

Development of a Concise Synthesis of Ouabagenin and Hydroxylated Corticosteroid Analogs

Hans Renata,[†] Qianghui Zhou,[†] Georg Dünstl,[‡] Jakob Felding,[‡] Rohan R. Merchant, Chien-Hung Yeh,
and Phil S. Baran*

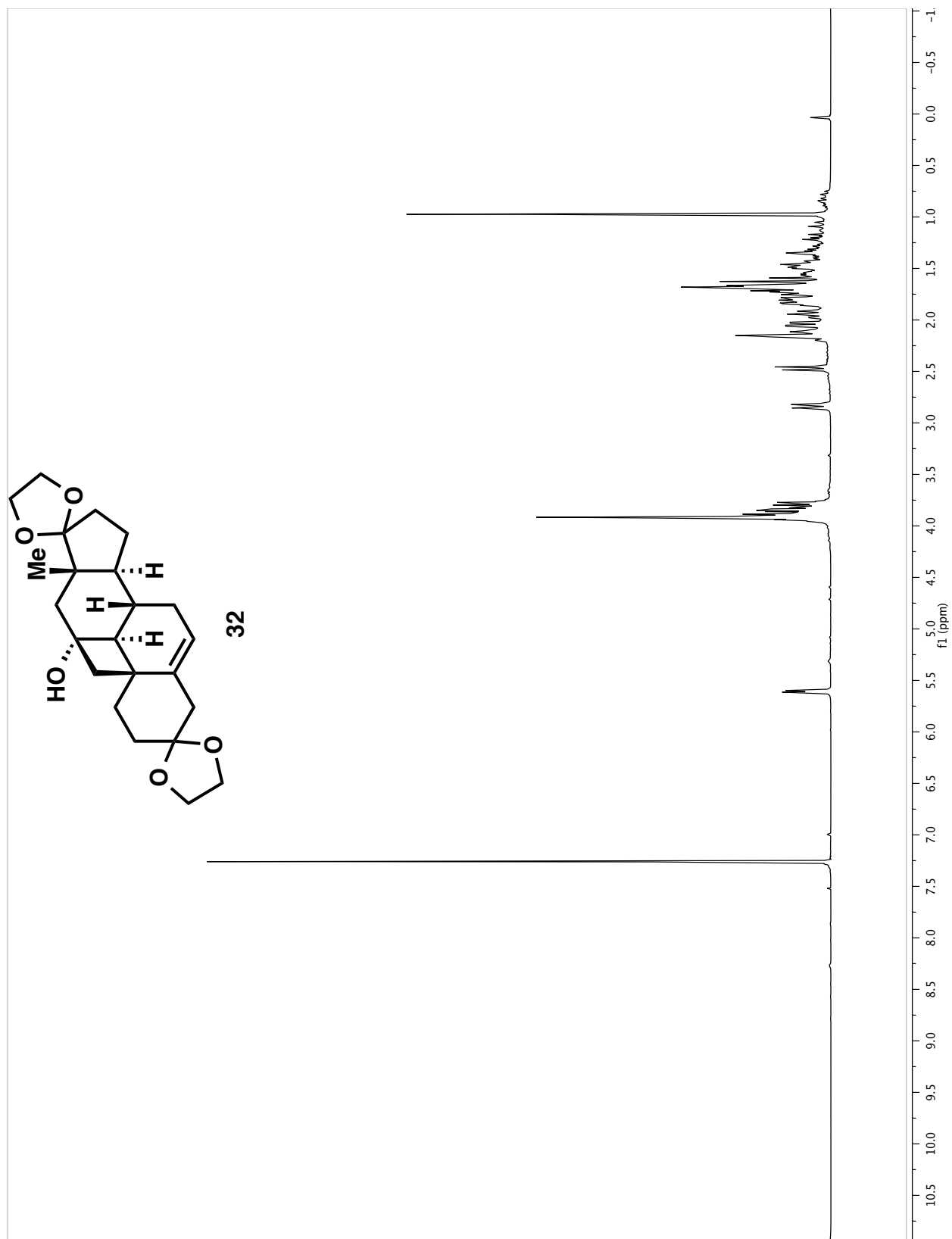
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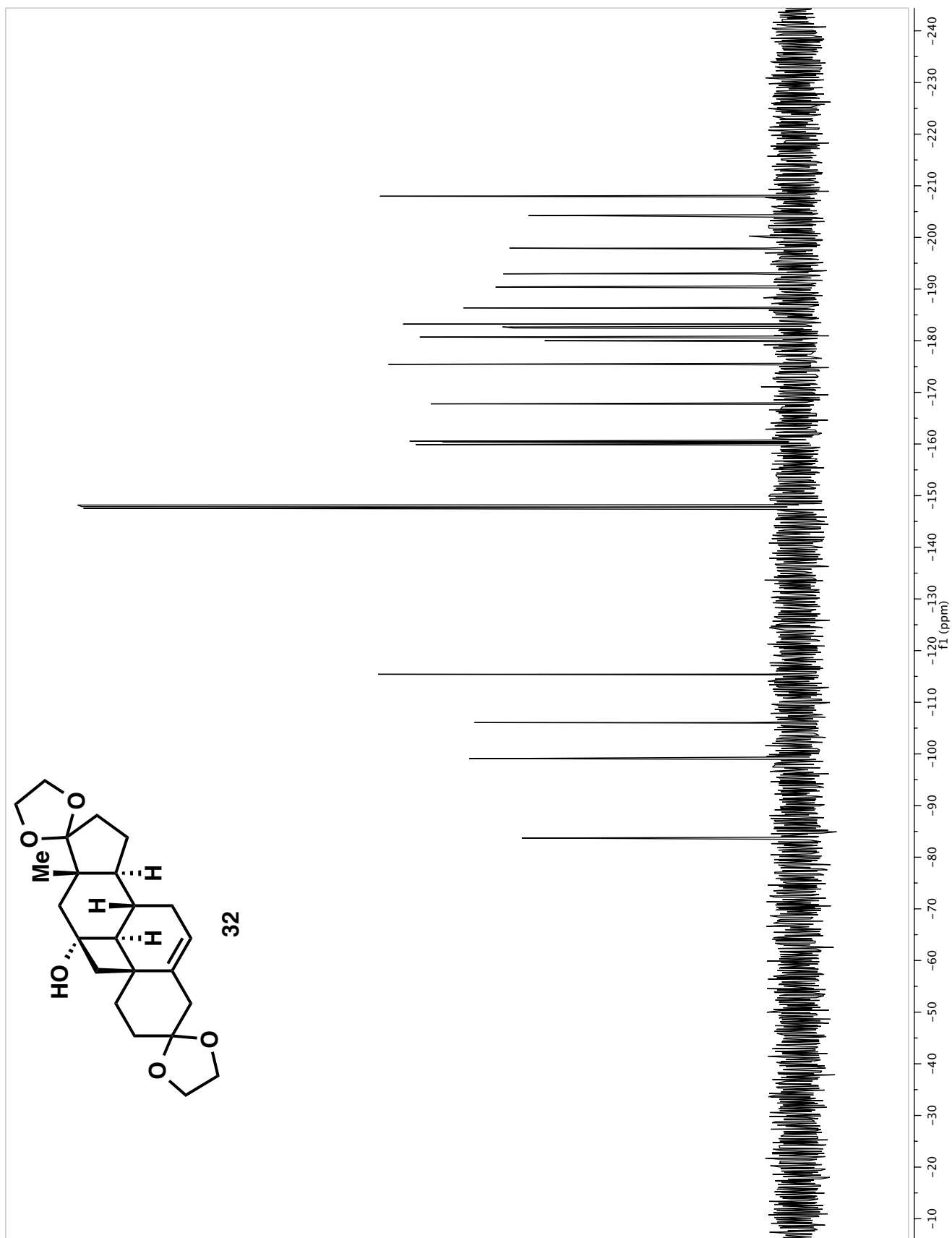
SUPPLEMENTARY MATERIAL – PART 2 – SPECTRA

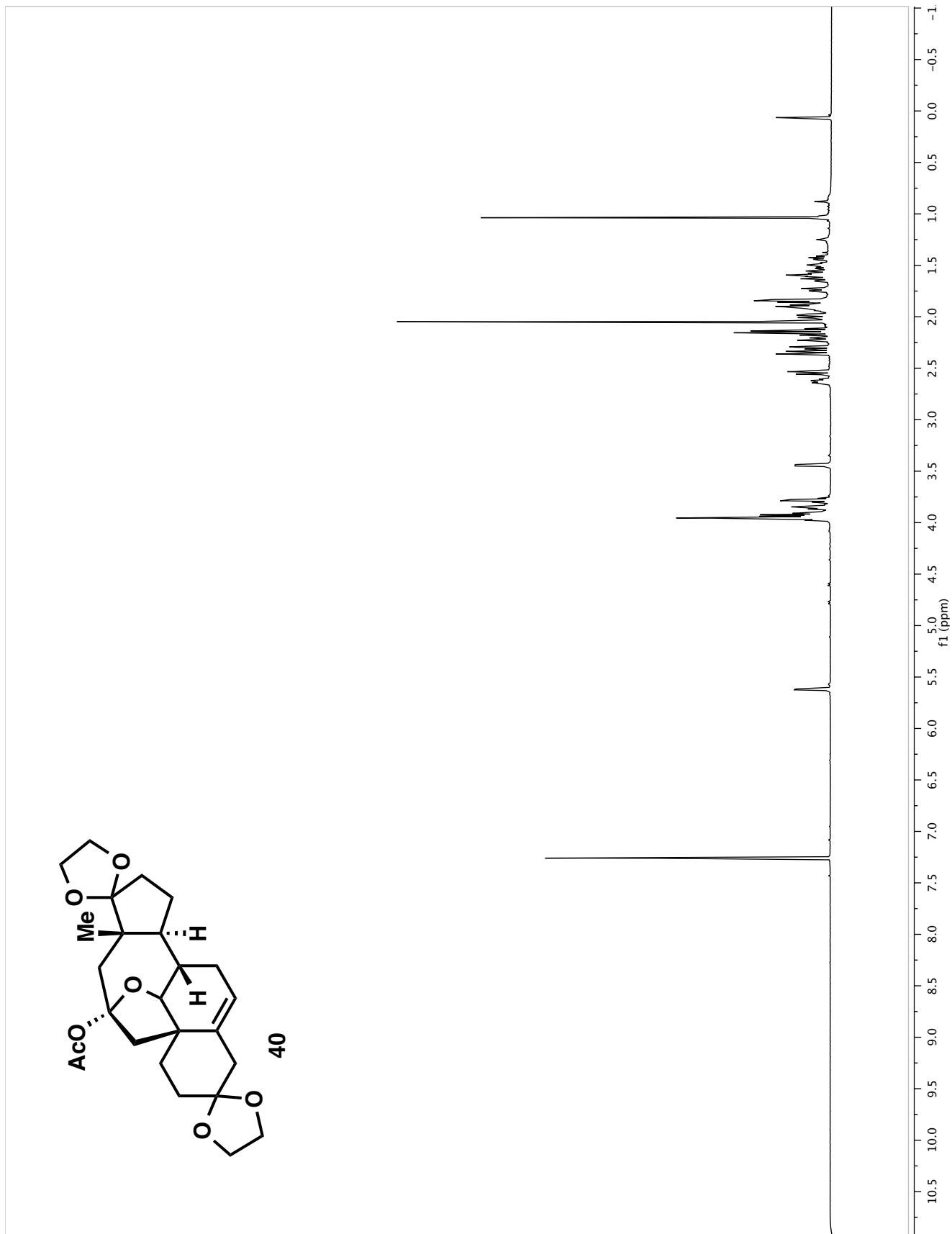
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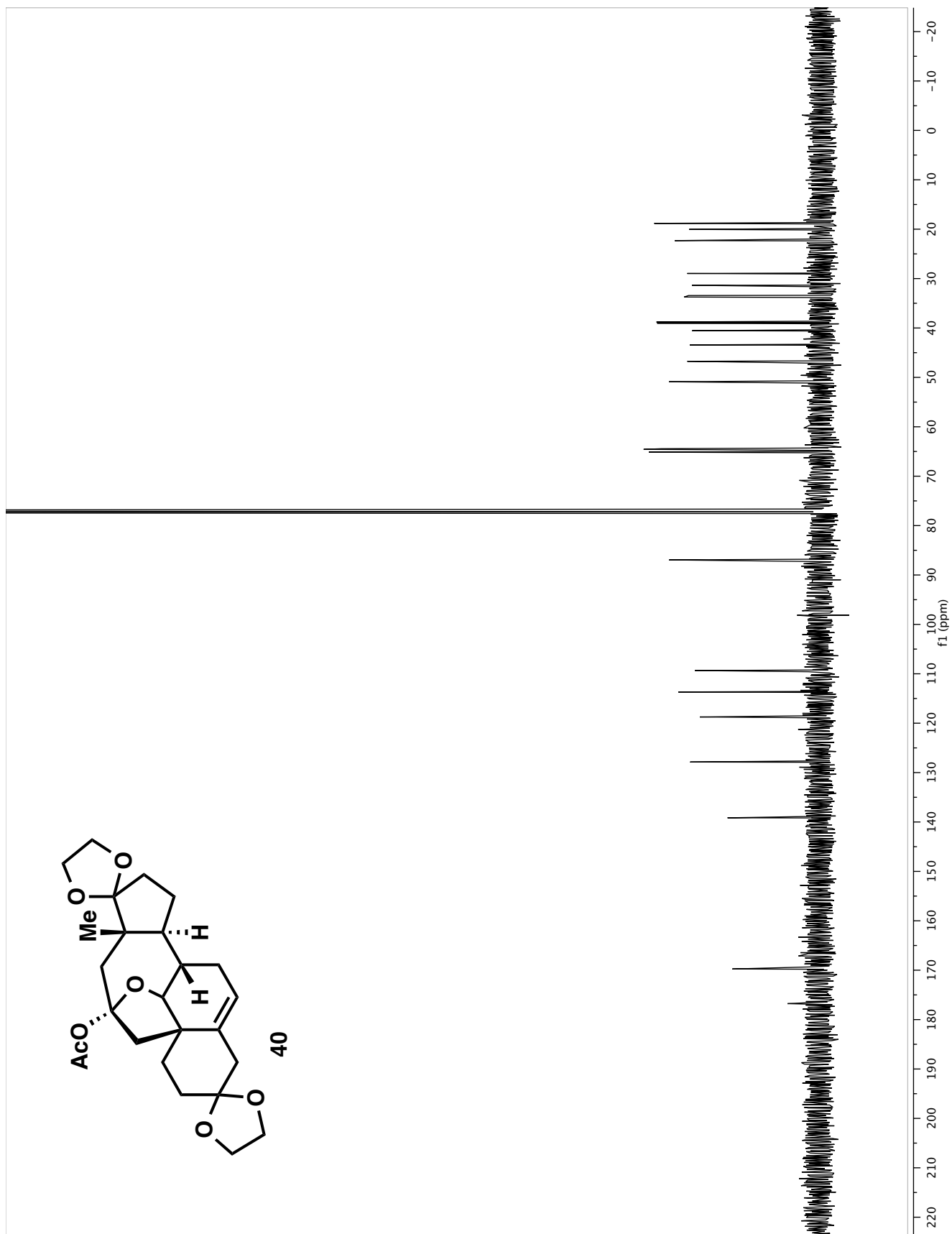
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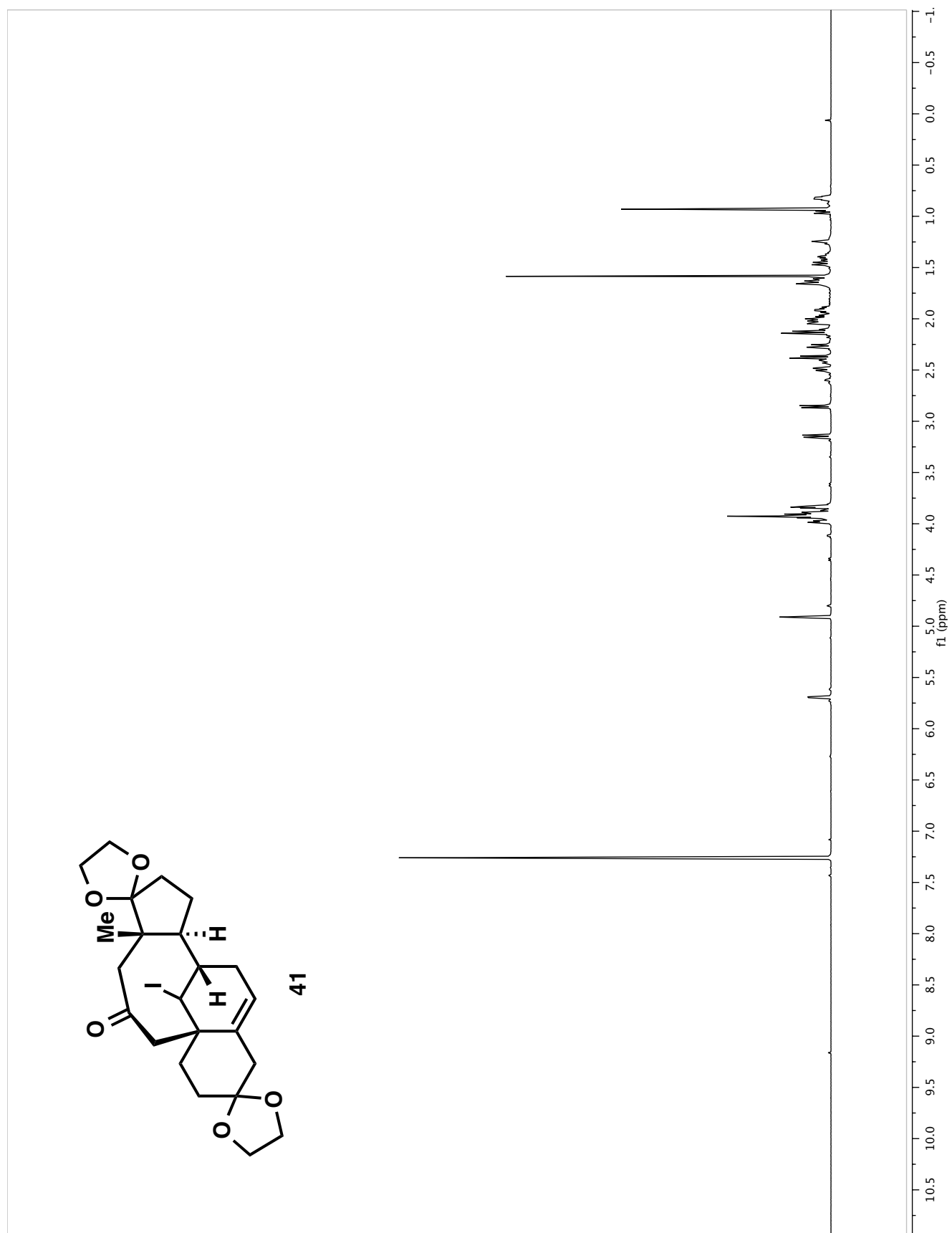
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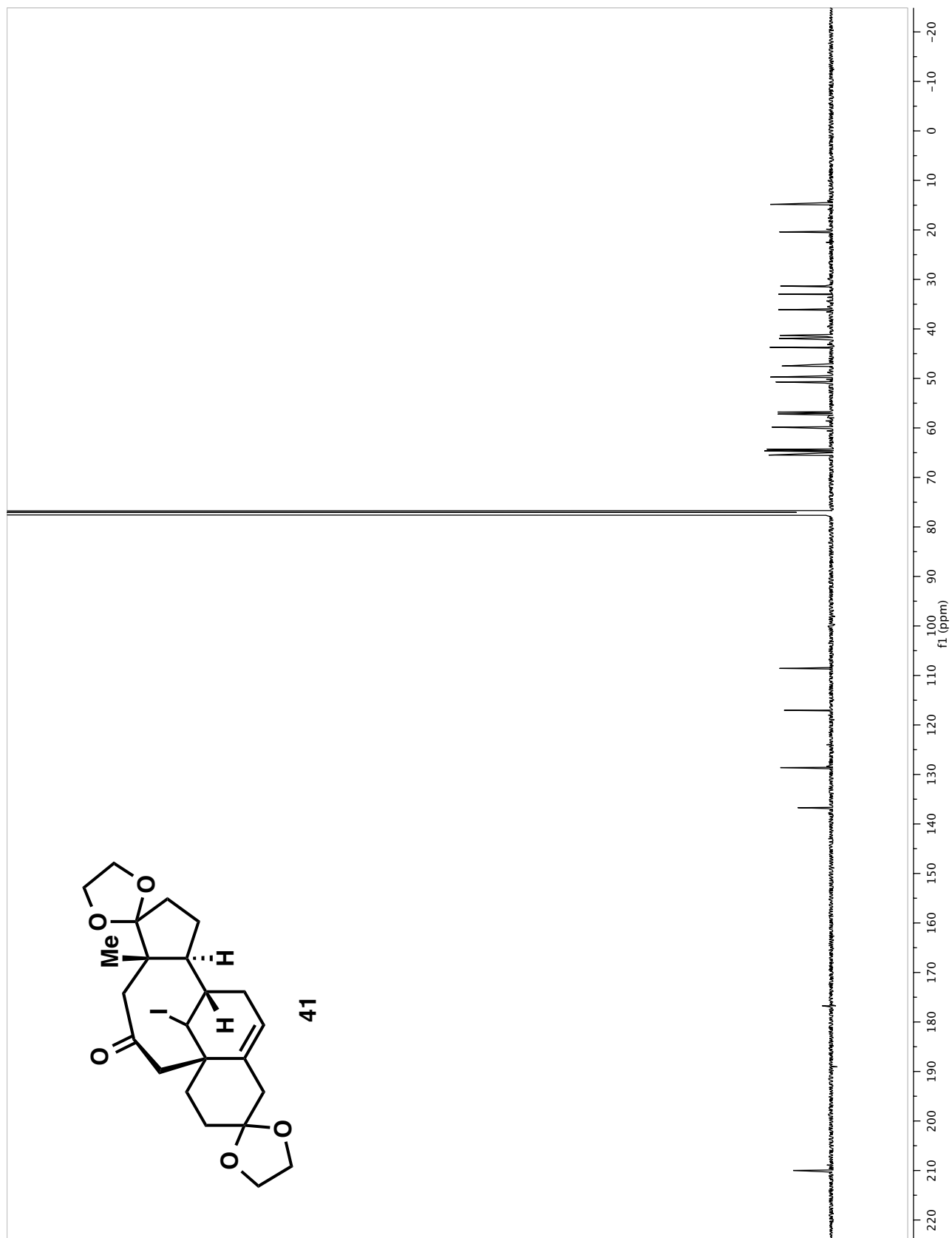


