Electronic Supplementary Information (ESI)

C-N bond formation *via* Cu-catalyzed cross-coupling with boronic acids leading to methyl carbazole-3-carboxylate: Synthesis of carbazole alkaloids

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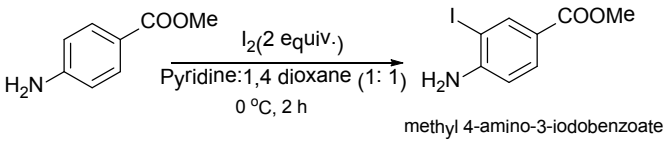
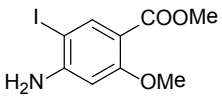
General procedure for the synthesis of methyl 4-amino-3-iodobenzoate: [1]



methyl 4-amino-3-iodobenzoate

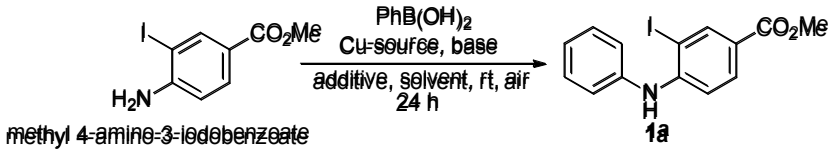
Methyl 4-amino-5-iodo benzoate (2 g, 1.3 mmol) dissolved in pyridine and 1,4-dioxane(1:1) and allow the reaction mixture to cool down to 0 °C. Molecular iodine (6.7g, 2.6 mmol), was added to the reaction mixture stirred at 0 °C for 2 h. The progress of the reaction was monitored by TLC. After completion the reaction mixture was diluted with ethyl acetate and washed with sodium thiosulfate solution (40 mL), followed by washed with brine (2 x 10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum and purified by column chromatography over silica gel by using hexane-EtOAc (7:3) as eluent to afford methyl 4-amino-3-iodobenzoate (3.6 g, 95%). Colourless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 1.9 Hz, 1H), 7.78 (dd, J = 8.4, 1.9 Hz, 1H), 6.68 (d, J = 8.4 Hz, 1H), 4.65 (s, 2H), 3.84 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 150.7, 141.0, 131.1, 121.1, 113.1, 82.1, 51.9; MS(ESI): m/z = 278$[M+H]^+$; HRMS (ESI): calcd. for $C_8H_9INO_3$ $[M+H]^+$ 277.9673; found:277.9708 .



methyl 4-amino-5-iodo-2-methoxybenzoate

Methyl 4-amino-5-iodo-2-methoxybenzoate synthesized from methyl 4-amino-2-methoxybenzoate (2 g, 1.1 mmol) and molecular iodine (5.6 g, 2.2 mmol), by following the procedure as discussed above. Purification: Hexane/EtOAc (1:1); yield (3.4 g, 96%). Colourless solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (s, 1H), 6.28 (s, 1H), 4.51 (br, 2H), 3.84 (s, 3H), 3.83 (s,3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 161.7, 151.6, 142.9, 111.0, 97.1, 71.5, 55.9, 51.7.; MS(ESI): m/z = 307$[M+H]^+$; HRMS (ESI): calcd. for $C_9H_{11}INO_3$ $[M+H]^+$ 307.9778; found: 307.9770.

Table 1. ***N*-arylation of methyl-4-amino-3-iodobenzene with phenylboronic acid:**



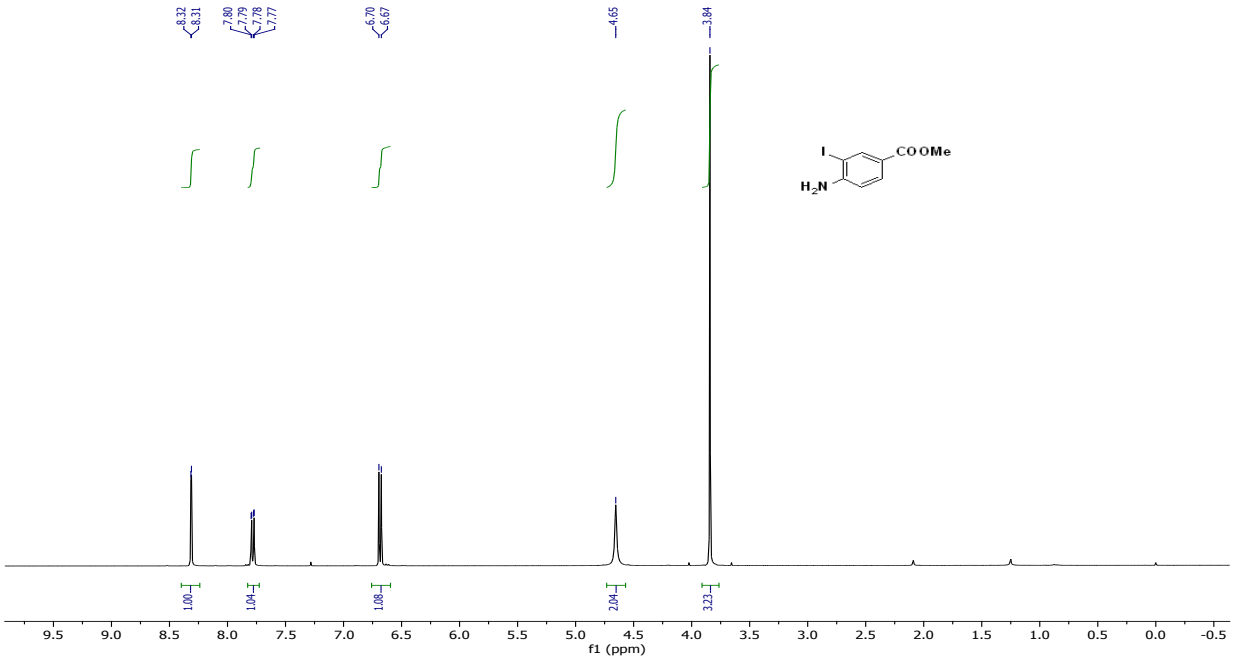
methyl 4-amino-3-iodobenzoate

Entry	Cu-source	mol%	Additive	mol%	Base	Temp.	Time(h)	Solvent	Conv %	Yield(%)[c]
1	$Cu(OAc)_2$	100	-	-	Et_3N	rt	24	DCM	40	30
2[a]	$Cu(OAc)_2$	100	-	-	Py	rt	48	DCM	30	20
3	$Cu(OAc)_2$	100	-	-	Et_3N	50 ^oC	50	DCM	40	40
4[a]	$Cu(OAc)_2$	100	-	-	Py	50 ^oC	24	DCM	50	44
5[b]	$Cu(OAc)_2$	100	-	-	Et_3N	rt	48	DMF	50	45
6[b]	$Cu(OAc)_2$	100	-	-	Py	rt	24	DMF	60	50
7	$Cu(OAc)_2$	100	A_1	100	2,6-lutidine	rt	24	Toluene	60	55
8[a]	$Cu(OAc)_2$	100	A_2	100	2,6-lutidine	rt	24	Toluene	60	55
9	$Cu(OAc)_2$	100	A_2	20	2,6-lutidine	rt	24	Toluene	70	60
10	**$Cu(OAc)_2$**	**10**	**A_2**	**20**	**2,6-lutidine**	**rt**	**24**	**Toluene**	**80**	**70**
11	$Cu(OAc)_2$	10	A_2	20	2,6-lutidine	rt	24	DCE	60	50
12	$CuBr_2$	10	A_2	20	2,6-lutidine	rt	24	Toluene	40	30
13	$Cu(OTf)_2$	10	A_2	20	2,6-lutidine	rt	24	Toluene	30	20
14	$CuCl_2$	10	A_2	20	2,6-lutidine	rt	24	Toluene	20	10
15[a]	$Cu(OAc)_2$	10	A_2	20	2,6-lutidine	rt	24	Toluene	80	70

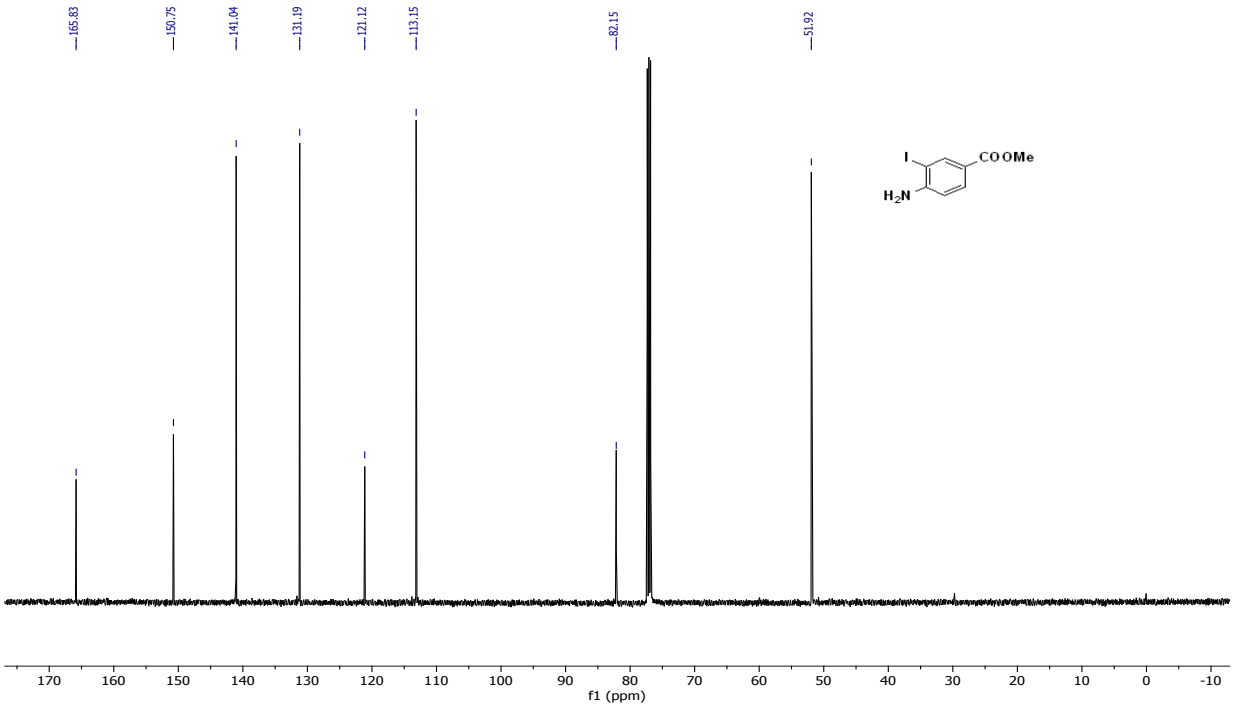
[a] O_2 (1atm.) used in place of air as oxidant; [b] TEMPO used in place of air as oxidant; [c] isolated yield. A_1 = Lauric acid; A_2 = *n*-Decanoic acid,

^{1}HNMR and ^{13}CNMR

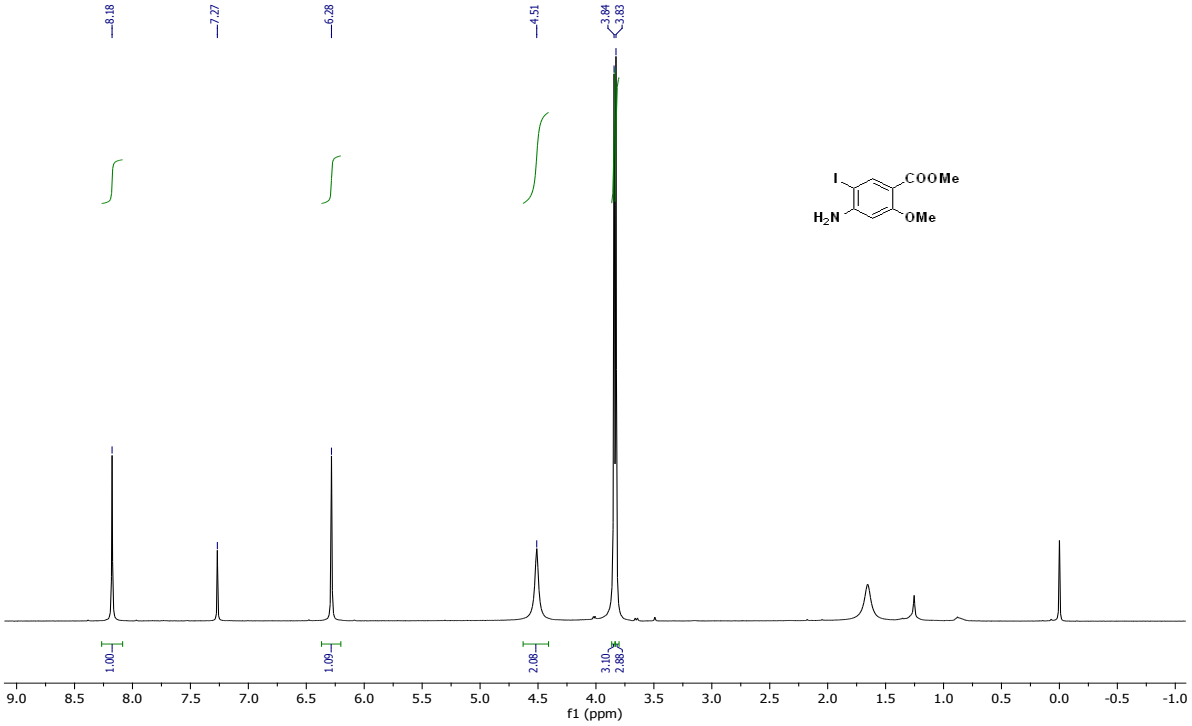
Methyl 4-amino-3-iodobenzoate: ^{1}H NMR



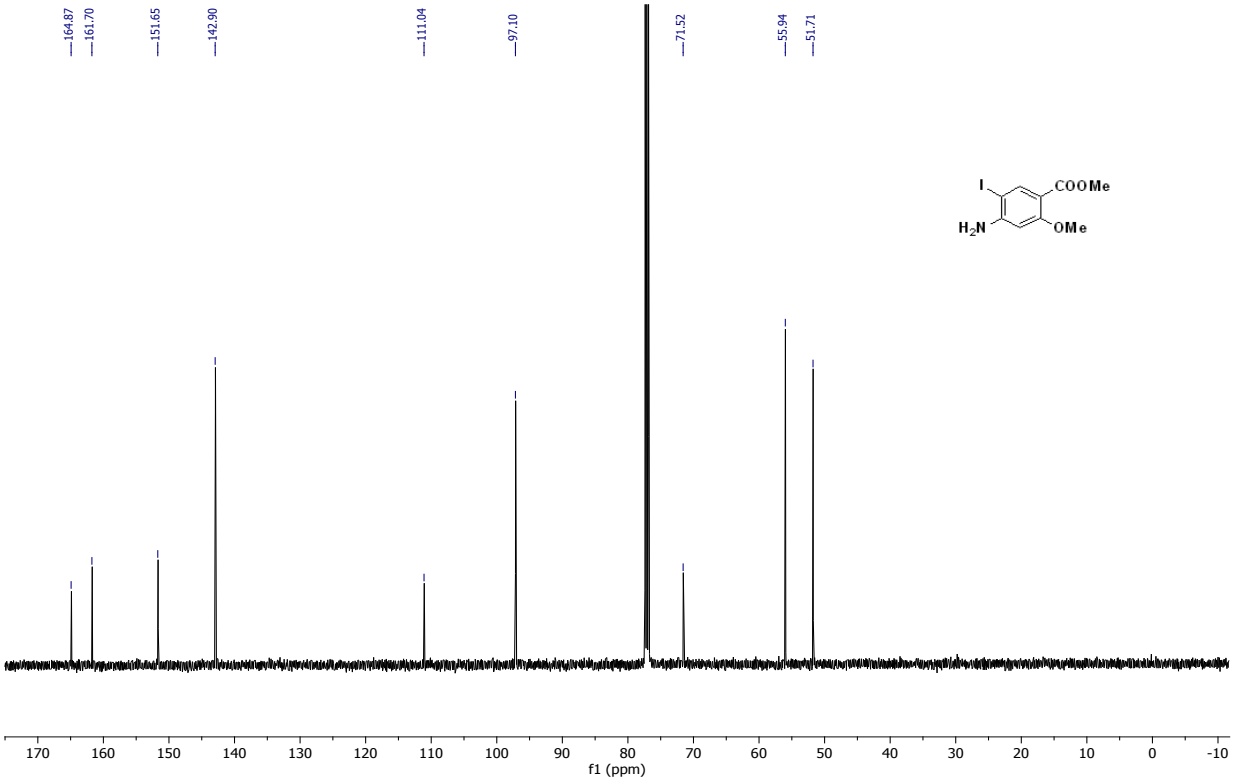
Methyl 4-amino-3-iodobenzoate: ^{13}C NMR



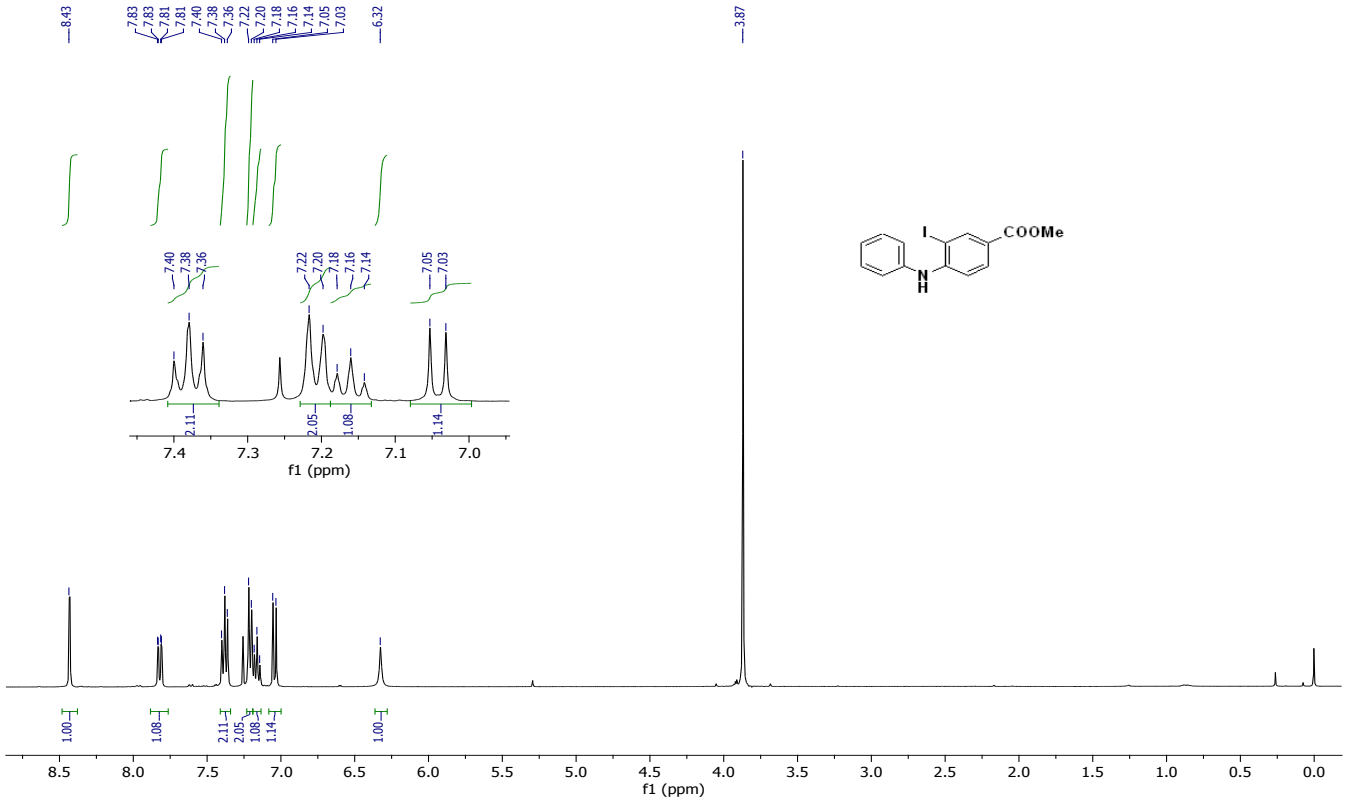
Methyl 4-amino-5-iodo-2-methoxybenzoate: ^{1}H NMR



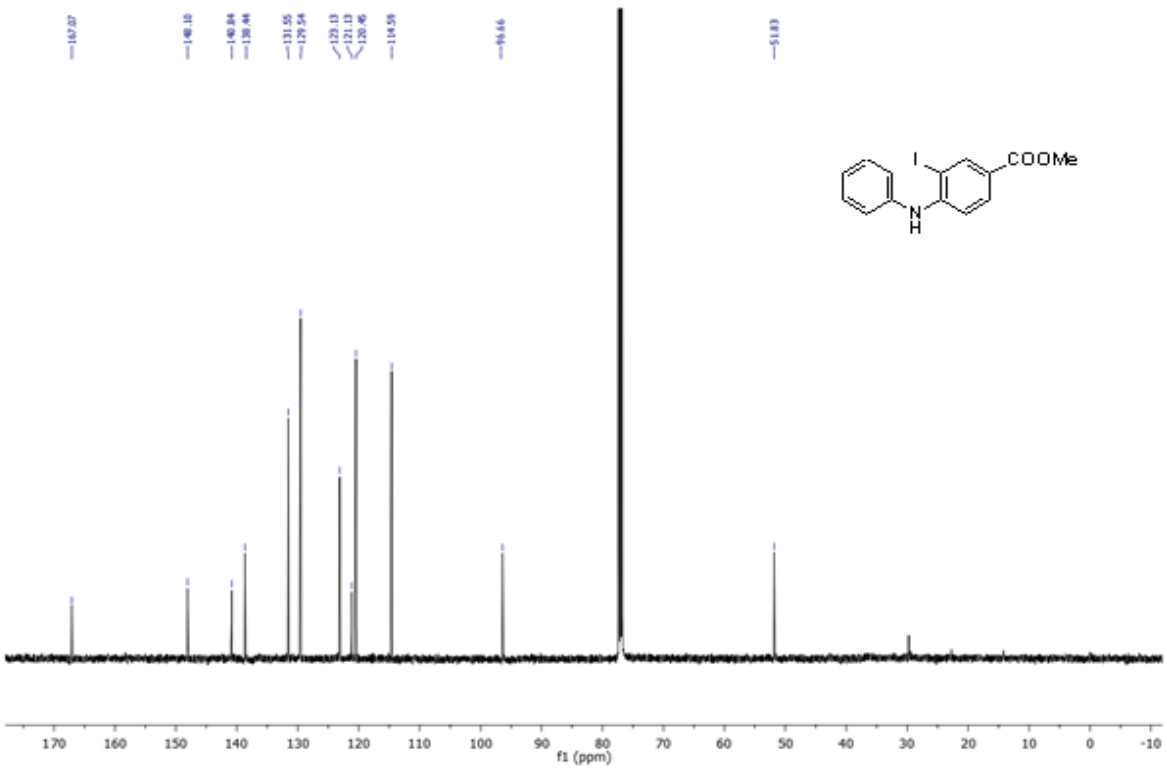
Methyl 4-amino-5-iodo-2-methoxybenzoate: ^{13}C NMR



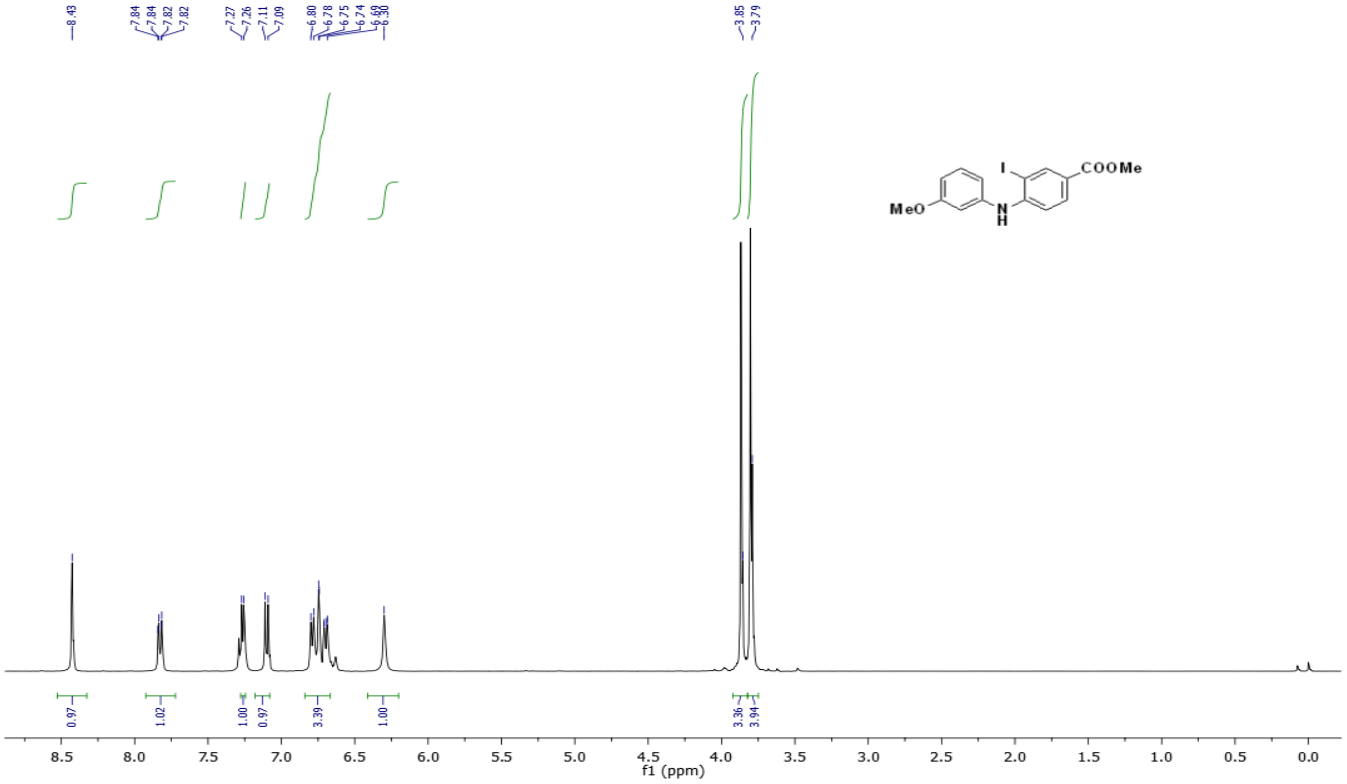
Methyl 3-iodo-4-(phenylamino)benzoate (1a): ^{1}H NMR



