Supporting Information

Acid-catalyzed 1,3-dipolar cycloaddition of 2*H*-azirines with nitrones: an unexpected access to 1,2,4,5-tetrasubstituted imidazoles

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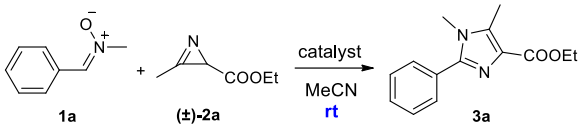
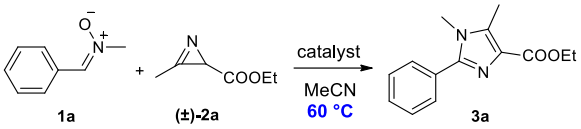
1. Optimization of the reaction conditions: HPLC yields and conversions in (3), 8 and 24 h

Table S1. Catalyst screening at rt and 60 °C[a]





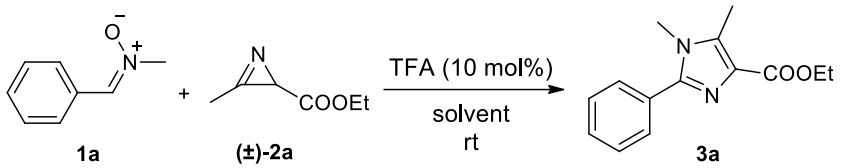
Entry	Catalyst	t (h)	Conv. (%) 1a	Conv. (%) 2a	Yield (%)[b]
1	–	8	0	0	0
2		24	1	2	0
3	HCOOH	8	18	24	10
4		24	45	62	36
5	AcOH	8	0	0	0
6		24	0	0	0
7	TFA	8	74	98	59
8		24	77	100	62
9	$MeSO_3H$	8	58	86	50
10		24	59	100	52
11	PTSA×H_2O	8	60	100	56
12		24	63	100	57
13	$HClO_4$ (70%)	8	63	100	56
14		24	63	100	56
15	H_2SO_4	8	53	60	36
16		24	67	78	49
17	$NaHSO_4$	8	18	20	14
18		24	35	38	28
19	$B(OH)_3$	8	0	0	0
20		24	50	77	35
21	PTA[†]	8	66	100	52
22		24	68	100	54
23	BINOL-phosphoric acid[††]	8	48	70	41
24		24	58	87	52
25	Silica gel[d,e]	8	5	6	1
26		24	18	40	16
27	Amberlyst 15[d]	8	77	52	0
28		24	82	83	1
29	Montmorillonite K10[d]	8	20	38	9
30		24	46	82	22
31	$ZnCl_2$	8	14	100	7
32		24	26	100	8
33	$Zn(OAc)_2$	8	22	100	6
34		24	28	100	7
35	ZnF_2	8	0	0	0
36		24	0	0	0
37	$InCl_3$	8	15	100	11
38		24	18	100	12
39	$In(OAc)_3$	8	0	0	0
40		24	4	11	2
41	$In(OTf)_3$	8	46	100	37
42		24	48	100	39

Entry	Catalyst	t (h)	Conv. (%) 1a	Conv. (%) 2a	Yield (%)[c]
63	–	8	2	4	0
64		24	5	7	0
65	HCOOH	8	67	100	42
66		24	68	100	42
67	AcOH	8	9	28	4
68		24	44	87	17
69	TFA	8	62	97	50
70		24	64	100	50
71	$MeSO_3H$	8	54	96	40
72		24	58	100	42
73	PTSA×H_2O	8	53	100	43
74		24	54	100	44
75	$HClO_4$ (70%)	8	58	98	49
76		24	59	100	48
77	H_2SO_4	8	72	100	42
78		24	74	100	41
79	$NaHSO_4$	8	48	61	23
80		24	61	82	30
81	$B(OH)_3$	8	53	97	38
82		24	54	100	39
83	PTA	8	70	98	47
84		24	72	100	49
85	BINOL-phosphoric acid	8	52	100	42
86		24	52	100	43
87	Silica gel[d,e]	8	51	76	34
88		24	65	100	41
89	Amberlyst 15[d]	8	91	86	1
90		24	94	100	1
91	Montmorillonite K10[d]	8	59	98	21
92		24	64	100	22
93	$ZnCl_2$	8	30	100	21
94		24	33	100	22
95	$Zn(OAc)_2$	8	27	100	10
96		24	29	100	9
97	ZnF_2	8	2	31	1
98		24	46	100	22
99	$InCl_3$	8	28	100	20
100		24	41	100	21
101	$In(OAc)_3$	8	26	100	19
102		24	28	100	20
103	$In(OTf)_3$	8	49	100	33
104		24	51	100	35

43	$FeCl_2 \times 4H_2O$	8	28	75	3		105	$FeCl_2 \times 4H_2O$	8	87	100	30
44		24	48	100	4		106		24	93	100	31
45	$FeCl_3 \times 6H_2O$	8	39	81	6		107	$FeCl_3 \times 6H_2O$	8	87	100	21
46		24	59	100	7		108		24	100	100	20
47	CuCl	8	50	70	2		109	CuCl	8	42	99	12
48		24	65	100	2		110		24	60	100	13
49	$CuCl_2$	8	56	100	3		111	$CuCl_2$	8	42	100	16
50		24	82	100	3		112		24	66	100	16
51	$Cu(OAc)_2$	8	14	49	0		113	$Cu(OAc)_2$	8	23	100	2
52		24	42	100	2		114		24	39	100	2
53	$Cu(OTf)_2$	8	40	100	11		115	$Cu(OTf)_2$	8	45	100	24
54		24	54	100	12		116		24	59	100	23
55	$Mg(OTf)_2$	8	58	100	52		117	$Mg(OTf)_2$	8	35	100	34
56		24	63	100	56		118		24	39	100	37
57	$Yb(OTf)_3$	8	58	100	56		119	$Yb(OTf)_3$	8	54	100	39
58		24	60	100	57		120		24	55	100	39
59	$Sc(OTf)_3$	8	61	94	53		121	$Sc(OTf)_3$	8	60	100	41
60		24	65	100	56		122		24	61	100	42
61	$Dy(OTf)_3$	8	63	94	57		123	$Dy(OTf)_3$	8	53	97	36
62		24	66	100	59		124		24	51	100	39

[a]Reaction conditions: nitrone **1a** (0.10 mmol), 2*H*-azirine **(±)-2a** (0.10 mmol), anhydrous MeCN (0.3 mL), catalyst (10 mol%). [b]Room temperature. Yields were determined by HPLC-MS analysis. [c]60 °C. Yields were determined by HPLC-MS analysis. [d]10 w/v % was applied. [e]60 Å, 70–230 mesh. [†]Phosphotungstic acid. [††]1,1′-Binaphthyl-2,2′-diyl hydrogen phosphate.

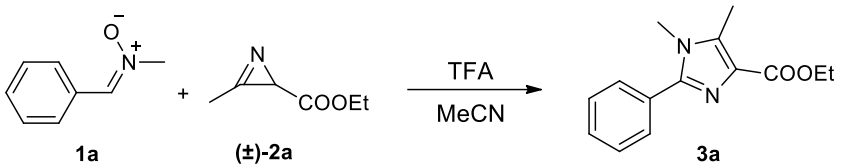
Table S2. Solvent screening[a]



Entry	Solvent	t (h)	Conv. (%) 1a	Conv. (%) 2a	Yield (%)[b]
1	MeOH	3	32	53	20
2		8	47	81	34
3		24	55	89	39
4	EtOH	3	29	44	21
5		8	47	71	37
6		24	57	88	46
7	IPA	3	14	26	10
8		8	31	54	23
9		24	54	87	33
10	TFE[c]	3	7	18	2
11		8	9	25	5
12		24	23	50	14
13	HFIP[c]	3	4	15	1
14		8	5	16	1
15		24	9	20	3
16	$CHCl_3$	3	25	40	18
17		8	47	69	27
18		24	56	93	39
19	CH_2Cl_2	3	38	60	46
20		8	58	90	52
21		24	65	94	55
22	Toluene	3	42	70	35
23		8	54	100	41
24		24	56	100	42
25	THF	3	47	71	39
26		8	56	100	48
27		24	65	100	54
28	Dioxane	3	49	54	16
29		8	51	72	41
30		24	64	89	47
31	DMF	3	12	7	6
32		8	30	31	22
33		24	64	76	48
34	DMSO	3	2	3	1
35		8	7	10	3
36		24	24	33	13
37	MeCN	3	69	79	55
38		8	74	98	59
39		24	77	100	62

[a]Reaction conditions: nitrone **1a** (0.10 mmol), 2*H*-azirine **(±)-2a** (0.10 mmol), anhydrous solvent (0.3 mL), TFA (10 mol%). [b]Yields were determined by HPLC-MS analysis. [c]Non-dried.

Table S3. Optimization of the reaction conditions[a]



Entry	2a (equiv.)	Cat. load (mol%)	Temp.	t (h)	Conv. (%) 1a	Equiv. of 2a reacted	Yield (%)[b]
1				3	69	0.79	55
2	1.0	10	rt	8	74	0.98	59
3				24	77	1.0	62
4				3	71	0.95	57
5	1.25	10	rt	8	82	1.10	66
6				24	90	1.25	70
7				3	74	0.94	58
8	1.5	10	rt	8	85	1.11	68
9				24	96	1.24	74
10				3	78	0.98	59
11	2.0	10	rt	8	89	1.13	68
12				24	98	1.21	74
13				3	22	0.42	22
14	1.5	1	rt	8	30	0.53	29
15				24	51	0.82	43
16				3	50	0.64	41
17	1.5	2.5	rt	8	57	0.82	49
18				24	74	0.97	60
19				3	54	0.88	52
20	1.5	5	rt	8	66	0.99	64
21				24	84	1.18	73
22				3	78	0.90	59
23	1.5	15	rt	8	90	1.08	67
24				24	94	1.15	72
25				3	82	0.62	54
26	1.5	20	rt	8	90	0.97	63
27				24	100	1.16	68
28				3	75	0.71	26
29	1.5	40	rt	8	89	0.89	34
30				24	99	1.11	41
31				3	83	0.97	67
32	1.5	10	40 °C	6	93	1.14	73
33				12	99	1.20	76
34				2	90	0.98	66
35	1.5	5	60 °C	4	94	1.10	69
36				6	96	1.25	69
37				2	95	1.09	76
38	1.5	10	60 °C	4	97	1.13	77
39				6	99	1.15	78
40				2	97	1.13	58
41	1.5	10	80 °C	4	99	1.25	59
42				6	100	1.32	59

[a]Reaction conditions: nitrone **1a** (0.10 mmol), 2*H*-azirine **(±)-2a** (0.10–0.20 mmol), anhydrous MeCN (0.3 mL), TFA (10 mol%). [b]Yields were determined by HPLC-MS analysis.

2. ^{1}H and ^{13}C{^{1}H} NMR spectra of all compounds, ^{19}F NMR spectra of 3c, 3r, 4d and 5d, 2D NMR spectra of 3a

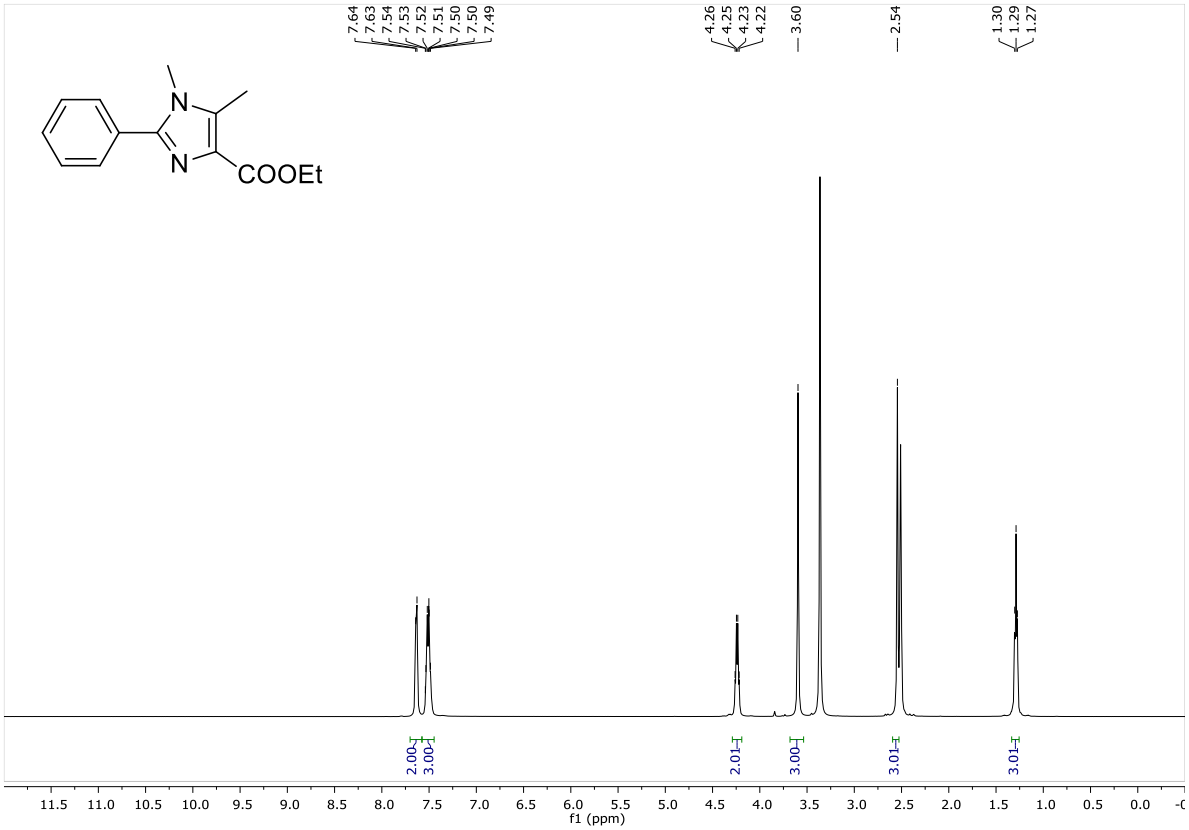


Figure S1. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of the compound **3a**

