

Supplementary Materials

From quinoxaline, pyrido[2,3-*b*]pyrazine and pyrido[3,4-*b*]pyrazine to pyrazino-fused carbazoles and carbolines

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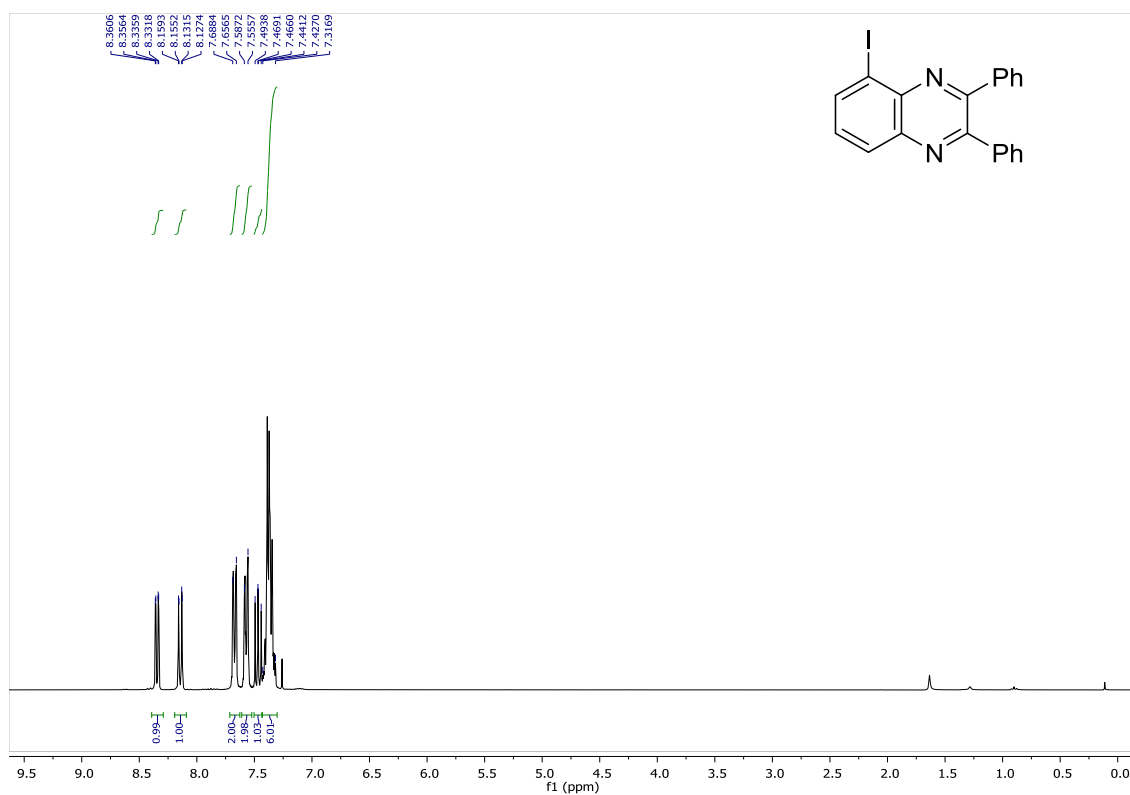
NMR data of compounds 1b-g, 1b', 1k', 2b-I, 2b-Br, 2b-Cl, 2d-g, 2i-v, 3b, 3g', 3h, 4a and 4b

Inhibitory activities of synthesized compounds against a short panel of disease-related protein kinases

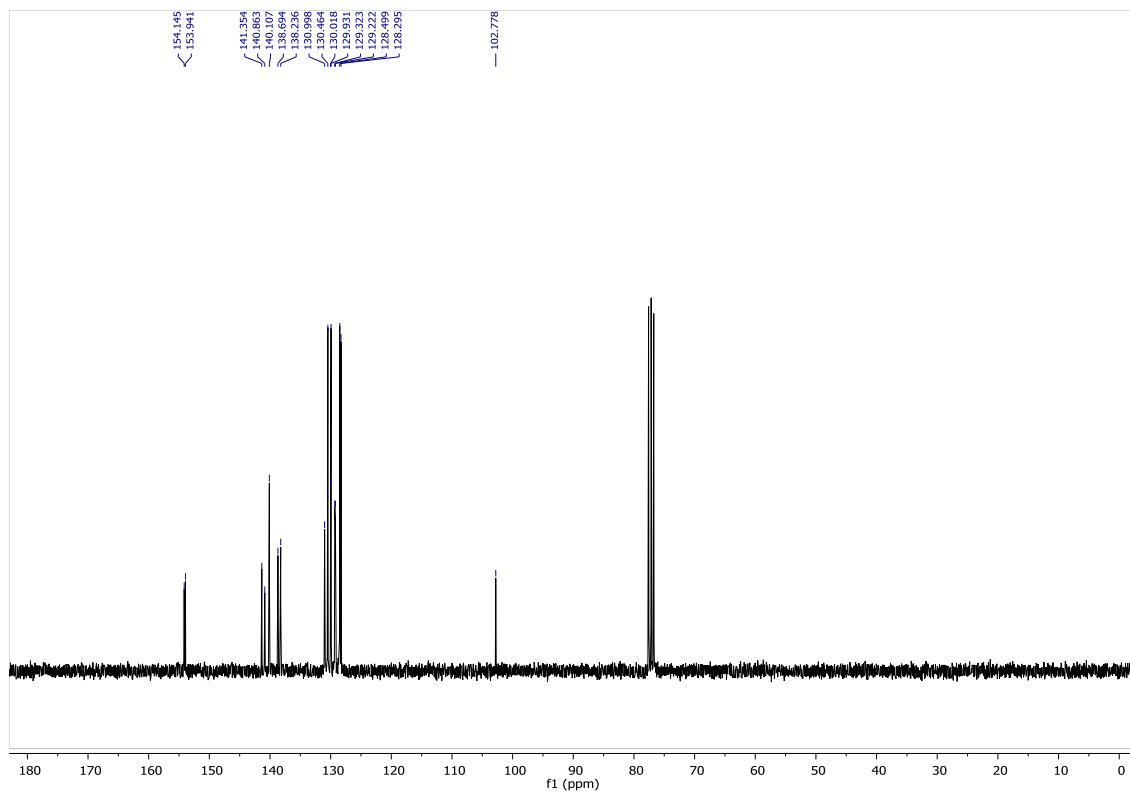
NMR data of compounds 1b-g, 1b', 1k', 2b-I, 2b-Br, 2b-Cl, 2d-g, 2i-v, 3b, 3g', 3h, 4a and 4b

Compound 1b

^1H NMR (300 MHz, CDCl_3)

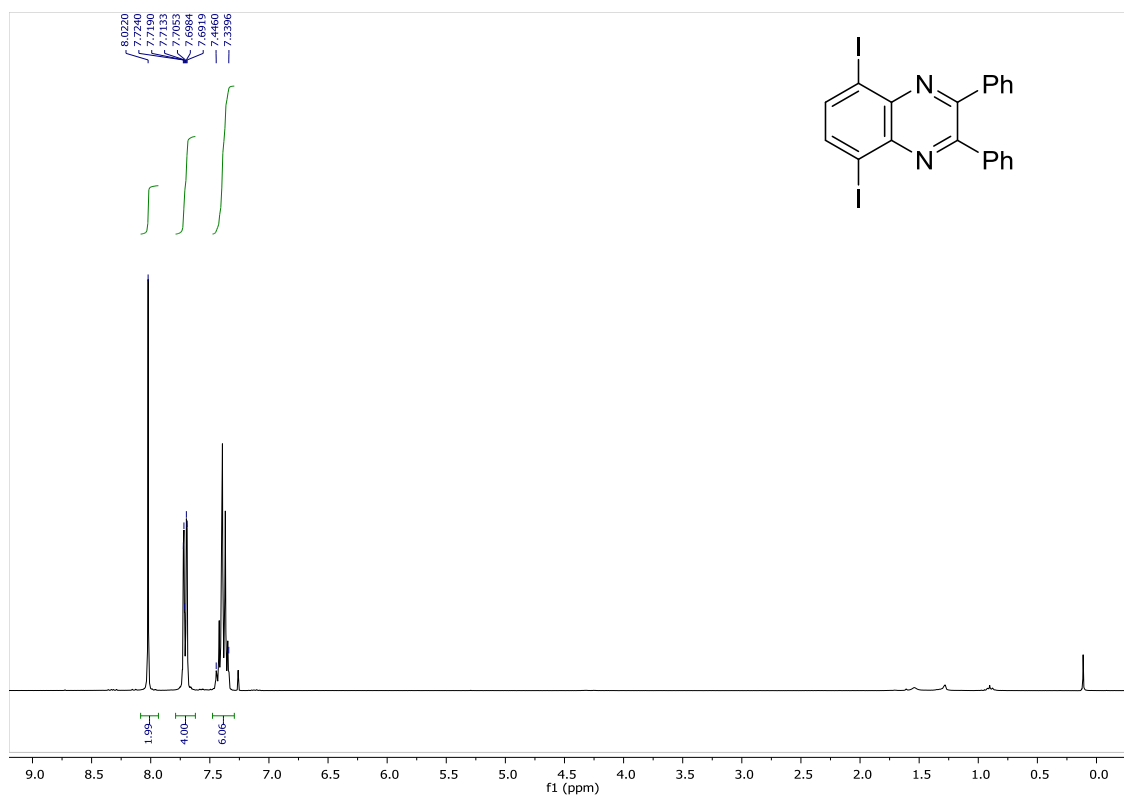


^{13}C NMR (75 MHz, CDCl_3)

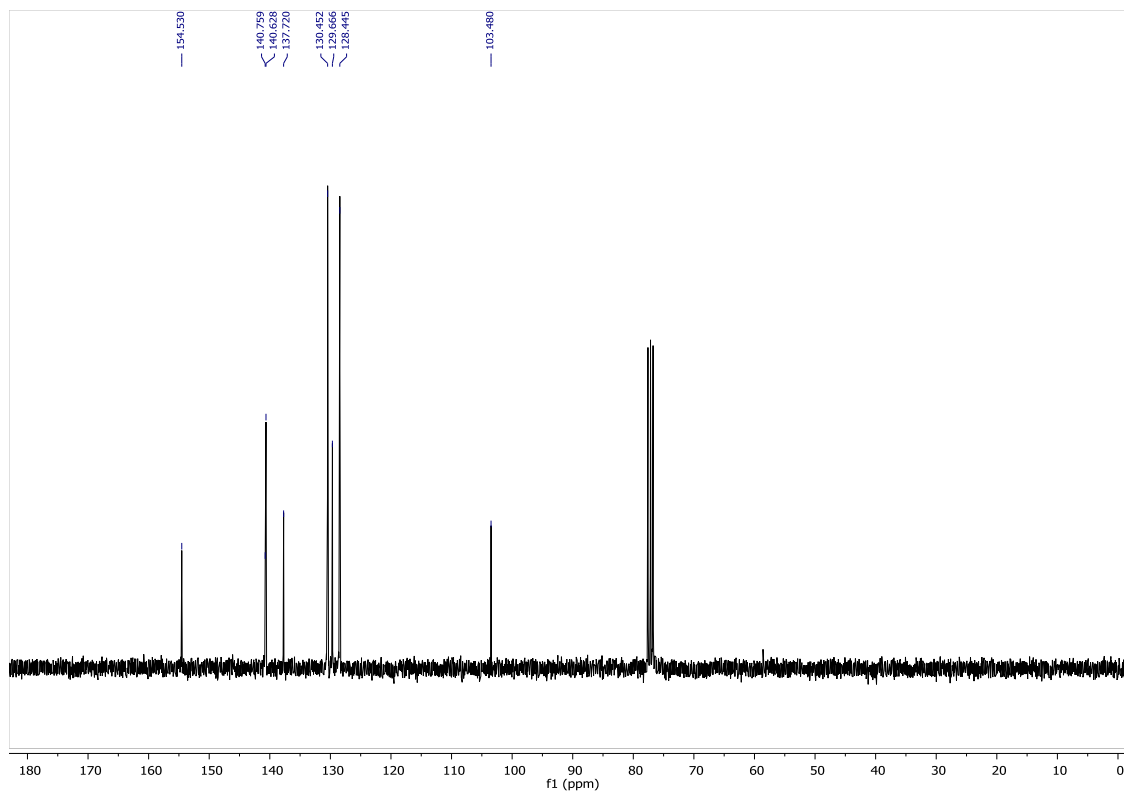


Compound 1b'

^1H NMR (300 MHz, CDCl_3)

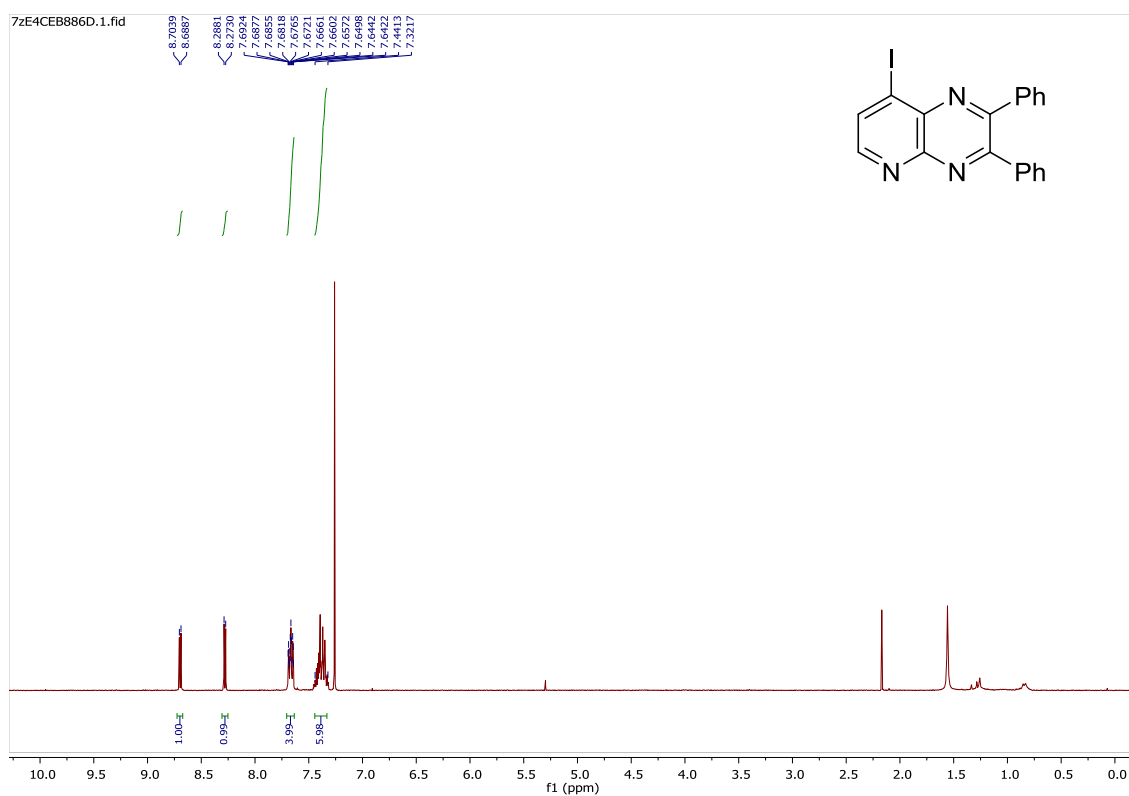


^{13}C NMR (75 MHz, CDCl_3)

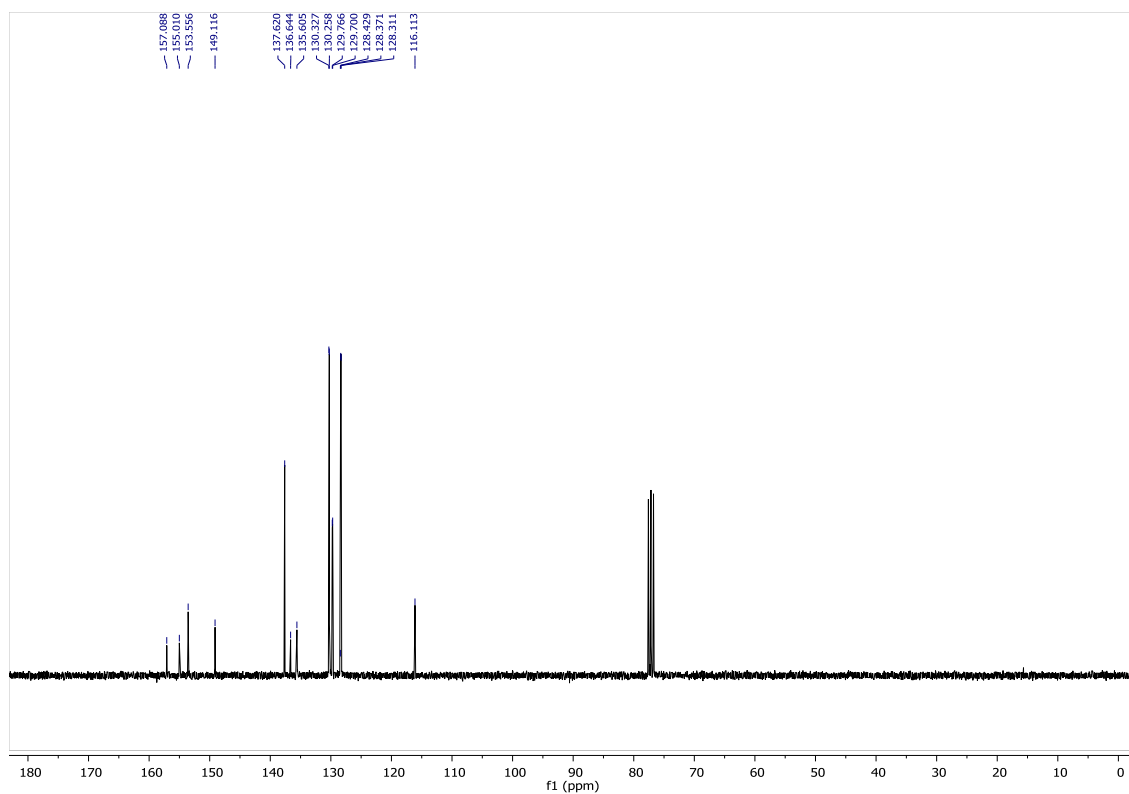


Compound 2b-I

^1H NMR (300 MHz, CDCl_3)

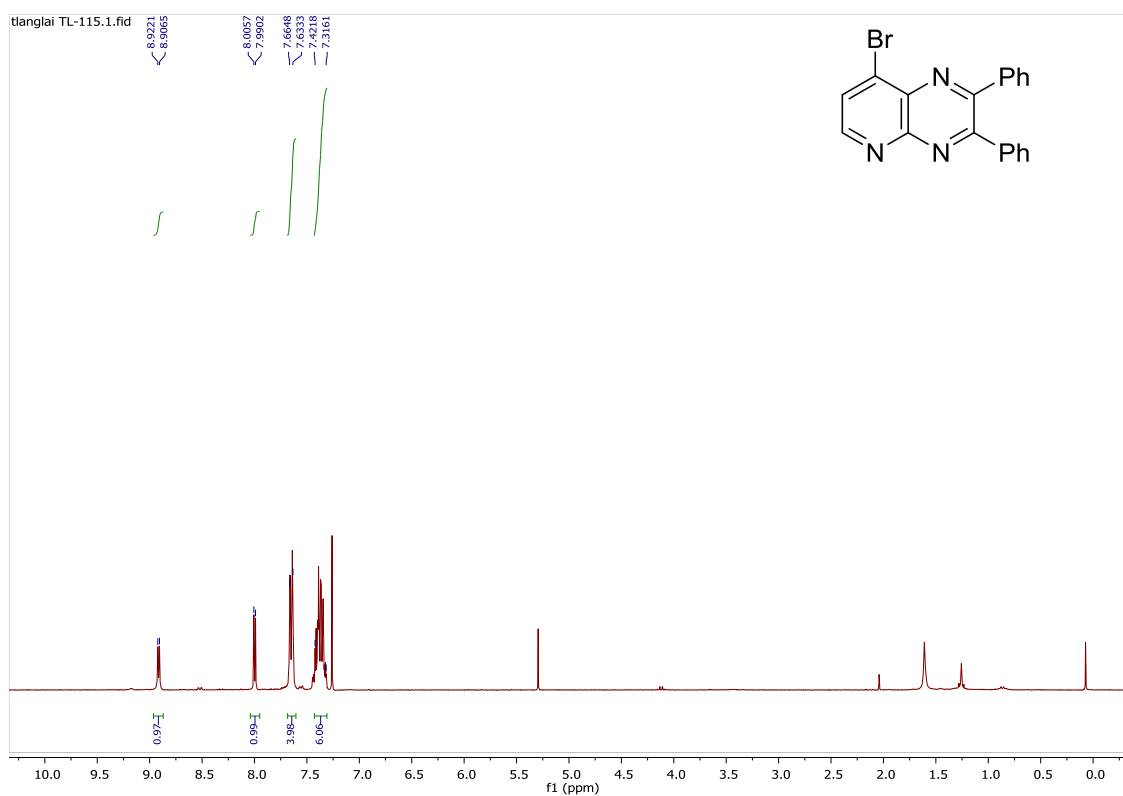


^{13}C NMR (75 MHz, CDCl_3)

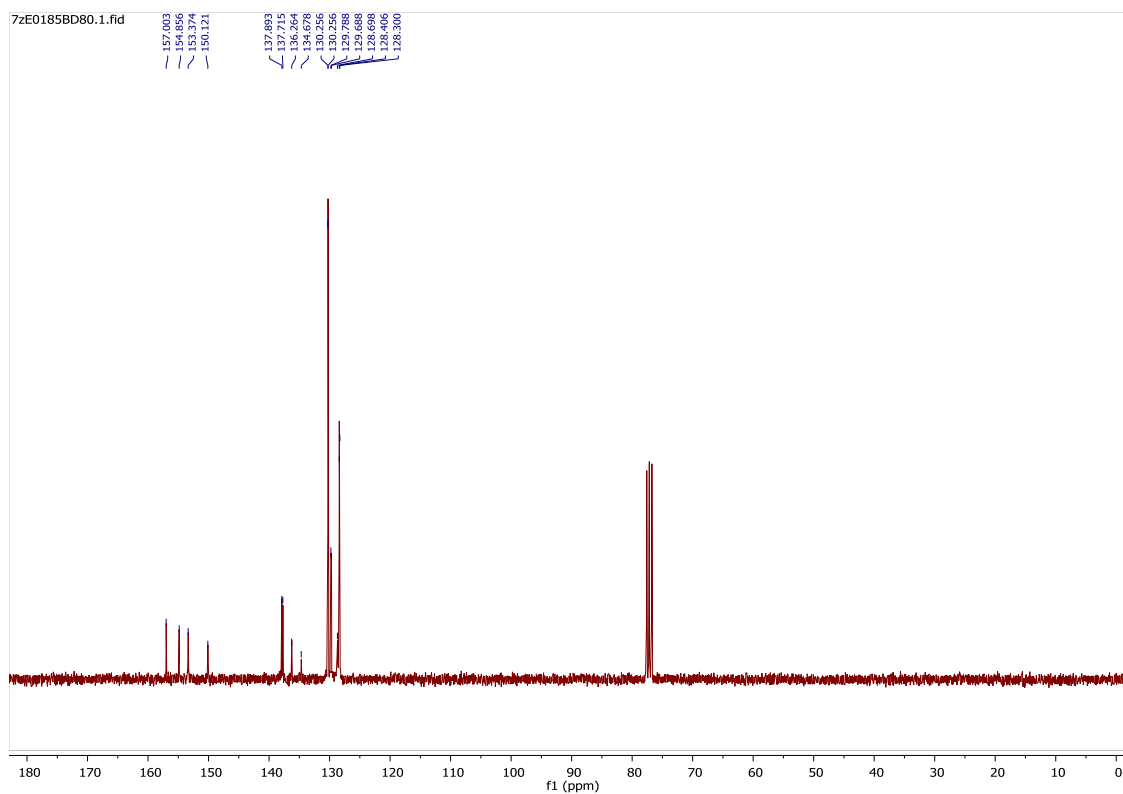


Compound 2b-Br

^1H NMR (300 MHz, CDCl_3)

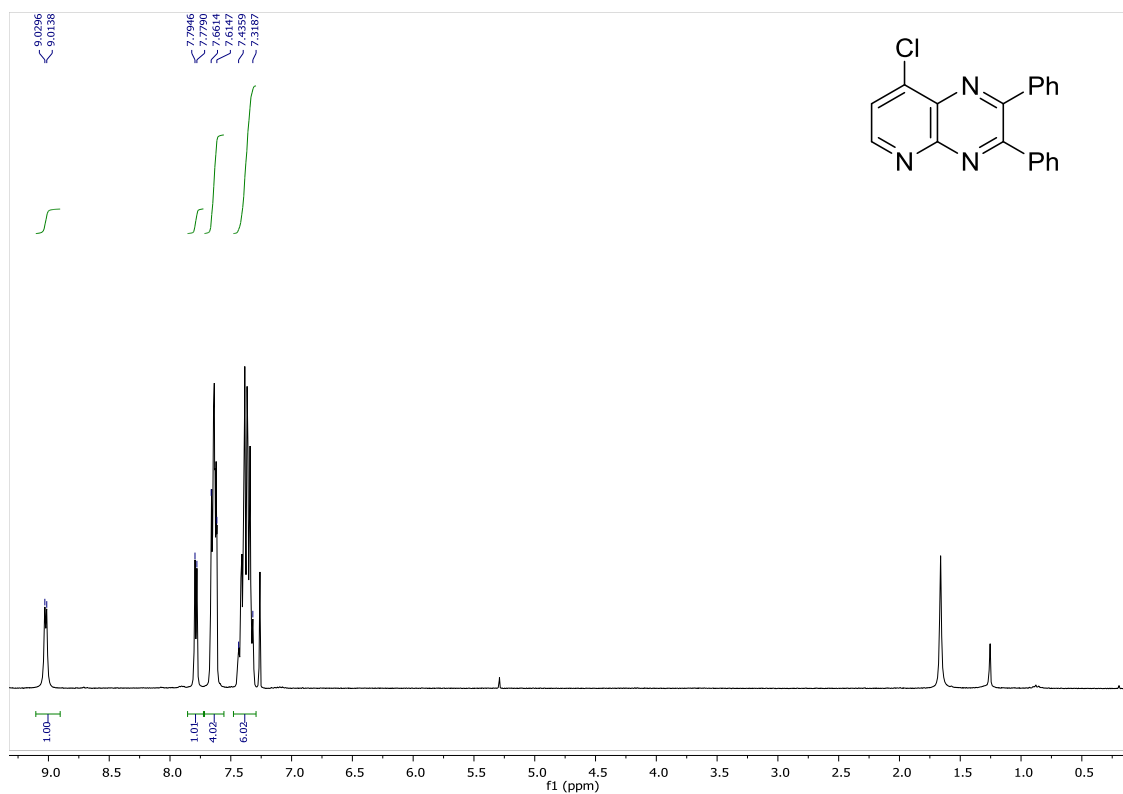


^{13}C NMR (75 MHz, CDCl_3)

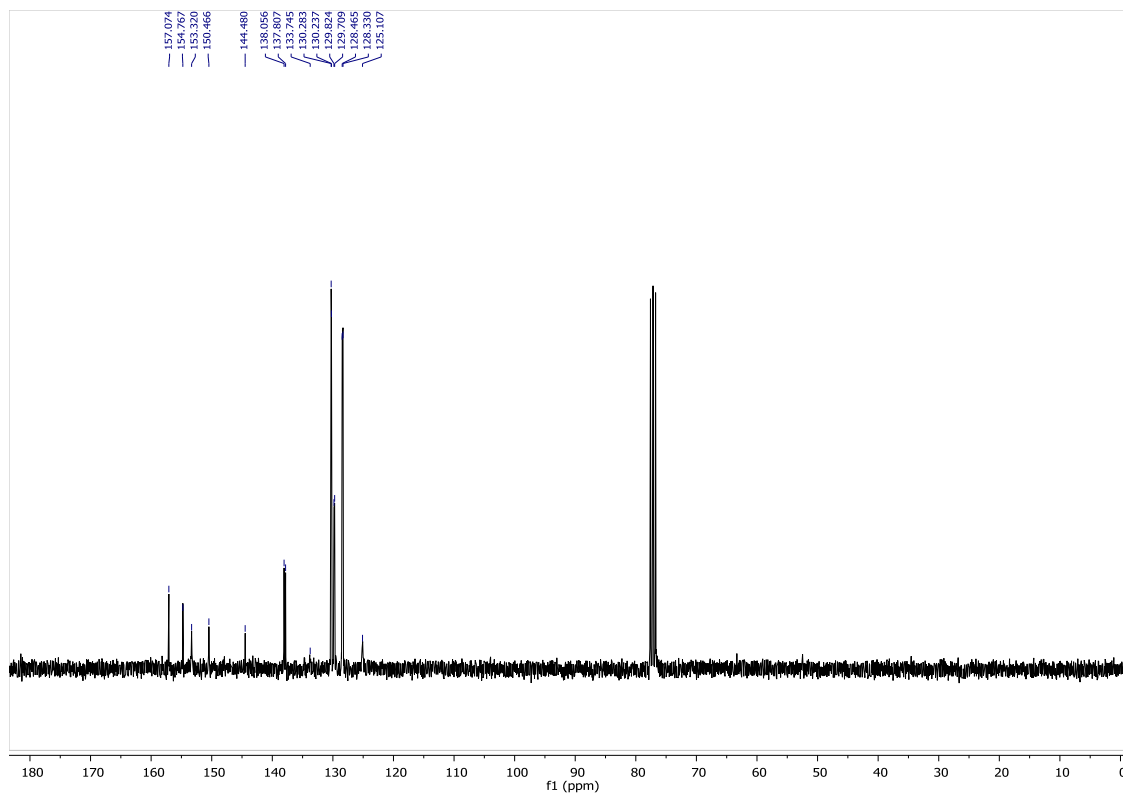


Compound 2b-Cl

^1H NMR (300 MHz, CDCl_3)

