

SUPPLEMENTAL MATERIALS

The Parallel Structure–Activity Relationship Screening of Three Compounds Identifies the Common Agonist Pharmacophore of Pyrrolidine Bis-Cyclic Guanidine Melanocortin-3 Receptor (MC3R) Small Molecule Ligands

Mark D. Ericson ¹, Katie T. Freeman ¹, Travis M. LaVoi ², Haley M. Donow ², Radleigh G. Santos ³, Marc A. Giulianotti ², Clemencia Pinilla ², Richard A. Houghten ² and Carrie Haskell-Luevano ^{1,*}

¹Department of Medicinal Chemistry & Institute for Translational Neuroscience, University of Minnesota, Minneapolis, MN 55455, USA

²Center for Translational Science, Florida International University, Port St. Lucie, FL 34987, USA

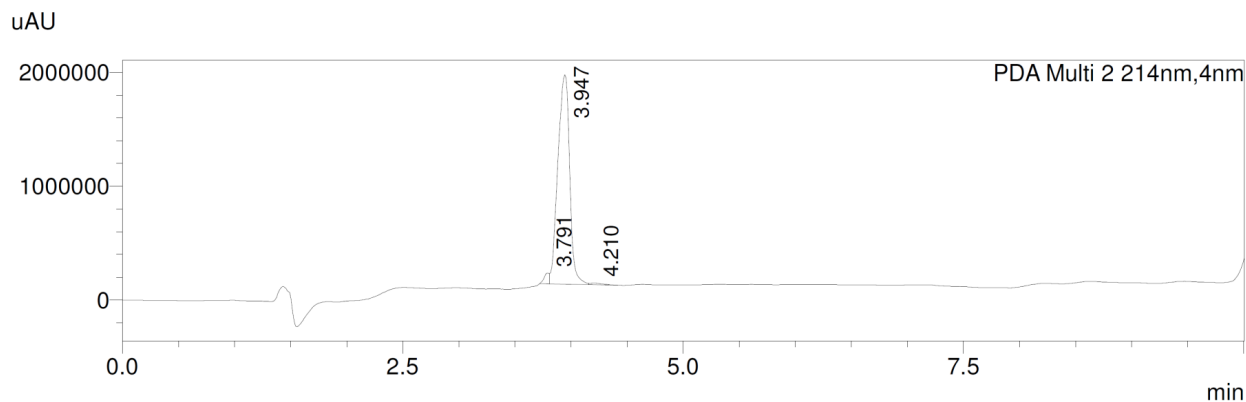
³Department of Mathematics, Nova Southeastern University, Fort Lauderdale, FL 33314, USA

* Correspondence: chaskell@umn.edu

Compound purification and characterization. All reagents were commercially available and used without further purification. Pyrrolidine bis-cyclic guanidine compounds were synthesized using Scheme 1. The final compounds were purified using preparative HPLC with a dual pump Shimadzu LC-20AB system equipped with a Luna C18 preparative column (21.5 x 150 mm, 5 micron) at $\lambda = 214$ nm, with a mobile phase of (A) H₂O (+0.1% formic acid)/(B) acetonitrile (ACN) (+0.1% formic acid) at a flow rate of 15 mL/min; gradients varied by compound based on hydrophobicity. ¹H NMR and ¹³C NMR spectra were recorded in DMSO-d₆ on a Bruker Ascend 400 MHz spectrometer at 400.14 and 100.62 MHz, respectively. The purities of synthesized compounds were assessed by liquid chromatography and mass spectrometry on a Shimadzu LCMS-2020 instrument with ESI Mass Spec and SPD-20A Liquid Chromatograph with a mobile phase of (A) H₂O (+0.1% formic acid)/(B) ACN (+0.1% formic acid) (5-95% over 6 min with a 4 min rinse).

2718.001 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

yl)imidazolidin-4-yl)ethanol. Compound 2718.001 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.9mg, **¹H NMR** (400 MHz, DMSO-d₆) ppm 8.62 (br. s., 2 H) 7.23 (br. s., 2 H) 4.69 (br. s., 1 H) 3.94 (br. s., 3 H) 3.79 (br. s., 1 H) 3.74 (br. s., 1 H) 3.68 (br. s., 1 H) 3.60 (br. s., 2 H) 3.39 - 3.55 (m, 2 H) 3.30 (br. s., 2 H) 3.11 (br. s., 1 H) 2.99 (d, J=13.20 Hz, 3 H) 2.61 - 2.85 (m, 2 H) 2.46 (d, J=11.49 Hz, 1 H) 2.34 (br. s., 1 H) 1.79 - 1.99 (m, 2 H) 1.69 (br. s., 2 H) 1.36 - 1.63 (m, 7 H) 1.26 (br. s., 2 H) 1.15 (br. s., 3 H) 1.00 (br. s., 4 H) 0.86 - 0.97 (m, 5 H) 0.83 (br. s., 9 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.55 (MS ESI) **Purity** LC-MS: >96% (214 nm, peak area).

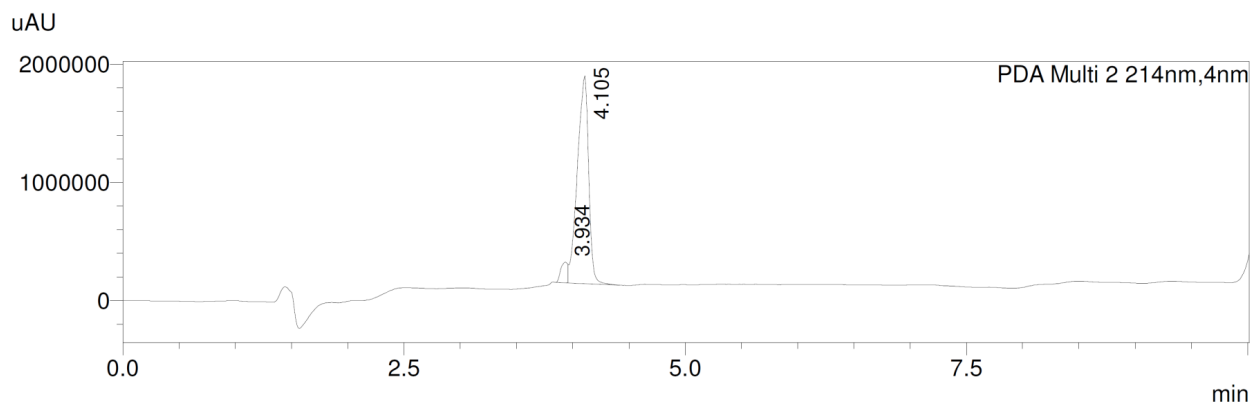


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.791	317255	95200	2.297	2.297
2	3.947	13371844	1840711	96.820	96.820
3	4.210	121955	16020	0.883	0.883
Total		13811055	1951931	100.000	

2718.002 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-

iminoimidazolidin-4-yl)ethanol. Compound 2718.002 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.9mg, **¹H NMR** (400 MHz, DMSO-*d*₆) δ ppm 8.23 (br. s., 1 H) 3.99 (br. s., 1 H) 3.71 - 3.95 (m, 3 H) 3.66 (t, *J*=9.29 Hz, 1 H) 3.43 - 3.58 (m, 3 H) 3.38 (br. s., 6 H) 3.09 - 3.34 (m, 7 H) 3.04 (d, *J*=3.42 Hz, 1 H) 2.89 (br. s., 1 H) 2.74 (d, *J*=3.91 Hz, 1 H) 2.53 (br. s., 1 H) 2.10 - 2.35 (m, 2 H) 1.76 - 1.94 (m, 2 H) 1.63 - 1.76 (m, 4 H) 1.53 - 1.63 (m, 4 H) 1.31 - 1.53 (m, 6 H) 1.17 - 1.31 (m, 2 H) 1.12 (d, *J*=7.83 Hz, 3 H) 0.84 (s, 8 H) 0.79 - 1.09 (m, 11 H) **m/z** calcd C₃₇H₆₉N₇O [M+H]⁺ 628.56, found 628.95 (MS ESI) **Purity** LC-MS: >94% (214 nm, peak area).

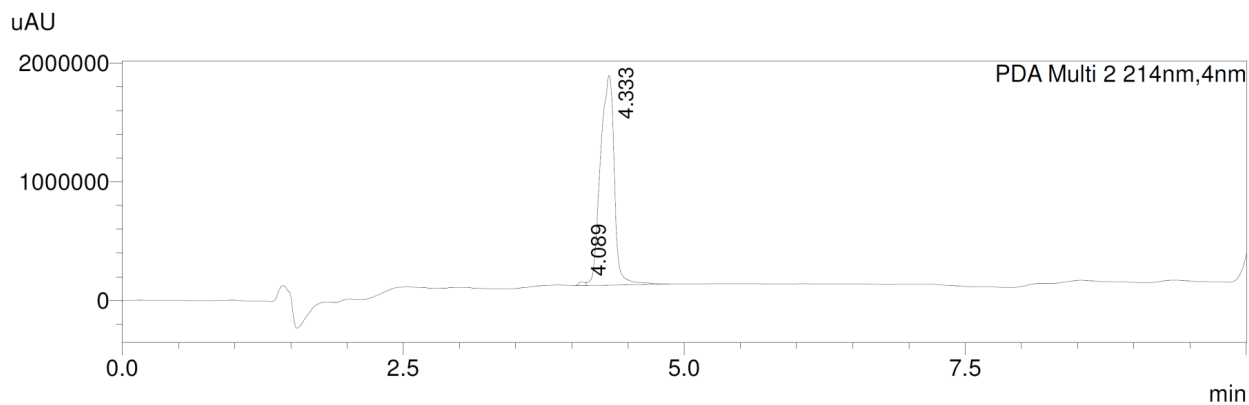


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.934	768969	176689	5.901	5.901
2	4.105	12261866	1760305	94.099	94.099
Total		13030834	1936995	100.000	

2718.003 (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-

propylimidazolidin-2-imine. Compound 2718.003 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.3mg, ¹H NMR (400 MHz, DMSO-d₆) δ ppm 10.42 (br. s., 1 H) 8.35 (br. s., 1 H) 3.78 - 4.03 (m, 4 H) 3.41 - 3.71 (m, 7 H) 3.19 - 3.41 (m, 4 H) 3.11 - 3.17 (m, 1 H) 2.78 - 3.08 (m, 3 H) 2.22 - 2.48 (m, 2 H) 2.18 (dt, J=6.76, 3.29 Hz, 1 H) 2.08 (br. s., 1 H) 1.64 - 1.93 (m, 7 H) 1.61 (br. s., 2 H) 1.34 - 1.55 (m, 6 H) 1.05 - 1.32 (m, 7 H) 0.79 - 1.05 (m, 17 H) 0.74 (d, J=6.72 Hz, 3 H) **m/z** calcd C₃₇H₆₉N₇ [M+H]⁺ 612.56, found 613.0 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

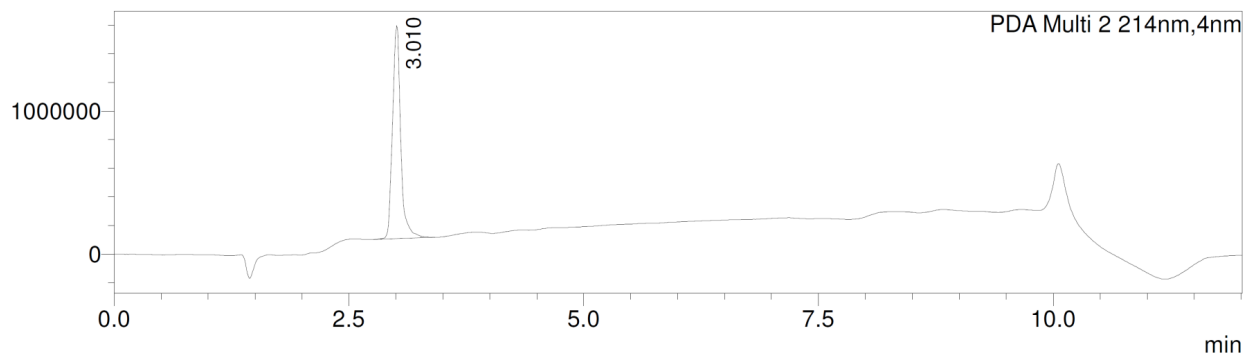


Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.089	130945	30839	0.856	0.856
2	4.333	15162360	1769533	99.144	99.144
Total		15293305	1800372	100.000	

2718.004 (S)-1-((S)-3-ethyl-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Compound

2718.004 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and Acetic Anhydride (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 7.1mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.44 (br. s., 1 H) 7.17 - 7.36 (m, 4 H) 4.23 - 4.33 (m, 1 H) 3.77 - 4.02 (m, 2 H) 3.54 - 3.77 (m, 3 H) 3.17 - 3.47 (m, 13 H) 2.92 - 3.08 (m, 2 H) 2.65 - 2.92 (m, 3 H) 2.29 - 2.48 (m, 1 H) 2.23 (q, J=8.27 Hz, 1 H) 1.75 - 1.92 (m, 1 H) 1.52 - 1.75 (m, 3 H) 1.29 - 1.52 (m, 2 H) 1.03 (d, J=6.24 Hz, 2 H) 0.93 (dd, J=18.52, 5.93 Hz, 5 H) 0.83 (t, J=7.03 Hz, 2 H) **m/z** calcd C₂₈H₄₇N₇O [M+H]⁺ 498.4, found 498.3 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

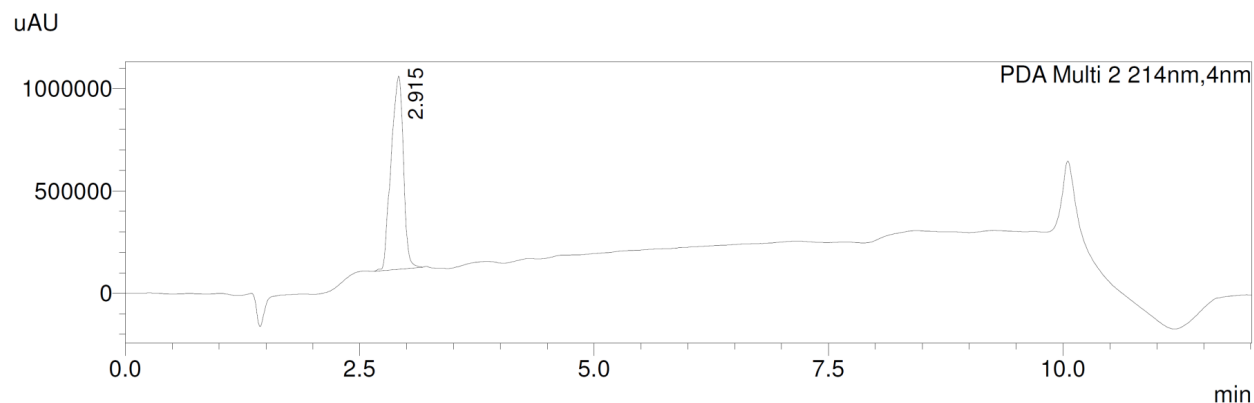
uAU



PDA Ch2 214nm

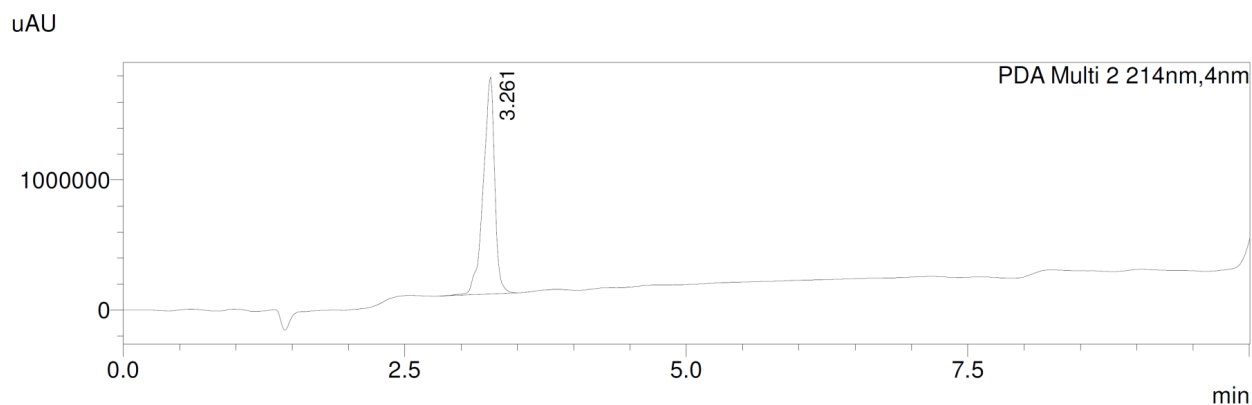
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.010	9095706	1489523	100.000	100.000
Total		9095706	1489523	100.000	

2718.006 (R)-1-(((S)-1-((R)-2-(2-iminoimidazolidin-1-yl)-3-phenylpropyl)pyrrolidin-2-yl)methyl)-5-isobutylimidazolidin-2-imine. Compound 2718.006 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), and Boc-Glycine-OH (R₄). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.3mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.30 (br. s., 1 H) 9.94 (br. s., 1 H) 8.39 (br. s., 2 H) 7.21 - 7.34 (m, 4 H) 4.17 (br. s., 1 H) 3.86 - 4.05 (m, 2H) 3.59 - 3.86 (m, 4 H) 3.51 (d, J=5.14 Hz, 1 H) 3.45 - 3.56 (m, 1 H) 3.38 - 3.44 (m, 1 H) 3.13 - 3.33 (m, 3 H) 3.00 - 3.12 (m, 1 H) 2.72 - 2.99 (m, 3H) 2.22 - 2.48 (m, 2 H) 1.76 - 1.91 (m, 1 H) 1.52 - 1.75 (m, 3 H) 1.24 - 1.50 (m, 2 H) 0.80 - 0.98 (m, 6 H) **m/z** calcd C₂₄H₃₉N₇ [M+H]⁺ 426.3, found 426.25 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	2.915	8585807	943626	100.000	100.000
Total		8585807	943626	100.000	

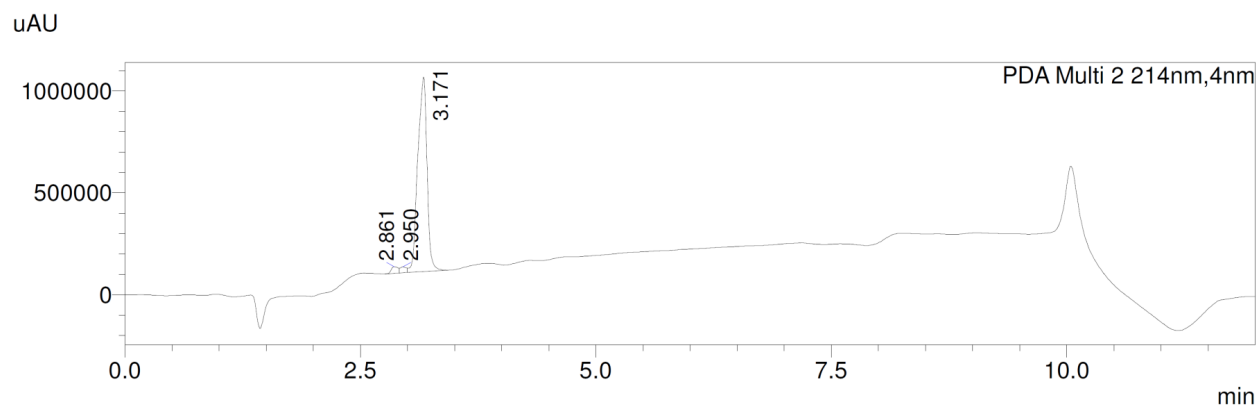
2718.010 (S)-1-((S)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-3-ethyl-2-iminoimidazolidin-4-yl)ethanol. Compound 2718.010 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and Acetic Anhydride (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.8mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.35 (br. s., 1 H) 8.27 (br. s., 1 H) 3.78 - 4.06 (m, 7 H) 3.43 - 3.71 (m, 5 H) 3.09 - 3.31 (m, 4 H) 3.02 - 3.08 (m, 1 H) 2.79 - 2.94 (m, 1 H) 2.72 - 2.79 (m, 1 H) 2.28 (d, J=9.05 Hz, 2 H) 1.75 - 1.89 (m, 2 H) 1.52 - 1.74 (m, 8 H) 1.26 - 1.48 (m, 4 H) 1.12 - 1.23 (m, 3 H) 1.03 - 1.12 (m, 6 H) 0.79 - 1.02 (m, 8 H) **m/z** calcd C₂₈H₅₃N₇O [M+H]⁺ 504.4, found 504.35 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.261	11822142	1673131	100.000	100.000
Total		11822142	1673131	100.000	

2718.011 (S)-1-((S)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-iminoimidazolidin-4-yl)ethanol. Compound

2718.011 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), and Boc-D-Threonine(Bzl)-OH (R₄). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.7mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.05 (br. s., 1 H) 9.98 (br. s., 1 H) 8.65 (br. s., 2 H) 4.23 (br. s., 1 H) 4.01 (br. s., 1 H) 3.79 - 3.95 (m, 3 H) 3.64 - 3.76 (m, 3 H) 3.48 - 3.61 (m, 3 H) 3.04 - 3.30 (m, 5 H) 2.71 - 2.94 (m, 2 H) 2.17 - 2.35 (m, 2 H) 1.62 - 1.88 (m, 6 H) 1.52 - 1.62 (m, 3 H) 1.33 - 1.49 (m, 3 H) 1.03 - 1.30 (m, 7 H) 0.80 - 1.00 (m, 8 H) **m/z** calcd C₂₆H₄₉N₇O [M+H]⁺ 476.4, found 476.65 (MS ESI) **Purity** LC-MS: >95% (214 nm, peak area).

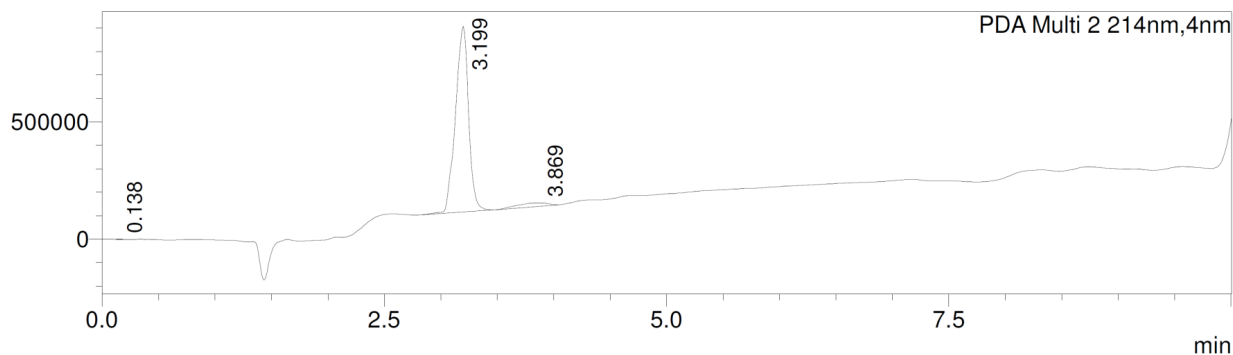


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	2.861	168560	32582	2.474	2.474
2	2.950	132609	28825	1.946	1.946
3	3.171	6512817	955412	95.580	95.580
Total		6813986	1016818	100.000	

2718.012 (R)-1-(((S)-1-((R)-3-cyclohexyl-2-(2-iminoimidazolidin-1-yl)propyl)pyrrolidin-2-yl)methyl)-5-isobutylimidazolidin-2-imine. Compound 2718.012 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), and Boc-Glycine-OH (R₄). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.3mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.19 (br. s., 1 H) 8.40 (br. s., 2 H) 8.27 (br. s., 1 H) 3.78 - 4.06 (m, 3 H) 3.43 - 3.71 (m, 9 H) 3.08 - 3.31 (m, 4 H) 2.71 - 2.87 (m, 2 H) 2.17 - 2.35 (m, 2 H) 1.75 - 1.91 (m, 2 H) 1.54 - 1.75 (m, 8 H) 1.31 - 1.46 (m, 3 H) 1.08 - 1.28 (m, 5 H) 0.80 - 1.00 (m, 8 H) **m/z** calcd C₂₄H₄₅N₇ [M+H]⁺ 432.4, found 432.25 (MS ESI) **Purity** LC-MS: >95% (214 nm, peak area).

uAU



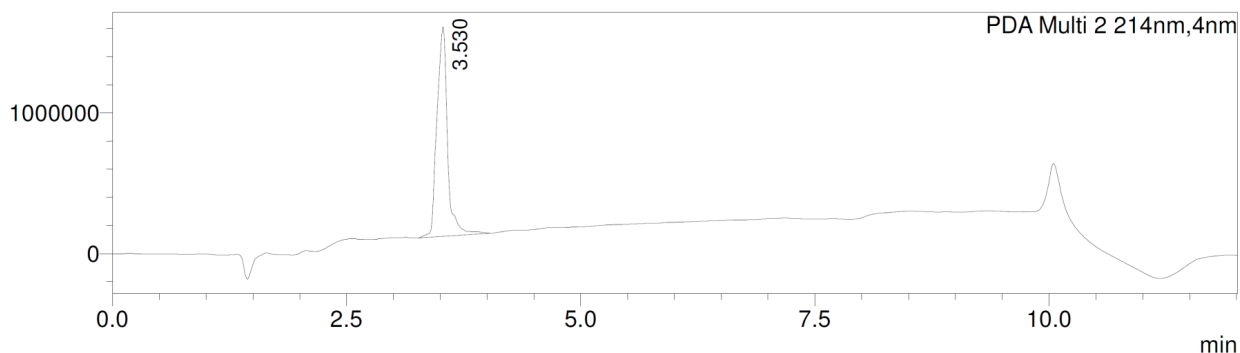
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	0.138	1464	442	0.022	0.022
2	3.199	6401103	792014	95.196	95.196
3	3.869	321539	15306	4.782	4.782
Total		6724107	807762	100.000	

2718.014 (R)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-3-ethyl-4-propylimidazolidin-2-imine. Compound

2718.014 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Norvaline-OH (R₄), and Acetic Anhydride (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.6mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.43 (br. s., 1 H) 3.75 - 4.05 (m, 3 H) 3.55 - 3.63 (m, 2 H) 3.27 - 3.52 (m, 10 H) 3.18 - 3.23 (m, 1 H) 3.08 - 3.15 (m, 1 H) 2.98 (dd, J=14.37, 4.10 Hz, 1 H) 2.76 - 2.92 (m, 2 H) 2.53 (br. s., 1 H) 2.23 - 2.48 (m, 2 H) 2.07 - 2.23 (m, 1 H) 1.93 - 2.07 (m, 1 H) 1.57 - 1.87 (m, 7 H) 1.19 - 1.49 (m, 6 H) 1.11 - 1.19 (m, 2 H) 1.05 (t, J=7.03 Hz, 3 H) 0.81 - 1.01 (m, 6 H) 0.74 (d, J=6.72 Hz, 2 H) **m/z** calcd C₂₈H₅₃N₇ [M+H]⁺ 488.4, found 488.8 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

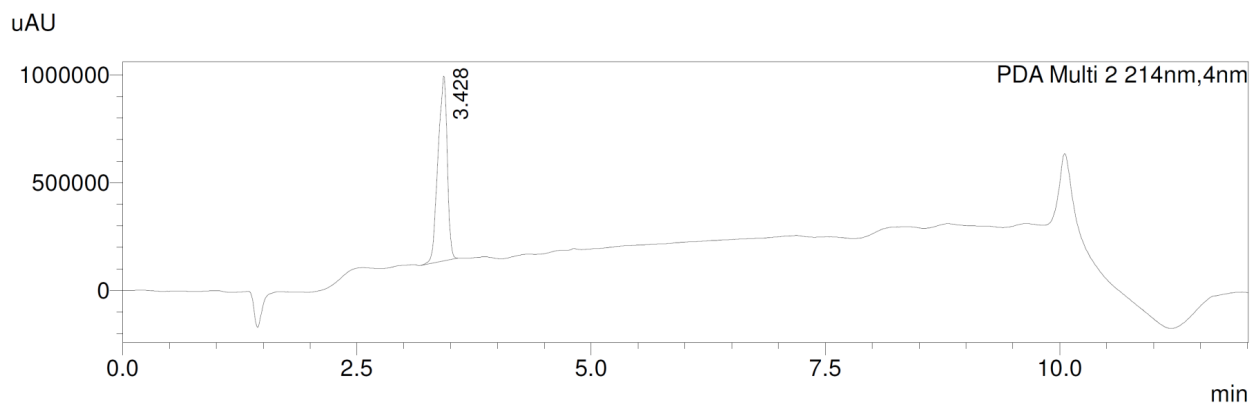
uAU



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.530	11660131	1489871	100.000	100.000
Total		11660131	1489871	100.000	

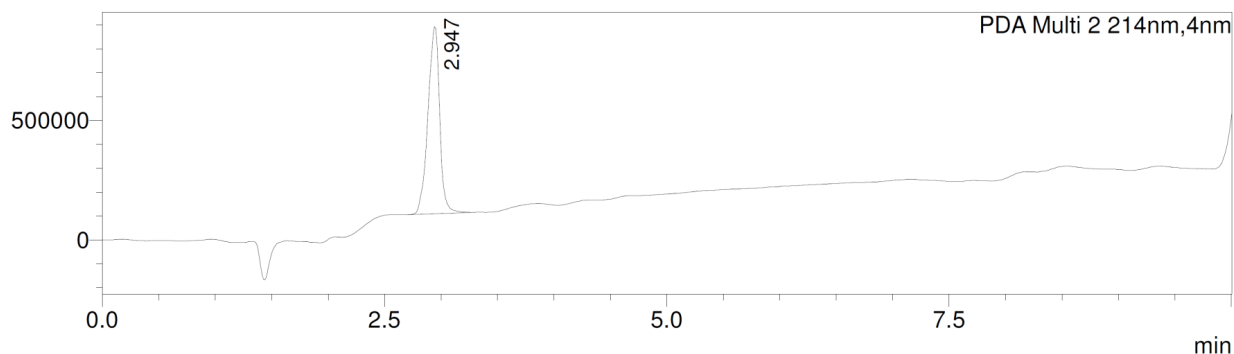
2718.015 (R)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-propylimidazolidin-2-imine. Compound 2718.015 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), and Boc-D-Norvaline-OH (R₄). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.8mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.52 (br. s., 1 H) 10.14 (br. s., 1 H) 8.70 (br. s., 1 H) 8.33 (br. s., 2 H) 3.83 - 4.09 (m, 2 H) 3.69 - 3.80 (m, 2 H) 3.31 - 3.60 (m, 6 H) 3.18 - 3.29 (m, 2 H) 2.95 - 3.14 (m, 2 H) 2.72 - 2.94 (m, 2 H) 2.46 (br. s., 1 H) 2.00 - 2.27 (m, 2 H) 1.52 - 1.81 (m, 6 H) 1.30 - 1.52 (m, 4 H) 1.01 - 1.27 (m, 5 H) 0.73 - 0.91 (m, 7 H) 0.67 (d, J=6.72 Hz, 3 H) **m/z** calcd C₂₆H₄₉N₇ [M+H]⁺ 460.4, found 460.7 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.428	5887893	858040	100.000	100.000
Total		5887893	858040	100.000	

2718.016 (R)-1-(((S)-1-((R)-3-cyclohexyl-2-(2-iminoimidazolidin-1-yl)propyl)pyrrolidin-2-yl)methyl)-5-isopropylimidazolidin-2-imine. Compound 2718.016 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), and Boc-Glycine-OH (R₄). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.9mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 9.80 (br. s., 1 H) 8.70 (br. s., 2 H) 4.08 - 4.37 (m, 1 H) 3.70 - 3.98 (m, 5 H) 3.41 - 3.69 (m, 6 H) 3.26 - 3.36 (m, 2 H) 3.04 - 3.20 (m, 2 H) 2.78 - 2.91 (m, 2 H) 2.53 (br. s., 1 H) 2.10 - 2.34 (m, 2 H) 1.78 - 1.89 (m, 2 H) 1.58 - 1.76 (m, 5 H) 1.35 - 1.56 (m, 2 H) 1.07 - 1.30 (m, 4 H) 0.90 - 1.02 (m, 1 H) 0.86 (d, J=6.85 Hz, 3 H) 0.76 (d, J=6.72 Hz, 3 H) **m/z** calcd C₂₃H₄₃N₇ [M+H]⁺ 418.4, found 418.25 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU

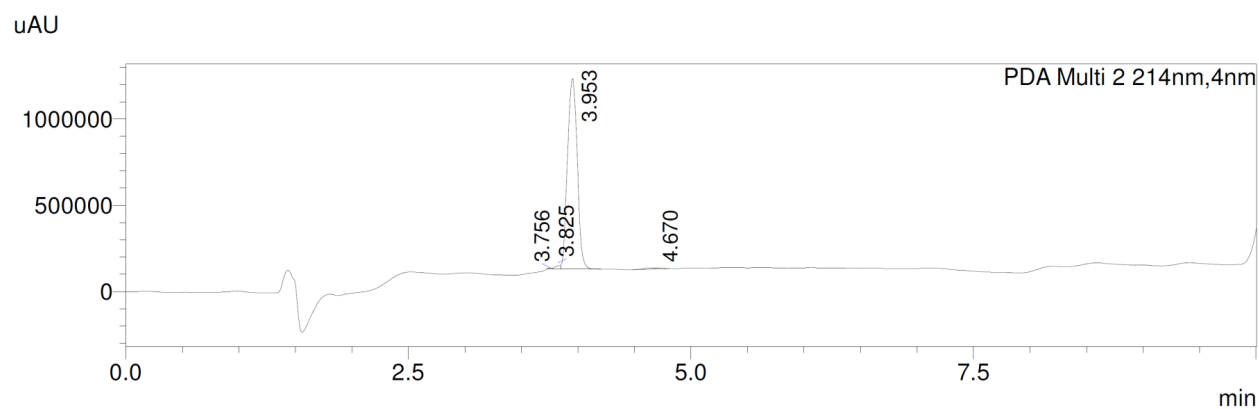


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	2.947	5667516	785224	100.000	100.000
Total		5667516	785224	100.000	

2718.020 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-iminoimidazolidin-4-yl)ethanol.

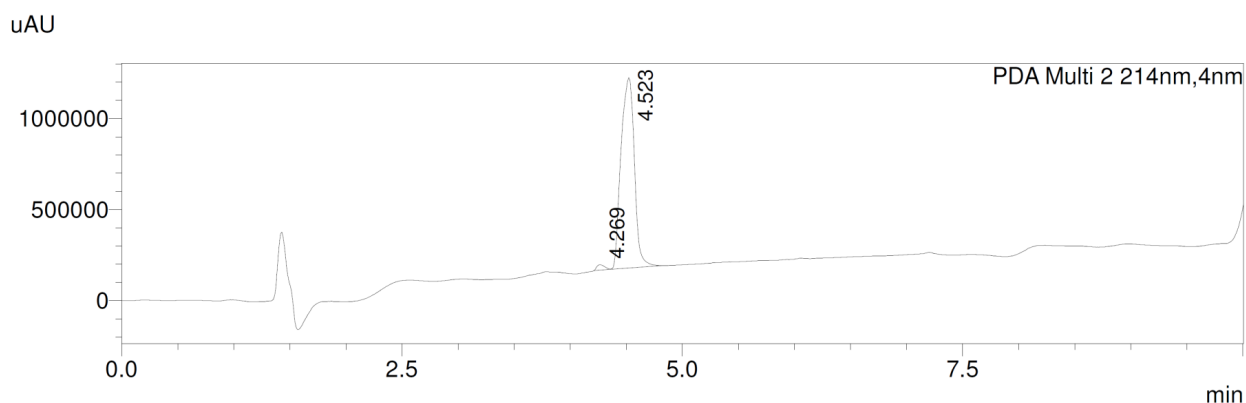
Compound 2718.020 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.8mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.62 (br. s., 1 H) 3.72 - 4.00 (m, 2 H) 3.46 - 3.72 (m, 2 H) 3.26 - 3.46 (m, 4 H) 3.16 (dd, J=14.55, 5.99 Hz, 1 H) 2.12 (br. s., 1 H) 1.59 (br. s., 2 H) 1.30 - 1.56 (m, 4 H) 1.06 - 1.30 (m, 1 H) 0.88 - 1.06 (m, 4 H) 0.58 - 0.88 (m, 8 H) **m/z** calcd C₁₆H₃₁N₃O [M+H]⁺ 282.3, found 282.55 (MS ESI) **Purity** LC-MS: >97% (214 nm, peak area).



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.756	21681	8351	0.318	0.318
2	3.825	78630	20815	1.153	1.153
3	3.953	6638793	1106908	97.358	97.358
4	4.670	79855	7381	1.171	1.171
Total		6818959	1143456	100.000	

2718.021 (R)-1-((4-(tert-butyl)cyclohexyl)methyl)-5-propylimidazolidin-2-imine. Compound 2718.021 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 5.6mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.20 (br. s., 1 H) 3.87 (d, J=8.80 Hz, 1 H) 3.55 - 3.75 (m, 2 H) 3.25 (dd, J=9.72, 5.69 Hz, 1 H) 2.95 (br. s., 1 H) 2.03 (br. s., 1 H) 1.62 (dt, J=10.09, 3.03 Hz, 2 H) 1.34 - 1.55 (m, 6 H) 1.25 (d, J=7.34 Hz, 2 H) 1.13 (br. s., 2 H) 0.87 - 1.00 (m, 5 H) 0.84 (s, 8 H) 0.83 (br. s., 1 H) **m/z** calcd C₁₇H₃₃N₃ [M+H]⁺ 280.3, found 280.6 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).



PDA Ch2 214nm

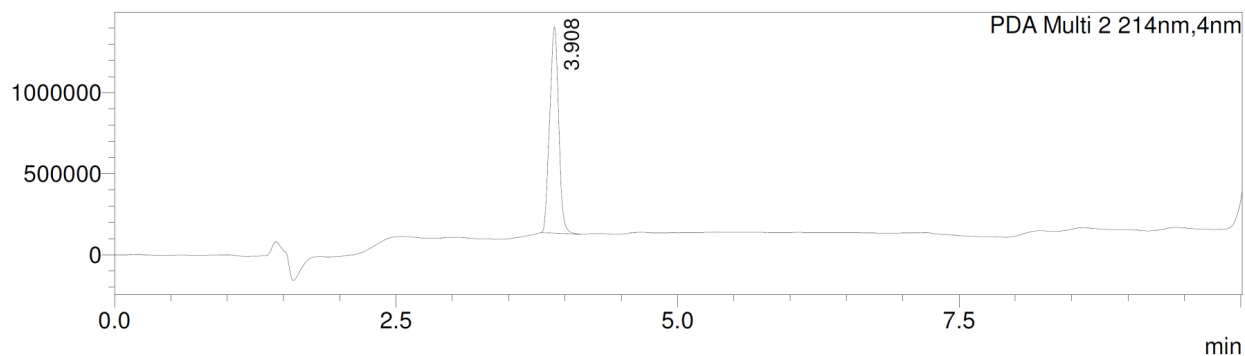
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.269	145522	29146	1.651	1.651
2	4.523	8667181	1046010	98.349	98.349
Total		8812703	1075156	100.000	

2718.022

1-((4-(tert-butyl)cyclohexyl)methyl)-3-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-2-

imine. Compound 2718.022 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-Glycine-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.8mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.13 (br. s., 1 H) 7.06 - 7.35 (m, 4 H) 4.31 - 4.41 (m, 1 H) 3.91 (q, J=8.15 Hz, 1 H) 3.65 (t, J=9.23 Hz, 2 H) 3.36 - 3.58 (m, 10 H) 3.15 - 3.36 (m, 5 H) 3.09 (dd, J=14.00, 7.76 Hz, 2 H) 2.97 (br. s., 1 H) 2.64 - 2.90 (m, 3 H) 2.20 - 2.48 (m, 2 H) 1.78 - 2.08 (m, 2 H) 1.64 - 1.78 (m, 2 H) 1.52 - 1.64 (m, 2 H) 1.32 - 1.52 (m, 5 H) 1.28 (br. s., 2 H) 0.86 - 1.12 (m, 7 H) 0.82 (s, 7 H) **m/z** calcd C₃₅H₅₉N₇ [M+H]⁺ 578.5, found 578.85 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU

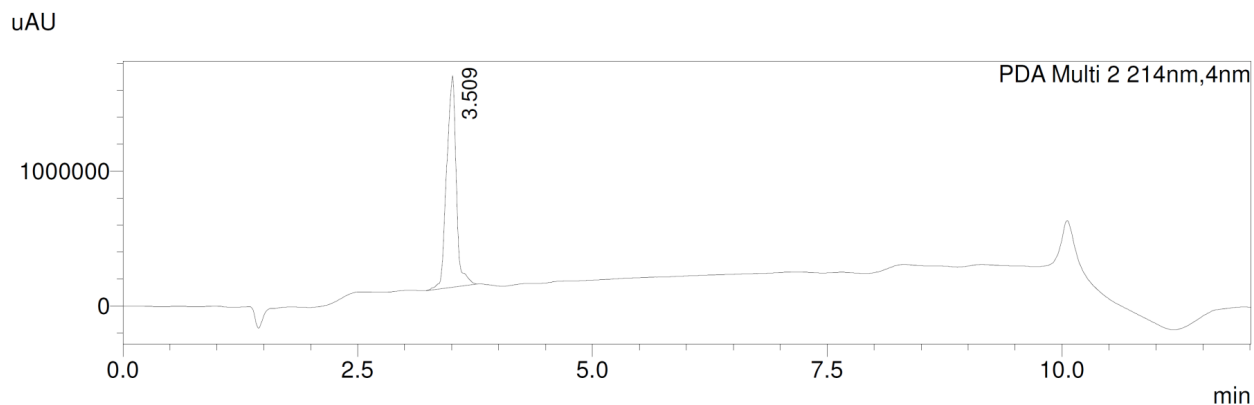


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.908	7076967	1275564	100.000	100.000
Total		7076967	1275564	100.000	

2718.023 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-(2-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)ethyl)imidazolidin-4-yl)ethanol.