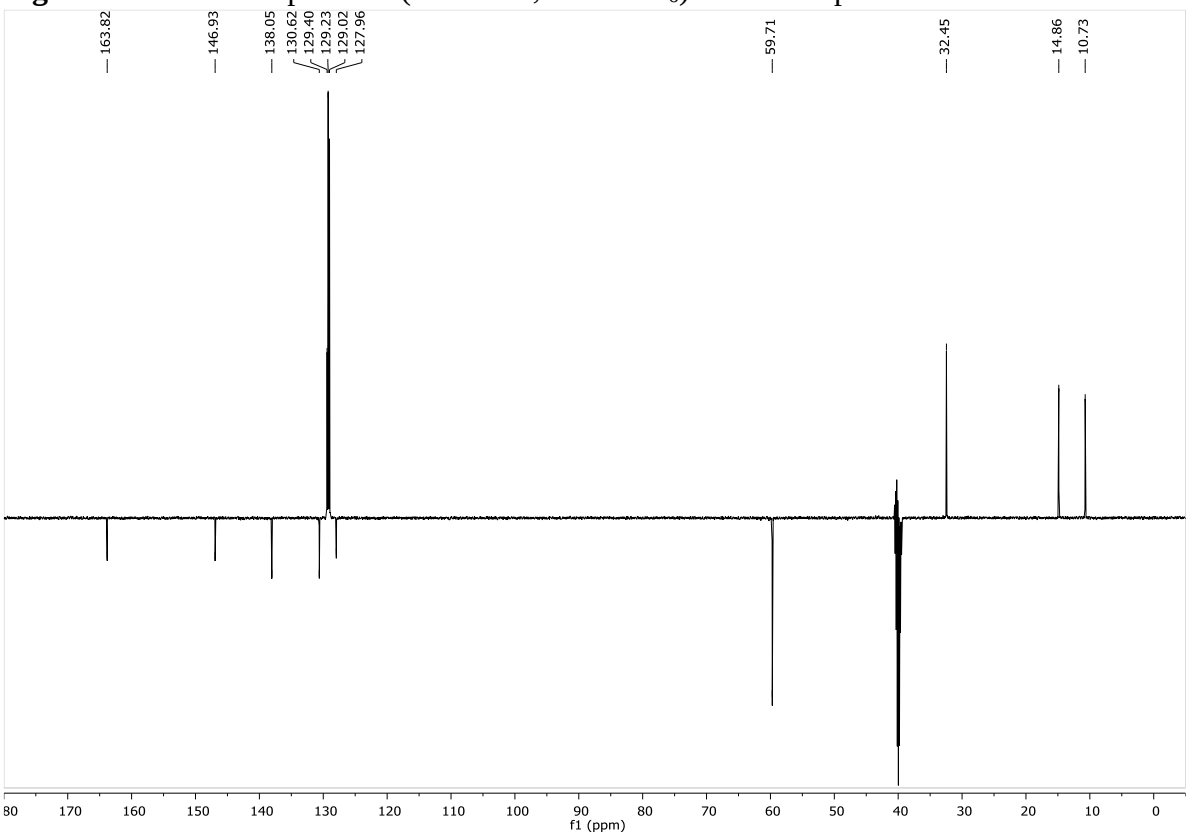


Figure S2. ^{13}C{^{1}H} NMR spectrum (126 MHz, DMSO-d_6) of the compound **3a**

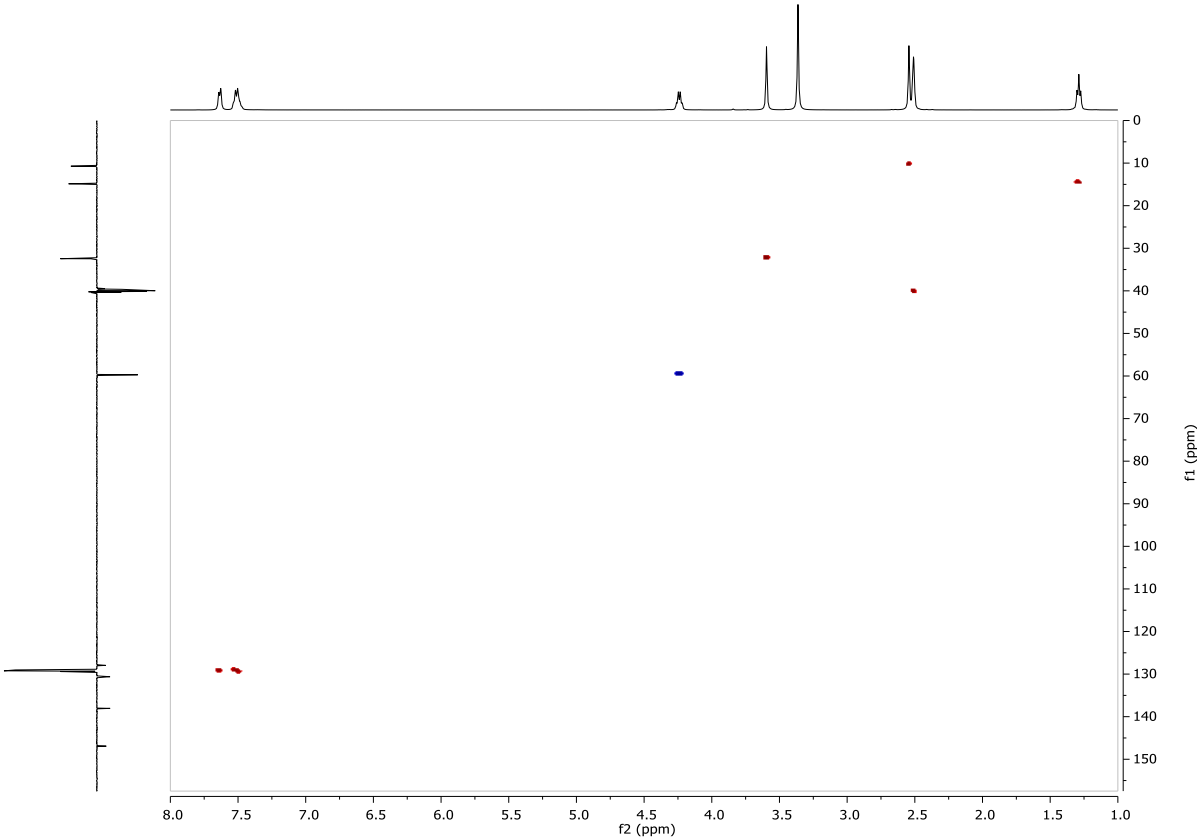


Figure S3. HSQC spectrum of the compound **3a** in DMSO-d_6

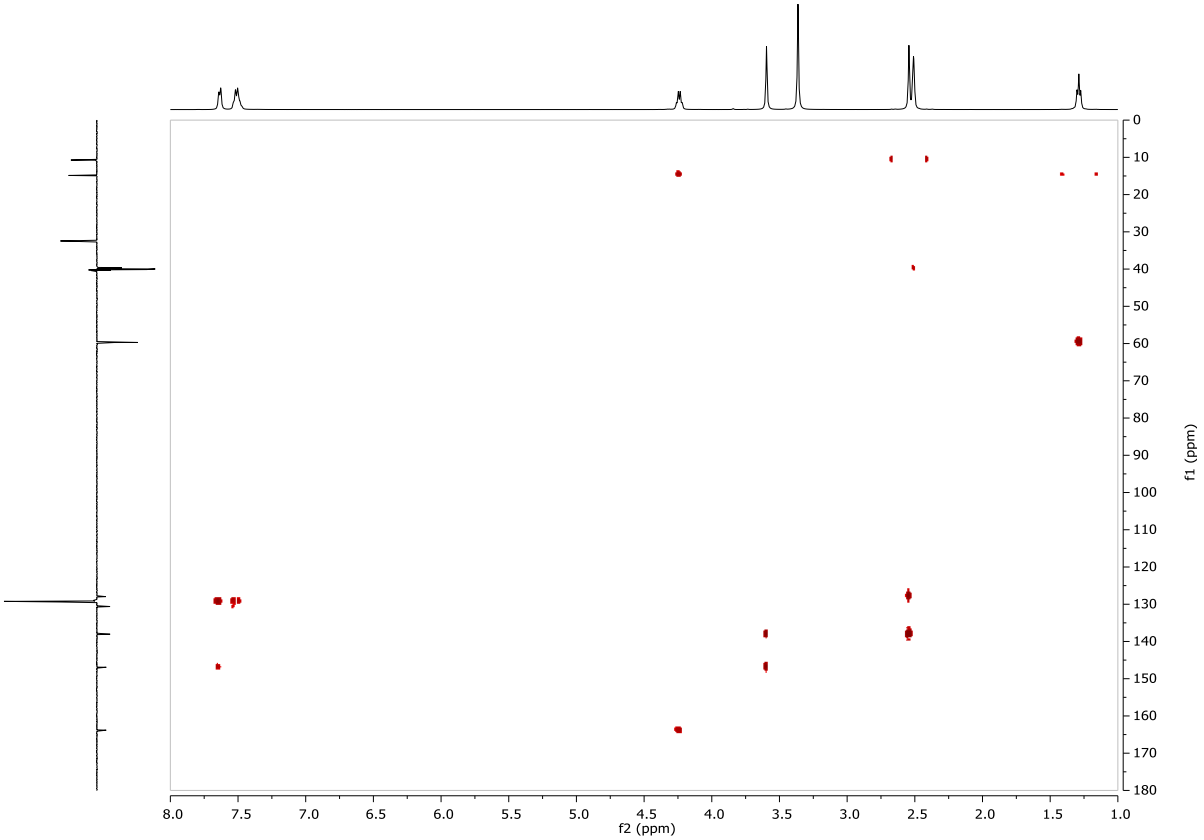


Figure S4. HMBC spectrum of the compound **3a** in DMSO-d_6

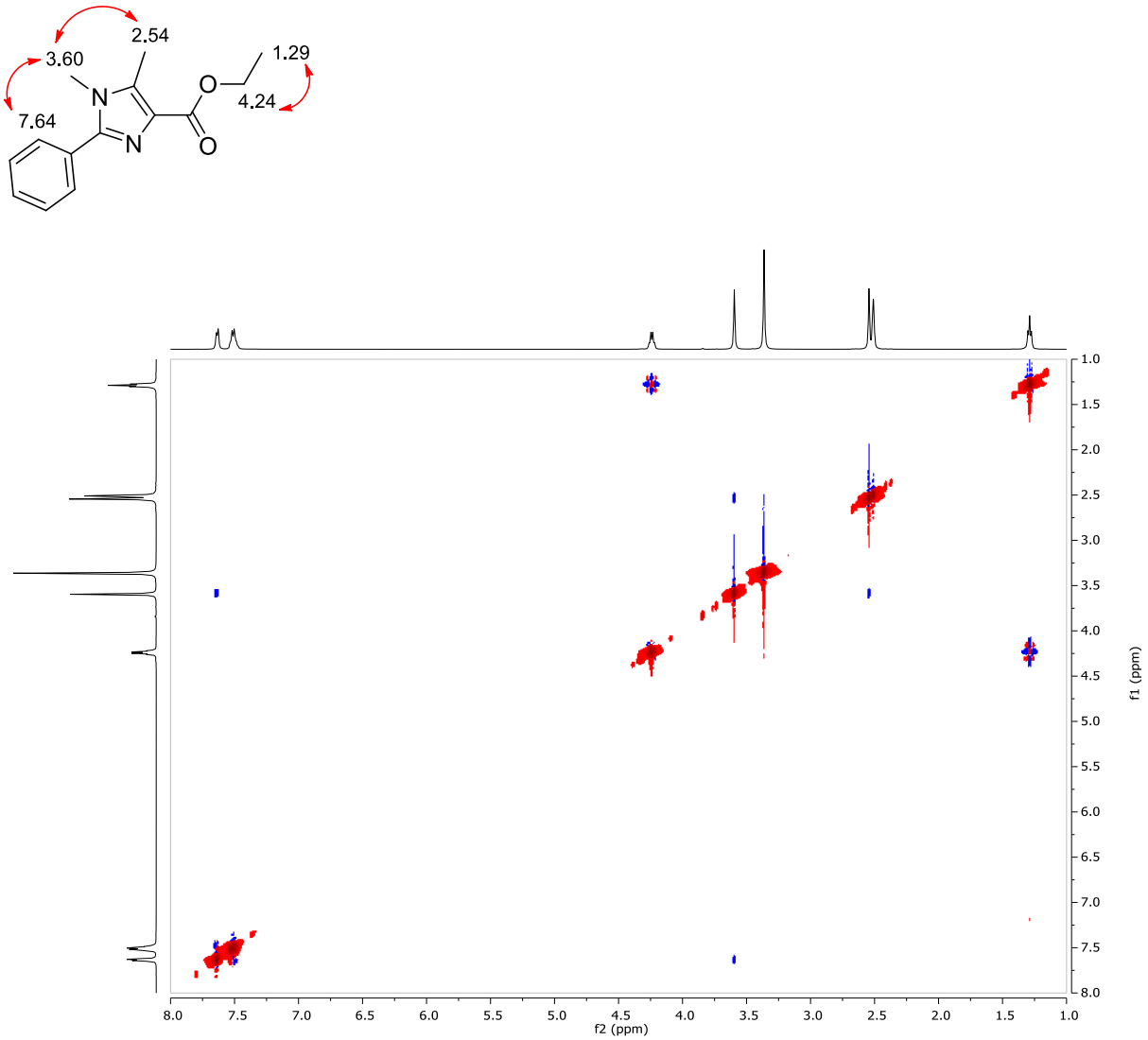


Figure S5. NOESY spectrum of the compound **3a** in DMSO-d_6

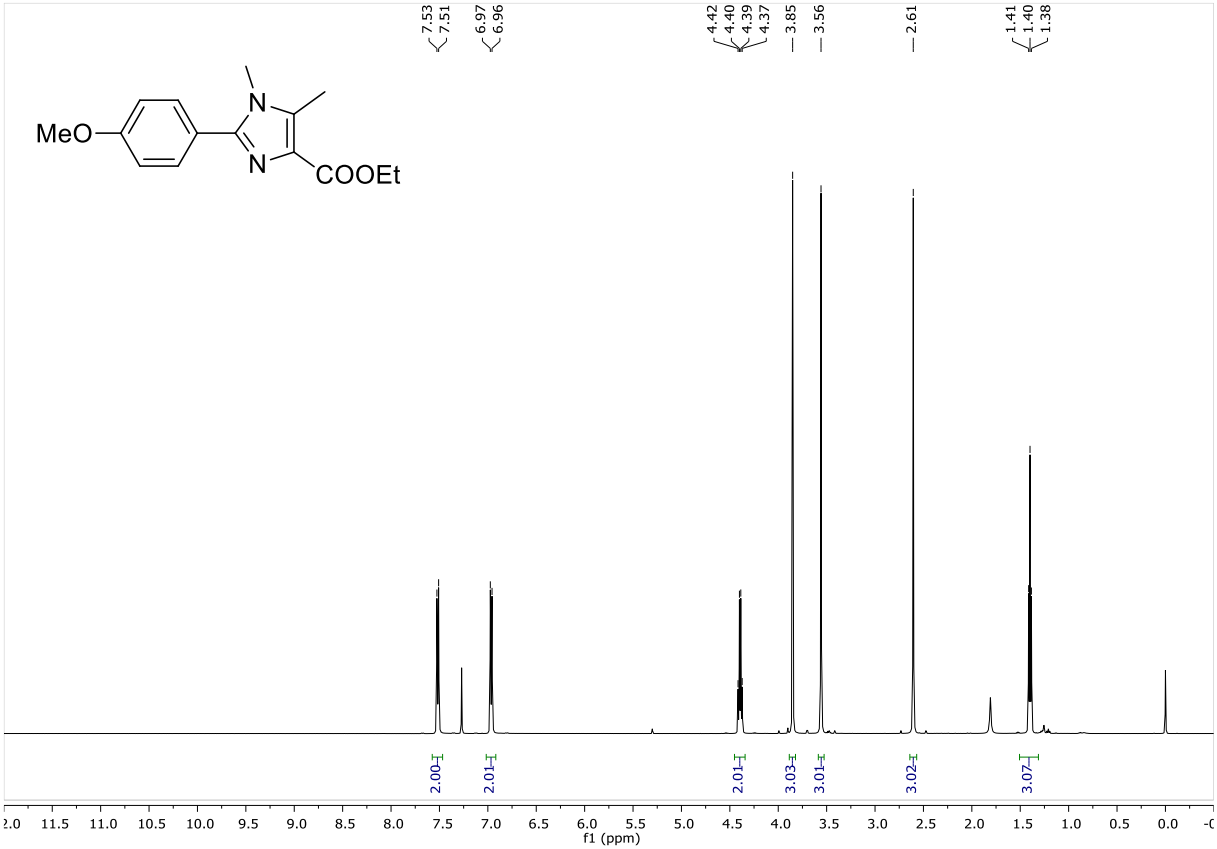


Figure S6. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3b**

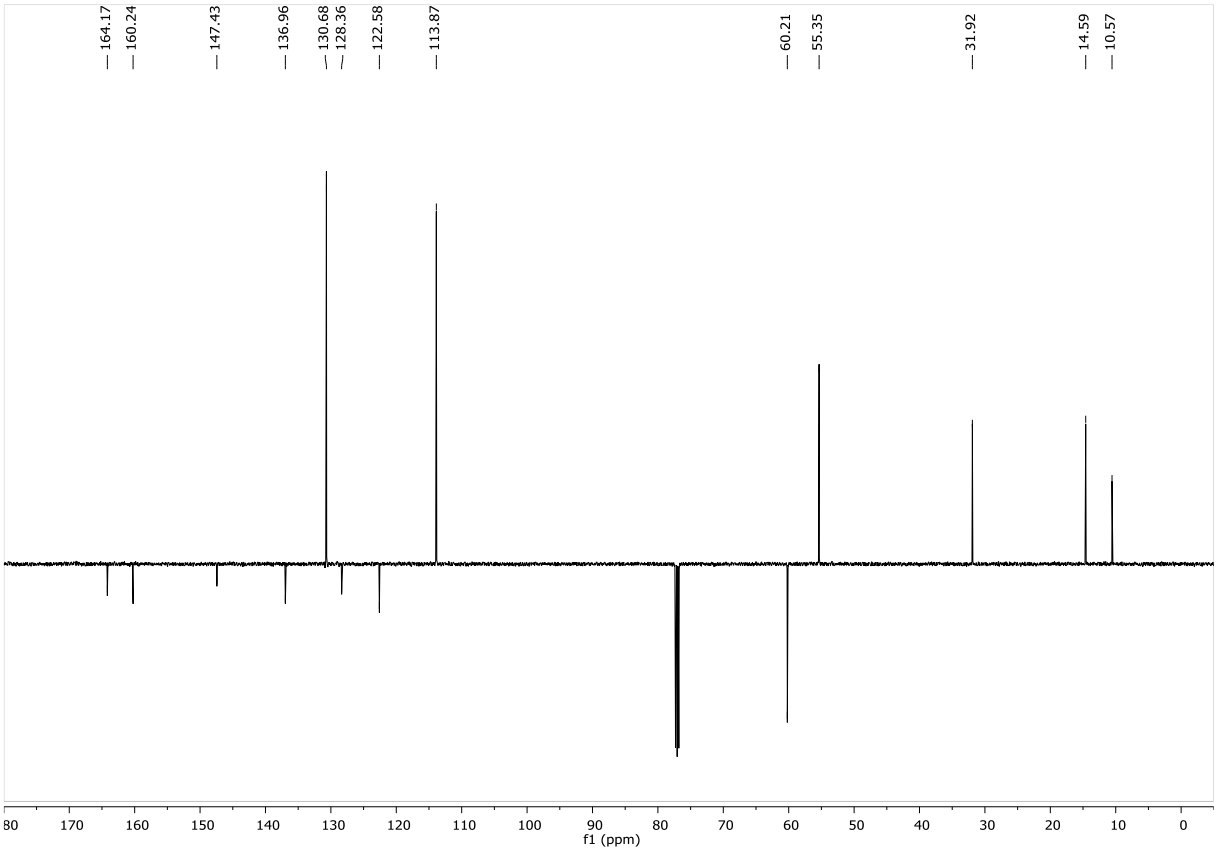


Figure S7. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3b**

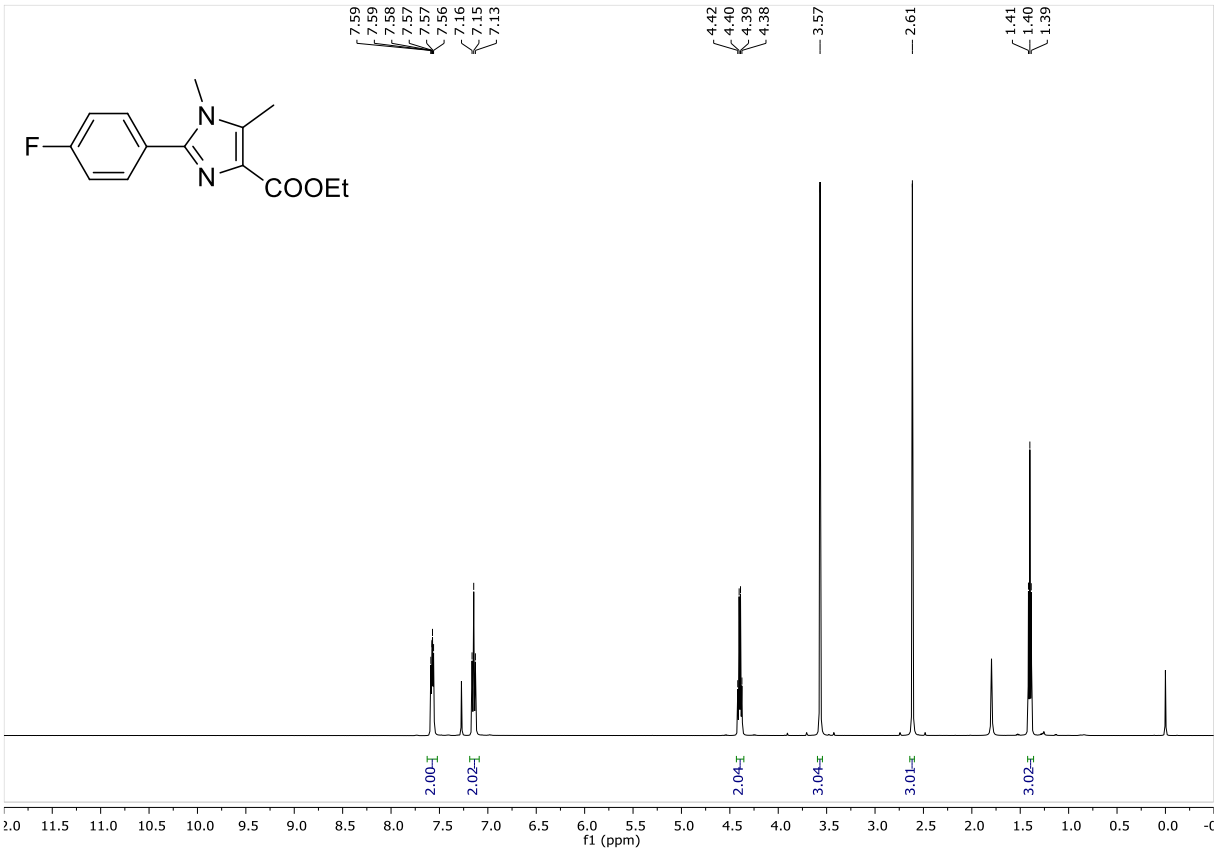


Figure S8. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3c**

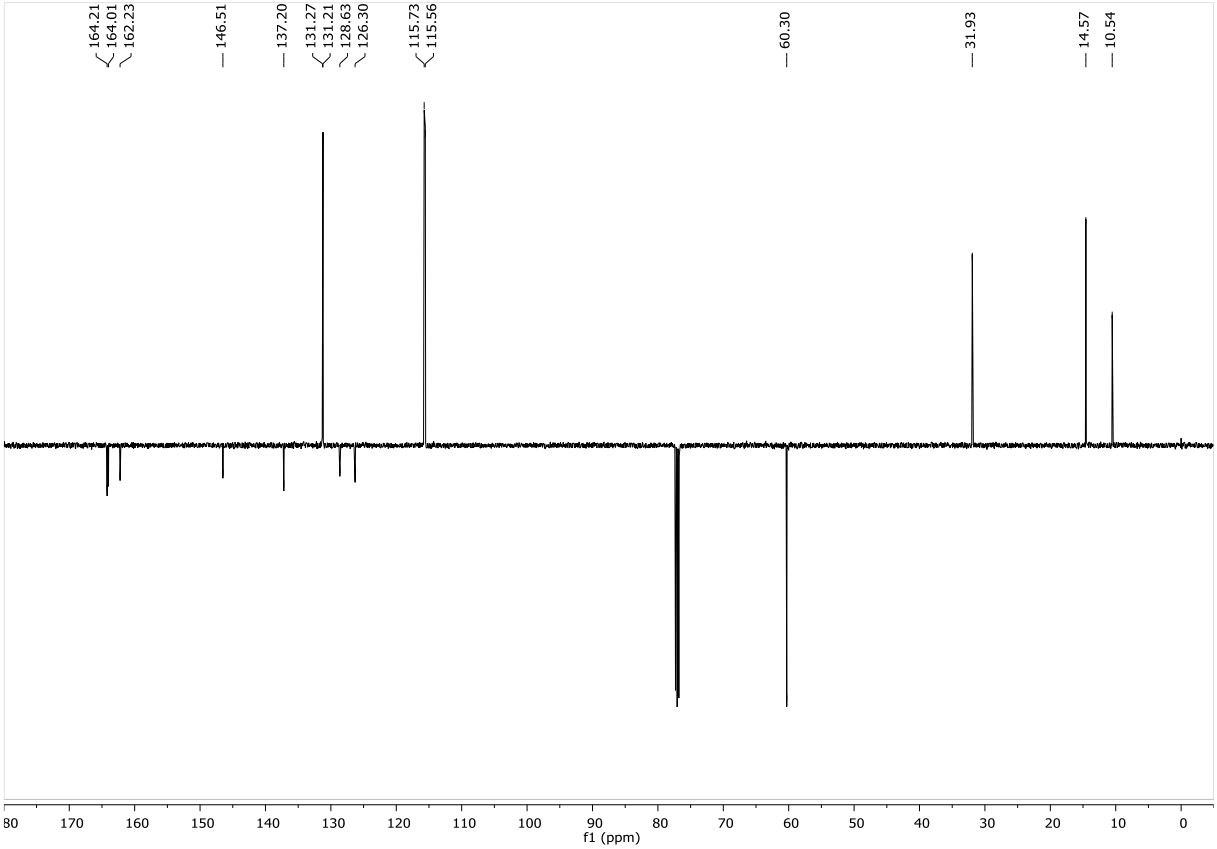


Figure S9. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3c**

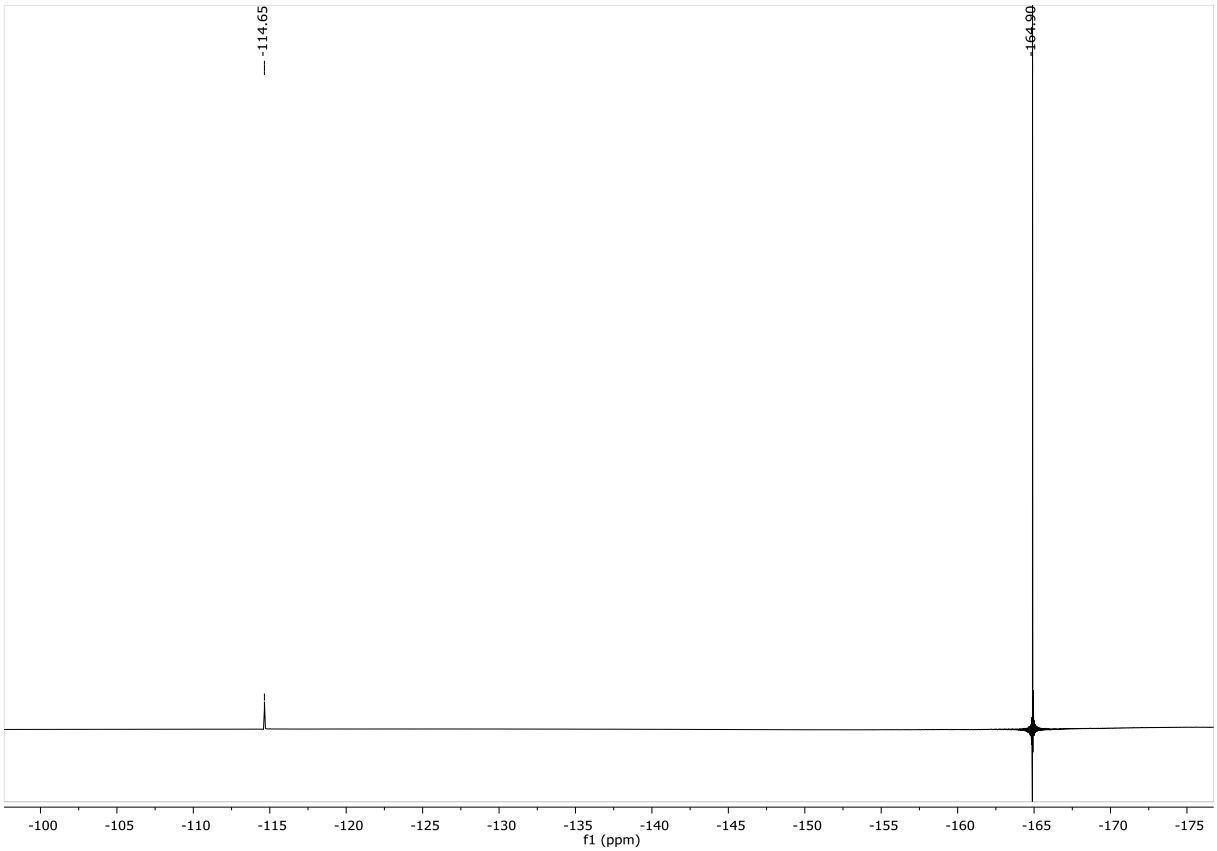


Figure S10. ^{19}F NMR spectrum (471 MHz, $CDCl_3$) of the compound **3c**

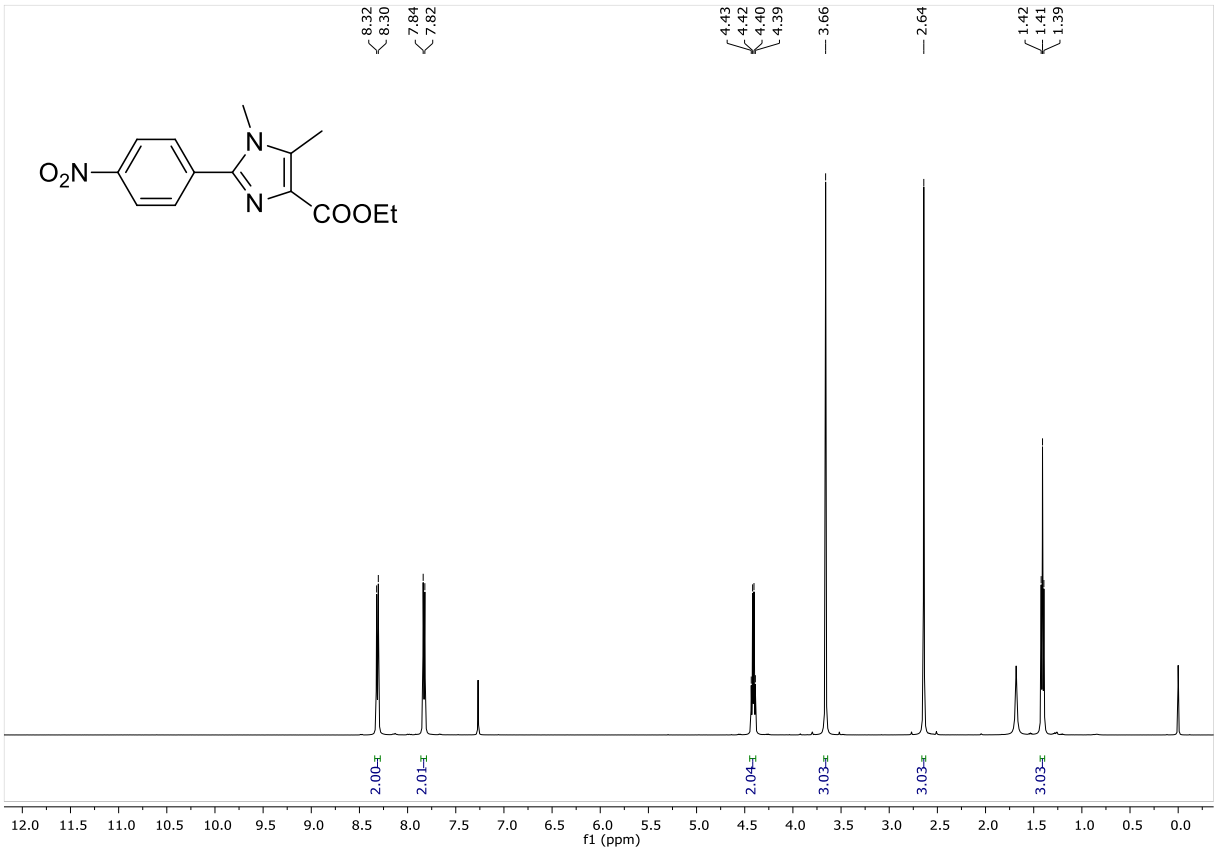


Figure S11. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3d**

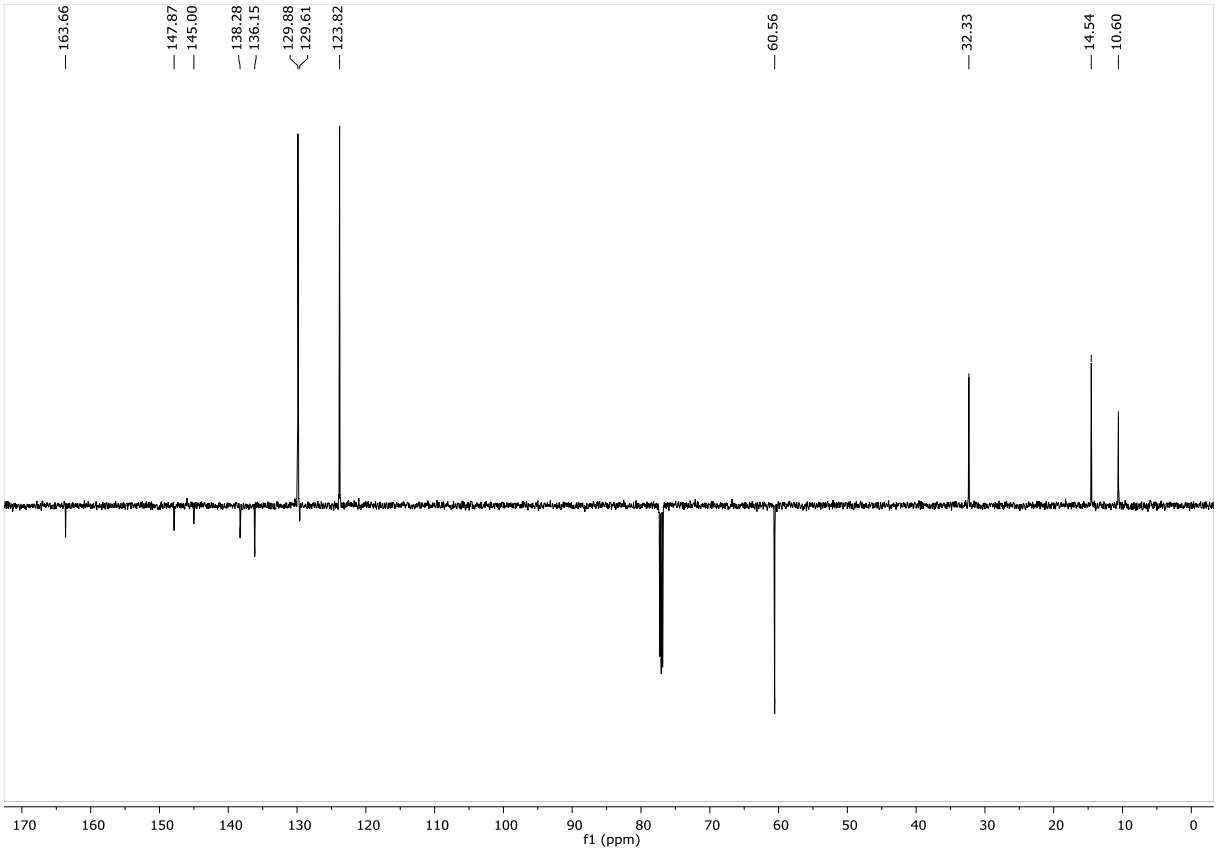


Figure S12. $^{13}C\{^{1}H\}$ NMR spectrum (126 MHz, $CDCl_3$) of the compound **3d**

