Supporting Information

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Abstract: Self-assembly of short peptides gives rise to versatile nanoassemblies capable of promoting efficient catalysis. We have semi-rationally designed a series of seven-residue peptides that form hemin-binding catalytic amyloids to facilitate enantioselective cyclopropanation with efficiencies that rival those of engineered hemin proteins. These results demonstrate that: 1. Catalytic amyloids can bind complex metallocofactors to promote practically important multisubstrate transformations; 2. Even essentially flat surfaces of amyloid assemblies can impart a substantial degree of enantioselectivity without the need for extensive optimization; 3. The ease of peptide preparation allows for straightforward incorporation of unnatural amino acids and preparation of peptides made of D-amino acids with complete reversal of enantioselectivity.

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Experimental Procedures

Reagents, methods of analysis, and instrumentation. Commercially available chemicals and reagents were used without further purification. Cyclopropanation reactions were carried out under argon in oven-dried glassware with magnetic stirring using standard gas-light syringes, cannula and septa. ^{1}H and ^{13}C NMR spectra were measured on a Bruker DPX-400 spectrometer. Chemical shifts are reported in parts per million (ppm) and are calibrated using residual undeuterated solvent as an internal standard ($CDCl_3$: 7.26 ppm and 77.0 ppm for ^{1}H and ^{13}C NMR, respectively). Purification of chemical compounds was done using Silia Flash® P60 silica gel (40-63 μm, Silicycle). Preparative thin layer chromatography was performed on TLC plates (Merck).

Enantiomeric excess and yields were determined by chiral gas chromatography (GC) using a (30 m x 0.25 mm x 0.25 μm film) Agilent J&W Cyclosil-B column on an Agilent 7820A instrument equipped with an FID detector. The flow rate was set to 5 mL/min for all tested compounds. Injector was in split mode 100:1, injection volume was 1 - 3 μL and injector temperature was set to 250 °C, whereas the detector temperature was set to 300 °C. The conditions for separation of individual product enantiomers can be found in the compound characterization section.

MALDI-TOF mass spectrometry was performed on a Bruker Autoflex III Smartbeam MALDI-TOF mass spectrometer. HPLC purification of peptides was done on a Shimadzu Prominence UFLC instrument equipped with C4 preparative column (Phenomenex), using a linear gradient of solvent A (0.1% TFA in water) and solvent B (90% CH_3CN, 10% H_2O, 0.1% TFA). For peptide analysis HPLC 1260 Agilent Infinity II equipped with an analytical Zorbax Eclipse XDB-C18 column (4.6 mm x 150 mm) was used.

CD spectra were collected on a Jasco J-715 CD spectrometer using continuous scan mode (50 nm/min, 4 s averaging time) in quartz cuvettes with a 0.1 cm pathlength. Each spectrum is an average of three scans. Care was taken so the sample absorbance never exceeded 1.5 at all wavelengths to produce reliable ellipticity values.

UV-Vis measurements were performed on Agilent Cary 60 UV-Vis spectrophotometer using 1 cm quartz cuvette.

TEM measurements were performed on a JEOL 2000EX instrument operated at 120 kV using formvar/carbon-coated, 200-mesh copper grids (Ted Pella, Redding, CA; glow-discharged prior to use) at the N.C. Brown Center for Ultrastructure studies at SUNY-ESF.

EPR measurements were performed on a Bruker EMX EPR spectrometer equipped with a cryostat using 0.2 mW or 2 mW power and frequency 9.39 GHz at 20 K. Each spectrum is an average of four scans.

Preparation of stock solutions. Stock solutions of peptides were prepared from pure (≥95%) lyophilized peptides by dissolving them in DMSO, so the final concentration was 15 mM or 50 mM (for EPR experiments), determined by weight. Hemin stock solutions were also prepared in DMSO, so the final concentration was 2 mM or 5 mM.
For CD spectroscopy, peptide stocks were prepared in 10 mM HCl. Concentration of peptides was calculated using the absorbance at 214 nm and the extinction coefficients calculated for peptides[1] ε_{214} (Table S1).

Table S1. Extinction coefficients of peptides used for this paper.

Peptide Sequence	Extinction coefficient, $M^{-1}cm^{-1}$
Ac-LHLHLFL-NH_2	22091
Ac-LHLALFL-NH_2	16988
Ac-LALHLFL-NH_2	16988
Ac-LHLFLFL-NH_2	22166
Ac-LFLHLFL-NH_2	22166
Ac-LTLHLFL-NH_2	17007
Ac-LLLHLFL-NH_2	17011
Ac-LGLHLFL-NH_2	16987
Ac-LVLHLFL-NH_2	17009
Ac-LMLHLFL-NH_2	17946
Ac-LILHLFL-NH_2	17011
(D)-Ac-LILHLFL-NH_2	17011
Ac-AHAHAFA-NH_2	22039
Ac-LHLH(L-NMe)-NH_2	22091
Ac-LHL(3Me-H)LFL-NH_2	22091

Hemin binding studies by UV-Vis spectroscopy. Working solutions of hemin or peptide-hemin were prepared by mixing hemin and peptide stock solutions with subsequent dilution with 100 mM pH 7 phosphate buffer to a desired concentration of peptide and hemin. The final DMSO amount was always kept below 2% (v/v). Samples were incubated for 24 hours prior to any experiment.

The stoichiometry of the Ac-LILHLFL-NH_2 -hemin binding was obtained from a Job plot (Figure S3c). The stocks of the peptide and hemin were mixed in different ratios so the total concentration of the peptide (as monomer) and the hemin in working solutions was 20 μM. Absorbance at 422 nm was used to construct a Job's plot.

Additionally, we titrated hemin (4 μM and 20 μM in two separate experiments) with Ac-LILHLFL-NH_2. Resulting absorbance at 422 nm was plotted against ratio of peptide to hemin and fitted (in the case of lower hemin concentration) to the modified equation reported by Fry and co-workers using Origin 9.5 software.[1]

$$\mathbf{A} = \mathbf{A_0} + \frac{\boldsymbol{\varepsilon_B l}}{\mathbf{2}} \times \left(\left(\frac{\mathbf{x}}{\mathbf{n}} \times \mathbf{M} + \mathbf{K_d} + \mathbf{M} \right) - \sqrt{\left(\frac{\mathbf{x}}{\mathbf{n}} \times \mathbf{M} + \mathbf{K_d} + \mathbf{M} \right)^2 - \mathbf{4} \times \frac{\mathbf{x}}{\mathbf{n}}} \right) \quad \text{(S1)}$$

where A_0, initial absorption; ε_B, extinction of bound hemin; x, ratio of peptide to hemin; n, set stoichiometry of peptide to heme, determined from Job plot and titrations of high hemin concentrations with peptide; K_d, dissociation constant; M, molar concentration of hemin; l, cuvette pathlength.

Determination of peptide secondary structure and hemin binding studies using CD spectroscopy. Peptide stock solutions in 10 mM HCl were diluted with 100 mM pH 7 phosphate buffer, so the final concentration of peptide was 50 μM. For CD spectra of the Soret band stocks of peptides in DMSO were mixed with hemin stock in DMSO and then diluted with same buffer to a desired concentration. CD spectra were taken after 24 hours of incubation.

EPR studies. For EPR experiments stock solutions of hemin (5 mM in DMSO) and peptide (50 mM in DMSO, freshly prepared) were mixed and then diluted with 100 mM pH 7 phosphate buffer to obtain a sample with 125 μM hemin and 935 μM peptide. After a 24 hour incubation, glycerol was added to the sample to a final concentration of 10% v/v, the sample was frozen and) and immediately used for EPR measurements.

TEM imaging. Hemin and peptide stocks were mixed in a 1:10 ratio (hemin:peptide) and then diluted with 100 mM pH 7 phosphate buffer. The samples were incubated for 24 hours and deposited onto carbon-coated copper grids, followed by application of staining

solution of 2% uranil acetate for 1 minute. The grids were carefully washed with deionized water and dried overnight prior to the imaging.

Cyclopropanation reactions setup. Reactions were carried out on a 500 µL scale. Initially, 100 mM pH 7 phosphate buffer was degassed under vacuum and kept under argon in a flask with a septum. To prepare catalyst, in a sealed vial 15 mM DMSO stock of peptide (5 µL) and 5 mM stock of hemin (2.5 µL) were mixed, diluted with the degassed buffer, so the final volume was 455 µL. Separately, solid $Na_2S_2O_4$ was placed in a vial equipped with septa and flushed with argon. Next, sodium dithionite was dissolved in degassed 100 mM phosphate buffer pH 7 under argon and kept on ice until necessary.
25 µL of sodium dithionite solution were added to the catalyst using a gas-tight syringe and the mixture was stirred for 1 minute. After that 10 µL of 0.4 M styrene in degassed ethanol were added followed by 10 µL of 1.2 M ethyl diazoacetate (EDA) in same solvent, so the final concentrations of the reagents were: 8 mM styrene, 24 mM EDA, 20 µM hemin and 150 µM peptide. Reaction mixture was stirred under positive argon pressure for 1 hour.

Cyclopropanation reactions workup and analysis. After 1 hour, 25 µL of each internal standard (100 mM anisole and 100 mM acetophenone) in ethylacetate were added to the reaction mixture, followed by extraction with 950 µL of ethylacetate. Organic layer was separated, dried with sodium sulfate and analyzed by GC. Calibration curves were prepared by GC analysis of the standard mixtures (*cis*- and *trans*- enantiomers of the corresponding cyclopropanes, see **Synthetic procedures** for detailed preparation protocols) with internal standards.

Kinetic experiments. To determine kinetic parameters we determined initial rates of the reaction by measuting the concentration of products after 2 minutes. This time point was experimentally determined from an extended kinetic trace of the reaction, where the yield of the product was determined at various time points (Figure S36). Reaction conditions were as described in **Cyclopropanation reactions setup**. Four stock solutions of 4-(trifluoromethyl)styrene in ethanol with concentrations of 0.4 M, 0.2 M, 0.1 M and 0.05 M were used in the experiment. Four stock solutions of EDA in ethanol with concentrations 1.2 M, 0.5 M, 0.25 M and 0.125 M were also prepared. 10 µL of 4-(trifluoromethyl)styrene stock solution was added to the reaction mixture followed by 10 µL of EDA stock solution. Final concentrations of 4-(trifluoromethyl)styrene were 1, 2, 4 and 8 mM. Final concentrations of EDA were 2.5, 5, 10 and 24 mM. Reaction mixture was stirred under positive argon pressure for 2 minutes. After that reaction was quenched by adding 30 µL of 3 M HCl. Finally, workup and analysis of the reaction mixtures were performed as described in **Cyclopropanation reactions workup and analysis** section. The initial rates of the reactions were globally fit to the ping-pong kinetic model (Eq. (S2)) using Origin 9.5 software:

$$\mathbf{v_0} = \frac{\mathbf{k_{cat}}\times[\mathbf{4-CF_3-styrene}]\times[\mathbf{EDA}]}{(\mathbf{K_M(EDA)}\times[\mathbf{4-CF_3-styrene}]+\mathbf{K_M(4-CF_3-styrene)}\times[\mathbf{EDA}]+[\mathbf{4-CF_3-styrene}]\times[\mathbf{EDA}])\times[\boldsymbol{hemin_p}]} \quad \text{(S2)}$$

where k_{cat} is the turnover rate of the reaction; [4-CF_3-styrene] is initial concentration of 4-(trifluoromethyl)styrene; [EDA], initial concentration of ethyl diazoacetate; [$hemin_p$], concentration of hemin; K_M(EDA) is the Michaelis constant for ethyl diazoacetate; K_M(4-CF3-stryrene) is the Michaelis constant for 4-(trifluoromethyl)styrene.

Synthetic Procedures

Peptide synthesis and purification. The peptides were synthesized by manual fluorenylmethyloxycarbonyl (Fmoc) solid phase synthesis at 60 °C using Rink Amid resin (Chem-Impex International). The resin was swelled in DMF then deprotected using 20% piperazine in DMF for 5 minutes. Each step consisted of 1. Fmoc-deprotection with 20% piperazine in DMF for 5 minutes; 2. washing with DMF four times; 3. coupling of the amino acid in the presence of HCTU [2-(6-chloro-1H-benzotriazol-1-yl)-1,1,3,3-tetramethylaminium-hexafluorophosphate] and DIEA (N,N-diisopropylethylamine) (AA:HCTU:DIEA:resin 3:2.8:6:1); 4. washing with DMF twice. Each amino acid coupling step took 7 minutes. Cleavage of the peptides from resin and simultaneous side chain deprotection was achieved by treatment with a mixture of trifluoroacetic acid (TFA)/H_2O/triethylsilane (TES) (95:2.5:2.5, v/v) for 2 hours at room temperature. The crude peptides were precipitated and washed thrice with cold methyl *tert*-butyl ether, then purified on a preparative reverse phase HPLC system. Purified peptides were lyophilized and their identities were confirmed by MALDI-TOF mass spectrometry and analytical HPLC.

Synthesis of cyclopropanes for GC calibration.[2] To obtain calibration curves for each product of cyclopropanation, we prepared standards using reaction of corresponding styrenes with EDA in the presence of $Pd(AcO)_2$. Briefly, to oven-dried round bottom flask 0.2 eq of $Pd(OAc)_2$ and 10 eq. of styrene were added under argon followed by dropwise addition of 1 eq. of EDA. The mixture was stirred under argon at room temperature for 3 hours followed by purification2 by column chromatography using hexane-ethyl acetate as eluent (from 90:10 to 70:30). Pure fractions were combined and solvents were removed on rotary evaporator. The residue was dried *in vacuo* leading to the products as colorless liquids. The identity of the products was confirmed by ^1H and ^{13}C NMR and was in full accordance with literature reports.

Ethyl 2-phenylcyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

Yield = 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 - 1.35 (m, 4 H) 1.49 - 1.71 (m, 1 H) 1.88 - 2.1 (m, 1 H) 2.47 - 2.63 (m, 1 H) 3.8 - 4.14 (m, 2 H) 7.02 - 7.11 (m, 2 H) 7.13 - 7.20 (m, 1 H) 7.20 - 7.30 (m, 2 H). 13C NMR (101 MHz, CDCl3) δ 11.07, 13.99, 14.24, 17.03, 21.78, 24.15, 25.43, 26.14, 60.13, 60.67, 126.14, 126.44, 126.60, 127.85, 128.44, 129.28, 136.55, 140.11, 170.93, 173.38.
GC separation gradient: column temperature set at 100 ºC for 5 min, then to 135 ºC at 1.5 ºC/min and was hold at this temperature for 11 minutes, then to 190 ºC at 20 ºC/min. Total run time was 46 min.

Ethyl 2-(4-acetoxyphenyl)cyclopropanecarboxylate[3] (mixture of *cis*- and *trans*- isomers)

Yield = 75%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, *J*=7.15 Hz, 1 H) 1.21 - 1.39 (m, 3 H) 1.52 - 1.74 (m, 1 H) 1.88 - 2.16 (m, 1 H) 2.29 (m, 3 H) 2.47 - 2.61 (m, 1 H) 3.89 (m, 1 H) 4.18 (q, *J*=7.09 Hz, 1 H) 6.95 - 7.06 (m, 2 H) 7.06 - 7.15 (m, 1 H) 7.23 - 7.34 (m, 1 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 11.30, 13.97, 14.21, 16.88, 21.04, 21.08, 21.86, 24.07, 24.82, 25.58, 60.23, 60.70, 120.91, 121.53, 127.22, 130.19, 134.16, 137.66, 149.18, 149.33, 169.39, 169.50, 170.82, 173.23.
GC separation gradient: column temperature set at 100 ºC for 4 min, then to 175 ºC at 0.7 ºC/min, then to 200 ºC at 25 ºC/min. Total run time was 112 min.

Ethyl-2-(4-chlorophenyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

Yield = 82%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.03 (t, *J*=7.09 Hz, 1 H) 1.21 - 1.41 (m, 3 H) 1.57 - 1.73 (m, 1 H) 1.78 - 1.98 (m, 1 H) 2.41 - 2.62 (m, 1 H) 3.91 (q, *J*=7.13 Hz, 1 H) 4.18 (q, *J*=7.09 Hz, 1 H) 7.04 (d, *J*=8.44 Hz, 1 H) 7.12 - 7.27 (m, 3 H) ^{13}C NMR (101 MHz, $CDCl_3$) δ 11.24, 14.02, 14.18, 16.91, 21.75, 24.09, 24.73, 25.40, 60.23, 60.71, 127.49, 127.94, 128.48, 130.55, 132.09, 132.32, 135.04, 138.57, 170.64, 173.00.
GC separation gradient: column temperature set at 85 ºC for 3 min, then to 160 ºC at 0.5 ºC/min. Total run time was 153 min.

