Supporting Information

Synthesis of 3,4-dihydroisoquinolin-1(2*H*)-one derivatives and their antioomycete activity against the phytopathogen *Pythium recalcitrans*

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Contents:

Table S1. X-ray diffraction data for compound **I6** (CCDC Deposition No. 2180985)

	Compound **I6**
Chemical formula	$C_{21}H_{17}NO_4$
Chemical formula weight	347.36
Temperature (K)	120.01(10)
Wavelength	1.54184 Å
Crystal system	monoclinic
Space group	*P*1 2_1/*n* 1
Unit cell dimension	*a*=8.61550(10) Å, *b*=13.21640(10) Å, *c*=15.09880(10) Å *α*=90°, *β*=99.6980(10)°, *γ*=90°
Volume (Å^3)	1694.67(3)
Z	4
Calculated density (g/cm^3)	1.361
Radiation type	Cu *K*α
Absorpt coefficient (mm^{-1})	0.776
Crystal description	colourless block
Crystal size (mm)	0.3 × 0.2 × 0.1
Diffractometer	XtaLAB Synergy R, HyPix
Absorpt correction type	multi-scan
T_{max}	1.00000
T_{min}	0.87479
Theta range for data collection	4.474° to 67.684°
F(000)	728
Limiting indices	$-10 \le h \le 10$, $-15 \le k \le 16$, $-18 \le l \le 17$
Reflection number/cell measurement reflection used	16914/14765
R_{int}, R_{sigma}	0.0151, 0.0087
Refinement method	Full-matrix
No. of refinement reflections	3424
No. of reflections ($I > 2\sigma(I)$)	3340
No. of parameters	236
No. of restraints	0
H-atom treatment	H-atom parameters constrained
Goodness-of-fit on F^2	1.041
R indices (all data)	$R_1 = 0.0388$, $wR_2 = 0.1000$
Final *R* indices ($I > 2\sigma(I)$)	$R_1 = 0.0380$, $wR_2 = 0.0995$
Extinction method	none
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	0.304, -0.252

Table S2. The relative configuration ratios of the synthesized target compounds in the present study

Compd.	*trans*/*cis* ratio	Compd.	*trans*/*cis* ratio
I1	1:0 (*trans* only)	**I31**	0:1
I2	1:0	**I32**	0:1
I3	1:0	**I33**	0:1
I4	0:1 (*cis* only)	**I34**	0:1
I5	1:0	**II1**	0:1
I6	1:0	**II2**	0:1
I7	1:0	**II3**	0:1
I8	1:0	**II4**	1:6.3
I9	5.6:1	**II5**	0:1
I10	1:0	**II6**	1:9
I11	1:0	**II7**	0:1
I12	1:0	**II8**	0:1
I13	1:0	**II9**	1:3.1
I14	1:0	**II10**	1:6.3
I15	0:1	**II11**	0:1
I16	0:1	**II12**	1:0
I17	0:1	**II13**	1:7.1
I18	0:1	**II14**	0:1
I19	0:1	**II15**	0:1
I20	0:1	**II16**	0:1
I21	0:1	**II17**	1:5.3
I22	1:0	**II18**	0:1
I23	0:1	**II19**	1:4.8
I24	0:1	**II20**	1:3.2
I25	1:6.6	**III1**	1:0
I26	0:1	**III2**	1:0
I27	0:1	**III3**	1:0
I28	0:1	**III4**	1:0
I29	0:1	**III5**	1:0
I30	0:1		

Table S3. Experimental and predicted activities of compounds **I1–I34**, **II1–II20** and **III1–III5** for the 3D-QSAR models

Compd.	EC_{50} ($\times 10^{-3}$ mM)	Actual pEC_{50}	CoMFA		CoMSIA	
			Predicated	Residual	Predicated	Residual
I1*	46.6	1.332	1.311	–0.021	1.340	0.008
I2	45.8	1.339	1.359	0.020	1.335	–0.004
I3*	29.5	1.530	1.405	–0.125	1.412	–0.118
I4	45.4	1.343	1.362	0.019	1.357	0.014
I5	53.7	1.270	1.365	0.095	1.319	0.049
I6	46.8	1.330	1.178	–0.152	1.238	–0.092
I7	43.6	1.360	1.359	–0.001	1.354	–0.006
I8*	59.8	1.223	1.130	–0.093	1.190	–0.033
I9	57.4	1.241	1.406	0.165	1.380	0.139
I10	54.0	1.268	1.310	0.042	1.313	0.045
I11	46.5	1.333	1.315	–0.018	1.320	–0.013
I12	67.8	1.169	1.351	0.182	1.323	0.154
I13	65.1	1.187	1.292	0.105	1.308	0.121
I14*	40.6	1.392	1.347	–0.045	1.334	–0.058
I15*	42.8	1.369	1.585	0.216	1.531	0.162
I16	20.9	1.681	1.518	–0.163	1.456	–0.225
I17*	23.2	1.635	1.643	0.008	1.578	–0.057
I18	25.1	1.601	1.710	0.109	1.599	–0.002
I19	21.5	1.668	1.653	–0.015	1.581	–0.087
I20	23.2	1.635	1.533	–0.102	1.578	–0.057
I21	14.7	1.833	1.593	–0.240	1.620	–0.213
I22	20.8	1.682	1.544	–0.138	1.634	–0.048
I23	14.0	1.855	1.537	–0.318	1.54	–0.315
I24	38.9	1.411	1.506	0.095	1.498	0.087
I25	33.2	1.479	1.566	0.087	1.543	0.064
I26	29.6	1.528	1.574	0.046	1.553	0.025
I27	26.0	1.585	1.592	0.007	1.569	–0.016
I28	29.4	1.532	1.646	0.114	1.588	0.056
I29	41.7	1.380	1.351	–0.029	1.368	–0.012
I30*	26.0	1.585	1.541	–0.044	1.463	–0.122
I31	36.3	1.440	1.465	0.025	1.418	–0.022
I32	26.9	1.570	1.648	0.078	1.547	–0.023
I33	43.1	1.365	1.399	0.034	1.513	0.148
I34	40.9	1.389	1.424	0.035	1.374	–0.015
II1*	18.2	1.739	1.636	–0.103	1.609	–0.13
II2	27.7	1.558	1.555	–0.003	1.558	0
II3	32.0	1.494	1.552	0.058	1.578	0.084
II4	38.5	1.415	1.562	0.147	1.588	0.173
II5*	45.3	1.344	1.472	0.128	1.515	0.171

II6	43.0	1.366	1.430	0.064	1.400	0.034
II7	31.5	1.502	1.472	–0.030	1.540	0.038
II8	47.1	1.327	1.424	0.097	1.477	0.150
II9	31.3	1.504	1.473	–0.031	1.523	0.019
II10	41.3	1.384	1.502	0.118	1.534	0.150
II11	16.9	1.773	1.615	–0.158	1.613	–0.160
II12*	35.8	1.446	1.529	0.083	1.567	0.121
II13	29.6	1.529	1.511	–0.018	1.500	–0.029
II14	47.8	1.321	1.366	0.045	1.434	0.113
II15*	31.3	1.505	1.397	–0.108	1.391	–0.114
II16*	48.7	1.313	1.287	–0.026	1.444	0.131
II17	30.3	1.519	1.573	0.054	1.548	0.029
II18	33.1	1.480	1.511	0.031	1.523	0.043
II19*	32.2	1.492	1.514	0.022	1.509	0.017
II20	34.0	1.469	1.506	0.037	1.523	0.054
III1	951.4	0.022	–0.185	–0.207	-0.094	–0.116
III2	1258.1	–0.097	0.066	0.163	0.007	0.104
III3	874.3	0.060	0.035	–0.025	-0.034	–0.094
III4*	895.7	0.051	0.186	0.135	0.141	0.090
III5	1055.2	–0.021	0.174	0.195	0.132	0.153

* The compounds were in the test set for external validation of the optimal 3D-QSAR models.

Table S4. *In vivo* control efficacy of compound **I23** against *Pythium recalcitrans* on *Nicotiana benthamiana* seedings in pot experiment

Compound	Dose (mg/pot)	Control efficacy (%)	
		Preventive effect	Curative effect
I23	1.0	37.8 ± 10.7c	3.3 ± 2.9c
	2.0	75.4 ± 12.6b	33.3 ± 12.6ab
	5.0	96.5 ± 3.1a	55.0 ± 10.0a
Hymexazol	2.0	63.9 ± 3.5b	21.7 ± 10.4b

The results were expressed as the mean ± SD of three independent replicates.

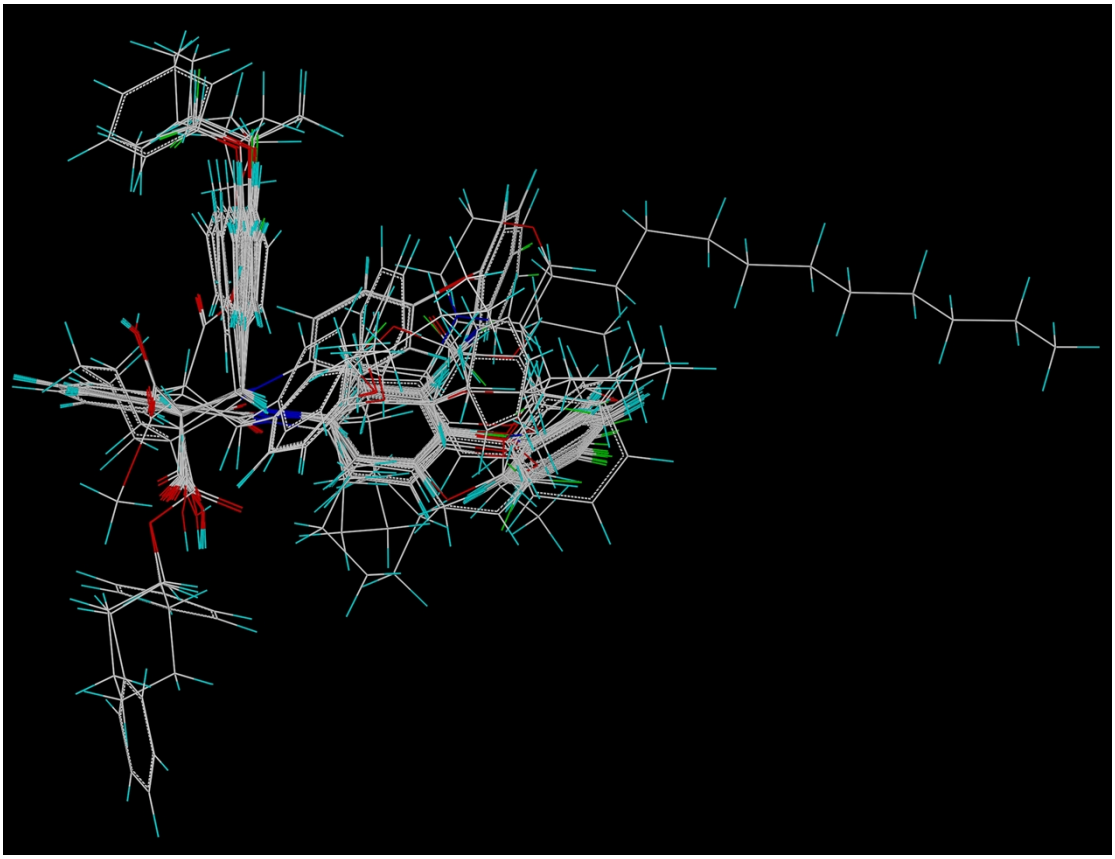

Figure S1. The results of molecular superposition based on the common backbone of the most potent compound **I23**.

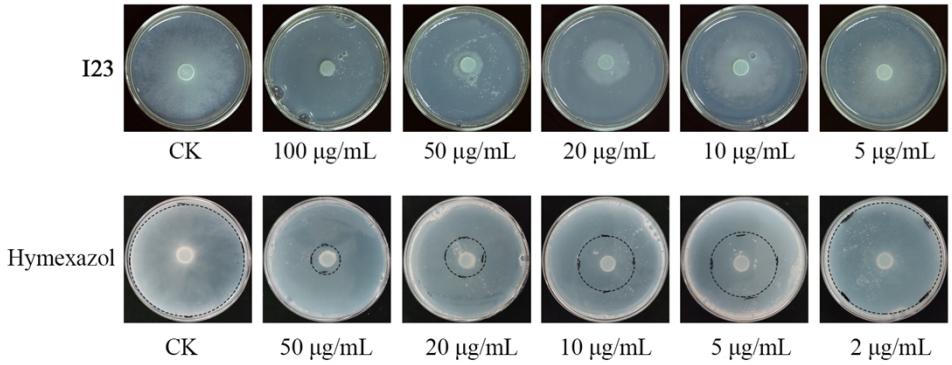

Figure S2. The representative photos of the inhibition effect of compounds **I23** and hymexazol on the mycelial growth of *Pythium recalcitrans* at different concentrations.

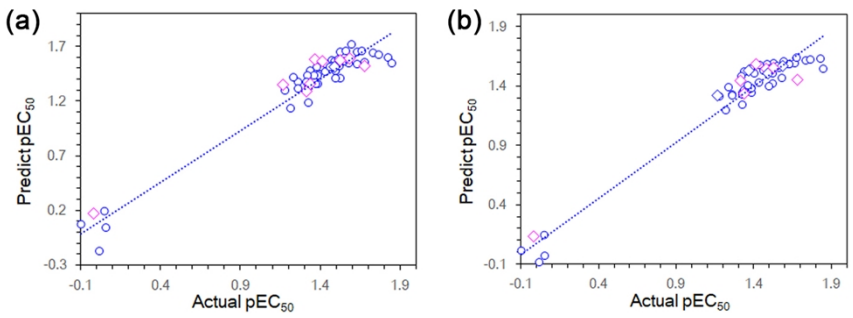

Figure S3. The correlation plots of the experimental versus predicted activities (pEC_{50} values) of training (○) and test (✸) set based on the CoMFA (**a**) and CoMSIA (**b**) models.

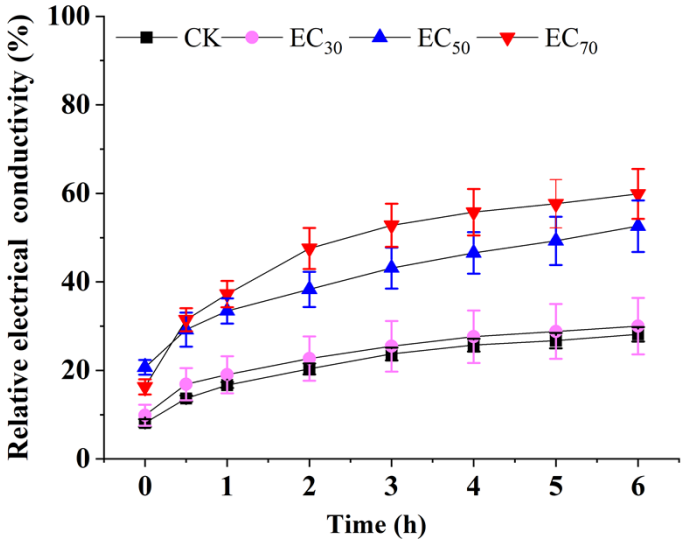

Figure S4. Effect of **I23** on cell membrane permeability of *P. recalcitrans*.

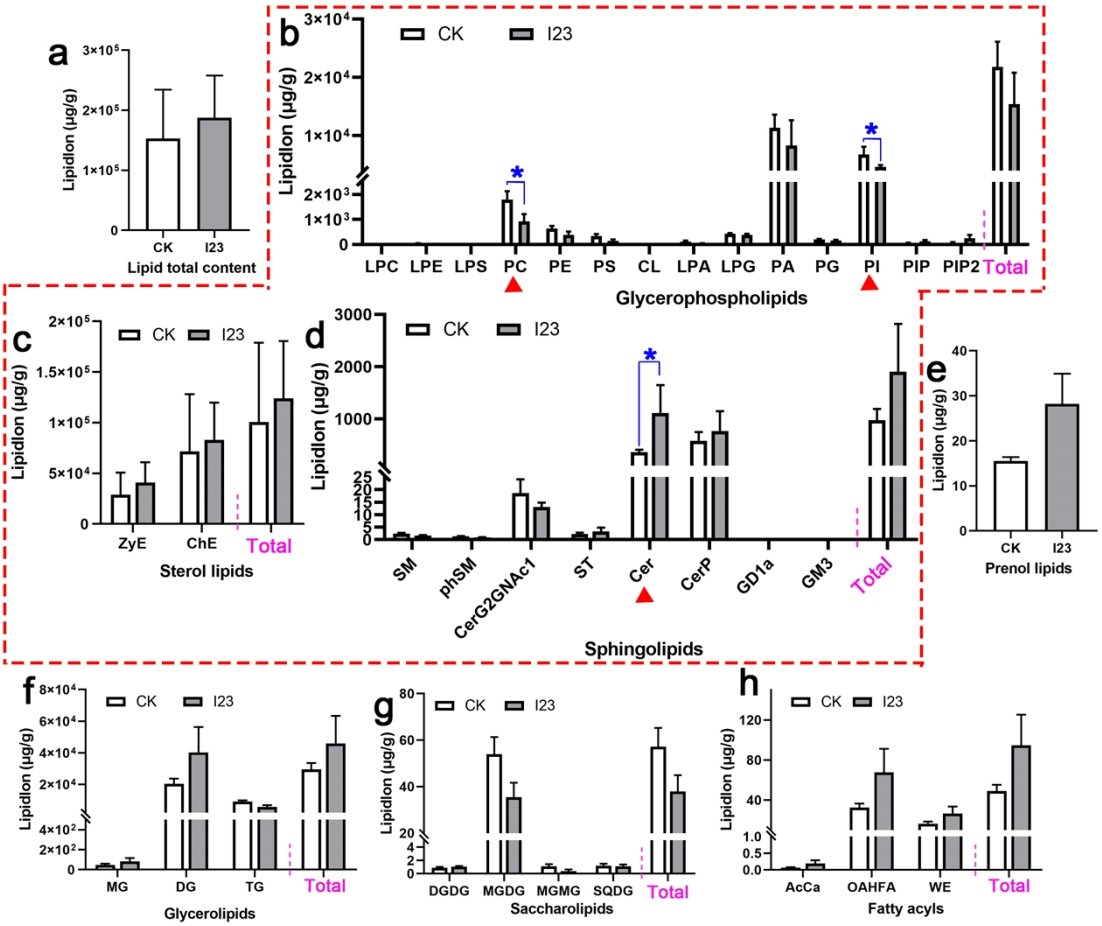

Figure S5. Comparison between the mean levels of the different lipid classes with the contents higher than 1%.

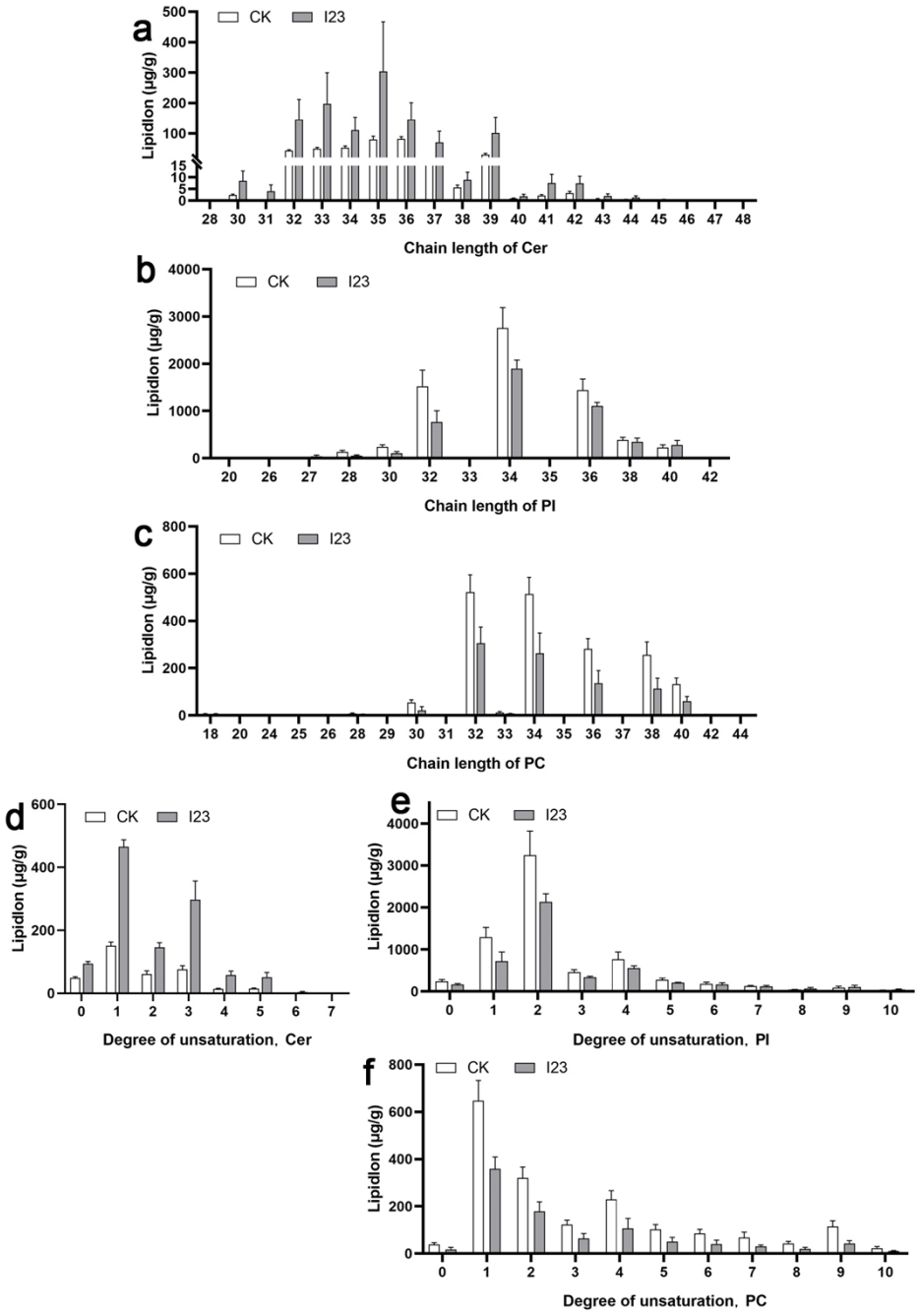

Figure S6. The distribution of the chain lengths and degrees of unsaturation of lipid classes Cer, PI and PC.

