

Discovery of phenolic 2-arylidene-isoquinolinones with antioxidant and α -glucosidase inhibition dual action.

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^1H -NMR and ^{13}C -NMR spectra of α -acylamino
carboxamides **9a–r**.

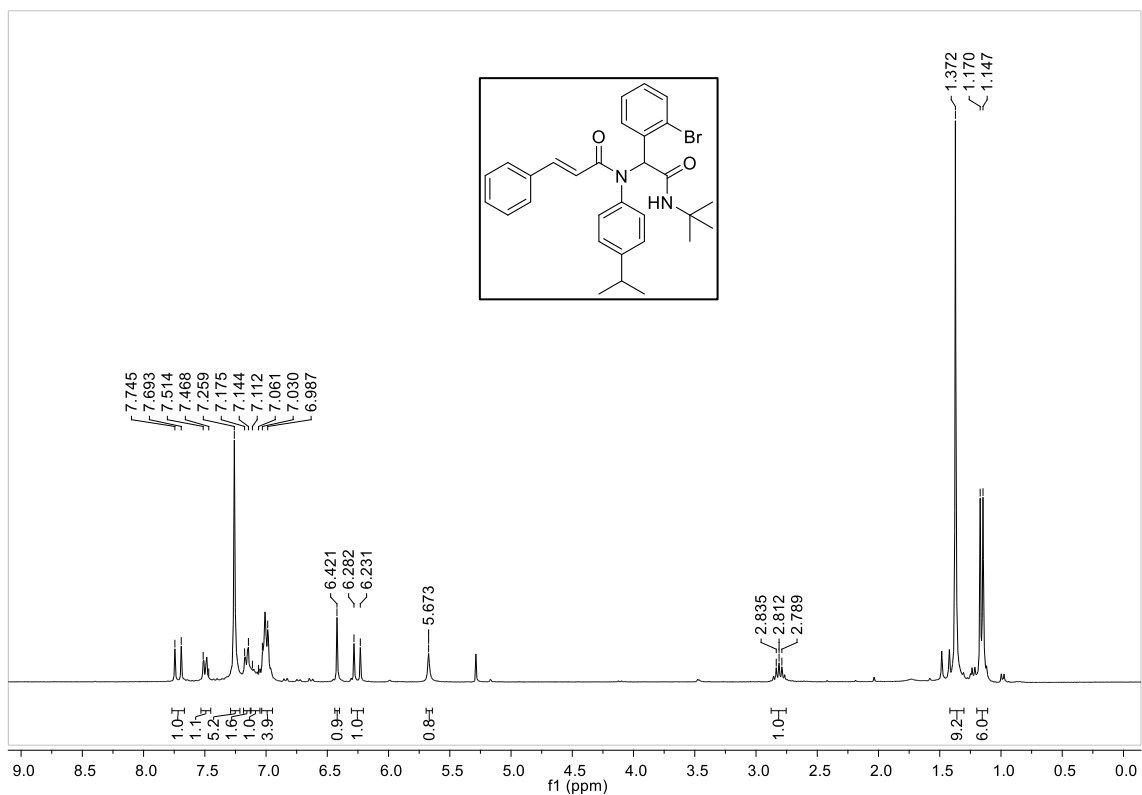


Figure S1. $^1\text{H-NMR}$ of 9a.

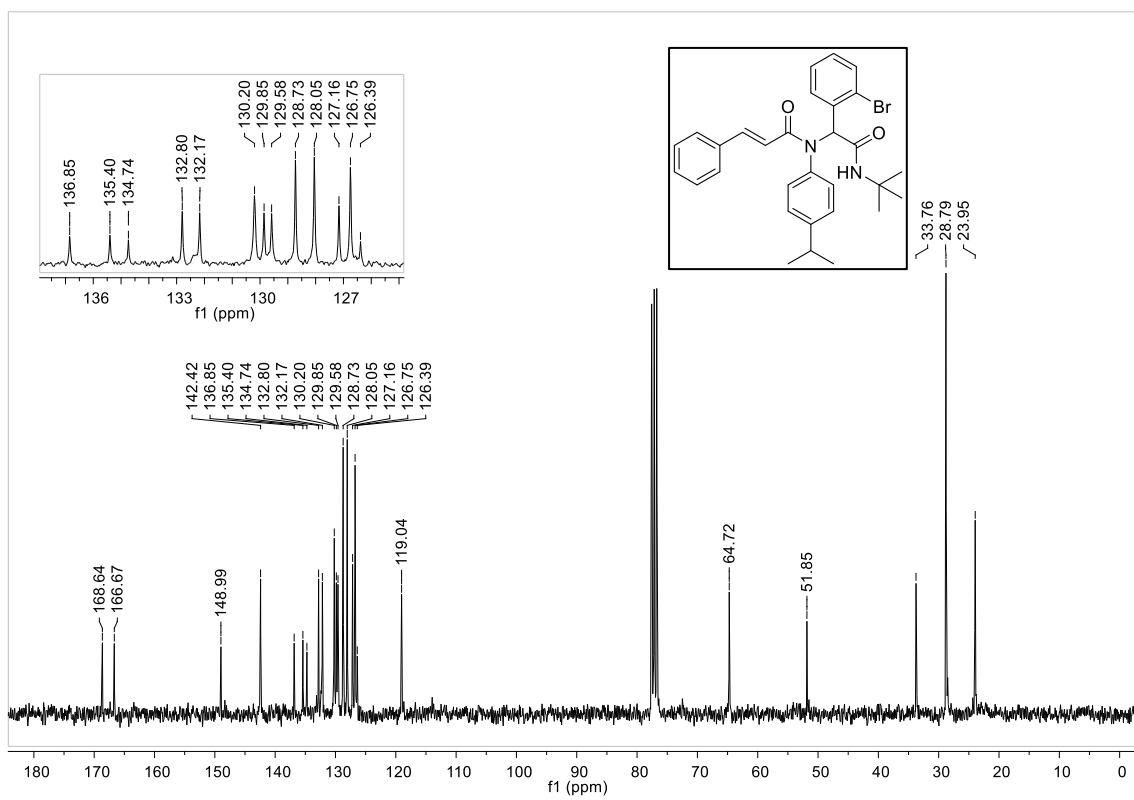


Figure S2. $^{13}\text{C-NMR}$ of 9a.



Figure S3. ¹H-NMR of 9b.

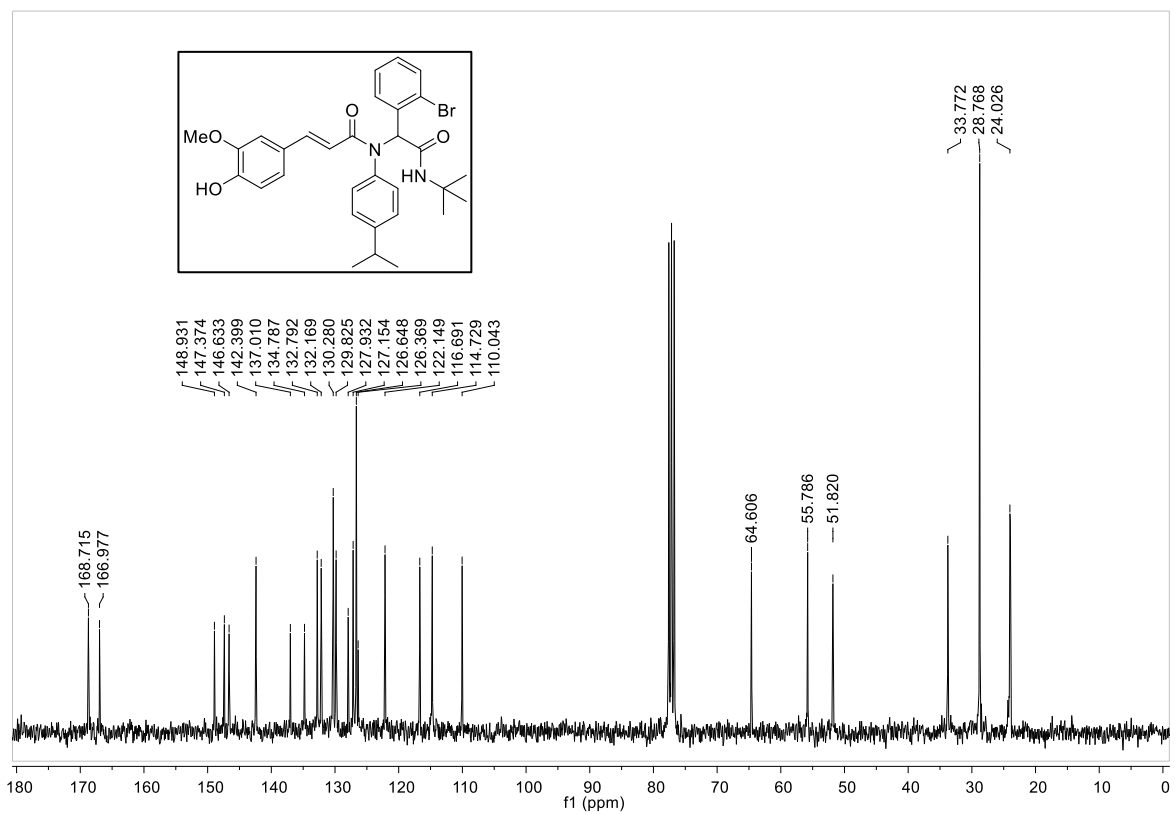


Figure S4. ¹³C-NMR of 9b.

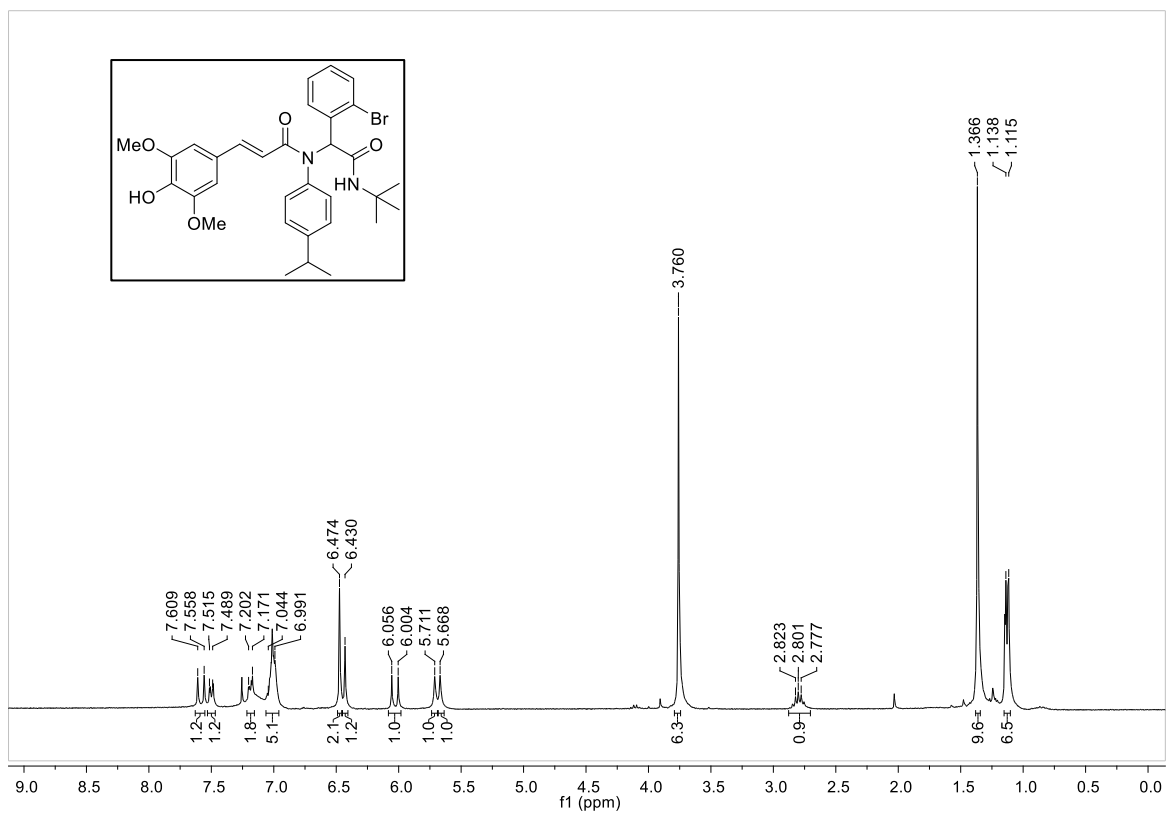


Figure S5. ¹H-NMR of 9c.

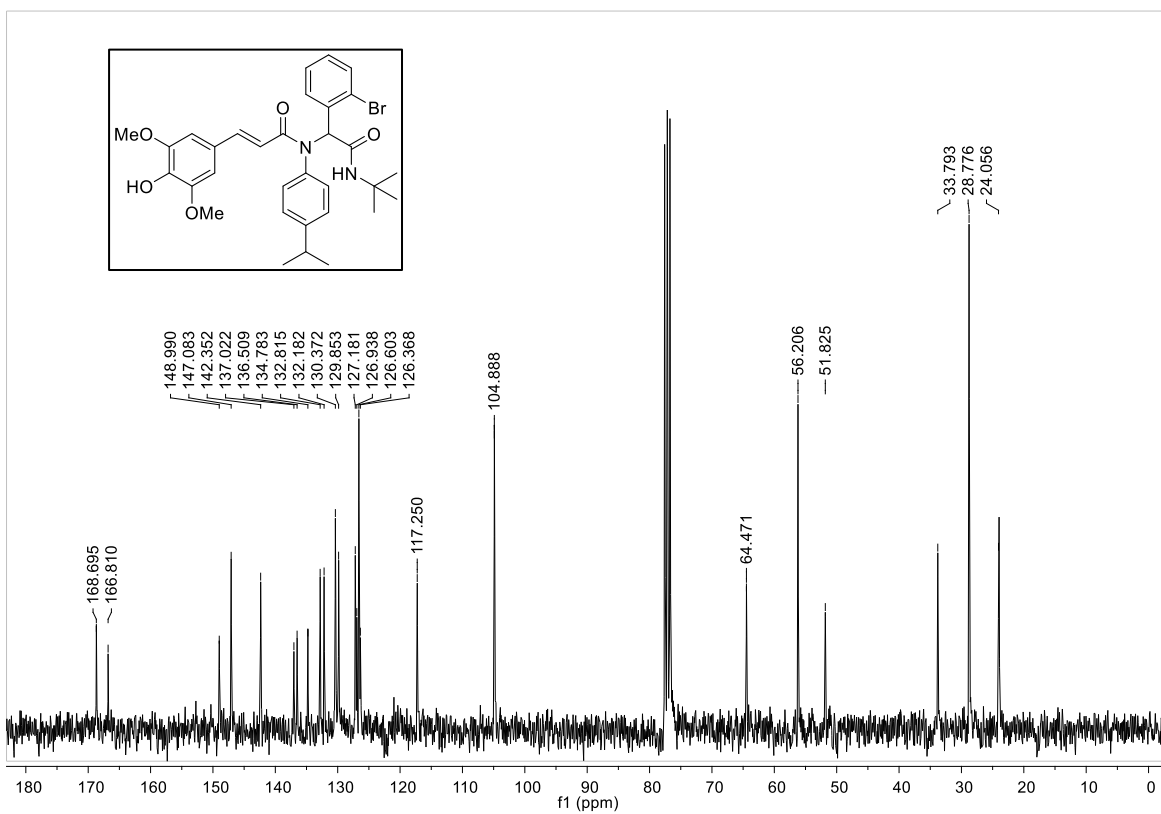


Figure S6. ^{13}C -NMR of 9c.

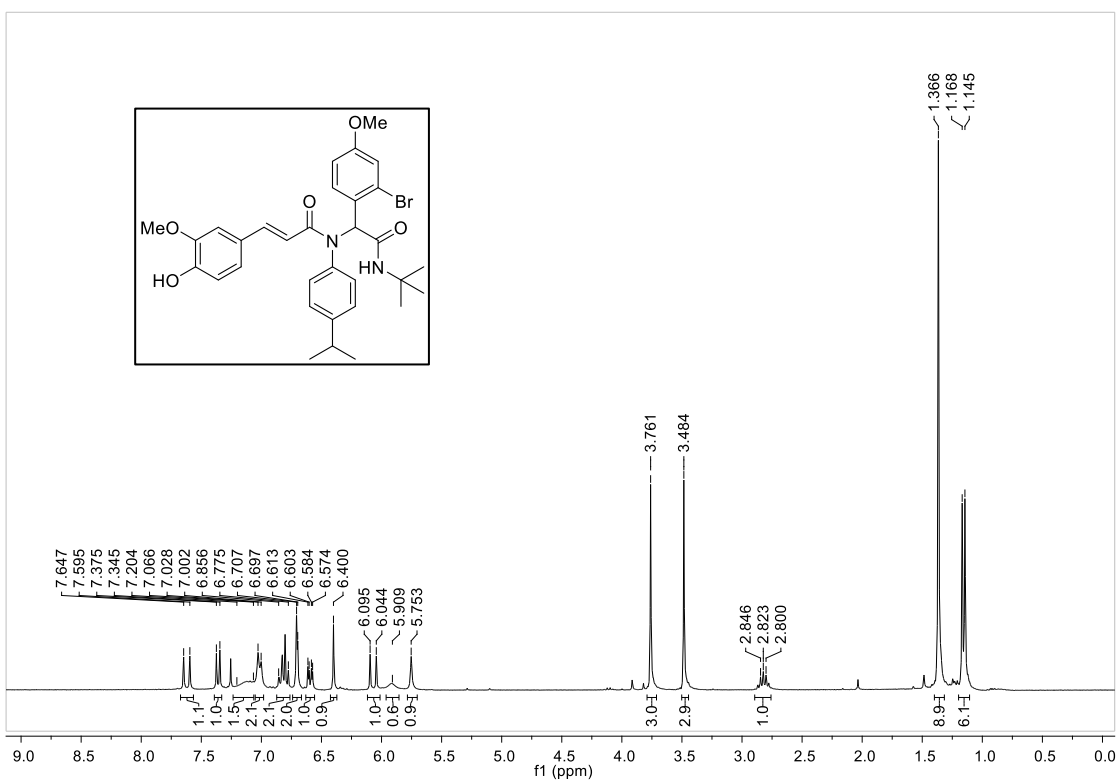


Figure S7. ^1H -NMR of 9d.

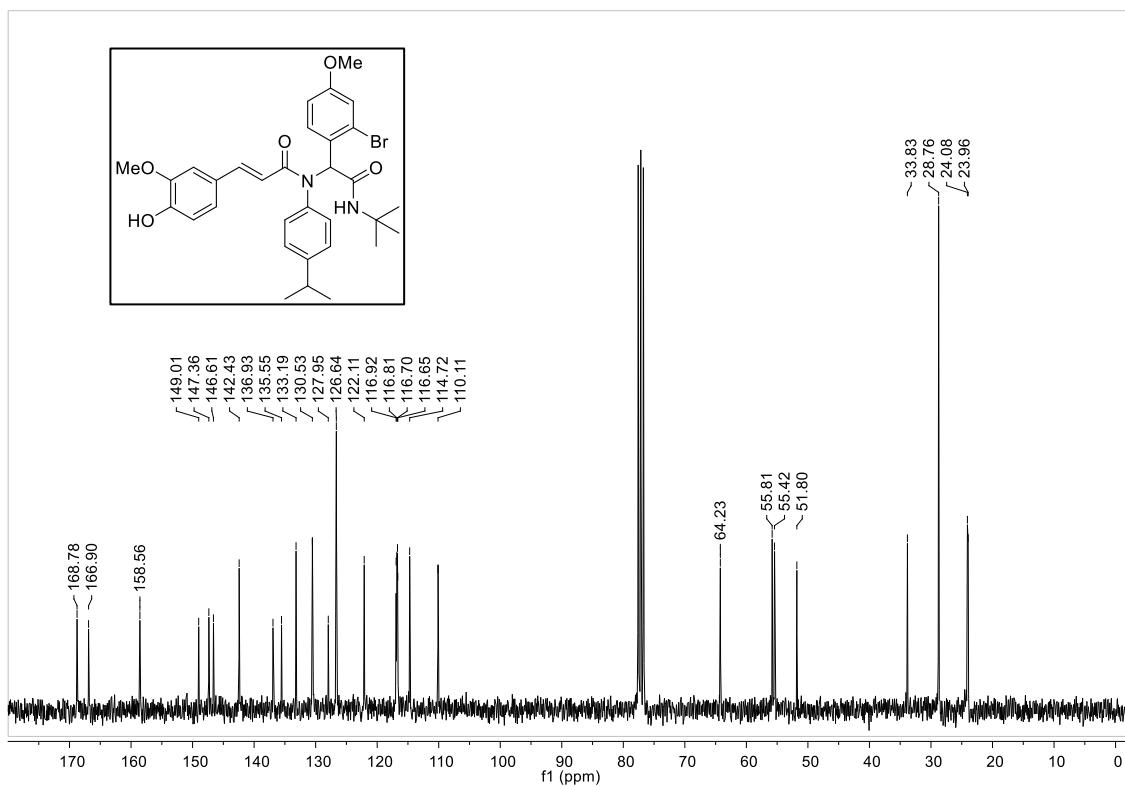


Figure S8. ¹³C-NMR of 9d.

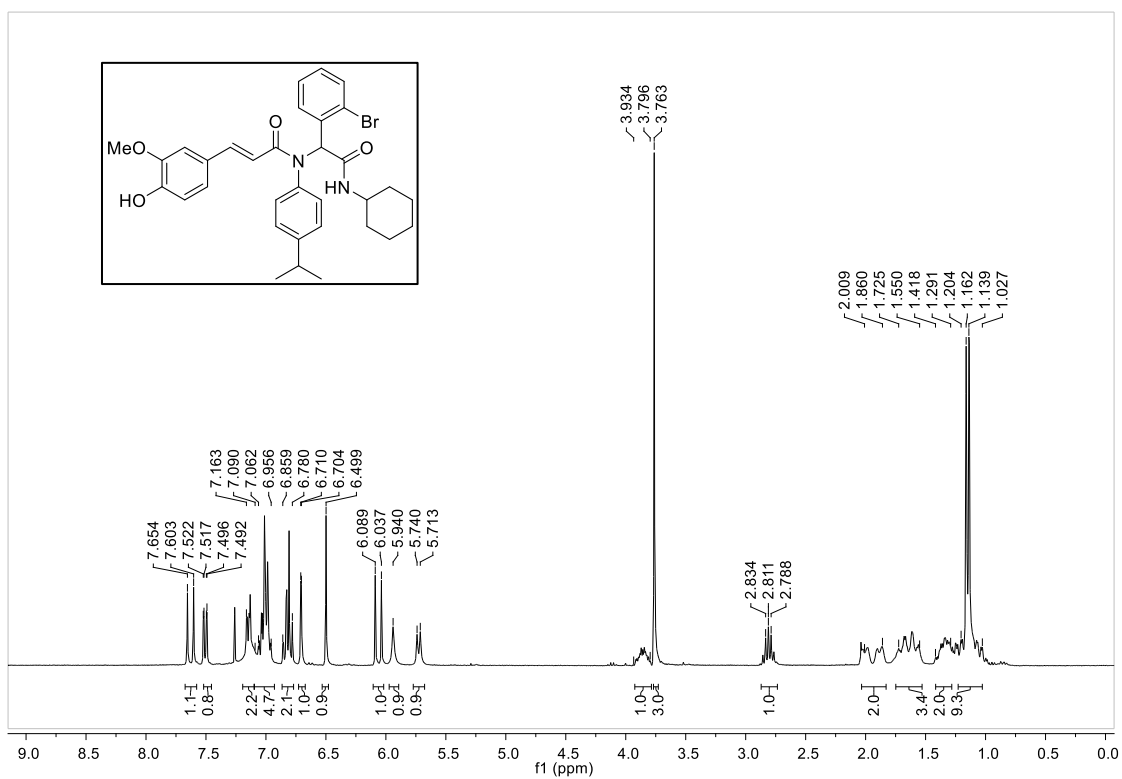


Figure S9. ¹H-NMR of 9e.

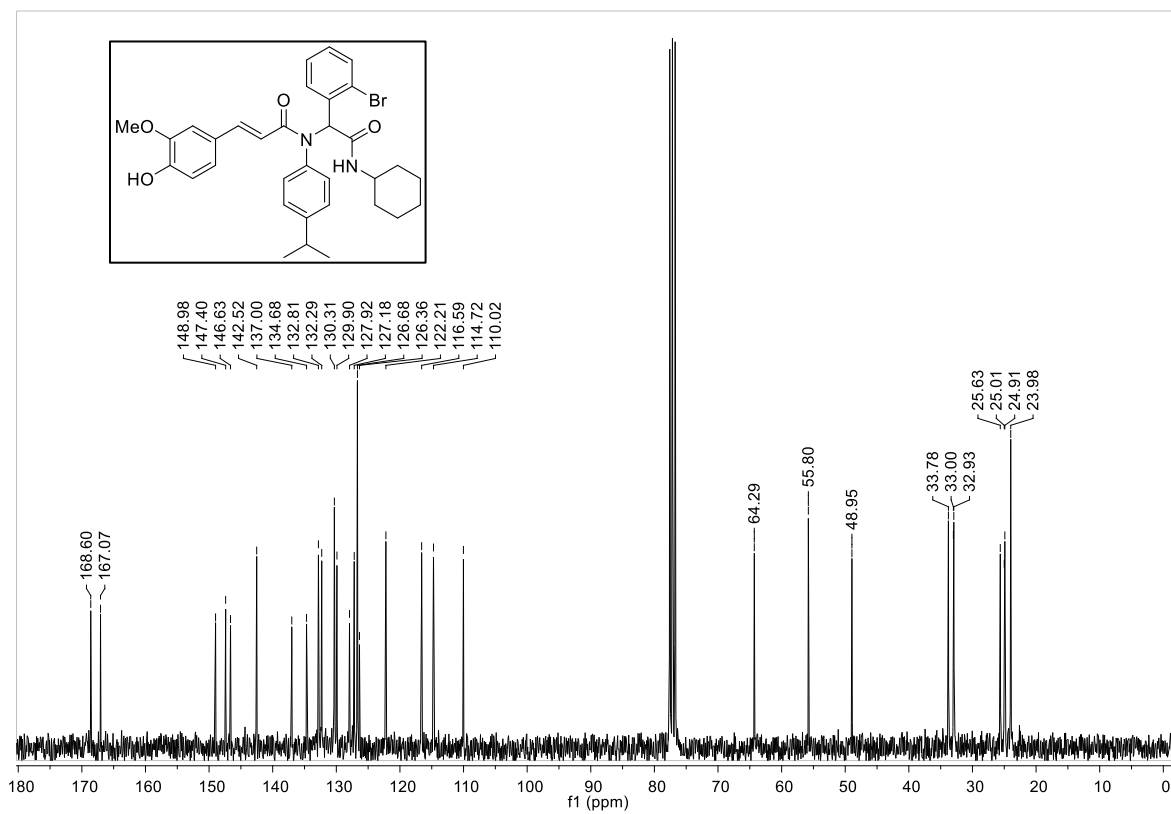


Figure S10. ¹³C-NMR of 9e.

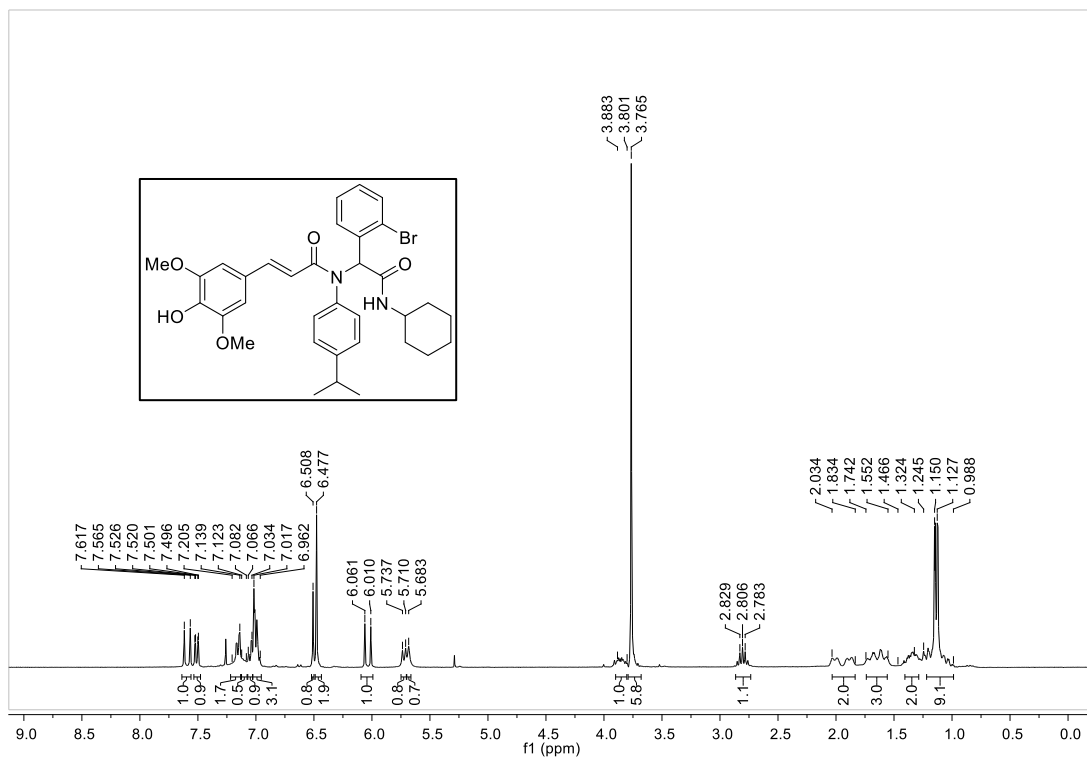


Figure S11. ¹H-NMR of 9f.