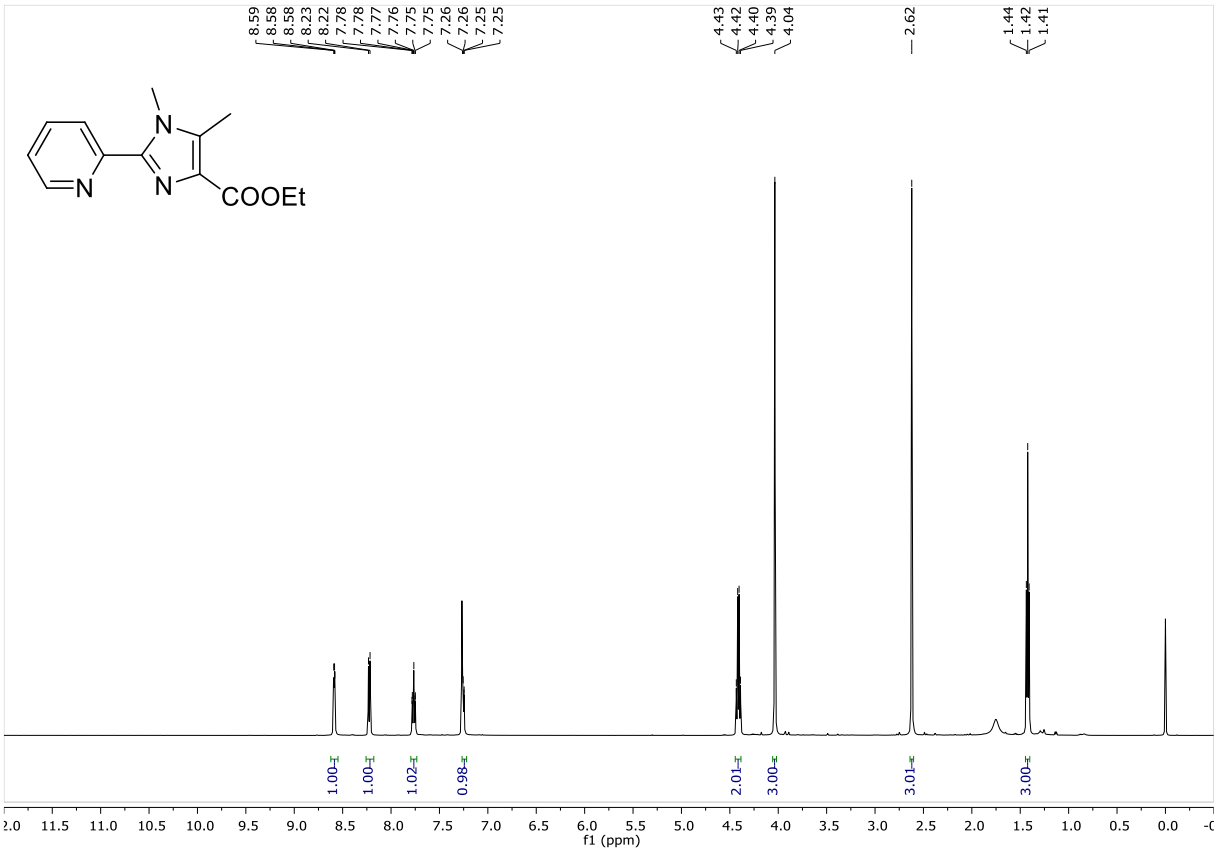


Figure S13. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3e**

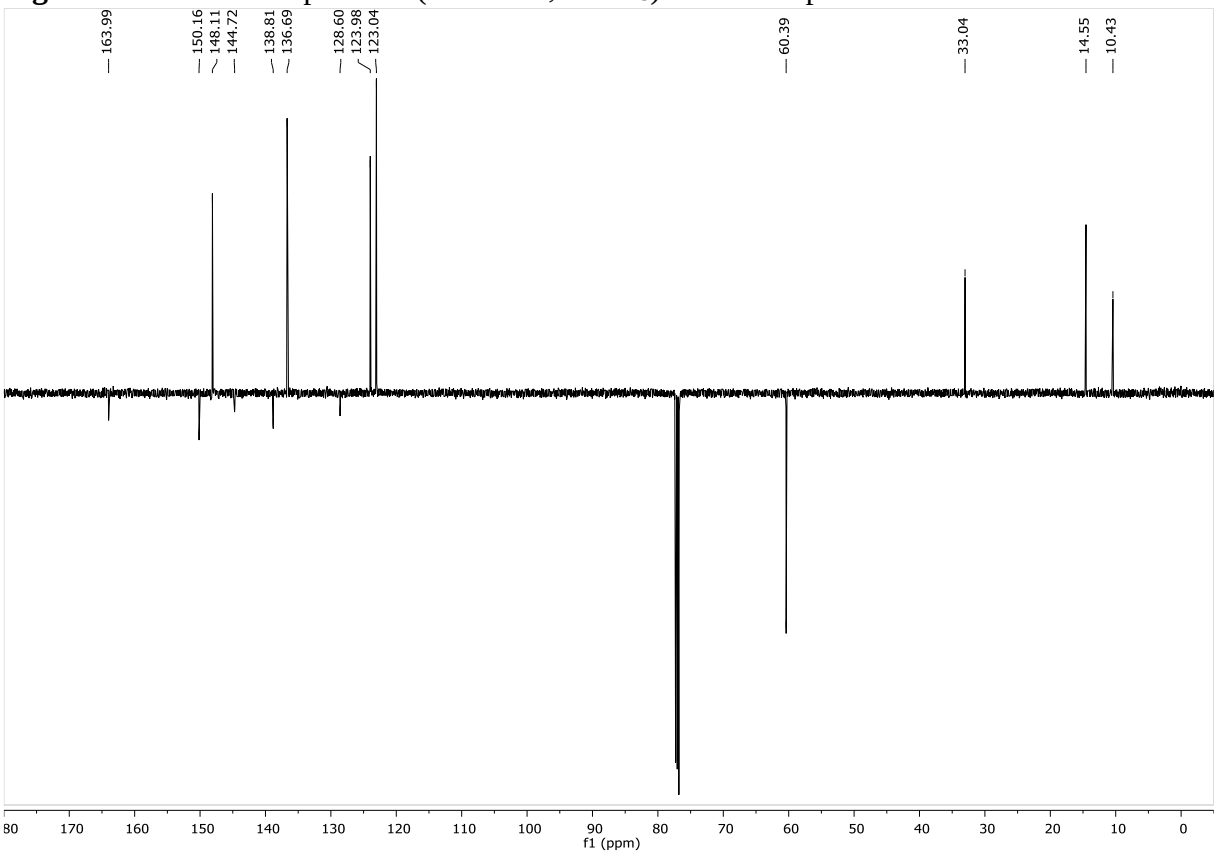


Figure S14. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3e**

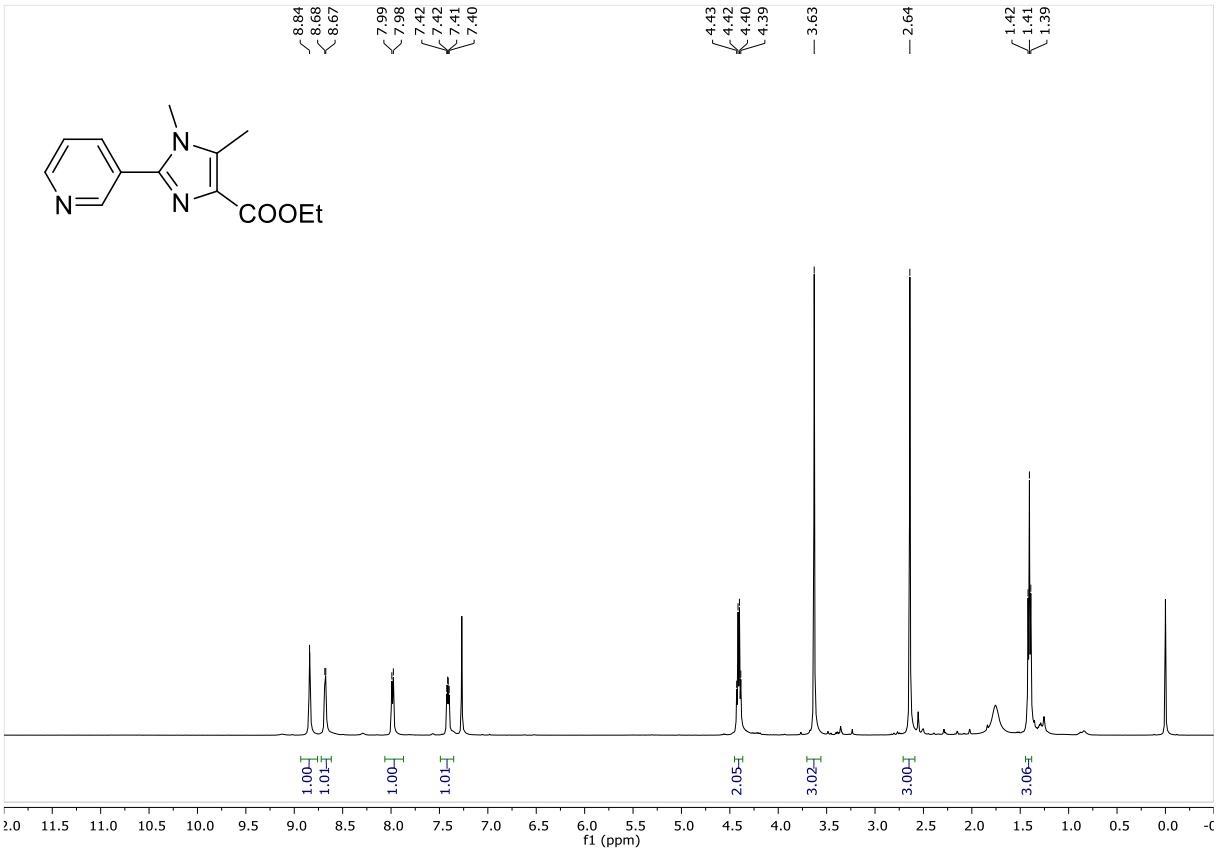


Figure S15. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3f**

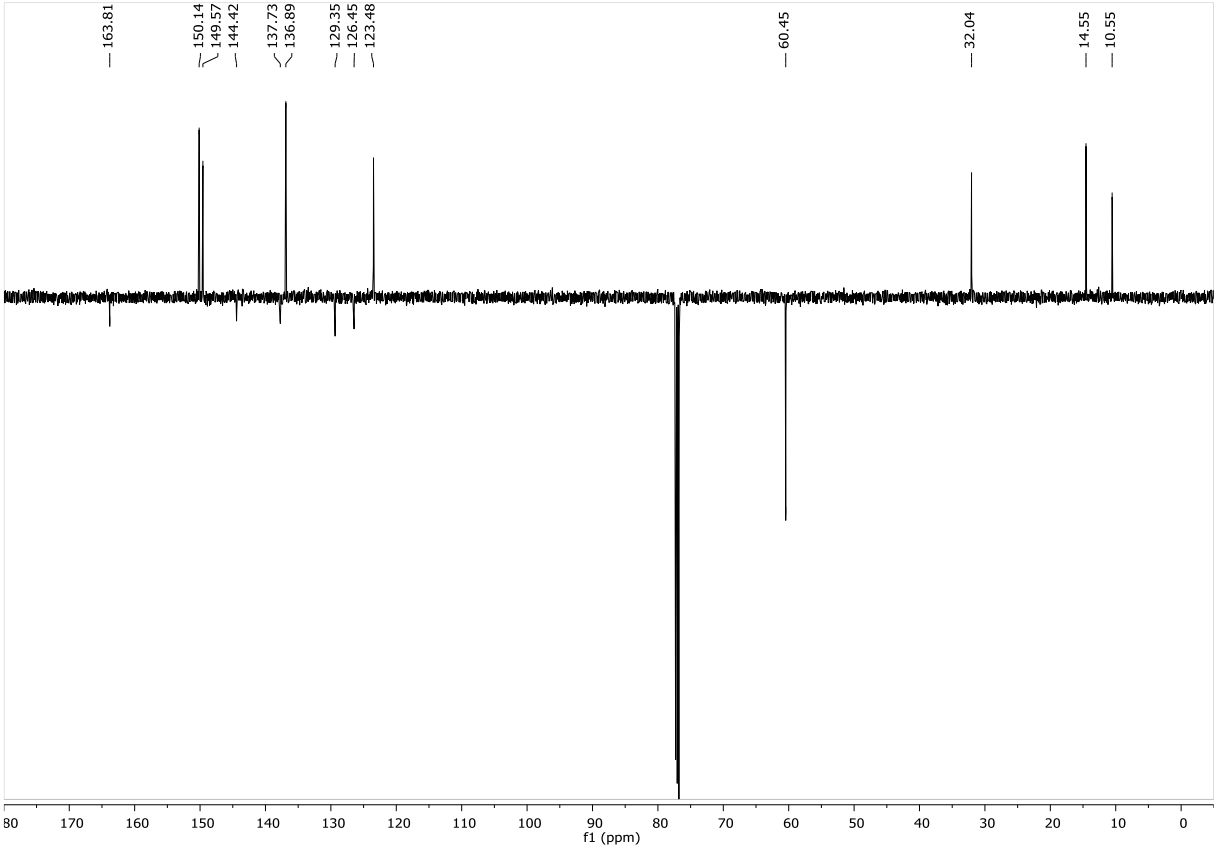


Figure S16. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3f**

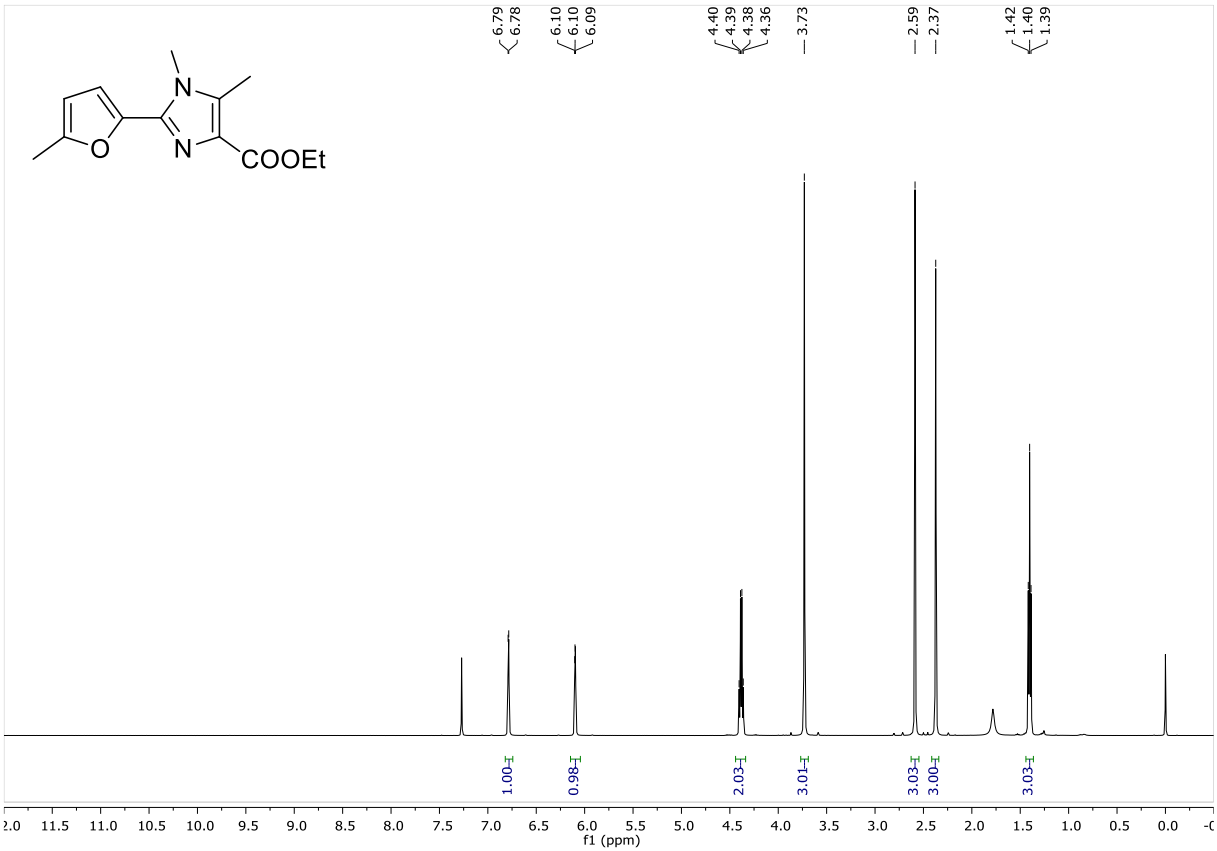


Figure S17. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3g**

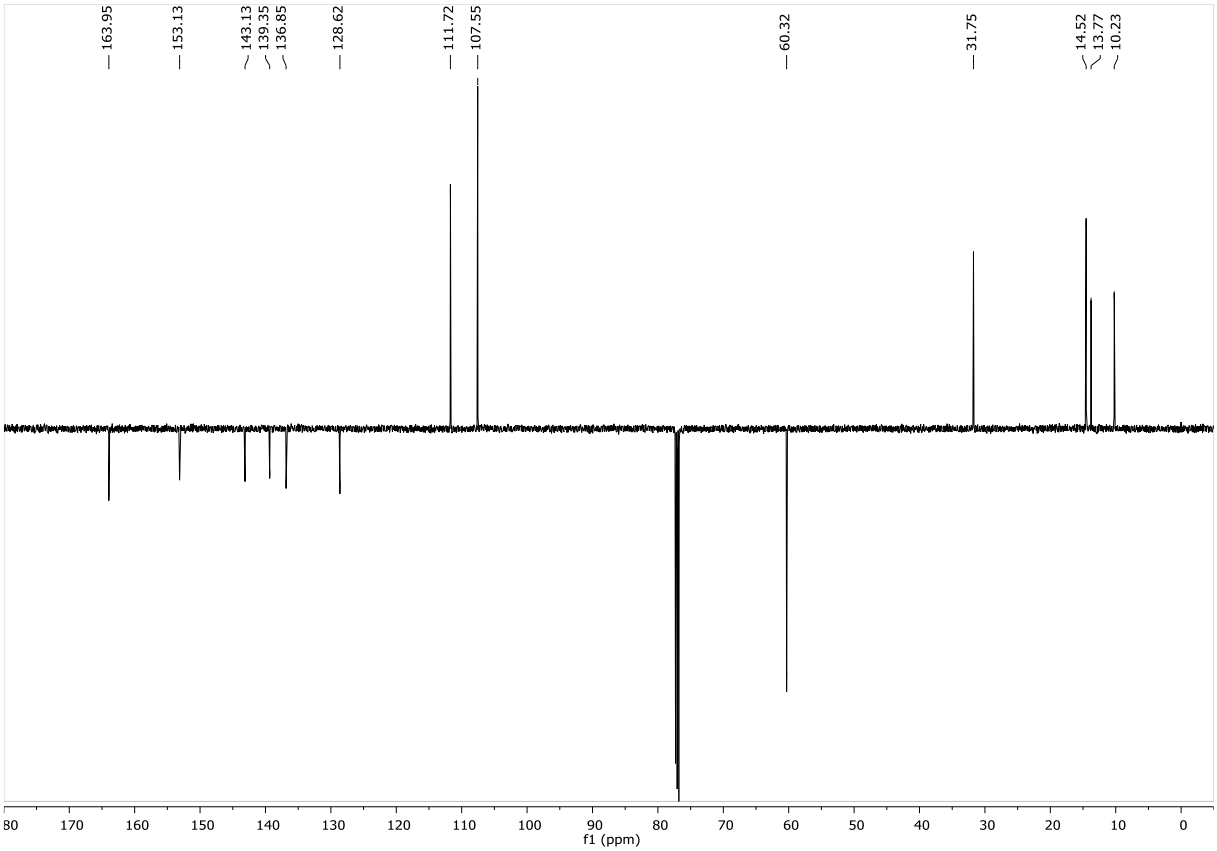


Figure S18. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3g**

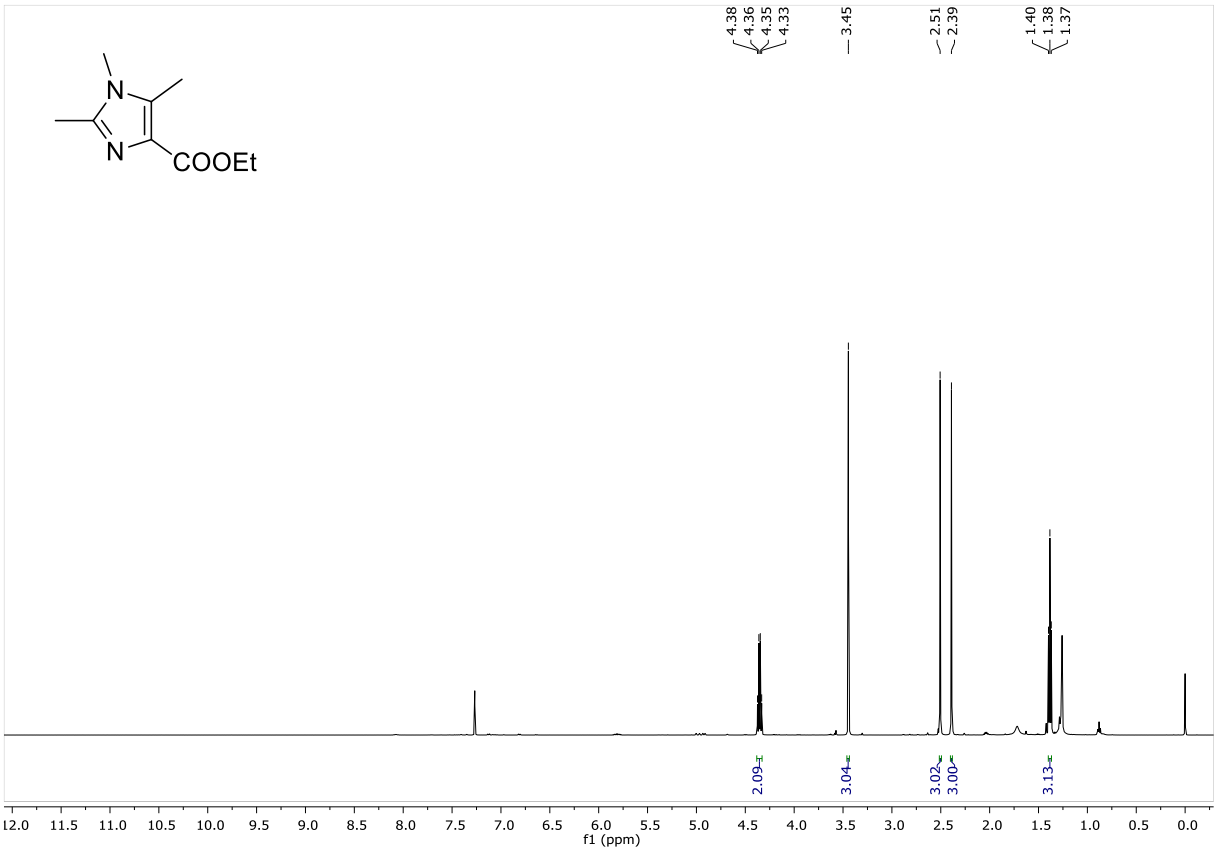


Figure S19. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3h**

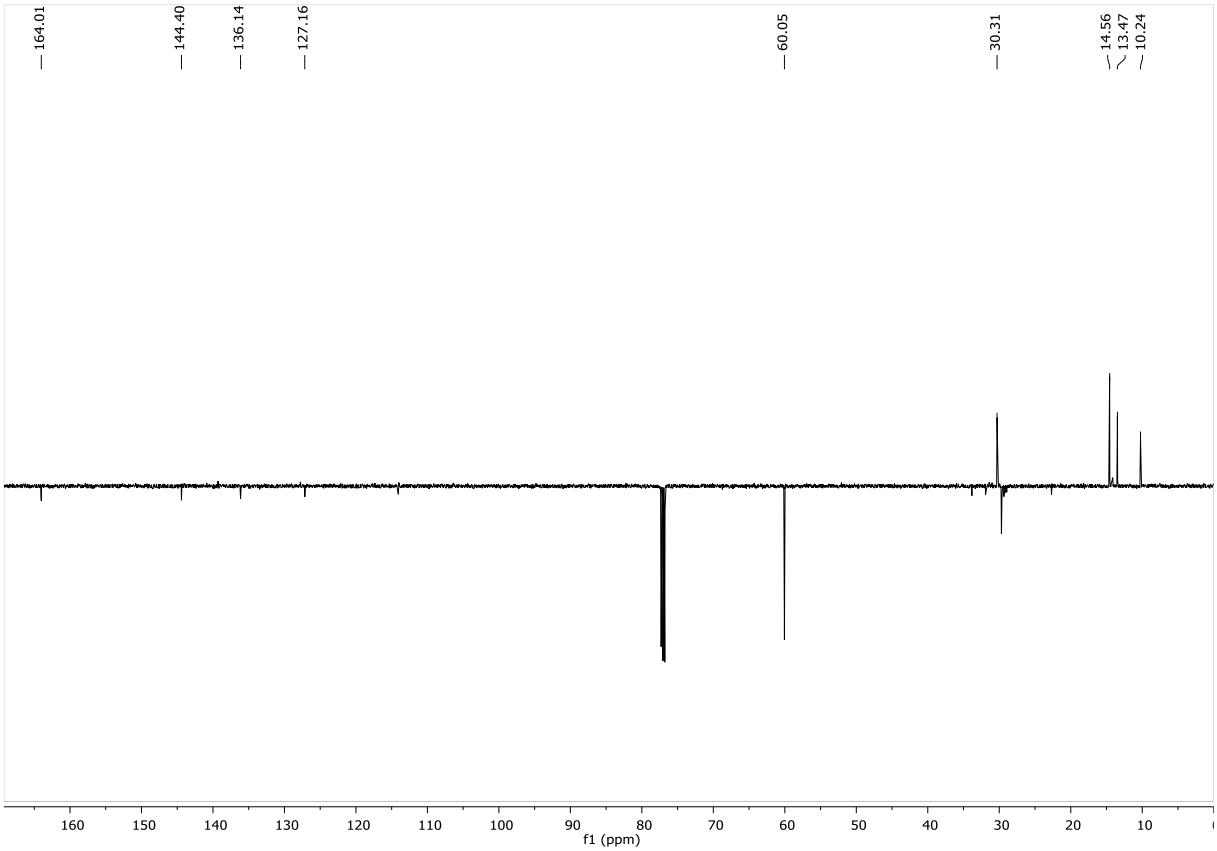


Figure S20. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3h**

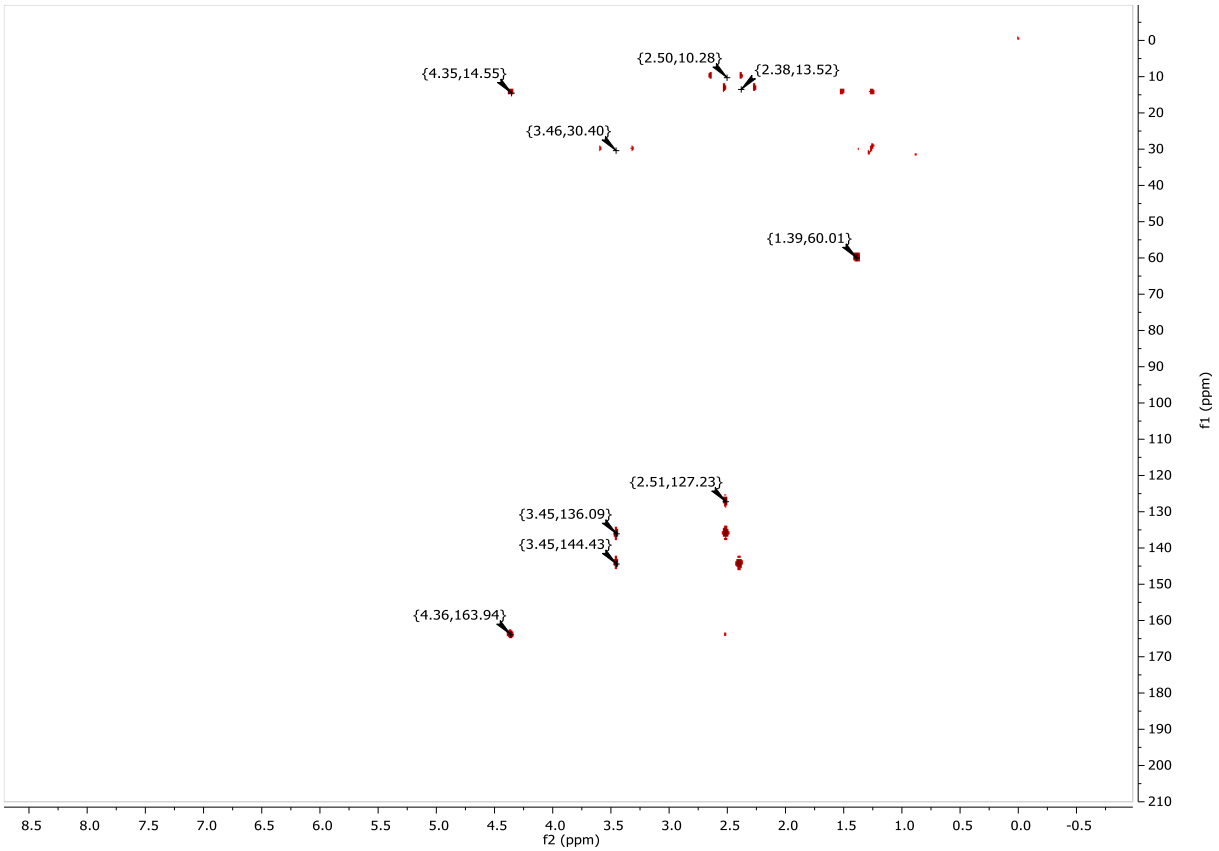


Figure S21. HMBC spectrum ($CDCl_3$) of the compound **3h**

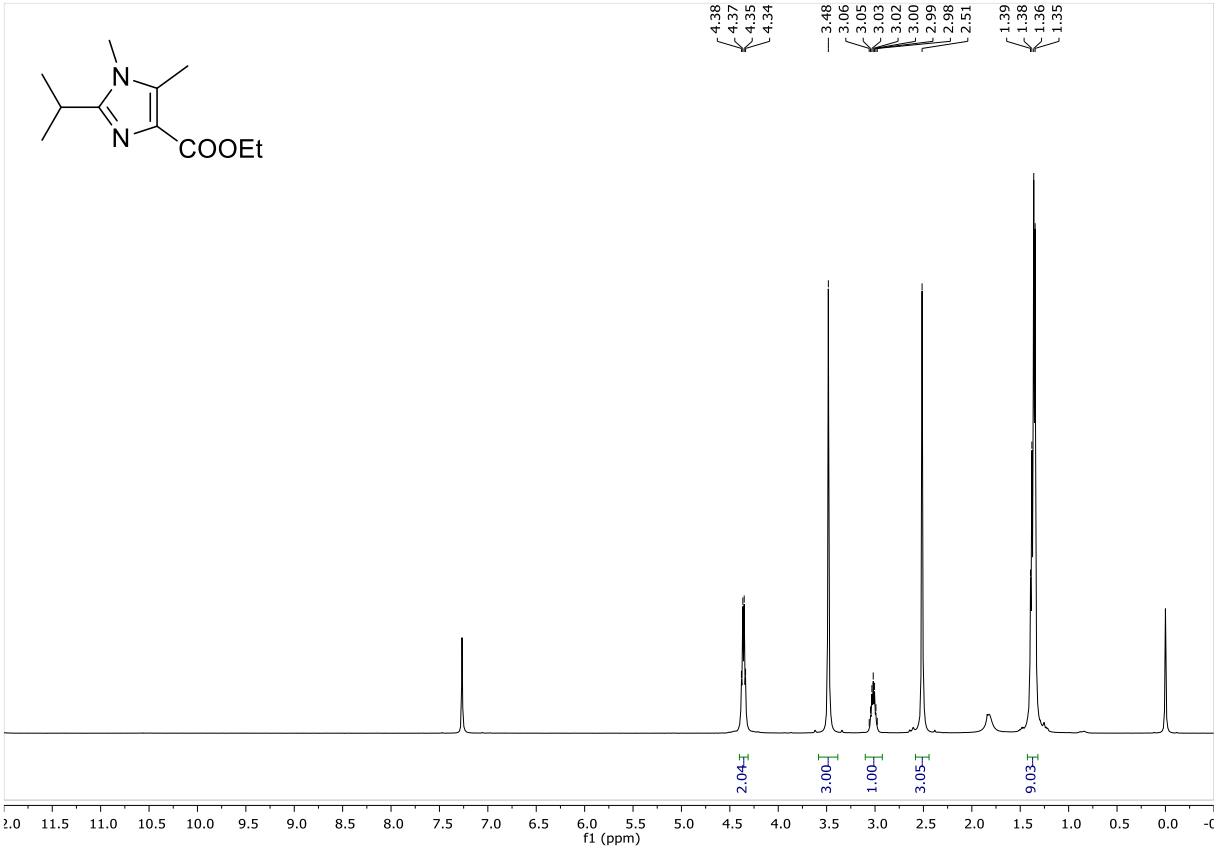


Figure S22. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3i**

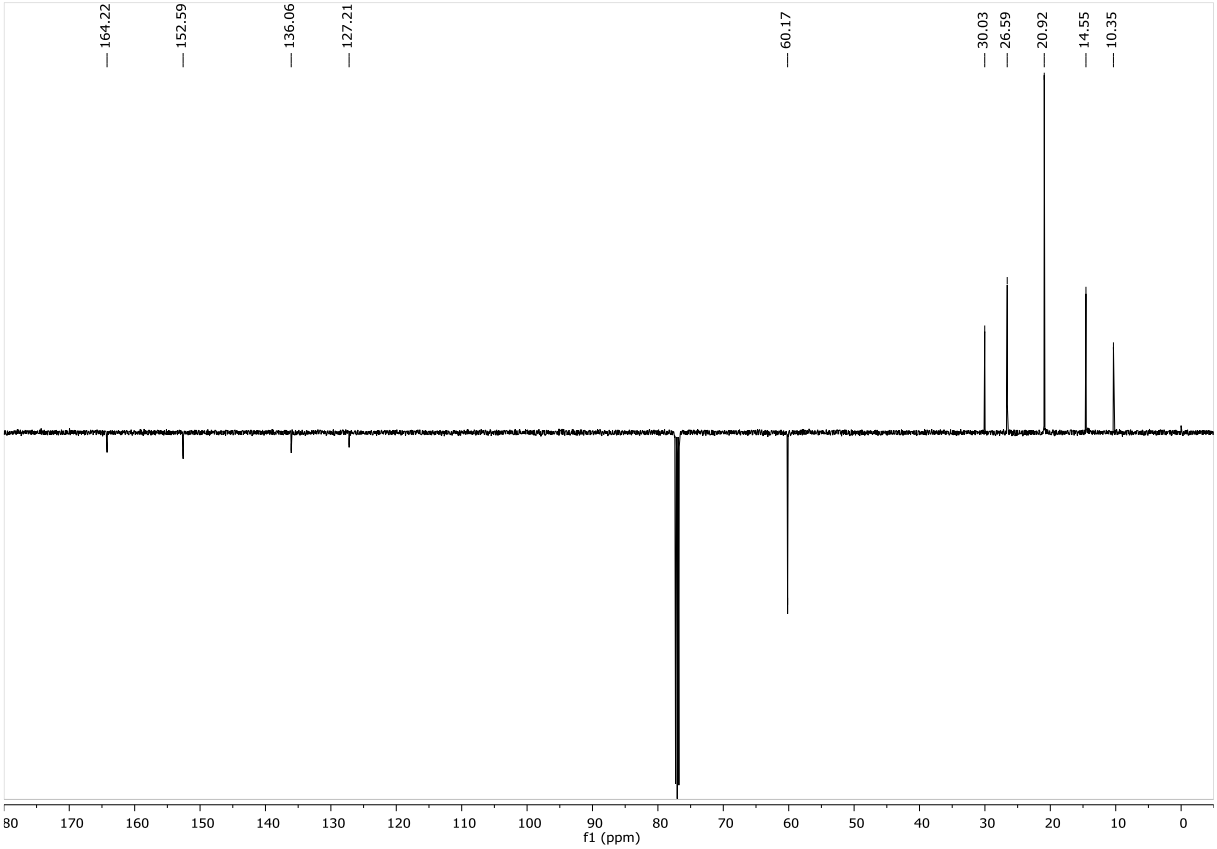


Figure S23. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3i**

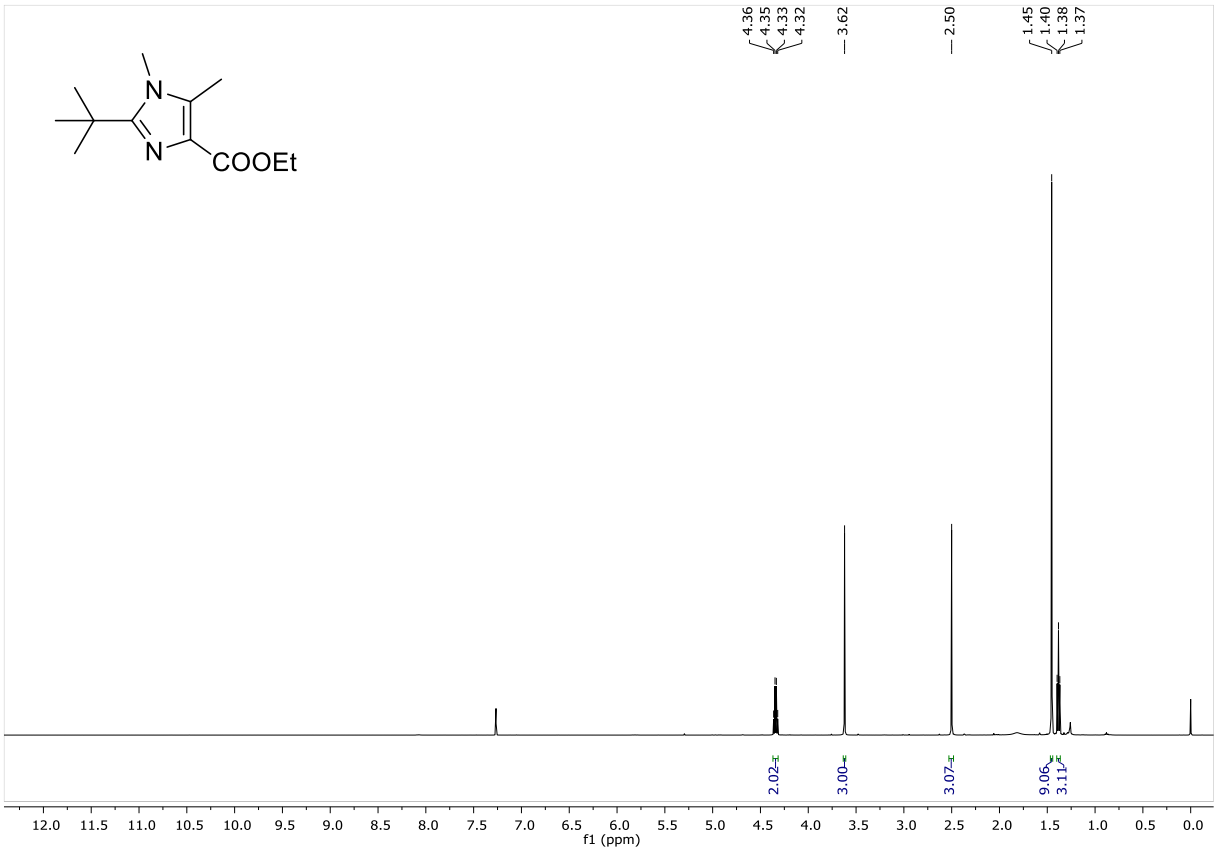


Figure S24. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3j**

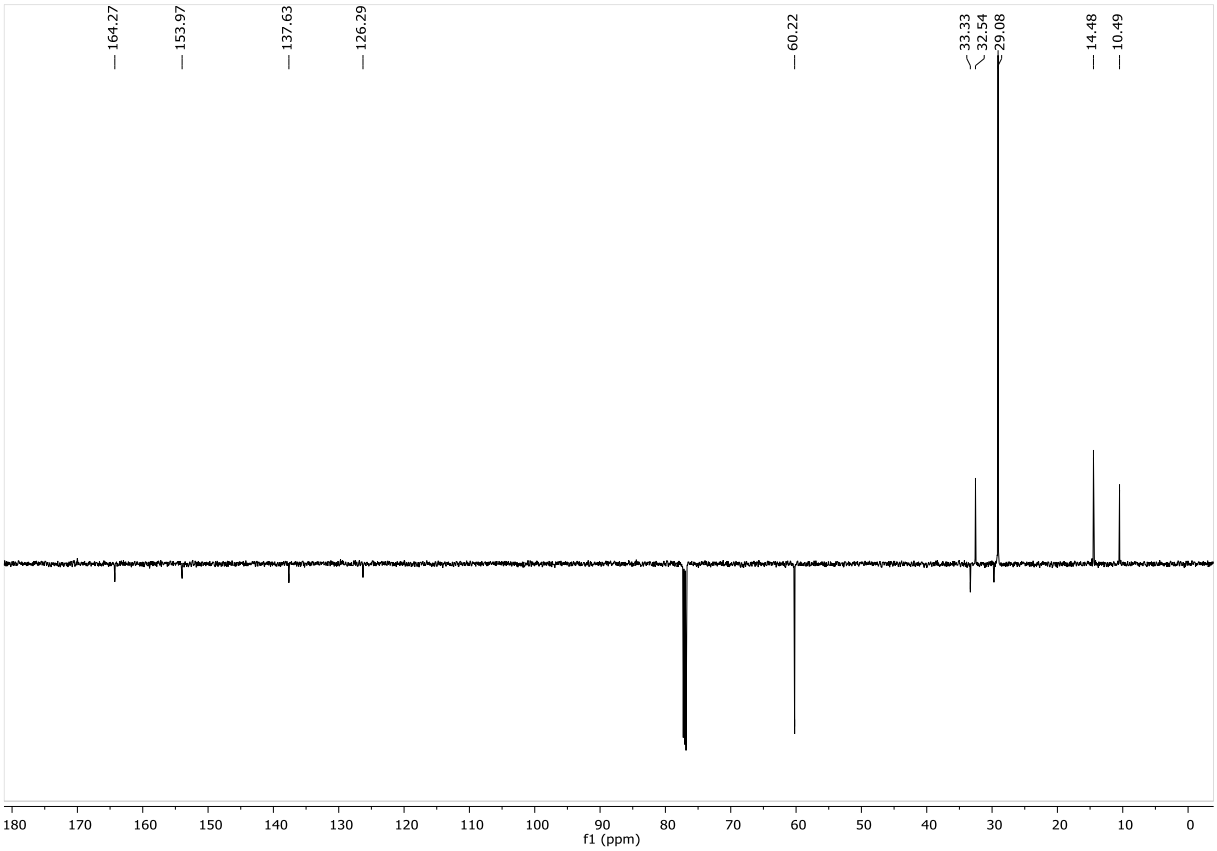


Figure S25. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3j**

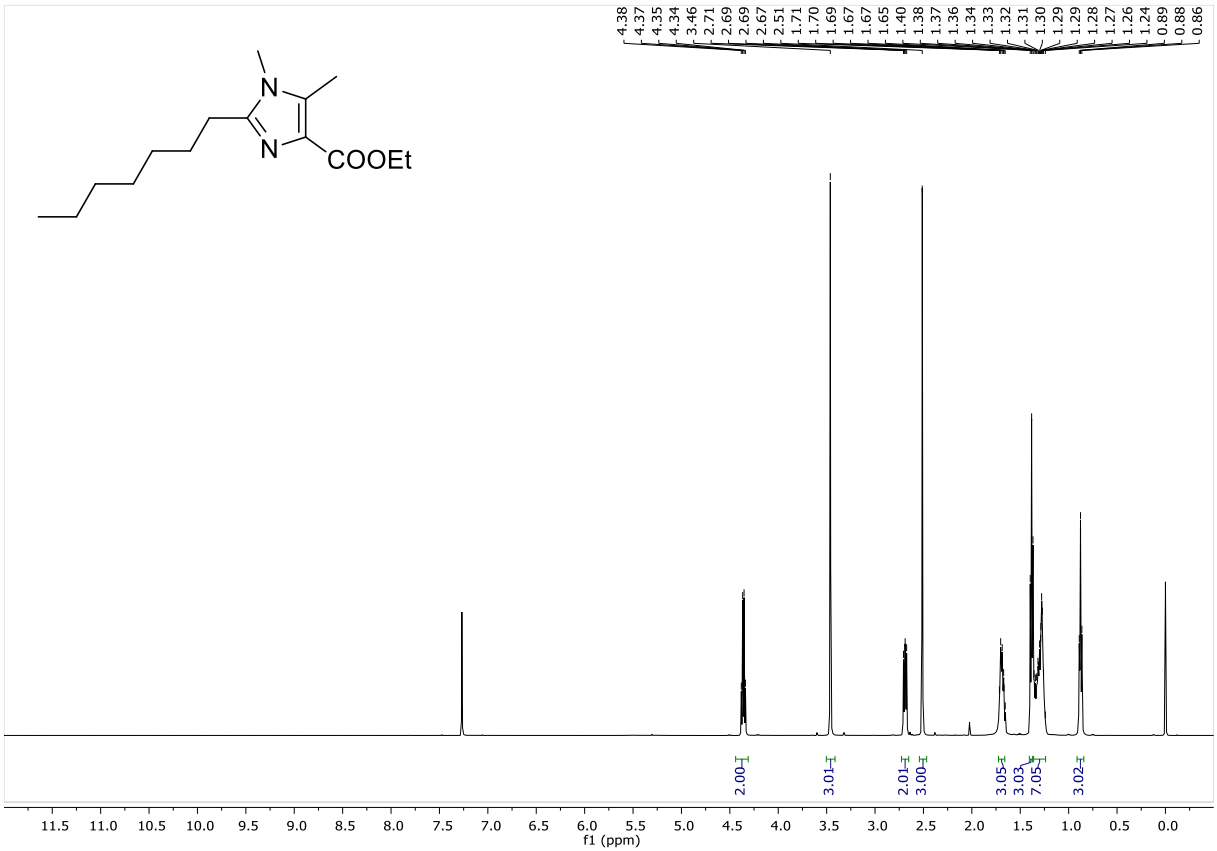


Figure S26. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3k**

