Supporting information

Short, Lipidated Dendrimeric γ-AApeptides as New Antimicrobial Peptidomimetics

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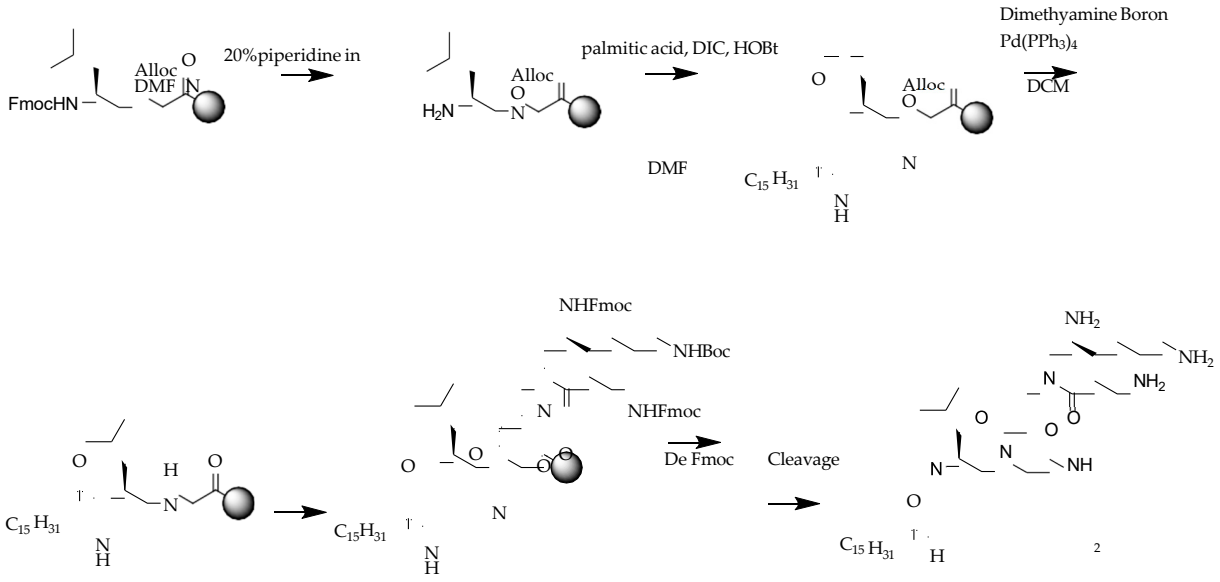
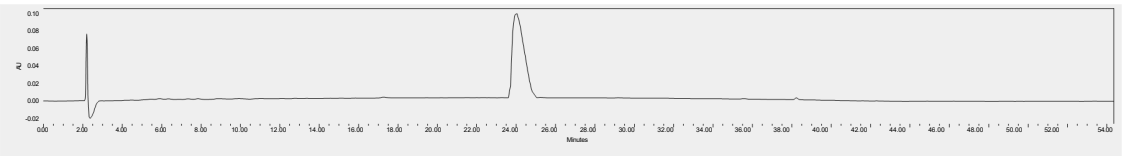
1. General Synthesis of Compound

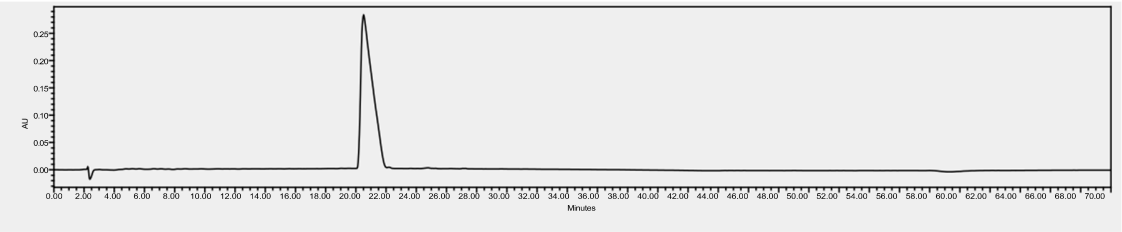
The Fmoc-protected amino acids were bought from Chemimpex, and the reagents used in the reaction were bought from Fisher Scientific and Sigma Aldrich. The building blocks were synthesized according to a previously published paper [1]. Next, the building block was loaded on Rink-Amide beads with DIC and HOBt in DMF, reacting for 4 hours. After deprotecting the Fmoc protecting, palmitic acid was coupled with DIC and HOBt again. The Alloc protecting group of the secondary amine was removed with dimethylamine boron ((CH3)2NH.BH3), and tetrakis (triphenylphosphine) palladium, the second building, was coupled similarly to the first building block. The Alloc protecting group was deprotected again, then the couple Fmoc-protected beta alanine was also deprotected. Subsequently, the Fmoc was removed, and the beads were cleaved with 50% TFA in DCM. The solvent was removed, and the solid was precipitated with cold ether. Finally, the oil was purified by HPLC, and the final product was obtained.



2. HPLC Data



YW-1



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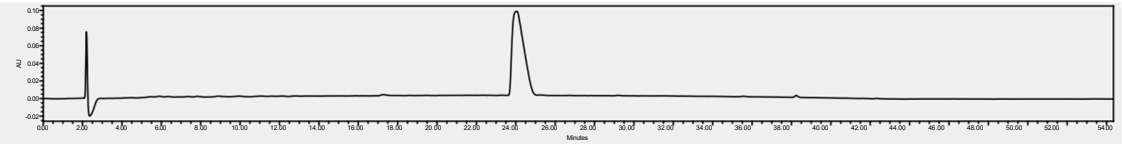

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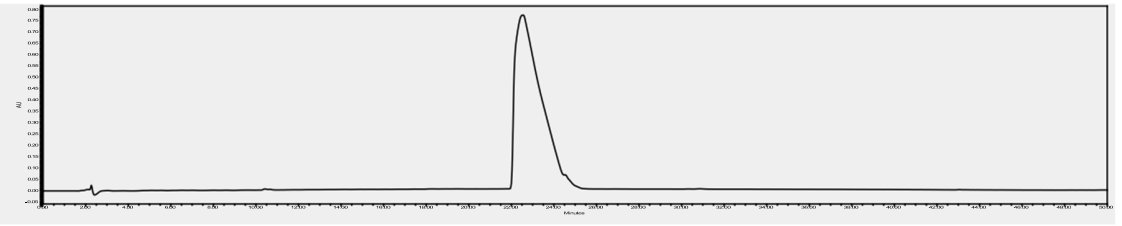

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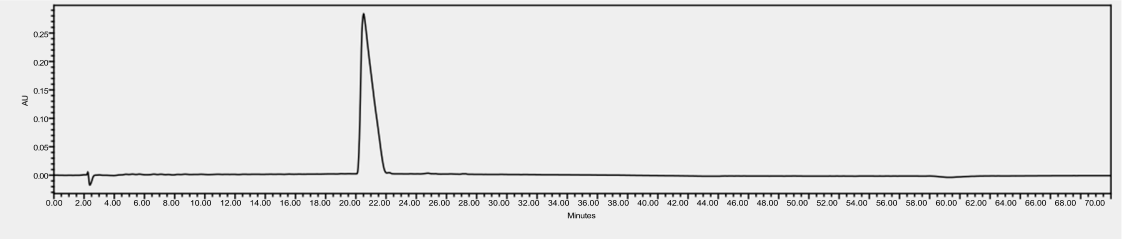

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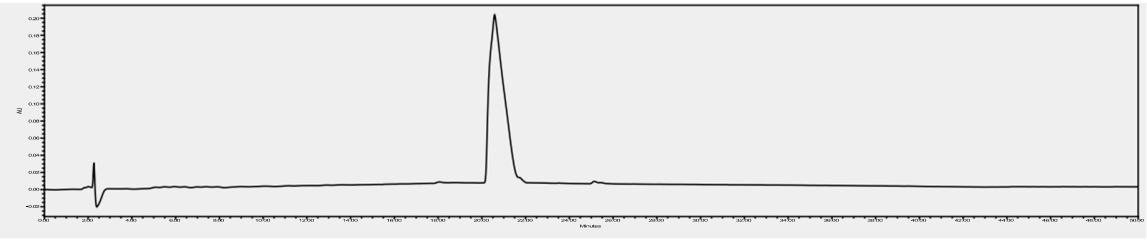

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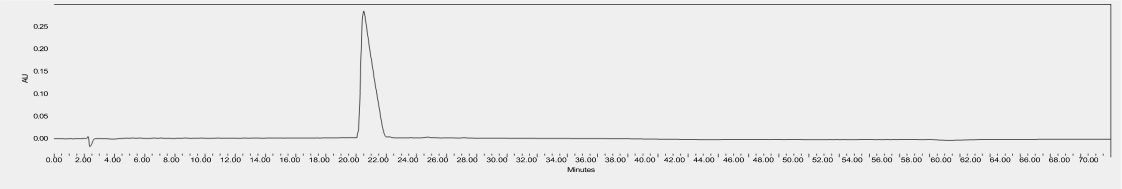

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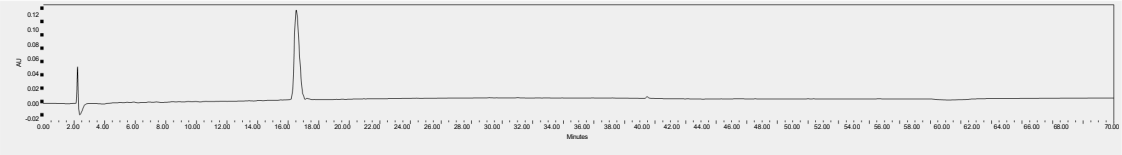

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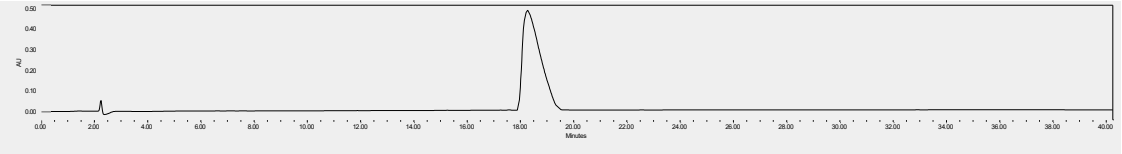

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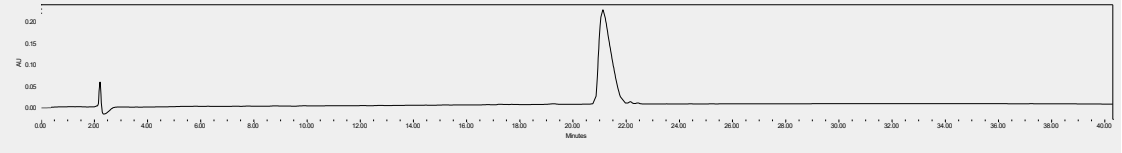