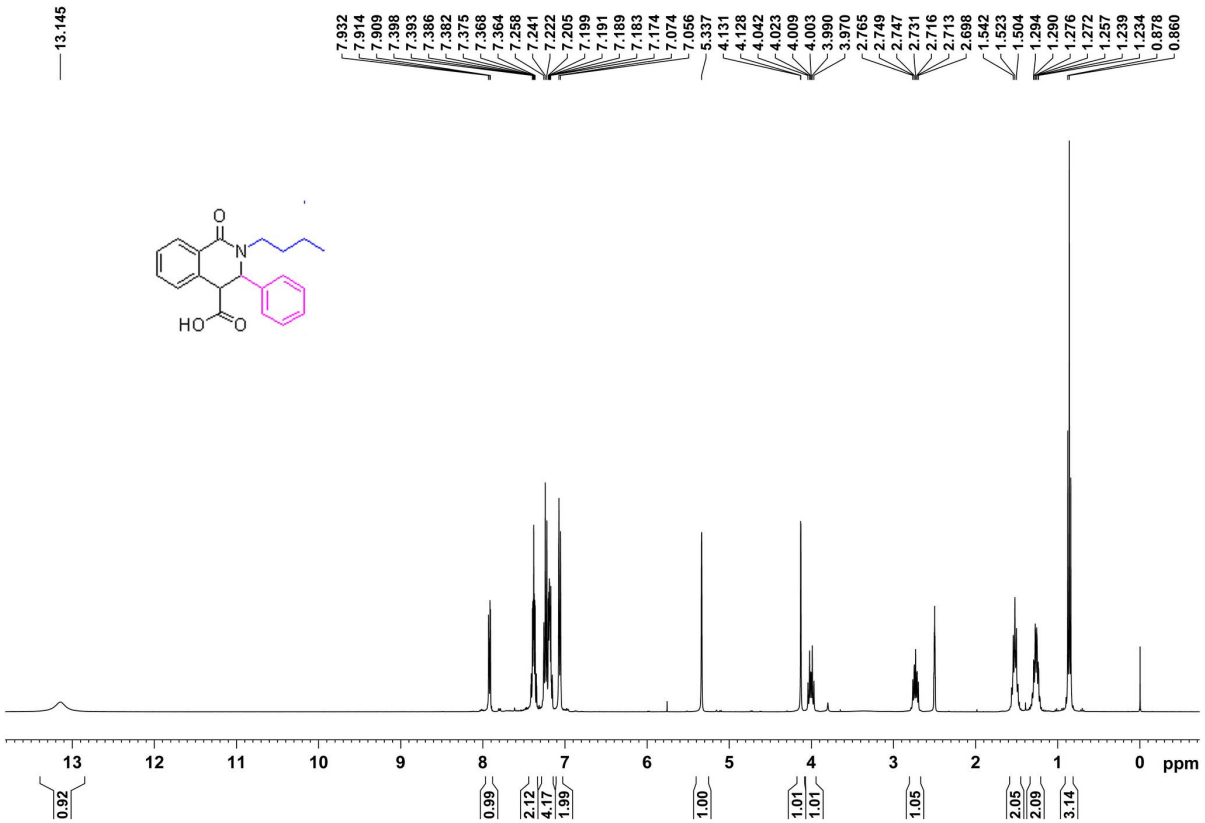

Figure S7. The ^{1}H NMR spectrum of compound **I1**

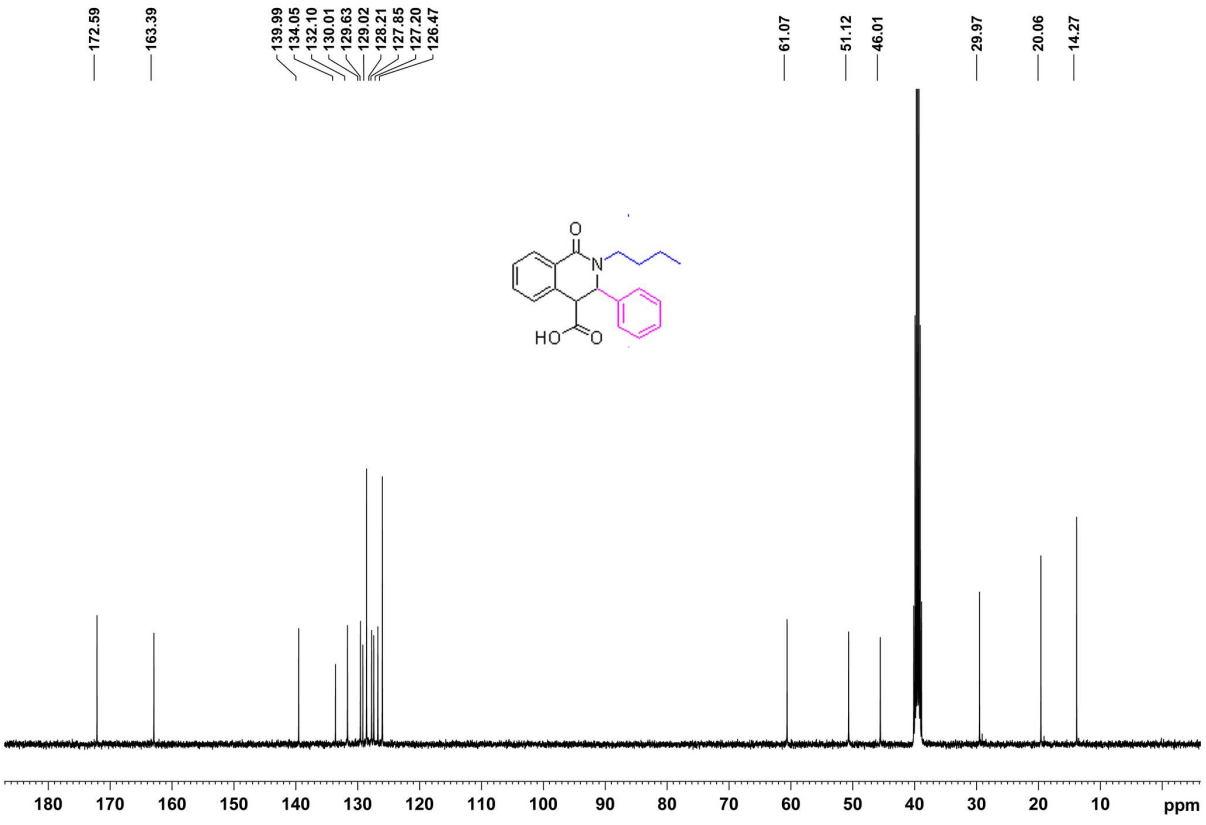

Figure S8. The ^{13}C NMR spectrum of compound **I1**

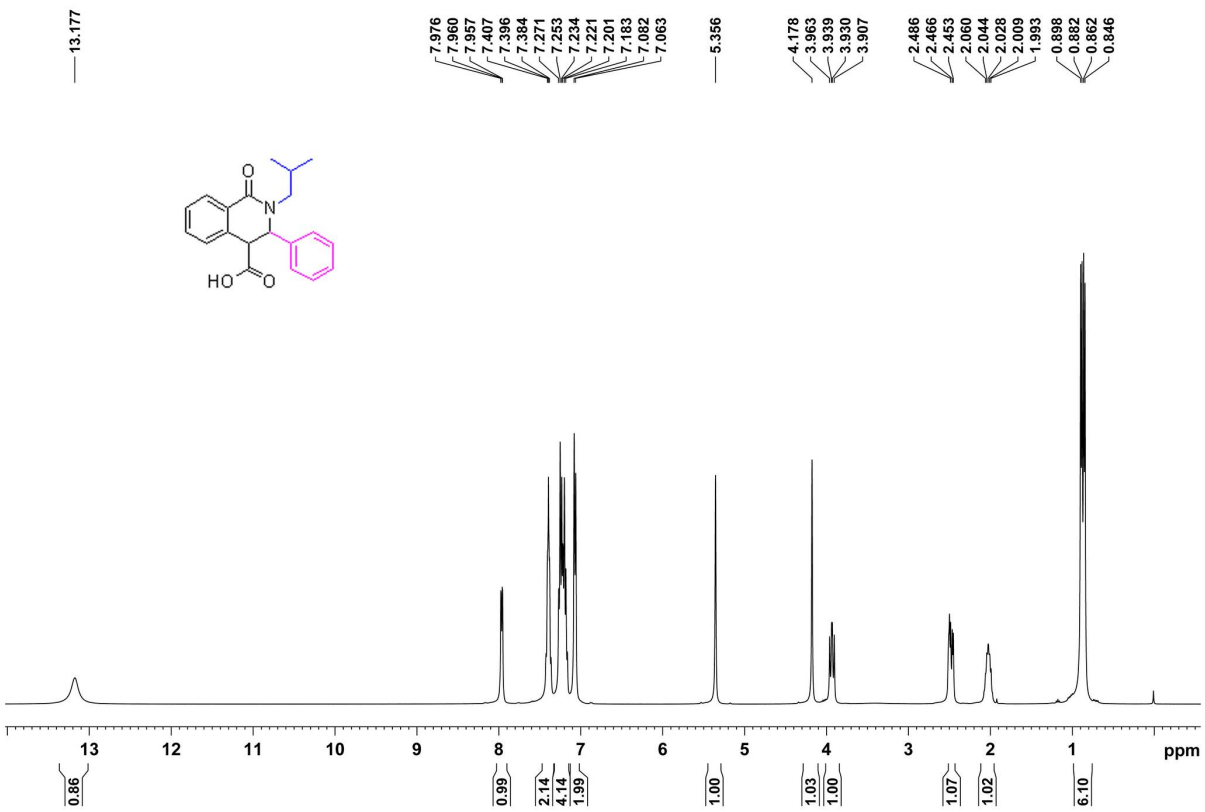

Figure S9. The ^{1}H NMR spectrum of compound **I2**

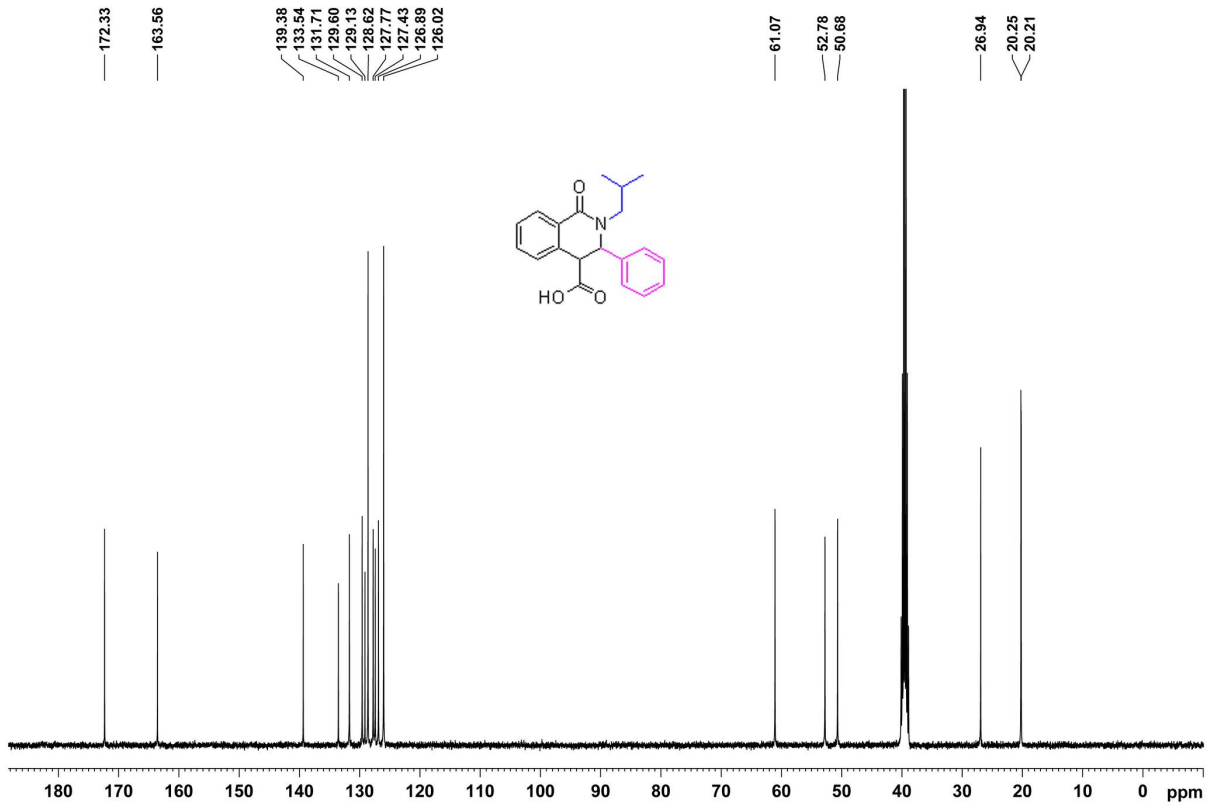

Figure S10. The ^{13}C NMR spectrum of compound **I2**

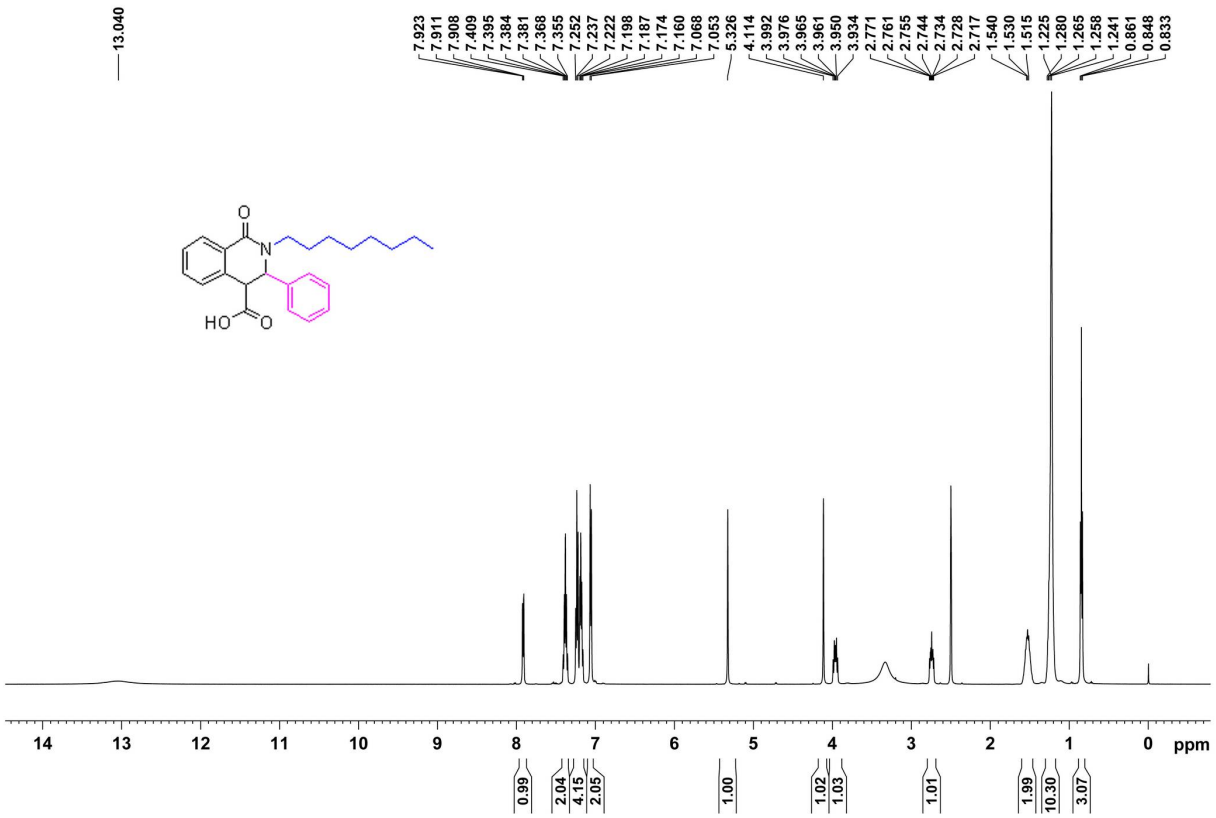

Figure S11. The ^{1}H NMR spectrum of compound **I3**

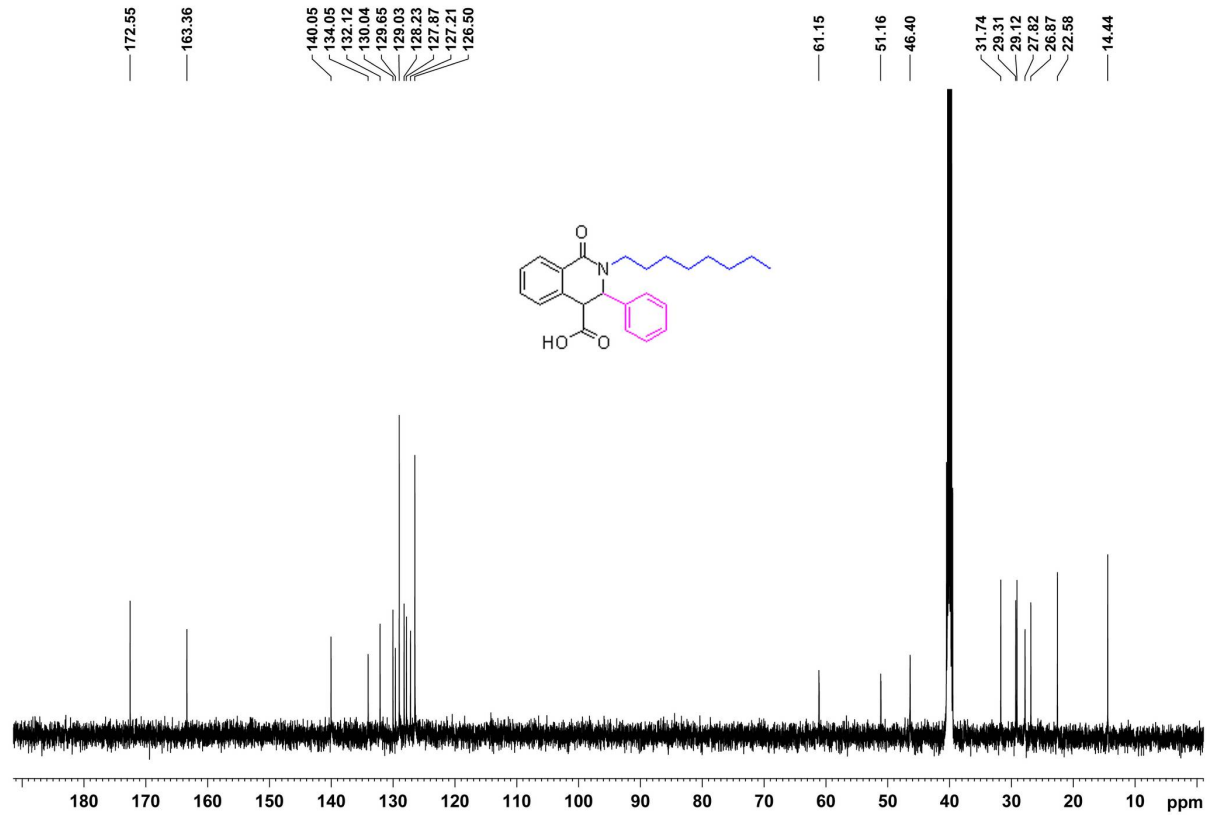

Figure S12. The ^{13}C NMR spectrum of compound **I3**

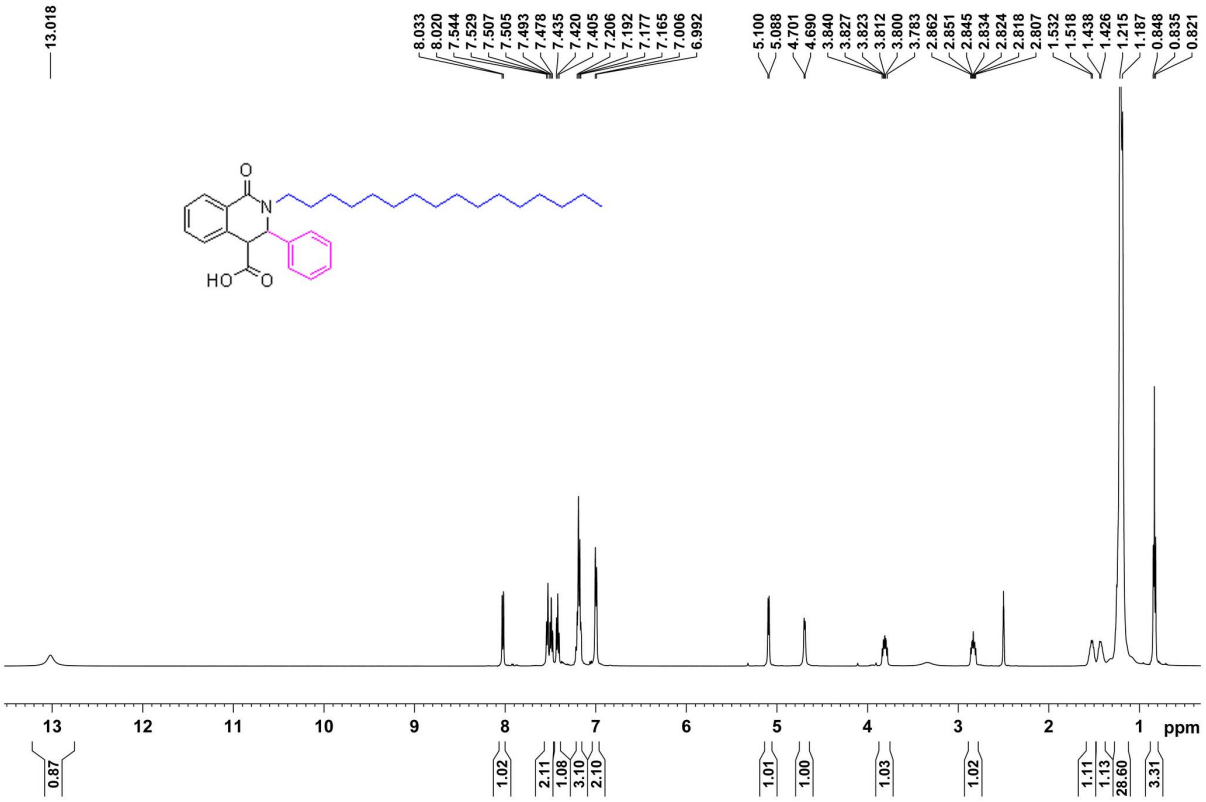

Figure S13. The ^{1}H NMR spectrum of compound **I4**

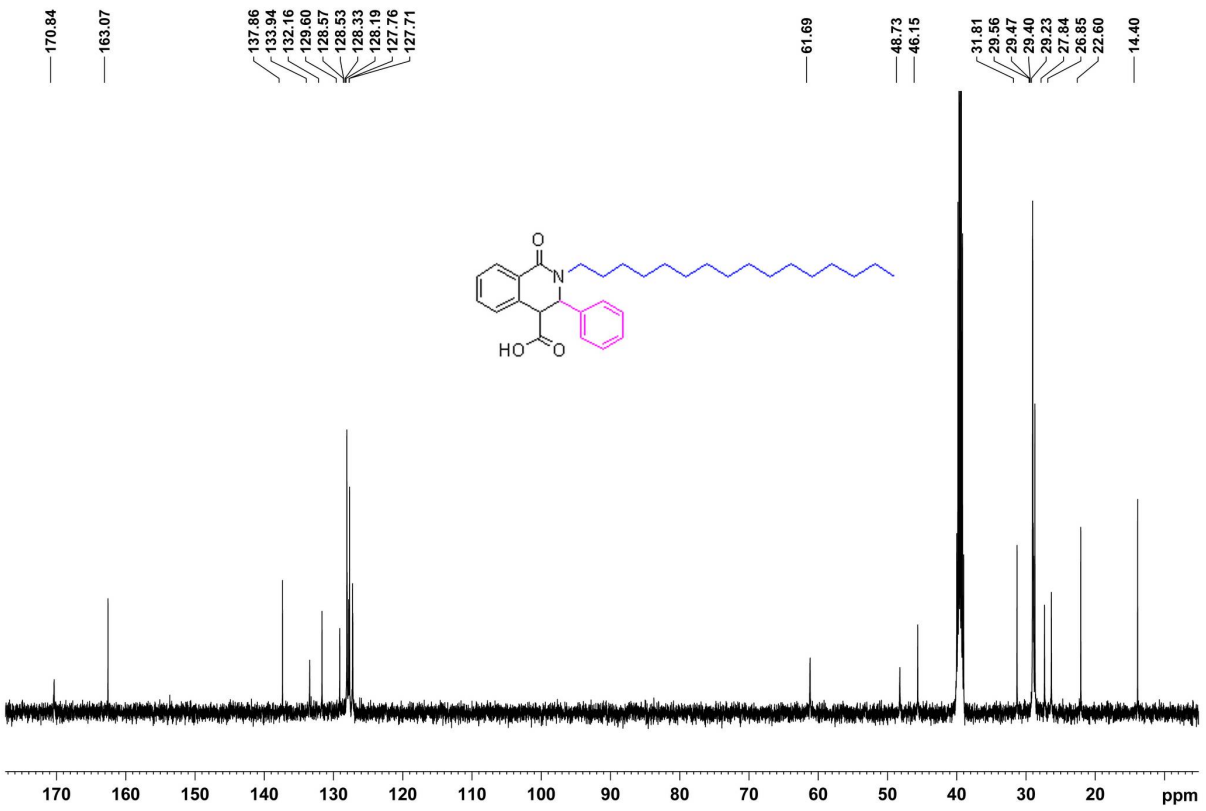

Figure S14. The ^{13}C NMR spectrum of compound **I4**

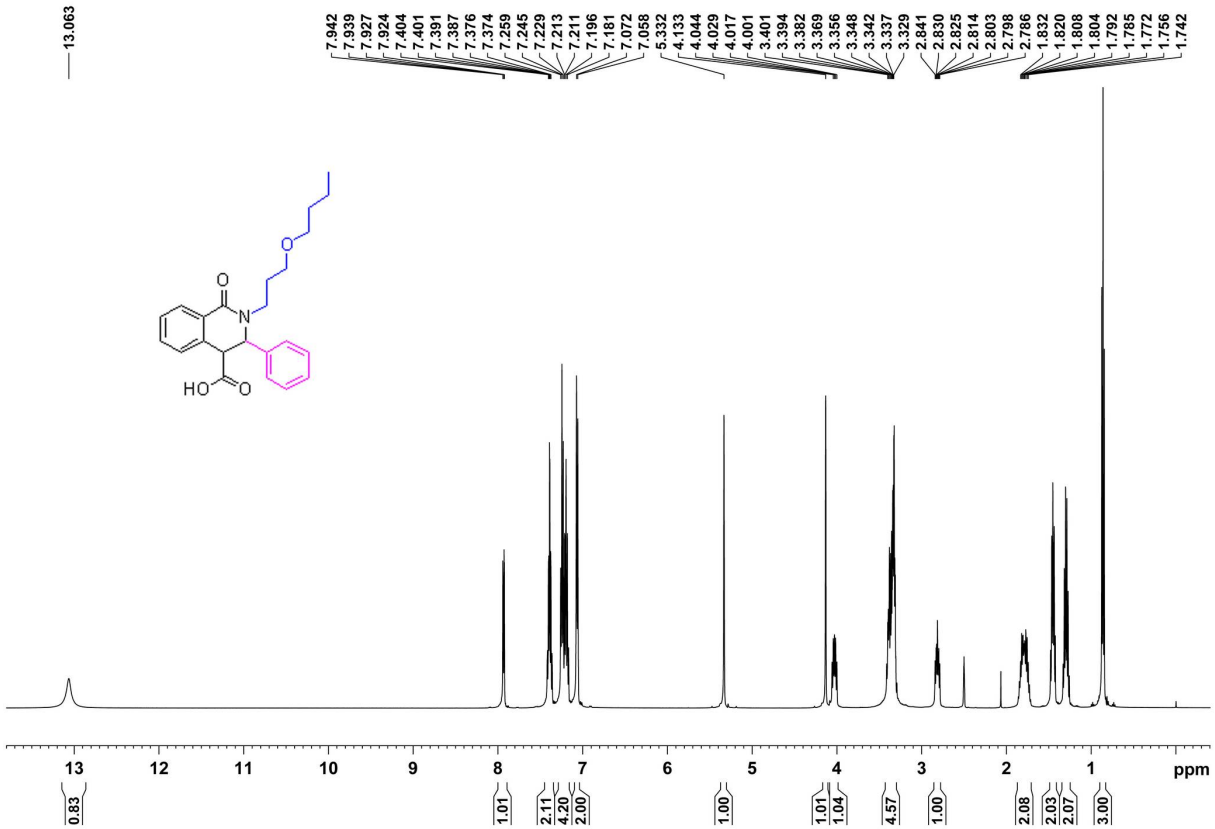

Figure S15. The ^{1}H NMR spectrum of compound **I5**

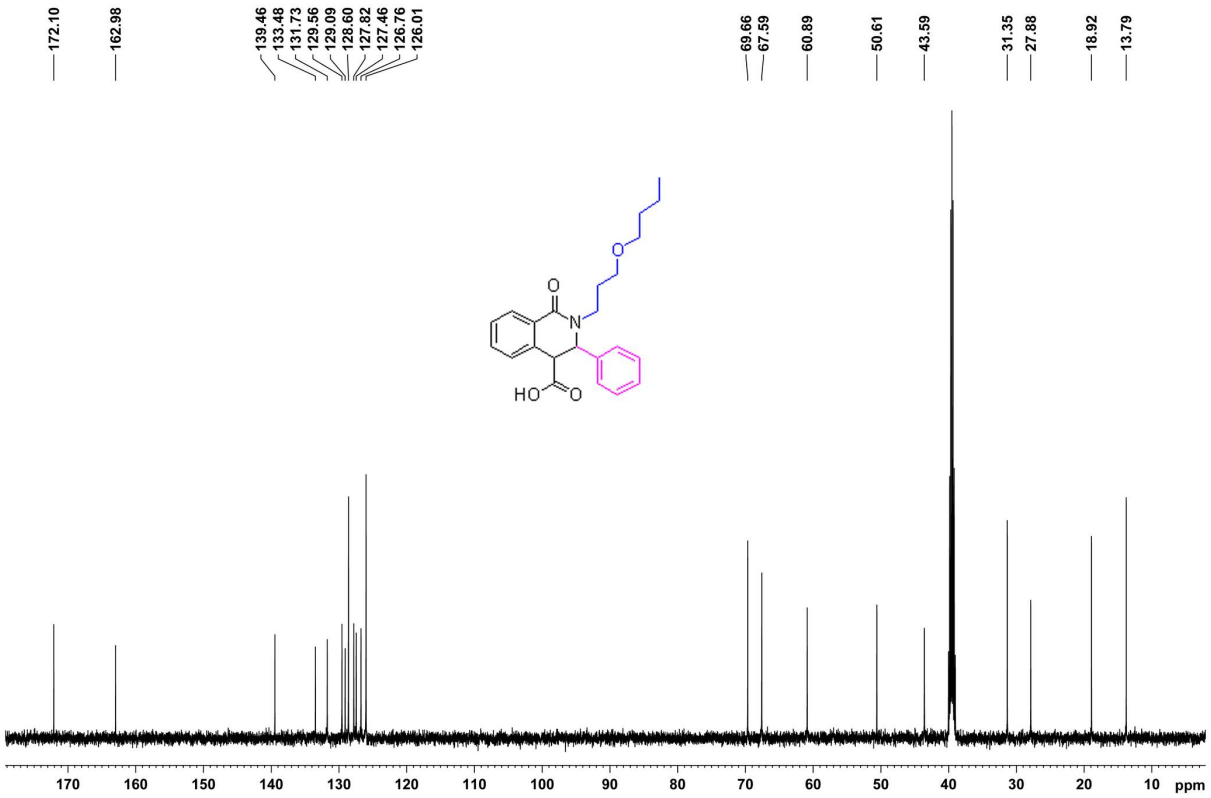

Figure S16. The ^{13}C NMR spectrum of compound **I5**

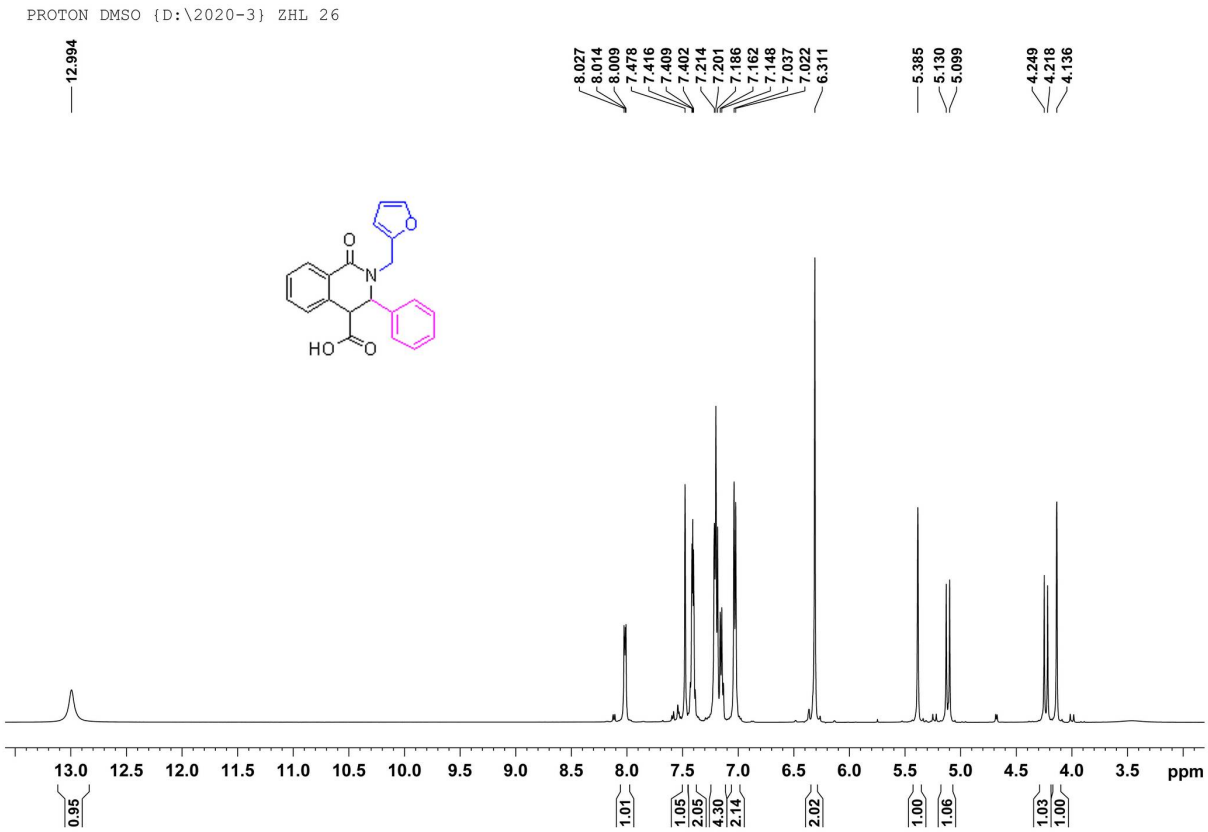

Figure S17. The ^{1}H NMR spectrum of compound **I6**

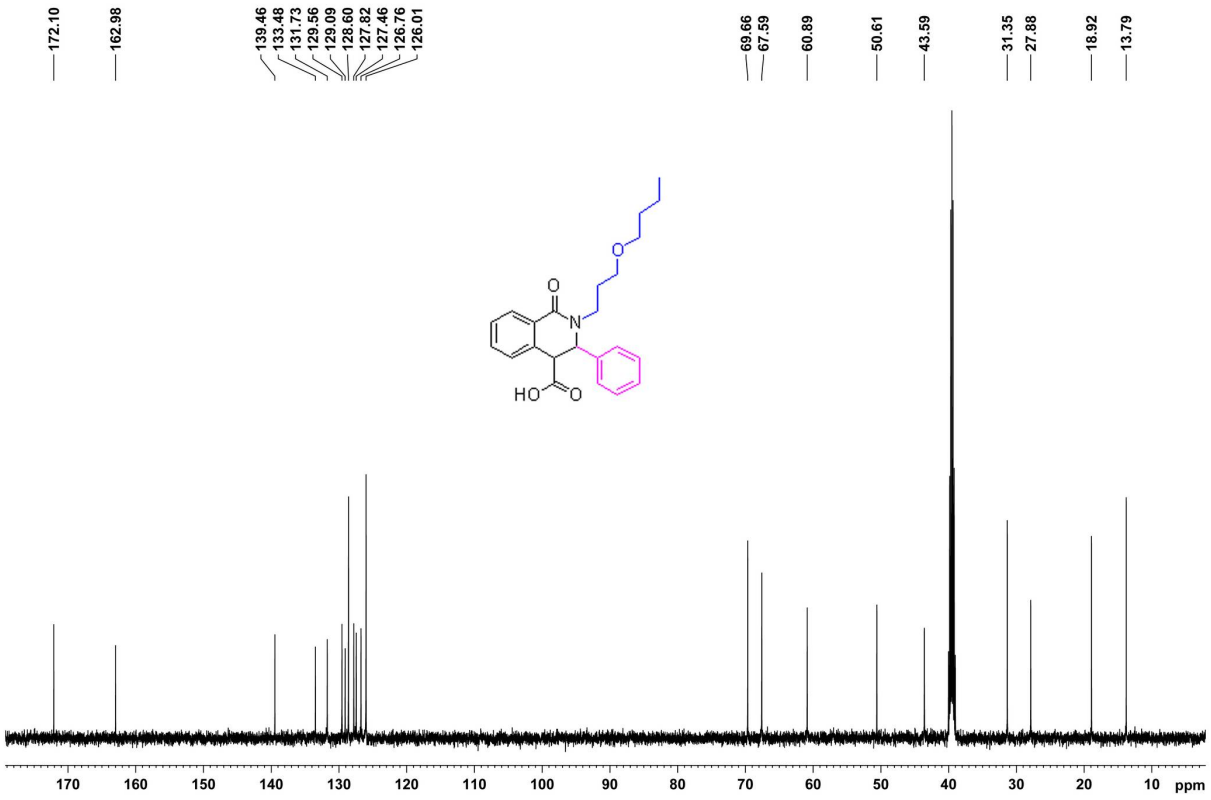

Figure S18. The ^{13}C NMR spectrum of compound **I6**

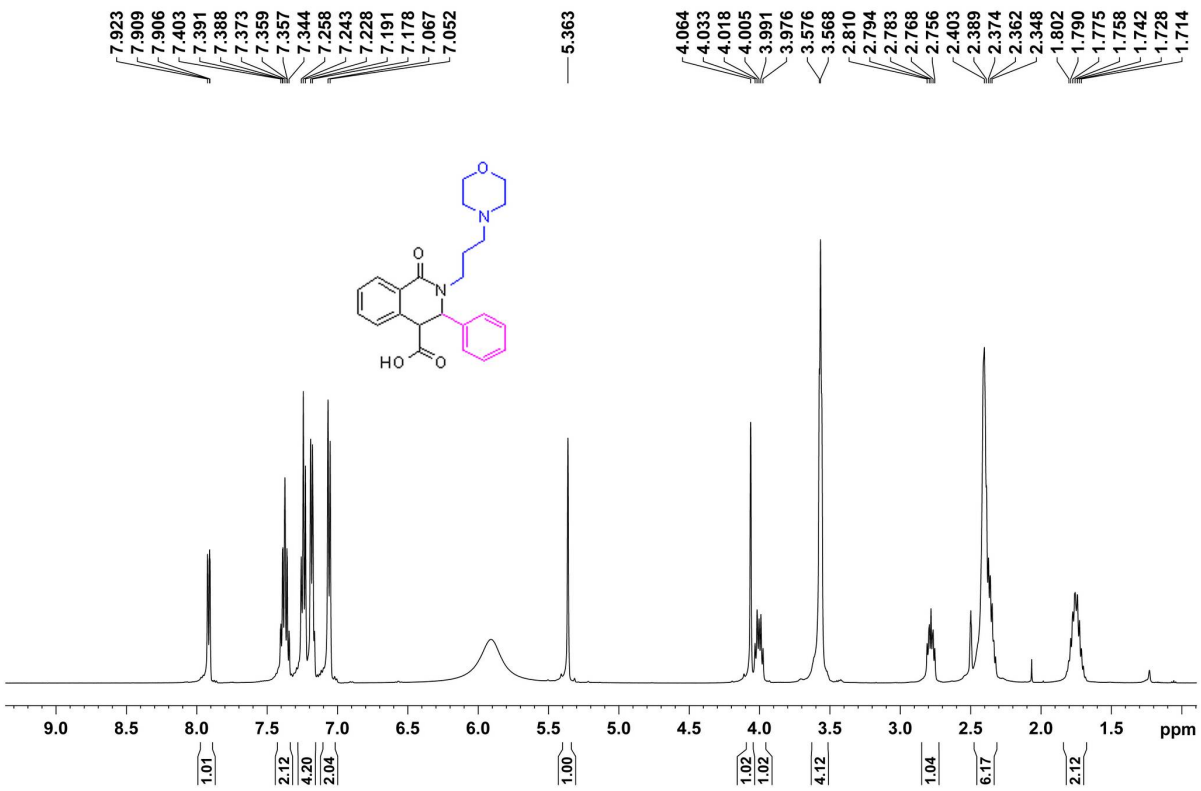

Figure S19. The ^{1}H NMR spectrum of compound **I7**

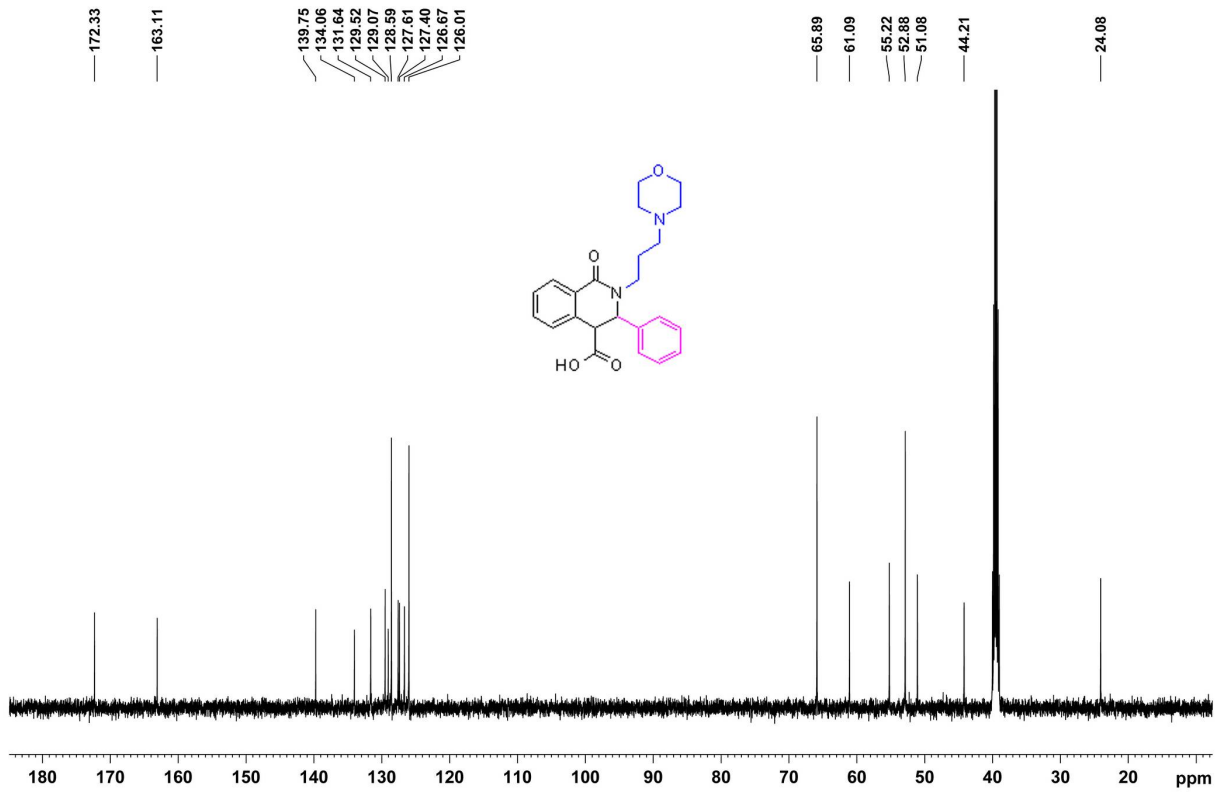

Figure S20. The ^{13}C NMR spectrum of compound **I7**

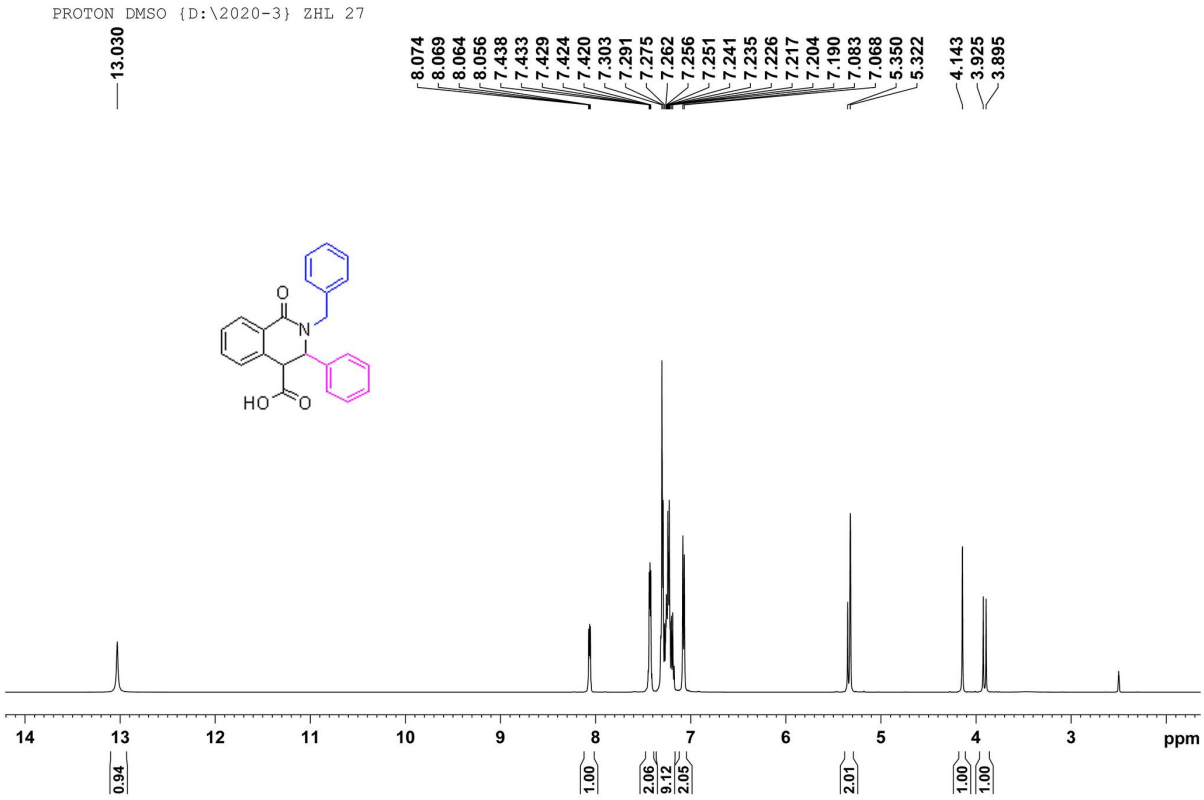

Figure S21. The ^{1}H NMR spectrum of compound **I8**

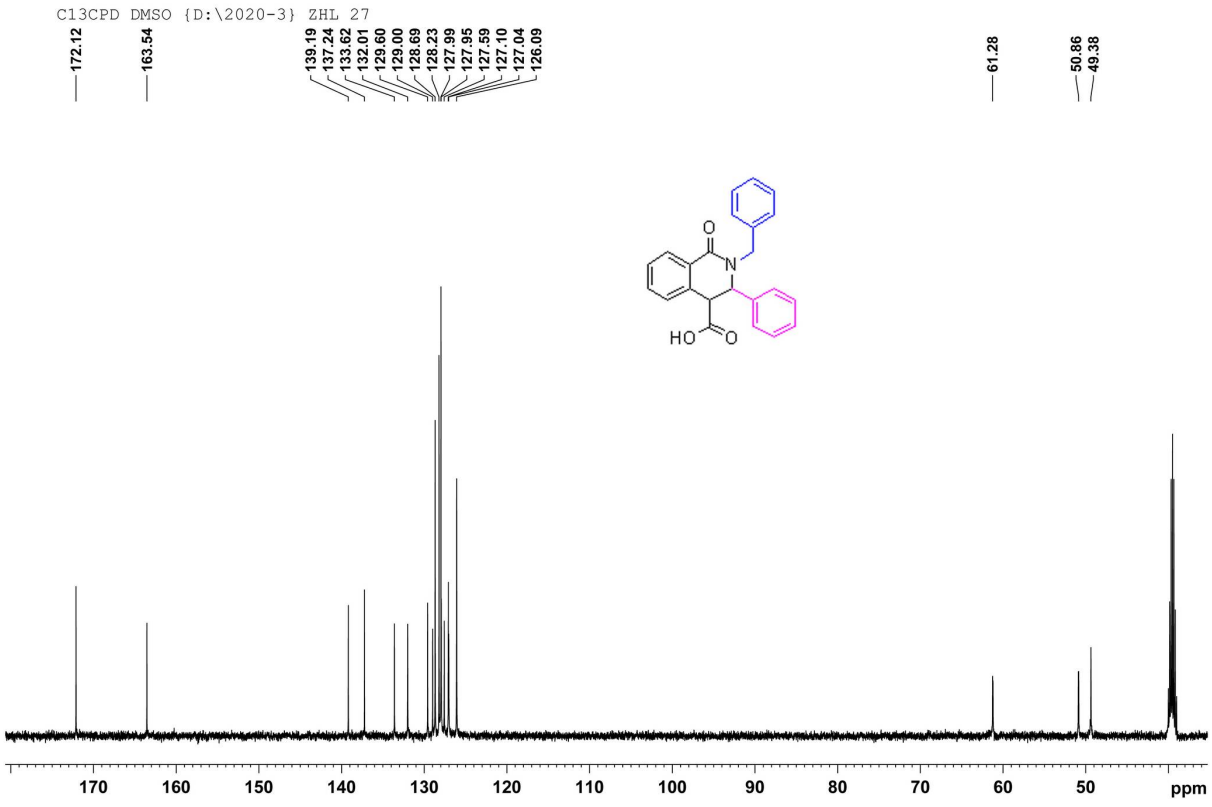

Figure S22. The ^{13}C NMR spectrum of compound **I8**

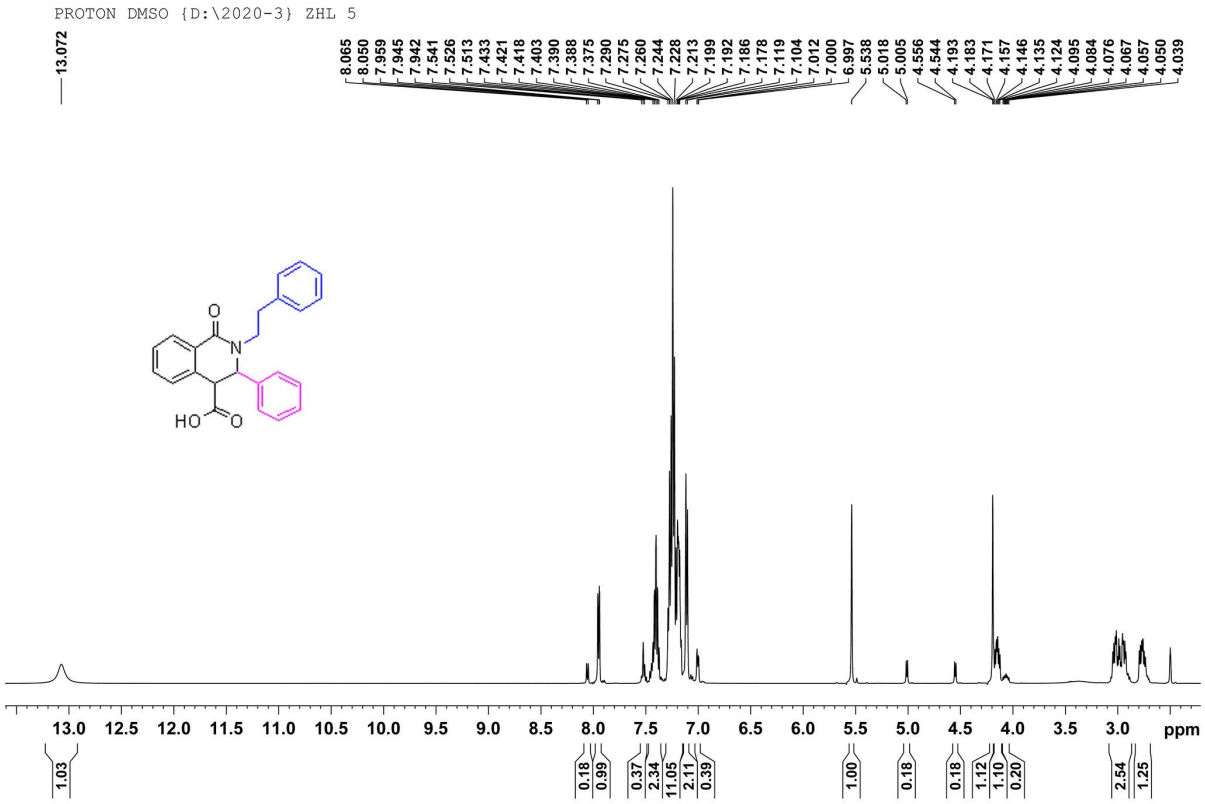

Figure S23. The ^{1}H NMR spectrum of compound **I9**