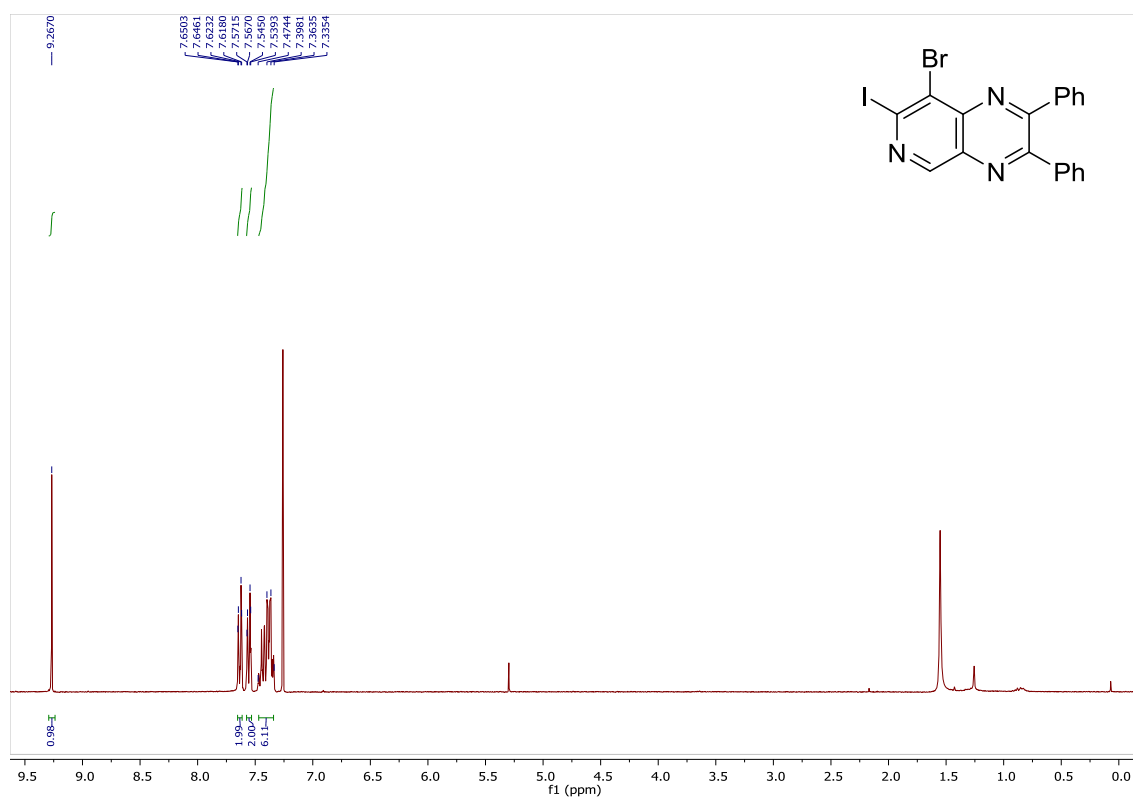


^{13}C NMR (75 MHz, CDCl_3)

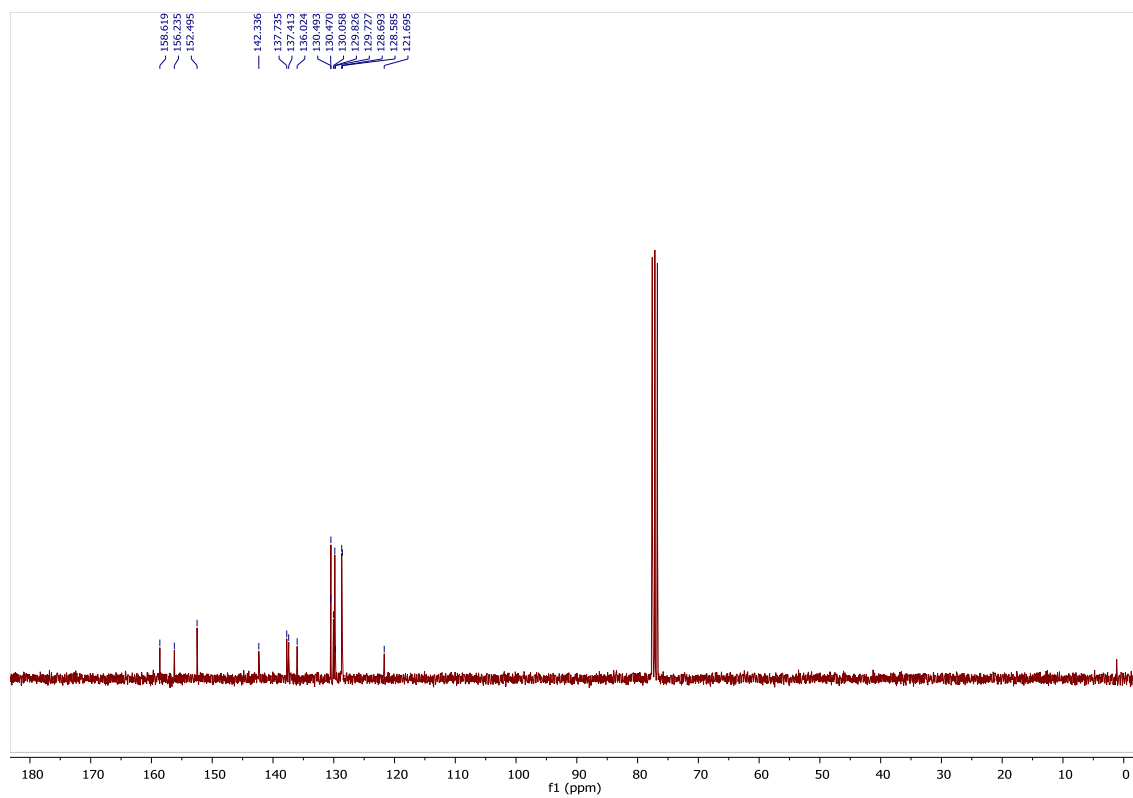


Compound 3b

^1H NMR (300 MHz, CDCl_3)

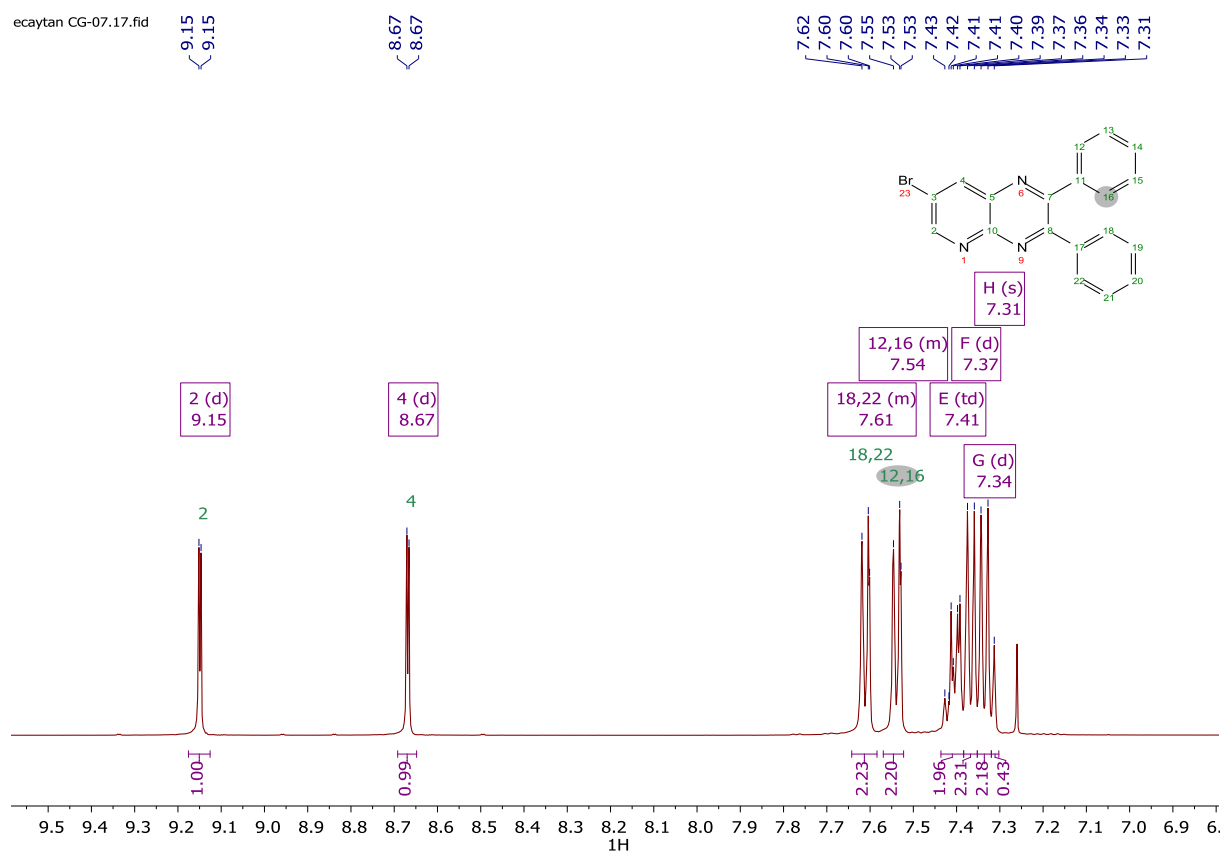


^{13}C NMR (75 MHz, CDCl_3)

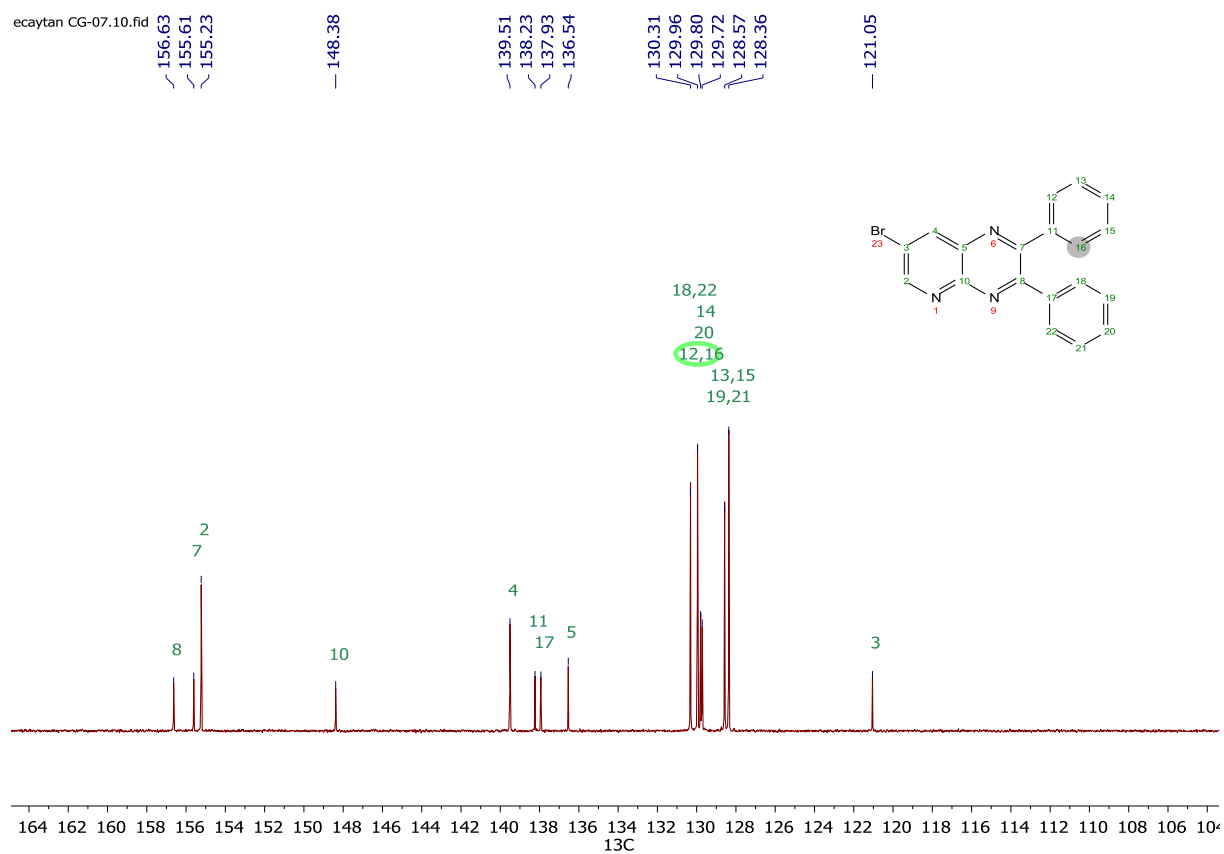


Compound 4a

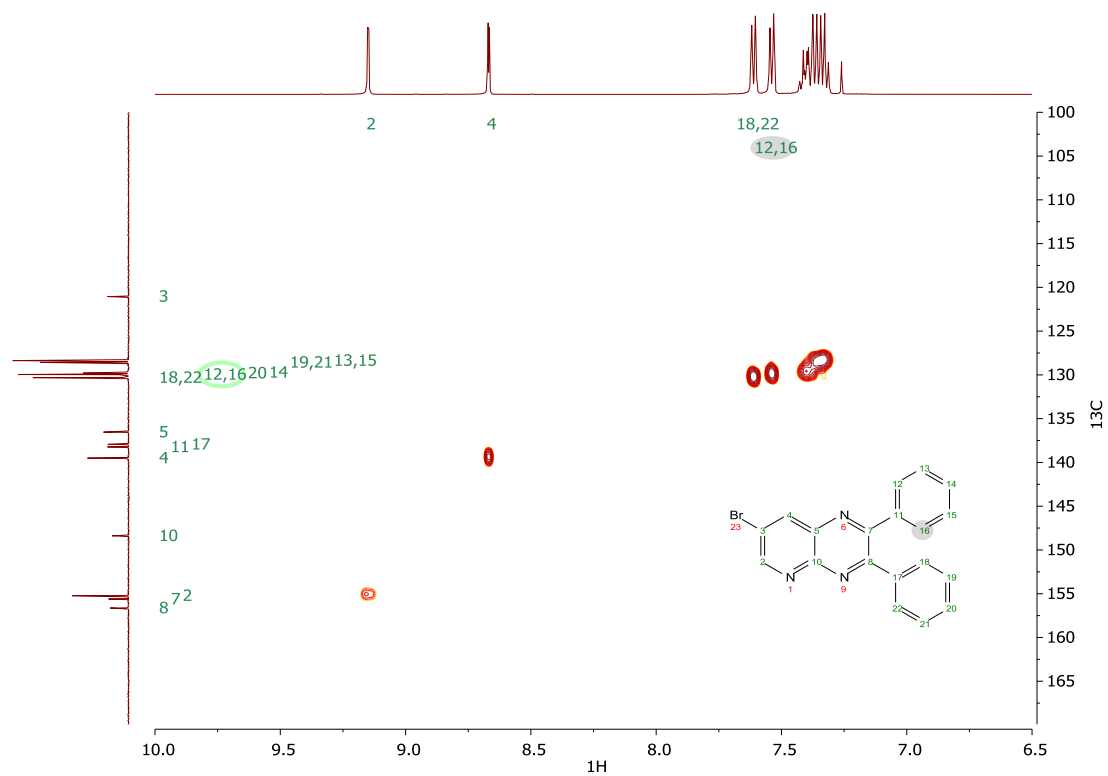
^1H NMR (500 MHz, CDCl_3)



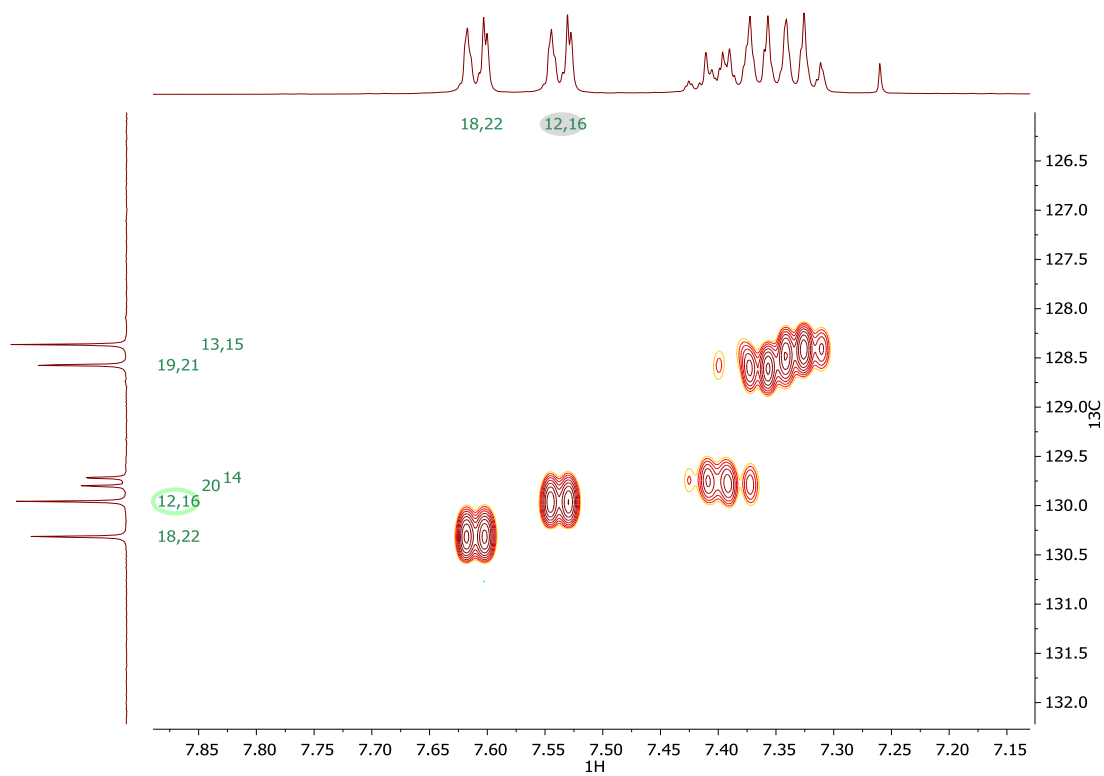
^{13}C NMR (126 MHz, CDCl_3)



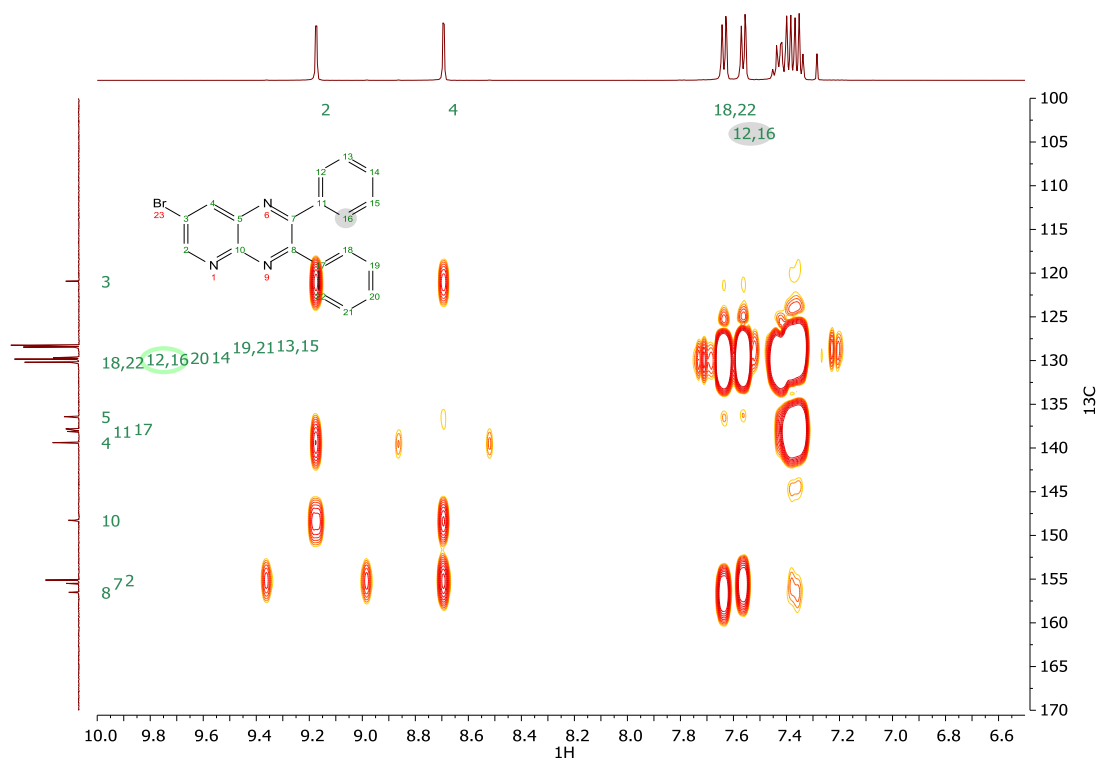
HSQC spectrum (500MHz, 126 MHz, CDCl₃)



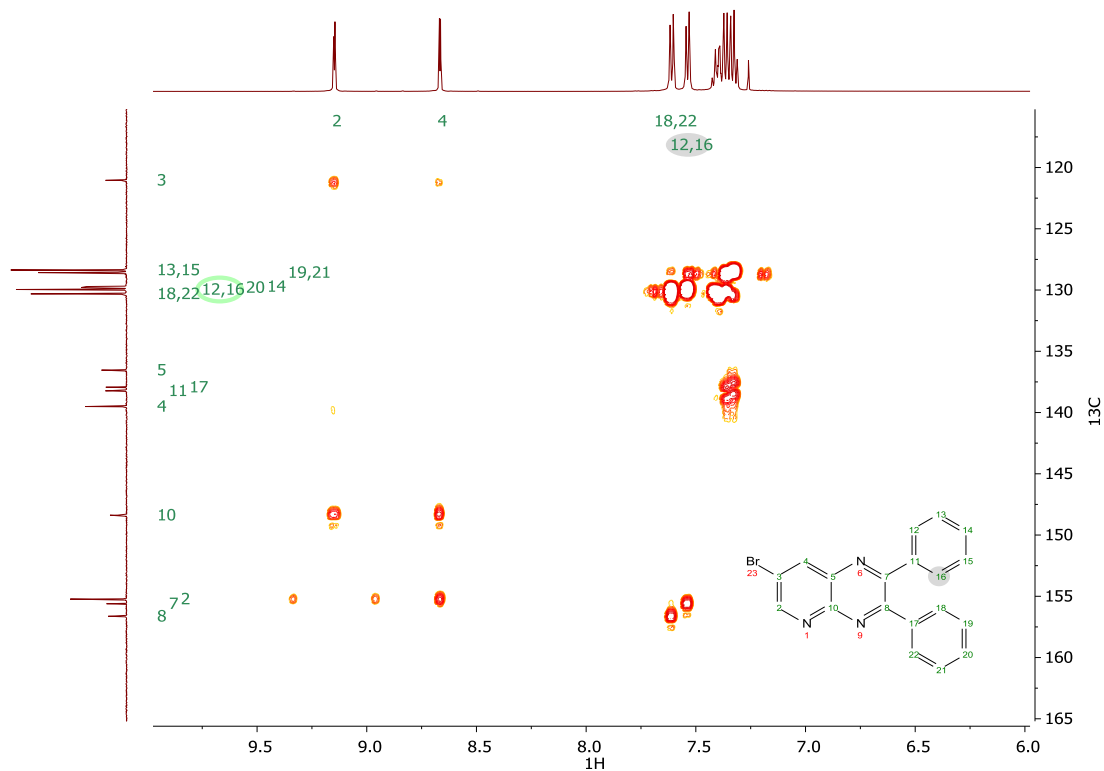
¹³C-Band-selective HSQC spectrum (500 MHz, 126 MHz, CDCl₃)



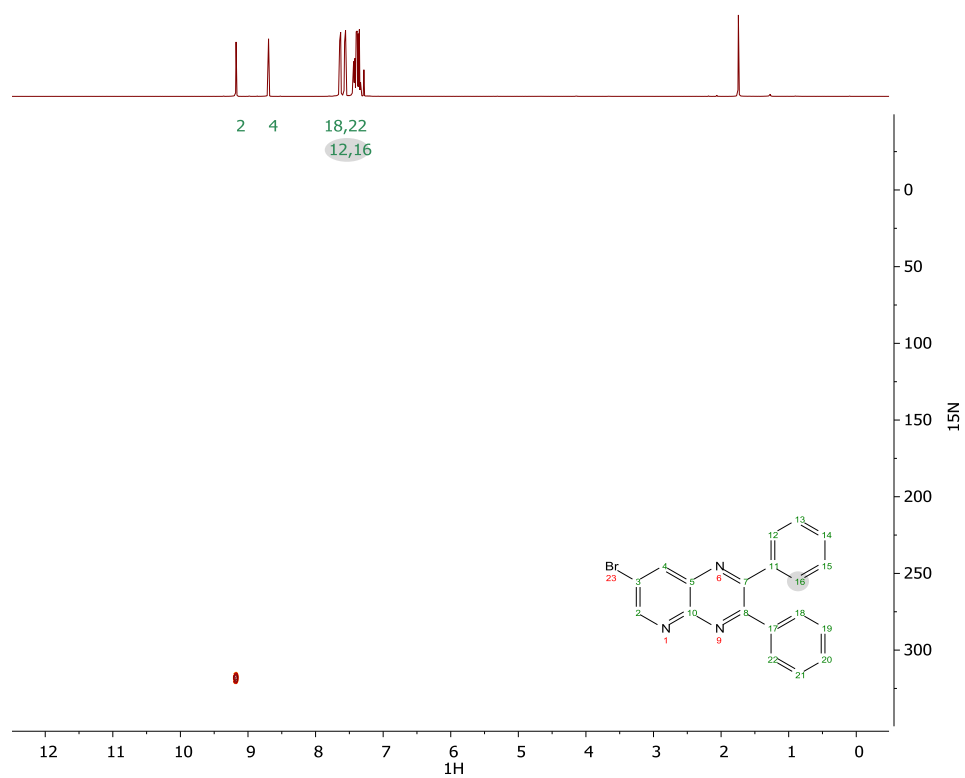
HMBC spectrum (500 MHz, 126 MHz, CDCl₃)



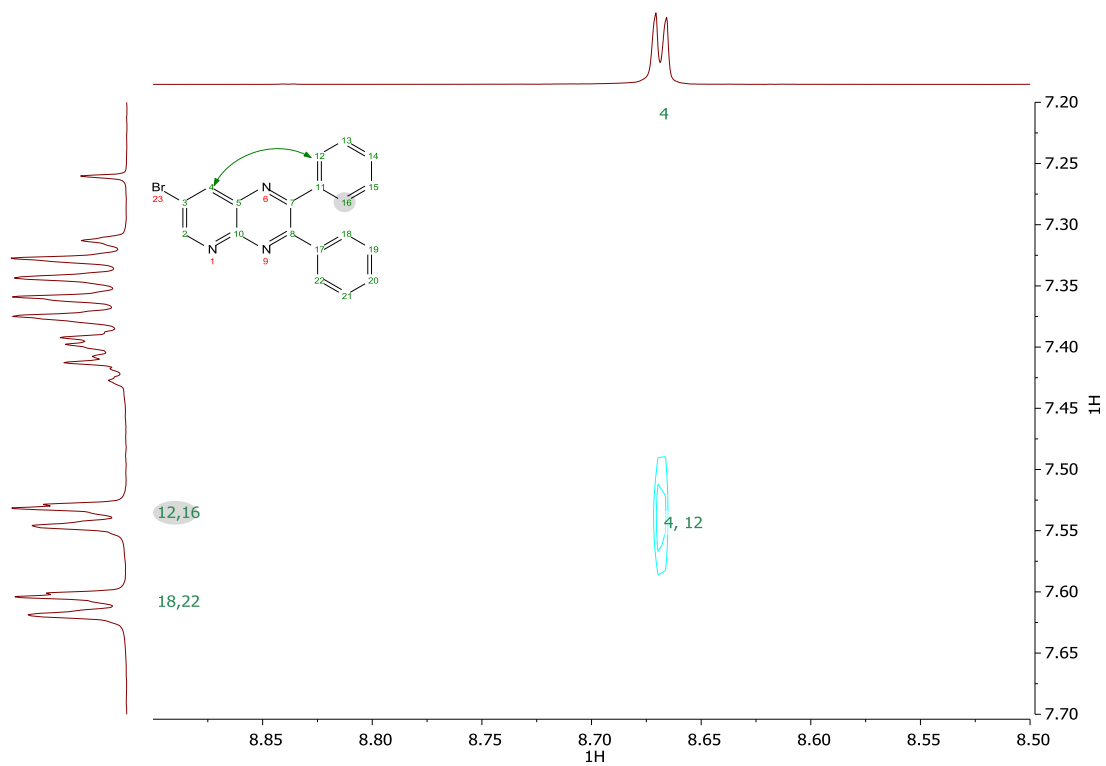
¹³C-Band-selective HMBC spectrum (500 MHz, 126 MHz, CDCl₃)