Ethyl-2-[4-(trifluoromethyl)phenyl]cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

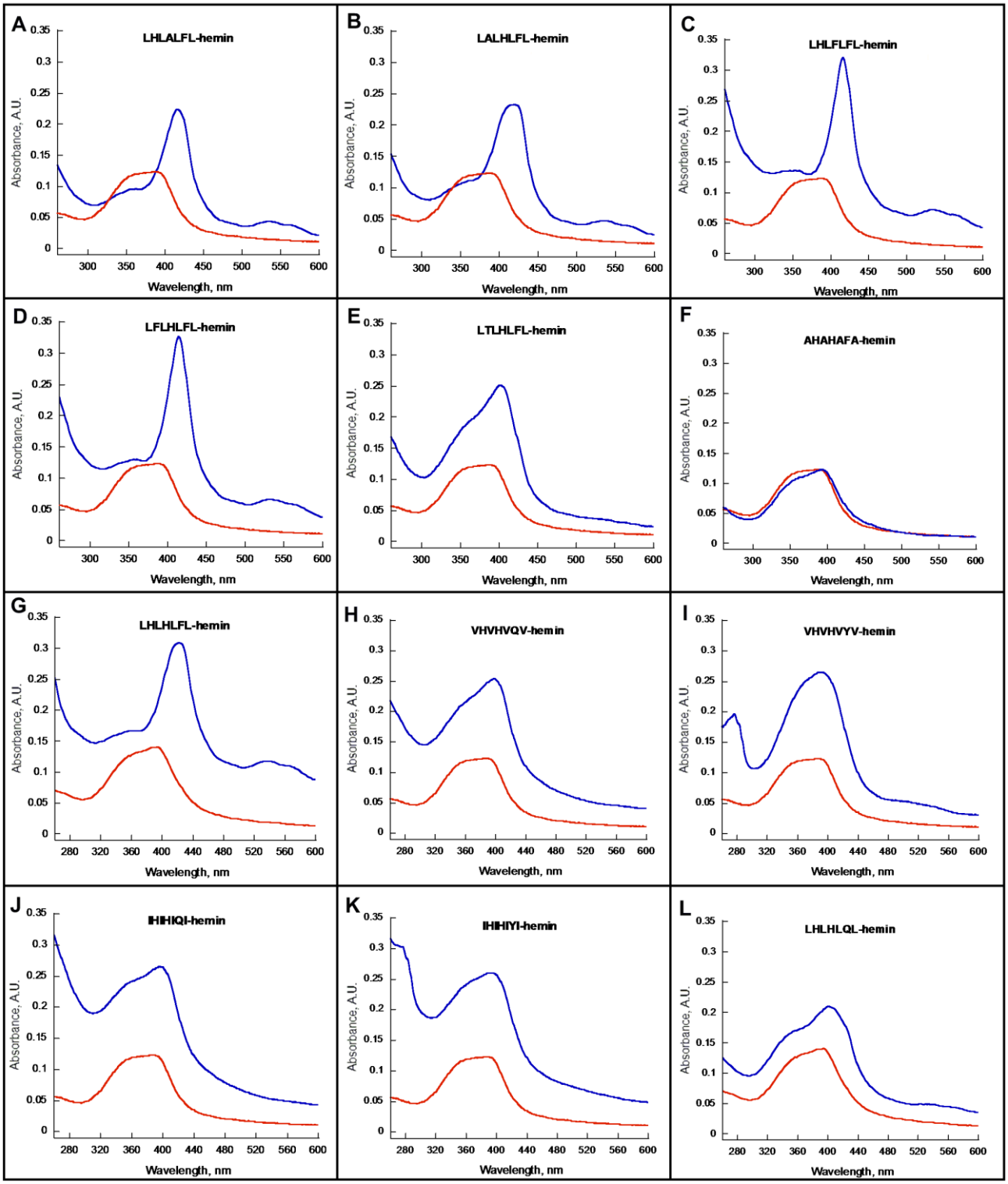
Yield = 72%, purity 90%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (t, *J*=7.15 Hz, 1 H) 1.20 - 1.48 (m, 3 H) 1.61 - 1.81 (m, 1 H) 1.90 - 2.05 (m, 1 H) 2.49 - 2.67 (m, 1 H) 3.90 (m, 1 H) 4.19 (q, *J*=7.13 Hz, 1 H) 7.20 (d, *J*=8.19 Hz, 1 H) 7.39 (d, *J*=8.19 Hz, 1 H) 7.53 (dd, *J*=8.01, 4.22 Hz, 2 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 11.31, 13.93, 14.16, 17.23, 21.97, 24.47, 25.04, 25.63, 60.35, 60.86, 124.68-124.80, 125.30 - 125.41, 126.38, 129.59, 140.78, 144.35, 144.36, 170.54, 172.81.
GC separation gradient: column temperature set at 87 ºC for 4 min, then to 145 ºC at 1 ºC/min, then to 185 ºC at 20 ºC/min. Total run time was 69 min.

Ethyl-2-(m-tolyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

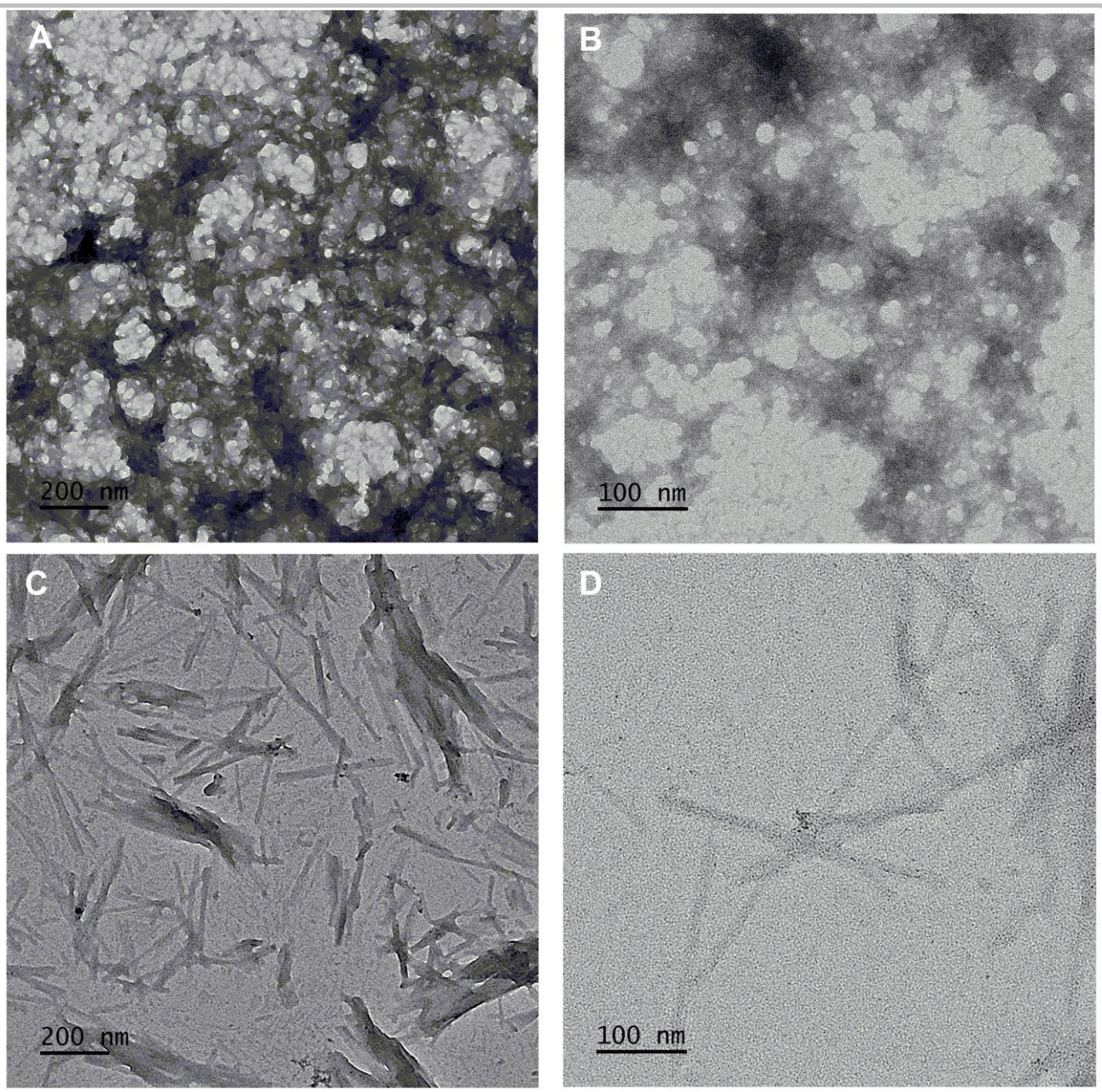
Yield = 62%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (t, *J*=7.09 Hz, 1 H) 1.21 - 1.39 (m, 3 H) 1.49 - 1.72 (m, 1 H) 1.90 - 2.10 (m, 1 H) 2.24 - 2.39 (m, 3 H) 2.42 - 2.62 (m, 1 H) 3.90 - 4.18 (m, 2 H) 6.85 - 6.96 (m, 1 H) 6.96 - 7.24 (m, 3 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 11.05, 13.99, 14.23, 16.94, 21.30, 21.32, 21.65, 24.06, 25.36, 26.09, 60.07, 60.60, 123.11, 126.26, 126.94, 127.18, 127.35, 127.72, 128.33, 130.09, 136.45, 137.27, 138.04, 140.03, 170.97, 173.41.
GC separation gradient: column temperature set at 100 ºC for 4 min, then to 140 ºC at 1.2 ºC/min, then to 150 ºC at 0.75 ºC/min, then to 170 ºC at 20 ºC/min. Total run time was 55 min.

Ethyl-2-methyl-2-phenylcyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

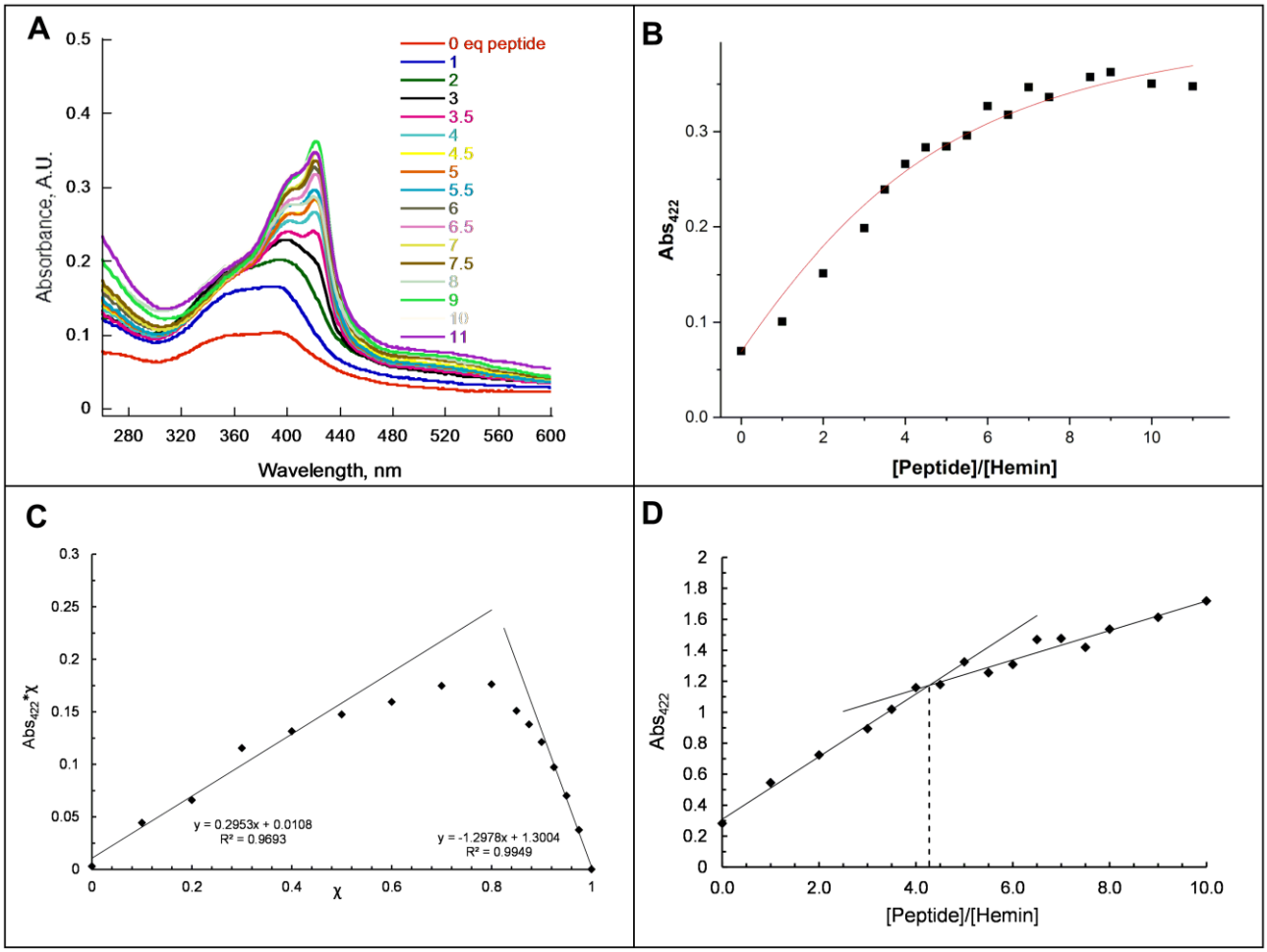
Yield = 70%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, *J*=7.09 Hz, 1 H) 1.16 (dd, *J*=7.76, 4.58 Hz, 1 H) 1.31 (t, *J*=7.15 Hz, 2 H) 1.40 - 1.46 (m, 1 H) 1.48 - 1.54 (m, 2 H) 1.87 - 2.02 (m, 2 H) 3.76 - 4.25 (m, 2 H) 7.24 (s, 1 H) 7.27 - 7.34 (m, 4 H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 13.95, 14.10, 14.41, 19.42, 19.87, 20.78, 27.86, 28.54, 30.55, 32.03, 60.04, 60.49, 126.43, 126.62, 127.29, 128.14, 128.43, 128.75, 133.62, 141.90, 145.92, 171.23, 172.18.
GC separation gradient: column temperature set at 87 ºC for 4 min, then to 136 ºC at 1.0 ºC/min, then to 170 ºC at 20 ºC/min. Total run time was 59 min.



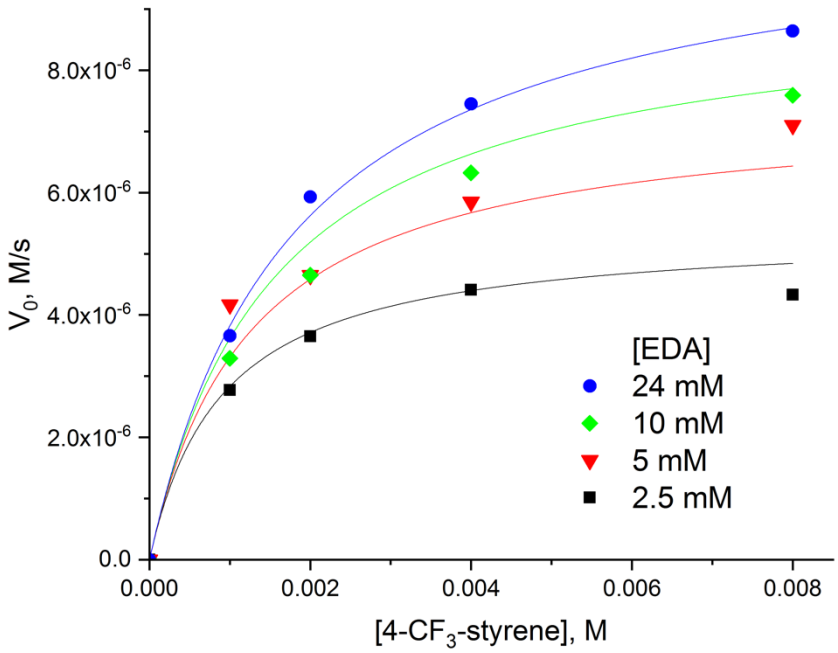
Supplementary Figure S1. UV-Vis spectra of 30 μM peptide mixed with 4 μM hemin in 100 mM phosphate buffer at pH 7 (blue trace) and 4 μM hemin in same buffer (red trace). Spectra were taken after 24 hours of incubation.



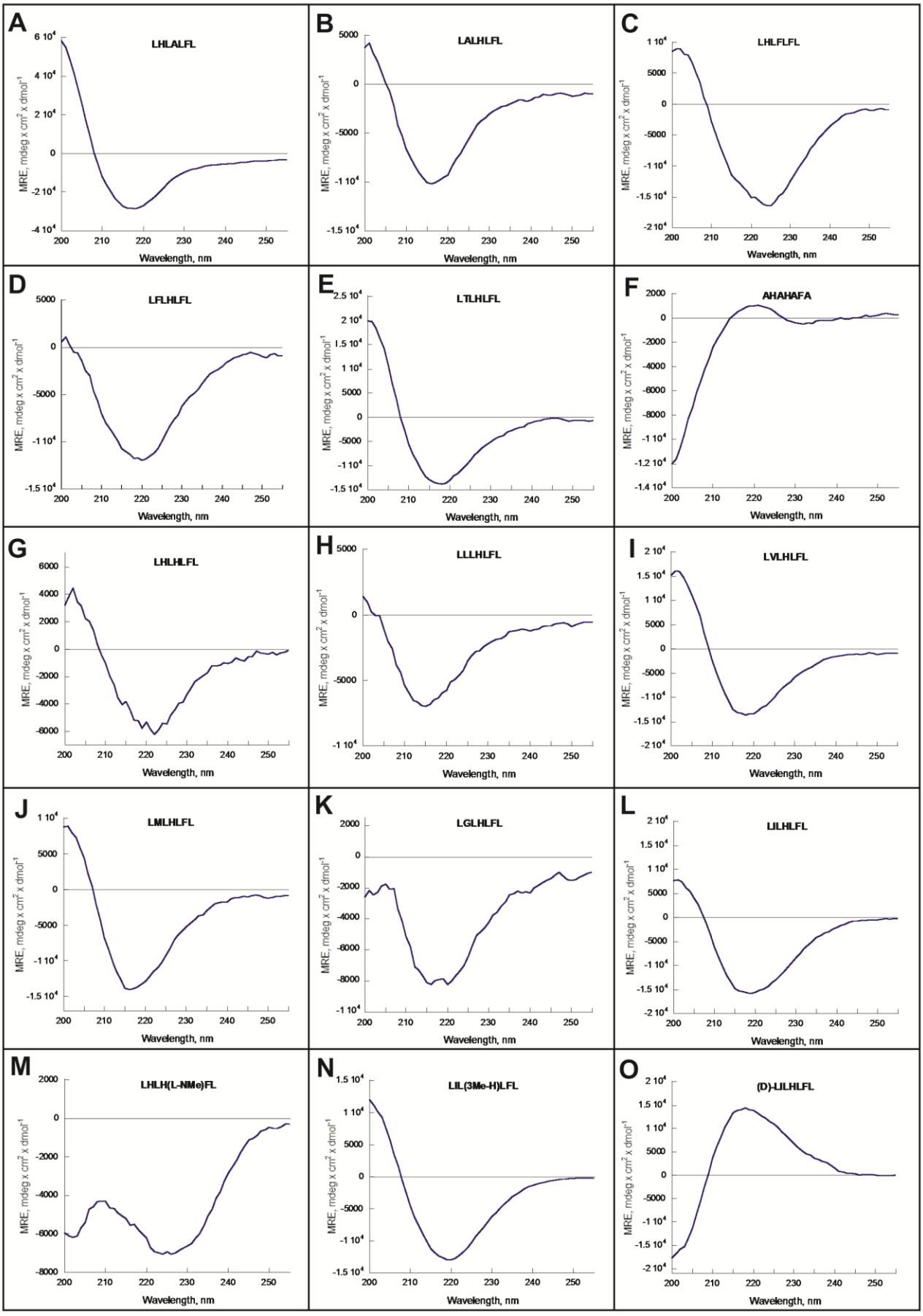
Supplementary Figure S2. Representative TEM image of (A,B) 100 μM Ac-LHLHLFL-$CONH_2$ with 10 μM hemin and (C,D) 100 μM of (D)-Ac-LILHLFL-NH_2 with 10 μM hemin. Samples were incubated for 24 hours in 100 mM pH 7 phosphate buffer prior to the deposition onto the grids.