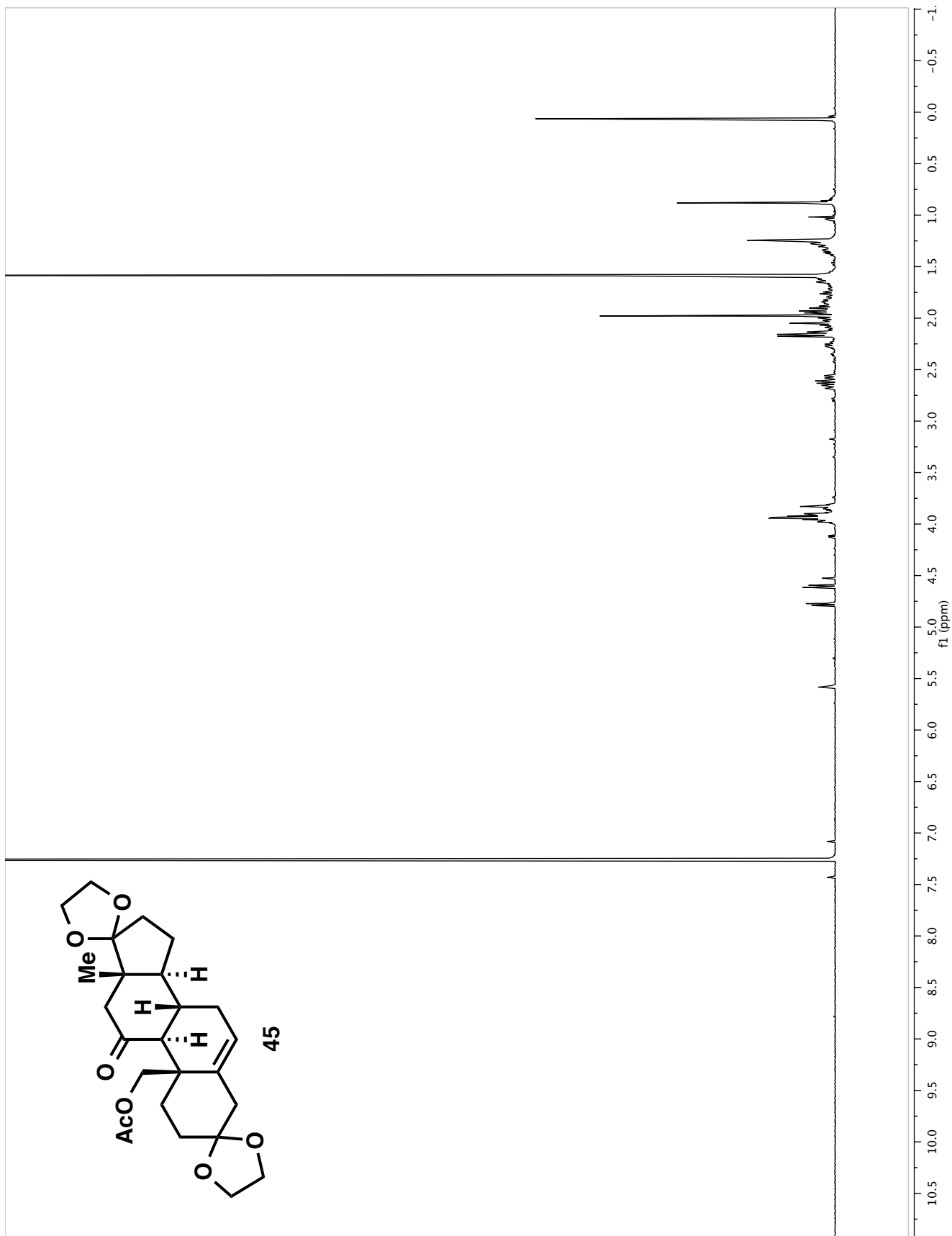


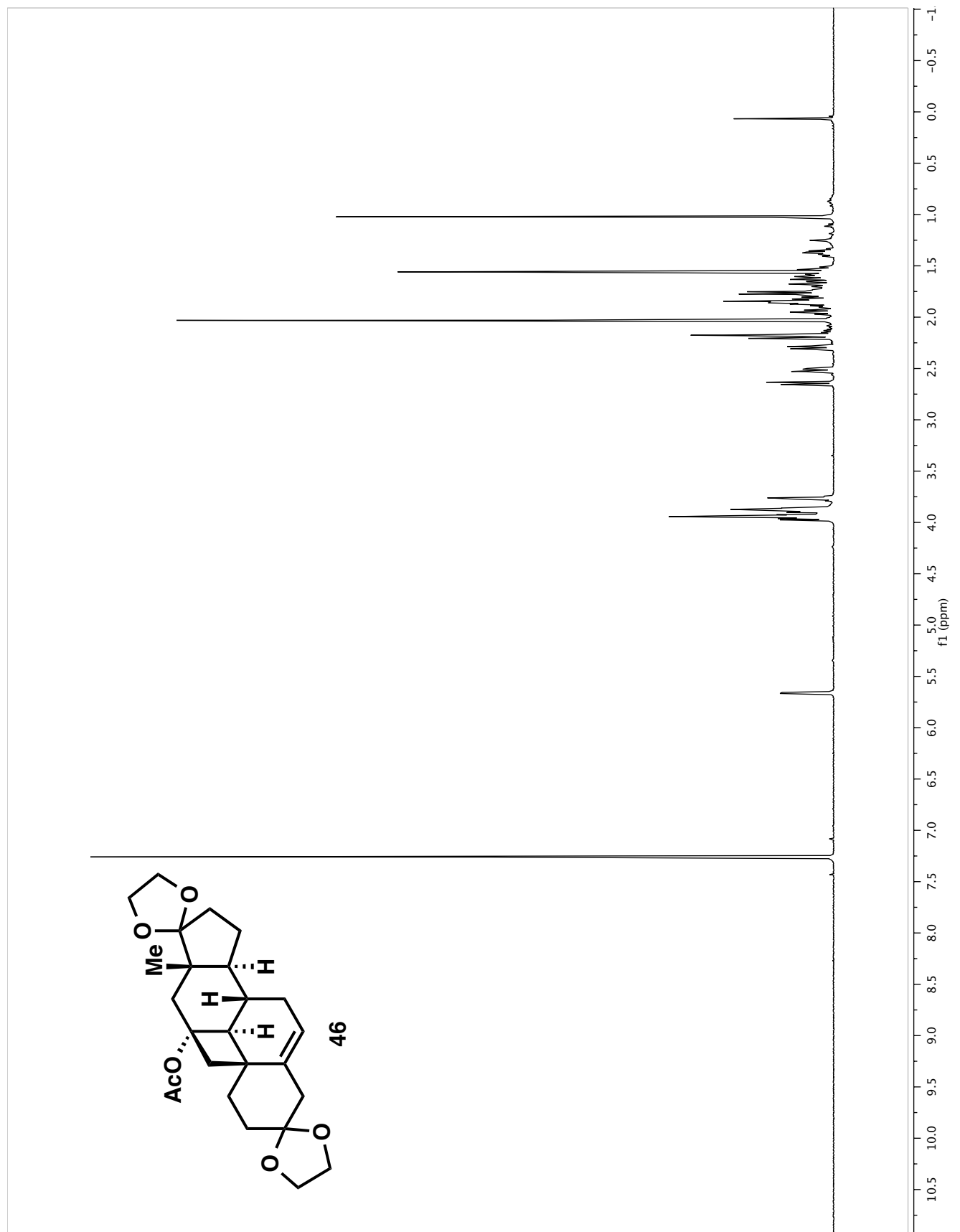


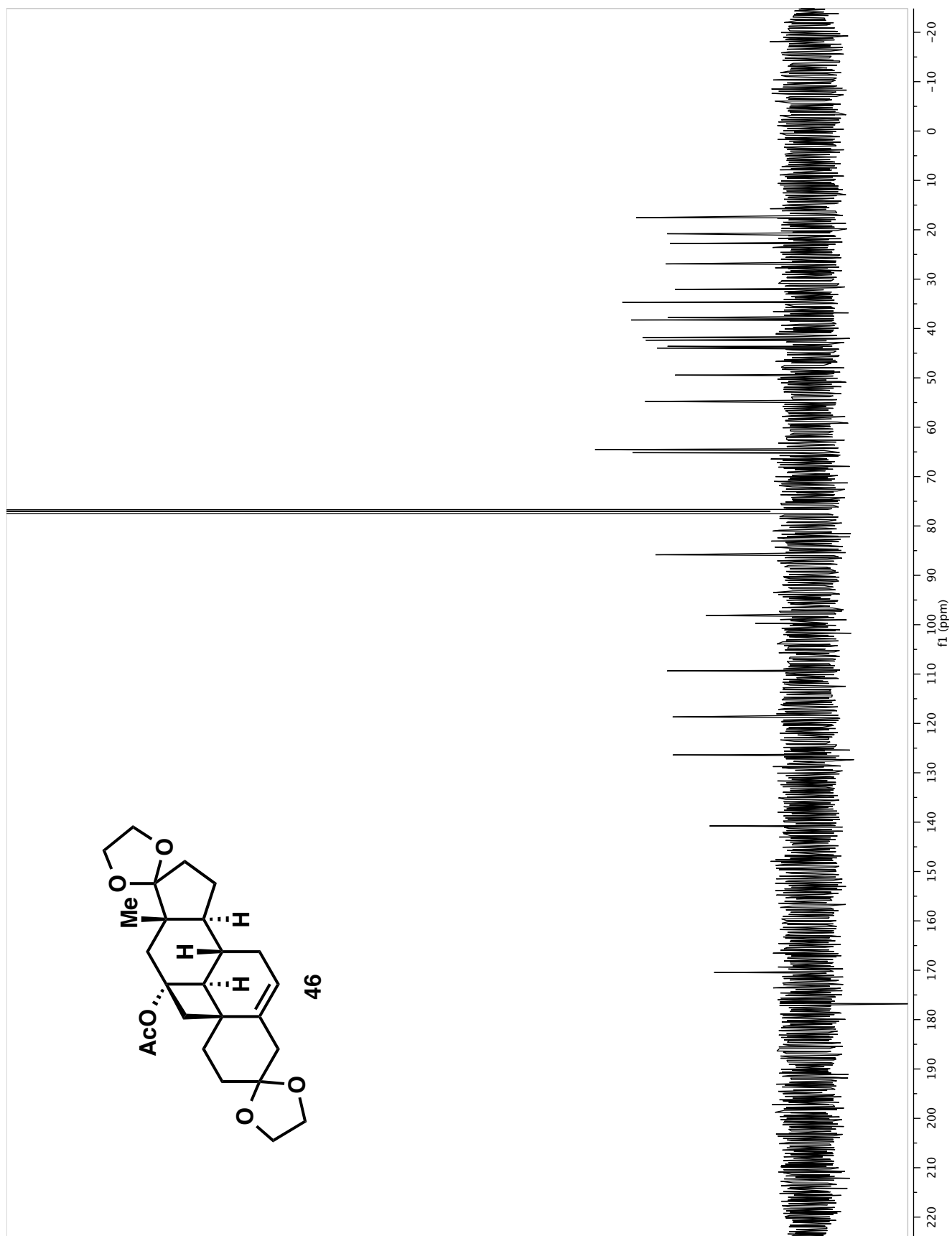


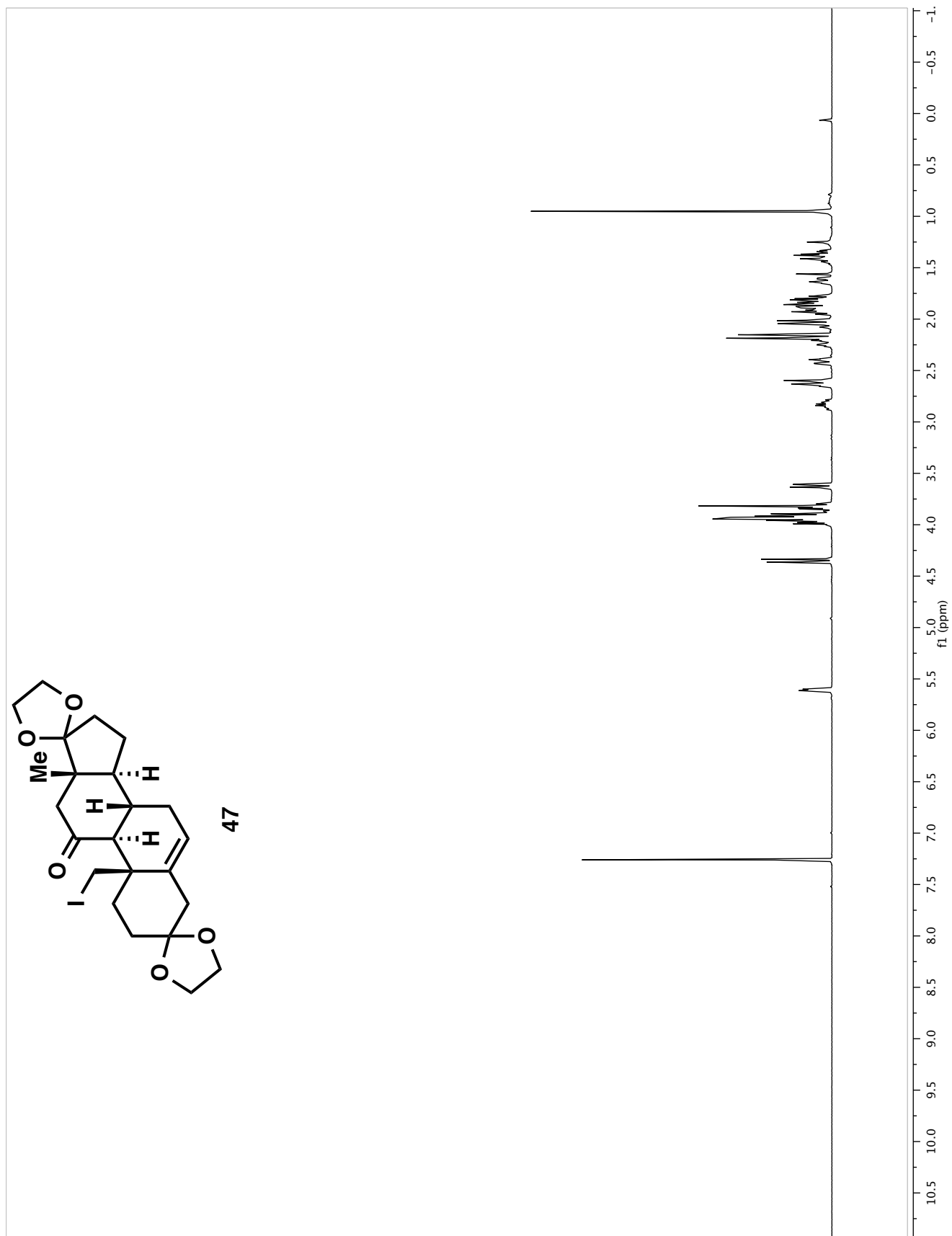


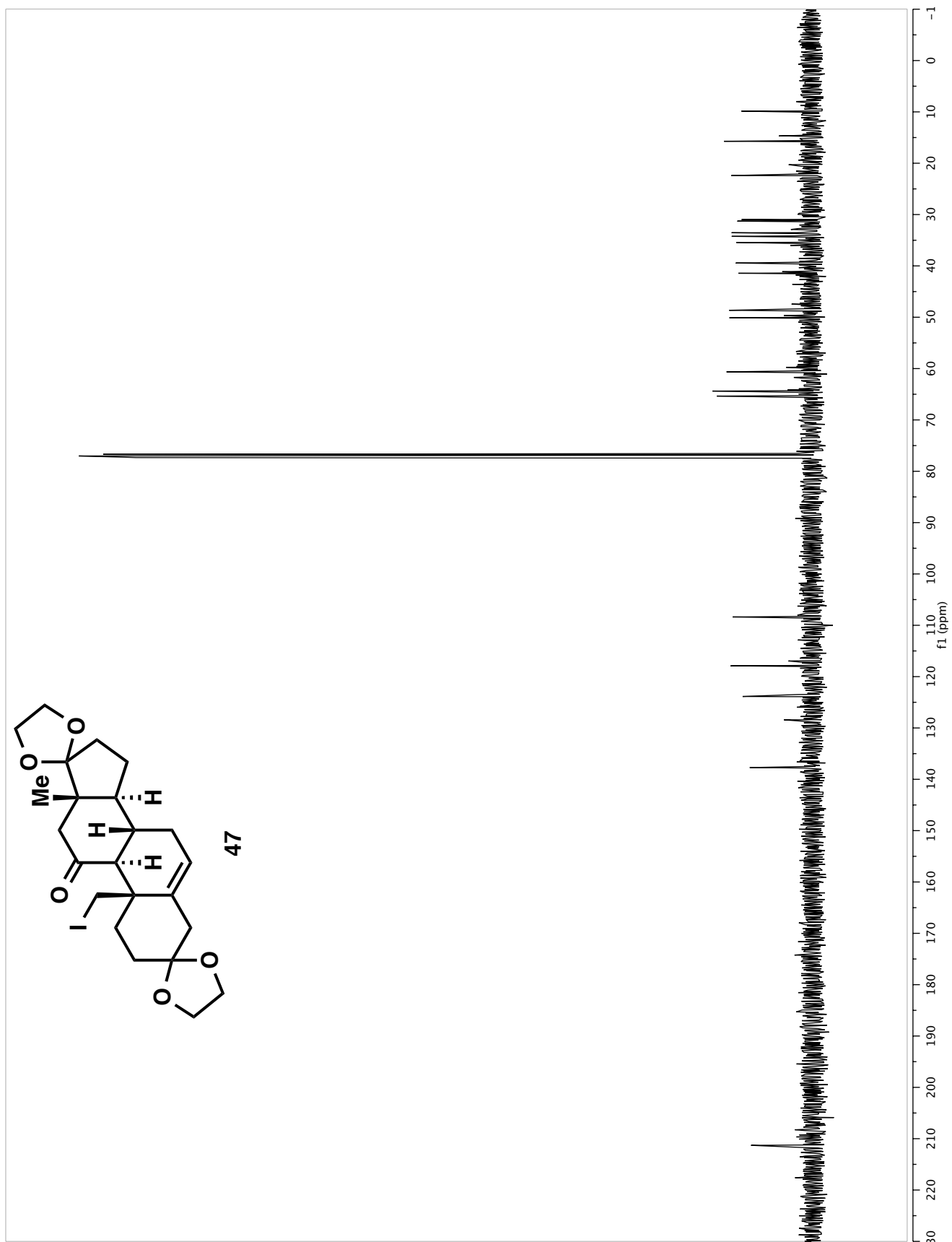


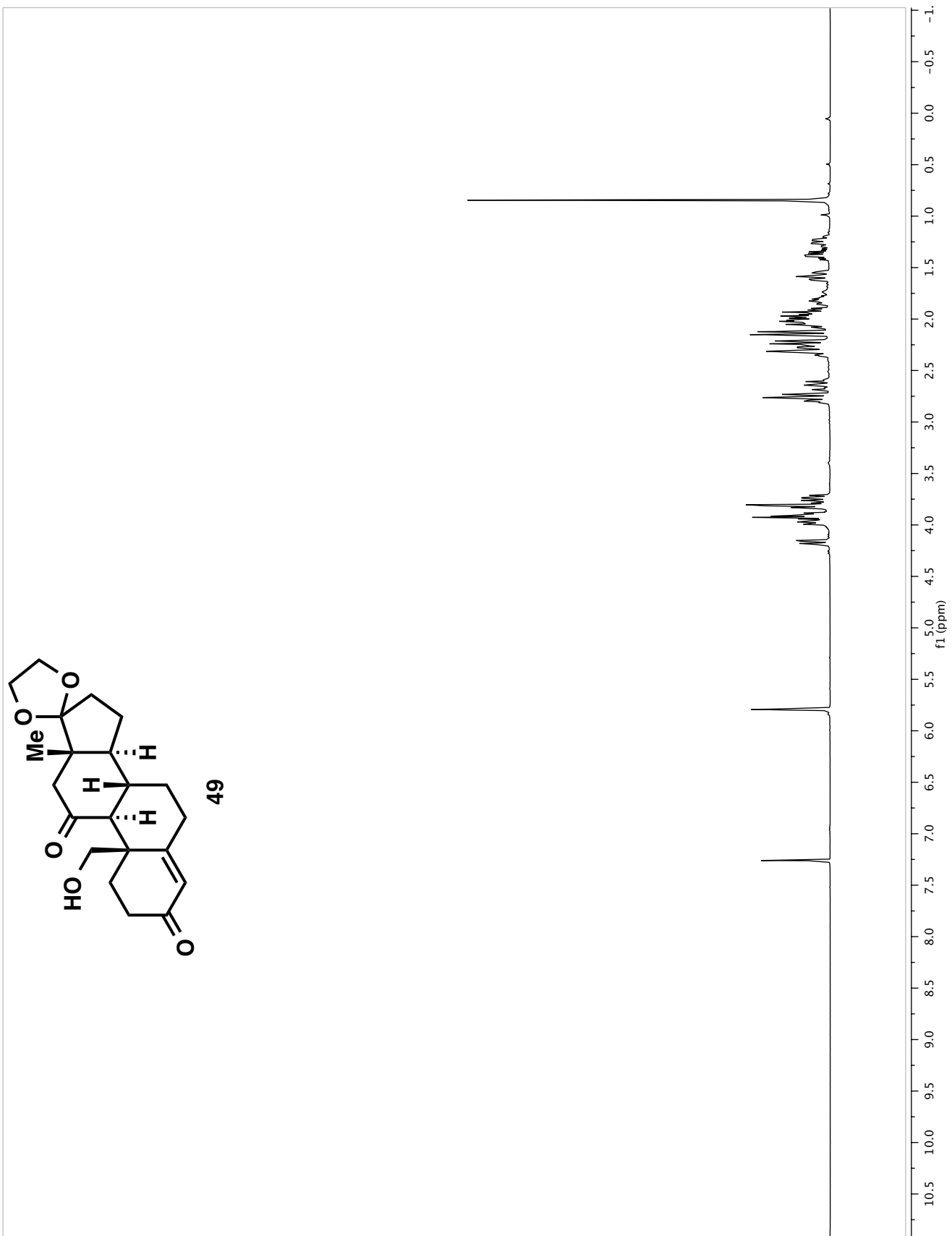


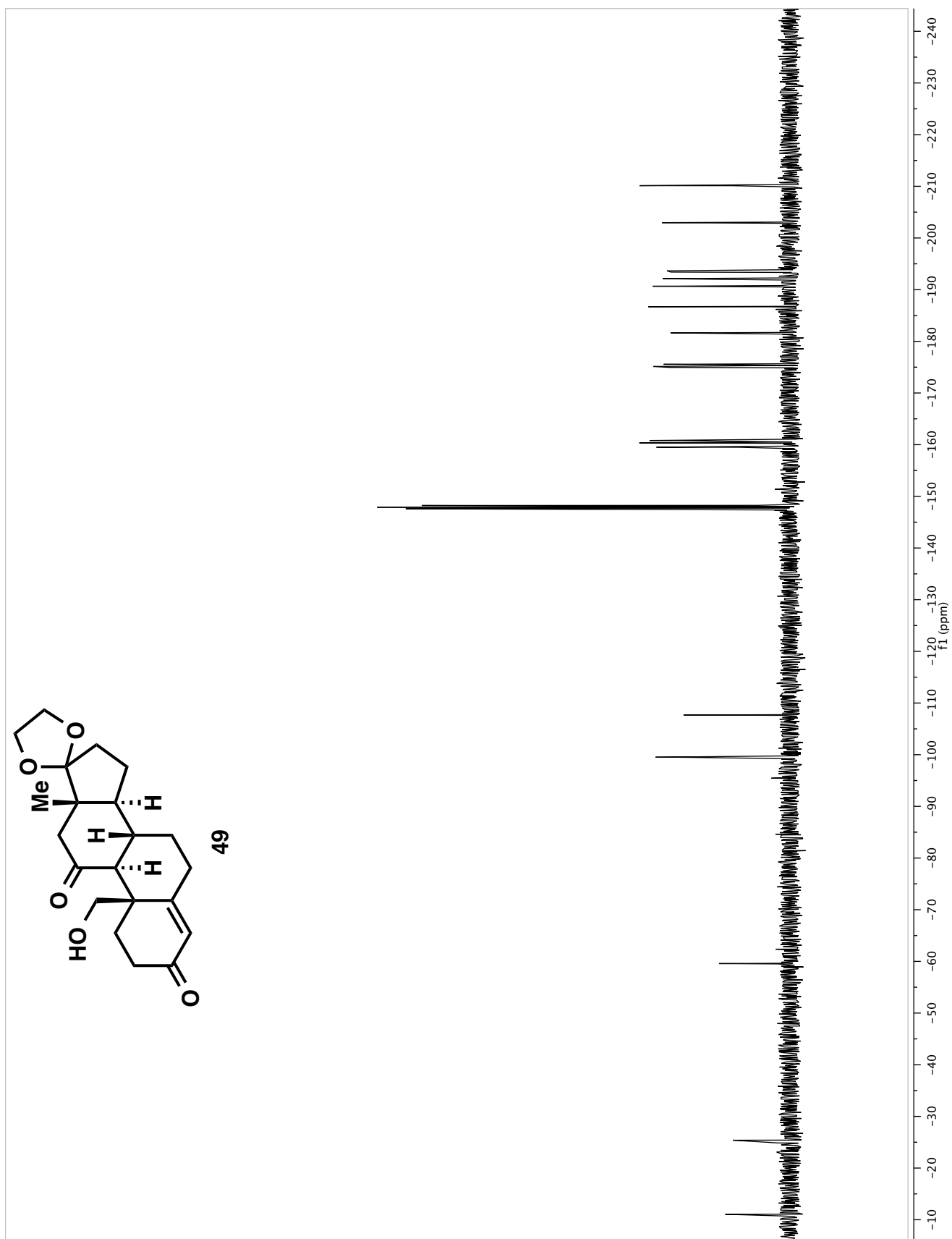


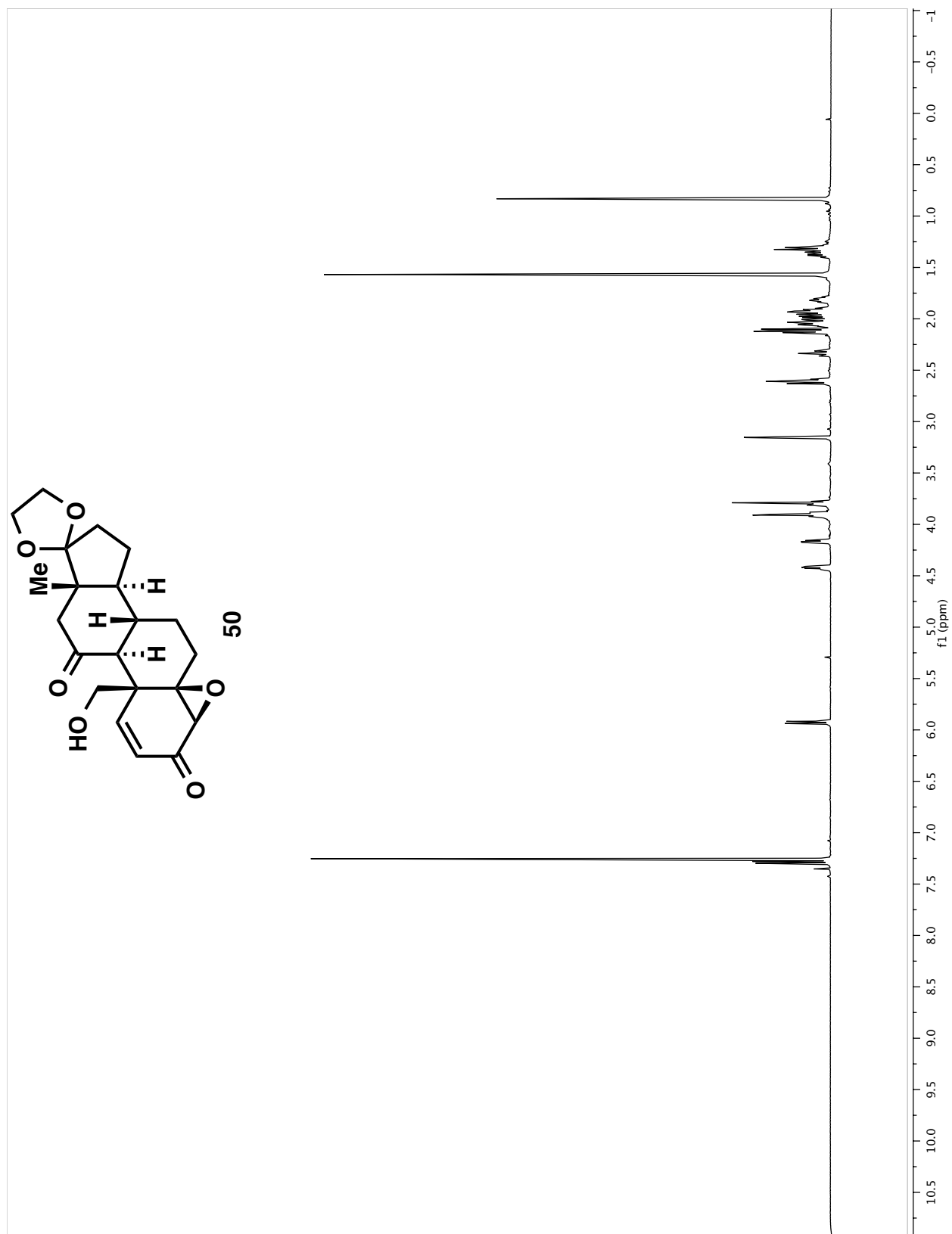


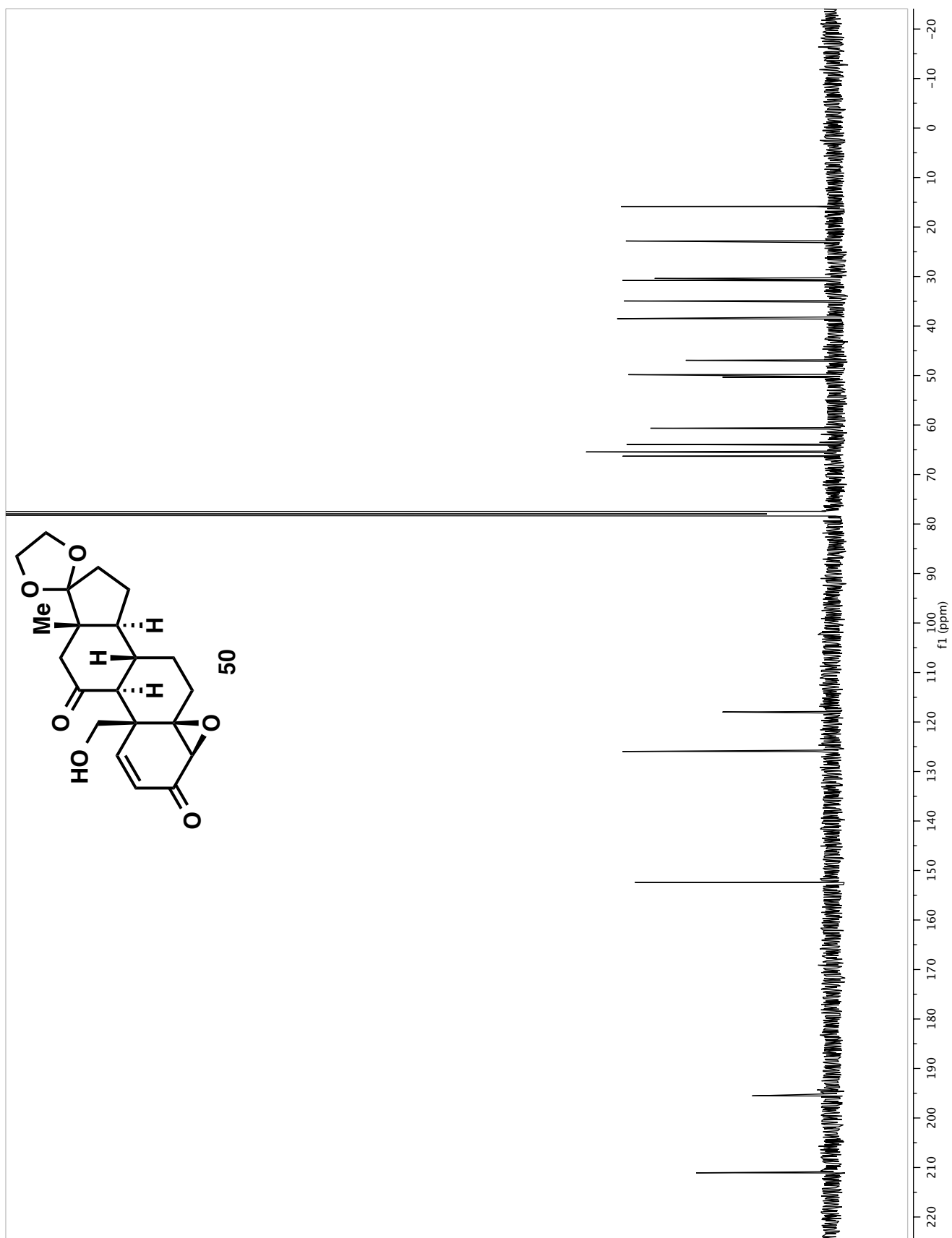


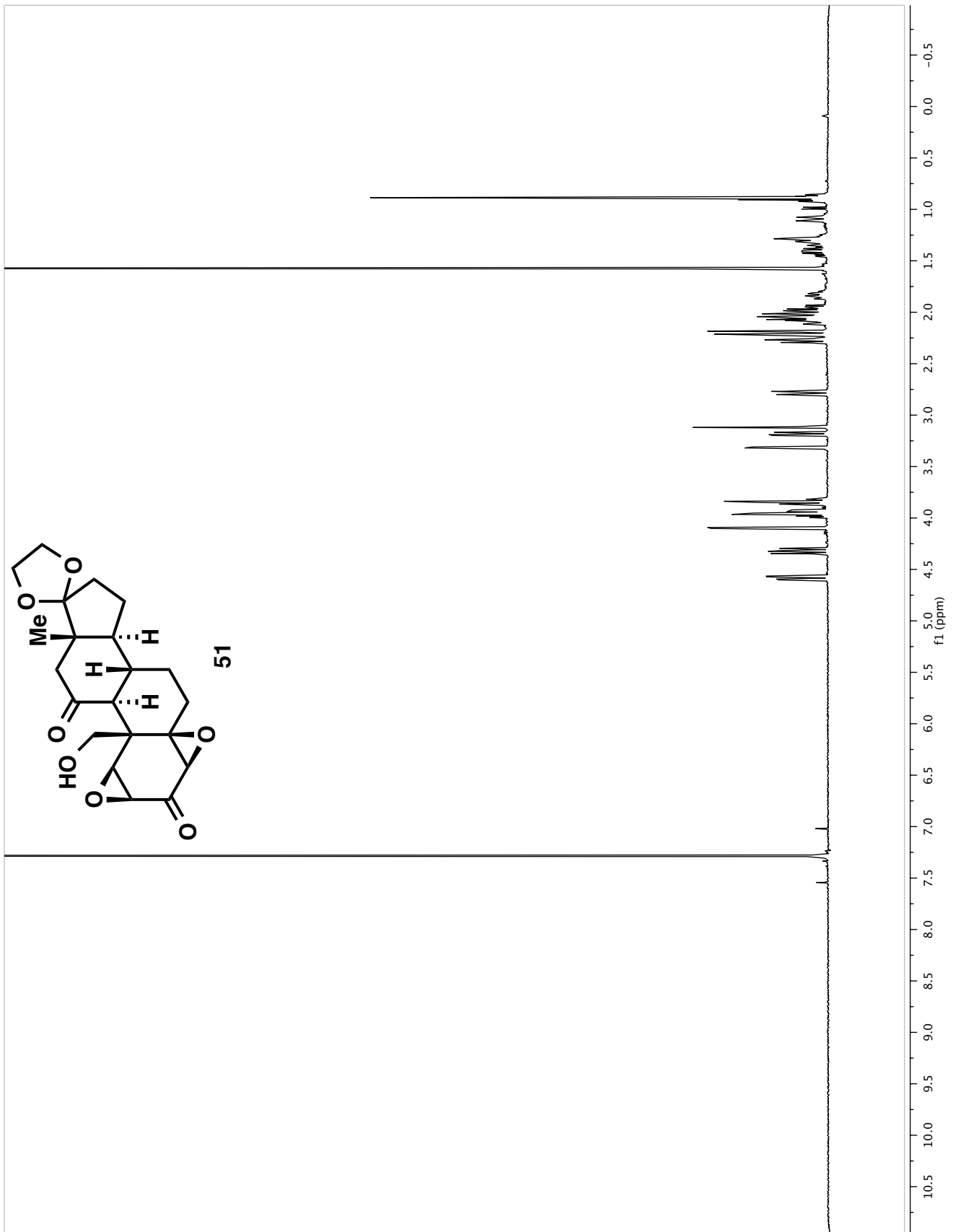


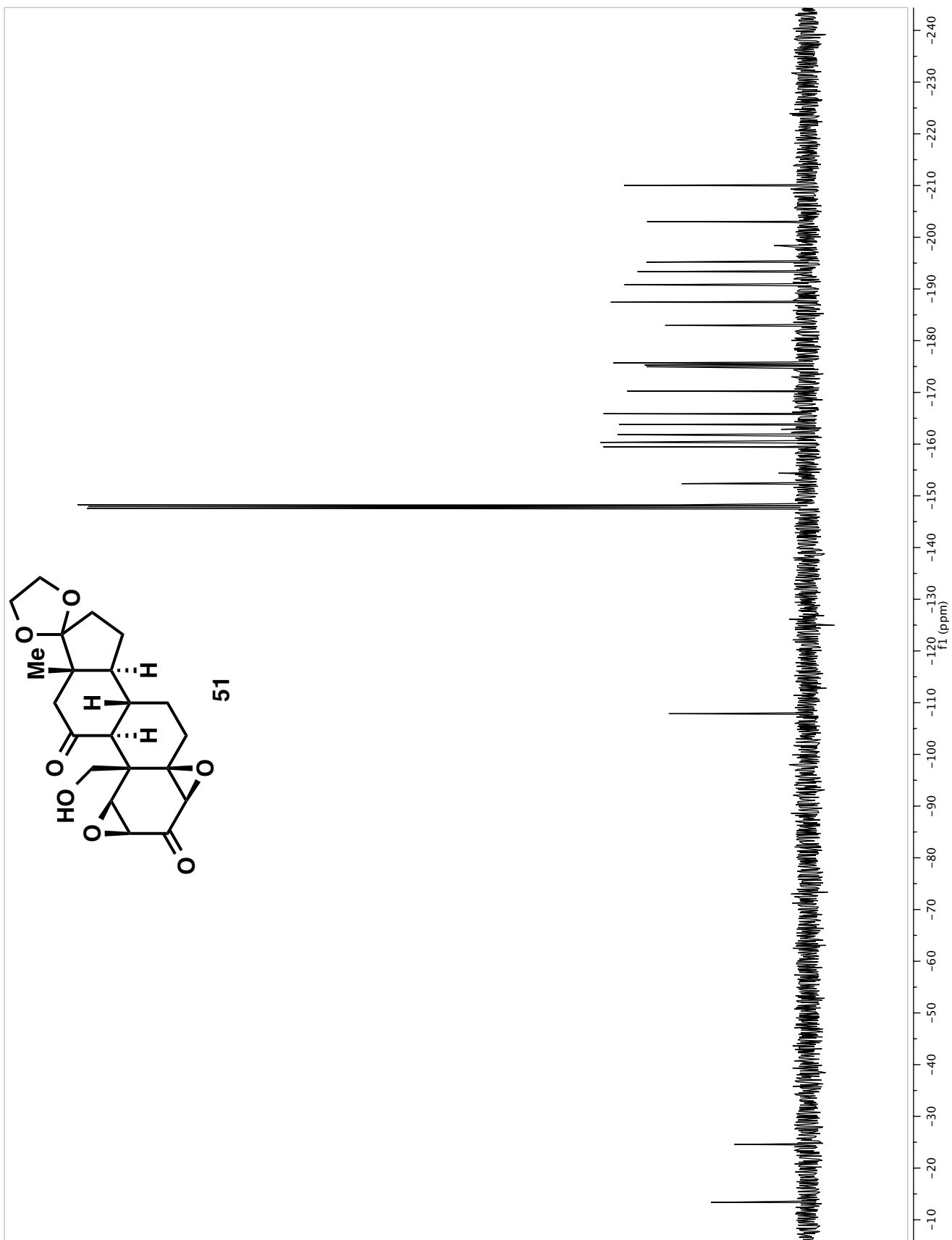


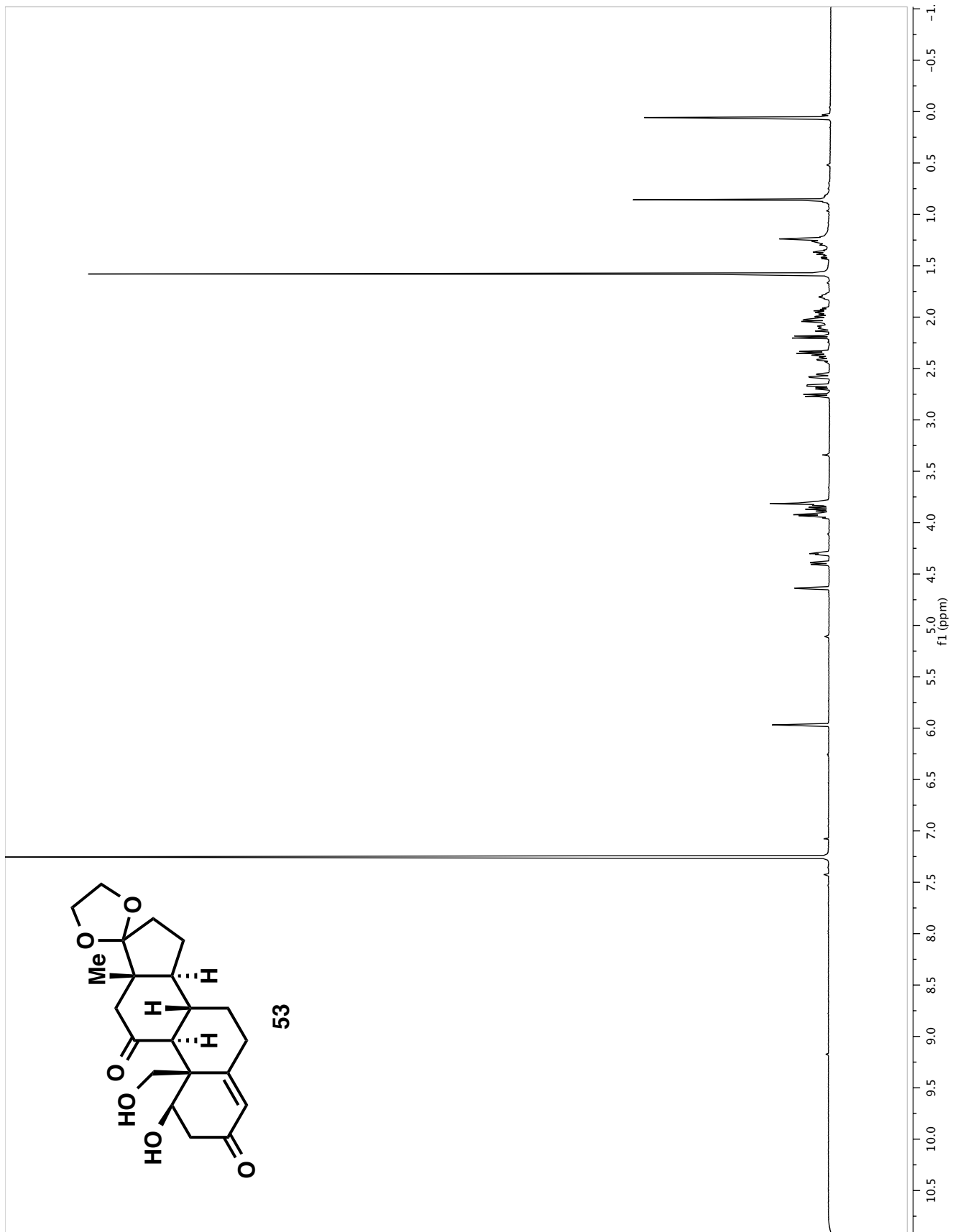


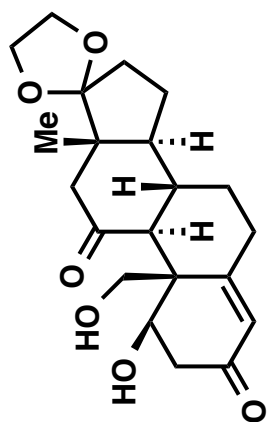




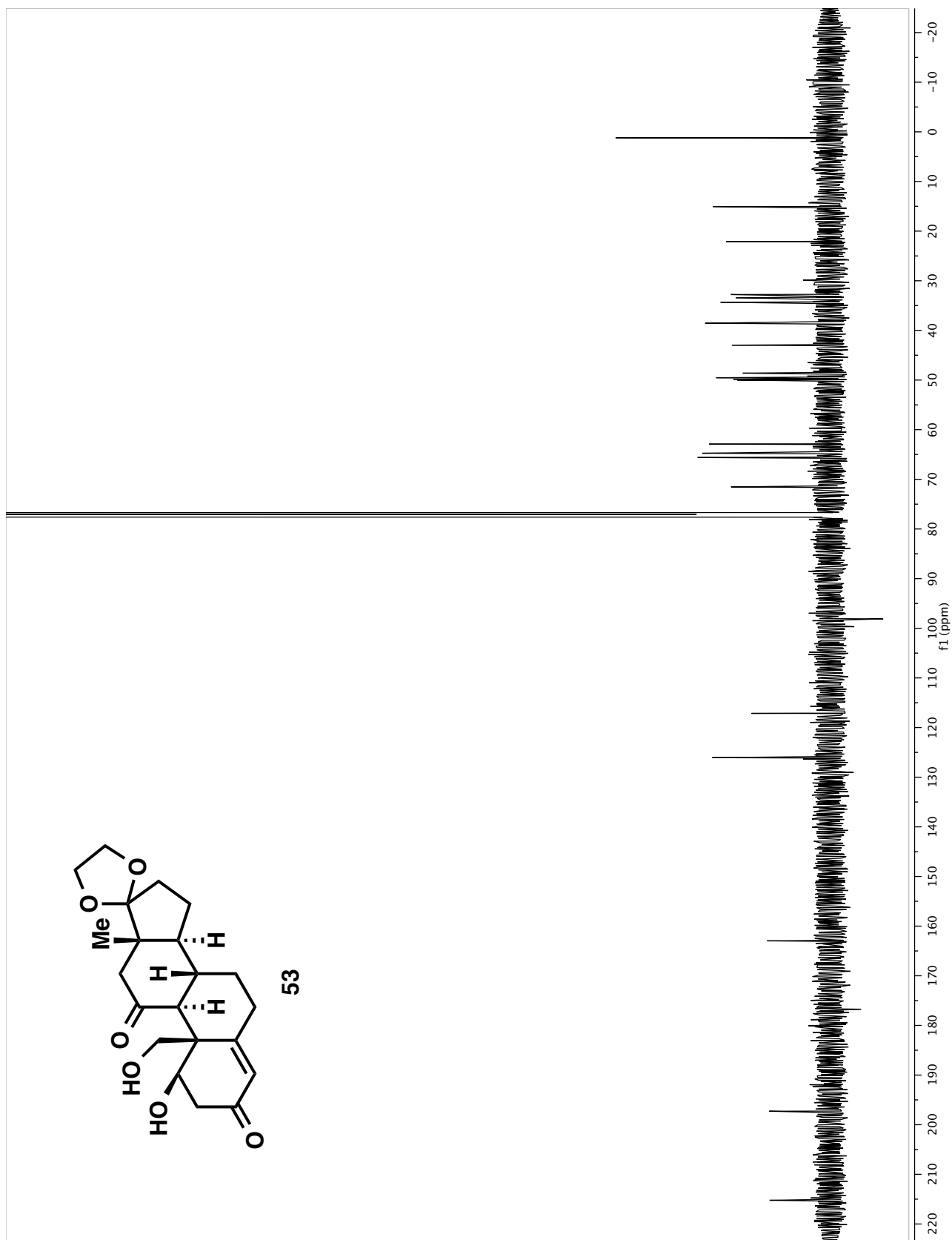


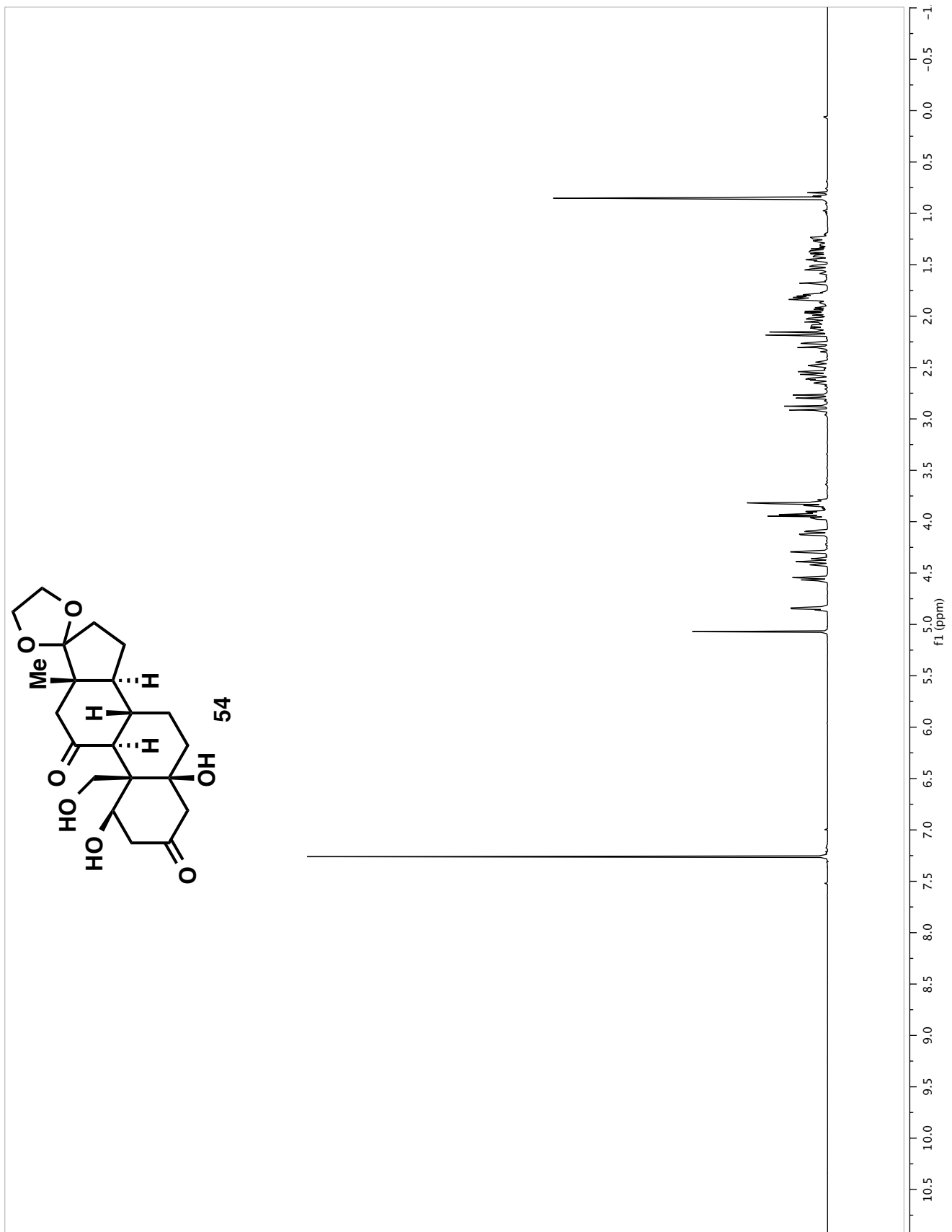


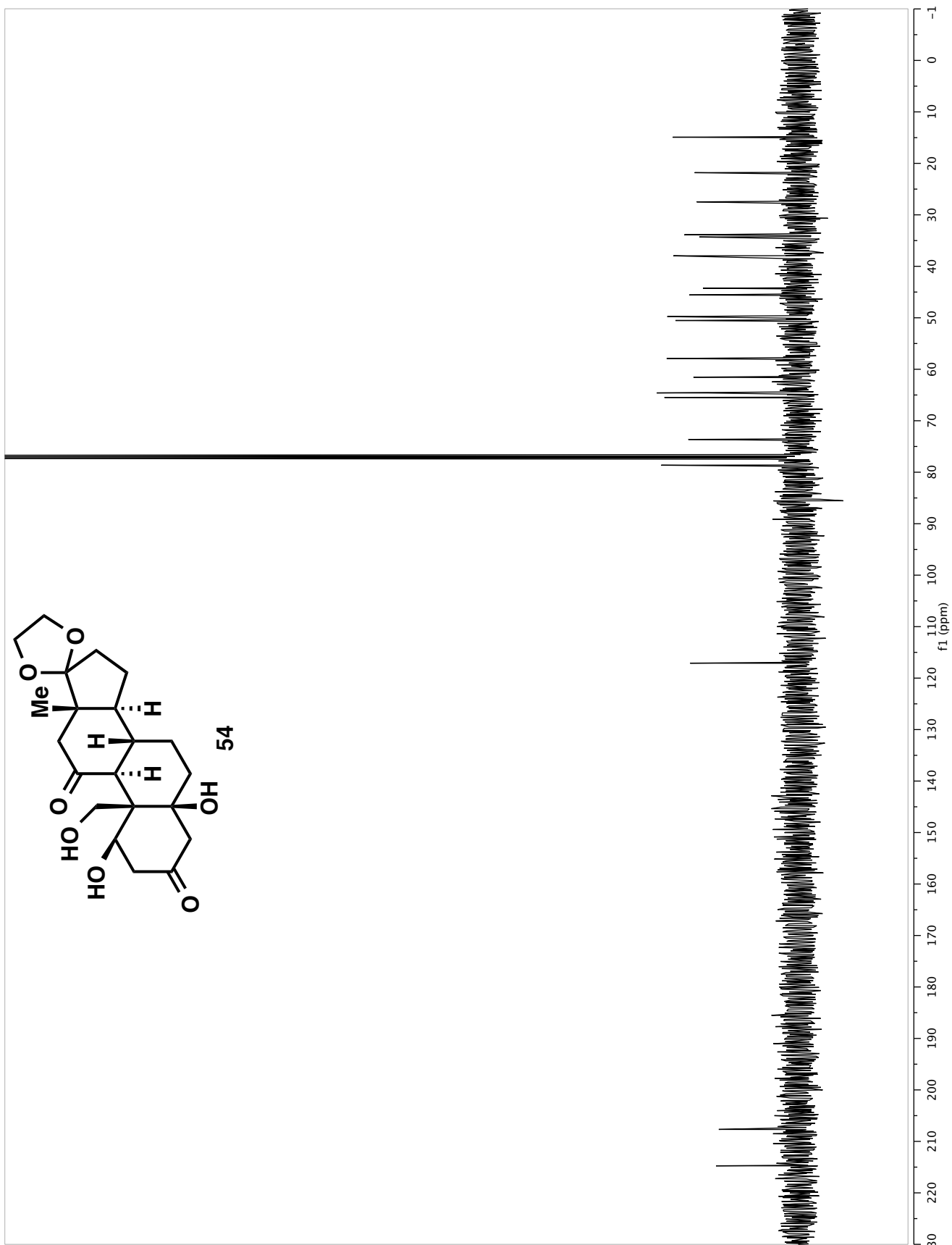


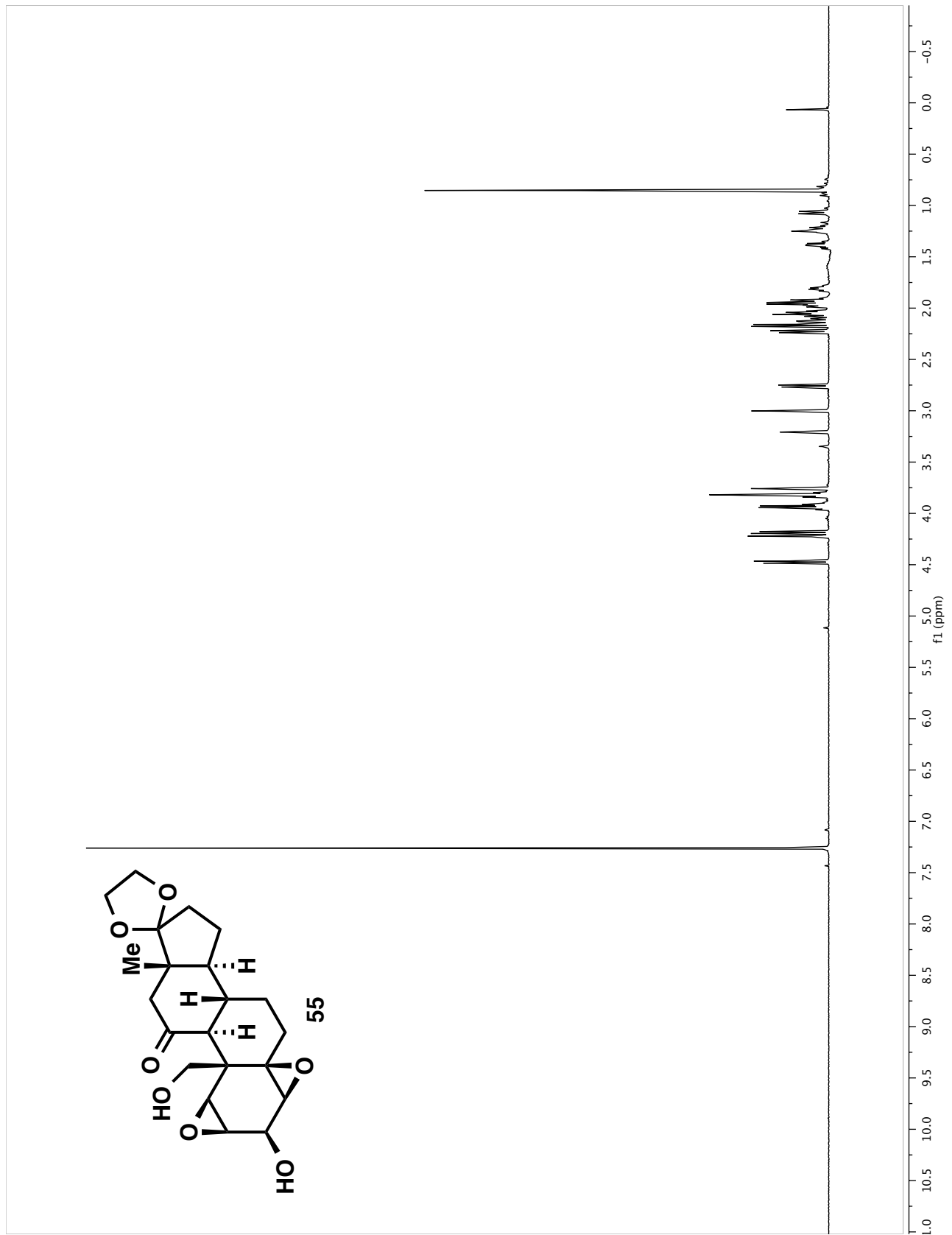


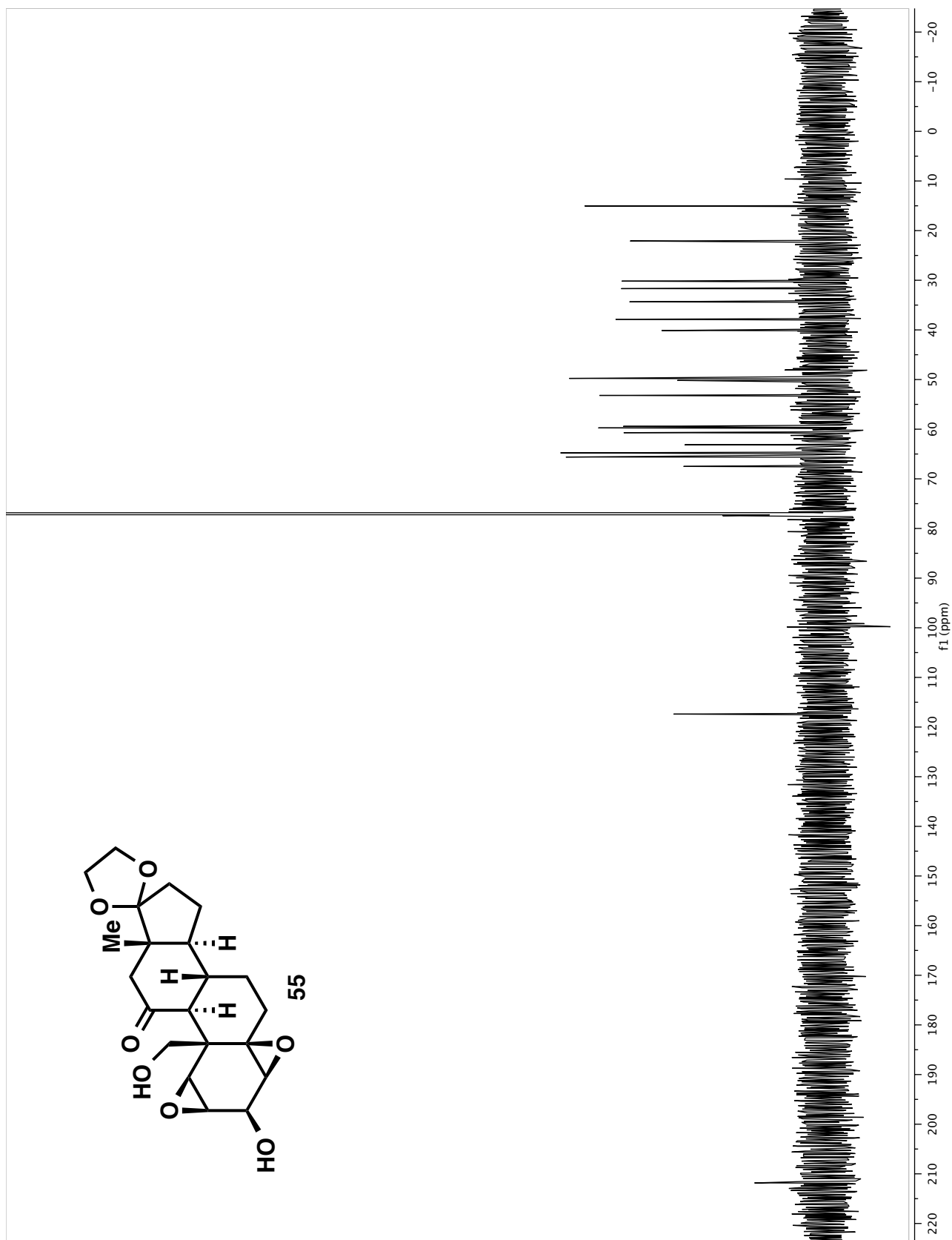
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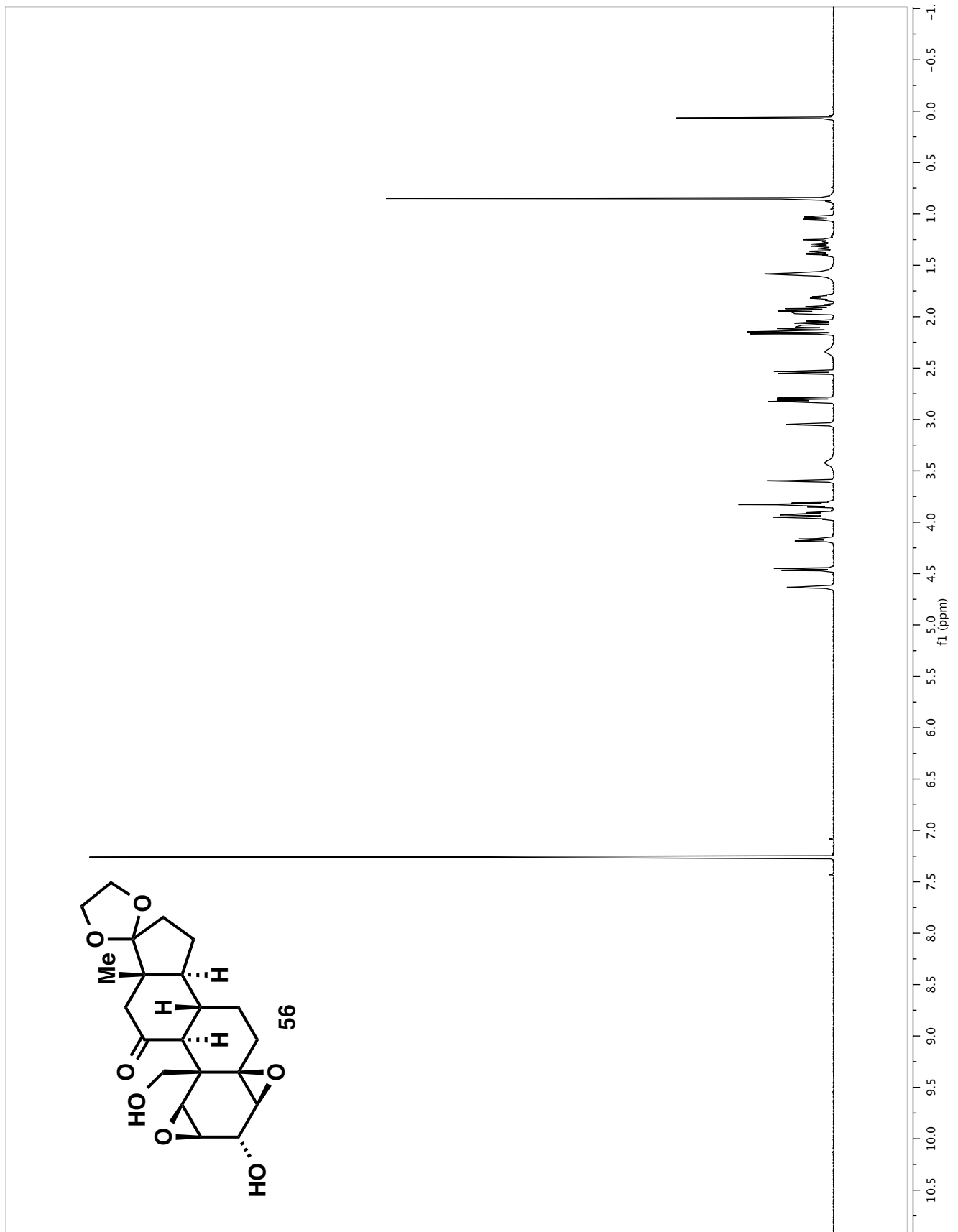