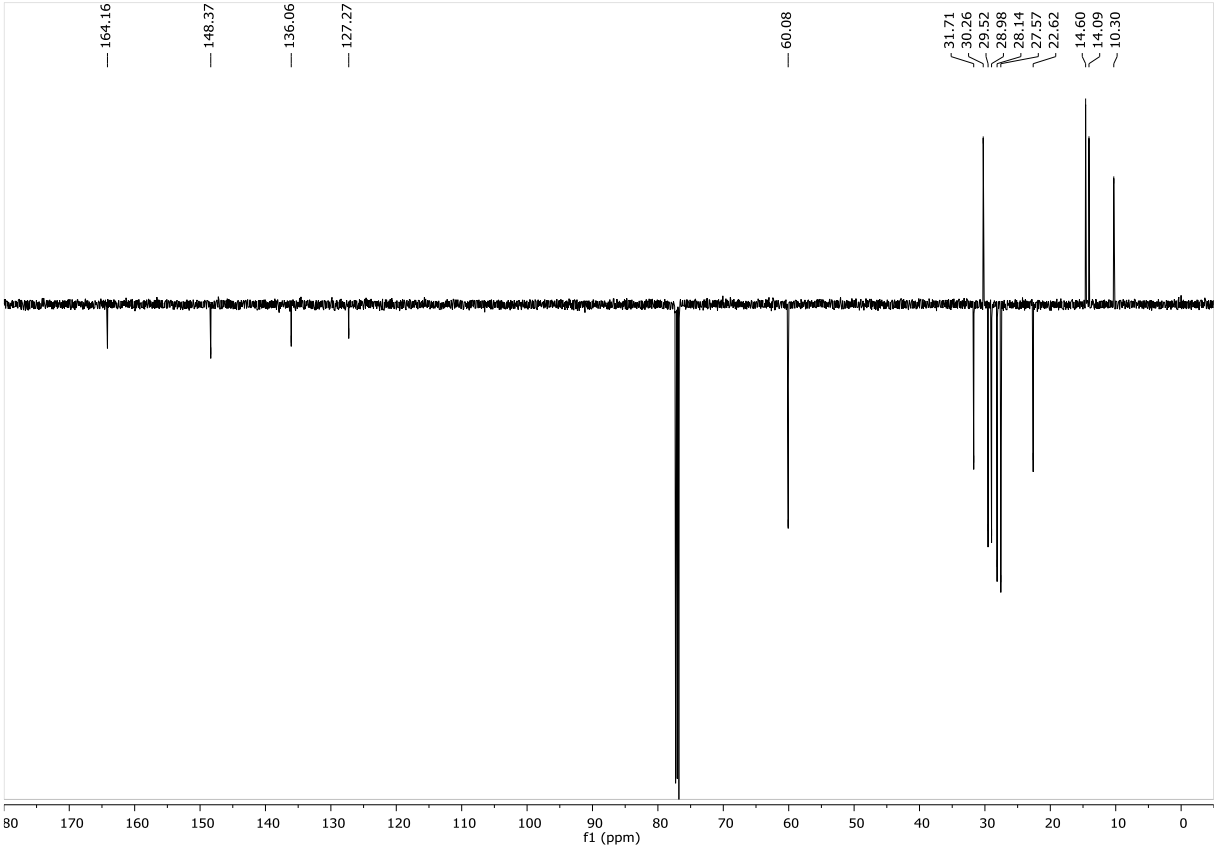


Figure S27. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3k**

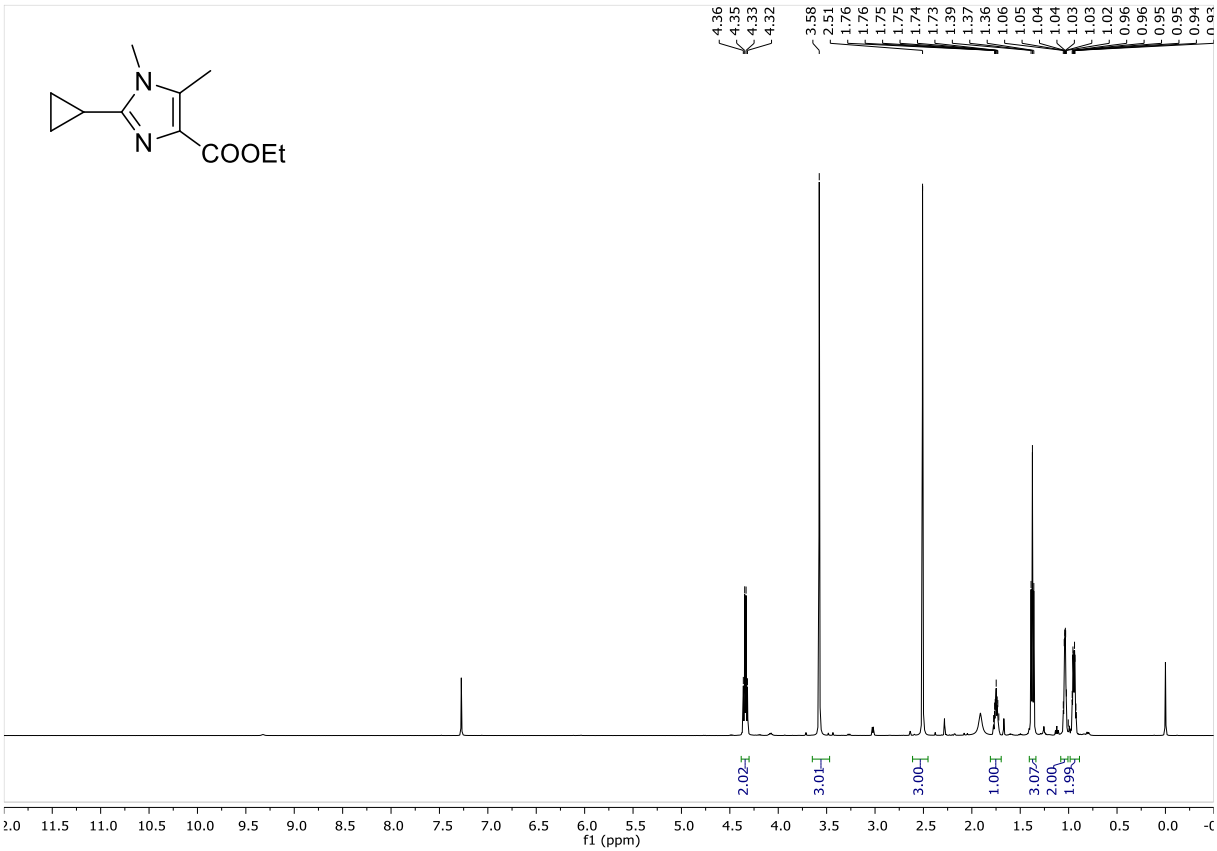


Figure S28. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3l**

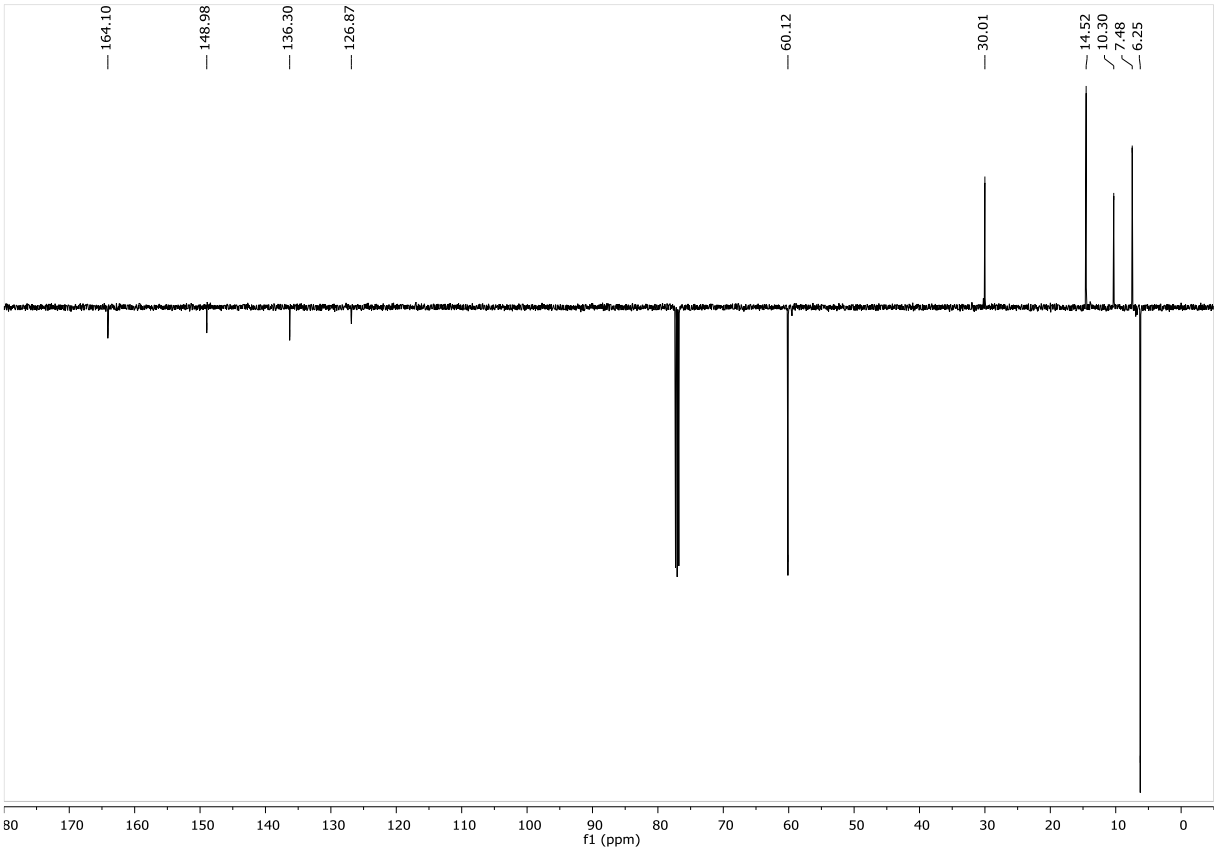


Figure S29. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3l**

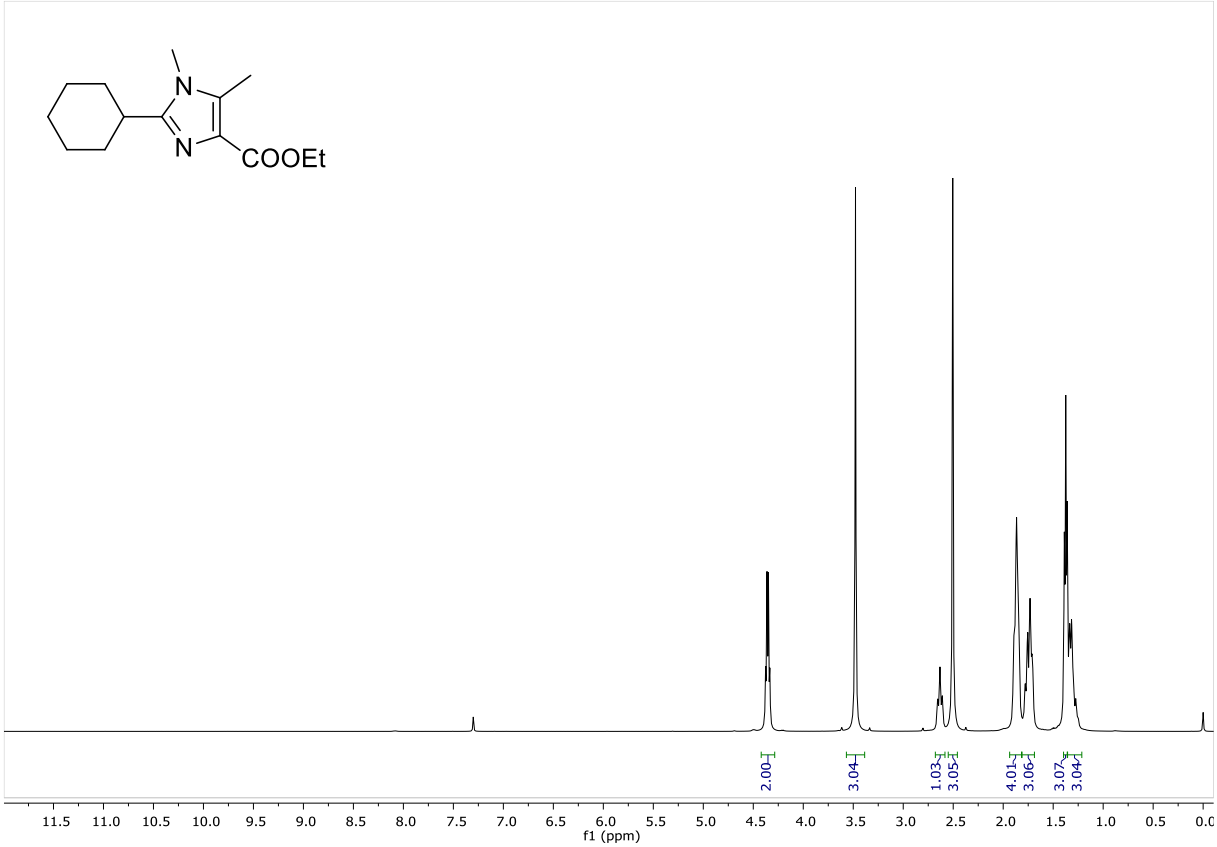


Figure S30. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3m**

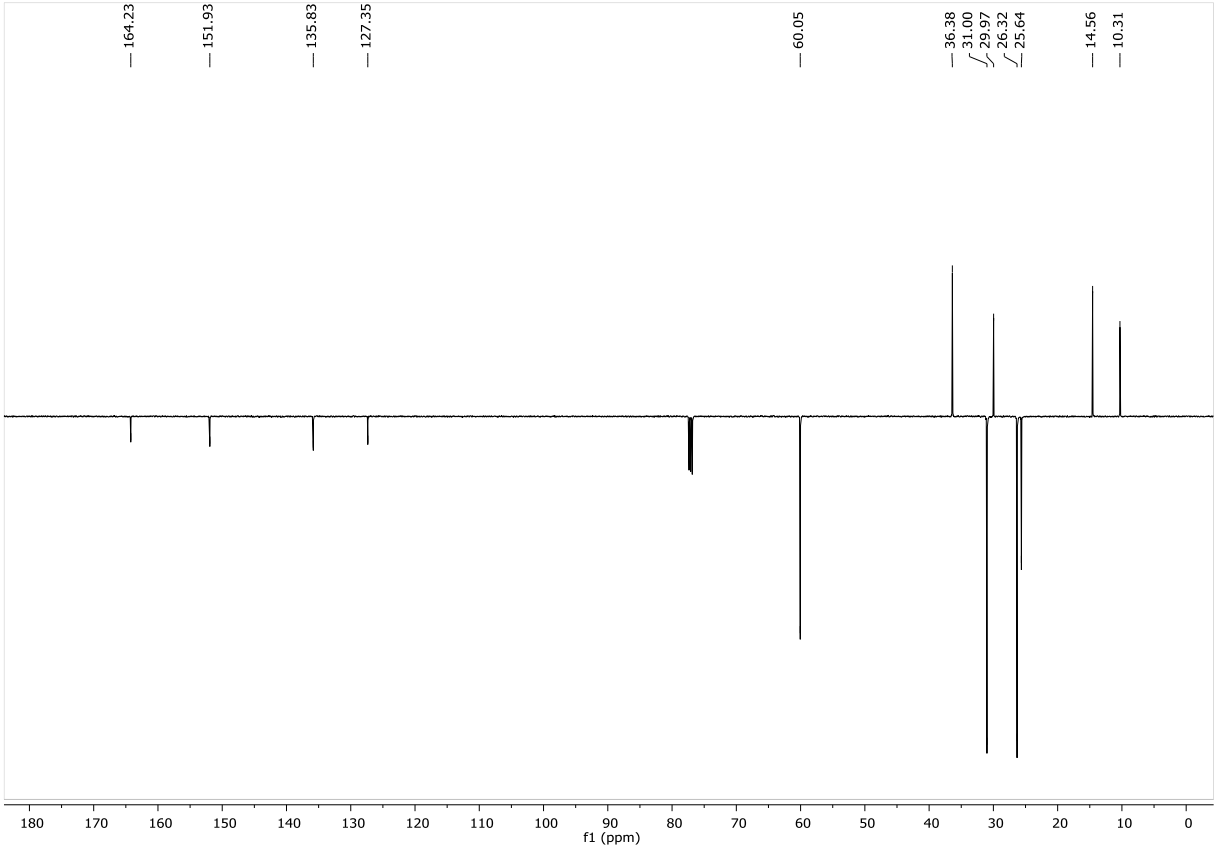


Figure S31. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3m**

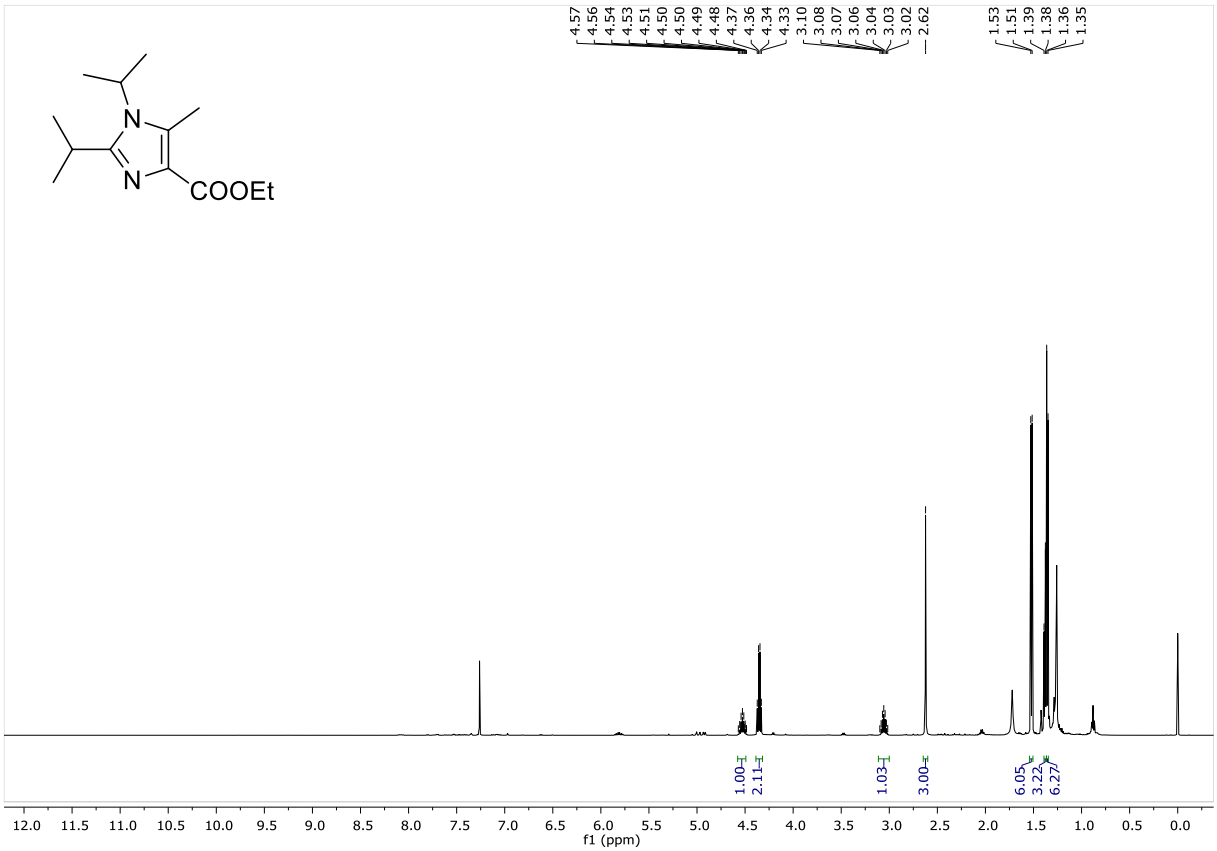


Figure S32. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3n**

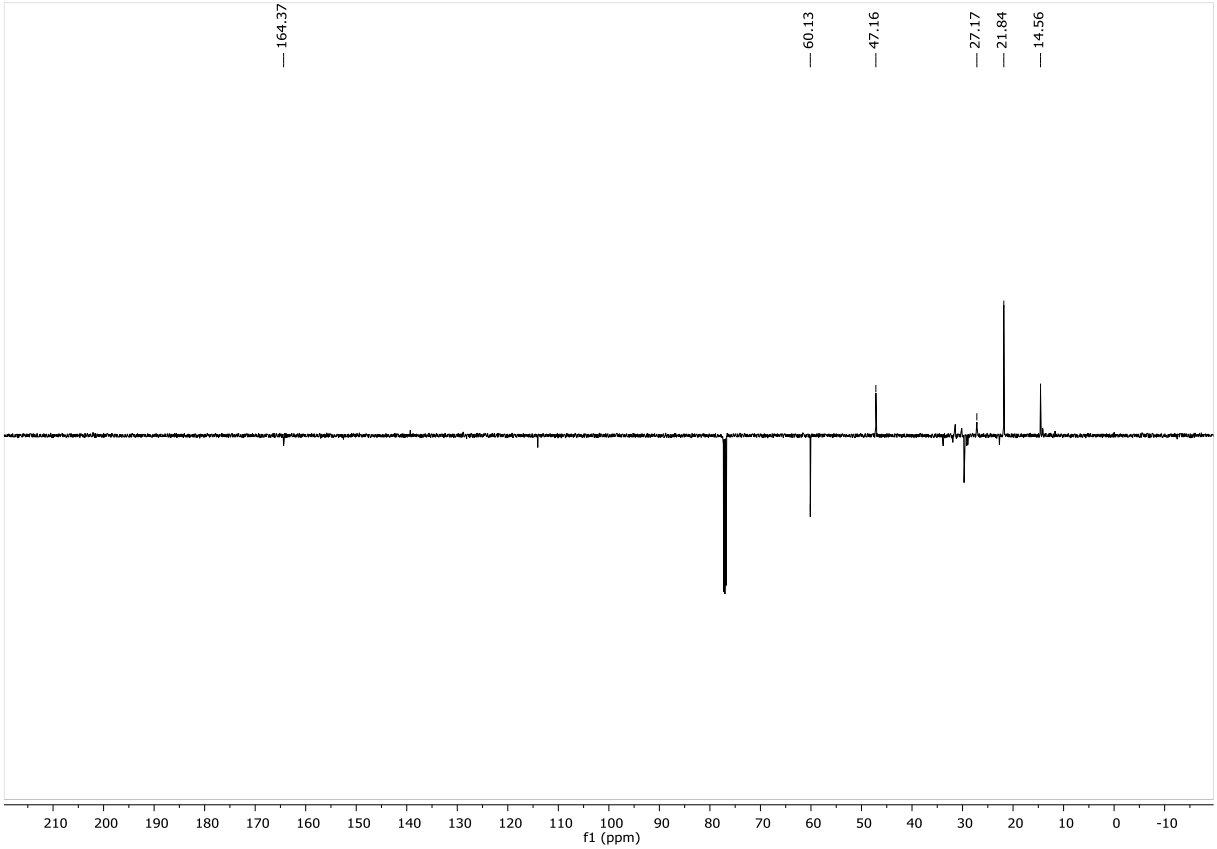


Figure S33. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3n**

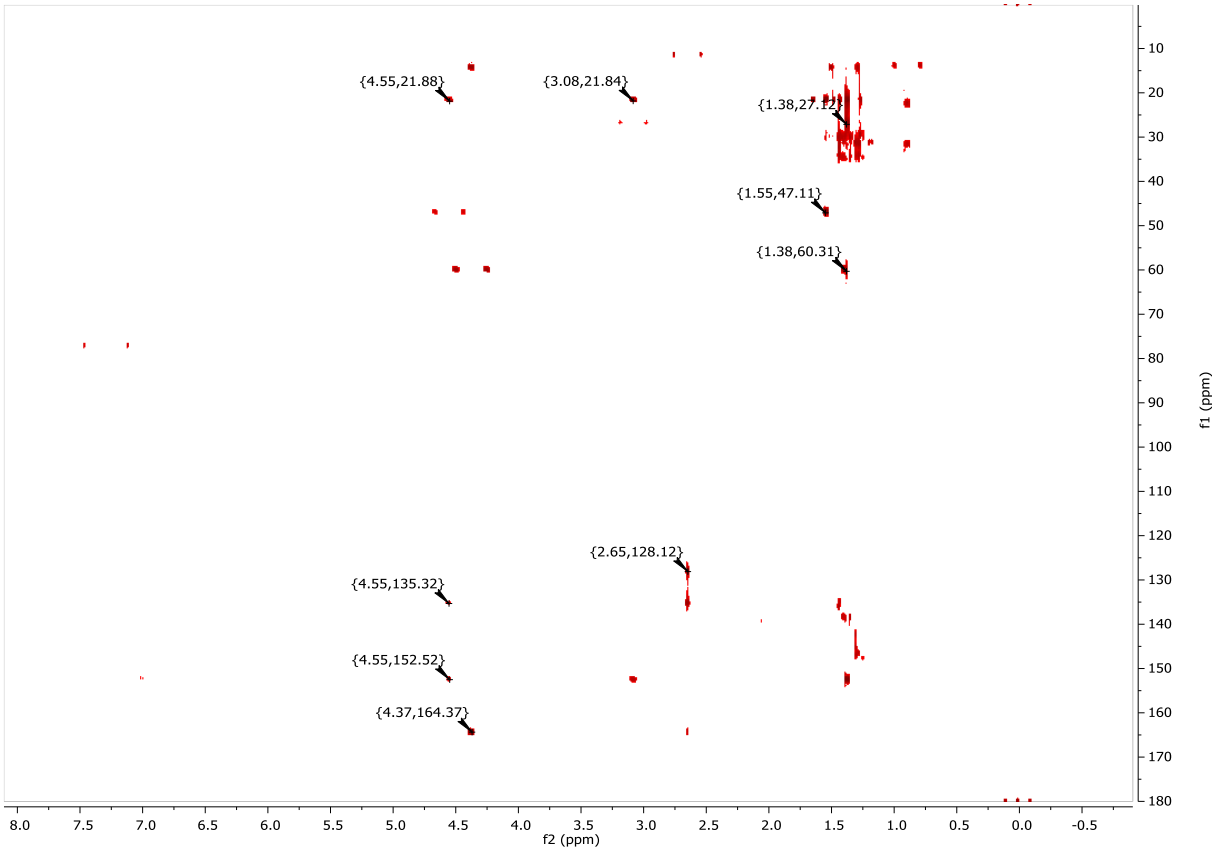


Figure S34. HMBC spectrum ($CDCl_3$) of the compound **3n**

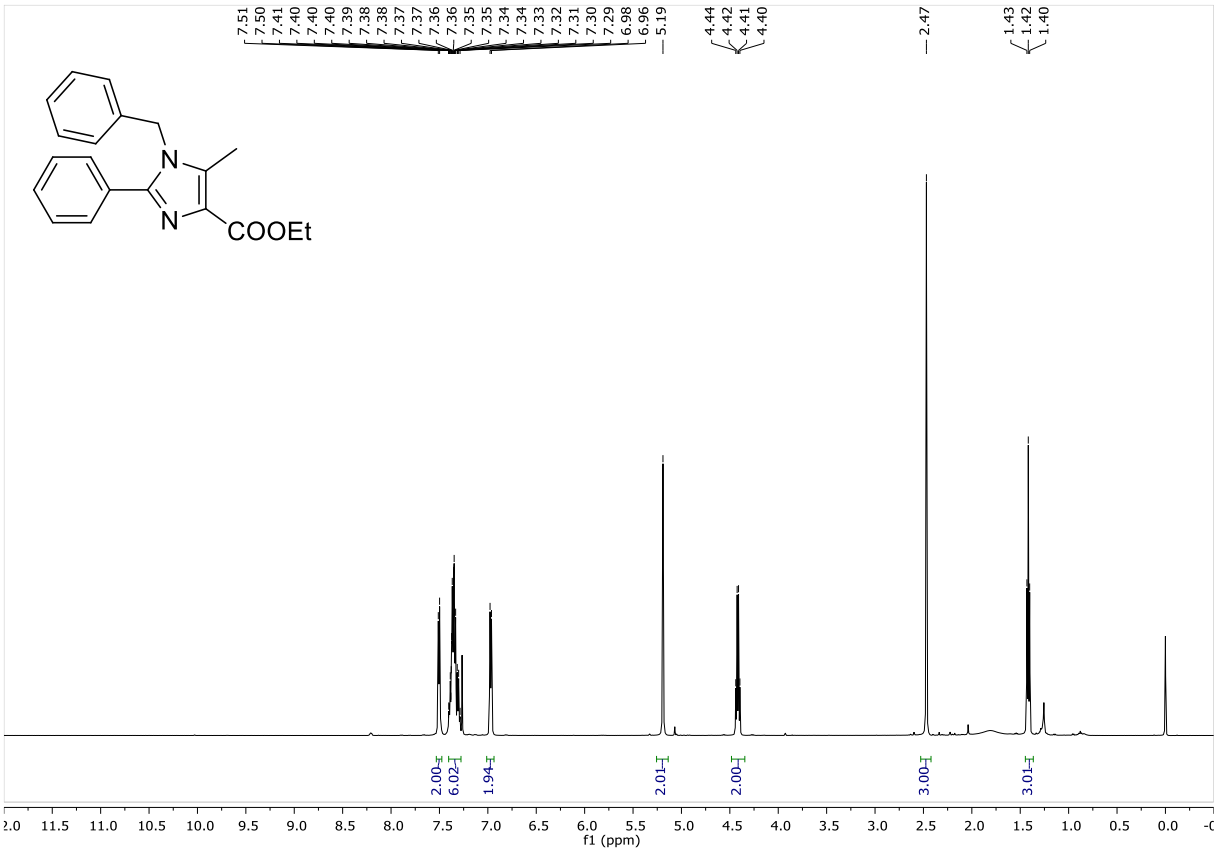


Figure S35. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3o**

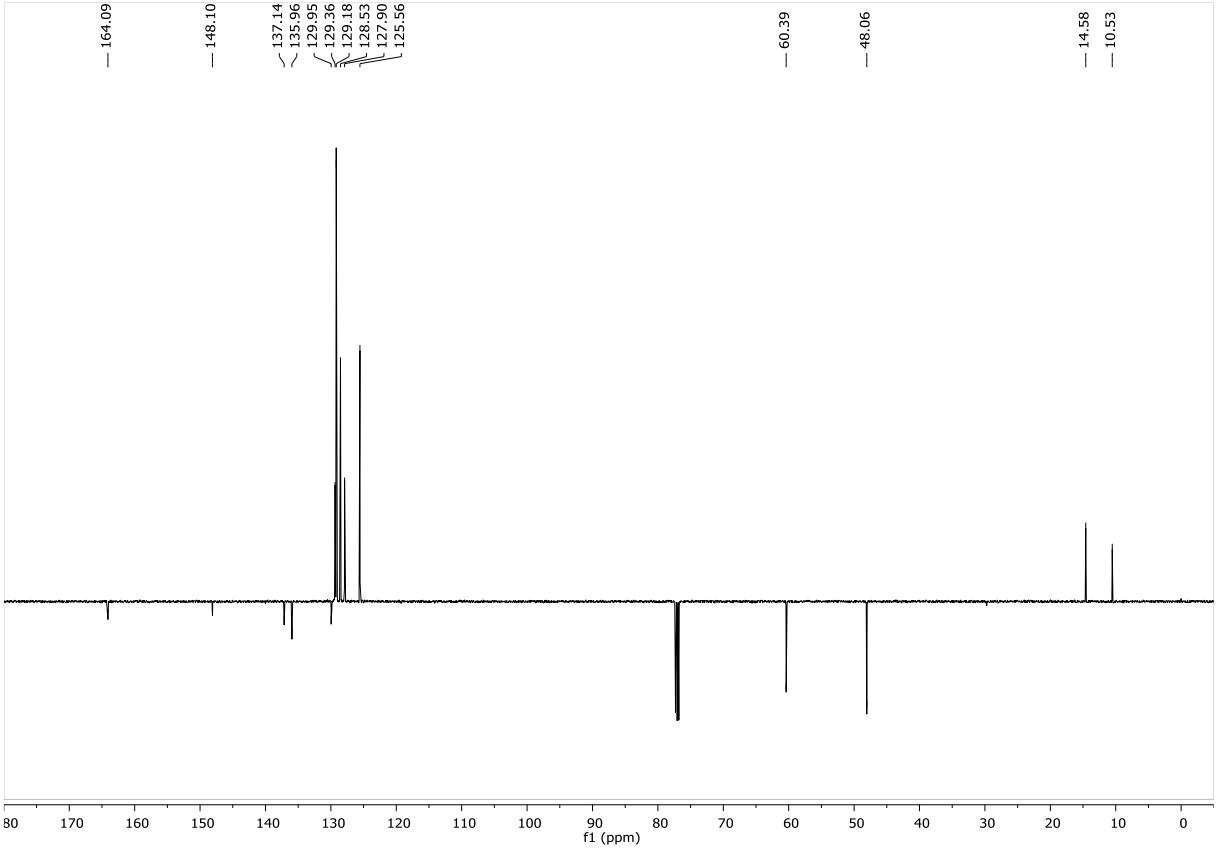


Figure S36. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3o**

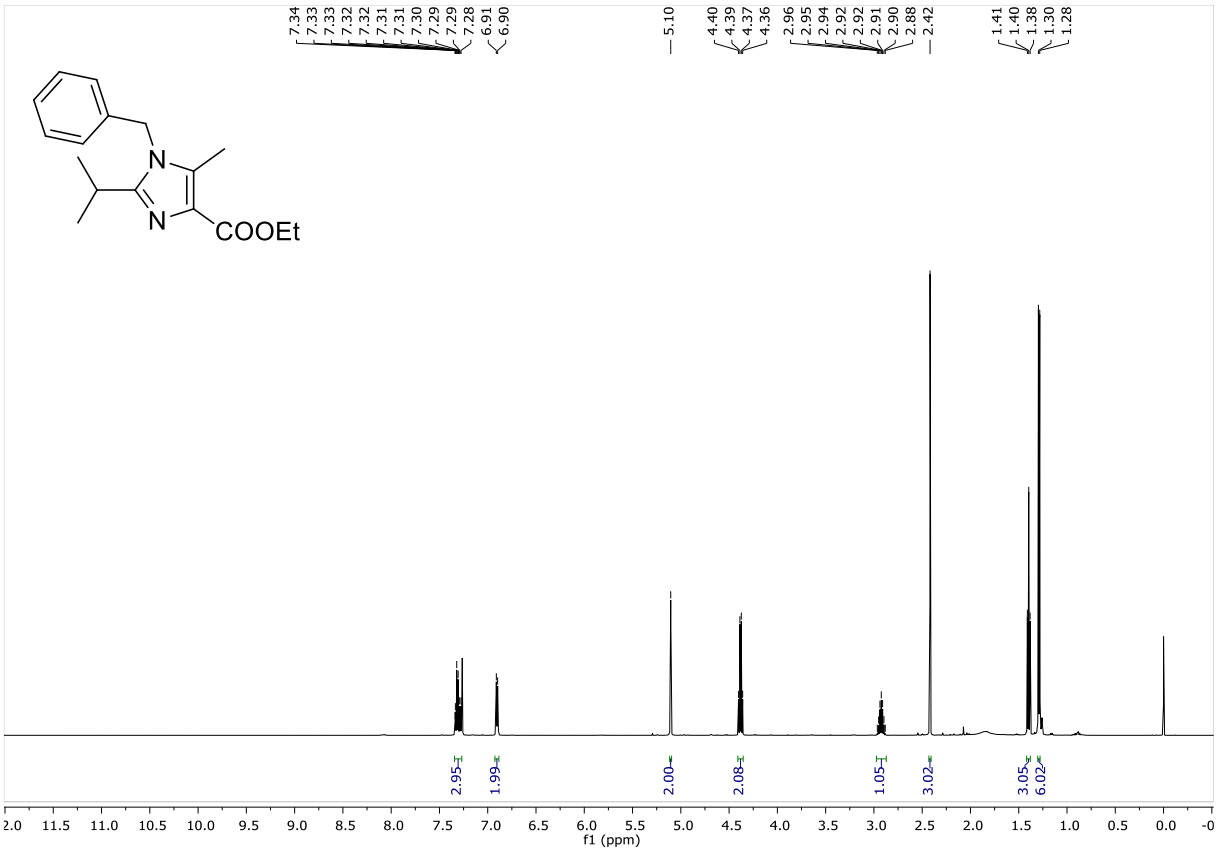


Figure S37. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3p**

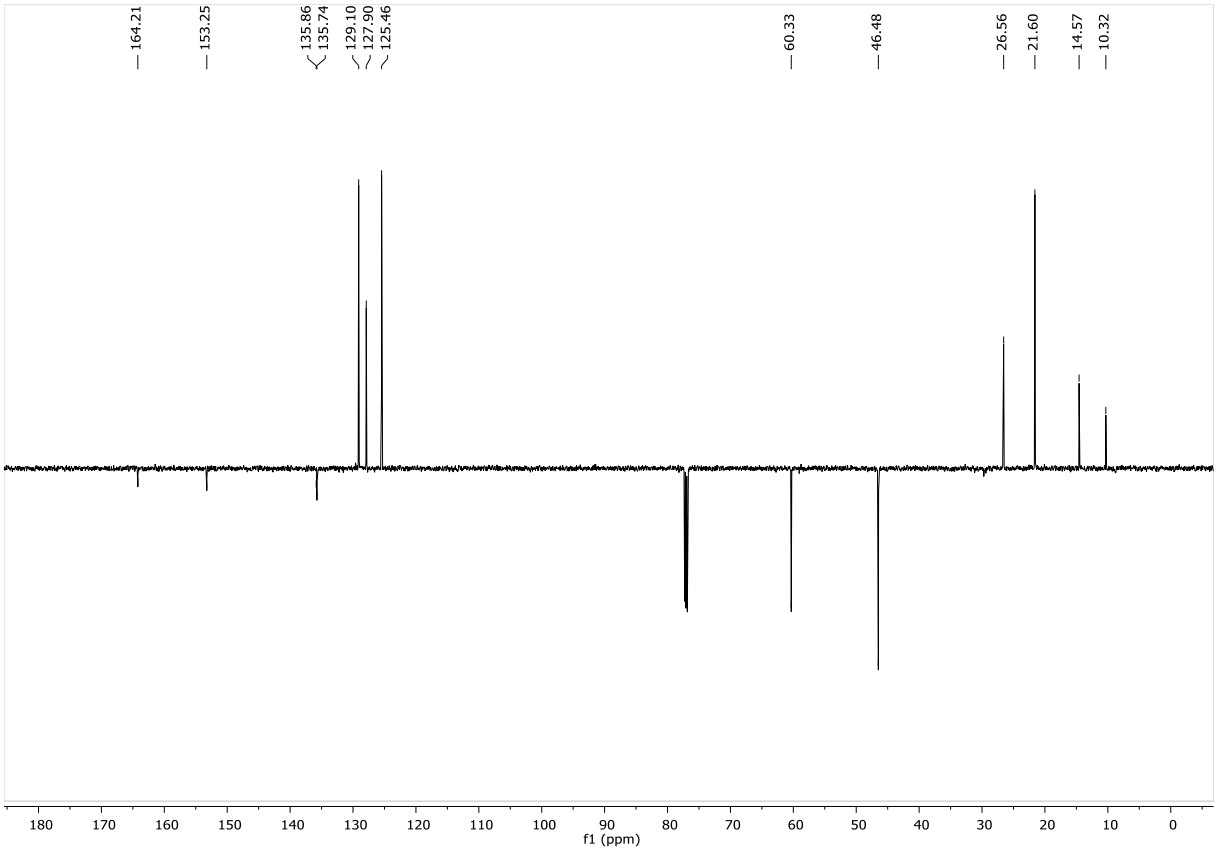


Figure S38. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3p**

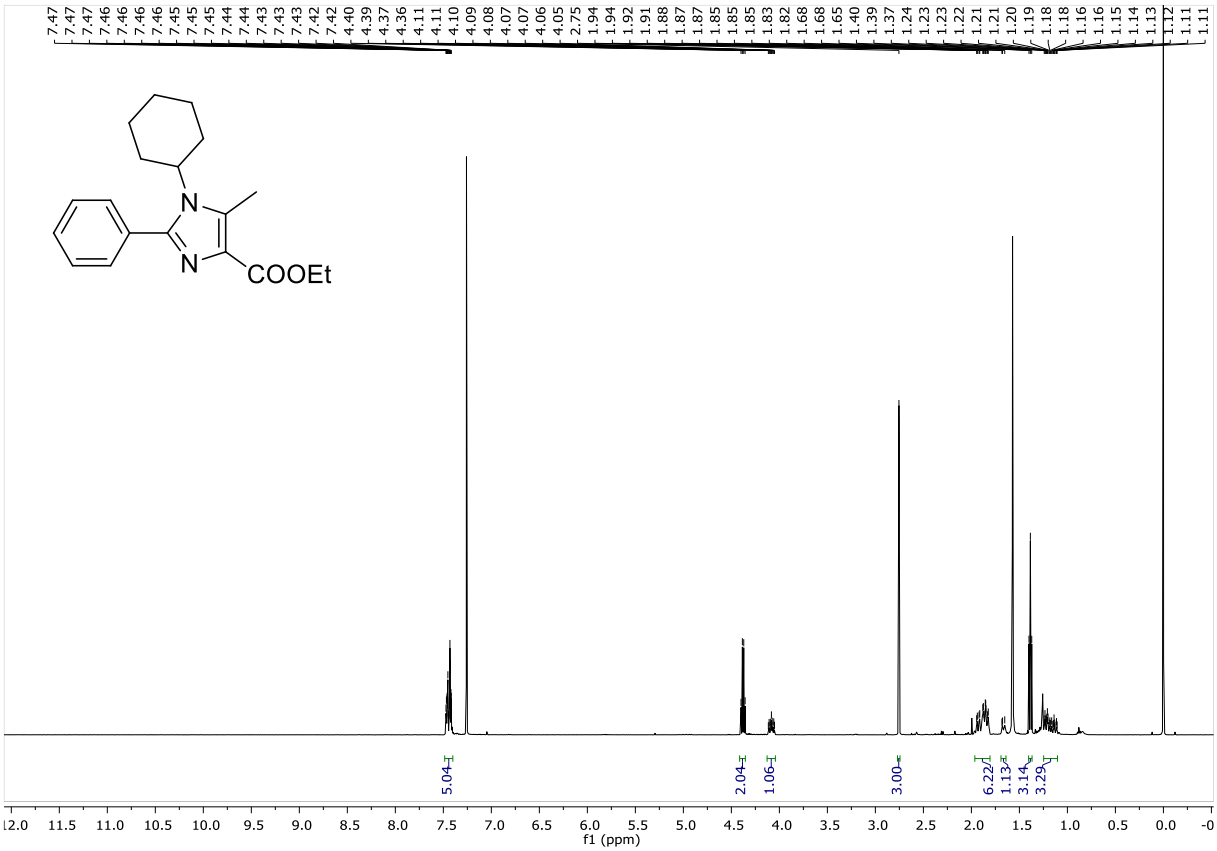


Figure S39. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3q**

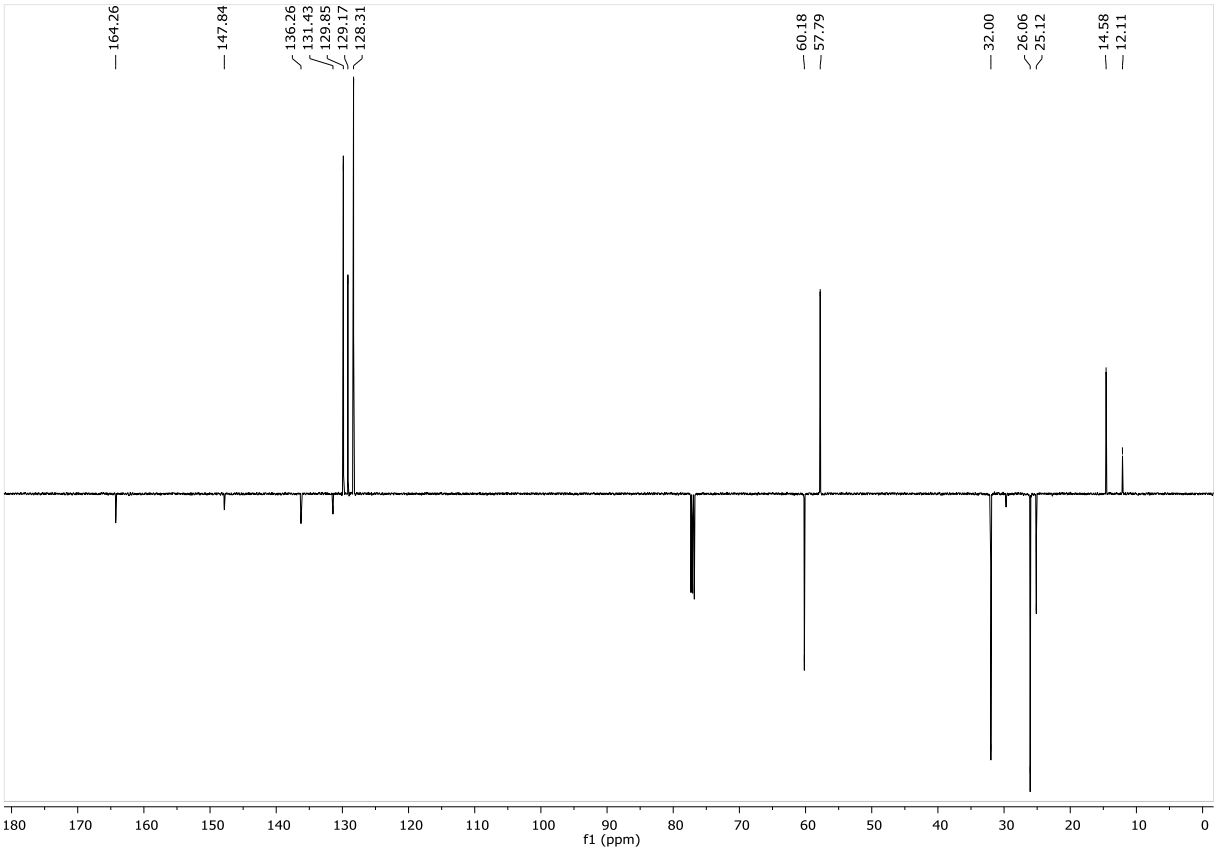


Figure S40. $^{13}C\{^{1}H\}$ NMR spectrum (126 MHz, $CDCl_3$) of the compound **3q**