Compound 2718.023 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-Glycine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.7mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.46 (br. s., 1 H) 8.47 (br. s., 2 H) 3.75 - 3.95 (m, 6 H) 3.64 - 3.70 (m, 2 H) 3.31 - 3.59 (m, 5 H) 2.99 - 3.24 (m, 4 H) 2.67 - 2.95 (m, 2 H) 2.30 (q, J=8.03 Hz, 2 H) 2.09 (d, J=12.84 Hz, 1 H) 1.67 - 1.89 (m, 3 H) 1.40 - 1.63 (m, 7 H) 1.32 - 1.38 (m, 1 H) 1.08 - 1.18 (m, 2 H) 0.84 (s, 8 H) 0.81 - 1.05 (m, 12 H) **m/z** calcd C₃₀H₅₇N₇O [M+H]⁺ 532.5, found 532.55 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

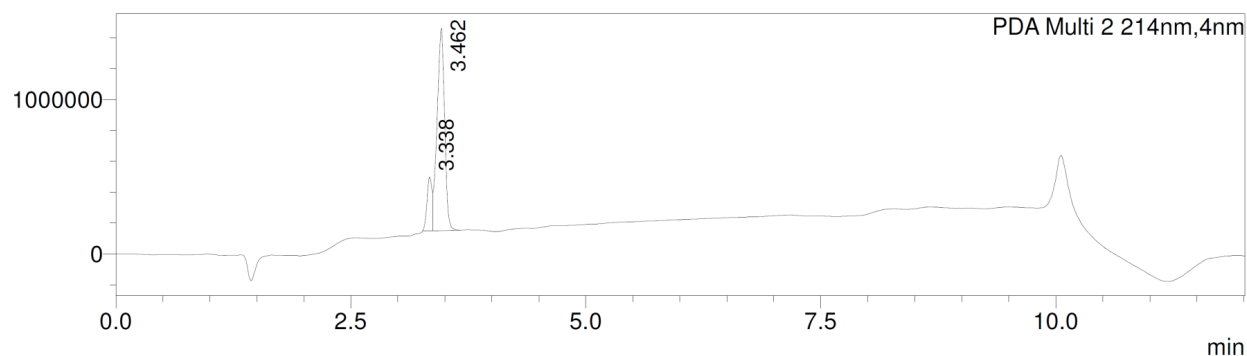


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.509	11159595	1569912	100.000	100.000
Total		11159595	1569912	100.000	

2718.024 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-((2-iminoimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.024 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-Glycine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.4mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 7.97 (br. s., 1 H) 7.32 - 7.37 (m, 2 H) 7.12 - 7.31 (m, 3 H) 4.23 - 4.40 (m, 1 H) 3.74 - 4.00 (m, 2 H) 3.58 - 3.69 (m, 4 H) 3.37 - 3.56 (m, 6 H) 3.02 - 3.27 (m, 3 H) 3.00 (br. s., 1 H) 2.87 (d, J=4.03 Hz, 1 H) 2.74 (dd, J=13.88, 10.09 Hz, 2 H) 2.38 (d, J=8.80 Hz, 1 H) 2.08 - 2.32 (m, 1 H) 1.78 - 2.04 (m, 2 H) 1.57 - 1.76 (m, 2 H) 1.41 - 1.54 (m, 3 H) 1.38 (br. s., 1 H) 1.28 (d, J=11.74 Hz, 1 H) 1.01 (d, J=6.24 Hz, 4 H) 0.97 - 1.20 (m, 2 H) 0.82 (s, 9 H) 0.75 - 0.94 (m, 1 H) **m/z** calcd C₃₃H₅₅N₇O [M+H]⁺ 566.45, found 566.40 (MS ESI) **Purity** LC-MS: >84% (214 nm, peak area).

uAU

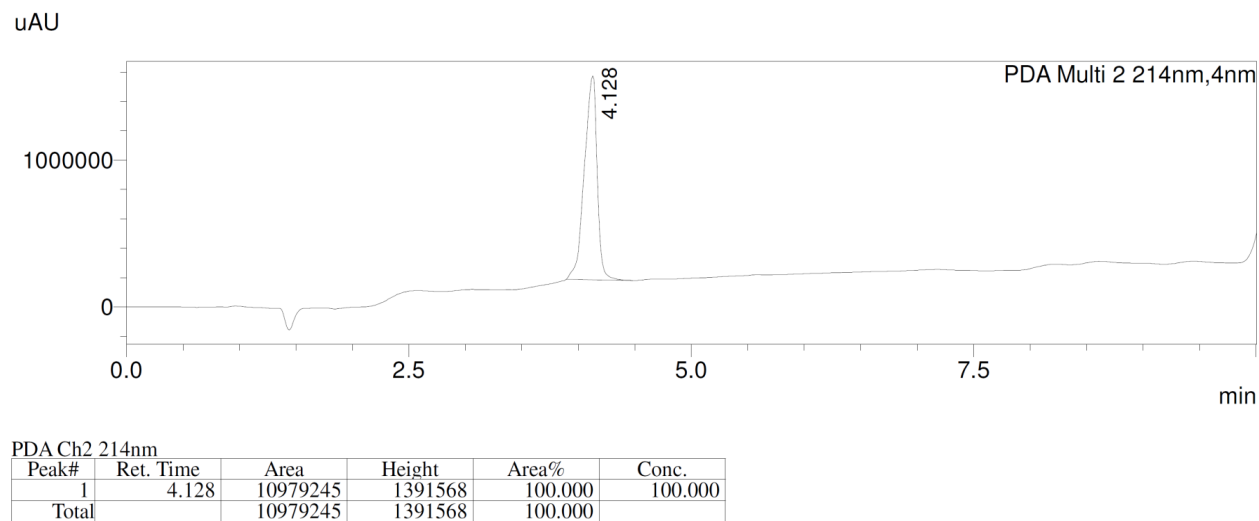


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.338	1339002	349181	15.580	15.580
2	3.462	7255339	1311674	84.420	84.420
Total		8594340	1660855	100.000	

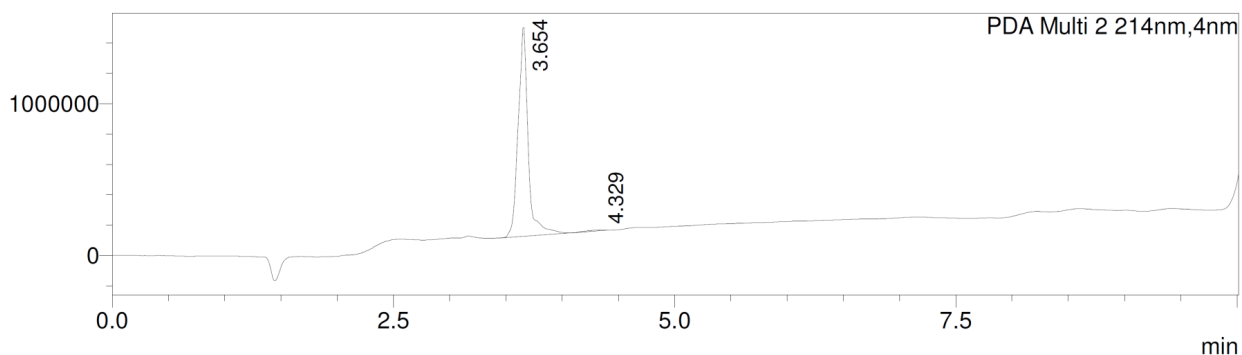
2718.025 1-((4-(tert-butyl)cyclohexyl)methyl)-3-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)imidazolidin-2-imine.

Compound 2718.025 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-Glycine-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 5.9mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.30 (br. s., 1 H) 8.28 (br. s., 1 H) 4.02 (t, J=9.72 Hz, 1 H) 3.78 - 3.97 (m, 1 H) 3.38 - 3.67 (m, 11 H) 3.15 - 3.38 (m, 5 H) 2.98 - 3.15 (m, 1 H) 2.85 (br. s., 1 H) 2.78 (br. s., 1 H) 2.53 (br. s., 1 H) 2.20 - 2.37 (m, 2 H) 2.06 (br. s., 1 H) 1.76 - 1.98 (m, 2 H) 1.54 - 1.70 (m, 7 H) 1.39 - 1.53 (m, 5 H) 1.27 (br. s., 1 H) 1.06 - 1.23 (m, 5 H) 0.84 (s, 9 H) 0.73 - 1.02 (m, 7 H) **m/z** calcd C₃₆H₆₅N₇ [M+H]⁺ 584.5, found 584.45 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



2718.026 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-((2-iminoimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-iminoimidazolidin-4-yl)ethanol. Compound 2718.026 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-Glycine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.7mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.42 (br. s., 2 H) 8.27 (br. s., 2 H) 3.92 - 4.22 (m, 2 H) 3.57 - 3.87 (m, 9 H) 3.45 - 3.55 (m, 3 H) 3.18 - 3.40 (m, 3 H) 2.89 - 3.18 (m, 3 H) 2.60 - 2.83 (m, 1 H) 2.04 - 2.29 (m, 3 H) 1.77 - 2.04 (m, 2 H) 1.58 - 1.72 (m, 5 H) 1.40 - 1.57 (m, 5 H) 1.28 (d, J=3.79 Hz, 1 H) 1.19 (br. s., 1 H) 0.89 - 1.16 (m, 9 H) 0.84 (s, 8 H) **m/z** calcd C₃₃H₆₁N₇O [M+H]⁺ 572.5, found 572.55 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU



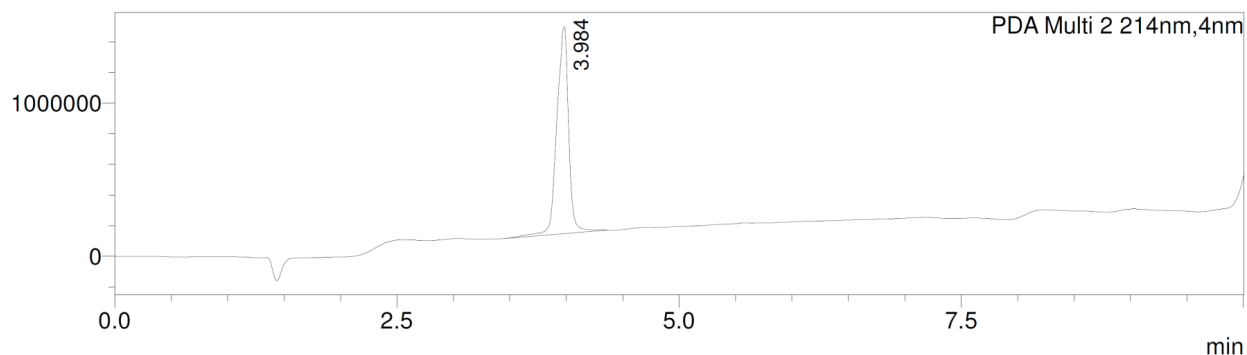
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.654	8523568	1375667	99.134	99.134
2	4.329	74439	5115	0.866	0.866
Total		8598007	1380783	100.000	

2718.027 1-((4-(tert-butyl)cyclohexyl)methyl)-3-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)imidazolidin-2-imine.

Compound 2718.027 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-Glycine-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.8mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.45 (br. s., 2 H) 3.75 - 4.05 (m, 2 H) 3.58 (d, J=8.31 Hz, 1 H) 3.26 - 3.55 (m, 19 H) 3.07 - 3.16 (m, 2 H) 2.77 - 2.98 (m, 2 H) 2.53 (br. s., 2 H) 2.21 - 2.35 (m, 2 H) 1.77 - 1.93 (m, 2 H) 1.59 - 1.77 (m, 5 H) 1.56 (br. s., 1 H) 1.33 - 1.53 (m, 5 H) 1.27 (br. s., 1 H) 1.05 - 1.23 (m, 5 H) 0.96 (t, J=11.49 Hz, 2 H) 0.84 (s, 8 H) 0.87 (s, 1 H) 0.76 (d, J=6.72 Hz, 2 H) **m/z** calcd C₃₄H₆₃N₇ [M+H]⁺ 570.5, found 570.9 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU



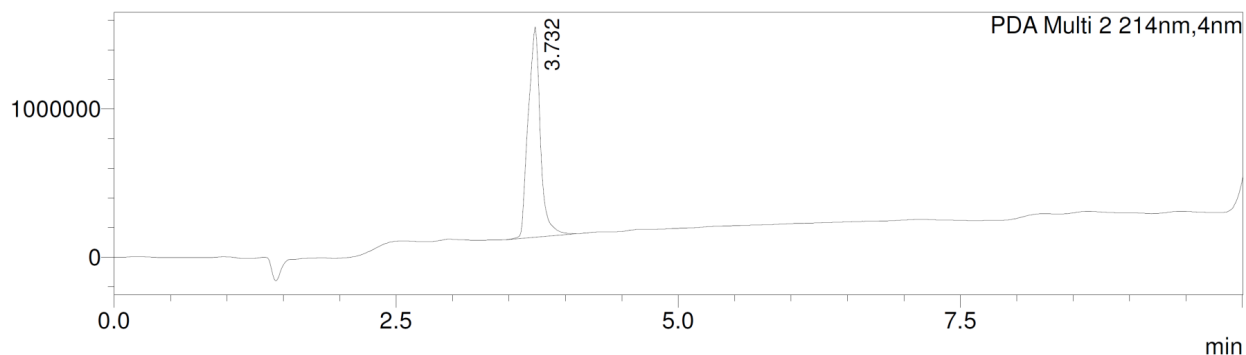
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.984	9850854	1351317	100.000	100.000
Total		9850854	1351317	100.000	

2718.028 (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-(2-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)ethyl)-4-propylimidazolidin-2-imine.

Compound 2718.028 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-Glycine-OH (R₃), Boc-D-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.2mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.47 (br. s., 1 H) 8.57 (br. s., 1 H) 3.94 (ddd, J=9.75, 5.84, 3.61 Hz, 2 H) 3.61 - 3.88 (m, 6 H) 3.31 - 3.61 (m, 8 H) 3.12 (dt, J=9.54, 4.89 Hz, 1 H) 2.77 - 3.06 (m, 3 H) 2.24 - 2.41 (m, 1 H) 2.11 (td, J=6.82, 3.48 Hz, 1 H) 2.01 (br. s., 1 H) 1.68 - 1.91 (m, 3 H) 1.56 - 1.68 (m, 2 H) 1.35 - 1.56 (m, 5 H) 1.19 - 1.35 (m, 2 H) 1.03 - 1.19 (m, 2 H) 0.84 (s, 7 H) 0.79 - 1.03 (m, 7 H) 0.76 (d, J=6.72 Hz, 3 H) **m/z** calcd C₃₀H₅₇N₇ [M+H]⁺ 516.5, found 516.55 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU

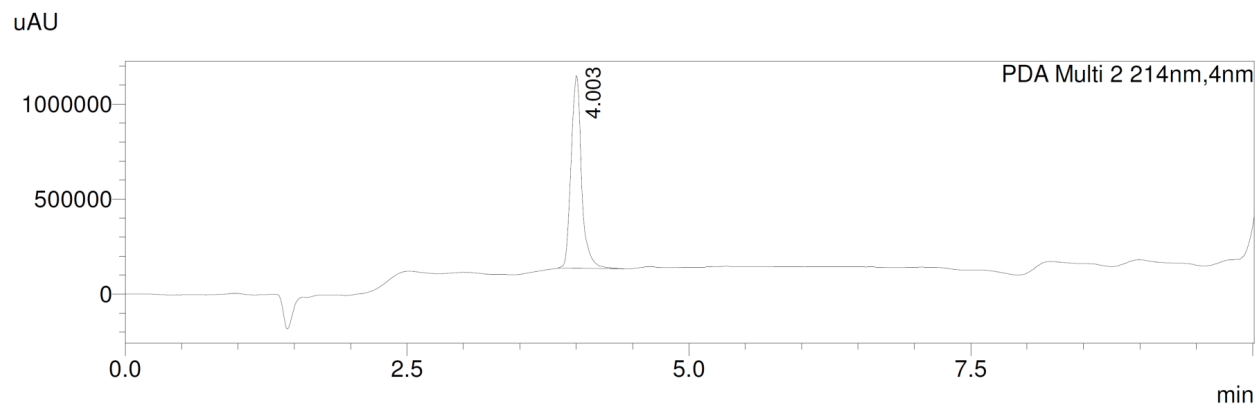


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.732	10653792	1422252	100.000	100.000
Total		10653792	1422252	100.000	

2718.029 (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-((2-iminoimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-propylimidazolidin-2-imine.

Compound 2718.029 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-Glycine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.1mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.29 (br. s., 1 H) 4.00 (br. s., 1 H) 3.70 - 3.93 (m, 3 H) 3.41 - 3.70 (m, 10 H) 3.16 - 3.41 (m, 4 H) 2.87 - 3.16 (m, 4 H) 2.63 - 2.84 (m, 1 H) 2.14 - 2.35 (m, 2 H) 2.07 (br. s., 1 H) 1.77 - 1.95 (m, 2 H) 1.64 - 1.77 (m, 4 H) 1.61 (br. s., 2 H) 1.35 - 1.55 (m, 6 H) 1.24 - 1.34 (m, 2 H) 1.05 - 1.20 (m, 4 H) 0.87 - 1.05 (m, 5 H) 0.84 (s, 8 H) **m/z** calcd C₃₄H₆₃N₇ [M+H]⁺ 570.5, found 570.9 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.003	6593125	1015319	100.000	100.000
Total		6593125	1015319	100.000	

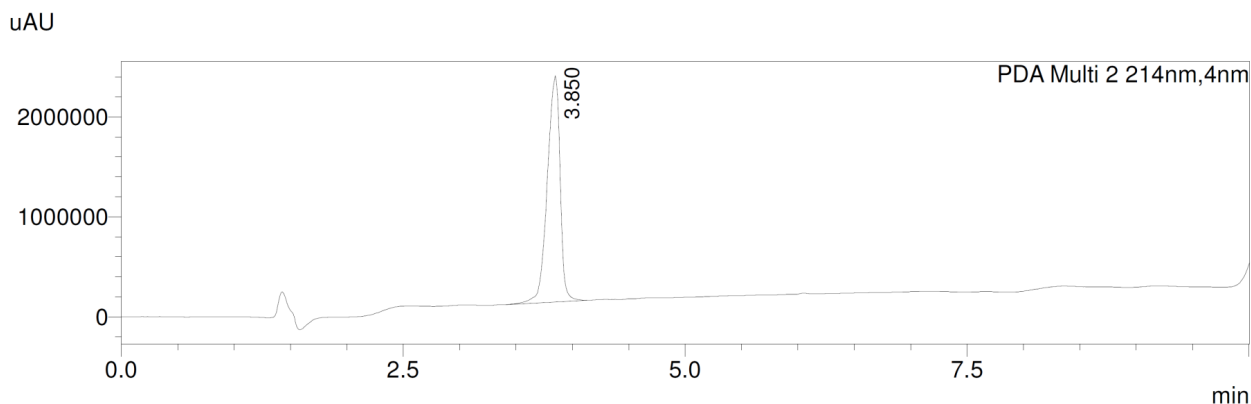
2718.030 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

yl)imidazolidin-4-yl)ethanol. Compound 2718.030 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.1mg,

¹H NMR (400 MHz, DMSO-d₆) δ ppm 10.58 (br. s., 1 H) 8.42 (br. s., 2 H) 8.21 (br. s., 1 H) 7.14 - 7.40 (m, 4 H) 4.16 - 4.46 (m, 2 H) 3.90 (dd, J=9.66, 5.38 Hz, 4 H) 3.48 - 3.78 (m, 5 H) 3.40 (dd, J=10.09, 4.34 Hz, 1 H) 3.14 - 3.35 (m, 3 H) 2.99 - 3.14 (m, 3 H) 2.92 (dd, J=14.31, 5.87 Hz, 1 H) 2.81 (dd, J=14.24, 9.11 Hz, 1 H) 2.67 (d, J=1.71 Hz, 1 H) 2.26 (d, J=9.05 Hz, 1 H) 2.16 (d, J=8.31 Hz, 1 H) 2.10 (br. s., 1 H) 1.73 - 1.90 (m, 1 H) 1.33 - 1.62 (m, 9 H) 1.09 (t, J=12.41 Hz, 1 H) 0.86 - 1.00 (m, 7 H) 0.82 (s, 8 H) 0.78 (d, J=6.36 Hz, 3 H) **m/z** calcd C₃₇H₆₃N₇ [M+H]⁺ 622.5, found 622.9 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.850	17957846	2264806	100.000	100.000
Total		17957846	2264806	100.000	

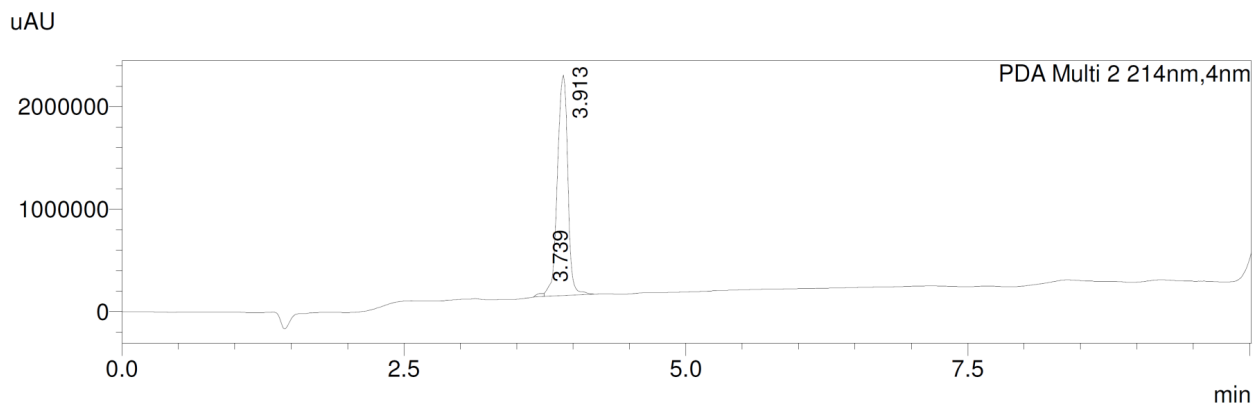
2718.031 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

yl)imidazolidin-4-yl)ethanol. Compound 2718.031 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.1mg,

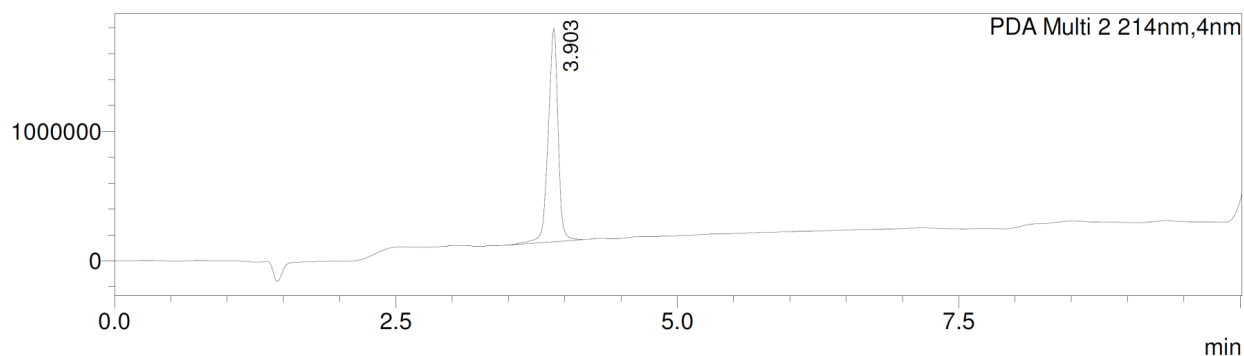
¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.45 (br. s., 2 H) 7.08 - 7.37 (m, 4 H) 4.26 - 4.50 (m, 1 H) 3.89 (d, J=8.44 Hz, 1 H) 3.72 (dd, J=9.84, 4.58 Hz, 1 H) 3.46 - 3.69 (m, 7 H) 3.27 - 3.46 (m, 4 H) 2.98 - 3.27 (m, 5 H) 2.72 - 2.94 (m, 3 H) 2.61 (dd, J=13.14, 6.79 Hz, 1 H) 2.44 (d, J=8.80 Hz, 1 H) 2.05 (br. s., 1 H) 1.76 - 1.95 (m, 1 H) 1.65 - 1.76 (m, 2 H) 1.37 - 1.65 (m, 7 H) 1.23 - 1.37 (m, 2 H) 0.98 - 1.23 (m, 2 H) 0.82 (s, 8 H) 0.74 - 0.98 (m, 7 H) 0.45 - 0.74 (m, 3 H) **m/z** calcd C₃₇H₆₃N₇ [M+H]⁺ 622.5, found 622.9 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.739	145399	29507	1.044	1.044
2	3.913	13784971	2152242	98.956	98.956
Total		13930370	2181750	100.000	

2718.032 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((R)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.032 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.1mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.44 (br. s., 2 H) 8.14 (br. s., 1 H) 7.15 - 7.36 (m, 4 H) 4.14 - 4.39 (m, 1 H) 3.87 - 4.14 (m, 2 H) 3.75 - 3.81 (m, 1 H) 3.43 - 3.73 (m, 9 H) 3.26 (dd, J=9.60, 6.42 Hz, 2 H) 2.93 - 3.21 (m, 5 H) 2.77 - 2.93 (m, 1 H) 2.70 (dd, J=14.55, 11.37 Hz, 1 H) 2.47 (br. s., 1 H) 2.24 - 2.43 (m, 1 H) 1.68 - 1.98 (m, 4 H) 1.49 - 1.65 (m, 3 H) 1.32 - 1.47 (m, 3 H) 1.26 (d, J=12.59 Hz, 2 H) 0.82 (s, 8 H) 0.76 - 1.04 (m, 10 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.55 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.903	10039379	1649962	100.000	100.000
Total		10039379	1649962	100.000	

2718.033 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

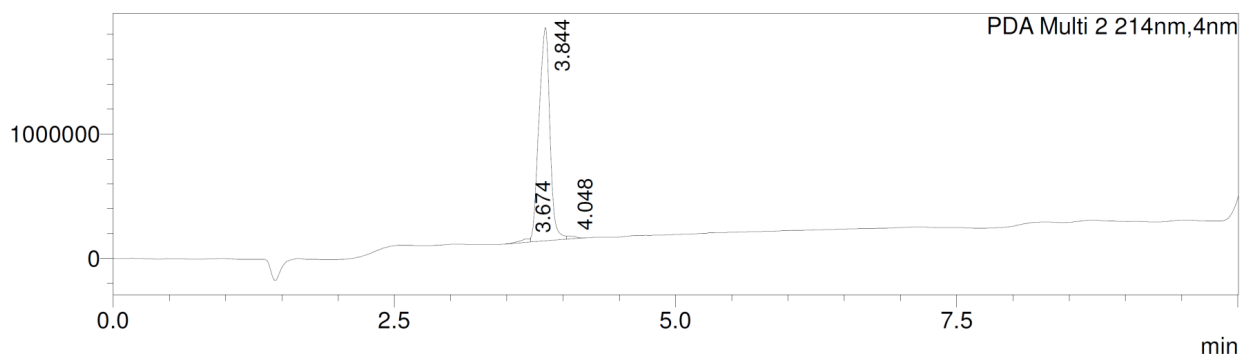
yl)imidazolidin-4-yl)ethanol. Compound 2718.033 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.8mg,

¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.46 (br. s., 1 H) 7.97 (br. s., 1 H) 7.35 (d, J=7.21 Hz, 2 H) 7.16 - 7.31 (m, 2 H) 4.34 (br. s., 1 H) 3.87 - 4.15 (m, 2 H) 3.76 - 3.87 (m, 2 H) 3.56 - 3.76 (m, 7 H) 3.36 - 3.56 (m, 5 H) 3.21 - 3.34 (m, 3 H) 2.85 - 3.15 (m, 4 H) 2.69 - 2.82 (m, 1 H) 2.63 (d, J=4.77 Hz, 1 H) 2.53 (br. s., 1 H) 2.35 (dd, J=12.35, 3.67 Hz, 1 H) 2.22 (d, J=8.93 Hz, 1 H) 1.91 - 2.12 (m, 1 H) 1.87 (br. s., 1 H) 1.70 (d, J=4.89 Hz, 1 H) 1.36 - 1.65 (m, 6 H) 1.29 (d, J=11.37 Hz, 1 H) 1.18 (br. s., 1 H) 1.01 (d, J=6.24 Hz, 3 H) 0.97 - 1.14 (m, 1 H) 0.82 (s, 7 H) 0.72 - 0.97 (m, 7 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.9 (MS ESI) **Purity** LC-MS: >97% (214 nm, peak area).

uAU



PDACh2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.674	190654	27134	1.604	1.604
2	3.844	11582394	1714248	97.423	97.423
3	4.048	115724	23497	0.973	0.973
Total		11888772	1764878	100.000	

2718.034 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((R)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

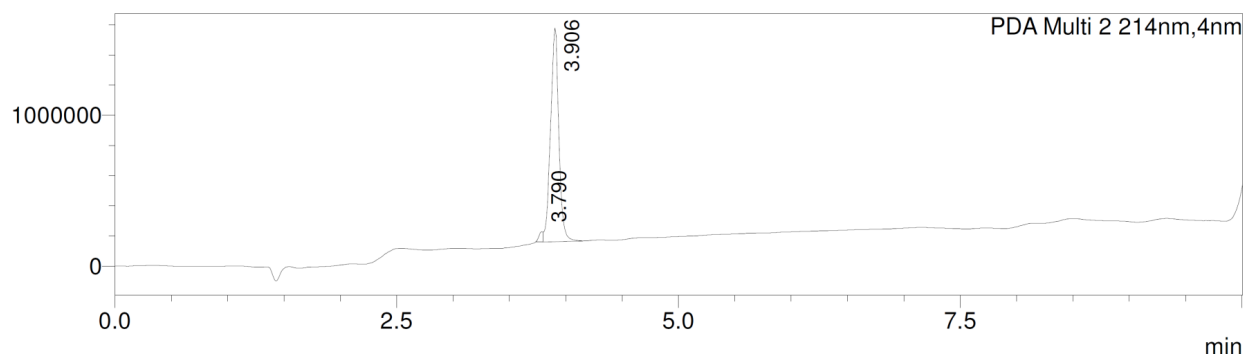
yl)imidazolidin-4-yl)ethanol. Compound 2718.034 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 5.8mg,

¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.44 (br. s., 2 H) 8.01 (br. s., 1 H) 7.15 - 7.38 (m, 4 H) 4.12 - 4.39 (m, 1 H) 3.77 - 4.06 (m, 3 H) 3.44 - 3.73 (m, 10 H) 3.27 - 3.44 (m, 4 H) 3.16 - 3.27 (m, 2 H) 2.97 - 3.14 (m, 3 H) 2.83 - 2.95 (m, 1 H) 2.77 (dd, J=14.00, 10.09 Hz, 2 H) 2.38 (dd, J=12.72, 3.67 Hz, 1 H) 2.10 - 2.32 (m, 1 H) 1.75 - 1.95 (m, 2 H) 1.53 - 1.75 (m, 3 H) 1.34 - 1.53 (m, 4 H) 1.29 (d, J=11.13 Hz, 1 H) 1.00 - 1.11 (m, 4 H) 0.82 (s, 8 H) 0.79 - 0.98 (m, 6 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.4 (MS ESI) **Purity** LC-MS: >97% (214 nm, peak area).

uAU



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.790	175204	67794	2.365	2.365
2	3.906	7233056	1418164	97.635	97.635
Total		7408260	1485958	100.000	

2718.035 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

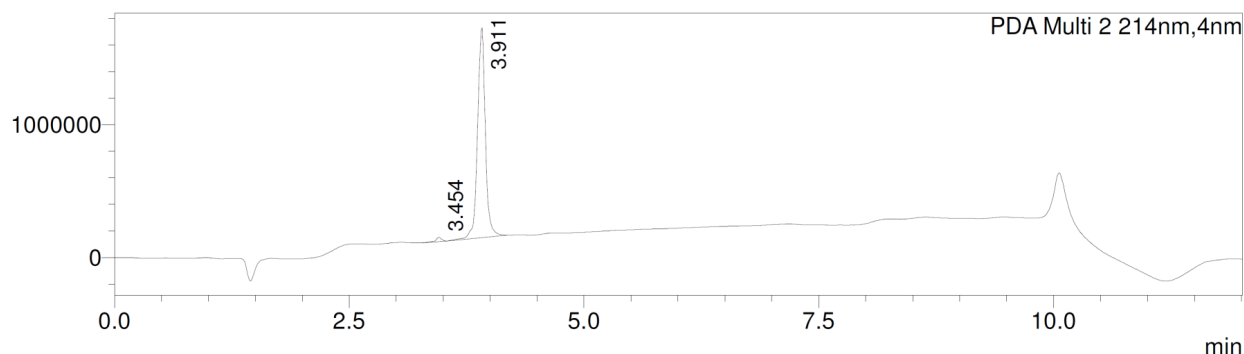
yl)imidazolidin-4-yl)ethanol. Compound 2718.035 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 5.8mg,

¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.17 (br. s., 1 H) 7.16 - 7.45 (m, 4 H) 4.32 (br. s., 1 H) 3.85 - 4.14 (m, 2 H) 3.73 - 3.85 (m, 2 H) 3.40 - 3.68 (m, 11 H) 3.38 (d, J=6.72 Hz, 1 H) 3.13 - 3.32 (m, 4 H) 3.02 - 3.11 (m, 2 H) 2.88 - 3.00 (m, 1 H) 2.84 (br. s., 1 H) 2.52 - 2.81 (m, 3 H) 2.19 - 2.48 (m, 1 H) 1.80 - 2.10 (m, 2 H) 1.69 - 1.80 (m, 2 H) 1.63 (d, J=8.56 Hz, 2 H) 1.32 - 1.54 (m, 4 H) 1.26 (d, J=11.00 Hz, 1 H) 1.13 (d, J=13.20 Hz, 1 H) 1.01 - 1.09 (m, 1 H) 0.71 - 1.01 (m, 16 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.6 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).

uAU



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.454	130631	30357	1.402	1.402
2	3.911	9188223	1582183	98.598	98.598
Total		9318854	1612540	100.000	

2718.036 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((R)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

yl)imidazolidin-4-yl)ethanol. Compound 2718.036 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-

D-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as

described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.0mg,

¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.42 (br. s., 1 H) 7.12 - 7.39 (m, 5 H) 4.30 - 4.56 (m, 1 H)

3.81 - 4.11 (m, 2 H) 3.43 - 3.73 (m, 8 H) 3.16 - 3.38 (m, 4 H) 2.90 - 3.16 (m, 5 H) 2.80 - 2.90 (m,

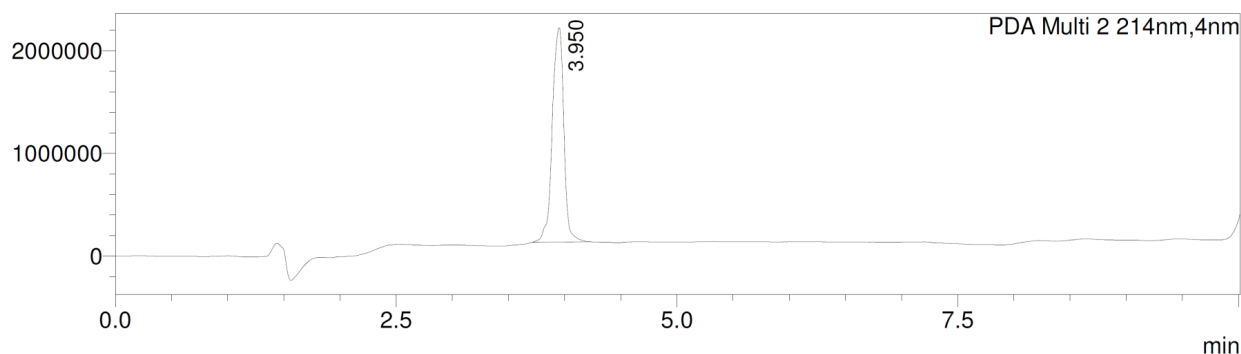
1 H) 2.74 (dd, J=14.92, 10.64 Hz, 1 H) 2.52 - 2.65 (m, 1 H) 2.19 - 2.48 (m, 1 H) 2.04 (br. s., 1 H)

1.90 (td, J=7.95, 4.16 Hz, 1 H) 1.64 - 1.80 (m, 2 H) 1.32 - 1.62 (m, 8 H) 0.98 - 1.25 (m, 2 H) 0.91

(dd, J=11.68, 5.93 Hz, 7 H) 0.82 (s, 9 H) 0.45 - 0.74 (m, 3 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5,

found 622.9 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU



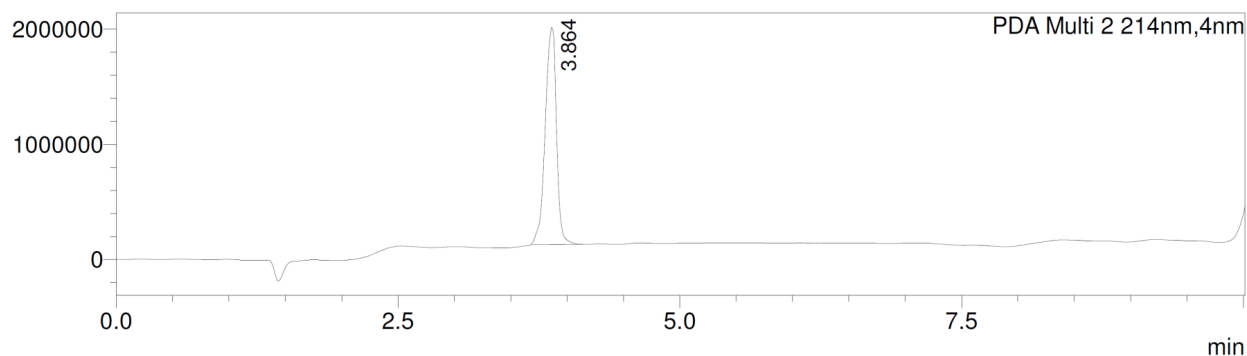
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.950	14936669	2089721	100.000	100.000
Total		14936669	2089721	100.000	