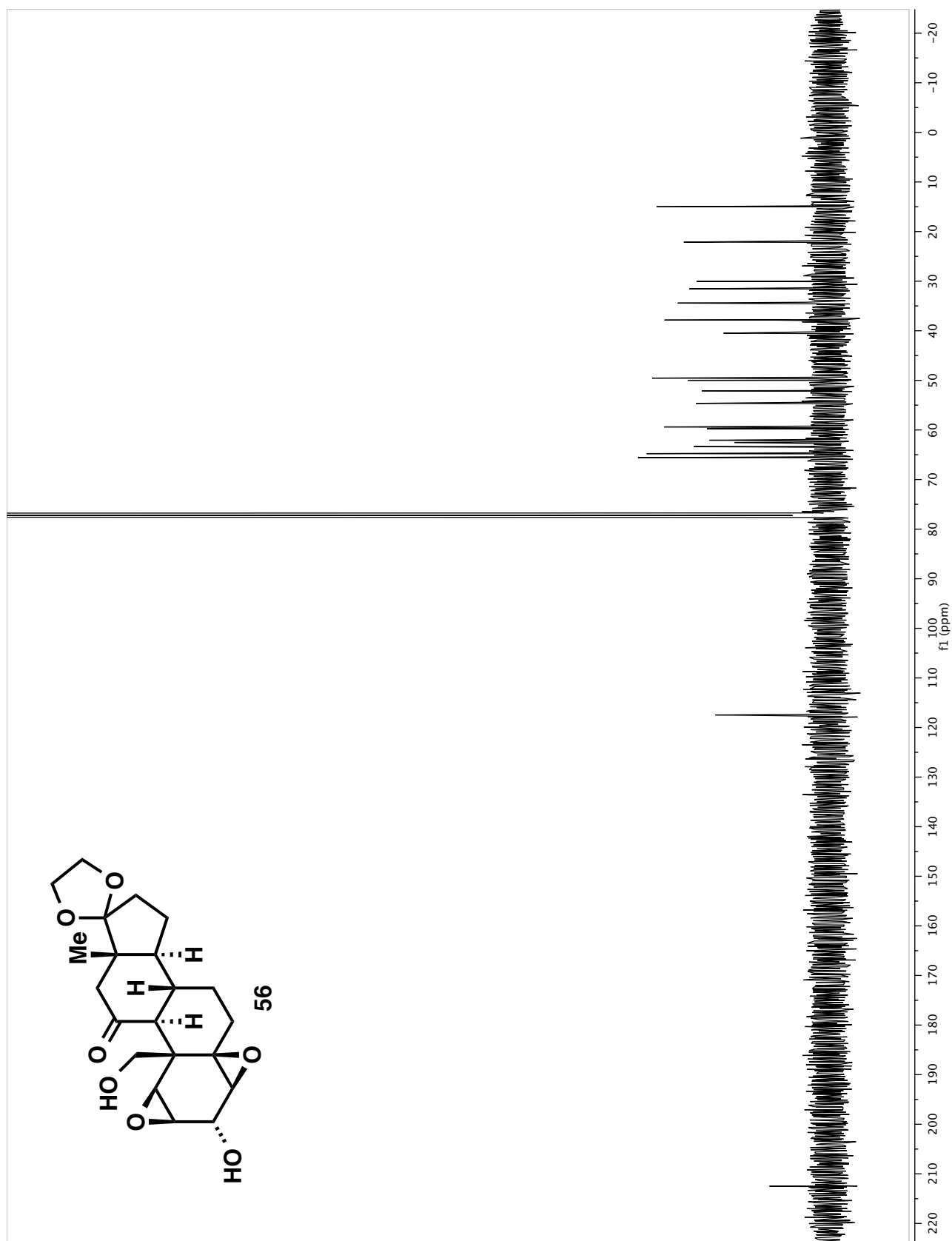


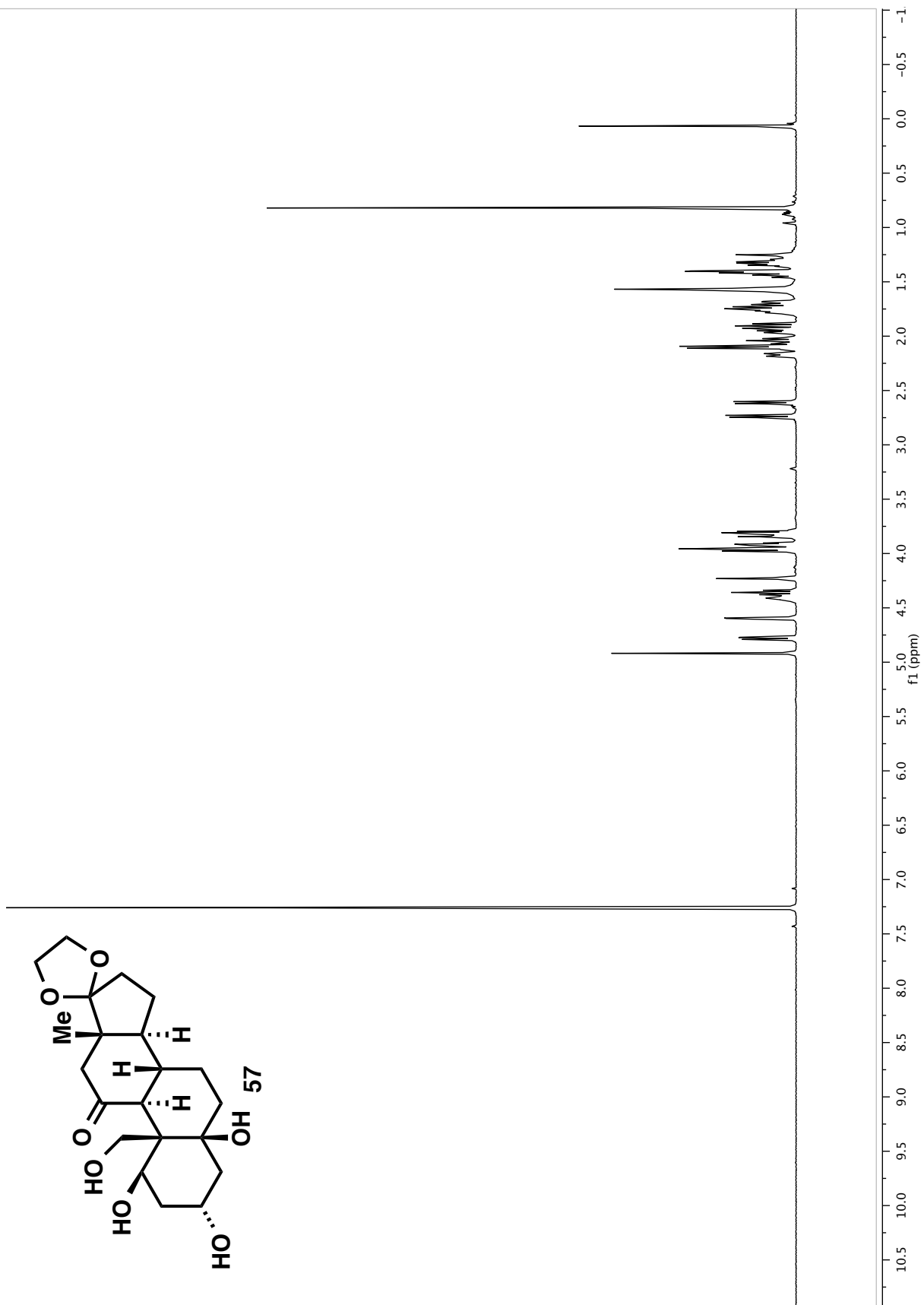


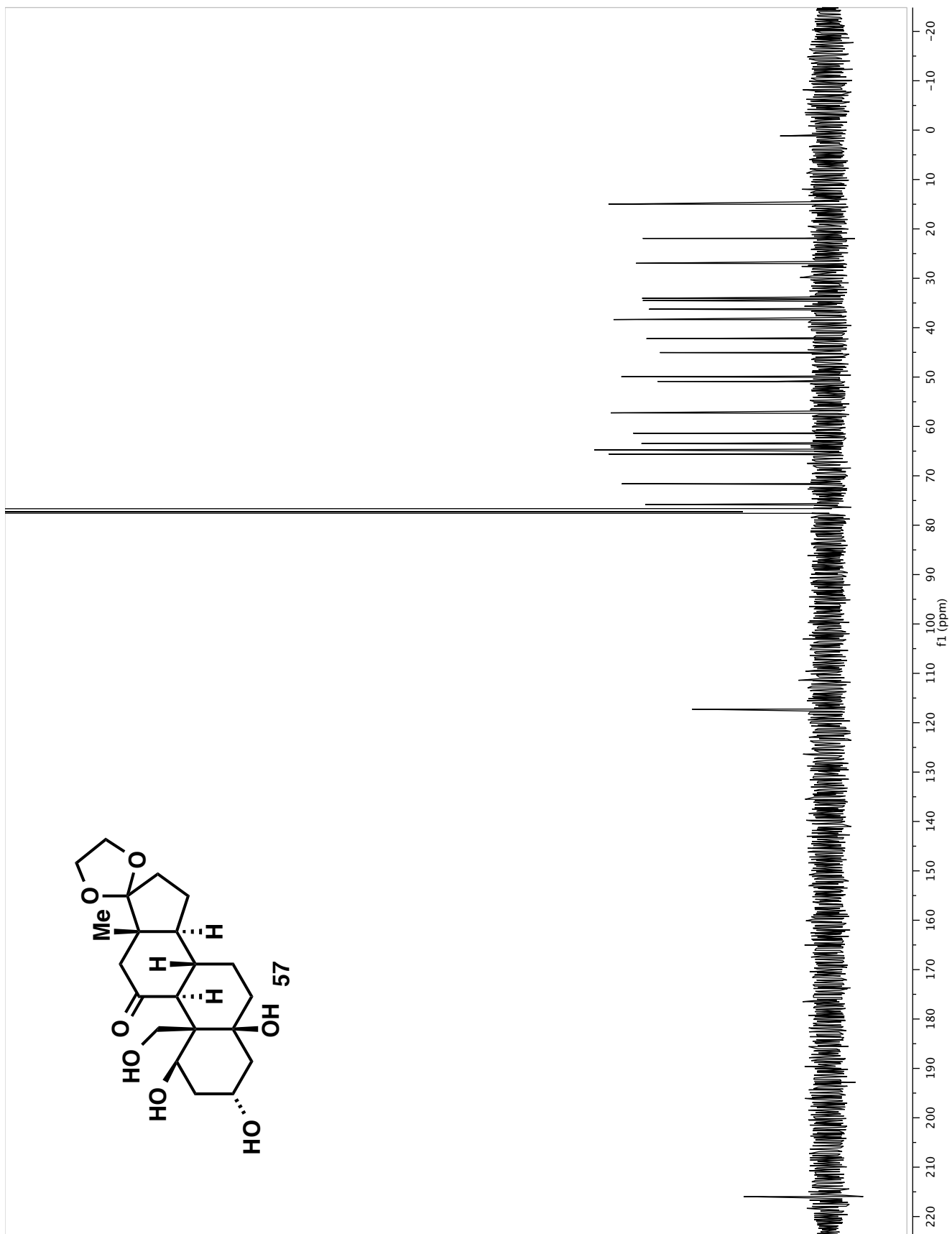


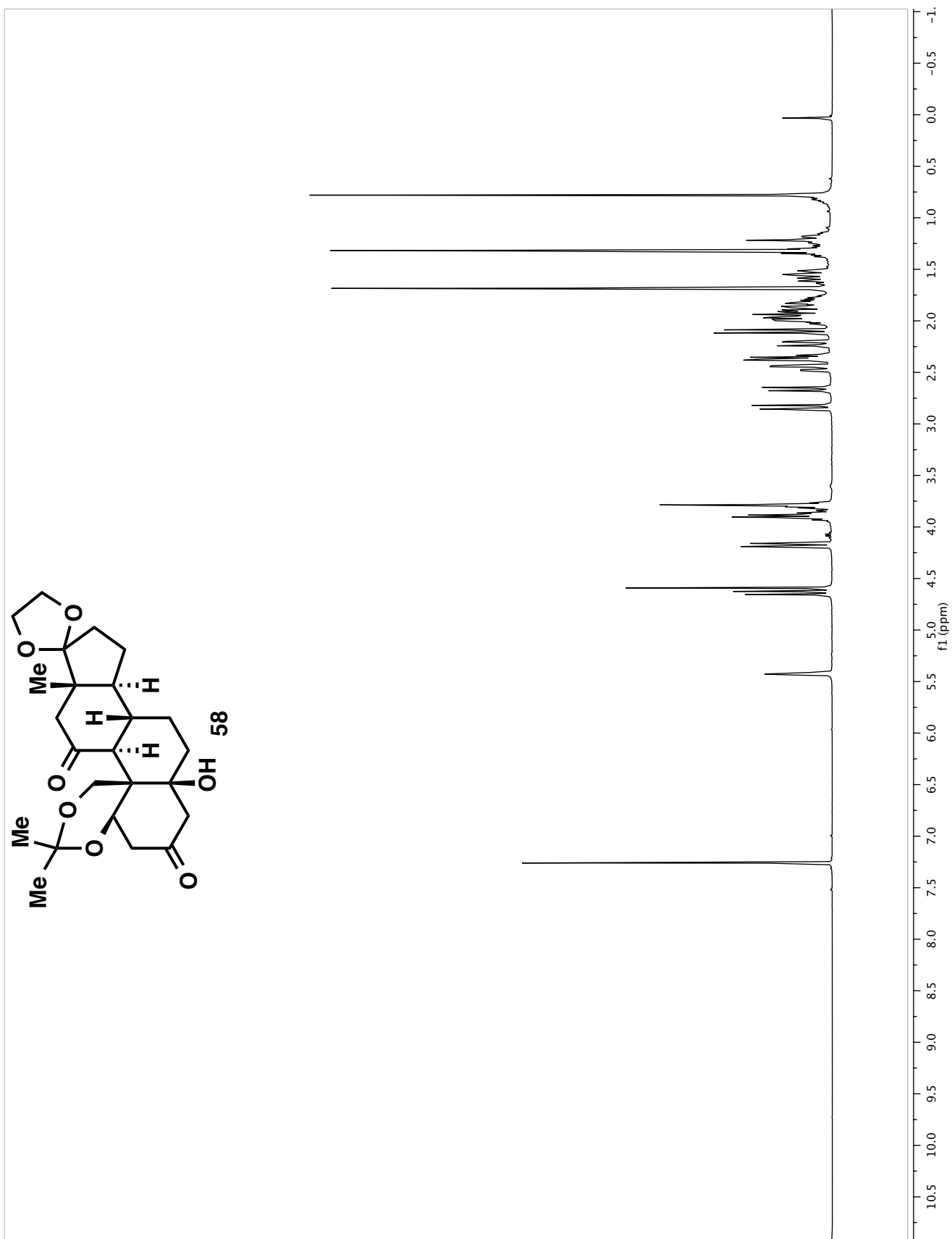


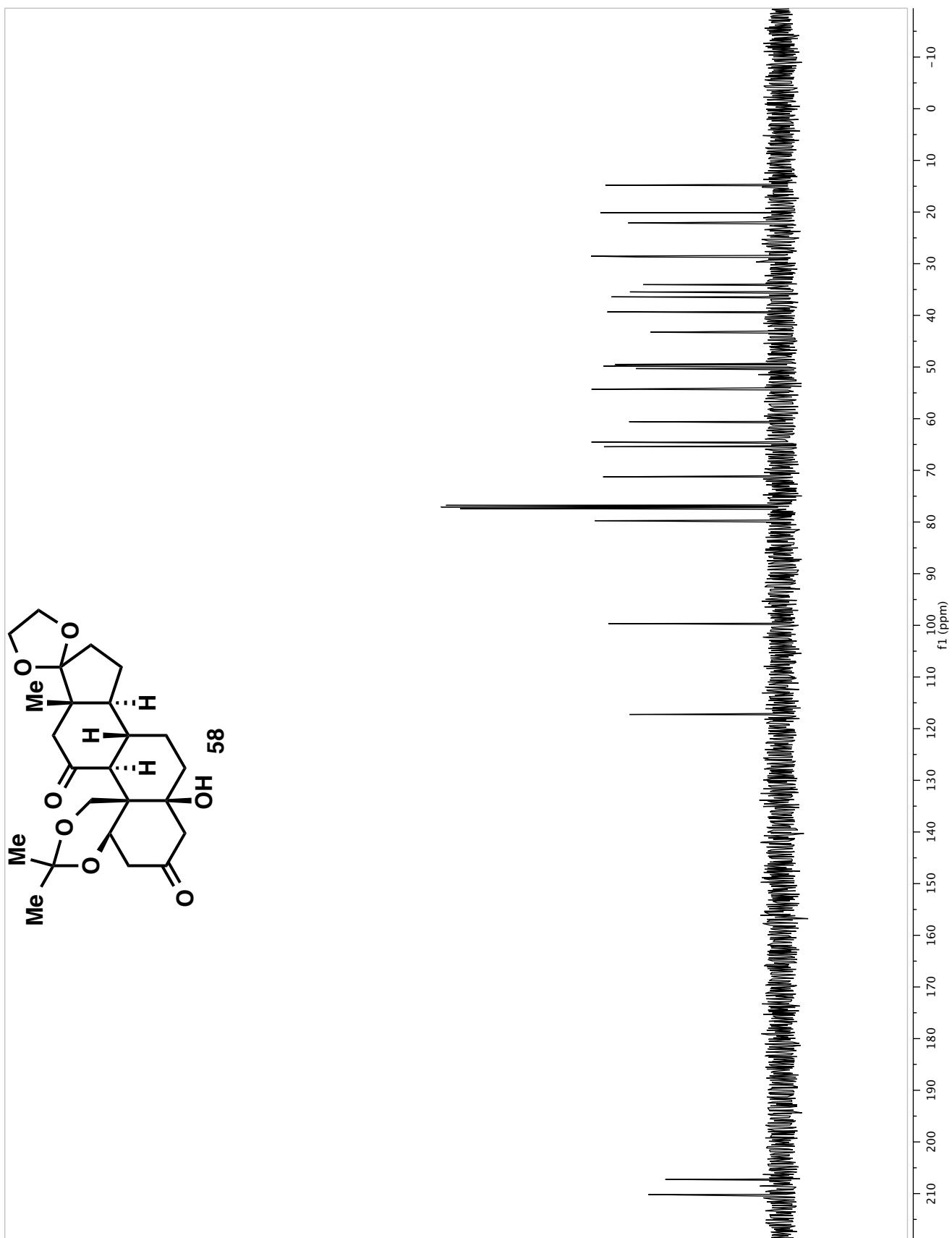


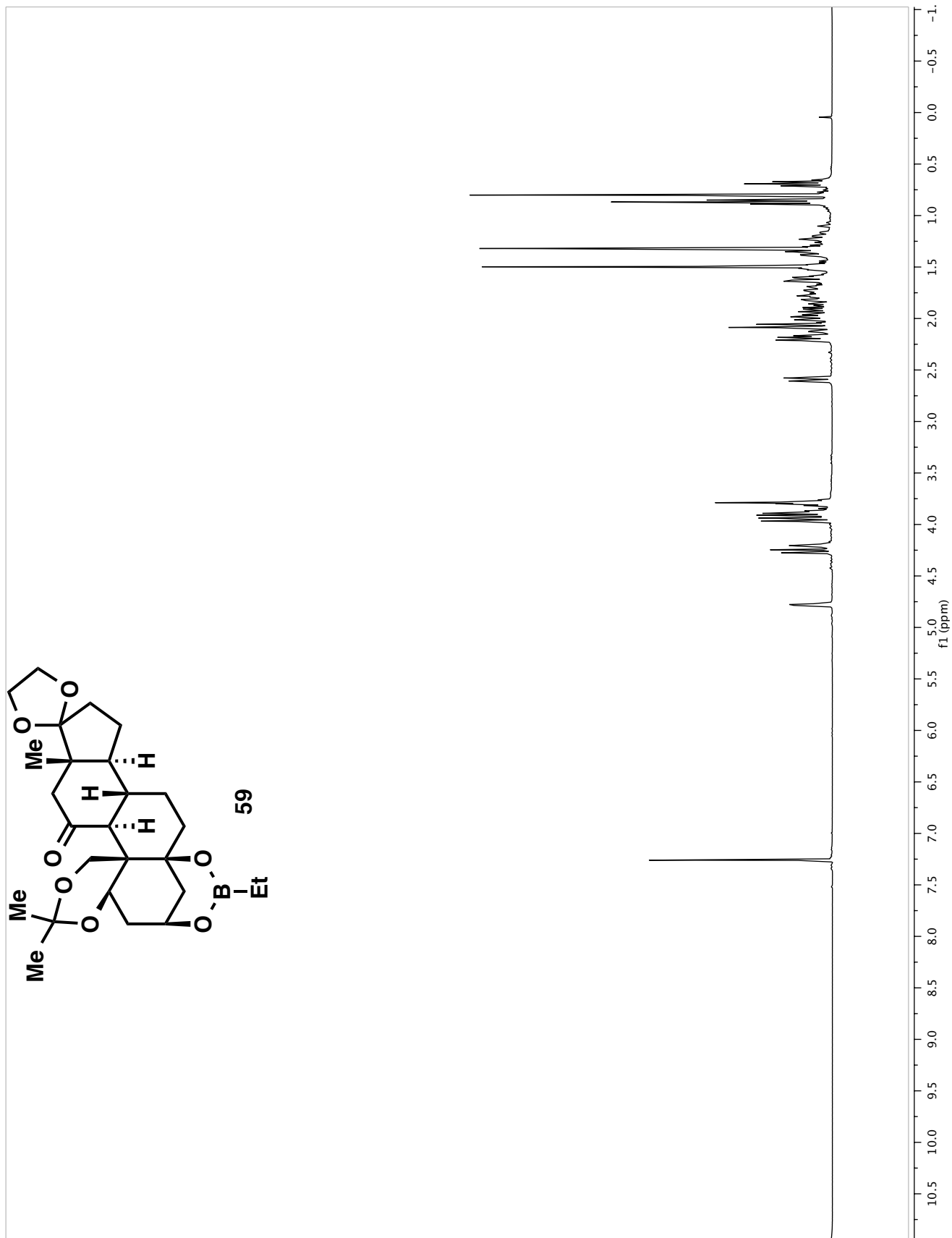


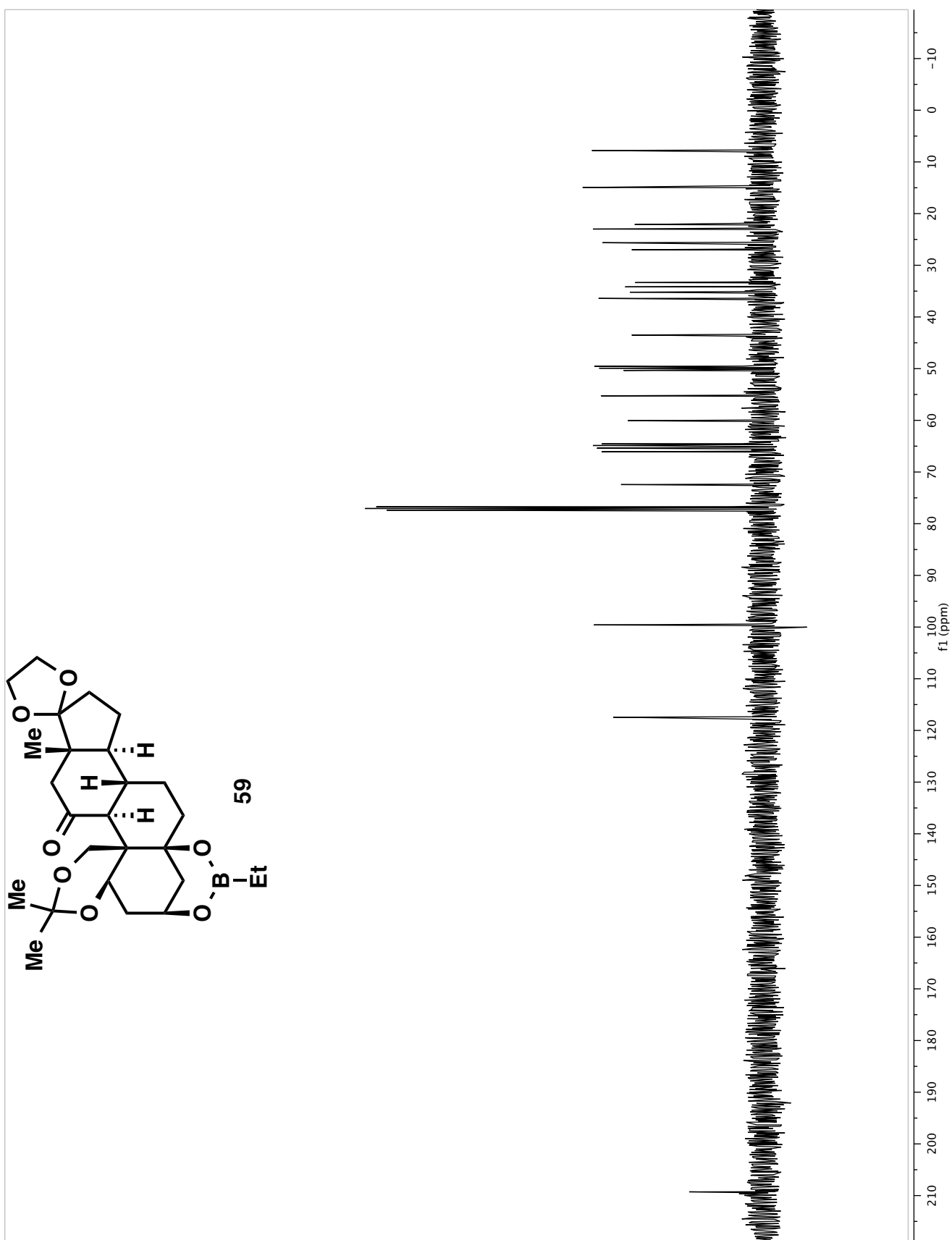


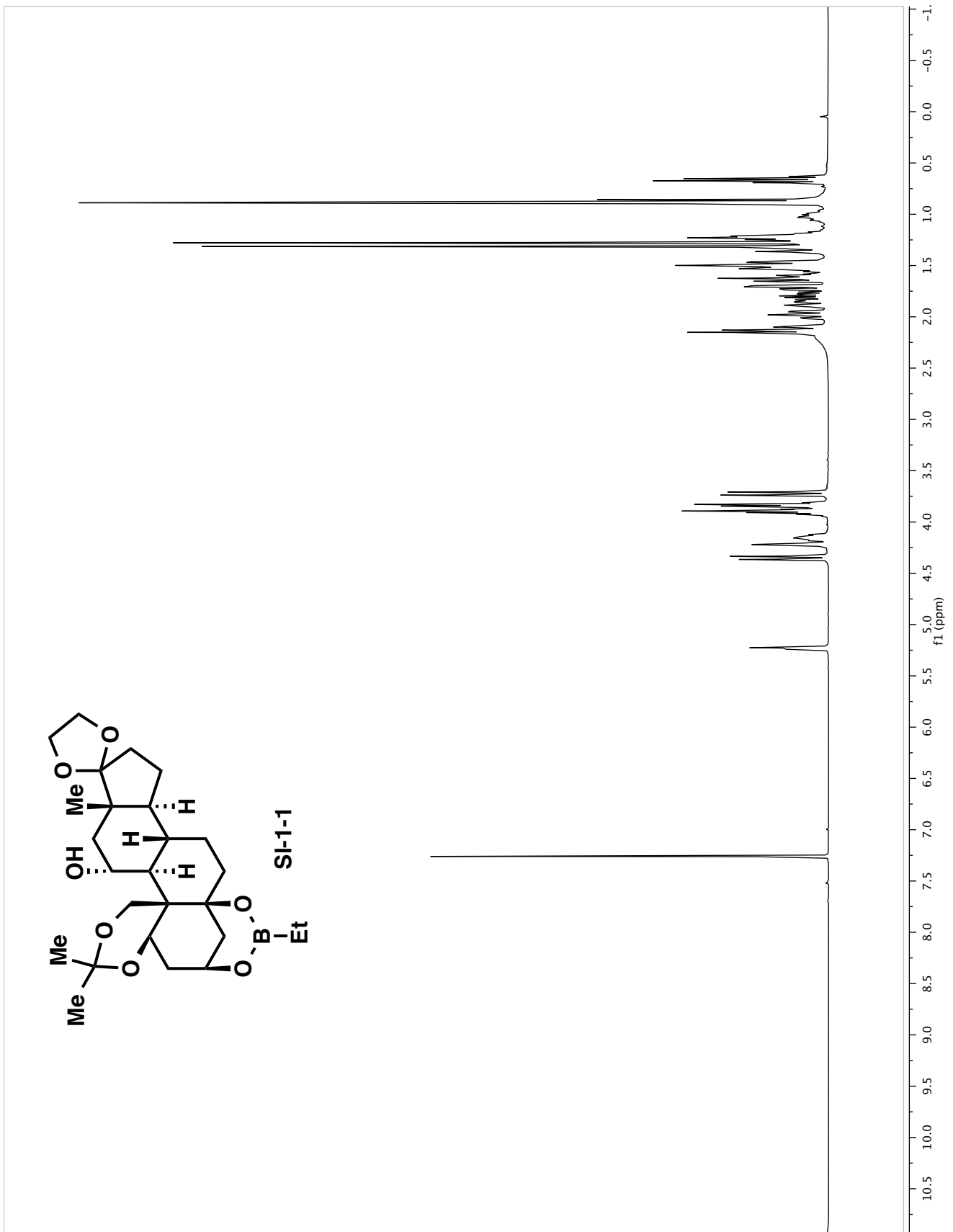


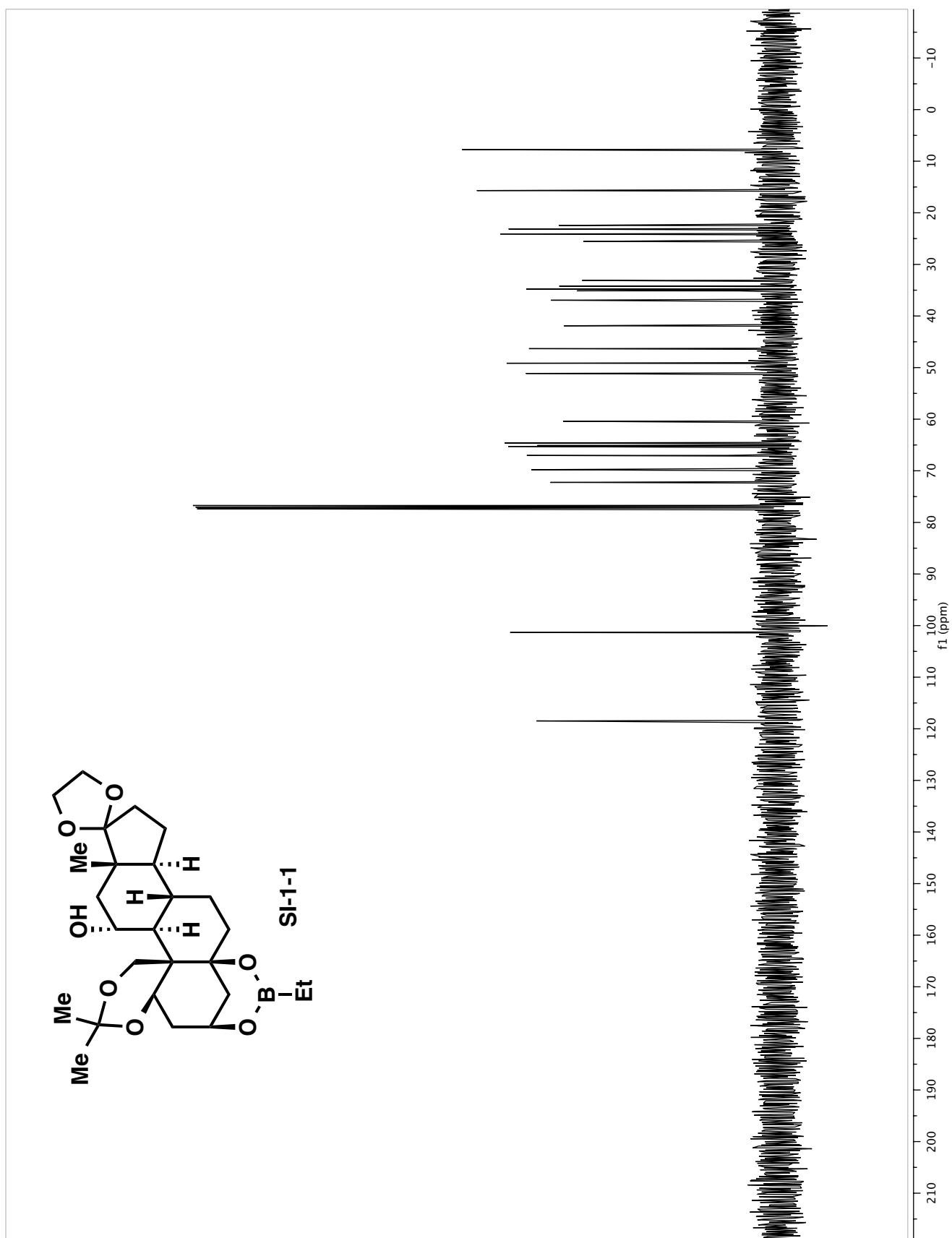


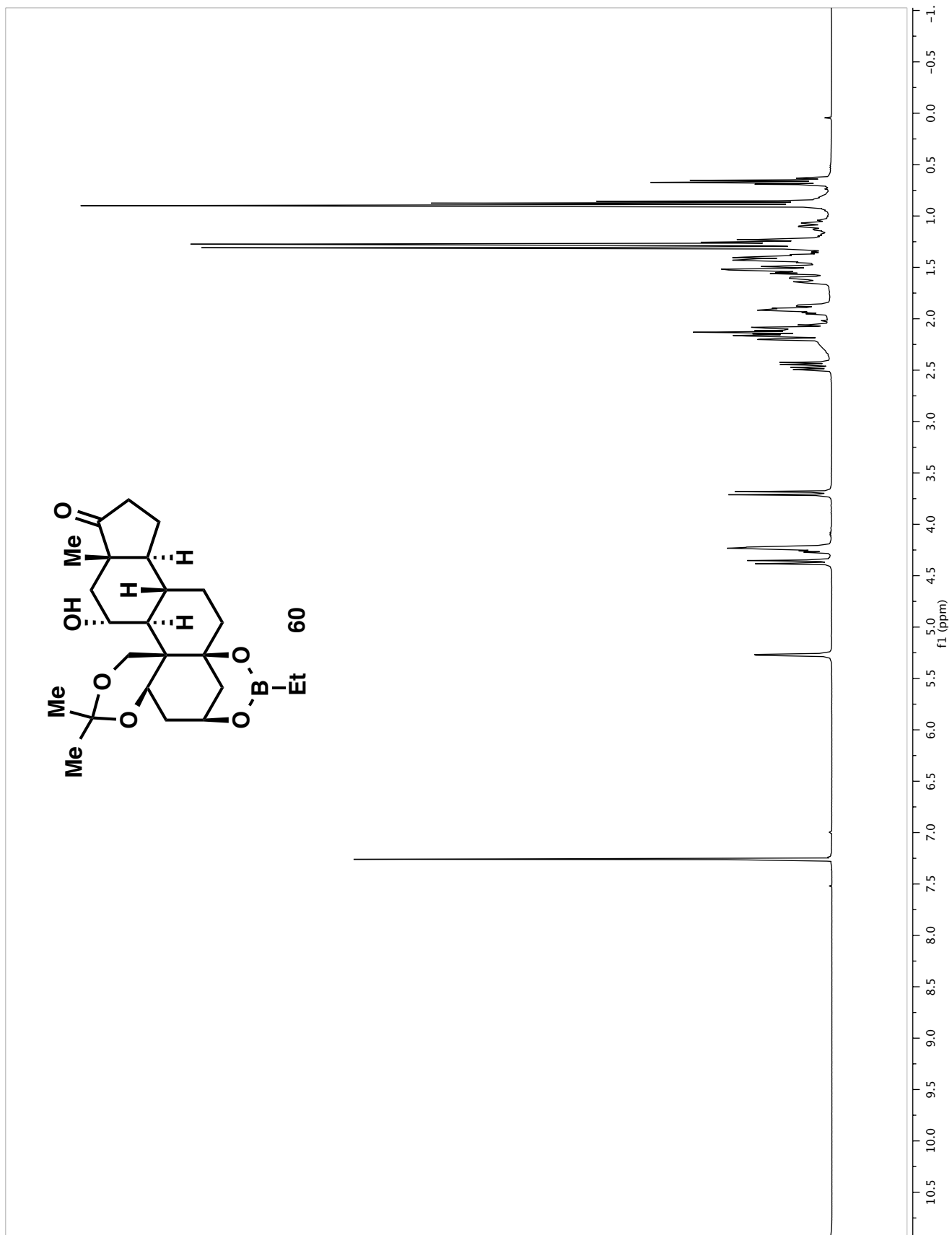


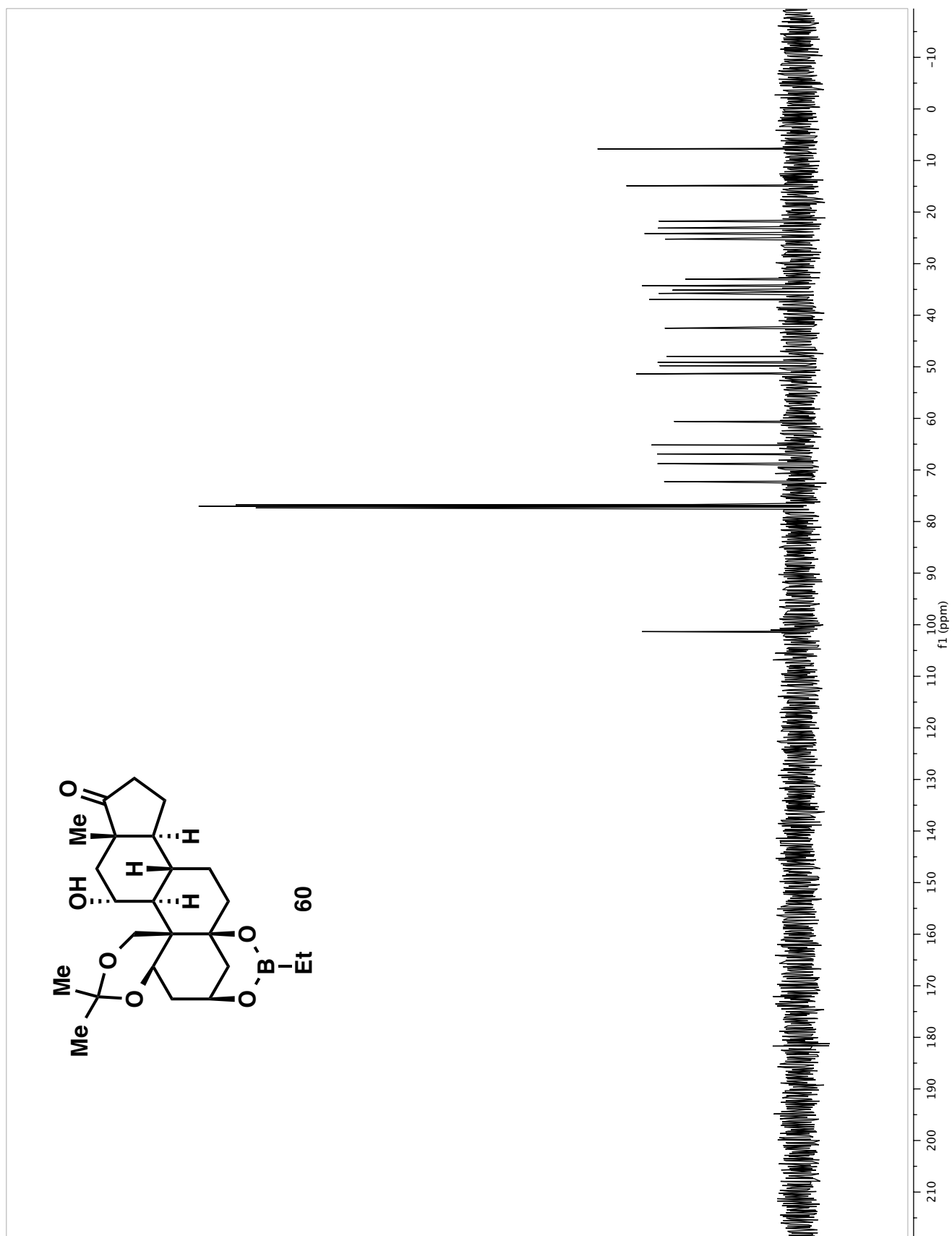


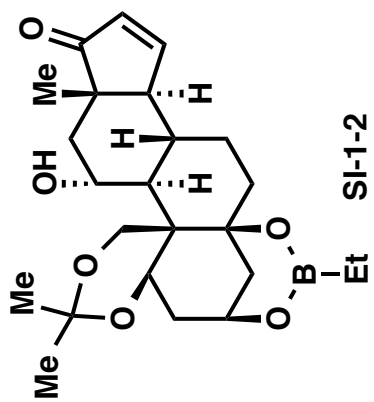












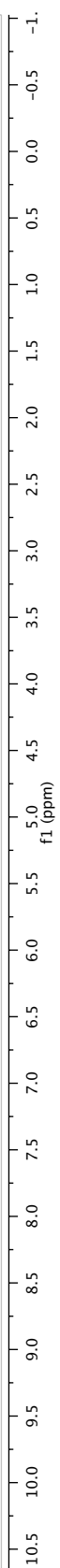
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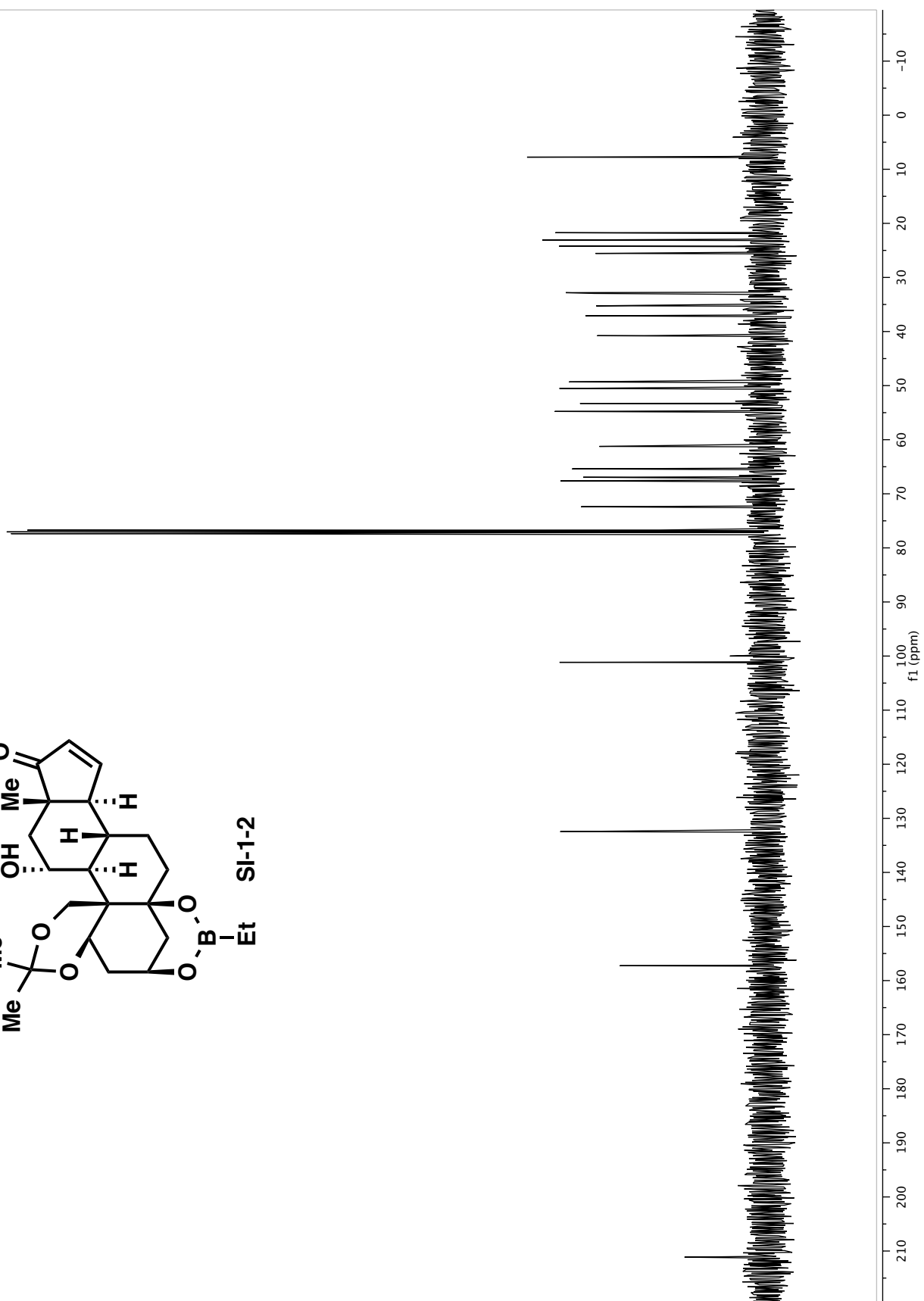
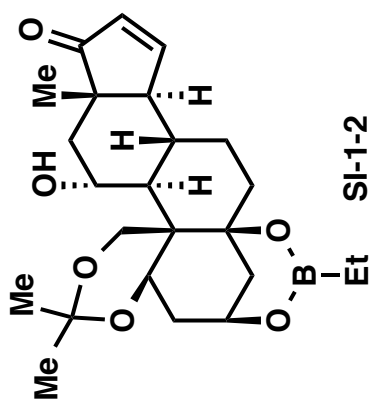
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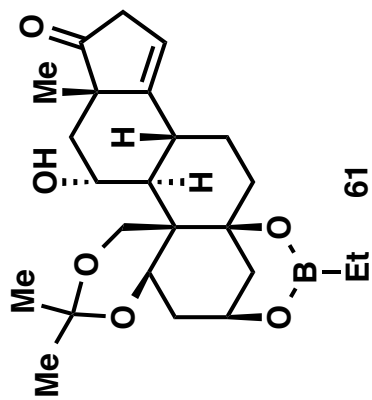
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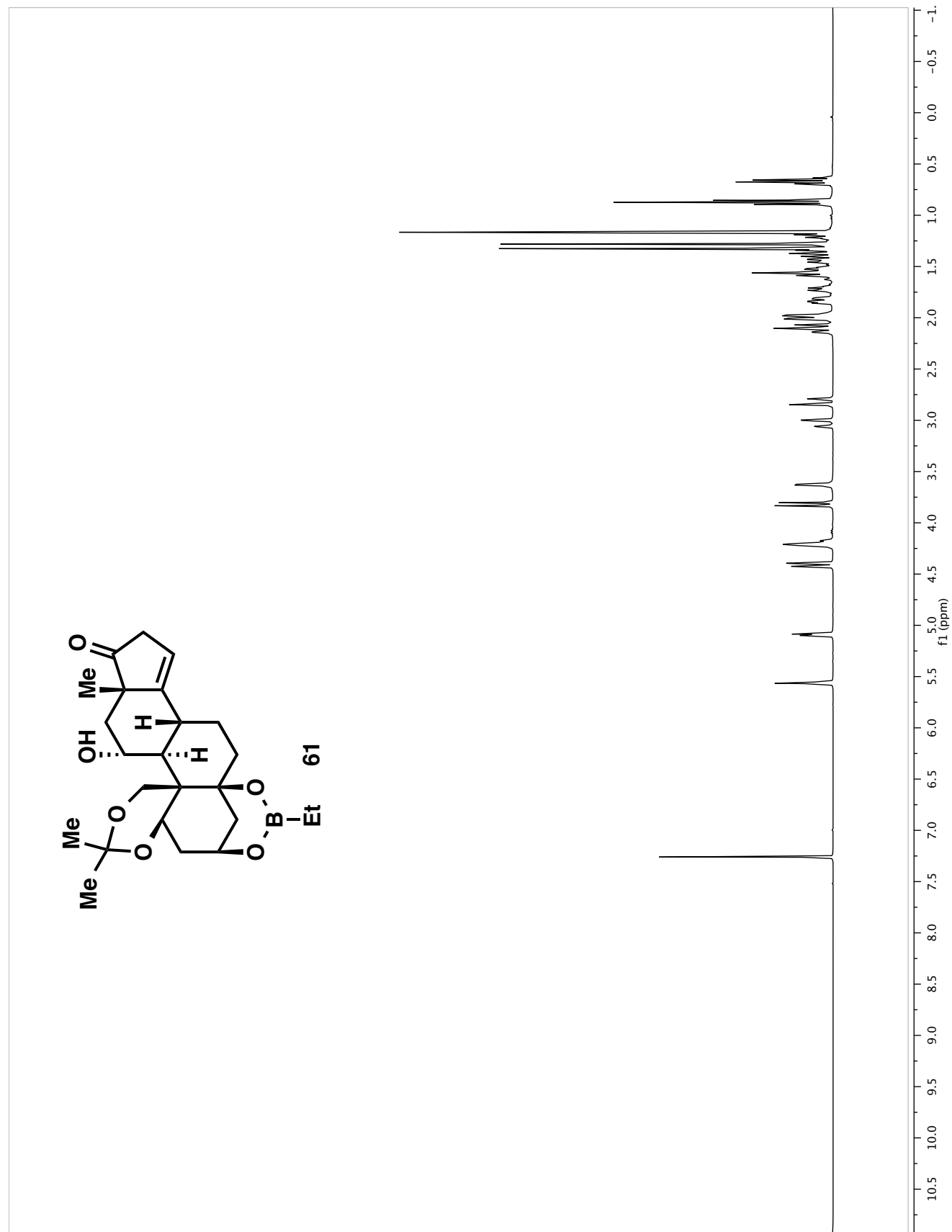
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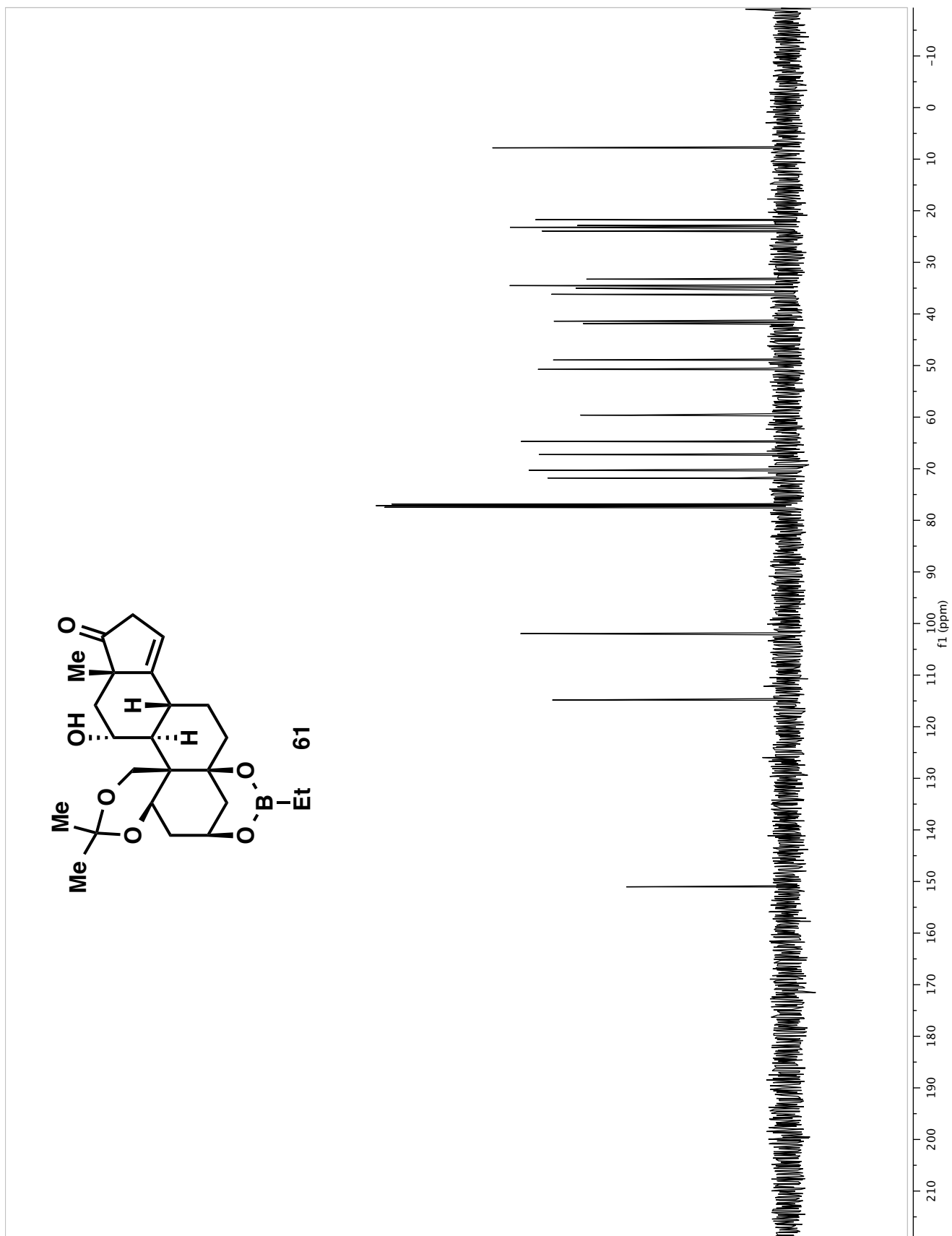


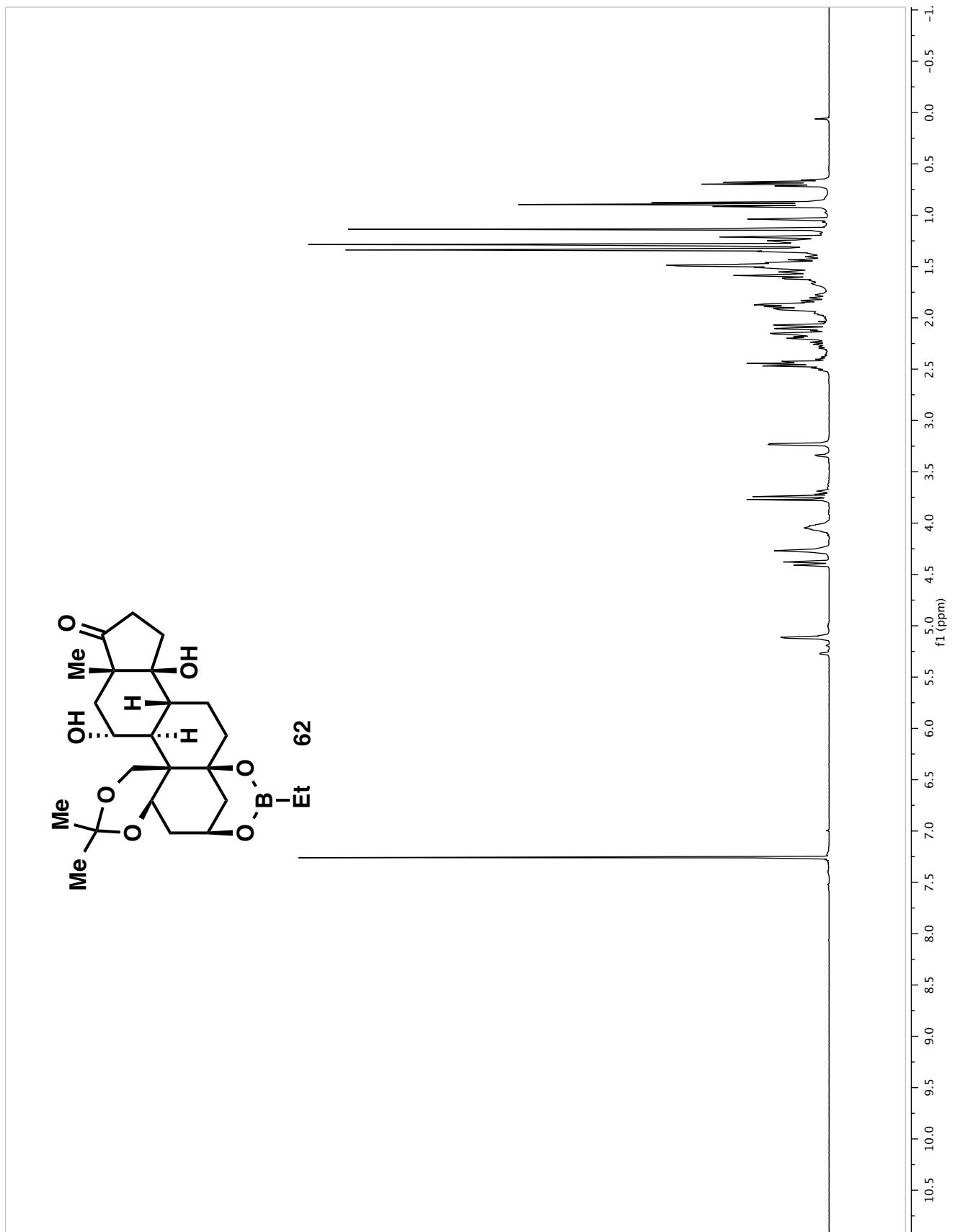


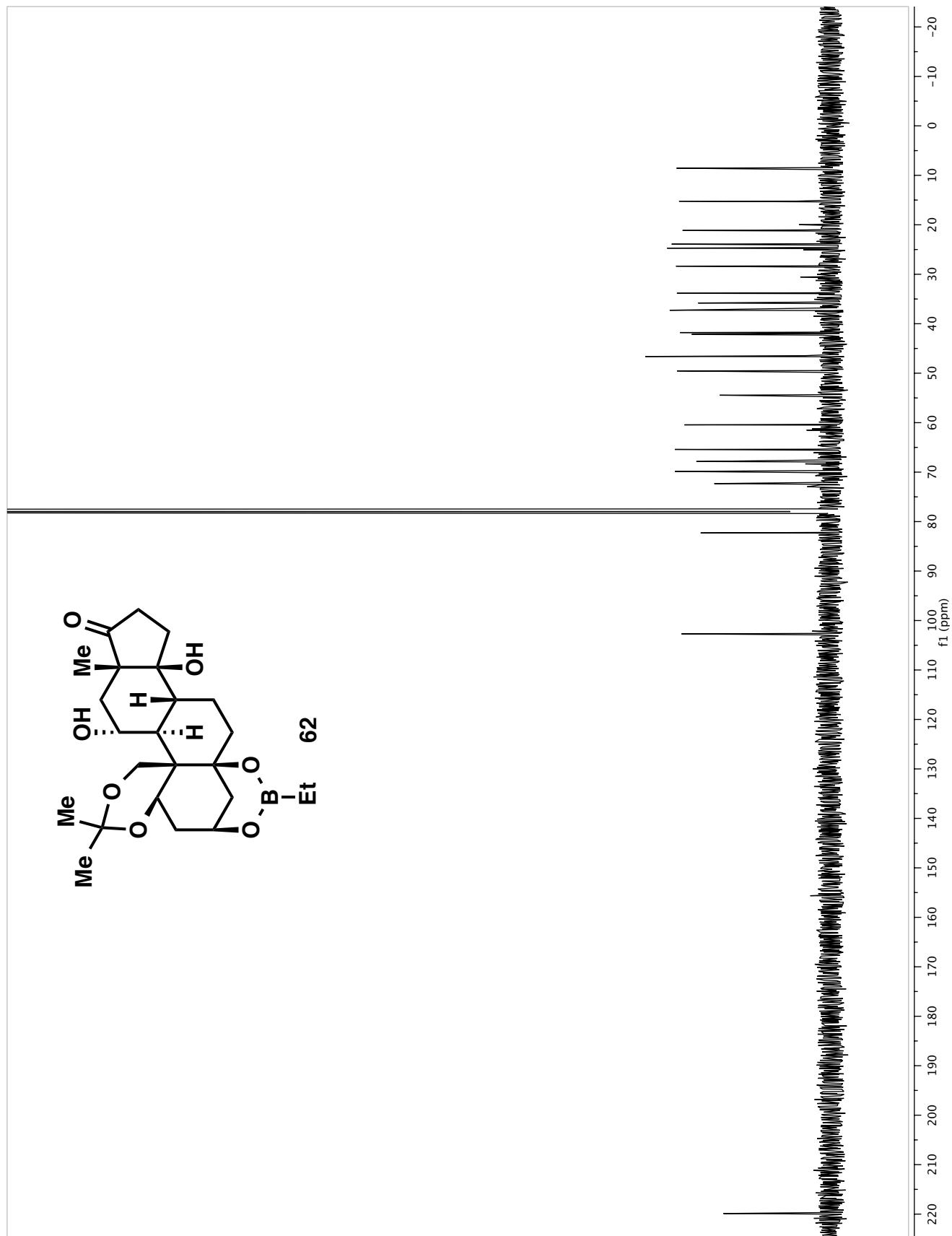
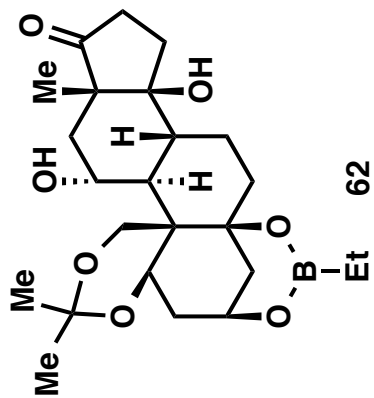


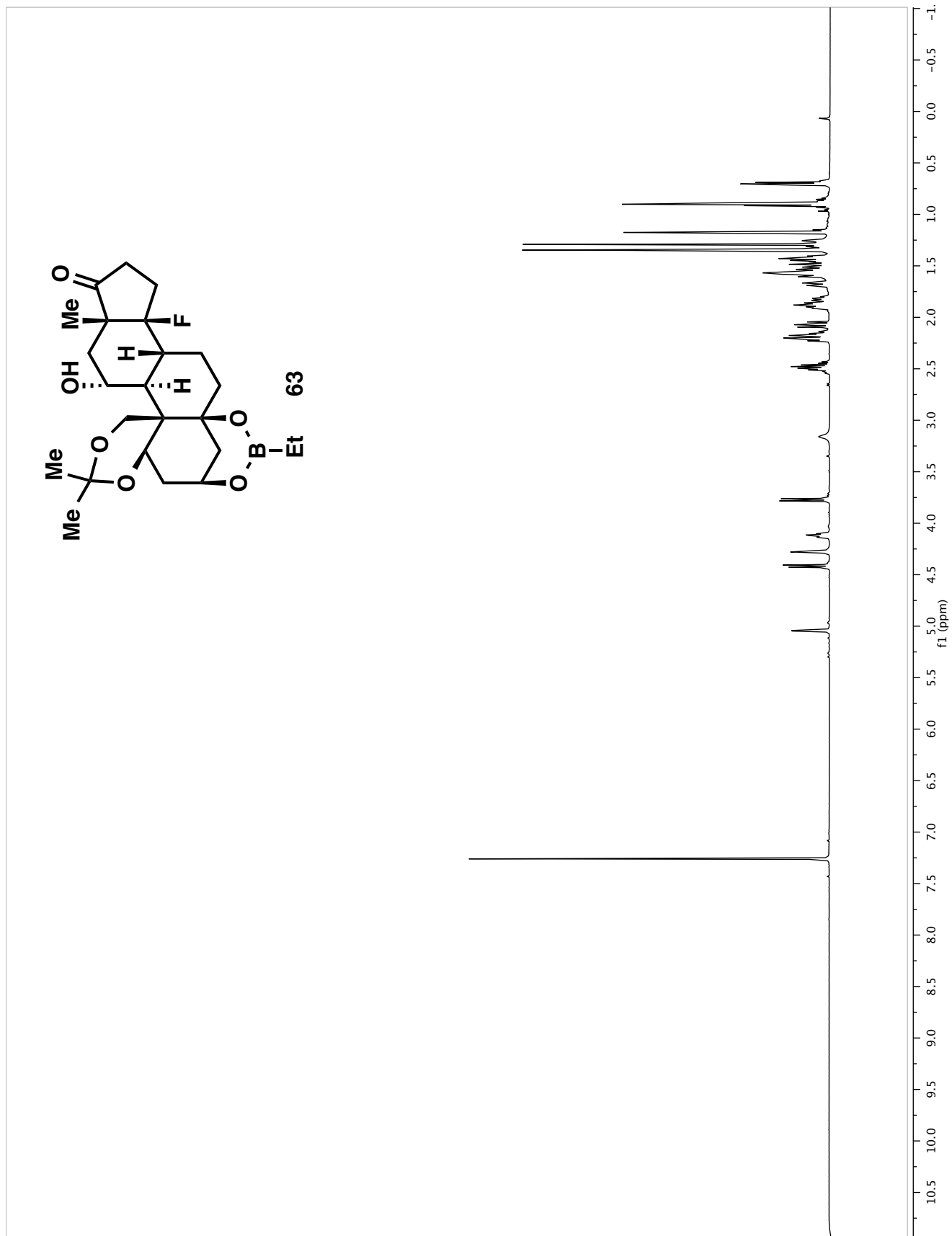
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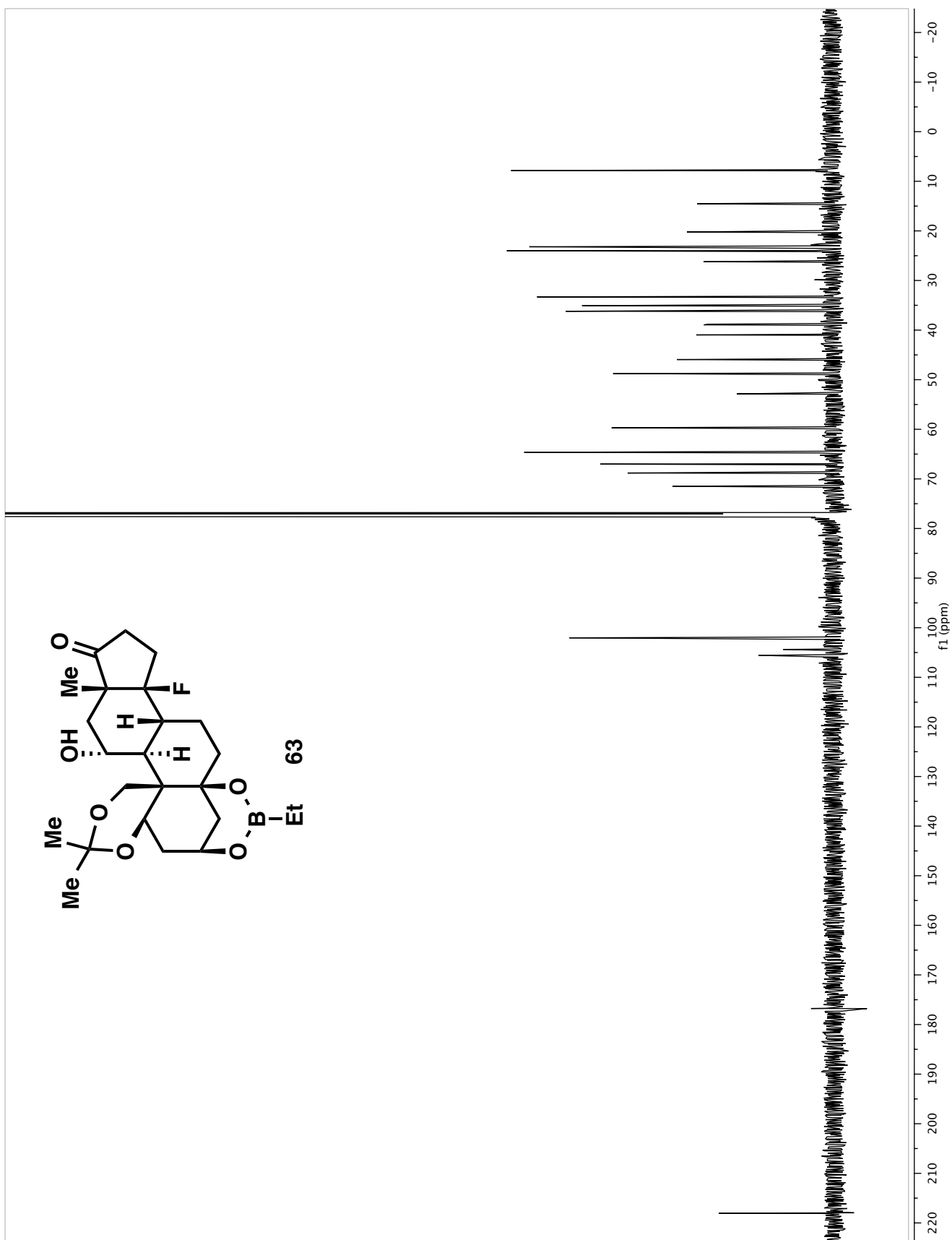