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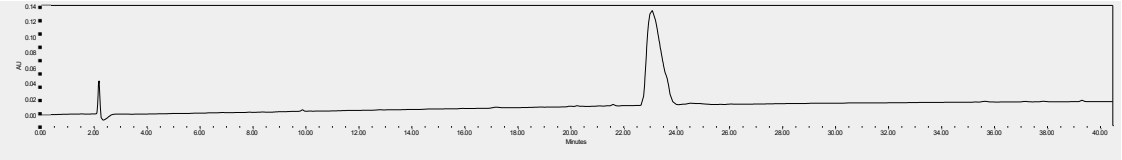


YW-11

3. 1H NMR Spectrum and 13C NMR Spectrum

YW-1:

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.09 (s, 1H), 7.96 – 7.71 (m, 9H), 7.57 (d, *J* = 8.9 Hz, 1H), 7.37 (d, *J* = 22.1 Hz, 1H),
7.17 (d, *J* = 12.8 Hz, 1H), 6.99 (d, *J* = 14.9 Hz, 1H), 4.10 – 3.88 (m, 3H), 3.74 (d, *J* = 16.5 Hz, 1H), 3.50 (ddd, *J* = 33.1,
14.7, 7.5 Hz, 4H), 3.26 – 3.16 (m, 1H), 3.02 (qd, *J* = 6.4, 3.2 Hz, 2H), 2.75 (dddd, *J* = 28.1, 13.9, 6.9, 3.1 Hz, 5H), 2.11
– 1.95 (m, 2H), 1.64 – 1.30 (m, 10H), 1.24 (s, 26H), 0.89 – 0.83 (m, 6H), 0.80 (dd, *J* = 10.4, 6.5 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.72, 172.49, 170.78, 158.82, 158.61, 38.94, 36.02, 35.73, 31.74, 30.46, 29.50, 29.15, 28.97, 27.14, 24.78, 23.80, 22.55, 22.01, 21.72, 14.41.

YW-2:

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.20 – 7.96 (m, 1H), 7.94 – 7.71 (m, 9H), 7.30 – 7.10 (m, 6H), 4.27 – 4.09 (m, 1H),
4.08 – 3.94 (m, 1H), 3.93 – 3.75 (m, 1H), 3.56 (ddd, *J* = 87.1, 13.0, 5.8 Hz, 4H), 3.02 (p, *J* = 6.4 Hz, 2H), 2.94 (dd, *J* =
13.4, 7.4 Hz, 1H), 2.85 – 2.53 (m, 7H), 2.45 (q, *J* = 7.0 Hz, 1H), 1.93 (td, *J* = 7.3, 4.0 Hz, 2H), 1.53 (dtt, *J* = 17.2, 10.4,
5.2 Hz, 4H), 1.45 – 1.10 (m, 27H), 1.09 – 0.94 (m, 2H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 171.27, 170.78, 158.54, 129.45, 128.50, 128.39, 118.54, 116.71,49.99, 47.31, 44.32, 38.95, 31.75, 29.52, 29.38, 29.16, 27.17, 25.67, 22.55, 22.02, 14.42.

YW-3:

^{1}H NMR (600 MHz, DMSO-d_6) δ 7.95 – 7.69 (m, 9H), 4.07 – 3.76 (m, 3H), 3.50 (dd, *J* = 17.8, 10.9 Hz, 4H), 3.24 (dd, *J*
= 7.3, 3.6 Hz, 1H), 3.01 (h, *J* = 6.2 Hz, 2H), 2.85 – 2.63 (m, 5H), 2.02 (dq, *J* = 12.1, 7.0 Hz, 2H), 1.62 – 1.49 (m, *J* = 6.5
Hz, 4H), 1.49 – 1.35 (m, 4H), 1.24 (s, 24H), 1.05 (d, *J* = 6.7 Hz, 1H), 0.97 (d, *J* = 6.7 Hz, 1H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.19, 171.93, 158.82, 158.62, 117.72, 116.43, 49.91, 47.31, 43.58, 38.95, 35.74,
31.75, 30.39, 29.51, 29.47, 29.16, 27.16, 25.70, 22.55, 22.01, 18.70, 18.46, 14.42.

YW-4

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.11 (d, *J* = 7.8 Hz, 1H), 7.98 – 7.68 (m, 9H), 7.03 – 6.91 (m, 3H), 6.67 – 6.58 (m, 2H),
4.17 – 3.75 (m, 3H), 3.57 (td, *J* = 13.7, 6.2 Hz, 2H), 3.41 – 3.28 (m, 3H), 3.25 (dd, *J* = 15.1, 9.2 Hz, 1H), 3.01 (h, *J* = 6.2
Hz, 2H), 2.92 (dd, *J* = 13.4, 7.7 Hz, 1H), 2.83 – 2.56 (m, 6H), 2.43 (dd, *J* = 13.5, 9.3 Hz, 1H), 1.95 (tt, *J* = 7.6, 3.1 Hz,
2H), 1.55 (tt, *J* = 14.0, 5.2 Hz, 4H), 1.46 – 1.30 (m, 4H), 1.30 – 1.13 (m, 22H), 1.09 (h, *J* = 7.0 Hz, 2H), 0.85 (t, *J* = 7.0 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.62, 171.79, 170.95, 158.97, 158.76, 156.14, 130.27, 128.92, 118.51, 116.53, 115.34, 115.23, 49.92, 47.40, 38.93, 37.31, 36.07, 35.72, 31.75, 29.47, 29.17, 27.16, 25.68, 22.55, 22.02, 14.41.

YW-5

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.03 (s, 1H), 7.89 – 7.63 (m, 9H), 4.08 – 3.76 (m, 4H), 3.57 – 3.38 (m, 6H), 3.03 (dp, *J*
= 17.3, 6.8, 6.0 Hz, 3H), 2.84 – 2.63 (m, 6H), 2.10 – 1.99 (m, 2H), 1.53 (h, *J* = 6.4, 5.4 Hz, 4H), 1.43 (dt, *J* = 30.3, 7.3 Hz, 4H), 1.24 (s, 24H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.75, 171.00, 159.29, 158.54, 50.10,49.42, 38.97, 35.75, 31.75, 30.40, 29.53, 29.31, 29.17, 27.18, 25.72, 22.56, 14.42.

YW-6:

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.06 (s, 1H), 7.78 (d, *J* = 31.6 Hz, 13H), 3.95 (dd, *J* = 20.6, 4.1 Hz, 2H), 3.88 (d, *J* =
14.1 Hz, 1H), 3.72 (d, *J* = 16.5 Hz, 1H), 3.58 – 3.40 (m, 4H), 3.01 (s, 2H), 2.95 (dd, *J* = 13.7, 8.3 Hz, 1H), 2.76 (dtd, *J* =

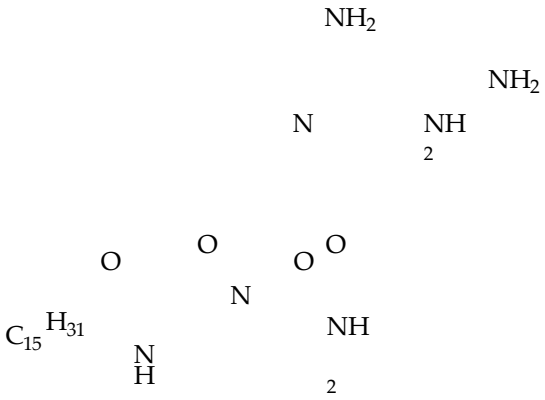
31.4, 17.3, 14.7, 7.3 Hz, 8H), 2.45 – 2.35 (m, 1H), 2.03 (dq, *J* = 9.5, 7.0, 6.6 Hz, 2H), 1.62 – 1.36 (m, 13H), 1.24 (s, 31H), 0.86 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 171.75, 169.58, 159.06, 158.32, 47.62, 45.31, 43.94, 39.03, 31.75, 29.54, 29.17, 22.55, 14.42.

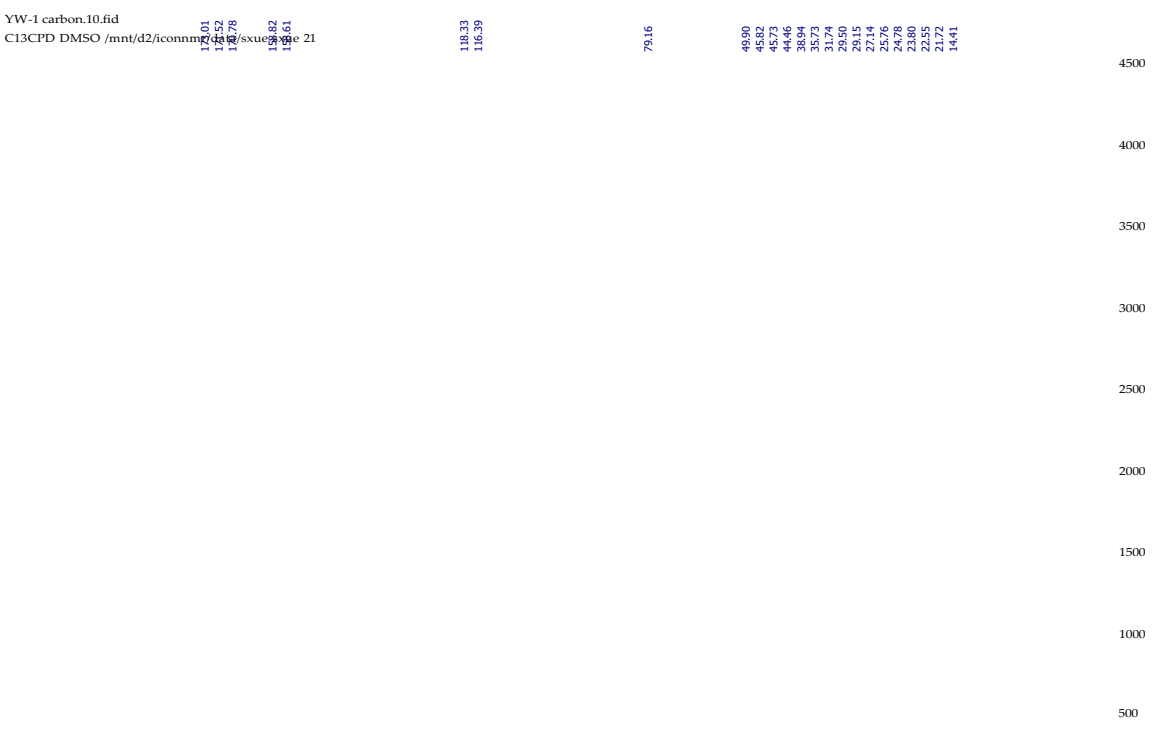
YW-1:

^{1}H NMR (600 MHz, DMSO-d_6) δ 8.05 (s, 1H), 7.95 – 7.53 (m, 11H), 4.09 – 3.84 (m, 3H), 3.73 (d, *J* = 16.5 Hz, 1H), 3.51
(s, 6H), 3.25 (s, 2H), 3.10 – 2.88 (m, 4H), 2.85 – 2.63 (m, 5H), 2.46 – 2.35 (m, 1H), 2.02 (dq, *J* = 10.1, 6.9 Hz, 2H), 1.60 – 1.05 (m, 38H), 0.85 (t, *J* = 6.9 Hz, 3H).

