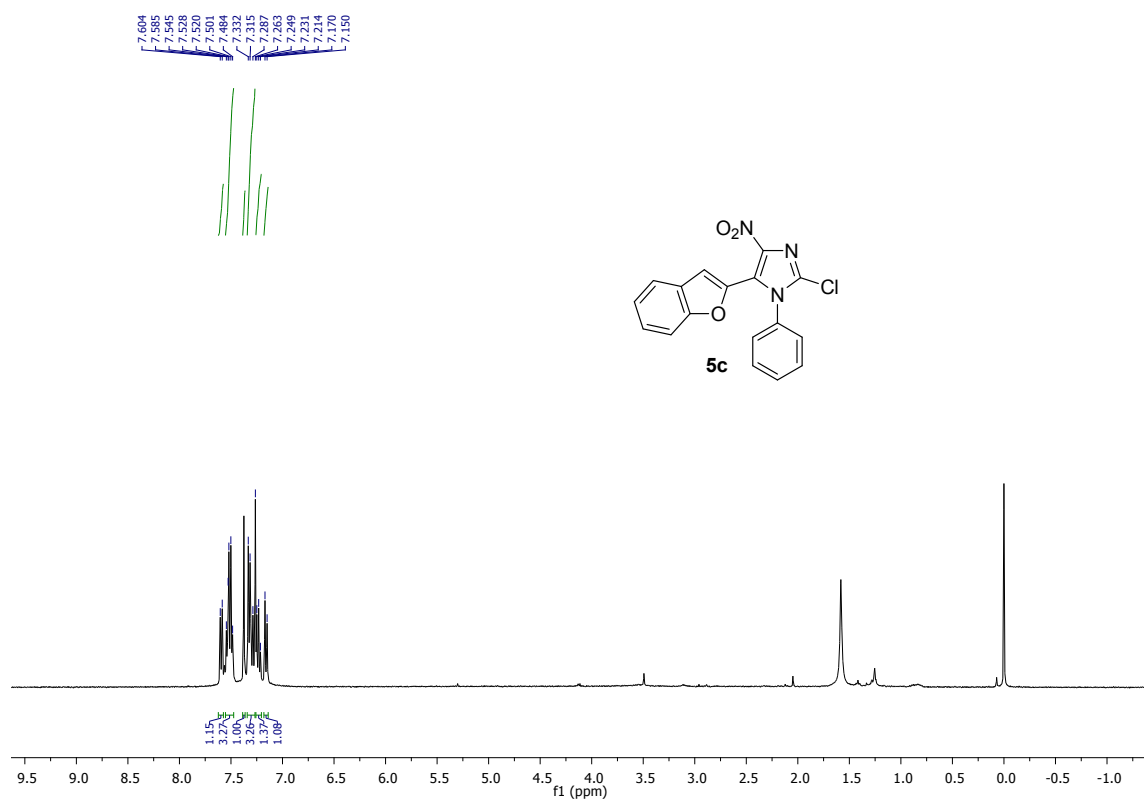
2-Chloro-4-nitro-1-phenyl-5-(thiophen-2-yl)-1*H*-imidazole (5a):



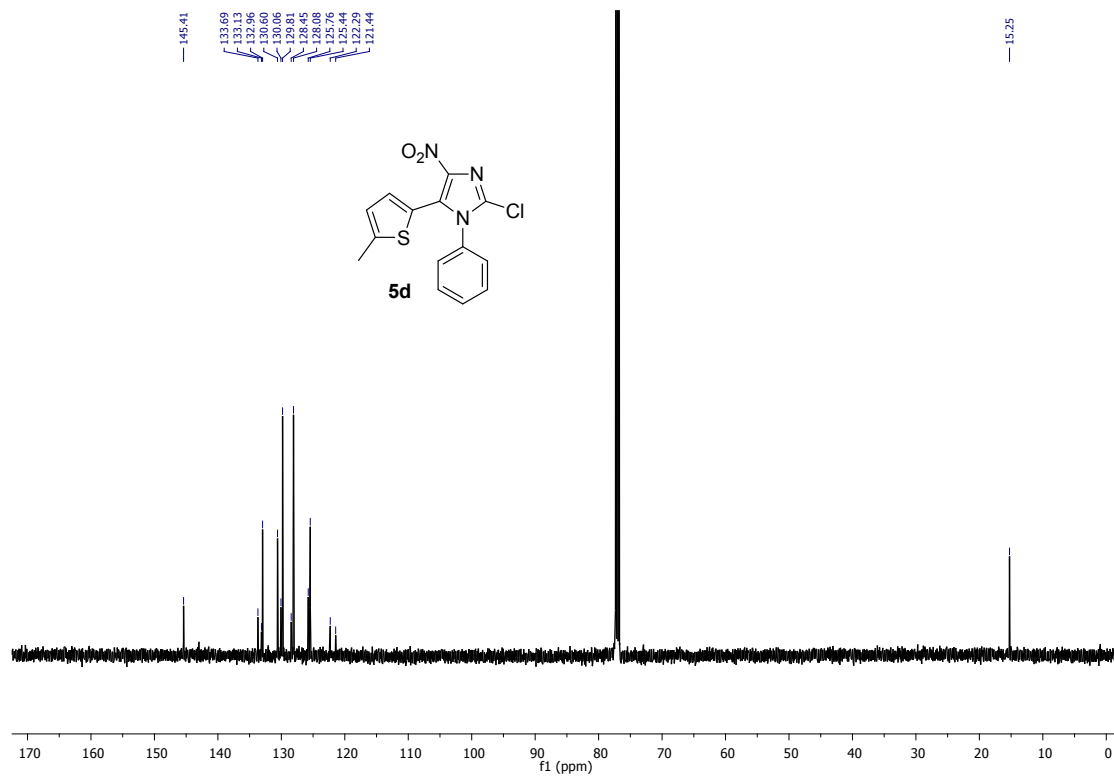
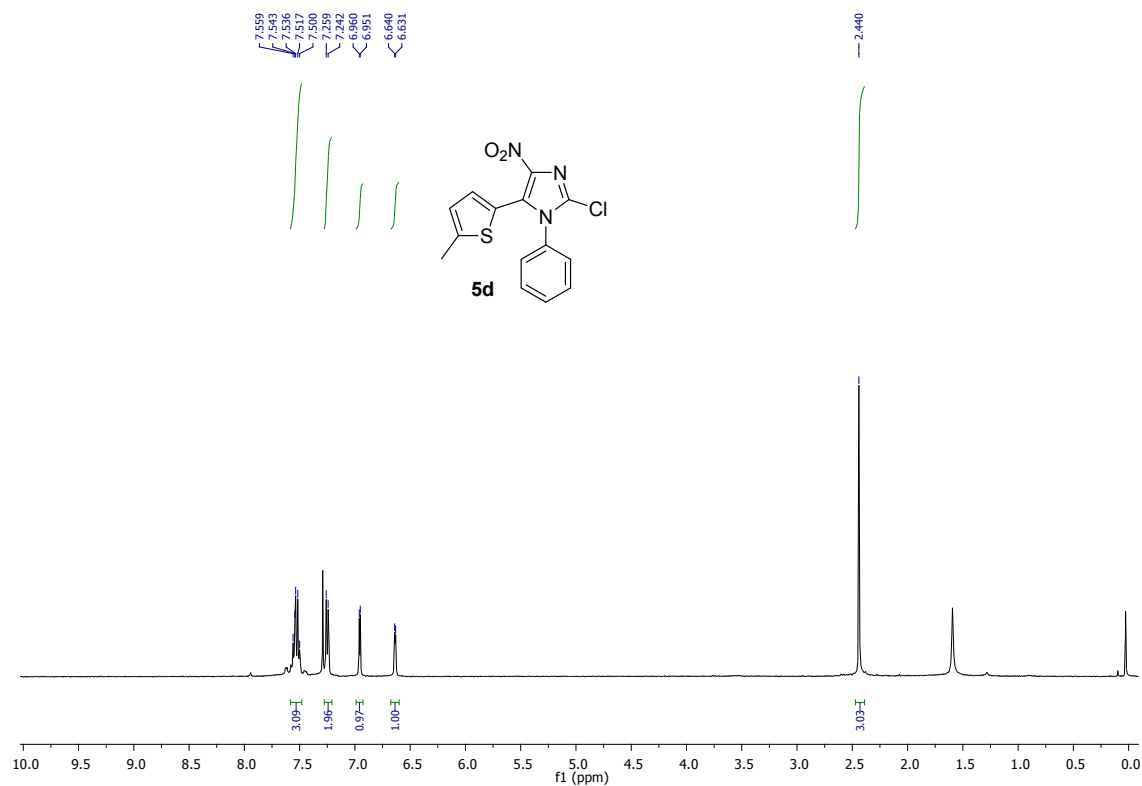
5-(Benzo[b]thiophen-2-yl)-2-chloro-4-nitro-1-phenyl-1H-imidazole (5b) :



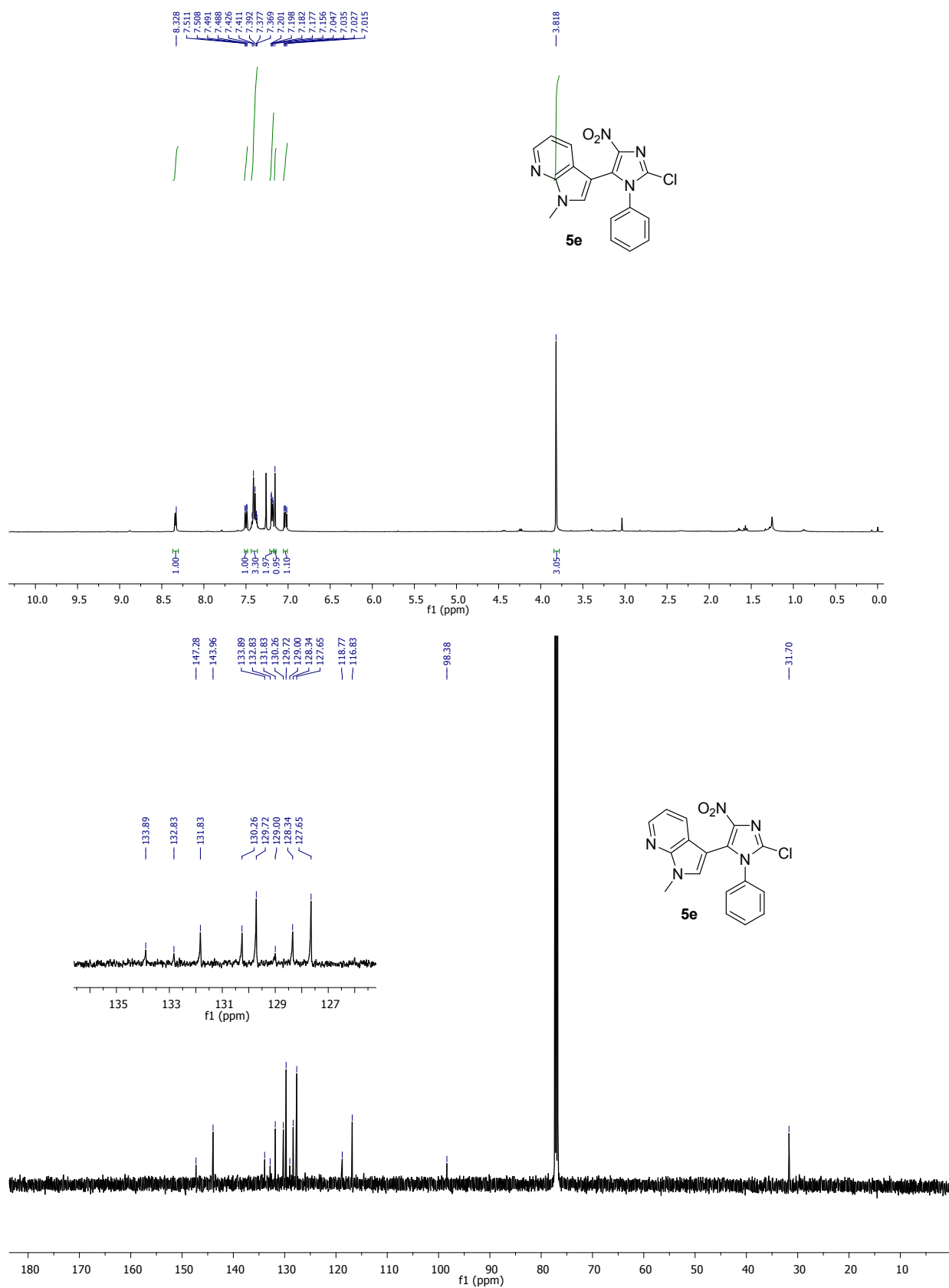
5-(Benzofuran-2-yl)-2-chloro-4-nitro-1-phenyl-1H-imidazole (5c):



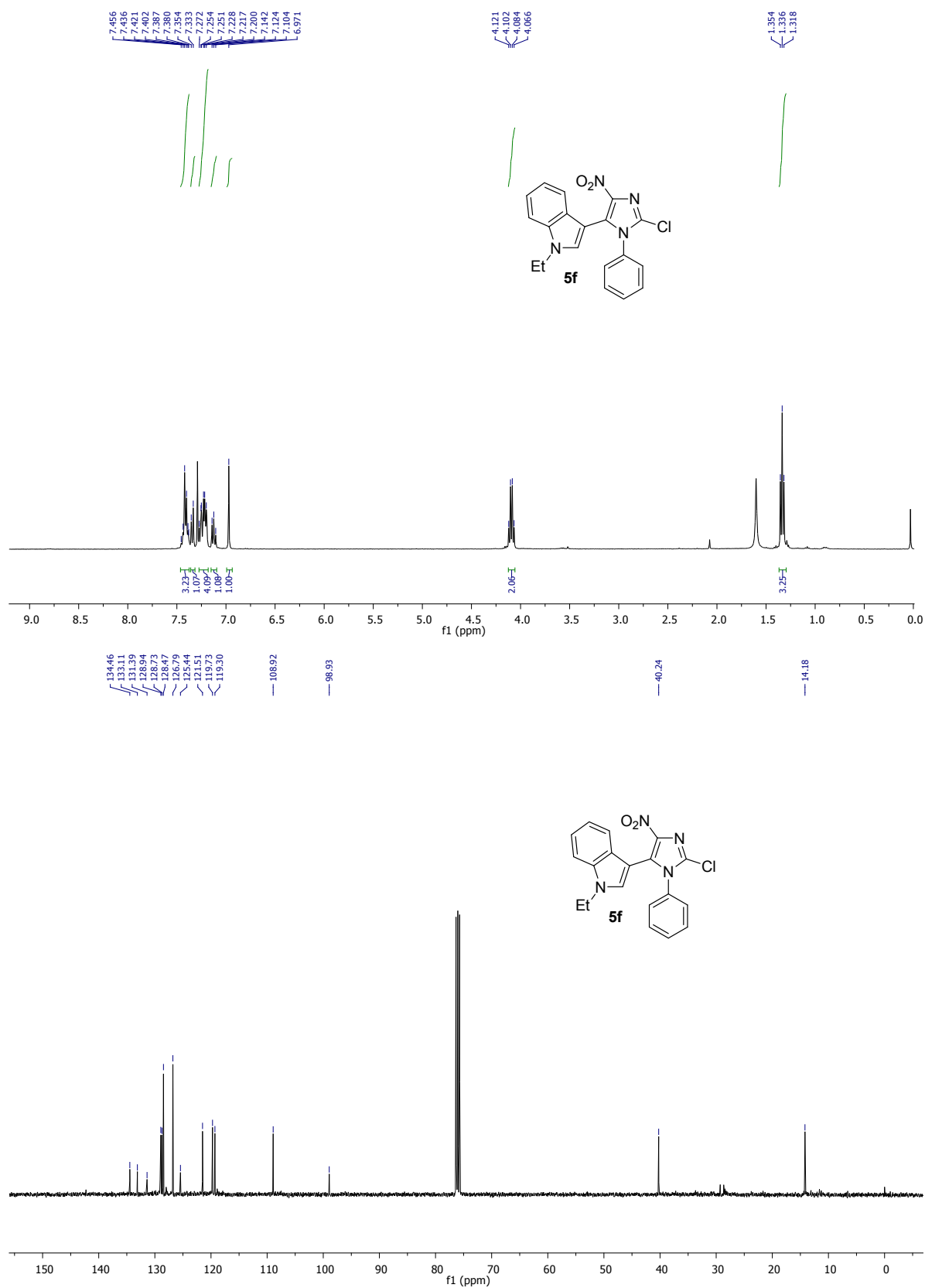
2-Chloro-5-(5-methylthiophen-2-yl)-4-nitro-1-phenyl-1H-imidazole (5d):

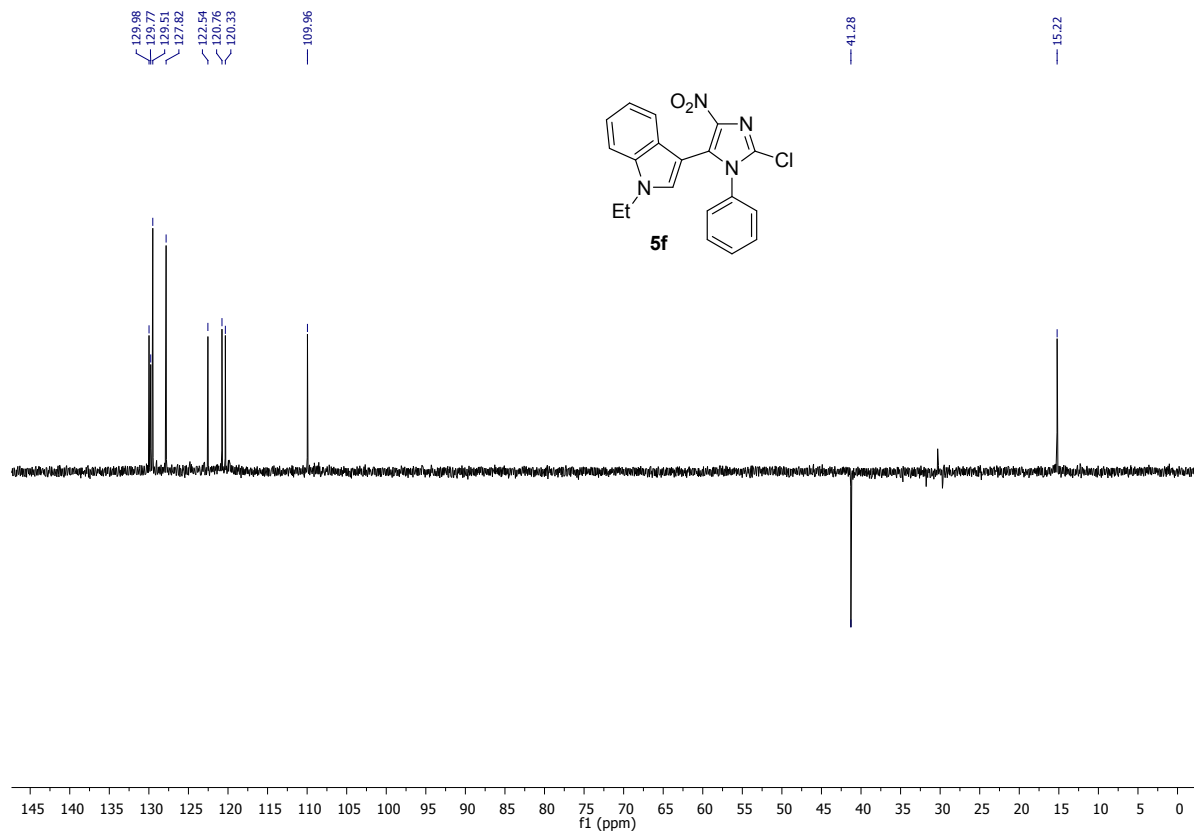


3-(2-Chloro-4-nitro-1-phenyl-1*H*-imidazol-5-yl)-1-methyl-1*H*-pyrrolo[2,3-*b*]pyridine (5e):