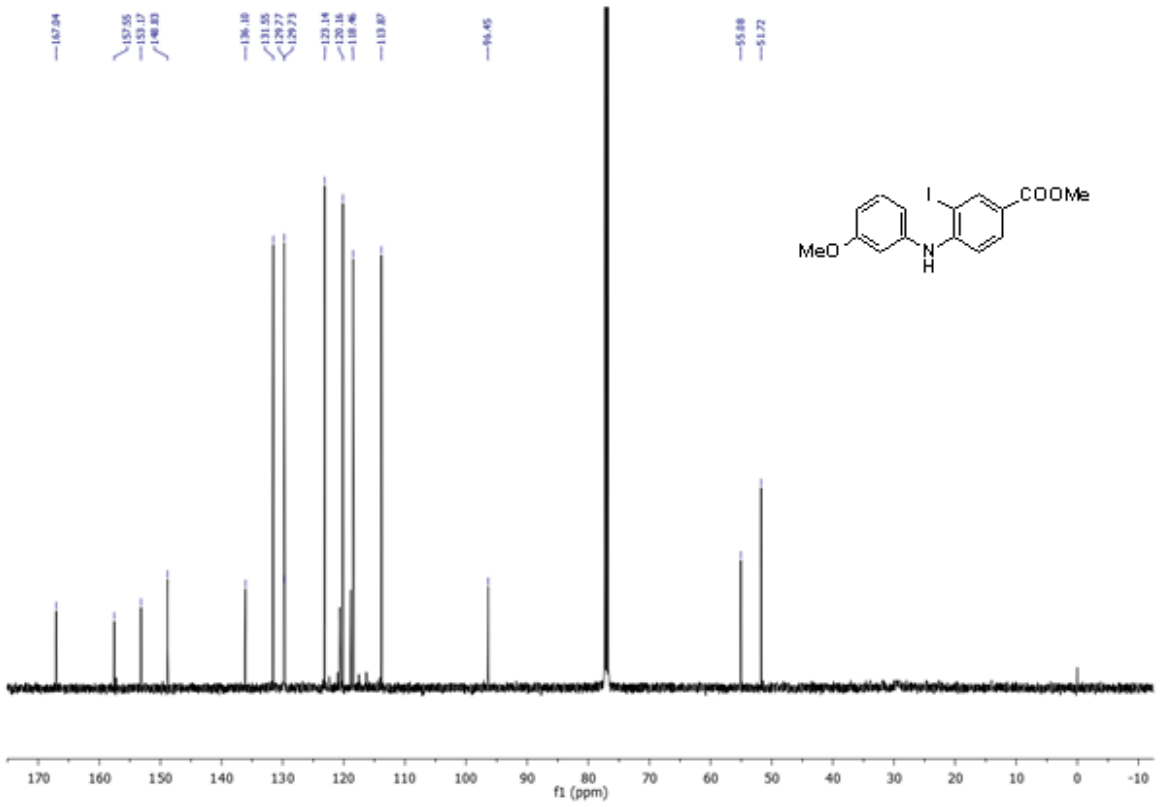
Methyl 3-iodo-4-(phenylamino)benzoate (1a): ^{13}C NMR



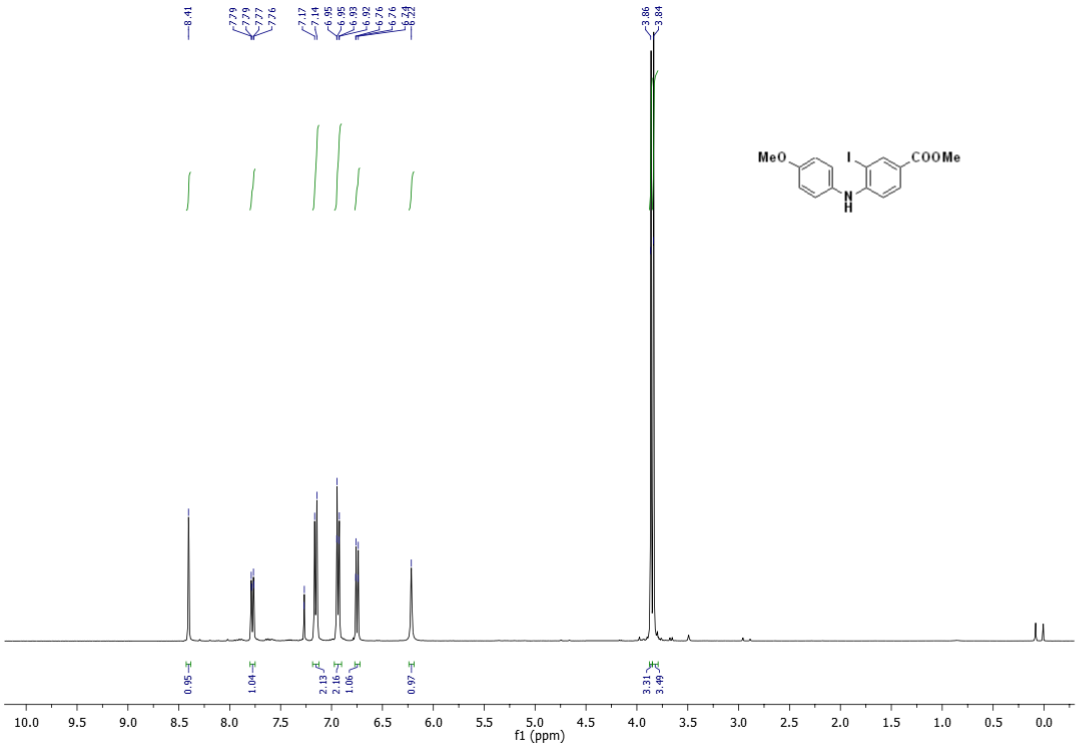
Methyl 3-iodo-4-(3-methoxyphenylamino)benzoate (1b): ^{1}H NMR



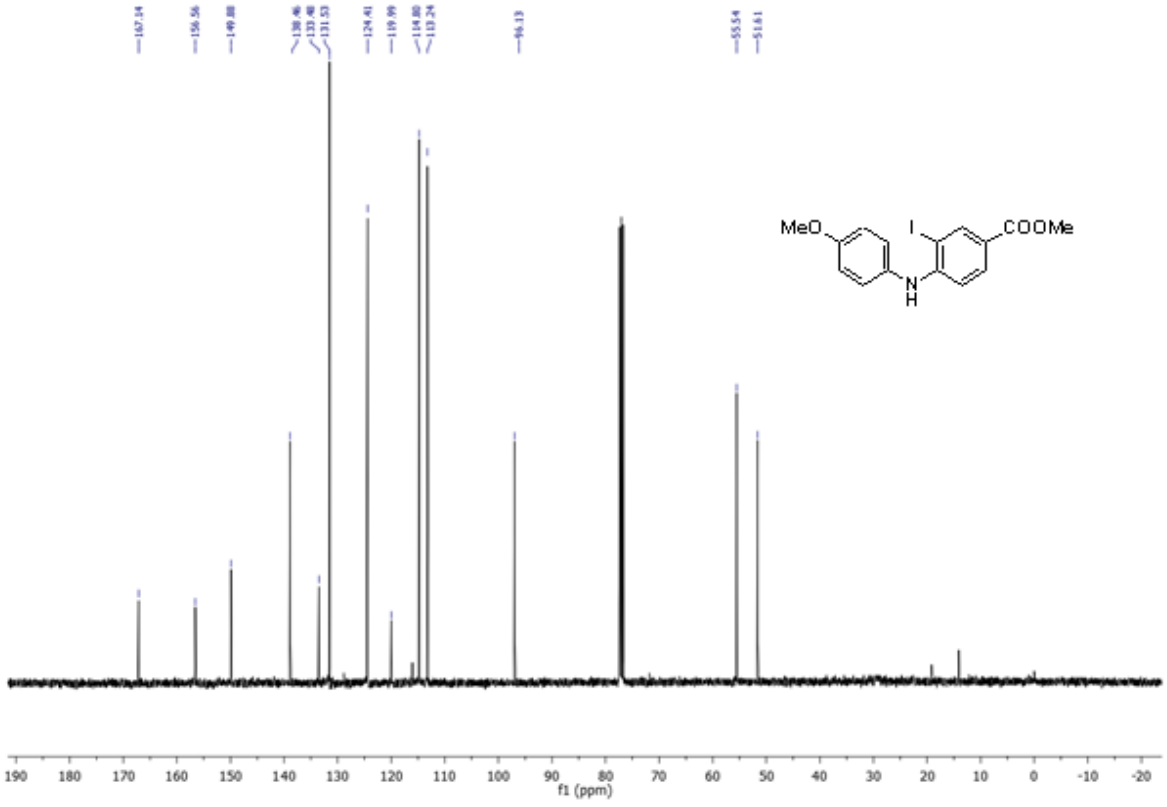
Methyl 3-iodo-4-(3-methoxyphenylamino)benzoate (1b): ^{13}C NMR



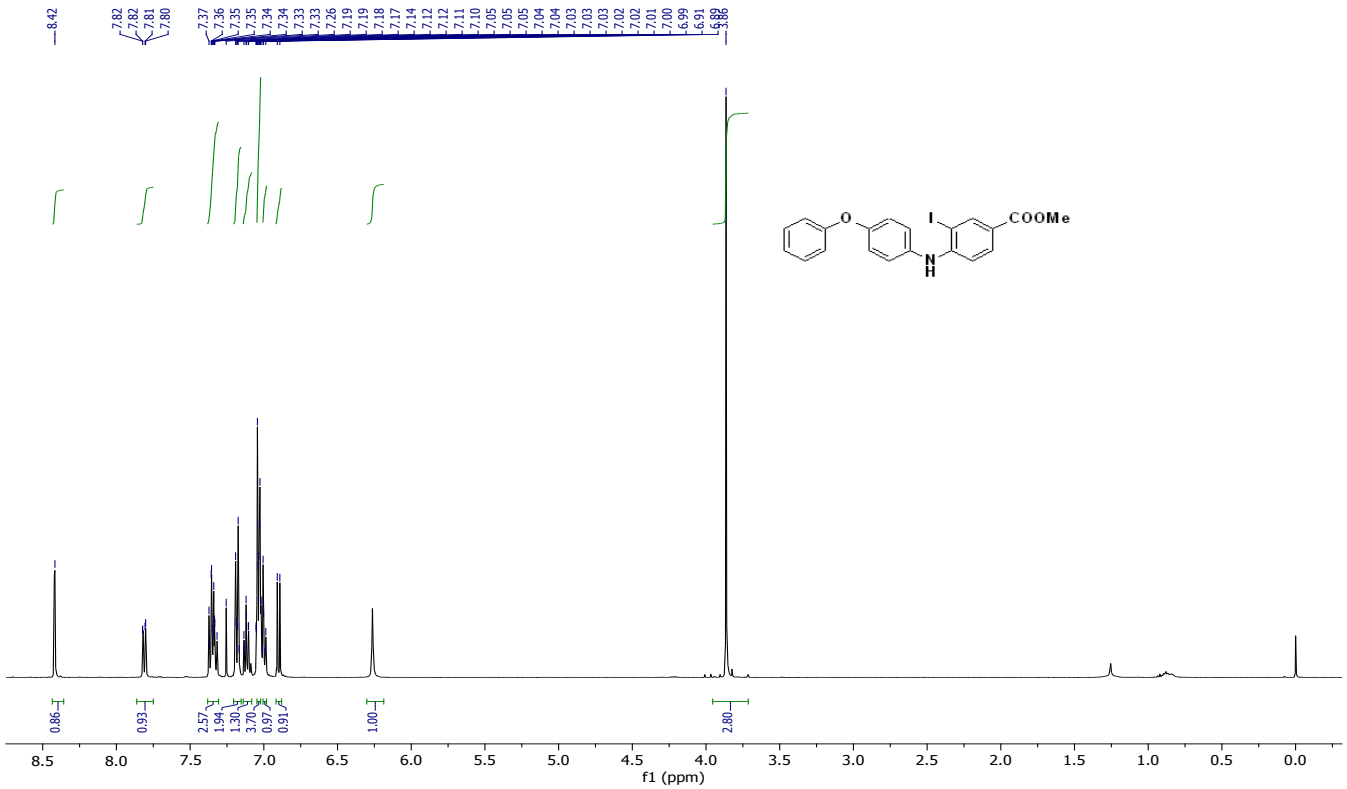
Methyl 3-iodo-4-(4-methoxyphenylamino)benzoate (1c): ^{1}H NMR



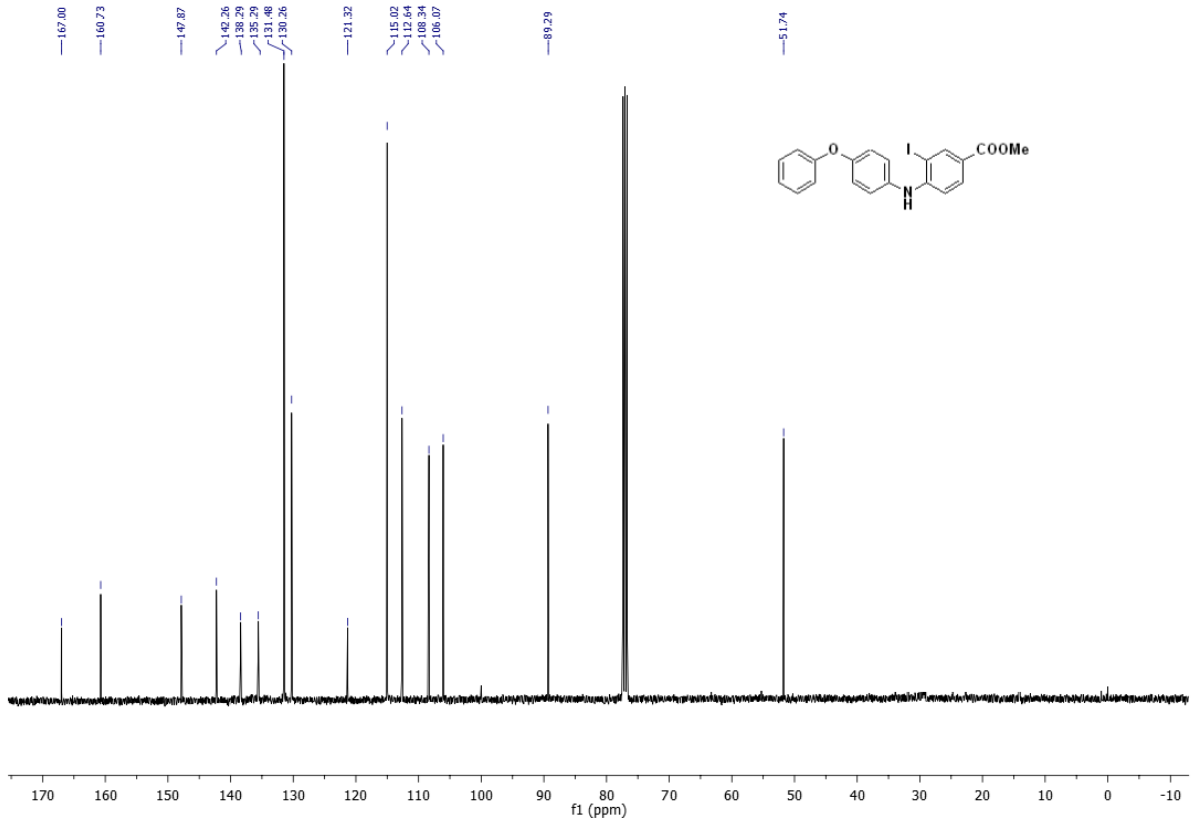
Methyl 3-iodo-4-(4-methoxyphenylamino)benzoate (1c): ^{13}C NMR



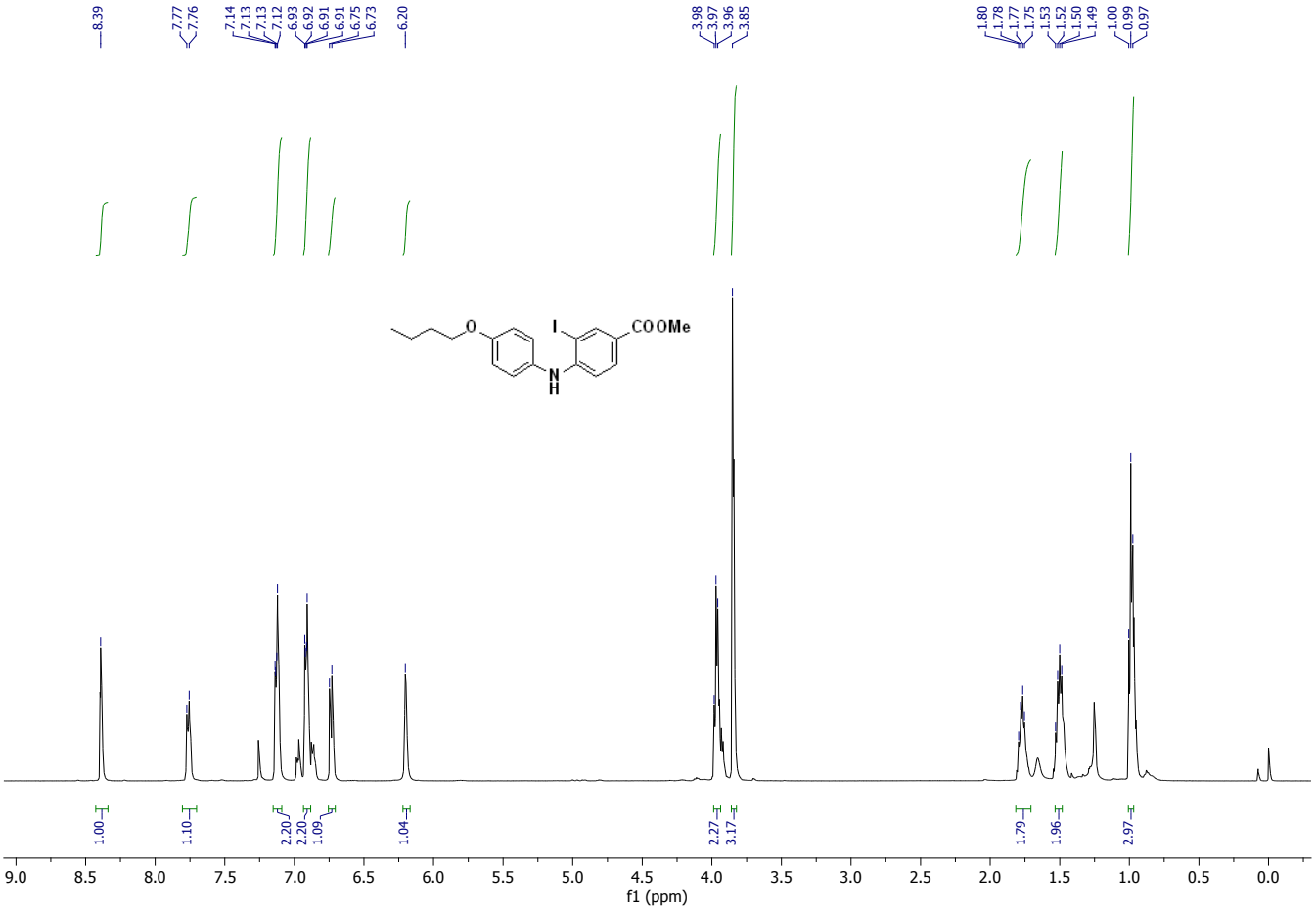
Methyl 3-iodo-4-(4-phenoxyphenylamino)benzoate (1d): ^{1}H NMR



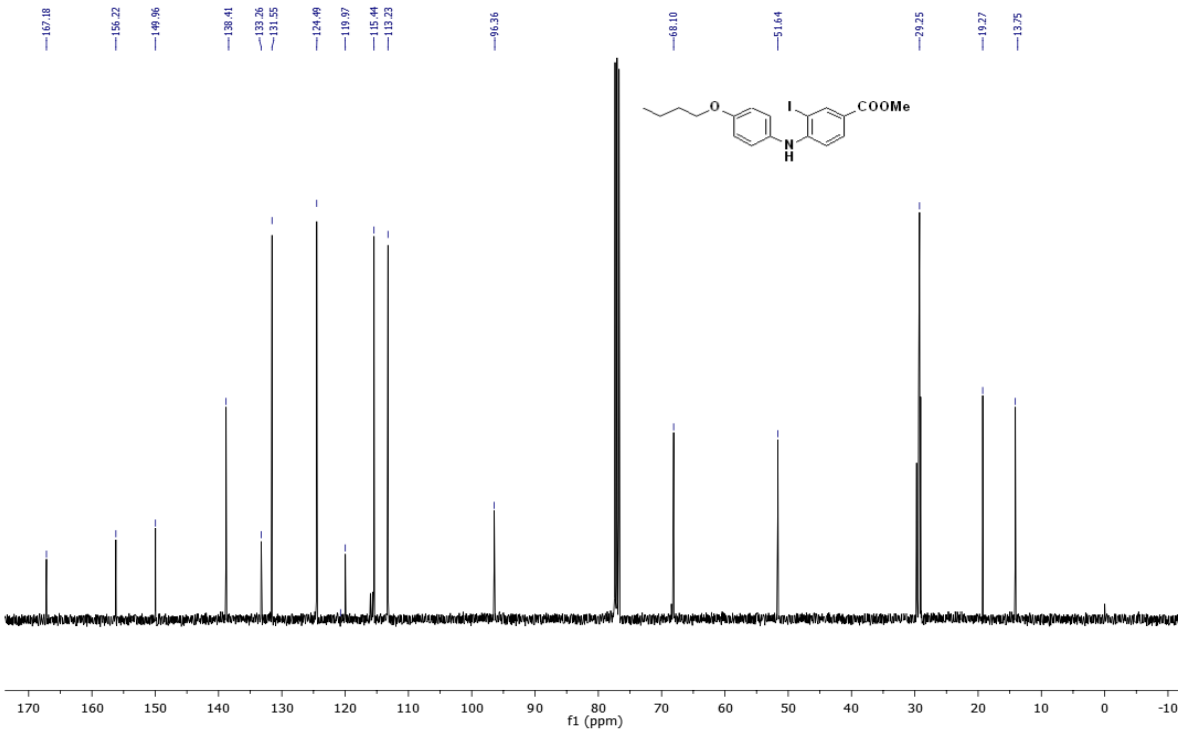
Methyl 3-iodo-4-(4-phenoxyphenylamino)benzoate (1d): ^{13}C NMR



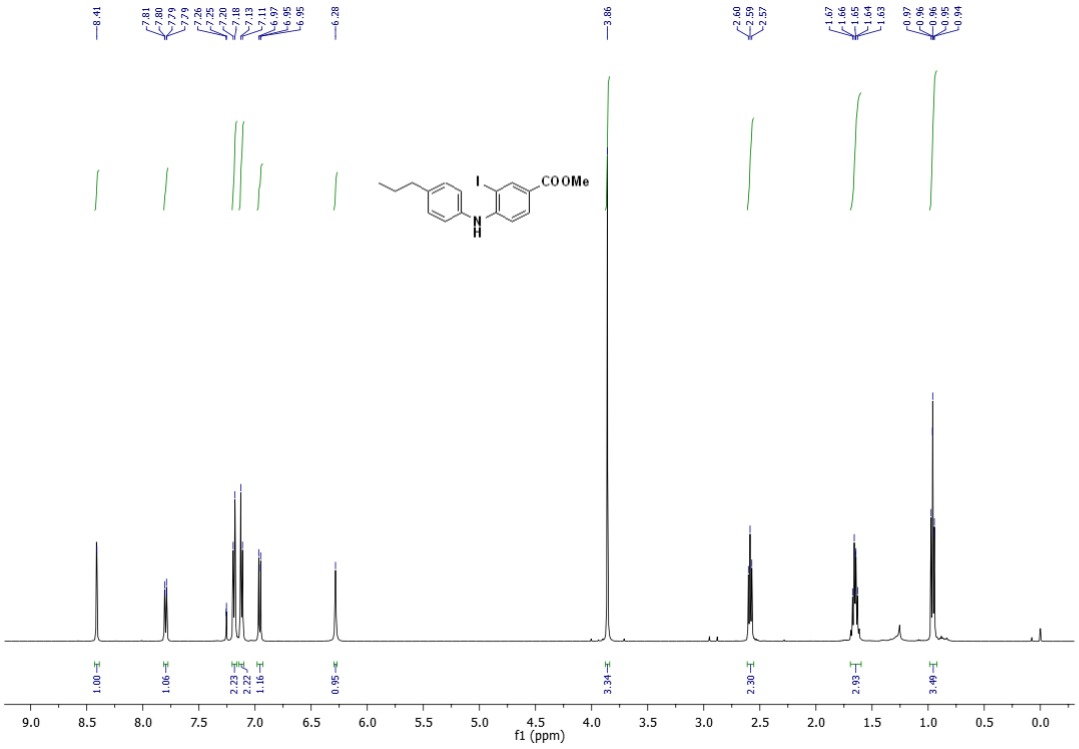
Methyl 4-(4-butoxyphenylamino)-3-iodobenzoate (1e): ^{1}H NMR



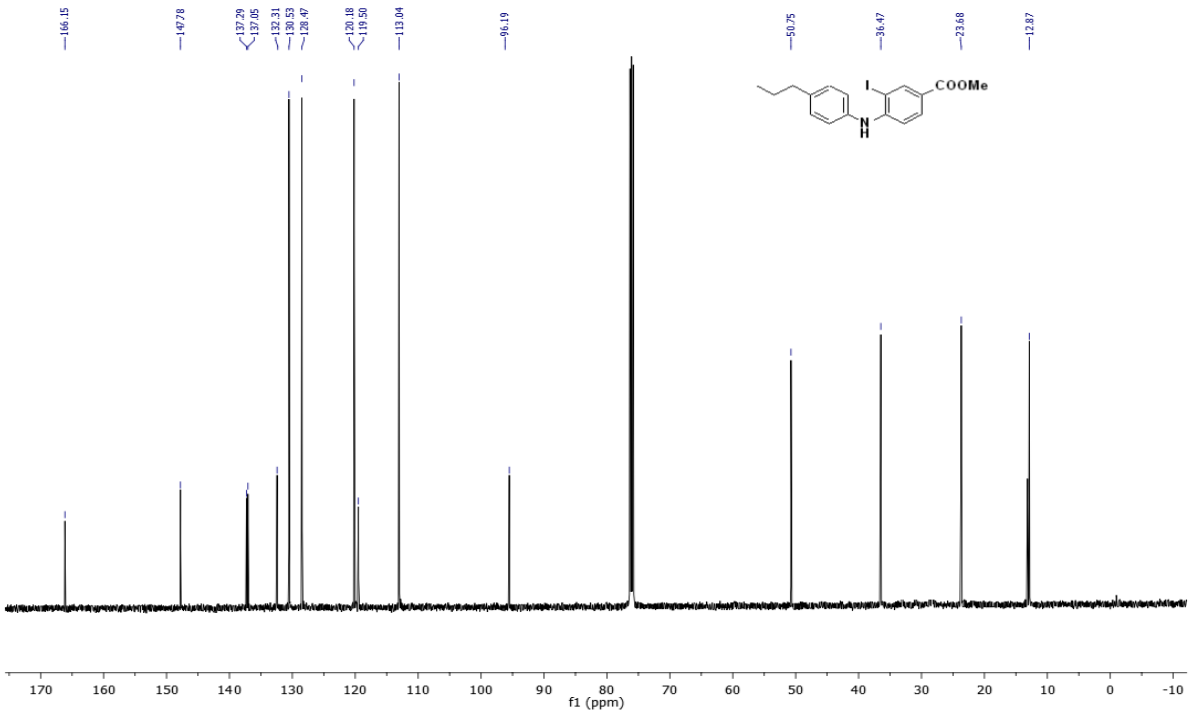
Methyl 4-(4-butoxyphenylamino)-3-iodobenzoate (1e): ^{13}C NMR



