

Experimental Supporting Information

Dehydrative formation and biological evaluation of allylic sulfonamides from allylic alcohols using recyclable silica-supported acid catalysts

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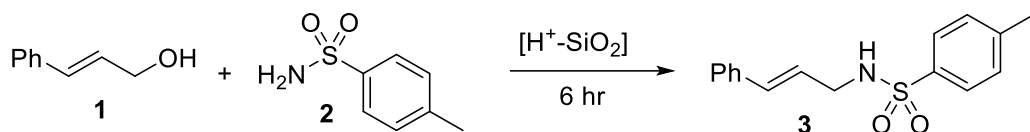
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Entry	Equiv 1	Equiv 2	SiO ₂ catalyst	[H ⁺ -SiO ₂] amount (mg)	Temp (°C)	Solvent Concentration	Solvent	% Yld 3 (¹ H NMR)
1	1	1.1	SA (3 mol%)	55	65	0.25	CDCl ₃	15
2	1	1.1	TfOH (3 mol%)	55	65	0.25	CDCl ₃	24
3	1	1.1	HClO ₄ (3 mol%)	55	65	0.25	CDCl ₃	32
4	1	1.1	PTSA (3 mol%)	55	65	0.25	CDCl ₃	43
5	1	1.1	SA (6 mol%)	55	65	0.25	CDCl ₃	5
6	1	1.1	TfOH (6 mol%)	55	65	0.25	CDCl ₃	3
7	1	1.1	HClO ₄ (6 mol%)	55	65	0.25	CDCl ₃	9
8	1	1.1	PTSA (6 mol%)	55	65	0.25	CDCl ₃	49
9	1	1.1	SA (3 mol%)	30	65	0.25	CDCl ₃	26
10	1	1.1	SA (3 mol%)	80	65	0.25	CDCl ₃	15
11	1	1.1	SA (6 mol%)	30	65	0.25	CDCl ₃	34
12	1	1.1	SA (6 mol%)	80	65	0.25	CDCl ₃	8
13	1	1.1	TfOH (3 mol%)	30	65	0.25	CDCl ₃	11
14	1	1.1	TfOH (3 mol%)	80	65	0.25	CDCl ₃	14
15	1	1.1	TfOH (6 mol%)	30	65	0.25	CDCl ₃	13
16	1	1.1	TfOH (6 mol%)	80	65	0.25	CDCl ₃	14
17	1	1.1	HClO ₄ (3 mol%)	30	65	0.25	CDCl ₃	11
18	1	1.1	HClO ₄ (3 mol%)	80	65	0.25	CDCl ₃	8
19	1	1.1	HClO ₄ (6 mol%)	30	65	0.25	CDCl ₃	9
20	1	1.1	HClO ₄ (6 mol%)	80	65	0.25	CDCl ₃	12
21	1	1.1	PTSA (3 mol%)	30	65	0.25	CDCl ₃	46
22	1	1.1	PTSA (3 mol%)	80	65	0.25	CDCl ₃	48
23	1	1.1	PTSA (6 mol%)	30	65	0.25	CDCl ₃	48
24	1	1.1	PTSA (6 mol%)	80	65	0.25	CDCl ₃	42
25	1	2	PTSA (3 mol%)	55	65	0.25	CDCl ₃	58
26	1	0.5	PTSA (3 mol%)	55	65	0.25	CDCl ₃	32
27	1	3	PTSA (3 mol%)	55	65	0.25	CDCl ₃	63
28	1	1.5	PTSA (3 mol%)	55	65	0.25	CDCl ₃	64
29	1	2.5	PTSA (3 mol%)	55	65	0.25	CDCl ₃	61
30	1	2	PTSA (6 mol%)	55	65	0.25	CDCl₃	68
31	1	3	PTSA (6 mol%)	55	65	0.25	CDCl ₃	63
32	1	1.5	PTSA (6 mol%)	55	65	0.25	CDCl ₃	52
33	1	2.5	PTSA (6 mol%)	55	65	0.25	CDCl ₃	58
34	1	1.1	PTSA (3 mol%)	55	85	0.25	CDCl ₃	45
35	1	1.1	PTSA (3 mol%)	55	105	0.25	CDCl ₃	50
36	1	2	PTSA (6 mol%)	55	105	0.33	CDCl ₃	50
37	1	2	PTSA (6 mol%)	30	105	0.25	CDCl ₃	59
38	1	2	PTSA (6 mol%)	55	105	0.25	CDCl ₃	44
39	1	1.1	PTSA (3 mol%)	55	65	0.33	CDCl ₃	55
40	1	1.1	PTSA (3 mol%)	55	65	0.17	CDCl ₃	48
41	1	2	PTSA (3 mol%)	30	65	0.25	CDCl ₃	64
42	1	2	PTSA (3 mol%)	80	65	0.25	CDCl ₃	48
43	1	3	PTSA (3 mol%)	30	65	0.25	CDCl ₃	66
44	1	2	PTSA (6 mol%)	30	65	0.33	CDCl ₃	66

45	1	2	PTSA (6 mol%)	30	65	0.33	CDCl ₃	66
46	1	2	PTSA (6 mol%)	30	65	0.25	CDCl ₃	65
47	1	2	PTSA (6 mol%)	55	65	0.33	CDCl ₃	62
48	1	3	PTSA (6 mol%)	30	65	0.33	CDCl ₃	52
49	1	2	PTSA (6 mol%)	55	65	0.33	CDCl ₃	67
50	1	2	PTSA (6 mol%)	55	65	0.17	CDCl ₃	60
51	1	3	PTSA (3 mol%)	55	65	0.33	CDCl ₃	56
52	1	3	PTSA (3 mol%)	55	65	0.17	CDCl ₃	58
53	1	1.1	PTSA (3 mol%)	55	65	0.25	THF	0
54	1	1.1	PTSA (3 mol%)	55	65	0.25	DCE	32
55	1	1.1	PTSA (3 mol%)	55	65	0.25	DCM	38
56	1	1.1	PTSA (3 mol%)	55	65	0.25	CDCl ₃	36 (2 hrs)
57	1	1.1	PTSA (3 mol%)	55	65	0.25	CDCl ₃	42 (4 hrs)
58	1	1.1	PTSA (3 mol%)	55	65	0.25	CDCl ₃	43 (6 hrs)

All yields determined by ¹H NMR using 1,3-dinitrobenzene as internal standard. SA = sulfuric acid; TfOH = triflic acid; HClO₄ = perchloric acid; PTSA = p-toluenesulfonic acid. THF = tetrahydrofuran; DCE = dichloroethane; DCM = dichloromethane.

Table S1. Optimization of reaction conditions.

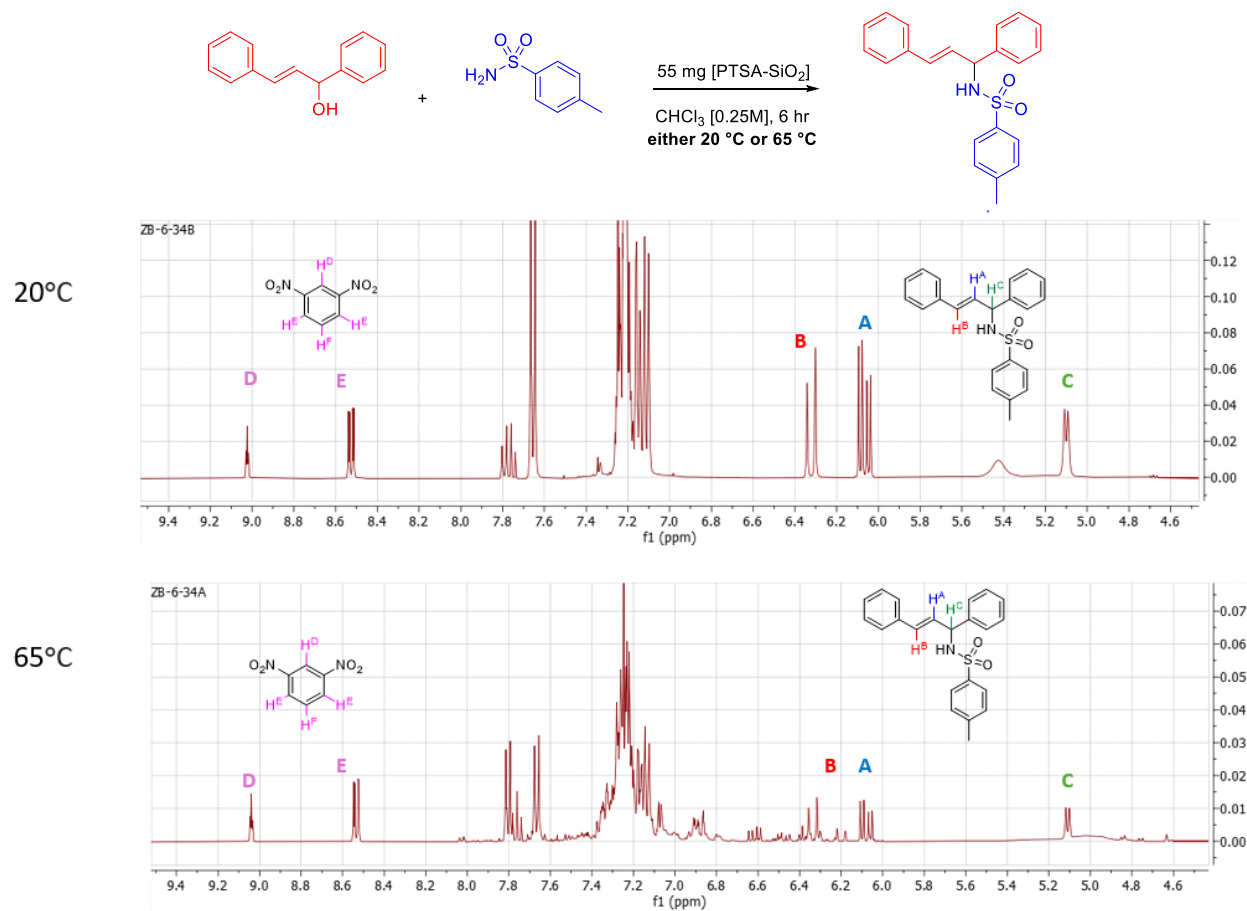


Figure S1. Comparison of reactions performed at 20 °C and 65 °C for 6 hours. 400 MHz ^1H -NMR in CDCl_3 of Product **4** with 1,3-dinitrobenzene as internal standard.

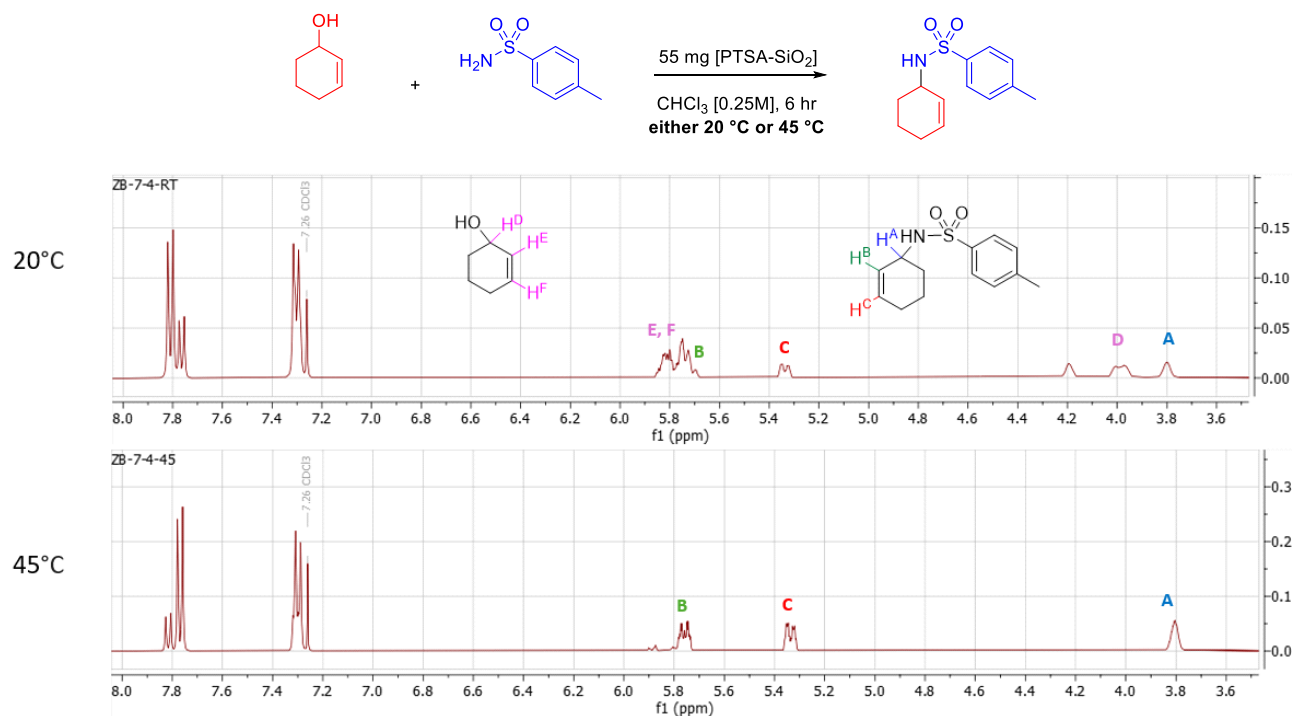


Figure S2. Comparison of reactions performed at 20 °C and 45 °C for 6 hours. 400 MHz ^1H -NMR in CDCl_3 of cyclohex-2-en-1-ol starting material and Product **22**.

Product Characterization (spectra):

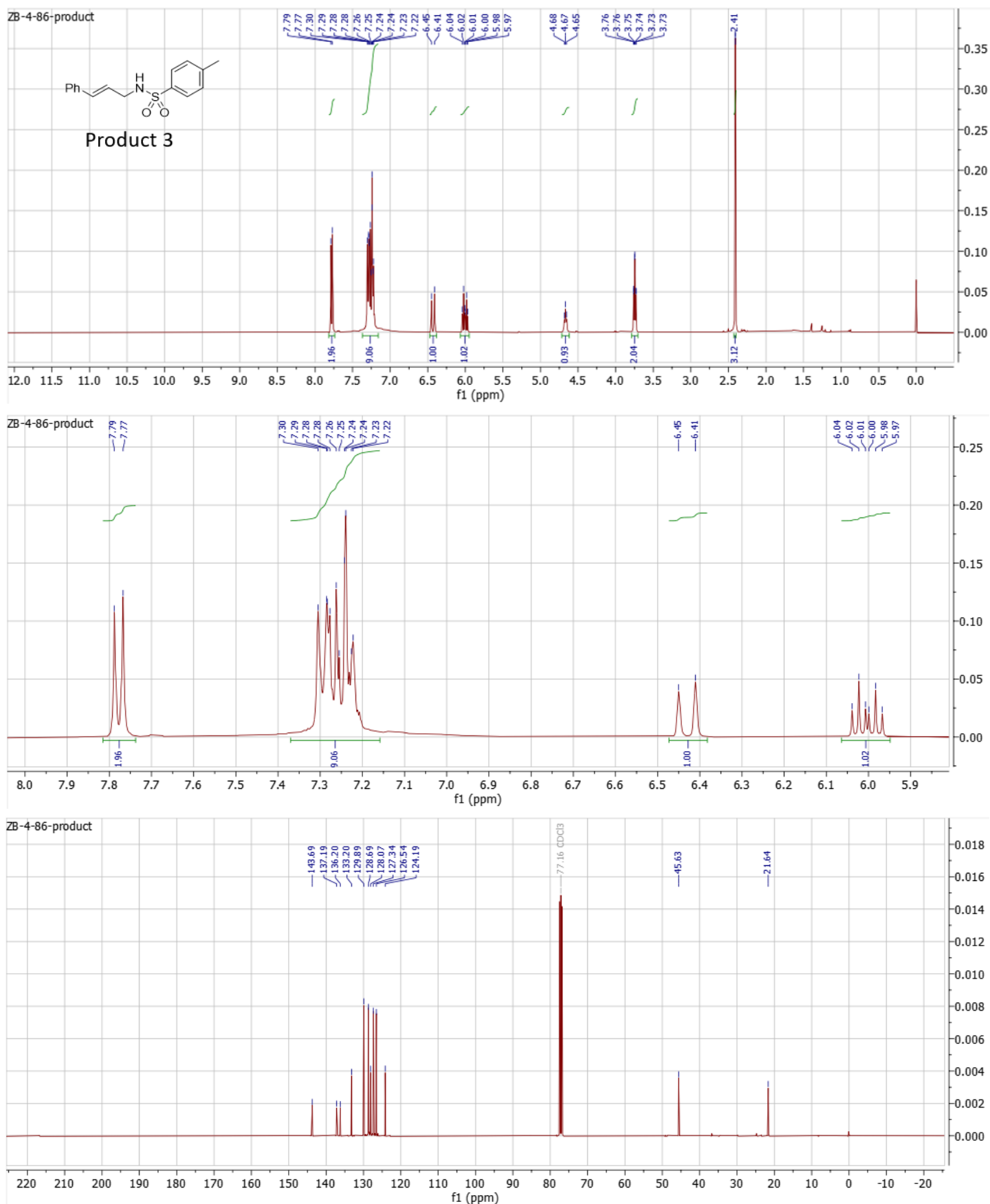


Figure S3. 400 MHz ¹H-NMR in CDCl₃ (full and zoom-in of aromatic region) and 101 MHz ¹³C{¹H} NMR in CDCl₃ of Product 3.