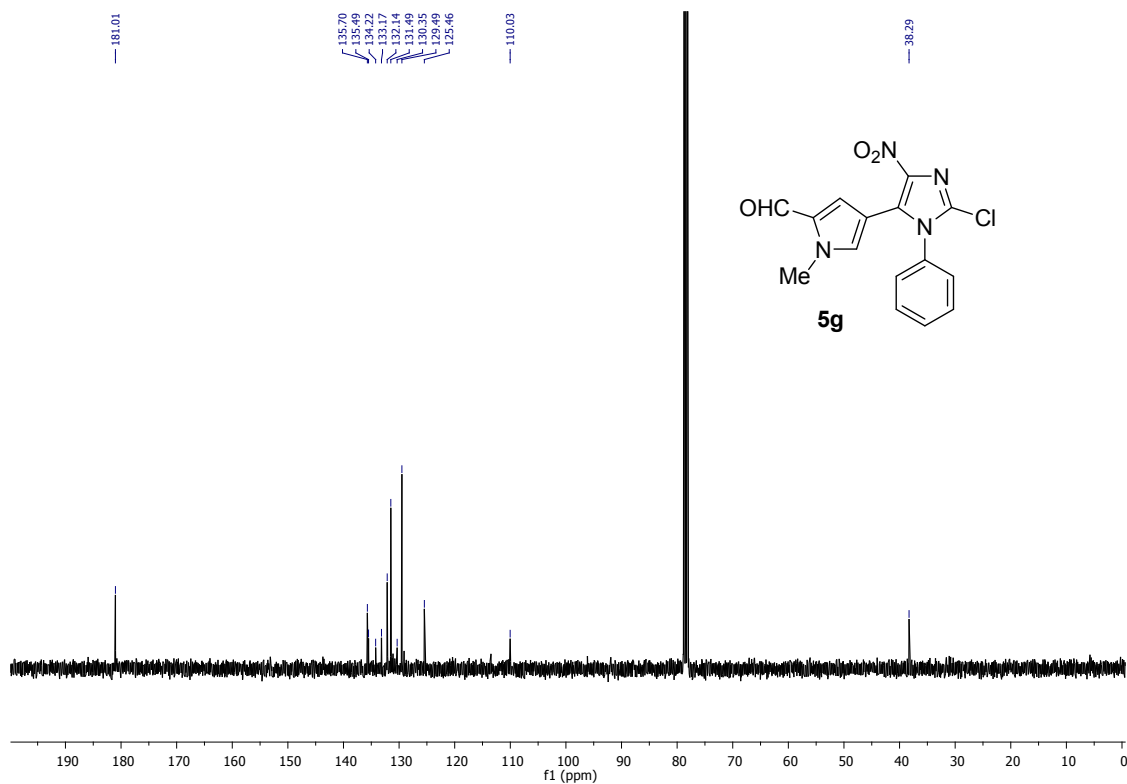
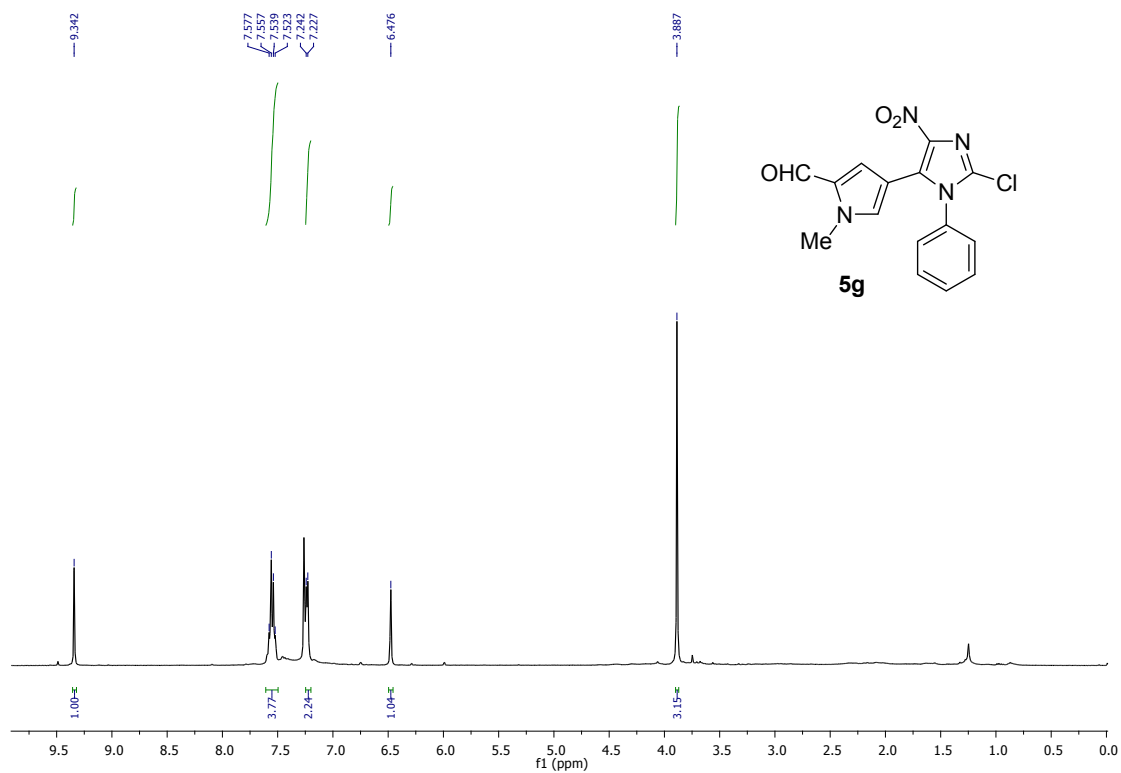


3-(2-Chloro-4-nitro-1-phenyl-1*H*-imidazol-5-yl)-1-ethyl-1*H*-indole (5f):

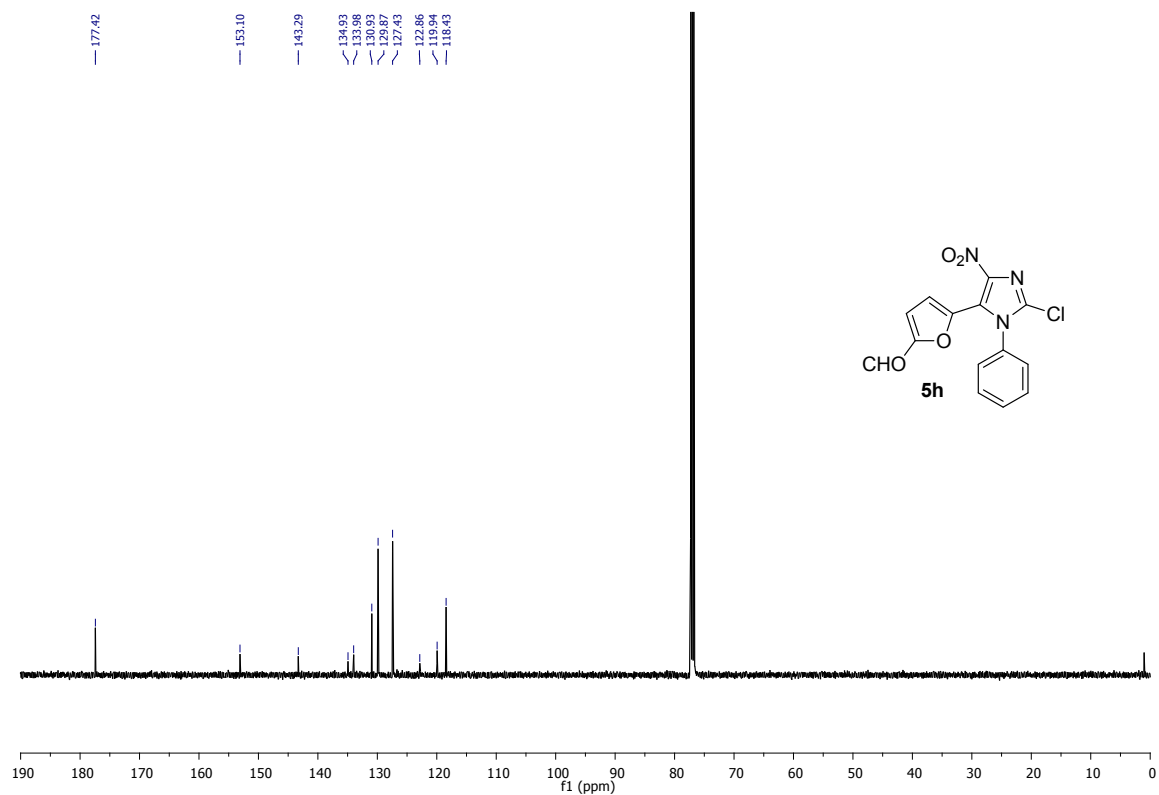
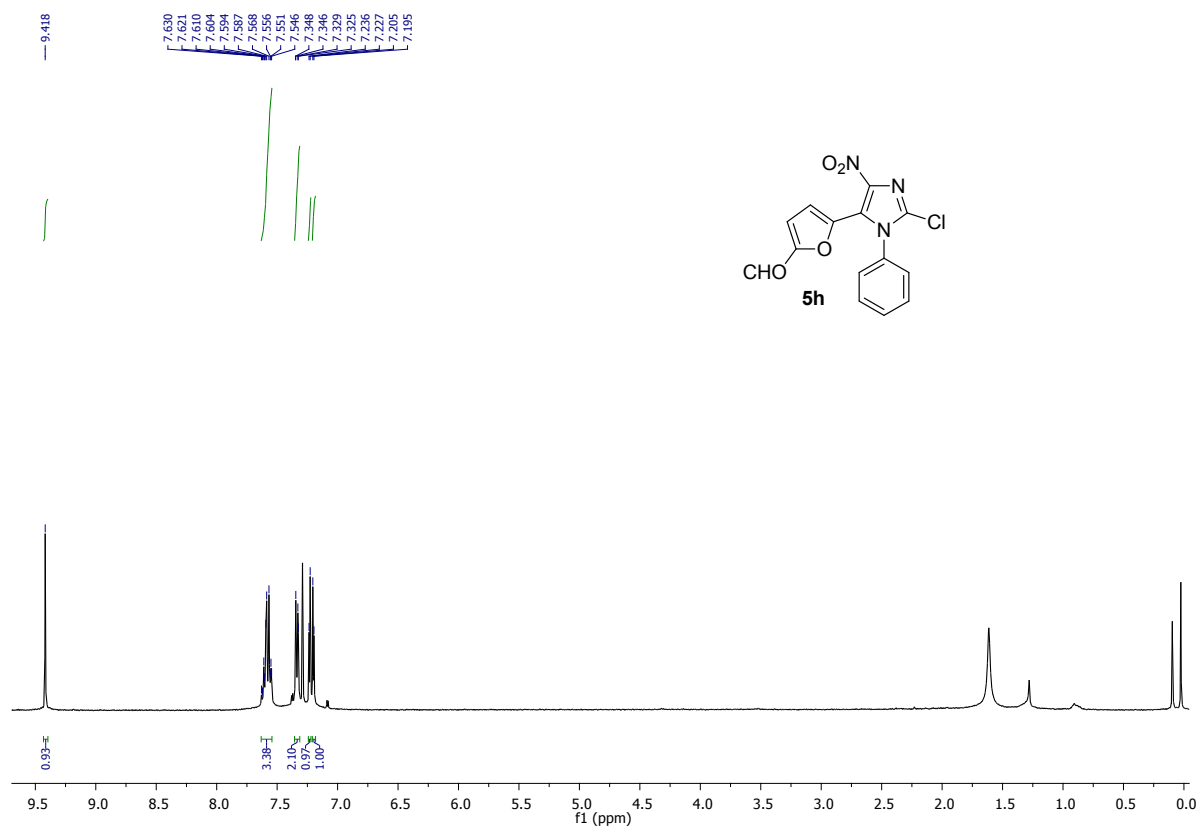




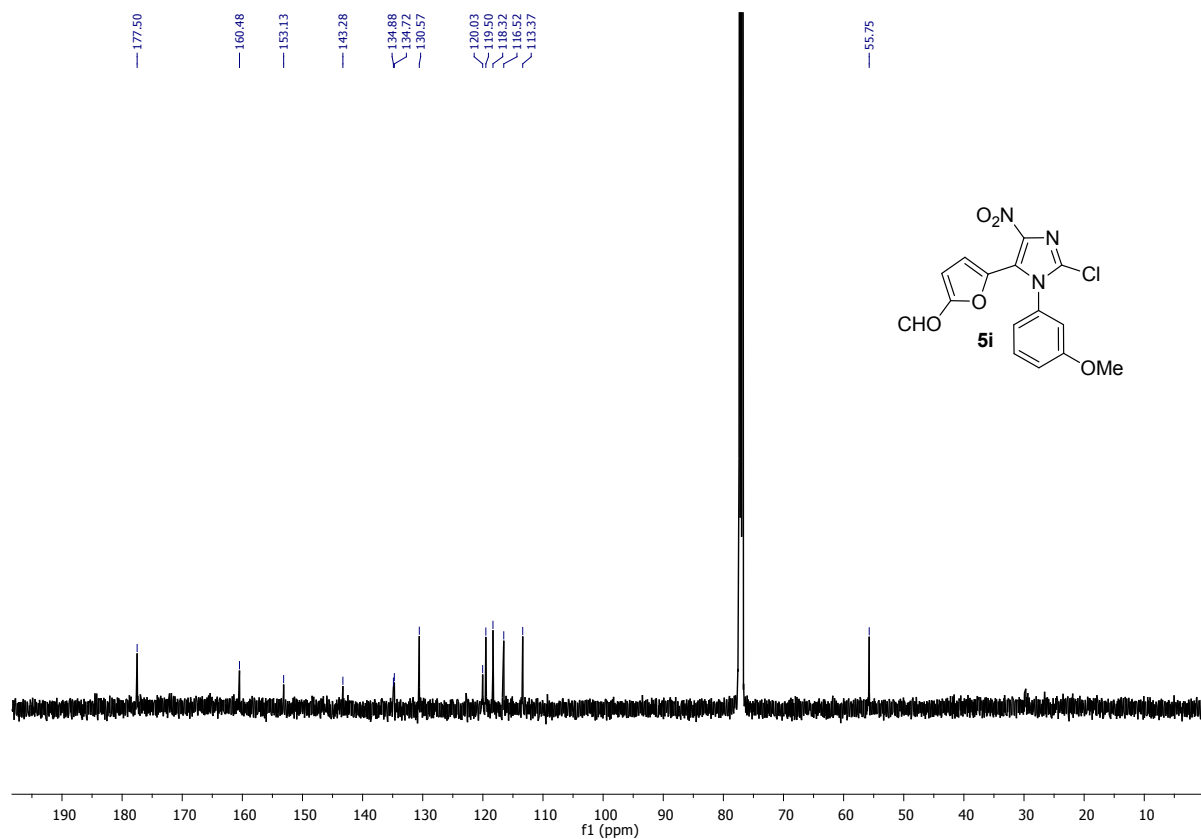
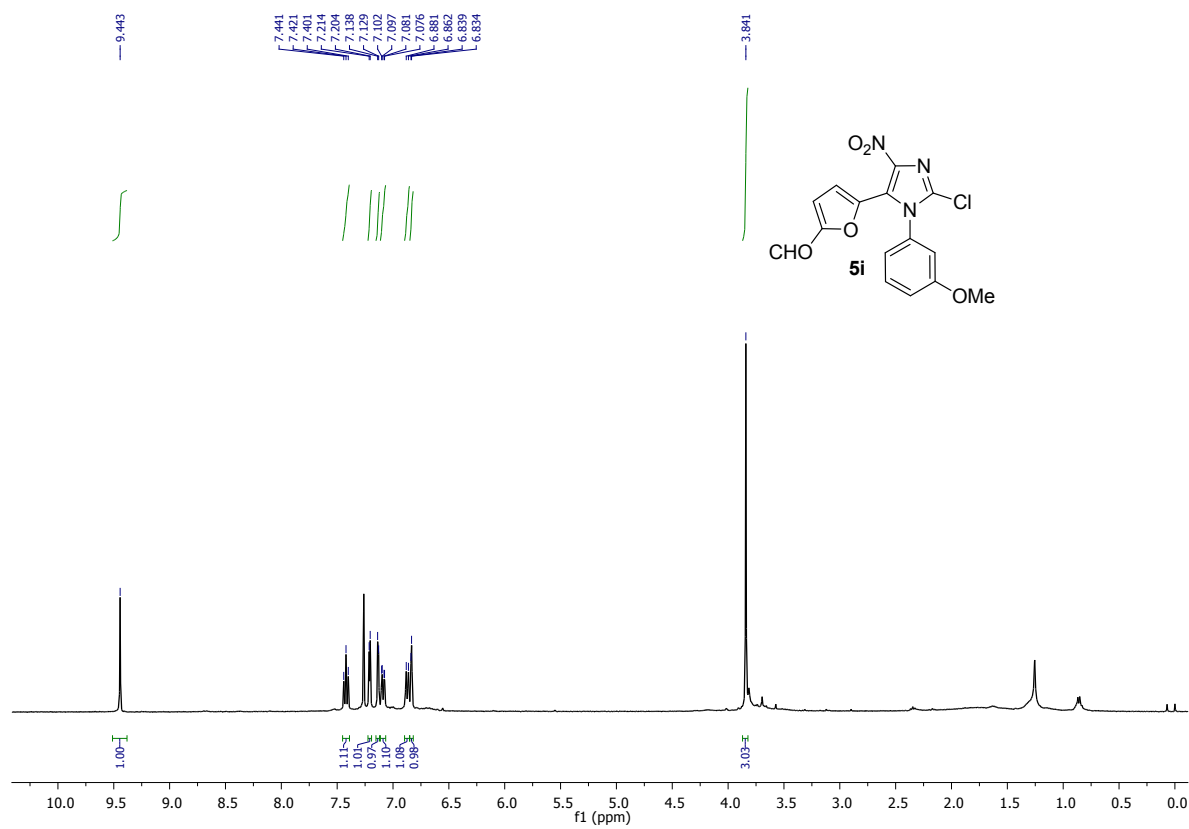
5-(2-Chloro-4-nitro-1-phenyl-1*H*-imidazol-5-yl)-1-methyl-1*H*-pyrrole-2-carbaldehyde (5g):