^1H - ^{15}N HMBC spectrum (500 MHz, 51 MHz, CDCl_3)

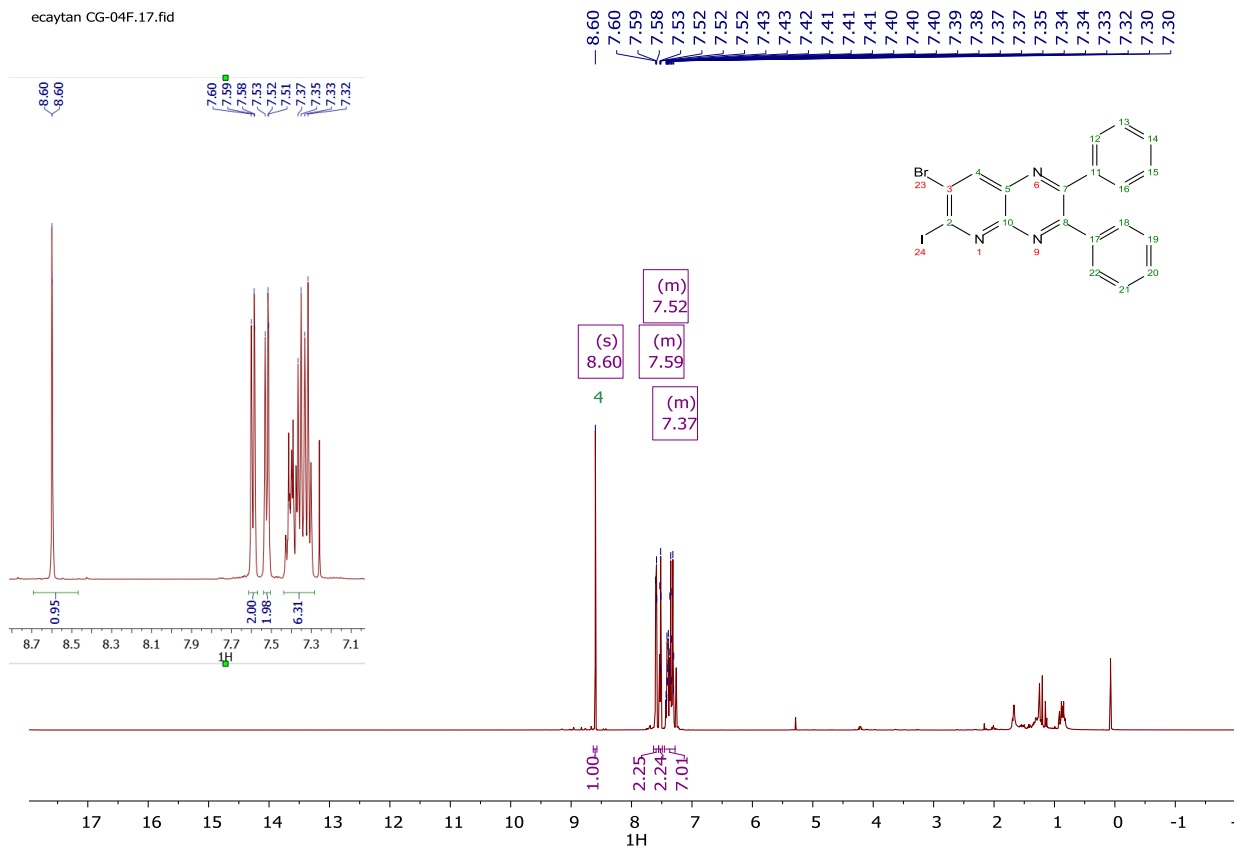


^1H NOESY spectrum (500 MHz, CDCl_3)

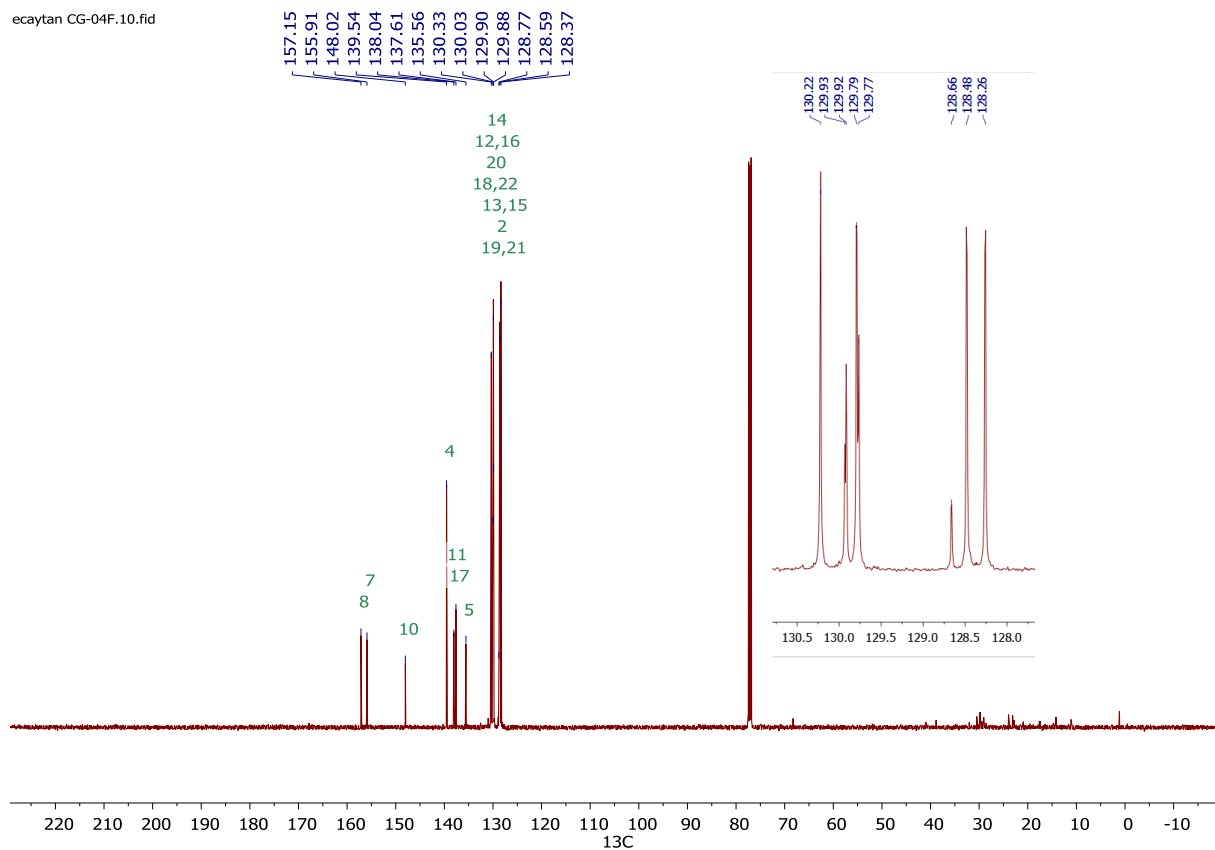


Compound 4b

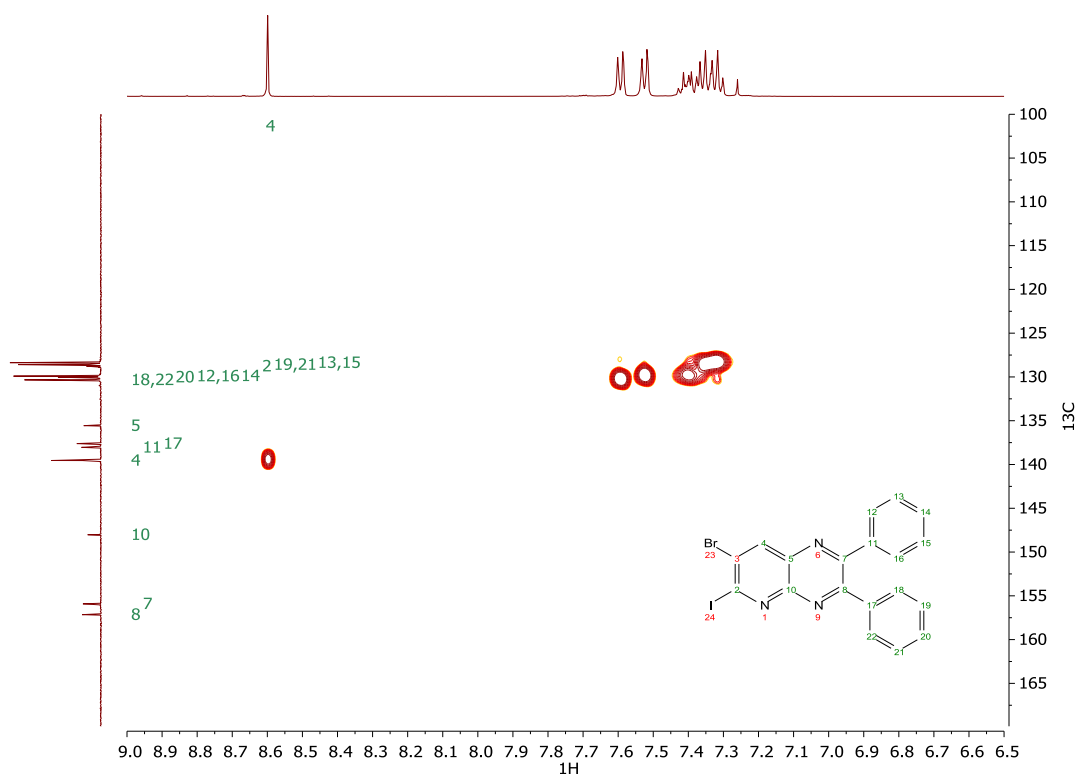
^1H NMR (500 MHz, CDCl_3)



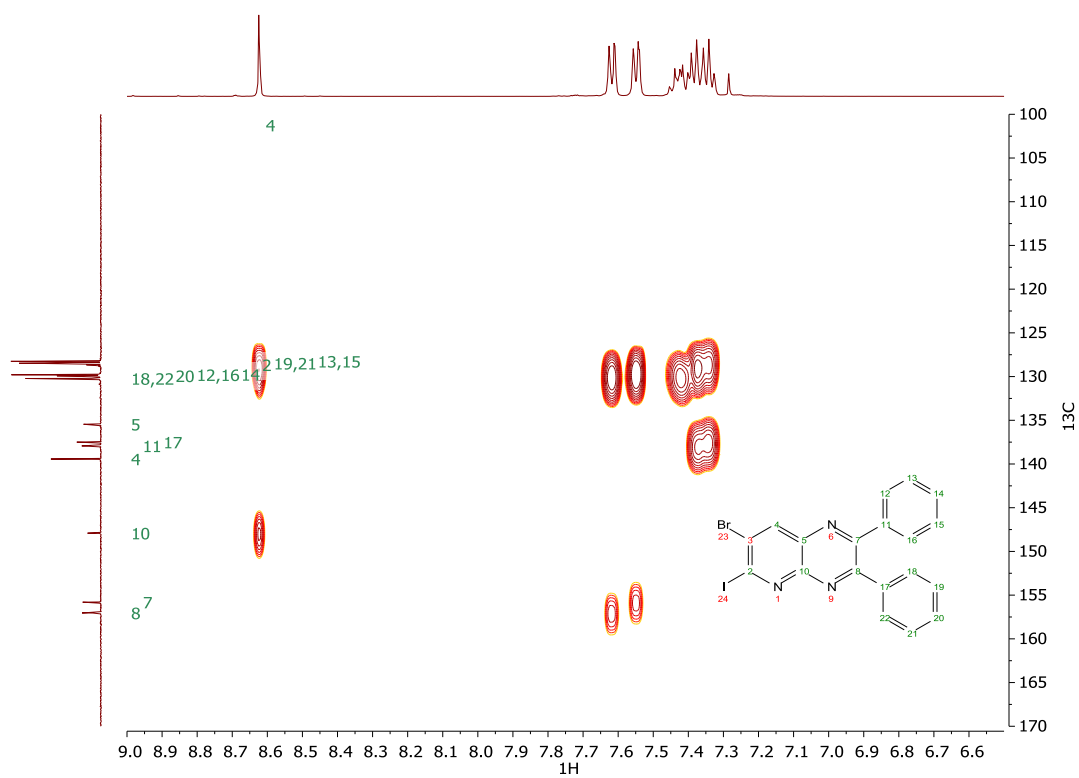
^{13}C NMR (126 MHz, CDCl_3)



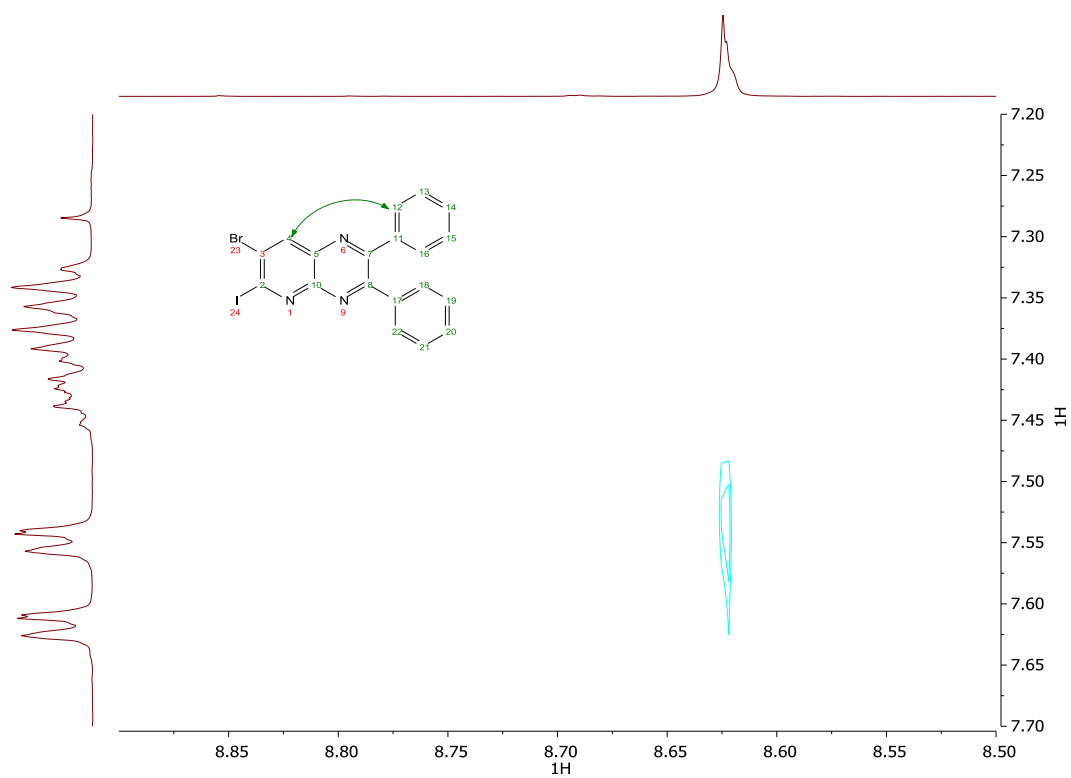
HSQC spectrum (500 MHz, 126 MHz, CDCl₃)



HMBC spectrum (500 MHz, 126 MHz, CDCl₃)

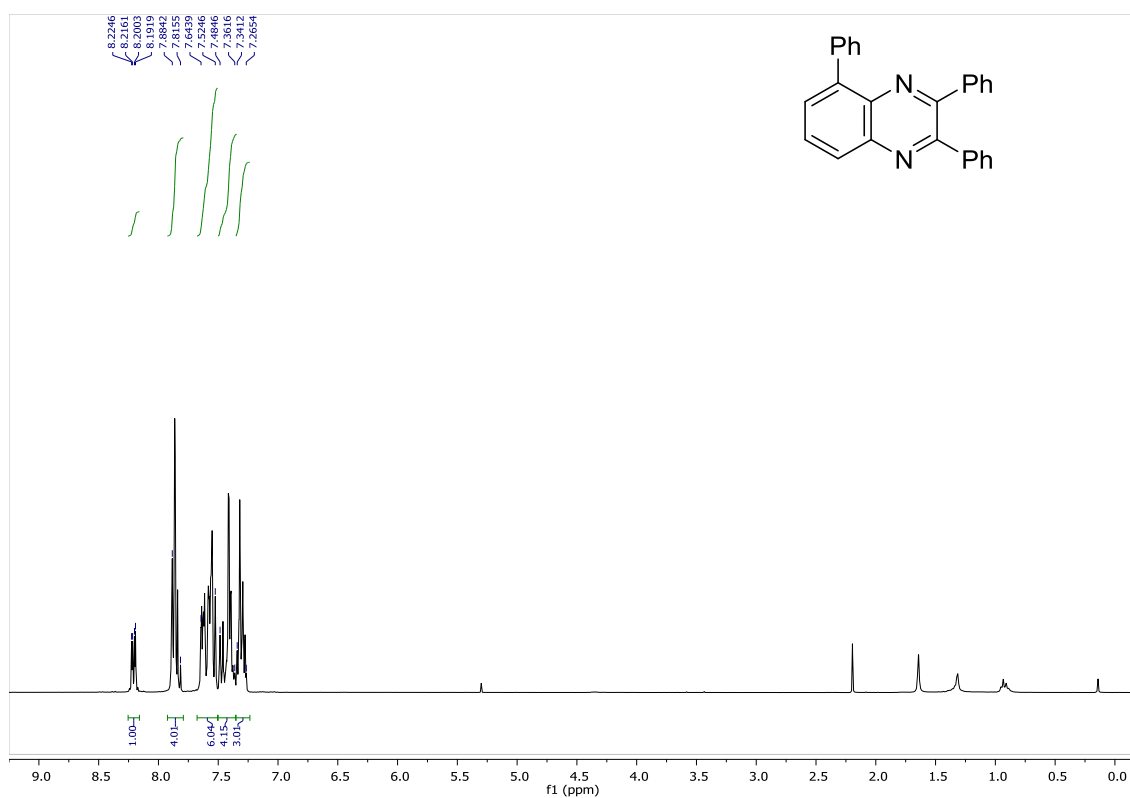


^1H NOESY spectrum (500 MHz, CDCl_3)

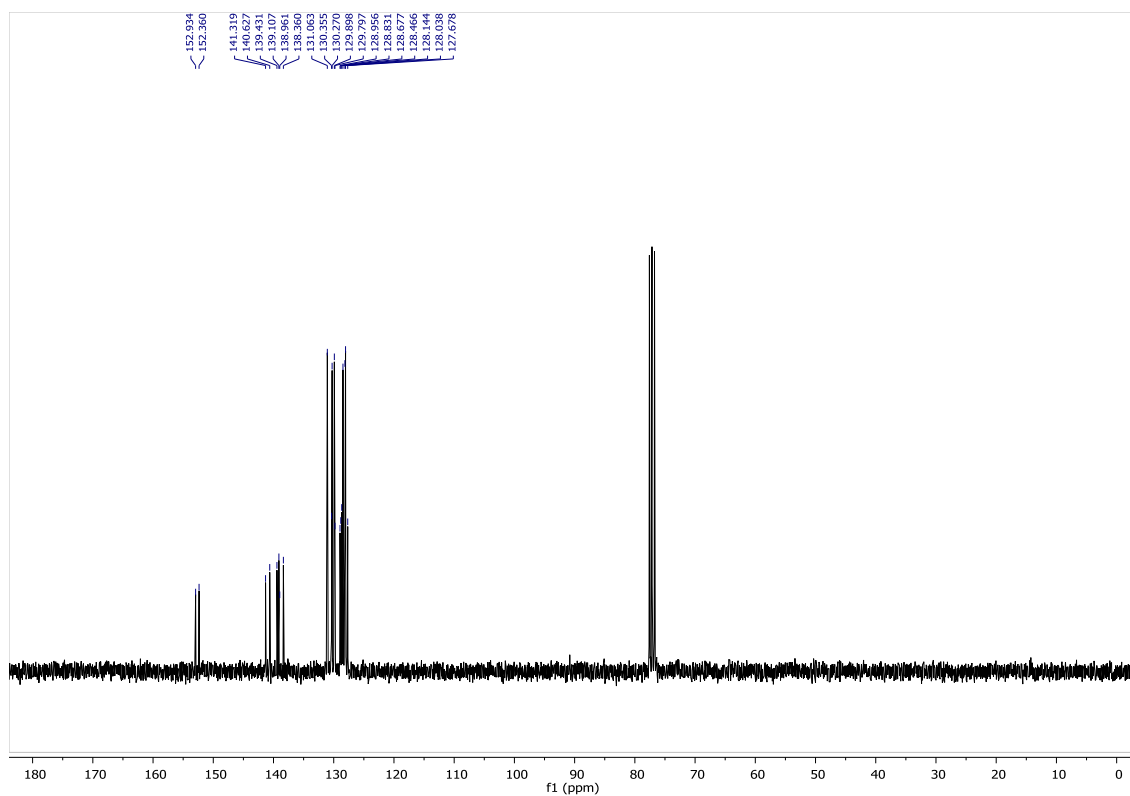


Compound 1c

^1H NMR (300 MHz, CDCl_3)

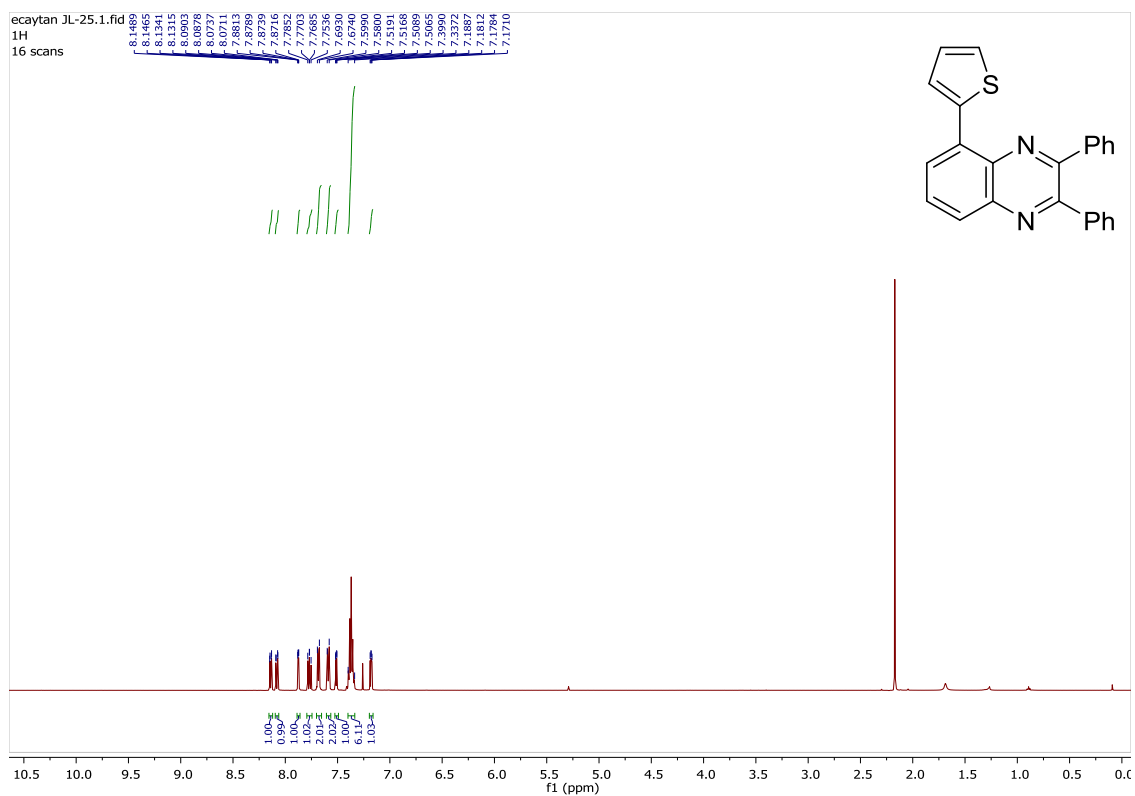


^{13}C NMR (75 MHz, CDCl_3)

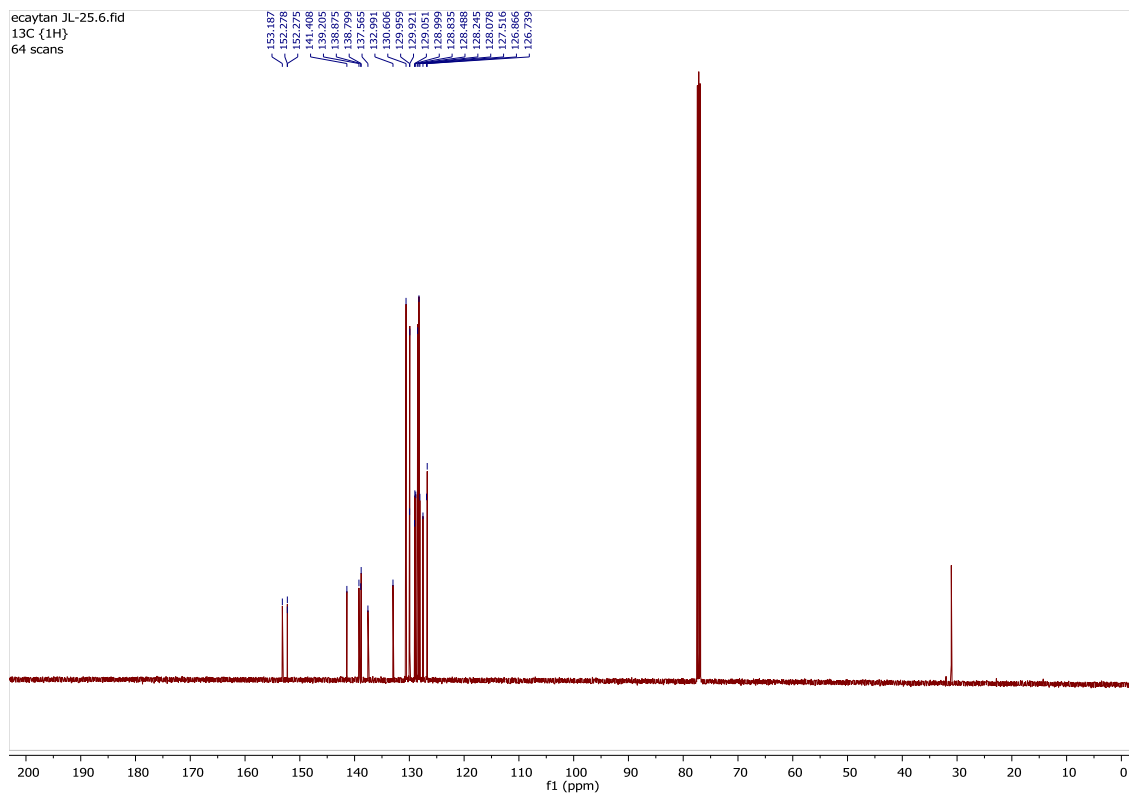


Compound 1d

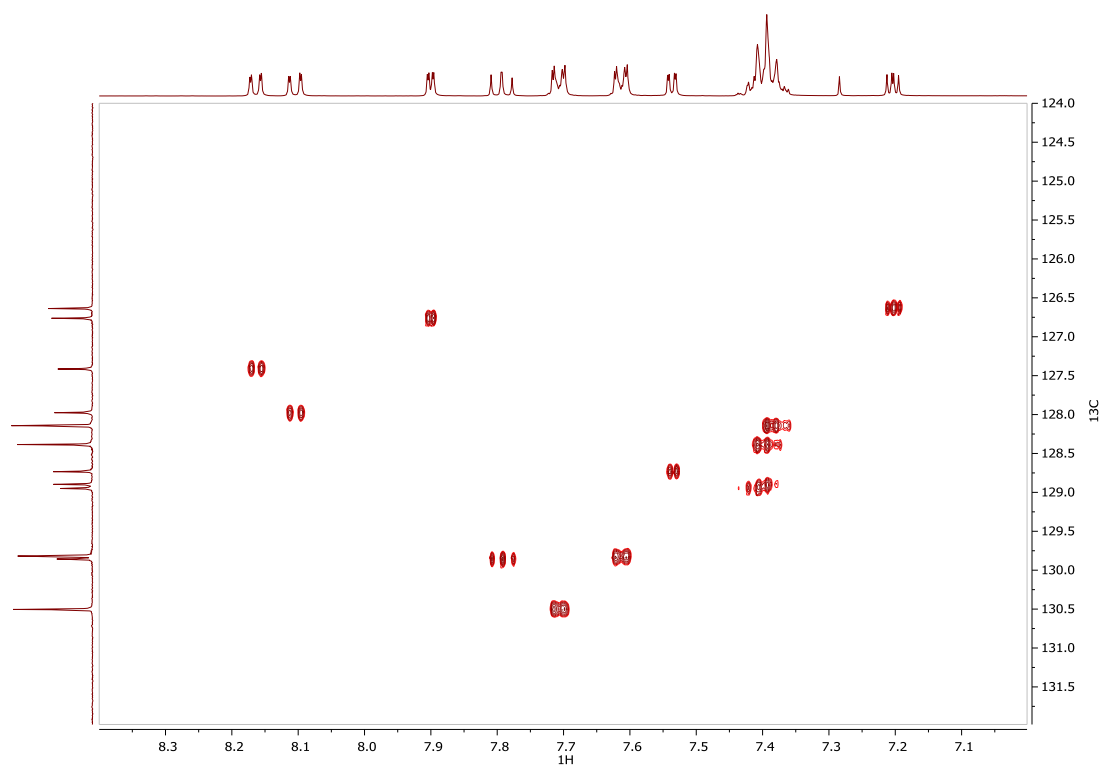
^1H NMR (500 MHz, CDCl_3)