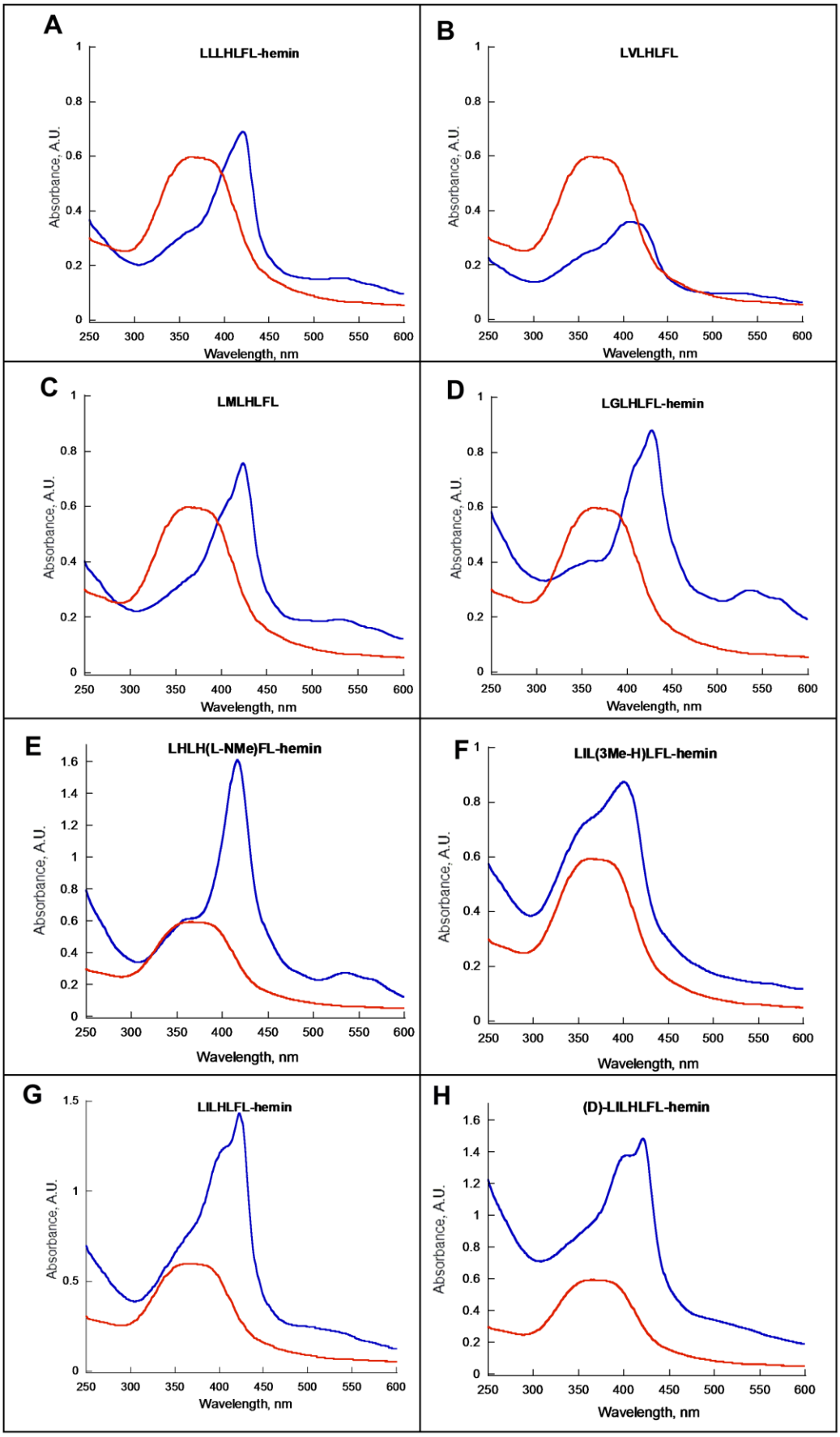
Supplementary Figure S3. (A) UV-Vis spectra of 4 μM hemin titrated with various amounts of Ac-LILHLFL-$CONH_2$ (B) Plot of Ac-LILHLFL-$CONH_2$-hemin absorbance maxima *vs*. peptide/hemin ratio (equivalents of the added peptide). Red trace represents the binding constant analysis fit and was obtained in Origin v9.5 by applying Equation S1. (C) Job plot – absorbance at 422 nm of 20 μM mixtures of hemin and peptide *vs*. mole fraction of peptide χ. (D) UV-Vis spectra of 20 μM hemin titrated with various amounts of Ac-LILHLFL-$CONH_2$. All samples were prepared in 100 mM pH 7 phosphate buffer and spectra were taken after 24 hours of incubation.



Supplementary Figure S4. Plot of initial rates of 4-(trifluoromethyl)styrene cyclopropanation catalysed by Ac-LALHLFL-NH_2-hemin complex (20 μM hemin and 150 μM peptide) at pH 7 in 100 mM phosphate buffer. Reactions were performed using various concentrations of both EDA and 4-(trifluoromethyl)styrene. Resulting rates were plotted in Origin v9.5 and globally fitted by applying Equation S2.



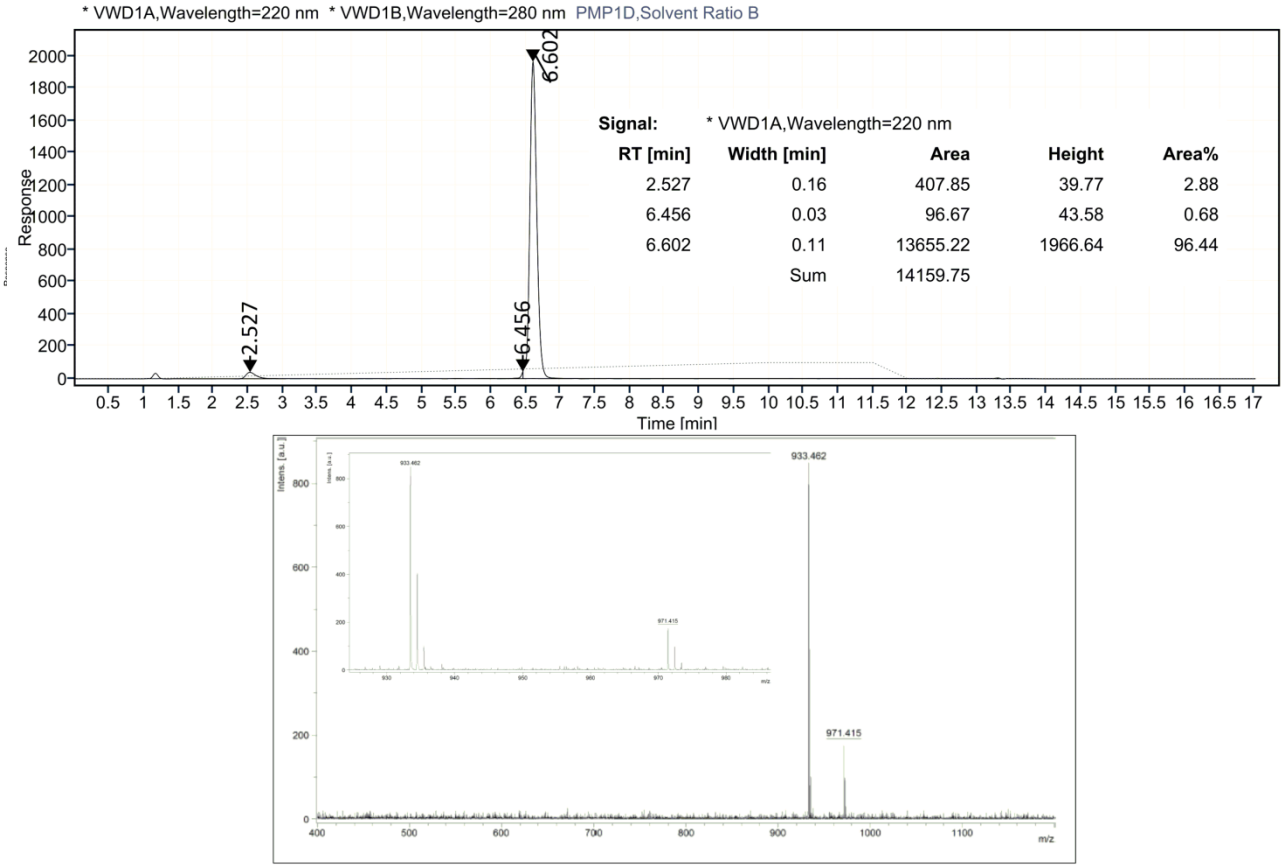
Supplementary Figure S5. (A)-(O) CD spectra of 50 μM peptides in 100 mM pH 7 phosphate buffer taken after 24 hours of incubation.



Supplementary Figure S6. (A)-(H) UV-Vis spectra of 20 μM hemin mixed with 150 uM of peptide (blue trace) and hemin alone (red trace). All measurements were conducted at pH 7 in 100 mM phosphate buffer after 24 hour of incubation.

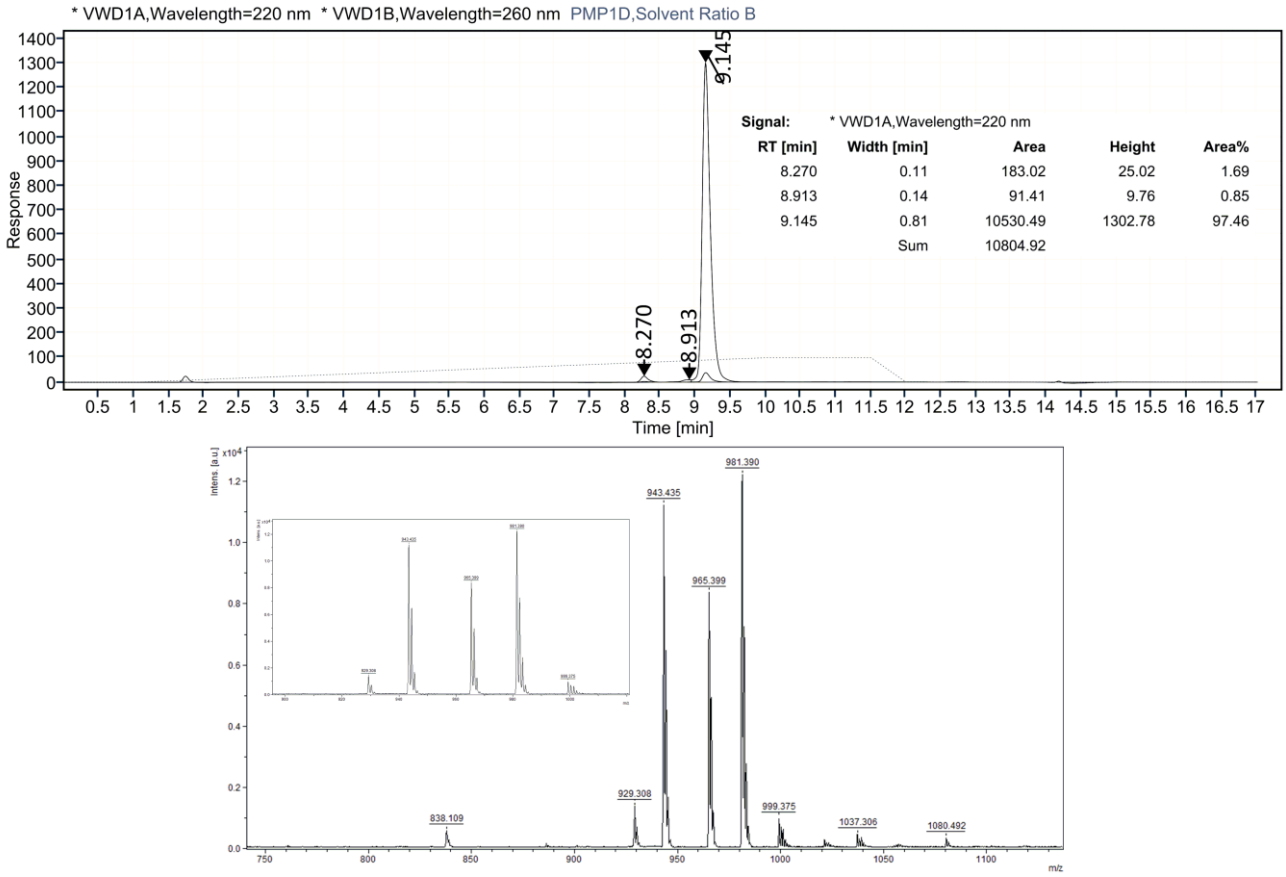
HPLC traces and MALDI spectra of peptides

Ac-LHLHLFL-NH_2



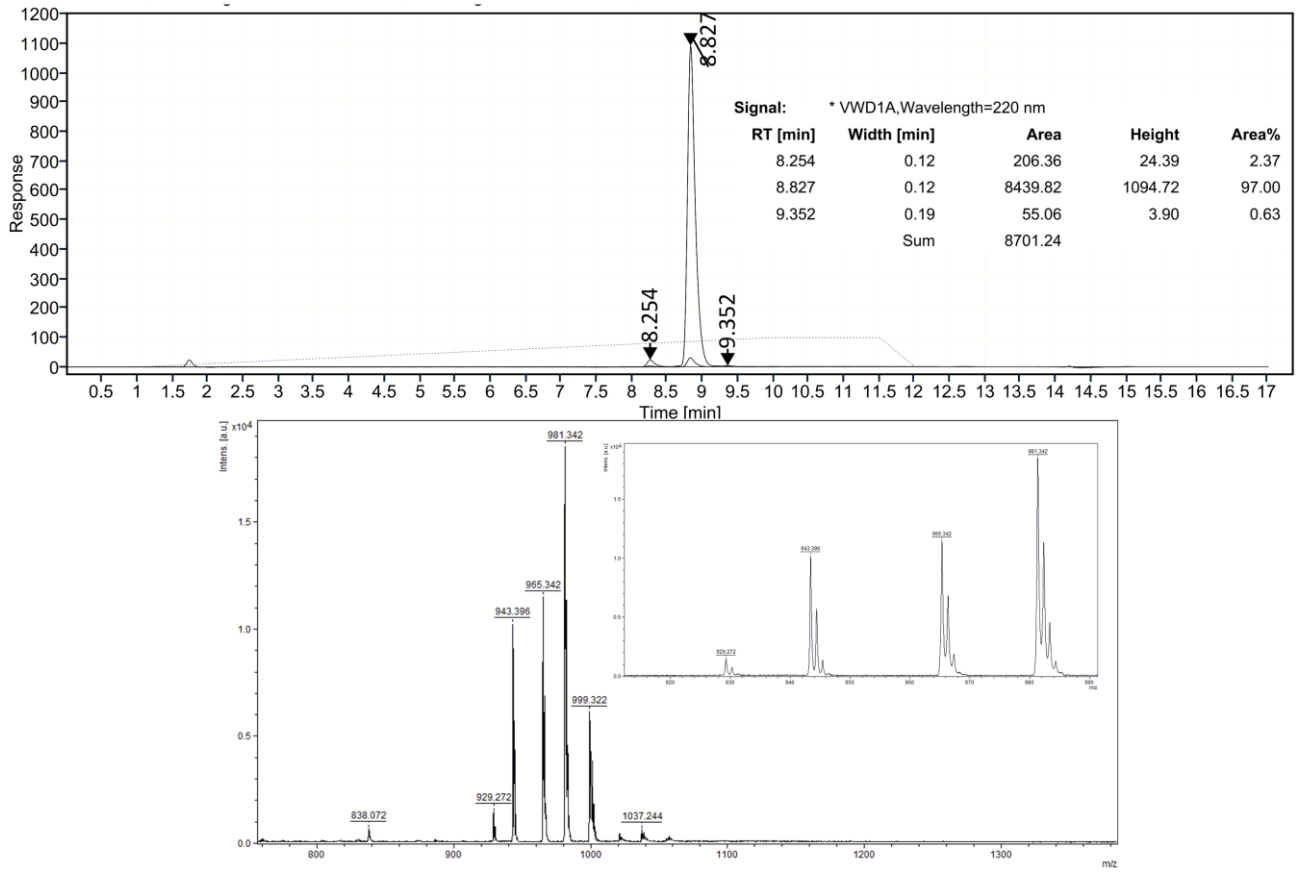
Supplementary Figure S7. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LHLHLFL-NH_2.