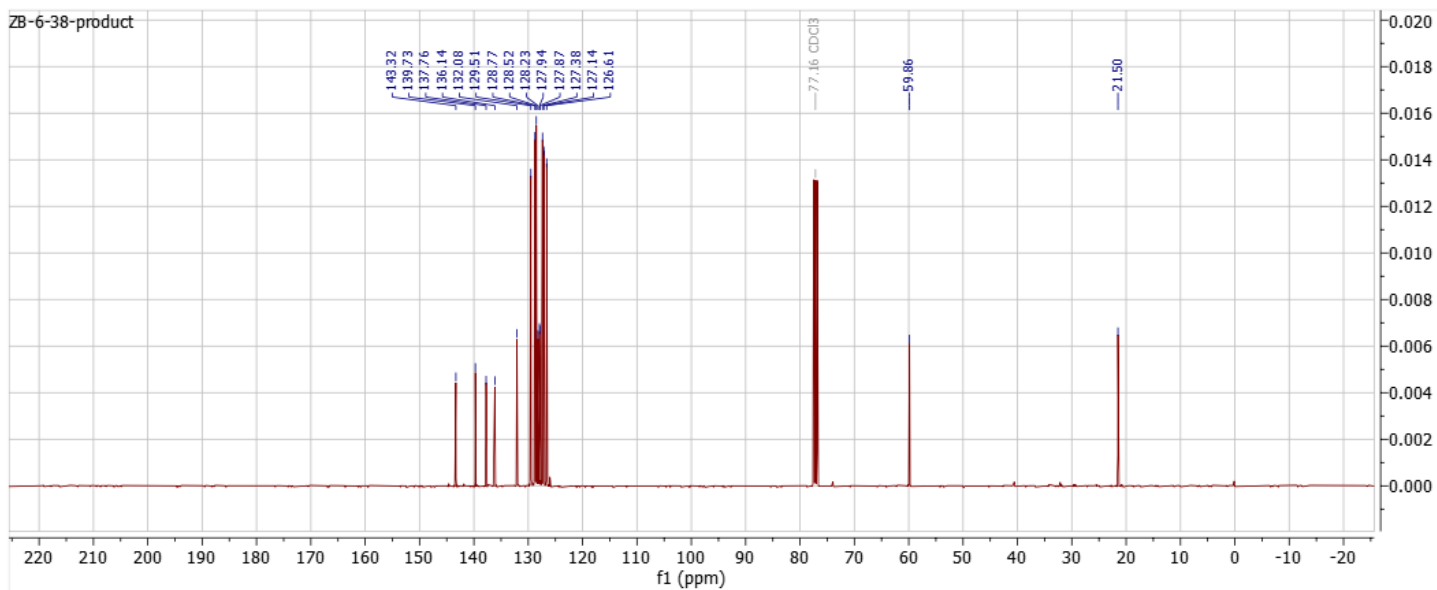
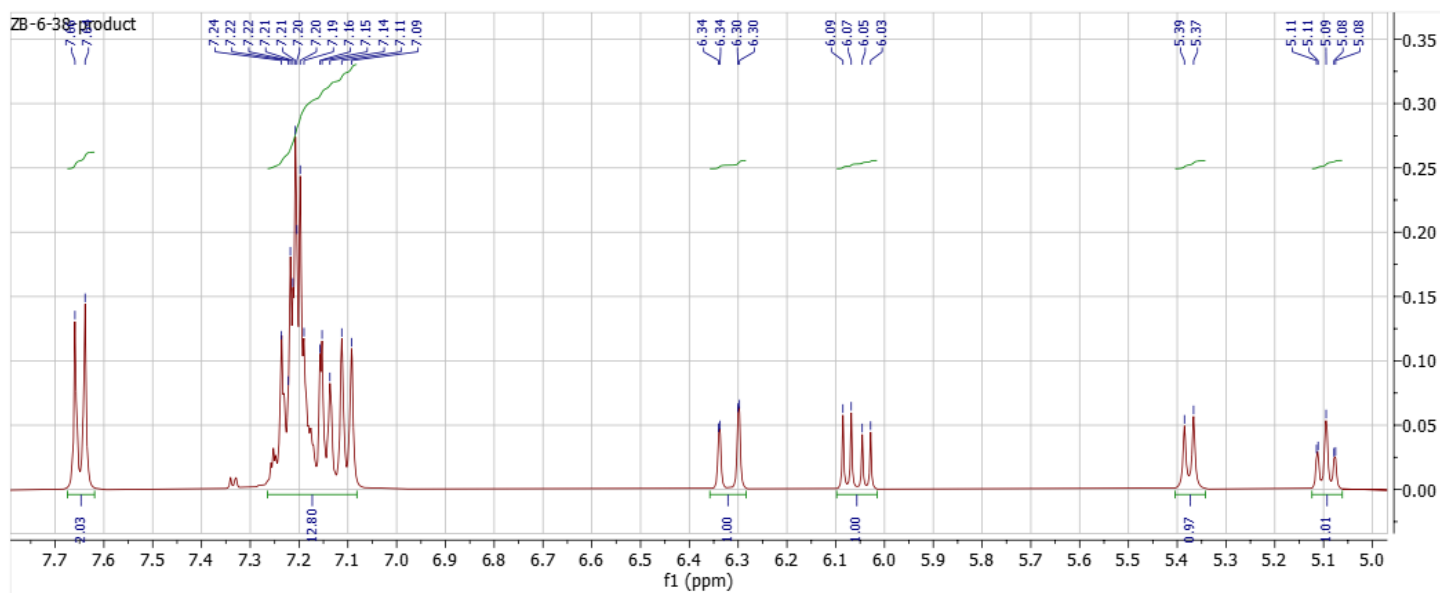
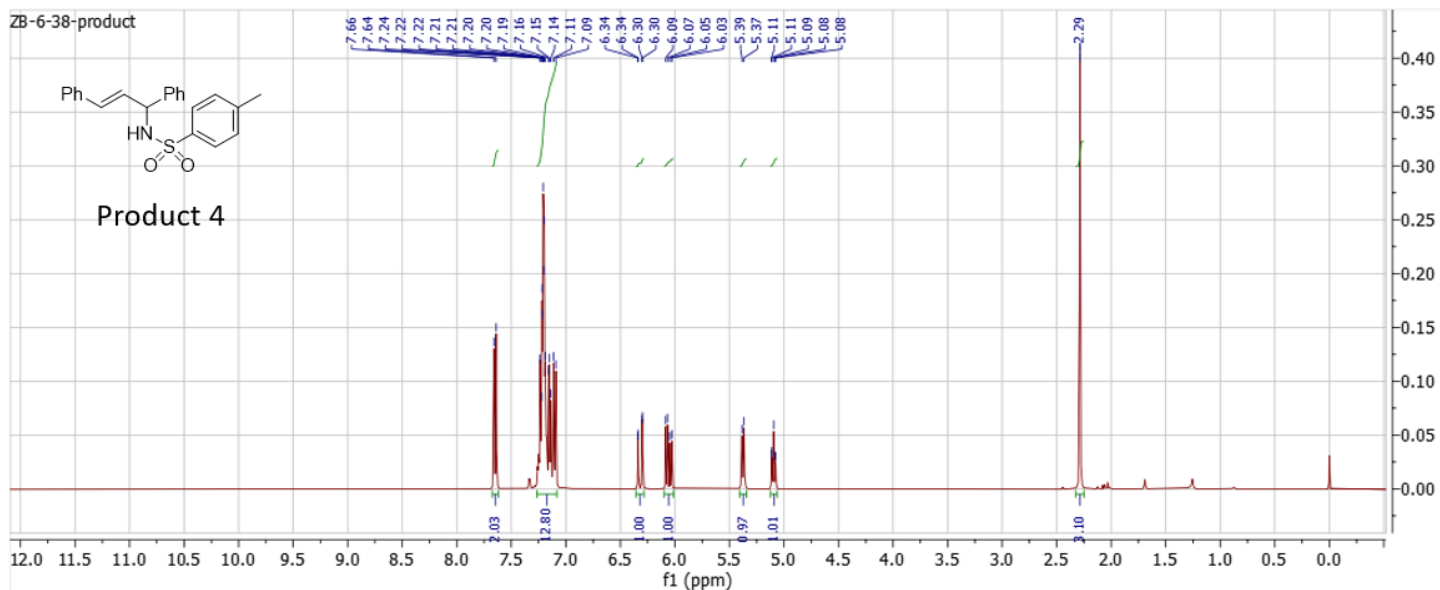


Figure S4. 400 MHz ^1H -NMR in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 4.

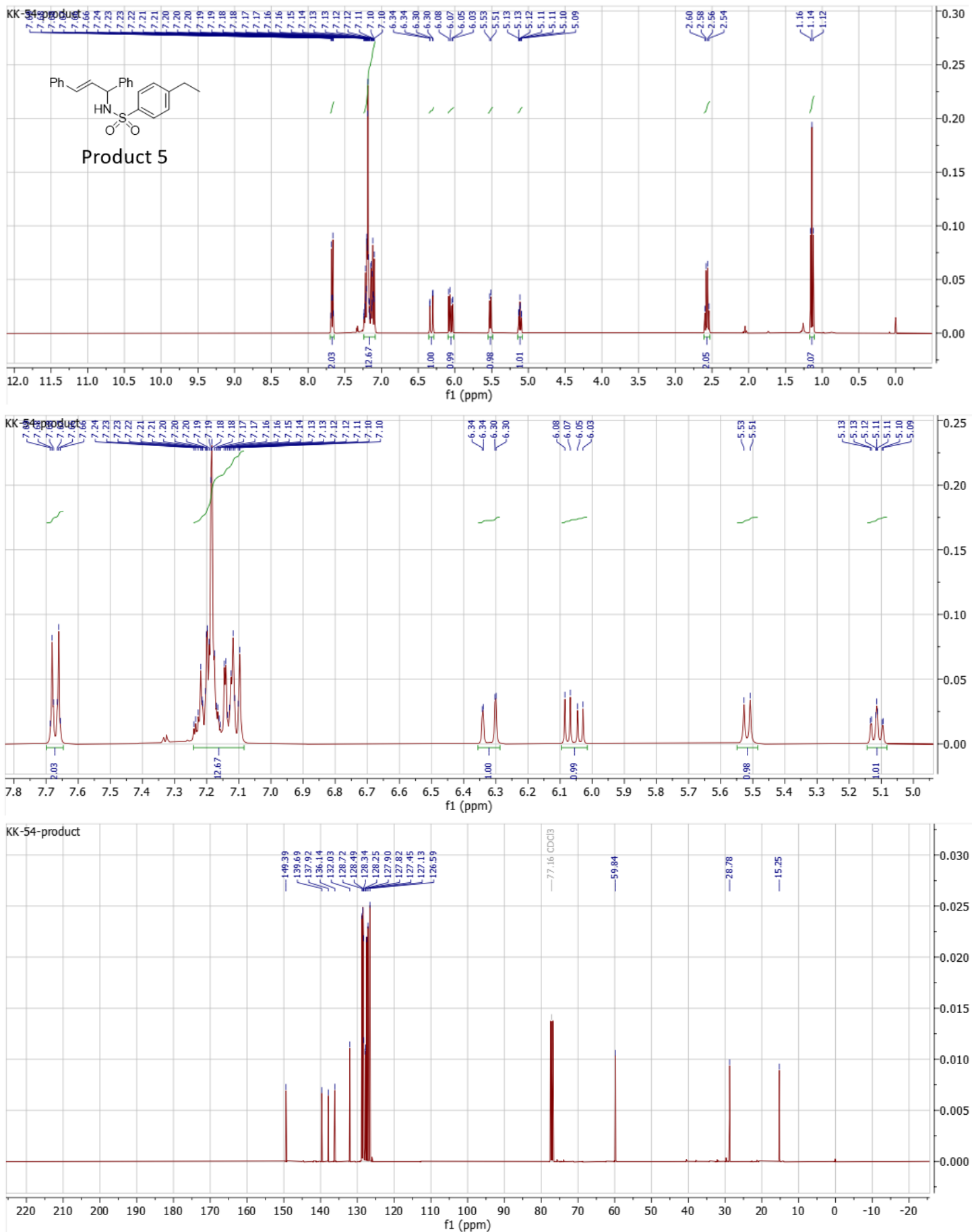


Figure S5. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 5.

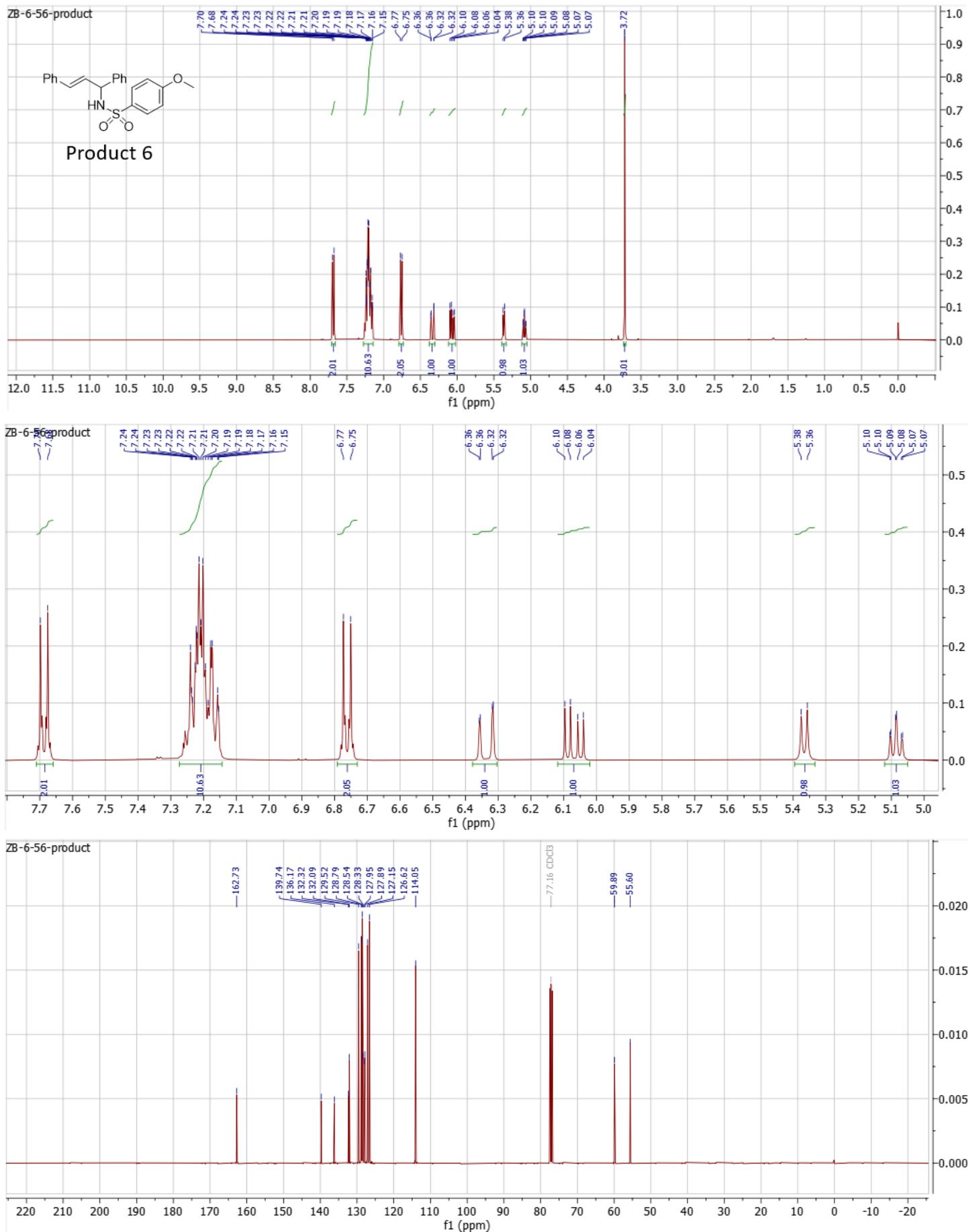


Figure S6. 400 MHz ¹H-NMR in CDCl₃ (full and zoom-in of aromatic region) and 101 MHz ¹³C{¹H} NMR in CDCl₃ of Product 6.