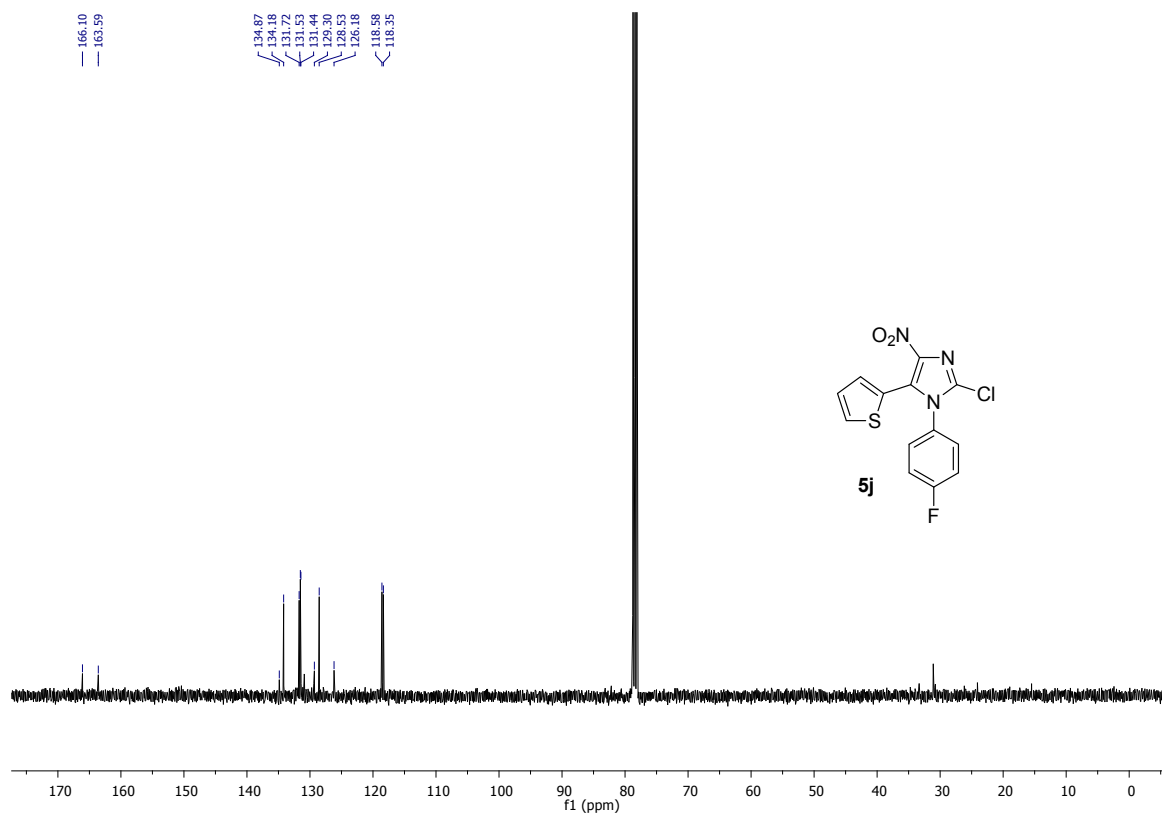
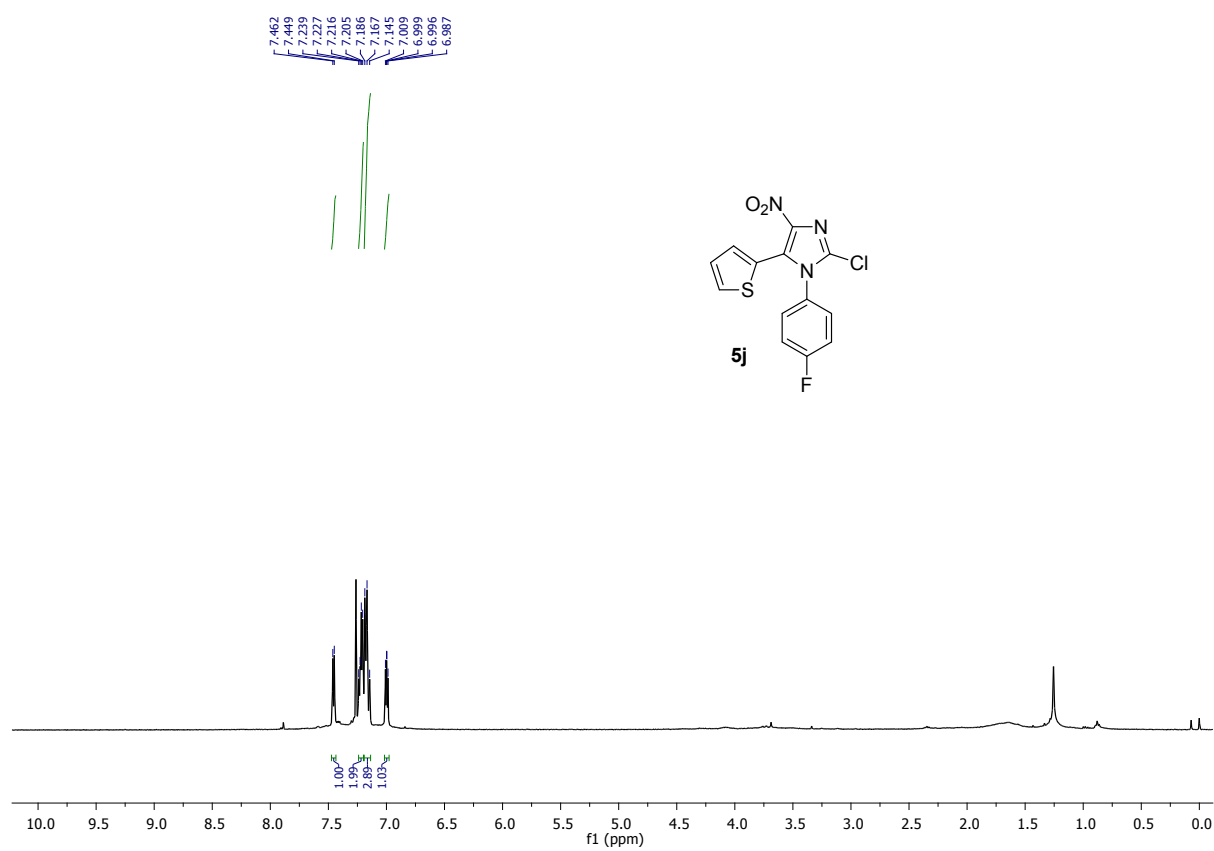
5-(2-Chloro-4-nitro-1-phenyl-1*H*-imidazol-5-yl)furan-2-carbaldehyde (5h):

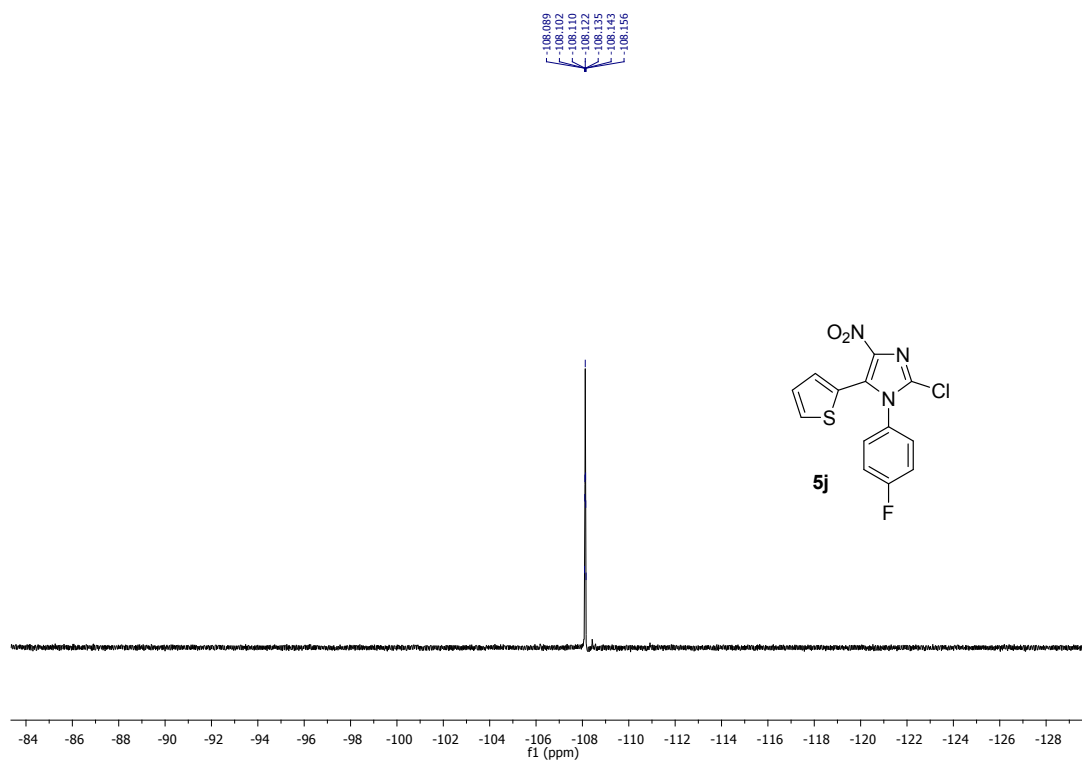


5-(2-Chloro-1-(3-methoxyphenyl)-4-nitro-1H-imidazol-5-yl)furan-2-carbaldehyde (5i):

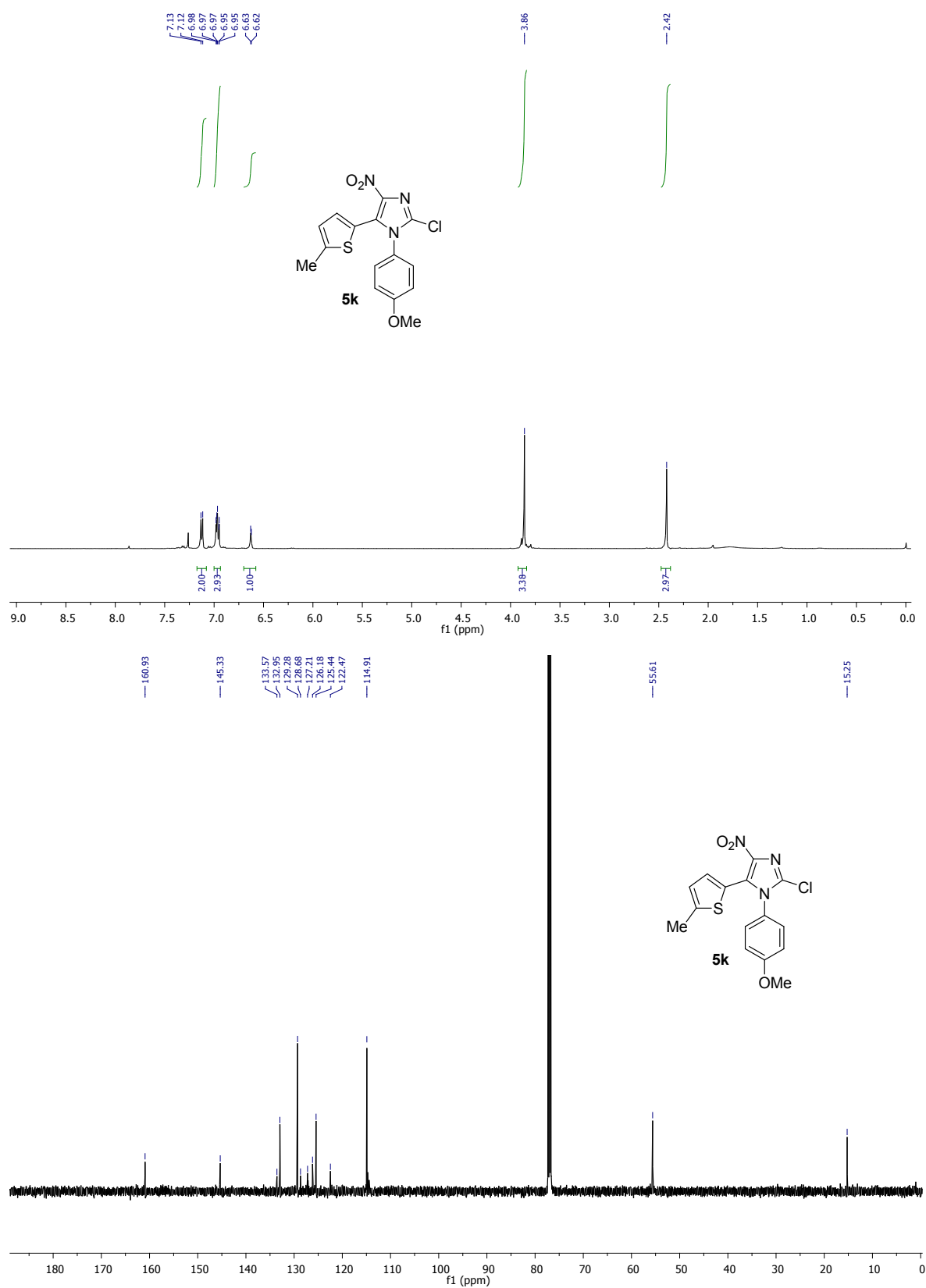


2-Chloro-1-(4-fluorophenyl)-4-nitro-5-(thiophen-2-yl)-1*H*-imidazole (5j):

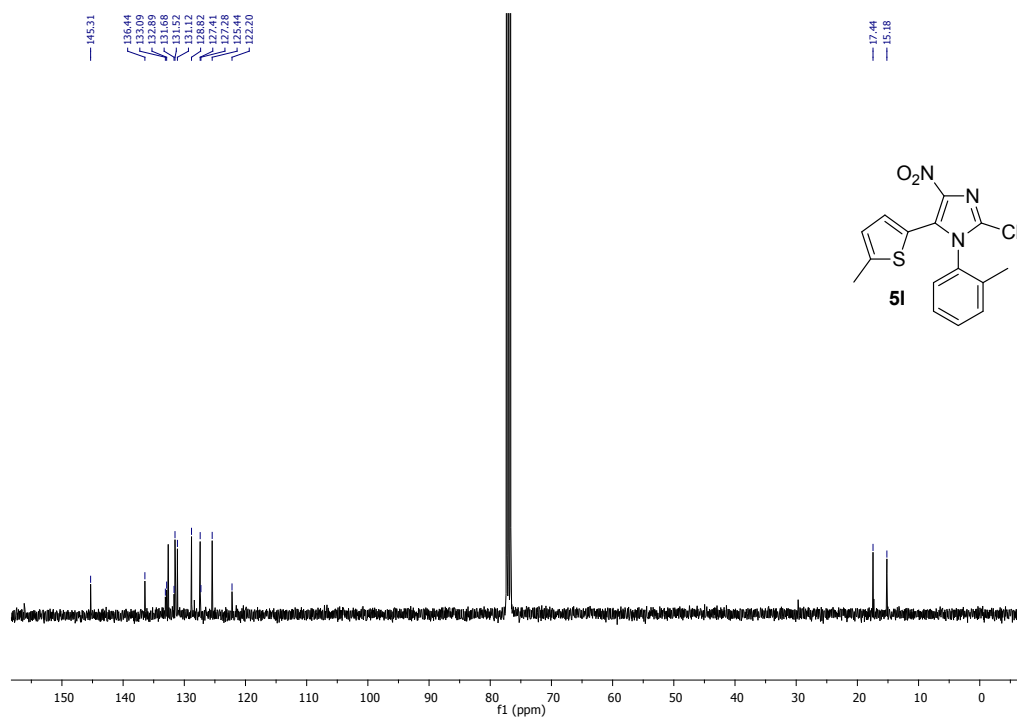
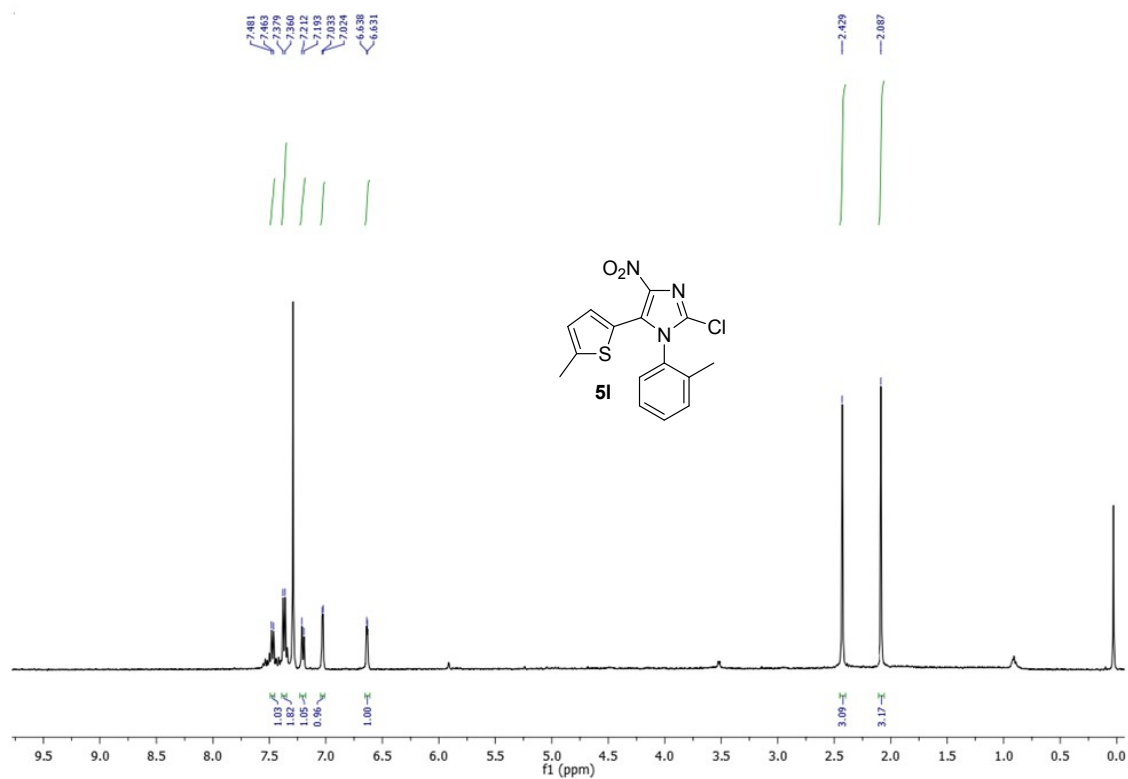




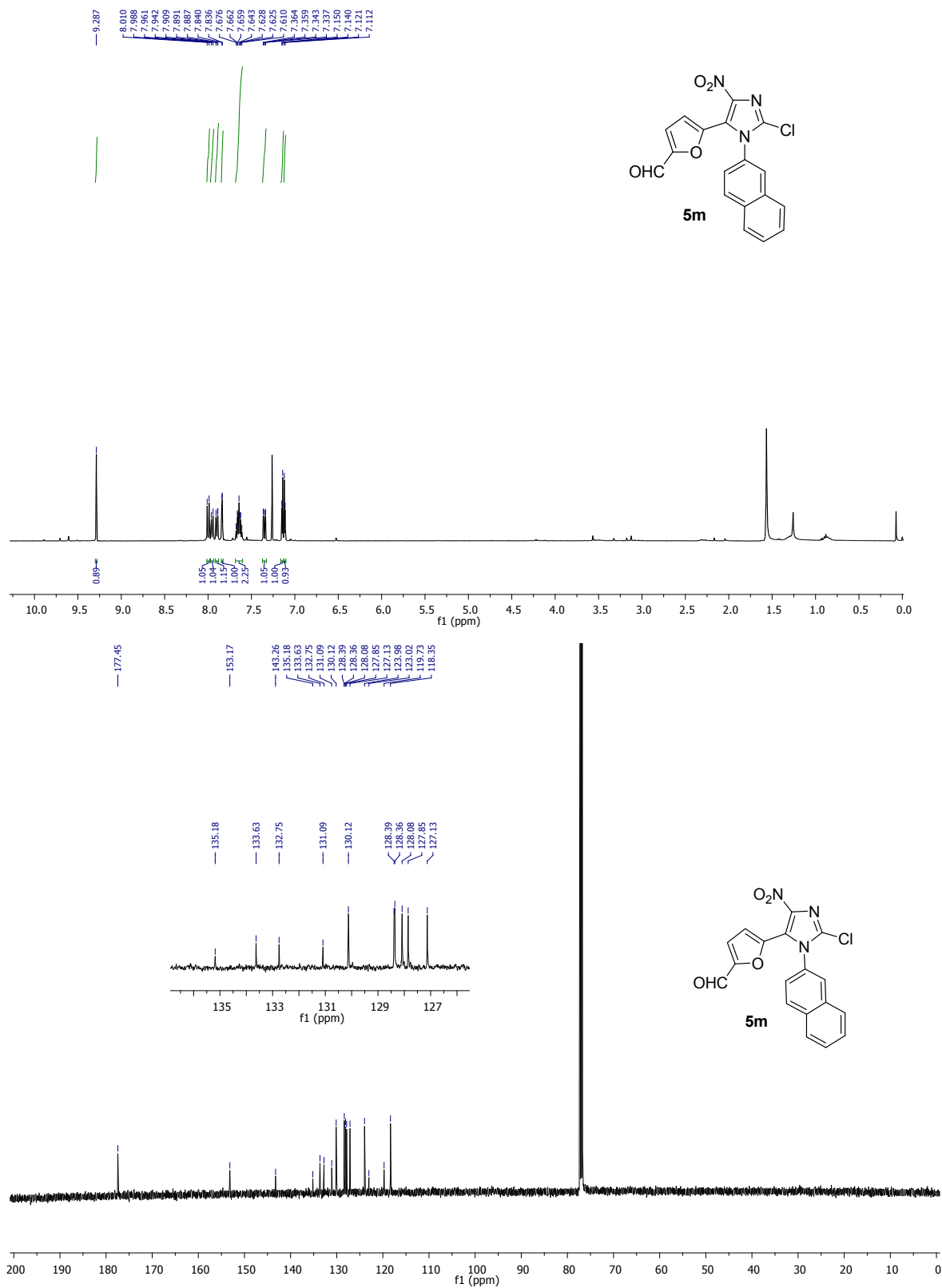
2-Chloro-1-(4-methoxyphenyl)-5-(5-methylthiophen-2-yl)-4-nitro-1*H*-imidazole (5k):