2718.037 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

yl)imidazolidin-4-yl)ethanol. Compound 2718.037 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.5mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.20 (br. s., 1 H) 7.13 - 7.40 (m, 4 H) 4.44 (br. s., 1 H) 3.94 (d, J=8.68 Hz, 1 H) 3.79 (td, J=10.51, 5.26 Hz, 2 H) 3.42 - 3.72 (m, 9 H) 3.16 - 3.42 (m, 5 H) 2.98 - 3.16 (m, 2 H) 2.69 - 2.98 (m, 3 H) 2.64 (br. s., 2 H) 2.13 - 2.36 (m, 2 H) 2.11 (br. s., 1 H) 1.83 - 2.07 (m, 1 H) 1.65 - 1.83 (m, 2 H) 1.44 - 1.65 (m, 5 H) 1.27 - 1.44 (m, 3 H) 1.01 - 1.27 (m, 2 H) 0.85 - 1.01 (m, 7 H) 0.82 (s, 7 H) 0.74 (dd, J=13.45, 6.24 Hz, 3 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.9 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.864	13127579	1886421	100.000	100.000
Total		13127579	1886421	100.000	

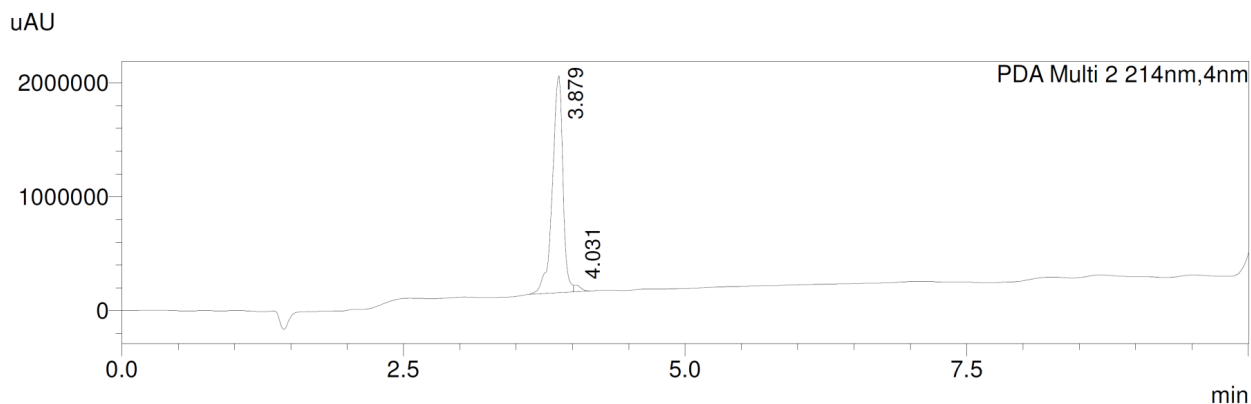
2718.038 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((R)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

yl)imidazolidin-4-yl)ethanol. Compound 2718.038 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.9mg,

¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.46 (br. s., 1 H) 8.22 (br. s., 1 H) 7.09 - 7.38 (m, 4 H) 4.43 (br. s., 1 H) 3.93 (d, J=9.66 Hz, 1 H) 3.72 - 3.88 (m, 1 H) 3.45 - 3.72 (m, 6 H) 3.38 (br. s., 4 H) 3.16 - 3.35 (m, 6 H) 2.99 - 3.16 (m, 2 H) 2.85 - 2.99 (m, 1 H) 2.77 (dd, J=14.55, 9.05 Hz, 2 H) 2.52 - 2.71 (m, 1 H) 2.13 - 2.36 (m, 2 H) 2.10 (br. s., 1 H) 2.00 (dd, J=13.20, 6.24 Hz, 1 H) 1.64 - 1.86 (m, 2 H) 1.34 - 1.64 (m, 8 H) 0.98 - 1.27 (m, 2 H) 0.85 - 0.98 (m, 7 H) 0.82 (s, 7 H) 0.62 - 0.80 (m, 3 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.85 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.879	12400151	1907510	98.160	98.160
2	4.031	232439	56993	1.840	1.840
Total		12632590	1964503	100.000	

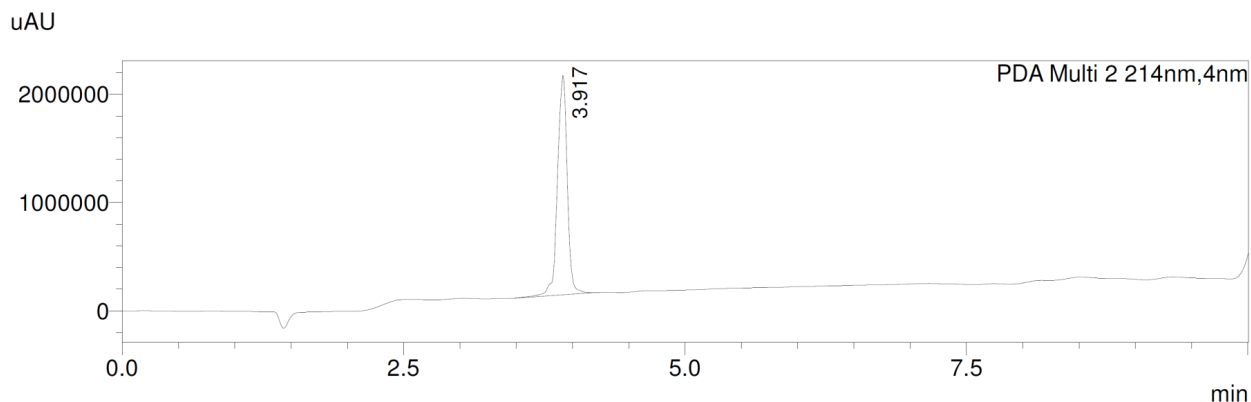
2718.039 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((S)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

yl)imidazolidin-4-yl)ethanol. Compound 2718.039 was synthesized using the following reagents:

(100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-

Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.1mg,

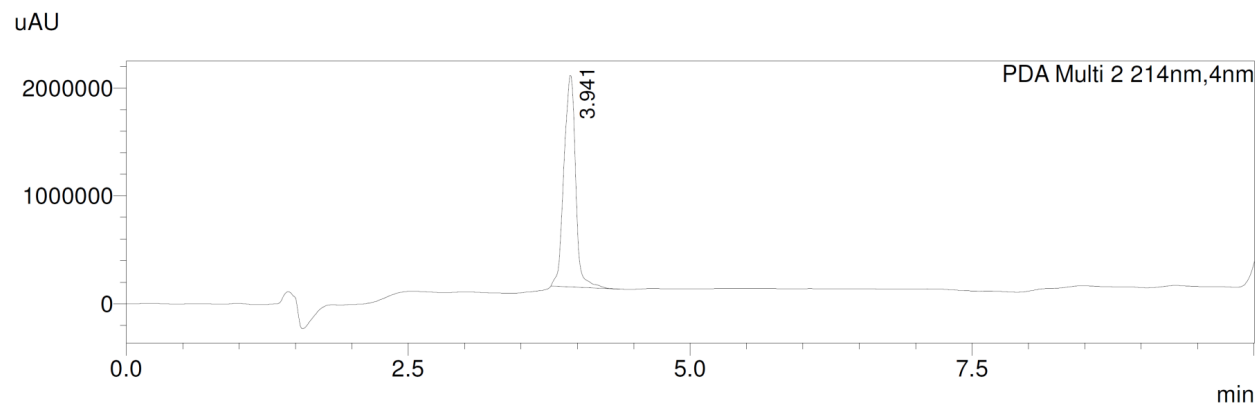
¹H NMR (400 MHz, DMSO-d₆) δ ppm 10.58 (br. s., 1 H) 8.45 (br. s., 2 H) 7.13 - 7.38 (m, 4 H) 4.46 (br. s., 1 H) 3.84 - 4.13 (m, 3 H) 3.44 - 3.74 (m, 11 H) 3.16 - 3.39 (m, 3 H) 2.90 - 3.16 (m, 5 H) 2.80 - 2.90 (m, 1 H) 2.74 (dd, J=14.92, 10.76 Hz, 1 H) 2.57 (d, J=5.99 Hz, 1 H) 2.37 - 2.48 (m, 1 H) 2.04 (br. s., 1 H) 1.80 - 1.98 (m, 1 H) 1.65 - 1.80 (m, 2 H) 1.32 - 1.62 (m, 8 H) 0.99 - 1.23 (m, 2 H) 0.82 (s, 8 H) 0.74 - 0.99 (m, 6 H) 0.64 (d, J=6.24 Hz, 2 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.55 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.917	12276638	2030768	100.000	100.000
Total		12276638	2030768	100.000	

2718.040 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((R)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

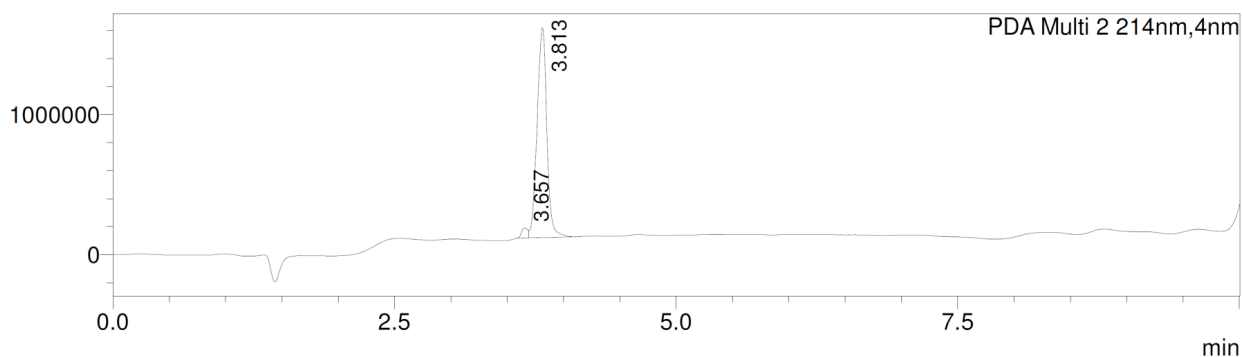
yl)imidazolidin-4-yl)ethanol. Compound 2718.040 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.9mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.25 (br. s., 1 H) 7.10 - 7.38 (m, 5 H) 4.36 (br. s., 1 H) 3.86 - 4.15 (m, 2 H) 3.79 (dt, J=11.95, 5.95 Hz, 1 H) 3.48 - 3.73 (m, 6 H) 3.33 - 3.48 (m, 3 H) 3.13 - 3.33 (m, 4 H) 2.91 - 3.12 (m, 3 H) 2.84 (br. s., 1 H) 2.75 (dd, J=14.31, 11.00 Hz, 1 H) 2.19 - 2.48 (m, 1 H) 1.86 (dt, J=11.52, 7.99 Hz, 2 H) 1.69 - 1.80 (m, 2 H) 1.54 - 1.69 (m, 2 H) 1.32 - 1.54 (m, 5 H) 1.26 (d, J=10.51 Hz, 1 H) 1.05 - 1.19 (m, 1 H) 0.82 (s, 8 H) 0.75 - 1.05 (m, 12 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.85 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.941	14098173	1962609	100.000	100.000
Total		14098173	1962609	100.000	

2718.041 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((R)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.041 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 5.3mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 7.92 (br. s., 1 H) 7.35 (d, J=7.09 Hz, 1 H) 7.12 - 7.32 (m, 2 H) 4.14 - 4.44 (m, 1 H) 3.88 - 4.14 (m, 1 H) 3.56 - 3.86 (m, 6 H) 3.38 - 3.56 (m, 5 H) 3.13 - 3.38 (m, 5 H) 2.83 - 3.13 (m, 3 H) 2.75 (dd, J=14.00, 10.45 Hz, 1 H) 2.63 (d, J=4.52 Hz, 1 H) 2.30 - 2.48 (m, 1 H) 2.23 (q, J=8.40 Hz, 1 H) 1.91 - 2.11 (m, 1 H) 1.87 (br. s., 1 H) 1.50 - 1.80 (m, 3 H) 1.33 - 1.50 (m, 3 H) 1.29 (d, J=11.25 Hz, 1 H) 1.14 - 1.24 (m, 1 H) 1.04 (d, J=6.11 Hz, 12 H) 0.97 - 1.14 (m, 1 H) 0.91 (dd, J=10.70, 6.05 Hz, 5 H) 0.82 (s, 7 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.6 (MS ESI) **Purity** LC-MS: >96% (214 nm, peak area).

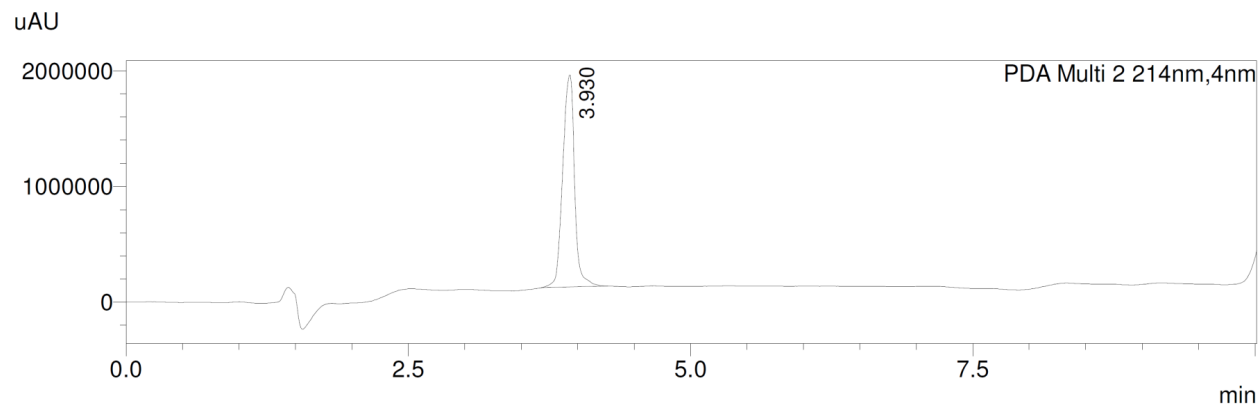
uAU



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.657	279213	71788	3.012	3.012
2	3.813	8991569	1494188	96.988	96.988
Total		9270782	1565976	100.000	

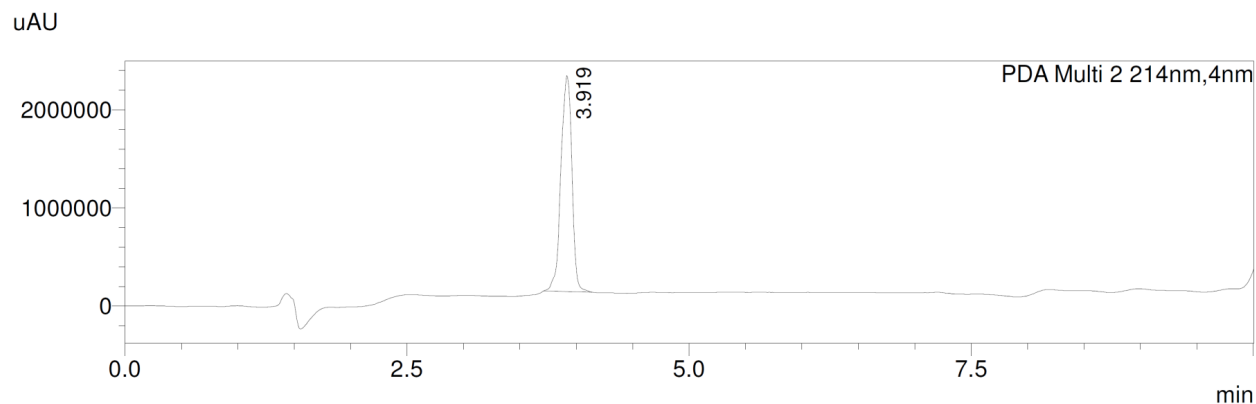
2718.042 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((S)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.042 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.4mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.15 (br. s., 1 H) 7.09 - 7.37 (m, 4 H) 4.36 (br. s., 1 H) 3.88 - 4.18 (m, 2 H) 3.73 - 3.81 (m, 2 H) 3.62 - 3.72 (m, 3 H) 3.46 - 3.60 (m, 4 H) 2.99 - 3.29 (m, 6 H) 2.77 - 2.90 (m, 1 H) 2.52 - 2.77 (m, 1 H) 2.19 - 2.48 (m, 2 H) 1.81 - 2.04 (m, 1 H) 1.69 - 1.81 (m, 2 H) 1.58 - 1.69 (m, 2 H) 1.52 (dd, J=12.47, 6.11 Hz, 1 H) 1.31 - 1.47 (m, 3 H) 1.25 (d, J=11.74 Hz, 1 H) 0.79 - 1.07 (m, 24 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.9 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.930	13397855	1833665	100.000	100.000
Total		13397855	1833665	100.000	

2718.043 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((R)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.043 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-D-Phenylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.6mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.44 (br. s., 1 H) 7.10 - 7.40 (m, 5 H) 4.35 - 4.51 (m, 1 H) 3.81 - 4.10 (m, 2 H) 3.73 (dd, J=10.64, 5.26 Hz, 1 H) 3.46 - 3.69 (m, 7 H) 3.27 - 3.46 (m, 4 H) 2.98 - 3.27 (m, 5 H) 2.71 - 2.95 (m, 3 H) 2.61 (d, J=6.36 Hz, 1 H) 2.45 (d, J=8.68 Hz, 1 H) 2.06 (d, J=7.70 Hz, 1 H) 1.66 - 1.93 (m, 3 H) 1.38 - 1.60 (m, 6 H) 1.30 - 1.36 (m, 1 H) 1.00 - 1.17 (m, 2 H) 0.82 (s, 8 H) 0.75 - 0.99 (m, 7 H) 0.45 - 0.75 (m, 3 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.85 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

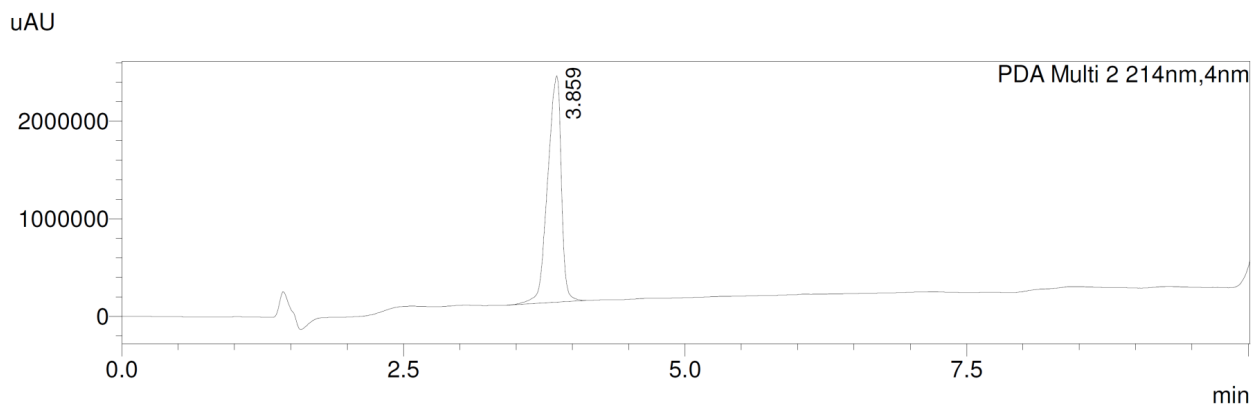


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.919	14916863	2203116	100.000	100.000
Total		14916863	2203116	100.000	

2718.044 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((S)-1-((R)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-phenylpropan-2-

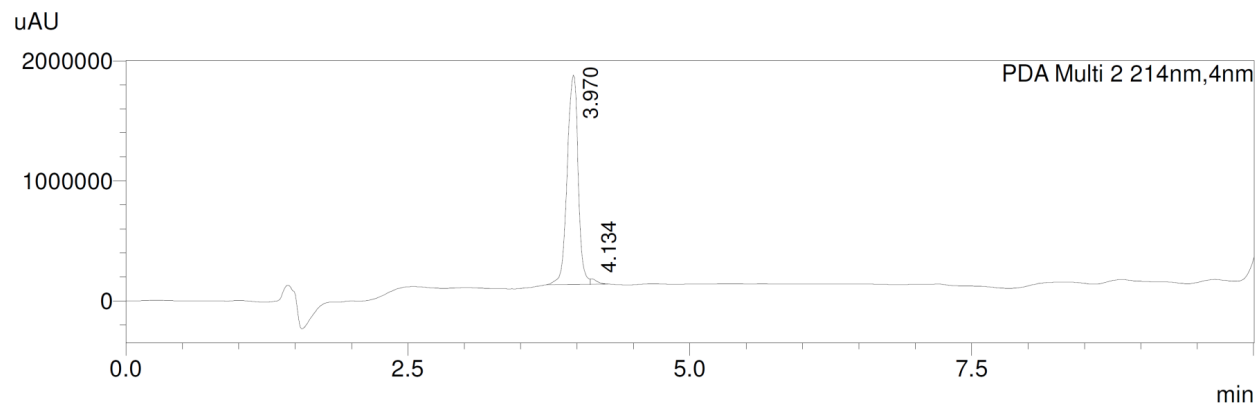
yl)imidazolidin-4-yl)ethanol. Compound 2718.044 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-L-Phenylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.2mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.54 (br. s., 1 H) 8.41 (br. s., 2 H) 8.21 (br. s., 1 H) 7.13 - 7.39 (m, 4 H) 4.15 - 4.45 (m, 4 H) 3.89 (dd, J=9.96, 5.81 Hz, 2 H) 3.48 - 3.77 (m, 4 H) 3.40 (dd, J=10.09, 4.34 Hz, 1 H) 3.14 - 3.35 (m, 3 H) 2.99 - 3.14 (m, 3 H) 2.92 (dd, J=14.37, 5.93 Hz, 1 H) 2.81 (dd, J=14.18, 9.05 Hz, 1 H) 2.61 - 2.74 (m, 1 H) 2.05 - 2.31 (m, 2 H) 1.75 - 1.90 (m, 1 H) 1.33 - 1.62 (m, 9 H) 1.00 - 1.25 (m, 2 H) 0.86 - 1.00 (m, 6 H) 0.82 (s, 8 H) 0.78 (d, J=6.36 Hz, 3 H) **m/z** calcd C₃₇H₆₃N₇O [M+H]⁺ 622.5, found 622.4 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.859	19583202	2324147	100.000	100.000
Total		19583202	2324147	100.000	

2718.045 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-

iminoimidazolidin-4-yl)ethanol. Compound 2718.045 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.2mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.22 (br. s., 1 H) 3.99 (dd, J=8.99, 4.58 Hz, 2 H) 3.82 - 3.94 (m, 2 H) 3.58 - 3.82 (m, 2 H) 3.42 - 3.58 (m, 4 H) 3.19 - 3.42 (m, 10 H) 3.11 - 3.18 (m, 1 H) 3.06 - 3.09 (m, 1 H) 2.93 (t, J=11.74 Hz, 1 H) 2.52 - 2.76 (m, 1 H) 2.09 - 2.28 (m, 2 H) 1.74 - 1.96 (m, 2 H) 1.55 - 1.71 (m, 8 H) 1.51 (d, J=12.35 Hz, 2 H) 1.43 - 1.46 (m, 1 H) 1.35 - 1.41 (m, 2 H) 1.18 - 1.31 (m, 2 H) 1.06 - 1.18 (m, 4 H) 0.86 - 1.06 (m, 11 H) 0.59 - 0.86 (m, 9 H) **m/z** calcd C₃₇H₆₉N₇O [M+H]⁺ 628.6, found 628.9 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).



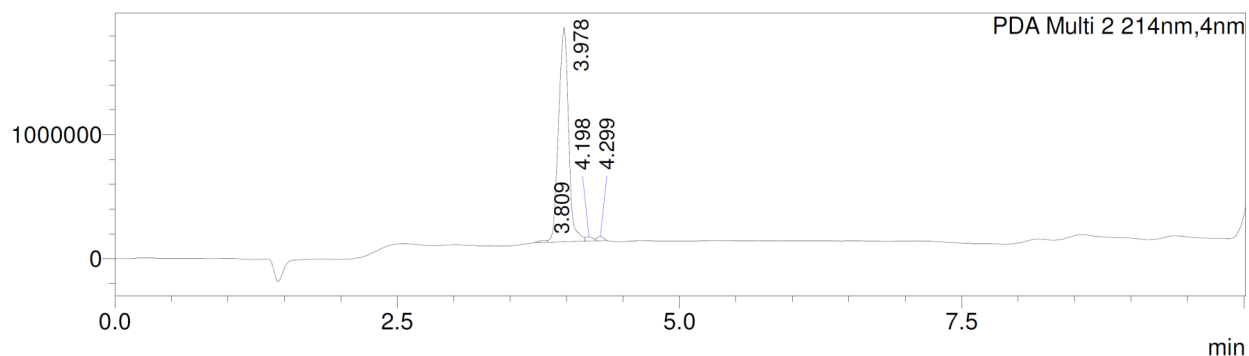
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.970	11767788	1745486	98.595	98.595
2	4.134	167655	43003	1.405	1.405
Total		11935443	1788490	100.000	

2718.046 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((S)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-

iminoimidazolidin-4-yl)ethanol. Compound 2718.046 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-L-Cyclohexylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.4mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.37 (br. s., 1 H) 8.41 (br. s., 1 H) 3.81 - 4.10 (m, 5 H) 3.55 - 3.81 (m, 5 H) 3.48 (dd, J=14.73, 7.89 Hz, 1 H) 3.29 - 3.42 (m, 2 H) 3.05 - 3.29 (m, 3 H) 2.87 - 3.05 (m, 1 H) 2.66 - 2.87 (m, 2 H) 2.23 - 2.48 (m, 2 H) 2.11 (br. s., 1 H) 1.76 - 1.97 (m, 2 H) 1.64 - 1.76 (m, 5 H) 1.35 - 1.64 (m, 11 H) 1.05 - 1.21 (m, 5 H) 0.86 - 1.04 (m, 11 H) 0.57 - 0.86 (m, 10 H) **m/z** calcd C₃₇H₆₉N₇O [M+H]⁺ 628.6, found 629.0 (MS ESI) **Purity** LC-MS: >96% (214 nm, peak area).

uAU

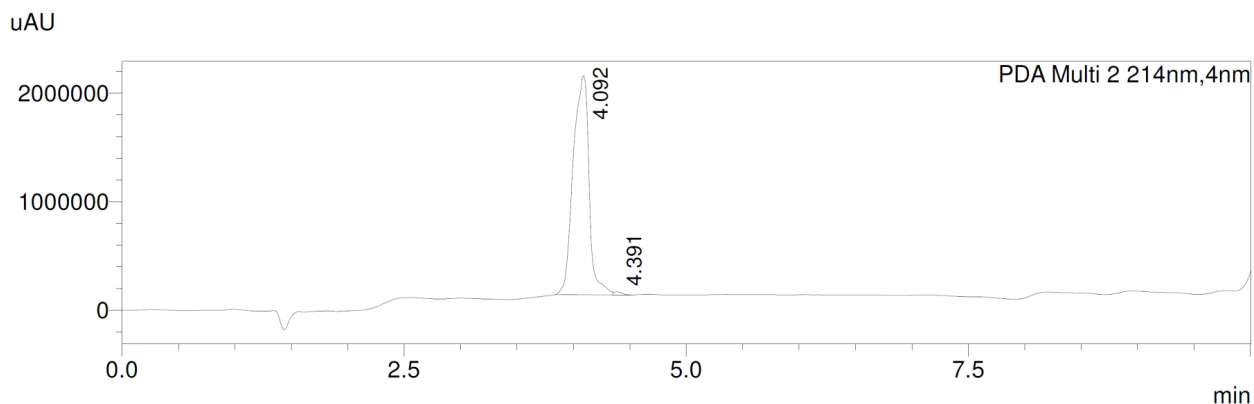


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.809	82922	14876	0.753	0.753
2	3.978	10635030	1731798	96.553	96.553
3	4.198	162543	36484	1.476	1.476
4	4.299	134202	35791	1.218	1.218
Total		11014696	1818950	100.000	

2718.047 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((R)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-

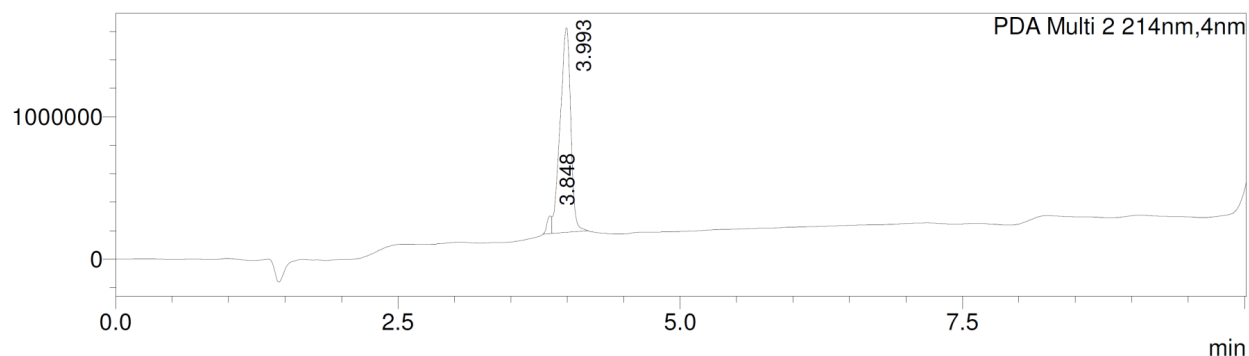
iminoimidazolidin-4-yl)ethanol. Compound 2718.047 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.5mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.29 (br. s., 1 H) 3.86 - 3.99 (m, 2 H) 3.58 - 3.86 (m, 4 H) 3.32 - 3.58 (m, 13 H) 3.05 - 3.32 (m, 6 H) 2.81 - 3.05 (m, 2 H) 2.63 - 2.81 (m, 1 H) 2.22 - 2.48 (m, 2 H) 2.16 (br. s., 1 H) 1.78 - 2.03 (m, 2 H) 1.64 - 1.72 (m, 3 H) 1.56 - 1.63 (m, 4 H) 1.43 - 1.53 (m, 4 H) 1.40 (d, J=6.36 Hz, 1 H) 0.88 - 1.18 (m, 14 H) 0.75 - 0.87 (m, 8 H) **m/z** calcd C₃₇H₆₉N₇O [M+H]⁺ 628.6, found 628. (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.092	19744725	2017931	99.340	0.000
2	4.391	131174	27216	0.660	0.000
Total		19875898	2045147	100.000	

2718.048 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-iminoimidazolidin-4-yl)ethanol. Compound 2718.048 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.2mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.28 (br. s., 1 H) 4.03 (t, J=9.84 Hz, 1 H) 3.73 - 3.96 (m, 4 H) 3.68 (t, J=9.23 Hz, 1 H) 3.42 - 3.62 (m, 5 H) 3.36 (dd, J=10.09, 3.85 Hz, 5 H) 3.09 - 3.29 (m, 4 H) 2.97 - 3.09 (m, 1 H) 2.90 (dd, J=14.92, 8.44 Hz, 1 H) 2.52 - 2.78 (m, 1 H) 2.09 - 2.30 (m, 3 H) 1.78 - 2.04 (m, 2 H) 1.42 - 1.72 (m, 13 H) 1.39 (d, J=9.29 Hz, 1 H) 1.02 - 1.21 (m, 7 H) 0.84 (s, 8 H) 0.81 - 1.01 (m, 8 H) **m/z** calcd C₃₇H₆₉N₇O [M+H]⁺ 628.6, found 628.9 (MS ESI) **Purity** LC-MS: >96% (214 nm, peak area).

uAU



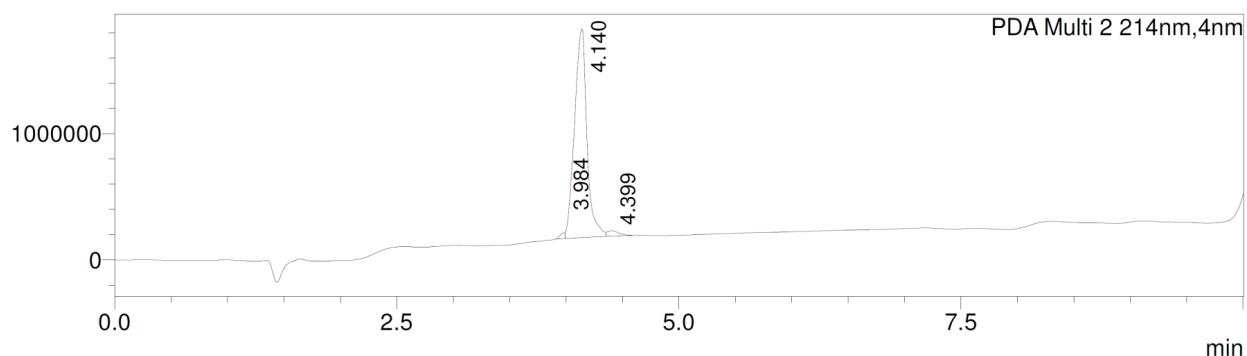
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.848	372759	124950	3.844	3.844
2	3.993	9325539	1438128	96.156	96.156
Total		9698297	1563078	100.000	

2718.049 (R)-1-((R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((S)-1-cyclohexyl-3-((R)-2-(((S)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-2-

iminoimidazolidin-4-yl)ethanol. Compound 2718.049 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Leucine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-L-Cyclohexylalanine-OH (R₃), Boc-L-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.3mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.25 (br. s., 1 H) 3.73 - 4.03 (m, 4 H) 3.66 (t, J=9.29 Hz, 1 H) 3.43 - 3.59 (m, 3 H) 3.37 (br. s., 7 H) 3.09 - 3.34 (m, 7 H) 2.97 - 3.09 (m, 1 H) 2.81 - 2.97 (m, 1 H) 2.67 - 2.81 (m, 1 H) 2.20 - 2.35 (m, 1 H) 2.18 (br. s., 1 H) 1.75 - 1.96 (m, 2 H) 1.63 - 1.75 (m, 4 H) 1.59 (d, J=5.62 Hz, 4 H) 1.31 - 1.54 (m, 6 H) 1.18 - 1.31 (m, 2 H) 1.12 (d, J=7.21 Hz, 3 H) 0.87 - 1.09 (m, 11 H) 0.67 - 0.87 (m, 8 H) **m/z** calcd C₃₇H₆₉N₇O [M+H]⁺ 628.6, found 628.65 (MS ESI) **Purity** LC-MS: >96% (214 nm, peak area).

uAU



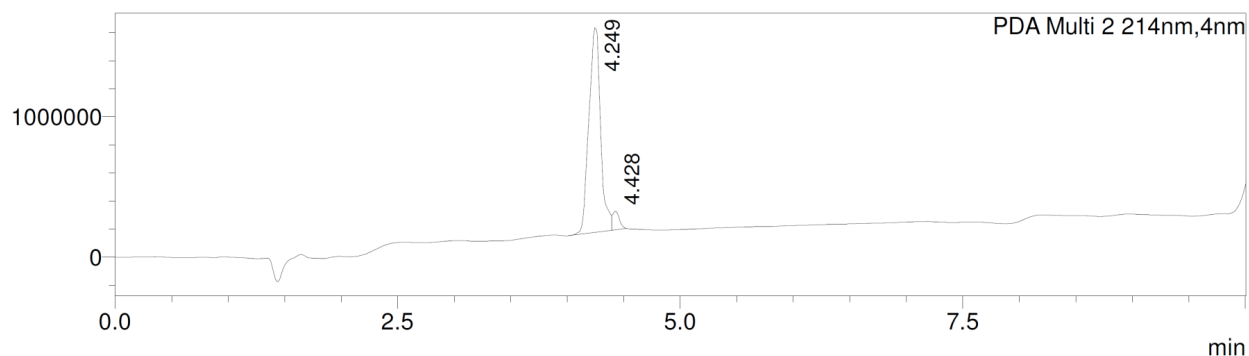
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.984	132509	42573	1.014	1.014
2	4.140	12636104	1653554	96.678	96.678
3	4.399	301750	43107	2.309	2.309
Total		13070364	1739233	100.000	

2718.050 (S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-

propylimidazolidin-2-imine. Compound 2718.050 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-L-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.9mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 10.38 (br. s., 1 H) 8.28 (br. s., 1 H) 3.97 - 4.14 (m, 1 H) 3.84 - 3.97 (m, 2 H) 3.62 - 3.84 (m, 2 H) 3.32 - 3.62 (m, 7 H) 3.21 - 3.31 (m, 2 H) 3.05 - 3.20 (m, 2 H) 2.99 (dd, J=14.67, 5.99 Hz, 1 H) 2.63 - 2.92 (m, 2 H) 2.15 - 2.36 (m, 2 H) 2.09 (dt, J=6.91, 3.39 Hz, 1 H) 1.73 - 1.94 (m, 2 H) 1.57 - 1.73 (m, 8 H) 1.32 - 1.54 (m, 6 H) 1.23 - 1.31 (m, 3 H) 1.09 - 1.21 (m, 5 H) 0.84 (s, 7 H) 0.73 - 1.02 (m, 13 H) **m/z** calcd C₃₇H₆₉N₇ [M+H]⁺ 612.6, found 612.65 (MS ESI) **Purity** LC-MS: >95% (214 nm, peak area).

uAU



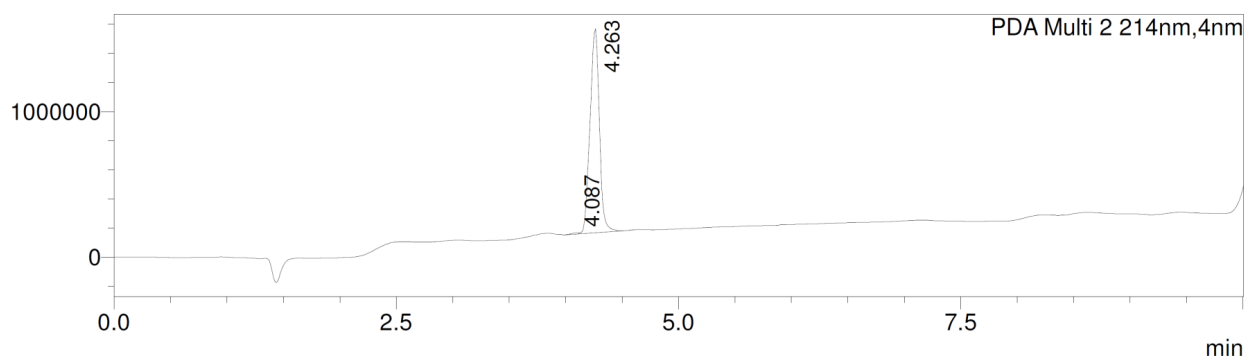
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.249	10513682	1459516	95.213	95.213
2	4.428	528618	132762	4.787	4.787
Total		11042300	1592278	100.000	

2718.051 (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((S)-1-cyclohexyl-3-((S)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-

propylimidazolidin-2-imine. Compound 2718.051 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-L-Cyclohexylalanine-OH (R₃), Boc-D-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.6mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.39 (br. s., 1 H) 3.79 - 4.08 (m, 3 H) 3.56 - 3.79 (m, 2 H) 3.42 - 3.56 (m, 3 H) 3.30 - 3.42 (m, 12 H) 3.25 (dd, J=10.09, 4.34 Hz, 2 H) 2.94 - 3.17 (m, 3 H) 2.85 - 2.92 (m, 1 H) 2.67 - 2.80 (m, 1 H) 2.32 - 2.48 (m, 2 H) 2.13 (td, J=6.72, 3.67 Hz, 1 H) 2.03 (br. s., 1 H) 1.77 - 1.90 (m, 2 H) 1.58 - 1.75 (m, 6 H) 1.33 - 1.54 (m, 7 H) 1.27 (dd, J=15.04, 7.46 Hz, 1 H) 1.03 - 1.21 (m, 5 H) 0.84 (s, 8 H) 0.81 - 1.03 (m, 6 H) 0.77 (d, J=6.72 Hz, 3 H) **m/z** calcd C₃₇H₆₉N₇ [M+H]⁺ 612.6, found 613.0 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU



