

Supporting Information

Pyridine C3-arylation of nicotinic acids accessible via multicomponent reaction: An entry to all-substituted-3,4- diaryled pyridines

Sankar K Guchhait,^a Neha Hura,^a Kanchan Sinha^b and Dulal Panda^b

^a*Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), S. A. S. Nagar (Mohali)–160062, India*

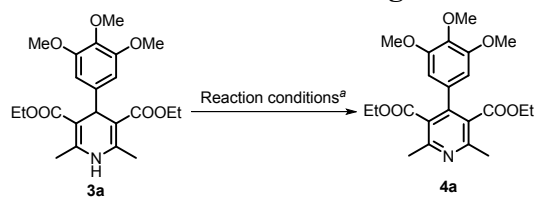
E-mail: skguchhait@niper.ac.in; Fax: +91 172 2214692; Tel: +91 172 2214683

^b*Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Powai, Mumbai 400076, India*

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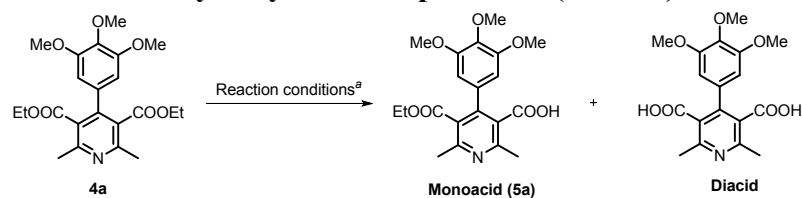
1. Dehydrogenative aromatization reactions utilizing different conditions (Table1)



Entry	Reaction conditions ^a	Time (h)	% Yield ^b
1 ¹	NaClO ₂ (1.5 equiv), EtOH:Water(1:1), conc. HCl (0.2 mL), 20 °C	3	70
2 ²	Mn(OAc) ₃ , (2 equiv), AcOH (5 mL), rt	2	90
3 ³	Fe(ClO ₄) ₃ (2 mol%), AcOH (5 mL), rt	4	60

^a Reaction was done at 1 mmol scale, ^bYield obtained after recrystallization

2. Optimization for mono-hydrolysis of compound 4a (Table 2)^{4,5}



Entry	Base (equiv)	Solvent	T (°C)	Yield (%) ^b		
				Monoacid	Diacid	Substrate recovered
1	KOH(2)	EtOH:Water (3:1)	80	50	29	20
2	KOH(2)	EtOH:Water (3:1)	65	60	20	20
3	KOH(2)	EtOH:Water (3:1)	50	65	7	26
4	NaOH(2)	EtOH:Water (3:1)	50	67	5	27
5	KOH(2)	EtOH	50	55	25	20
6	KOH(2)	MeOH	50	60	30	10
7	NaOH (2)	THF:Water (1:10)	0-50	0	0	100
8	KOH(2), TBAB(1)	EtOH:Water (3:1)	50	65	10	25

^a Reactions were performed at 0.5 mmol scale, reaction time 24 h; ^b Isolated yield

3. Inhibition of cell proliferation upon treatment of HeLa cells with 5 μ M compounds (Table 3)

Diaryled-pyridine compounds (5 μ M)	% Inhibition
8a	11 \pm 9
8b	64 \pm 5
8c	52 \pm 5
8d	50 \pm 10
8e	3 \pm 2
8f	73 \pm 5
8g	41 \pm 12
8h	45 \pm 11
8i	40 \pm 11
8j	65 \pm 8
8k	8 \pm 4
8l	60 \pm 2
8m	47 \pm 15
8n	8 \pm 2
8o	48 \pm 10
8p	64 \pm 2
8q	54 \pm 12
8r	28 \pm 3
8s	18 \pm 3
8t	29 \pm 19

4. Effects of compounds 8b, 8f, 8j, 8p on the assembly of tubulin *in vitro*

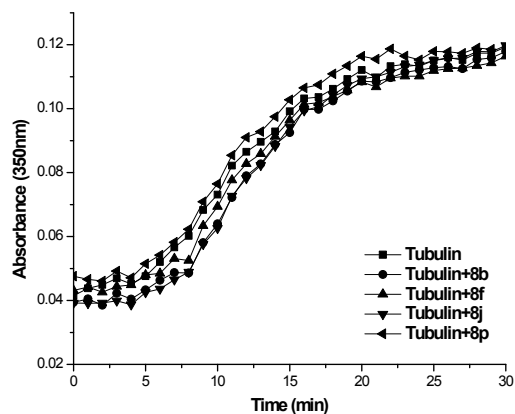


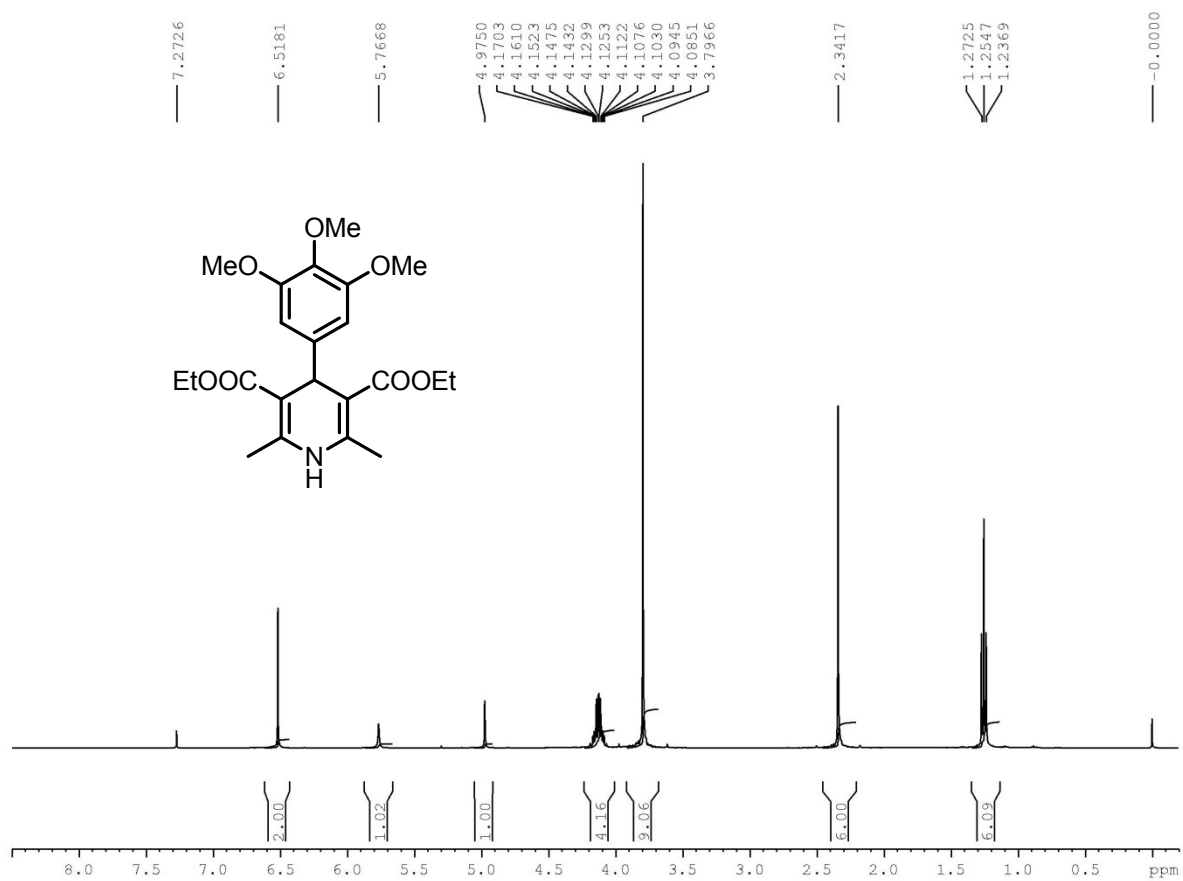
Figure 1: Effects of compounds 8b, 8f, 8j, 8p on the assembly of tubulin *in vitro*. Tubulin(12 μ M) was polymerized in the presence of 1 mM GTP and 10% DMSO without or with 20 μ M of compound 8b, 8f, 8j, 8p. Three independent sets of experiments were performed for each compound. Here is one of the representative set.

5. References

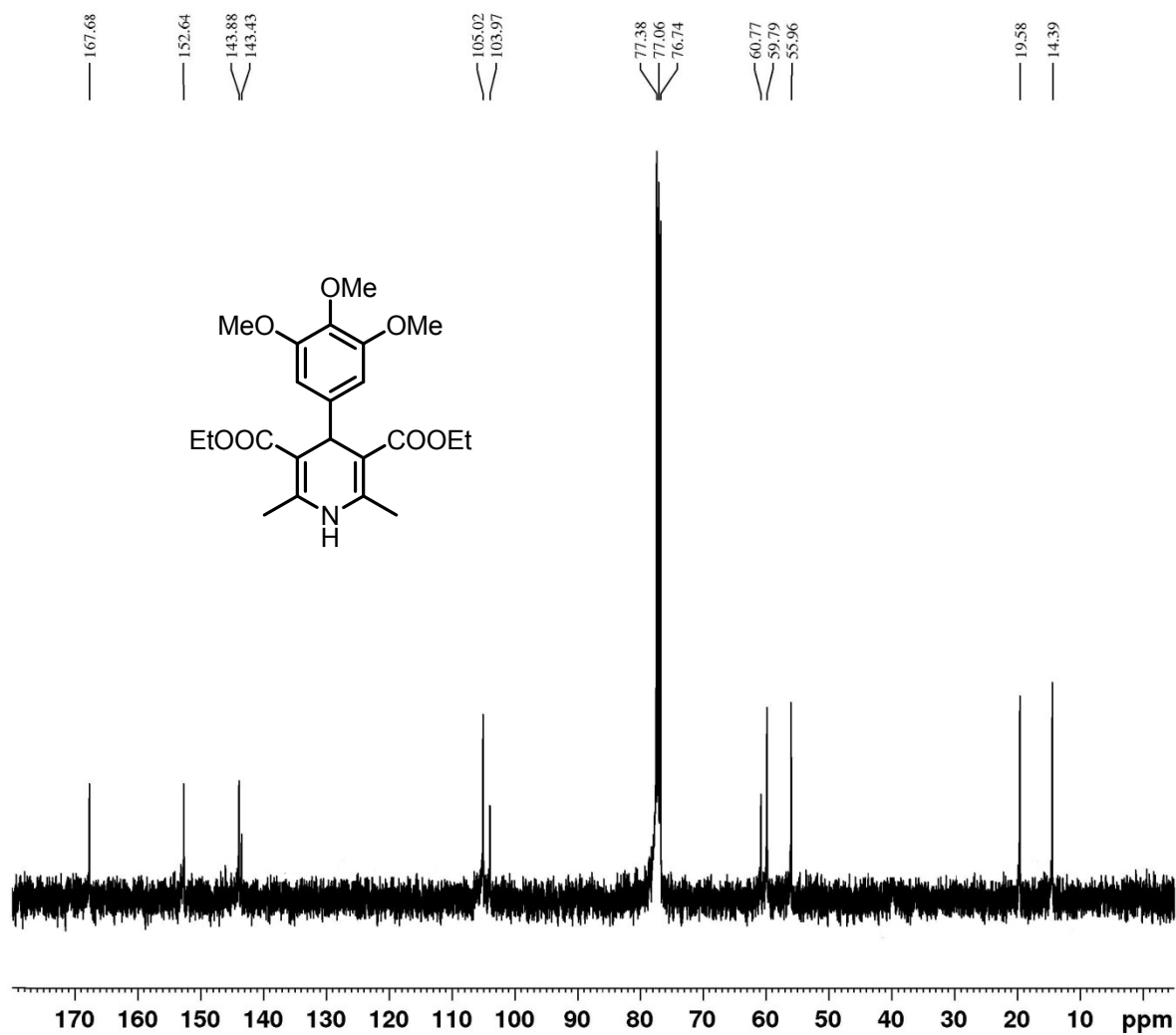
1. R. S. Varma and D. Kumar, *Tet. Lett.*, 1999, **40**, 21.
2. X. Liao, W. Lin, J. Lu and C. Wang, *Tet. Lett.*, 2010, **51**, 3859.
3. M. M. Heravi, F. K. Behbahani, H. A. Oskooie and R. H. Shoar, *Tet. Lett.*, 2005, **46**, 2775.
4. J. Duan, X. Song, H. Yan and X. Song, *Molecules*, 2011, **16**, 3845.
5. M. Chouhan, R. Sharma and V. A. Nair, *Org. Lett.*, 2012, **14**, 5672.