Ac-LFLHLFL-NH_2



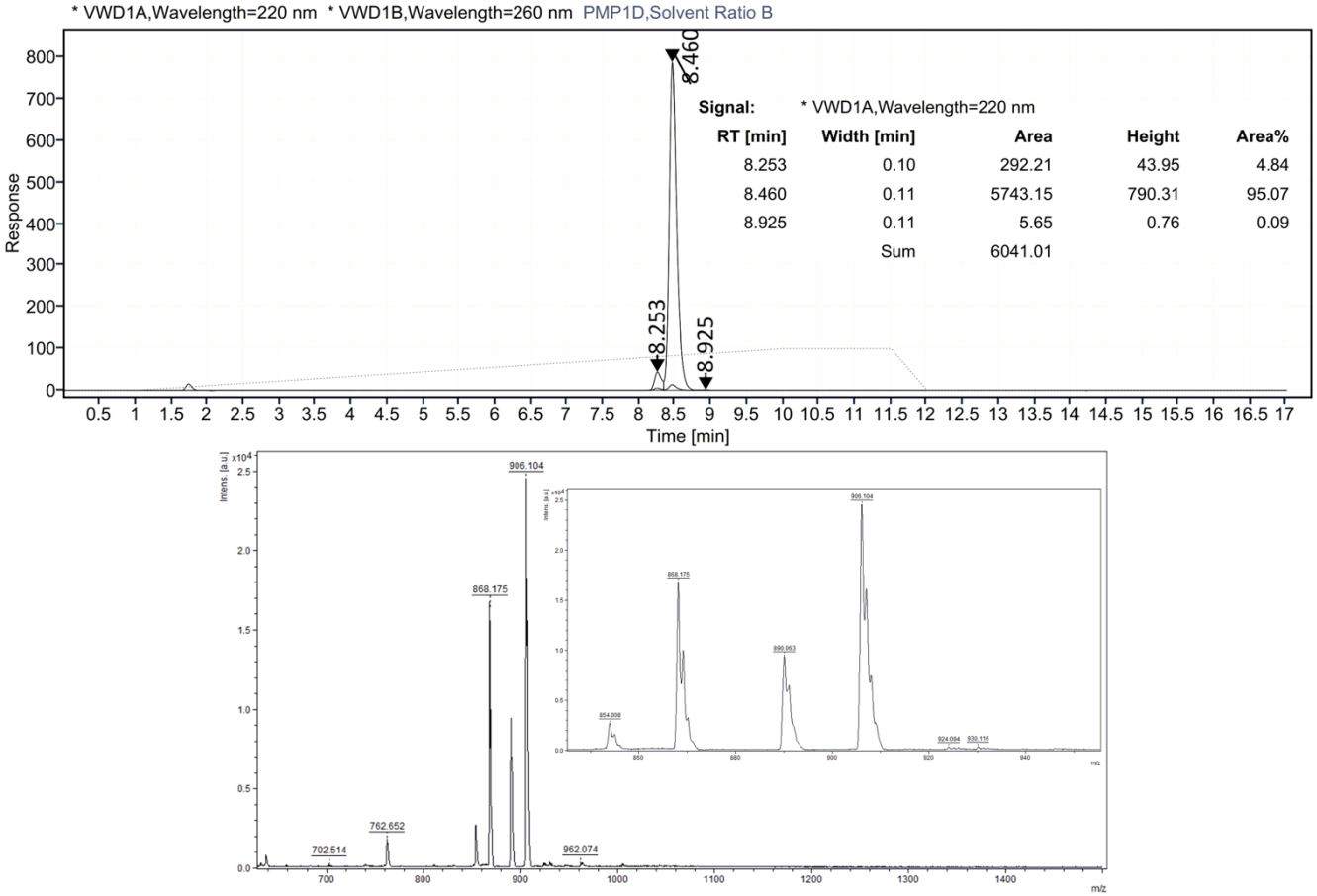
Supplementary Figure S8. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LFLHLFL-NH_2.

Ac-LHLFLFL-NH_2



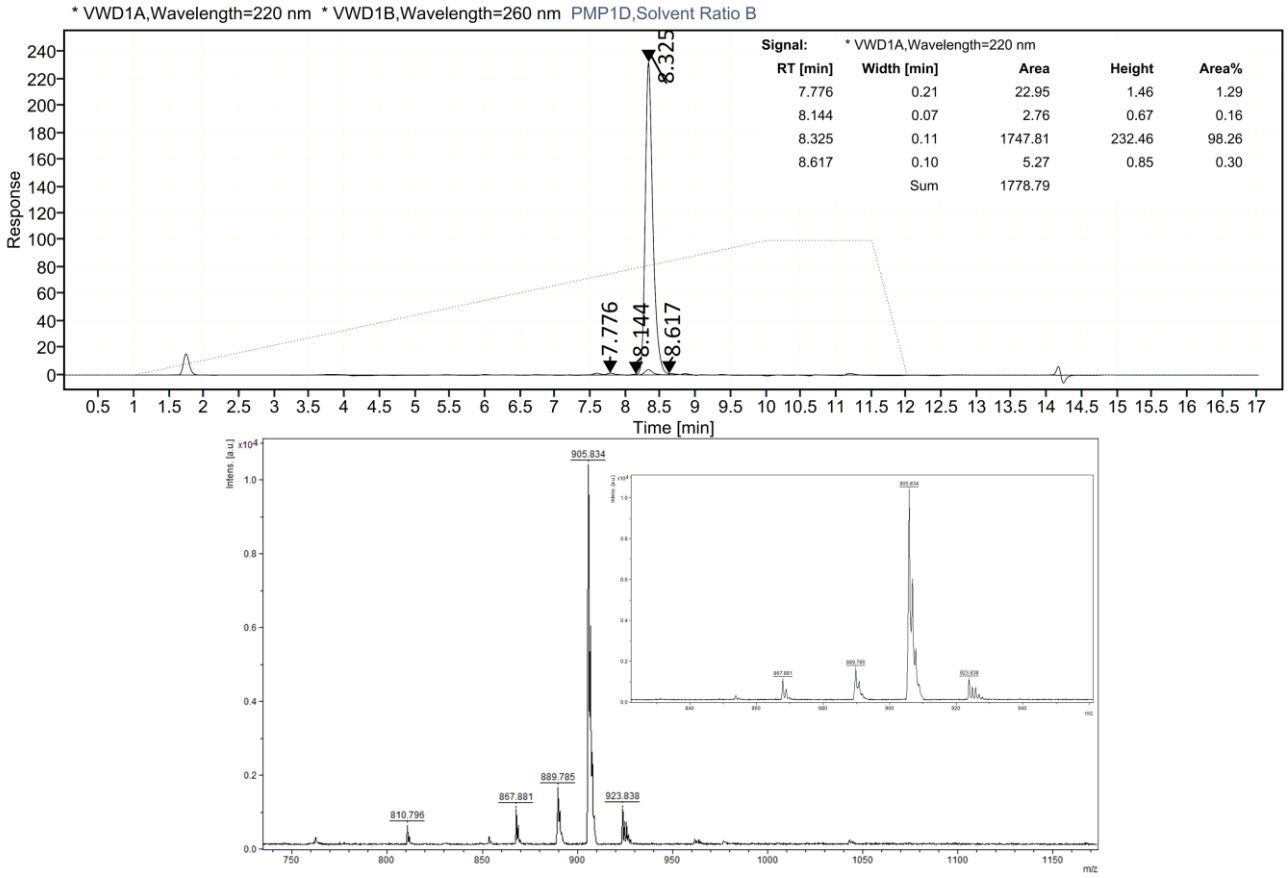
Supplementary Figure S9. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LHLFLFL-NH_2.

Ac-LALHLFL-NH_2



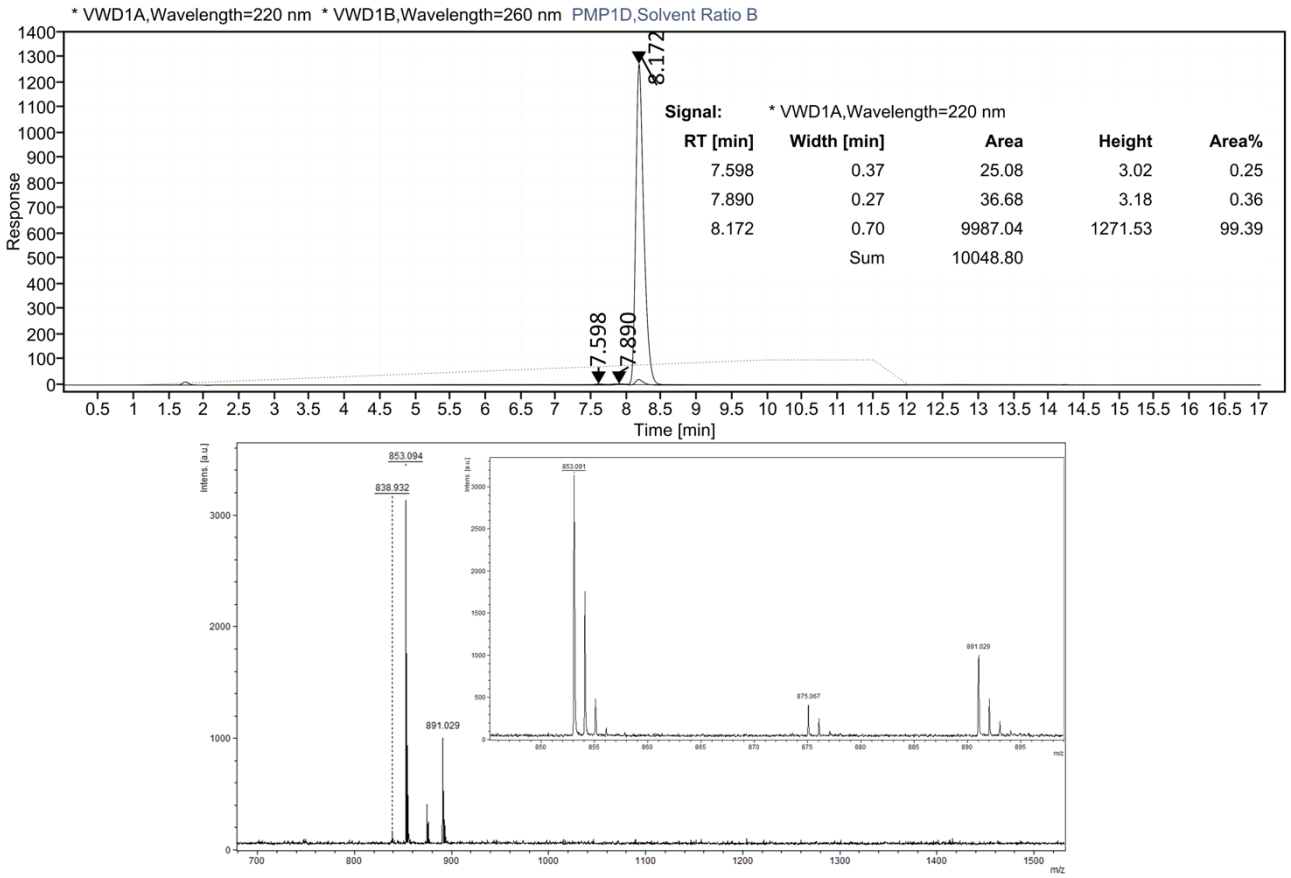
Supplementary Figure S10. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LALHLFL-NH_2.

Ac-LHLALFL-NH_2



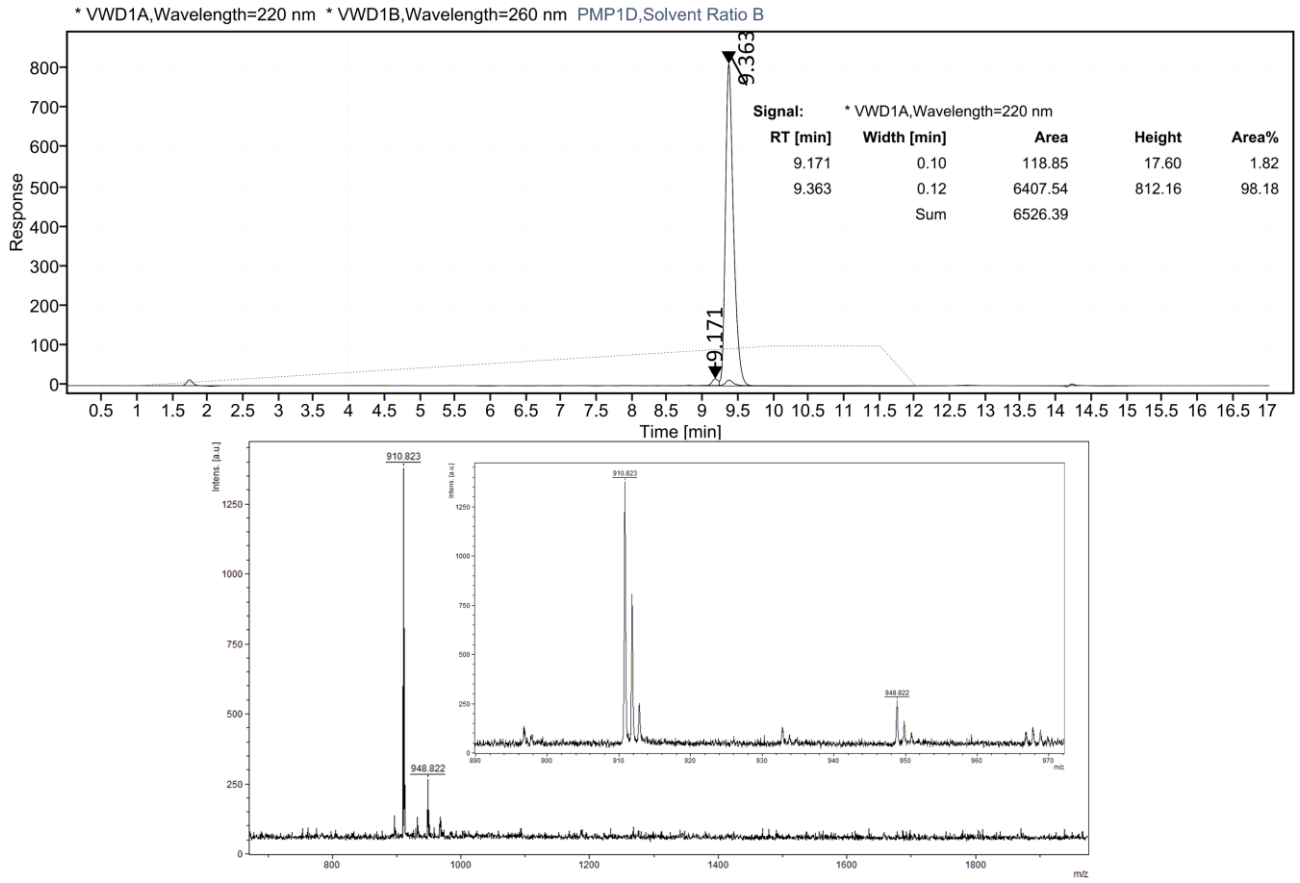
Supplementary Figure S21. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LHLALFL-NH_2.

Ac-LGLHLFL-NH_2



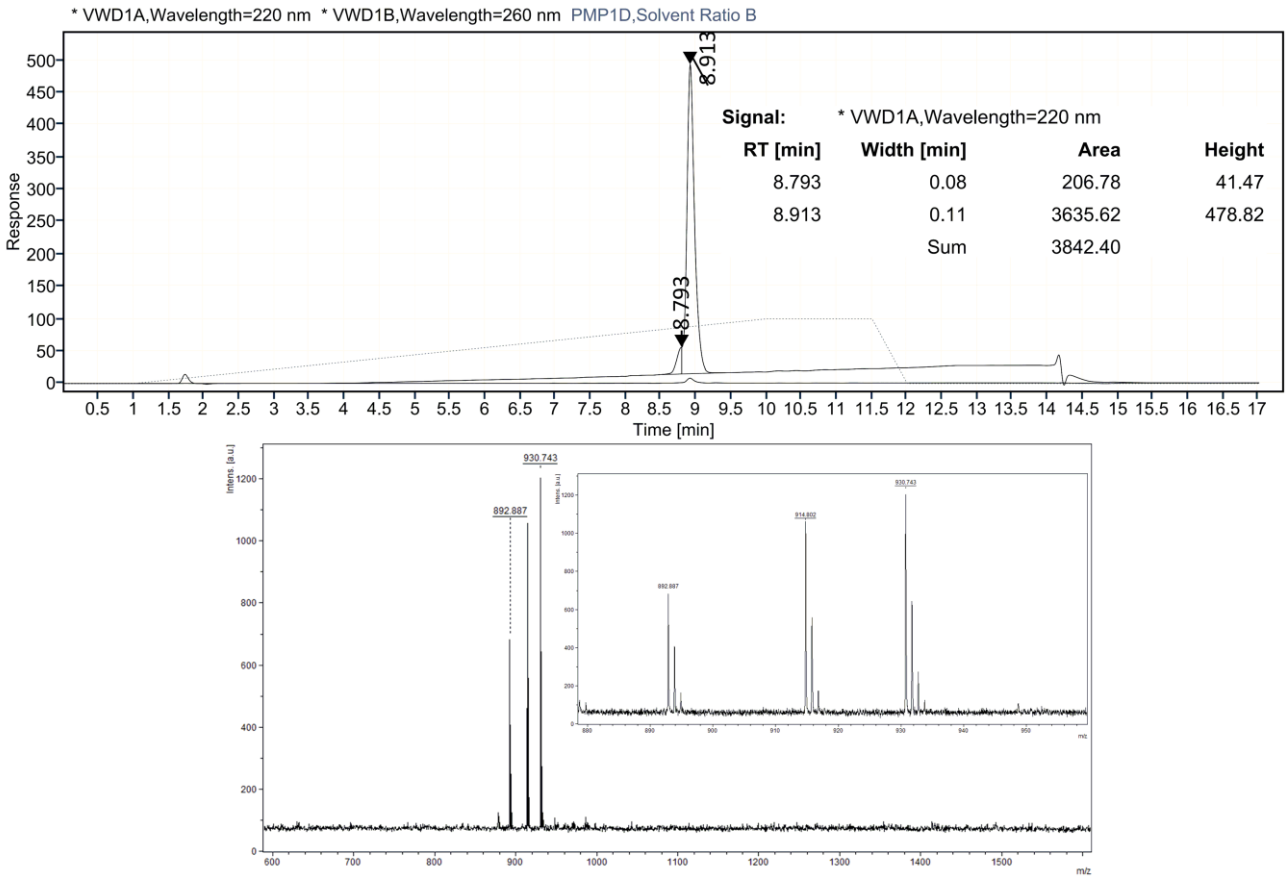
Supplementary Figure S32. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LGLHLFL-NH_2.