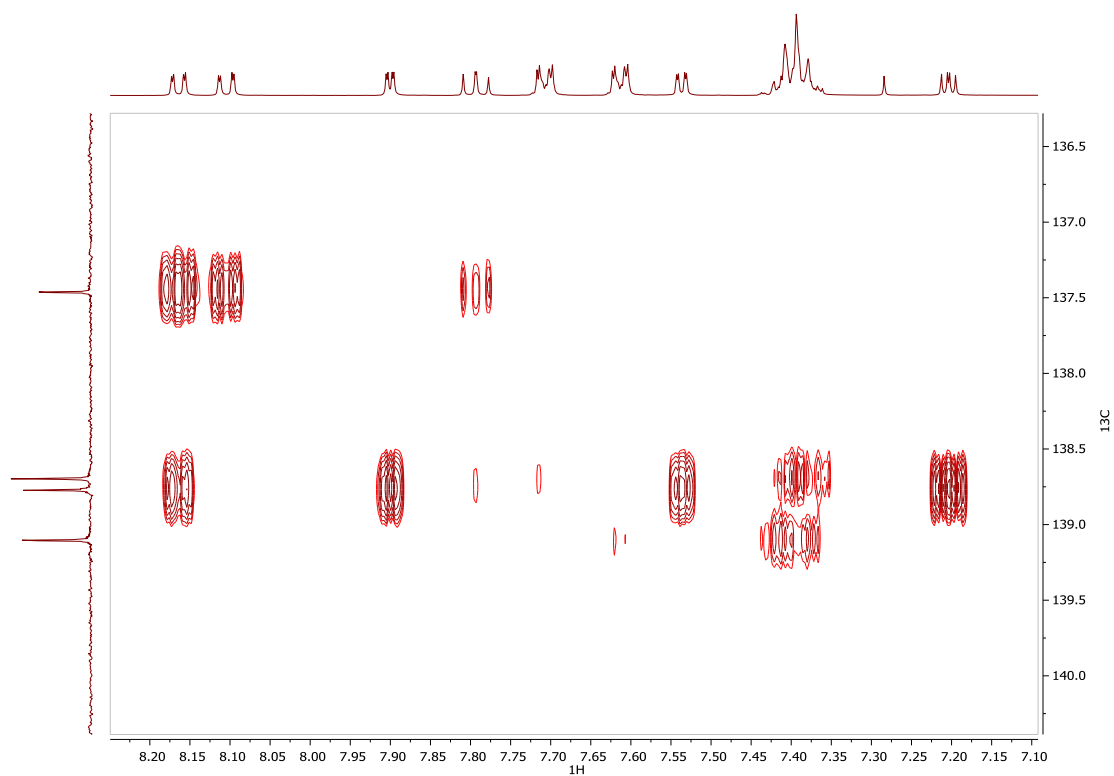
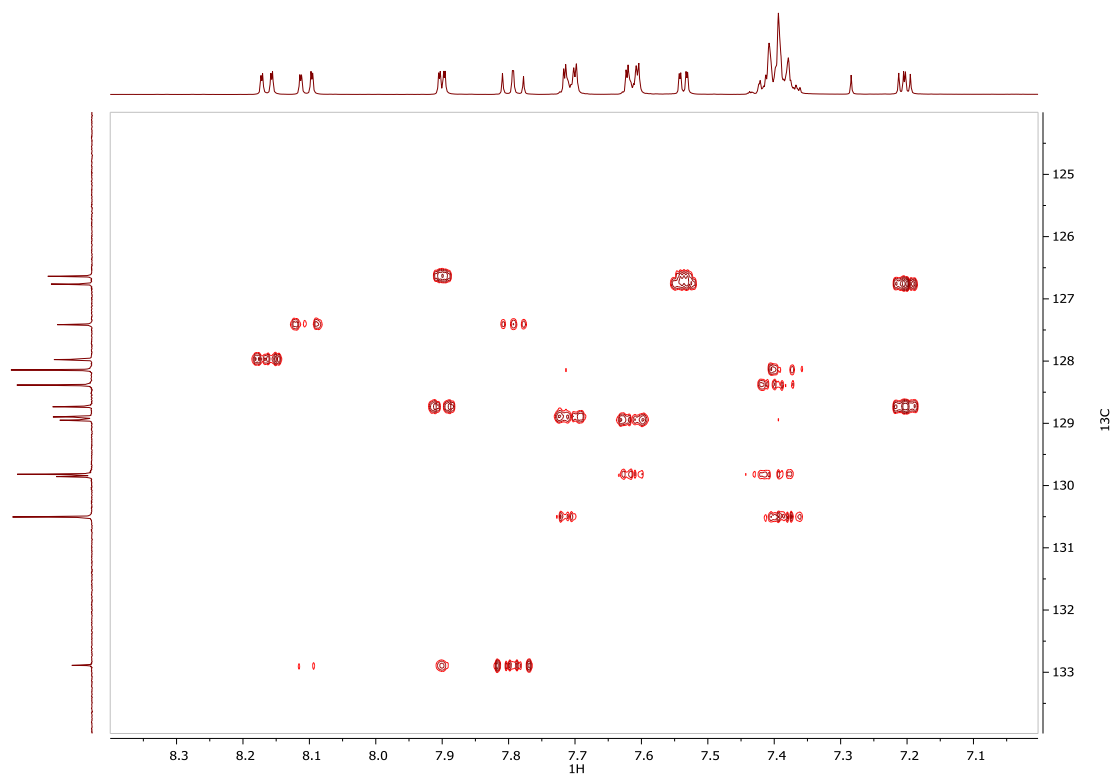
^{13}C NMR (126 MHz, CDCl_3)



^{13}C -Band-selective HSQC spectrum (500 MHz, 126 MHz, CDCl_3)

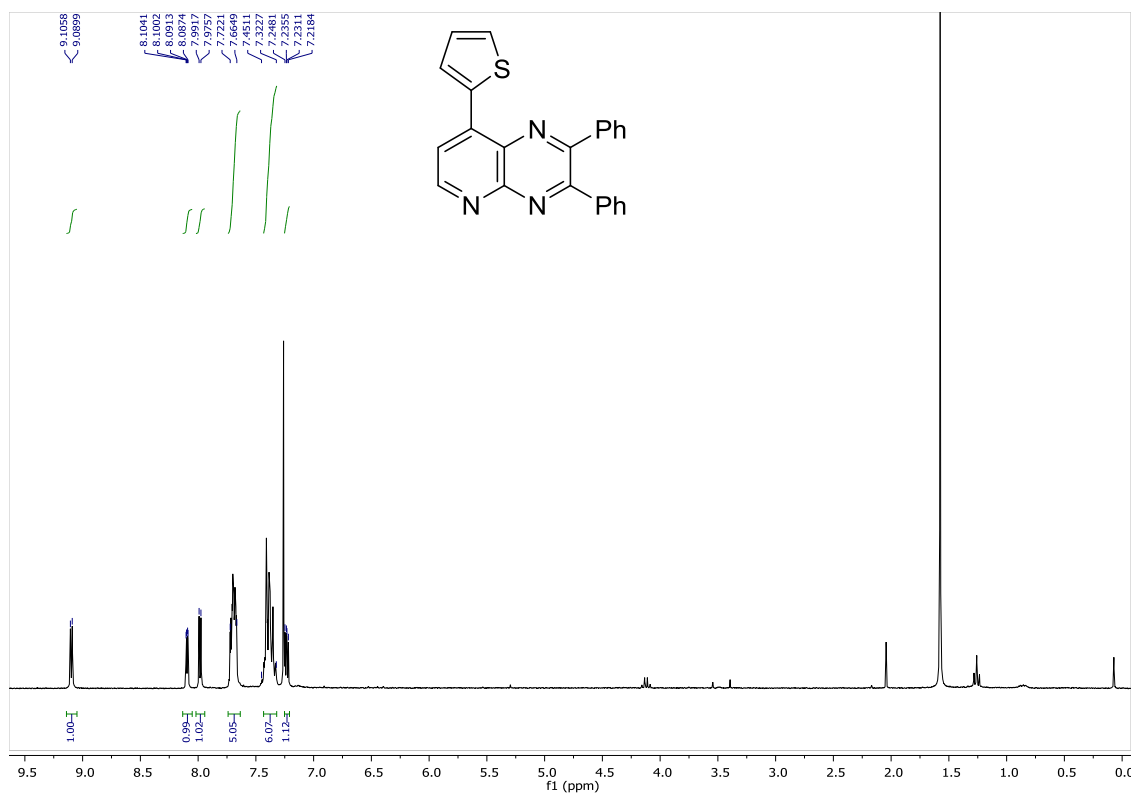


^{13}C -Band-selective HMBC spectra (500 MHz, 126 MHz, CDCl_3)

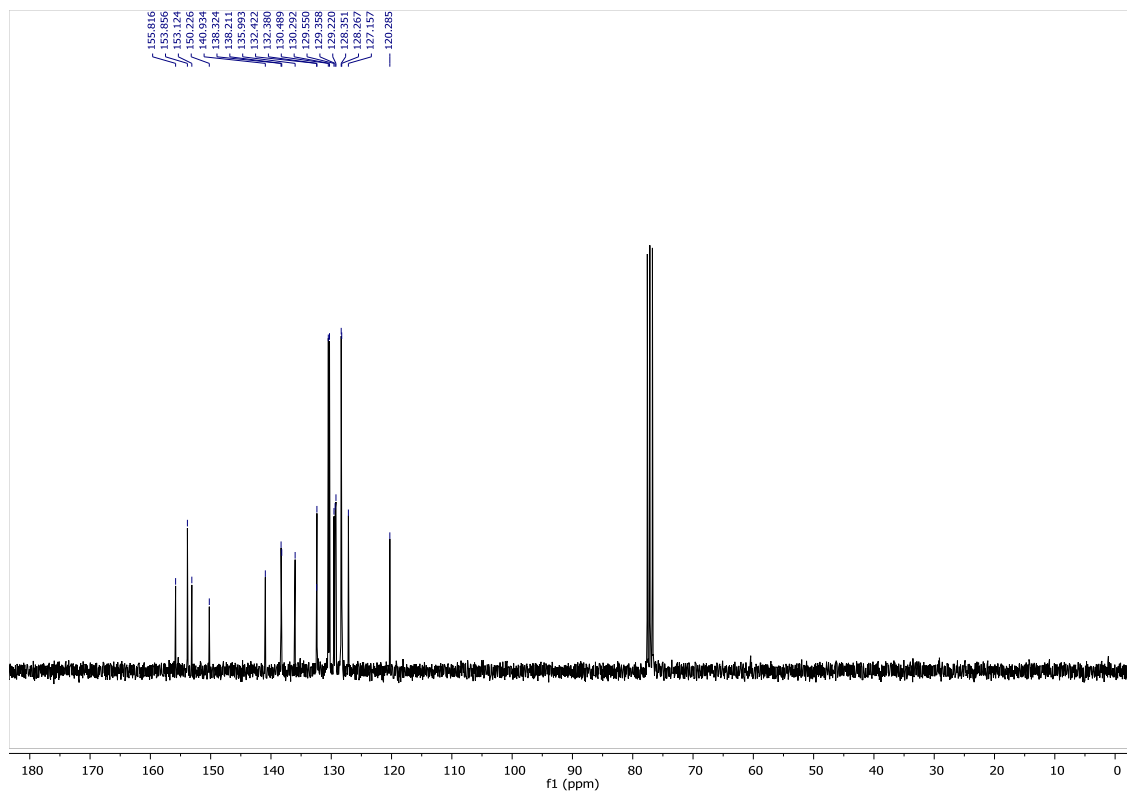


Compound 2d

^1H NMR (300 MHz, CDCl_3)

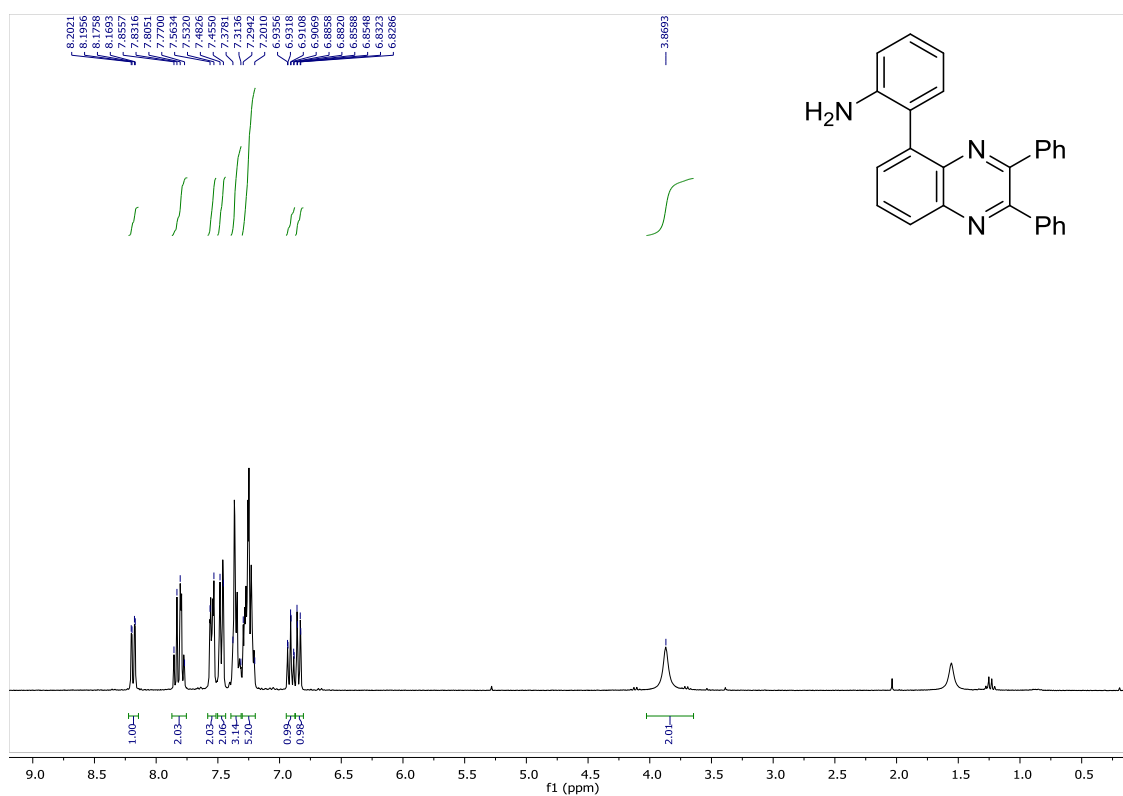


^{13}C NMR (75 MHz, CDCl_3)

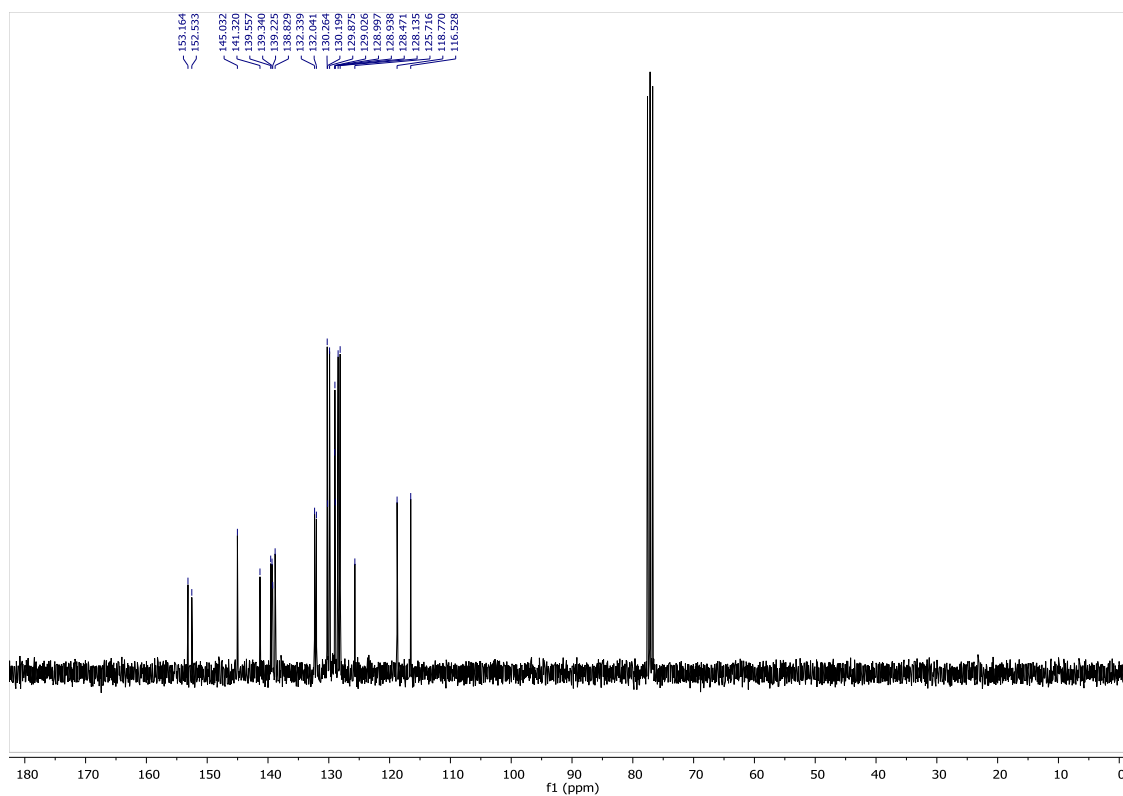


Compound 1e

^1H NMR (300 MHz, CDCl_3)

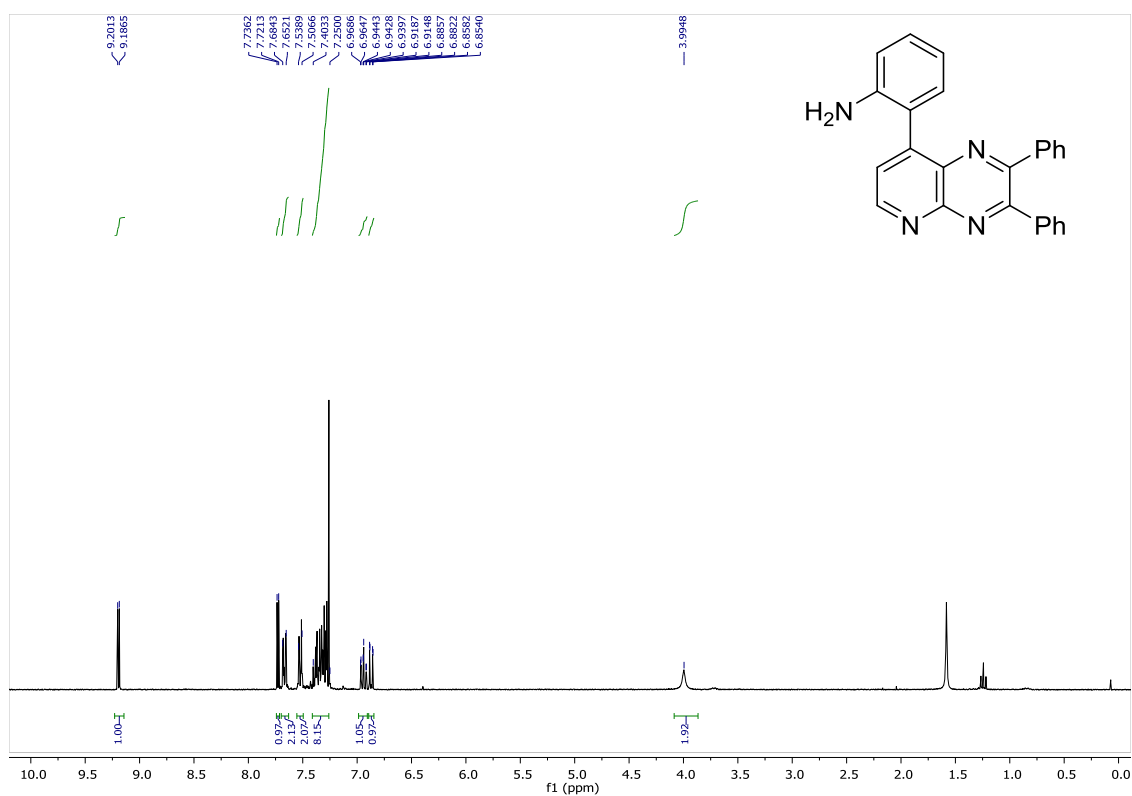


^{13}C NMR (75 MHz, CDCl_3)

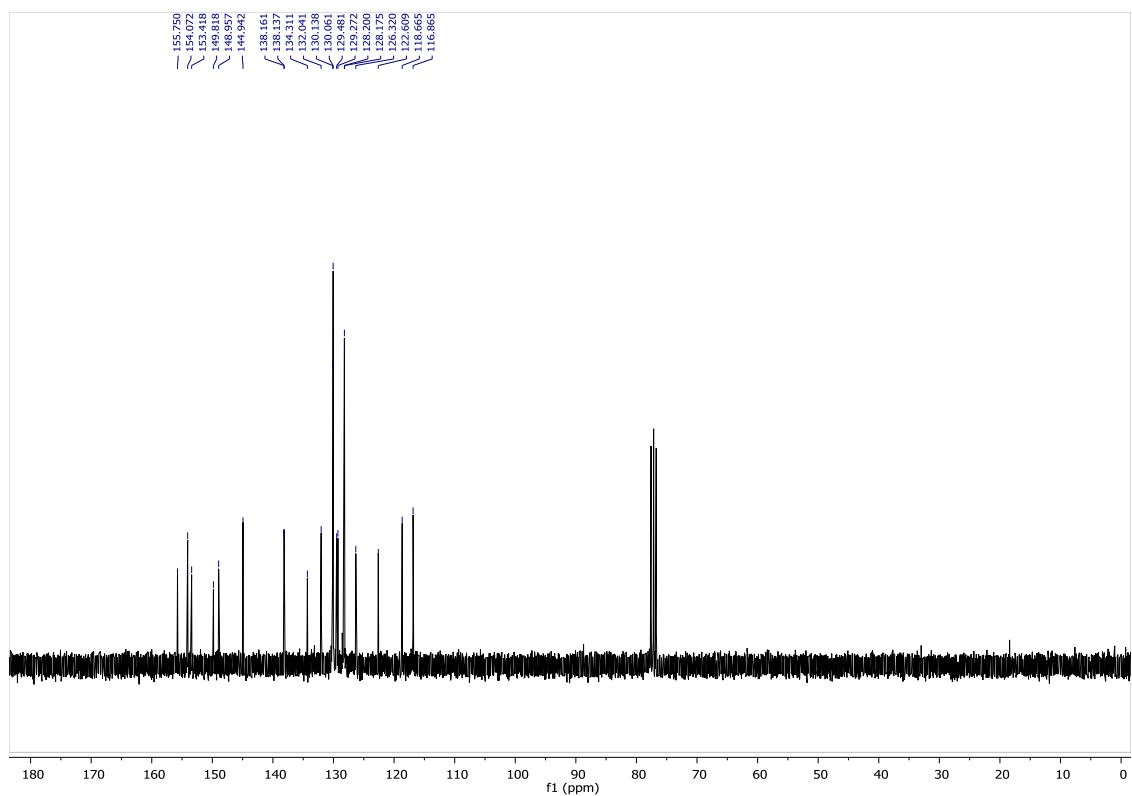


Compound 2e

^1H NMR (300 MHz, CDCl_3)

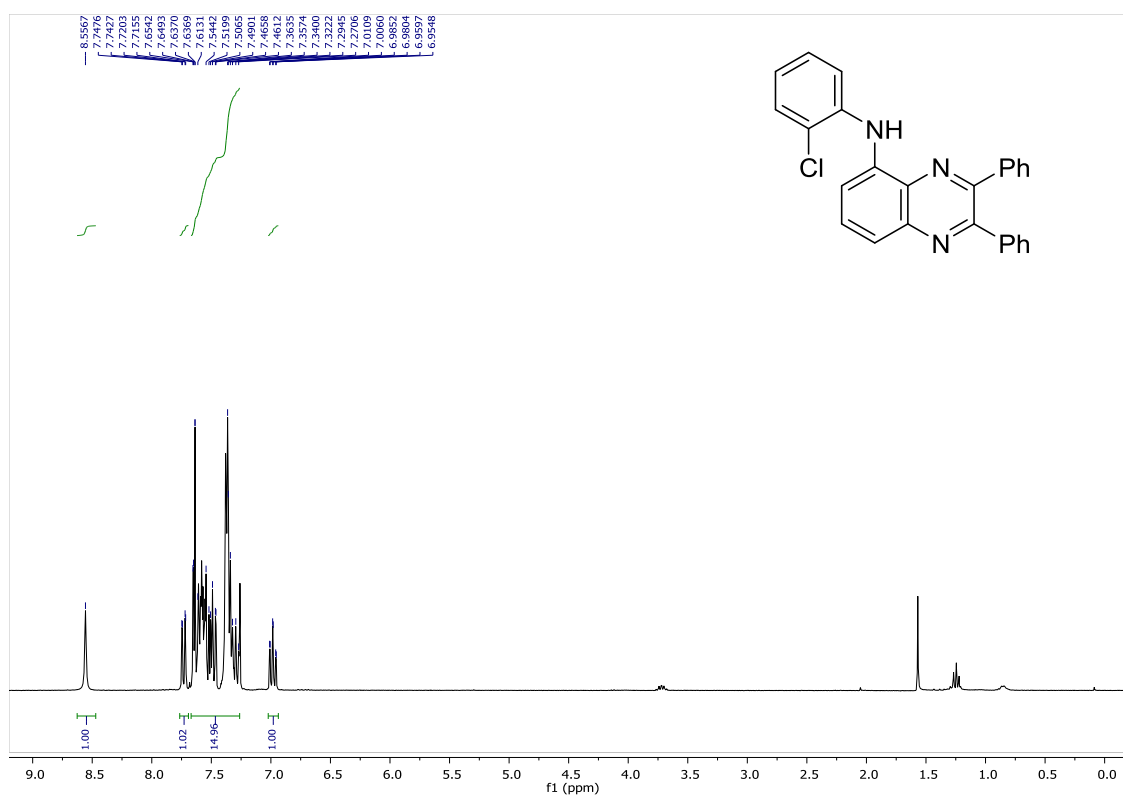


^{13}C NMR (75 MHz, CDCl_3)

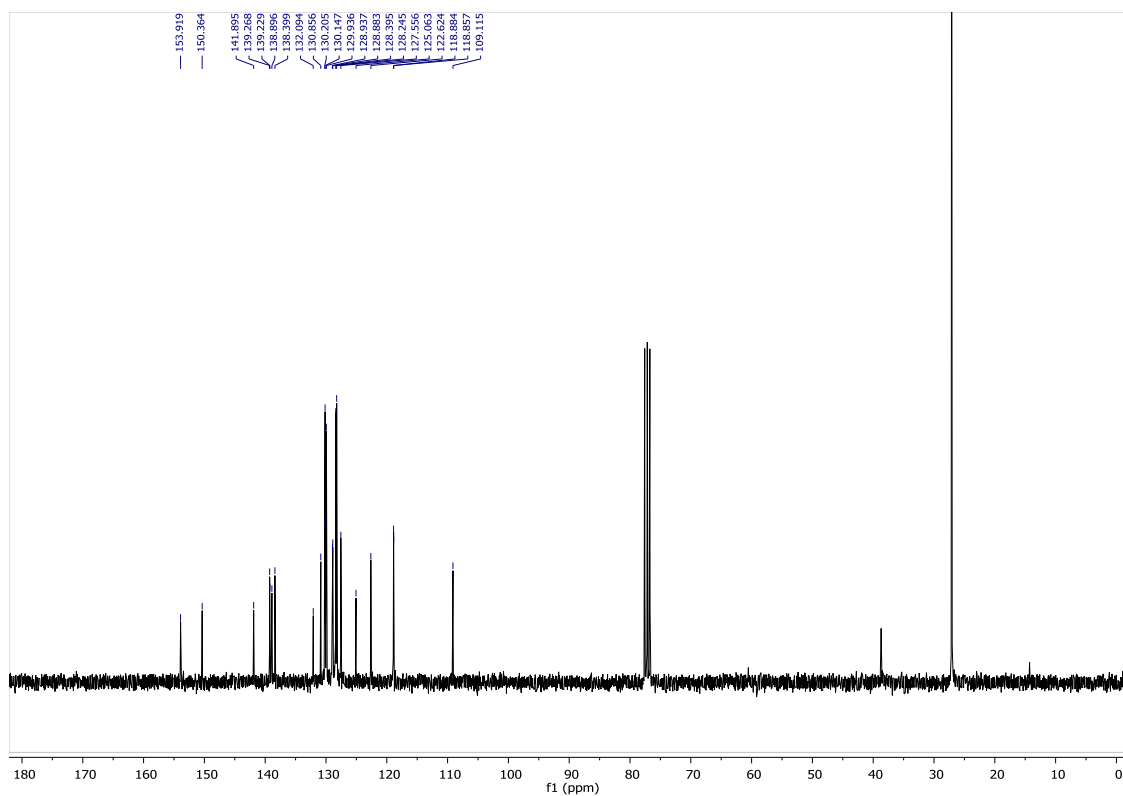


Compound 1f

^1H NMR (300 MHz, CDCl_3)

