Supporting information

Hydrazineyl-linked imidazole[1,2-*a*]pyrimidine -thiazole hybrids: Design, synthesis, and in-vitro biological evaluation studies

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Contents:

Table 1: Calculation of global reactivity parameters using DFT.

Comp	HOMO (eV)	LUMO (eV)	ΔE (eV)	IP (eV)	EA (eV)	η (eV)	σ (eV)	μ (eV)	ω (eV)	χ (eV)
K4	-5.0978	-2.061	3.0368	5.0978	2.061	1.5184	0.3292	-1.5184	0.7592	3.5794
K5	-5.0806	-2.0559	3.0247	5.0806	2.0559	1.5123	0.3306	-1.5123	0.75615	3.5682
K6	-4.9588	-1.9365	3.0223	4.9588	1.9365	1.5111	0.3308	-1.5111	0.75555	3.4476
K7	-5.2099	-2.2713	2.9386	5.2099	2.2713	1.4693	0.3402	-1.4693	0.73465	3.7406
K8	-4.9944	-1.9469	3.0475	4.9944	1.9469	1.5237	0.3281	-1.5237	0.76185	3.4706
K9	-4.9925	-1.9875	3.005	4.9925	1.9875	1.5025	0.3327	-1.5025	0.75125	3.49
K10	-4.9333	-1.9667	2.9666	4.9333	1.9667	1.4833	0.3370	-1.4833	0.74165	3.45
K11	-5.1371	-2.1119	3.0252	5.1371	2.1119	1.5126	0.3305	-1.5126	0.7563	3.6245
K12	-5.1454	-2.1275	3.0179	5.1454	2.1275	1.5089	0.3313	-1.5089	0.75445	3.6364
K13	-5.1286	-2.1230	3.0056	5.1286	2.1230	1.5028	0.3327	-1.5028	0.7514	3.6258
K14	-5.2602	-2.3126	2.9476	5.2602	2.3126	1.4738	0.3392	-1.4738	0.7369	3.7864
K15	-5.0412	-2.0203	3.0209	5.0412	2.0203	1.5104	0.3310	-1.5104	0.7552	3.5307
K16	-5.0151	-2.0385	2.9766	5.0151	2.0385	1.4883	0.3359	-1.4883	0.74415	3.5268
K17	-5.404	-2.0355	3.3685	5.4040	2.0355	1.6842	0.3033	-1.6842	0.8421	3.7197
K18	-5.1585	-2.1619	2.9966	5.1585	2.1619	1.4983	0.3337	-1.4983	0.74915	3.6602
K19	-5.1664	-2.1776	2.9888	5.1664	2.1776	1.4944	0.3345	-1.4944	0.7472	3.672
K20	-5.1474	-2.1657	2.9817	5.1474	2.1657	1.4908	0.3353	-1.4908	0.7454	3.6565
K21	-5.0252	-2.0643	2.9609	5.0252	2.0643	1.4804	0.3377	-1.4804	0.7402	3.5447
K22	-5.0645	-2.0735	2.991	5.0645	2.0735	1.4955	0.3343	-1.4955	0.74775	3.569
K23	-5.3414	-2.4386	2.9028	5.3414	2.4386	1.4514	0.3444	-1.4514	0.7257	3.89
K24	-5.2320	-2.4211	2.8109	5.2320	2.4211	1.4054	0.3557	-1.4054	0.7027	3.8265
K25	-5.5061	-2.5416	2.9645	5.5061	2.5416	1.4822	0.3373	-1.4822	0.7411	4.0238
K26	-5.5128	-2.5534	2.9594	5.5128	2.5534	1.4797	0.3379	-1.4797	0.73985	4.0331

Table 2: Binding energy and interactions between target molecules (K1-K26) and receptor 1P44 and 4KTF.

	1P44			**4KTF**		
Compound code	**Docking score (Kcal/mol)**	**H-boding**	**Pi-Pi stacking**	**Docking score (Kcal/mol)**	**H-boding**	**Pi-Pi stacking**
K4	-11.1	Ile194	The196	-5.6	-	Ile236
K5	-7.6	Tyr158, Ile194	Tyr158	-5.6	-	-
K6	-7.8	Tyr158, Ile194	Tyr158	-5.1	-	Trp168
K7	-8.3	-	-	-5.9	-	Phe168
K8	-8.8	Tyr158, Ile194	Phe149	-7.9	Thr77, Arg72	Trp182
K9	-7.3	Tyr158, Gyl104	Tyr158	-7.7	Gln385	Phe168, Trp182
K10	-9.4	Tyr158, Ile194	Phe149	-7.6	Thr77	Trp182
K11	-8.3	Ile 194	-	-7.6	Thr77	Phe168, Trp182
K12	-6.9	Tyr158, Ile194	Tyr158	-7.9	Thr77, Arg72	Trp182
K13	-7.5	Ile194	-	-8.4	-	Trp182

K14	-8.8	Tyr158, Ile194	Tyr158, Phe149	-7.8	Gln385	Trp182, Phe168
K15	-11.9	Tyr158, Ile194	Phe149	-6.5	Val82	Ile236
K16	-10.9	Tyr158, Ile194	Phe149	-8.1	Ser170, Met86	Trp182, Phe168
K17	-8.8	Tyr158, Ile194	Phe149	-8.3	Gln385	Trp182
K18	-11.3	Tyr158, Ile194	Phe149	-6.0	-	Trp182
K19	-9.2	Tyr158, Ile194	-	-7.9	Gln385, Thr229	Trp182, Phe168
K20	-7.5	Tyr158, Ile194	Tyr158	-8.2	-	Gln385
K21	-9.1	Tyr158, Ile194	Tyr158, Phe149	-8.7	Thr229, Met86	Trp182, Phe168
K22	-9.2	Lys165	Phe149	-6.4	-	-
K23	-8.3	Tyr158, Lys165	Tyr158	-7.8	Asn85	Phe168
K24	-8.8	Lys165	Tyr158, Phe149	-7.8	Asn74	Trp182
K25	-8.6	-	-	-4.1	Ser170	Trp182, Phe168
K26	-6.4	Tyr158	Tyr158	-7.3	Gln385, Asn74, Val82	-