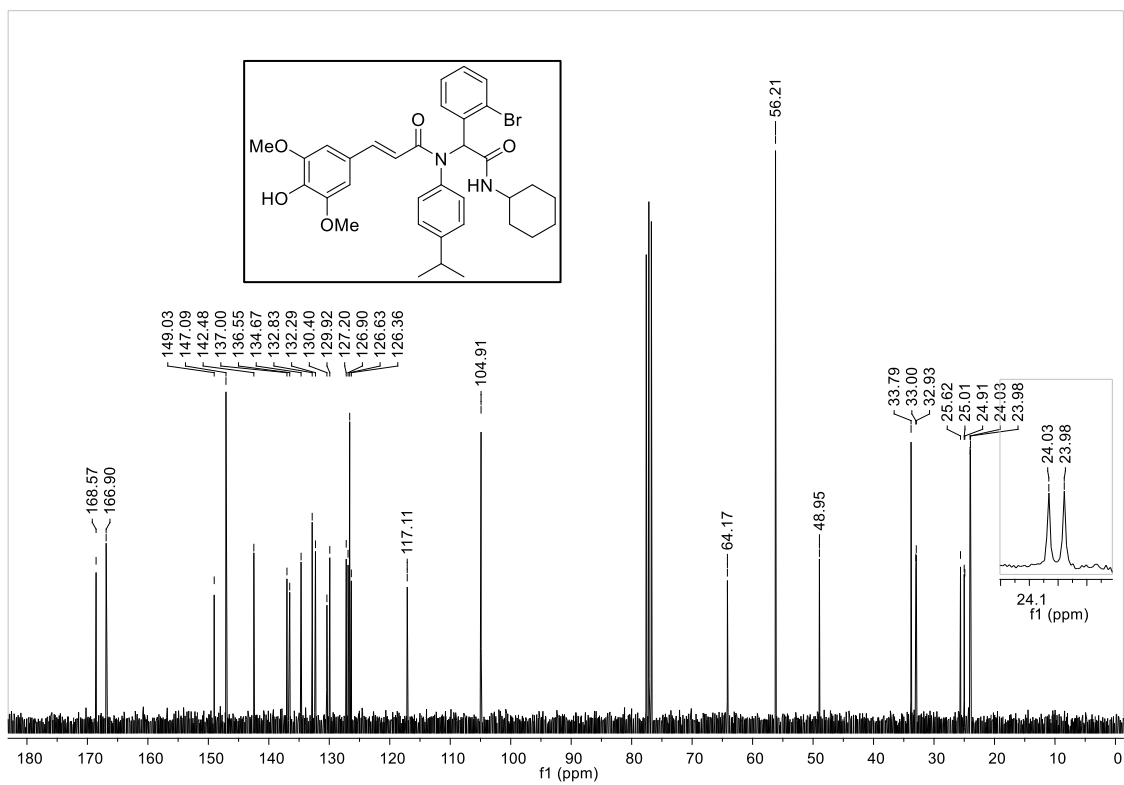


Figure S12. ¹³C-NMR of 9f.

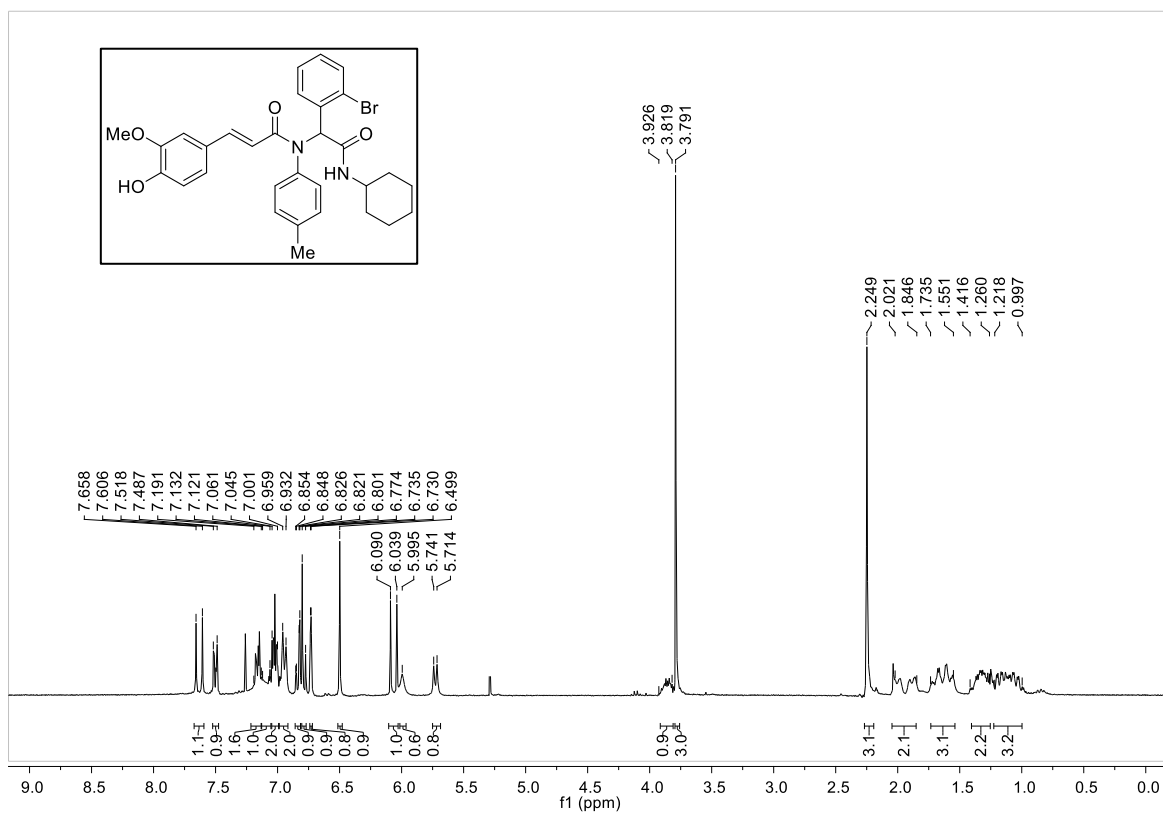


Figure S13. ¹H-NMR of 9g.

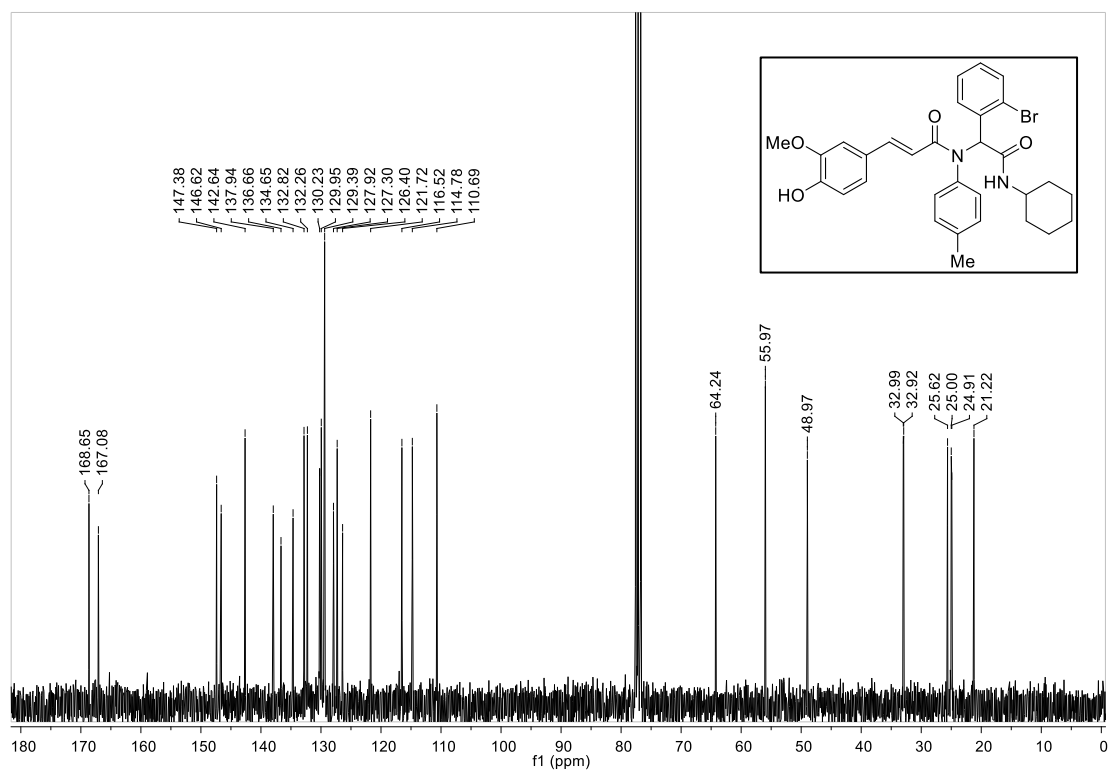


Figure S14. ¹³C-NMR of 9g.

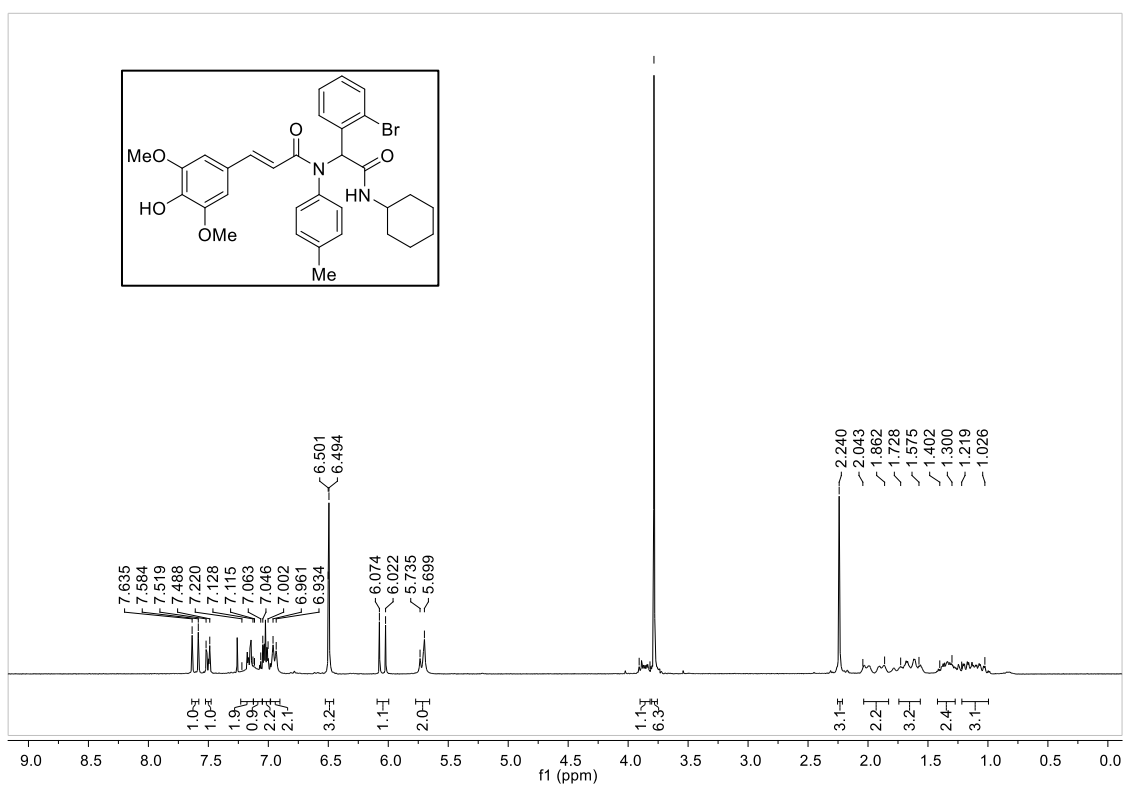


Figure S15. ¹H-NMR of 9h.

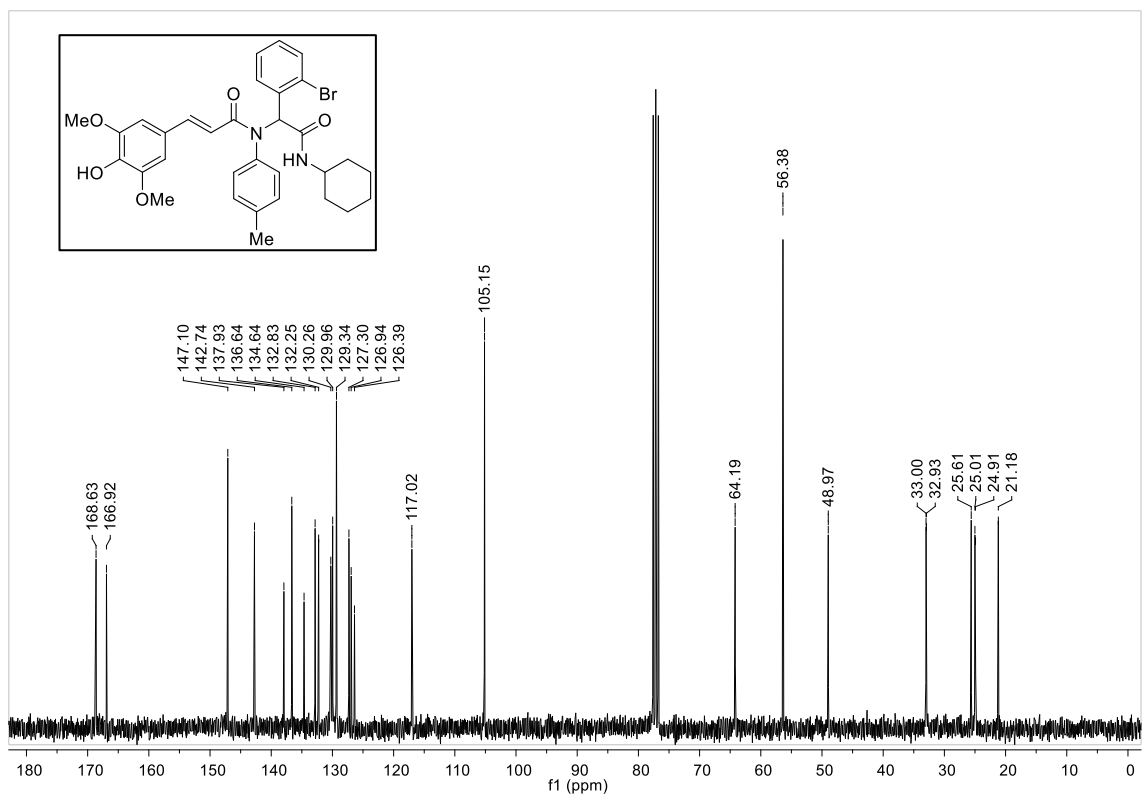


Figure S16. ¹³C-NMR of 9h.

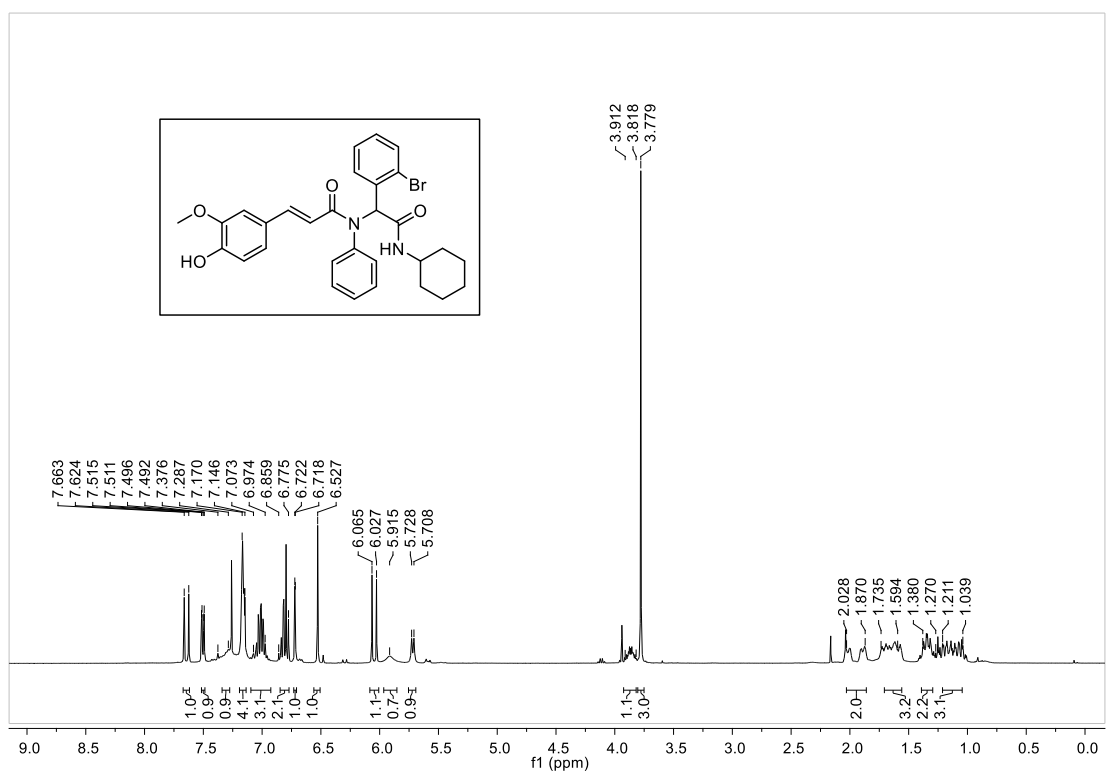
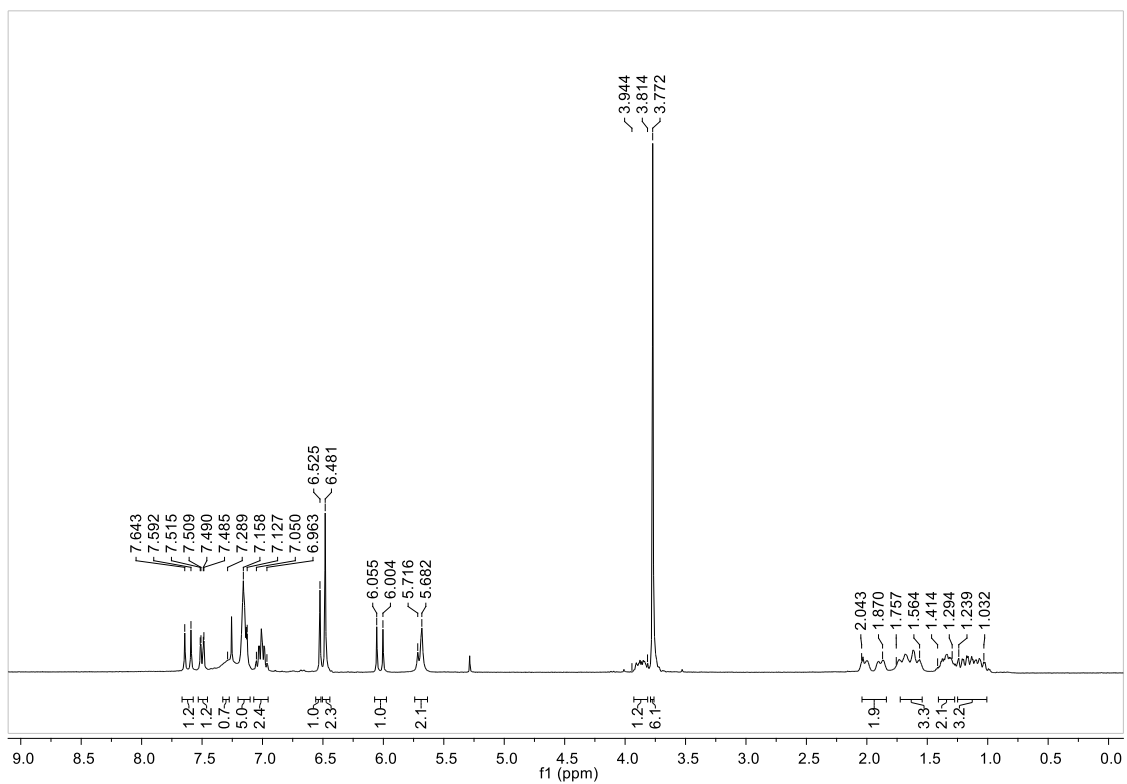
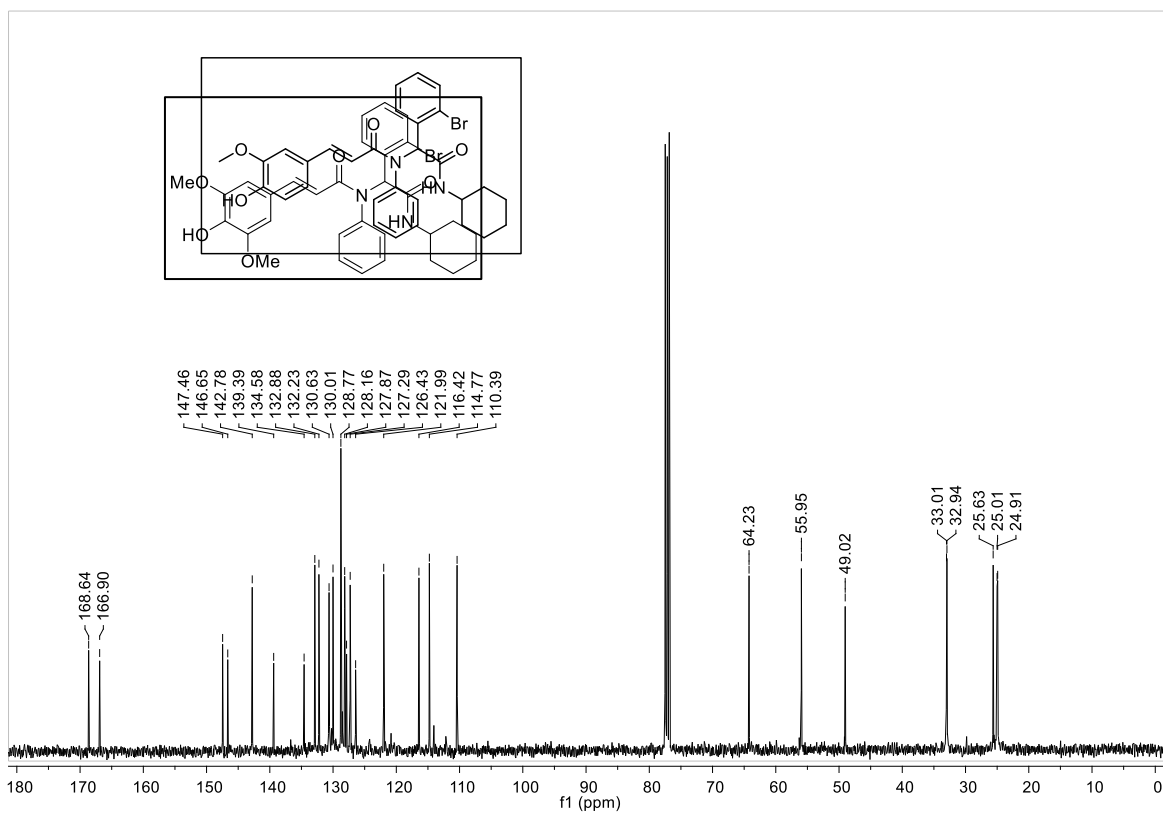


Figure S17. ¹H-NMR of 9i.



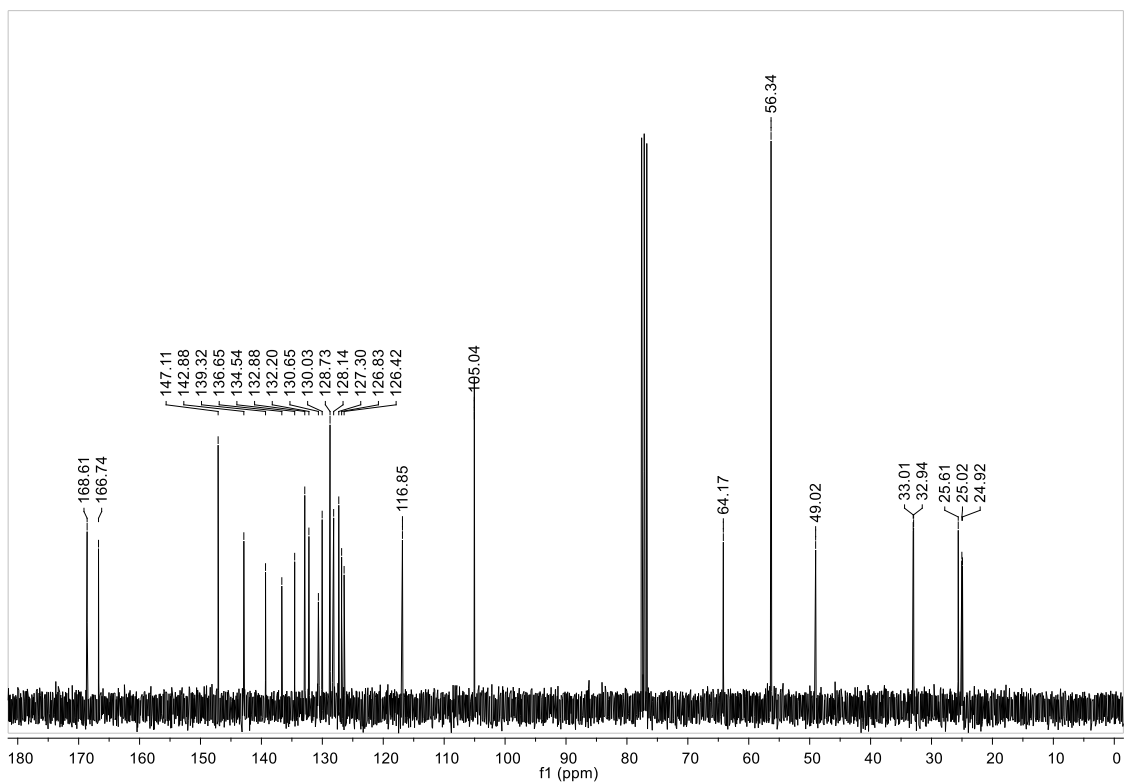


Figure S20. ^{13}C -NMR of 9j.

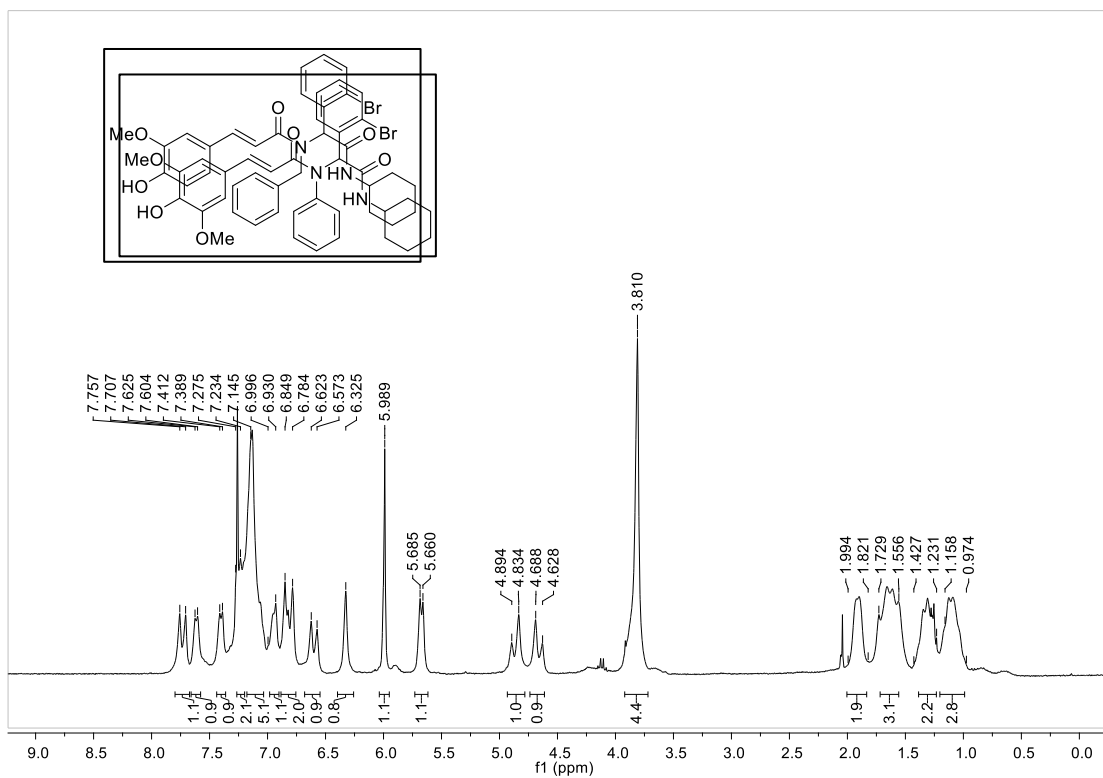


Figure S21. ^1H -NMR of 9k.