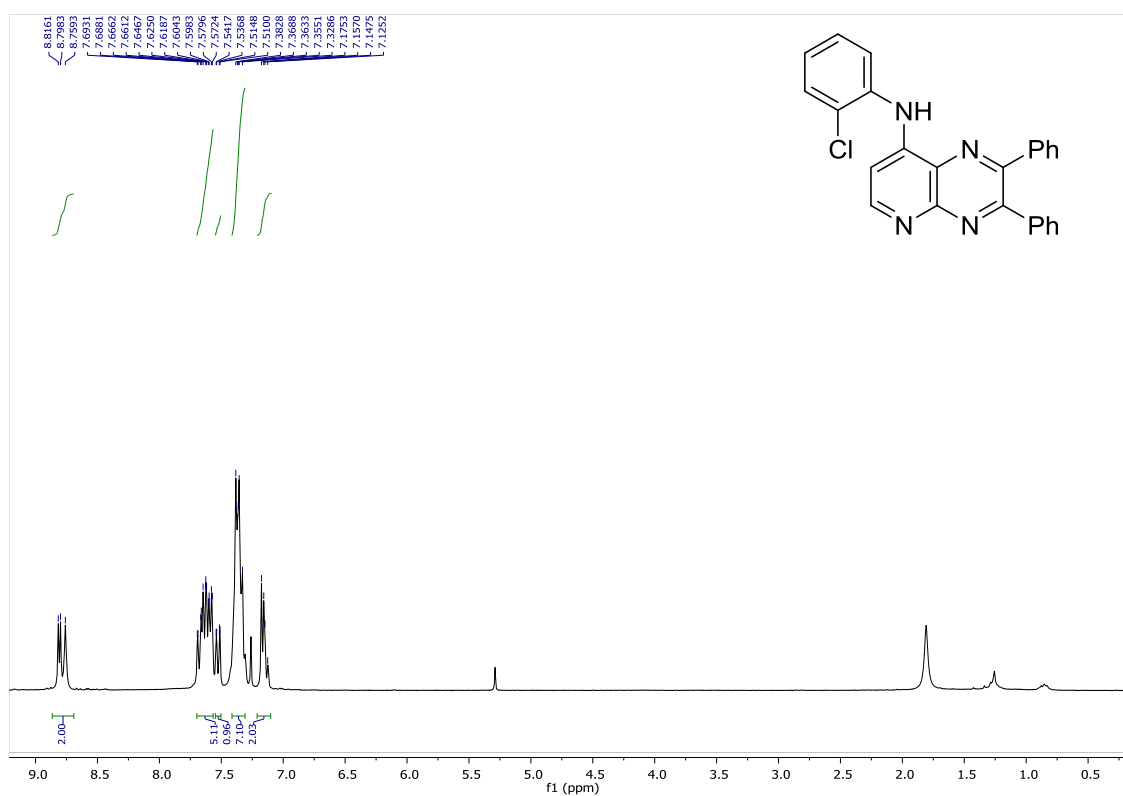


^{13}C NMR (75 MHz, CDCl_3)

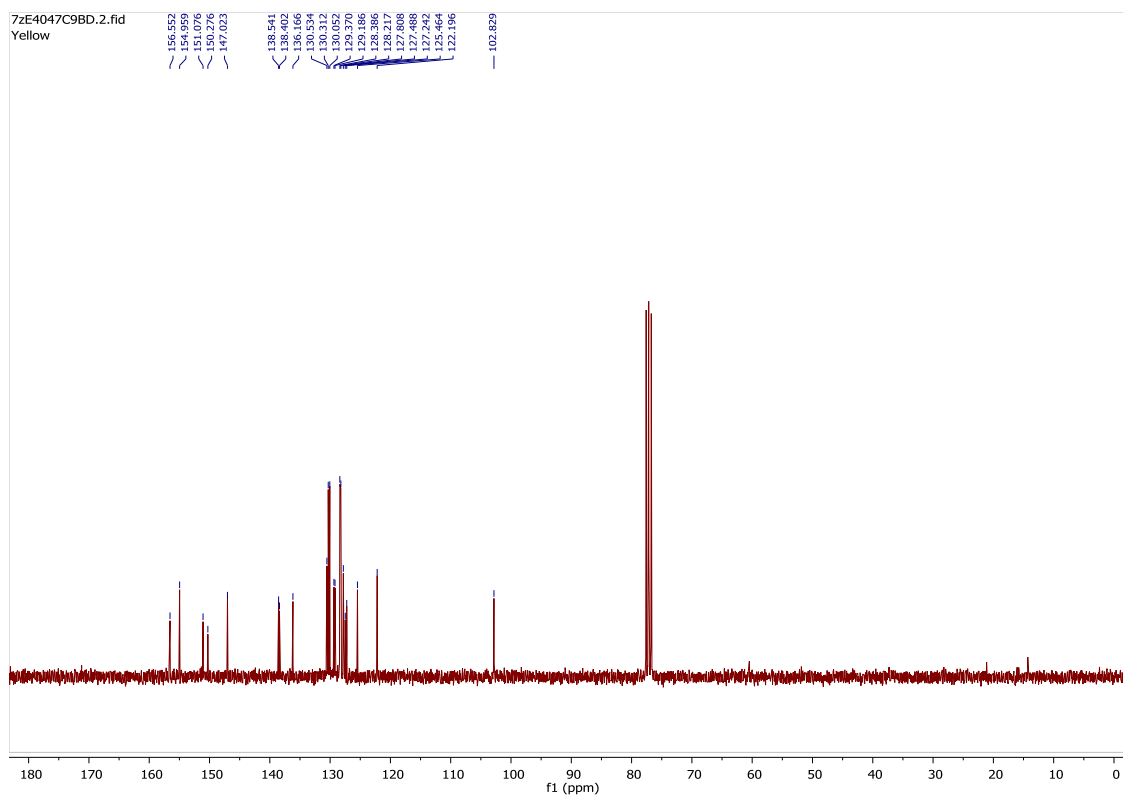


Compound 2f

^1H NMR (300 MHz, CDCl_3)

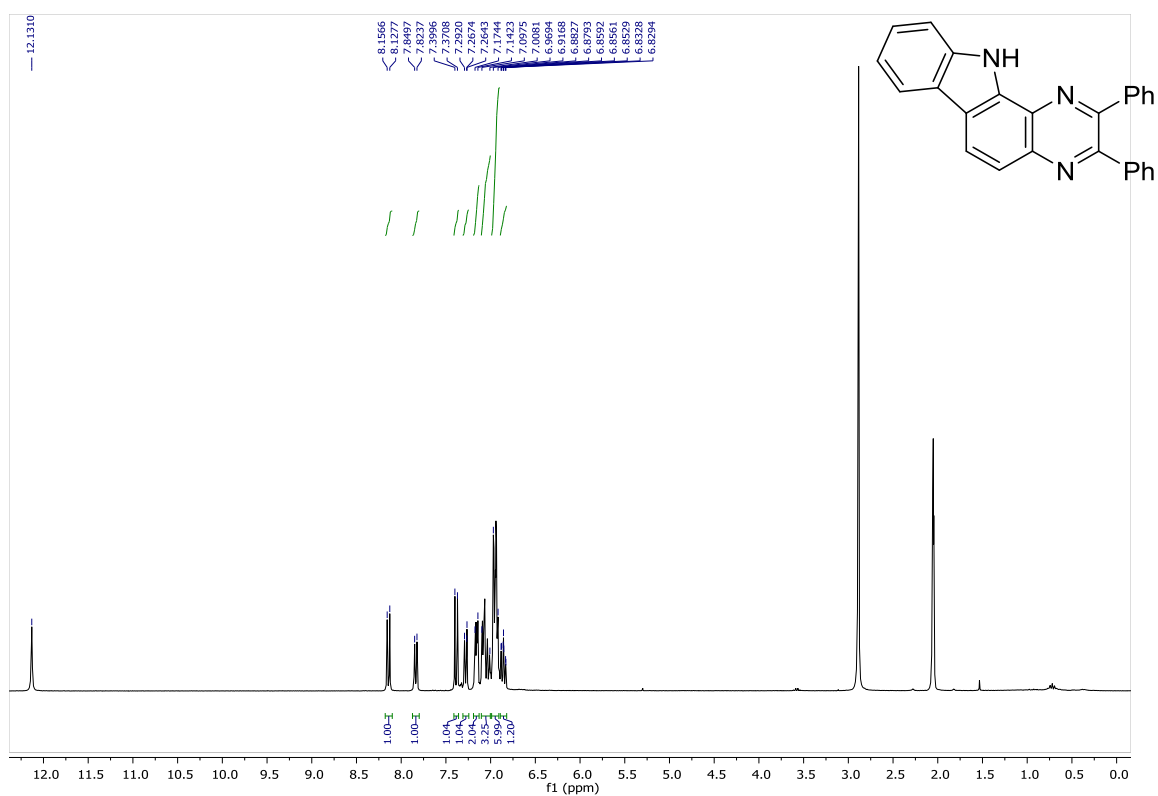


^{13}C NMR (75 MHz, CDCl_3)

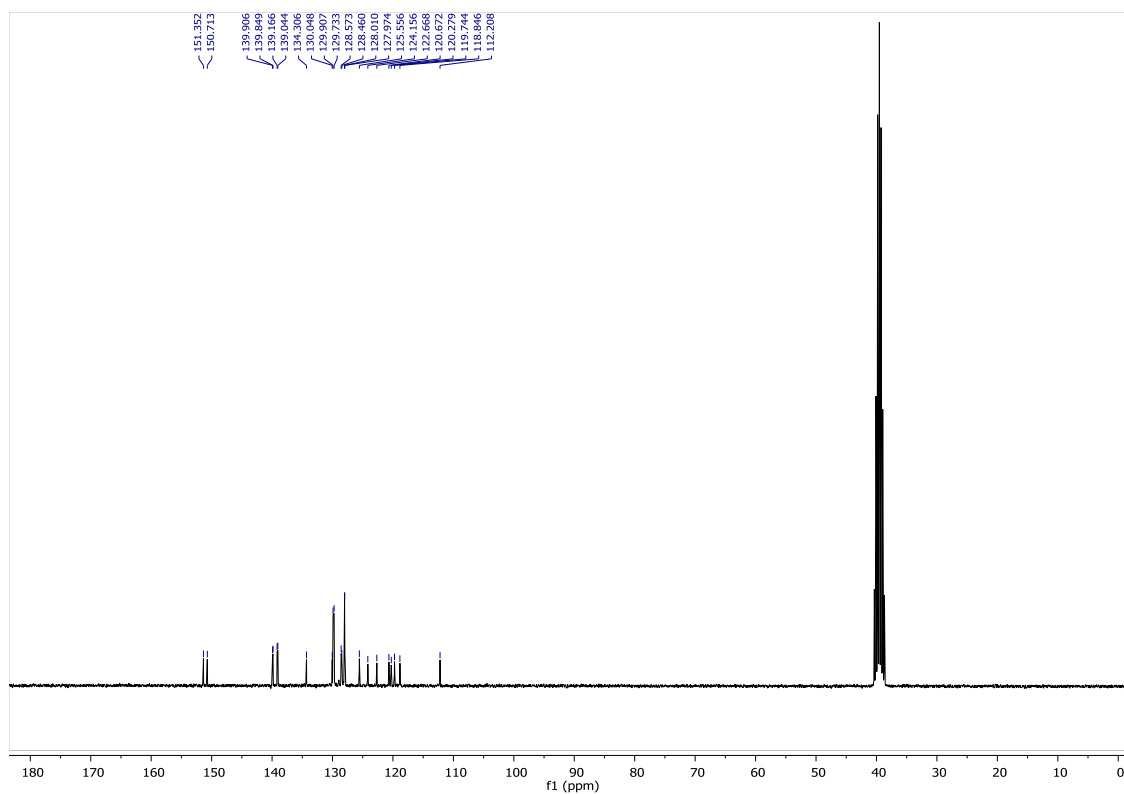


Compound 1g

^1H NMR (300 MHz, $(\text{CD}_3)_2\text{SO}$)

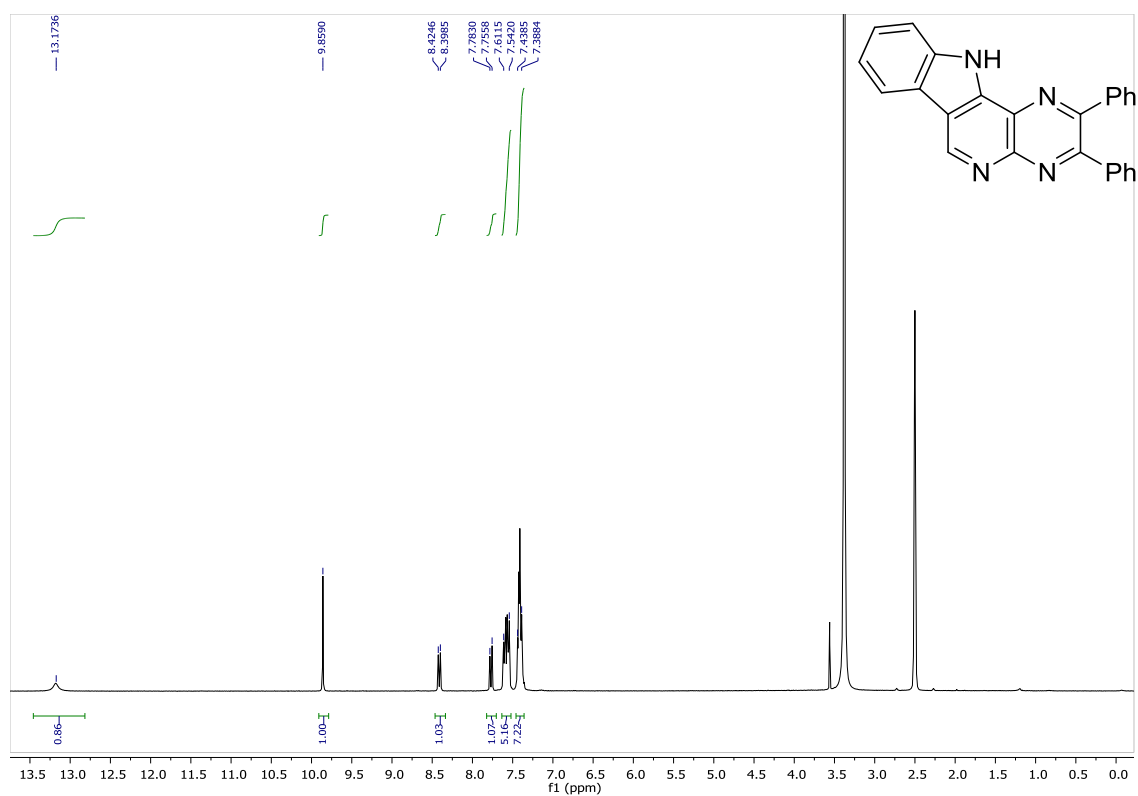


^{13}C NMR (75 MHz, $(\text{CD}_3)_2\text{SO}$)

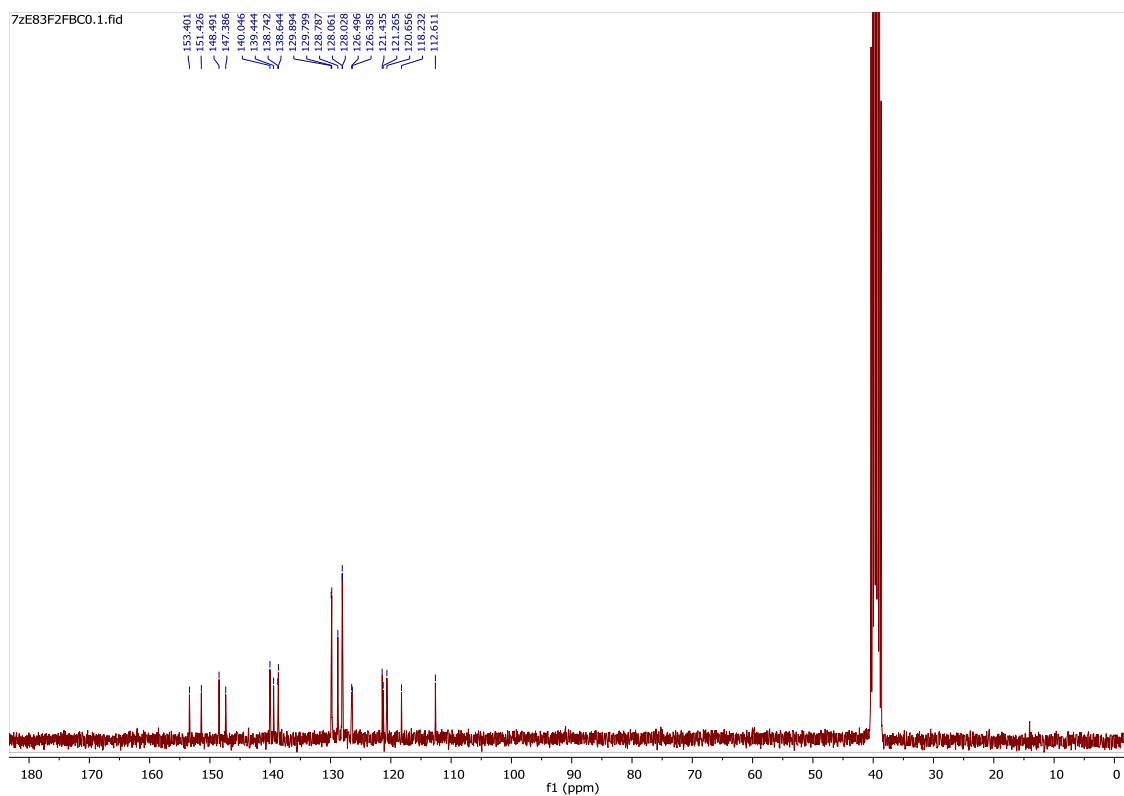


Compound 2g

^1H NMR (300 MHz, $(\text{CD}_3)_2\text{SO}$)

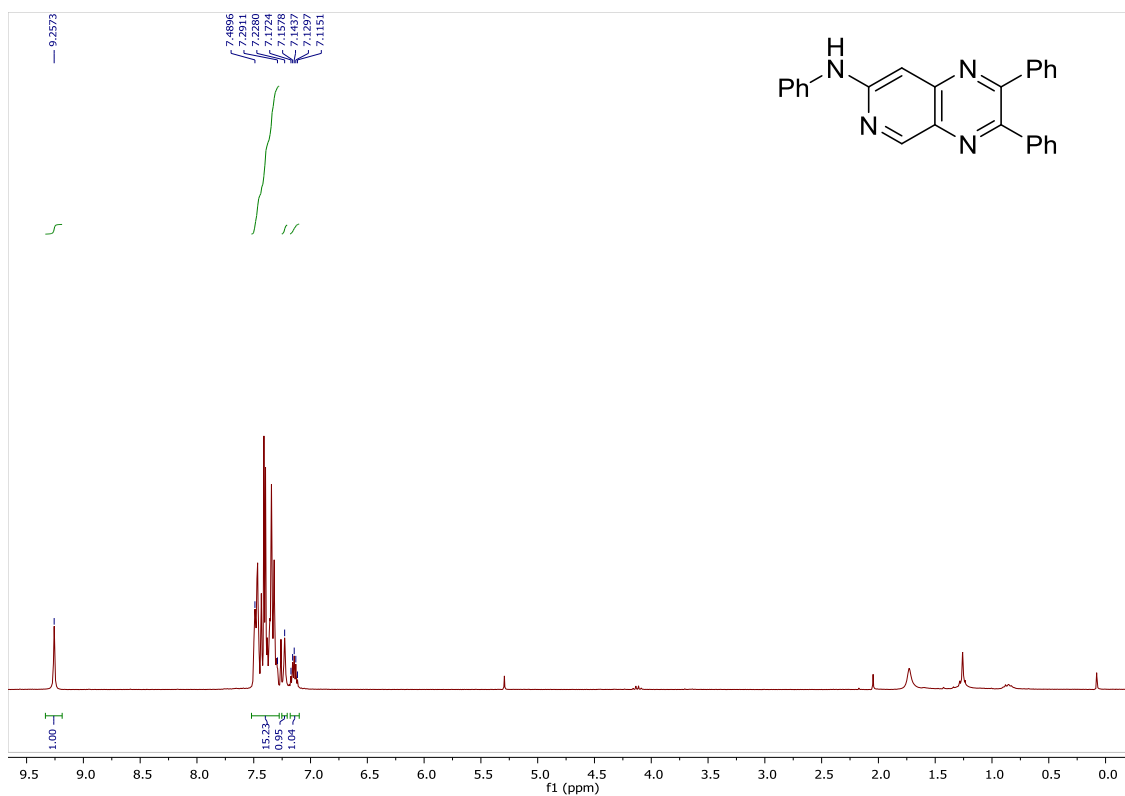


^{13}C NMR (75 MHz, $(\text{CD}_3)_2\text{SO}$)

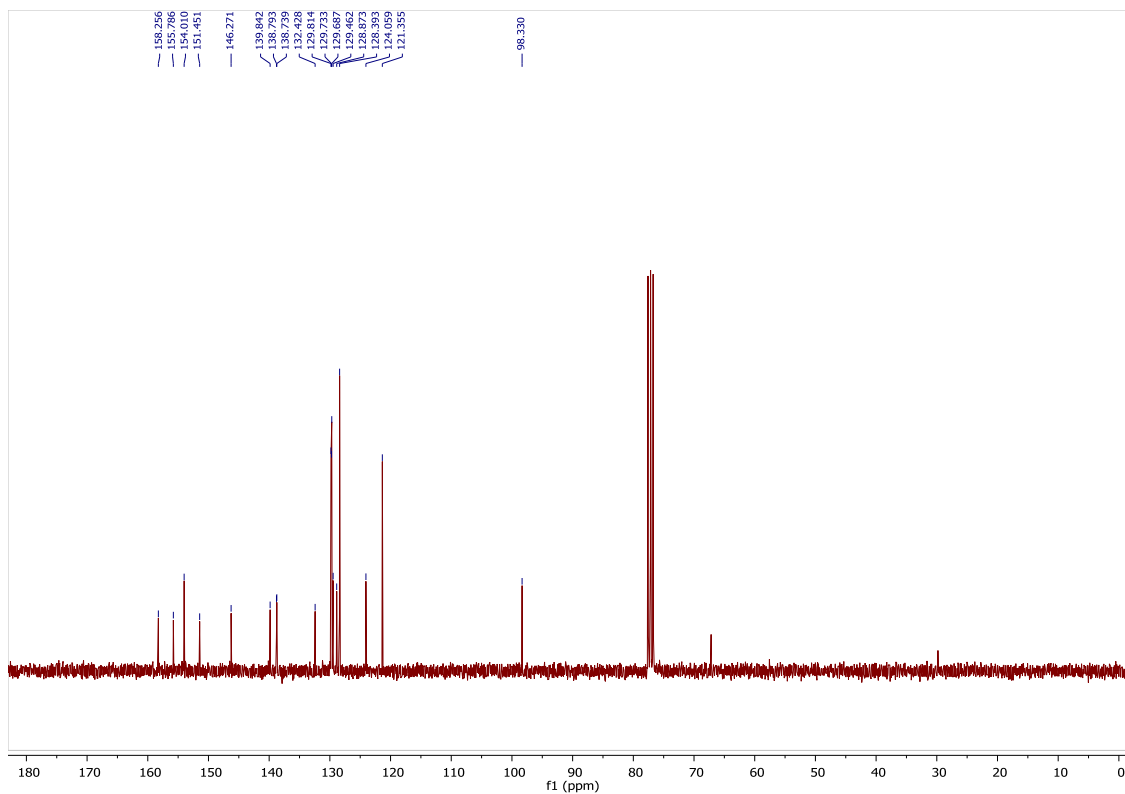


Compound 3g'

^1H NMR (300 MHz, CDCl_3)

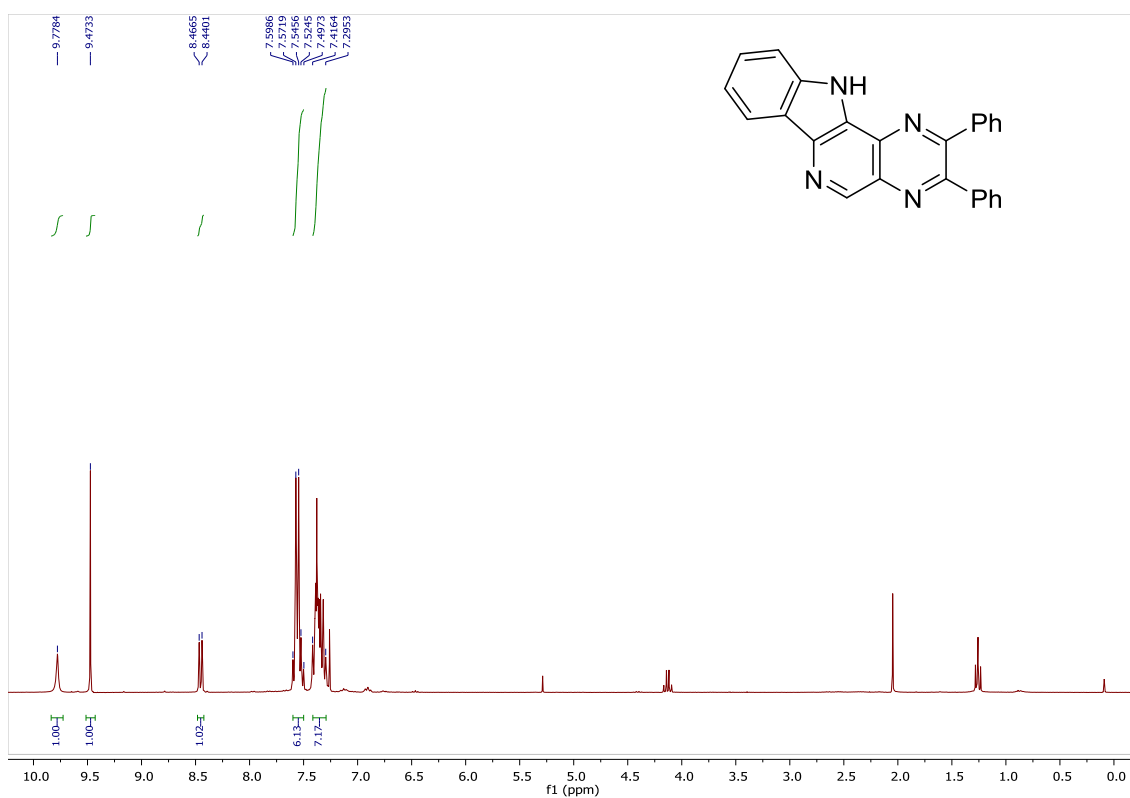


^{13}C NMR (75 MHz, CDCl_3)

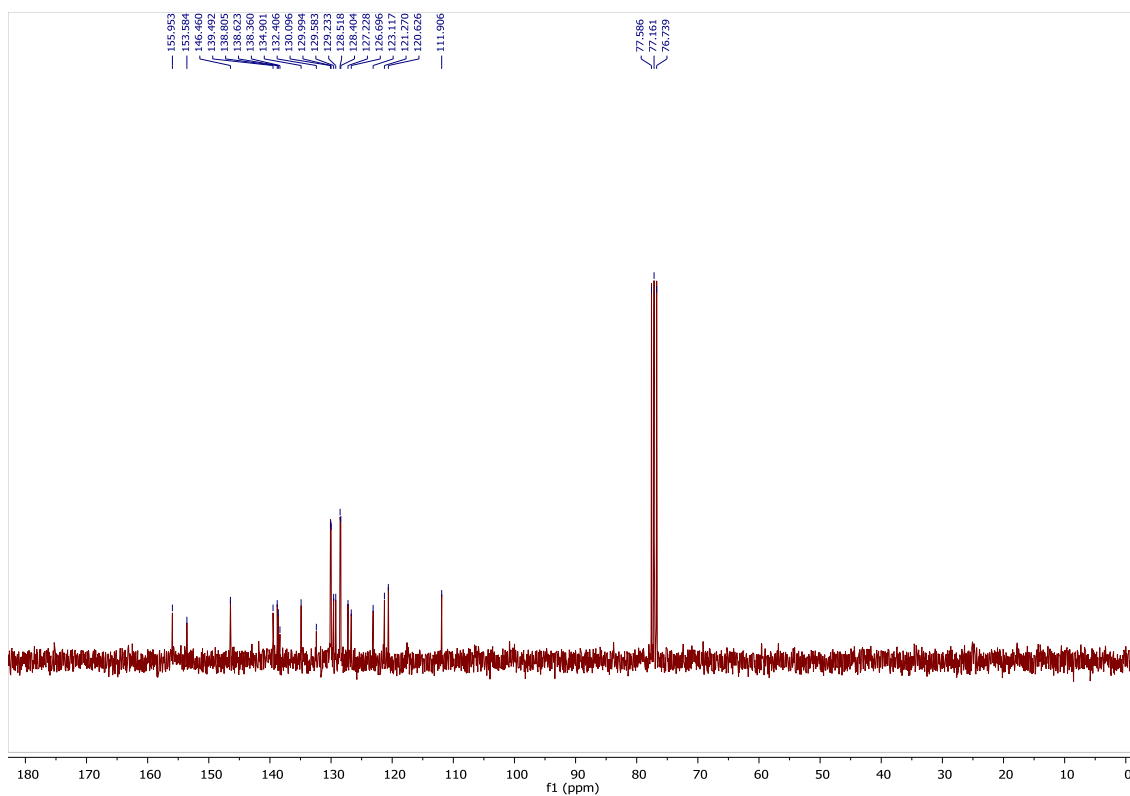


Compound 3h

^1H NMR (300 MHz, CDCl_3)