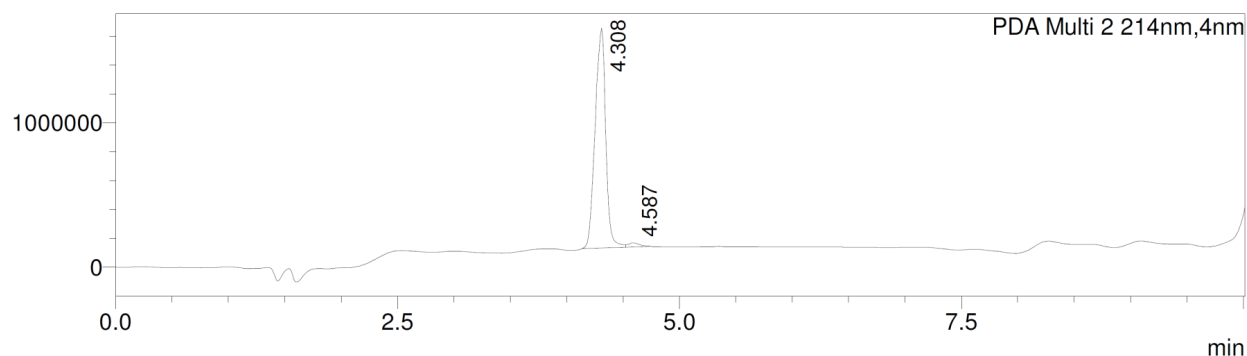
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.087	35387	7045	0.438	0.438
2	4.263	8038237	1403566	99.562	99.562
Total		8073624	1410610	100.000	

2718.052 (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((R)-2-(((R)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-

propylimidazolidin-2-imine. Compound 2718.052 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Valine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.5mg, ¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.42 (br. s., 1 H) 4.04 (dt, J=9.26, 4.72 Hz, 1 H) 3.96 (br. s., 1 H) 3.67 - 3.92 (m, 2 H) 3.31 - 3.61 (m, 11 H) 3.16 - 3.31 (m, 2 H) 2.93 - 3.16 (m, 3 H) 2.65 - 2.93 (m, 2 H) 2.22 - 2.40 (m, 2 H) 2.15 (td, J=6.60, 3.79 Hz, 1 H) 2.07 (br. s., 1 H) 1.78 - 1.95 (m, 2 H) 1.56 - 1.78 (m, 7 H) 1.33 - 1.56 (m, 7 H) 1.02 - 1.30 (m, 6 H) 0.72 - 1.02 (m, 19 H) **m/z** calcd C₃₇H₆₉N₇ [M+H]⁺ 612.6, found 612.65 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).

uAU

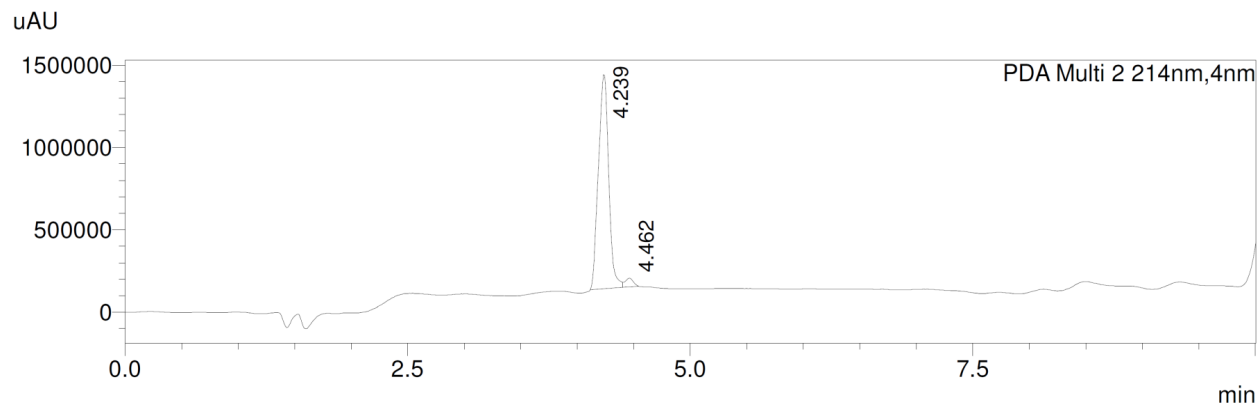


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.308	9941972	1522385	98.057	98.057
2	4.587	196973	27430	1.943	1.943
Total		10138946	1549815	100.000	

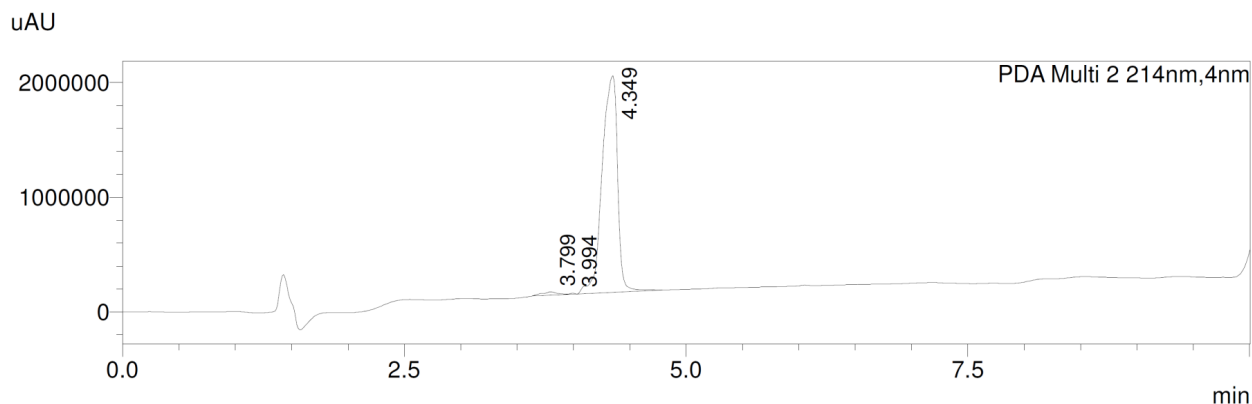
2718.053 (R)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-3-((S)-2-(((S)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-

propylimidazolidin-2-imine. Compound 2718.053 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Valine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylalanine-OH (R₃), Boc-D-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.8mg, ¹H NMR (400 MHz, DMSO-d₆) δ ppm 8.29 (br. s., 1 H) 3.97 - 4.05 (m, 1 H) 3.73 - 3.95 (m, 3 H) 3.52 - 3.60 (m, 2 H) 3.29 - 3.50 (m, 8 H) 3.04 - 3.19 (m, 2 H) 2.97 (dd, J=14.86, 5.69 Hz, 1 H) 2.59 - 2.88 (m, 2 H) 2.13 - 2.42 (m, 2 H) 2.02 - 2.13 (m, 2 H) 1.80 - 2.02 (m, 2 H) 1.57 - 1.80 (m, 8 H) 1.32 - 1.55 (m, 7 H) 1.22 - 1.30 (m, 2 H) 1.07 - 1.21 (m, 5 H) 0.80 - 1.05 (m, 17 H) 0.75 (d, J=6.85 Hz, 3 H) **m/z** calcd C₃₇H₆₉N₇ [M+H]⁺ 612.6, found 613.0 (MS ESI) **Purity** LC-MS: >96% (214 nm, peak area).



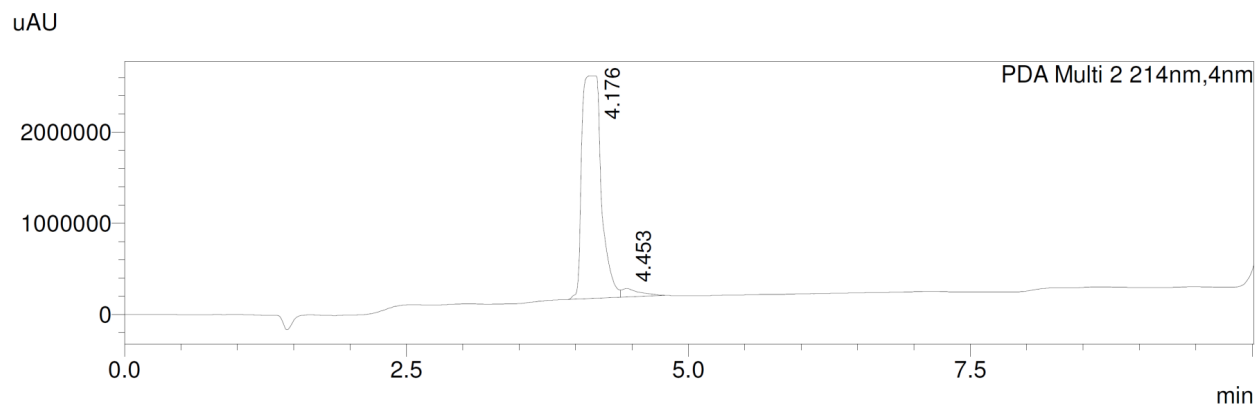
PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.239	8276647	1301200	96.949	96.949
2	4.462	260469	53744	3.051	3.051
Total		8537116	1354944	100.000	

2718.054 (S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((S)-1-cyclohexyl-3-((R)-2-(((S)-2-imino-5-isopropylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)-4-propylimidazolidin-2-imine. Compound 2718.054 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-L-Valine-OH (R₁), Boc-D-Proline-OH (R₂), Boc-L-Cyclohexylalanine-OH (R₃), Boc-L-Norvaline-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 7.0mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.31 (br. s., 1 H) 3.86 - 4.07 (m, 2 H) 3.79 (dd, J=14.86, 10.94 Hz, 2 H) 3.42 - 3.69 (m, 5 H) 3.38 (br. s., 11 H) 3.09 - 3.34 (m, 5 H) 2.81 - 3.07 (m, 3 H) 2.11 - 2.35 (m, 2 H) 2.08 (br. s., 1 H) 1.64 - 1.92 (m, 5 H) 1.61 (br. s., 2 H) 1.34 - 1.56 (m, 6 H) 1.05 - 1.32 (m, 6 H) 0.84 (s, 7 H) 0.80 - 1.05 (m, 6 H) 0.74 (d, J=6.72 Hz, 2 H) **m/z** calcd C₃₇H₆₉N₇ [M+H]⁺ 612.6, found 612.95 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).



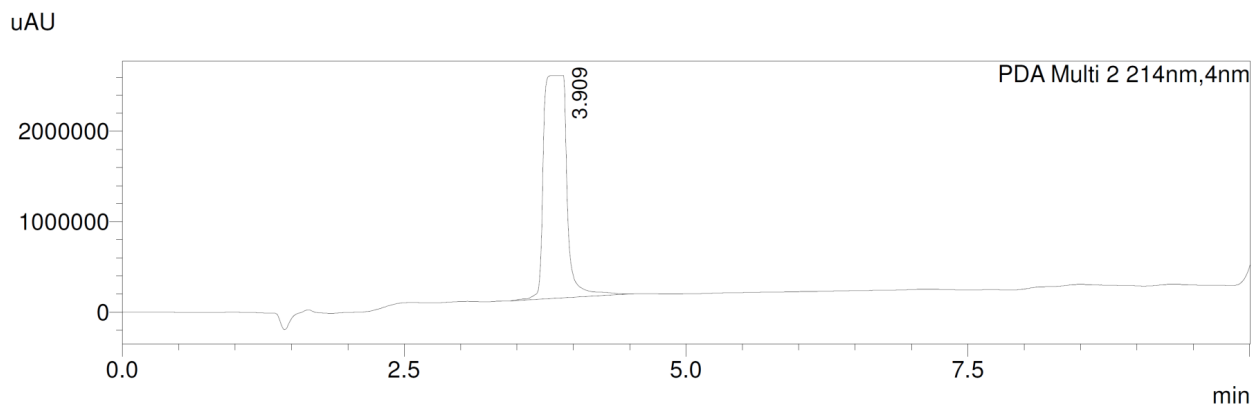
PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.799	261366	28444	1.435	1.435
2	3.994	27753	9816	0.152	0.152
3	4.349	17927279	1889802	98.413	98.413
Total		18216398	1928063	100.000	

2718.055 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-(naphthalen-2-yl)propan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.055 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-2-Naphthylalanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.8mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 7.99 (br. s., 1 H) 7.71 - 7.93 (m, 4 H) 7.52 - 7.63 (m, 1 H) 7.21 - 7.50 (m, 2 H) 4.43 - 4.59 (m, 1 H) 3.79 - 4.04 (m, 2 H) 3.50 - 3.79 (m, 5 H) 3.28 - 3.50 (m, 6 H) 3.02 - 3.28 (m, 5 H) 2.85 - 3.02 (m, 2 H) 2.78 (dd, J=7.64, 3.73 Hz, 1 H) 2.45 (br. s., 1 H) 2.10 - 2.40 (m, 1 H) 1.77 - 1.95 (m, 1 H) 1.56 - 1.77 (m, 4 H) 1.35 - 1.56 (m, 2 H) 1.31 (d, J=11.49 Hz, 1 H) 1.21 (d, J=14.31 Hz, 1 H) 0.87 - 1.11 (m, 9 H) 0.83 (d, J=6.24 Hz, 1 H) 0.55 - 0.78 (m, 10 H) **m/z** calcd C₄₁H₆₅N₇O [M+H]⁺ 672.5, found 672.6 (MS ESI) **Purity** LC-MS: >96% (214 nm, peak area).



PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	4.176	29124056	2441848	96.671	96.671
2	4.453	1002828	93208	3.329	3.329
Total		30126884	2535056	100.000	

2718.056 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)-3-(1H-indol-3-yl)propan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.056 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Tryptophan-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.4mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.08 - 8.27 (m, 1 H) 7.14 - 7.25 (m, 1 H) 6.93 - 7.13 (m, 1 H) 6.87 (t, J=7.89 Hz, 1 H) 3.89 - 3.99 (m, 1 H) 3.73 - 3.86 (m, 2 H) 3.65 (d, J=9.17 Hz, 1 H) 3.60 (d, J=5.50 Hz, 1 H) 3.28 - 3.54 (m, 8 H) 3.14 - 3.27 (m, 3 H) 2.84 - 3.14 (m, 4 H) 2.76 (br. s., 1 H) 2.45 (br. s., 1 H) 2.17 - 2.41 (m, 1 H) 2.08 (s, 1 H) 1.84 (dd, J=12.10, 8.07 Hz, 1 H) 1.63 - 1.76 (m, 2 H) 1.60 (br. s., 2 H) 1.30 - 1.56 (m, 4 H) 1.04 (d, J=6.11 Hz, 10 H) 0.99 - 1.09 (m, 1 H) 0.77 - 0.97 (m, 13 H) **m/z** calcd C₃₉H₆₄N₈O [M+H]⁺ 661.5, found 661.4 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).



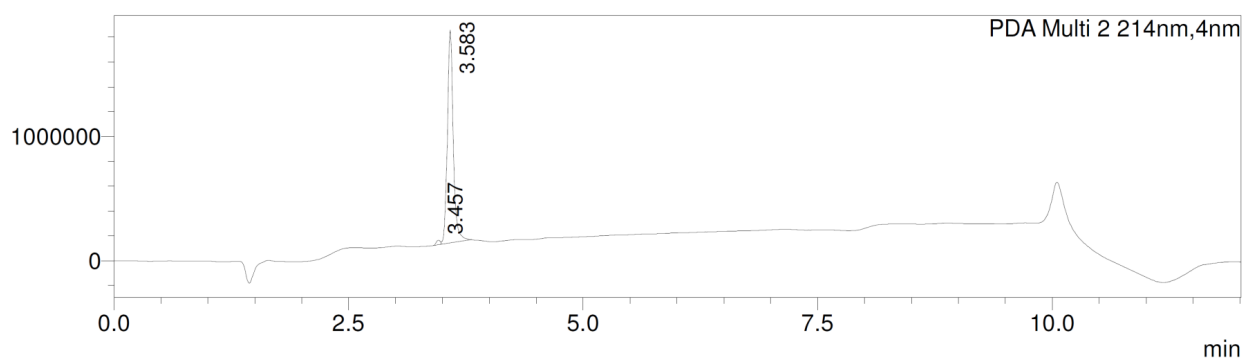
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.909	34845962	2459477	100.000	100.000
Total		34845962	2459477	100.000	

2718.057 4-((R)-2-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-4-((S)-1-hydroxyethyl)-2-iminoimidazolidin-1-yl)-3-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propyl)phenol.

Compound 2718.057 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Tyrosine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.0mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.44 (br. s., 1 H) 7.92 (br. s., 1 H) 7.08 (d, J=8.44 Hz, 1 H) 6.65 (d, J=8.44 Hz, 1 H) 4.19 (d, J=4.65 Hz, 2 H) 3.73 - 3.95 (m, 5 H) 3.46 - 3.71 (m, 5 H) 3.15 - 3.43 (m, 4 H) 3.10 (dd, J=14.73, 6.54 Hz, 1 H) 2.95 - 3.05 (m, 1 H) 2.74 (dd, J=13.69, 4.52 Hz, 1 H) 2.63 (dd, J=14.06, 9.90 Hz, 1 H) 2.36 (dd, J=12.53, 3.48 Hz, 1 H) 2.11 - 2.30 (m, 1 H) 1.74 - 1.96 (m, 1 H) 1.54 - 1.74 (m, 3 H) 1.29 - 1.54 (m, 4 H) 1.11 - 1.29 (m, 1 H) 1.04 (d, J=6.11 Hz, 19 H) 0.80 - 1.10 (m, 6 H) **m/z** calcd C₃₇H₆₃N₇O₂ [M+H]⁺ 638.5, found 638.4 (MS ESI) **Purity** LC-MS: >98% (214 nm, peak area).

uAU

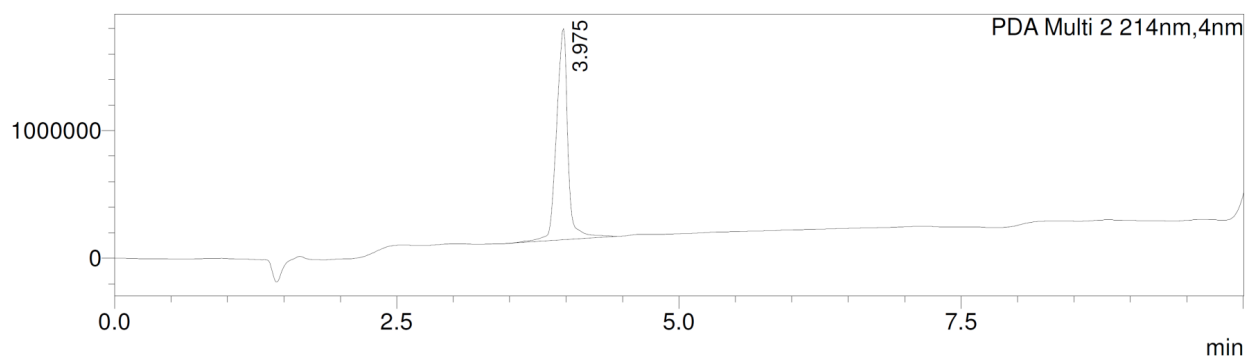


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.457	120191	35924	1.595	1.595
2	3.583	7414747	1716757	98.405	98.405
Total		7534938	1752681	100.000	

2718.059 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-1-((R)-1-cyclohexyl-2-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)ethyl)-2-iminoimidazolidin-4-yl)ethanol. Compound 2718.059 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Cyclohexylglycine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 6.5mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.25 (br. s., 1 H) 3.86 - 3.95 (m, 2 H) 3.63 - 3.81 (m, 6 H) 3.43 - 3.62 (m, 4 H) 3.13 - 3.43 (m, 6 H) 2.79 - 3.06 (m, 2 H) 2.68 (dt, J=3.76, 1.85 Hz, 1 H) 2.43 (dd, J=12.41, 3.24 Hz, 1 H) 1.96 - 2.25 (m, 2 H) 1.78 - 1.93 (m, 1 H) 1.54 - 1.78 (m, 7 H) 1.47 - 1.54 (m, 3 H) 1.28 - 1.47 (m, 4 H) 1.04 (d, J=6.11 Hz, 12 H) 1.02 - 1.21 (m, 2 H) 0.92 (dd, J=12.65, 5.93 Hz, 5 H) 0.84 (s, 6 H) **m/z** calcd C₃₆H₆₇N₇O [M+H]⁺ 614.5, found 614.65 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

uAU

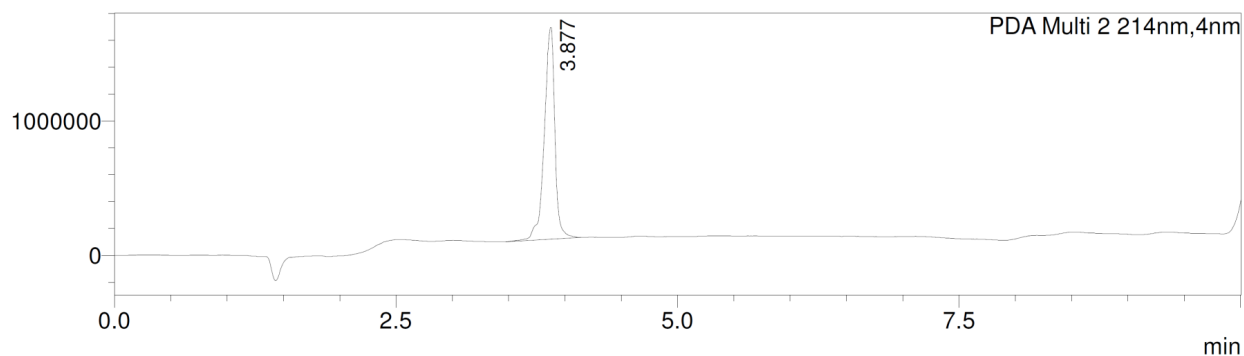


PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.975	11621561	1655802	100.000	100.000
Total		11621561	1655802	100.000	

2718.060 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)hexan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.060 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Norleucine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/27, 25/30, 27/98, 30/98. **Isolated Mass** 5.4mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.27 (br. s., 1 H) 3.84 - 4.03 (m, 3 H) 3.71 - 3.83 (m, 4 H) 3.42 - 3.70 (m, 6 H) 3.13 - 3.42 (m, 6 H) 2.81 - 3.08 (m, 2 H) 2.60 - 2.81 (m, 1 H) 2.18 - 2.38 (m, 1 H) 2.15 (br. s., 1 H) 1.76 - 1.90 (m, 1 H) 1.54 - 1.76 (m, 4 H) 1.34 - 1.54 (m, 6 H) 1.27 (td, J=14.27, 7.52 Hz, 2 H) 1.04 (d, J=6.11 Hz, 13 H) 1.02 - 1.17 (m, 1 H) 0.84 (s, 7 H) 0.81 - 1.00 (m, 6 H) **m/z** calcd C₃₄H₆₅N₇O [M+H]⁺ 588.9, found 588.9 (MS ESI) **Purity** LC-MS: >99% (214 nm, peak area).

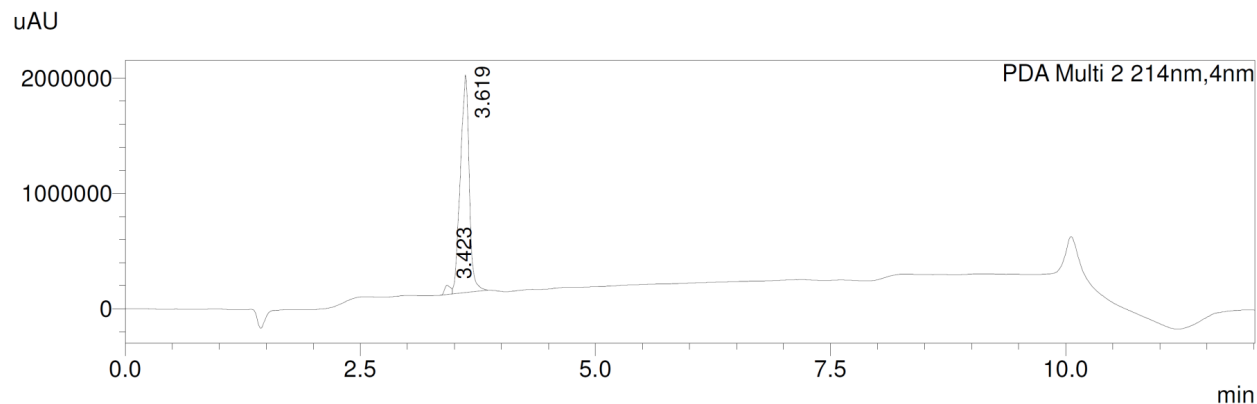
uAU



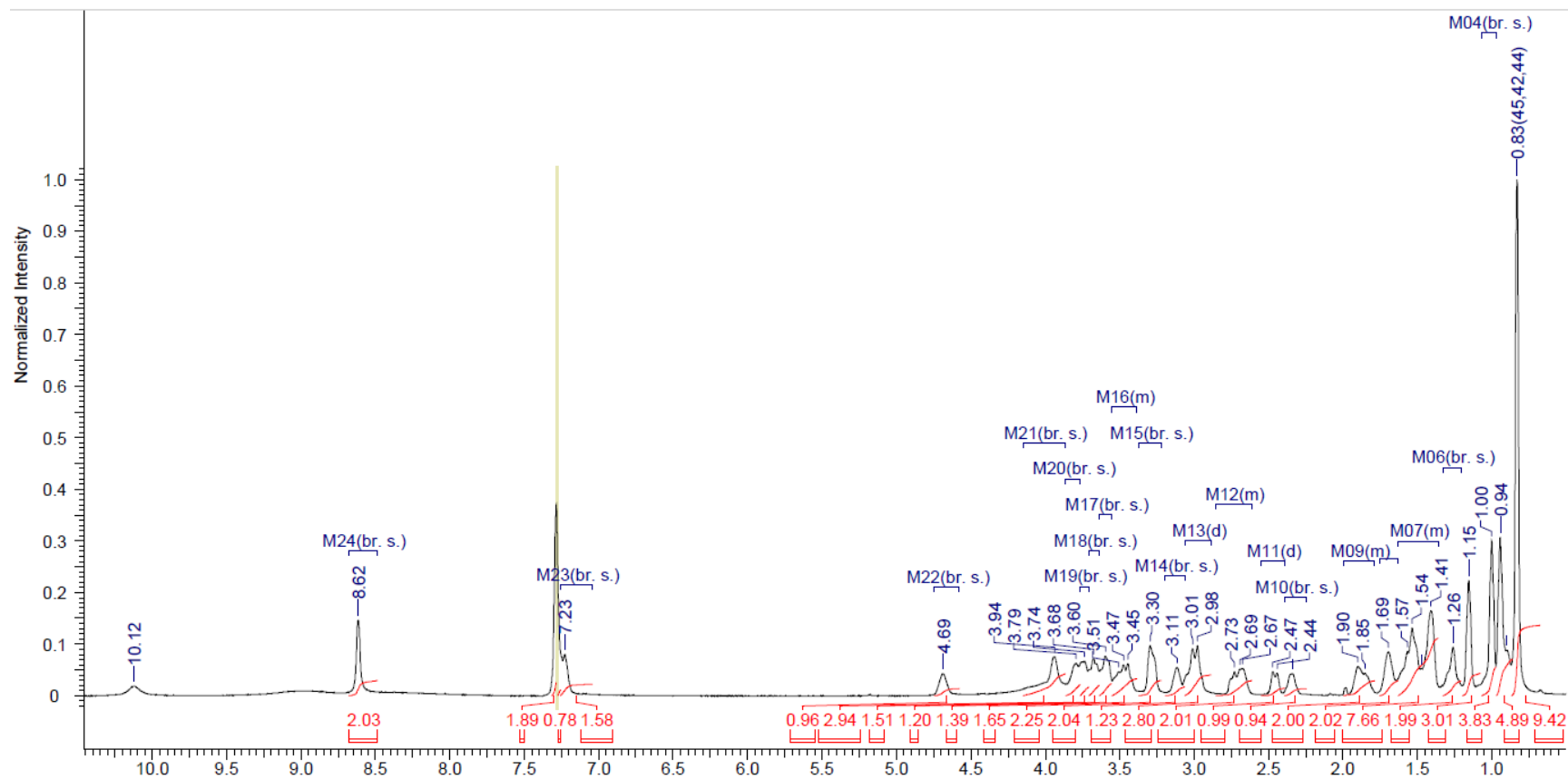
PDA Ch2 214nm

Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.877	10286842	1574625	100.000	100.000
Total		10286842	1574625	100.000	

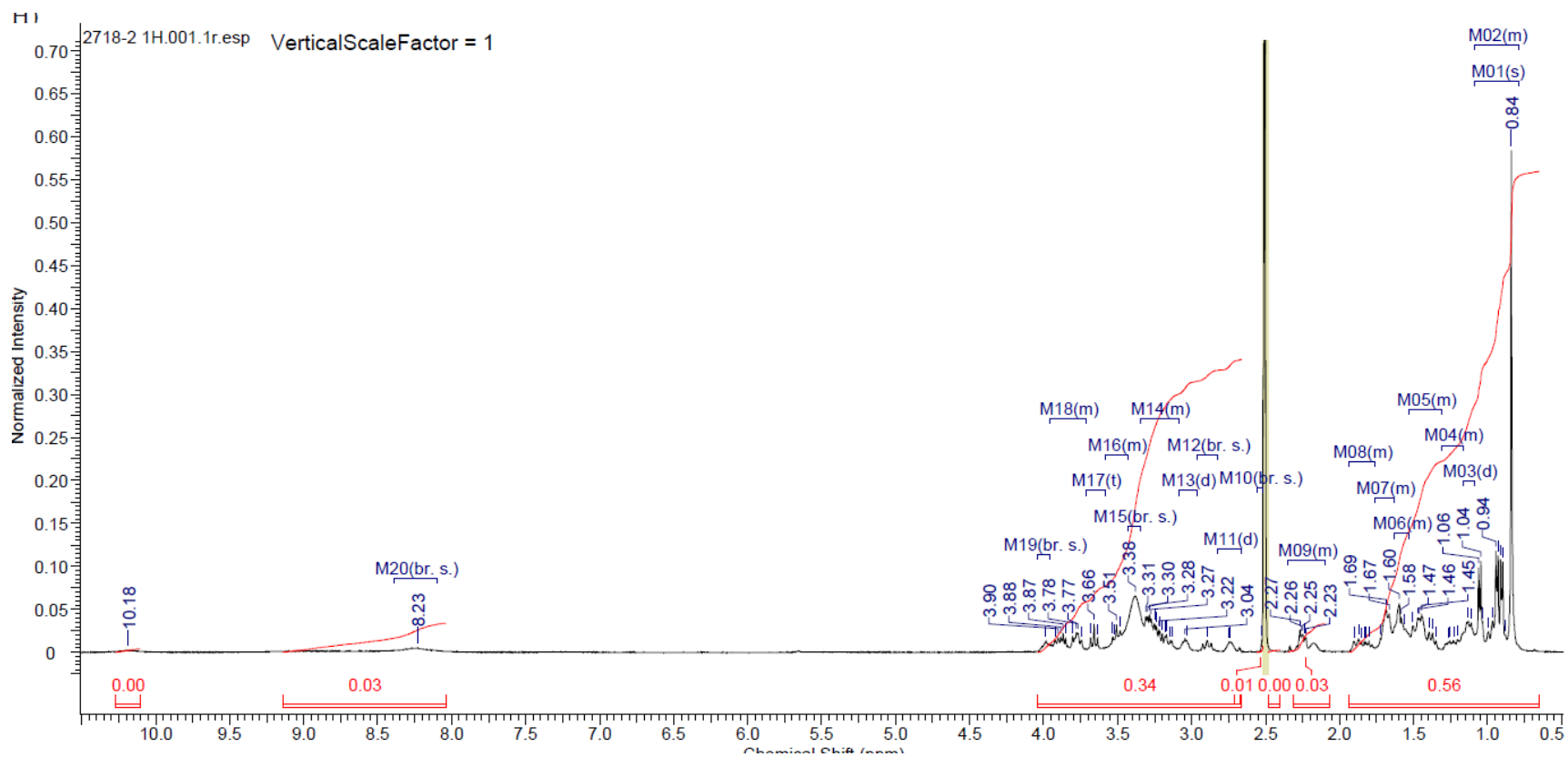
2718.061 (S)-1-((S)-3-((4-(tert-butyl)cyclohexyl)methyl)-2-imino-1-((R)-1-((S)-2-(((R)-2-imino-5-isobutylimidazolidin-1-yl)methyl)pyrrolidin-1-yl)propan-2-yl)imidazolidin-4-yl)ethanol. Compound 2718.061 was synthesized using the following reagents: (100mg) MBHA resin starting material, Boc-D-Leucine-OH (R₁), Boc-L-Proline-OH (R₂), Boc-D-Alanine-OH (R₃), Boc-D-Threonine(Bzl)-OH (R₄), and 4-tert-Butylcyclohexanecarboxylic acid (R₅). The final crude product was purified using HPLC as described above, with a gradient of (B) 0/2, 2/2, 20/26, 25/29, 27/98, 30/98. **Isolated Mass** 6.3mg, **¹H NMR** (400 MHz, DMSO-d₆) δ ppm 8.44 (br. s., 2 H) 4.02 - 4.32 (m, 1 H) 3.85 - 4.02 (m, 2 H) 3.52 - 3.81 (m, 8 H) 3.28 - 3.49 (m, 4 H) 3.12 - 3.28 (m, 3 H) 2.83 - 3.01 (m, 2 H) 2.58 - 2.83 (m, 1 H) 2.16 - 2.35 (m, 2 H) 2.04 - 2.16 (m, 1 H) 1.76 - 1.94 (m, 1 H) 1.66 - 1.73 (m, 1 H) 1.35 - 1.64 (m, 7 H) 1.04 (d, J=6.11 Hz, 13 H) 1.01 - 1.28 (m, 1 H) 0.84 (s, 6 H) 0.79 - 1.01 (m, 4 H) **m/z** calcd C₃₁H₅₉N₇O [M+H]⁺ 546.5, found 546.65 (MS ESI) **Purity** LC-MS: >97% (214 nm, peak area).

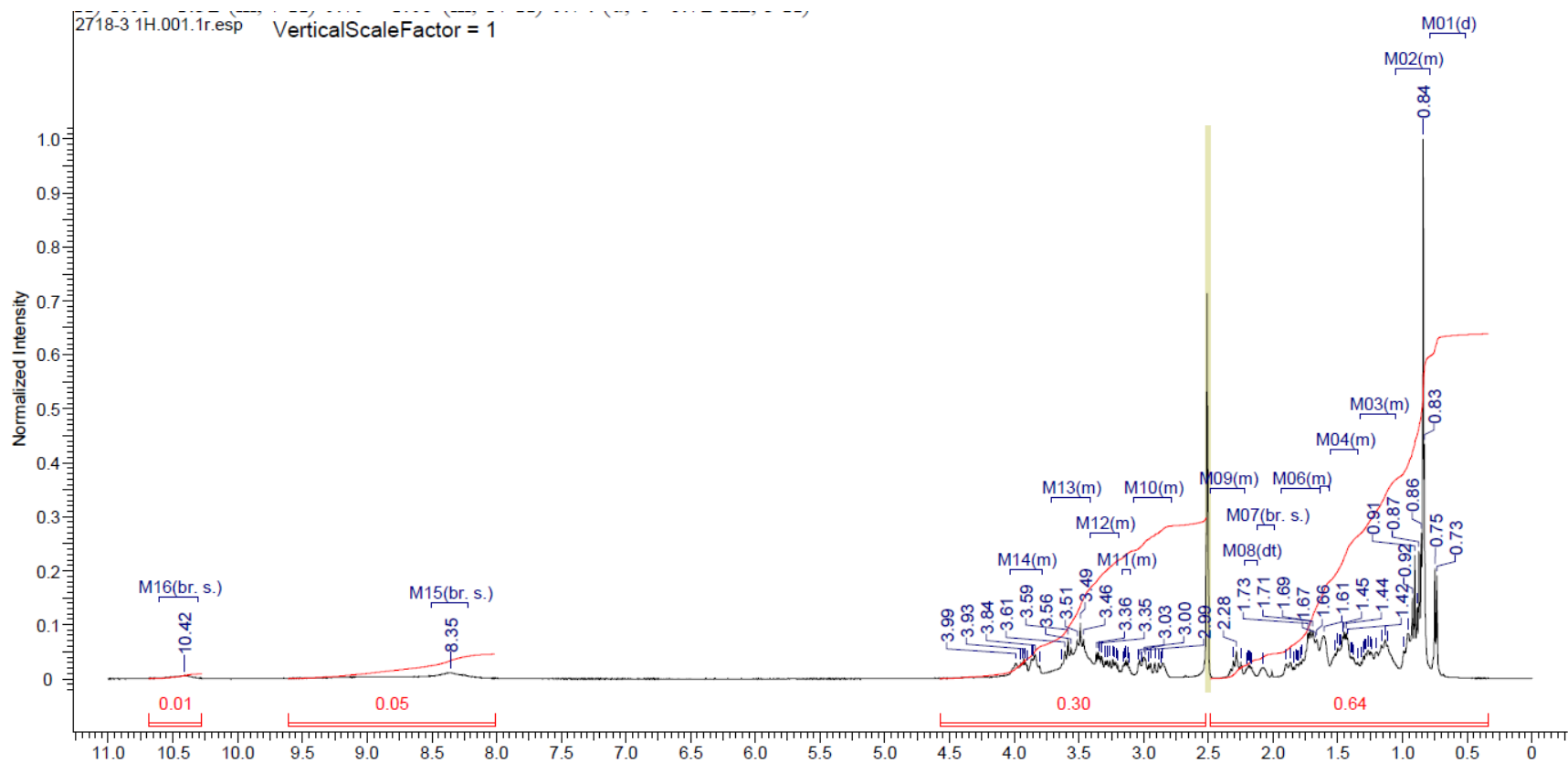


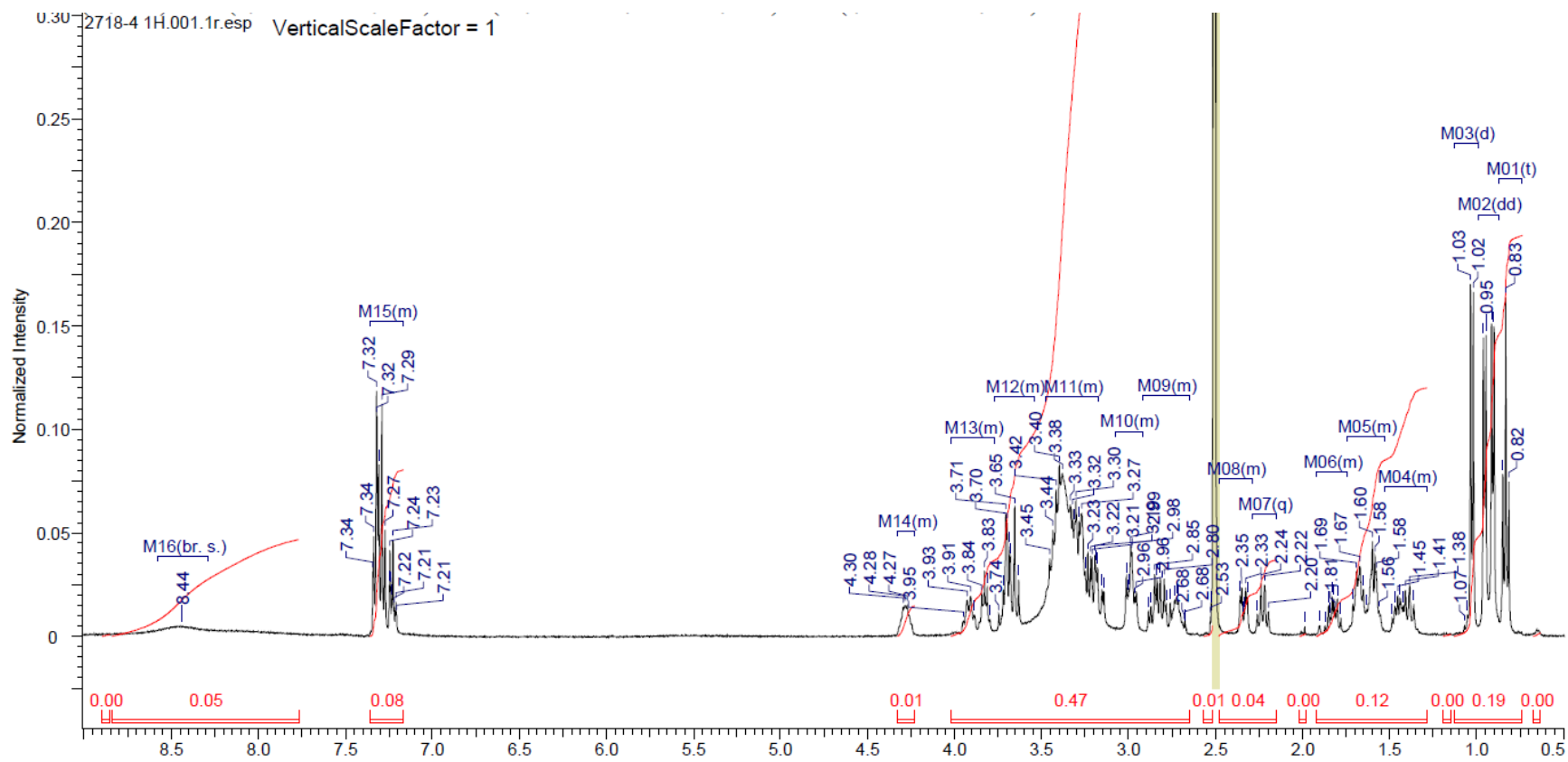
PDA Ch2 214nm					
Peak#	Ret. Time	Area	Height	Area%	Conc.
1	3.423	371550	81843	2.912	2.912
2	3.619	12389467	1889955	97.088	97.088
Total		12761017	1971798	100.000	