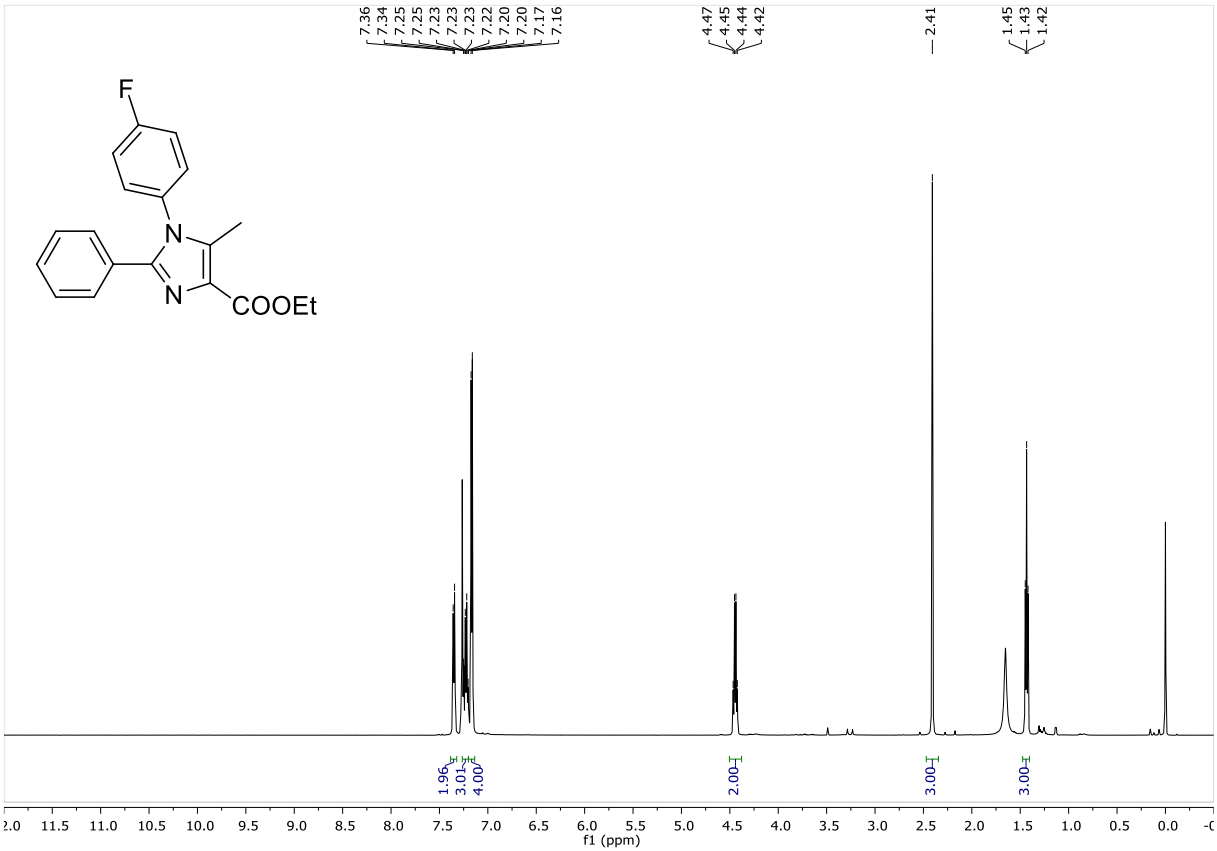


Figure S41. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **3r**

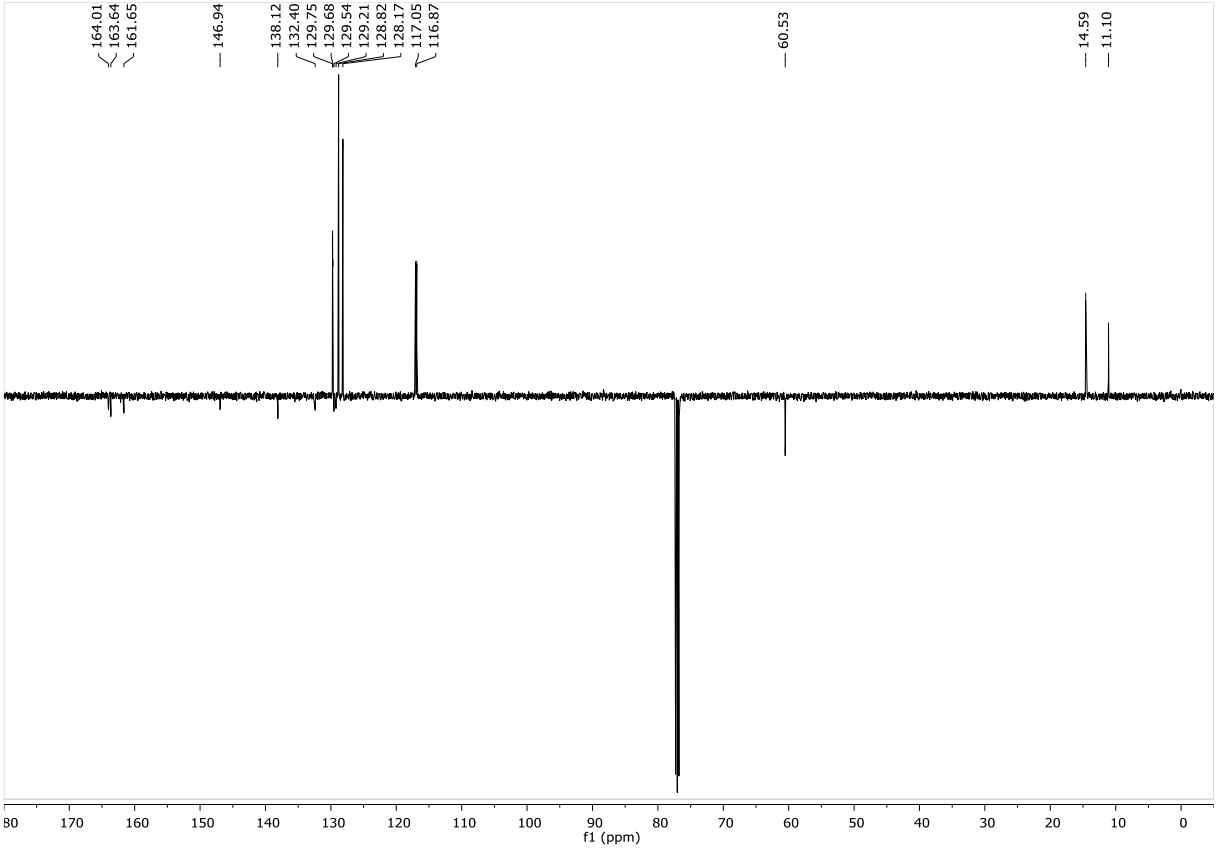


Figure S42. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **3r**

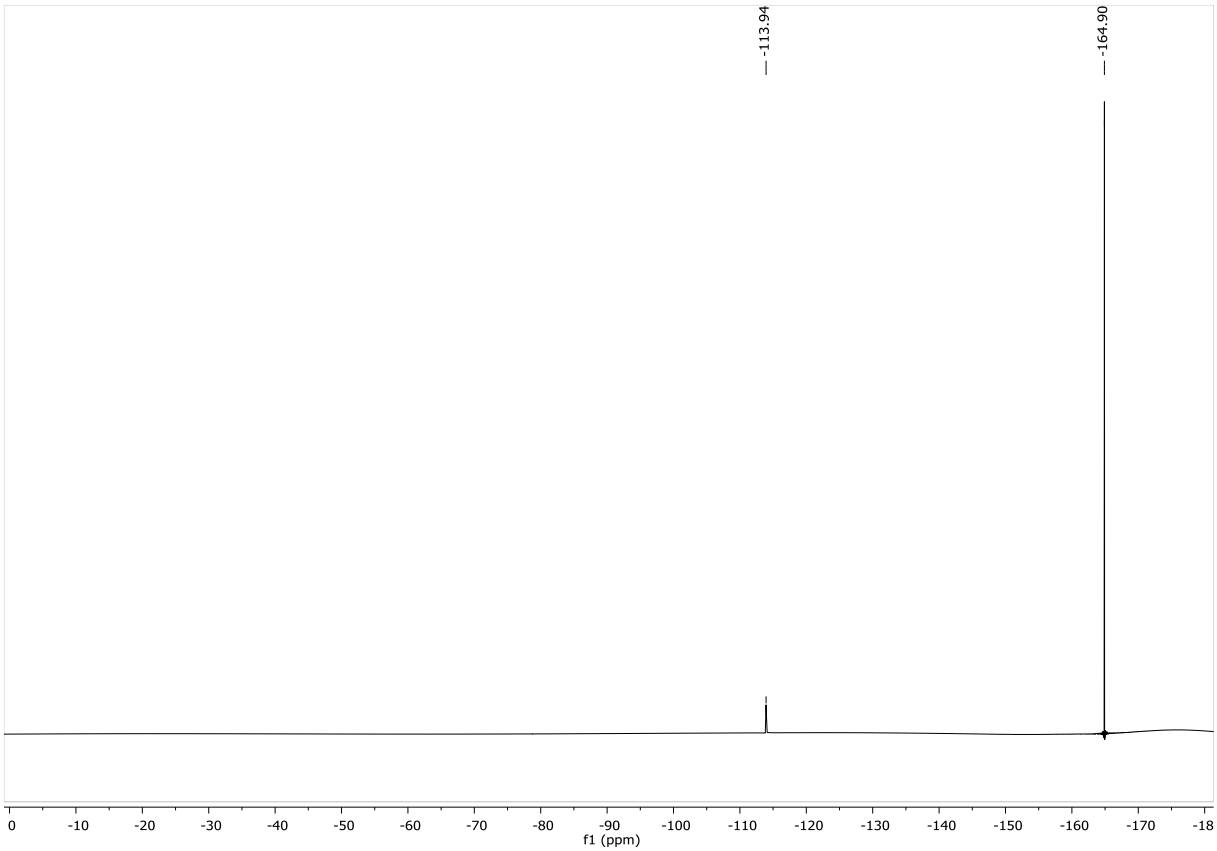


Figure S43. ^{19}F NMR spectrum (471 MHz, $CDCl_3$) of the compound **3r**

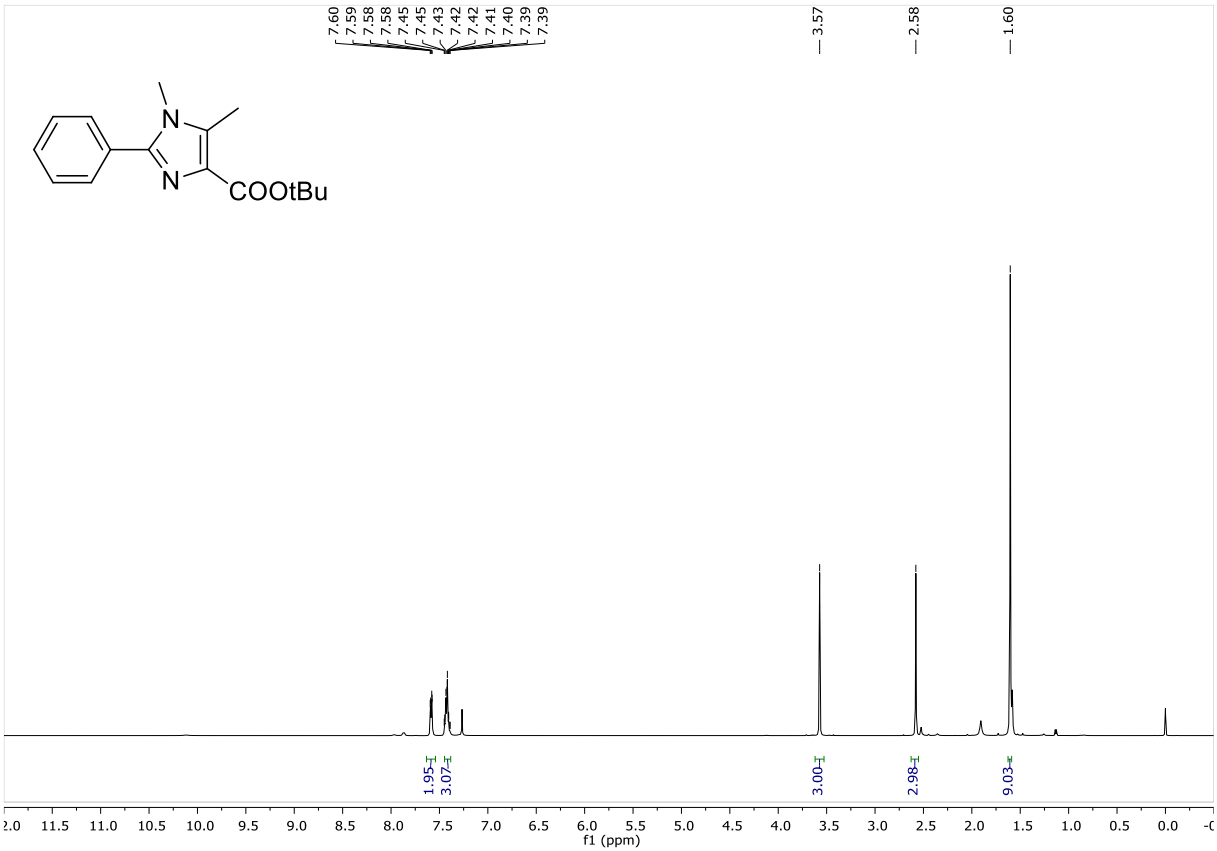


Figure S44. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **4a**

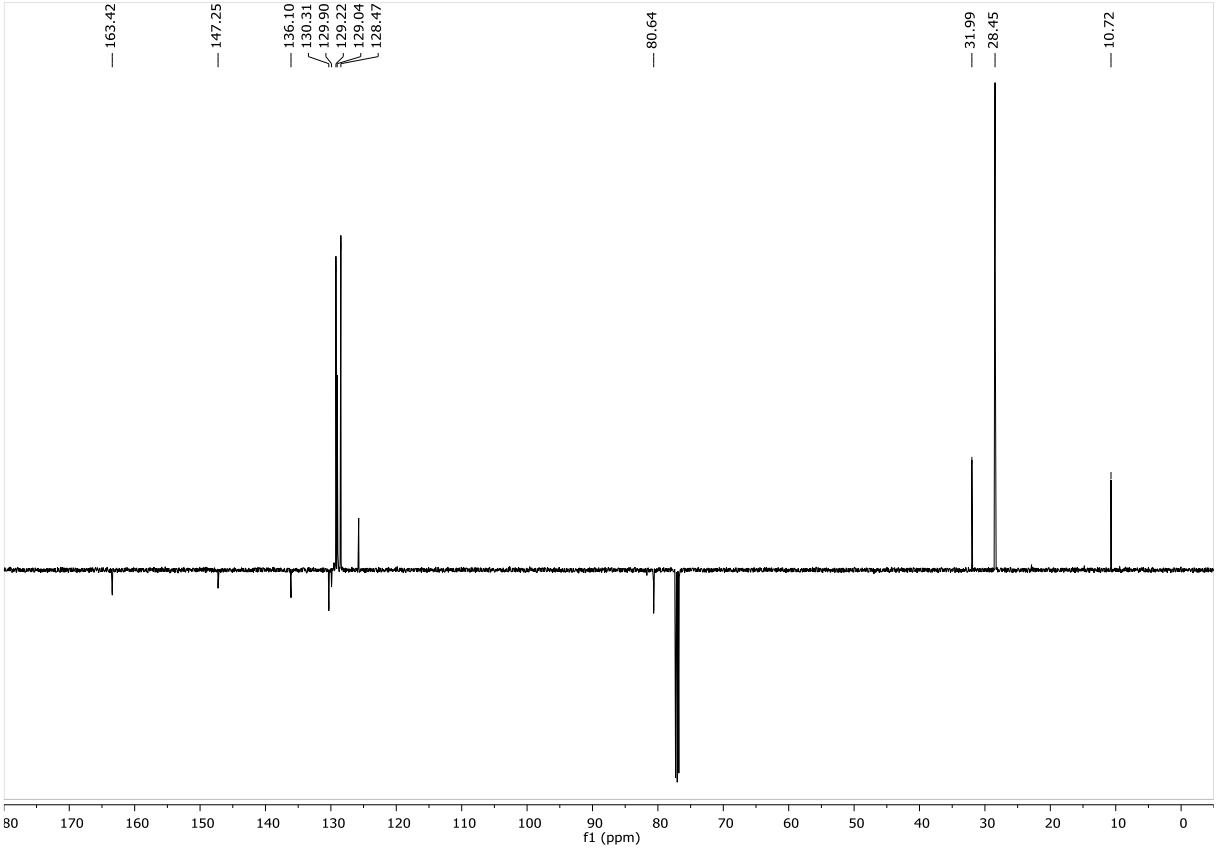


Figure S45. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **4a**

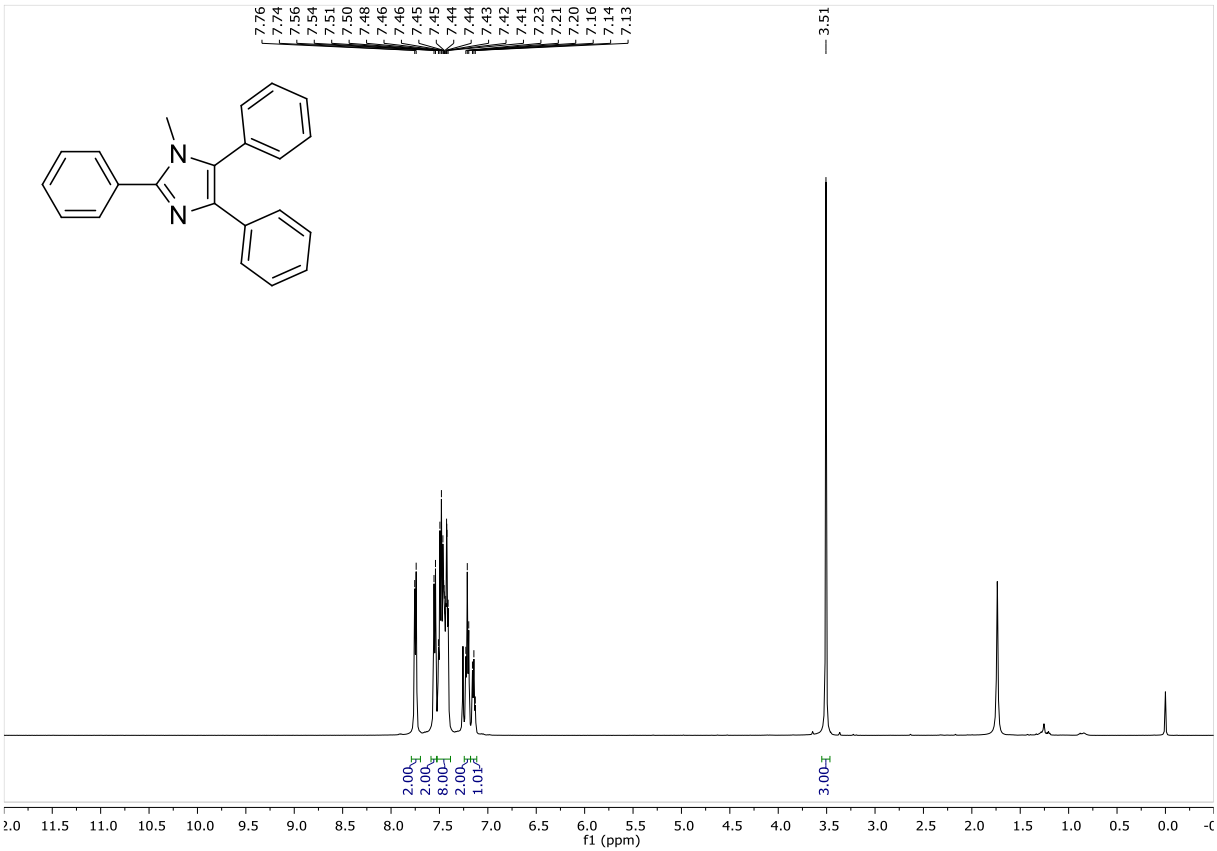


Figure S46. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **4b**

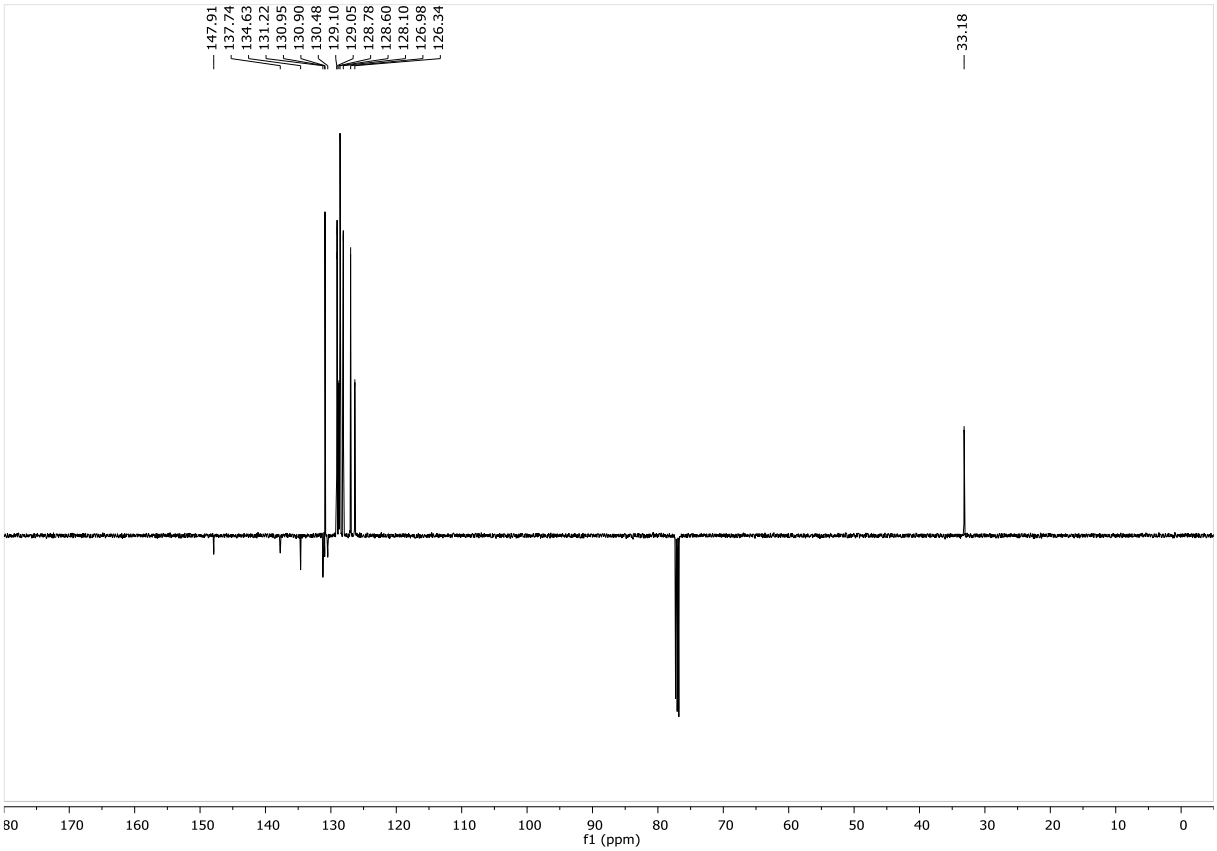


Figure S47. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **4b**

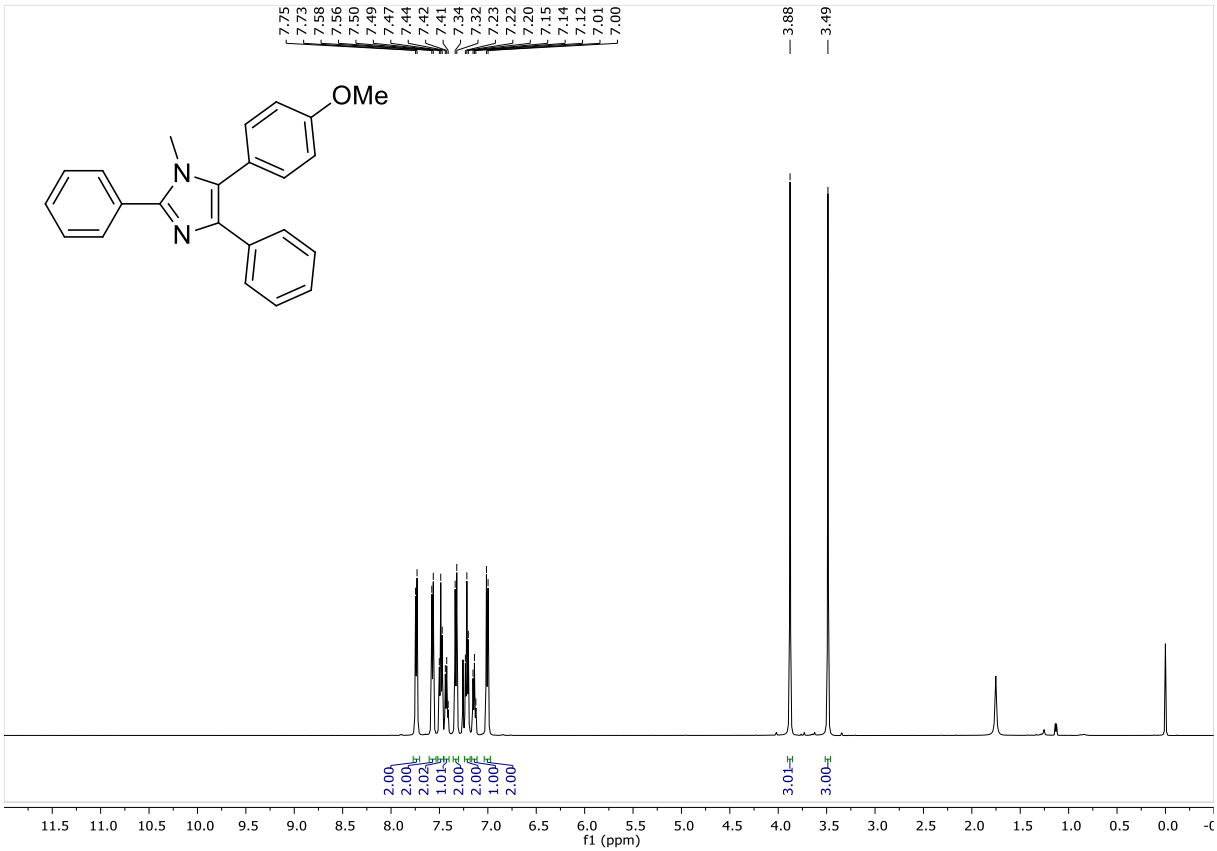


Figure S48. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **4c**

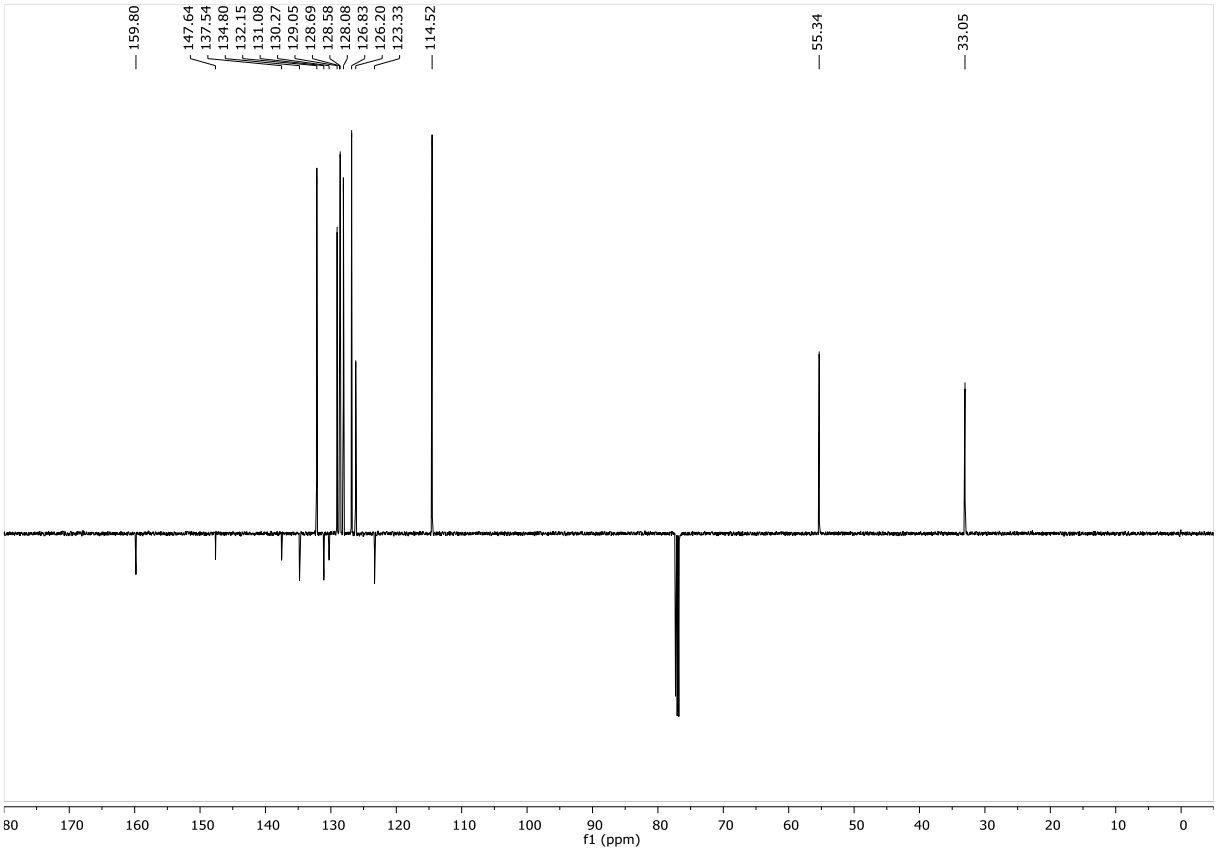


Figure S49. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **4c**

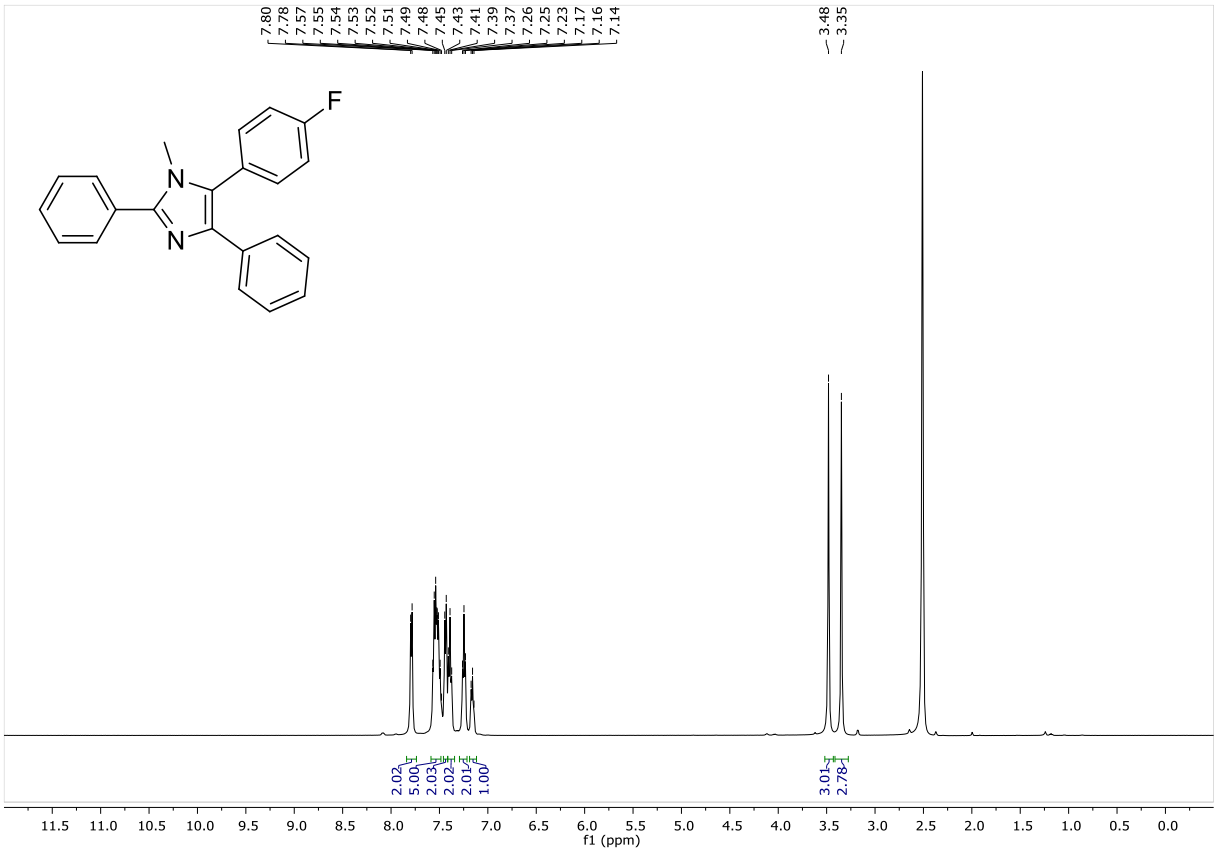


Figure S50. ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of the compound **4d**

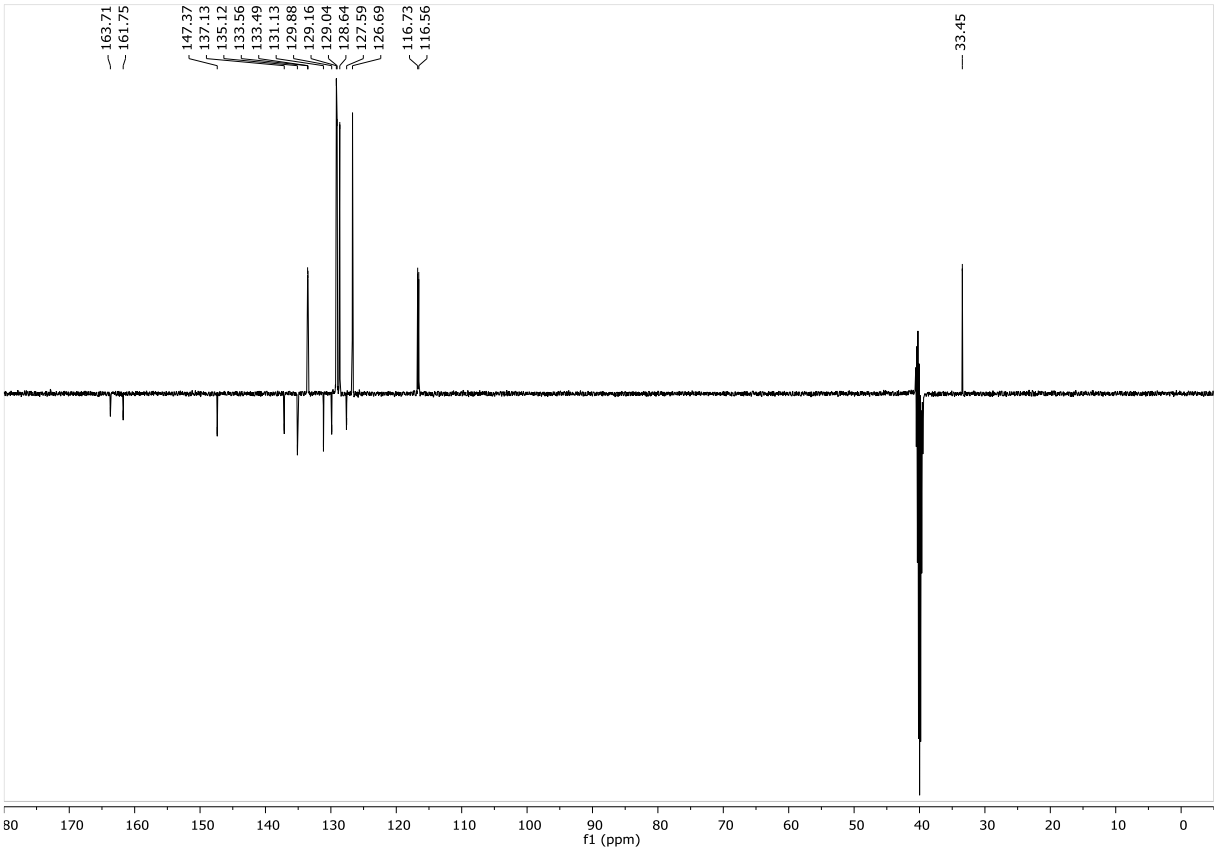


Figure S51. ^{13}C{^{1}H} NMR spectrum (126 MHz, DMSO-d_6) of the compound **4d**