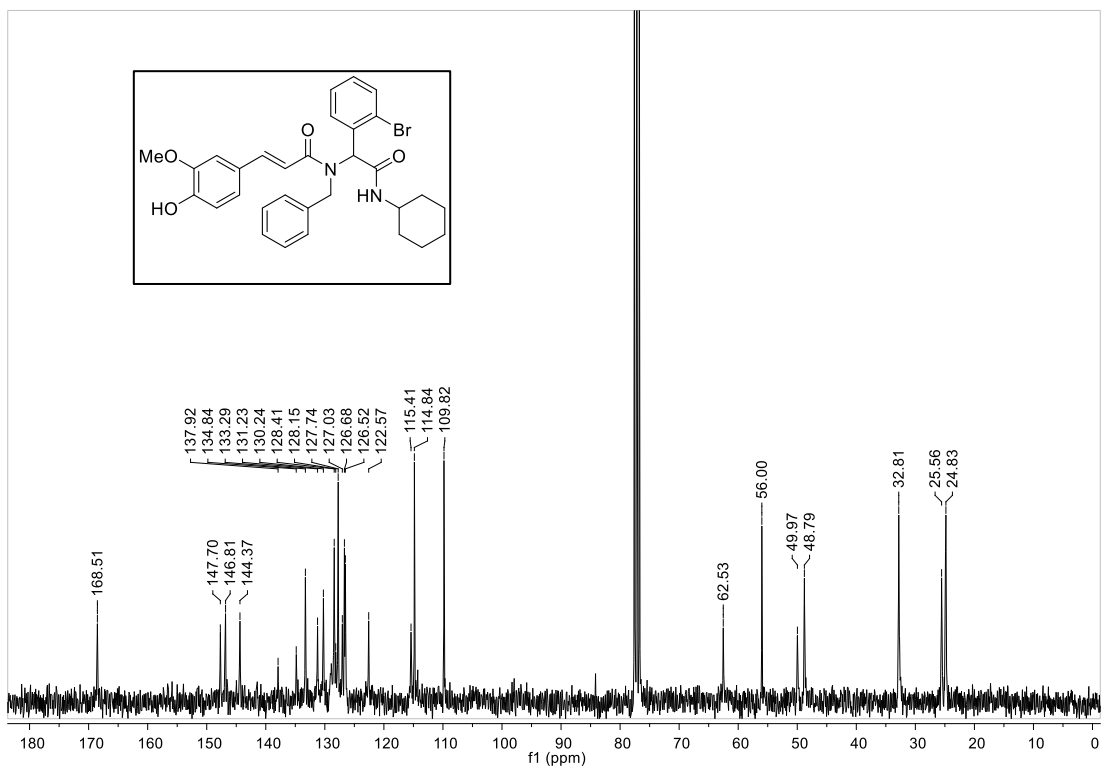


Figure S22. ¹³C-NMR of 9k.

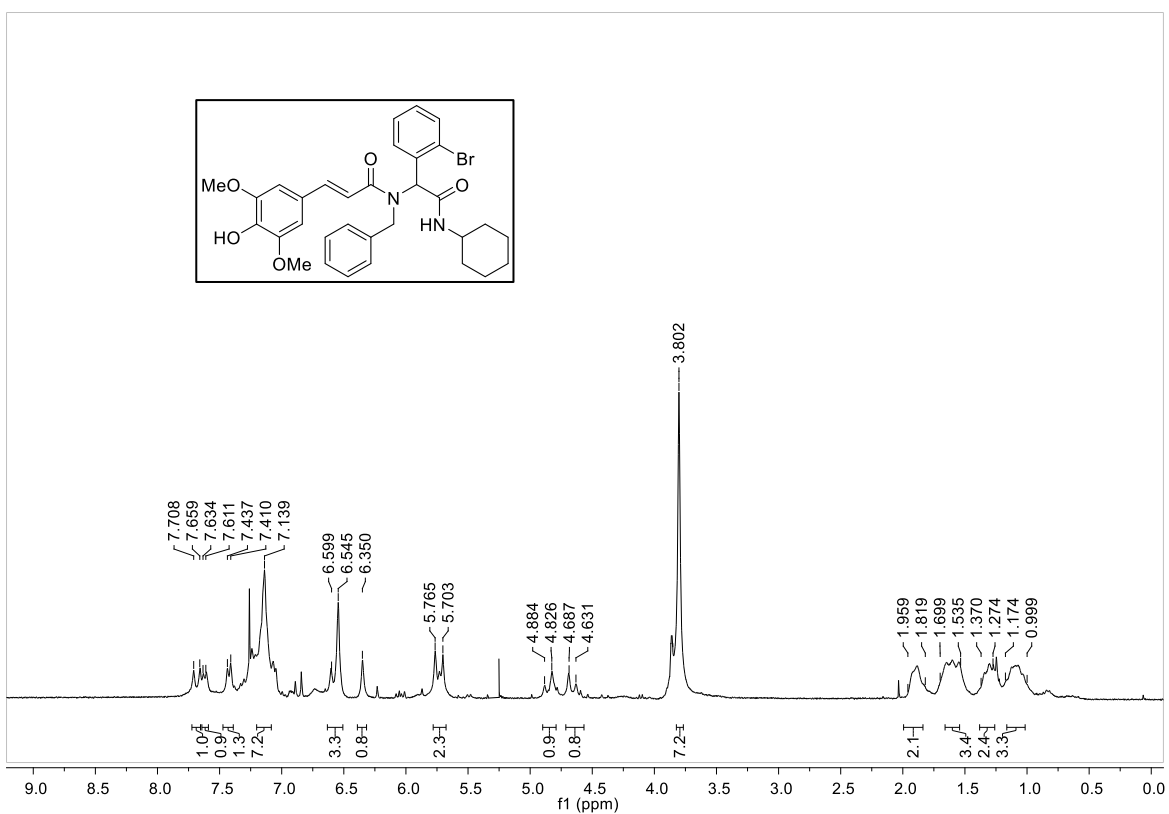


Figure S23. ¹H-NMR of 9l.

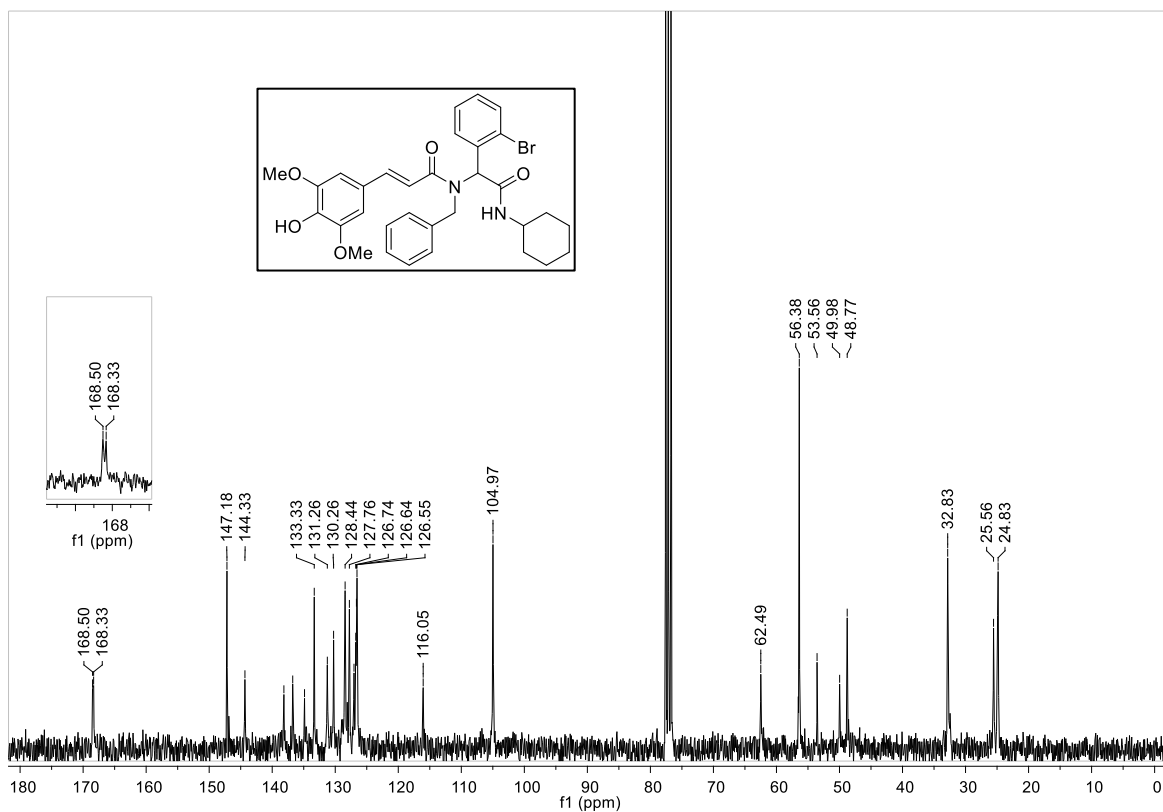


Figure S24. ¹³C-NMR of 9l.

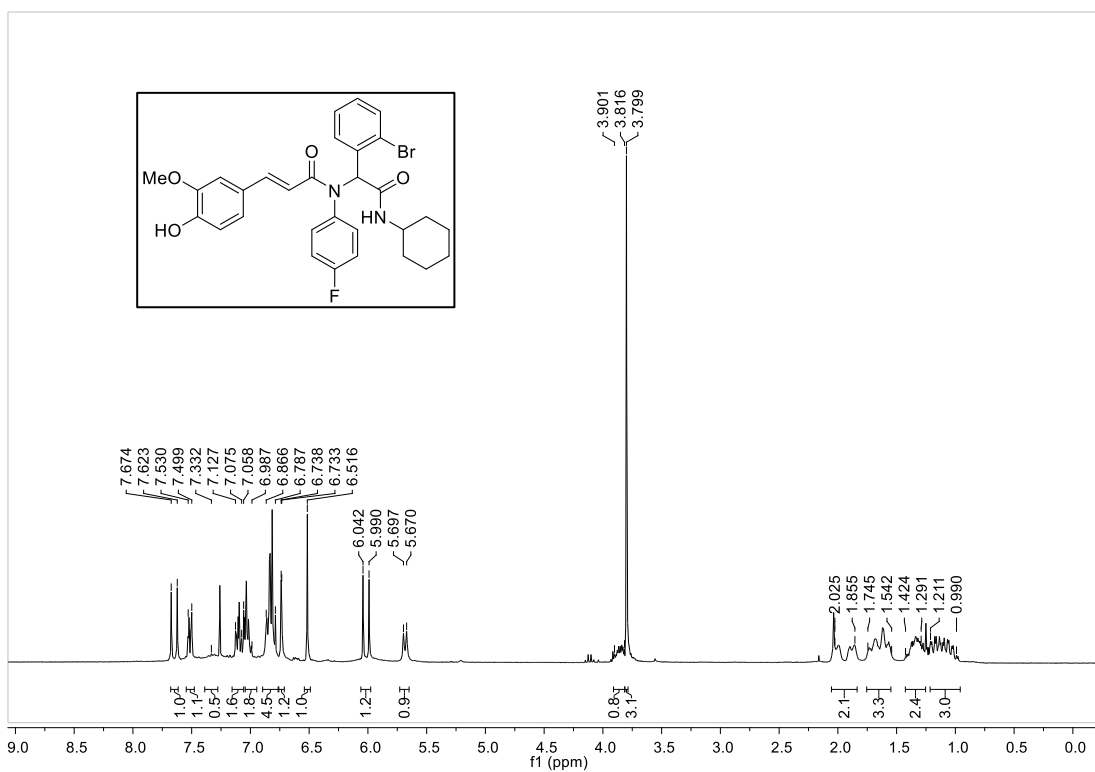


Figure S25. ¹H-NMR of 9m.

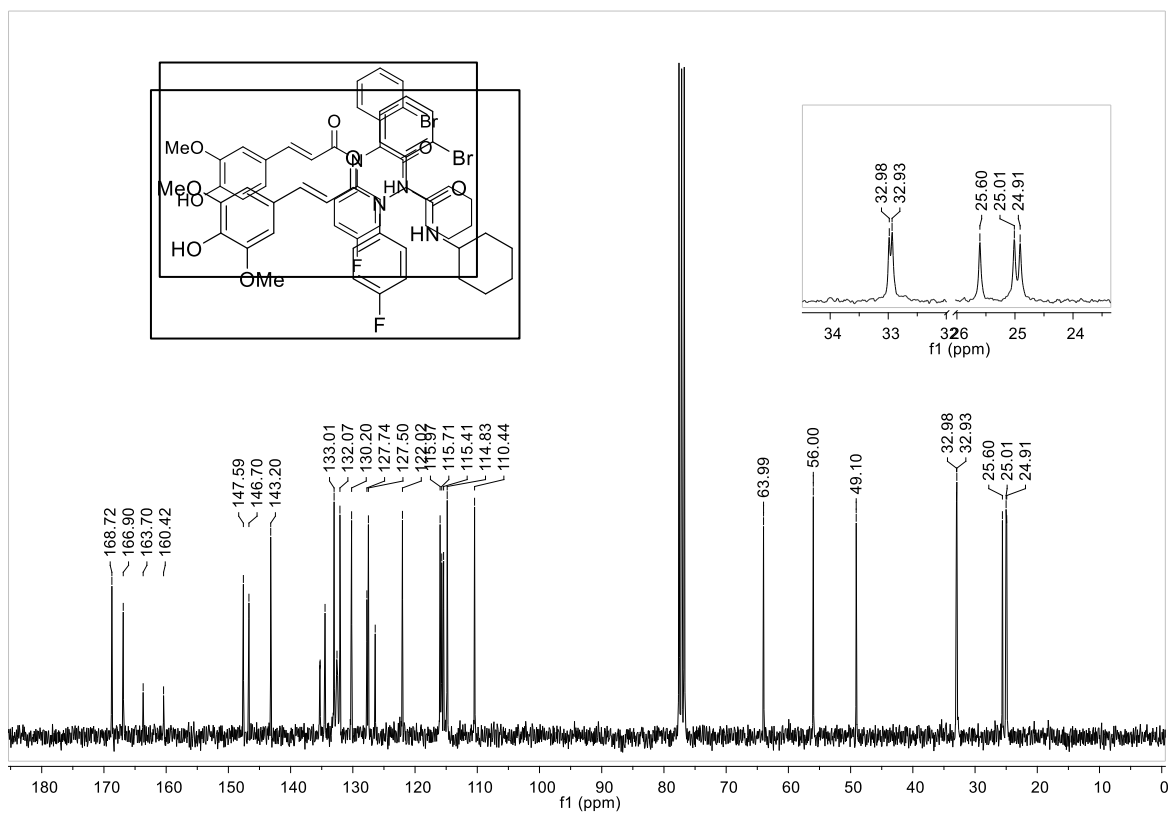


Figure S26. ¹³C-NMR of 9m.

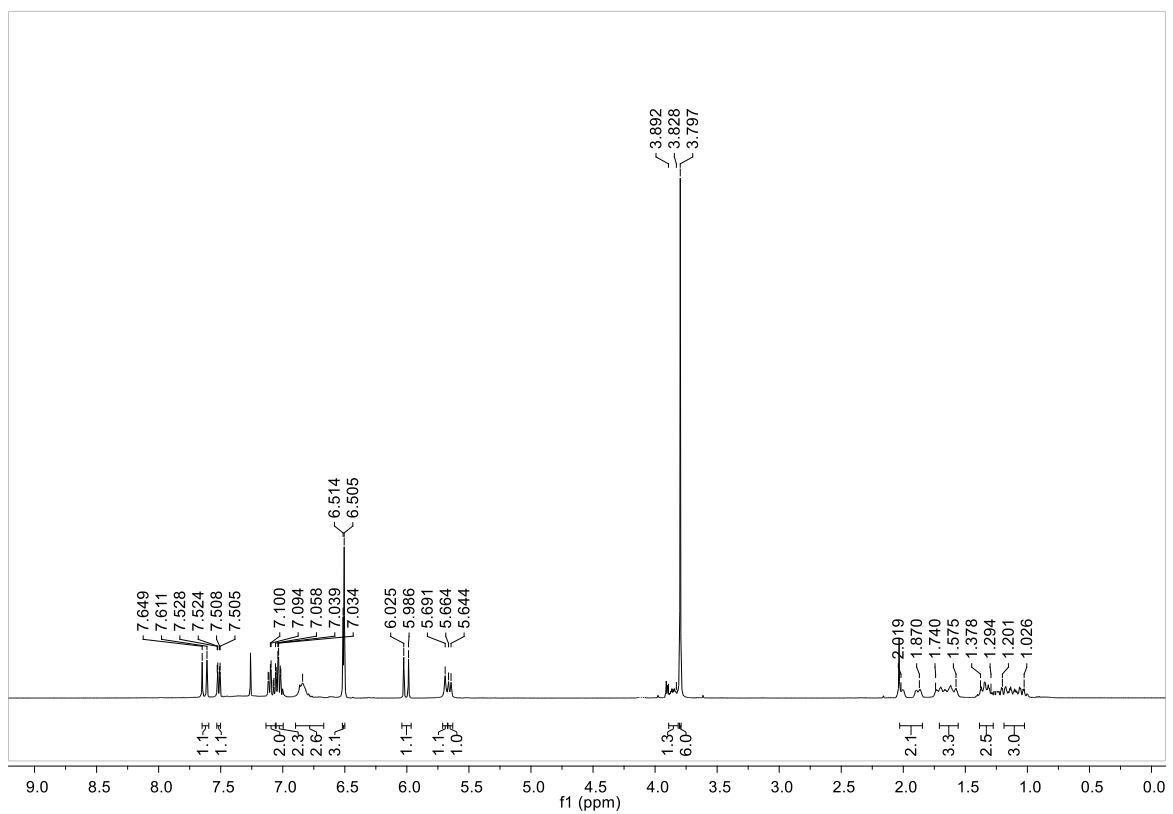


Figure S27. ¹H-NMR of 9n.

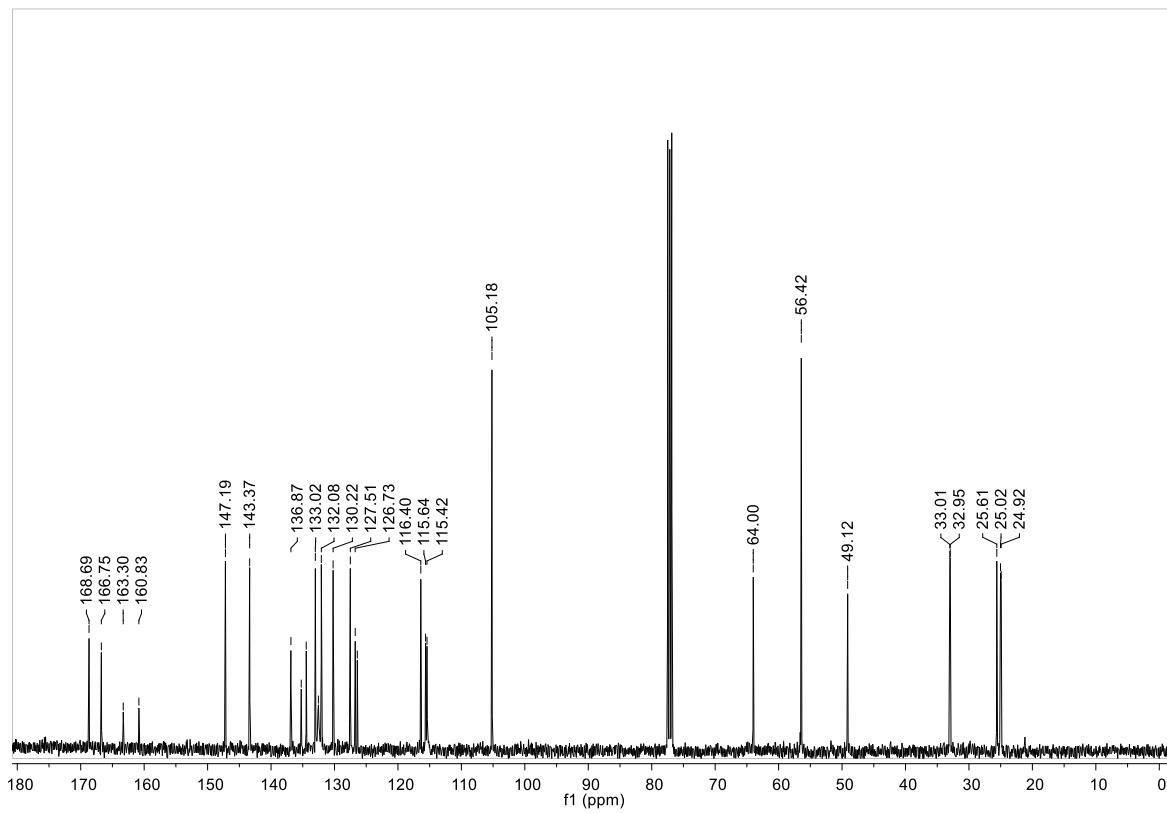
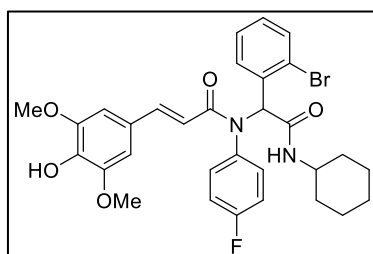


Figure S28. ¹³C-NMR of 9n.



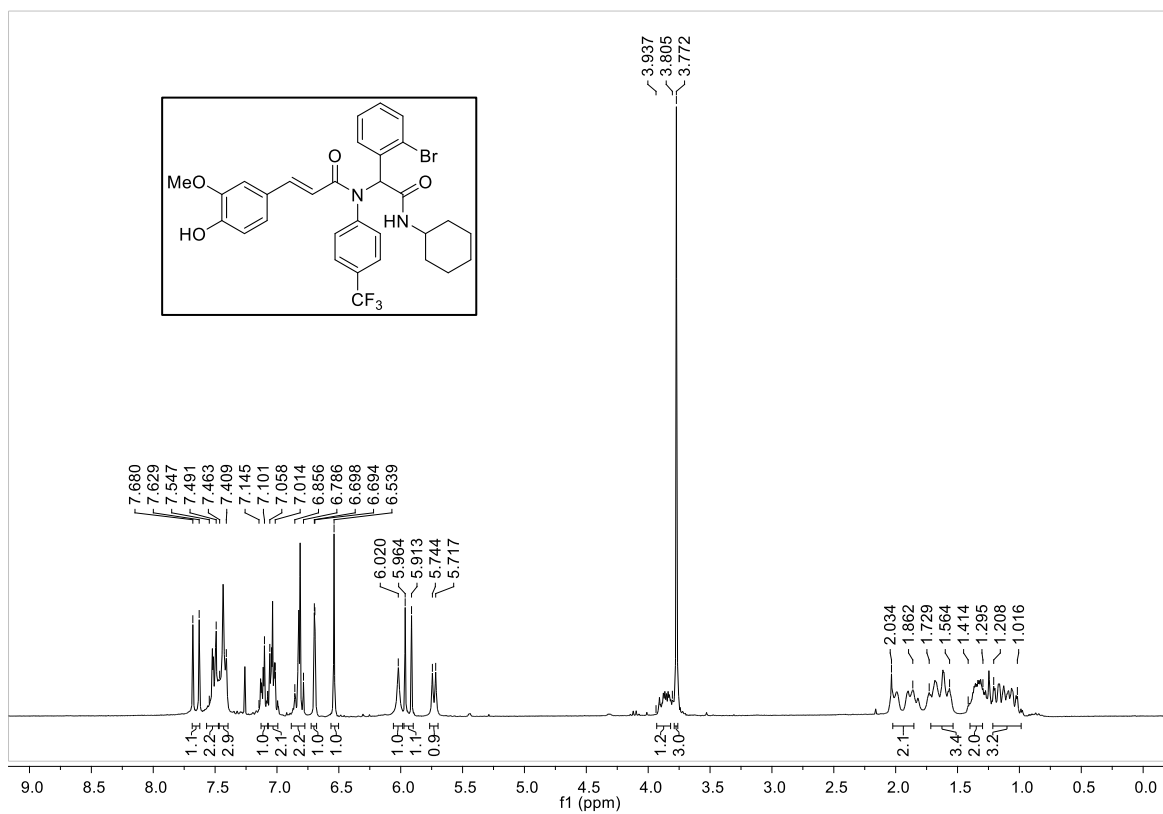


Figure S29. ¹H-NMR of **9o**.

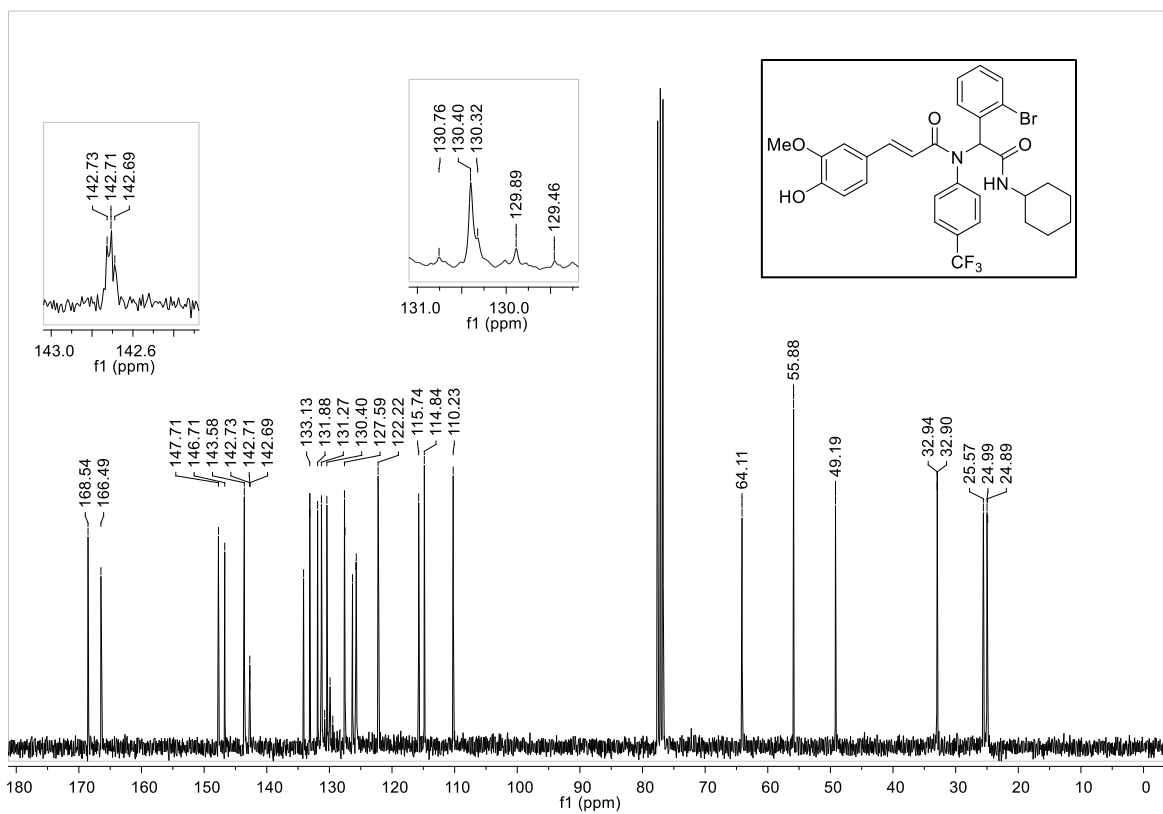


Figure S30. ¹³C-NMR of 9o.

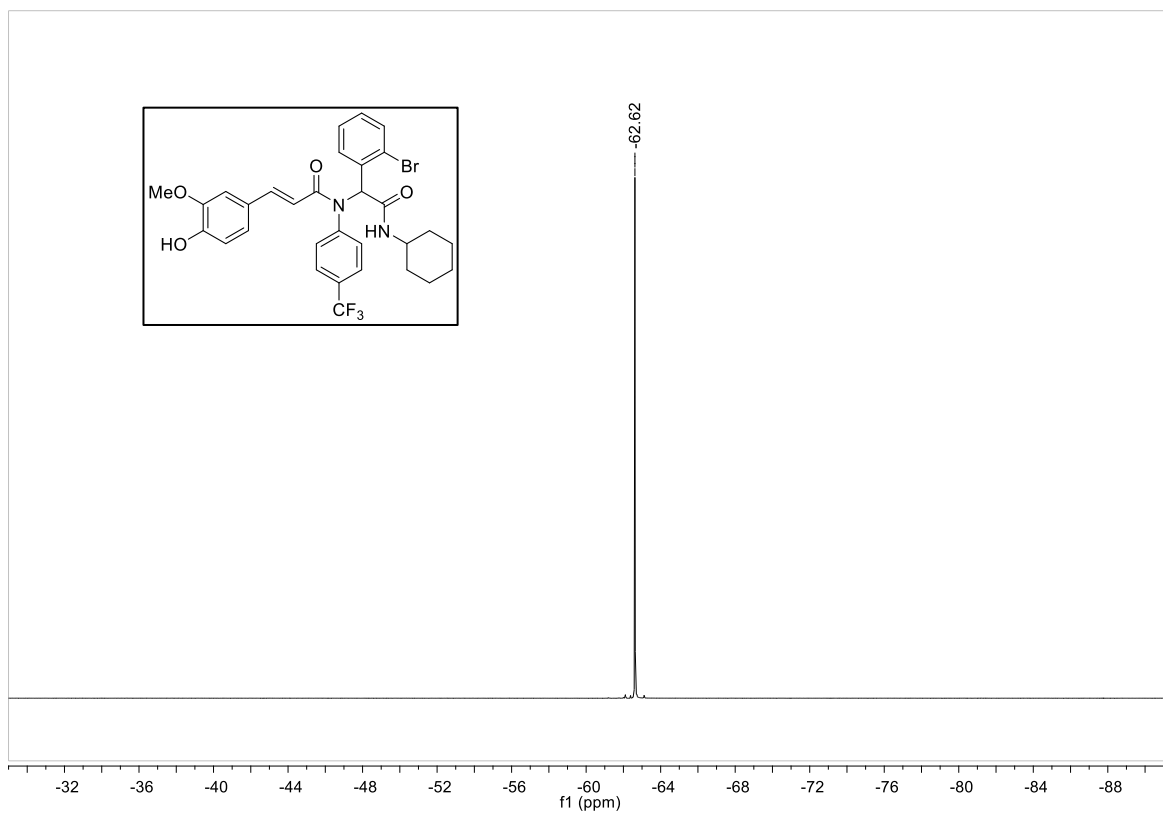


Figure S31. ^{19}F -NMR of 9o.