Ac-LLLHLFL-NH_2



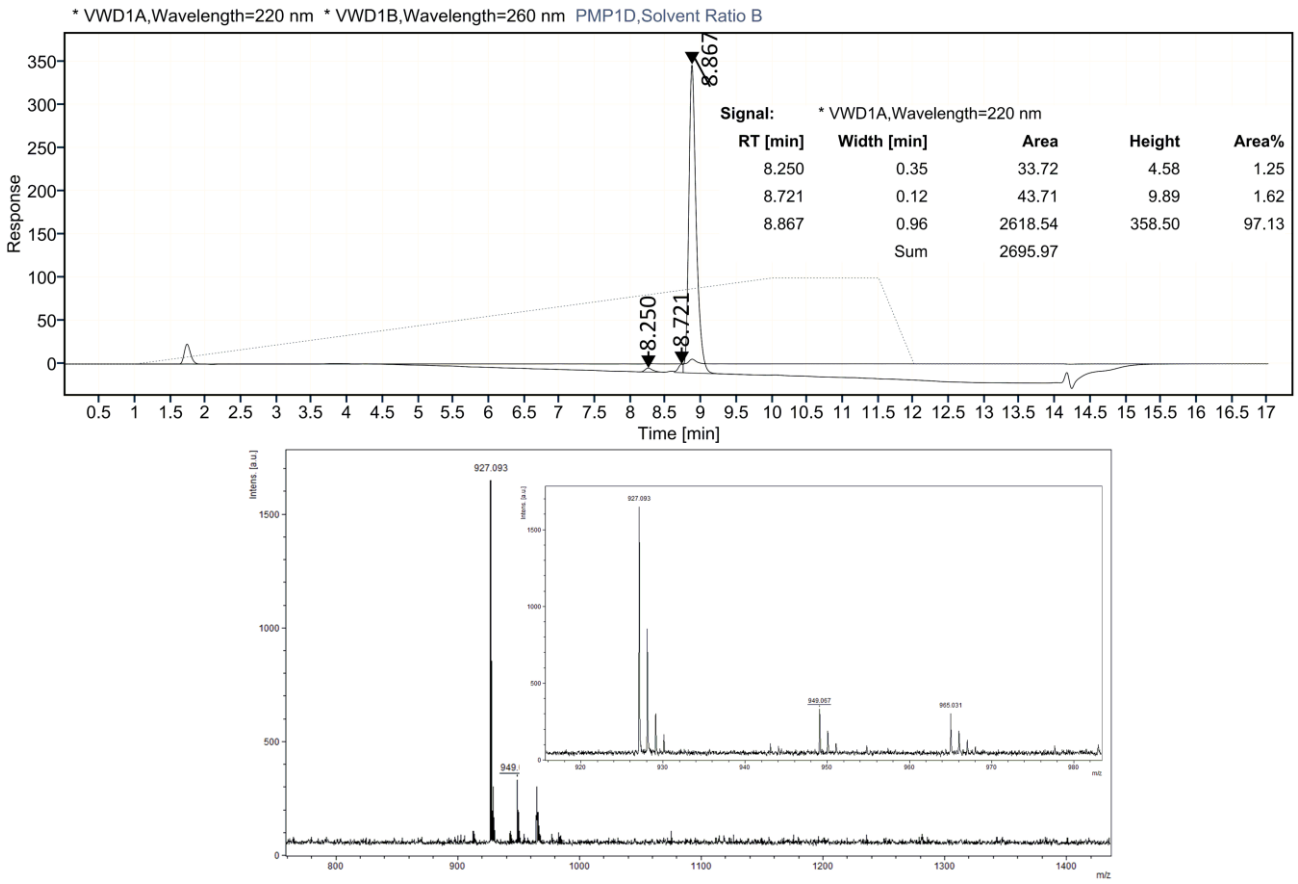
Supplementary Figure S43. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LLLHLFL-NH_2.

Ac-LVLHLFL-NH_2



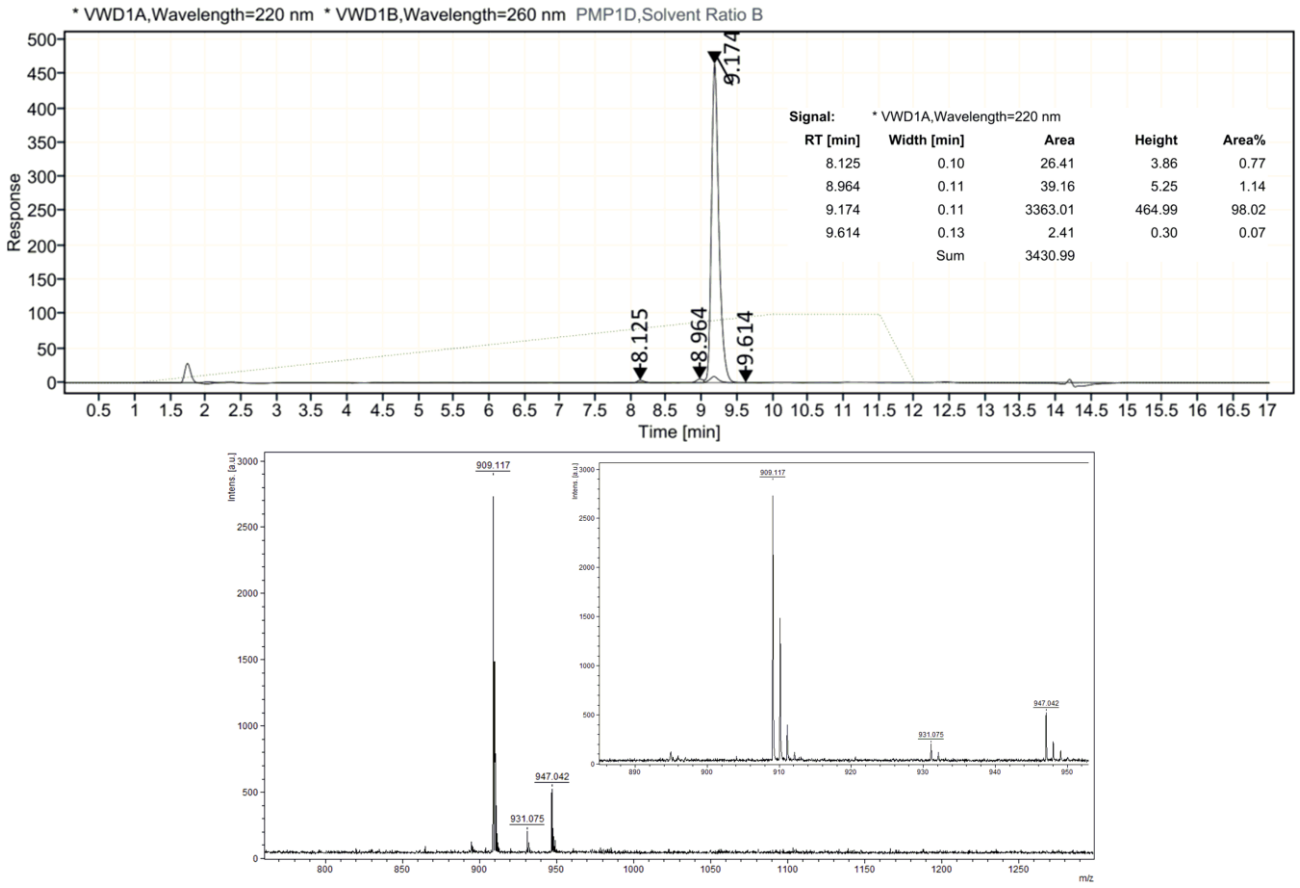
Supplementary Figure S54. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LVLHLFL-NH_2.

Ac-LMLHLFL-NH_2



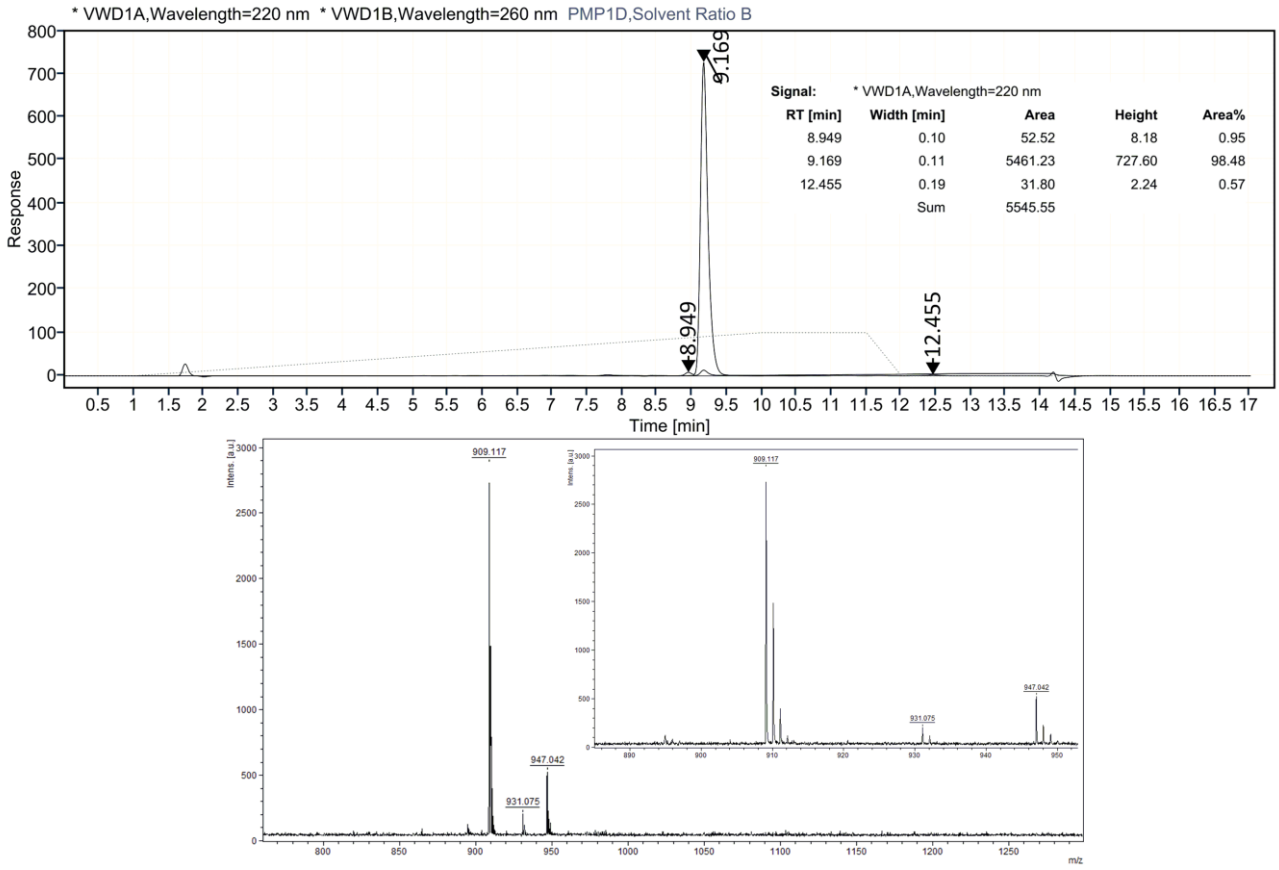
Supplementary Figure S15. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LMLHLFL-NH_2.

Ac-LILHLFL-NH_2



Supplementary Figure S16. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure Ac-LILHLFL-NH_2.

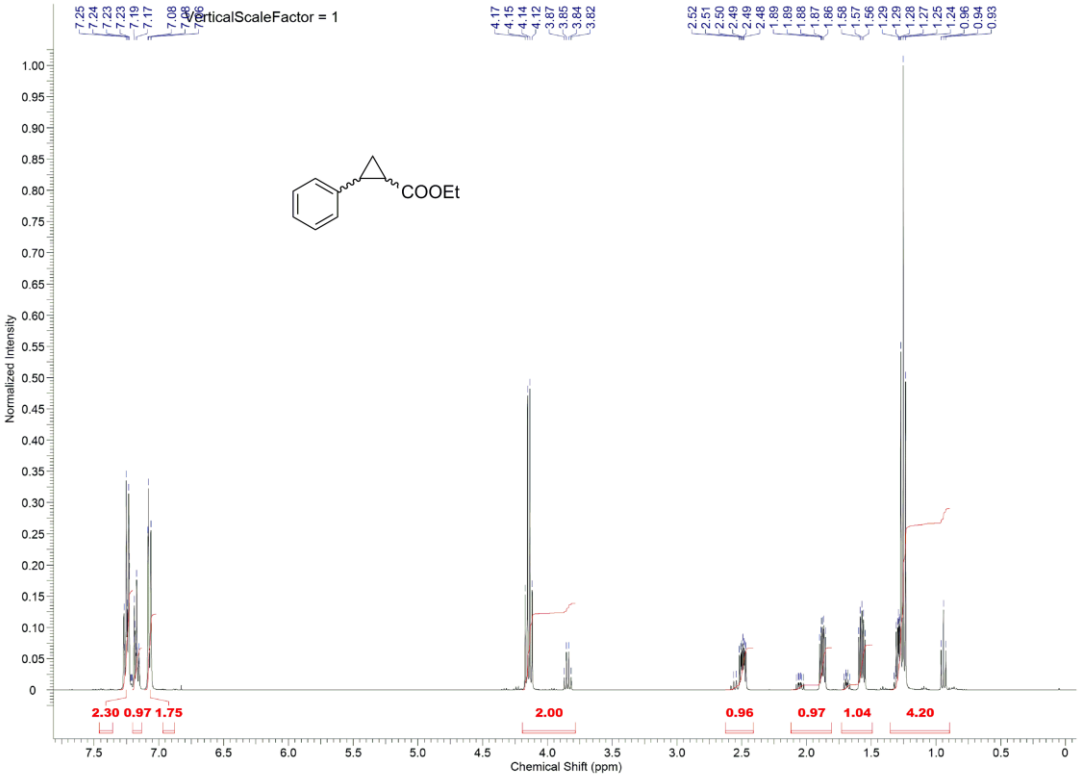
(D)-Ac-LILHLFL-NH$_2$



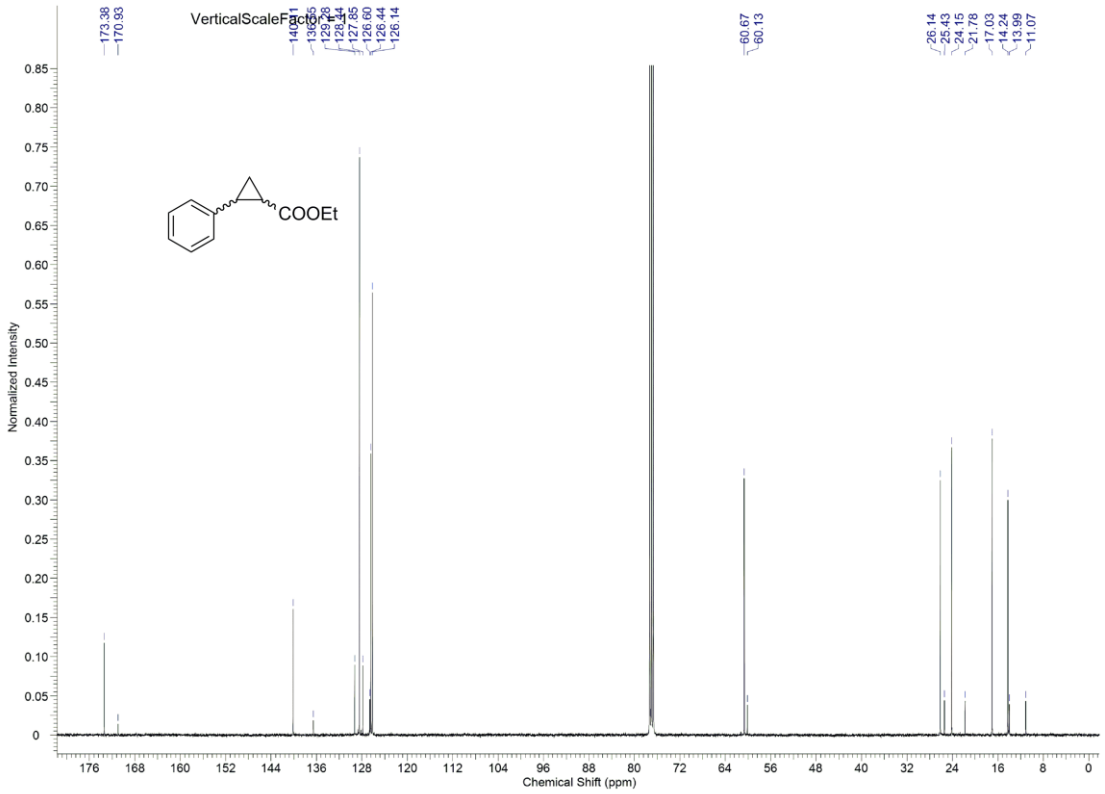
Supplementary Figure S17. HPLC chromatogram (top) and MALDI spectrum (bottom) of pure d-Ac-LILHLFL-NH$_2$.