6. NMR spectra of compounds (3a, 4a, 5a, 8a-8t)

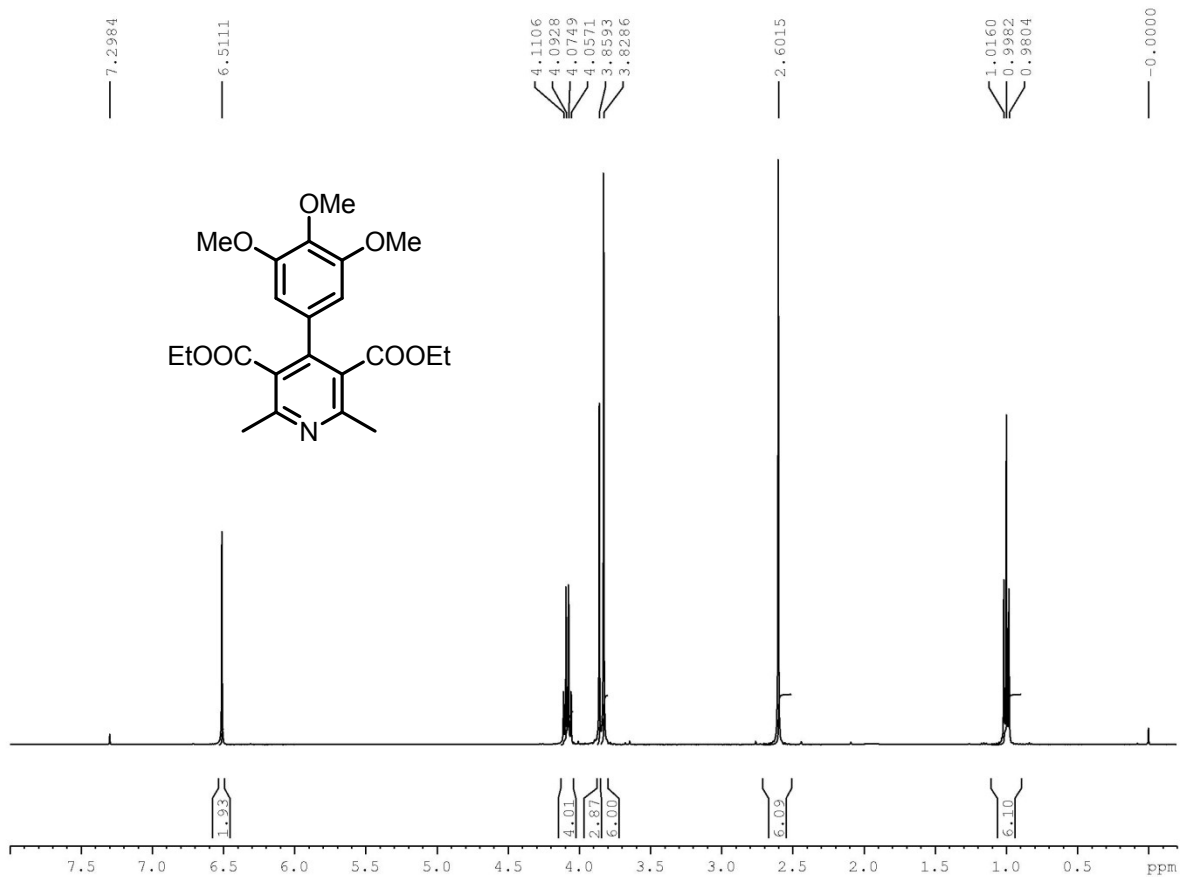
Scheme 1, (3a): ¹H NMR



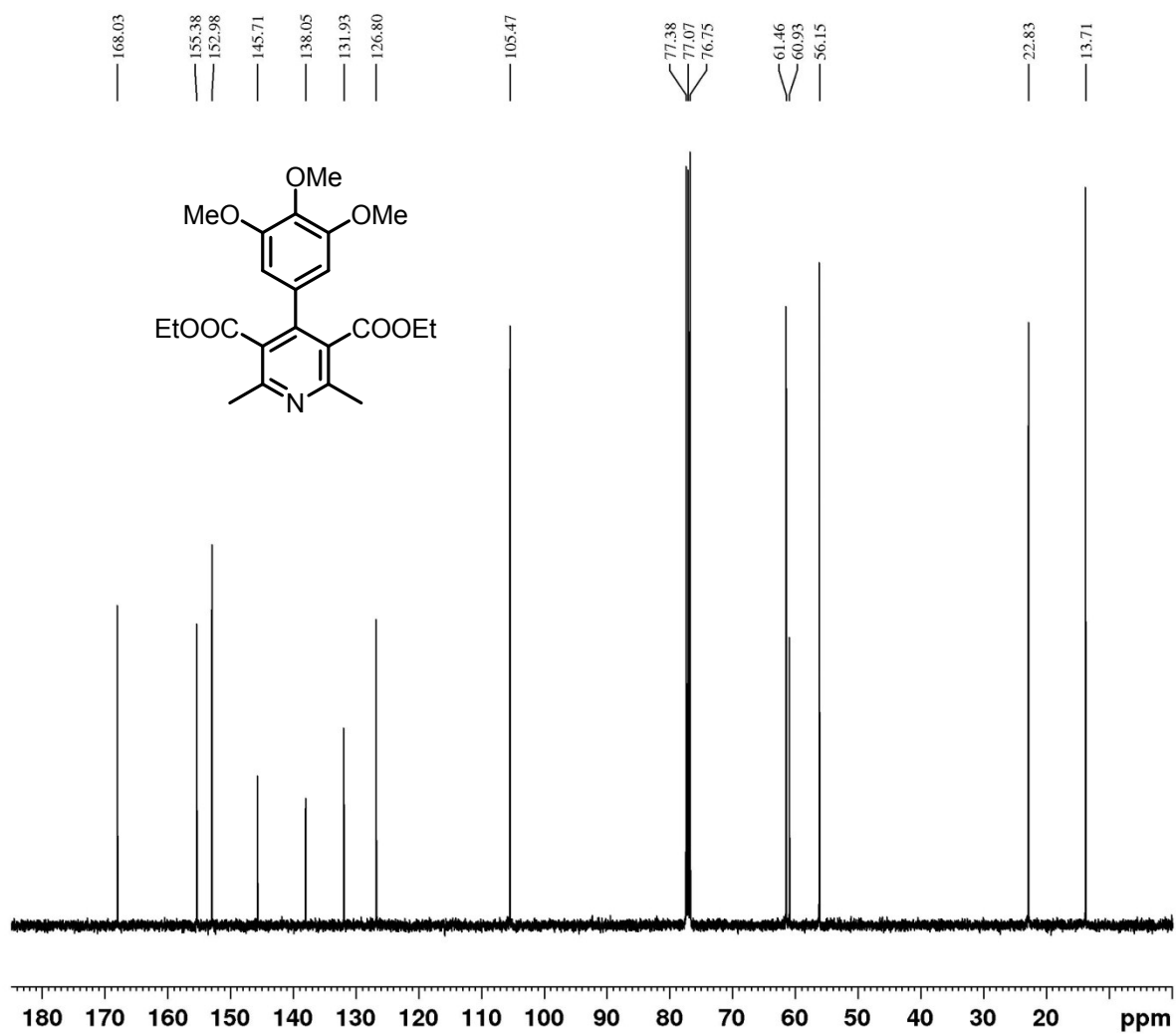
Scheme 1 (3a): ¹³C NMR



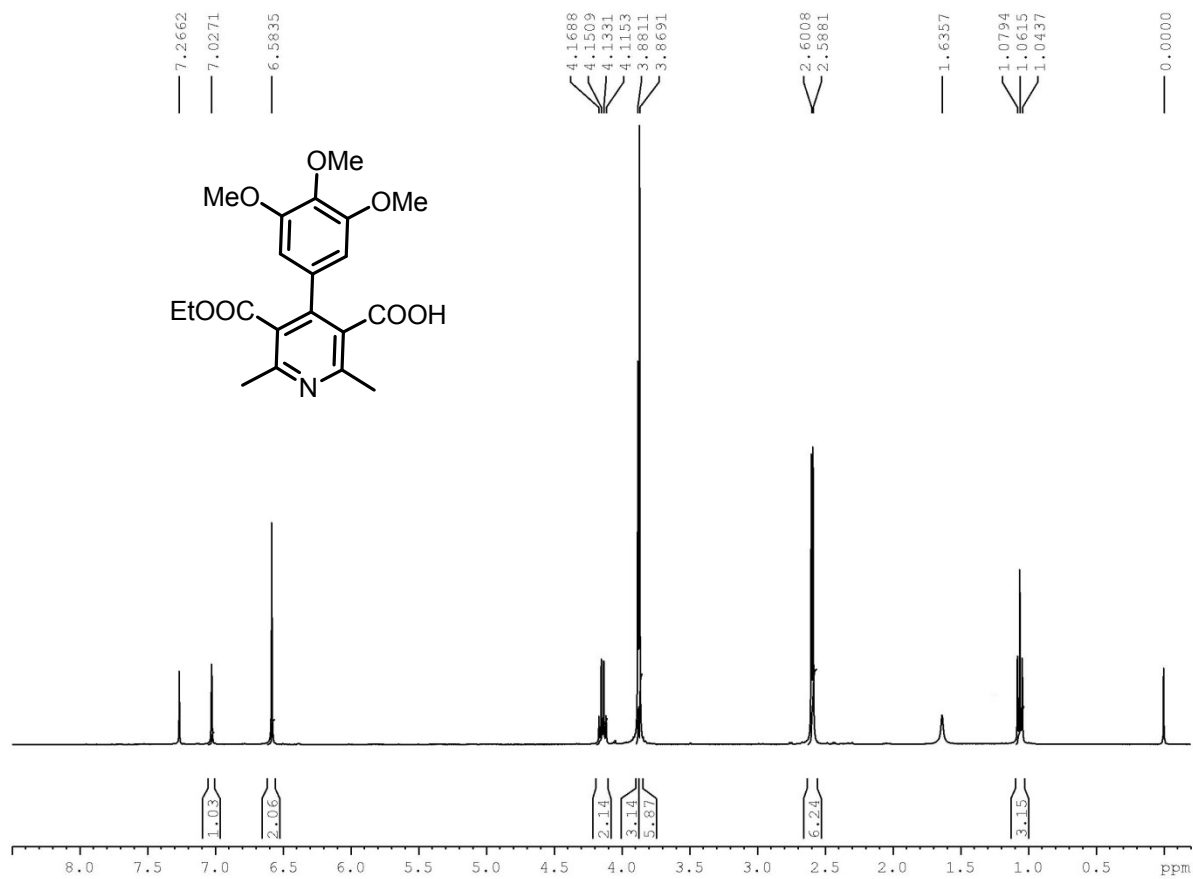
Scheme 1, (4a): ¹H NMR



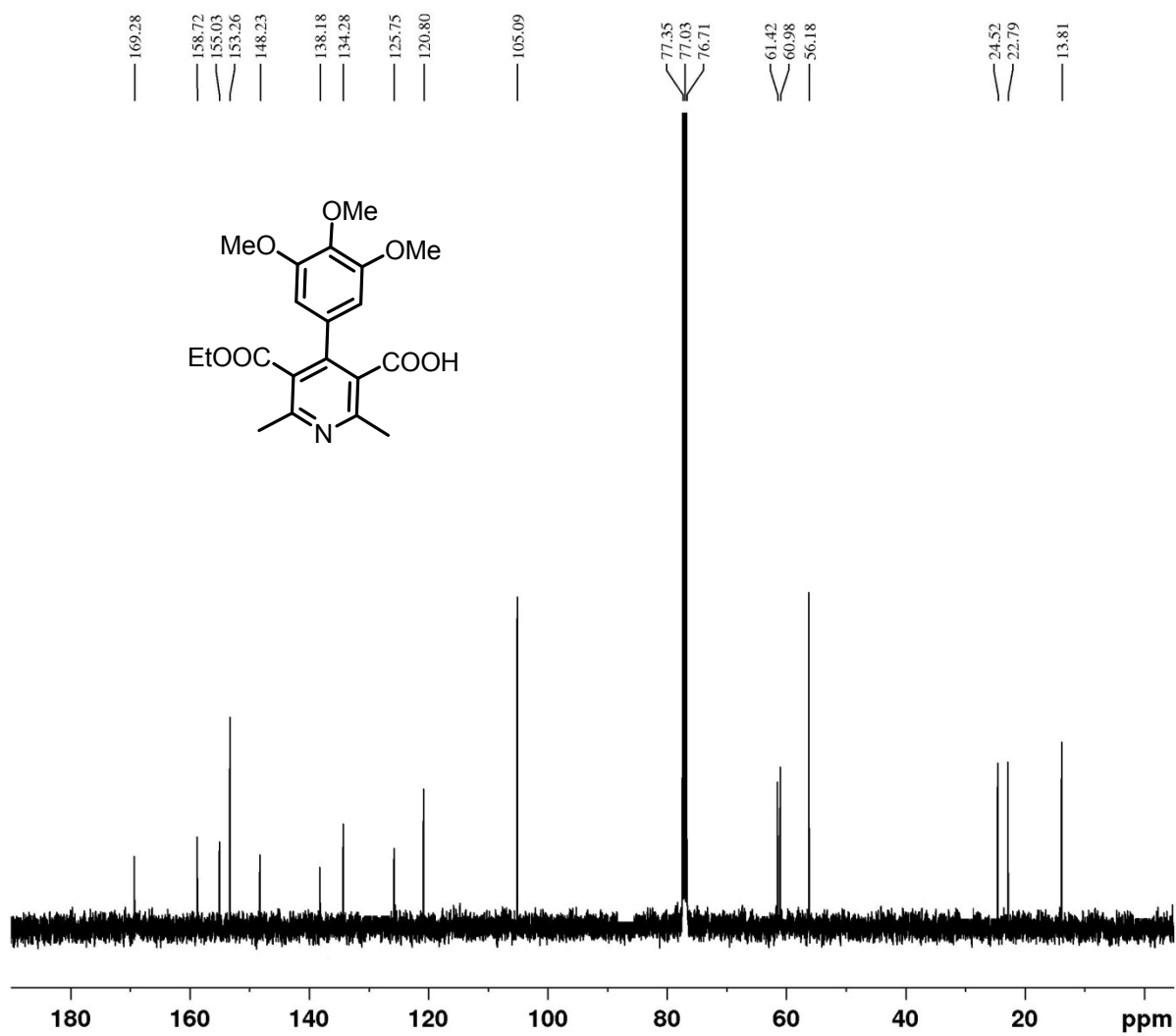
Scheme 1 (4a): ¹³C NMR



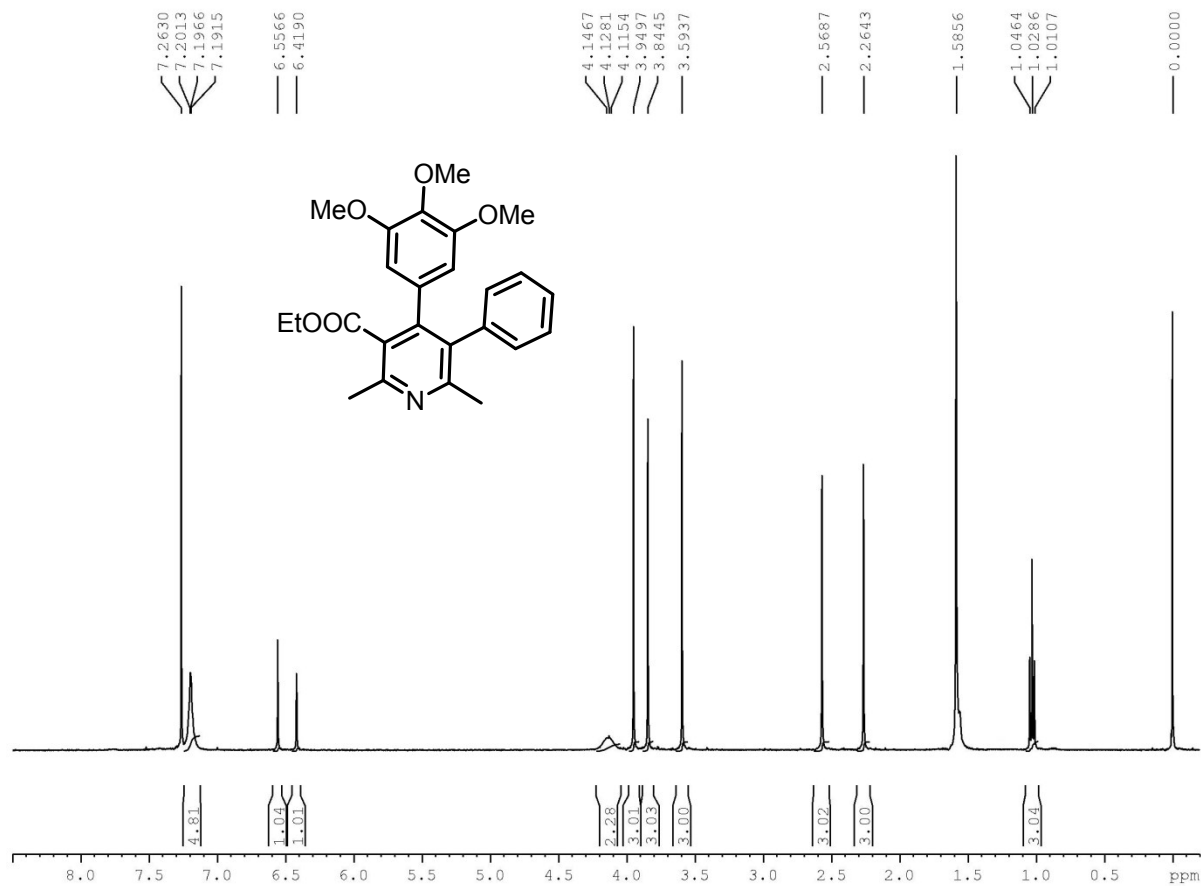
Scheme 1, (5a): ¹H NMR



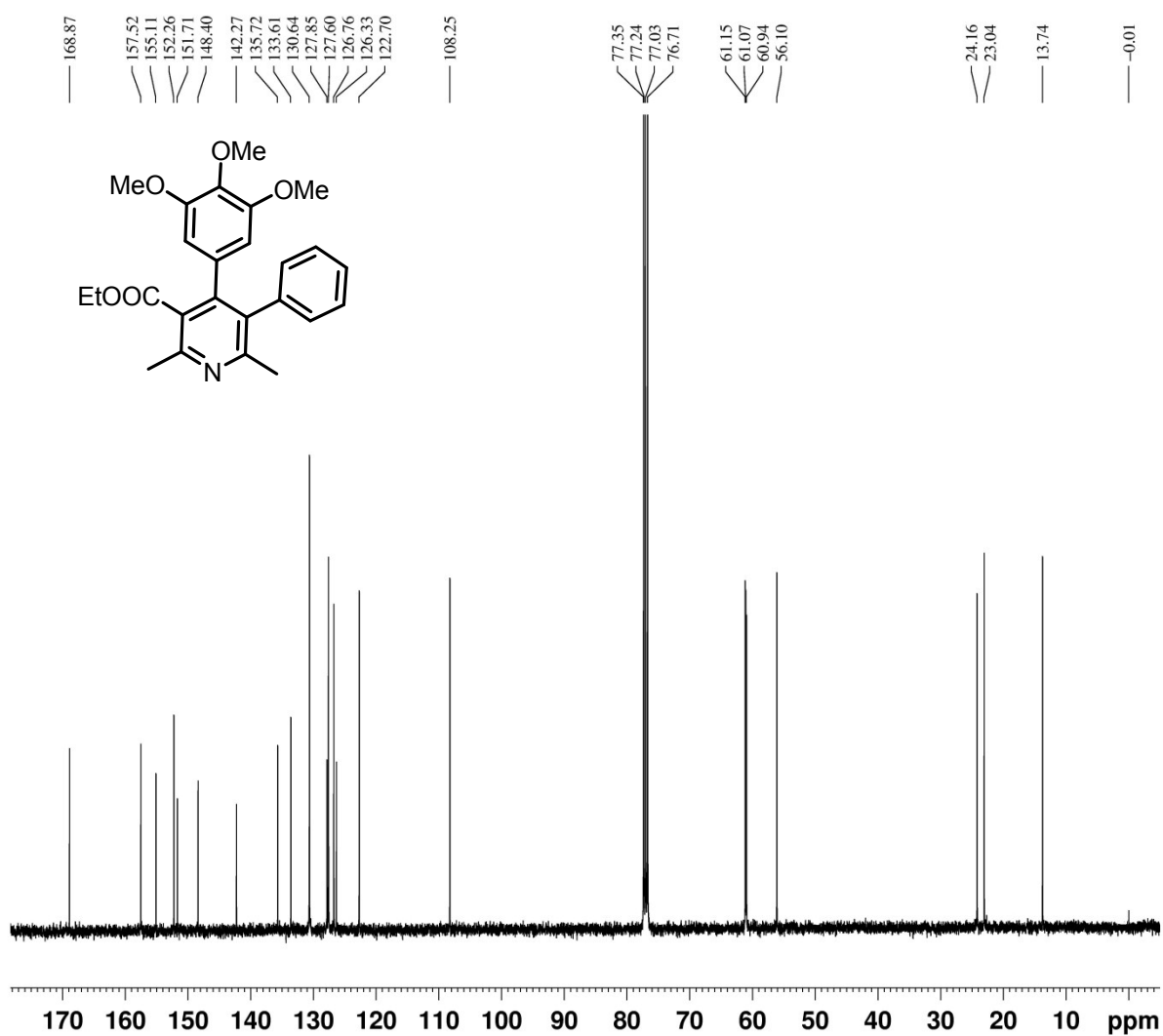
Scheme 1 (5a): ^{13}C NMR



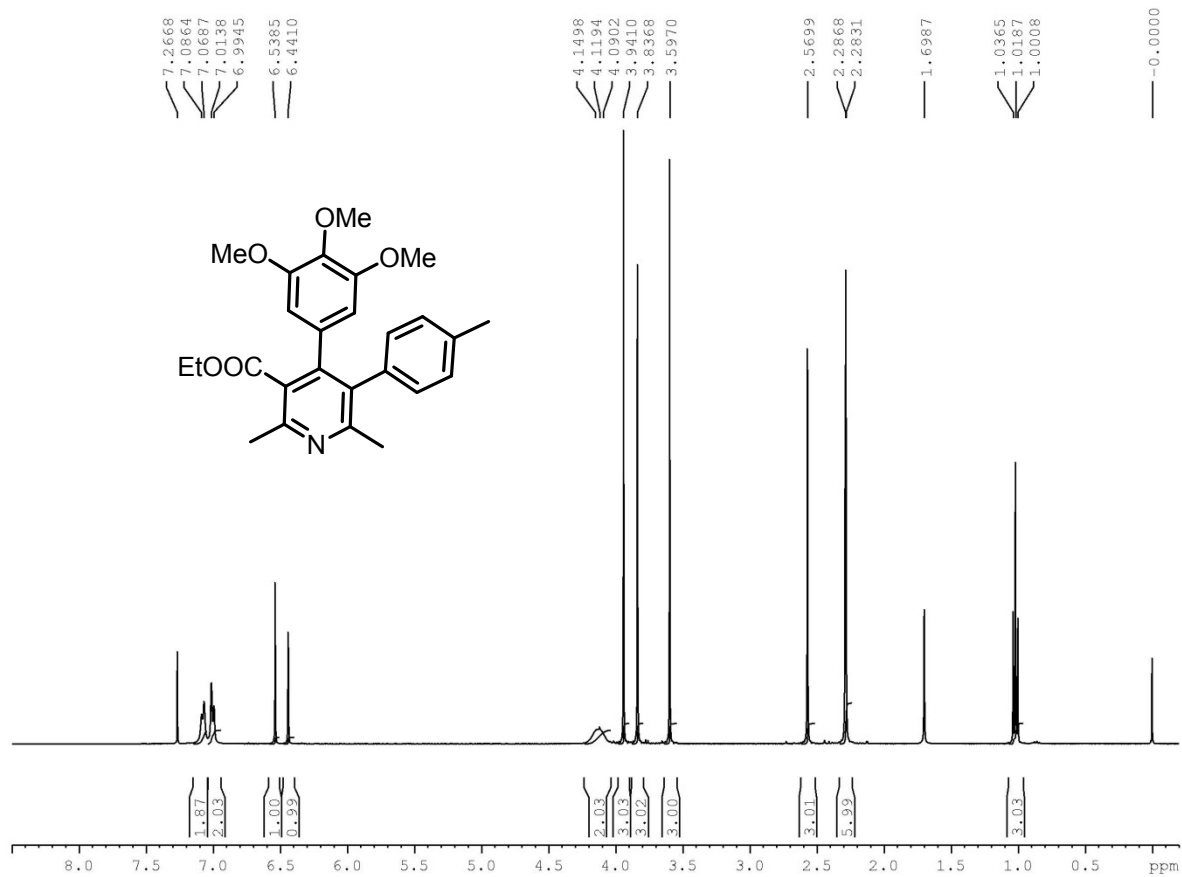