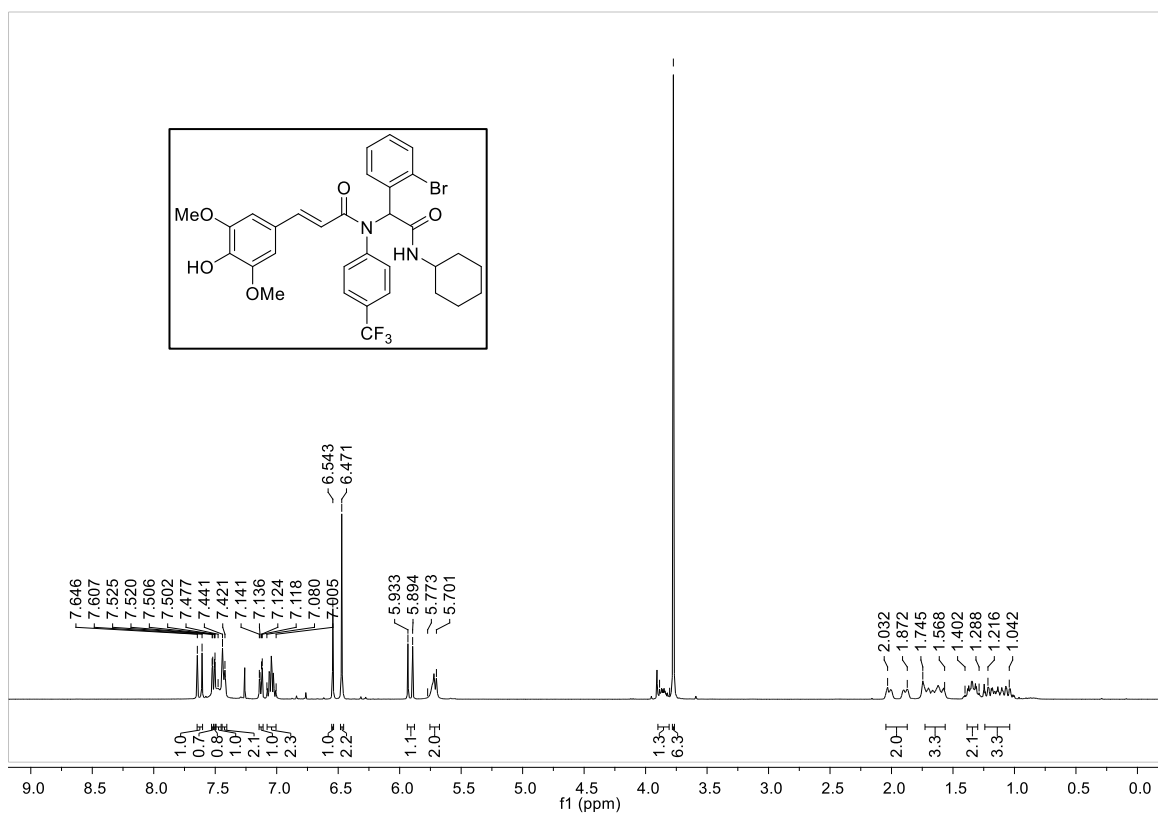
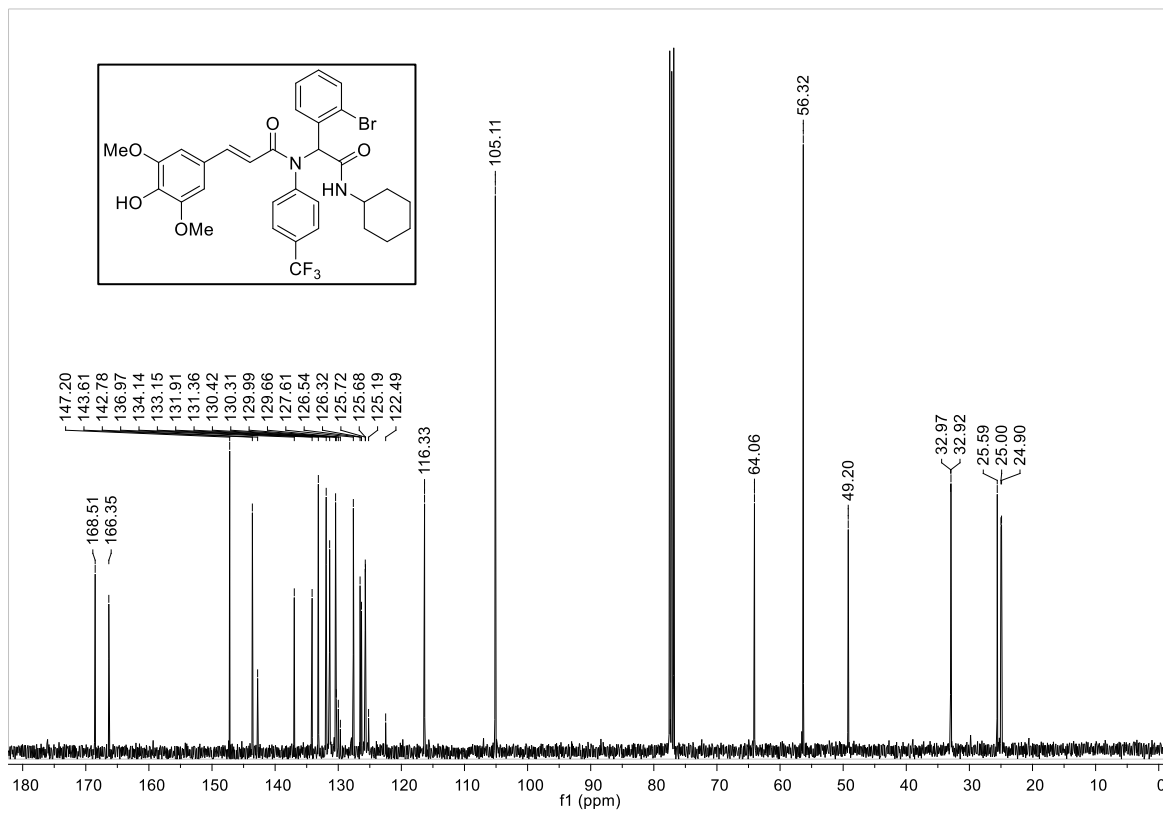


Figure S32. ¹H-NMR of 9p.



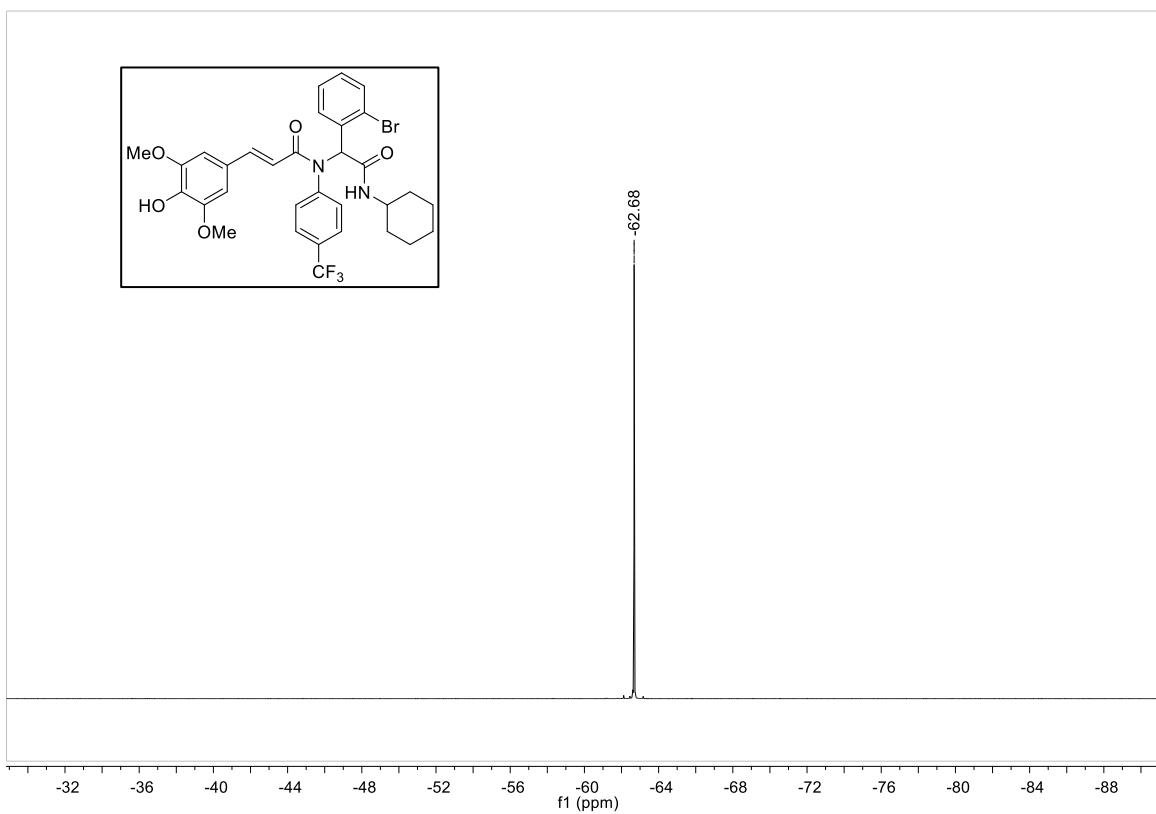


Figure S34. ^{19}F -NMR of **9p**.

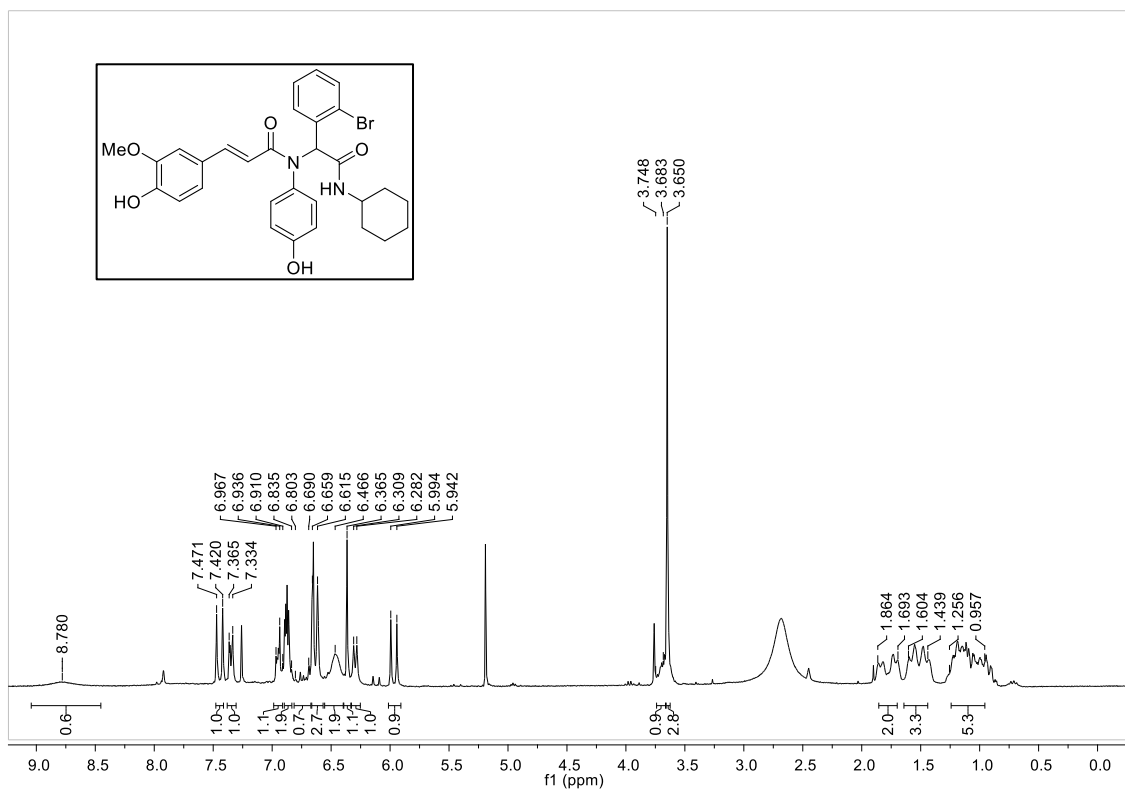


Figure S35. ¹H-NMR of 9q.

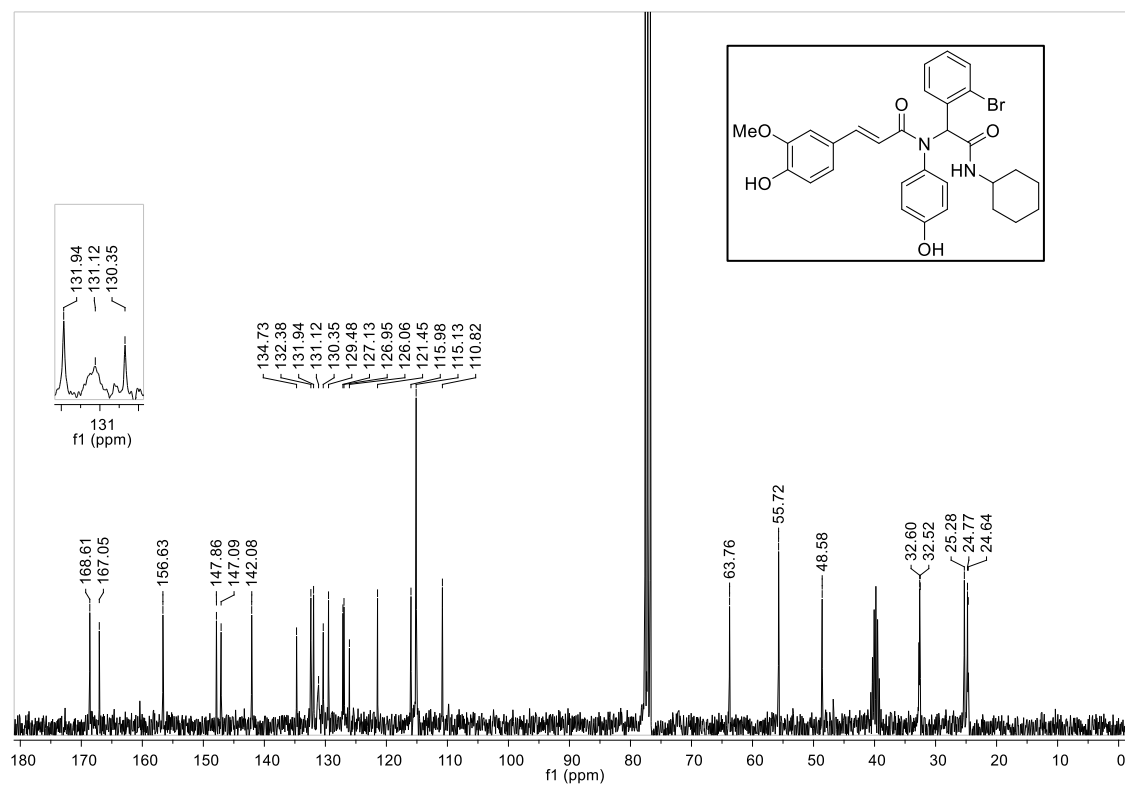


Figure S36. ¹³C-NMR of 9q.

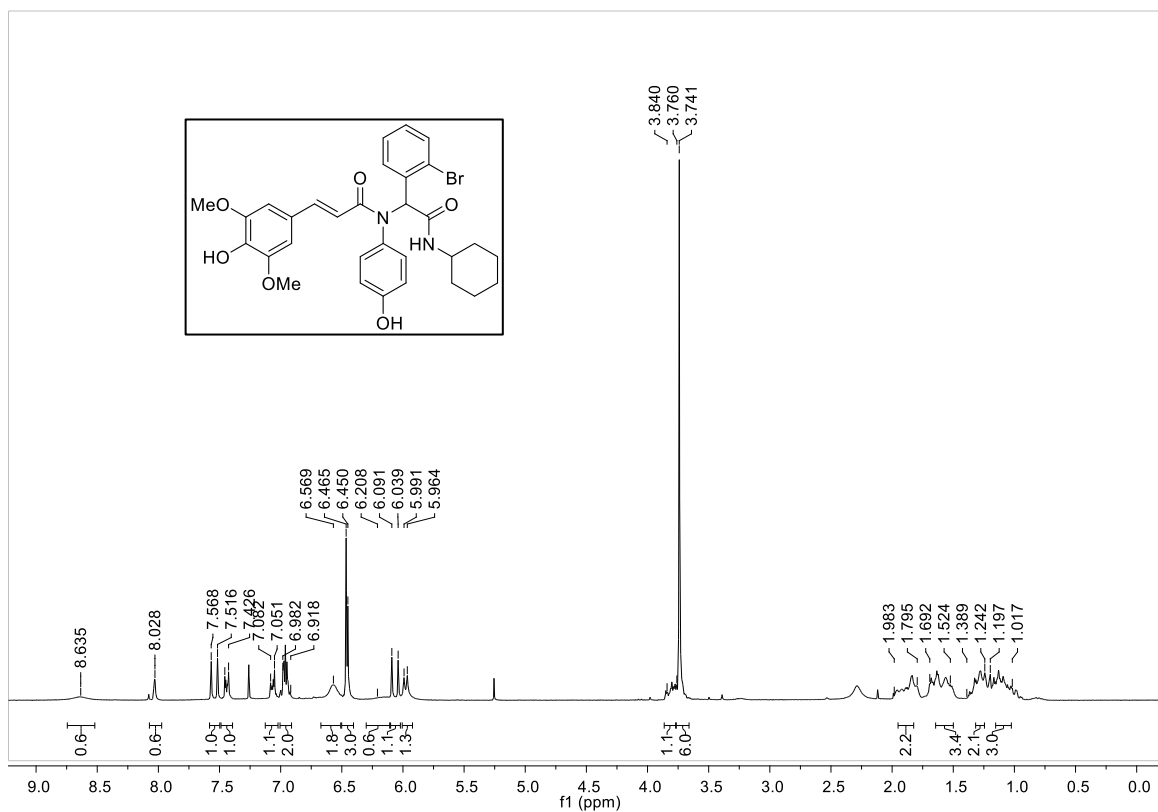


Figure S37. ¹H-NMR of 9r.

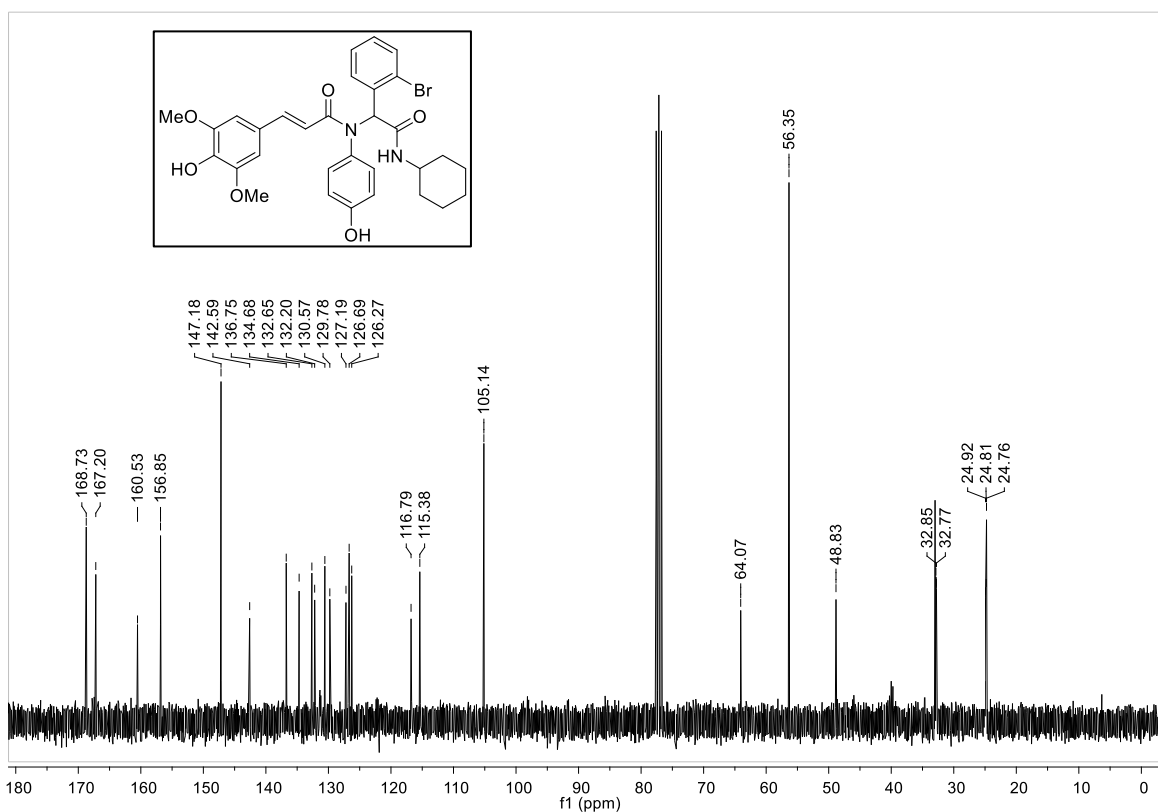


Figure S38. ¹³C-NMR of 9r.

^1H -NMR and ^{13}C -NMR spectra of isoquinolinones
10a–r.

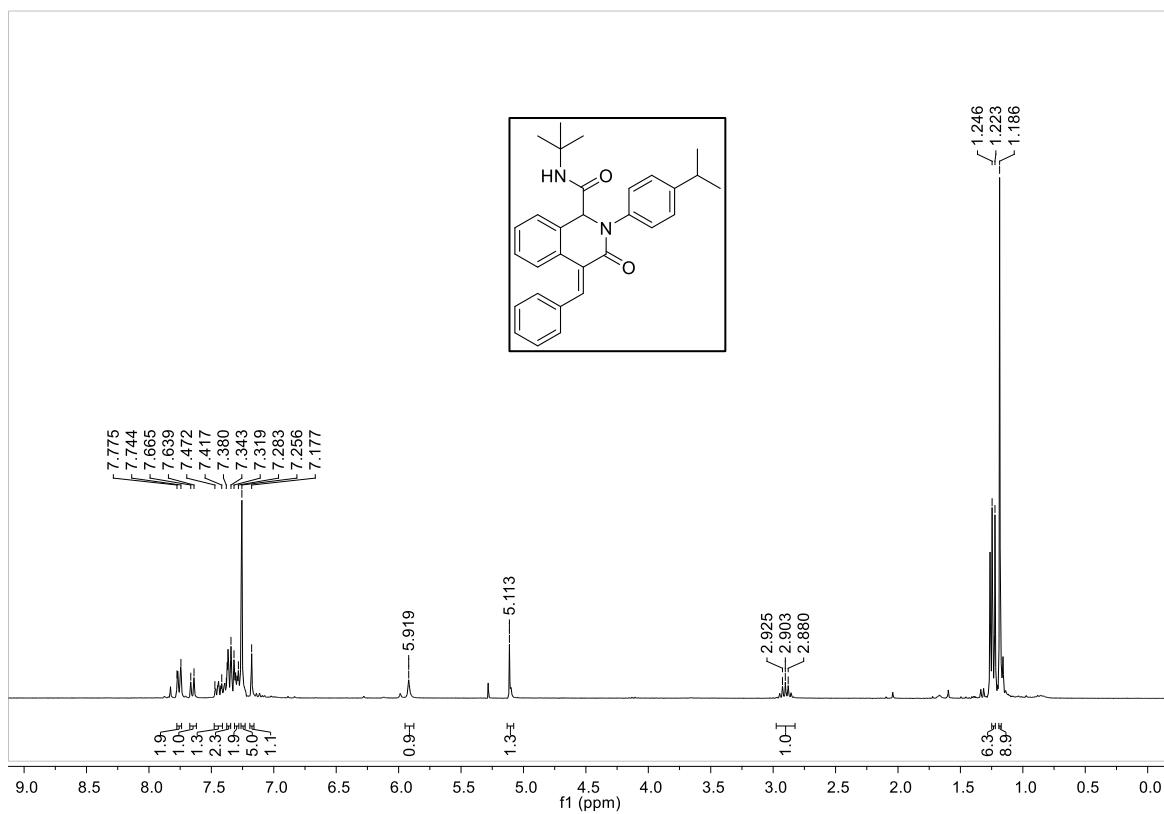


Figure S39. $^1\text{H-NMR}$ of 10a.

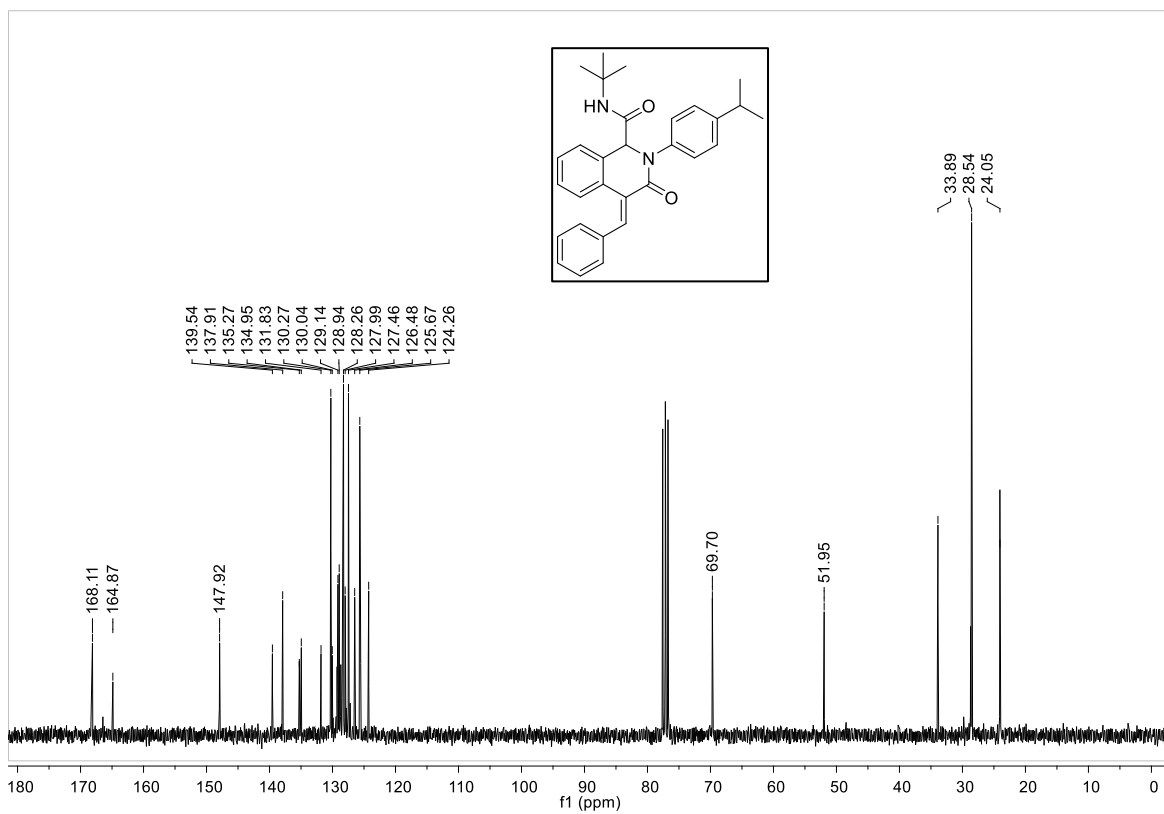


Figure S40. ^{13}C -NMR of 10a.

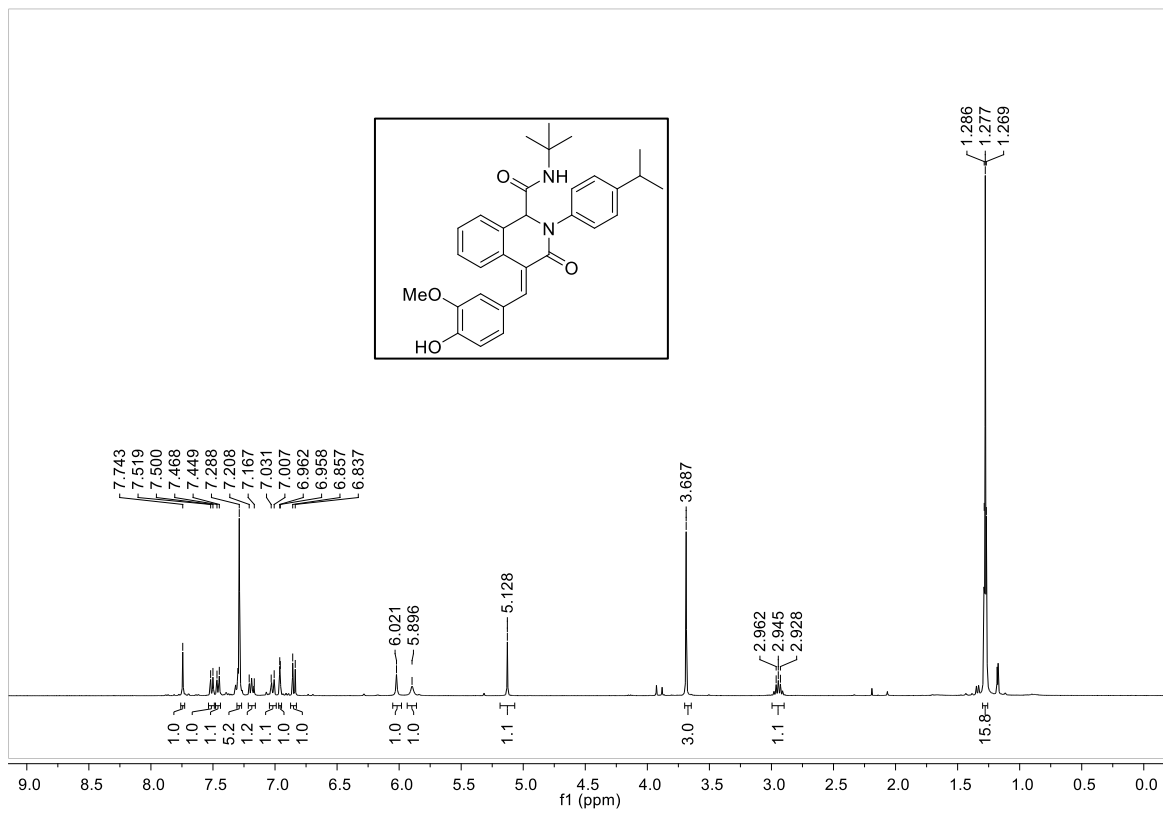


Figure S41. ^1H -NMR of 10b.