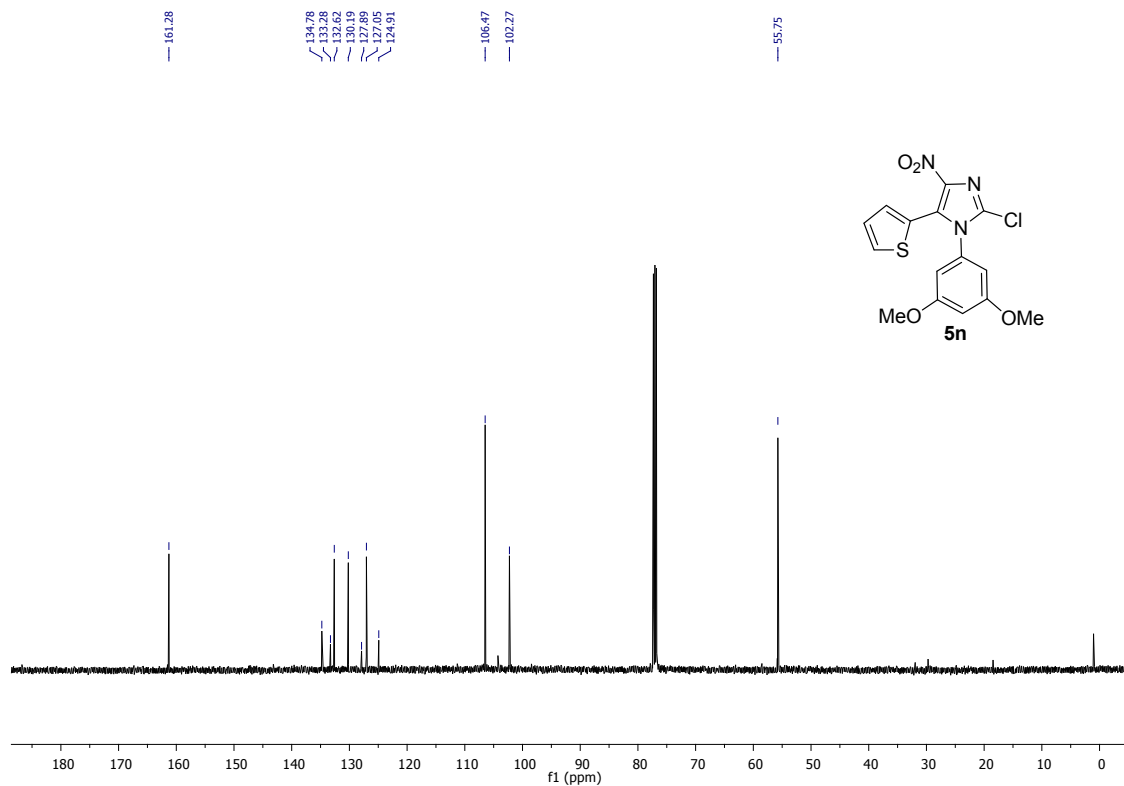
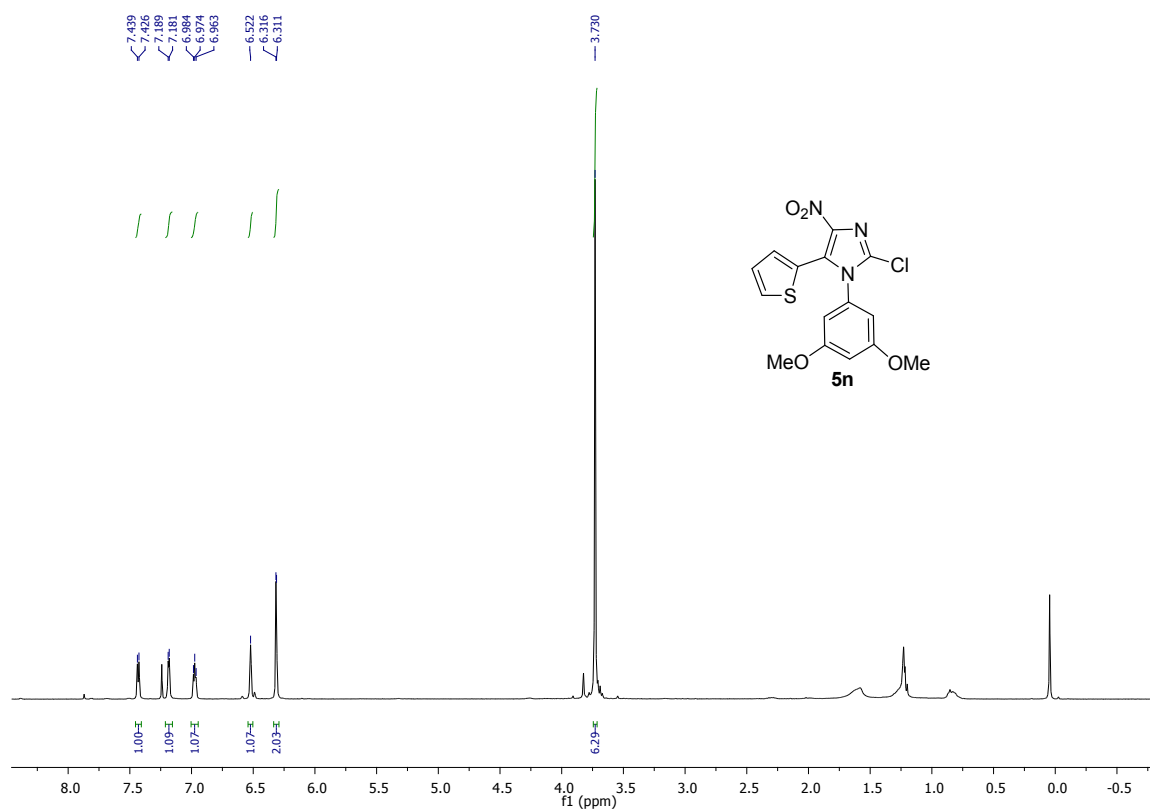
2-Chloro-5-(5-methylthiophen-2-yl)-4-nitro-1-(*o*-tolyl)-1*H*-imidazole (5I):



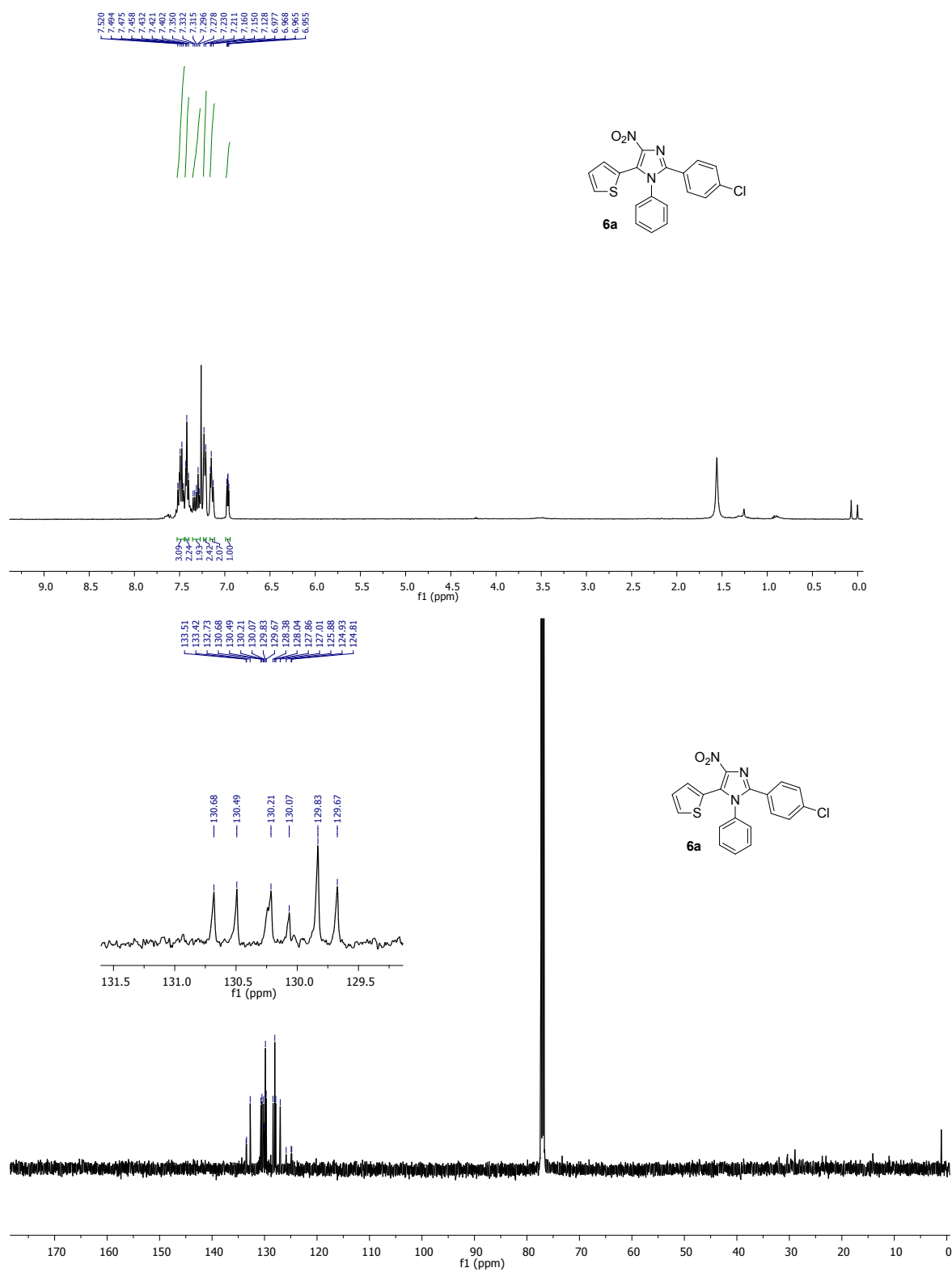
5-(2-Chloro-1-(naphthalen-2-yl)-4-nitro-1H-imidazol-5-yl)furan-2-carbaldehyde (5m):



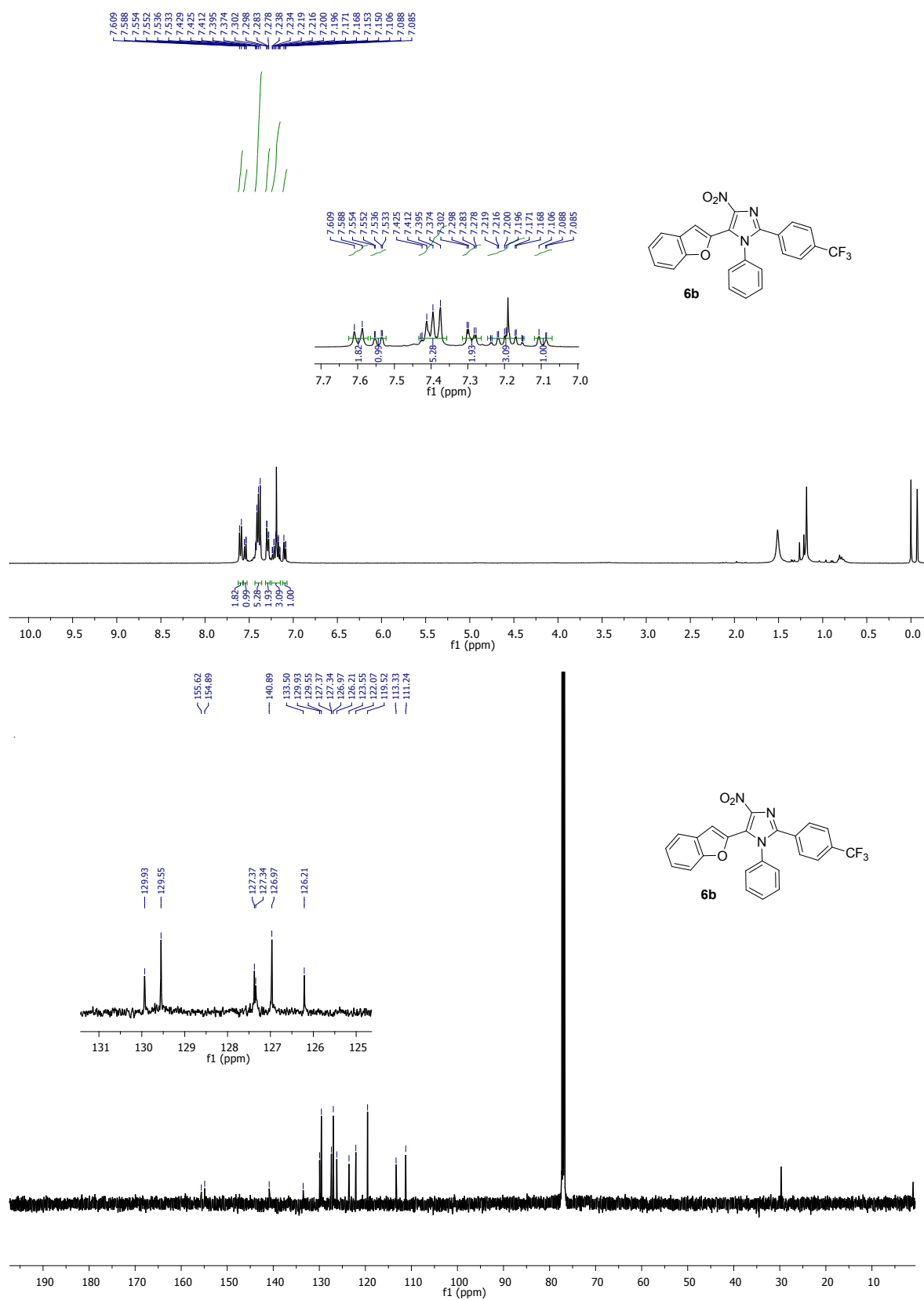
2-Chloro-1-(3,5-dimethoxyphenyl)-4-nitro-5-(thiophen-3-yl)-1H-imidazole (5n):

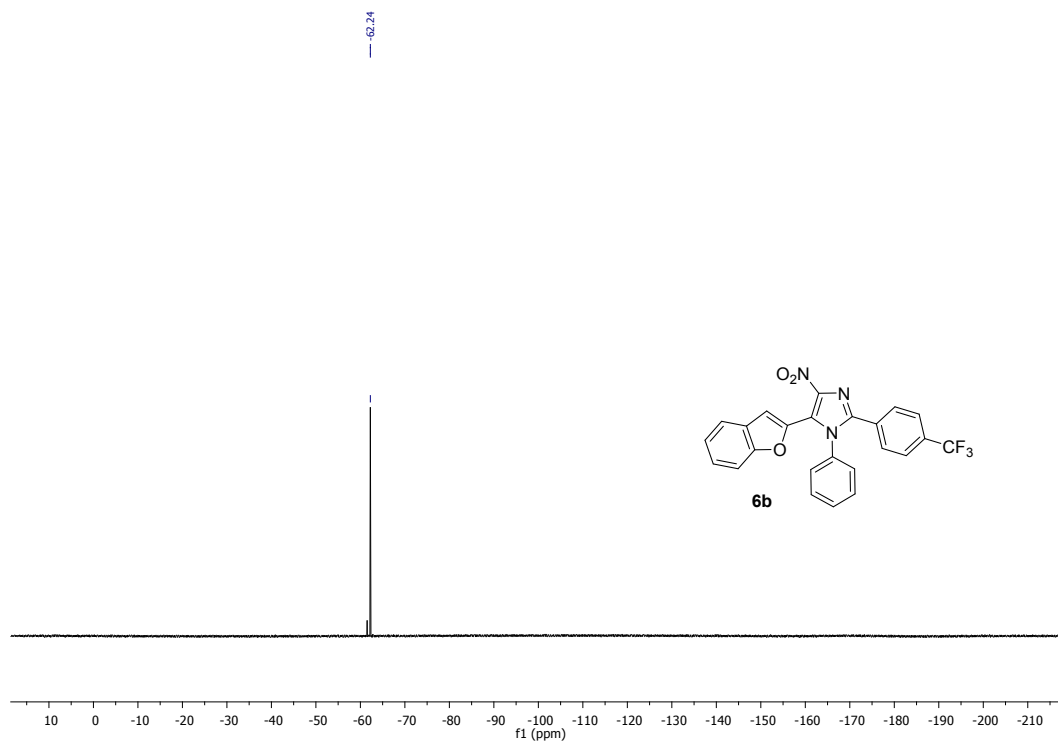


2-(4-Chlorophenyl)-4-nitro-1-phenyl-5-(thiophen-2-yl)-1*H*-imidazole (6a):



5-(Benzofuran-2-yl)-4-nitro-1-phenyl-2-(4-(trifluoromethyl)phenyl)-1*H*-imidazole (6b):





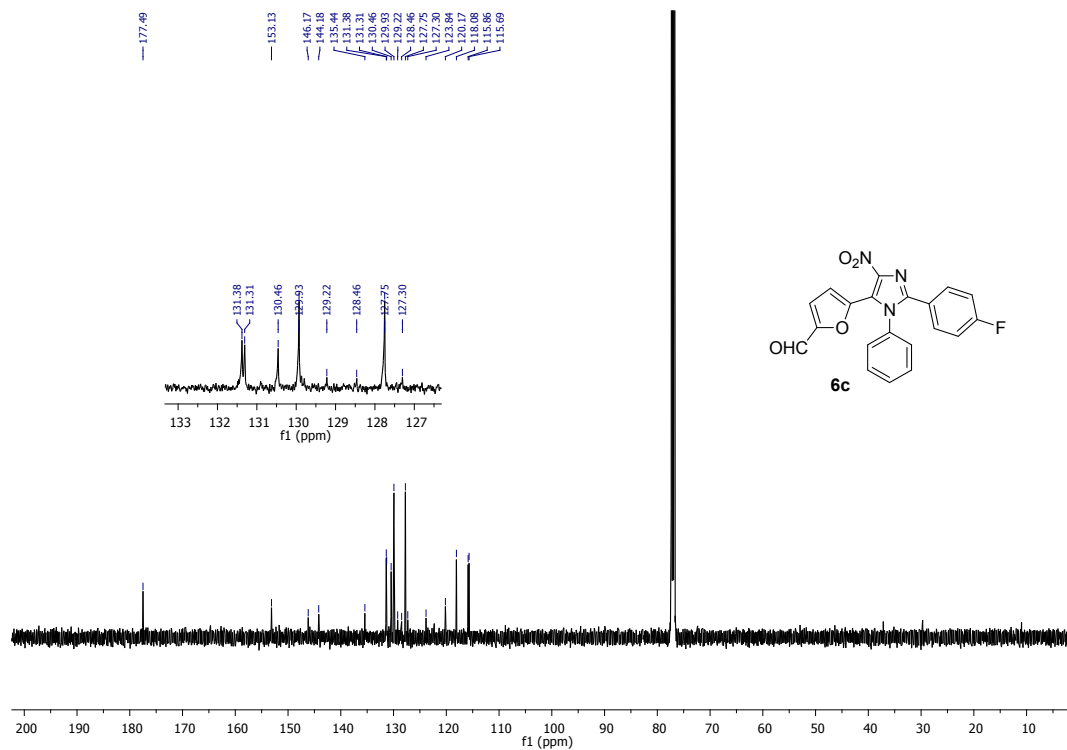
Chemical structure of **6c** is shown in the top right corner. The structure is a benzimidazole derivative with a 4-fluorophenyl group, a phenyl group, and a 2-formyl-5-nitrophenyl group.

