Supporting Information

Divergent total syntheses of kavaratamide A, B and C

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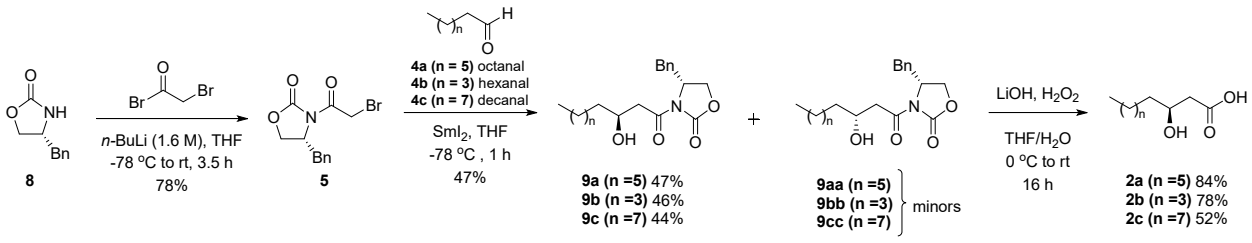
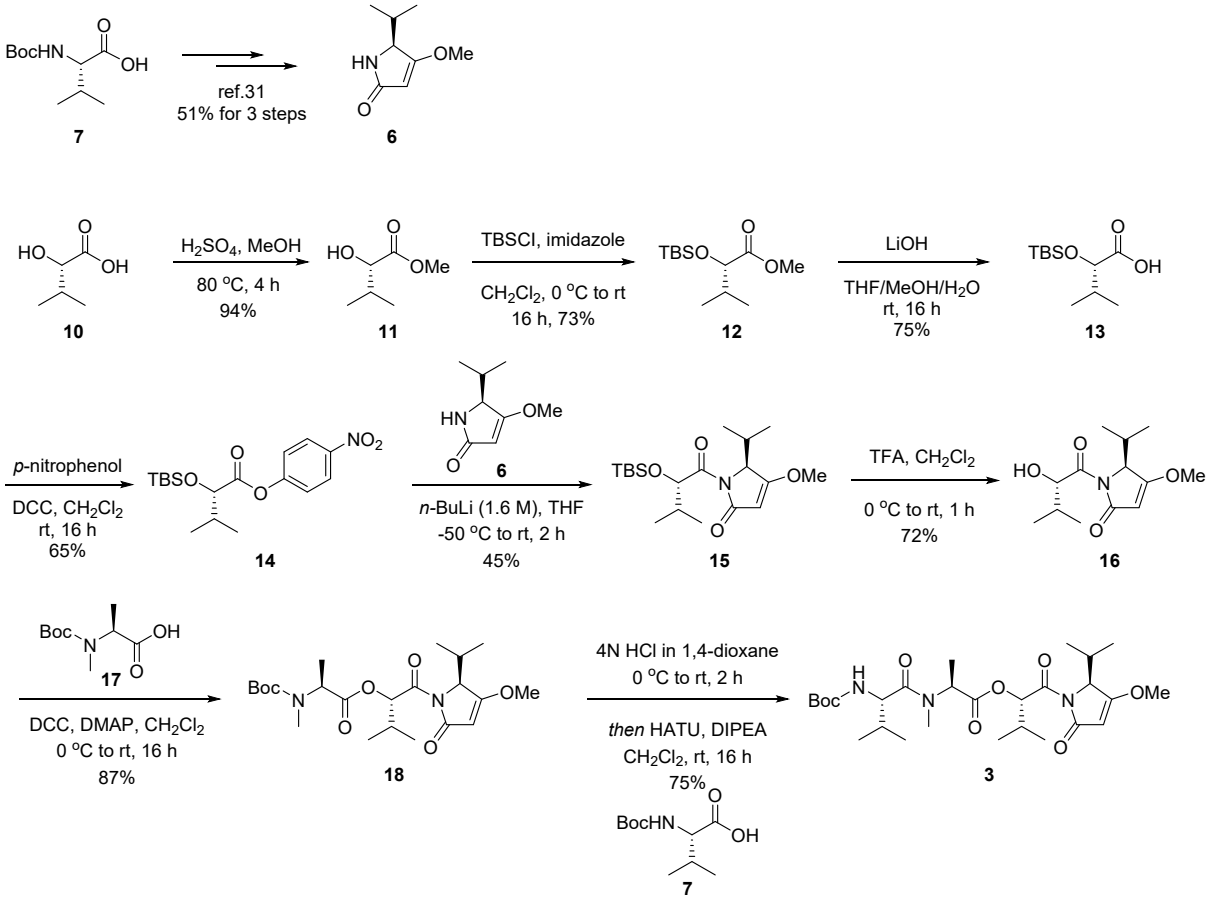
I. General information:

All the chemicals and solvents used were of LR grade purchased from Sigma Aldrich, Combi-block, and TCI and used as received. ^{1}H NMR spectra were recorded on JNM-ECZL500R (JEOL) NMR spectrometer using tetramethylsilane (TMS) as an internal standard and $CDCl_3$/DMSO-d_6 as a solvent. The purity determination of the starting materials and reaction monitoring was accomplished by thin-layer chromatography (TLC) on Merck silica gel GF_{254} plates. The reaction products were purified by column chromatography using silica gel (200-300 mesh). High resolution mass spectrometry was performed using Field desorption Ionization (FDI). All the known compounds were identified by ^{1}H NMR spectroscopy for structural identification. All chemical shifts δ are in ppm. The chemical shift (δ ppm) is related to the resonance of the deuterated solvent as the internal references ($CDCl_3$ δH= 7.26 ppm, δC = 77.16 ppm, DMSO-d_6 δH= 2.50 ppm, δC = 39.60 ppm).

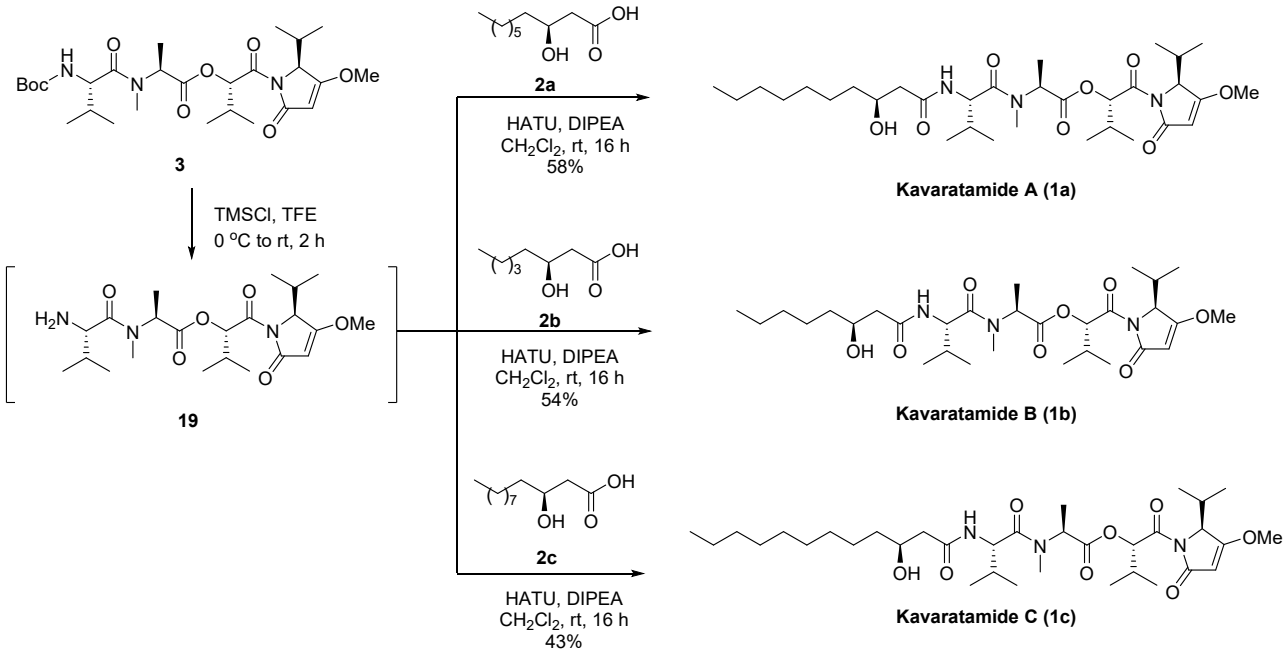
II. General route of synthesis:



Scheme 1. Synthesis of β-hydroxy carboxylic acid



Scheme 2. Synthesis of key intermediate of kavaratamide A, B and C



Scheme 3. Completion of synthesis of kavaratamide A, B and C

III. General procedures

Preparations of (R)-4-benzyl-3-(2-bromoacetyl)oxazolidine-2-one (5).

To a solution of (*R*)-4-benzyloxazolidin-2-one (**8)** (500 mg, 2.82 mmol) in dry THF (10 mL) was added dropwise *n*-BuLi (2.11 mL, 3.39 mmol, 1.6 M solution in THF) at -78 °C in the presence of nitrogen gas. The resulting solution was stirred at -78 °C for 30 min. 2-bromoacetyl bromide (678 mg, 3.39 mmol,) in THF (5 mL) was added dropwise to above solution and resulting solution was stirred at -78 °C for 30 min. After 30 min reaction mixture was warmed to rt and stirred for 2.5h at rt. After completion of the reaction, the reaction mixture was quenched with NH_4Cl (aq) (3 mL), and then extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (3:7) as the eluent to obtain (*R*)-4-benzyl-3-(2-bromoacetyl)oxazolidine-2-one **5** (650 mg, 77.5%) as off white solid. $[\alpha]^{20}$ = -65.73 (*c* = 2.19 in Dichloromethane), λ: 589.3 nm; ^{1} ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.32 (m, 2H), 7.28 (t, *J* = 6.2 Hz, 1H), 7.20 (d, *J* = 6.6 Hz, 2H), 4.72-4.67 (m, 1H), 4.53 (dd, *J* = 17.3, 12.7 Hz, 2H), 4.28-4.21 (m, 2H), 3.32 (dd, *J* = 13.5, 3.2 Hz, 1H), 2.80 (dd, *J* = 13.5, 9.6 Hz, 1H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 166.1, 153.0, 134.8, 129.5, 129.2, 127.6, 66.8, 55.6, 37.6, 28.3.

Preparations of (R)-4-benzyl-3-((S)-3-hydroxydecanoyl)oxazolidine-2-one (9a).

To a solution of SmI_2 (20 mL, 2.01 mmol, 0.1 M solution in THF) in dry THF (5 mL) was added dropwise solution of (*R*)-*4*-benzyl-*3*-(*2*-bromoacetyl)oxazolidine-*2*-one **(5)** (200 mg, 0.67 mmol) and octanal (**4a)** (86 mg, 0.67 mmol) in THF (5 mL) over 5 min at -78 °C in the presence of nitrogen gas. The resulting solution was stirred at -78 °C for 1h. After completion of the reaction, the reaction mixture was quenched with 1N HCl (2 mL), and then extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with aqueous Sodium thiosulfate pentahydrate, brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (4:6) as the eluent to obtain (*R*)-4-benzyl-3-((*S*)-3-hydroxydecanoyl)oxazolidine-2-one **9a** (110 mg, 47%) as off white solid. Diastereomeric ratio (dr = 8.8:1.2, determined by isolated yield). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.28-7.25 (m, 1H), 7.21-7.19 (m, 2H), 4.71-4.66 (m, 1H), 4.23-4.20 (m, 1H), 4.18 (d, *J* = 2.9 Hz, 1H), 4.15-4.10 (m, 1H), 3.30 (dd, *J* = 13.3, 3.4 Hz, 1H), 3.17 (dd, *J* = 17.5, 2.5 Hz, 1H), 2.97 (dd, *J* = 17.4, 9.5 Hz, 1H), 2.81-2.75 (m, 1H), 1.62-1.46 (m, 5H), 1.38-1.24 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 173.0, 153.5, 135.2, 129.5, 129.1, 127.5, 68.0, 66.4, 55.2, 42.8, 38.0, 36.7, 31.9, 29.6, 29.3, 25.6, 22.7, 14.2.

(S)-3-hydroxydecanoic acid (2a).

To a solution of (*R*)-4-benzyl-3-((*S*)-3-hydroxydecanoyl)oxazolidine-*2*-one **(9a)** (100 mg, 0.288 mmol,) in THF: H_2O 1:1 (10 mL) was added H_2O_2 30 % (w/w) in H_2O (0.25 mL, 1.44 mmol) and LiOH (21 mg, 0.864 mmol) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 16h. After completion of the reaction, the reaction mixture was quenched with aqueous sodium thiosulfate pentahydrate (2 mL), and then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and

concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using MeOH–DCM (1:9) as the eluent to obtain (*S*)-3-hydroxydecanoic acid **2a** (45 mg, 84%) as off white solid. $[\alpha]_D^{25}$ = +32.5 (*c* = 0.1 in MeOH), [2] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.04-4.00 (m, 1H), 2.56 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.46 (dd, *J* = 16.6, 8.9 Hz, 1H), 1.58-1.52 (m, 1H), 1.48-1.40 (m, 2H), 1.33-1.26 (m, 10H), 0.85 (t, *J* =7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.9, 68.1, 41.1, 36.6, 31.9, 29.5, 29.3, 25.5, 22.7, 14.2. HRMS (ES $^+$) m/z [M-H] $^+$ calcd 187.1340.; found 187.1337. [2]

(S)-tert-butyl 3-hydroxy-2-isopropyl-5-oxo-2,5-dihydro-1H-pyrrole-1-carboxylate (6a).

To a solution of Meldrum's acid (2.85 g, 19.8 mmol,), DCC (4.9 g, 23.8 mmol,) and DMAP (4.84 g, 39.6 mmol,) in CH_2Cl_2 (50 mL) was added Boc-*N*-L-Valine **(7)** (4.3 g, 19.8 mmol,) at rt in the presence of nitrogen gas. The resulting solution was stirred at rt for 3h. After completion of the reaction, the reaction mixture was filtered. The filtrate was diluted with CH_2Cl_2, transferred to a separatory funnel, and extracted. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the residue. The residue was then refluxed in methanol (300 mL) for 1h. The reaction mixture was concentrated on a rotary evaporator to afford the crude (*S*)-tert-butyl 3-hydroxy-2-isopropyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate **6a**, which was submitted to the next step without further purification.

(S)-tert-butyl 2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrole-1-carboxylate (6b).

To a solution of crude (*S*)-tert-butyl 3-hydroxy-2-isopropyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate **(6a)** (4.2 g, 17.4 mmol,) in dry THF (100 mL) was added TPP (5.93 g, 22.62 mmol,), and DIAD (3.8 g, 19.14 mmol,), and dry methanol (3.87 mL, 95.7 mmol,) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C for 30 min and 3h at rt. After completion of the reaction, the reaction mixture was diluted with water (50 mL), and then extracted with EtOAc (3 × 50 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (4:6) as the eluent to obtain (*S*)-tert-butyl 2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate **6b** (3.0 g, 60% over 2 steps) as off white solid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.04 (s, 1H), 4.34 (d, *J* = 2.4 Hz, 1H), 3.79 (s, 3H), 2.46-2.40 (m, 1H), 1.51 (s, 9H), 1.07 (d, *J* = 7.3 Hz, 3H), 0.78 (d, *J* = 7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 178.0, 169.4, 149.6, 95.0, 82.5, 64.7, 58.3, 29.6, 28.2, 18.8, 15.6. HRMS (ES $^+$) m/z [M+Na] $^+$ calcd for $C_{13}H_{21}NO_4Na$, 278.1354.; found 278.1363. [3]

(S)-5-isopropyl-4-methoxy-1H-pyrrol-2(5H)-one (6).

To a solution of (*S*)-tert-butyl 2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate **(6b)** (2.0 g, 7.84 mmol,) in dry CH_2Cl_2 (30 mL) was added TFA (10 mL,) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C for 30 min and 1h at rt. After completion of the reaction, TFA was removed under reduced pressure to give the crude. The crude was purified with column chromatography on silica gel using MeOH–DCM (0.5:9.5) as the eluent to obtain (*S*)-5-isopropyl-4-methoxy-1*H*-pyrrol-2(5*H*)-one **6** (1.0 g, 85%) as off white solid. $[\alpha]_D^{25}$ = +8.47 (*c* = 1.0 in $CHCl_3$), [3] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.78 (s, 1H), 5.02 (s, 1H), 3.97 (d, *J* = 3.1 Hz, 1H), 3.78 (s, 3H), 2.10-2.05 (m, 1H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.79 (d, *J* = 6.7 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.7, 175.0, 94.3, 62.7, 58.3, 29.4, 19.5, 15.2. HRMS (ES $^+$) m/z [M+H] $^+$ calcd for $C_8H_{14}NO_2$, 156.1019; found 156.1018. [3]

(S)-methyl 2-hydroxy-3-methylbutanoate (11).

To a solution of (*S*)-*2*-hydroxy-*3*-methylbutanoic acid **(10)** (1.0 g, 8.47 mmol,) in MeOH (10 mL) was added H_2SO_4 (cat.) at rt. The resulting solution was stirred at 80 °C for 4h. After completion of the reaction, the reaction mixture was concentrated on rotary evaporator to give the residue. Residue was diluted with water (20 mL), and then extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with aqueous sodium bicarbonate, brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (2:8) as the eluent to obtain (*S*)-methyl 2-hydroxy-3-methylbutanoate **11** (1.05 g, 94%) as colorless liquid. $[\alpha]^{20}$ = +23.7 (*c* = 1.0 in $CHCl_3$), λ: 589.3 nm; [4] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.04 (d, *J* = 3.7 Hz, 1H), 3.78 (s, 3H), 2.09-2.03 (m, 1H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 175.5, 75.1, 52.4, 32.2, 18.8, 16.1.

(S)-methyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate (12).

To a solution of (*S*)-methyl *2*-hydroxy-*3*-methylbutanoate **(11)** (1.0 g, 7.57 mmol,) in CH_2Cl_2 (20 mL) was added imidazole (695 mg, 10.22 mmol,) and TBSCl (1.41 g, 9.46 mmol,) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 16h. After completion of the reaction, the reaction mixture was diluted with water (20 mL), and then extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with aqueous sodium bicarbonate, brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (1:9) as the eluent to obtain (*S*)-methyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate **12** (1.35 g, 72.5%) as colorless liquid. $[\alpha]^{20}$ = -31.3 (*c* = 2.0 in CCl_4), λ: 589.3 nm; [5] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.95 (d, *J* = 4.9 Hz, 1H), 3.70 (s, 3H), 2.04-1.98 (m, 1H), 0.92 (d, *J* = 6.9 Hz, 3H), 0.90-0.87 (m, 12H), 0.04 (s, 3H), 0.02 (s, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 174.0, 51.5, 32.9, 25.8, 19.0, 18.4, 17.1, -5.0, -5.3.

(S)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoic acid (13).

To a solution of (*S*)-methyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate **(12)** (1.3 g, 5.28 mmol,) in THF: MeOH:H_2O 2:1:2 (15 mL) solvent mixture was added LiOH (380 mg, 15.85 mmol) at rt in the presence of nitrogen gas. The resulting solution was stirred at rt for 16h. After completion of the reaction, the reaction mixture was concentrated on rotary evaporator to give the residue. Residue was diluted with water (20 mL), acidified with 1N HCl, and extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using MeOH–DCM (1:9) as the eluent to obtain (*S*)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoic acid **13** (919 mg, 75%) as off white solid. $[\alpha]_D^{22}$ = -18.9 (*c* = 1.0 in MeOH), [6] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.07 (d, *J* = 3.7 Hz, 1H), 2.11-2.04 (m, 1H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.96-0.88 (m, 12H), 0.10 (d, *J* = 5.0 Hz, 6H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 53.5, 33.0, 25.7, 18.7, 18.2, 16.8, -5.0, -5.1.

(S)-4-nitrophenyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate (14).

To a solution of (*S*)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoic acid **(13)** (900 mg, 3.88 mmol,) in CH_2Cl_2 (20 mL) was added 4-nitrophenol (647 mg, 4.65 mmol,) and DCC (959 mg, 4.65 mmol,) at rt in the presence of nitrogen gas. The resulting solution was stirred at rt for 16h. After completion of the reaction, the reaction mixture

was diluted with water (20 mL), and then extracted with CH_2Cl_2 (3 × 30 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (1:9) as the eluent to obtain (*S*)-4-nitrophenyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate **14** (890 mg, 65%) as colorless liquid. ^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.2 Hz, 2H), 7.25 (d, *J* = 9.2 Hz, 2H), 4.23 (d, *J* = 4.6 Hz, 1H), 2.26-2.19 (m, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.94 (s, 9H), 0.11 (d, *J* = 4.4 Hz, 6H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 171.3, 155.4, 145.5, 125.4, 122.3, 33.1, 25.8, 19.1, 18.4, 16.9, -4.8, -5.2.

(S)-1-((S)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoyl)-5-isopropyl-4-methoxy-1H-pyrrol-2(5H)-one (15).