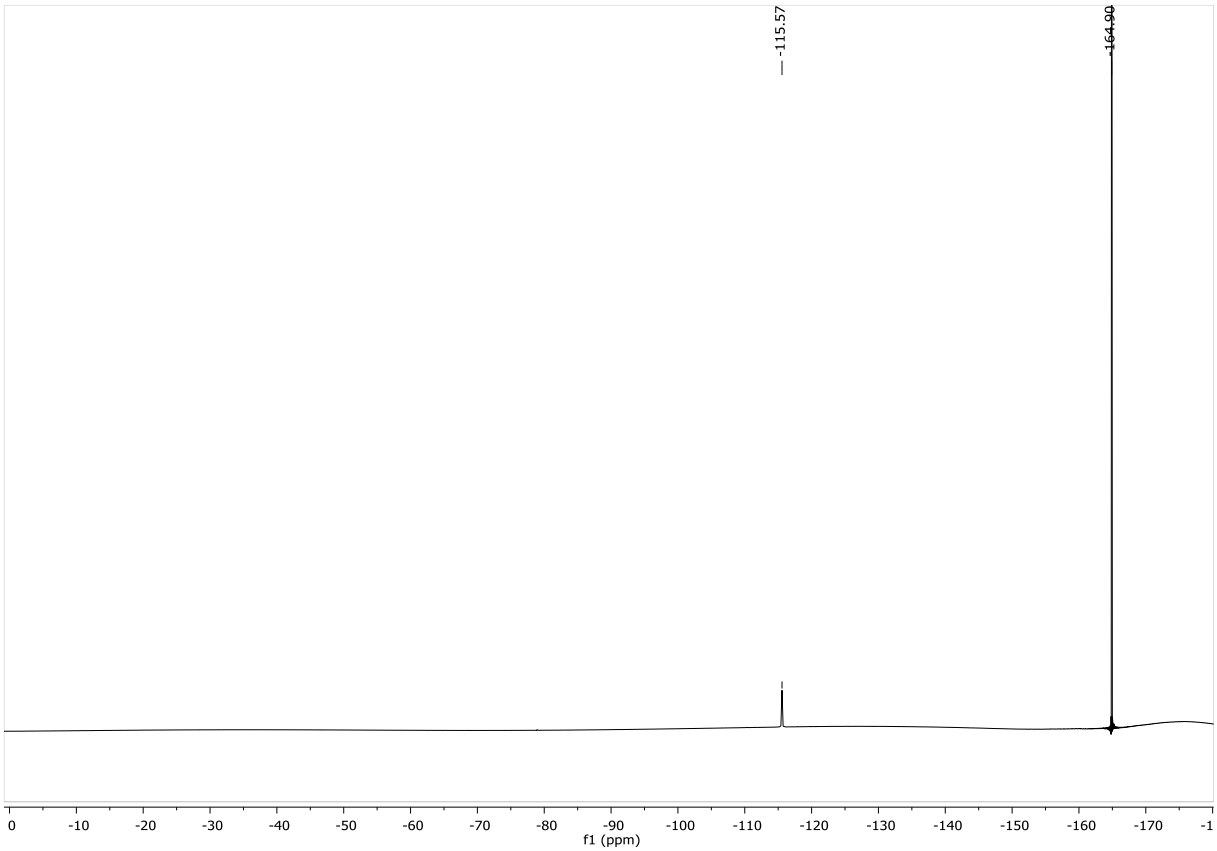


Figure S52. ^{19}F NMR spectrum (471 MHz, $CDCl_3$) of the compound **4d**

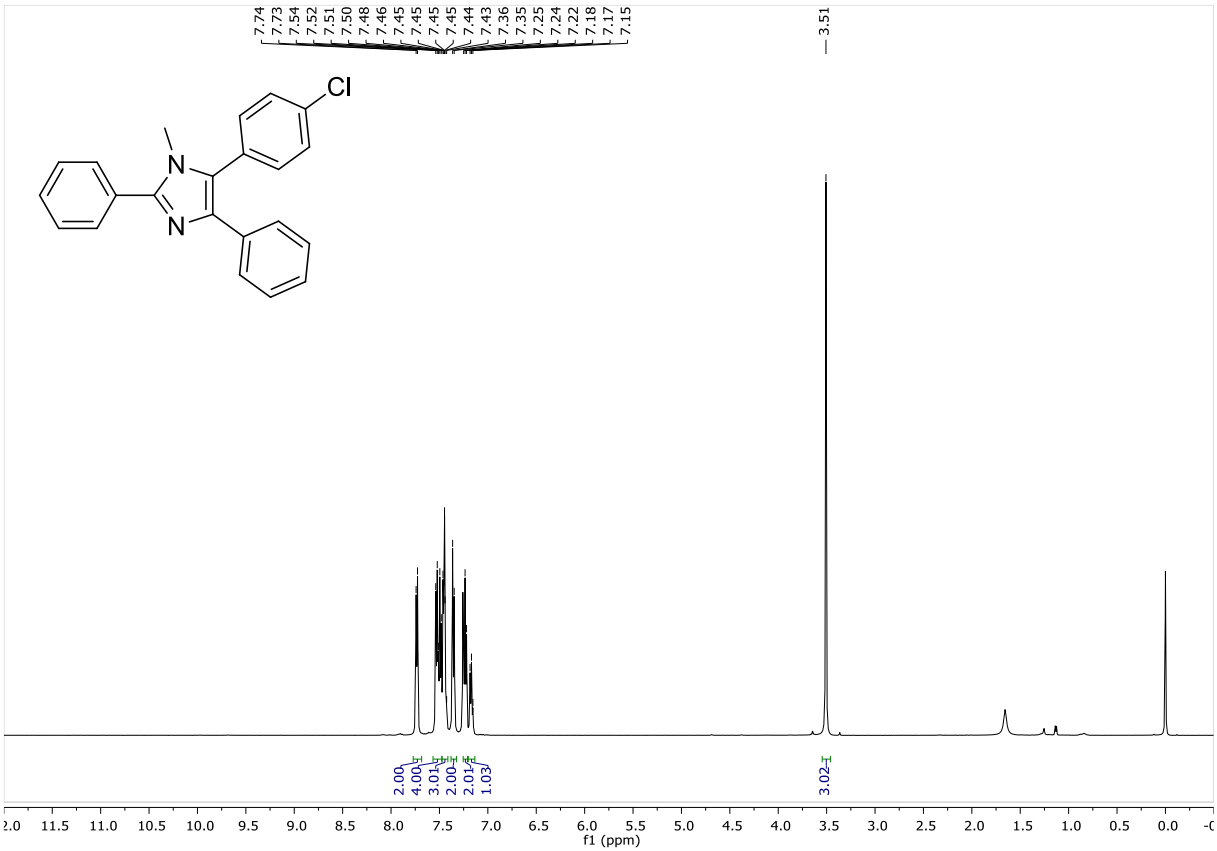


Figure S53. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **4e**

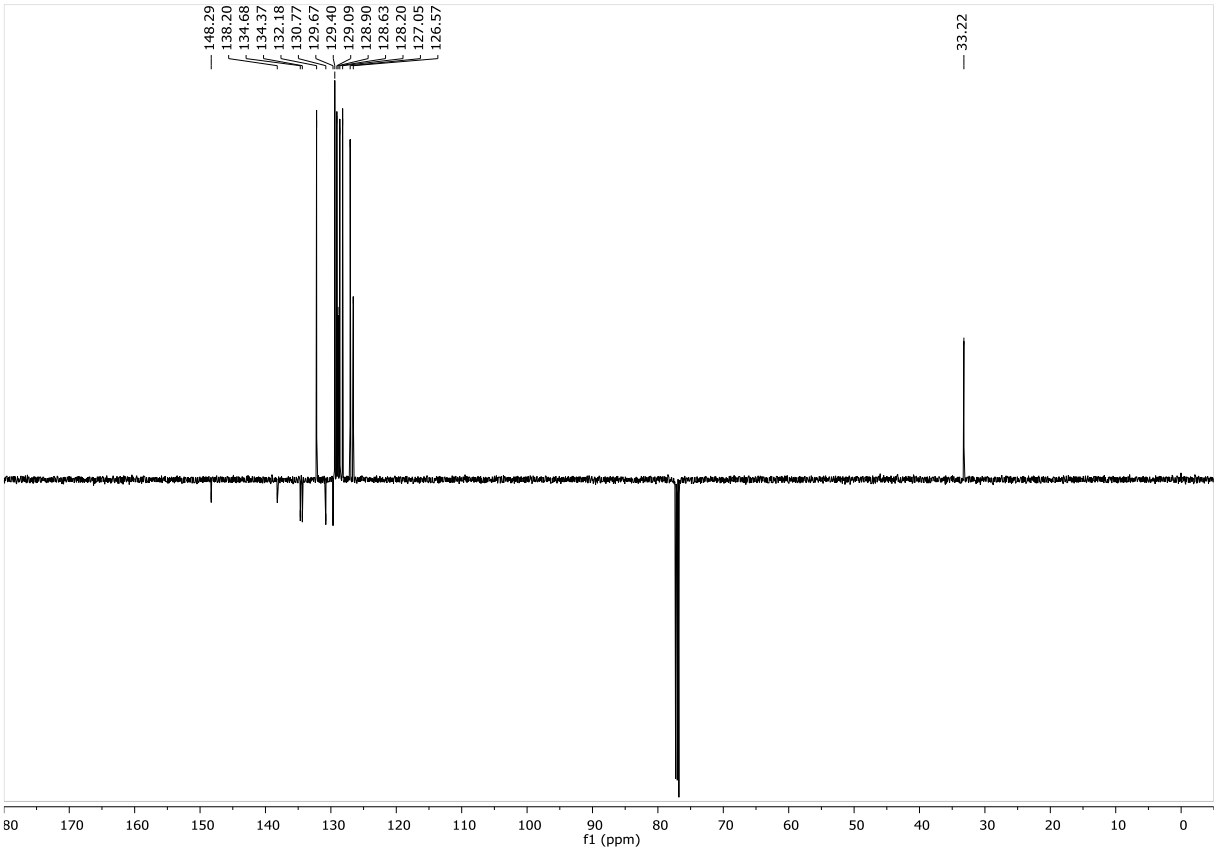


Figure S54. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **4e**

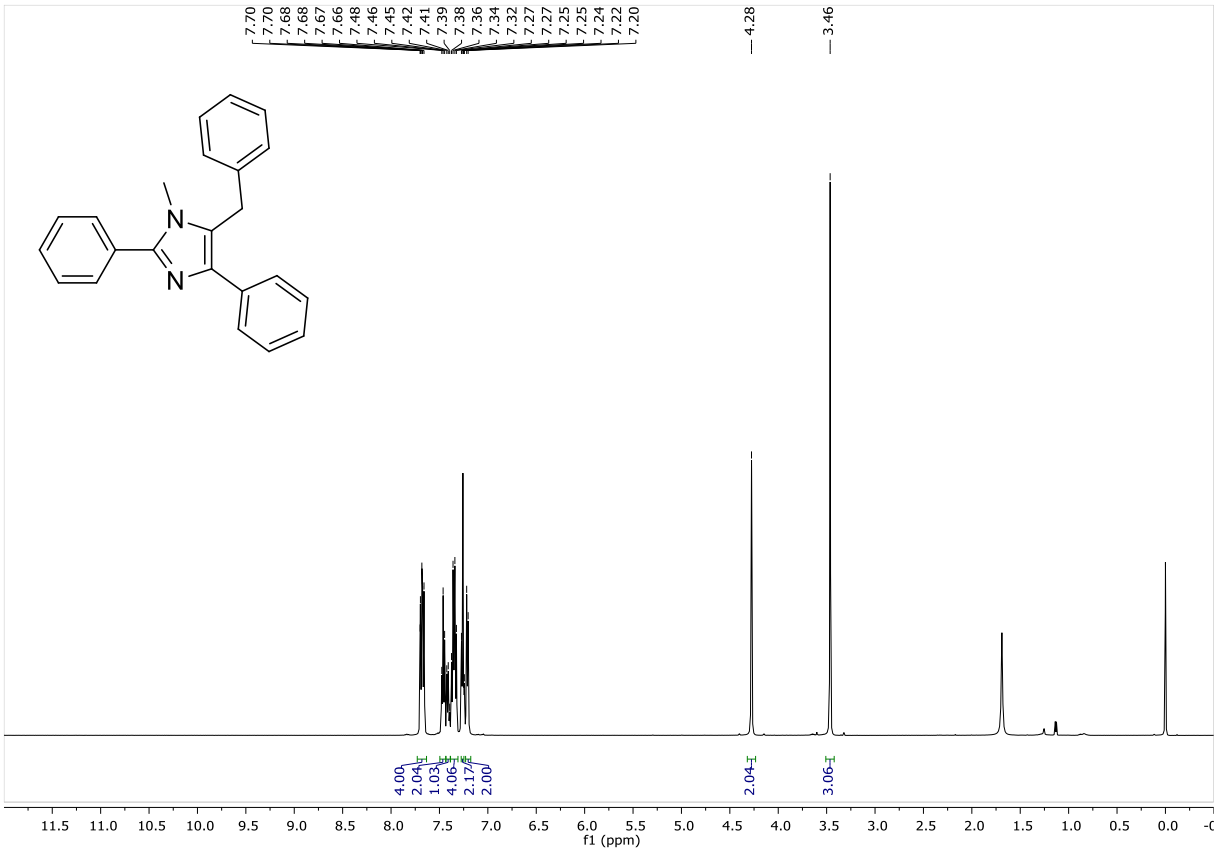


Figure S55. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **4f**

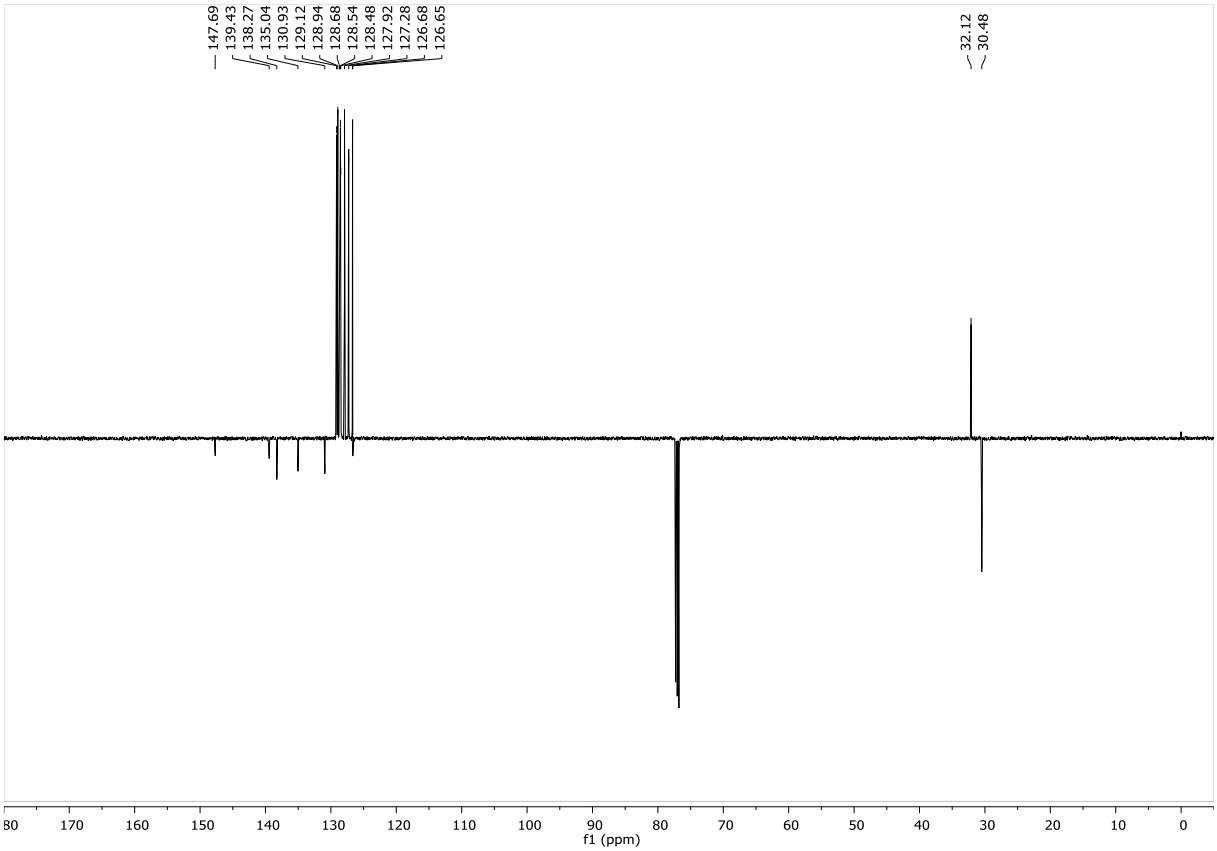


Figure S56. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **4f**

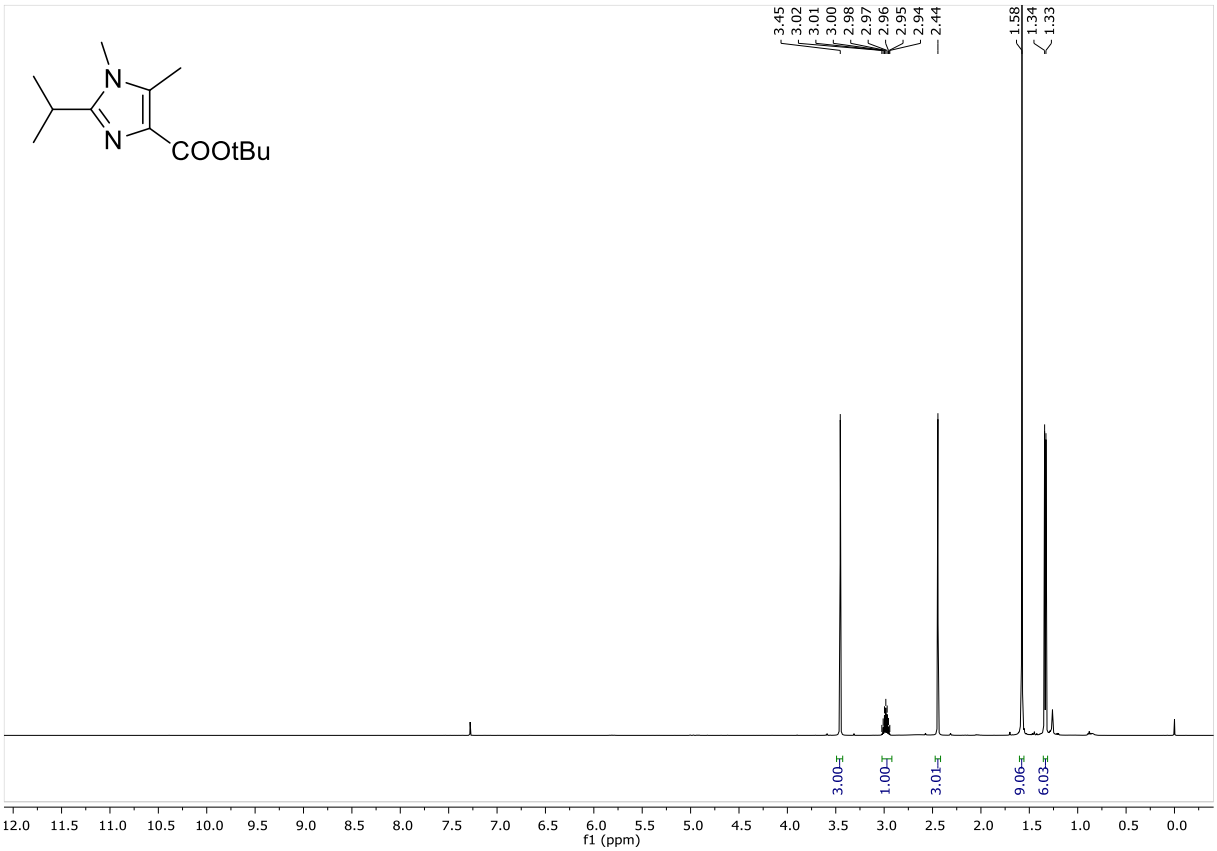


Figure S57. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **5a**

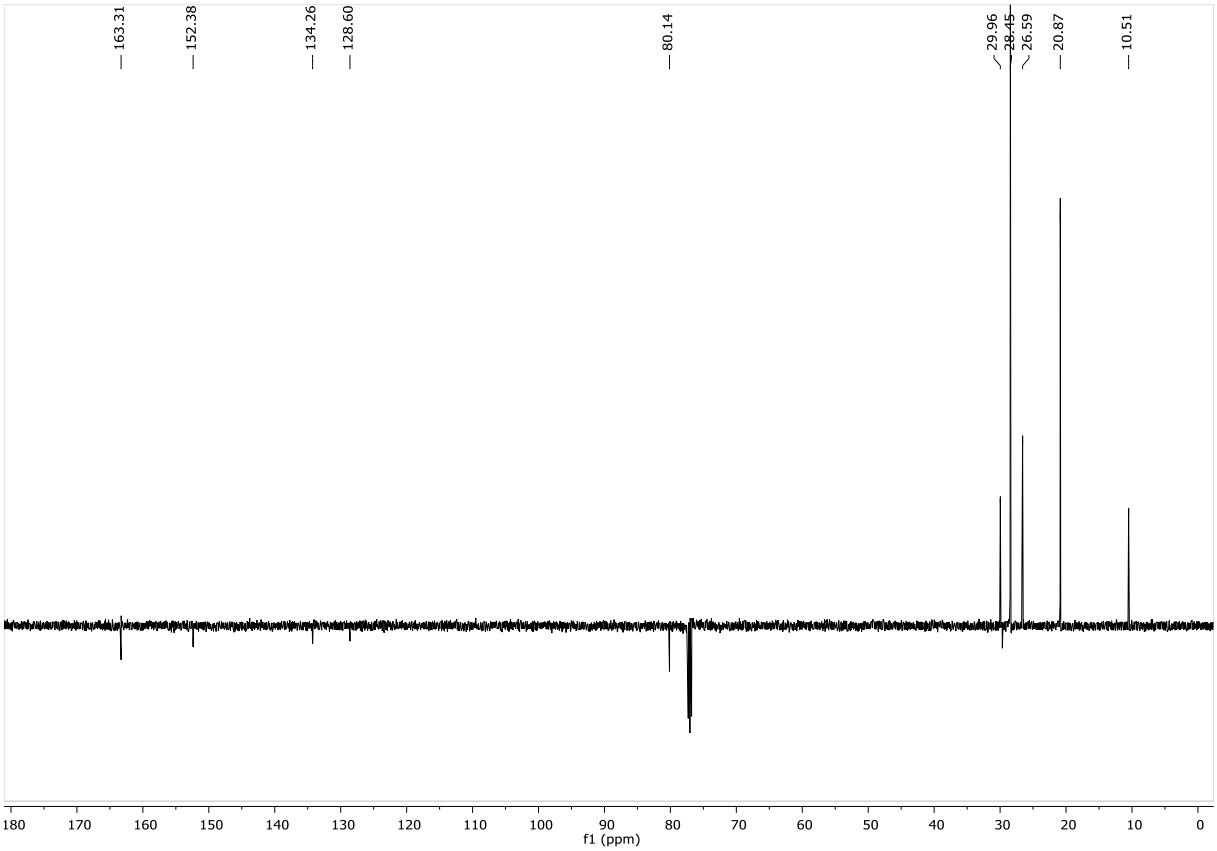


Figure S58. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **5a**

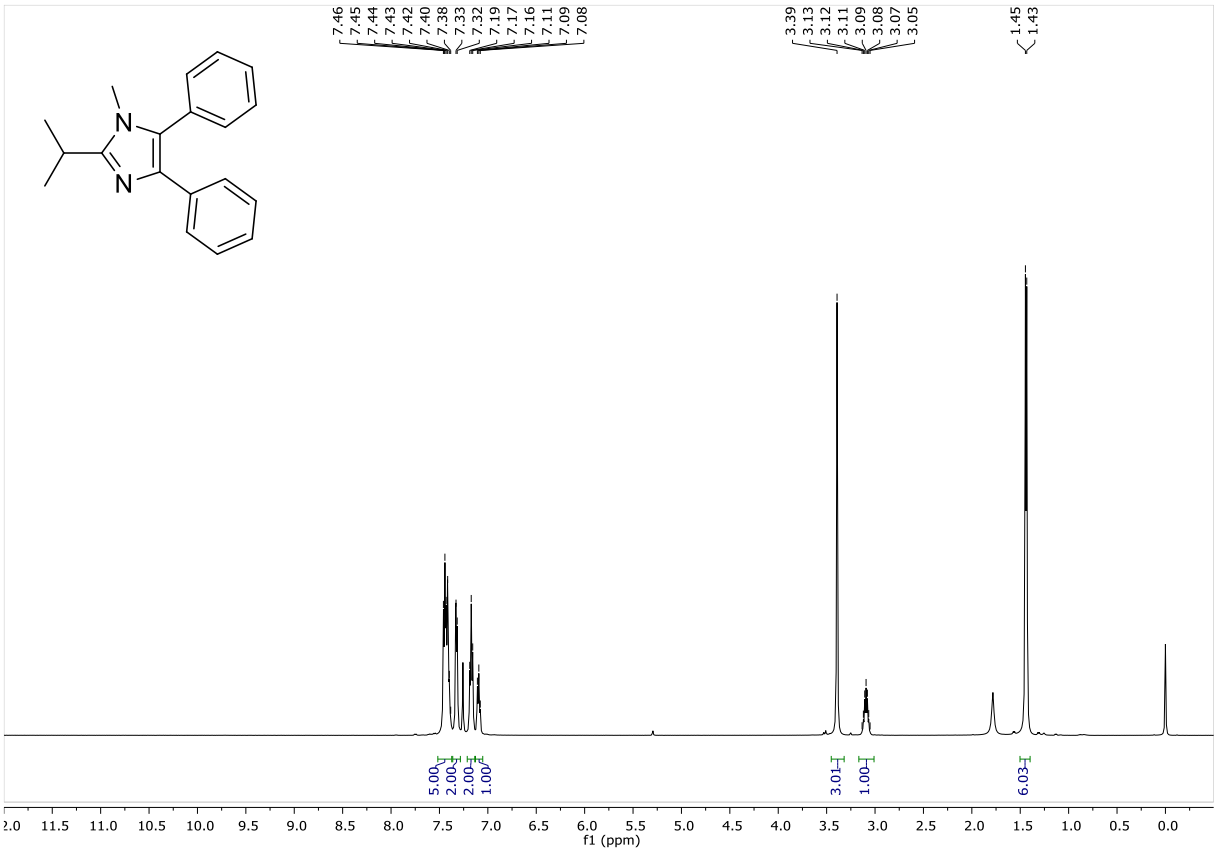


Figure S59. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **5b**

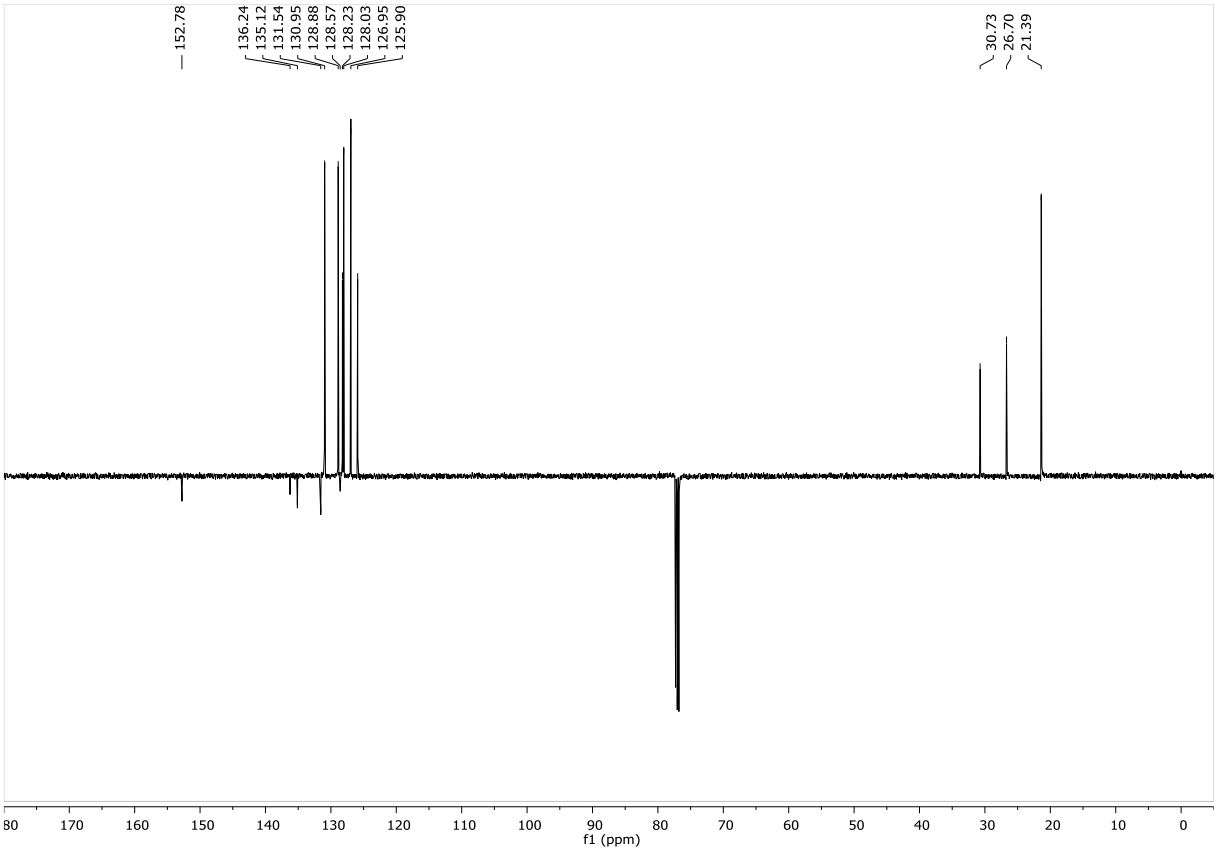


Figure S60. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **5b**

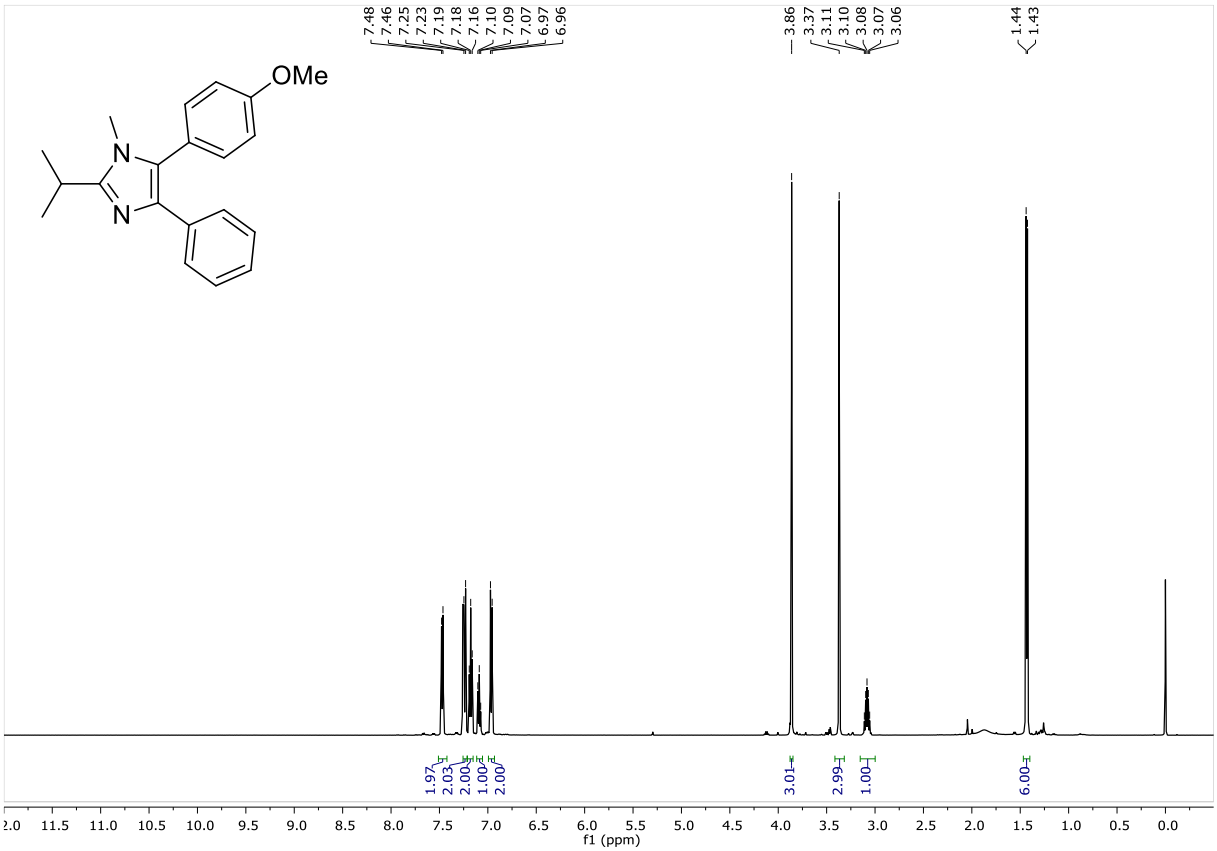


Figure S61. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **5c**

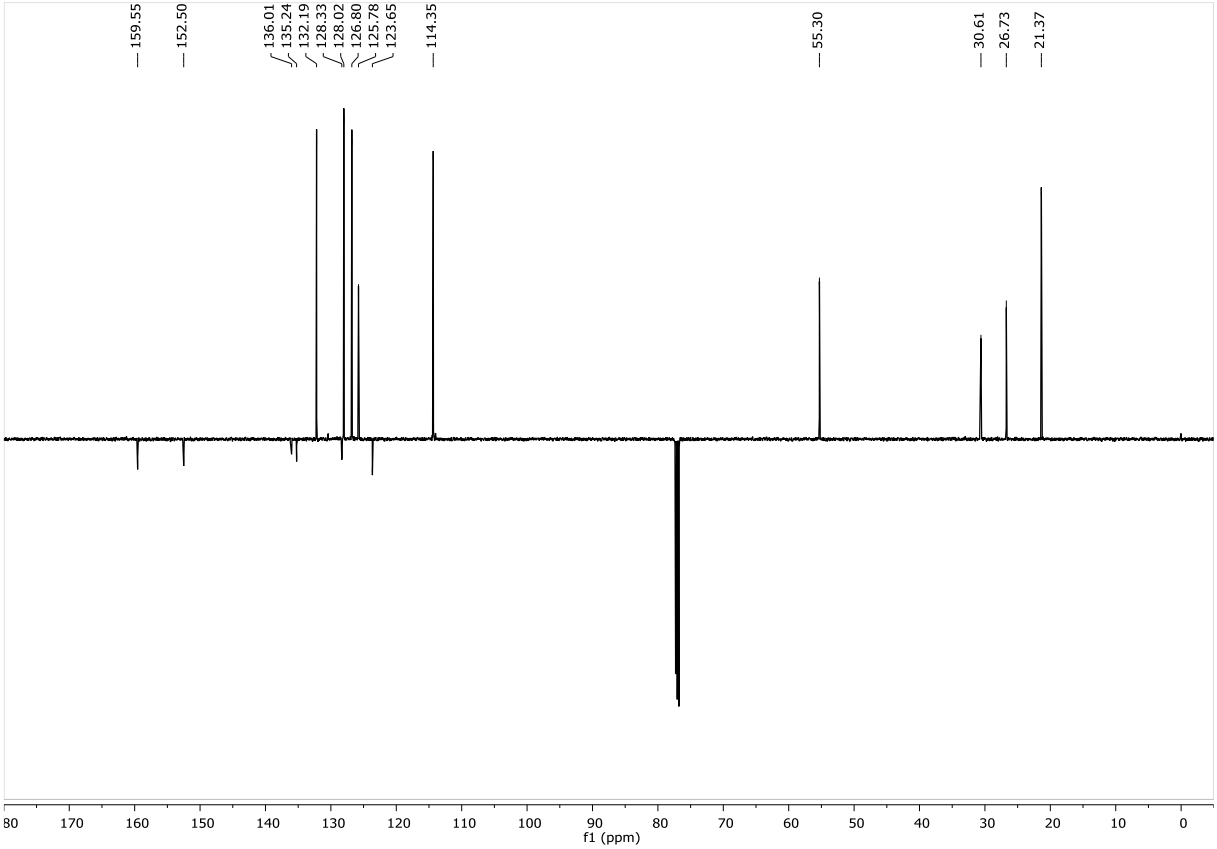


Figure S62. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **5c**