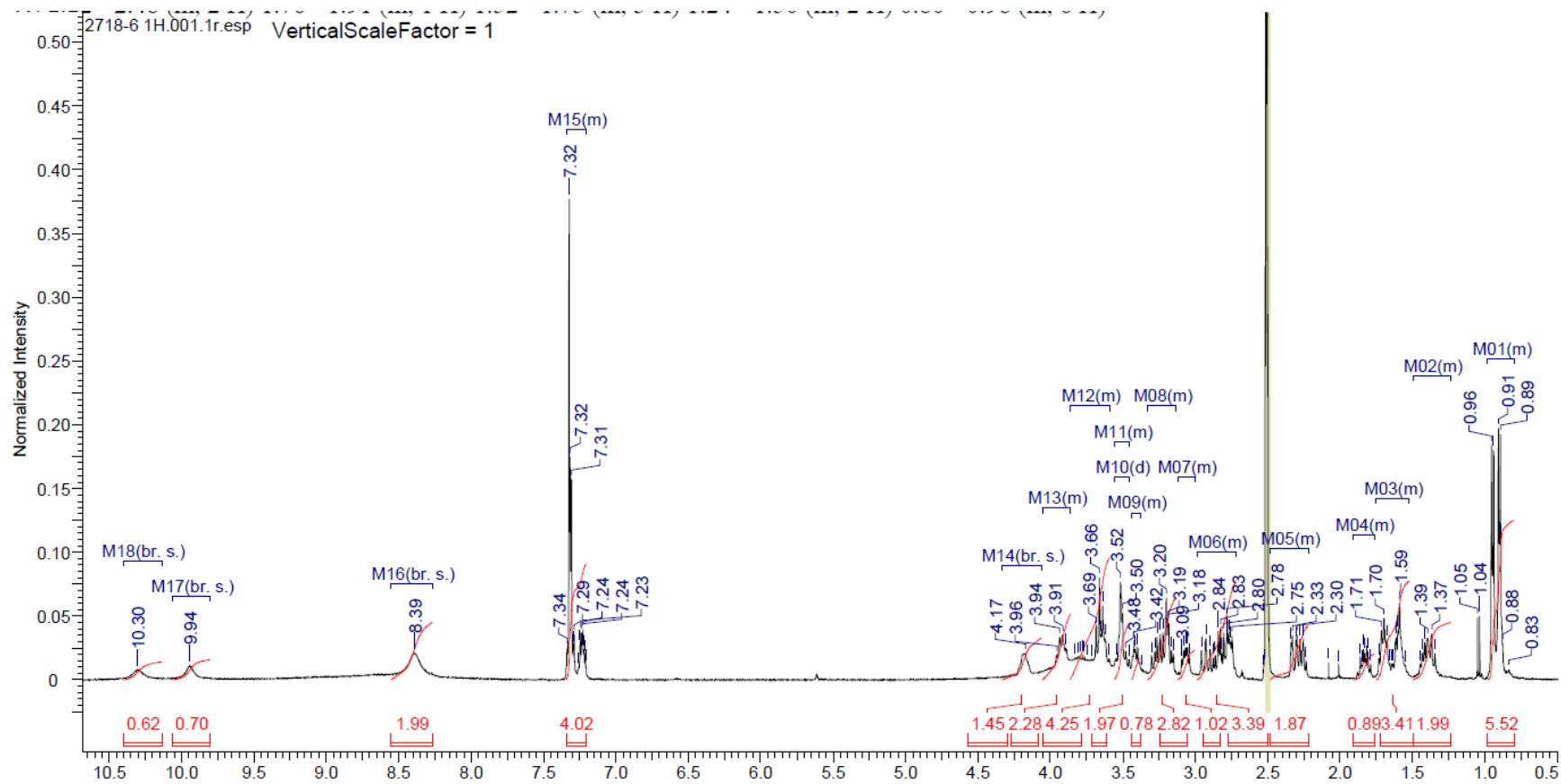


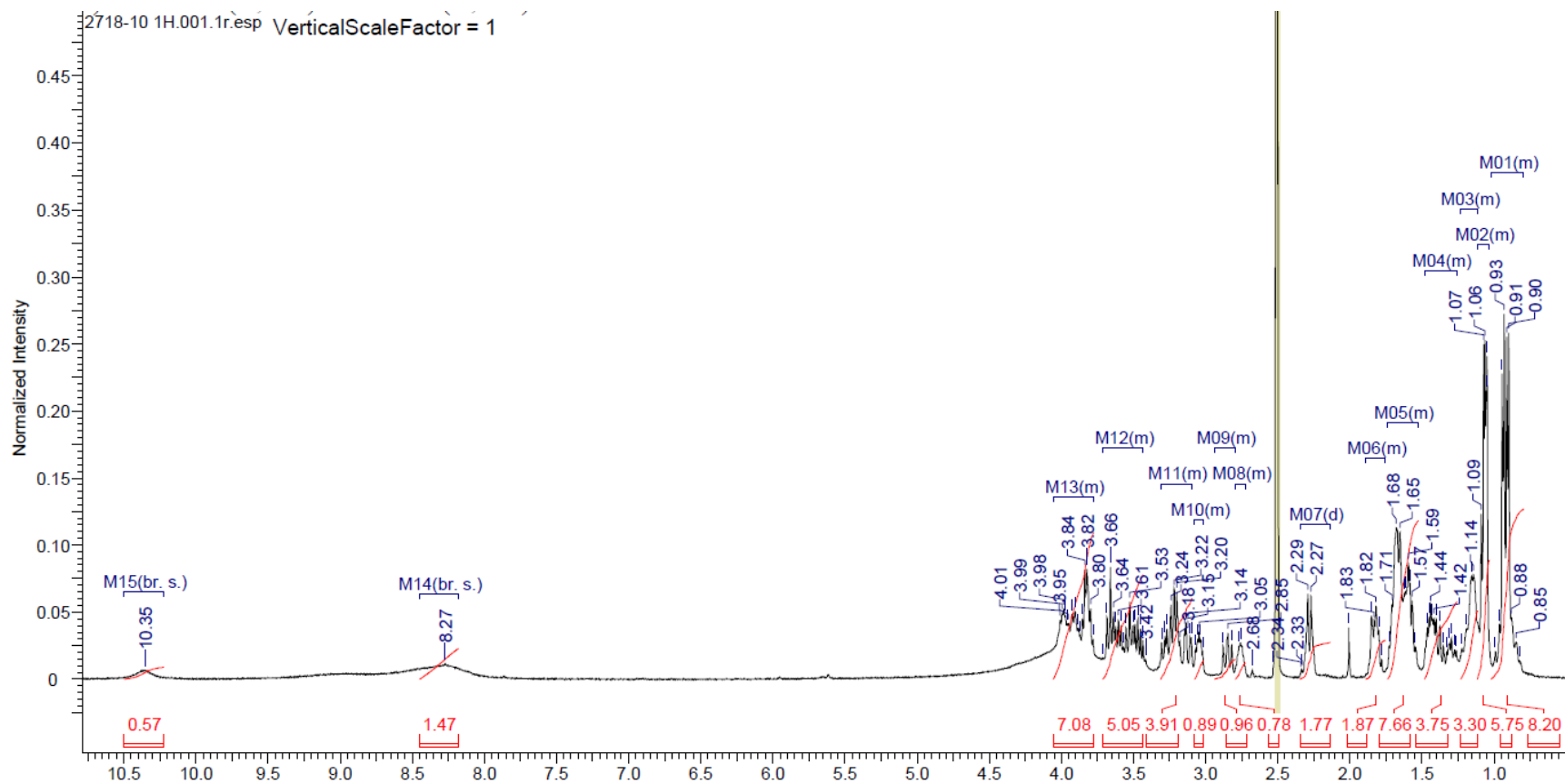
2718.001

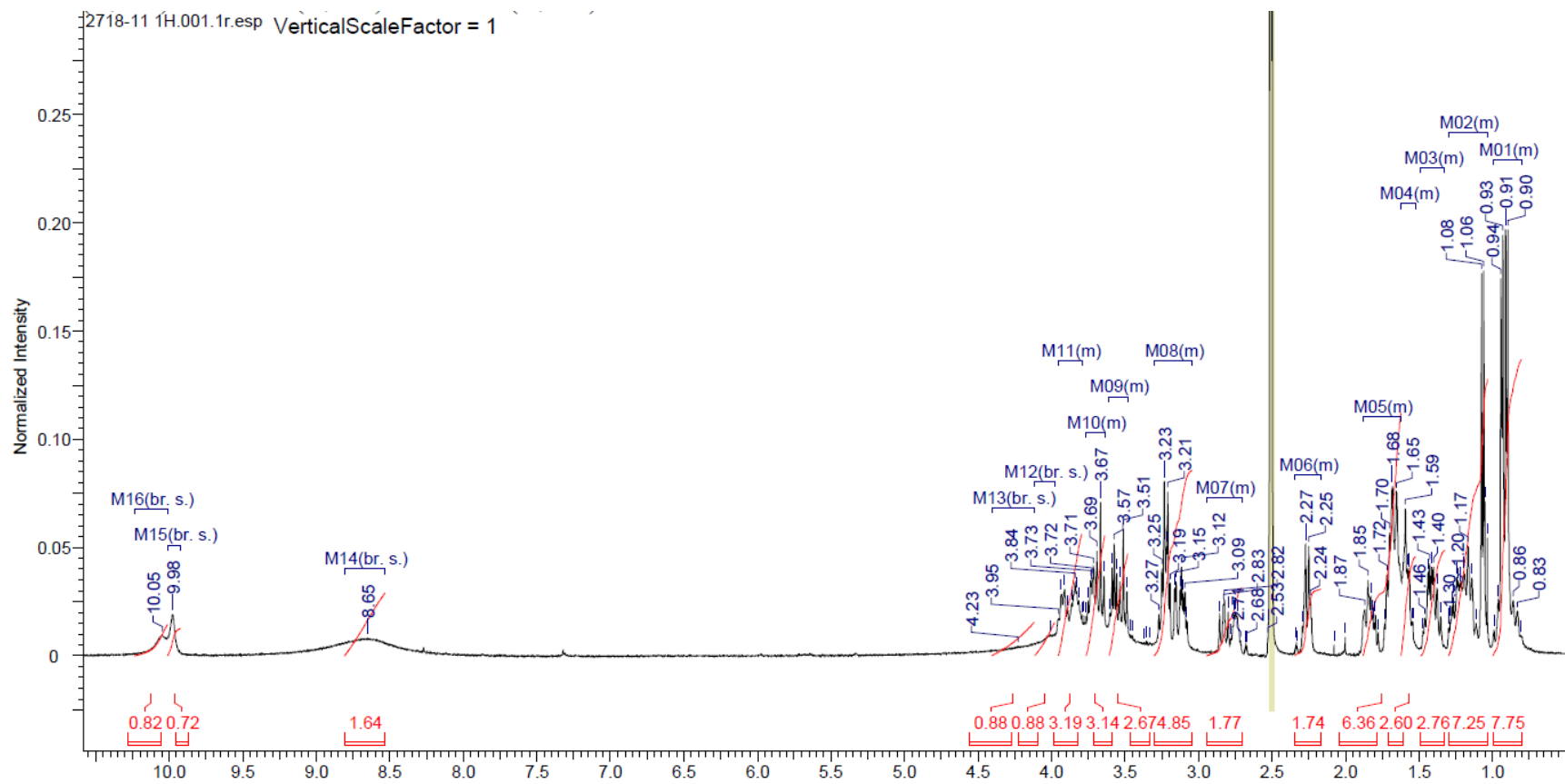


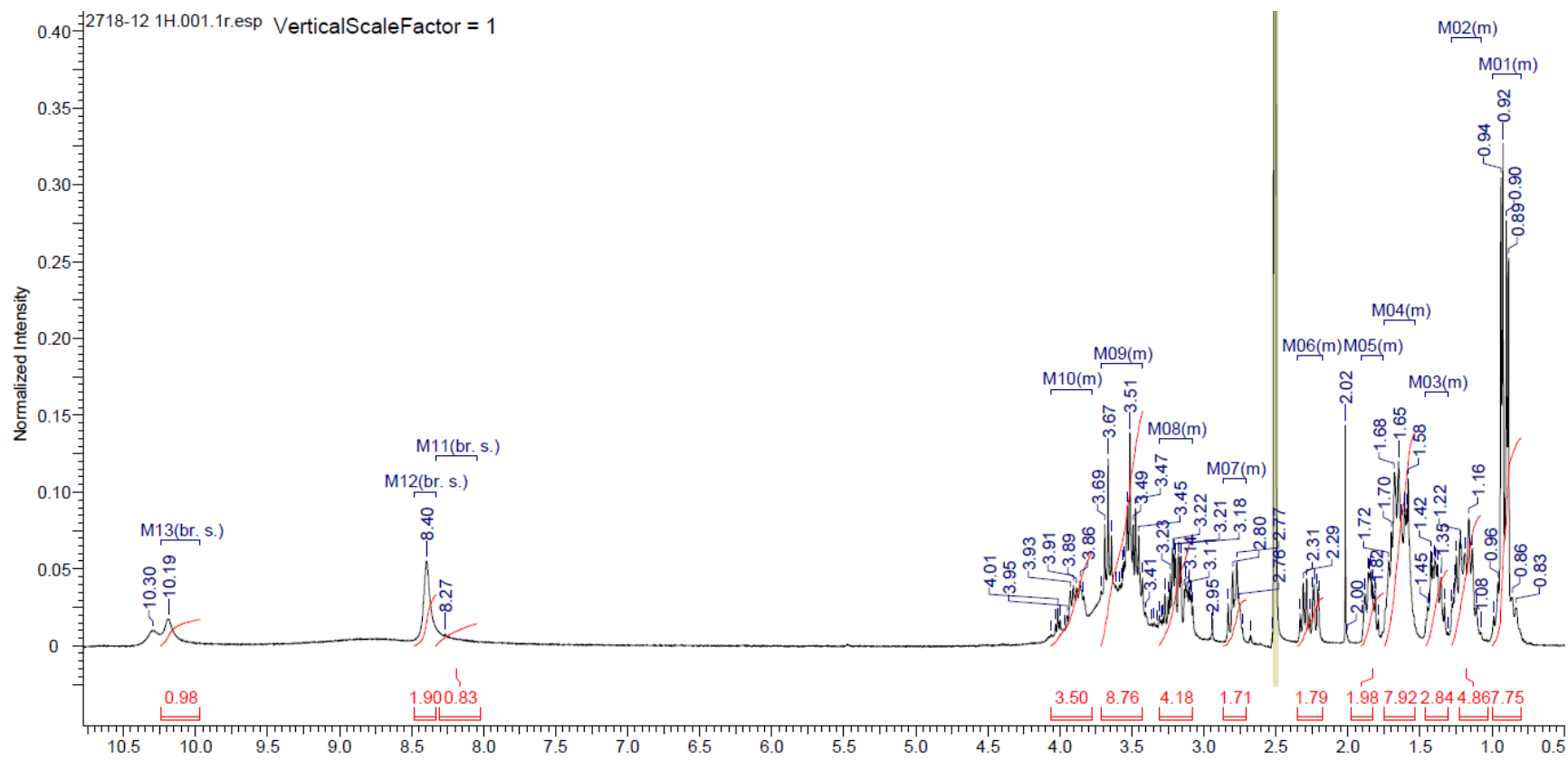


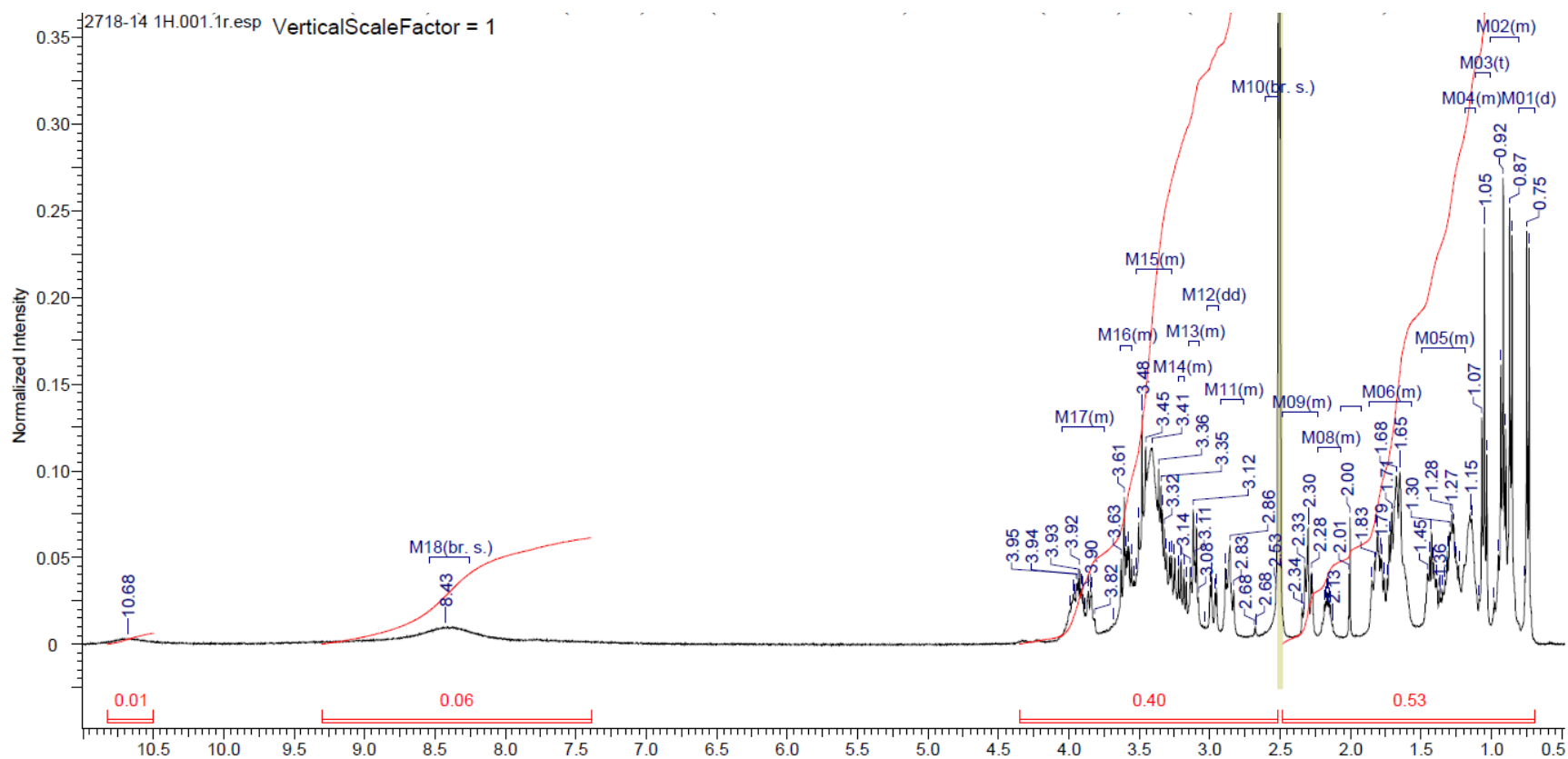


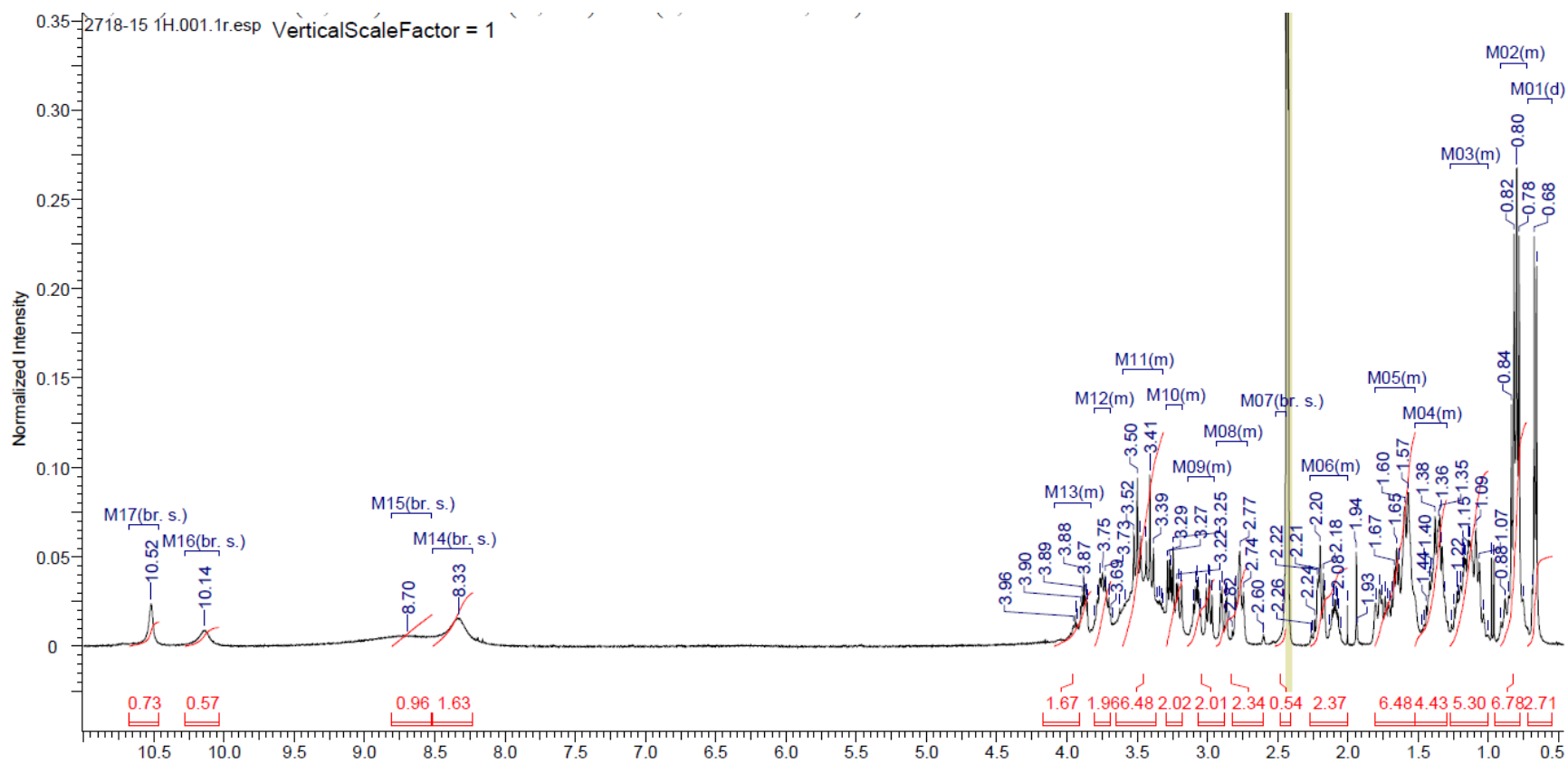


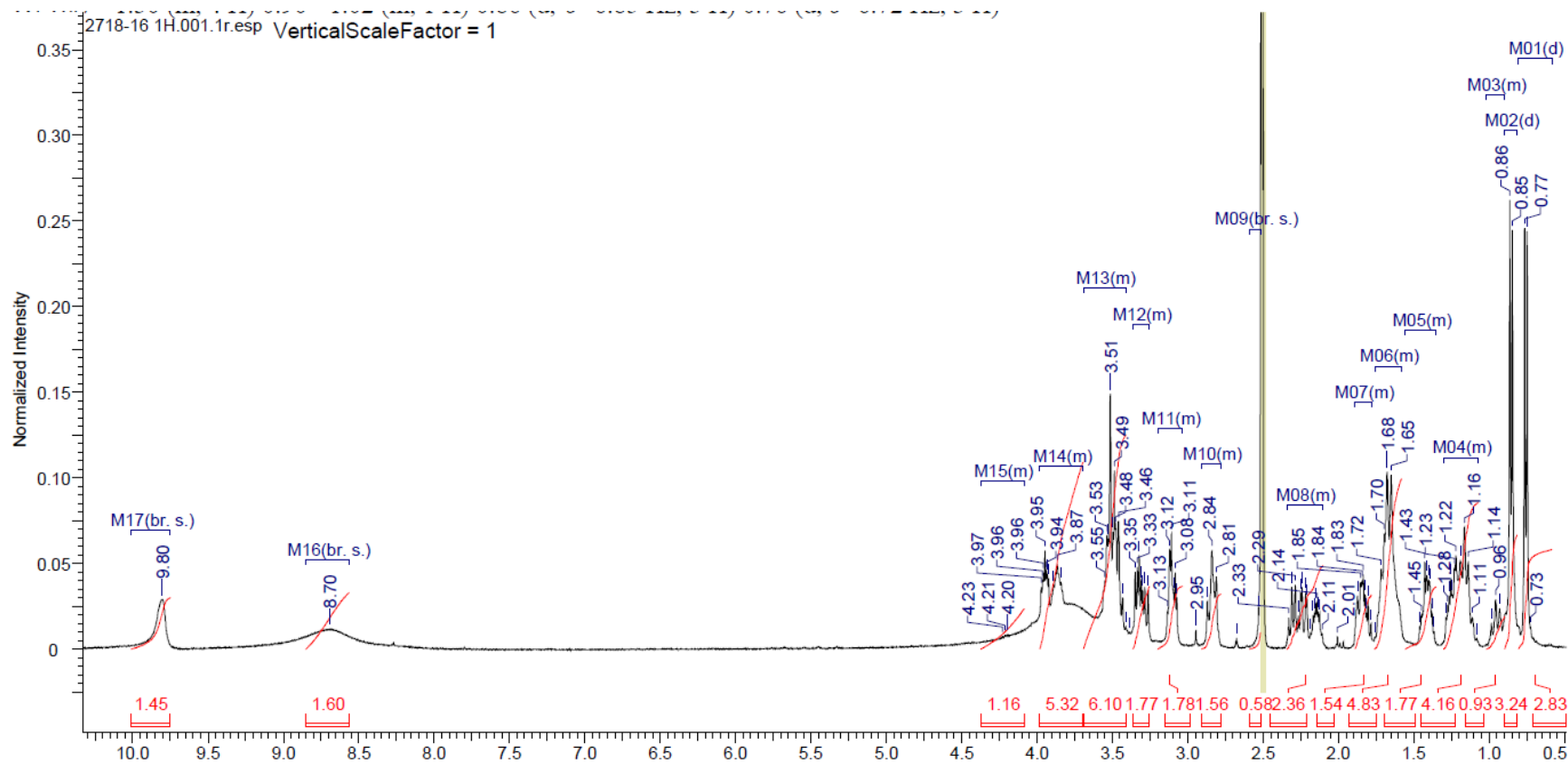


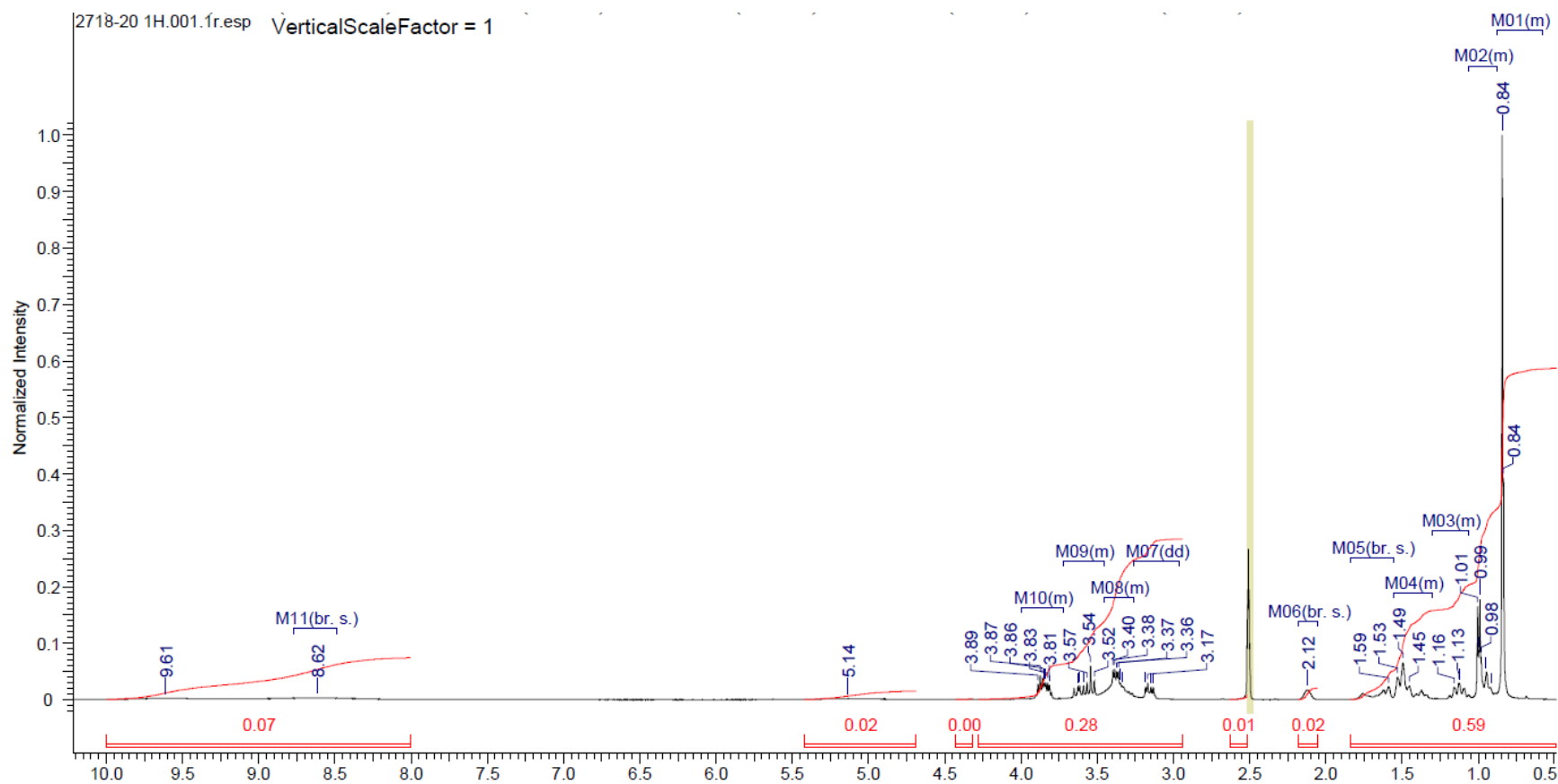


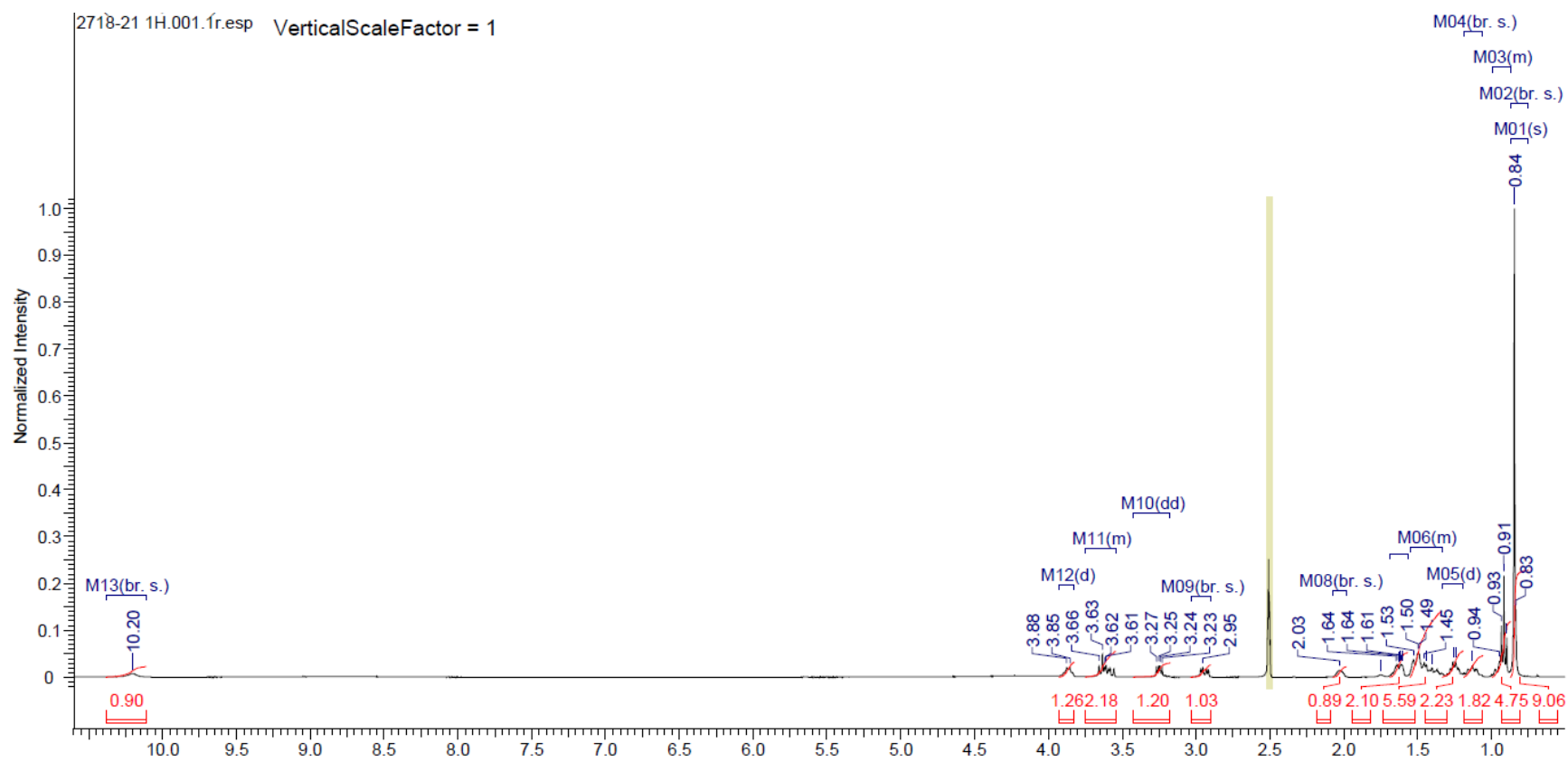


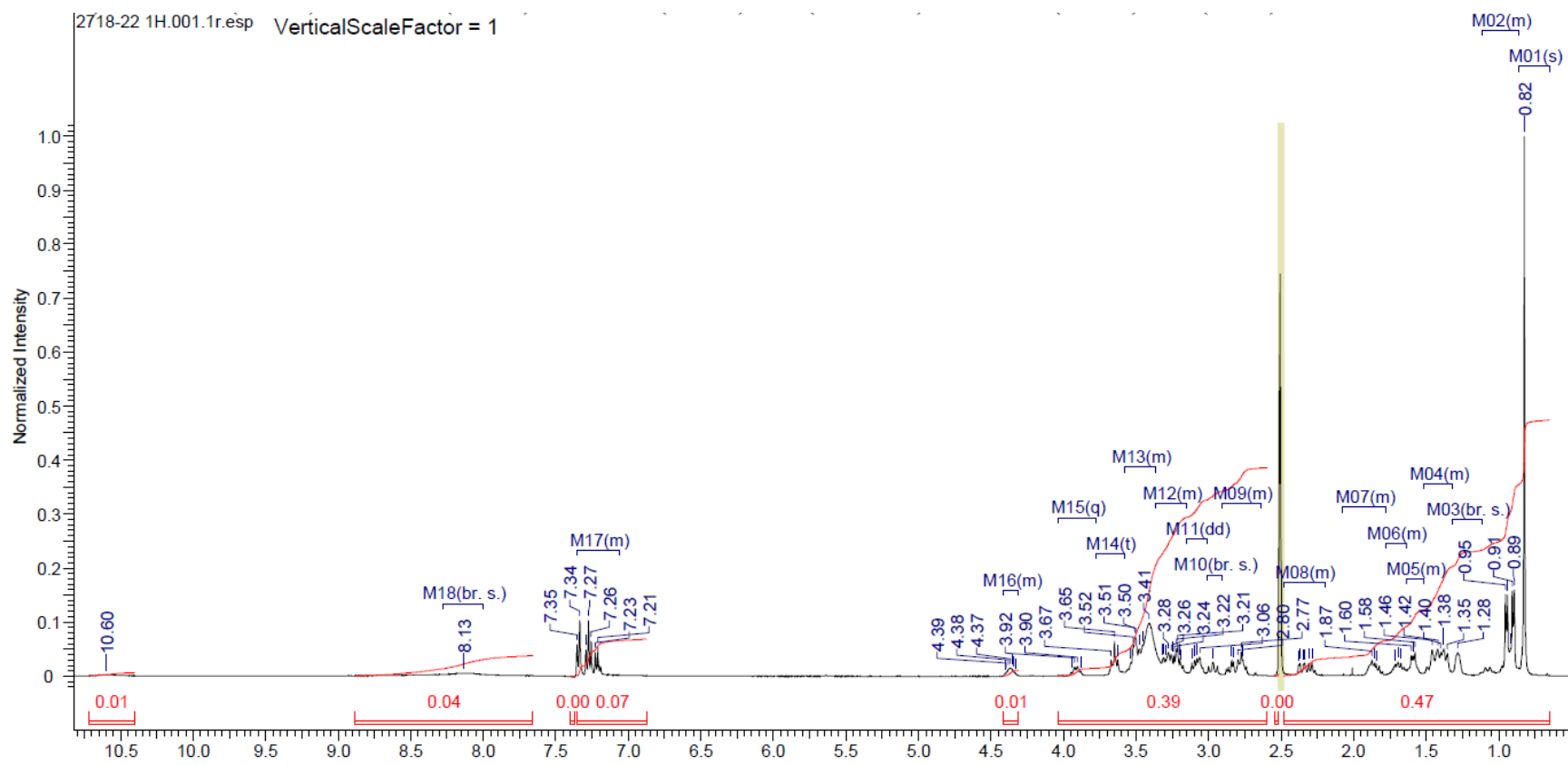


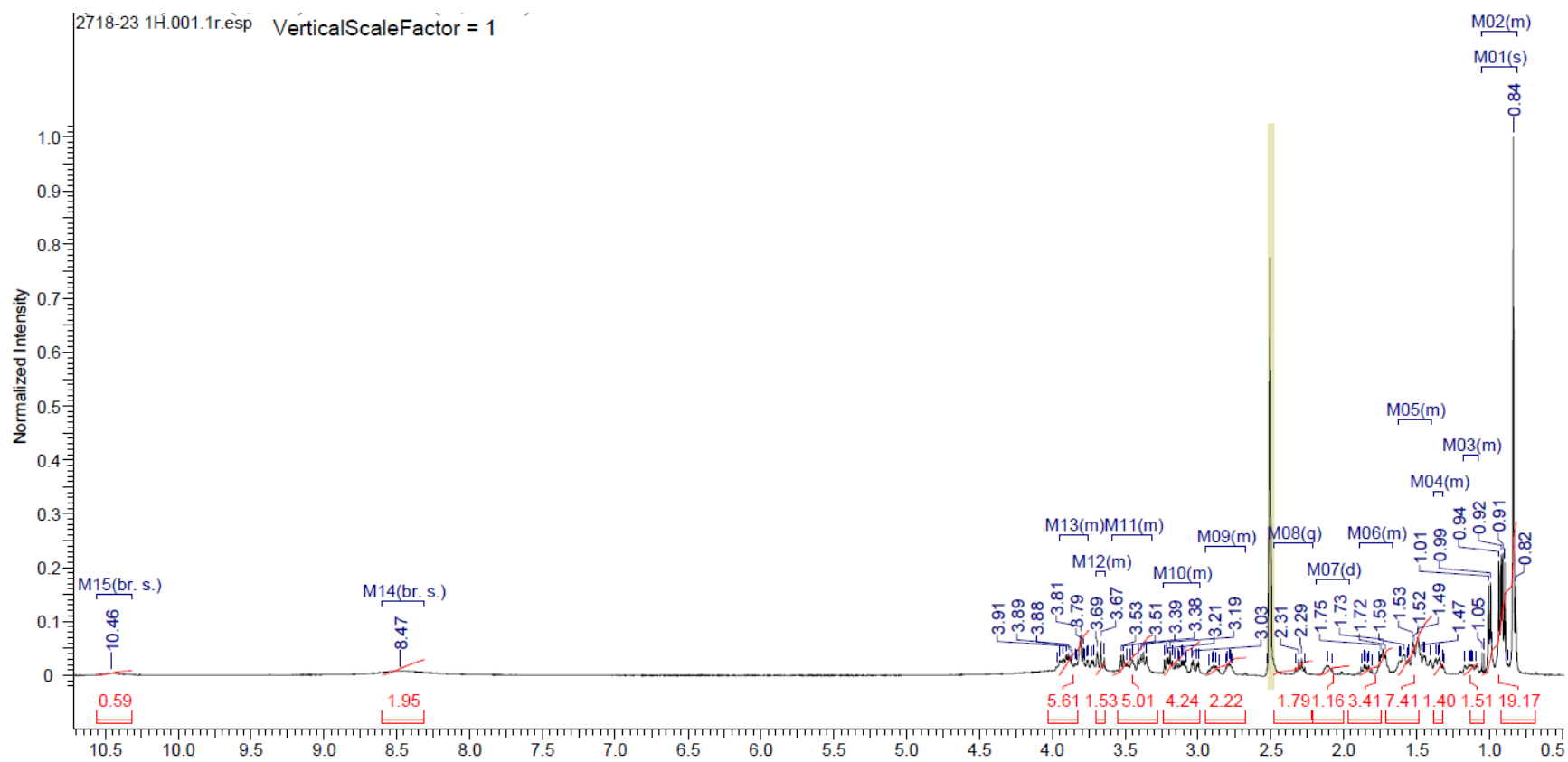


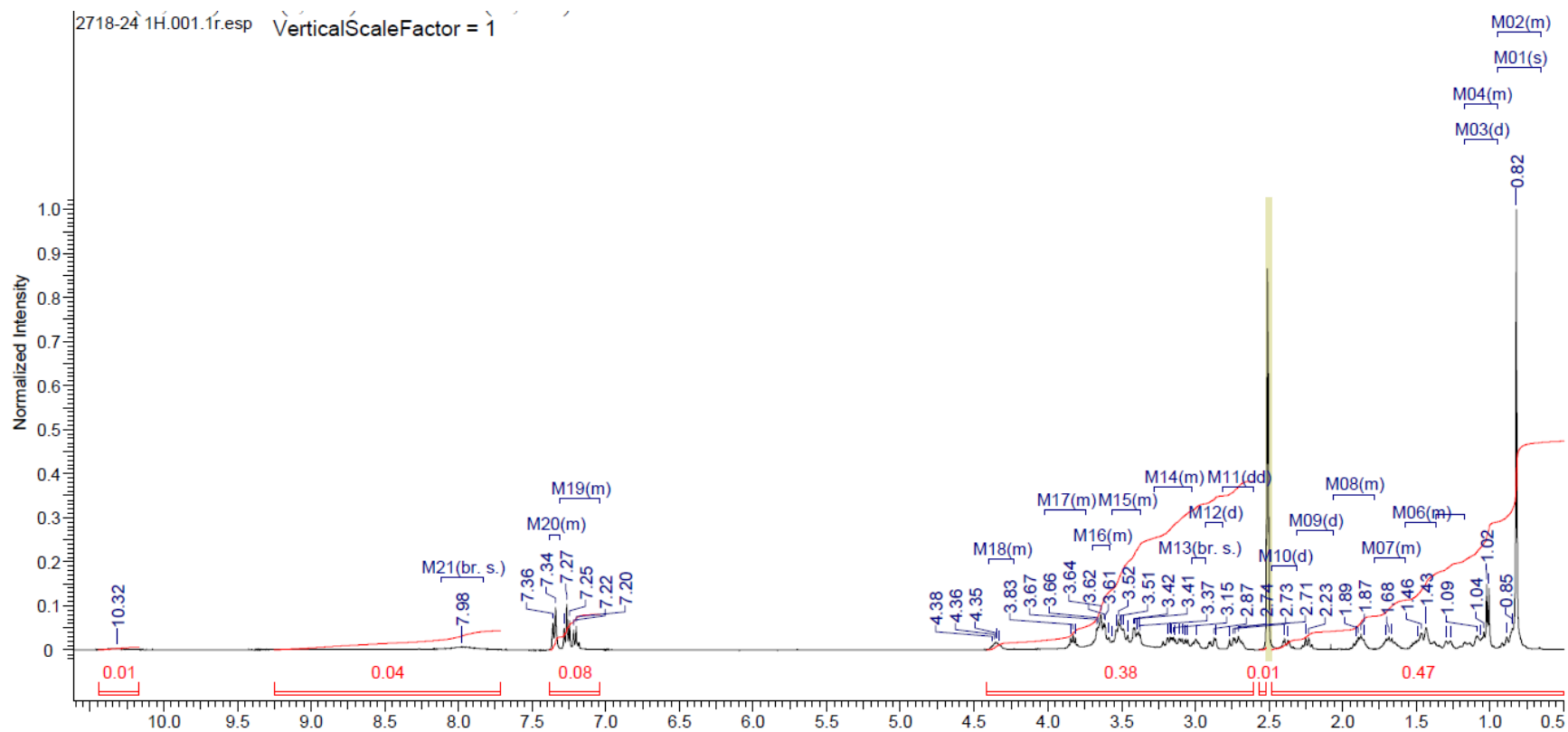