^{13}C NMR (151 MHz, DMSO-d_6) δ 172.04, 171.95, 158.82, 158.66, 157.24, 118.85, 117.36, 50.22, 47.53, 44.10, 39.00,
36.22, 36.07, 35.73, 31.75, 29.54, 29.17, 22.55, 14.42.



YW-1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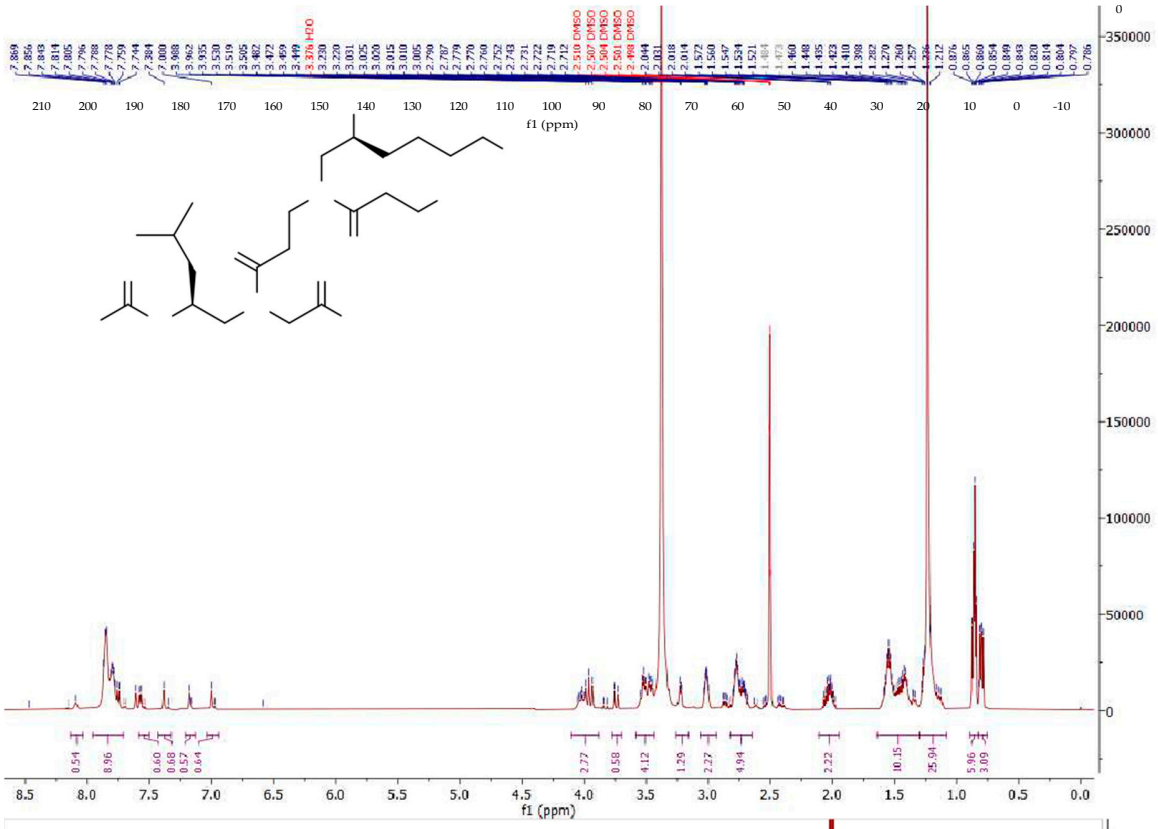
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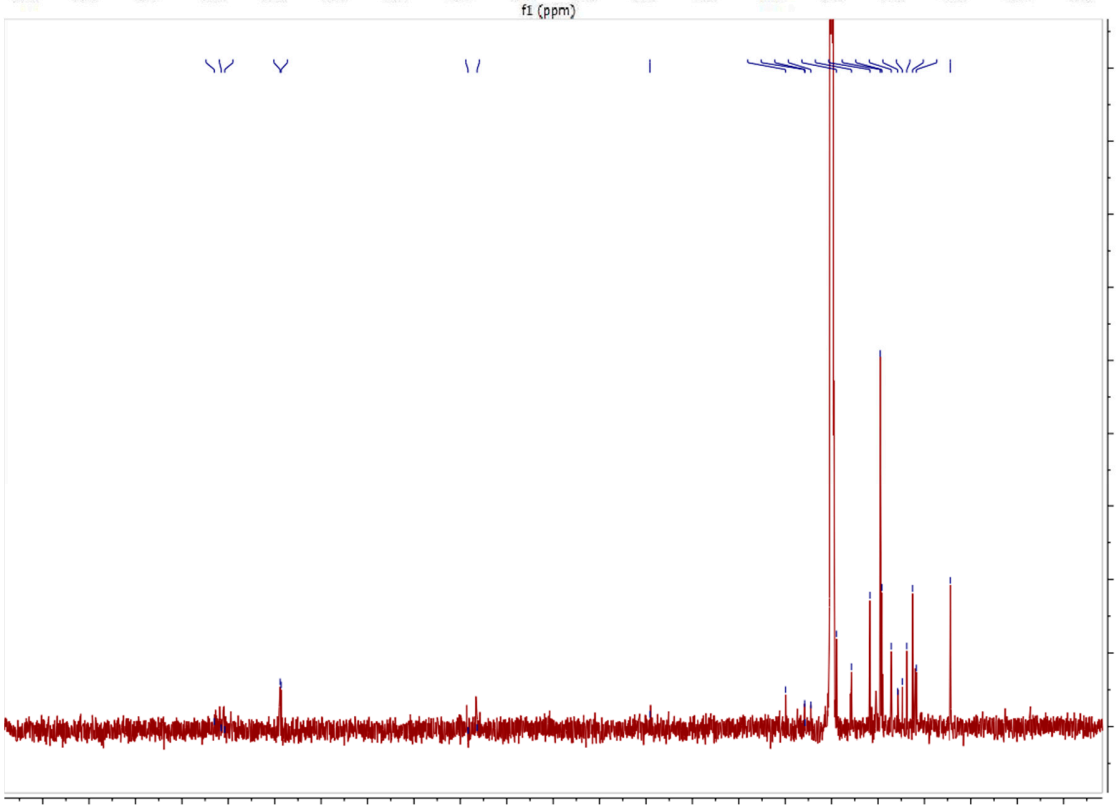