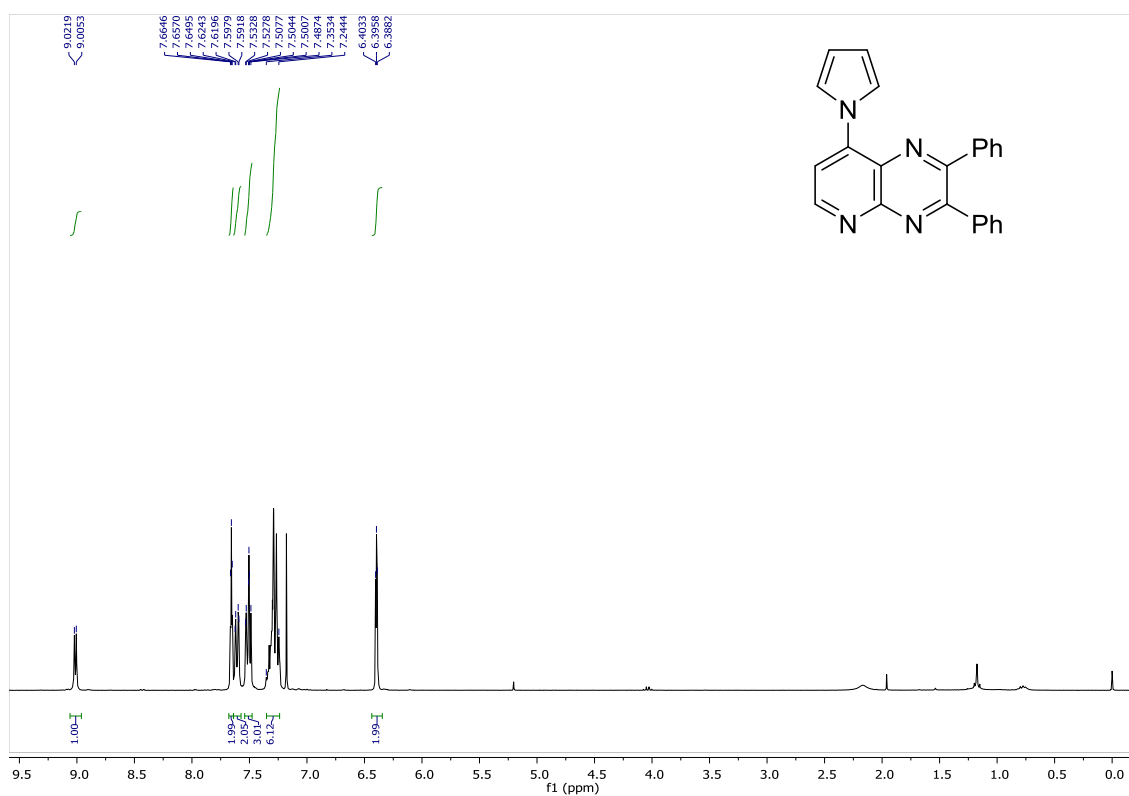


^{13}C NMR (75 MHz, CDCl_3)

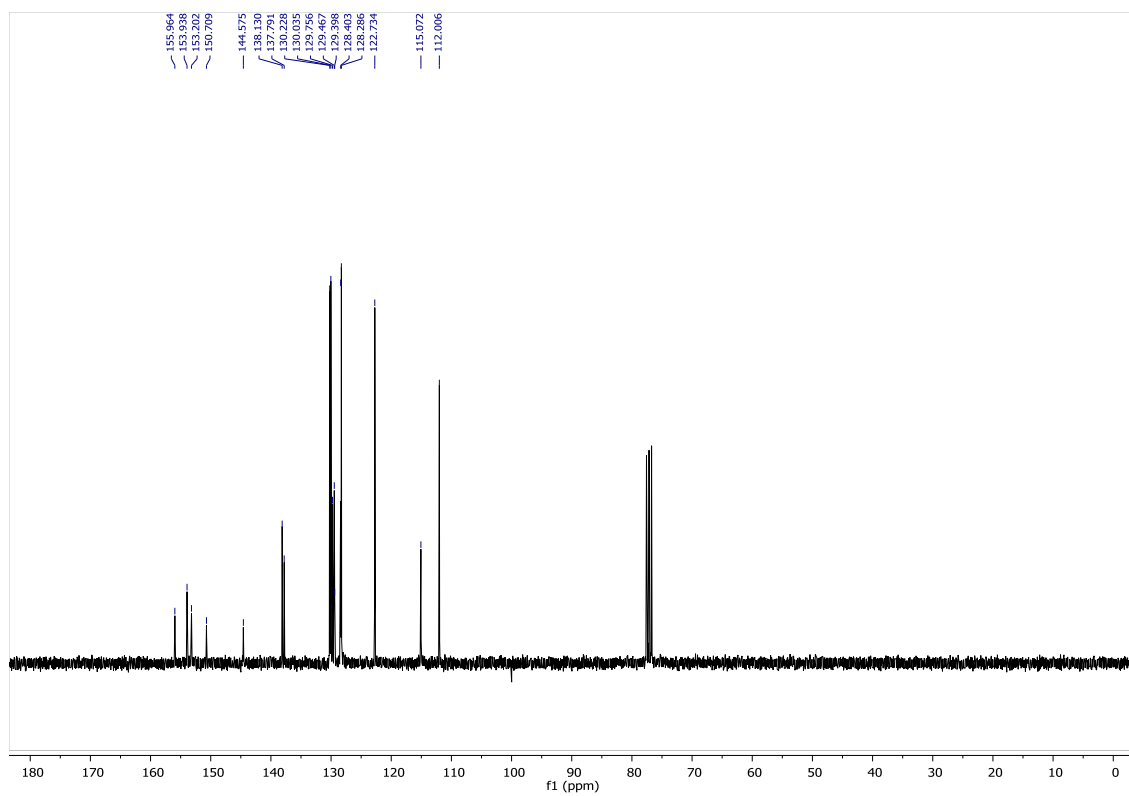


Compound 2i

^1H NMR (300 MHz, CDCl_3)

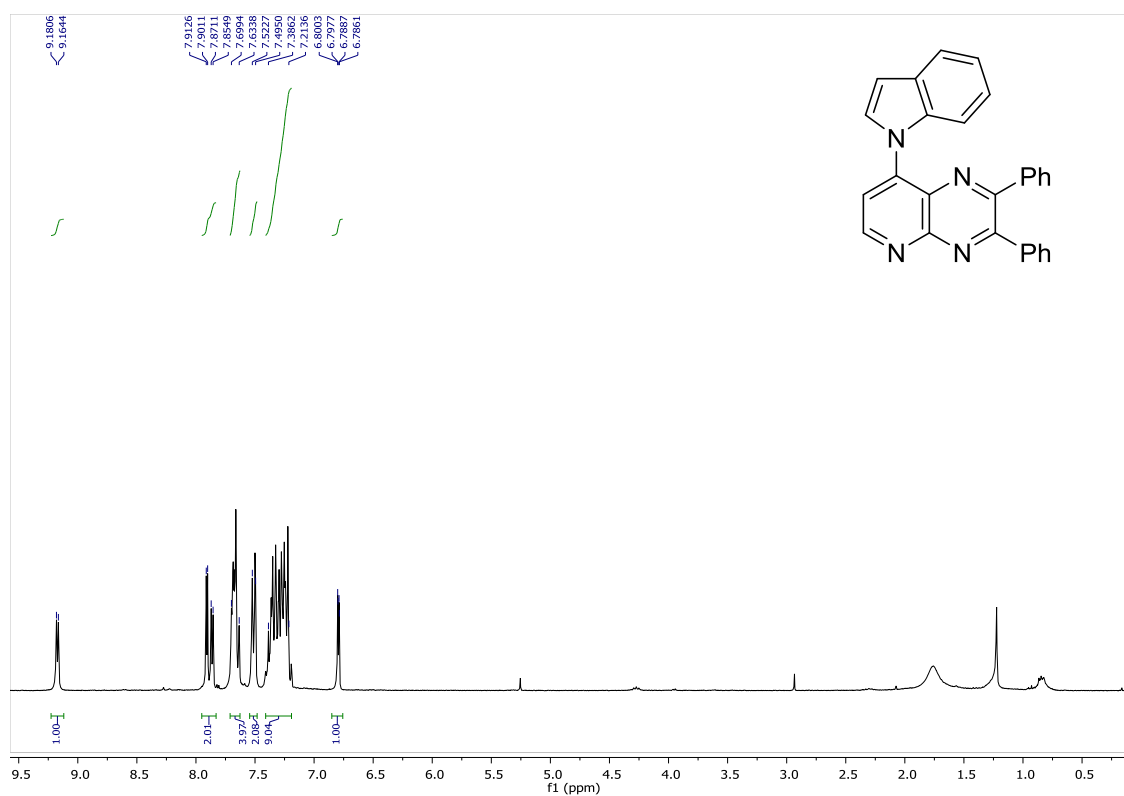


^{13}C NMR (75 MHz, CDCl_3)

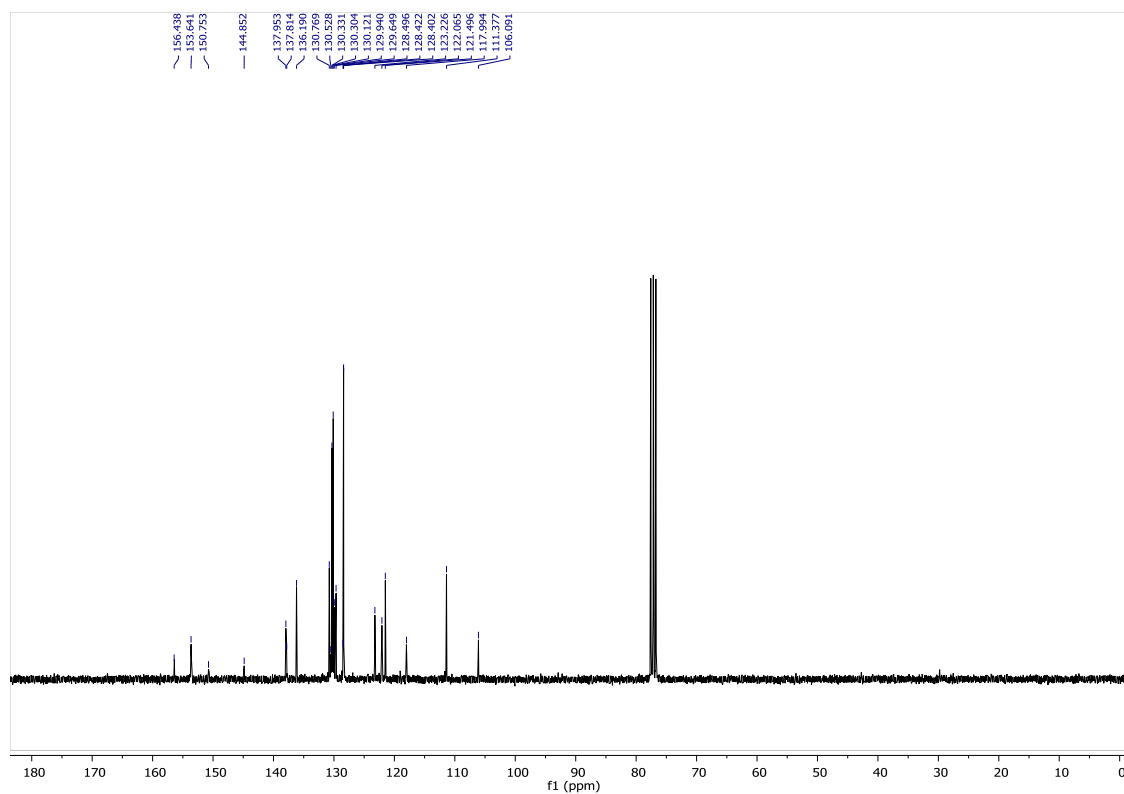


Compound 2j

^1H NMR (300 MHz, CDCl_3)

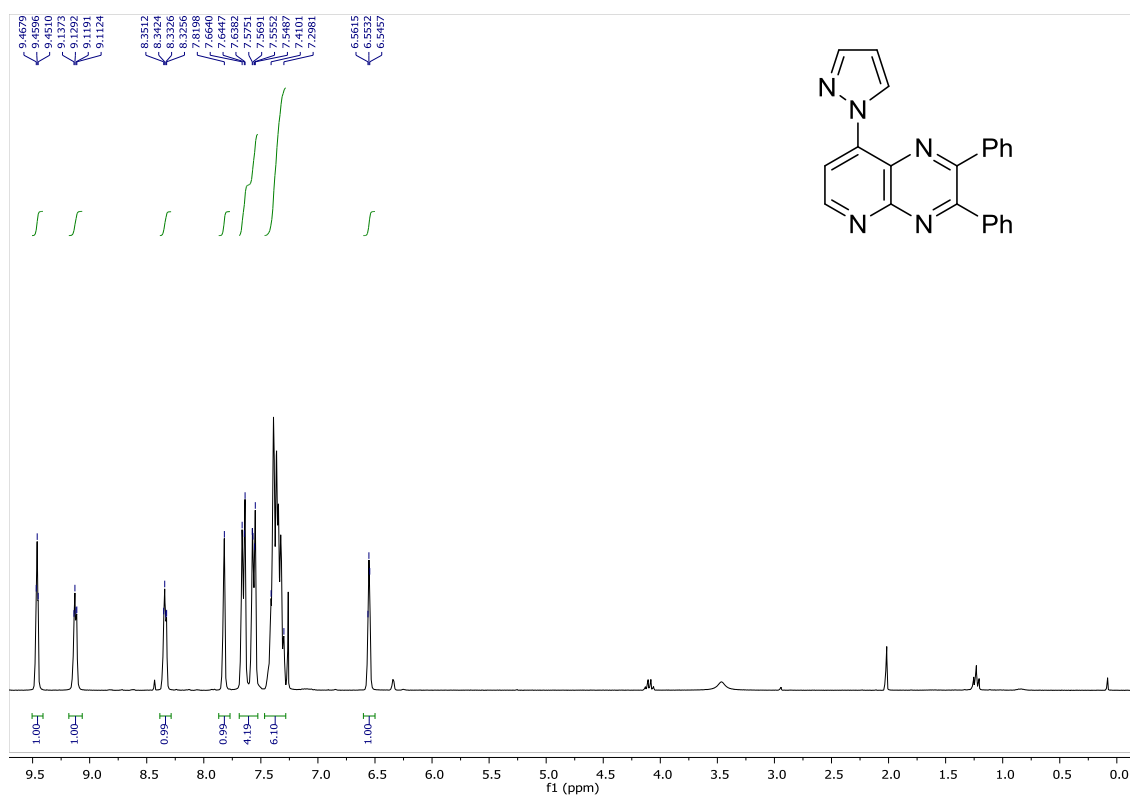


^{13}C NMR (75 MHz, CDCl_3)

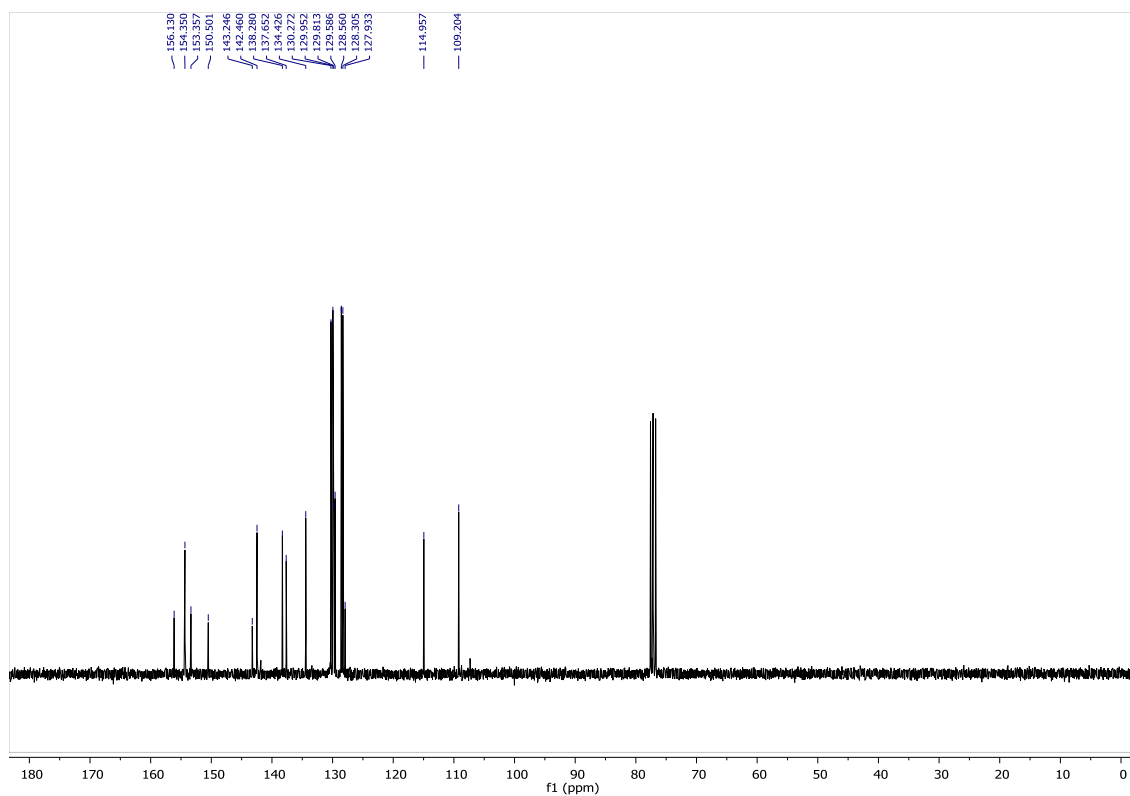


Compound 2k

^1H NMR (300 MHz, CDCl_3)

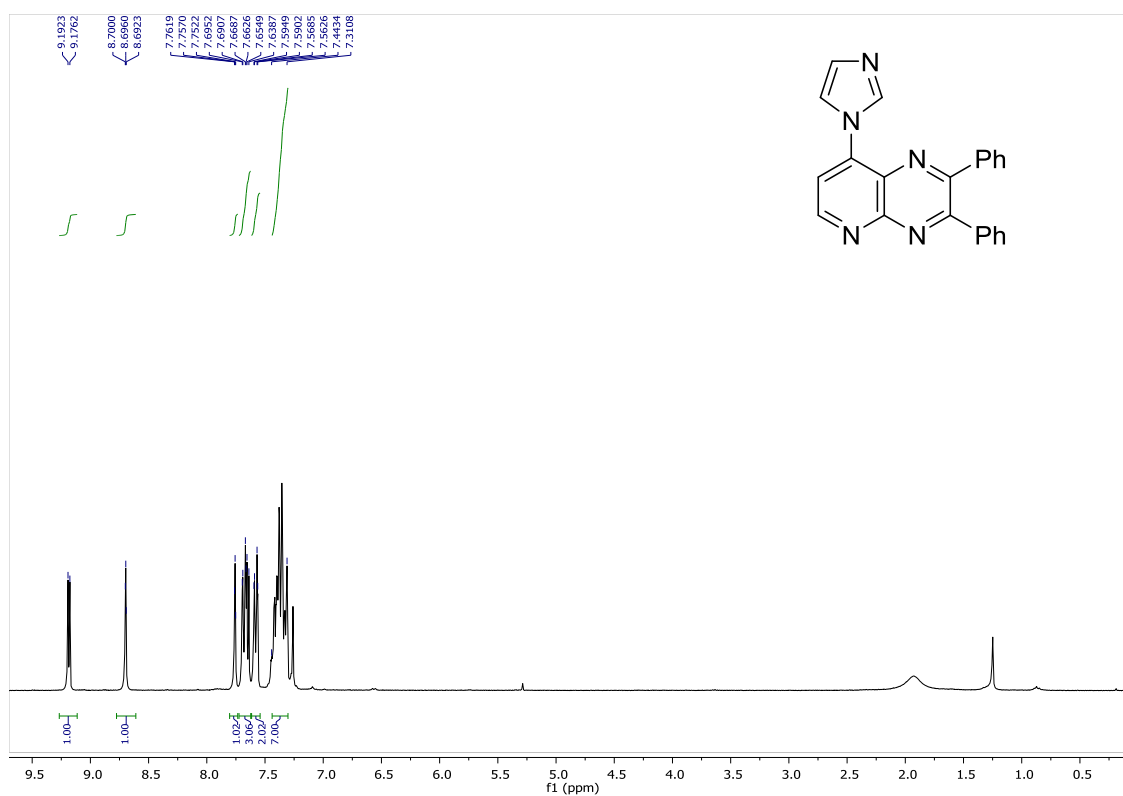


^{13}C NMR (75 MHz, CDCl_3)

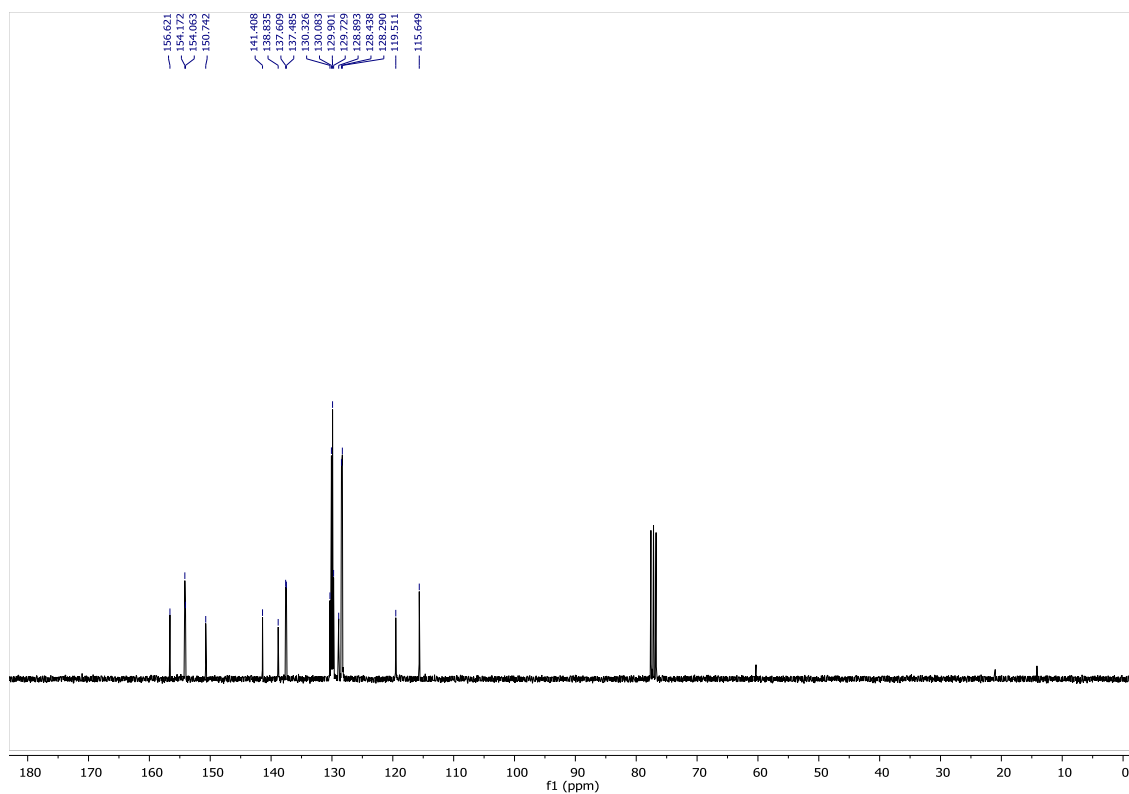


Compound 2l

^1H NMR (300 MHz, CDCl_3)

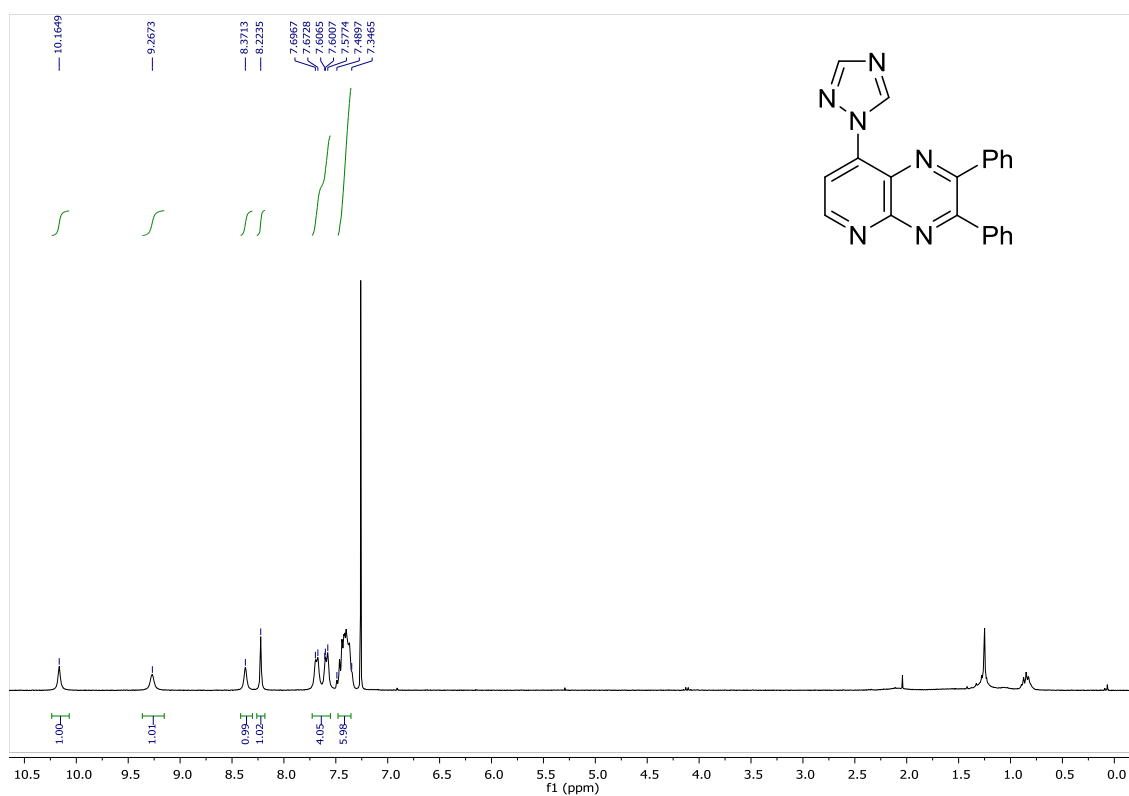


^{13}C NMR (75 MHz, CDCl_3)

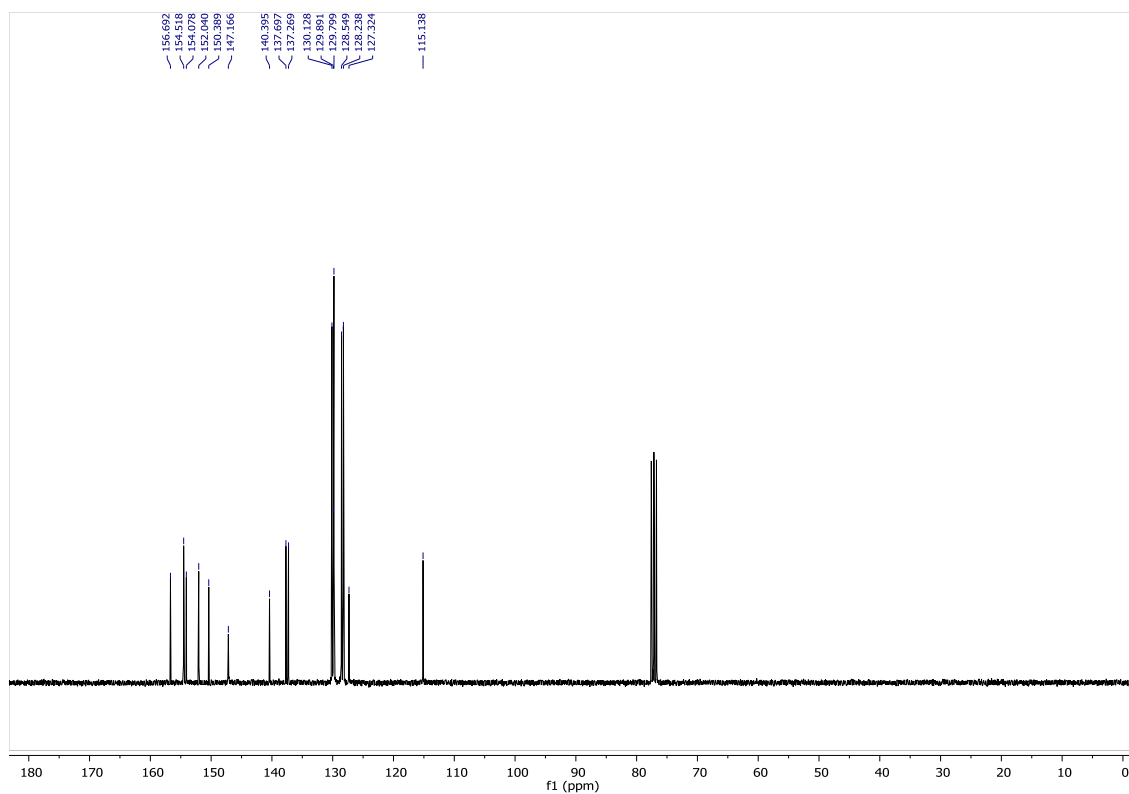


Compound 2m

^1H NMR (300 MHz, CDCl_3)