Scheme 4, Entry 1 (8a): ¹H NMR



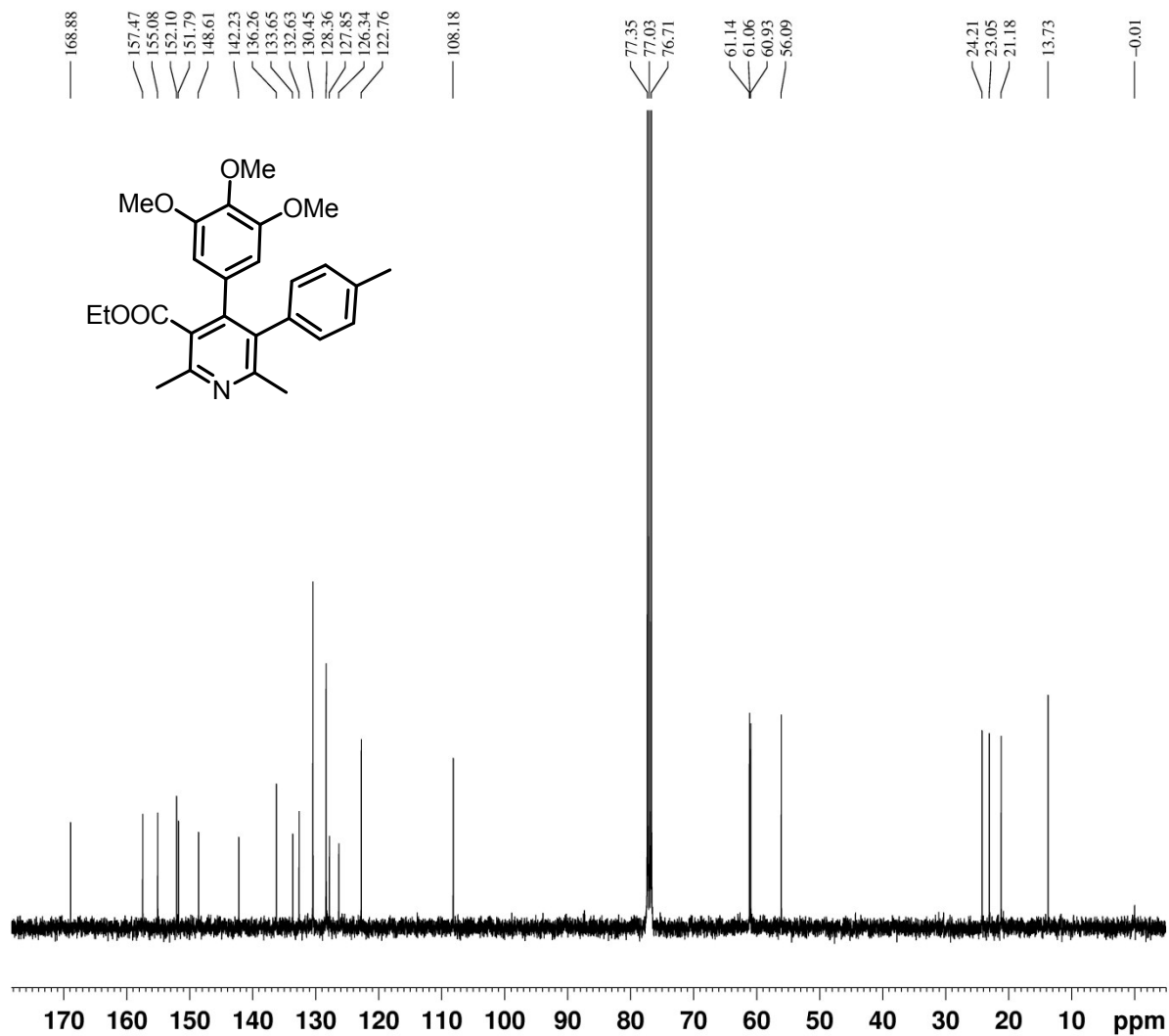
Scheme 4, Entry 1 (8a): ¹³C NMR



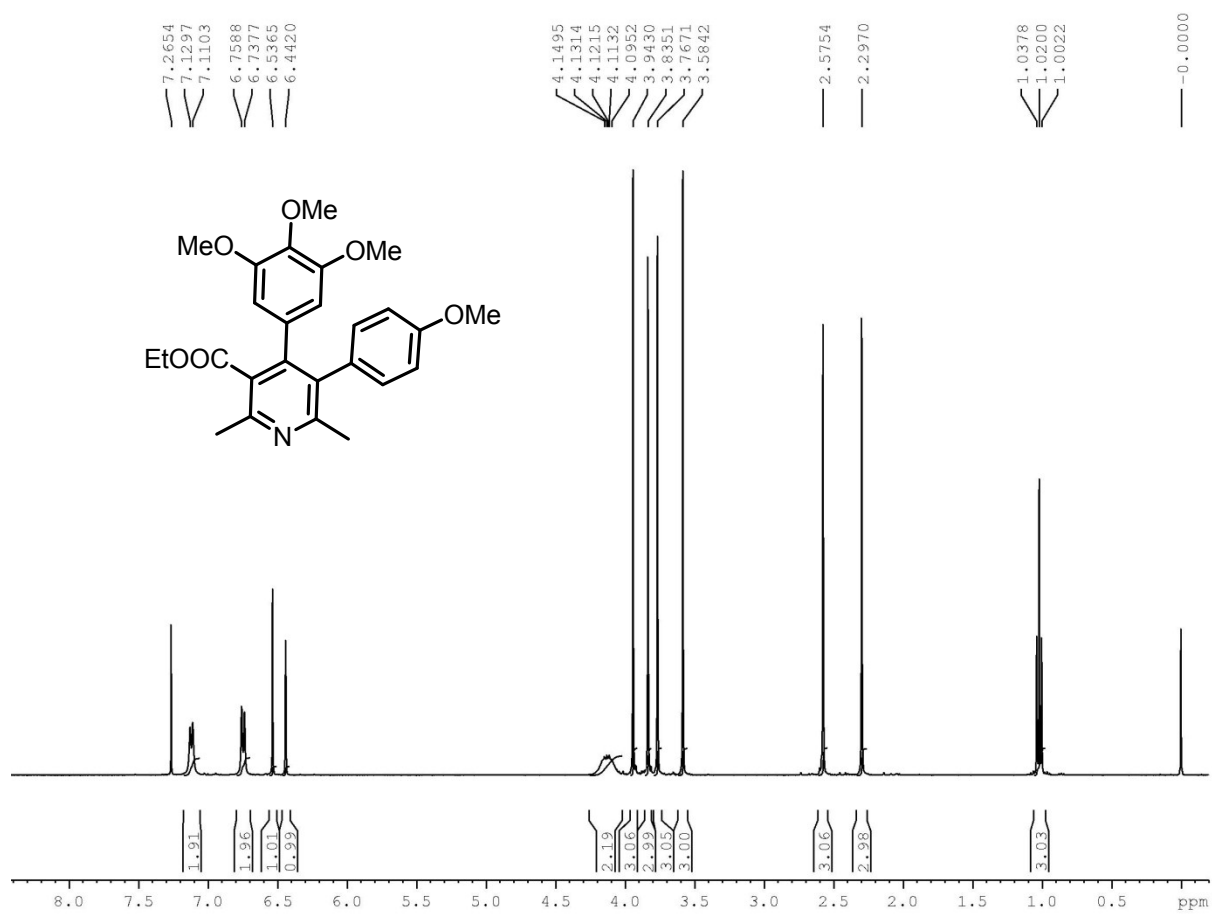
Scheme 4, Entry 2 (8b): ¹H NMR



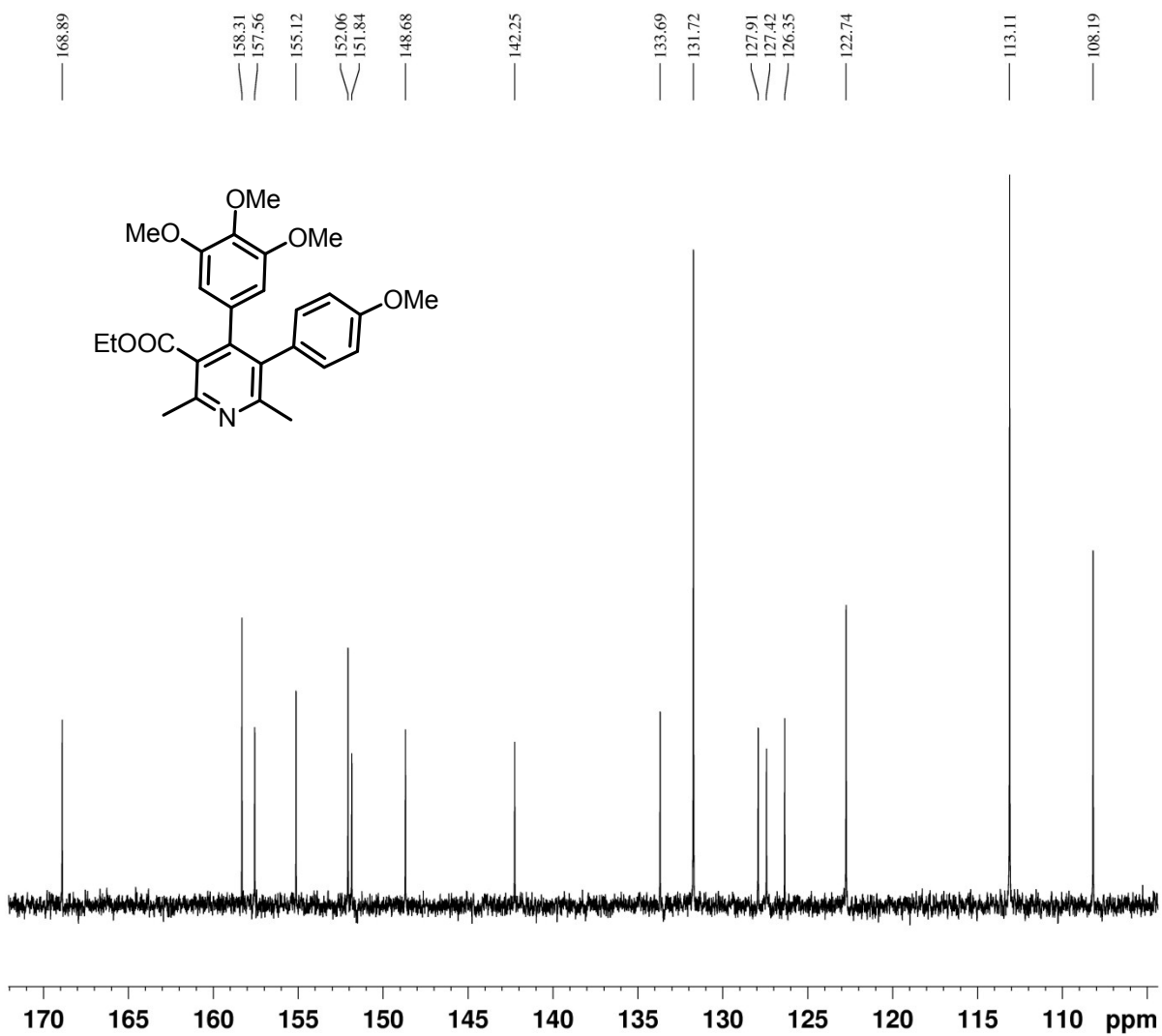
Scheme 4, Entry 2 (8b): ¹³C NMR



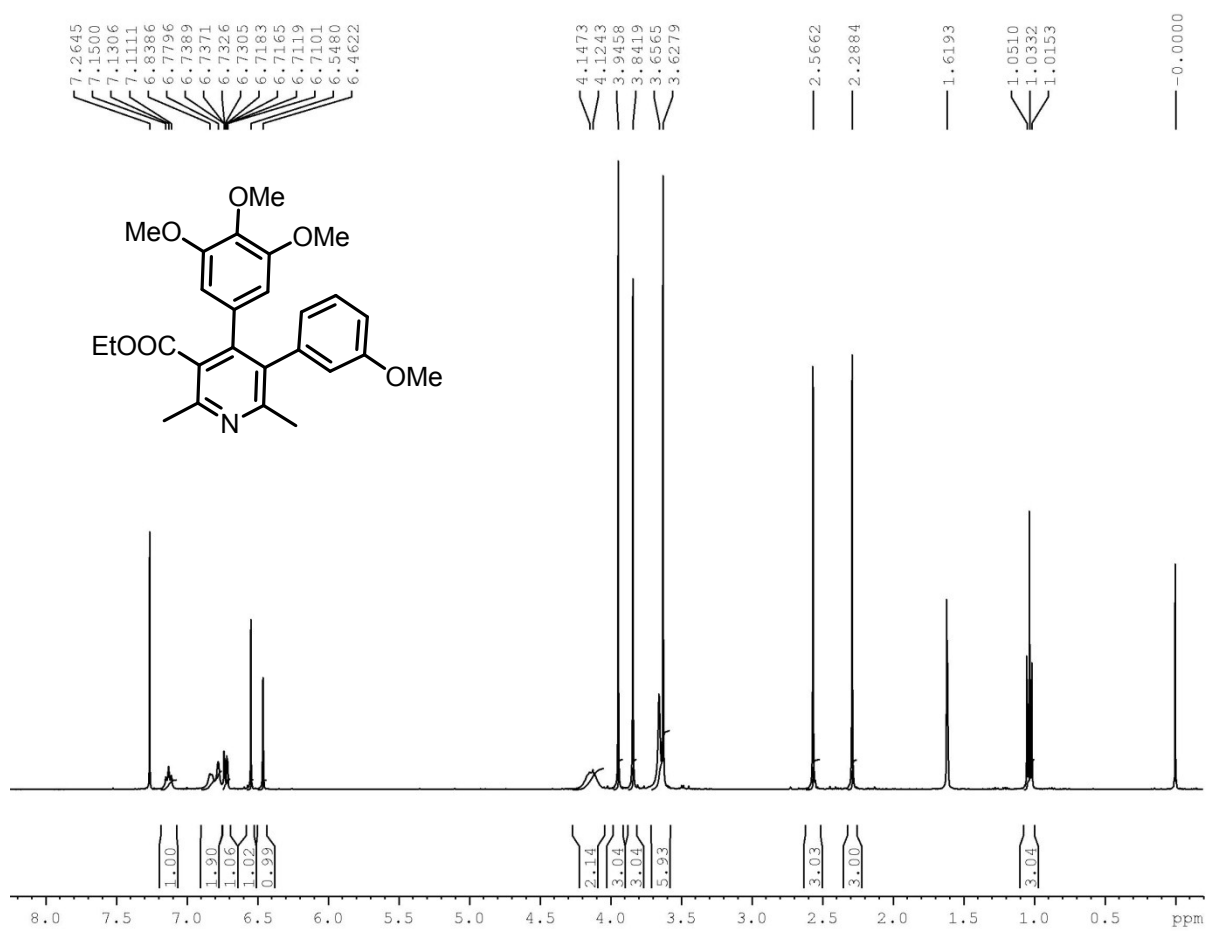
Scheme 4, Entry 3 (8c): ¹H NMR



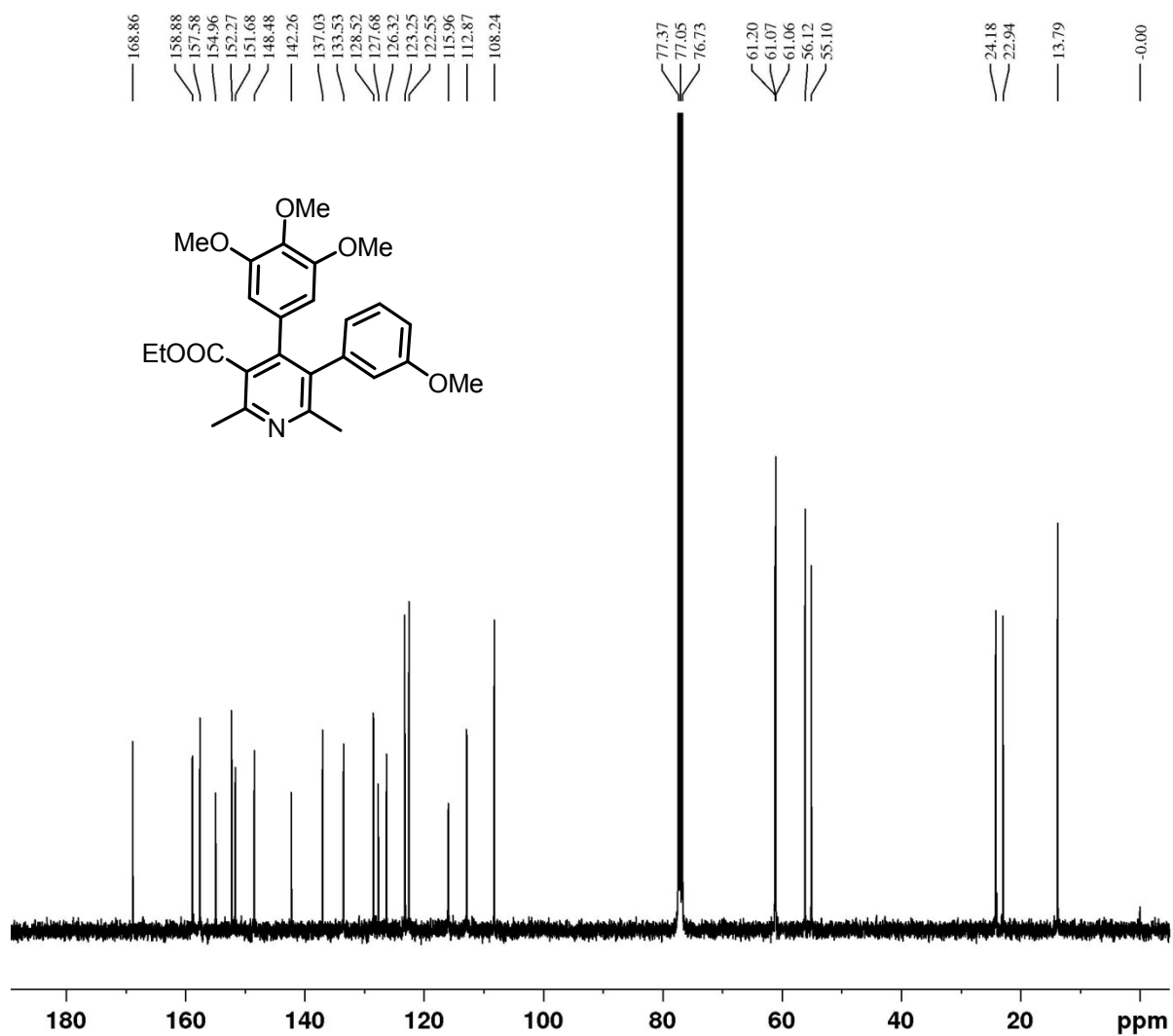
Scheme 4, Entry 3 (8c): ^{13}C NMR



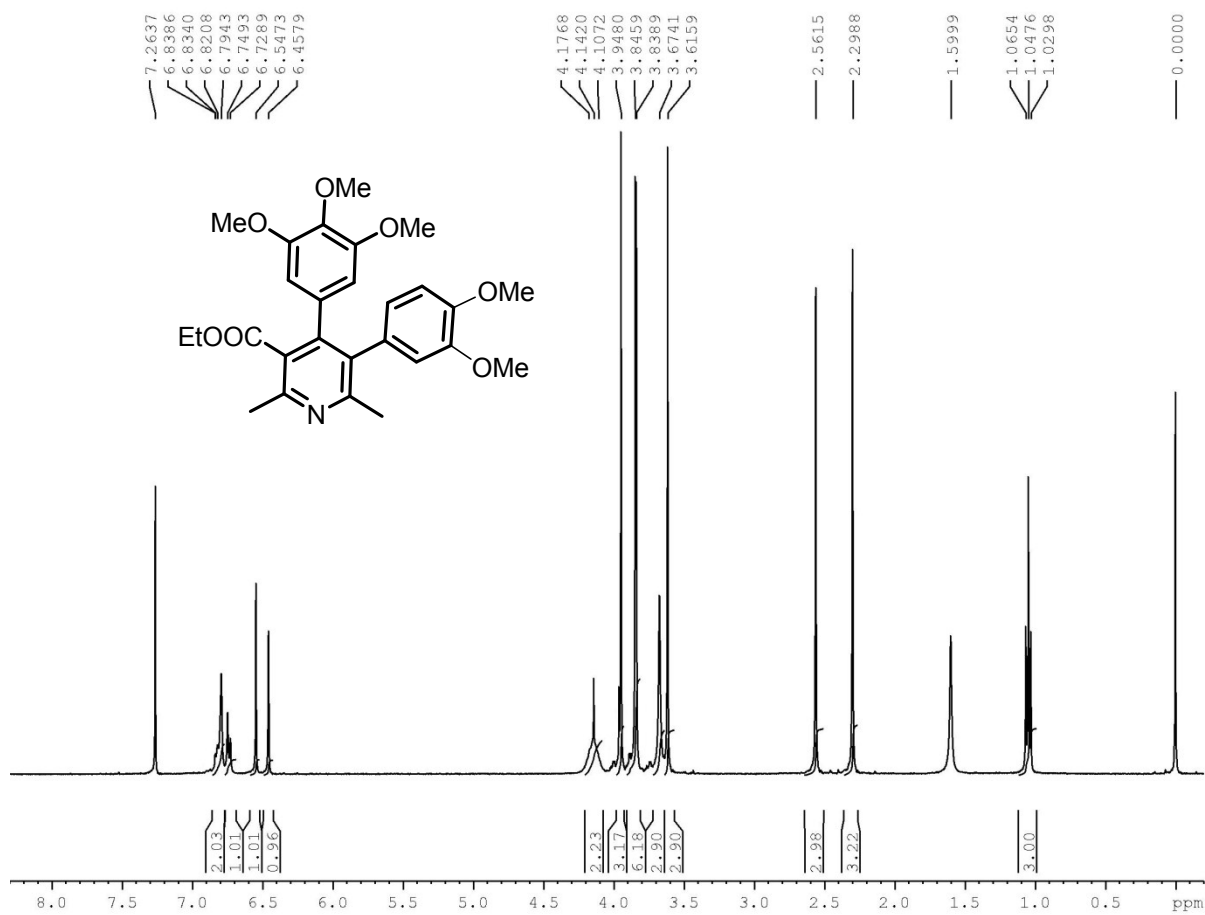