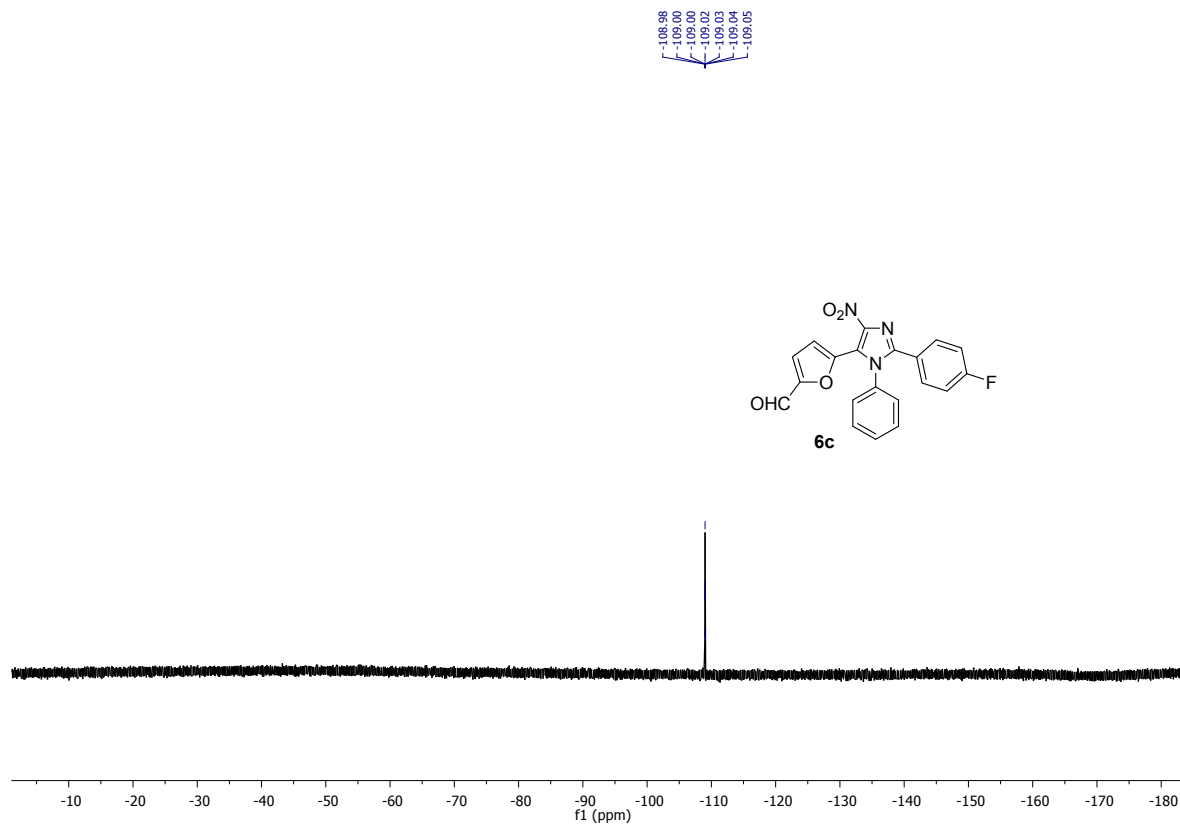
The ¹H NMR spectrum (CDCl₃) shows the following peaks (ppm):

- 9.44 (s, 1H, formyl proton)
- 7.53, 7.51, 7.49, 7.45, 7.43, 7.42, 7.41, 7.40, 7.24, 7.21, 7.18, 7.20, 7.04, 6.99, 6.95 (aromatic protons, 10H total)
- 7.24, 7.21, 7.20 (aromatic protons, 3H total)
- 7.05, 7.04, 6.99, 6.95 (aromatic protons, 4H total)
- 1.00 (s, 3H, methyl protons)
- 0.93 (s, 3H, methyl protons)
- 0.83 (s, 3H, methyl protons)
- 2.12 (s, 3H, methyl protons)

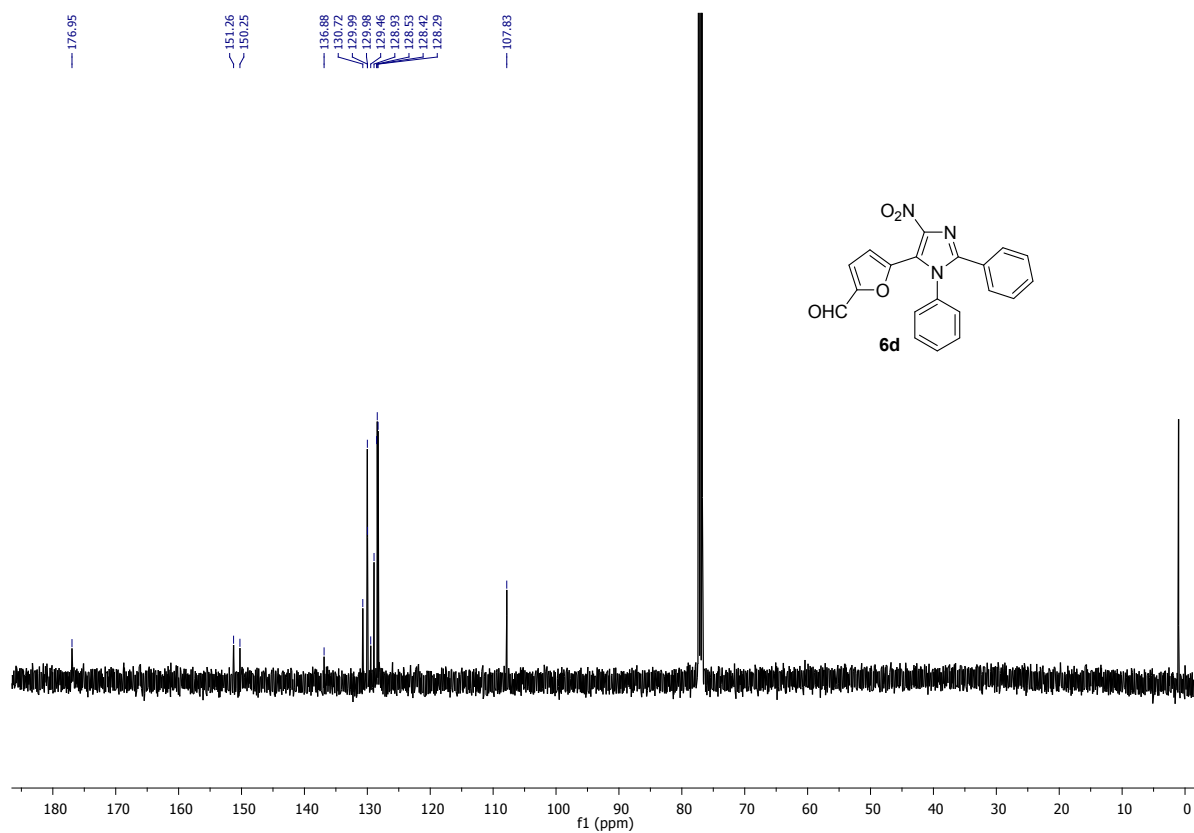
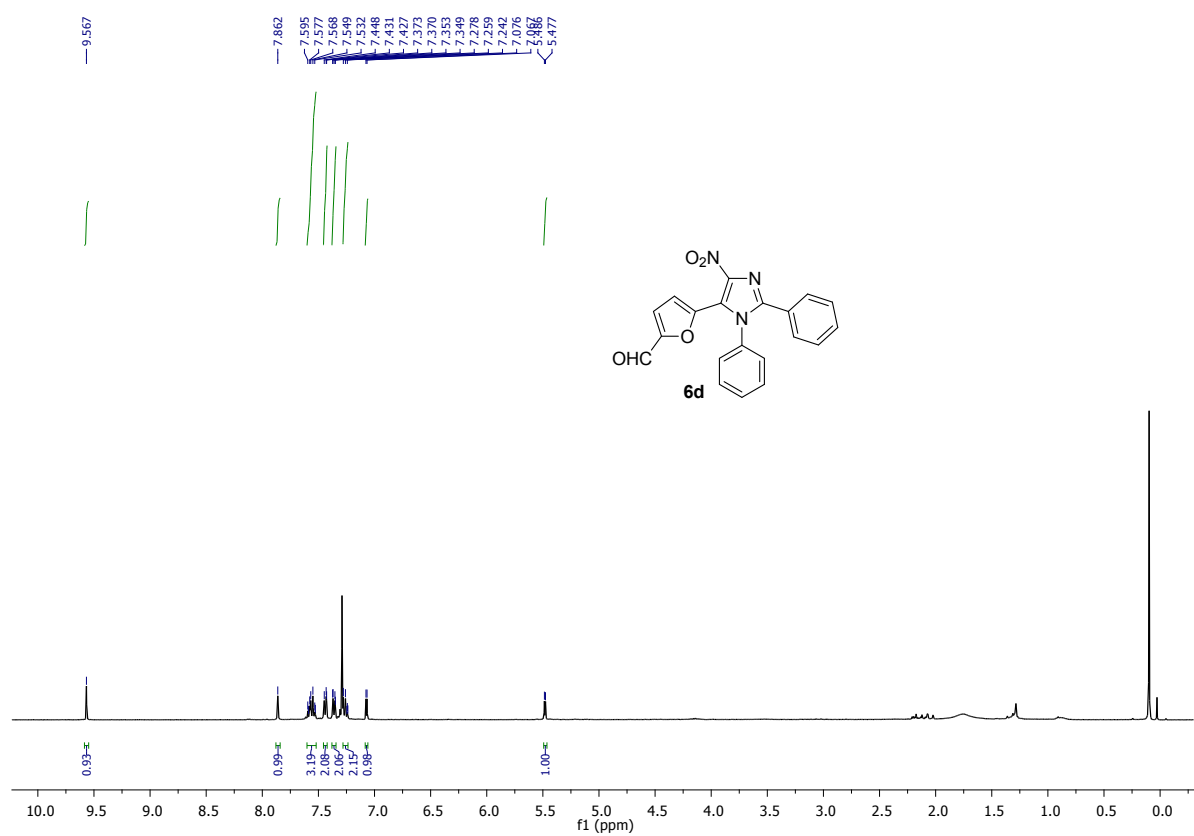
The inset spectrum shows the aromatic region (6.8-7.8 ppm) with the following peaks (ppm):

- 7.53, 7.51, 7.49, 7.45, 7.43, 7.42, 7.41, 7.40, 7.24, 7.21, 7.20, 7.05, 7.04, 6.99, 6.95

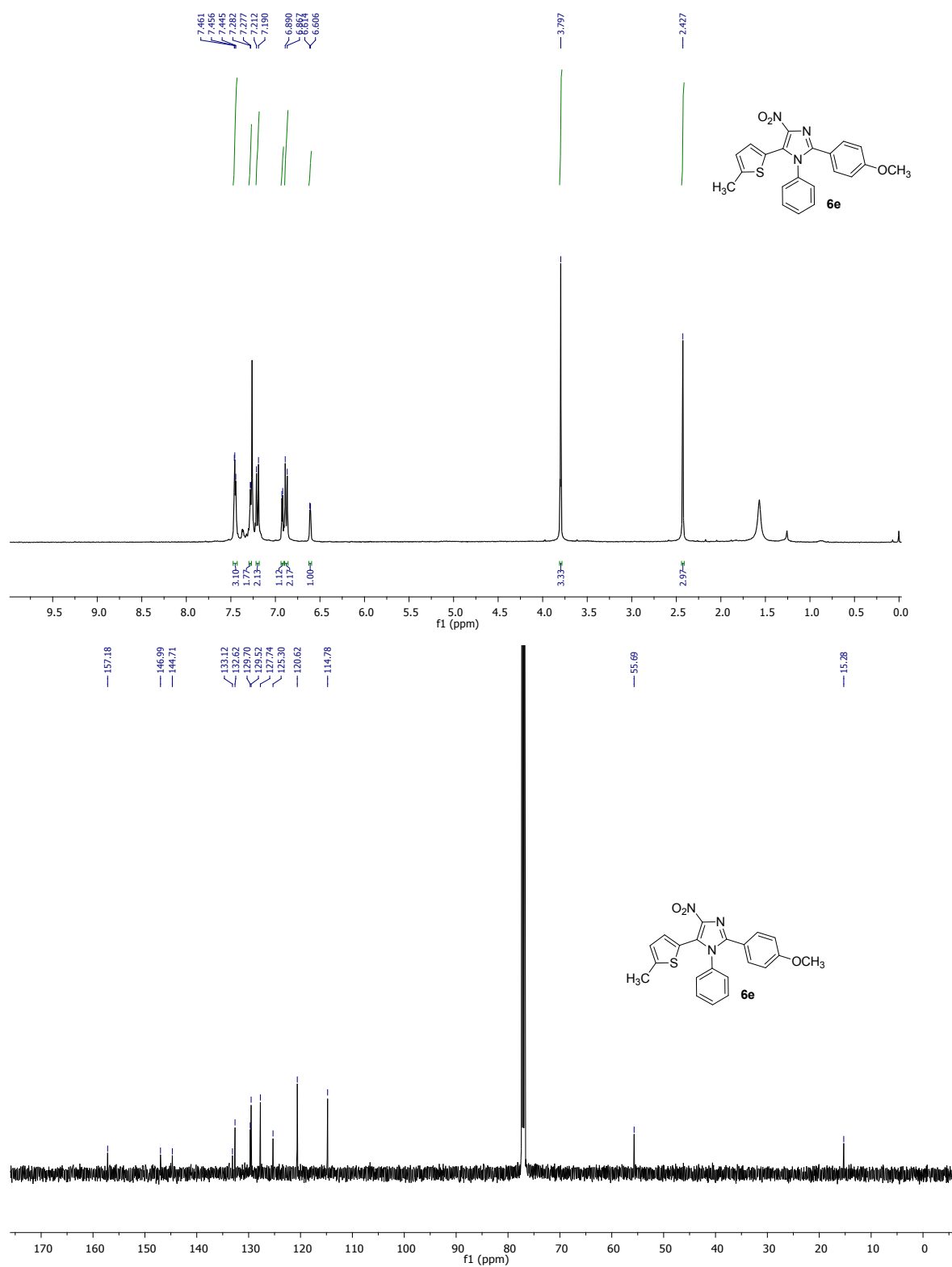




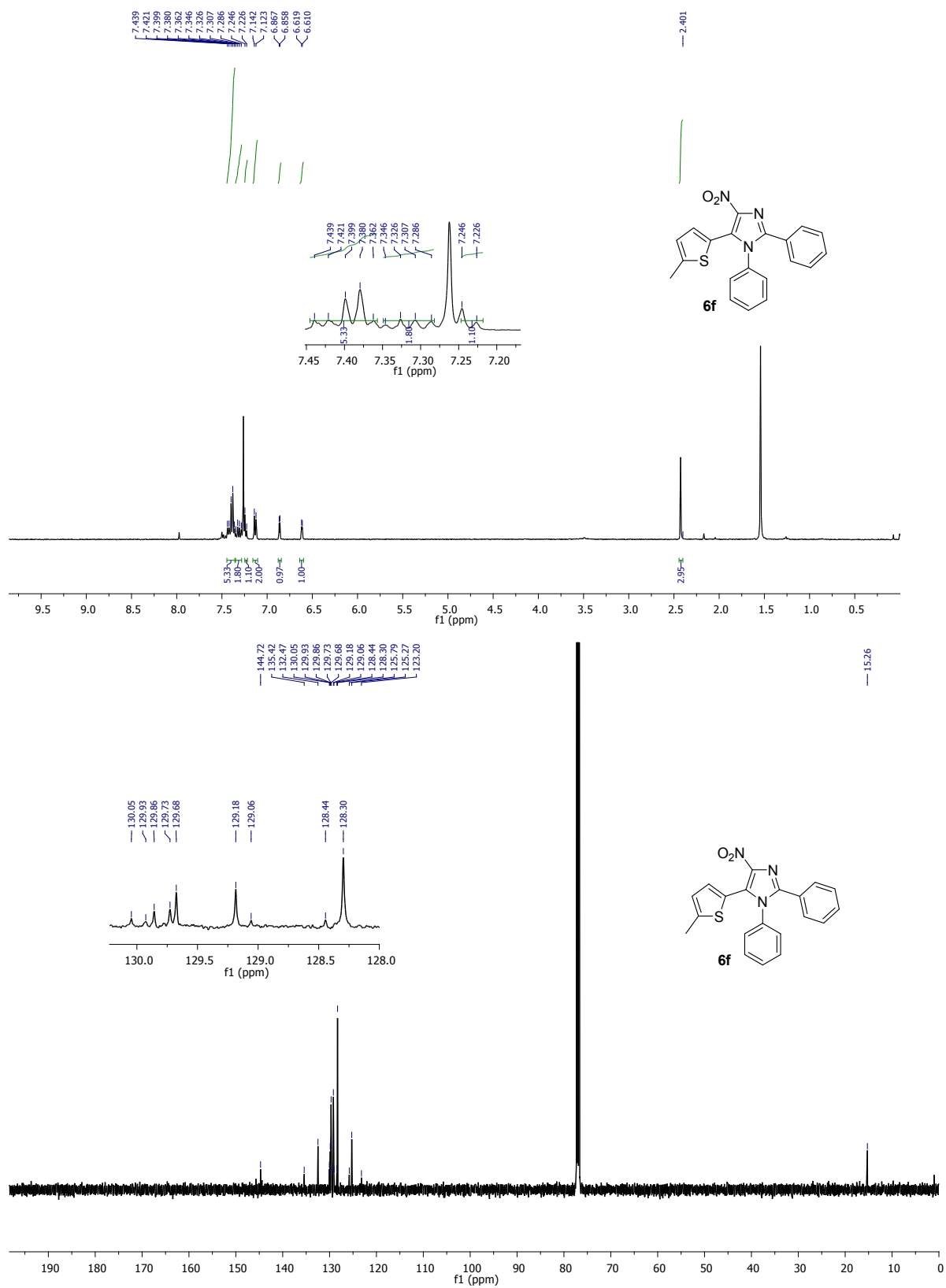
5-(4-Nitro-1,2-diphenyl-1*H*-imidazol-5-yl)furan-2-carbaldehyde (6d):



