SUPPORTING INFORMATION

Sucrose-fueled, Energy Dissipative, Transient Formation of Molecular Hydrogels Mediated by Yeast Activity.

César A. Angulo-Pachón, Juan F. Miravet*

1. GENERAL METHODS.

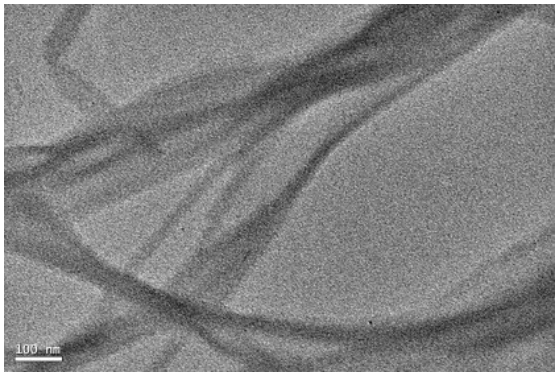
$^{1}H/^{13}C$ NMR spectra were recorded at 500/125 MHz or 300/75 MHz in the indicated solvent at 30 ºC. Signals of the deuterated solvent (DMSO-*d6* in all case, unless otherwise indicated) were taken as the reference in DMSO-*d6*, the singlet at δ 2.50 and the quadruplet centered at 39.52 ppm for ^{1}H and ^{13}C NMR, respectively. ^{1}H and ^{13}C signals were assigned with the aid of 2D methods (COSY, HSQC and HMBC). Reactions which required an inert atmosphere were carried out under N2. Commercially available reagents were used as received.

For the experiments we used fresh baker yeast "*Levital*"; composition: yeast (*saccharomyces cerevisiae*), water (70 %), nitrogenous material (13.5 %), cellulosic material (1.5 %), sugars (12 %), minerals (2 %) and vitamins (1 %).

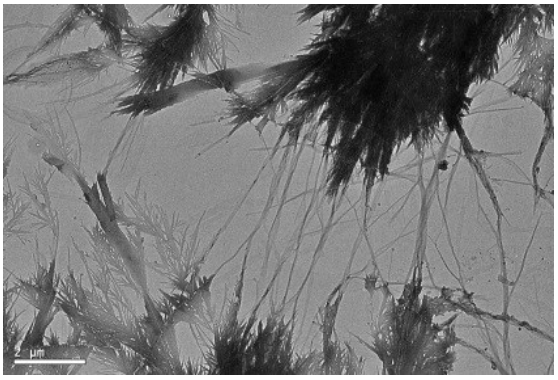
Mass spectra were run by the electro- spray mode (ESMS). Masses spectra were recorded at Mass Spectrometry triple Quadrupole Q-TOF Premier (Waters) with simultaneous Electrospray and APCI Probe.

2. TRANSMISSION ELECTRON MICROSCOPY (TEM).

Transmission electron microscopy micrographs were taken on a JEOL 2100 microscope equipped with a camera CCD (11 MP). The corresponding fresh gels were applied directly onto a 200 mesh carbon coated copper grids. Excess solvent was carefully removed by capillary action using filter paper. The grids were immediately stained with one drop of phosphotungstic acid 1 % for 1 min. Excess stain was removed by capillarity.



A



B

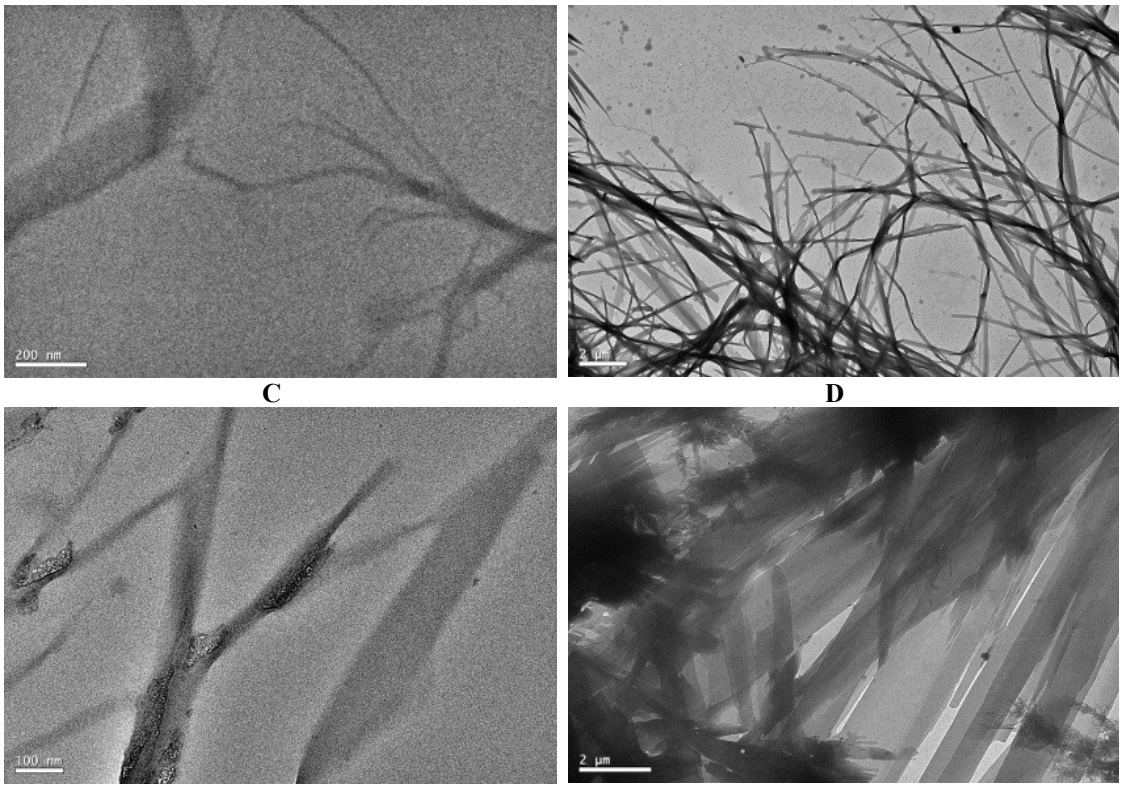


Figure S1. Electron microscopy (TEM) images obtained from gels of compounds (10 mg/mL) prepared by exposition of basic aqueous solutions to carbon dioxide pressure. **A - B** compound **1**; **C - D** compound **2** and **E – D** compound **3**.

3. pKa DETERMINATION: Potentiometric titrations to determine acid−base constants were carried out at 298 K. In a typical experiment 5 mL of basic solution of the corresponding amino acid derivative (10 mg) and NaOH (0.1 N) were titrated with normalized dissolution HCl 0.1 N commercially available and vigorous stirring. The acid was added with an NE-300 "Just Infusion" TM Syringe Pump (0,08 mL/min-inside diameter 14.57 mm) using a SGE Analytical Science syringe 10 mL which had connected a needle of stainless steel cono. Luer. Look 0,7mm x 300mm. The pH was monitored every 10 s (in a S220 Seven Compact pHmeter, Mettler Toledo).

Thermodynamic constants for the species in solution could be calculated with HYPERQUAD using titration data previous to the experimental aggregation onset. To assess the solubility product of the acids derivatives, titration was stopped when a solid precipitate was observed. Then the solubility product was calculated iteratively with HYSS2009, adjusting its value to fit the calculated and experimental pH.

4. FLUORESCENCE MEASUREMENTS: An aqueous solution (2 mL) sonicated and centrifuged (5000 rpm by 5 min) of the corresponding amino acid derivative (10 mg), K_2CO_3 (0.05 M), sucrose (80 mg) and fresh yeast (8 mg) was placed in a fluorescence cuvette (tetragonal prism, 1 cm width and deep); the cuvette was closed with an expanded polystyrene stopper (1.0 cm^3). Excitation was performed at 260 nm and the emission intensity at 294−296 nm monitored every 1 min for 3 h in a Jasco FP-8300 spectrofluorimeter at 37 ºC.

5. WIDE-ANGLE X-RAY DIFFRACTION: Data collection was performed at room temperature with a Bruker D4 Endeavor X-ray powder diffractometer by using Cu-α radiation. A sample of the respective freeze-dried powder was placed on a sample holder and data were collected for 2θ values between 2 and 40° with a step size of 0.03° and a time step of 10 s.

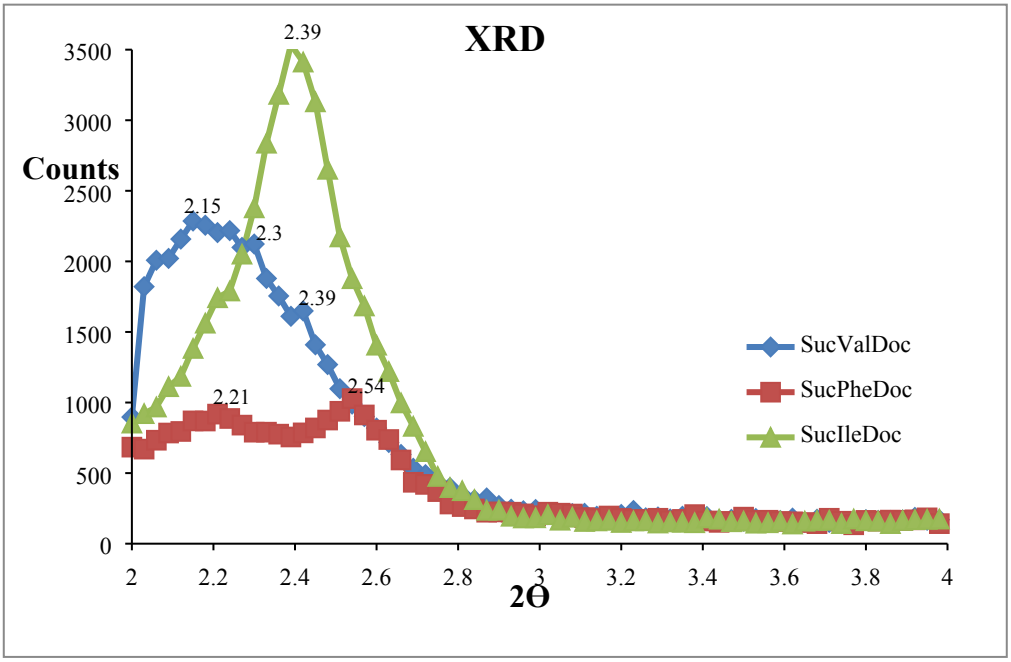


Figure S2. Diffractogram of compounds. Blue line: compound **1**; green line: compound **2** and red line: compound **3**.

6. CYTOTOXICITY TESTING:[1] A suspension of larvae (1 mL), containing 10 larvae, was added into each test vial (4 mL) and incubated for 48 hours. The test vials were then examined, and the number of dead larvae in each bottle was counted after 6, 12, and 24 hours. The total number of shrimps in each bottle was counted and recorded. The lethal concentration (LC_{50}) were determined using statistical analysis.[2]

6.1. Sample preparation: Samples were prepared dissolving 50 mg of compound in 5 mL of K_2CO_3 0.1 M (solution A). Amounts of solution A (5, 50 and 500 µL) were diluted to 4 mL with salt water for obtain concentrations of 10, 100 and 1000 µg/mL, respectively. The final dissolutions were prepared in cylindrical glass vial (diameter = 2 cm). A control was prepared diluting 5, 50, 500 µL of K_2CO_3 to 4 mL the artificial sea water. Three replicates were prepared for each dose level.