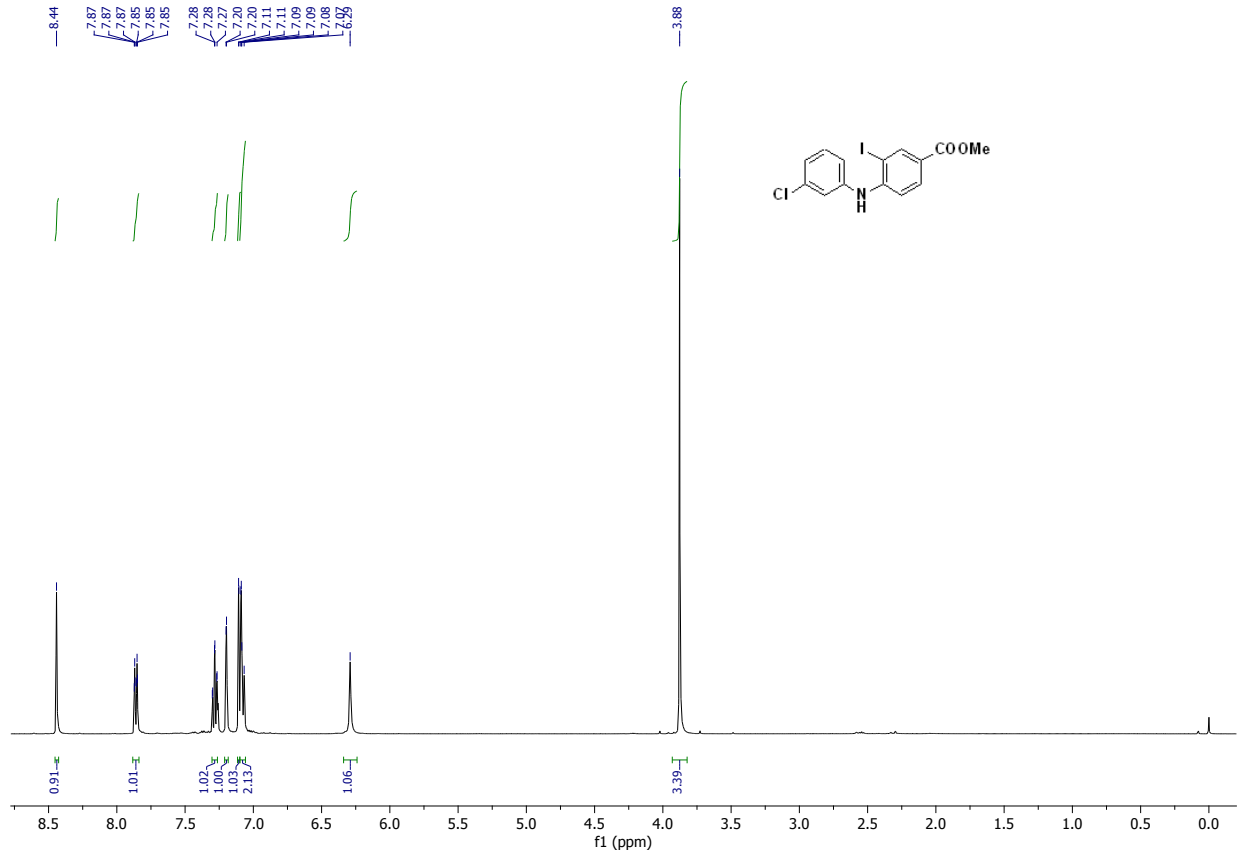
Methyl 3-iodo-4-(4-propylphenylamino)benzoate (1f): ^{1}H NMR



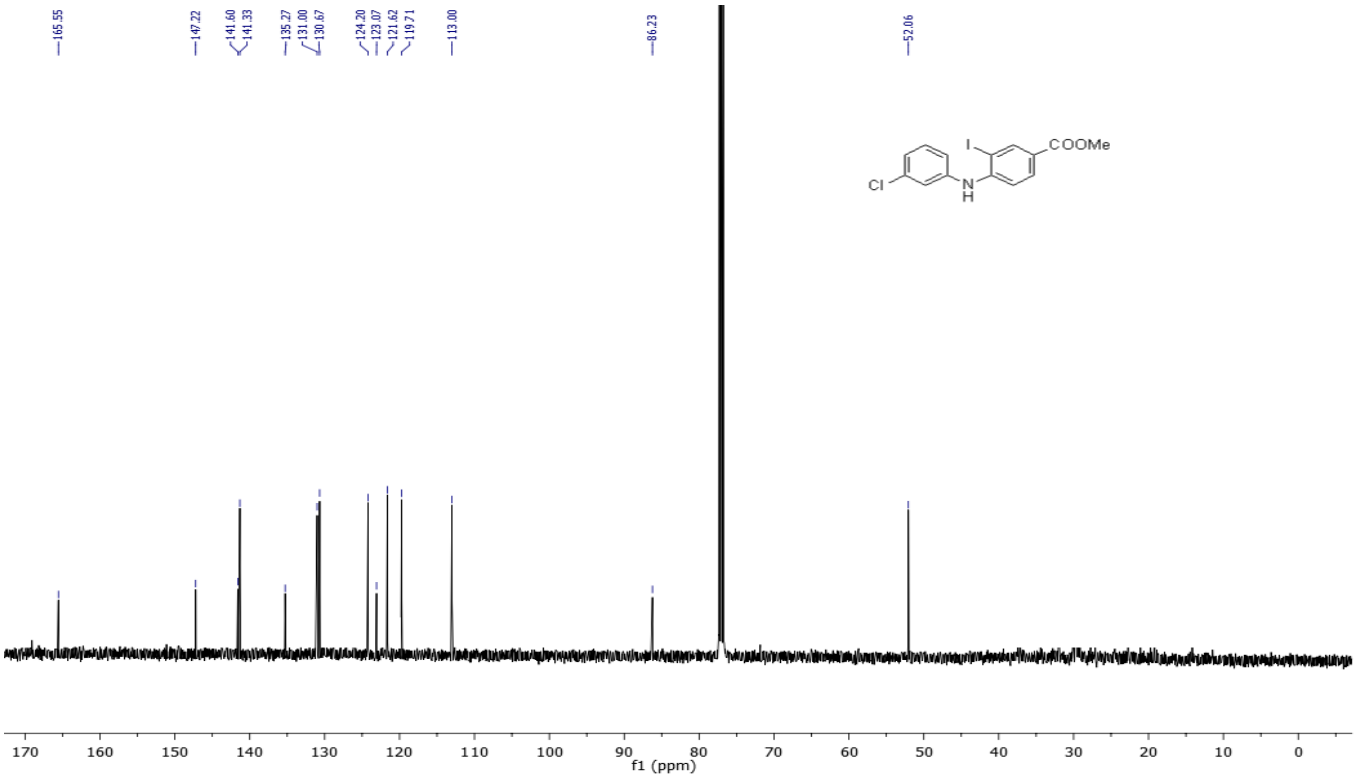
Methyl 3-iodo-4-(4-propylphenylamino)benzoate (1f): ^{13}C NMR



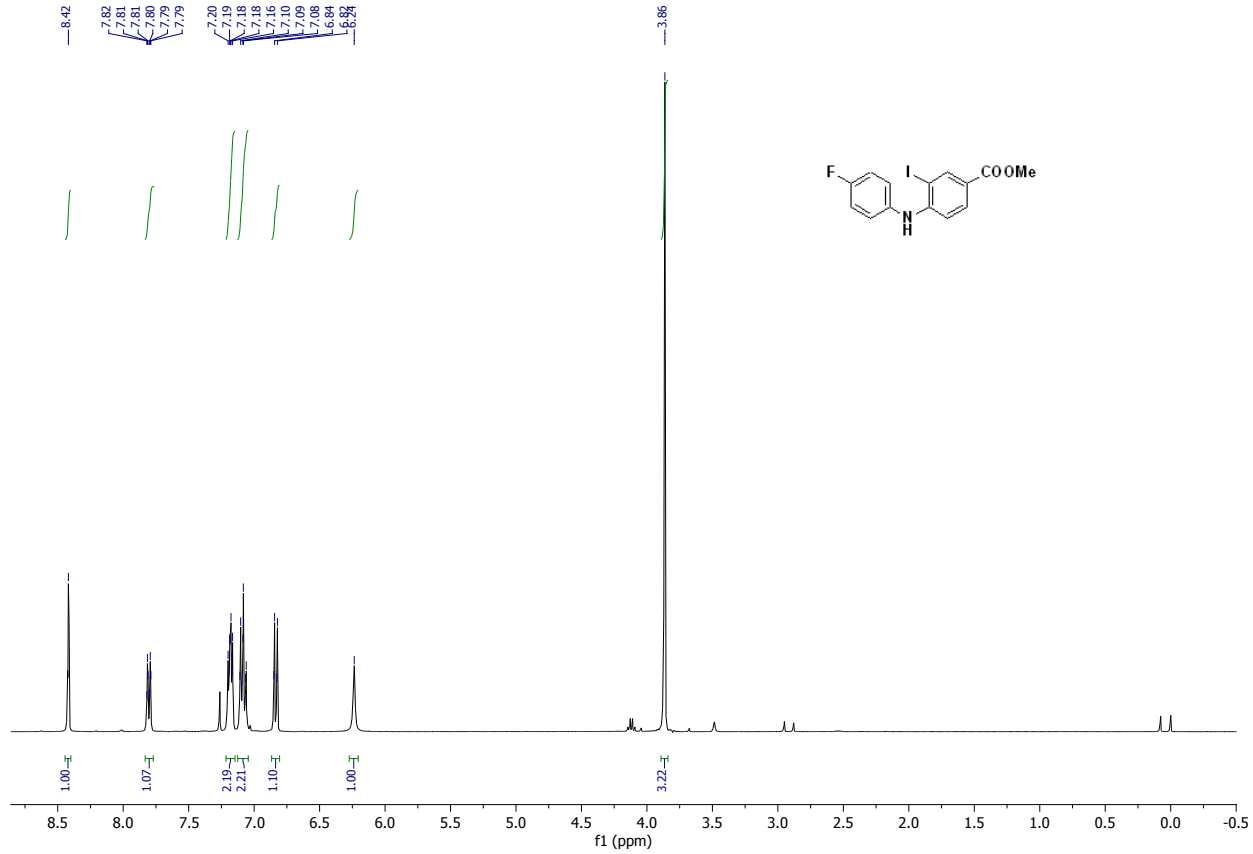
Methyl 4- (3-chlorophenylamino)-3-iodobenzoate (1g): ^{1}H NMR



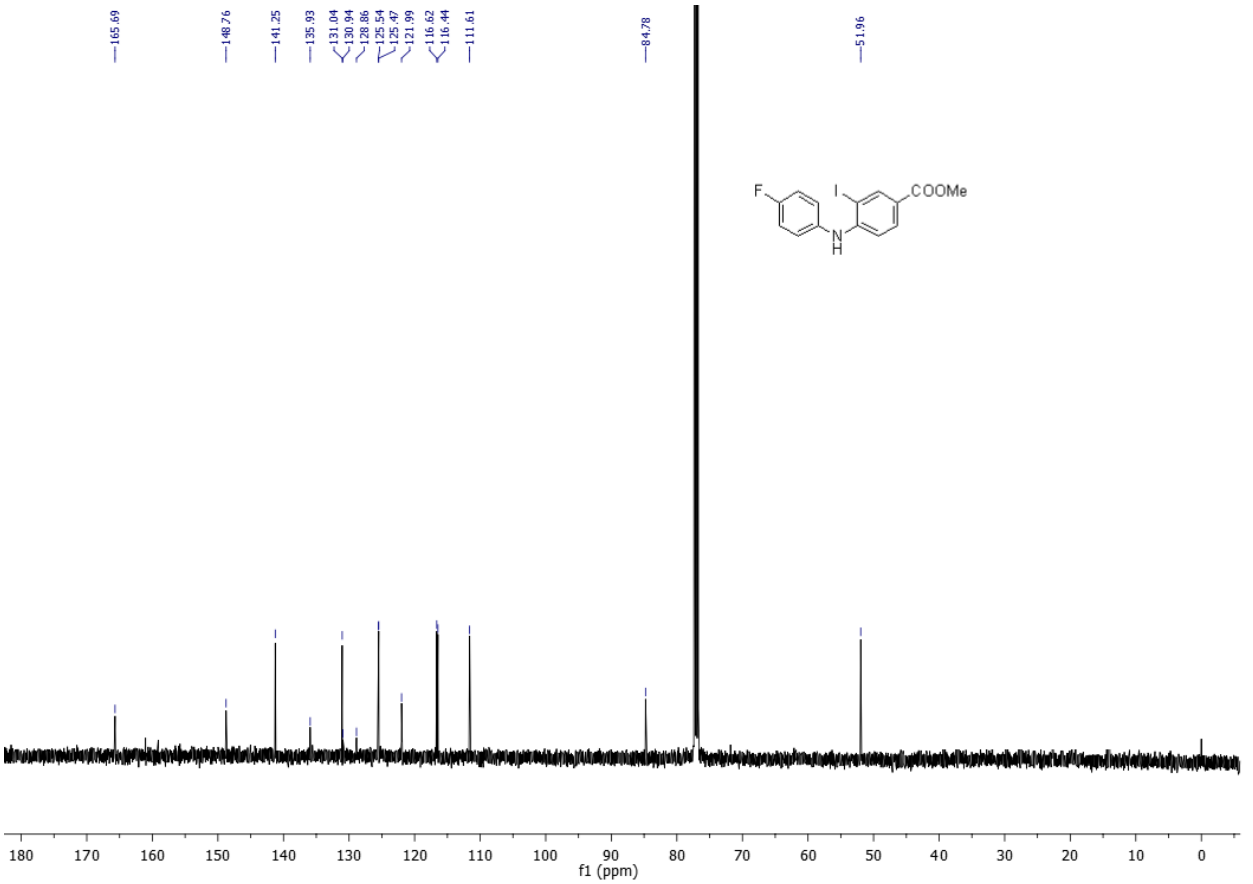
Methyl 4-(3-chlorophenylamino)-3-iodobenzoate (1g): ^{13}C NMR



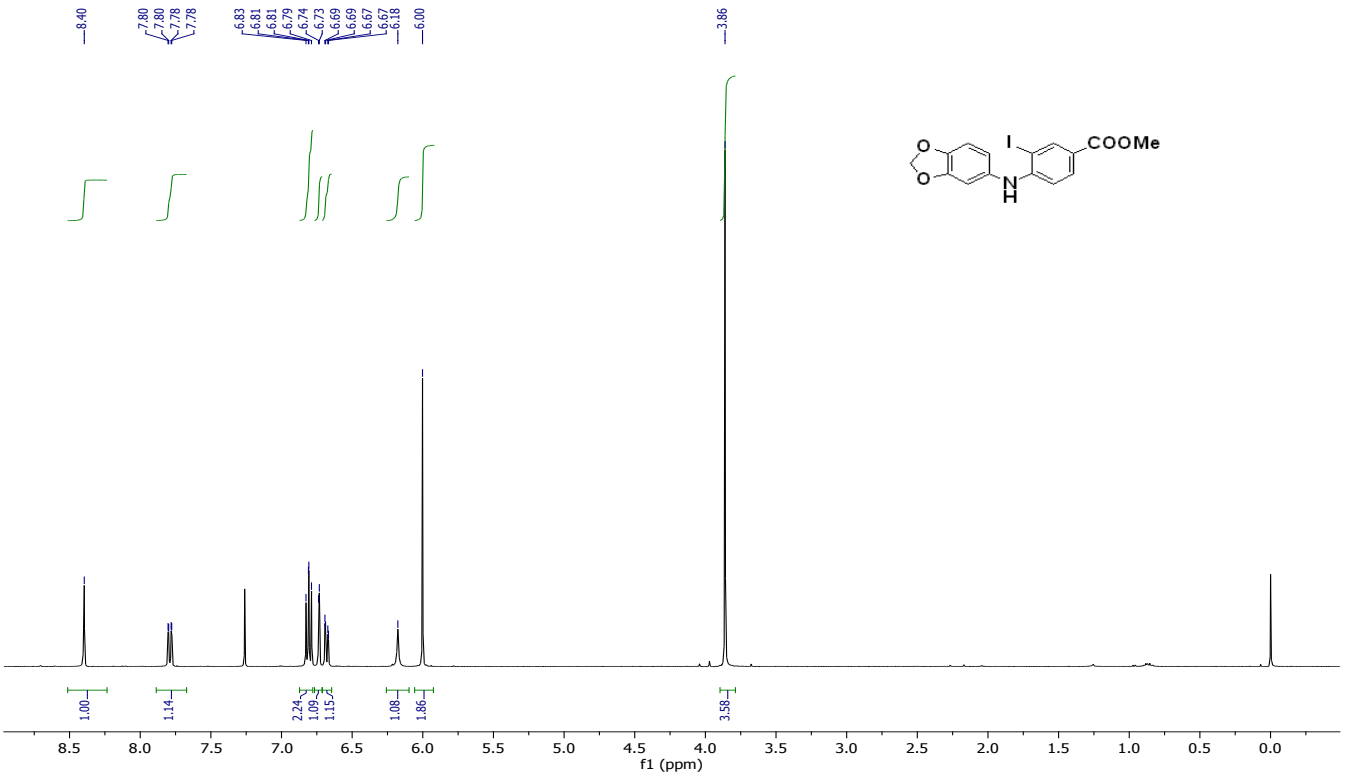
Methyl 4-(4-fluorophenylamino)-3-iodobenzoate (1h): ^{1}H NMR



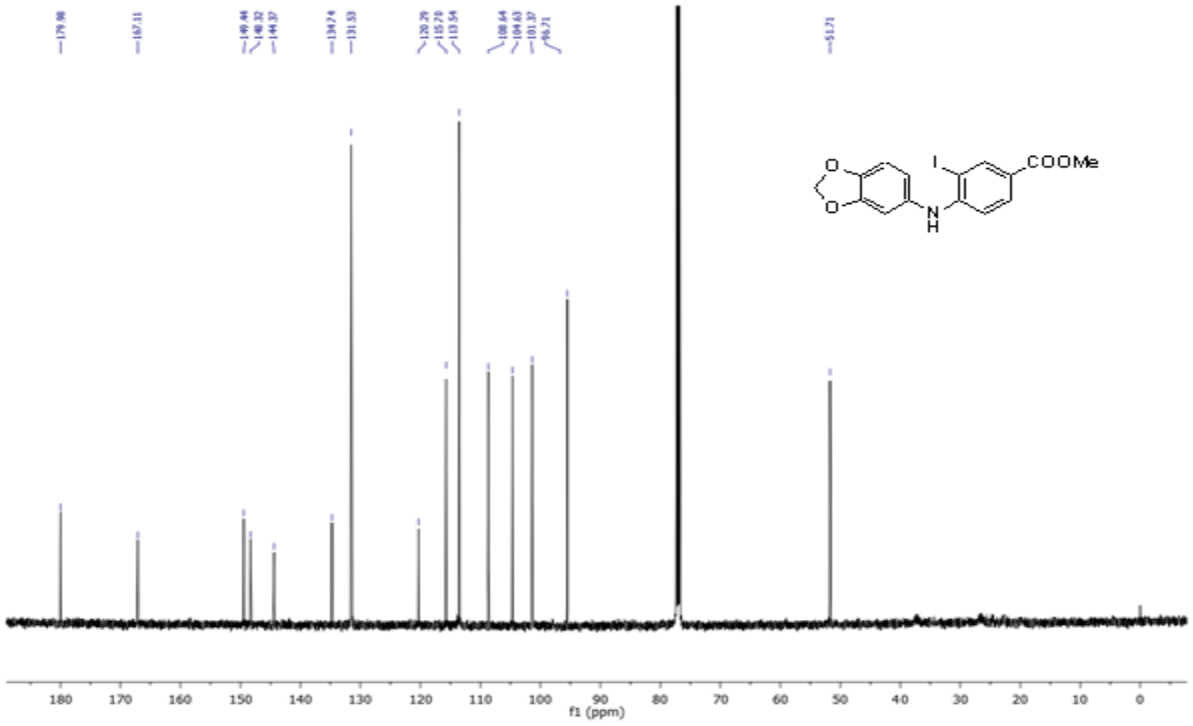
Methyl 4- (4-fluorophenylamino)-3-iodobenzoate (1h): ^{13}C NMR



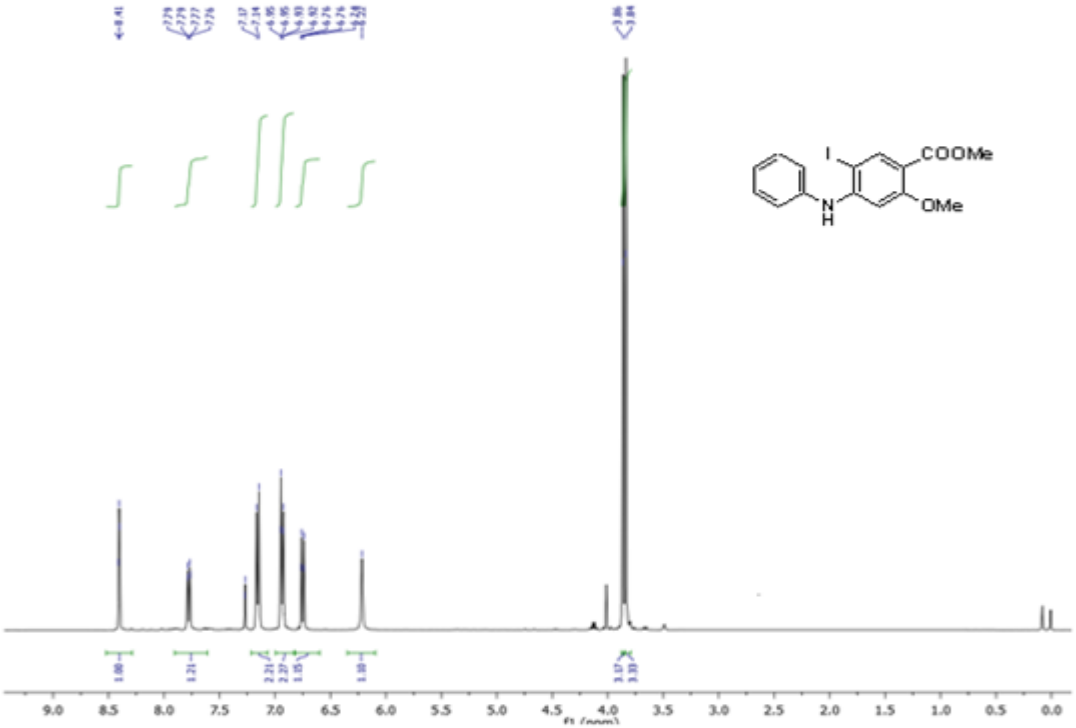
Methyl 4-(benzo[*d*][1,3]dioxol-5-ylamino)-3-iodobenzoate (1i): ^{1}H NMR



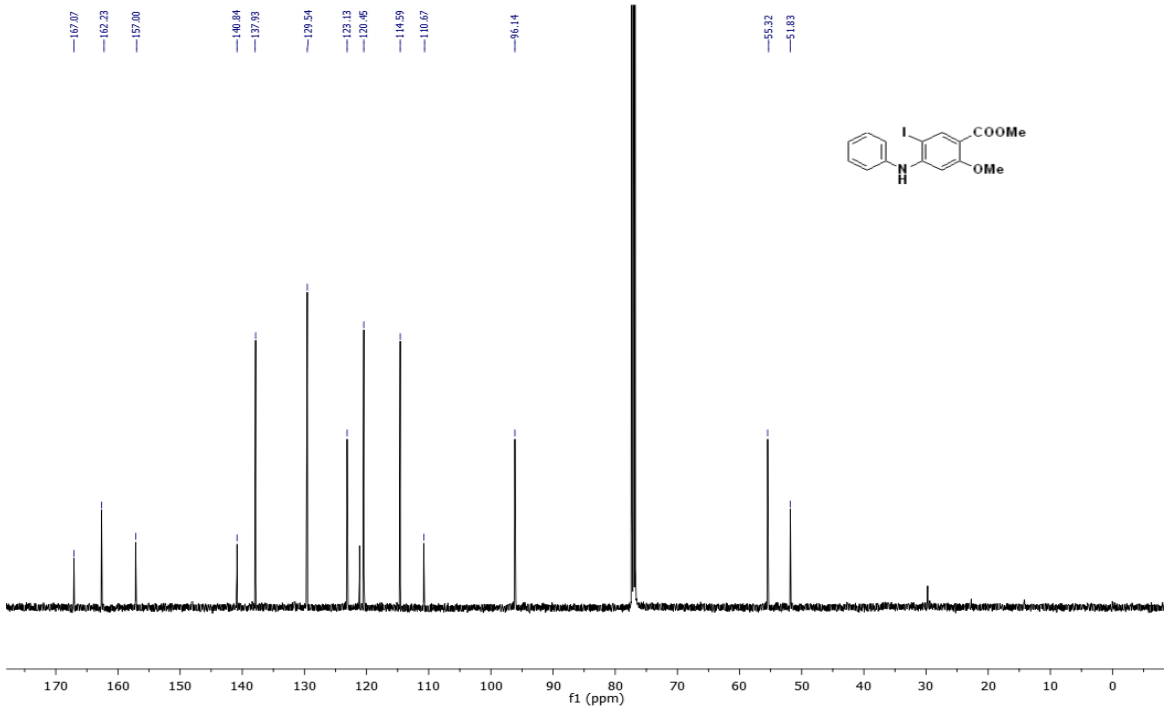
Methyl 4-(benzo[*d*][1,3]dioxol-5-ylamino)-3-iodobenzoate (1i): ^{13}C NMR