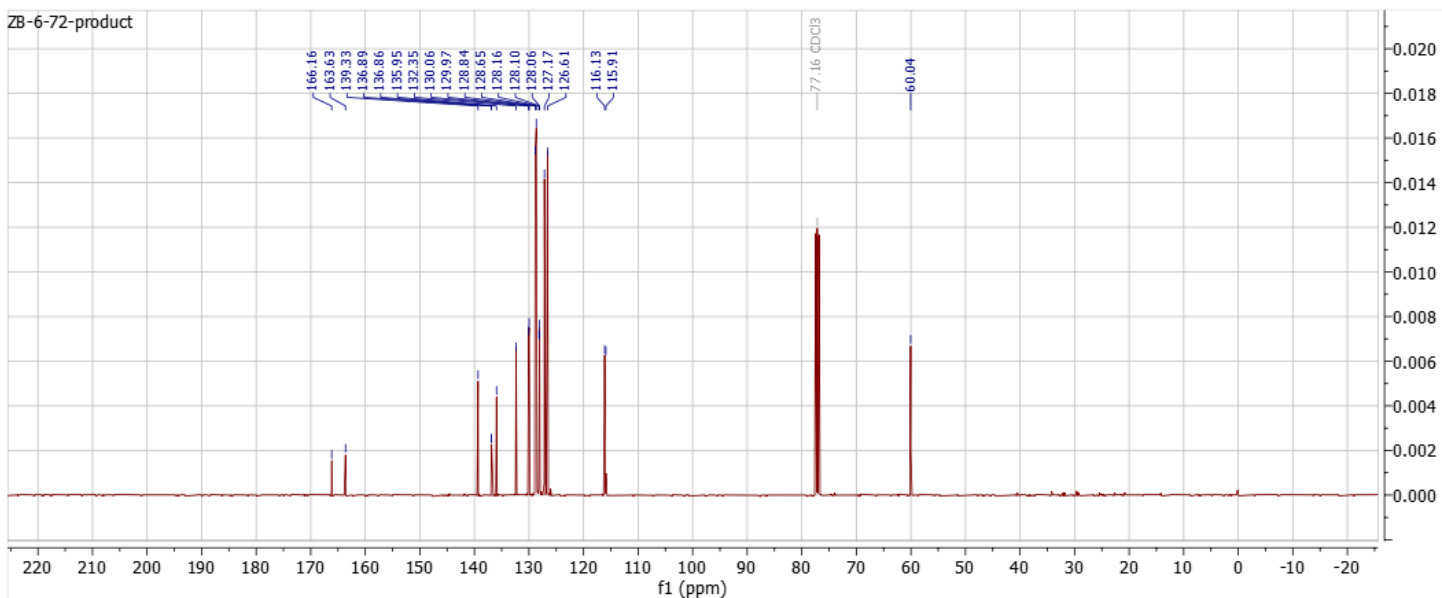
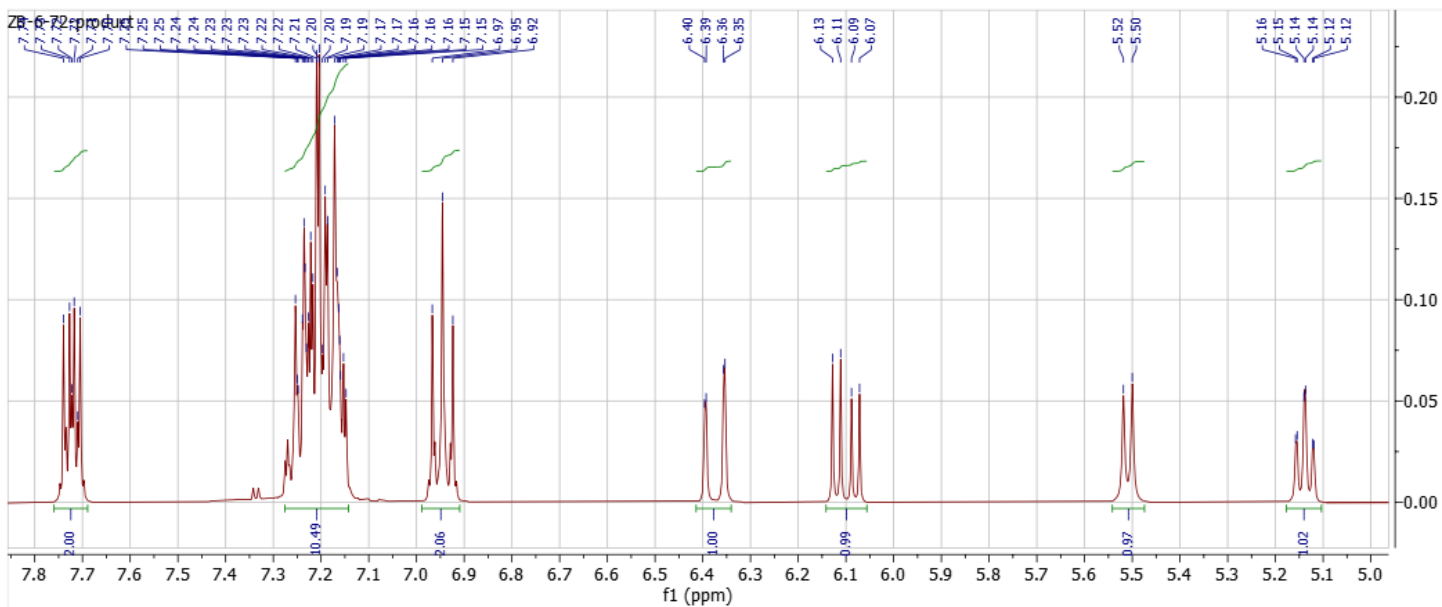
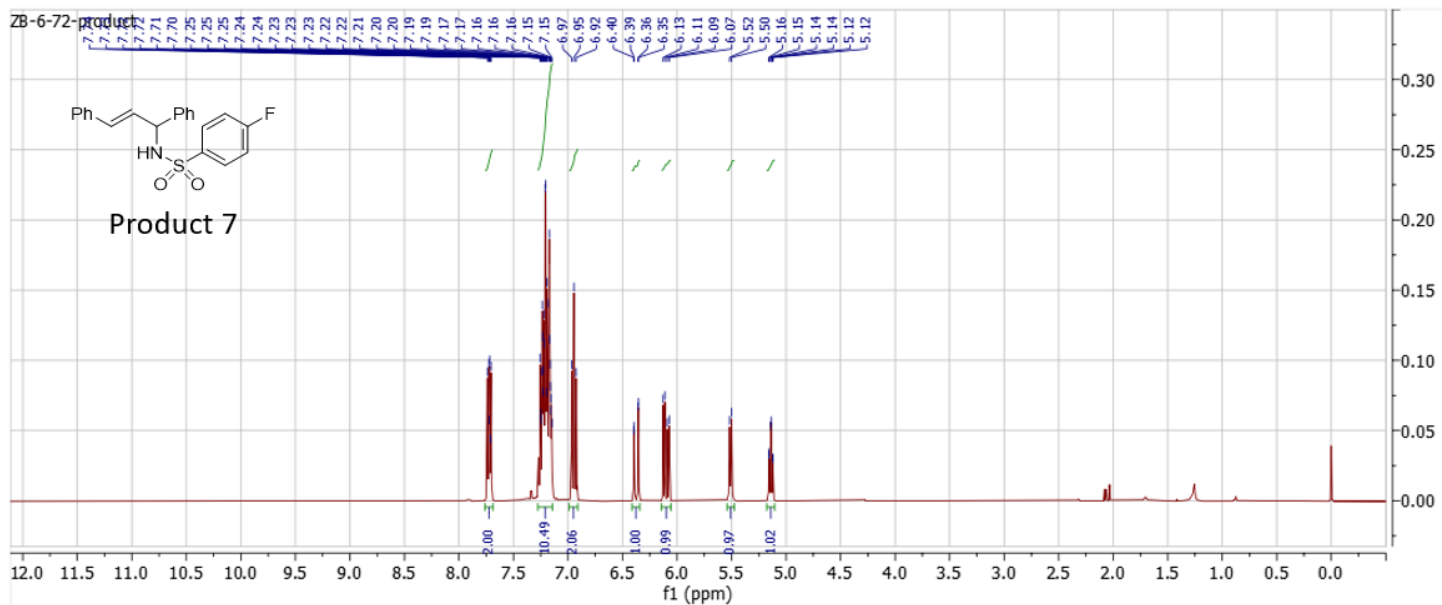


Figure S7. 400 MHz ^1H -NMR in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 7.

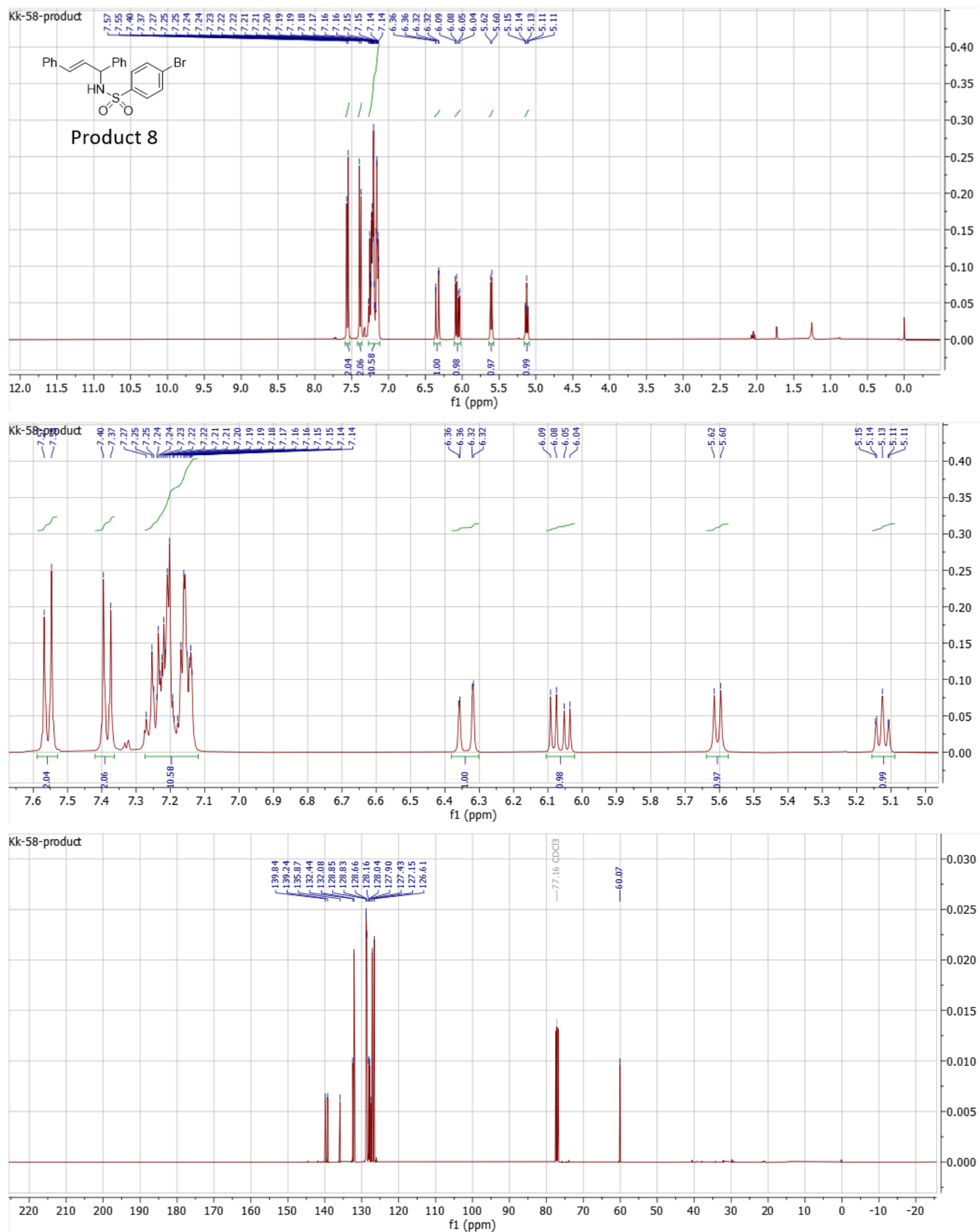


Figure S8. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 8.

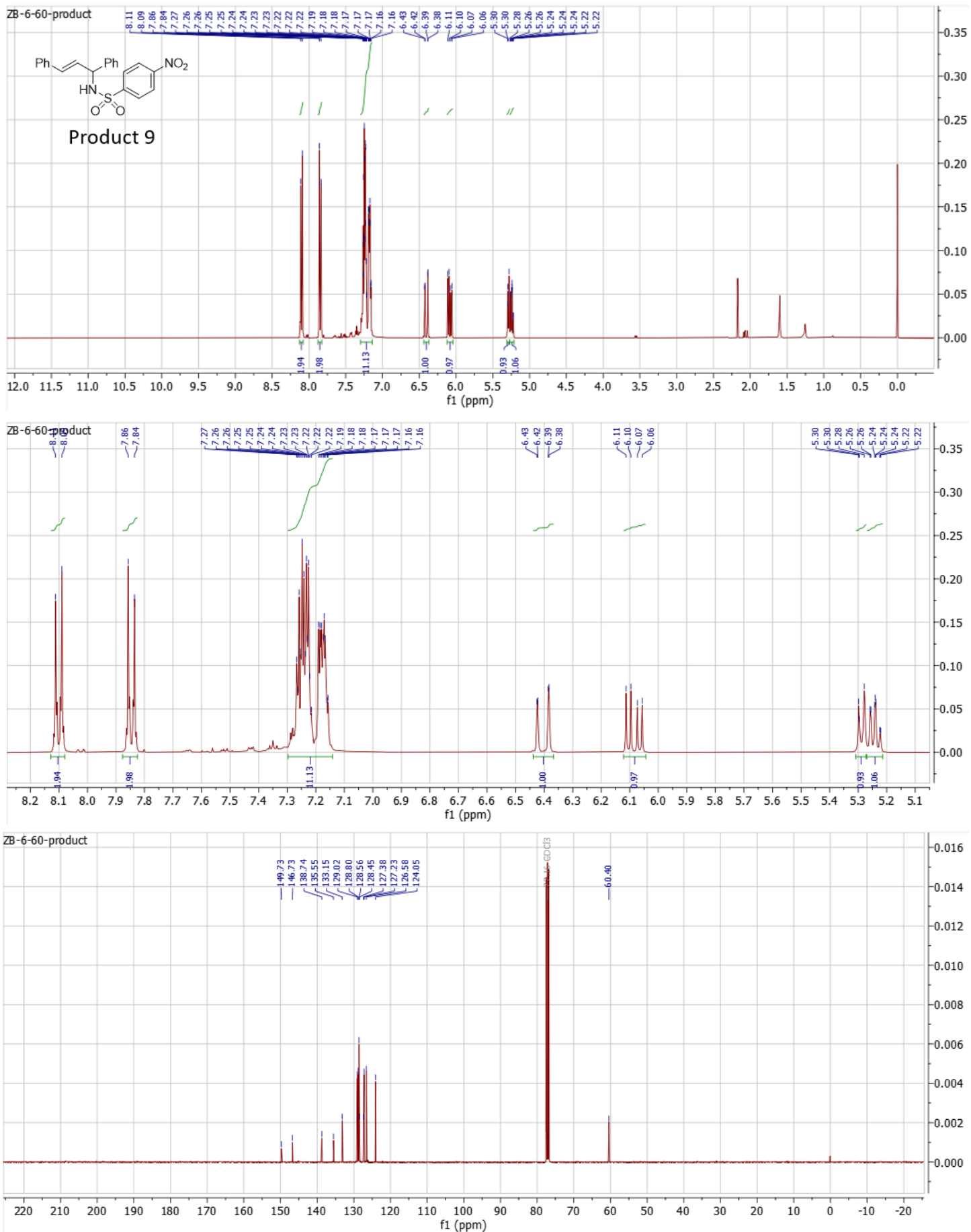
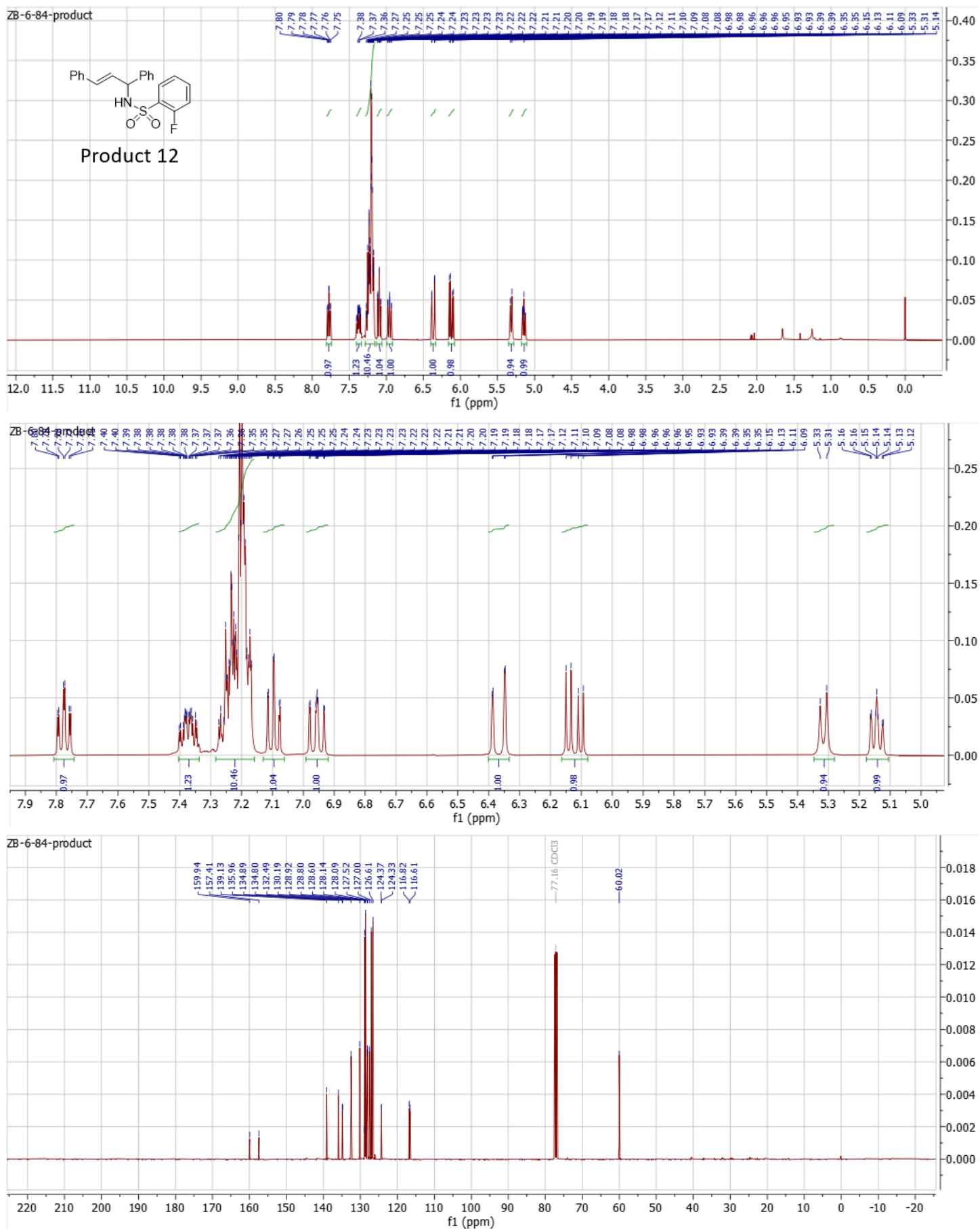


Figure S9. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 9.



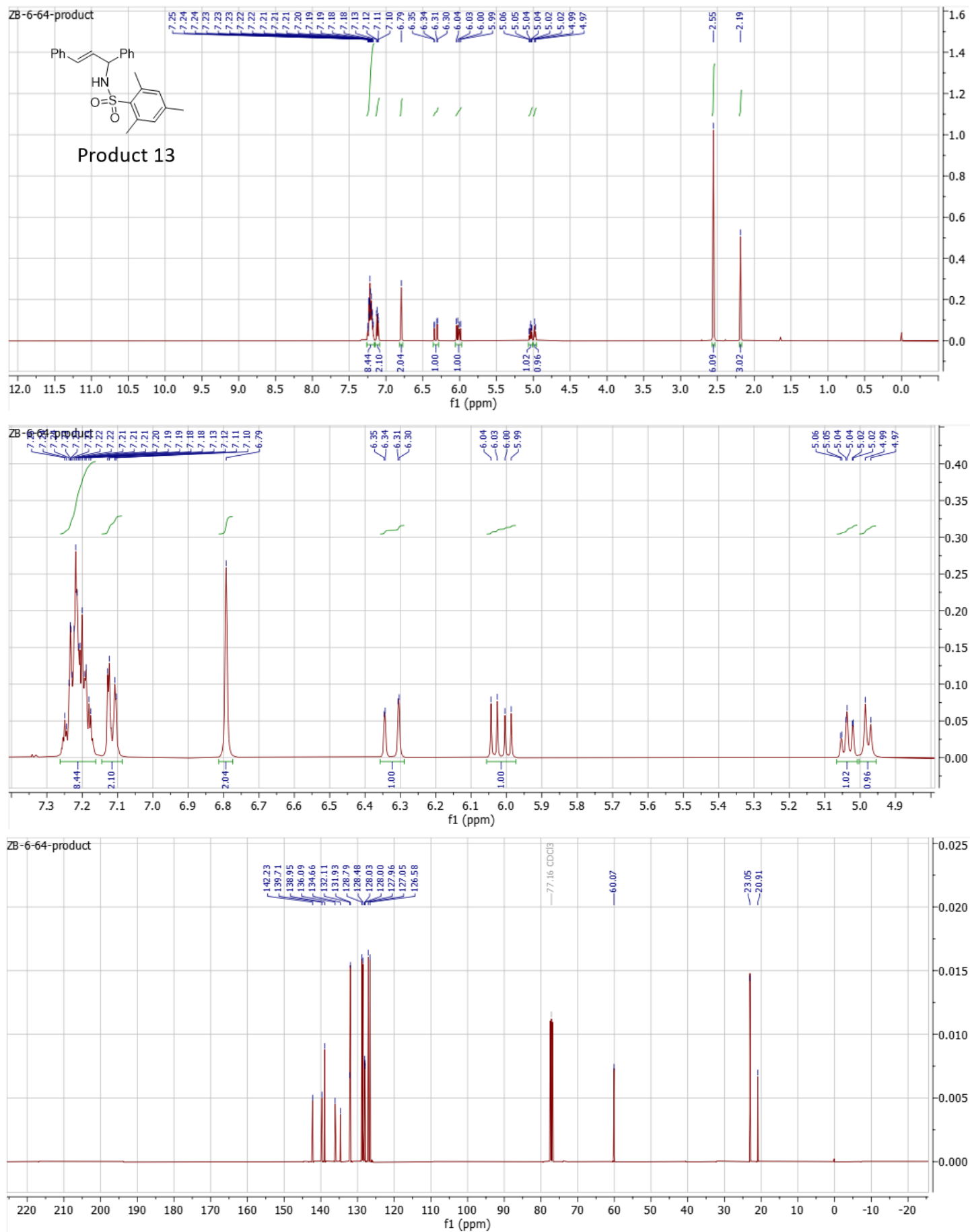


Figure S13. 400 MHz ¹H-NMR in CDCl₃ (full and zoom-in of aromatic region) and 101 MHz ¹³C{¹H} NMR in CDCl₃ of Product **13**.