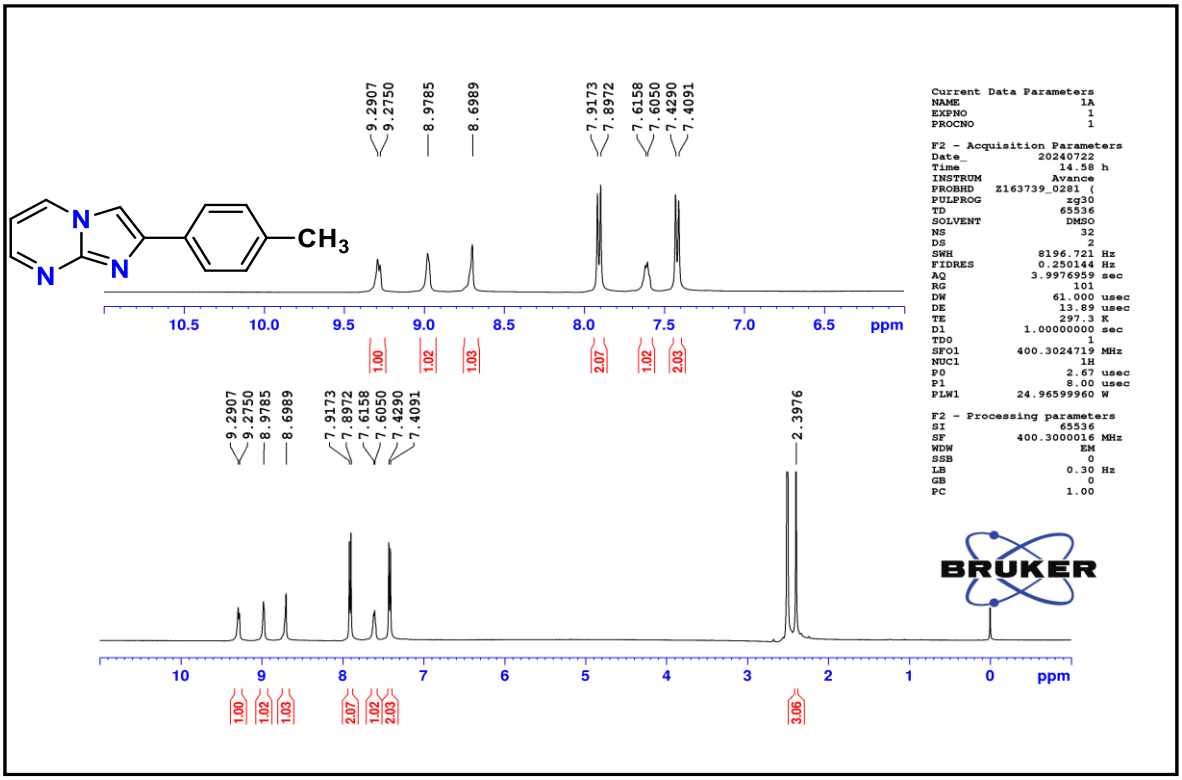


Figure S1: ^{1}H-NMR spectrum of compound **3a**

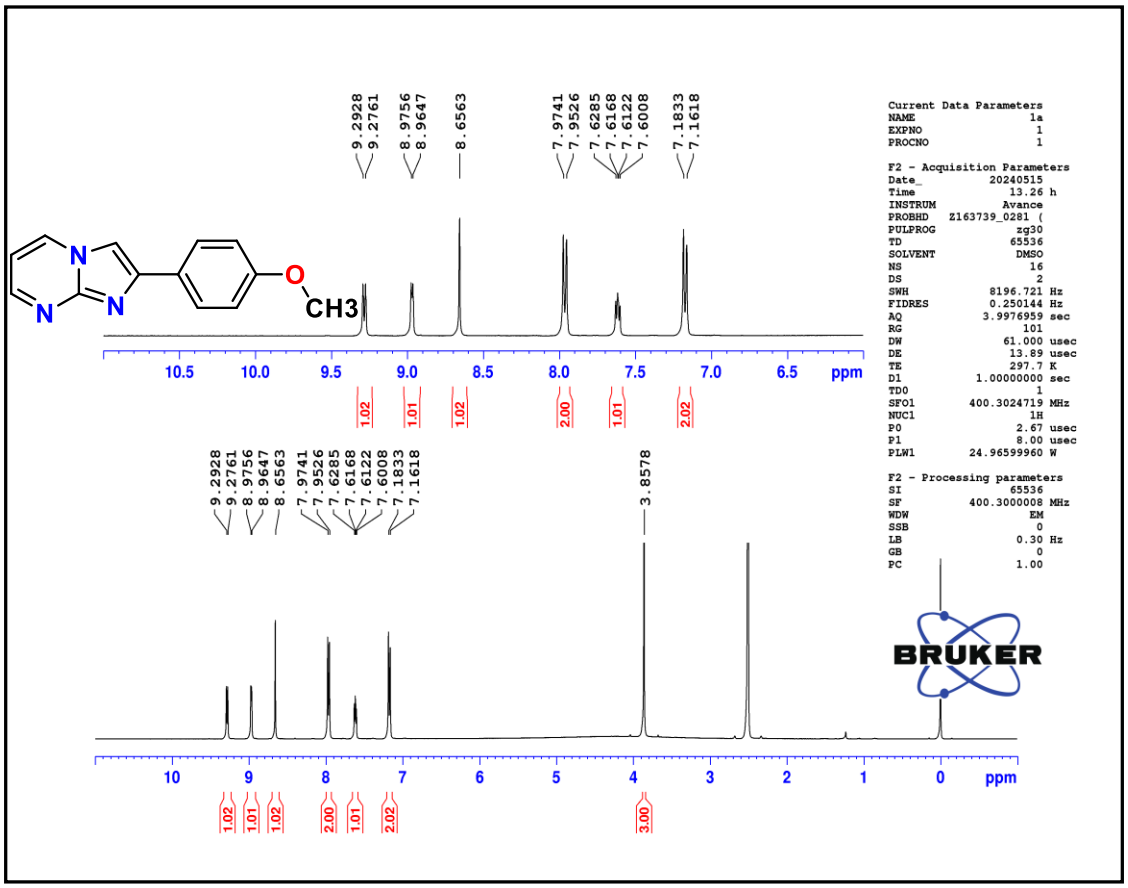


Figure S2: ^{1}H-NMR spectrum of compound **3b**

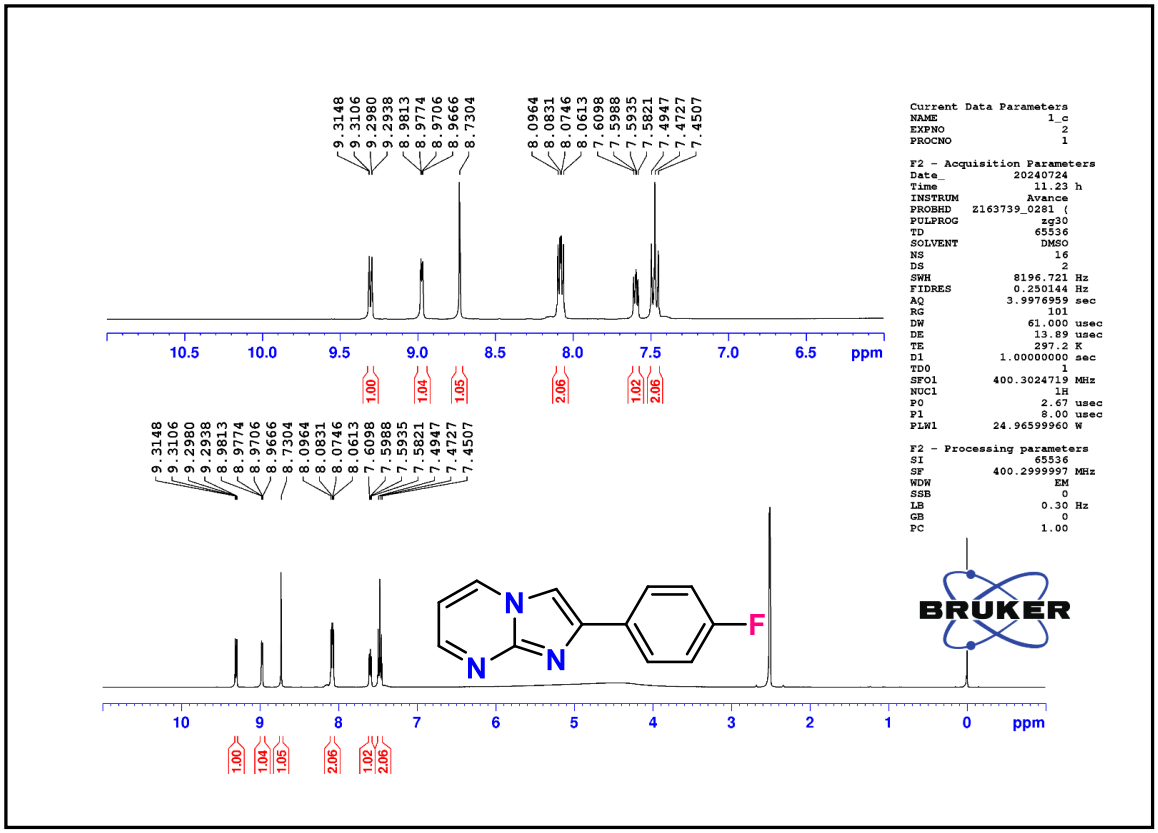


Figure S3: [1]H-NMR spectrum of compound **3c**

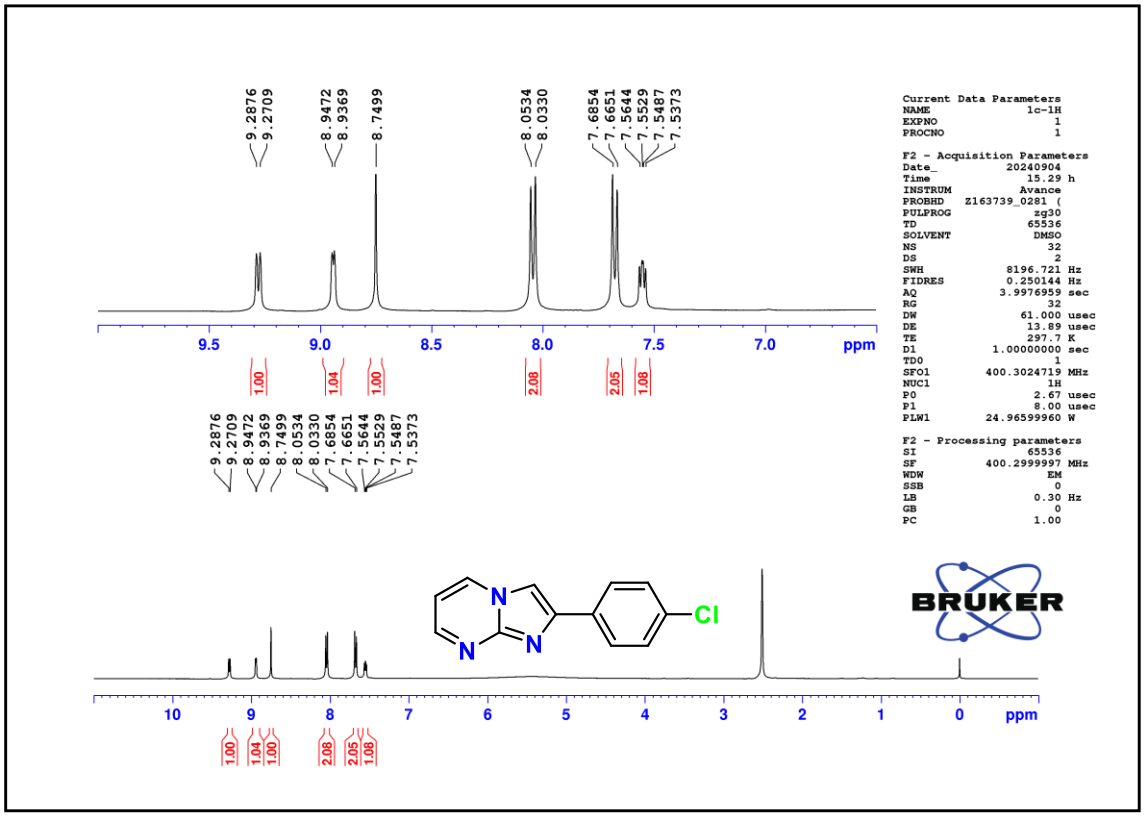


Figure S4: [1]H-NMR spectrum of compound **3d**

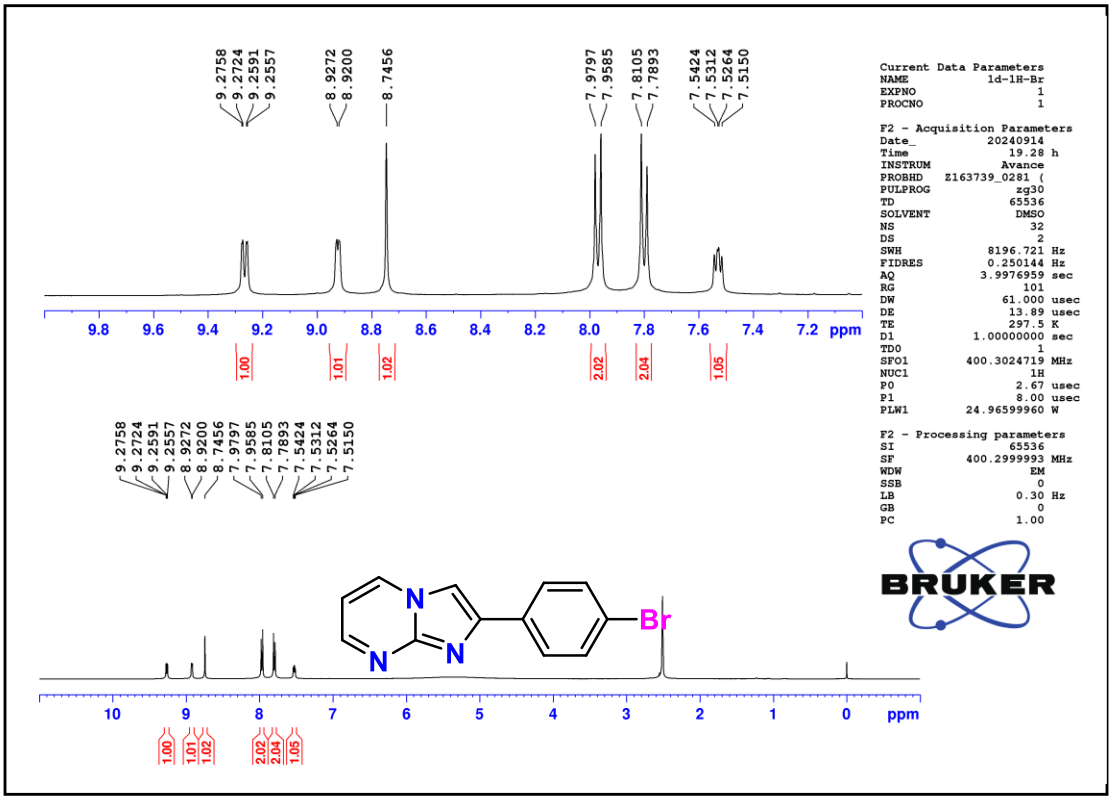


Figure S5: ^{1}H-NMR spectrum of compound **3e**

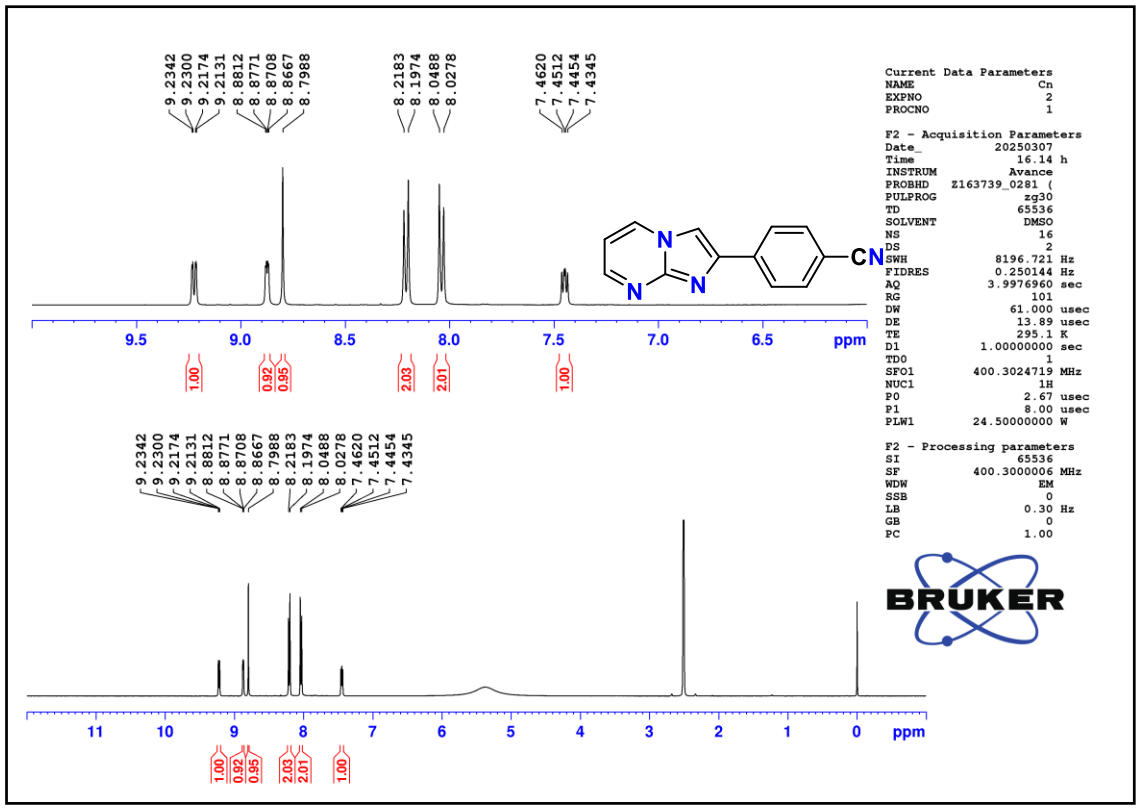


Figure S6: ^{1}H-NMR spectrum of compound **3f**

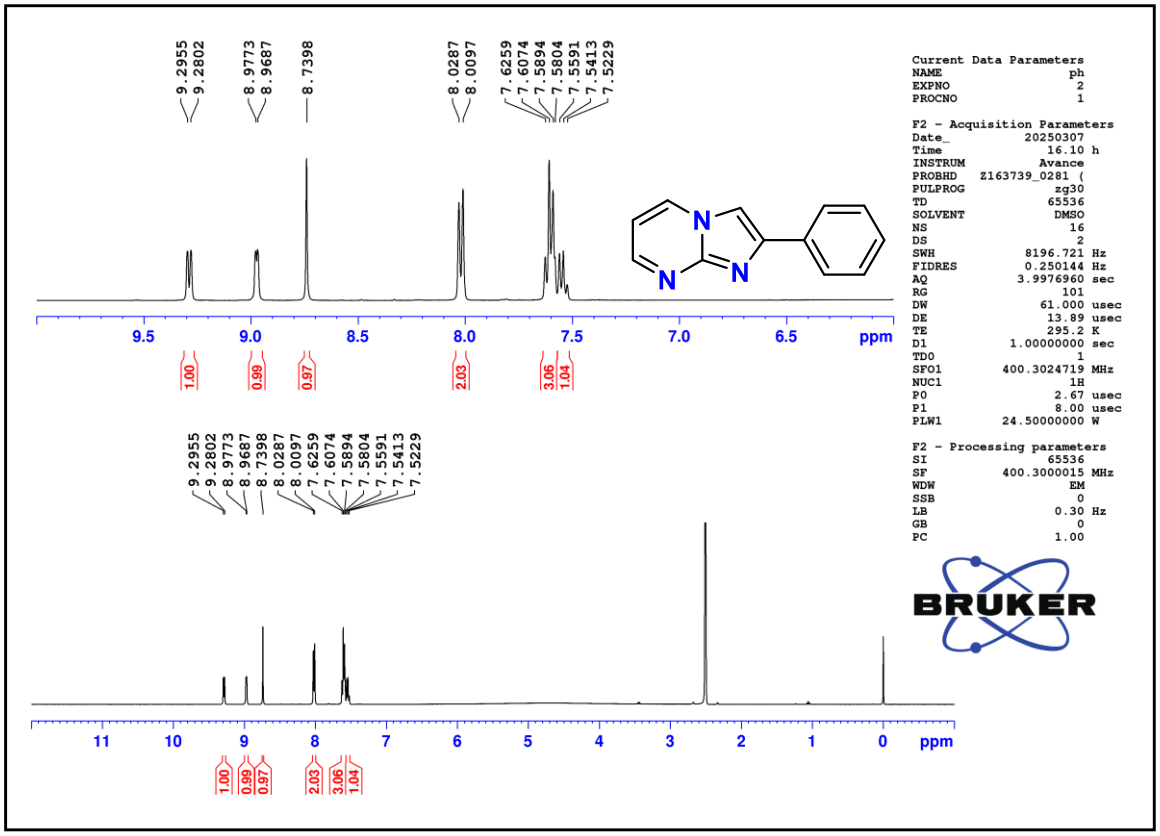


Figure S7: ^{1}H-NMR spectrum of compound **3g**

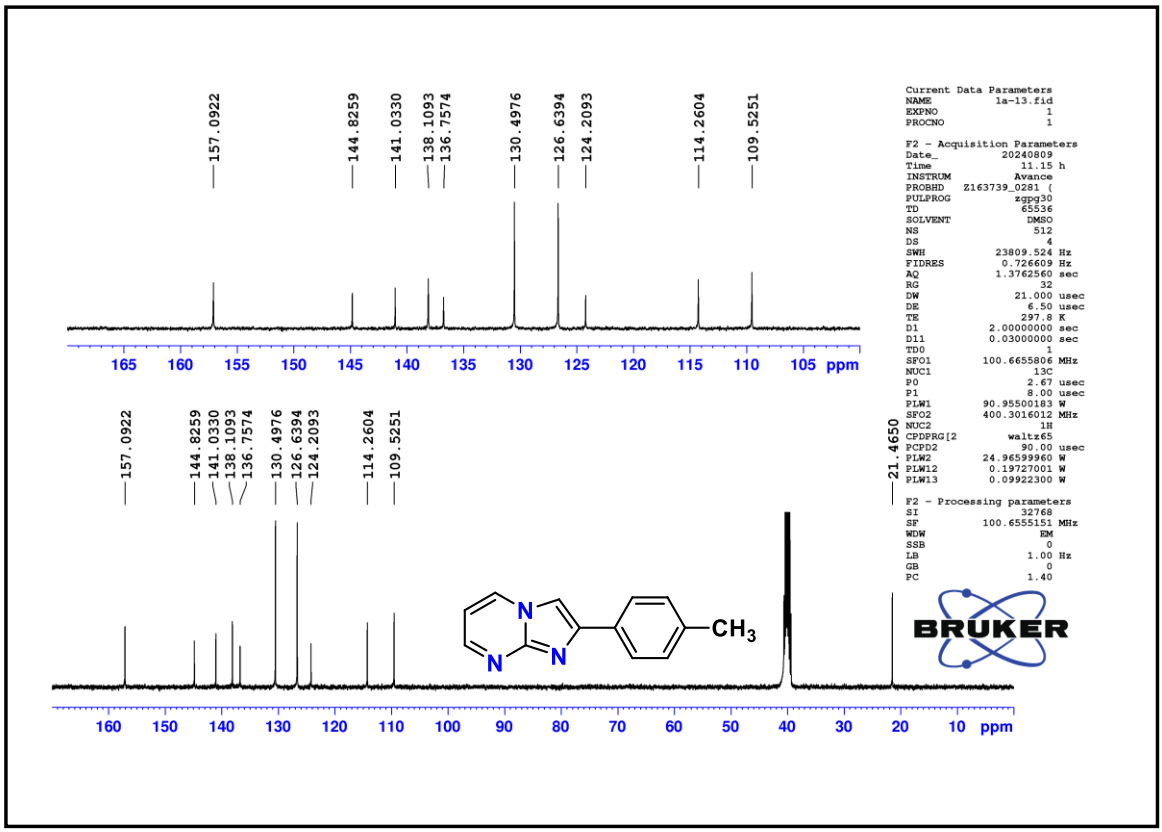


Figure S8: ^{13}C-NMR spectrum of compound **3a**

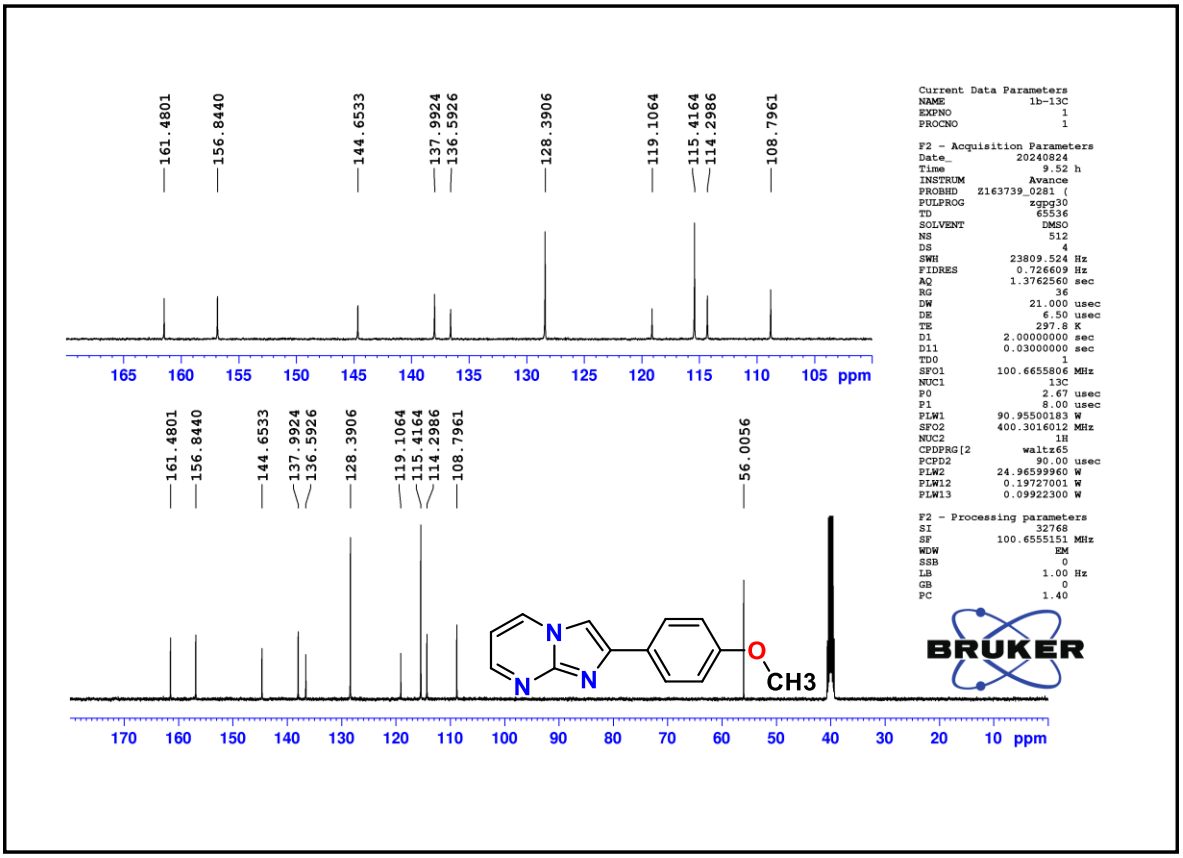


Figure S9: ^{13}C-NMR spectrum of compound **3b**

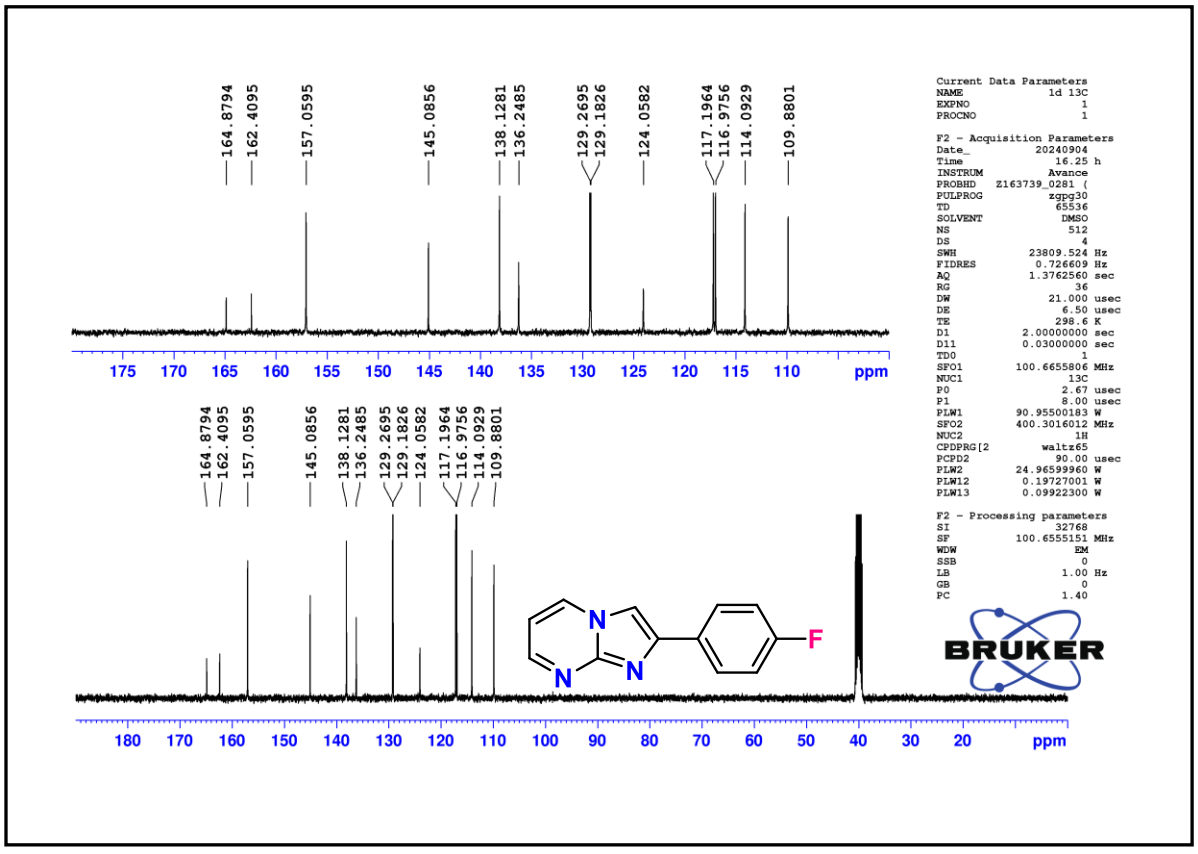


Figure S10: ^{13}C-NMR spectrum of compound **3c**

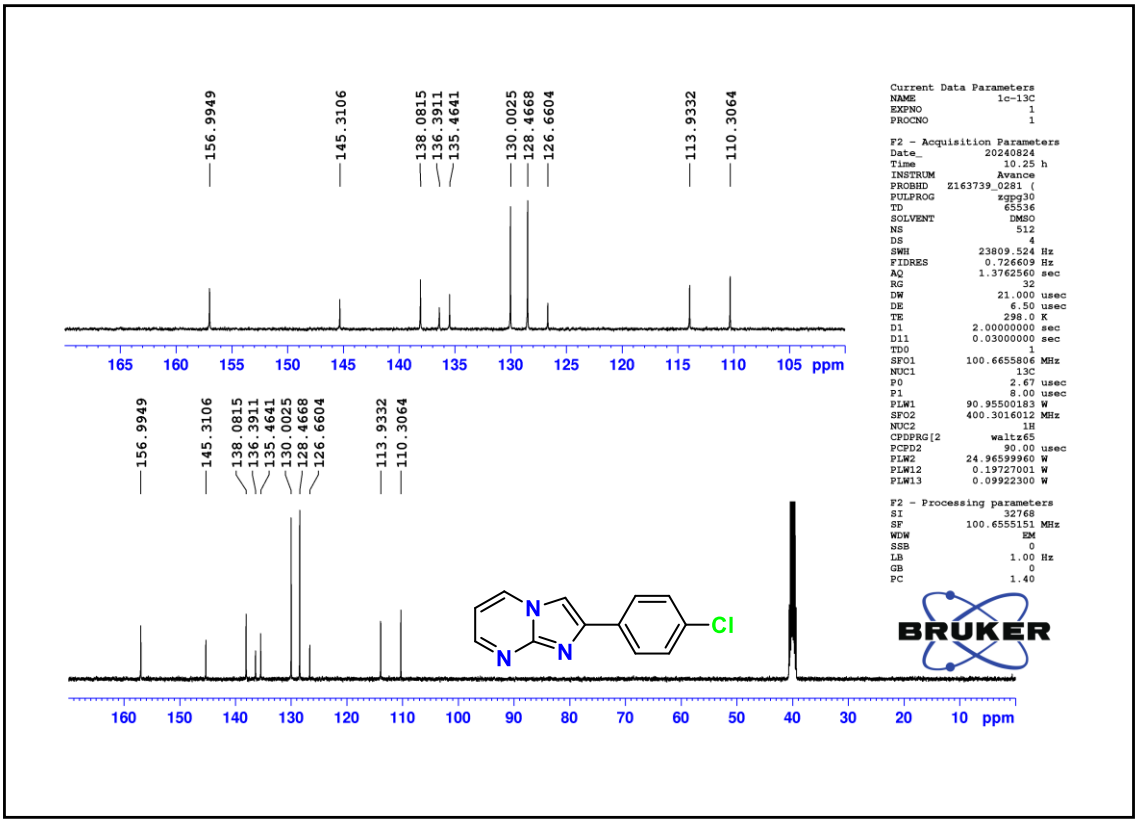


Figure S11: ^{13}C-NMR spectrum of compound **3d**

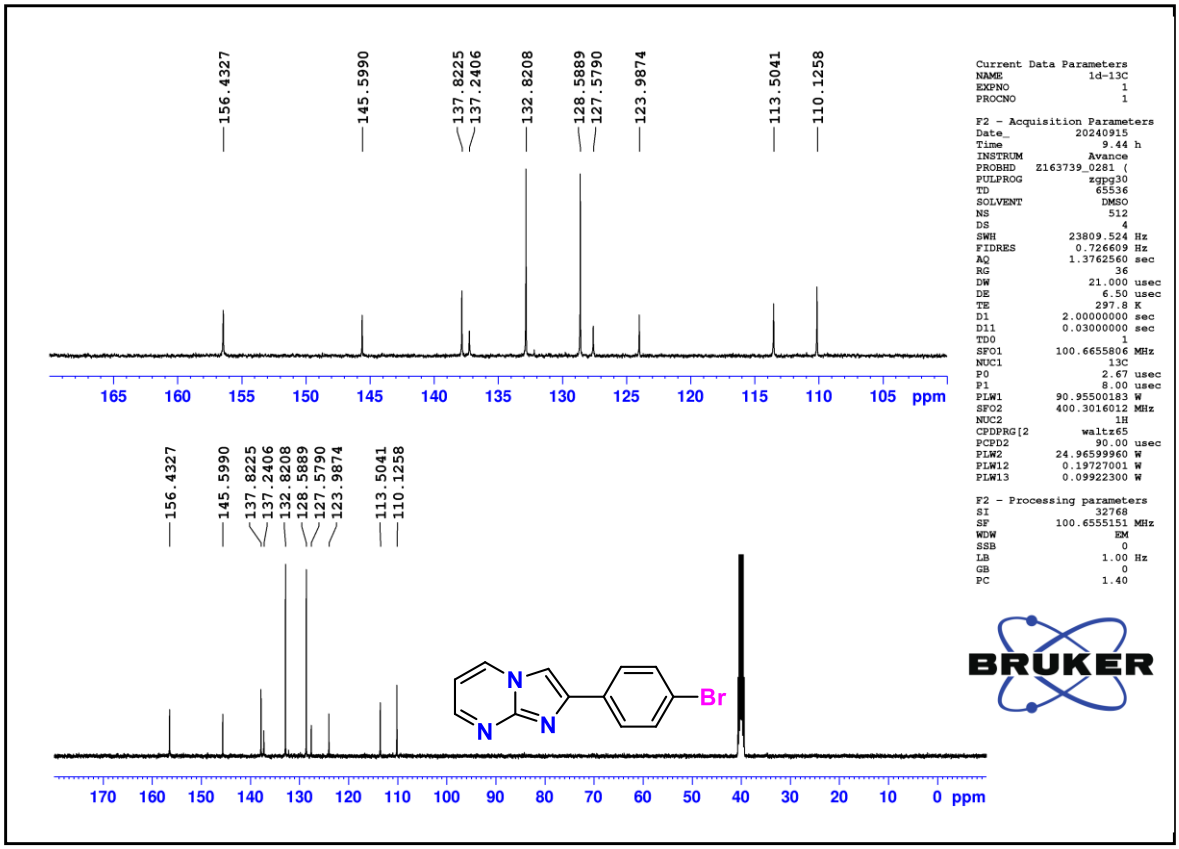


Figure S12: ^{13}C-NMR spectrum of compound **3e**

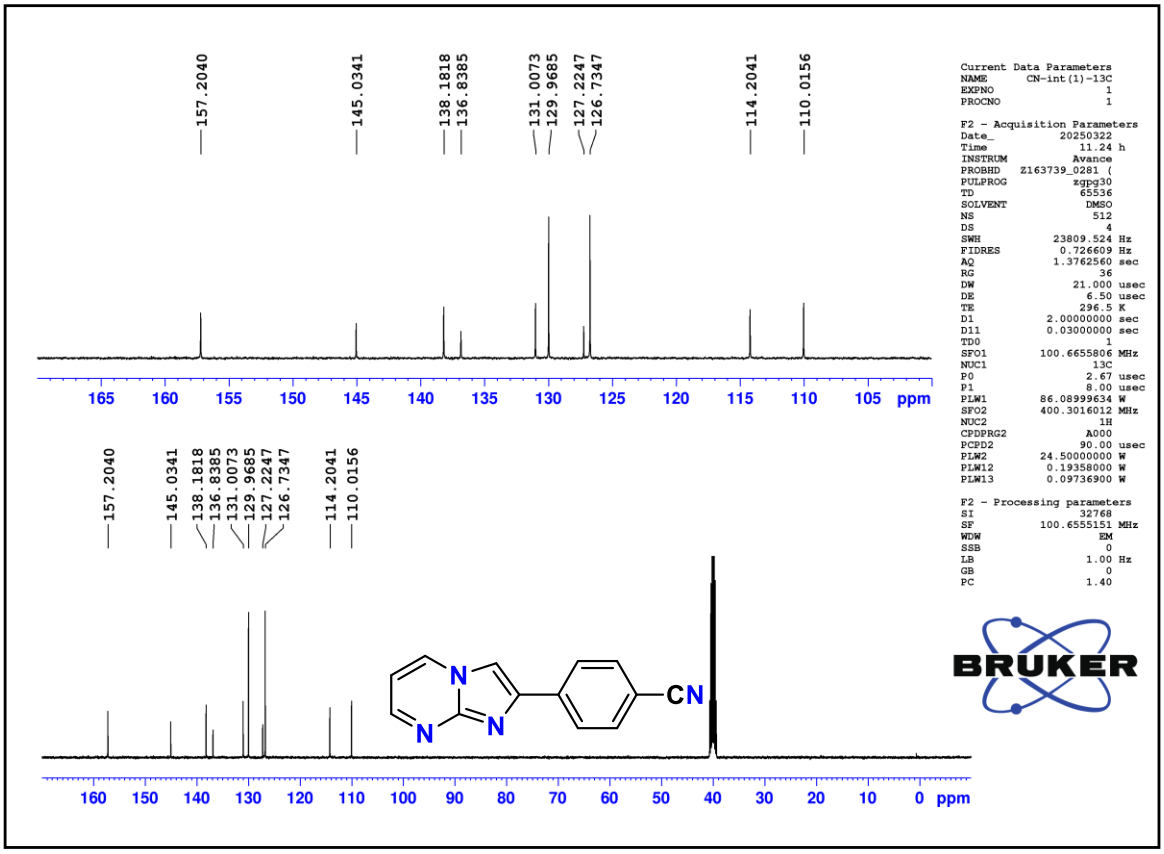


Figure S13: ^{13}C-NMR spectrum of compound **3f**

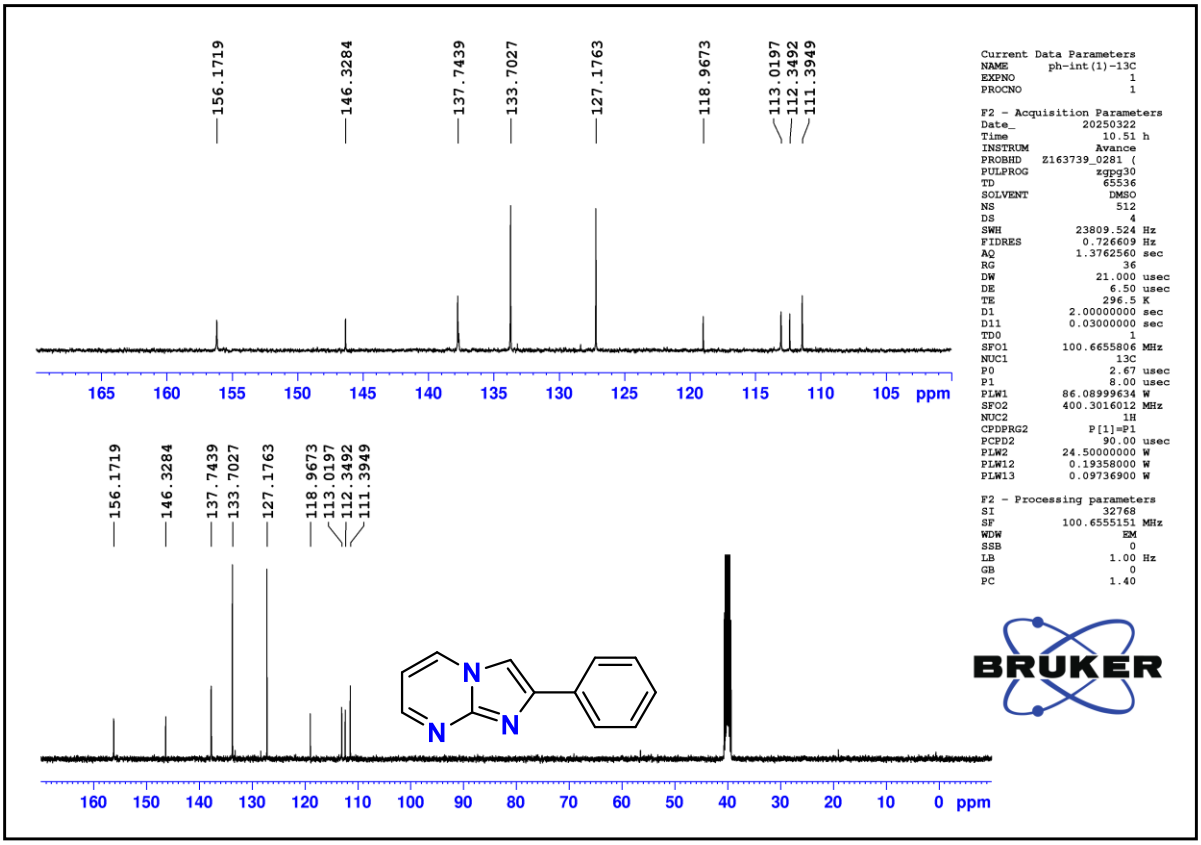


Figure S14: ^{13}C-NMR spectrum of compound **3g**

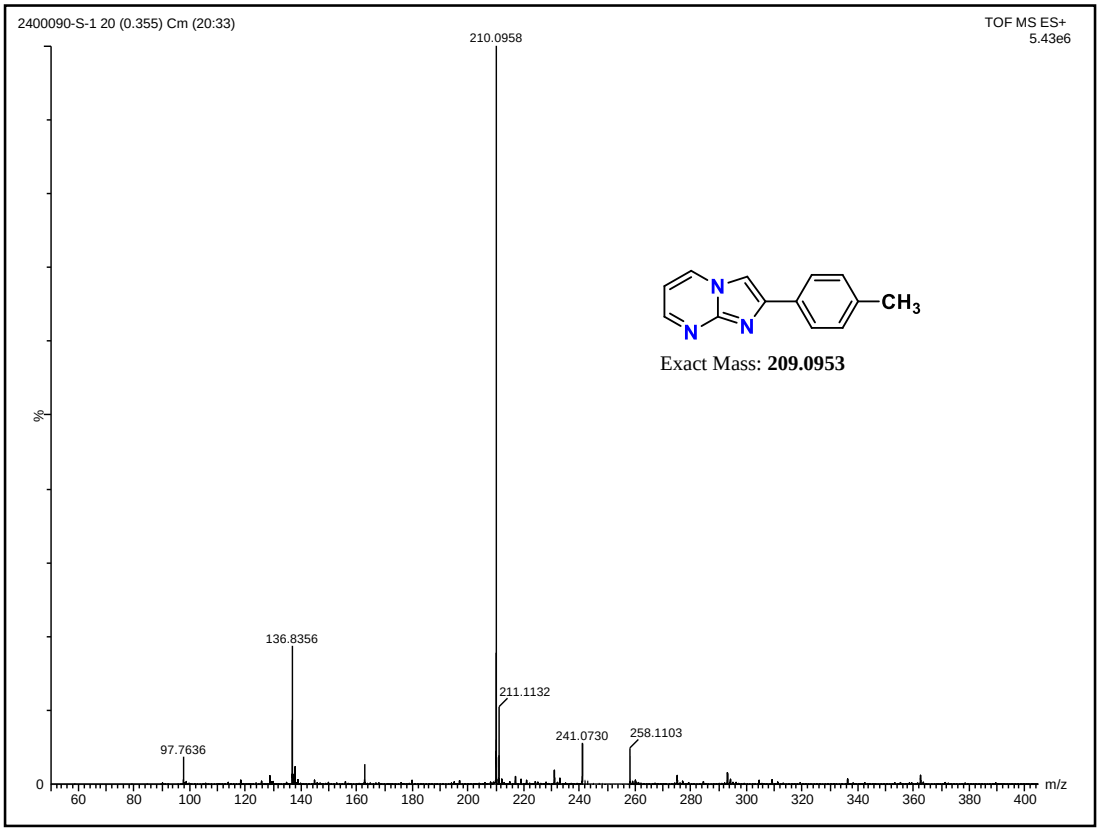


Figure S15: HR-MS spectrum of compound **3a**

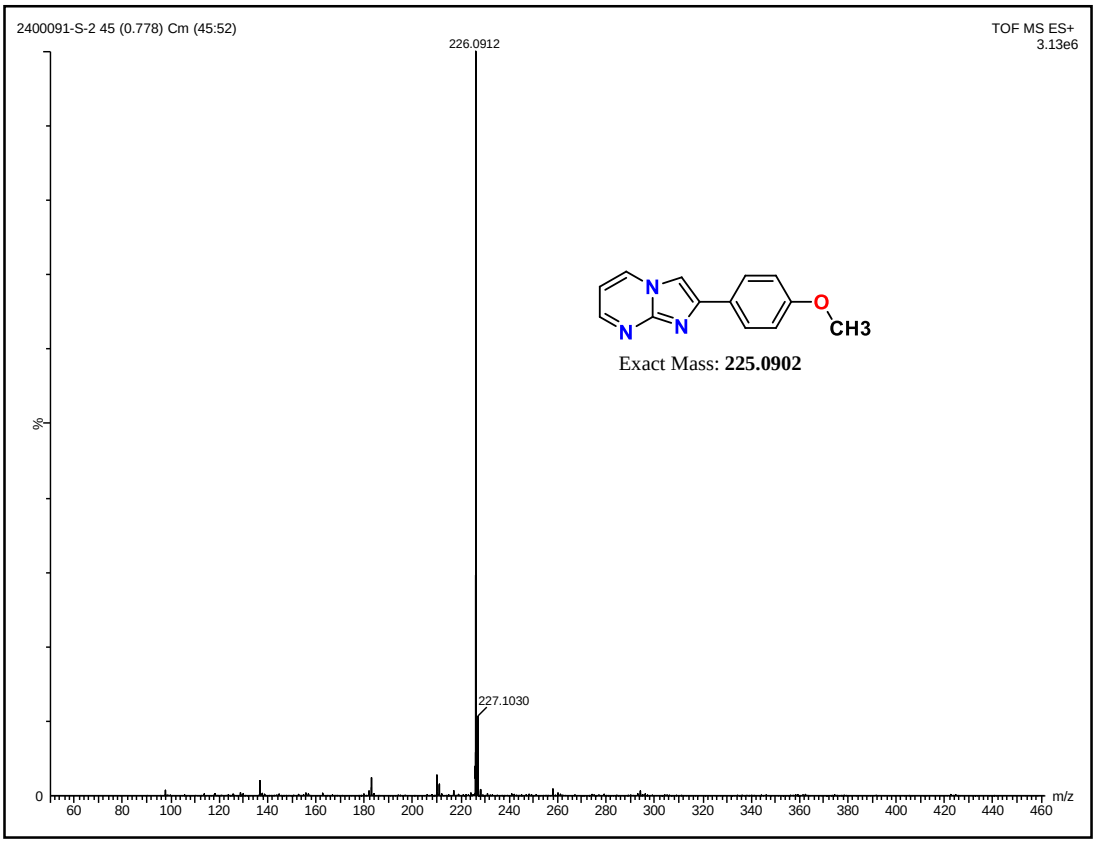


Figure S16: HR-MS spectrum of compound **3b**

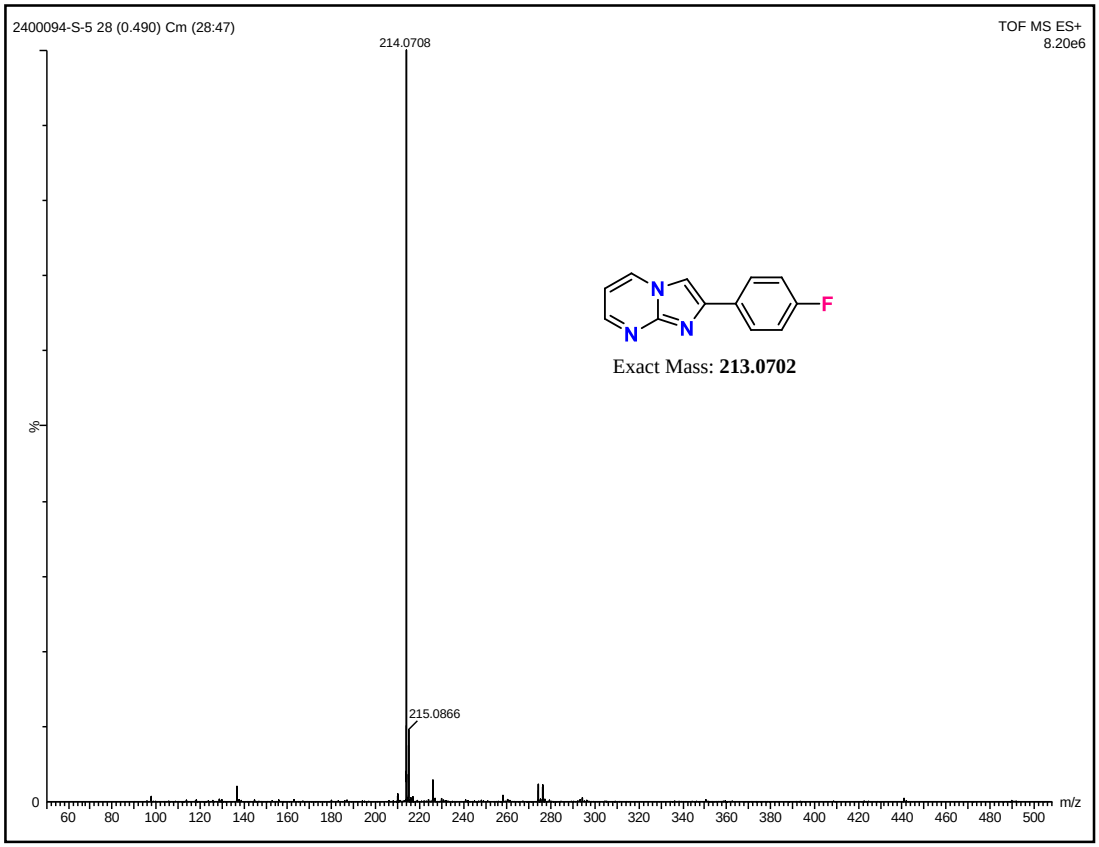


Figure S17: HR-MS spectrum of compound **3c**

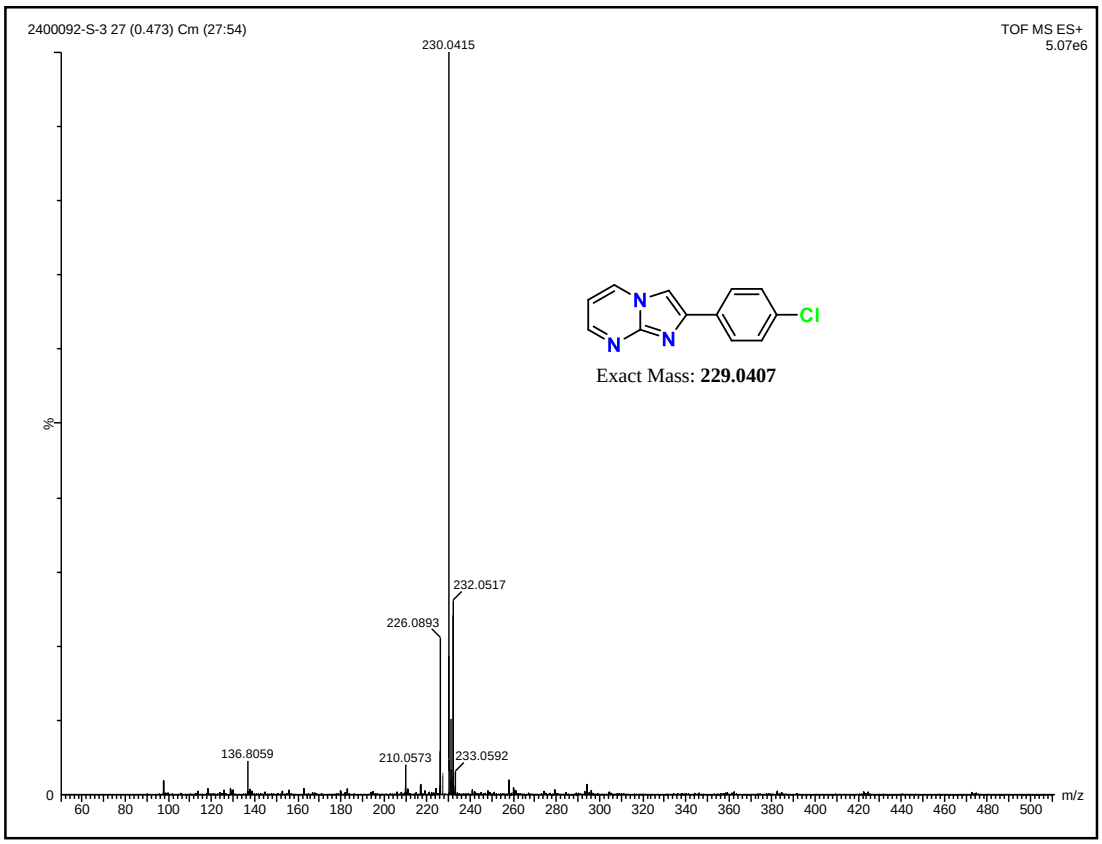


Figure S18: HR-MS spectrum of compound **3d**

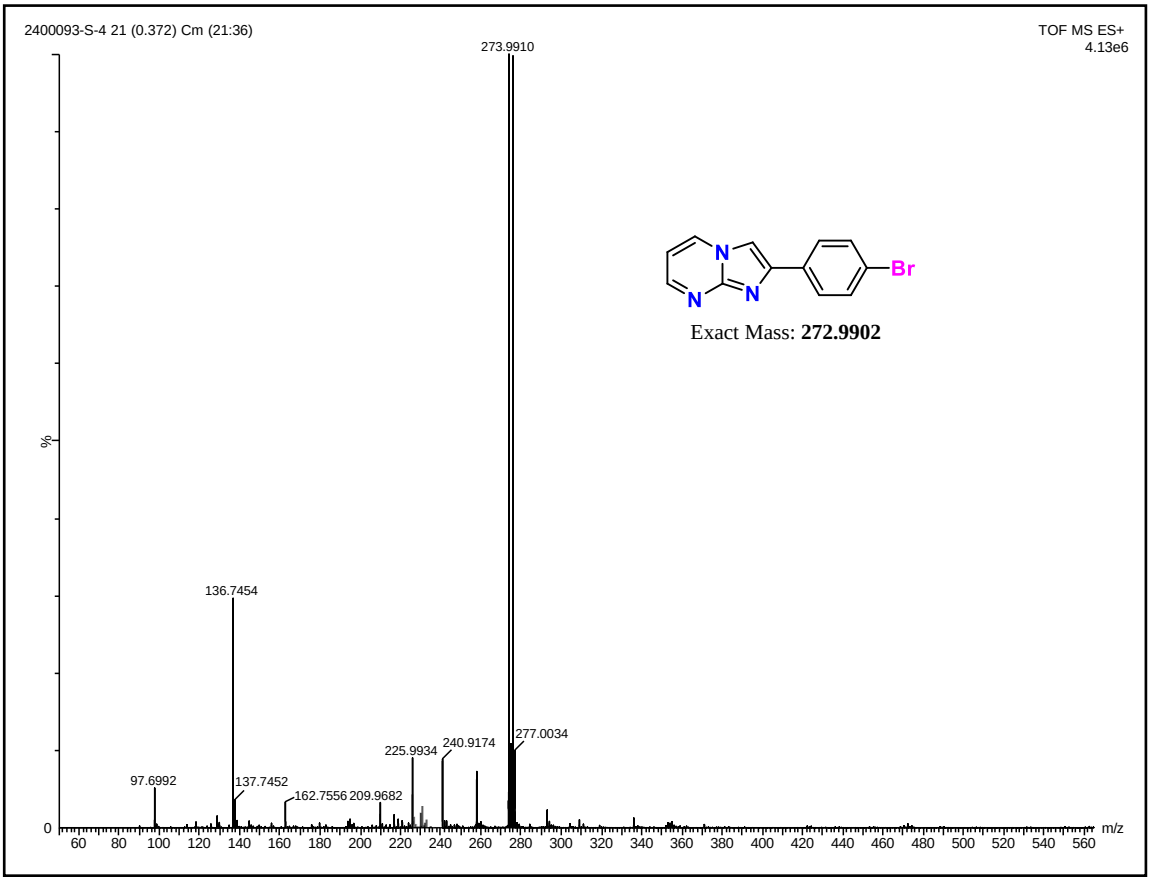


Figure S19: HR-MS spectrum of compound **3e**

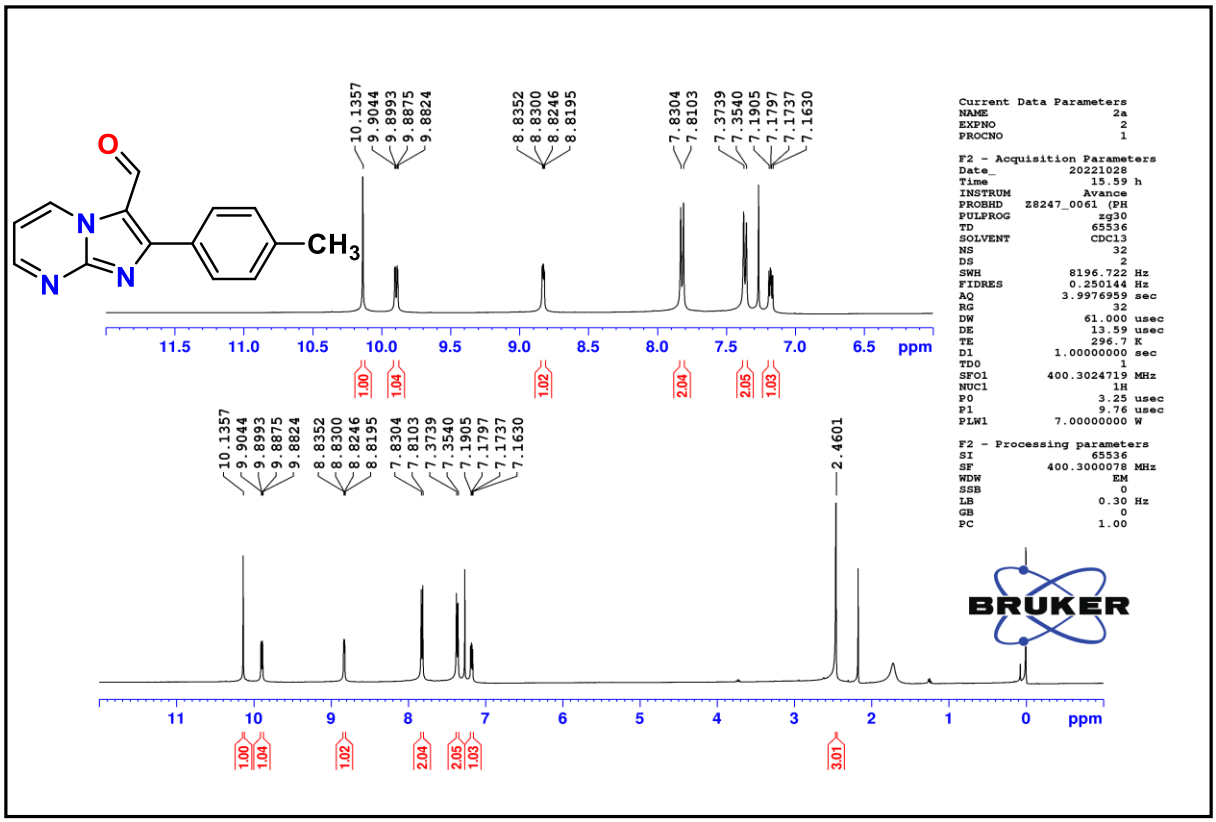


Figure S20: ^{1}H-NMR spectrum of compound **4a**

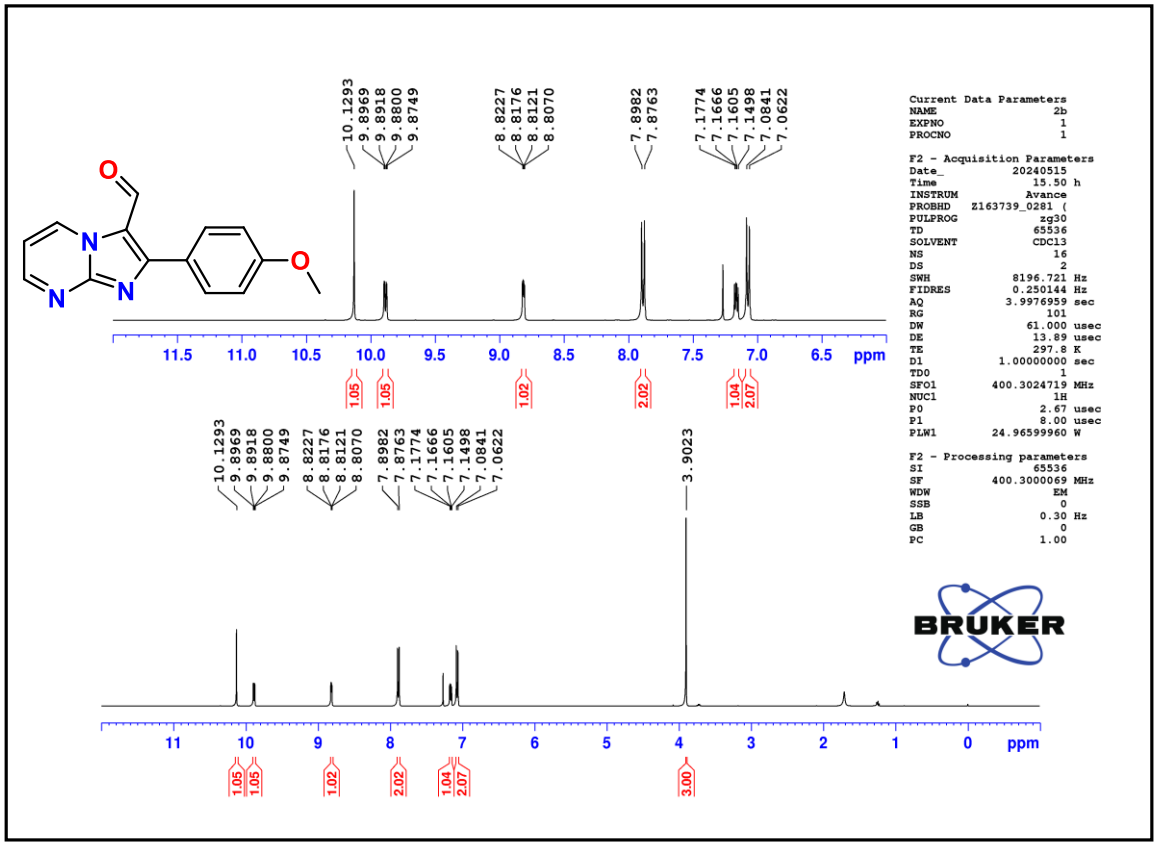