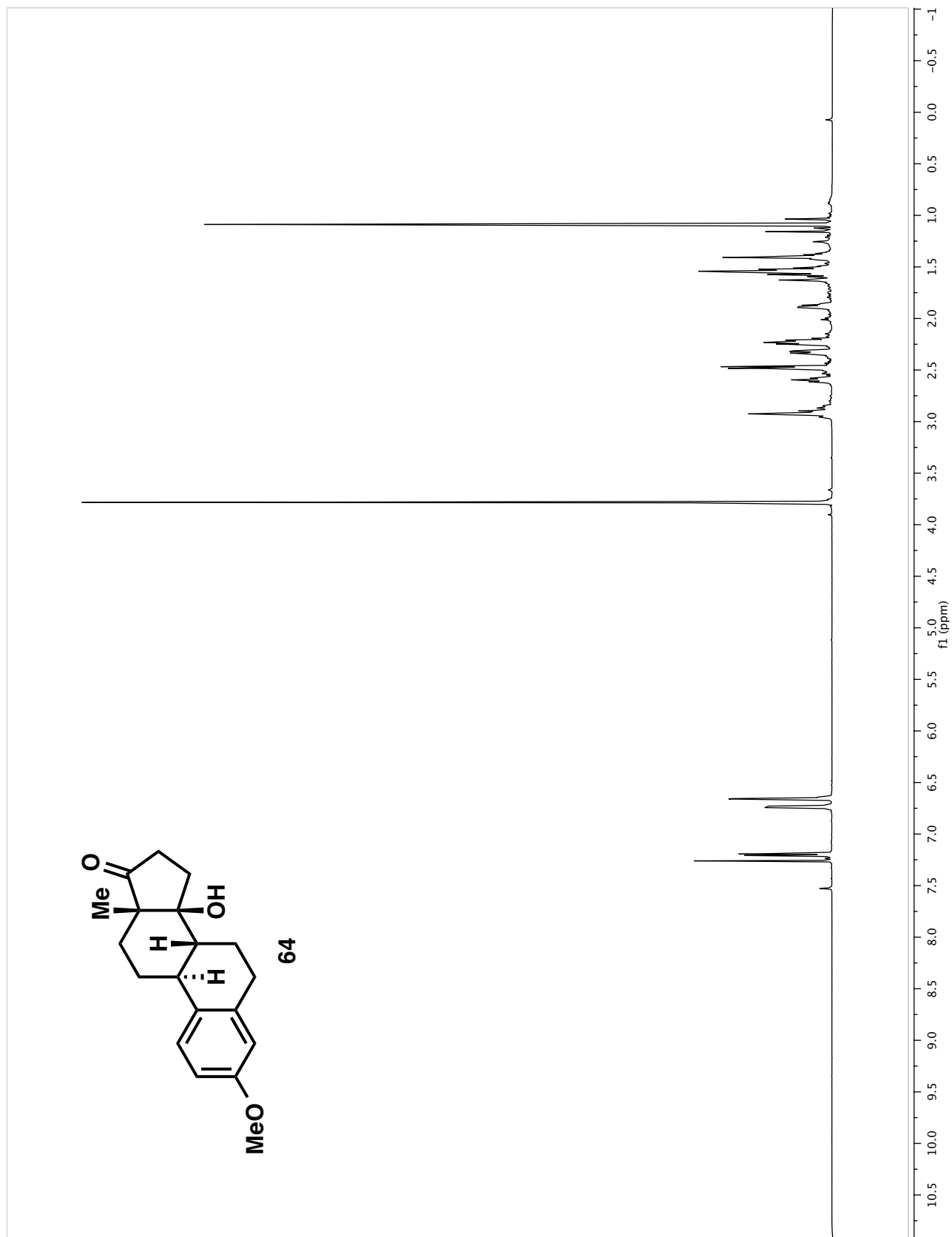


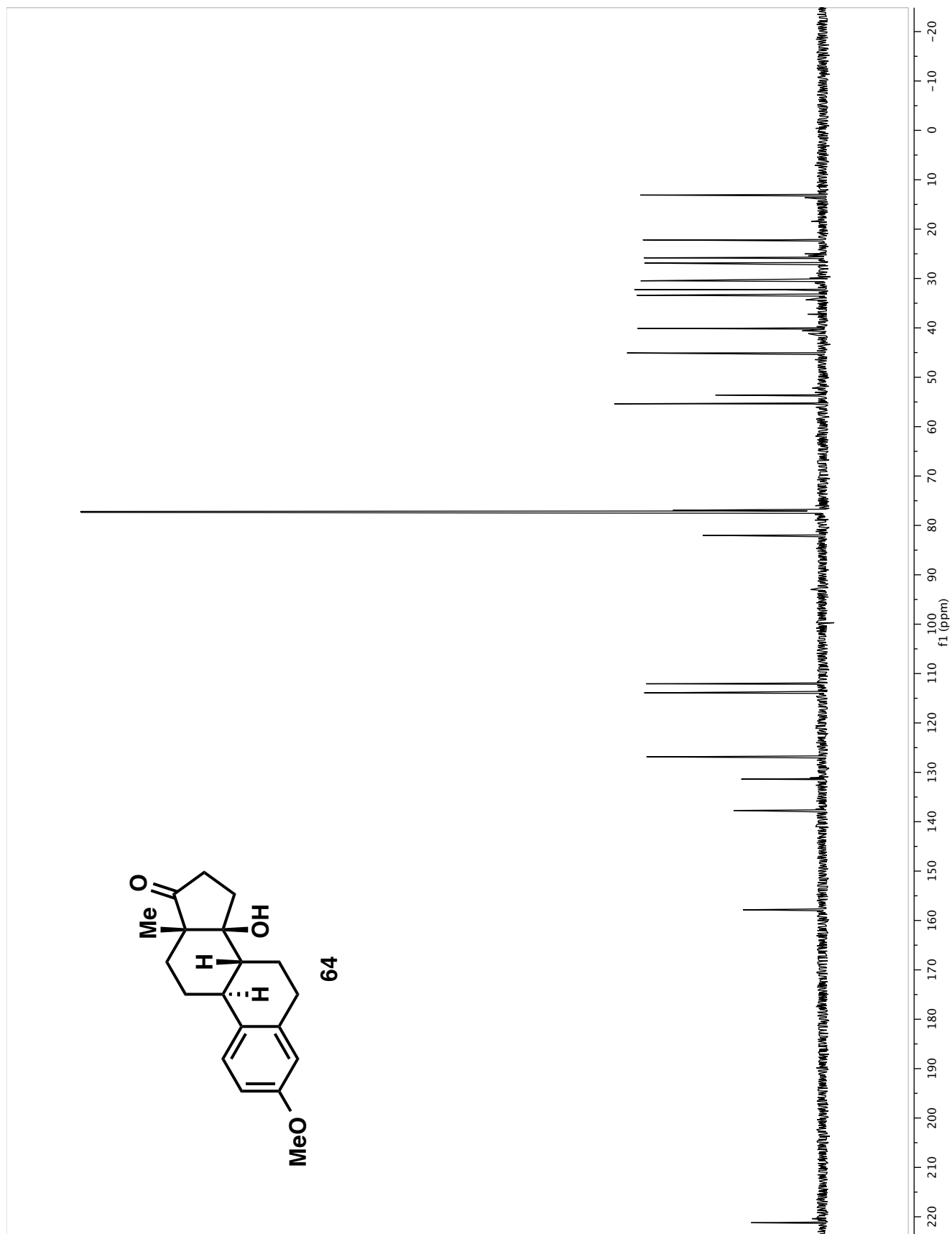


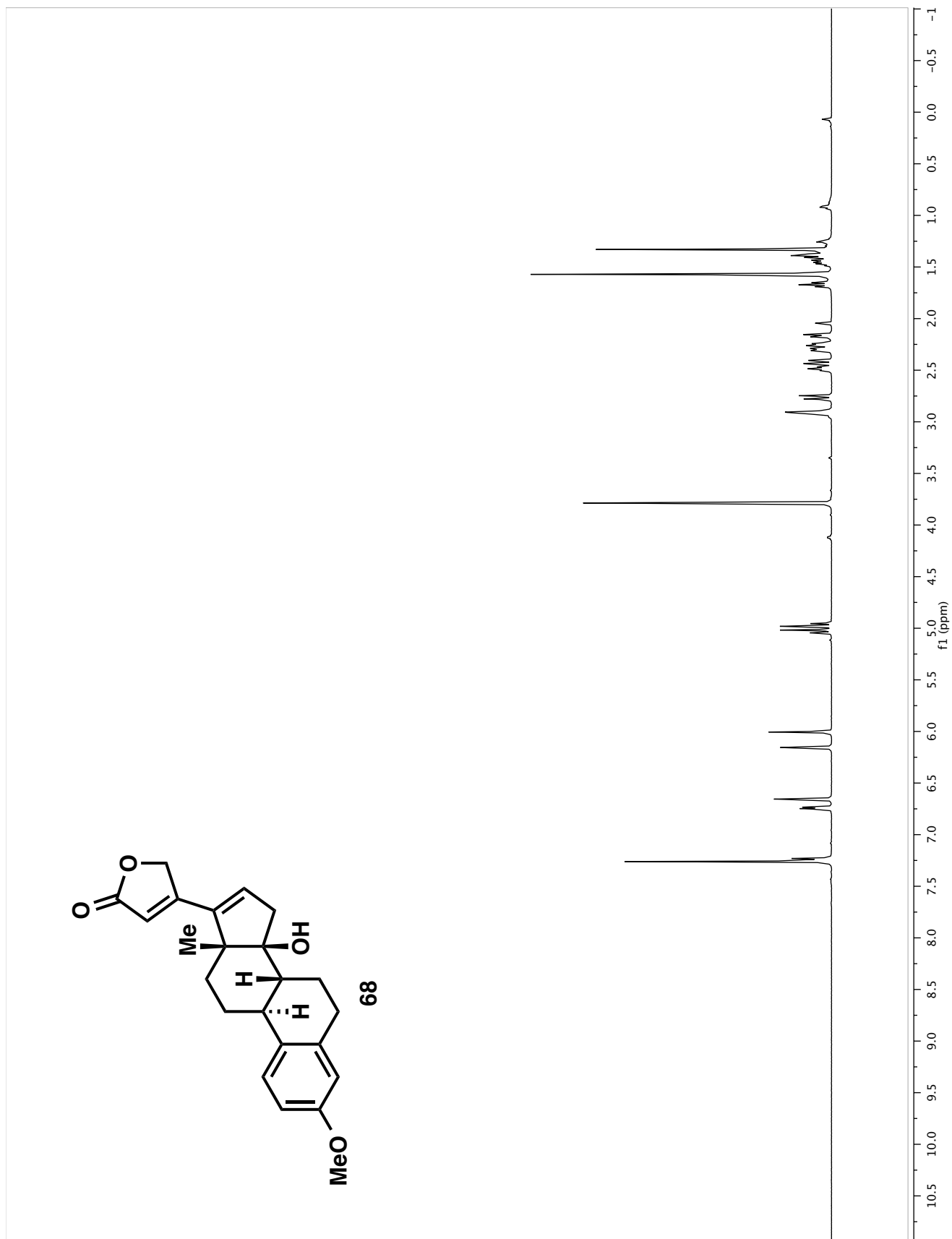


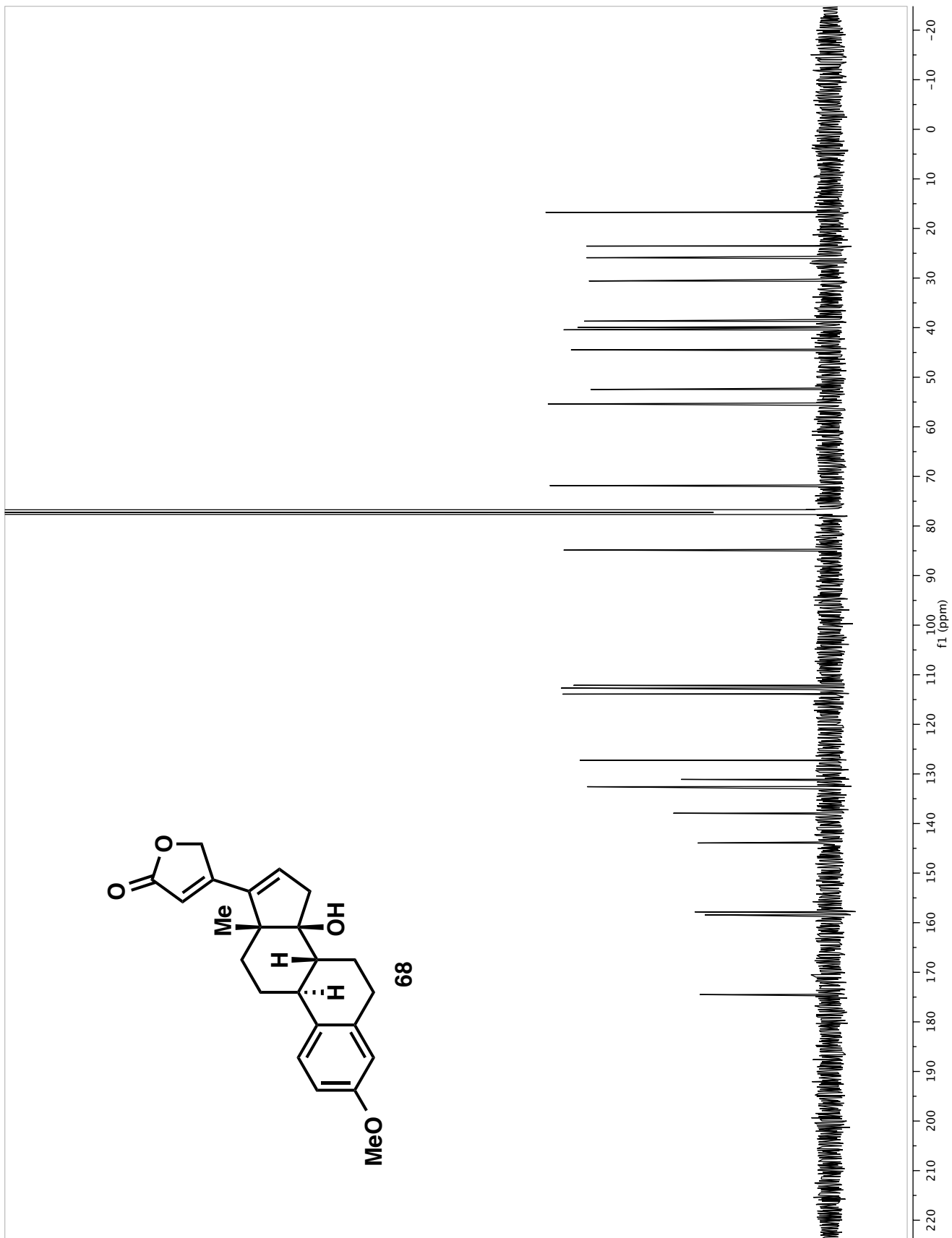


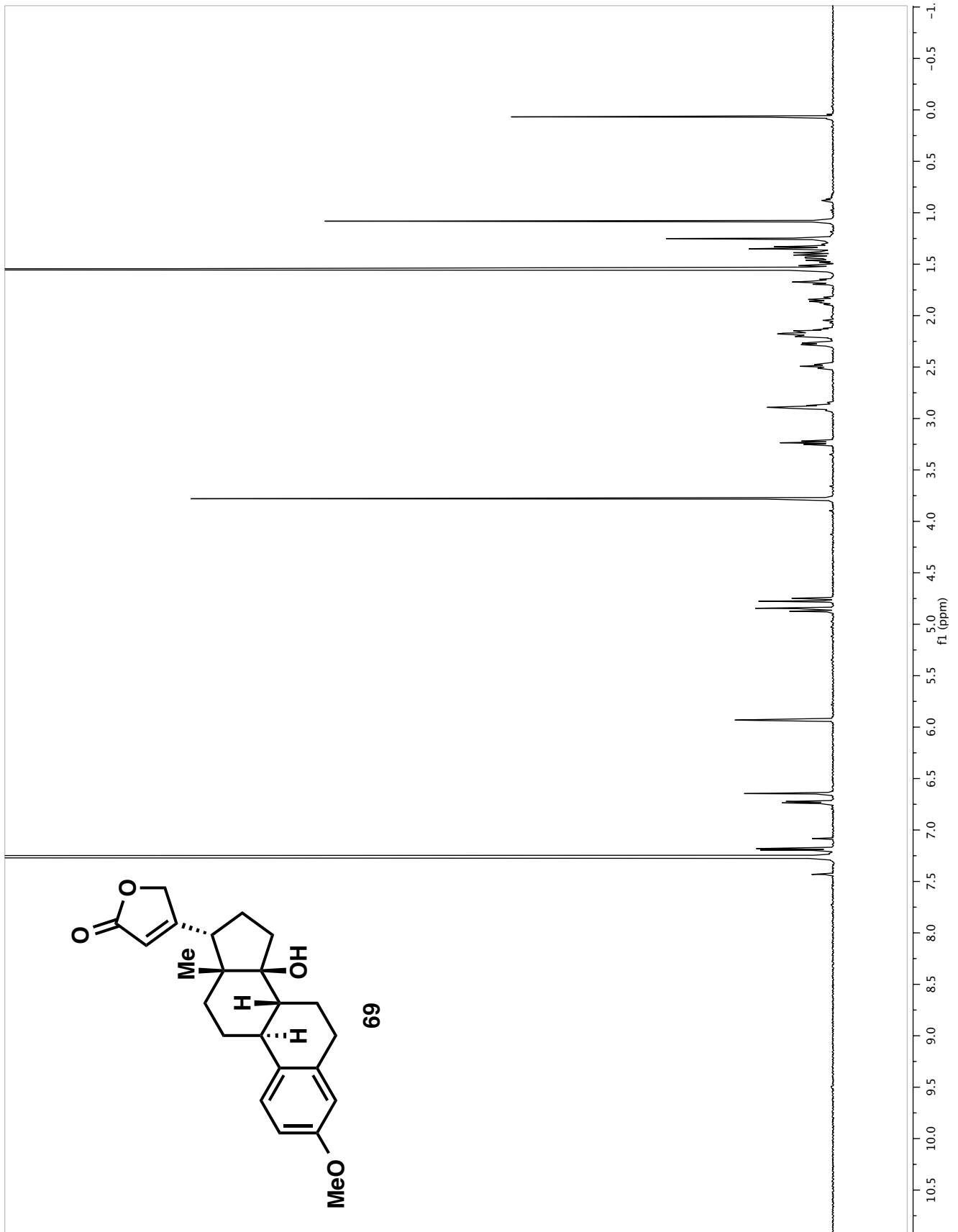


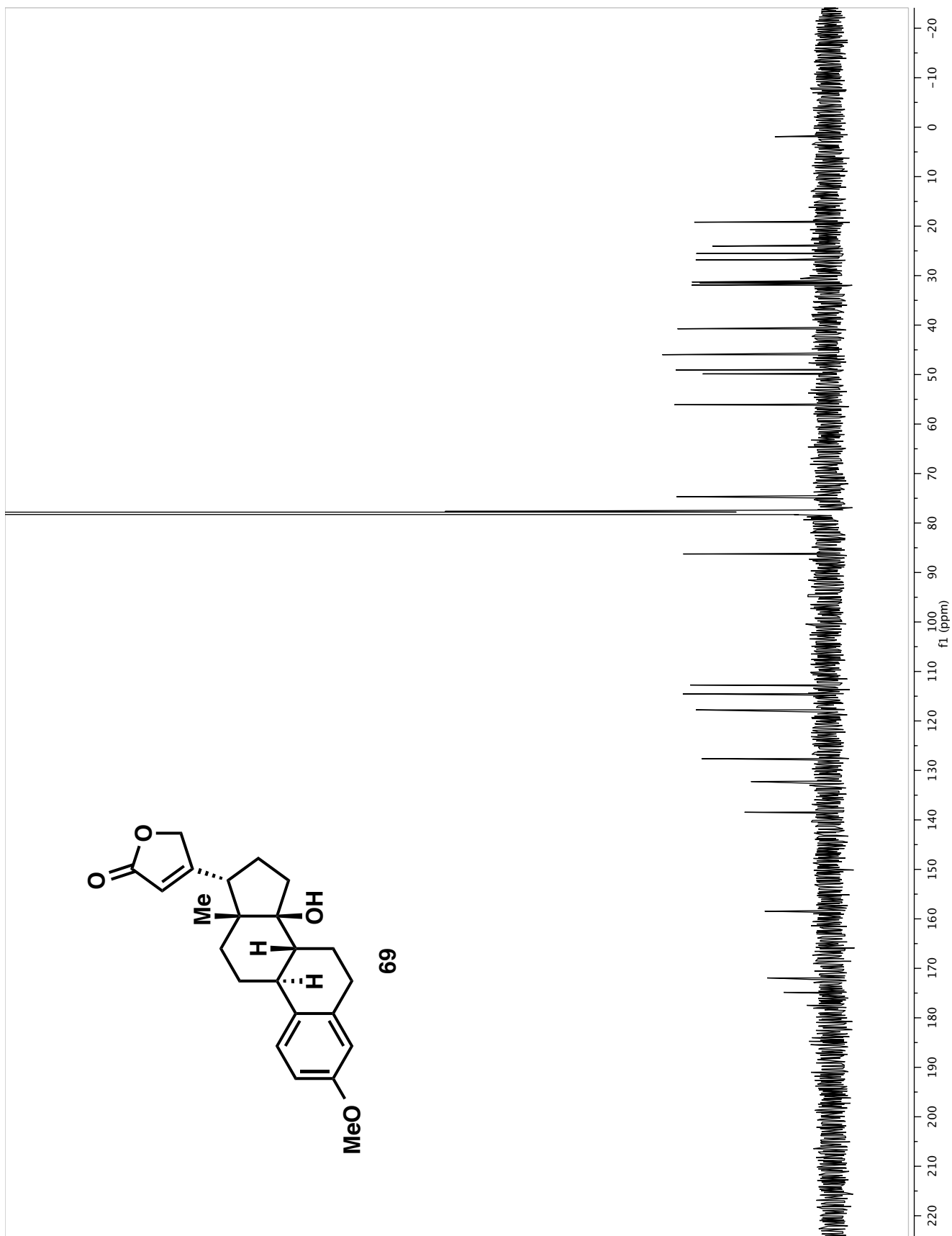


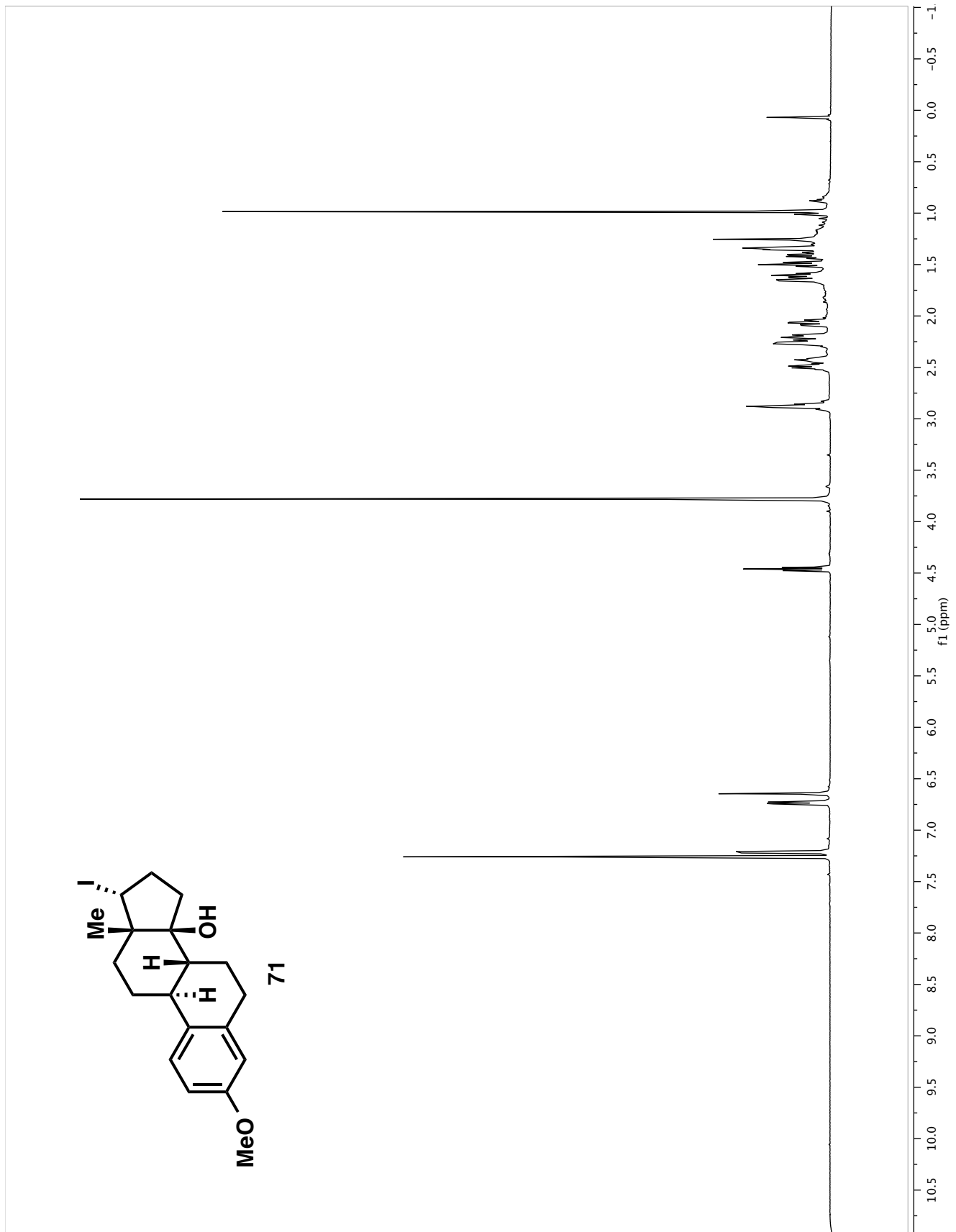


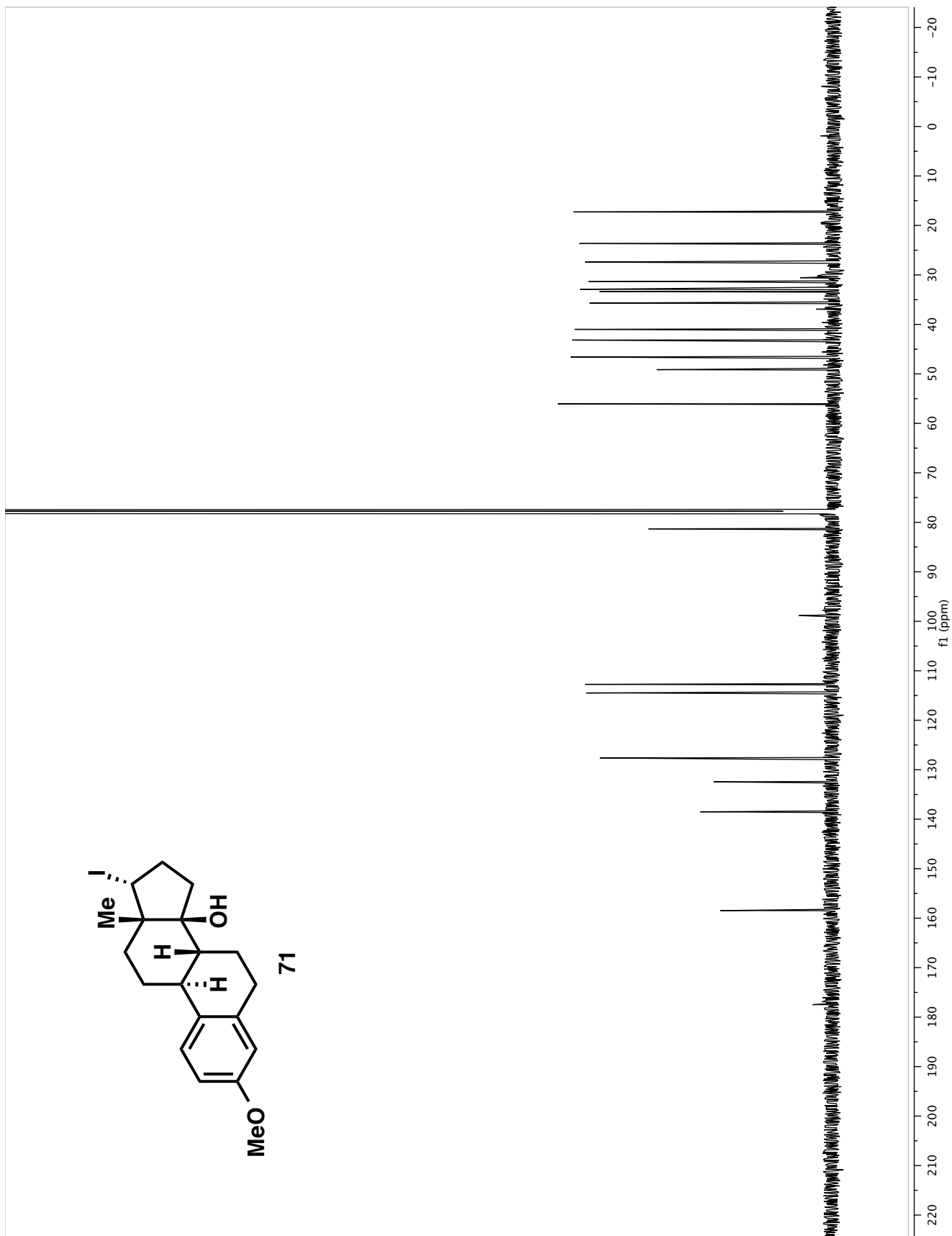


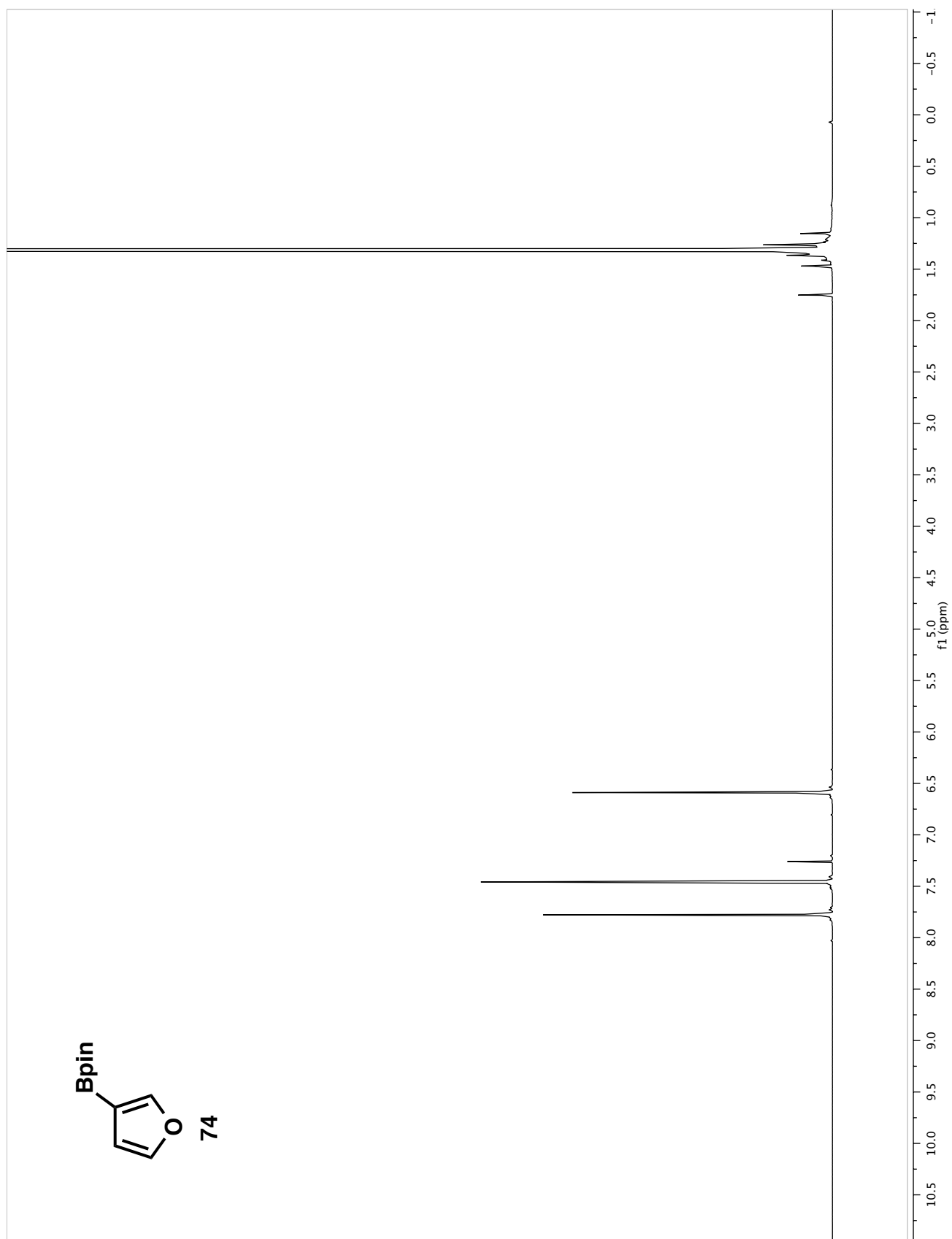


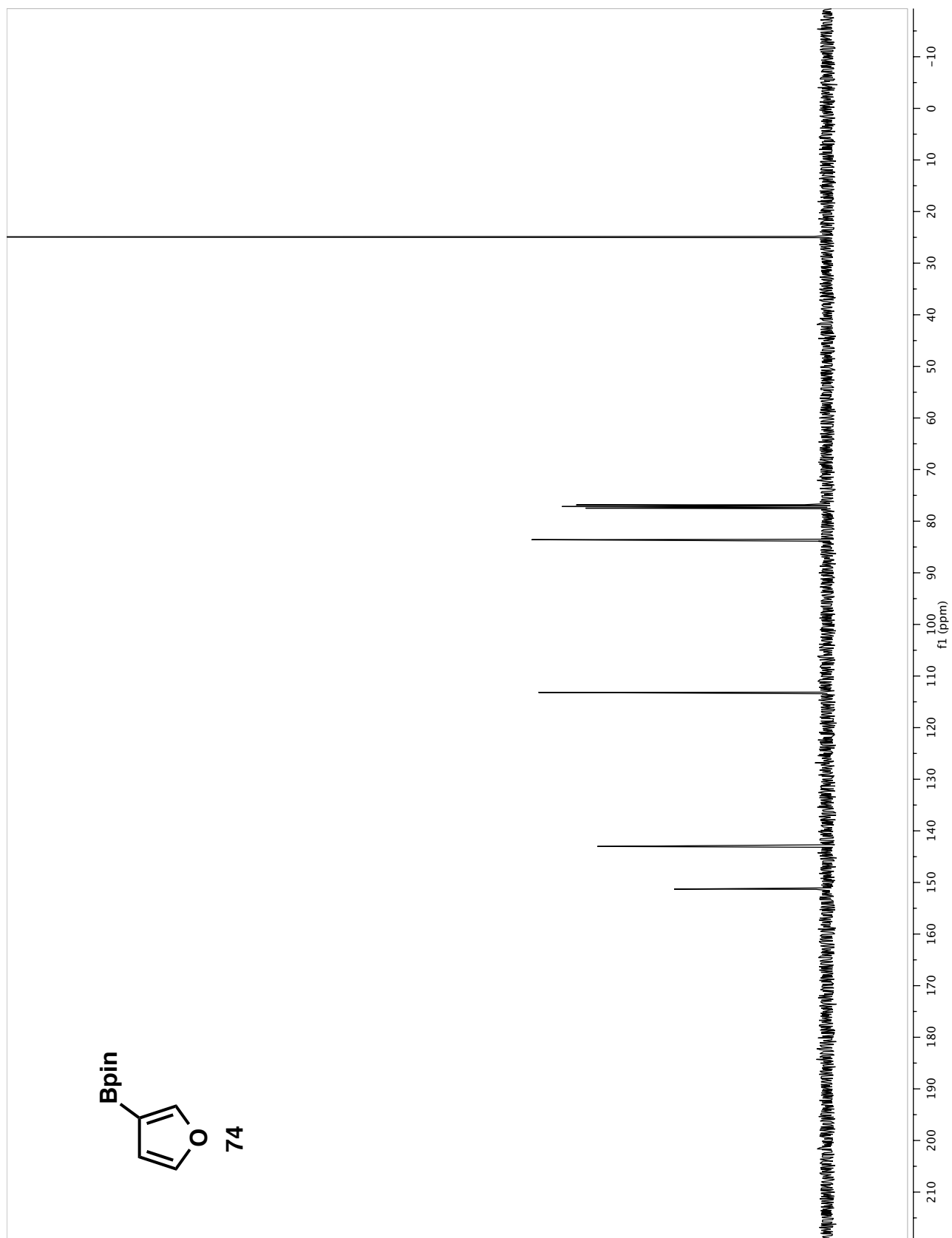


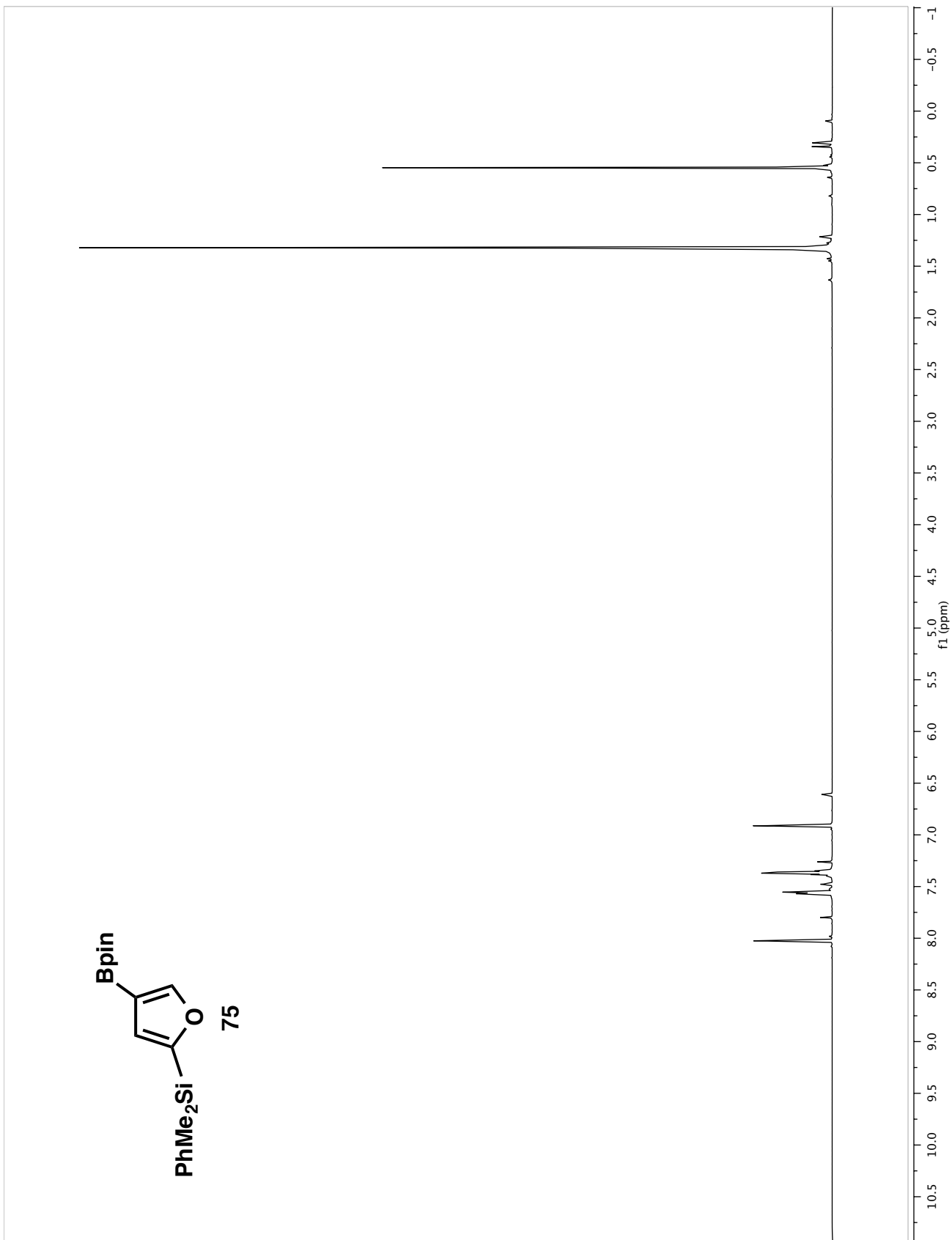


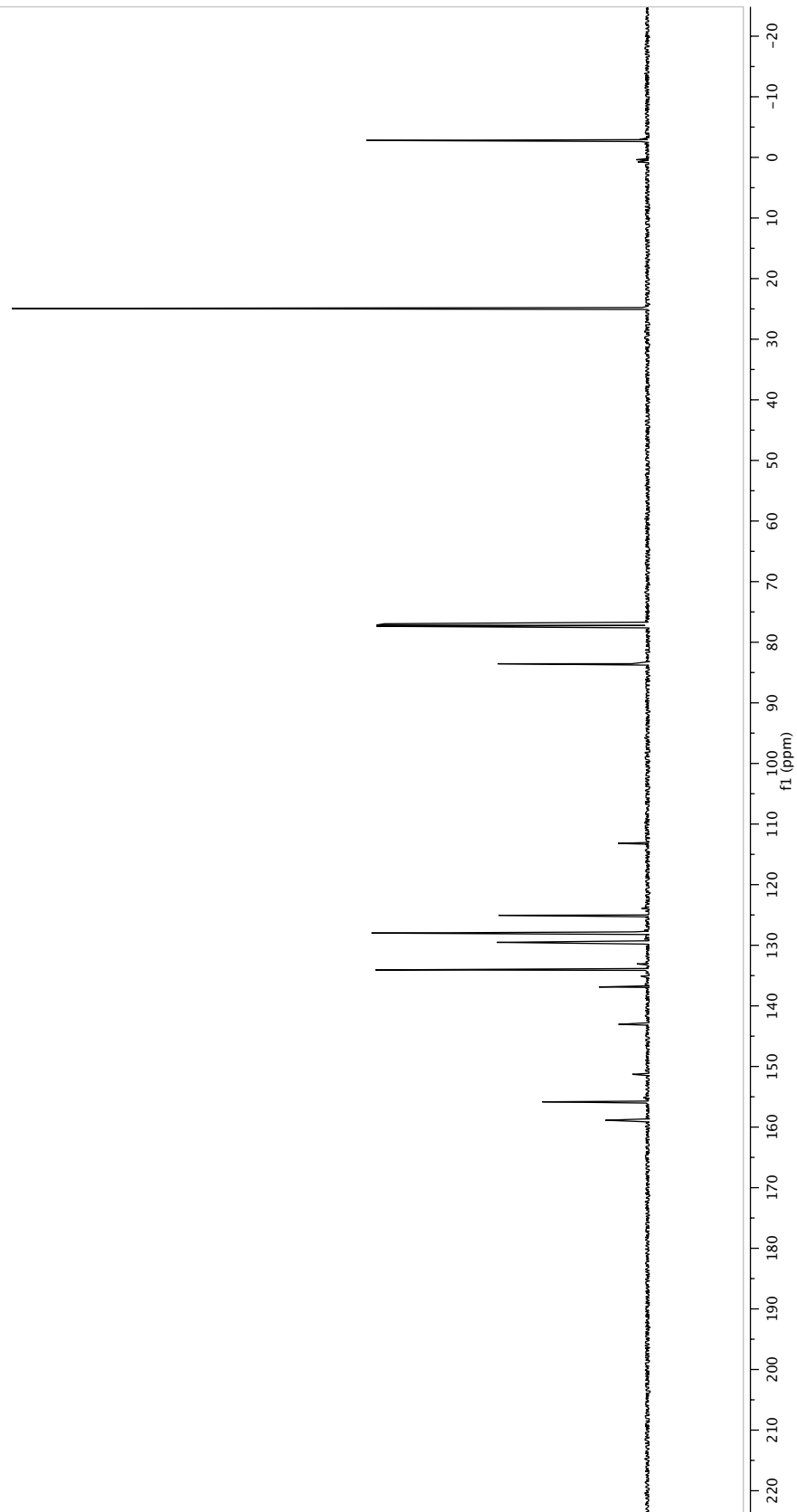
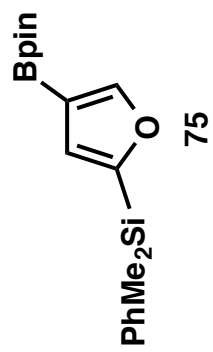