To a solution of (*S*)-5-isopropyl-4-methoxy-1*H*-pyrrol-2(5*H*)-one (**6)** (373 mg, 2.40 mmol) in dry THF (10 mL) was added dropwise *n*-BuLi (1.65 mL, 2.64 mmol, 1.6 M solution in THF) at -50 °C in the presence of nitrogen gas. The resulting solution was stirred at -50 °C for 10 min and added (*S*)-4-nitrophenyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate (**14)** (850 mg, 2.40 mmol,) in THF (5 mL) dropwise to above solution and resulting solution was stirred at -50 °C to rt for 2h. After completion of the reaction, the reaction mixture was quenched with NH_4Cl (aq) (3 mL), and then extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (2:8) as the eluent to obtain (*S*)-1-((*S*)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoyl)-5-isopropyl-4-methoxy-1*H*-pyrrol-2(5*H*)-one **15** (400 mg, 45%) as off white solid. $[\alpha]_D^{22}$ = +44.9 (*c* = 1.0 in MeOH), [7] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.26 (d, *J* = 3.8 Hz, 0.67H), 5.25 (d, *J* = 2.8 Hz, 0.3H), 5.03 (s, 0.65H), 5.03 (s, 0.3H), 4.65 (d, *J* = 2.8 Hz, 0.3H), 4.50 (d, *J* = 2.6 Hz, 0.68H), 3.83 (s, 1H), 3.82 (s, 2H), 2.69-2.64 (m, 0.63H), 2.48-2.42 (m, 0.23H), 2.12-2.07 (m, 0.26H), 1.99-1.93 (m, 0.62H), 1.11 (t, *J* = 7.5 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 1H), 0.96 (d, *J* = 6.9 Hz, 2H), 0.91 (d, *J* = 3.5 Hz, 9H), 0.85 (d, *J* = 6.9 Hz, 2H), 0.81 (d, *J* = 6.9 Hz, 1H), 0.71 (dd, *J* = 6.9, 4.9 Hz, 3H), 0.02 (d, *J* = 8.4 Hz, 7H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.8, 173.4, 170.5, 94.9, 75.9, 64.3, 58.5, 31.9, 28.6, 25.9, 19.7, 19.0, 18.4, 16.0, 15.1, -4.7, -5.1. HRMS (ES $^+$) m/z [M+H] $^+$ calcd for $C_{19}H_{35}NO_4Si$, 370.2401; found 370.2408. [7]

(S)-1-((S)-2-hydroxy-3-methylbutanoyl)-5-isopropyl-4-methoxy-1H-pyrrol-2(5H)-one (16).

To a solution of (*S*)-1-((*S*)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoyl)-5-isopropyl-4-methoxy-1*H*-pyrrol-2(5*H*)-one **(15)** (400 mg, 1.08 mmol,) in dry CH_2Cl_2 (10 mL) was added TFA (2 mL,) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 1h. After completion of the reaction, TFA was removed under reduced pressure to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (3:7) as the eluent to obtain (*S*)-1-((*S*)-2-hydroxy-3-methylbutanoyl)-5-isopropyl-4-methoxy-1*H*-pyrrol-2(5*H*)-one **16** (200 mg, 72%) as off white solid. $[\alpha]_D^{25}$ = -36.4 (*c* = 1.0 in MeOH), [2] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.08 (s, 1H), 4.74 (d, *J* = 3.7 Hz, 1H), 4.52 (d, *J* = 2.8 Hz, 1H), 3.85 (s, 3H), 2.69-2.63 (m, 1H), 2.13-2.07 (m, 1H), 1.11 (d, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.74 (d, *J* = 6.9 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 180.3, 173.9, 170.7, 94.6, 76.2, 64.5, 58.7, 30.5, 28.7, 20.0, 18.8, 15.6, 15.3. HRMS (ES $^+$) m/z [M+Na] $^+$ calcd 278.1363; found 278.1373. [2]

(S)-2-((tert-butoxycarbonyl)(methyl)amino)propanoic acid (17).

To a solution of (*S*)-2-(methylamino)propanoic acid (400 mg, 3.88 mmol,) in dry Ether (10 mL) was added Boc anhydride (2.54 g, 11.65 mmol,) and 4N aqueous NaOH (2.5 mL) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 16h. After completion of the reaction, the reaction mixture was diluted with water (20 Ml), and then extracted with EtOAc (3 × 20 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (5:5) as the eluent to obtain (*S*)-2-((*tert*-butoxycarbonyl)(methyl)amino)propanoic acid **17** (600 mg, 76%) as off white solid. $[\alpha]_{}^{20}$ = -41.7 (*c* = 0.92 in Dichloromethane), λ: 589.3 nm; [8] ^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.53 (s, 1H), 4.37 (d, *J* = 128.6 Hz, 1H), 2.70 (s, 3H), 1.34 (d, *J* = 20.6 Hz, 9H), 1.25 (s, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 178.0, 177.6, 156.4, 155.3, 80.7, 55.1, 53.7, 31.4, 30.8, 28.4, 15.1, 14.7.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((tert-butoxycarbonyl)(methyl)amino)propanoate (18).

To a solution of (*S*)-2-((*tert*-butoxycarbonyl)(methyl)amino)propanoic acid **(17)** (191 g, 0.94 mmol,) and (*S*)-1-((*S*)-2-hydroxy-3-methylbutanoyl)-5-isopropyl-4-methoxy-1*H*-pyrrol-2(5*H*)-one **(16)** (200 mg, 0.78 mmol,) in CH_2Cl_2 (5 mL) was added DCC (194 mg, 0.94 mmol,) and DMAP (95 mg, 0.78 mmol,) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 16h. After completion of the reaction, the reaction mixture was diluted with water (10 mL), and then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (2:8) as the eluent to obtain (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*tert*-butoxycarbonyl)(methyl)amino)propanoate **18** (300 mg, 87%) as colorless liquid. $[\alpha]_{D}^{25}$ = -2.4 (*c* = 1.0 in $CHCl_3$), [3] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.79 (d, *J* = 3.2 Hz, 1H), 5.06 (s, 1H), 4.92-4.54 (m, 1H), 4.49 (d, *J* = 2.6 Hz, 1H), 3.83 (s, 3H), 2.82 (d, *J* = 38.0 Hz, 3H), 2.63-2.57 (m, 1H), 2.24-2.18 (m, 1H), 1.44 (s, 9H), 1.42 (d, *J* = 7.3 Hz, 3H), 1.06 (dd, *J* = 12.7, 7.0 Hz, 6H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.9, 172.0, 170.1, 169.1, 94.7, 78.0, 64.3, 58.6, 55.0, 53.5, 31.3, 30.7, 28.9, 28.4, 19.8, 18.8, 16.1, 15.3, 14.8. HRMS (FD $^+$) m/z $[M+H]^+$ calcd for $C_{22}H_{36}N_2O_7$, 440.2517; found 440.2518.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((tert-butoxycarbonyl)amino)-N,3-dimethylbutanamido)propanoate (3).

A solution of compound (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((tert-butoxycarbonyl)(methyl)amino)propanoate **(18)** (250 mg, 0.57 mmol,) in HCl dioxane (4 N) (2 mL) was stirred at 0 °C to rt for 2h in the presence of nitrogen gas. After completion of the reaction, the reaction mixture was concentrated to afford a hydrochloride compound. The product would be used to next step without further purification. To a solution of hydrochloride compound and (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-methylbutanoic acid **(7)** (148 mg, 0.68 mmol,) in CH_2Cl_2 (5 mL) was added DIPEA (220 mg, 1.71 mmol,) and HATU (325 mg, 0.85 mmol,) at rt in the presence of nitrogen gas. The resulting solution was stirred at rt for 16h. After completion of the reaction, the reaction mixture was diluted with water (10 mL), and then extracted with

CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (4:6) as the eluent to obtain (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-*N*,3-dimethylbutanamido)propanoate **3** (230 mg, 75%) as off white solid. $[\alpha]_D^{25}$ = -6.66 (*c* = 1.0 in $CHCl_3$), [3] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.80 (d, *J* = 3.2 Hz, 1H), 5.28 (q, *J* = 7.1 Hz, 2H), 5.06 (s, 1H), 4.49 (d, *J* = 2.8 Hz, 1H), 4.47-4.46 (m, 1H), 3.84 (s, 4H), 3.01 (s, 3H), 2.61-2.55 (m, 1H), 2.23-2.18 (m, 1H), 1.99 (m, 1H), 1.43 (d, *J* = 7.3 Hz, 3H), 1.42 (s, 9H), 1.08 (d, *J* = 7.1 Hz, 3H), 1.05-1.03 (m, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (dd, *J* = 14.4, 6.7 Hz, 6H), 0.77 (d, *J* = 6.8 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.9, 172.5, 171.2, 170.0, 169.1, 156.0, 94.6, 79.5, 78.3, 64.3, 58.6, 55.2, 52.6, 31.8, 31.4, 28.8, 28.4, 19.7, 19.6, 18.8, 17.2, 16.0, 15.3, 14.2. HRMS (FD $^+$) m/z [M+H] $^+$ calcd for $C_{27}H_{45}N_3O_8$, 539.3201; found 539.3201.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxydecanamido)-N,3-dimethylbutanamido)propanoate (1a).

To a solution of (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-*N*,3-dimethylbutanamido)propanoate **(3)** (60 mg, 0.11 mmol,) in 2,2,2 trifluoroethanol, (1 mL) was added TMSCl, (0.15 mL) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 2h. After completion of the reaction, the reaction mixture was concentrated to afford a compound **(19).** The product would be used to next step without further purification. To a solution of hydrochloride compound and (*S*)-3-hydroxydecanoic acid **(2a)** (21 mg, 0.11 mmol,) in CH_2Cl_2 (5 mL) was added DIPEA (43 mg, 0.33 mmol,) and HATU (62.7 mg, 0.165 mmol,) at rt in the presence of nitrogen gas. The resulting solution was stirred at rt for 16h. After completion of the reaction, the reaction mixture was diluted with water (10 mL), and then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (5:5) as the eluent to obtain (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*S*)-2-((*S*)-3-hydroxydecanamido)-*N*,3-dimethylbutanamido)propanoate **1a** (40 mg, 58%) as white solid. $[\alpha]_D^{25}$ = −8.70 (*c* = 1.0 in MeOH), lit: $[\alpha]_D^{25}$ = −17 (*c* = 1.0 in MeOH);[7] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.45 (d, *J* = 8.8 Hz, 1H), 5.81 (d, *J* = 3.1 Hz, 1H), 5.25 (q, *J* = 7.2 Hz, 1H), 5.06 (s, 1H), 4.86 (dd, *J* = 8.8, 5.7 Hz, 1H), 4.49 (d, *J* = 2.6 Hz, 1H), 3.94 (s, 1H), 3.84 (s, 3H), 3.03 (s, 3H), 2.56 (tt, *J* = 7.1, 2.7 Hz, 1H), 2.38 (dd, *J* = 15.4, 2.4 Hz, 1H), 2.30 (d, *J* = 8.8 Hz, 1H), 2.25-2.17 (m, 1H), 2.04 (dt, *J* = 12.5, 6.5 Hz, 1H), 1.53 (dd, *J* = 8.8, 7.8 Hz, 1H), 1.44 (d, *J* = 7.3 Hz, 3H), 1.42-1.38 (m, 1H), 1.27 (m, 10H), 1.07 (d, *J* = 7.3 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.3 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 180.0, 173.1, 172.2, 170.9, 170.2, 169.0, 94.6, 78.4, 68.8, 64.3, 58.6, 53.9, 52.9, 42.1, 36.9, 32.1, 31.9, 31.4, 29.6, 29.3, 28.8, 28.4, 25.5, 22.7, 19.7, 19.6, 18.7, 17.5, 16.0, 15.3, 14.2. HRMS (FD $^+$) m/z [M+H] $^+$ calcd for $C_{32}H_{56}N_3O_8$, 610.4061; found 610.4063.

(R)-4-benzyl-3-((S)-3-hydroxyoctanoyl)oxazolidine-2-one (9b).

To a solution of SmI_2 (20 mL, 2.0 mmol, 0.1 M solution in THF) in dry THF (5 mL) was added dropwise solution

of (*R*)-*4*-benzyl-*3*-(*2*-bromoacetyl)oxazolidine-*2*-one **(5)** (200 mg, 0.67 mmol) and hexanal (**4b)** (67 mg, 0.67 mmol) in THF (5 mL) over 5 min at -78 °C in the presence of nitrogen gas. The resulting solution was stirred at -78 °C for 1h. After completion of the reaction, the reaction mixture was quenched with 1N HCl (2 mL), diluted with water, and then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with aqueous Sodium thiosulfate pentahydrate, brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (4:6) as the eluent to obtain (*R*)-4-benzyl-3-((*S*)-3-hydroxyoctanoyl)oxazolidine-2-one **9b** (100 mg, 46%) as off white solid. Diastereomeric ratio (dr = 9.1:0.9, determined by isolated yield). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 7.29-7.25 (m, 1H), 7.20-7.18 (m, 2H), 4.71-4.66 (m, 1H), 4.23-4.16 (m, 1H), 4.15-4.11 (m, 1H), 3.30 (dd, *J* = 13.4, 3.3 Hz, 1H), 3.17 (dd, *J* = 17.4, 2.5 Hz, 1H), 2.97 (dd, *J* = 17.4, 9.5 Hz, 1H), 2.77 (dd, *J* = 13.4, 9.7 Hz, 1H), 2.64 (s, 1H), 1.61-1.55 (m, 1H), 1.50-1.45 (m, 2H), 1.38-1.24 (m, 5H), 0.89 (t, *J* = 6.9 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 172.9, 153.5, 135.2, 129.5, 129.1, 127.5, 68.0, 66.4, 55.2, 42.8, 38.0, 36.6, 31.8, 25.3, 22.7, 14.1.

(S)-3-hydroxyoctanoic acid (2b).

To a solution of (*R*)-4-benzyl-3-((*S*)-3-hydroxyoctanoyl)oxazolidine-2-one **(9b)** (90 mg, 0.28 mmol,) in THF: H_2O 1:1 (5 mL) was added H_2O_2 30 % (w/w) in H_2O (0.25 mL, 1.41 mmol) and LiOH (20 mg, 0.84 mmol) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 16h. After completion of the reaction, the reaction mixture was quenched with aqueous sodium thiosulfate pentahydrate (2 mL), and then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using MeOH–DCM (1:9) as the eluent to obtain (*S*)-3-hydroxydecanoic acid **2b** (35 mg, 78%) as off white solid. $[\alpha]_D^{22}$ = +29.3 (*c* = 1.0 in $CHCl_3$),[9] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.05-4.00 (m, 1H), 2.56 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.46 (dd, *J* = 16.6, 8.9 Hz, 1H), 1.57-1.51 (m, 1H), 1.48-1.41 (m, 2H), 1.34-1.24 (m, 6H), 0.88 (t, *J* =7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.9, 68.1, 41.1, 36.5, 31.7, 25.2, 22.6, 14.1.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxyoctanamido)-N,3-dimethylbutanamido)propanoate (1b).

To a solution of (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-*N*,3-dimethylbutanamido)propanoate **(3)** (60 mg, 0.11 mmol,) in 2,2,2 trifluoroethanol, (1 mL) was added TMSCl, (0.15 mL) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 2h. After completion of the reaction, the reaction mixture was concentrated to afford a compound **(19).** The product would be used to next step without further purification. To a solution of hydrochloride compound and (*S*)-3-hydroxydecanoic acid **(2b)** (18 mg, 0.11 mmol,) in CH_2Cl_2 (5 mL) was added DIPEA (43 mg, 0.33 mmol,) and HATU (62.7 mg, 0.16 mmol,) at rt in the presence of nitrogen gas. The resulting solution was stirred at rt for 16h. After completion of the reaction, the reaction mixture was diluted with water (10 mL), and then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (5:5) as the eluent to obtain (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-

methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*S*)-2-((*S*)-3-hydroxyoctanamido)-*N*,3-dimethylbutanamido)propanoate **1b** (35 mg, 54%) as white solid. $[\alpha]_D^{25}$ = -14.07 (*c* = 1.0 in MeOH); lit: $[\alpha]_D^{22}$ = −32.6 (*c* = 1.0 in MeOH), [7] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.51 (d, *J* = 8.8 Hz, 1H), 5.81 (d, *J* = 3.2 Hz, 1H), 5.25 (q, *J* = 7.2 Hz, 1H), 5.06 (s, 1H), 4.85 (dd, *J* = 8.9, 5.7 Hz, 1H), 4.48 (d, *J* = 2.8 Hz, 1H), 3.95 (s, 1H), 3.83 (s, 3H), 3.04 (s, 3H), 2.56 (tt, *J* = 7.1, 2.7 Hz, 1H), 2.39 (dd, *J* = 15.4, 2.4 Hz, 1H), 2.29 (dd, *J* = 15.3, 8.8 Hz, 1H), 2.24-2.18 (m, 1H), 2.04 (td, *J* = 13.1, 6.6 Hz, 1H), 1.53 (dd, *J* = 8.8, 7.8 Hz, 1H), 1.44 (d, *J* = 7.1 Hz, 3H), 1.42-1.38 (m, 1H), 1.33-1.24 (m, 6H), 1.07 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.3 Hz, 3H), 0.87 (d, *J* = 6.3 Hz, 3H), 0.85 (t, *J* = 6.7 Hz, 3H),0.76 (d, *J* = 7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 180.0, 172.9, 172.1, 170.9, 170.1, 169.0, 94.6, 78.4, 68.7, 64.3, 58.6, 53.8, 52.8, 42.2, 36.9, 32.0, 31.8, 31.4, 28.8, 28.4, 25.2, 22.6, 19.8, 19.7, 19.6, 18.7, 17.4, 16.0, 15.3, 14.2, 14.1. HRMS (FD $^+$) m/z $[M+H]^+$ calcd for $C_{30}H_{52}N_3O_8$, 582.3748; found 582.3743.

(R)-4-benzyl-3-((S)-3-hydroxydodecanoyl)oxazolidine-2-one (9c).

To a solution of SmI_2 (20 mL, 2.0 mmol, 0.1 M solution in THF) in dry THF (5 mL) was added dropwise solution of (*R*)-*4*-benzyl-*3*-(*2*-bromoacetyl)oxazolidine-*2*-one **(5)** (200 mg, 0.67 mmol) and decanal (**4c)** (105 mg, 0.67 mmol) in THF (5 mL) over 5 min at -78 °C in the presence of nitrogen gas. The resulting solution was stirred at -78 °C for 1h. After completion of the reaction, the reaction mixture was quenched with 1N HCl (2 mL), diluted with water, and then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with aqueous Sodium thiosulfate pentahydrate, brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (4:6) as the eluent to obtain (*R*)-4-benzyl-3-((*S*)-3-hydroxydodecanoyl)oxazolidine-2-one **9c** (110 mg, 44%) as off white solid. Diastereomeric ratio (dr = 8.1:1.9, determined by isolated yield). ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34-7.32 (m, 2H), 7.29-7.25 (m, 1H), 7.20-7.18 (m, 2H), 4.71-4.66 (m, 1H), 4.23-4.16 (m, 2H), 4.15-4.10 (m, 1H), 3.30 (dd, *J* = 13.5, 3.2 Hz, 1H), 3.17 (dd, *J* = 17.4, 2.5 Hz, 1H), 2.97 (dd, *J* = 17.4, 9.5 Hz, 1H), 2.77 (dd, *J* = 13.5, 9.6 Hz, 1H), 1.62-1.56 (m, 1H), 1.53-1.44 (m, 2H), 1.38-1.26 (m, 14H), 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 173.0, 153.5, 135.2, 129.5, 129.1, 127.5, 68.0, 66.4, 55.2, 42.8, 38.0, 36.7, 32.0, 29.7, 29.4, 25.6, 22.8, 14.2.

(S)-3-hydroxydodecanoic acid (2c).

To a solution of (*R*)-4-benzyl-3-((*S*)-3-hydroxydodecanoyl)oxazolidine-2-one **(9c)** (100 mg, 0.26 mmol,) in THF: H_2O 1:1 (5 mL) was added H_2O_2 30 % (w/w) in H_2O (0.25 mL, 1.33 mmol) and LiOH (20 mg, 0.80 mmol) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 16h. After completion of the reaction, the reaction mixture was quenched with aqueous sodium thiosulfate pentahydrate (2 mL), and then extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using MeOH–DCM (1:9) as the eluent to obtain (*S*)-3-hydroxydodecanoic acid **2c** (30 mg, 52%) as off white solid. $[\alpha]_D^{22}$ = +18.7 (*c* = 1.0 in $CHCl_3$), [10] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.04-4.00 (m, 1H), 2.57 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.47 (dd, *J* = 16.6, 9.0 Hz, 1H), 1.57-1.52 (m, 1H), 1.50-1.42 (m, 2H), 1.33-1.25 (m, 14H), 0.87 (t, *J* =7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.7, 68.1, 41.1, 36.6, 32.0, 29.6, 29.5, 29.4, 25.5, 22.7, 14.2.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxydodecanamido)-N,3-dimethylbutanamido)propanoate (1c).