Figure S21: ^{1}H-NMR spectrum of compound **4b**

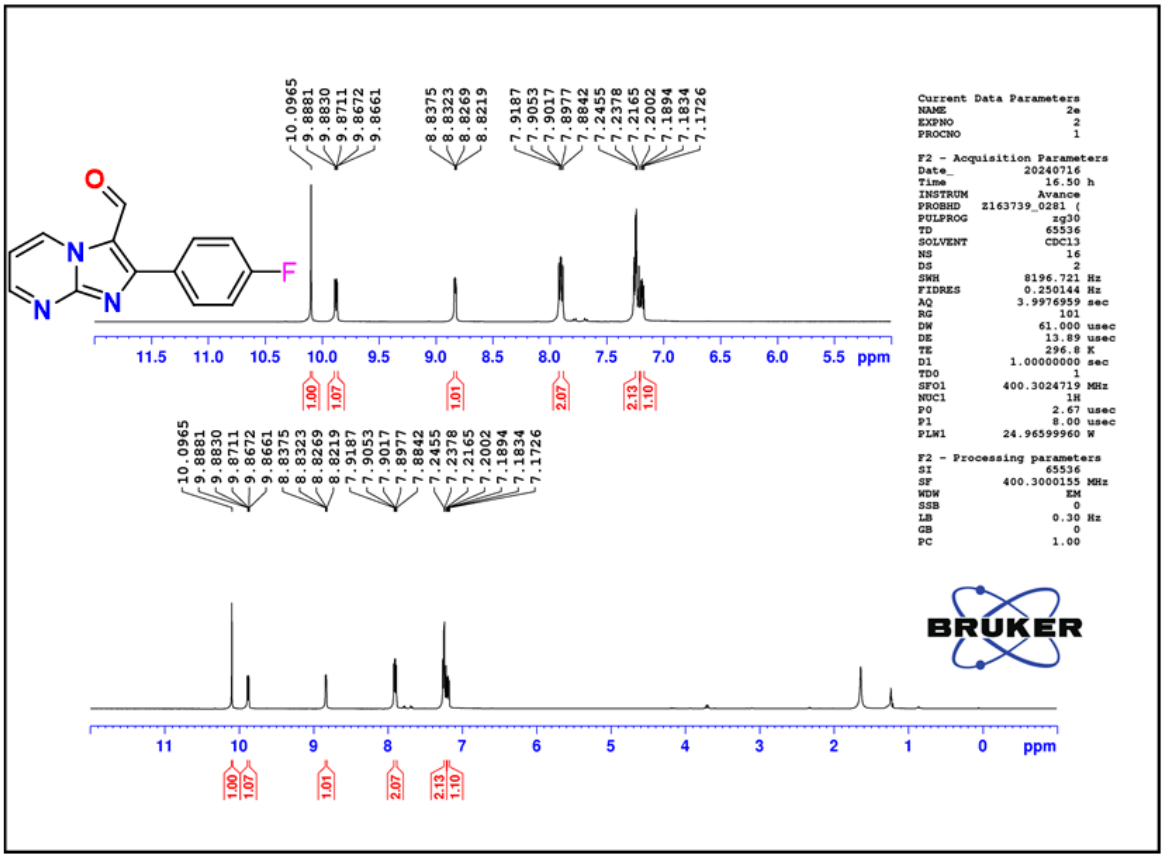


Figure S22: ^{1}H-NMR spectrum of compound **4c**

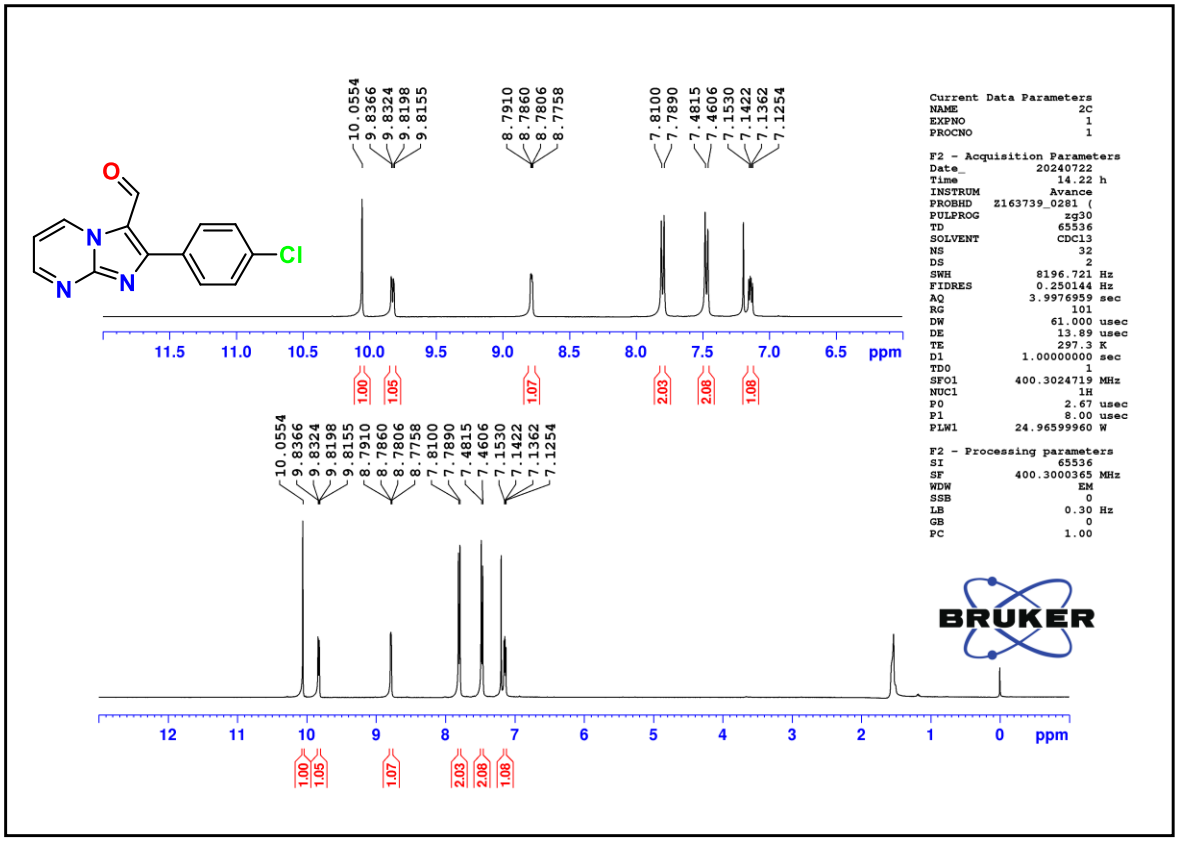


Figure S23: ^{1}H-NMR spectrum of compound **4d**

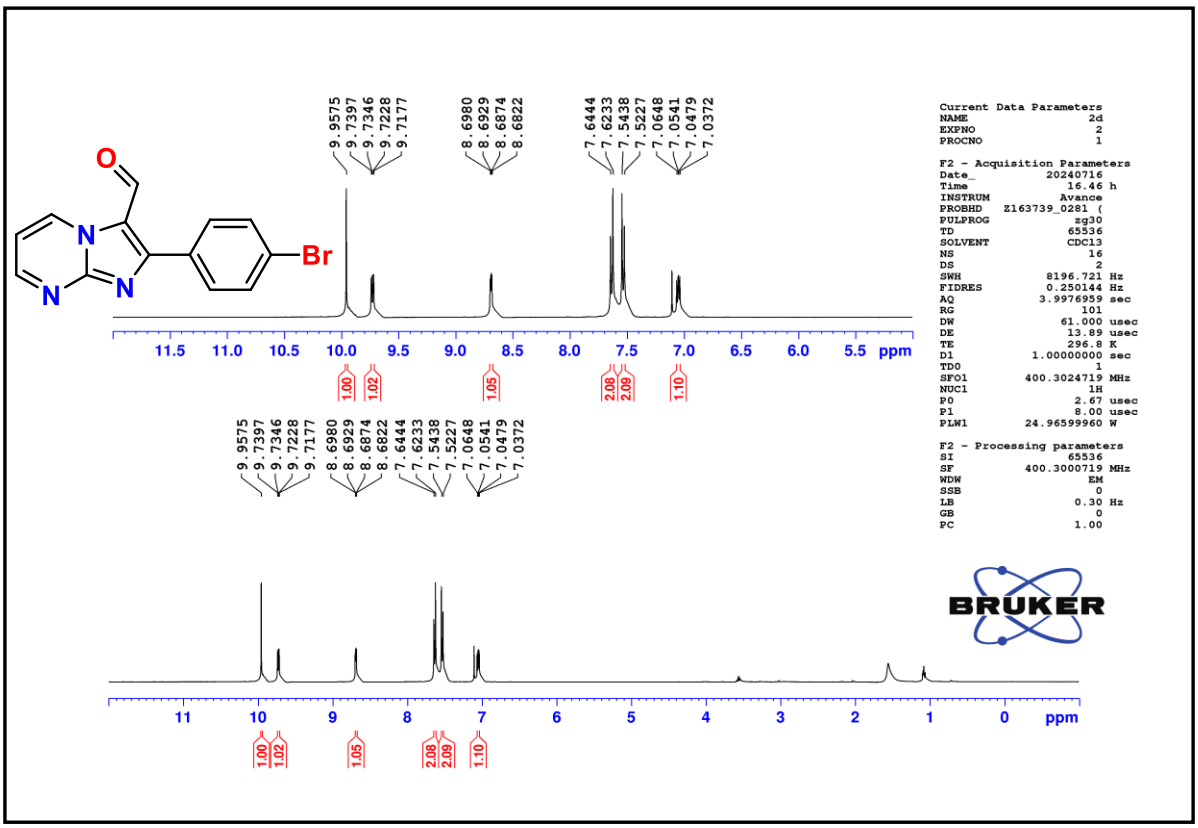


Figure S24: ^{1}H-NMR spectrum of compound **4e**

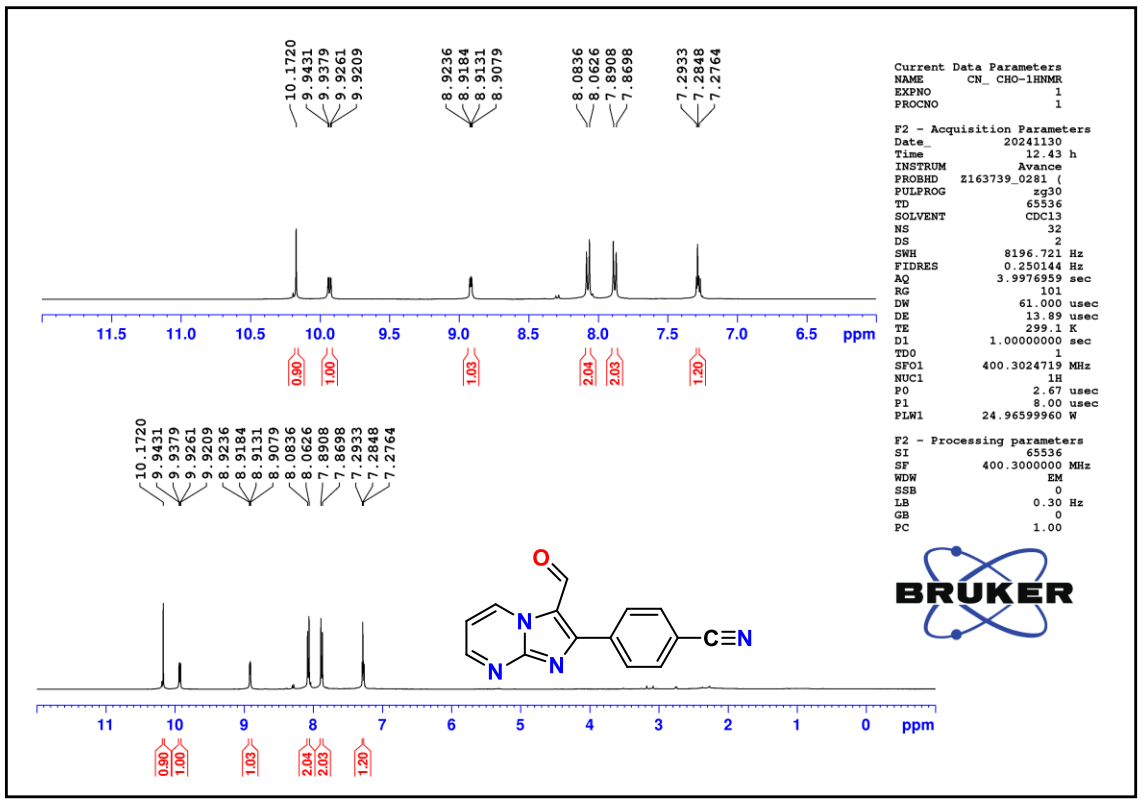


Figure S25: ^{1}H-NMR spectrum of compound **4f**

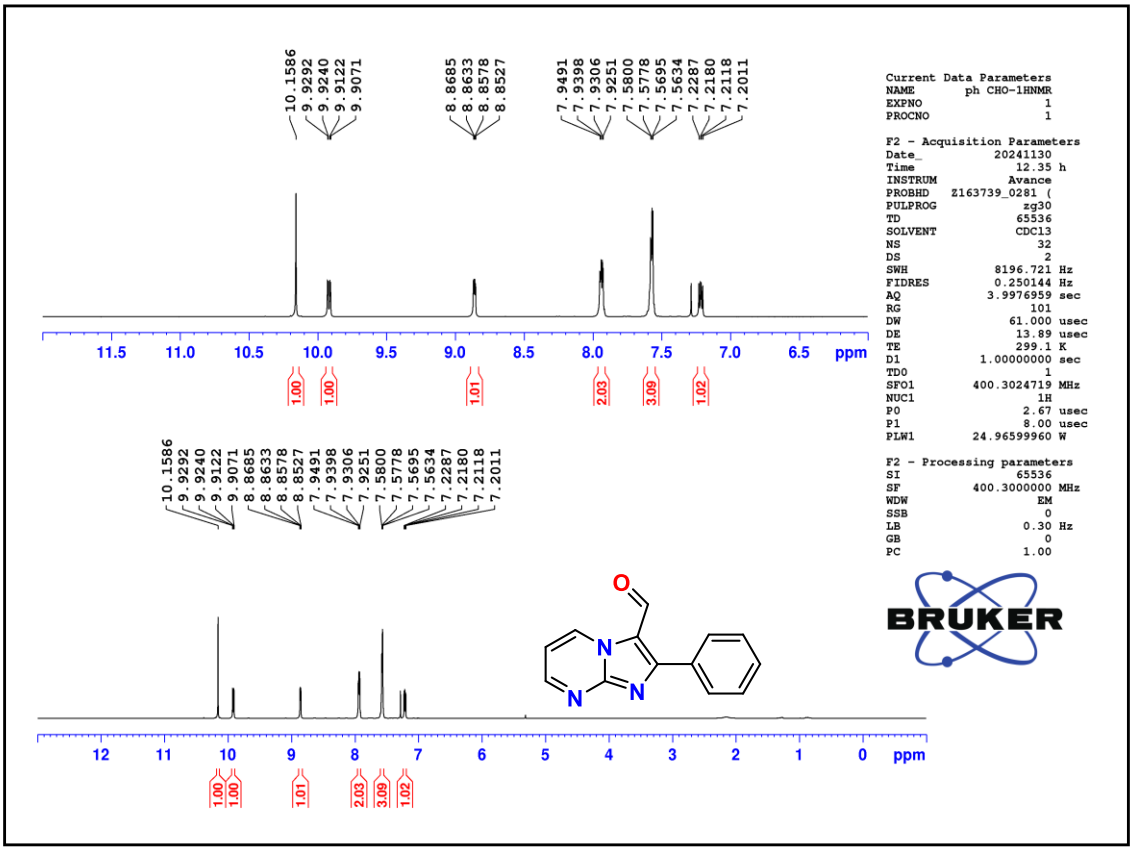


Figure S26: ^{1}H-NMR spectrum of compound **4g**

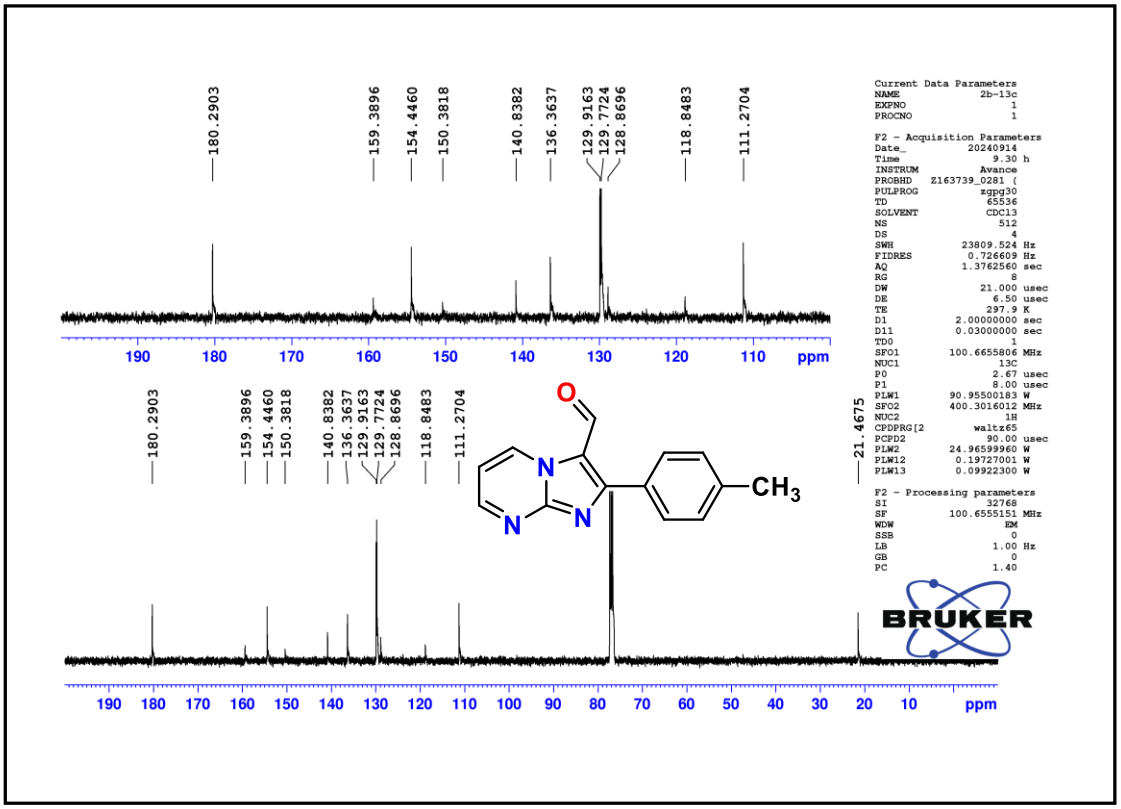


Figure S27: ^{13}C-NMR spectrum of compound **4a**

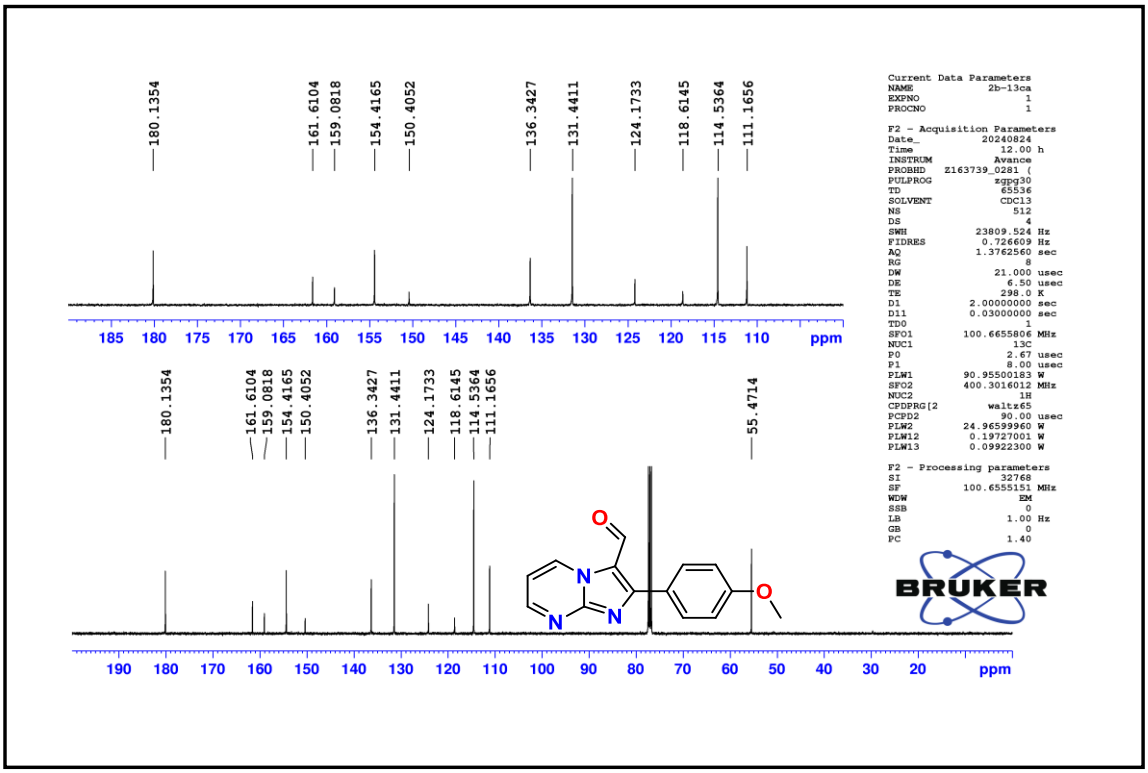


Figure S28: ^{13}C-NMR spectrum of compound **4b**

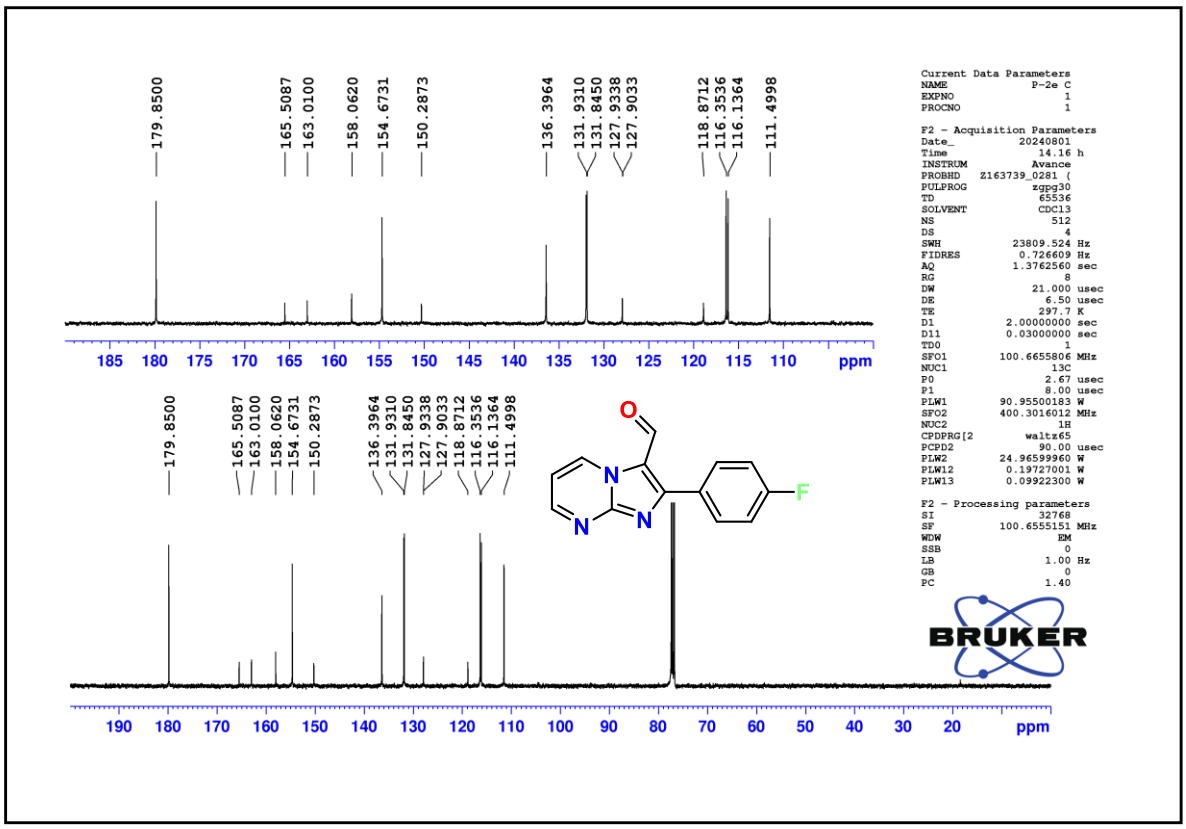


Figure S29: ^{13}C-NMR spectrum of compound **4c**

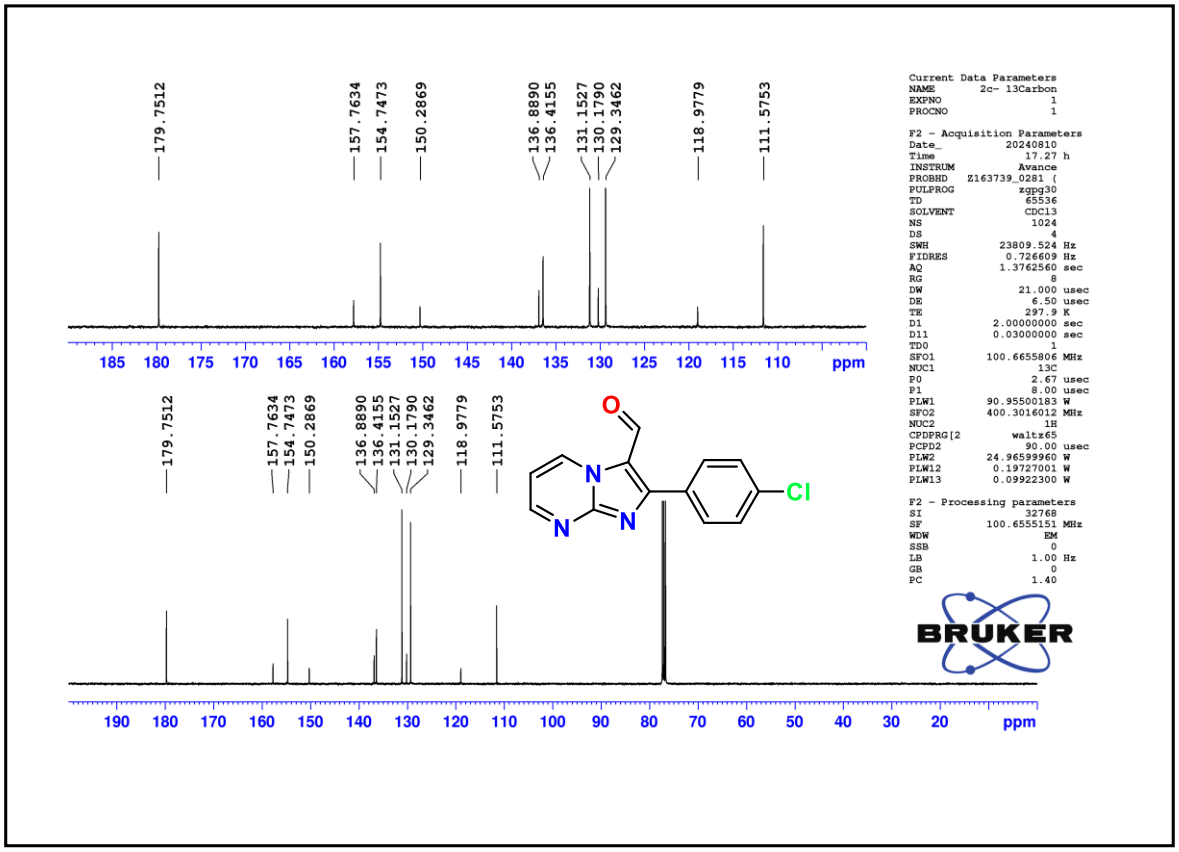


Figure S30: ^{13}C-NMR spectrum of compound **4d**

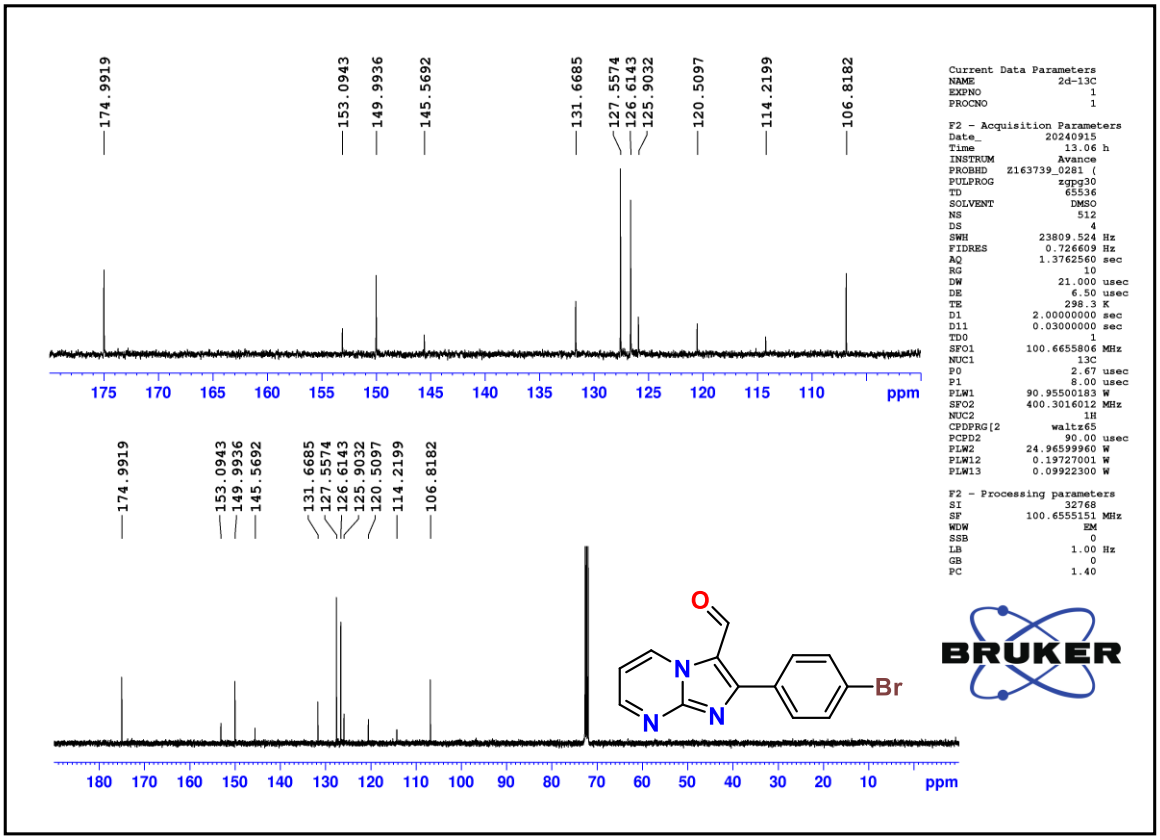


Figure S31: ^{13}C-NMR spectrum of compound **4e**

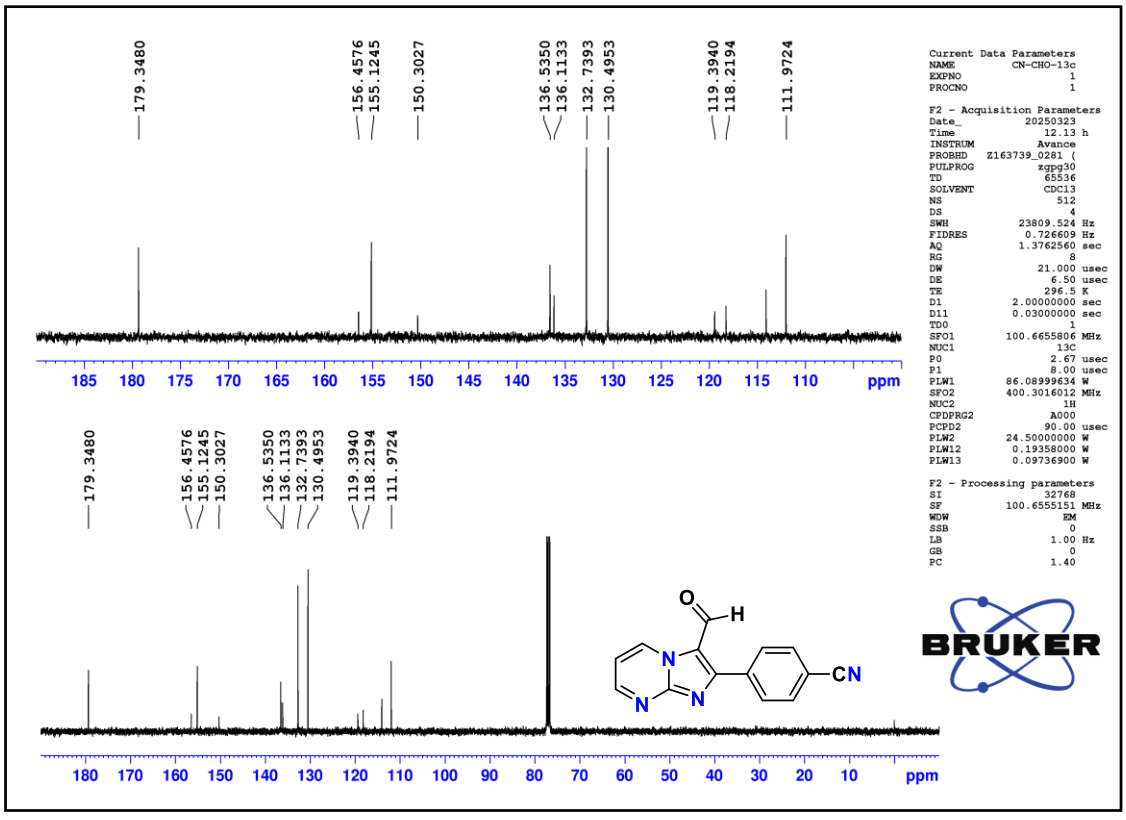


Figure S32: ^{13}C-NMR spectrum of compound **4f**

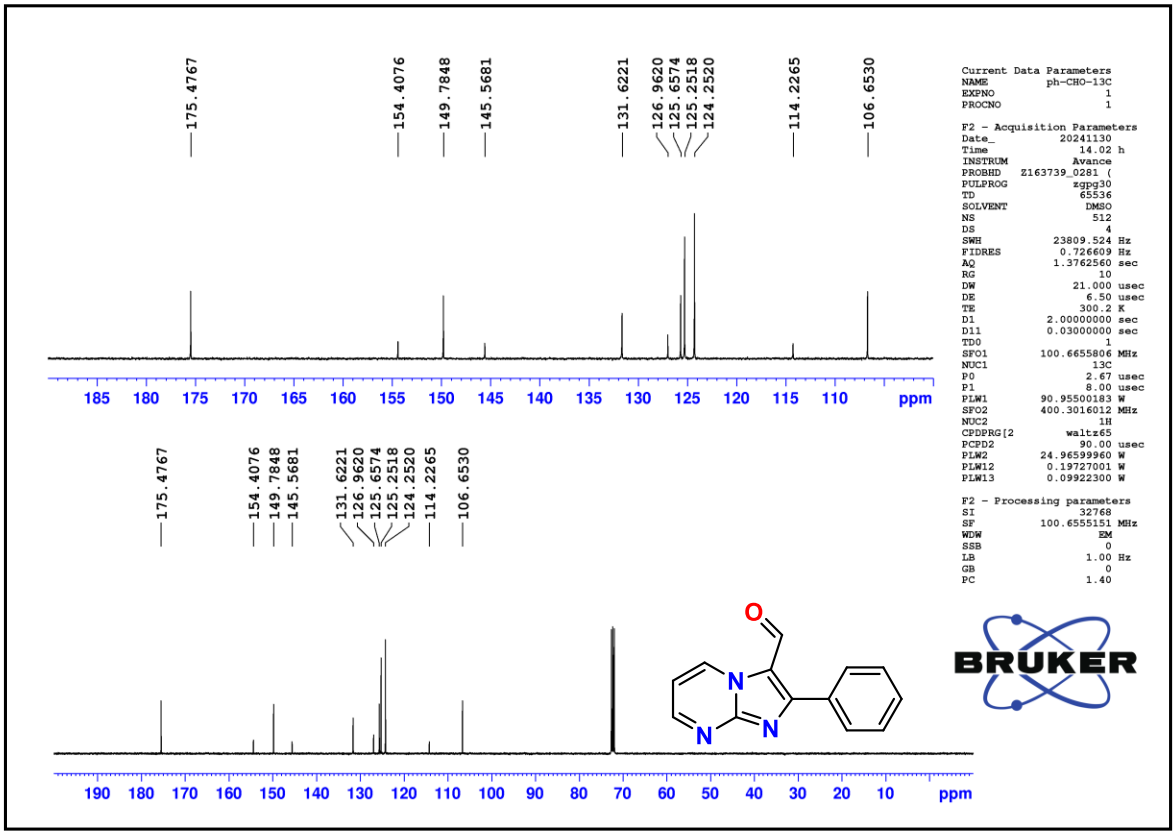


Figure S33: ^{13}C-NMR spectrum of compound **4g**

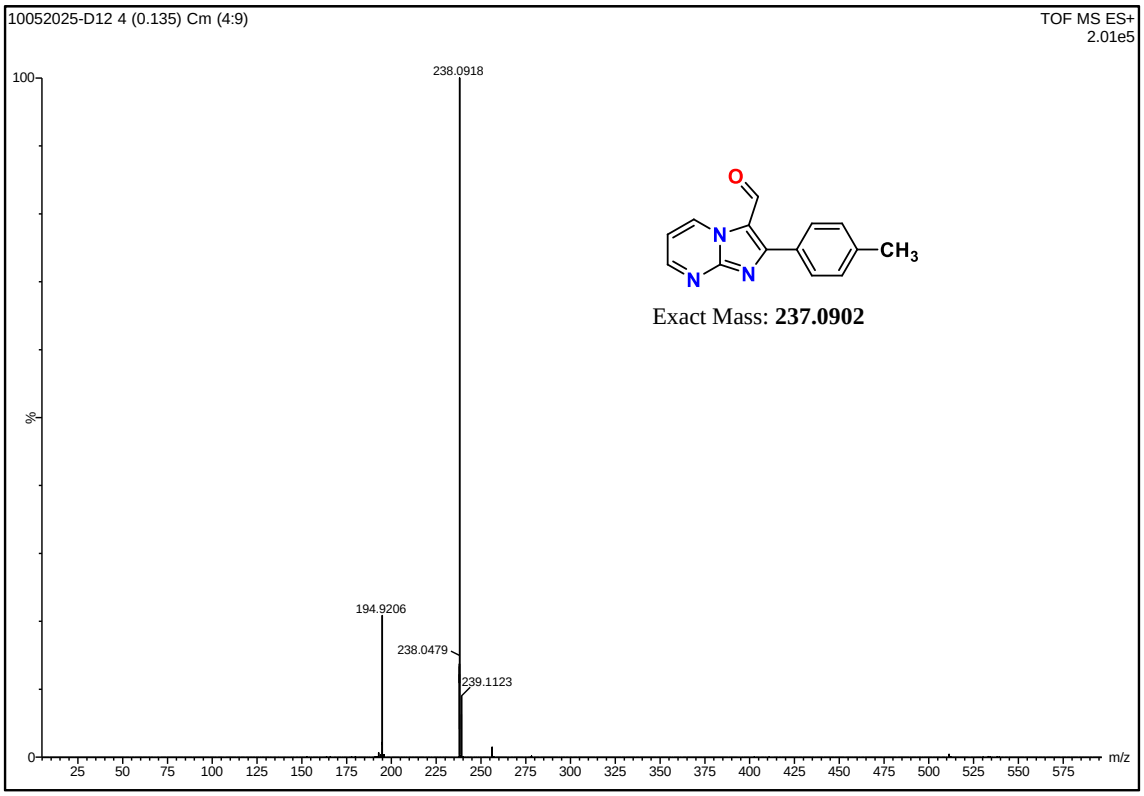


Figure S34: ^{13}C-NMR spectrum of compound **4a**

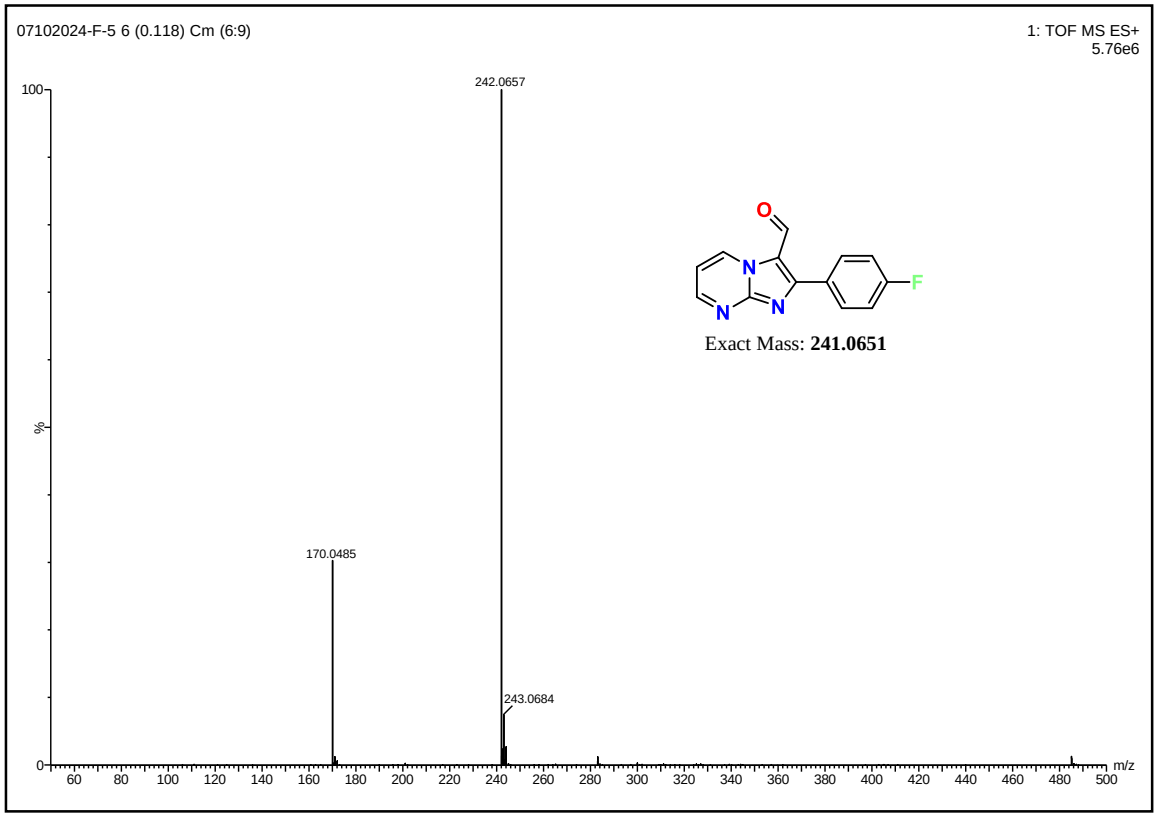


Figure S36: HR-MS spectrum of compound **4c**

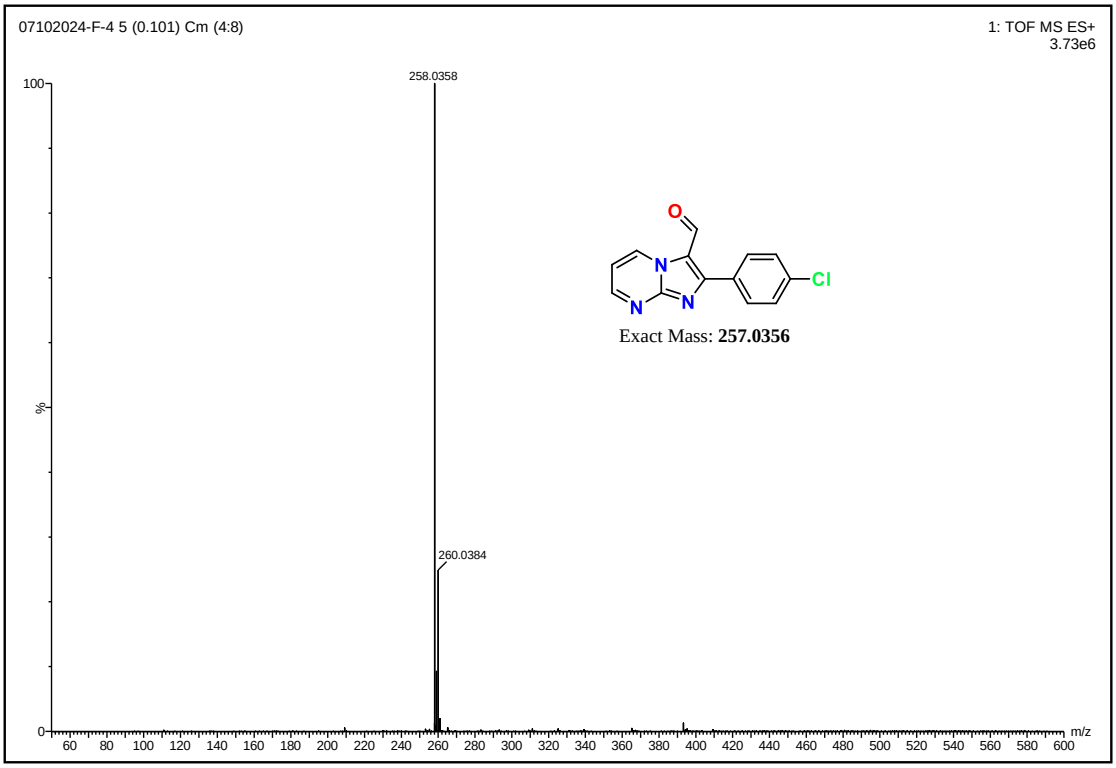


Figure S35: HR-MS spectrum of compound **4d**

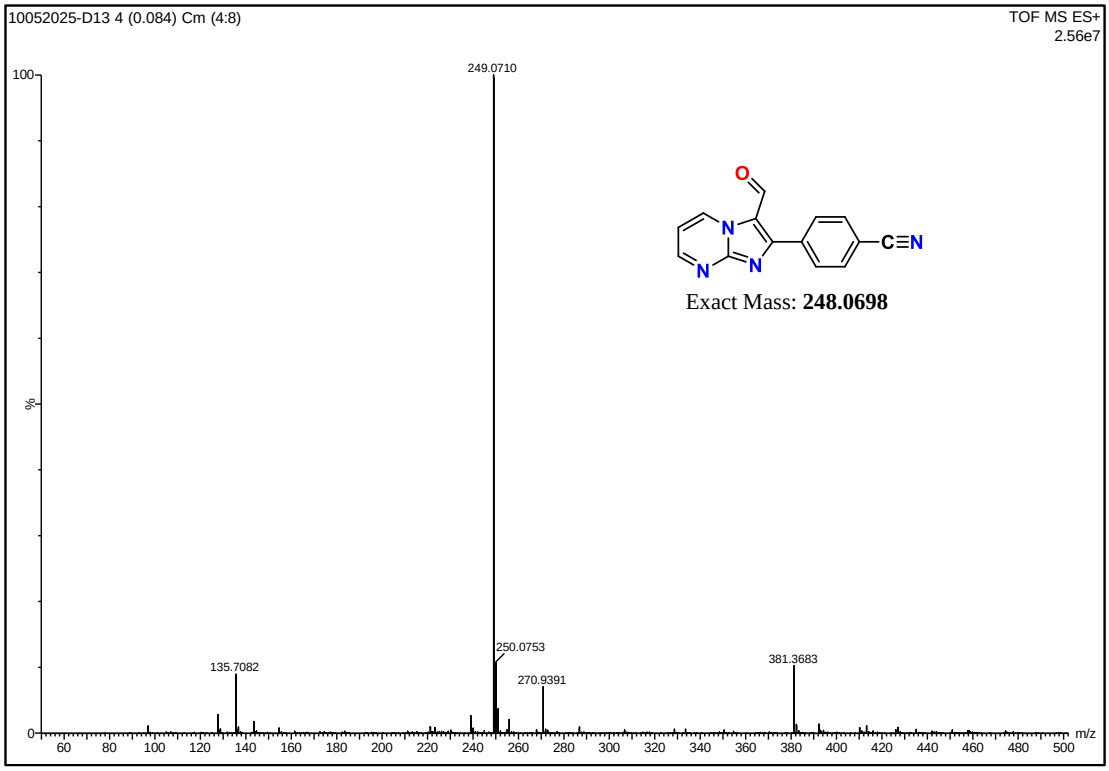


Figure S37: HR-MS spectrum of compound **4f**

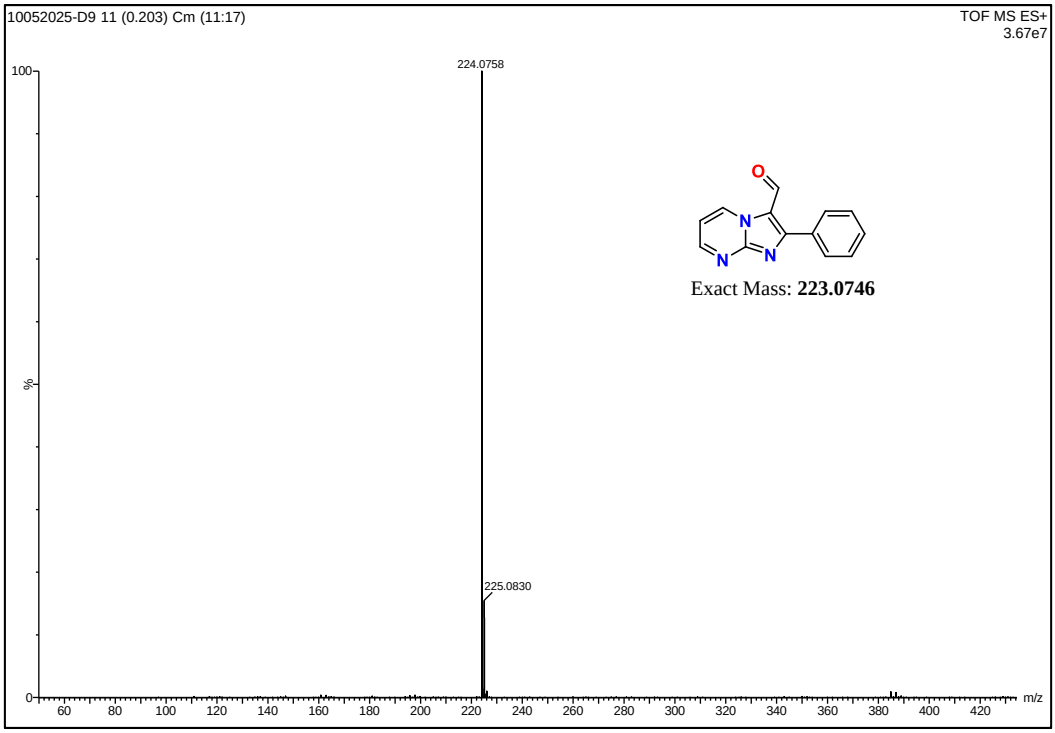


Figure S38: HR-MS spectrum of compound **4g**

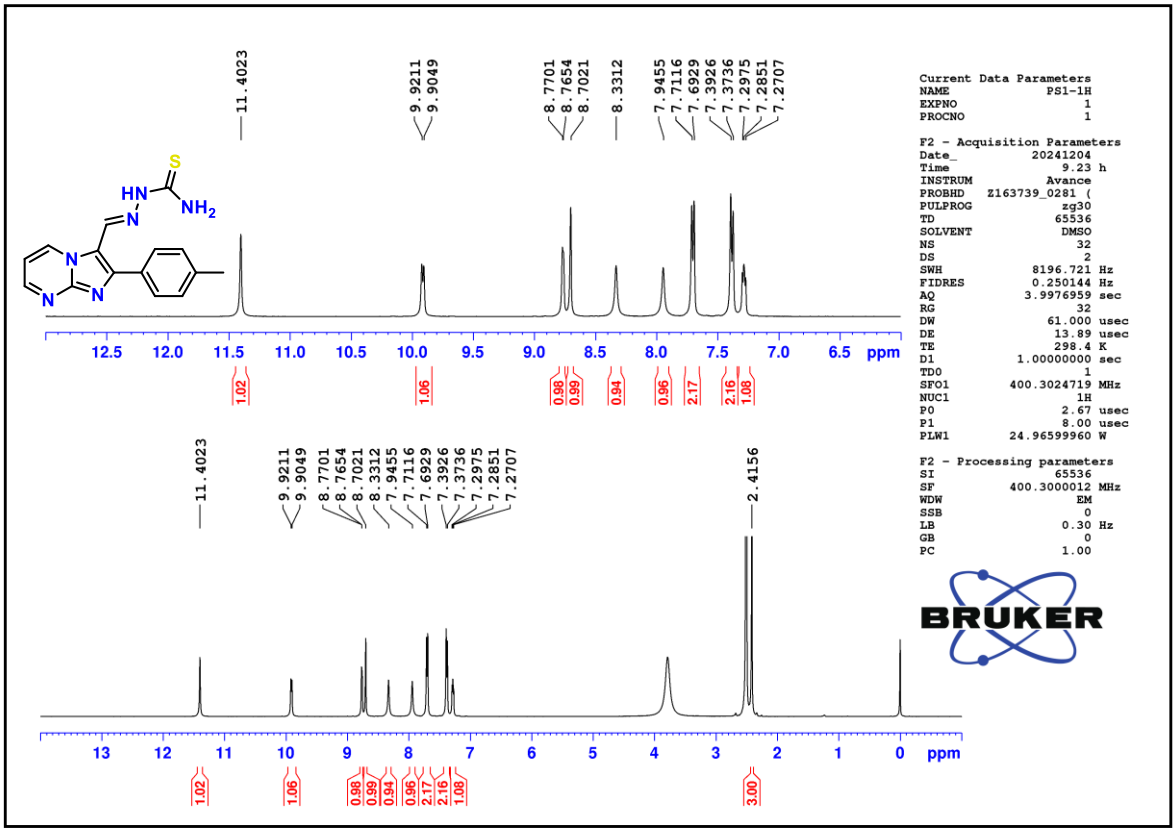


Figure S39: ^{1}H-NMR spectrum of compound **5a**

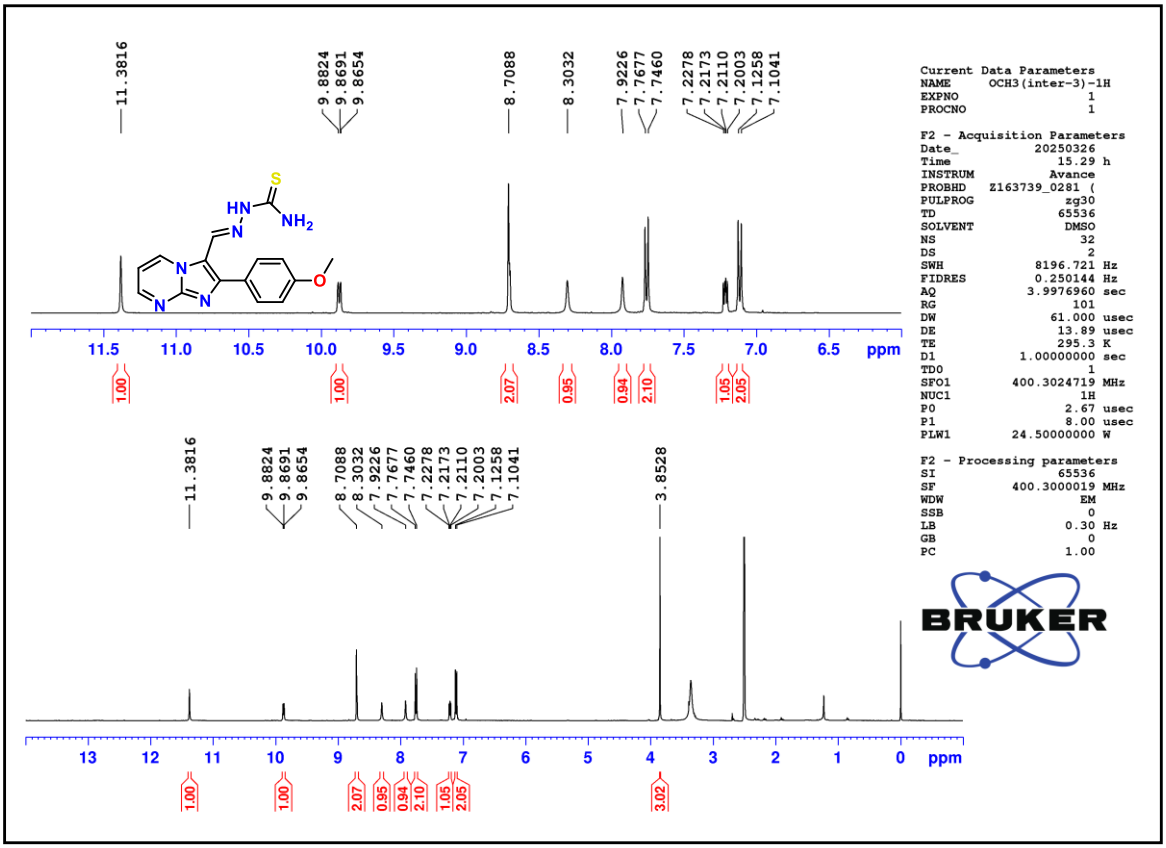


Figure S40: ^{1}H-NMR spectrum of compound **5b**

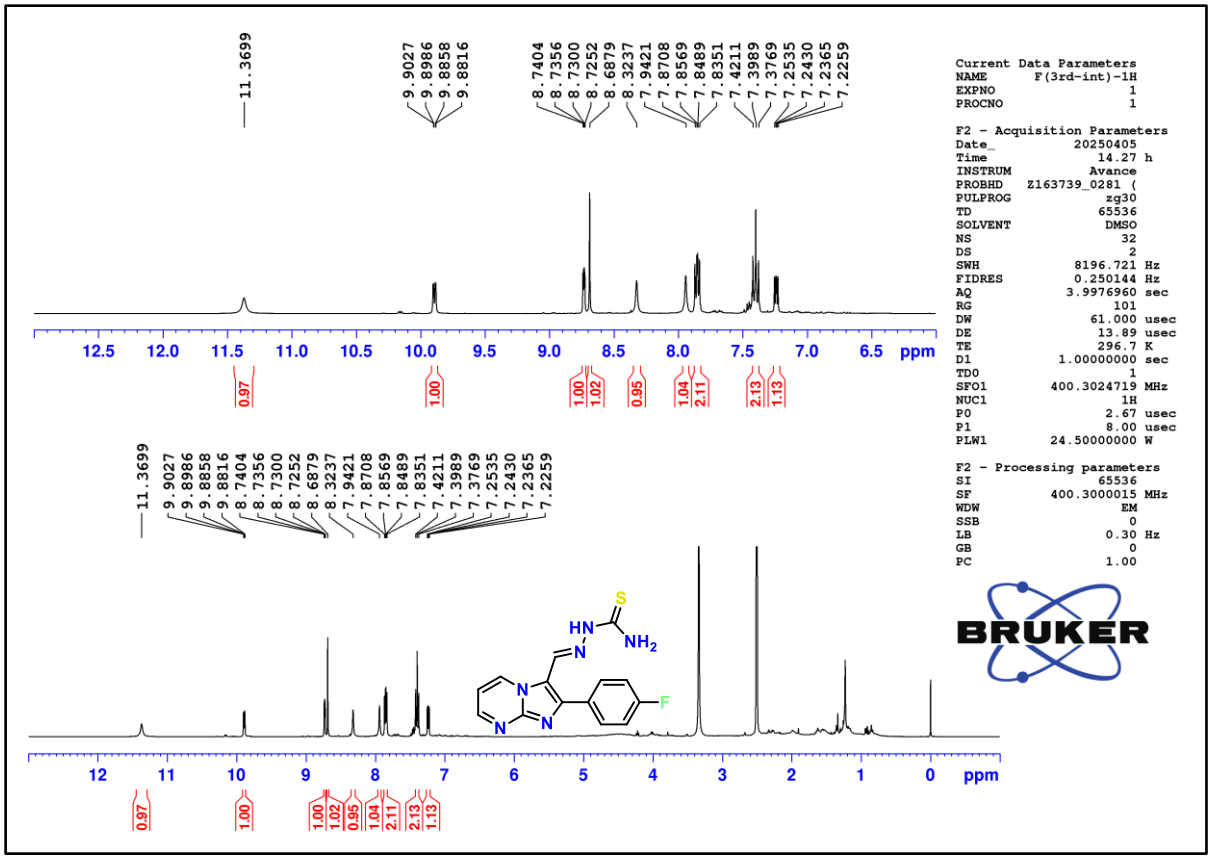