NMR spectra of cyclopropanes

Ethyl 2-phenylcyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

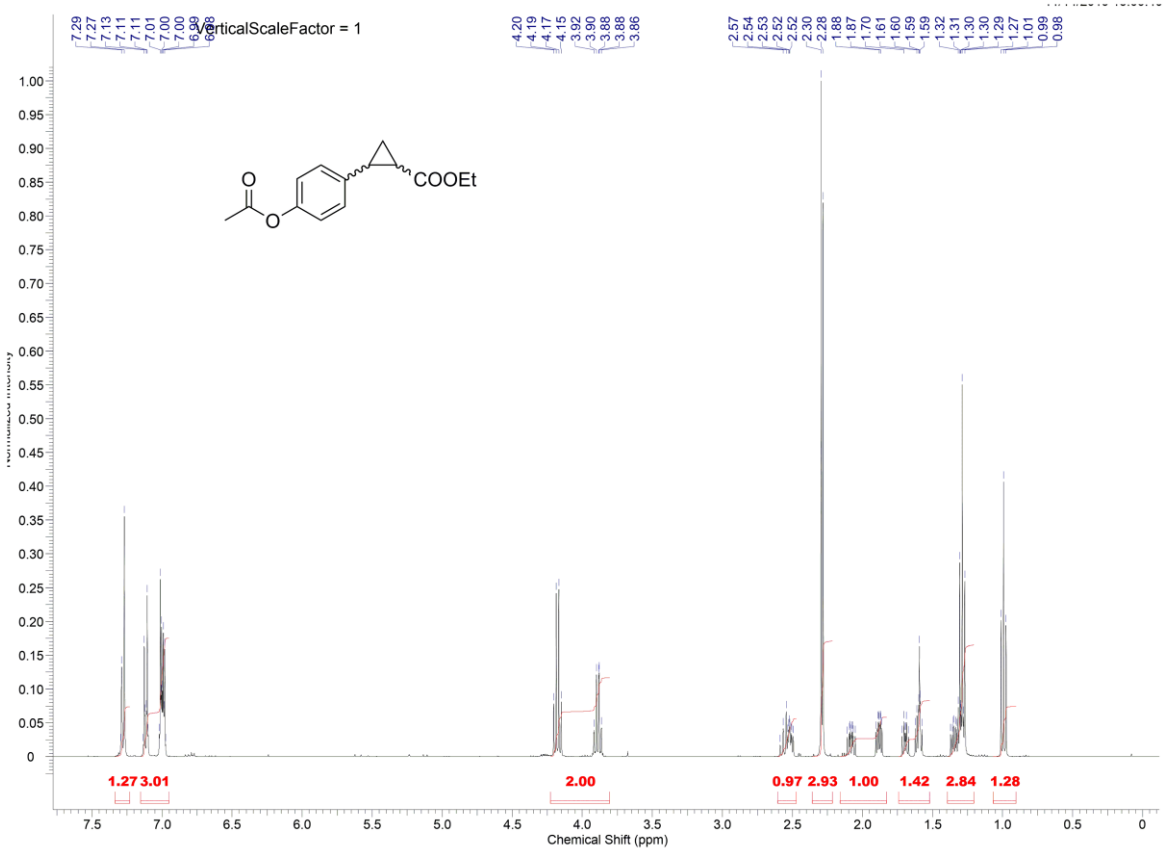


Supplementary Figure S18. ^{1}H-NMR spectrum of ethyl 2-phenylcyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

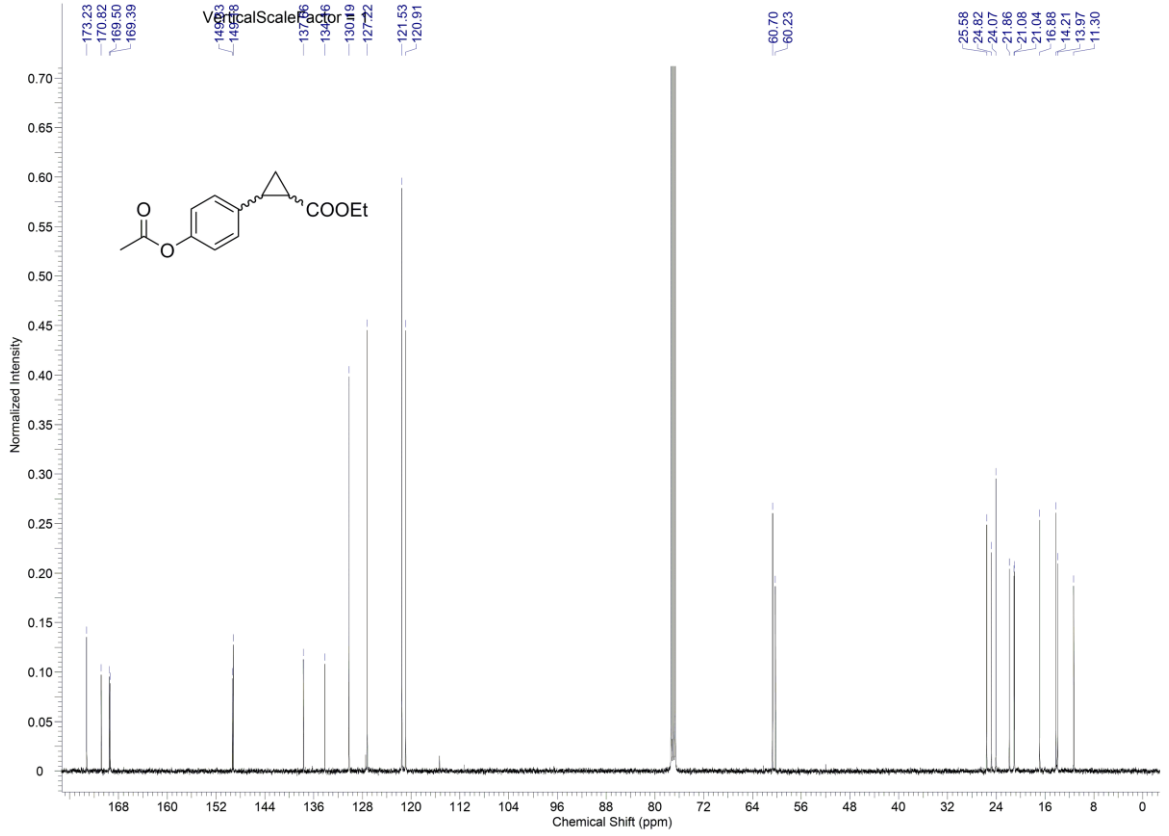


Supplementary Figure S19. ^{13}C-NMR spectrum of ethyl 2-phenylcyclopropanecarboxylate (mixture of cis- and trans- isomers).

Ethyl 2-(4-acetoxyphenyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

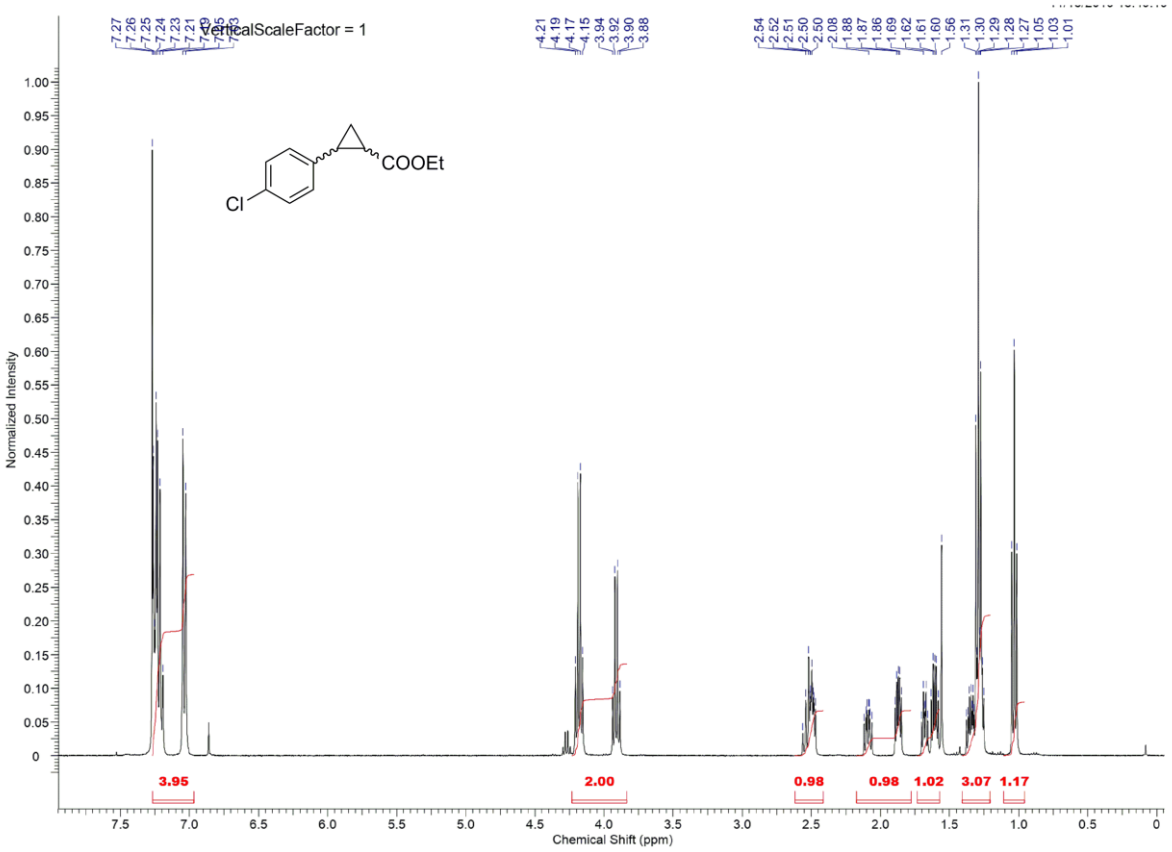


Supplementary Figure S20. ^{1}H NMR of ethyl 2-(4-acetoxyphenyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

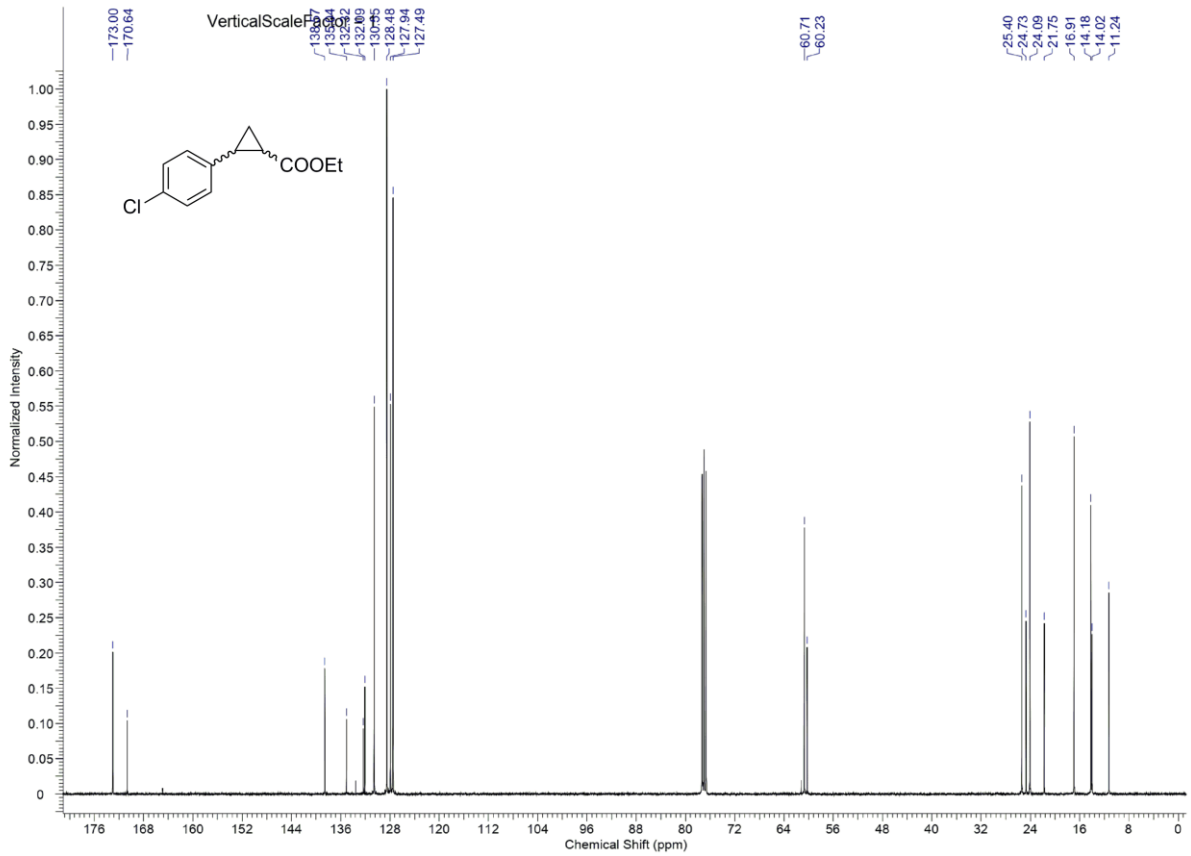


Supplementary Figure S61. ^{13}C NMR of Ethyl 2-(4-acetoxyphenyl)cyclopropanecarboxylate (mixture of cis- and trans- isomers).

Ethyl-2-(4-chlorophenyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

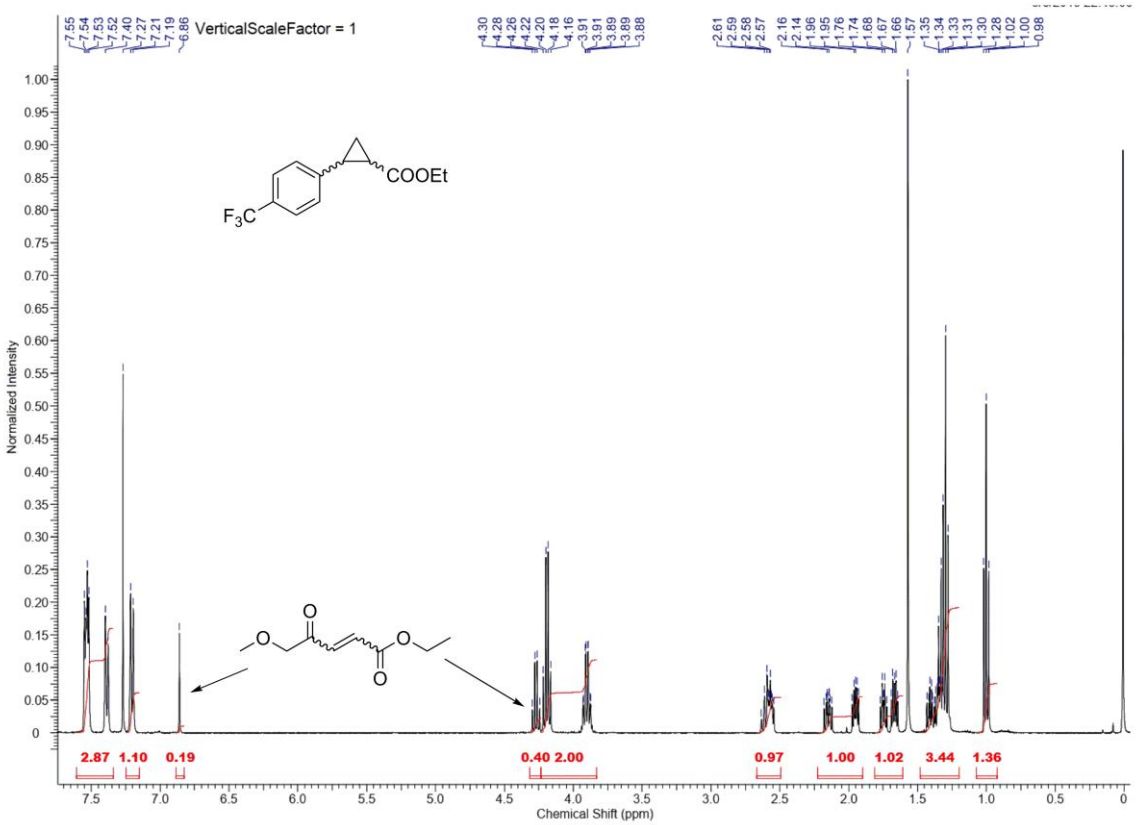


Supplementary Figure S72. ^{1}H NMR spectrum of ethyl-2-(4-chlorophenyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

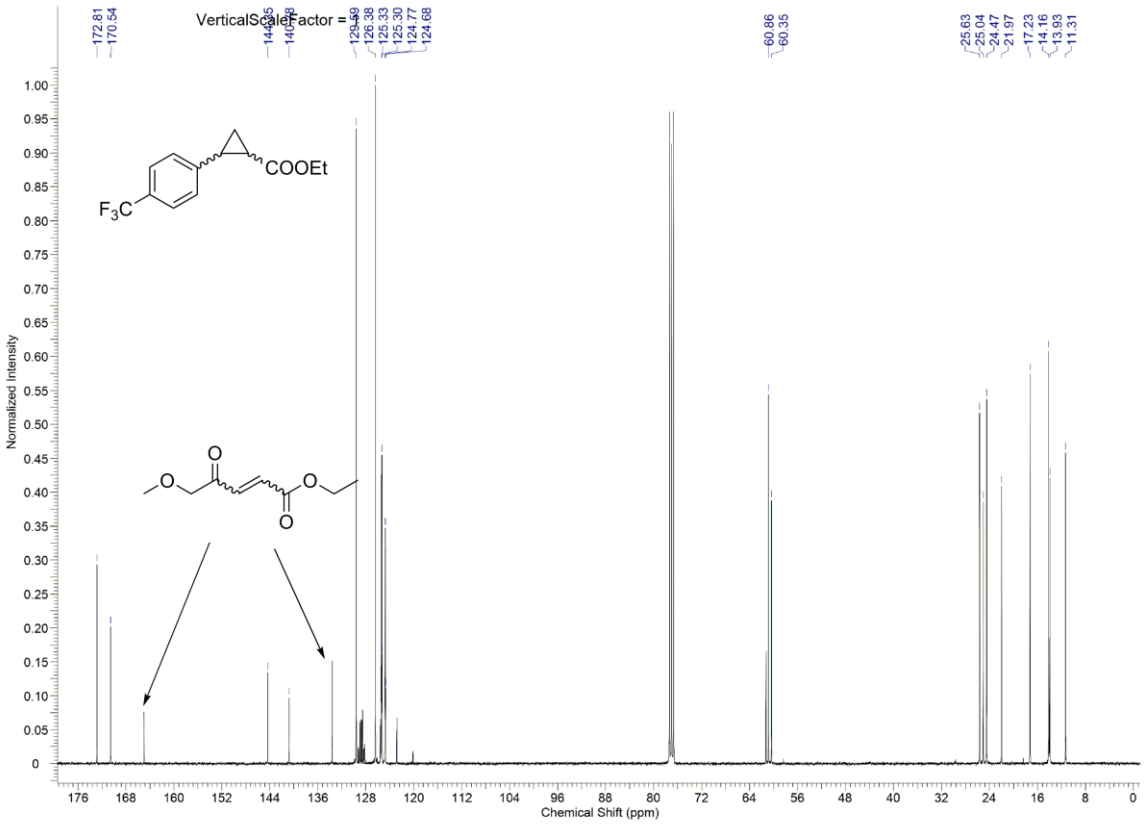


Supplementary Figure S83. ^{13}C NMR spectrum of ethyl-2-(4-chlorophenyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

Ethyl-2-[4-(trifluoromethyl)phenyl]cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