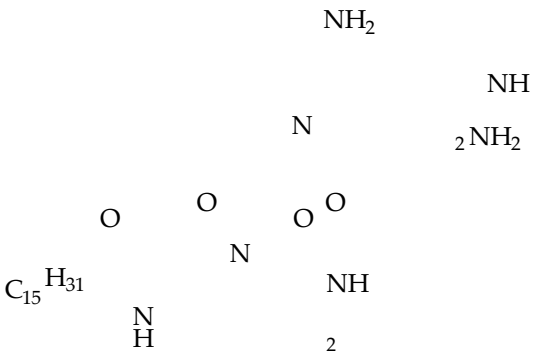
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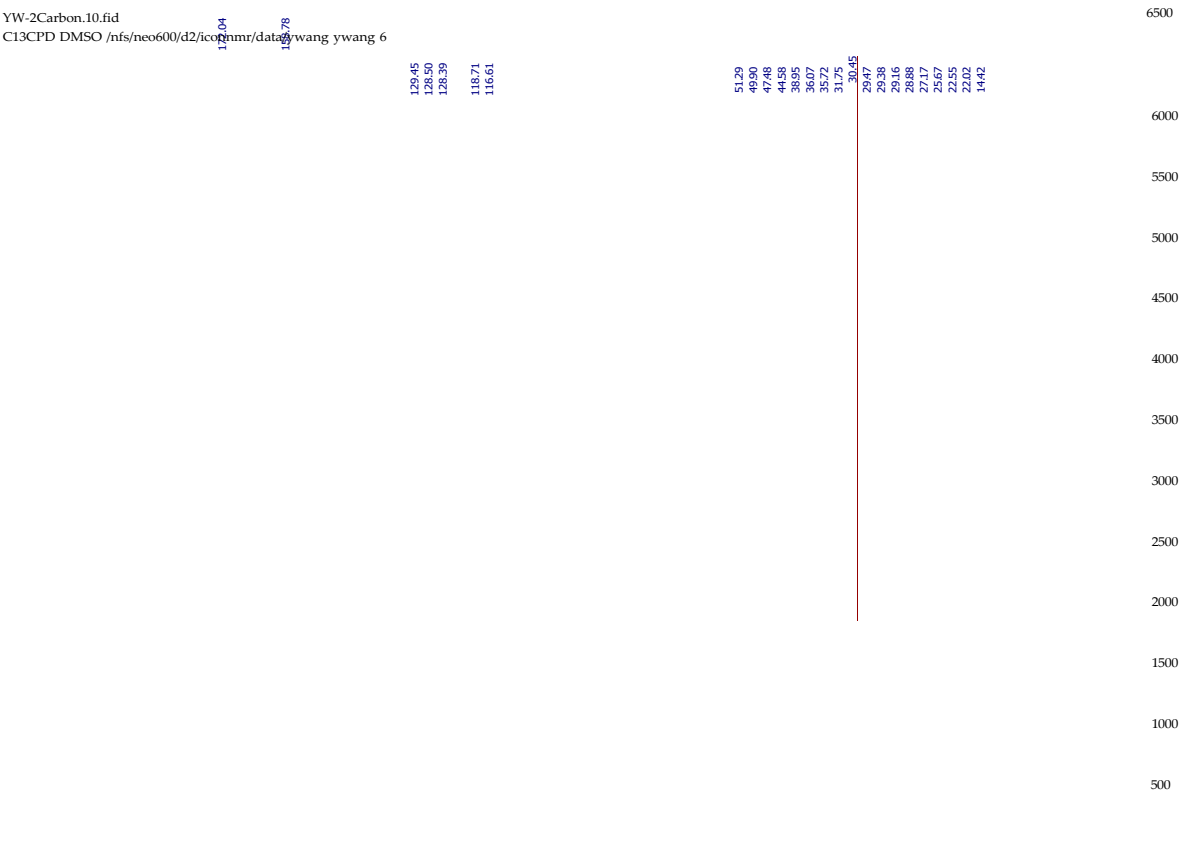
YW-2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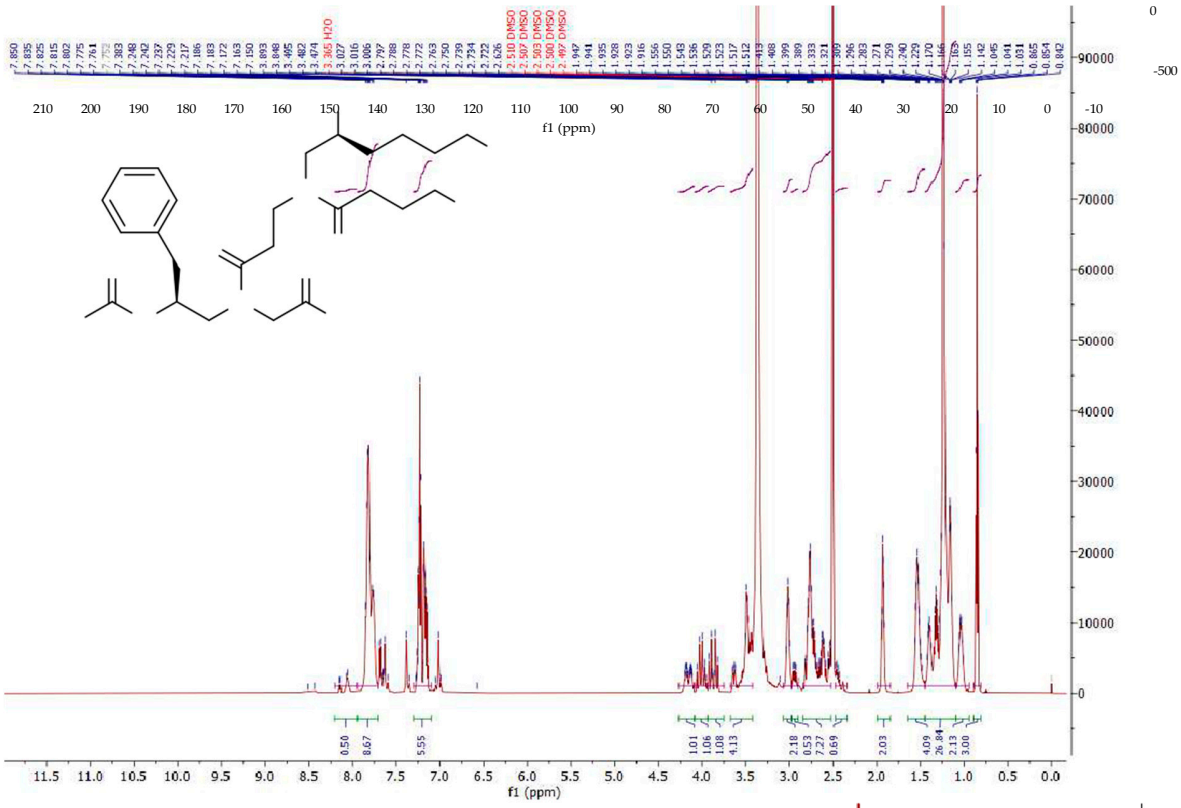
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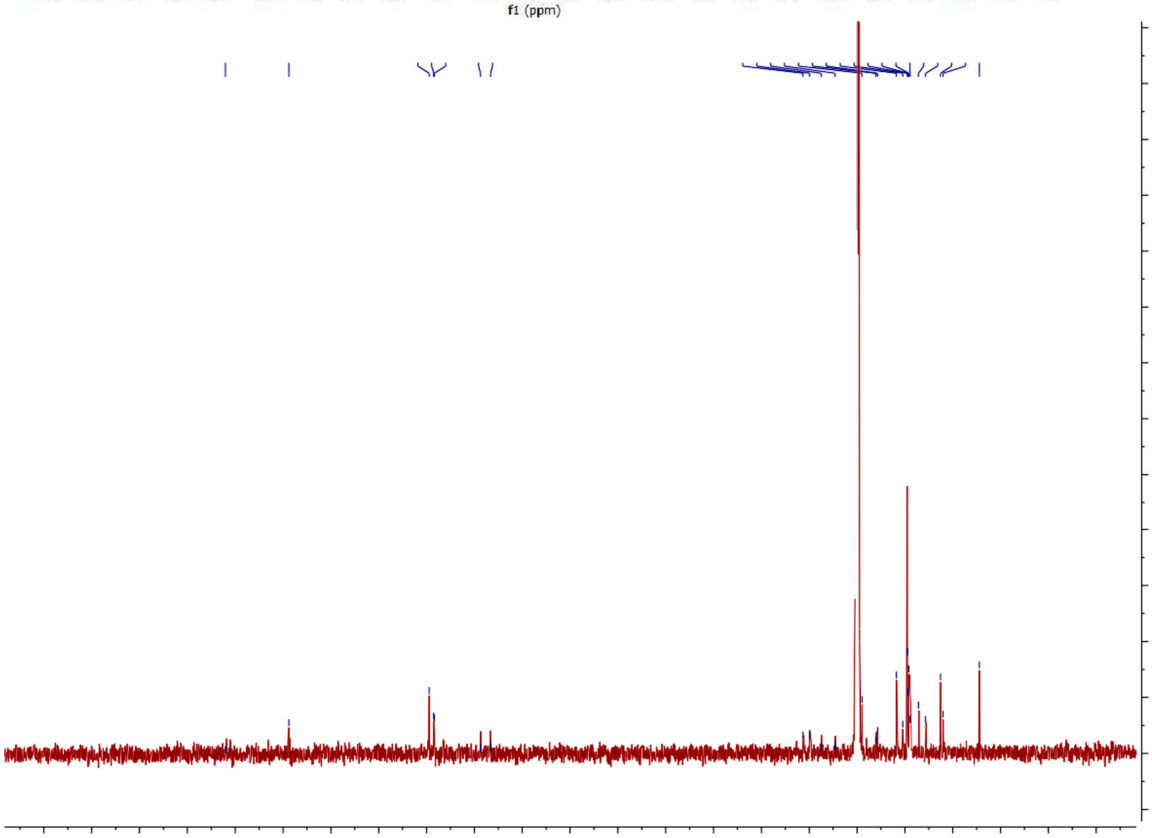