To a solution of (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*S*)-2-((*tert*-butoxycarbonyl)amino)-*N*,3-dimethylbutanamido)propanoate **(3)** (50 mg, 0.092 mmol,) in 2,2,2 trifluoroethanol, (1 mL) was added TMSCl, (0.15 mL) at 0 °C in the presence of nitrogen gas. The resulting solution was stirred at 0 °C to rt for 2h. After completion of the reaction, the reaction mixture was concentrated to afford a compound **(19).** The product would be used to next step without further purification. To a solution of hydrochloride compound and (S)-3-hydroxydodecanoic acid **(2c)** (20 mg, 0.092 mmol,) in CH_2Cl_2 (5 mL) was added DIPEA (36 mg, 0.278 mmol,) and HATU (52.5 mg, 0.138 mmol,) at rt in the presence of nitrogen gas. The resulting solution was stirred at rt for 16h. After completion of the reaction, the reaction mixture was diluted with water (10 mL), and then extracted with CH_2Cl_2 (3 × 10 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated on rotary evaporator to give the crude. The crude was purified with column chromatography on silica gel using EtOAc–hexane (5:5) as the eluent to obtain (*S*)-(*S*)-1-((*S*)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1*H*-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((*S*)-2-((*S*)-3-hydroxydodecanamido)-*N*,3-dimethylbutanamido)propanoate **1c** (25 mg, 43%) as white solid. $[\alpha]_D^{25}$ = -23.00 (*c* = 1.0 in MeOH); lit: $[\alpha]_D^{21} = -16.5$ (*c* = 1.0 in MeOH), [7] ^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.44 (d, *J* = 8.9 Hz, 1H), 5.81 (d, *J* = 3.2 Hz, 1H), 5.25 (q, *J* = 7.2 Hz, 1H), 5.06 (s, 1H), 4.86 (dd, *J* = 8.9, 5.7 Hz, 1H), 4.49 (d, *J* = 2.6 Hz, 1H), 3.96-3.91 (m, 1H), 3.84 (s, 3H), 3.03 (s, 3H), 2.56 (tt, *J* = 7.1, 2.7 Hz, 1H), 2.40 (dd, *J* = 15.3, 2.7 Hz, 1H), 2.29 (d, *J* = 8.9 Hz, 1H), 2.25-2.19 (m, 1H), 2.04 (dt, *J* = 12.5, 6.5 Hz, 1H), 1.53 (dd, *J* = 8.8, 7.8 Hz, 1H), 1.44 (d, *J* = 7.1 Hz, 3H), 1.42-1.38 (m, 1H), 1.25 (m, 14H), 1.07 (d, *J* = 7.3 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.3 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H), 0.76 (d, *J* = 7.0 Hz, 3H). ^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.9, 172.5, 172.0, 171.0, 170.1, 169.1, 94.6, 78.3, 68.7, 64.3, 58.6, 53.5, 52.7, 42.4, 36.9, 32.0, 31.9, 31.4, 29.6, 29.6, 29.4, 28.8, 28.4, 25.6, 22.7, 19.7, 19.7, 18.8, 17.4, 16.0, 15.3, 14.2. HRMS (FD $^+$) m/z $[M+H]^+$ calcd for $C_{34}H_{60}N_3O_8$, 638.4375; found 638.4376.

IV. NMR comparison of natural Kavaratamide A [500 MHz (^{1}H) and 125 MHz (^{13}C) in $CDCl_3$] and synthetic Kavaratamide A [500 MHz (^{1}H) and 125 MHz (^{13}C) in $CDCl_3$].

Position		Natural **Kavaratamide A**		Synthetic **Kavaratamide A**		Difference value	
		δH (*J* in Hz)	δC	δH (*J* in Hz)	δC	δH	δC
iPr-O-Me-Pyr	1	3.85, s	58.7, CH_3	3.84, s	58.6	-0.01	-0.1
	2		170.2, C		170.2		0.0
	3	5.07, s	94.7, CH	5.06, s	94.6	-0.01	-0.1
	4		180.0, C		180.0		0.0
	5	4.50, d (2.5)	64.4, CH	4.49, d (2.6)	64.3	-0.01	-0.1
	6	2.56, sepd (7.5, 2.5)	28.5, CH	2.56, sepd (7.1, 2.7)	28.4,	0.0	-0.1
	7	1.09, d (7.5)	18.8, CH_3	1.07, d (7.3)	18.7	-0.02	-0.1
	8	0.78, d (7.0)	15.3, CH_3	0.77, d (6.8)	15.3	-0.01	0.0
Hiva	9		169.1, C		169.0		-0.1
	10	5.82, d (3.5)	78.4, CH	5.81, d (3.1)	78.4	-0.01	0.0
	11	2.23, sepd (6.5, 3.0)	28.9, CH	2.23, sepd (7.5, 2.5)	28.8	0.0	-0.1
	12	1.05, d (6.5)	19.8, CH_3	1.03, d (6.8)	19.7	-0.02	-0.1
	13	0.92, d (7.0)	16.1, CH_3	0.90, d (6.5)	16.0	-0.02	-0.1
N-Me-Ala	14		171.1, C		170.9		-0.2
	15	5.29, q (7.0)	52.8, CH	5.25, q (7.2)	52.9	-0.04	0.1
	16	1.46, d (7.0)	14.2, CH_3	1.44, d (7.3)	14.2	-0.01	0.0
	17	3.04, s	31.9, CH_3	3.03, s	31.9	-0.01	0.0
Val	18		172.3, C		172.2		-0.1
	19	4.84, dd (8.5, 5.5)	53.9, CH	4.86, dd (8.8, 5.7)	53.9	0.02	0.0
	20	2.06, sepd (7.0)	31.3, CH	2.04, dt (12.5, 6.5)	31.4	-0.02	0.1
	21	1.01, d (7.0)	19.8, CH_3	0.99, d (6.8)	19.6	-0.02	-0.2
	22	0.91, d (6.5)	17.4, CH_3	0.88, d (6.3)	17.5	-0.02	0.1
	19-NH	6.54, d (8.5)		6.45, d (8.8)		-0.09	
3-HDA	23		172.9, C		173.1		0.2
	24a	2.38, dd (15, 2.5)	42.9, CH_2	2.38, dd (15.4, 2.4)	42.1	0.0	-0.8
	24b	2.29, dd (15, 9.5)		2.30 d (8.8)		0.01	
	25		69.0, CH	3.94, br s	68.8	0.0	-0.2
	26a	1.54, dd (17.0, 7.5) 1.42, overlap	37.1, CH_2	1.53, dd (8.8, 7.8) 1.44, overlap	36.9	0.0	-0.2
	26b					0.0	0.0
	27	1.43-1.24, m	25.6, CH_2	1.43-1.24, m	25.5	0.0	-0.1

	28	1.43-1.24, m	29.7c, CH_2	1.43-1.24, m	29.6	0.0	-0.1
	29	1.43-1.24, m	29.4c, CH_2	1.43-1.24, m	29.3	0.0	-0.1
	30	1.43-1.24, m	31.9, CH_2	1.43-1.24, m	32.1	0.0	0.2
	31	1.43-1.24, m	22.8, CH_2	1.43-1.24, m	22.7	0.0	-0.1
	32	0.88, t (7.0)	14.3, CH_3	0.87, t (6.7)	14.2	0.0	-0.1

V. NMR values of synthetic Kavaratamide B & Kavaratamide C [500 MHz (^{1}H) and 125 MHz (^{13}C) in $CDCl_3$].

Position		Synthetic **Kavaratamide B**		Synthetic **Kavaratamide C**	
		δH (*J* in Hz)	δC	δH (*J* in Hz)	δC
iPr-O-Me-Pyr	1	3.83, s	58.6, CH_3	3.84, s	58.6
	2		170.1, C		170.1
	3	5.06, s	94.6, CH	5.06, s	94.6
	4		180.0, C		179.9
	5	4.48, d (2.8)	64.3, CH	4.49, d (2.6)	64.3
	6	2.56, sepd (7.1, 2.7)	28.4, CH	2.56, sepd (7.1, 2.7)	28.4,
	7	1.07, d (7.1)	18.7, CH_3	1.07, d (7.3)	18.8
	8	0.76, d (7.0)	15.3, CH_3	0.76, d (7.0)	15.3
Hiva	9		169.0, C		169.1
	10	5.81, d (3.2)	78.4, CH	5.81, d (3.2)	78.3
	11	2.23, sepd (6.5, 3.0)	28.8, CH	2.23, sepd (7.5, 2.5)	28.8
	12	1.03, d (6.9)	19.7, CH_3	1.03, d (6.8)	19.7
	13	0.89, d (6.3)	16.0, CH_3	0.90, d (6.5)	16.0
N-Me-Ala	14		170.9, C		171.0
	15	5.25, q (7.2)	52.8, CH	5.25, q (7.2)	52.7
	16	1.44, d (7.1)	14.1, CH_3	1.44, d (7.1)	14.2
	17	3.04, s	31.8, CH_3	3.03, s	31.9
Val	18		172.1, C		172.0
	19	4.85, dd (8.9, 5.7)	53.8, CH	4.86, dd (8.9, 5.7)	53.5
	20	2.04, sepd (7.0)	31.4, CH	2.04, dt (12.5, 6.5)	31.4
	21	0.99, d (6.8)	19.8, CH_3	0.99, d (6.8)	19.7
	22	0.87, d (6.3)	17.4, CH_3	0.88, d (6.3)	17.4
	19-NH	6.51, d (8.8)		6.44, d (8.9)	
3-HDA	23		172.9, C		172.5
	24a	2.39, dd (15.4, 2.4)	42.2, CH_2	2.40, dd (15.3, 2.7)	42.4
	24b	2.29, dd (15.3, 8.8)		2.29 d (8.9)	
	25	3.95, br s	68.7, CH	3.94, br s	68.7
	26a	1.53, dd (17.0, 7.8) 1.44, overlap	36.9, CH_2	1.53, dd (8.8, 7.8) 1.42, overlap	36.9
	26b				
	27	1.43-1.24, m	25.2, CH_2	1.43-1.24, m	25.6
	28	---	---	1.43-1.24, m	29.6

	29	---	---	1.43-1.24, m	29.6
	30	---	---	1.43-1.24, m	29.4
	31	1.43-1.24, m	32.0, CH_2	1.43-1.24, m	32.0
	32	1.43-1.24, m	22.6, CH_2	1.43-1.24, m	22.7
	33	0.85, t (6.7)	14.2, CH_3	0.86, t (6.7)	14.2

VI. Comparison of optical rotation of Kavaratamide A, B and C

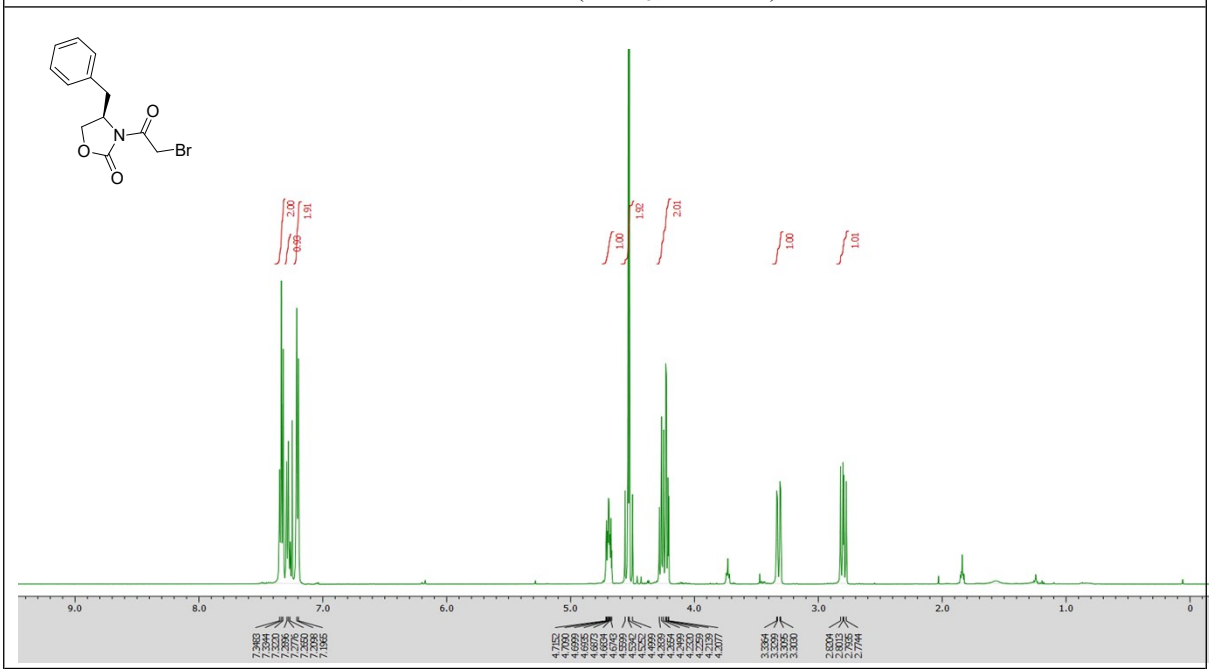
Compound	Optical rotation for Natural **compound**	Optical rotation for Synthetic **compound**
Kavaratamide A	−17	−8.70
Kavaratamide B	NA	-14.07
Kavaratamide C	NA	-23.0

Note: all optical rotation recorded under the condition of $[\alpha]_D^{25}$ and c = 1.0, MeOH

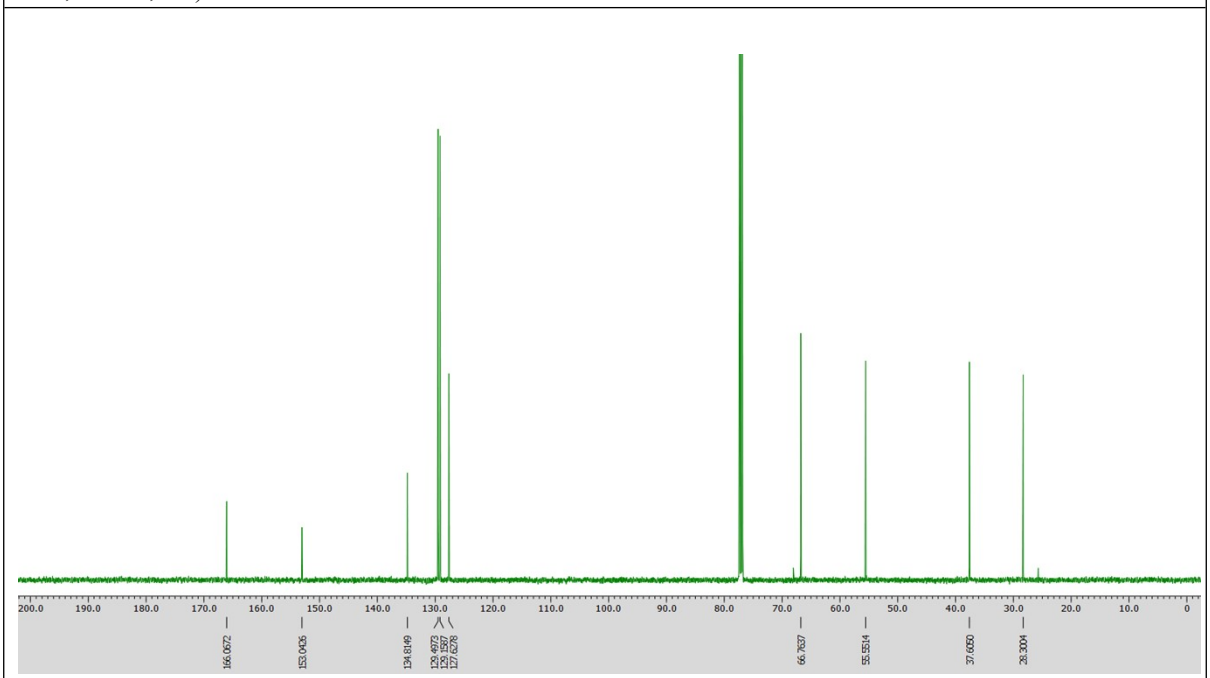
VII. The copies of ^{1}H and ^{13}C NMR spectra

(R)-4-benzyl-3-(2-bromoacetyl)oxazolidine-2-one (5)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)

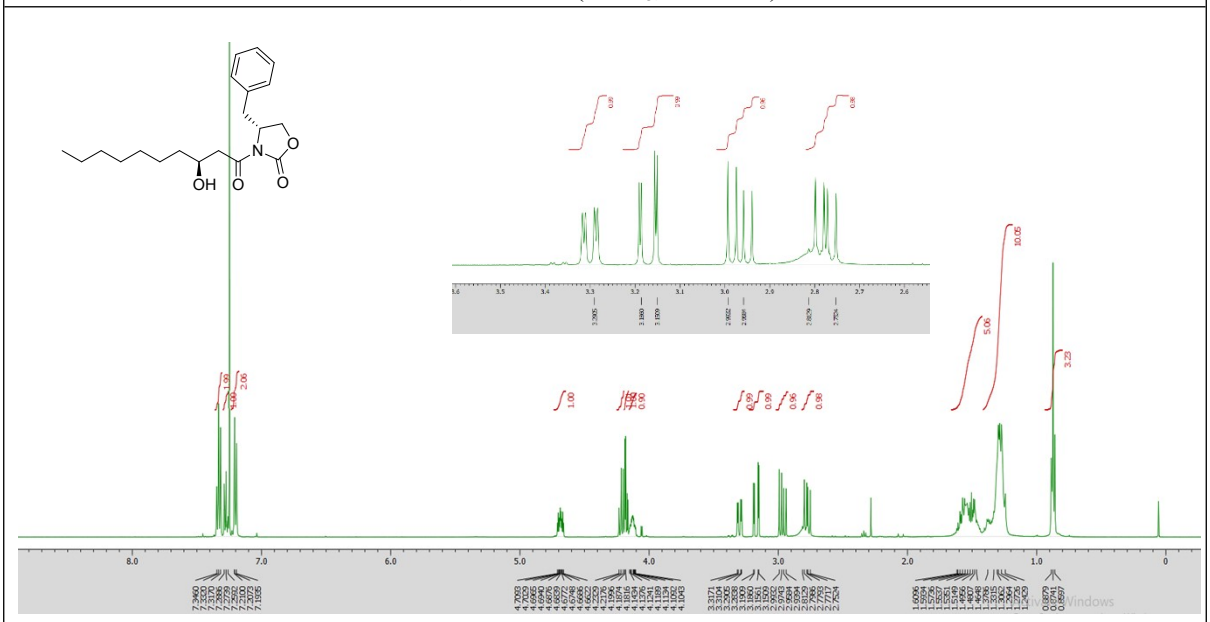
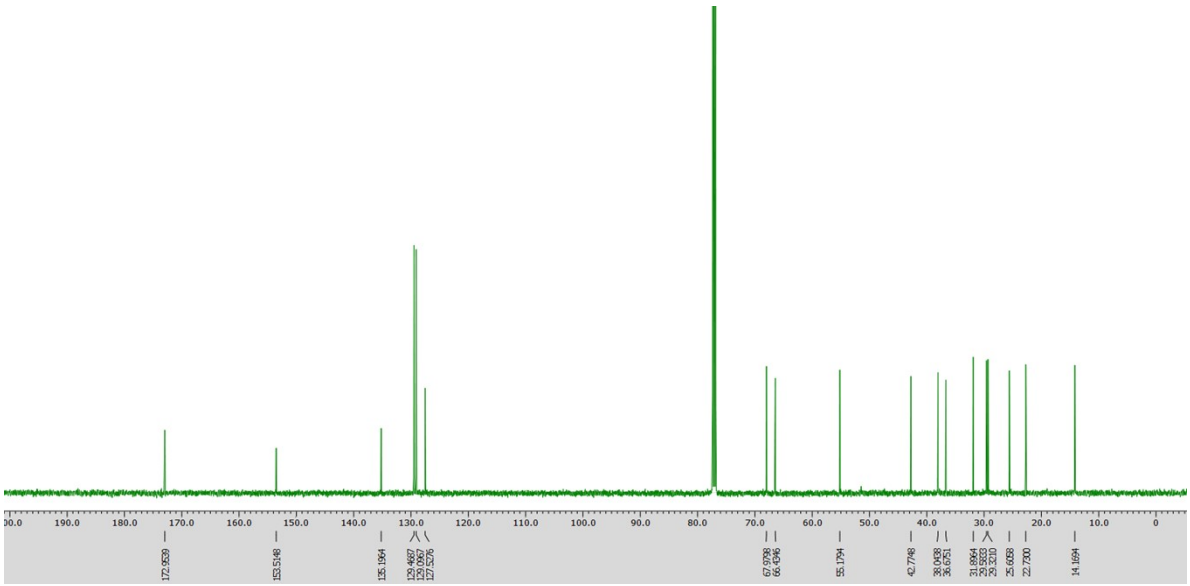


^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.32 (m, 2H), 7.28 (t, *J* = 6.2 Hz, 1H), 7.20 (d, *J* = 6.6 Hz, 2H), 4.72-4.67 (m, 1H), 4.53 (dd, *J* = 17.3, 12.7 Hz, 2H), 4.28-4.21 (m, 2H), 3.32 (dd, *J* = 13.5, 3.2 Hz, 1H), 2.80 (dd, *J* = 13.5, 9.6 Hz, 1H).