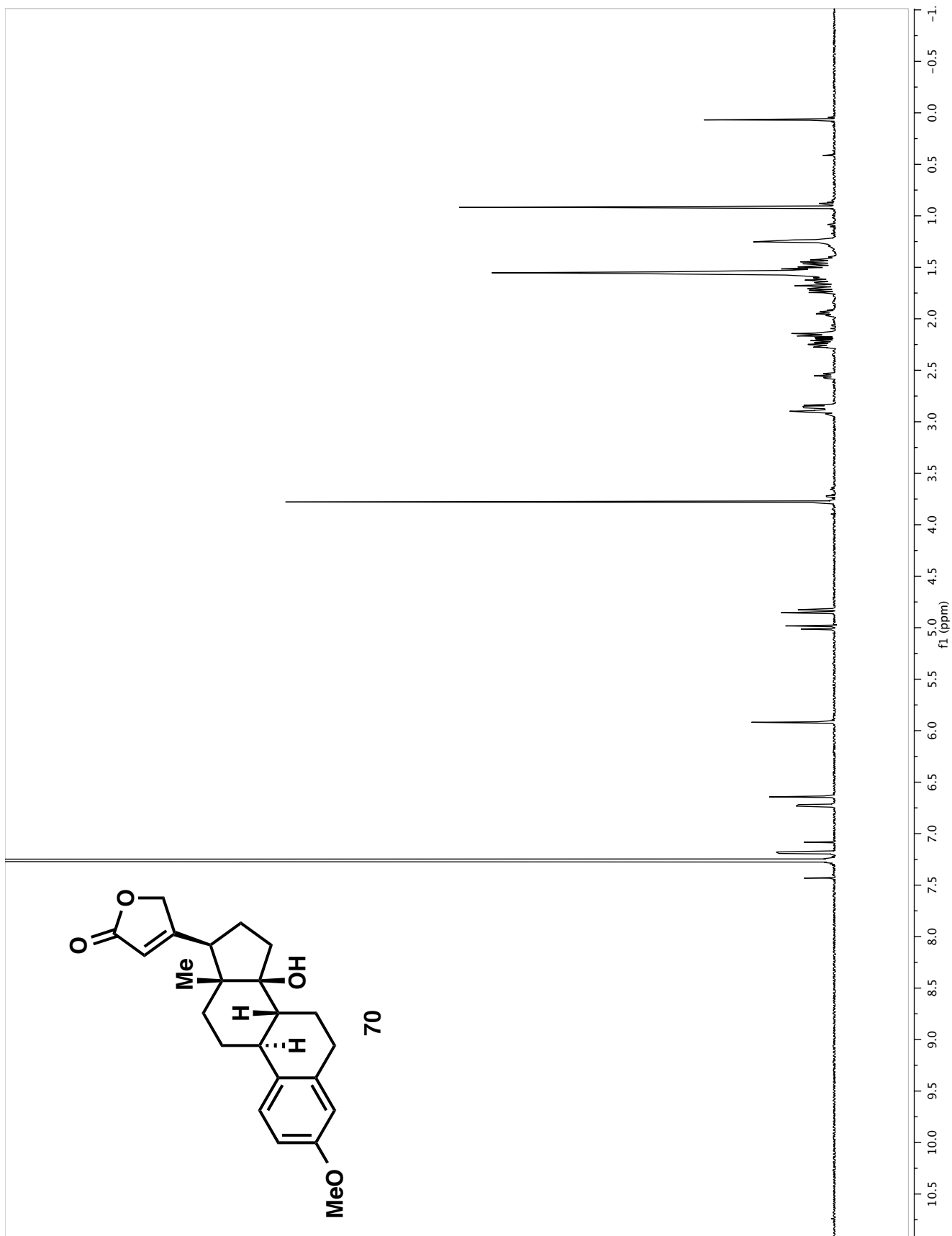


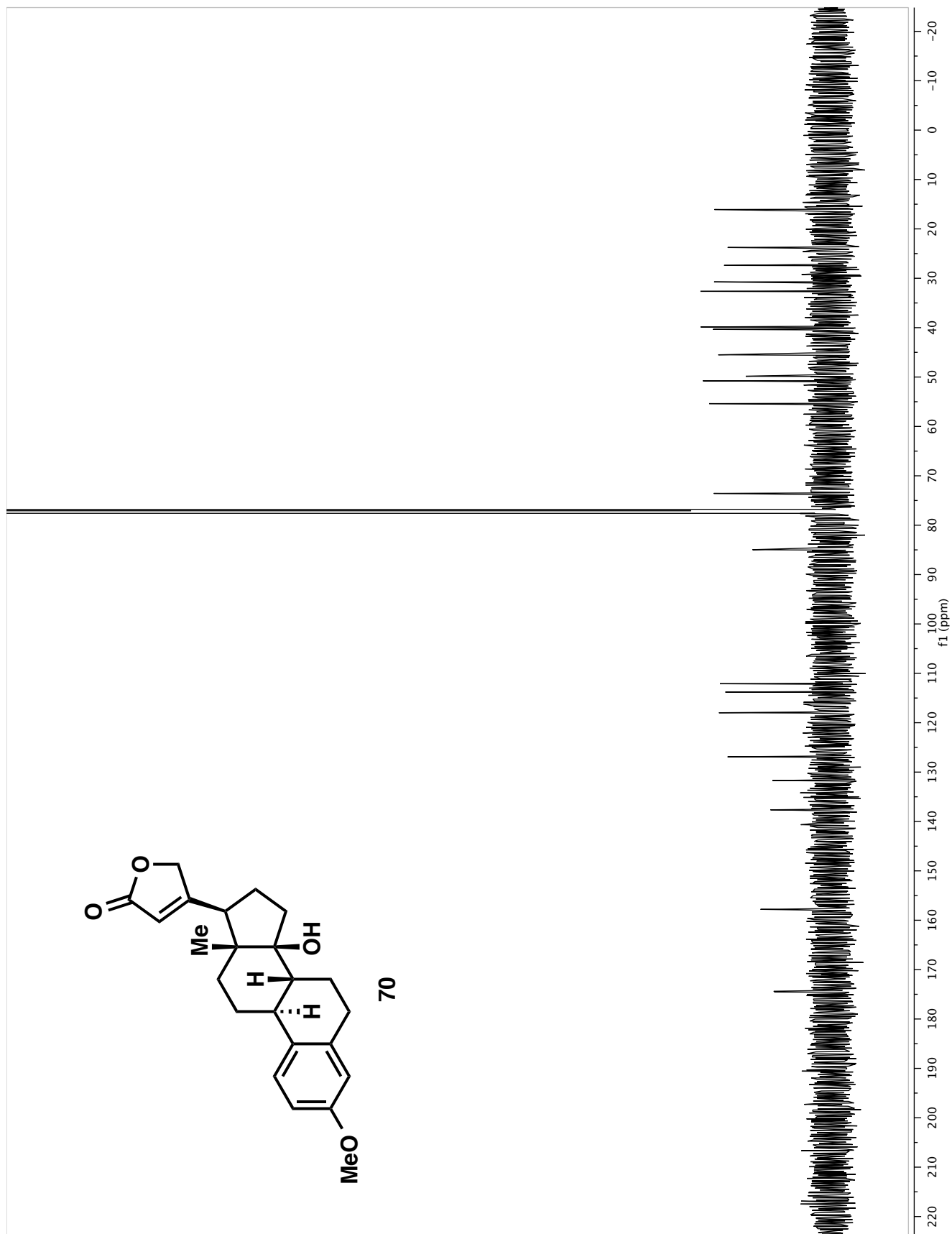


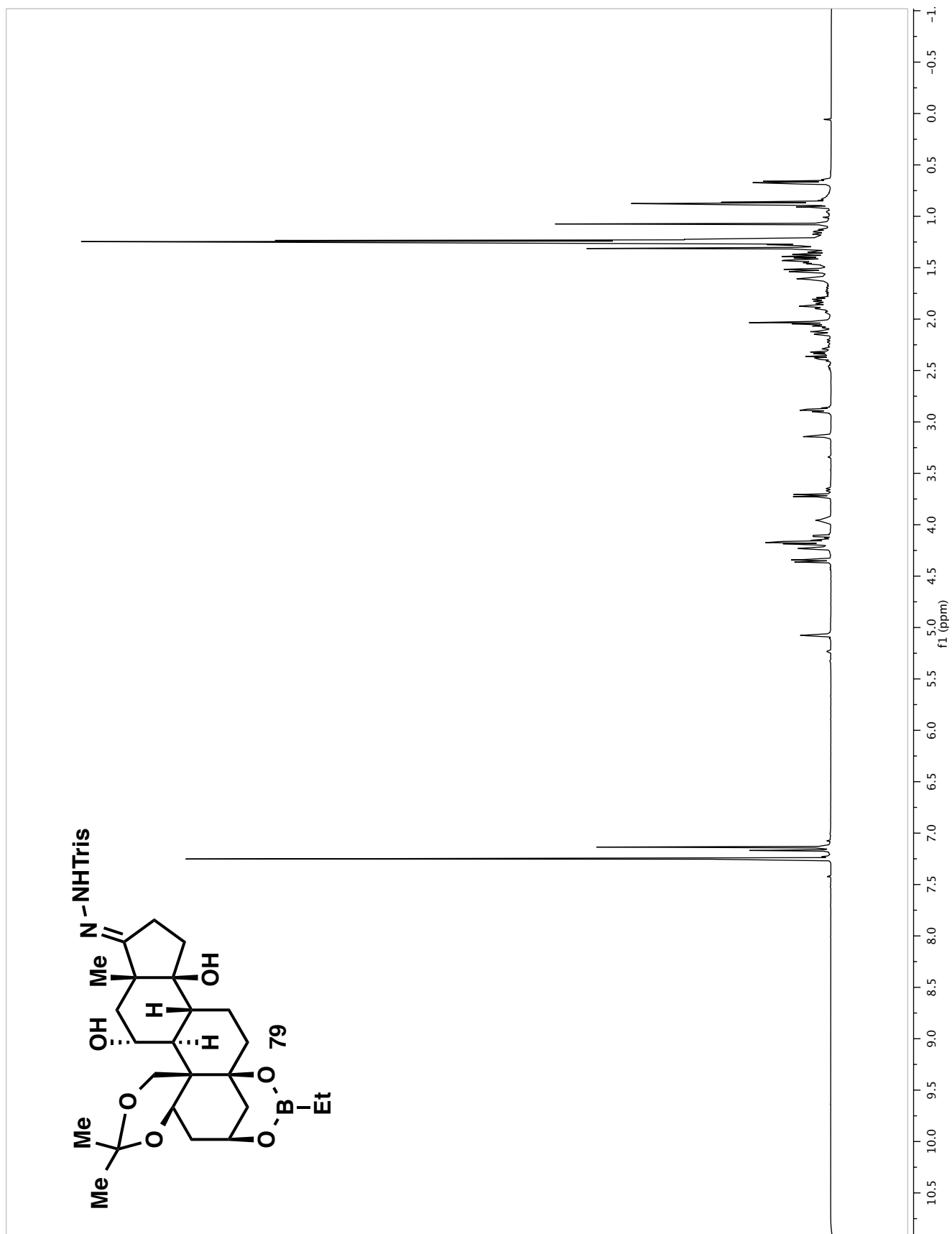


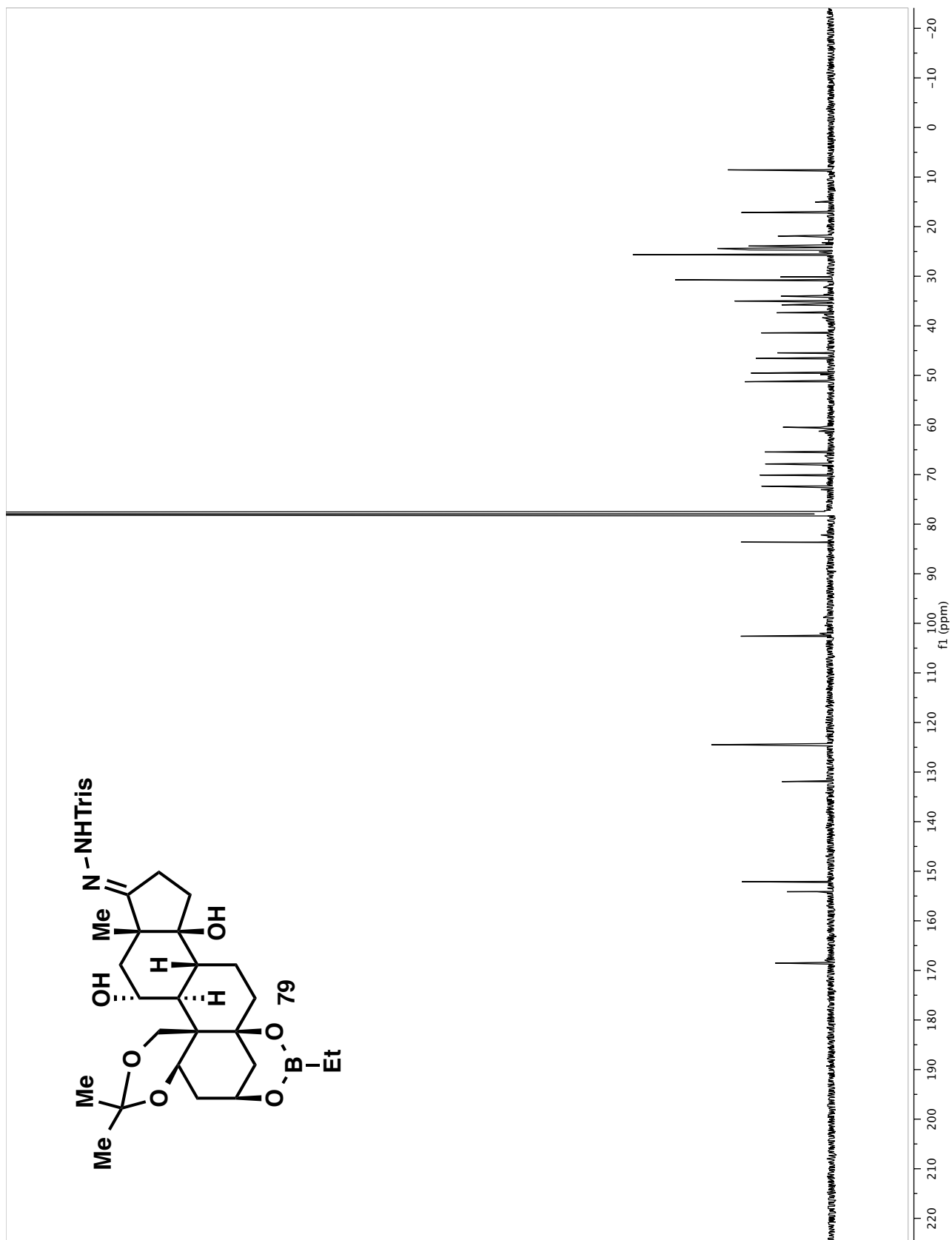


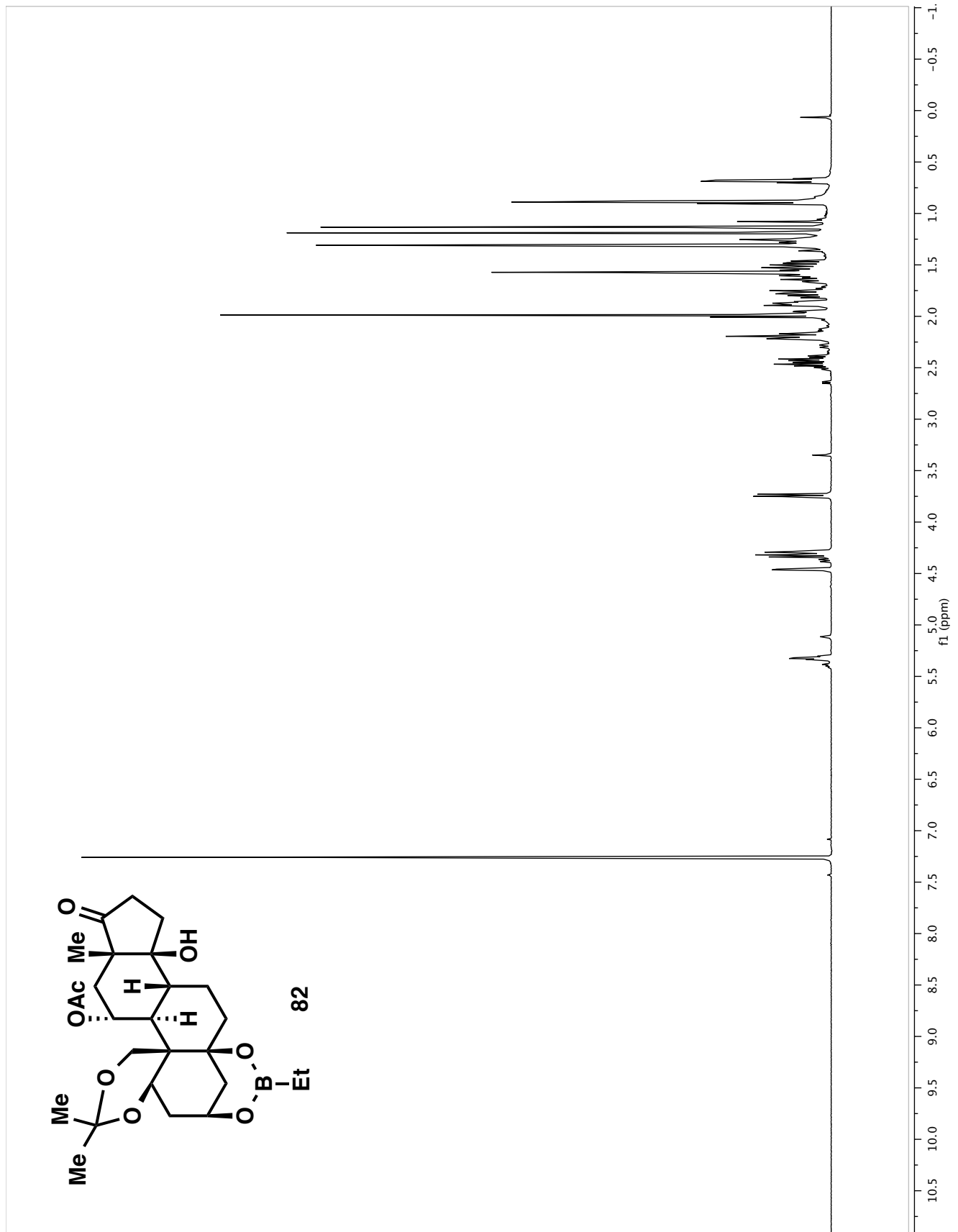


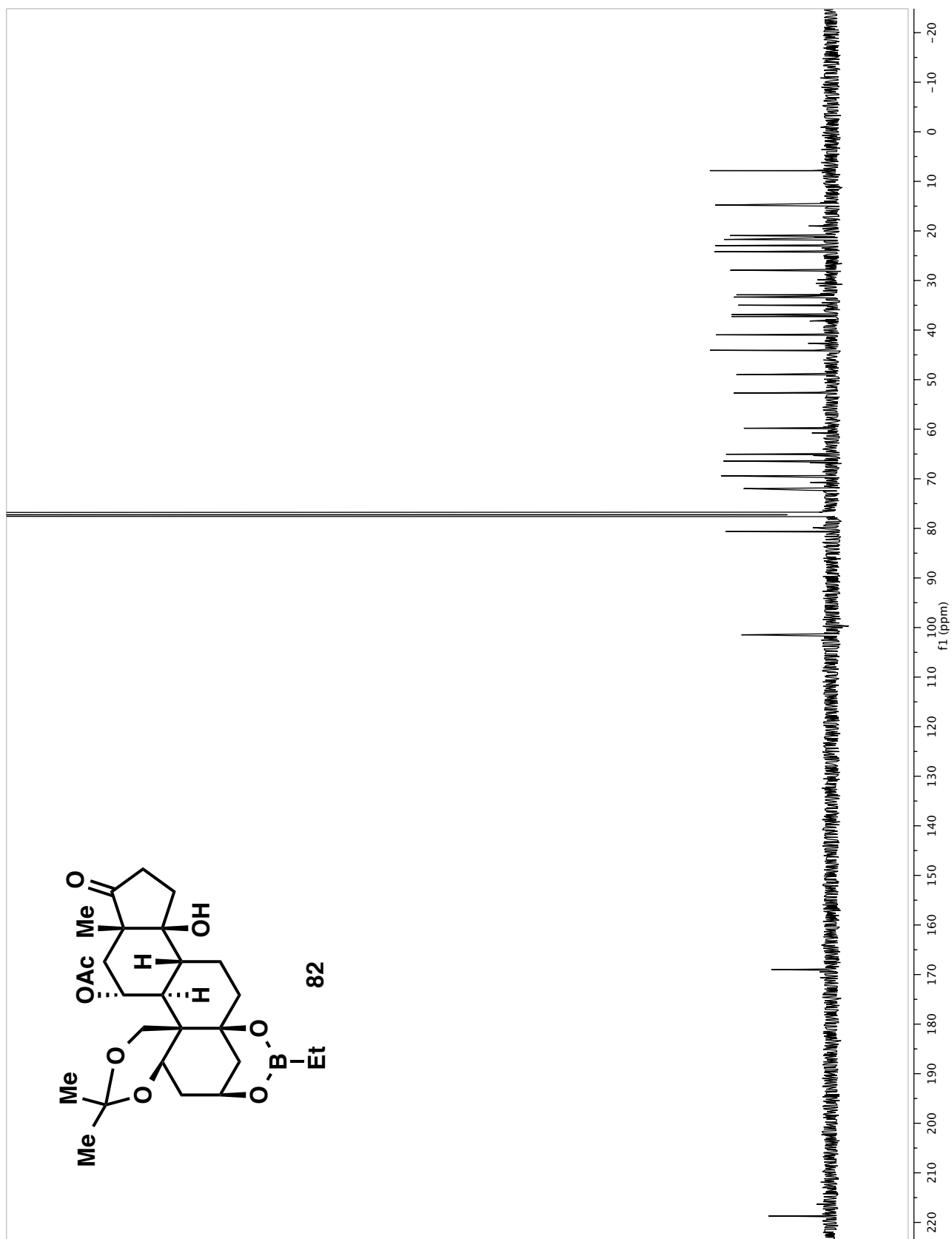


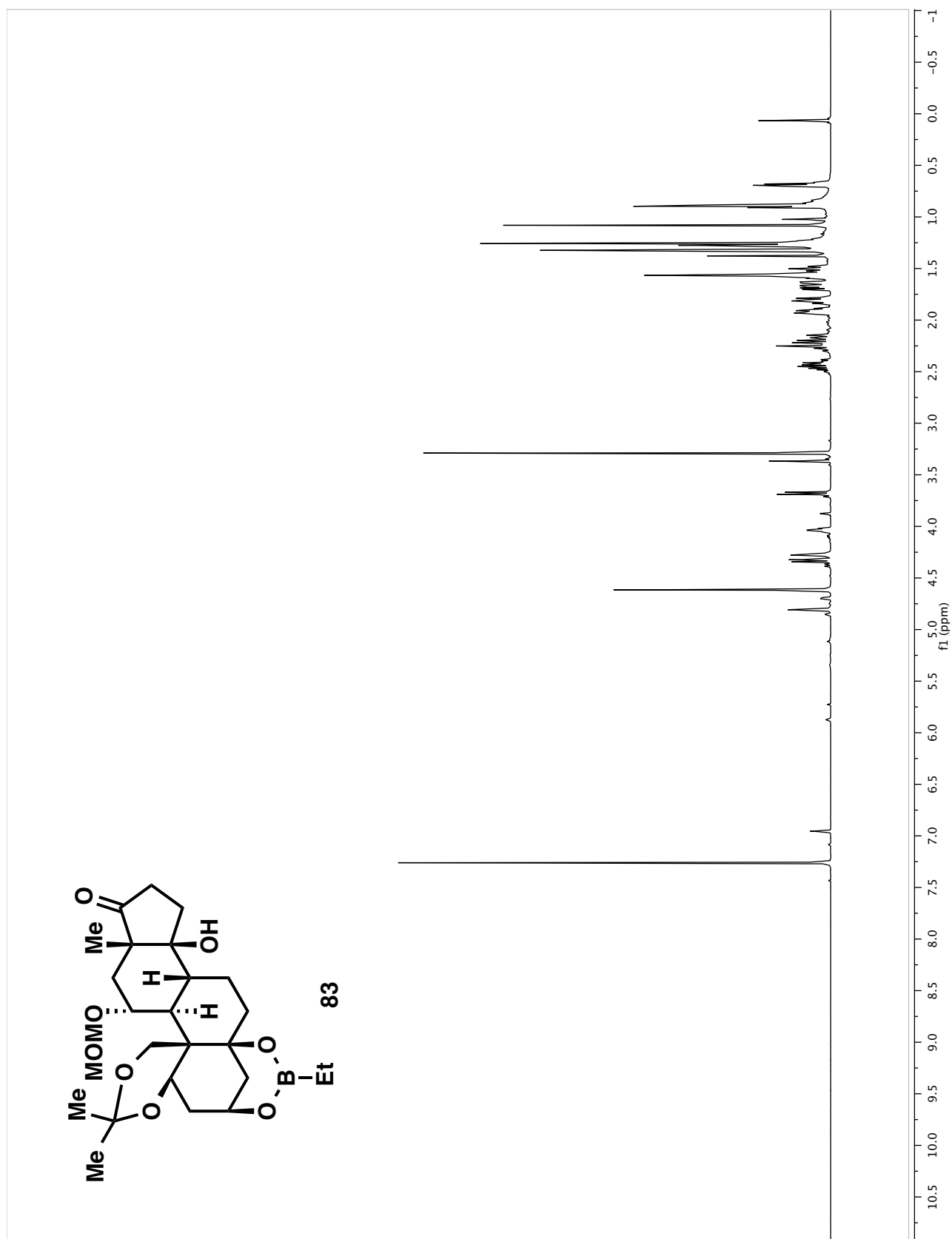


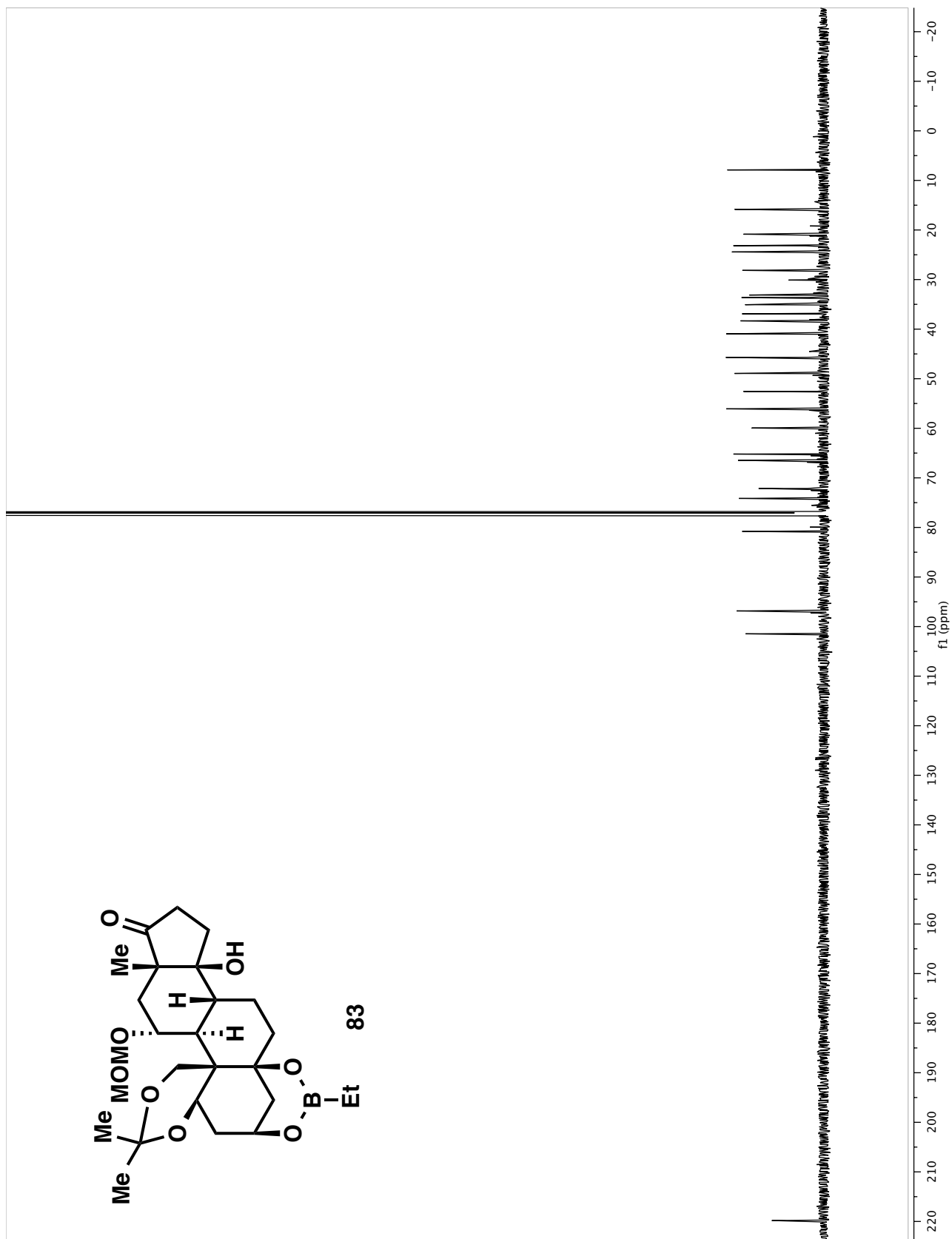


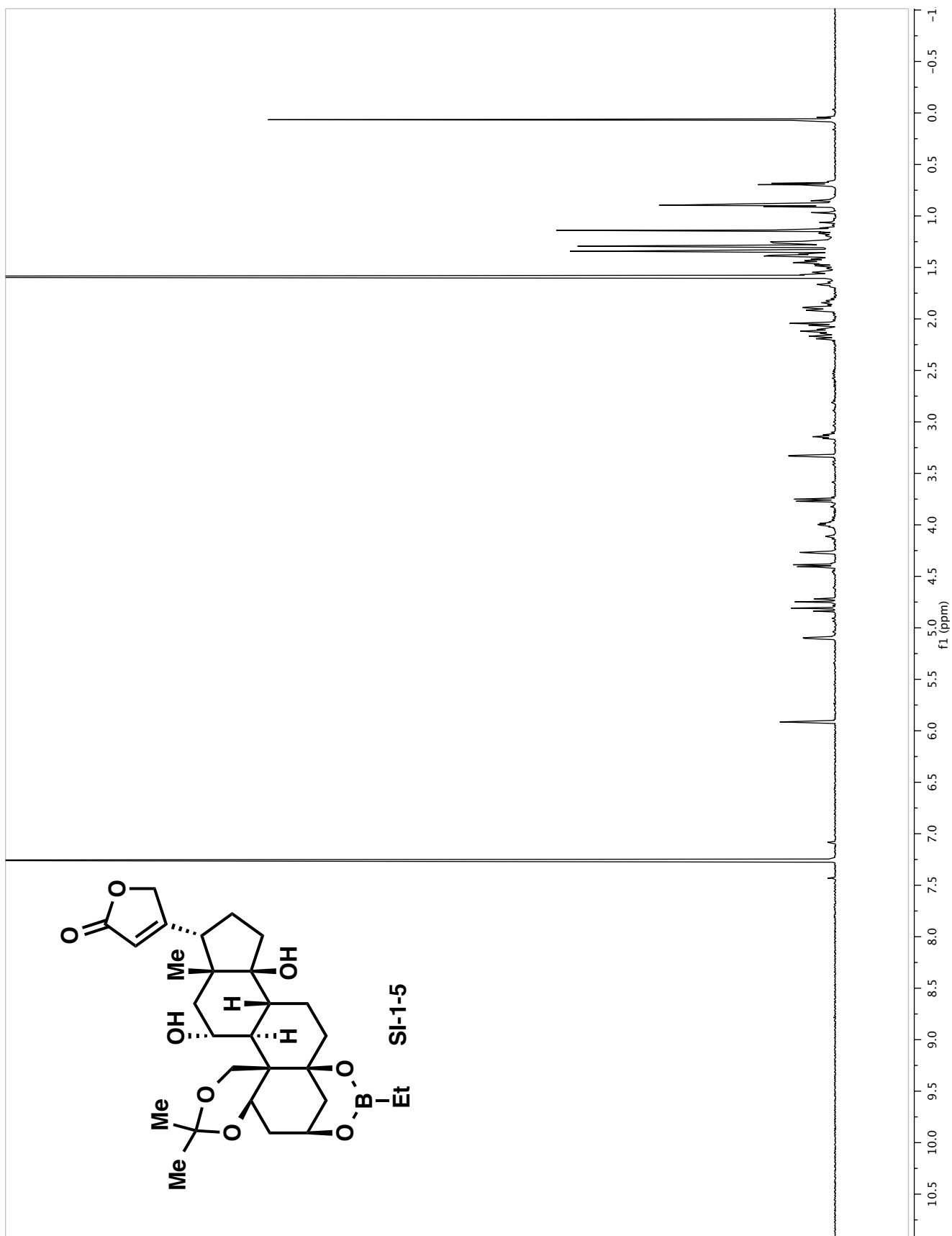


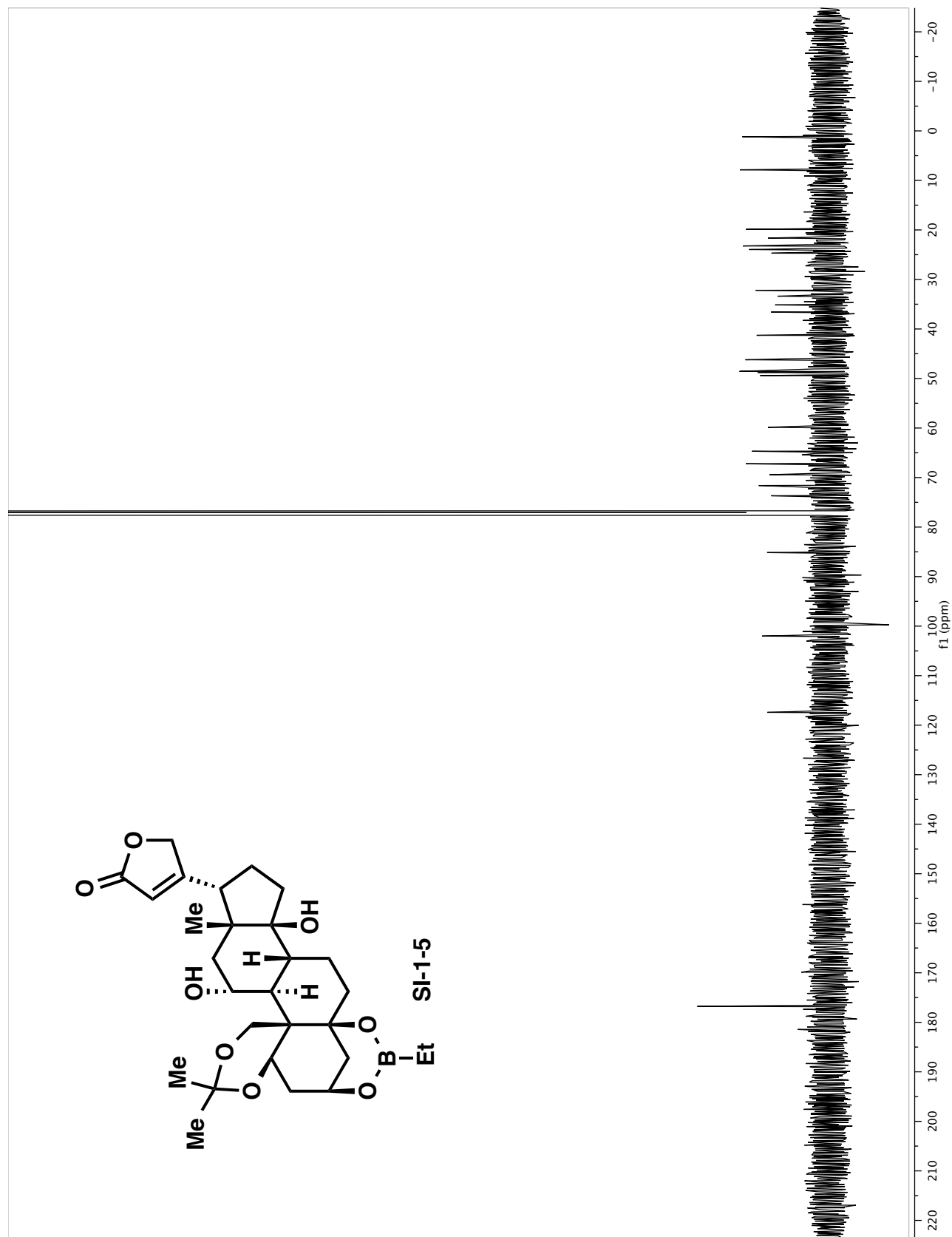


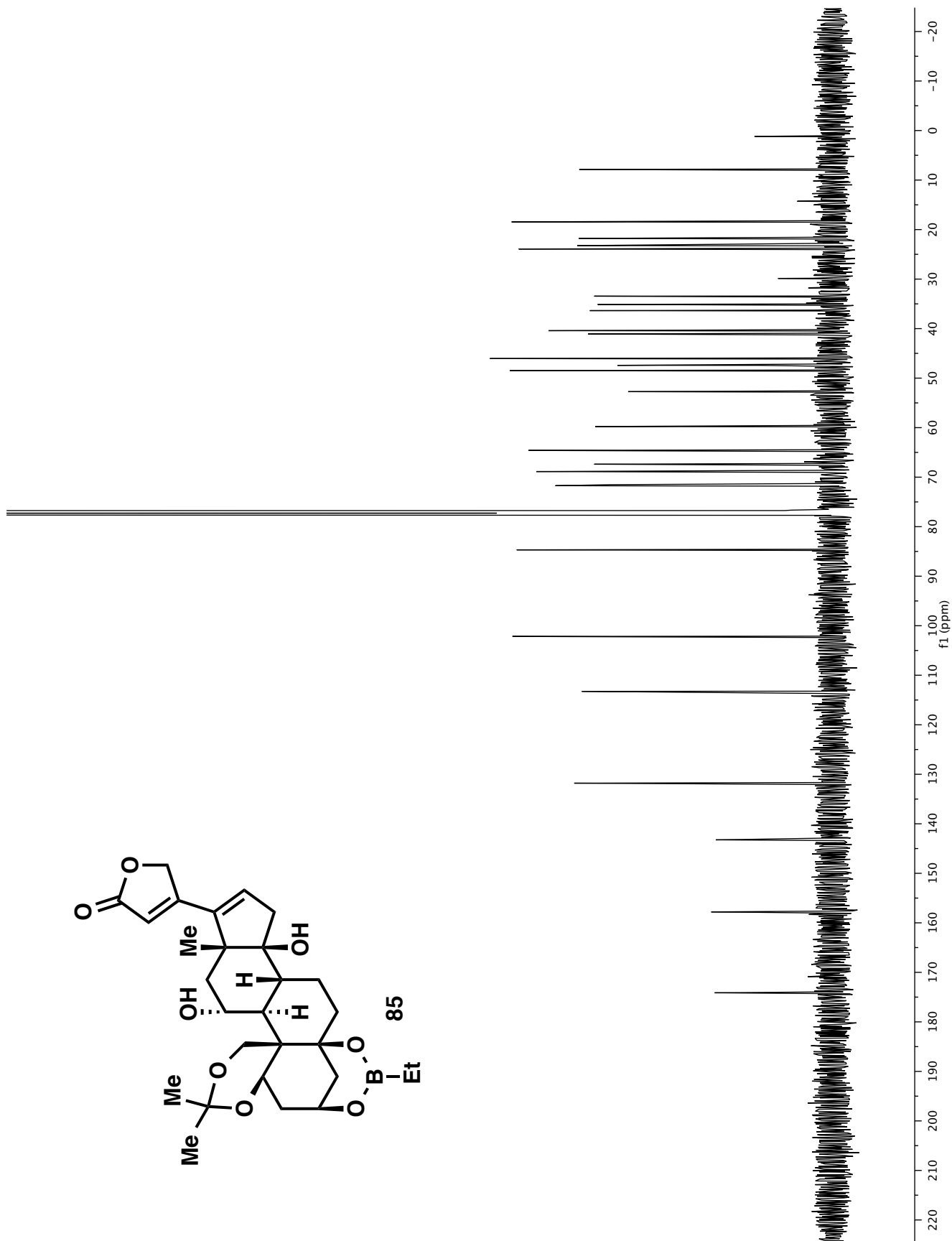


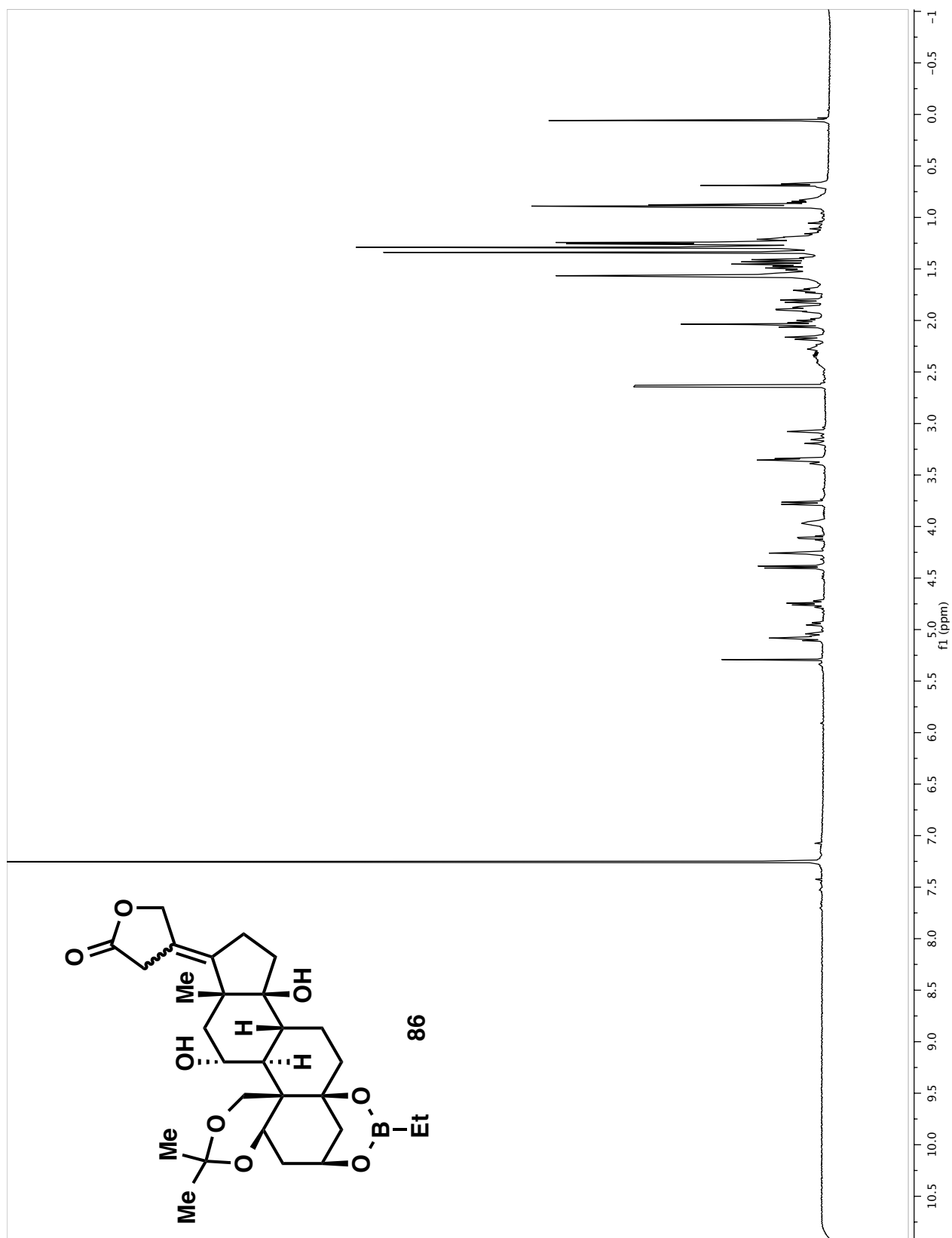


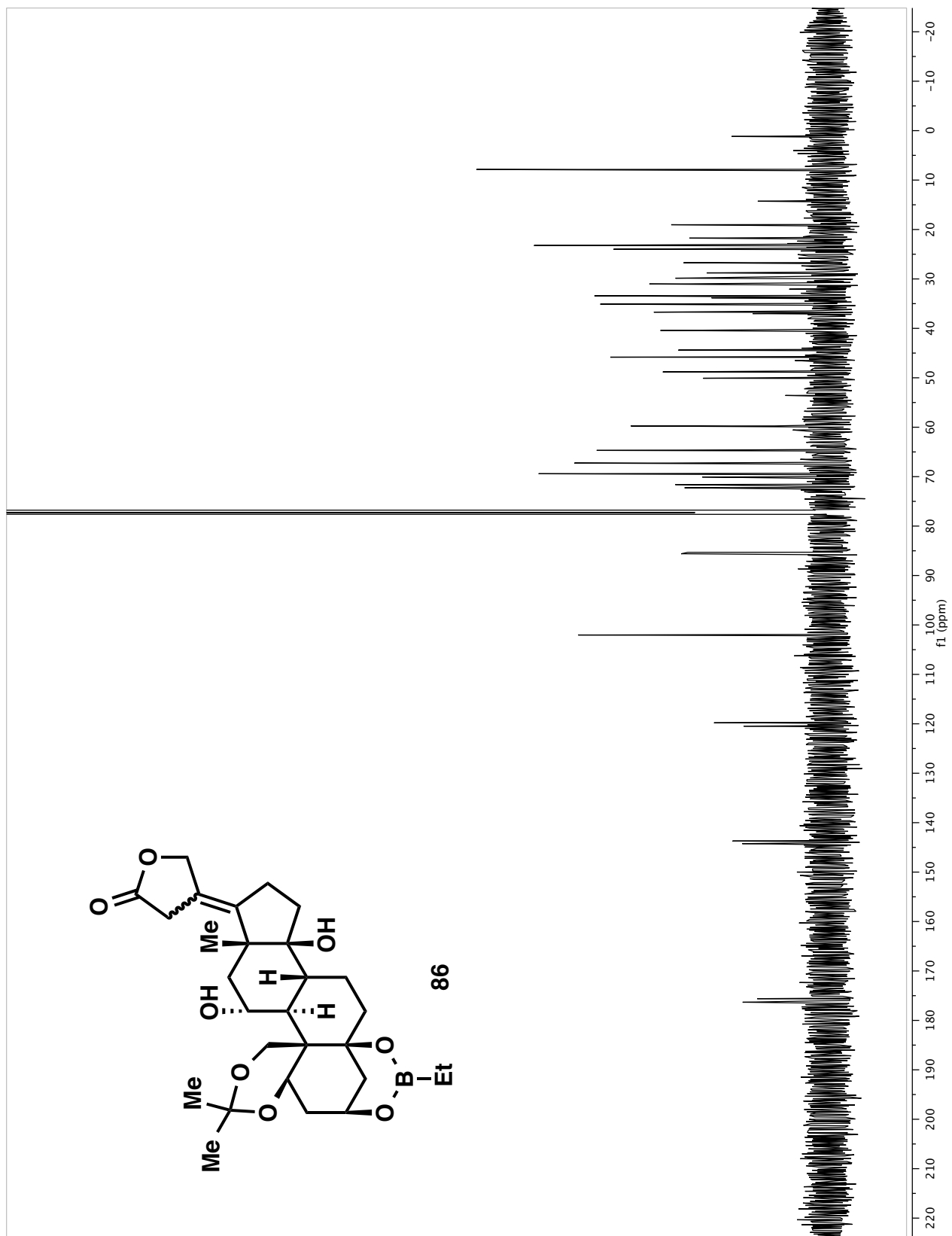


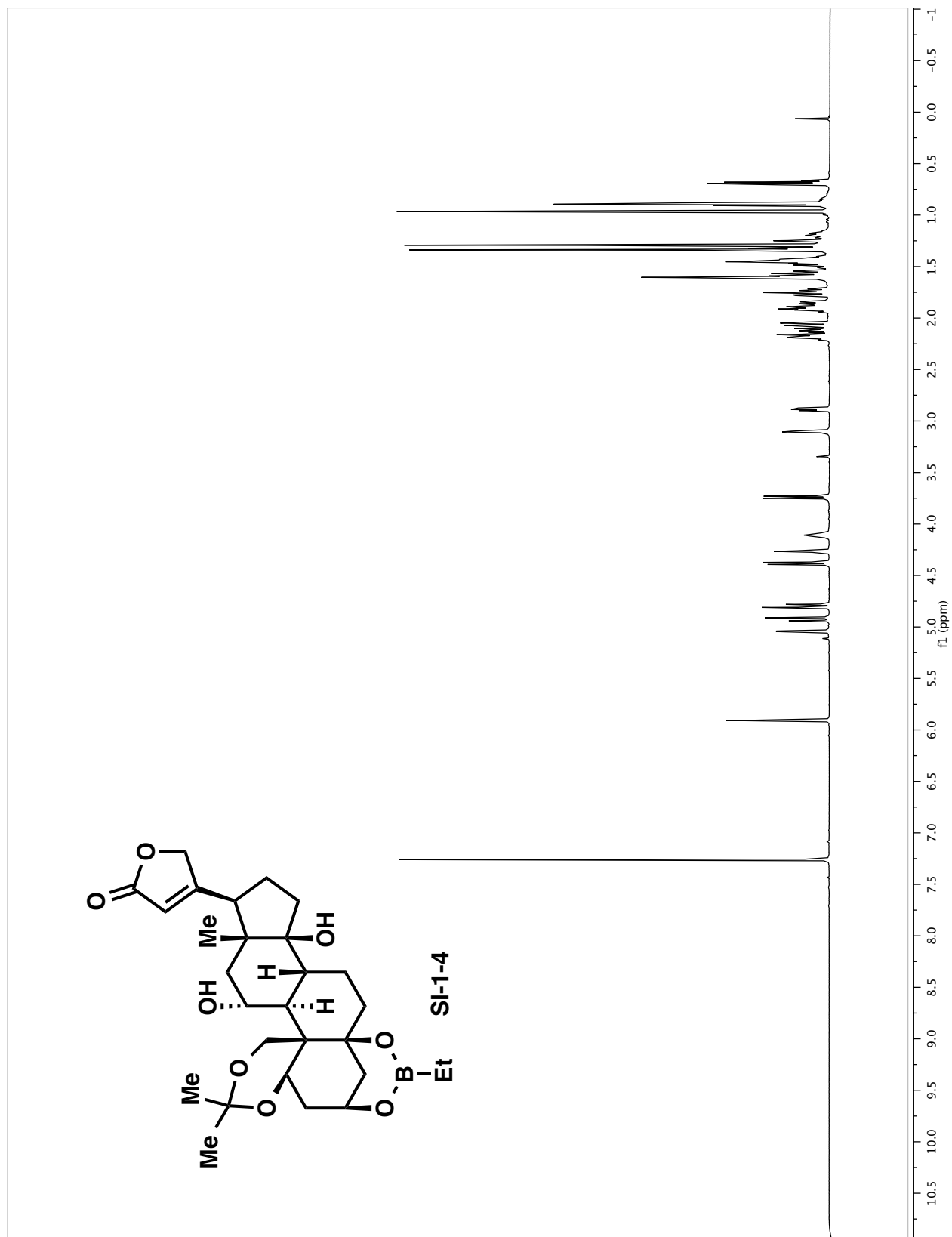


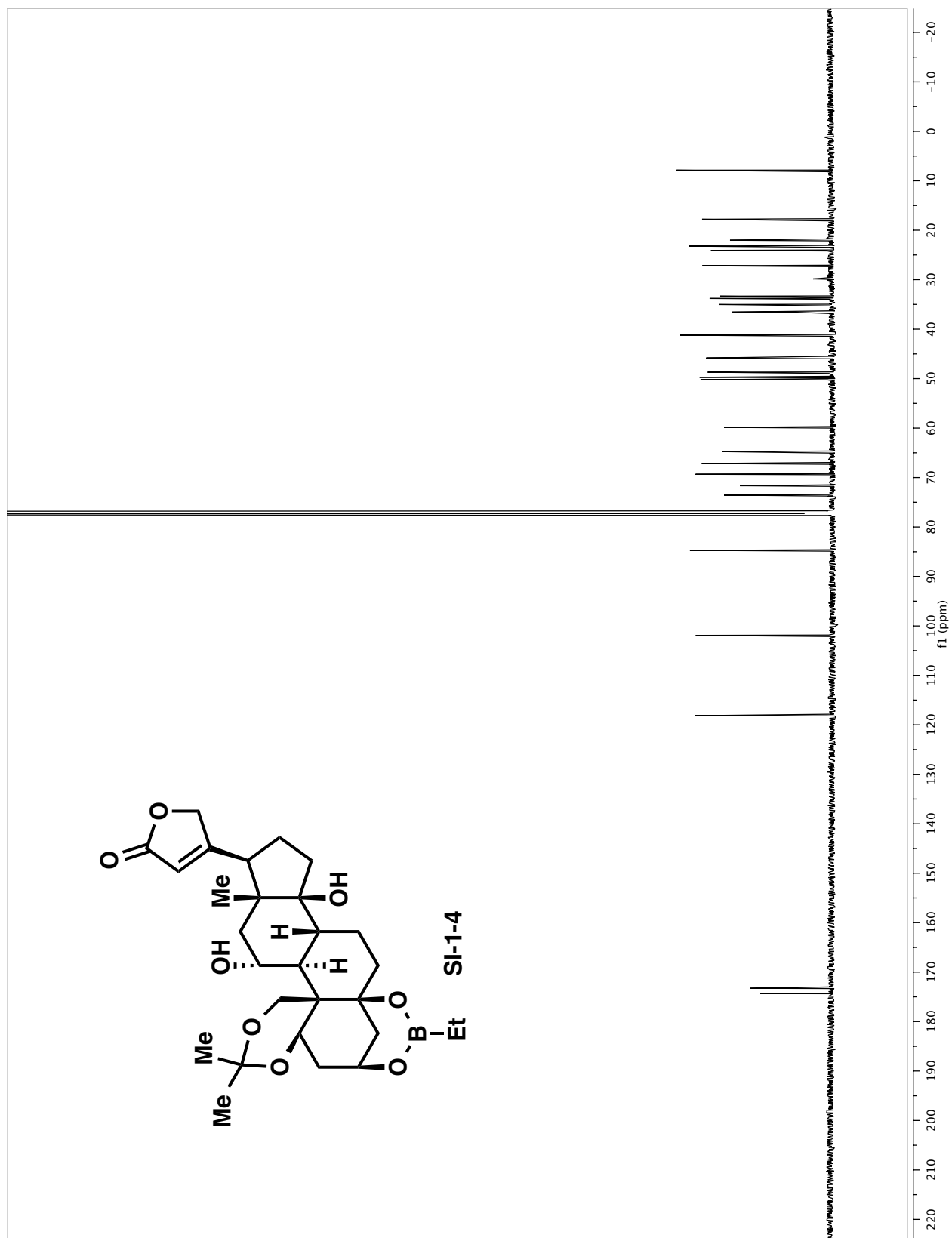


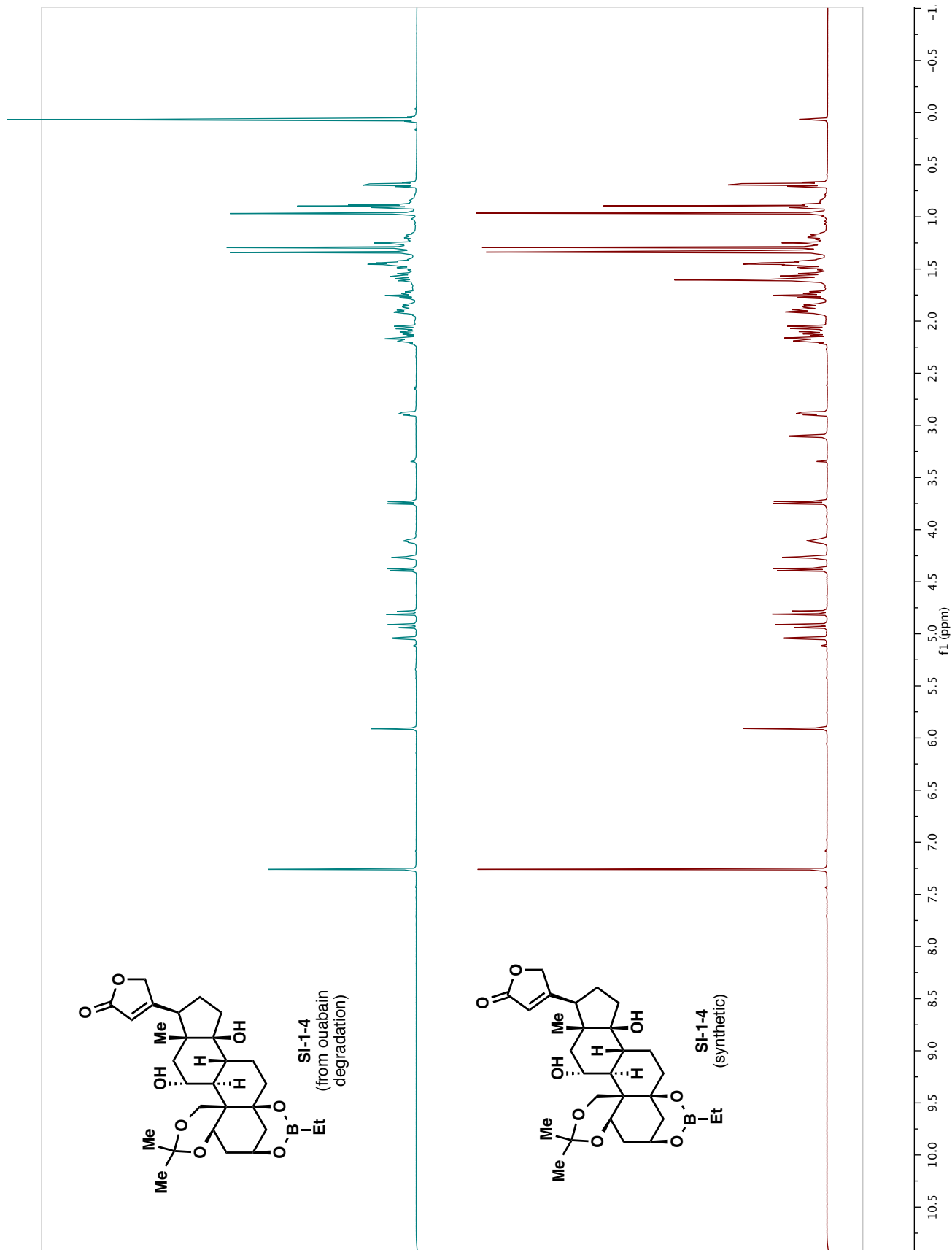


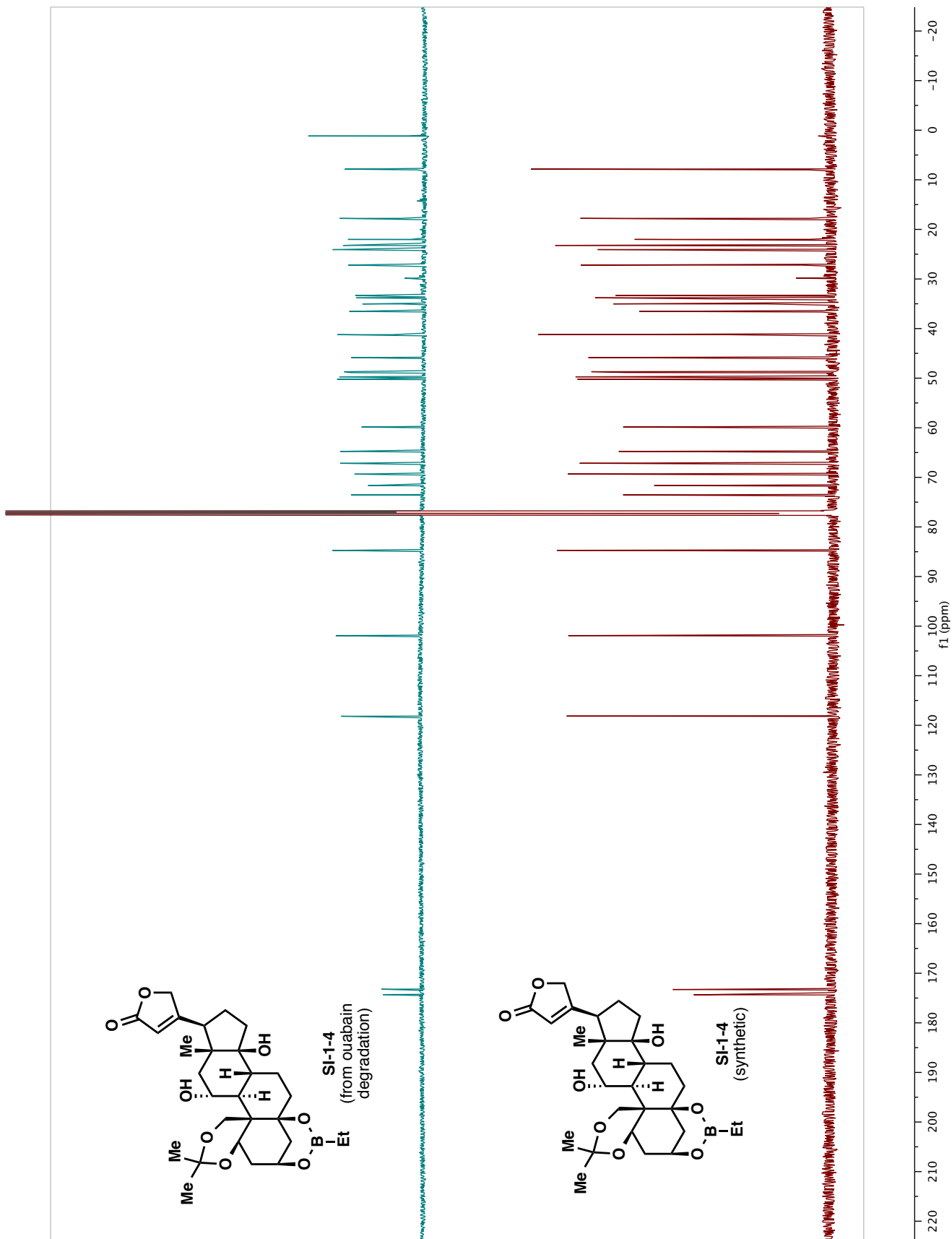


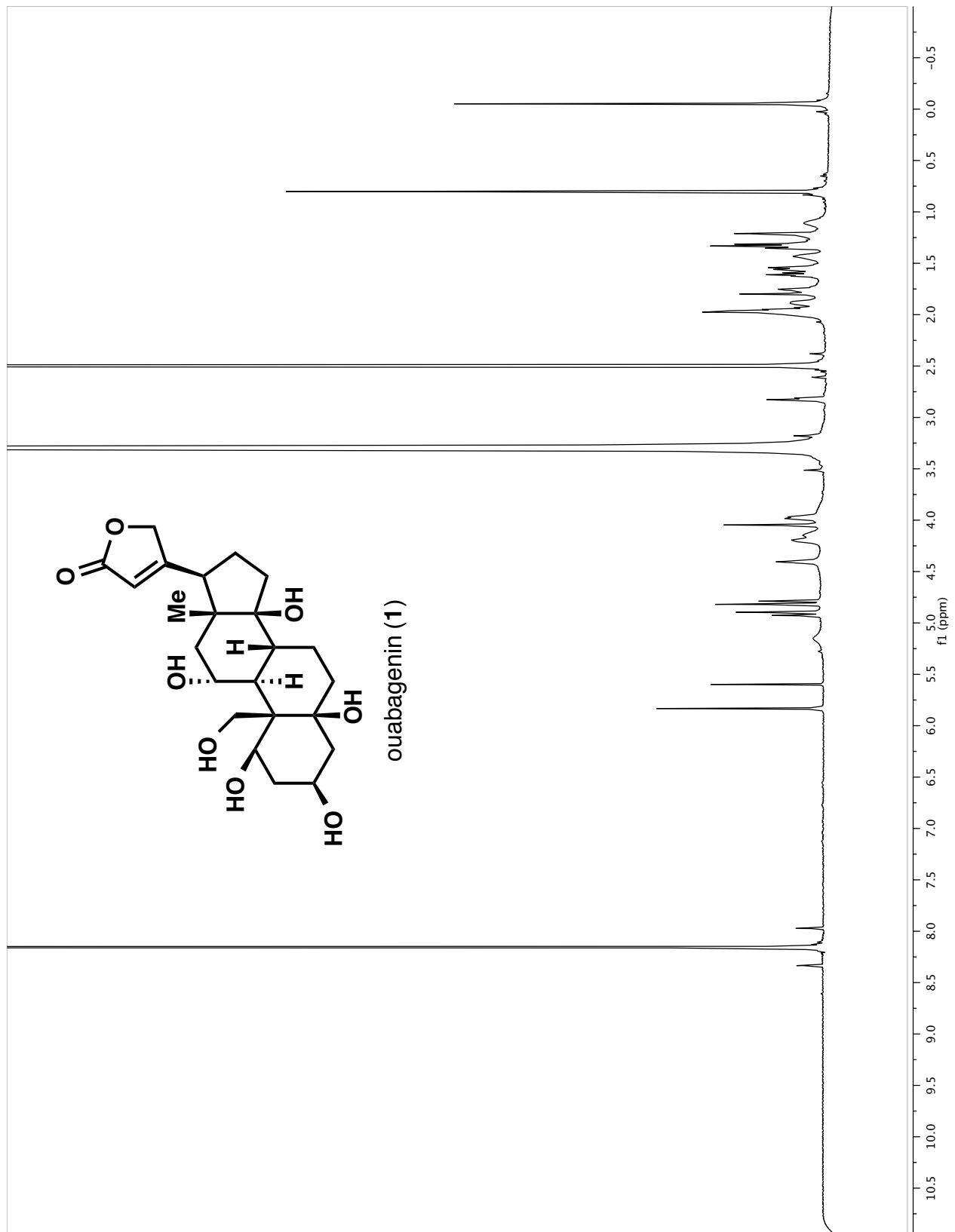


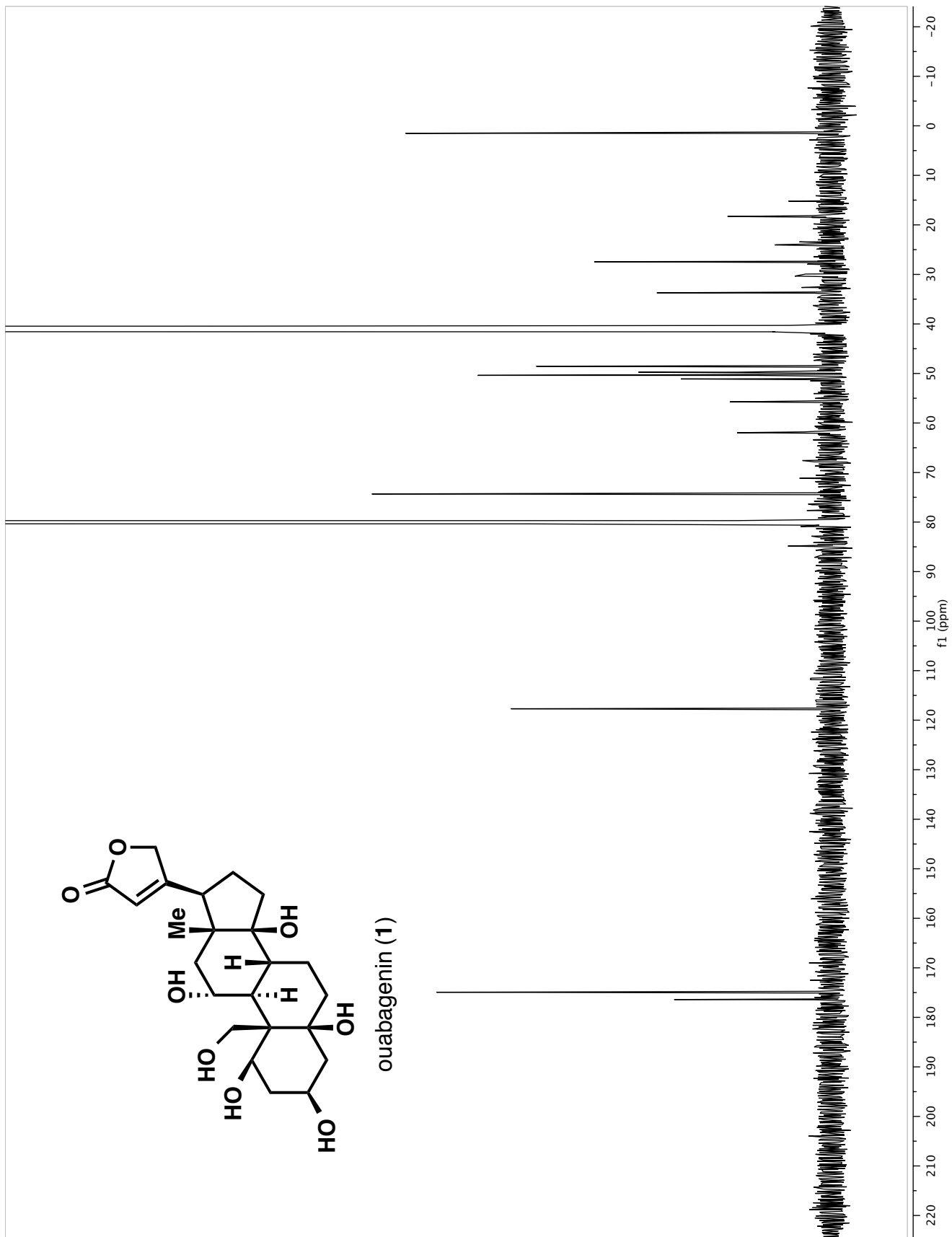


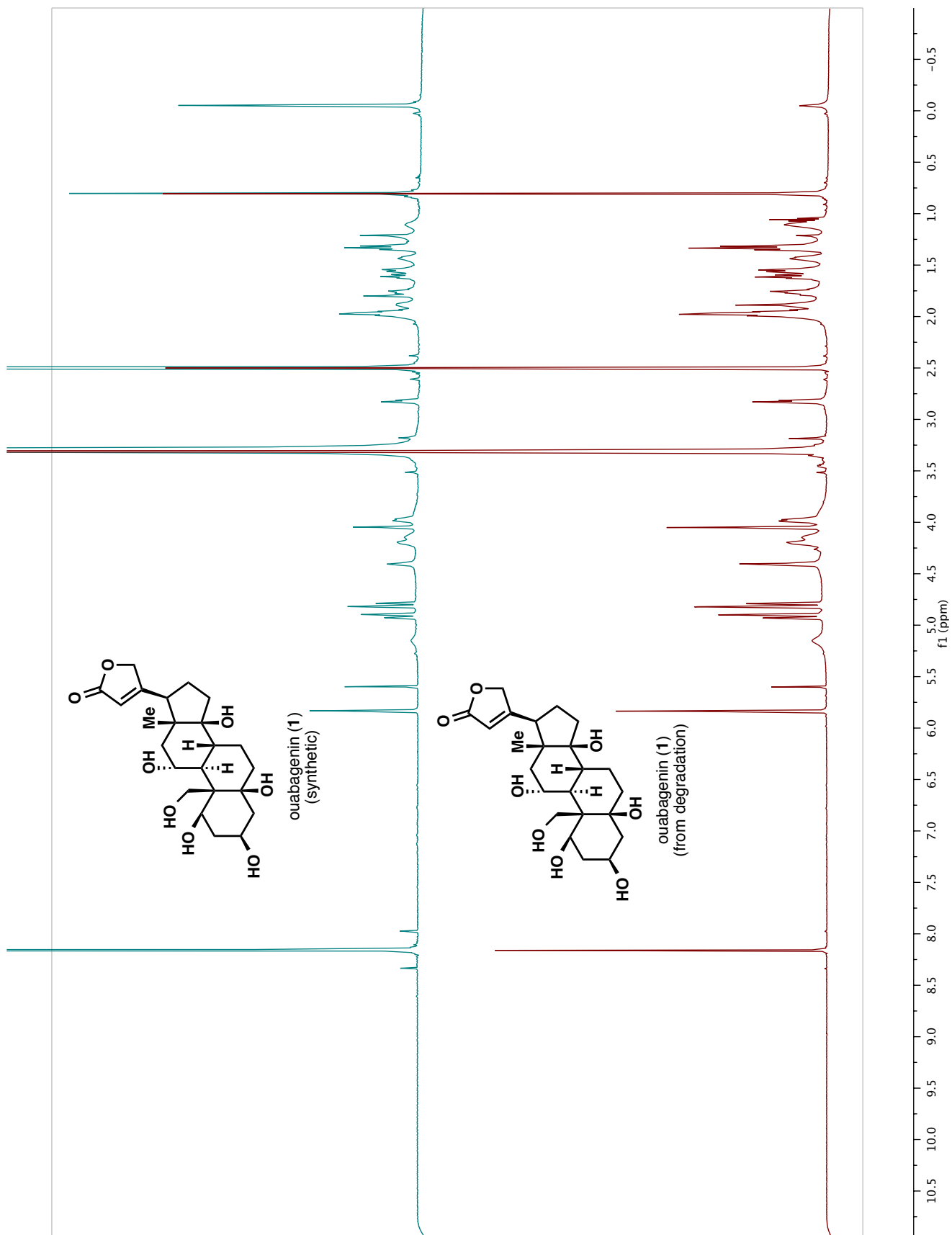












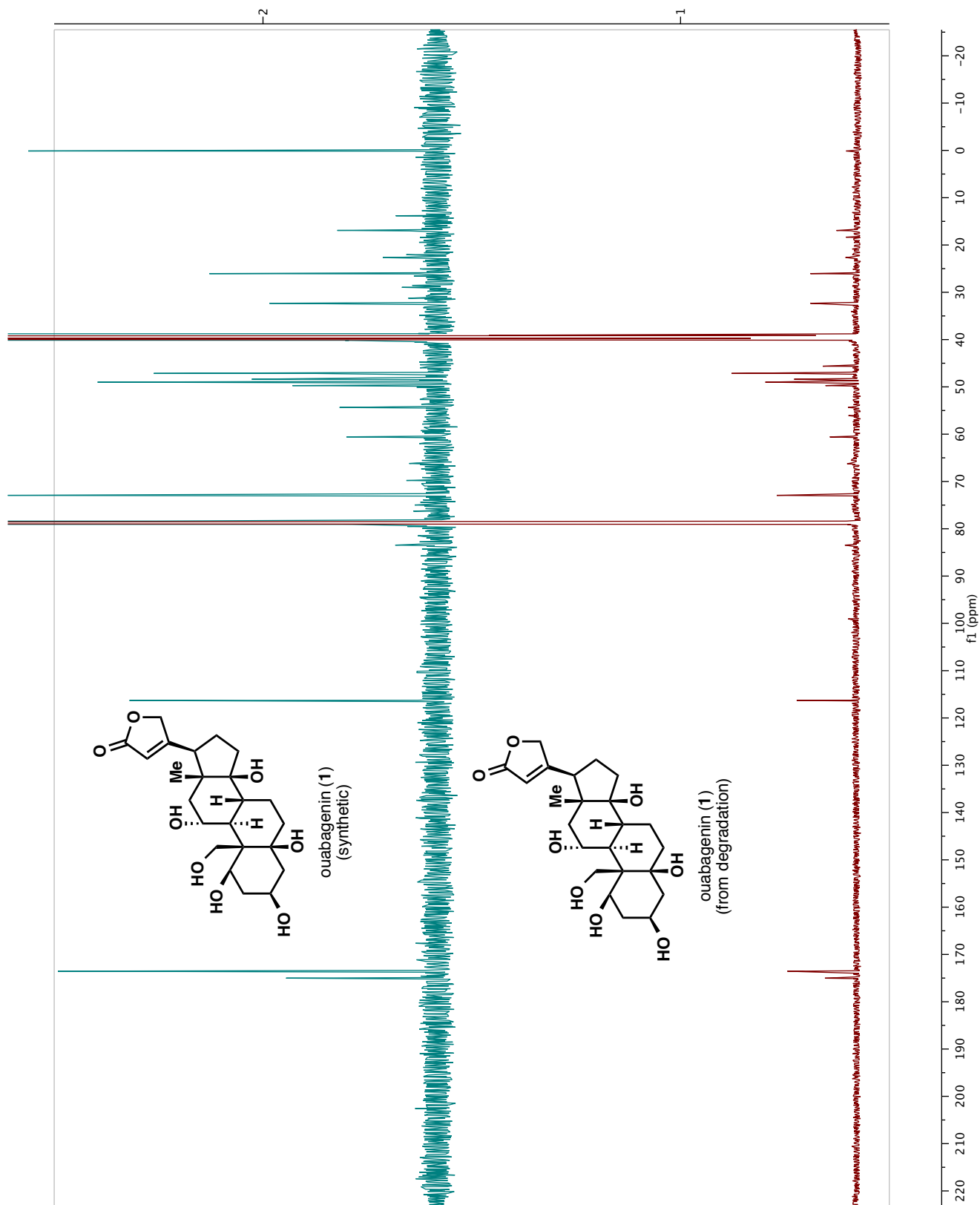


Table S10. ^1H NMR data comparison between synthetic **SI-1-4** and that obtained from ouabain degradation

Synthetic SI-1-4 (CDCl_3 , 600 MHz)	SI-1-4 from degradation (CDCl_3 , 600 MHz)
5.91 (s, 1 H)	5.91 (s, 1 H)
5.04 (dd, $J = 5.3, 1.8$ Hz, 1 H)	5.04 (dd, $J = 5.2, 1.8$ Hz, 1 H)
4.93 (dd, $J = 18, 1.7$ Hz, 1 H)	4.93 (dd, $J = 18.0, 1.8$ Hz, 1 H)
4.80 (dd, $J = 17.9, 1.7$ Hz, 1 H)	4.80 (dd, $J = 17.9, 1.8$ Hz, 1 H)
4.38 (d, $J = 12.1$ Hz, 1 H)	4.39 (d, $J = 12.0$ Hz, 1 H)
4.27 (s, 1 H)	4.27 (s, 1 H)
4.11 (td, $J = 7.9, 4.0$ Hz, 1 H)	4.11 (td, $J = 8.1, 3.9$ Hz, 1 H)
3.74 (d, $J = 12.1$ Hz, 1 H)	3.74 (d, $J = 12.2$ Hz, 1 H)
3.10 (d, $J = 4.2$ Hz, 1 H)	2.89 (dd, $J = 9.2, 6.3$ Hz, 1 H)
2.89 (dd, $J = 9.0, 6.2$ Hz, 1 H)	2.89 (dd, $J = 9.2, 6.3$ Hz, 1 H)
2.22–2.15 (m, 2 H)	2.22–2.15 (m, 2 H)
2.11 (dt, 13.7, 9.7 Hz, 1 H)	2.11 (dt, $J = 13.5, 9.6$ Hz, 1 H)
2.06 (dd, 13.7, 1.9 Hz, 1 H)	2.06 (dd, $J = 13.7, 1.9$ Hz, 1 H)
1.95–1.82 (m, 3 H)	1.95–1.82 (m, 3 H)
1.80–1.70 (m, 2 H)	1.80–1.71 (m, 2 H)
1.61 (dt, $J = 13.9, 2.8$ Hz, 1 H)	1.62–1.58 (m, 1 H)
1.55 (dt, $J = 13.9, 2.8$ Hz, 1 H)	1.56 (dt, $J = 13.8, 3.0$ Hz, 1 H)
1.53–1.39 (m, 3 H)	1.53–1.39 (m, 3 H)
1.34 (s, 3 H)	1.34 (s, 3 H)
1.29 (s, 3 H)	1.30 (s, 3 H)
1.19 (m, 1 H)	1.20 (ddd, $J = 16.0, 11.6, 5.4$ Hz, 1 H)
0.97 (s, 3 H)	0.97 (s, 3 H)
0.90 (t, $J = 7.7$ Hz, 3 H)	0.90 (t, $J = 7.8$ Hz, 2 H)
0.69 (q, $J = 7.7$ Hz, 2 H)	0.69 (q, $J = 7.8$ Hz, 3 H)