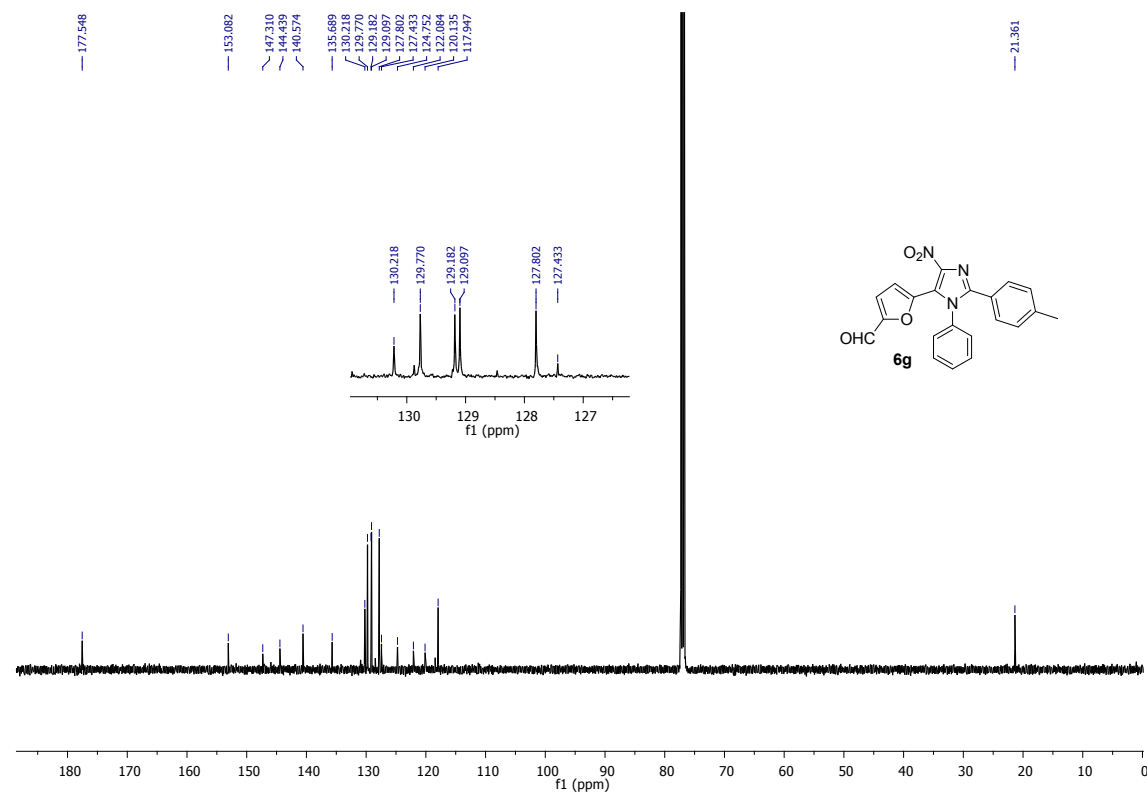
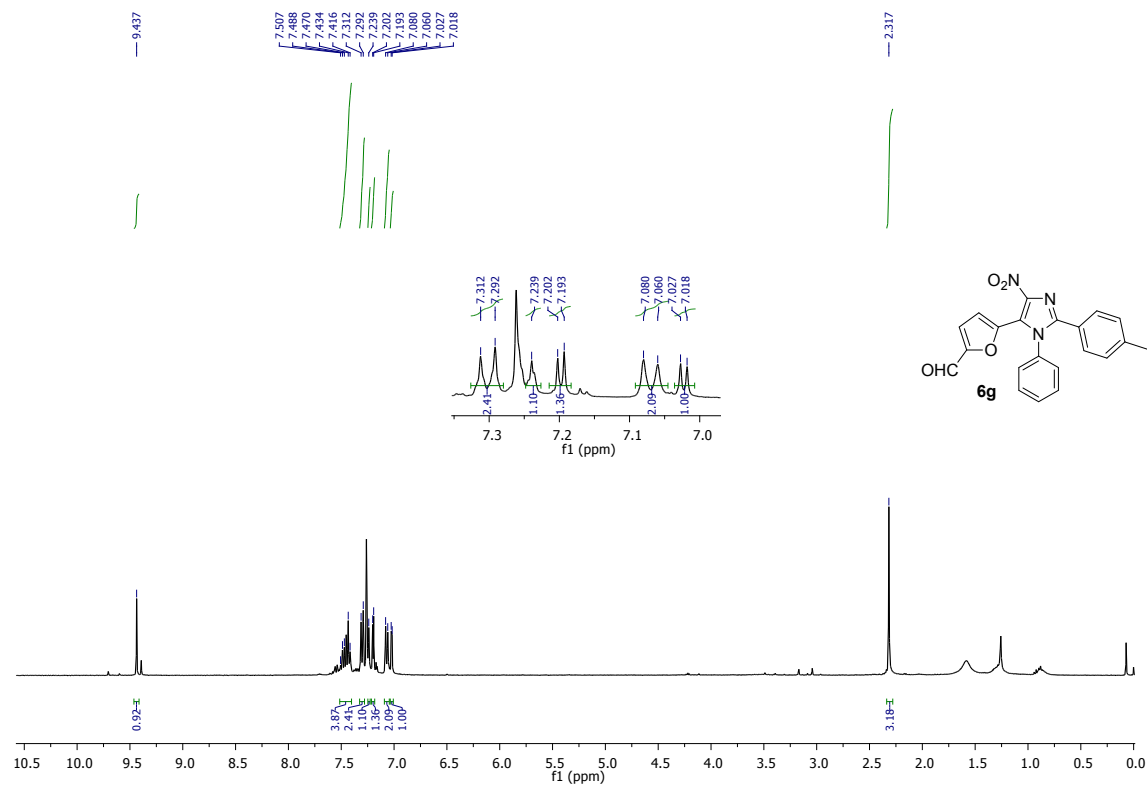
2-(4-Methoxyphenyl)-5-(5-methylthiophen-2-yl)-4-nitro-1-phenyl-1*H*-imidazole (6e):



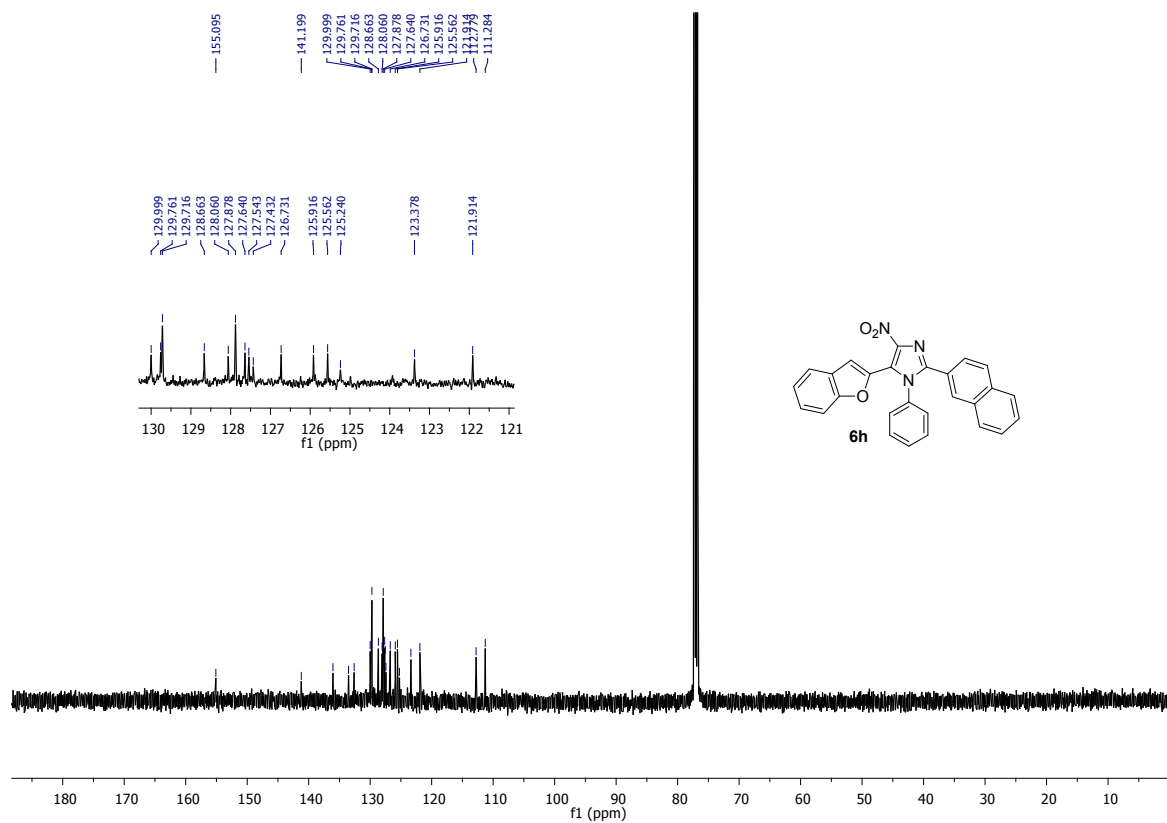
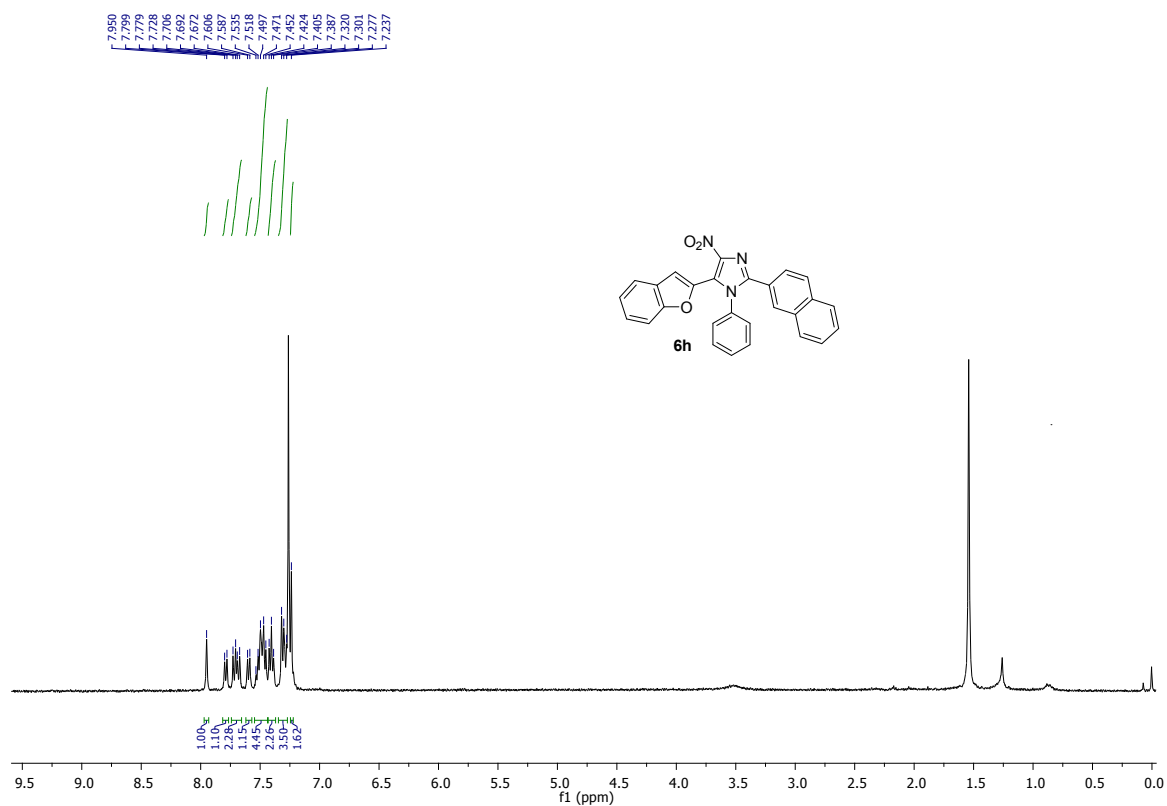
5-(5-Methylthiophen-2-yl)-4-nitro-1,2-diphenyl-1*H*-imidazole (6f):



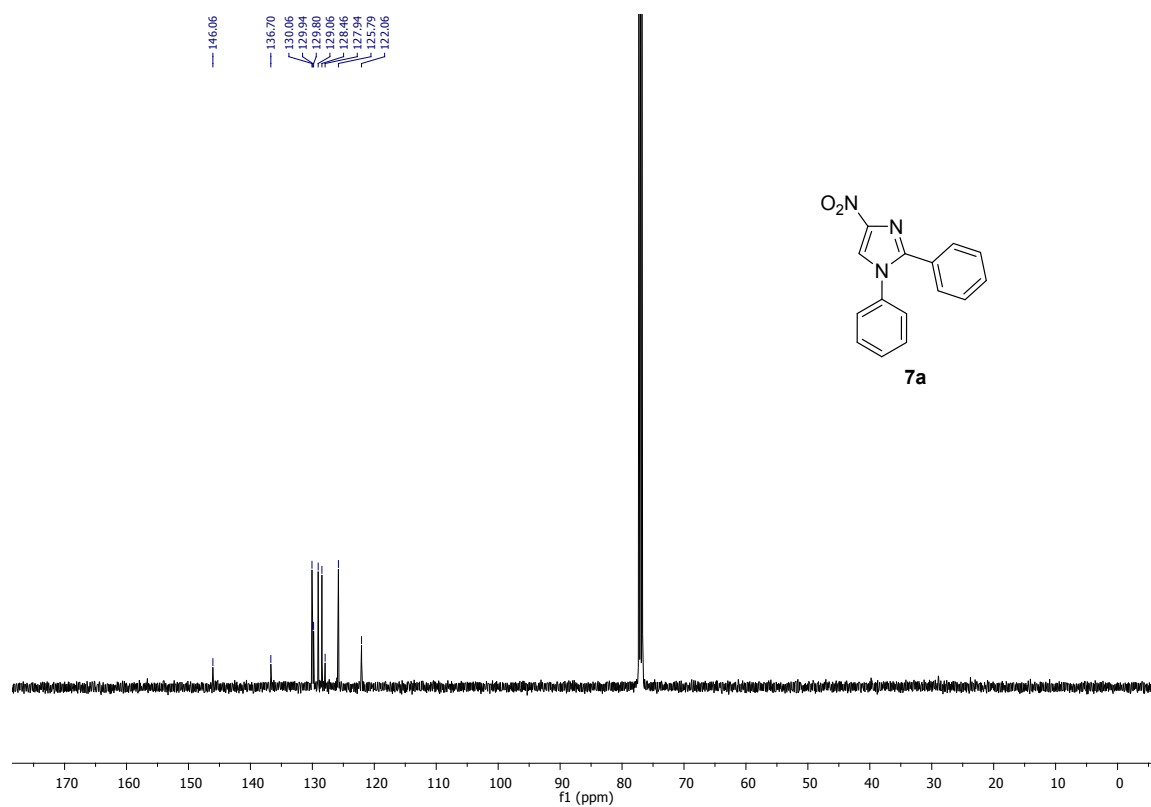
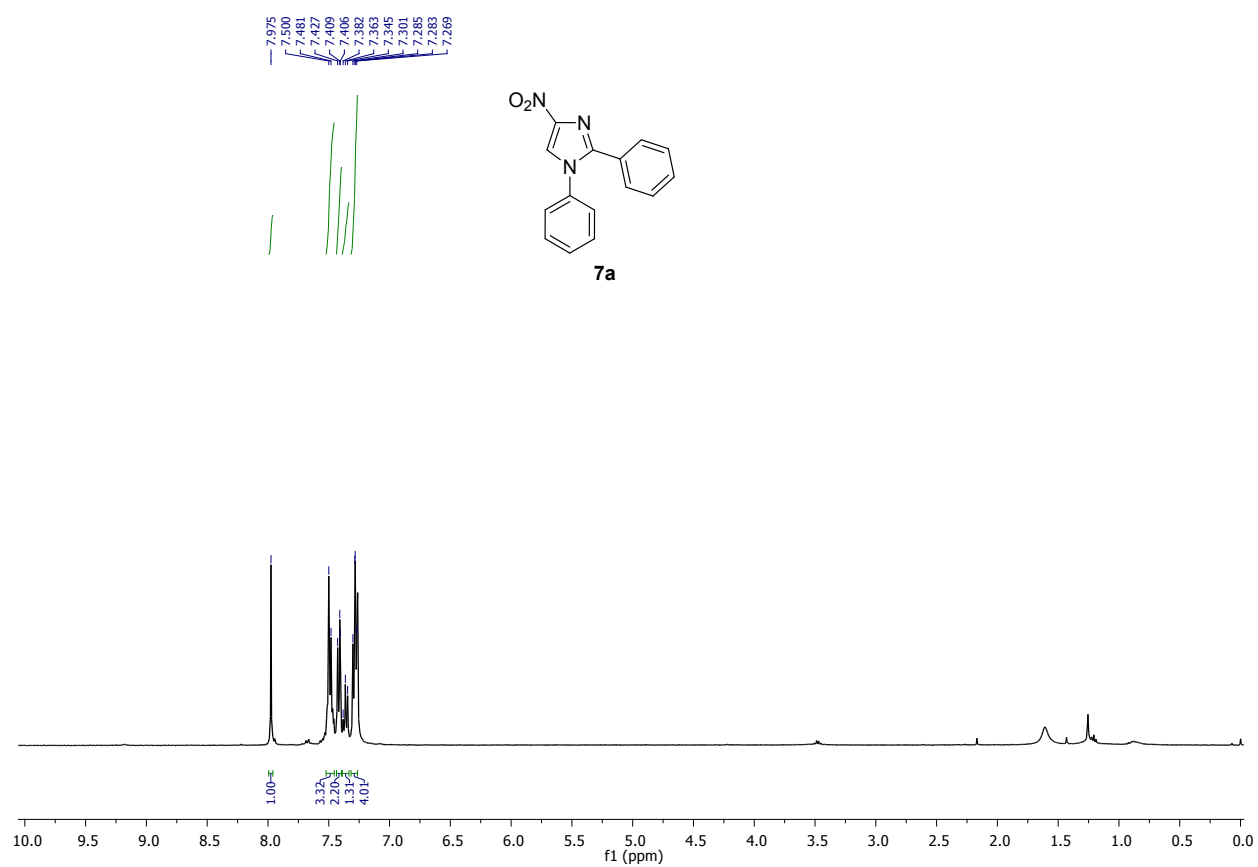
5-(4-5-(4-Nitro-1-phenyl-2-(*p*-tolyl)-1*H*-imidazol-5-yl)furan-2-carbaldehyde (6g):



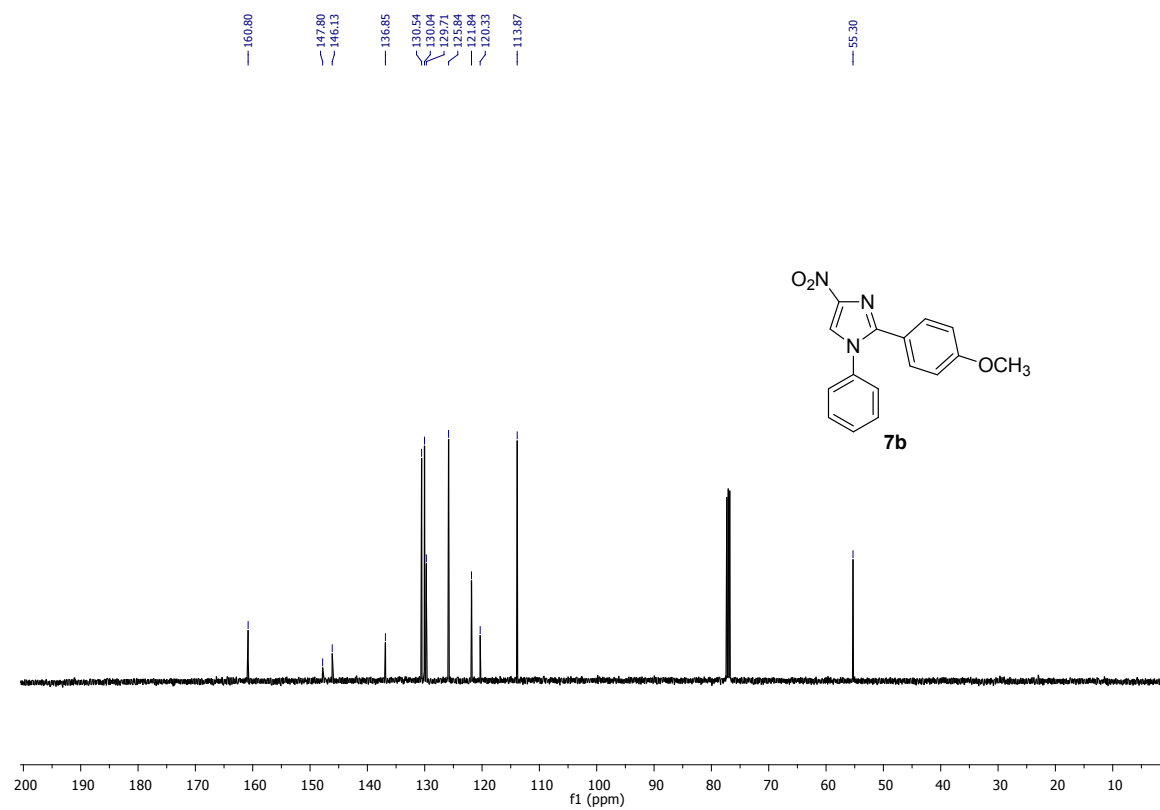
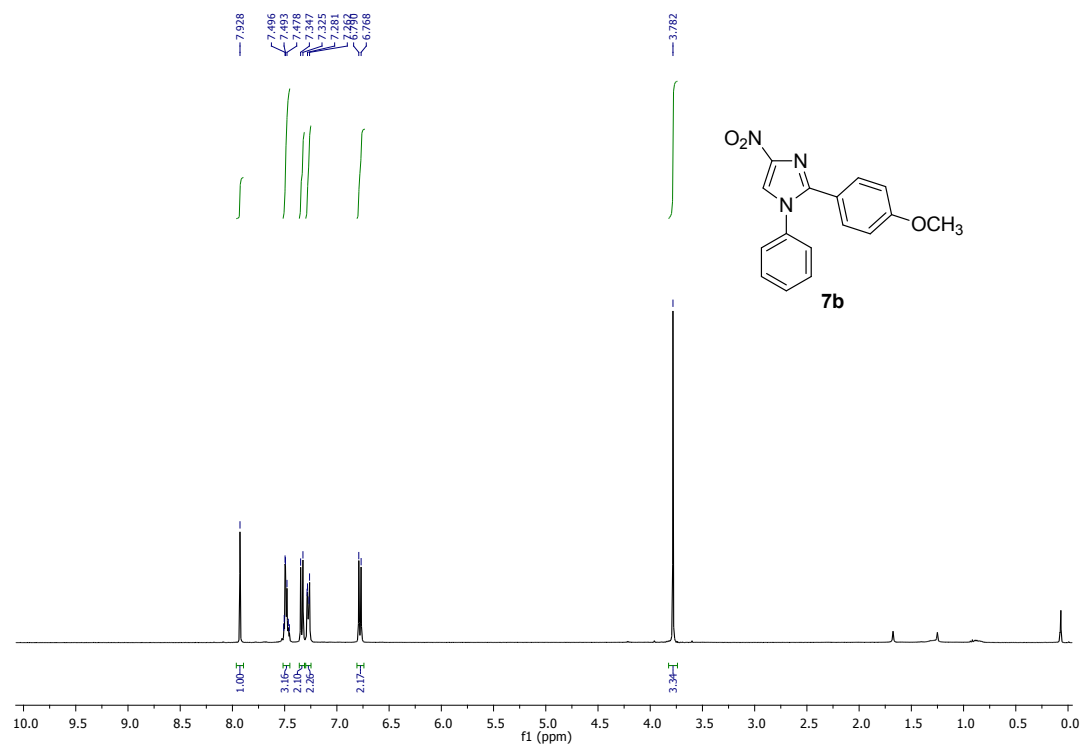
5-(Benzofuran-2-yl)-2-(naphthalen-2-yl)-4-nitro-1-phenyl-1H-imidazole (6h):