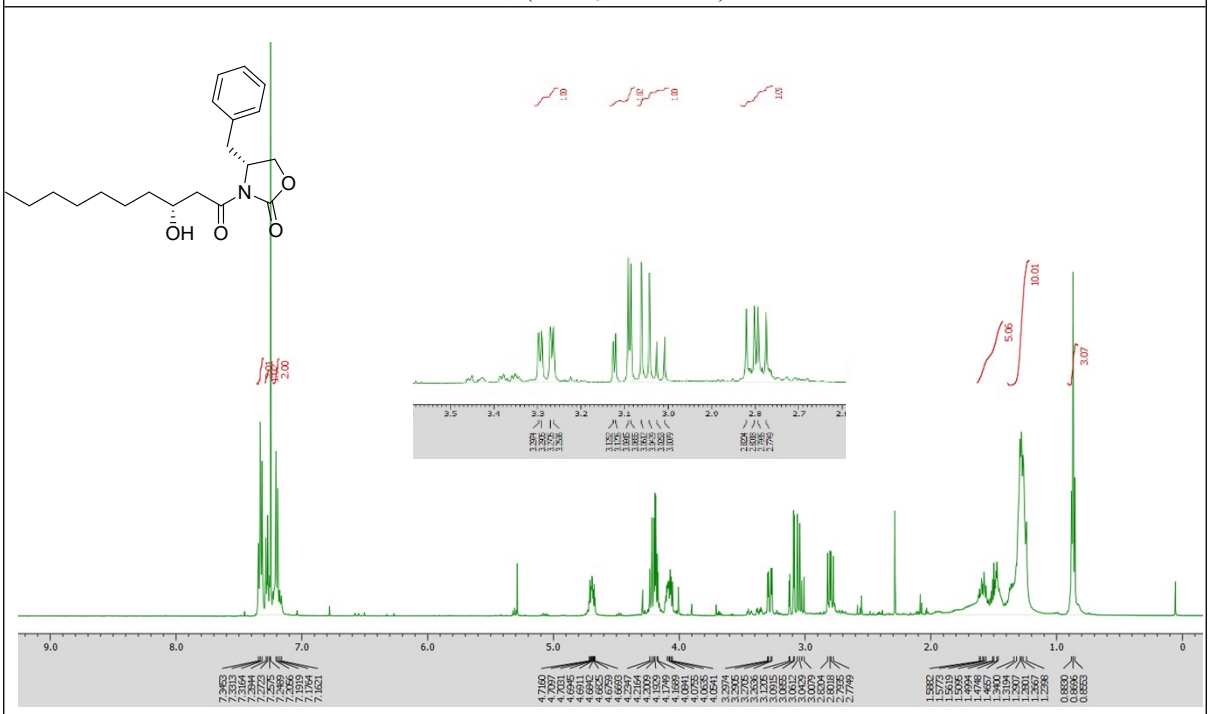


^{13}C-NMR (126 MHz, $CDCl_3$) δ 166.1, 153.0, 134.8, 129.5, 129.2, 127.6, 66.8, 55.6, 37.6, 28.3.

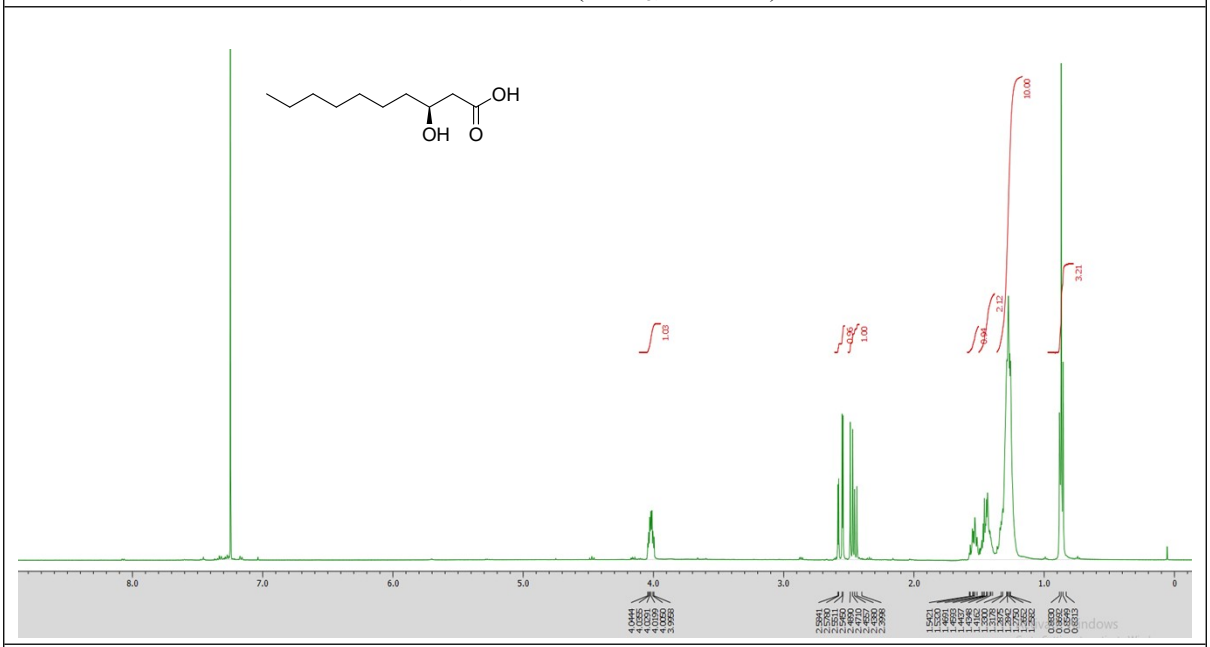
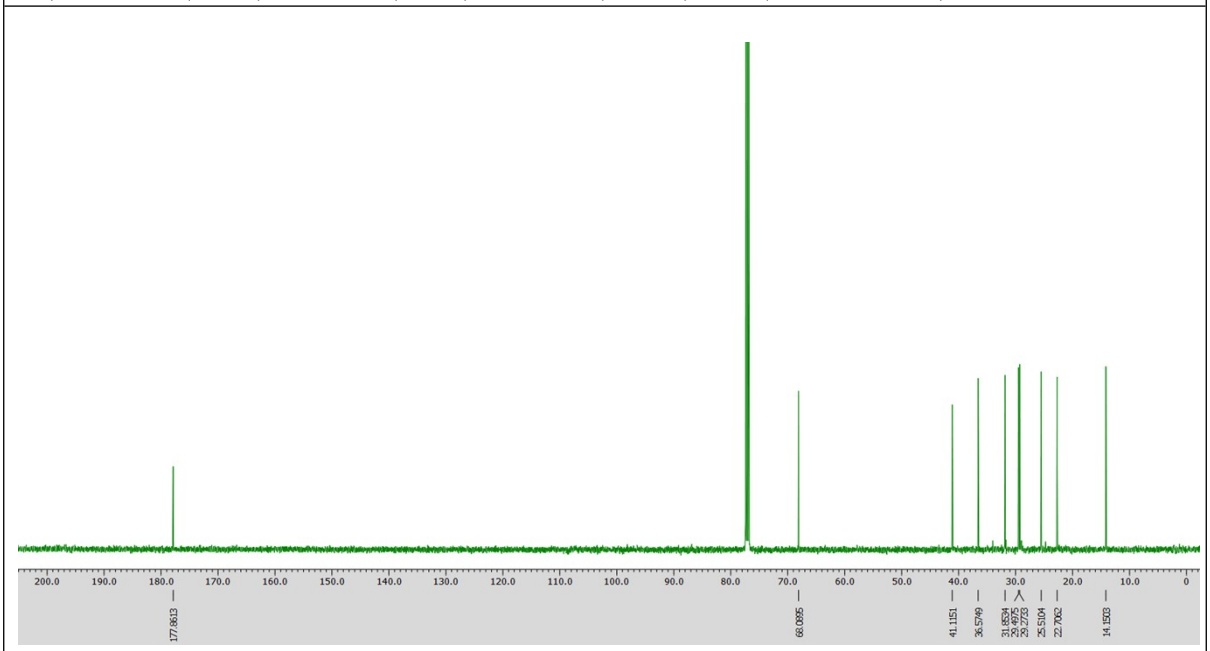
(R)-4-benzyl-3-((S)-3-hydroxydecanoyl)oxazolidine-2-one (9a)

$^{1}H,^{13}C$ NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.28-7.25 (m, 1H), 7.21-7.19 (m, 2H), 4.71-4.66 (m, 1H), 4.23-4.20 (m, 1H), 4.18 (d, *J* = 2.9 Hz, 1H), 4.15-4.10 (m, 1H), 3.30 (dd, *J* = 13.3, 3.4 Hz, 1H), 3.17 (dd, *J* = 17.5, 2.5 Hz, 1H), 2.97 (dd, *J* = 17.4, 9.5 Hz, 1H), 2.81-2.75 (m, 1H), 1.62-1.46 (m, 5H), 1.38-1.24 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 173.0, 153.5, 135.2, 129.5, 129.1, 127.5, 68.0, 66.4, 55.2, 42.8, 38.0, 36.7, 31.9, 29.6, 29.3, 25.6, 22.7, 14.2.

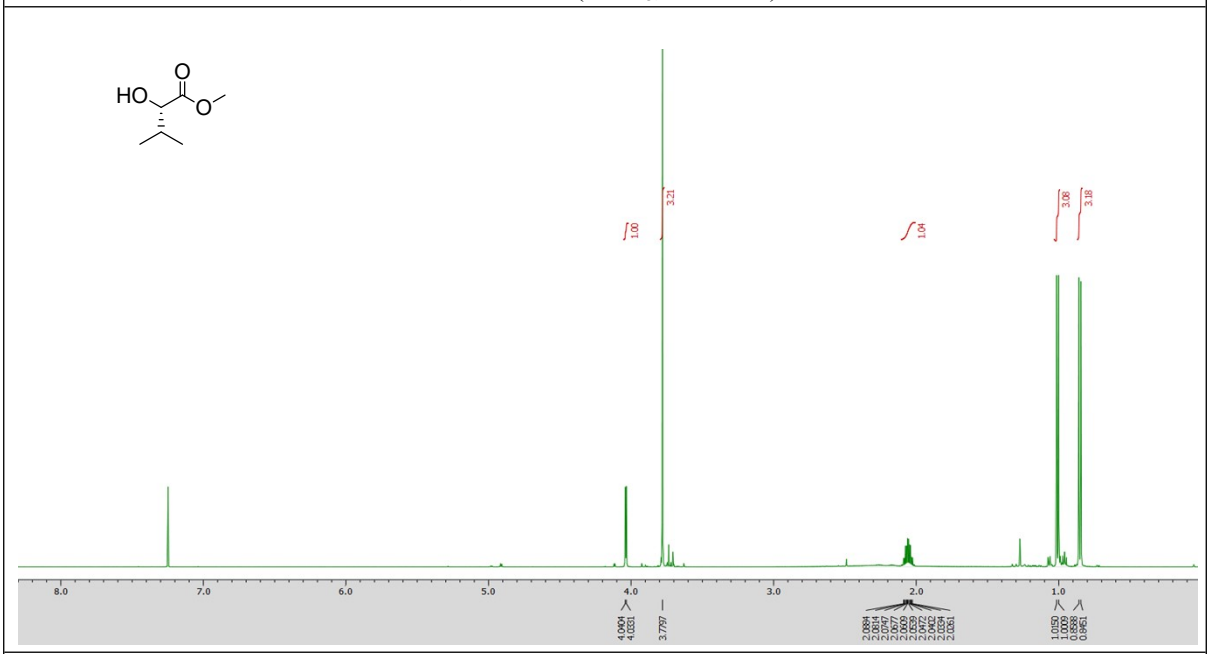
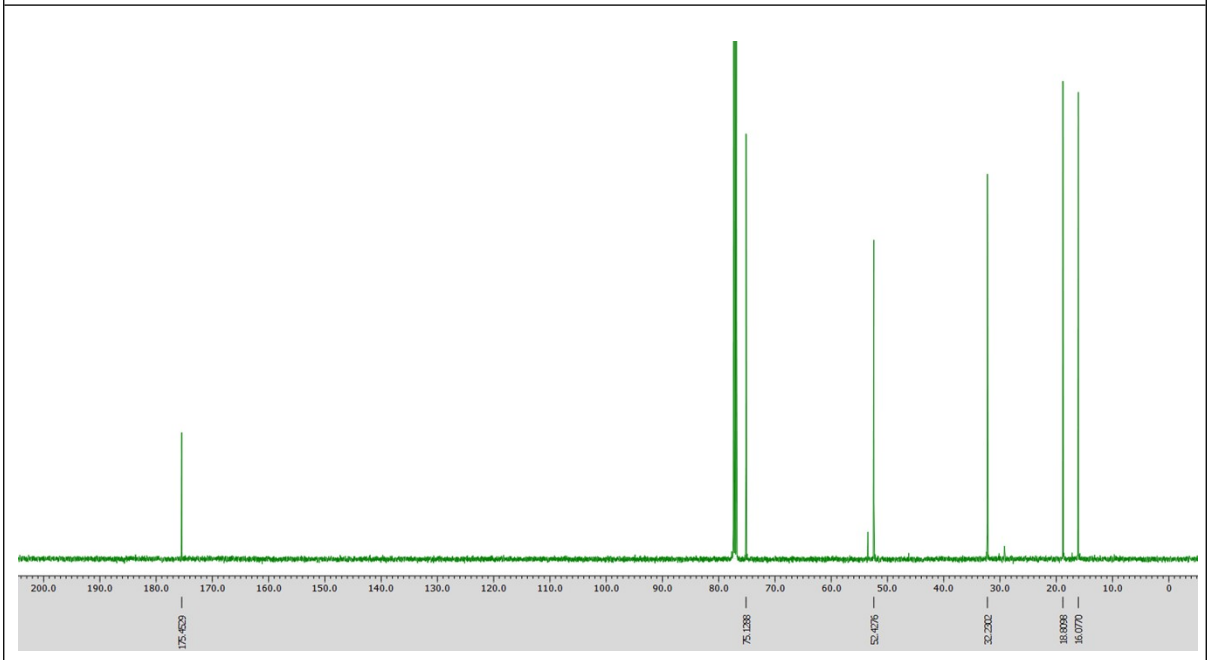
(R)-4-benzyl-3-((R)-3-hydroxydecanoyl)oxazolidine-2-one(9aa)

^{1}H, ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34-7.31 (m, 2H), 7.28-7.25 (m, 1H), 7.23-7.16 (m, 2H), 4.71-4.66 (m, 1H), 4.23-4.16 (m, 2H), 4.10-4.04 (m, 1H), 3.28 (dd, *J* = 13.3, 3.4 Hz, 1H), 3.10 (dd, *J* = 17.5, 2.5 Hz, 1H), 3.03 (dd, *J* = 17.4, 9.5 Hz, 1H), 2.80 (dd, *J* = 13.4, 9.3 Hz, 1H), 1.61-1.46 (m, 5H), 1.34-1.24 (m, 10H), 0.87 (t, *J* = 7.0 Hz, 3H).

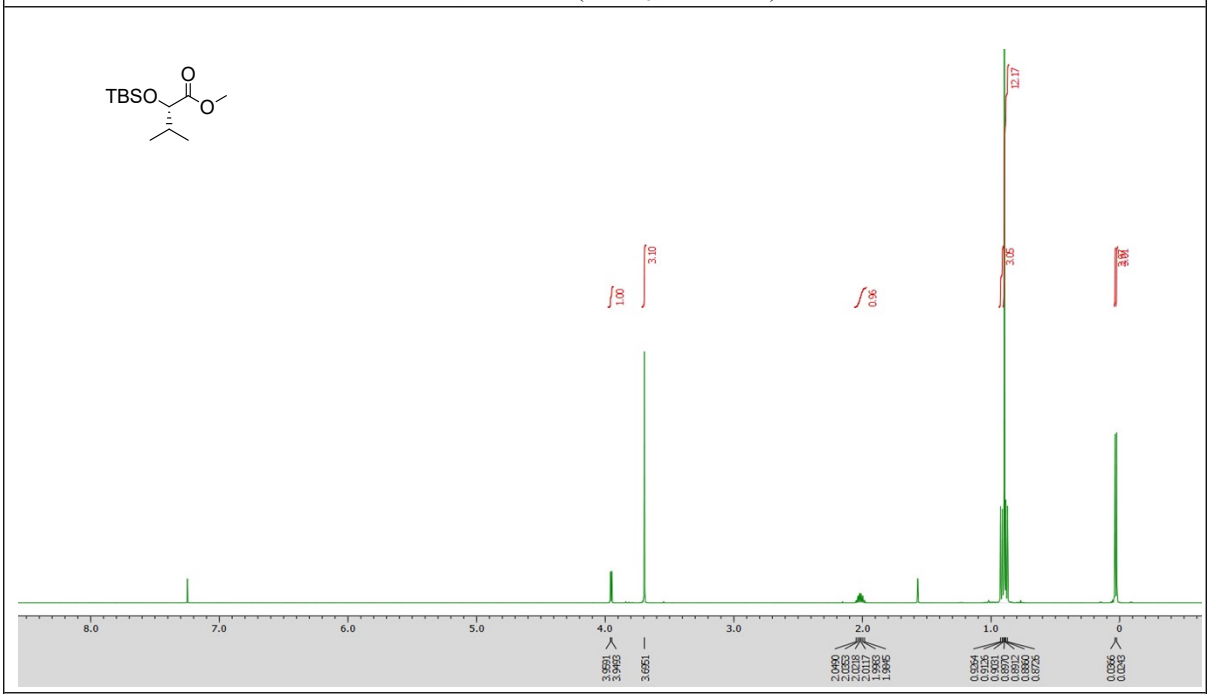
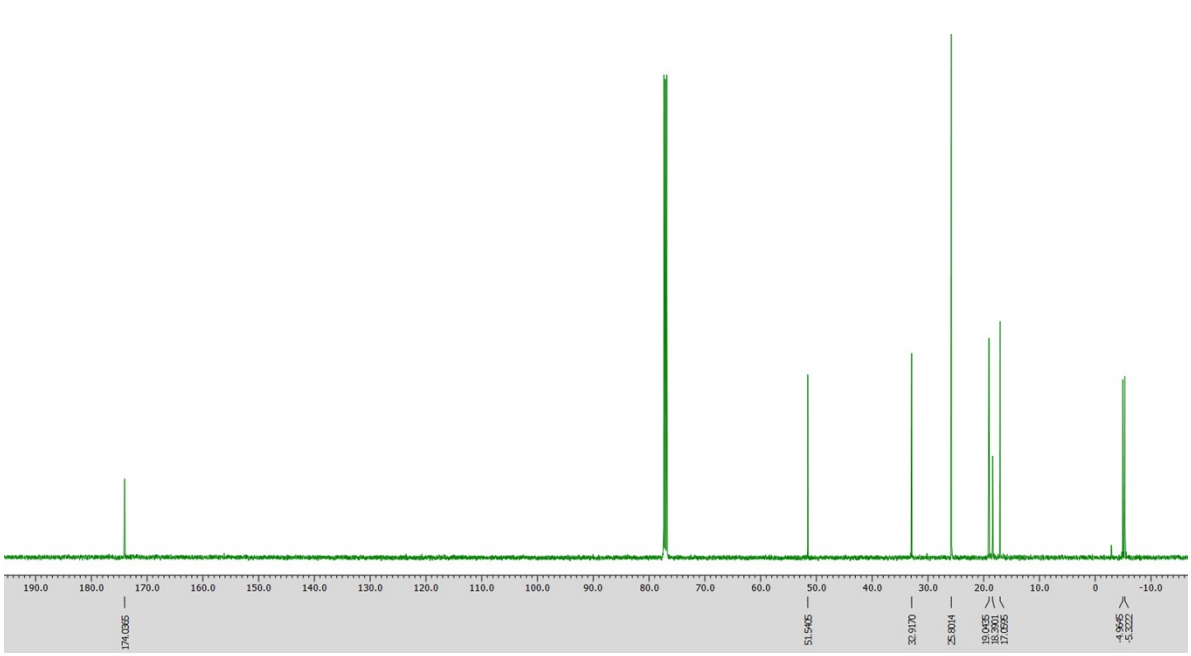
(S)-3-hydroxydecanoic acid (2a)

$^{1}H,^{13}C$ NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.04-4.00 (m, 1H), 2.56 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.46 (dd, *J* = 16.6, 8.9 Hz, 1H), 1.58-1.52 (m, 1H), 1.48-1.40 (m, 2H), 1.33-1.26 (m, 10H), 0.85 (t, *J* =7.0 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.9, 68.1, 41.1, 36.6, 31.9, 29.5, 29.3, 25.5, 22.7, 14.2.