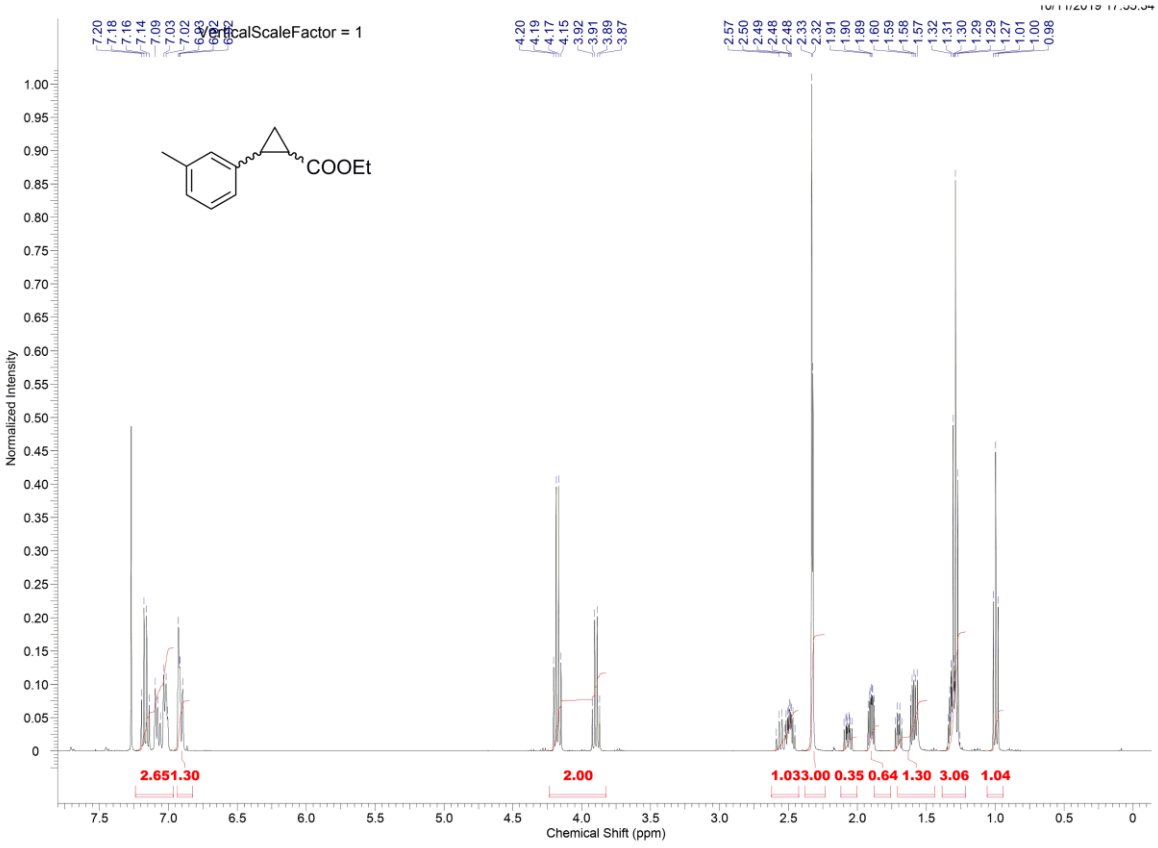


Supplementary Figure S94. ^{1}H NMR spectrum of ethyl-2-[4-(trifluoromethyl)phenyl]cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

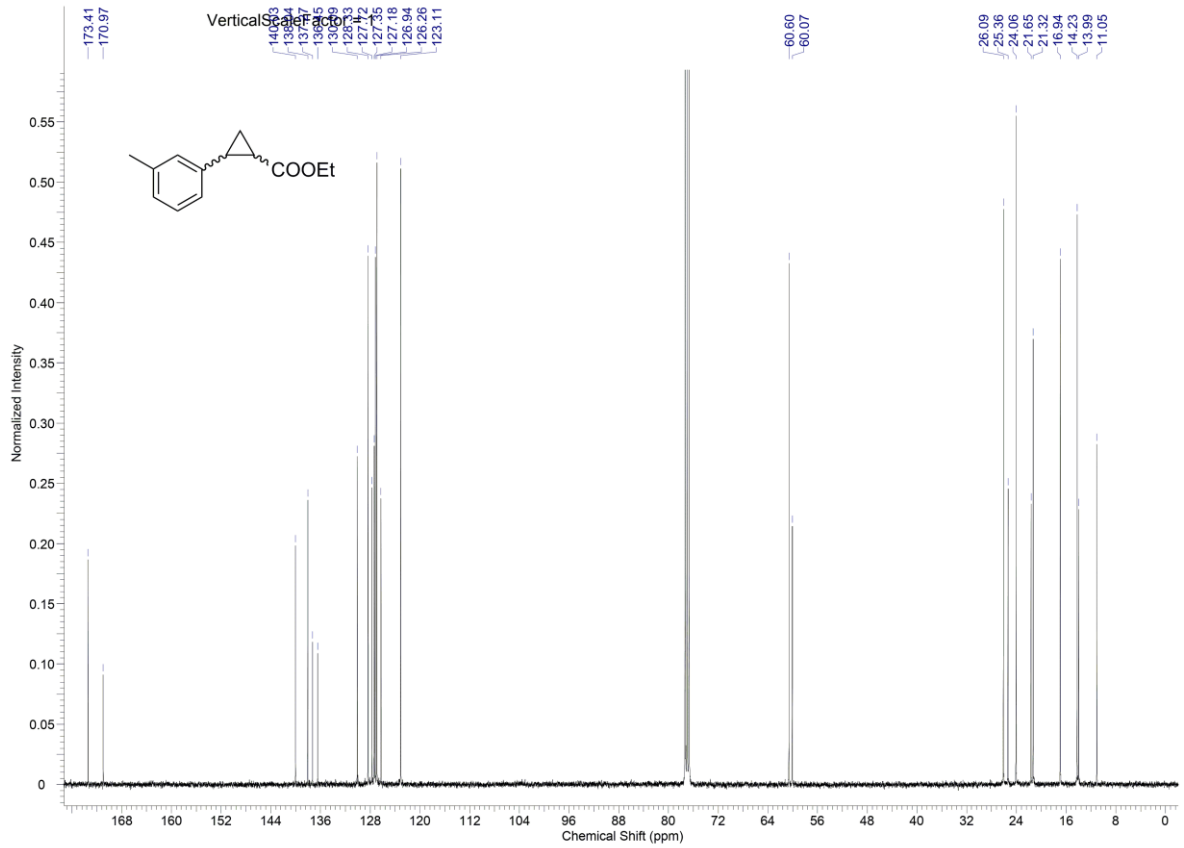


Supplementary Figure S25. ^{13}C NMR spectrum of ethyl-2-[4-(trifluoromethyl)phenyl]cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

Ethyl-2-(m-tolyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

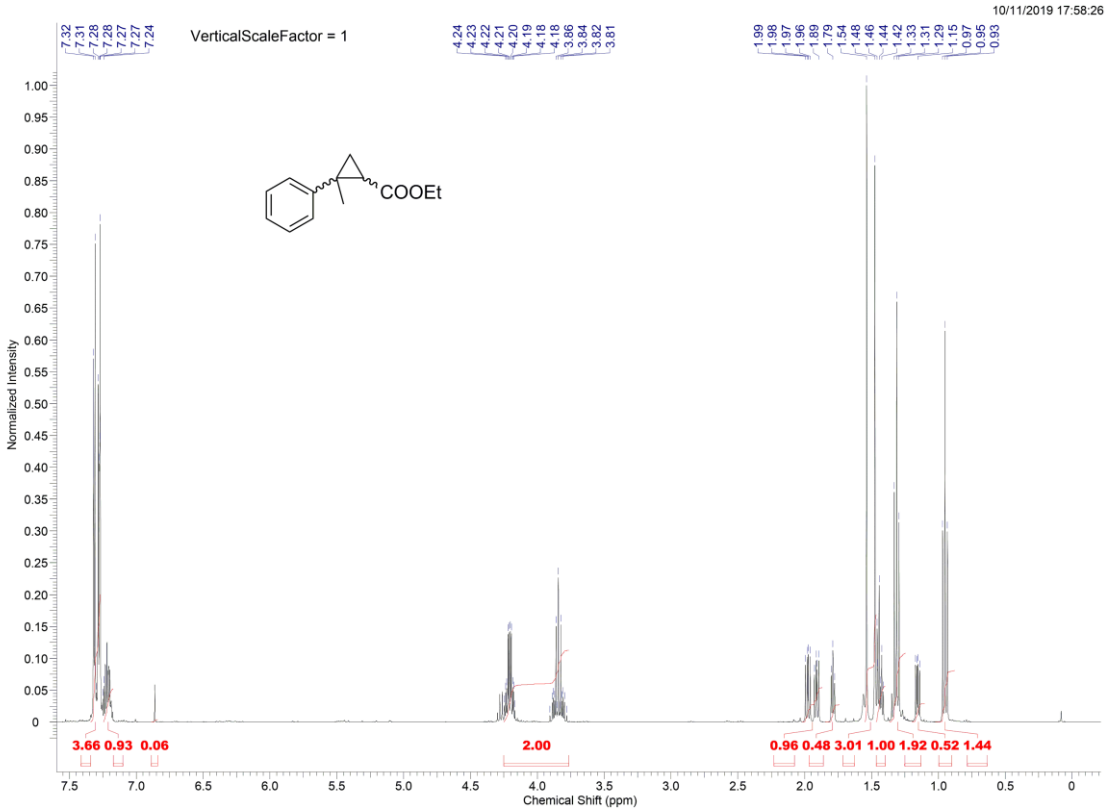


Supplementary Figure S26. ^{1}H NMR spectrum of ethyl-2-(m-tolyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

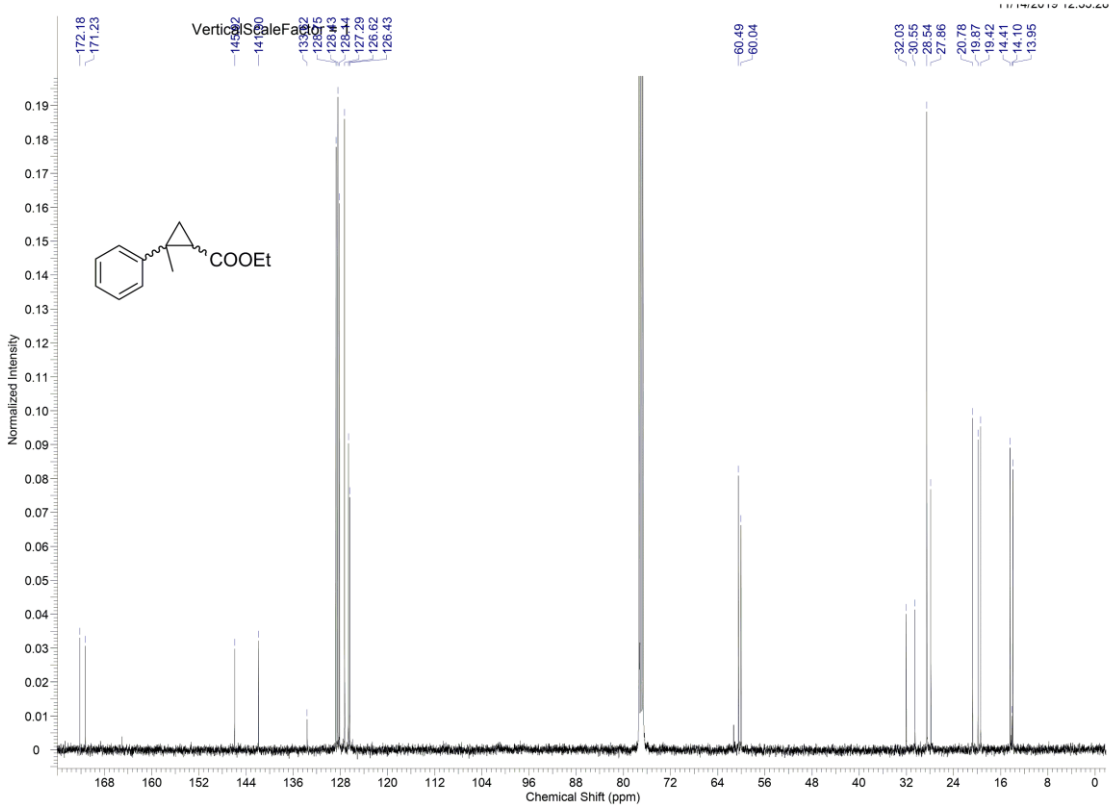


Supplementary Figure S27. ^{13}C NMR spectrum of ethyl-2-(m-tolyl)cyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

Ethyl-2-methyl-2-phenylcyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers)

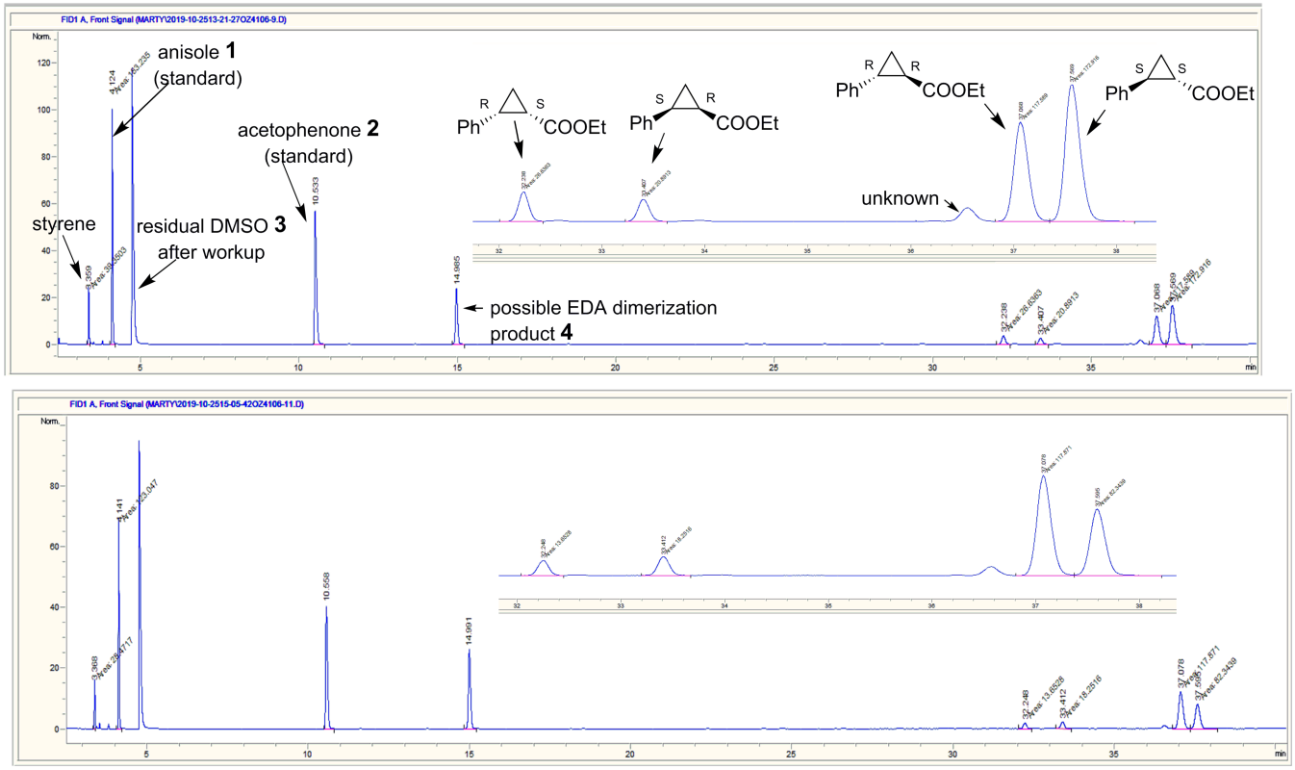


Supplementary Figure S28. ^{1}H NMR spectrum of ethyl-2-methyl-2-phenylcyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

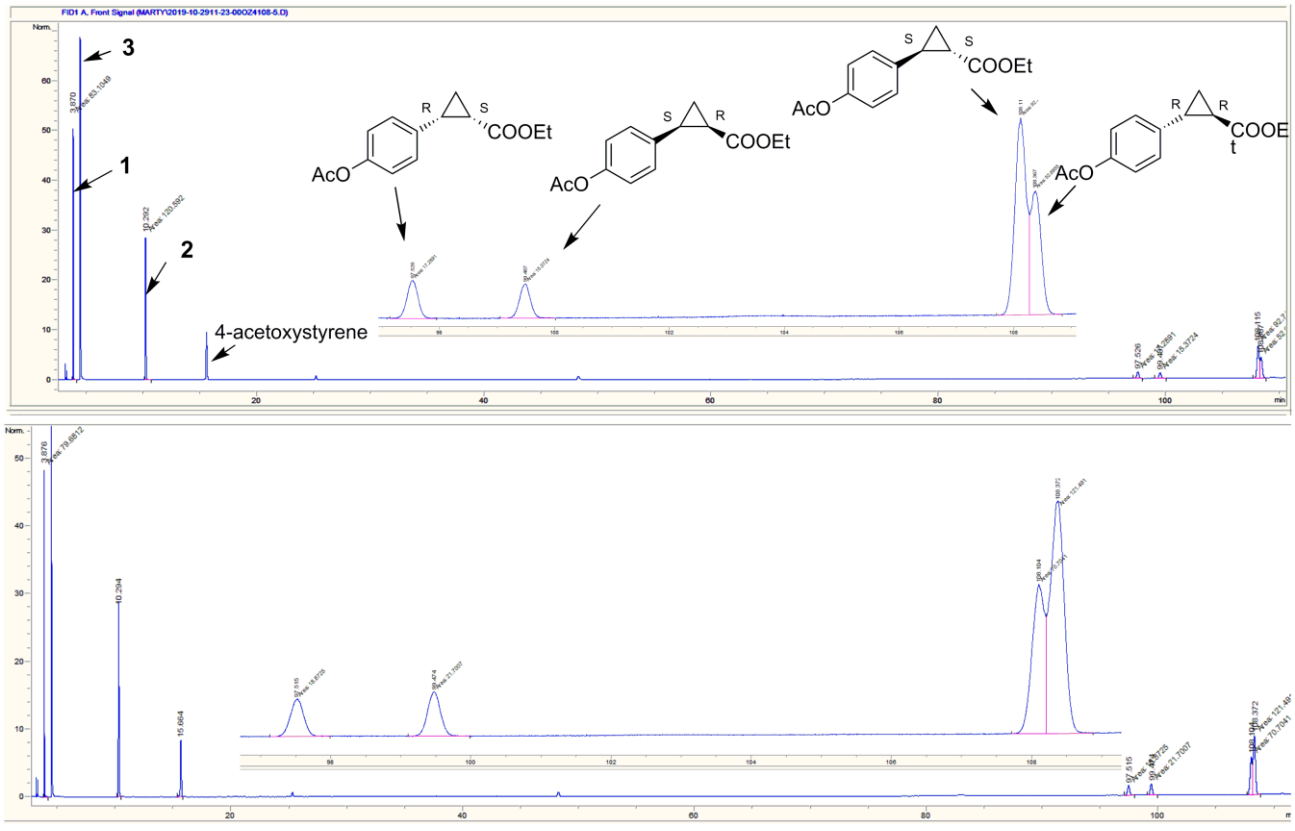


Supplementary Figure S29. ^{13}C NMR spectrum of Ethyl-2-methyl-2-phenylcyclopropanecarboxylate (mixture of *cis*- and *trans*- isomers).