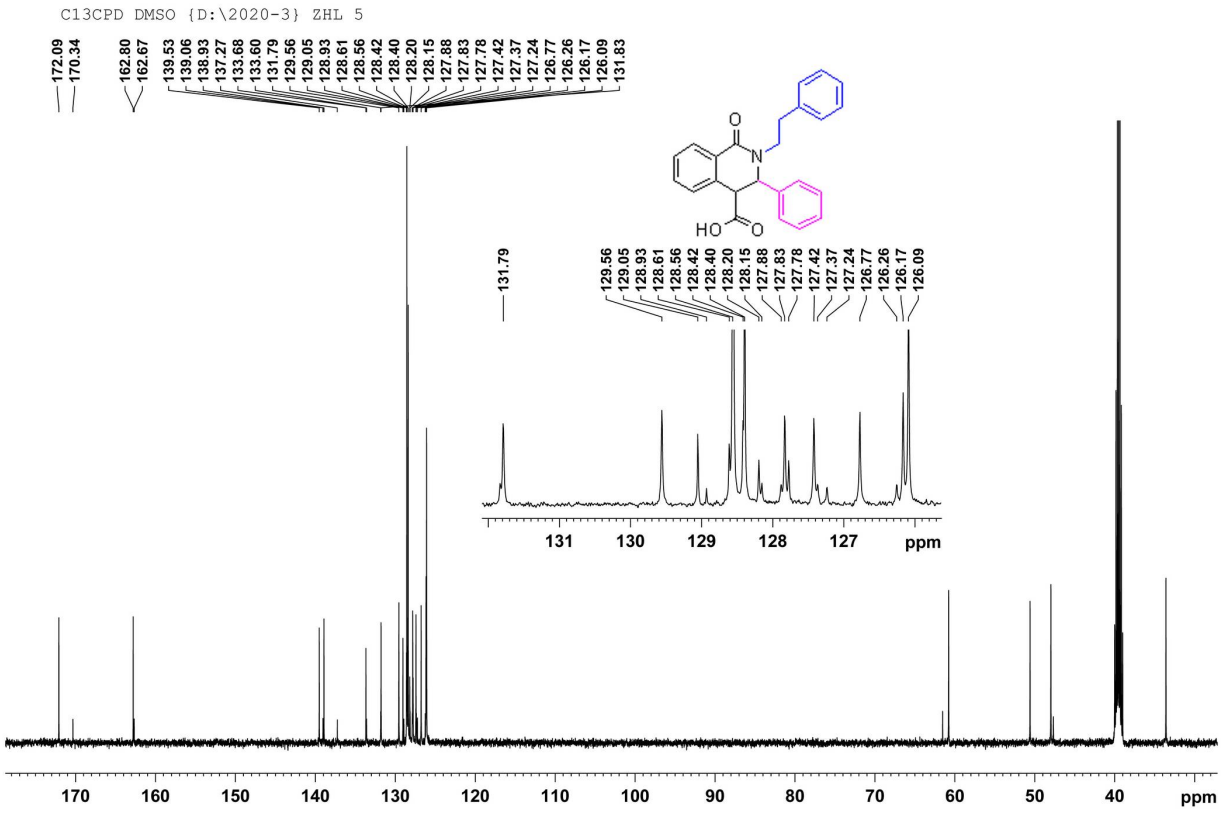

Figure S24. The ^{13}C NMR spectrum of compound **I9**

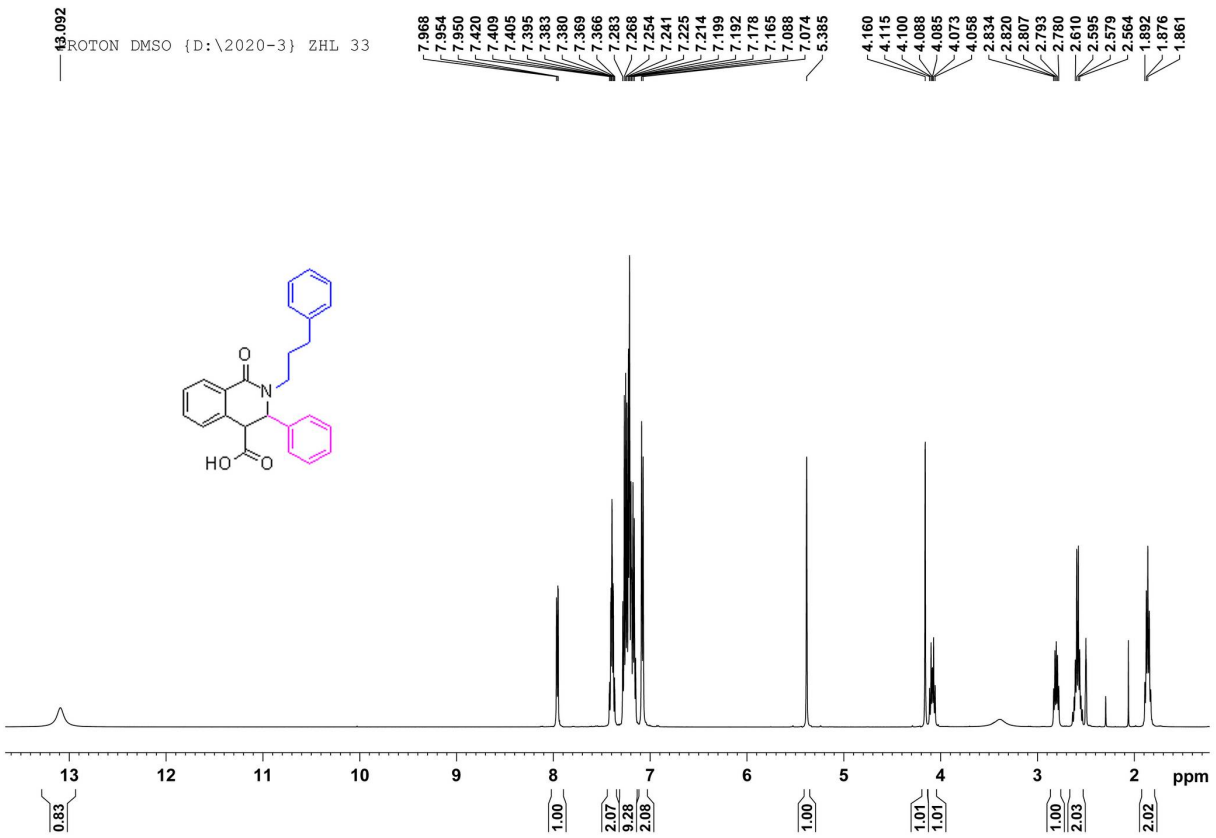

Figure S25. The ^{1}H NMR spectrum of compound **I10**

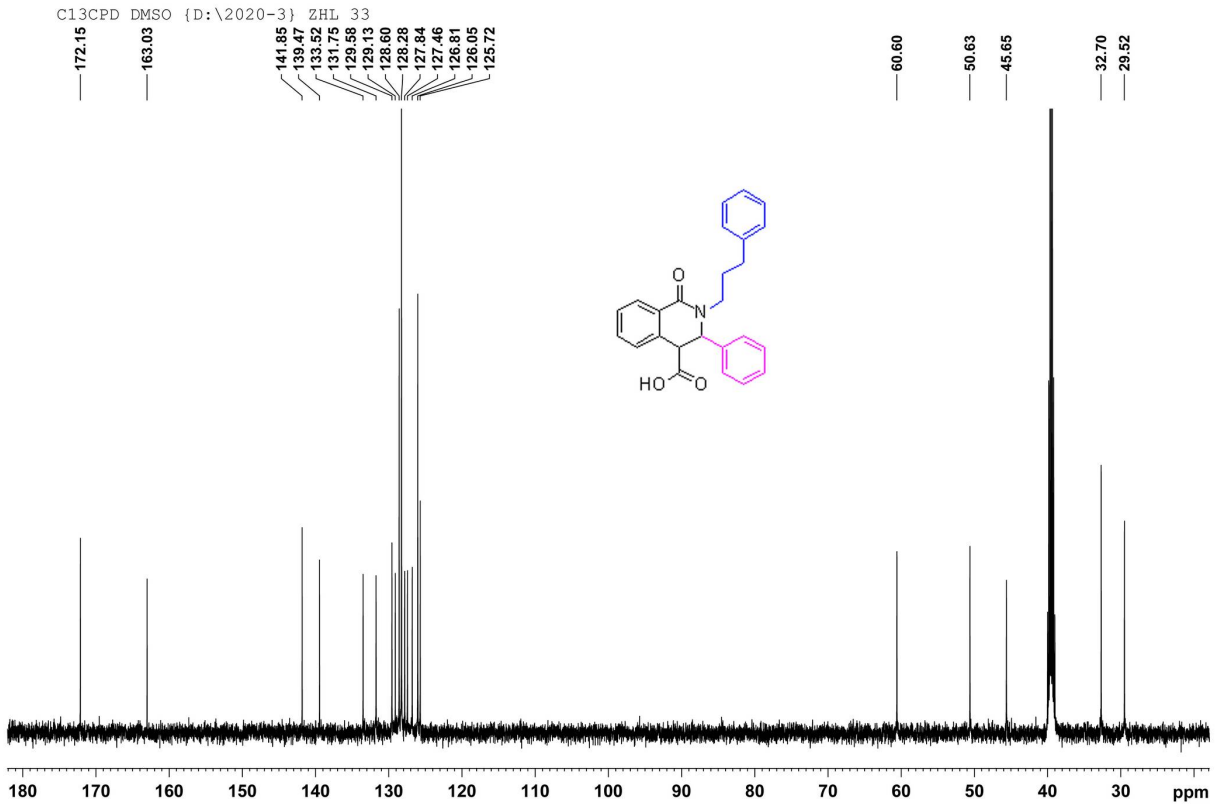

Figure S26. The ^{13}C NMR spectrum of compound **I10**

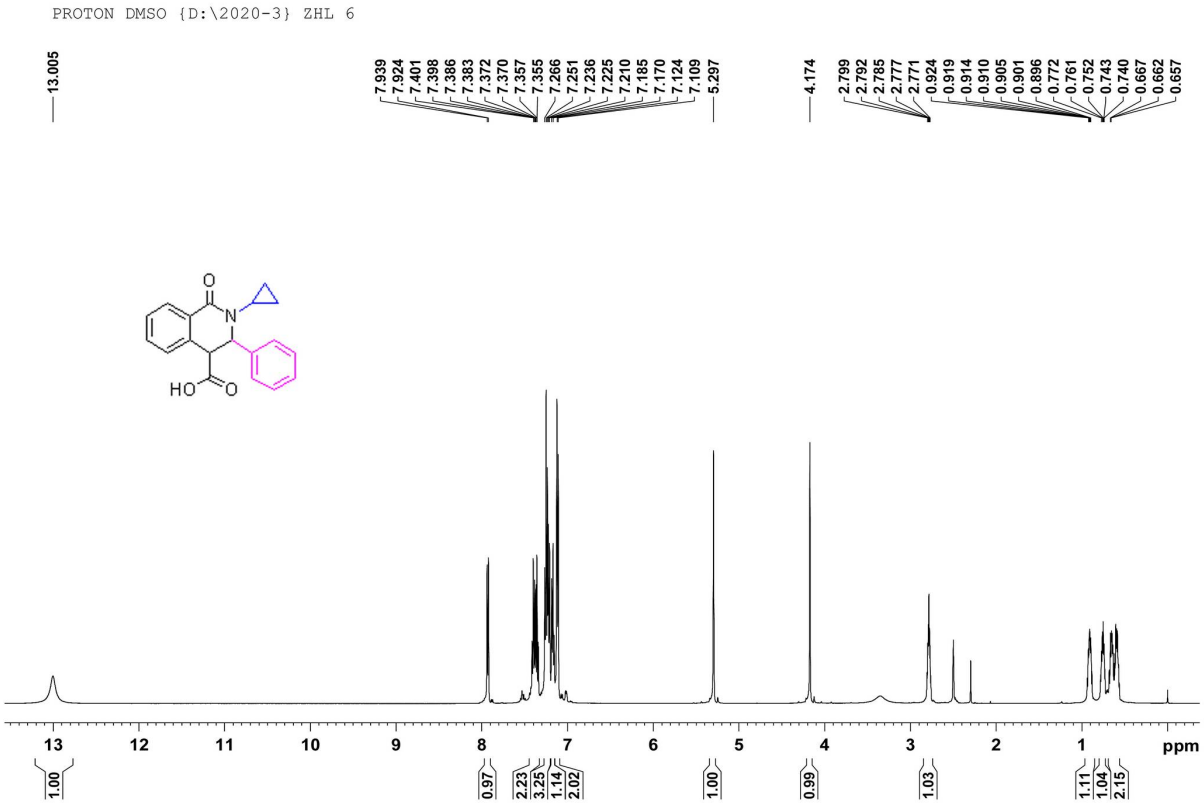

Figure S27. The ^{1}H NMR spectrum of compound **I11**

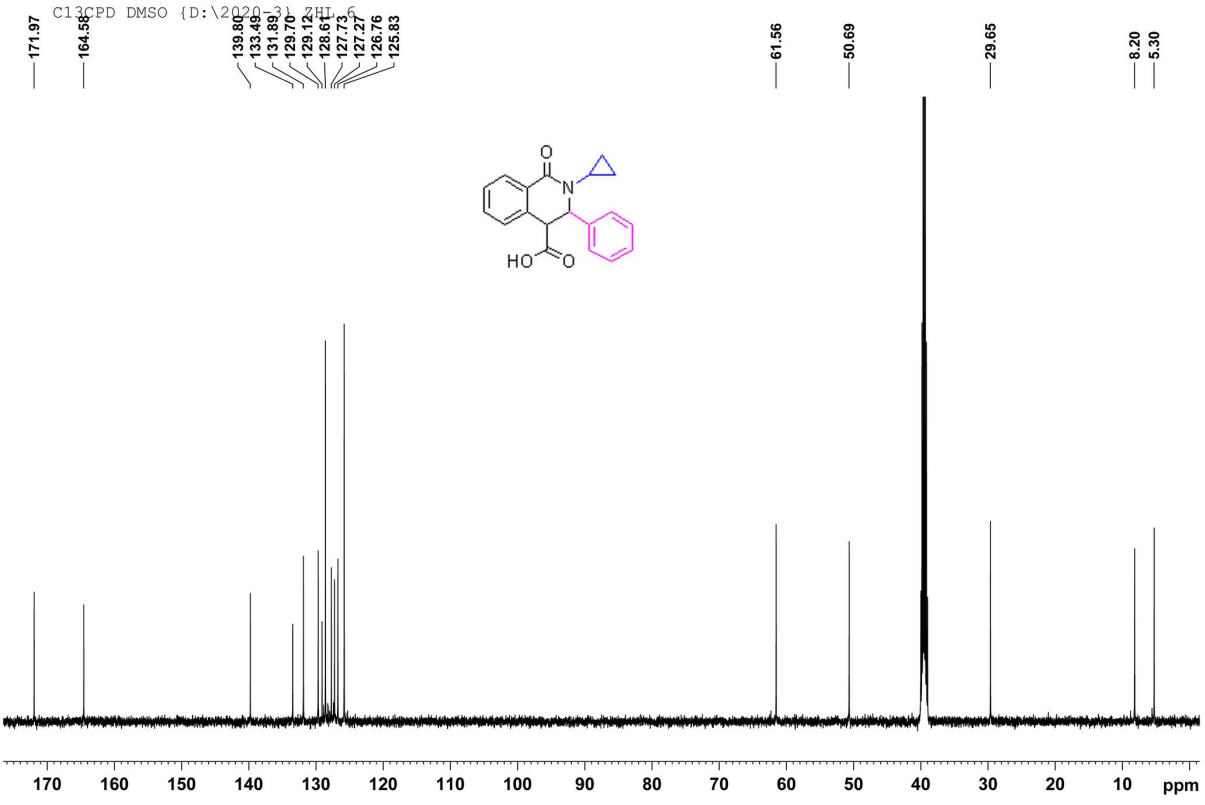

Figure S28. The ^{13}C NMR spectrum of compound **I11**

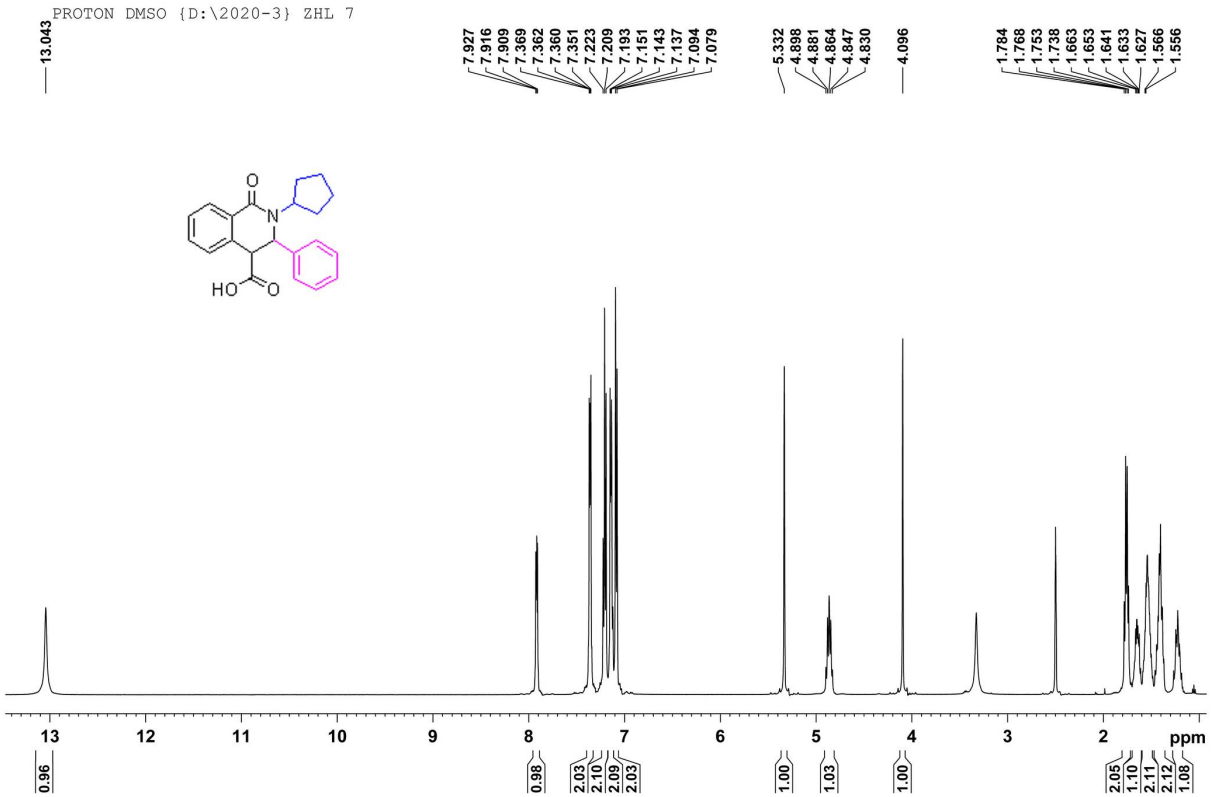

Figure S29. The ^{1}H NMR spectrum of compound **I12**

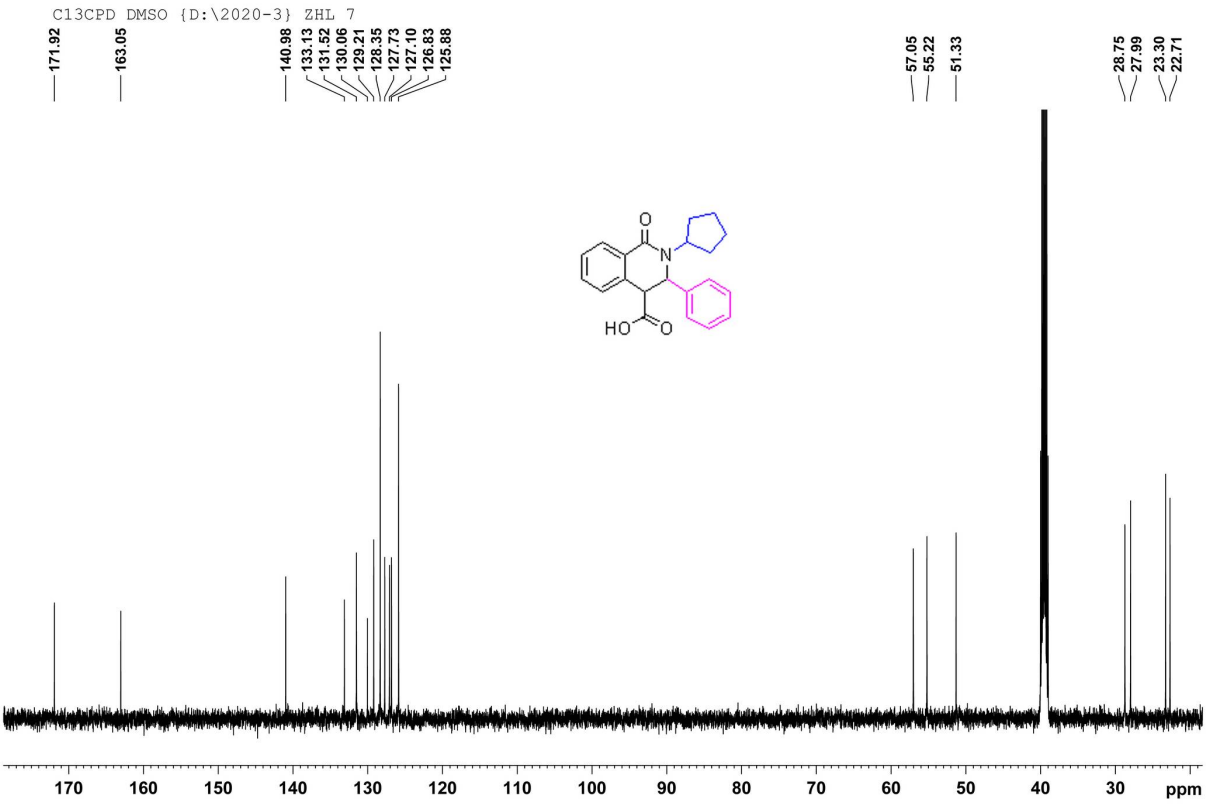

Figure S30. The ^{13}C NMR spectrum of compound **I12**

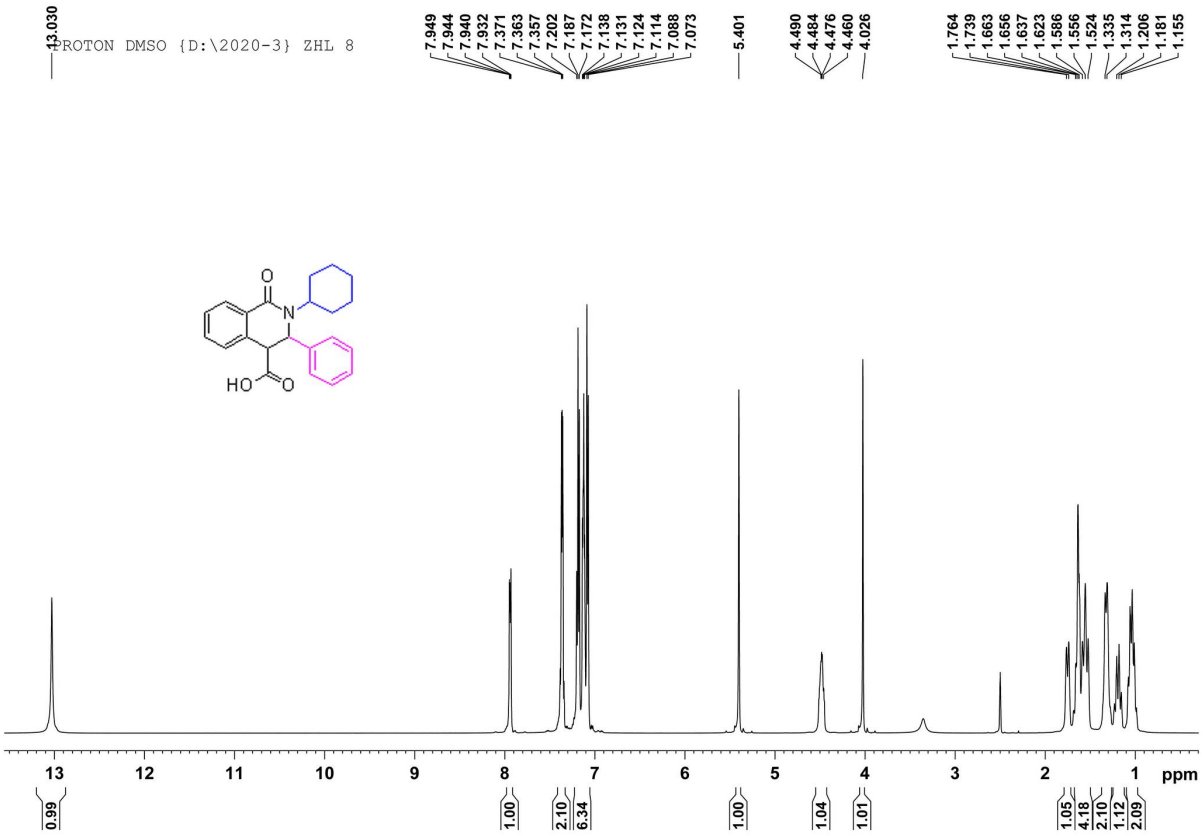

Figure S31. The ^{1}H NMR spectrum of compound **I13**

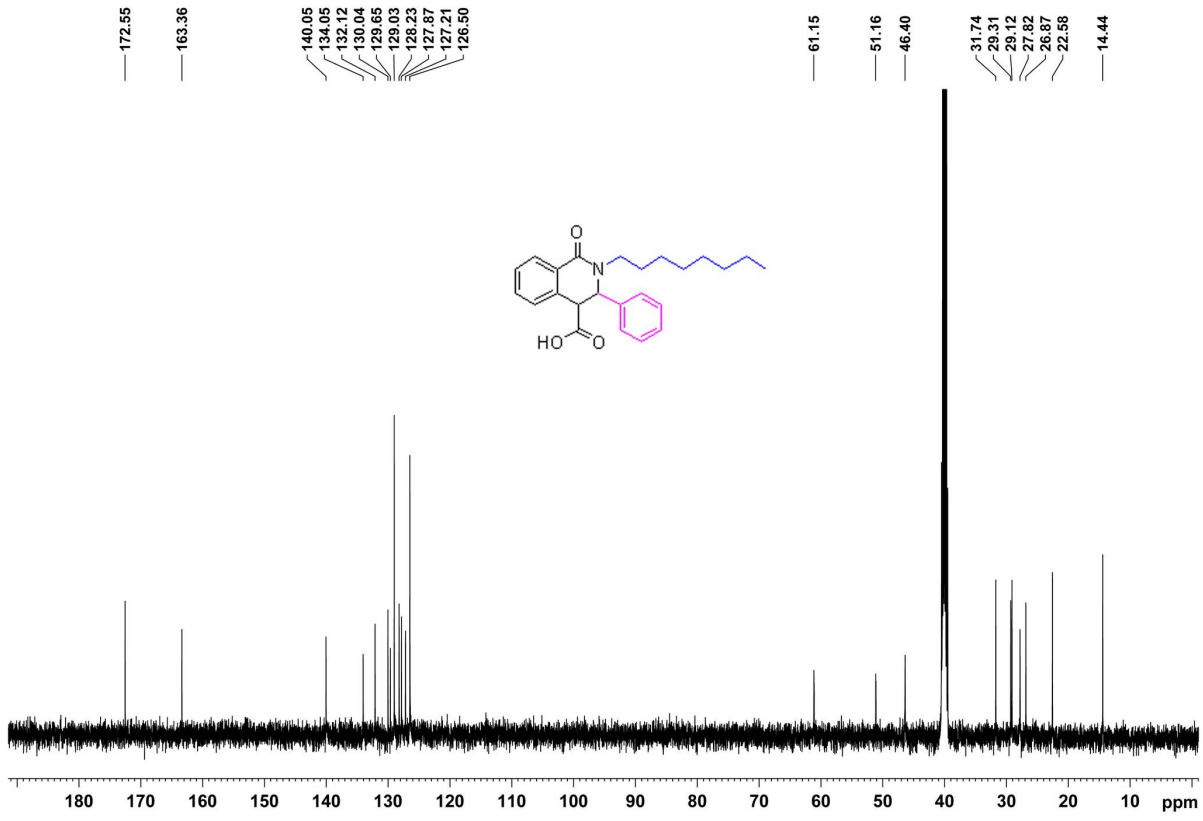

Figure S32. The ^{13}C NMR spectrum of compound **I13**

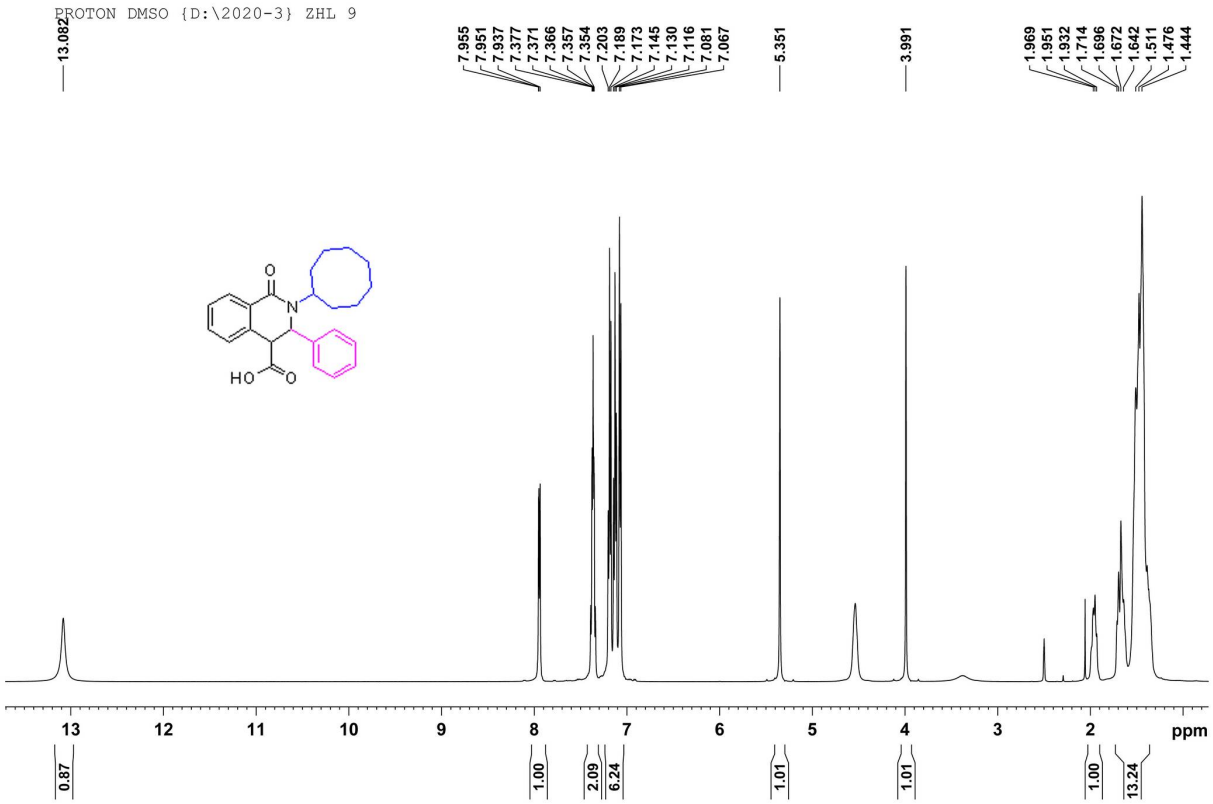

Figure S33. The ^{1}H NMR spectrum of compound **I14**

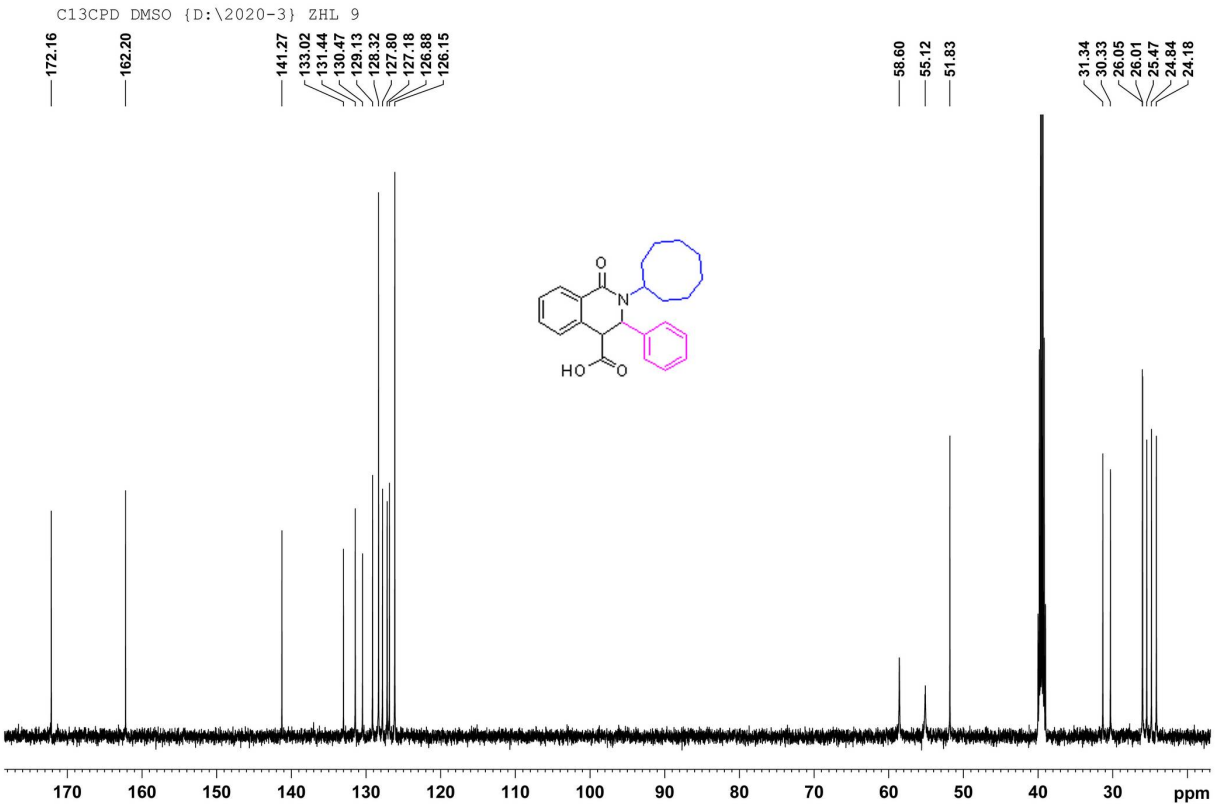

Figure S34. The ^{13}C NMR spectrum of compound **I14**

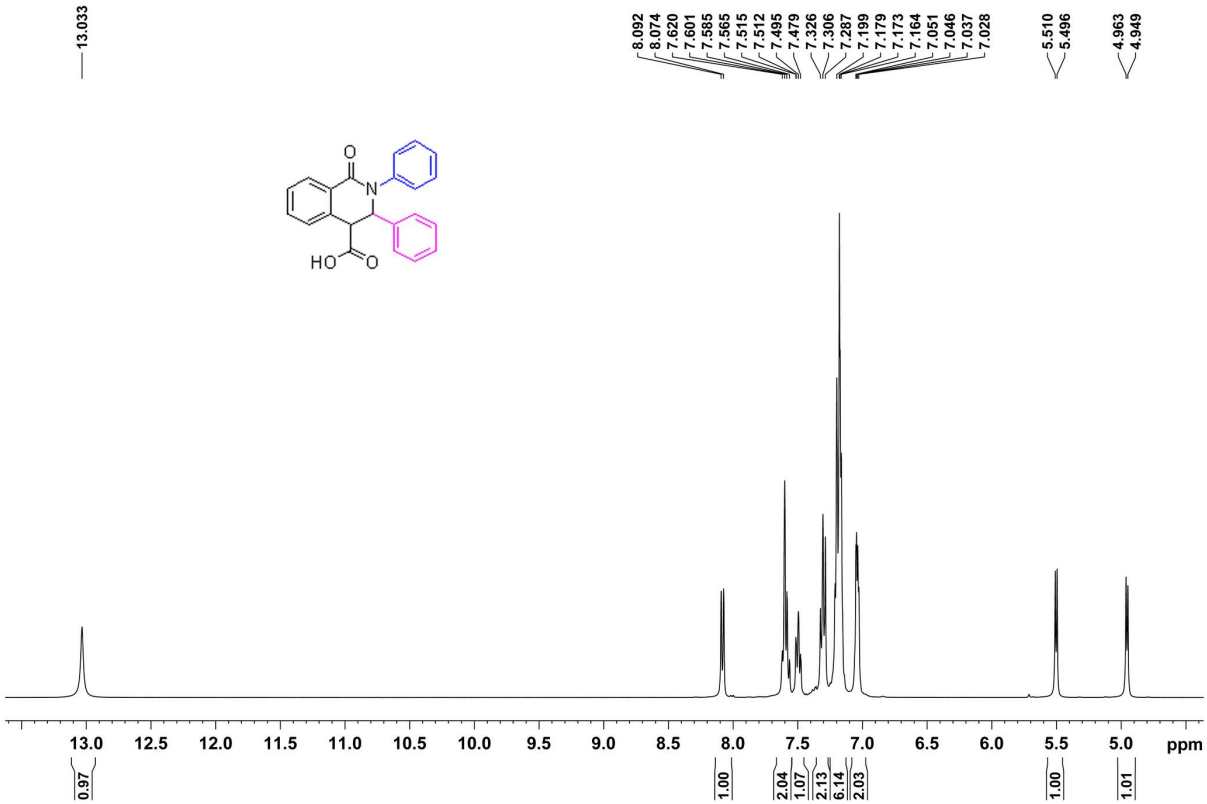

Figure S35. The ^{1}H NMR spectrum of compound **I15**

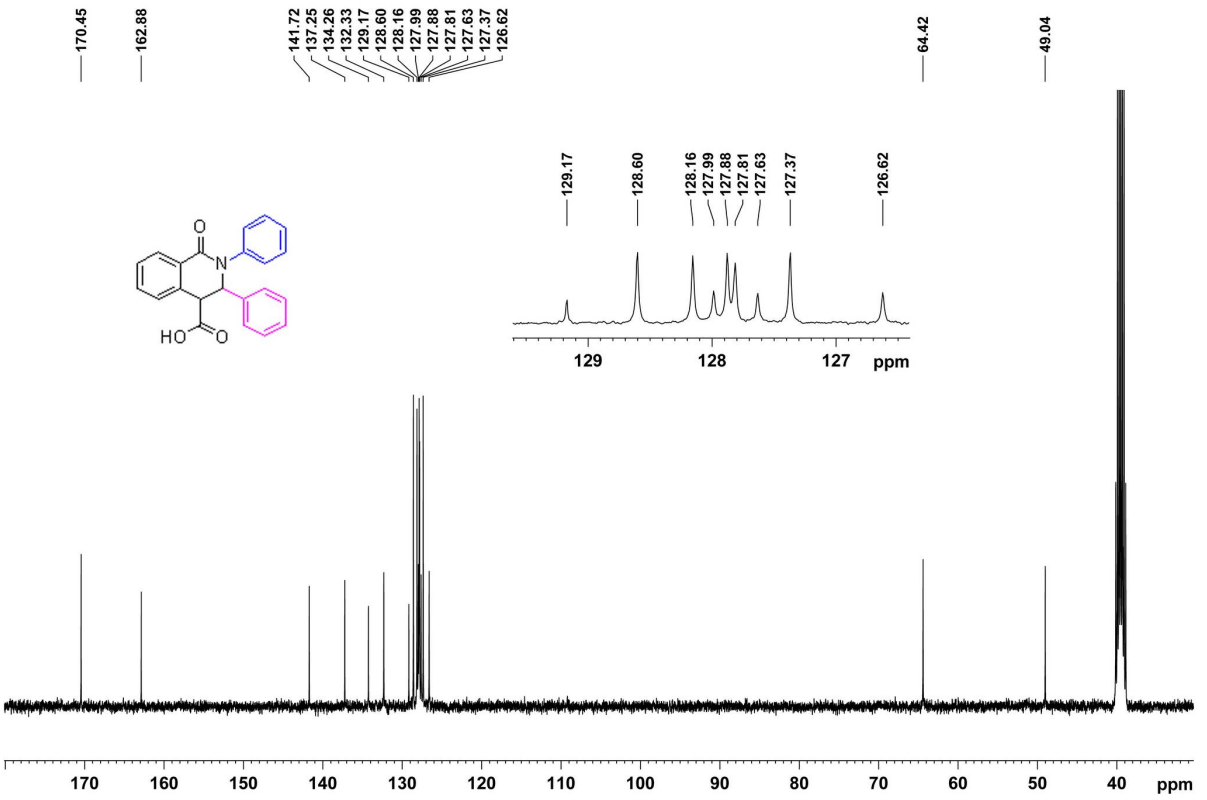

Figure S36. The ^{13}C NMR spectrum of compound **I15**

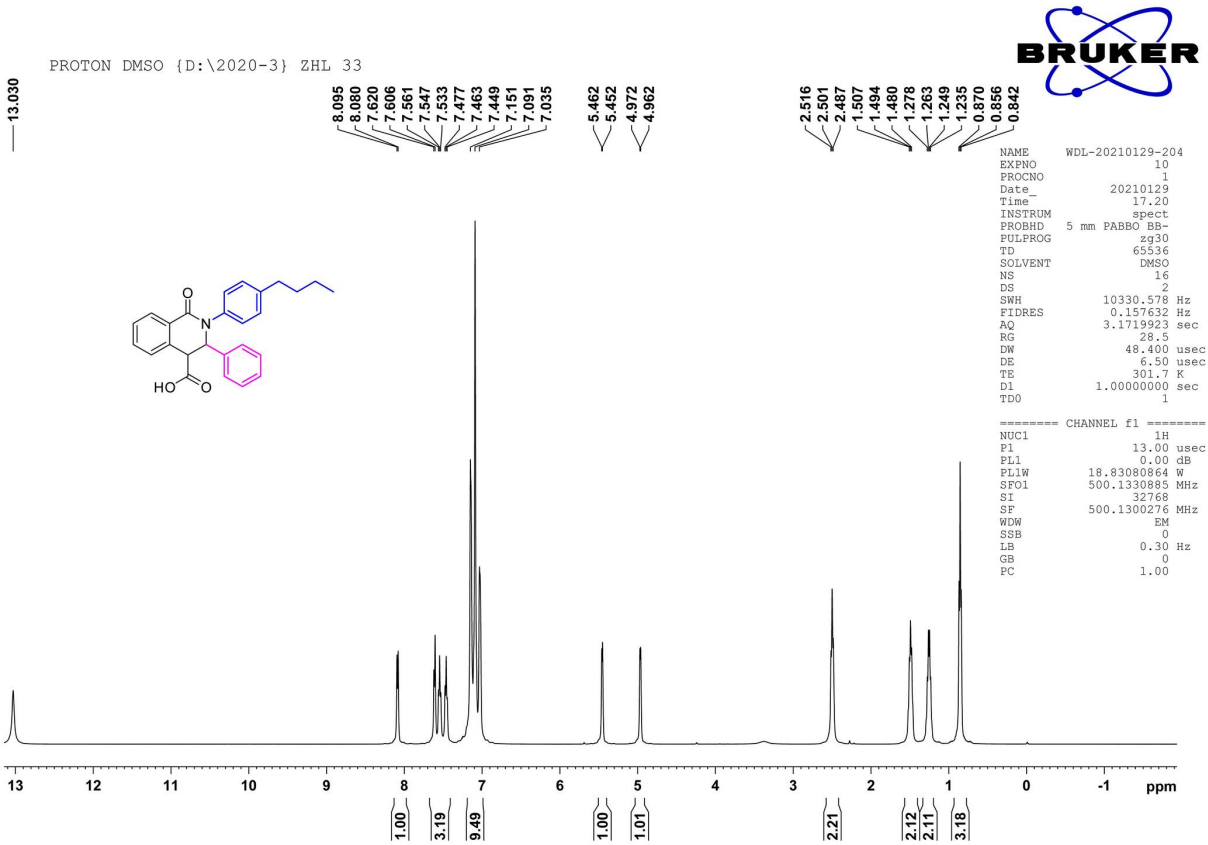

Figure S37. The ^{1}H NMR spectrum of compound **I16**

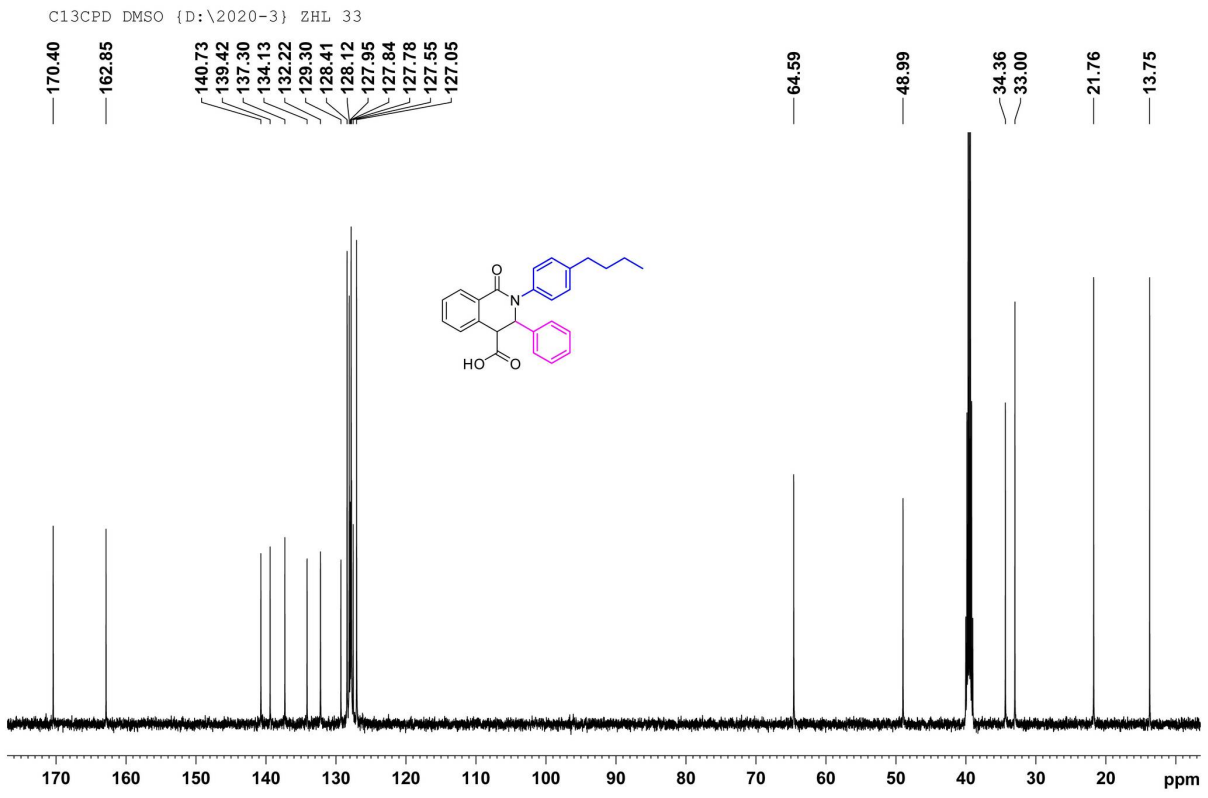

Figure S38. The ^{13}C NMR spectrum of compound **I16**

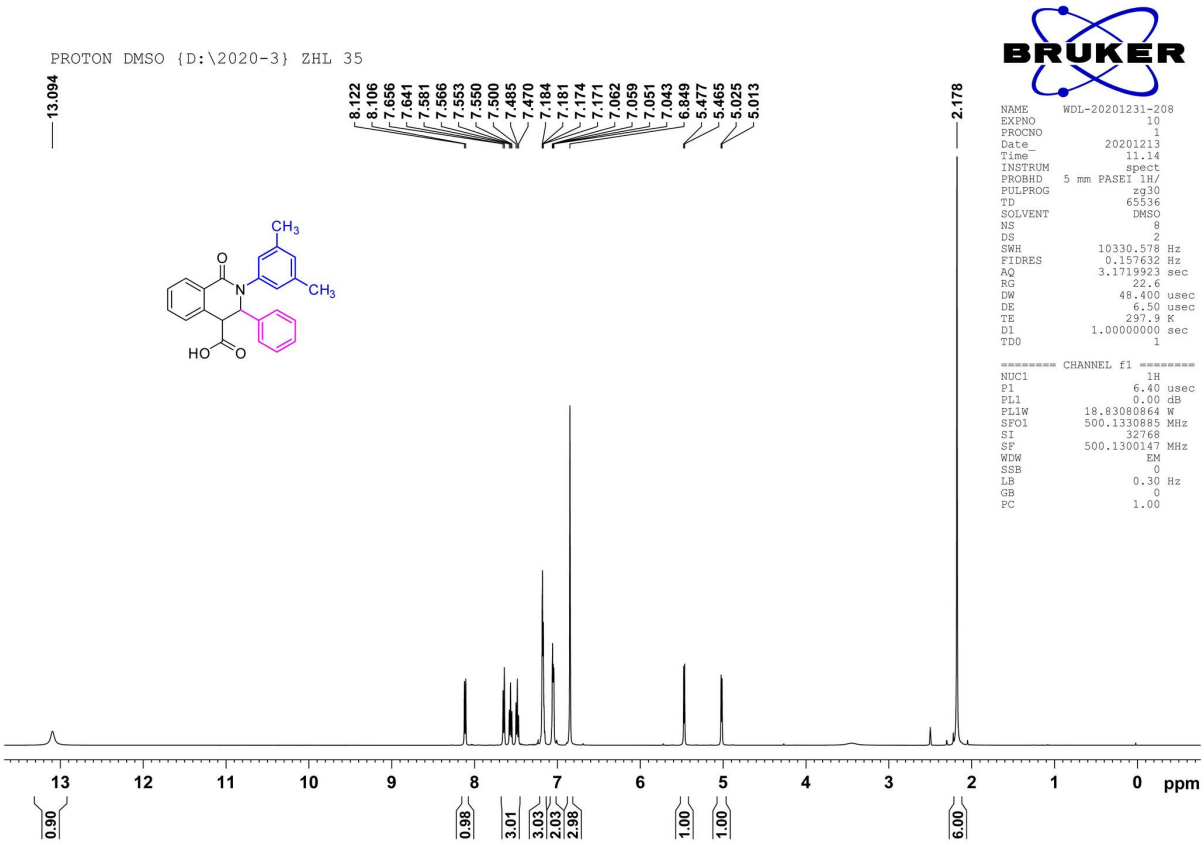

Figure S39. The ^{1}H NMR spectrum of compound **I17**

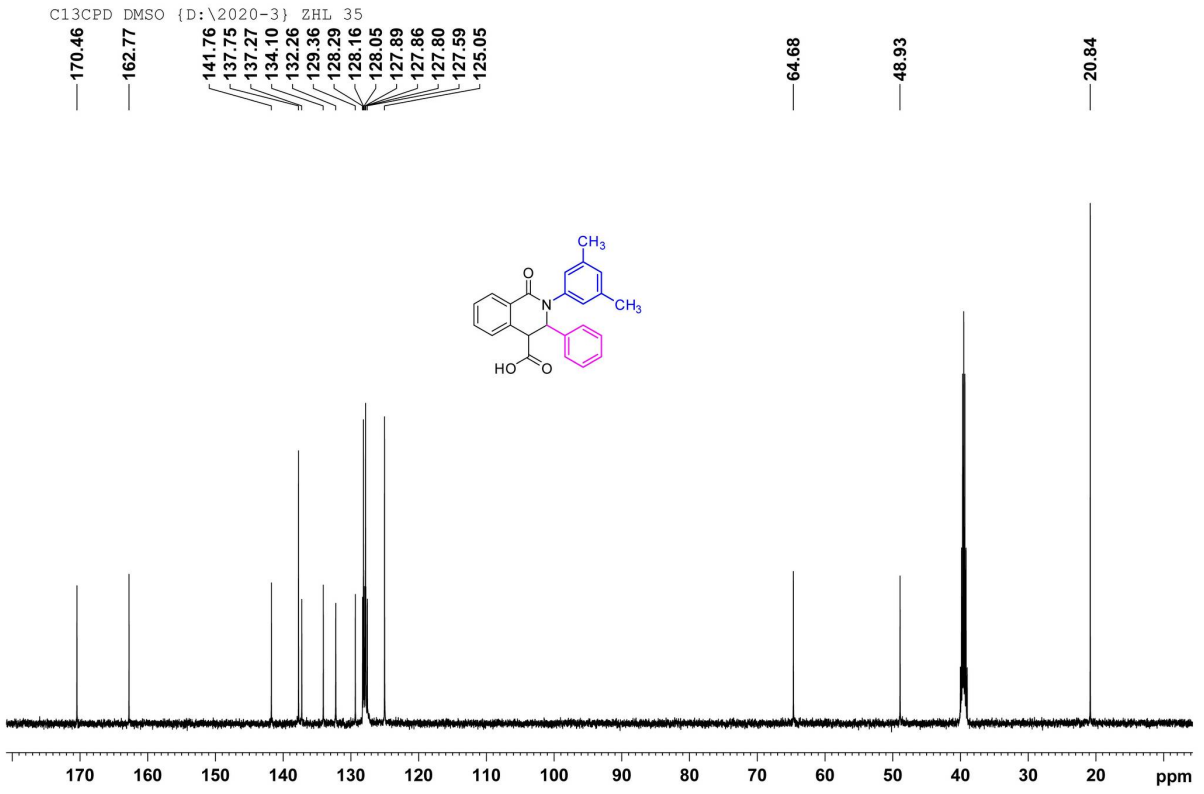

Figure S40. The ^{13}C NMR spectrum of compound **I17**