Scheme 4, Entry 4 (8d): ¹H NMR



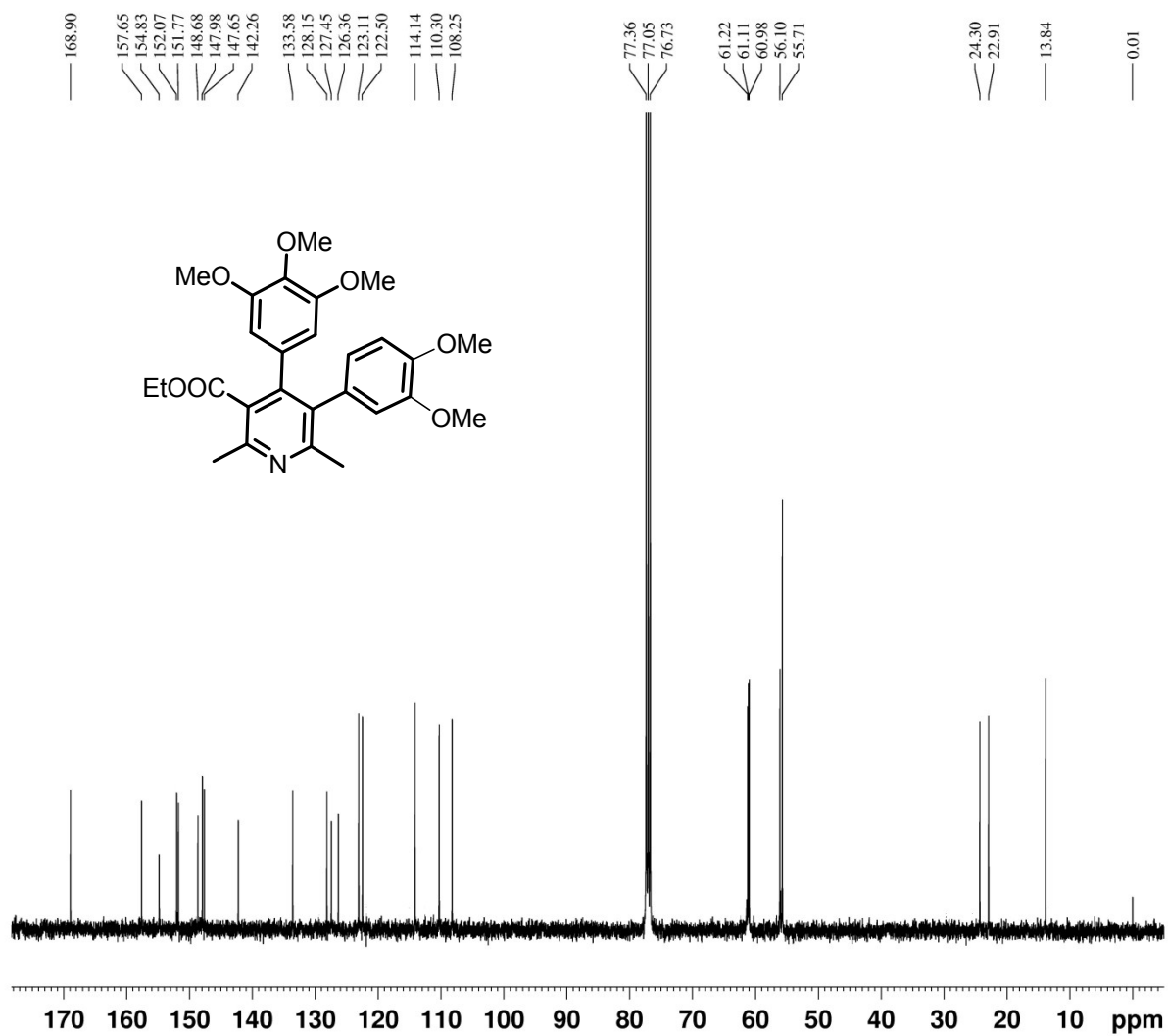
Scheme 4, Entry 4 (8d): ¹³C NMR



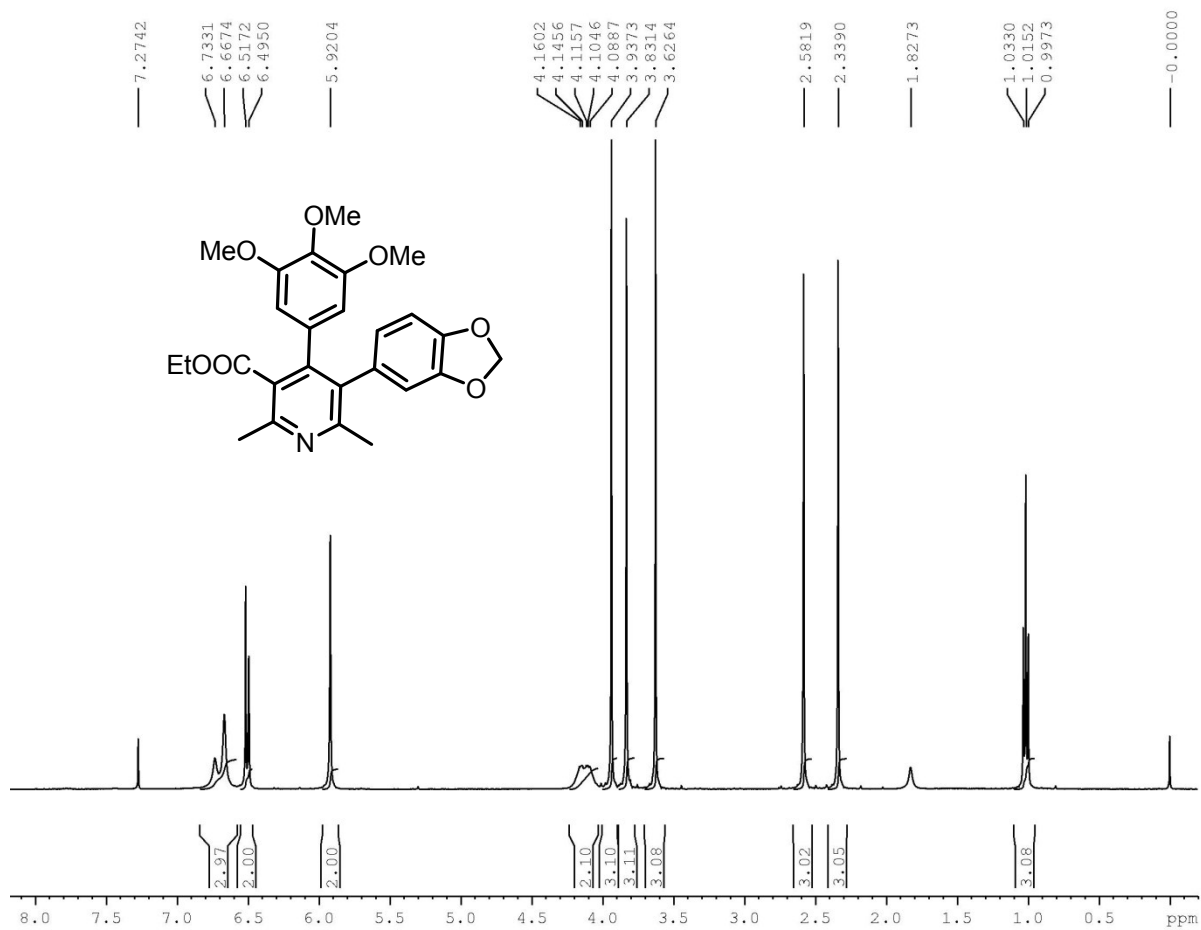
Scheme 4, Entry 5 (8e): ¹H NMR



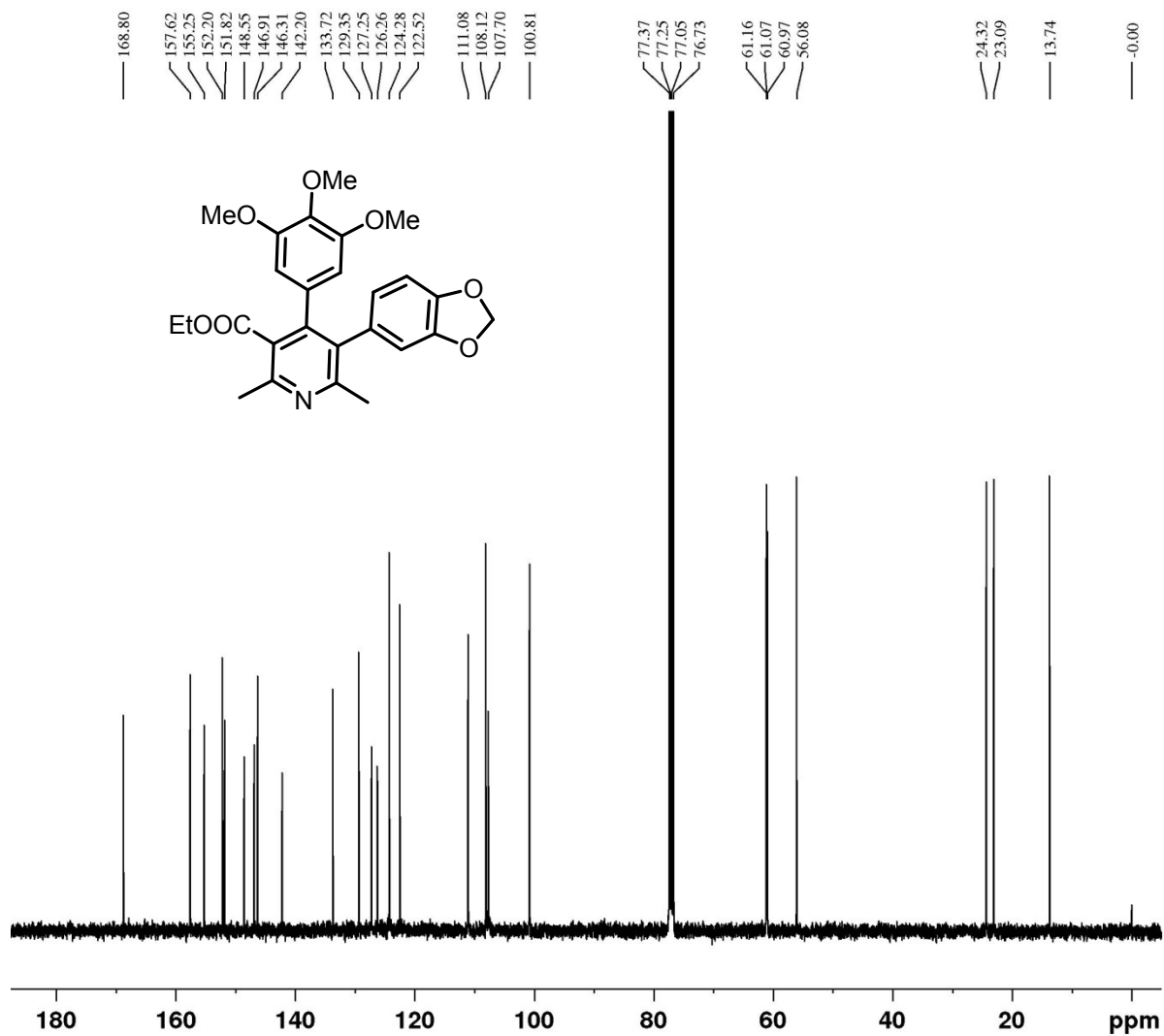
Scheme 4, Entry 5 (8e): ¹³C NMR



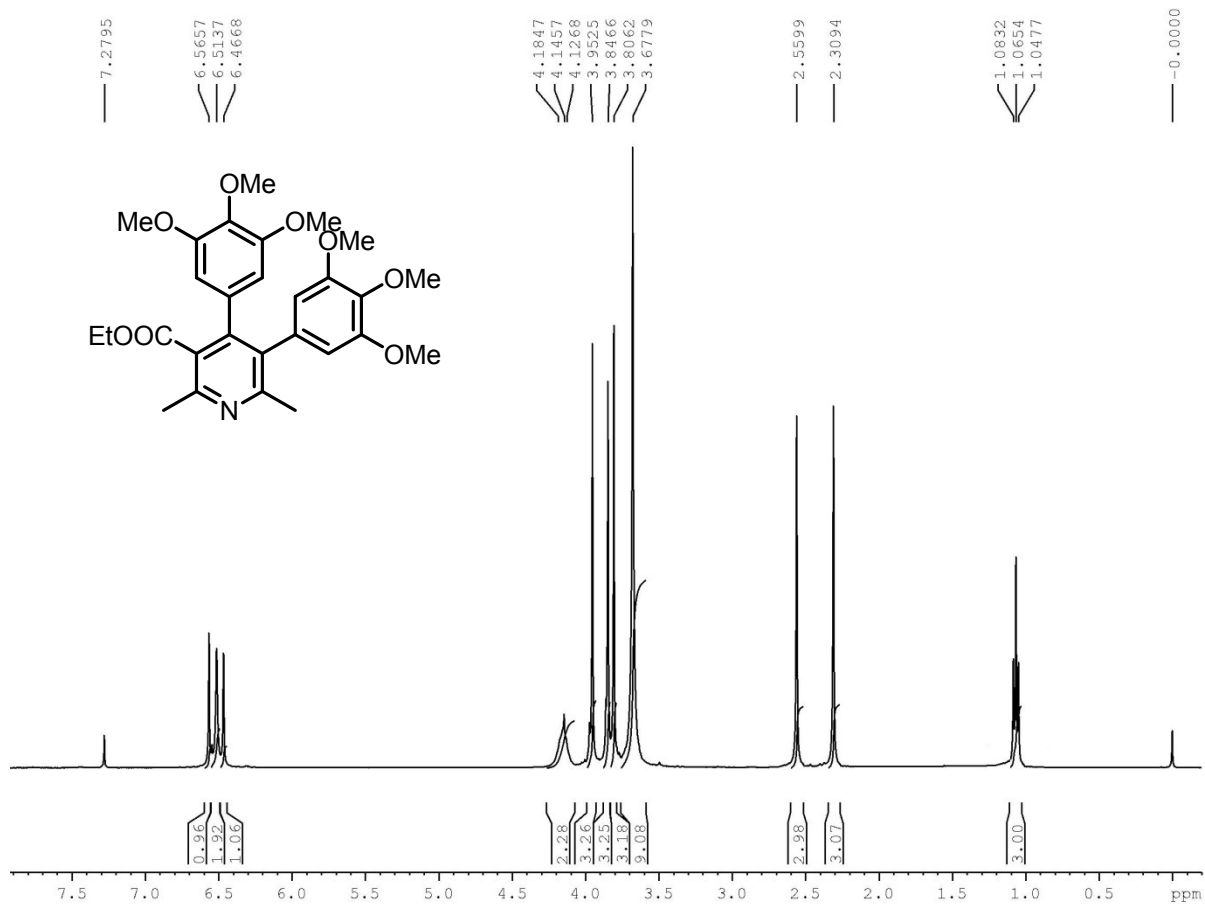
Scheme 4, Entry 6 (8f): ¹H NMR



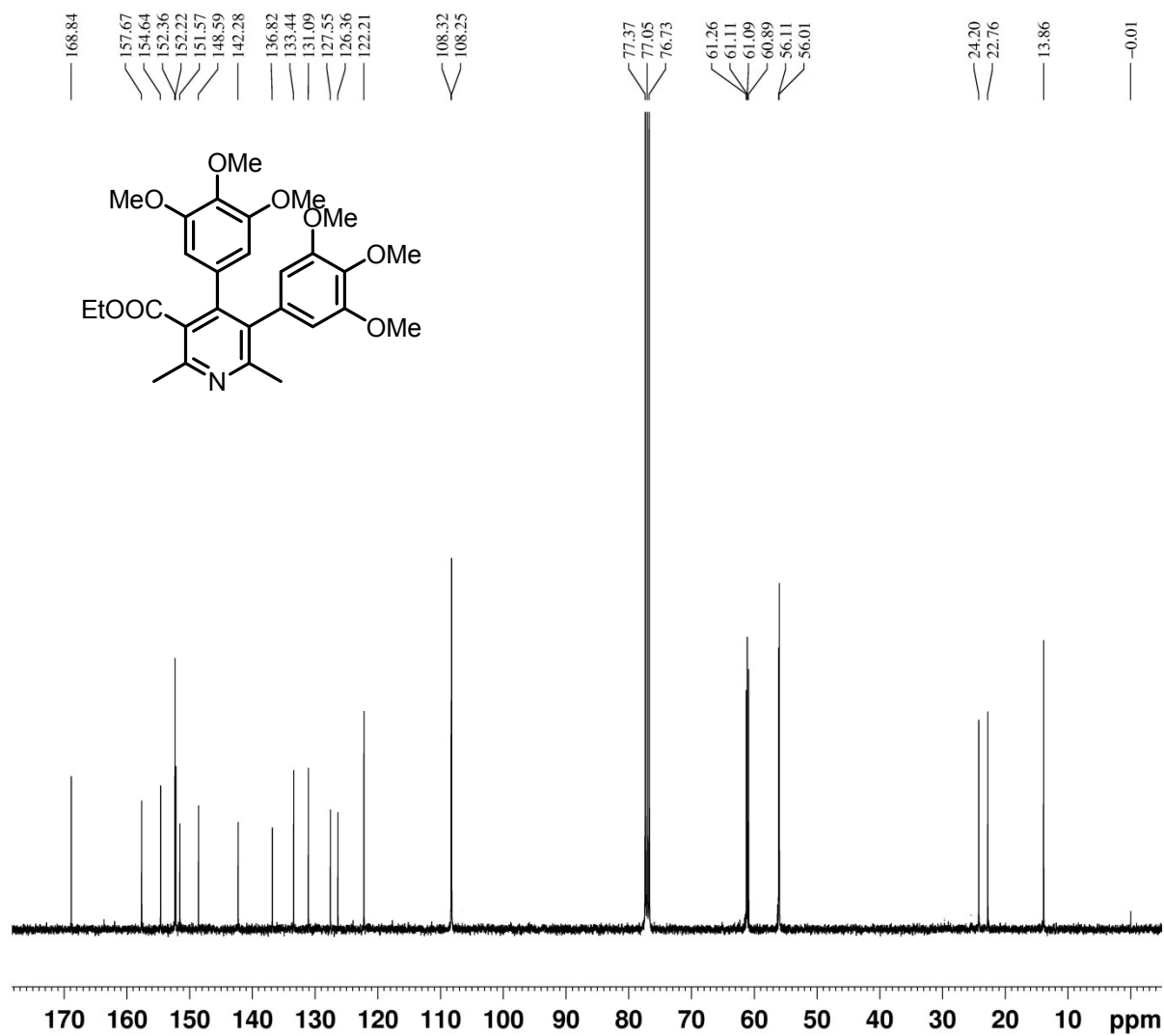
Scheme 4, Entry 6 (8f): ¹³C NMR



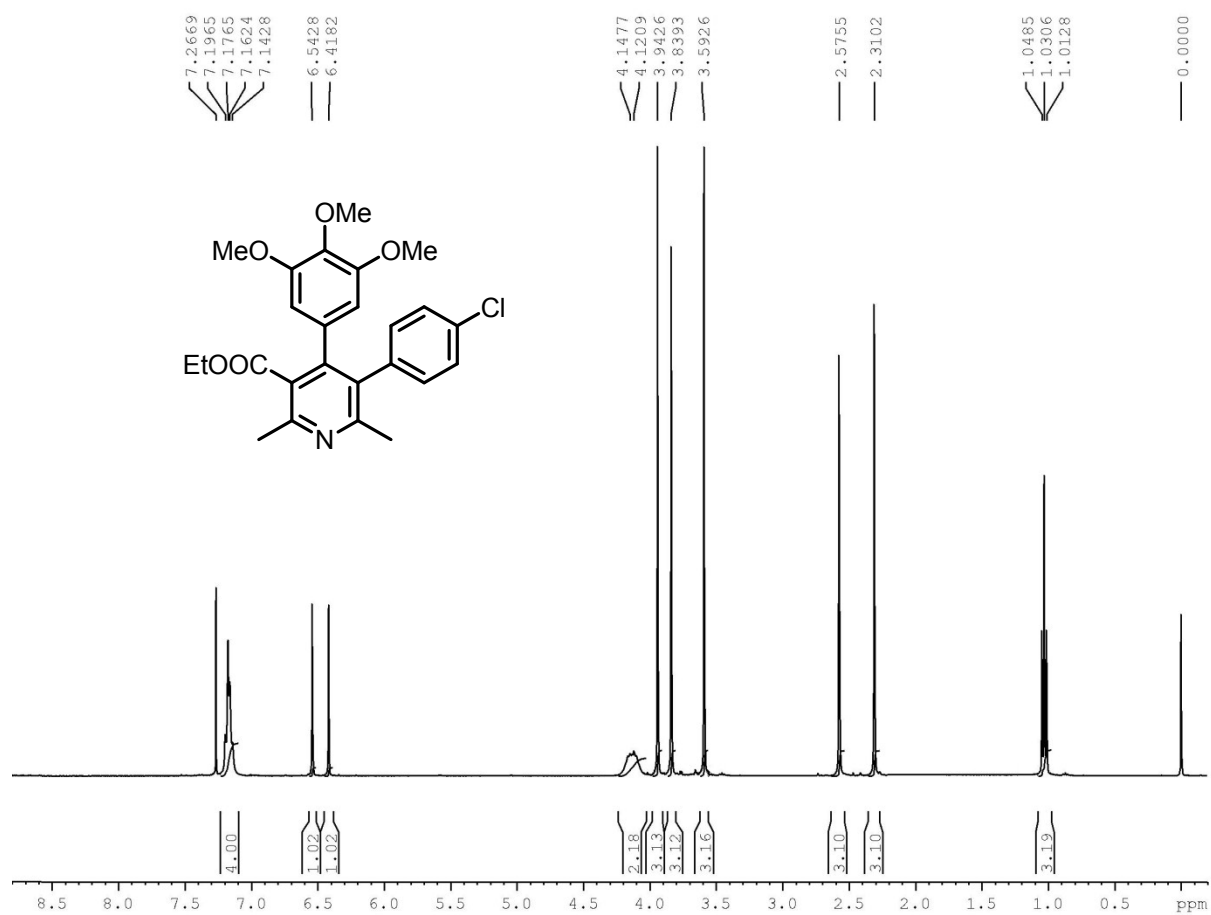
Scheme 4, Entry 7 (8g): ¹H NMR