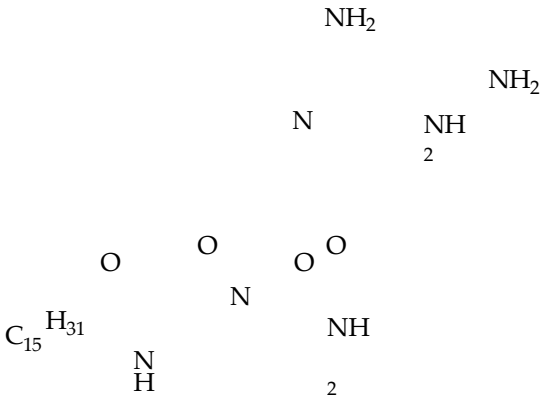
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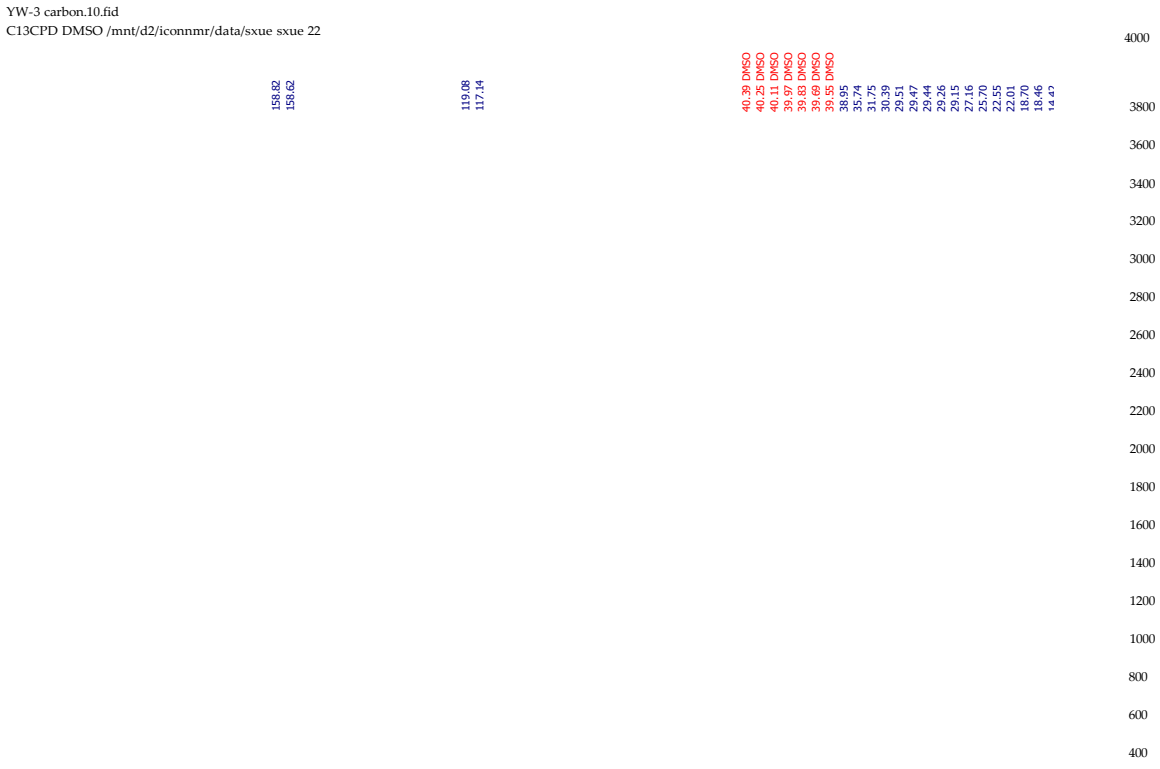
YW-3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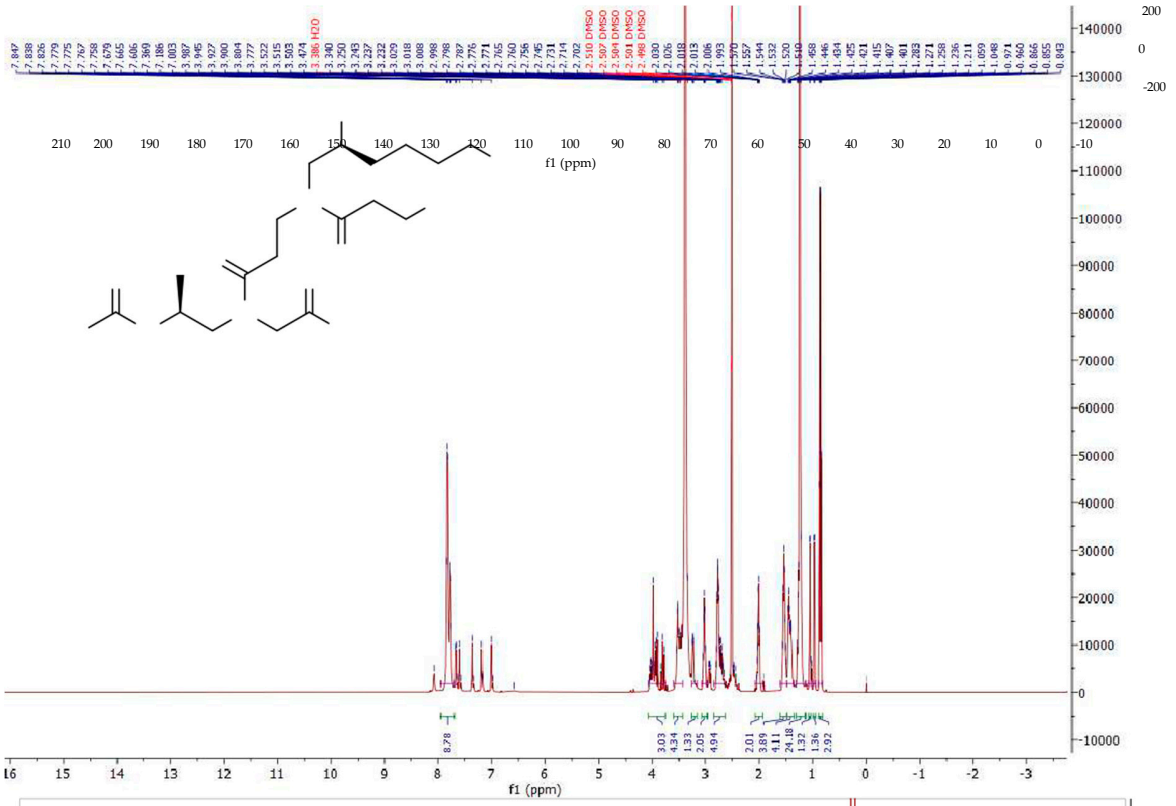
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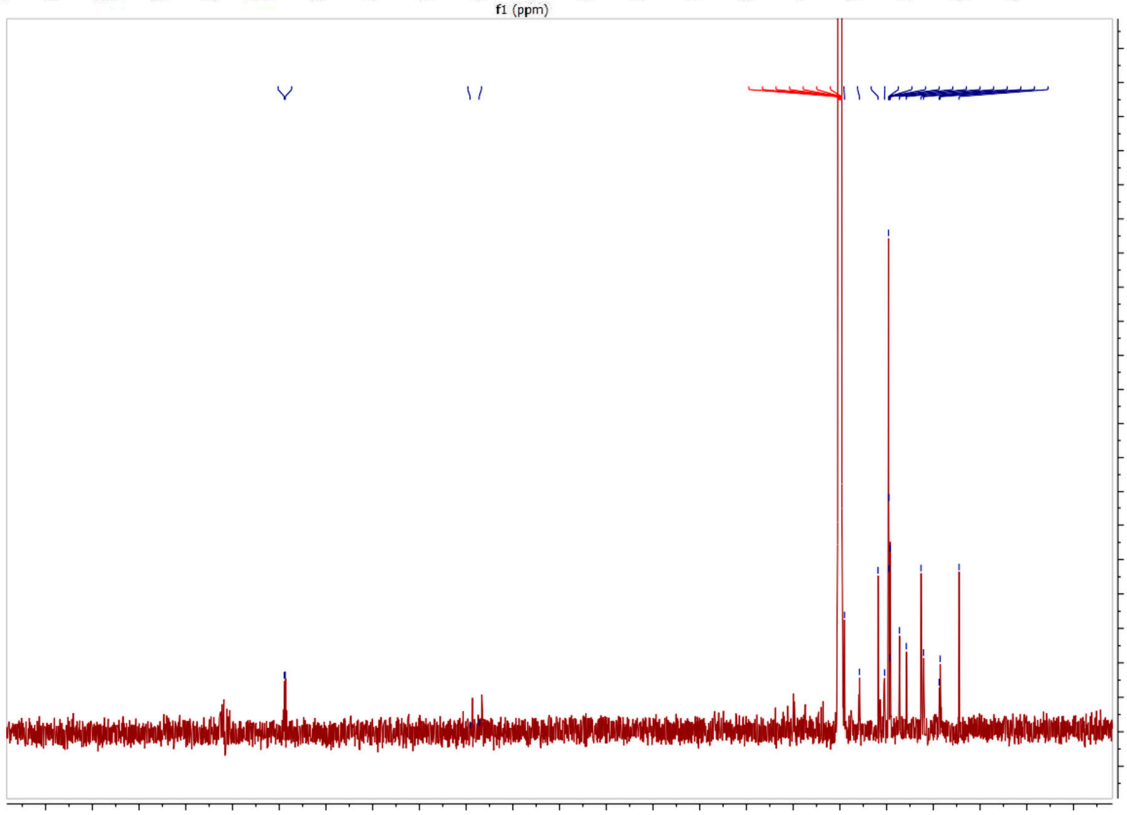