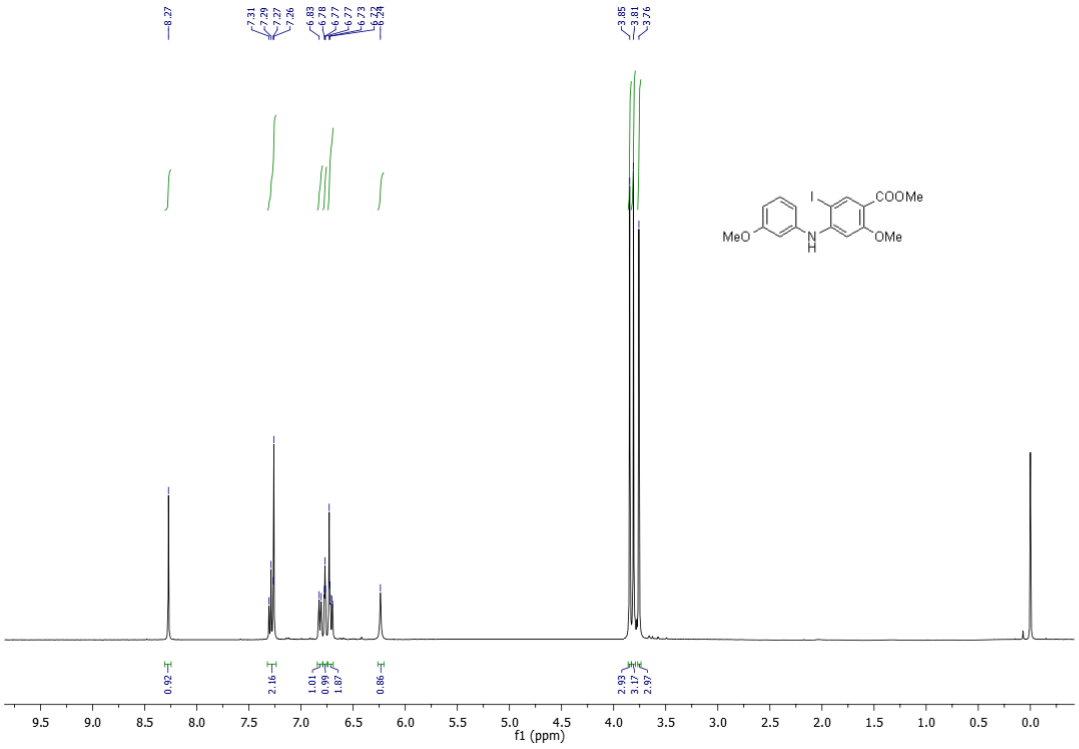
Methyl 5-iodo-2-methoxy-4-(phenylamino)benzoate (1j): ^{1}H NMR



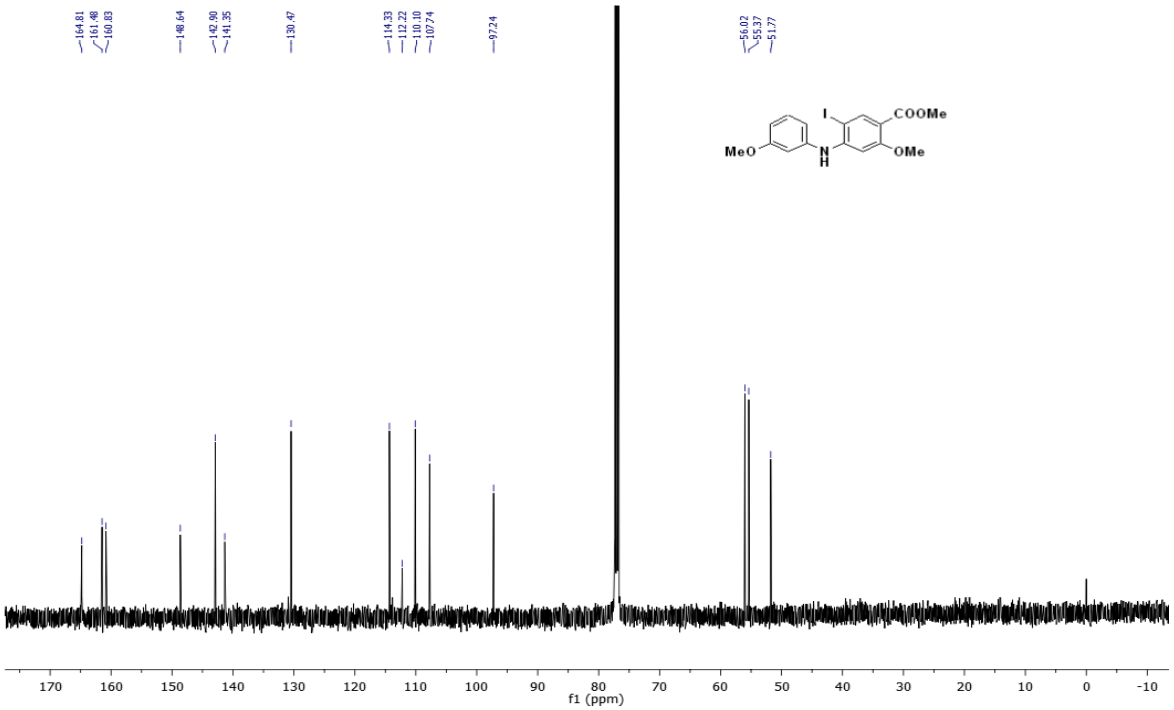
Methyl 5-iodo-2-methoxy-4-(phenylamino)benzoate (1j): ^{13}C NMR



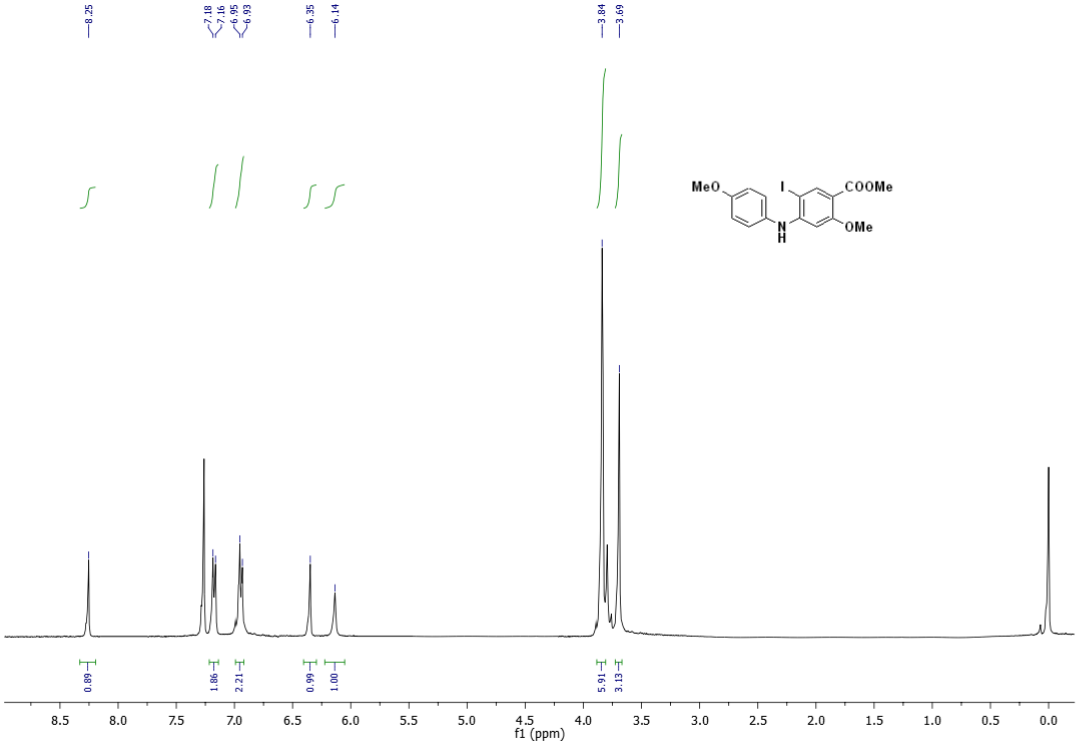
Methyl 5-iodo-2-methoxy-4-(3-methoxyphenylamino)benzoate (1k): ^{1}H NMR



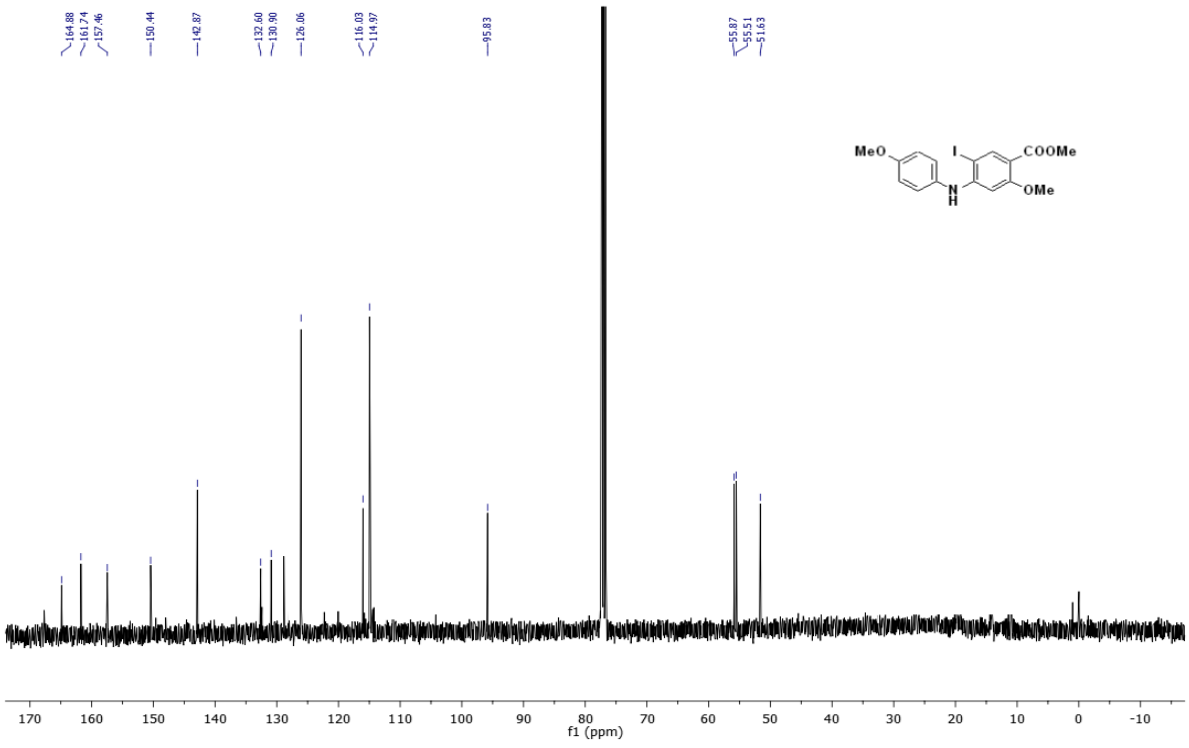
Methyl 5-iodo-2-methoxy-4-(3-methoxyphenylamino)benzoate (1k): ^{13}C NMR



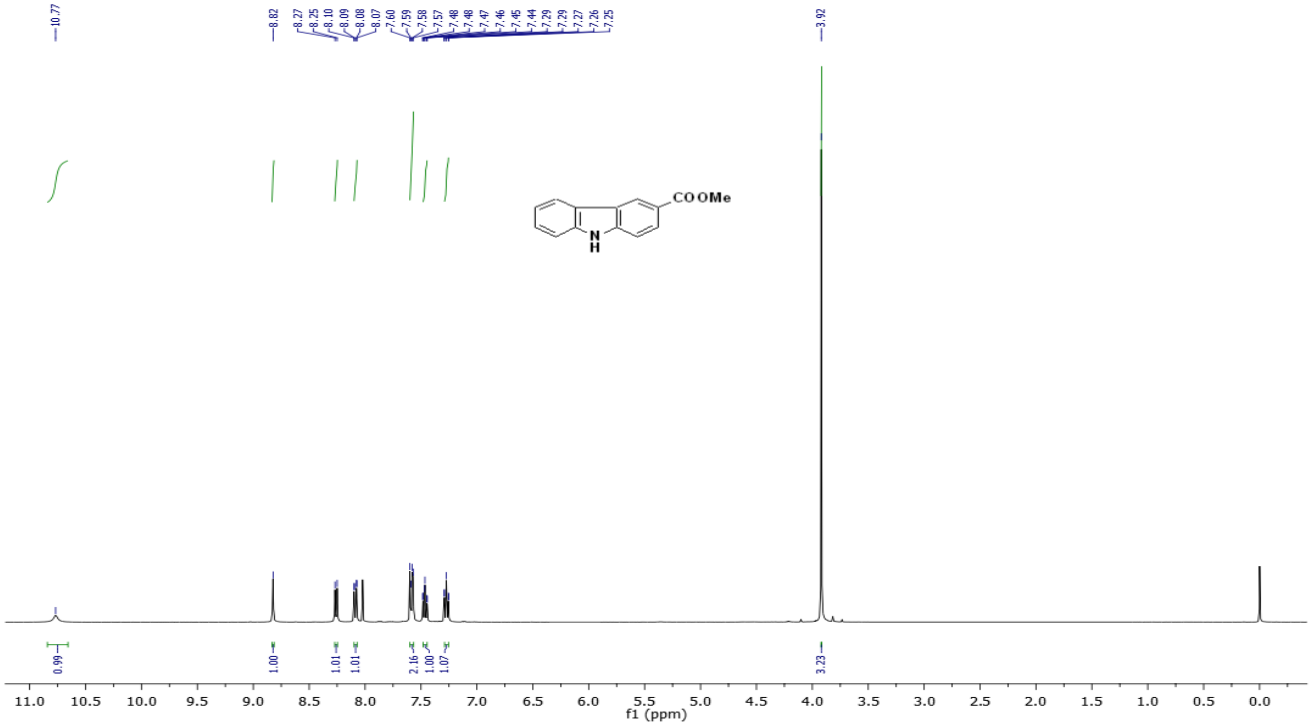
Methyl 5-iodo-2-methoxy-4-(4-methoxyphenylamino) benzoate (1l): ^{1}H NMR



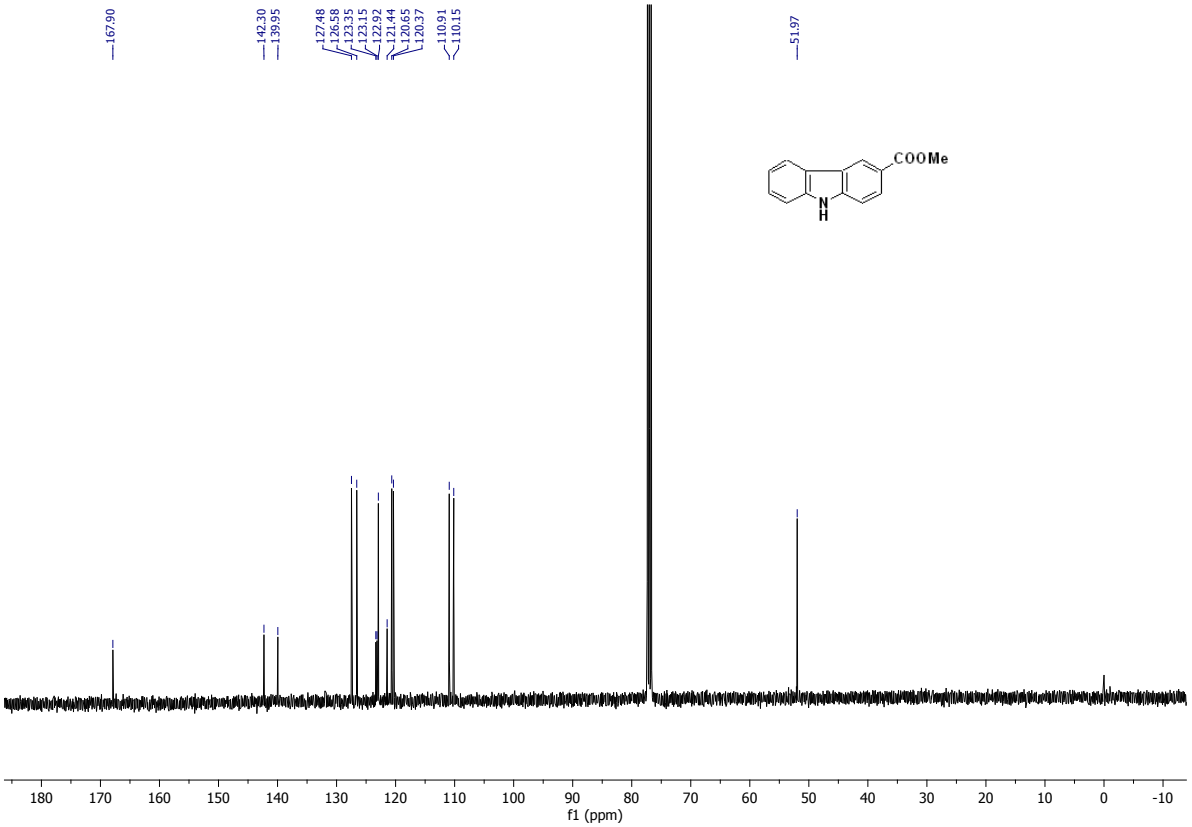
Methyl 5-iodo-2-methoxy-4-(4-methoxyphenylamino) benzoate (1l): ^{13}C NMR



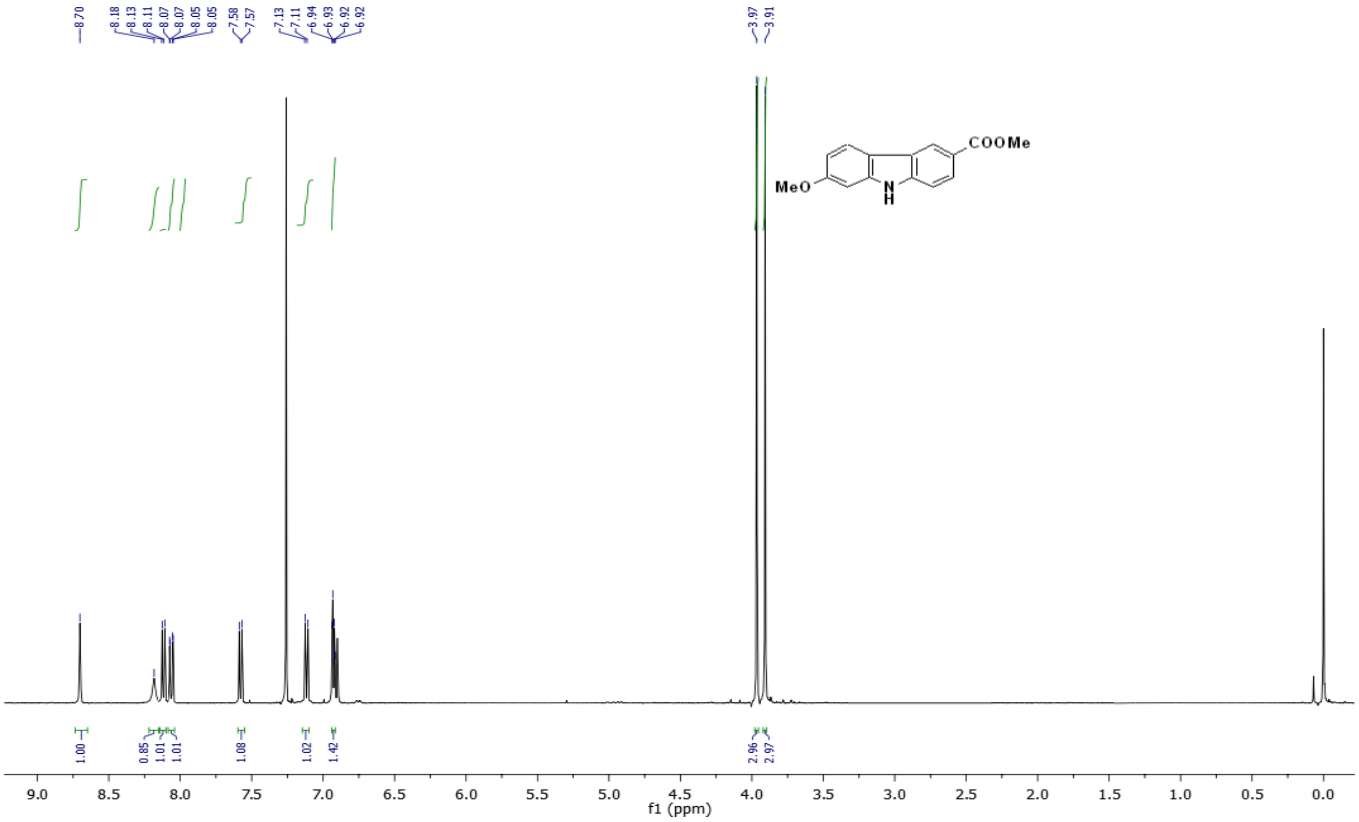
Methyl 9H-carbazole-3-carboxylate (2a): ^{1}H NMR



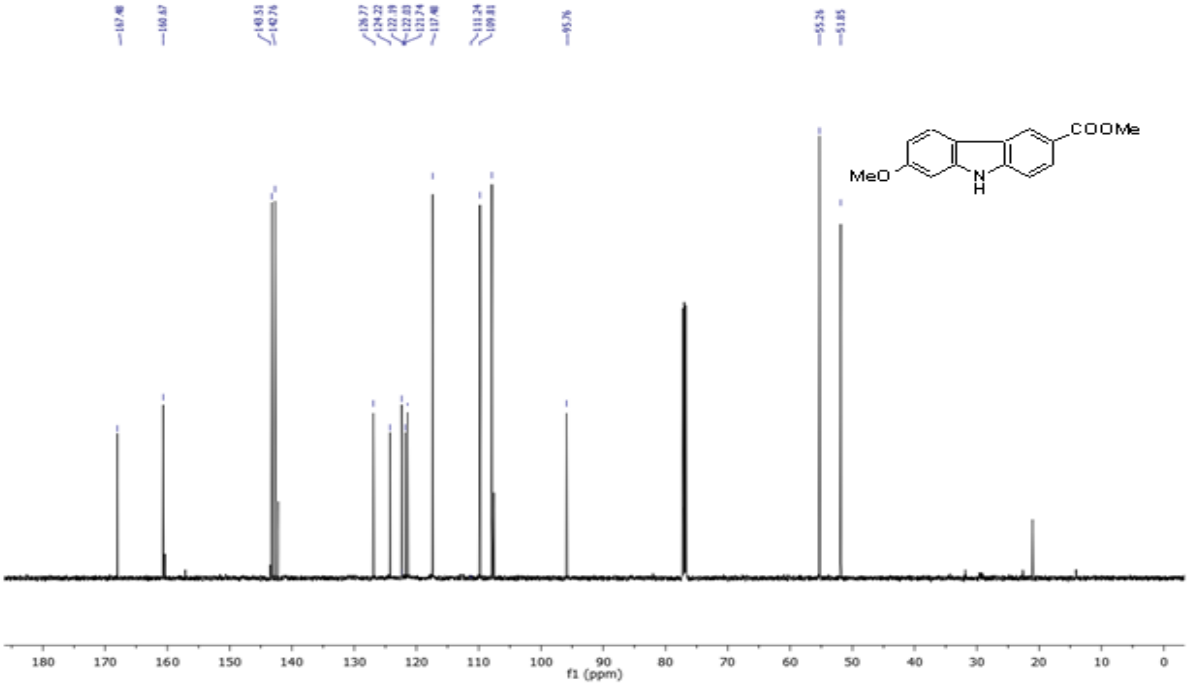
Methyl 9*H*-carbazole-3-carboxylate (2a): ^{13}C NMR