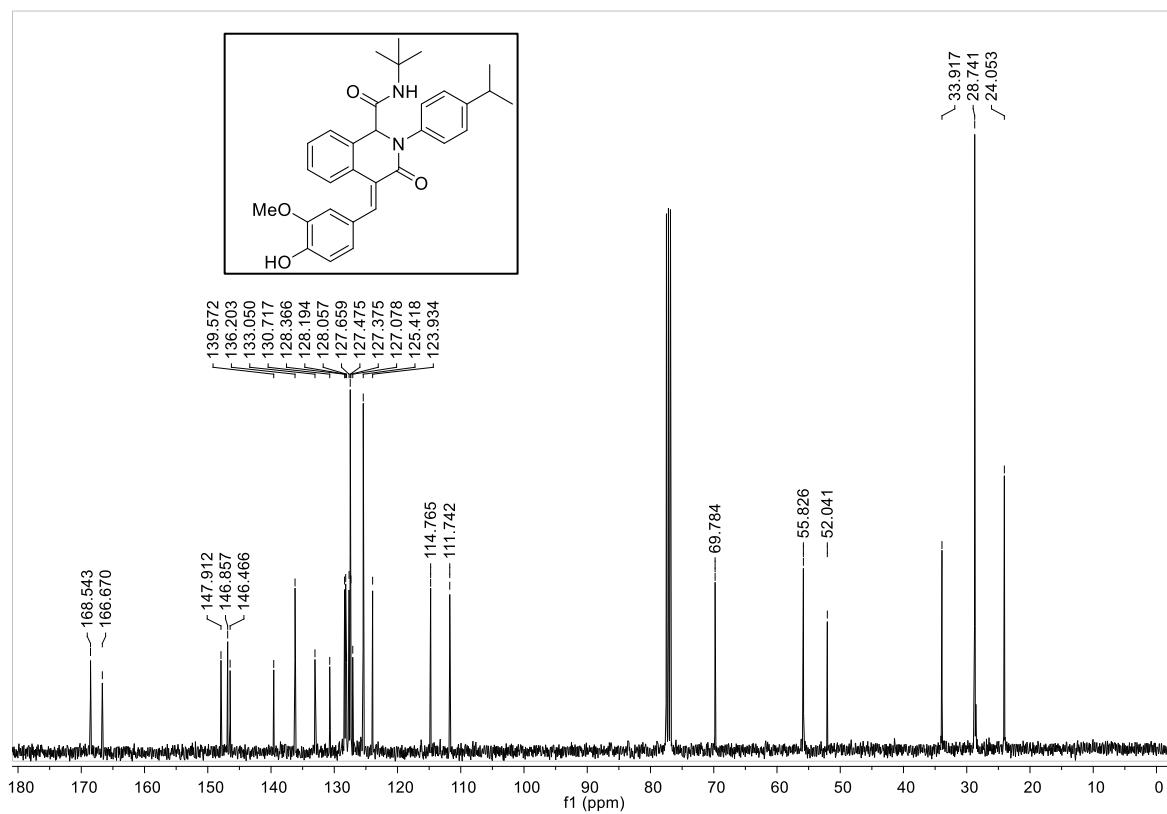


Figure S42. ¹³C-NMR of 10b.

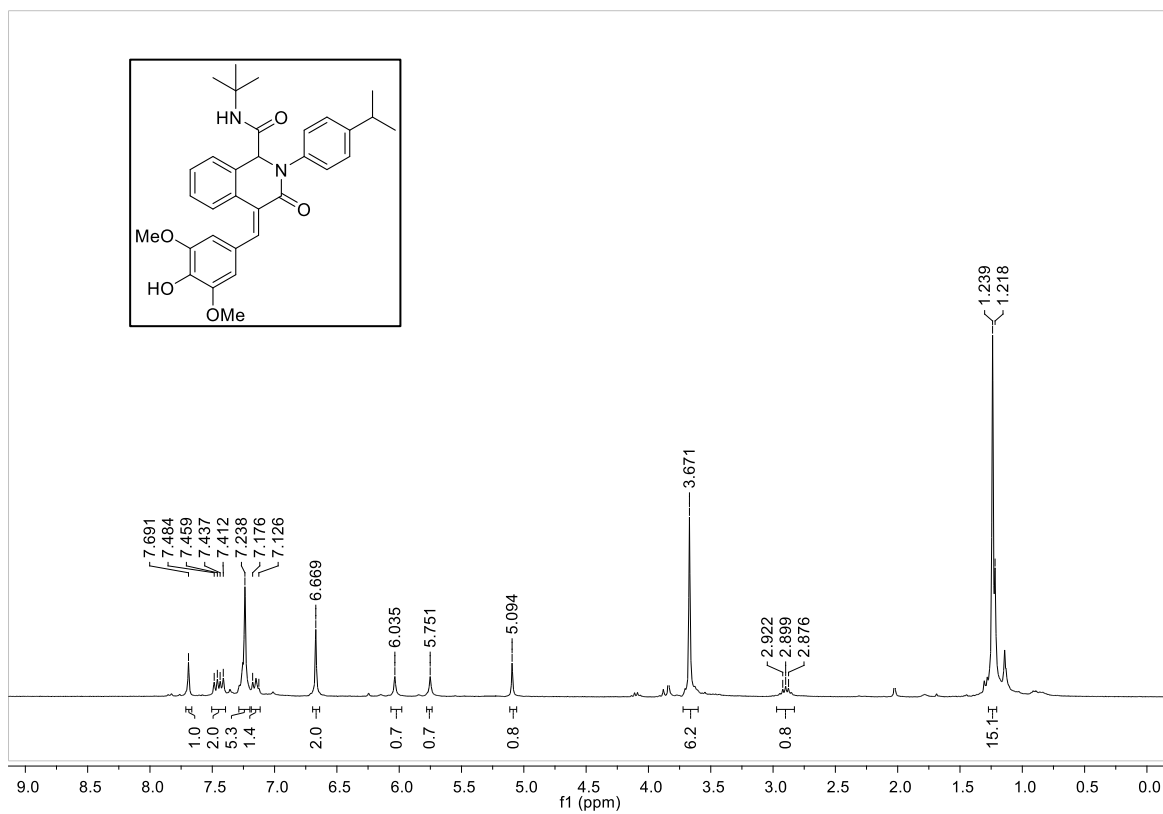
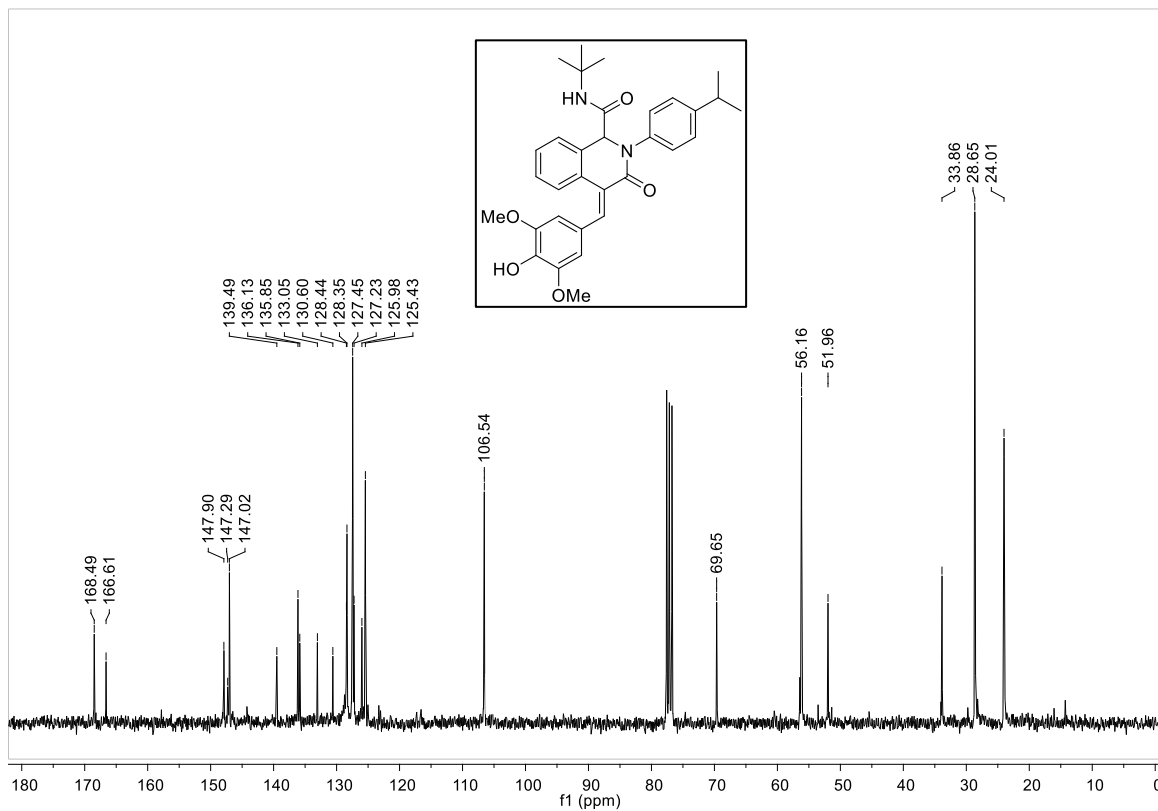


Figure S43. ¹H-NMR of 10c.



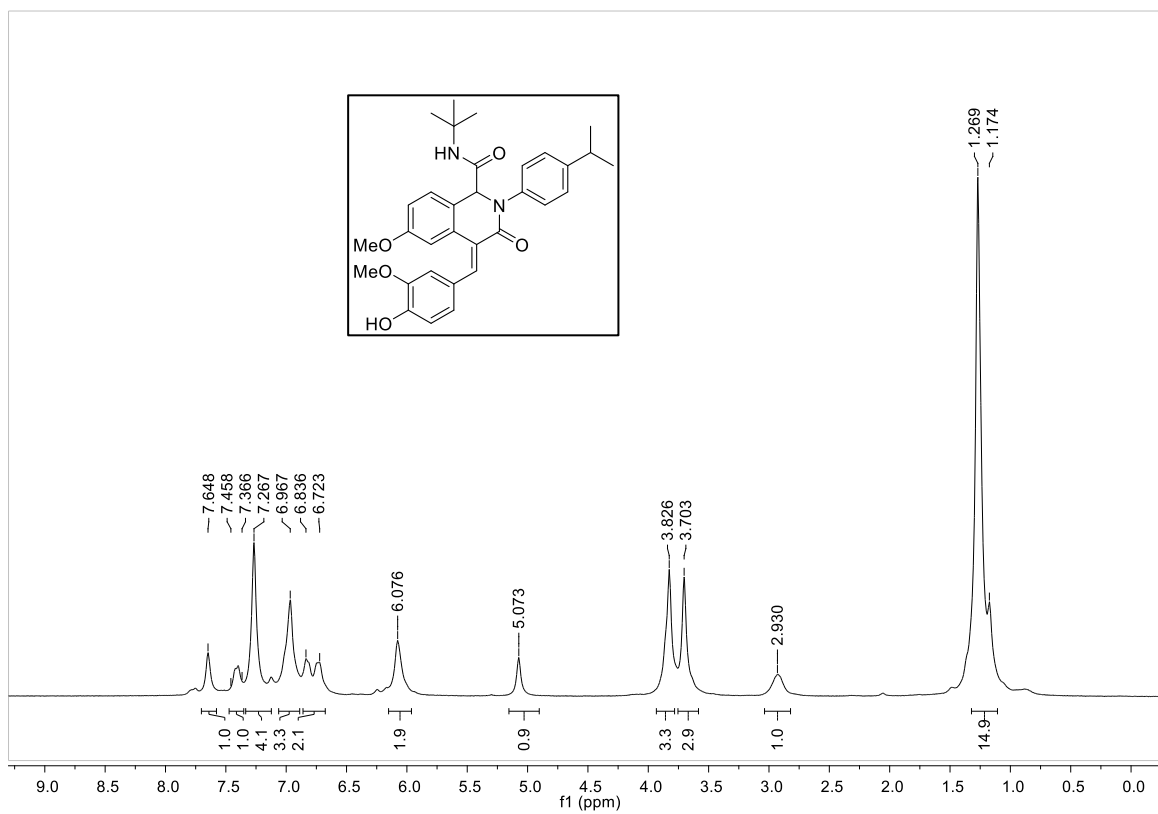
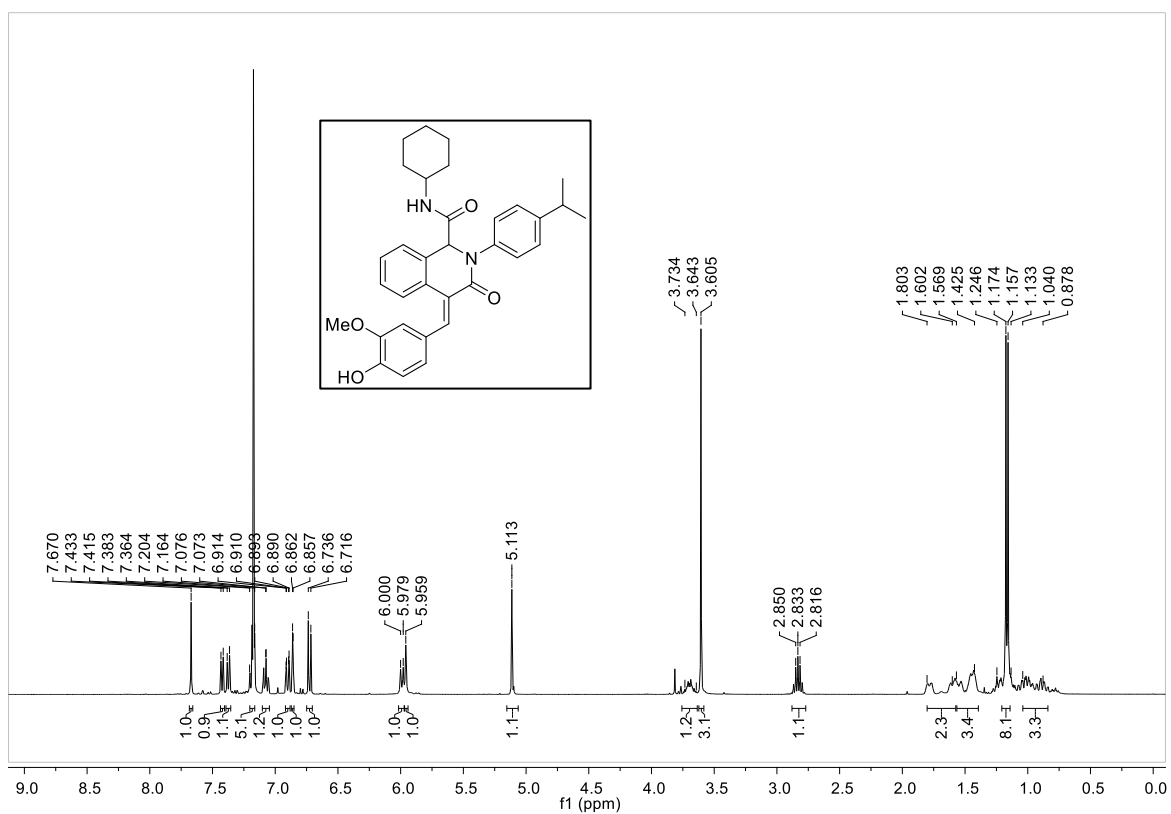
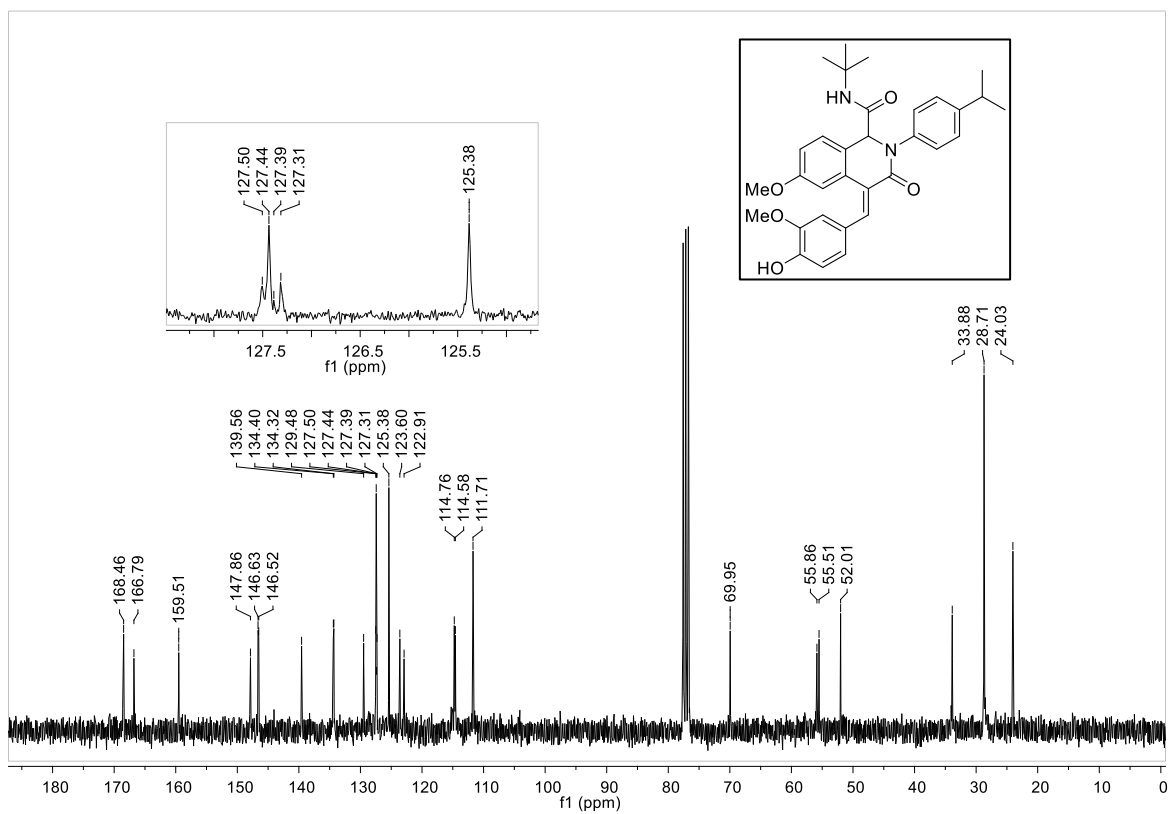


Figure S45. ¹H-NMR of 10d.



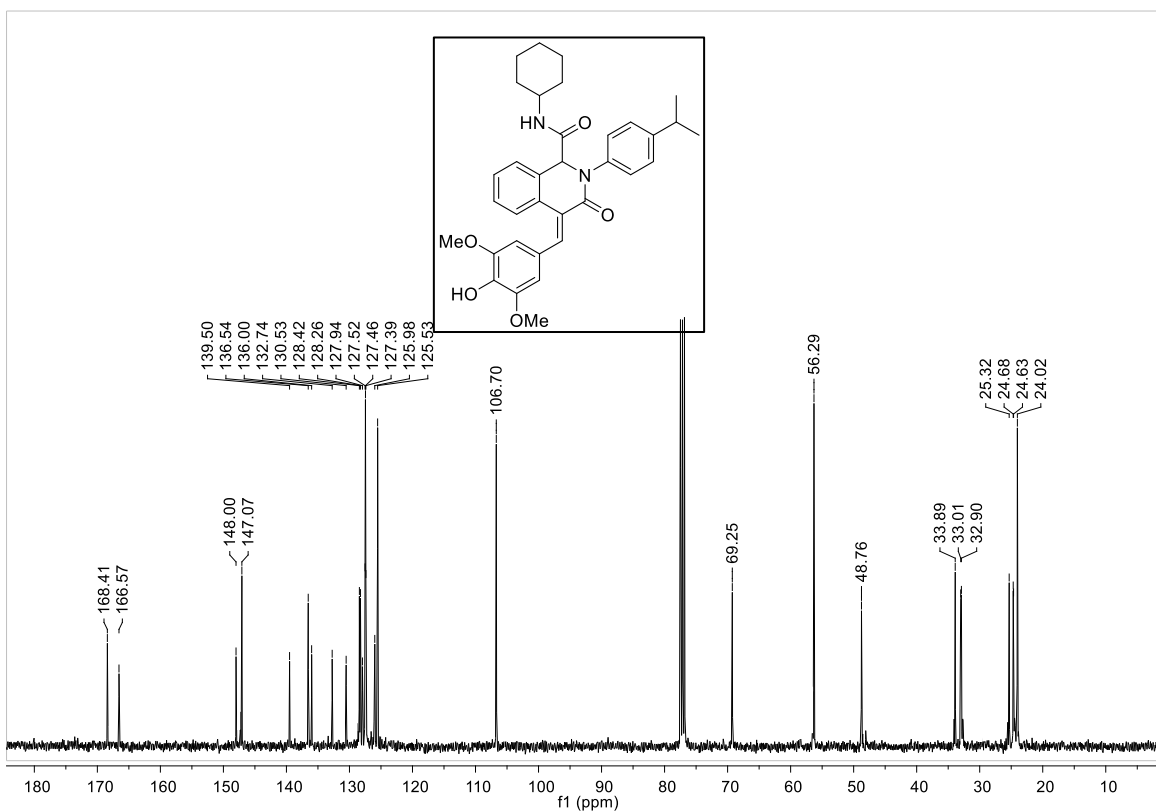


Figure S50. ¹³C-NMR of 10f.

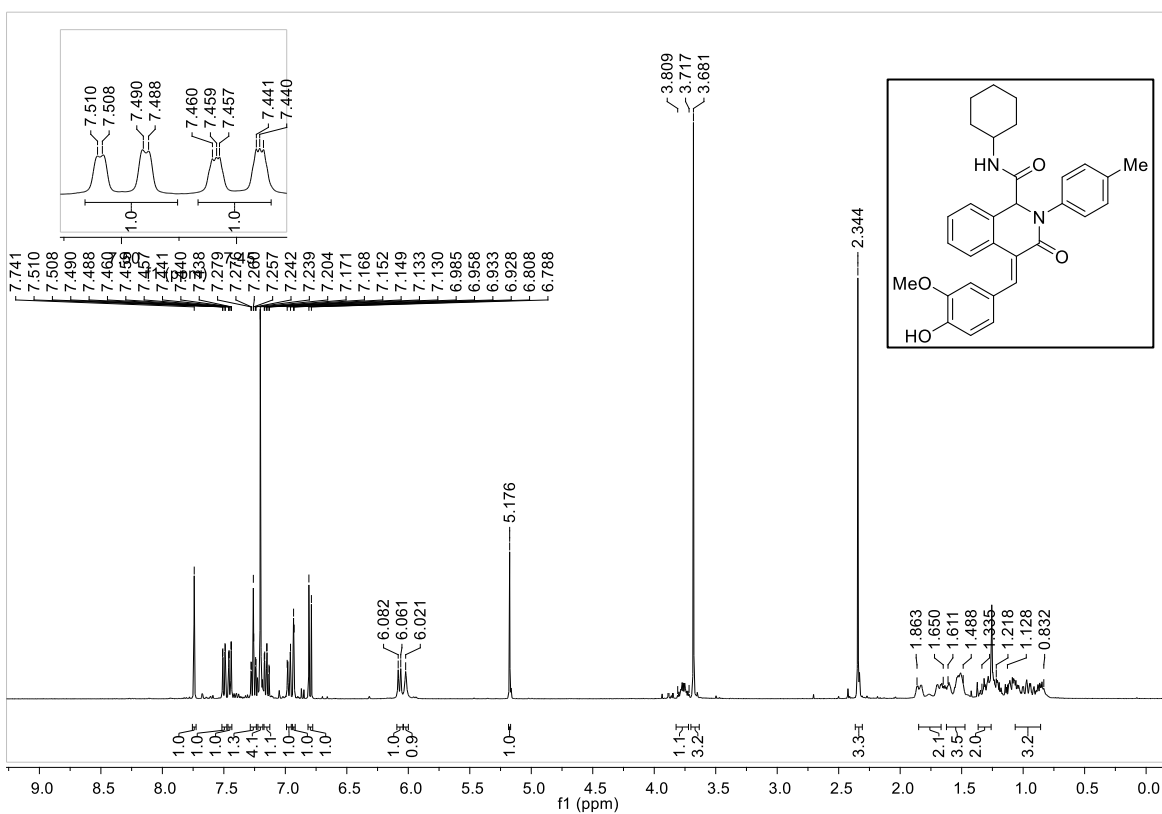
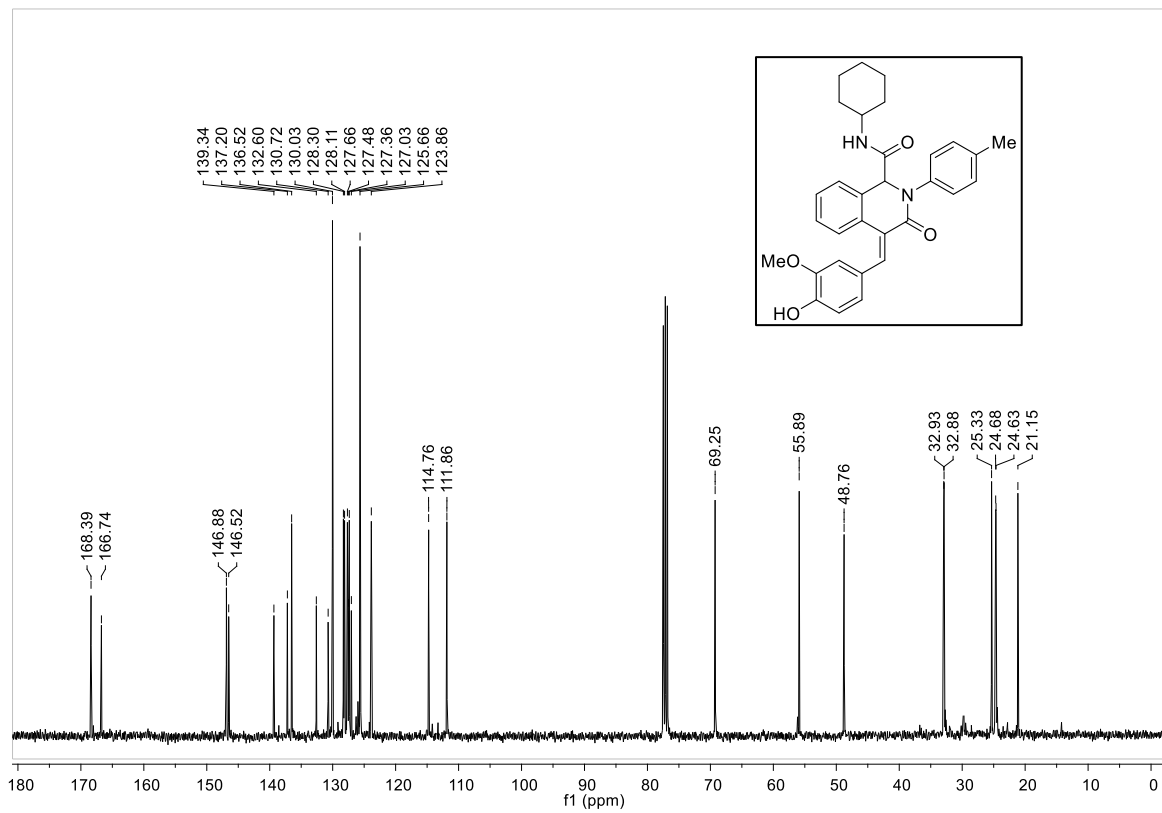


Figure S51. ¹H-NMR of 10g.



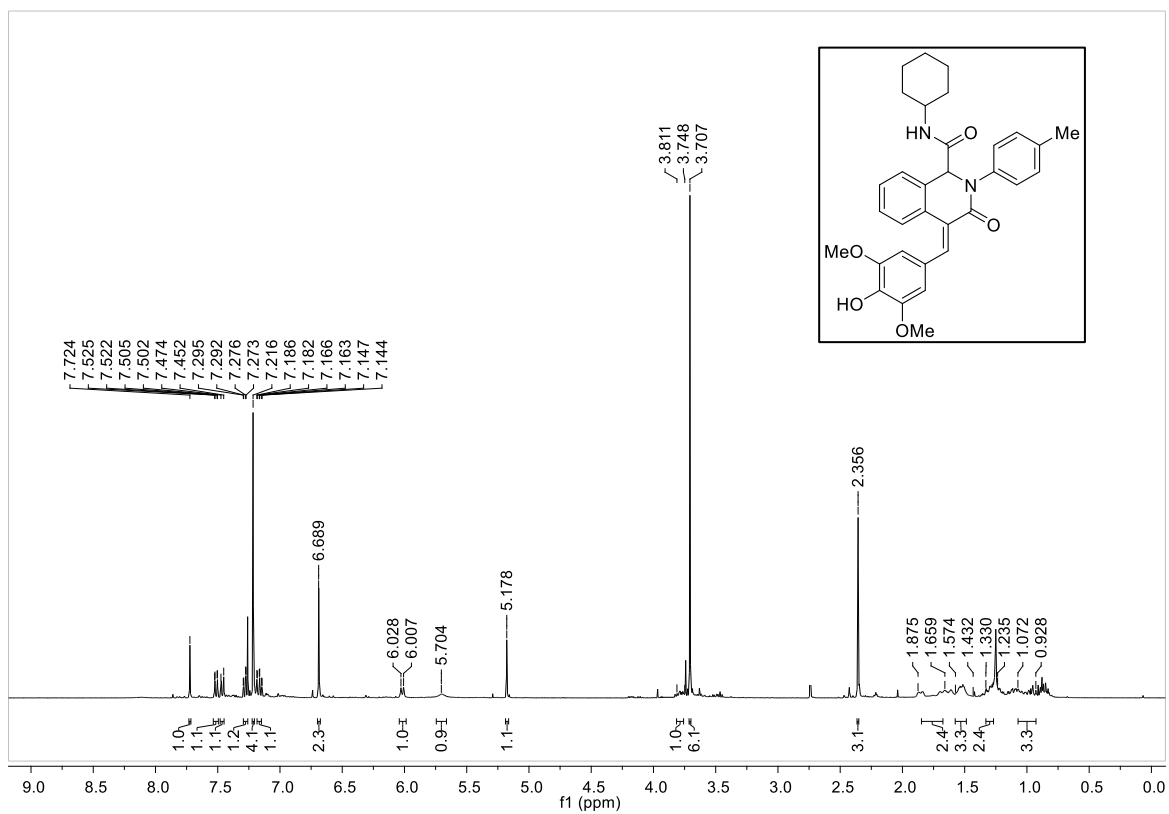


Figure S53. ¹H-NMR of 10h.