6.2. Hatching the Shrimp: Brine shrimp (*Artemia salina*) eggs (Hobby®, Dohse Aquaristik GmbH & Co. KG D-53501, Gelsdorf, Germany) were hatched in a shallow square glass dish (5 x 14 x 14 cm) filled with artificial sea water which was prepared with a commercial

[1] (a) B. N., Meyer; N. R., Ferrigni; J. E., Putnam; L. B., Jacobsen; D. E. Nichols; J. L. MacLaughlin. *J. Med. Plants Res.* **1982**, *45*, 31 – 34. (b) G., Sahgal; S., Ramanathan; S., Sasidharan; M. N., Mordi; S. Ismail; S. M. Mansor. *Pharmacogn. Res*. **2010**, *4*, 215 – 220.
[2] IBM® SPSS® Statistics Software. Version 23.0.0.0.

sodium chloride (Scharlab S. L.) and distillated water. The eggs (ca. 25 mg) were sprinkled into the square glass dish (5 x 14 x 14 cm). Then, was added artificial sea water (500 mL) and air was bubbled; after 48 hours, the shrimps matured as nauplii (*Artemia salina*) and were ready for the assay.

6.3. Bioassay: Ten shrimp were transfererred to each sample vial using a Pasteur pipette. The nauplii can be counted macroscopically in the stem of the pipette against a lighted background. The vials were maintained under illumination. Survivors were counted, with aid of magnifying glass.

	Percent deaths at 24 h				
Compound	*10 μg/mL*	*100 μg/mL*	*1000 μg/mL*	*LC_{50} μg/mL*	*(95 % confidence interval)[a]*
SucValDoc (**1**)	1	3	6	51199	(3.411 – 97.246)
SucIleDoc (**2**)	2	6	8	23714	(3.169 – 74.545)
SucPheDoc (**3**)	1	12	30	19962	– –
SucValHx (**4**)	2	3	4	$> 10^5$	– –

Table S1. *Artemia Salina* bioassay results of succinic acid derivatives. [a)] For concentration in logarithm = 10. Where data were insufficient for probit analysis not provide confidence intervals.

7. METHODS OF GELATION.

7.1. Gelation by carbon dioxide pressure: Inside a vial was weighted 10 mg of succinic acid derivate. Then we added 1 mL of K_2CO_3 0.1 M, the vial was closed and was sonicated until complete dissolution of the compound.
To continue, the vials were put carefully inside a two necks flask with PTFE stopcock glass flow control adapter for have the control of flux carbon dioxide. Finally, we was applied a pressure of carbon dioxide 0.6 bars until formation of gel (2 – 3 hours approximately).

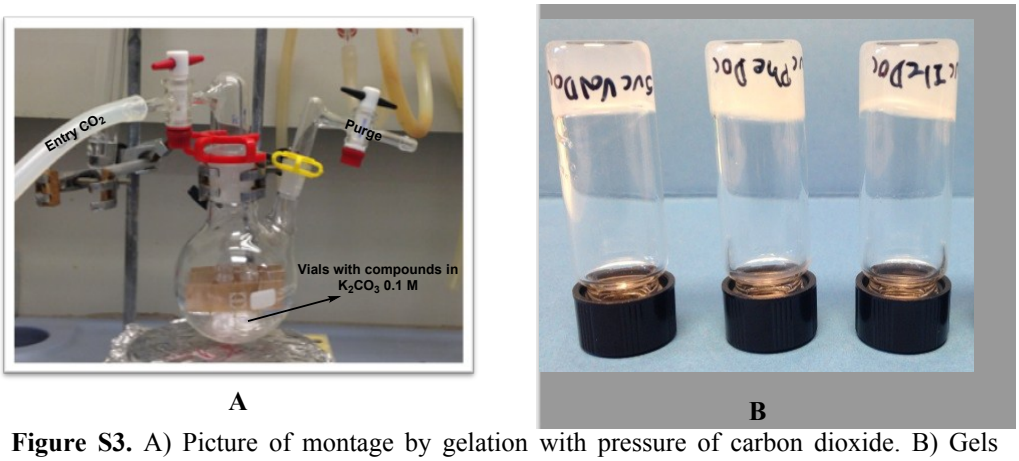
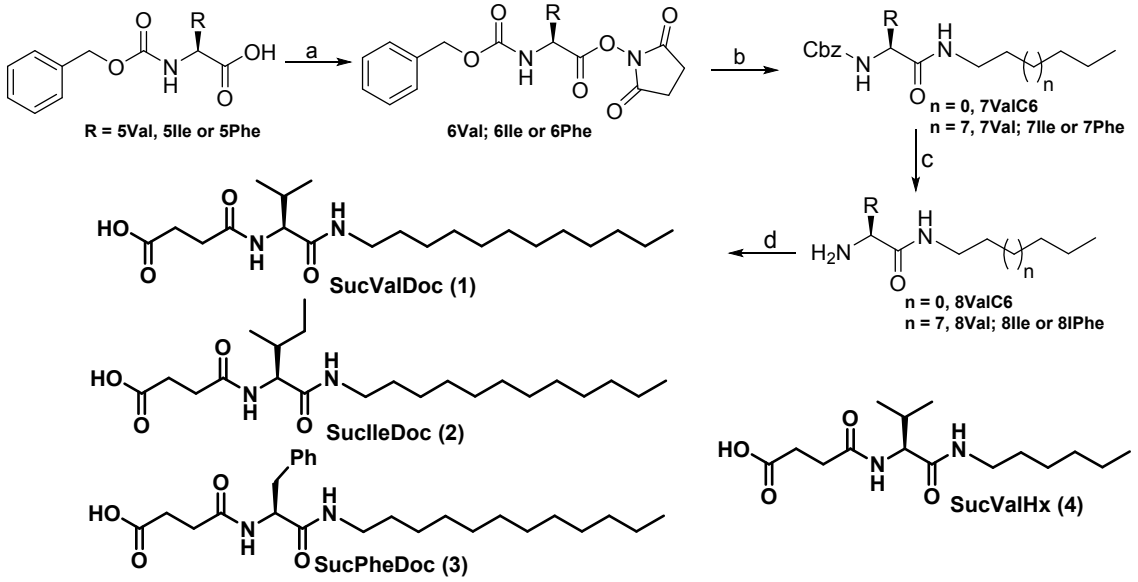


Figure S3. A) Picture of montage by gelation with pressure of carbon dioxide. B) Gels formed by pressure of carbon dioxide.

7.2. Gelation carbon dioxide produced by yeast: Inside a vial was put 1 mL of distilled water, to continue was added 10 mg of compound (1, 2 and 3) and 5.3 mg of potassium carbonate, the vials were placed sonicated until complete dissolution of the compounds. Then 43 mg of sucrose were added, resulting mixture was again sonicated until the dissolution of the sucrose, finally 8 mg of fresh yeast is put in the final solution and close

hermetically the vial. The vial was sealed and allowed to stand at room temperature until formation of gel (between 2 – 4 hours).

8. SYNTHESIS OF COMPOUNDs 1 – 4.



Scheme S1. Reagents and conditions: a) DCC, *N*-hydroxisuccinimide, THF, 2 h, 94 – 97%; b) *n*-dodecylamine or *n*-hexylamine, THF, 16 h, 92 – 96%; d) Pd/C, H_2, MeOH, 4 – 6 h, 95 – 98%; e) Succinic anhydride, K_2CO_3, THF, 16 h, 89 – 95%.

8.1. General procedure for activation of amino acid: A solution of commercial available carbobenzyloxy-*L*-amino acid (**5Val, 5Ile or 5Phe**) (40 mmol) and *N*-hydroxysuccinimide (40 mmol, 1.0 eq.) in dry THF (150 mL) was added dropwise under N_2 at 0 ºC with a dropping funnel to a solution of *N,N′*-dicyclohexylcarbodiimide (10.9 mmol, 1.01 eq.) in dry THF (75 mL). The mixture was further stirred for 1 h at 0 ºC. The solution was then allowed to stand into refrigerator for 2 h, which caused precipitation of *N,N′*-dicyclohexylurea. After this time, the mixture was filtered under vacuum, and the filtrate was removed under reduced pressure and the crude residue was purified by crystallization in isopropanol to yield the respective activated ester.

2,5-dioxopyrrolidin-1-yl ((benzyloxy)carbonyl)-L-valinate ***(6Val)***: A white solid was obtained (yield 97%); the NMR spectra were consistent with those described in the literature.[3]

2,5-dioxopyrrolidin-1-yl ((benzyloxy)carbonyl)-L-alloisoleucinate ***(6Ile)***: Pure crystals were obtained (yield 95%) as a white solid. The NMR spectra were consistent with those described in the literature.[4]

2,5-dioxopyrrolidin-1-yl ((benzyloxy)carbonyl)-L-phenylalaninate ***(6Phe)***: The ester 6Phe was previously recrystallized. Pure crystals were obtained (yield 94%) as a white solid; NMR spectra were consistent with those described in the literature.[3]

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[3] J., Becerril; M., Bolte; M., I., Burguete; F., Galindo; E., García-España; S., V., Luis; J., F., Miravet. *J. Am. Chem. Soc*. **2003**, *125*, 6677 – 6686.

[4] C., Berdugo; B., Escuder; J. F., Miravet. *Org. Biomol. Chem*. **2015**, *13*, 592 – 600.

8.2. General procedure for coupling between activated ester and amine: A solution of carbobenzyloxy-L-amino ester activated (36.8 mmol) in THF (200 mL) was added dropwise under N_2 at room temperature with a dropping funnel to a solution of commercial available *n*-dodecylamine or *n*-hexylamine (40.5 mmol, 1.1 eq.) in THF (100 mL). The mixture was further stirred for 5 h at 55 ºC. After this time, the mix was cooled to room temperature and solvent was removed under reduced pressure and the residue was poured into dissolution aq. HCl 0.1, then the mix was sonicated during 5 minutes. It was filtered under vacuum, and the residue was washed with water until pH = 7. The residue was dried under reduced pressure at 50ºC overnight.

*(S)-benzyl (1-(dodecylamino)-3-methyl-1-oxobutan-2-yl)carbamate (***7Val***):* A white solid was obtained (yield 96%).
^{1}H NMR (300 MHz, DMSO-*d*$_6$): 7.84 (t, *J* = 5.1 Hz, 1H), 7.43 – 7.26 (m, 5H), 7.15, (d, *J* = 8.7 Hz, 1H), 5.03 (s, 2H), 3.79 (t, *J* = 7.8 Hz, 1H), 3.16 – 2.91 (m, 2H), 1.92 (sext, *J* = 6.6, 13.2 Hz, 1H), 1.45 – 1.33 (m, 2H), 1.32 – 1.17 (m, 20H), 0.84 (d, overlapped, *J* = 6.6 Hz, 9H).
^{13}C NMR (125 MHz, DMSO-*d6*): δ 170.8, 156.0 (C=O), 137.1 ©, 128.2 (x2), 127.6, 127.5 (x2) (CH), 65.3 (CH_2), 60.3 (CH), 38.3, 31.3 (CH_2), 30.2 (CH), 29.0 (x4) 28.9 (x2), 28.7, 26.3, 22.0 (CH_2), 19.1, 18.2, 13.9 (CH_3).
HR ESMS: *m/z:* calcd for $C_{25}H_{42}N_2O_3$: 441.3093; found: 441.3089 [$M + Na^+$].

*Benzyl ((2S,3R)-1-(dodecylamino)-3-methyl-1-oxopentan-2-yl)carbamate (***7Ile***):* The compound was obtained with a yield 92% as a white solid.
^{1}H NMR (300 MHz, DMSO-*d*$_6$): δ 7.85 (t, *J* = 5.1 Hz, 1H), 7.40 – 7.25 (m, 5H), 7.20 (d, *J* = 9 Hz, 1H) 5.02 (s, 2H), 3.82 (t, *J* = 8.1 Hz, 1H), 3.16 – 2.92 (m, 2H), 1.78-1.67 (m, overlapped, 1H), 1.45 – 1.32 (m, 2H), 1.29 – 1.15 (m, 20H), 0.87 (t, overlapped, *J* = 6.6 Hz, 3H), 0.83 – 0.76 (m, overlapped, 6H).
^{13}C NMR (75 MHz, DMSO-*d6*): δ 172.8, 170.9, 155.9 (C=O), 137.1, 128.3 (x2) (CH), 127.7 ©, 127.6 (CH), 65.3 (CH_2), 59.3 (CH), 38.4, 36.4 (CH_2), 31.3 (CH), 29.0 (x3), 28.7 (x2), 26.3, 25.2 (x2), 24.4, 22.1 (CH_2), 12.3, 14.0, 10.9 (CH_3).
HR ESMS: *m/z:* calcd for $C_{26}H_{44}N_2O_3$: 455.3250; found: 455.3251 [$M + Na^+$].