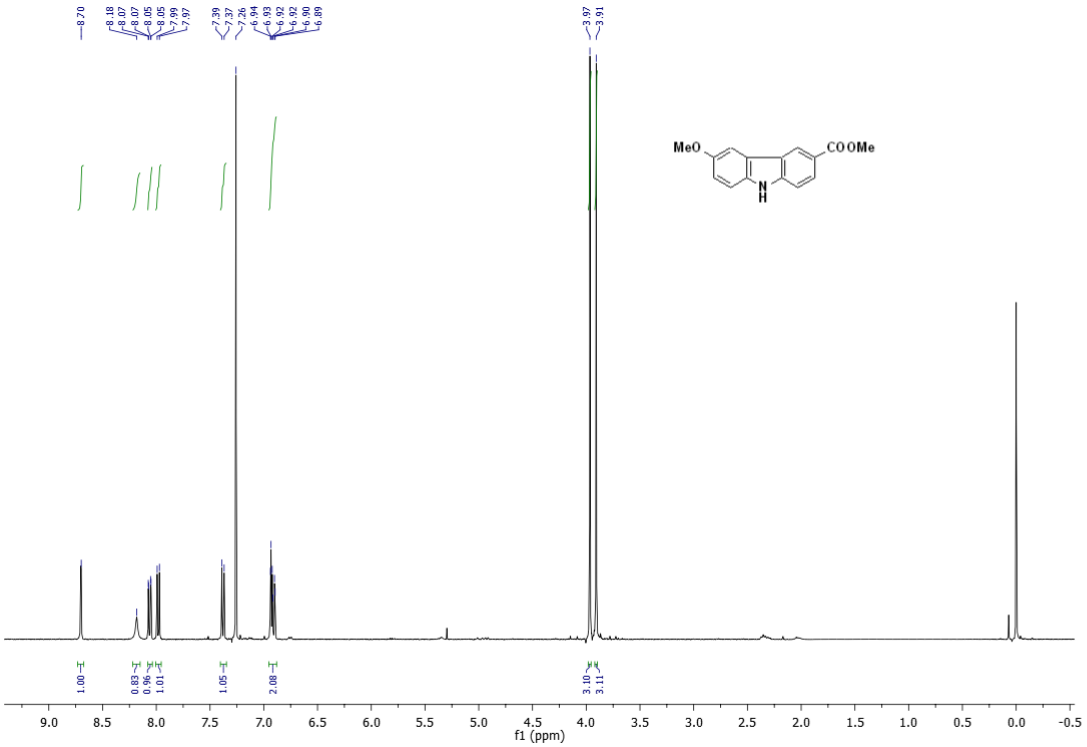
Clausine C (2b): ^{1}H NMR



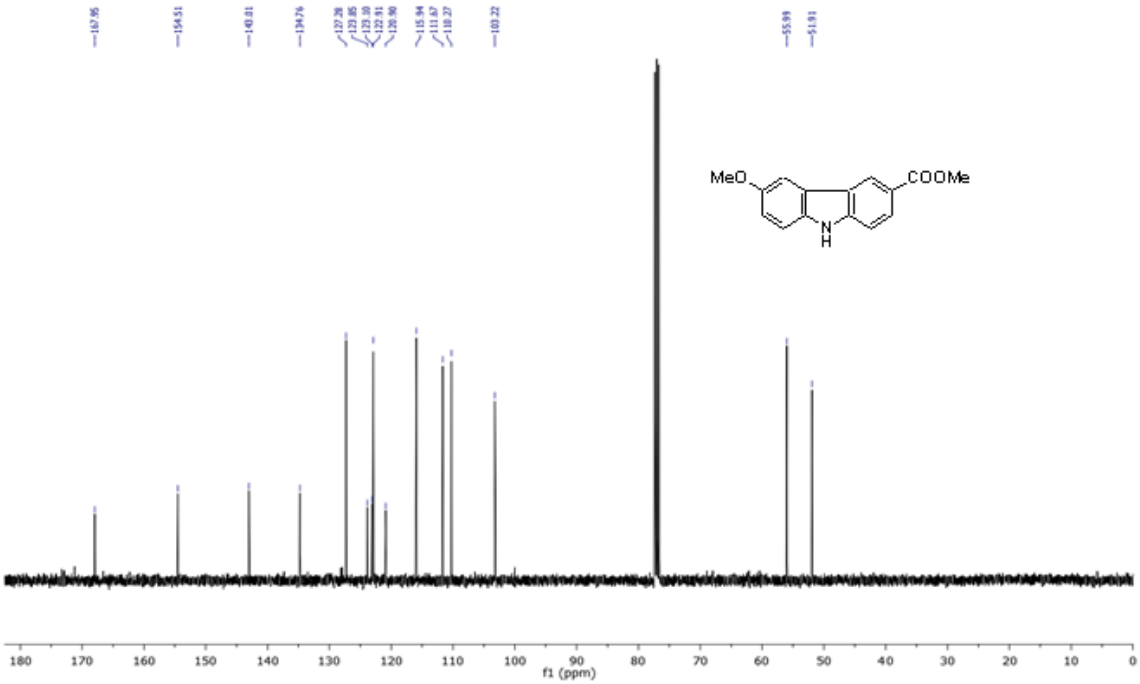
Clausine C (2b): ^{13}C NMR



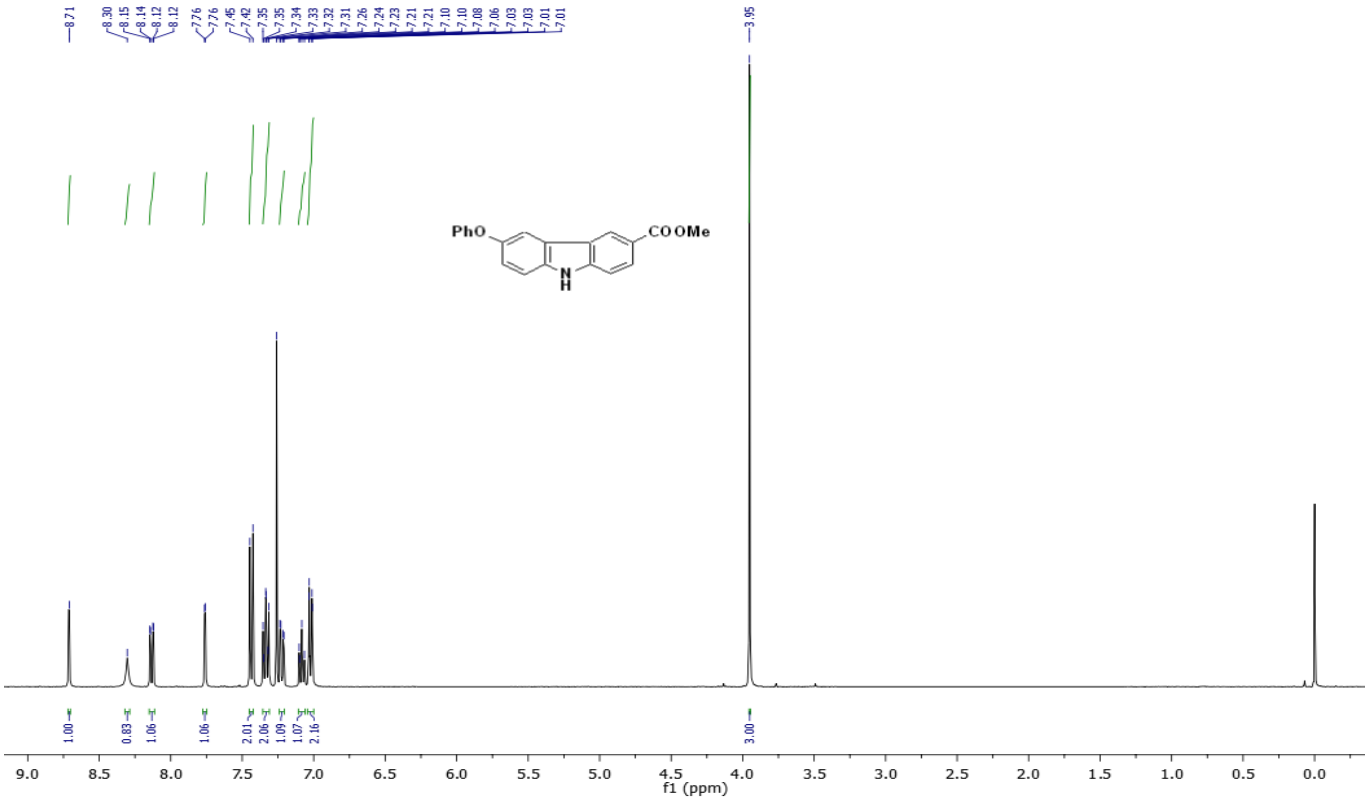
Methyl 6-methoxy-9*H*-carbazole-3-carboxylate (2c): ^{1}H NMR



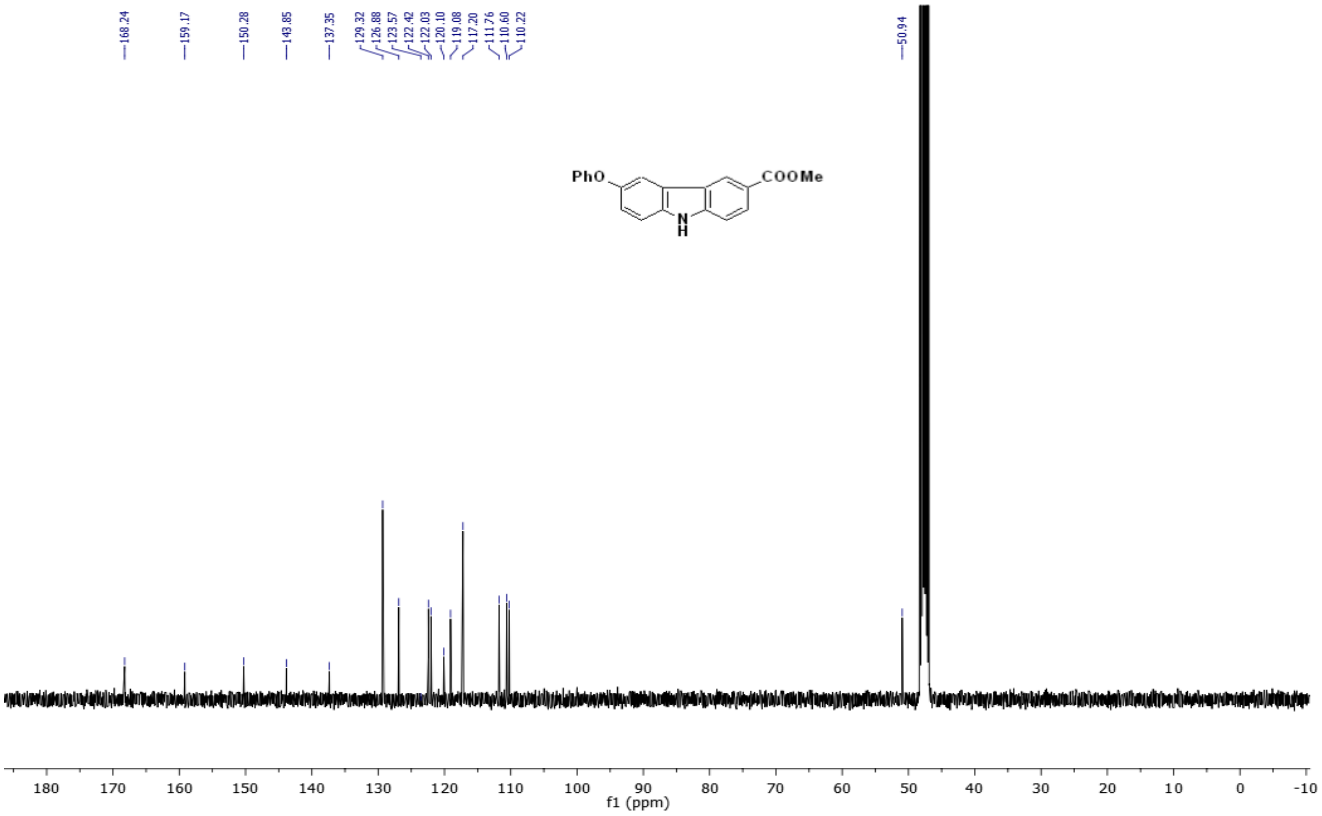
Methyl 6-methoxy-9*H*-carbazole-3-carboxylate (2c): ^{13}C NMR



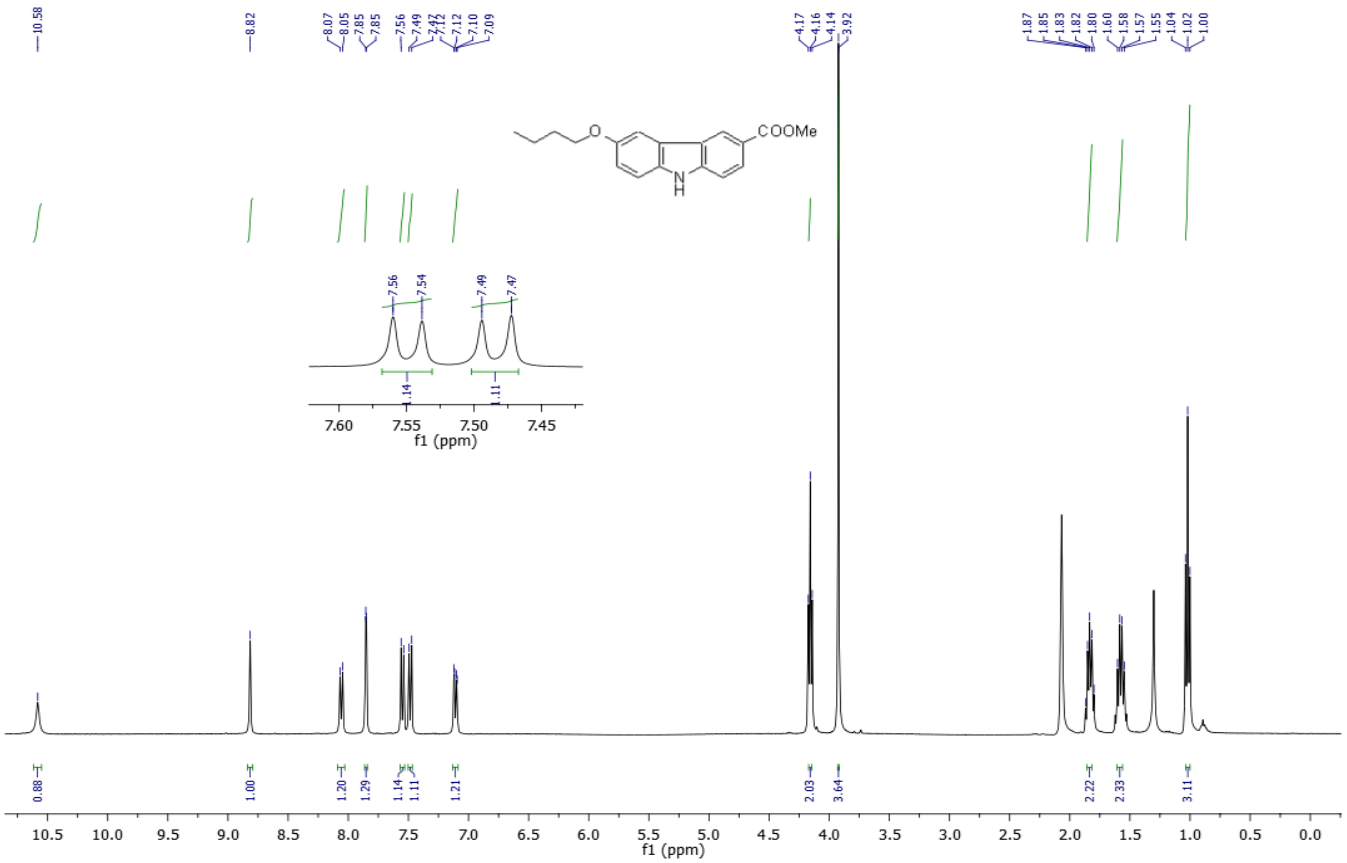
Methyl 6-phenoxy-9*H*-carbazole-3-carbaxylate (2d): ^{1}H NMR



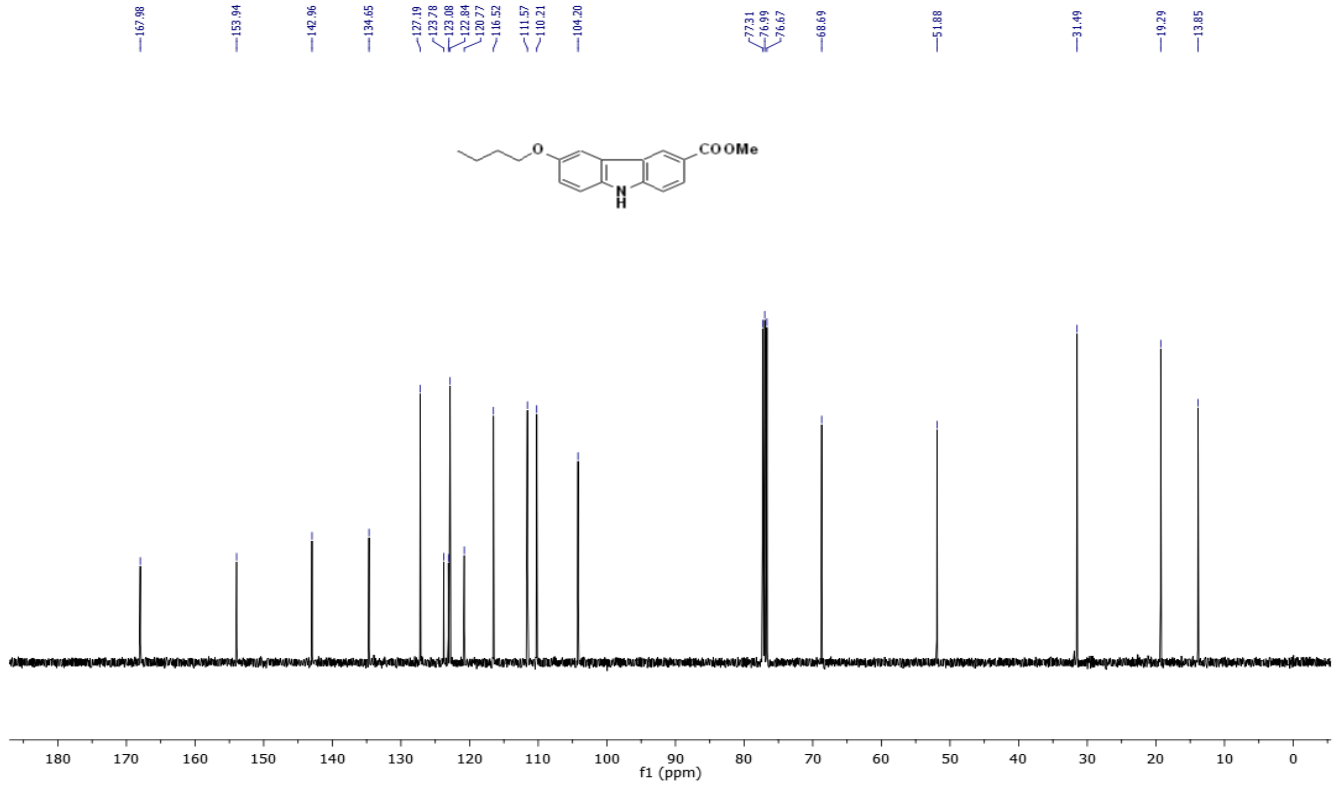
Methyl 6-phenoxy-9*H*-carbazole-3-carbaxylate (2d): ^{13}C NMR



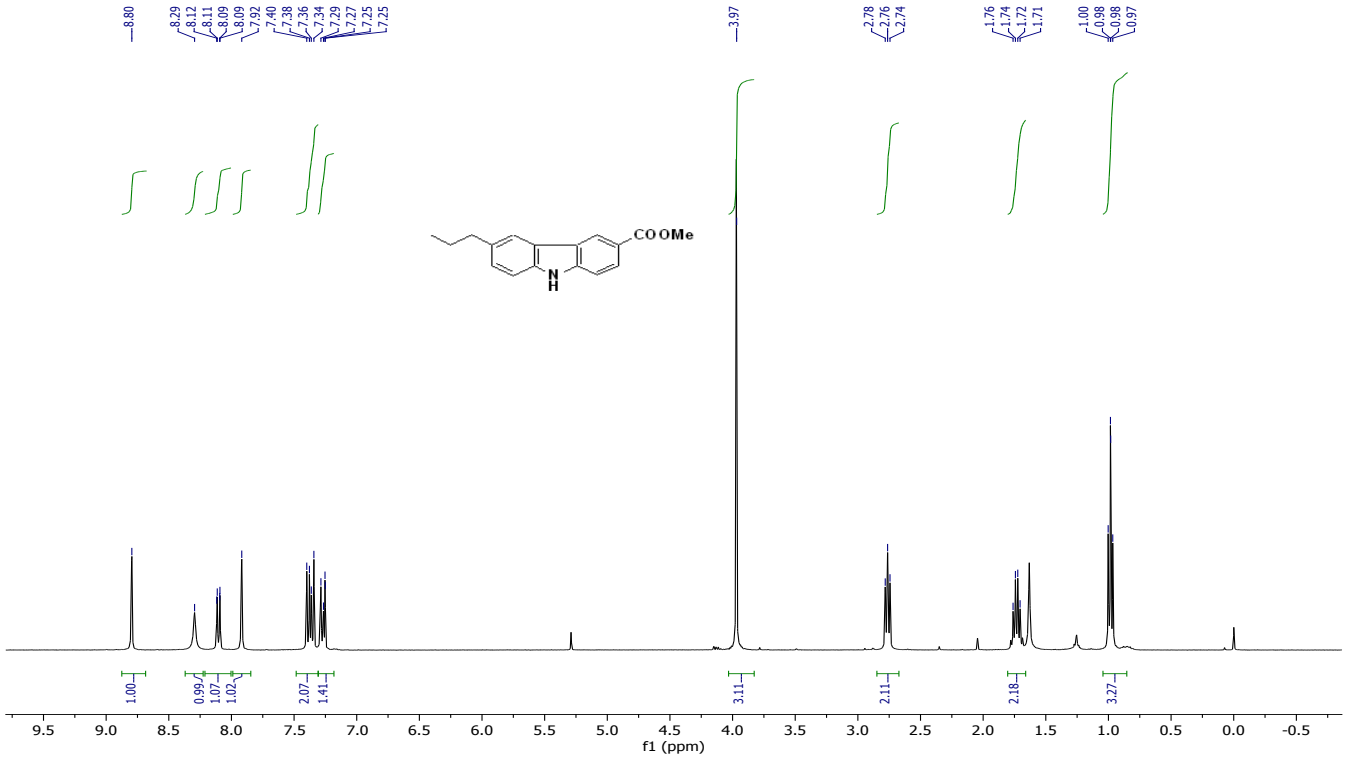
Methyl 6-butoxy-9H-carbazole-3-carbaxylate (2e): ^{1}H NMR



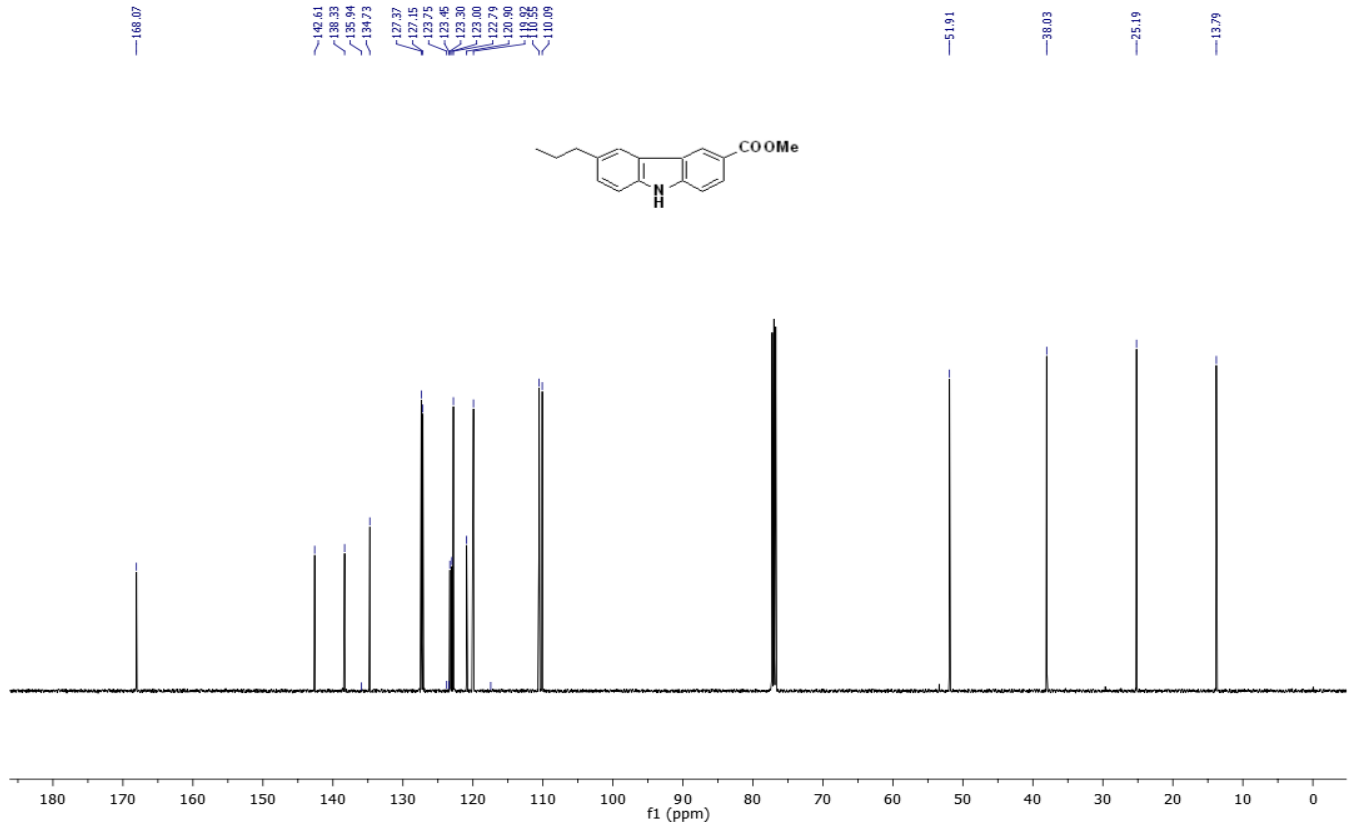
Methyl 6-butoxy-9H-carbazole-3-carbaxylate (2e): ^{13}C NMR



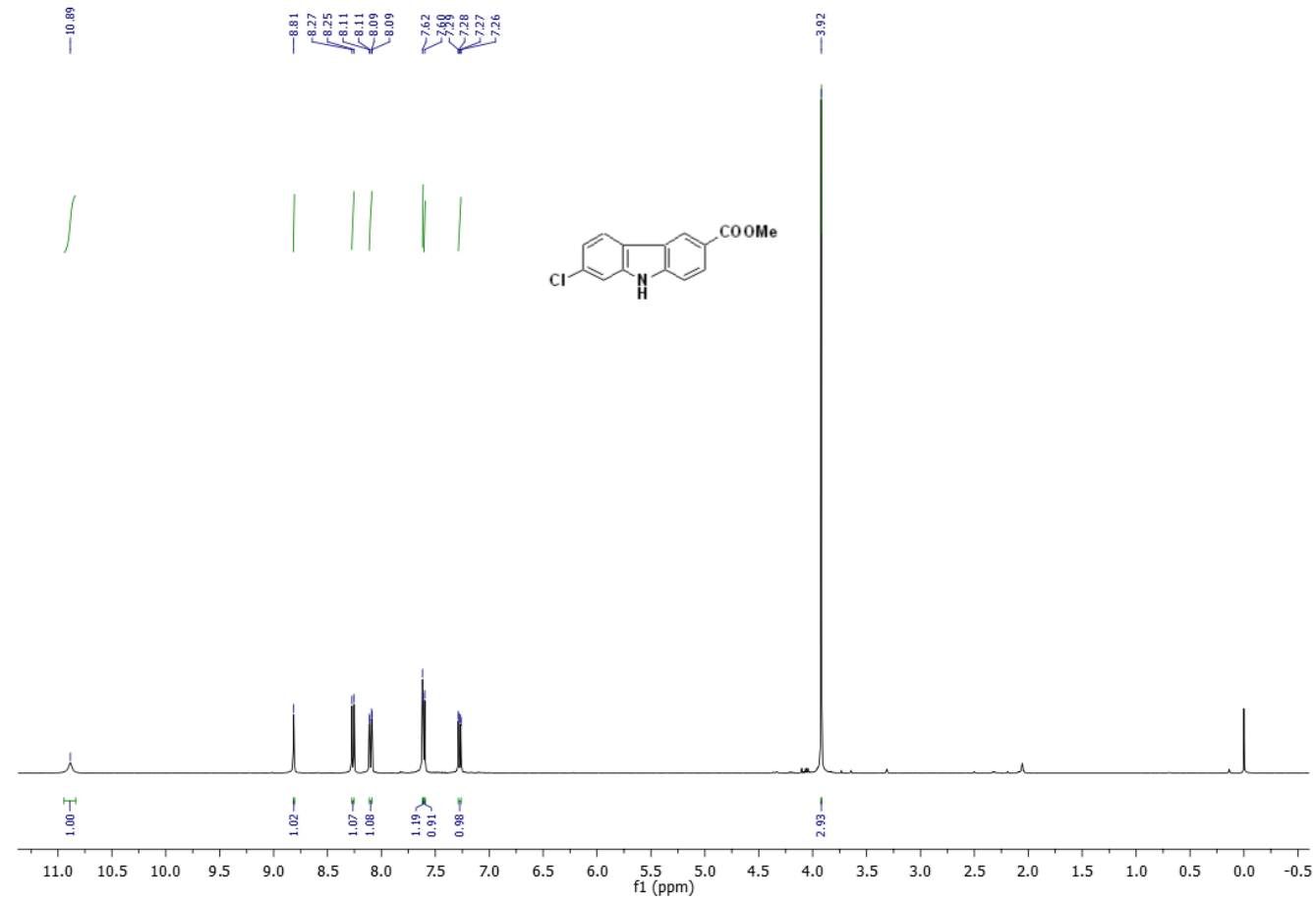
Methyl 6-propyl-9*H*-carbazole-3-carbaxylate (2f): ^{1}H NMR