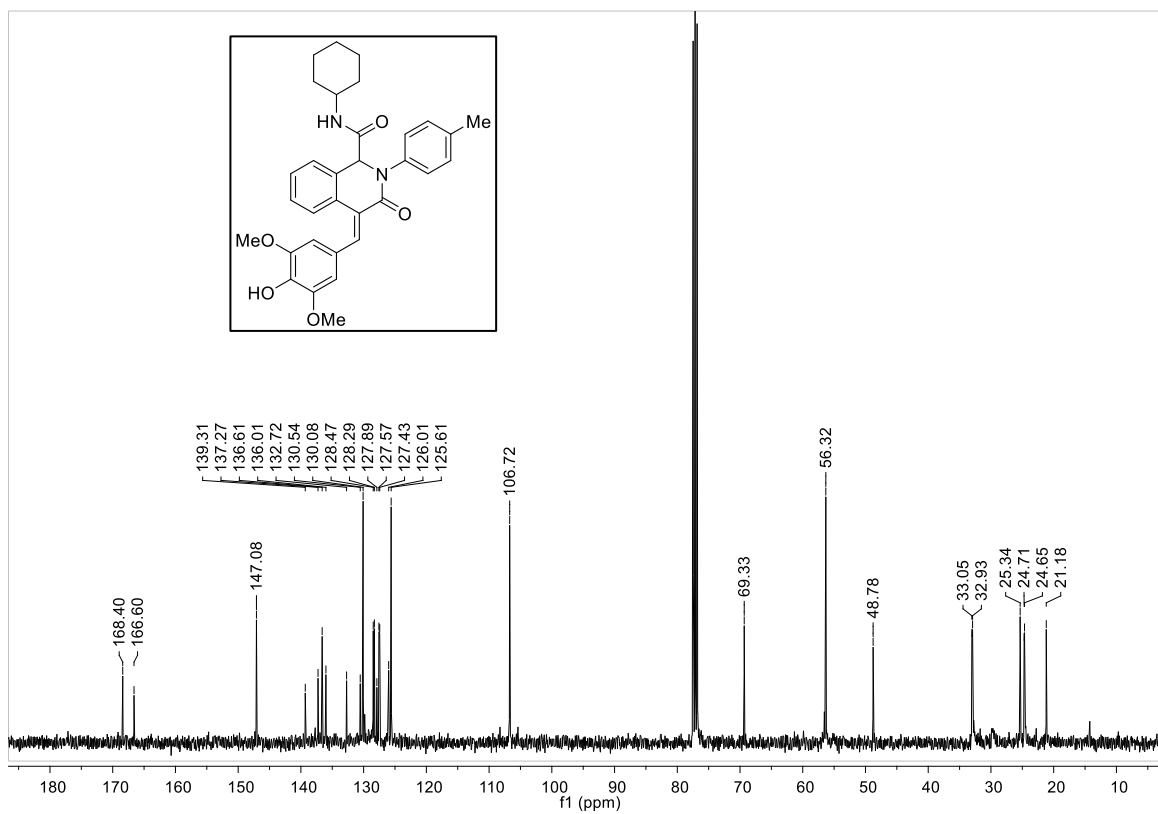


Figure S54. ¹³C-NMR of 10h.

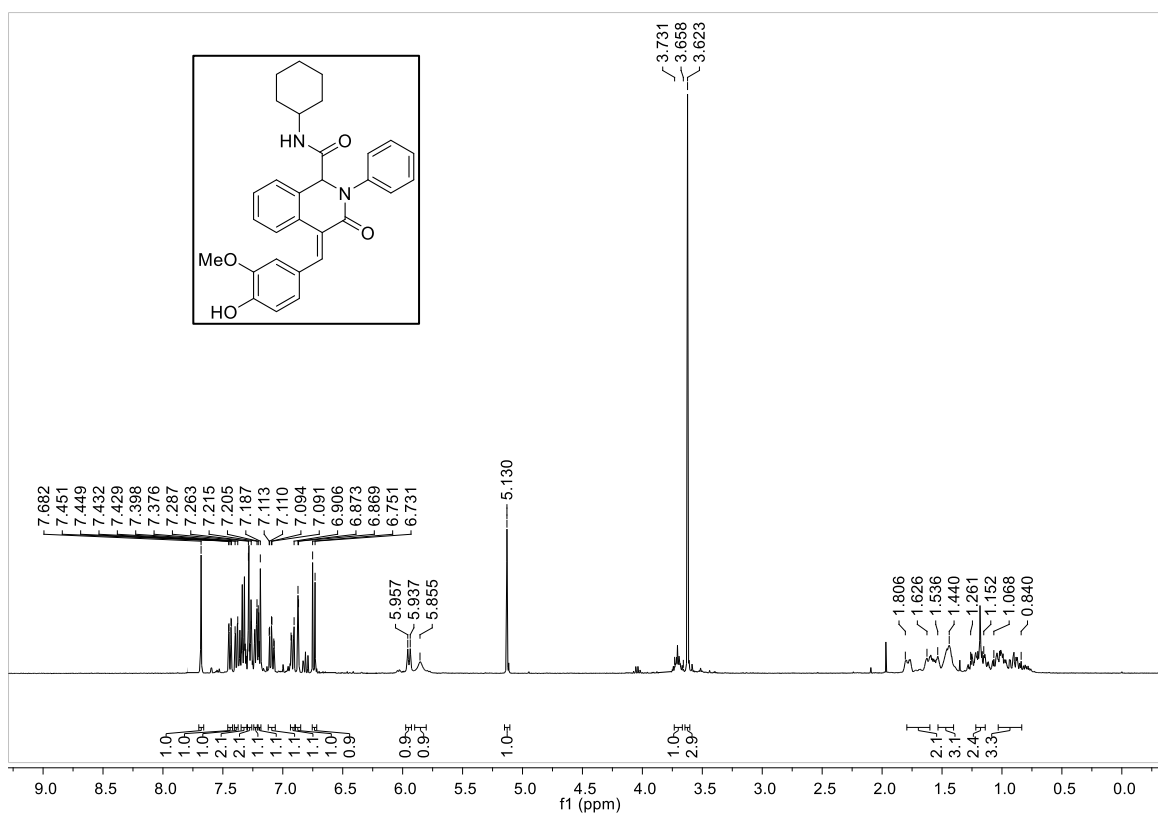


Figure S55. ¹H-NMR of 10i.

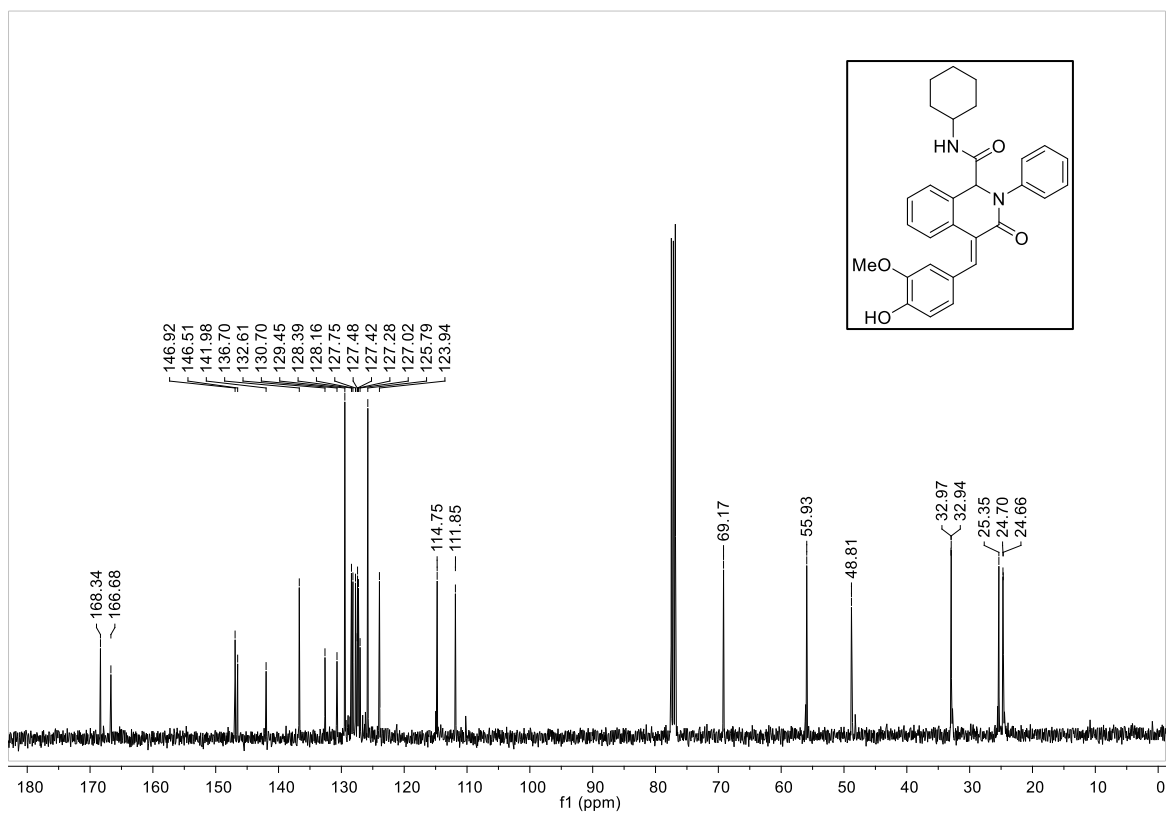


Figure S56. ¹³C-NMR of 10i.

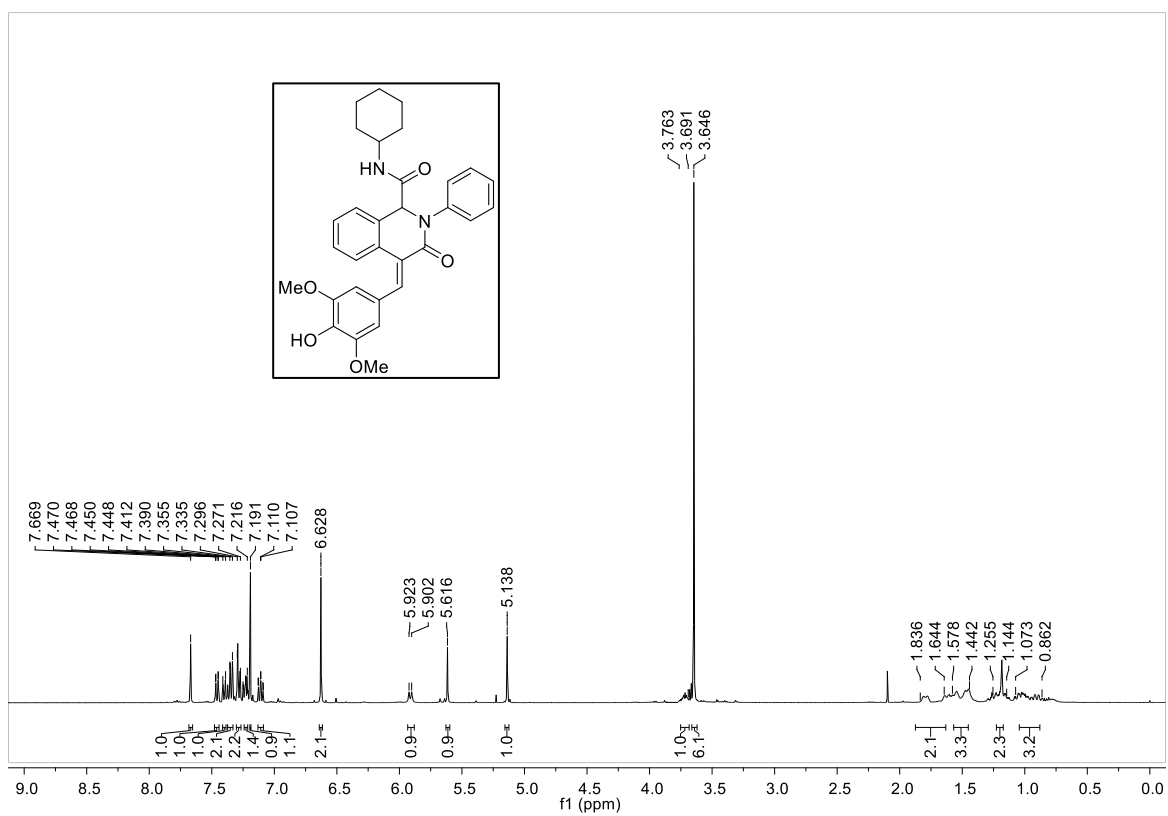


Figure S57. ¹H-NMR of 10j.

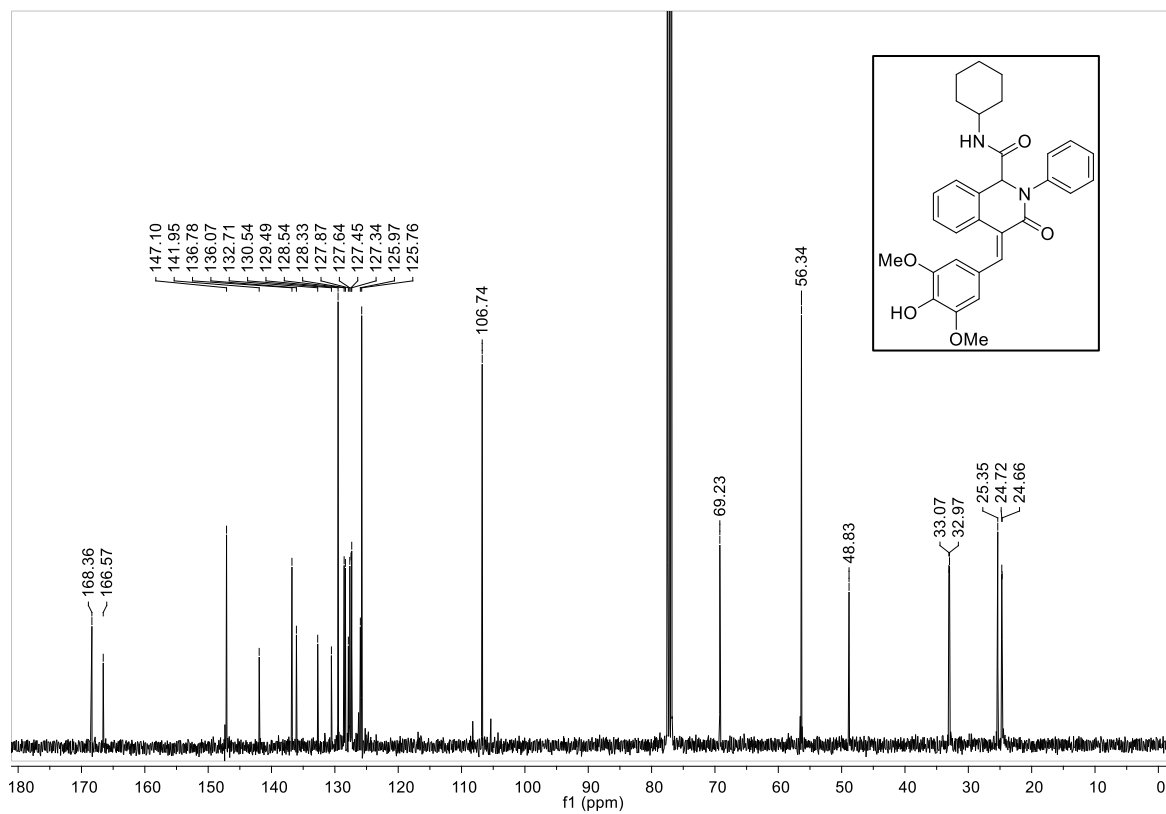


Figure S58. ¹³C-NMR of 10j.

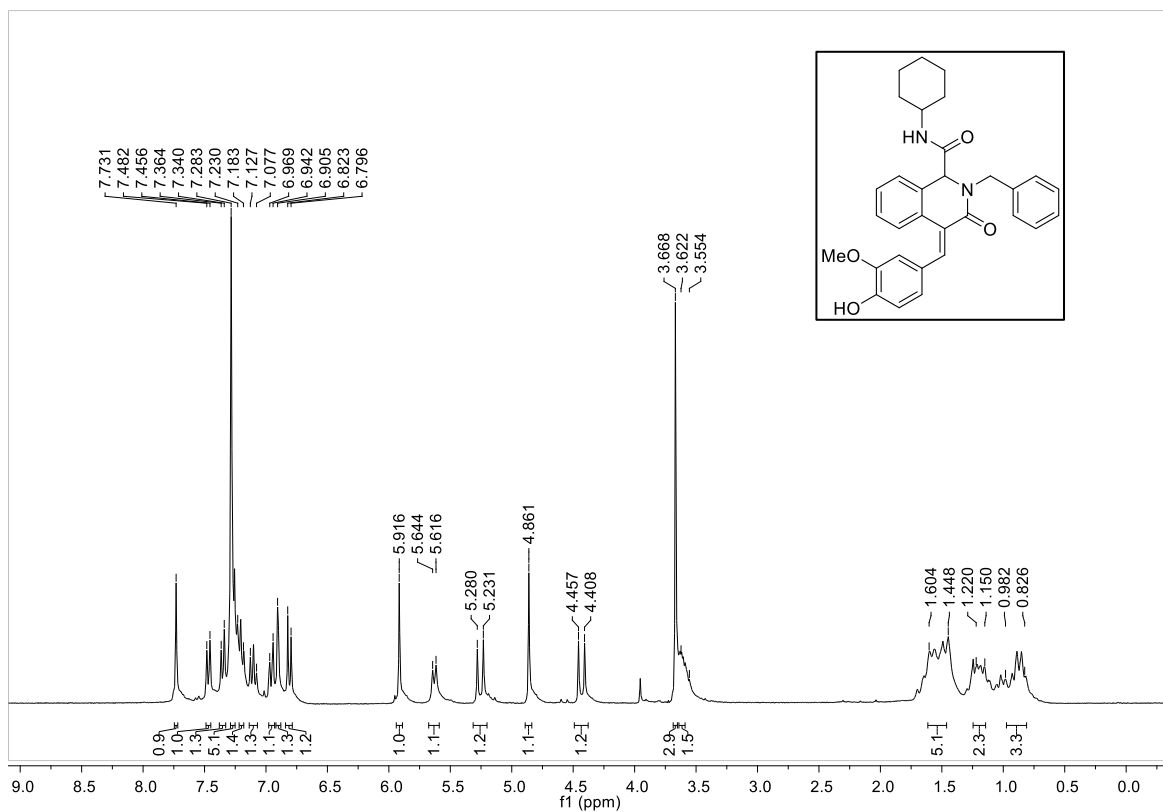


Figure S59. ¹H-NMR of 10k.

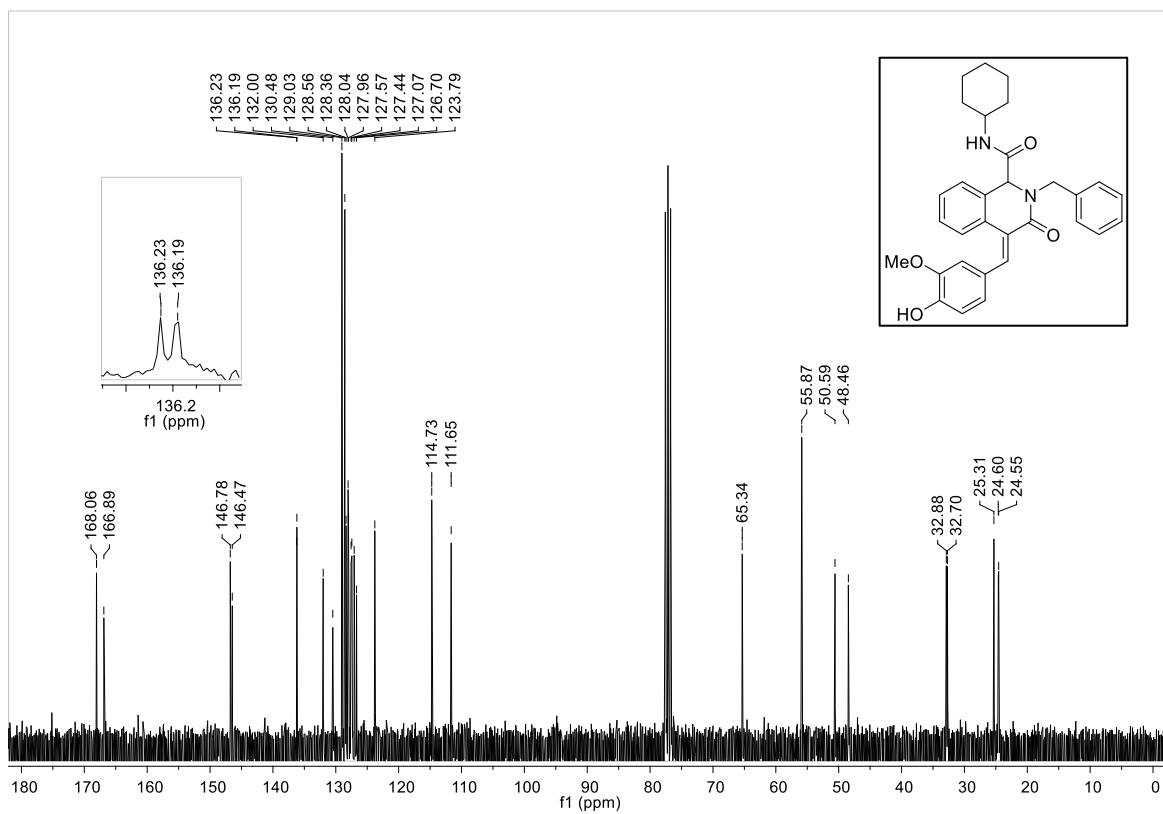


Figure S60. ¹³C-NMR of 10k.

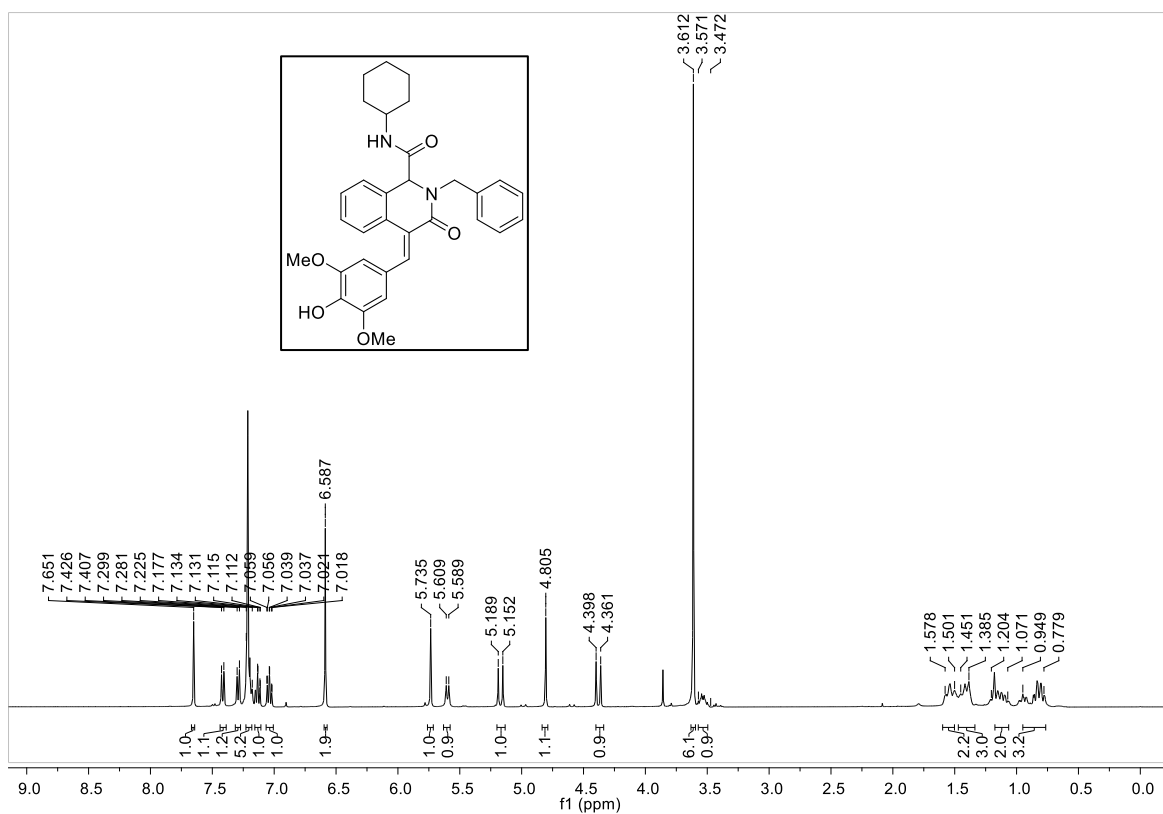
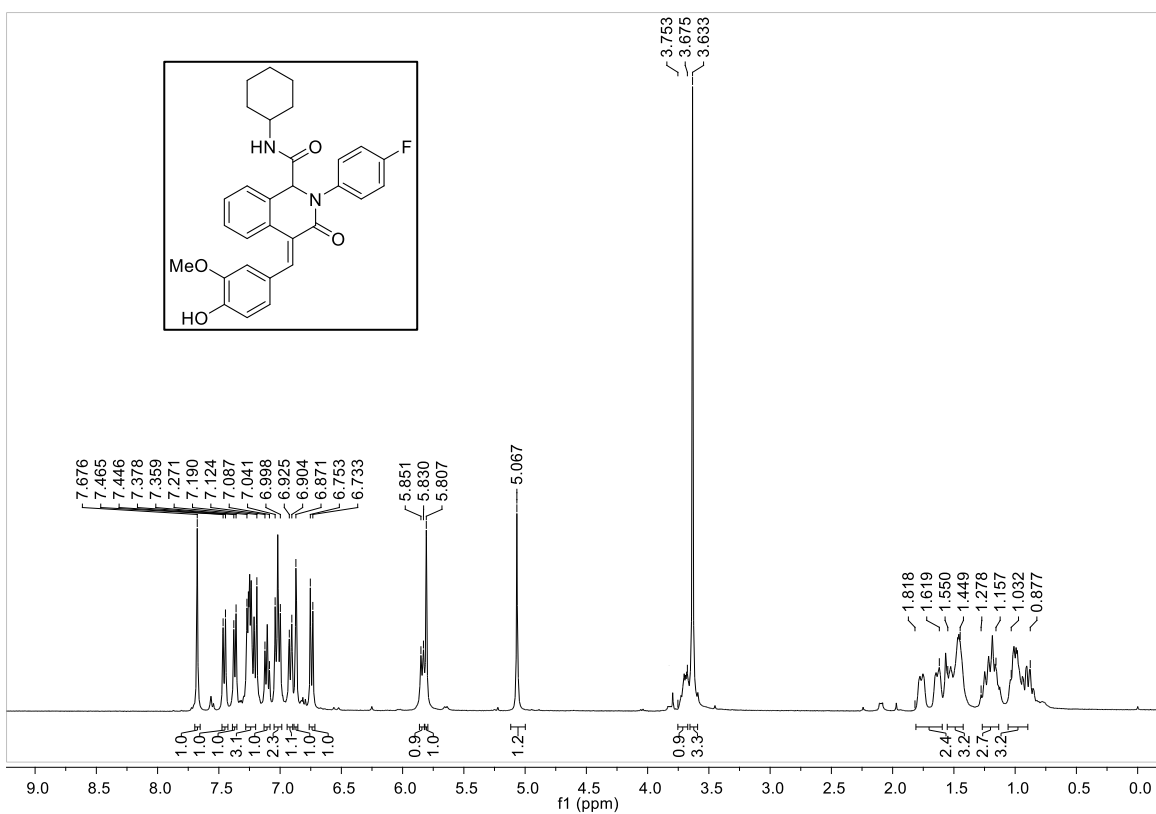
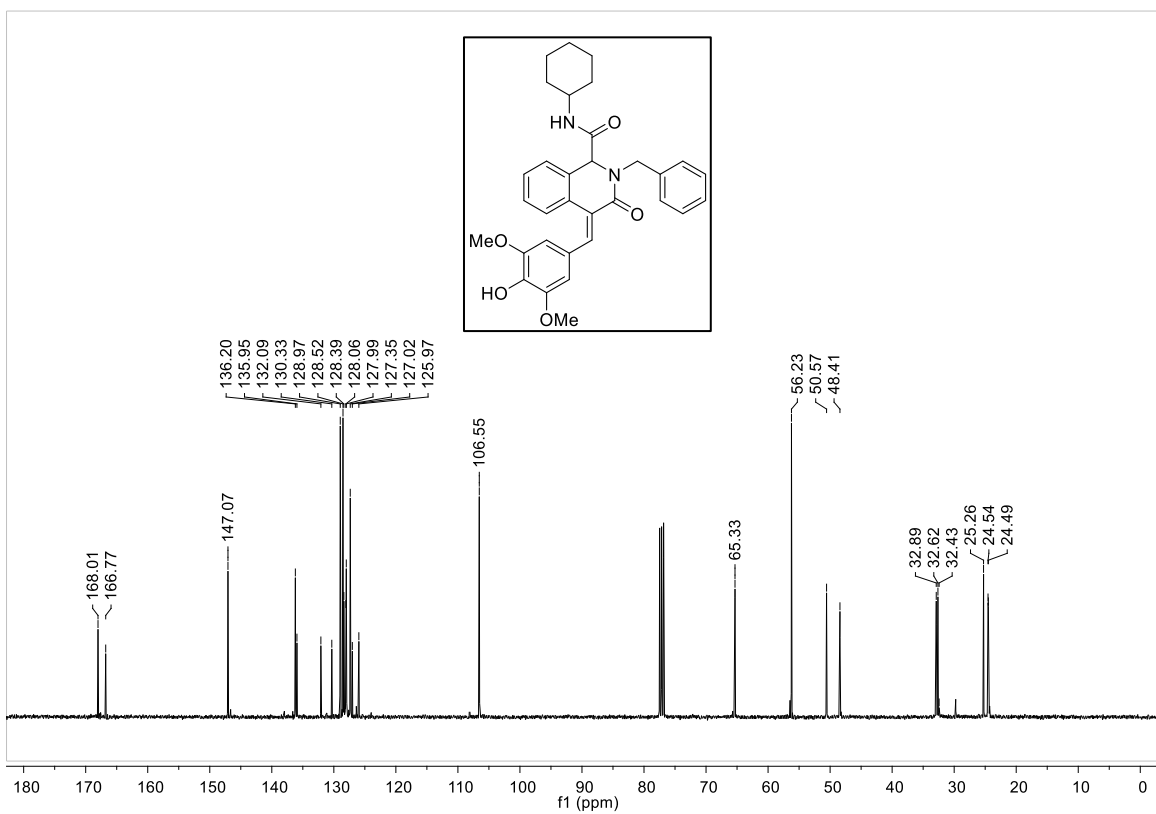


Figure S61. ¹H-NMR of 10l.