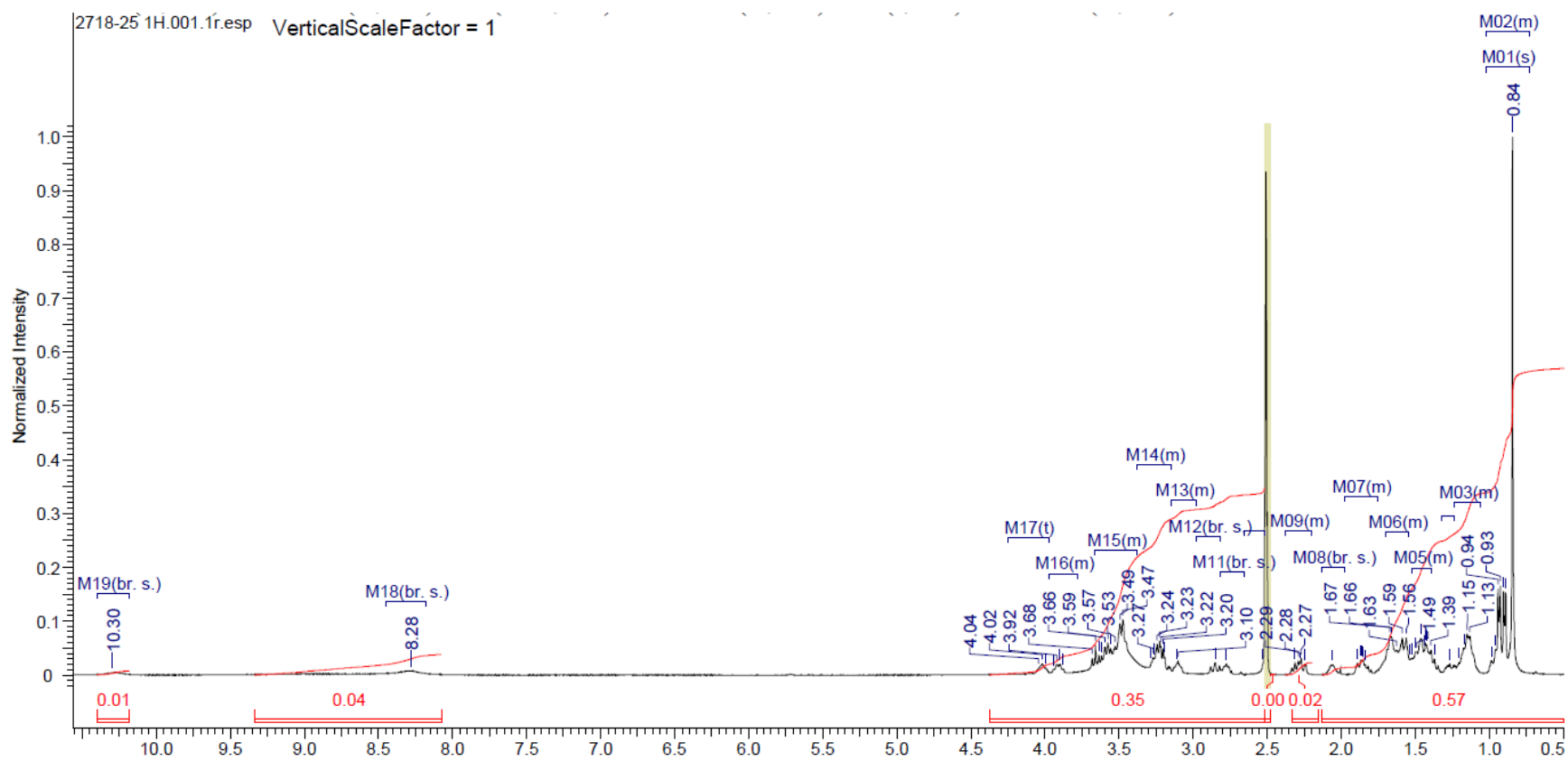


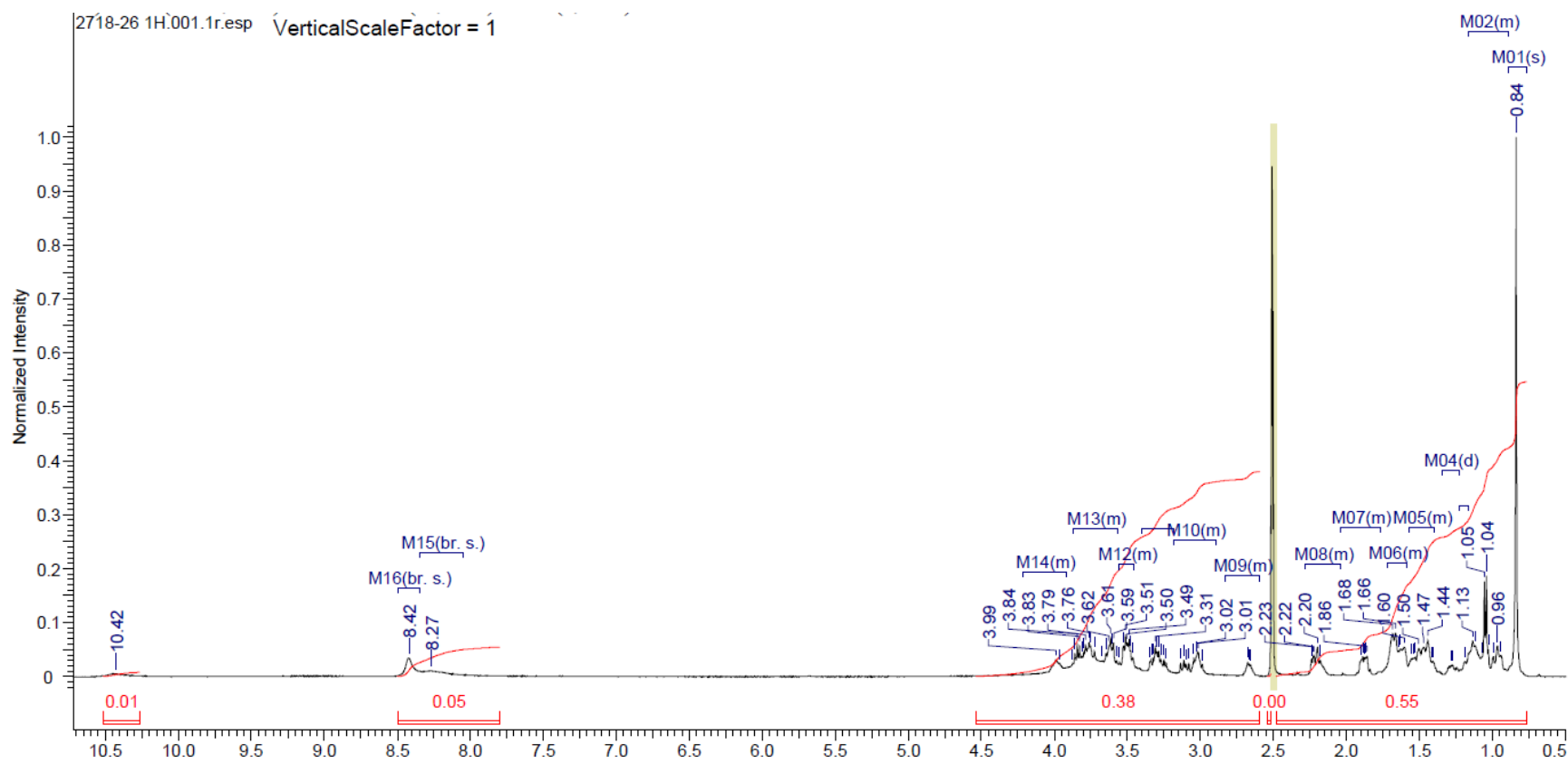


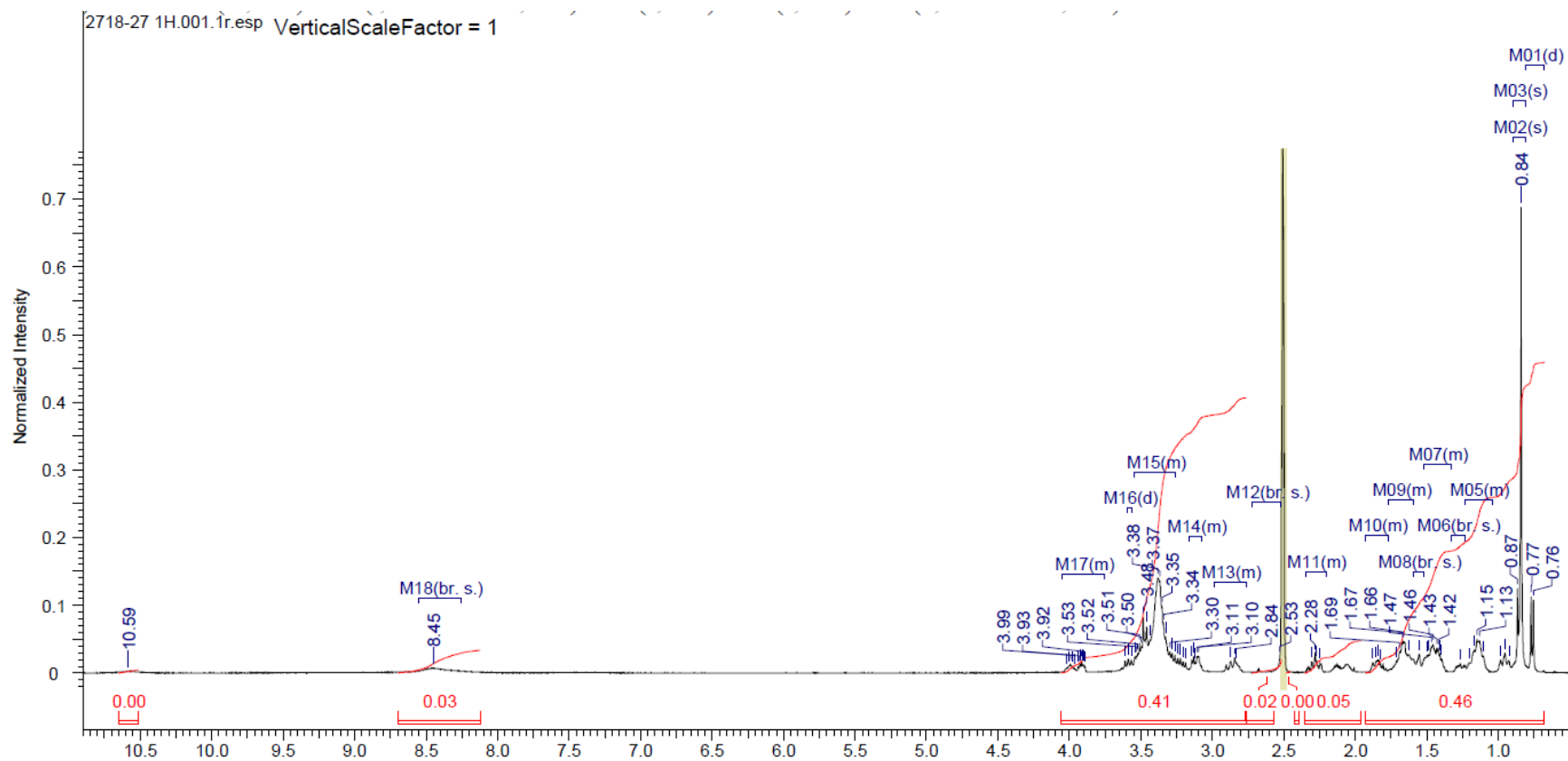


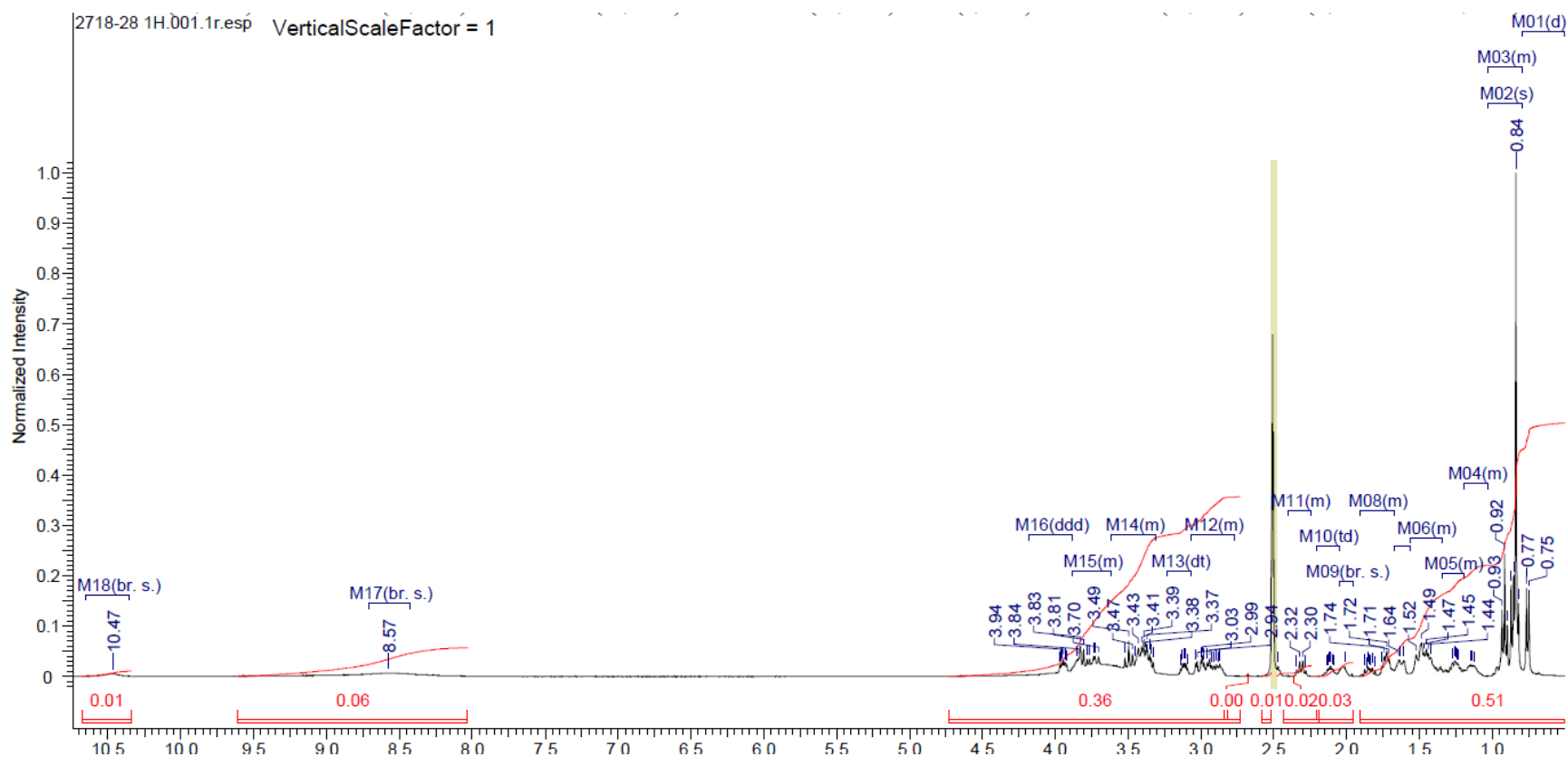


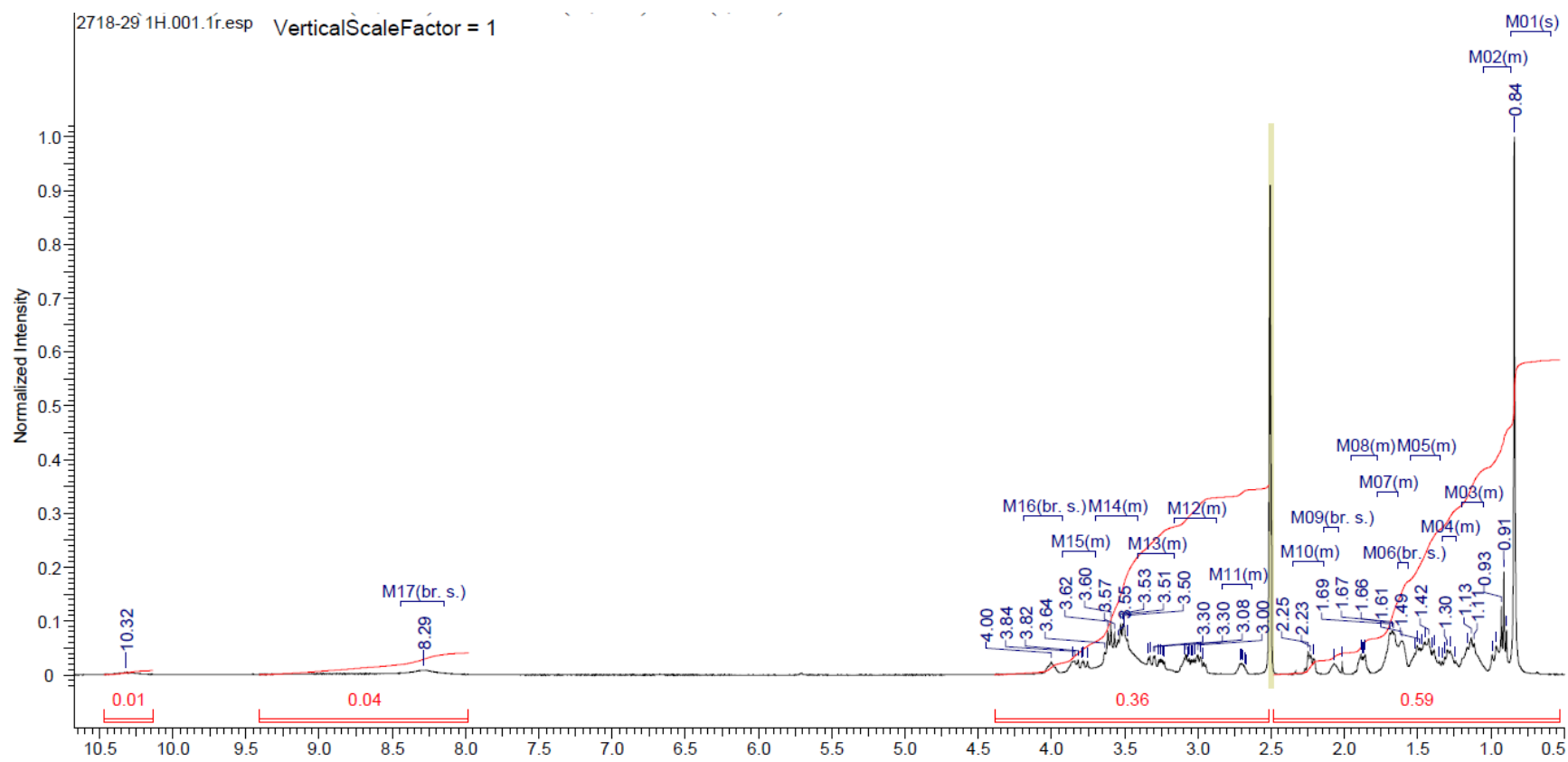


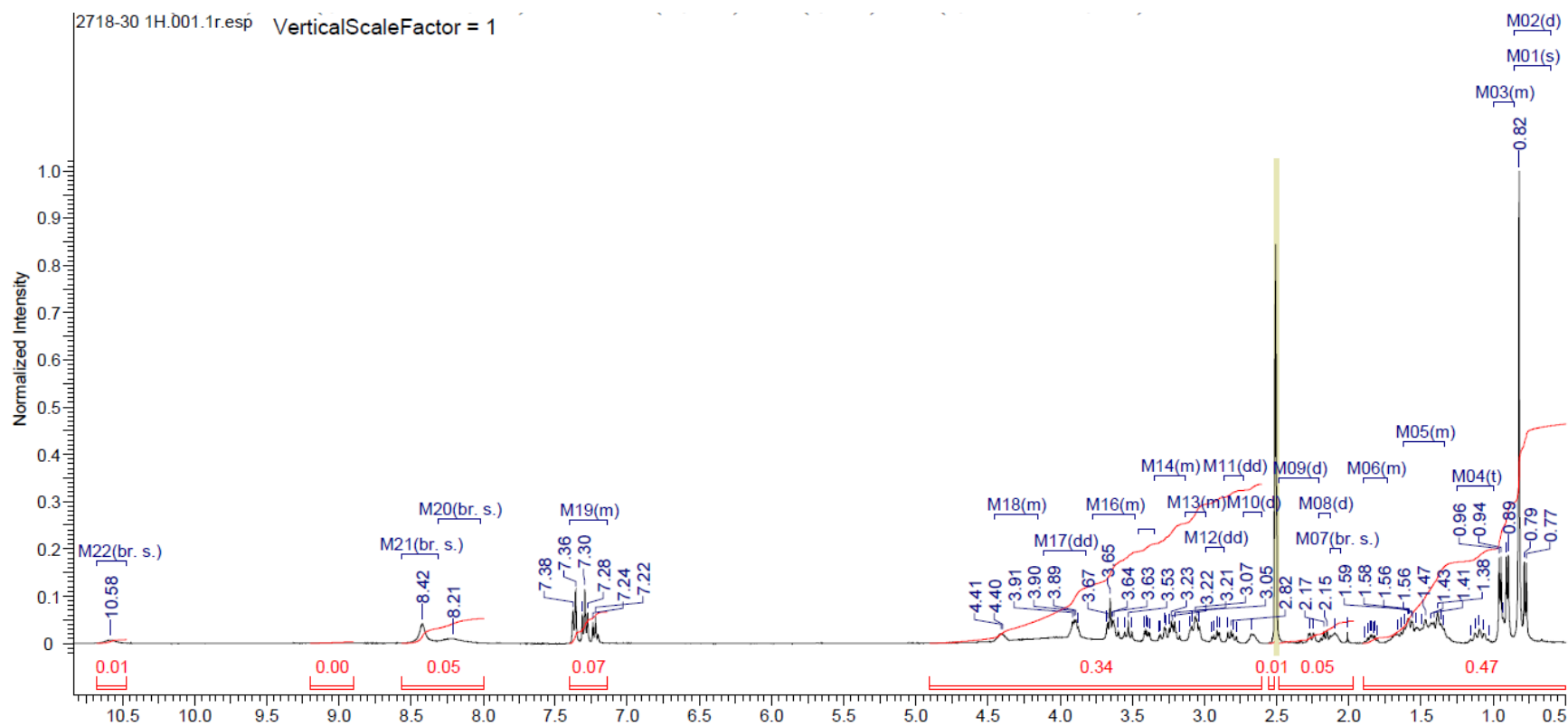


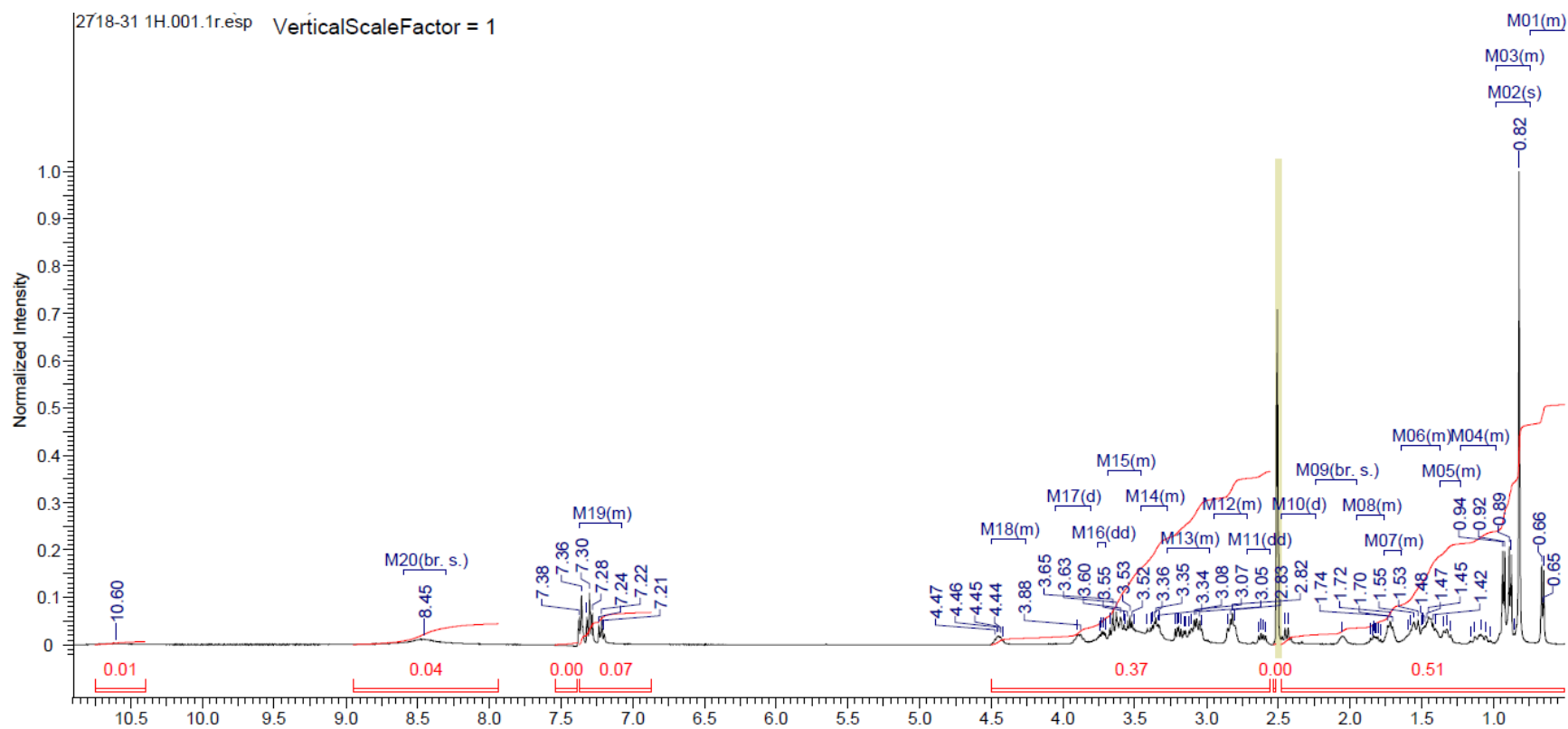


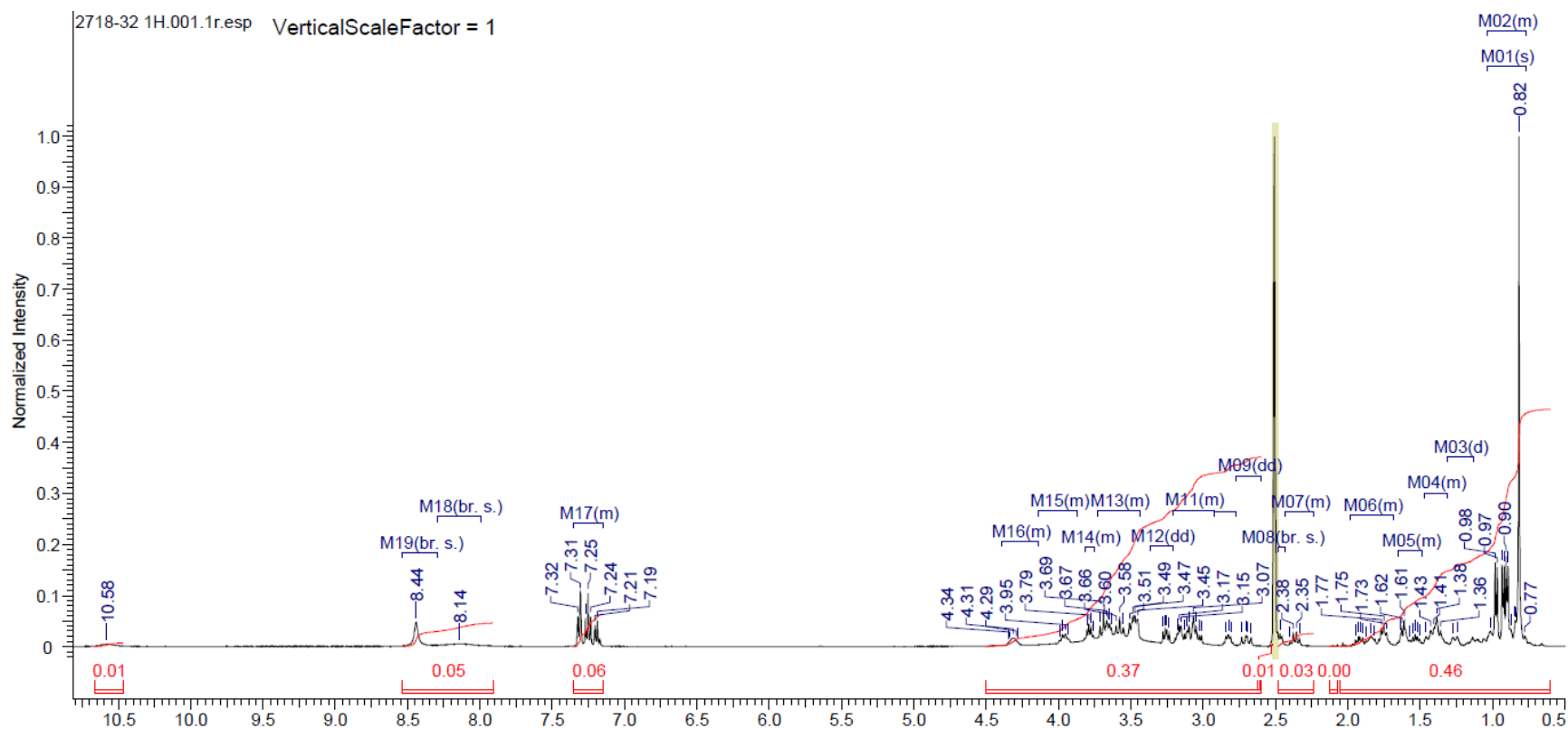




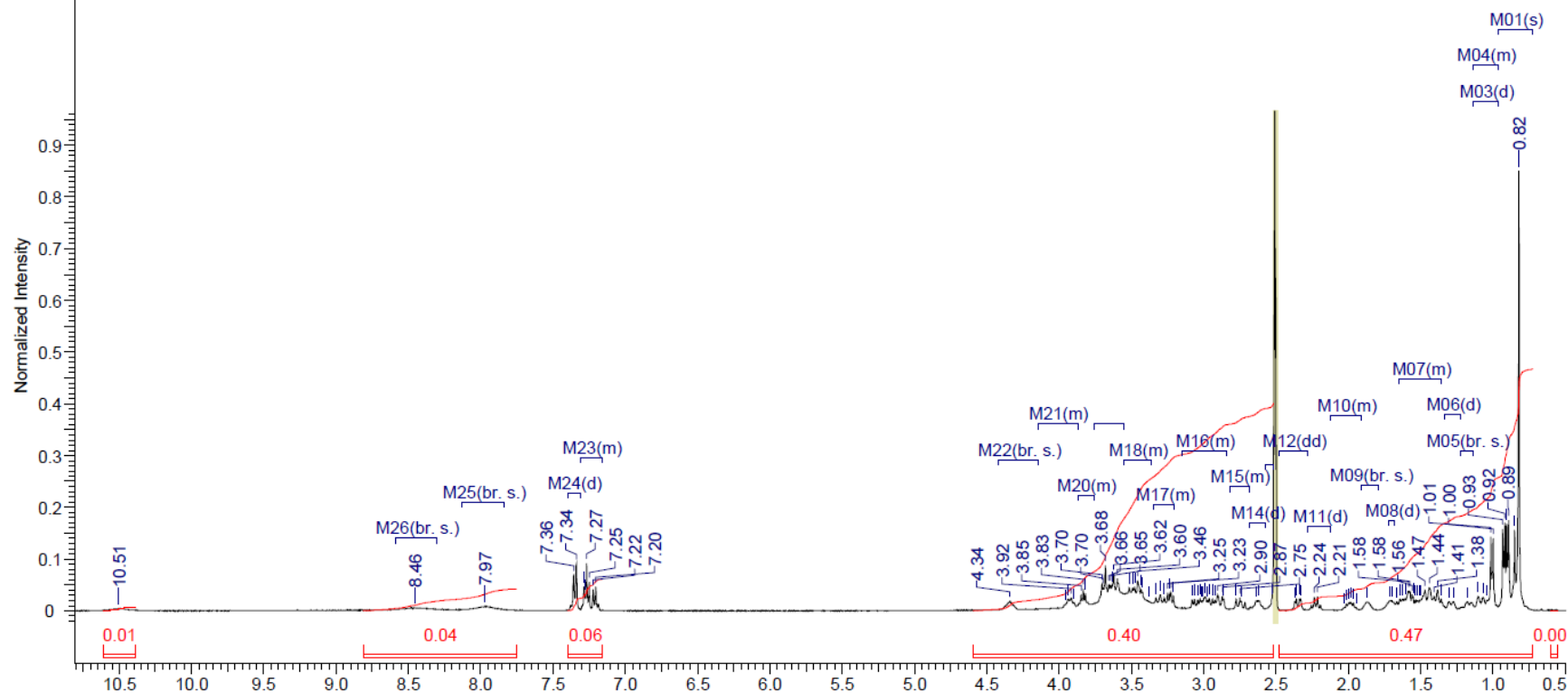


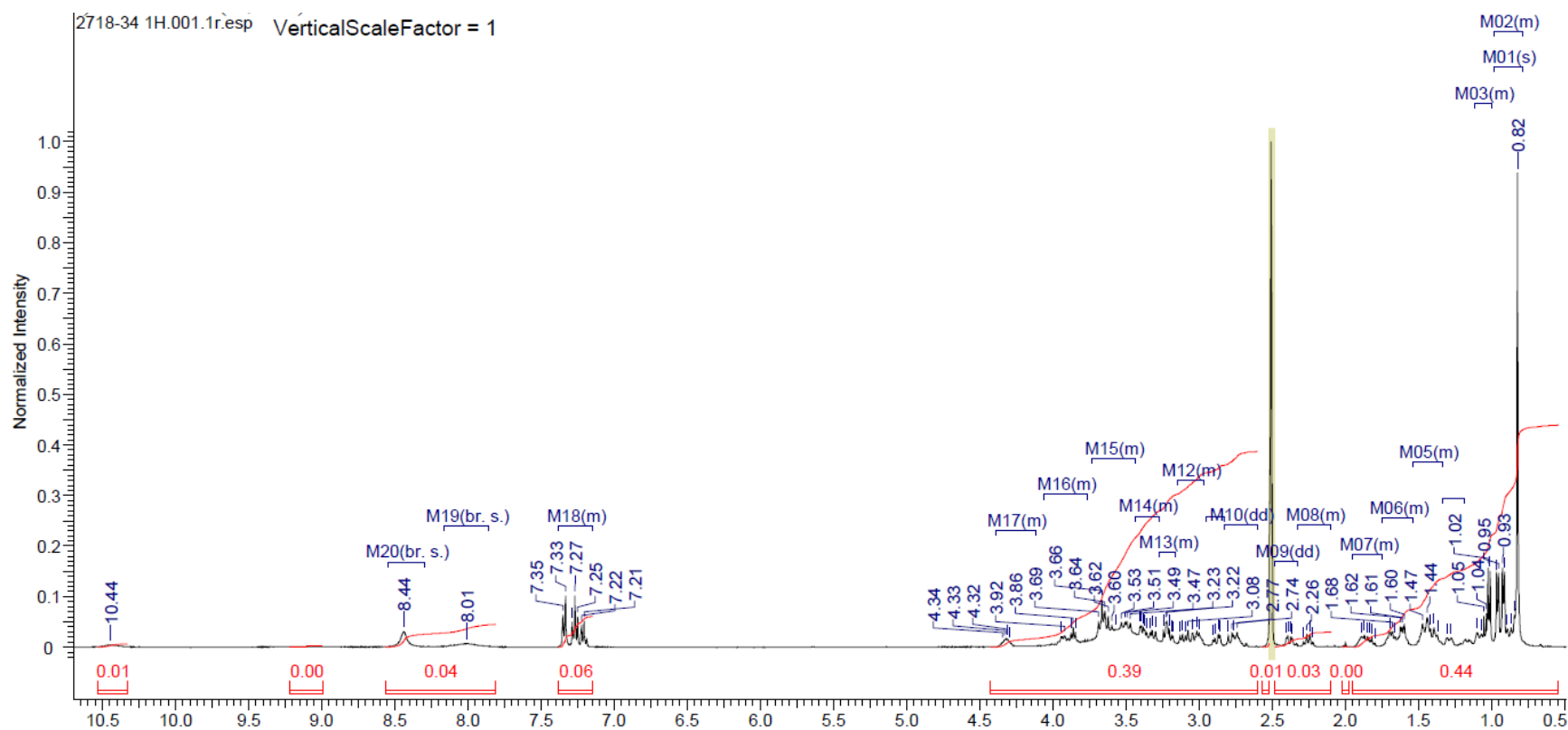


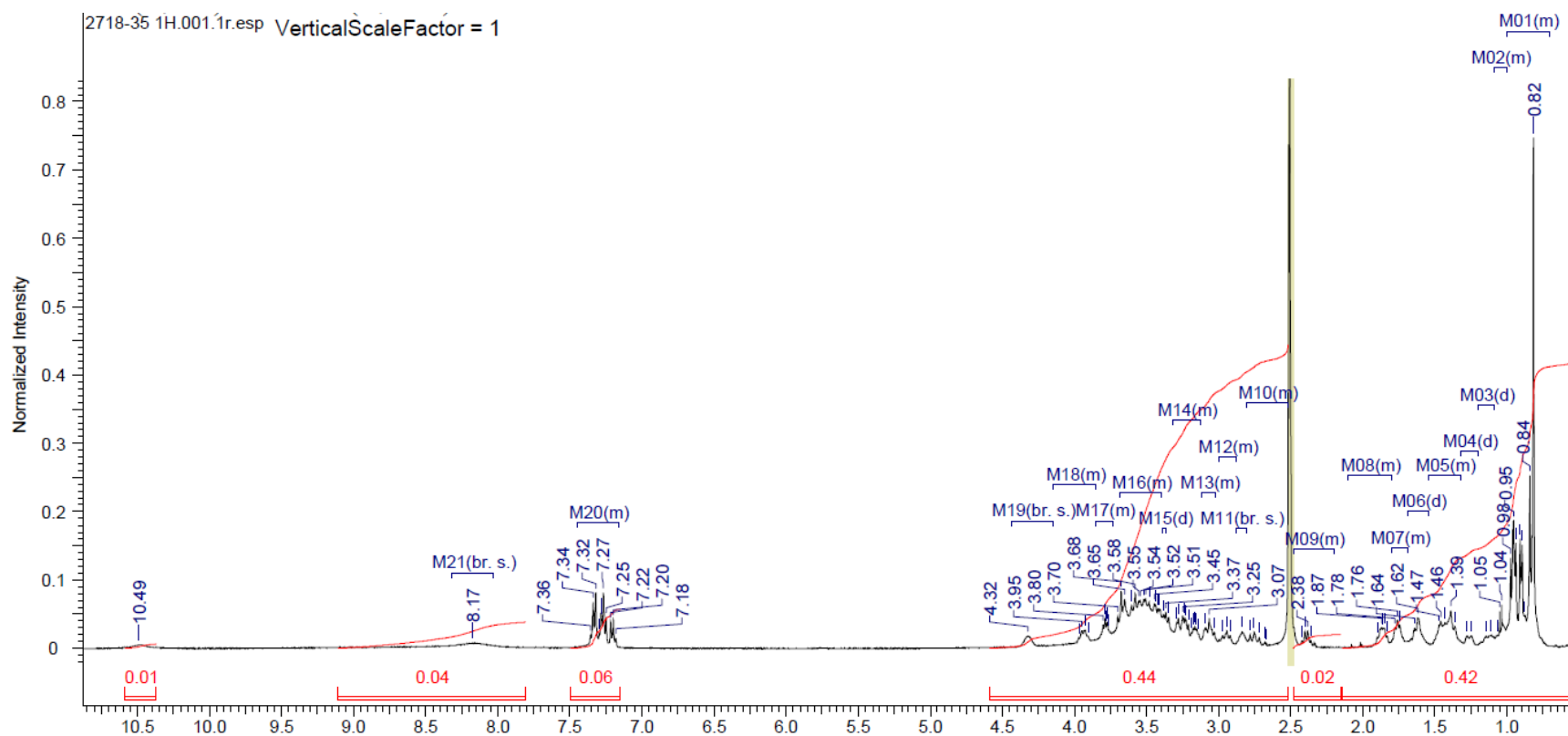


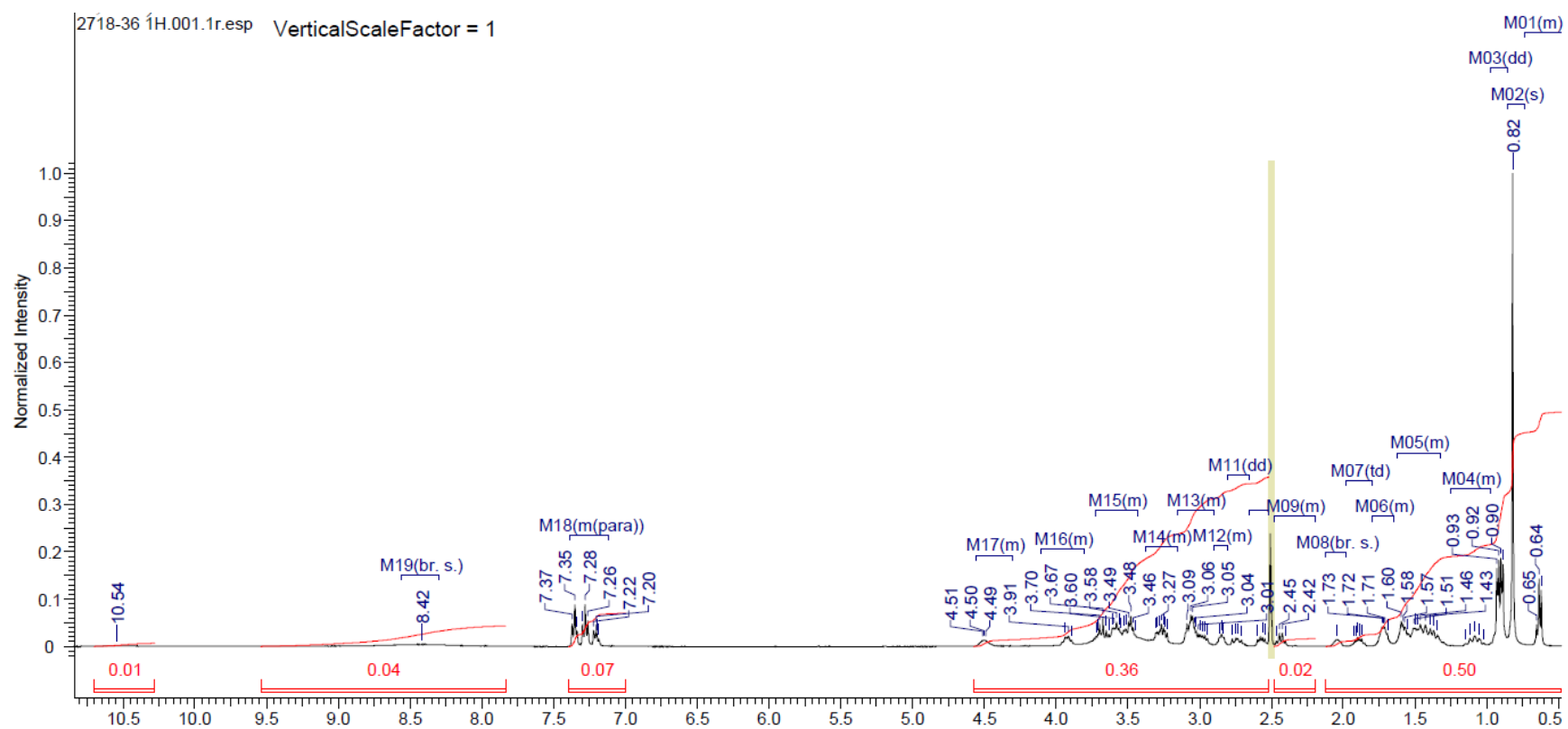