Table S11. ^{13}C NMR data comparison between synthetic **SI-1-4** and that obtained from ouabain degradation

Synthetic SI-1-4 (CDCl ₃ , 600 MHz)	SI-1-4 from degradation (CDCl ₃ , 600 MHz)
174.3	174.3
173.3	173.2
118.2	118.2
101.9	101.9
84.7	84.7
73.6	73.5
71.7	71.7
69.3	69.4
67.2	67.2
64.8	64.8
59.9	59.9
50.2	50.2
49.7	49.7
48.9	48.9
48.7	48.7
45.8	45.8
41.2	41.2
36.6	36.6
35.0	35.0
33.8	33.8
33.3	33.3
29.8	29.9
27.2	27.2
24.1	24.1
23.2	23.2
22.0	22.0
17.8	17.8
7.9	7.9

Table S12. ¹H NMR data comparison between synthetic ouabagenin (**1**) and that from degradation

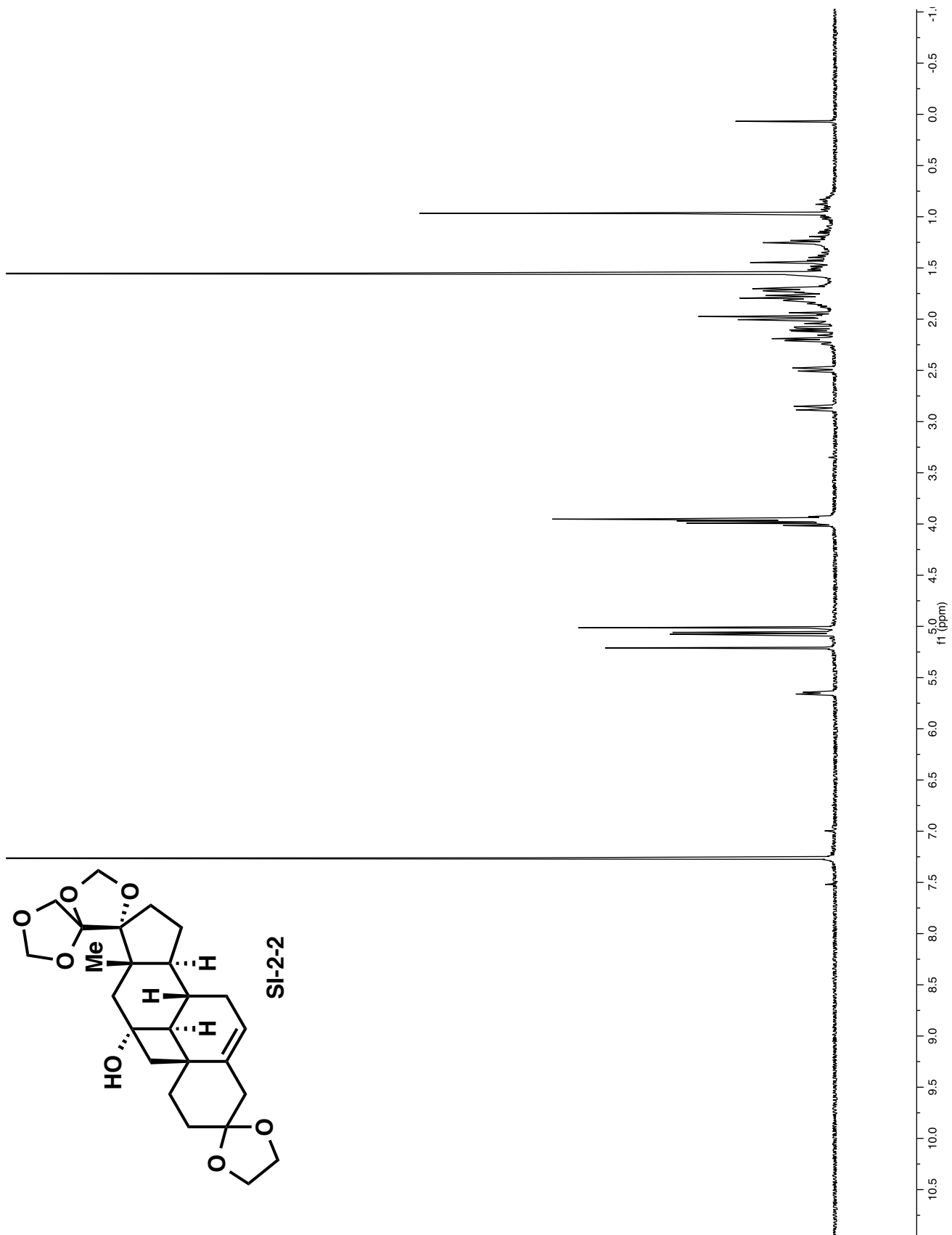
Synthetic 1 (2:1 (CD ₃) ₂ SO:CDCl ₃ , 151 MHz)	From degradation (2:1 (CD ₃) ₂ SO:CDCl ₃ , 151 MHz)
5.84 (s, 1 H)	5.84 (s, 1 H)
4.92 (d, J = 18.4 Hz, 1 H)	4.92 (d, J = 18.3 Hz, 1 H)
4.81 (dd, J = 18.4, 1.8 Hz, 1 H)	4.81 (dd, J = 18.3, 1.8 Hz, 1 H)
4.41 (s, 1 H)	4.41 (d, J = 4.8 Hz, 1 H)

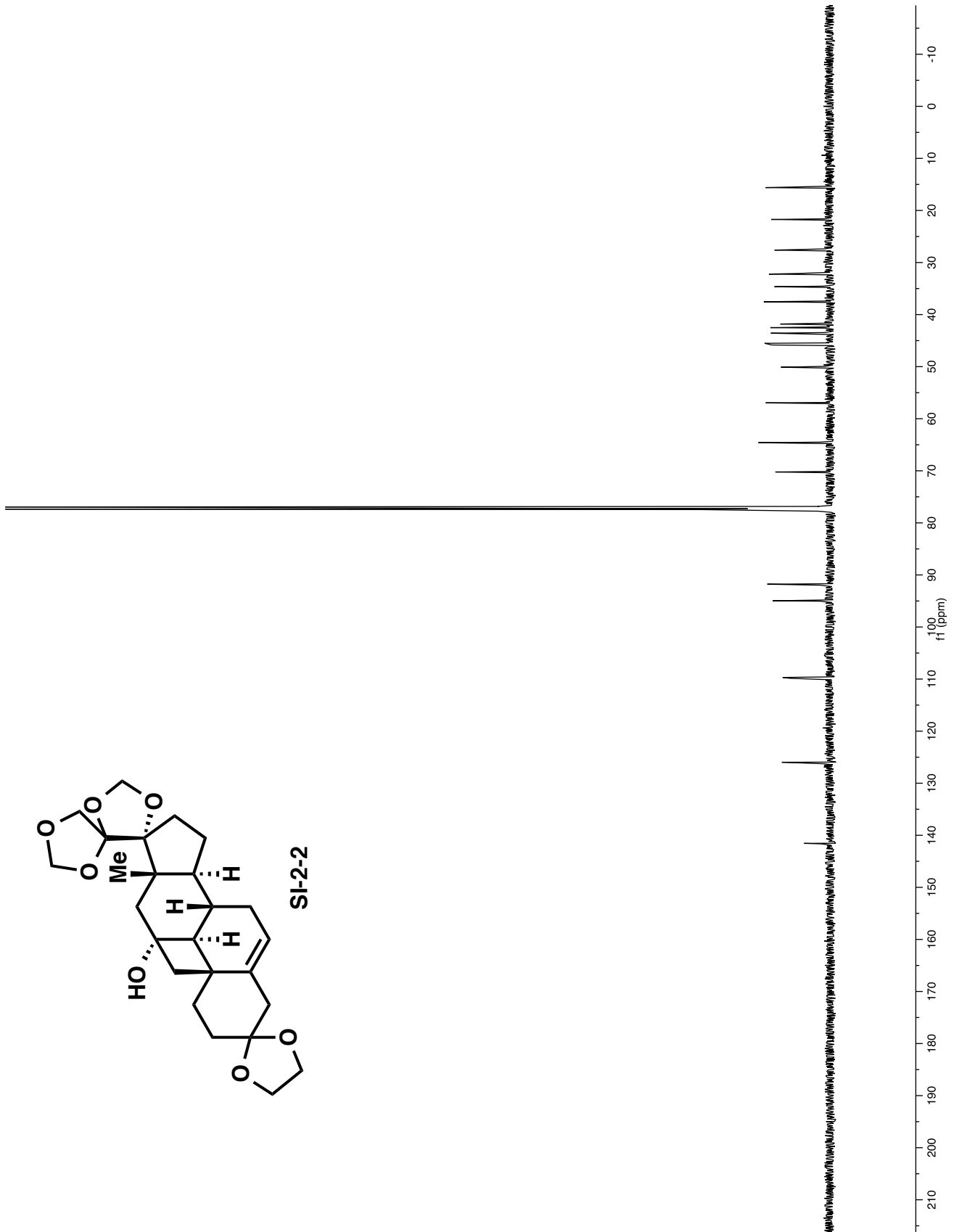
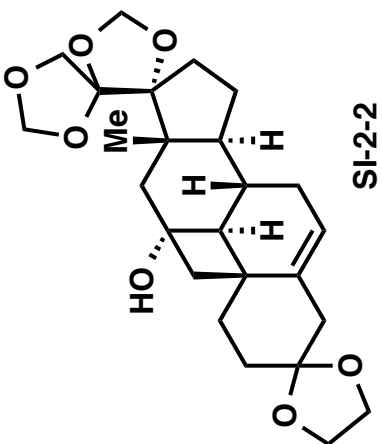
4.21 (d, J = 10.4 Hz, 1 H)	4.20 (d, J = 10.3 Hz, 1 H)
4.20–4.10 (m, 1 H)	4.20–4.10 (m, 1 H)
3.98 (d, J = 10.4 Hz, 1 H)	3.99 (d, J = 10.3 Hz, 1 H)
2.83 (t, J = 7.1 Hz, 1 H)	2.83 (t, J = 7.2 Hz, 1 H)
2.03–1.93 (m, 3 H)	2.03–1.93 (m, 3 H)
1.92–1.85 (m, 1 H)	1.92–1.85 (m, 1 H)
1.82–1.72 (m, 2 H)	1.81–1.70 (m, 2 H)
1.61 (dd, J = 11.4, 8.6 Hz, 1 H)	1.61 (dd, J = 11.4, 8.6 Hz, 1 H)
1.56 (dd, J = 13.5, 4.5 Hz, 1 H)	1.56 (dd, J = 13.5, 4.5 Hz, 1 H)
1.49–1.40 (m, 1 H)	1.44 (p, J = 7.9, 5.9 Hz, 1 H)
1.37–1.28 (m, 2 H)	1.37–1.28 (m, 2 H)
1.22 (s, 1 H)	
1.11 (s, 1 H)	1.11 (s, 1 H)
0.81 (s, 3 H)	0.81 (s, 3 H)

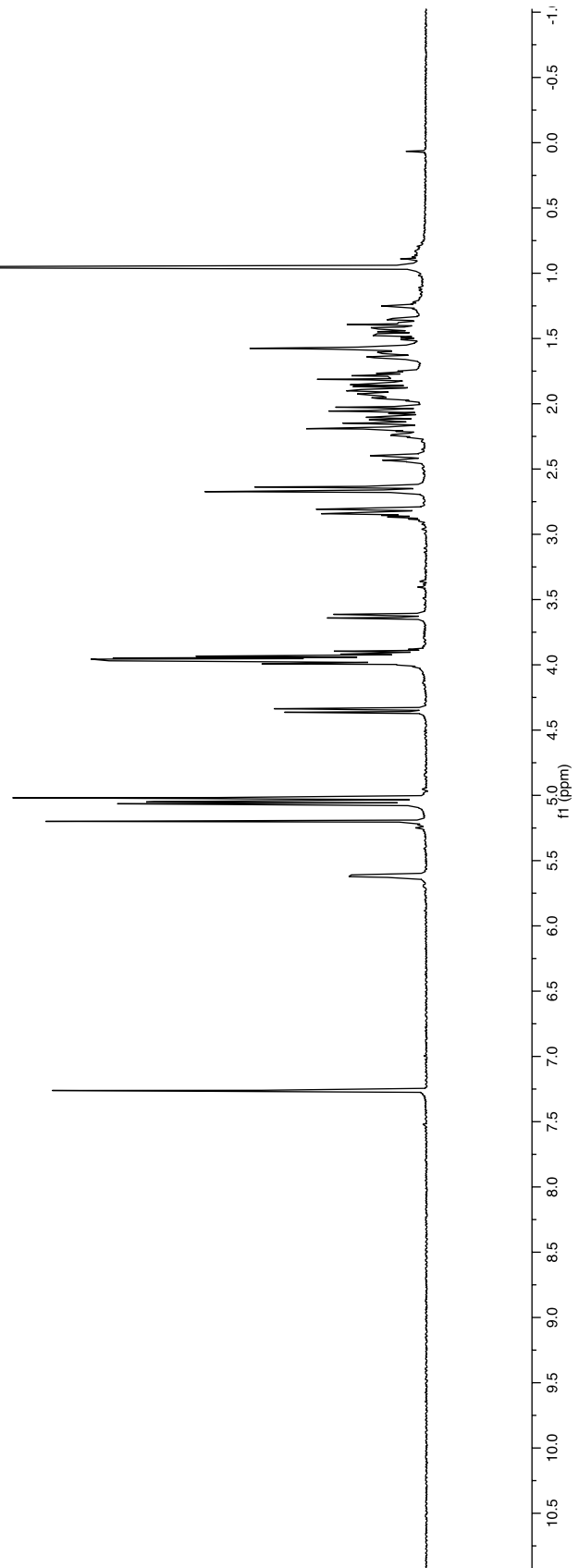
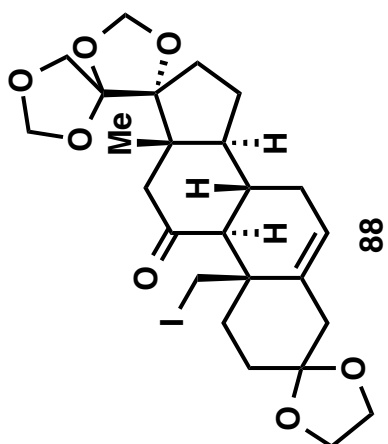
Table S13. ^{13}C NMR data comparison between synthetic ouabagenin (**1**) and that from degradation

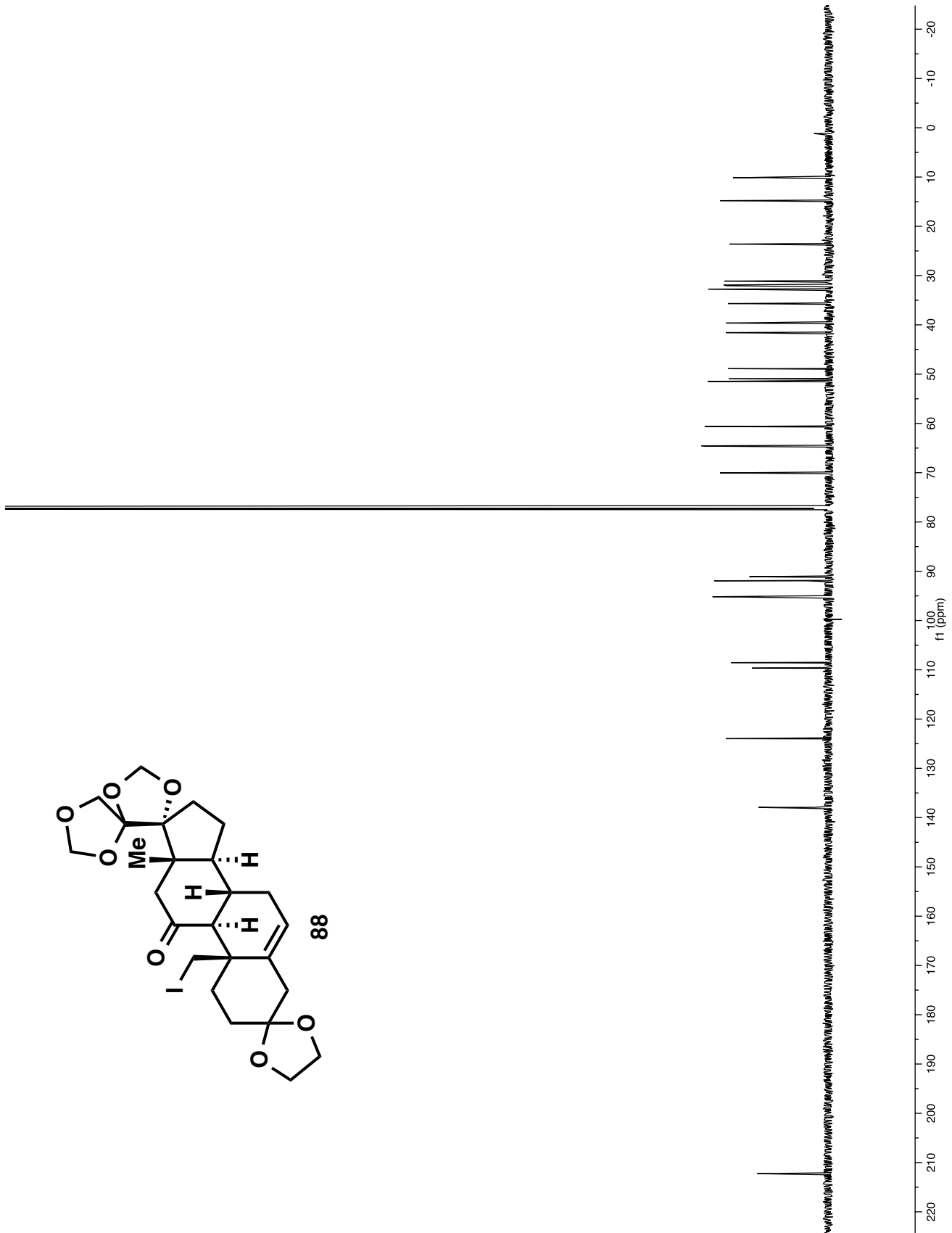
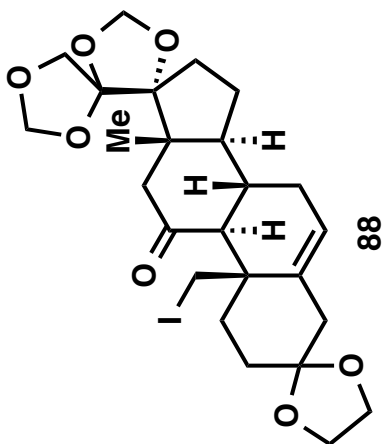
Synthetic 1 (2:1 (CD ₃) ₂ SO:CDCl ₃ , 151 MHz)	From degradation (2:1 (CD ₃) ₂ SO:CDCl ₃ , 151 MHz)
175.0	175.0
173.5	173.6
116.3	116.3
83.5	83.5
75.1	74.9
72.9	72.9
66.2	66.3
65.4	65.4
60.6	60.6
49.7	49.7
49.0	49.0
48.6	48.6
48.4	48.4
47.2	47.2
40.1	40.0
32.3	32.3

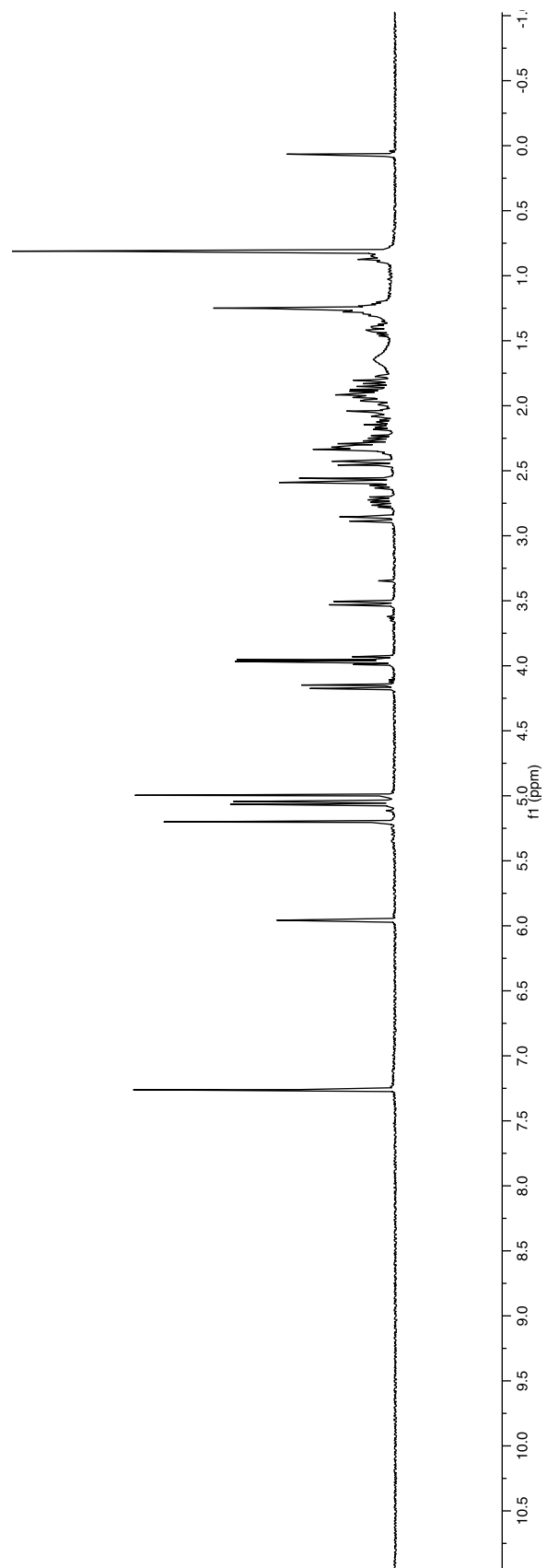
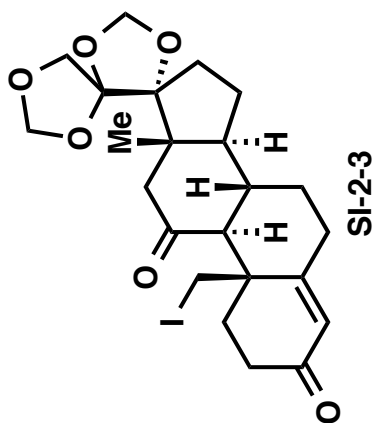
26.0	26.0
22.7	22.6
16.9	16.9

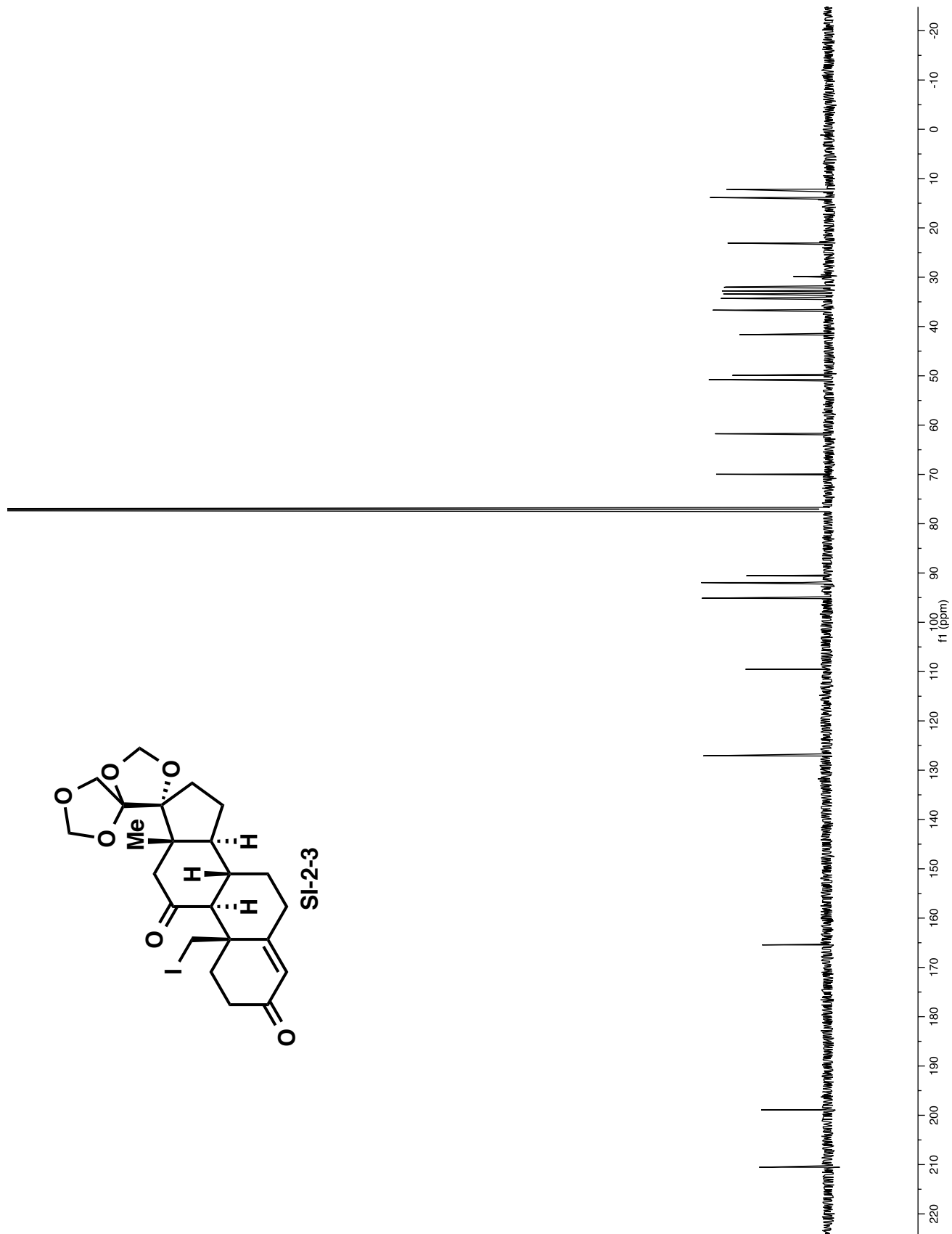
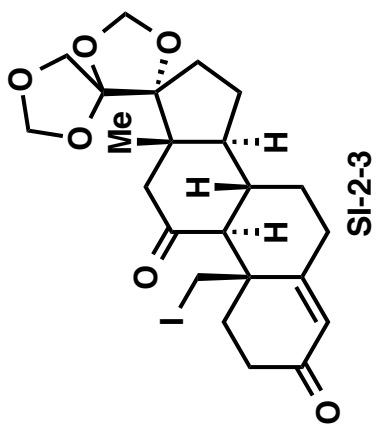