*(S)-benzyl (1-(dodecylamino)-1-oxo-3-phenylpropan-2-yl)carbamate (***7Phe***):* Compound **7Phe** was obtained (yield 92%) as a white solid. The NMR spectra were consistent with those described in the literature.[5]

*(S)-benzyl (1-(hexylamino)-3-methyl-1-oxobutan-2-yl)carbamate (***7ValC6***):* Compound **7ValC6**, was obtained following the same procedure as above except that *n*-hexylamine was used. A white solid was obtained (yield 96%).
^{1}H NMR (300 MHz, DMSO-*d*$_6$): *d* 7.85 (s, 1H), 7.42 – 7.25 (m, 5H), 7.18 (d, *J* = 8.8 Hz, 1H), 5.02 (s, 2H), 3.78 (t, *J* = 8.0 Hz, 1H), 3.17 – 2.88 (m, 2H), 1.93 (dt, *J* = 13.5, 6.8 Hz, 1H), 1.46 – 1.14 (m, 8H), 0.84 (m, 9H).

[5] K., Shigeki; K., Hiroki; Y., Takatoshi; N., Miharu; Y., Kentaro; N., Masaaki; M., Naoki; T., Akira. *Chem. Pharm. Bull*. **2000**, *48*, 920 – 934.

^{13}C NMR (75 MHz, DMSO-d_6): *d* 170.8, 156.0 (C=O), 128.3 (x3) (CH), 127.7 ©, 127.5 (x2) (CH), 65.3 (CH_2), 60.3 (CH), 38.3 (CH_2), 30.9 (CH), 30.2, 28.9, 25.9, 22.0 (CH_2), 19.2, 18.2, 13.8 (CH_3).
HR ESMS: *m/z*: calcd for $C_{19}H_{30}N_2O_3$: 335.2335; found: 335.2331 [$M + H^+$].

8.3. General procedure for deprotection of carbobenzyloxy group: Palladium catalyst (10% *w/w*) was suspended in MeOH (250 mL) and stirred under H_2 at room temperature for 10 min. Subsequently, a solution of carbobenzyloxy amino compound in MeOH (150 mL) was added via syringe, followed by stirring under H_2 at room temperature for 2 – 4 h. The reaction mixture was then filtered through Celite®, and the solvent was removed under reduced pressure to yield respective amine.

*(S)-2-amino-N-dodecyl-3-methylbutanamide (**8Val**):* White solid was obtained (yield 98%). The compound was used in crude form for the next reaction.
^{1}H NMR (500 MHz, DMSO-d_6): δ 7.75 (t, *J* = 4.5 Hz, 1H), 3.13 – 2.97 (m, 2H), 2.89 (d, *J* = 5.0, 1H), 1.83 (sext, 6.0, 13.0, 19.5, 1H), 1.44 – 1.32 (m, 2H), 1.31 – 1.15 (m, 18H), 0.91 – 0.81 (m, 6H), 0.77 (d, *J* = 6.5 Hz, 3H). The amine's signals (NH_2) are very broad and cannot distinguish in the spectrum.
^{13}C NMR (125 MHz, DMSO-d_6): δ 174.2 (C=O), 60.0 (CH), 38.2, 31.6 (CH_2), 31.3 (CH), 29.2, 28.9 (x2), 28.7 (x3), 26.4, 22.1 (x2) (CH_2), 19.5, 17.1, 13.9 (CH_3).
HR ESMS: *m/z:* calcd for $C_{17}H_{36}N_2O$: 258.2906; found: 258.2908 [$M + H^+$].

*(2S, 3R)-2-amino-N-dodecyl-3-methylpentanamide (**7Ile**):* The amine was obtained (yield 98%) as a white solid. The compound was used in crude form for the next reaction.
^{1}H NMR (500 MHz, $CDCl_3$): 7.27 (s, 1H), 3.31 – 3.13 (m, 3H), 2.00 – 1.91 (m, 1H), 1.51 – 1.41 (m, 2H), 1.31 – 1.16 (m, 18H), 1.11 – 1.00 (m, 2H), 0.93 (d, *J* = 7 Hz, 3H), 0.85 (dd, *J* = 7.4, 15.3 Hz, 6H). The amine's signals (NH_2) are very broad and cannot distinguish in the spectrum.
^{13}C NMR (125 MHz, $CDCl_3$): δ 174.3 (C=O), 60.1 (CH), 39.1, 38.0 (CH_2), 32.0 (CH), 29.8, 29.7 (x2), 29.6 (x2), 29.4 (x2), 27.1, 25.1, 23.7 (CH_2), 17.9, 16.3, 16.2 (CH_3).
HR ESMS: *m/z:* calcd for $C_{18}H_{38}N_2O$: 299.3062; found: 299.3061 [$M + H^+$].

*(S)-2-amino-N-dodecyl-3-phenylpropanamide **(8Phe)**:* The reaction furnished the amine in 98% as white solid. The compound was used in crude form for the next reaction.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.25 – 7.09 (m, 5H), 3.50 (dd, *J* = 4.2, 9.1 Hz, 1H), 3.21 – 3.09 (m, 3H), 2.62 (dd, *J* = 9.1, 13.7 Hz, 1H), 1.49 – 1.29 (m, 2H), 1.27 – 1.11 (m, 19H), 0.80 (t, *J* = 6.7 Hz, 3H). The amine's signals (NH_2) are very broad and cannot distinguish in the spectrum.
^{13}C NMR (75 MHz, $CDCl_3$): δ 174.1 (C=O), 138.1 ©, 129.3 (x2), 128.7 (x2), 126.1, 56.5 (CH), 41.2, 39.2, 32.0, 29.7 (x2), 29.6 (x2), 29.4 (x2), 27.0, 23.5, 22.7 (CH_2), 14.1 (CH_3).
HR ESMS: *m/z:* calcd for $C_{21}H_{36}N_2O$: 333.2906; found: 333.2902 [$M + H^+$].

*(S)-2-amino-N-hexyl-3-methylbutanamide (**8ValC6**):* Colorless oil was obtained (yield 95%). The compound was used in crude form for the next reaction.
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30 (s, 1H), 3.22 – 2.99 (m, 3H), 2.20 – 1.85 (m, 3H), 1.45 – 1.29 (m, 2H), 1.26 – 1.09 (m, 6H), 0.86 (d, *J* = 5.0 Hz, 3H), 0.80 – 0.68 (m, 6H).
^{13}C NMR (75 MHz, $CDCl_3$): δ 173.9 (C=O), 59.9 (CH), 38.8, 31.2, 30.7, 29.3, 26.4, 22.2, (CH_2), 19.4, 16.0, 13.7 (CH_3).

HR ESMS: *m/z*: calcd for $C_{11}H_{24}N_2O$: 201.1967; found: 201.1967 [$M + H^+$].

8.4. General procedure for preparing the final compounds: A solution of respective amine (16.3 mmol) in THF (150 mL) was treated at 0 ºC under N_2 with solid K_2CO_3 (61.9 mmol, 3.8 eq.). The mixture was stirred for 15 minutes at 0 ºC, after with a dropping funnel to a solution of commercial available succinic anhydride (32.6 mmol, 2.0 eq.) in THF (50 mL). The mixture was further stirred vigorously for 16 h at room temperature. After this time, the solution was concentrated under reduced pressure and the crude residue was dissolved in water (100 mL); then hydrochloric acid concentrate was added dropwise at 0 ºC until observe the formation of a white precipitate to pH = 4. The white solid obtained was filtered under vacuum, and the residue was washed with water (300 mL). The compound was dried under reduced pressure at 50 ºC overnight.

*(S)-4-((1-(dodecylamino)-3-methyl-1-oxobutan-2-yl)amino)-4-oxobutanoic acid (**1**):* A white solid was obtained (yield 95%).6 mmol, 95%) as a white solid.
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 12.0 (br s, 1H), 7.90 – 7.82 (m, 2H), 4.07 (t, *J* = 16 Hz, 1H), 3.12 – 2.92 (br m, 2H), 2.44 – 2.36 (m, 4H), 1.93 (sext, *J* = 10, 16 Hz, 1H), 1.40 – 1.31 (m, 2H), 1.30 – 1.18 (m, 18H), 0.85 (t, *J* = 5 Hz, 3H), 0.82 (d, J = 5 Hz, 6H).
^{13}C NMR (125 MHz, DMSO-*d*$_6$): δ 173.8, 171.0, 170.7 (C=O), 57.9 (CH), 38.3, 31.3 (CH_2), 30.4 (CH), 29.9, 29.3, 29.0 (x3), 29.0 (x2), 28.7, 26.3, 22.0 (CH_2), 19.15, 18.10, 13.89 (CH_3).
HR ESMS: *m/z*: calcd for $C_{21}H_{40}N_2O_4$: 383.2914; found: 383.2910 [$M - H^+$].

*4-(((2S,3R)-1-(dodecylamino)-3-methyl-1-oxopentan-2-yl)amino)-4-oxobutanoic acid (**2**):* This reaction furnished the succinic derivate **2** in 89% yield as white solid.
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 11.7 (br s, 1H), 7.84 – 7.79 (m, , 2H), 4.10 (t, *J* = 8 Hz, 1H), 3.13, – 2.91 (br m, 2H), 2.45 – 2.33 (m, 4H), 1.74 – 1.64 (m, 1H), 1.43 – 1.33 (m, 2H), 1.29 – 1.17 (m, 20H), 0.85 (t, *J* = 6 Hz, 3H), 0.83 – 0.76 (overlapped d, t, 6H).
^{13}C NMR (125 MHz, DMSO-*d6*): δ 173.8, 170.8, 170.7 (C=O), 56.8 (CH), 38.3, 36.6, 31.3 (CH_2), 31.3 (CH), 29.9, 29.3, 29.0 (x3), 28.9, 28.7 (x2), 24.3, 22.0 (x2) (CH_2), 15.3, 13.9, 11.1 (CH_3).
HR ESMS: *m/z:* calcd for $C_{22}H_{42}N_2O_4$: 399.3223; found: 399.3217 [$M + H^+$].

(S)-4-((1-(dodecylamino)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobutanoic acid (3): Acid **3** was obtained (yield 93%) as a white solid.
^{1}H NMR (500 MHz, DMSO-*d*$_6$): δ 11.96 (br s, 1H), 8.09 (d, *J* = 8 Hz, 1H), 7.84 (t, *J* = 6 Hz, 1H), 7.27 – 7.15 (m, 5H), 4.40 (sext, *J* = 9.0, 5.5 Hz, 1H), 3.08 – 2.91 (br m, 2H), 2.74 (dd, *J* = 9.0, 13.5 Hz, 1H), 2.37 – 2.18 (m, 5H), 1.37 – 1.12 (m, 20H), 0.85 (t, *J* = 5.5 Hz, 3H).
^{13}C NMR (125 MHz, DMSO-*d6*): δ 171.0, 170.7 (x2), (C=O), 138.0 (C), 129.0 (x2), 127.9 (x2), 126.1, 54.1 (CH), 38.5, 37.8, 31.3, 30.2, 29.5, 29.0 (x4), 28.9, 28.8, 28.7, 26.2, 22.1 (CH_2), 13.9 (CH_3).
HR ESMS: *m/z:* calcd for $C_{25}H_{40}N_2O_4$: 433.2563; found: 433.2564 [$M + H^+$].

*(S)-4-((1-(cyclohexylamino)-3-methyl-1-oxobutan-2-yl)amino)-4-oxobutanoic acid (**4**):* A white solid was obtained (yield 94%).