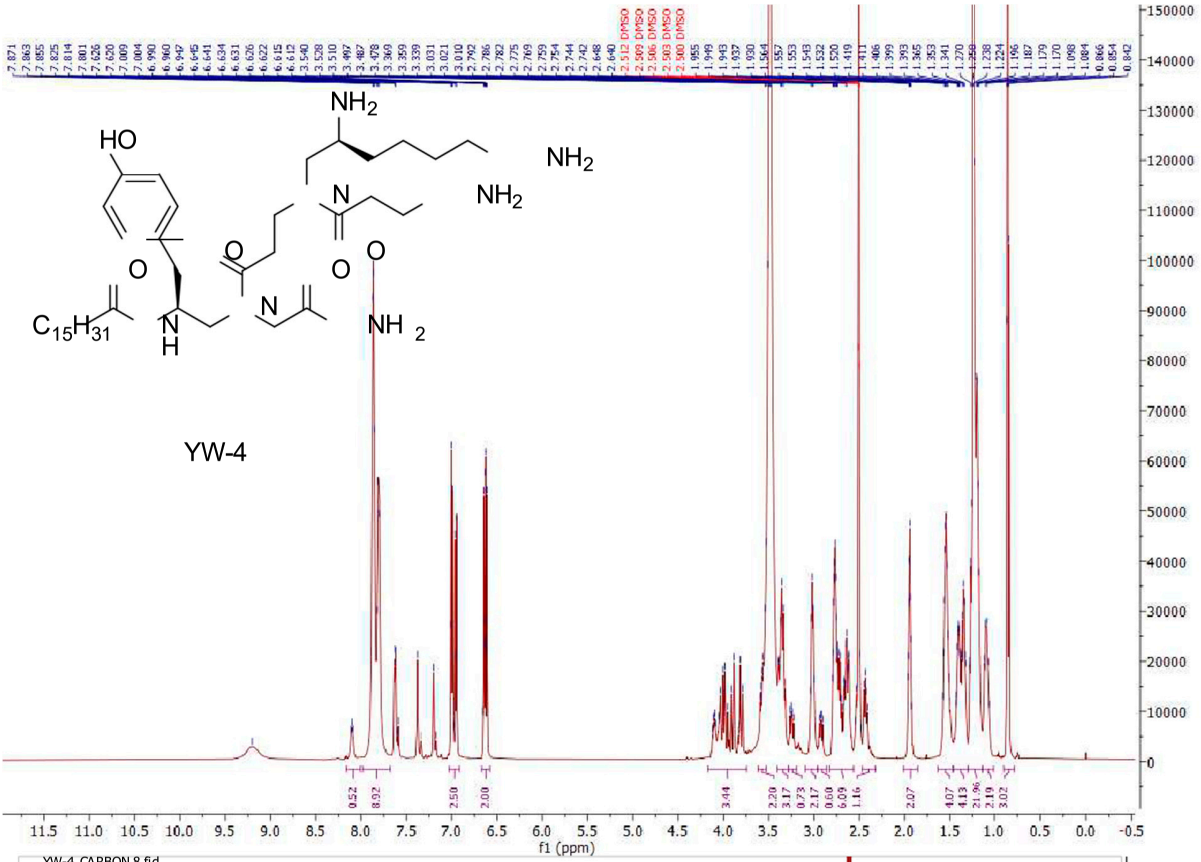
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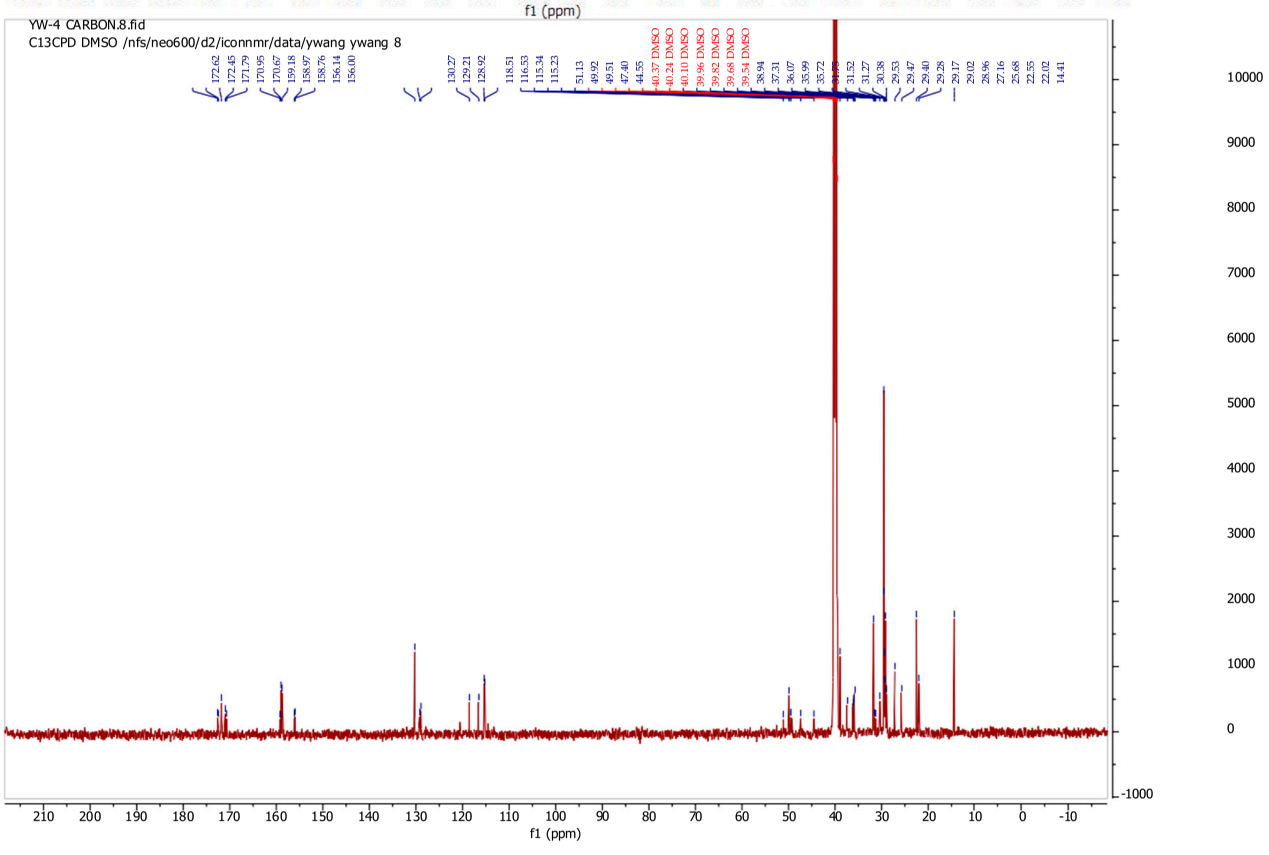
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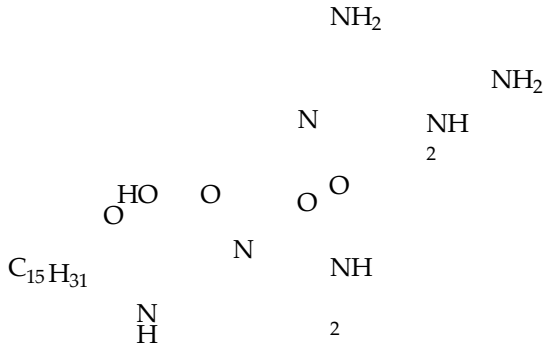
f1 (ppm)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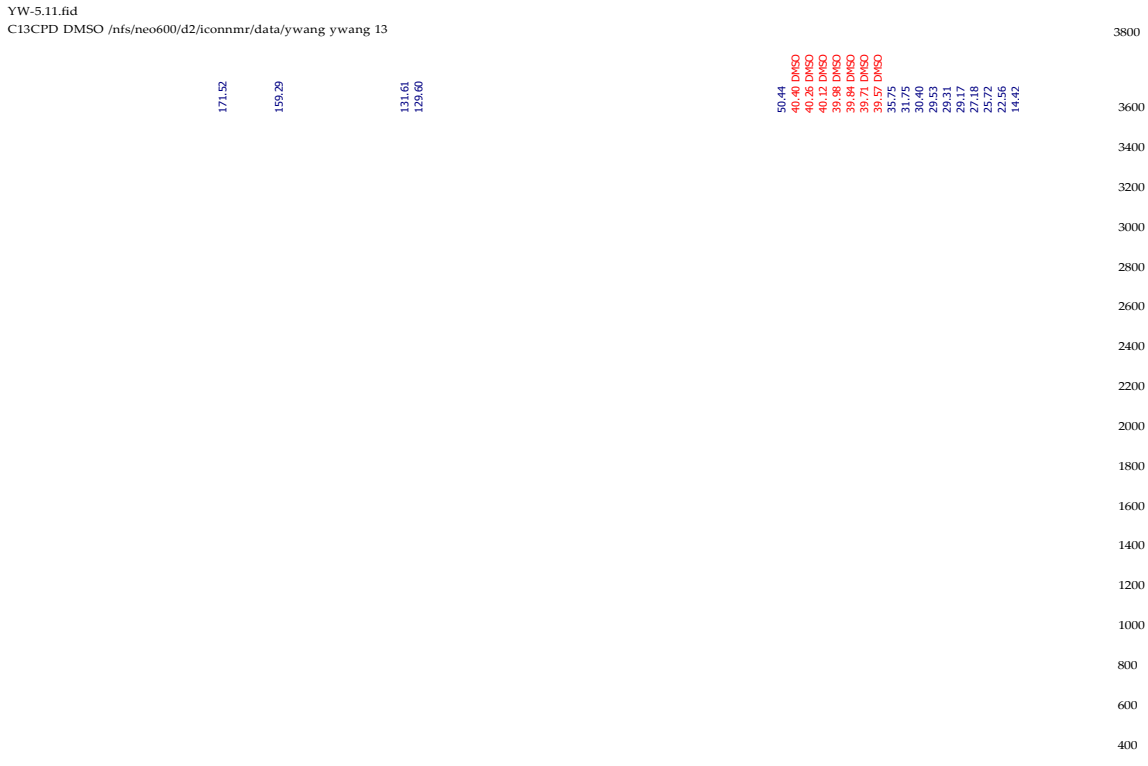
YW-5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39.98 DMSO
39.84 DMSO
39.71 DMSO
39.57 DMSO
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31.75
30.46
29.53
29.31
29.17
27.18
25.72
22.56
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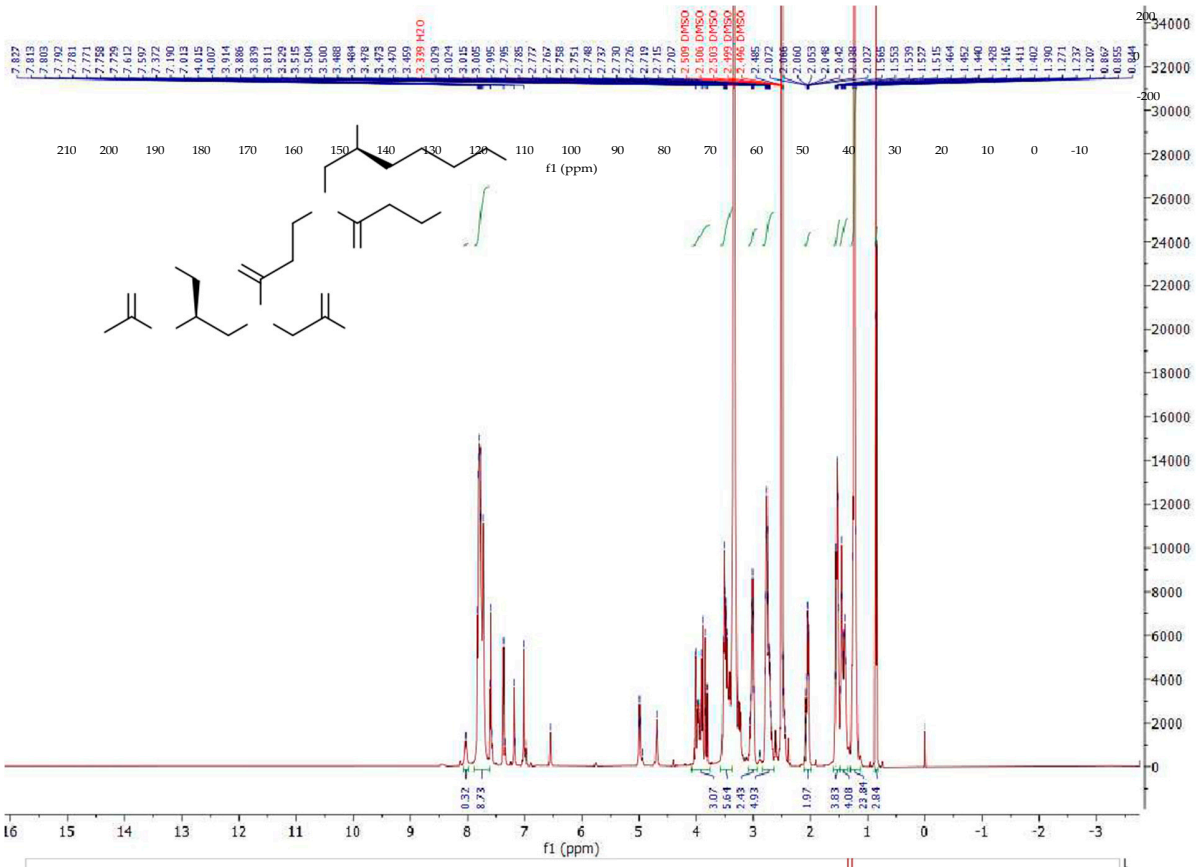
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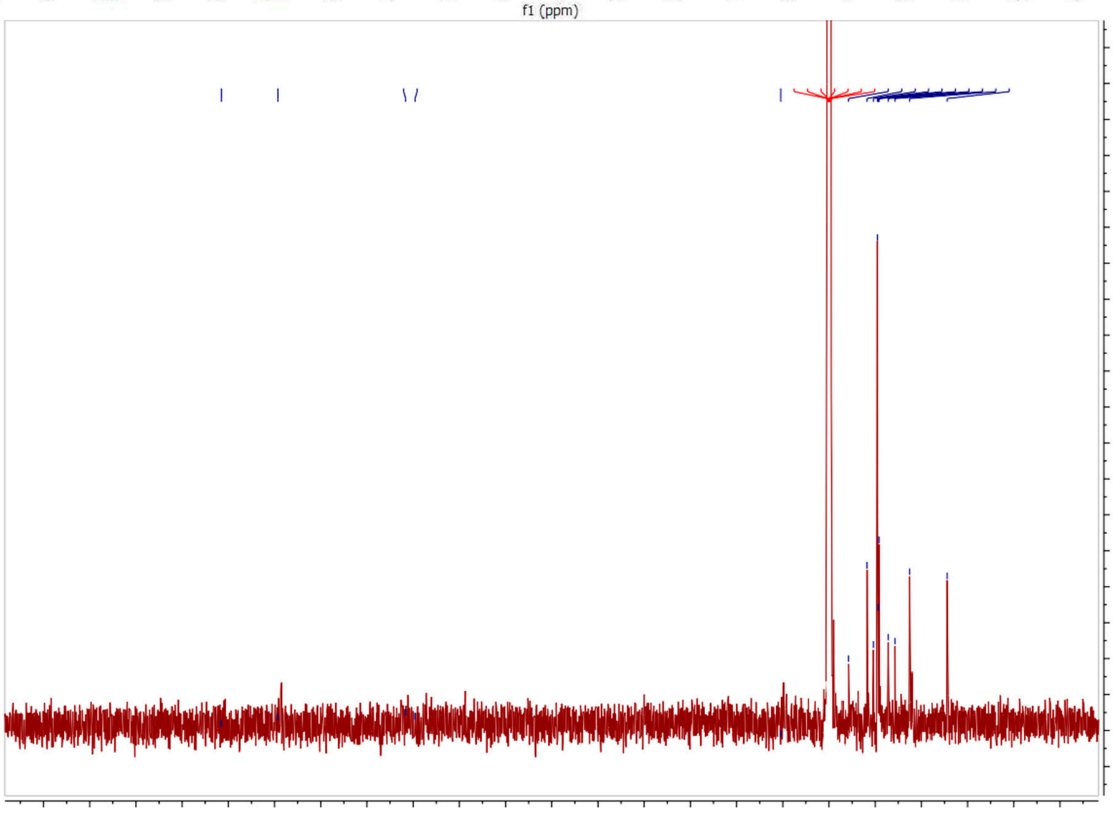