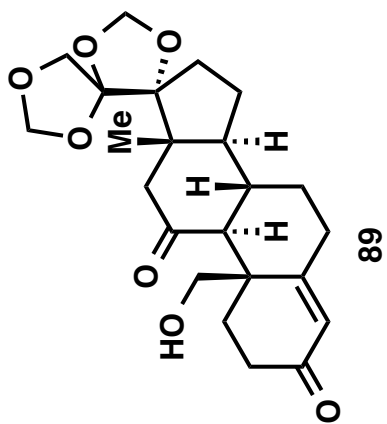




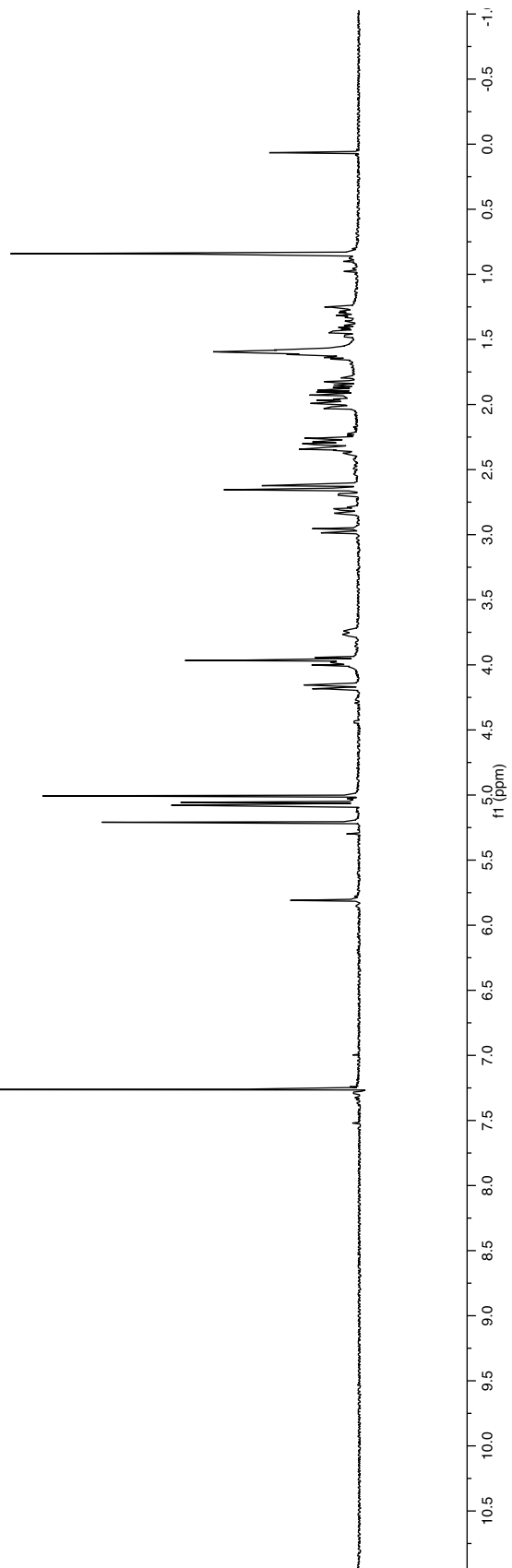


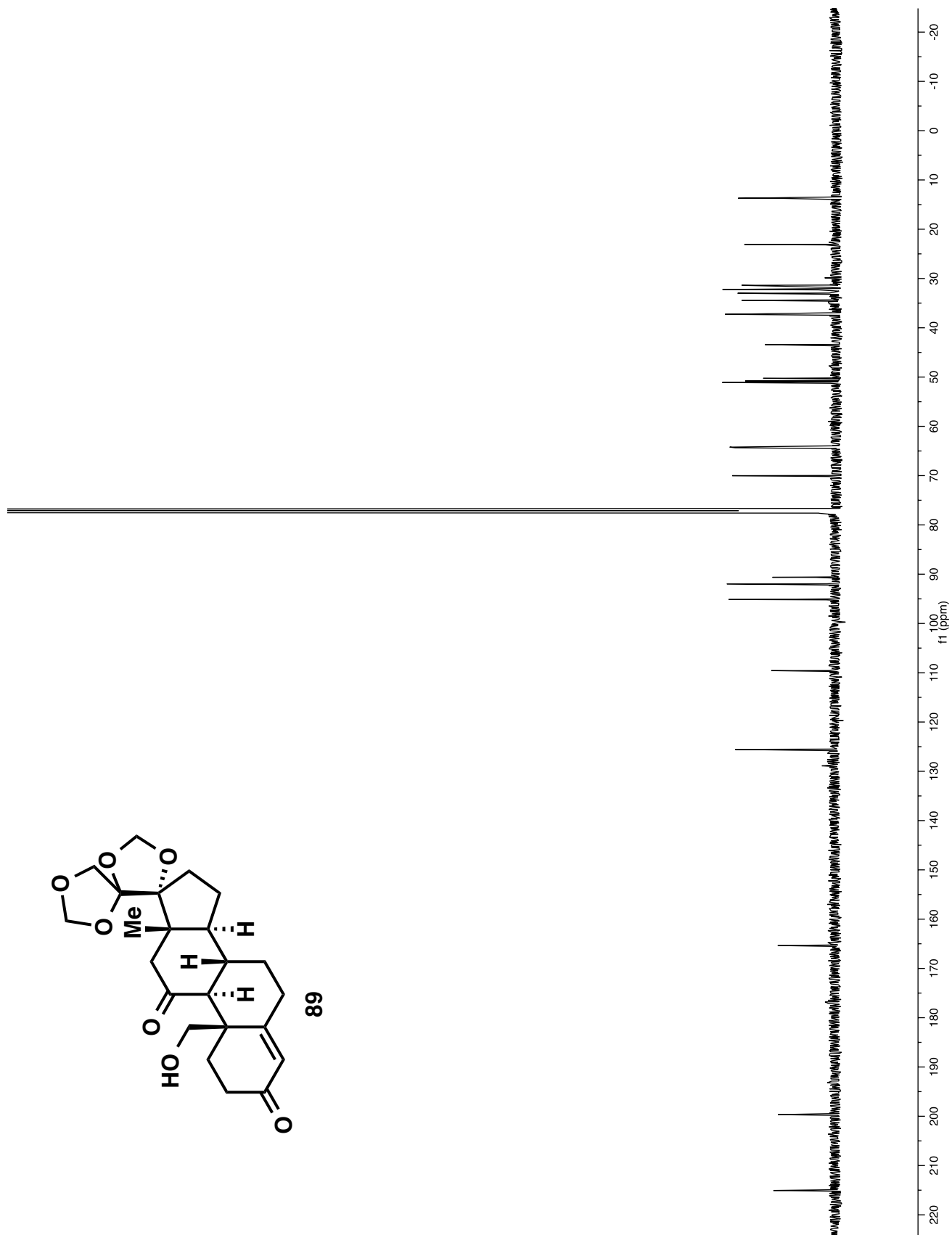
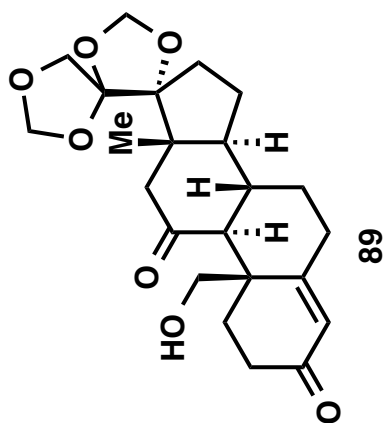


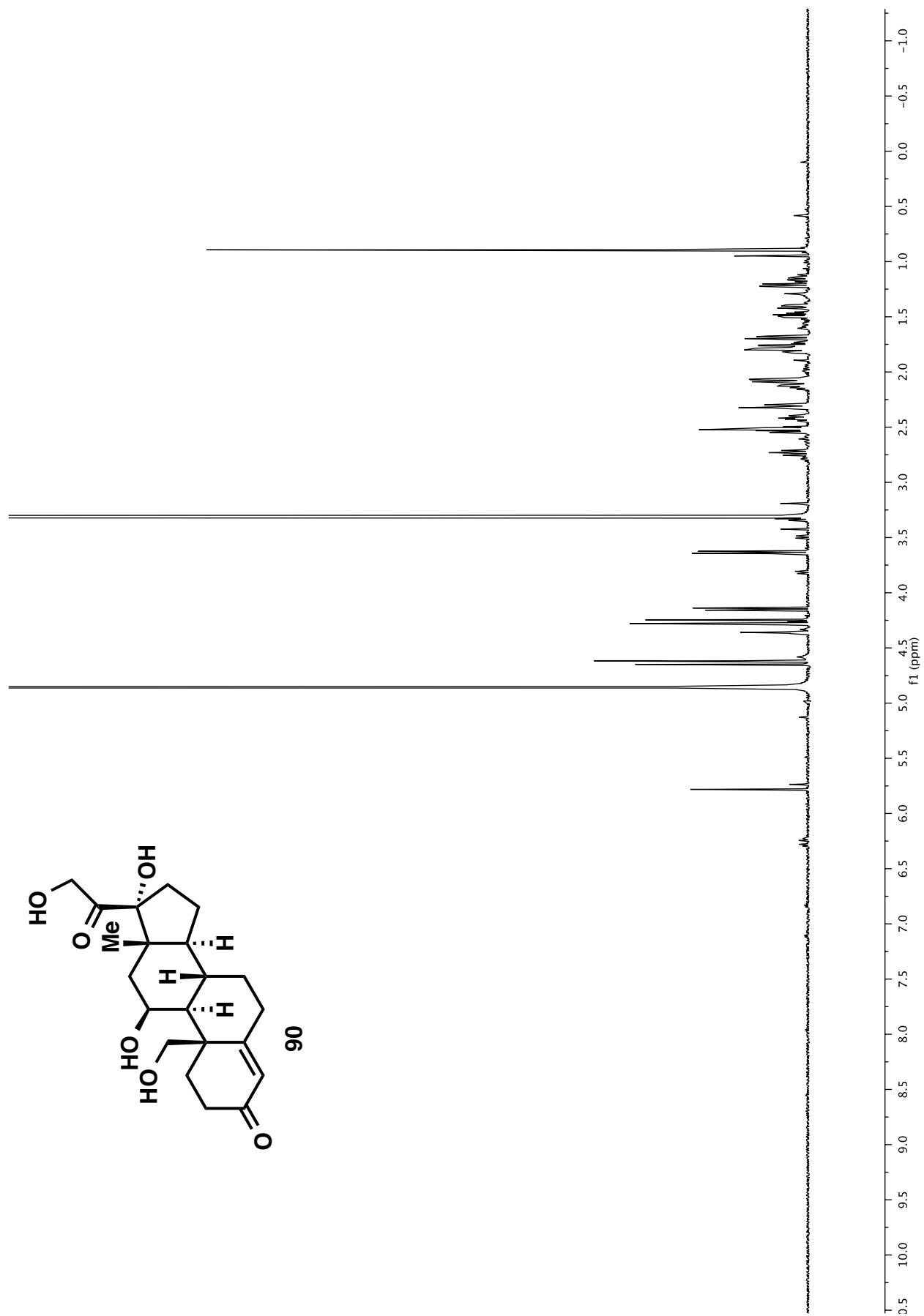
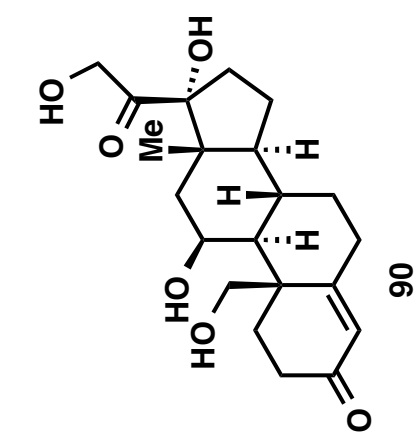


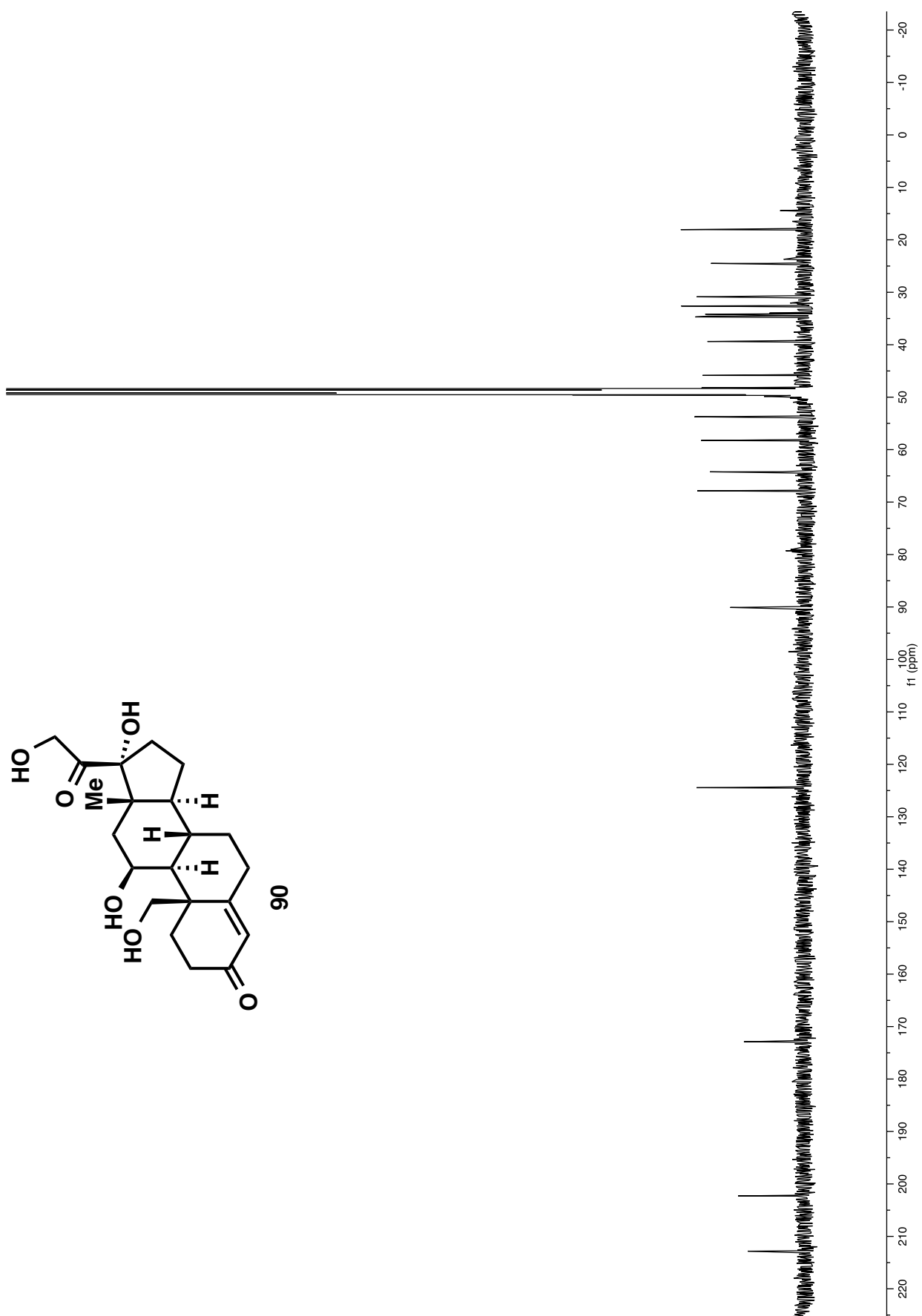


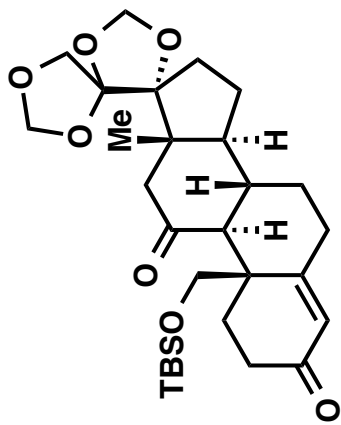
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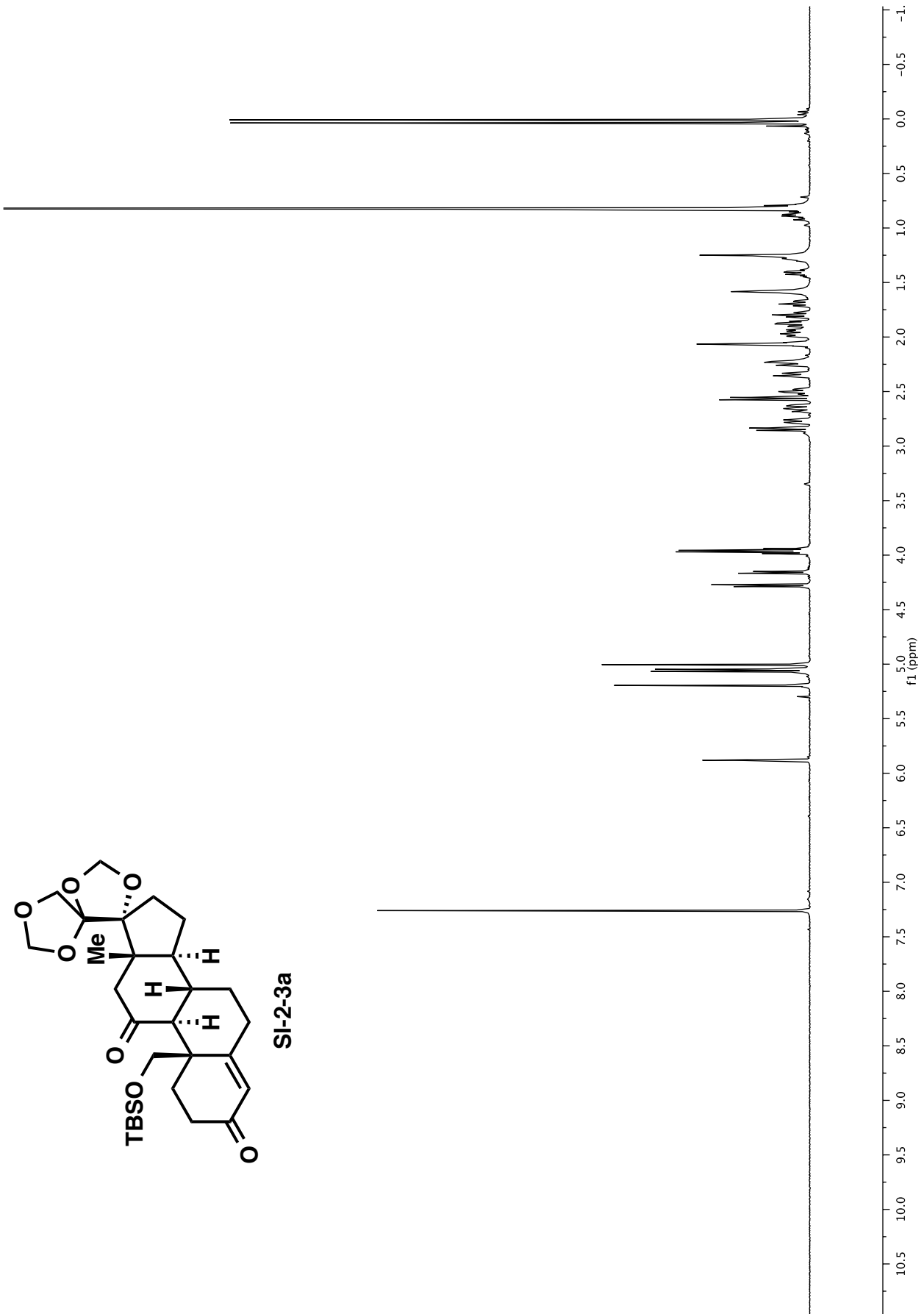


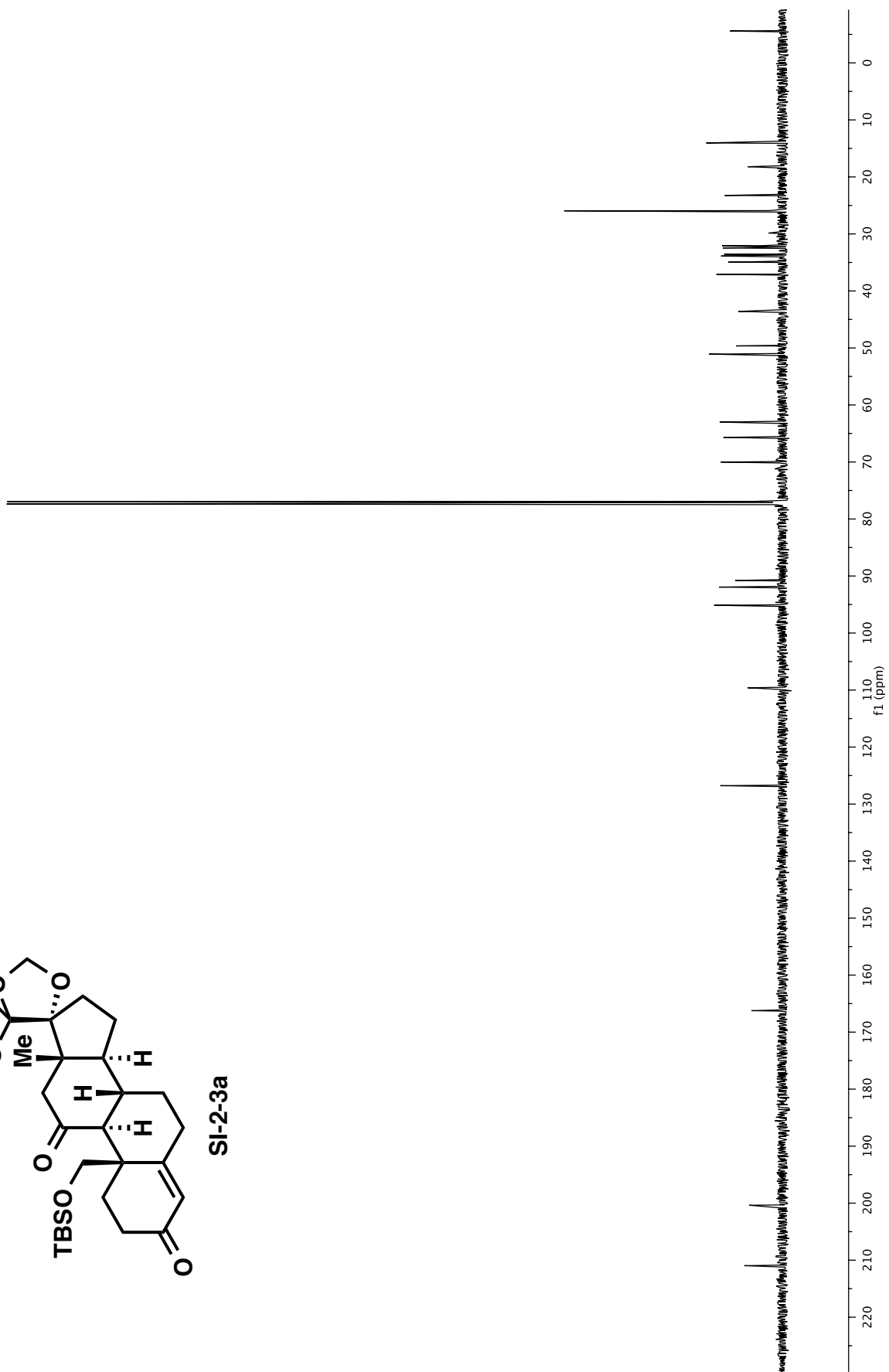
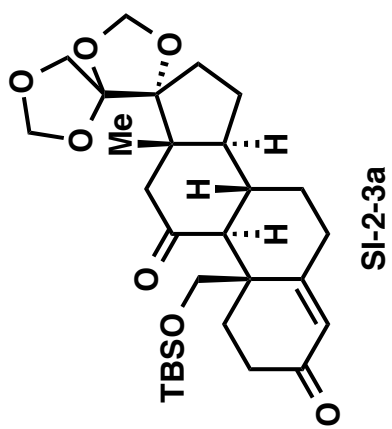


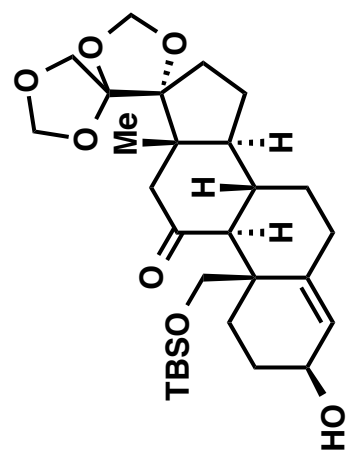


SI-2-3a

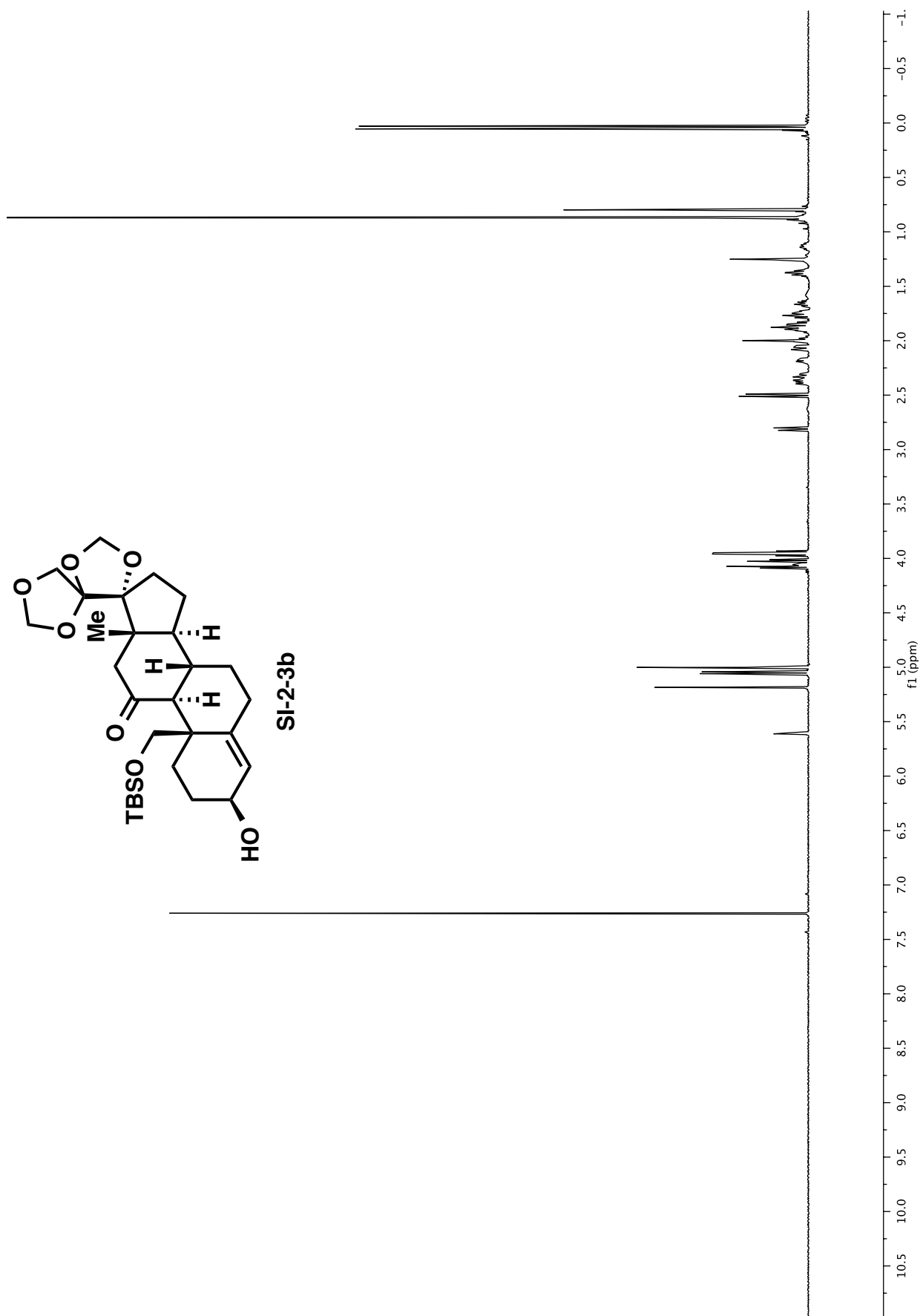
SI-94

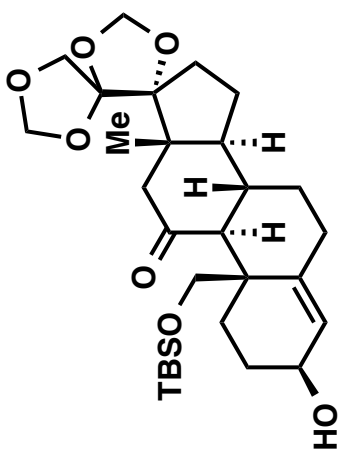




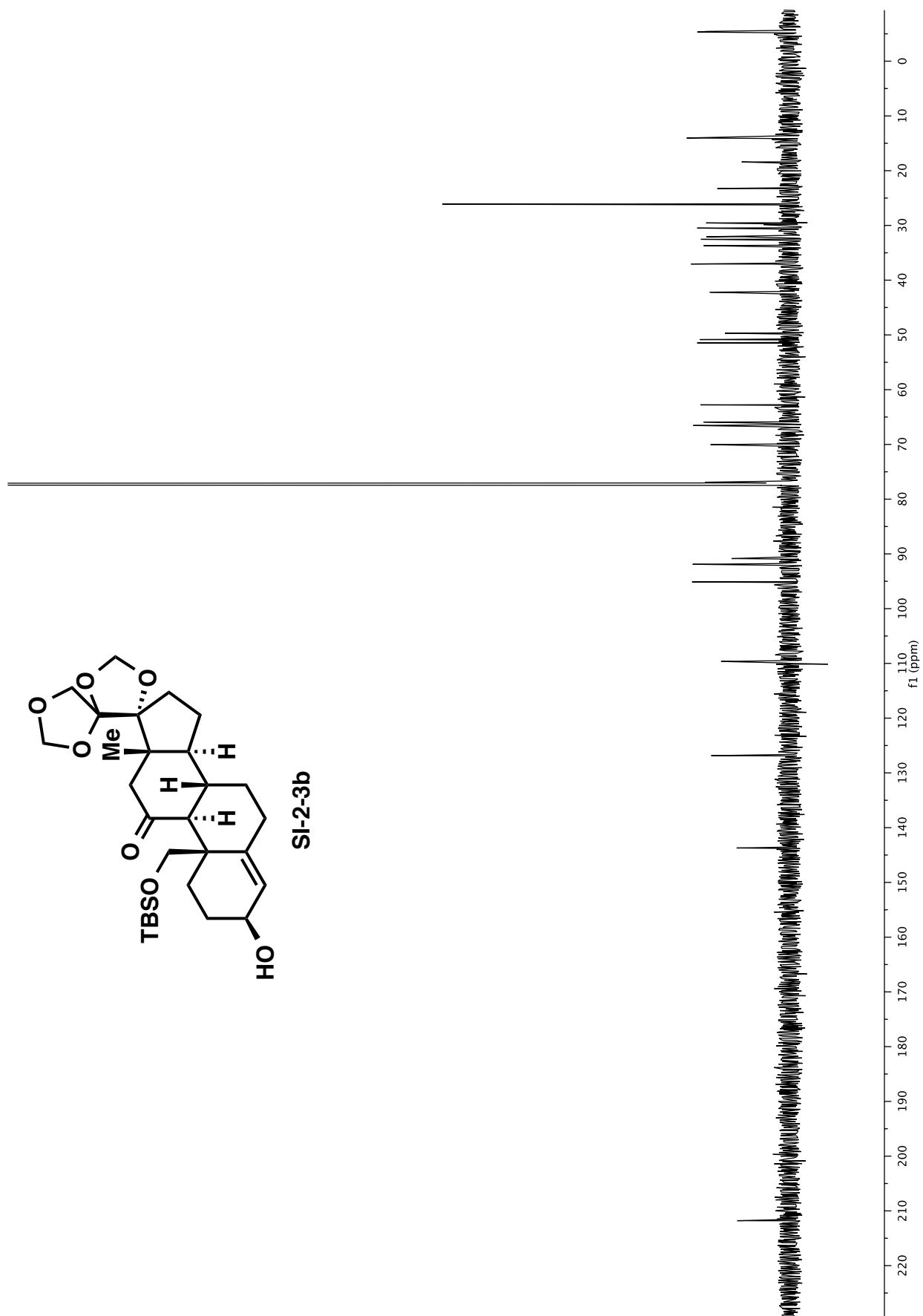


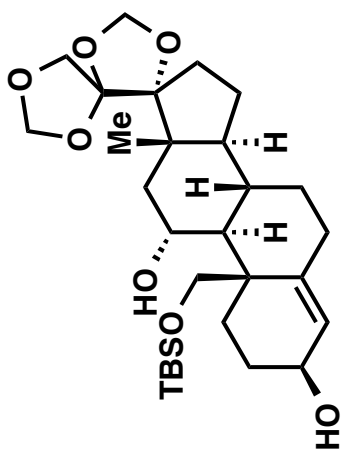
SI-2-3b



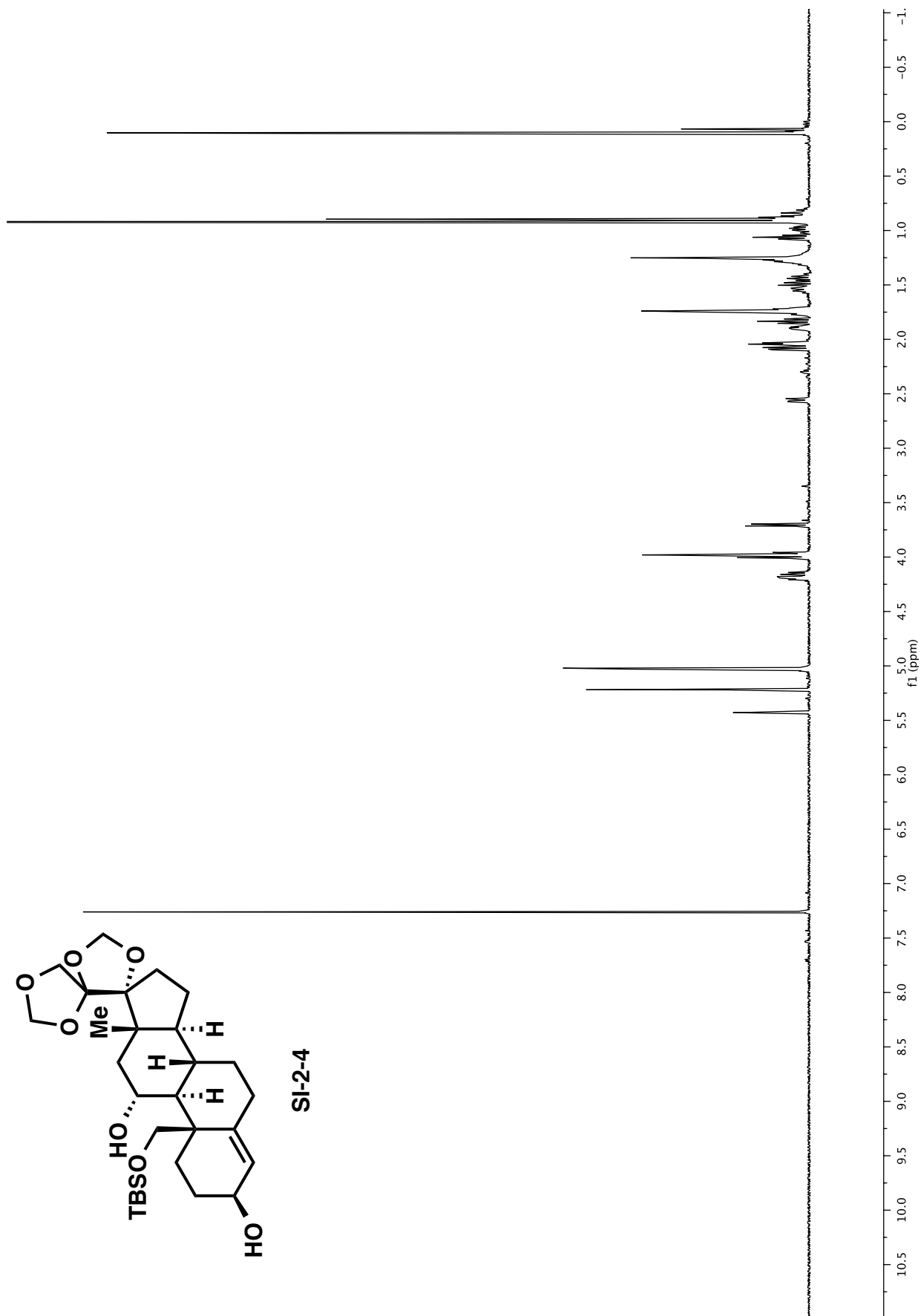


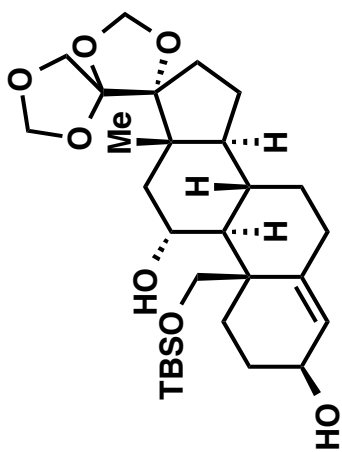
SI-2-3b



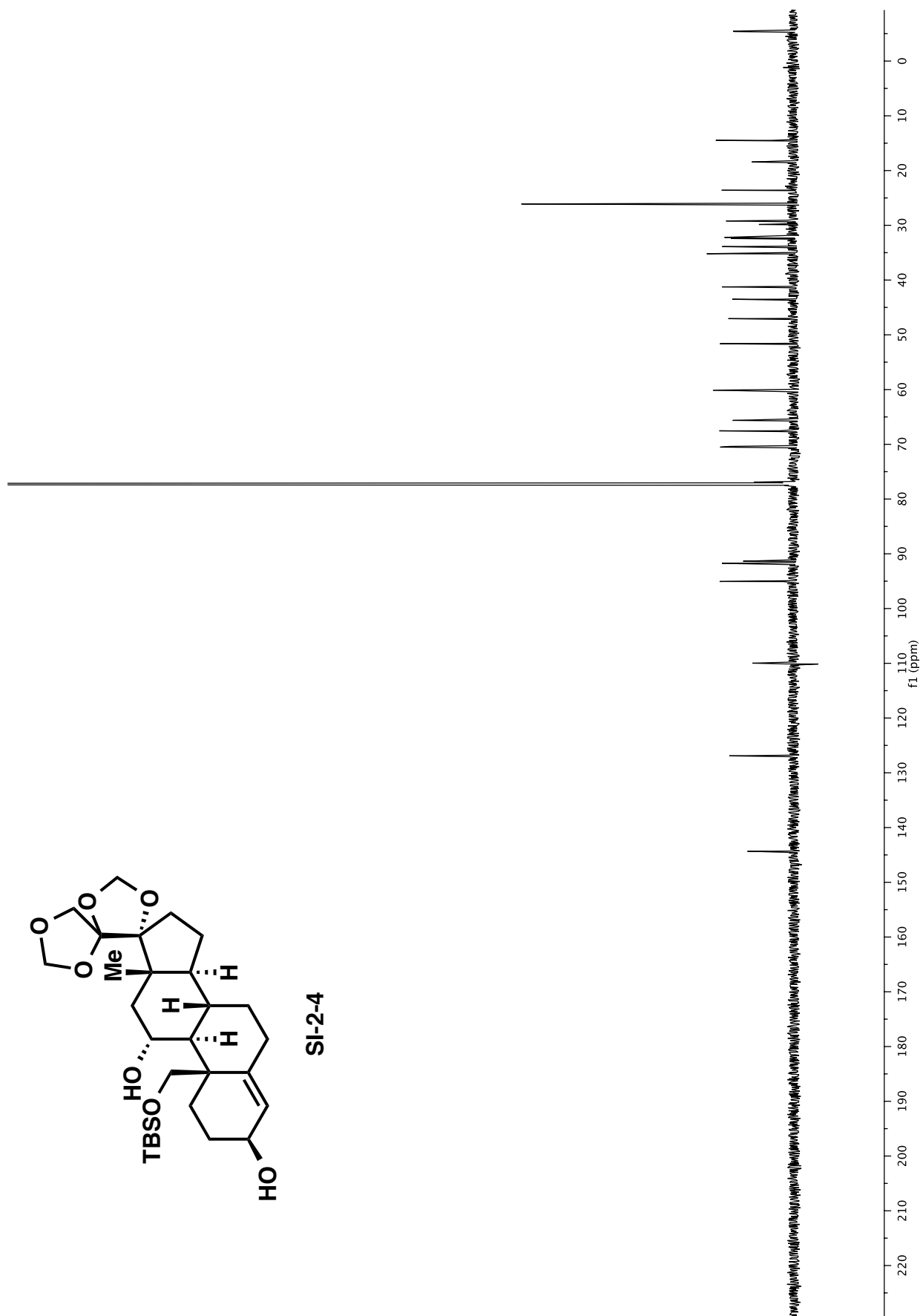


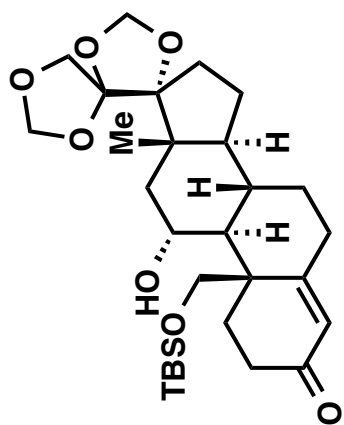
SI-2-4



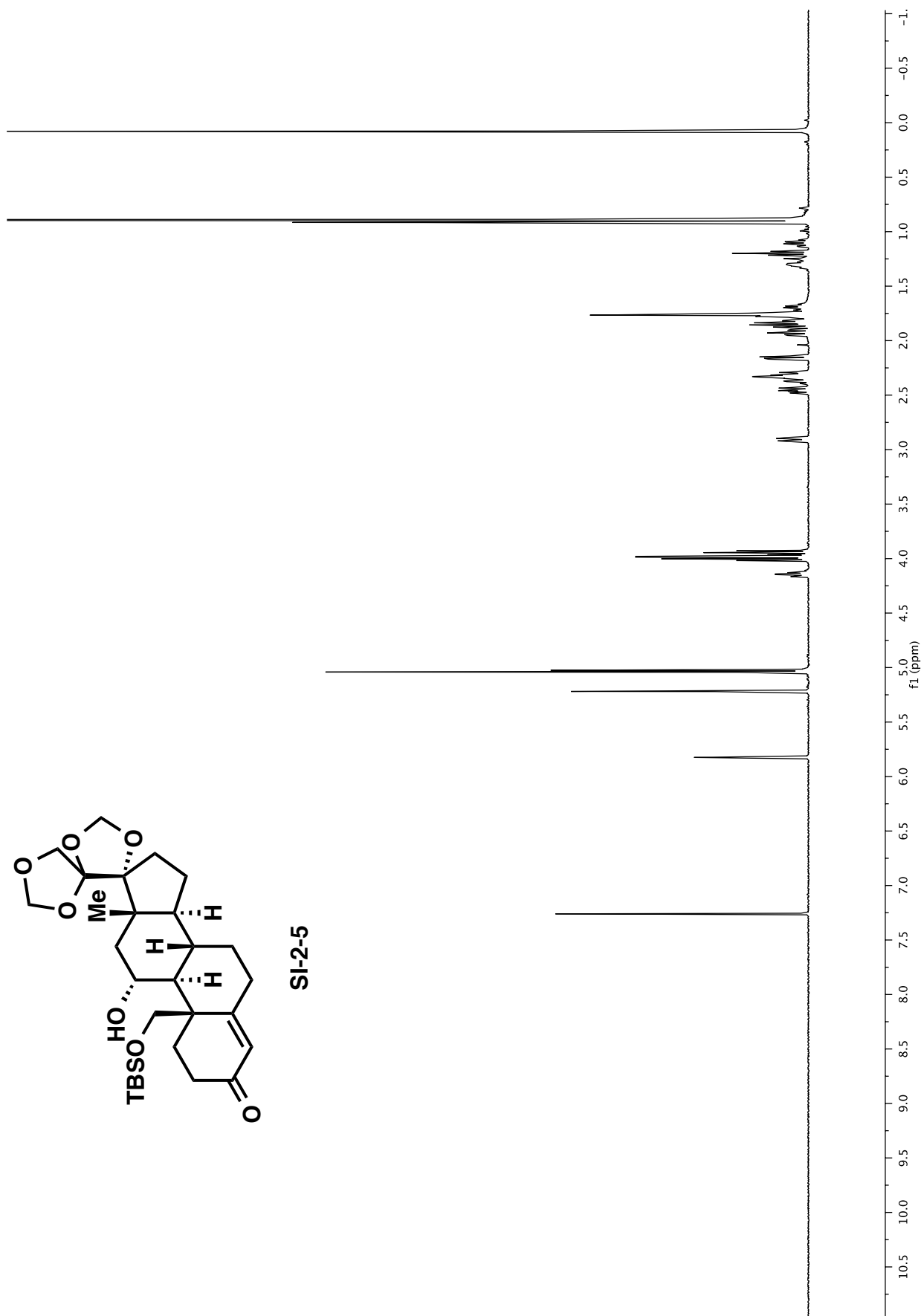


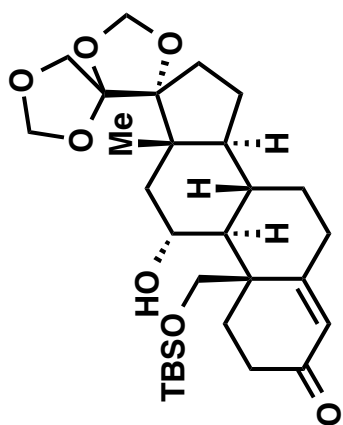
SI-2-4



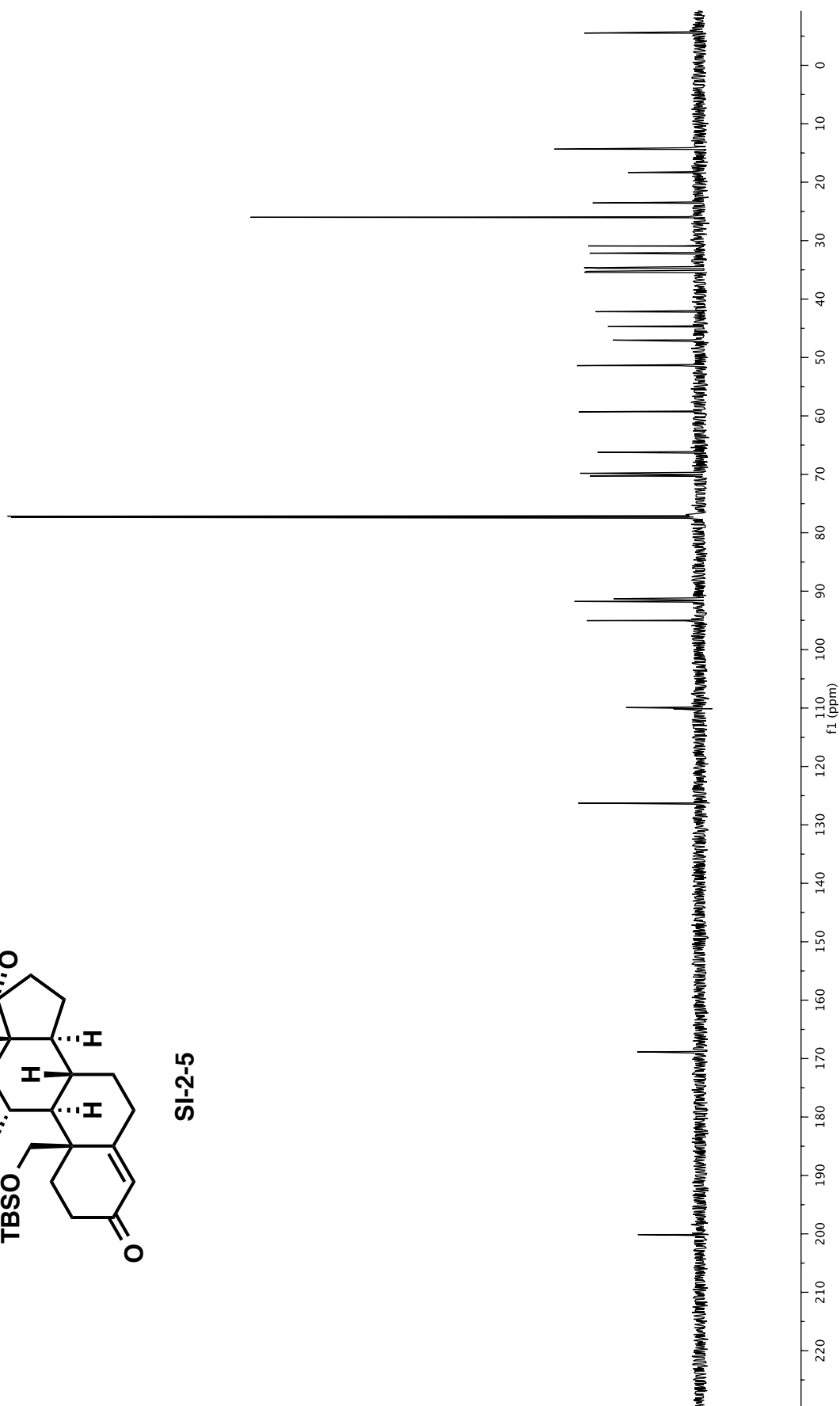


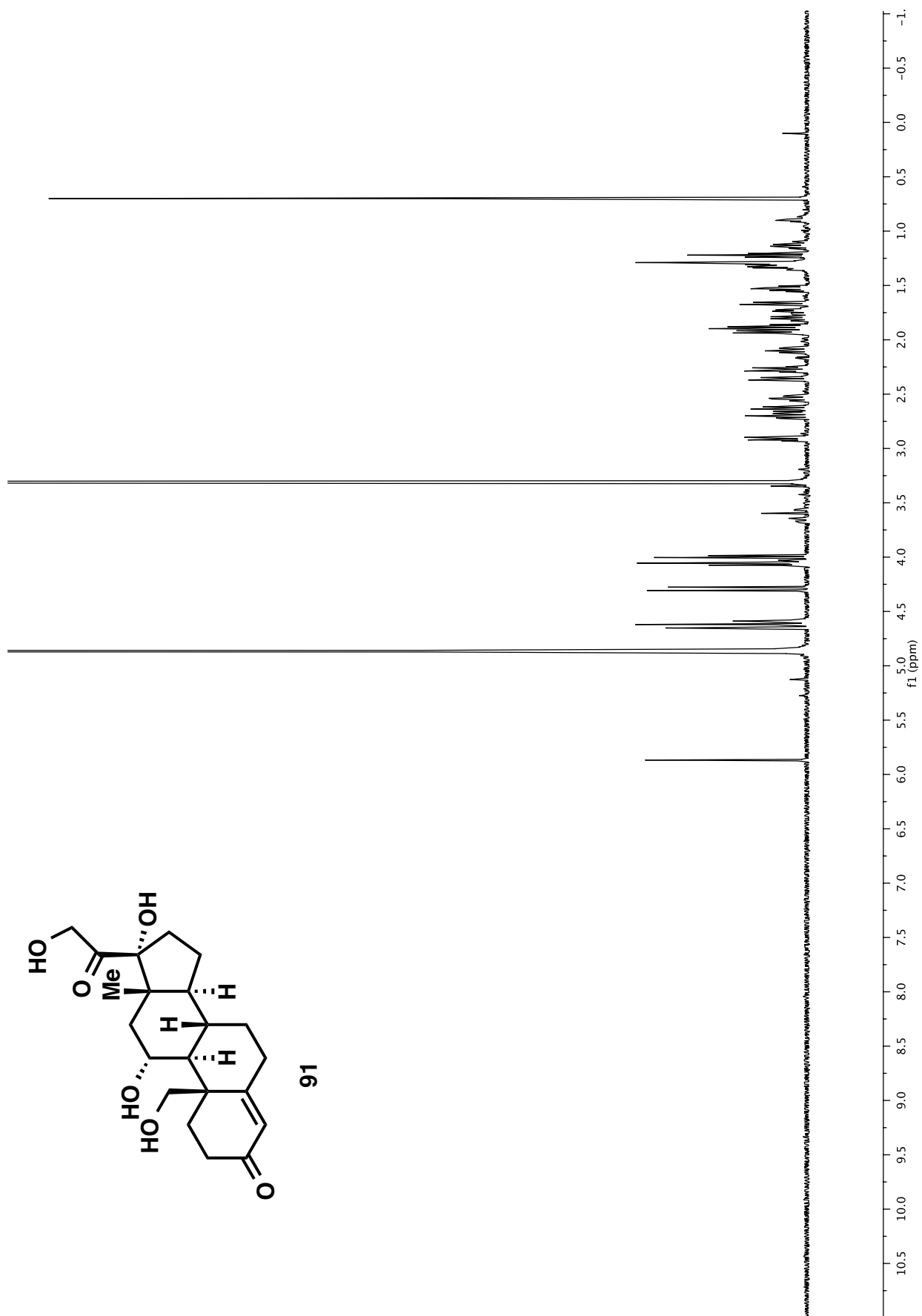
SI-2-5

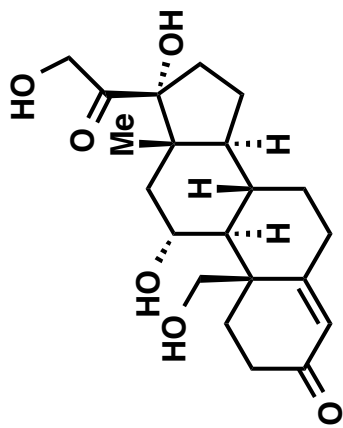




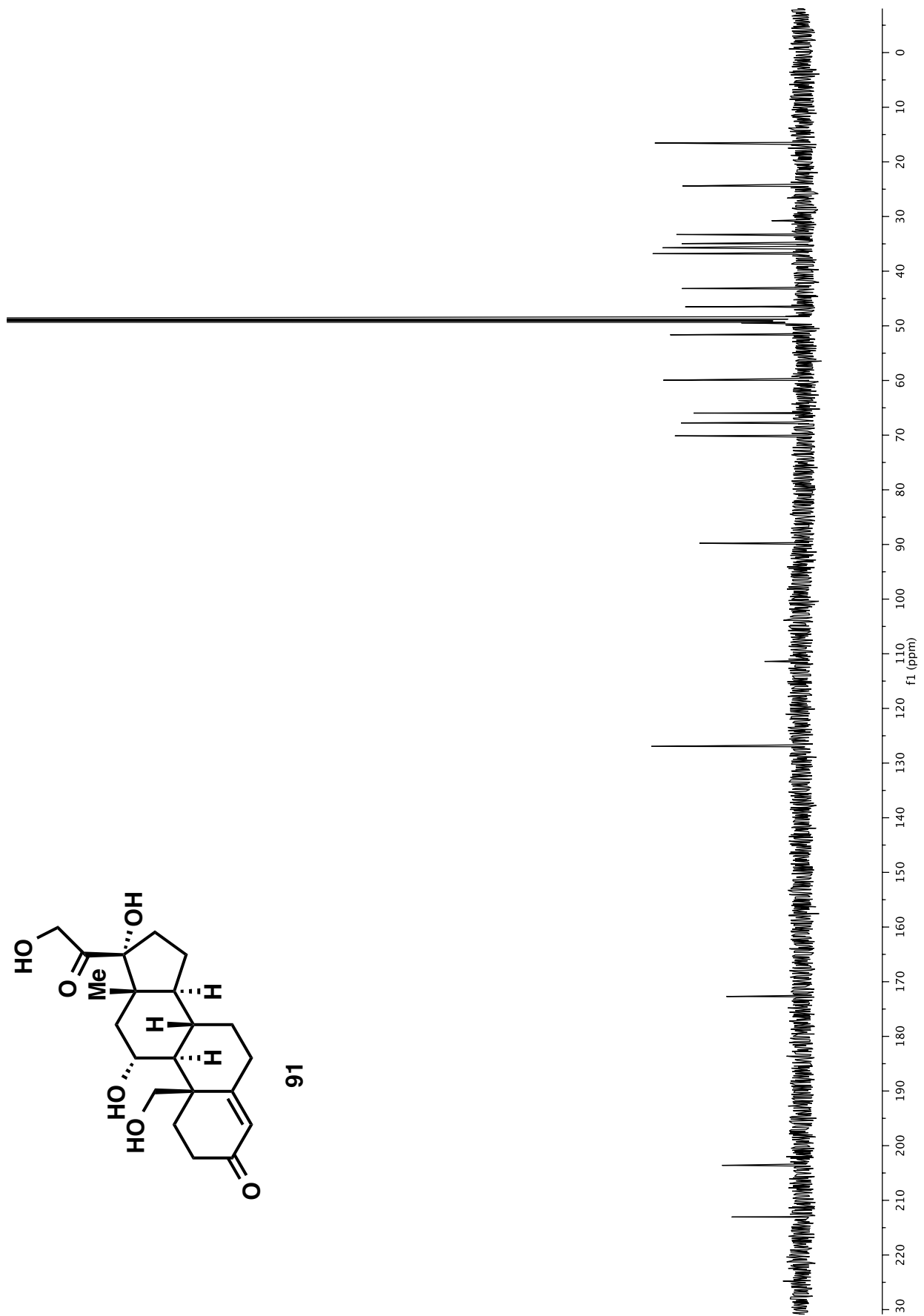
SI-2-5

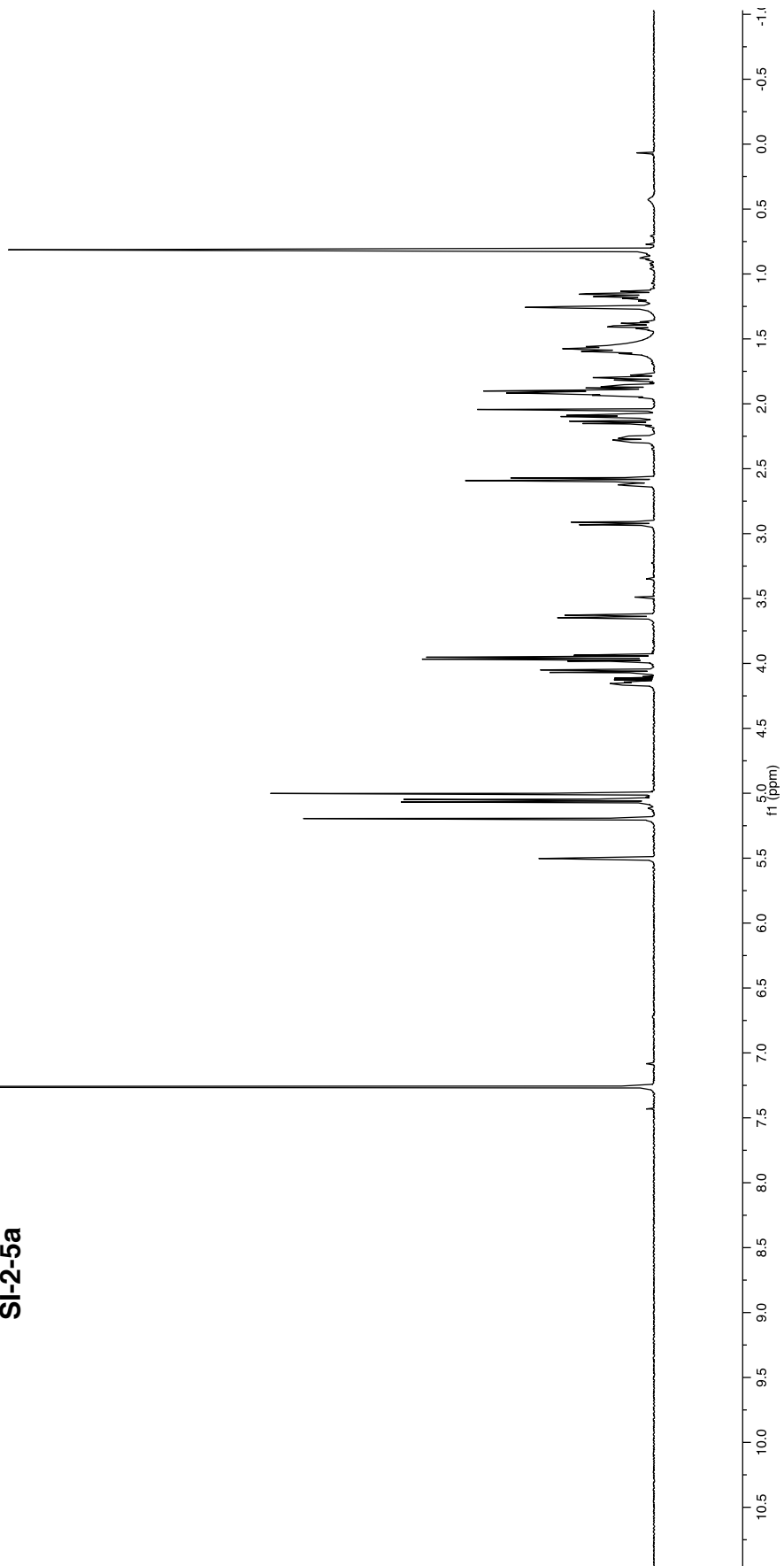
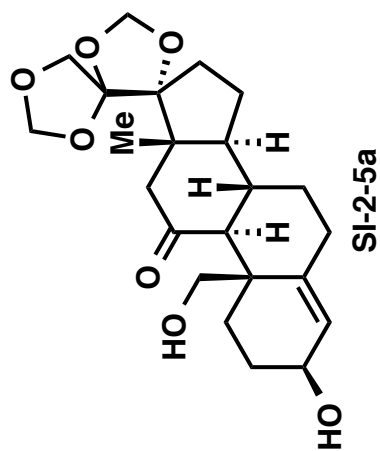