^{1}H NMR (300 MHz, DMSO-d_6): δ 12.00 (br s, 1H), 7.83 (d overlapped, 2H), 4.17 – 3.97 (dd, J = 6.9, 9.5 Hz, 1H), 3.16 – 2.90 (m, 2H), 2.41 (s, 4H), 2.02 – 1.82 (m, 1H), 1.53 – 1.11 (m, 8H), 0.98 – 0.71 (t app, 9 H).
^{13}C NMR (75 MHz, DMSO-d_6): δ 173.4, 171.5, 171.2 (C=O), 58.3 (CH), 38.8 (CH_2), 31.4 (CH), 30.8, 30.4 (CH_2), 29.8, 29.4, 26.5, 22.5 (CH_2), 19.6, 18.6, 14.3 (CH_3).
HR ESMS: m/z: calcd for $C_{15}H_{28}N_2O_4$: 323.1947; found: 323.1950 [M + Na^+].

9. RMN SPECTRA.

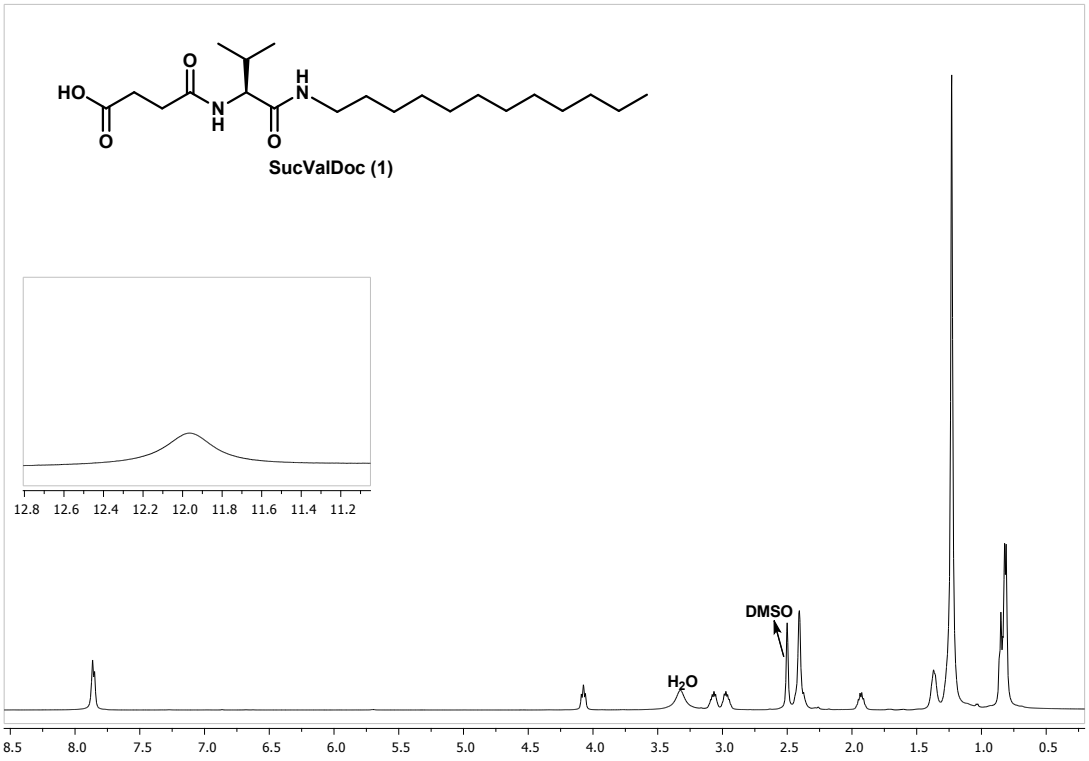

Figure S3. ^{1}H NMR spectrum of compound **1**.

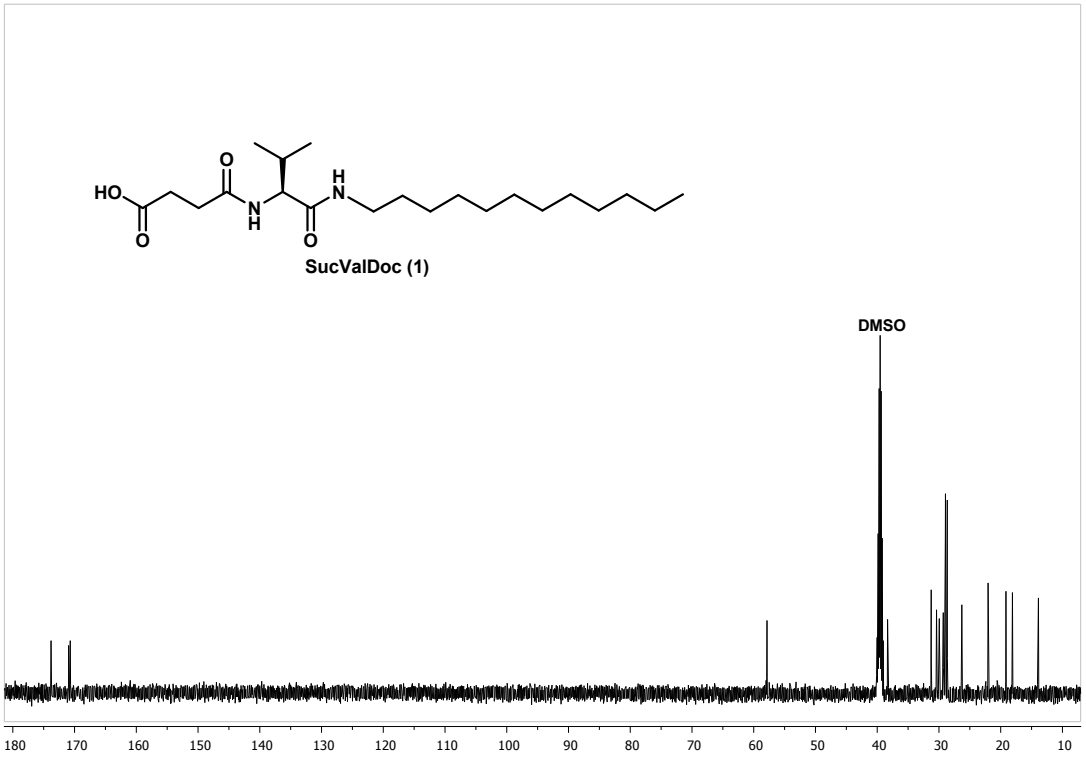

Figure S4. ^{13}C NMR spectrum of compound **1**.

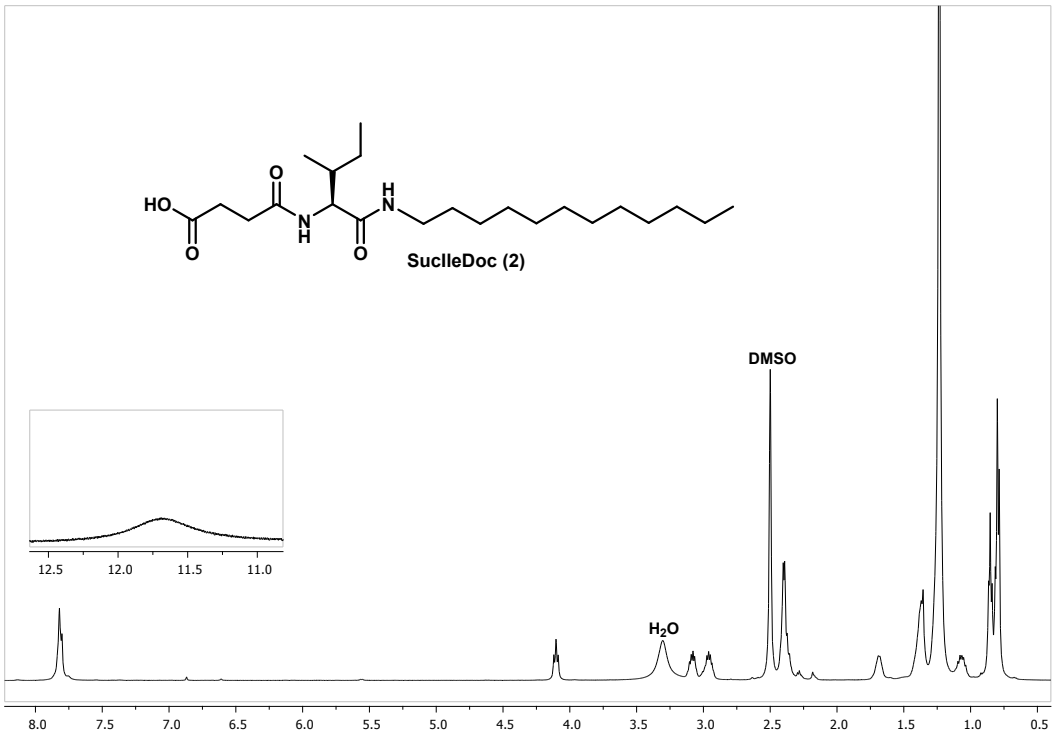

Figure S5. ^{1}H NMR spectrum of **2**.

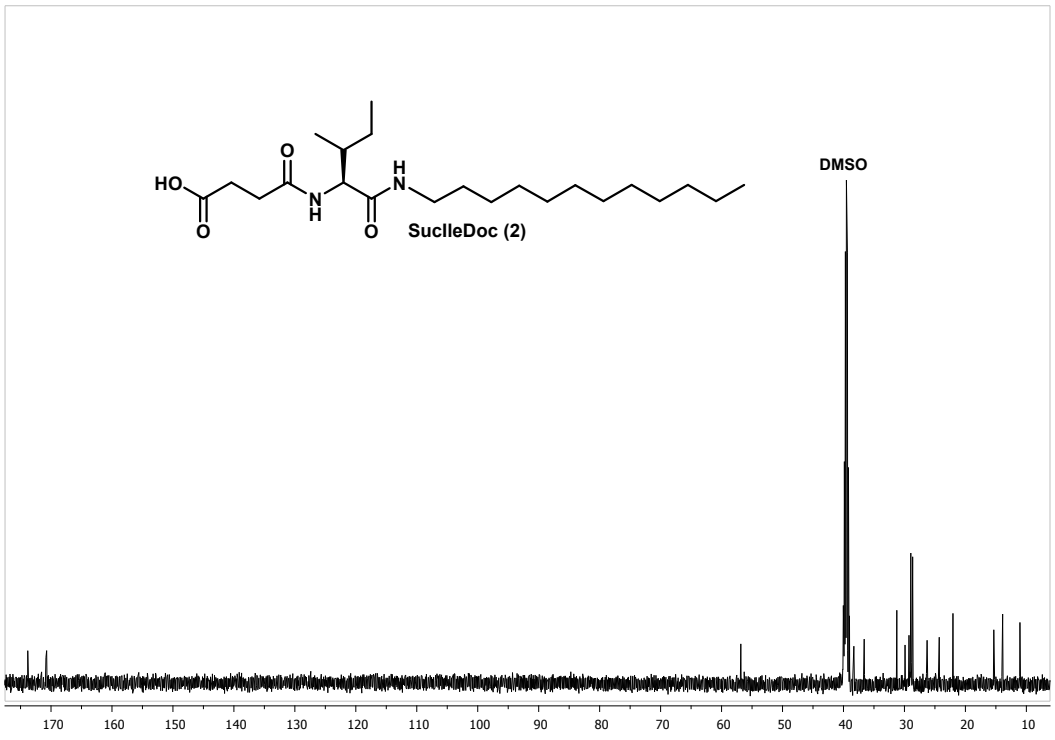

Figure S6. ^{13}C NMR spectrum of **3**.