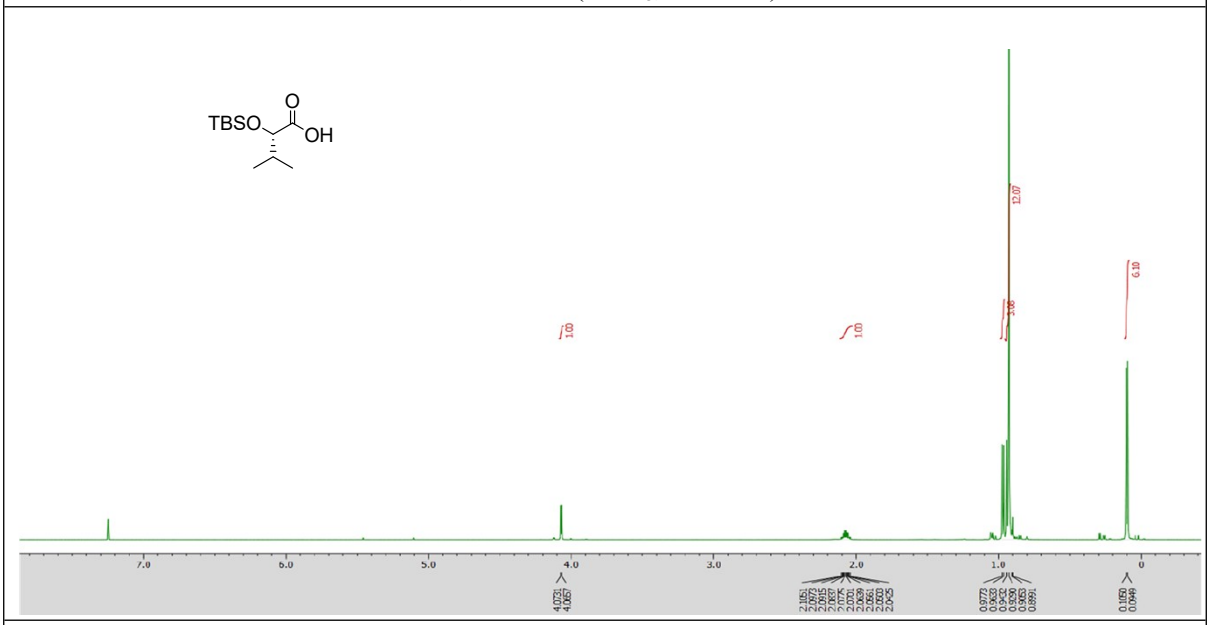
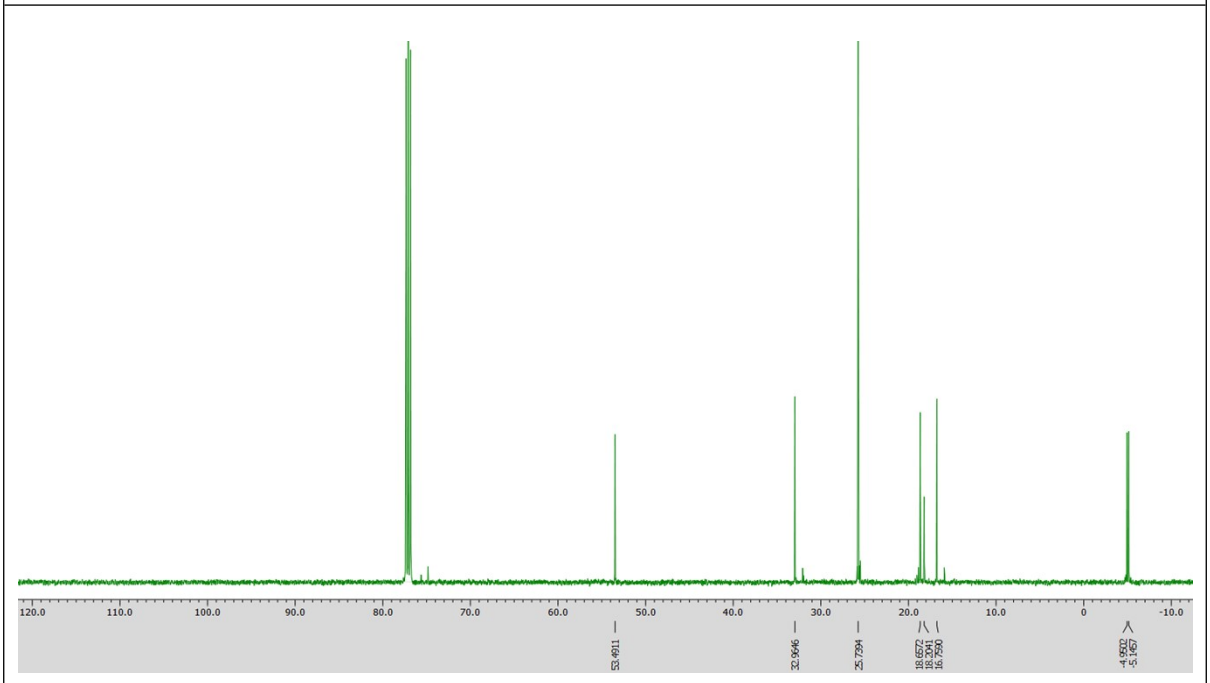
(S)-methyl 2-hydroxy-3-methylbutanoate (11)

$^{1}H,^{13}C$ NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.04 (d, *J* = 3.7 Hz, 1H), 3.78 (s, 3H), 2.09-2.03 (m, 1H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 175.5, 75.1, 52.4, 32.2, 18.8, 16.1.

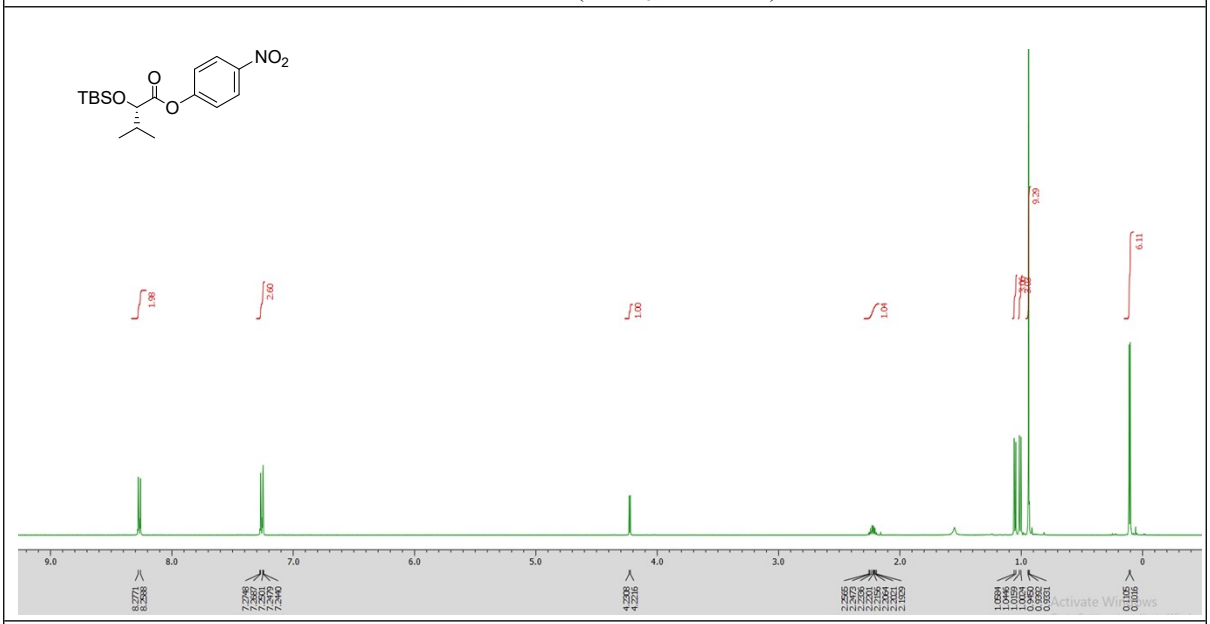
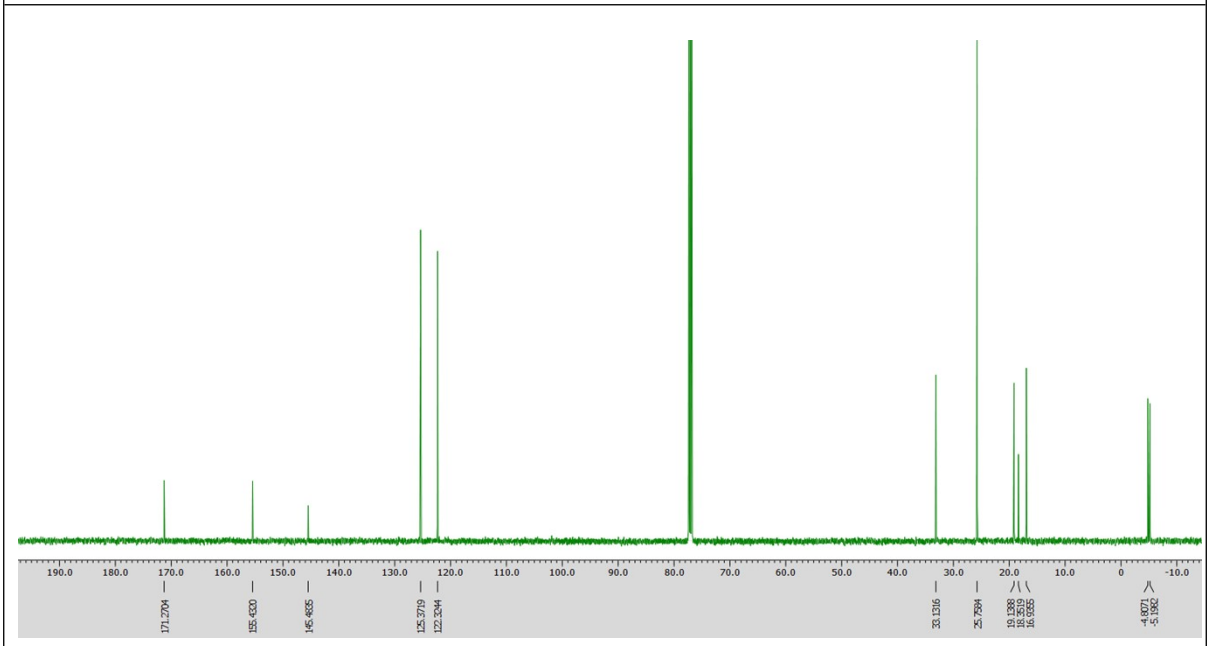
(S)-methyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate (12)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 3.95 (d, J = 4.9 Hz, 1H), 3.70 (s, 3H), 2.04-1.98 (m, 1H), 0.92 (d, J = 6.9 Hz, 3H), 0.90-0.87 (m, 12H), 0.04 (s, 3H), 0.02 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 174.0, 51.5, 32.9, 25.8, 19.0, 18.4, 17.1, -5.0, -5.3.

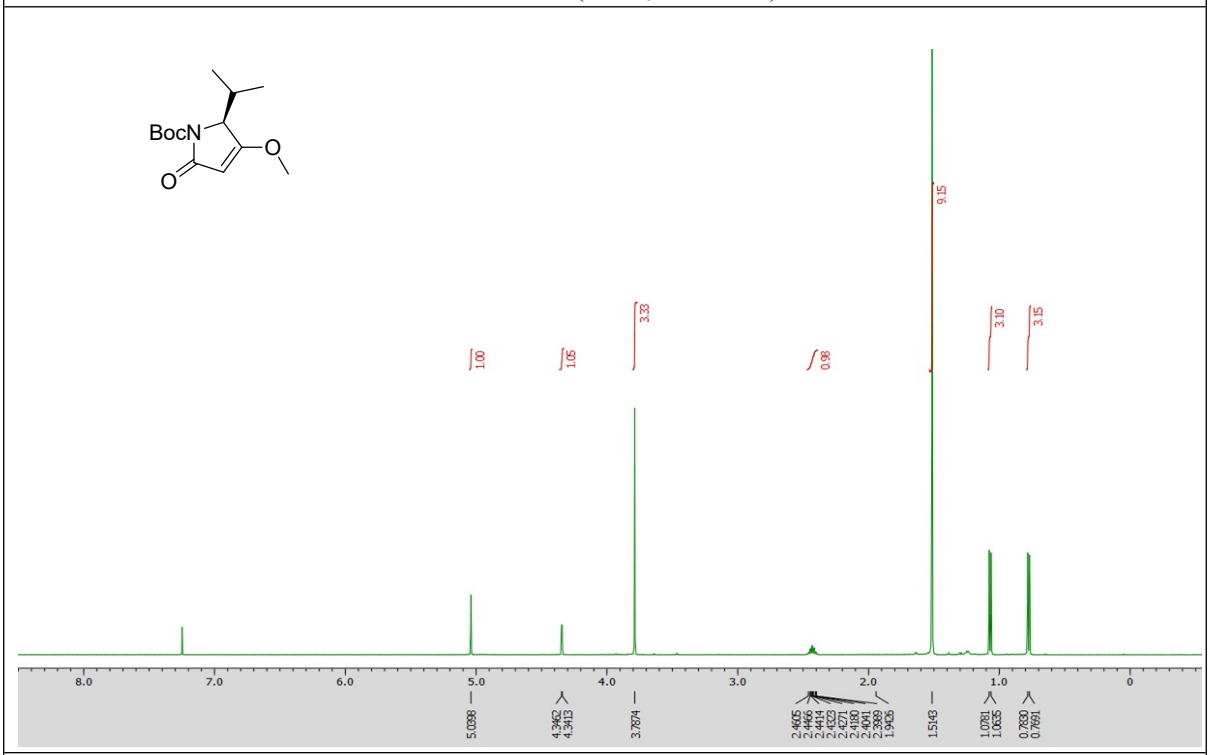
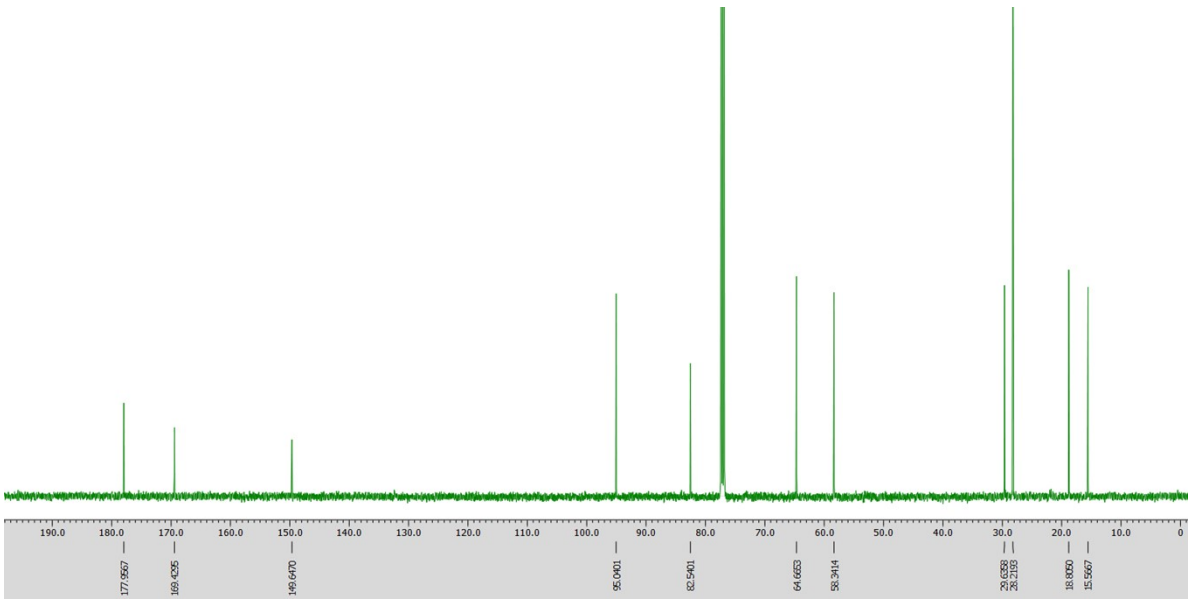
(S)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoic acid (13)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.07 (d, *J* = 3.7 Hz, 1H), 2.11-2.04 (m, 1H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.96-0.88 (m, 12H), 0.10 (d, *J* = 5.0 Hz, 6H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 53.5, 33.0, 25.7, 18.7, 18.2, 16.8, -5.0, -5.1.

(S)-4-nitrophenyl 2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoate (14)

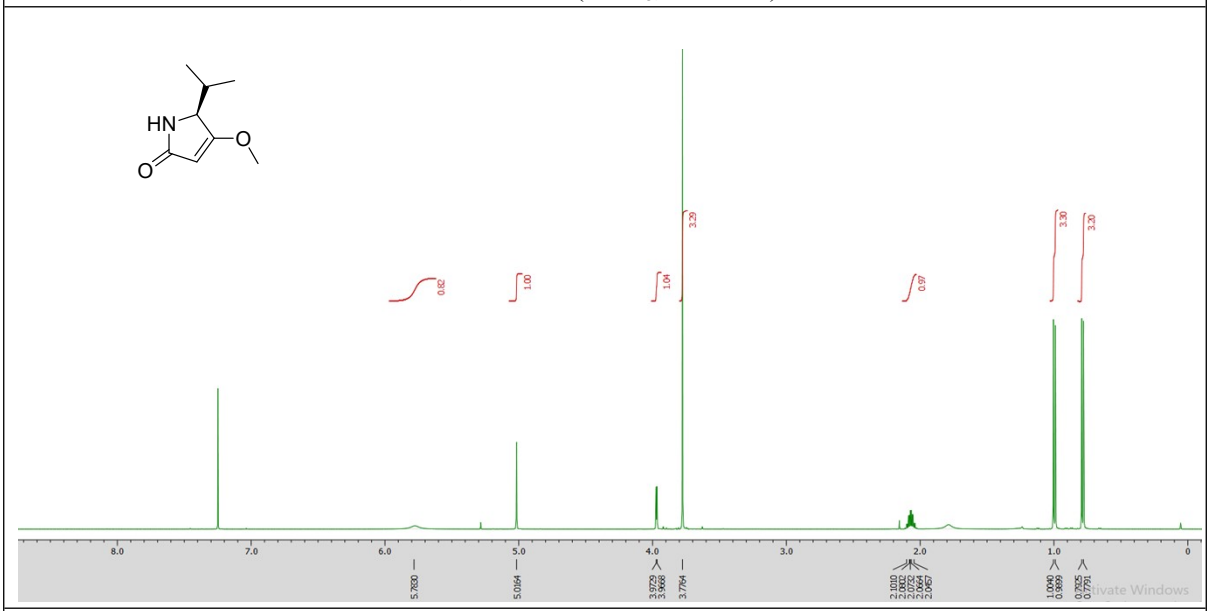
$^{1}H,^{13}C$ NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 9.2 Hz, 2H), 7.25 (d, *J* = 9.2 Hz, 2H), 4.23 (d, *J* = 4.6 Hz, 1H), 2.26-2.19 (m, 1H), 1.05 (d, *J* = 6.9 Hz, 3H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.94 (s, 9H), 0.11 (d, *J* = 4.4 Hz, 6H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 171.3, 155.4, 145.5, 125.4, 122.3, 33.1, 25.8, 19.1, 18.4, 16.9, -4.8, -5.2.

(S)-tert-butyl 2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrole-1-carboxylate (6b)

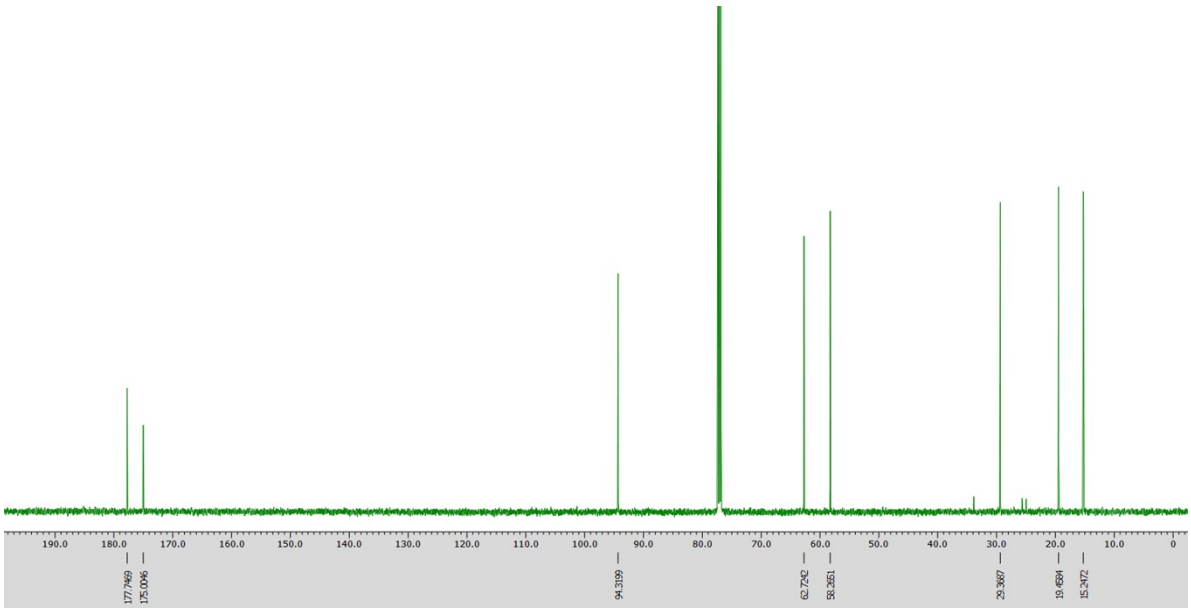
^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.04 (s, 1H), 4.34 (d, *J* = 2.4 Hz, 1H), 3.79 (s, 3H), 2.46-2.40 (m, 1H), 1.51 (s, 9H), 1.07 (d, *J* = 7.3 Hz, 3H), 0.78 (d, *J* = 7.0 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 178.0, 169.4, 149.6, 95.0, 82.5, 64.7, 58.3, 29.6, 28.2, 18.8, 15.6.