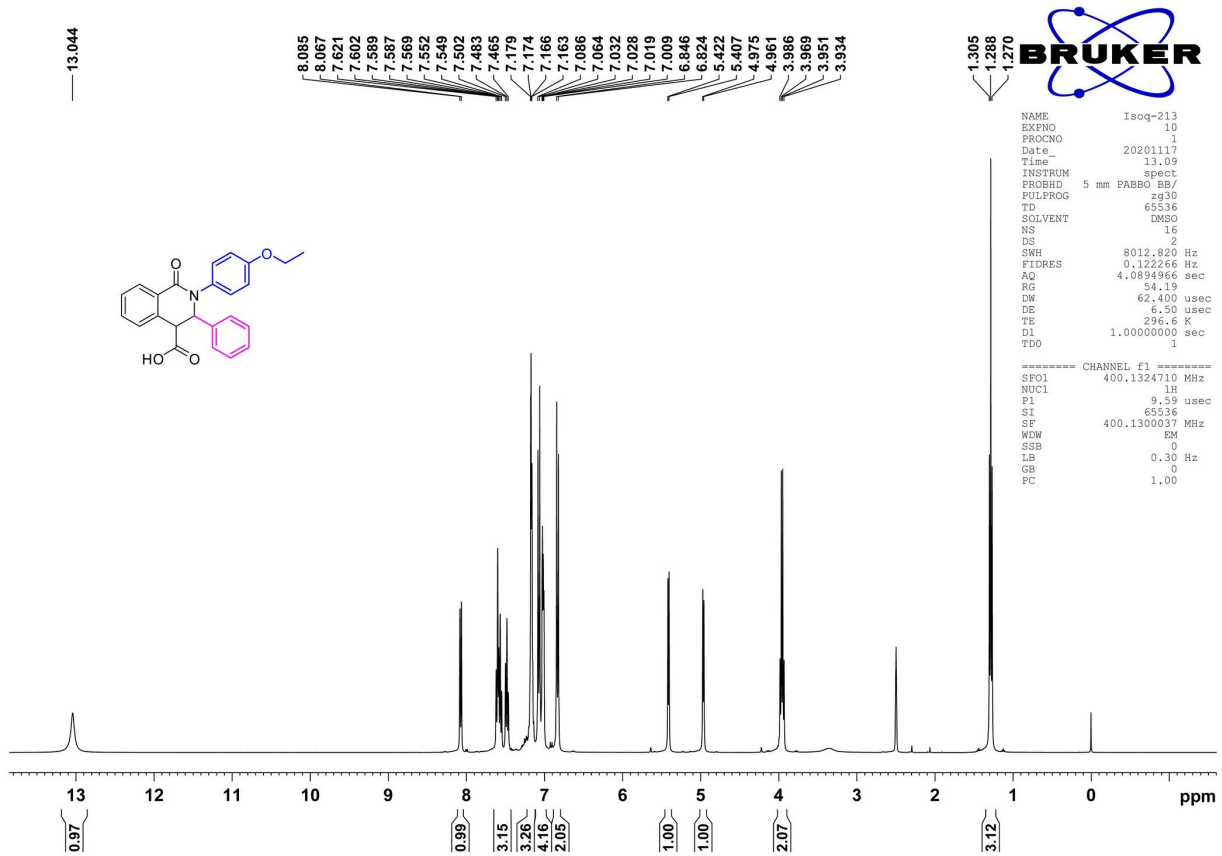

Figure S41. The ^{1}H NMR spectrum of compound **I18**

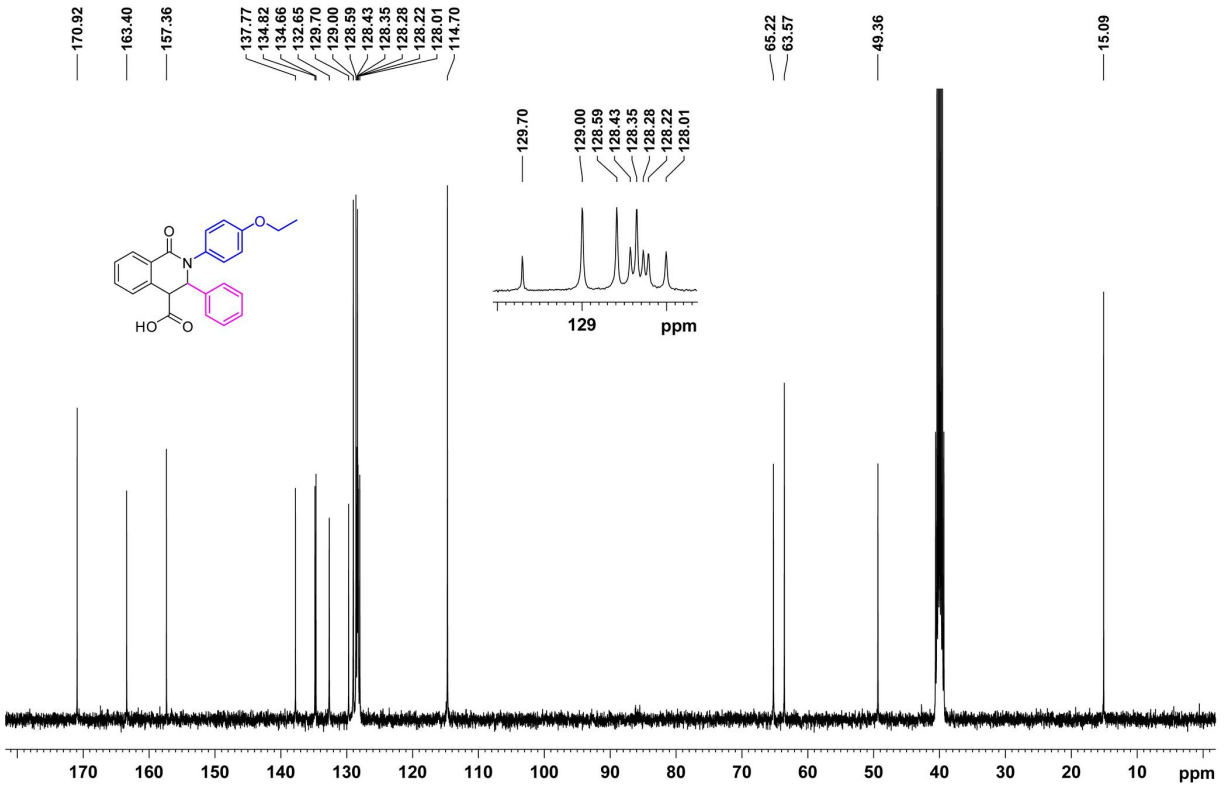

Figure S42. The ^{13}C NMR spectrum of compound **I18**

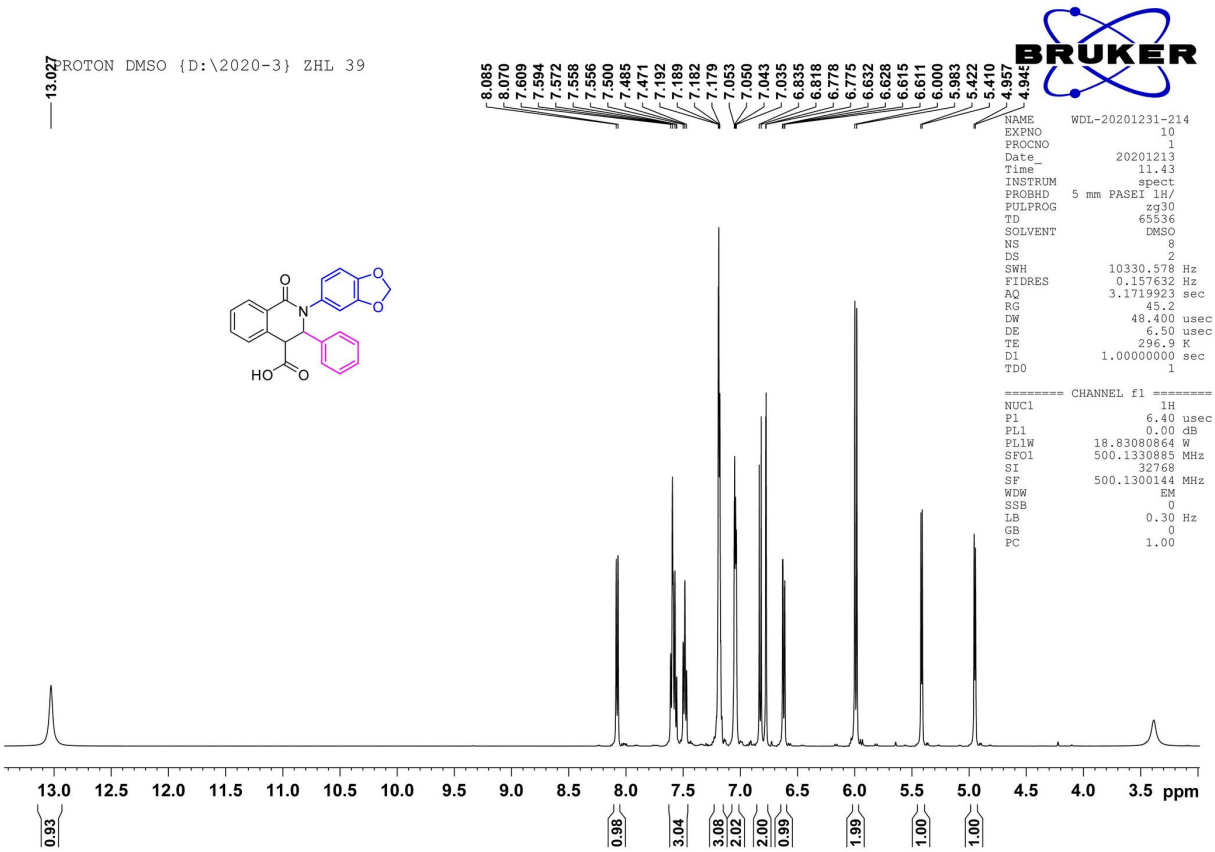

Figure S43. The ^{1}H NMR spectrum of compound **I19**

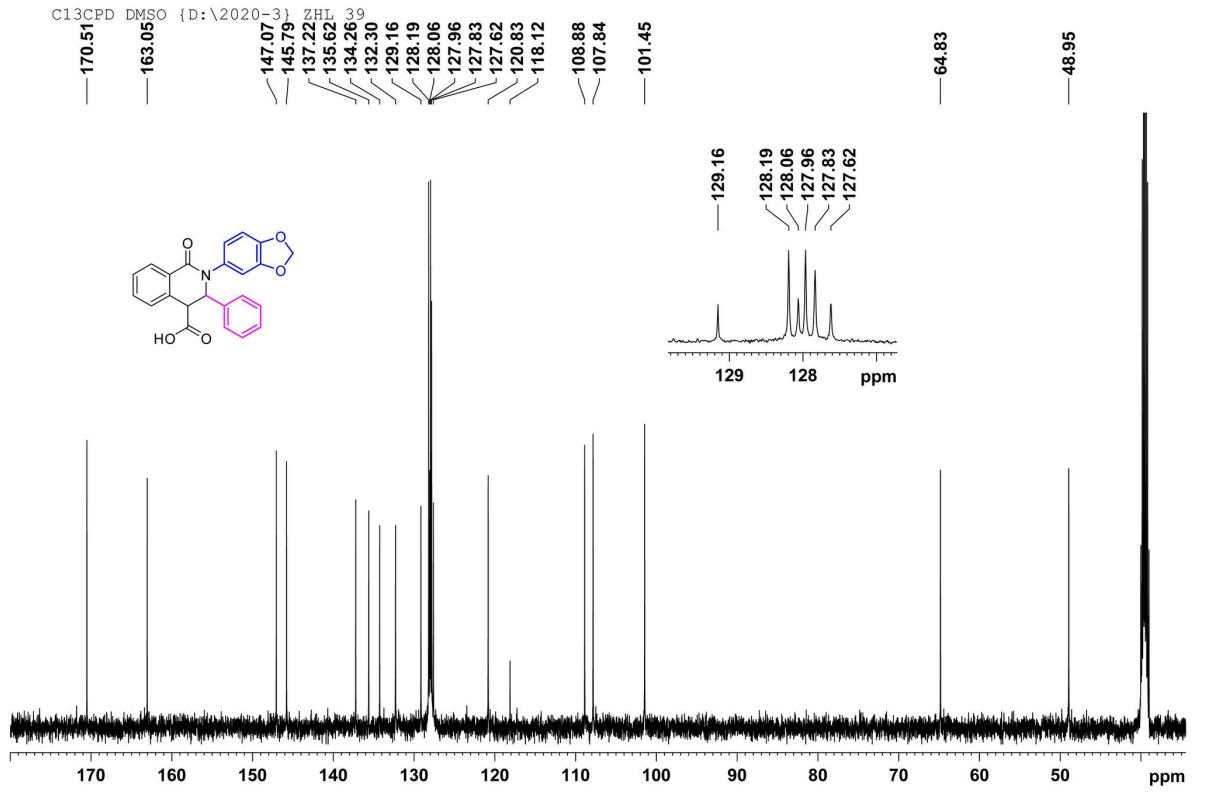

Figure S44. The ^{13}C NMR spectrum of compound **I19**

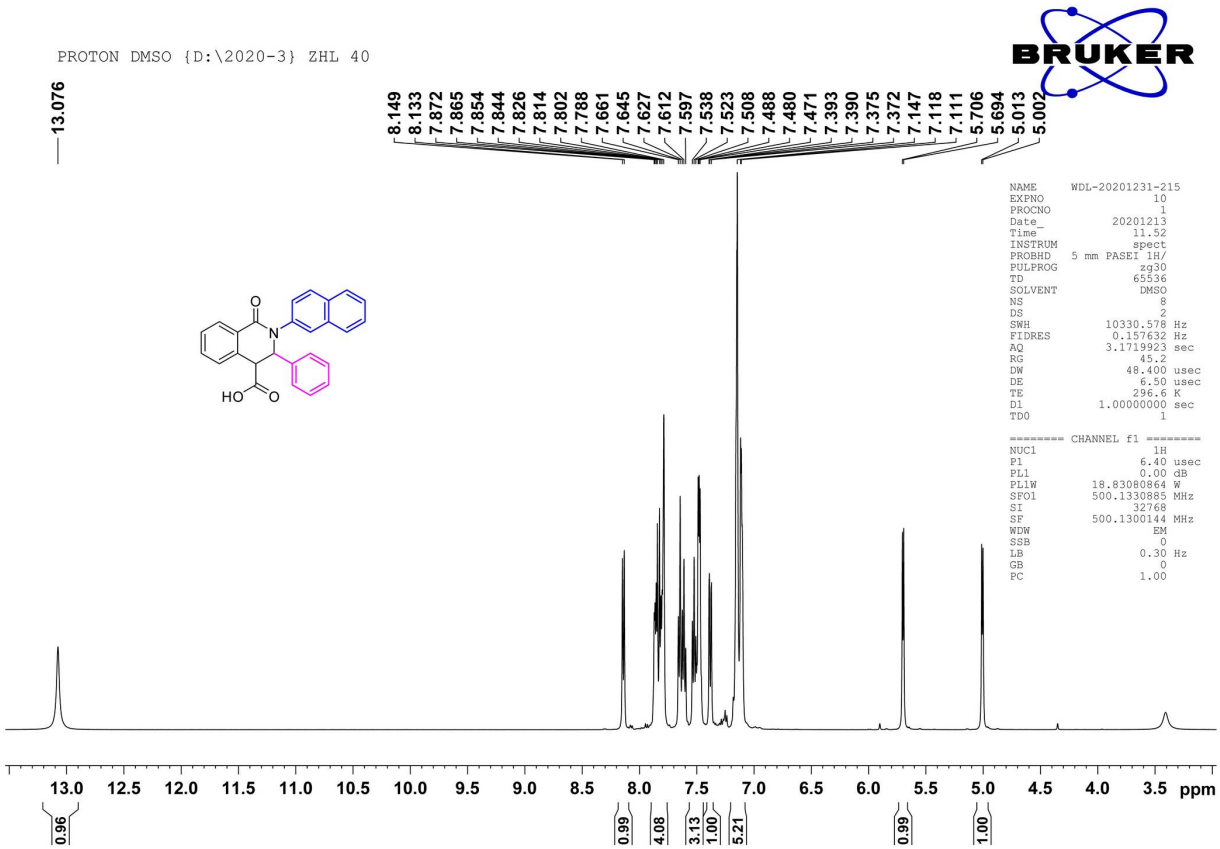

Figure S45. The ^{1}H NMR spectrum of compound **I20**

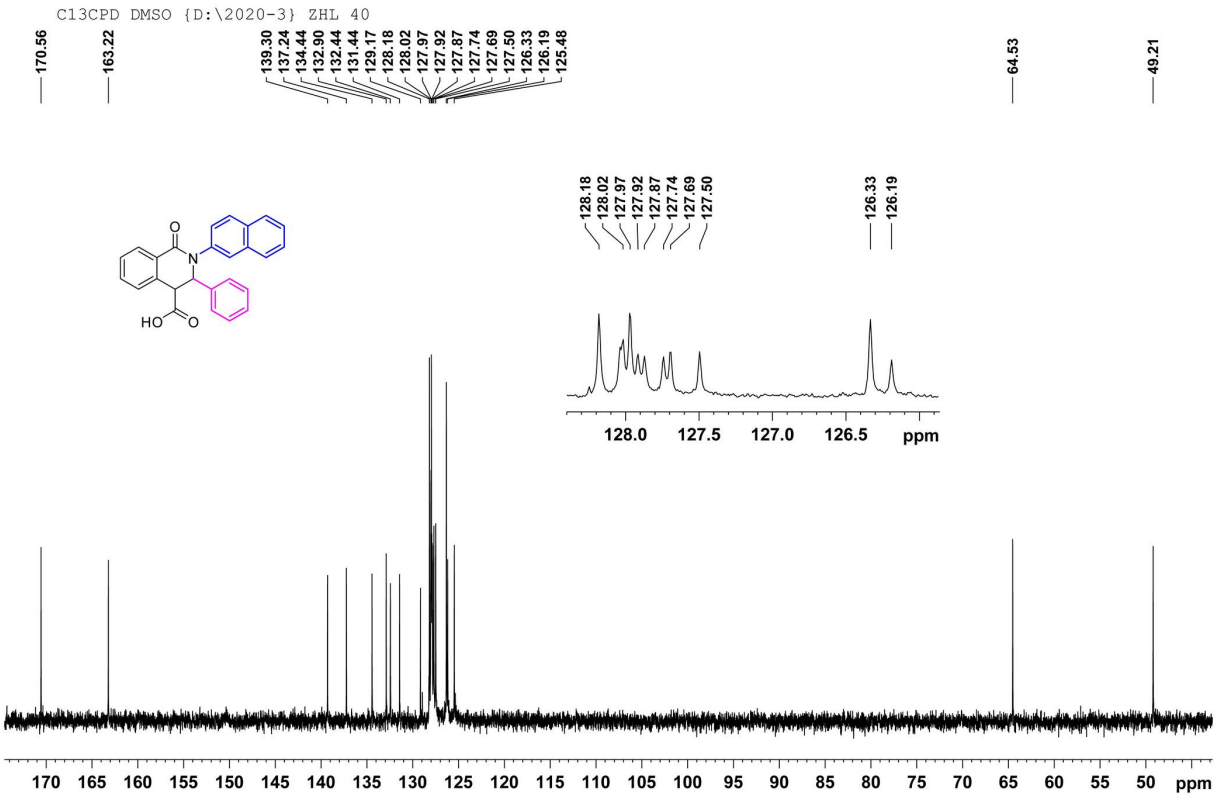

Figure S46. The ^{13}C NMR spectrum of compound **I20**

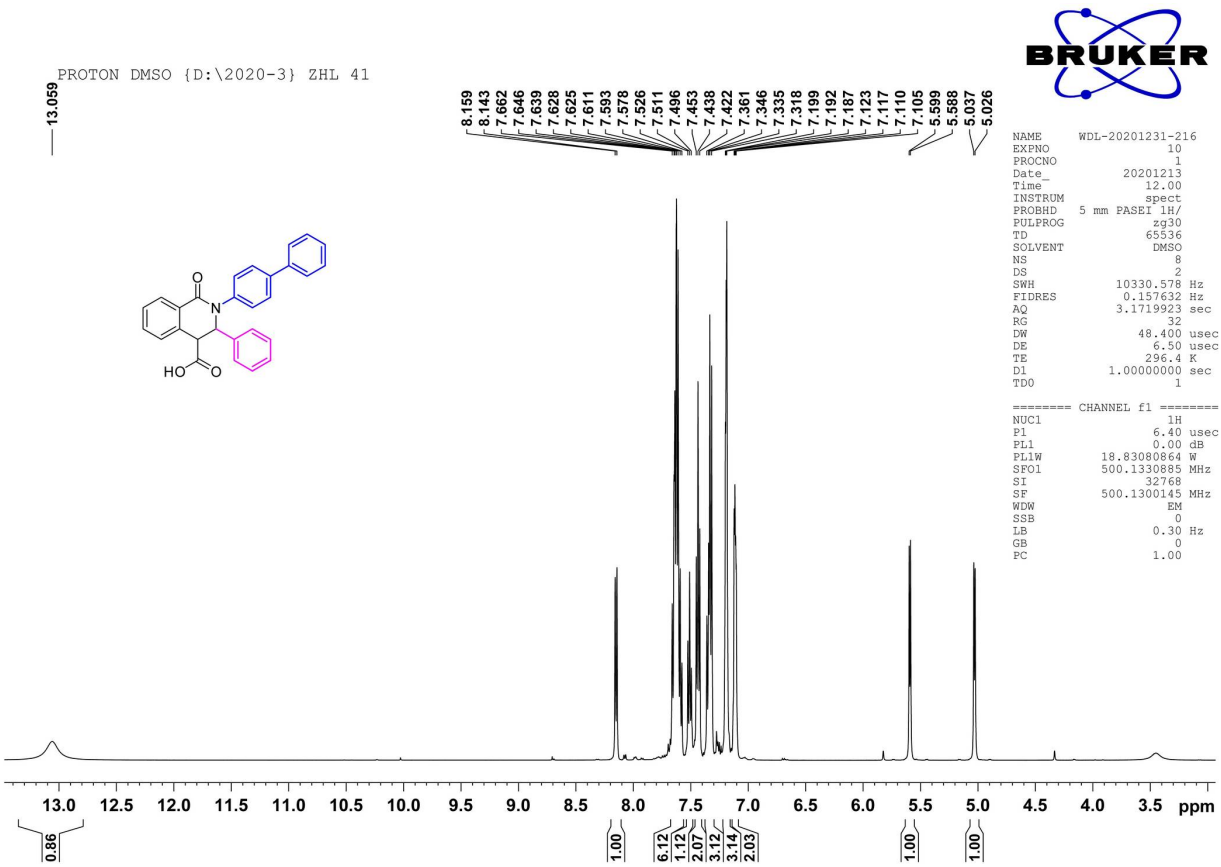

Figure S47. The ^{1}H NMR spectrum of compound **I21**

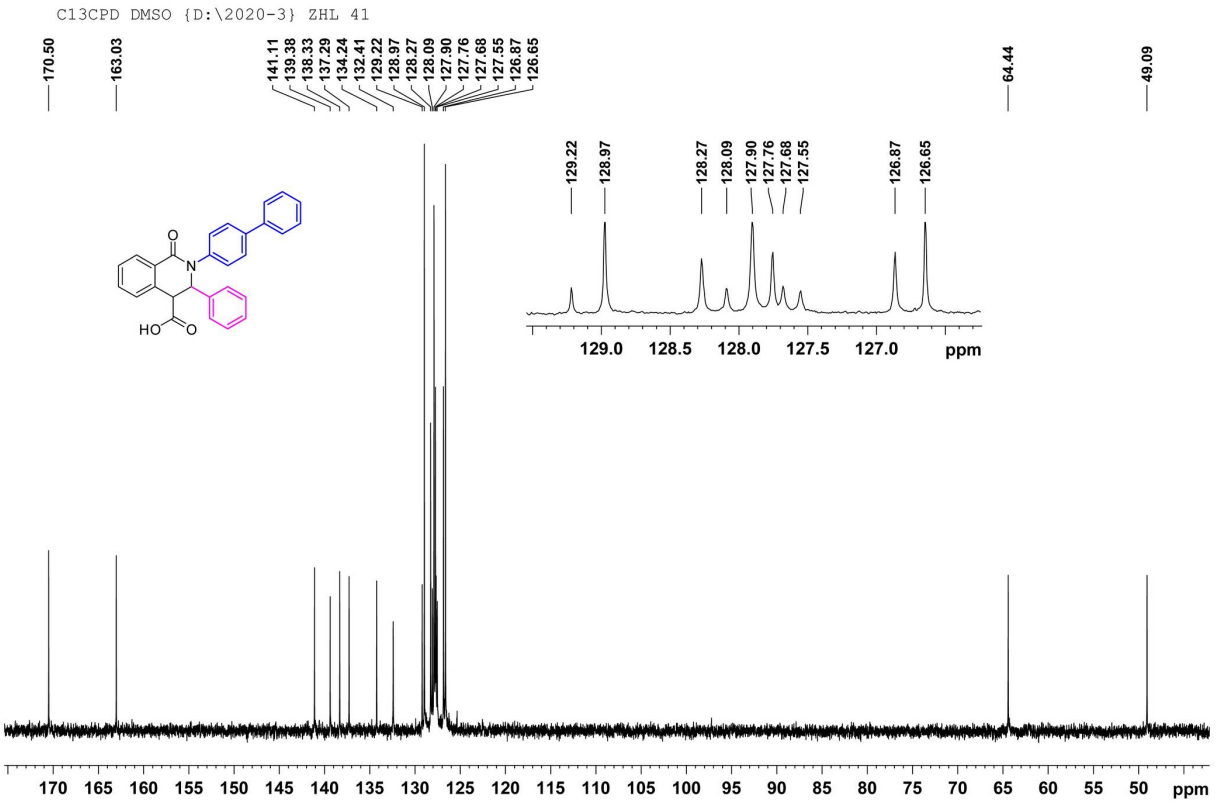

Figure S48. The ^{13}C NMR spectrum of compound **I21**

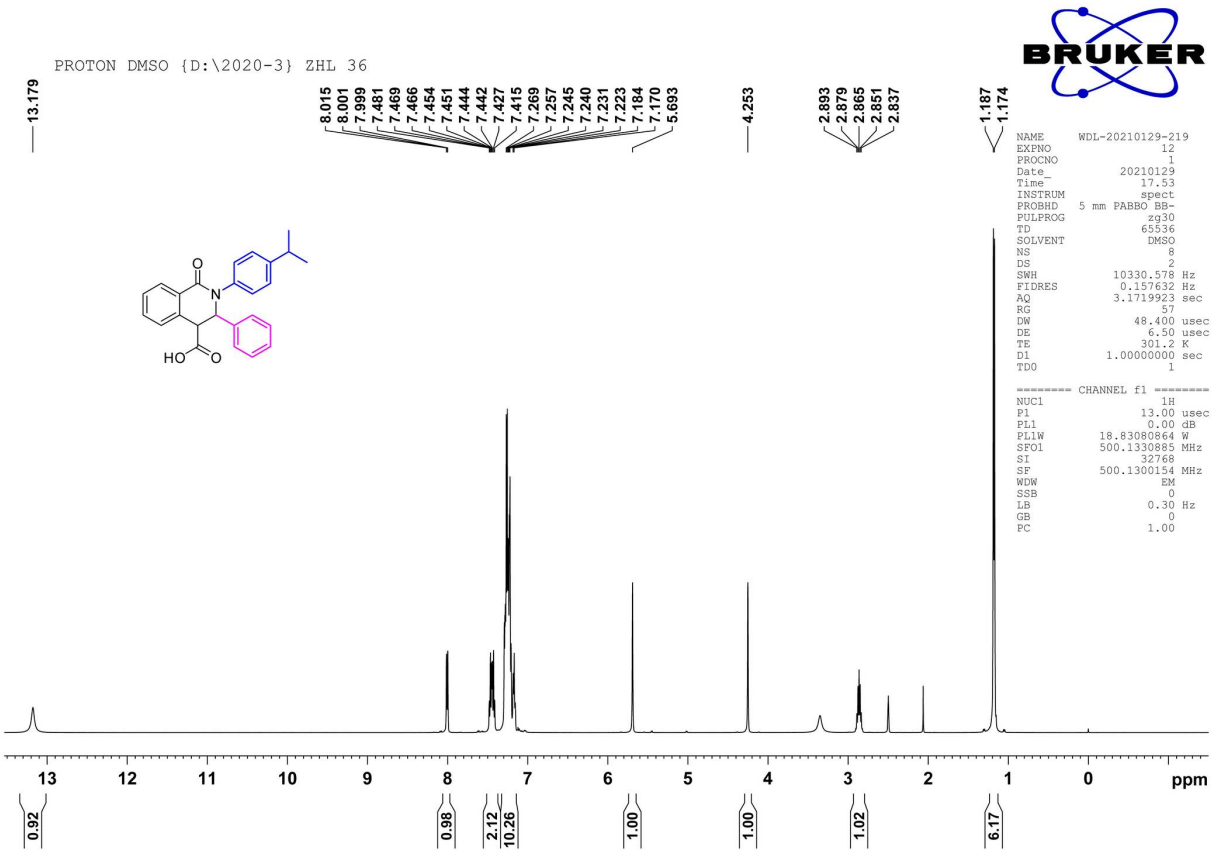

Figure S49. The ^{1}H NMR spectrum of compound **I22**

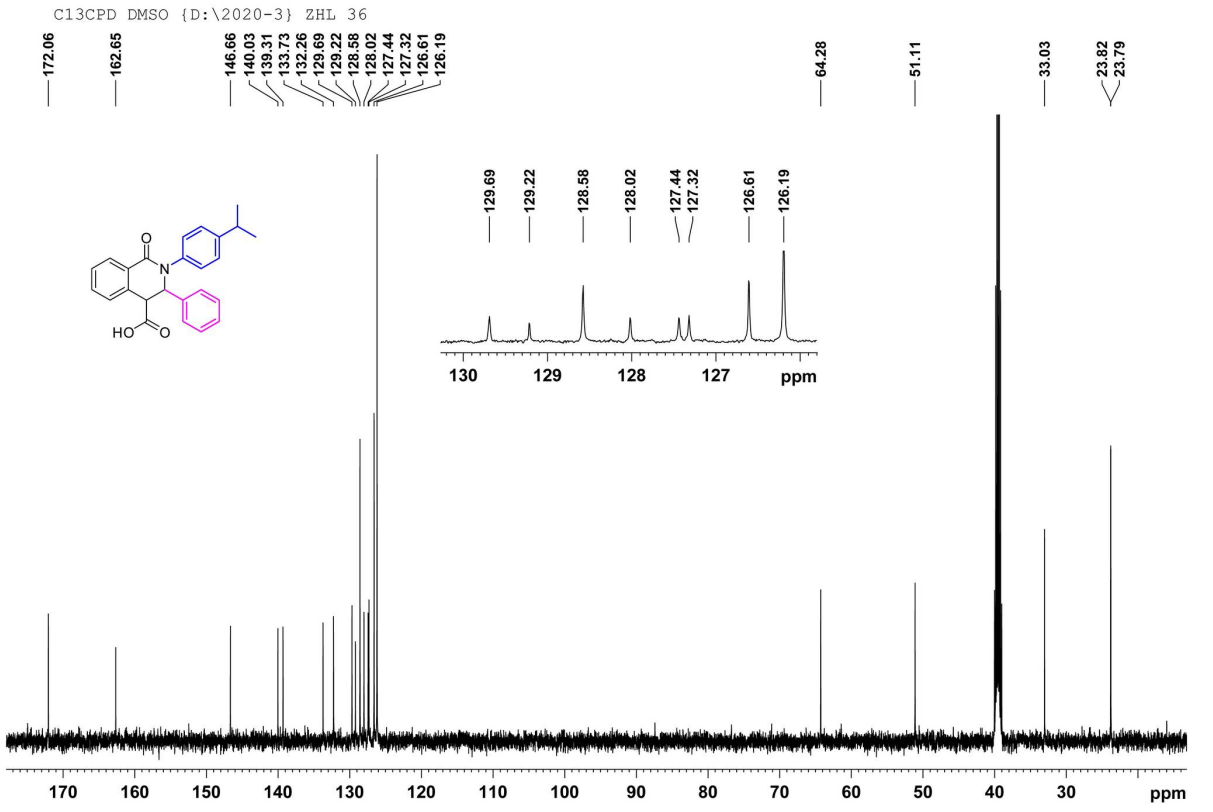

Figure S50. The ^{13}C NMR spectrum of compound **I22**

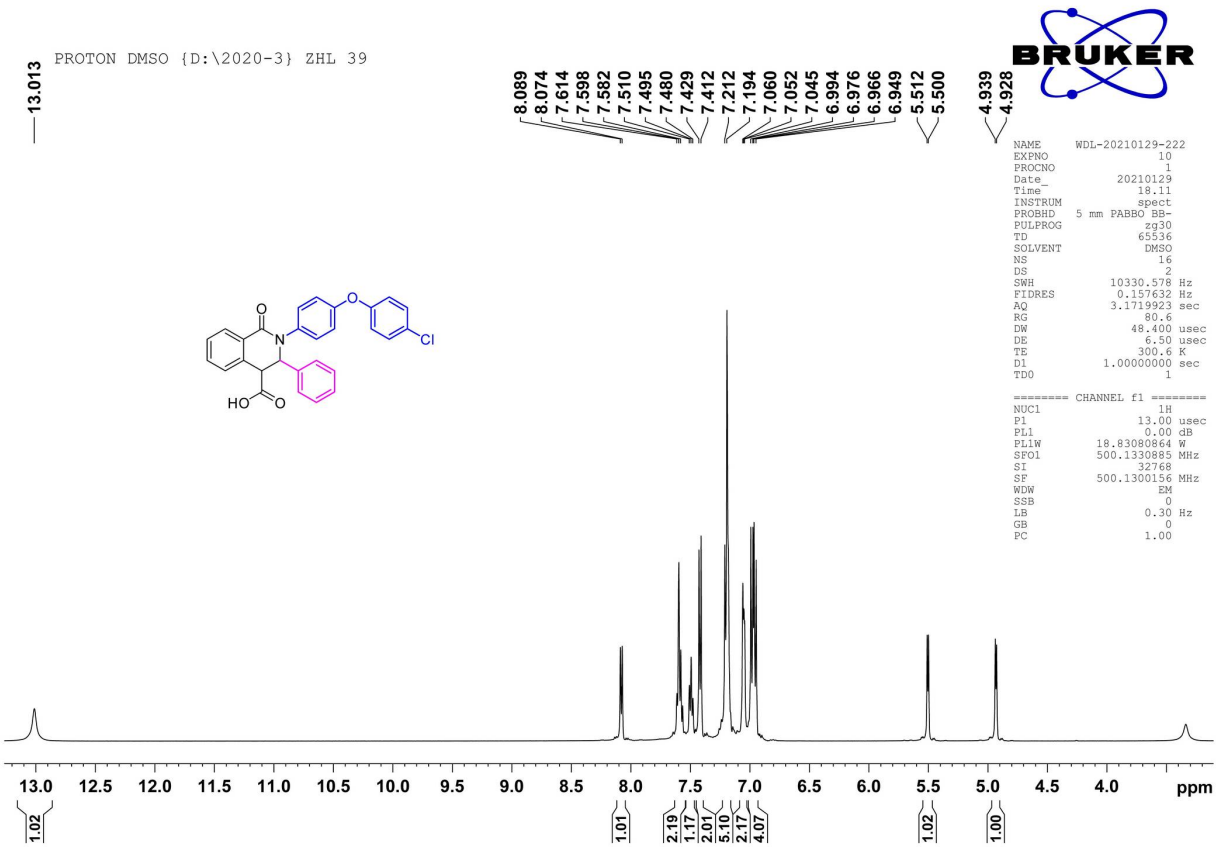

Figure S51. The ^{1}H NMR spectrum of compound **I23**

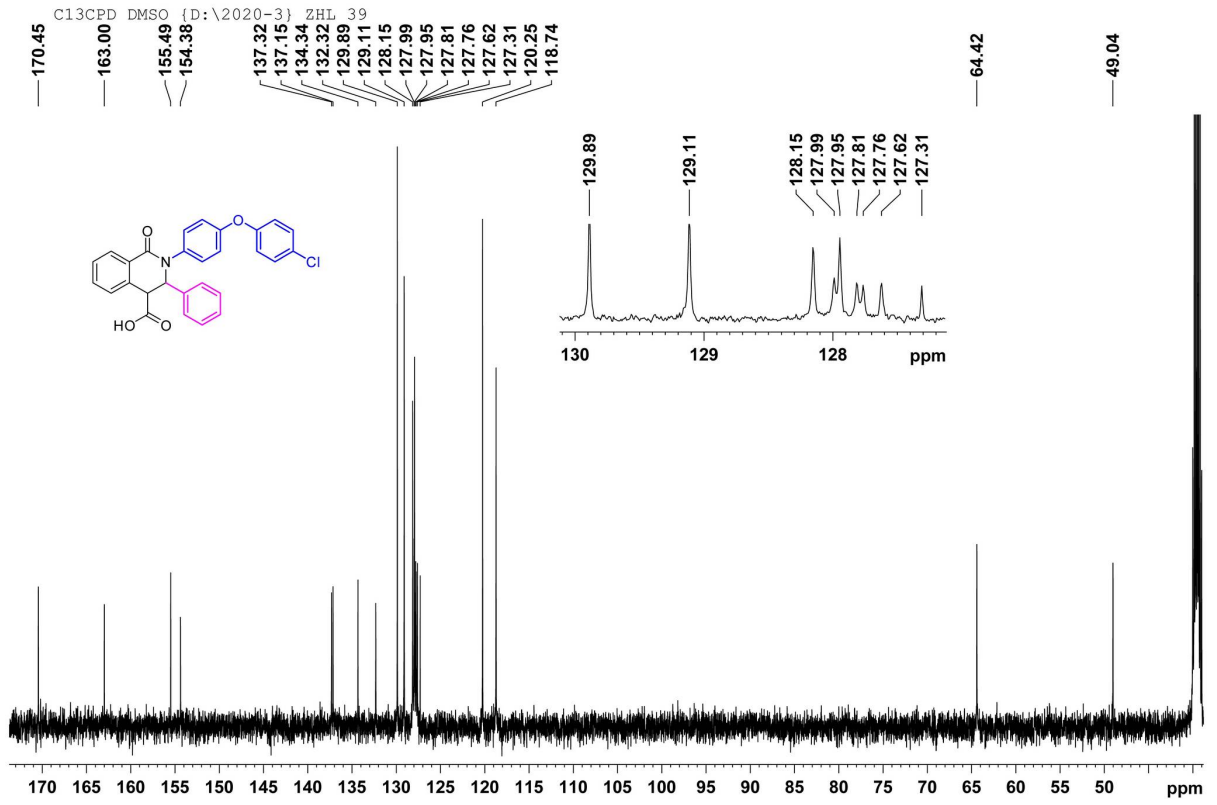

Figure S52. The ^{13}C NMR spectrum of compound **I23**

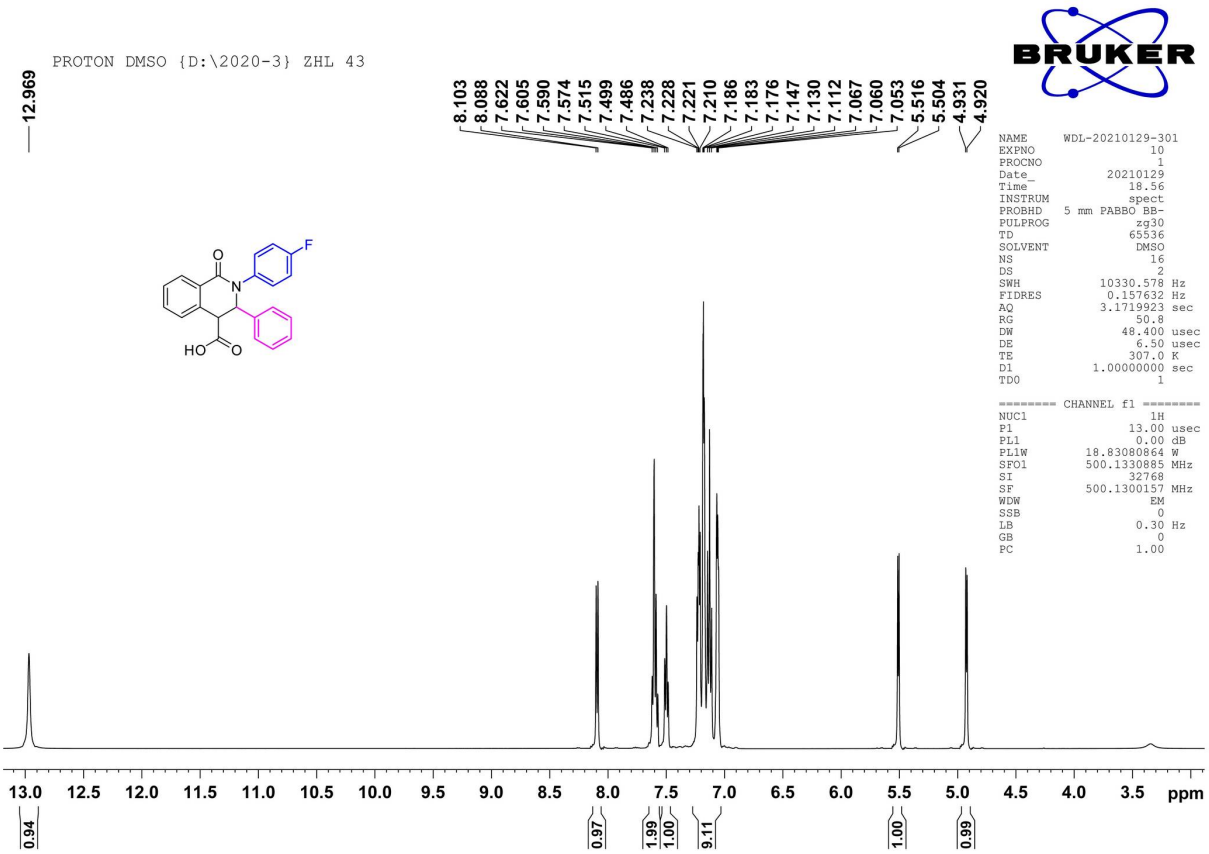

Figure S53. The ^{1}H NMR spectrum of compound **I24**

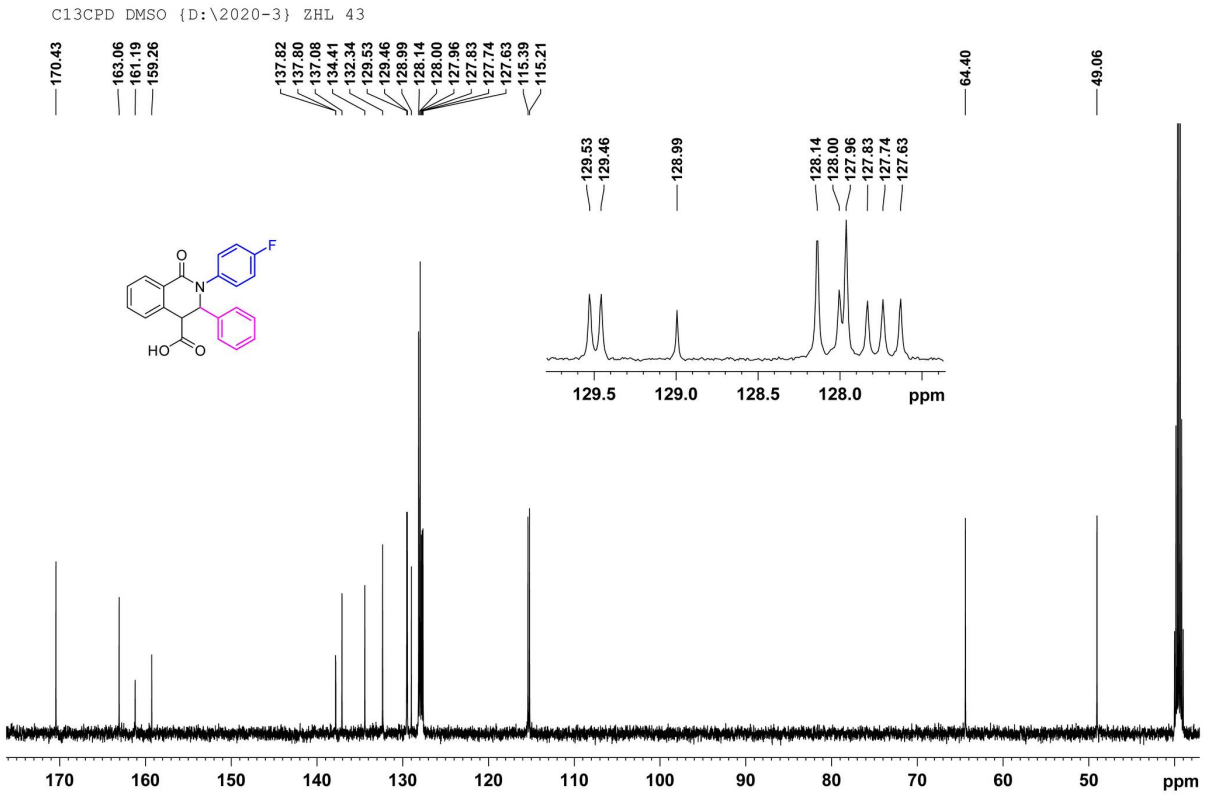

Figure S54. The ^{13}C NMR spectrum of compound **I24**

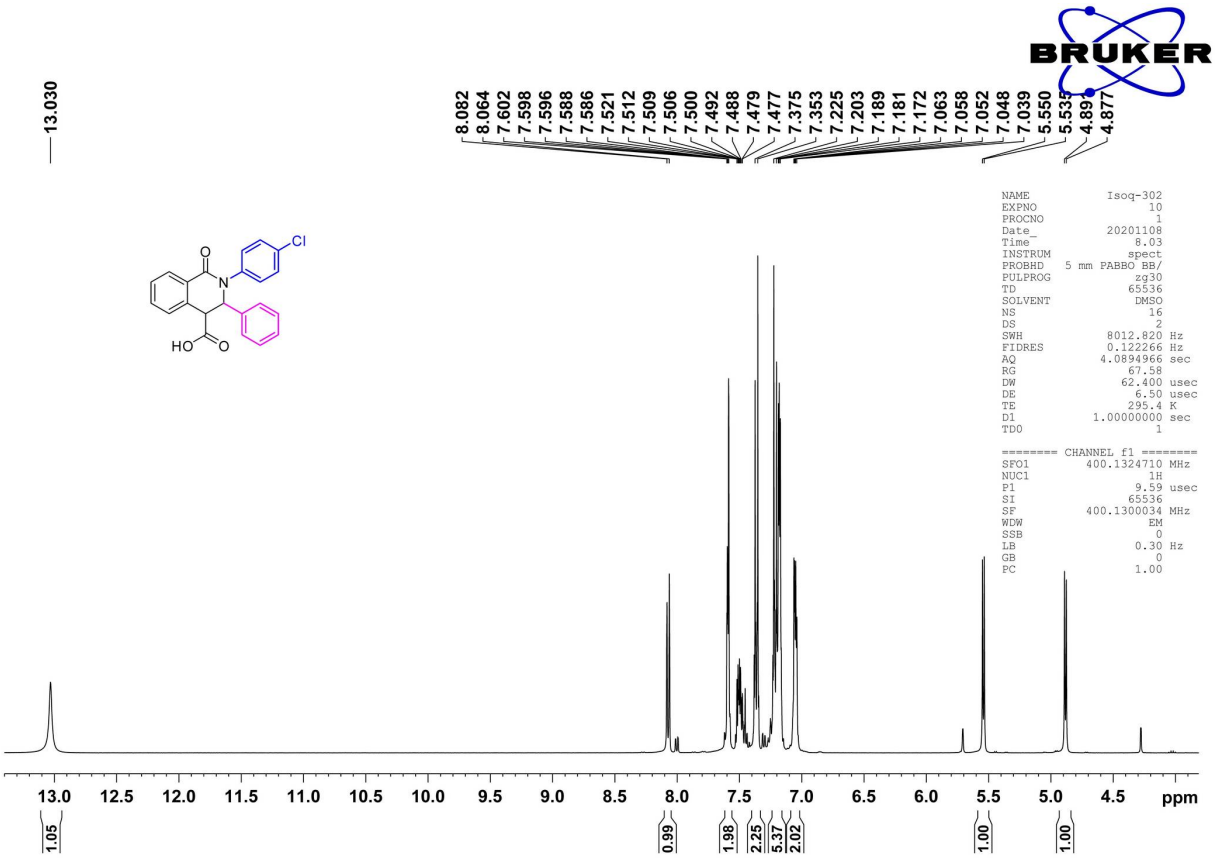

Figure S55. The ^{1}H NMR spectrum of compound **I25**

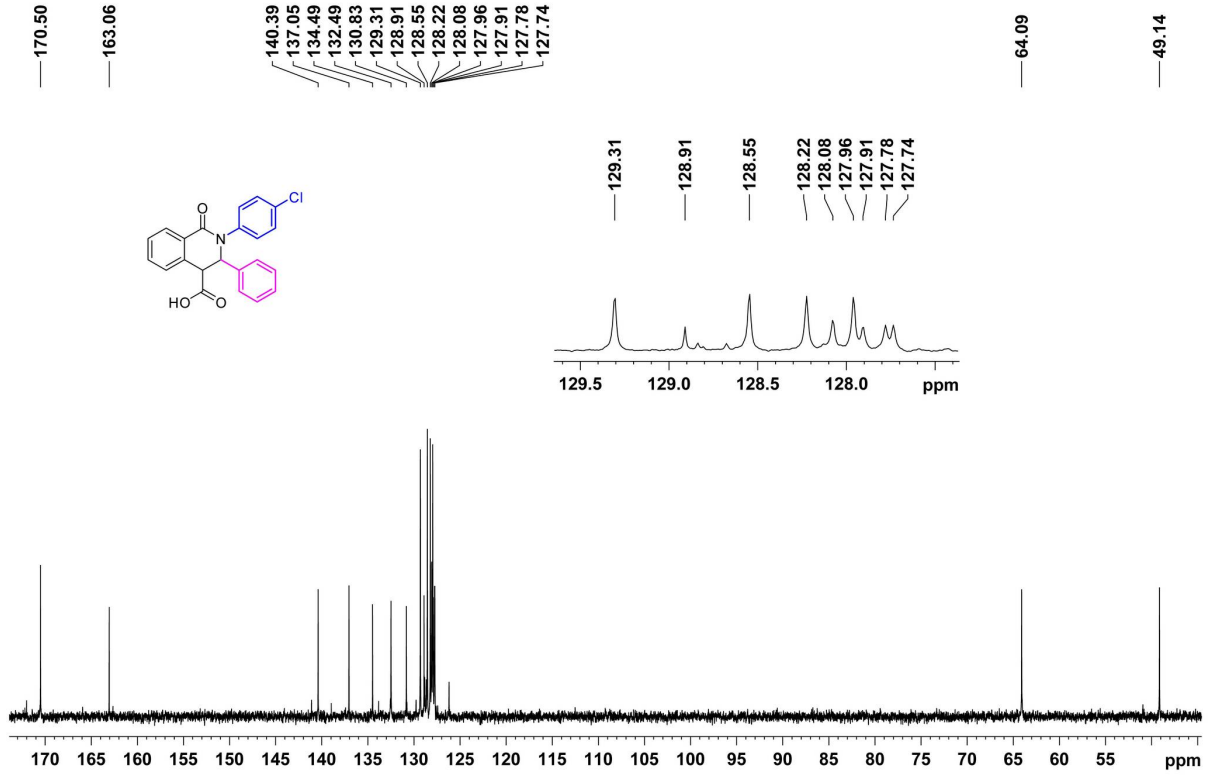

Figure S56. The ^{13}C NMR spectrum of compound **I25**

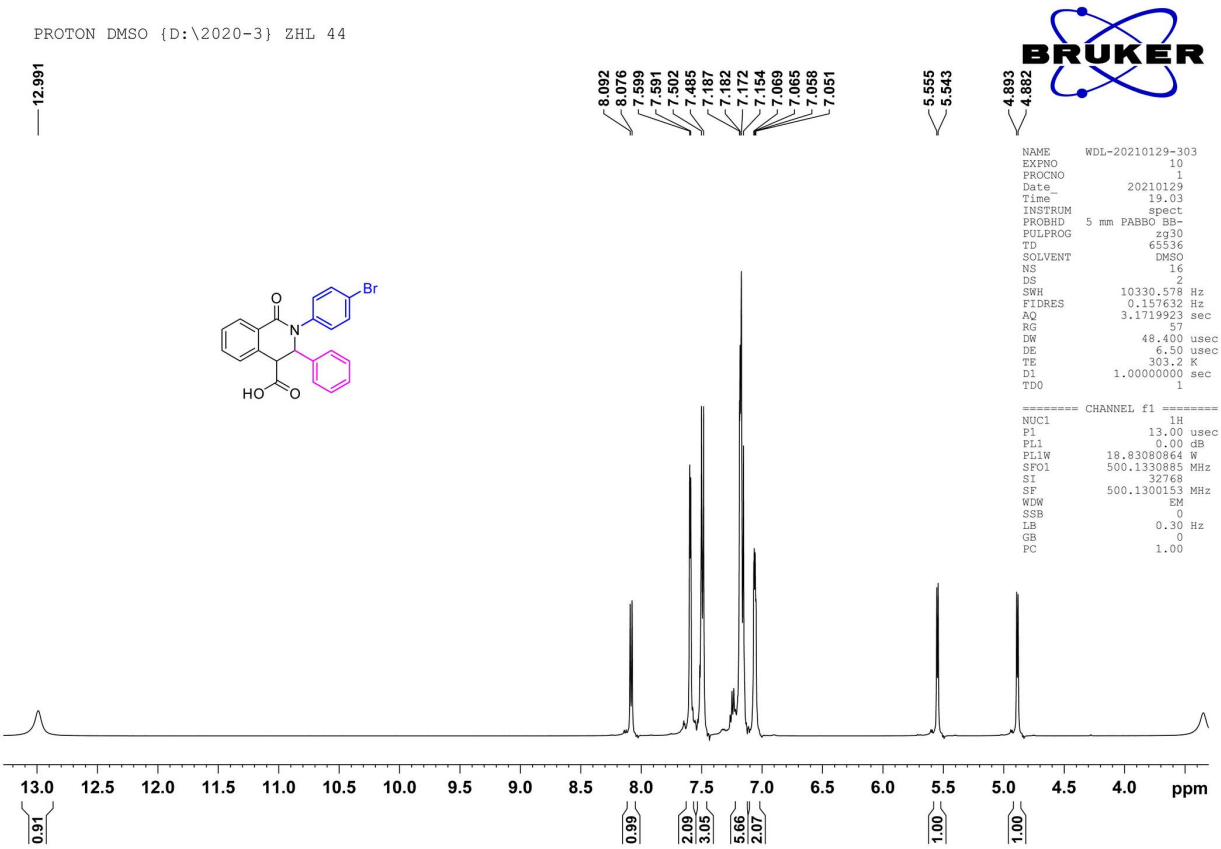

Figure S57. The ^{1}H NMR spectrum of compound **I26**