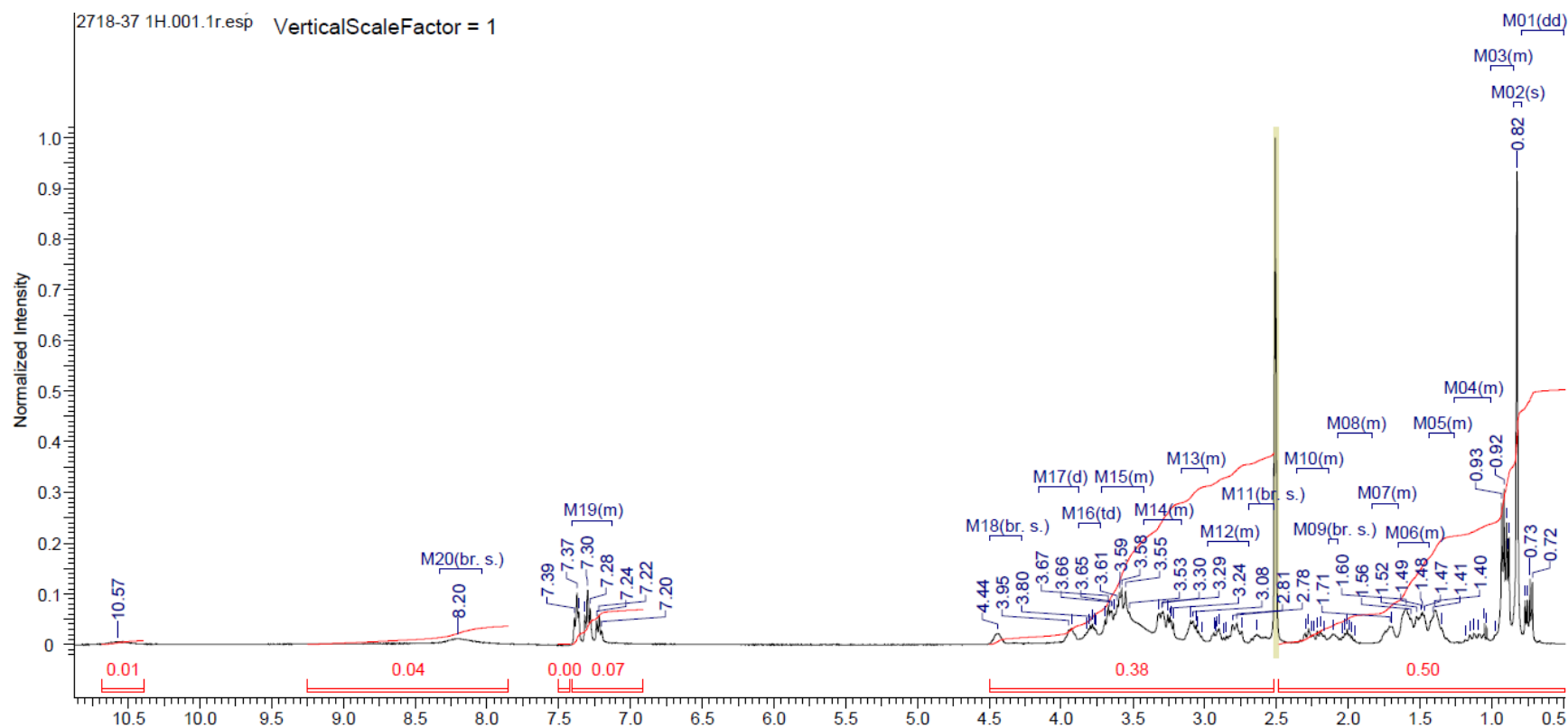
2718-33 1H.001.1r.esp VerticalScaleFactor = 1



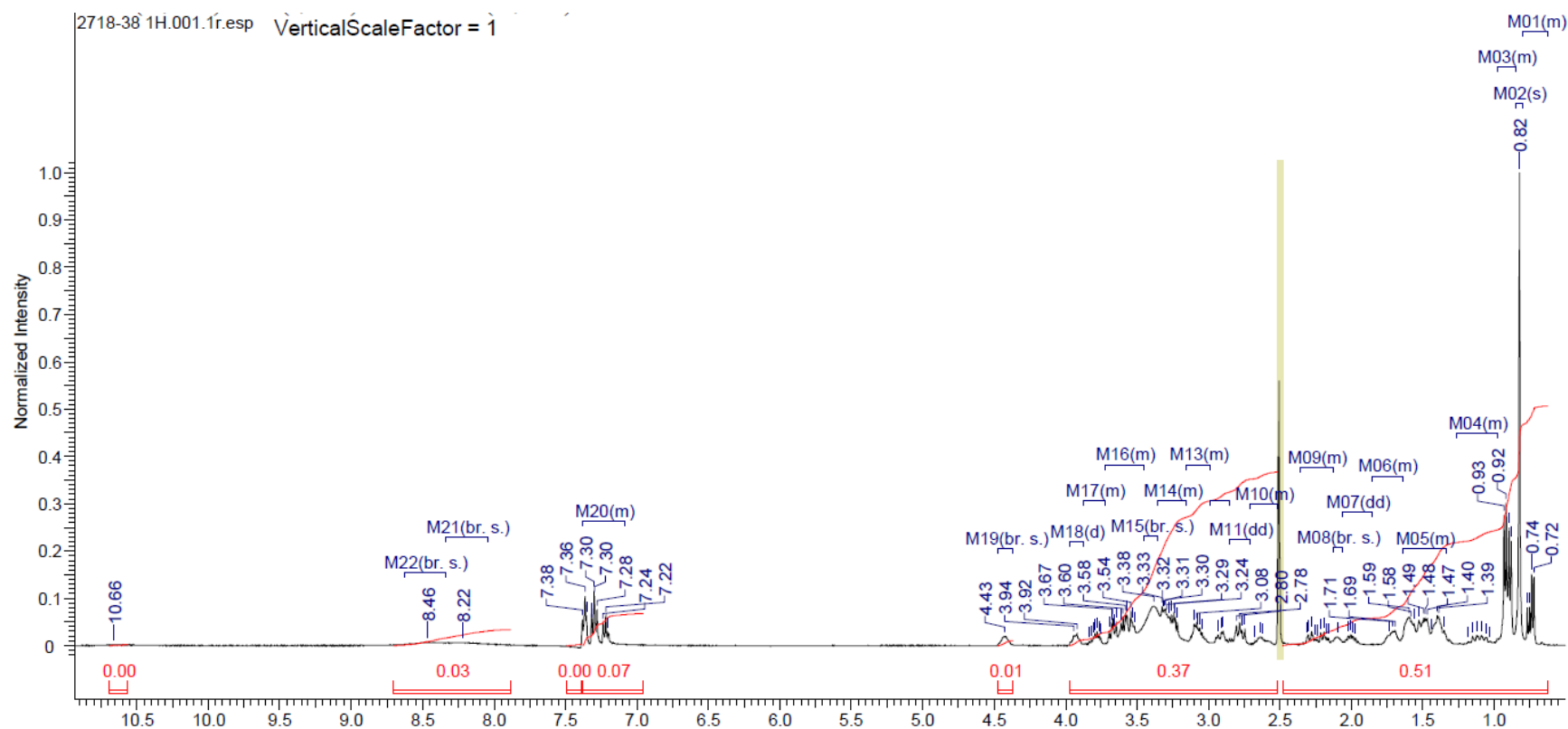


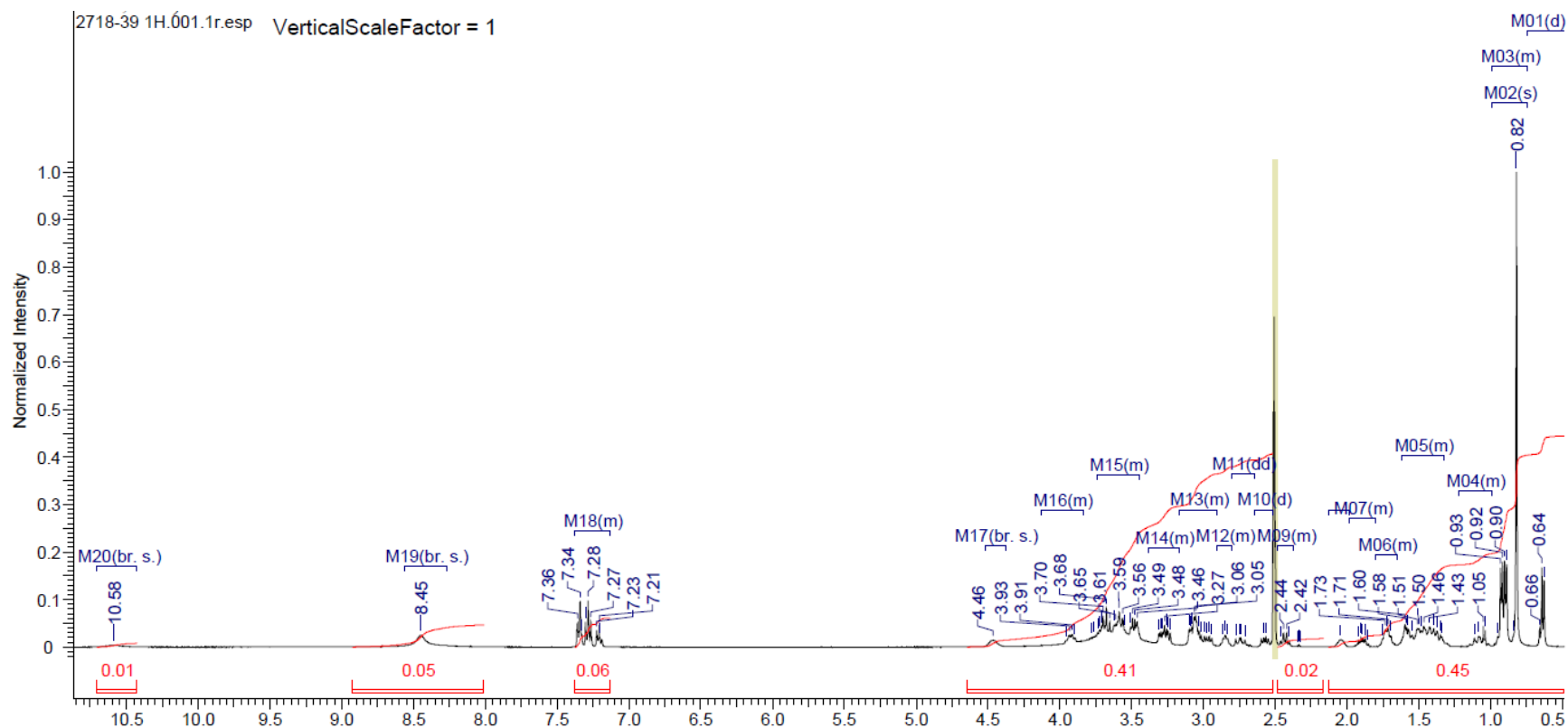


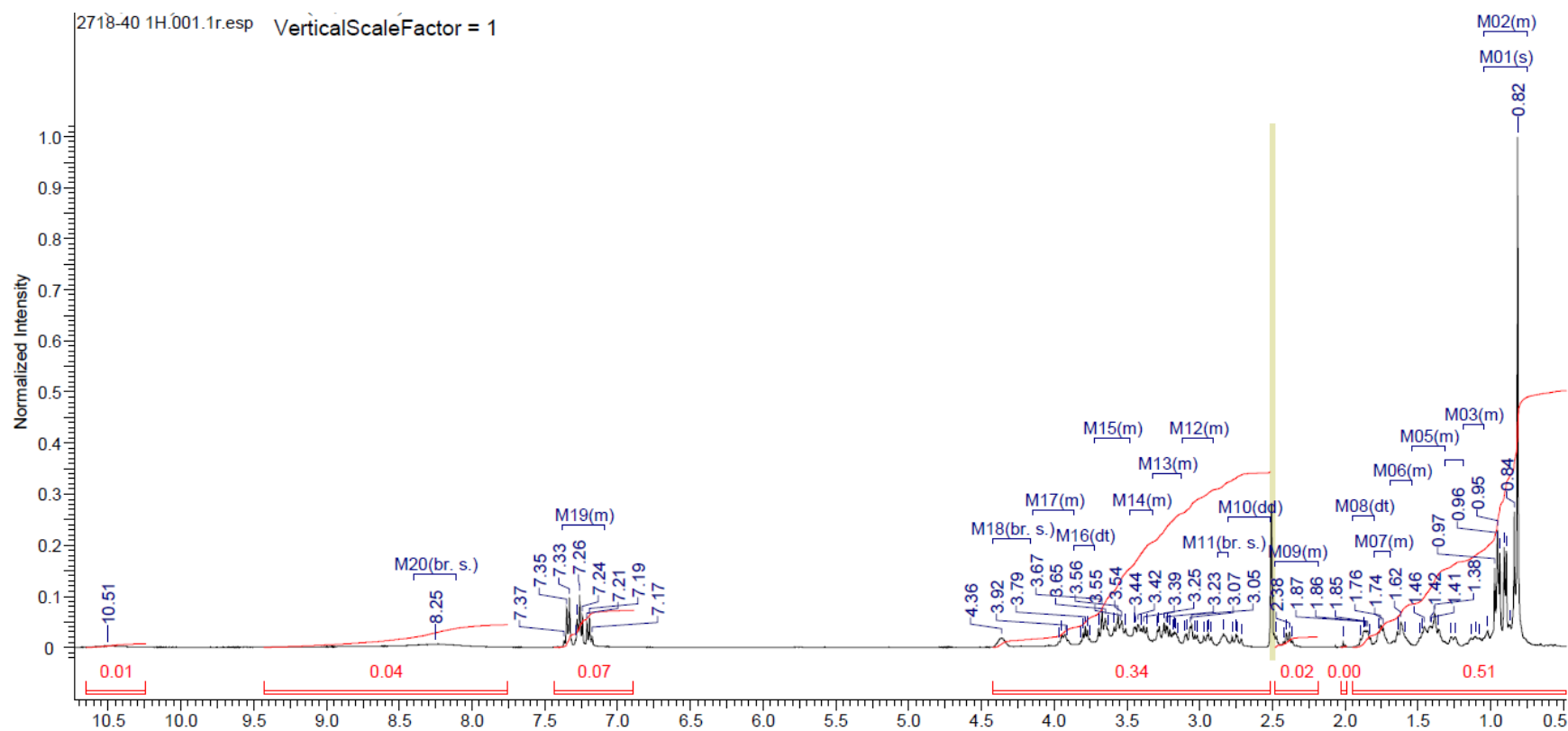




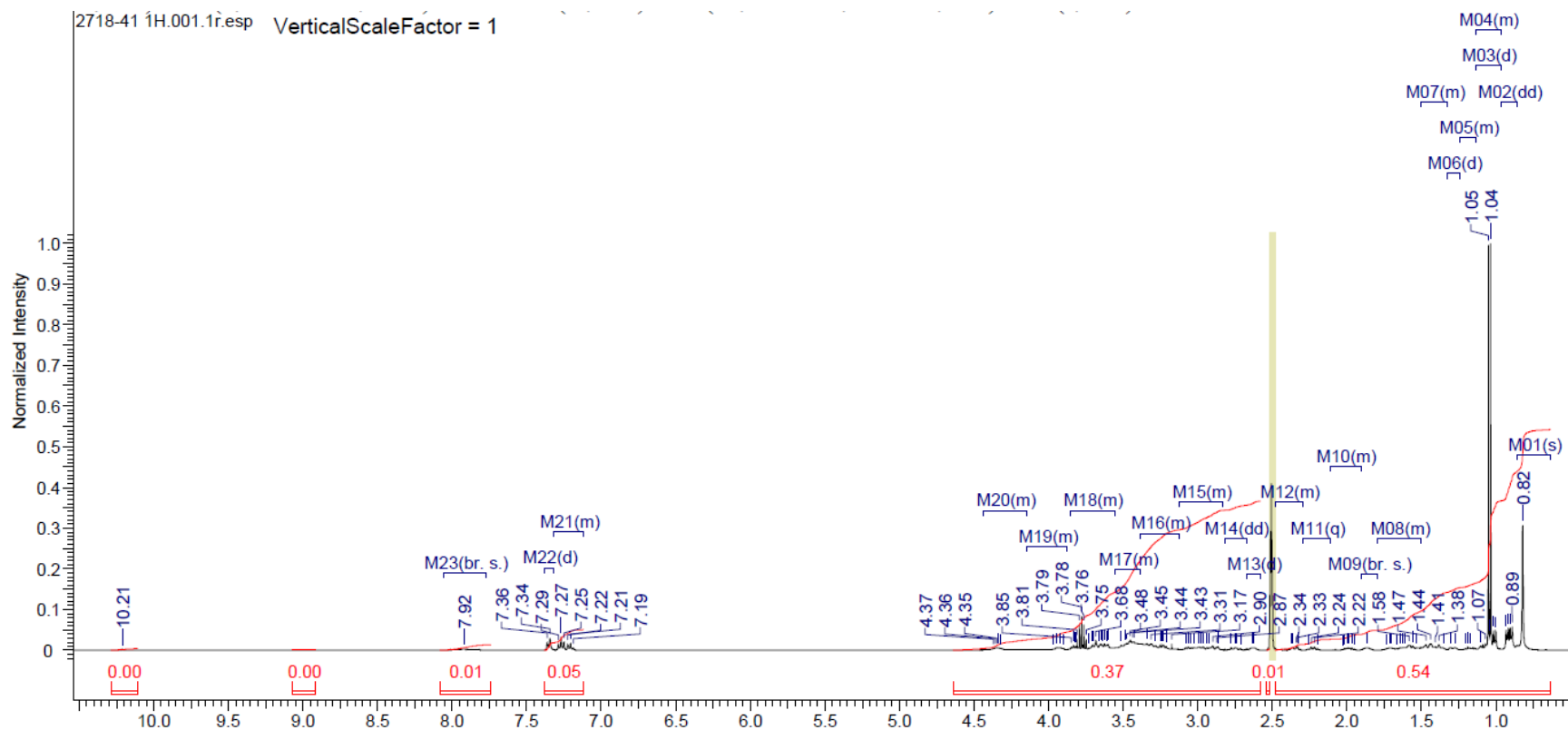
2718-38 1H.001.1r.esp VerticalScaleFactor = 1

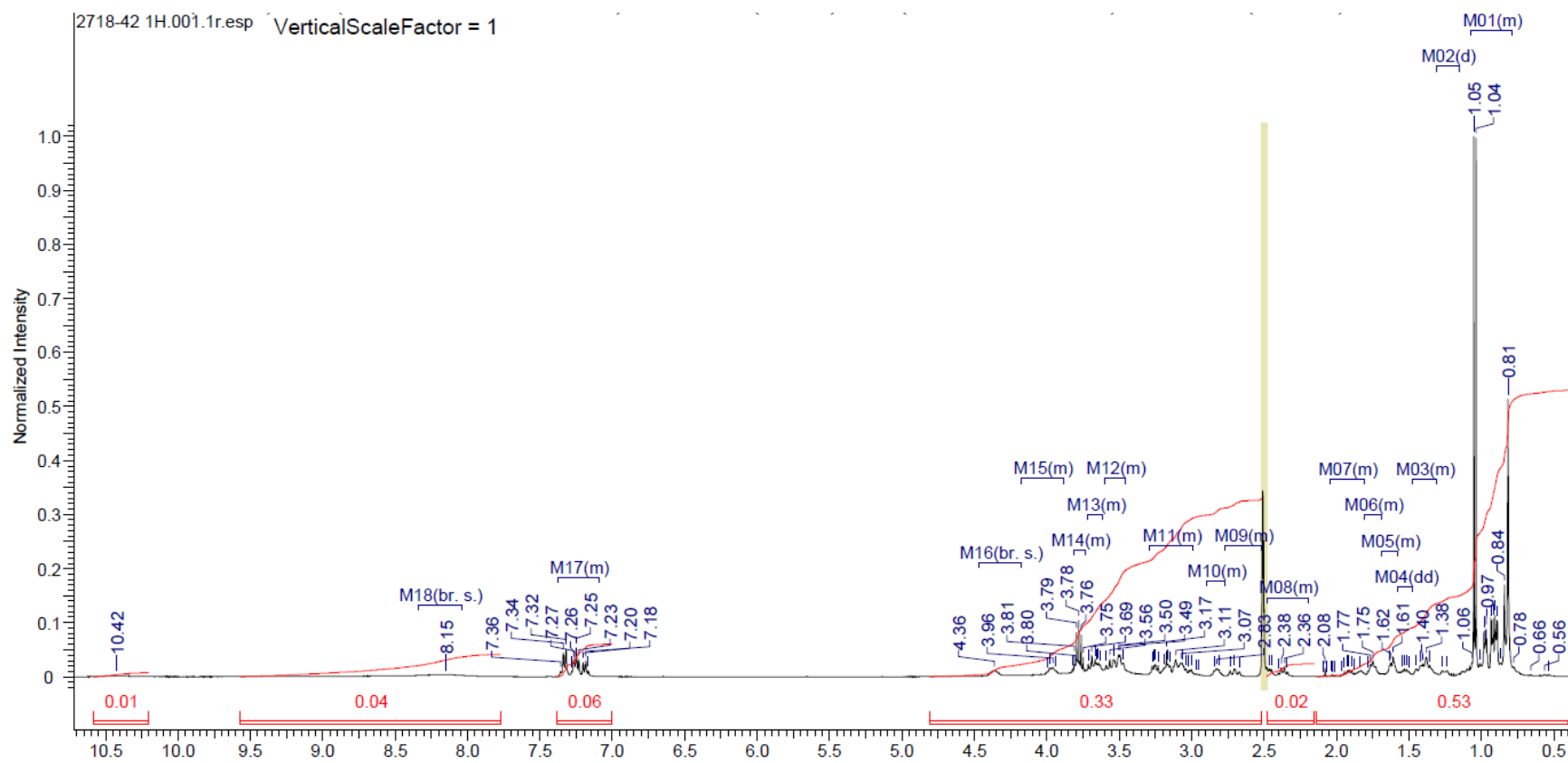


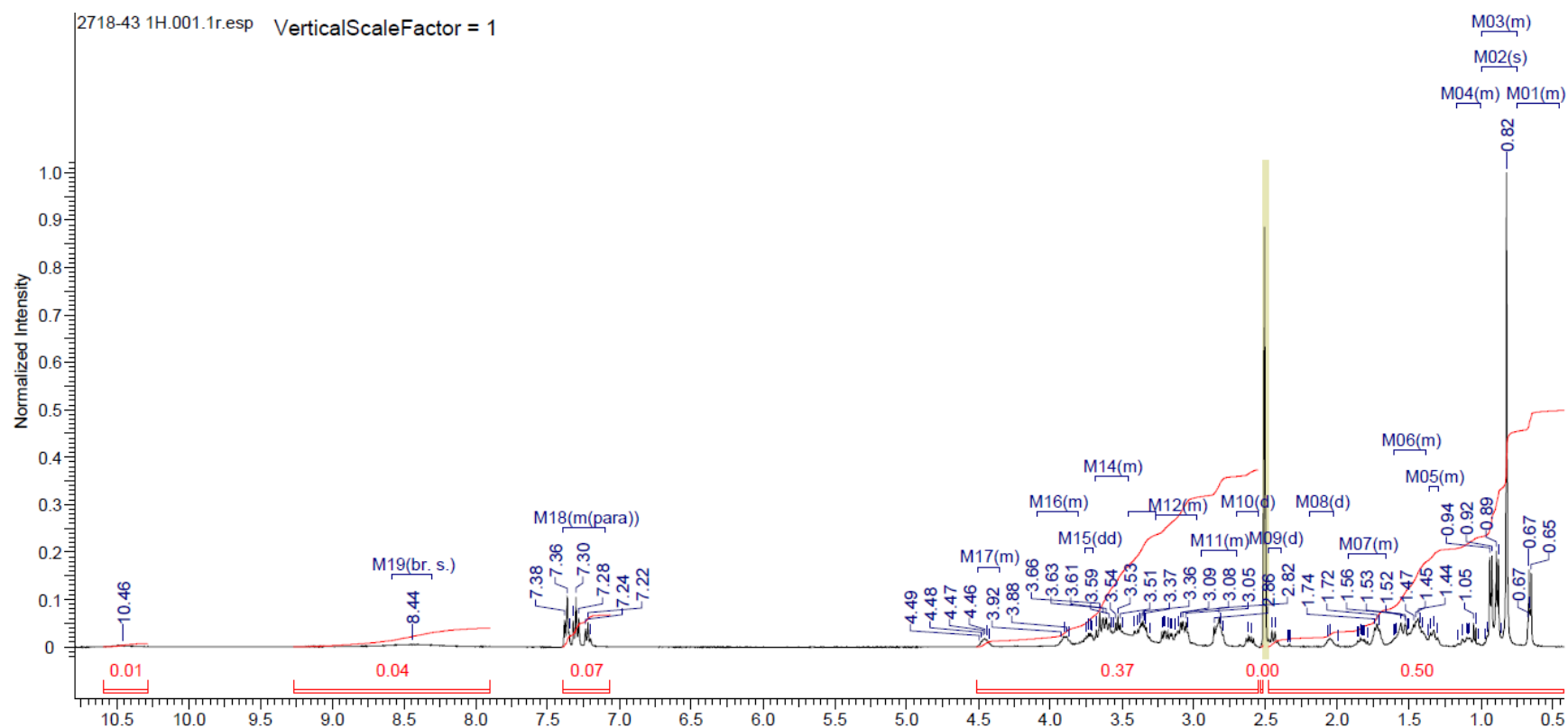


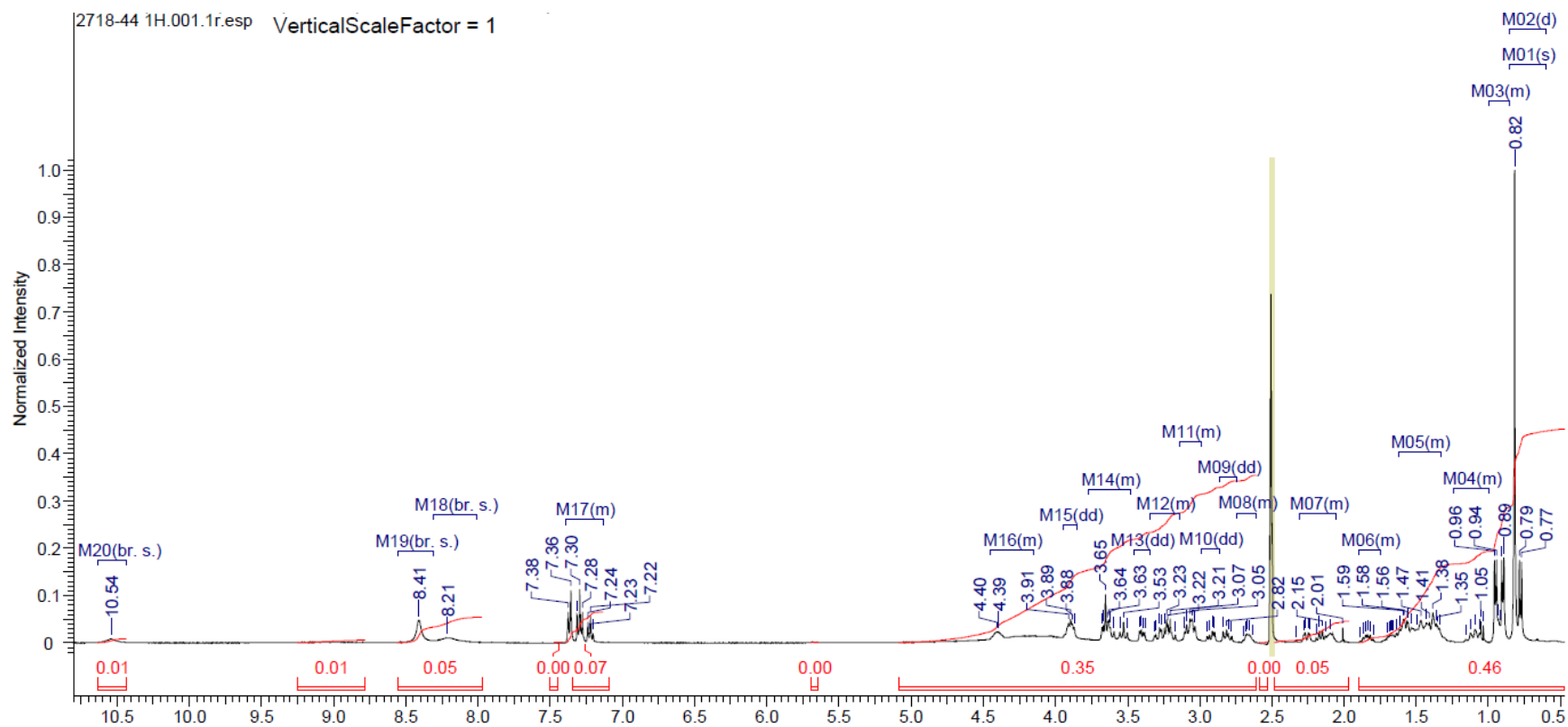


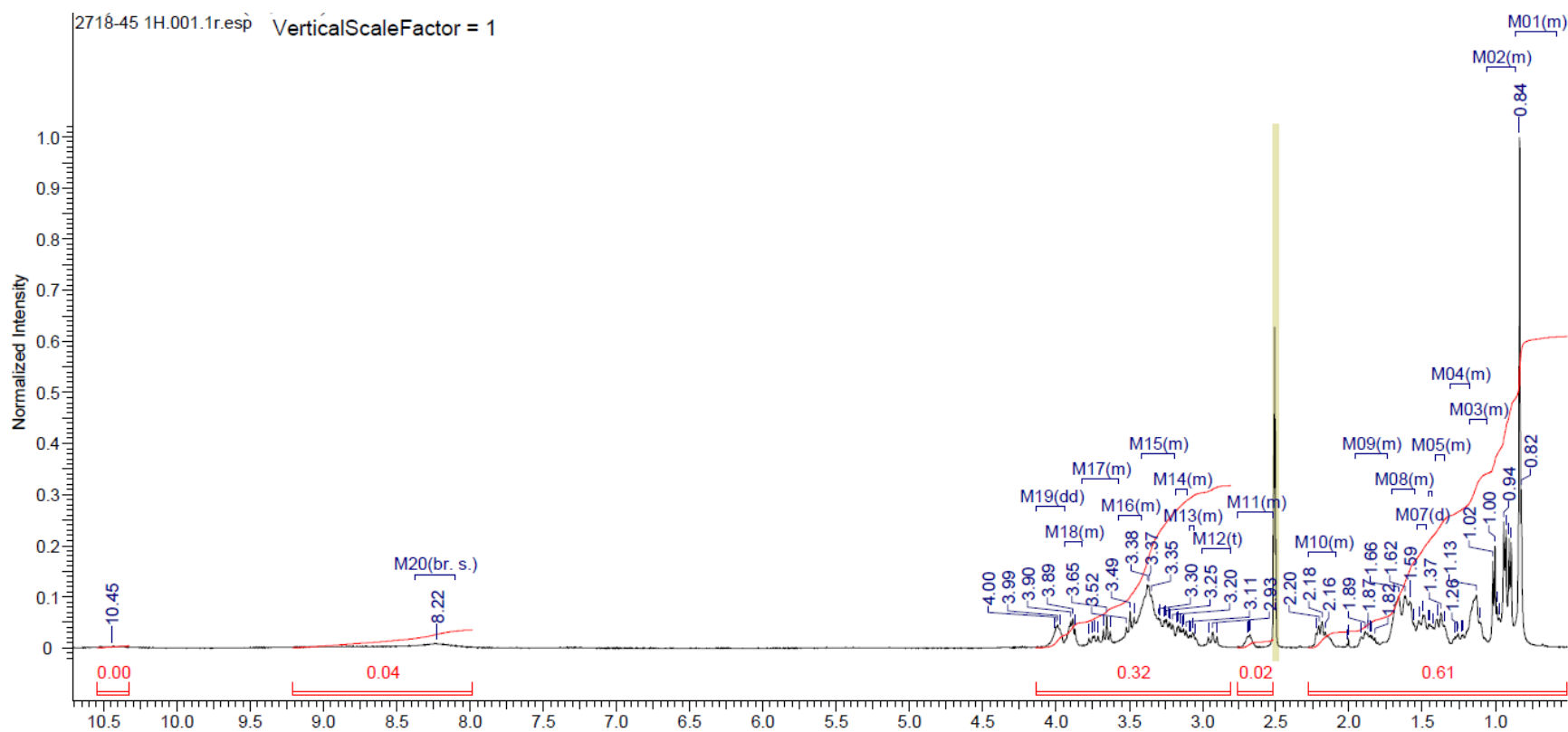
2718-41 1H.001.1r.esp VerticalScaleFactor = 1