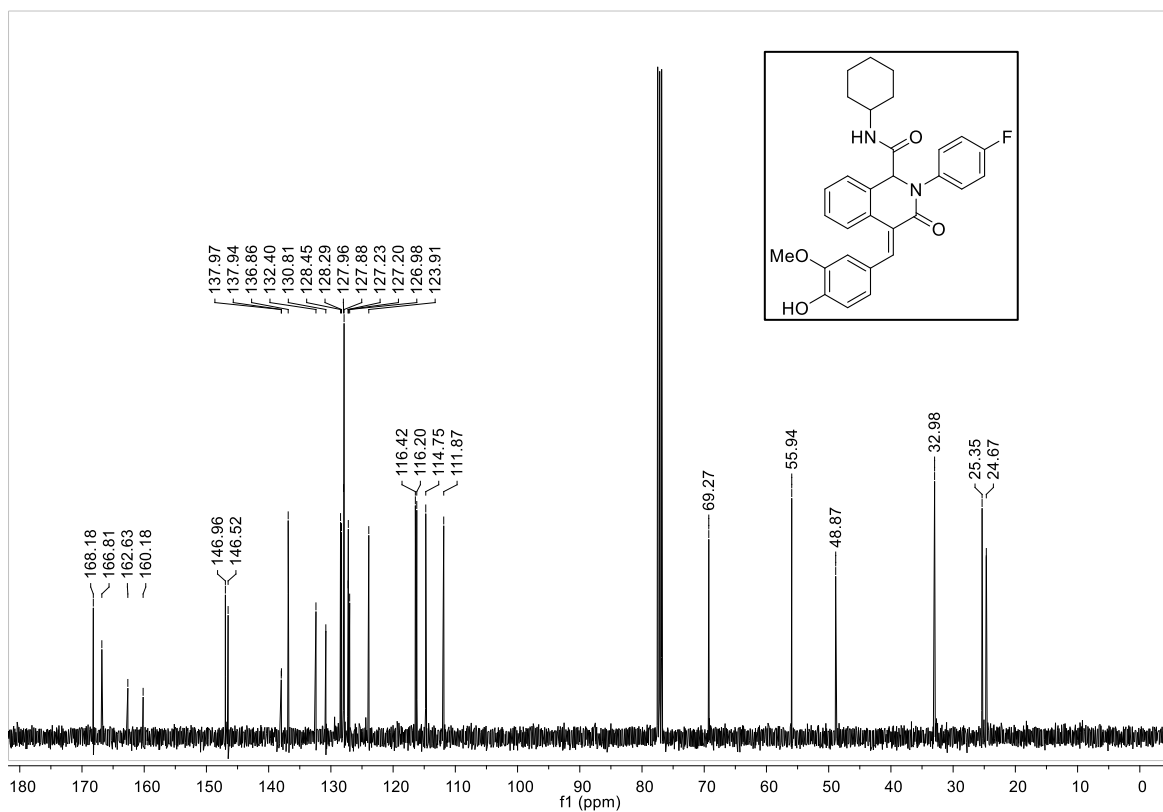


Figure S64. ^{13}C -NMR of 10m.

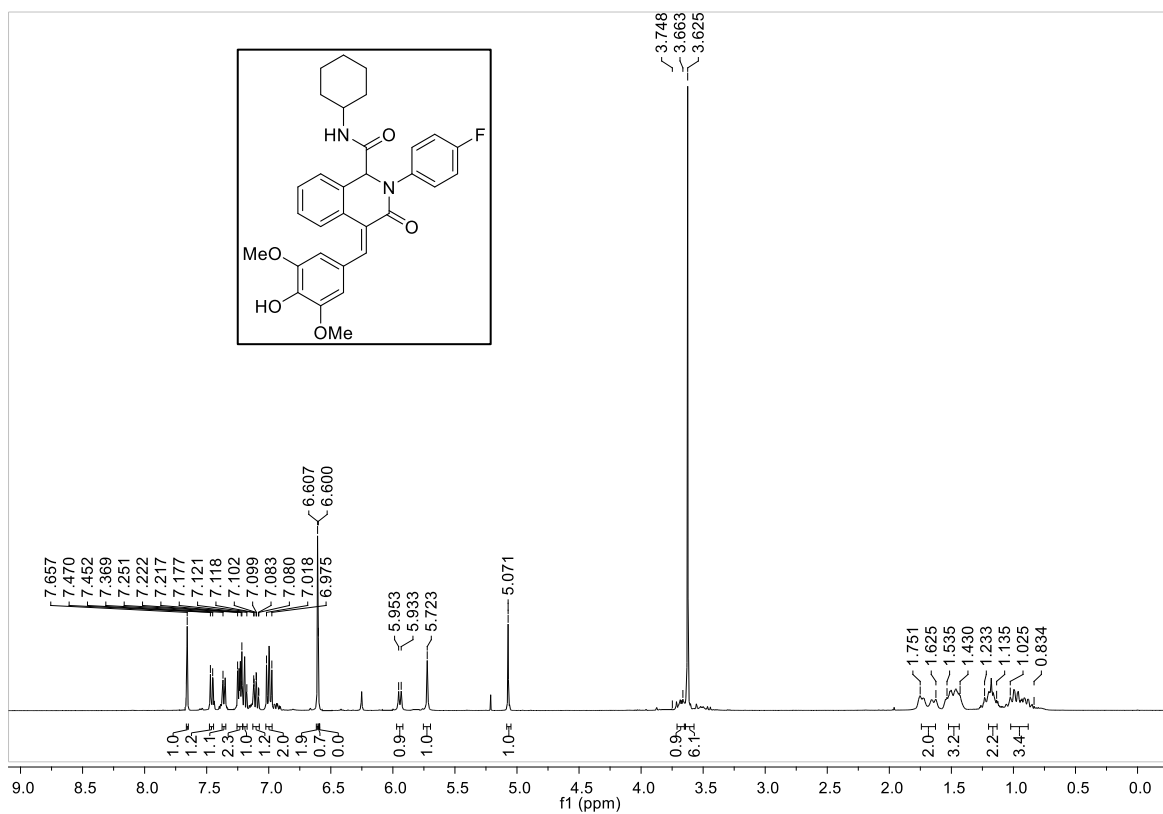


Figure S65. ^1H -NMR of 10n.

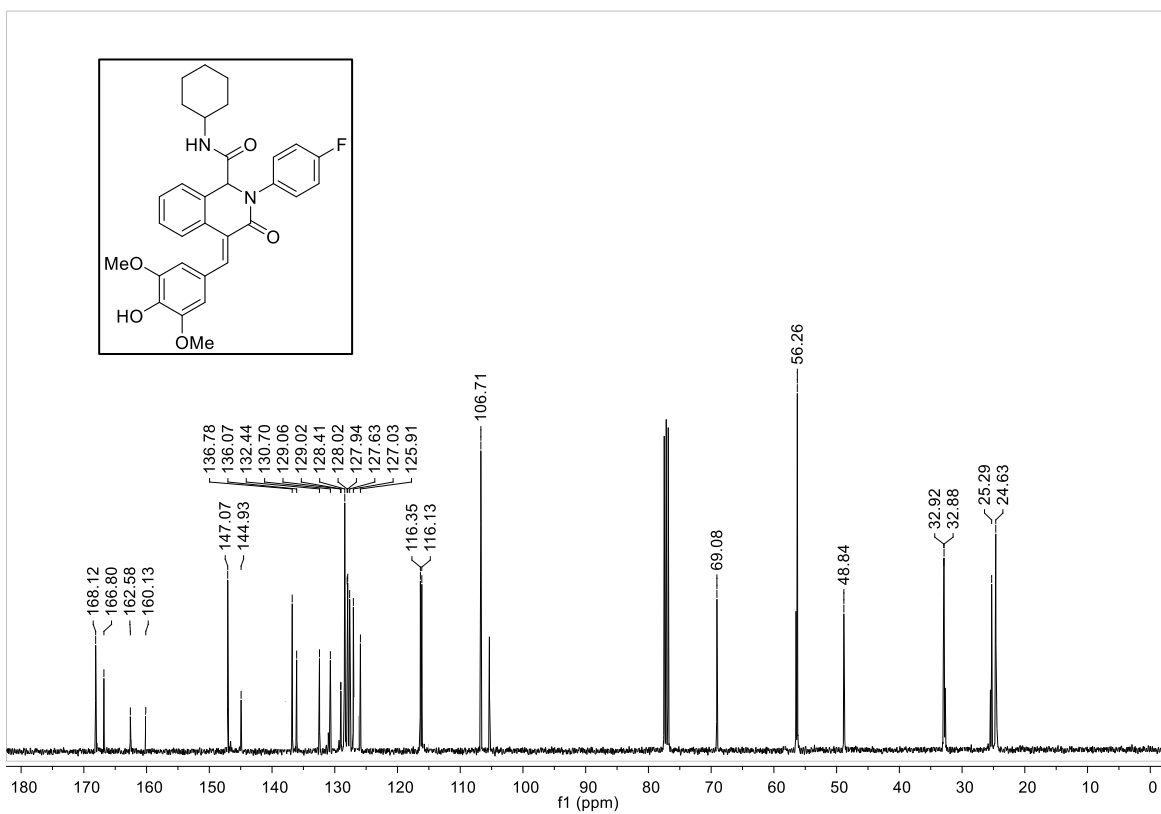


Figure S66. ¹³C-NMR of 10n.

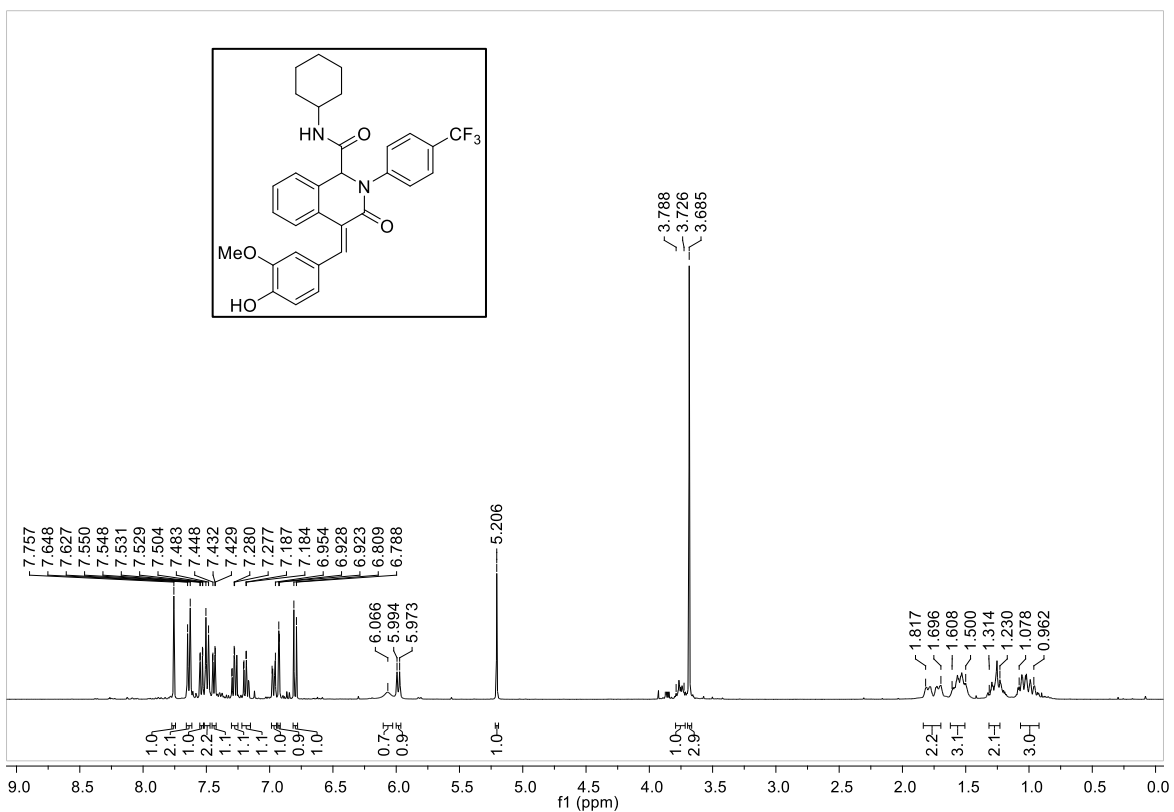


Figure S67. ¹H-NMR of 10o.

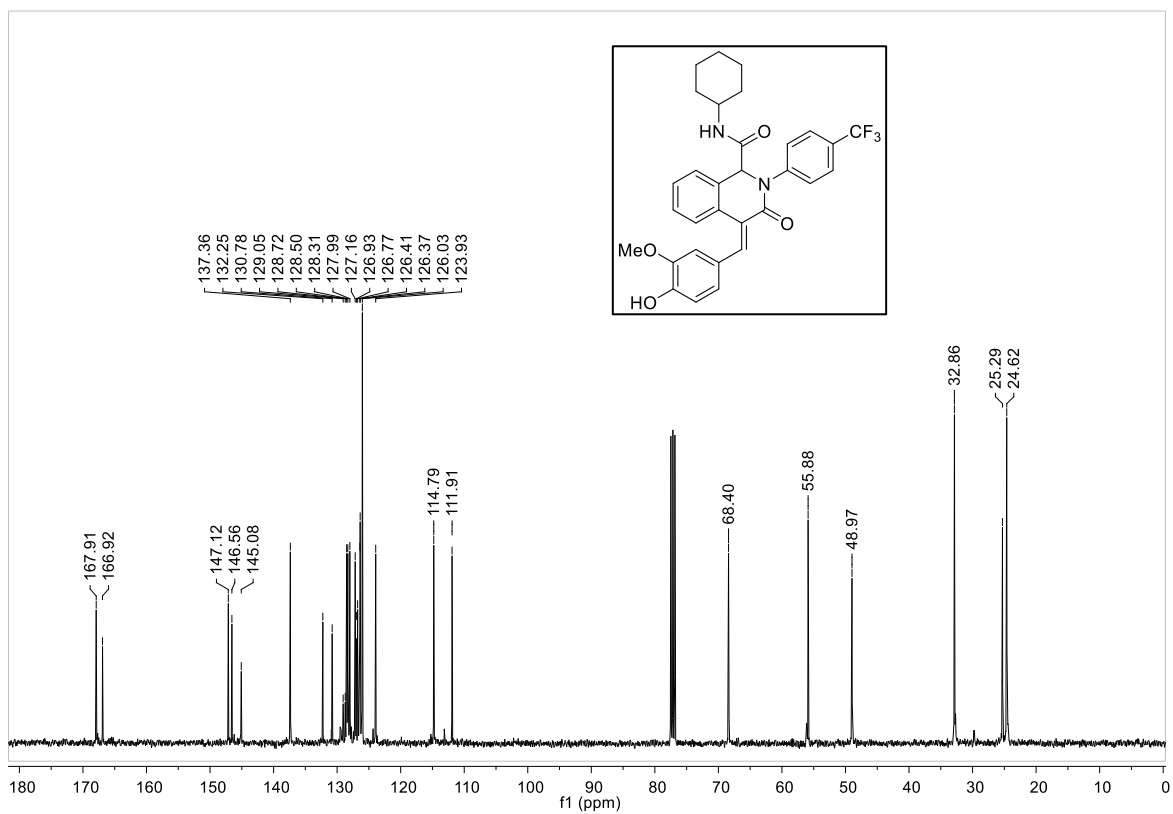


Figure S68. ^{13}C -NMR of 10o.

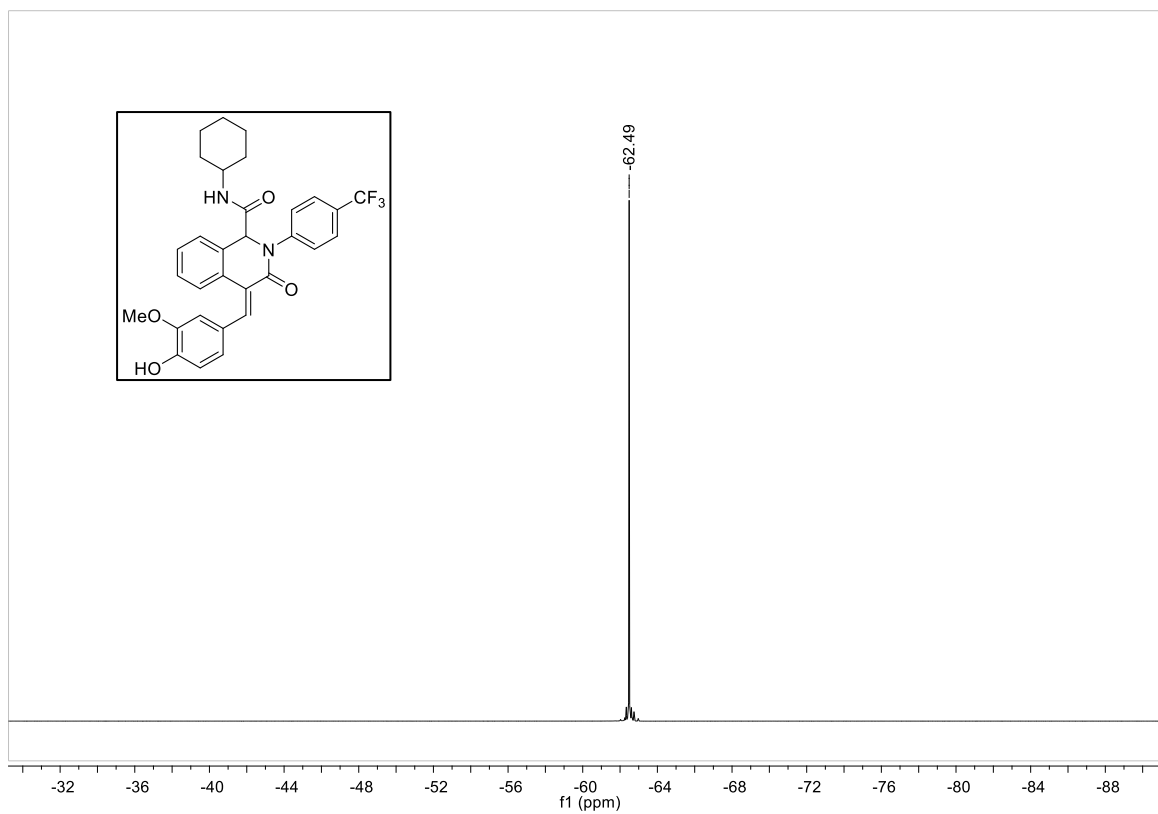


Figure S69. ^{19}F -NMR of **10c**.

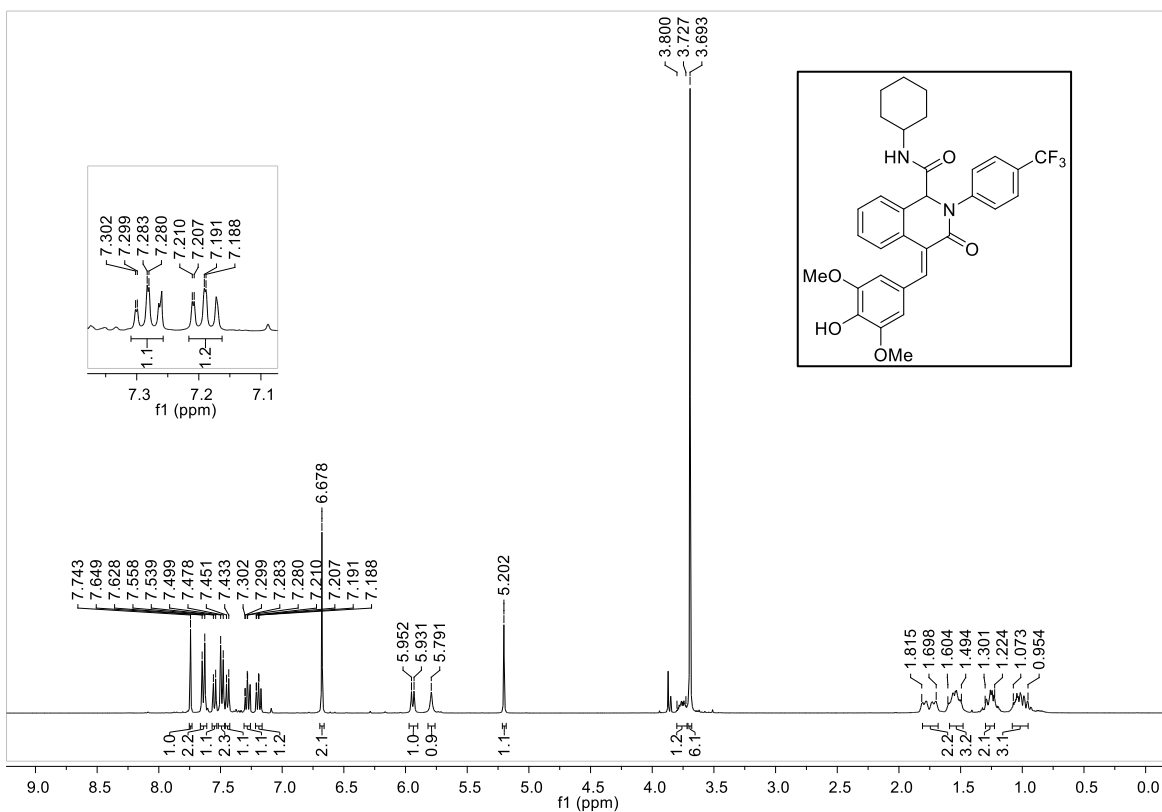


Figure S70. ^{19}F -NMR of 10p.

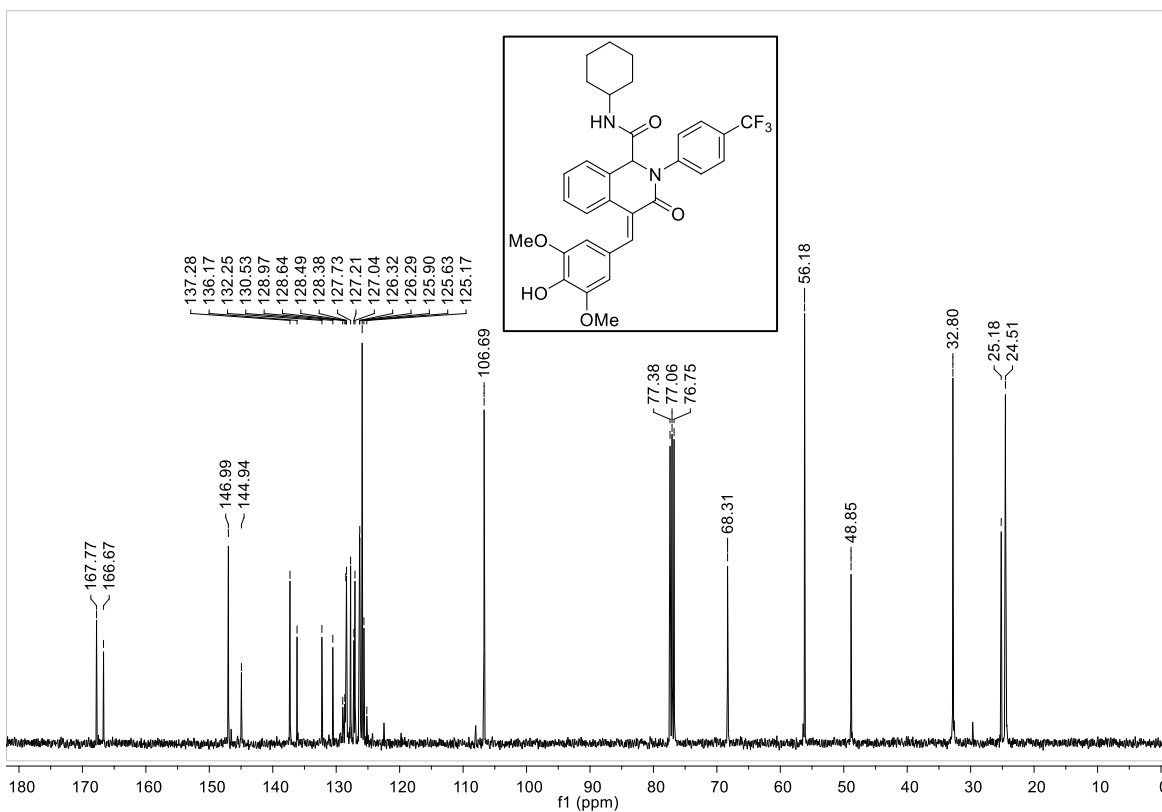


Figure S71. ^{13}C -NMR of 10p.

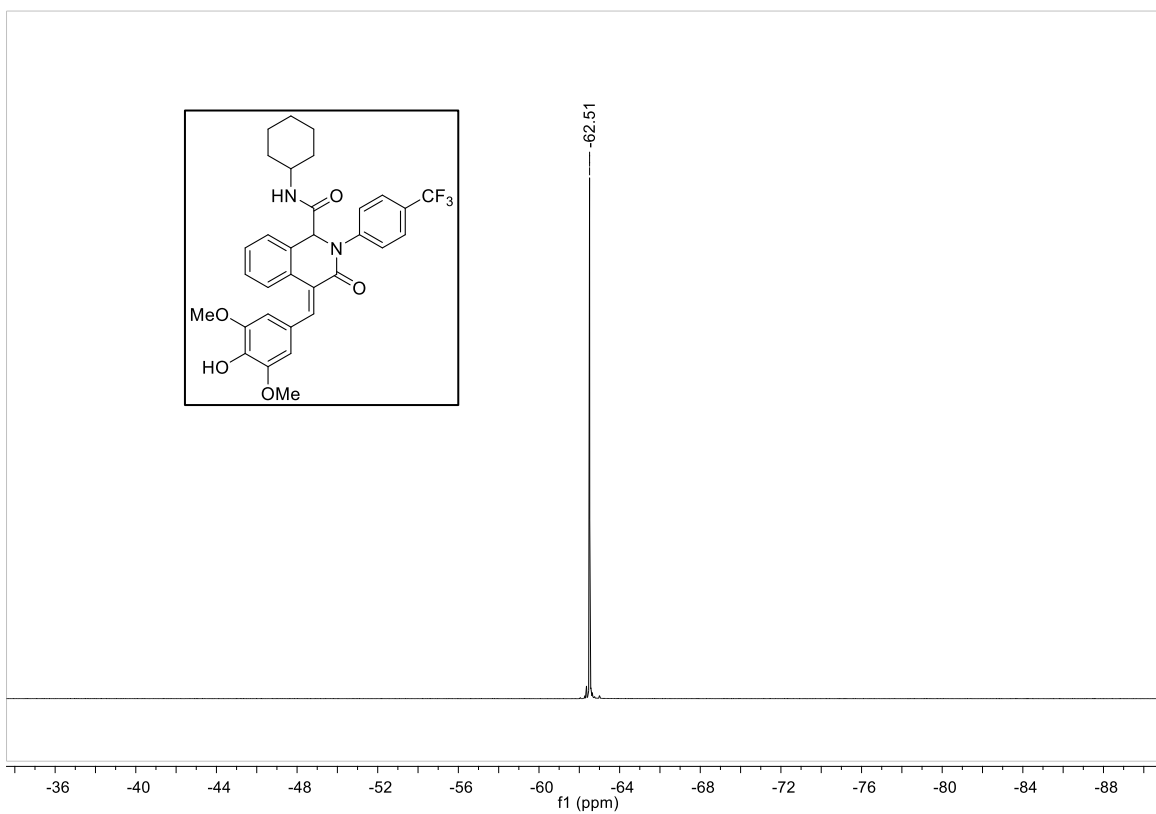


Figure S72. ^{19}F -NMR of 10p.