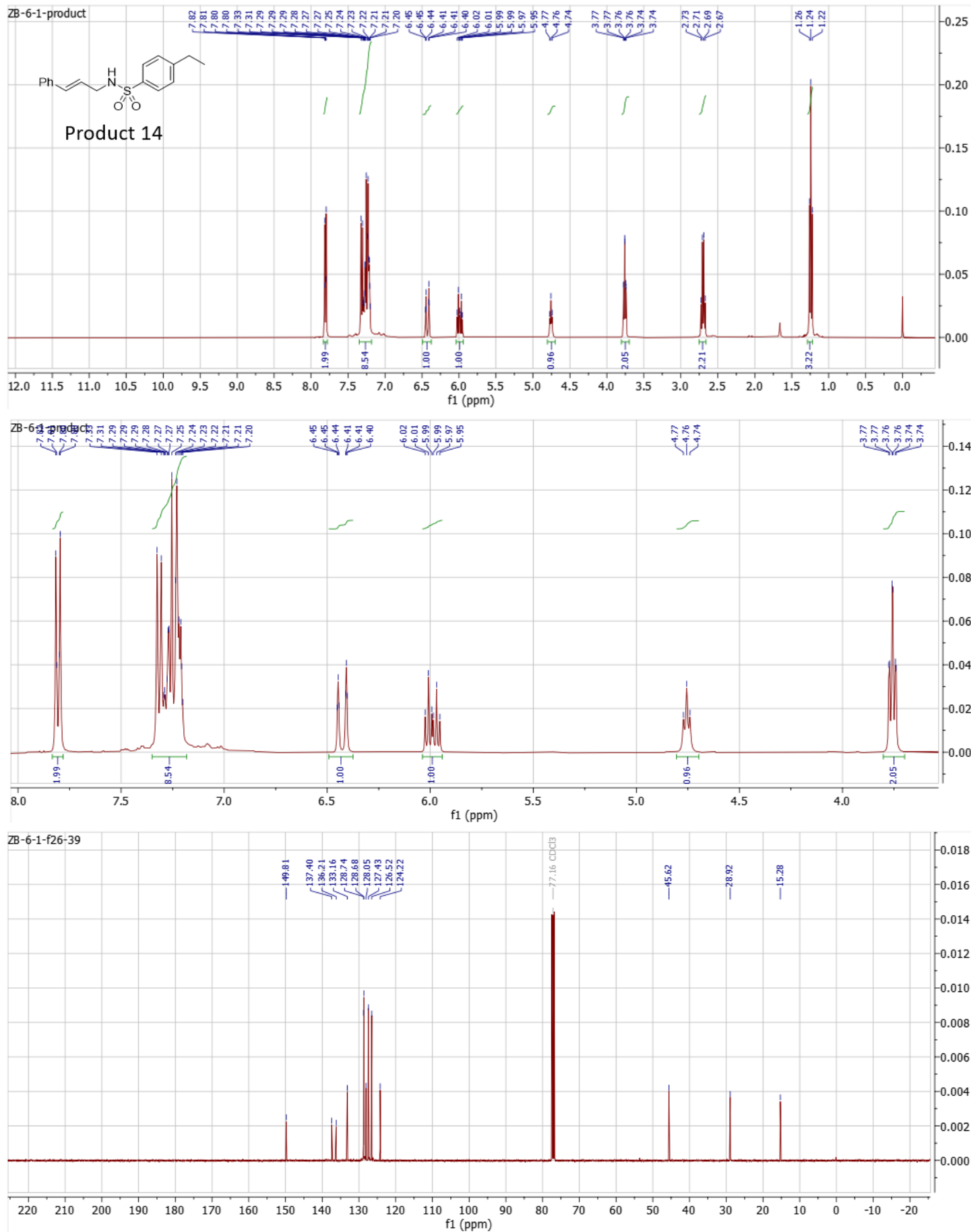


Figure S14. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 14.

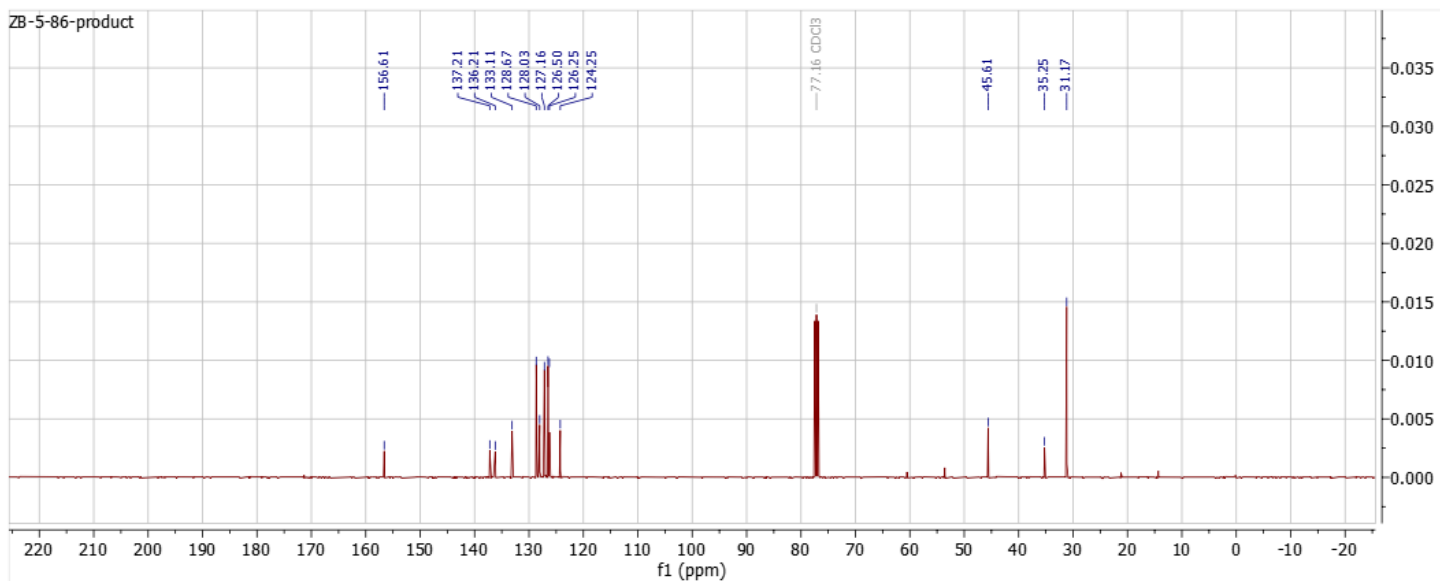
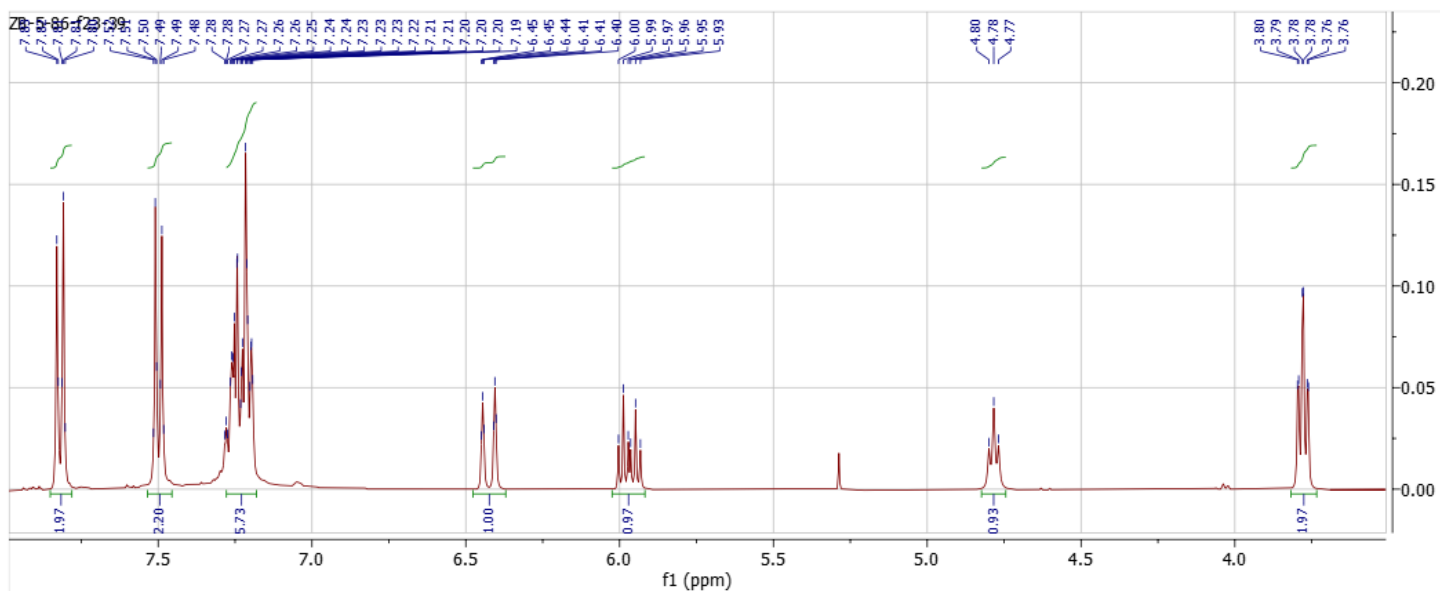
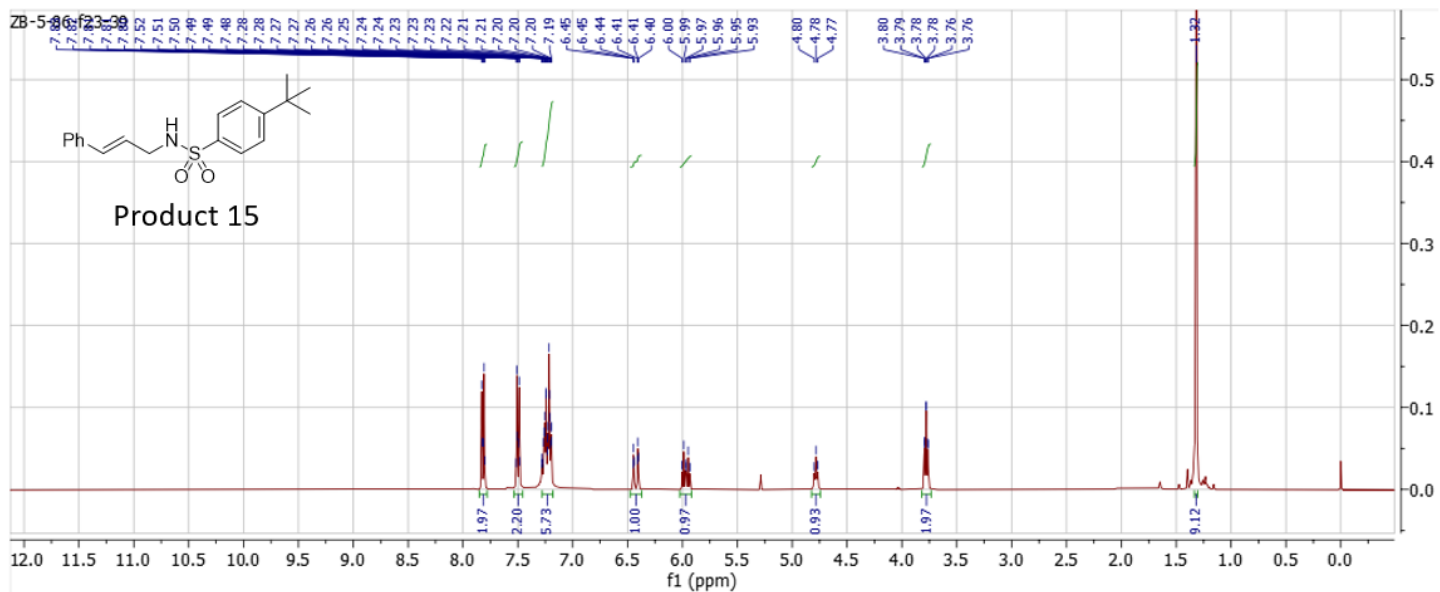


Figure S15. 400 MHz ^1H -NMR in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 15.

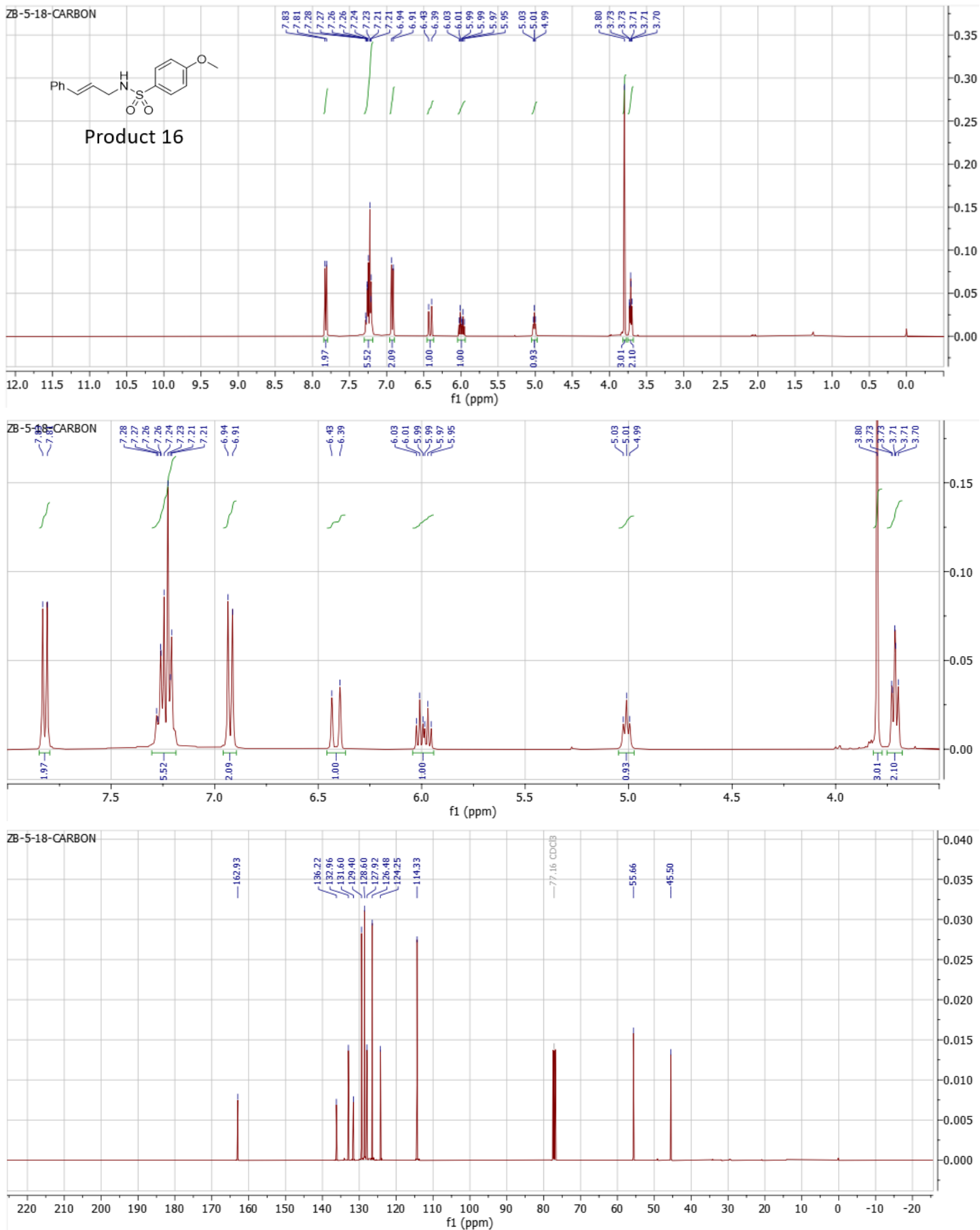


Figure S16. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product **16**.

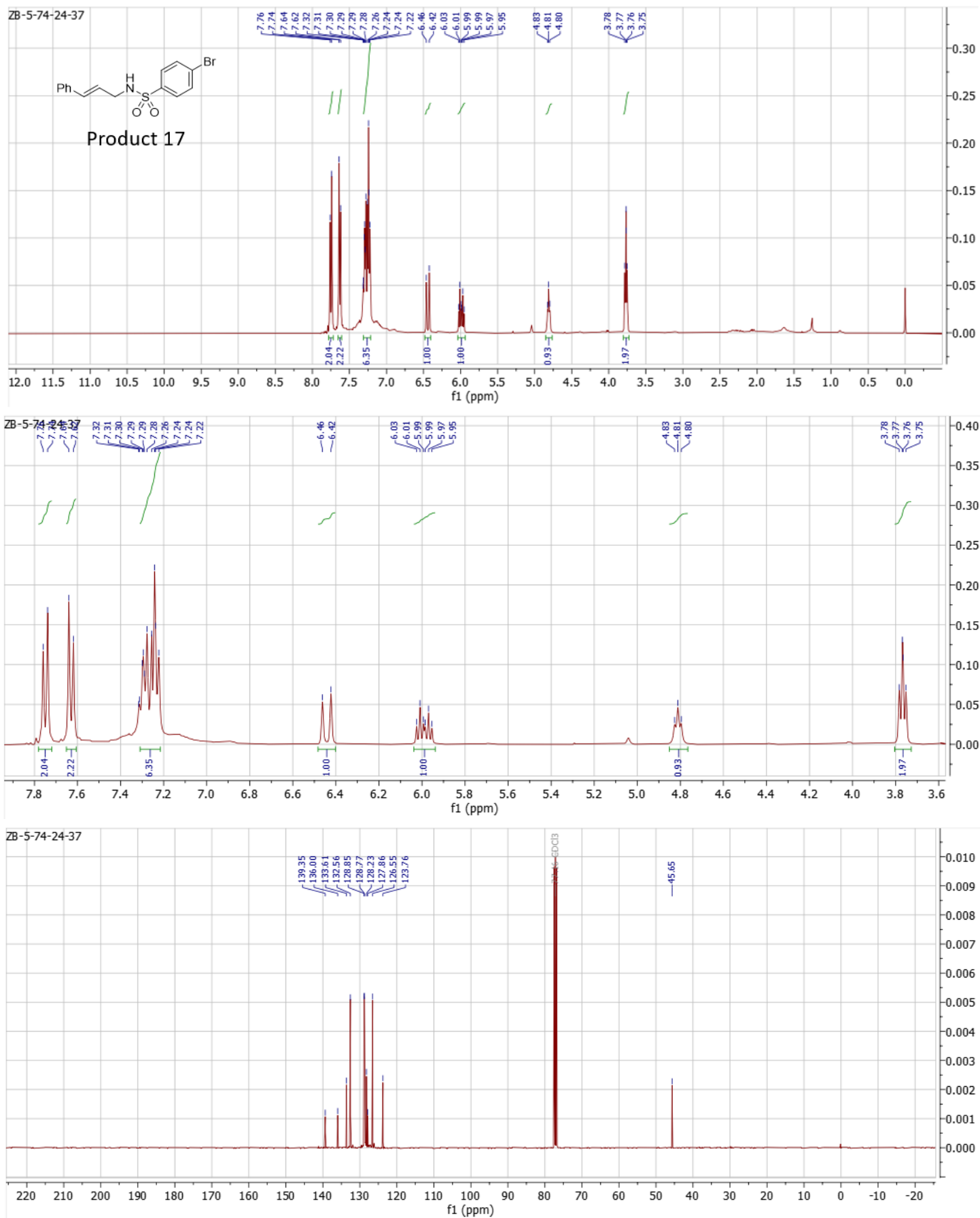


Figure S17. 400 MHz ^1H -NMR in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 17.