Figure S41: ^{1}H-NMR spectrum of compound **5c**

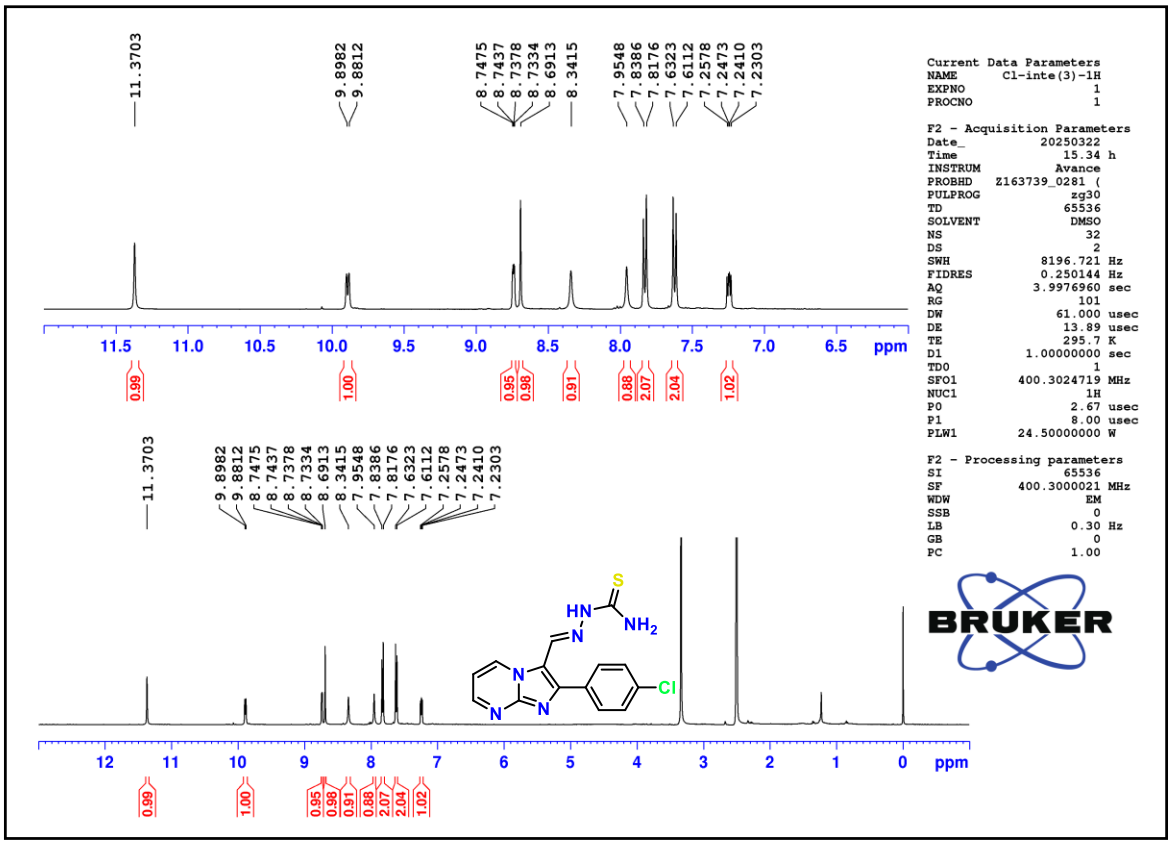


Figure S42: ^{1}H-NMR spectrum of compound **5d**

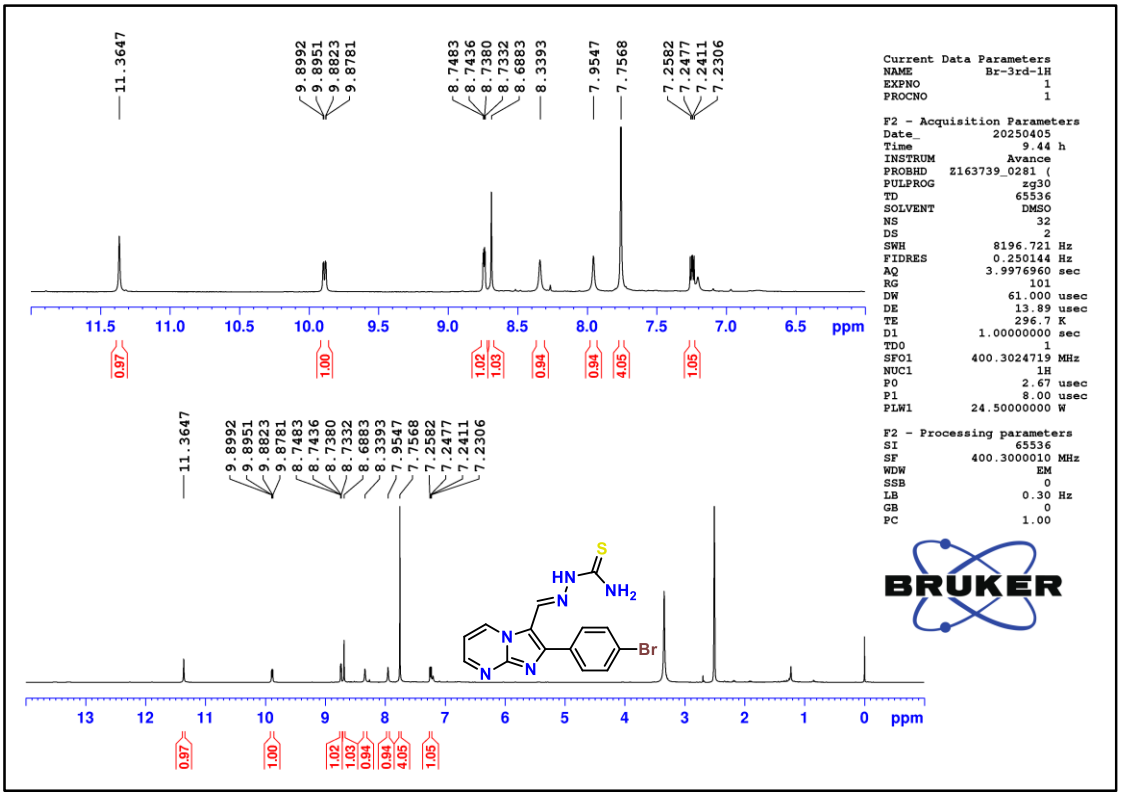


Figure S43: ^{1}H-NMR spectrum of compound **5e**

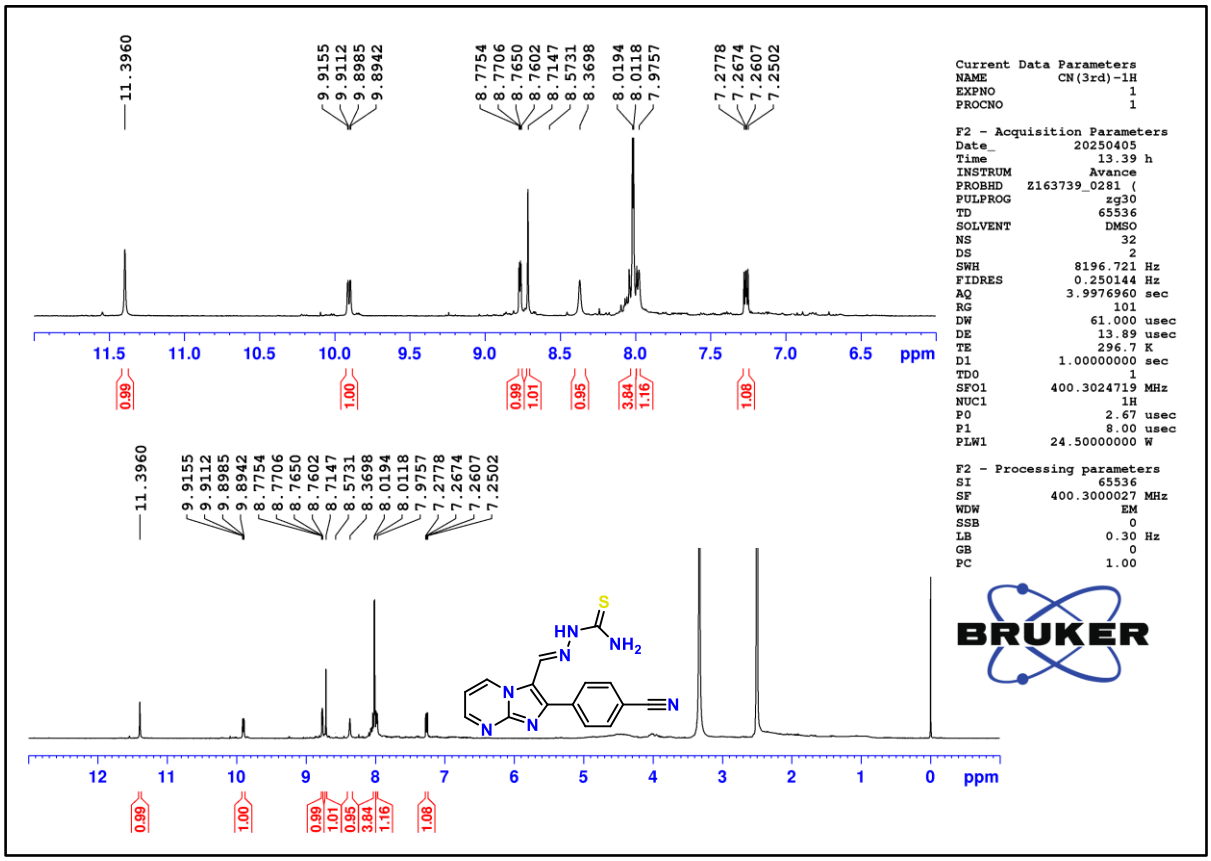


Figure S43: ^{1}H-NMR spectrum of compound **5f**

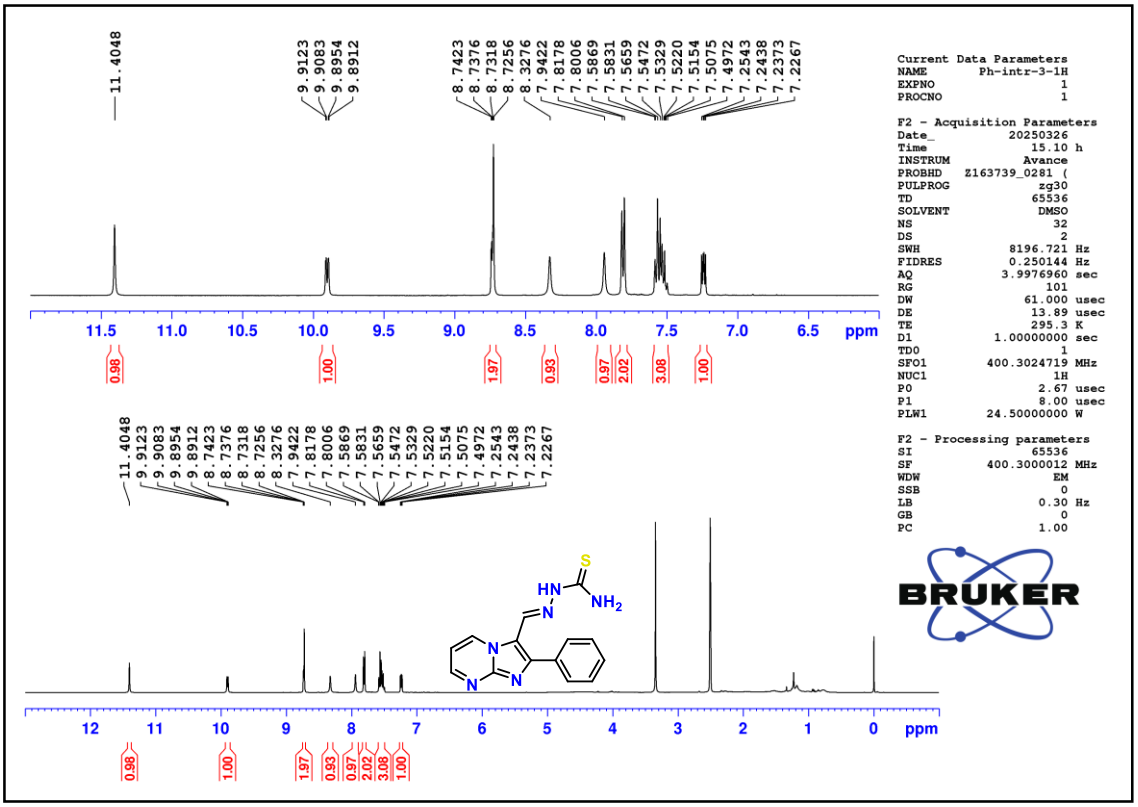


Figure S44: ^{1}H-NMR spectrum of compound **5g**

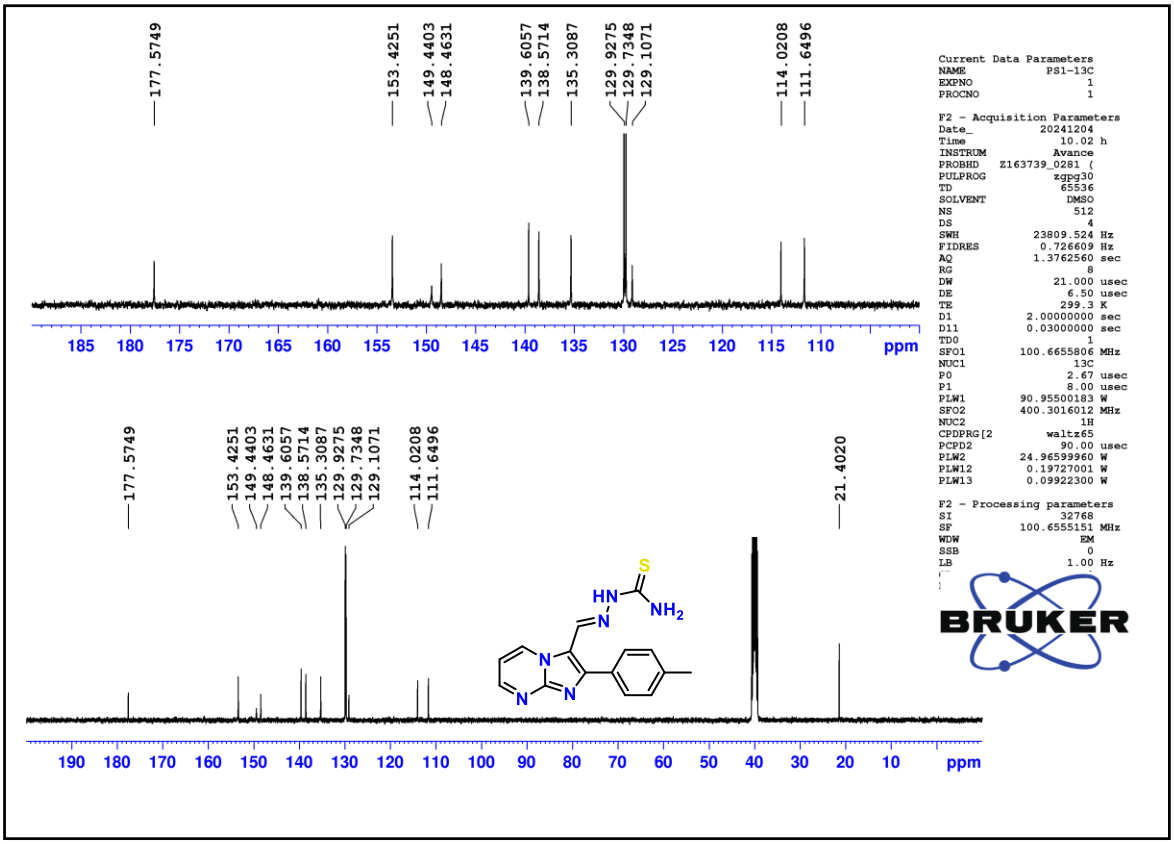


Figure S45: ^{13}C-NMR spectrum of compound **5a**

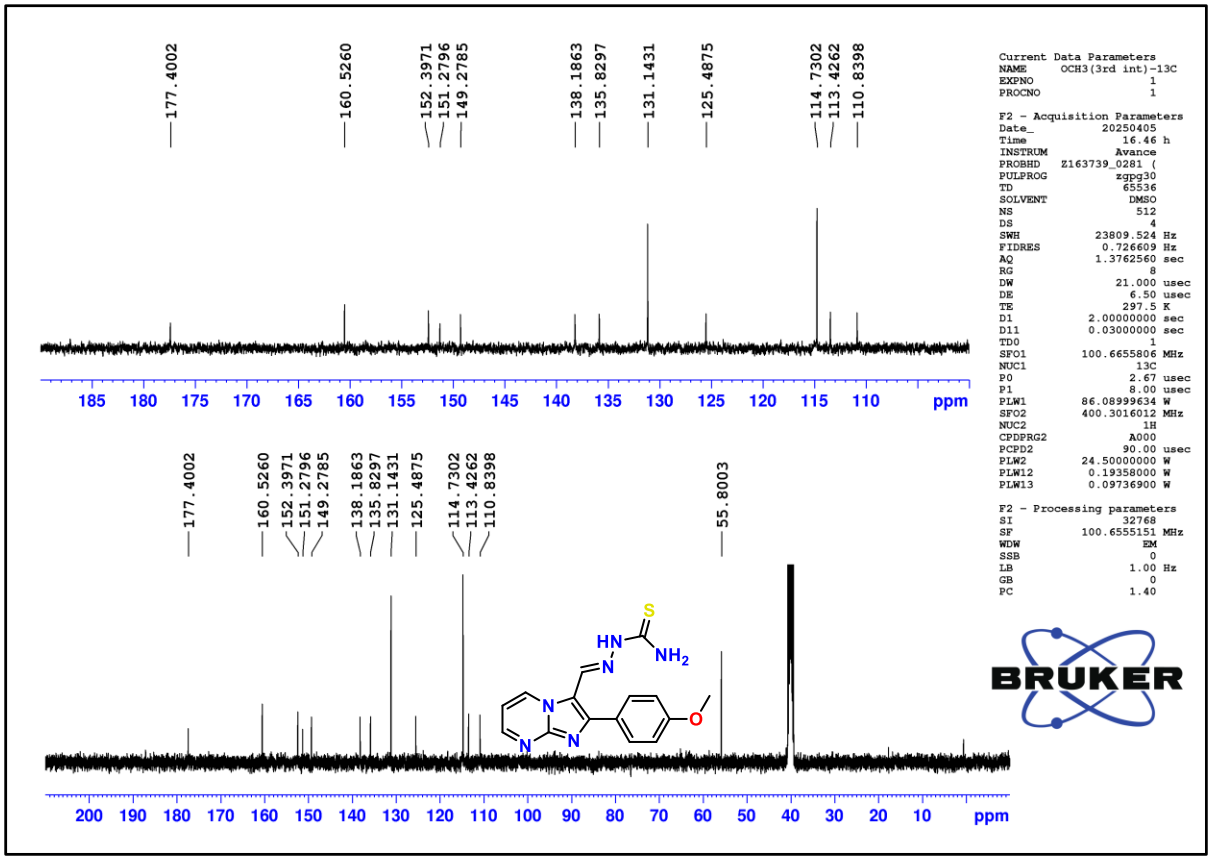


Figure S46: ^{13}C-NMR spectrum of compound **5b**

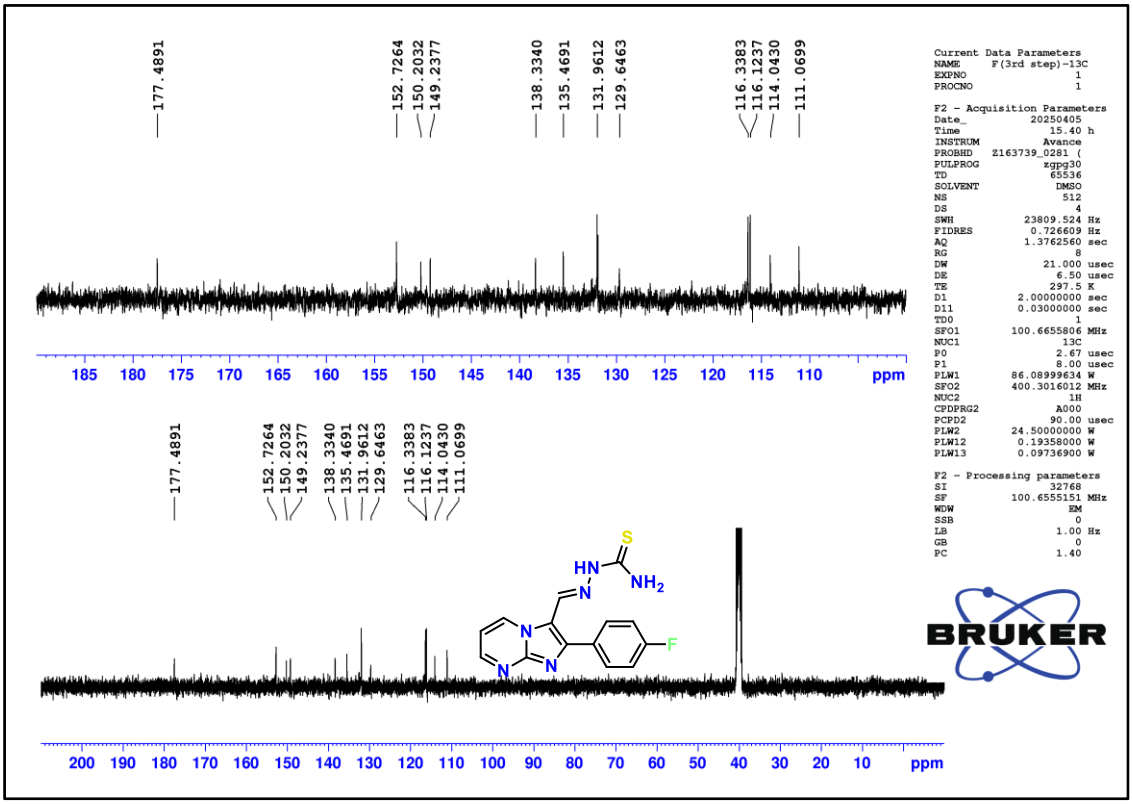


Figure S47: ^{13}C-NMR spectrum of compound **5c**

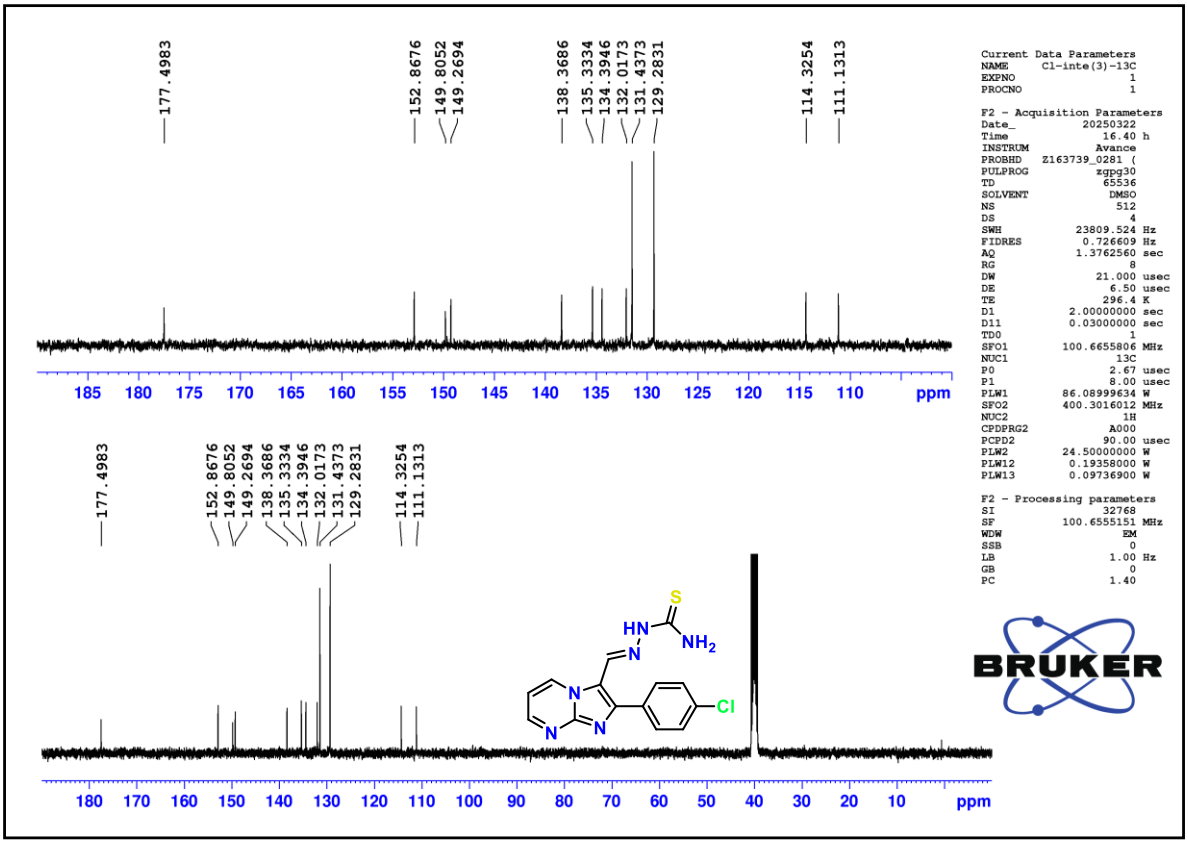


Figure S48: ^{13}C-NMR spectrum of compound **5d**

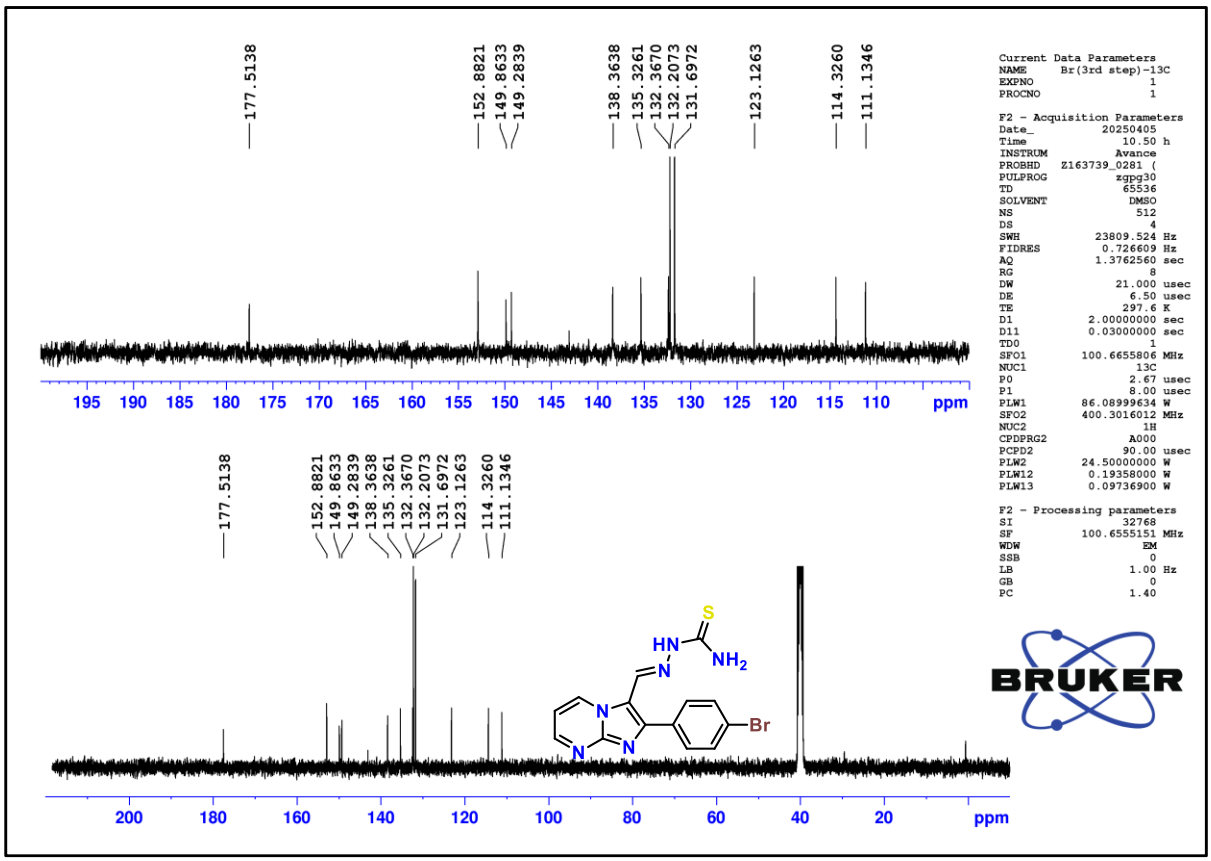


Figure S49: ^{13}C-NMR spectrum of compound **5e**

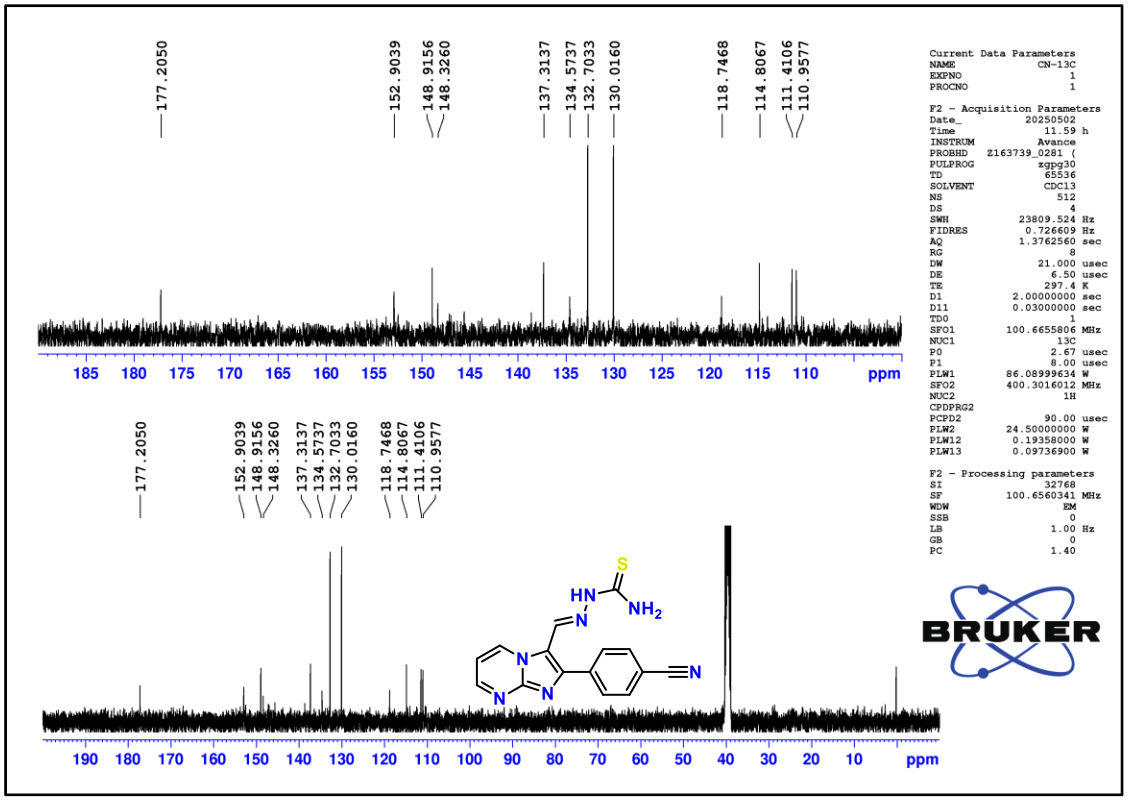


Figure S50: ^{13}C-NMR spectrum of compound **5f**

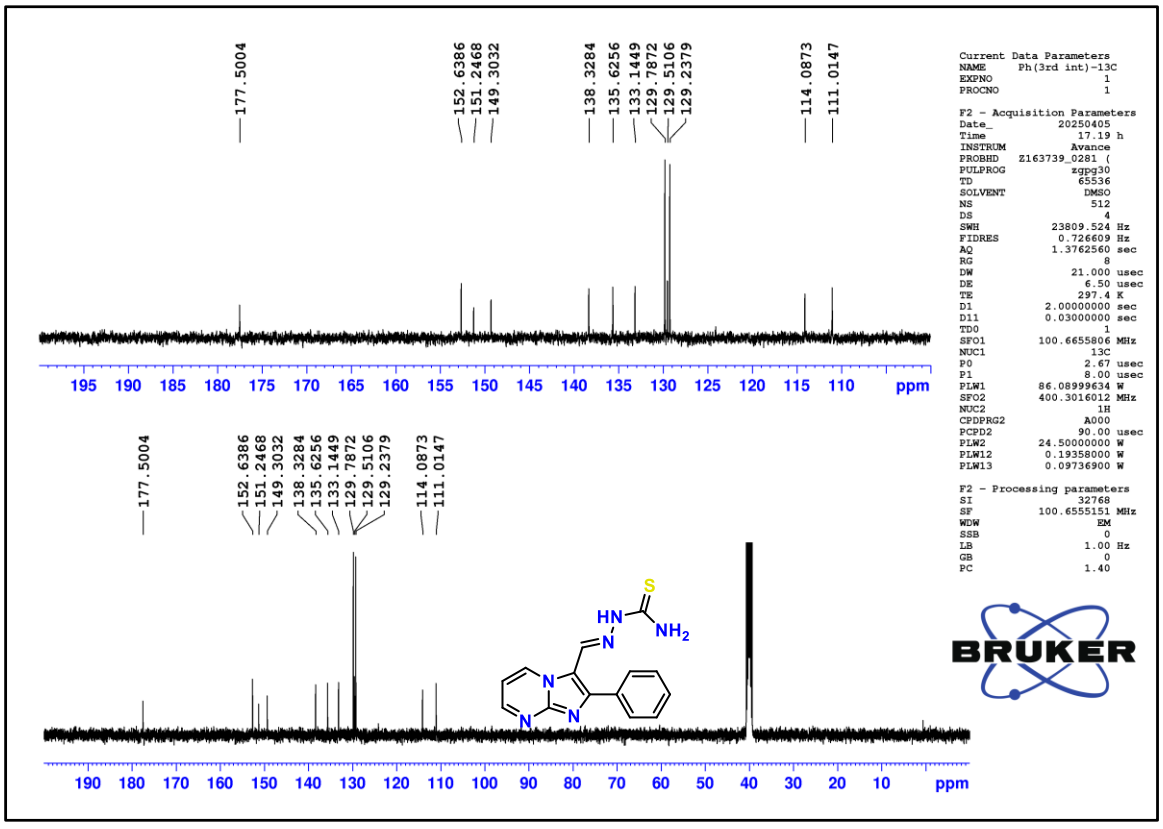


Figure S50: ^{13}C-NMR spectrum of compound **5g**

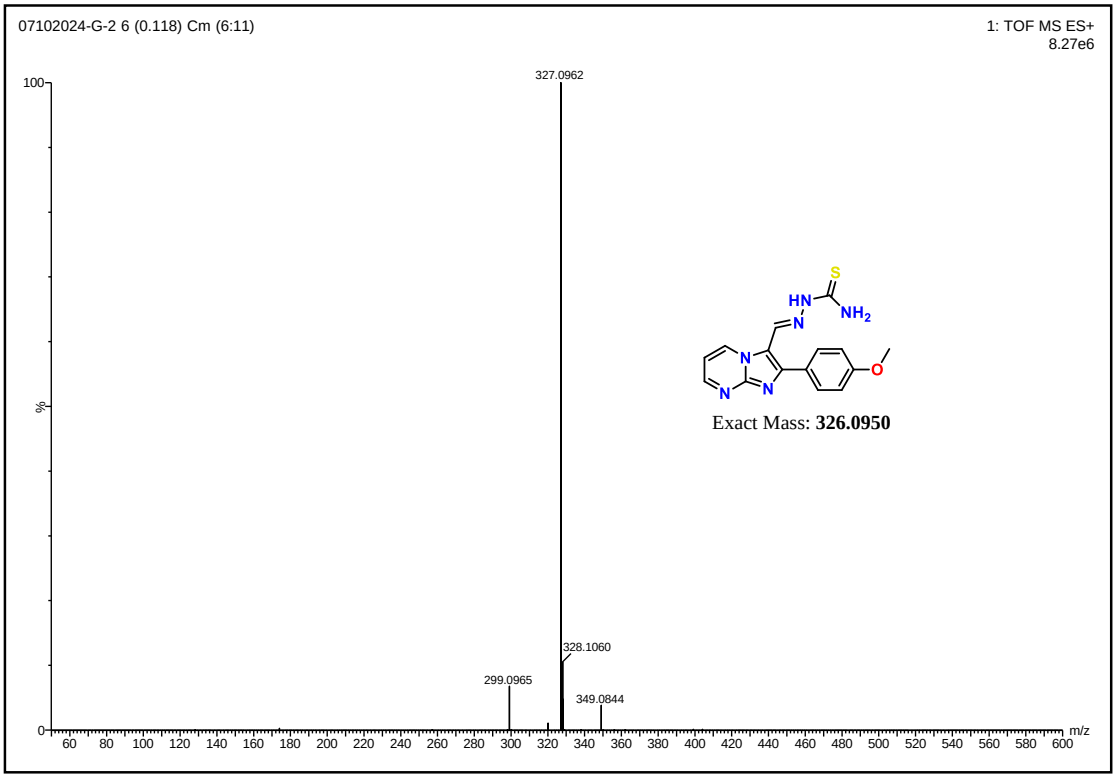


Figure S51: HR-MS spectrum of compound **5b**

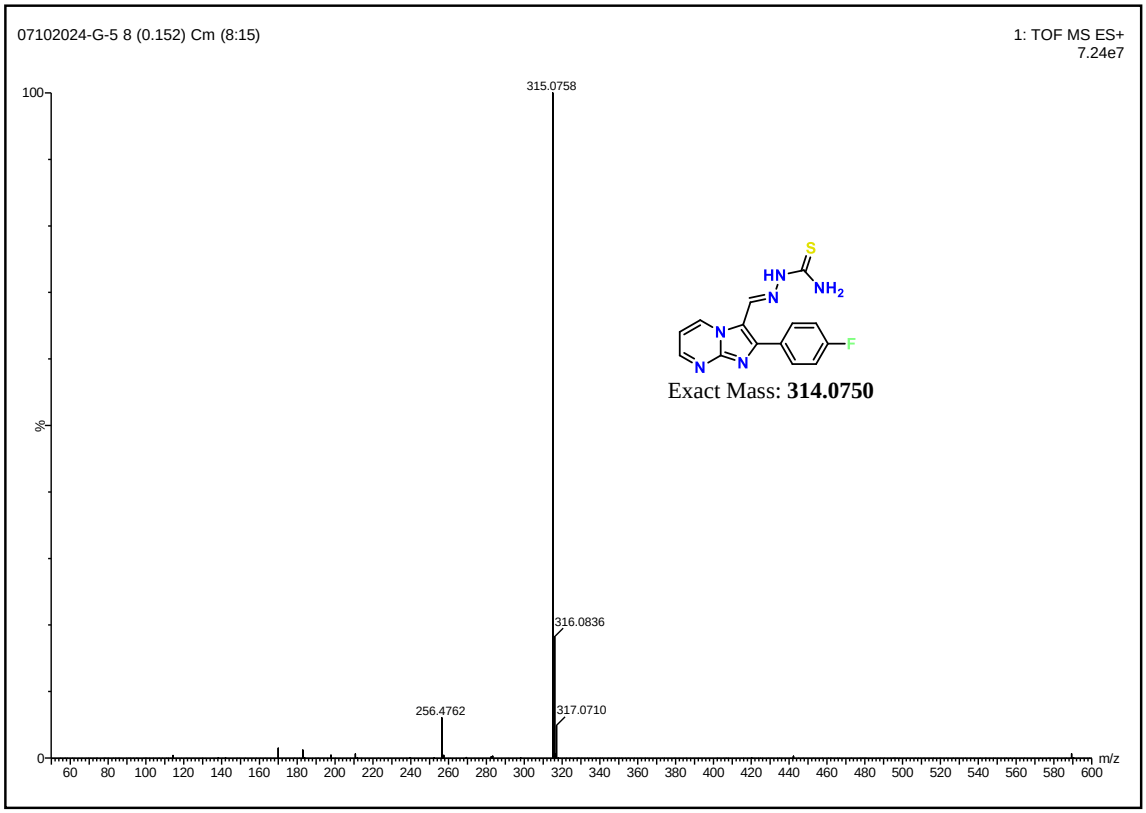


Figure S52: HR-MS spectrum of compound **5c**

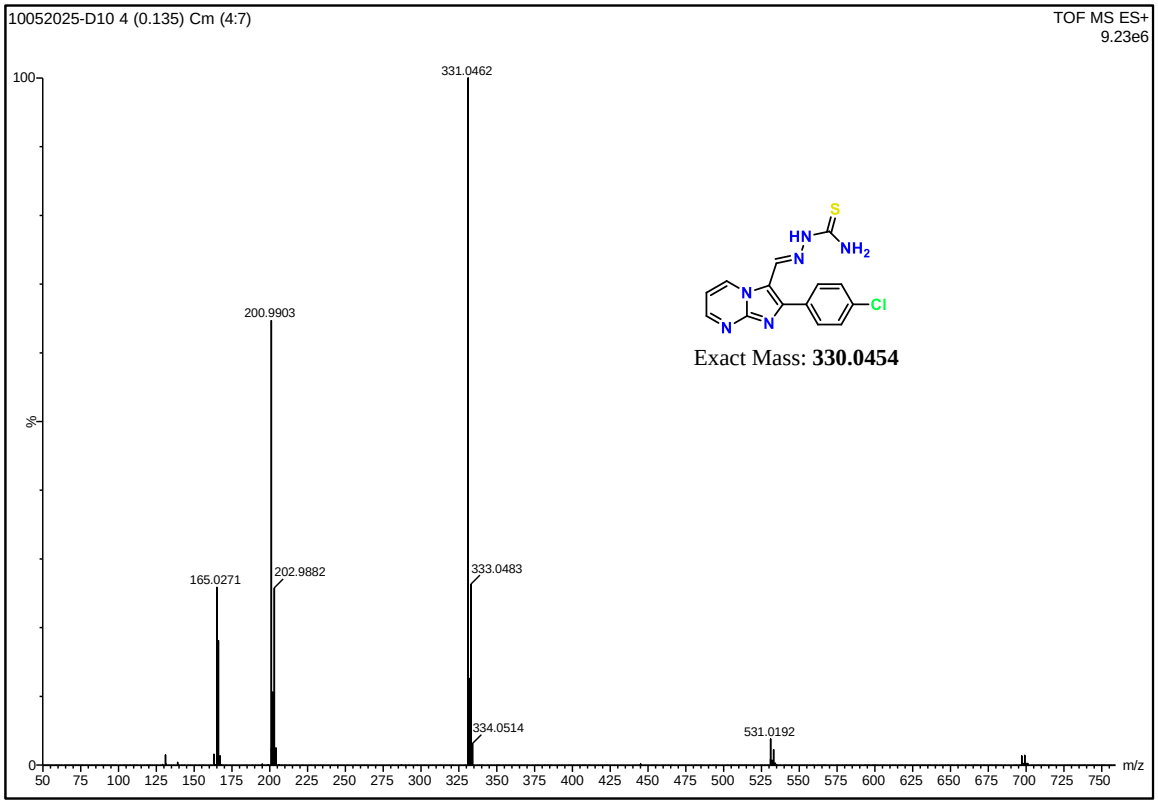


Figure S53: HR-MS spectrum of compound **5d**

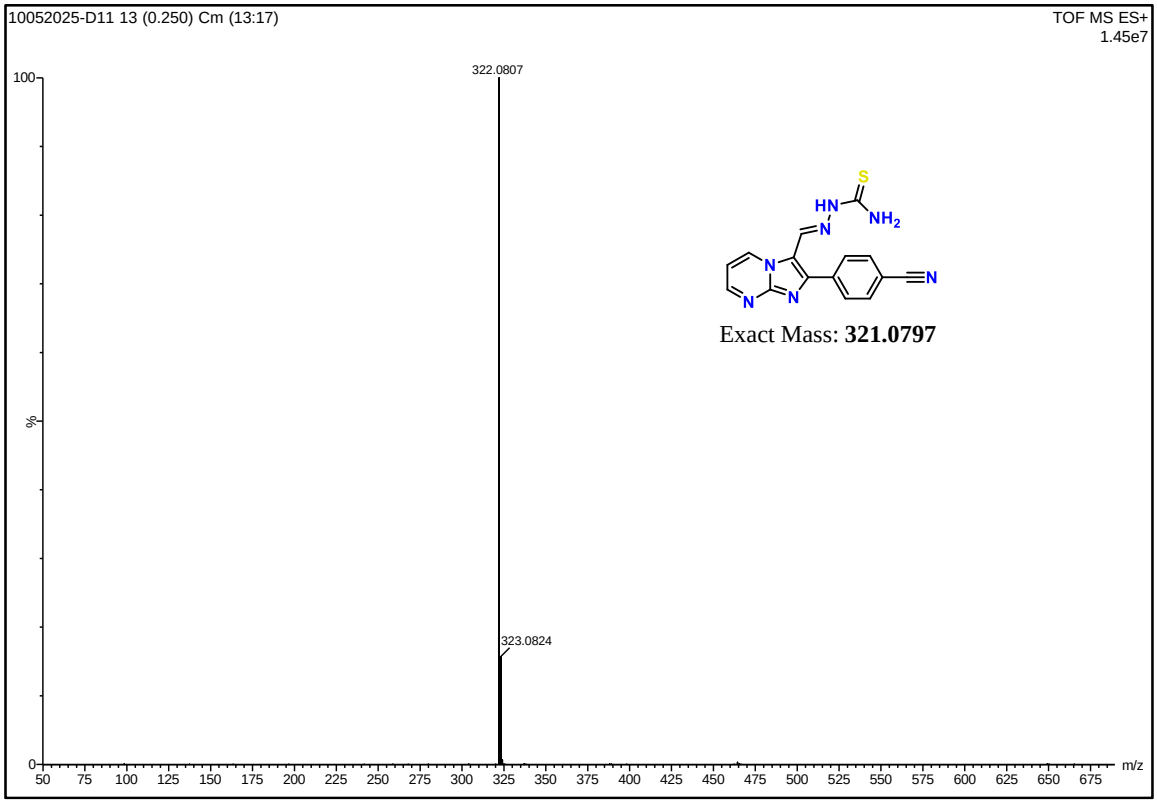


Figure S54: HR-MS spectrum of compound **5f**

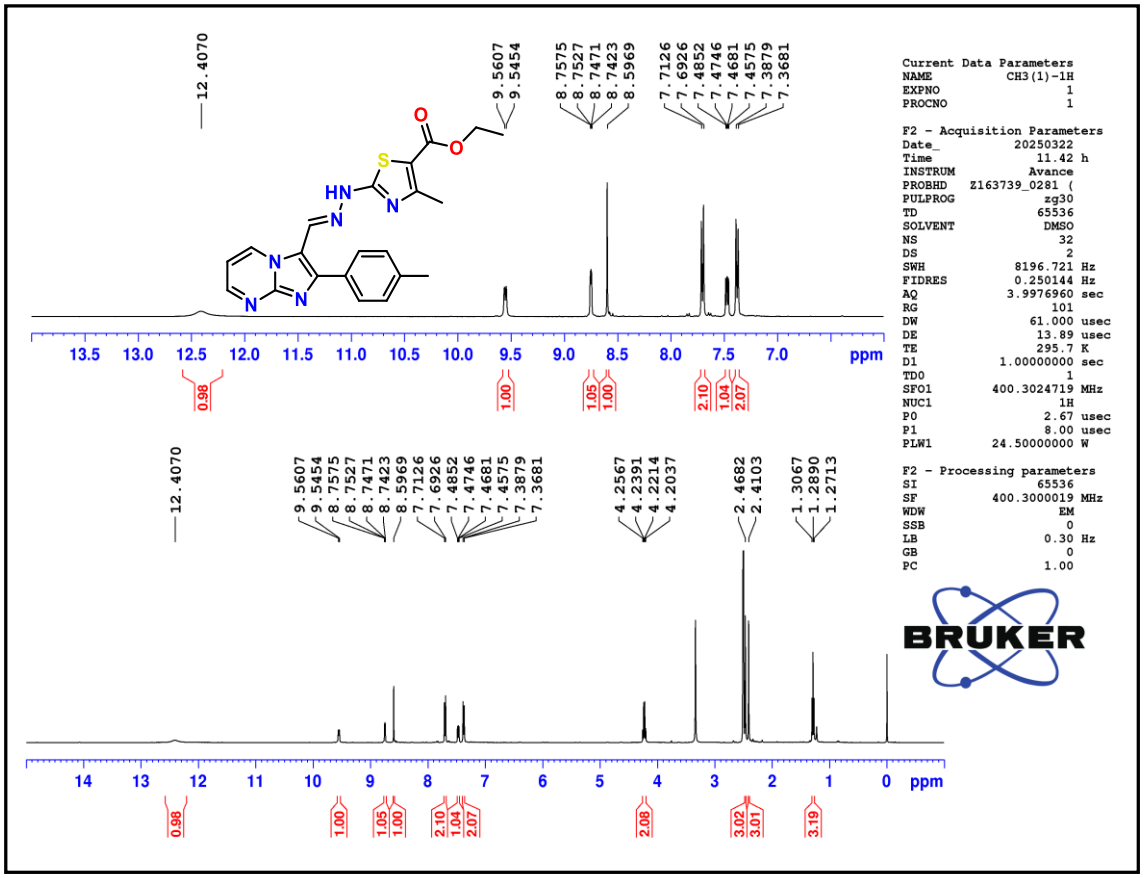


Figure S55: [1]H-NMR spectrum of compound **K1**

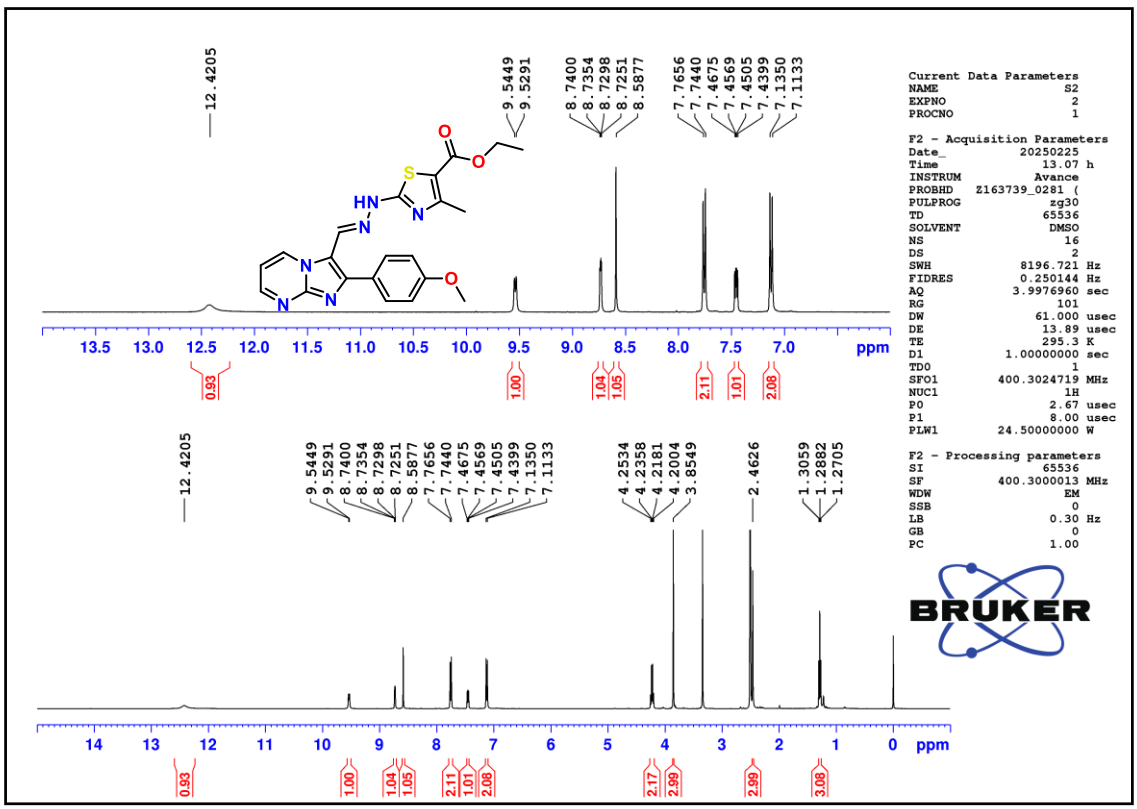


Figure S56: [1]H-NMR spectrum of compound **K2**

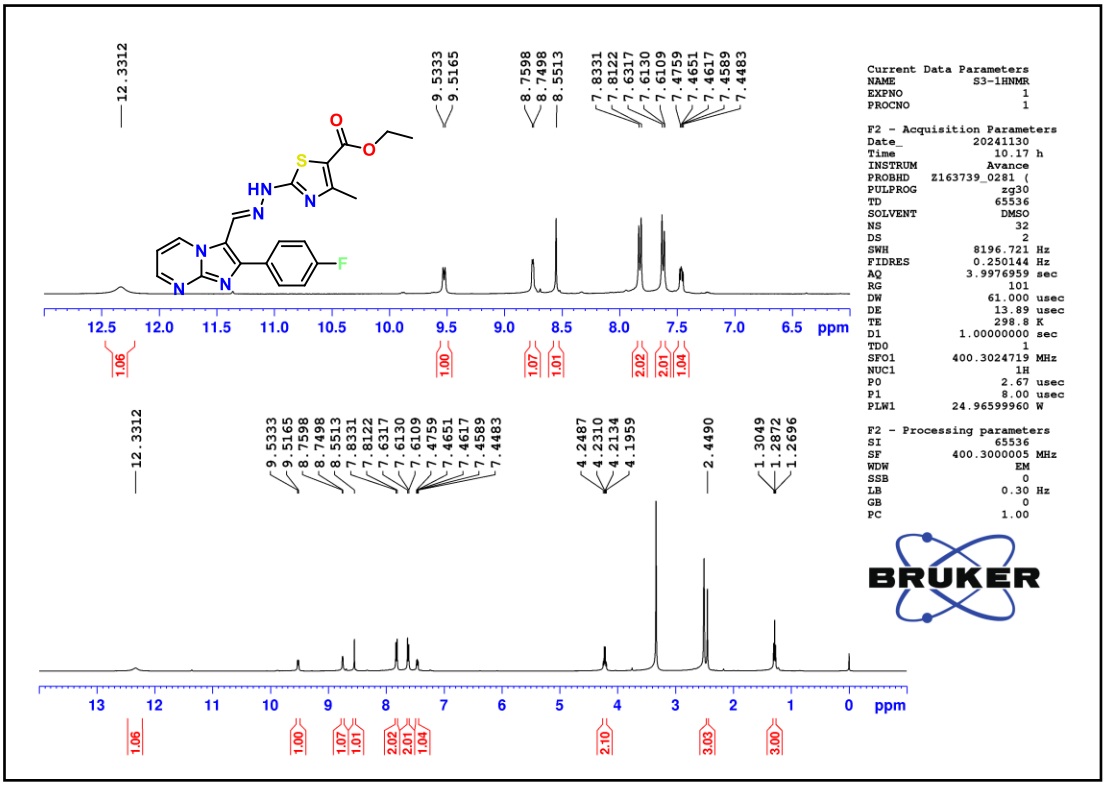


Figure S57: [1]H-NMR spectrum of compound **K3**

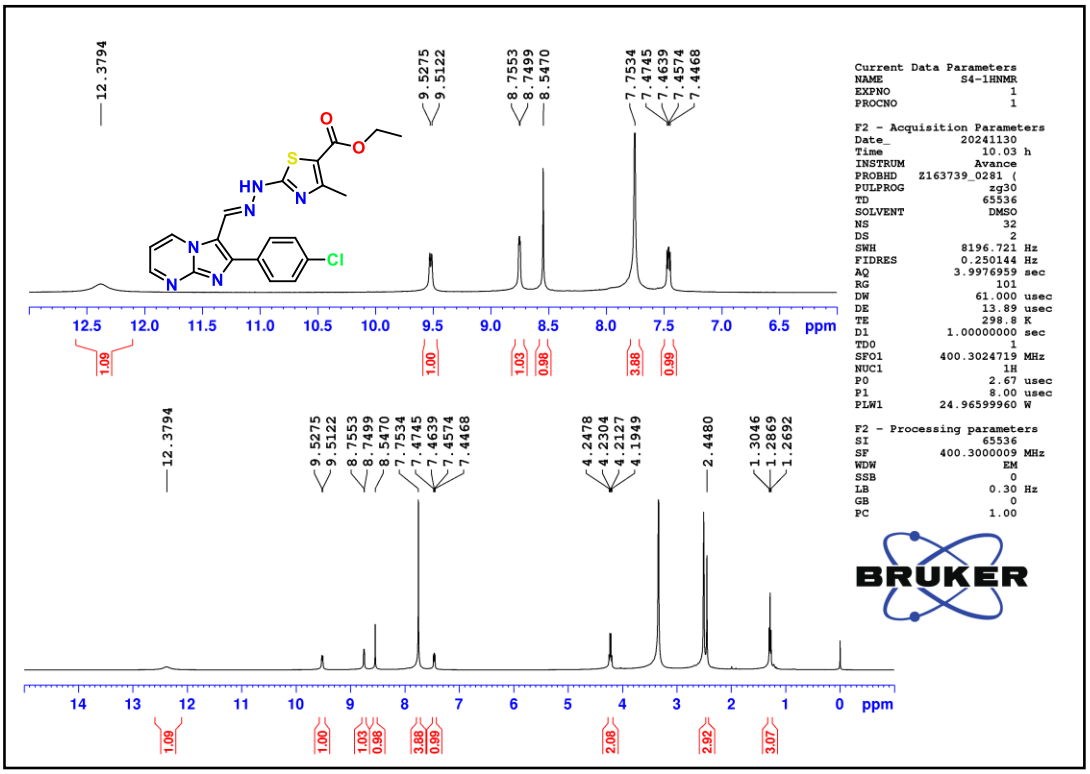


Figure S58: [1]H-NMR spectrum of compound **K4**

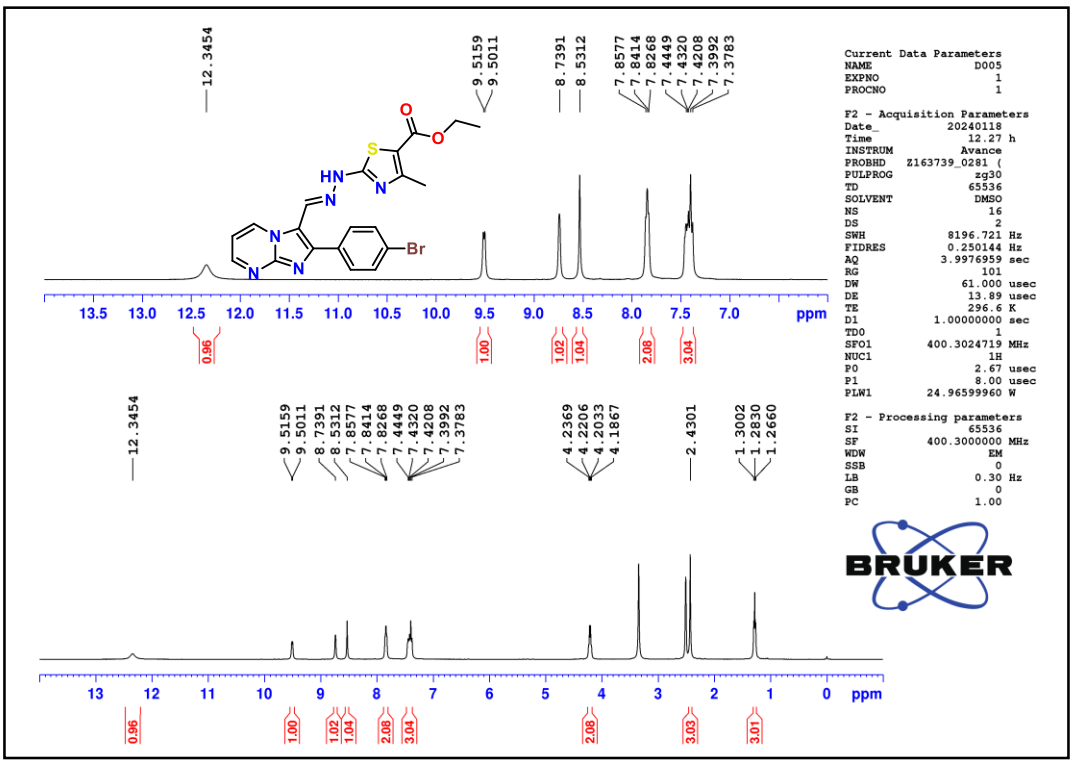


Figure S59: ^{1}H-NMR spectrum of compound **K5**