(S)-5-isopropyl-4-methoxy-1H-pyrrol-2(5H)-one (6)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)



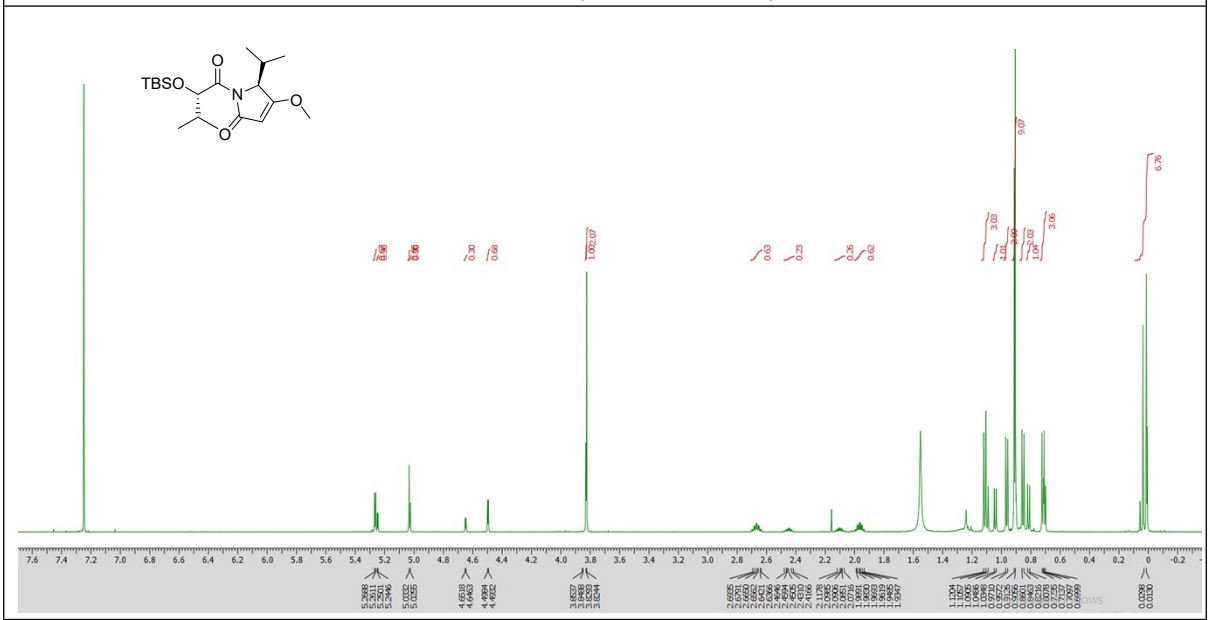
^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.78 (s, 1H), 5.02 (s, 1H), 3.97 (d, J = 3.1 Hz, 1H), 3.78 (s, 3H), 2.10-2.05 (m, 1H), 1.00 (d, J = 7.0 Hz, 3H), 0.79 (d, J = 6.7 Hz, 3H).



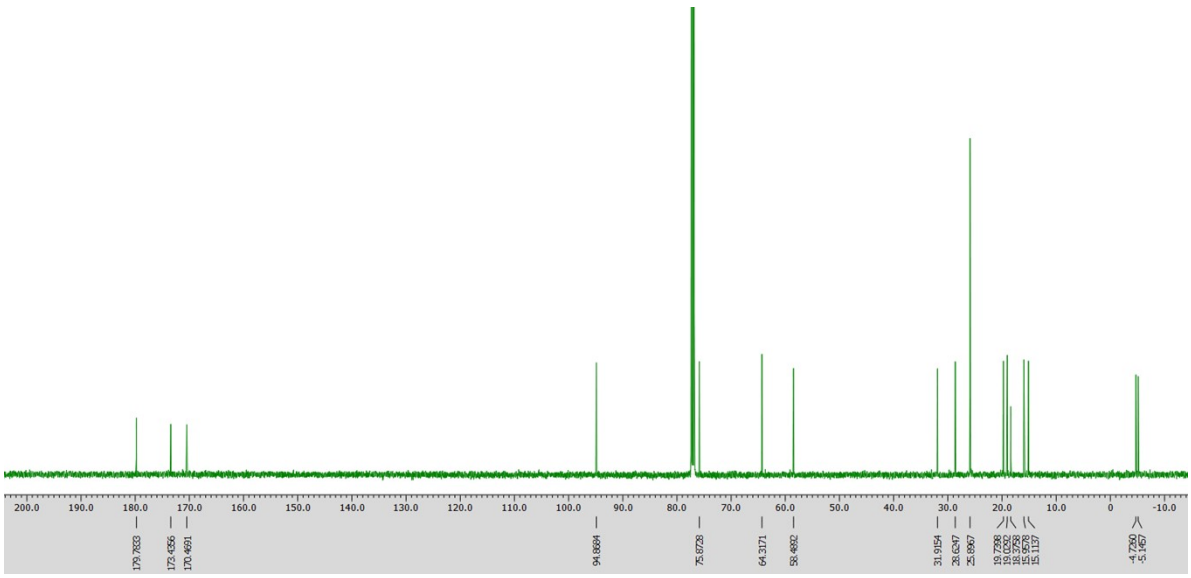
^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.7, 175.0, 94.3, 62.7, 58.3, 29.4, 19.5, 15.2.

(S)-1-((S)-2-((tert-butyldimethylsilyl)oxy)-3-methylbutanoyl)-5-isopropyl-4-methoxy-1H-pyrrol-2(5H)-one (15)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)

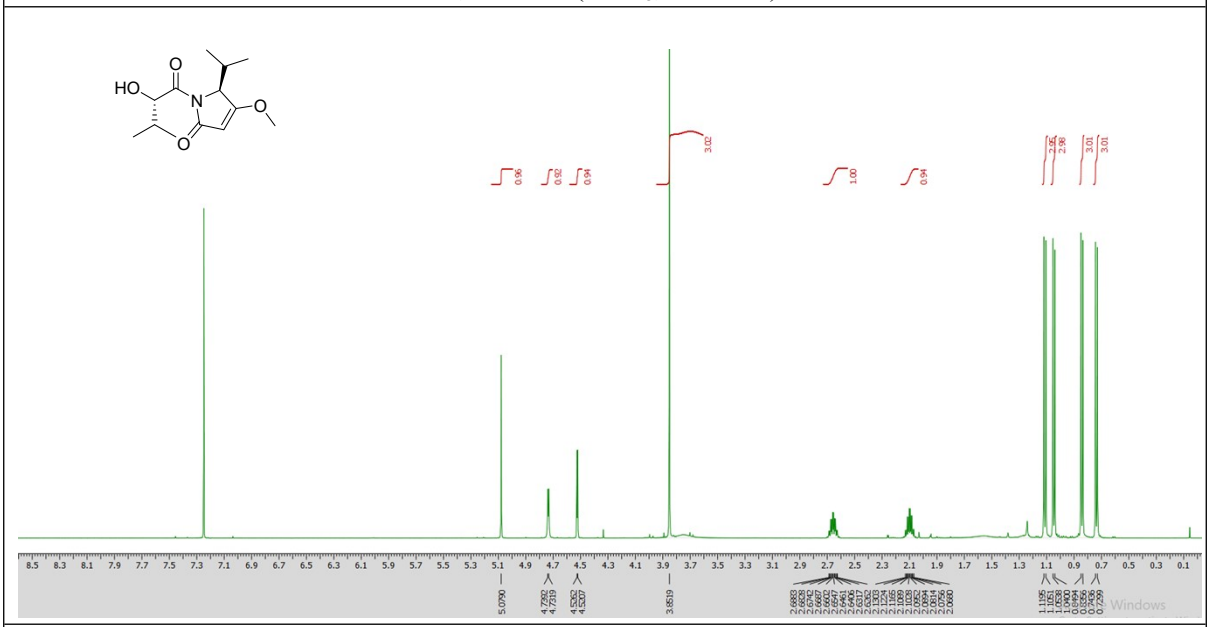
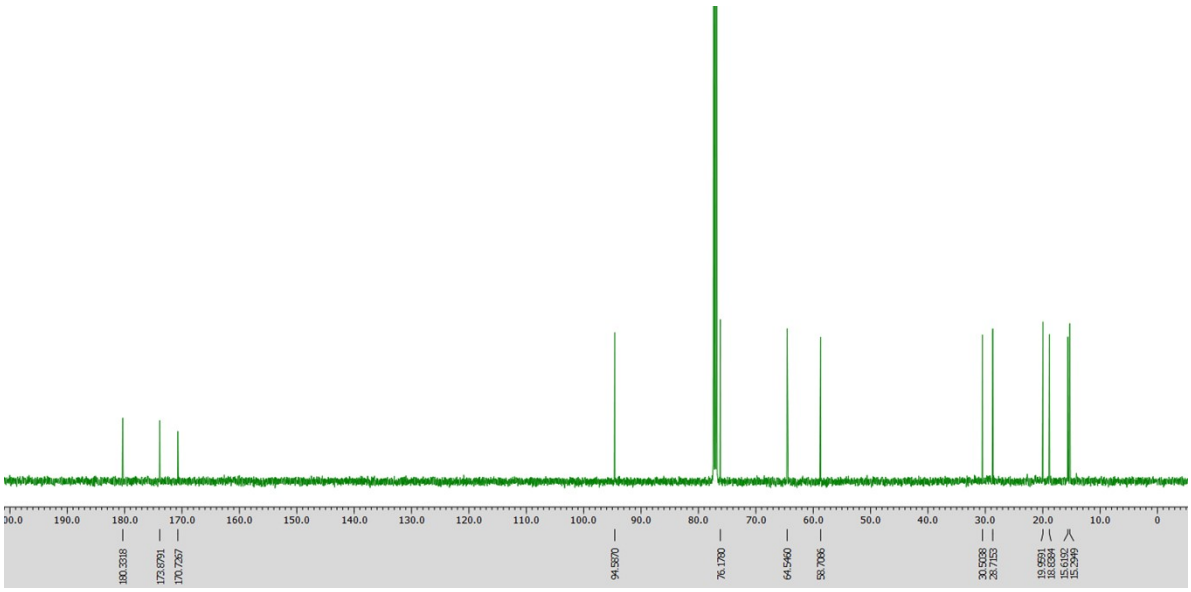


^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.26 (d, *J* = 3.8 Hz, 0.67H), 5.25 (d, *J* = 2.8 Hz, 0.3H), 5.03 (s, 0.65H), 5.03 (s, 0.3H), 4.65 (d, *J* = 2.8 Hz, 0.3H), 4.50 (d, *J* = 2.6 Hz, 0.68H), 3.83 (s, 1H), 3.82 (s, 2H), 2.69-2.64 (m, 0.63H), 2.48-2.42 (m, 0.23H), 2.12-2.07 (m, 0.26H), 1.99-1.93 (m, 0.62H), 1.11 (t, *J* = 7.5 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 1H), 0.96 (d, *J* = 6.9 Hz, 2H), 0.91 (d, *J* = 3.5 Hz, 9H), 0.85 (d, *J* = 6.9 Hz, 2H), 0.81 (d, *J* = 6.9 Hz, 1H), 0.71 (dd, *J* = 6.9, 4.9 Hz, 3H), 0.02 (d, *J* = 8.4 Hz, 7H).

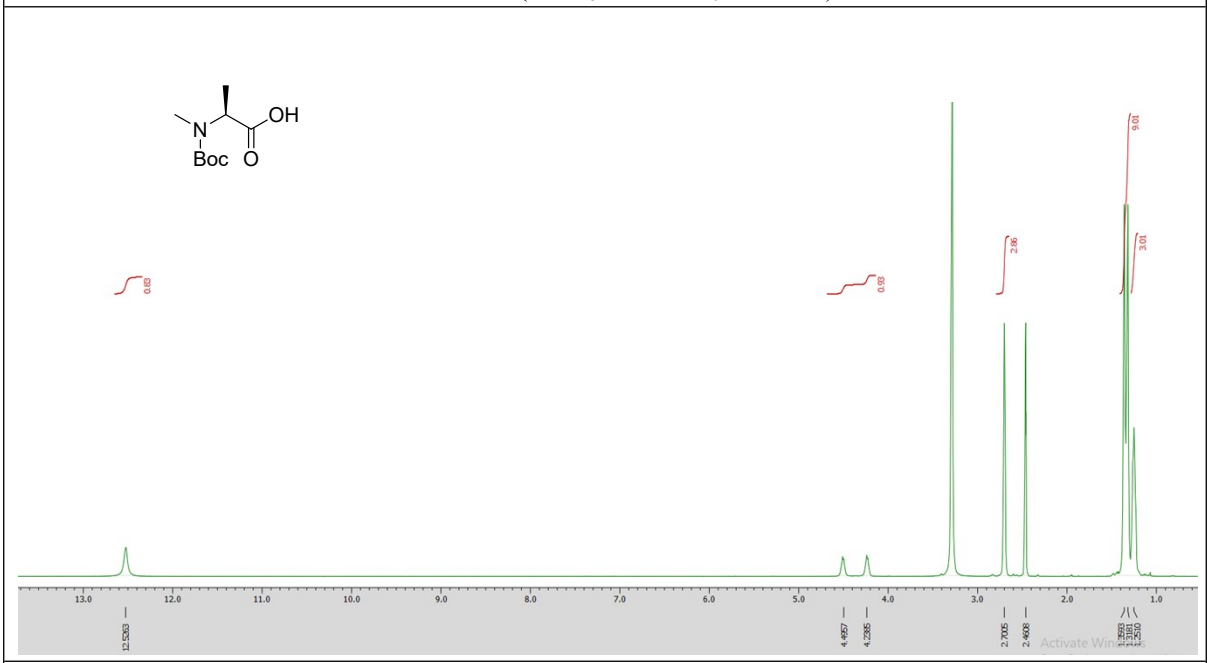
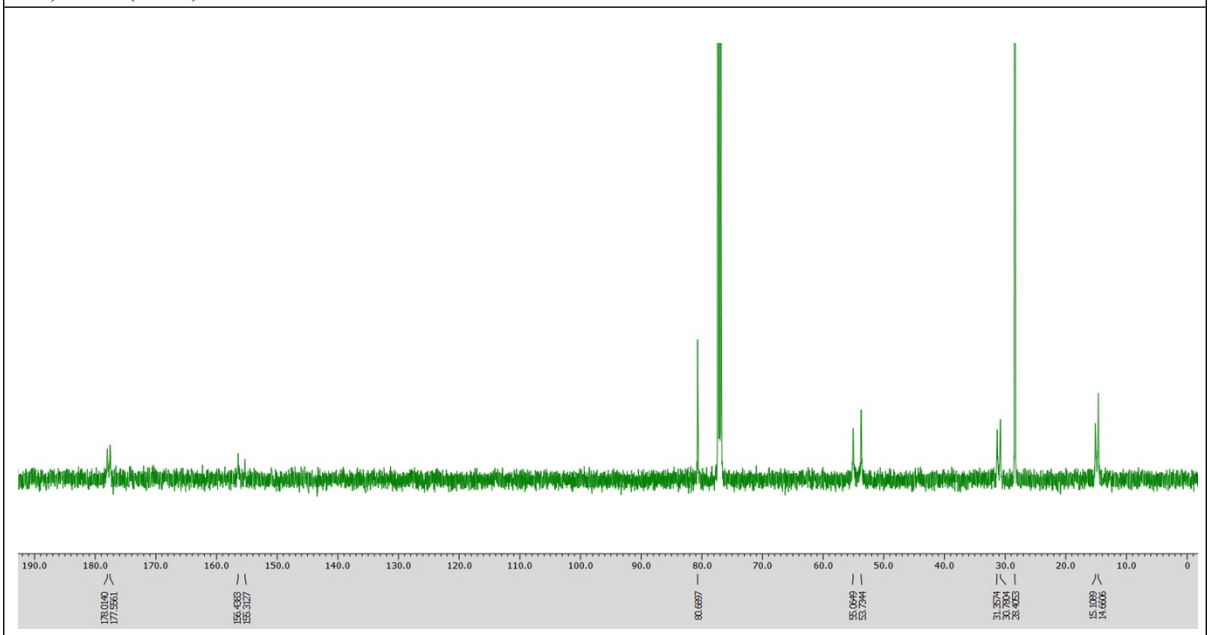


^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.8, 173.4, 170.5, 94.9, 75.9, 64.3, 58.5, 31.9, 28.6, 25.9, 19.7, 19.0, 18.4, 16.0, 15.1, -4.7, -5.1.

(S)-1-((S)-2-hydroxy-3-methylbutanoyl)-5-isopropyl-4-methoxy-1H-pyrrol-2(5H)-one (16)

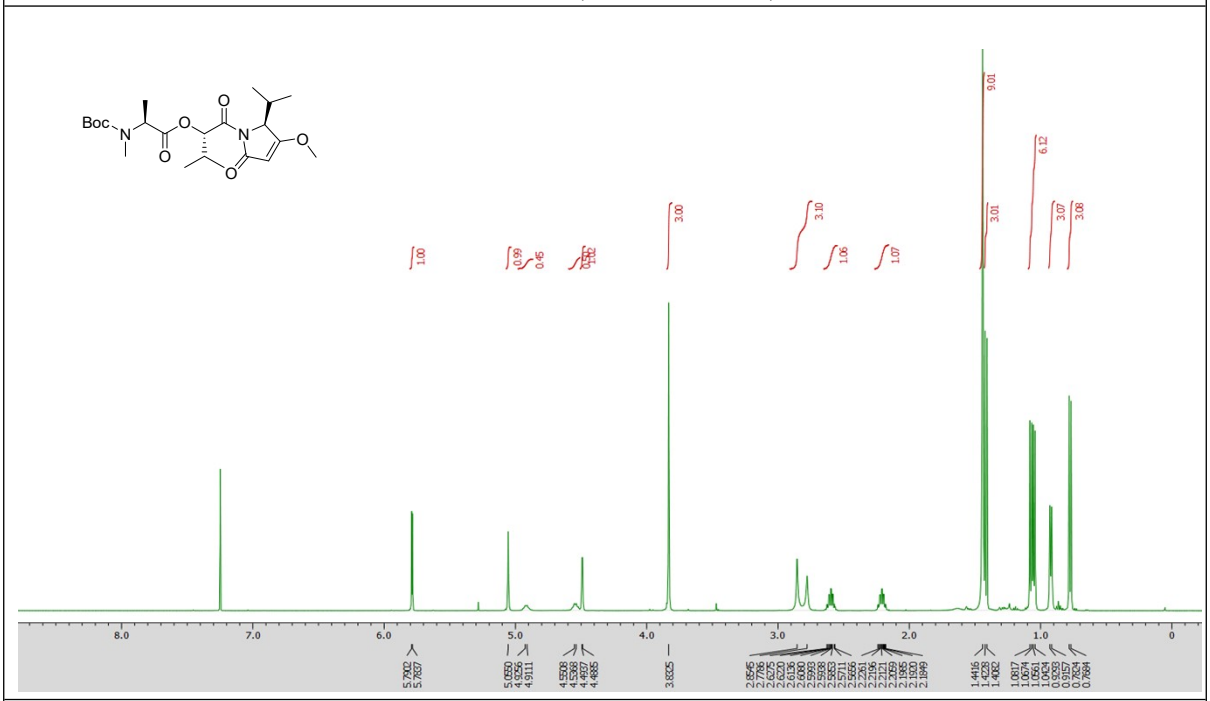
$^{1}H,^{13}C$ NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.08 (s, 1H), 4.74 (d, *J* = 3.7 Hz, 1H), 4.52 (d, *J* = 2.8 Hz, 1H), 3.85 (s, 3H), 2.69-2.63 (m, 1H), 2.13-2.07 (m, 1H), 1.11 (d, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 6.9 Hz, 3H), 0.84 (d, *J* = 6.9 Hz, 3H), 0.74 (d, *J* = 6.9 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 180.3, 173.9, 170.7, 94.6, 76.2, 64.5, 58.7, 30.5, 28.7, 20.0, 18.8, 15.6, 15.3.