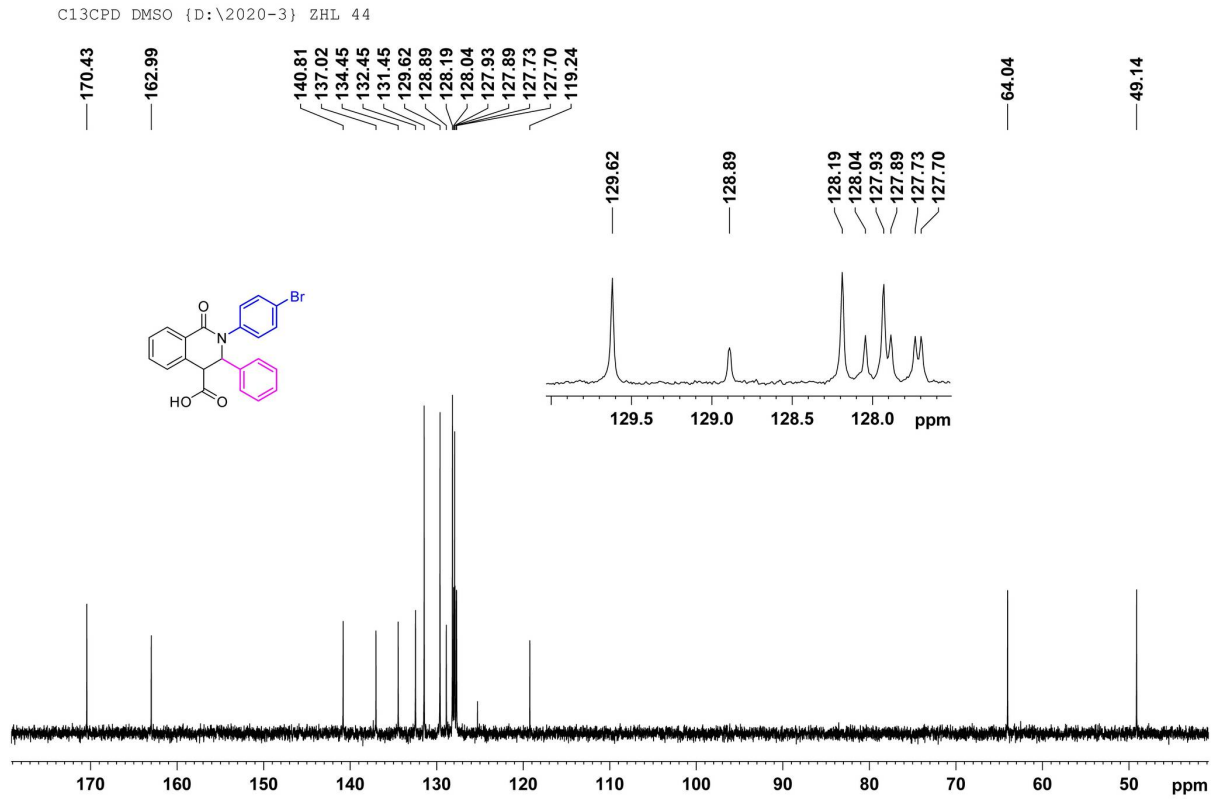

Figure S58. The ^{13}C NMR spectrum of compound **I26**

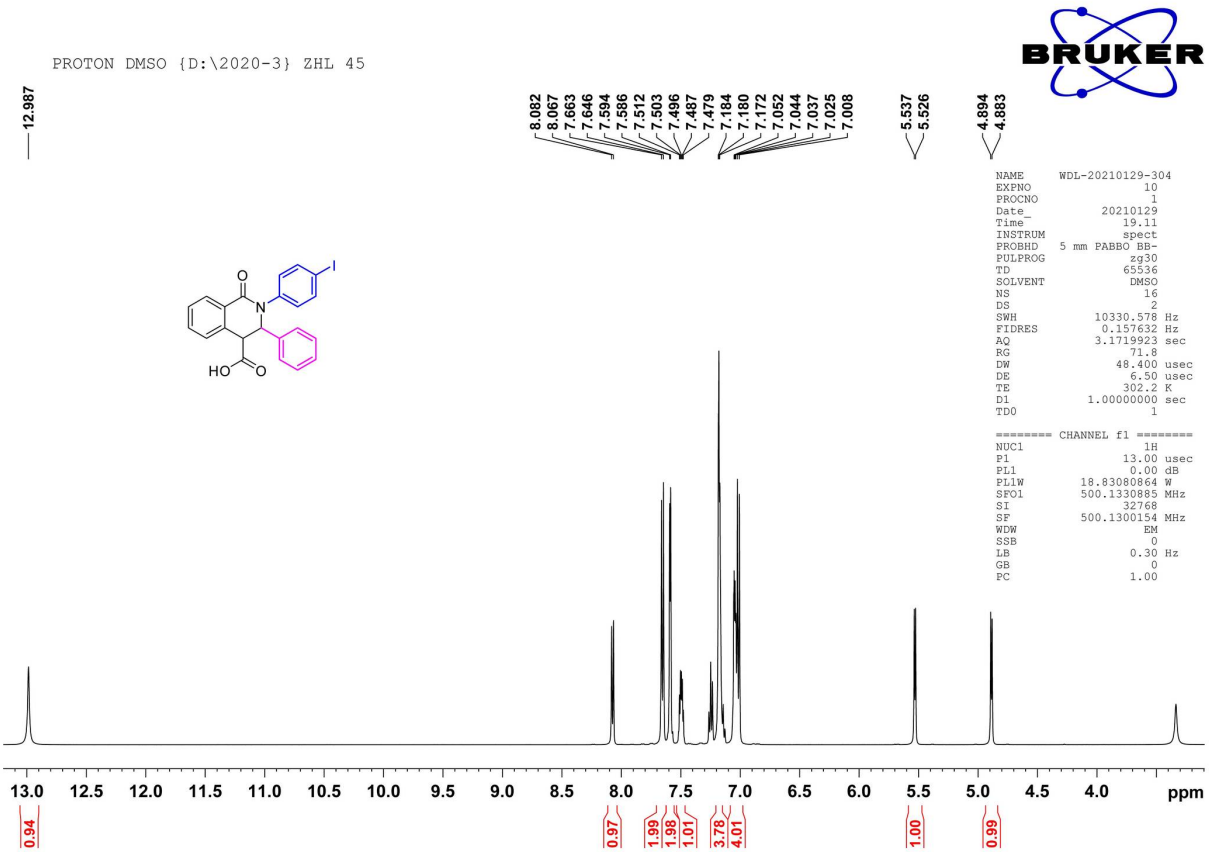

Figure S59. The ^{1}H NMR spectrum of compound **I27**

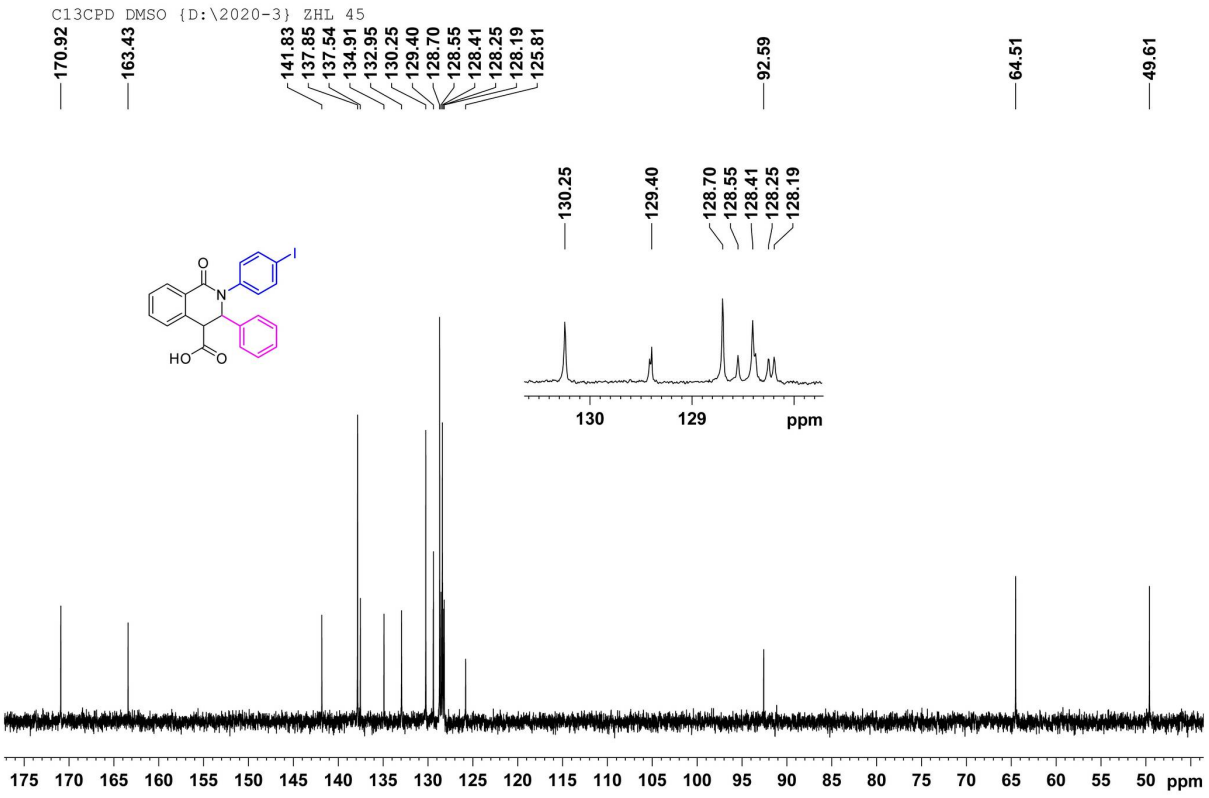

Figure S60. The ^{13}C NMR spectrum of compound **I27**

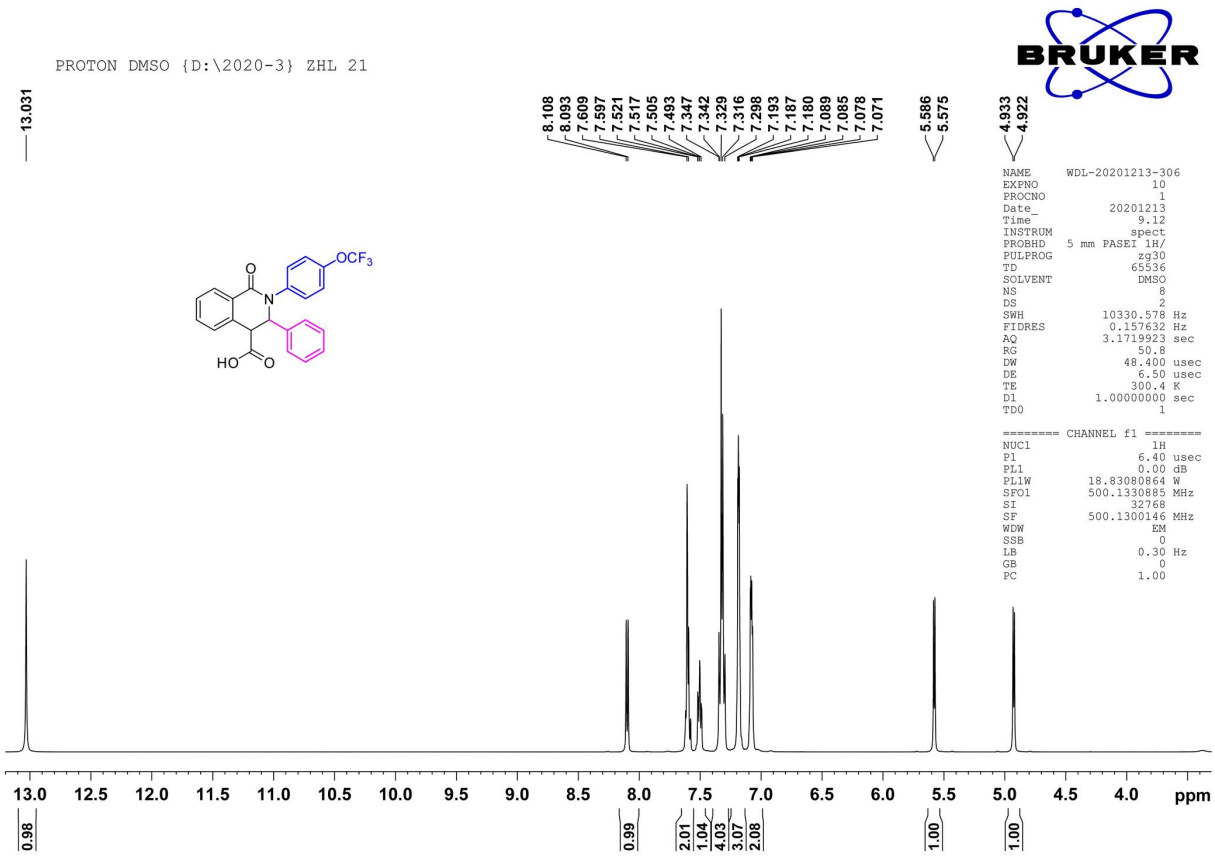

Figure S61. The ^{1}H NMR spectrum of compound **I28**

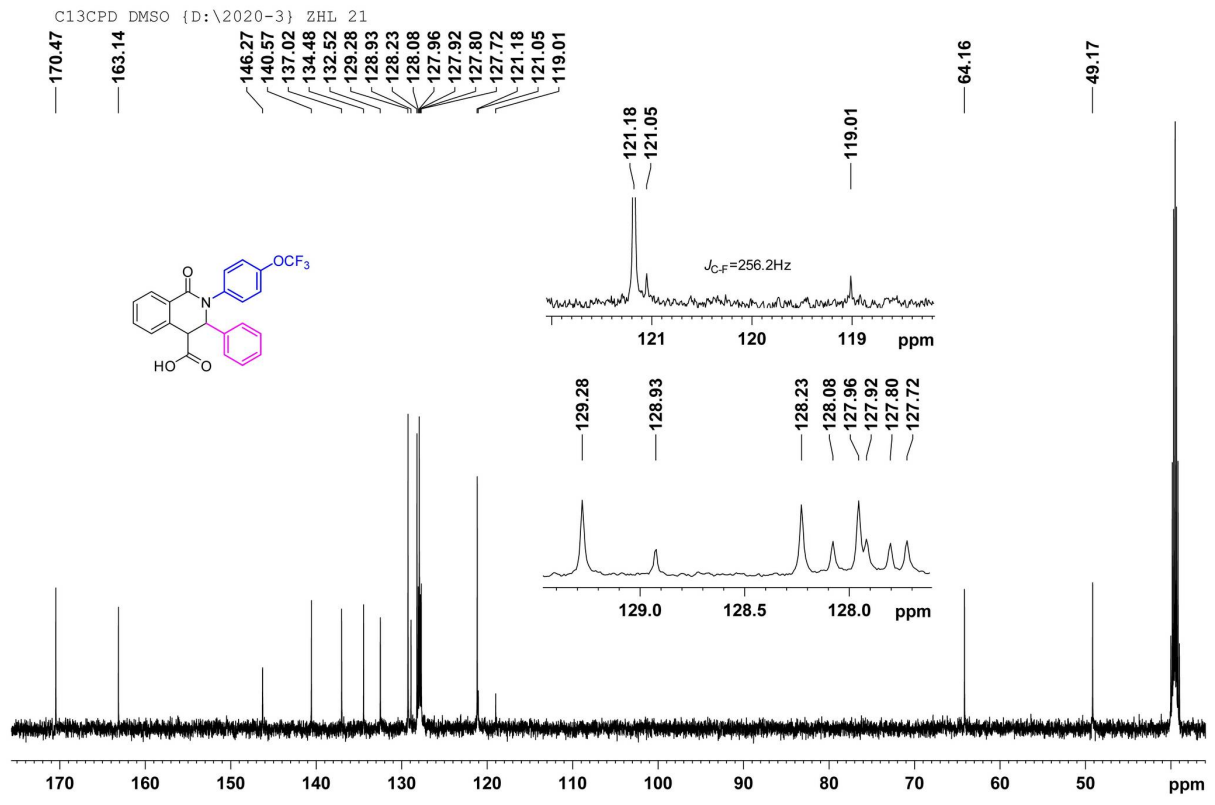

Figure S62. The ^{13}C NMR spectrum of compound **I28**

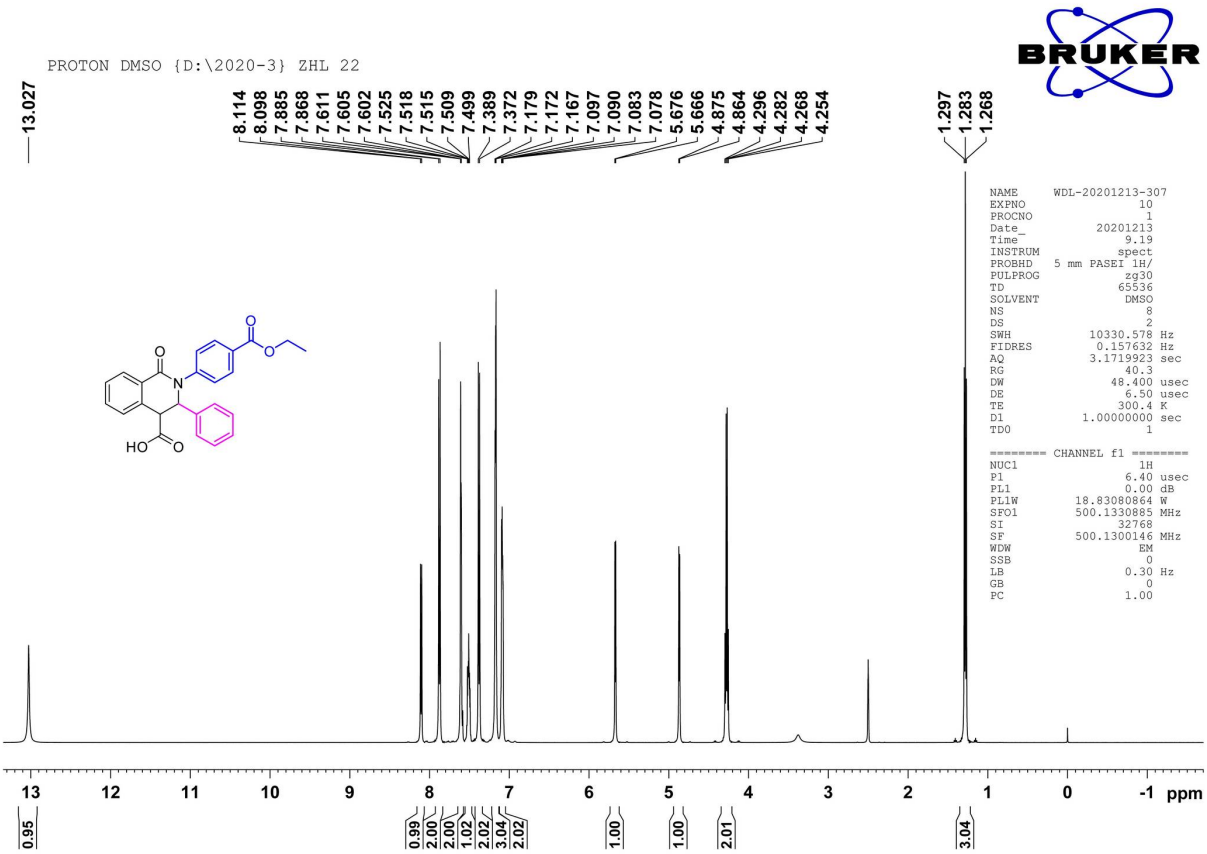

Figure S63. The ^{1}H NMR spectrum of compound **I29**

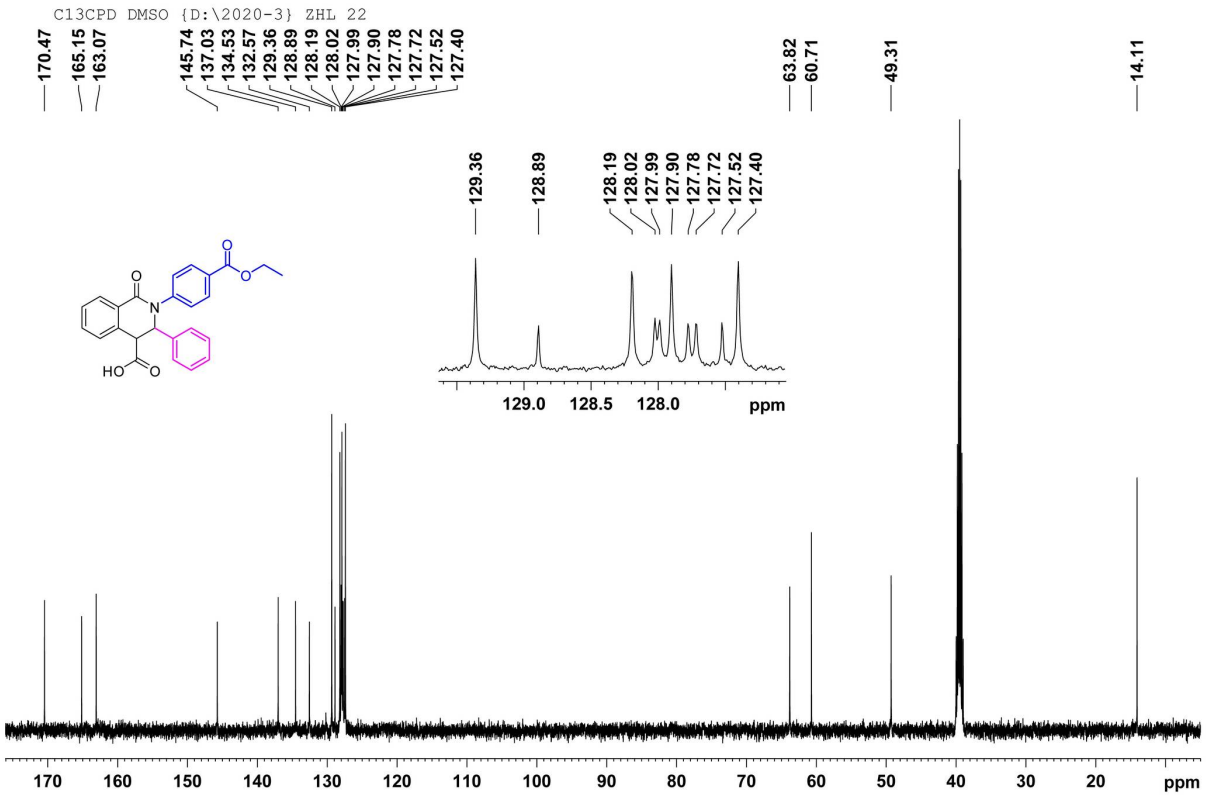

Figure S64. The ^{13}C NMR spectrum of compound **I29**

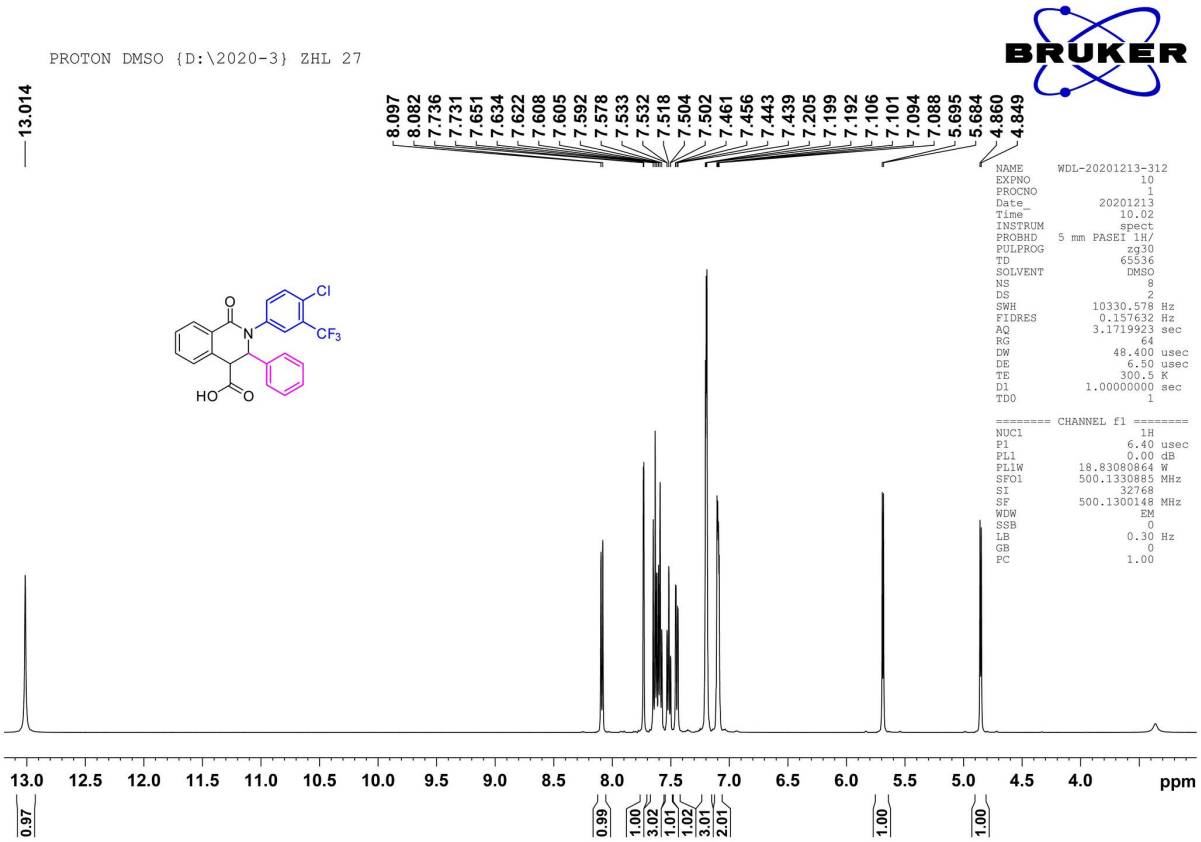

Figure S65. The ^{1}H NMR spectrum of compound **I30**

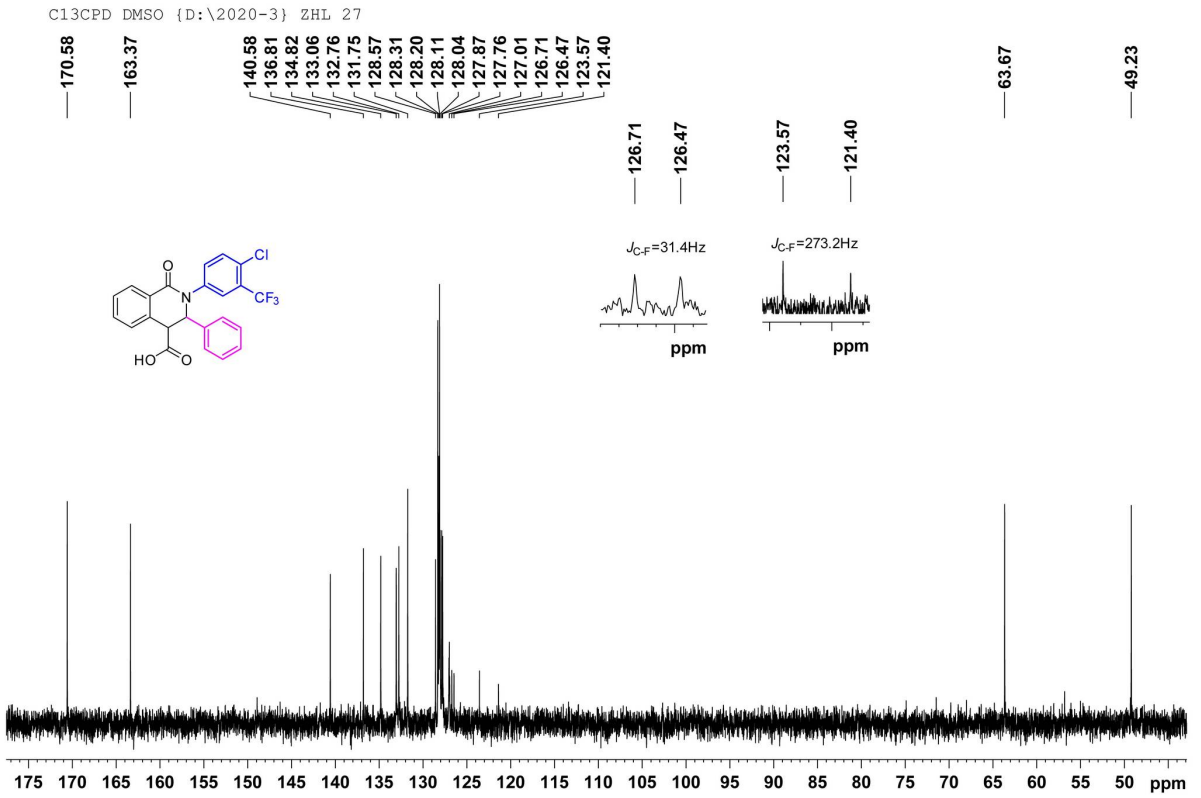

Figure S66. The ^{13}C NMR spectrum of compound **I30**

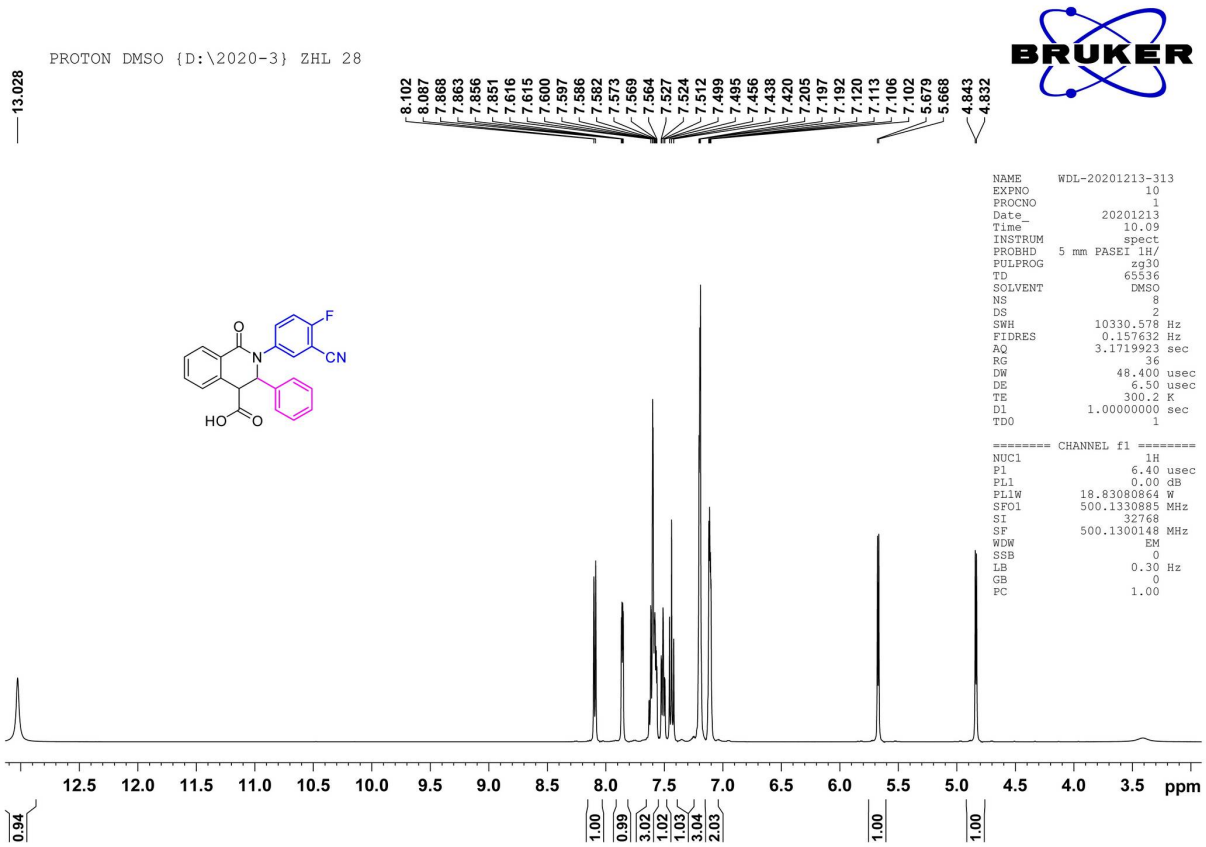

Figure S67. The ^{1}H NMR spectrum of compound **I31**

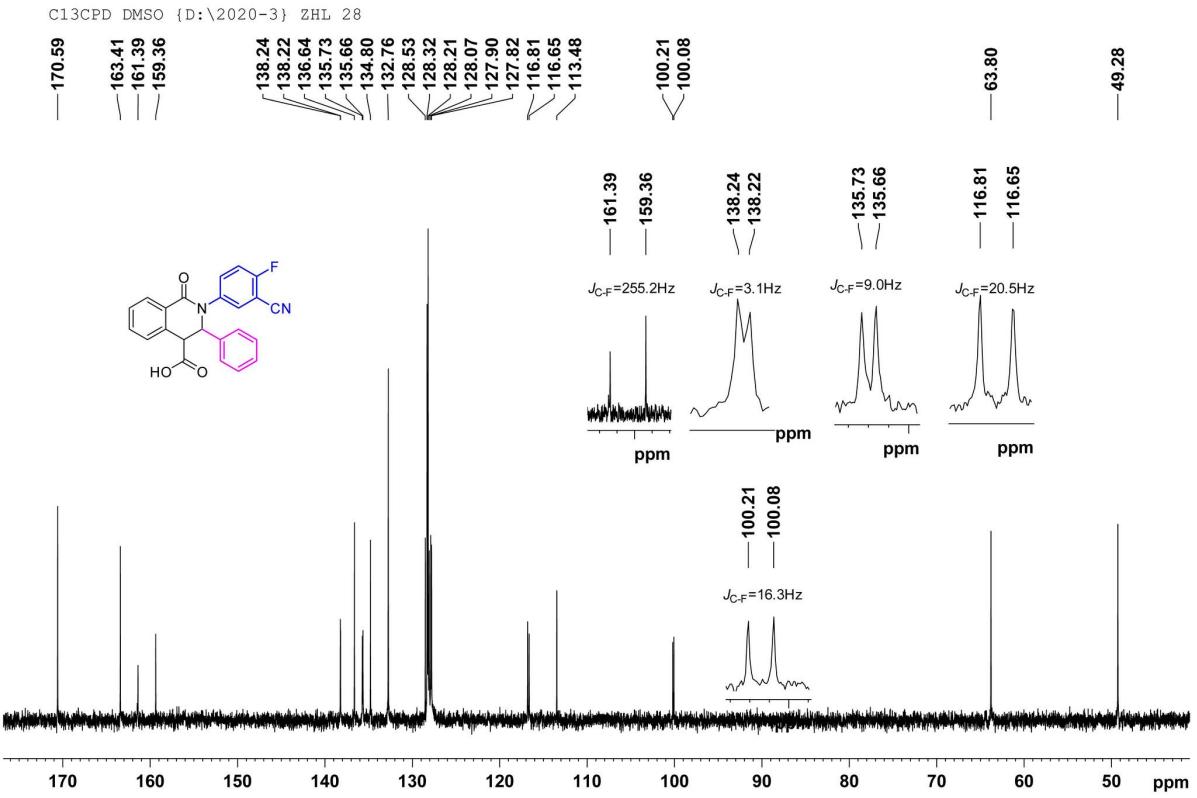

Figure S68. The ^{13}C NMR spectrum of compound **I31**

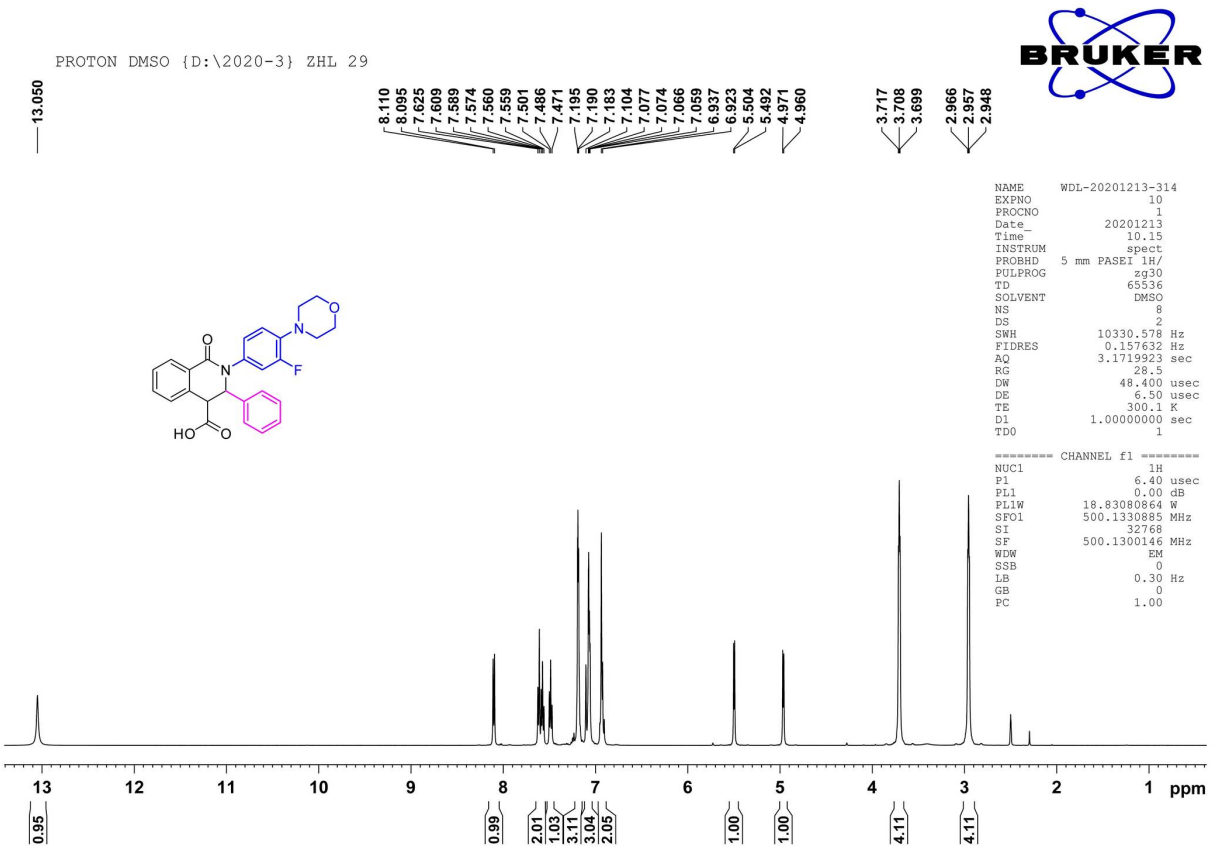

Figure S69. The ^{1}H NMR spectrum of compound **I32**

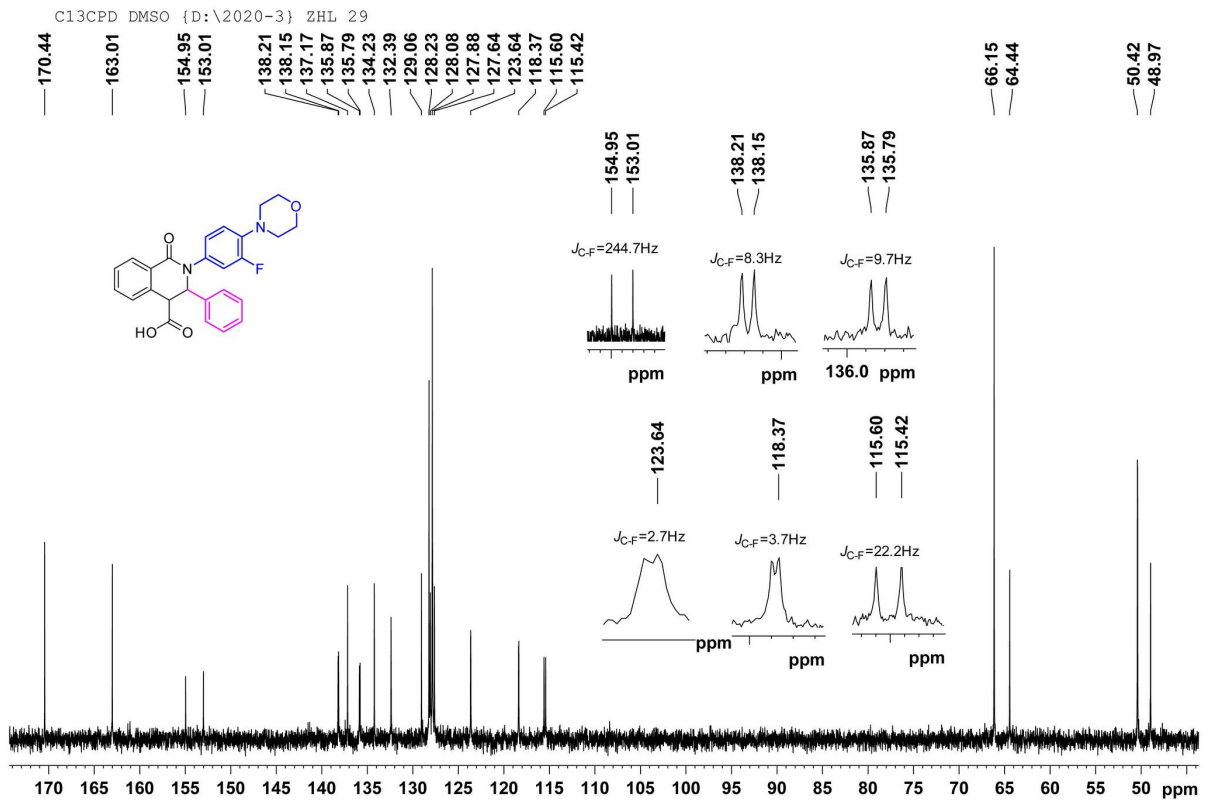

Figure S70. The ^{13}C NMR spectrum of compound **I32**

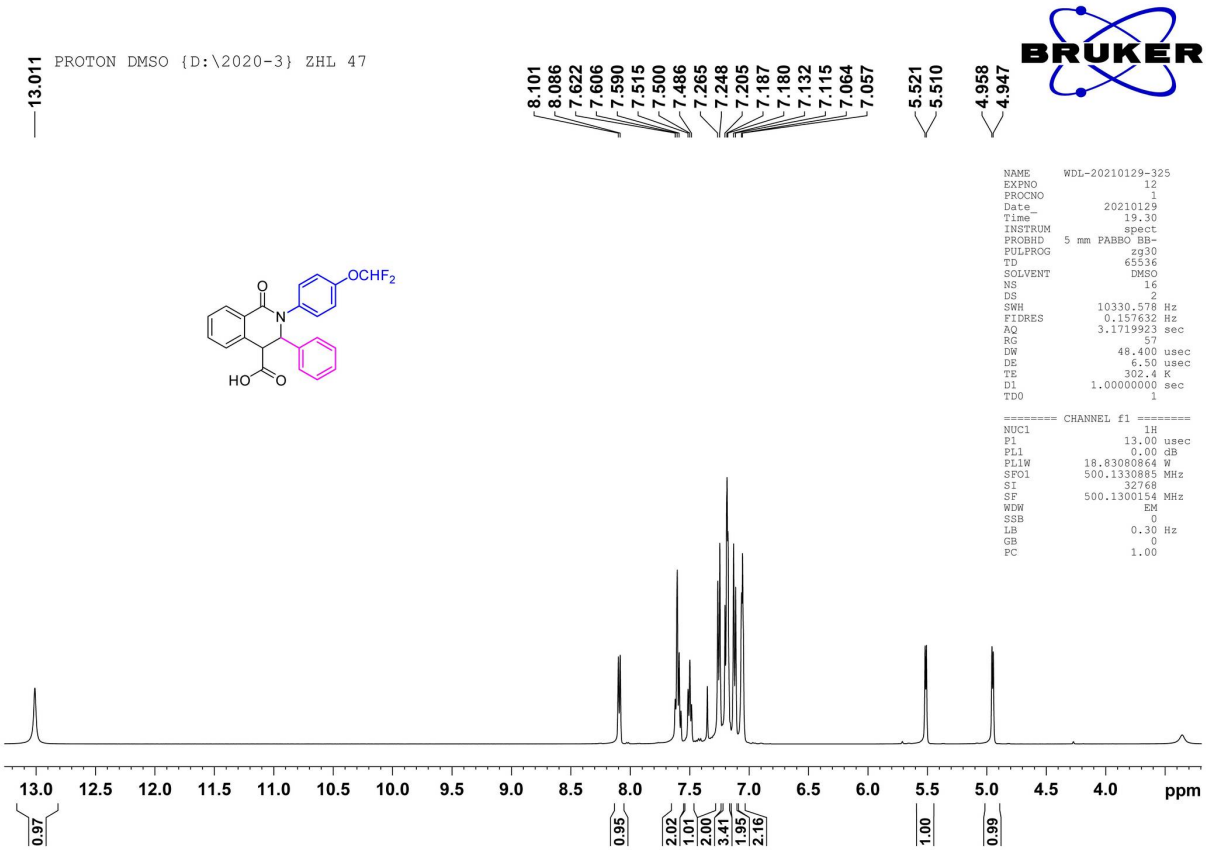

Figure S71. The ^{1}H NMR spectrum of compound **I33**

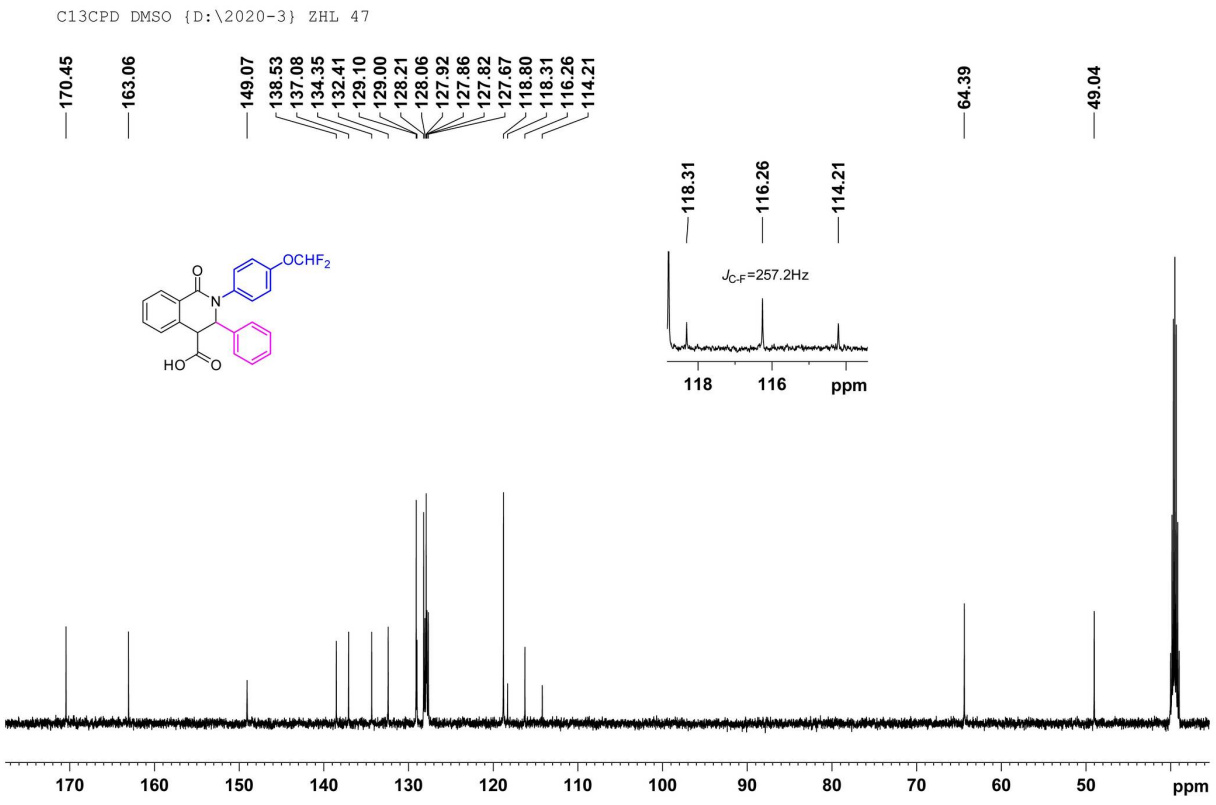

Figure S72. The ^{13}C NMR spectrum of compound **I33**

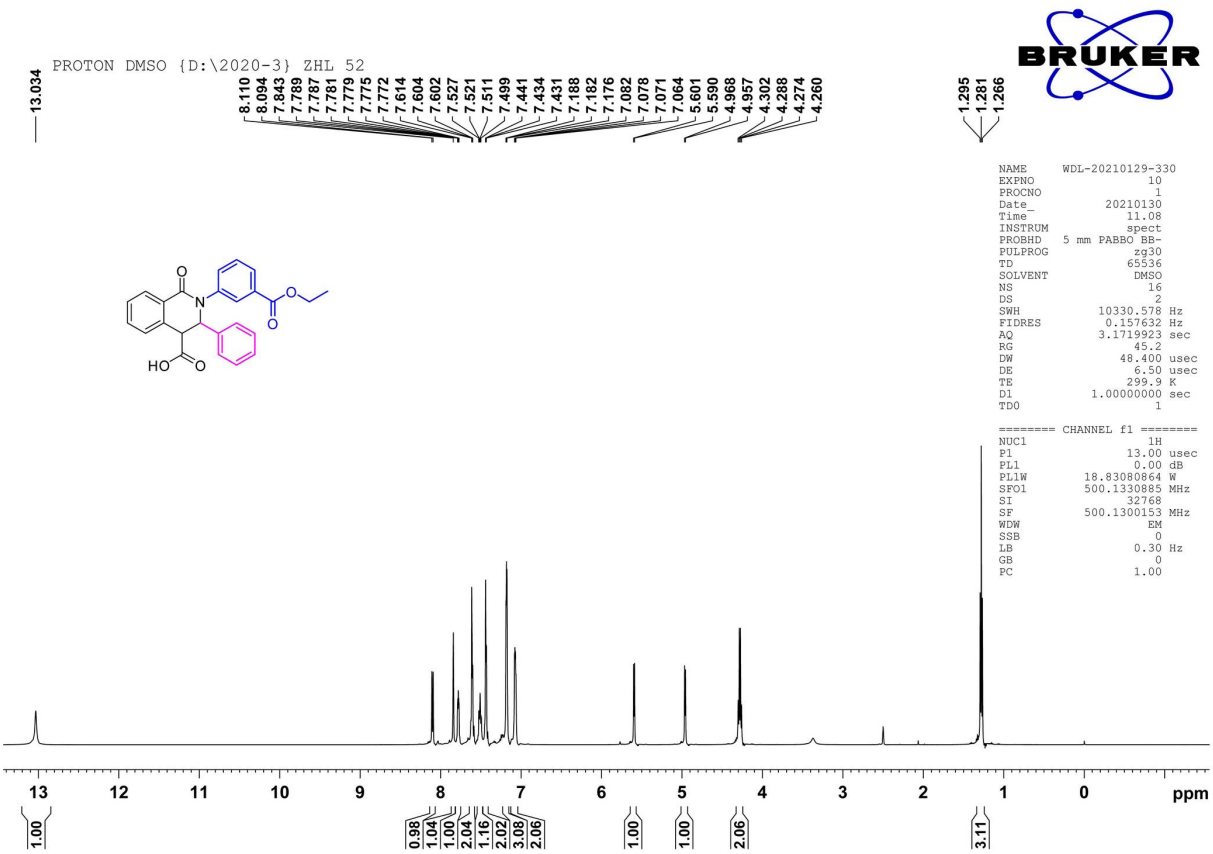

Figure S73. The ^{1}H NMR spectrum of compound **I34**

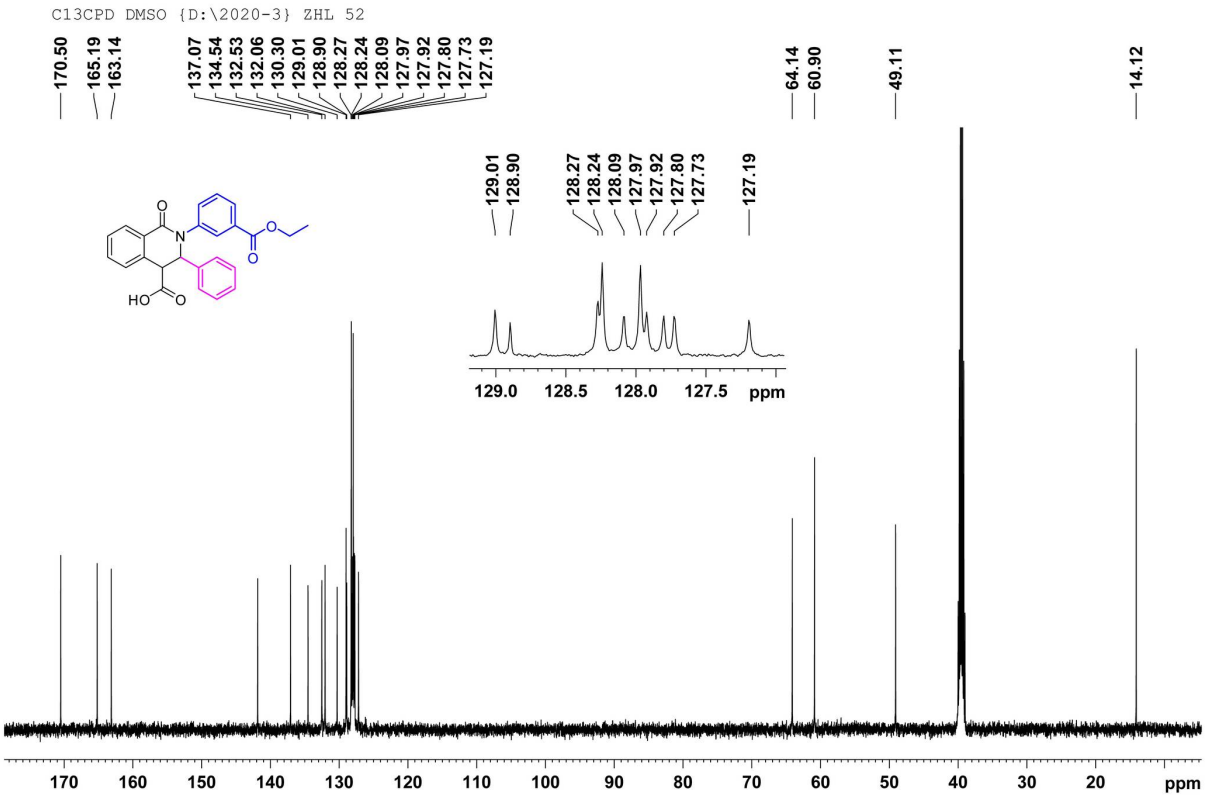

Figure S74. The ^{13}C NMR spectrum of compound **I34**