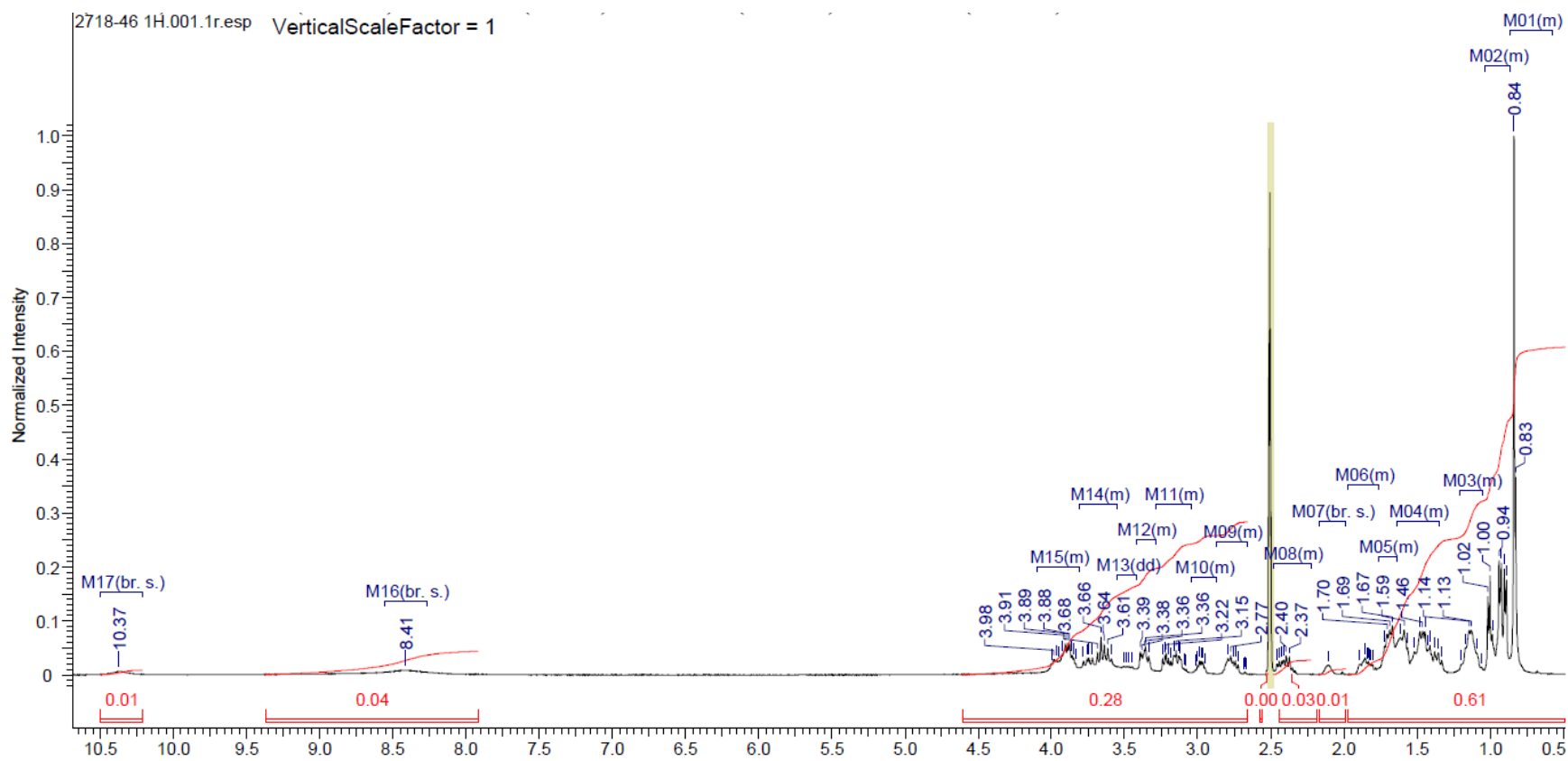


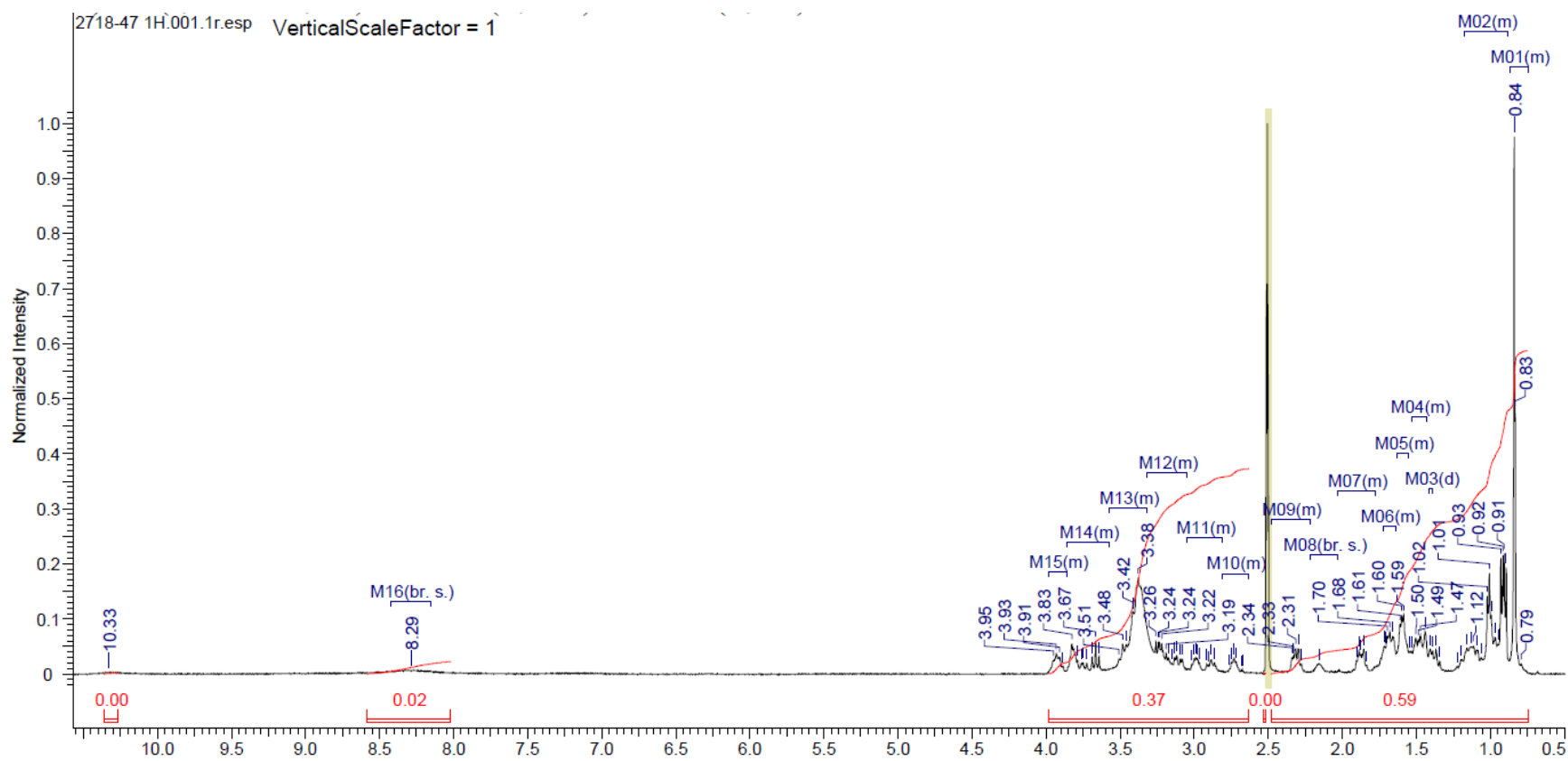


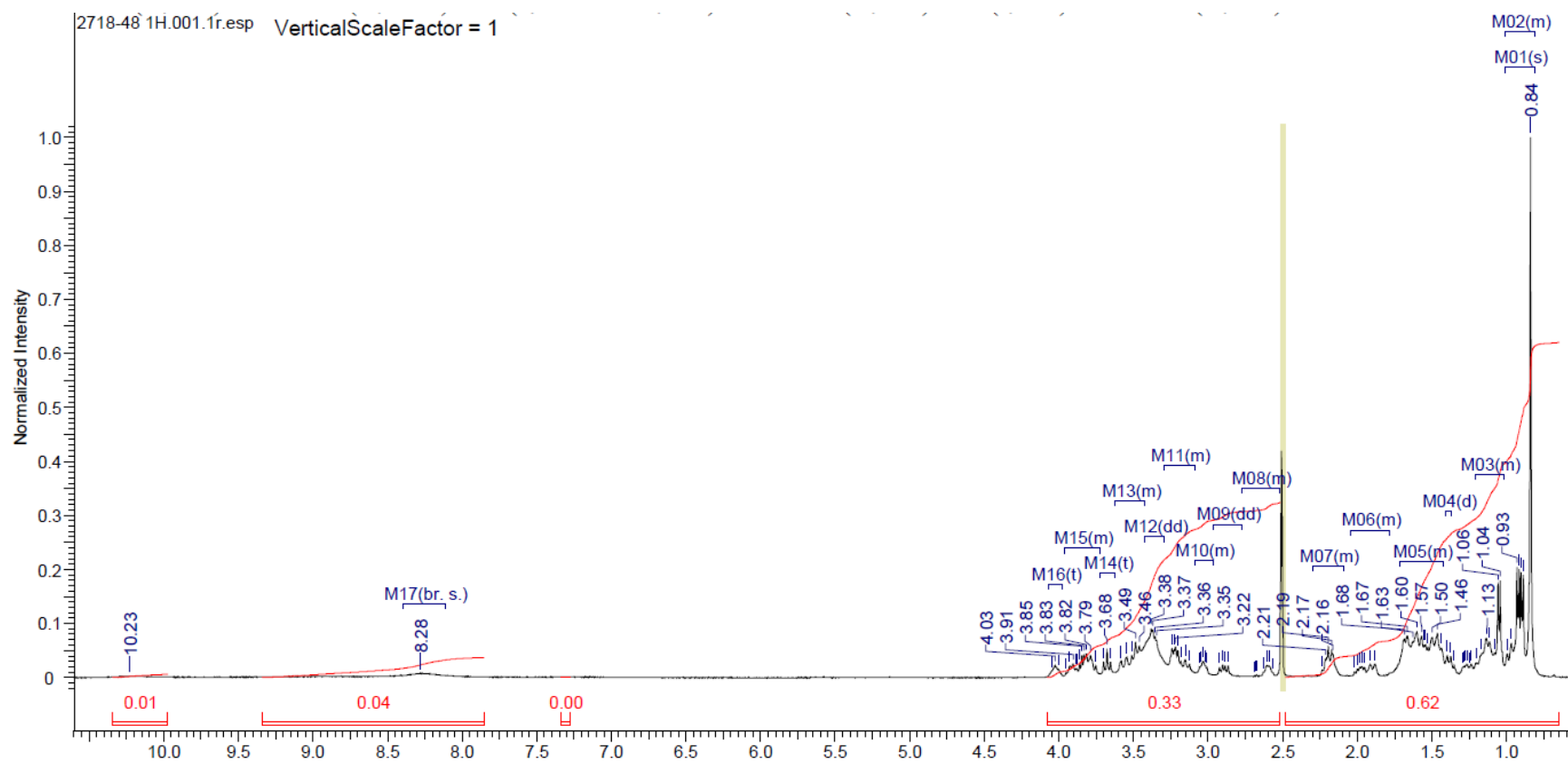


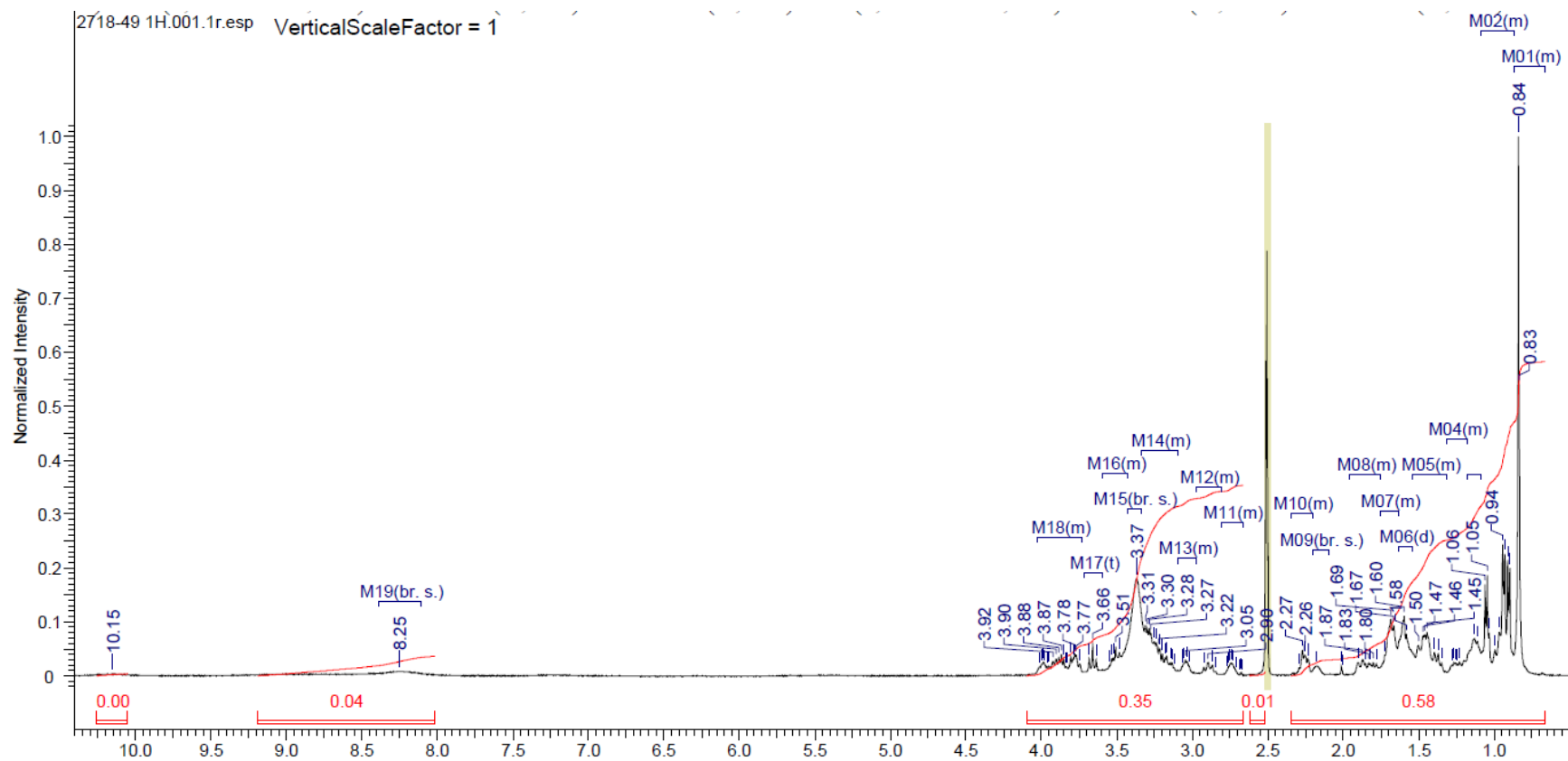


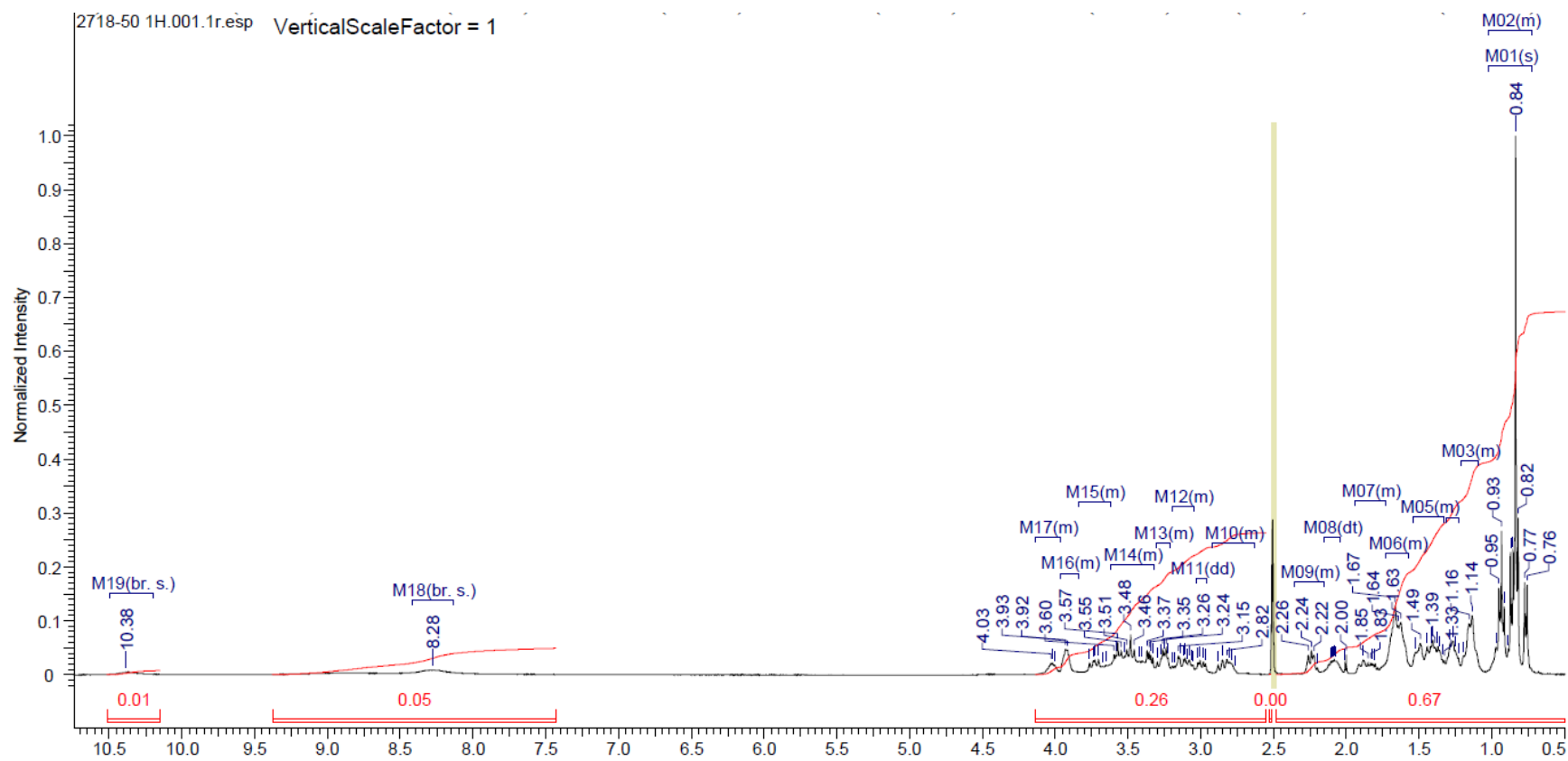


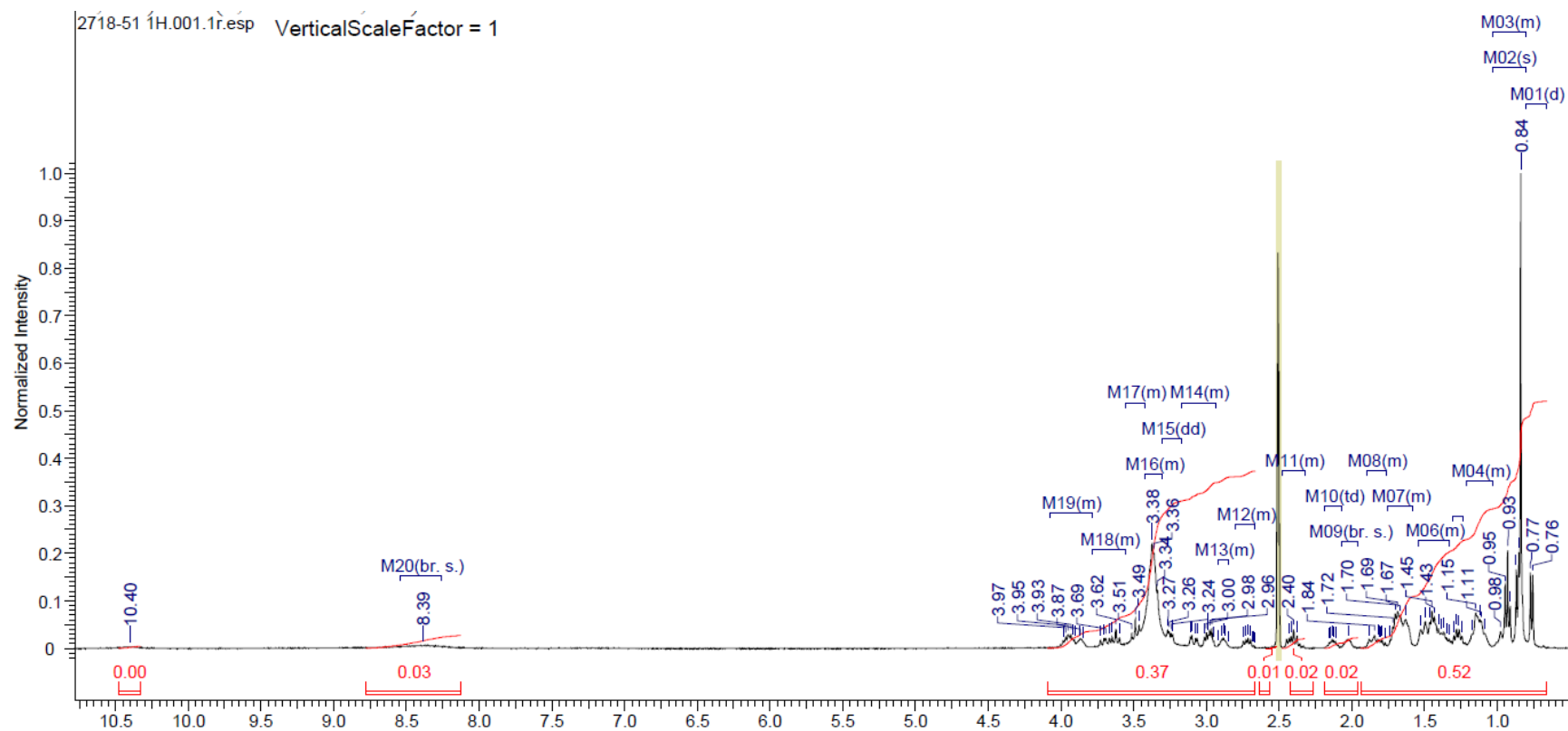


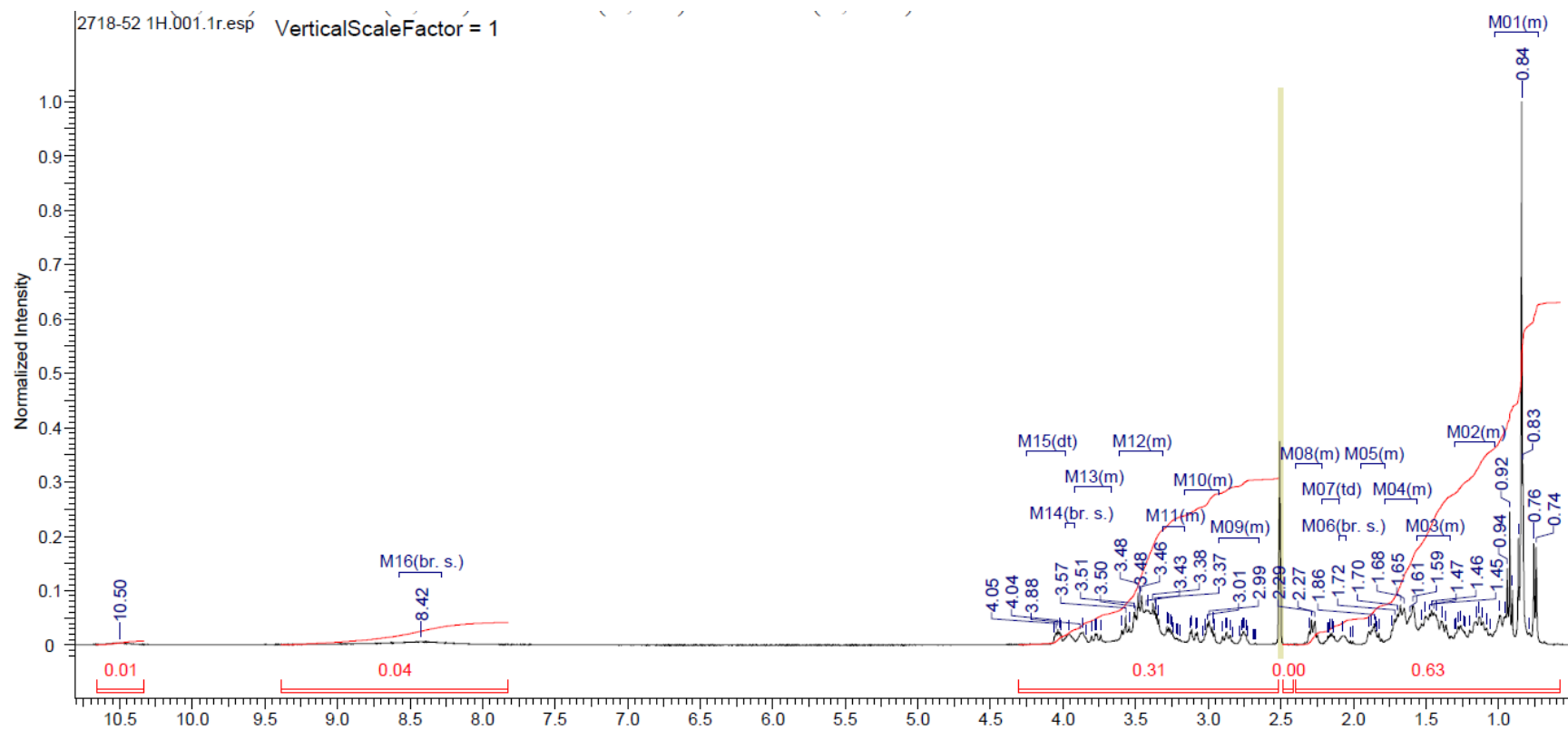


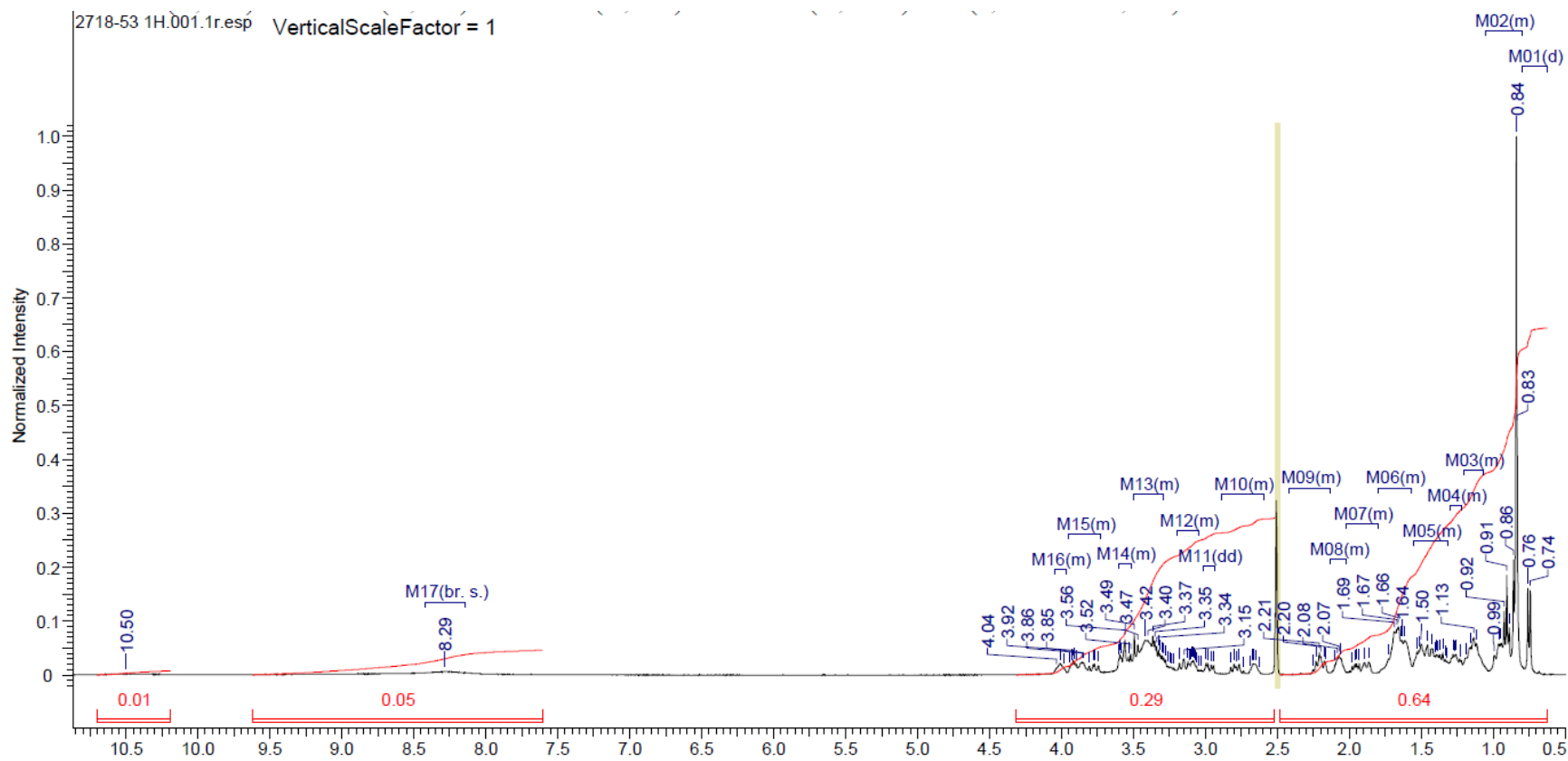


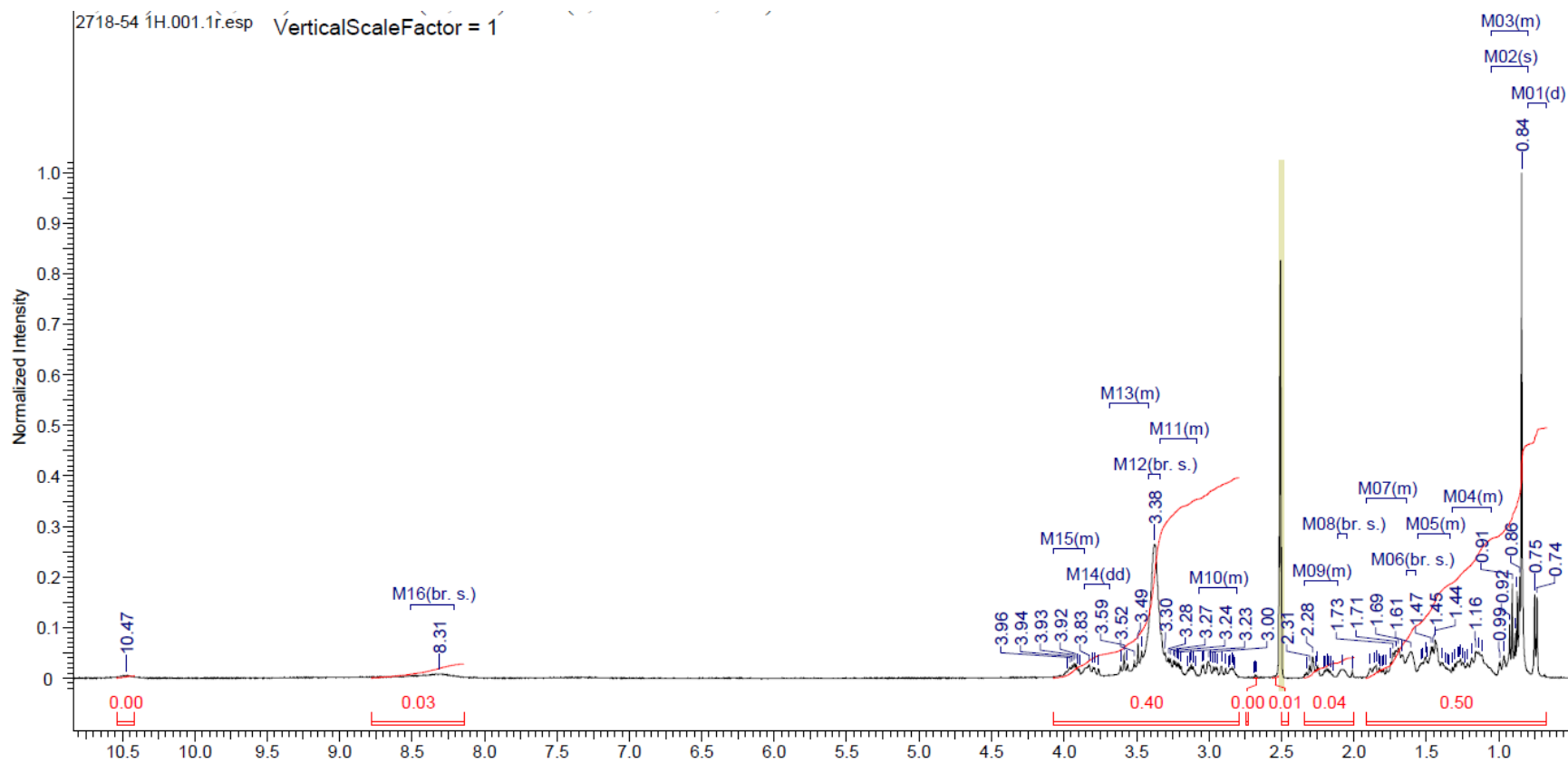


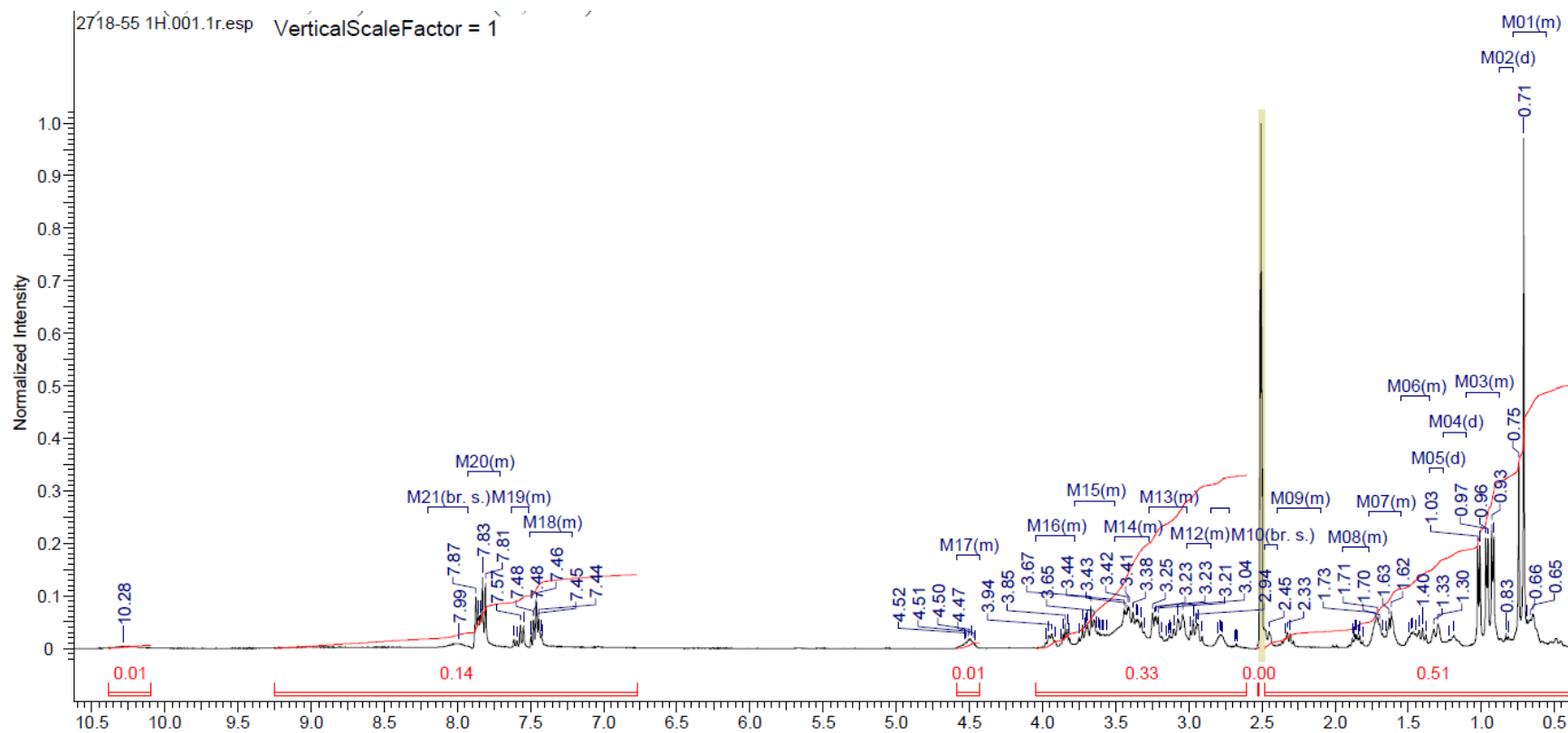












2718-56 1H.001.1r.esp VerticalScaleFactor = 1