(S)-2-((tert-butoxycarbonyl)(methyl)amino)propanoic acid (17)

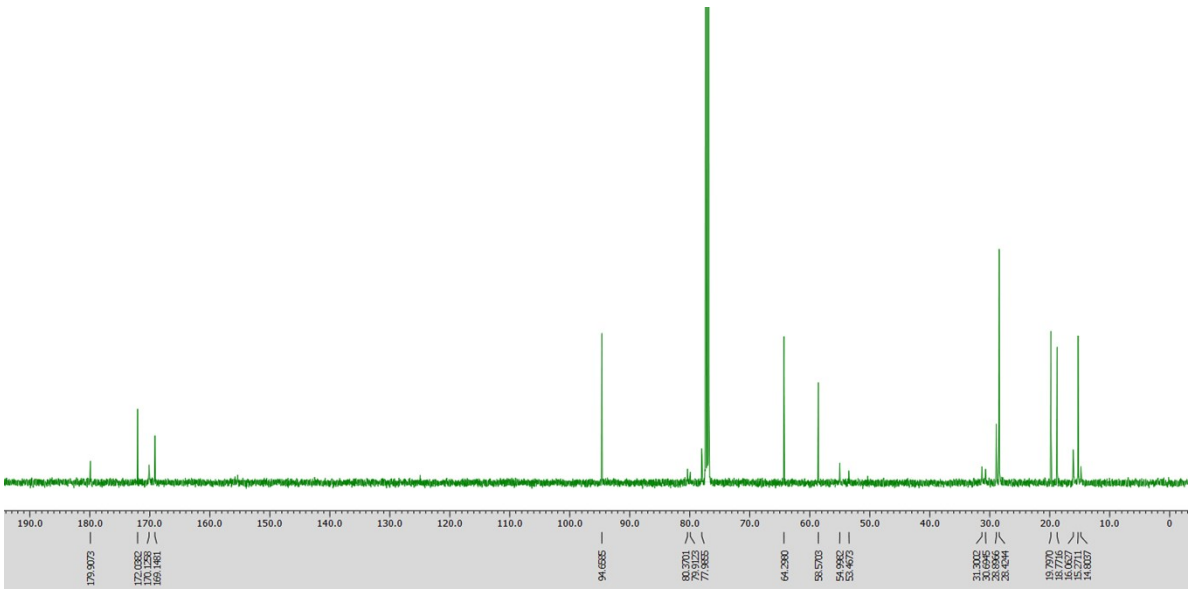
^{1}H,^{13}C NMR ($CDCl_3$, DMSO-d_6 500 MHz)

^{1}H-NMR (500 MHz, DMSO-d_6) δ 12.53 (s, 1H), 4.37 (d, J = 128.6 Hz, 1H), 2.70 (s, 3H), 1.34 (d, J = 20.6 Hz, 9H), 1.25 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 178.0, 177.6, 156.4, 155.3, 80.7, 55.1, 53.7, 31.4, 30.8, 28.4, 15.1, 14.7.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((tert-butoxycarbonyl)(methyl)amino)propanoate (18)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)



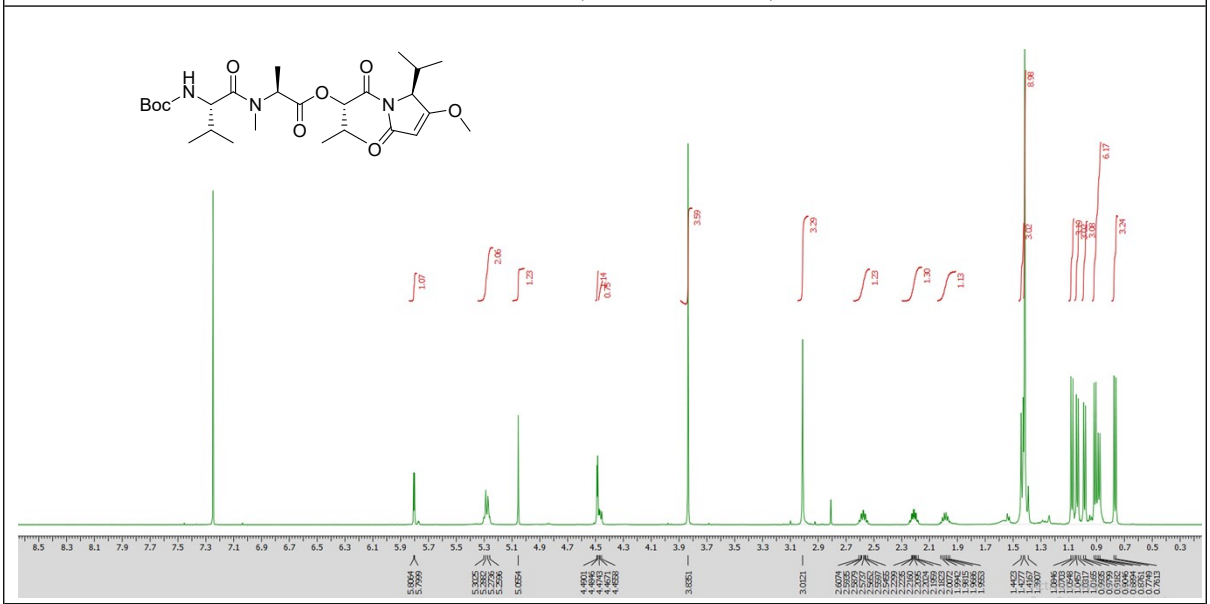
^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.79 (d, *J* = 3.2 Hz, 1H), 5.06 (s, 1H), 4.92-4.54 (m, 1H), 4.49 (d, *J* = 2.6 Hz, 1H), 3.83 (s, 3H), 2.82 (d, *J* = 38.0 Hz, 3H), 2.63-2.57 (m, 1H), 2.24-2.18 (m, 1H), 1.44 (s, 9H), 1.42 (d, *J* = 7.3 Hz, 3H), 1.06 (dd, *J* = 12.7, 7.0 Hz, 6H), 0.92 (d, *J* = 6.8 Hz, 3H), 0.78 (d, *J* = 7.0 Hz, 3H).



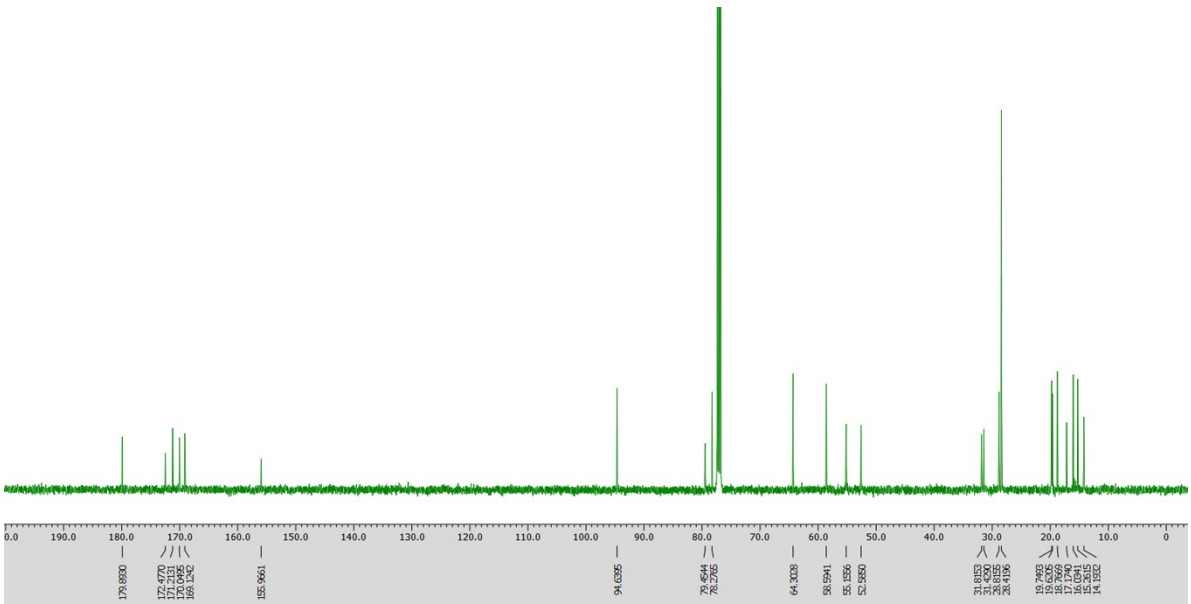
^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.9, 172.0, 170.1, 169.1, 94.7, 78.0, 64.3, 58.6, 55.0, 53.5, 31.3, 30.7, 28.9, 28.4, 19.8, 18.8, 16.1, 15.3, 14.8.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((tert-butoxycarbonyl)amino)-N,3-dimethylbutanamido)propanoate (3)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)



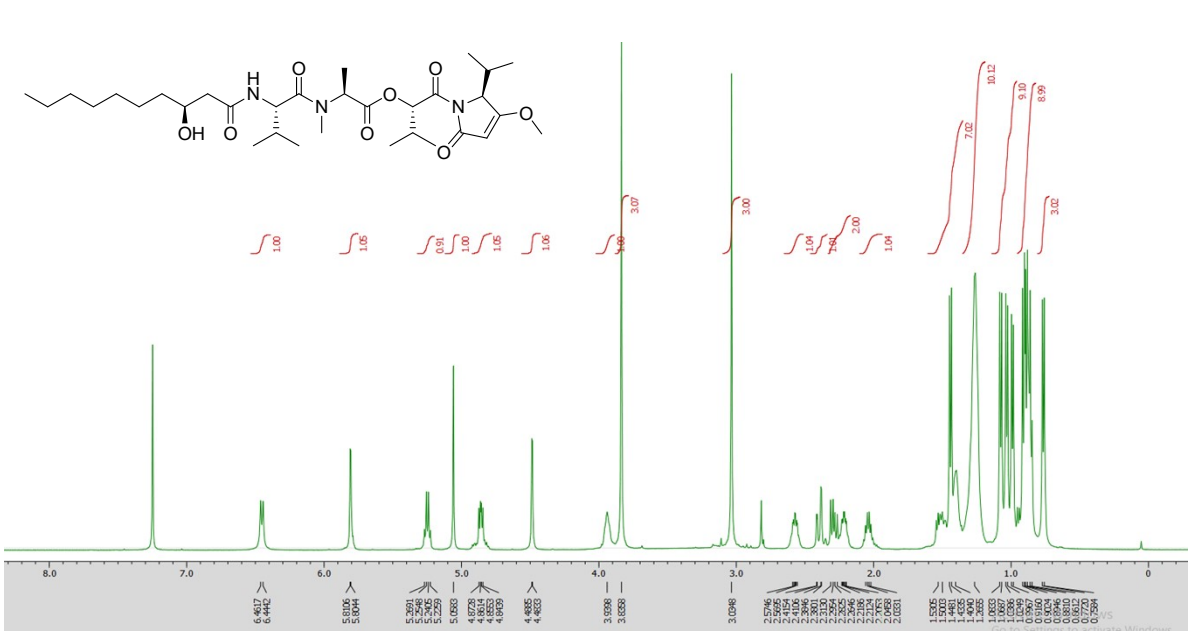
^{1}H-NMR (500 MHz, $CDCl_3$) δ 5.80 (d, *J* = 3.2 Hz, 1H), 5.28 (q, *J* = 7.1 Hz, 2H), 5.06 (s, 1H), 4.49 (d, *J* = 2.8 Hz, 1H), 4.47-4.46 (m, 1H), 3.84 (s, 4H), 3.01 (s, 3H), 2.61-2.55 (m, 1H), 2.23-2.18 (m, 1H), 1.99 (m, 1H), 1.43 (d, *J* = 7.3 Hz, 3H), 1.42 (s, 9H), 1.08 (d, *J* = 7.1 Hz, 3H), 1.05-1.03 (m, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (dd, *J* = 14.4, 6.7 Hz, 6H), 0.77 (d, *J* = 6.8 Hz, 3H).



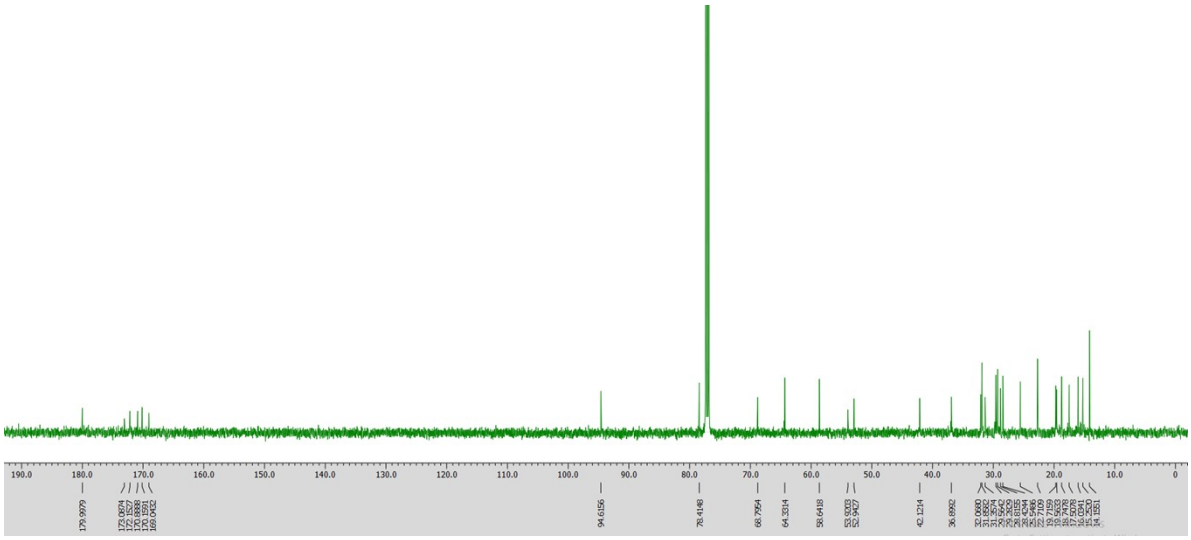
^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.9, 172.5, 171.2, 170.0, 169.1, 156.0, 94.6, 79.5, 78.3, 64.3, 58.6, 55.2, 52.6, 31.8, 31.4, 28.8, 28.4, 19.7, 19.6, 18.8, 17.2, 16.0, 15.3, 14.2.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxydecanamido)-N,3-dimethylbutanamido)propanoate (1a)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)



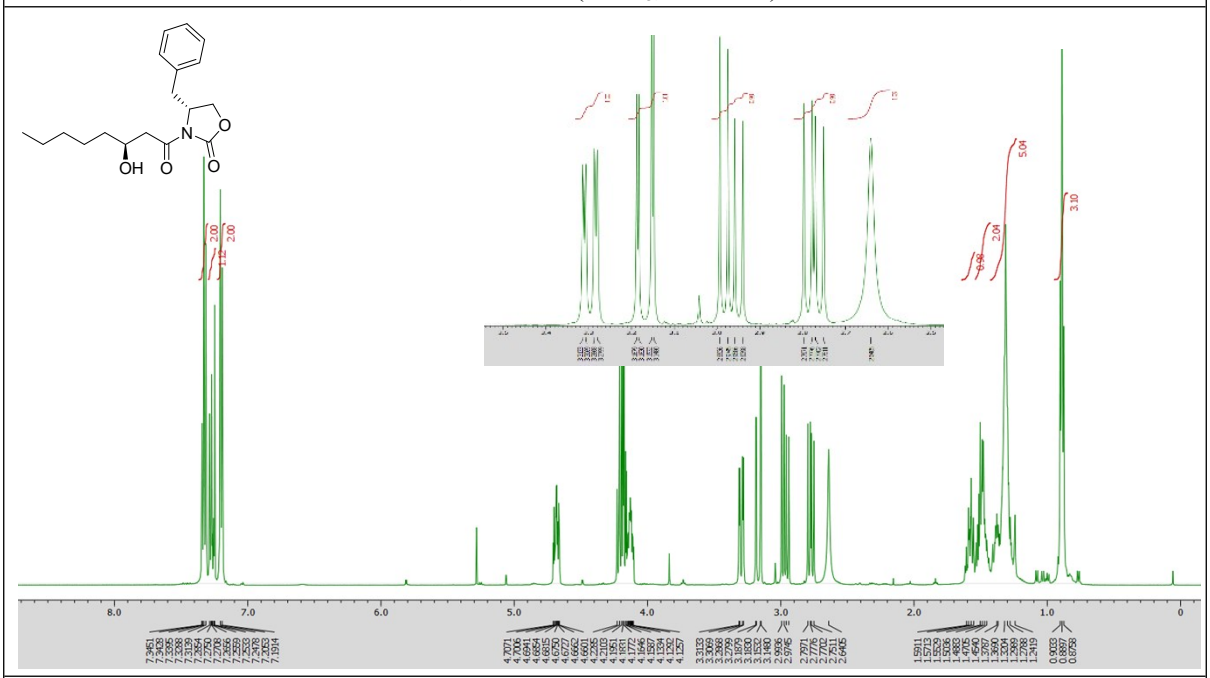
^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.45 (d, *J* = 8.8 Hz, 1H), 5.81 (d, *J* = 3.1 Hz, 1H), 5.25 (q, *J* = 7.2 Hz, 1H), 5.06 (s, 1H), 4.86 (dd, *J* = 8.8, 5.7 Hz, 1H), 4.49 (d, *J* = 2.6 Hz, 1H), 3.94 (s, 1H), 3.84 (s, 3H), 3.03 (s, 3H), 2.56 (tt, *J* = 7.1, 2.7 Hz, 1H), 2.38 (dd, *J* = 15.4, 2.4 Hz, 1H), 2.30 (d, *J* = 8.8 Hz, 1H), 2.25-2.17 (m, 1H), 2.04 (dt, *J* = 12.5, 6.5 Hz, 1H), 1.53 (dd, *J* = 8.8, 7.8 Hz, 1H), 1.44 (d, *J* = 7.3 Hz, 3H), 1.42-1.38 (m, 1H), 1.27 (m, 10H), 1.07 (d, *J* = 7.3 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.3 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H), 0.77 (d, *J* = 6.8 Hz, 3H).



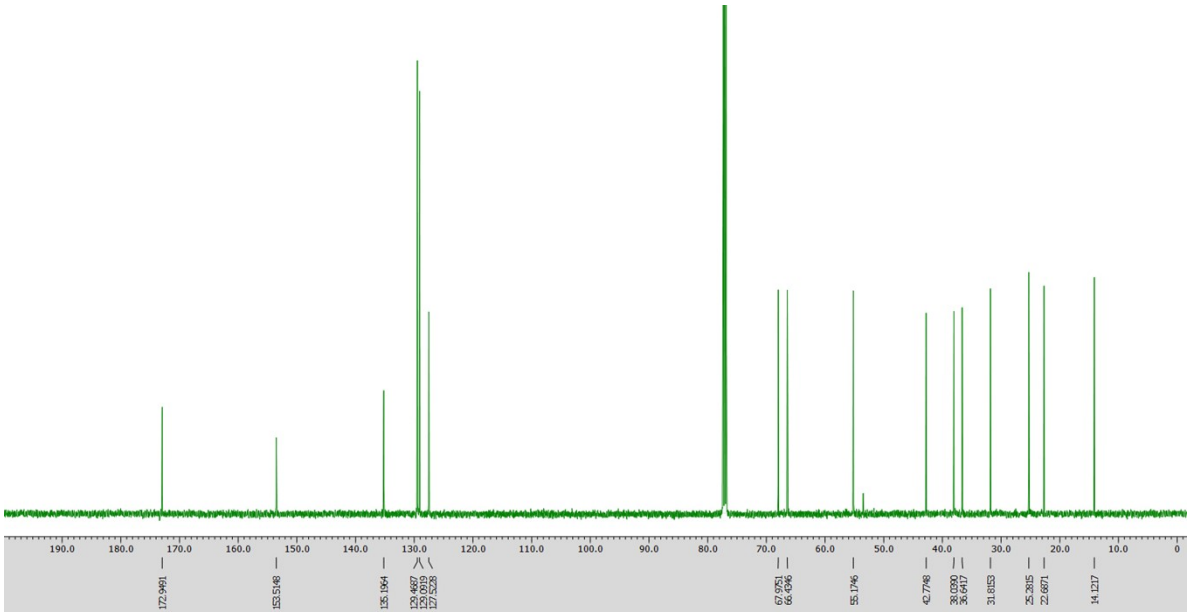
^{13}C-NMR (126 MHz, $CDCl_3$) δ 180.0, 173.1, 172.2, 170.9, 170.2, 169.0, 94.6, 78.4, 68.8, 64.3, 58.6, 53.9, 52.9, 42.1, 36.9, 32.1, 31.9, 31.4, 29.6, 29.3, 28.8, 28.4, 25.5, 22.7, 19.7, 19.6, 18.7, 17.5, 16.0, 15.3, 14.2.