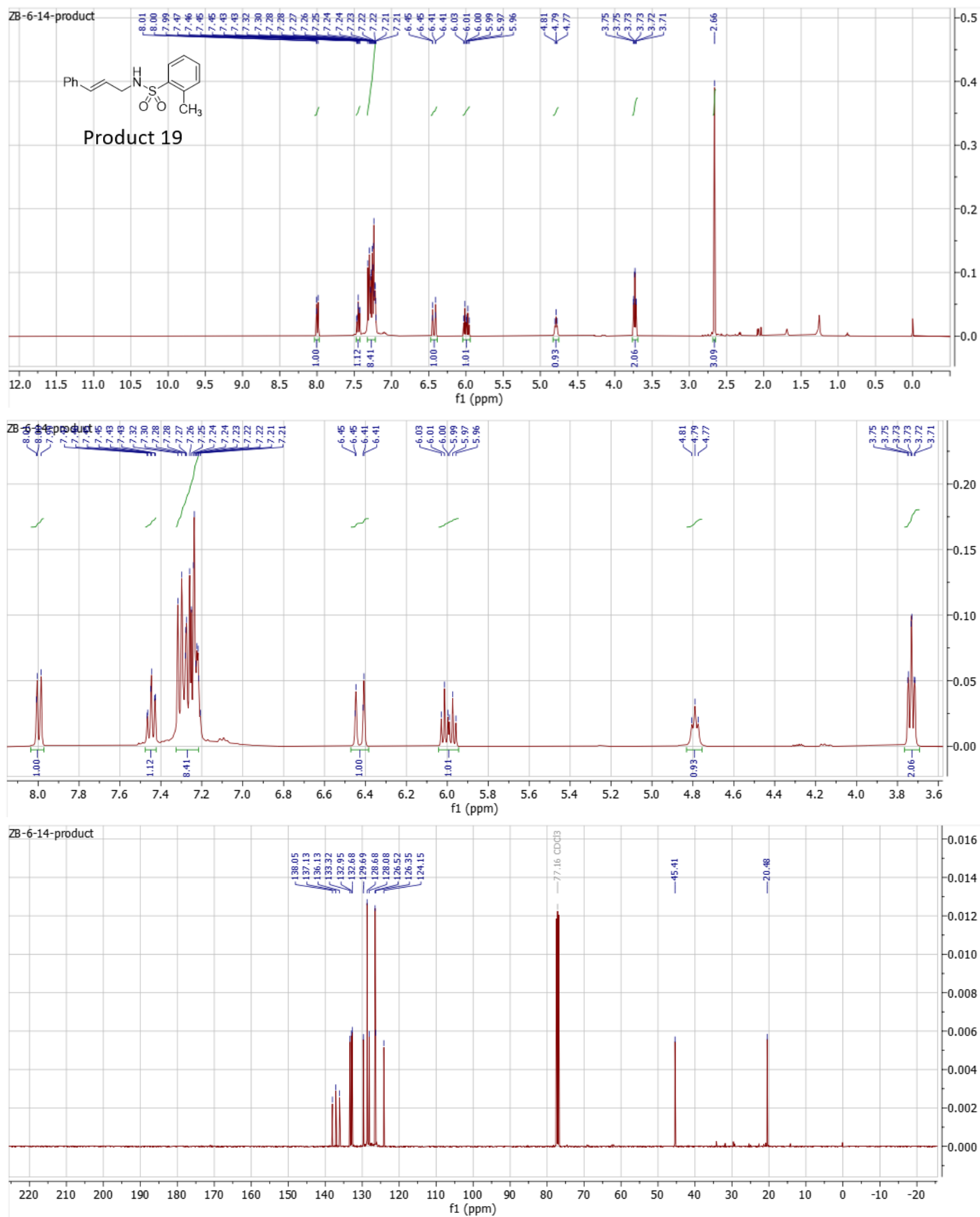


Figure S19. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 19.

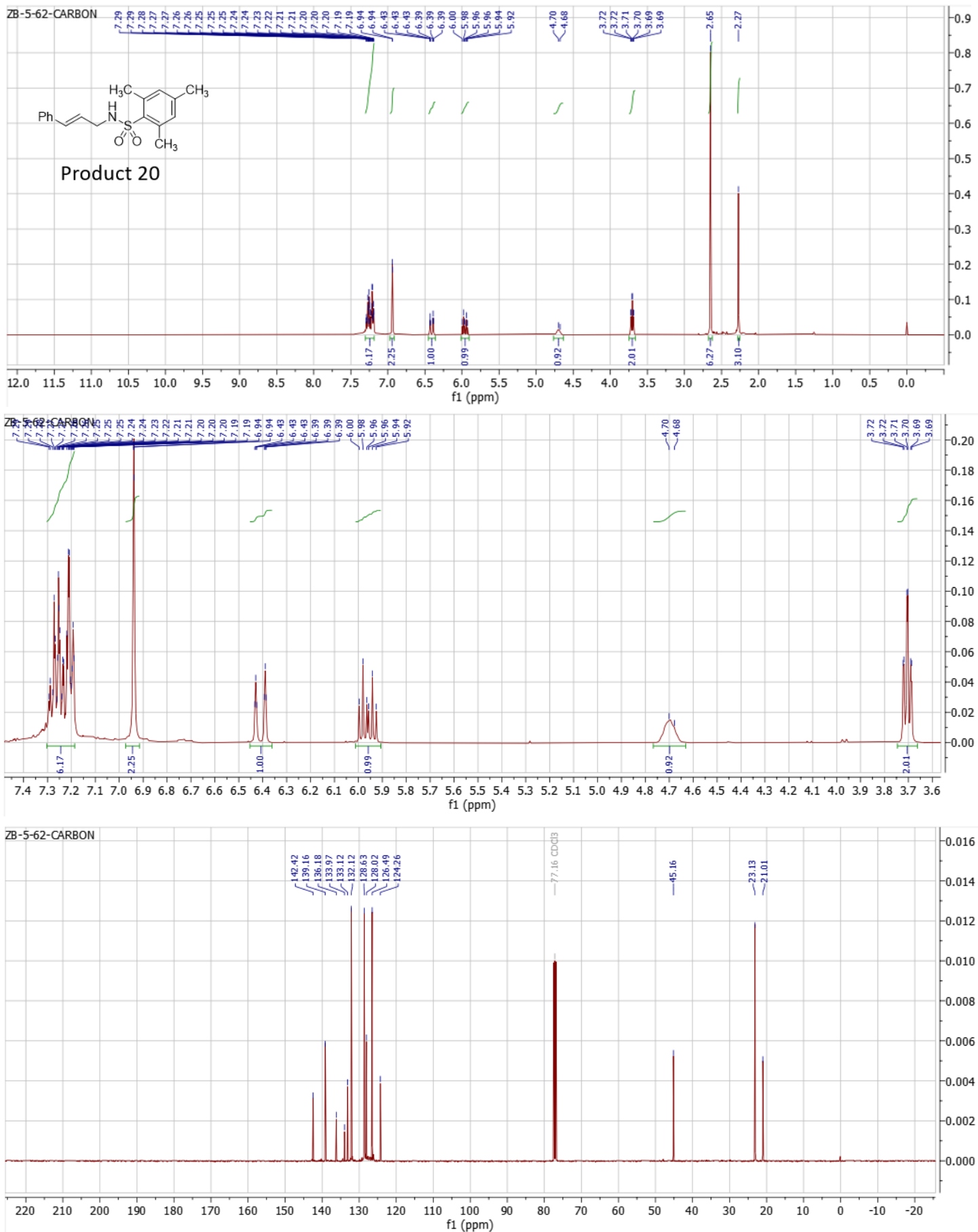


Figure S20. 400 MHz ¹H-NMR in CDCl₃ (full and zoom-in of aromatic region) and 101 MHz ¹³C{¹H} NMR in CDCl₃ of Product 20.

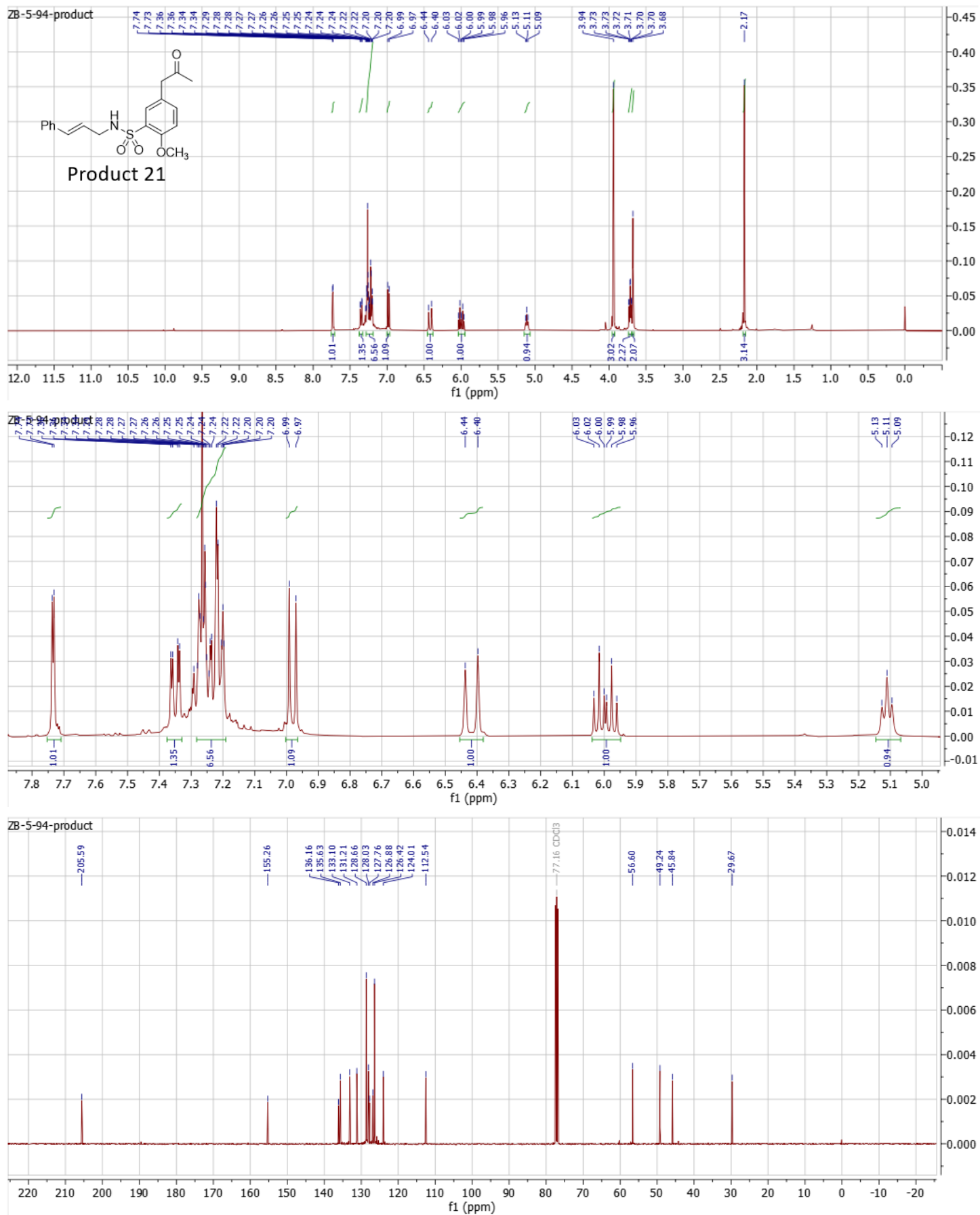


Figure S21. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 21.

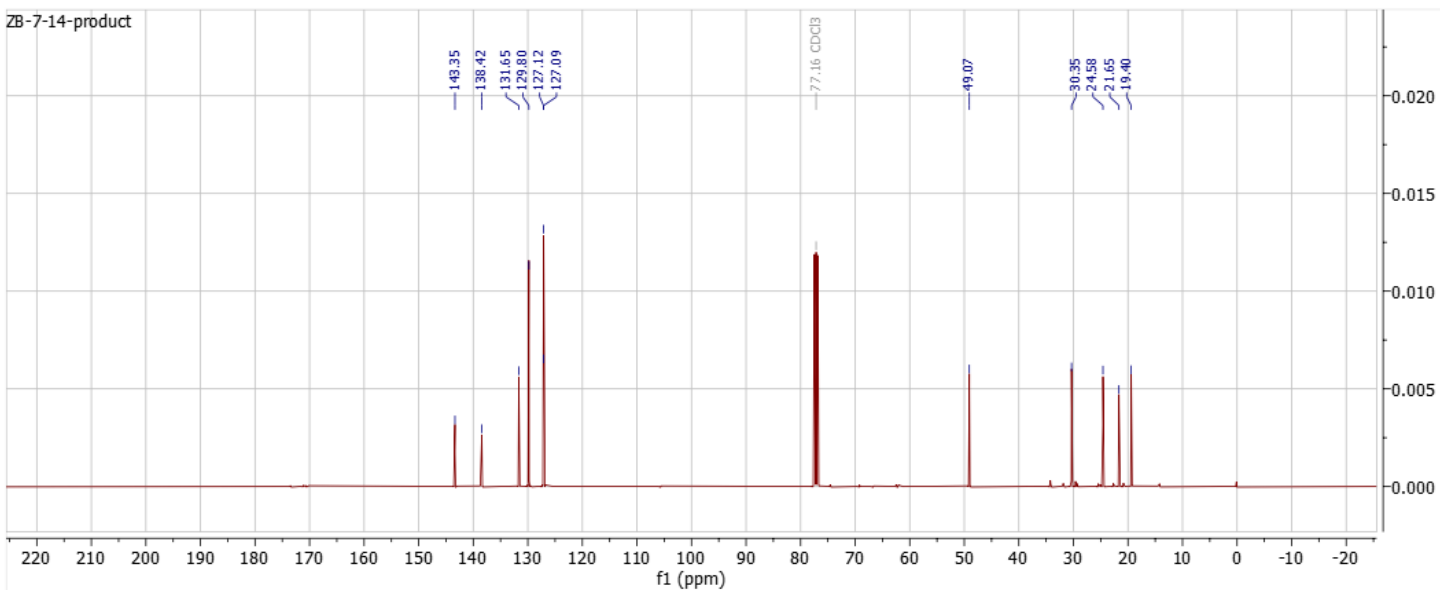
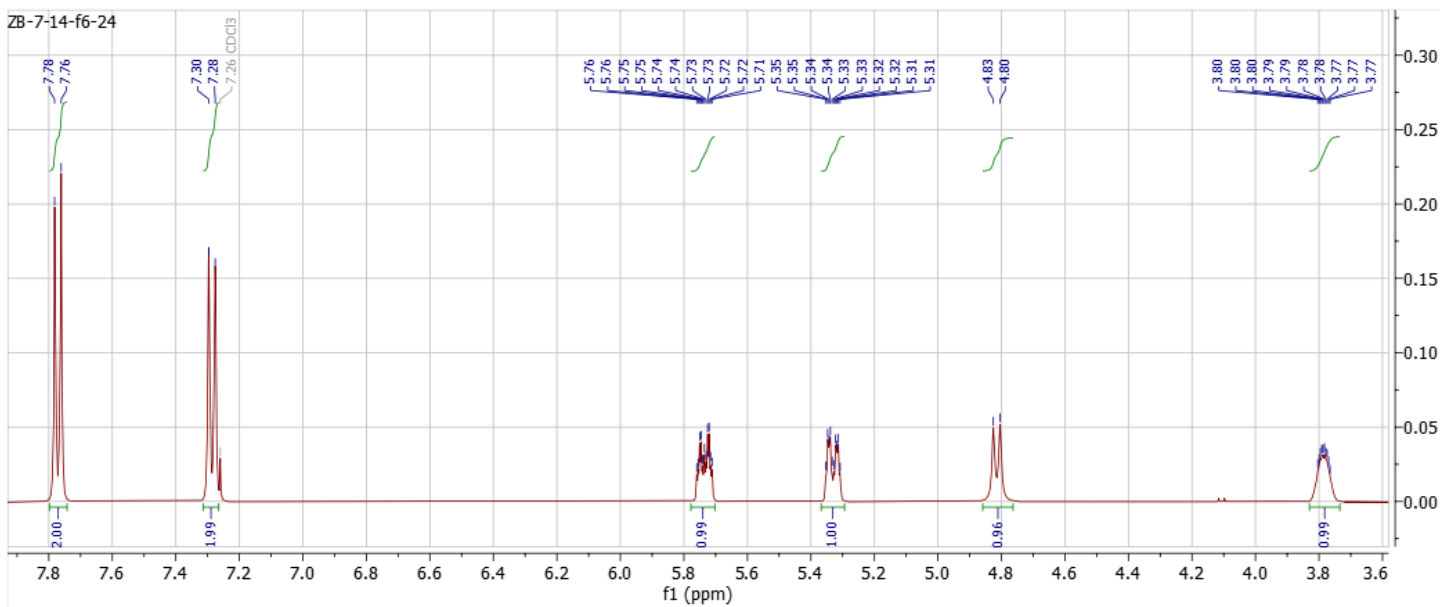
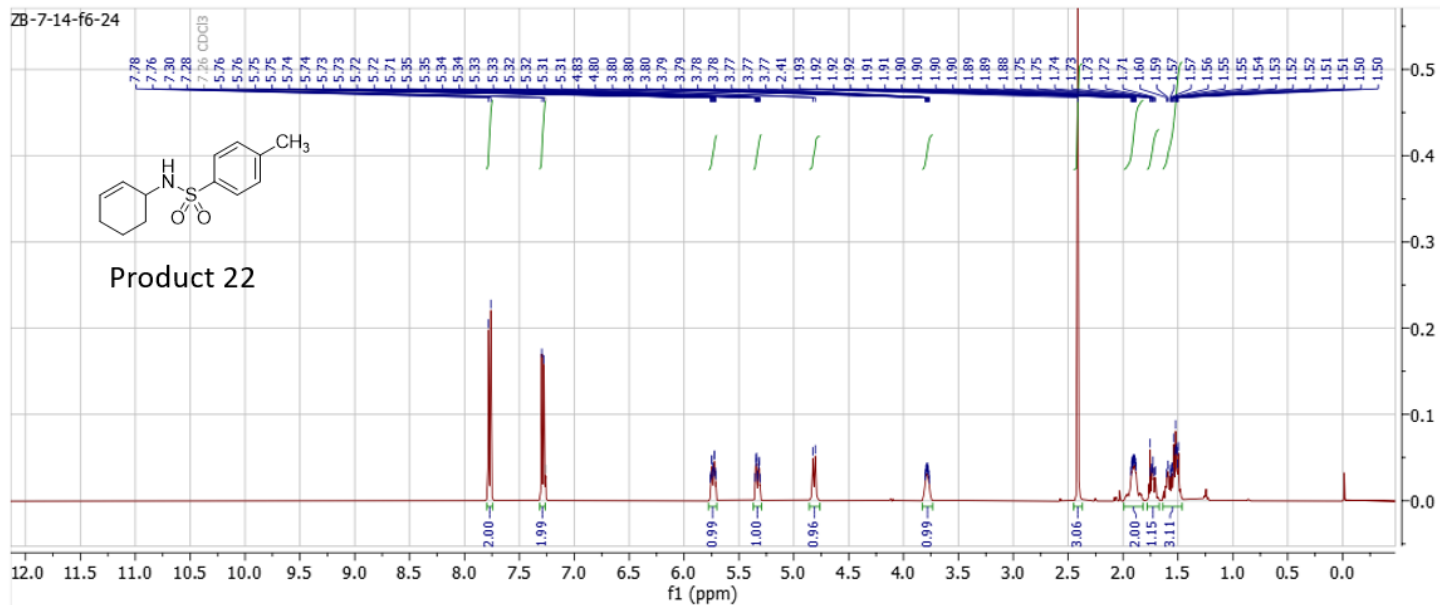


Figure S22. 400 MHz ¹H-NMR in CDCl₃ (full and zoom-in of aromatic region) and 101 MHz ¹³C{¹H} NMR in CDCl₃ of Product 22.