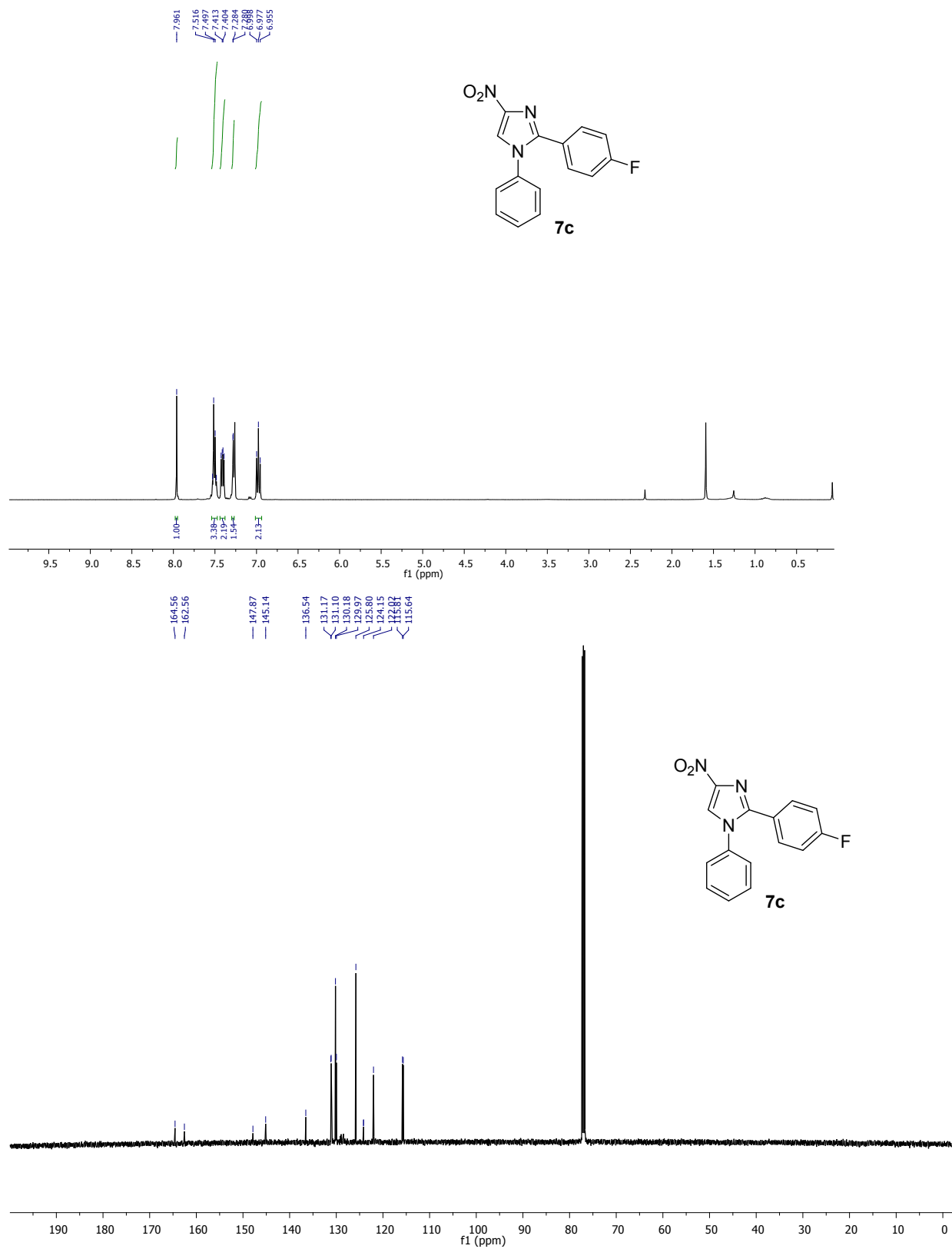
4-Nitro-1,2-diphenyl-1*H*-imidazole (7a):

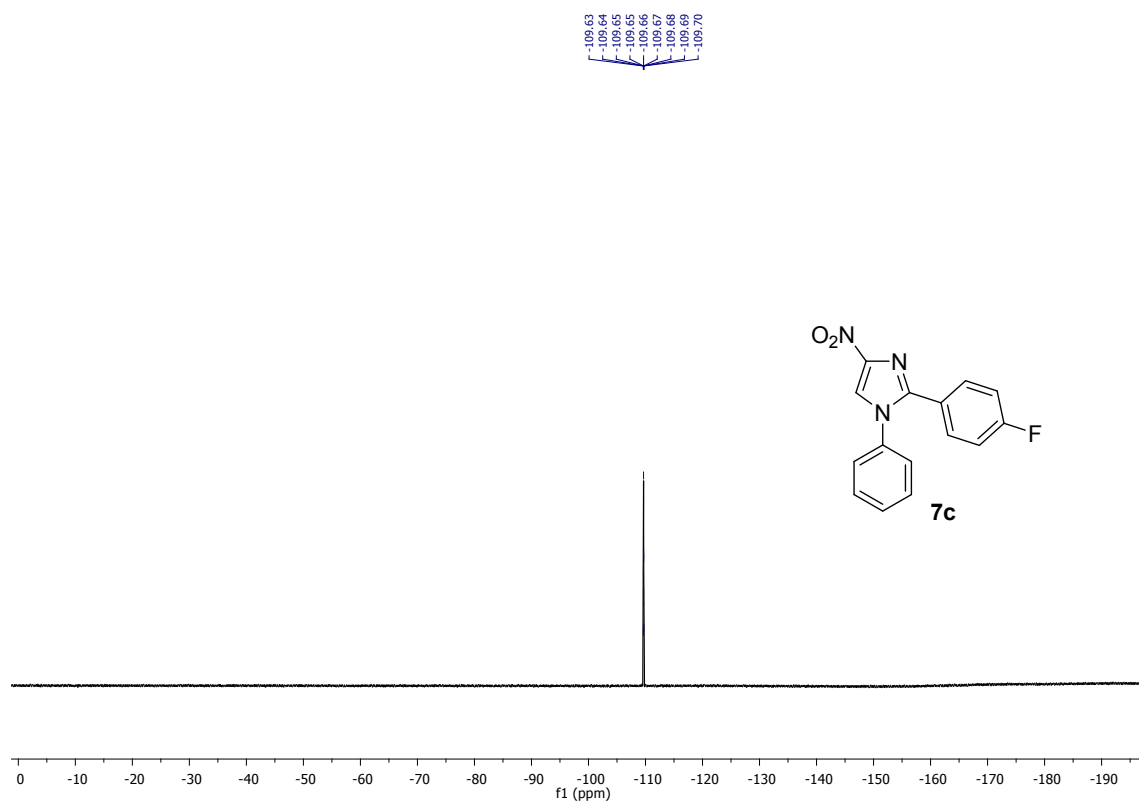


2-(4-Methoxyphenyl)-4-nitro-1-phenyl-1H-imidazole (7b):

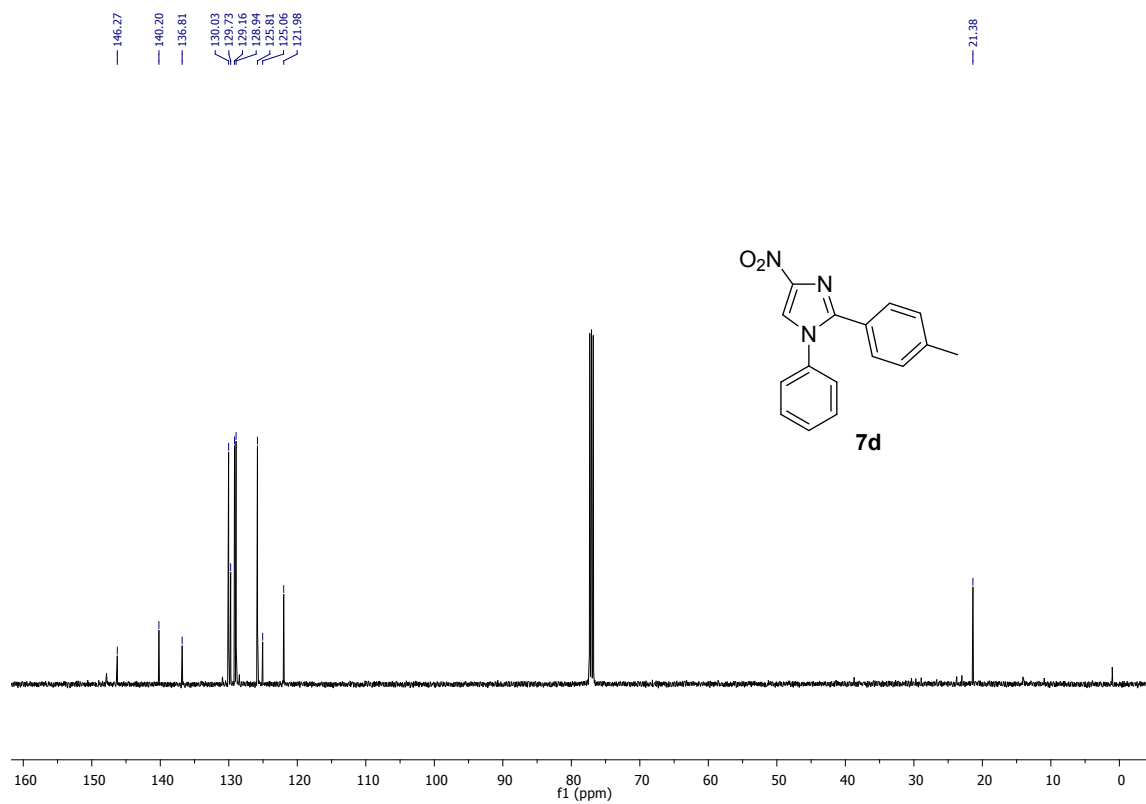
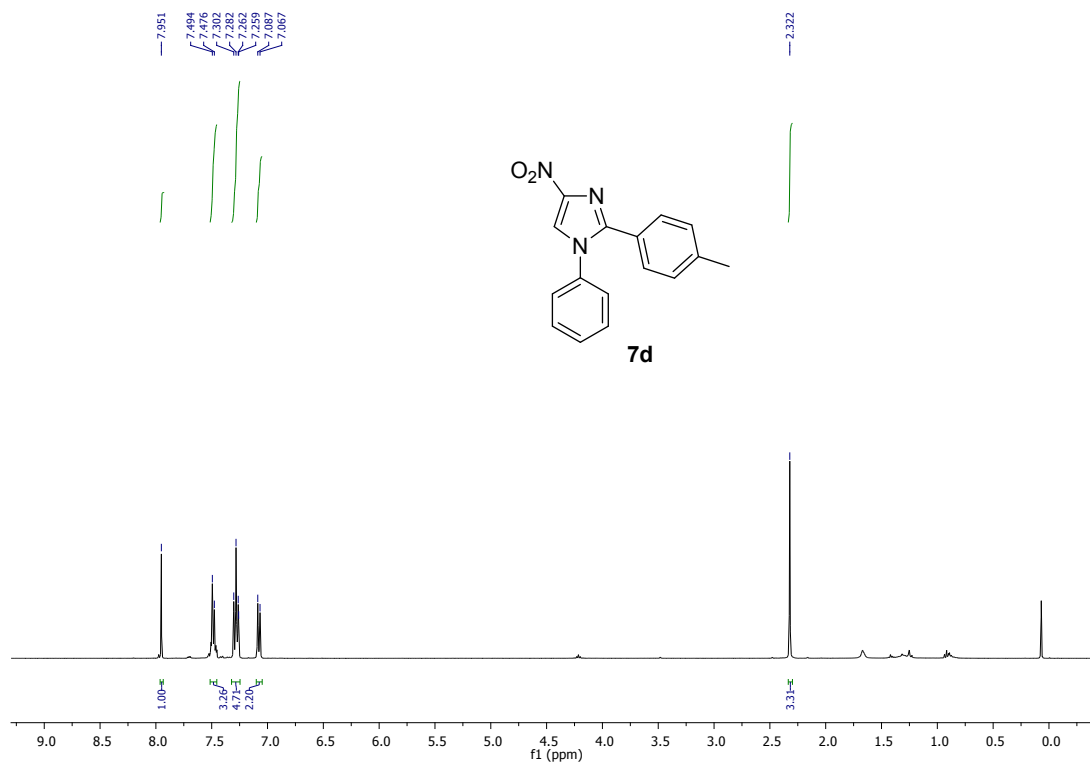


2-(4-Fluorophenyl)-4-nitro-1-phenyl-1*H*-imidazole (7c):

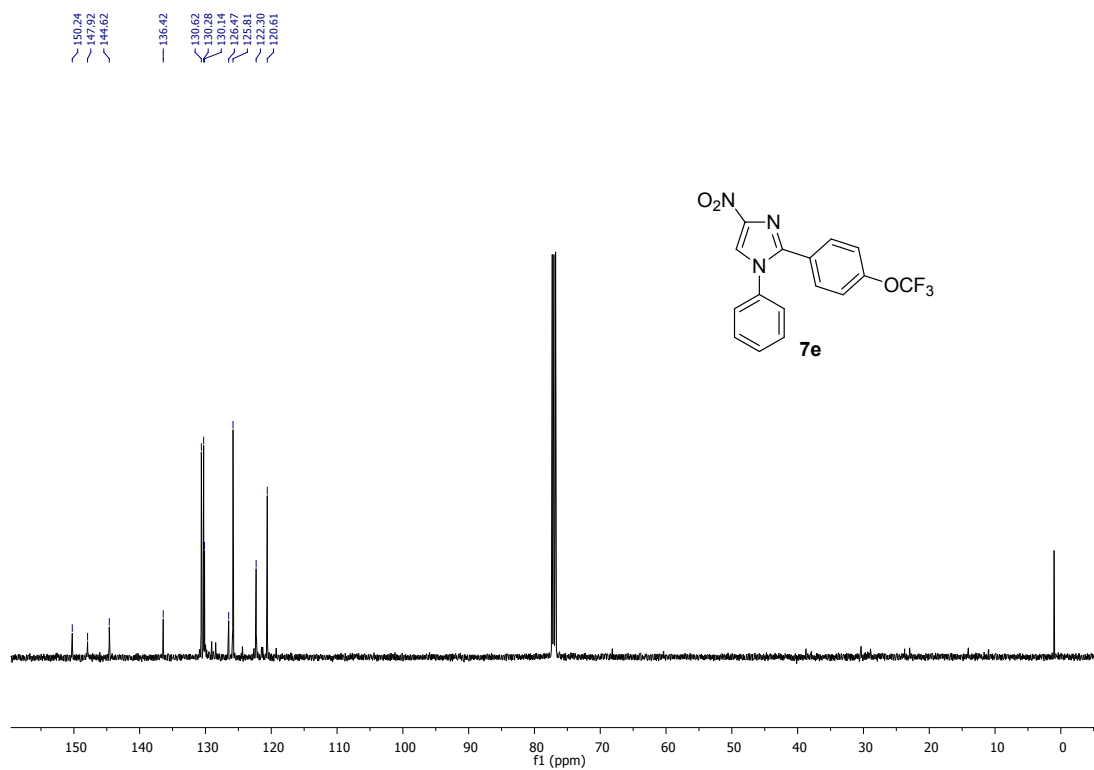
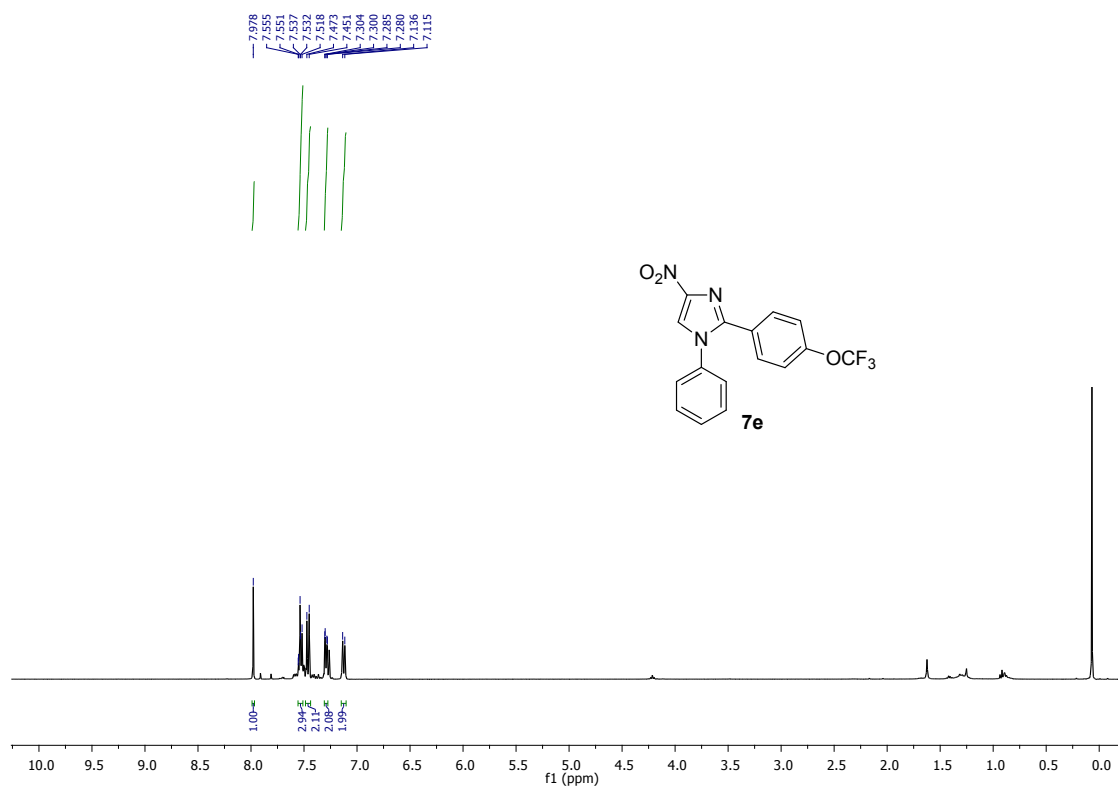