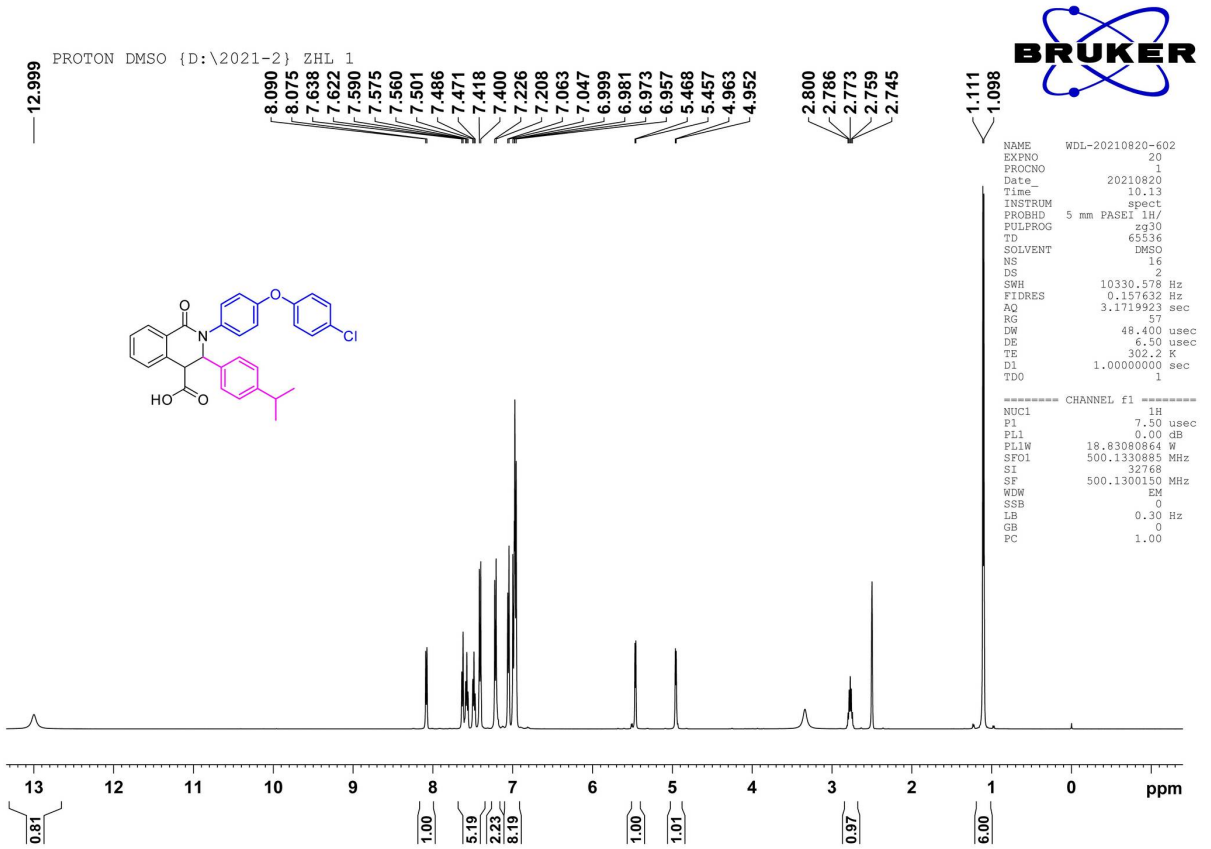

Figure S75. The ^{1}H NMR spectrum of compound **II1**

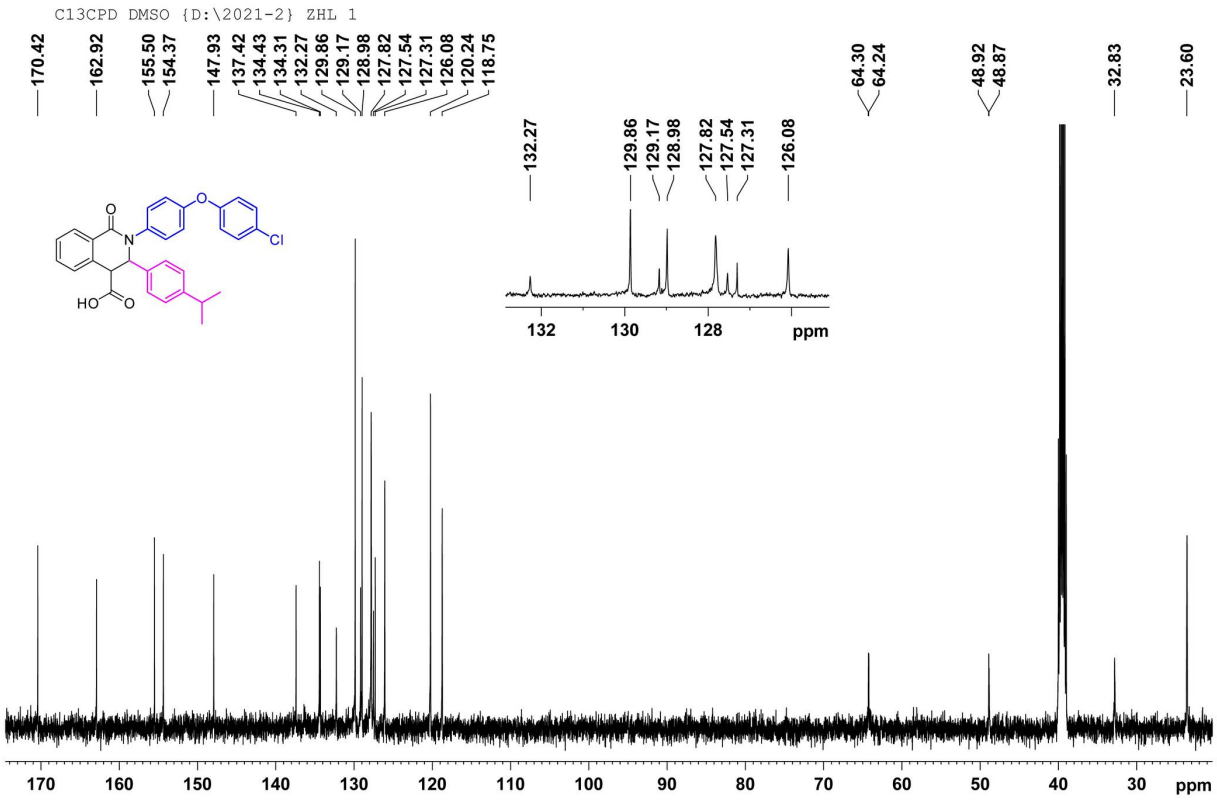

Figure S76. The ^{13}C NMR spectrum of compound **II1**

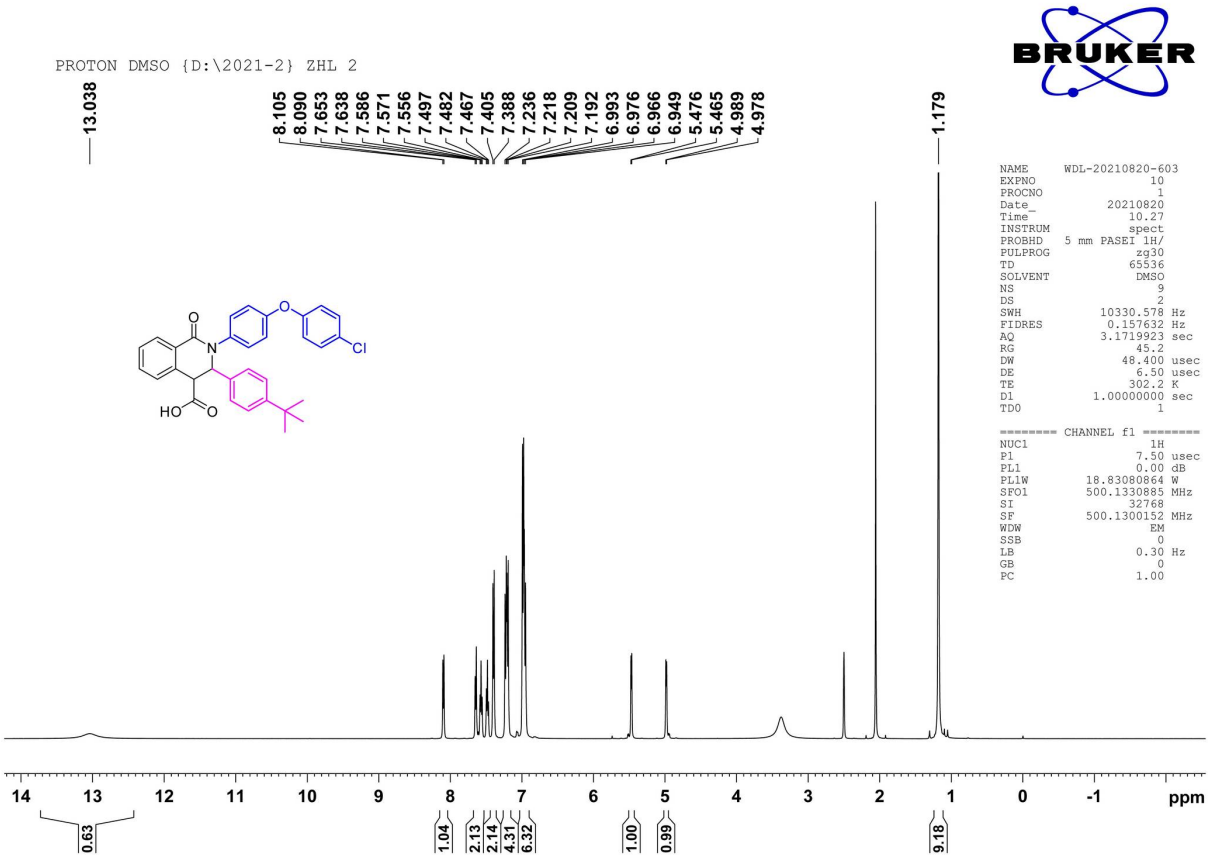

Figure S77. The ^{1}H NMR spectrum of compound **II2**

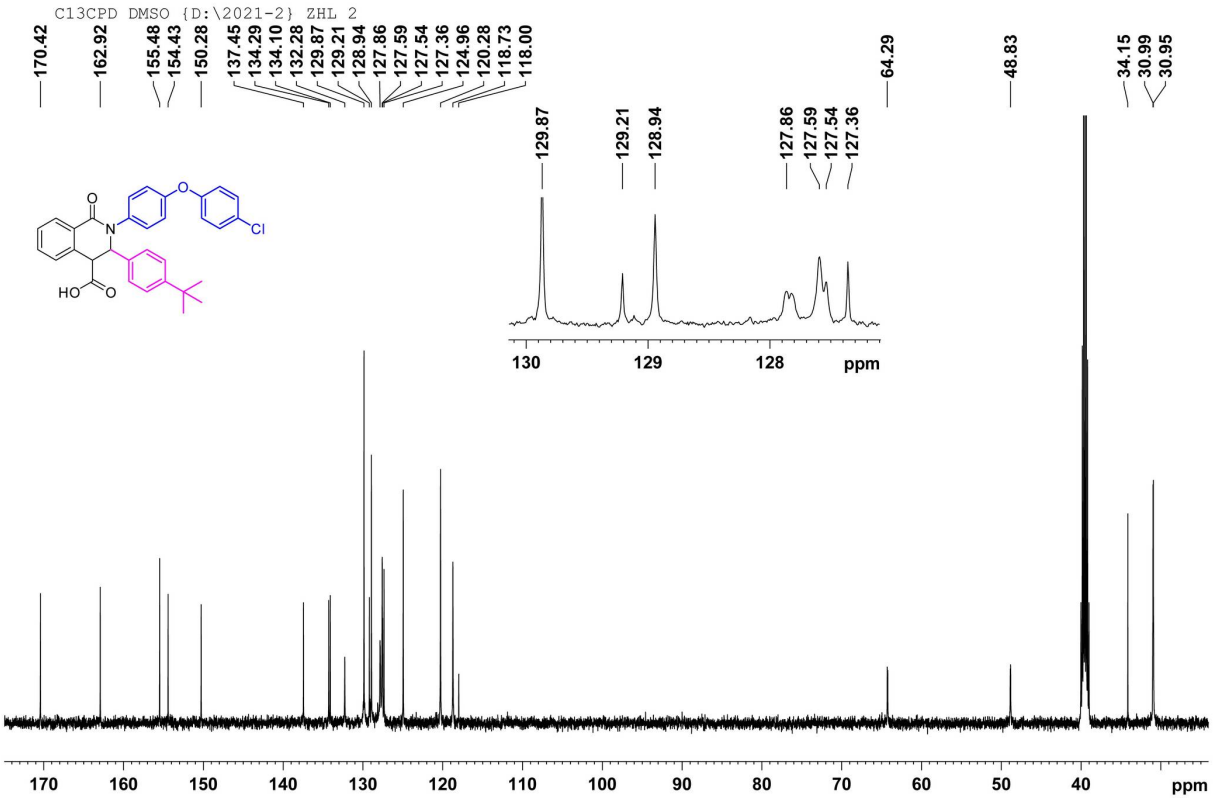

Figure S78. The ^{13}C NMR spectrum of compound **II2**

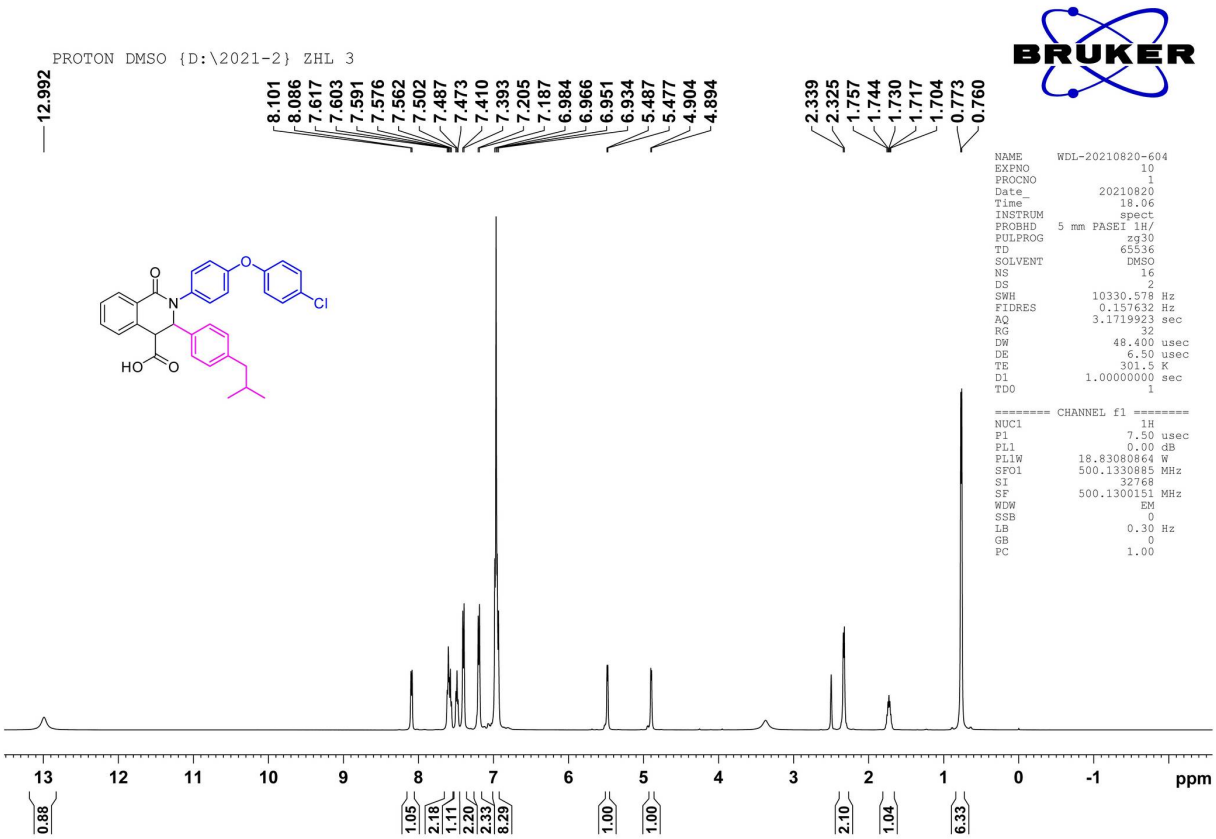

Figure S79. The ^{1}H NMR spectrum of compound **II3**

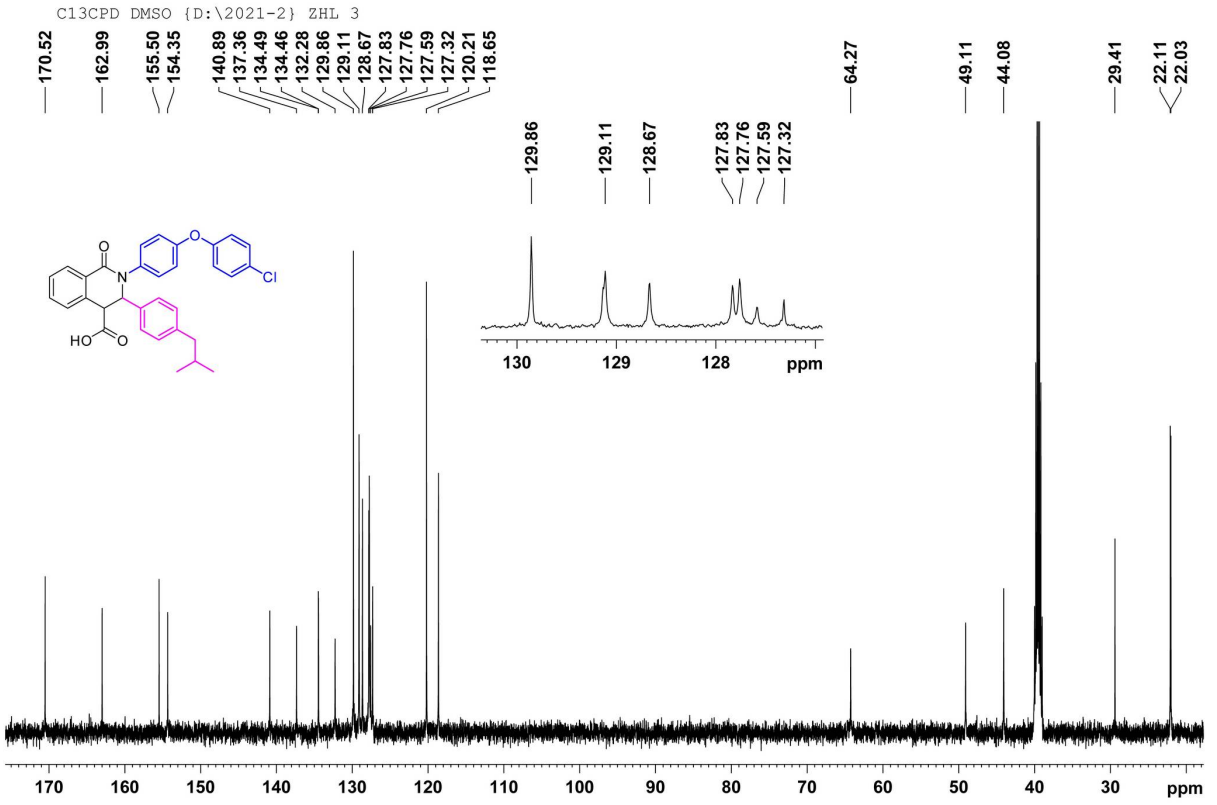

Figure S80. The ^{13}C NMR spectrum of compound **II3**

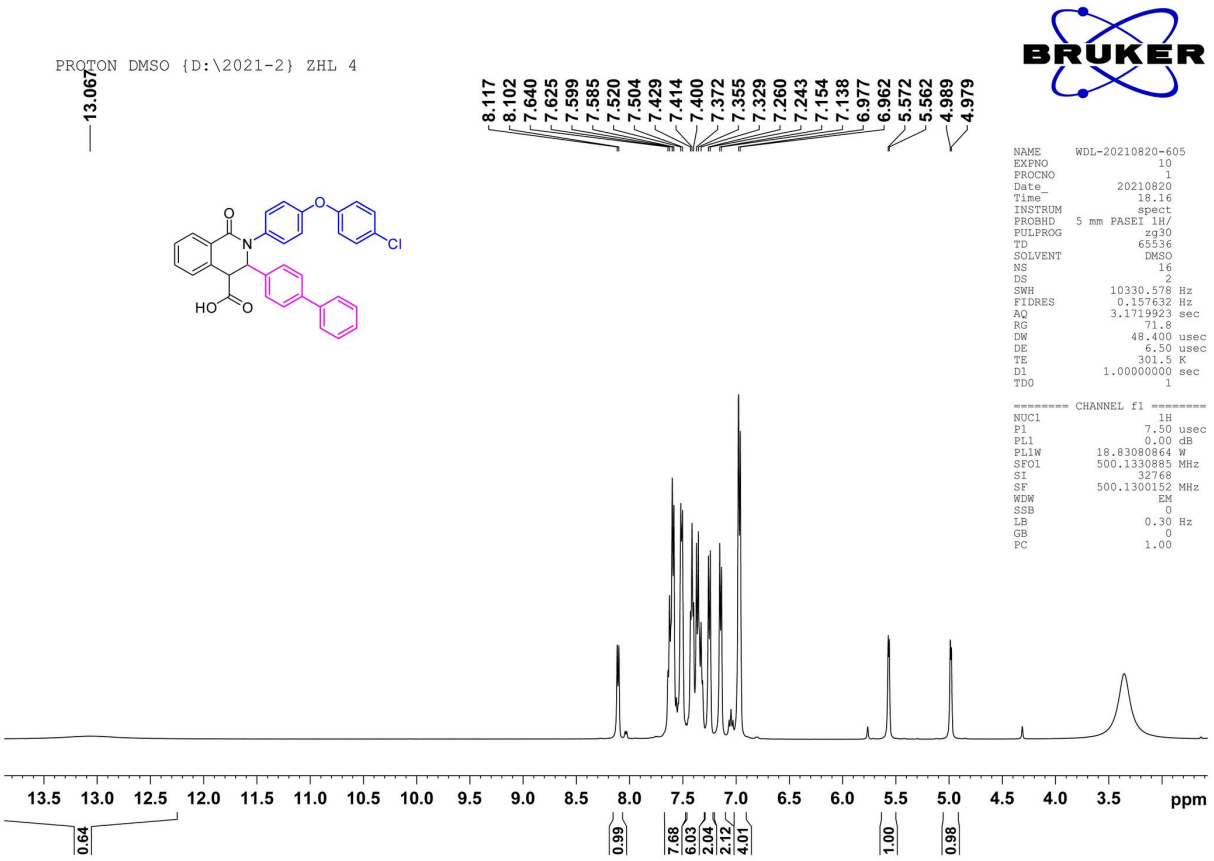

Figure S81. The ^{1}H NMR spectrum of compound **II4**

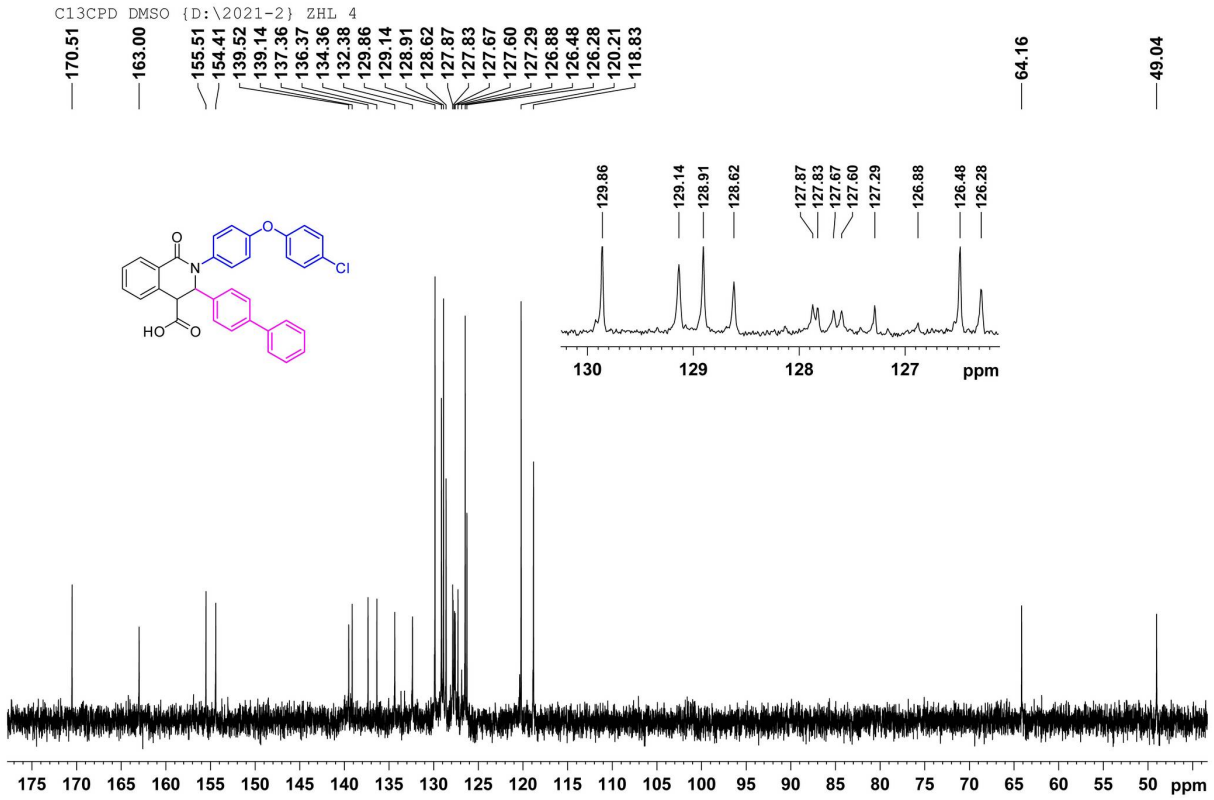

Figure S82. The ^{13}C NMR spectrum of compound **II4**

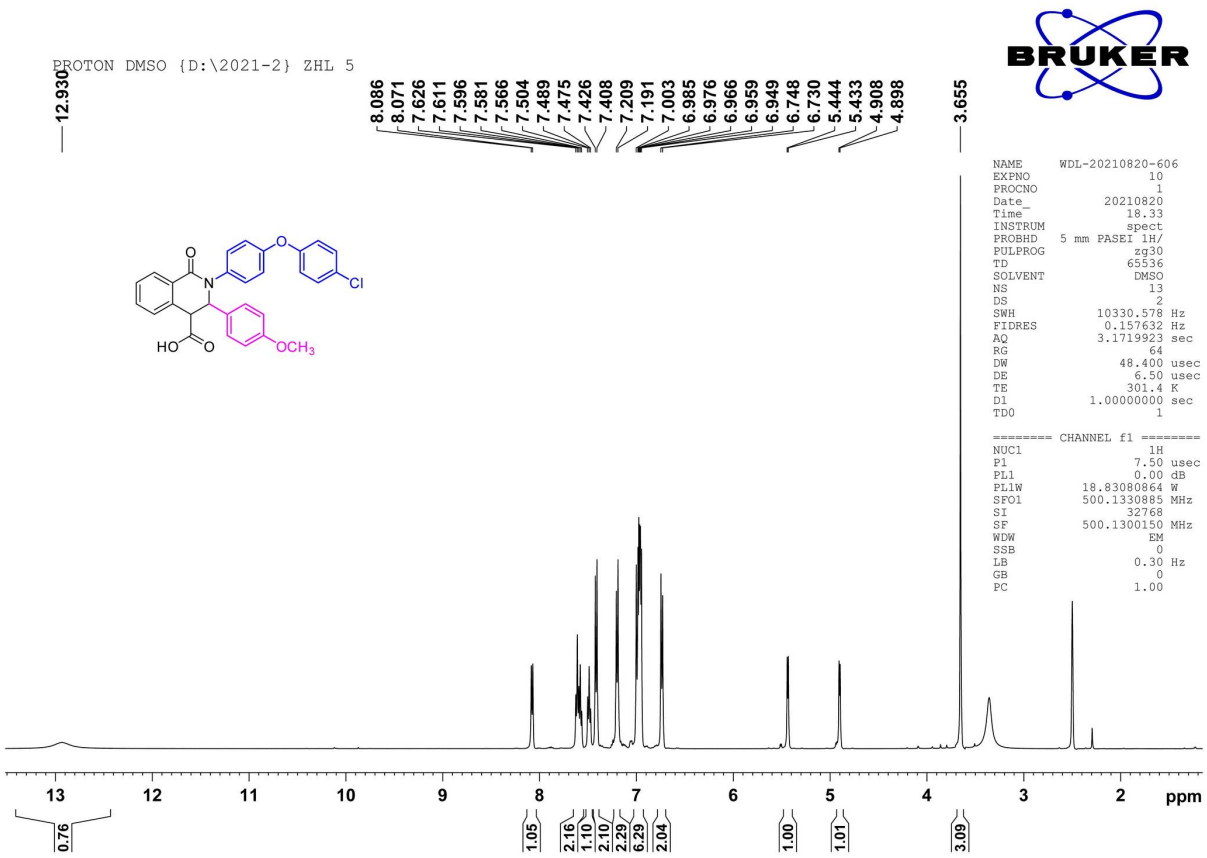

Figure S83. The ^{1}H NMR spectrum of compound **II5**

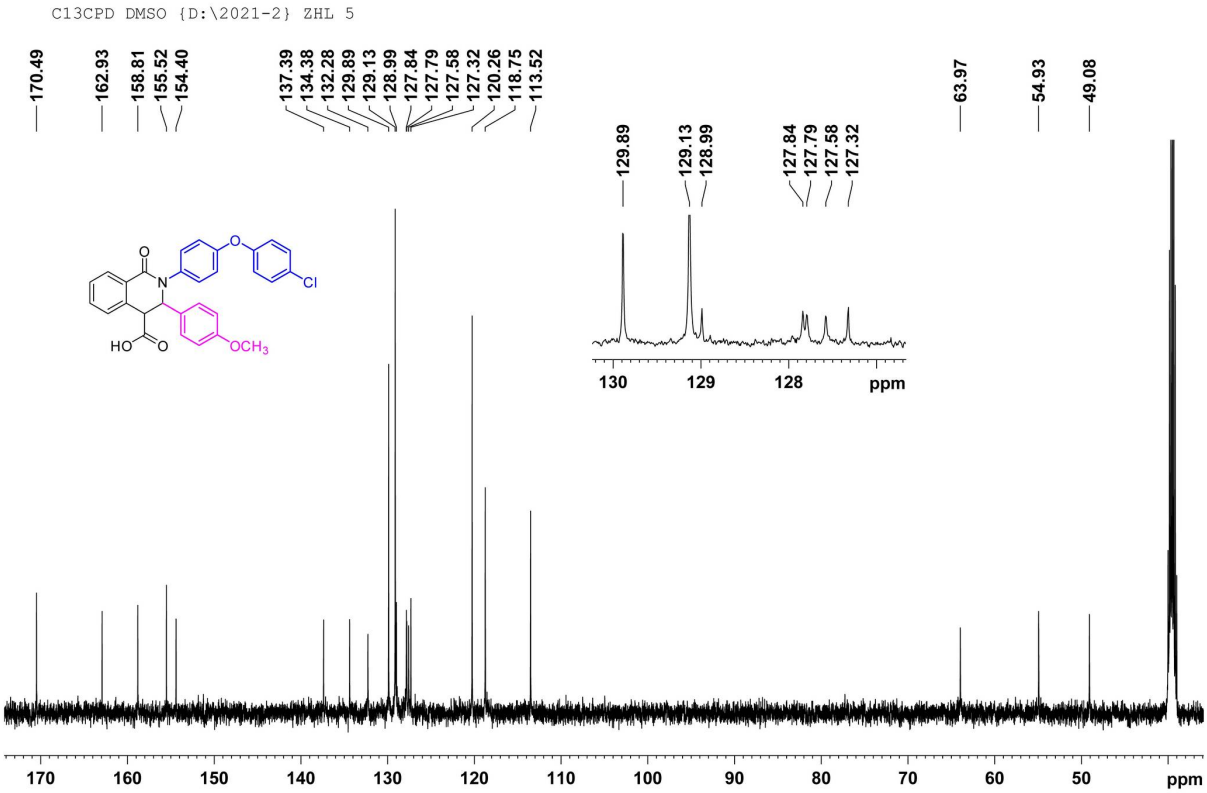

Figure S84. The ^{13}C NMR spectrum of compound **II5**

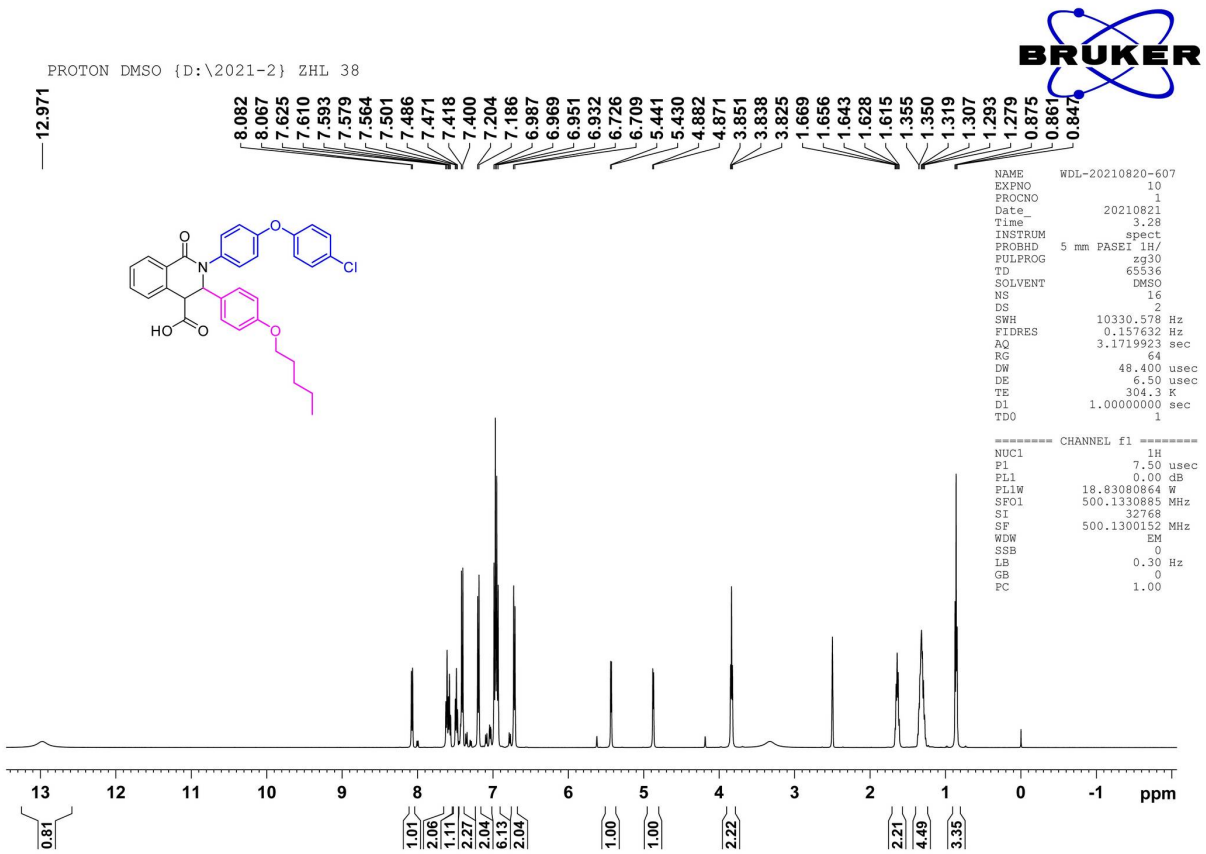

Figure S85. The ^{1}H NMR spectrum of compound **II6**

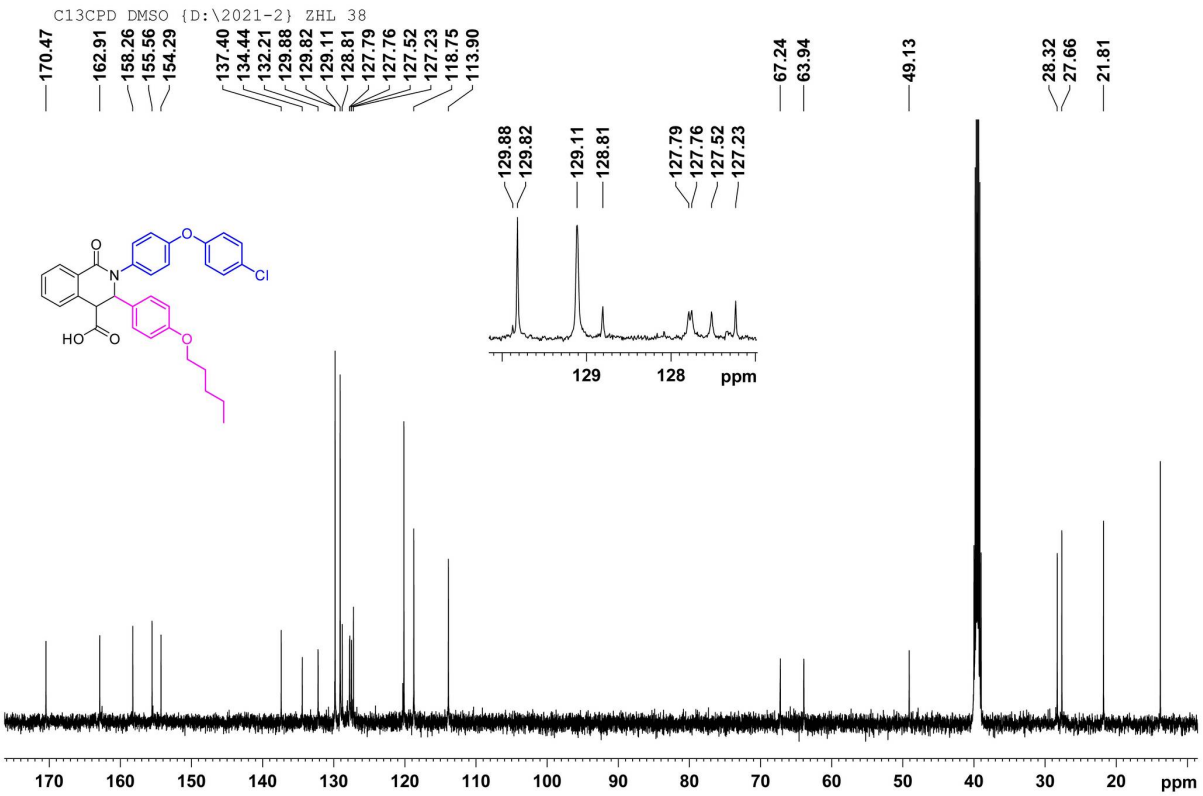

Figure S86. The ^{13}C NMR spectrum of compound **II6**

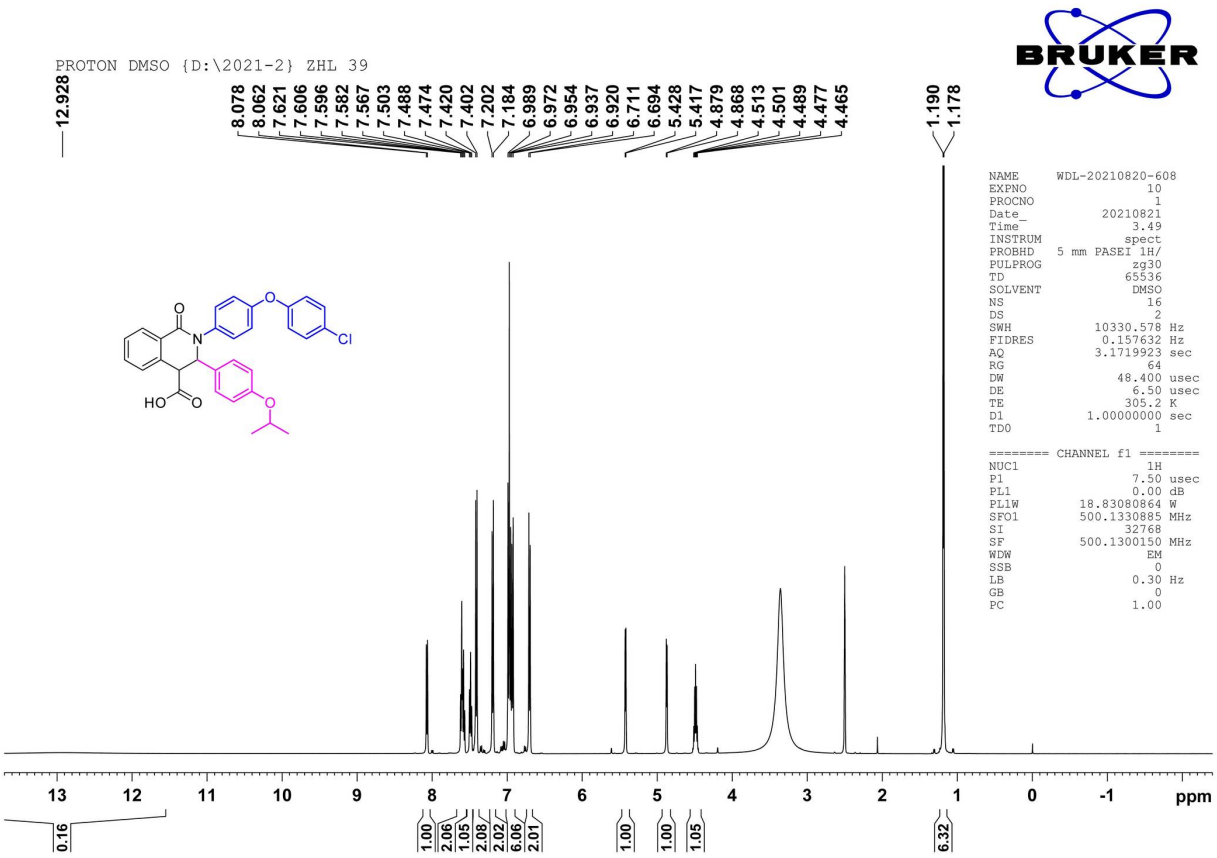

Figure S87. The ^{1}H NMR spectrum of compound **II7**

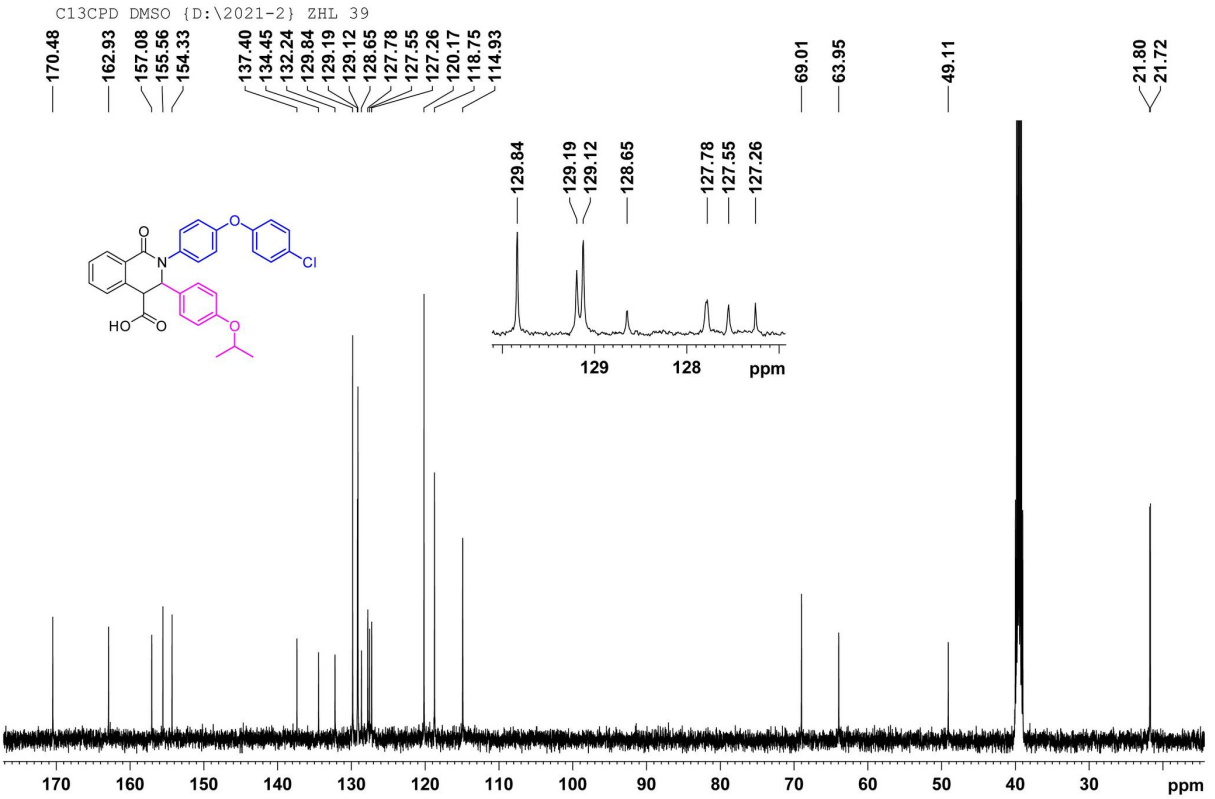

Figure S88. The ^{13}C NMR spectrum of compound **II7**

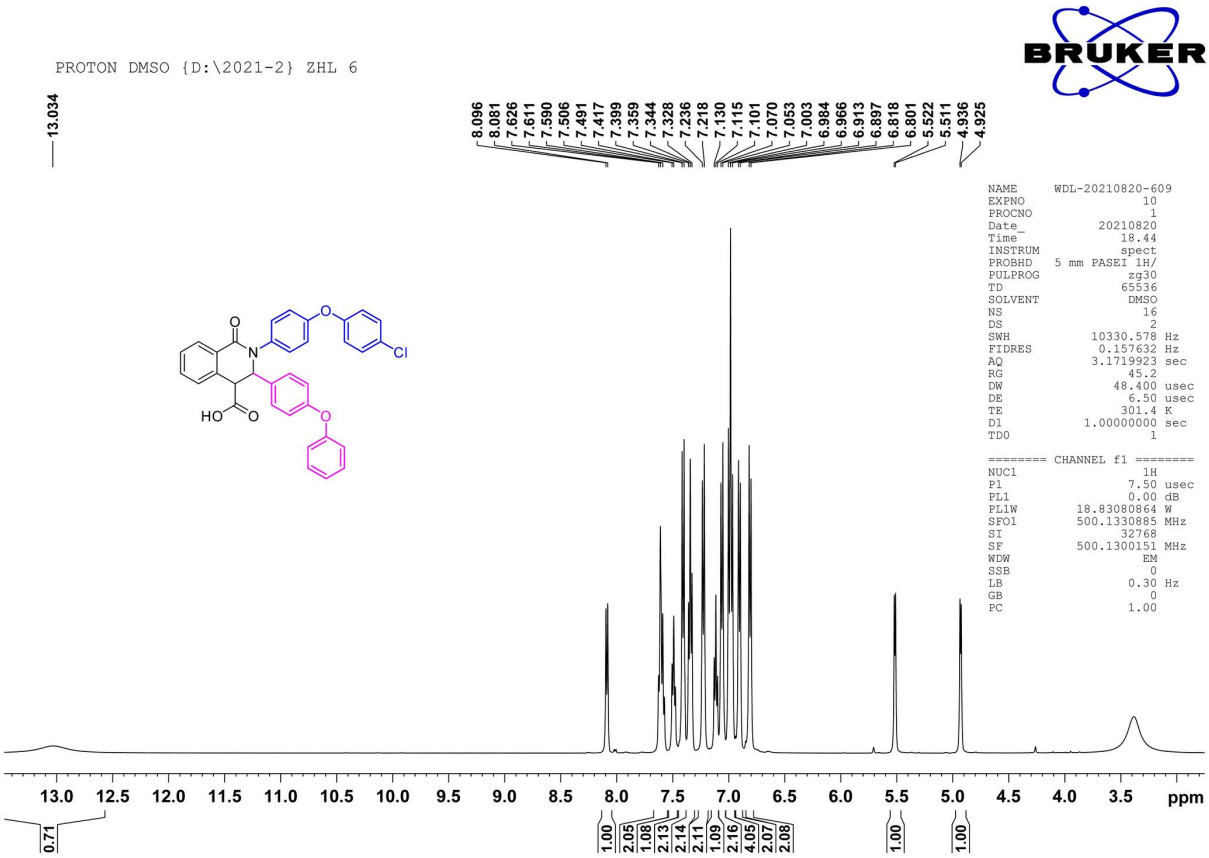

Figure S89. The ^{1}H NMR spectrum of compound **II8**

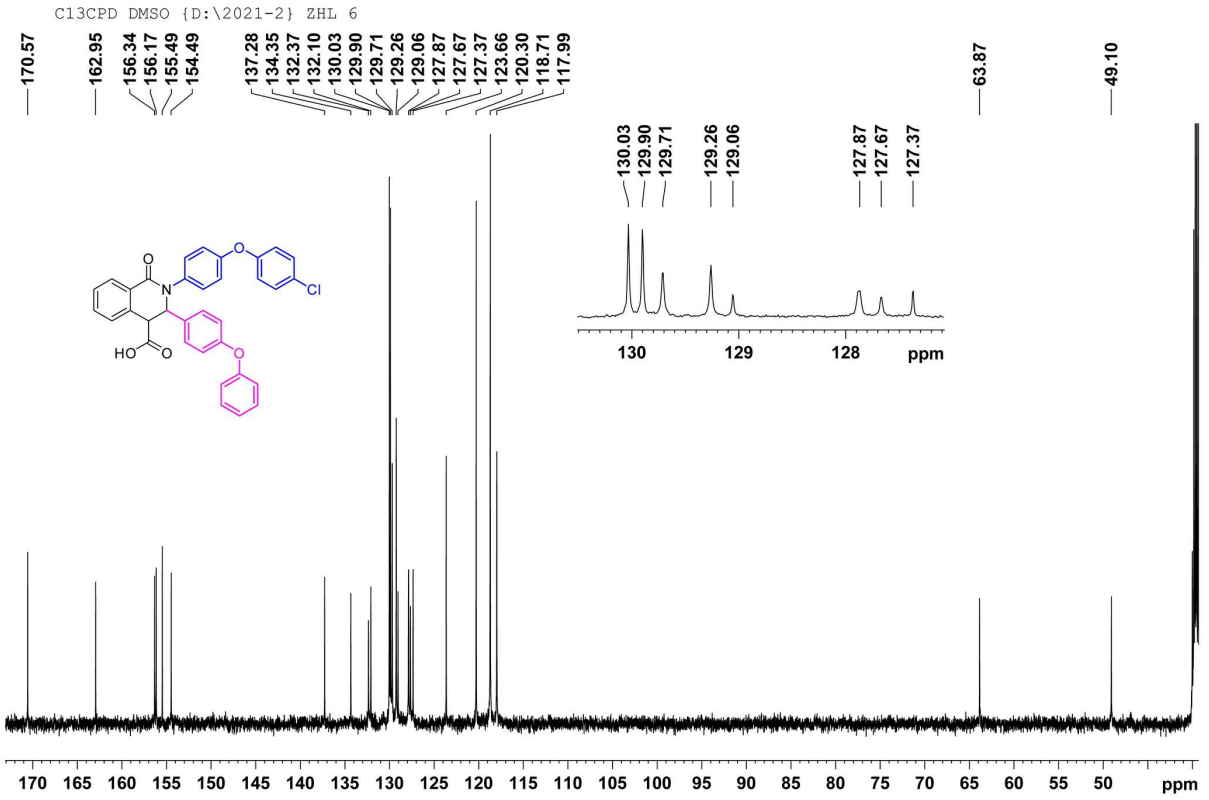

Figure S90. The ^{13}C NMR spectrum of compound **II8**

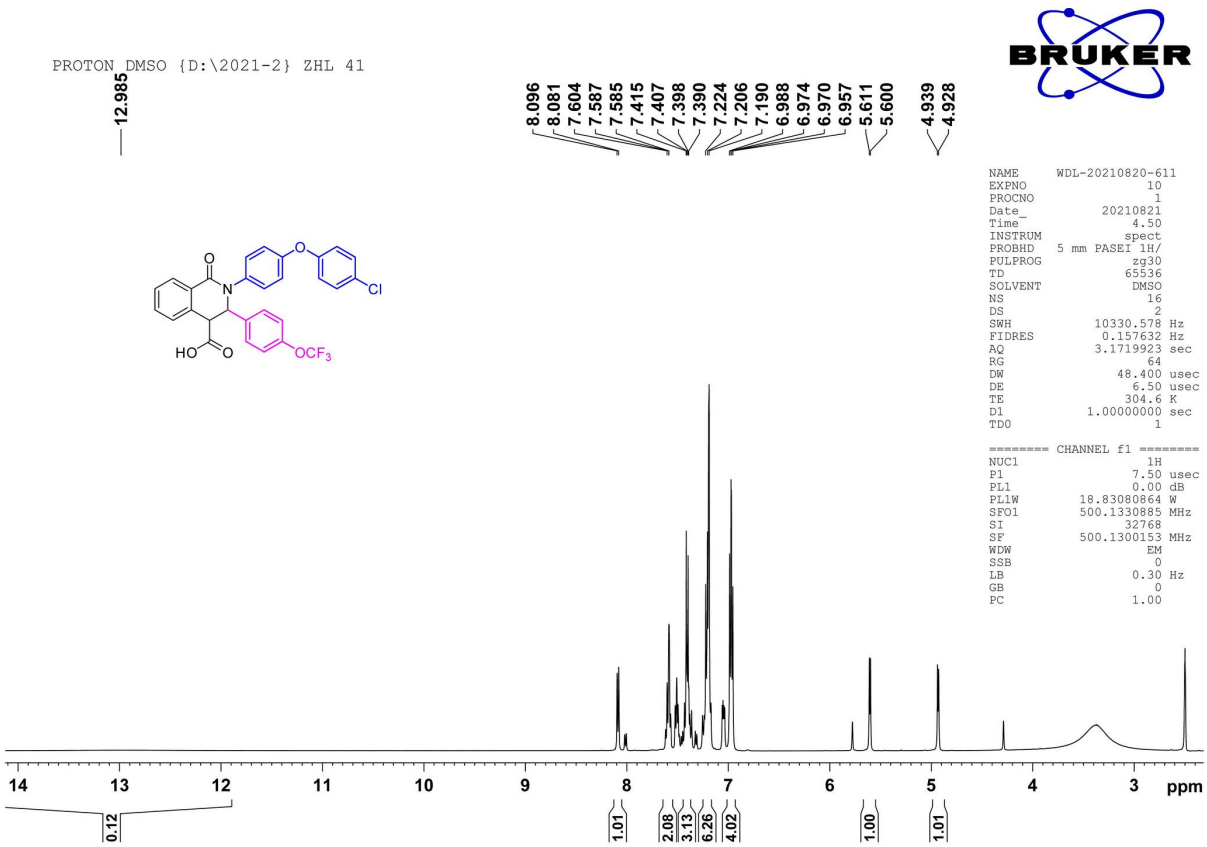

Figure S91. The ^{1}H NMR spectrum of compound **II9**