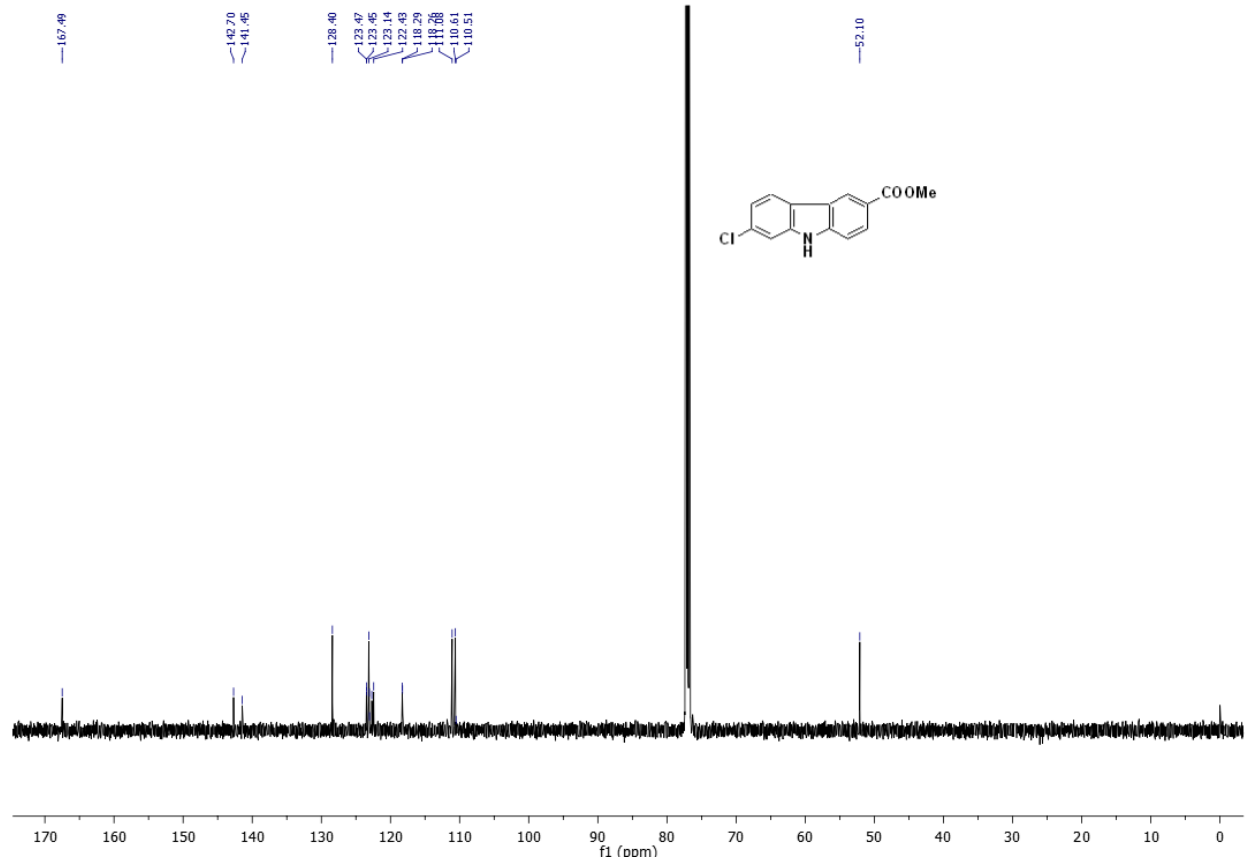
Methyl 6-propyl-9*H*-carbazole-3-carbaxylate (2f): ^{13}C NMR



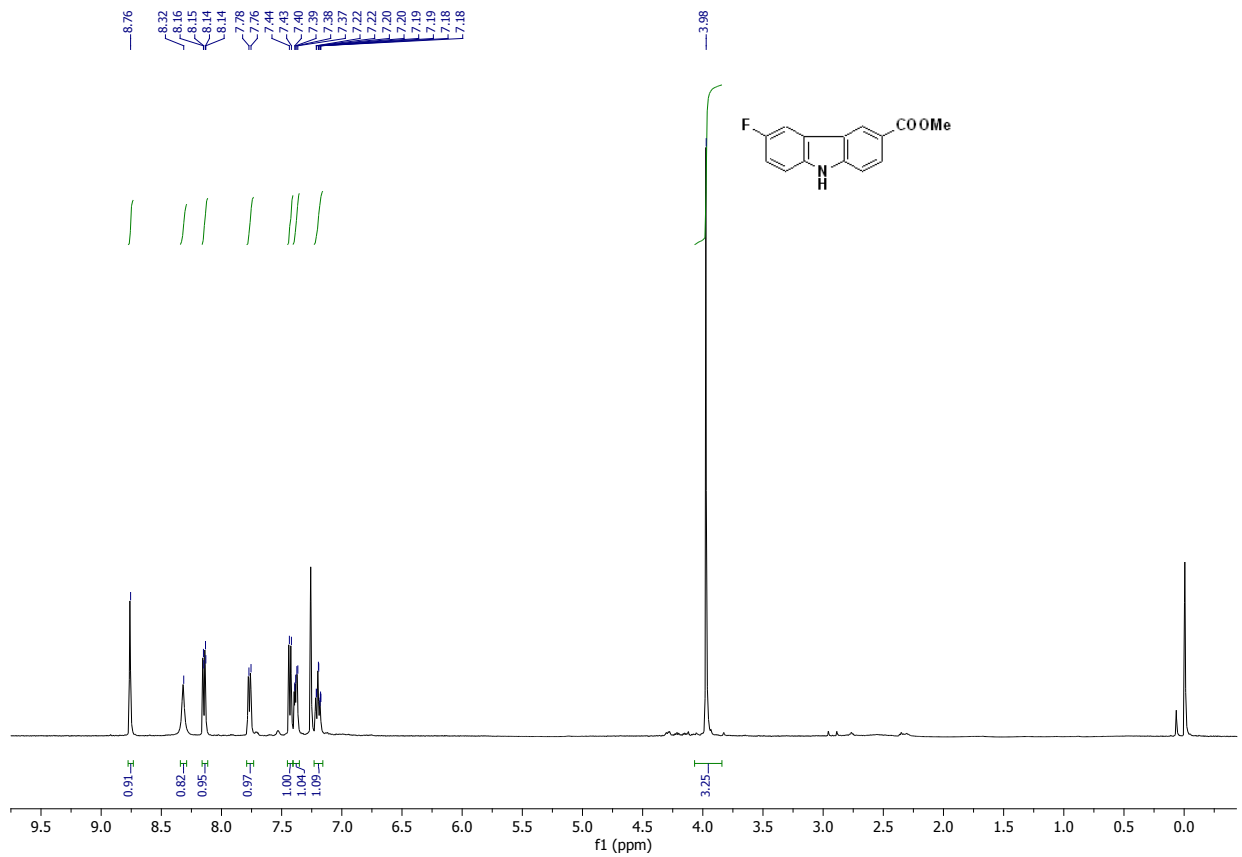
Methyl 7-chloro-9H-carbazole-3-carboxylate (2g): ^{1}H NMR



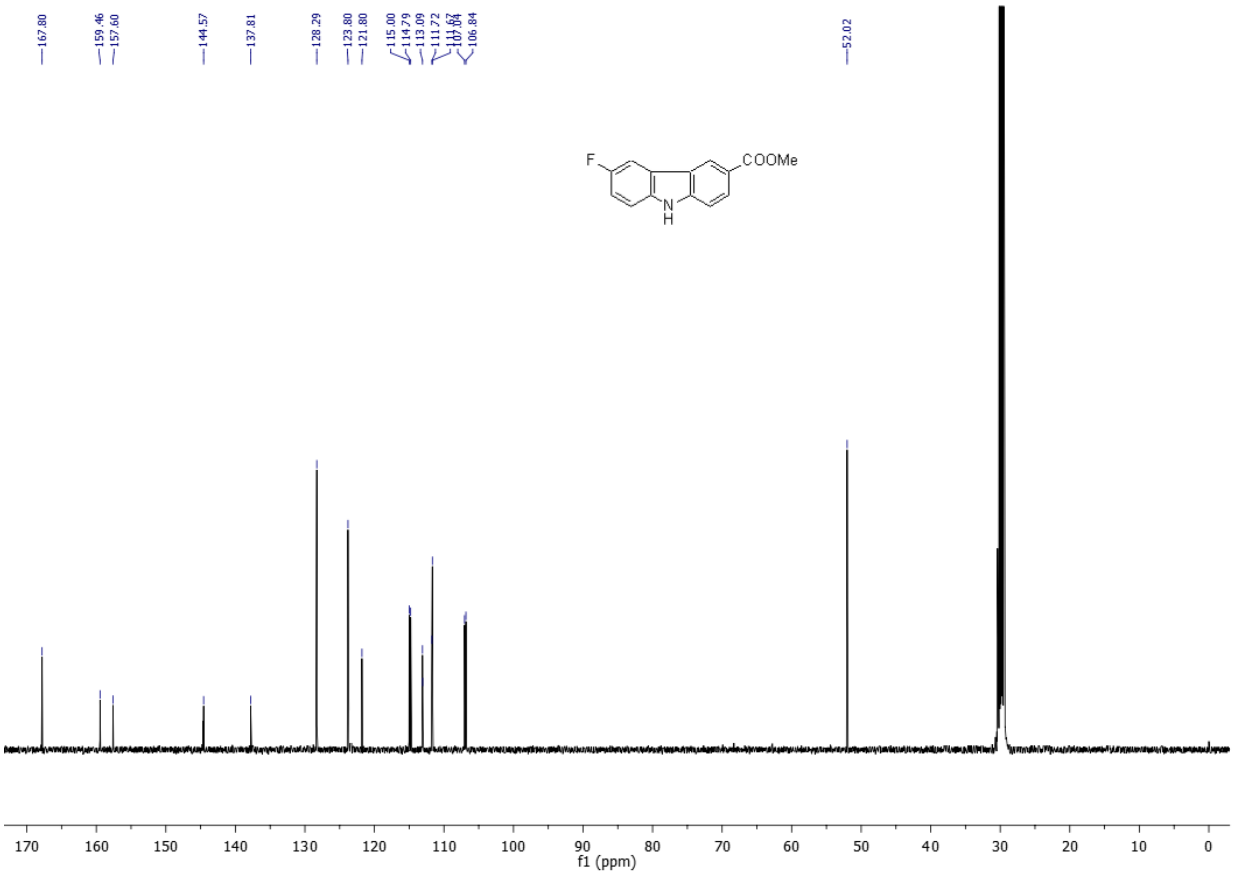
Methyl 7-chloro-9H-carbazole-3-carboxylate (2g): ^{13}C NMR



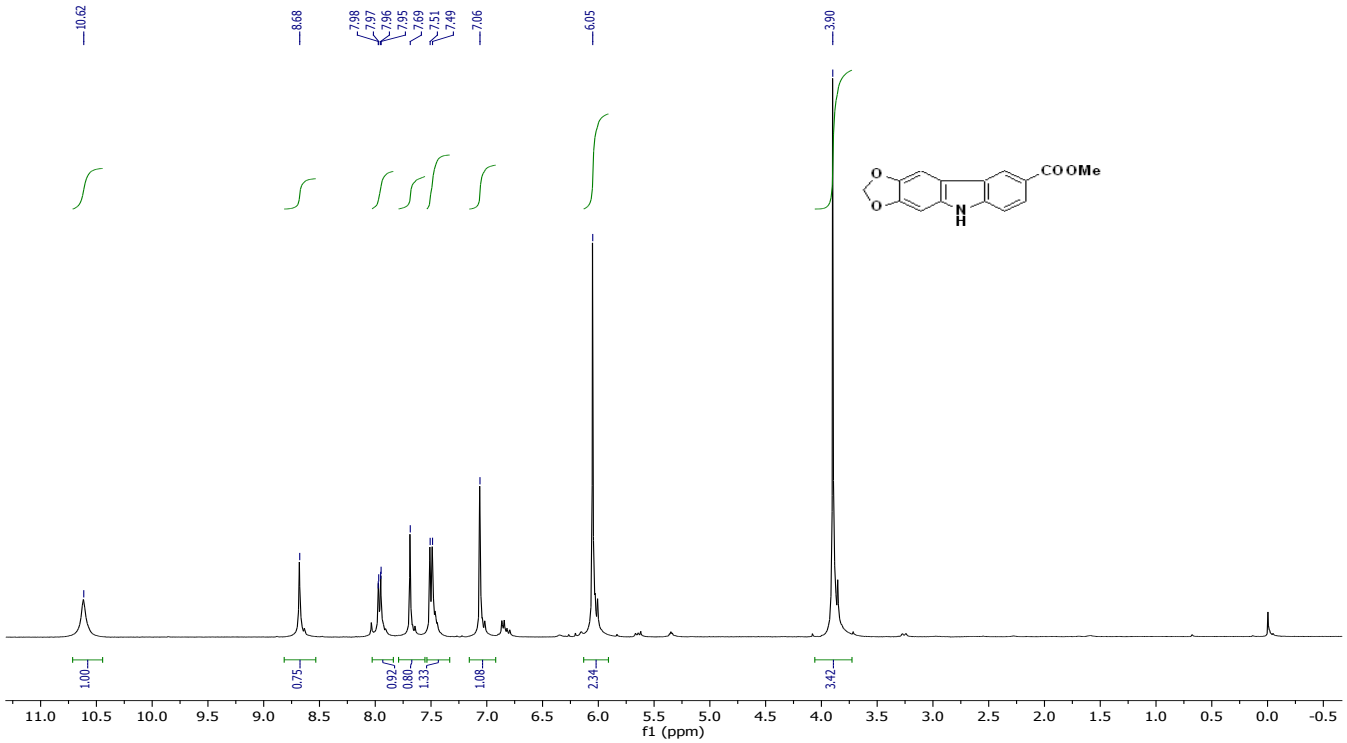
Methyl 6-fluoro-9H-carbazole-3-carboxylate (2h): ^{1}H NMR



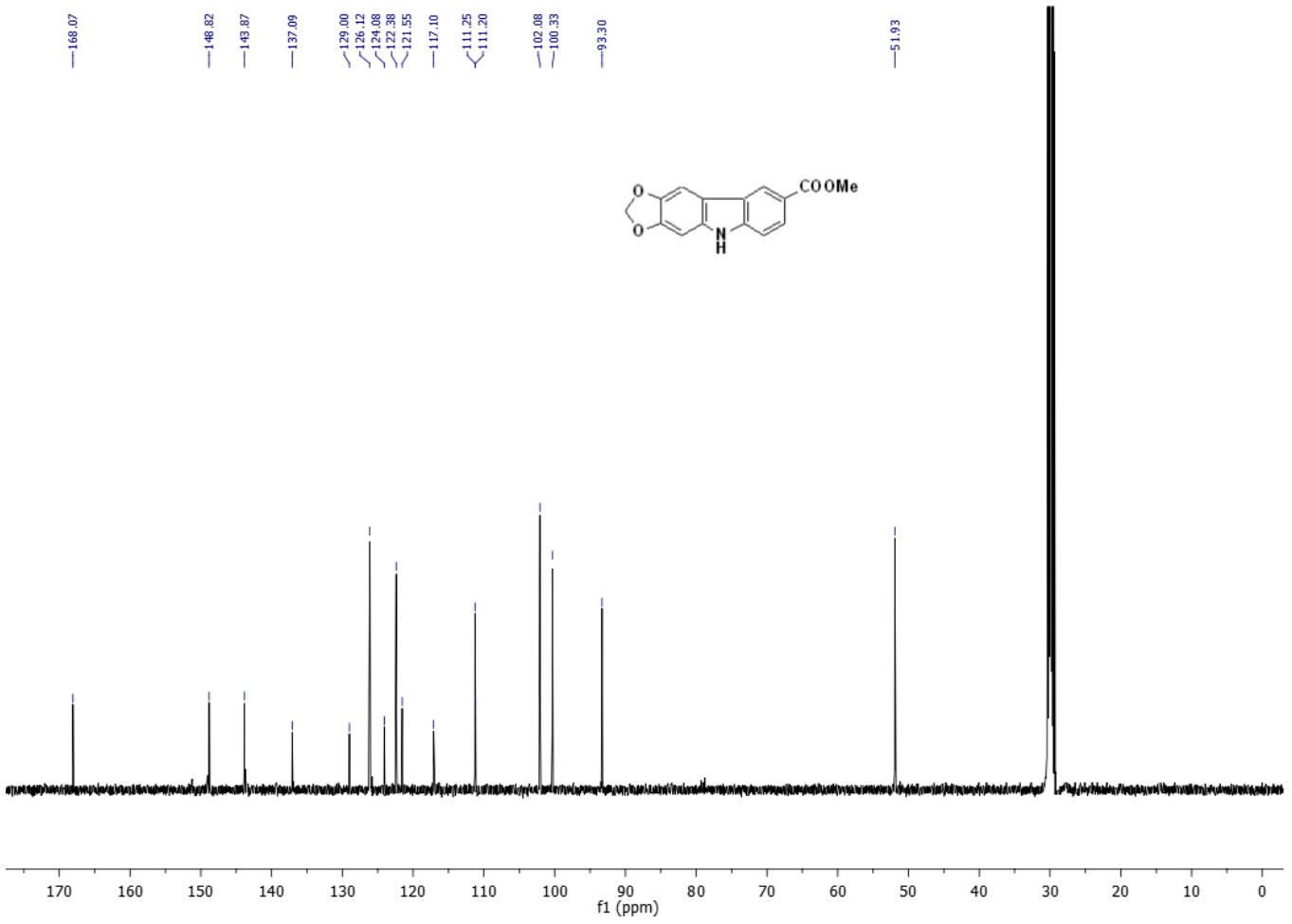
Methyl 6-fluoro-9H-carbazole-3-carboxylate (2h): ^{13}C NMR



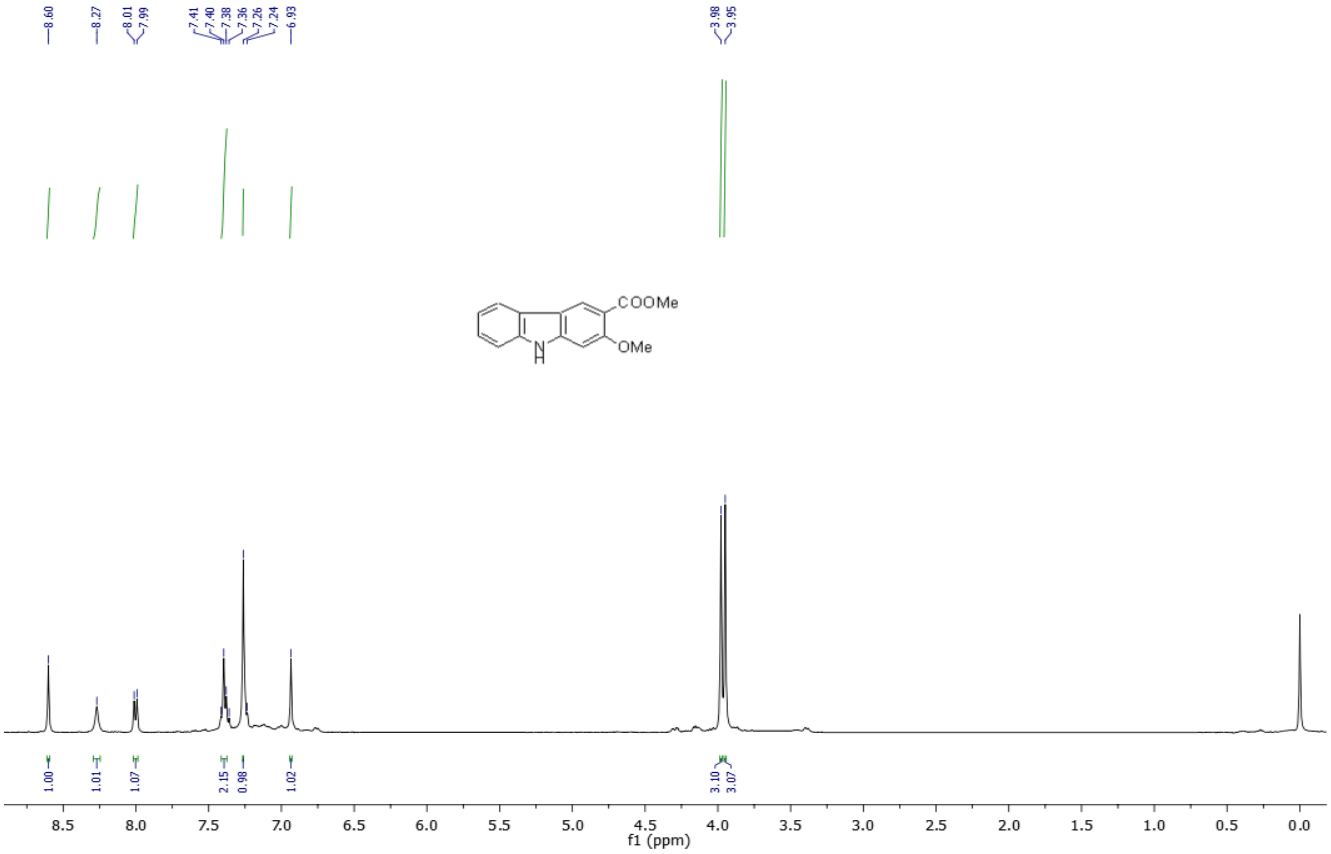
Methyl 5*H*-[1,3]dioxolo[4,5-b]carbazole-8-carbaxylate (2i): ^{1}H NMR



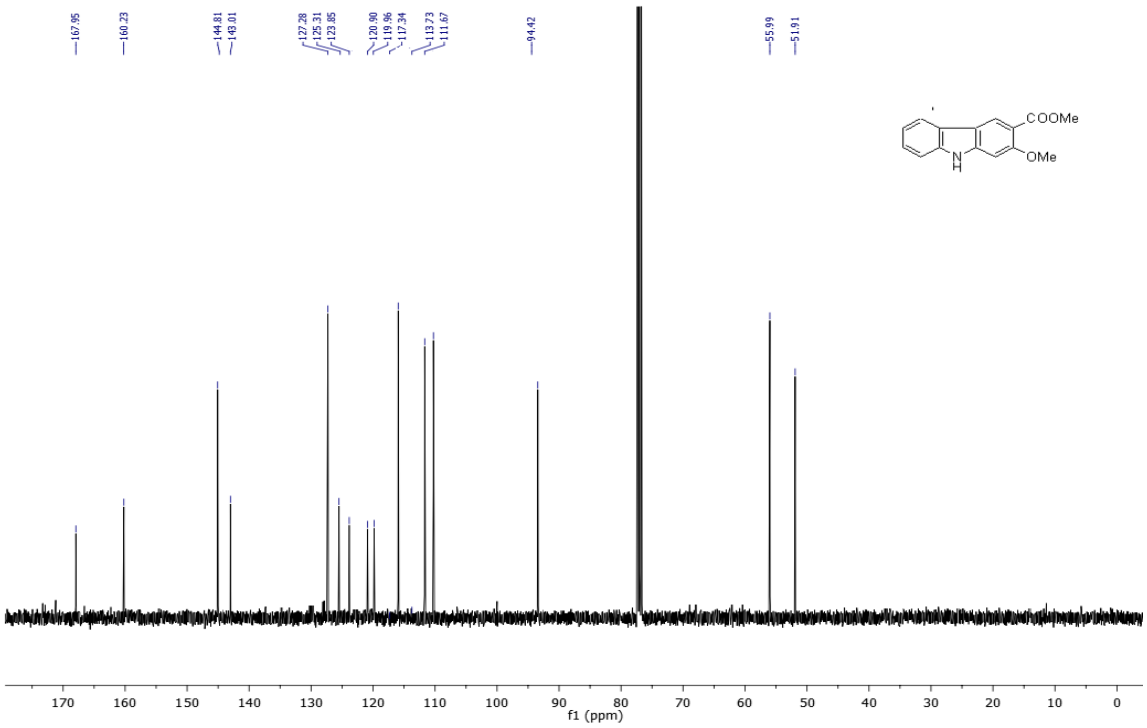
Methyl 5*H*-[1,3]dioxolo[4,5-b]carbazole-8-carbaxylate (2i): ^{13}C NMR