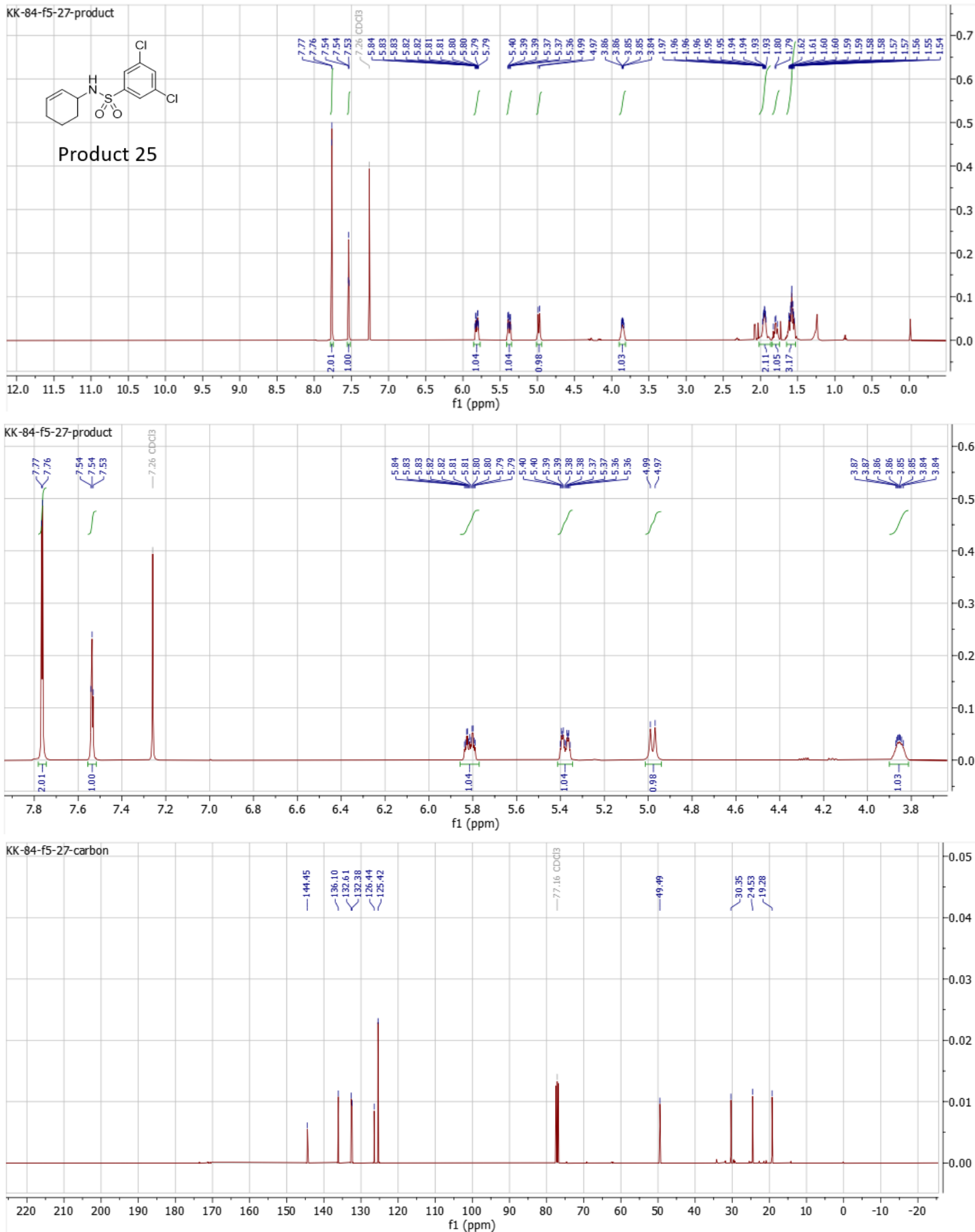


Figure S25. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product **25**.

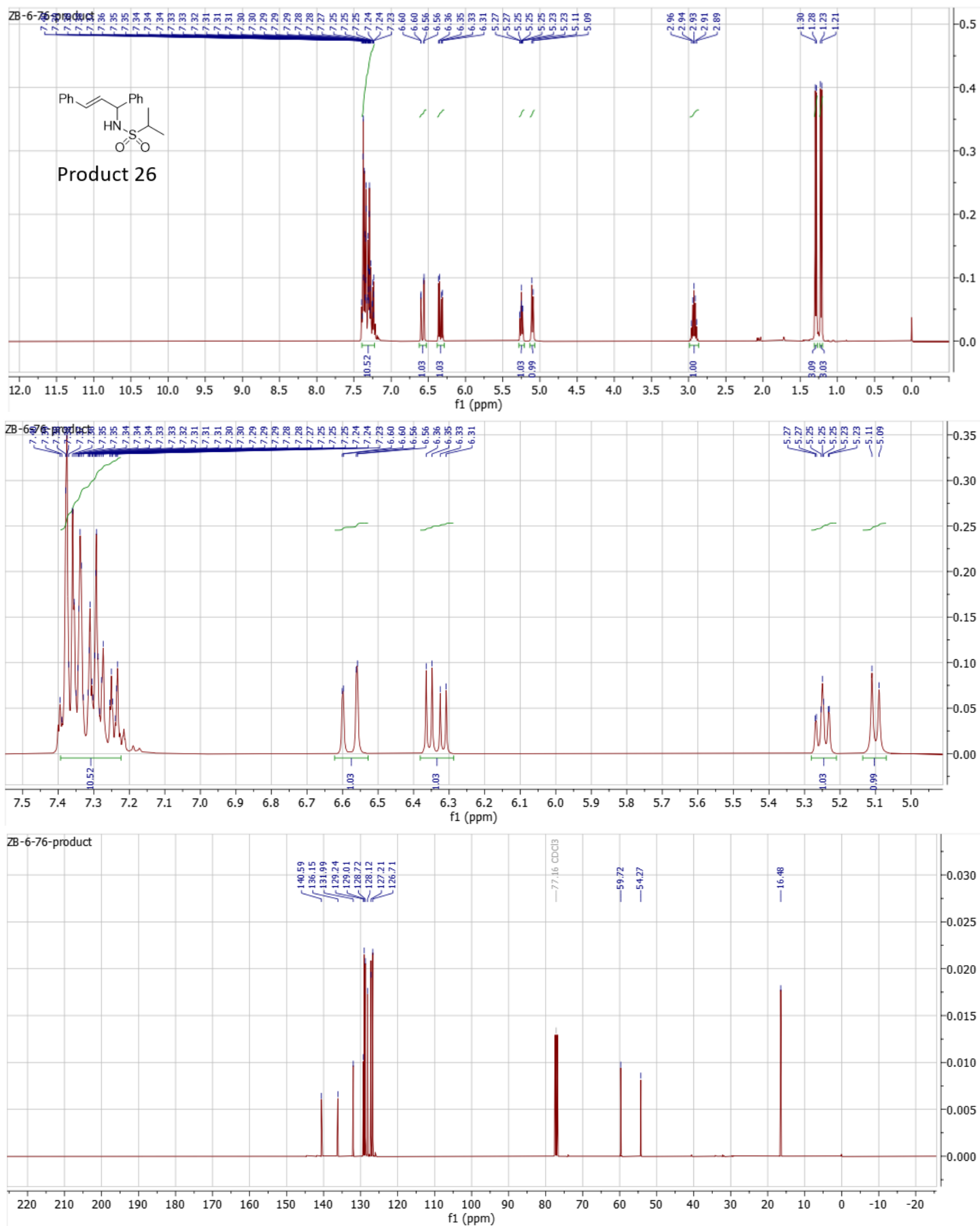


Figure S26. 400 MHz ¹H-NMR in CDCl₃ (full and zoom-in of aromatic region) and 101 MHz ¹³C{¹H} NMR in CDCl₃ of Product **26**.

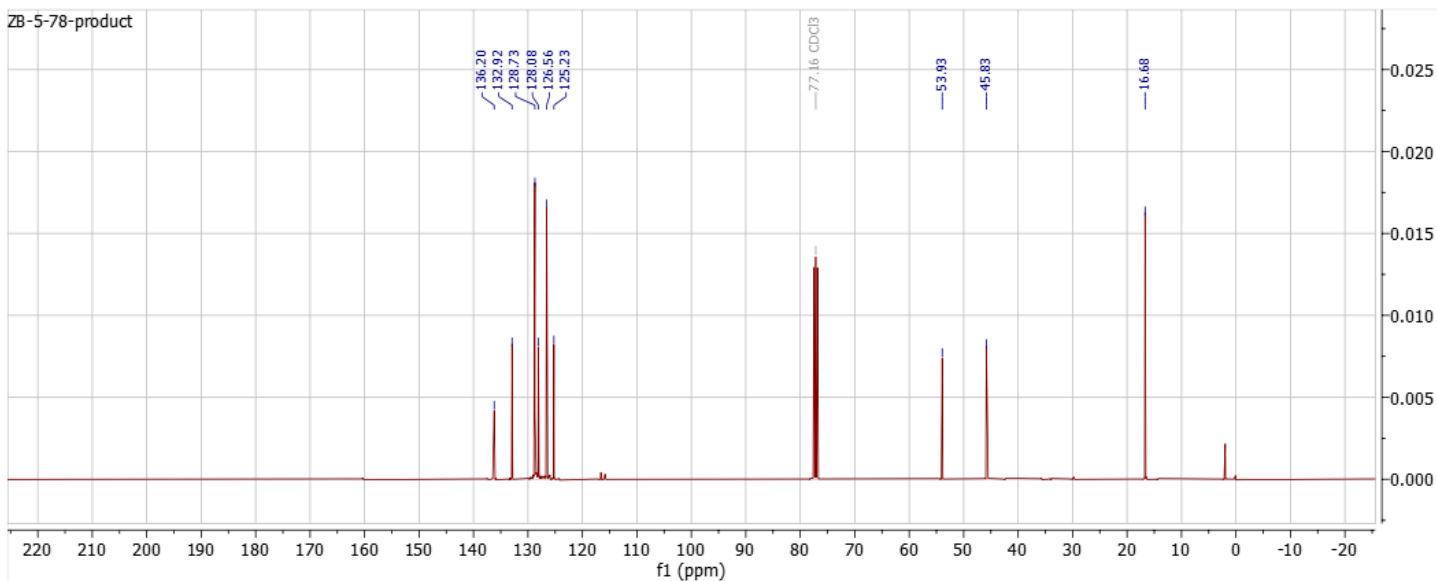
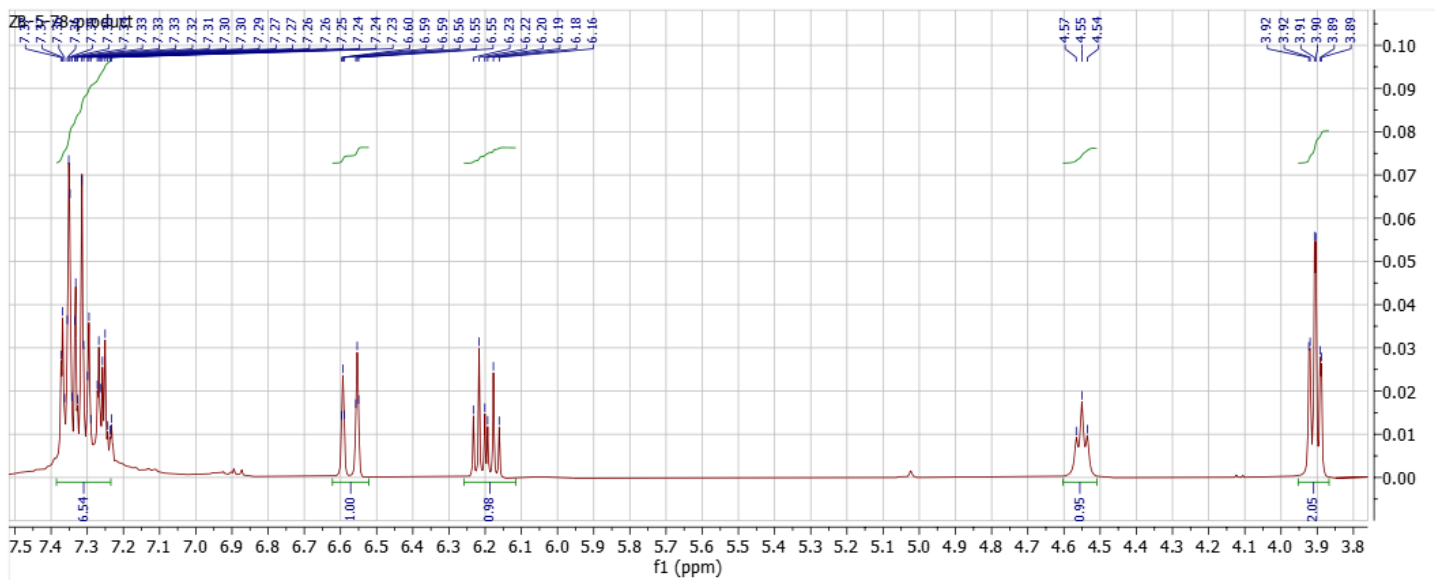
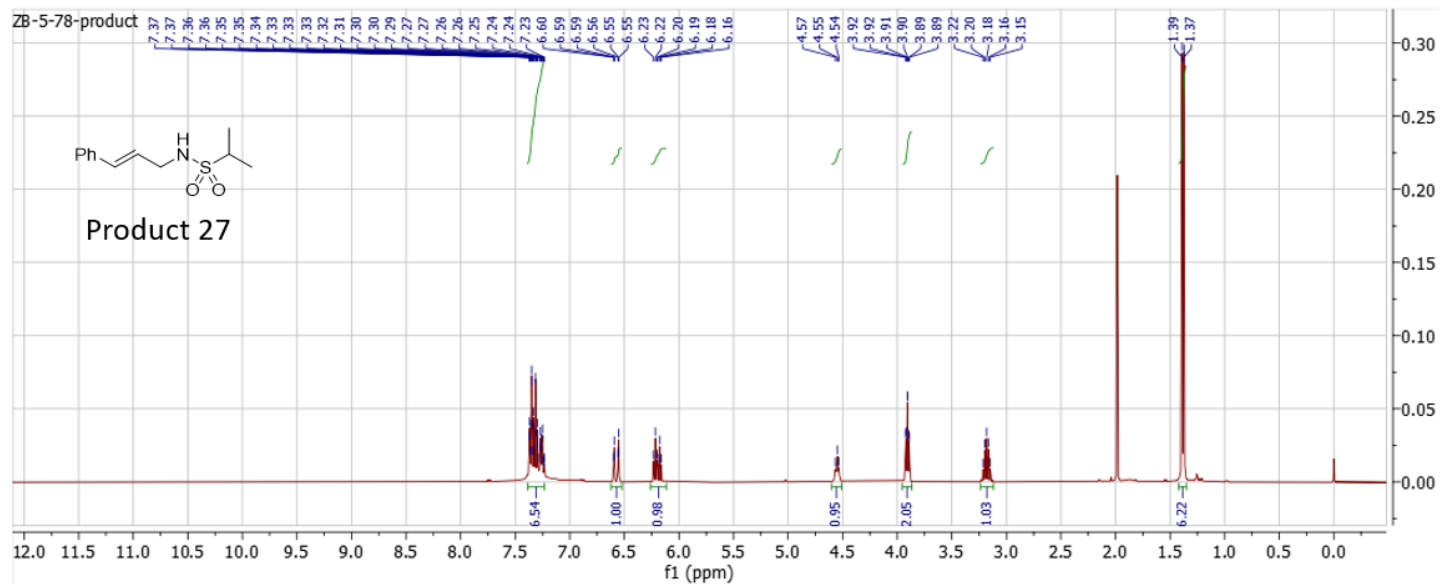


Figure S27. 400 MHz ^1H -NMR in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 27.