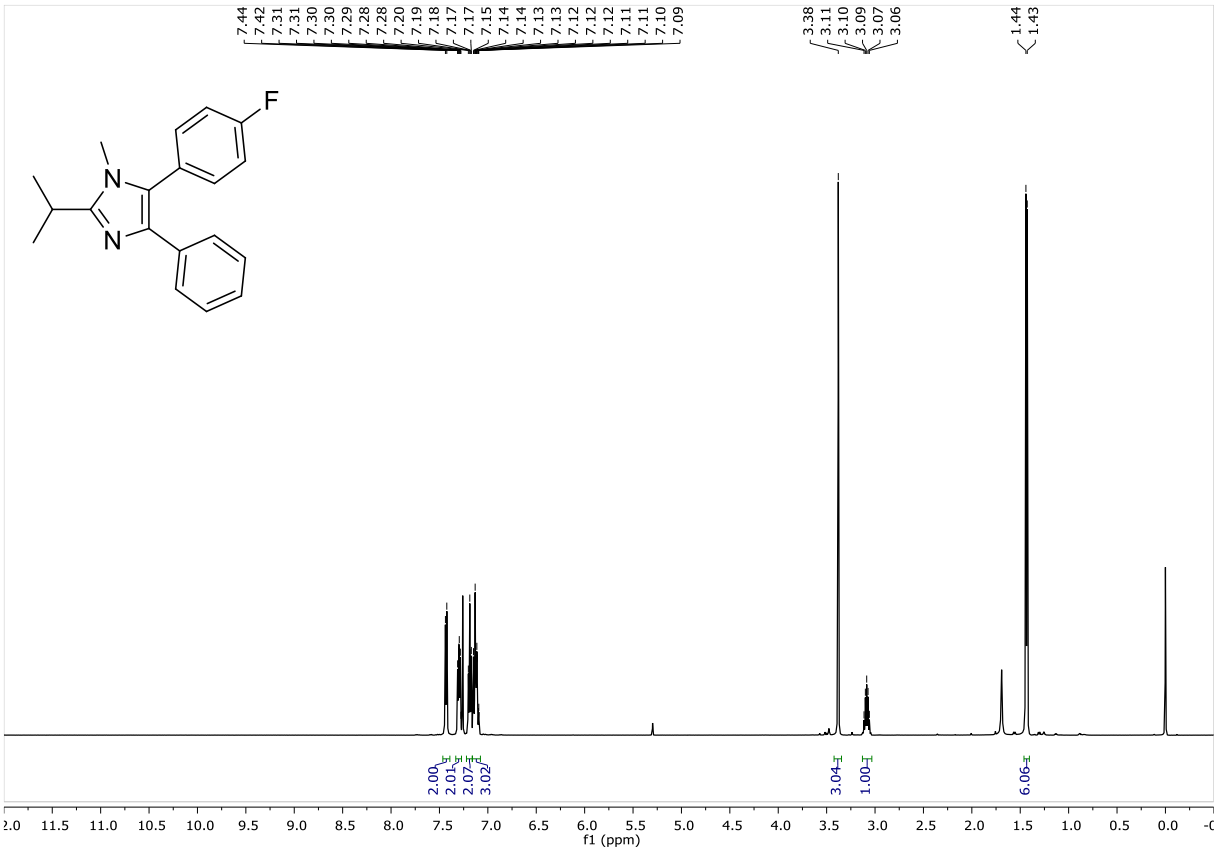


Figure S63. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **5d**

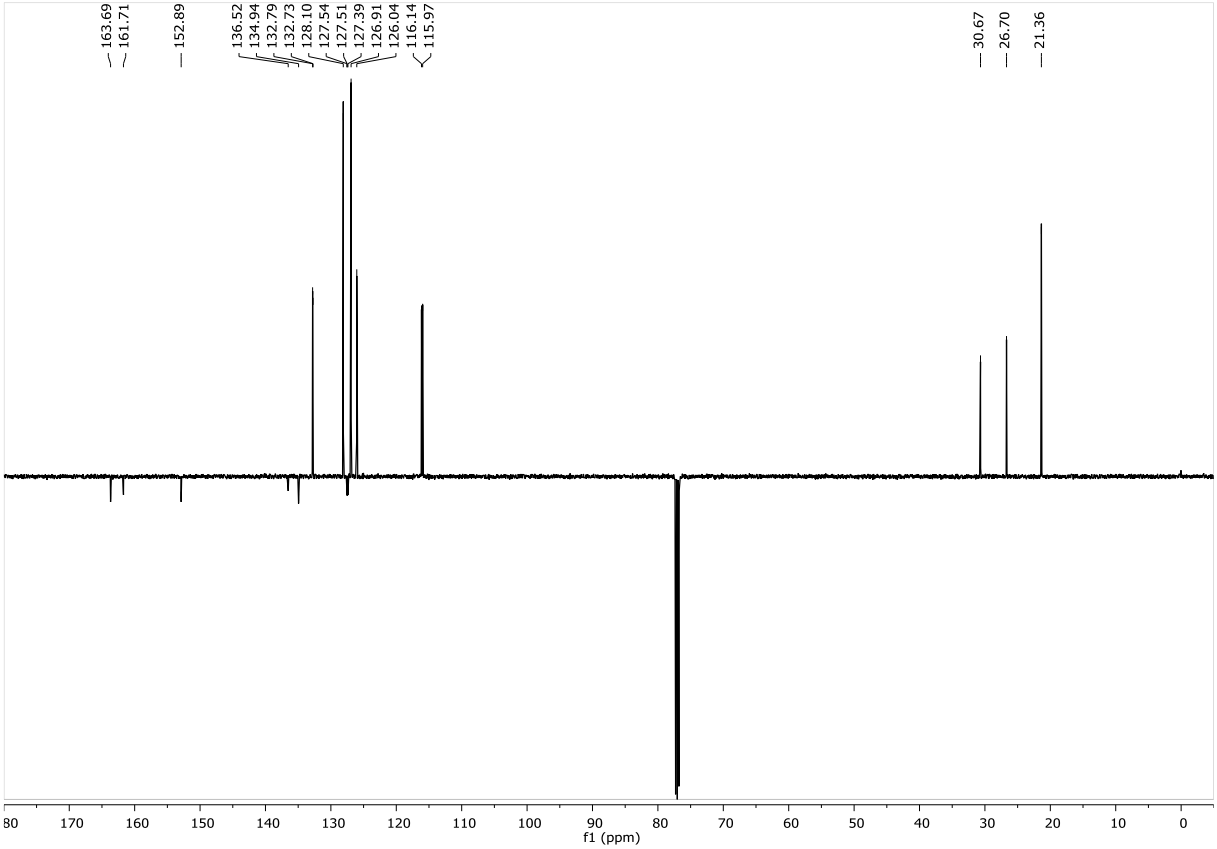


Figure S64. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **5d**

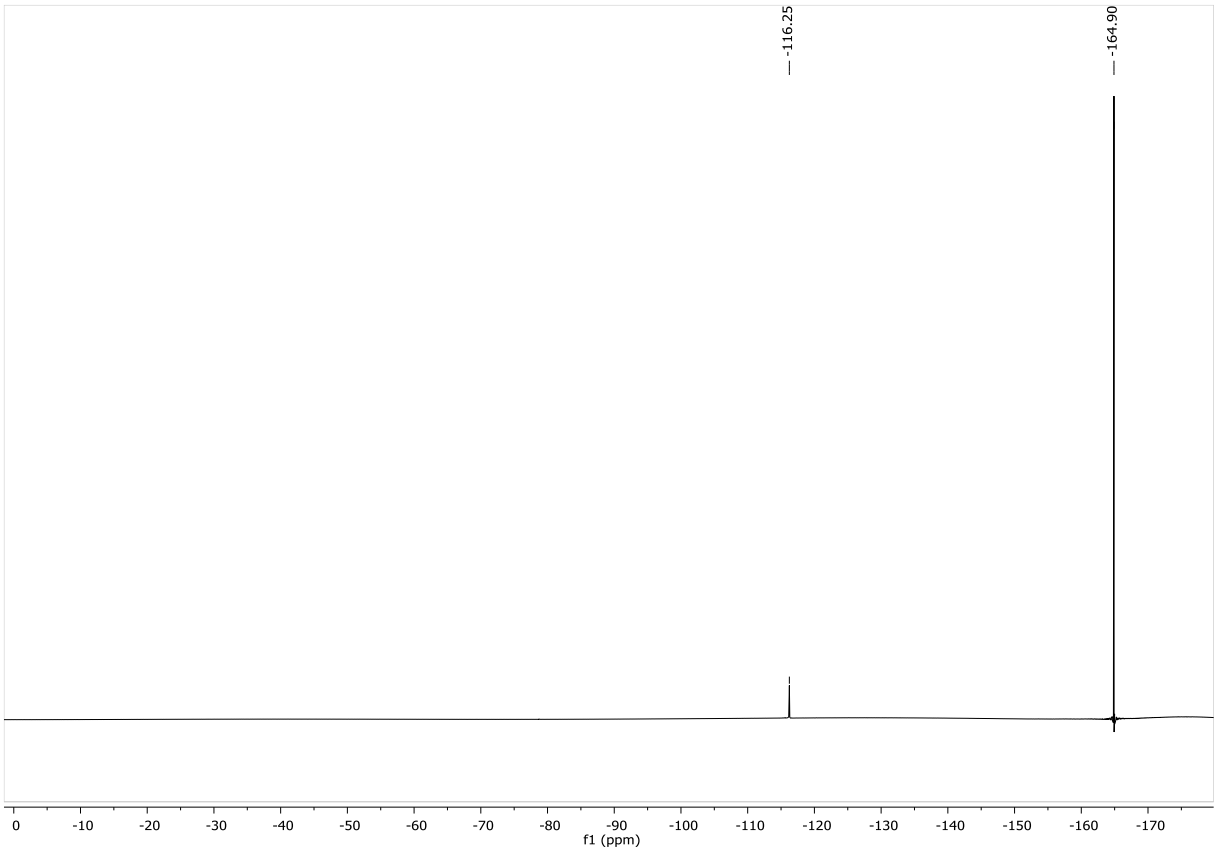


Figure S65. ^{19}F NMR spectrum (471 MHz, $CDCl_3$) of the compound **5d**

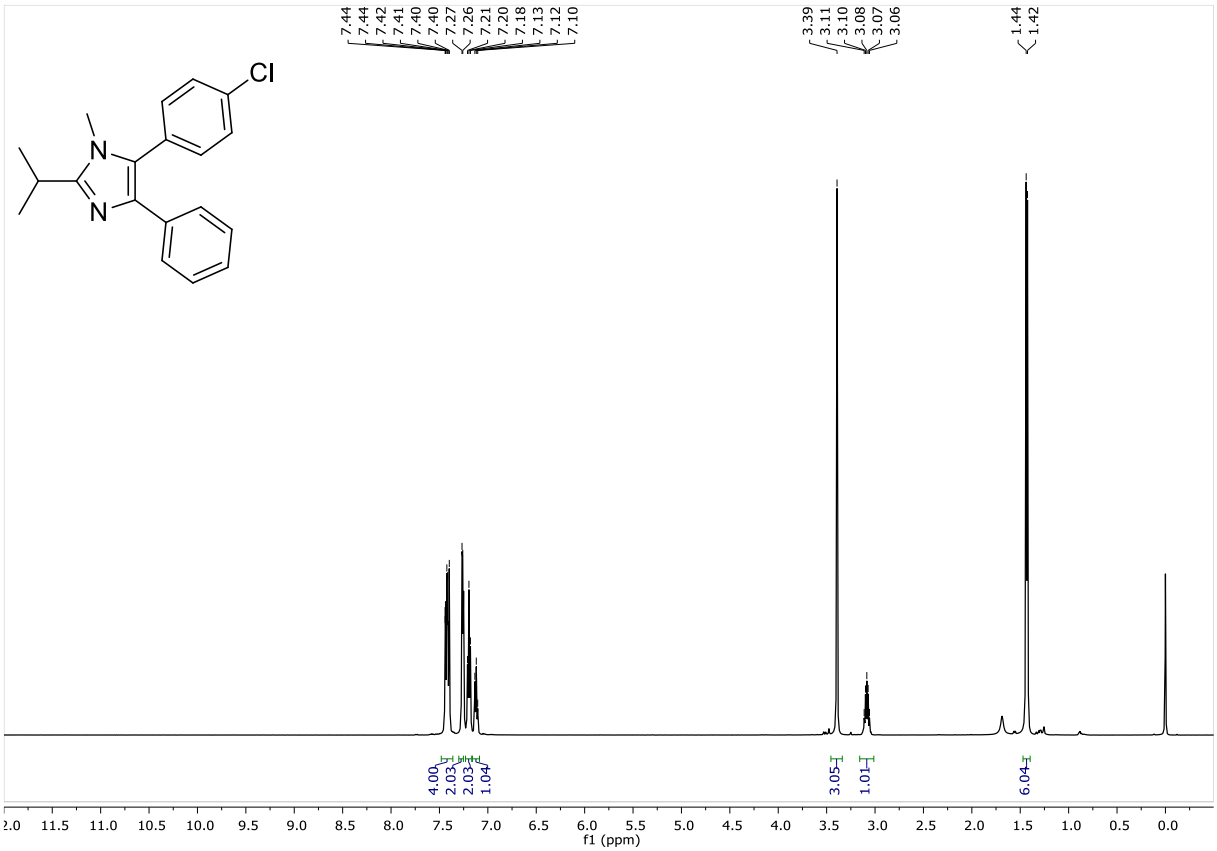


Figure S66. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **5e**

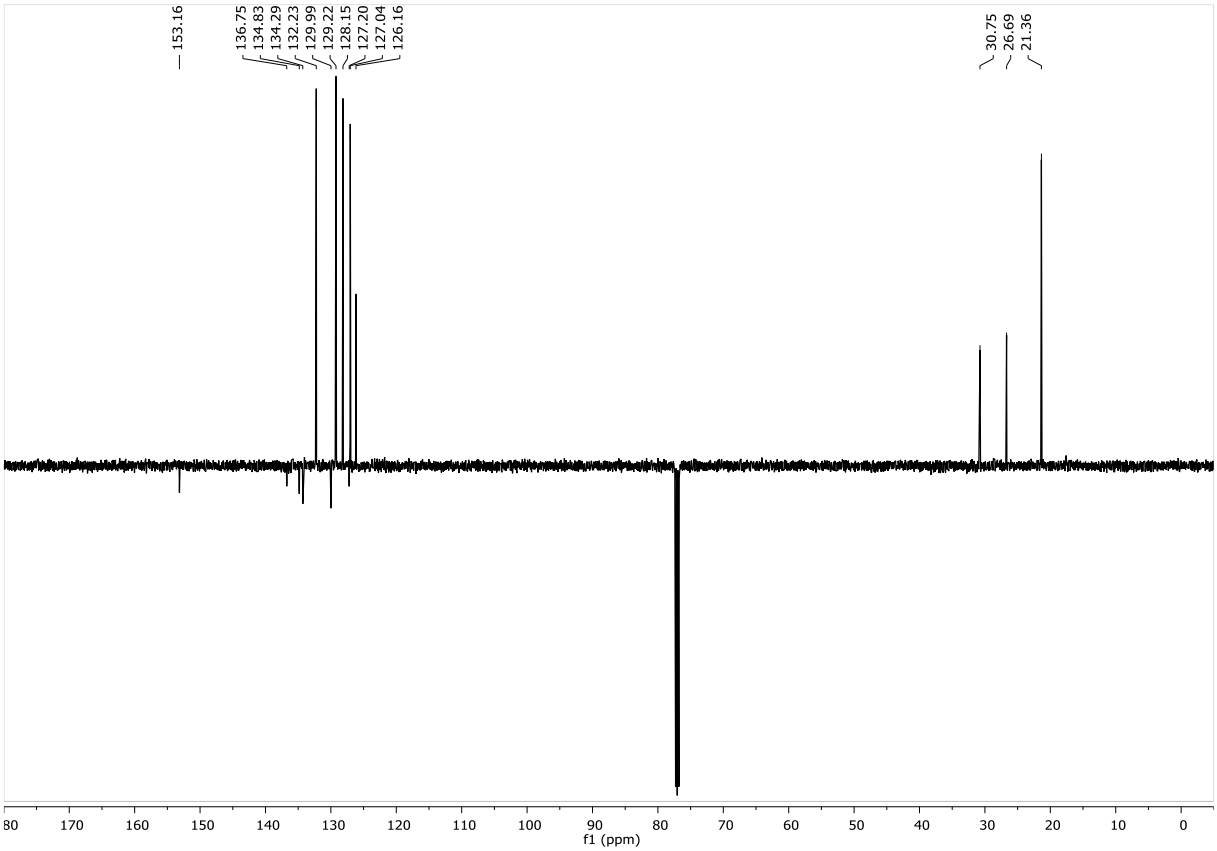


Figure S67. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **5e**

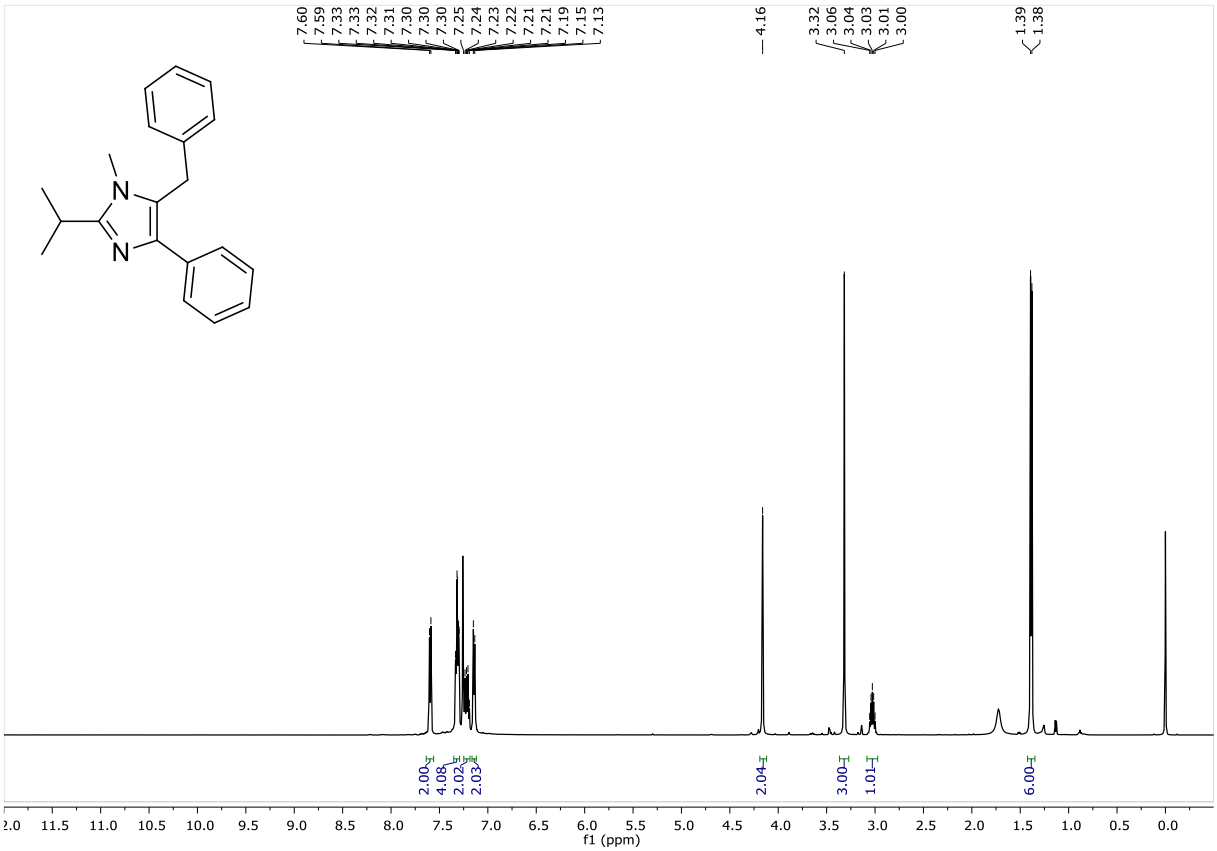


Figure S68. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **5f**

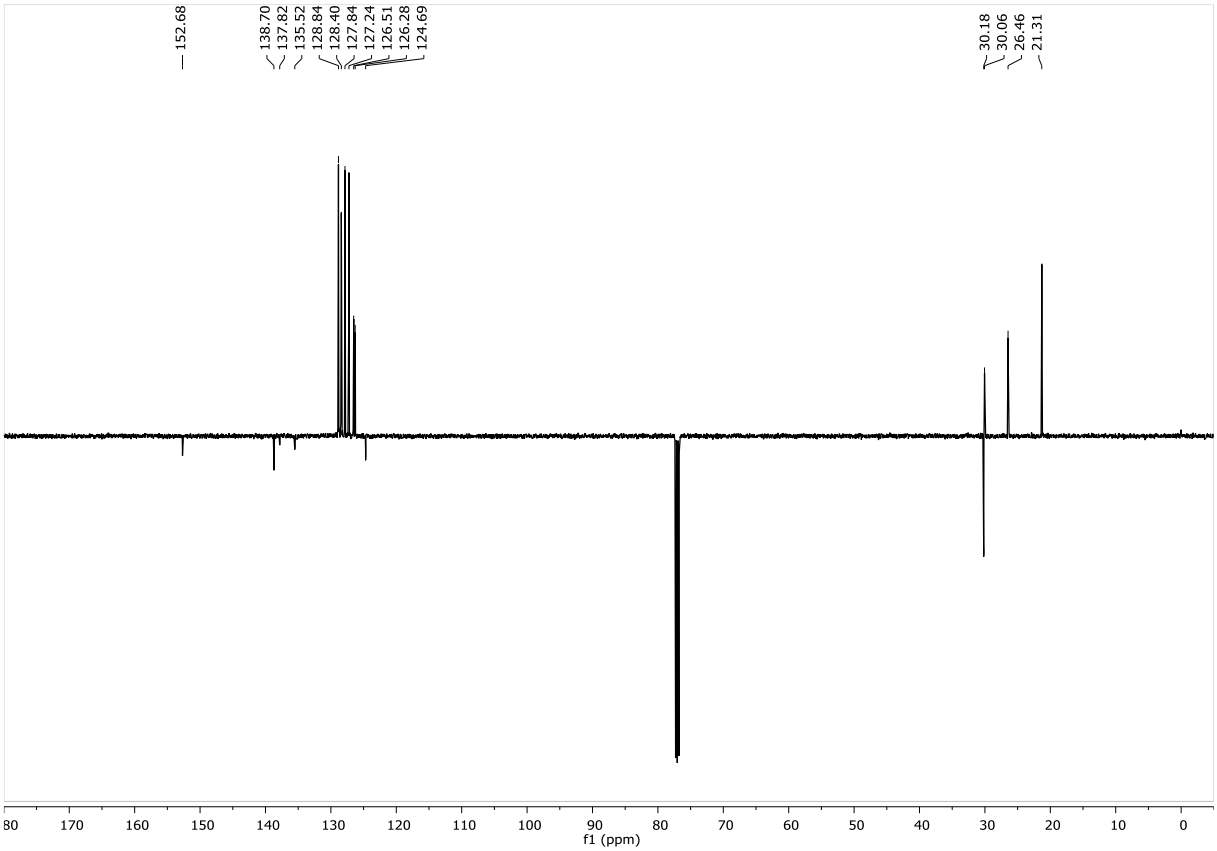


Figure S69. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **5f**

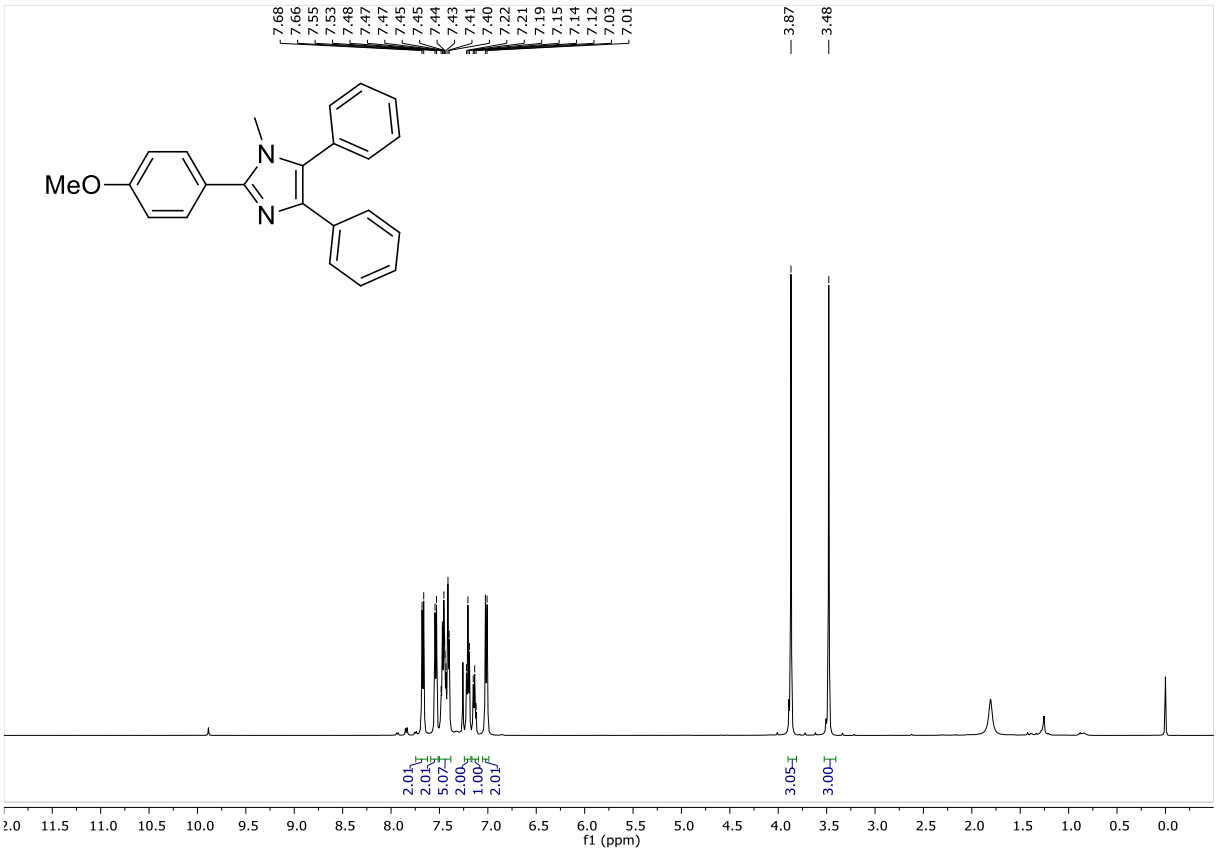


Figure S70. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6a**

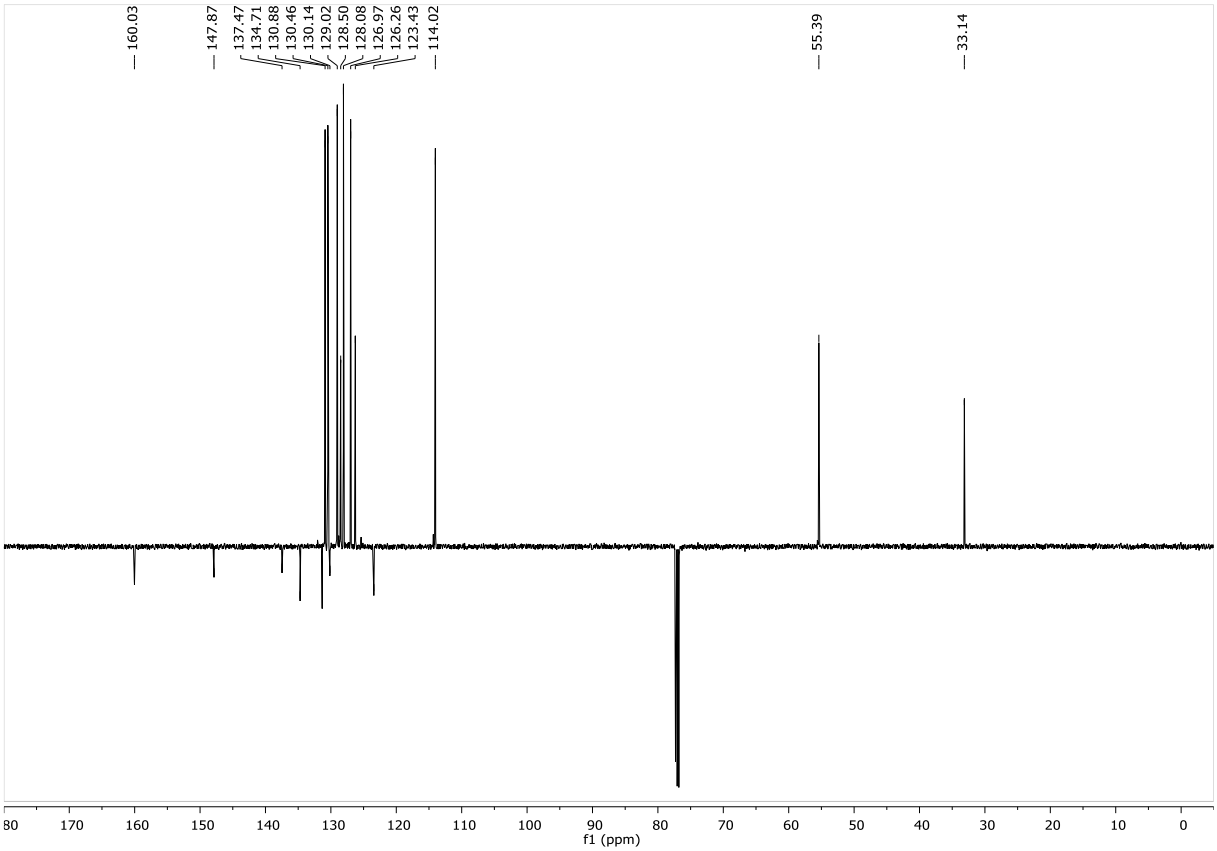


Figure S71. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **6a**

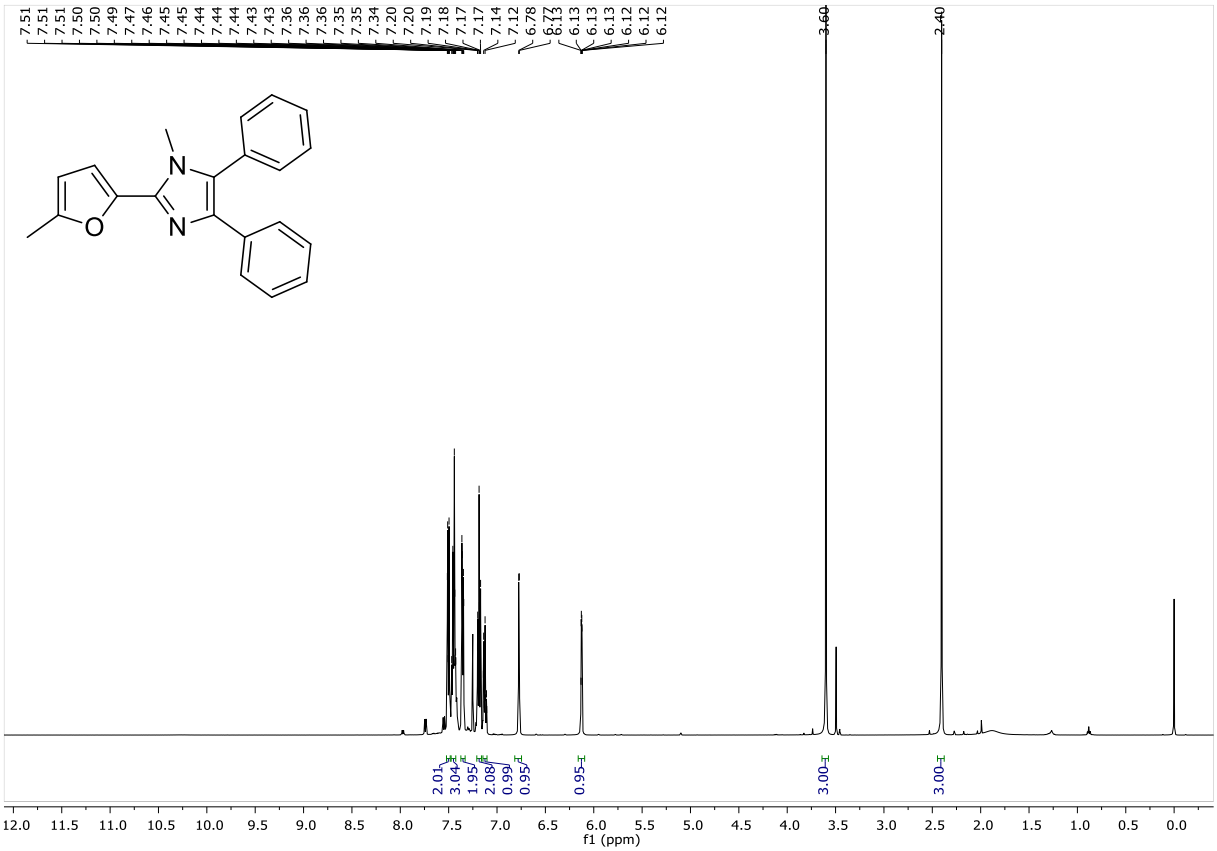


Figure S72. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6b**

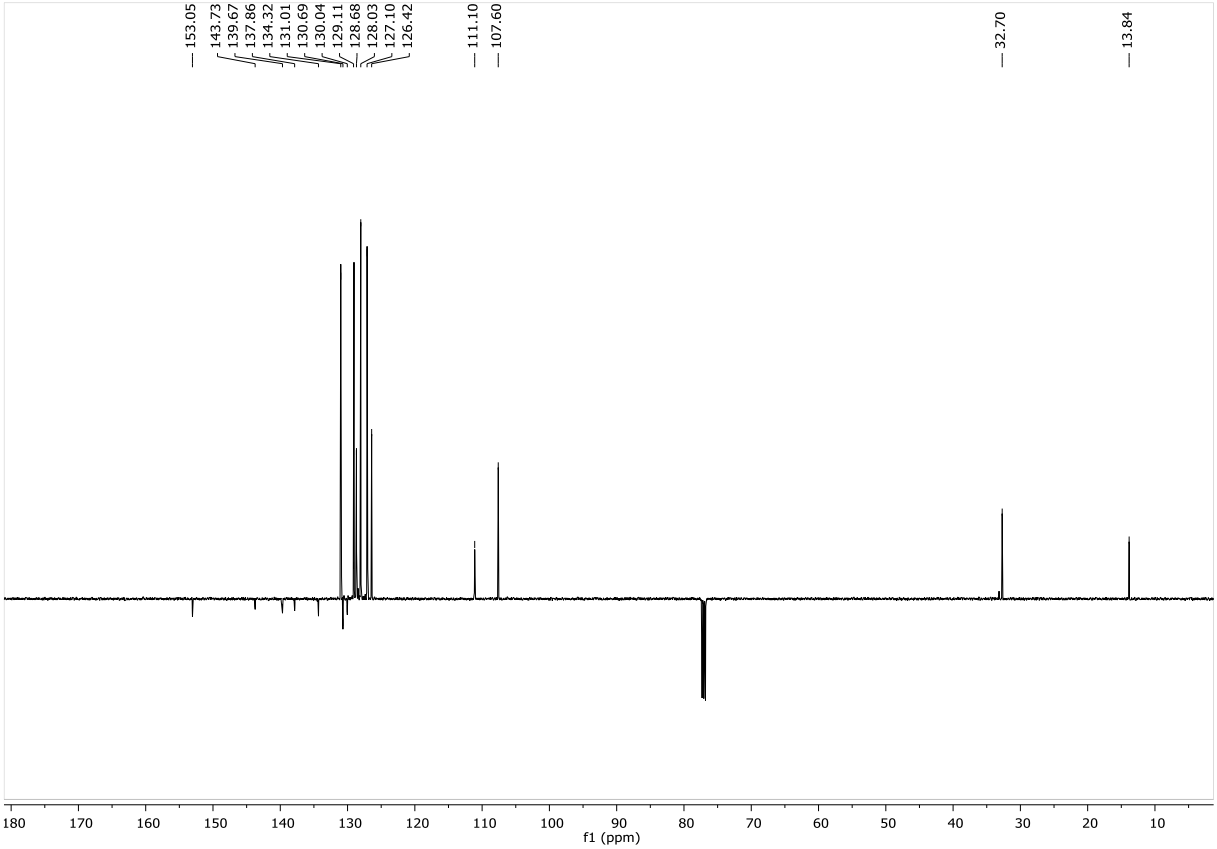


Figure S73. $^{13}C\{^{1}H\}$ NMR spectrum (126 MHz, $CDCl_3$) of the compound **6b**