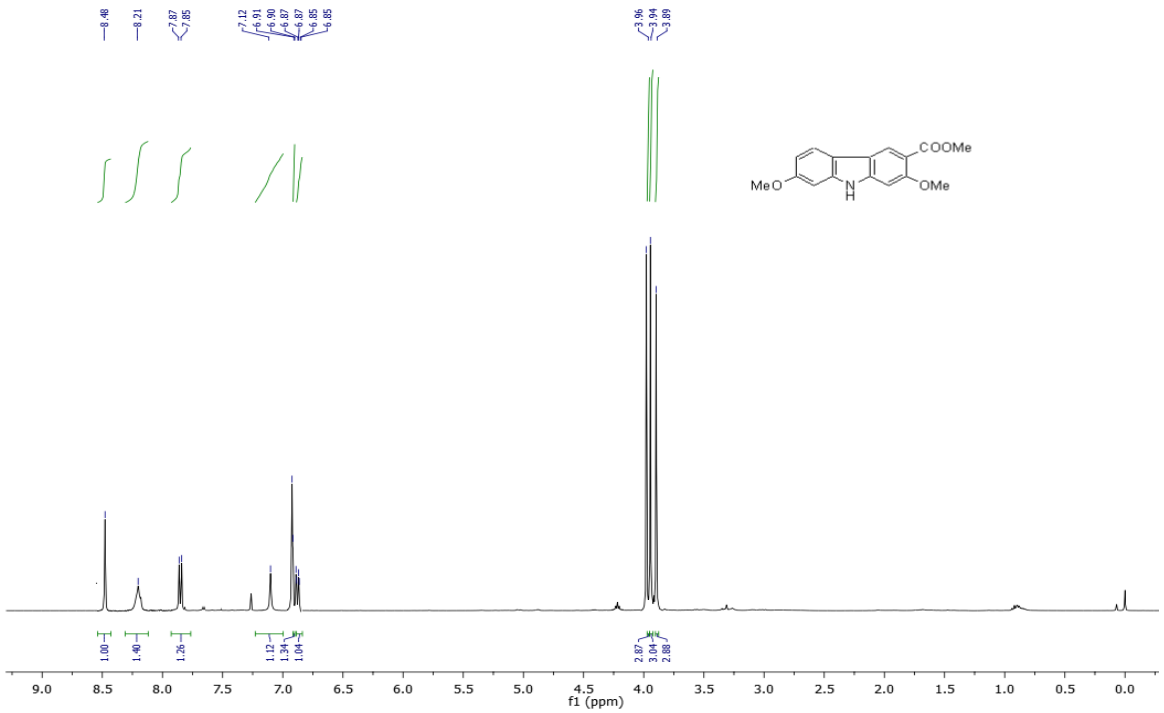
Clausine L (2j): ^{1}H NMR



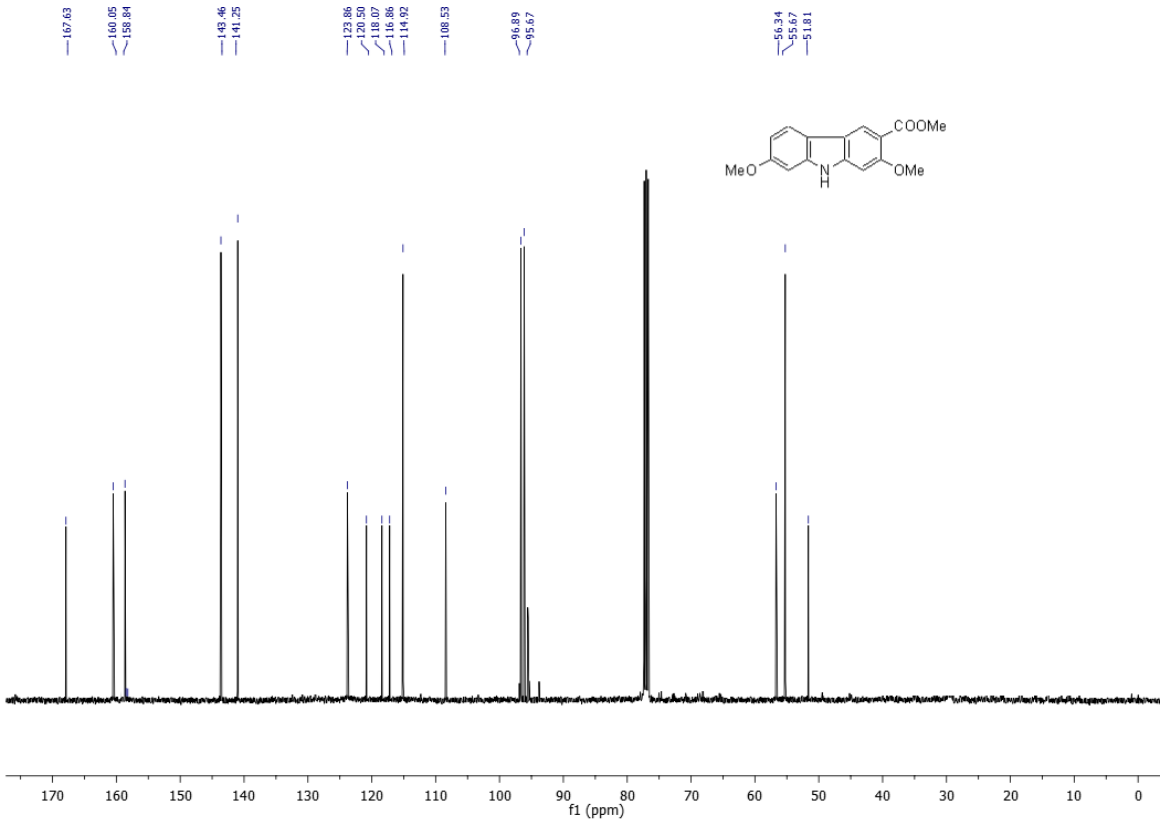
Clausine L (2j): ^{13}C NMR



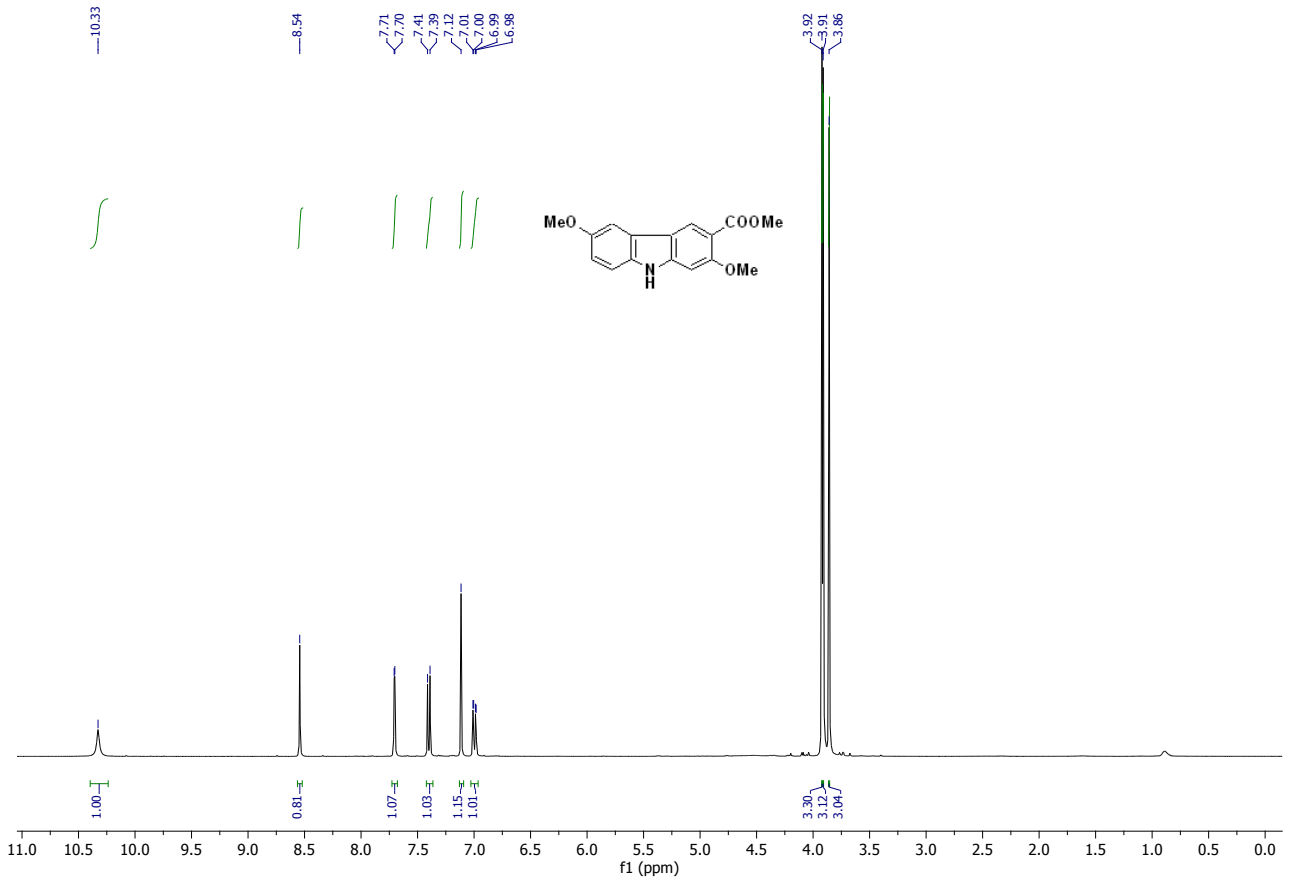
Clausine H (2k): ^{1}H NMR



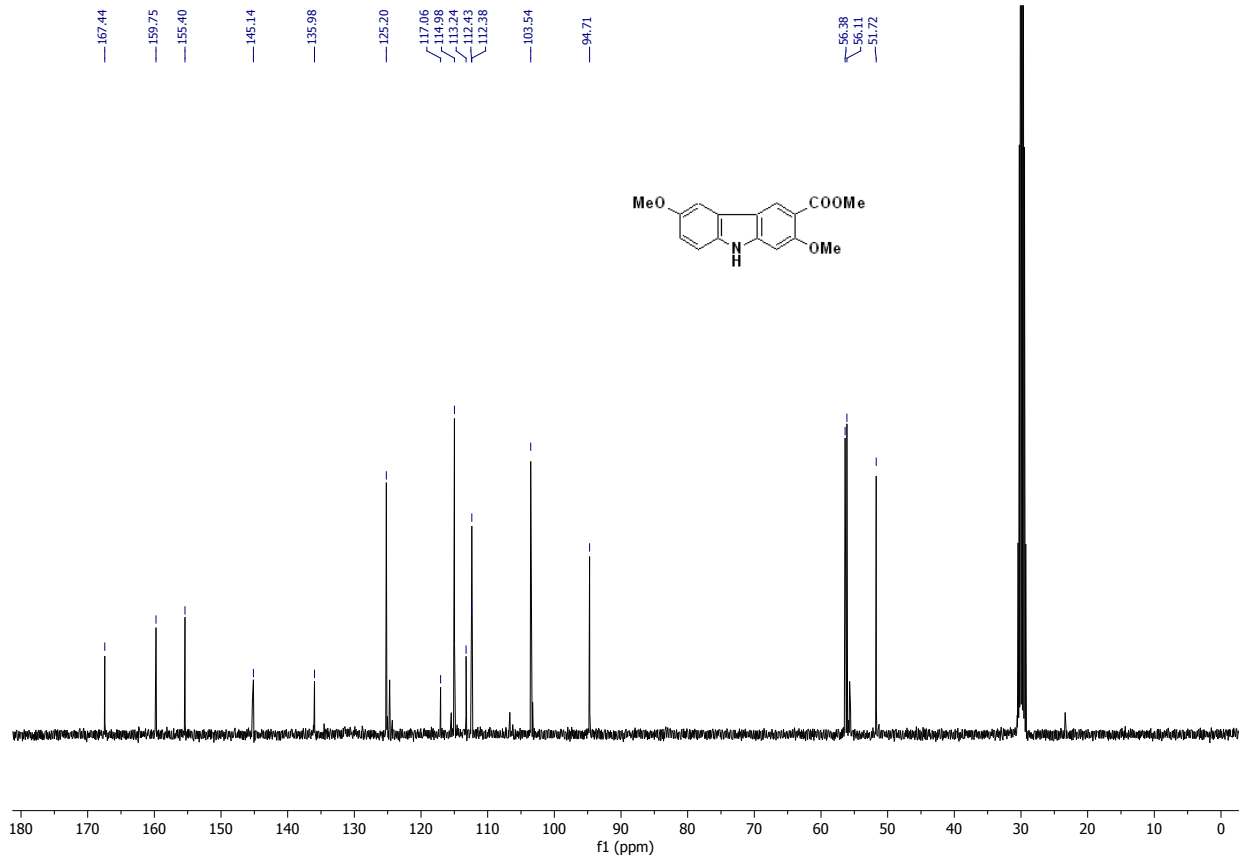
Clausine H (2k): ^{13}C NMR



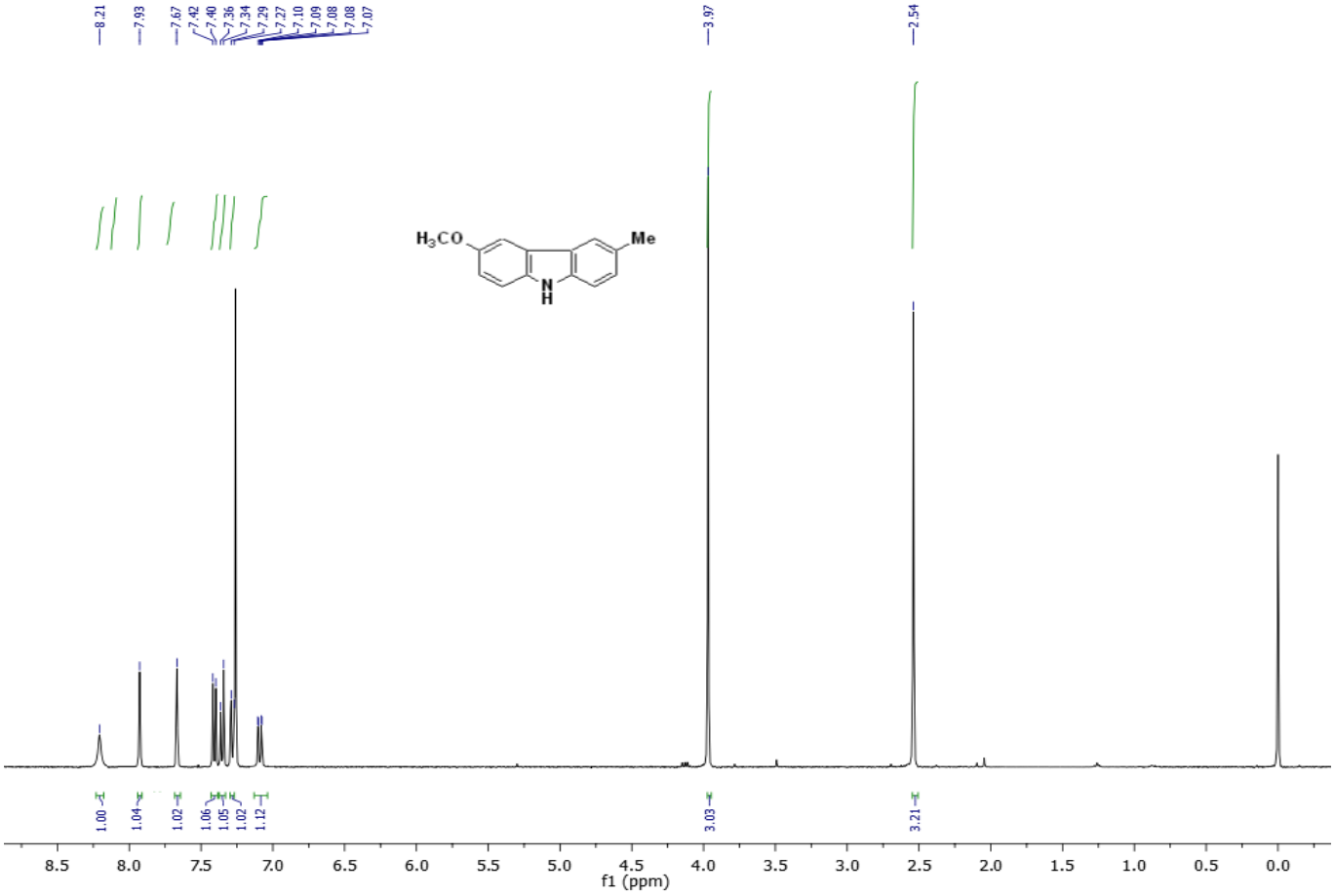
Methyl 2,6-dimethoxy-9*H*-carbazole-3-carboxylate (2l): ^{1}H NMR



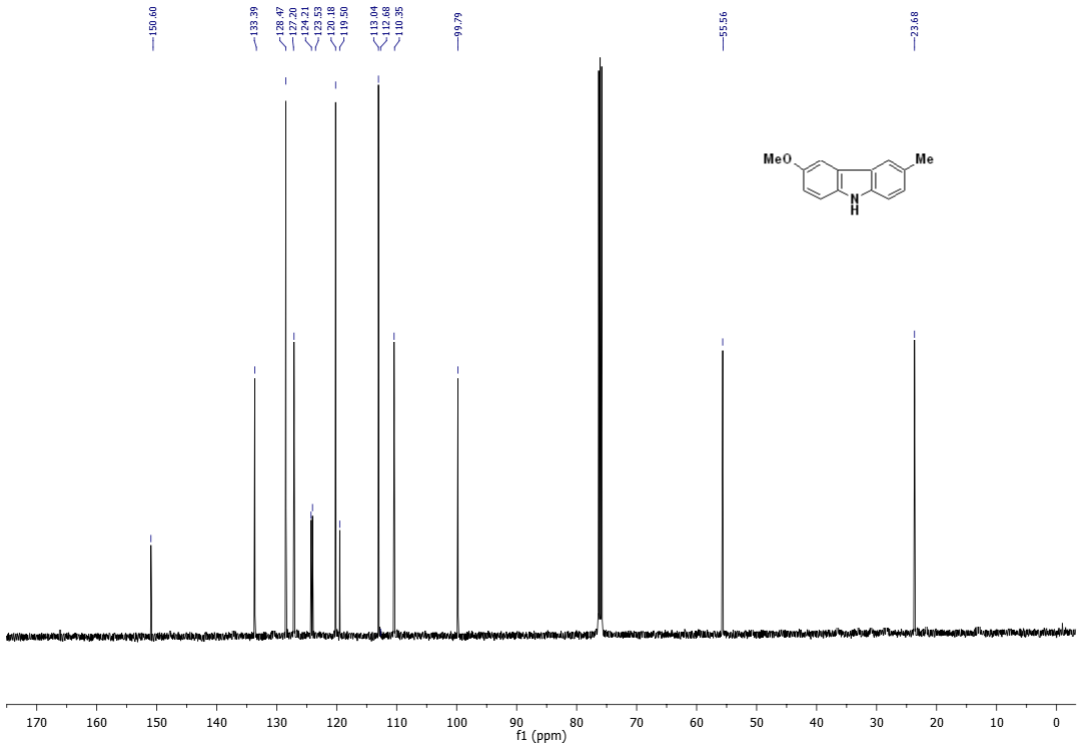
Methyl 2,6-dimethoxy-9*H*-carbazole-3-carboxylate (2l): ^{13}C NMR