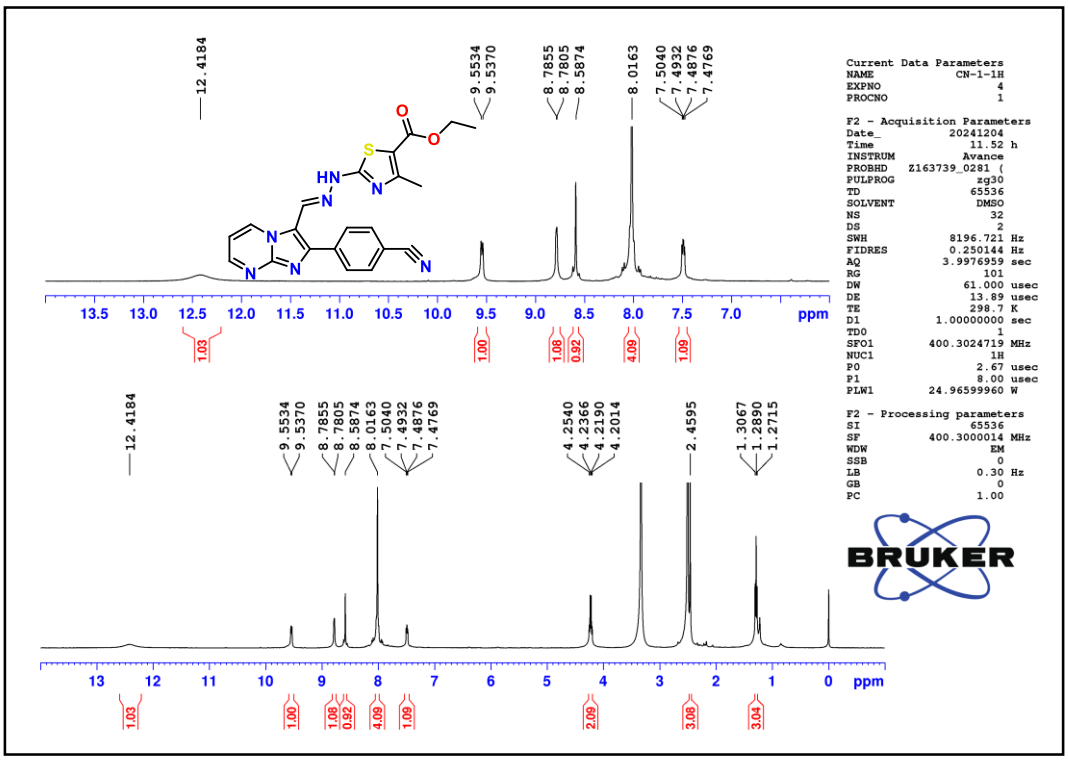


Figure S60: ^{1}H-NMR spectrum of compound **K6**

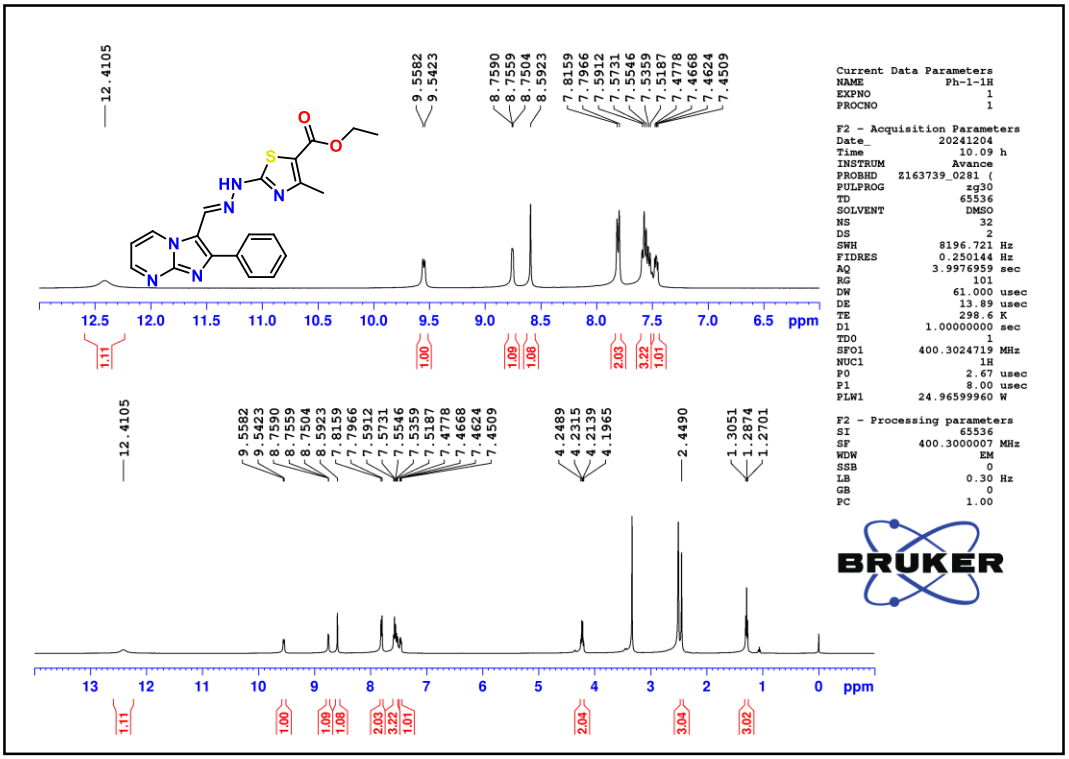


Figure S61: ^{1}H-NMR spectrum of compound **K7**

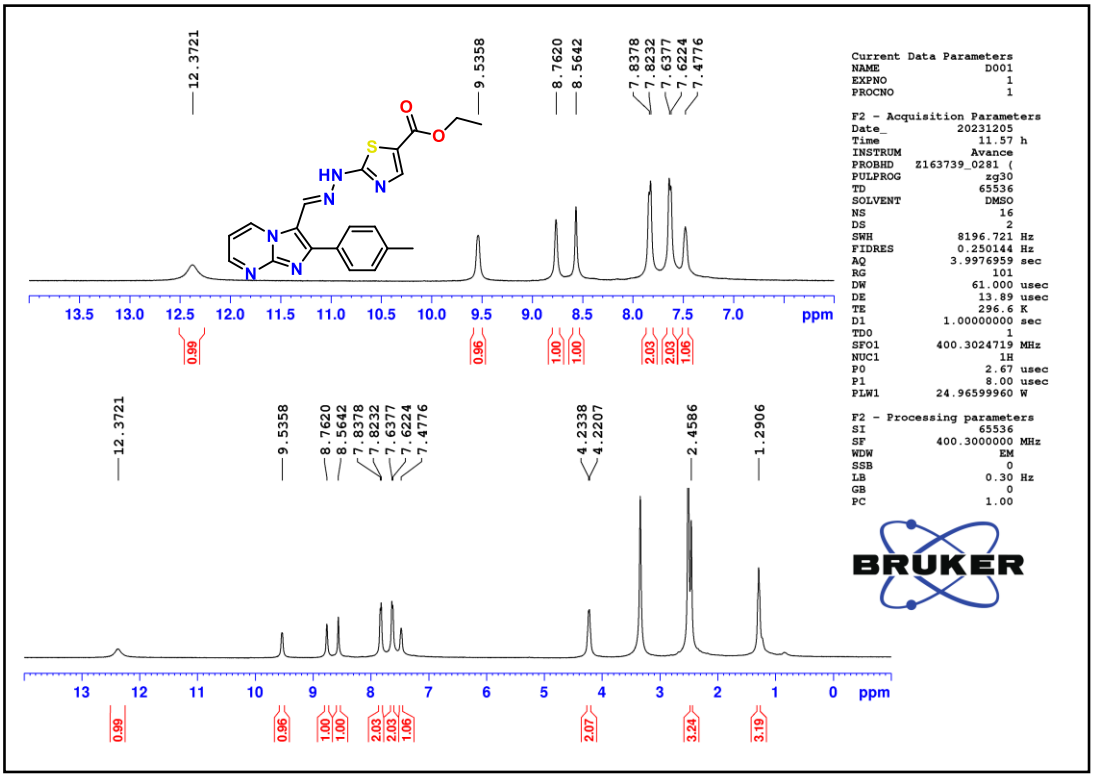


Figure S62: ^{1}H-NMR spectrum of compound **K8**

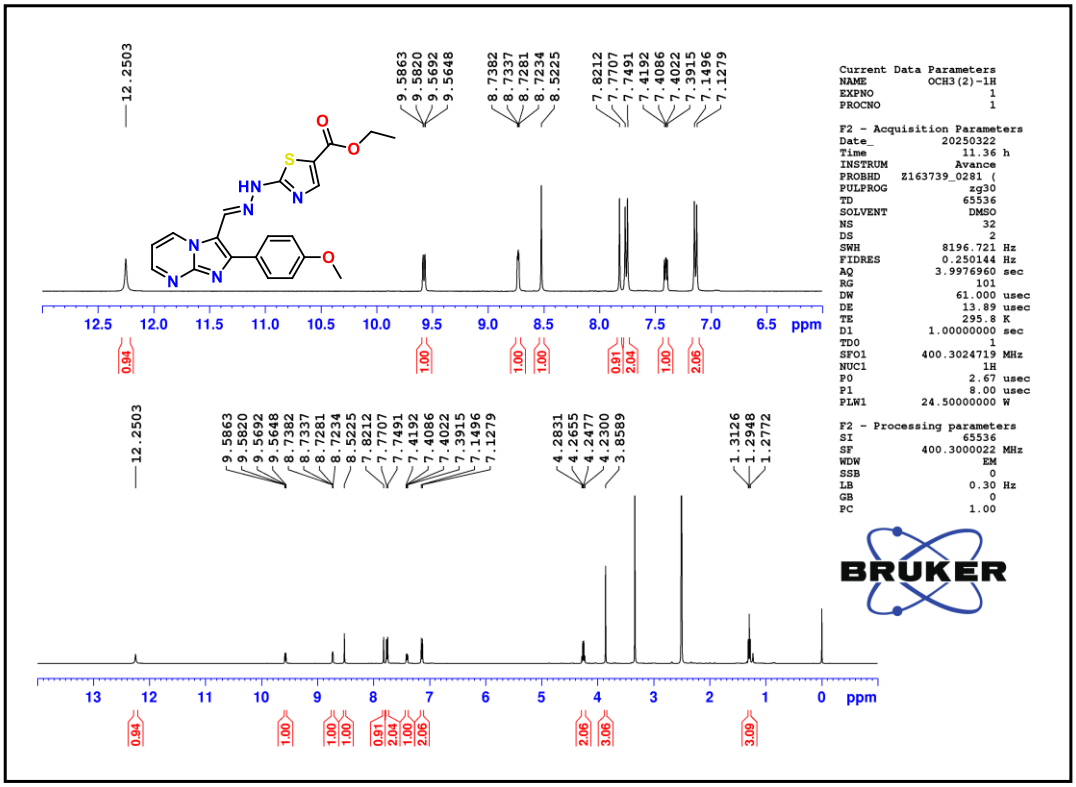


Figure S63: ^{1}H-NMR spectrum of compound **K9**

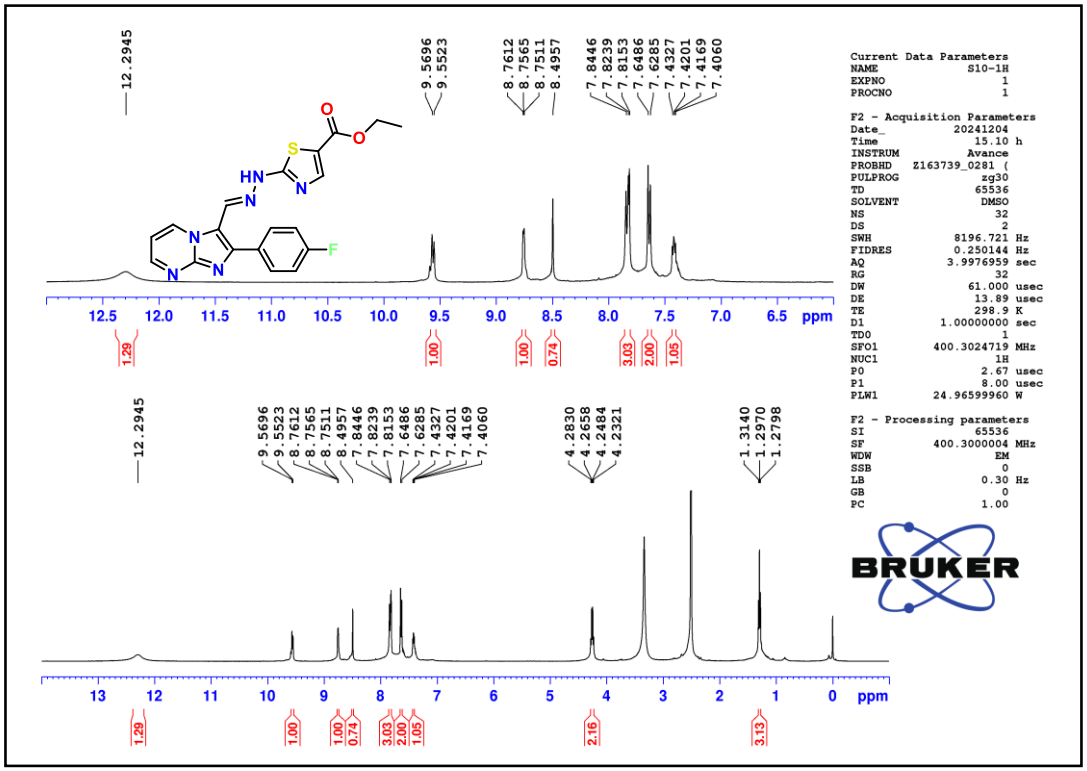


Figure S64: ^{1}H-NMR spectrum of compound **K10**

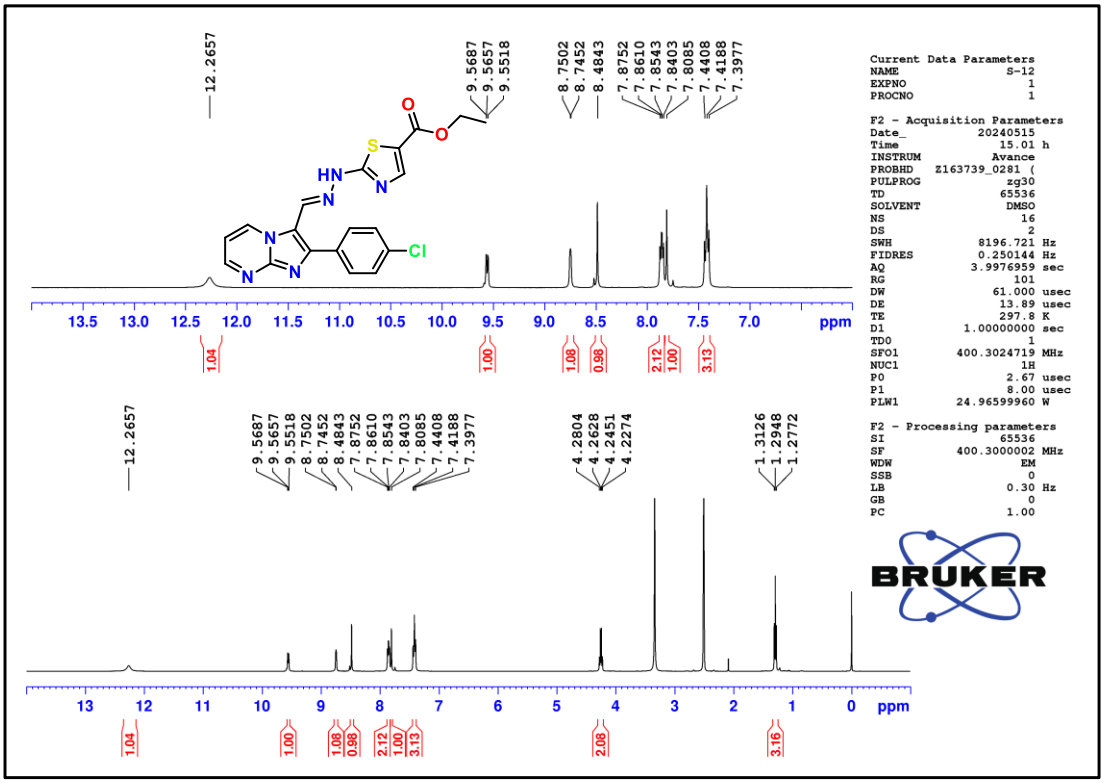


Figure S65: ^{1}H-NMR spectrum of compound **K11**

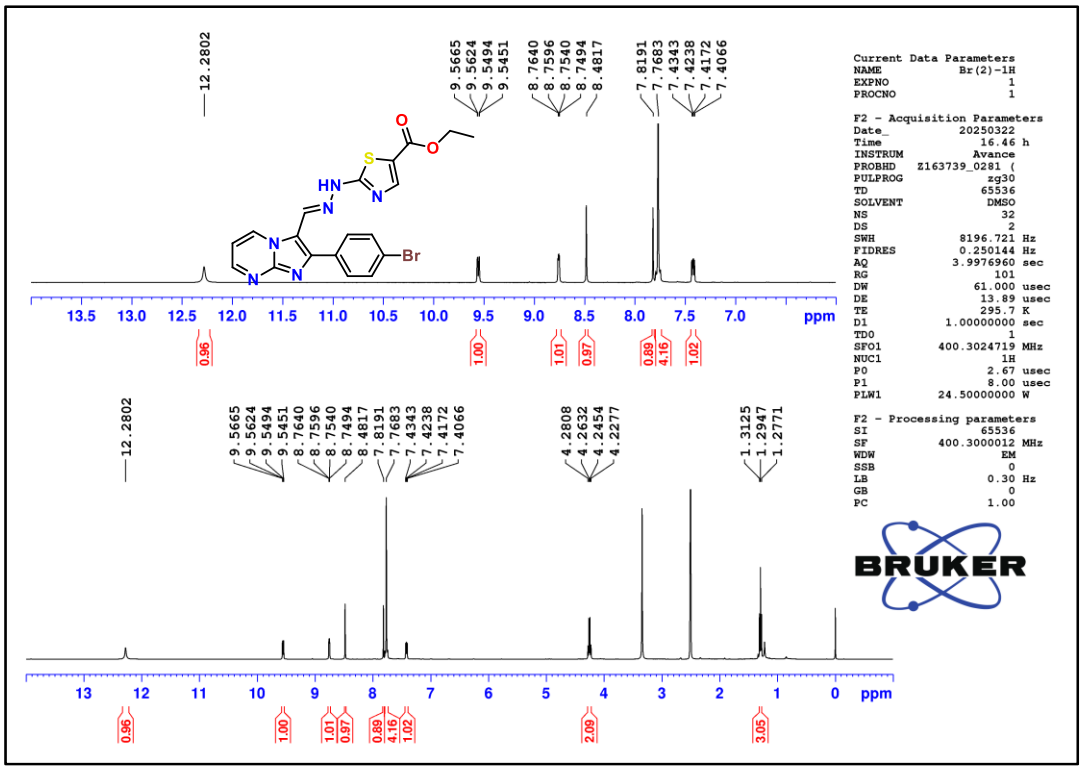


Figure S66: ^{1}H-NMR spectrum of compound **K12**

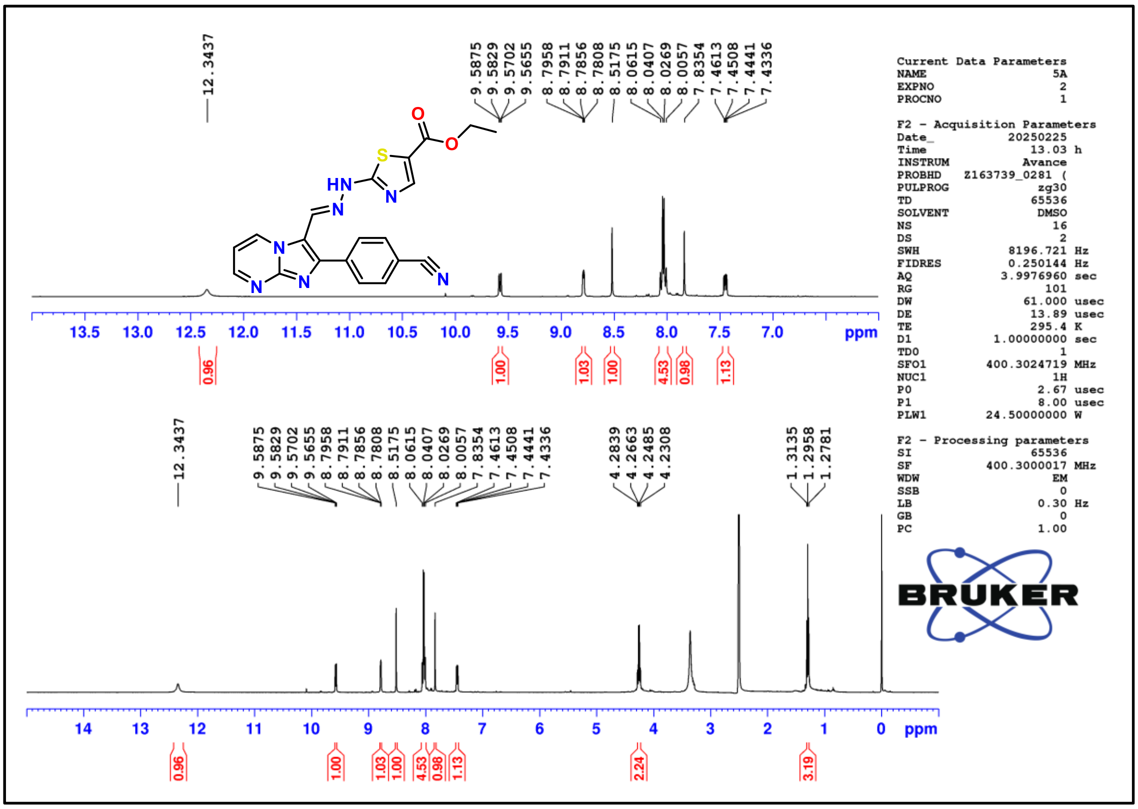


Figure S67: ^{1}H-NMR spectrum of compound **K13**

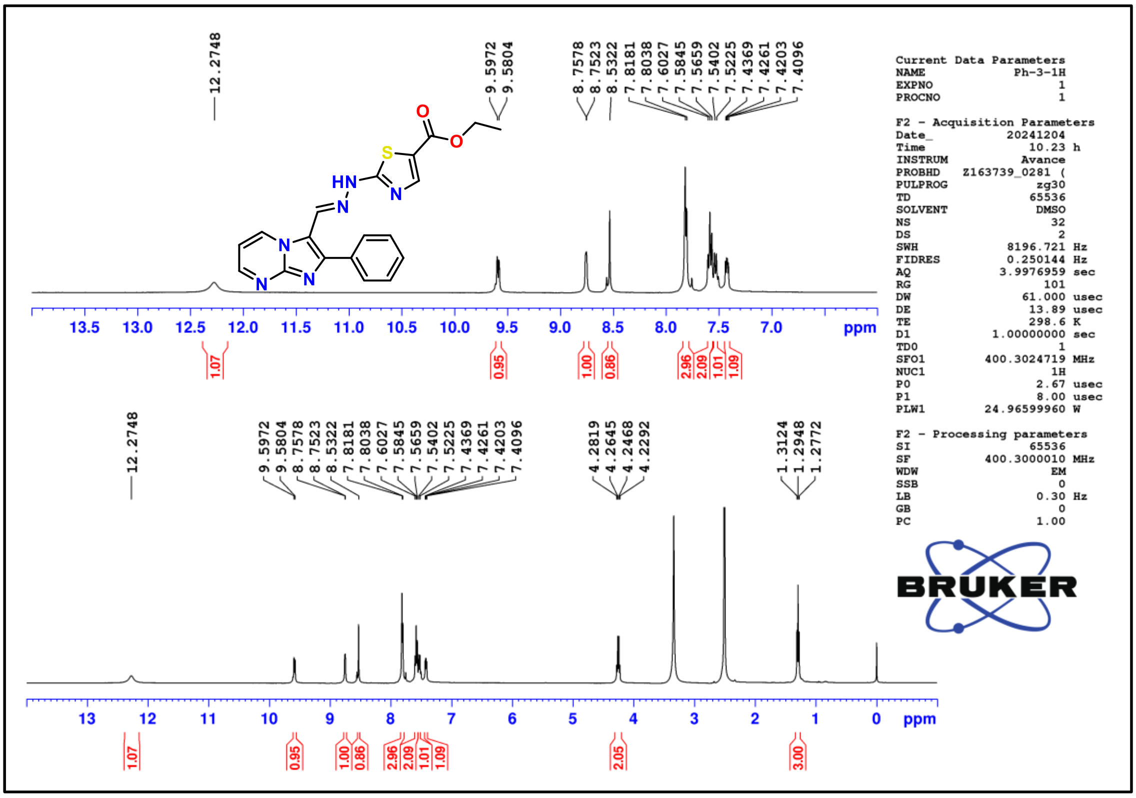


Figure S68: ^{1}H-NMR spectrum of compound **K14**

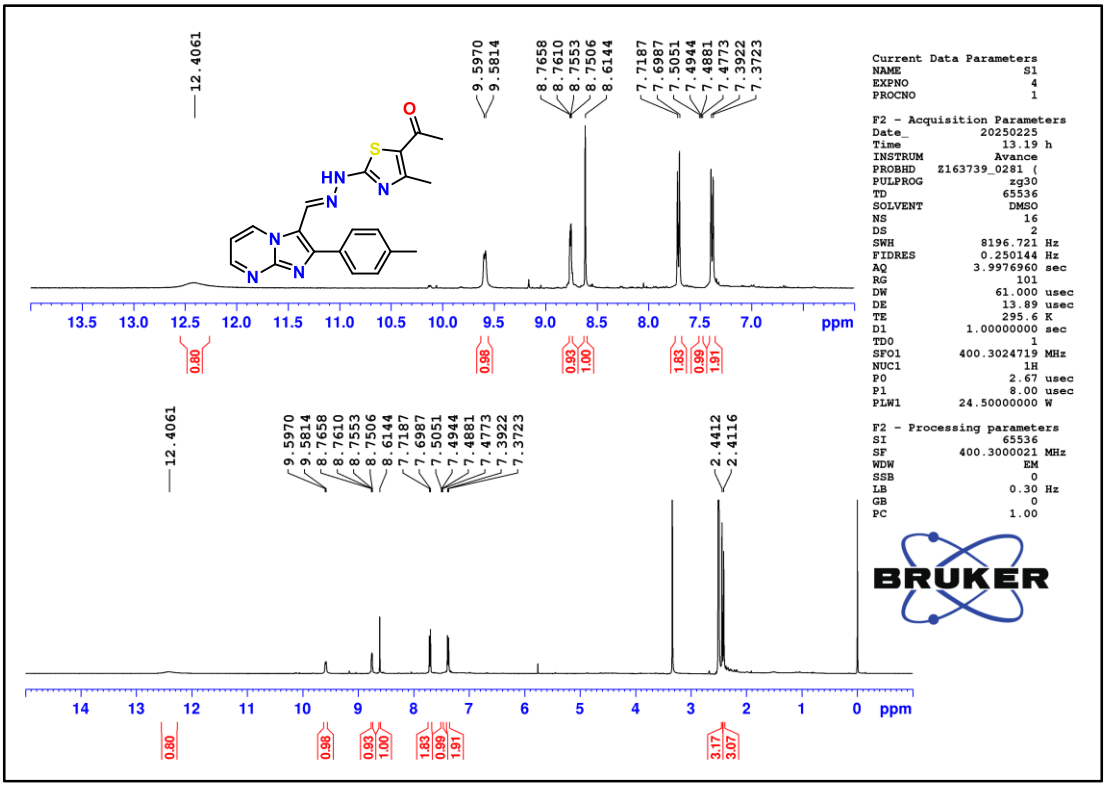


Figure S69: ^{1}H-NMR spectrum of compound **K15**

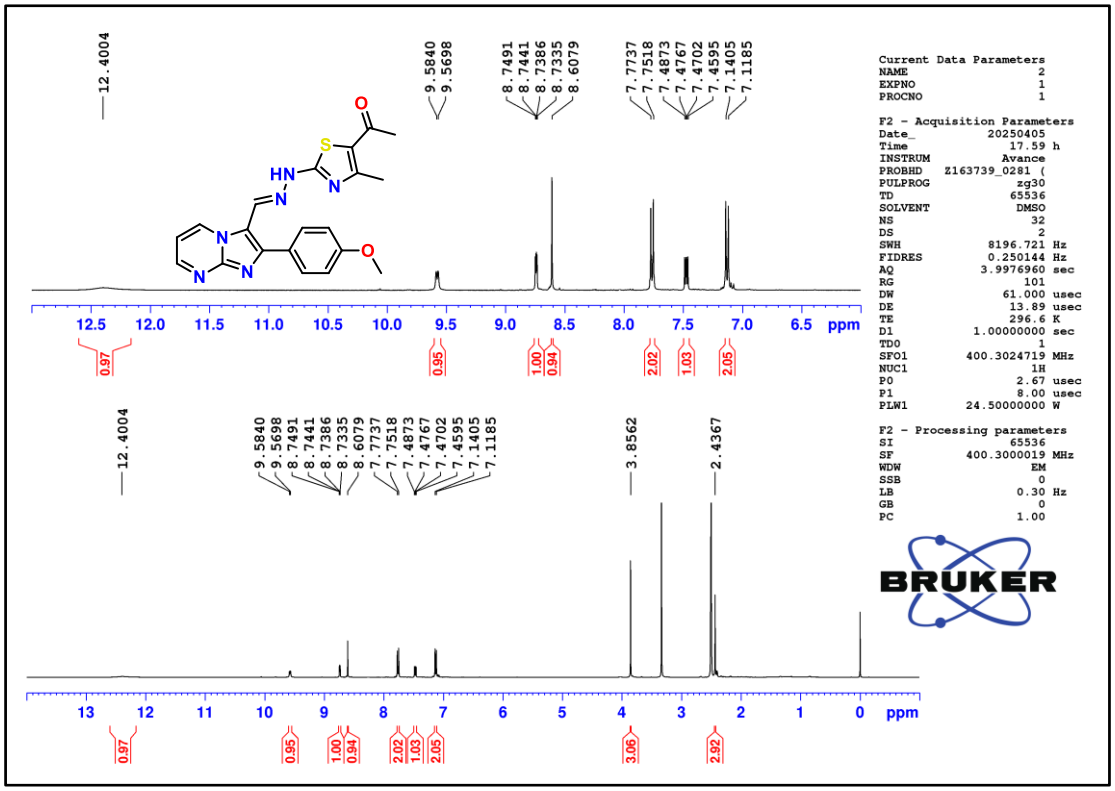


Figure S70: ^{1}H-NMR spectrum of compound **K16**

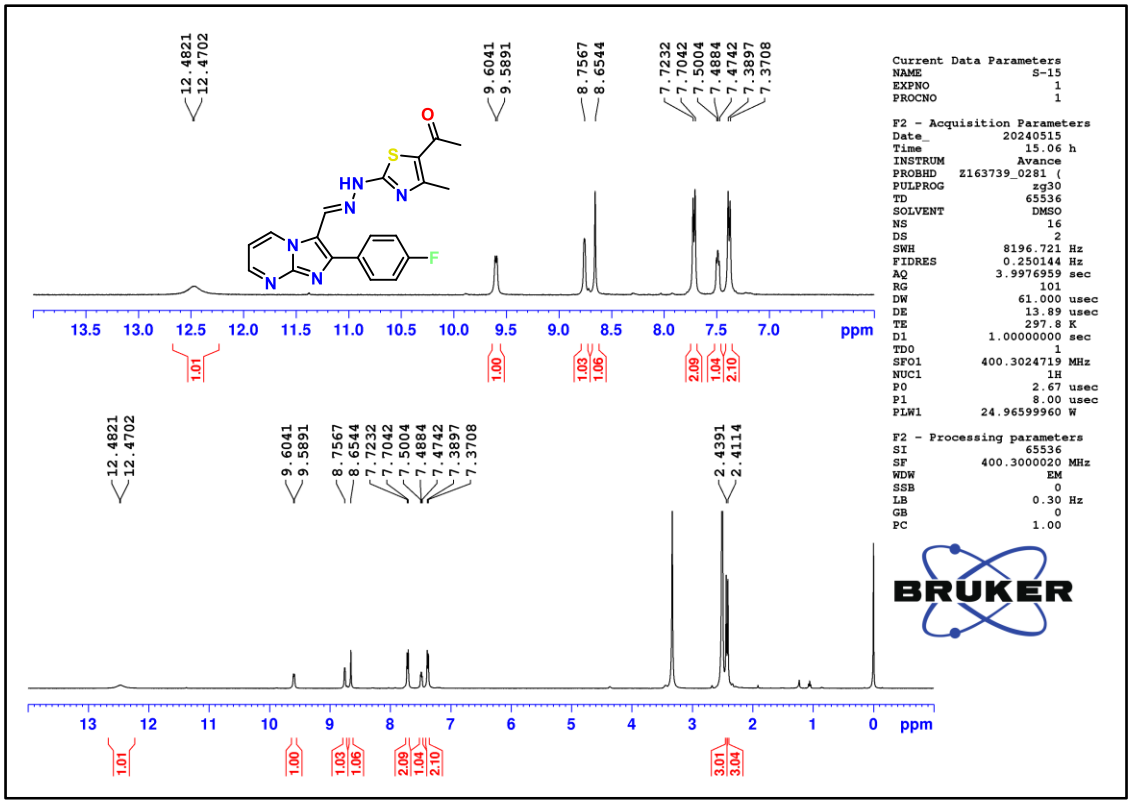


Figure S71: ^{1}H-NMR spectrum of compound **K17**

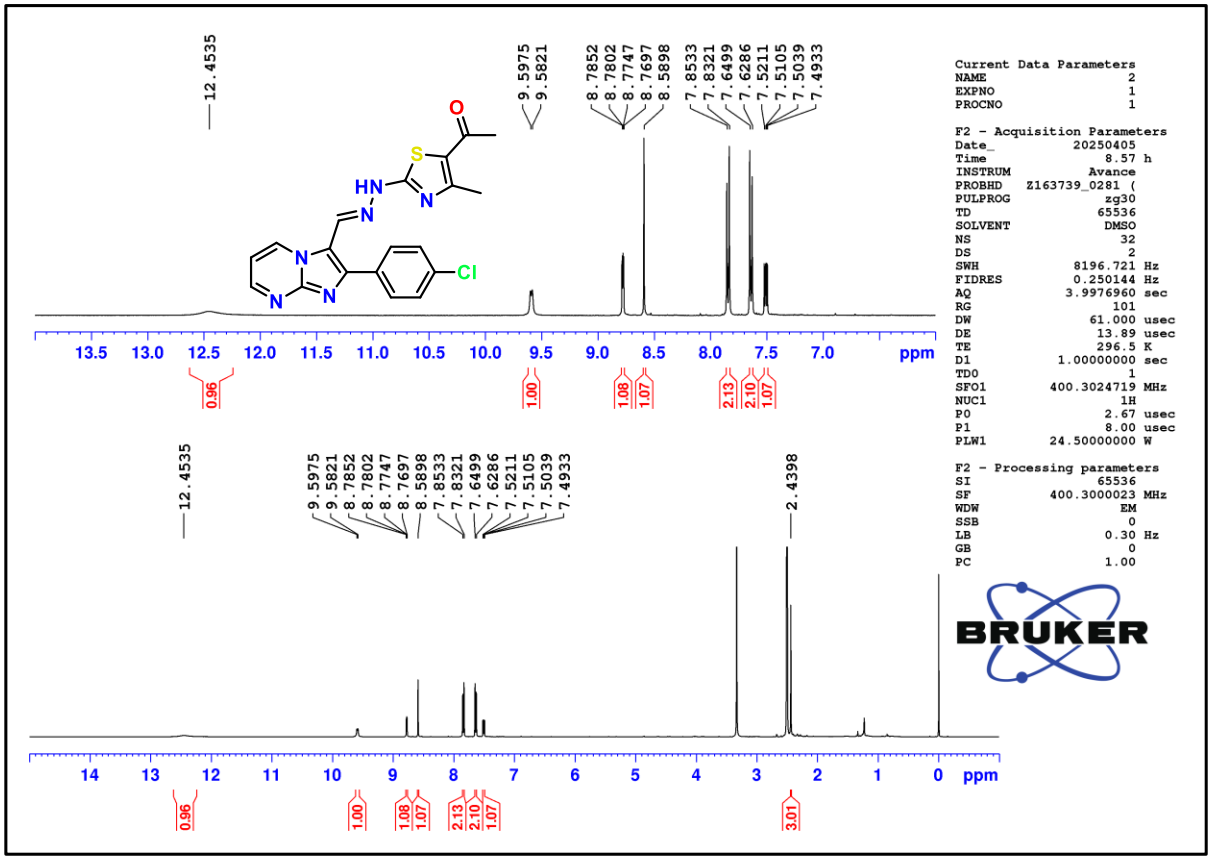


Figure S72: ^{1}H-NMR spectrum of compound **K18**

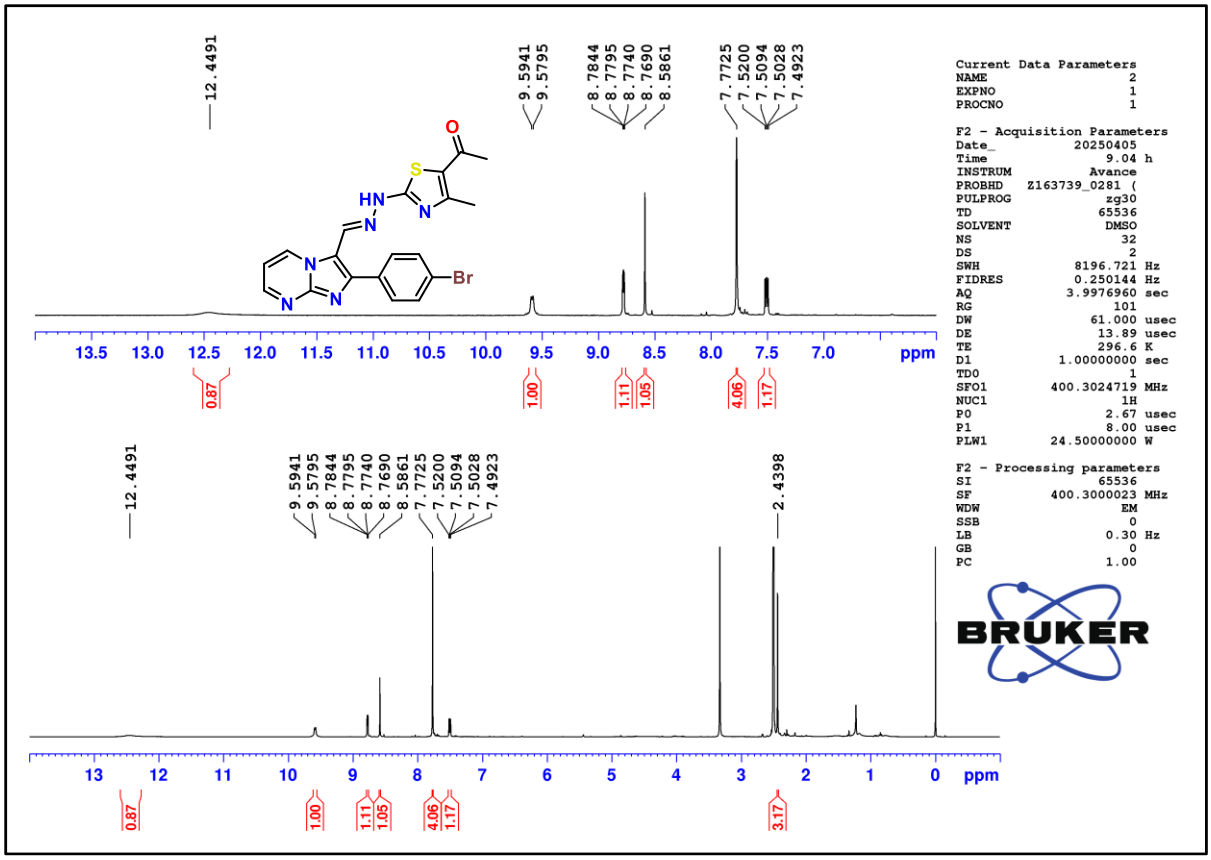


Figure S73: ^{1}H-NMR spectrum of compound **K19**

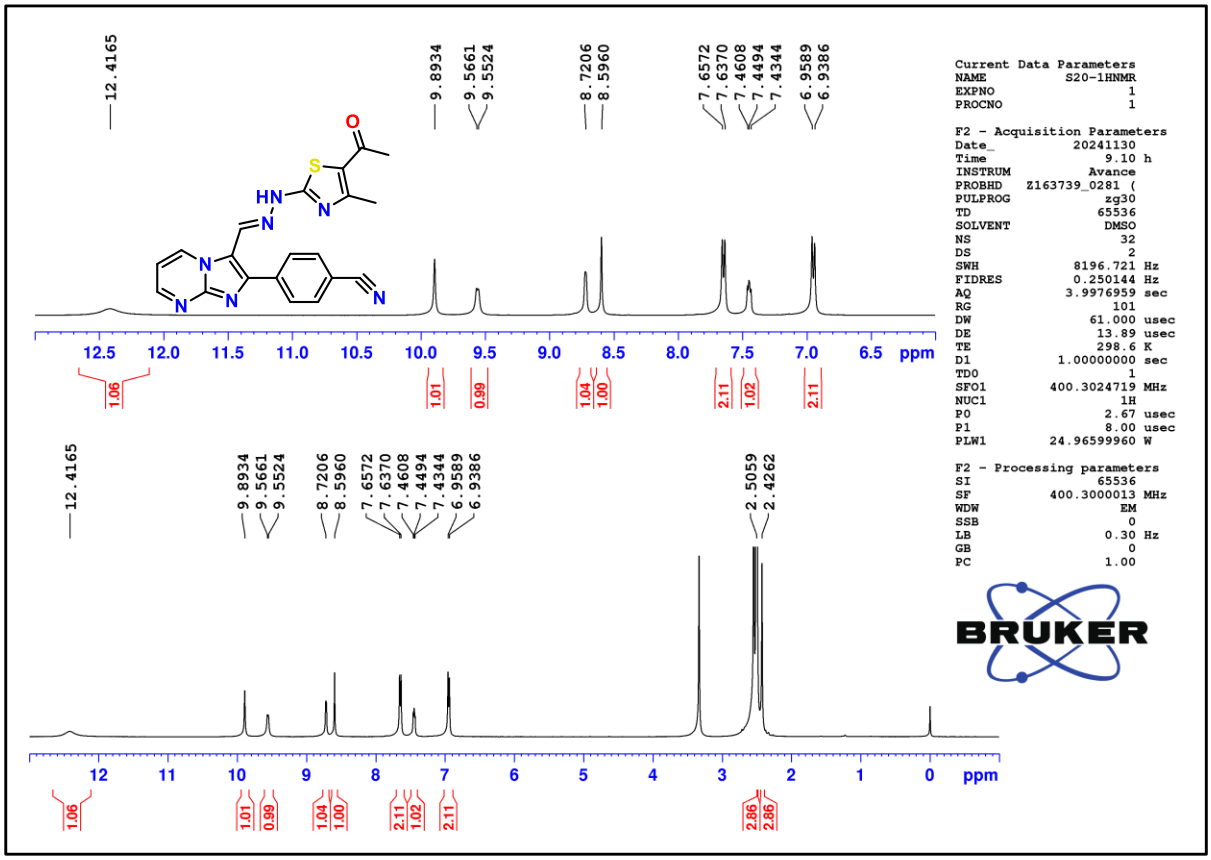


Figure S74: ^{1}H-NMR spectrum of compound **K20**

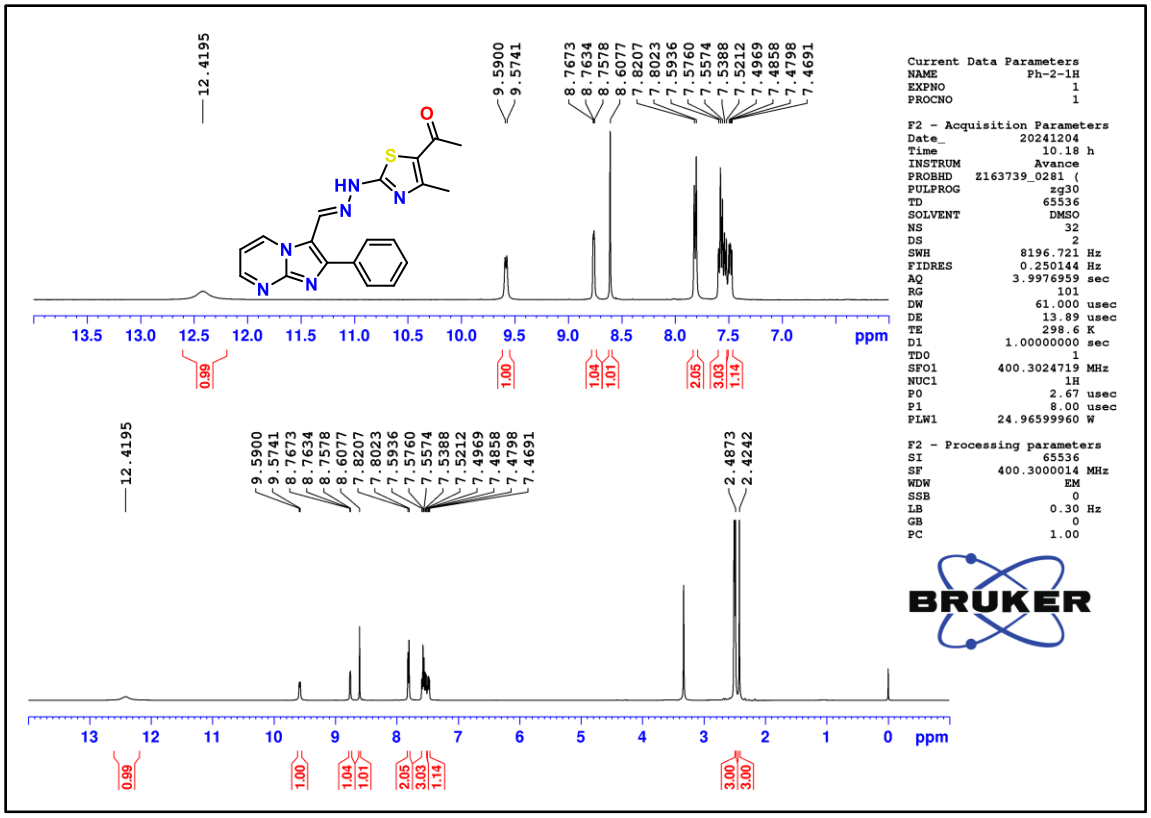


Figure S75: [1]H-NMR spectrum of compound **K21**

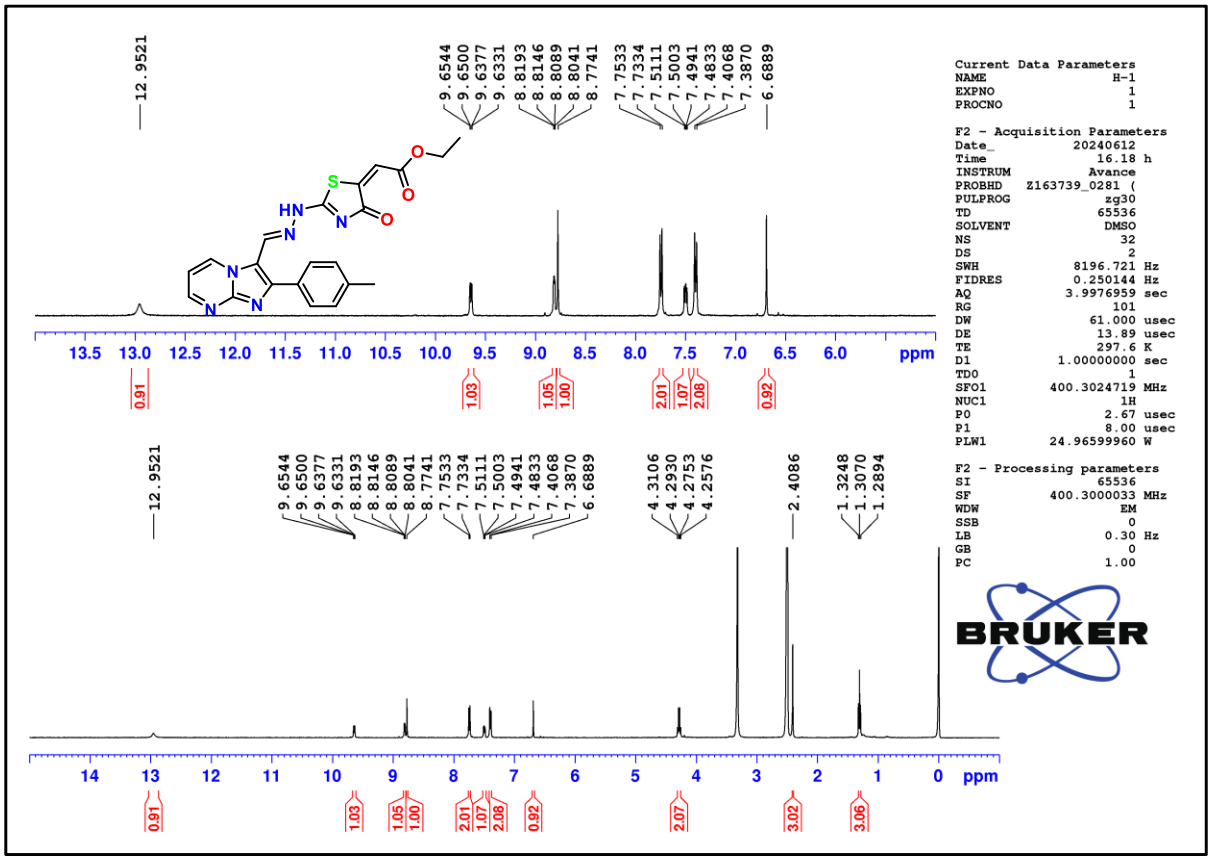


Figure S76: [1]H-NMR spectrum of compound **K22**

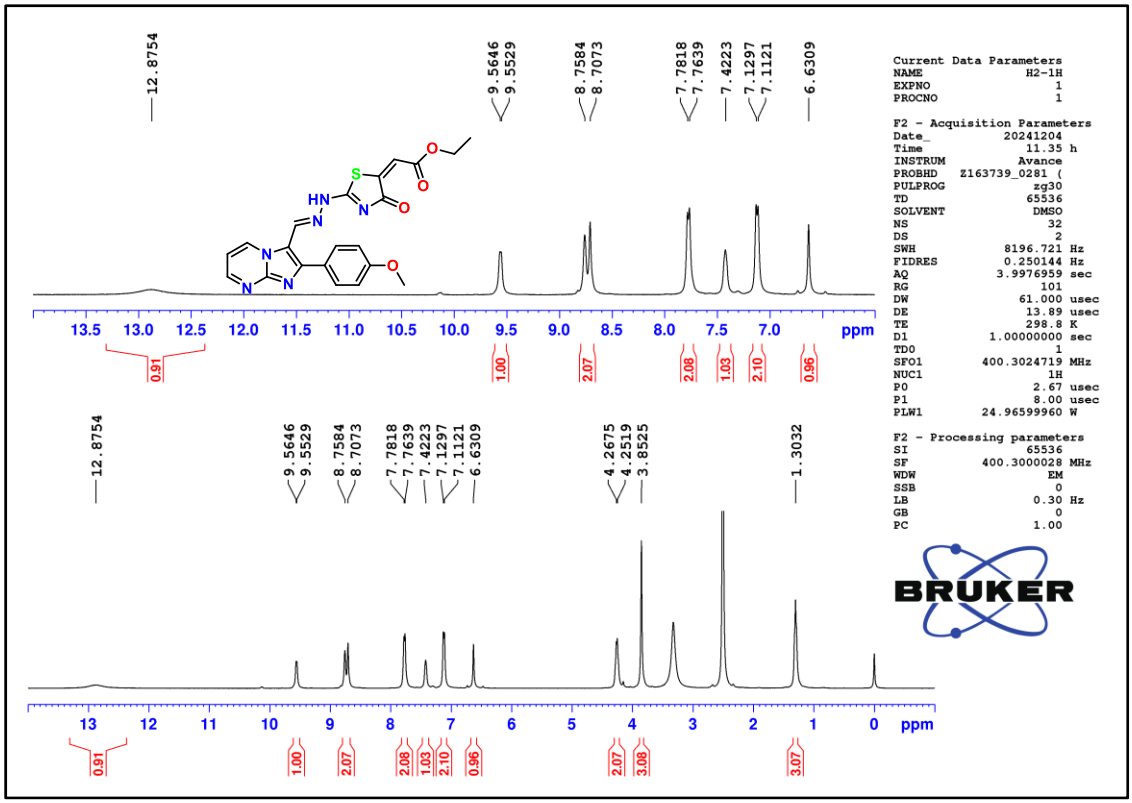


Figure S77: ^{1}H-NMR spectrum of compound **K23**

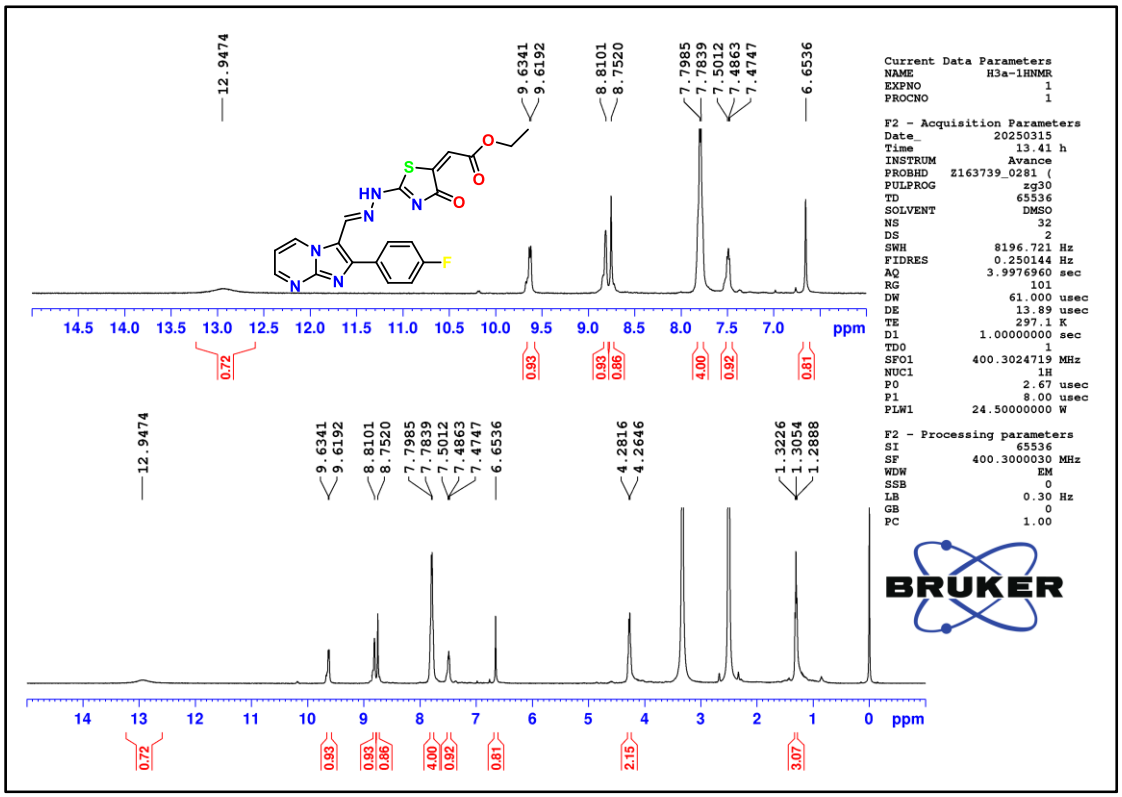


Figure S78: ^{1}H-NMR spectrum of compound **K24**

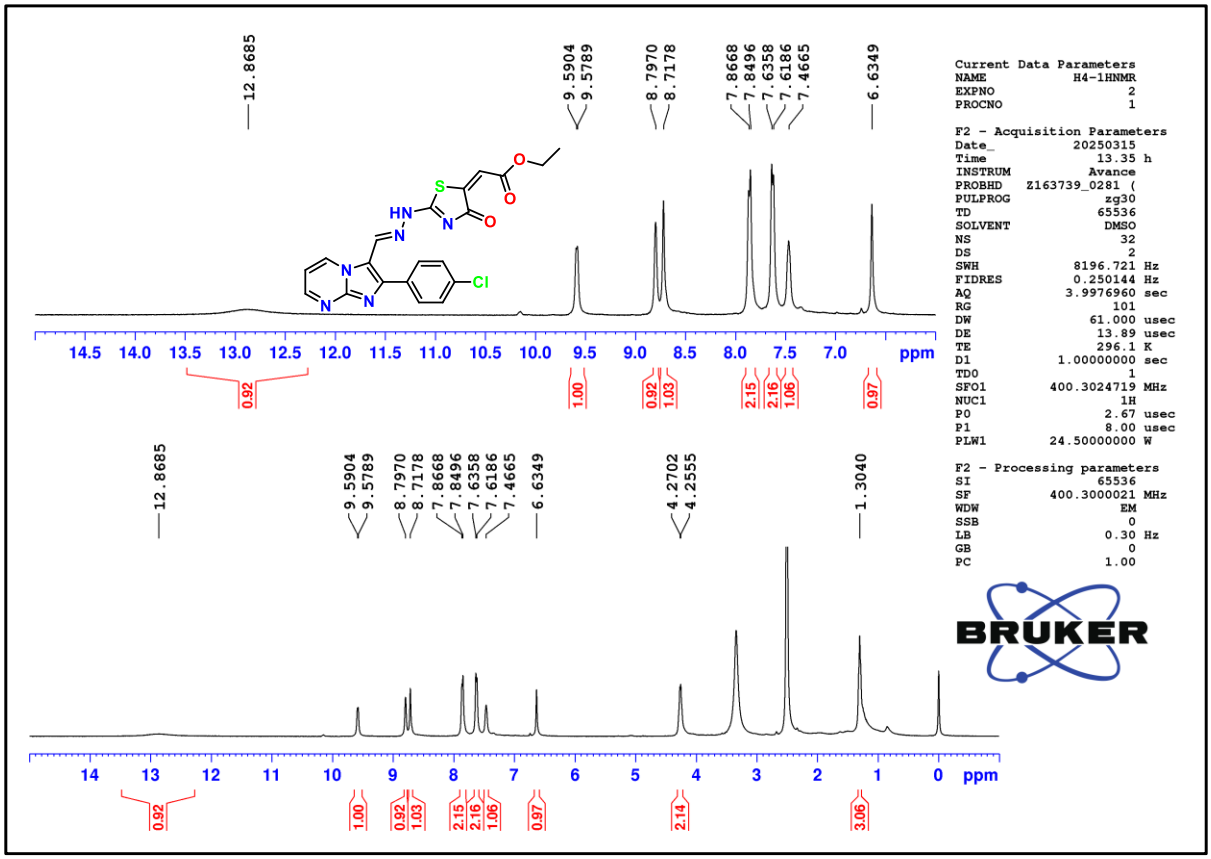


Figure S79: ^{1}H-NMR spectrum of compound **K25**