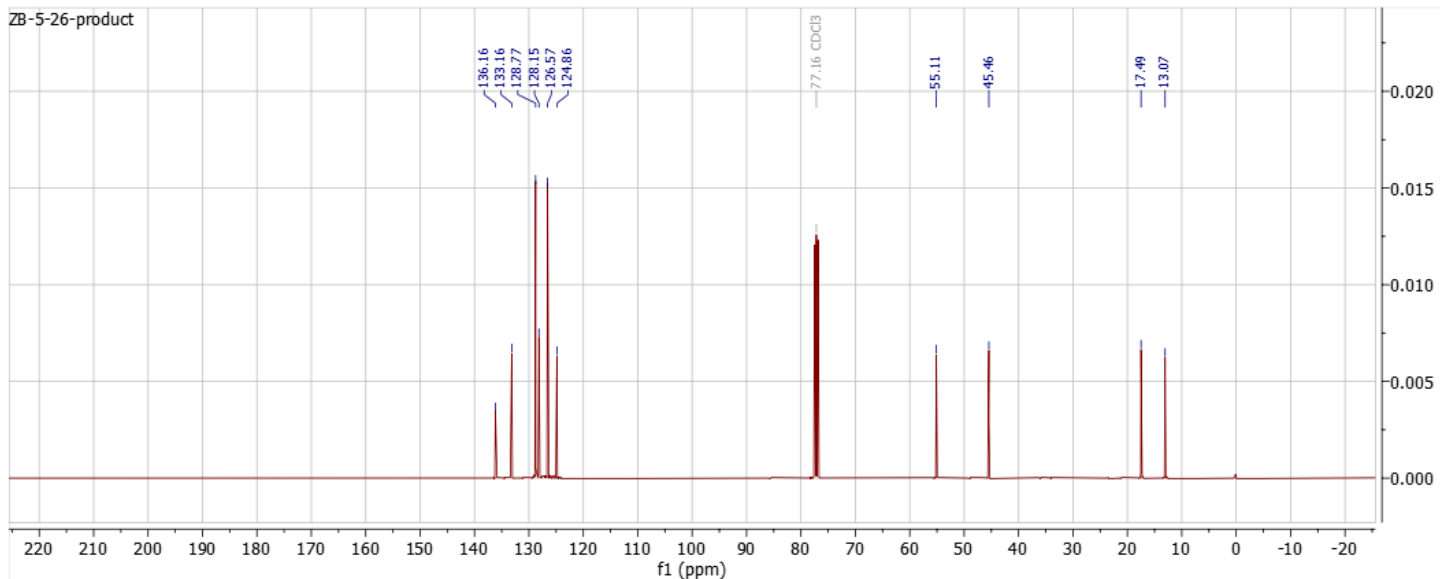
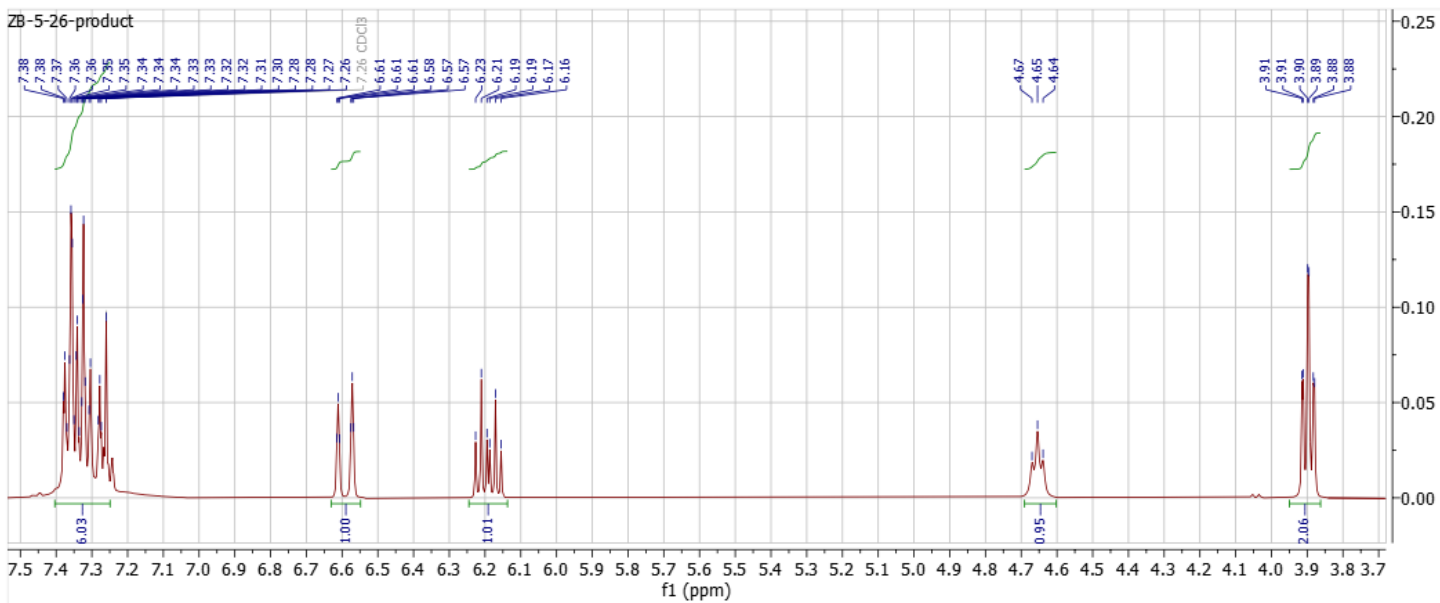
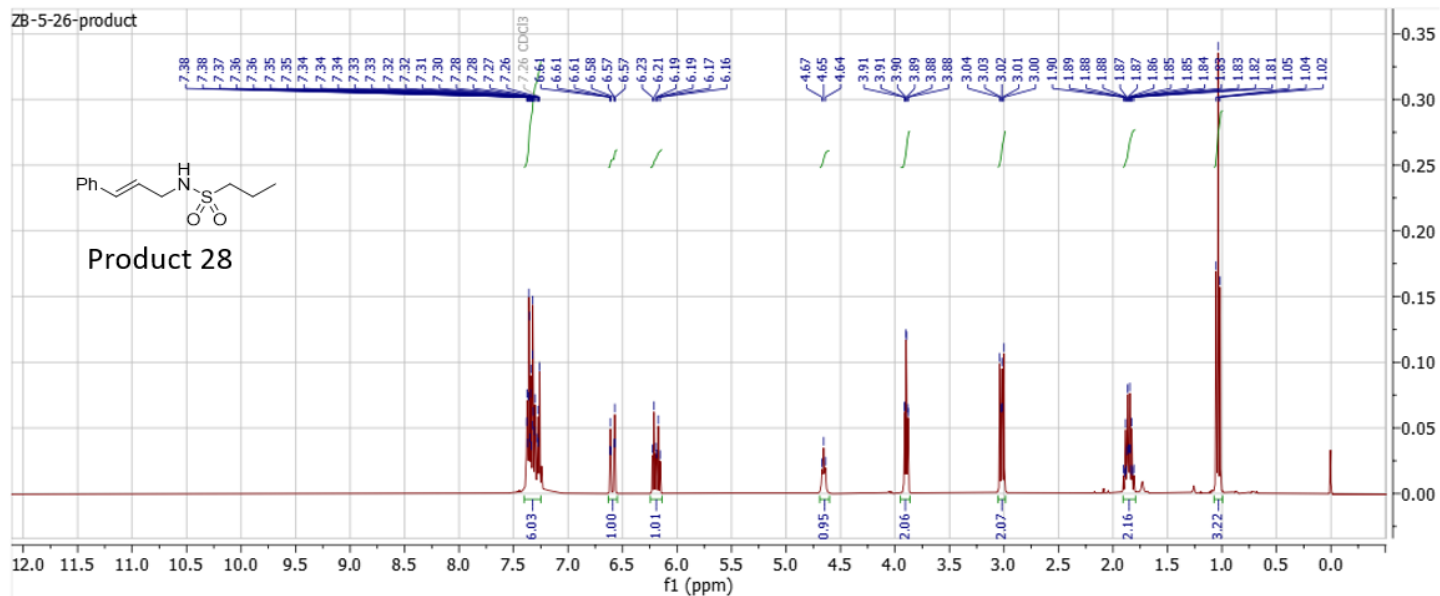


Figure S28. 400 MHz ¹H-NMR in CDCl₃ (full and zoom-in of aromatic region) and 101 MHz ¹³C{¹H} NMR in CDCl₃ of Product 28.

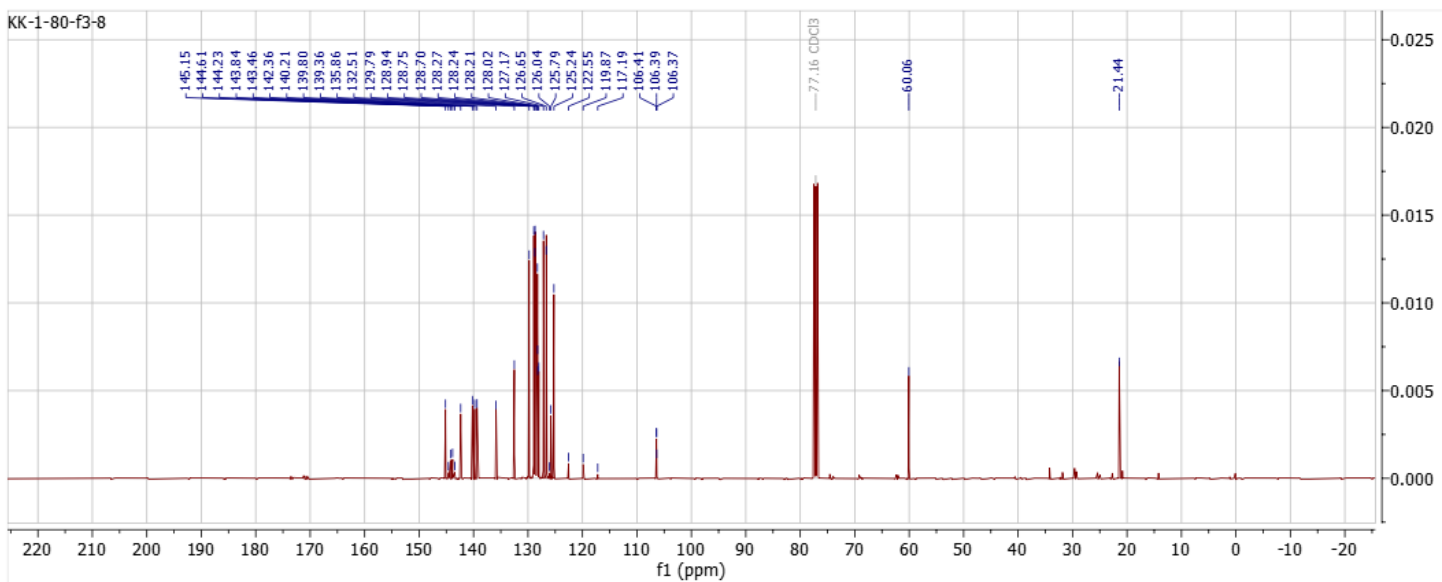
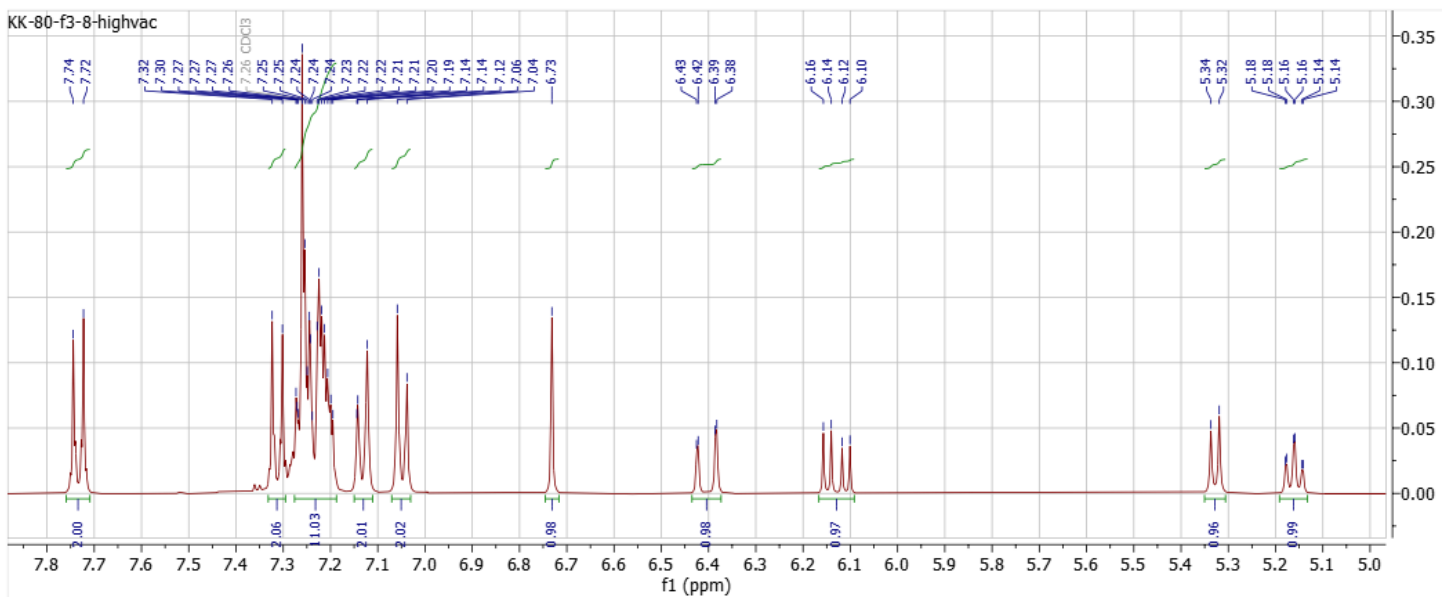
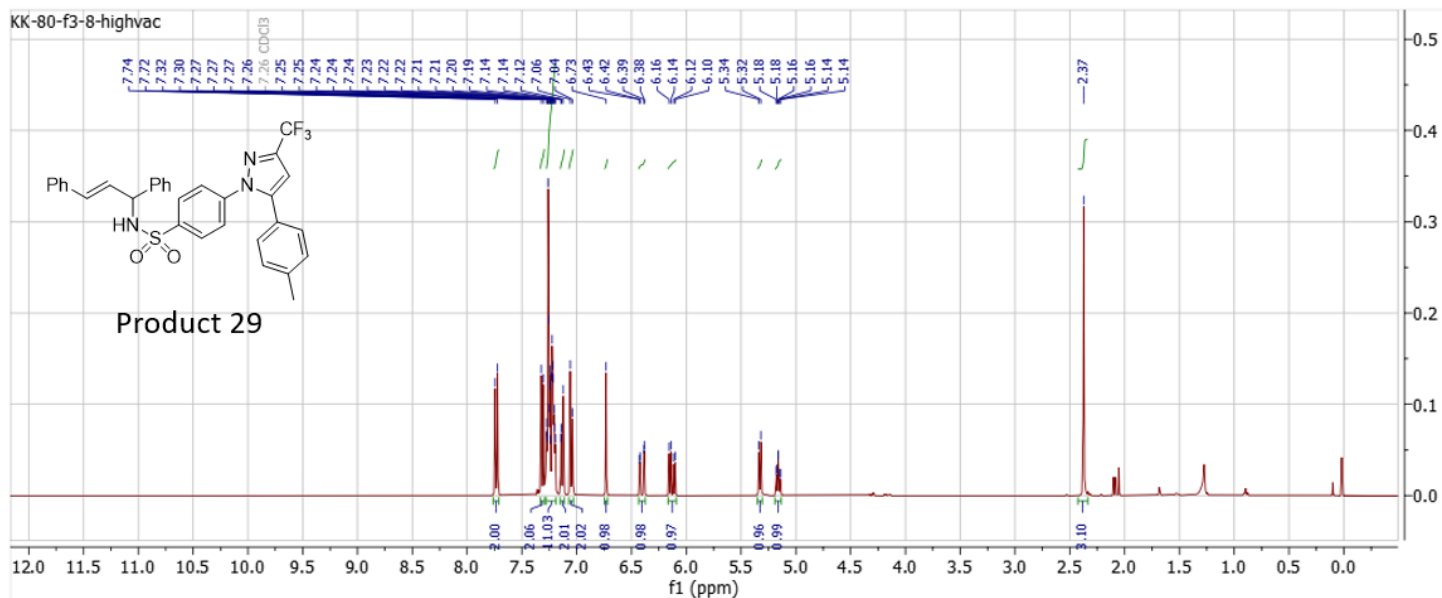


Figure S29. 400 MHz $^1\text{H-NMR}$ in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 29.