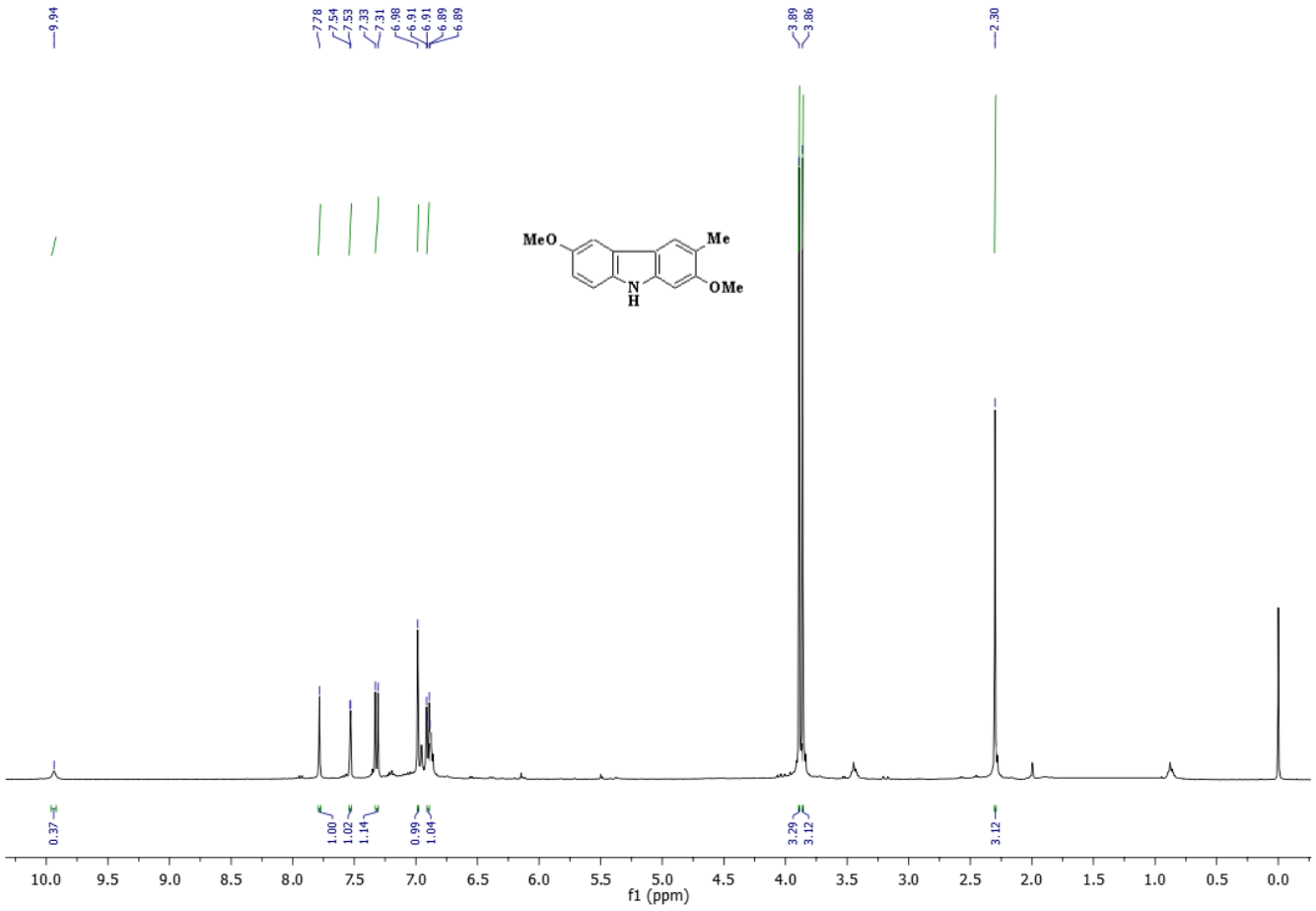
Glycozoline (3): ^{1}H NMR



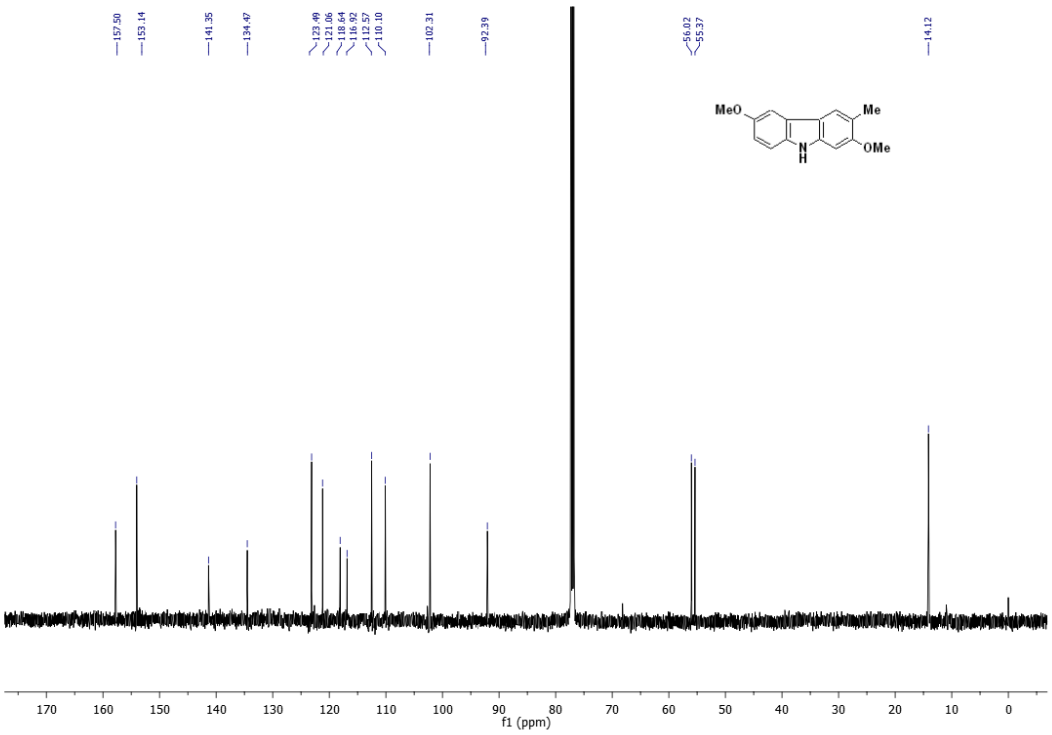
Glycozoline (3): ^{13}C NMR



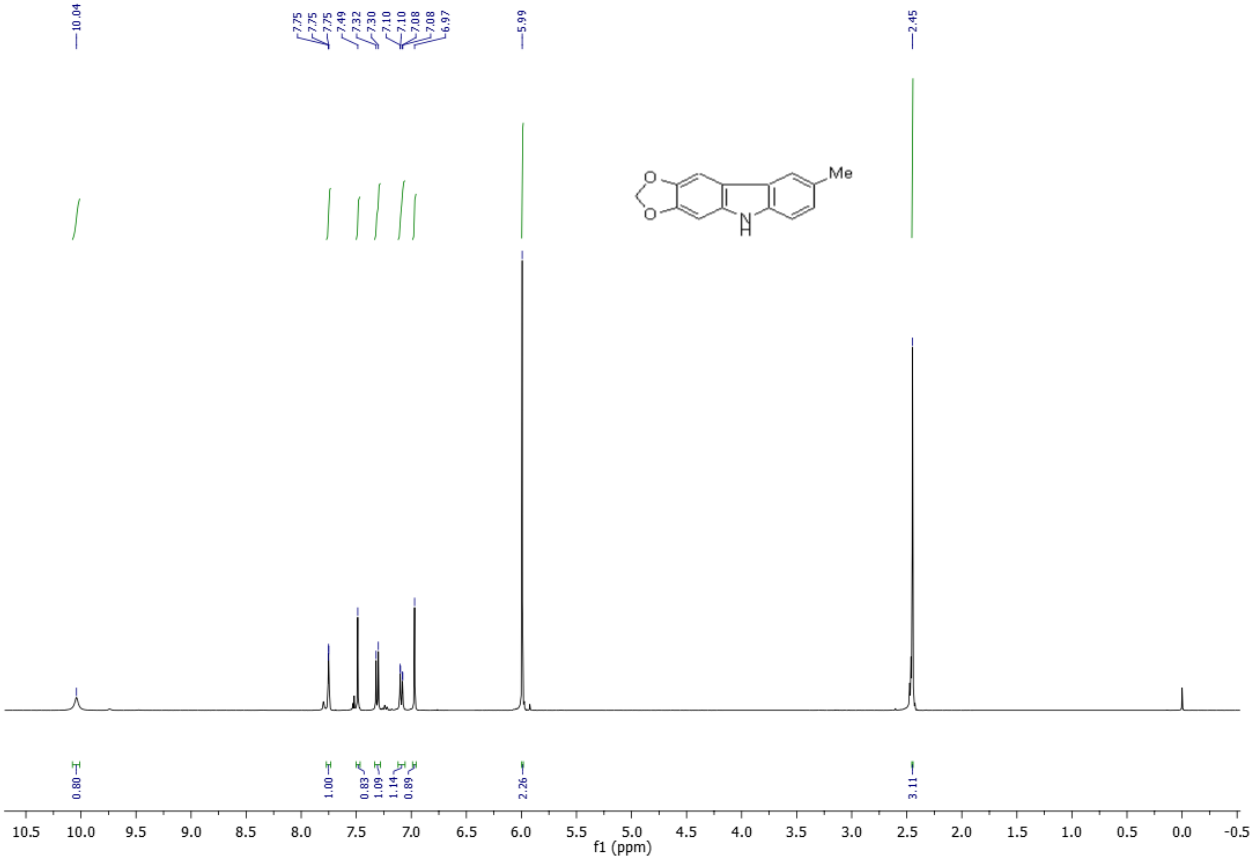
Glycozolidine (4): ^{1}H NMR



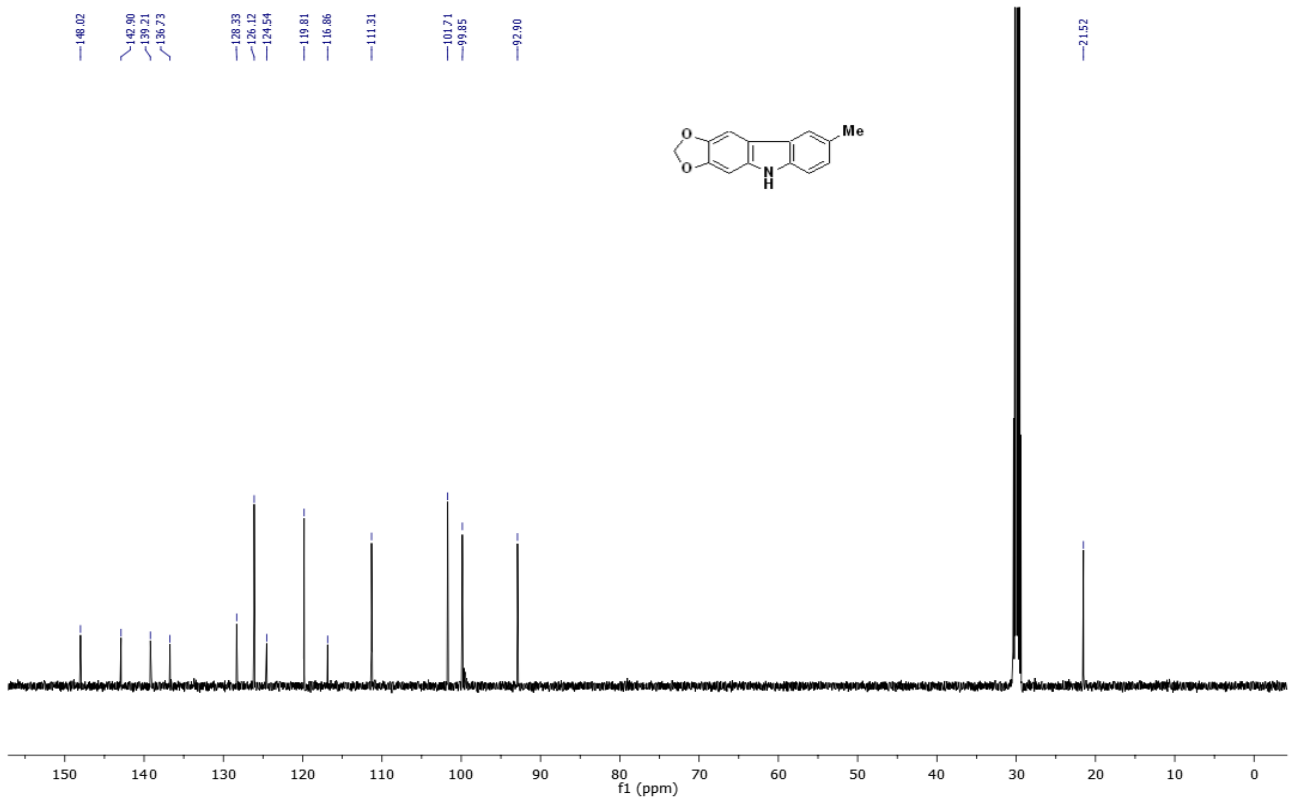
Glycozolidine (4): ^{13}C NMR



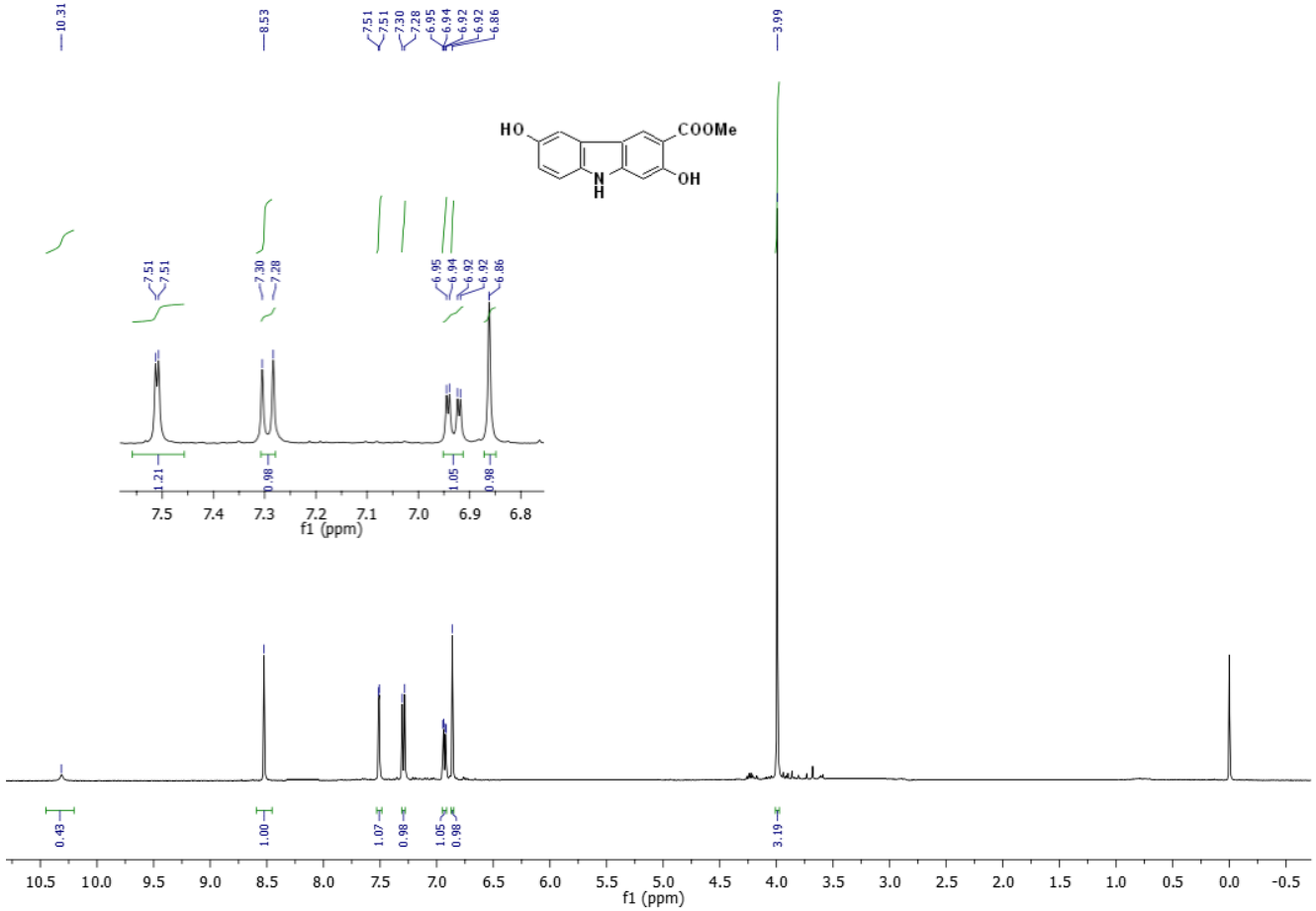
Clausenaline (5): ^{1}H NMR



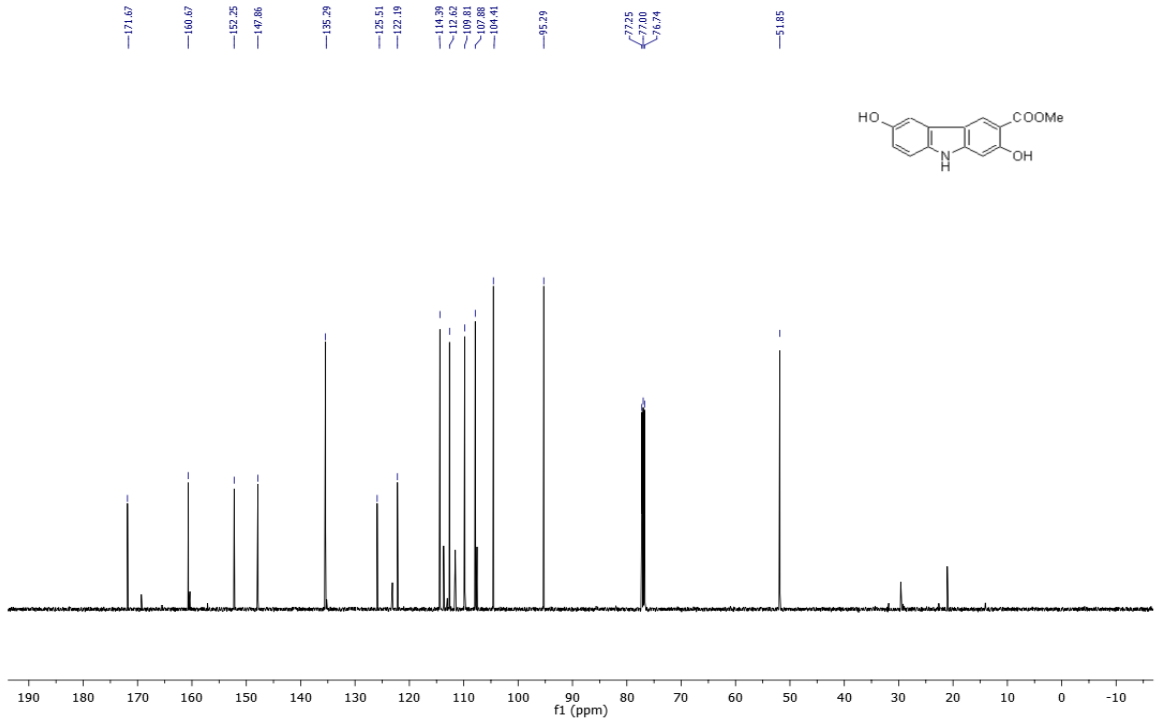
Clausenaline (5): ^{13}C NMR



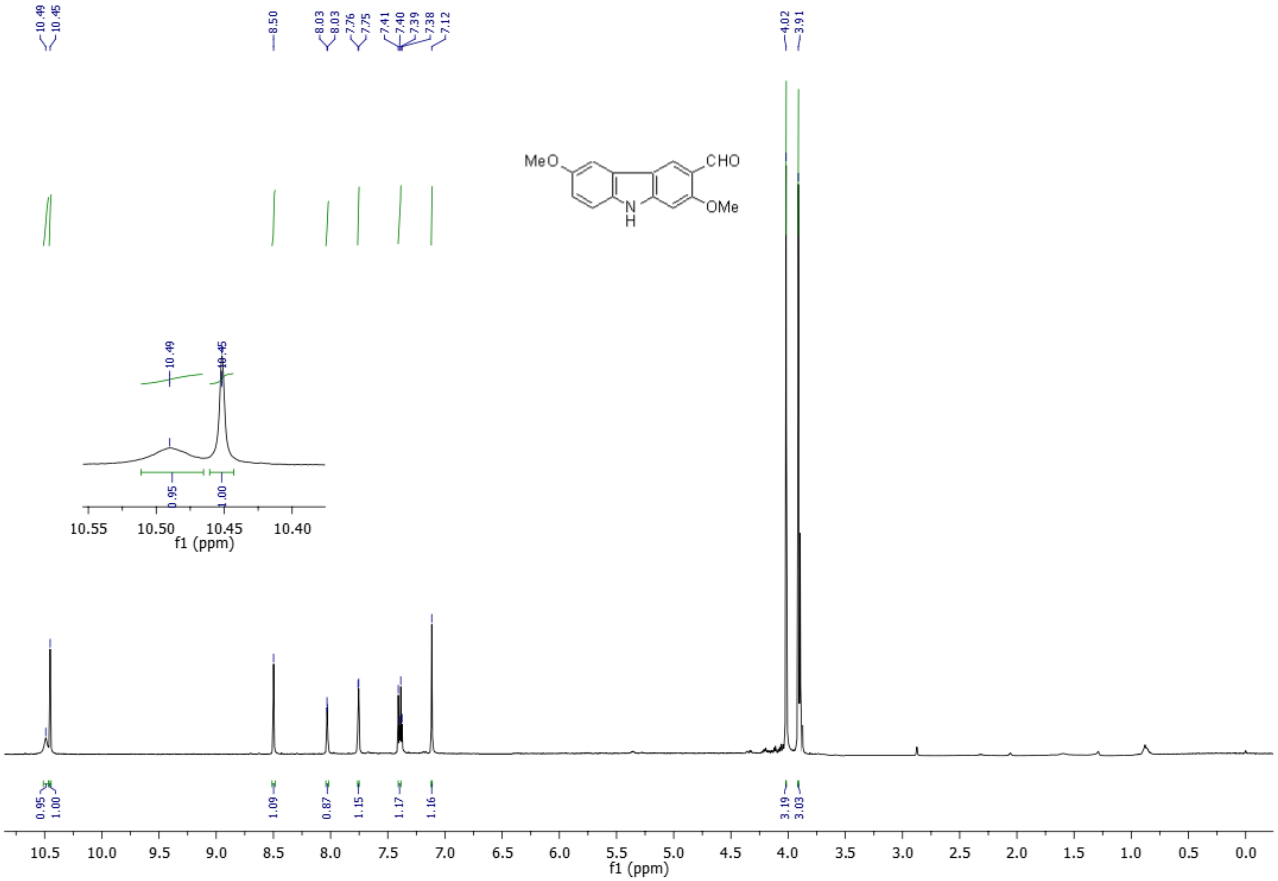
Sansoakamine (6): ^{1}H-NMR



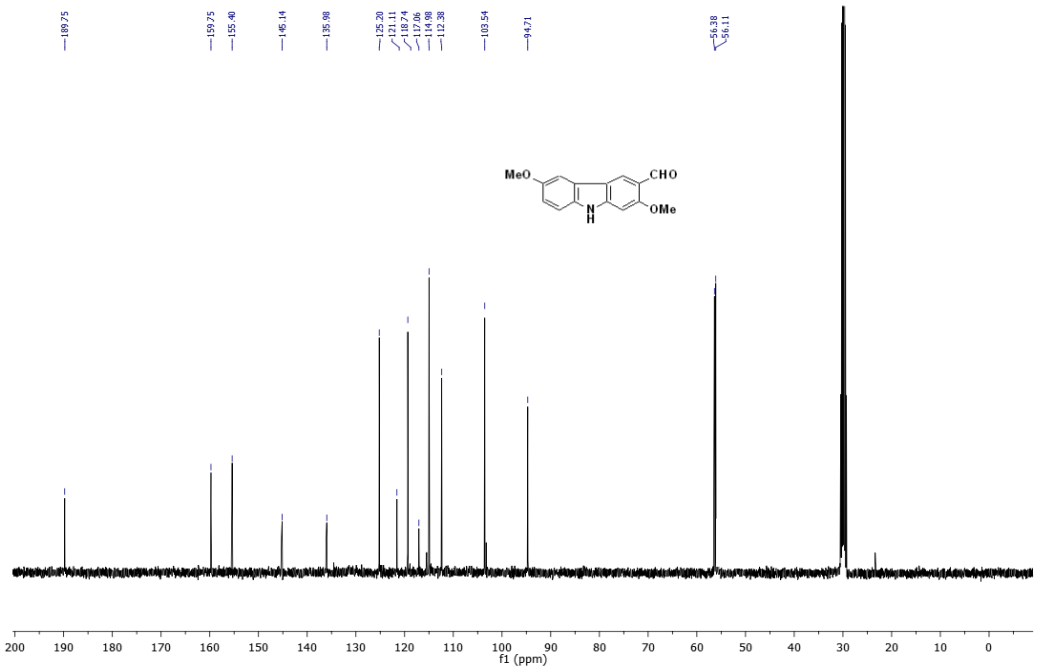
Sansoakamine (6): ^{13}C-NMR



Glycozolidal (7): ^{1}H NMR



Glycozolidal (7) : ^{13}C NMR



X-ray crystallography of methyl 6-propyl-9*H*-carbazole-3-carboxylate (2f):

A single crystal of methyl 6-propyl-9H-carbazole-3-carboxylatewas obtained by slow evaporation at room temperature, from a mixture of methanol/water. The X-ray data was collected from a dry crystal mounted on an 'Xcalibur, Sapphire3', Oxford diffractometer. The crystal structure was solved by direct method using SHELXS-97[2] followed by Full matrix anisotropic least square refinement using SHELXL-97.[2] All the hydrogen atoms were located from difference Fourier map except the methyl groups. For methyl group the hydrogen atom were fixed geometrically and refined in the final cycle as riding over the heavy atom they are bonded. All the relevant crystallographic data collection parameters and structure refinement details for **2f** is summarized in Table 2. Bond lengths and bond angles are given in Table 3.

Table 2. Crystal data and structure refinement for **2f**

Identification code	**2f**	
Empirical formula	$C_{17}\ H_{17}\ N_1\ O_2$	
Formula weight	267.32	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P\ 2_1/n$	
Unit cell dimensions	a = 12.8565(7) Å	α= 90°.
	b = 13.8210(7) Å	β= 98.229(5)°.
	c = 8.0271(4) Å	γ = 90°.
Volume	1411.63(13) $Å^3$	
Z	4	
Density (calculated)	1.258 Mg/m^3	
Absorption coefficient	0.082 mm^{-1}	
F(000)	568	
Crystal size	0.3 x 0.2 x 0.01 mm^3	
Theta range for data collection	3.9 to 27.0°.	
Index ranges	-16<=h<=16, -17<=k<=17, -9<=l<=10	
Reflections collected	11900	
Scan type	ω-scan	
Unique reflections	3031 [R(int) = 0.0305]	
Observed reflection [|F| >4σ(F)]	1989	
Completeness to theta = 26.74°	98.4 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3031 / 0 / 249	
Goodness-of-fit (S)	1.059	
Final R indices [I>2sigma(I)]	R1 = 0.0520, wR2 = 0.1298	

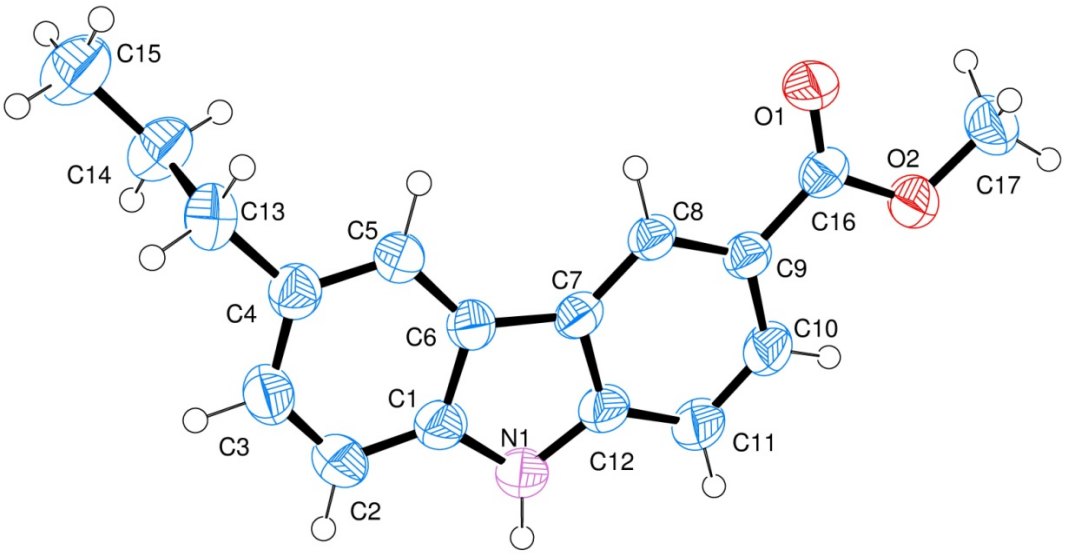
R indices (all data)	R1 = 0.0856, wR2 = 0.1561
Largest diff. peak and hole	0.158 and -0.213 e.Å^{-3}
CCDC number	909569

Table 3. Bond lengths [Å] and angles [°] for **2f**

C(1) - C(2)	1.391(3)	C(1) - C(6)	1.403(3)
C(1) - N(1)	1.382(3)	C(2) - C(3)	1.373(4)
C(2) - H(2)	0.94(3)	C(3) - C(4)	1.400(4)
C(3) - H(3)	0.98(3)	C(4) - C(5)	1.392(3)
C(4) - C(13)	1.502(4)	C(5) - C(6)	1.392(3)
C(5) - H(4)	0.99(3)	C(6) - C(7)	1.452(3)
C(7) - C(8)	1.387(3)	C(7) - C(12)	1.408(3)
C(8) - C(9)	1.388(3)	C(8) - H(5)	1.00(3)
C(9) - C(10)	1.404(3)	C(9) - C(16)	1.475(3)
C(10) - C(11)	1.368(4)	C(10) - H(6)	0.93(3)
C(11) - C(12)	1.392(3)	C(11) - H(7)	0.98(3)
C(12) - N(1)	1.374(3)	C(13) - C(14)	1.500(4)
C(13) - H(8)	0.99(3)	C(13) - H(9)	0.98(3)
C(14) - C(15)	1.510(5)	C(14) - H(10)	1.00(3)
C(14) - H(11)	1.00(3)	C(15) - H(12)	0.97(3)
C(15) - H(13)	0.96(4)	C(15) - H(14)	0.96(4)
C(16) - O(1)	1.207(3)	C(16) - O(2)	1.345(3)
C(17) - H(15)	1.01(4)	C(17) - H(16)	0.96(4)
C(17) - H(17)	1.05(4)	N(1) - H(1)	0.93(4)

C(2)-C(1)-C(6)	121.1(2)	C(2)-C(1)-N(1)	129.7(3)
C(6)-C(1)-N(1)	109.2(2)	C(1)-C(2)-C(3)	117.9(3)
C(1)-C(2)-H(2)	119.2(14)	C(3)-C(2)-H(2)	122.8(14)
C(2)-C(3)-C(4)	122.8(2)	C(2)-C(3)-H(3)	118.0(13)
C(4)-C(3)-H(3)	119.2(13)	C(3)-C(4)-C(5)	118.4(2)
C(3)-C(4)-C(13)	120.8(2)	C(5)-C(4)-C(13)	120.8(2)
C(4)-C(5)-C(6)	120.2(2)	C(4)-C(5)-H(4)	119.1(12)
C(6)-C(5)-H(4)	120.7(12)	C(1)-C(6)-C(5)	119.6(2)
C(1)-C(6)-C(7)	106.4(2)	C(5)-C(6)-C(7)	134.0(2)
C(6)-C(7)-C(8)	134.4(2)	C(6)-C(7)-C(12)	106.2(2)
C(8)-C(7)-C(12)	119.4(2)	C(7)-C(8)-C(9)	119.3(2)
C(7)-C(8)-H(5)	120.2(10)	C(9)-C(8)-H(5)	120.5(10)
C(8)-C(9)-C(10)	120.2(2)	C(8)-C(9)-C(16)	117.9(2)
C(10)-C(9)-C(16)	121.9(2)	C(9)-C(10)-C(11)	121.5(2)
C(9)-C(10)-H(6)	119.0(16)	C(11)-C(10)-H(6)	119.6(16)
C(10)-C(11)-C(12)	118.1(2)	C(10)-C(11)-H(7)	120.4(13)
C(12)-C(11)-H(7)	121.5(13)	C(7)-C(12)-C(11)	121.5(2)
C(7)-C(12)-N(1)	109.4(2)	C(11)-C(12)-N(1)	129.1(2)
C(4)-C(13)-C(14)	114.1(2)	C(4)-C(13)-H(8)	110.8(14)
C(4)-C(13)-H(9)	110.3(16)	C(14)-C(13)-H(8)	108.6(14)
C(14)-C(13)-H(9)	107.9(16)	H(8)-C(13)-H(9)	104.8(21)
C(13)-C(14)-C(15)	114.3(3)	C(13)-C(14)-H(10)	105.8(17)
C(13)-C(14)-H(11)	105.2(16)	C(15)-C(14)-H(10)	112.7(17)
C(15)-C(14)-H(11)	111.1(16)	H(10)-C(14)-H(11)	107.3(23)
C(14)-C(15)-H(12)	110.7(17)	C(14)-C(15)-H(13)	110.4(21)
C(14)-C(15)-H(14)	113.2(22)	H(12)-C(15)-H(13)	110.2(27)
H(12)-C(15)-H(14)	100.8(27)	H(13)-C(15)-H(14)	111.3(30)
C(9)-C(16)-O(1)	125.6(2)	C(9)-C(16)-O(2)	112.8(2)
O(1)-C(16)-O(2)	121.6(2)	H(15)-C(17)-H(16)	113.9(26)
H(15)-C(17)-H(17)	112.6(26)	H(16)-C(17)-H(17)	104.5(27)

C(1)-N(1)-C(12)	108.8(2)	C(1)-N(1)-H(1)	126.5(17)
C(12)-N(1)-H(1)	124.7(17)		



The ORTEP diagram showing numbering scheme and the molecular conformation of **2f** in crystals.

1 C. Monnereau, E. Blart and F. Odobel, *Tetrahedron Lett.*, 2005, **46**, 5421.

2 G. M. Sheldrick, short history of SHELX. *Acta Crystallogr.,* 2008, **A64**, 112.