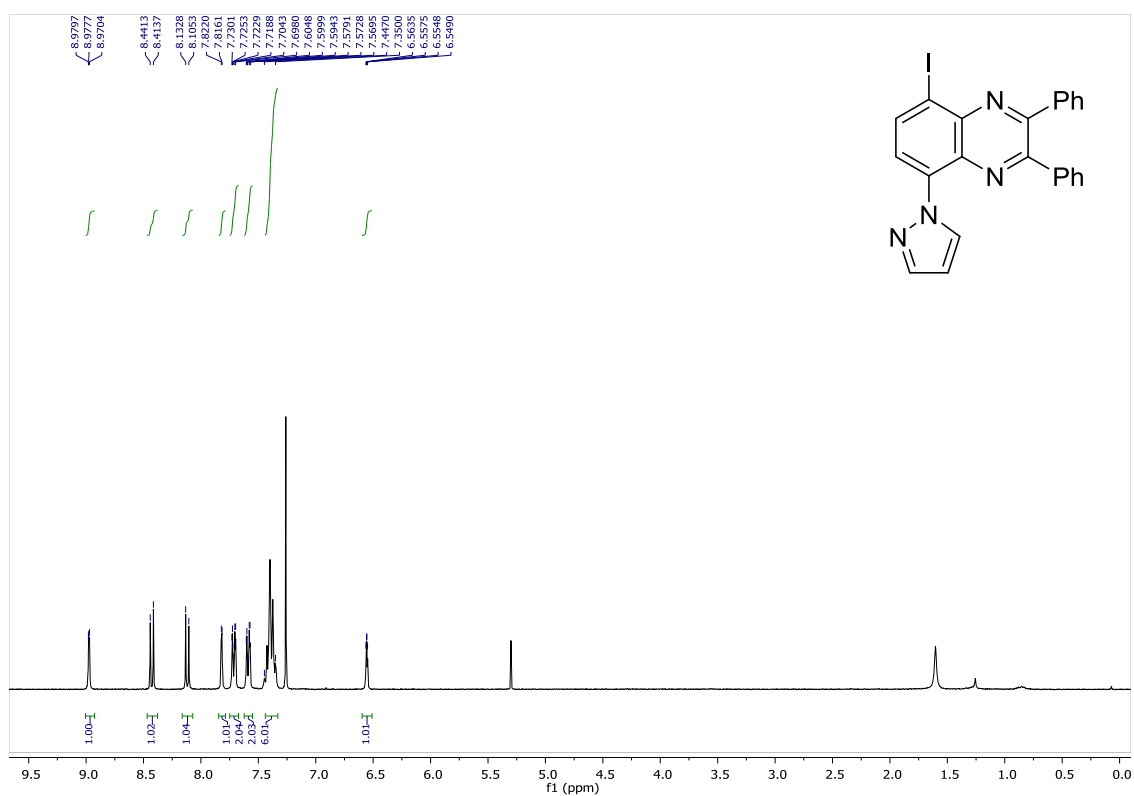


^{13}C NMR (75 MHz, CDCl_3)

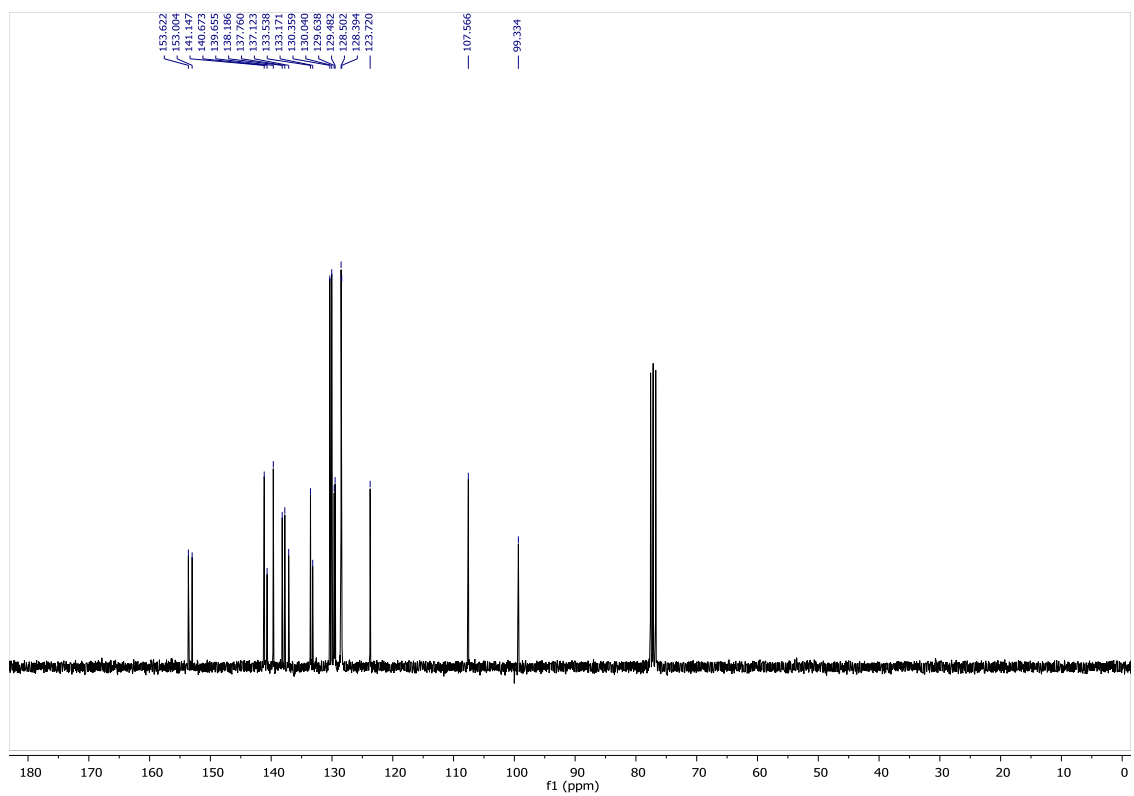


Compound 1k'

^1H NMR (300 MHz, CDCl_3)

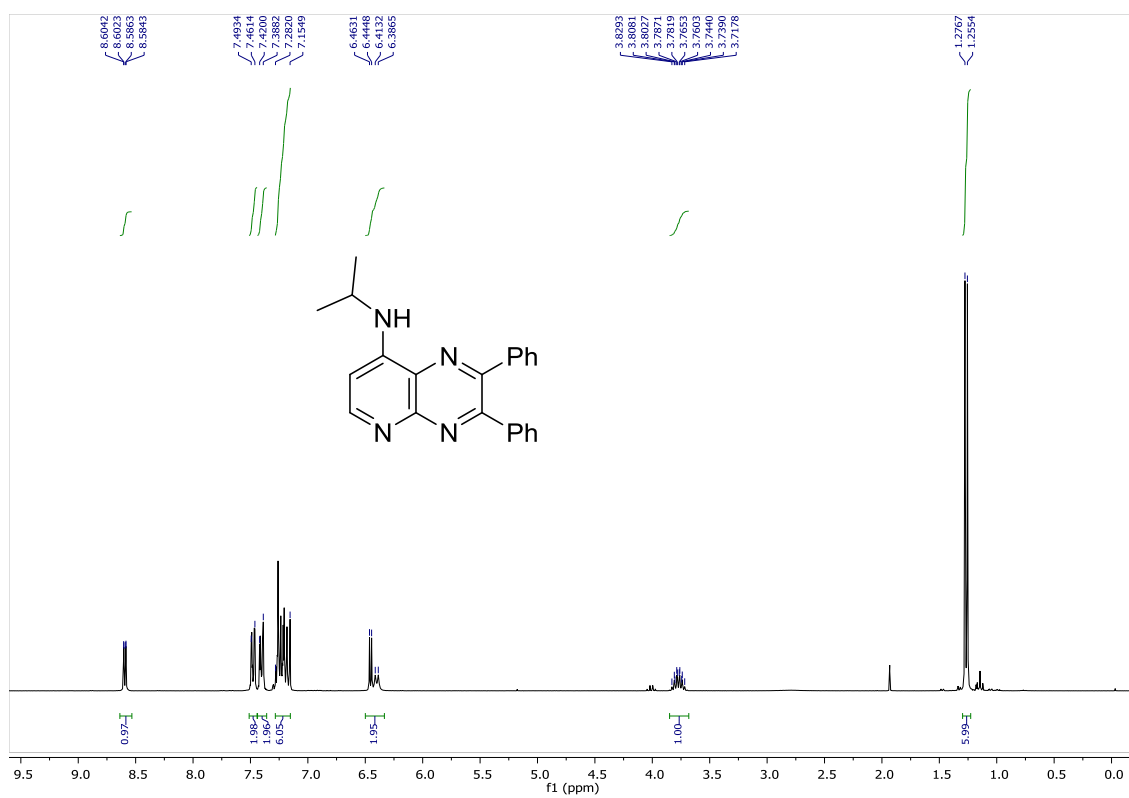


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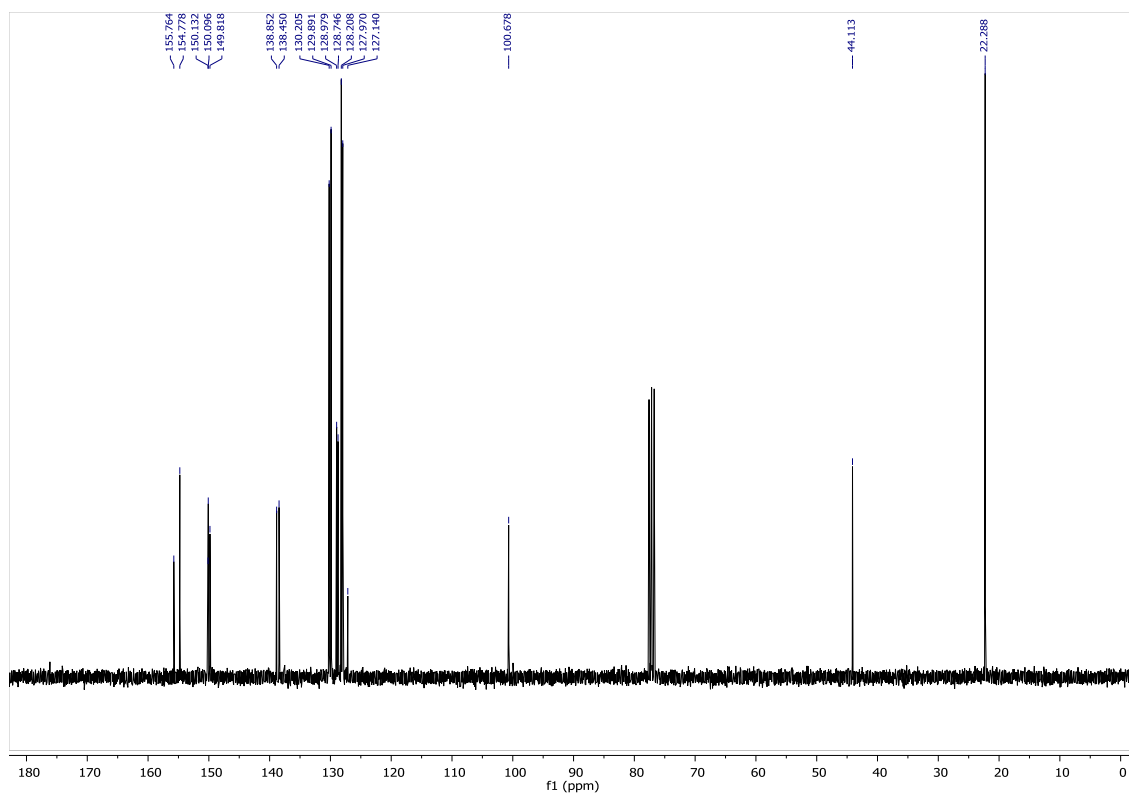


Compound 2n

^1H NMR (300 MHz, CDCl_3)

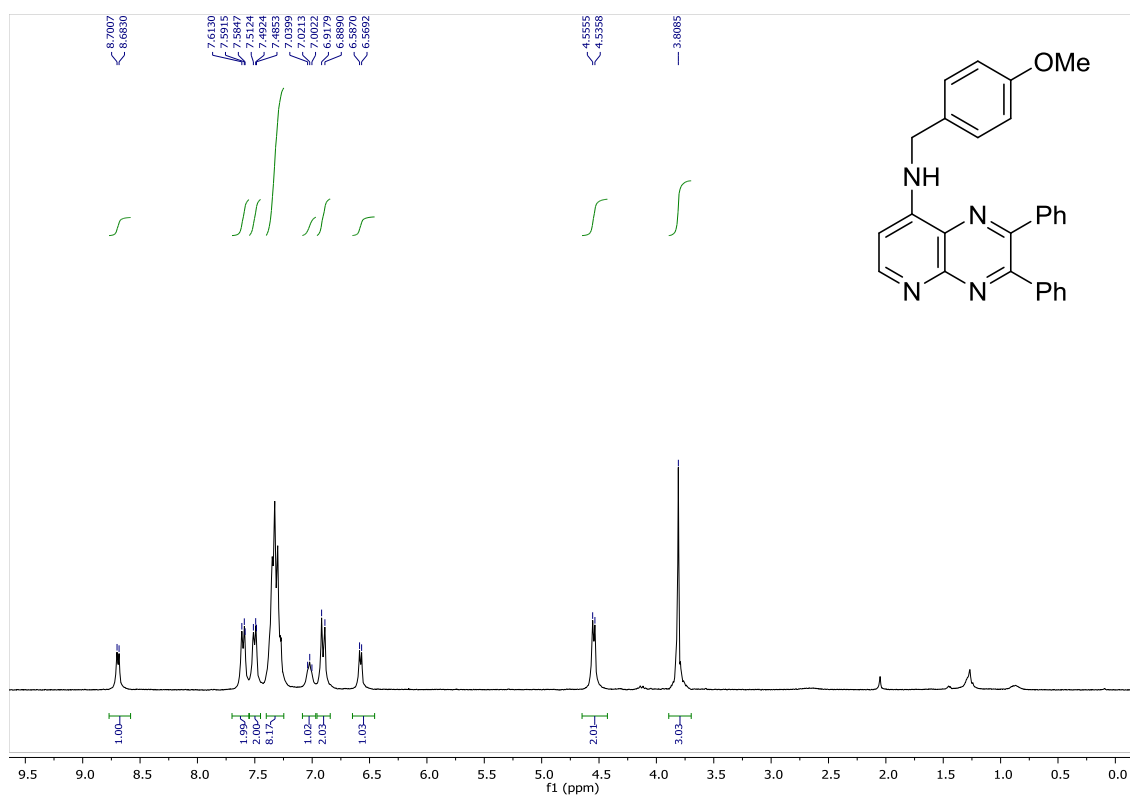


^{13}C NMR (75 MHz, CDCl_3)

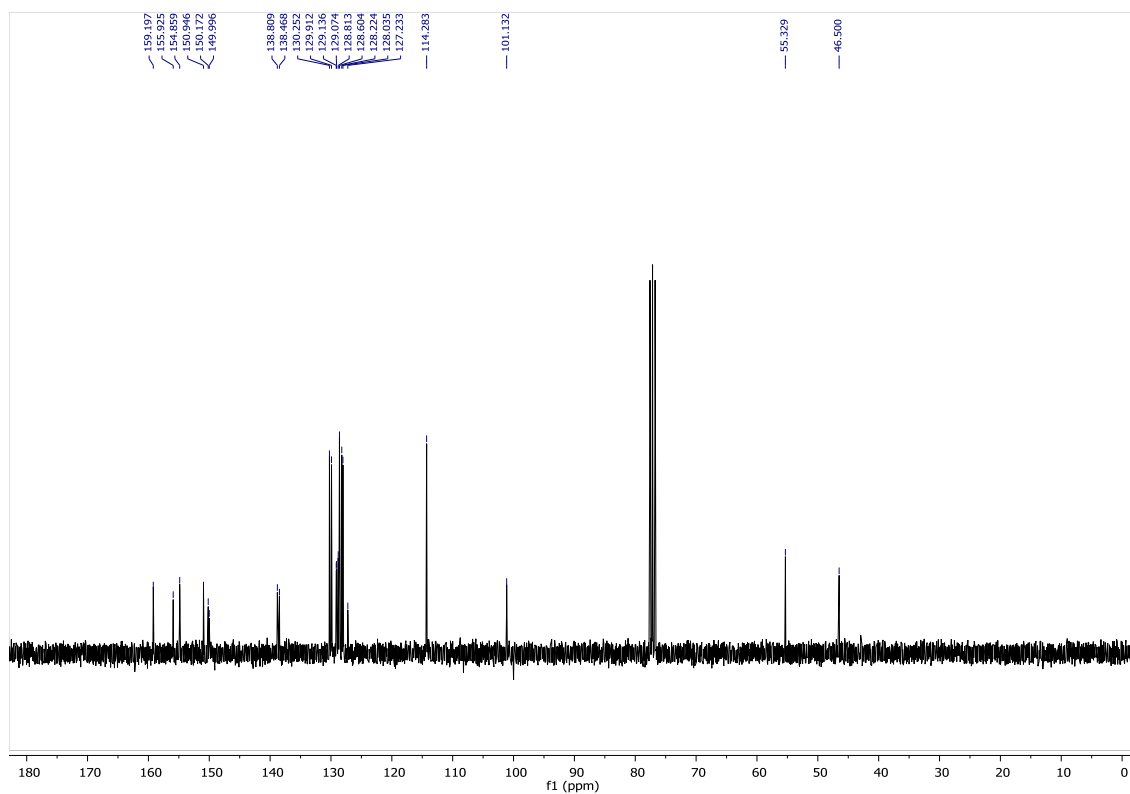


Compound 2o

^1H NMR (300 MHz, CDCl_3)

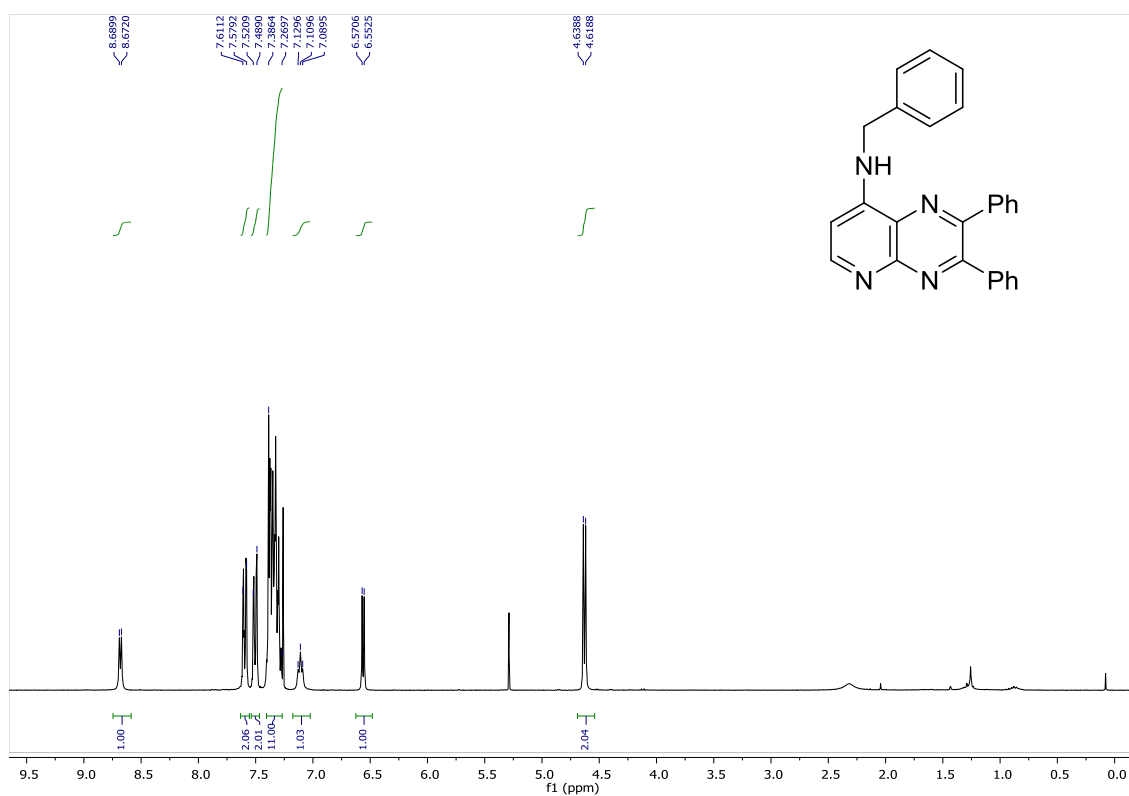


^{13}C NMR (75 MHz, CDCl_3)

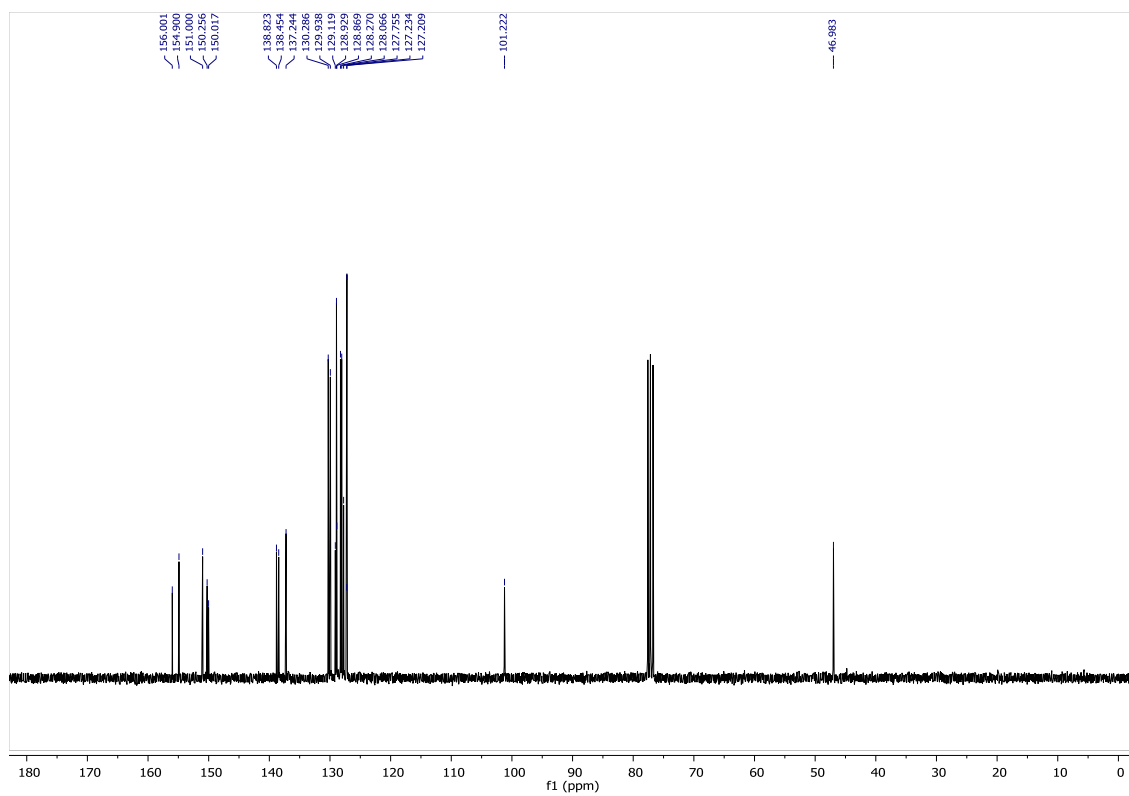


Compound 2p

^1H NMR (300 MHz, CDCl_3)

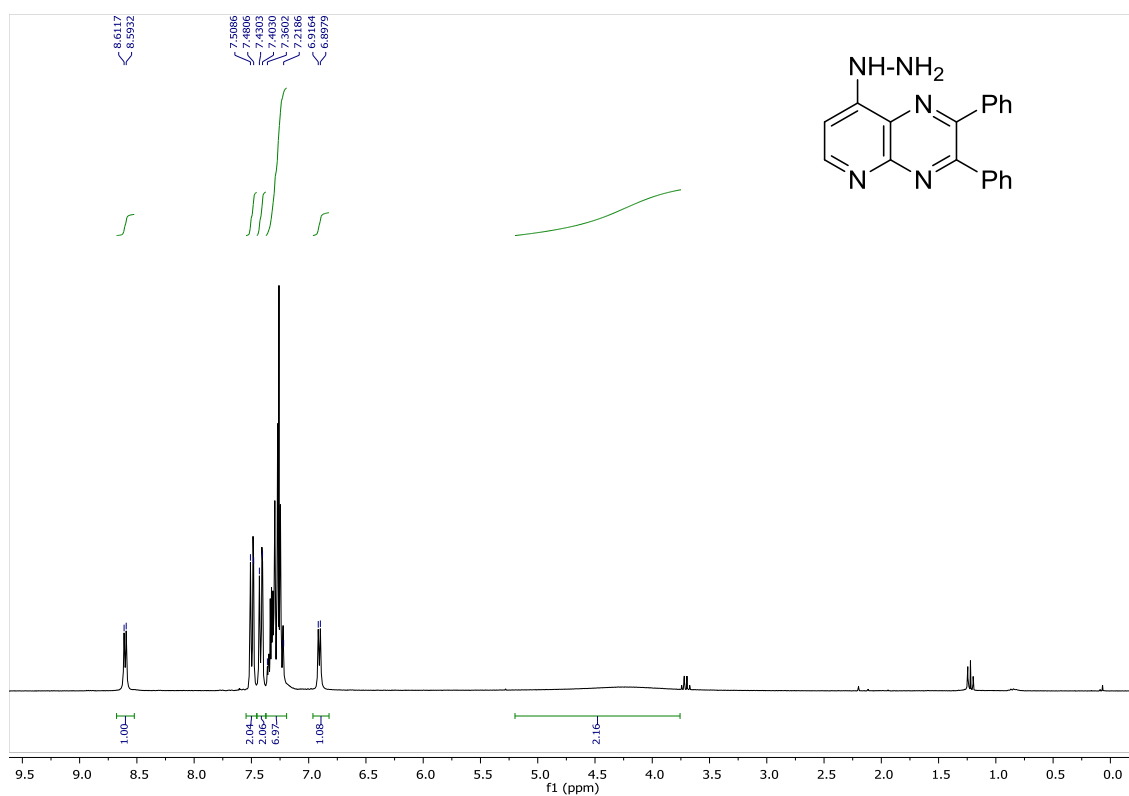


^{13}C NMR (75 MHz, CDCl_3)

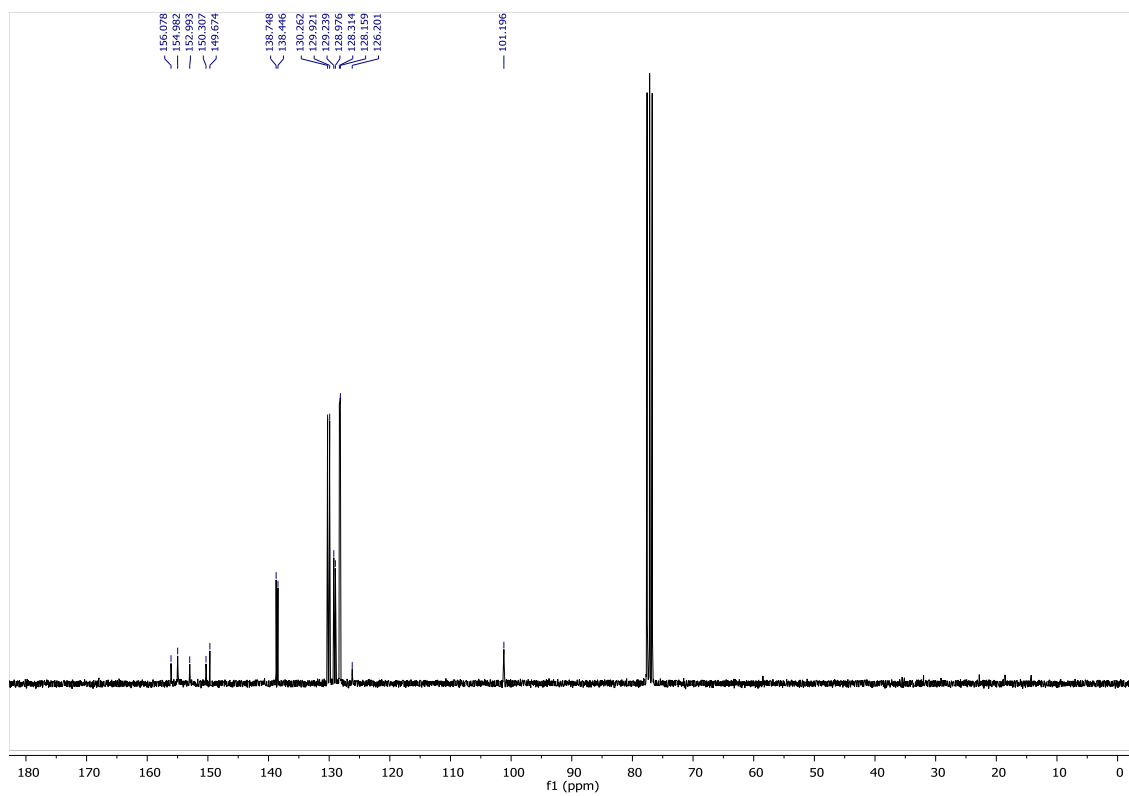


Compound 2q

^1H NMR (300 MHz, CDCl_3)