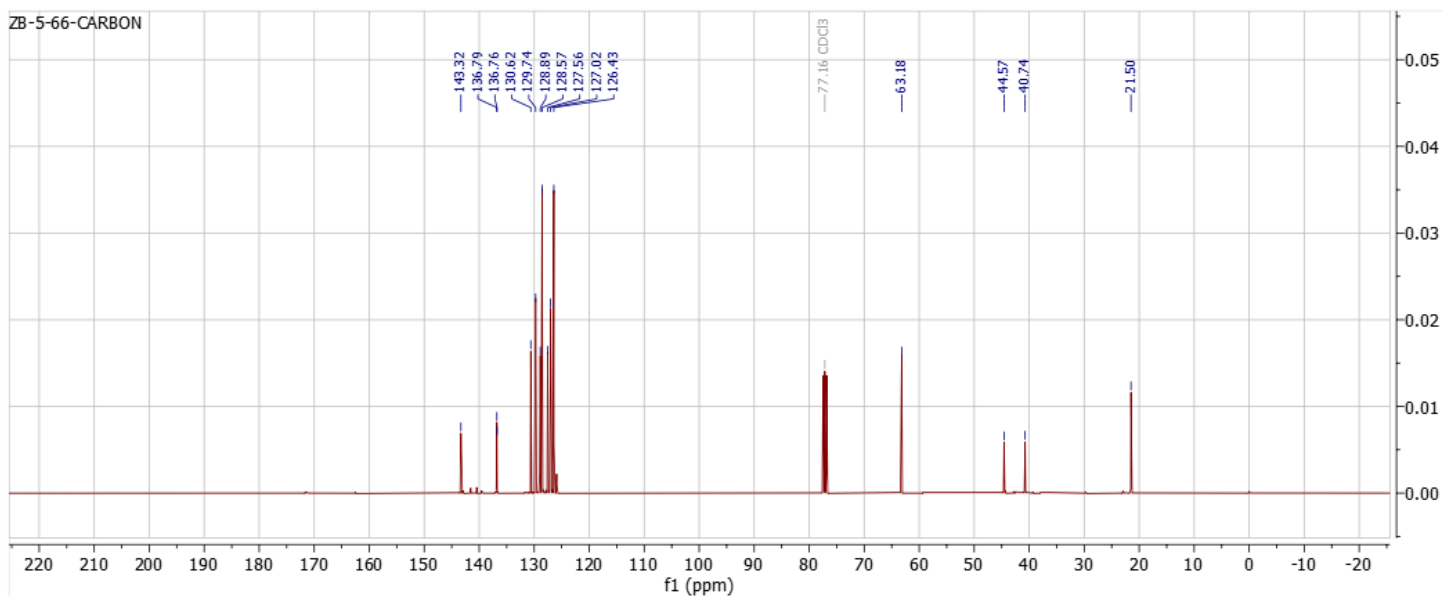
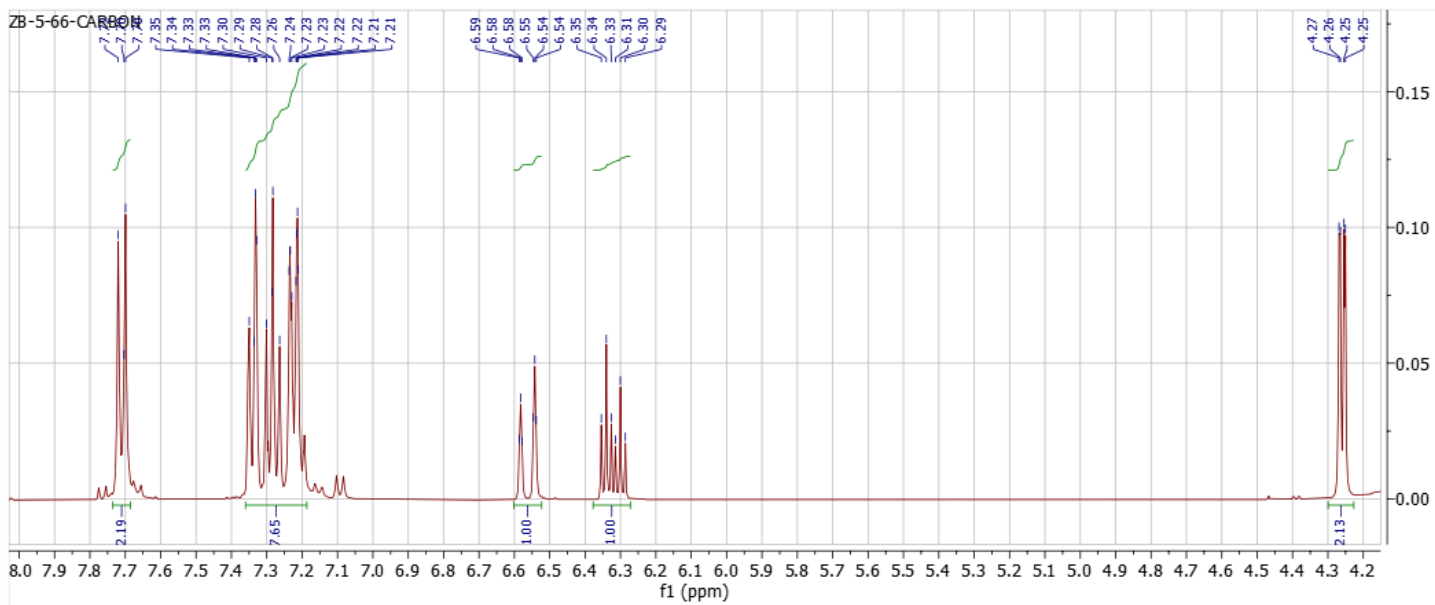
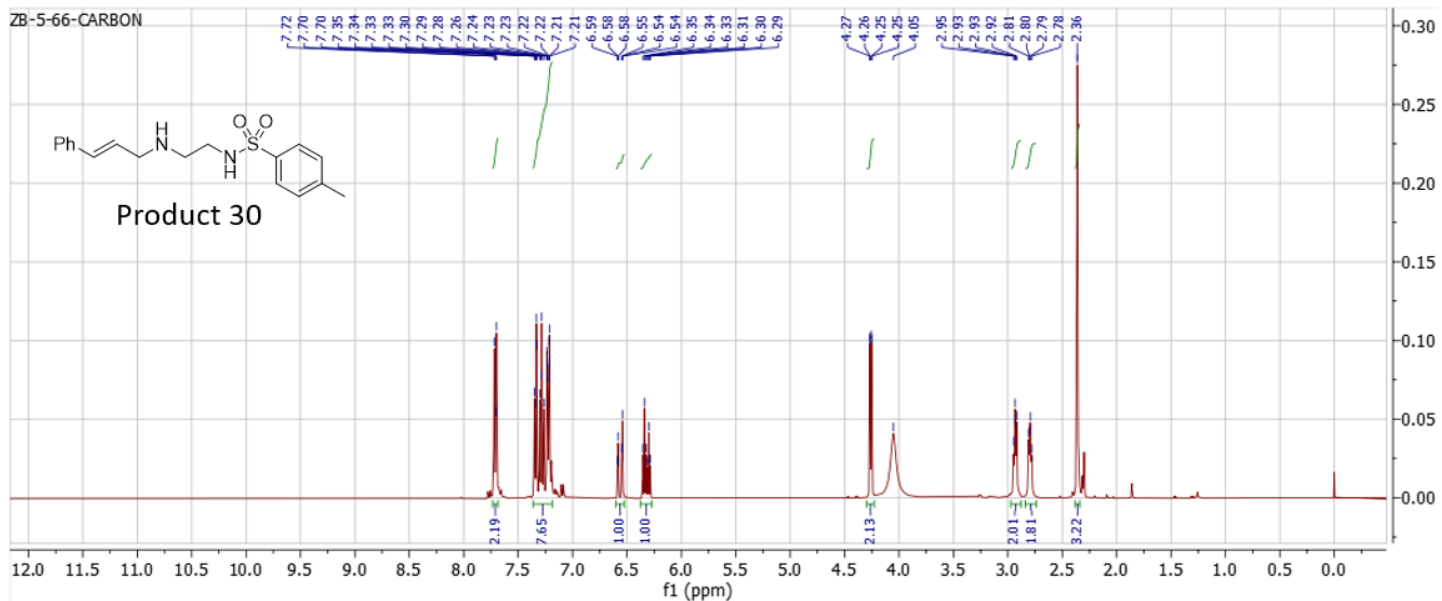


Figure S30. 400 MHz ^1H -NMR in CDCl_3 (full and zoom-in of aromatic region) and 101 MHz $^{13}\text{C}\{^1\text{H}\}$ NMR in CDCl_3 of Product 30.

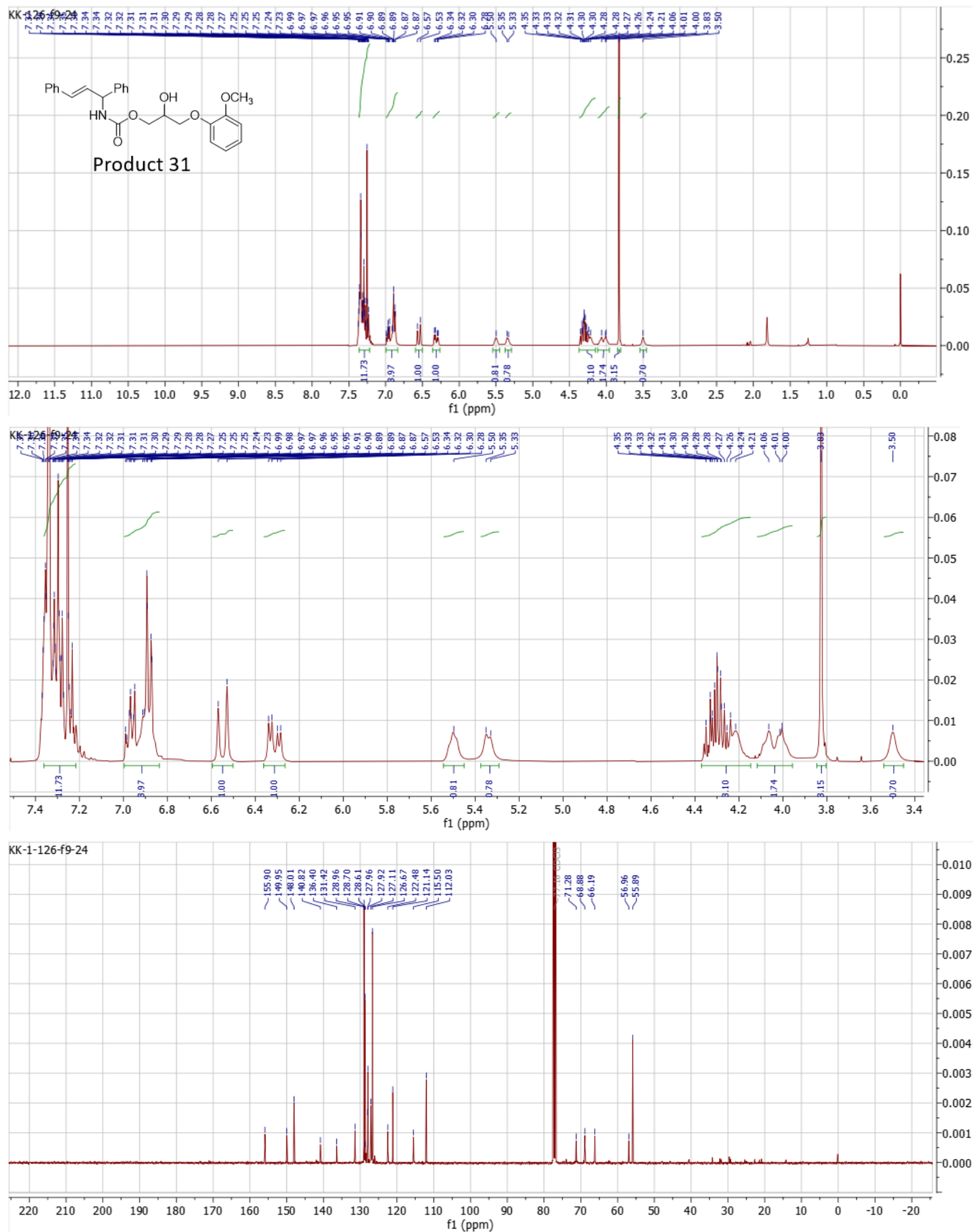


Table S2. Biological evaluation of compounds **3-31** (50 μ M) at 24-hour incubation time using CellTiter-Blue.

Compound	H293	A549	HDF
	DMEM media	DMEM media	DMEM media
3	102.8 \pm 6.7	77.7 \pm 9.3	85.4 \pm 4.0
4	76.8 \pm 3.3	94.8 \pm 11.5	82.8 \pm 2.0
5	75.6 \pm 5.4	96.1 \pm 5.8	82.0 \pm 2.0
6	85.9 \pm 2.4	95.1 \pm 1.4	77.2 \pm 0.1
7	44.9 \pm 10.8	48.2 \pm 8.4	41.1 \pm 0.5
8	47.2 \pm 1.5	37.2 \pm 6.9	49.4 \pm 5.8
9	63.5 \pm 0.2	65.9 \pm 6.7	52.3 \pm 8.3
10	76.1 \pm 4.4	78.1 \pm 4.2	70.0 \pm 1.2
11	75.2 \pm 3.5	71.5 \pm 12.5	68.3 \pm 1.7
12	64.3 \pm 1.3	77.4 \pm 15.4	55.6 \pm 10.2
13	69.0 \pm 4.9	55.3 \pm 3.3	52.4 \pm 9.4
14	89.7 \pm 10.7	74.0 \pm 15.6	78.9 \pm 1.3
15	88.9 \pm 2.8	61.6 \pm 2.0	56.8 \pm 8.5
16	87.6 \pm 5.7	83.9 \pm 5.3	81.1 \pm 0.5
17	91.3 \pm 3.5	89.6 \pm 3.4	83.9 \pm 12.5
18	91.5 \pm 4.4	64.1 \pm 3.7	69.4 \pm 2.4
19	97.2 \pm 9.5	65.4 \pm 16.0	71.9 \pm 13.4
20	58.8 \pm 1.2	65.5 \pm 14.2	48.8 \pm 0.1
21	94.4 \pm 9.0	78.0 \pm 2.3	79.2 \pm 1.6
22	89.3 \pm 1.5	90.2 \pm 6.3	76.0 \pm 10.5
23	64.4 \pm 0.9	54.7 \pm 15.1	51.9 \pm 0.9
24	94.1 \pm 6.5	85.0 \pm 19.4	72.5 \pm 0.3
25	79.3 \pm 3.8	66.9 \pm 5.1	62.2 \pm 0.9
26	105.8 \pm 4.2	86.2 \pm 6.9	81.4 \pm 5.8
27	99.9 \pm 0.9	69.1 \pm 8.5	78.1 \pm 1.2
28	102.2 \pm 1.5	77.8 \pm 19.2	85.7 \pm 6.7
29	93.7 \pm 3.5	82.6 \pm 4.3	70.3 \pm 2.4
30	96.0 \pm 2.1	71.5 \pm 5.7	83.8 \pm 3.3
31	88.0 \pm 4.0	71.3 \pm 5.6	61.4 \pm 12.1
DMSO	100.0 \pm 2.3	100.0 \pm 5.0	100.0 \pm 0.5
+C	59.0 \pm 2.8	48.5 \pm 6.0	55.6 \pm 2.6

Values displayed are percent of DMSO control (POC). All values (%) against cell lines were obtained as an average of duplicate measurements (standard deviations also displayed calculated at 85% CI by Microsoft Excel) via the CellTiter-Blue (Promega) assay at 50 μ M (24 h) in the described cell media. Lower values of POC indicate stronger hits. POC values below 25% of inhibition based upon positive control are highlighted in red. A combination of 1.5 μ M rotenone, a known OXPHOS inhibitor, and 10 mM 2-DG (a known glycolysis inhibitor) is used as positive control to determine maximum inhibition. DMSO serves as the negative control.

Table S3. Biological evaluation of compounds **3-31** (25 μ M) at 2-hour incubation time using CellTiter-Glo.

Compound	H293	H293
	Minimal media plus glucose	Minimal media plus glutamine
3	87.2 \pm 1.8	28.6 \pm 2.3
4	84.9 \pm 3.8	17.1 \pm 0.9
5	85.5 \pm 5.8	18.6 \pm 0.1
6	93.7 \pm 2.8	31.1 \pm 1.8
7	69.3 \pm 8.3	13.6 \pm 0.1
8	83.5 \pm 3.3	18.5 \pm 1.1
9	78.7 \pm 0.1	20.0 \pm 0.3
10	95.3 \pm 5.2	19.8 \pm 0.3
11	97.9 \pm 1.6	24.3 \pm 0.1
12	84.9 \pm 0.8	18.2 \pm 1.5
13	87.2 \pm 12.7	19.8 \pm 1.5
14	77.4 \pm 6.1	18.5 \pm 0.2
15	82.3 \pm 2.2	33.6 \pm 0.5
16	84.0 \pm 1.2	35.6 \pm 0.7
17	76.1 \pm 1.2	17.0 \pm 1.2
18	92.1 \pm 4.0	52.9 \pm 15.2
19	93.2 \pm 0.3	33.0 \pm 4.7
20	66.7 \pm 5.2	16.8 \pm 0.2
21	96.9 \pm 0.3	86.2 \pm 1.2
22	93.9 \pm 2.6	91.0 \pm 11.1
23	75.6 \pm 4.4	55.4 \pm 21.4
24	92.0 \pm 5.9	76.8 \pm 1.3
25	57.7 \pm 14.4	17.7 \pm 4.2
26	94.4 \pm 0.4	85.7 \pm 3.2
27	96.7 \pm 7.7	94.7 \pm 6.7
28	96.2 \pm 3.3	91.3 \pm 0.9
29	89.7 \pm 2.6	75.8 \pm 26.7
30	98.0 \pm 4.0	100.3 \pm 1.7
31	73.1 \pm 2.2	51.7 \pm 15.2
DMSO	100.0 \pm 1.8	100.0 \pm 6.1
Rotenone	80.6 \pm 3.3	16.4 \pm 1.9

Values displayed are percent of DMSO control (POC). All values (%) against cell lines were obtained as an average of duplicate measurements (standard deviations also displayed calculated at 85% CI by Microsoft Excel) via the CellTiter-Glo (Promega) assay at 25 μ M (2 h) in the described cell media. Lower values of POC indicate stronger hits. Rotenone, a known OXPHOS inhibitor, is used as positive control to determine maximum inhibition in "minimal media + glutamine". POC values below 25% of inhibition based upon positive control are highlighted in red. DMSO serves as the negative control.

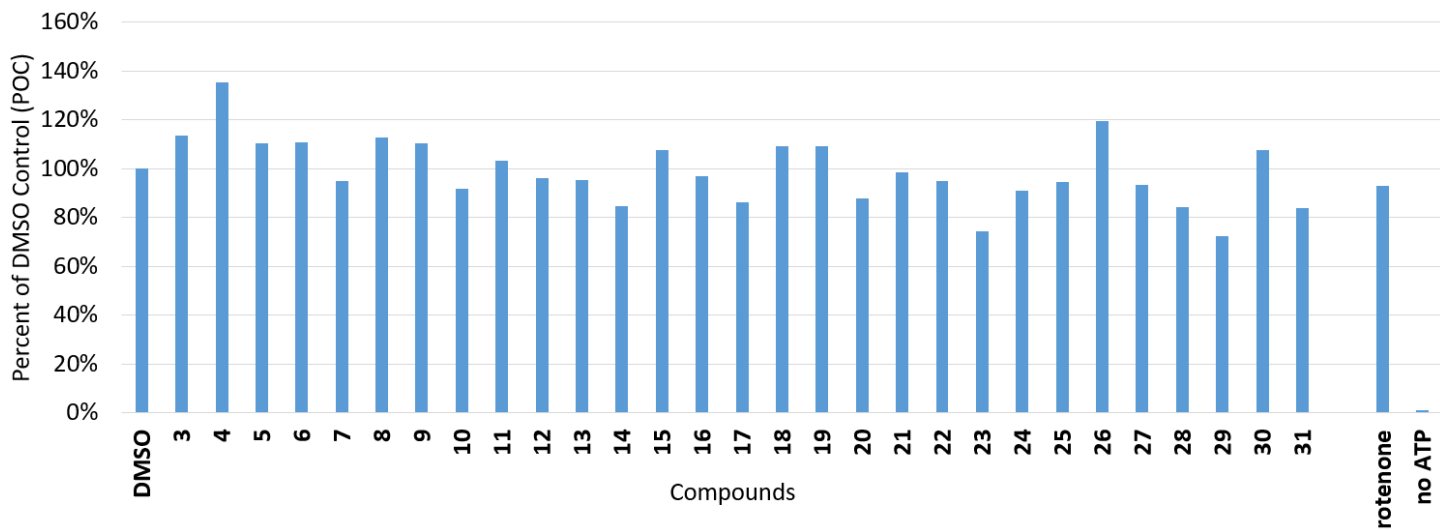


Figure S32. Luciferase inhibition assay using compounds **3-31** (50 μ M, 10 min exposure; CTG). Exogenous ATP was added to wells containing the compounds (no cells were used). Values are shown as percent of DMSO control (POC).