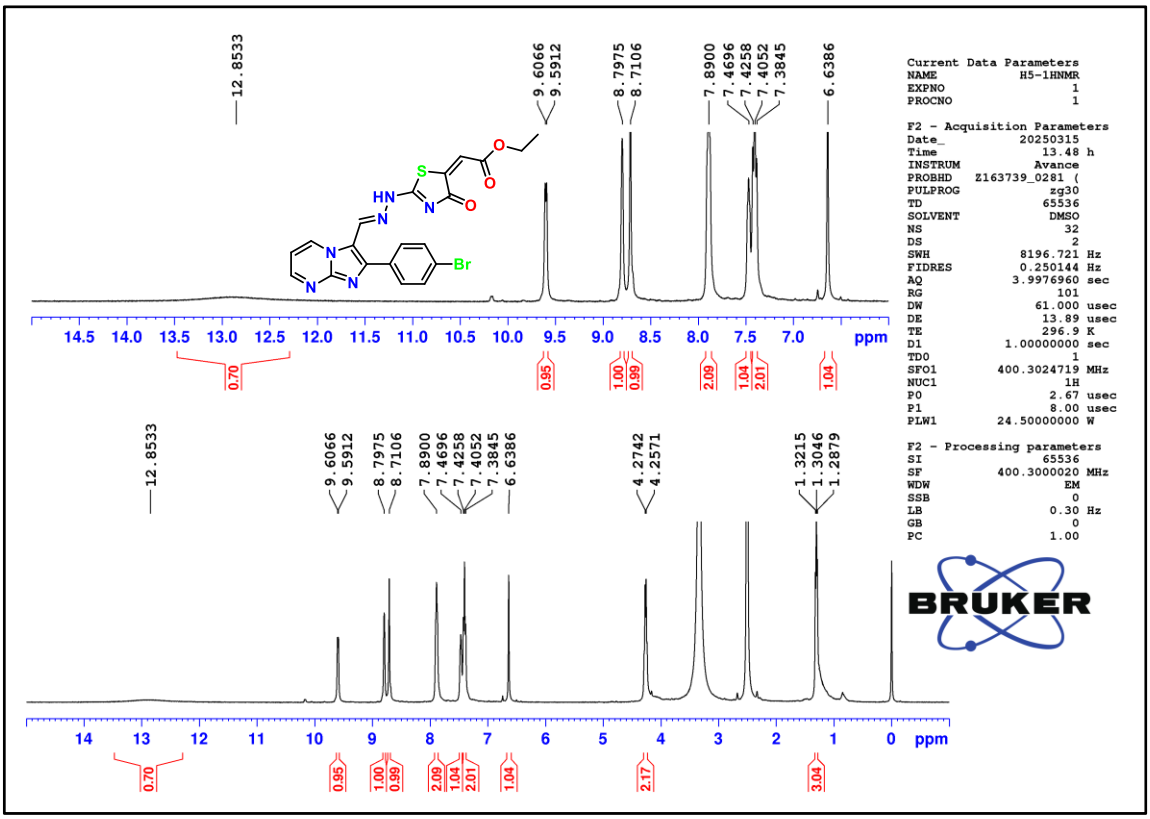


Figure S80: ^{1}H-NMR spectrum of compound **K26**

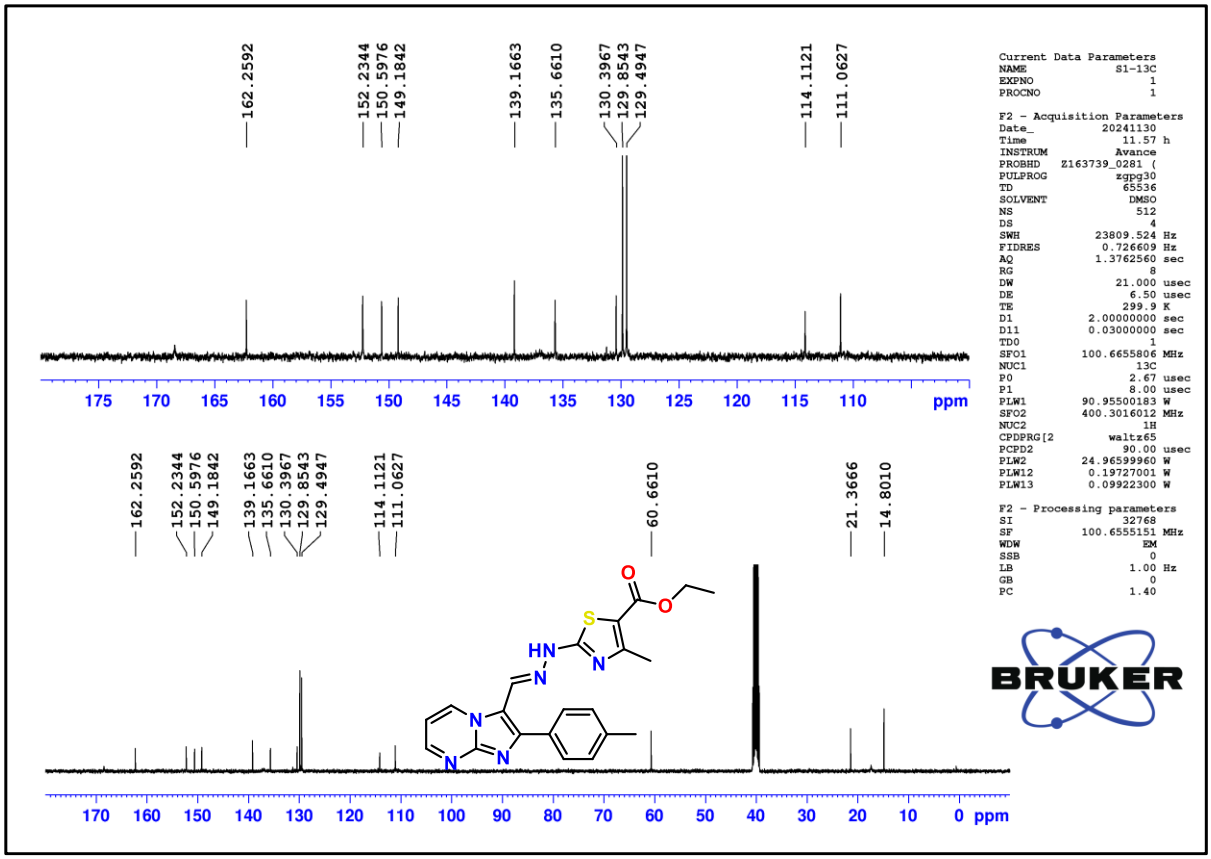


Figure S81: ^{13}C-NMR spectrum of compound **K1**

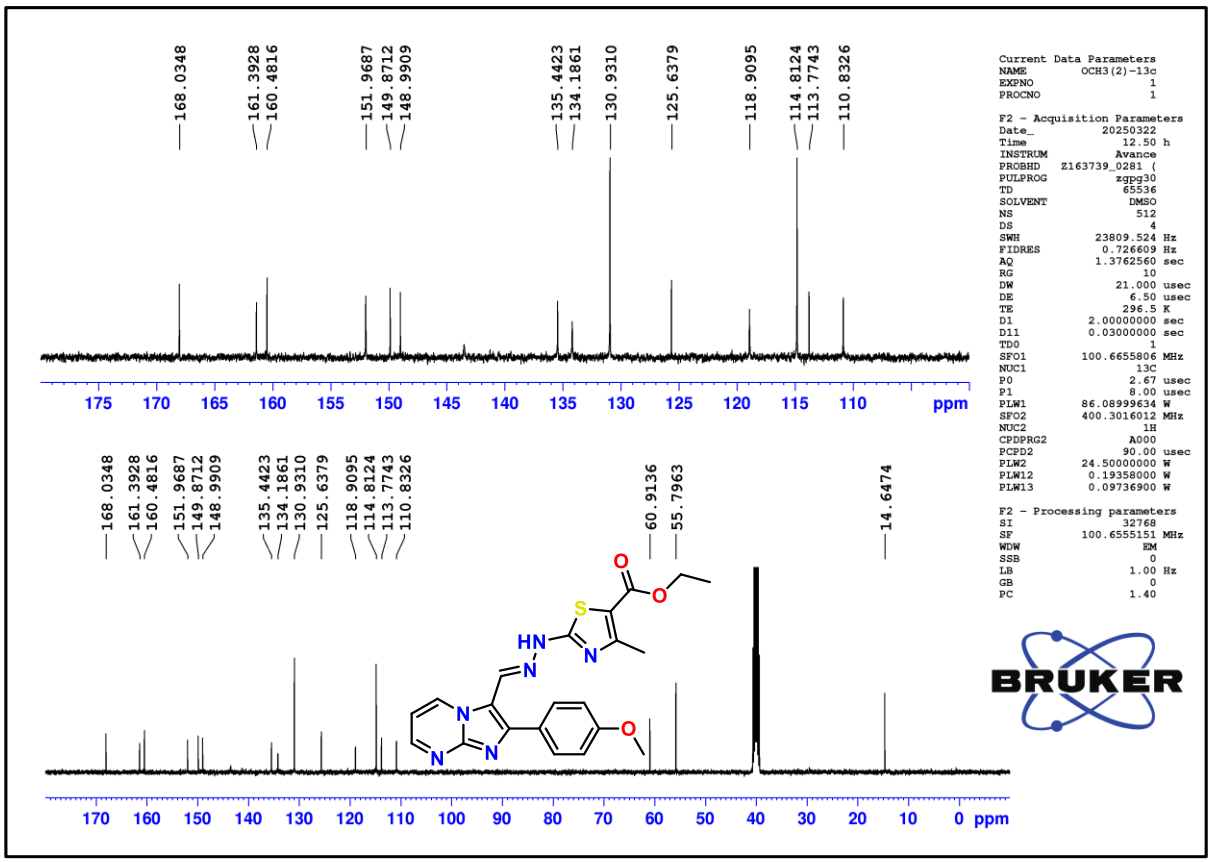


Figure S82: ^{13}C-NMR spectrum of compound **K2**

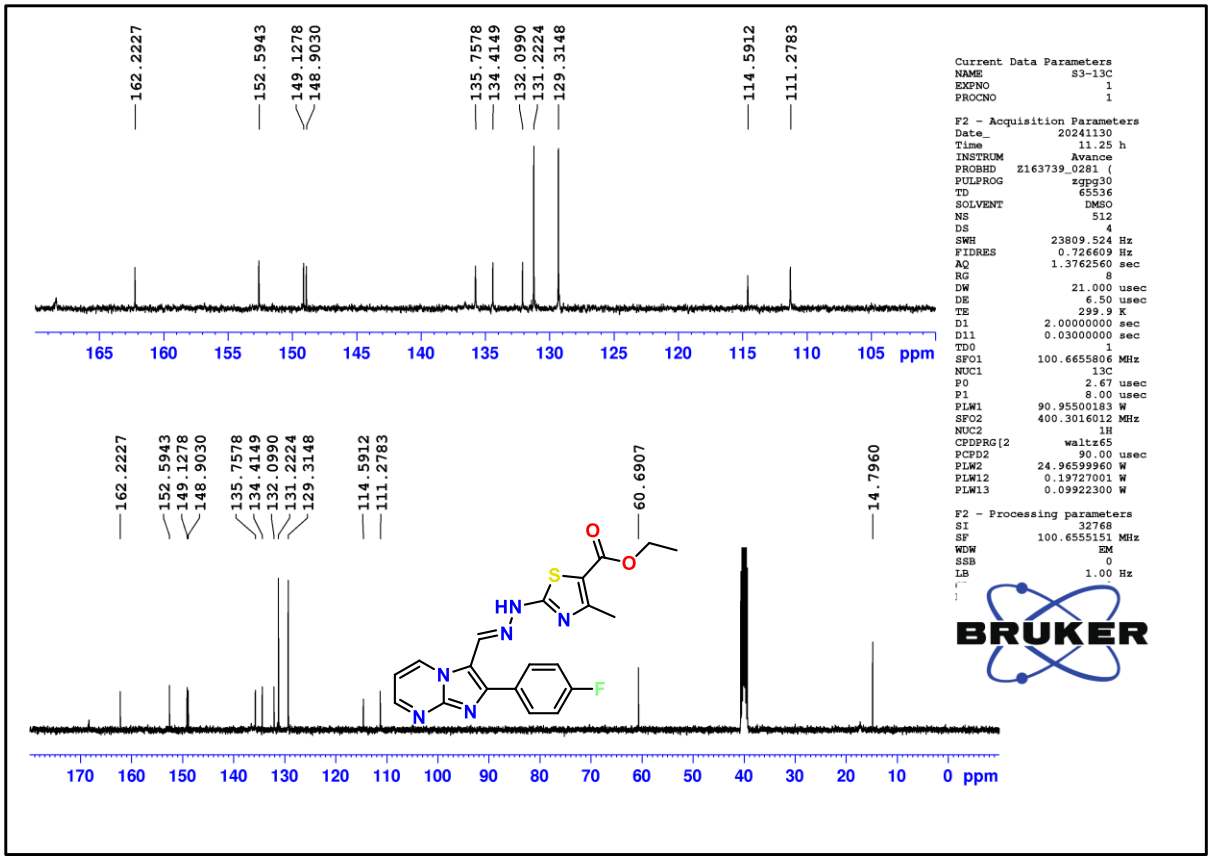


Figure S83: ^{13}C-NMR spectrum of compound **K3**

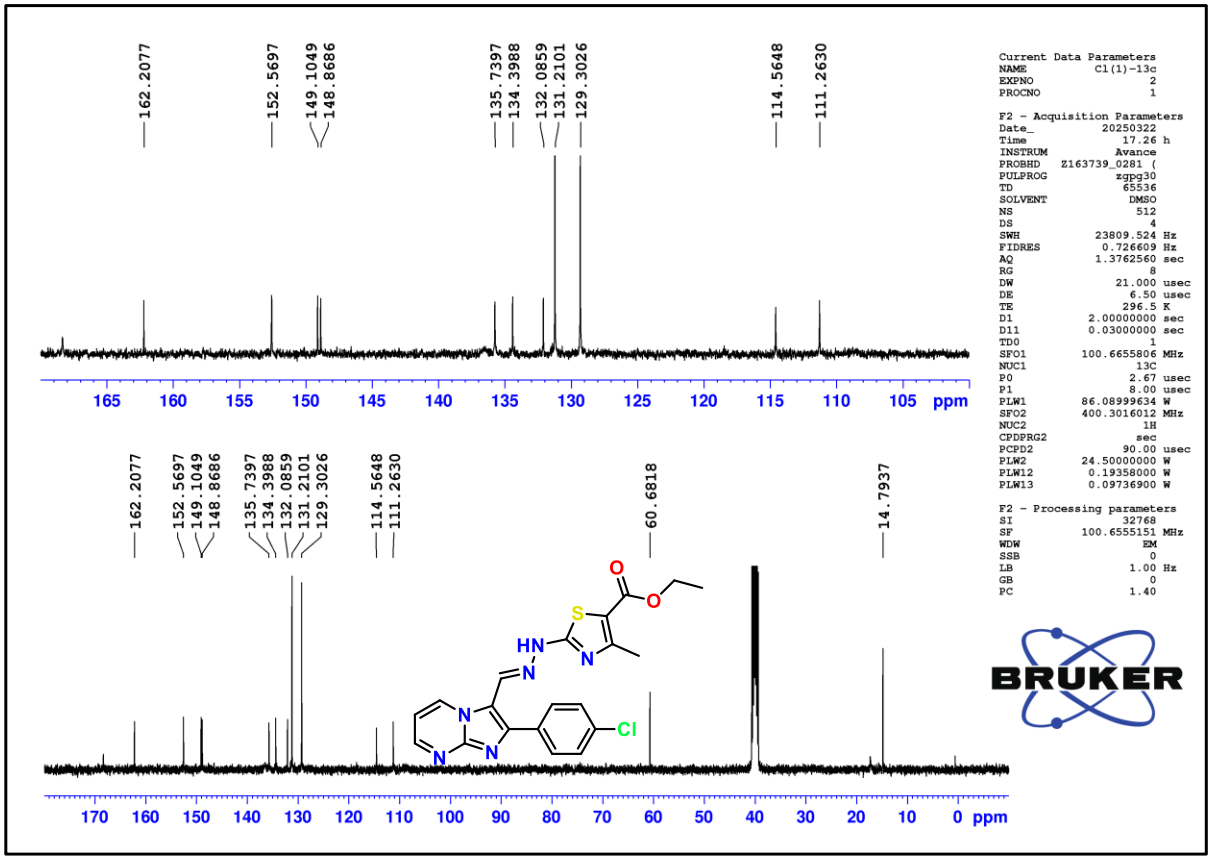


Figure S84: ^{13}C-NMR spectrum of compound **K4**

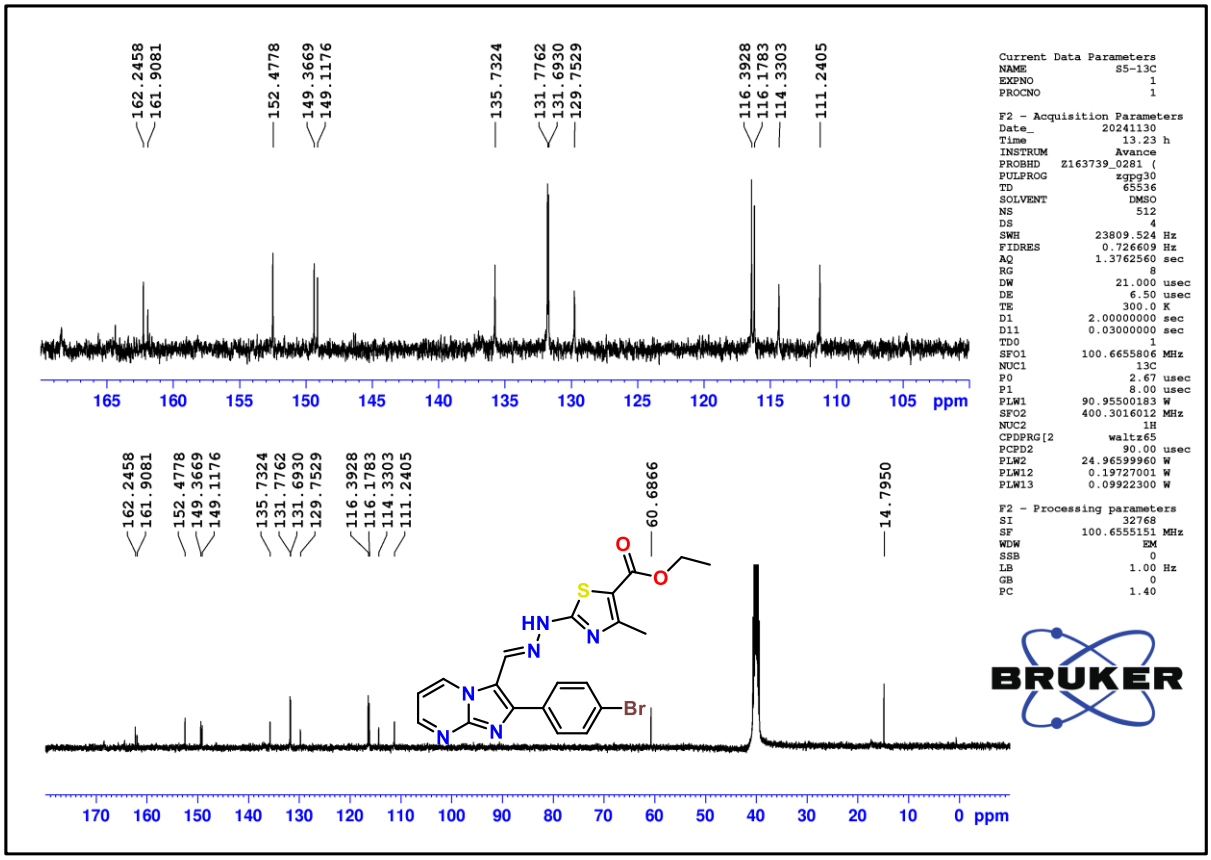


Figure S85: ^{13}C-NMR spectrum of compound **K5**

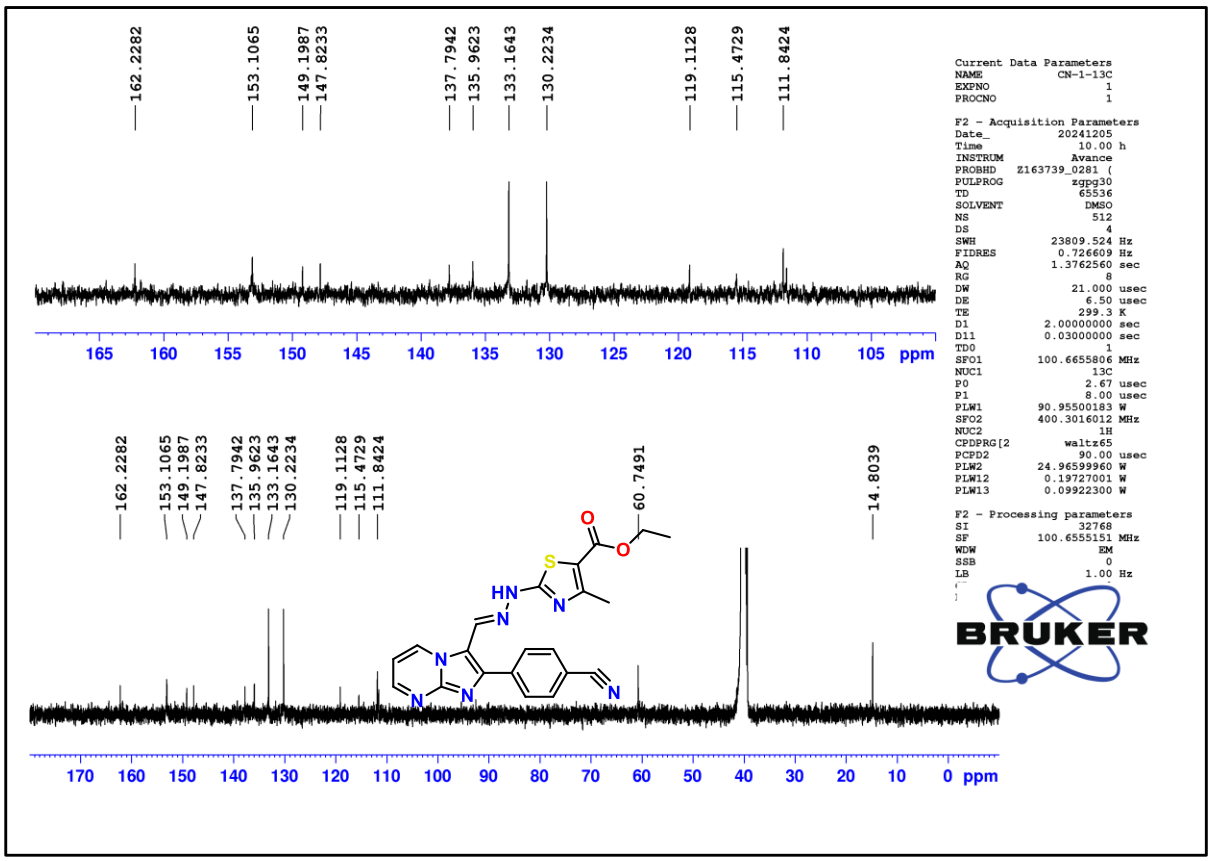


Figure S86: ^{13}C-NMR spectrum of compound **K6**

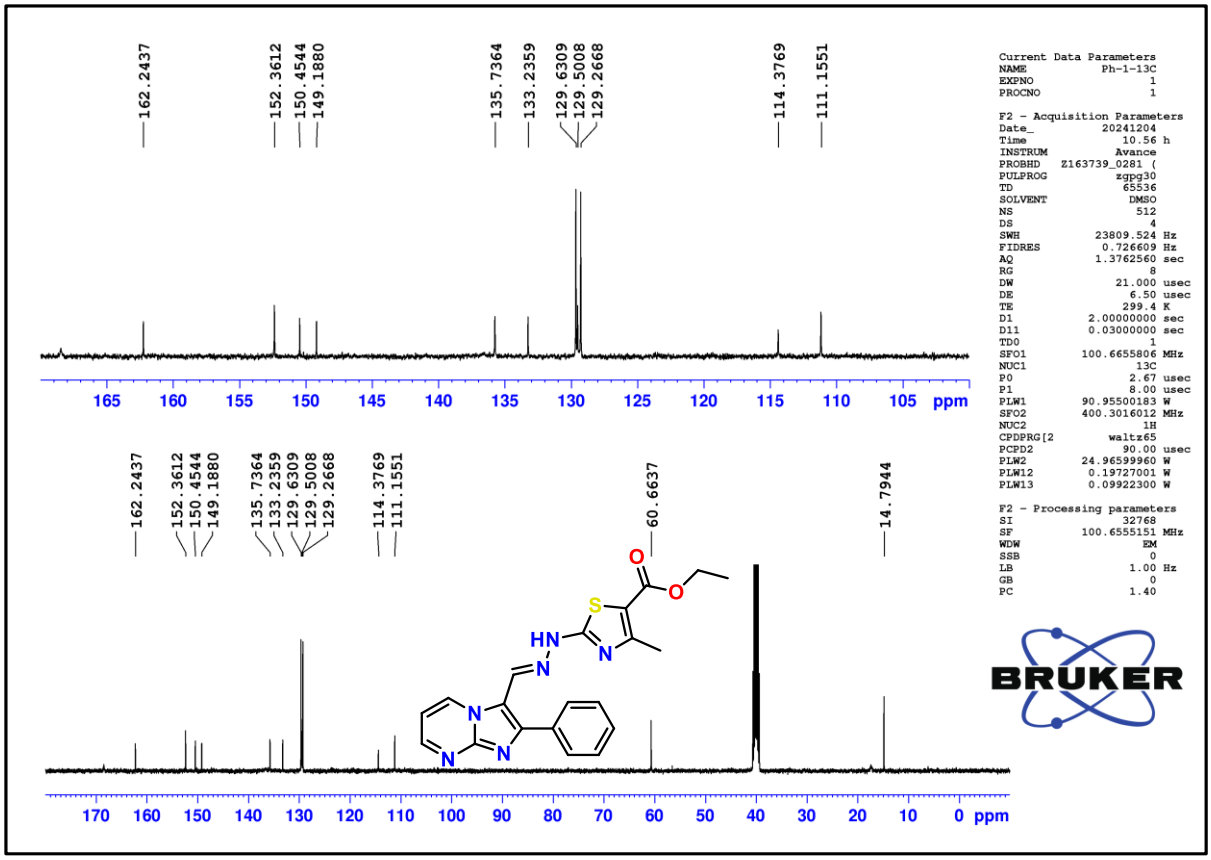


Figure S87: ^{13}C-NMR spectrum of compound **K7**

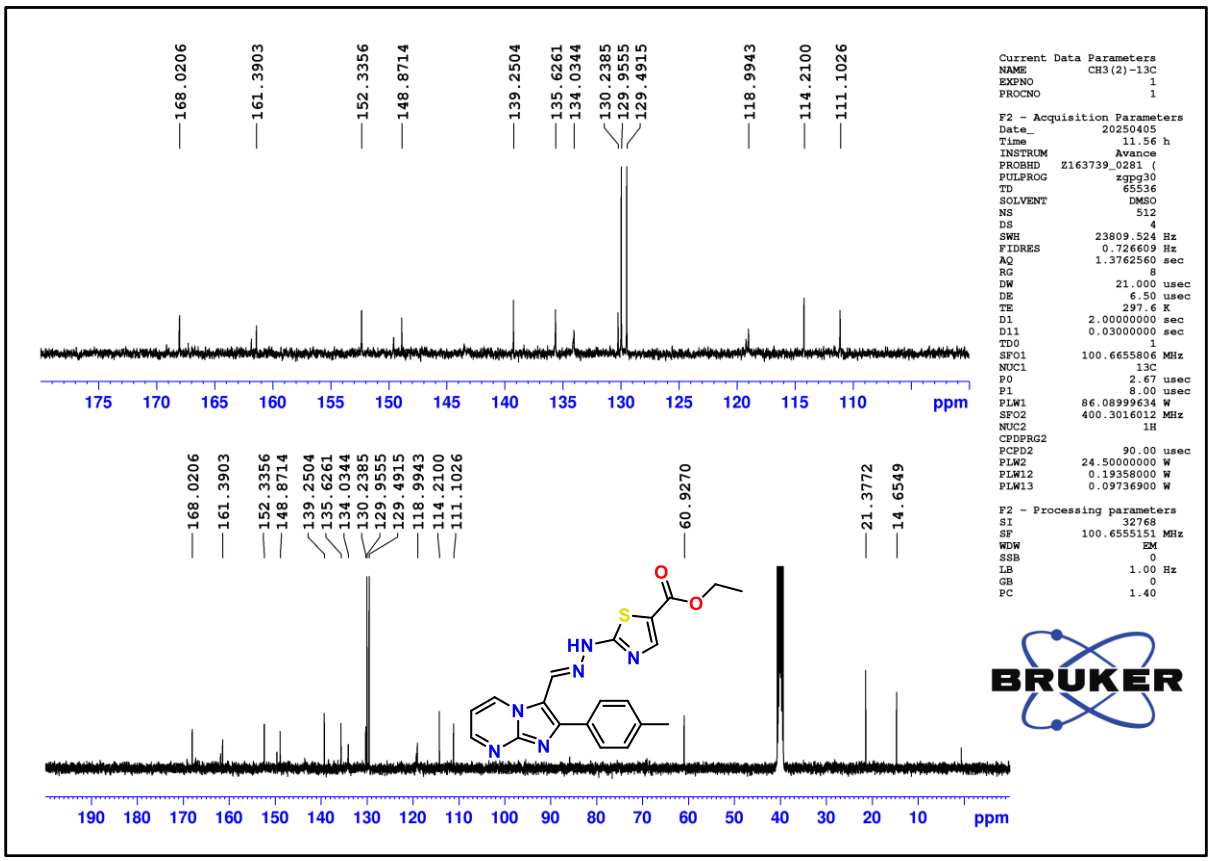


Figure S88: ^{13}C-NMR spectrum of compound **K8**

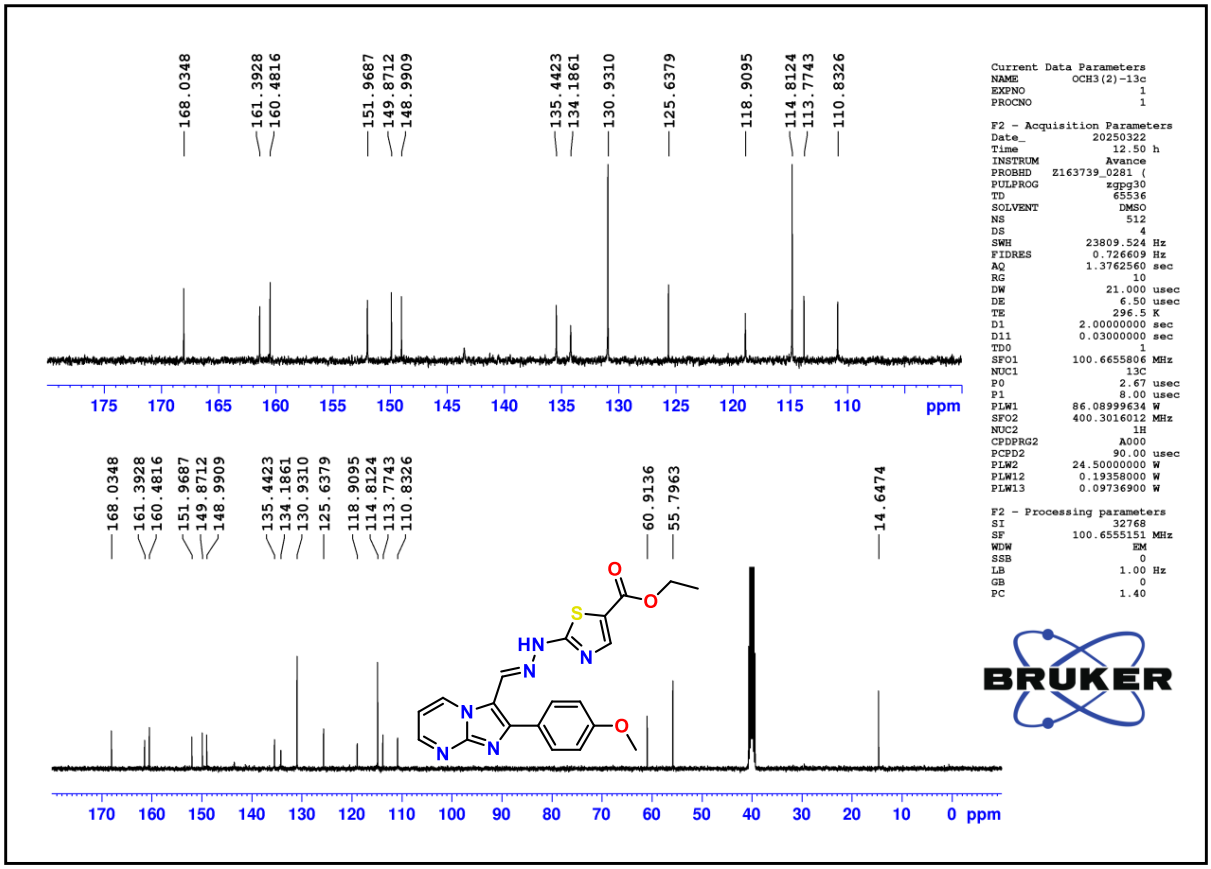


Figure S89: ^{13}C-NMR spectrum of compound **K9**

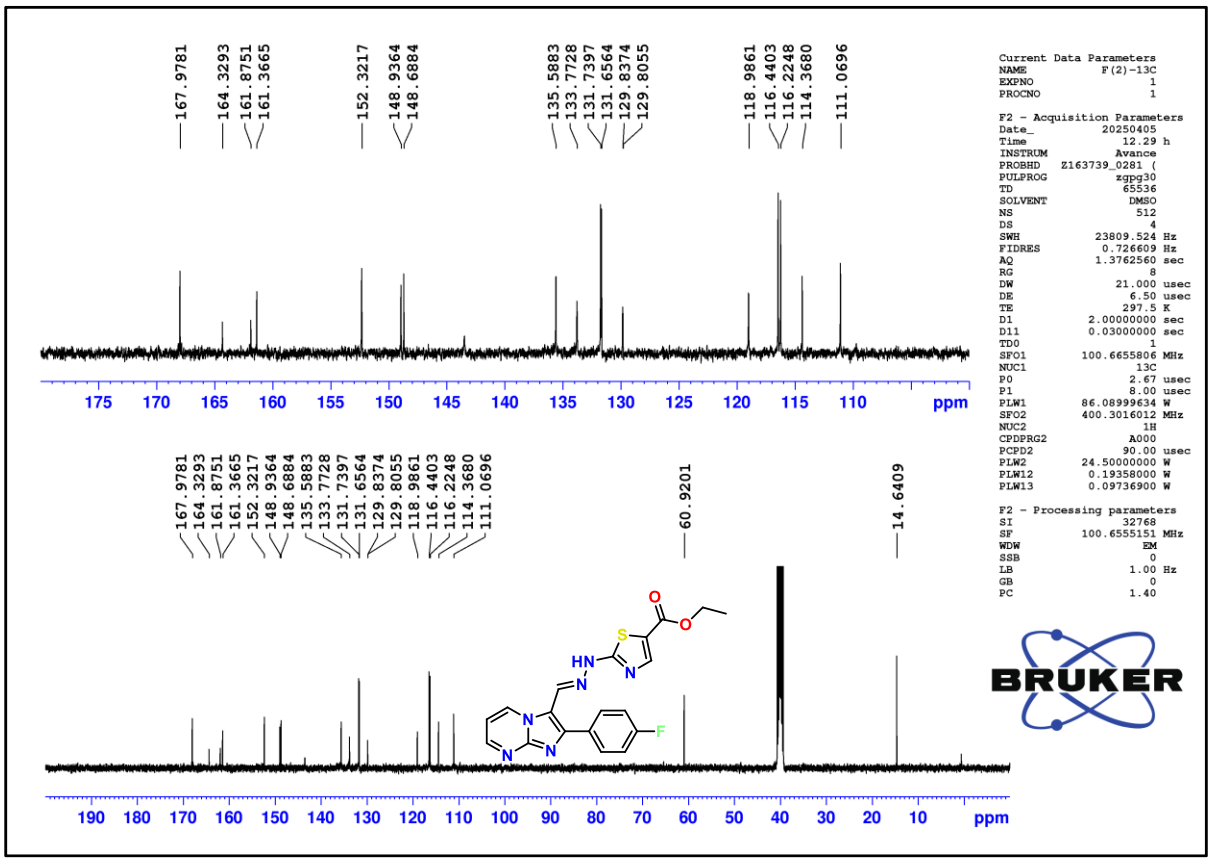


Figure S90: ^{13}C-NMR spectrum of compound **K10**

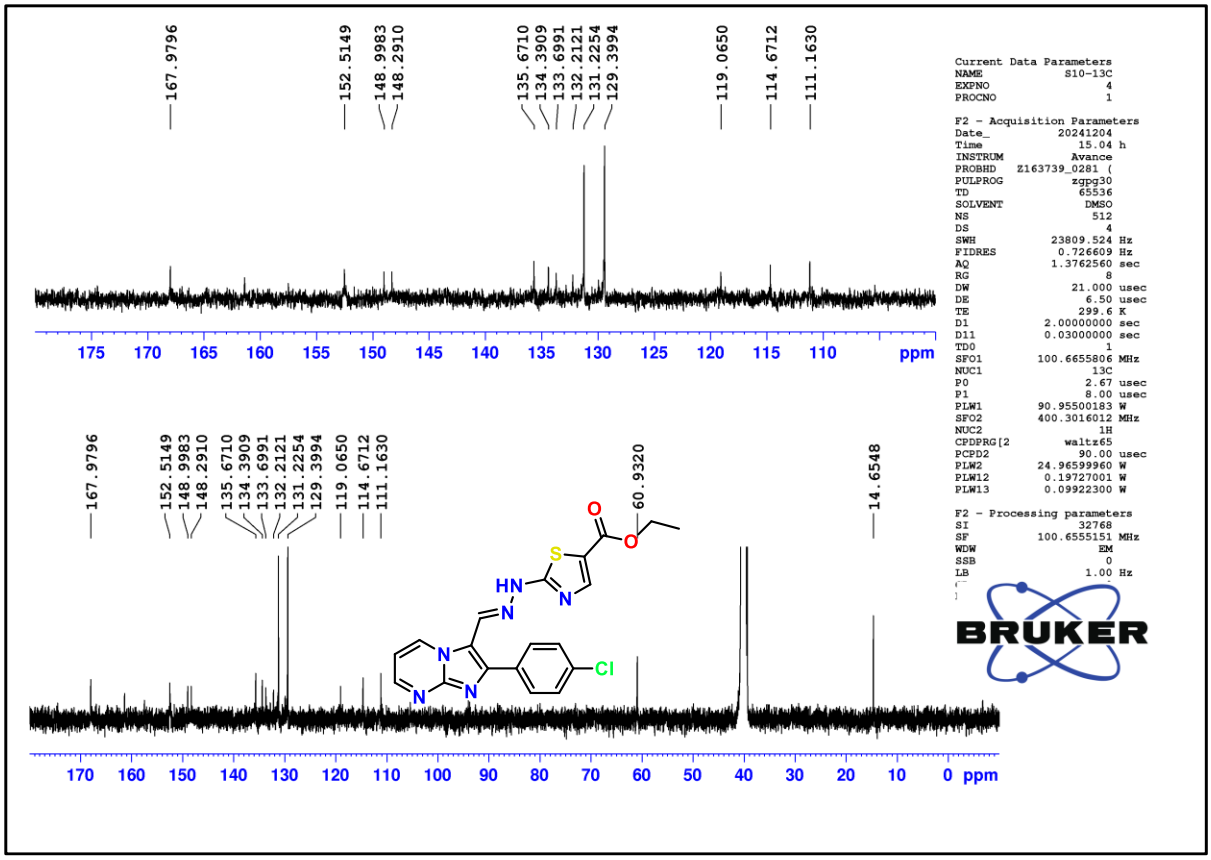


Figure S91: ^{13}C-NMR spectrum of compound K11

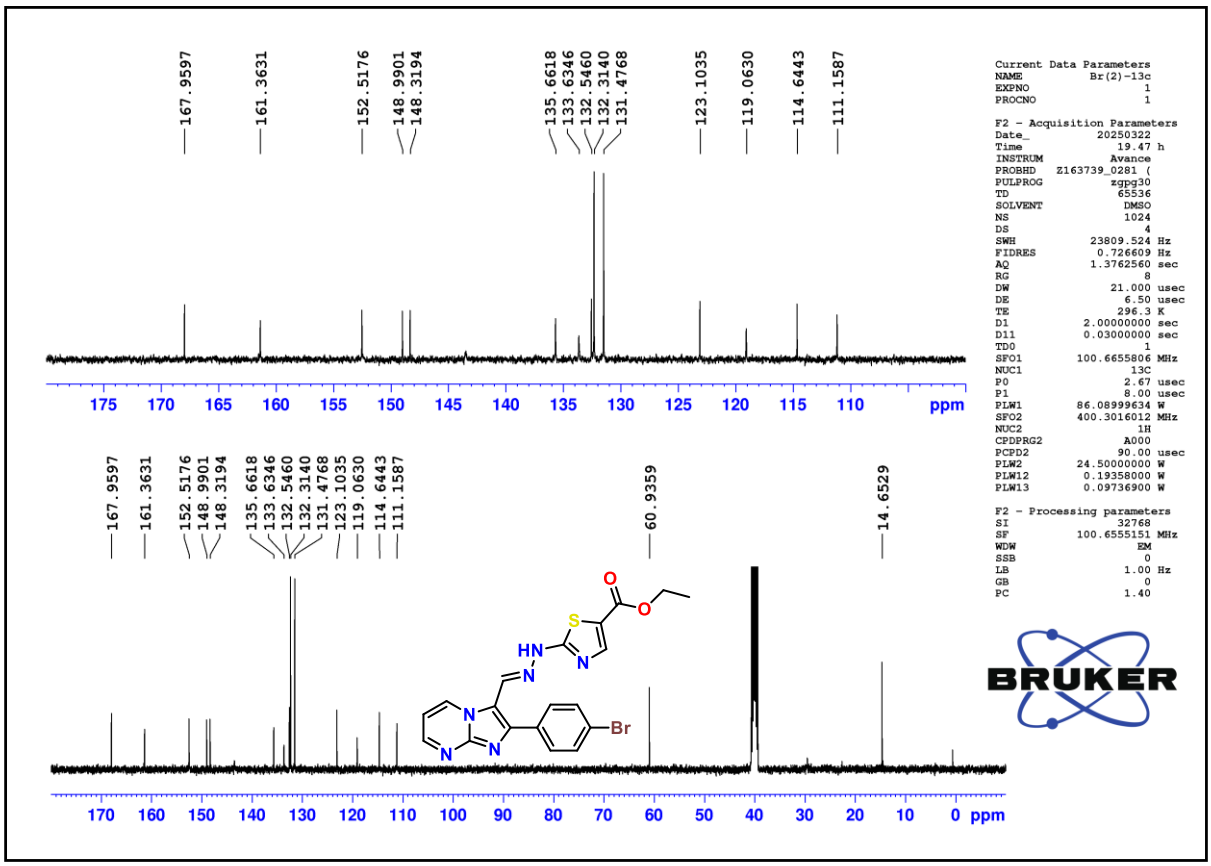


Figure S92: ^{13}C-NMR spectrum of compound **K12**

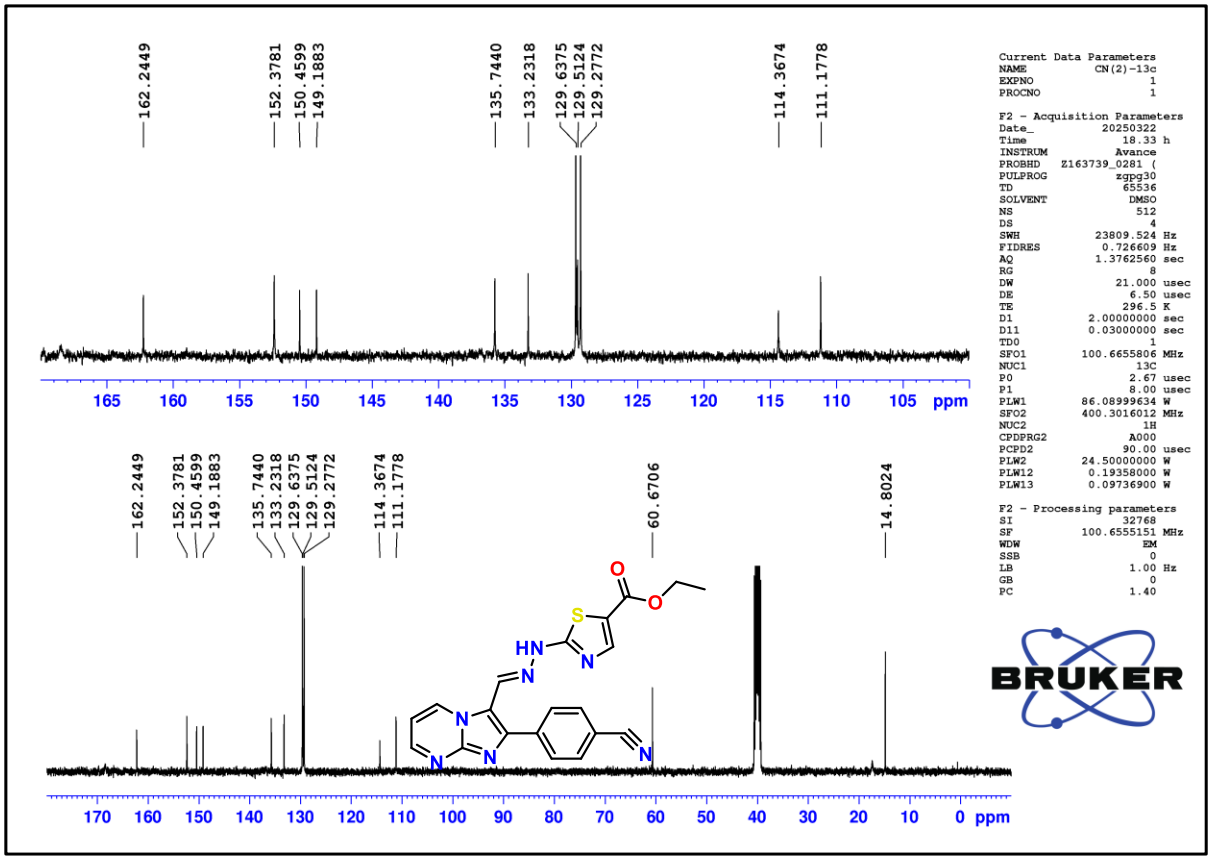


Figure S93: ^{13}C-NMR spectrum of compound **K13**

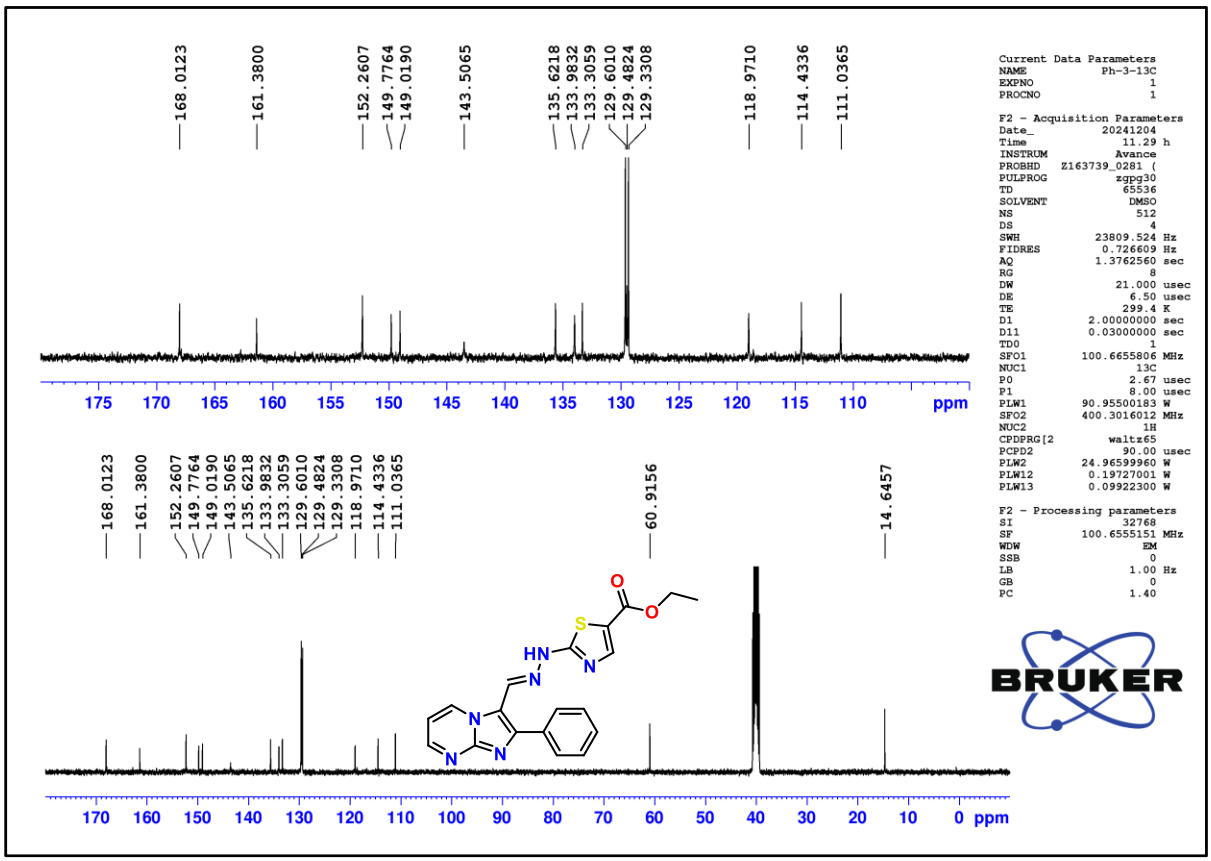


Figure S94: ^{13}C-NMR spectrum of compound **K14**

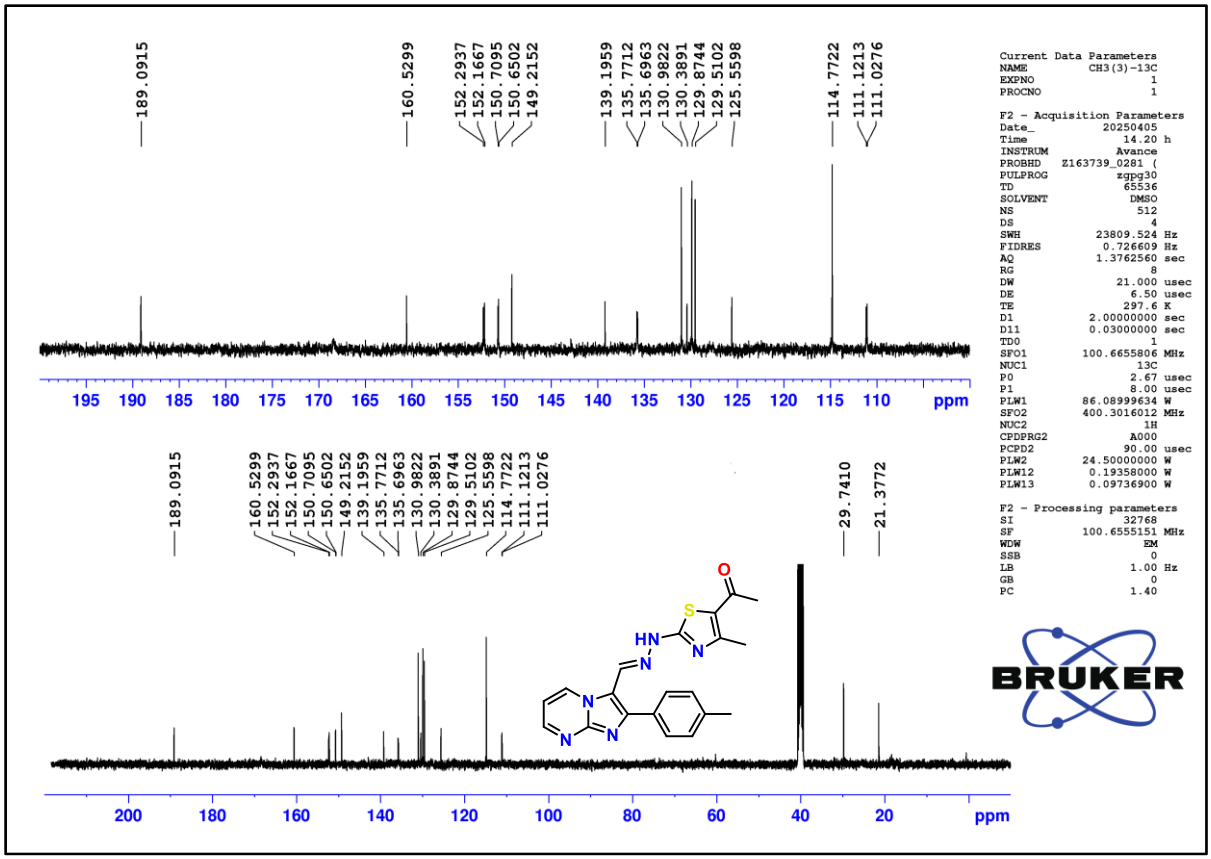


Figure S95: ^{13}C-NMR spectrum of compound **K15**

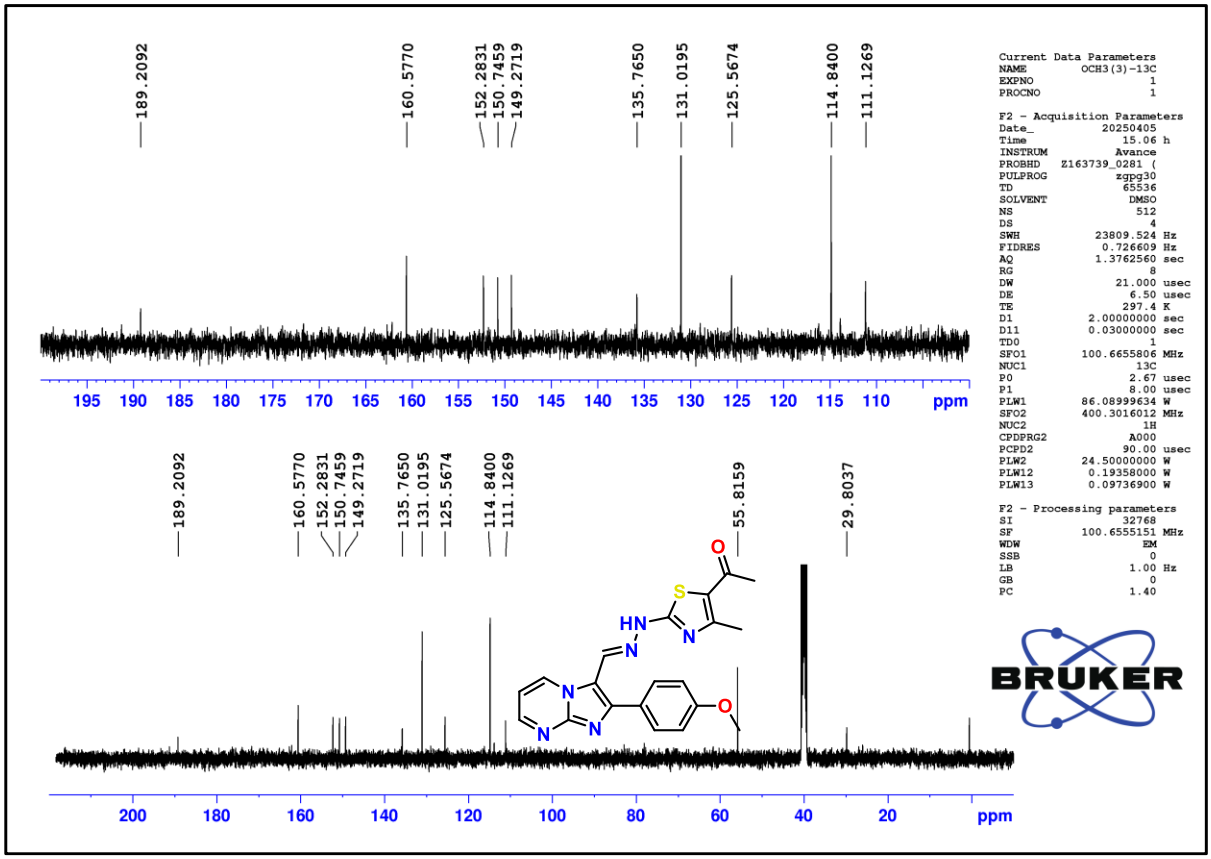


Figure S96: ^{13}C-NMR spectrum of compound **K16**

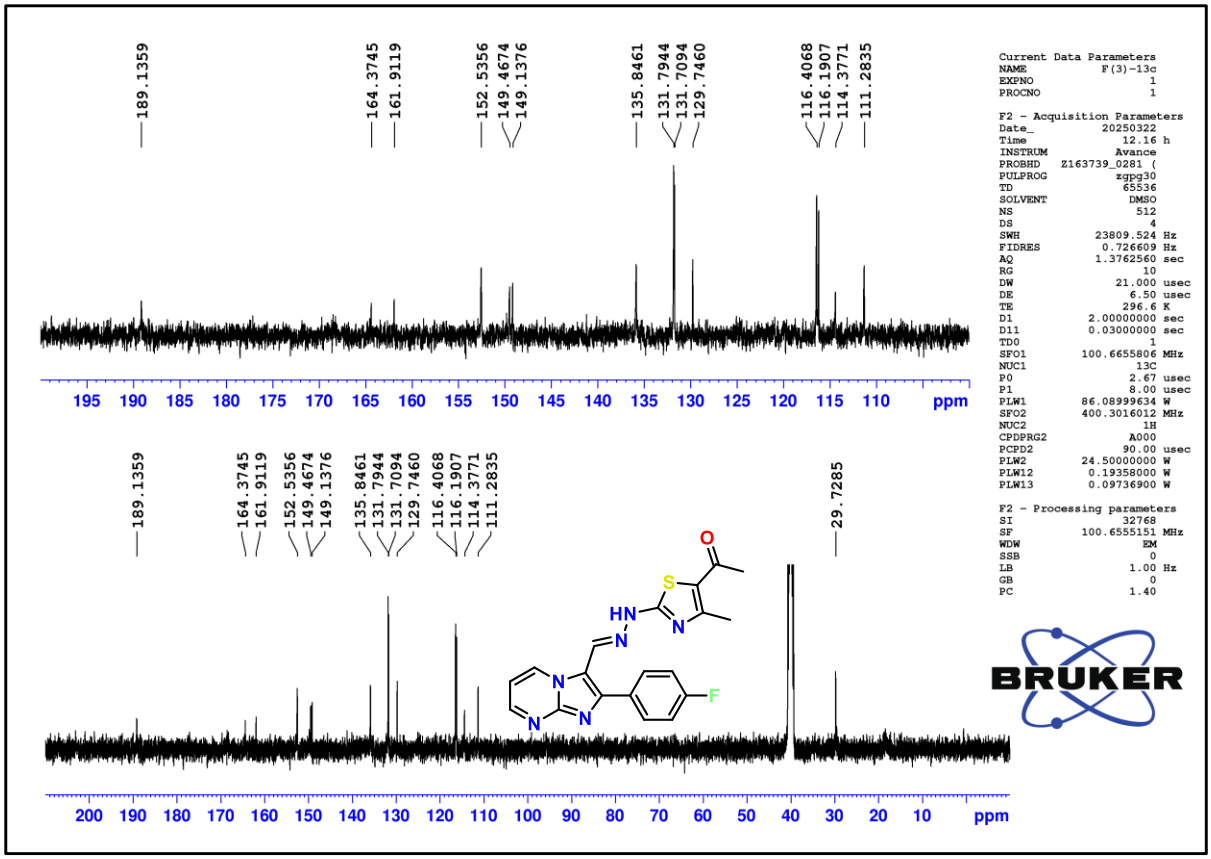


Figure S97: ^{13}C-NMR spectrum of compound **K17**

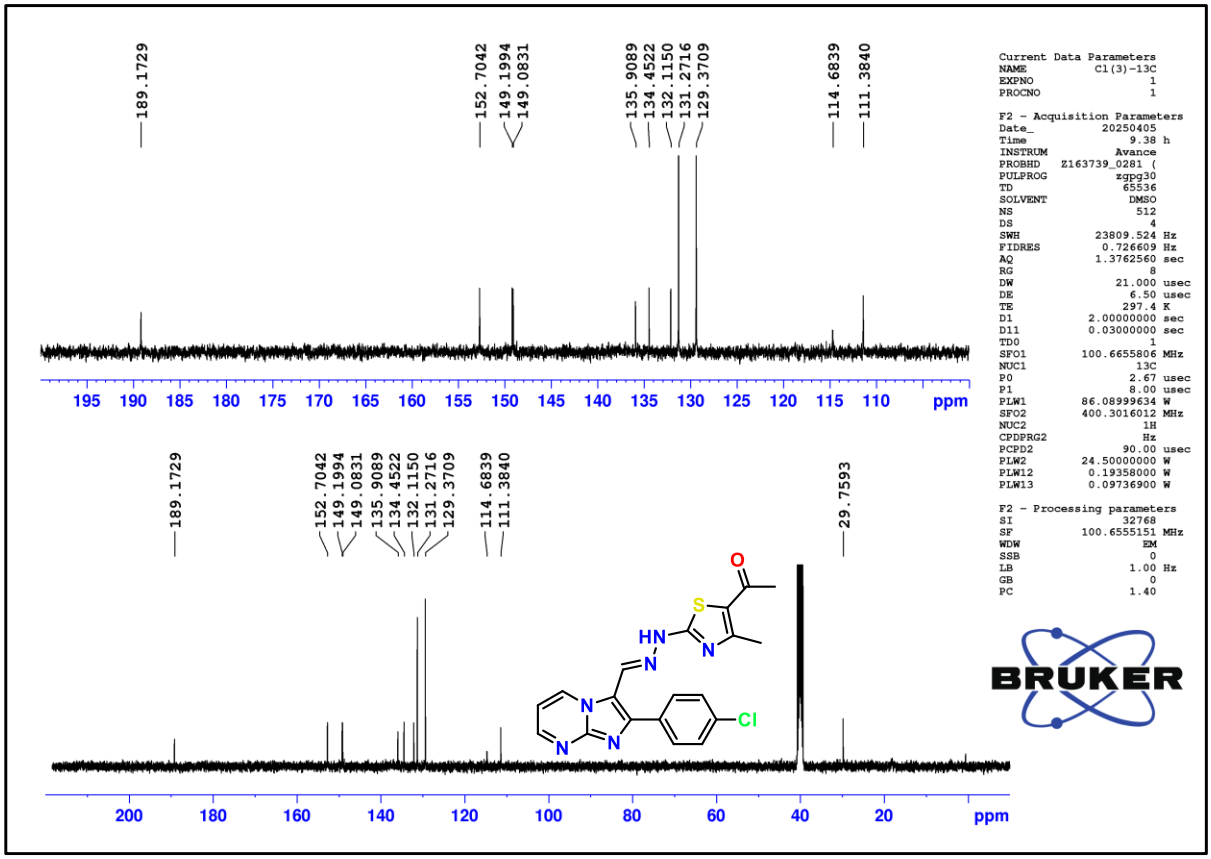


Figure S98: ^{13}C-NMR spectrum of compound **K18**

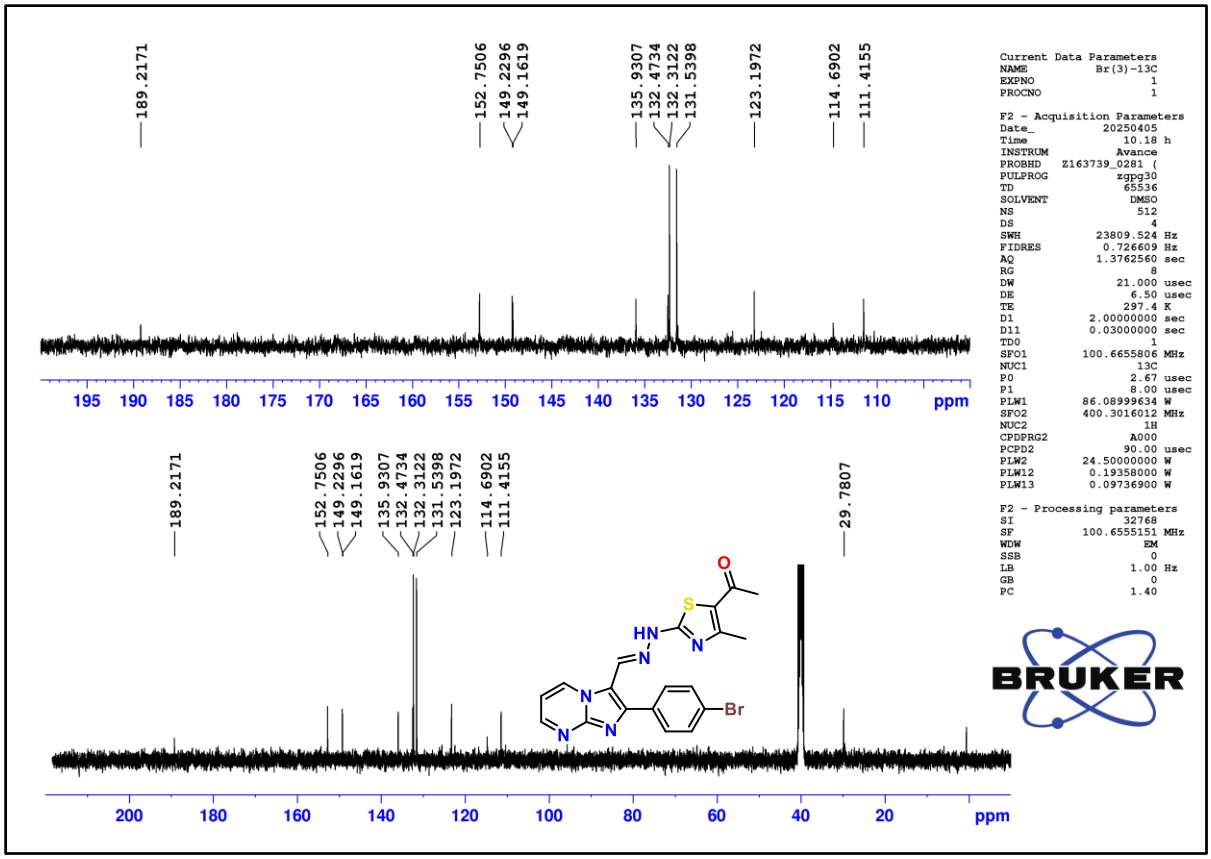


Figure S99: ^{13}C-NMR spectrum of compound **K19**