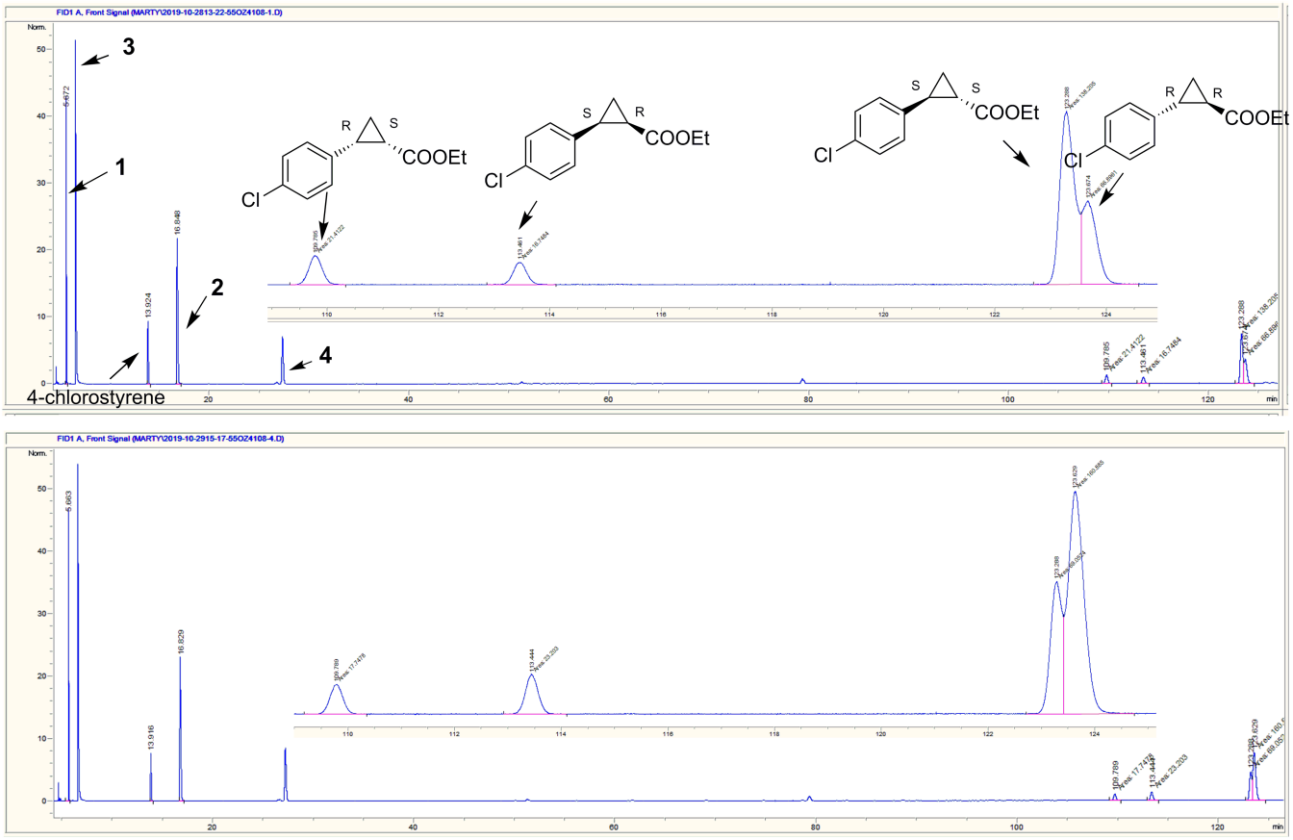
Representative GC chromatograms of cyclopropanes from cyclopropanation reaction



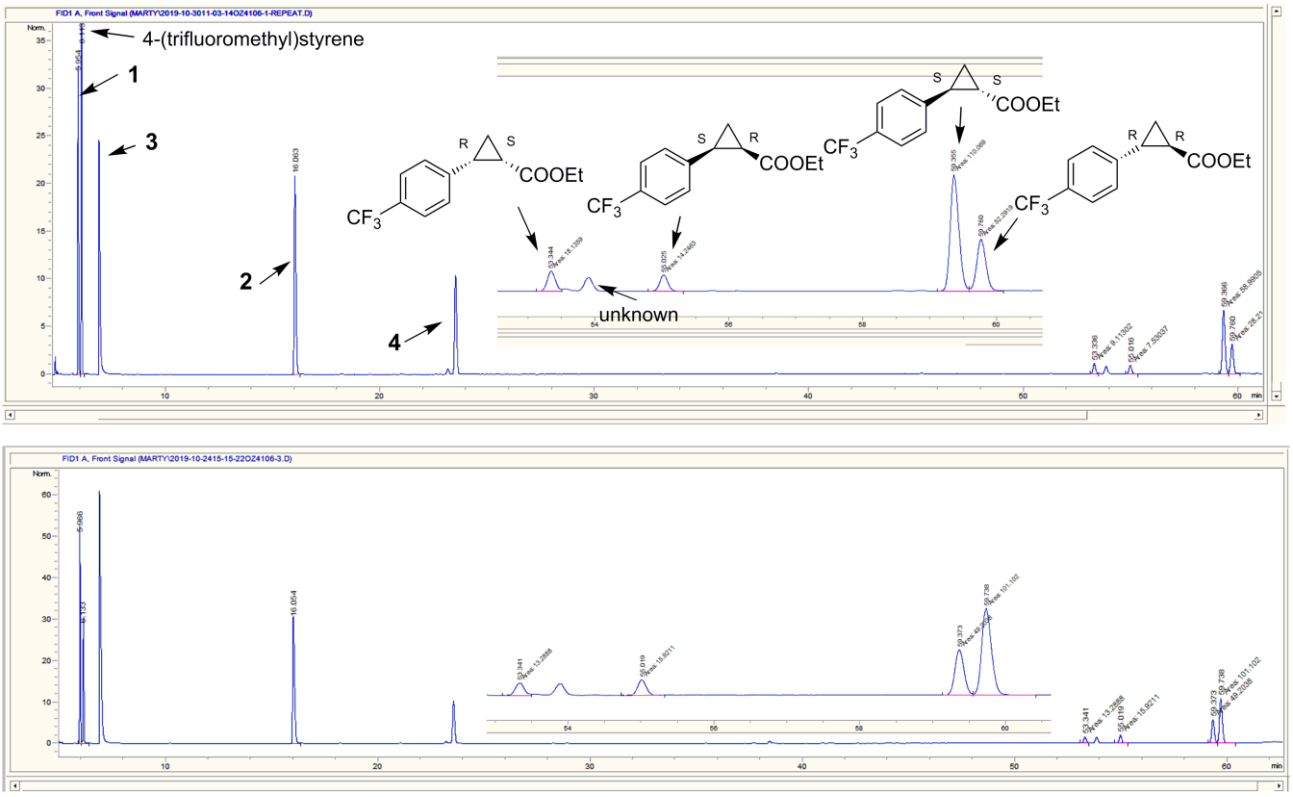
Supplementary Figure S30. Separation of ethyl 2-phenylcyclopropanecarboxylate. Reaction catalysed by hemin-Ac-LILHLFL-NH_2 (top) or hemin-(D)-Ac-LILHLFL-NH_2 (bottom) assembly. Here and further all known components of the analysis were labelled with names and/or numbers.



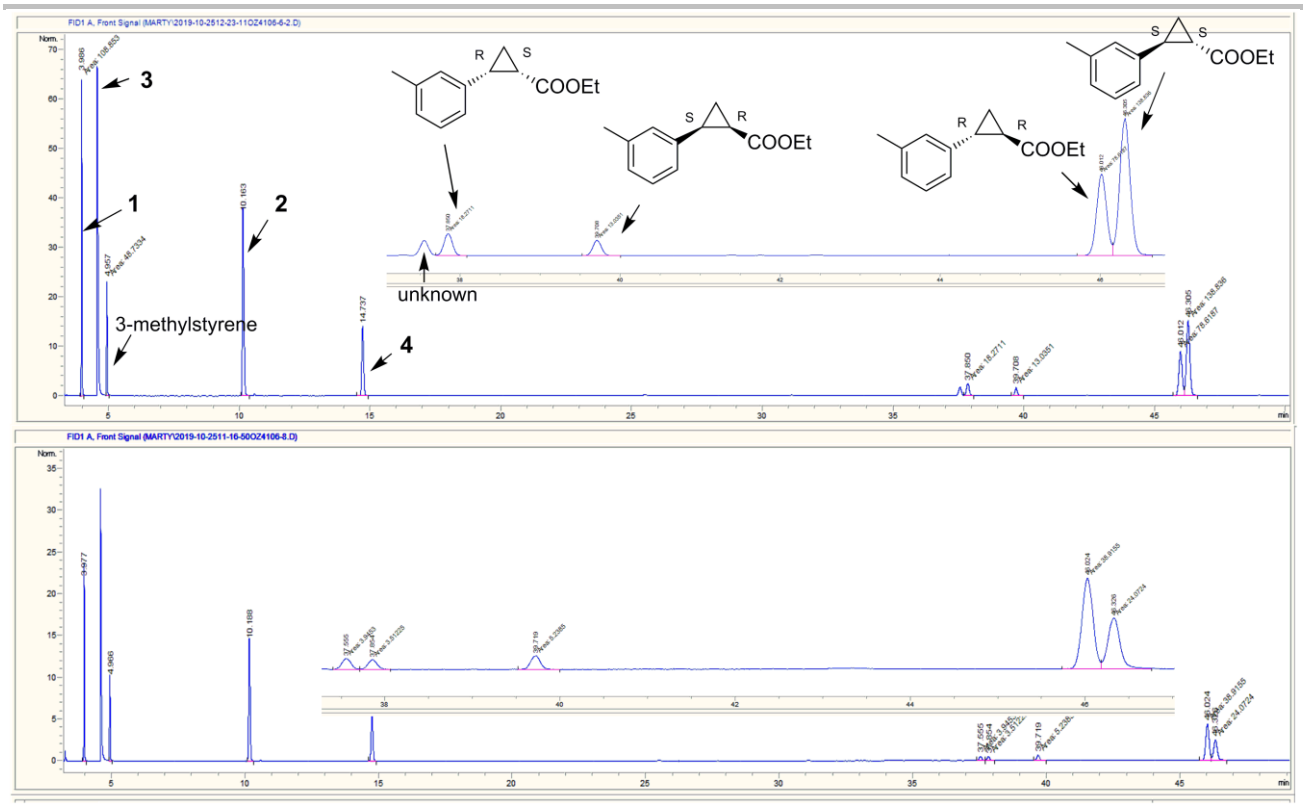
Supplementary Figure S101. Separation of ethyl 2-(4-acetoxyphenyl)cyclopropanecarboxylate. Reaction catalysed by hemin-Ac-LILHLFL-NH_2 (top) or hemin-(D)-Ac-LILHLFL-NH_2 (bottom) assembly.



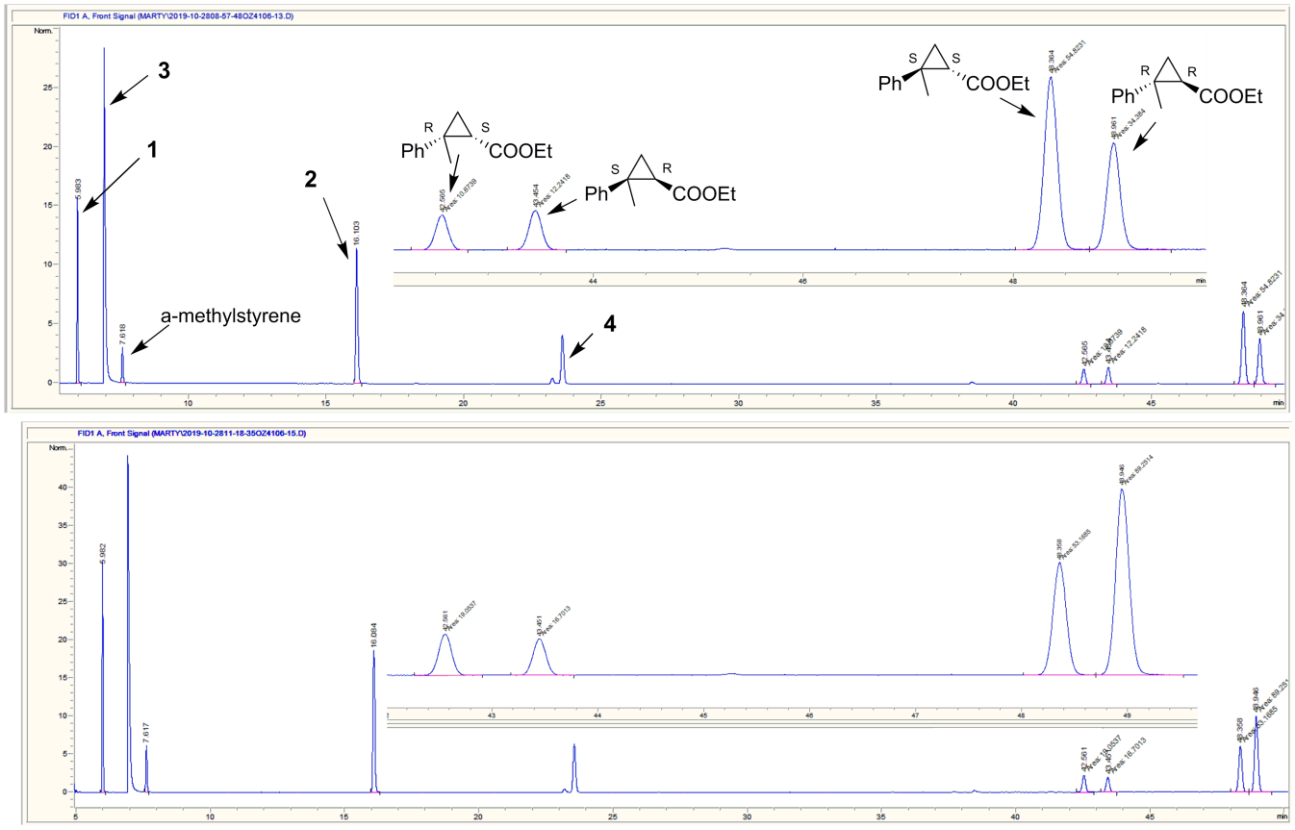
Supplementary Figure S112. Sepapration of ethyl-2-(4-chlorophenyl)cyclopropanecarboxylate. Reaction catalysed by hemin-Ac-LILHLFL-NH_2 (top) or hemin-(D)-Ac-LILHLFL-NH_2 (bottom) assembly.



Supplementary Figure S123. Sepapration of ethyl-2-[4-(trifluoromethyl)phenyl]cyclopropanecarboxylate. Reaction catalysed by hemin-Ac-LILHLFL-NH_2 (top) or hemin-(D)-Ac-LILHLFL-NH_2 (bottom) assembly.

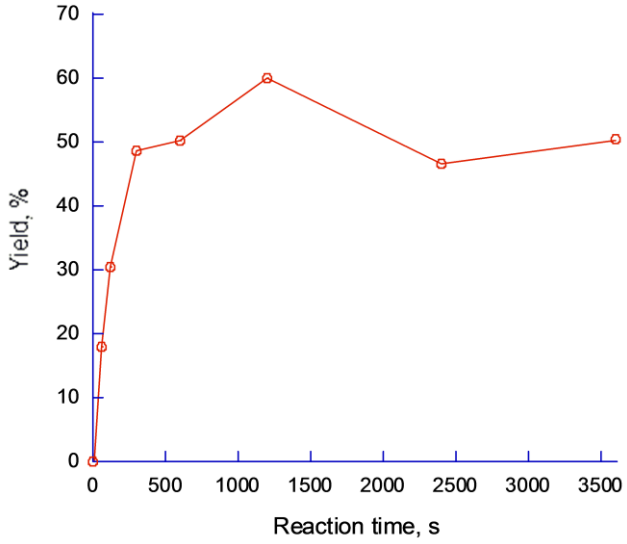


Supplementary Figure S134. Sepapration of ethyl-2-(m-tolyl)cyclopropanecarboxylate. Reaction catalysed by hemin-Ac-LILHLFL-NH_2 (top) or hemin-(D)-Ac-LILHLFL-NH_2 (bottom) assembly.



Supplementary Figure S35. Separation of ethyl-2-methyl-2-phenylcyclopropanecarboxylate. Reaction catalysed by hemin-Ac-LILHLFL-NH_2 (top) or hemin-(D)-Ac-LILHLFL-NH_2 (bottom) assembly.

Dependence of the yield on reaction time for cyclopropanation of 4-(trifluoromethyl)styrene



Supplementary Figure S36. Plot of the yield *vs*. reaction time of 4-(trifluoromethyl)styrene cyclopropanation catalyzed by Ac-LILHLFL-NH_2-hemin complex (20 μM hemin and 150 μM peptide) at pH 7 in 100 mM phosphate buffer.

References

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[3] A. J. Anciaux, A. J. Hubert, A. F. Noels, N. Petiniot, P. Teyssie, *J. Org. Chem.* **1980**, *45*, 695-702.
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