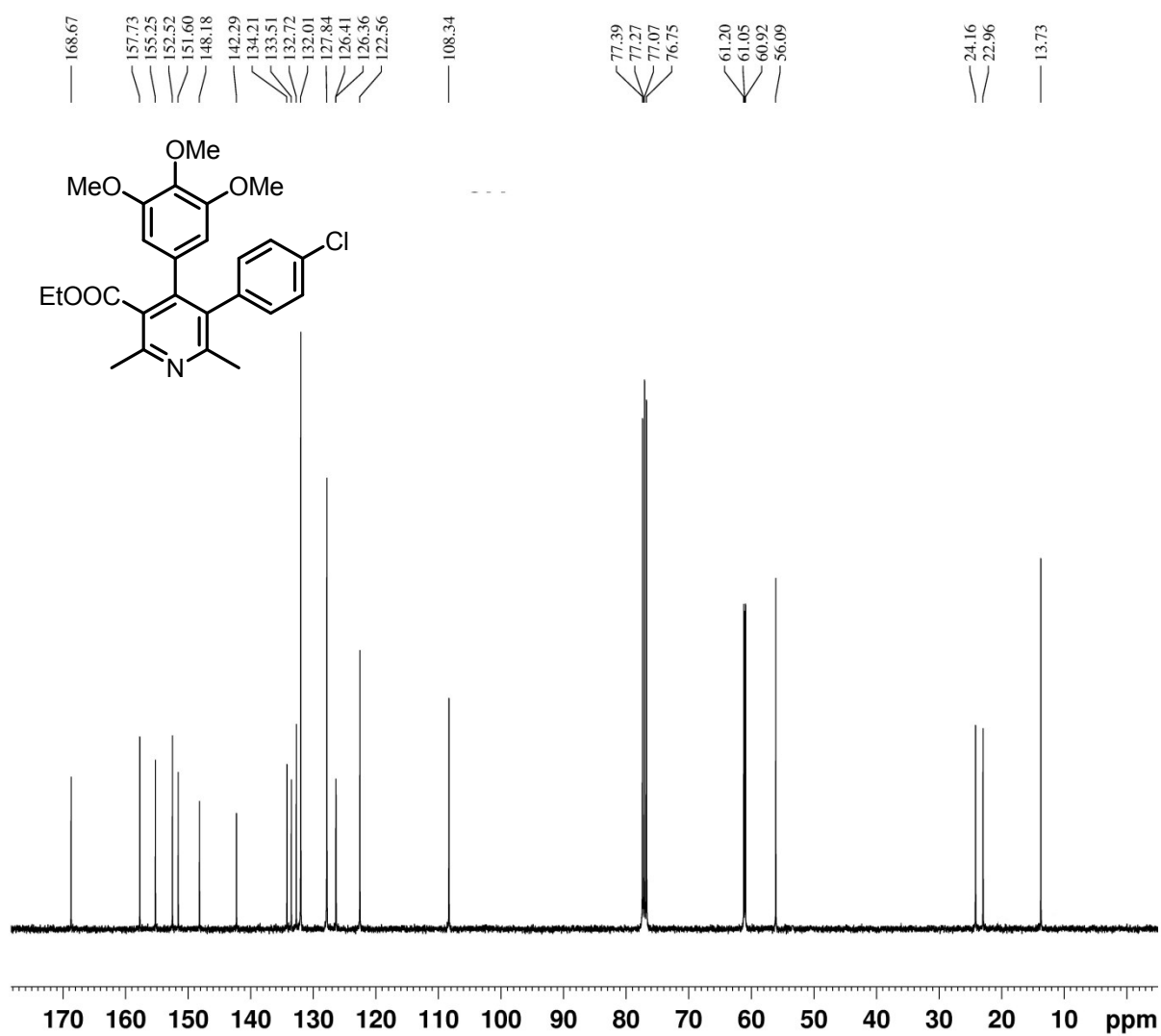
Scheme 4, Entry 7 (8g): ¹³C NMR



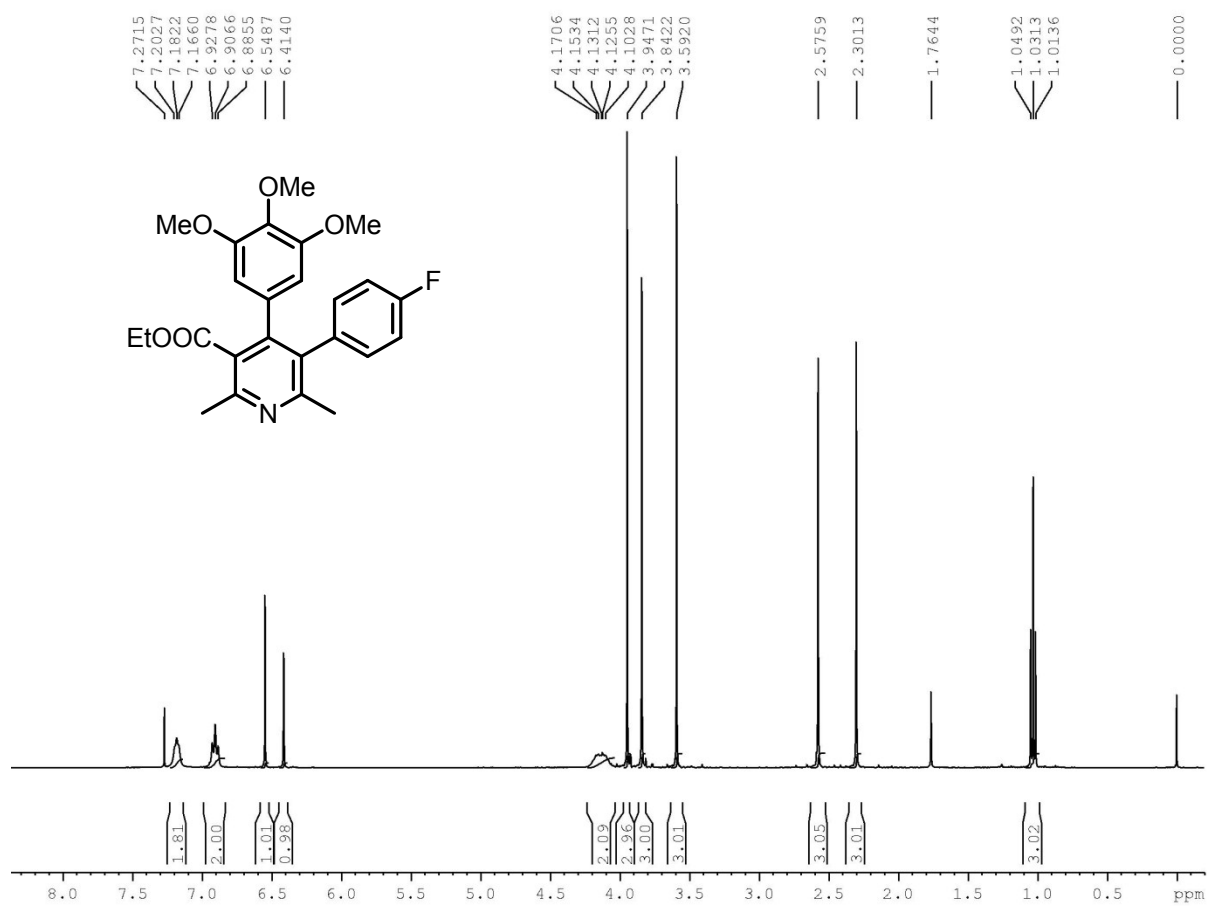
Scheme 4, Entry 8 (8h): ¹H NMR



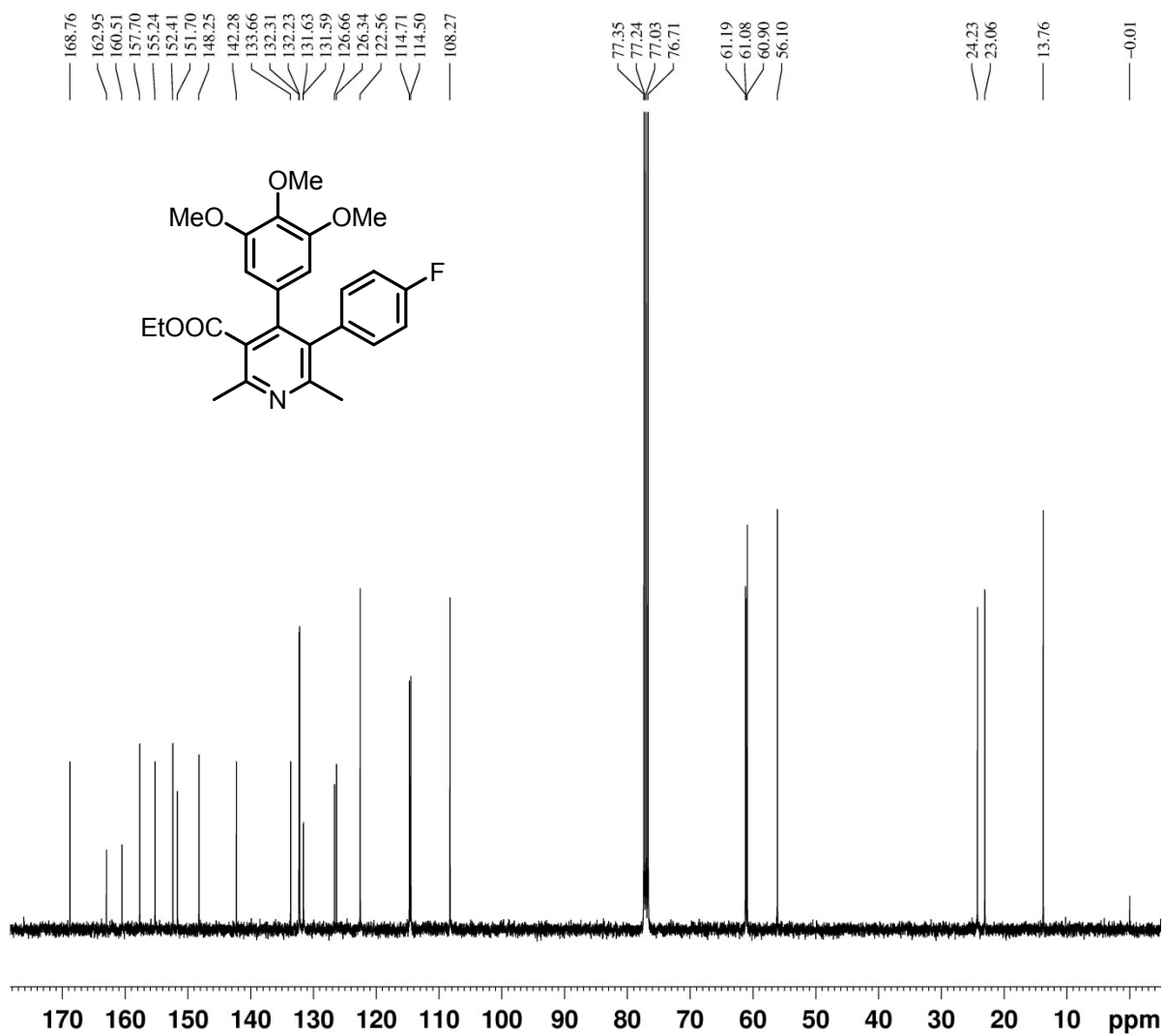
Scheme 4, Entry 8 (8h): ¹³C NMR



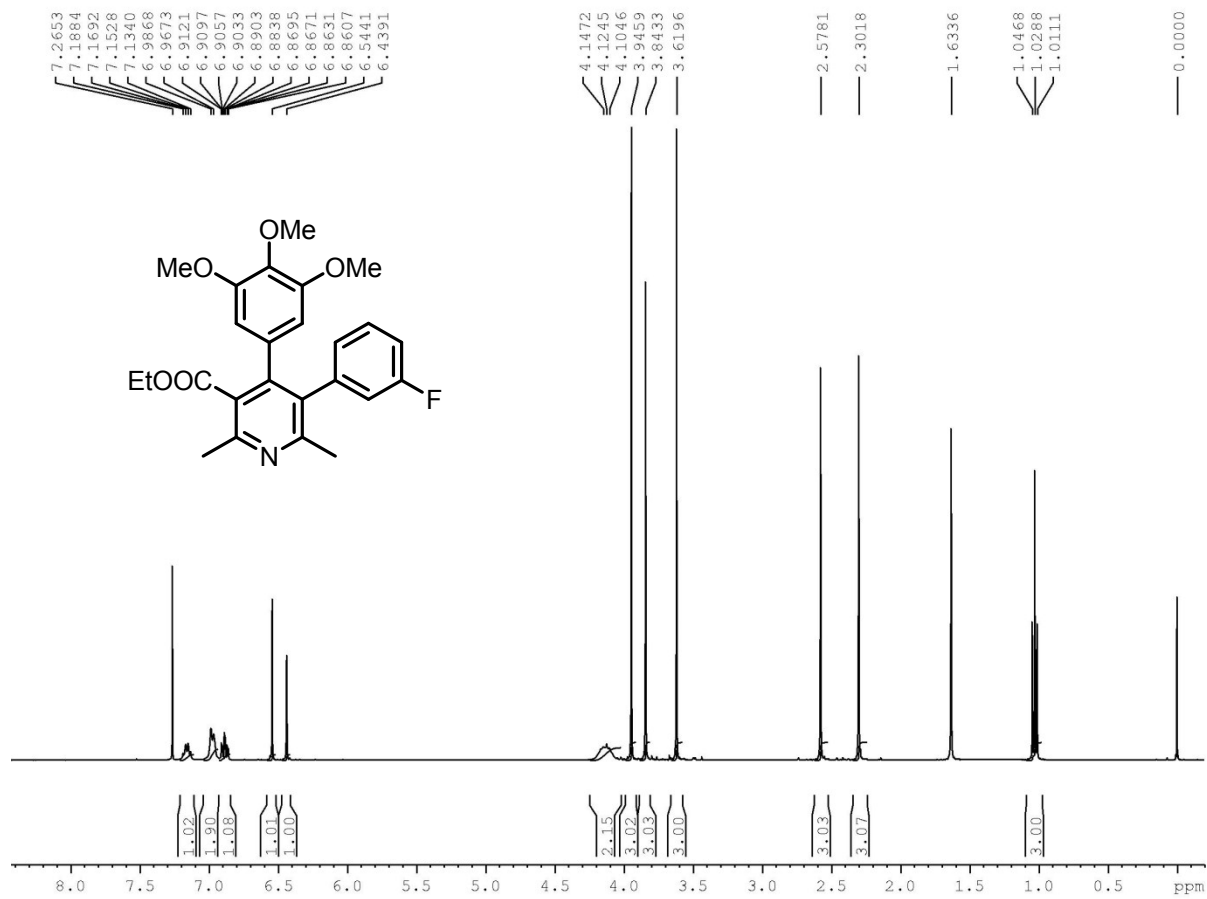
Scheme 4, Entry 9 (8i): ¹H NMR



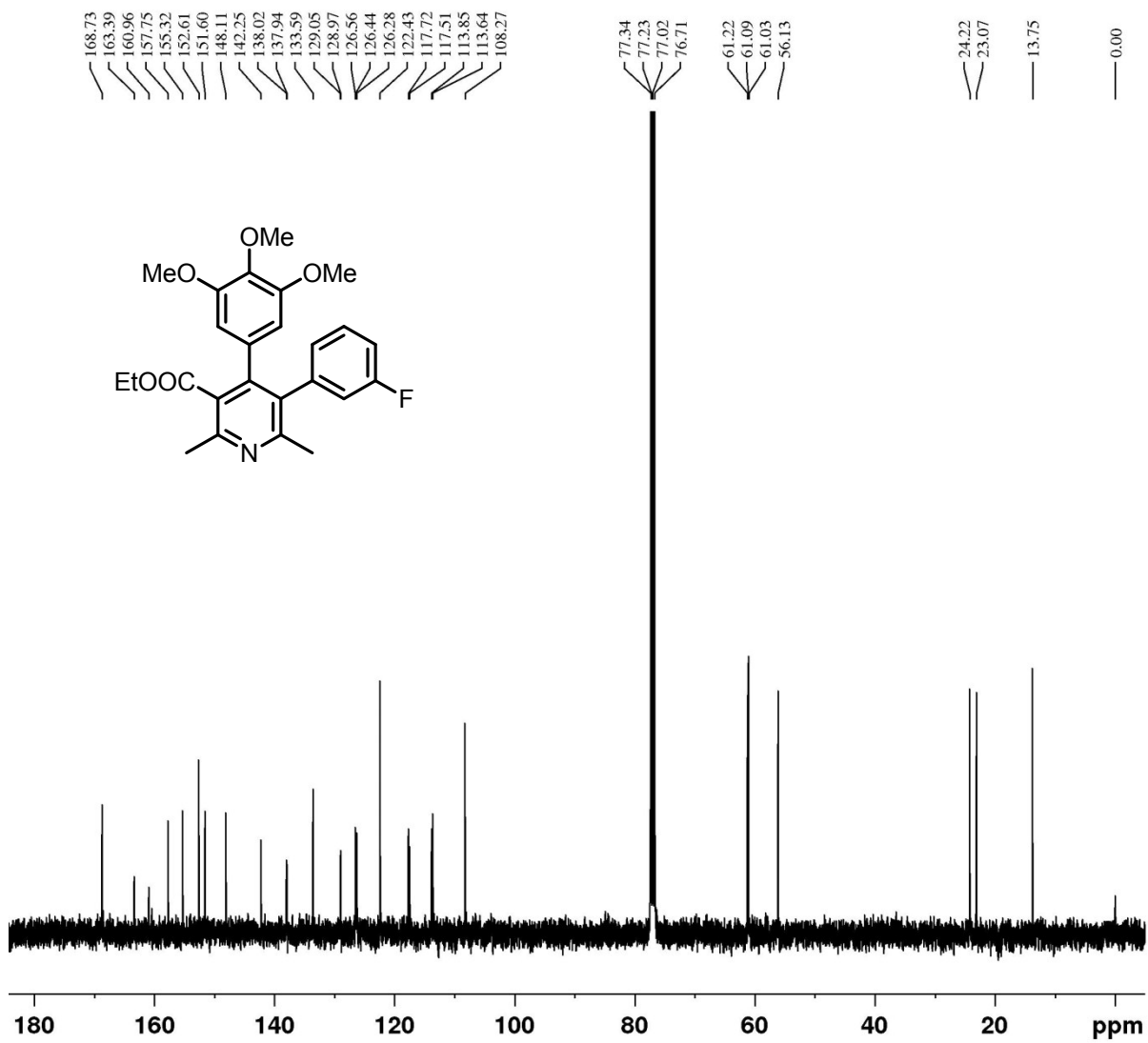
Scheme 4, Entry 9 (8i): ¹³C NMR



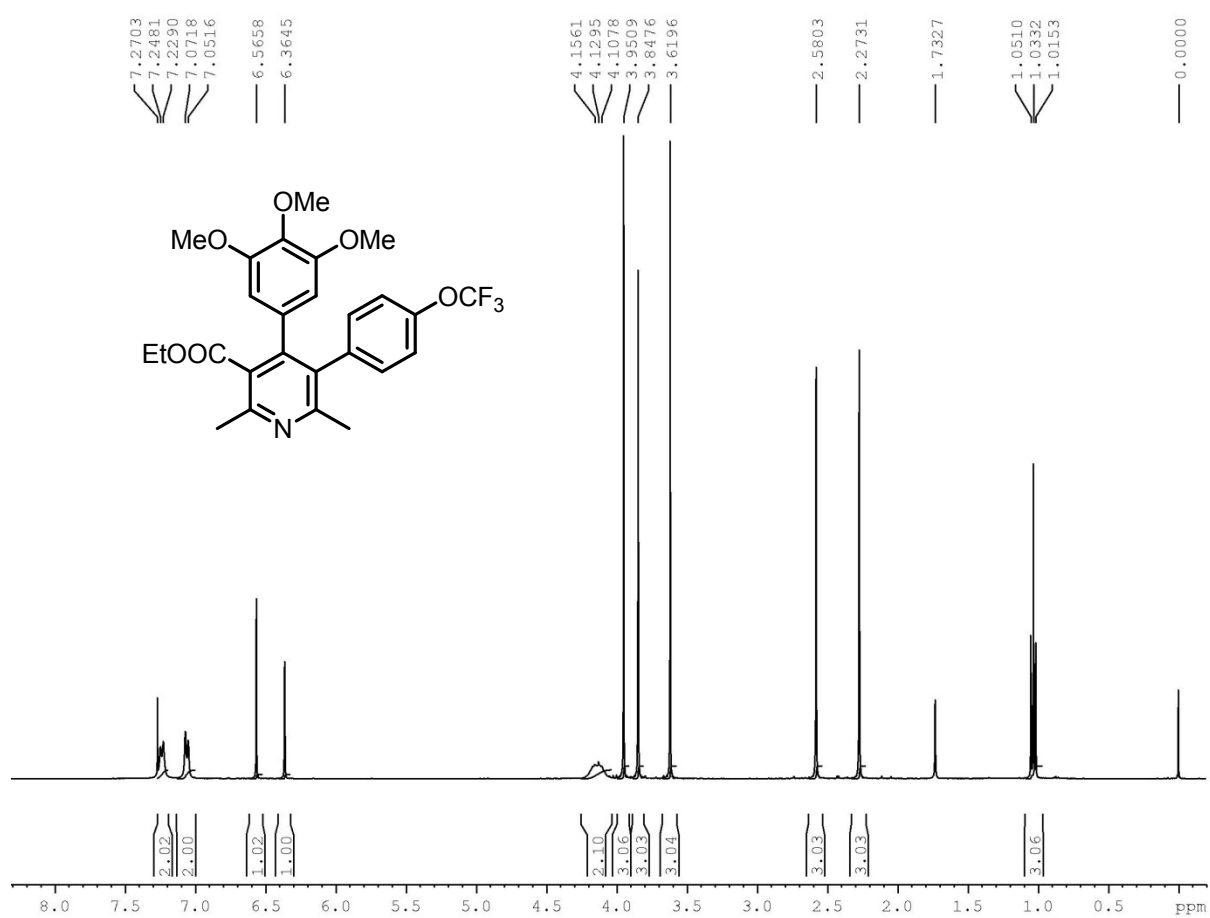
Scheme 4, Entry 10 (8j): ¹H NMR