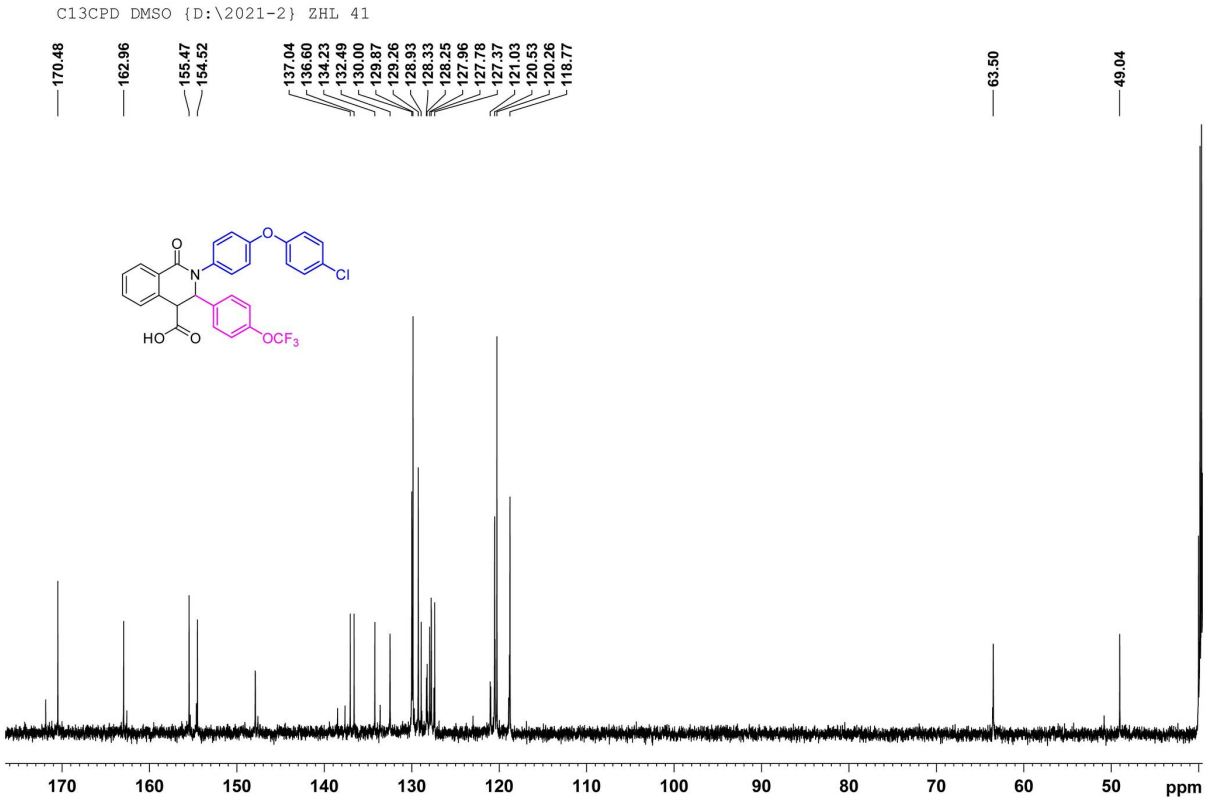

Figure S92. The ^{13}C NMR spectrum of compound **II9**

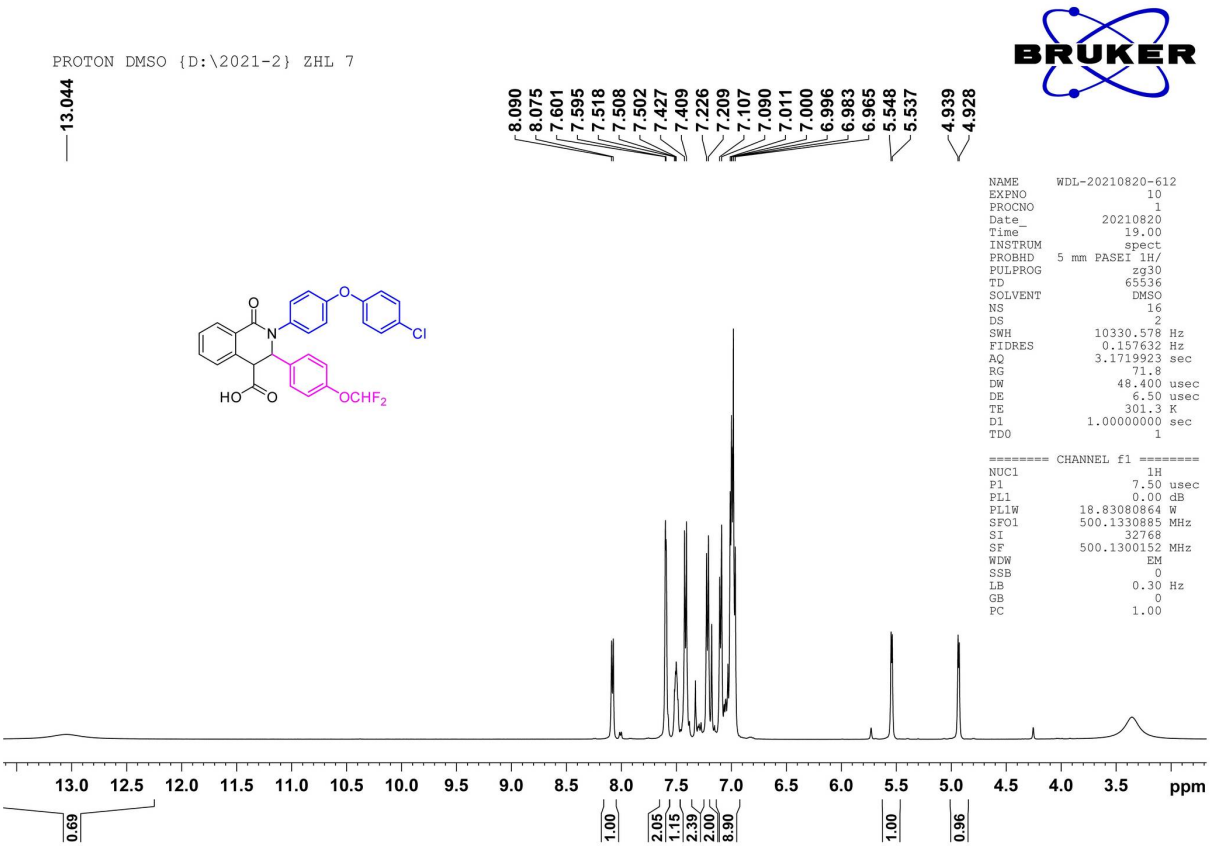

Figure S93. The ^{1}H NMR spectrum of compound **II10**

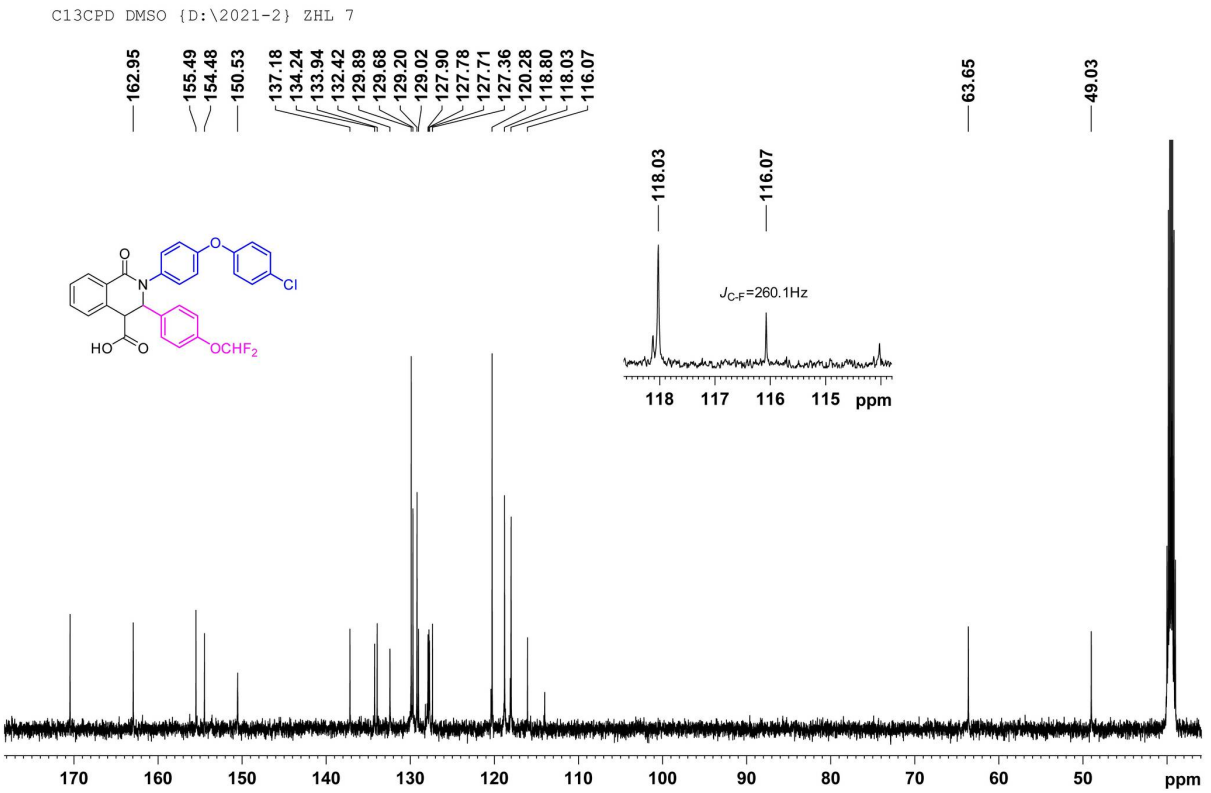

Figure S94. The ^{13}C NMR spectrum of compound **II10**

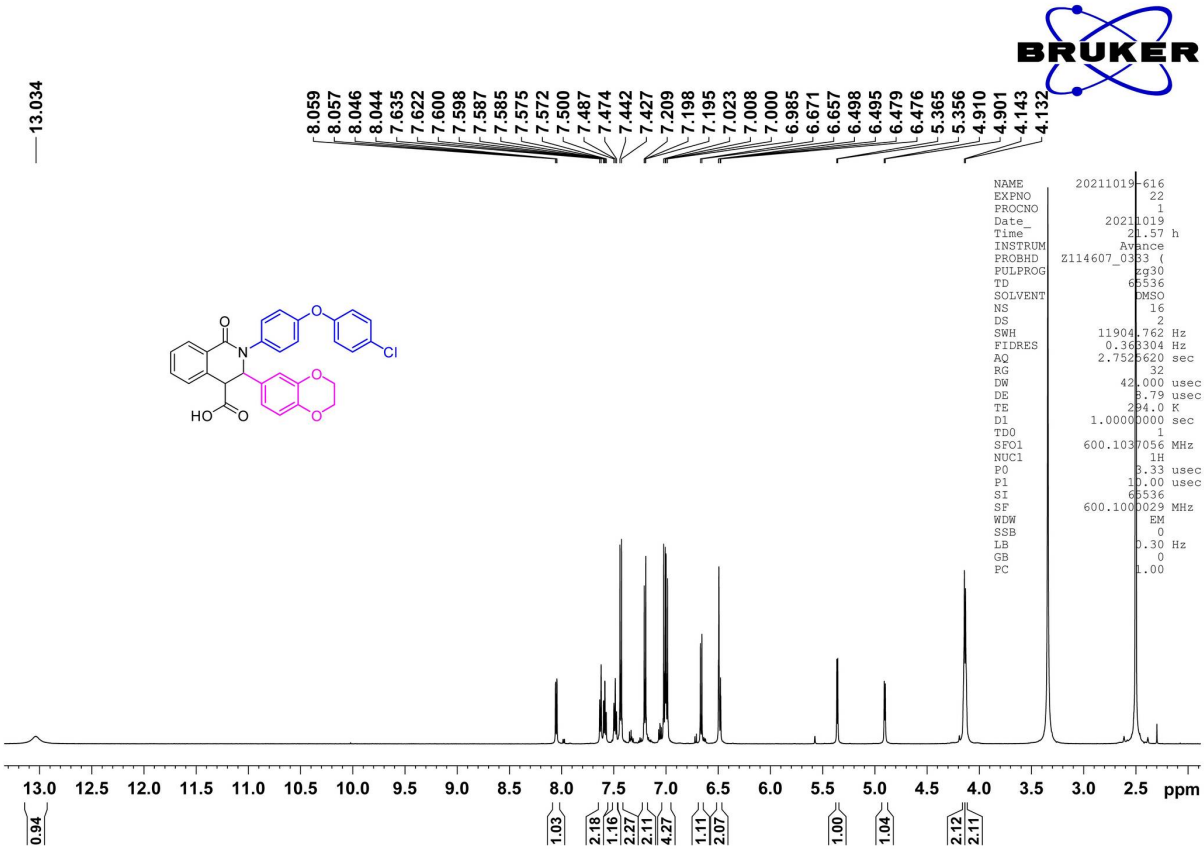

Figure S95. The ^{1}H NMR spectrum of compound **II11**

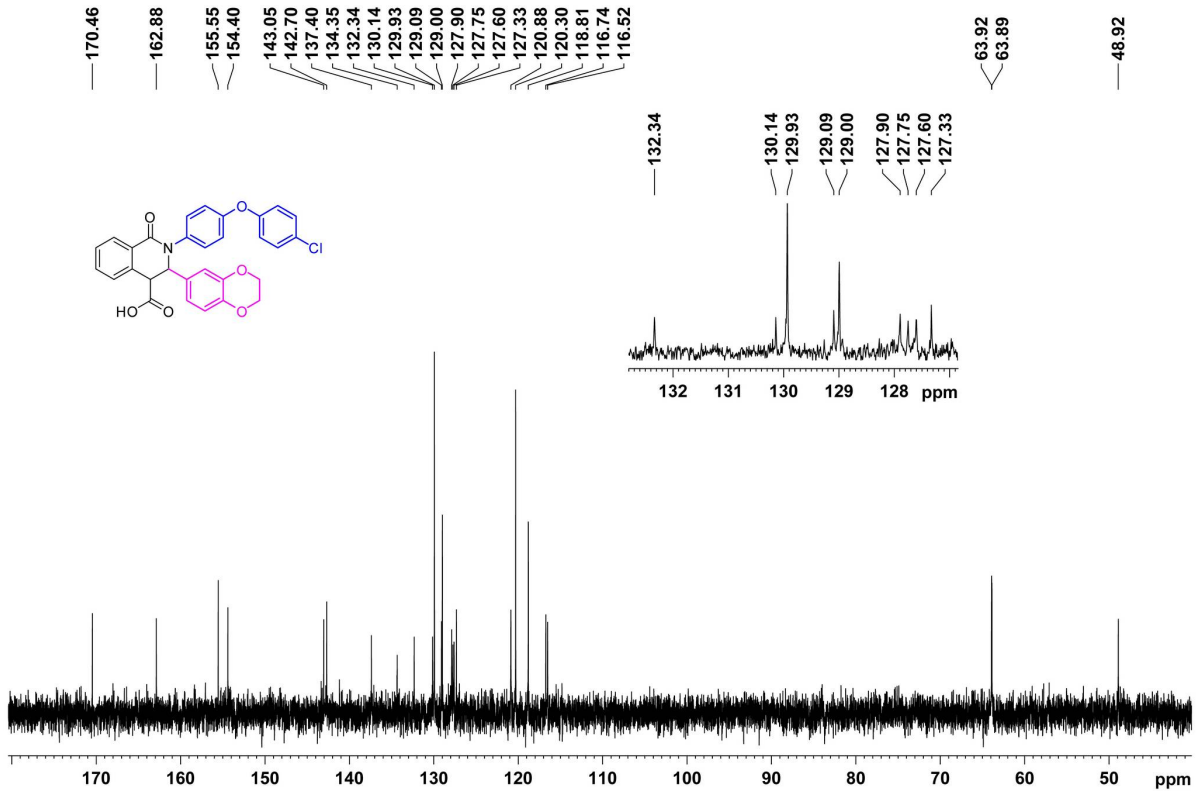

Figure S96. The ^{13}C NMR spectrum of compound **II11**

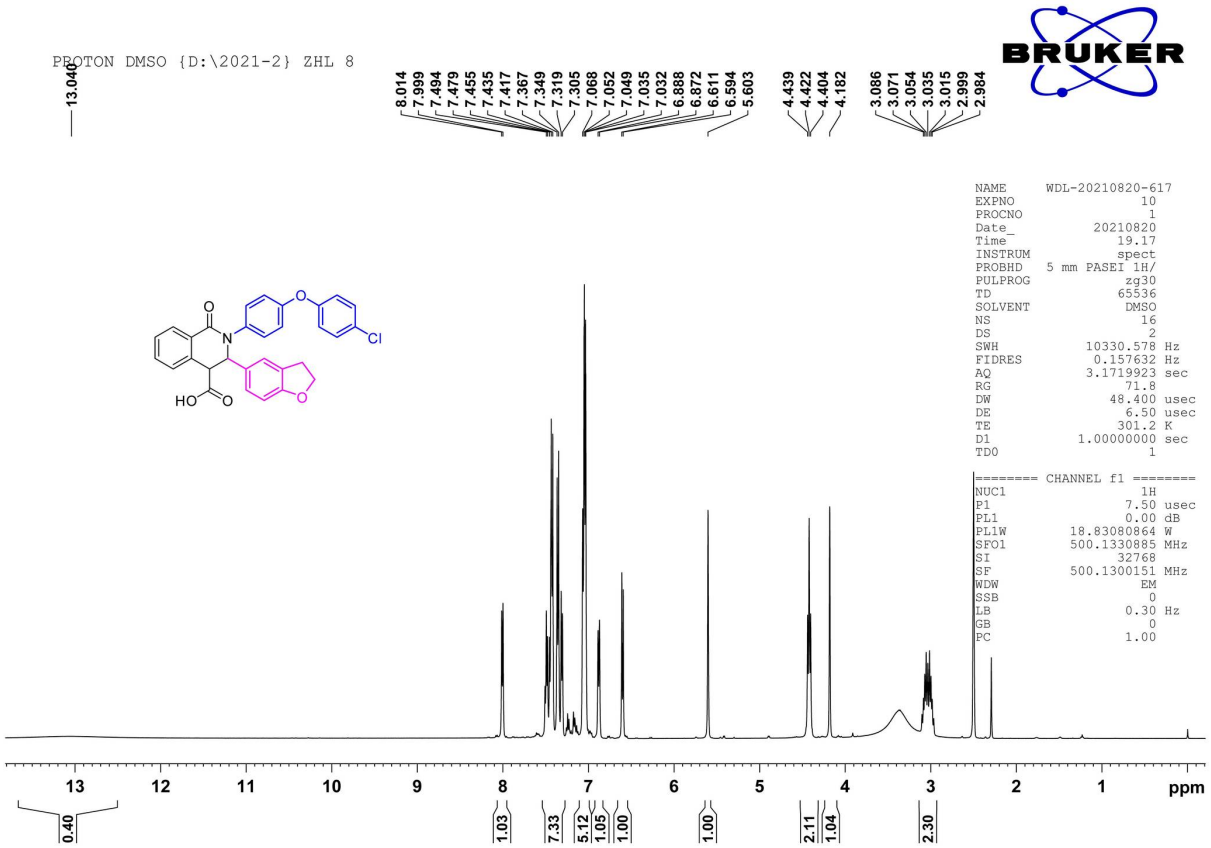

Figure S97. The ^{1}H NMR spectrum of compound **II12**

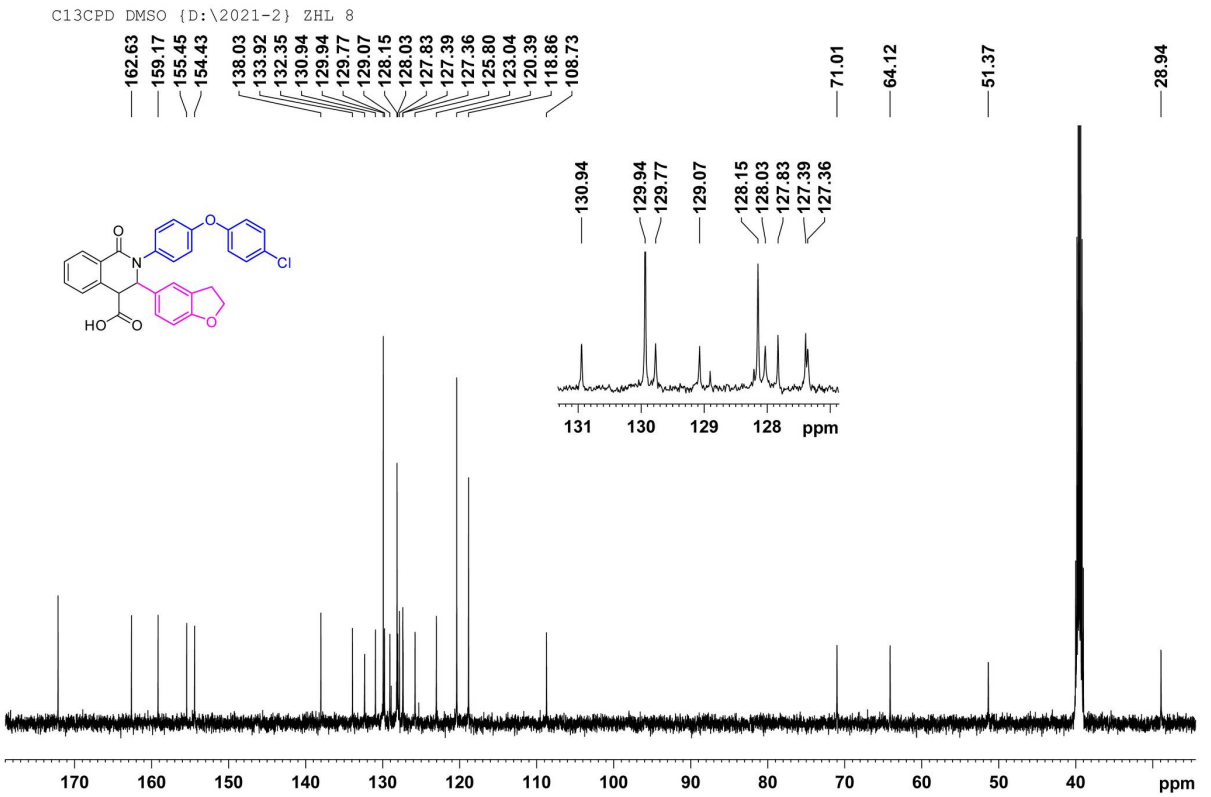

Figure S98. The ^{13}C NMR spectrum of compound **II12**

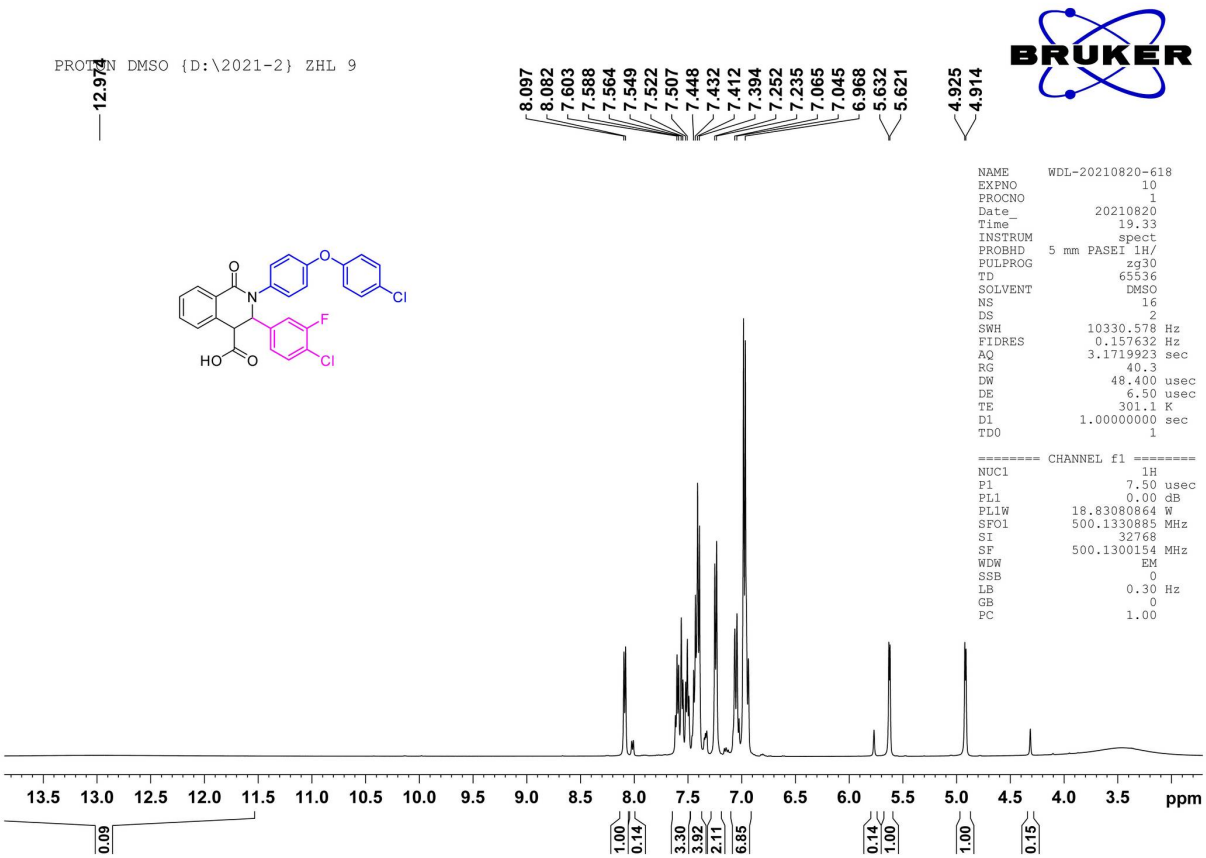

Figure S99. The ^{1}H NMR spectrum of compound **II13**

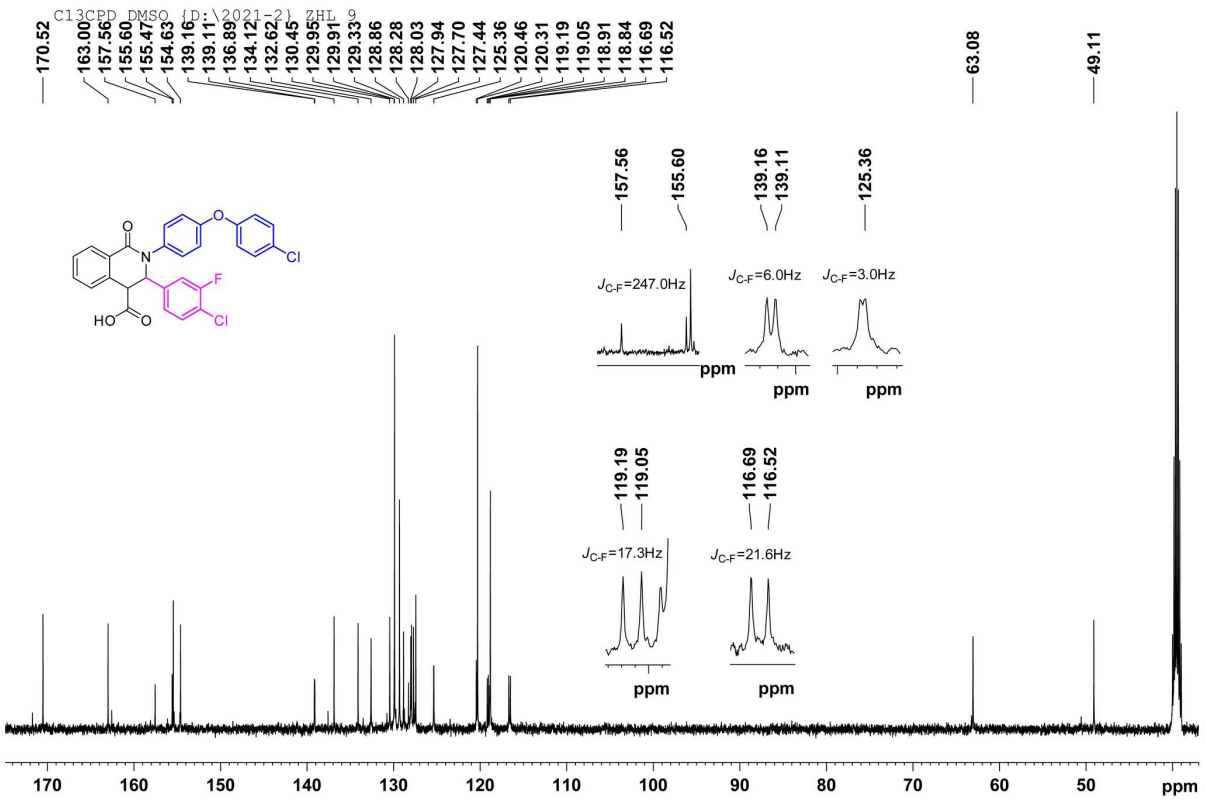

Figure S100. The ^{13}C NMR spectrum of compound **II13**

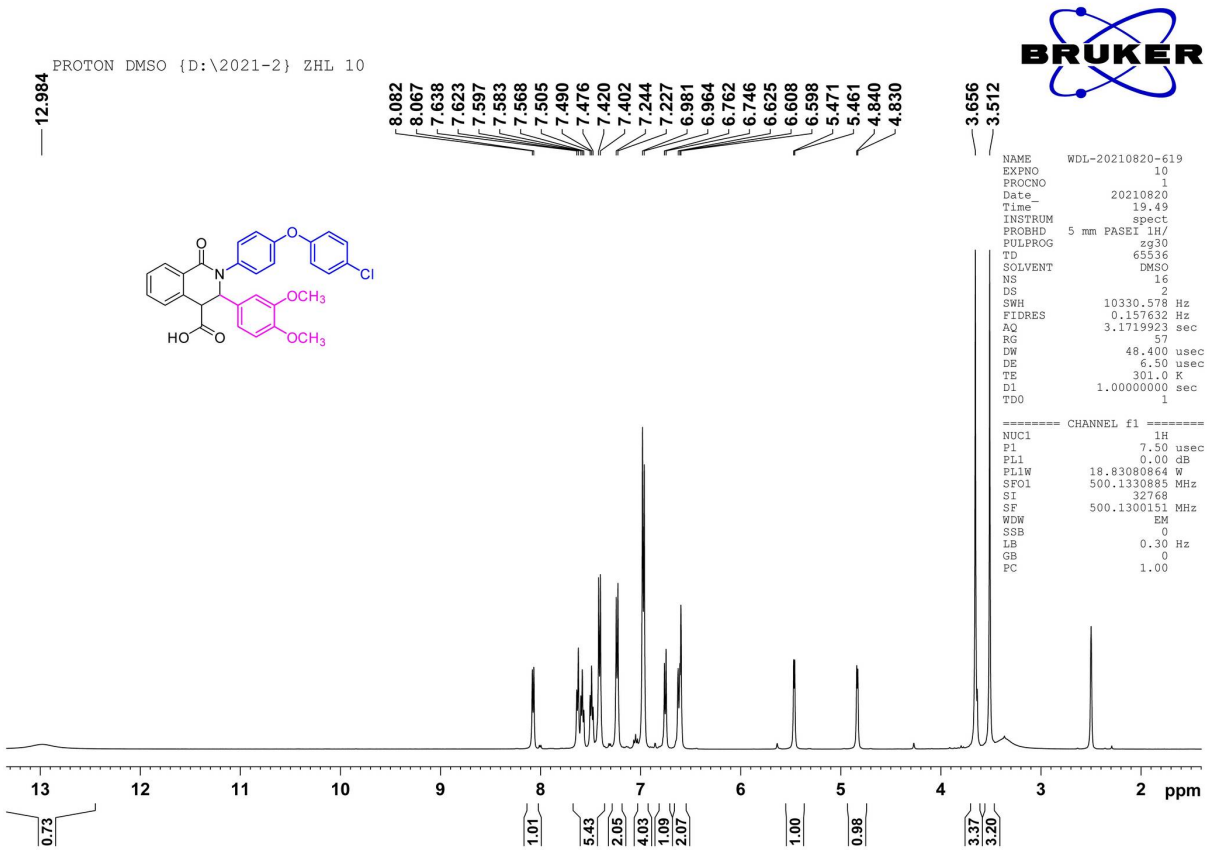

Figure S101. The ^{1}H NMR spectrum of compound **II14**

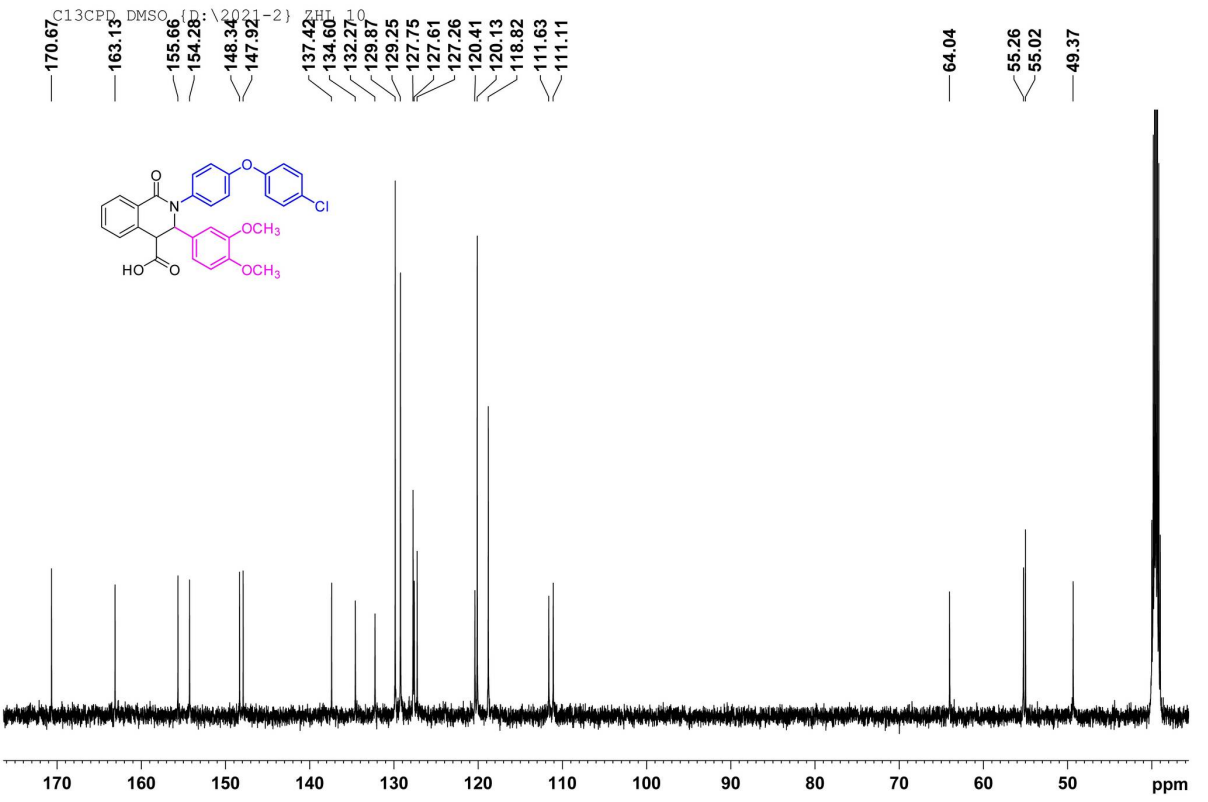

Figure S102. The ^{13}C NMR spectrum of compound **II14**

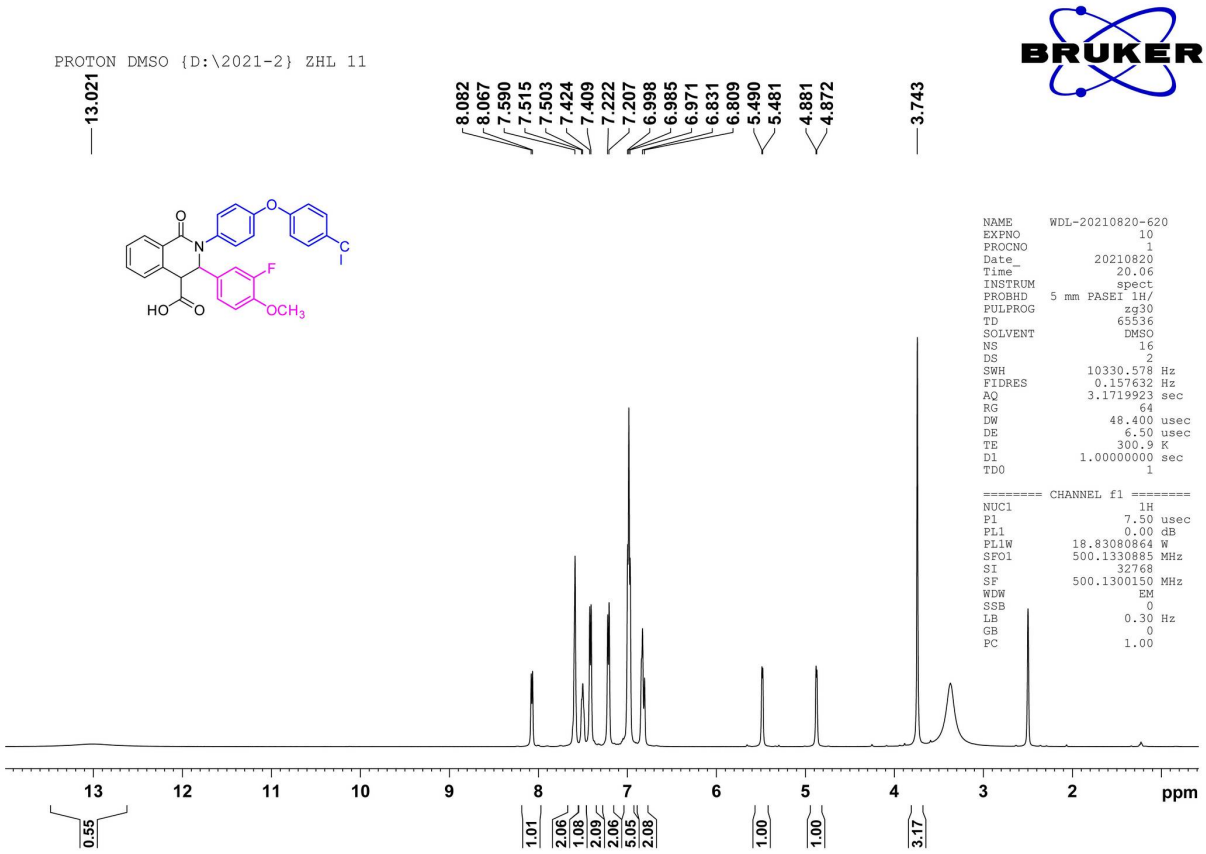

Figure S103. The ^{1}H NMR spectrum of compound **II15**

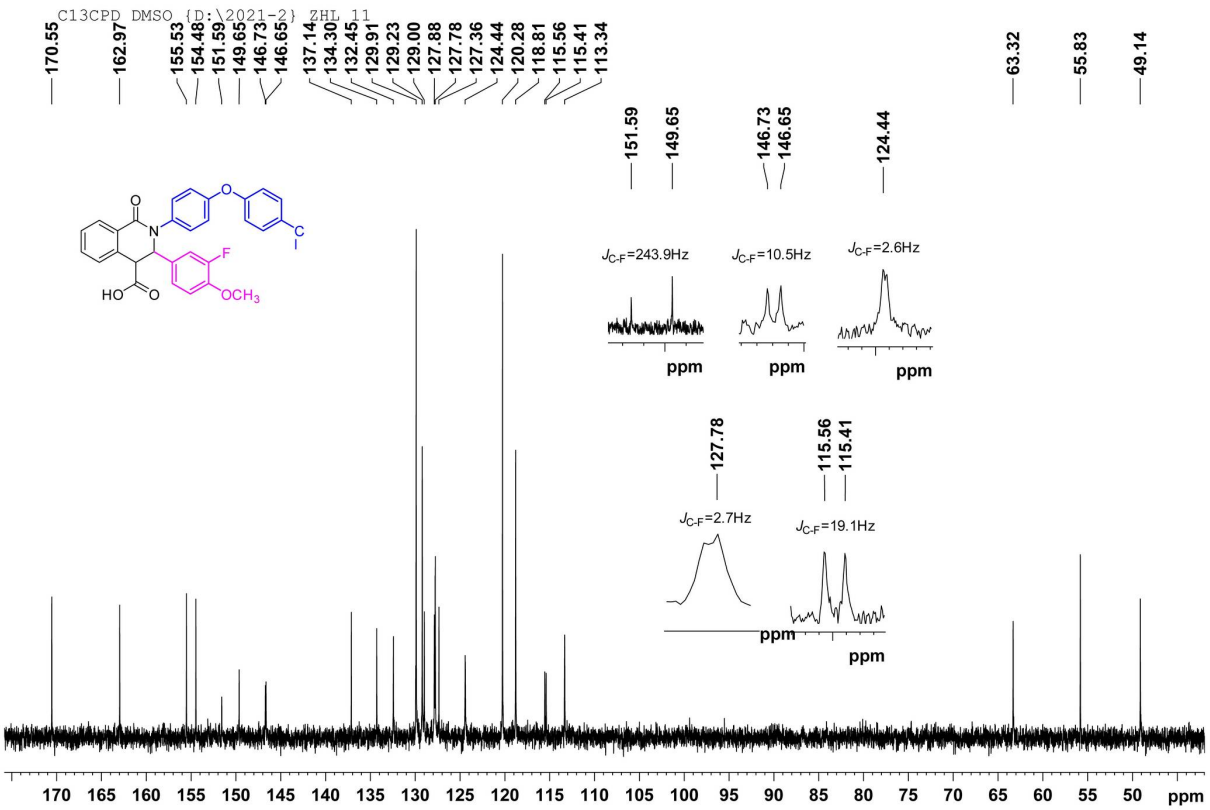

Figure S104. The ^{13}C NMR spectrum of compound **II15**

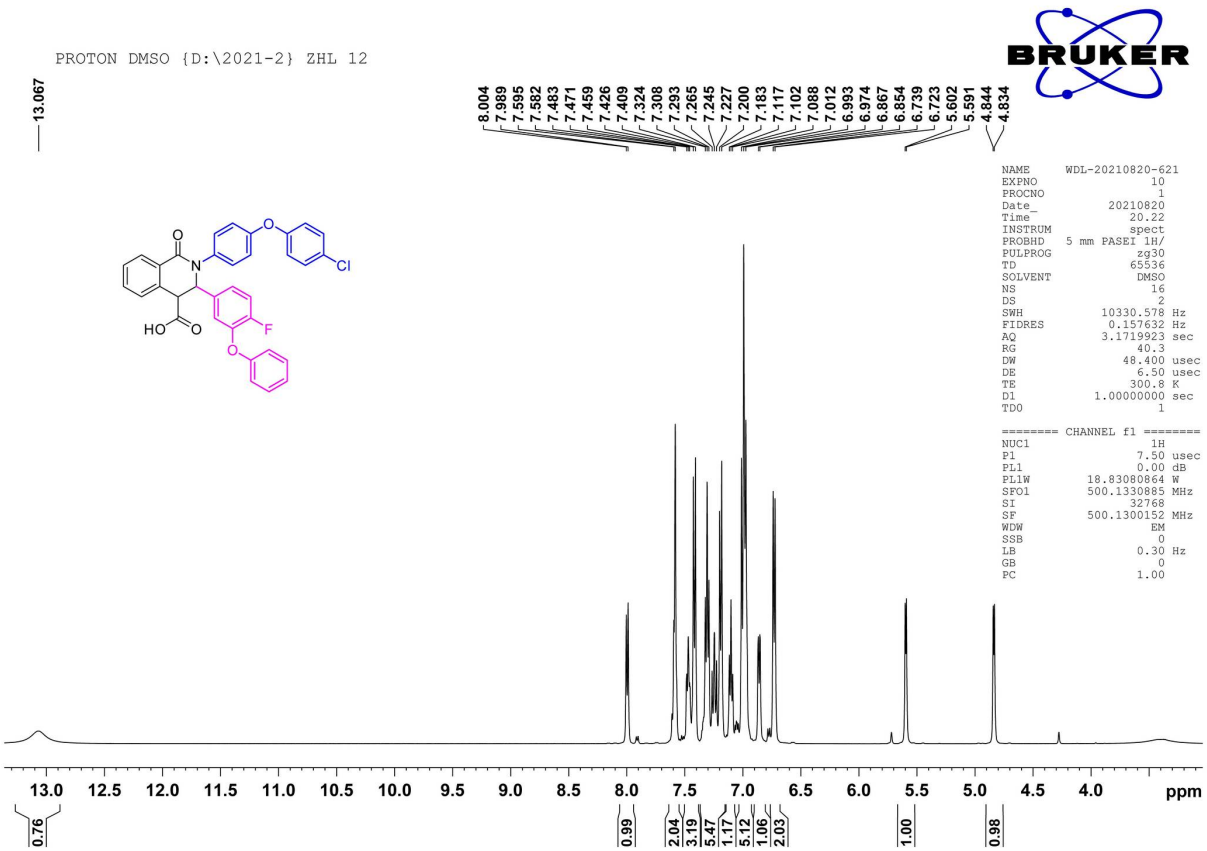

Figure S105. The ^{1}H NMR spectrum of compound **II16**

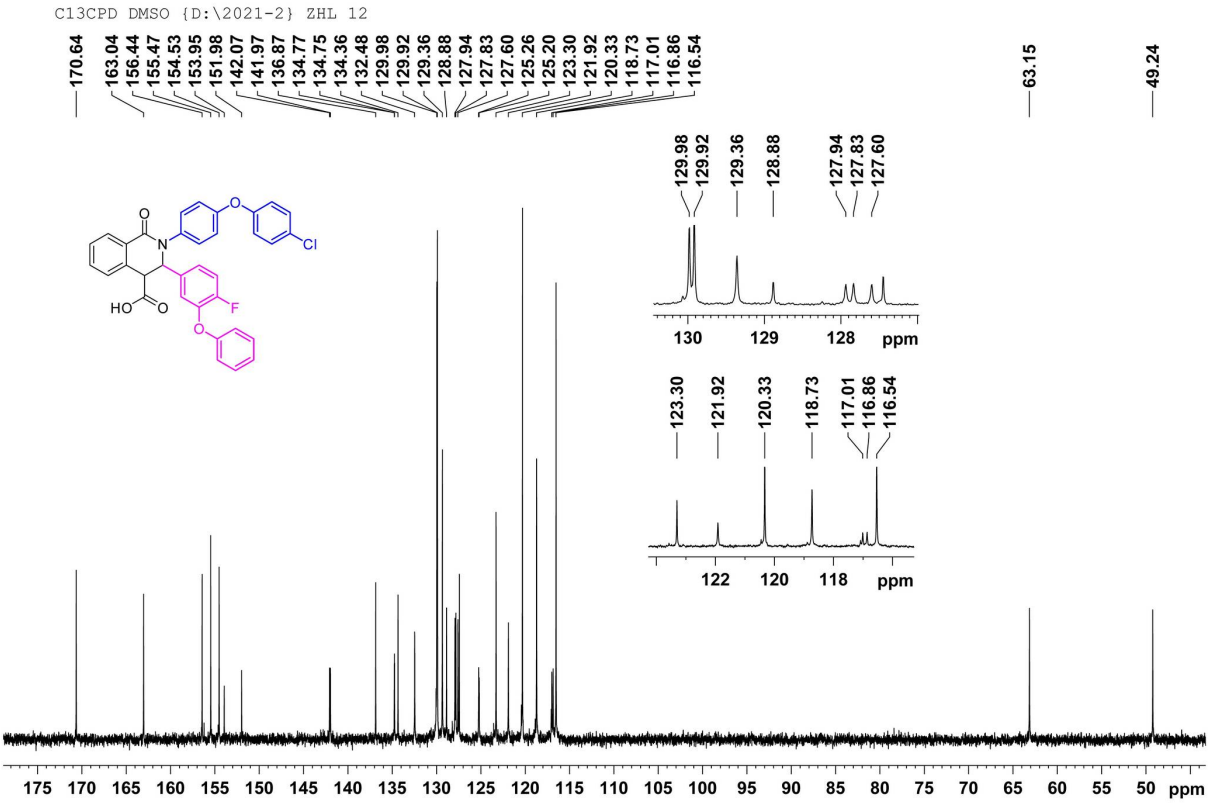

Figure S106. The ^{13}C NMR spectrum of compound **II16**

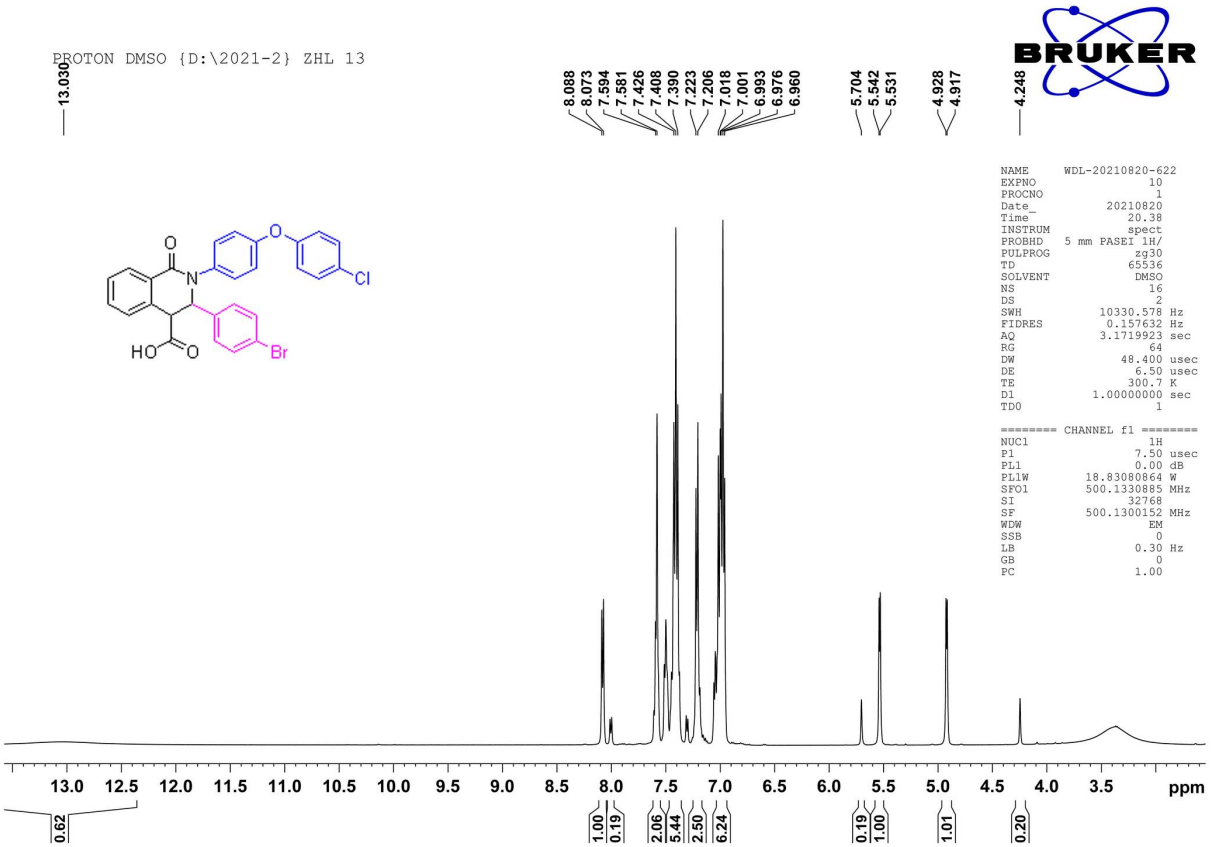

Figure S107. The ^{1}H NMR spectrum of compound **II17**

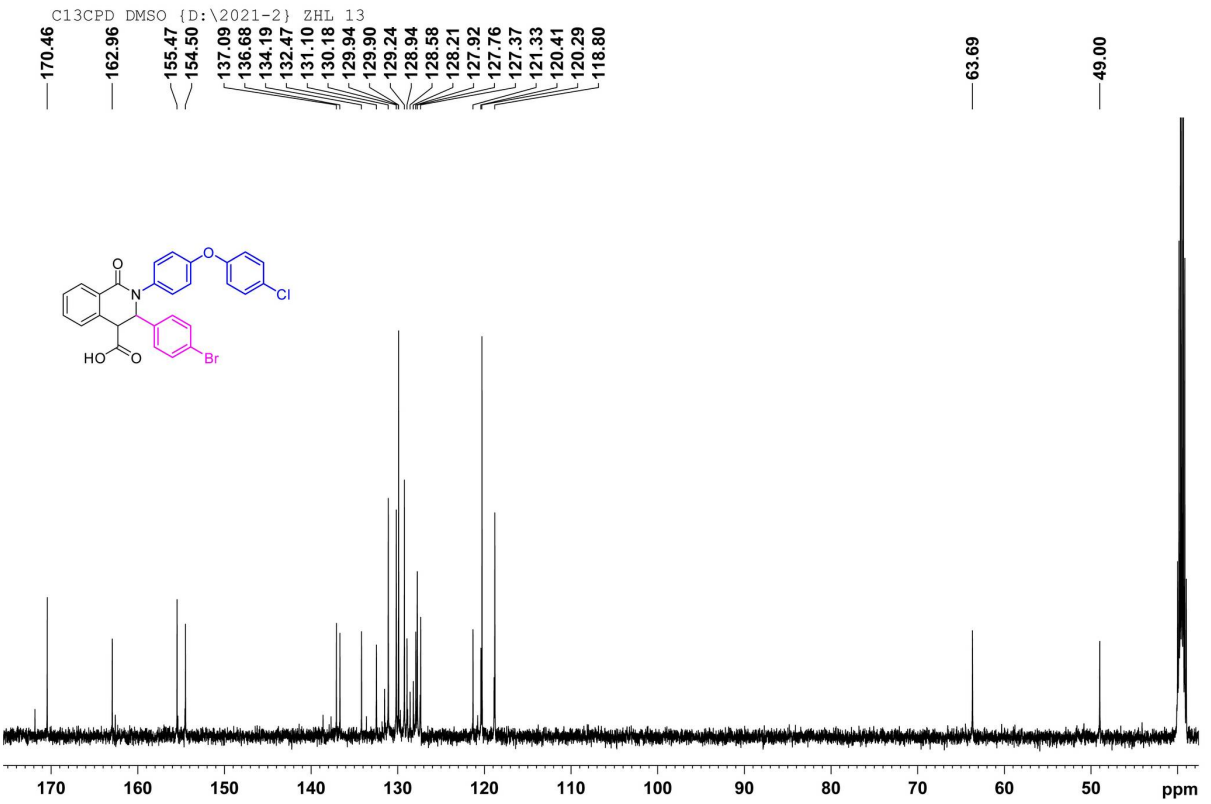