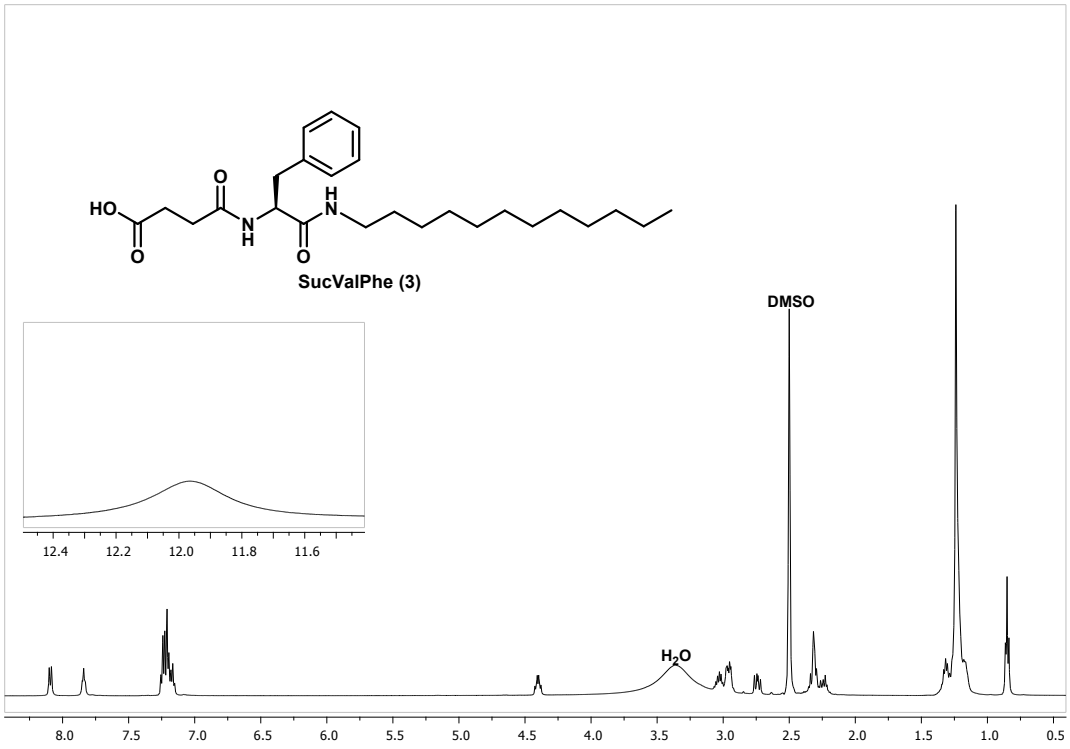

Figure S7. ^{1}H NMR spectrum of compound **3.**

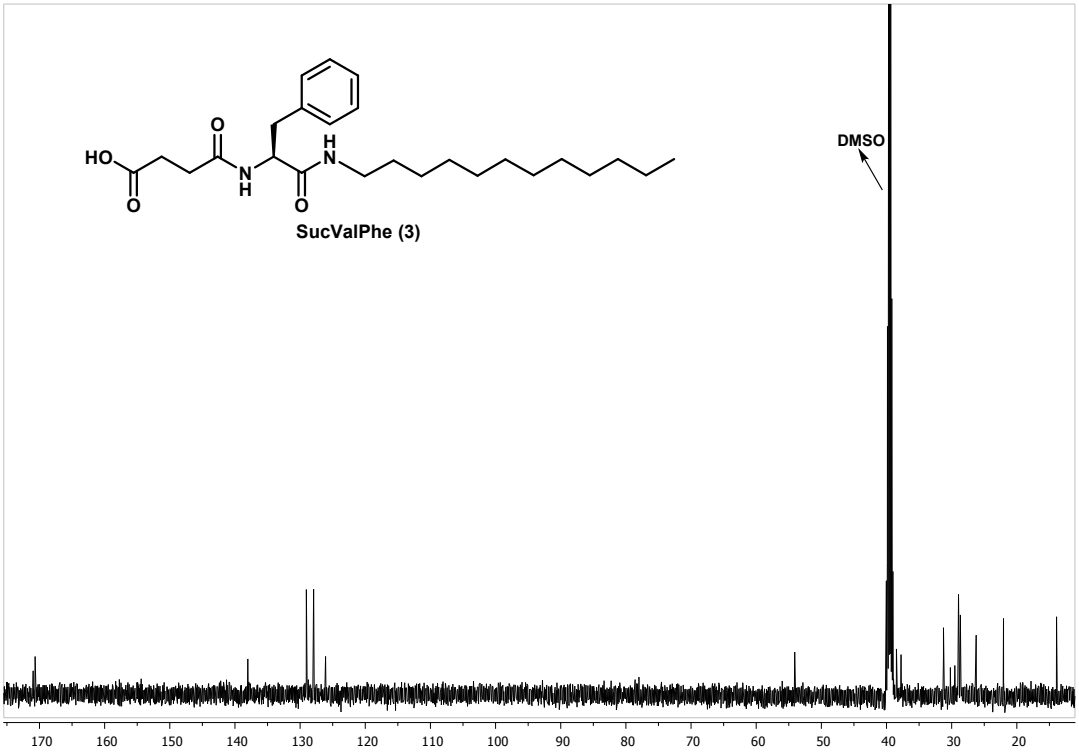

Figure S8. ^{13}C NMR spectrum of compound **3**.

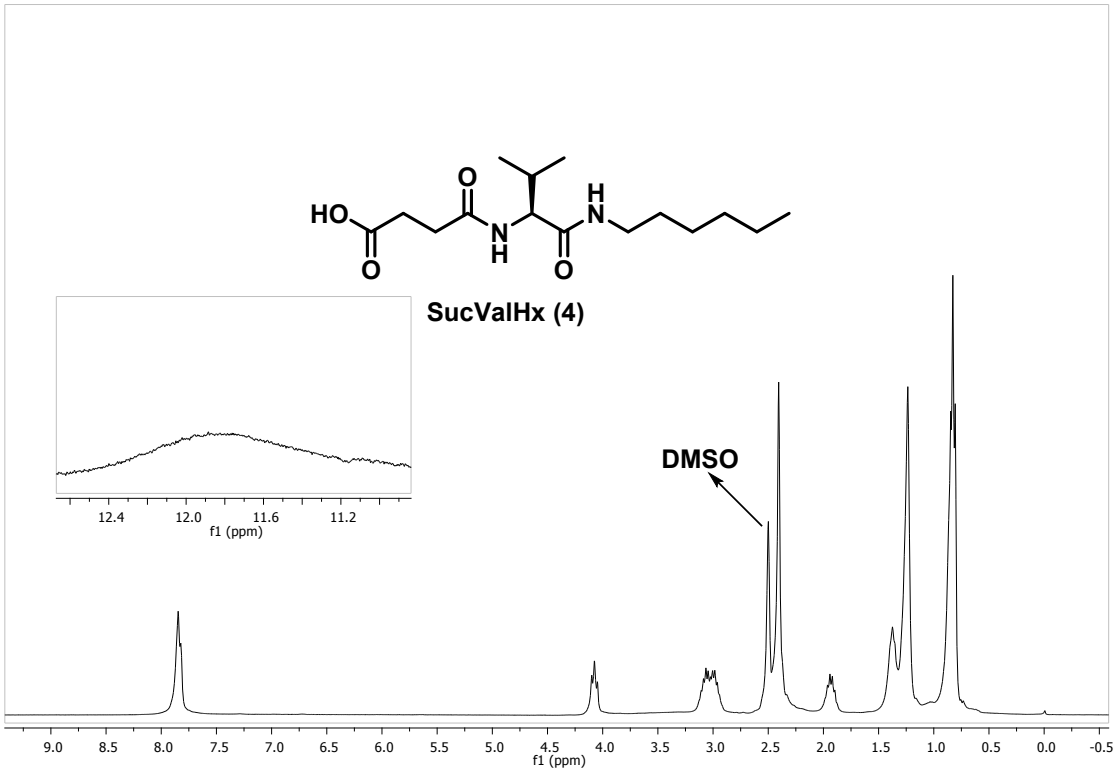

Figure S9. ^{1}H NMR spectrum of compound **4**.

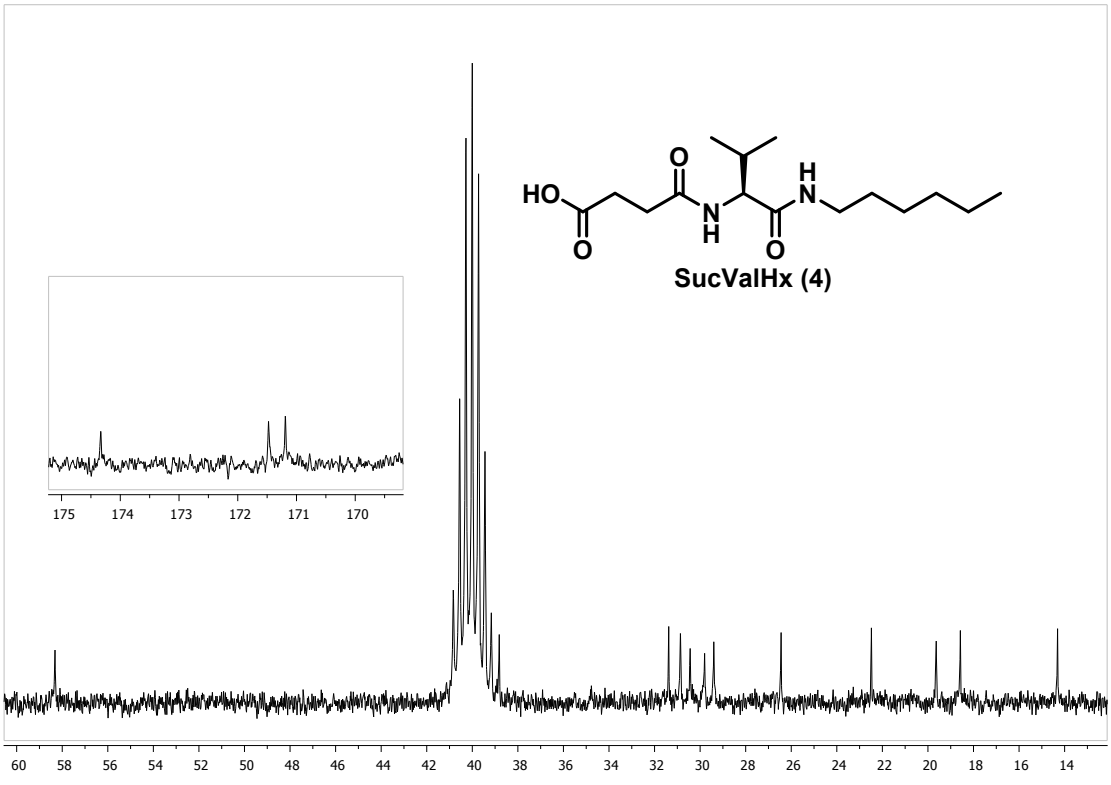

Figure S10. ^{13}C NMR spectrum of compound **4**.

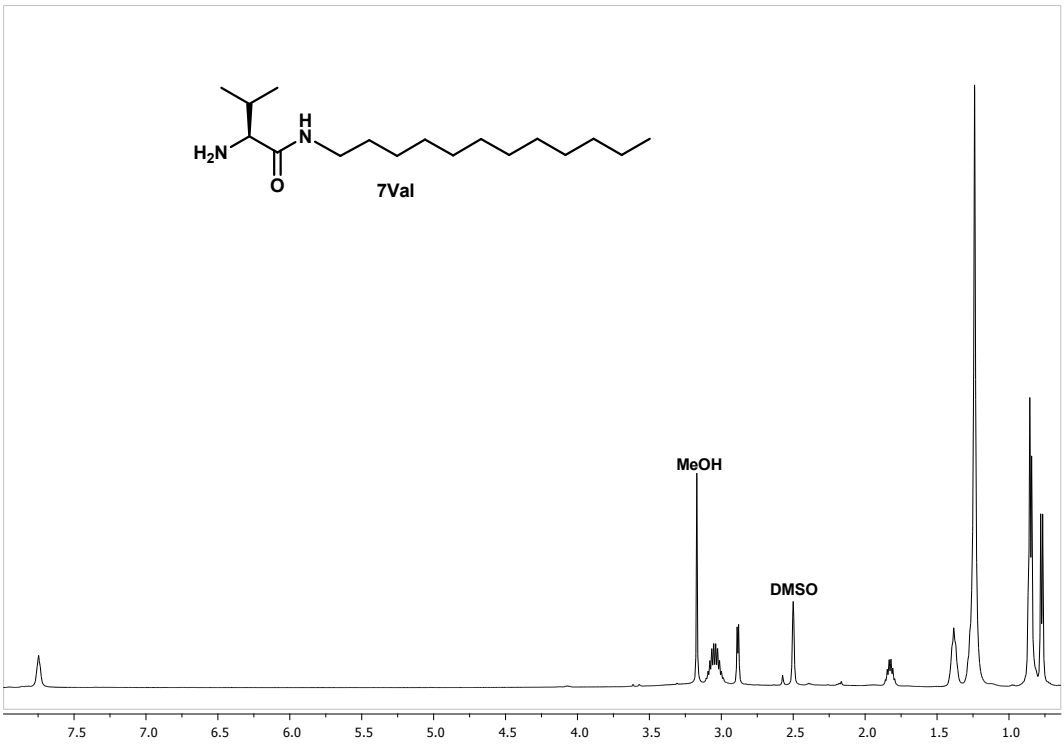

Figure S11. ^{1}H NMR spectrum of amine **8Val**.