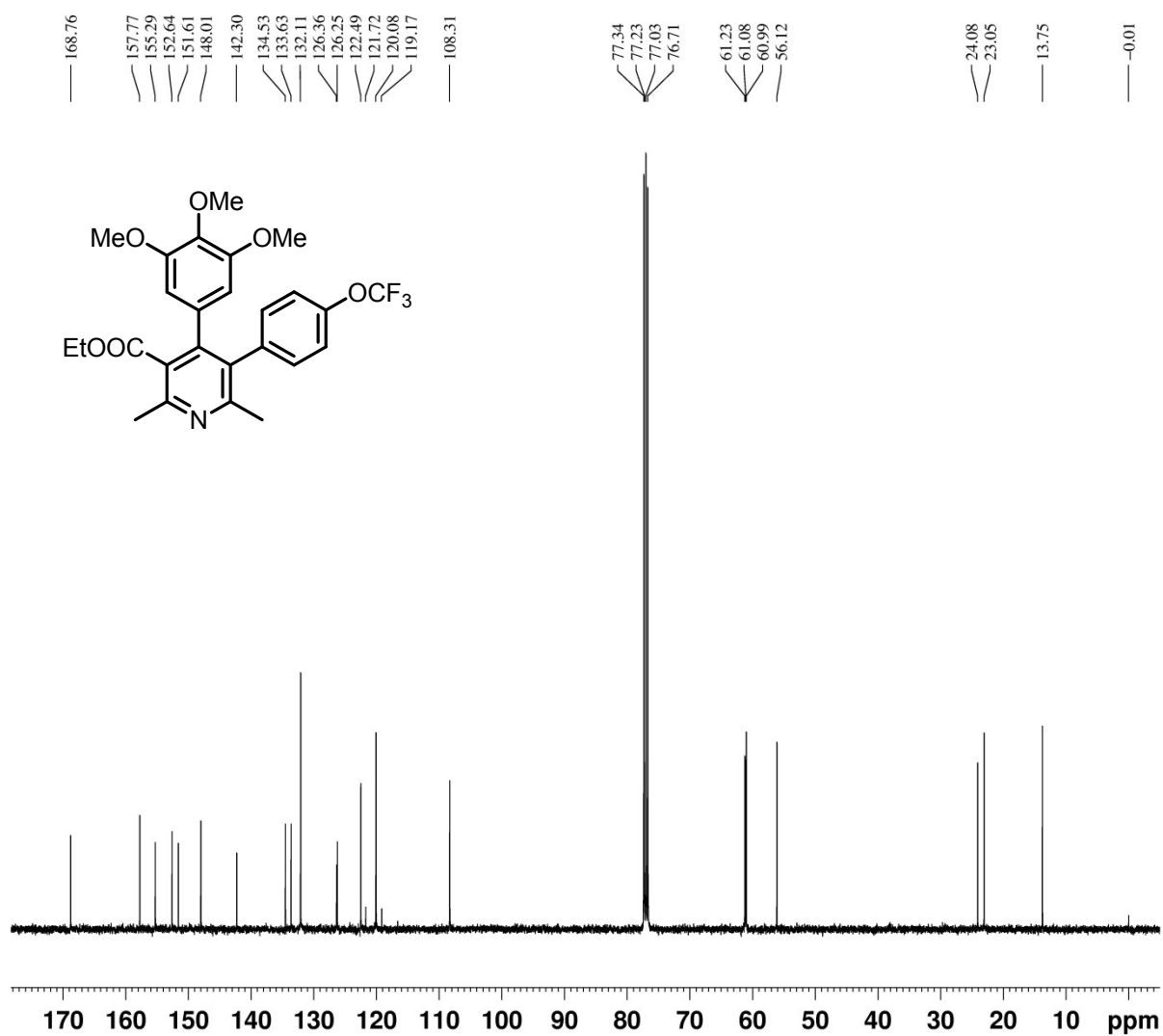
Scheme 4, Entry 10 (8j): ¹³C NMR



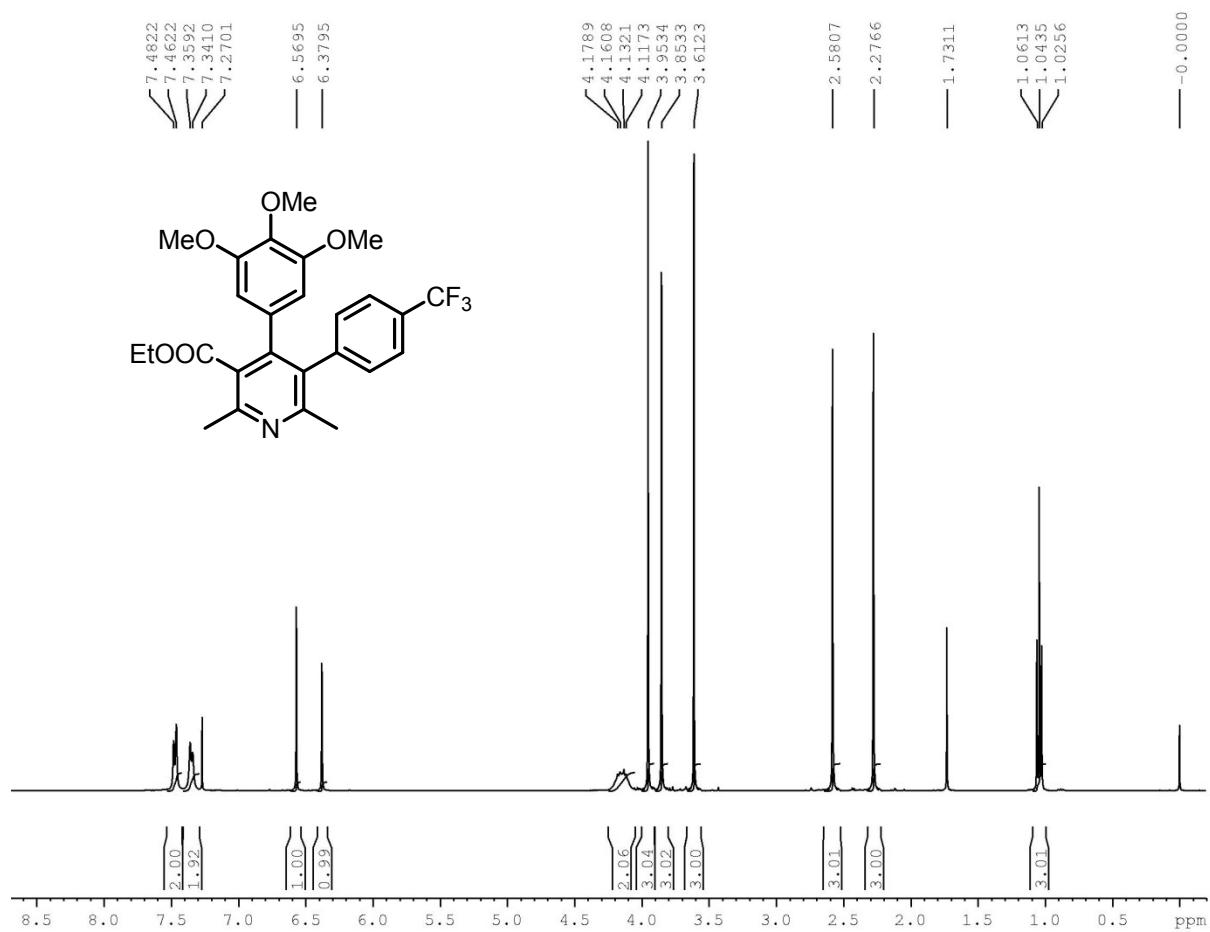
Scheme 4, Entry 11 (8k): ¹H NMR



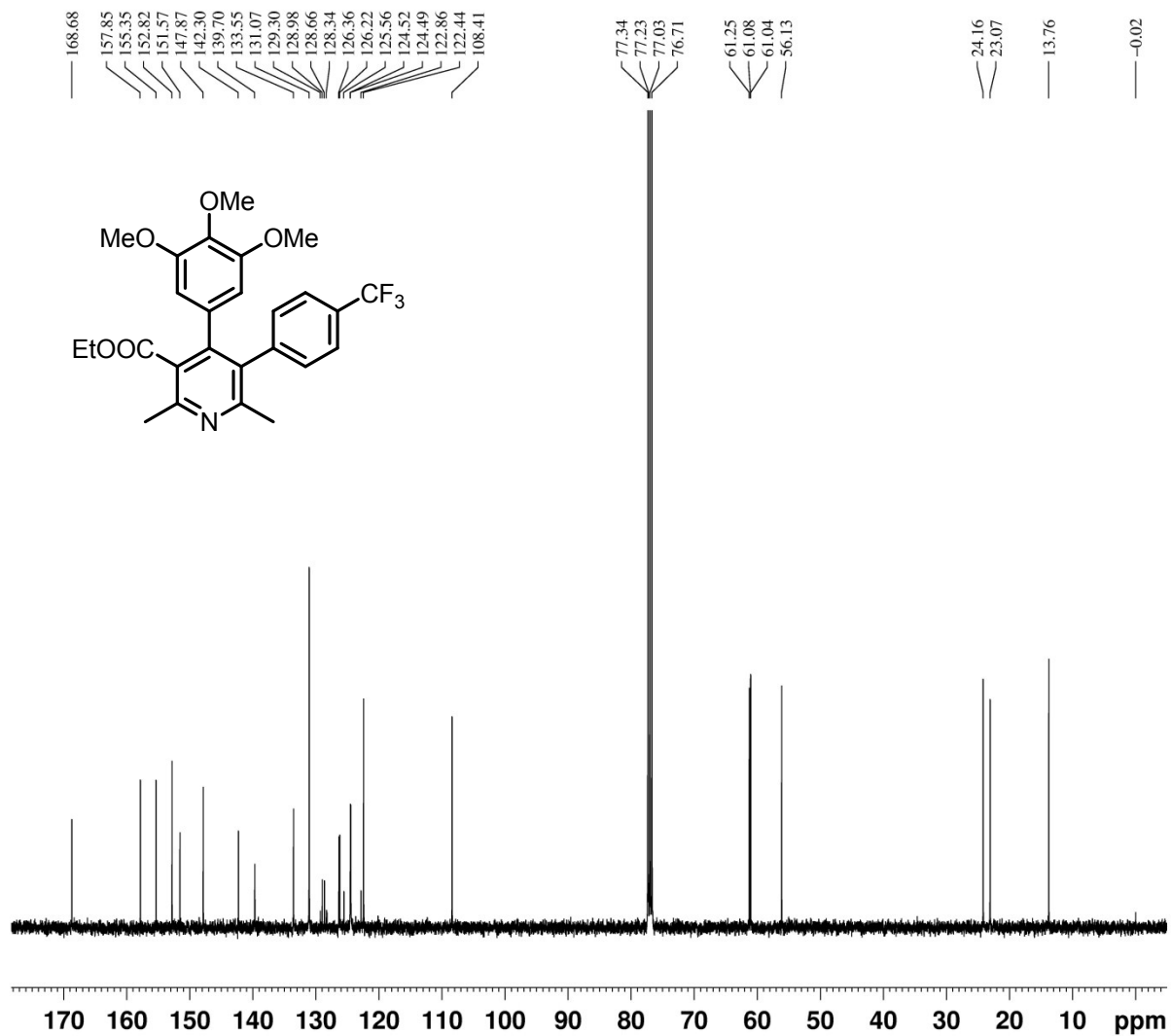
Scheme 4, Entry 11 (8k): ¹³C NMR



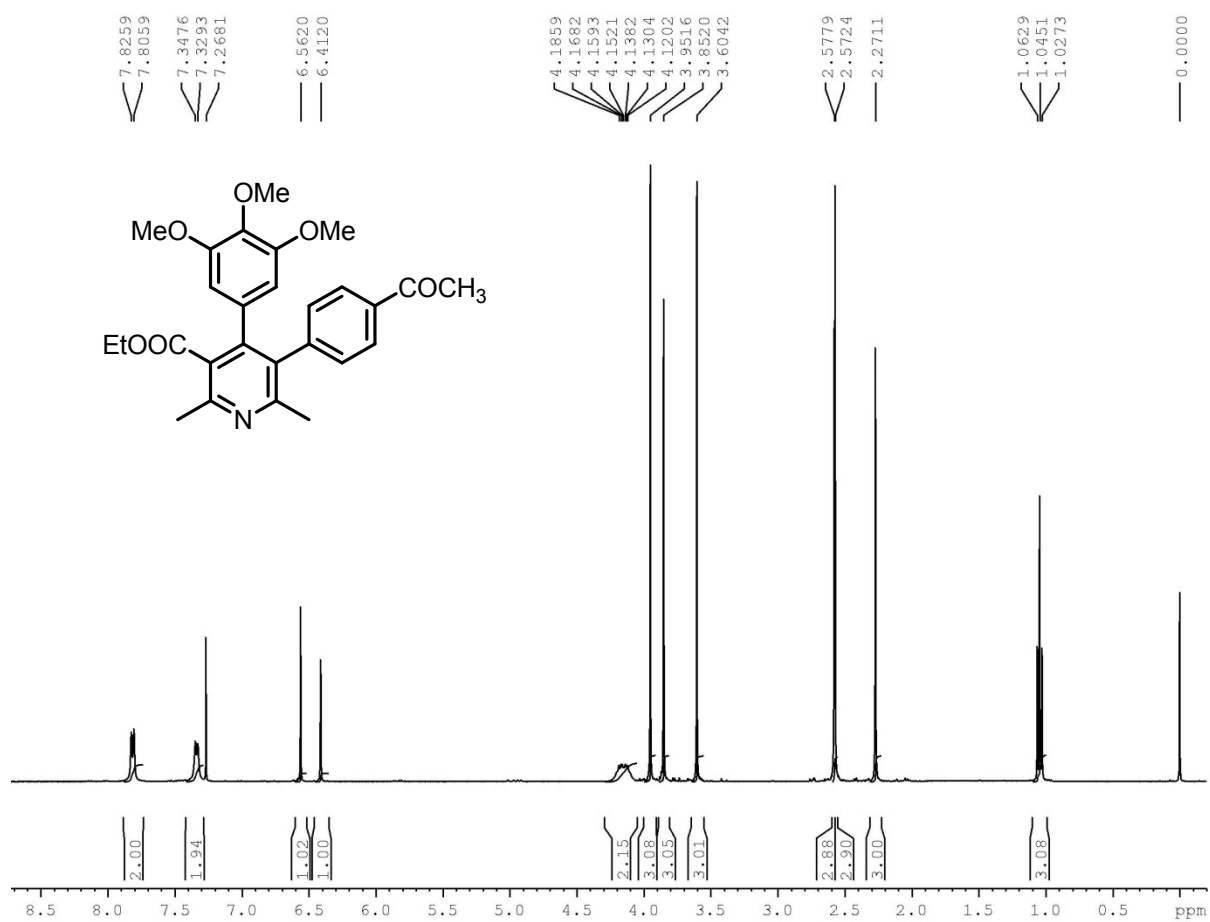
Scheme 4, Entry 12 (8l): ¹H NMR



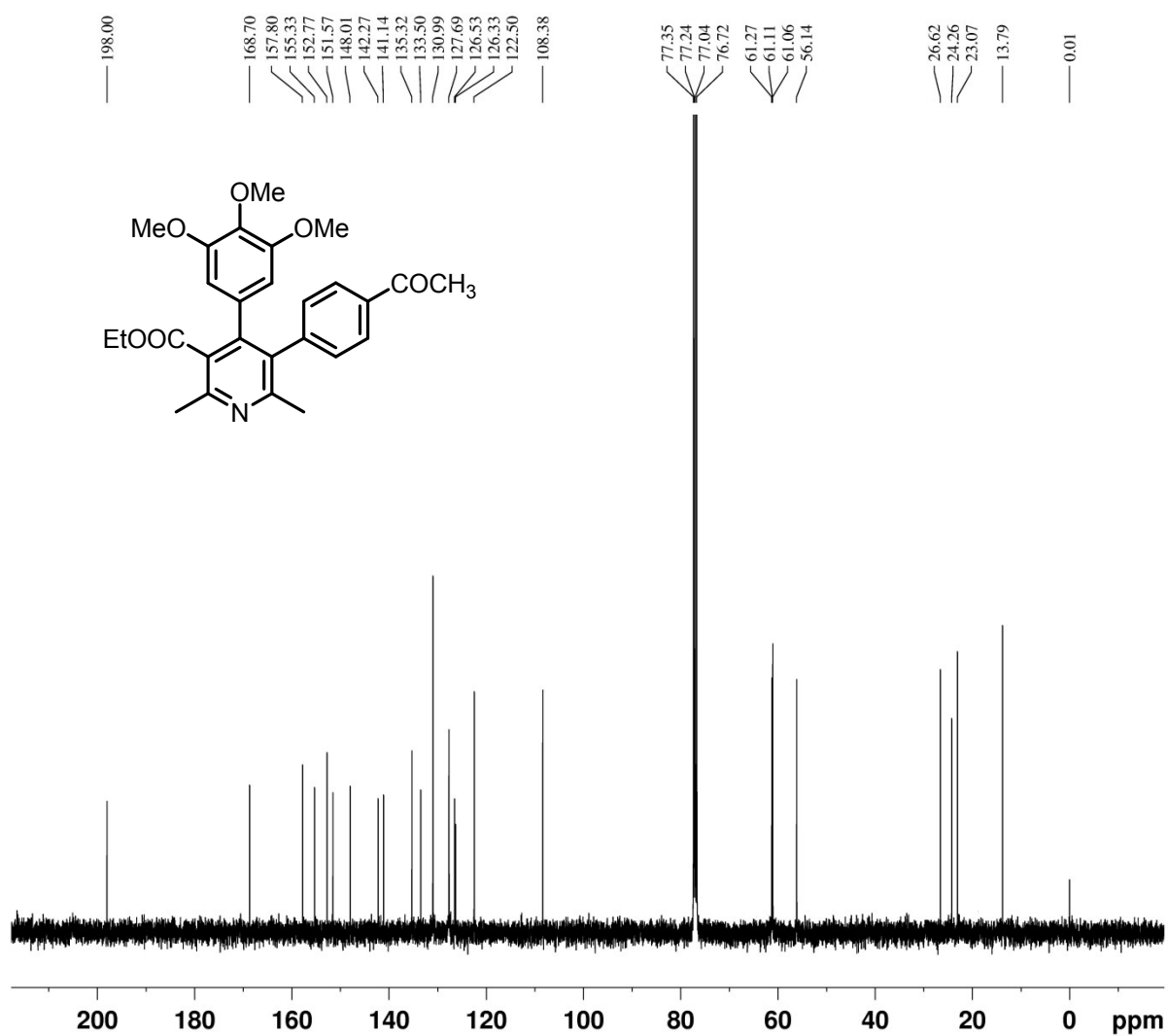
Scheme 4, Entry 12 (81): ¹³C NMR



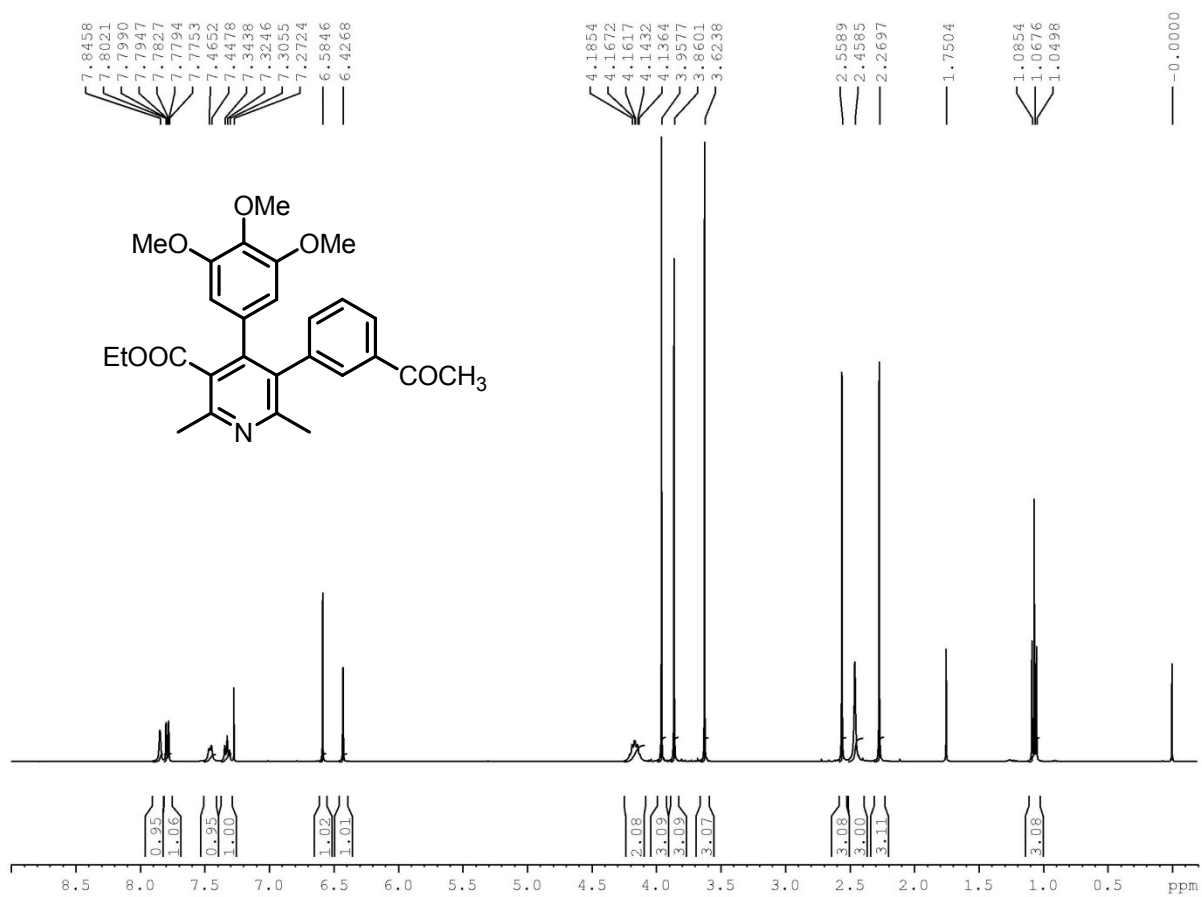
Scheme 4, Entry 13 (8m): ¹H NMR



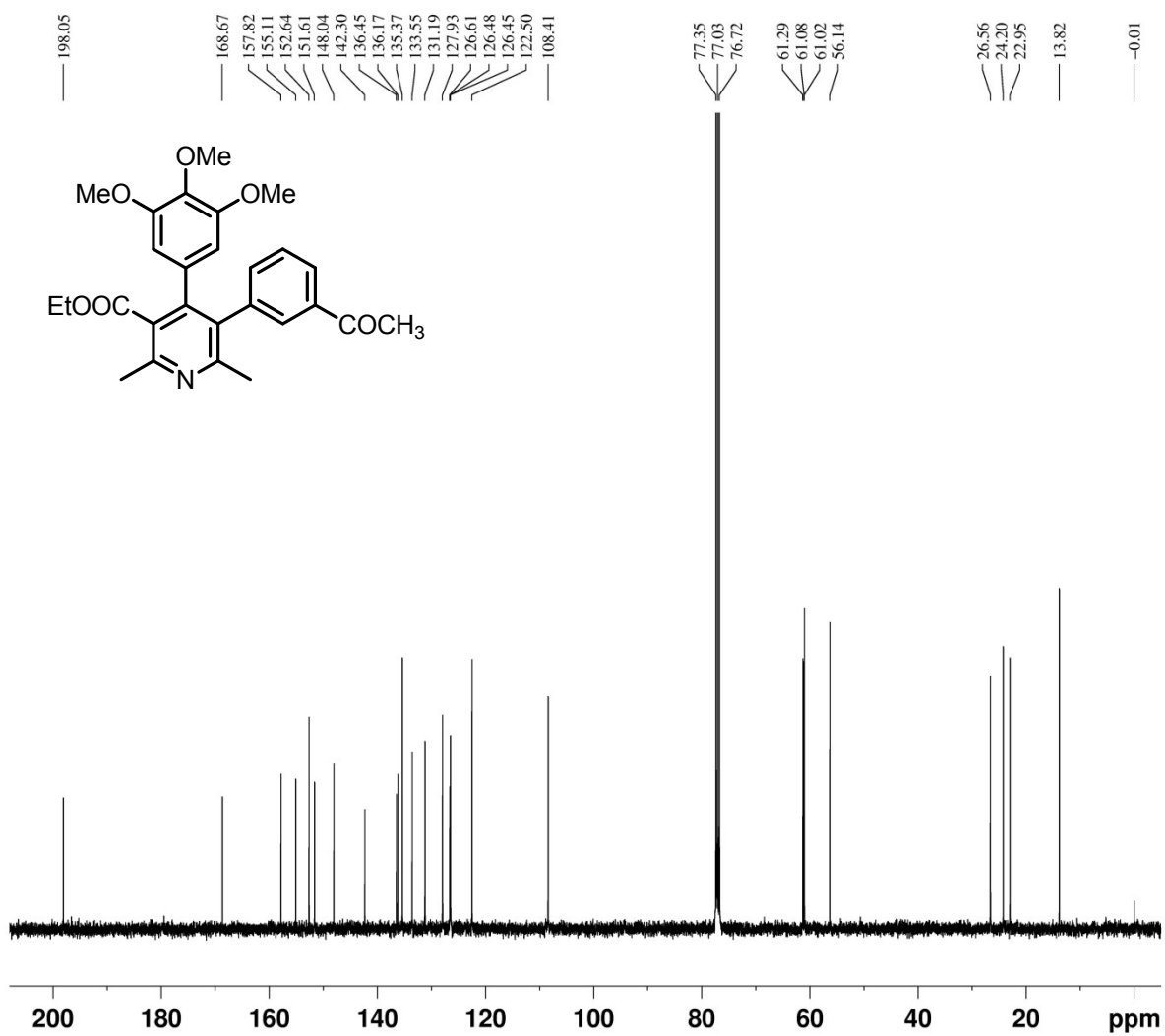