Figure S108. The ^{13}C NMR spectrum of compound **II17**

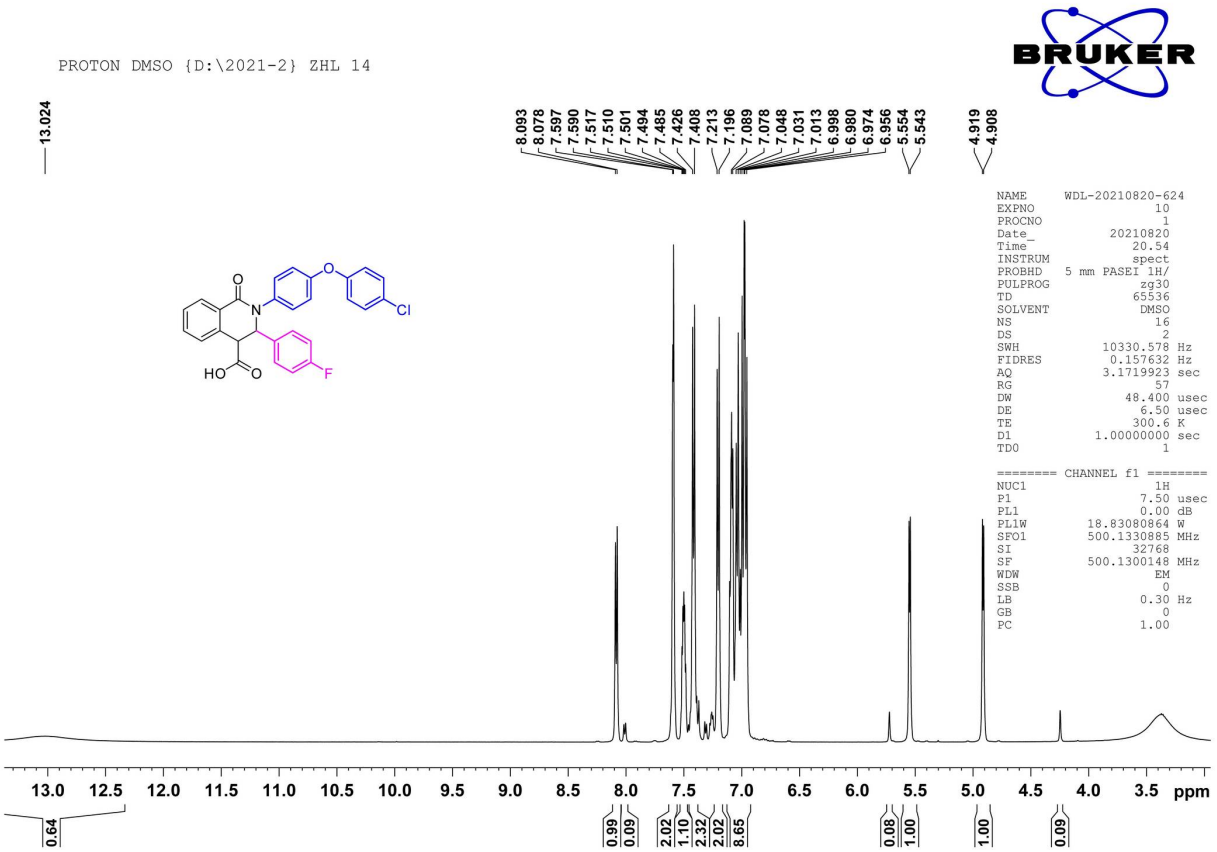

Figure S109. The ^{1}H NMR spectrum of compound **II18**

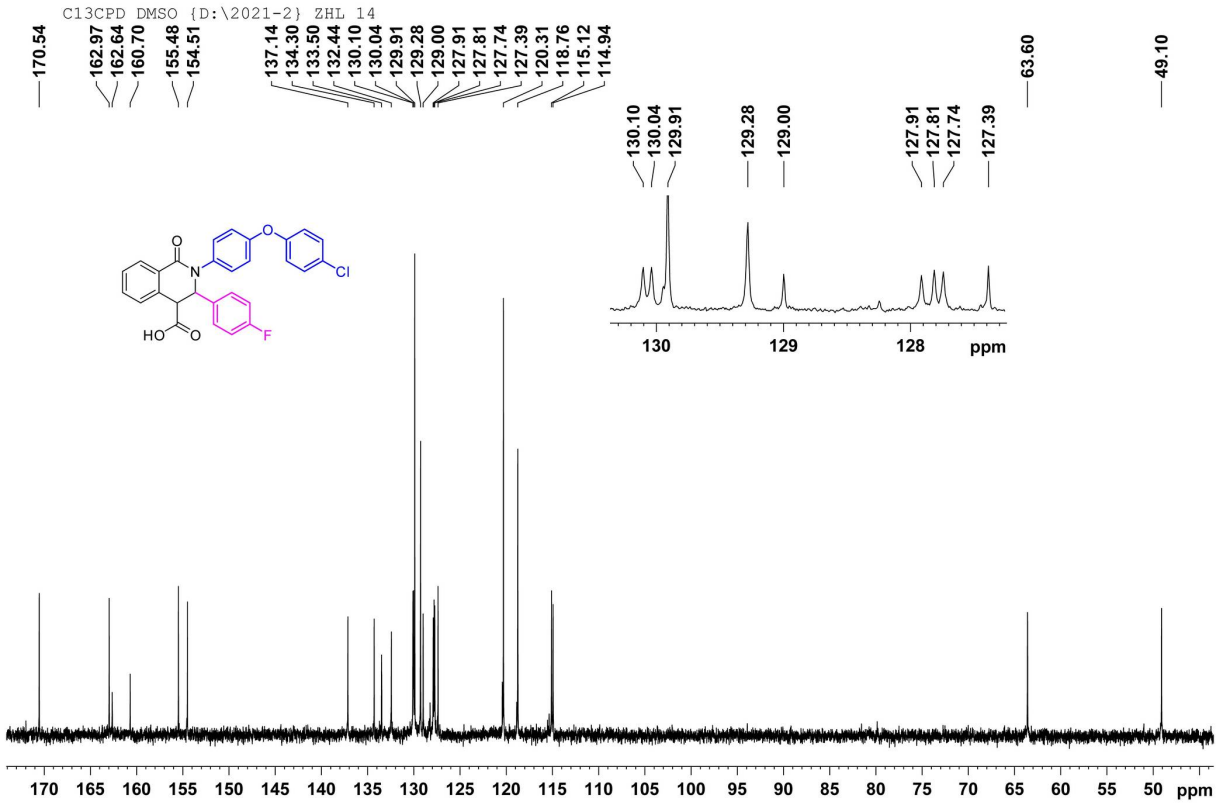

Figure S110. The ^{13}C NMR spectrum of compound **II18**

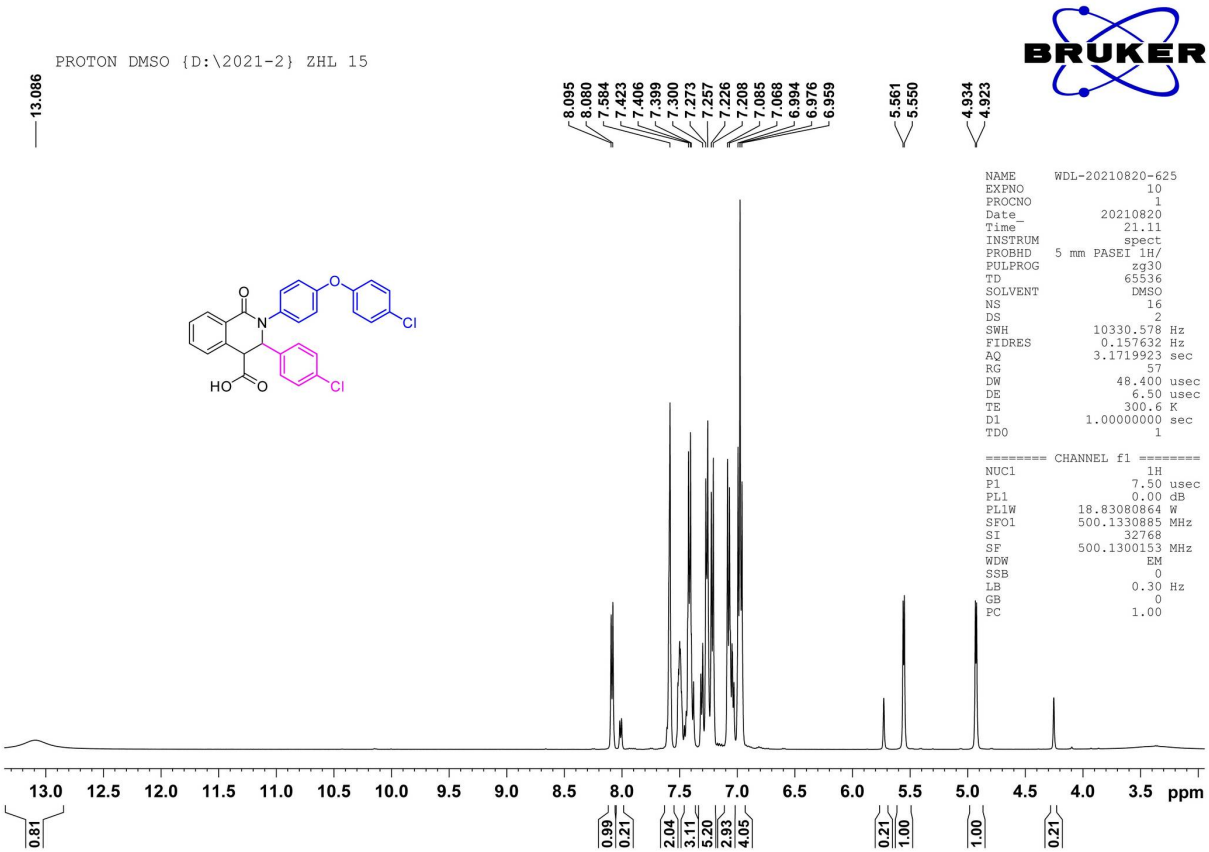

Figure S111. The ^{1}H NMR spectrum of compound **II19**

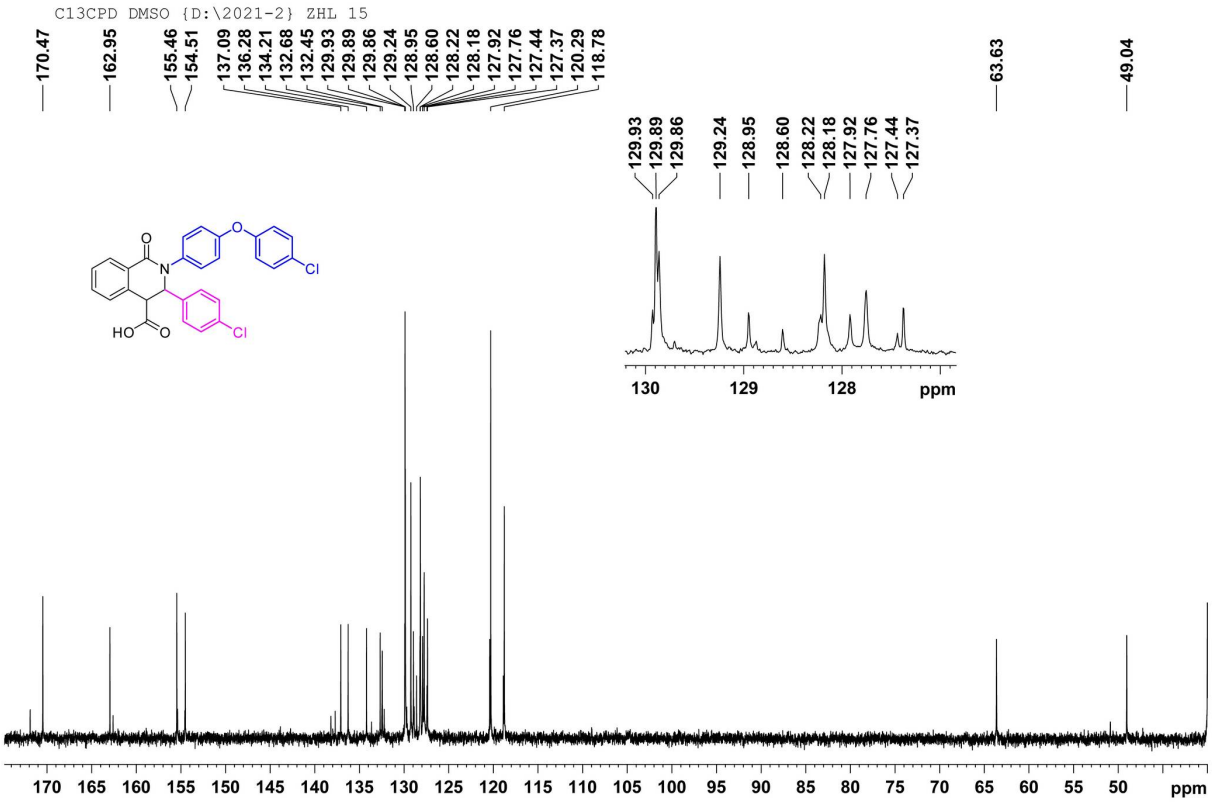

Figure S112. The ^{13}C NMR spectrum of compound **II19**

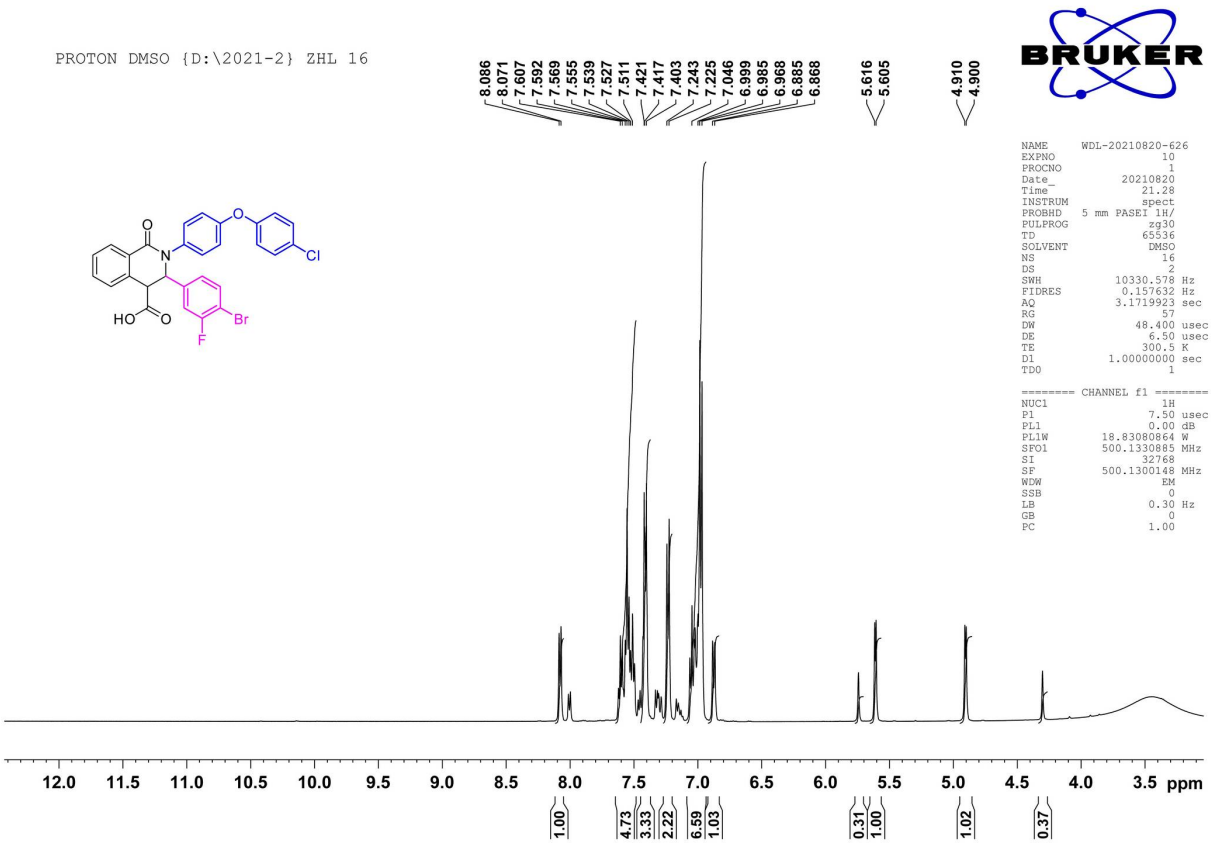

Figure S113. The ^{1}H NMR spectrum of compound **II20**

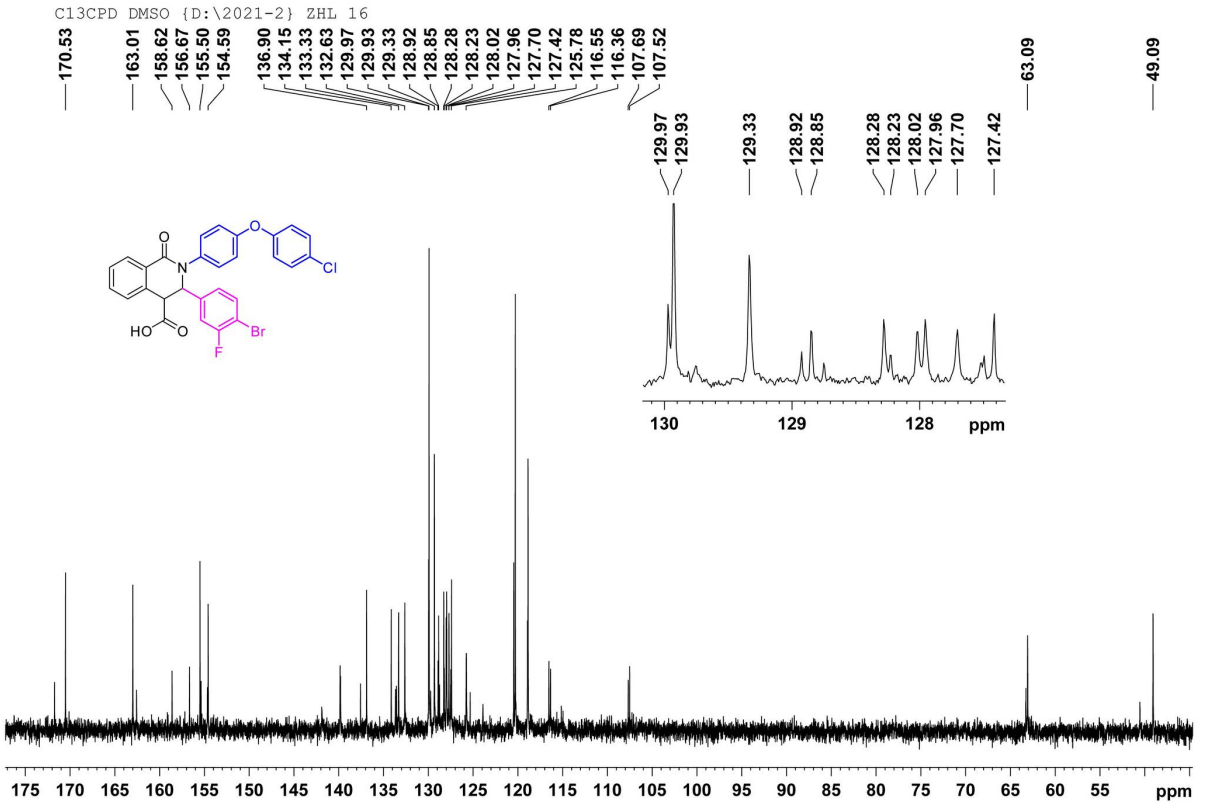

Figure S114. The ^{13}C NMR spectrum of compound **II20**

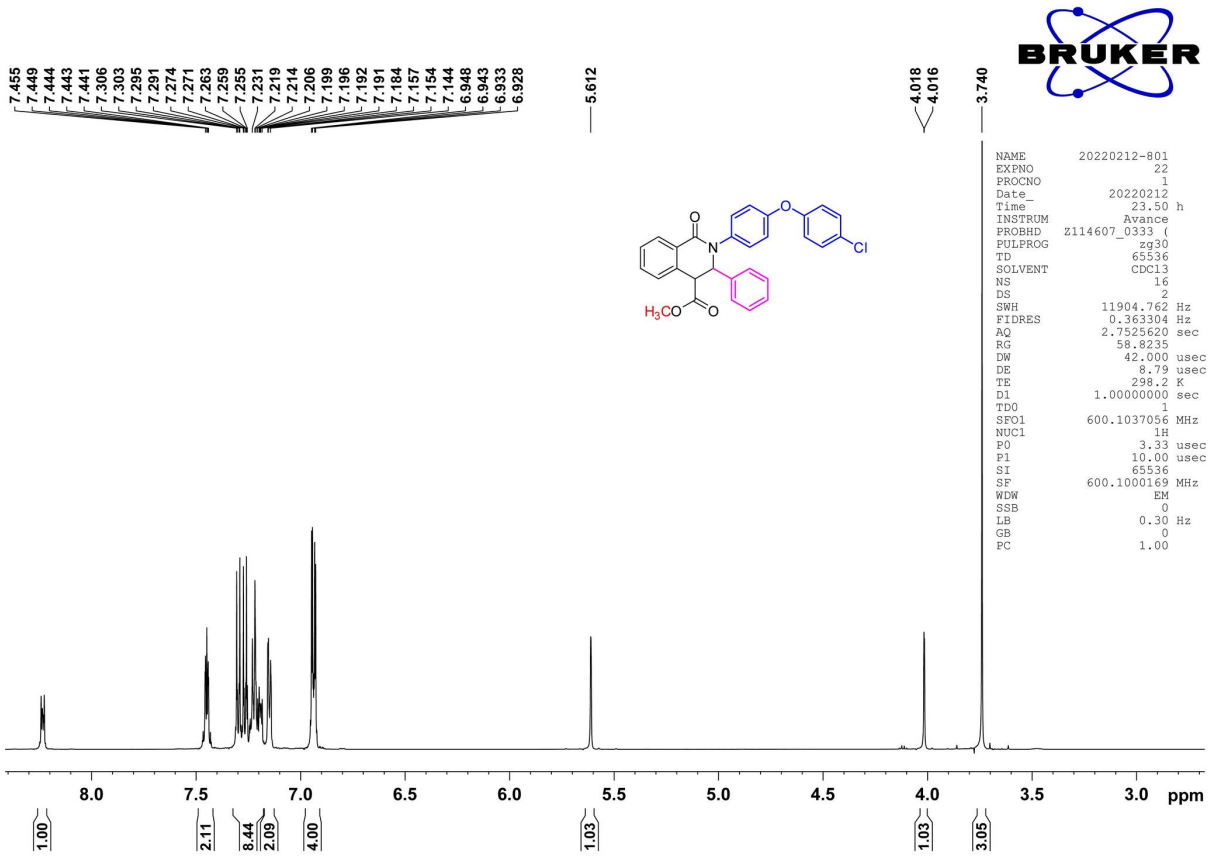

Figure S115. The ^{1}H NMR spectrum of compound **III1**

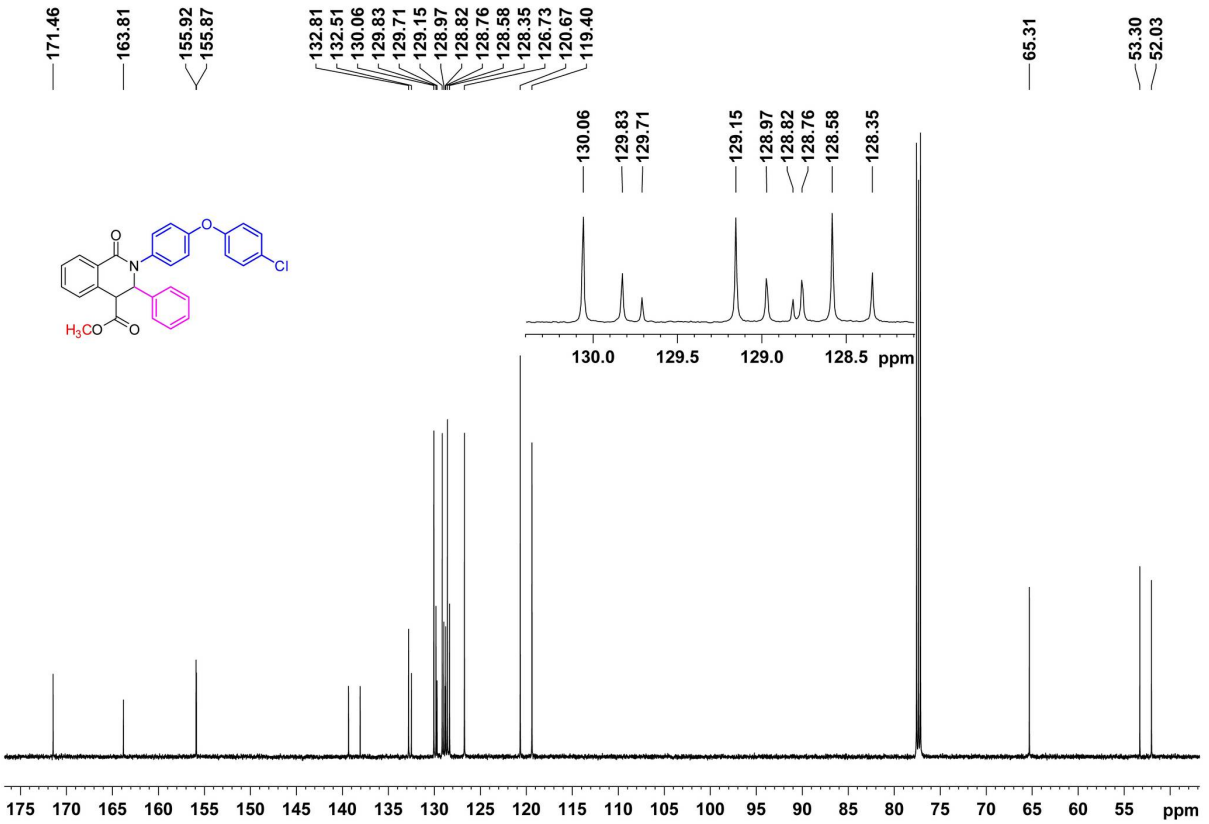

Figure S116. The ^{13}C NMR spectrum of compound **III1**

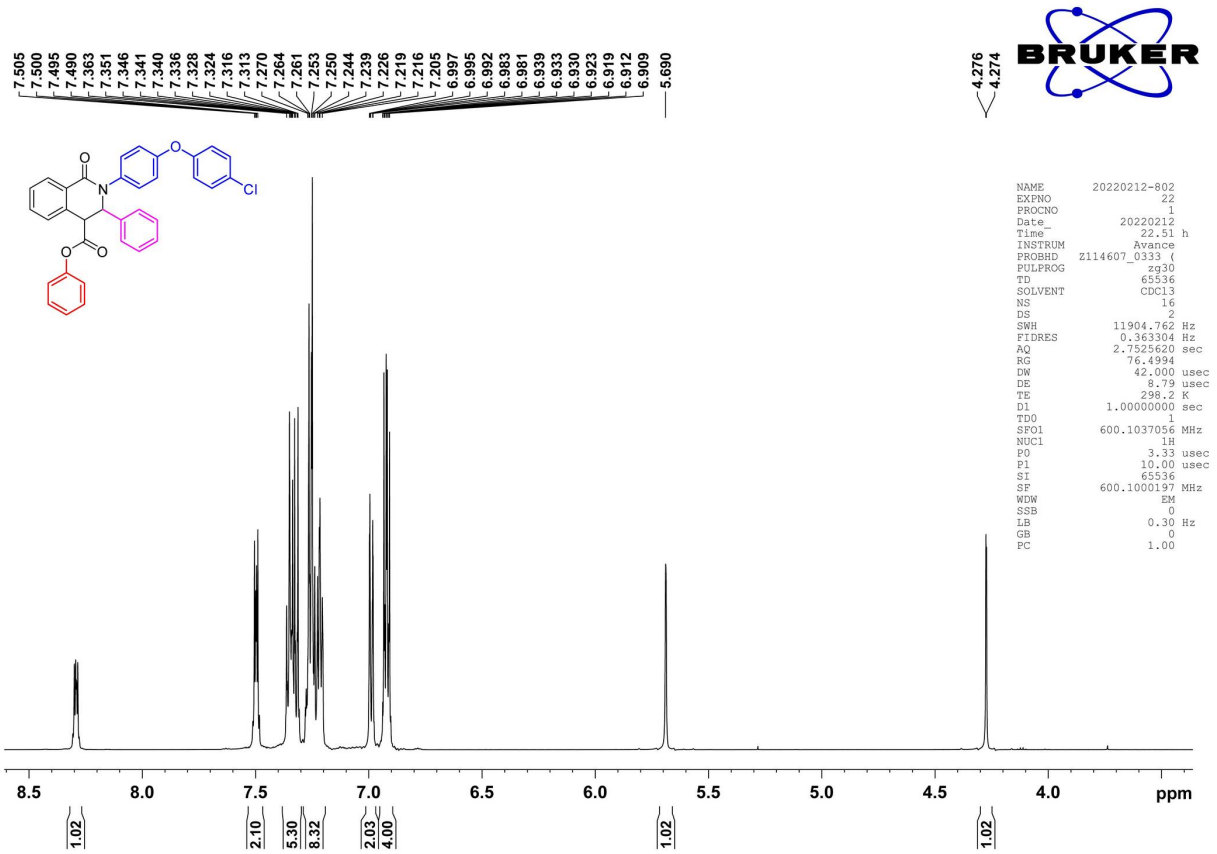

Figure S117. The ^{1}H NMR spectrum of compound **III2**

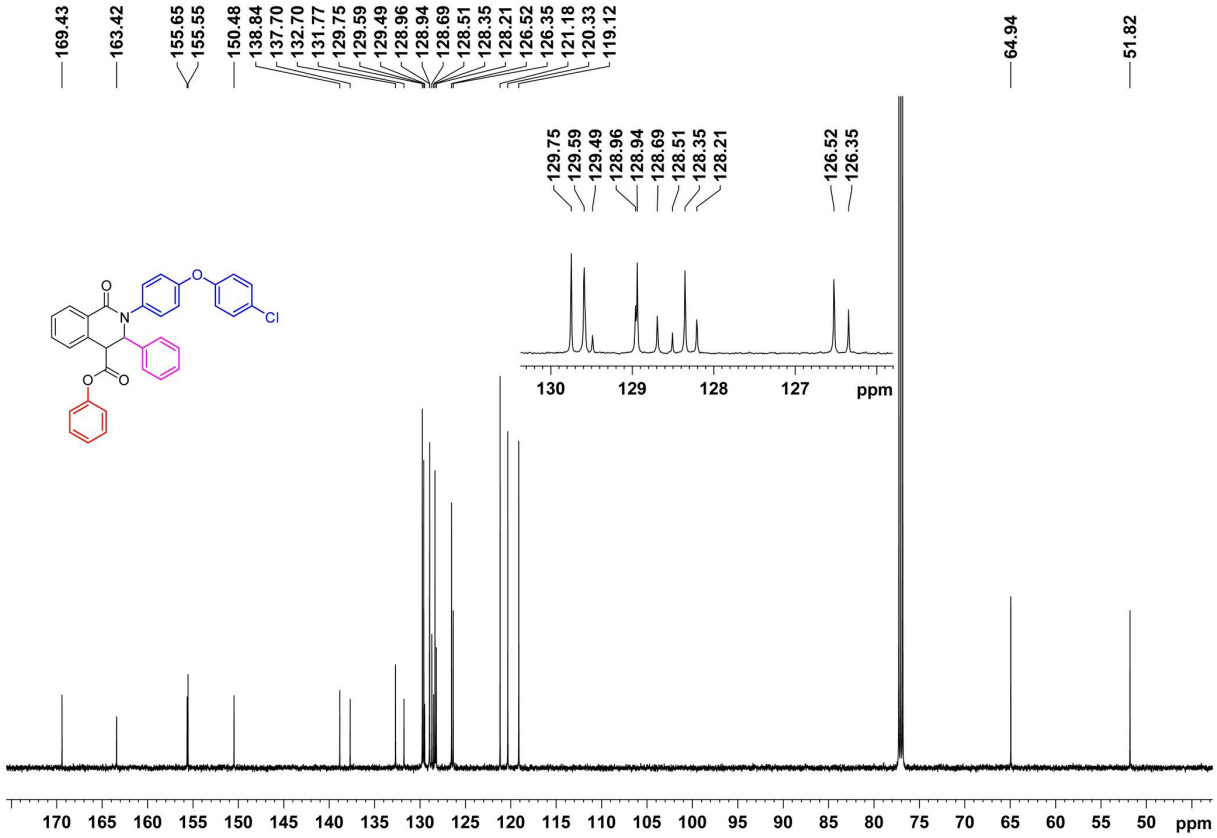

Figure S118. The ^{13}C NMR spectrum of compound **III2**

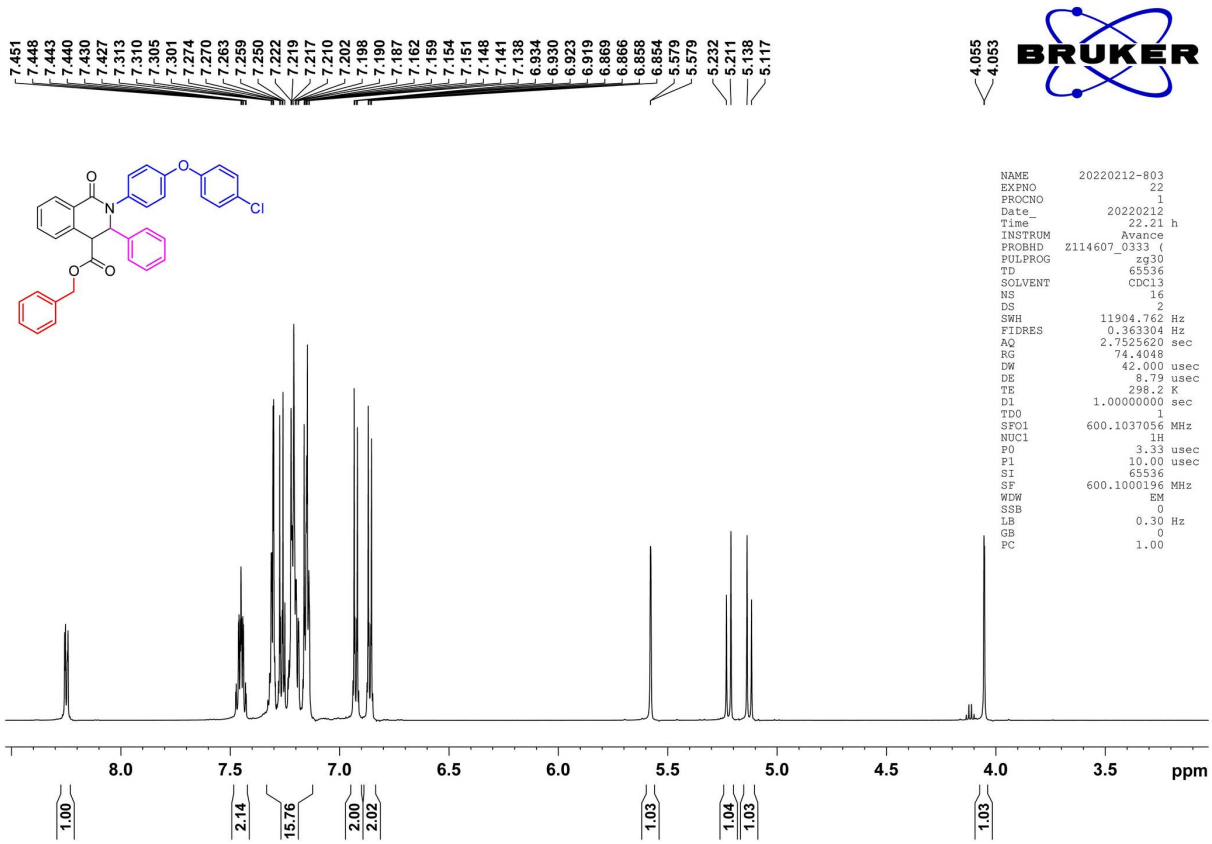

Figure S119. The ^{1}H NMR spectrum of compound **III3**

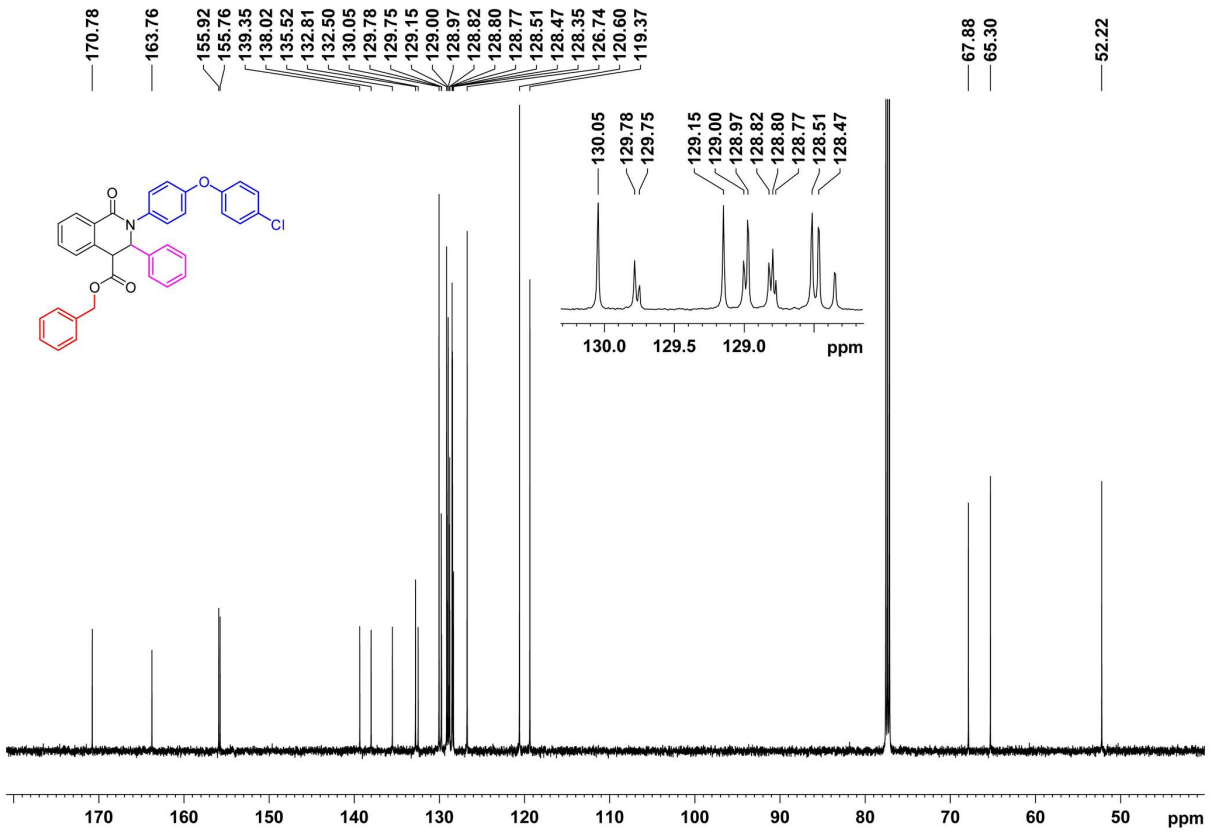

Figure S120. The ^{13}C NMR spectrum of compound **III3**

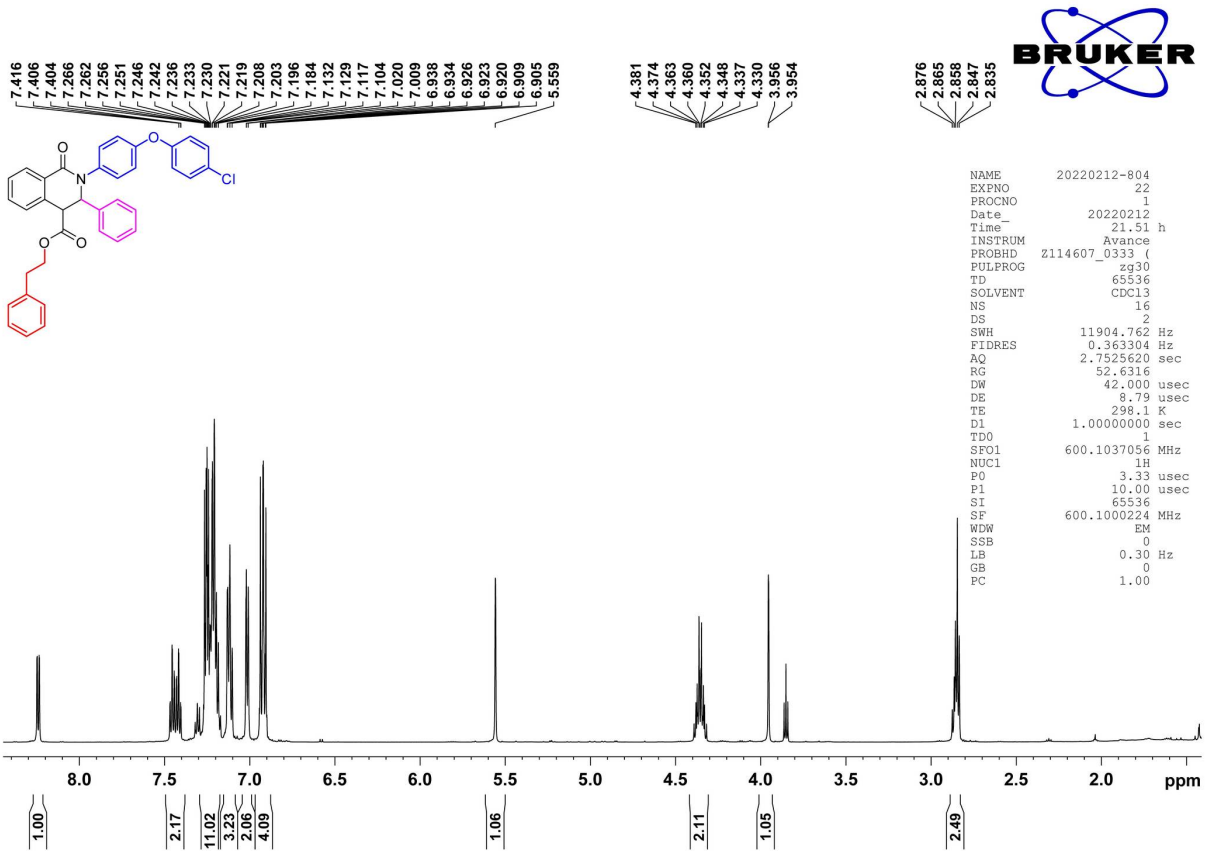

Figure S121. The ^{1}H NMR spectrum of compound **III4**

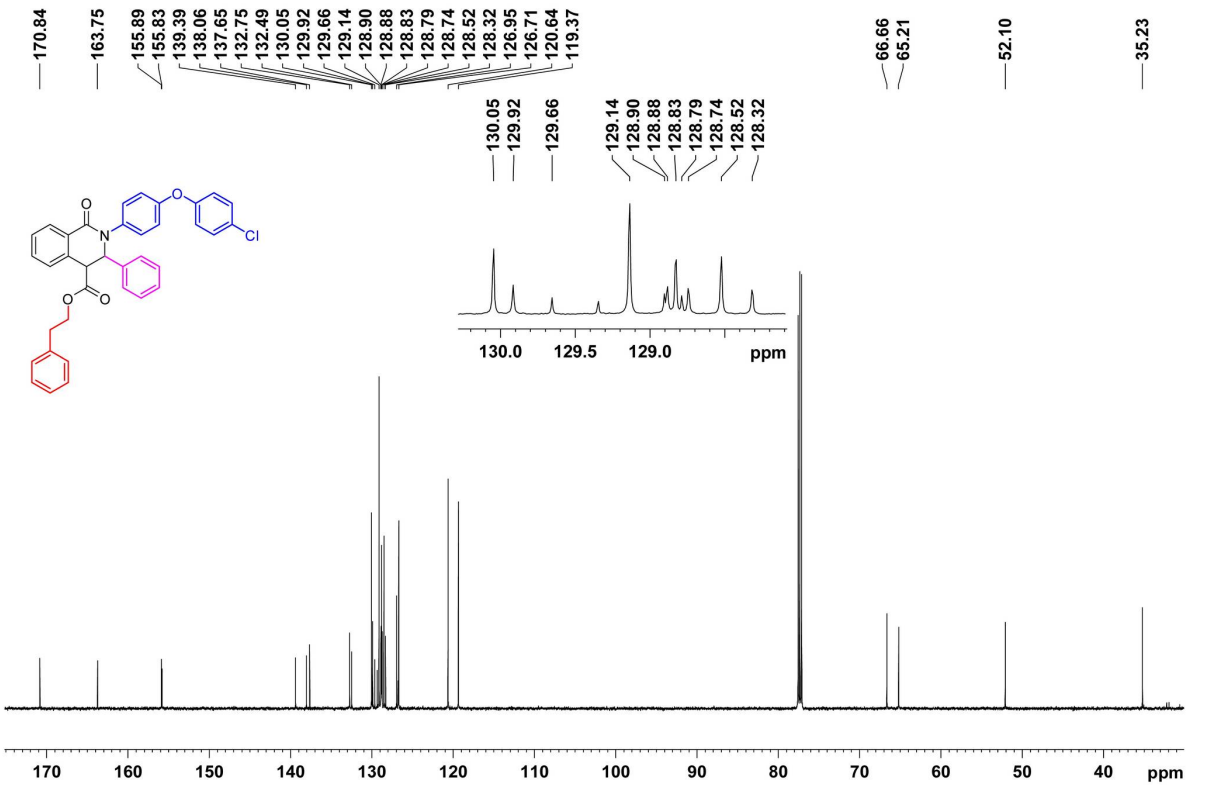

Figure S122. The ^{13}C NMR spectrum of compound **III4**

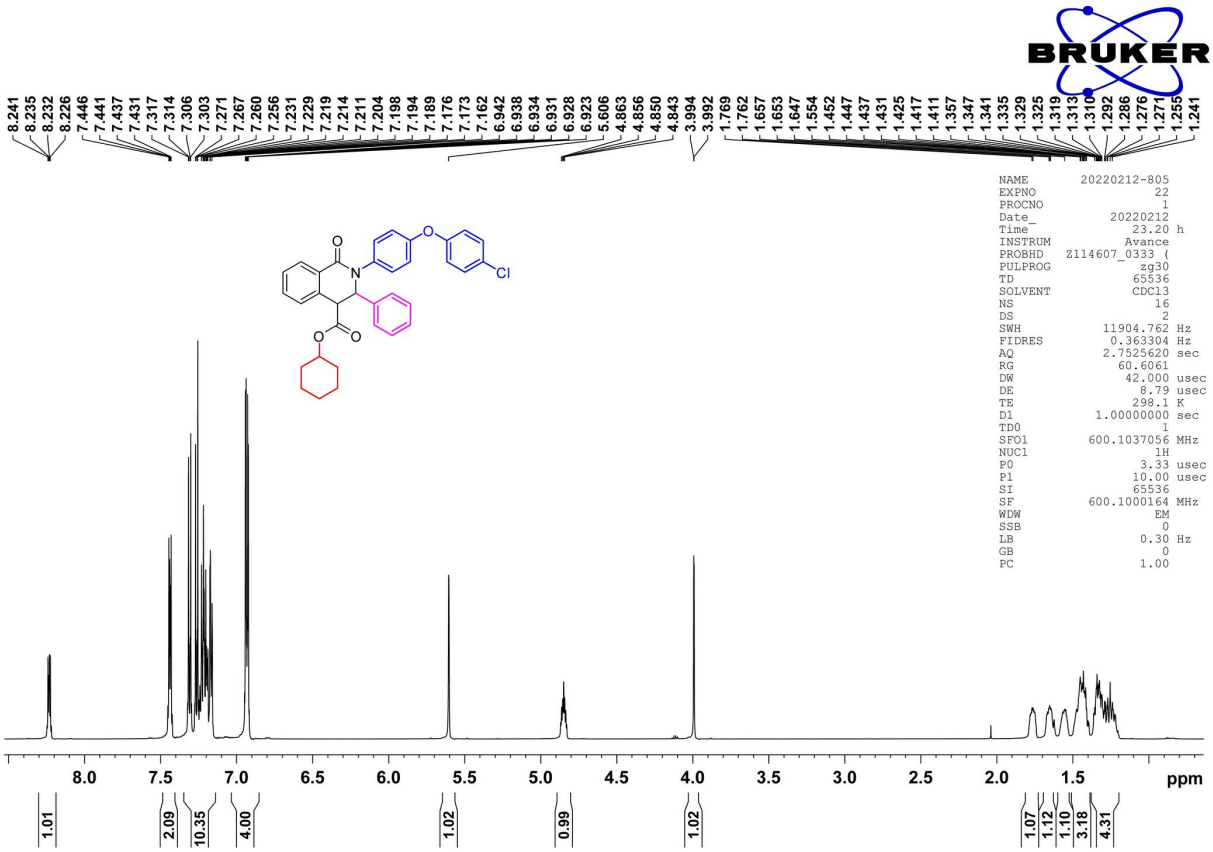

Figure S123. The ^{1}H NMR spectrum of compound **III5**

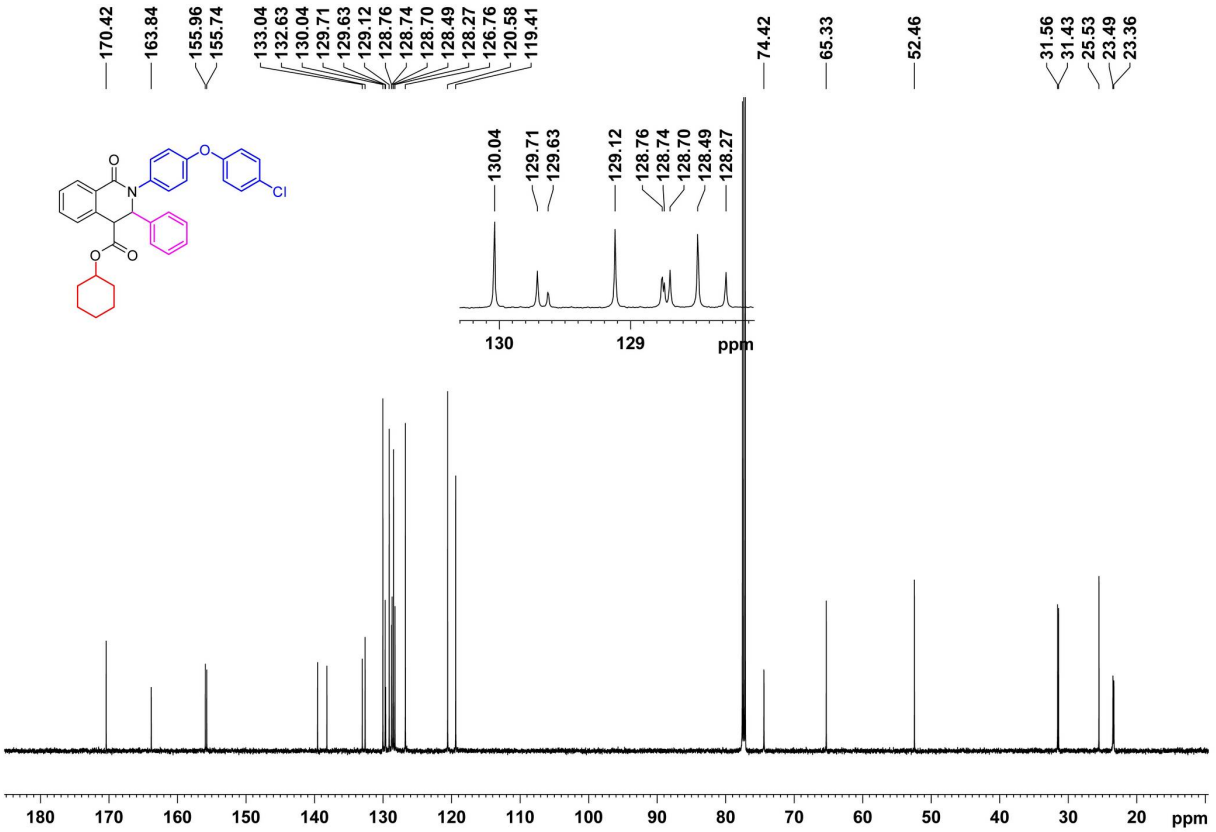

Figure S124. The ^{13}C NMR spectrum of compound **III5**