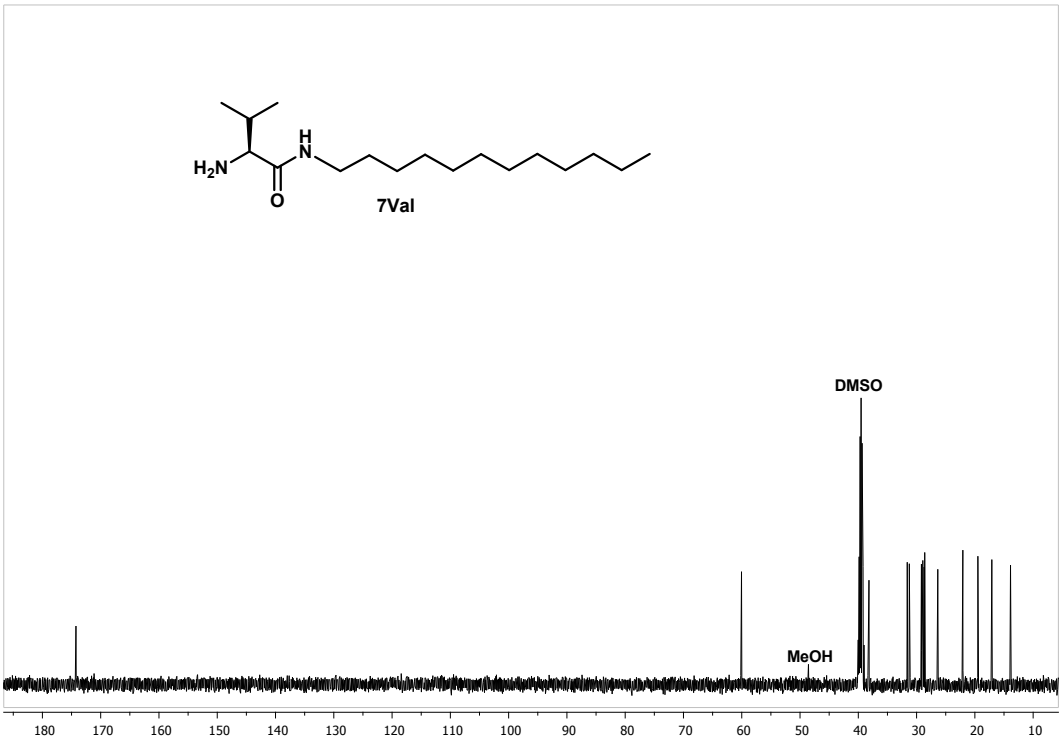

Figure S12. ^{13}C NMR spectrum of amine **8Val**.

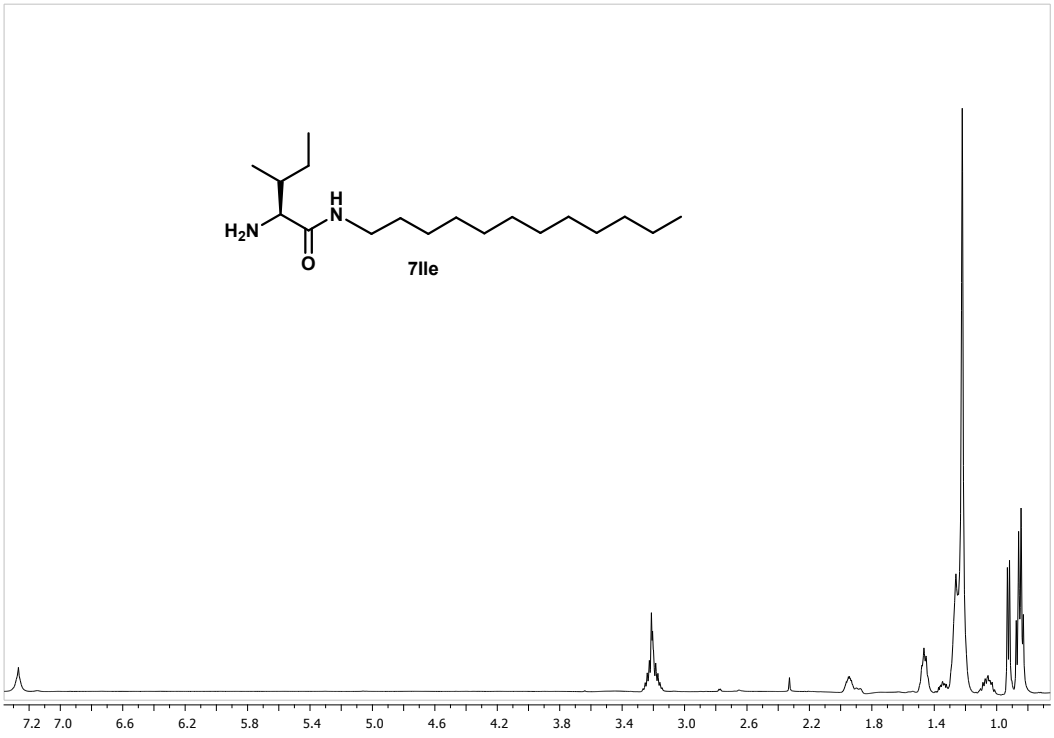

Figure S13. ^{1}H NMR spectrum of amine **8Ile**.

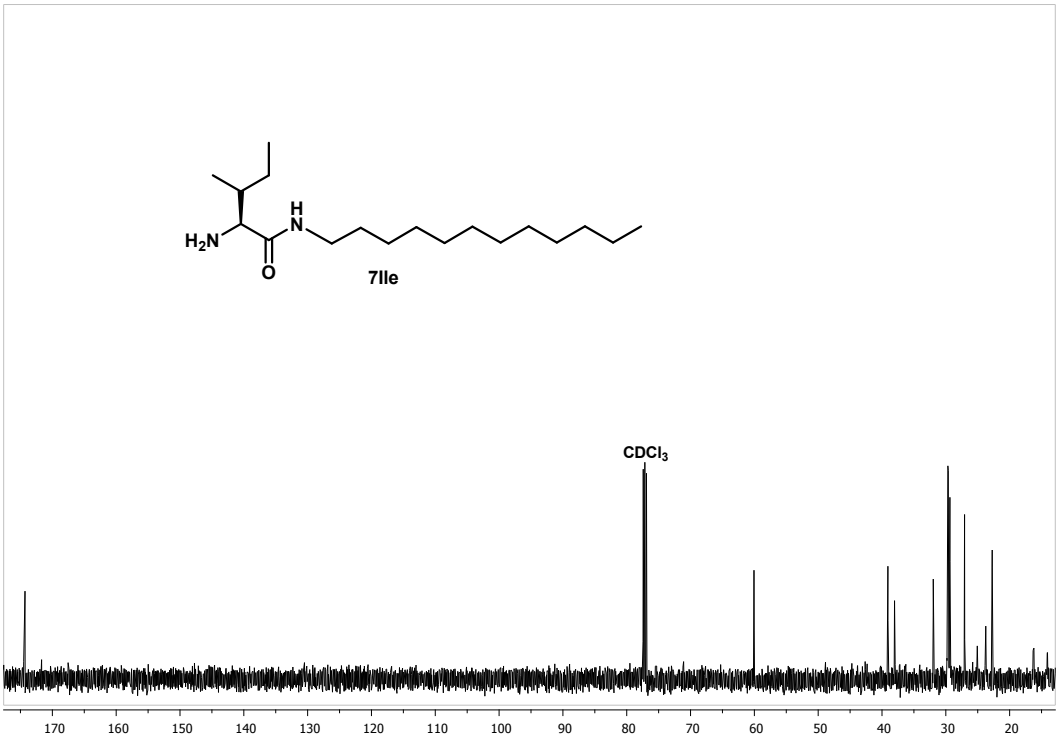

Figure S14. ^{13}C NMR spectrum of amine **8Ile**.

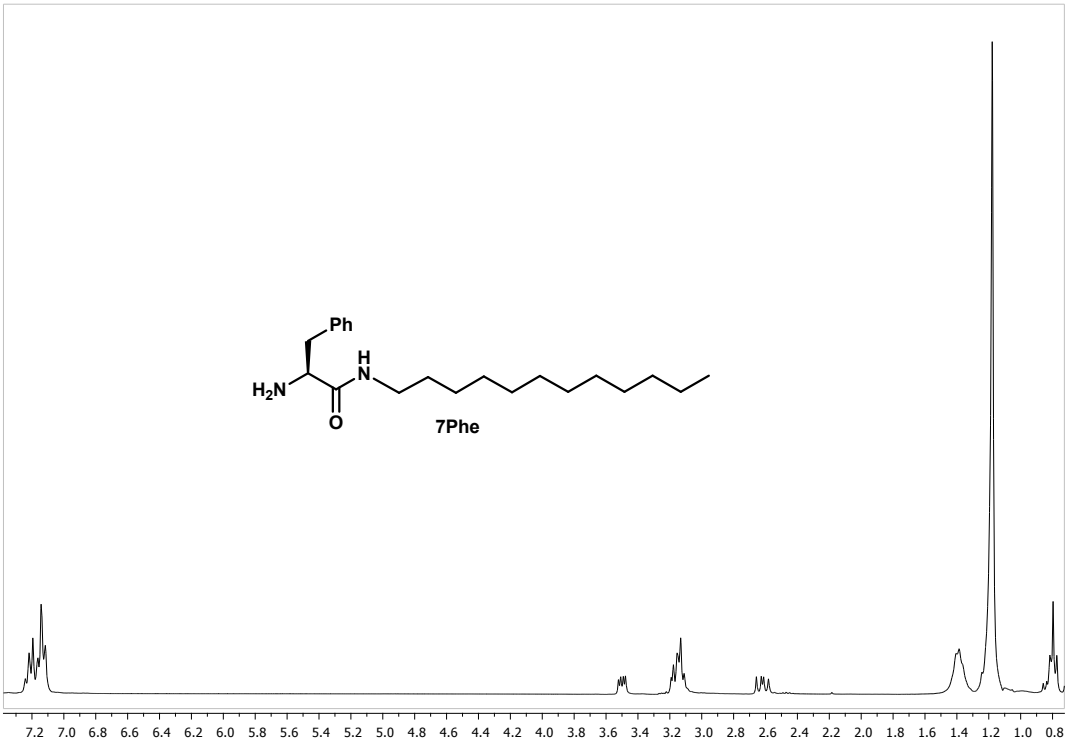

Figure S15. ^{1}H NMR spectrum of amine **8Phe**.