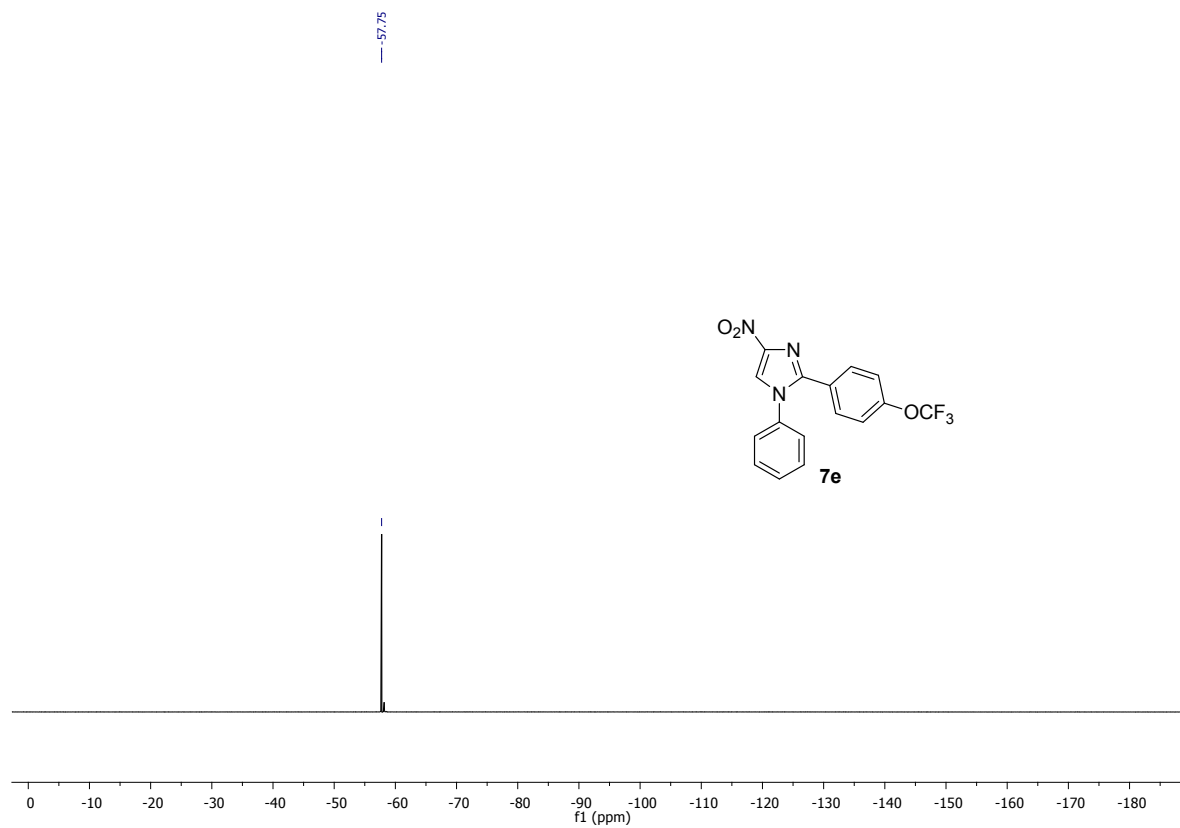


4-Nitro-1-phenyl-2-(*p*-tolyl)-1*H*-imidazole (7d):

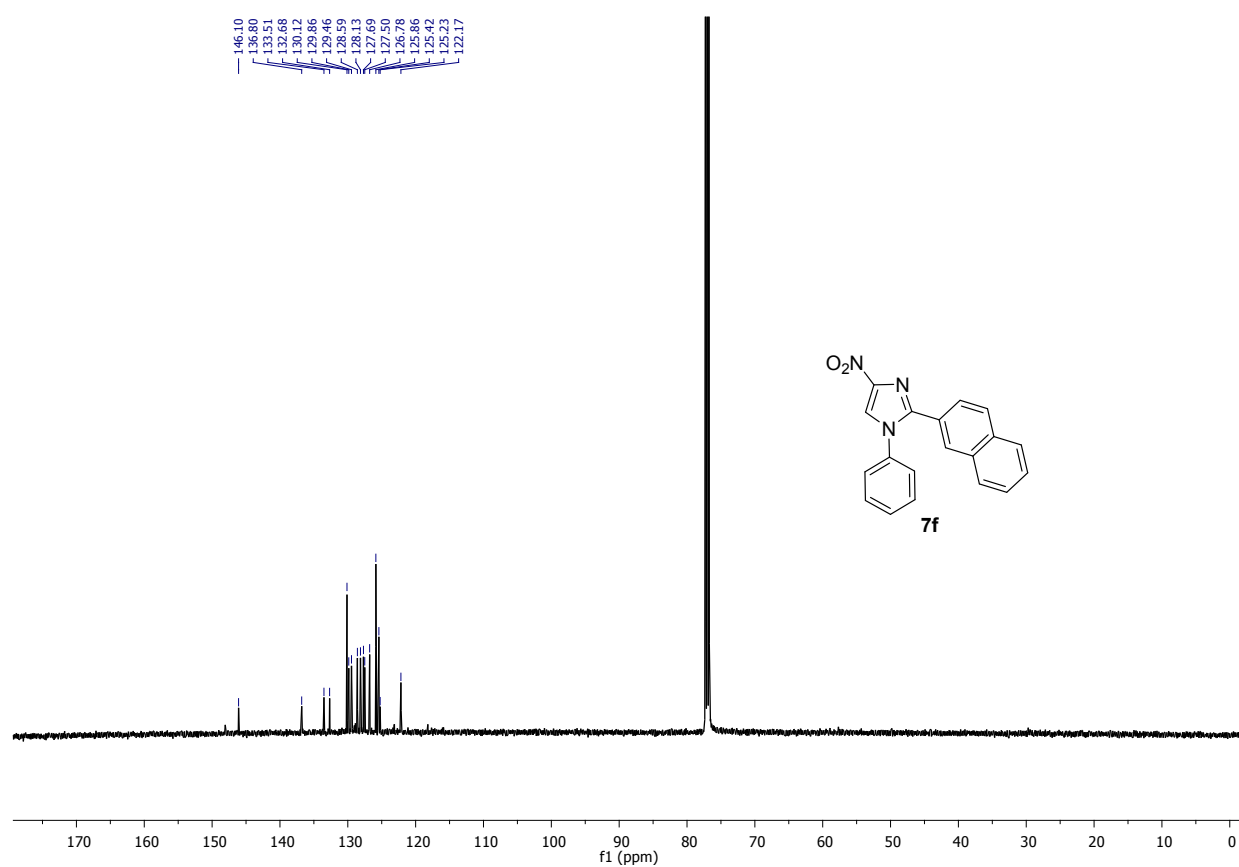
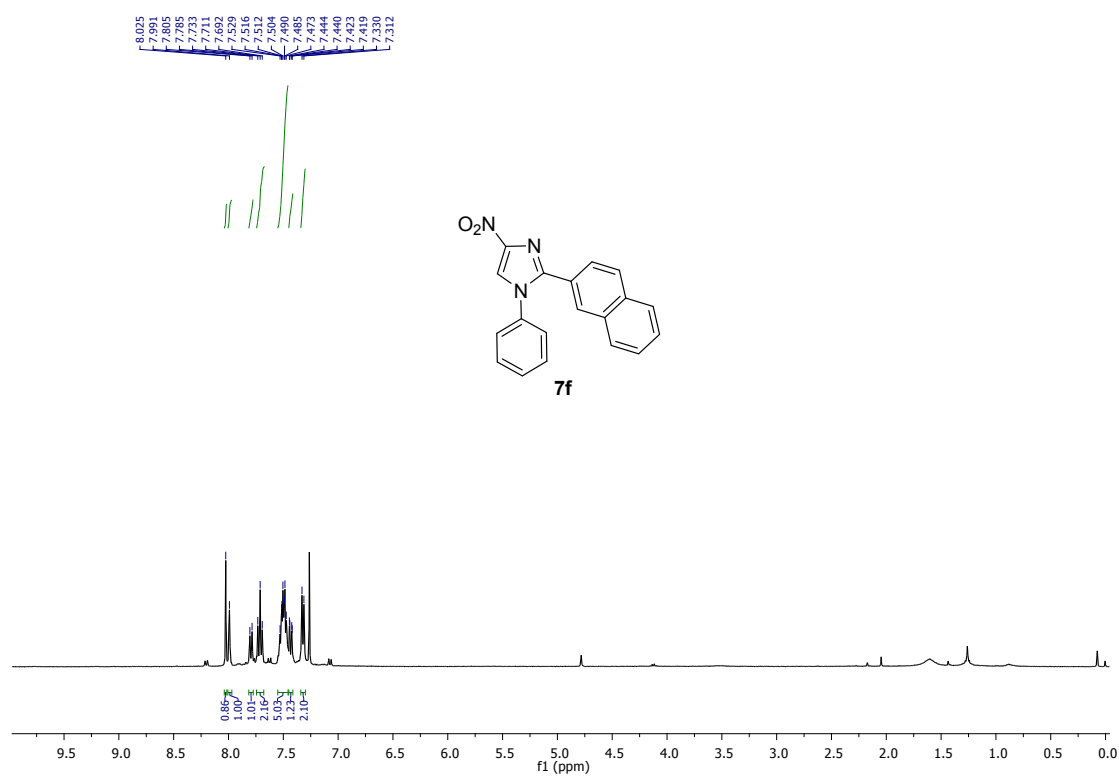


4-Nitro-1-phenyl-2-(4-(trifluoromethoxy)phenyl)-1H-imidazole (7e) :

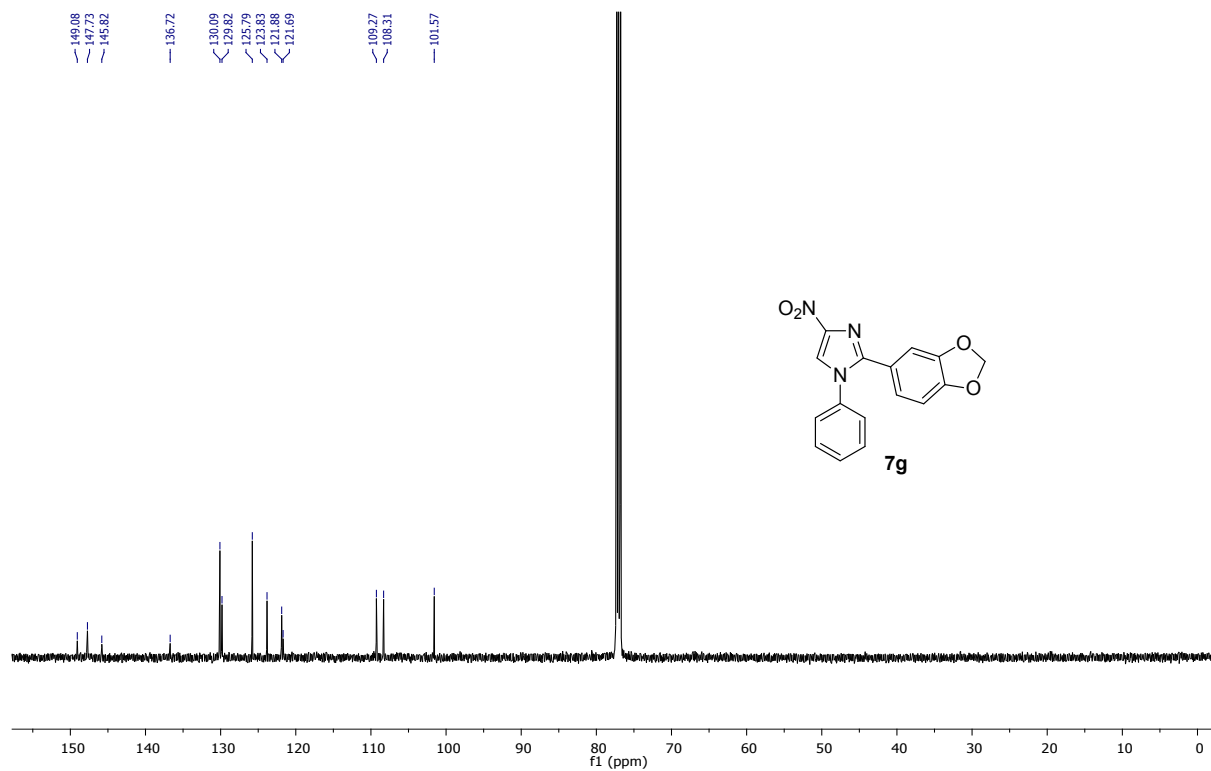
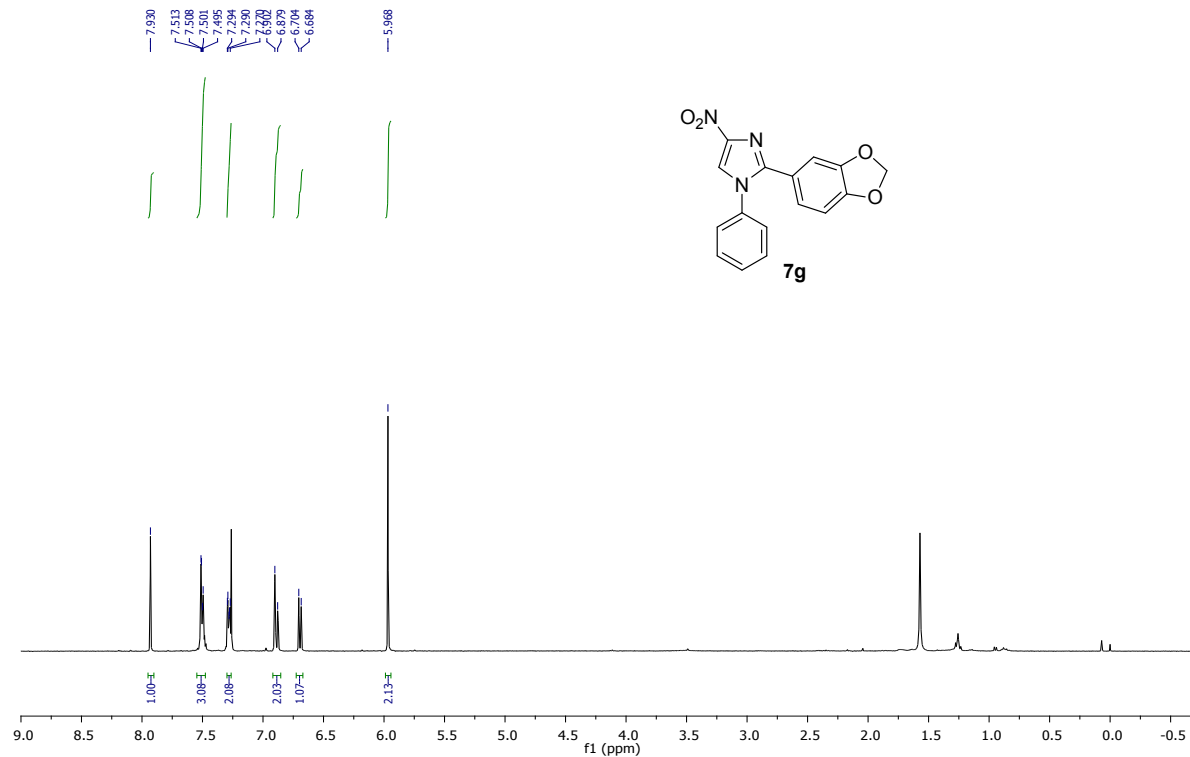




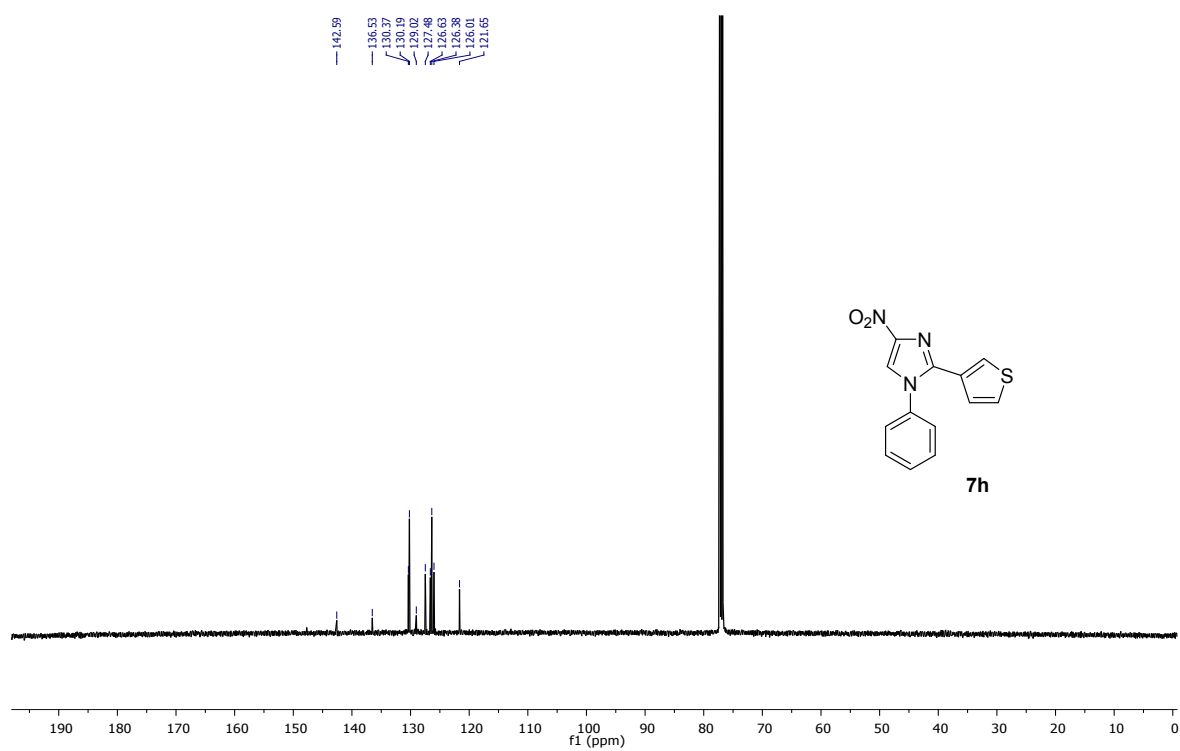
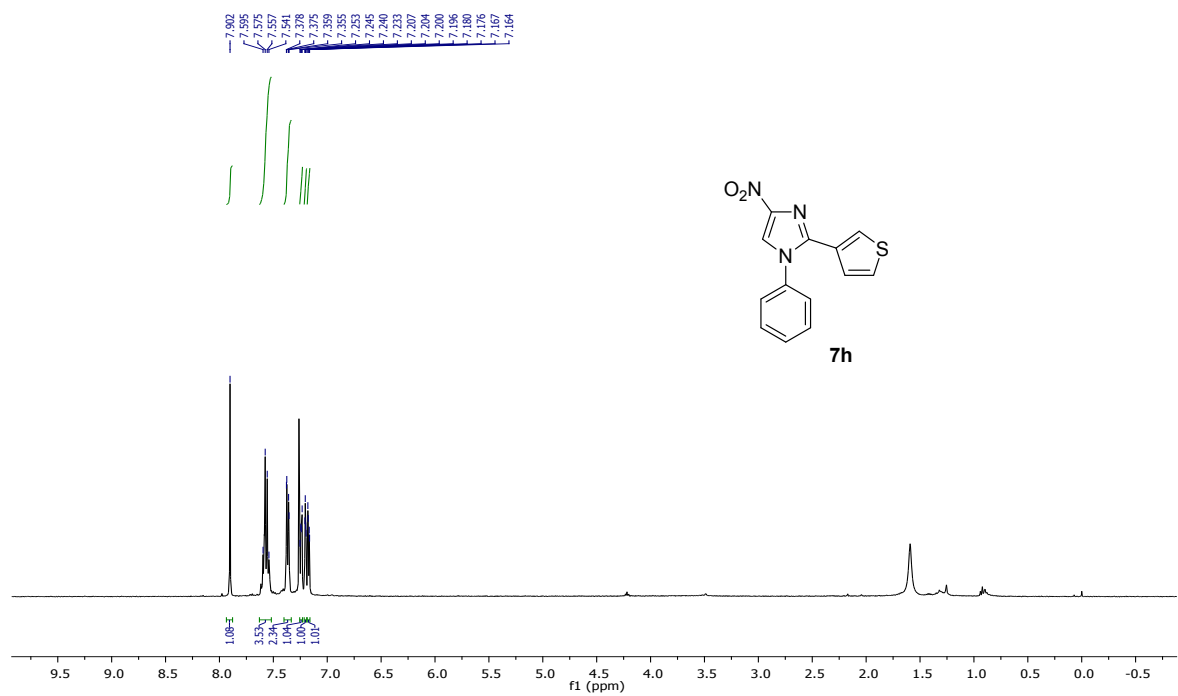
2-(Naphthalen-2-yl)-4-nitro-1-phenyl-1H-imidazole (7f):



2-(Benzo[d][1,3]dioxol-5-yl)-4-nitro-1-phenyl-1H-imidazole (7g):



4-Nitro-1-phenyl-2-(thiophen-3-yl)-1*H*-imidazole (7h):



2-chloro-4-nitro-1*H*-imidazole 1 :