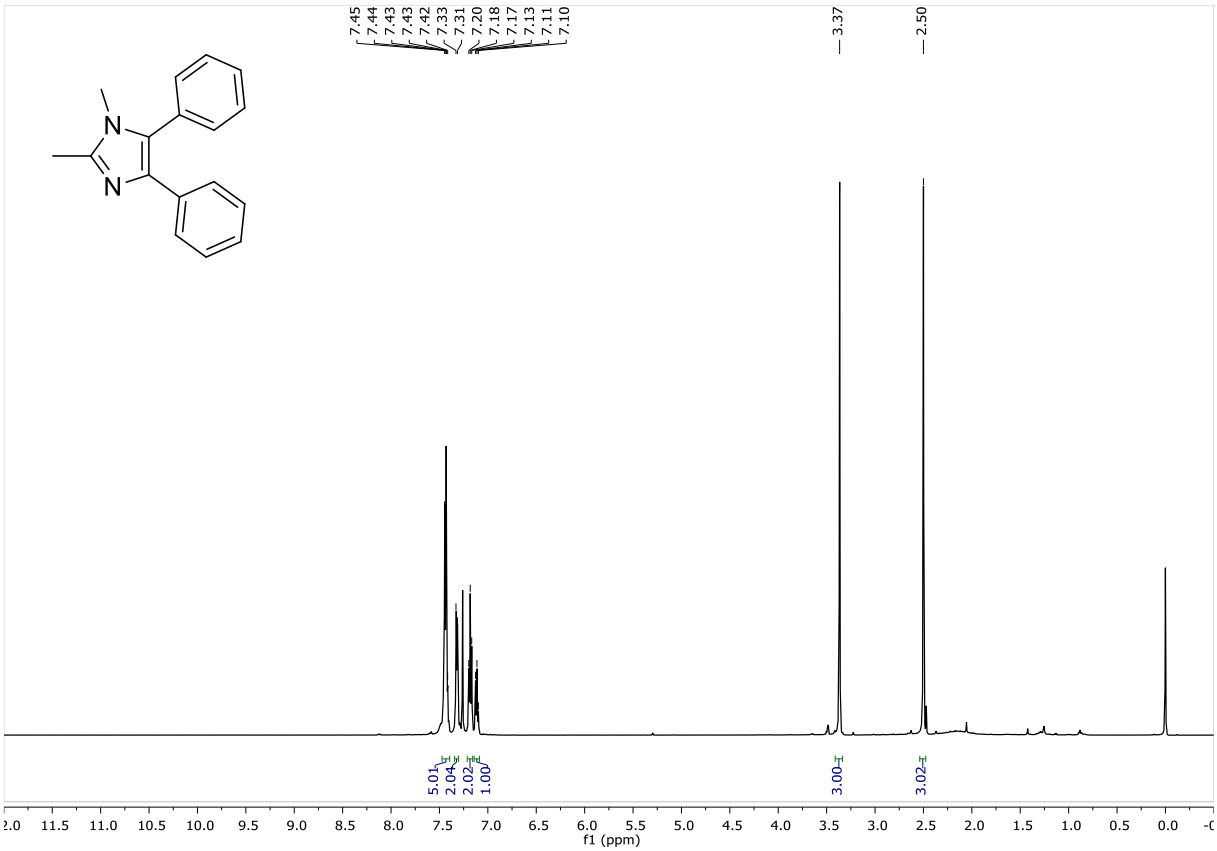


Figure S74. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6c**

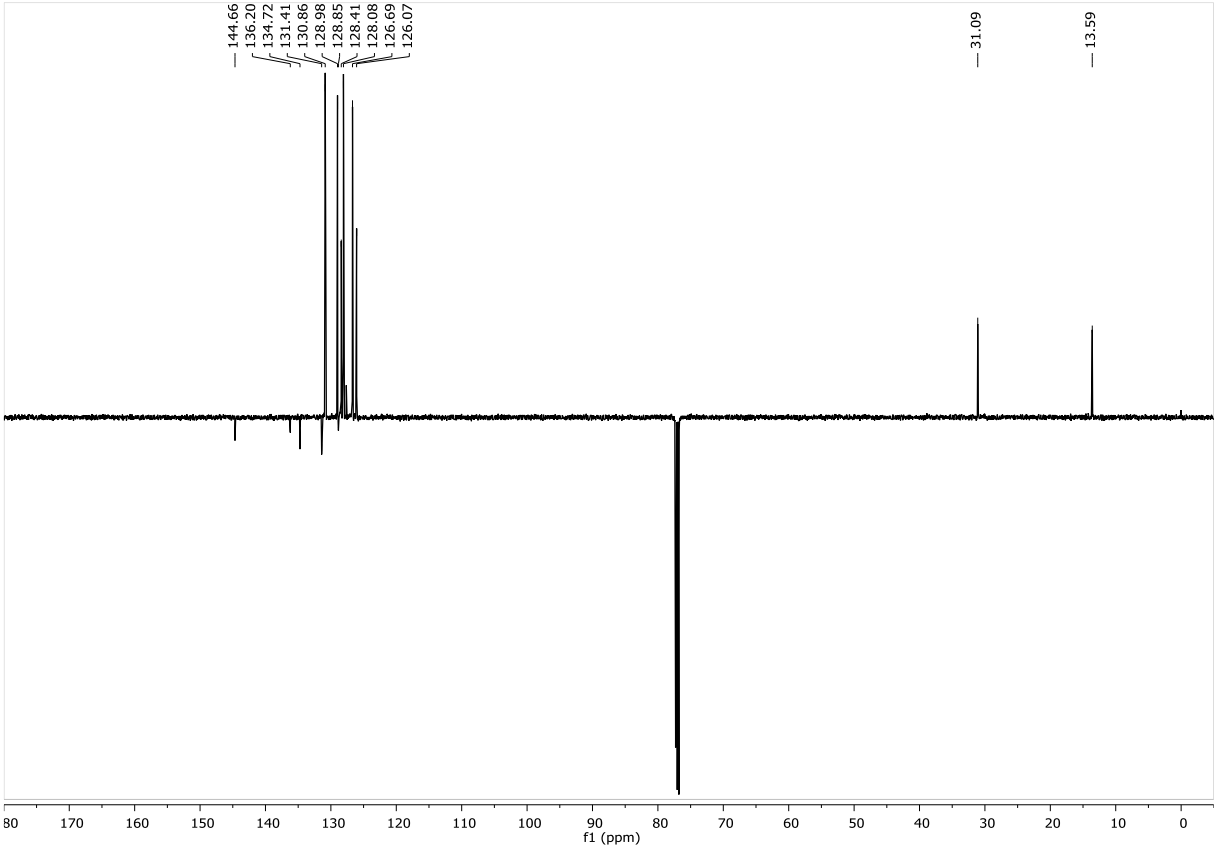


Figure S75. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **6c**

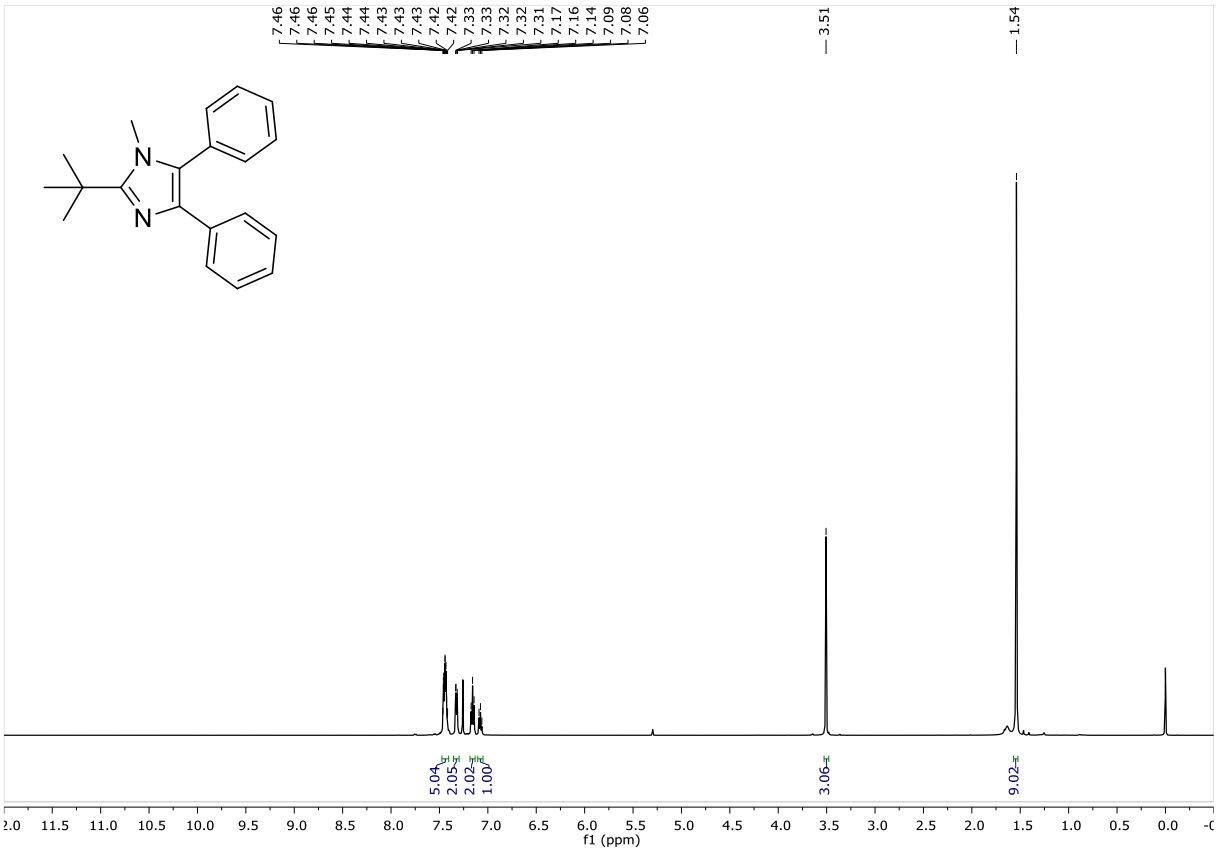


Figure S76. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6d**

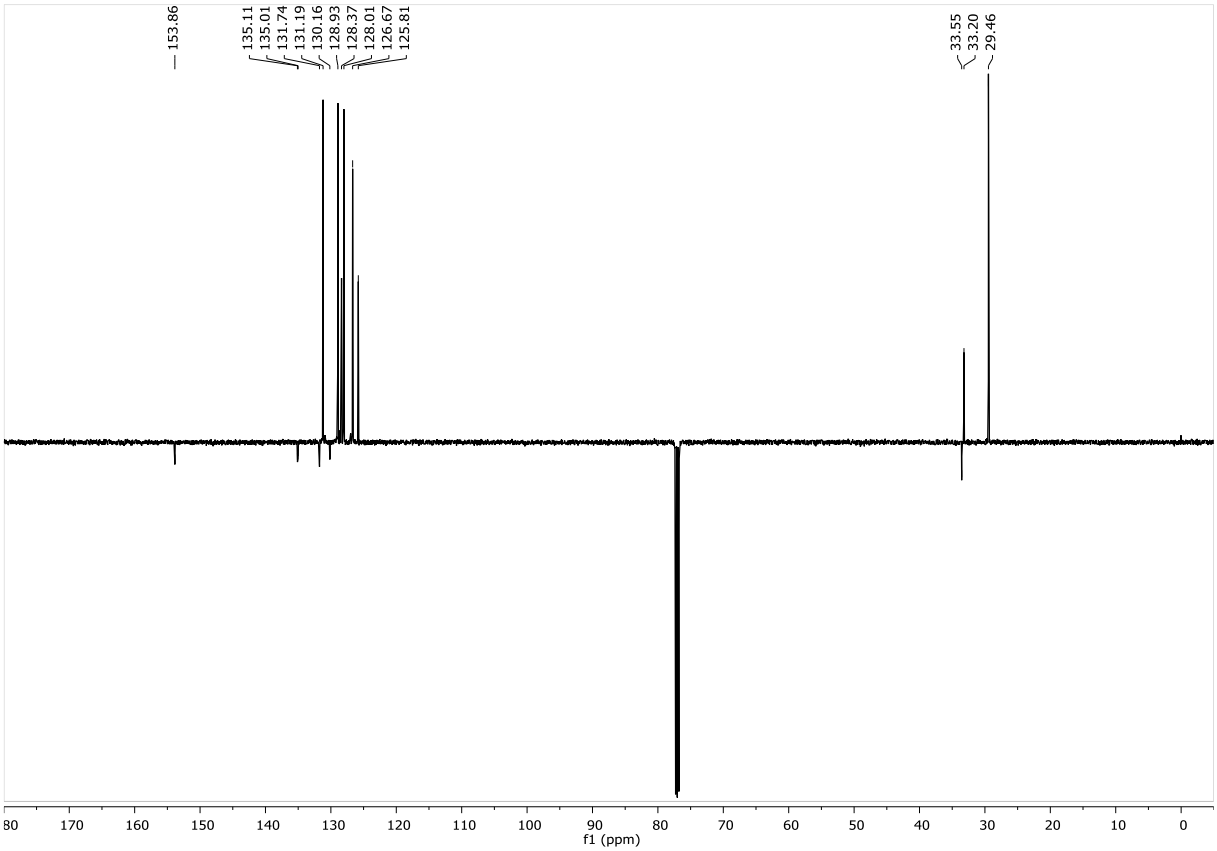


Figure S77. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **6d**

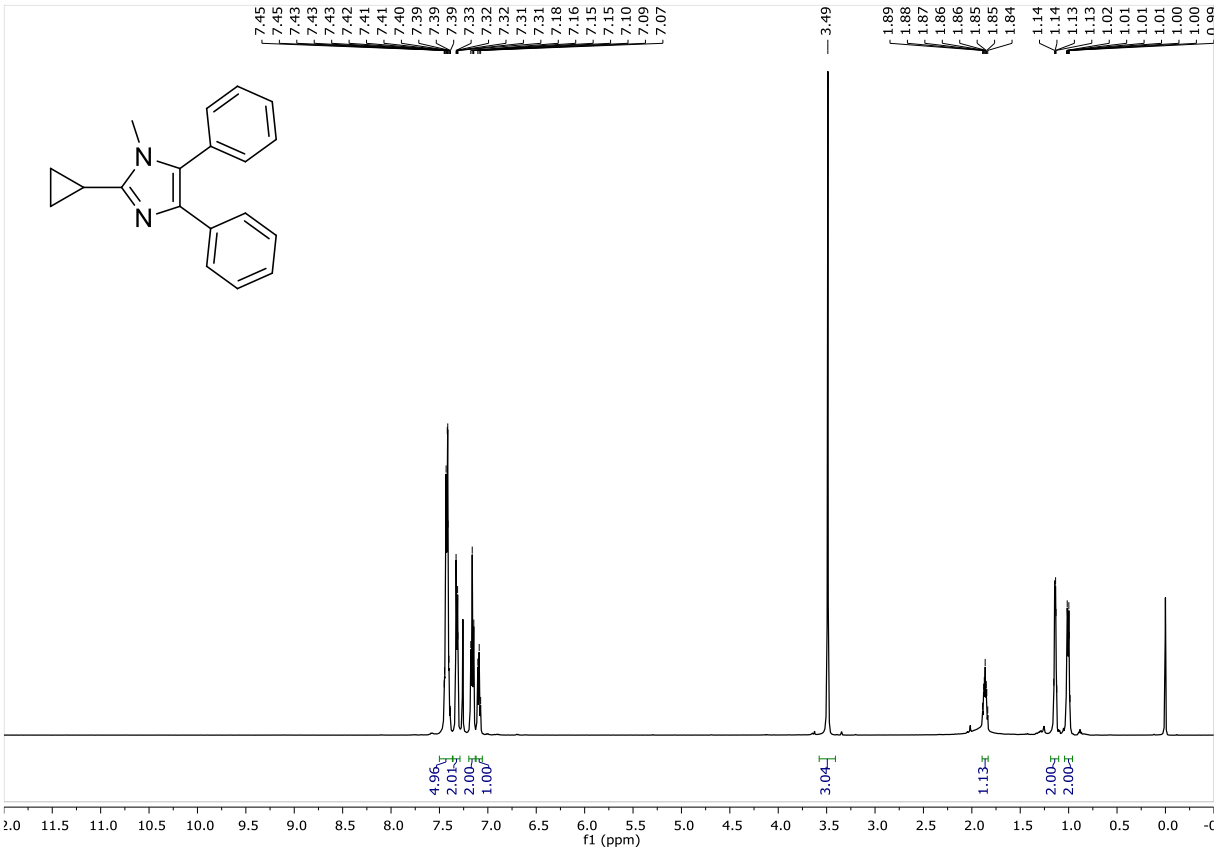


Figure S78. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6e**

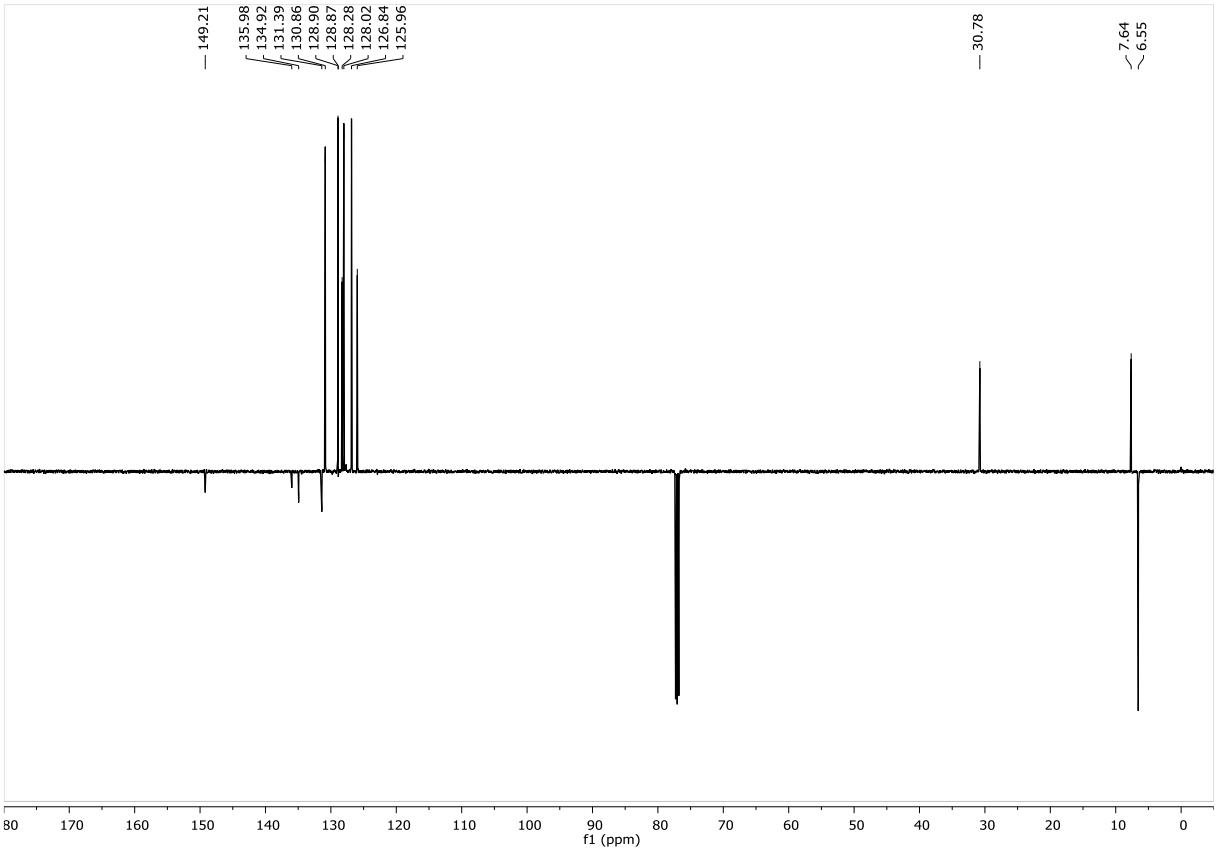


Figure S79. $^{13}C\{^{1}H\}$ NMR spectrum (126 MHz, $CDCl_3$) of the compound **6e**

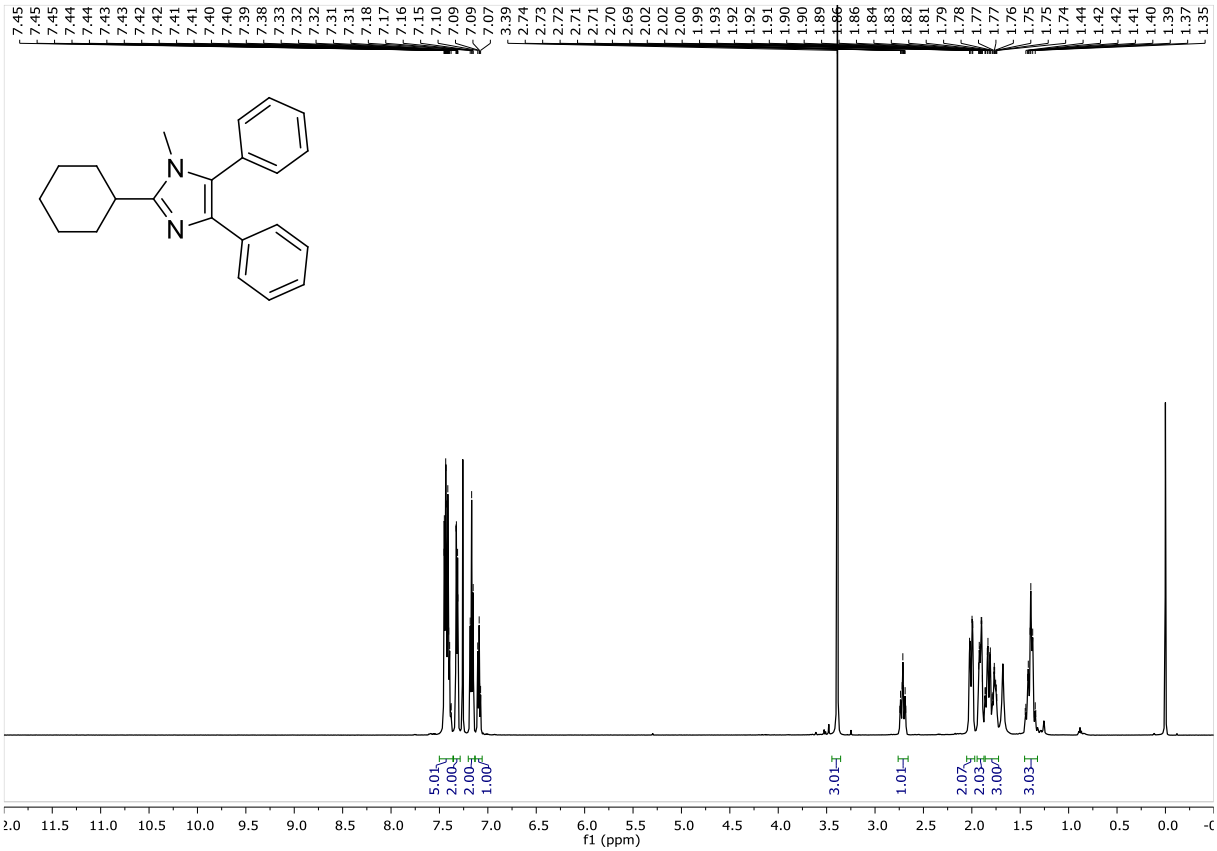


Figure S80. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6f**

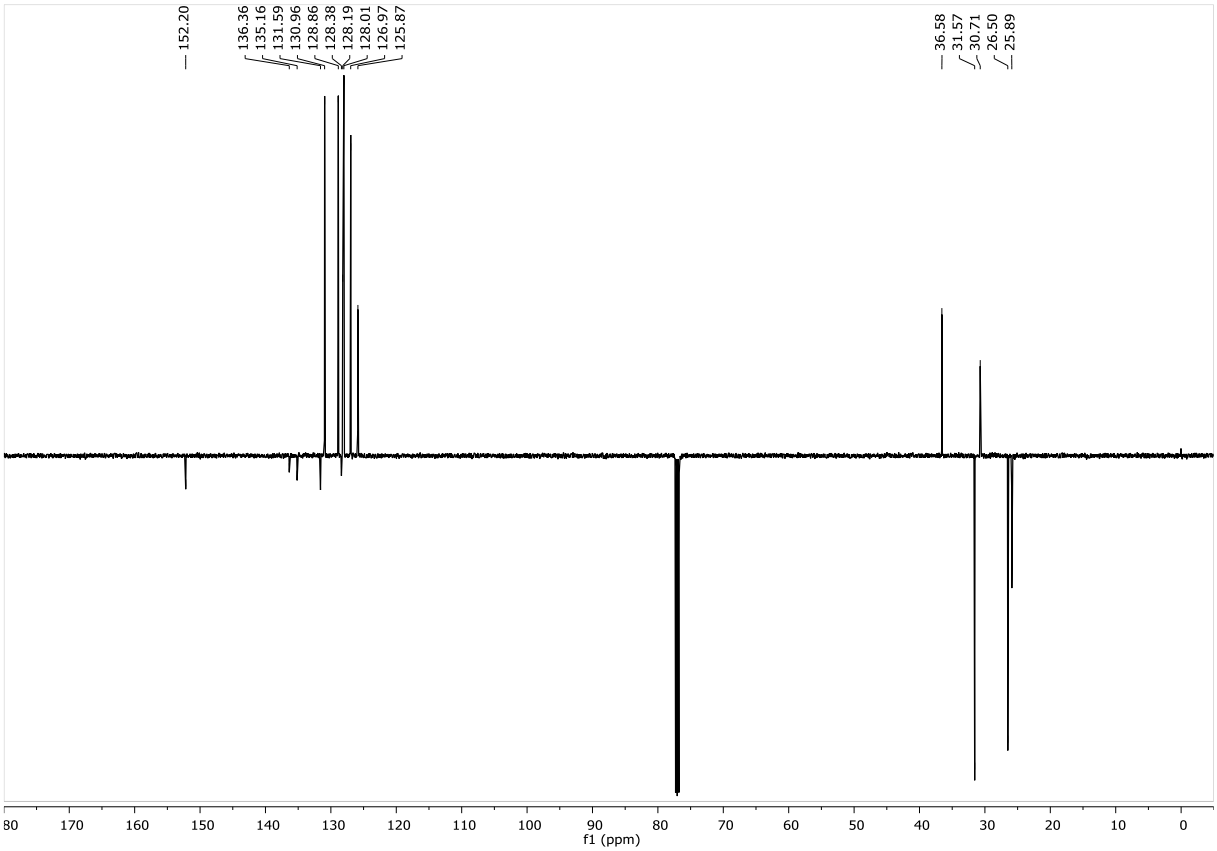


Figure S81. $^{13}C\{^{1}H\}$ NMR spectrum (126 MHz, $CDCl_3$) of the compound **6f**

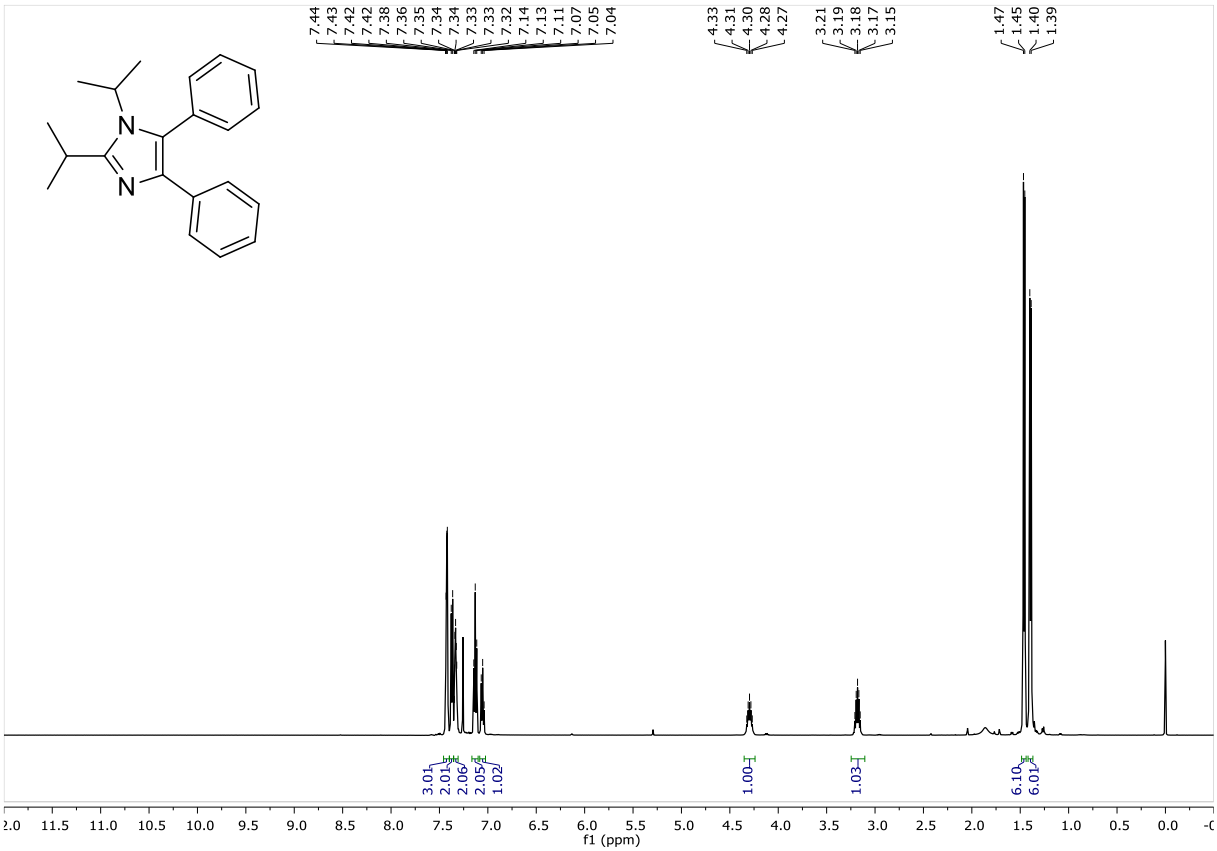


Figure S82. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6g**

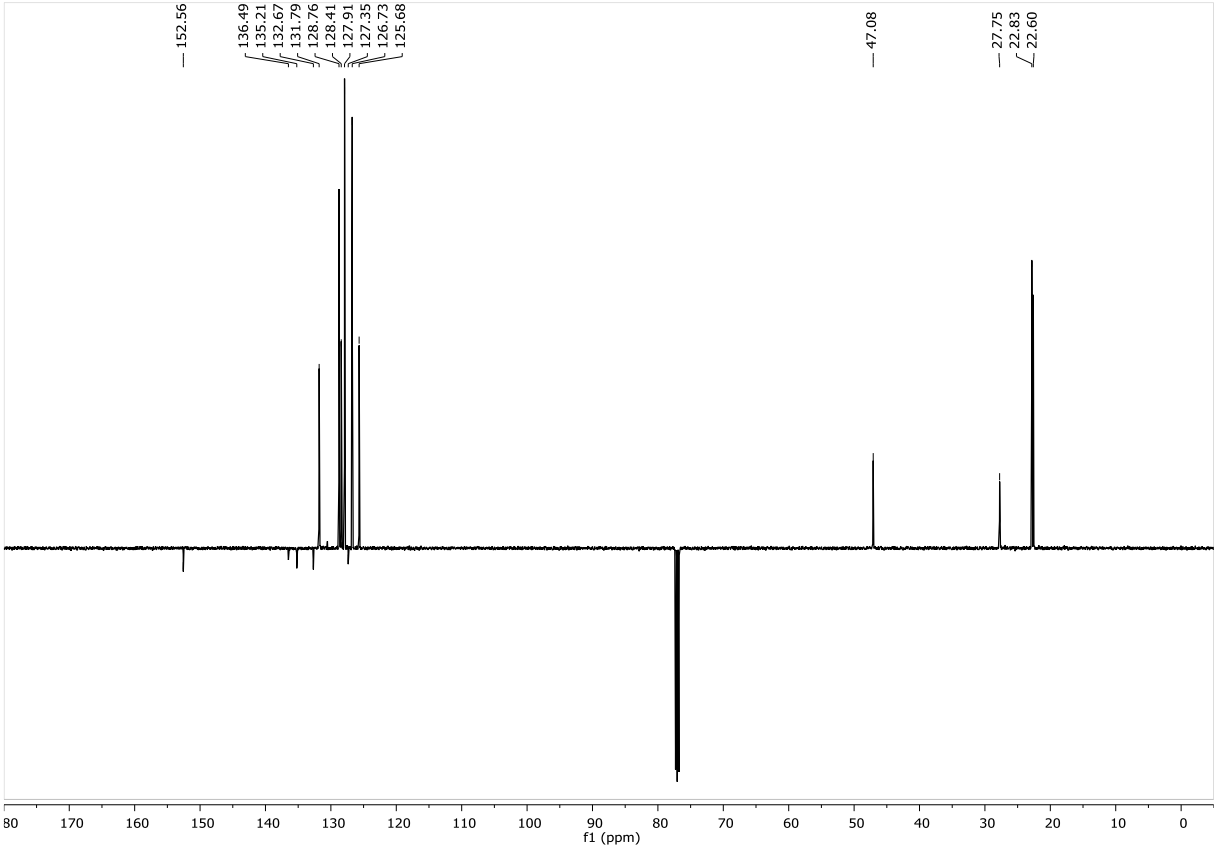


Figure S83. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **6g**

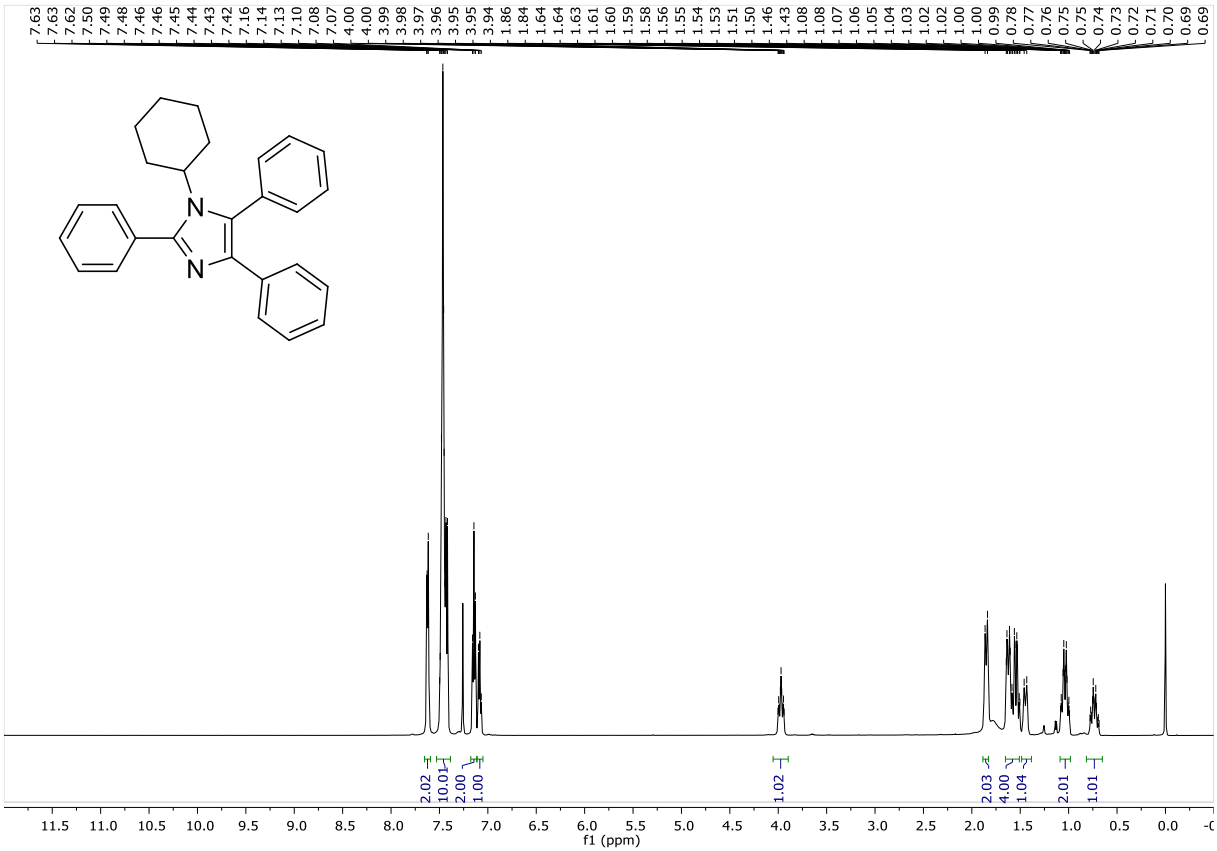


Figure S84. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6h**

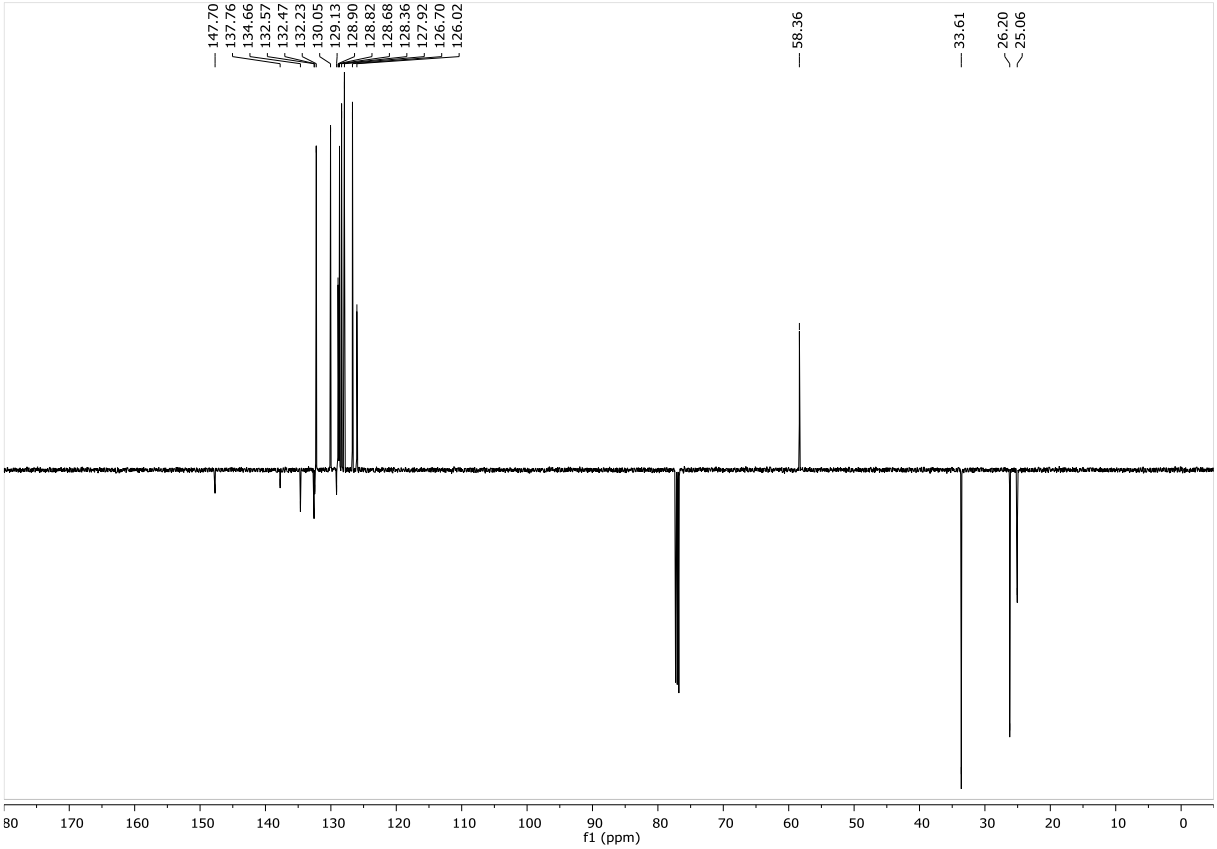


Figure S85. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **6h**

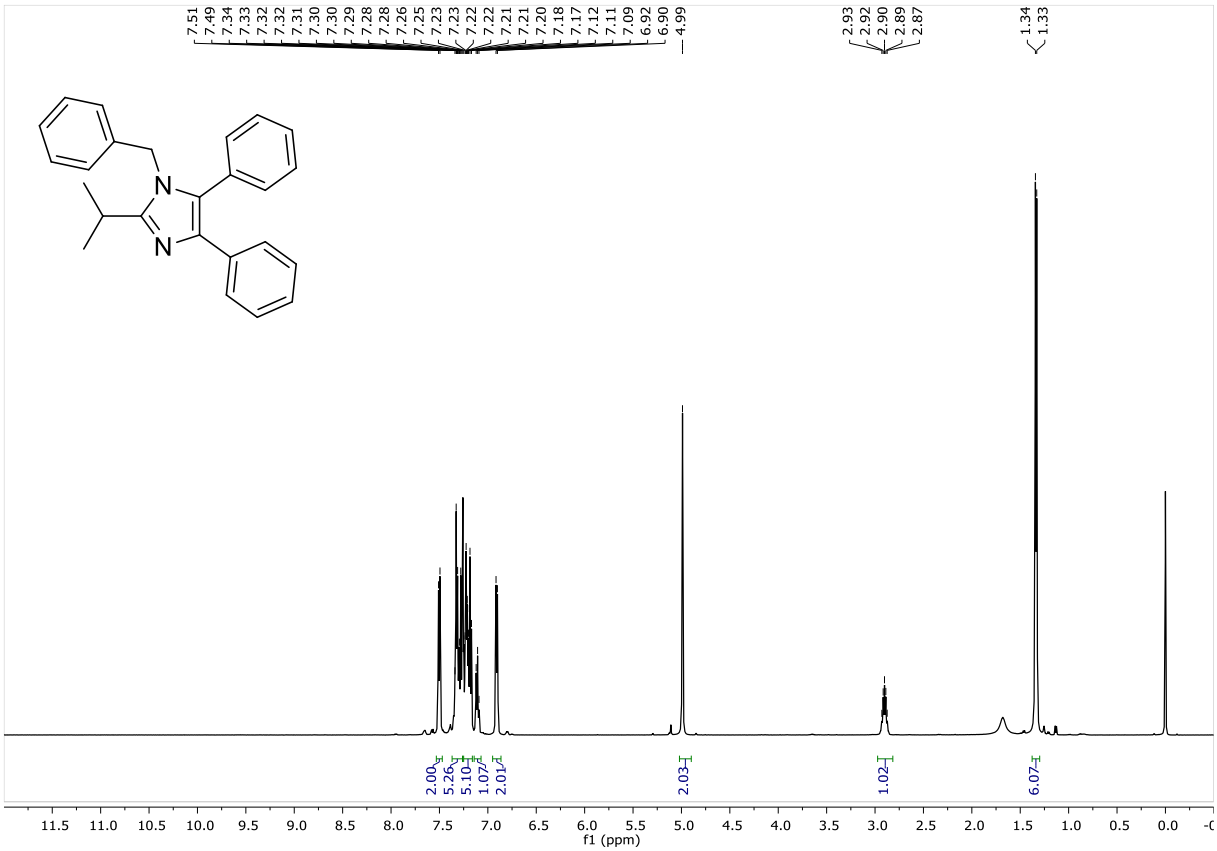


Figure S86. ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of the compound **6i**

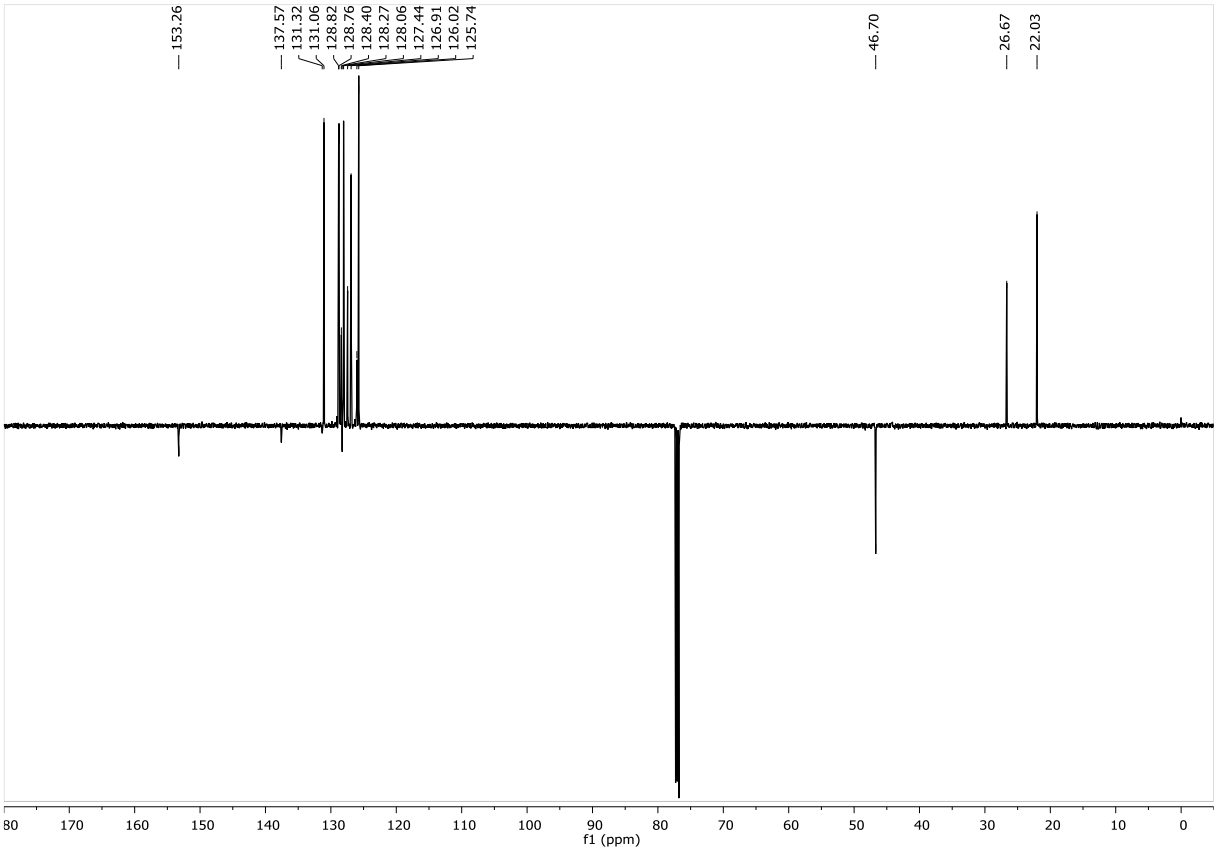


Figure S87. ^{13}C{^{1}H} NMR spectrum (126 MHz, $CDCl_3$) of the compound **6i**