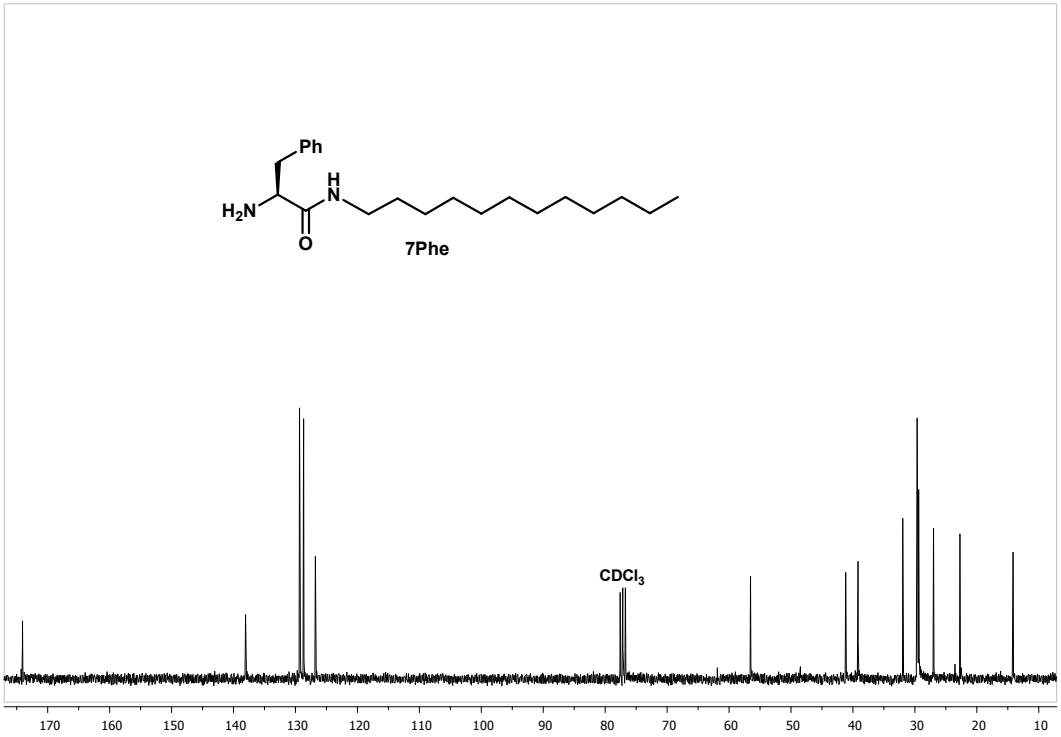

Figure S16. ^{13}C NMR spectrum of amine **8Phe**.

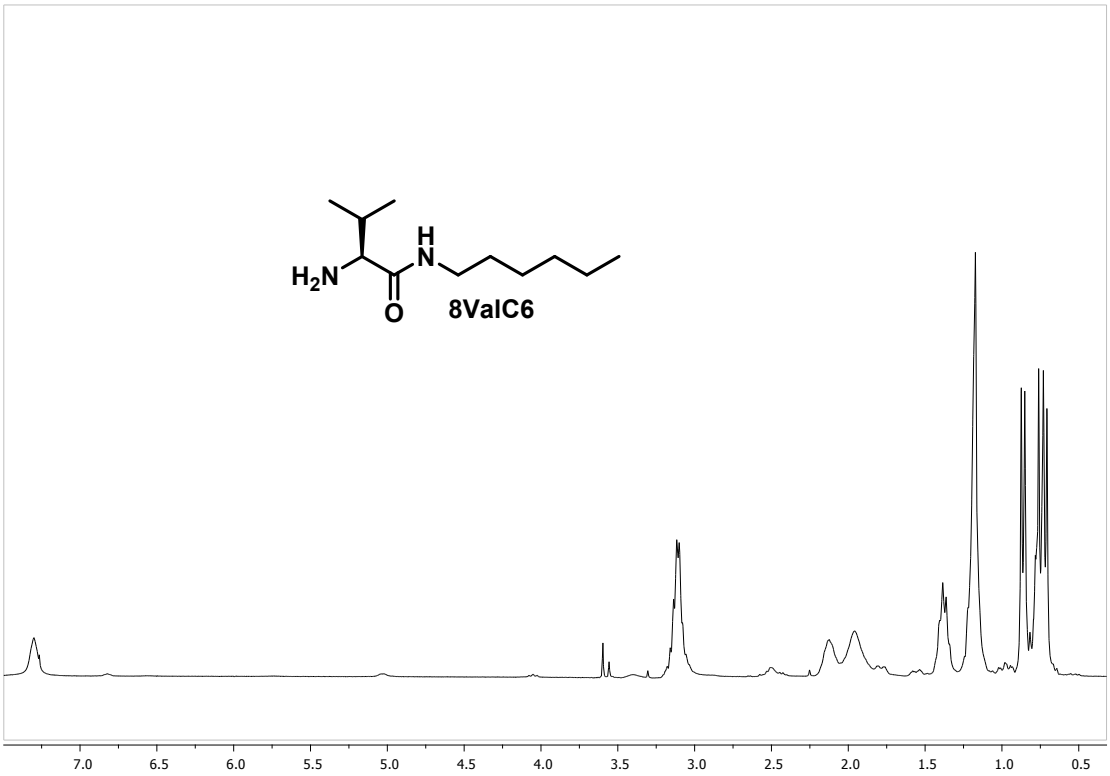

Figure S17. ^{1}H NMR spectrum of amine **8ValC6**.

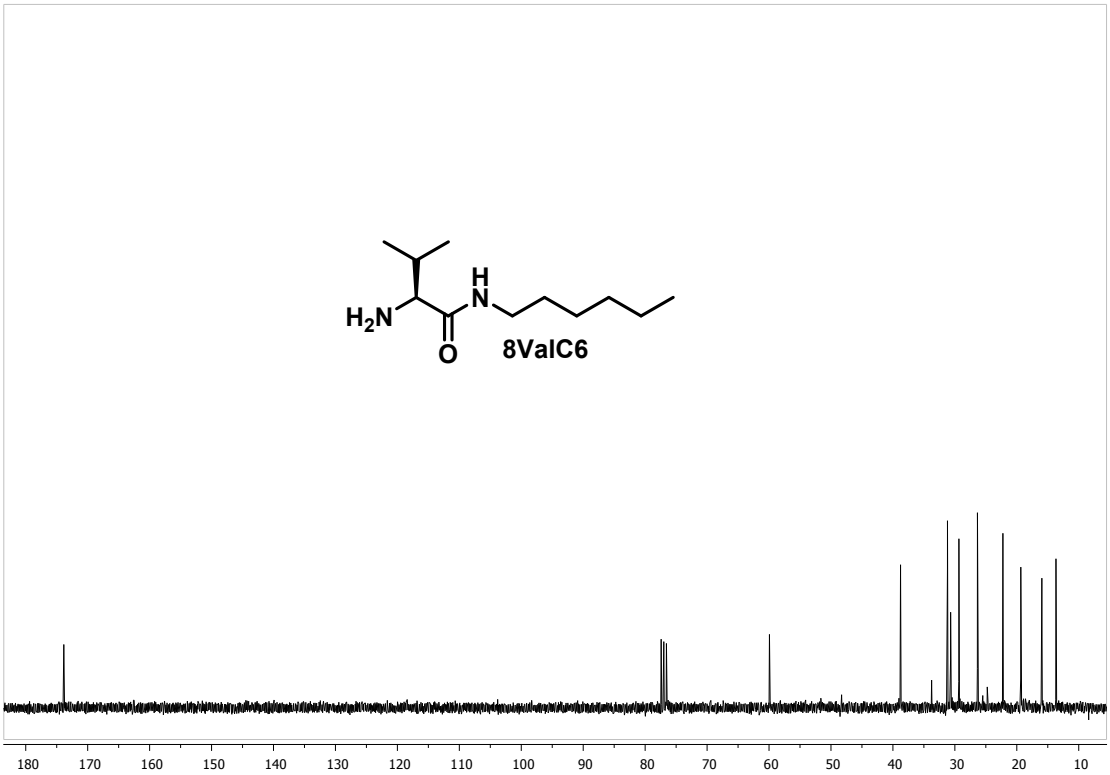

Figure S17. ^{13}C NMR spectrum of amine **8ValC6**.

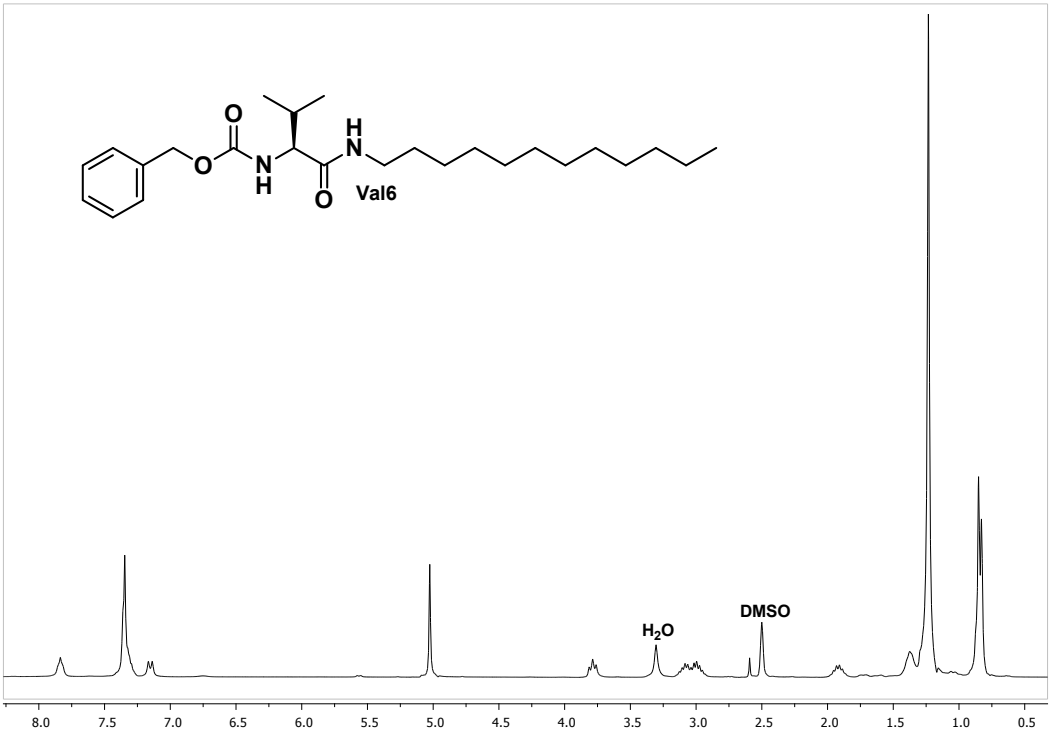

Figure S18. ^{1}H NMR spectrum of compound **7Val**.

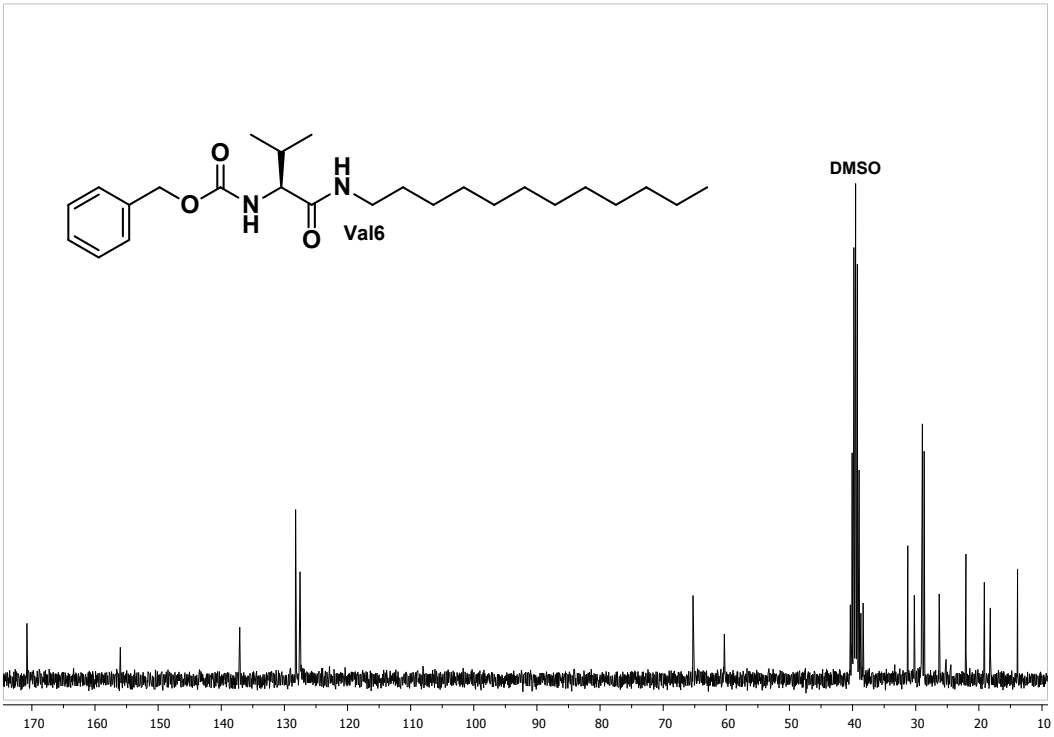

Figure S19. ^{13}C NMR spectrum of compound **7Val**.