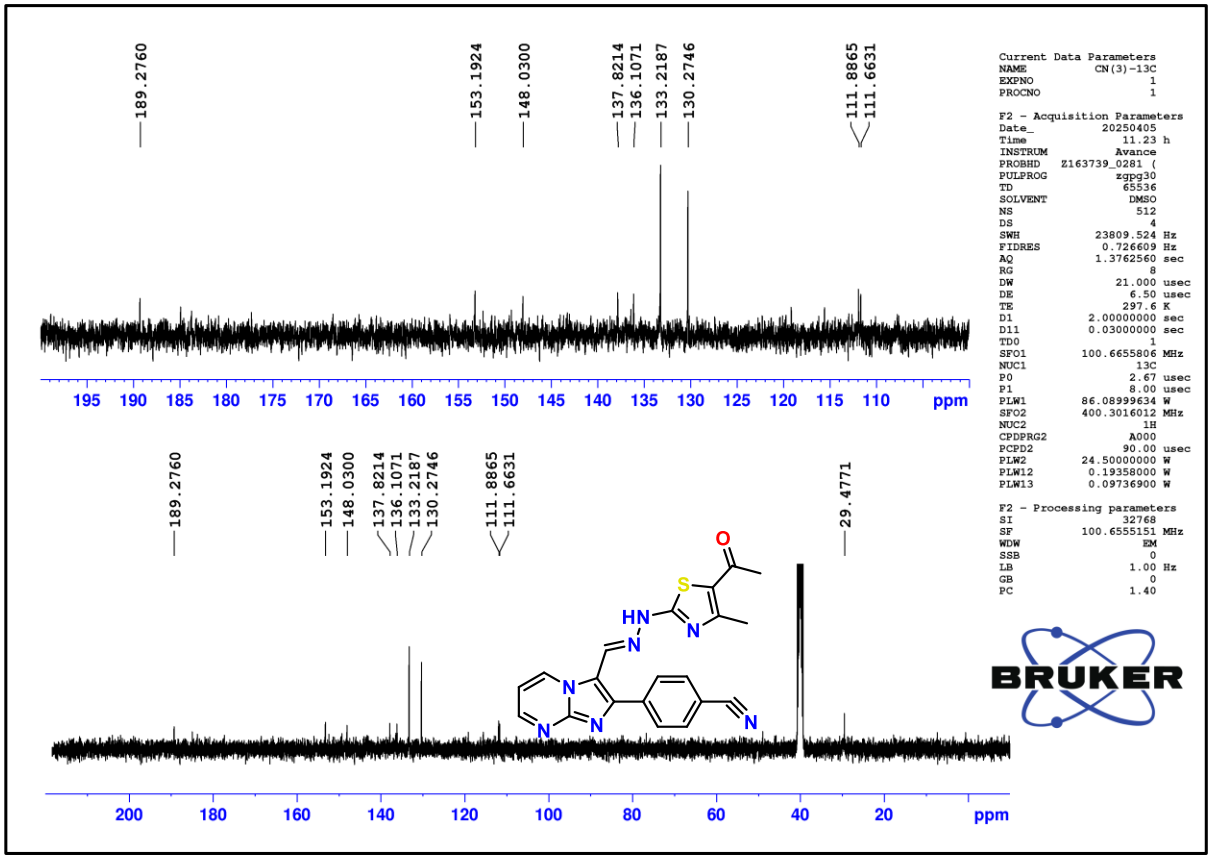


Figure S100: ^{13}C-NMR spectrum of compound **K20**

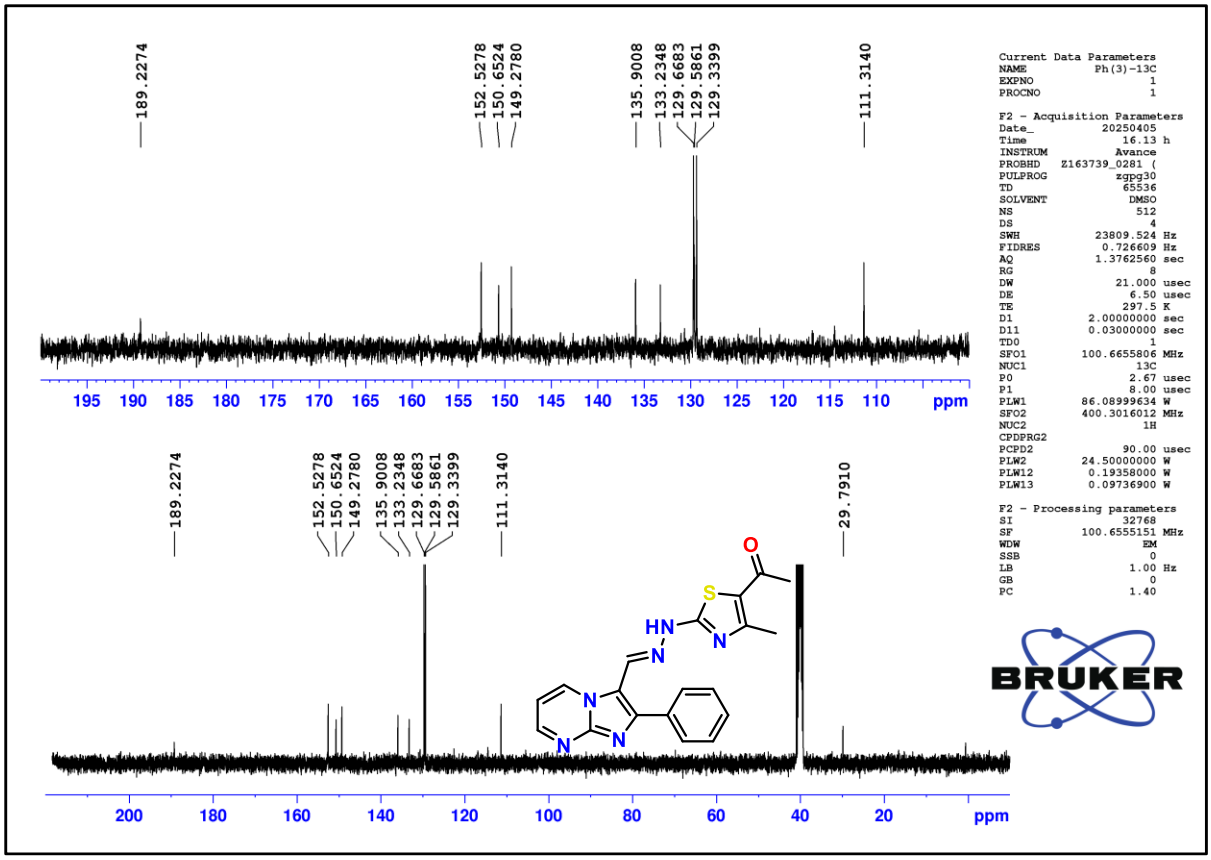


Figure S101: ^{13}C-NMR spectrum of compound **K21**

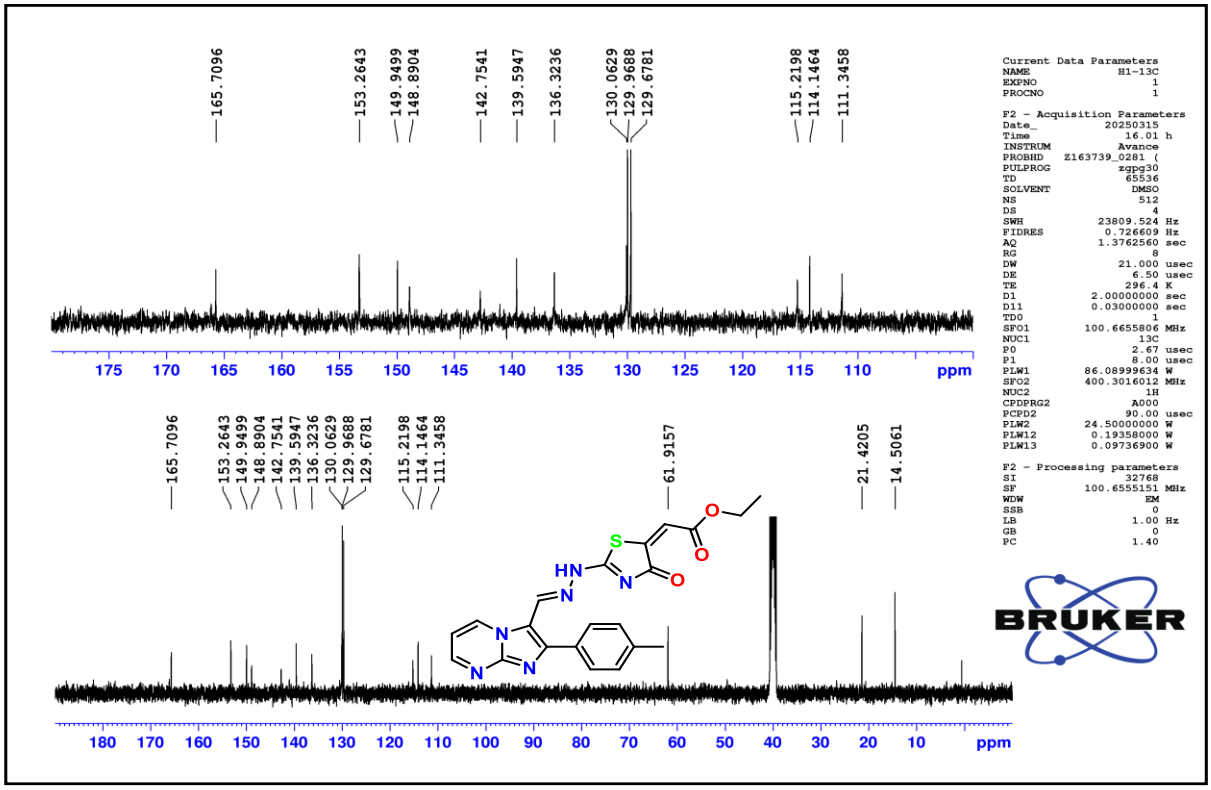


Figure S102: ^{13}C-NMR spectrum of compound **K22**

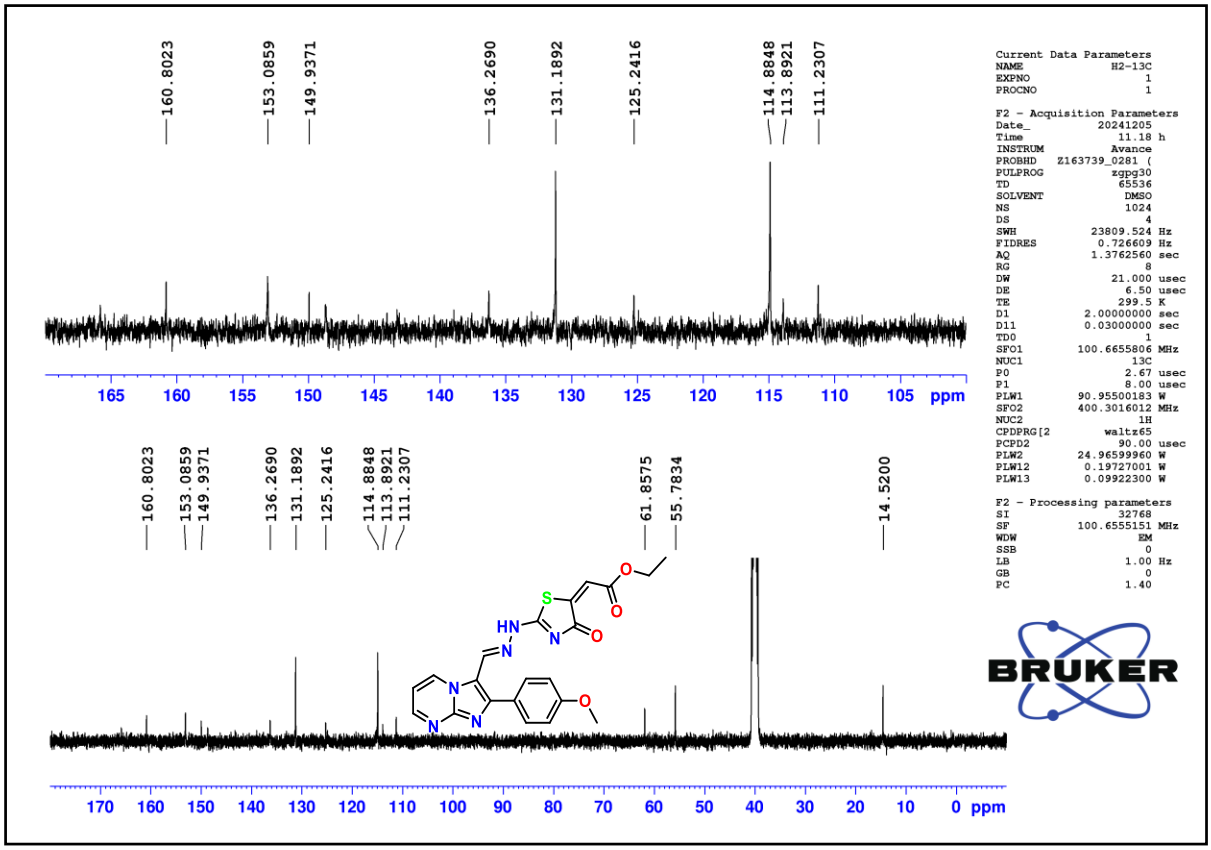


Figure S103: ^{13}C-NMR spectrum of compound **K23**

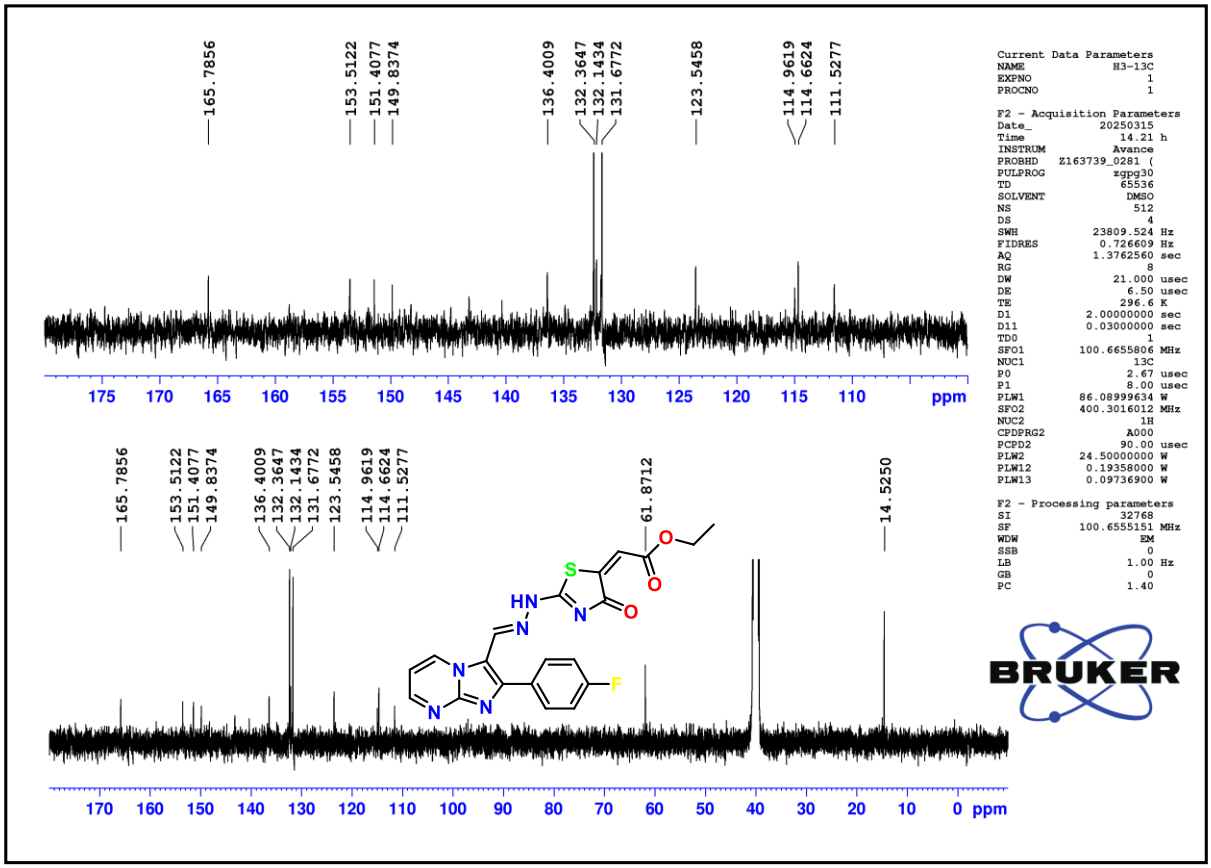


Figure S104: ^{13}C-NMR spectrum of compound **K24**

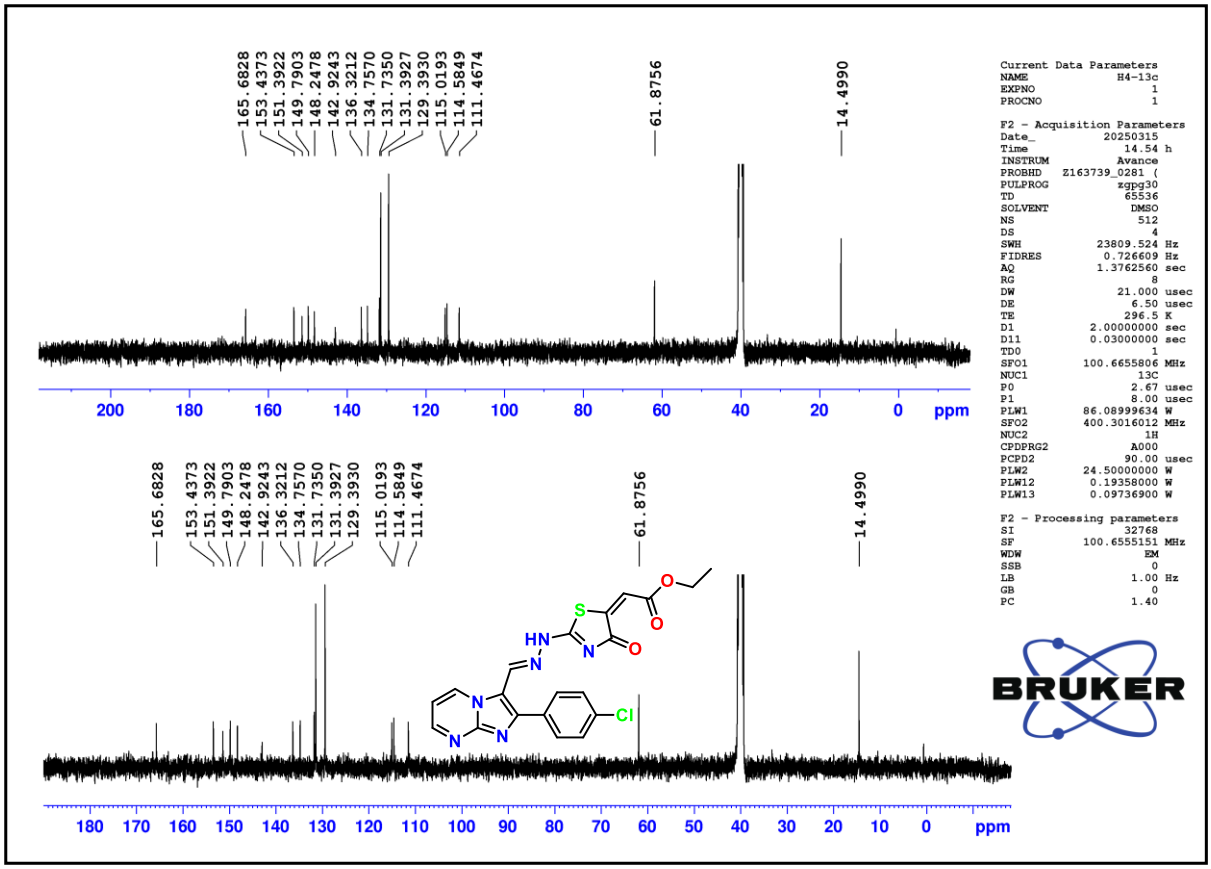


Figure S105: ^{13}C-NMR spectrum of compound **K25**

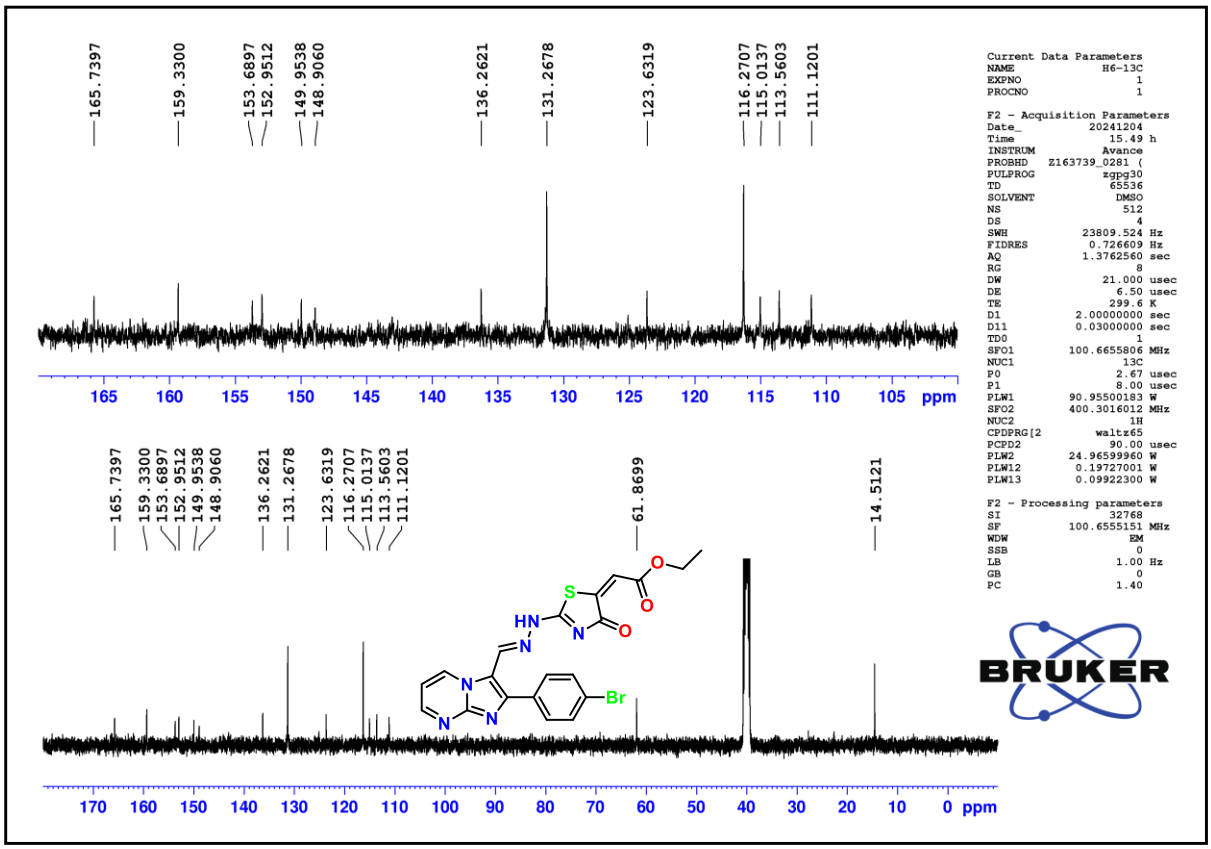


Figure S106: ^{13}C-NMR spectrum of compound **K26**

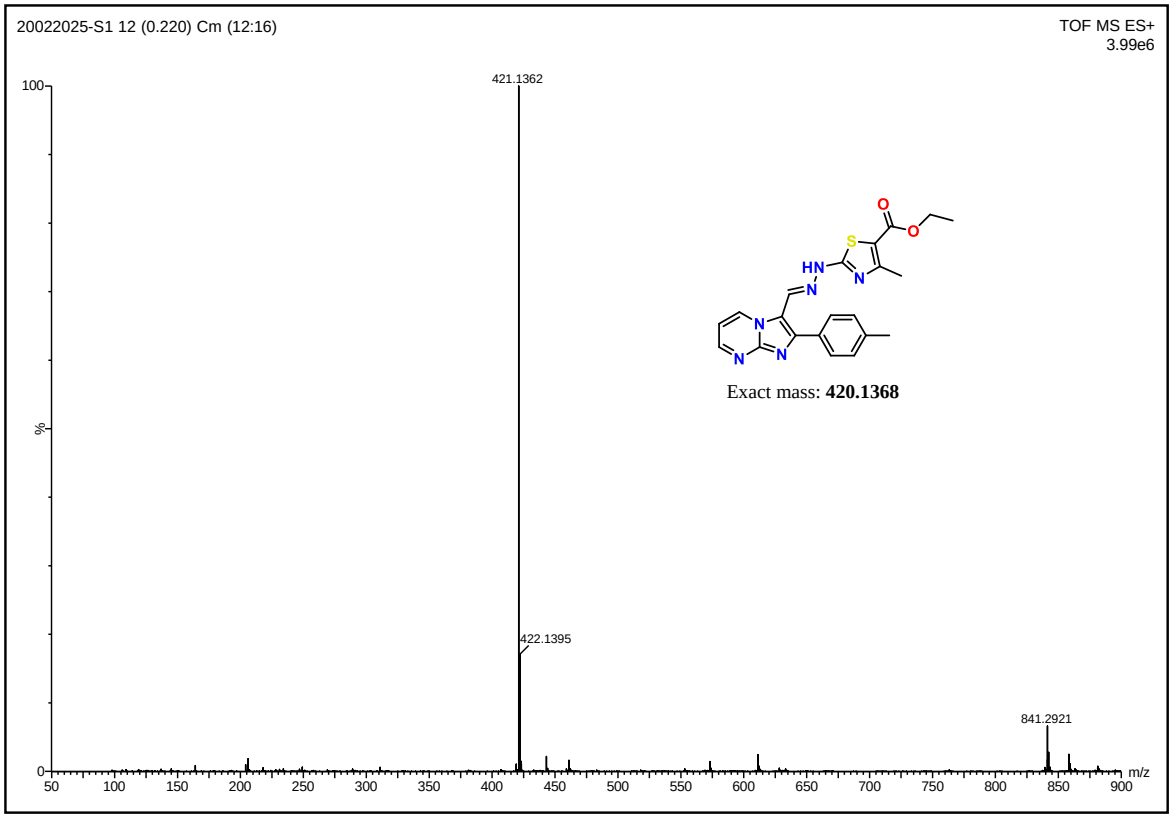


Figure S107: HR-MS spectrum of compound **K1**

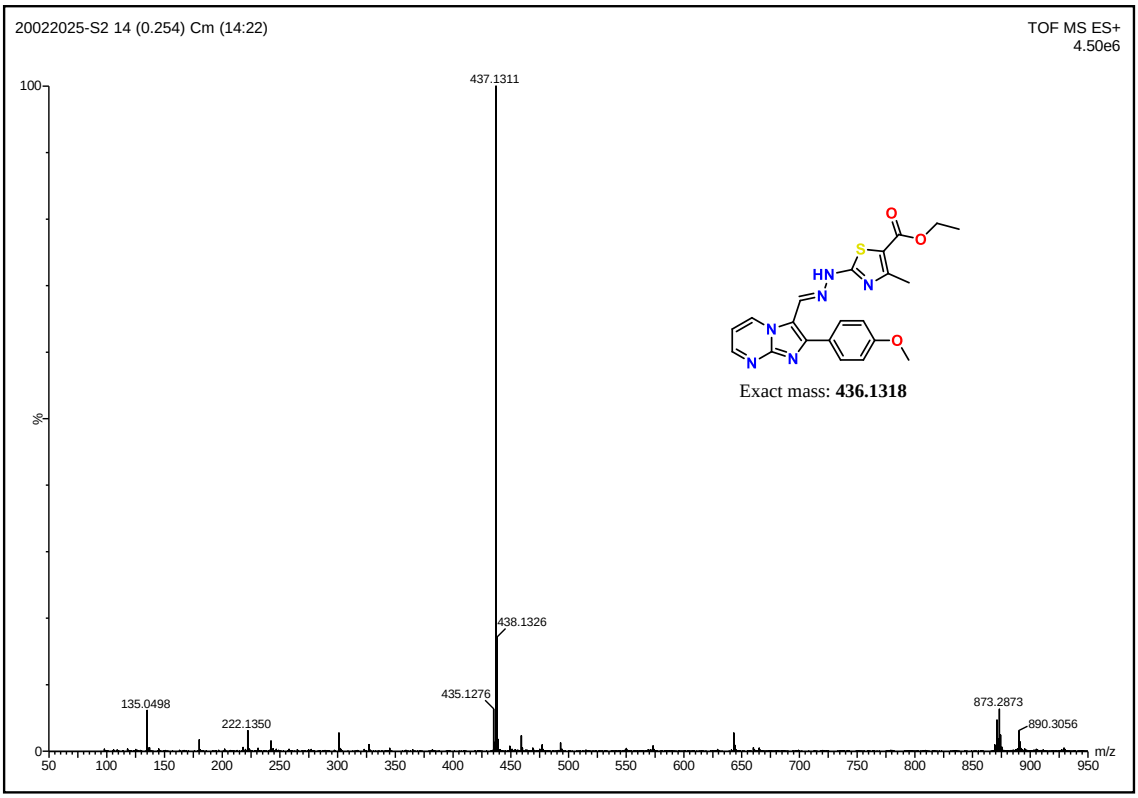


Figure S108: HR-MS spectrum of compound **K2**

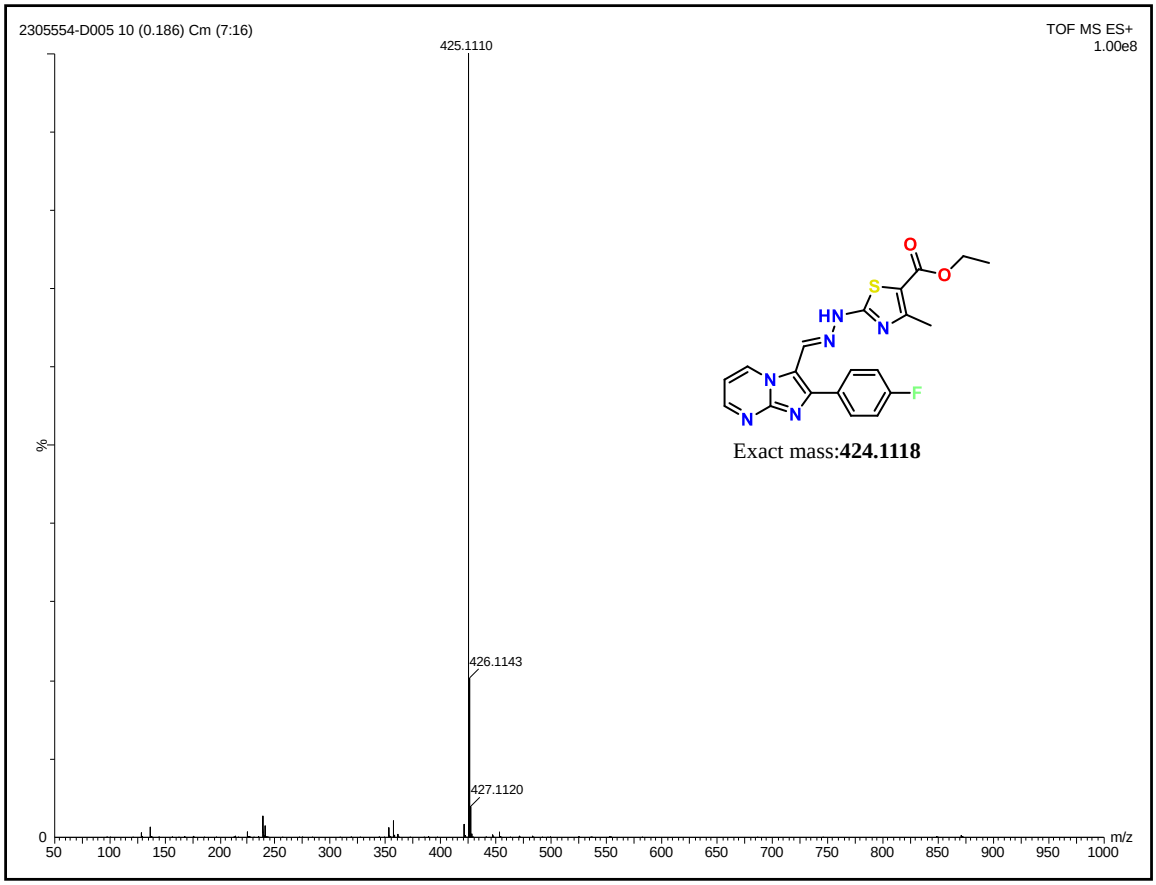


Figure S109: HR-MS spectrum of compound **K3**

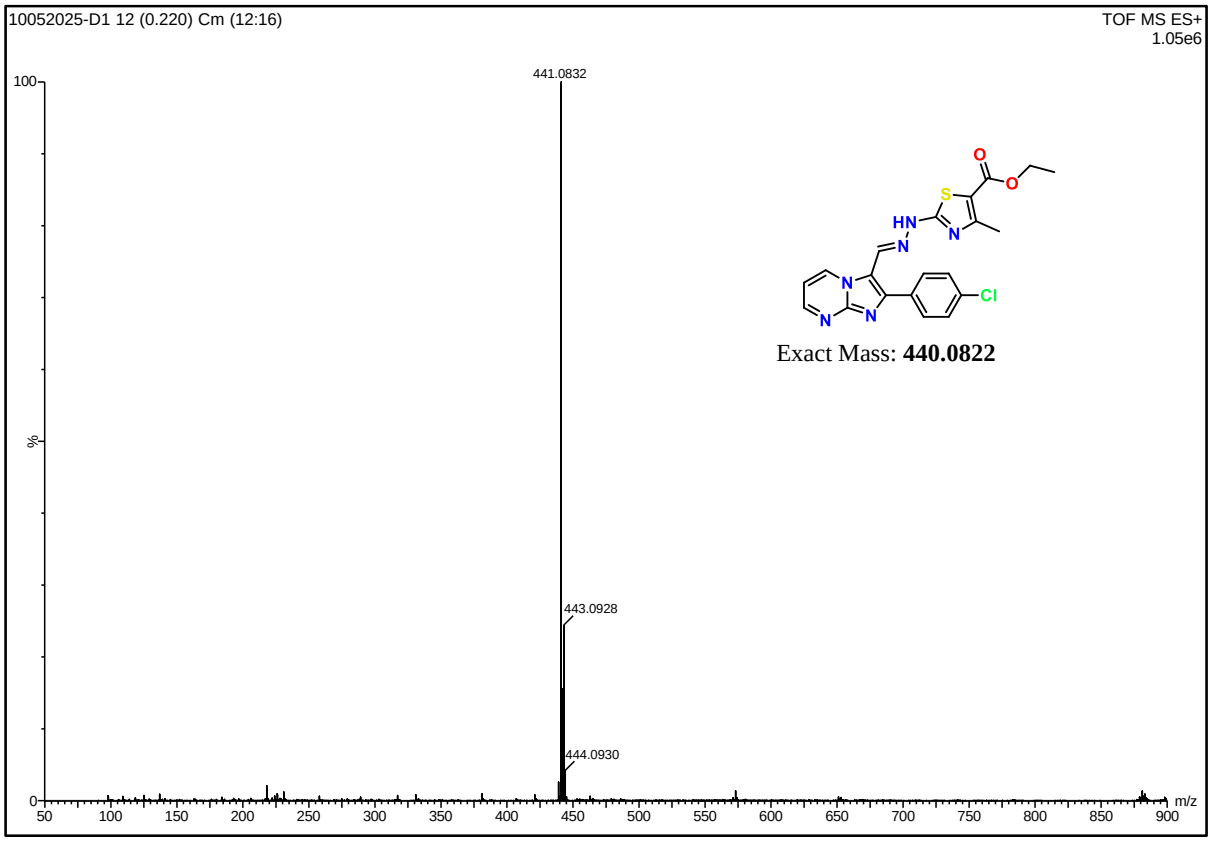


Figure S110: HR-MS spectrum of compound **K4**

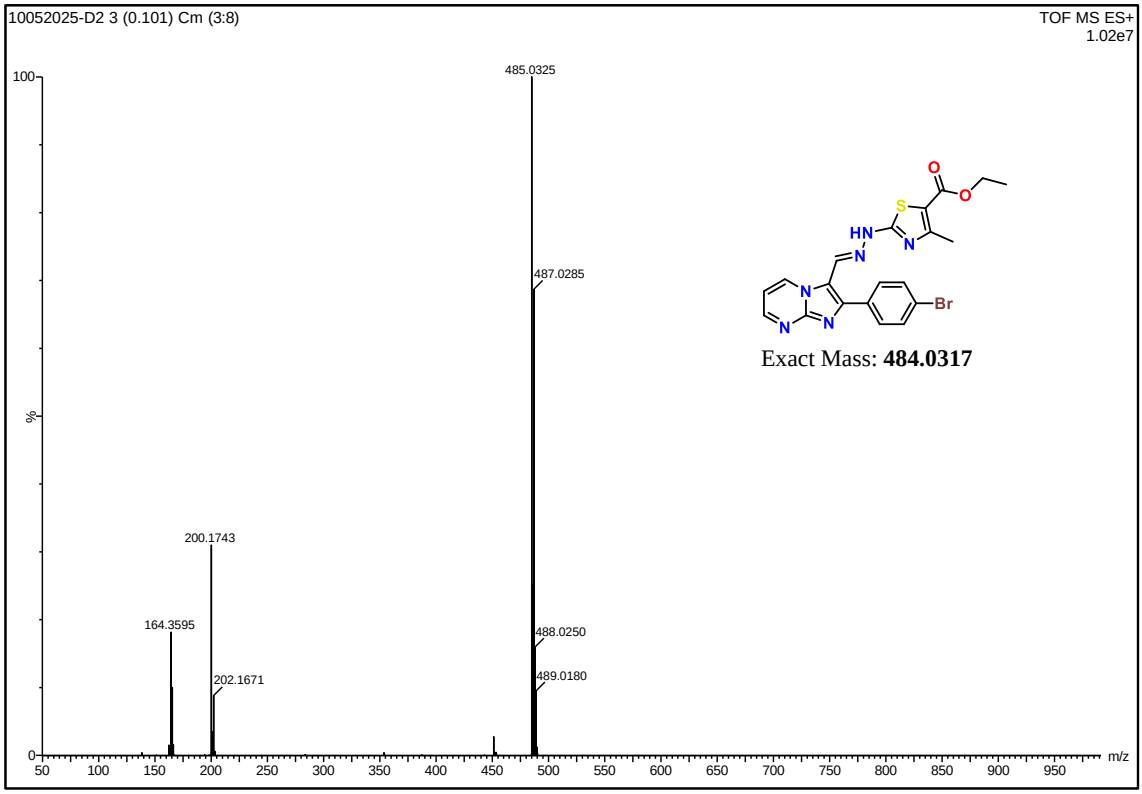


Figure S111: HR-MS spectrum of compound **K5**

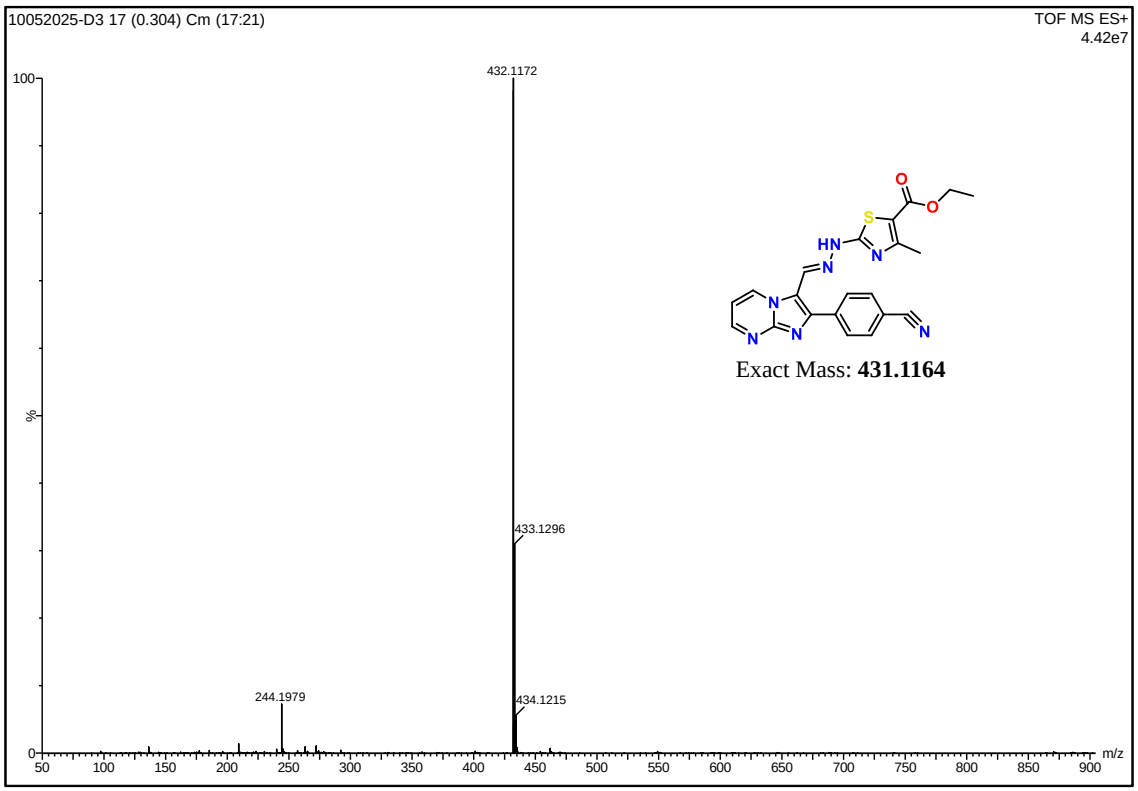


Figure S112: HR-MS spectrum of compound **K6**

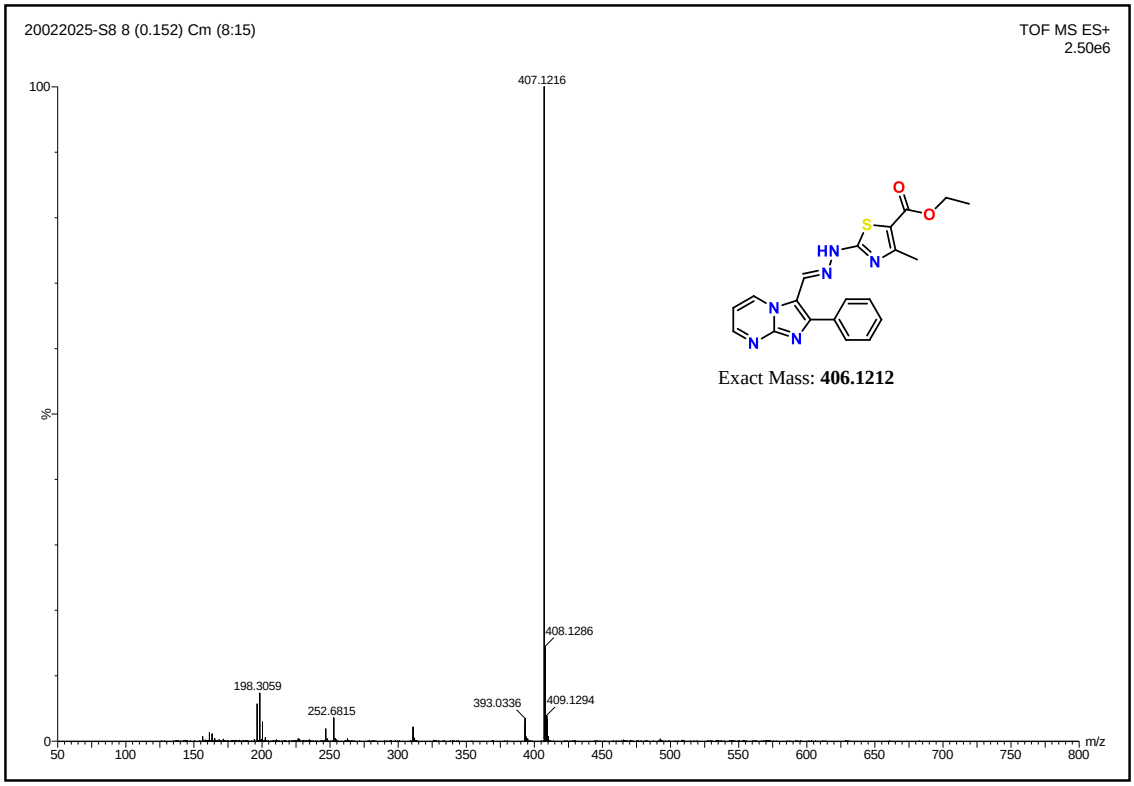


Figure S113: HR-MS spectrum of compound **K7**

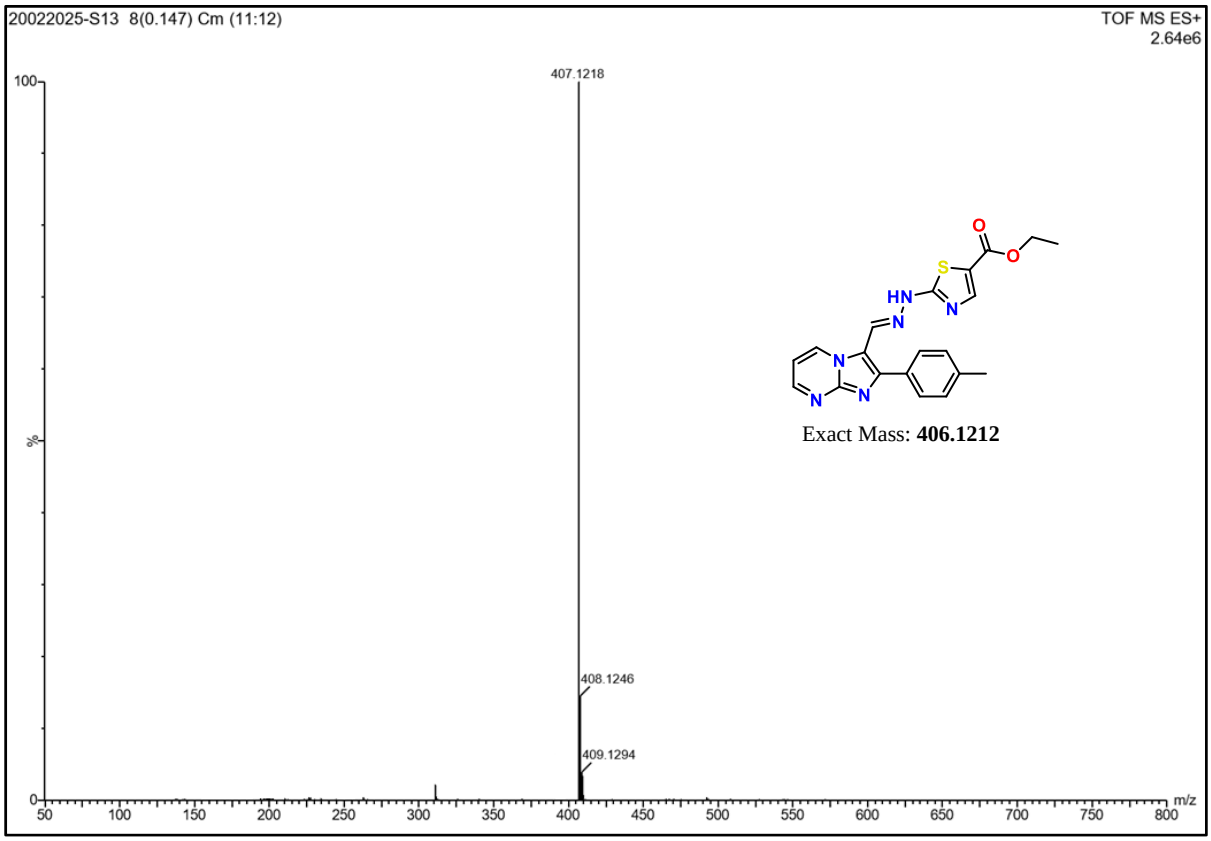


Figure S114: HR-MS spectrum of compound **K8**

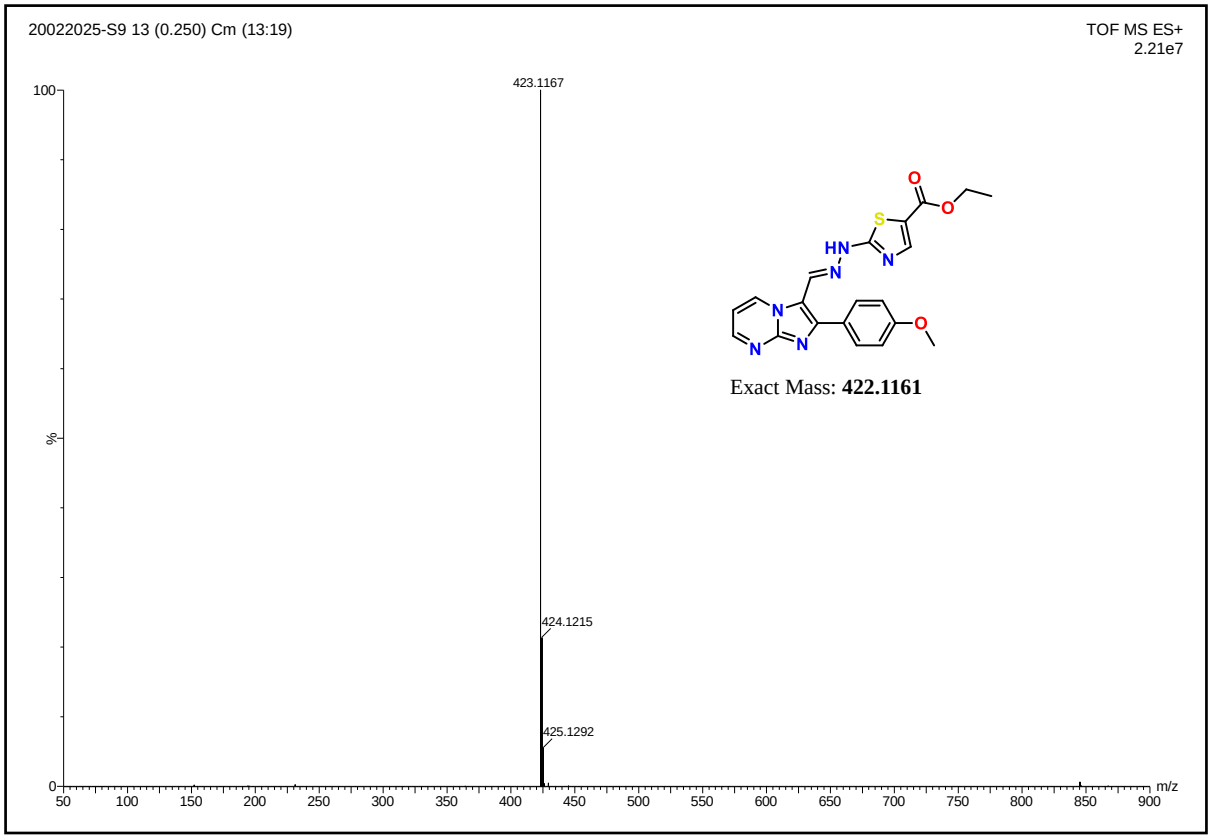


Figure S115: HR-MS spectrum of compound **K9**

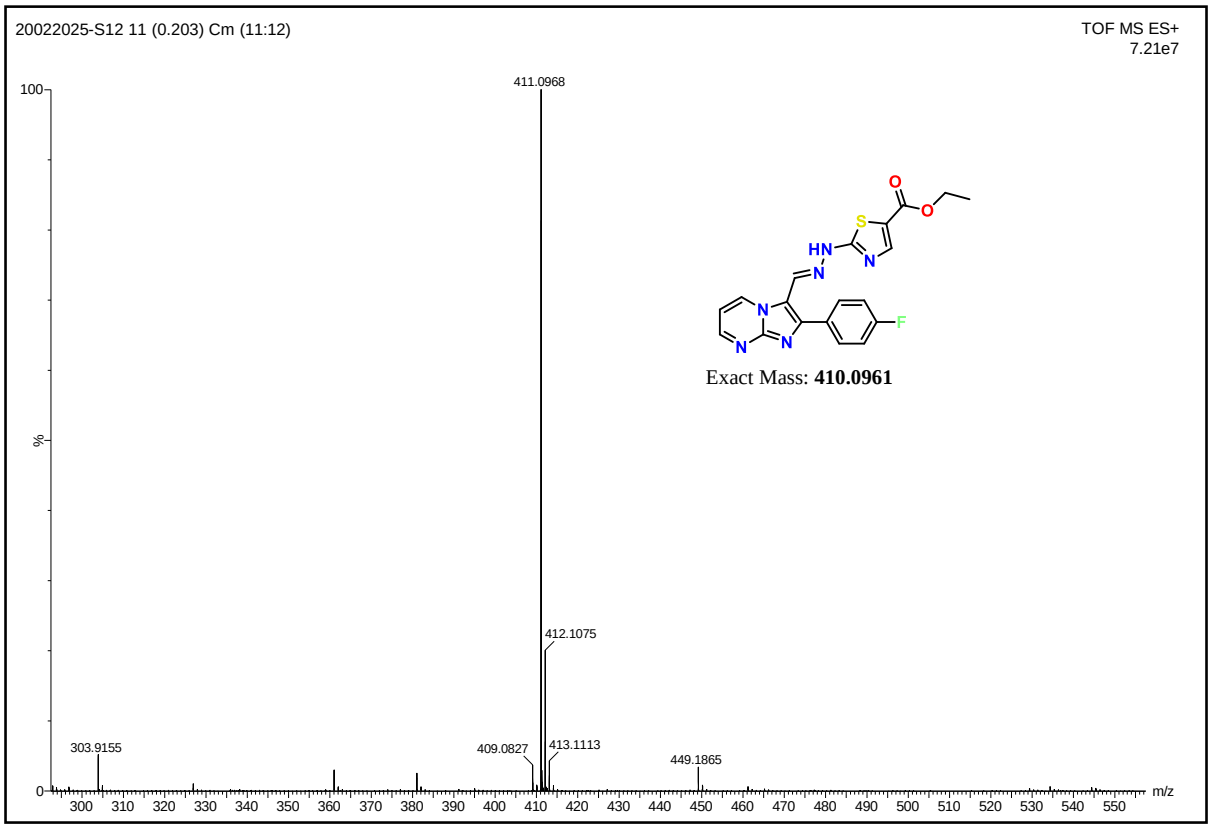


Figure S116: HR-MS spectrum of compound **K10**

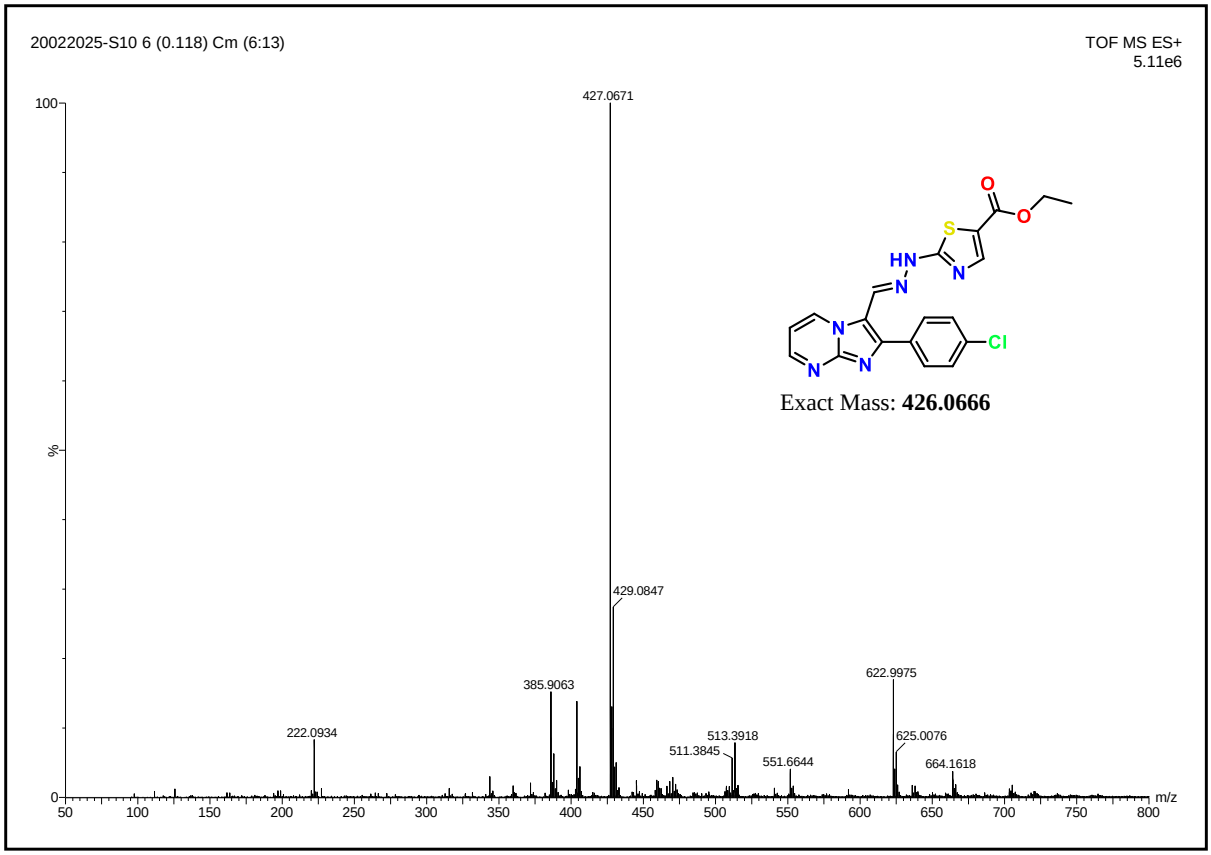


Figure S117: HR-MS spectrum of compound **K11**

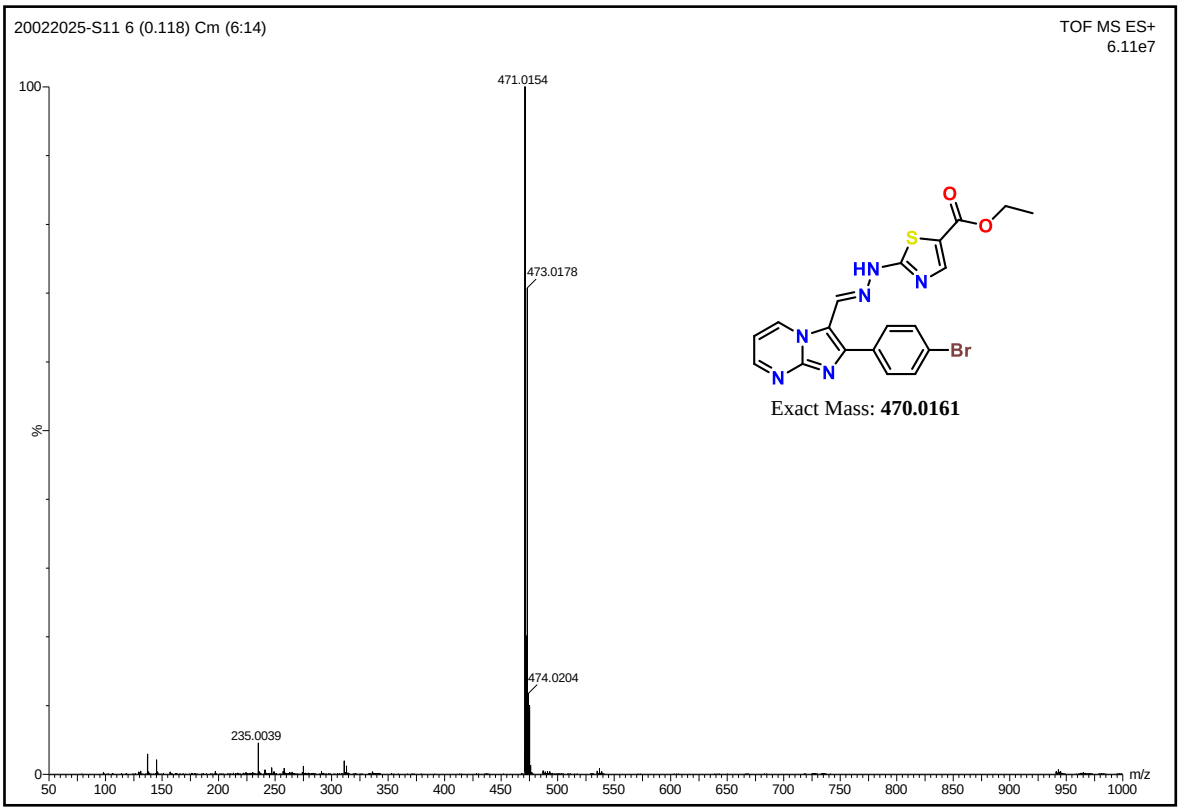


Figure S118: HR-MS spectrum of compound **K12**

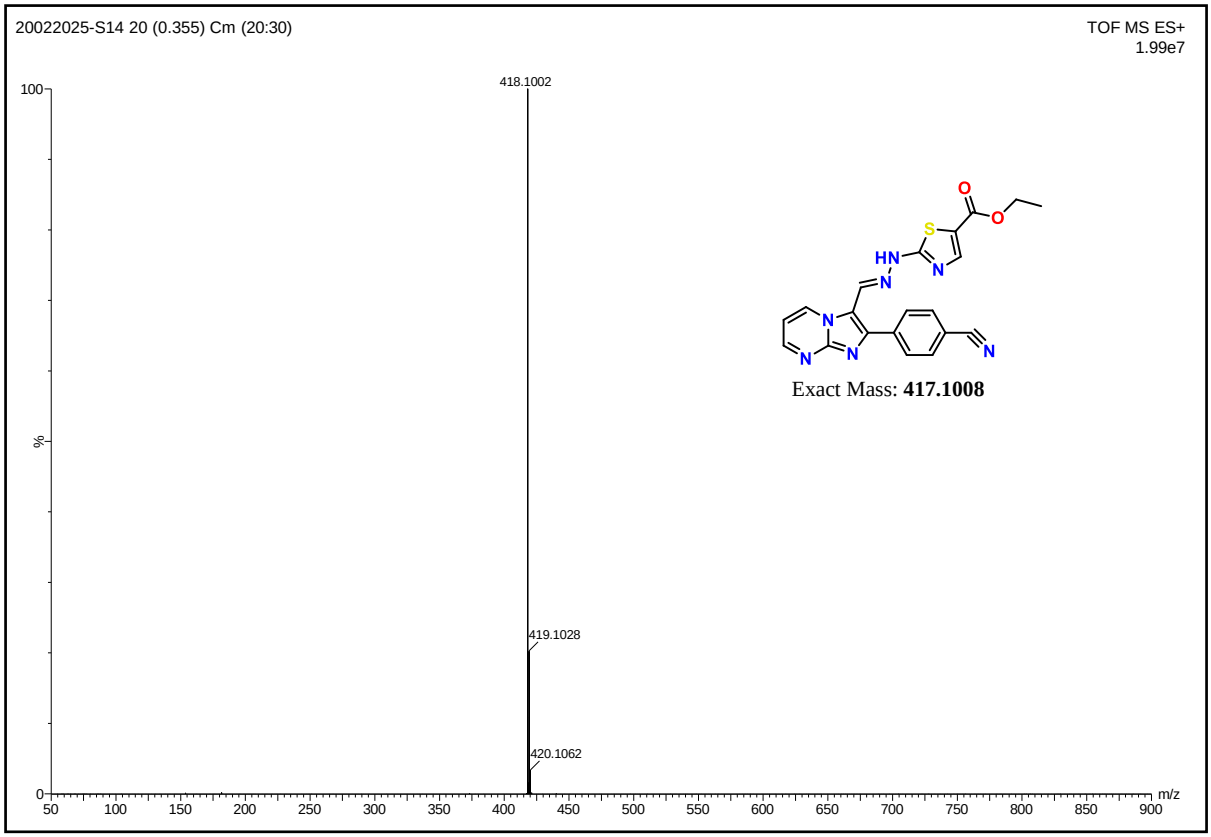


Figure S119: HR-MS spectrum of compound **K13**