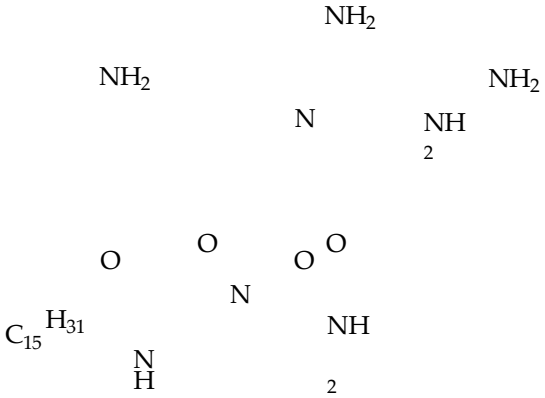
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O
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O
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C15H31
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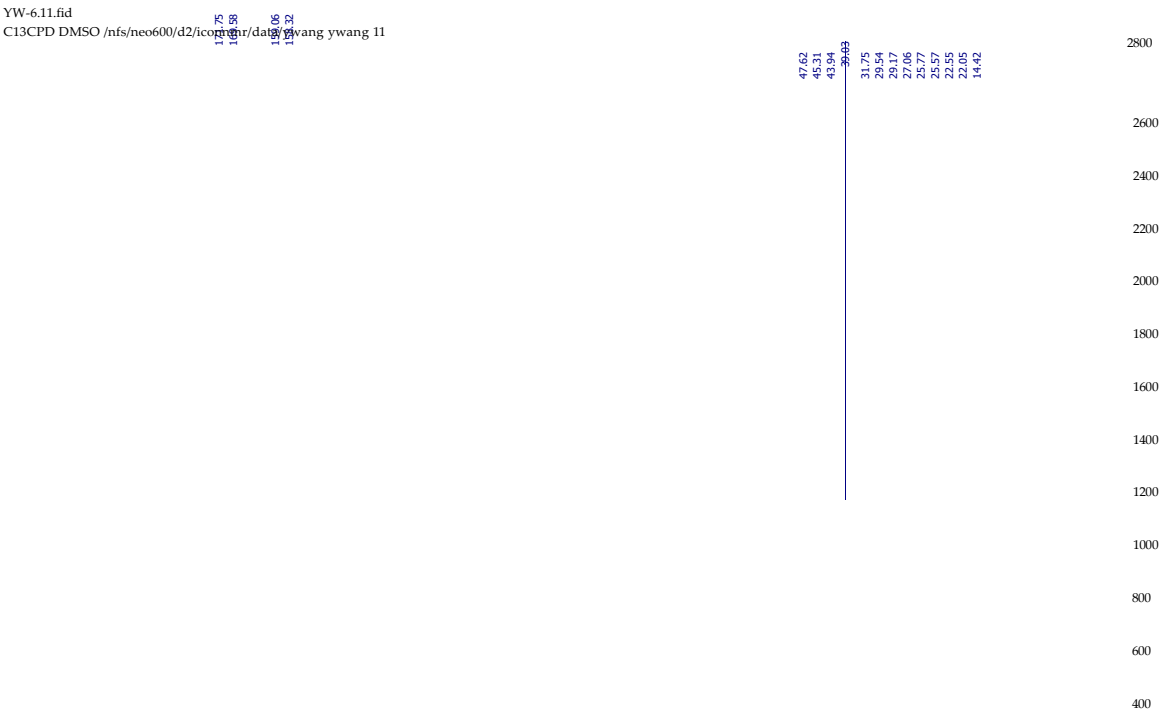
H
2

YW-6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27.06
25.77
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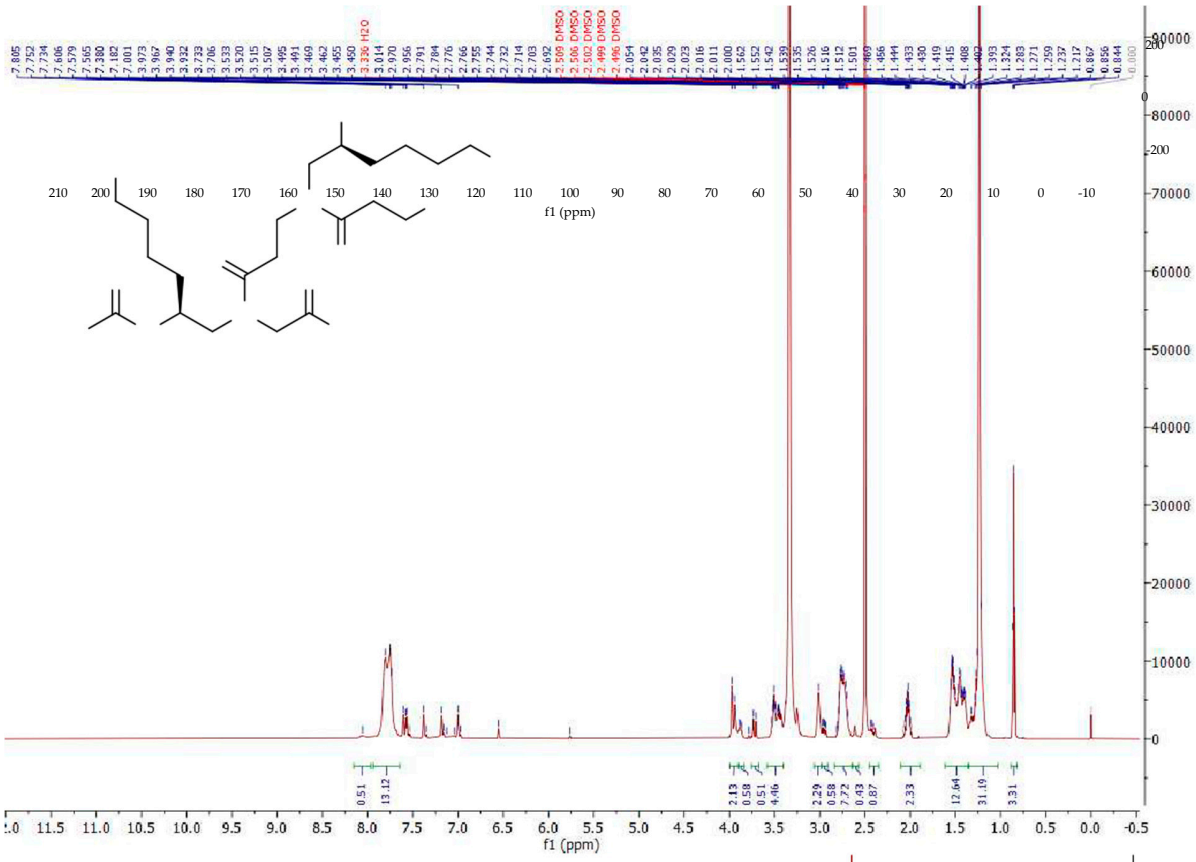
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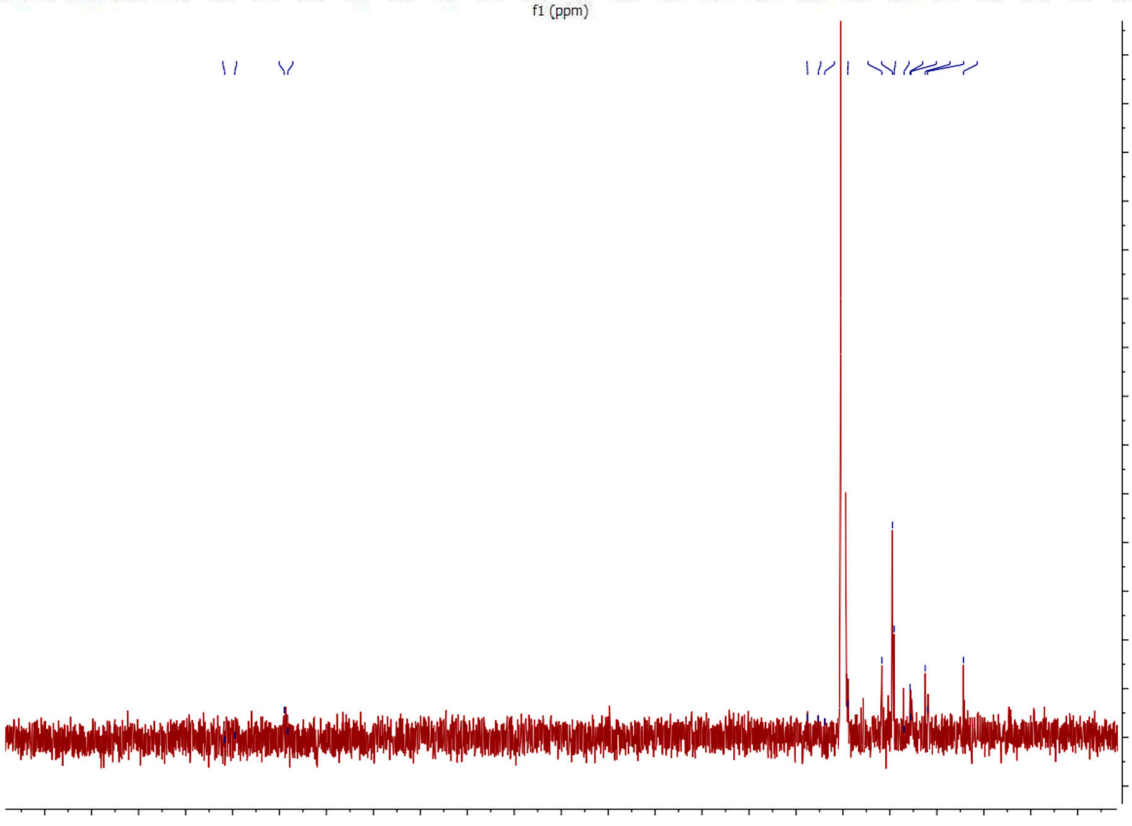