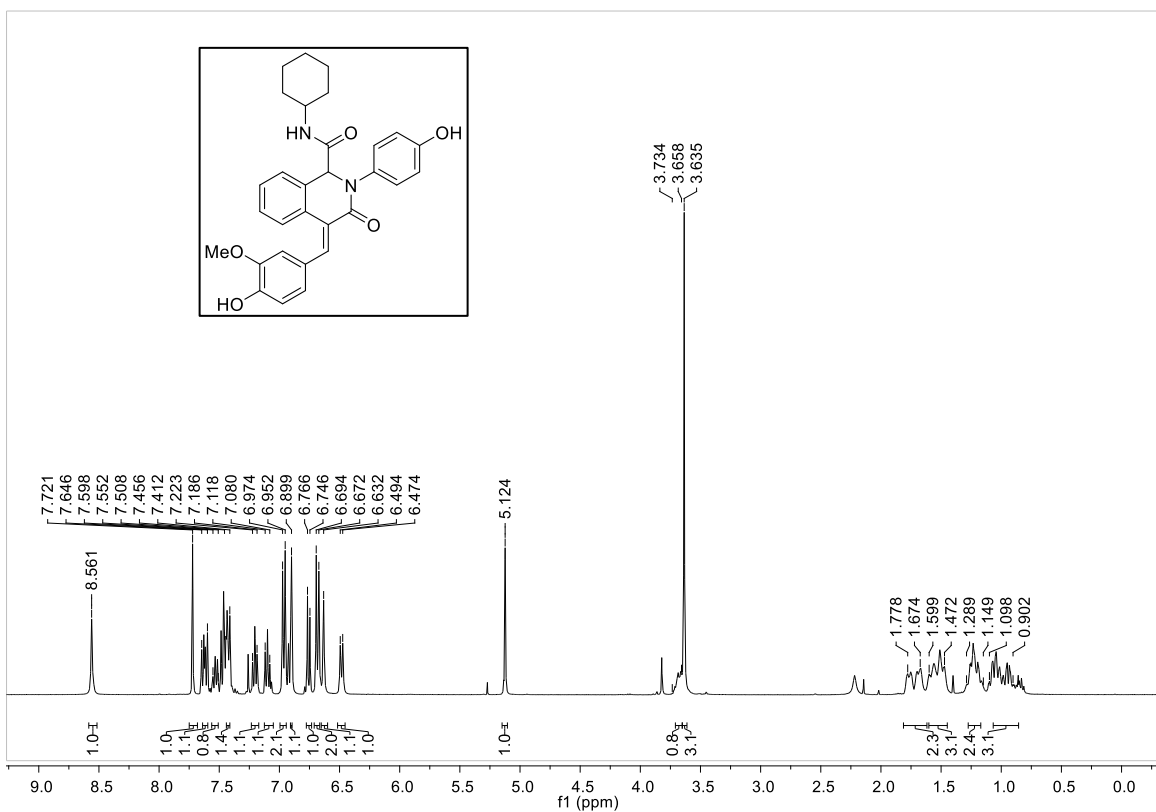


Figure S73. ¹H-NMR of 10q.

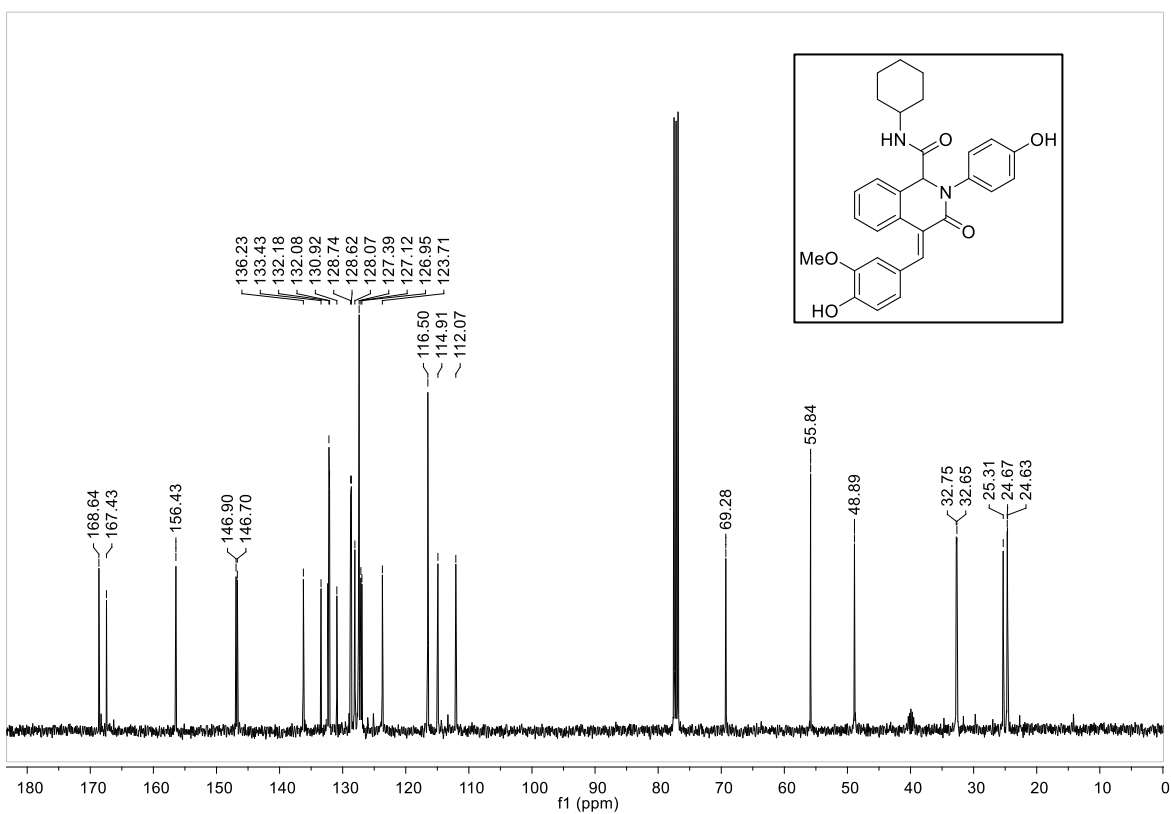


Figure S74. ¹³C-NMR of 10q.

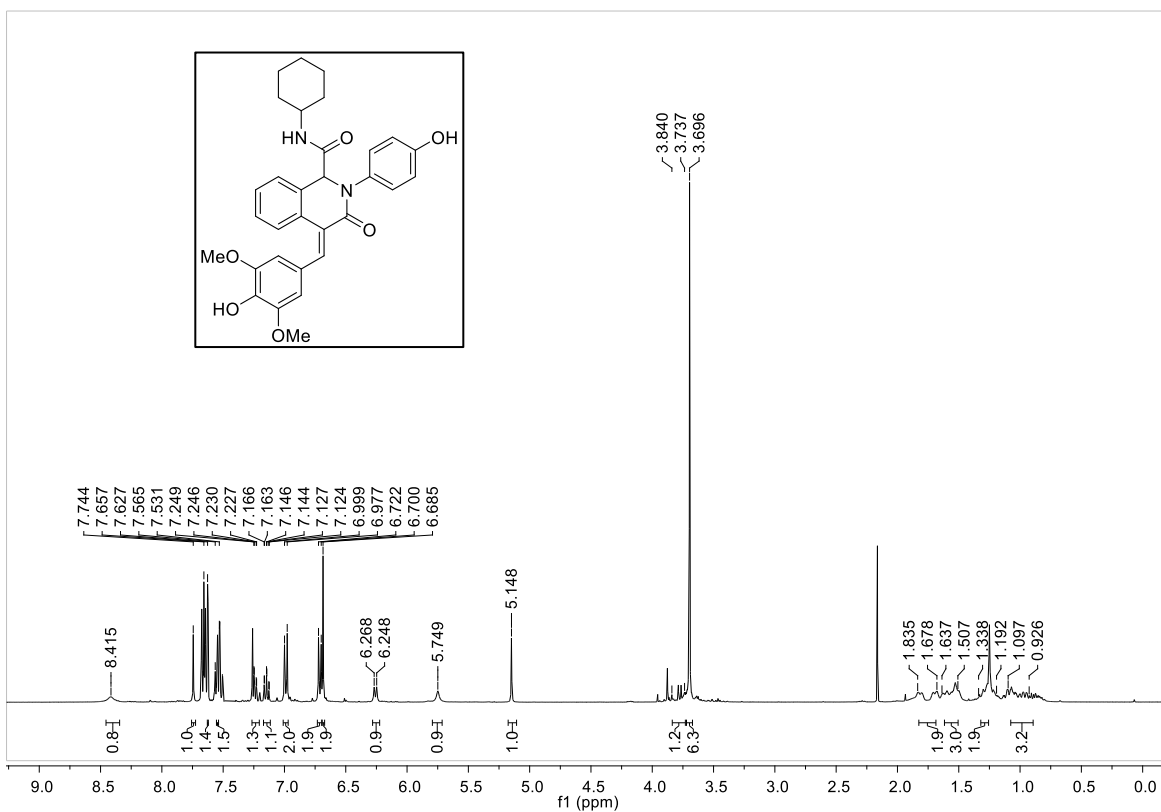


Figure S75. ¹H-NMR of 10r.

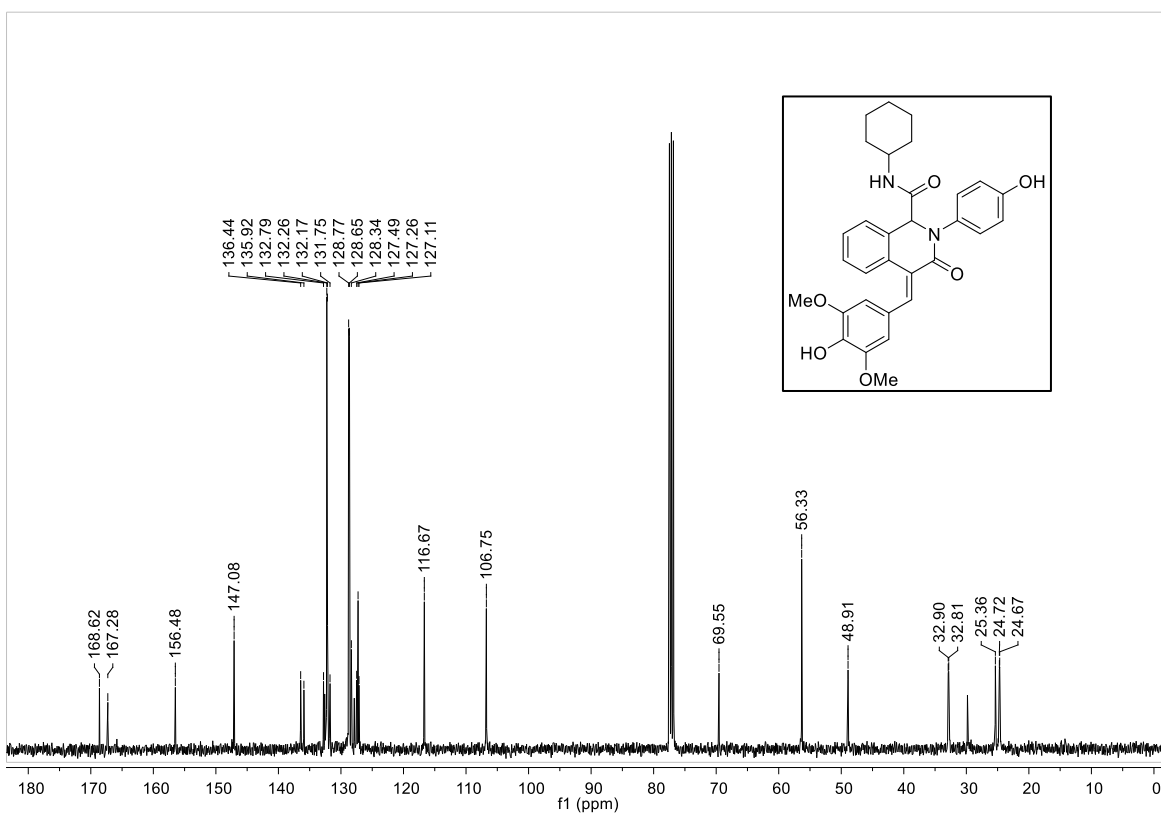
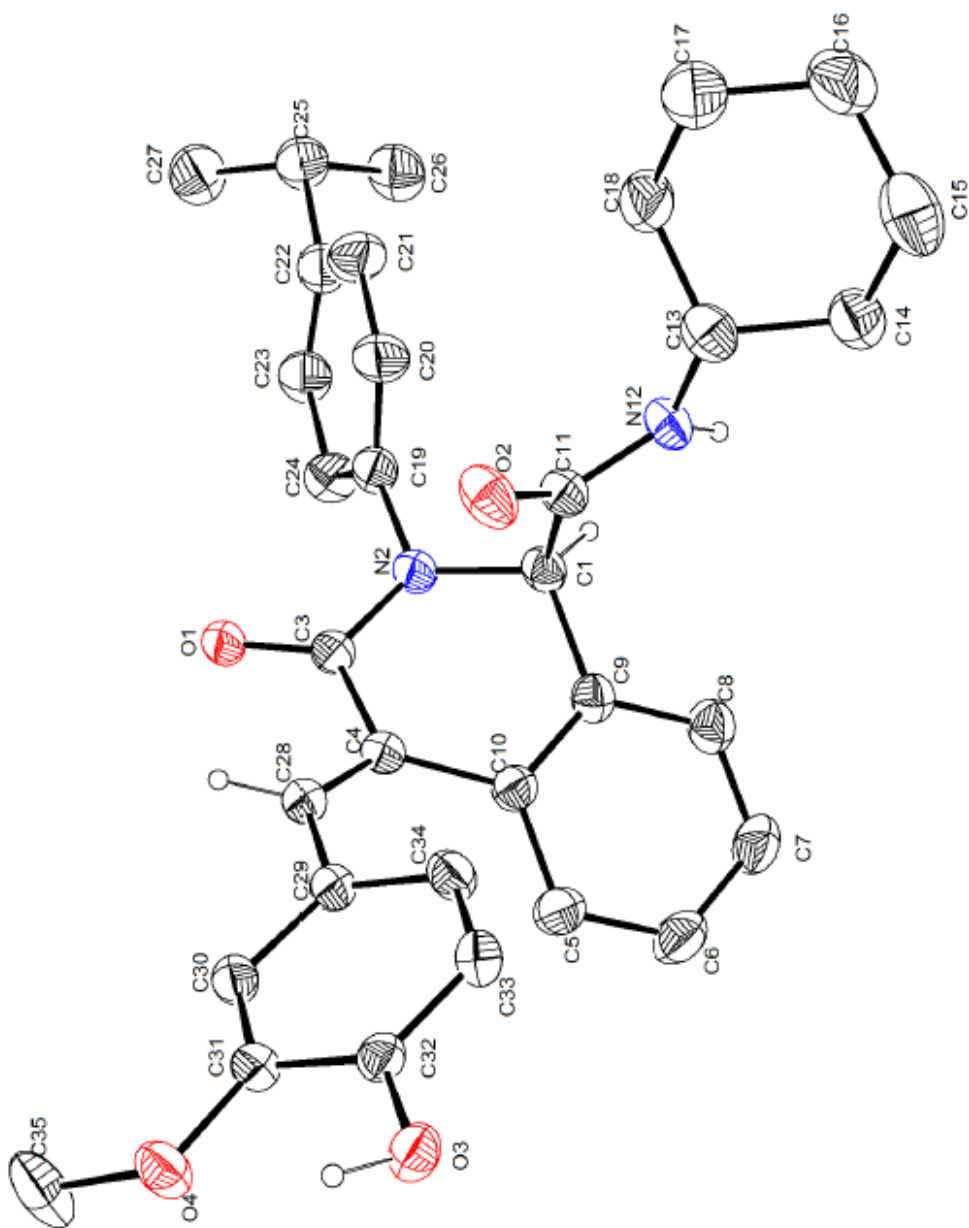


Figure S76. ¹³C-NMR of 10r.

X-Ray data





IC₅₀ data

Table S1. TBARS IC₅₀ data of isoquinolinones and controls.

Comp.	Concentration (μM)	Percentage of inhibition (%)	IC ₅₀ (μM)	Comp.	Concentration (μM)	Percentage of inhibition (%)	IC ₅₀ (μM)
10c	Basal	-	2.43±0.10	10l	Basal	-	2.23±0.15
	Control	-			Control	-	
	0.1	10.48±1.24			0.1	15.61±1.81	
	0.31	14.93±1.85			0.31	15.36±0.77	
	1	28.33±1.57			1	31.22±1.44	
	3.16	59.47±3.29			3.16	62.64±3.71	
10	95.33±0.75	10	93.93±1.42				
10d	Basal	-	11.30±1.69	10n	Basal	-	2.9±0.01
	Control	-			Control	-	
	1	14.27±0.79			0.1	5.25±2.08	
	3.16	28.00±2.86			0.31	9.23±5.71	
	10	48.19±5.39			1	21.99±4.09	
	31.62	70.84±5.61			3.16	51.75±0.75	
100	78.84±3.28	10	94.27±0.28				
10f	Basal	-	1.39±0.04	10p	Basal	-	1.55±0.33
	Control	-			Control	-	
	0.1	13.41±0.78			0.1	9.24±1.75	
	0.31	19.75±2.05			0.31	16.99±0.52	
	1	38.14±1.93			1	34.99±2.67	
	3.16	84.58±3.71			3.16	81.6±5.02	
10	96.86±0.24	10	96.63±0.19				
10h	Basal	-	3.49±0.03	10q	Basal	-	22.69±3.21
	Control	-			Control	-	
	0.1	5.23±1.37			1	9.55±0.80	
	0.31	14.9±1.51			3.16	17.47±2.04	
	1	23.48±0.18			10	31.51±3.32	
	3.16	45.41±0.69			31.62	60.82±5.22	
10	93.03±2.01	100	96.39±0.46				
10i	Basal	-	19.24±2.71	10r	Basal	-	9.81±0.87
	Control	-			Control	-	
	1	13.64±2.75			1	14.4±1.99	
	3.16	25.74±1.65			3.16	24.61±1.52	
	10	35.57±4.20			10	50.84±4.64	
	31.62	62.39±4.31			31.62	92.04±1.34	
100	76.16±2.07	100	97.24±0.10				
10j	Basal	-	4.75±0.55	α-TCP	Basal	-	6.78±2.16 μM
	Control	-			Control	-	
	1	19.70±3.82			0.1	4.62±0.57	
	3.16	39.72±4.55			0.32	8.26±1.31	
	10	74.00±2.95			1	21.13±2.56*	
	31.62	96.34±0.73			3.16	44.84±6.74**	
100	97.05±0.42	10	59.00±3.71**				
Quer	Basal	-	1.496±0.031 μM				
	Control	-					
	0.32	5.23±1.17					
	0.56	10.93±1.20					
	1	27.88±2.05**					
	1.78	62.68±1.93**					
	3.16	85.23±2.81**					
5.62	94.90±1.13**						
10	95.65±1.24**						

Table S2. α -glucosidase inhibition IC₅₀ data of isoquinolinones, acarbose and quercetin.

Comp.	Concentration (μ M)	Percentage of inhibition (%)	IC ₅₀ (μ M)	Comp.	Concentration (μ M)	Percentage of inhibition (%)	IC ₅₀ (μ M)
10a	Control	-	50.63 \pm 2.28	10j	Control	-	60.08 \pm 1.18
	31.62	3.48 \pm 9.53			31.62	9.46 \pm 2.22	
	42.17	15.17 \pm 6.62			42.17	16.16 \pm 1.25	
	56.23	26.77 \pm 4.37			56.23	39.92 \pm 1.95	
	74.13	55.81 \pm 3.43			74.13	81.08 \pm 4.6	
100	78.40 \pm 3.34	100	91.61 \pm 0.78				
10b	Control	-	68.04 \pm 0.28	10k	Control	-	50.05 \pm 3.07
	31.62	3.20 \pm 0.90			31.62	2.95 \pm 8.24	
	42.17	7.27 \pm 0.94			42.17	12.72 \pm 9.92	
	56.23	14.80 \pm 1.81			56.23	21.19 \pm 8.46	
	74.13	36.95 \pm 1.32			74.13	58.10 \pm 3.43	
100	81.70 \pm 1.12	100	96.50 \pm 3.08				
10c	Control	-	>100	10l	Control	-	61.31 \pm 1.72
	1	2.06			31.62	5.34 \pm 1.41	
	10	5.00			42.17	15.57 \pm 2.27	
	100	35.74			56.23	38.04 \pm 3.17	
10d	Control	-	31.49 \pm 0.82	10m	Control	-	52.47 \pm 4.16
	10	6.80 \pm 1.14			31.62	2.44 \pm 4.49	
	17.78	16.48 \pm 2.97			42.17	7.34 \pm 5.38	
	31.62	49.24 \pm 3.40			56.23	18.4 \pm 4.68	
	56.23	94.79 \pm 1.39			74.13	58.04 \pm 7.71*	
	100	93.83 \pm 0.28			100	93.68 \pm 2.35*	
10e	Control	-	14.75 \pm 0.30	10n	Control	-	57.21 \pm 0.17
	31.62	20.65 \pm 8.36			10	3.40 \pm 0.53	
	42.17	19.24 \pm 6.89			17.78	4.02 \pm 1.08	
	56.23	32.35 \pm 2.57			31.62	11.89 \pm 0.35	
	74.13	63.31 \pm 1.92			56.23	47.97 \pm 0.47	
	100	91.32 \pm 2.47			100	95.49 \pm 0.20	
10f	Control	-	33.07 \pm 1.73	10o	Control	-	13.70 \pm 0.56
	10	17.12 \pm 1.56			31.62	15.44 \pm 3.93	
	17.78	27.92 \pm 0.71			42.17	20.94 \pm 4.83	
	31.62	49.46 \pm 2.63			56.23	37.88 \pm 2.29	
	56.23	82.83 \pm 10.5			74.13	63.16 \pm 3.29	
	100	90.90 \pm 7.47			100	91.05 \pm 2.19	
10g	Control	-	30.22 \pm 1.07	10p	Control	-	>100
	31.62	-4.39 \pm 8.8			10	4.98 \pm 3.20	
	42.17	13.73 \pm 5.79			17.78	13.05 \pm 2.30	
	56.23	52.30 \pm 5.04			31.62	15.65 \pm 0.99	
	74.13	97.78 \pm 1.47			56.23	21.96 \pm 4.74	
	100	95.22 \pm 5.37			100	34.00 \pm 4.24	

Comp.	Concentration (μM)	Percentage of inhibition (%)	IC ₅₀ (μM)	Comp.	Concentration (μM)	Percentage of inhibition (%)	IC ₅₀ (μM)
10h	Control	-	44.37±2.39	10q	Control	-	92.78±1.31
	31.62	21.56±2.94			10	2.17±0.98	
	42.17	44.11±8.54			17.78	2.17±0.03	
	56.23	80.64±5.47			31.62	5.55±0.71	
	74.13	91.25±4.82			56.23	10.91±0.53	
	100	94.91±3.25			100	66.49±5.48	
10i	Control	-	50.52±1.81	10r	Control	-	>100
	31.62	13.44±1.36			10	2.74±1.97	
	42.17	29.26±3.22			17.78	8.59±1.1	
	56.23	66.33±7.01			31.62	9.5±1.46	
	74.13	91.27±1.91			56.23	8.32±4.81	
	100	98.64±2.26			100	29.08±2.17	
Acarbose	Control	-	4687.06±21 9.50	Quer	Control	-	15.61±1.68
	2040.09	29.9±2.17			1	6.71±0.40	
	3628.27	43.14±1.64			1.78	12.14±1.29	
	6456.00	59.17±1.66			3.16	24.24±4.94	
	11478.77	72.54±1.55			5.62	53.39±8.74	
	20413.87	82.93±0.10			10	82.89±3.44	

Cytotoxicity



Table S3. Percentage of inhibition against healthy cell line COS-7 of selected isoquinolinones at 50 μ M.

Compound	Percentage of growth inhibition of COS-7
10e	5.0
10f	NC
10g	NC
10o	NC
10p	7.6

Cytotoxicity assay was performed in accordance to our previous works without modifications.¹

¹ Á. Ramírez-Trinidad, K. Carrillo-Jaimes, J. A. Rivera-Chávez and E. Hernández-Vázquez, *Med Chem Res*, 2023, **32**, 144–157.

Sucrose tolerance assay

The area under the curve of sucrose tolerance test is shown herein.

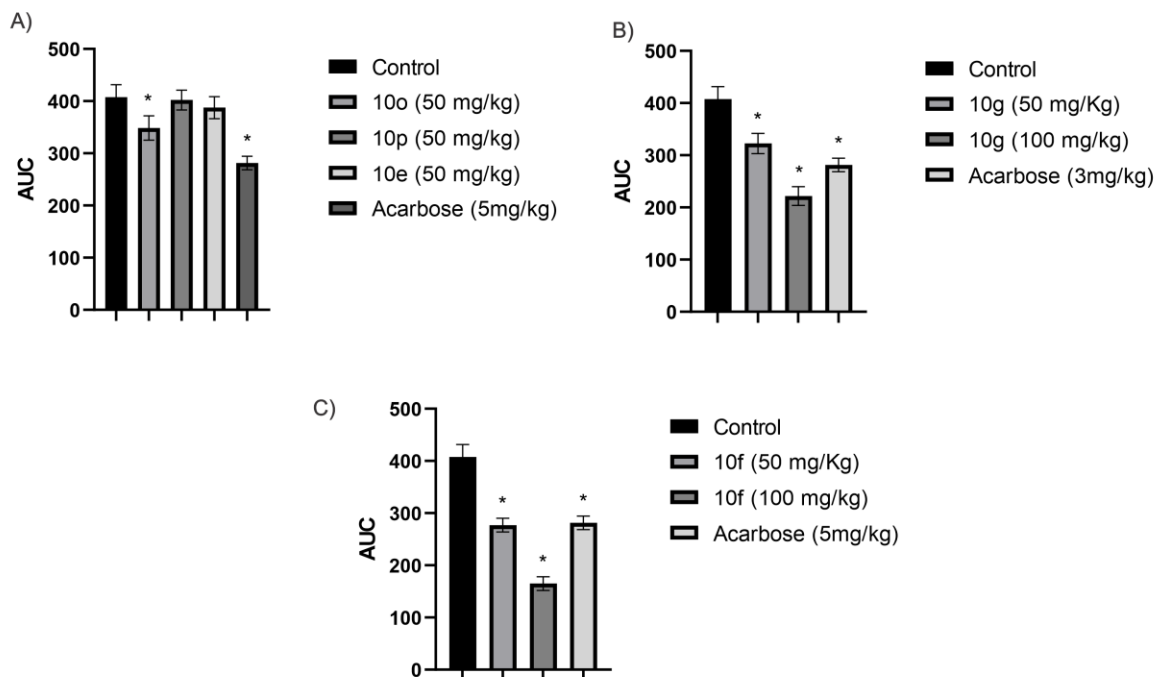


Figure S77. AUC of sucrose tolerance test. A) Less active compounds; only **10o** showed a significant reduction of glucose; b) Compound **10g**; c) Compound **10f**. Both compounds show a dose-dependent glucose reduction. *p < 0.05.

Glucose tolerance assay

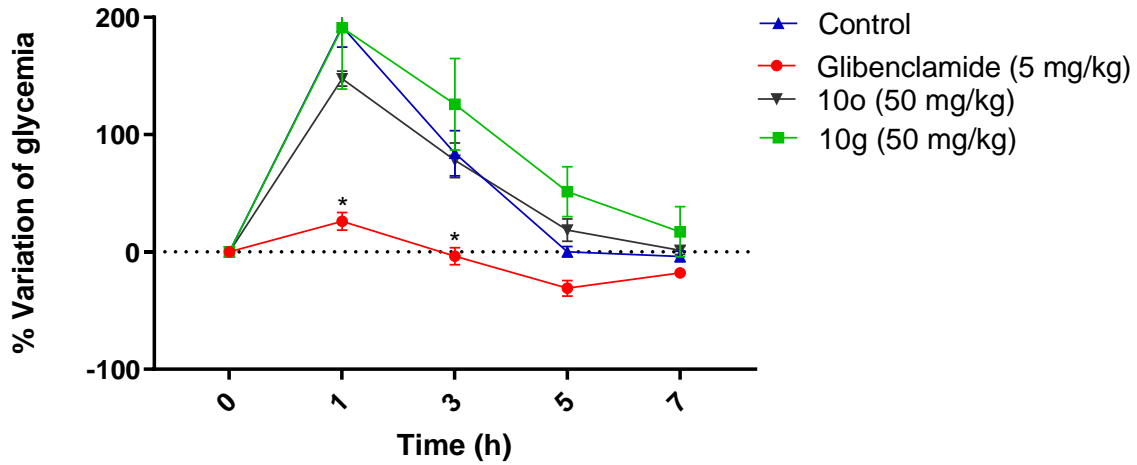


Figure S78. Oral glucose tolerance test of **10g** and **10o**, along with glibenclamide. No glucose reduction was observed with the isoquinolines. * $p < 0.05$.

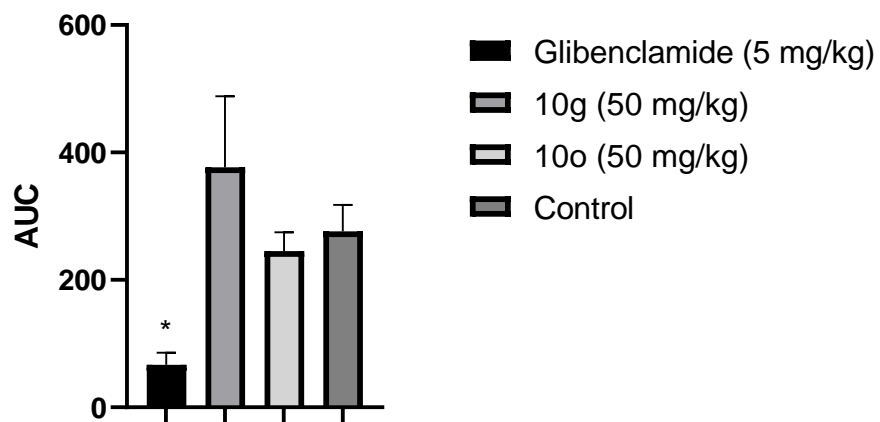


Figure S79. AUC of GTA. Only glibenclamide showed a significant difference against control.

* $p < 0.05$.