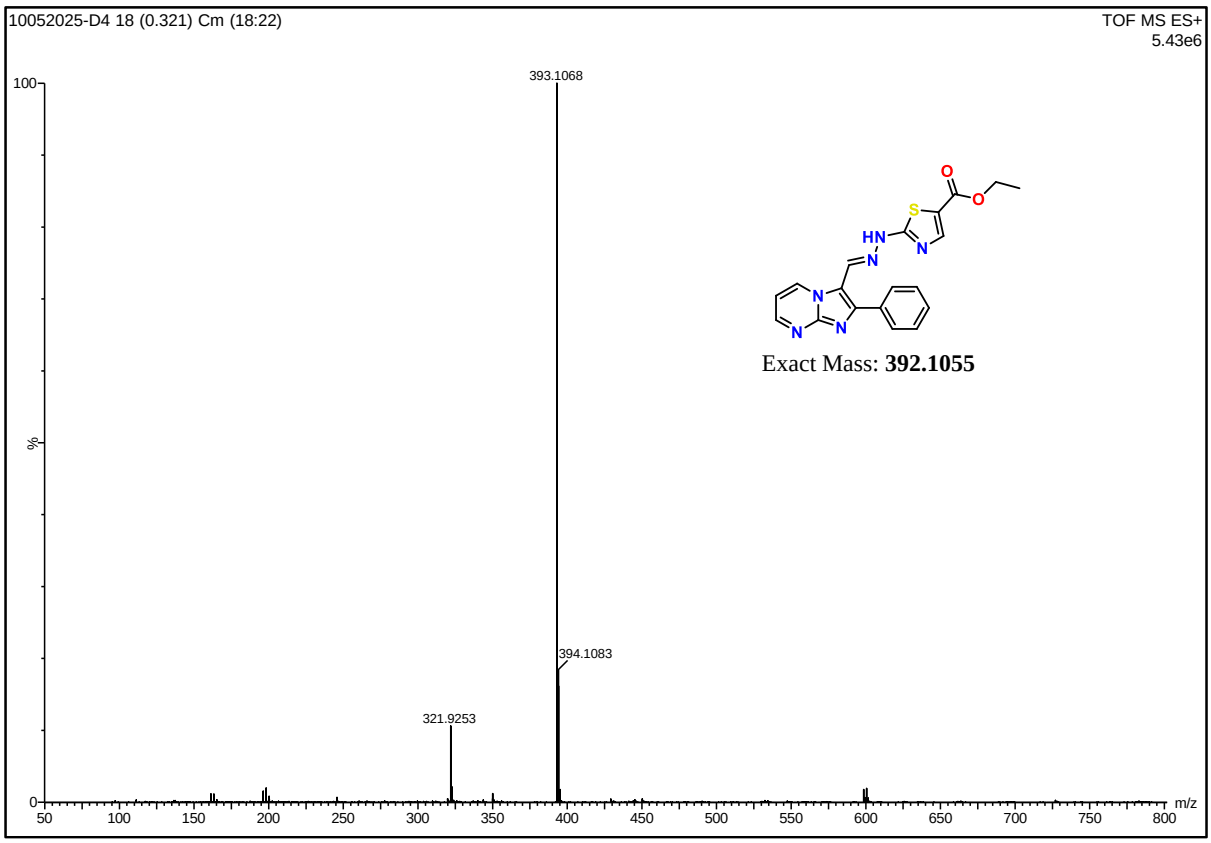


Figure S120: HR-MS spectrum of compound **K14**

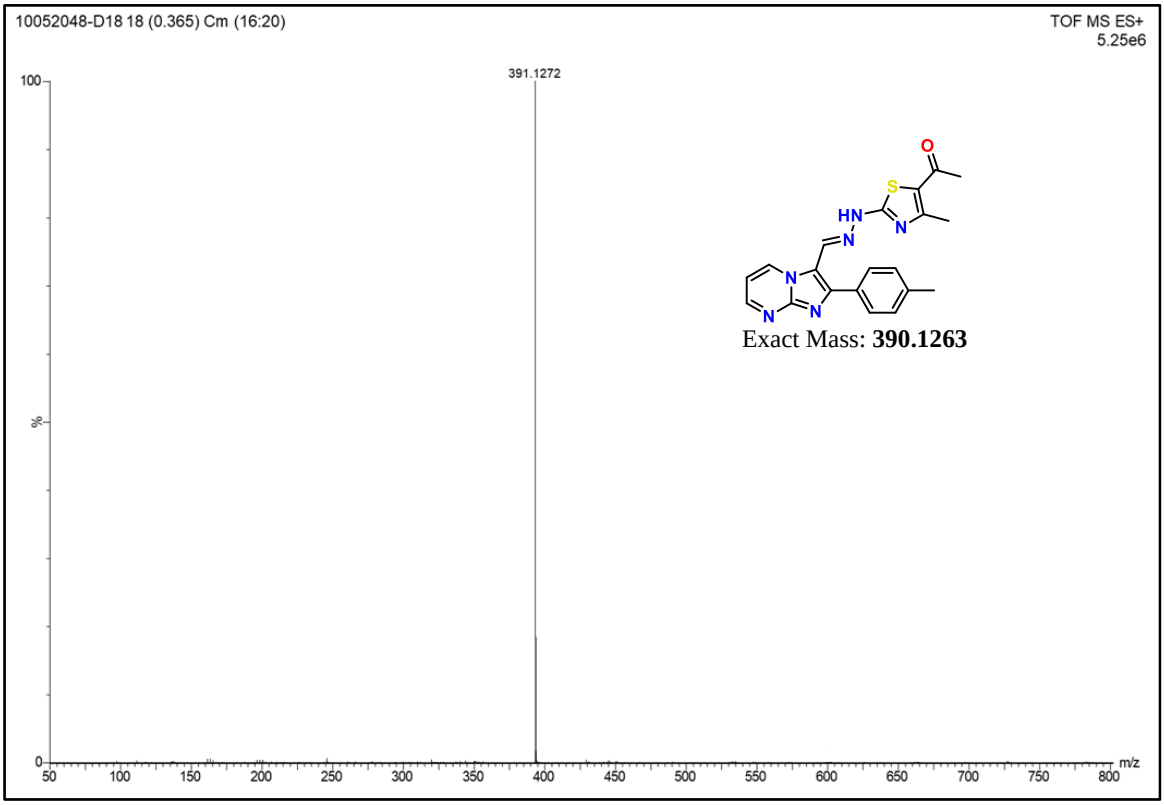


Figure S121: HR-MS spectrum of compound **K15**

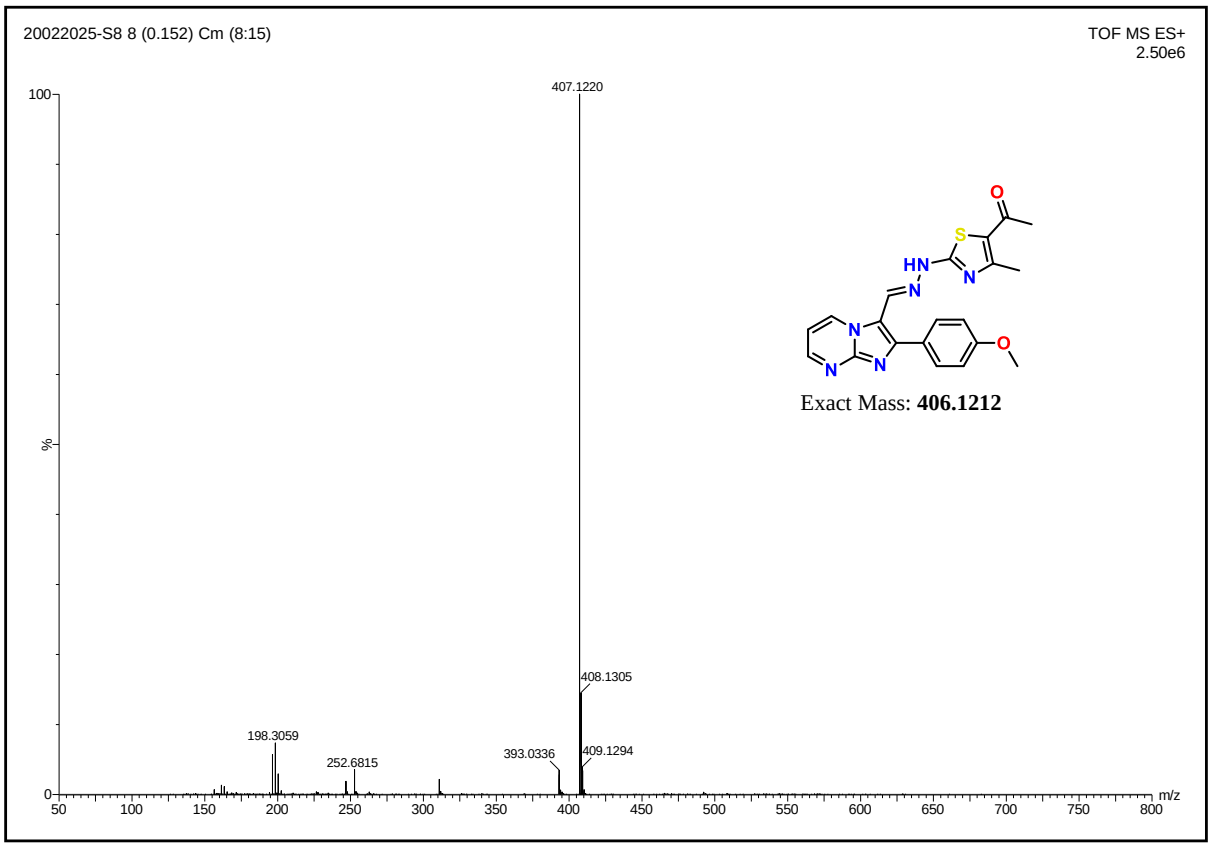


Figure S122: HR-MS spectrum of compound **K16**

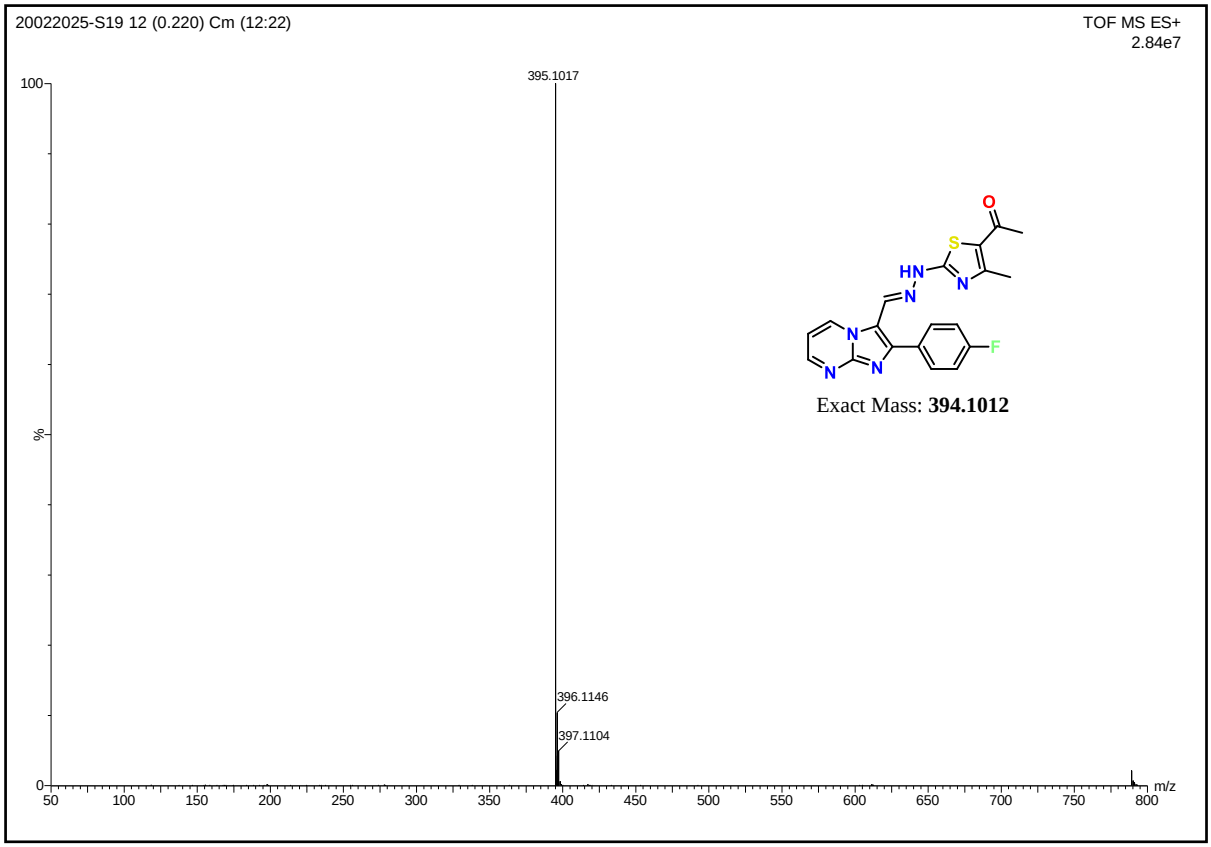


Figure S123: HR-MS spectrum of compound **K17**

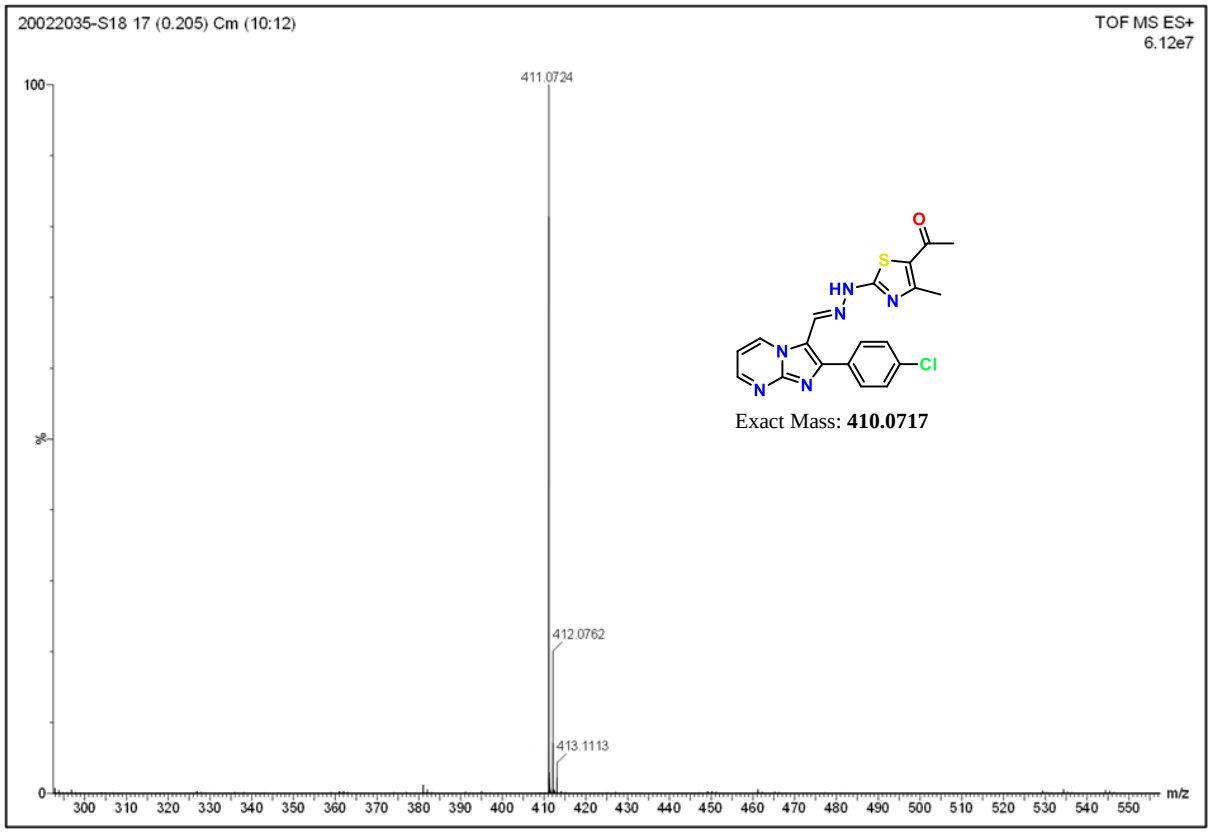


Figure S124: HR-MS spectrum of compound **K18**

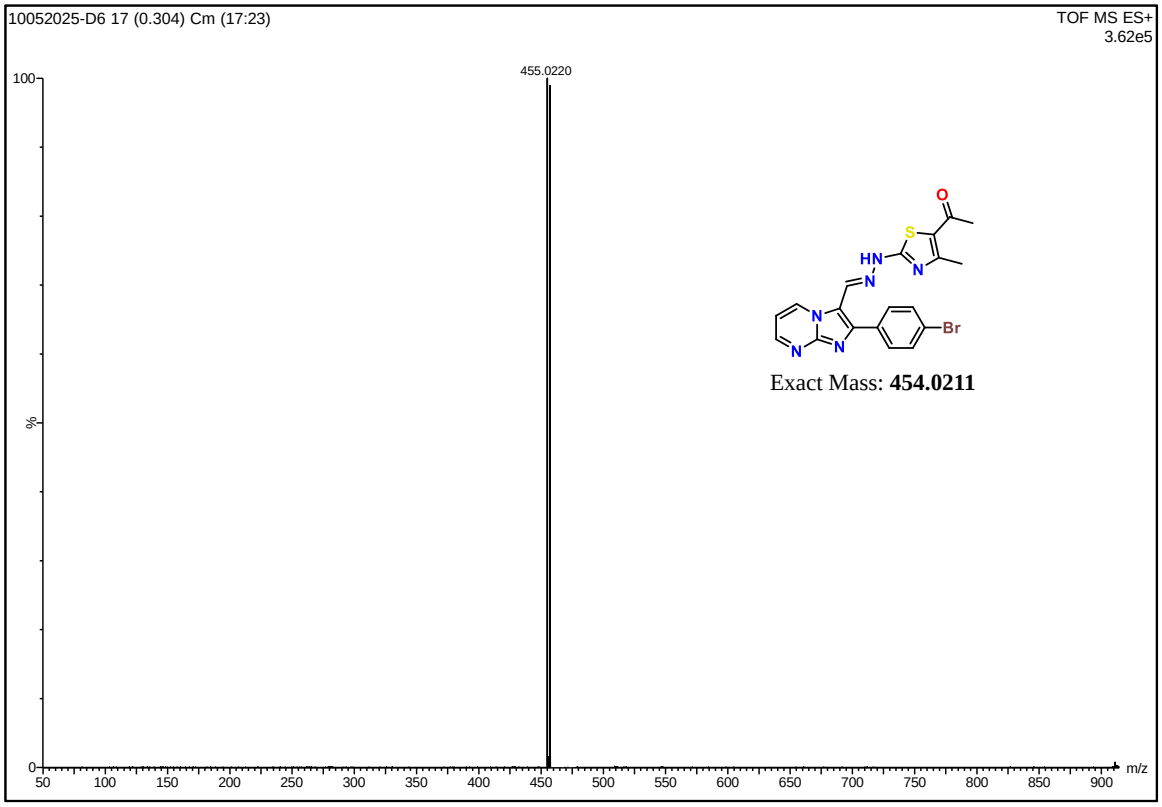


Figure S125: HR-MS spectrum of compound **K19**

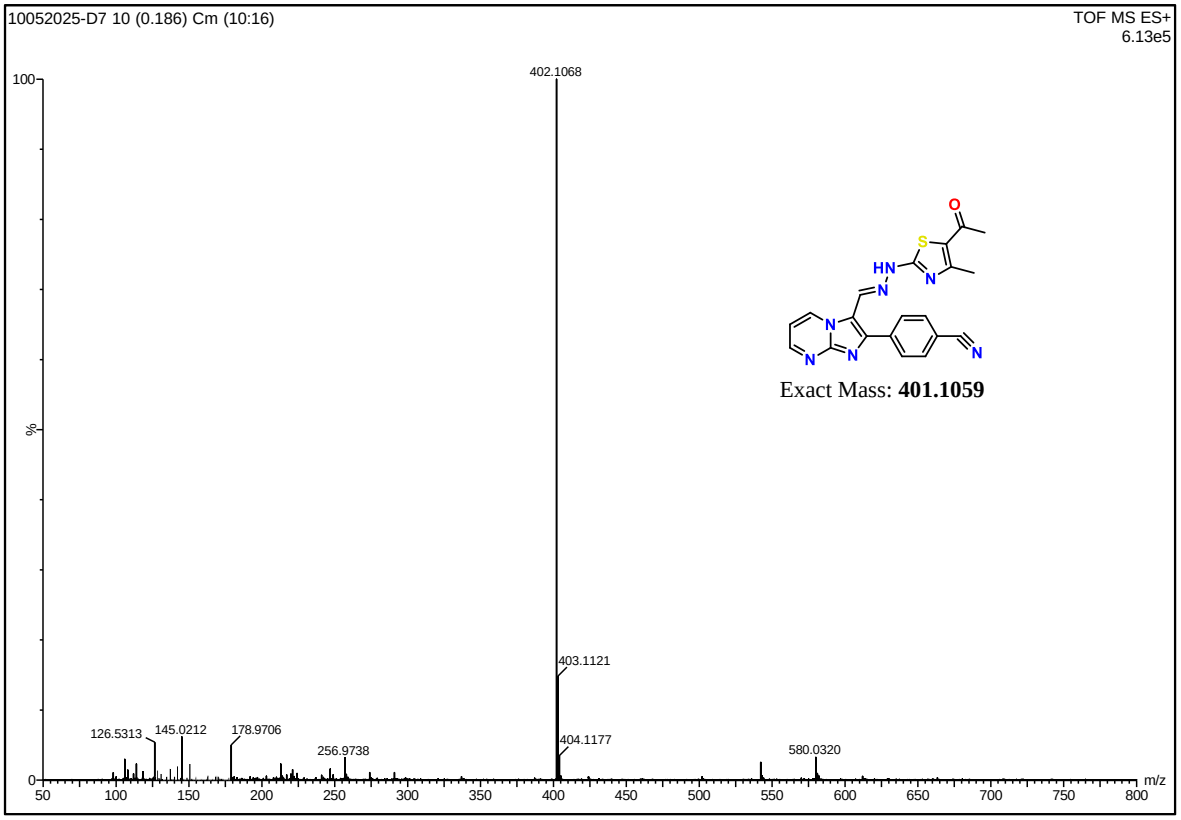


Figure S126: HR-MS spectrum of compound **K20**

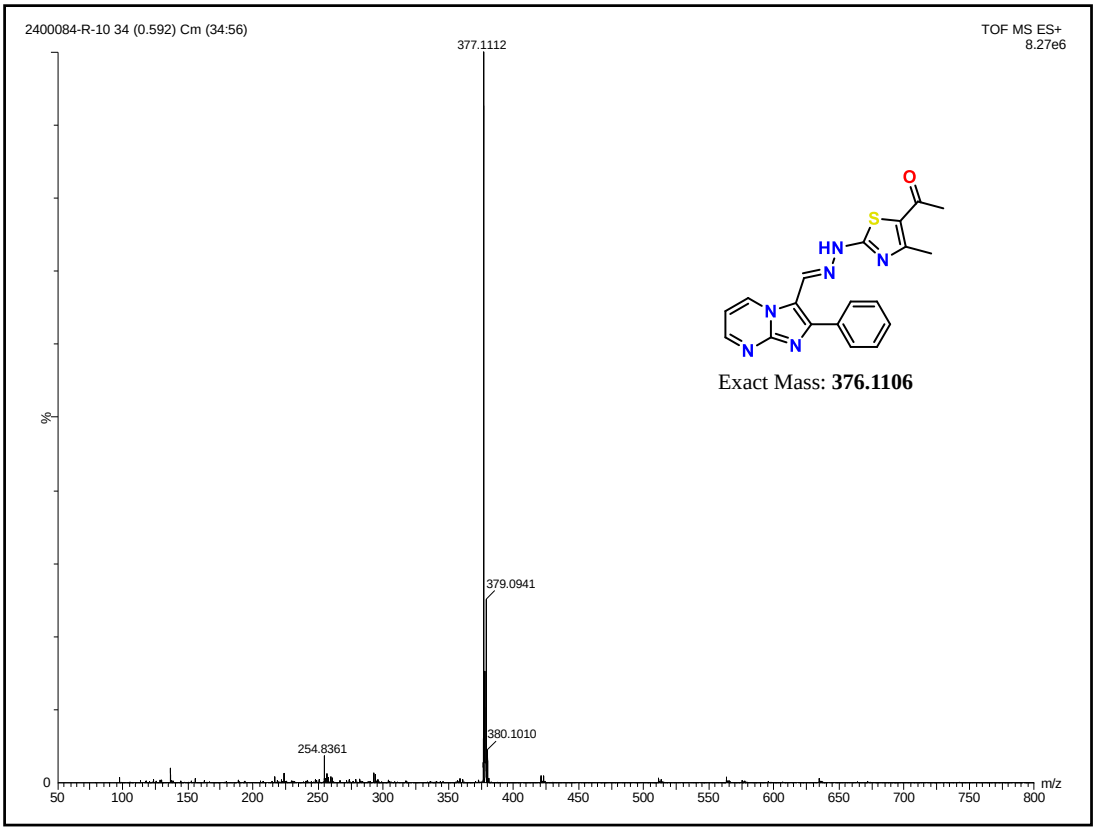


Figure S127: HR-MS spectrum of compound **K21**

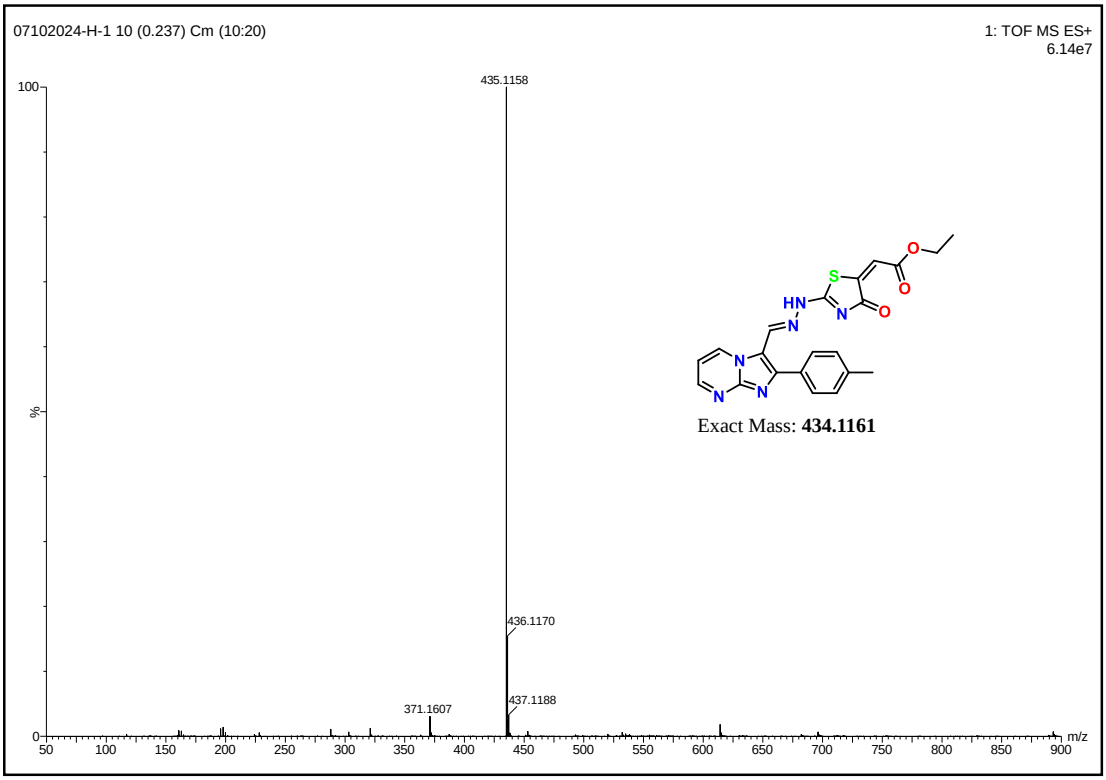


Figure S128: HR-MS spectrum of compound **K22**

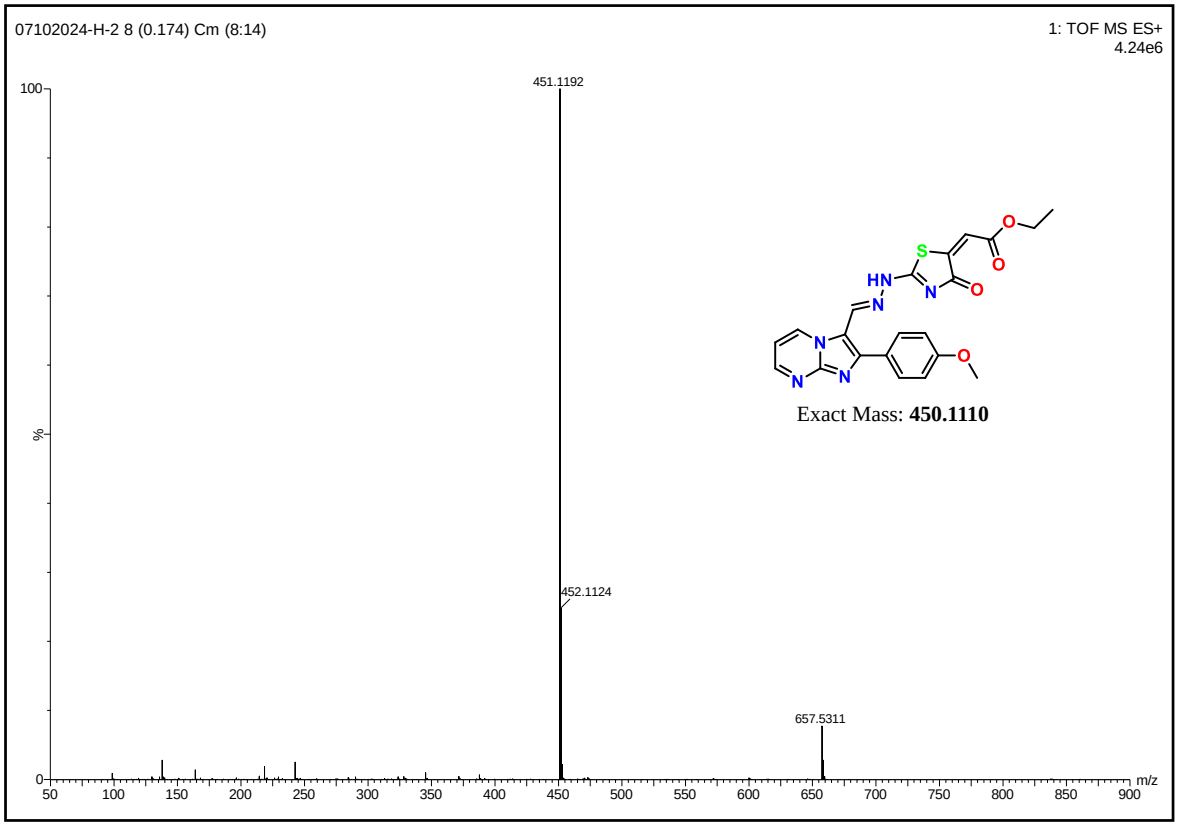


Figure S130: HR-MS spectrum of compound **K23**

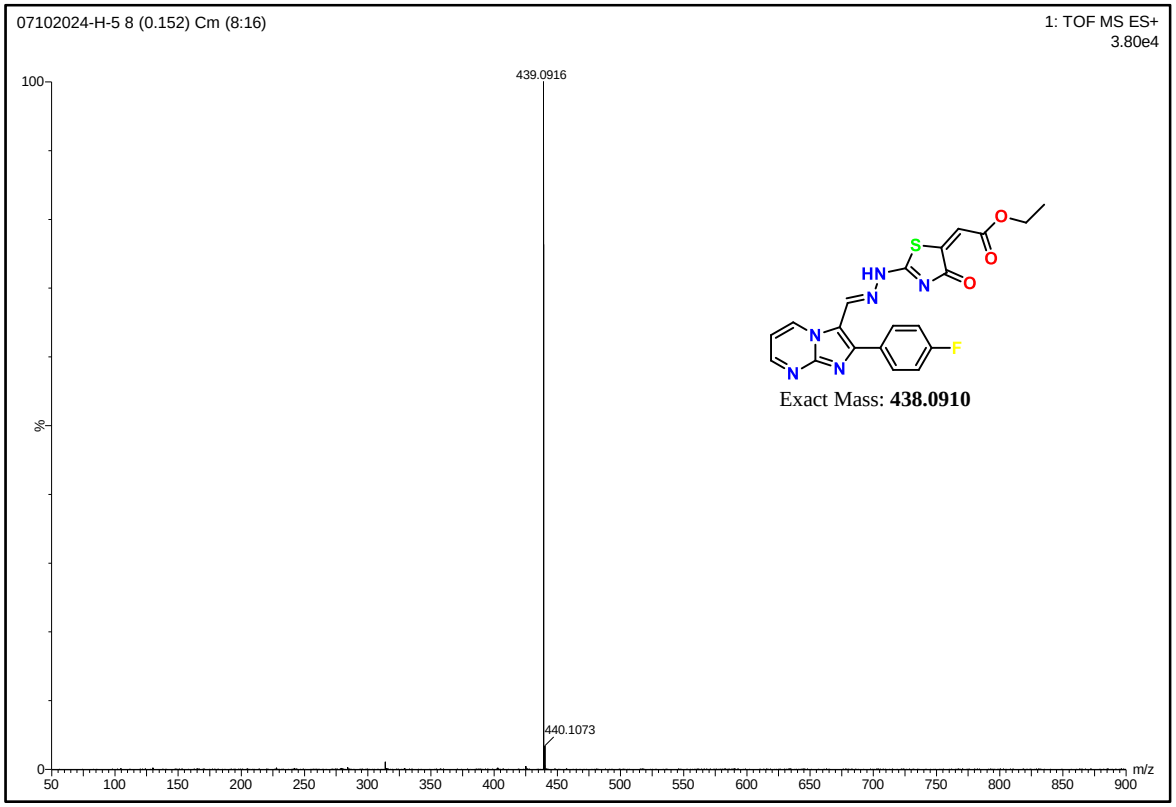


Figure S131: HR-MS spectrum of compound **K24**

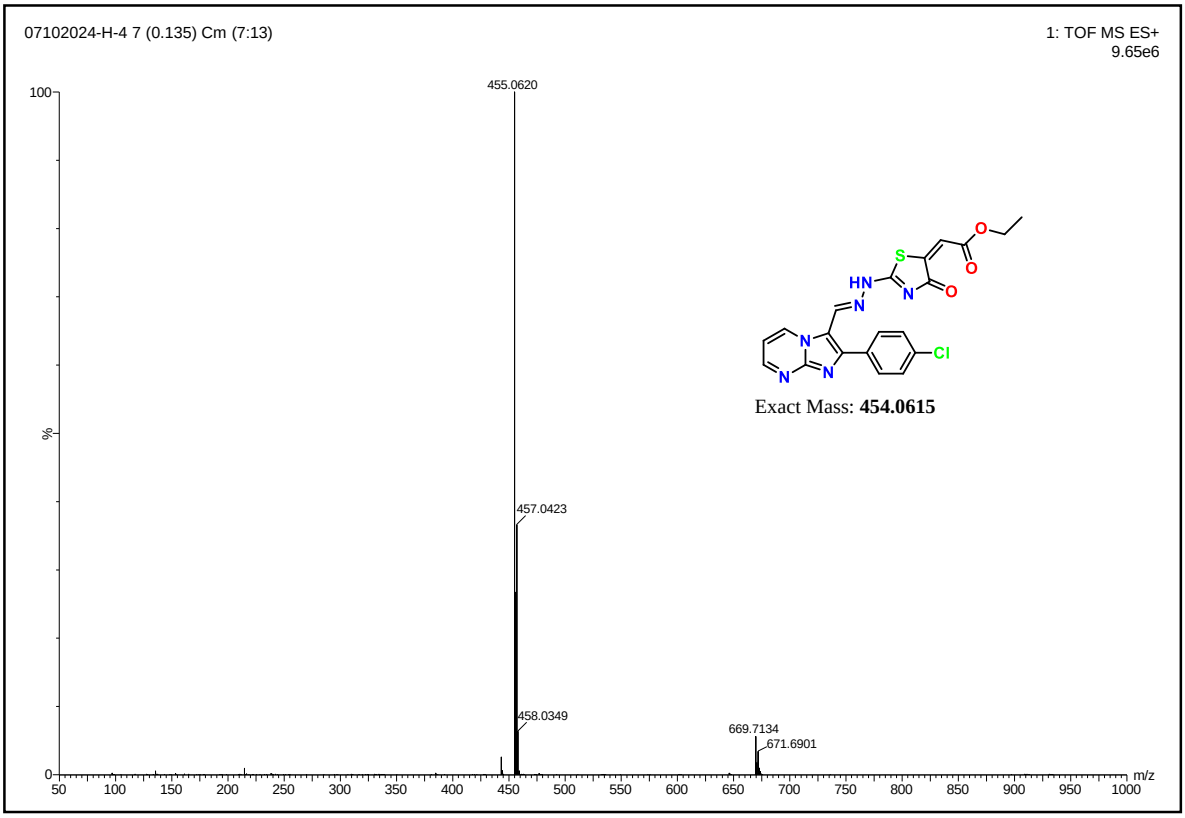


Figure S132: HR-MS spectrum of compound **K25**

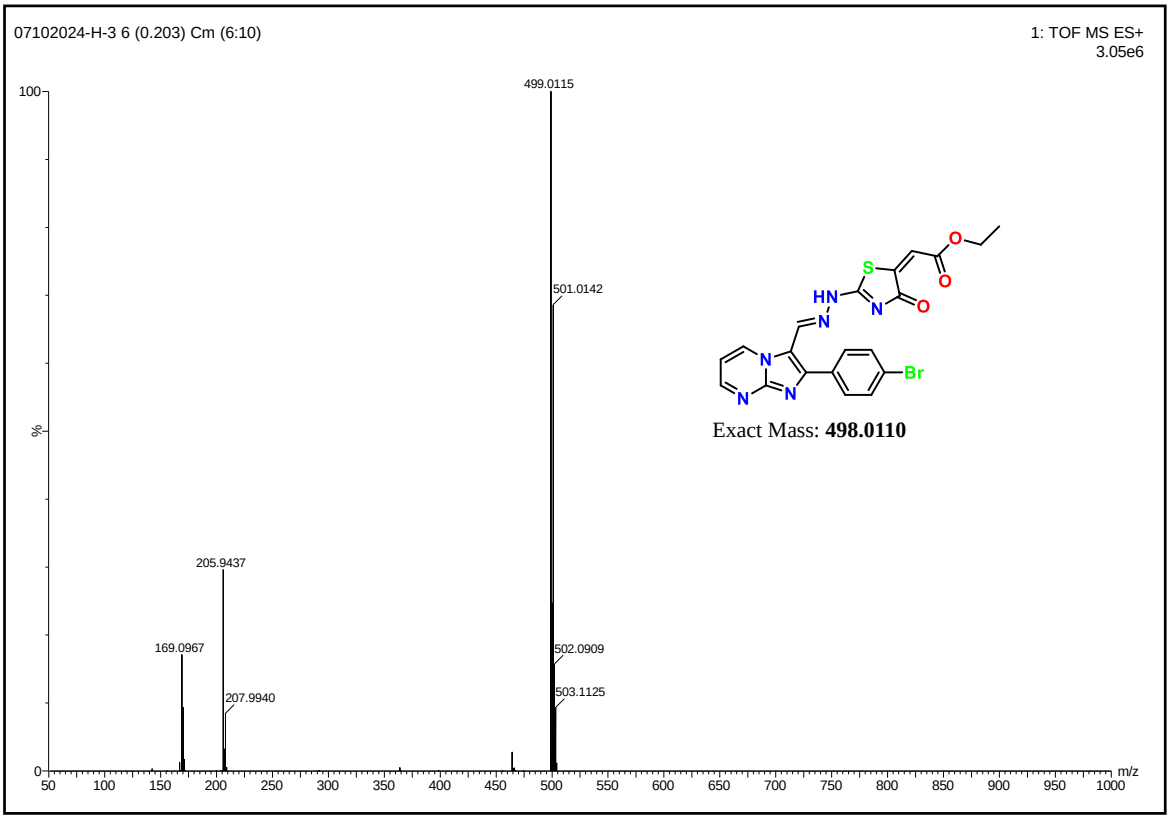
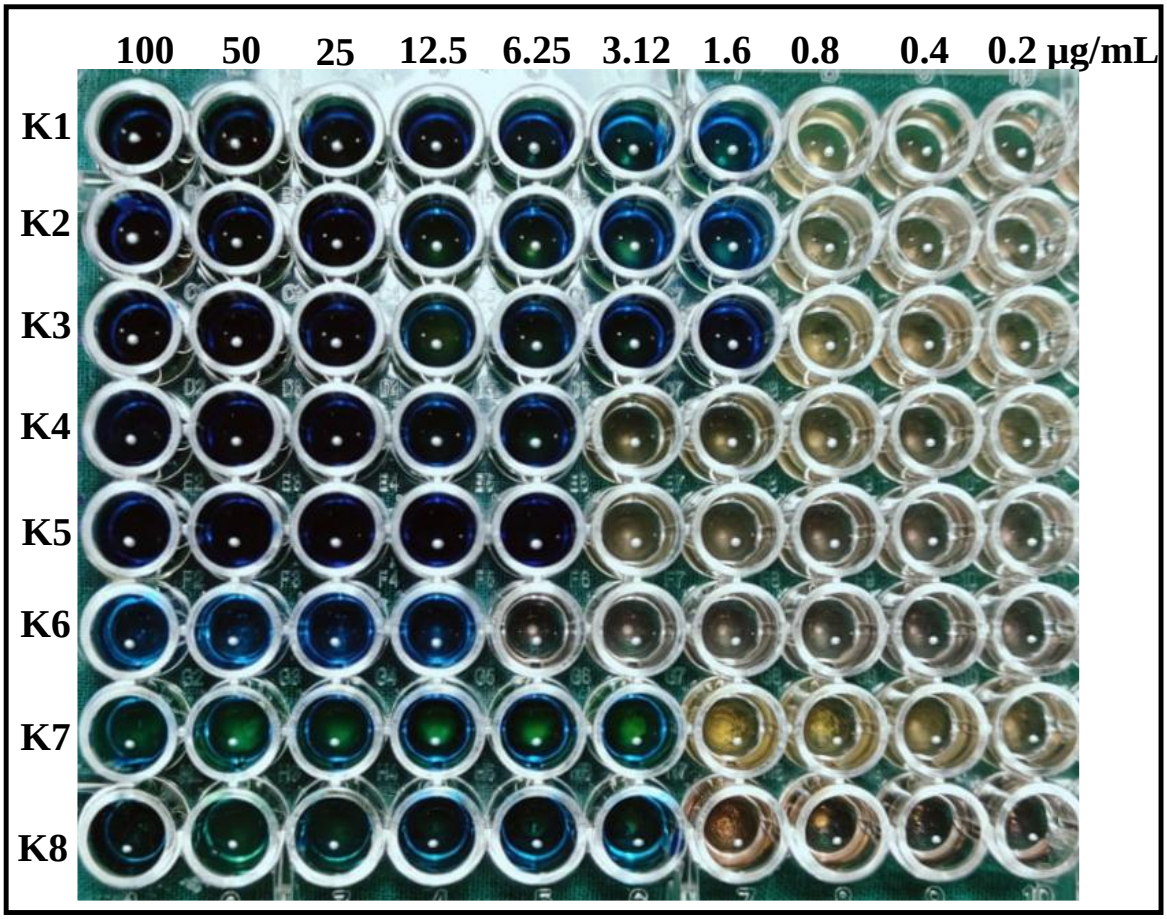
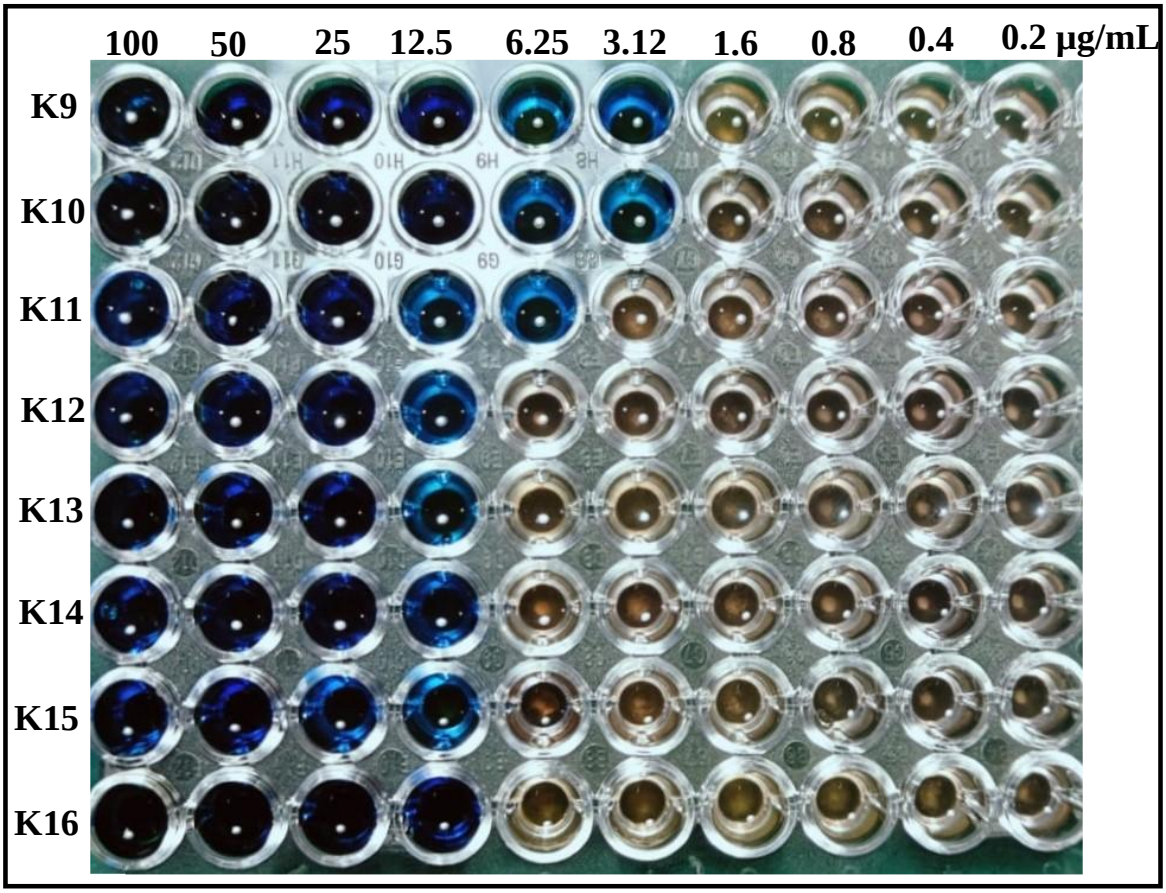
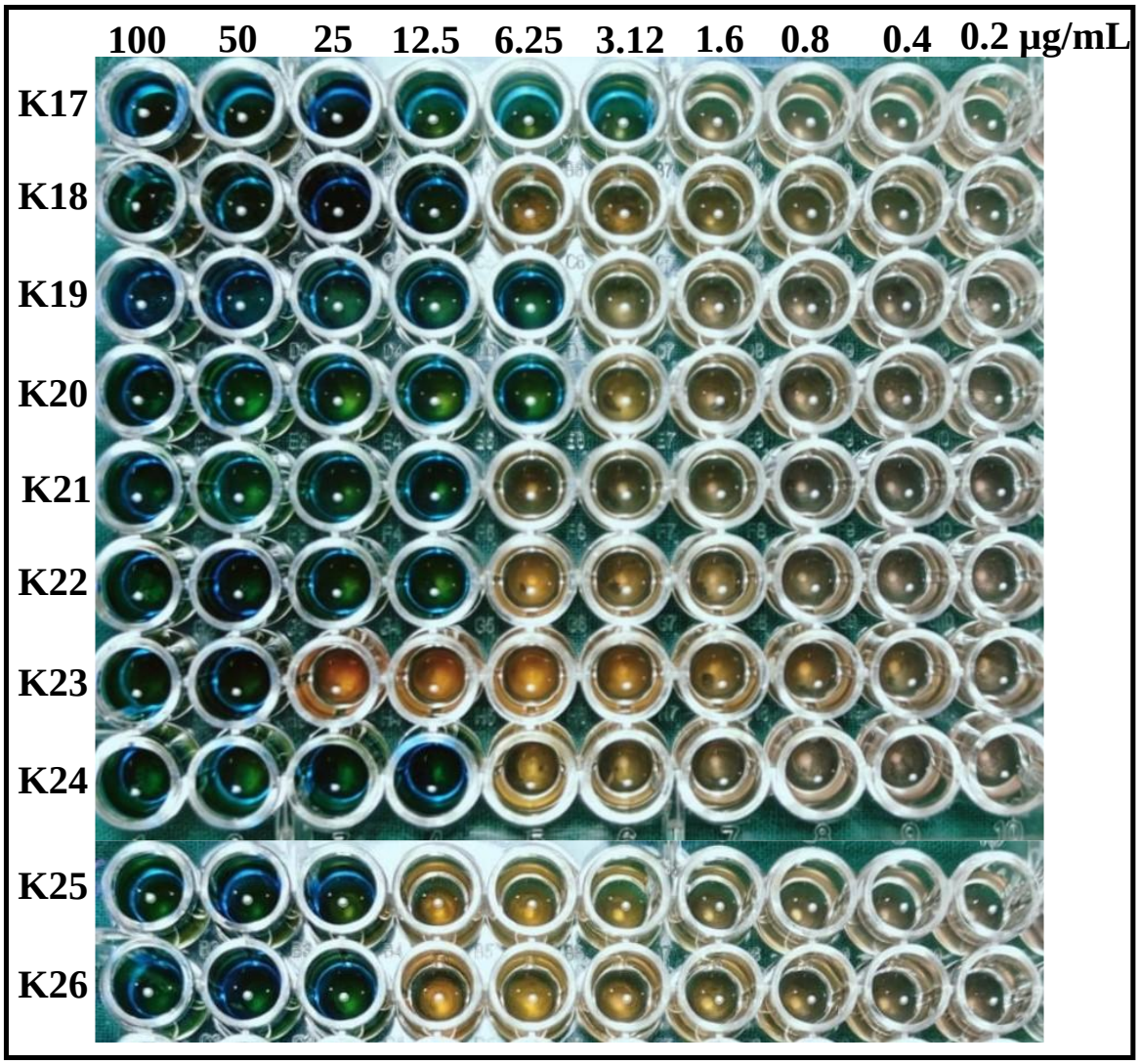


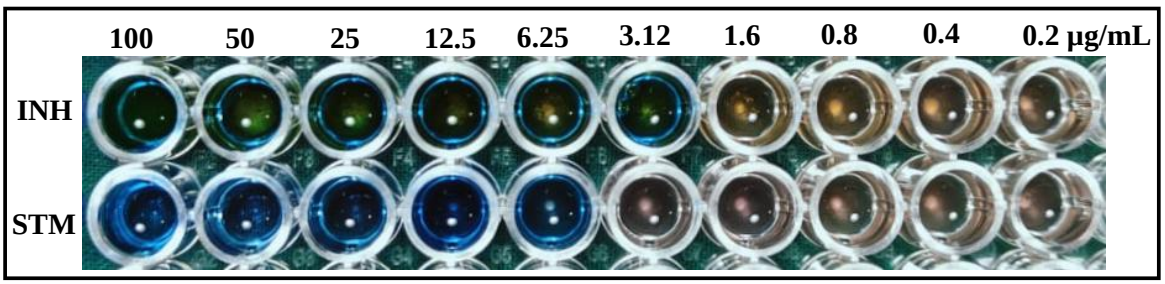
Figure S133: HR-MS spectrum of compound **K26**

In vitro antitubercular activity studies of the compounds **K1-K27**

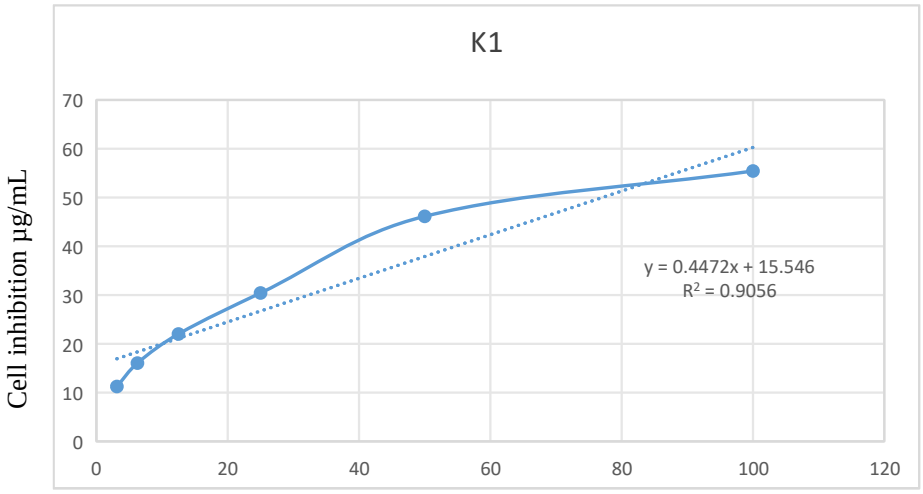



100
50
25
12.5
6.25
3.12
1.6
0.8
0.4
0.2 µg/mL
K9
K10
K11
K12
K13
K14
K15
K16

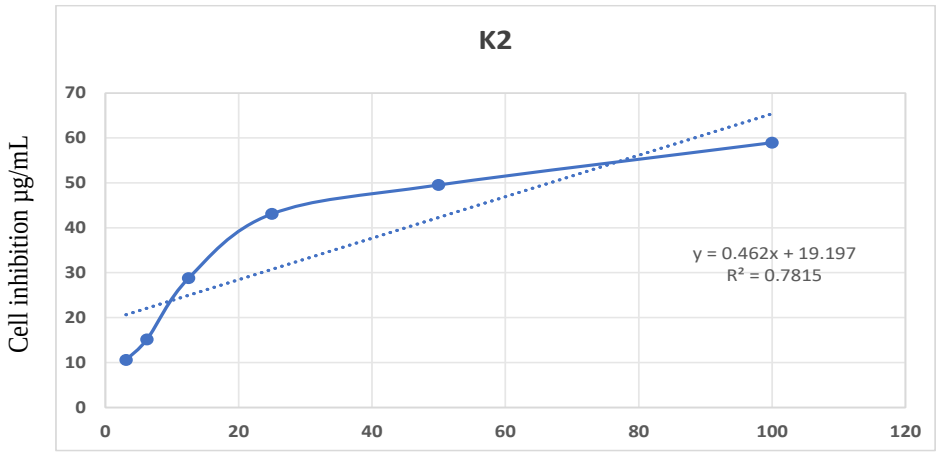

100 50 25 12.5 6.25 3.12 1.6 0.8 0.4 0.2 µg/mL
K17
K18
K19
K20
K21
K22
K23
K24
K25
K26


100 50 25 12.5 6.25 3.12 1.6 0.8 0.4 0.2 µg/mL
INH
STM

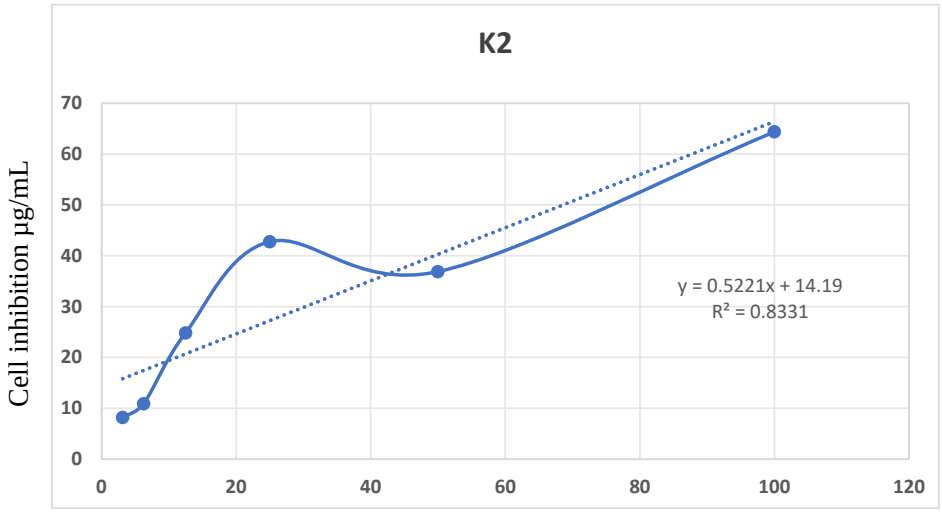
IC_{50} value curves for the active compounds (K1-K3).



Concentrations in µg/mL



Concentrations in µg/mL



Concentrations in µg/mL