Scheme 4, Entry 13 (8m): ¹³C NMR



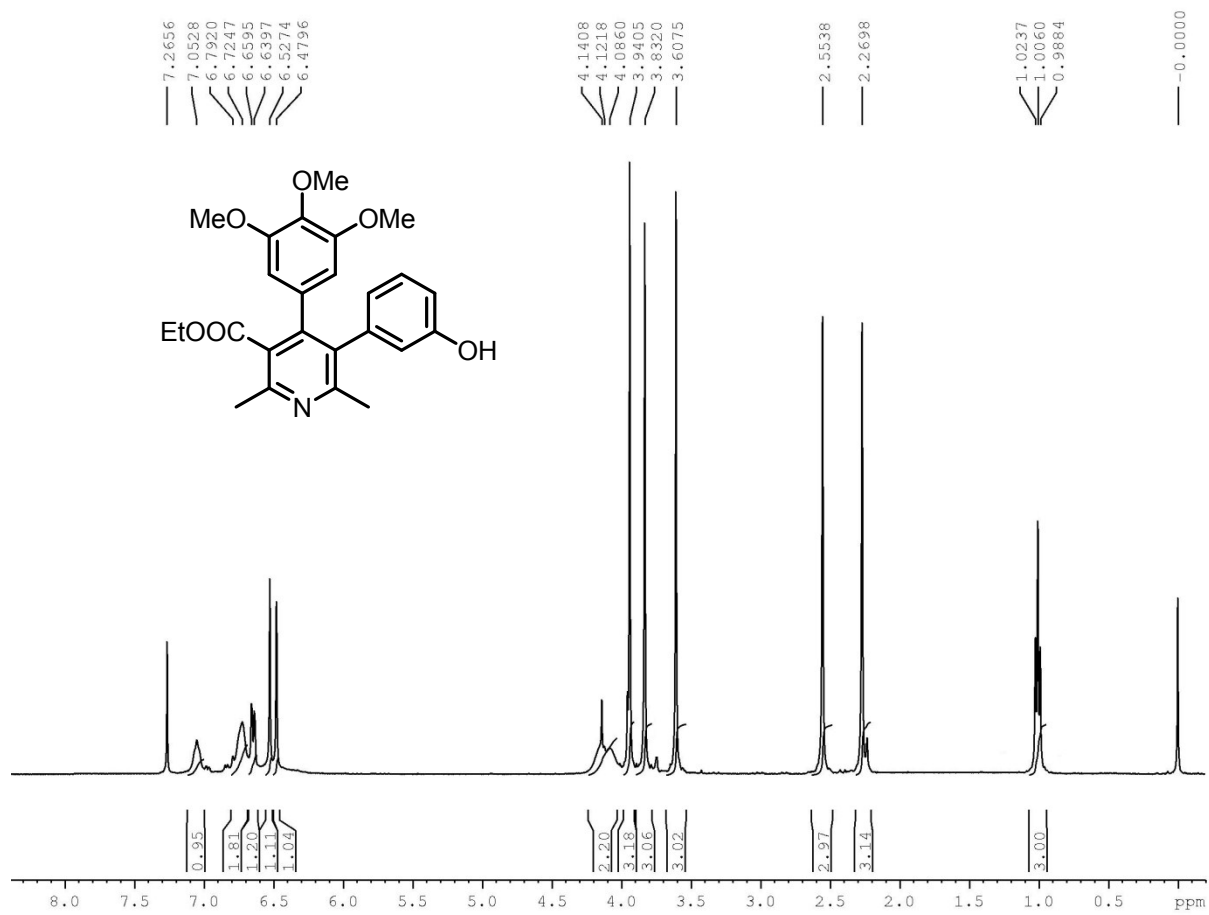
Scheme 4, Entry 14 (8n): ¹H NMR



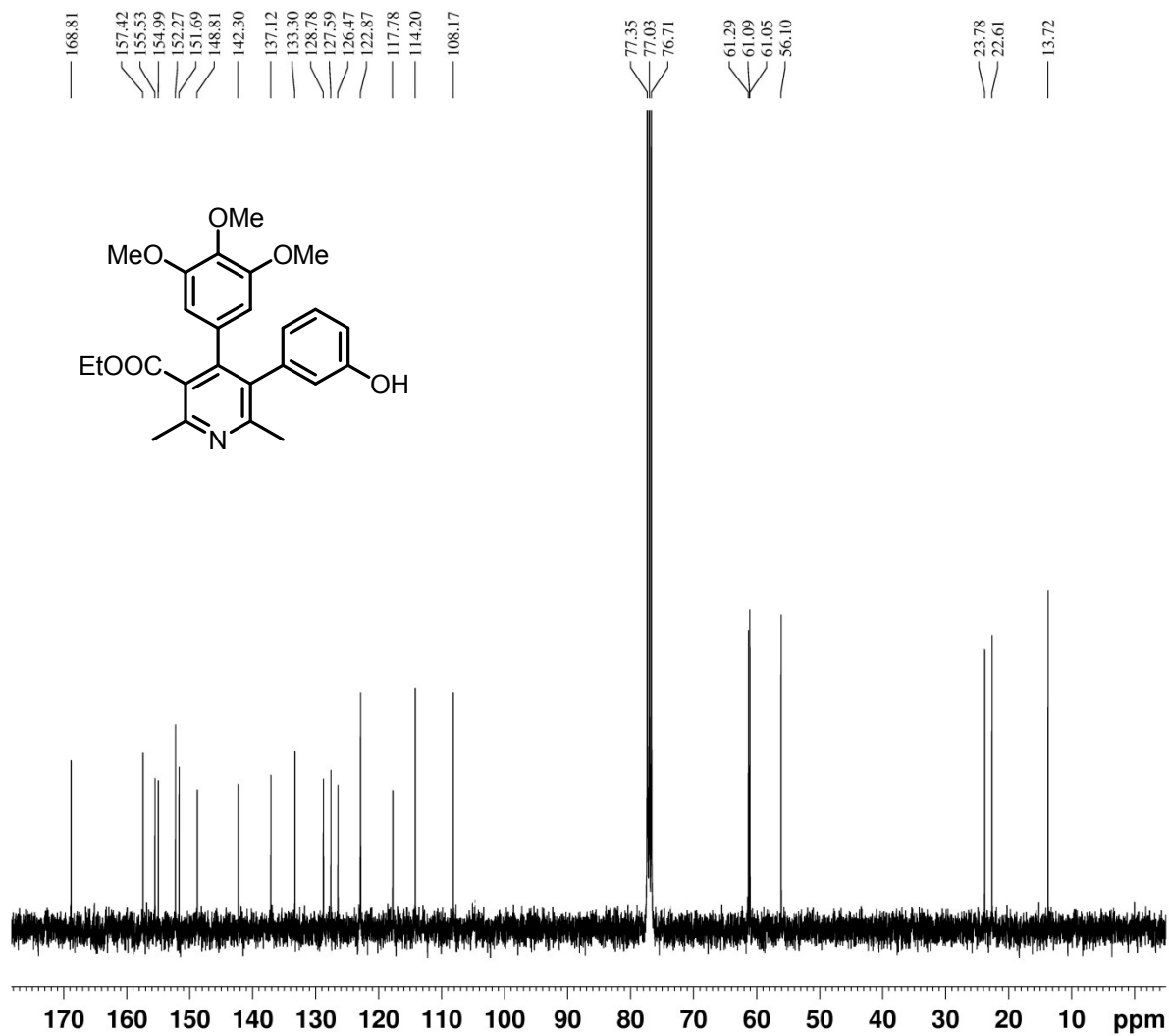
Scheme 4, Entry 14 (8n): ¹³C NMR



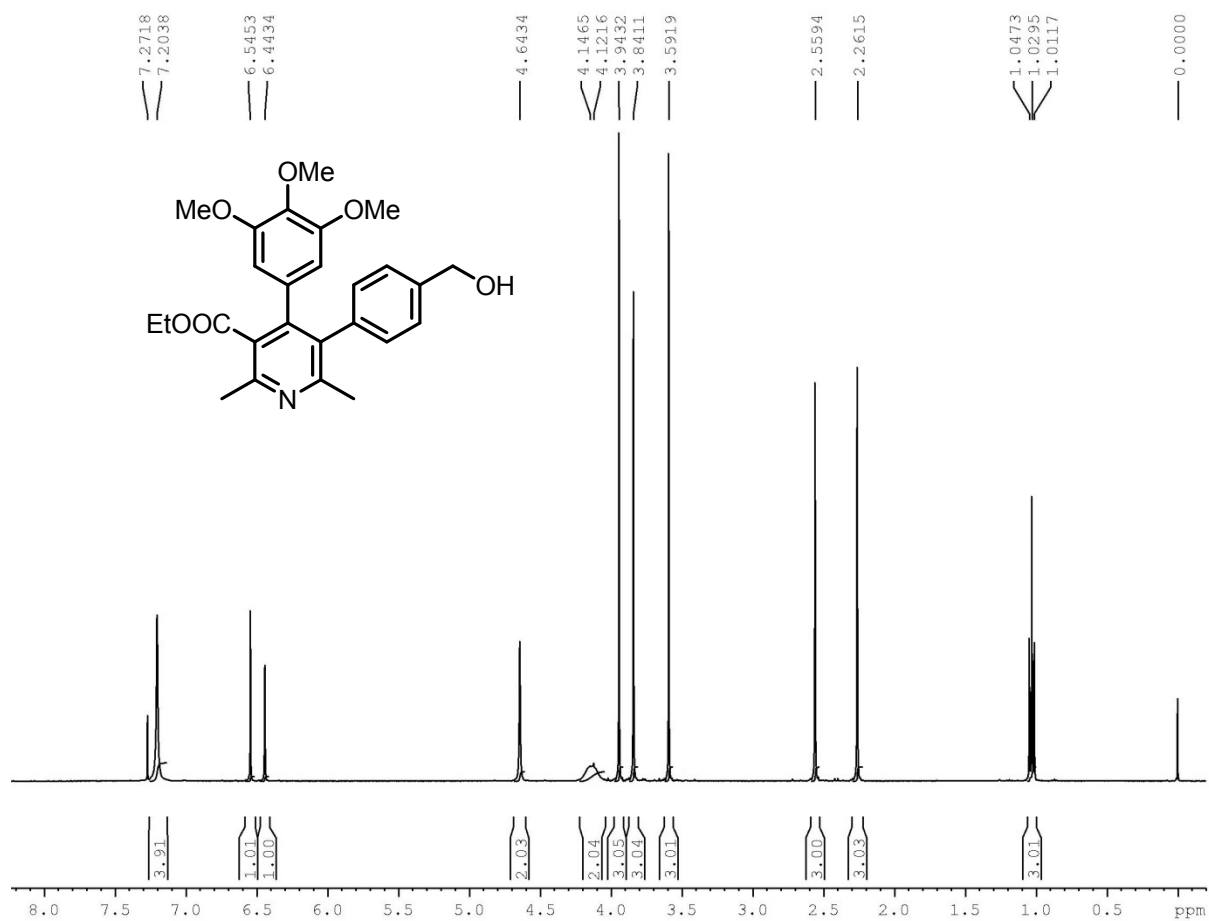
Scheme 4, Entry 15 (8o): ¹H NMR



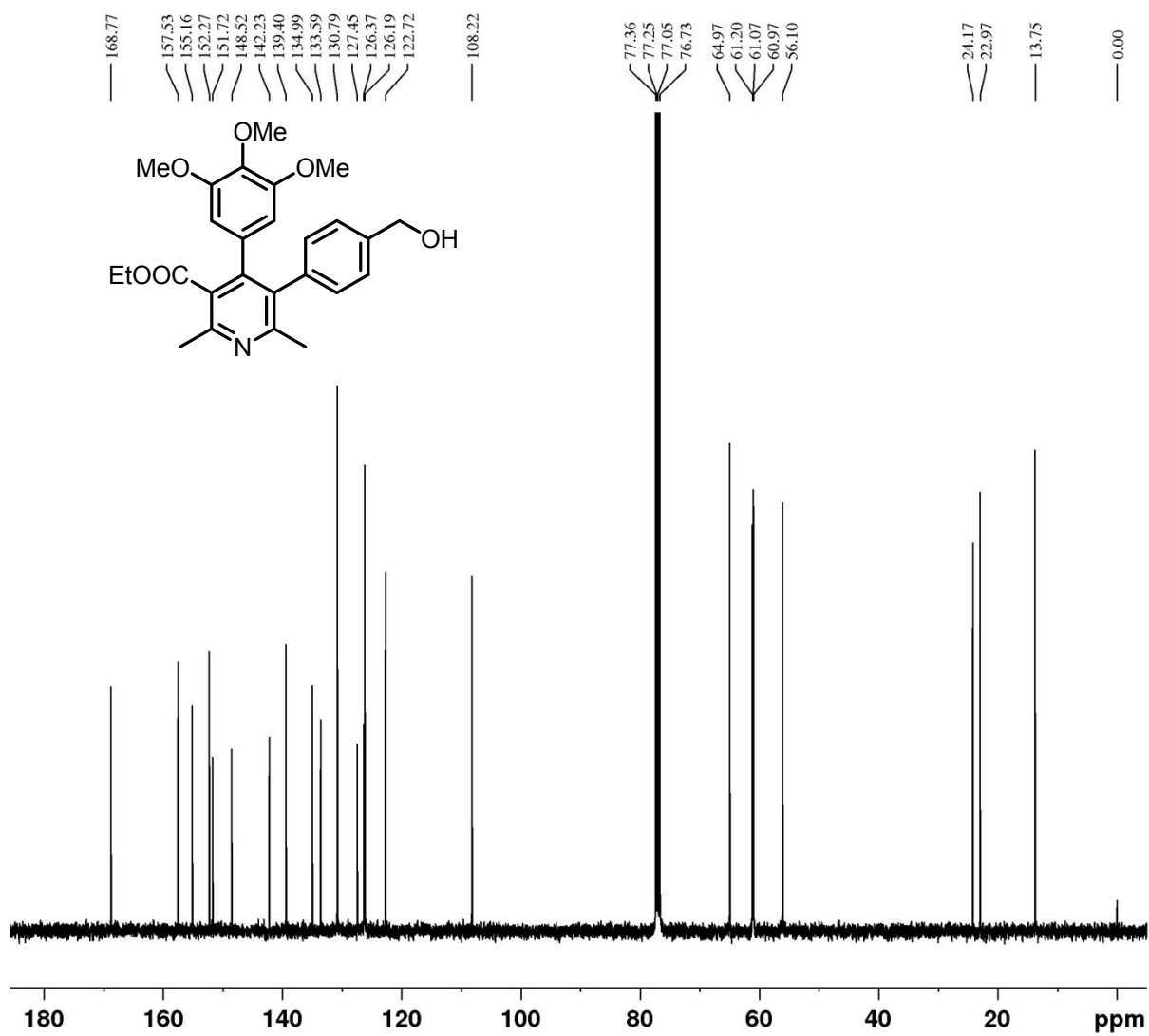
Scheme 4, Entry 15 (**8o**): ^{13}C NMR



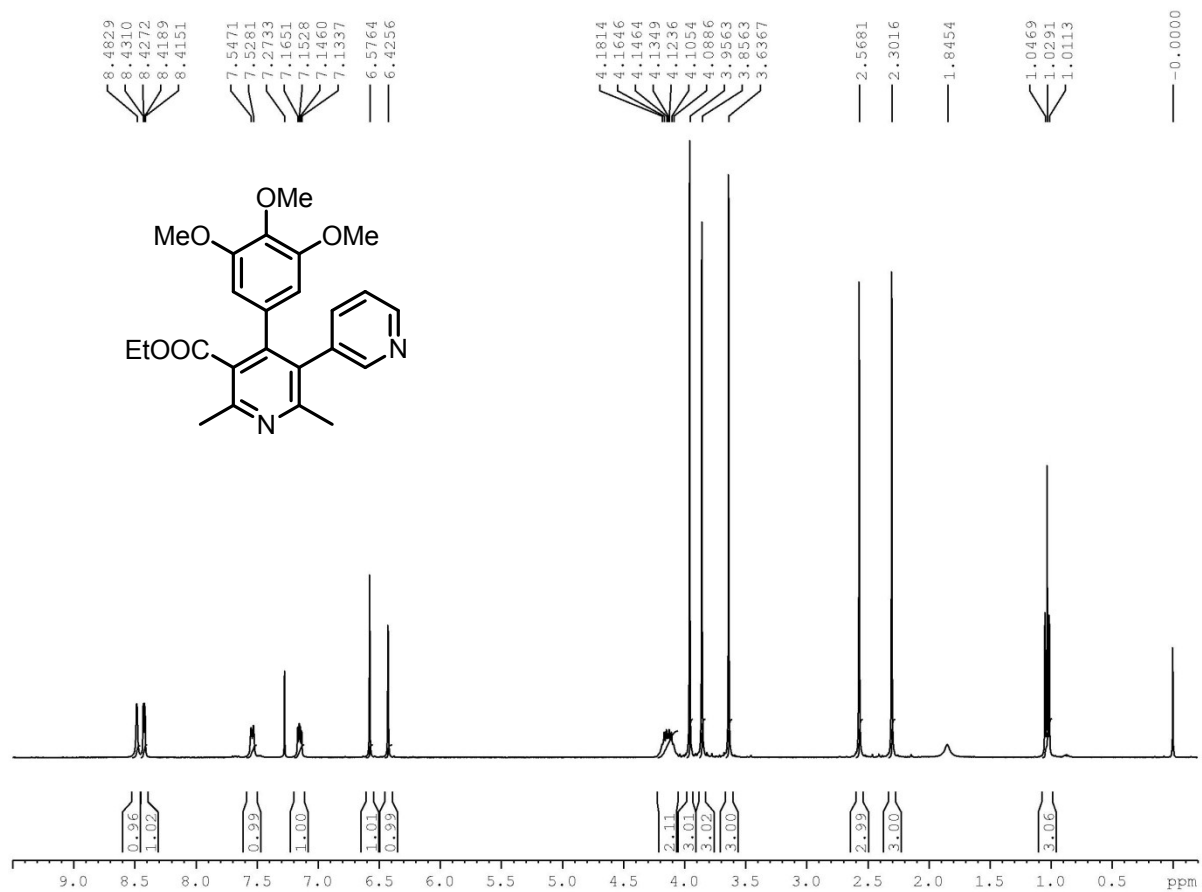
Scheme 4, Entry 16 (8p): ¹H NMR



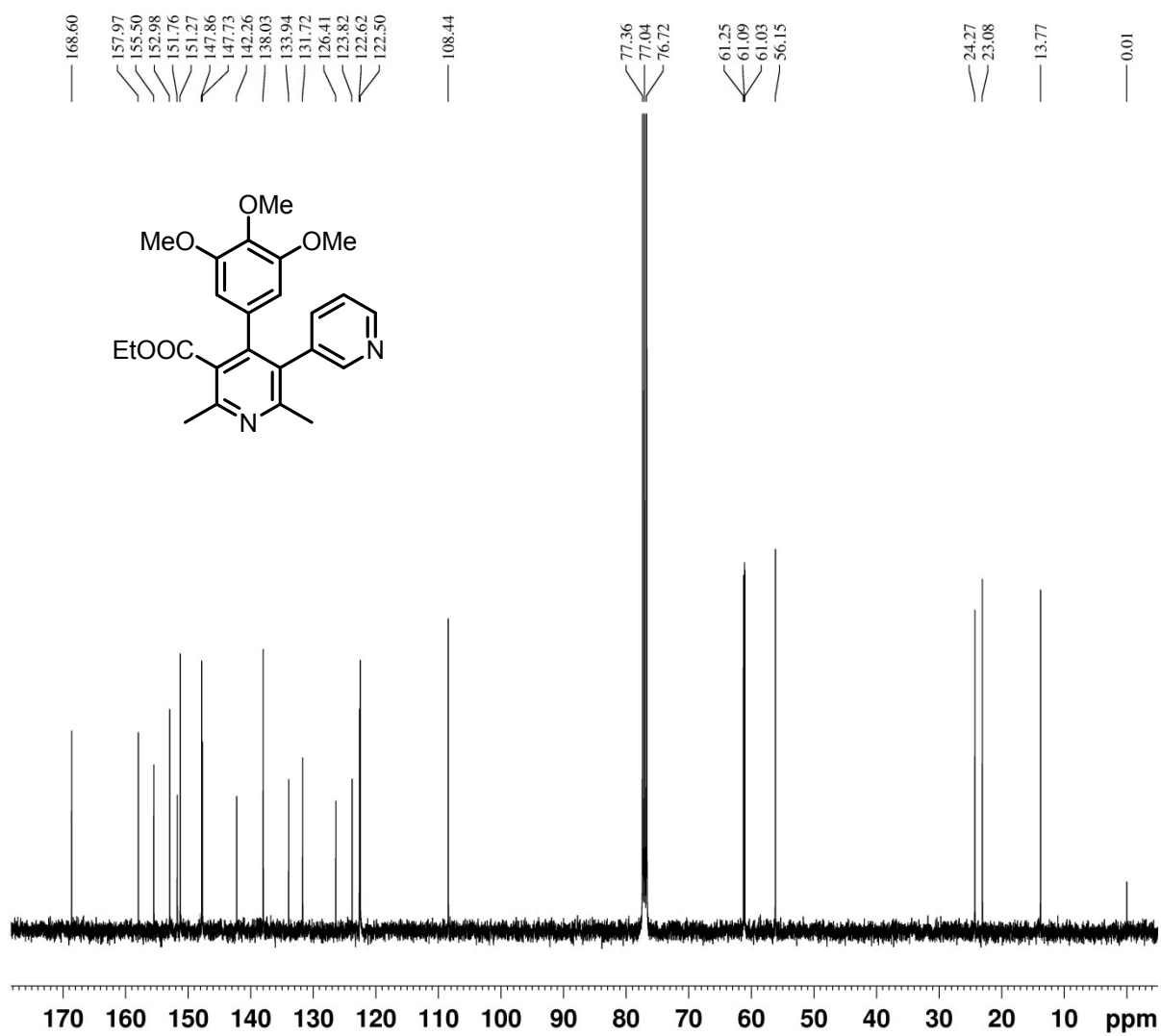