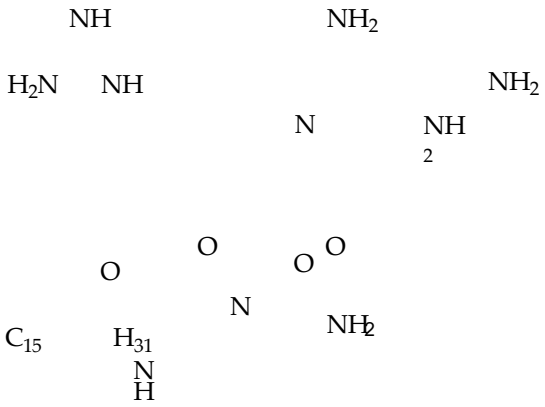
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NH2
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H31
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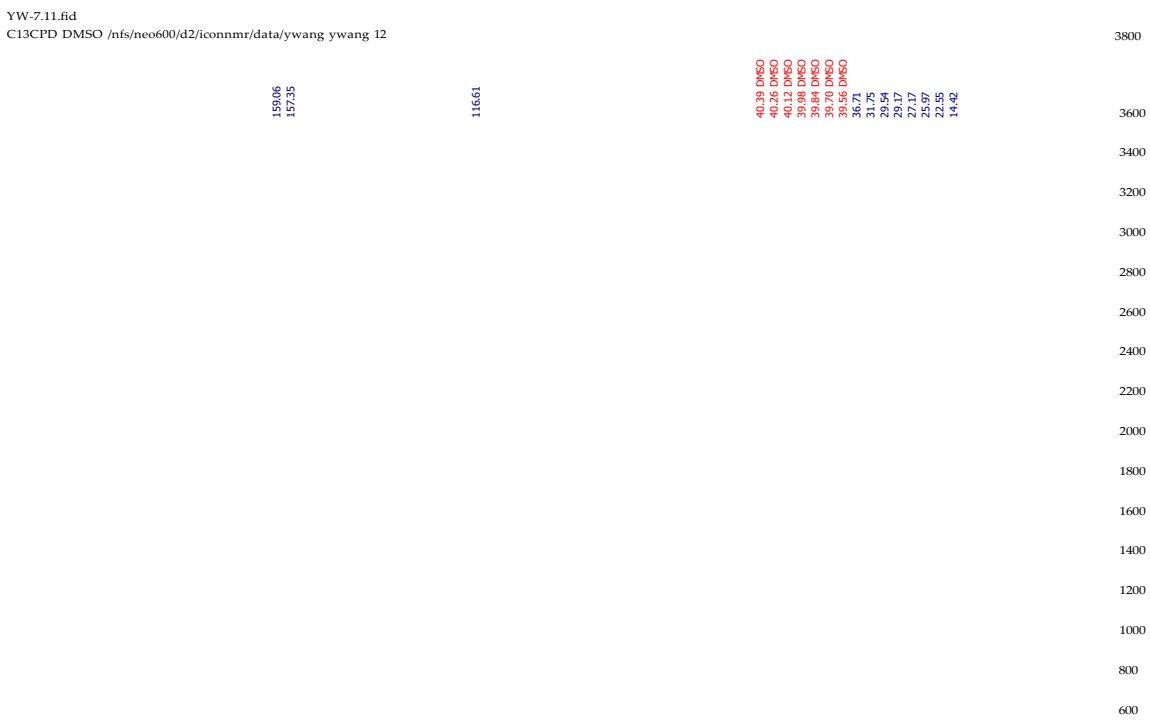
YW-7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27.17
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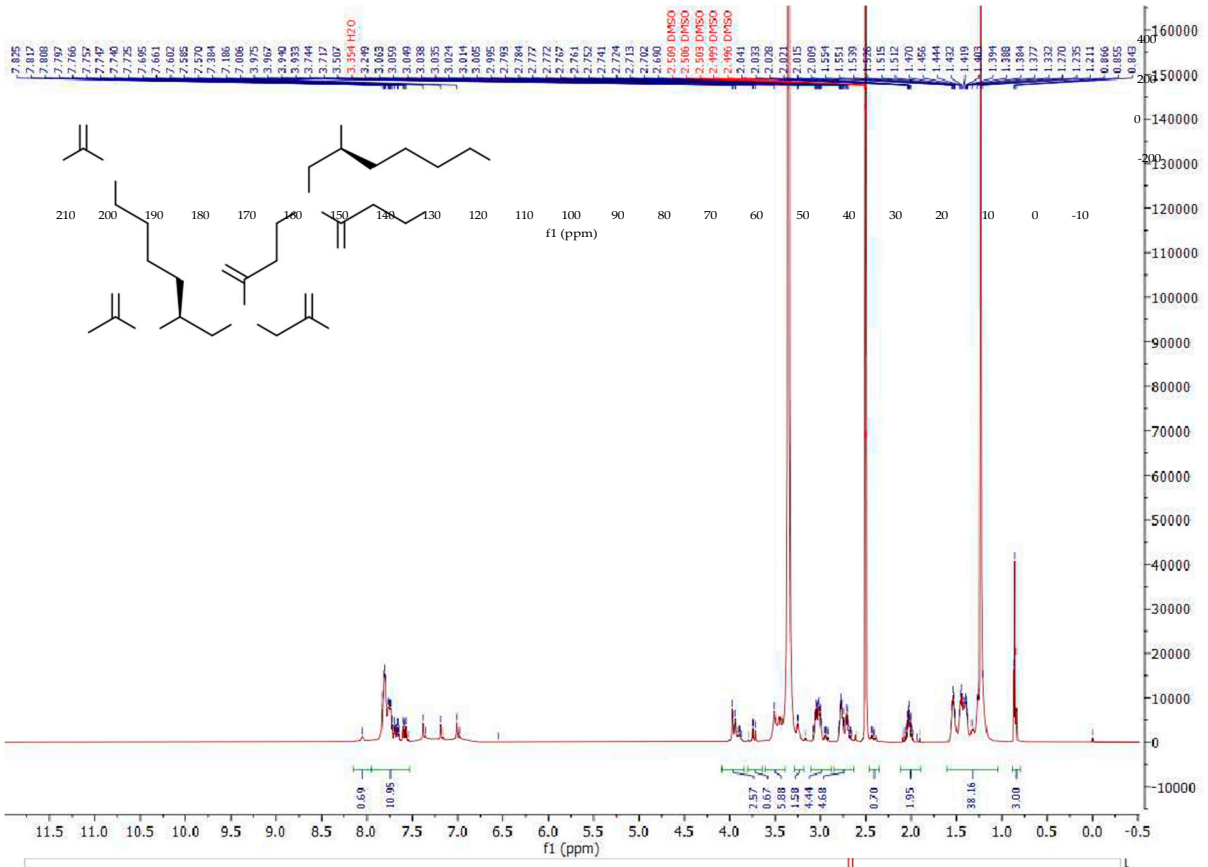
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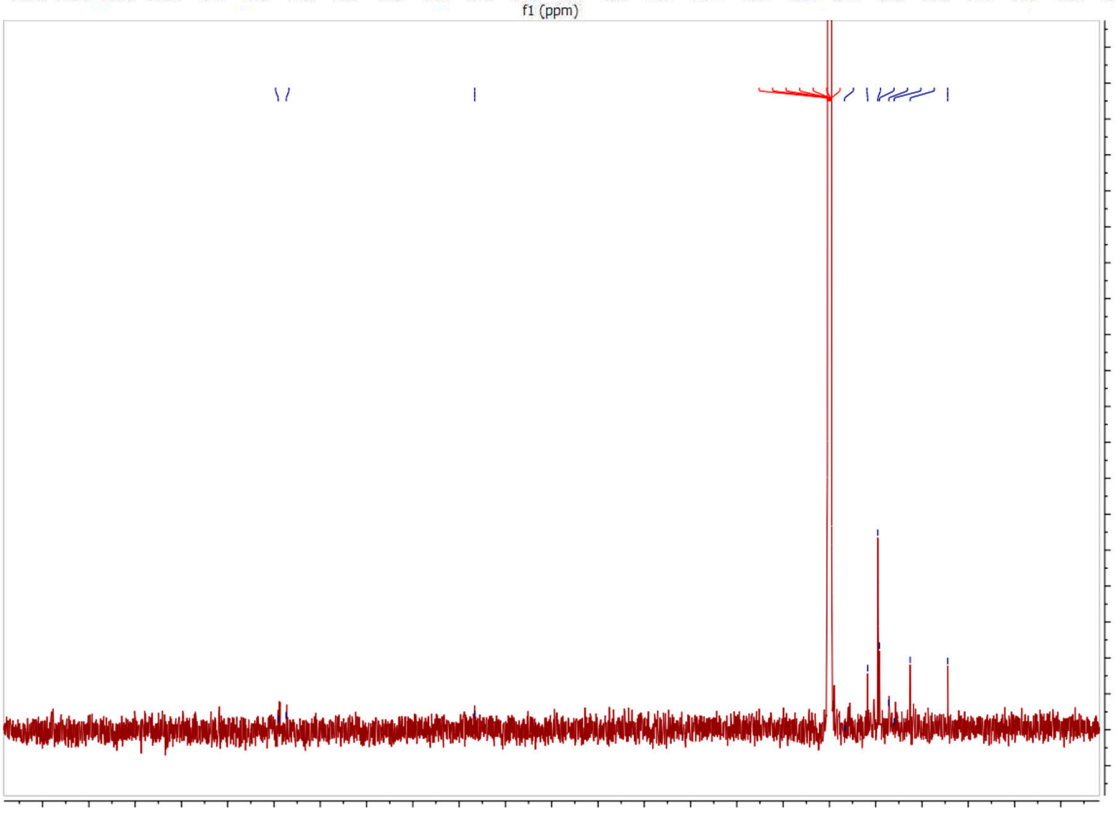

3. Table S1: HRMS data

Peptide	HRMS (ESI) [Exact Mass+H^+] calculated	HRMS (ESI) [Exact Mass+H^+] found
YW-1	667.5742	668.5747
YW-2	701.5568	702.5604
YW-3	625.5255	626.5286
YW-4	717.5517	718.5532
YW-5	641.5204	642.5214
YW-6	682.5833	683.5852
YW-7	724.6051	725.6050
YW-8	673.5255	674.5298
YW-9	645.4942	646.4979
YW-10	617.4629	618.4668
YW-11	589.4316	590.4355

References

1. Singh, S.; Wang, M.; Gao, R.; Teng, P.; Odom, T.; Zhang, E.; Xu, H.; Cai, J.; Hu, Y.; Amin, M.N.; et al. Lipo-γ-AApeptides as a New Class of Potent and Broad-Spectrum Antimicrobial Agents. *J. Med. Chem.* **2012**, *55*, 4003–4009. https://doi.org/10.1021/jm300274p