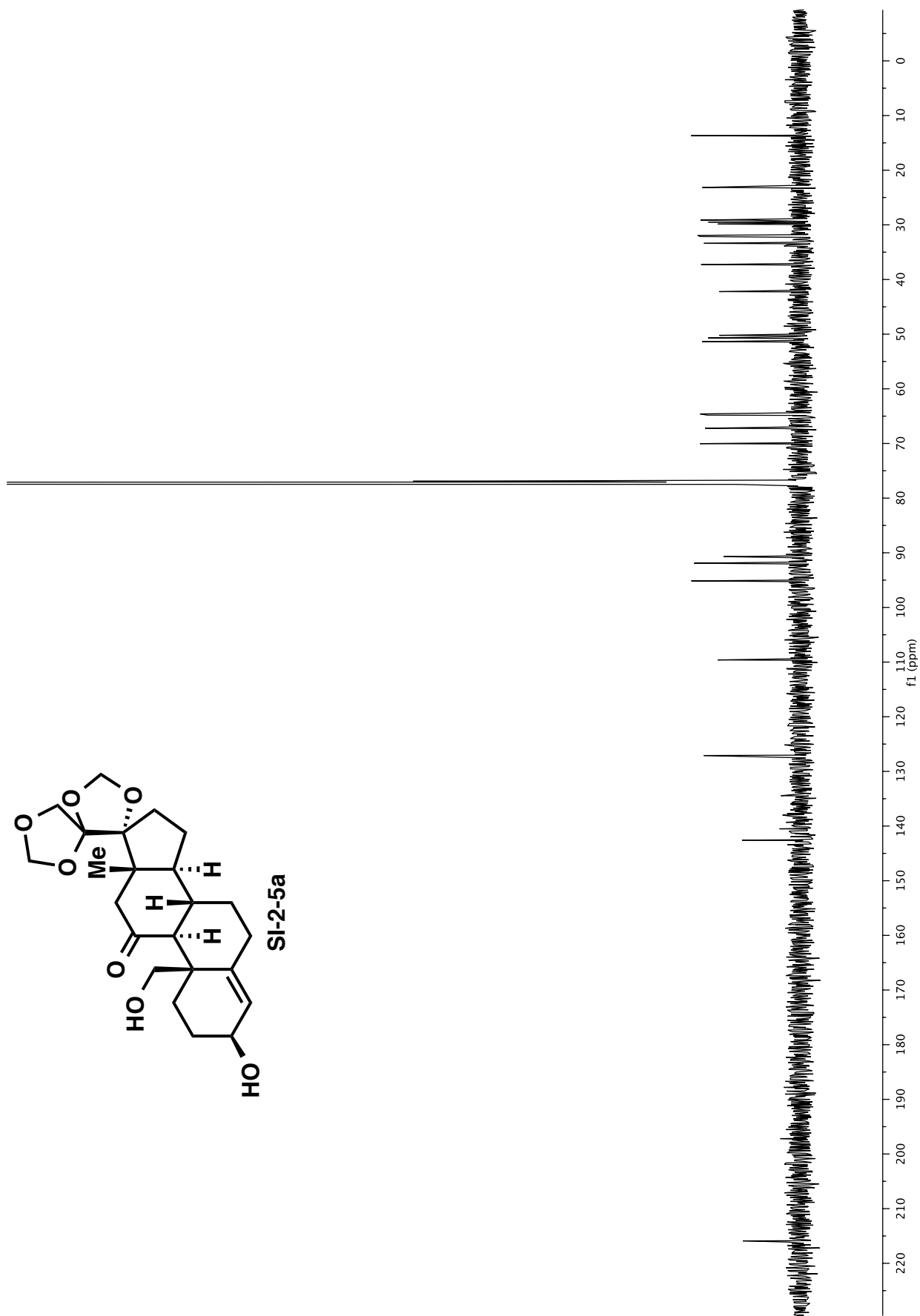
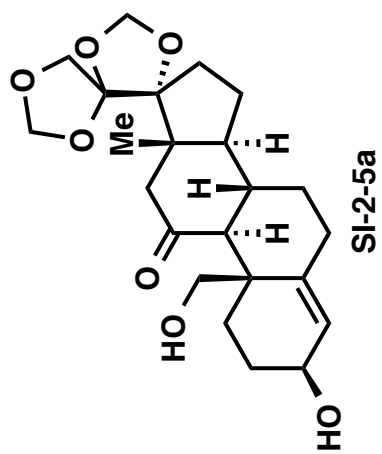


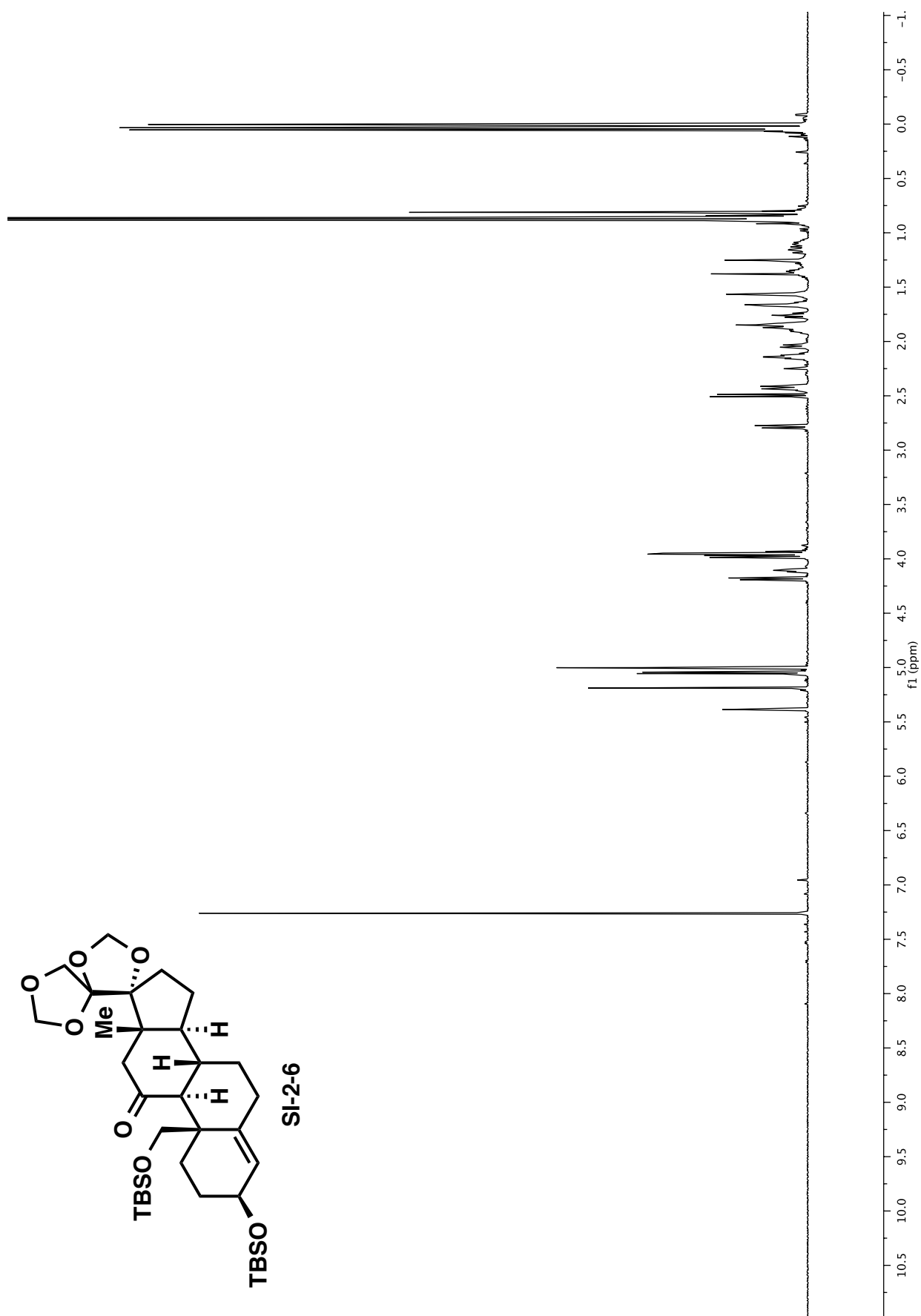


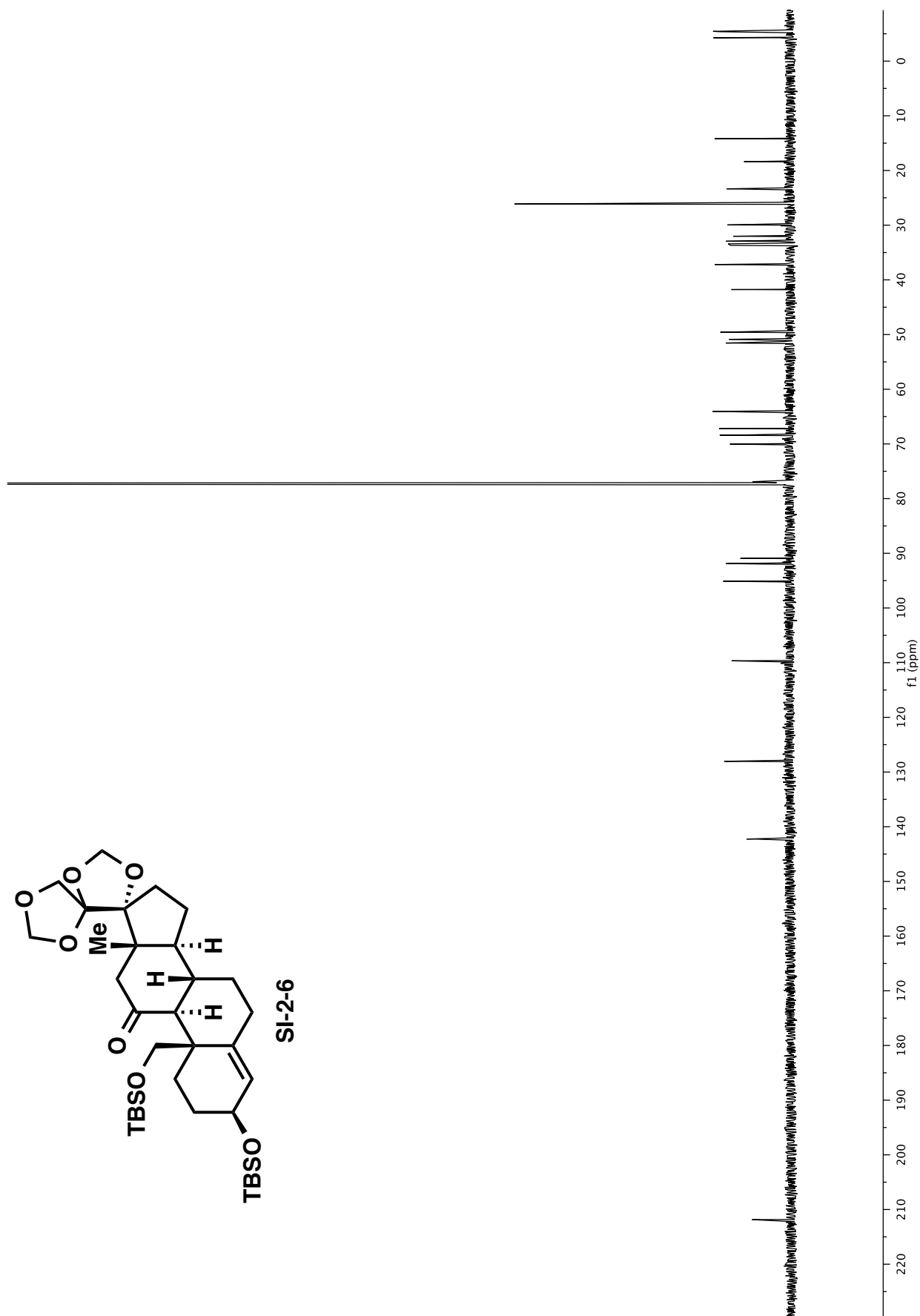
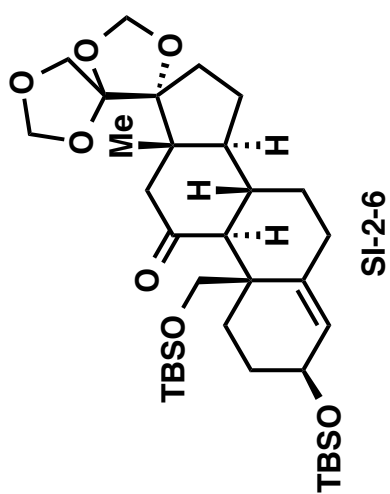
91

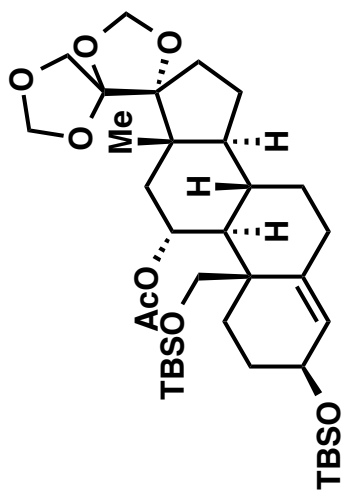




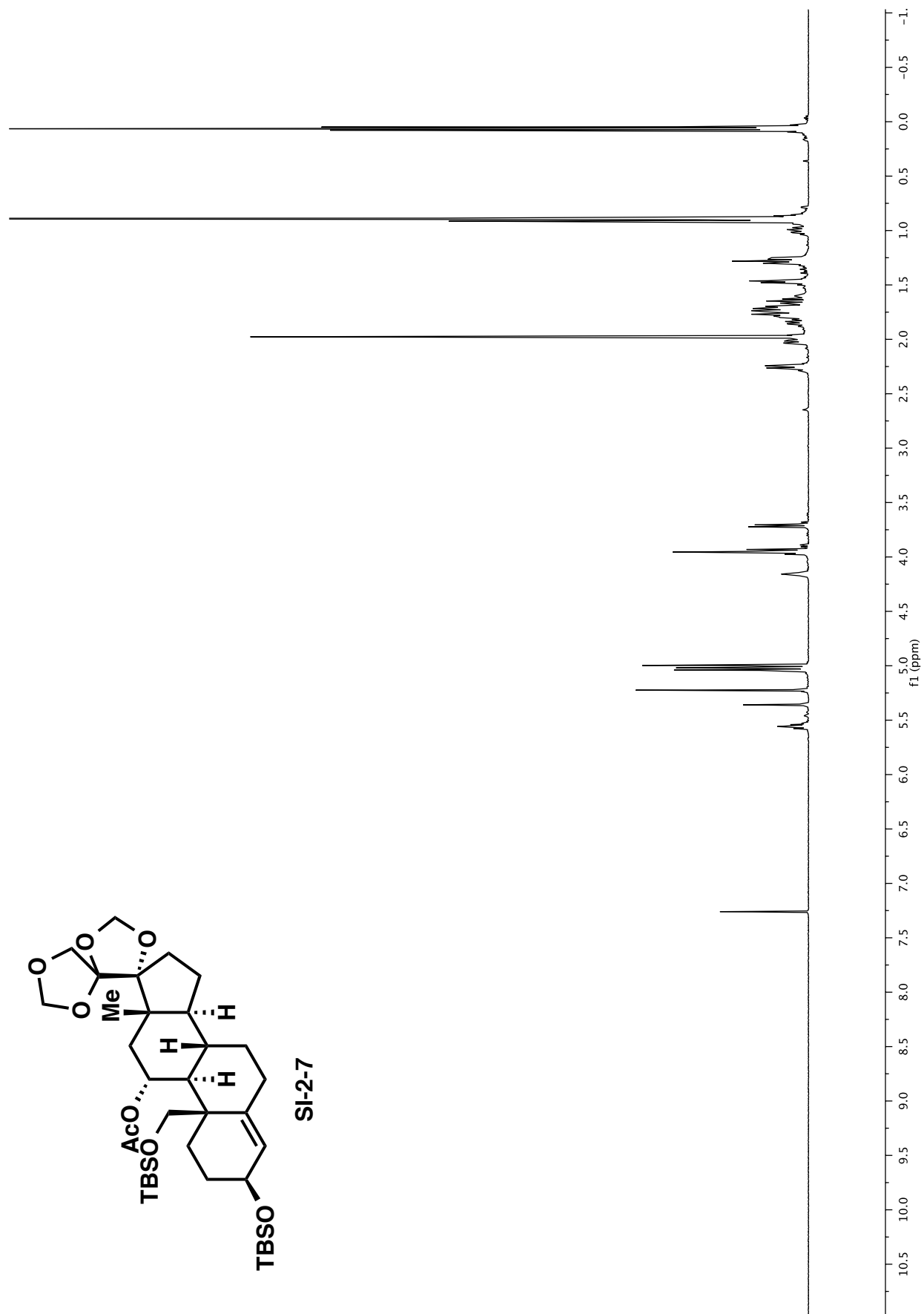


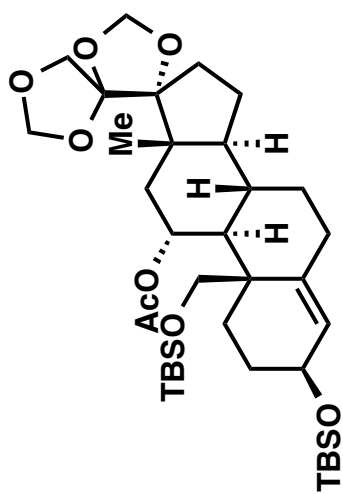




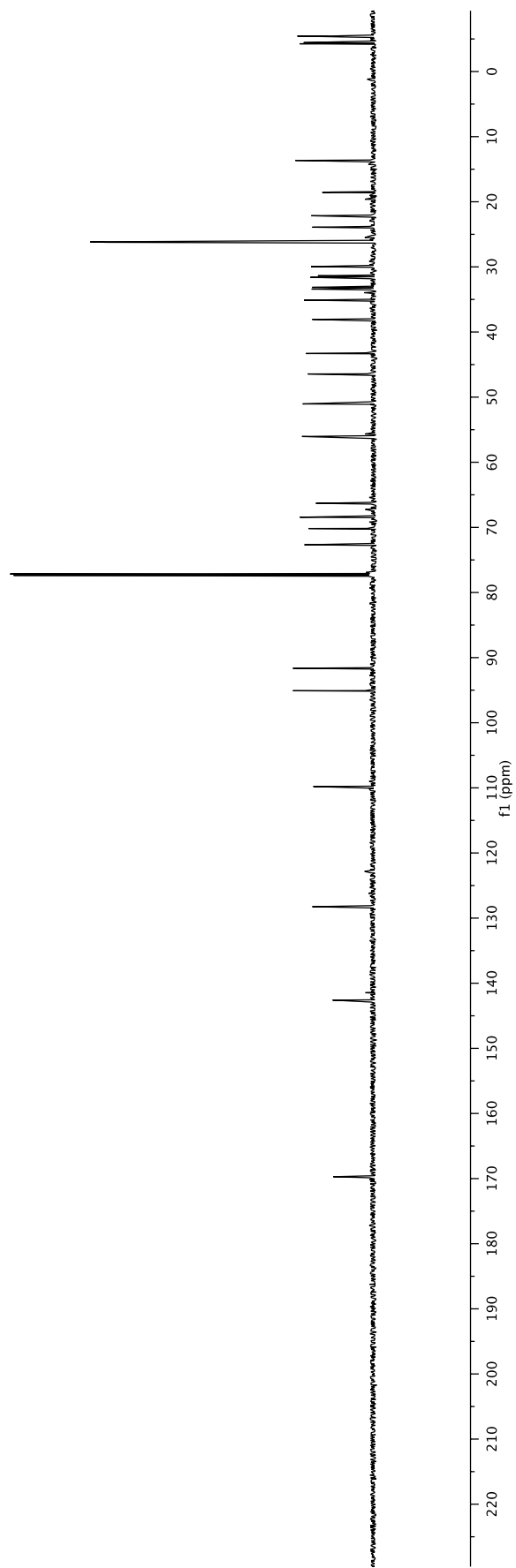


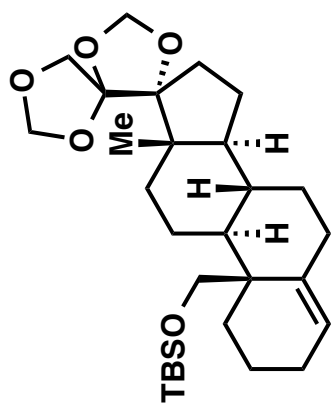
SI-2-7



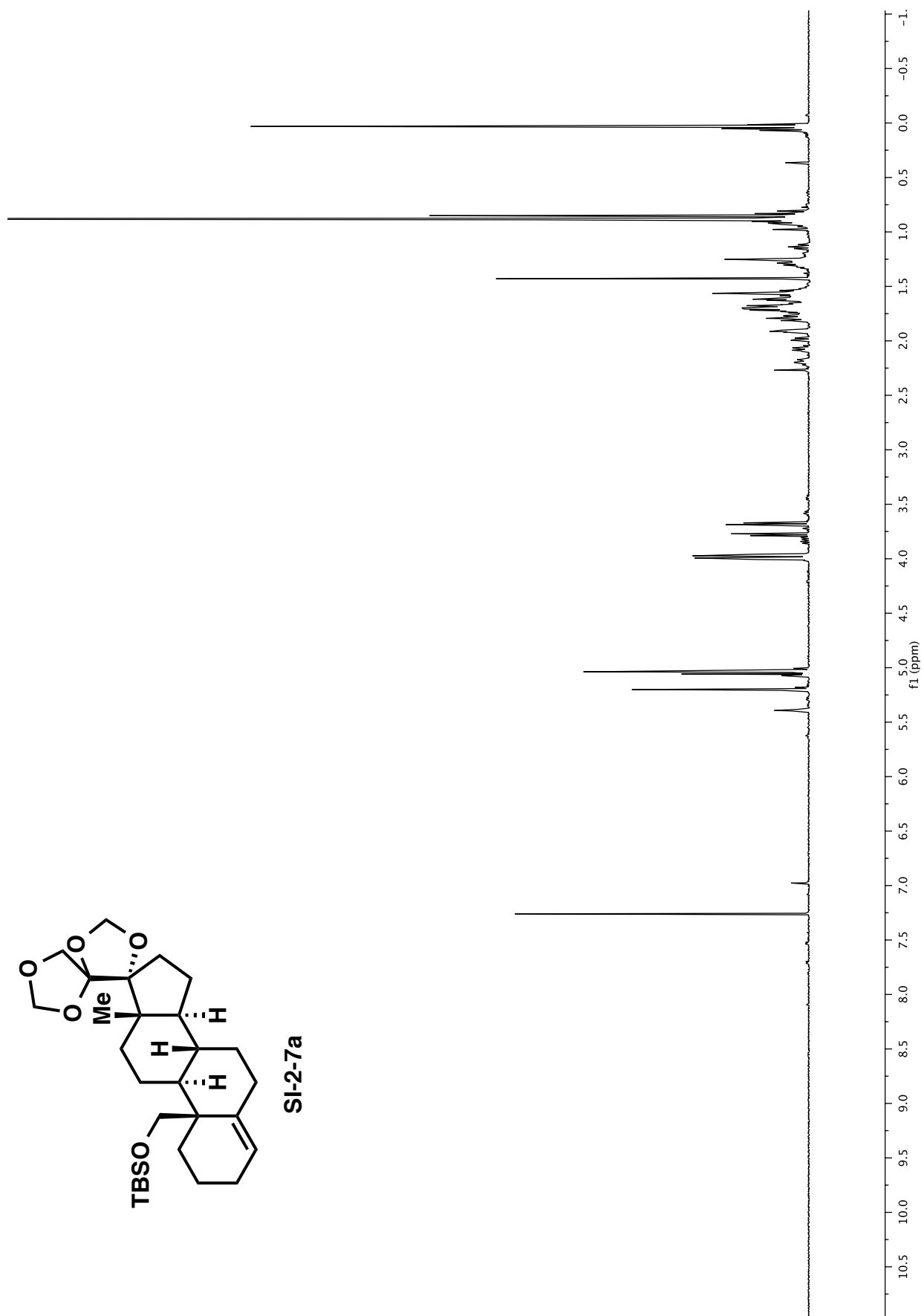


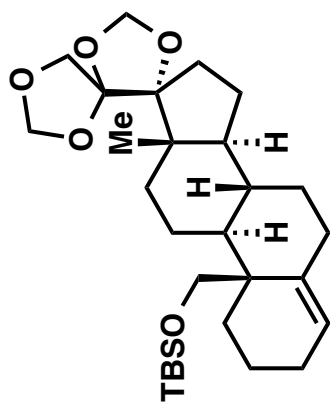
SI-2-7



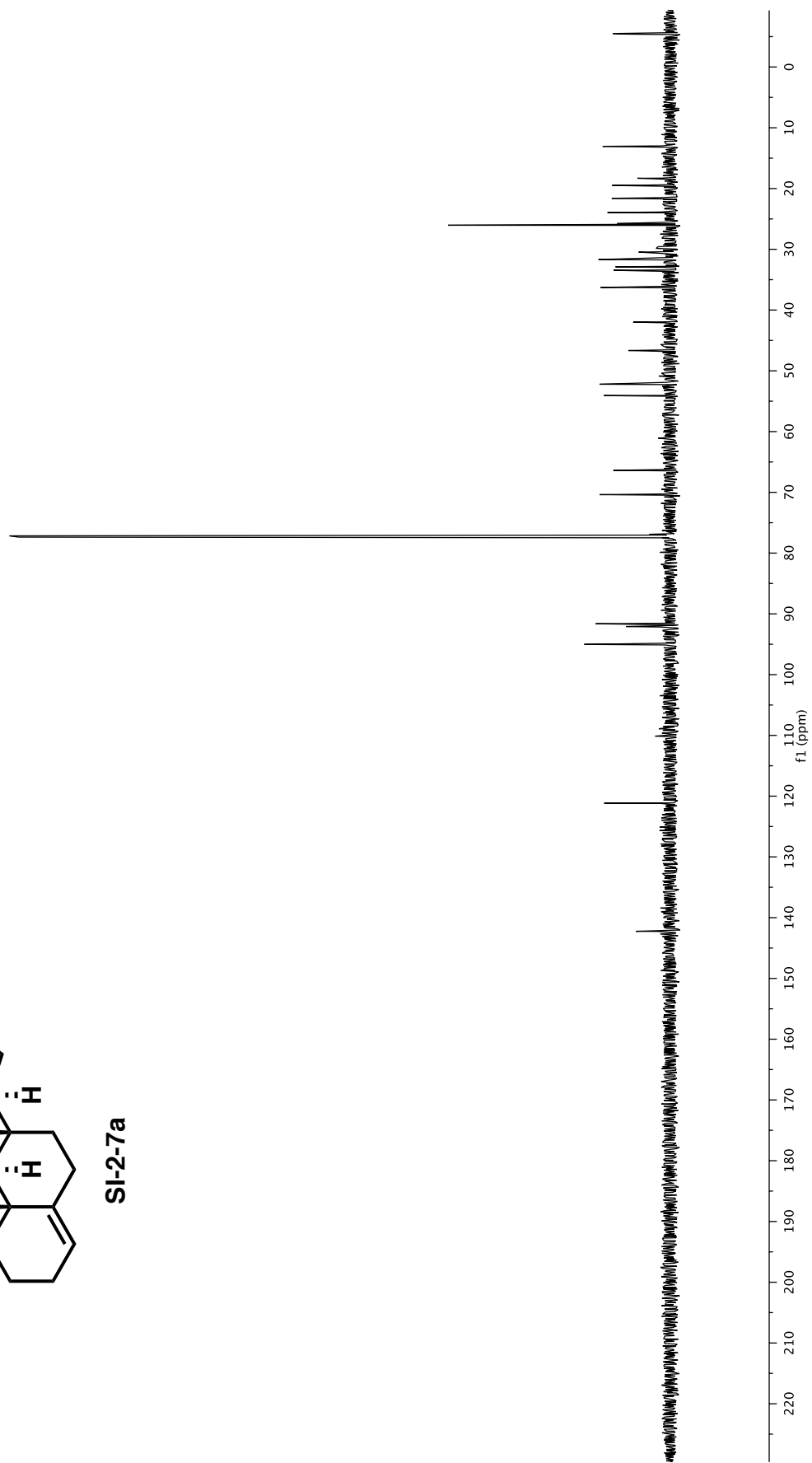


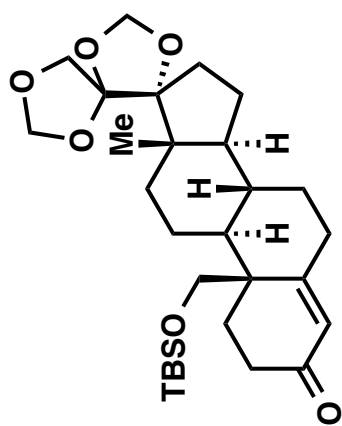
SI-2-7a



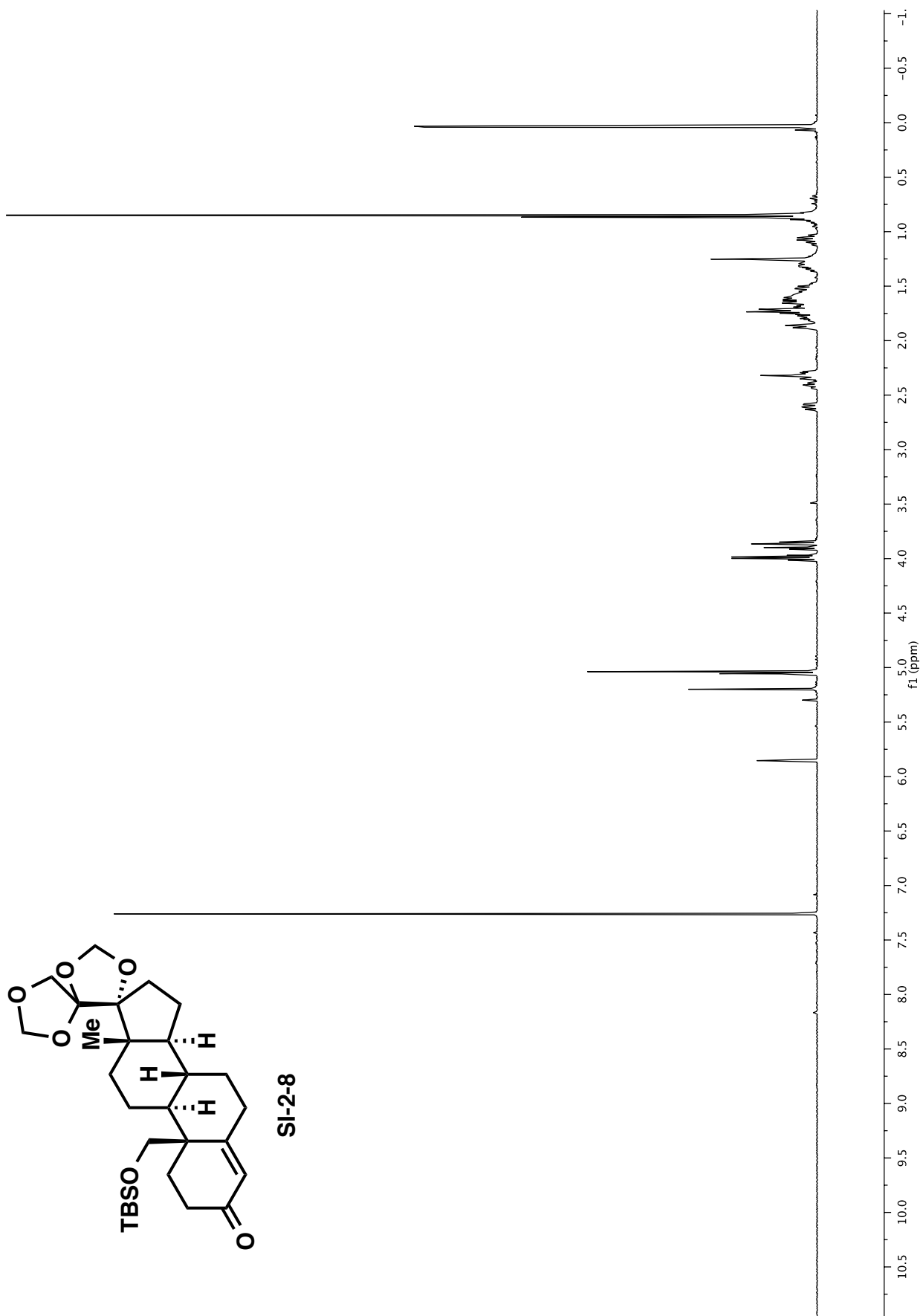


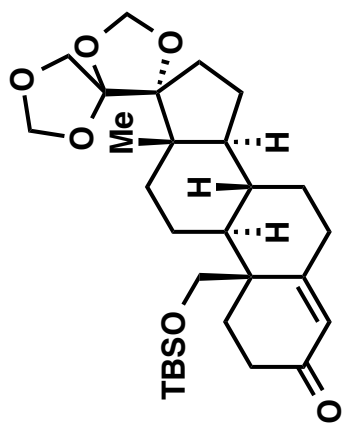
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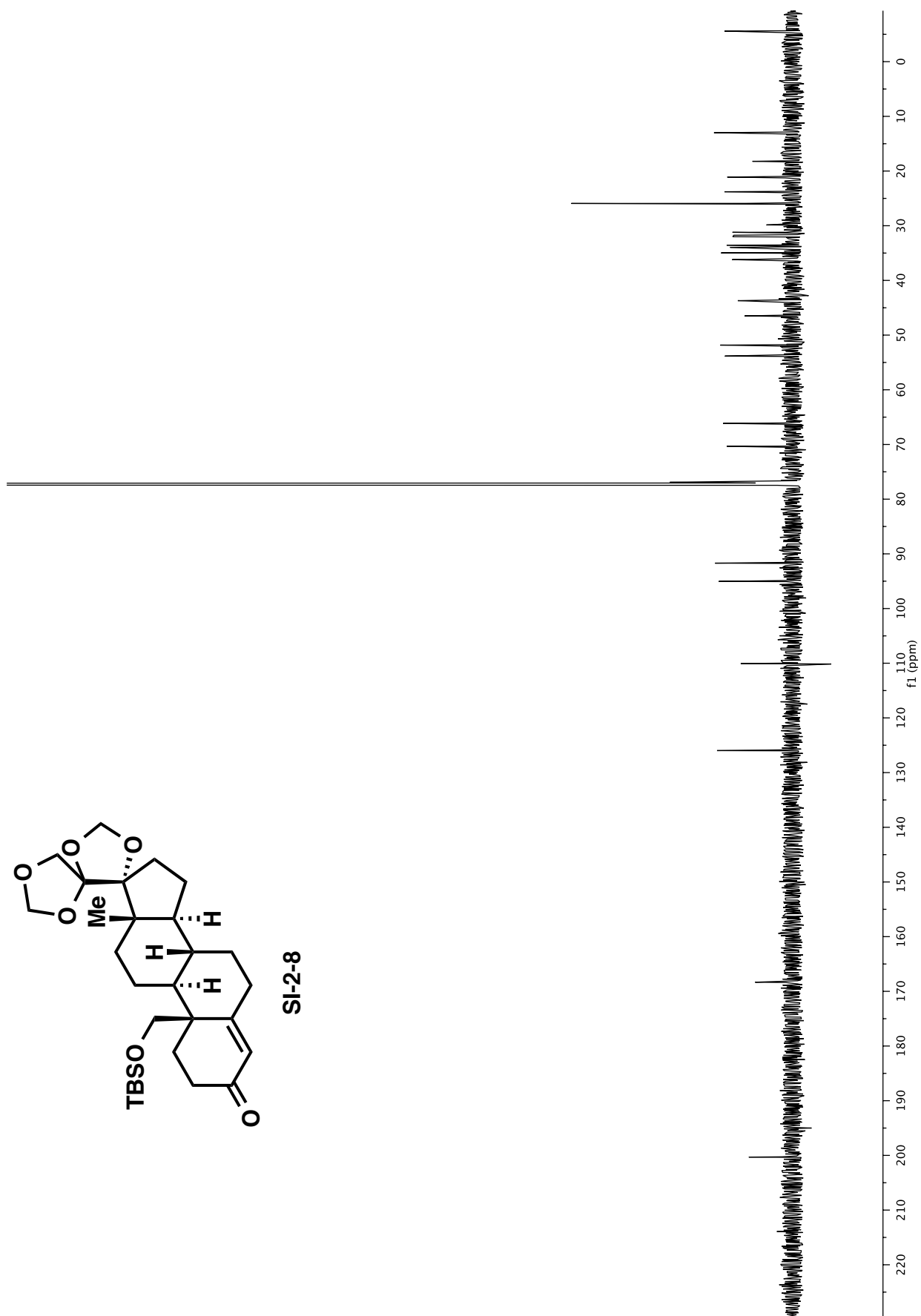


SI-2-8

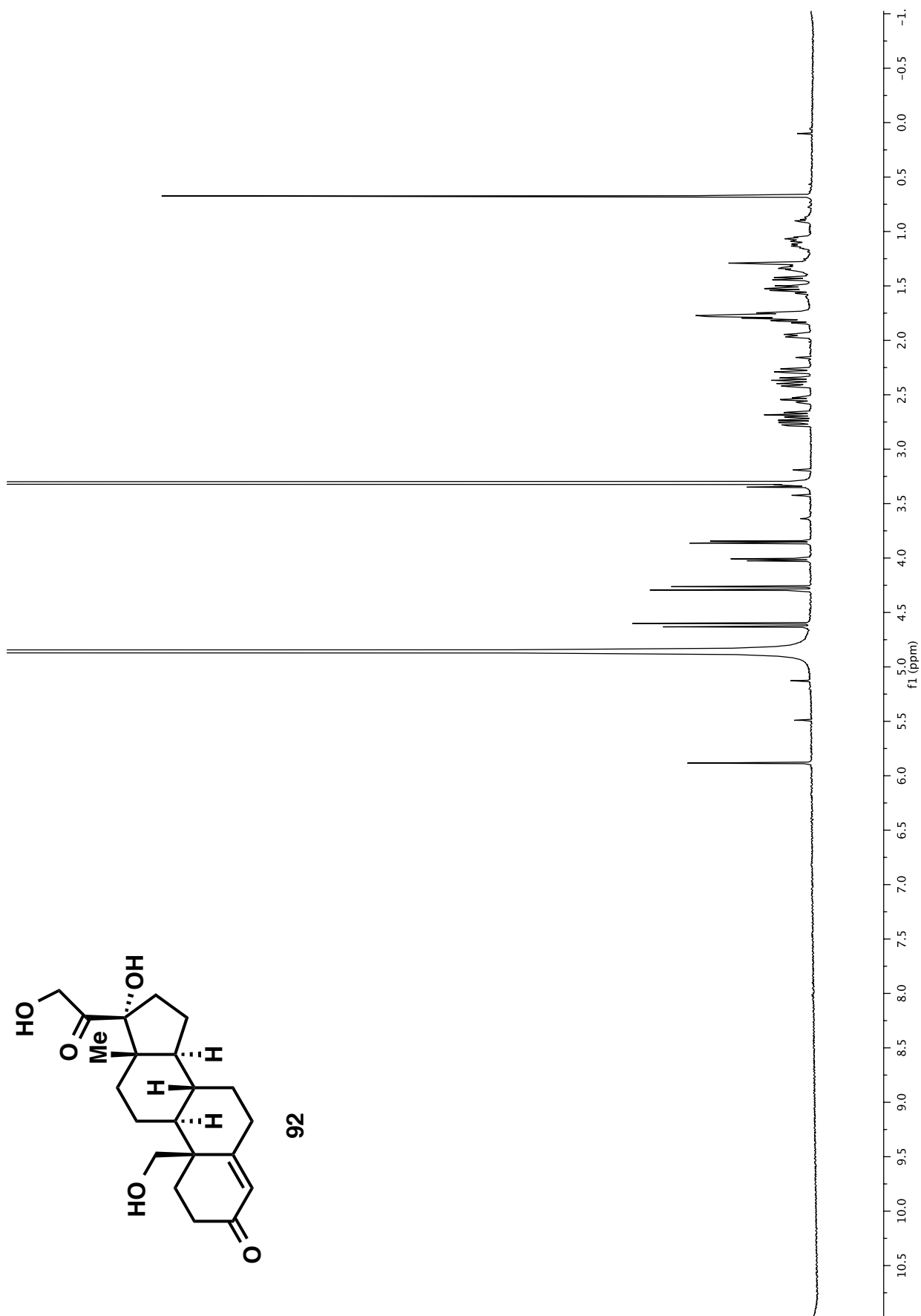
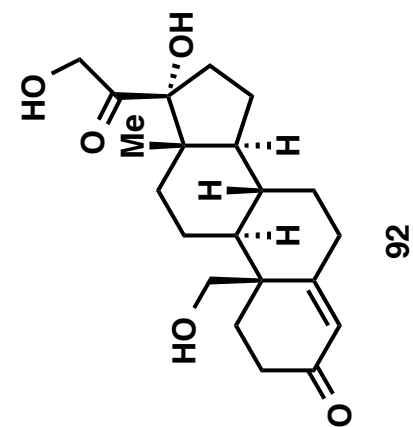


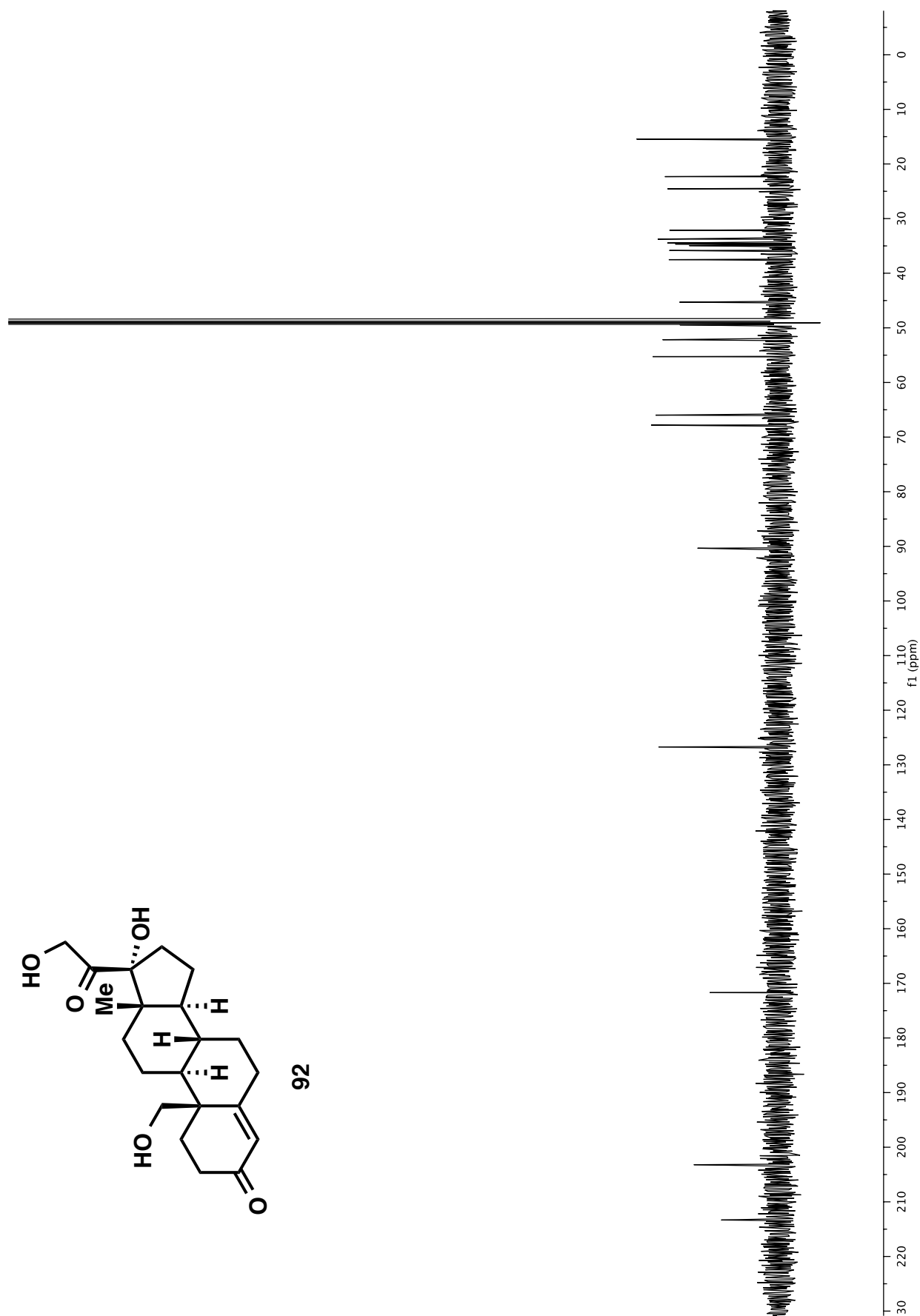
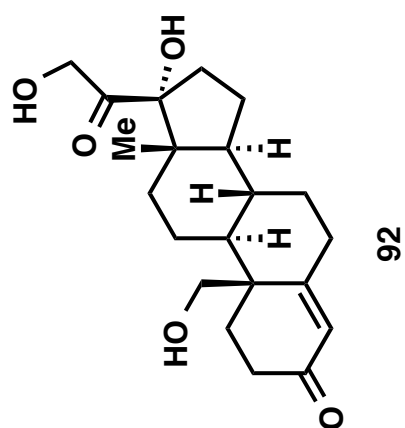


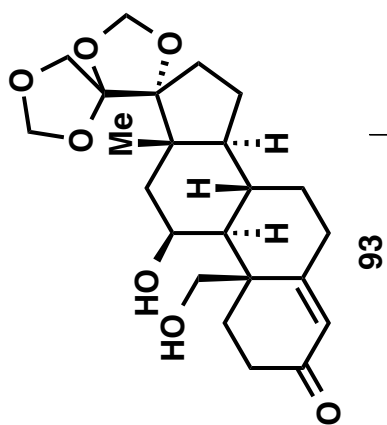
SI-2-8



SI-114







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