Scheme 4, Entry 16 (8p): ¹³C NMR



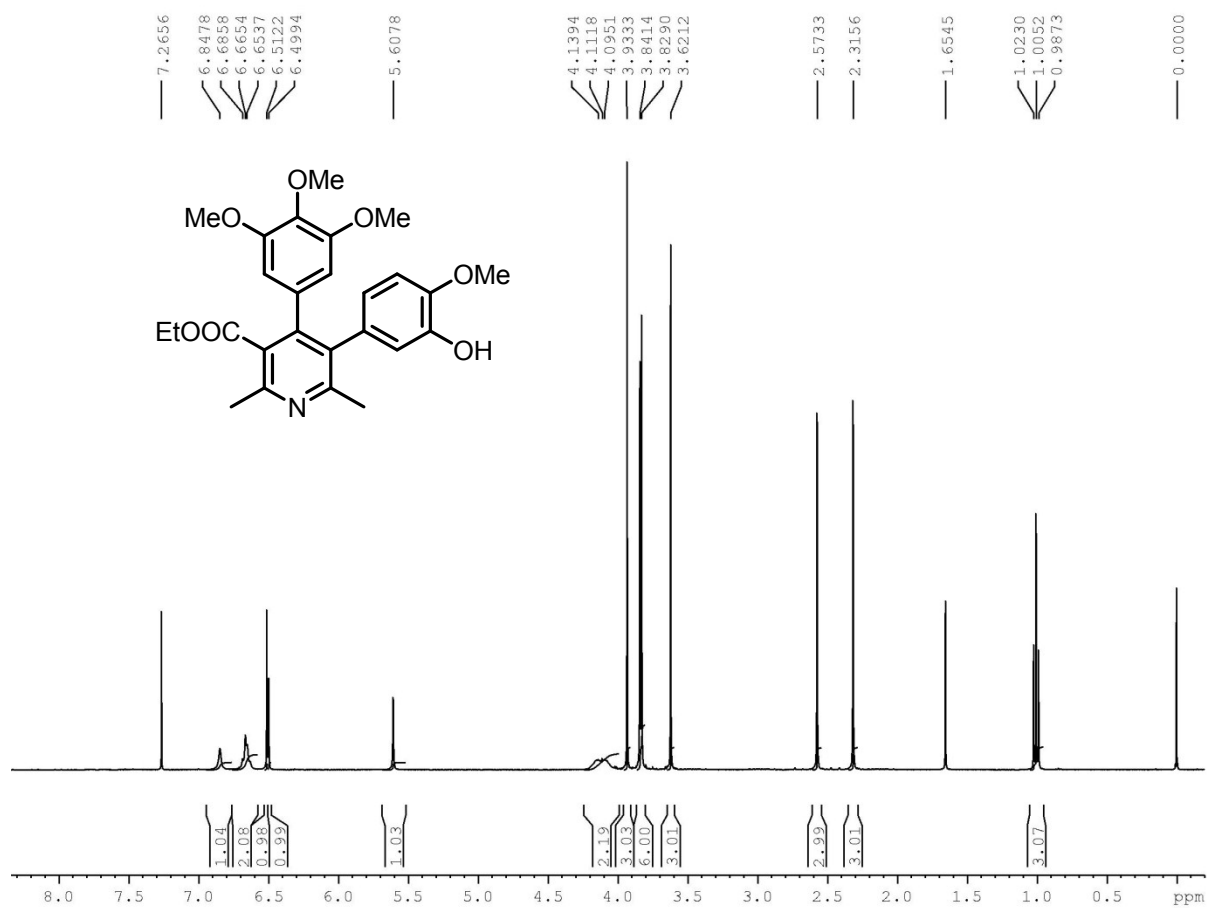
Scheme 4, Entry 17 (8q): ¹H NMR



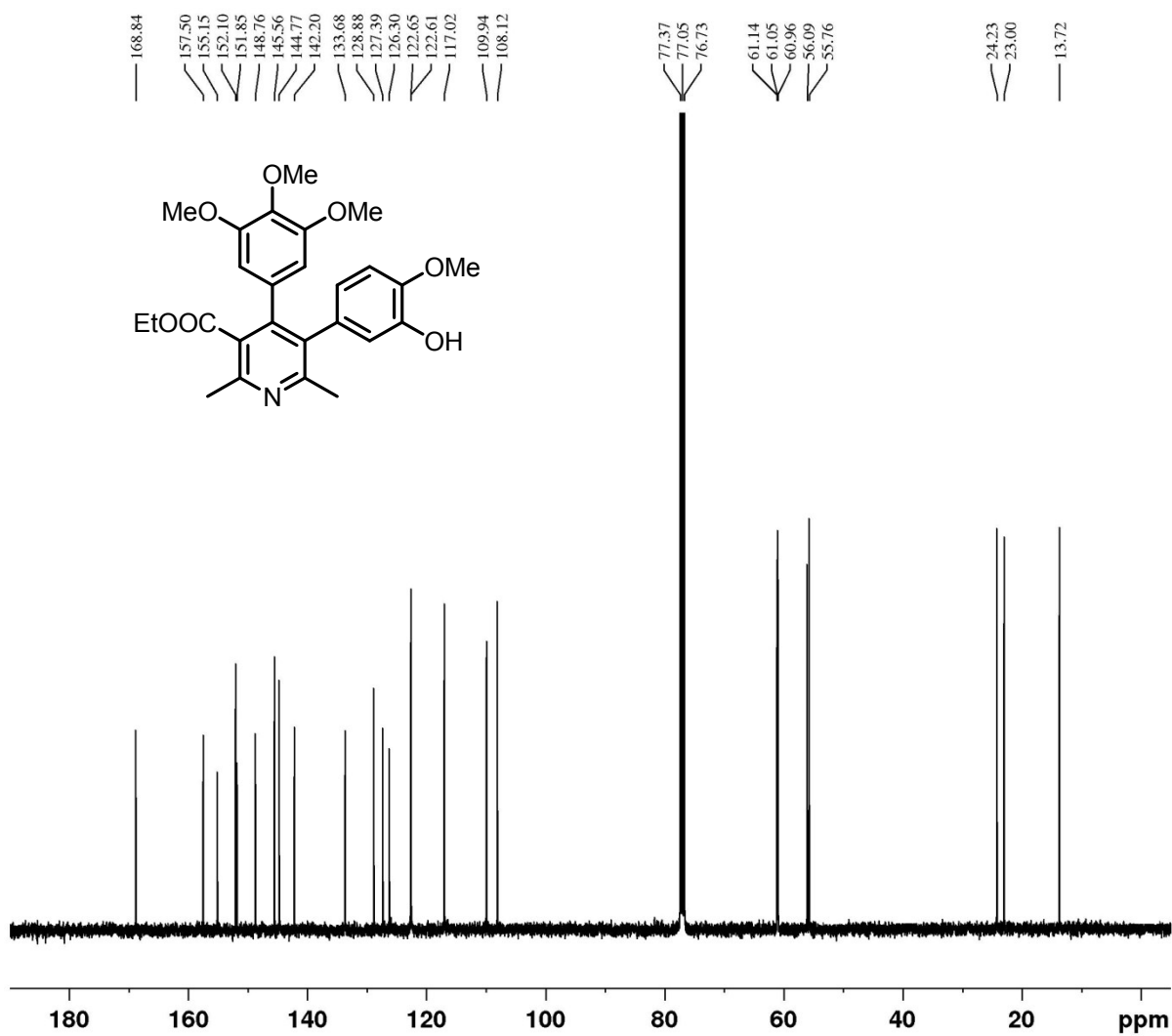
Scheme 4, Entry 17 (8q): ¹³C NMR



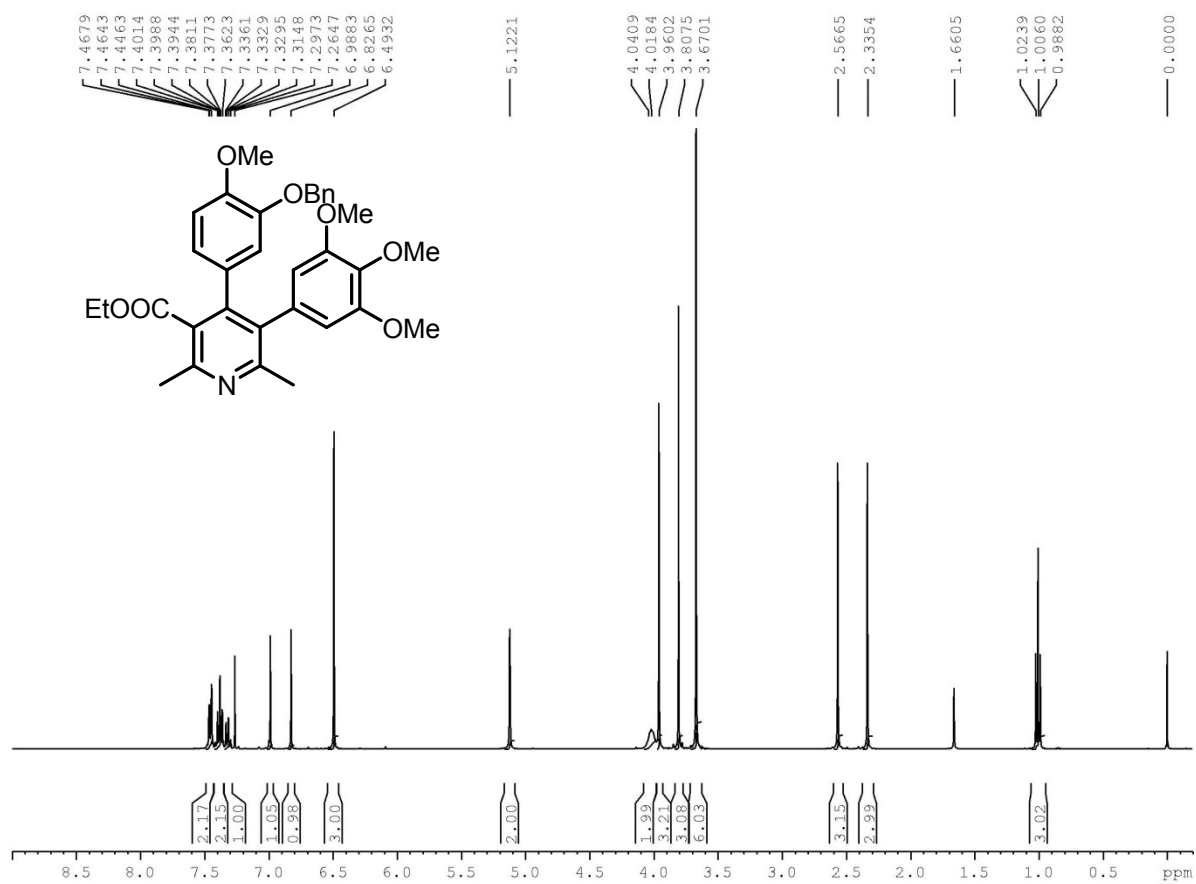
Scheme 5, 8r: ¹H NMR



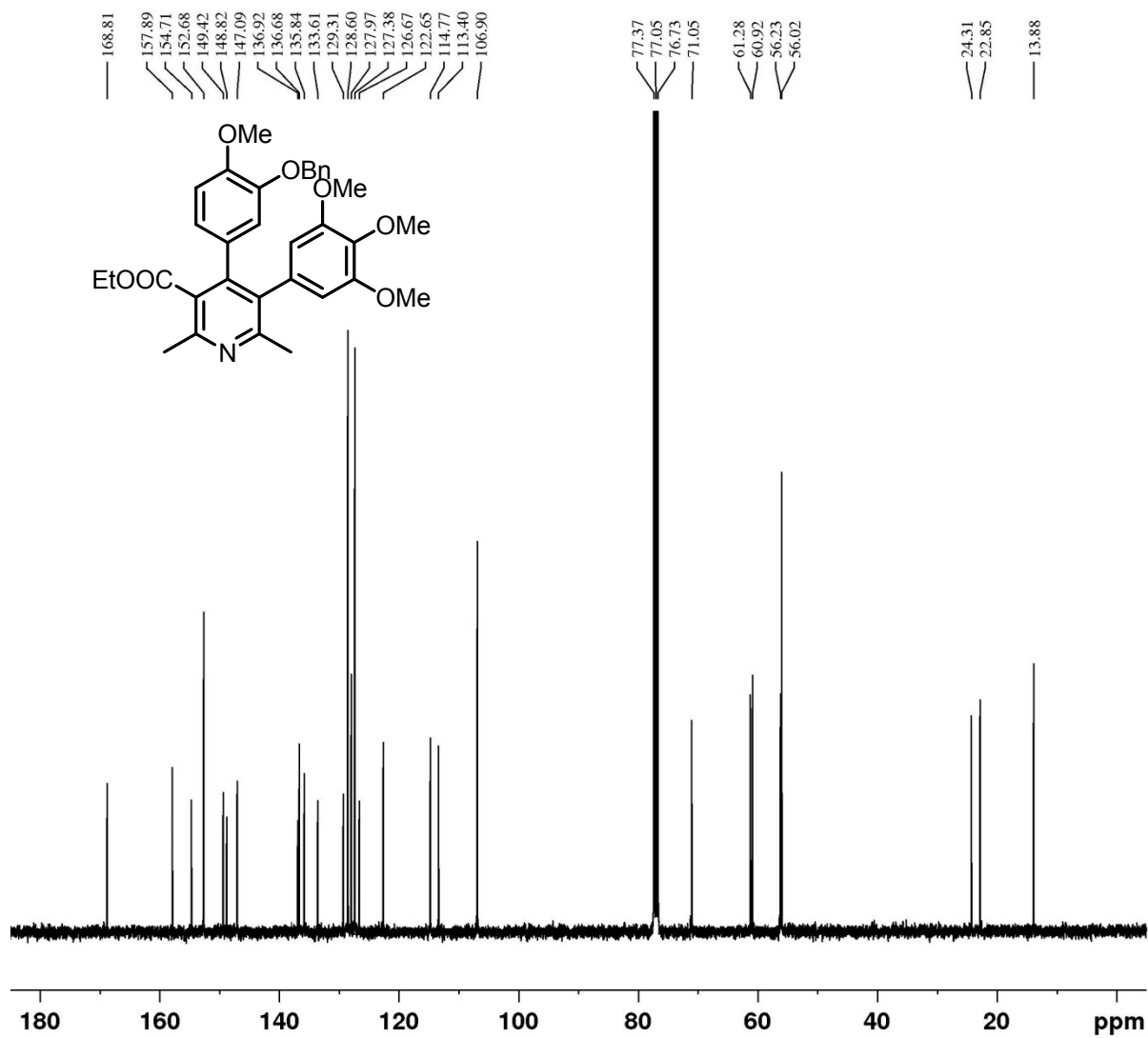
Scheme 5, 8r : ^{13}C NMR



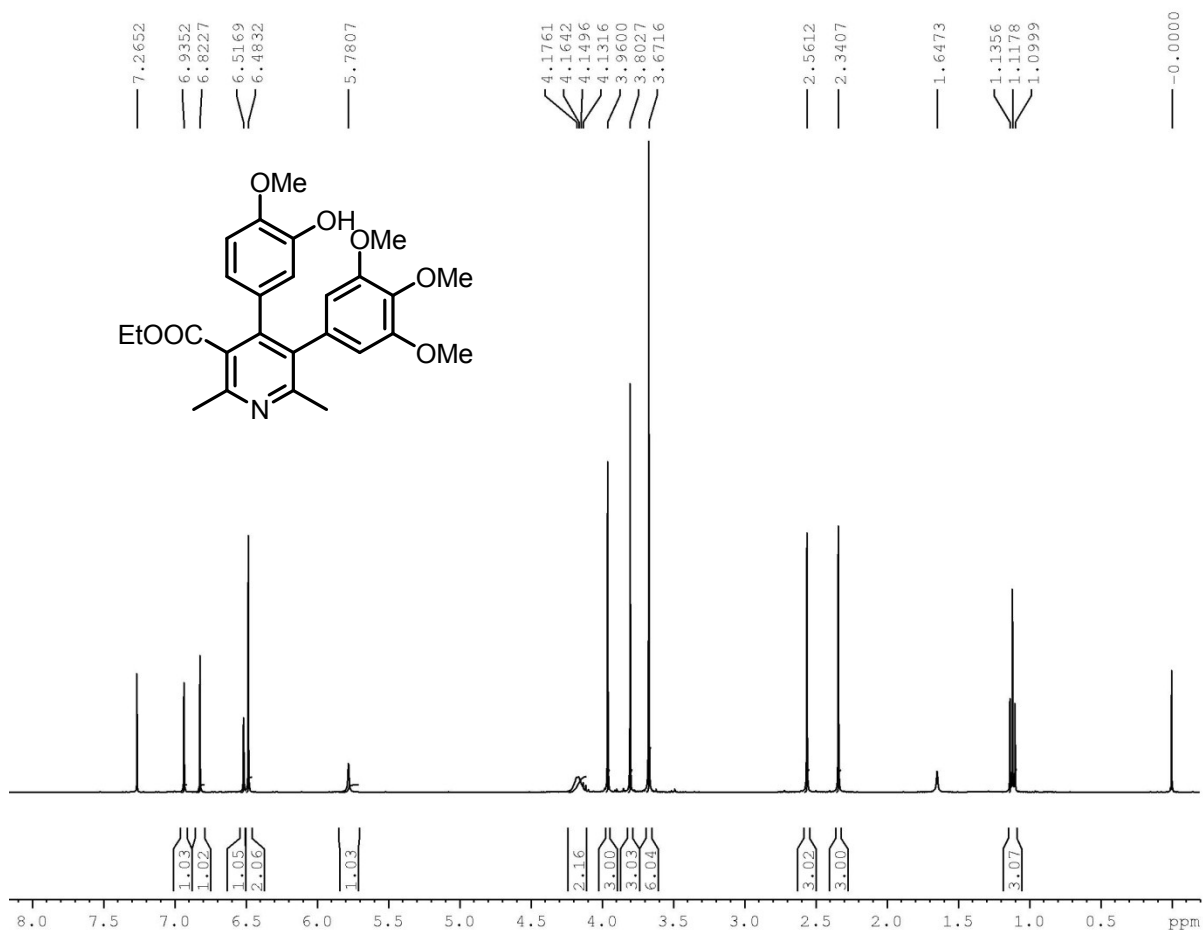
Scheme 6, 8s: ¹H NMR



Scheme 6, 8s : ^{13}C NMR



Scheme 6, 8t: ¹H NMR



Scheme 6, 8t: ¹³C NMR