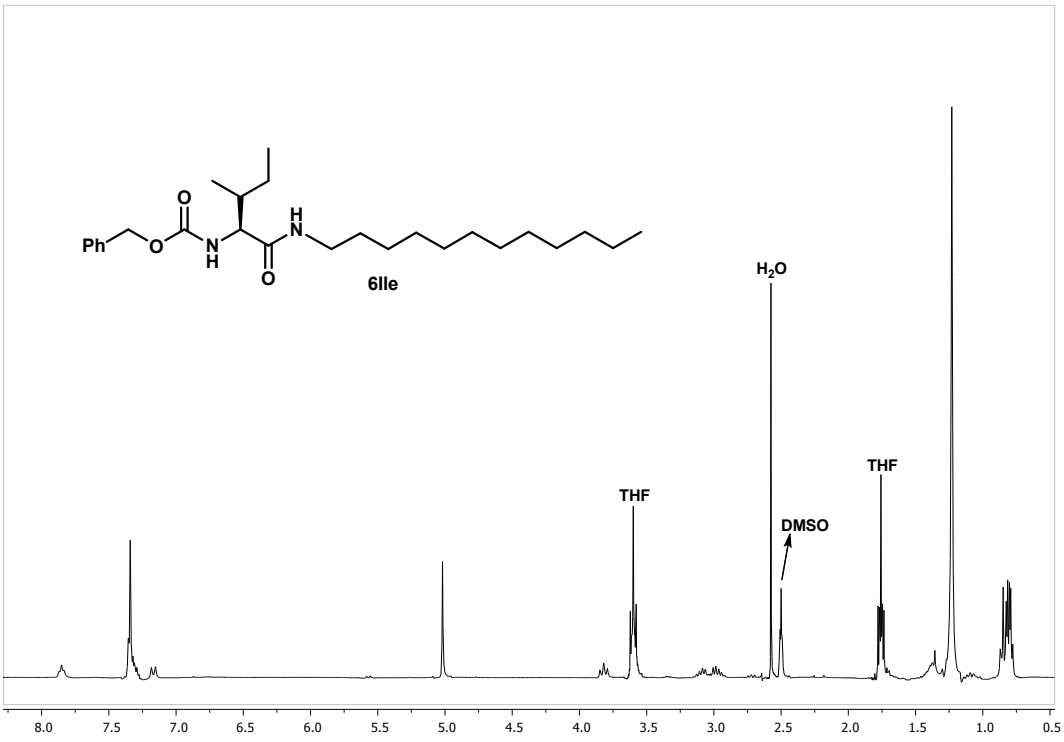

Figure S20. ^{1}H NMR spectrum of compound **7Ile**.

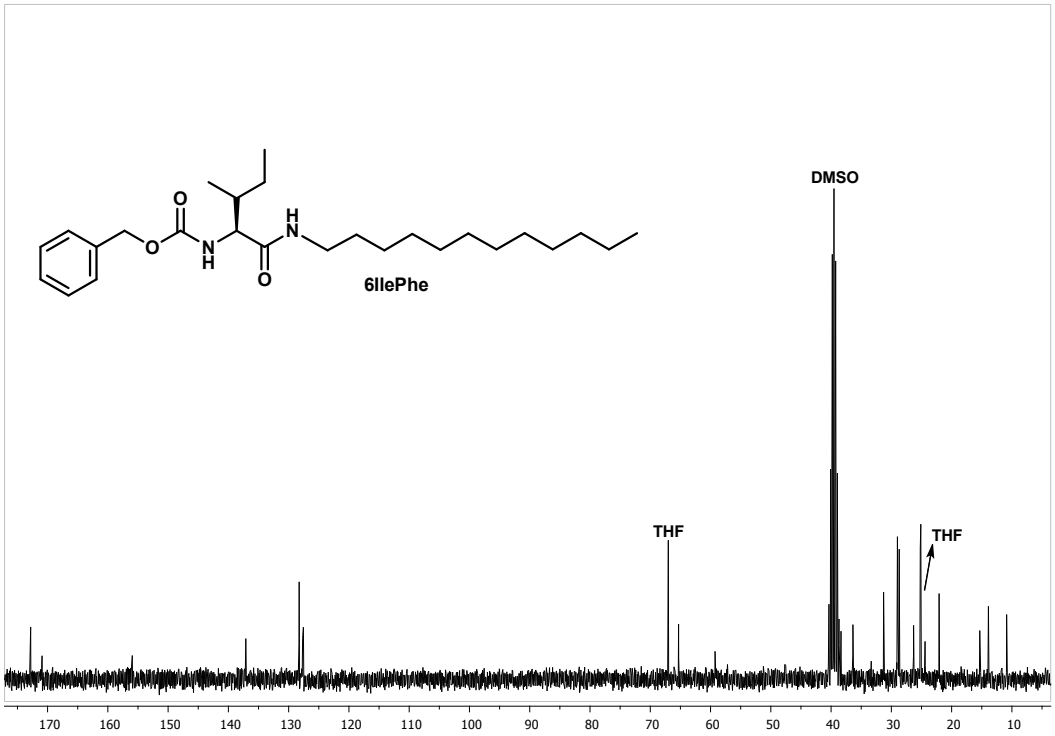

Figure S20. ^{13}C NMR spectrum of compound **7Ile**.

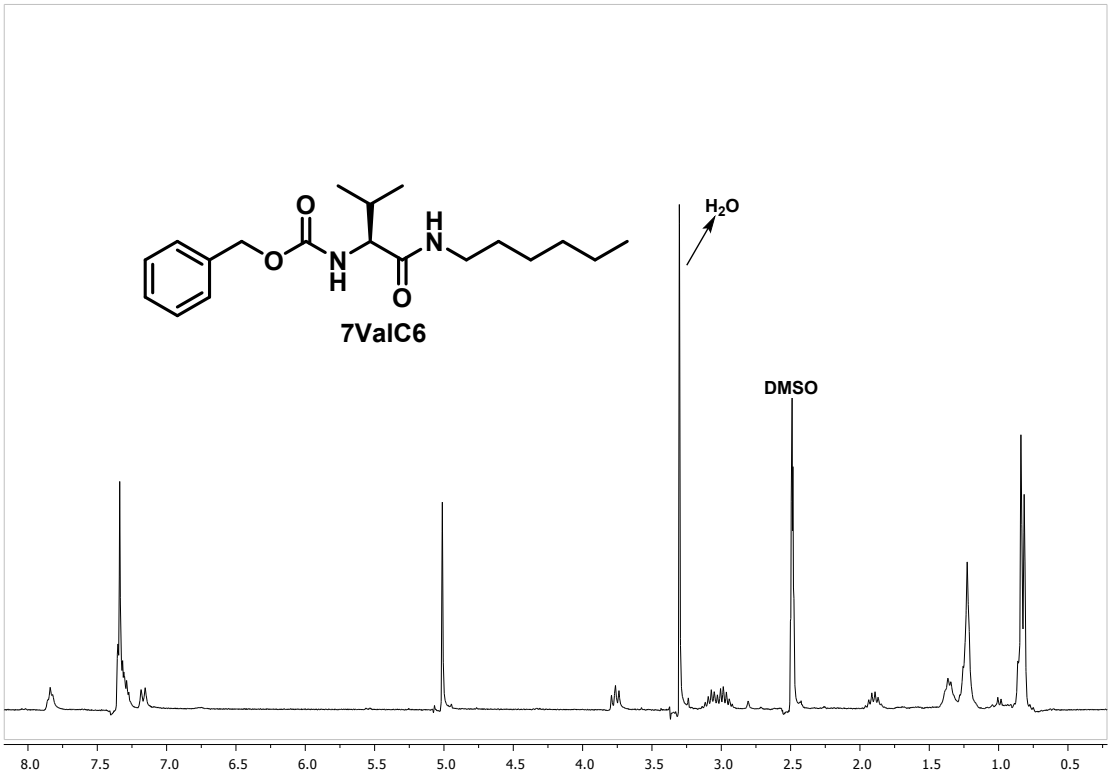

Figure S21. ^{1}H NMR spectrum of compound **7ValC6**.

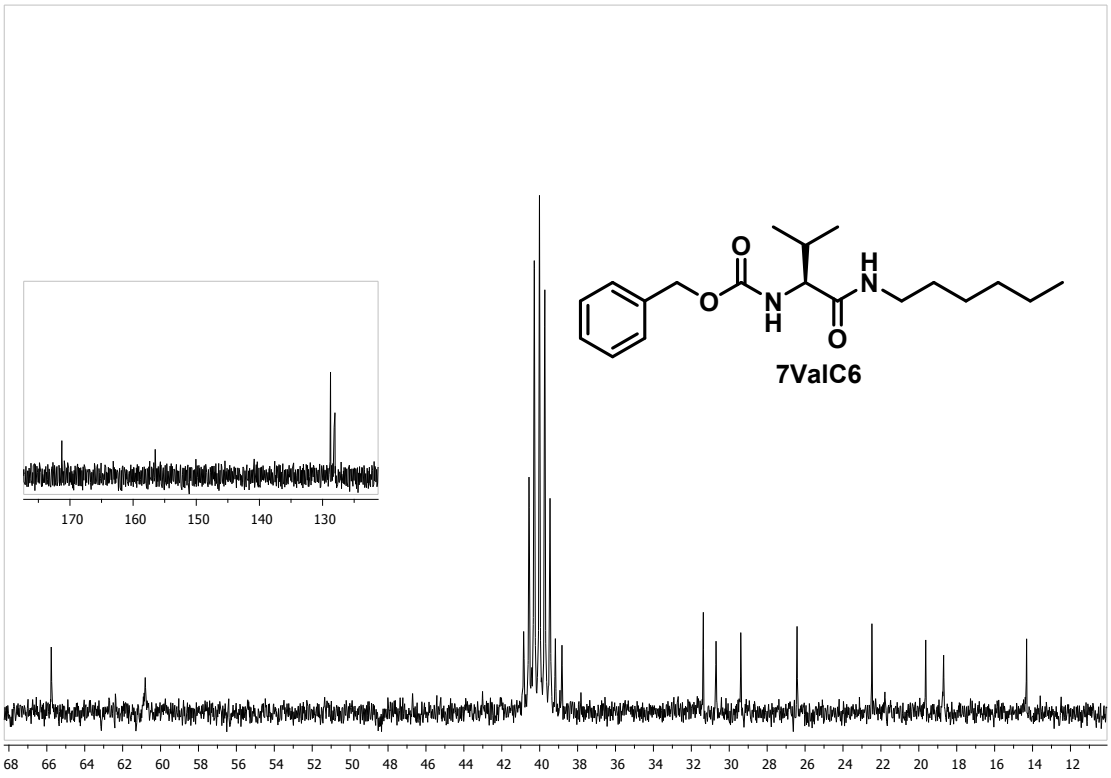

Figure S22. ^{13}C NMR spectrum of compound **7ValC6**.