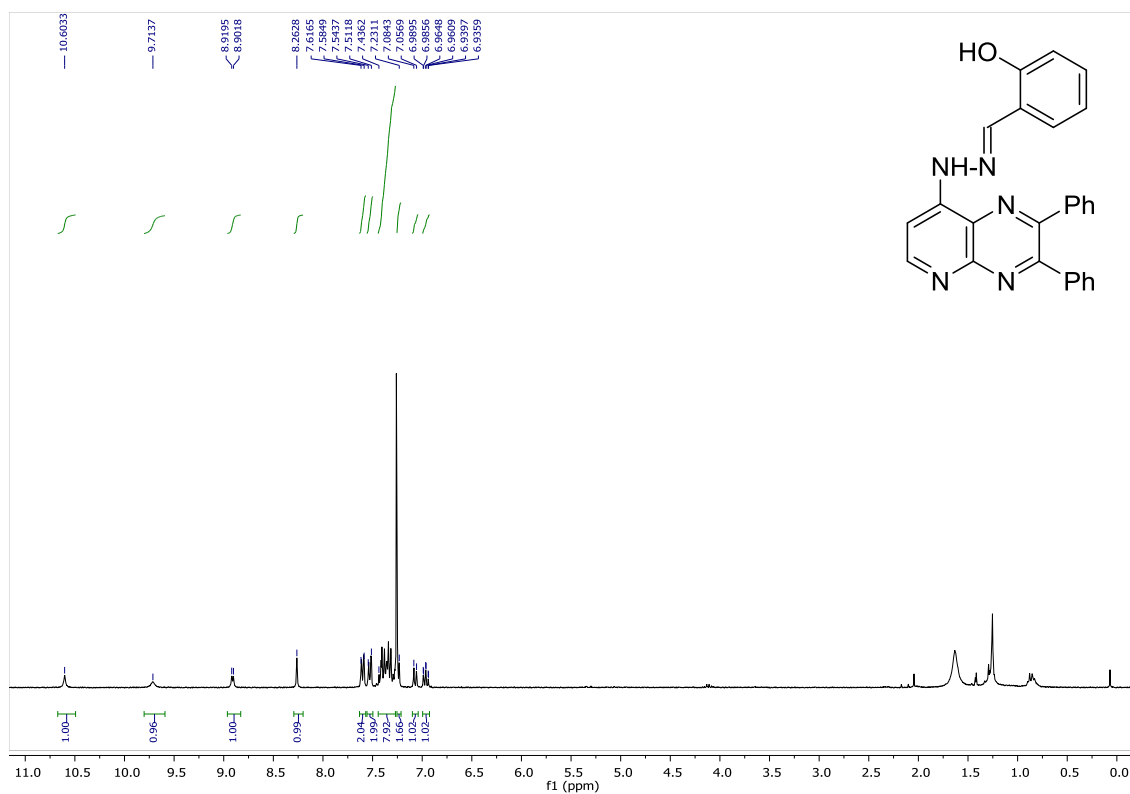


^{13}C NMR (75 MHz, CDCl_3)



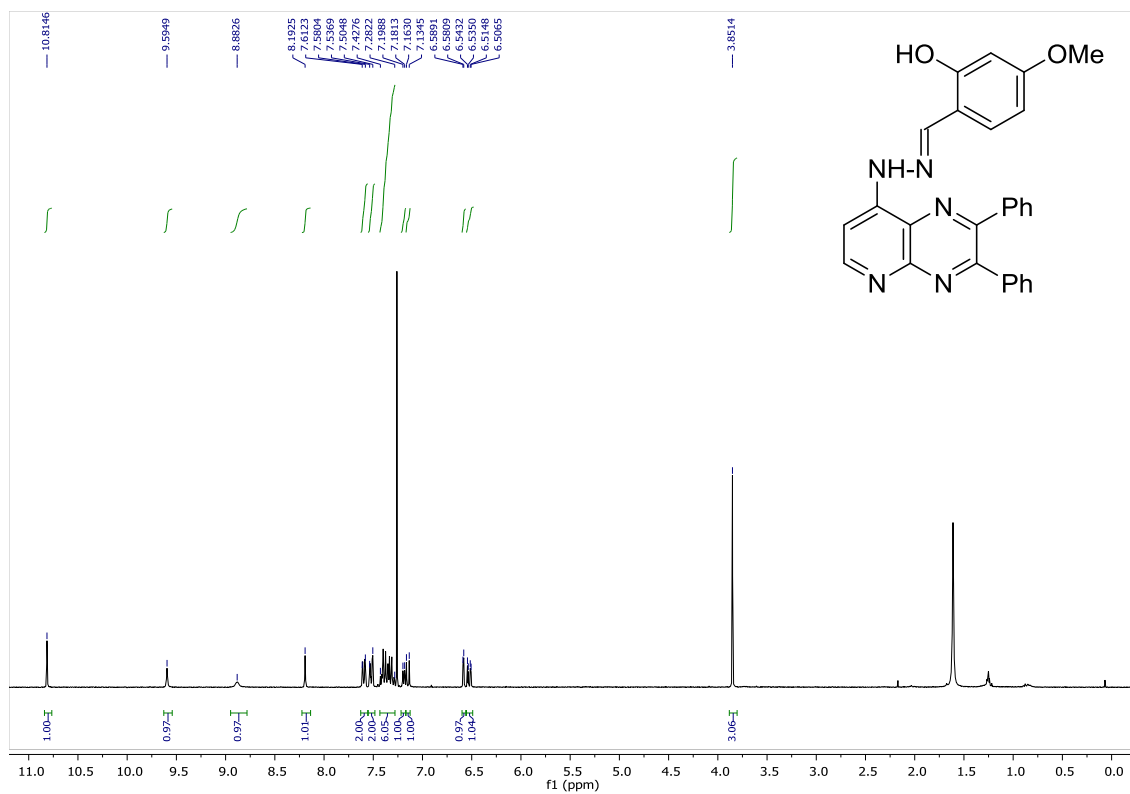
Compound 2r

^1H NMR (300 MHz, CDCl_3)



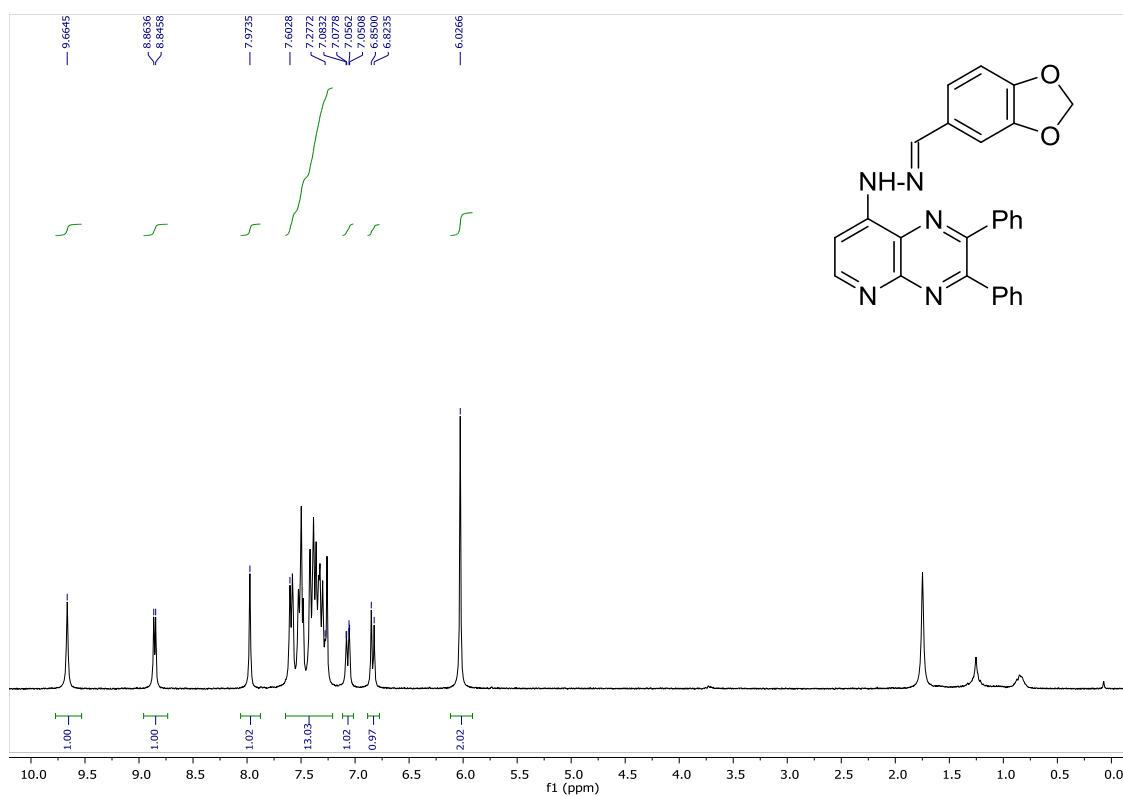
Compound 2t

^1H NMR (300 MHz, CDCl_3)

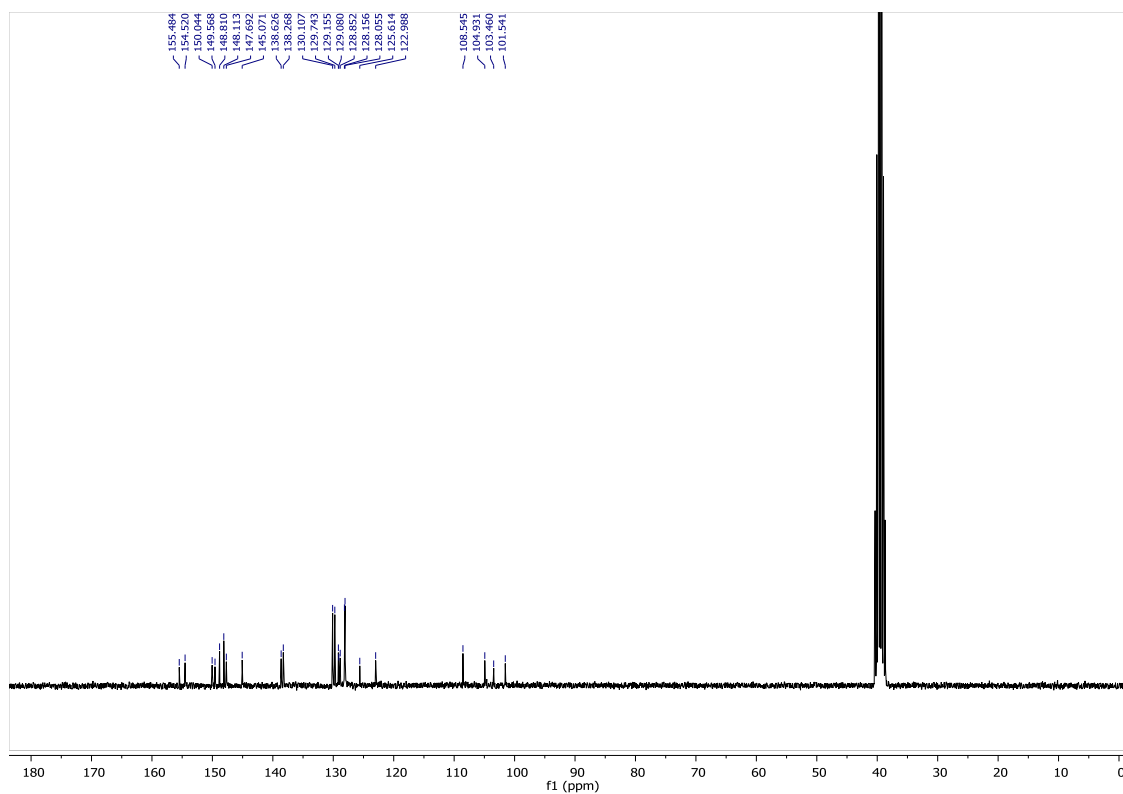


Compound 2s

^1H NMR (300 MHz, CDCl_3)

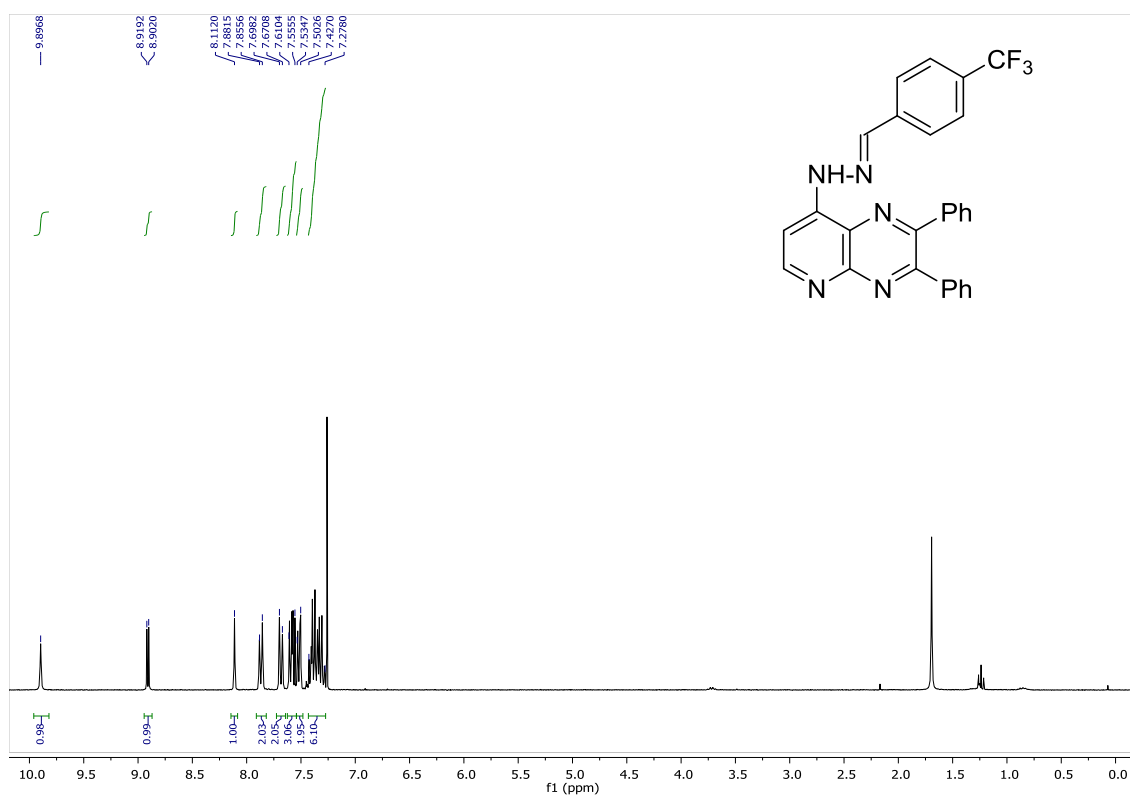


^{13}C NMR (75 MHz, $(\text{CD}_3)_2\text{SO}$)

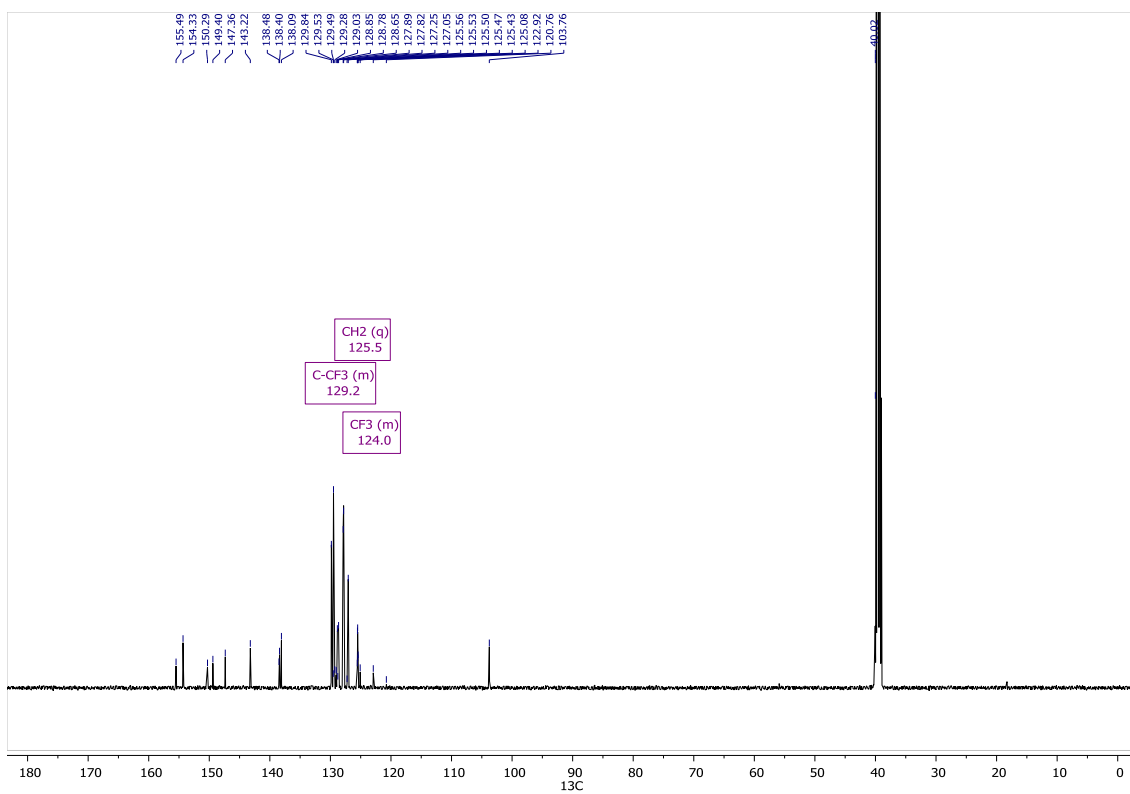


Compound 2u

^1H NMR (300 MHz, CDCl_3)

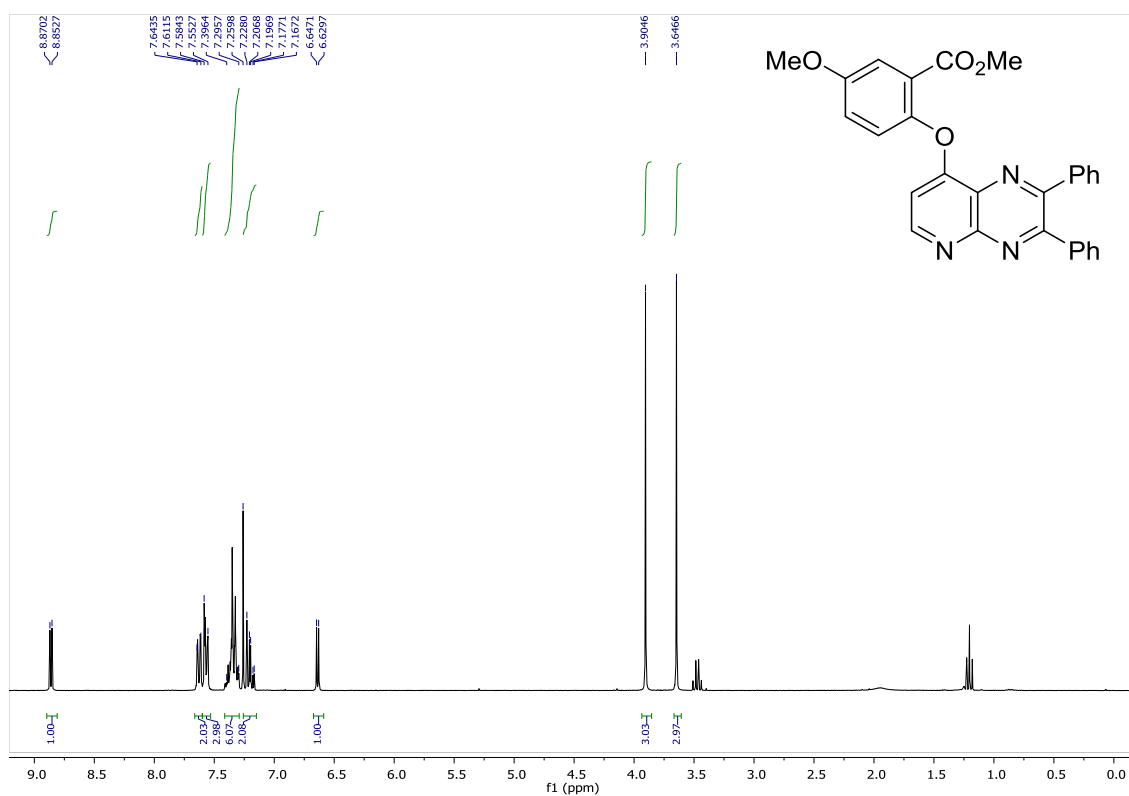


^{13}C NMR (126 MHz, $(\text{CD}_3)_2\text{SO}$, 333 K)

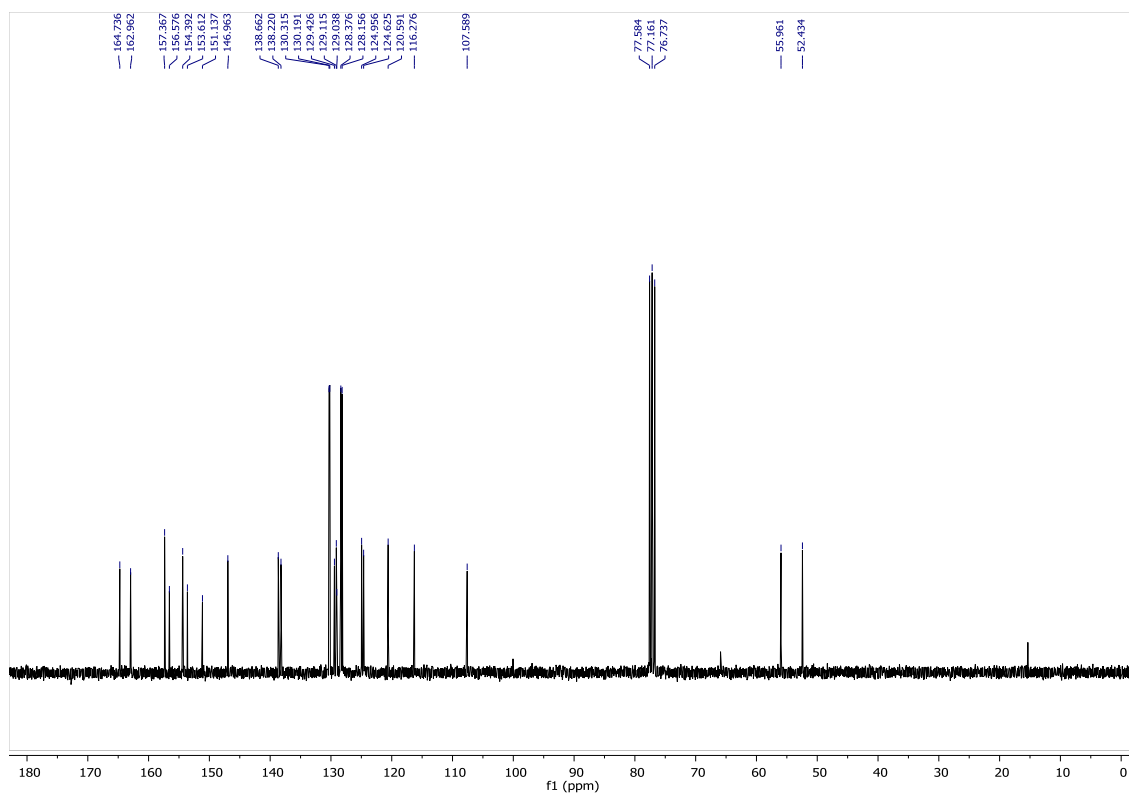


Compound 2v

^1H NMR (300 MHz, CDCl_3)



^{13}C NMR (75 MHz, CDCl_3)



Inhibitory activities of synthesized compounds against a short panel of disease-related protein kinases

Table S1. The table displays the remaining kinase activities detected after treatment with 10 μ M of the tested compounds. The values obtained after treatment with 1 μ M are given in brackets. Results are expressed in % of maximal activity, i.e. measured in the absence of inhibitor but with an equivalent dose of DMSO (solvent of the tested compounds). ATP concentration used in the kinase assays was 10 μ mol/L (values are means, n=2). Kinases are from human origin unless specified:

Mm, Mus musculus; Rn, Rattus norvegicus; Ssc, Sus scrofa domestica.

Compound	CDK2/Cyclin A	CDK5/p25	CDK9/Cyclin T	PIM1	<i>Mm</i> CLK1	<i>Rn</i> DYRK1A	DYRK1A	<i>Ssc</i> CSK3 α/β	GSK3 β	<i>Ssc</i> CK1 δ/ϵ	CK1 ϵ	Haspin
1c	99 (99)	- ¹	84 (97)	94 (100)	113 (108)	138 (146)	- ¹	110 (100)	- ¹	100 (114)	- ¹	108 (104)
1d	103 (95)	- ¹	116 (109)	103 (90)	115 (107)	86 (95)	- ¹	108 (91)	- ¹	112 (113)	- ¹	90 (102)
1e	100 (107)	- ¹	127 (93)	83 (94)	47 (108)	128 (119)	- ¹	114 (94)	- ¹	132 (107)	- ¹	116 (99)
1g	89 (103)	- ¹	83 (93)	93 (96)	118 (107)	139 (99)	- ¹	105 (97)	- ¹	125 (116)	- ¹	101 (97)
2d	109 (111)	- ¹	102 (102)	83 (99)	113 (109)	129 (114)	- ¹	147 (111)	- ¹	131 (101)	- ¹	110 (102)
2e	58 (92)	- ¹	98 (94)	90 (92)	130 (108)	181 (118)	- ¹	105 (116)	- ¹	86 (107)	- ¹	111 (114)
2f	107 (105)	- ¹	113 (106)	101 (90)	130 (107)	178 (128)	- ¹	122 (104)	- ¹	108 (108)	- ¹	130 (106)
2g	108 (101)	93 (101)	93 (69)	88 (108)	90 (99)	180 (125)	88 (101)	113 (94)	62 (95)	104 (106)	86 (88)	89 (107)
2i	- ¹	97 (81)	97 (56)	96 (67)	101 (114)	- ¹	64 (86)	101 (98)	- ¹	- ¹	- ¹	94 (96)
2j	- ¹	77 (99)	55 (74)	109 (105)	107 (107)	- ¹	83 (106)	106 (97)	- ¹	93 (91)	- ¹	59 (105)
2k	- ¹	93 (100)	72 (83)	51 (88)	92 (112)	- ¹	95 (83)	97 (100)	- ¹	- ¹	- ¹	100 (95)
2l	- ¹	79 (96)	66 (87)	50 (106)	72 (112)	- ¹	78 (95)	100 (110)	- ¹	- ¹	- ¹	73 (63)
2m	- ¹	101 (98)	59 (83)	77 (96)	86 (104)	- ¹	87 (90)	94 (101)	- ¹	86 (111)	- ¹	79 (83)
2n	- ¹	118 (100)	84 (69)	100 (107)	95 (97)	- ¹	74 (56)	101 (99)	- ¹	65 (78)	- ¹	82 (82)
2o	- ¹	100 (101)	78 (75)	74 (85)	103 (115)	- ¹	86 (94)	96 (109)	- ¹	69 (102)	- ¹	104 (106)
2p	- ¹	92 (114)	74 (76)	99 (108)	96 (102)	- ¹	59 (86)	103 (88)	- ¹	73 (57)	- ¹	101 (101)
2q	- ¹	110 (101)	71 (69)	81 (84)	98 (99)	- ¹	82 (80)	101 (104)	- ¹	80 (85)	- ¹	105 (95)
2r	- ¹	110 (99)	93 (84)	105 (90)	109 (113)	- ¹	114 (100)	108 (107)	- ¹	105 (117)	- ¹	120 (133)
2s	- ¹	99 (109)	85 (80)	102 (94)	95 (104)	- ¹	80 (89)	103 (105)	- ¹	91 (76)	- ¹	114 (81)
2t	- ¹	95 (107)	83 (92)	76 (113)	111 (112)	- ¹	98 (85)	109 (109)	- ¹	110 (89)	- ¹	109 (138)
2u	- ¹	103 (119)	80 (82)	110 (87)	98 (104)	- ¹	91 (84)	98 (103)	- ¹	77 (70)	- ¹	91 (87)
2v	- ¹	119 (113)	72 (72)	60 (78)	98 (107)	- ¹	85 (97)	103 (111)	- ¹	79 (72)	- ¹	118 (126)
3h	- ¹	103 (103)	77 (89)	106 (99)	92 (106)	- ¹	99 (102)	- ¹	60 (91)	- ¹	92 (99)	100 (110)

¹ Not performed.