(R)-4-benzyl-3-((S)-3-hydroxyoctanoyl)oxazolidine-2-one (9b)

$^{1}H,^{13}C$ NMR ($CDCl_3$, 500 MHz)

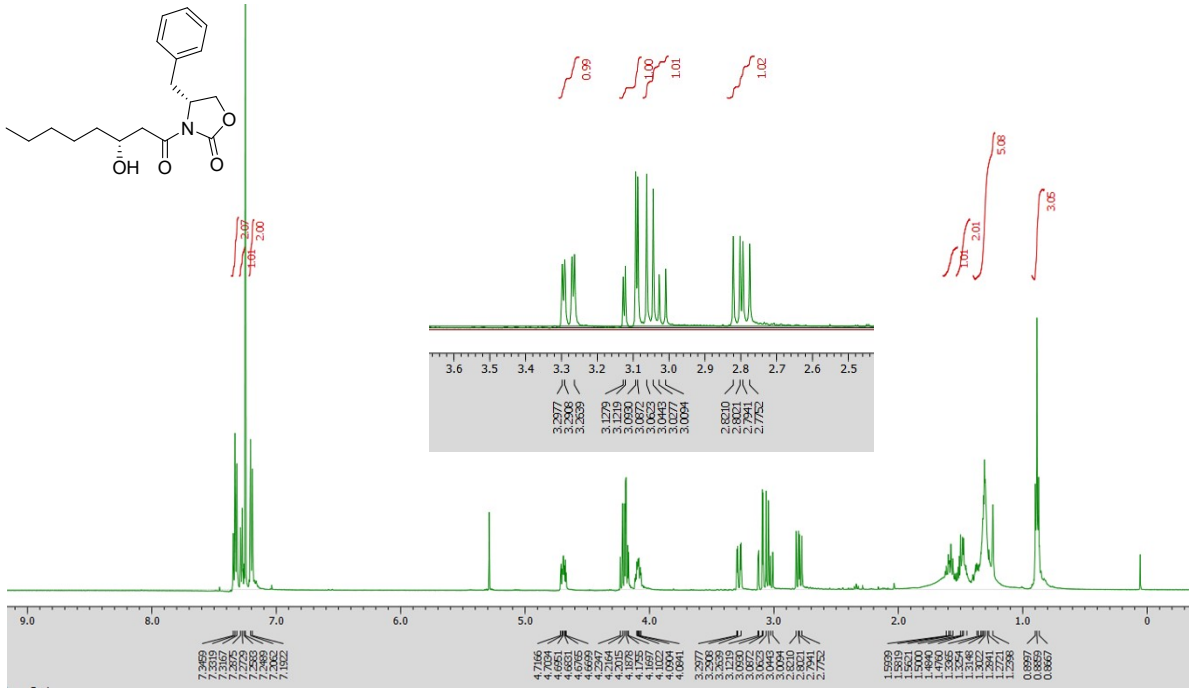


^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 7.29-7.25 (m, 1H), 7.20-7.18 (m, 2H), 4.71-4.66 (m, 1H), 4.23-4.16 (m, 1H), 4.15-4.11 (m, 1H), 3.30 (dd, *J* = 13.4, 3.3 Hz, 1H), 3.17 (dd, *J* = 17.4, 2.5 Hz, 1H), 2.97 (dd, *J* = 17.4, 9.5 Hz, 1H), 2.77 (dd, *J* = 13.4, 9.7 Hz, 1H), 2.64 (s, 1H), 1.61-1.55 (m, 1H), 1.50-1.45 (m, 2H), 1.38-1.24 (m, 5H), 0.89 (t, *J* = 6.9 Hz, 3H).



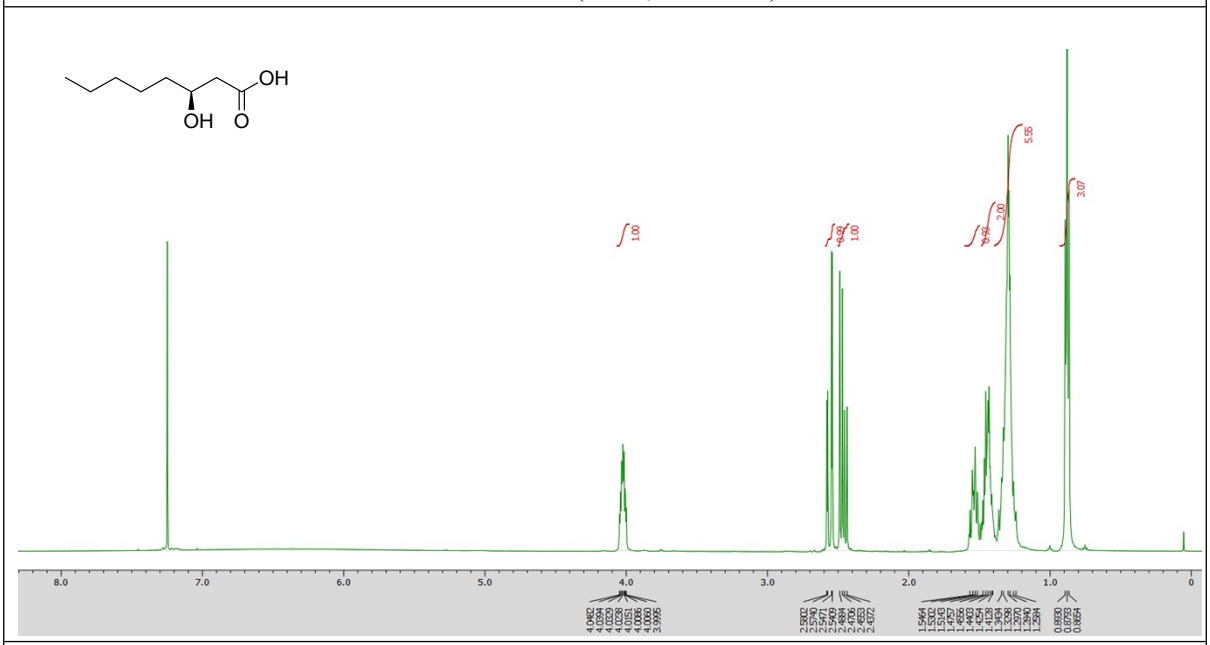
^{13}C-NMR (126 MHz, $CDCl_3$) δ 172.9, 153.5, 135.2, 129.5, 129.1, 127.5, 68.0, 66.4, 55.2, 42.8, 38.0, 36.6, 31.8, 25.3, 22.7, 14.1.

(R)-4-benzyl-3-((R)-3-hydroxydecanoyl)oxazolidine-2-one(9bb)

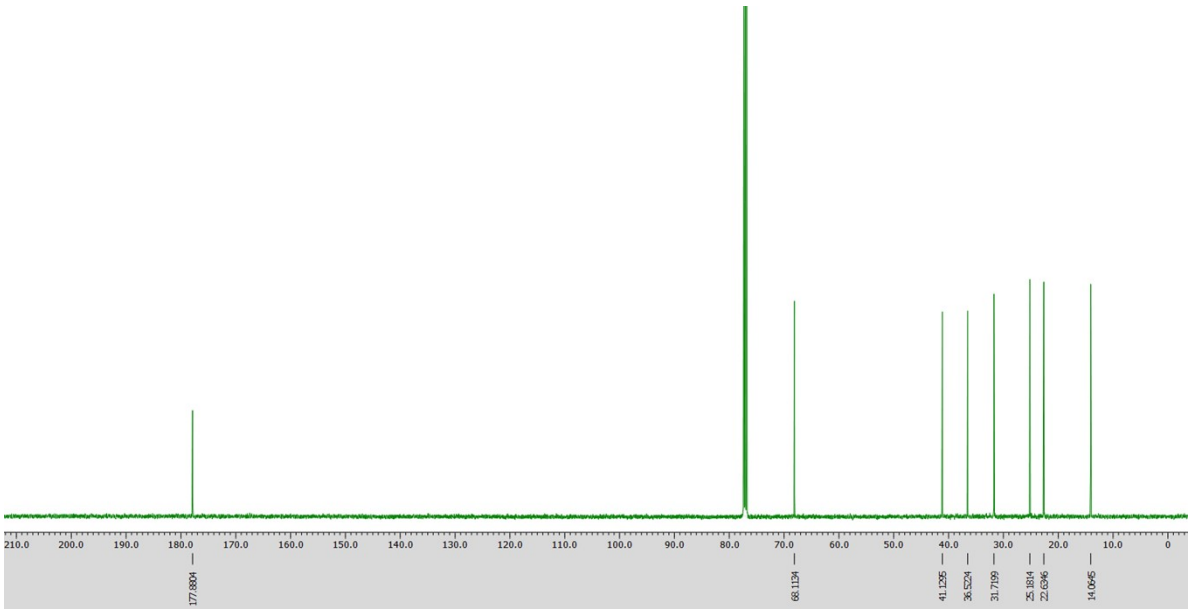
^{1}H, ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 7.29-7.25 (m, 1H), 7.21-7.19 (m, 2H), 4.71-4.66 (m, 1H), 4.24-4.17 (m, 2H), 4.11-4.06 (m, 1H), 3.30 (dd, *J* = 13.4, 3.3 Hz, 1H), 3.10 (dd, *J* = 17.4, 3.0 Hz, 1H), 3.03 (dd, *J* = 17.3, 9.0 Hz, 1H), 2.80 (dd, *J* = 13.4, 9.4 Hz, 1H), 1.61-1.55 (m, 1H), 1.50-1.44 (m, 2H), 1.37-1.23 (m, 5H), 0.88 (t, *J* = 6.9 Hz, 3H).

(S)-3-hydroxyoctanoic acid (2b)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)



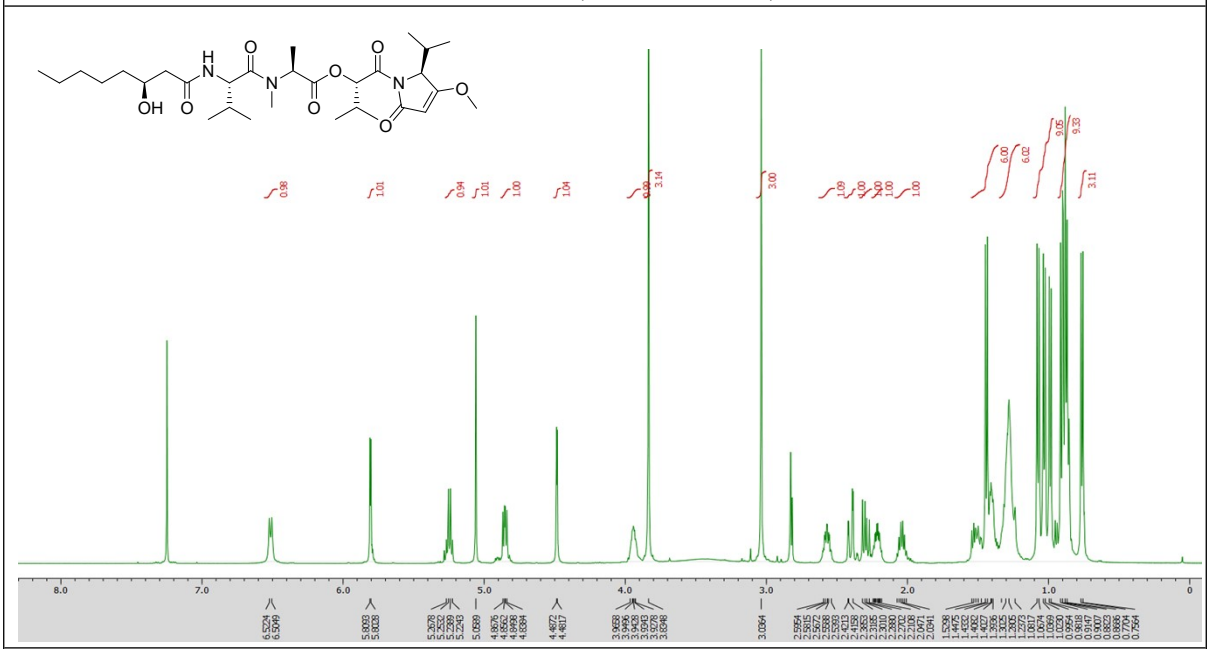
^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.05-4.00 (m, 1H), 2.56 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.46 (dd, *J* = 16.6, 8.9 Hz, 1H), 1.57-1.51 (m, 1H), 1.48-1.41 (m, 2H), 1.34-1.24 (m, 6H), 0.88 (t, *J* =7.0 Hz, 3H).



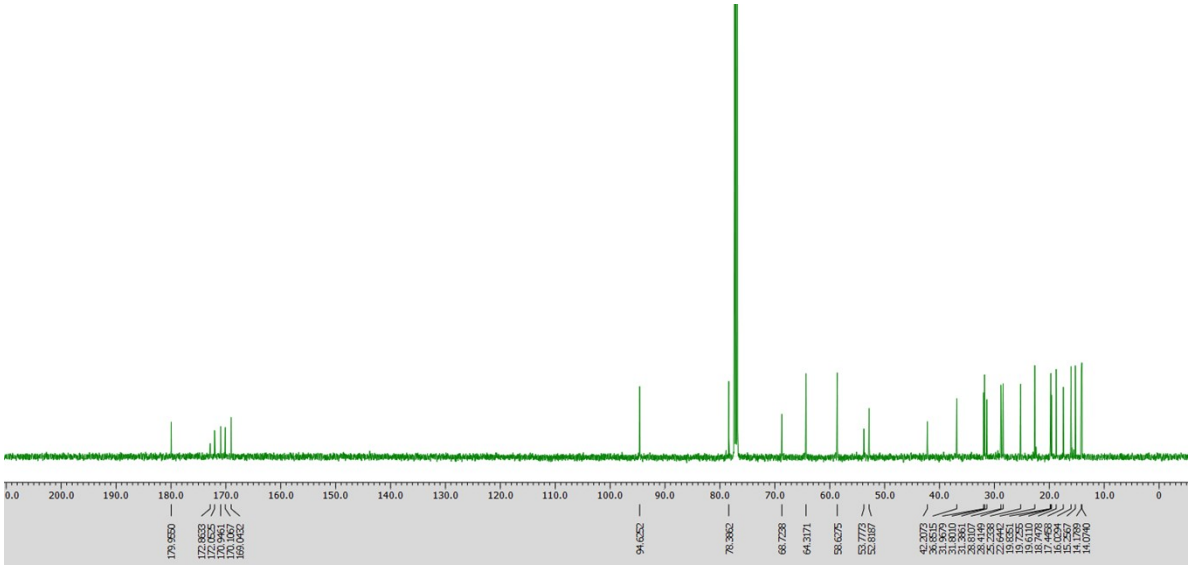
^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.9, 68.1, 41.1, 36.5, 31.7, 25.2, 22.6, 14.1.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxyoctanamido)-N,3-dimethylbutanamido)propanoate (1b)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)



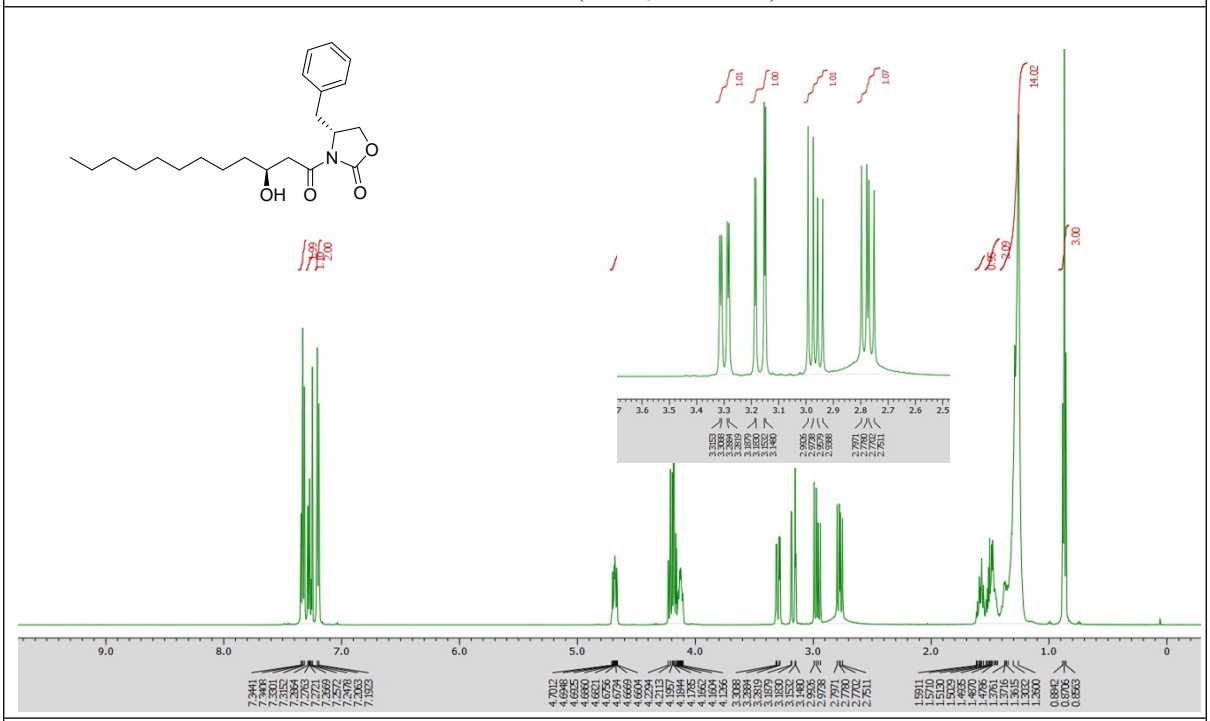
^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.51 (d, *J* = 8.8 Hz, 1H), 5.81 (d, *J* = 3.2 Hz, 1H), 5.25 (q, *J* = 7.2 Hz, 1H), 5.06 (s, 1H), 4.85 (dd, *J* = 8.9, 5.7 Hz, 1H), 4.48 (d, *J* = 2.8 Hz, 1H), 3.95 (s, 1H), 3.83 (s, 3H), 3.04 (s, 3H), 2.56 (tt, *J* = 7.1, 2.7 Hz, 1H), 2.39 (dd, *J* = 15.4, 2.4 Hz, 1H), 2.29 (dd, *J* = 15.3, 8.8 Hz, 1H), 2.24-2.18 (m, 1H), 2.04 (td, *J* = 13.1, 6.6 Hz, 1H), 1.53 (dd, *J* = 8.8, 7.8 Hz, 1H), 1.44 (d, *J* = 7.1 Hz, 3H), 1.42-1.38 (m, 1H), 1.33-1.24 (m, 6H), 1.07 (d, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.89 (d, *J* = 6.3 Hz, 3H), 0.87 (d, *J* = 6.3 Hz, 3H), 0.85 (t, *J* = 6.7 Hz, 3H),0.76 (d, *J* = 7.0 Hz, 3H).



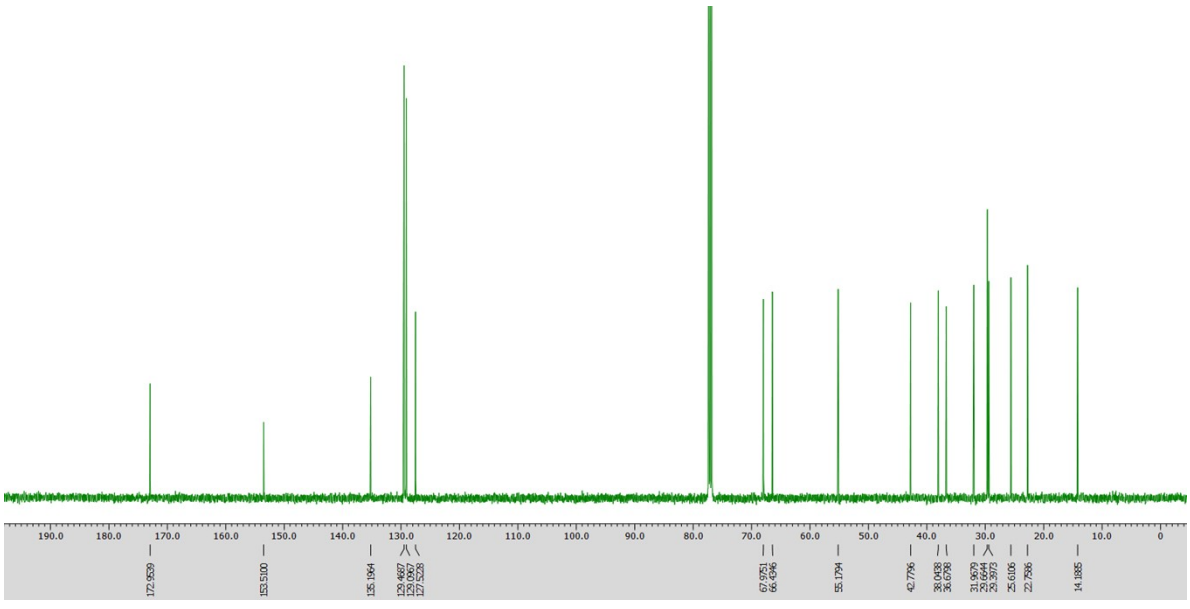
^{13}C-NMR (126 MHz, $CDCl_3$) δ180.0, 172.9, 172.1, 170.9, 170.1, 169.0, 94.6, 78.4, 68.7, 64.3, 58.6, 53.8, 52.8, 42.2, 36.9, 32.0, 31.8, 31.4, 28.8, 28.4, 25.2, 22.6, 19.8, 19.7, 19.6, 18.7, 17.4, 16.0, 15.3, 14.2, 14.1.

(R)-4-benzyl-3-((S)-3-hydroxydodecanoyl)oxazolidine-2-one (9c)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)

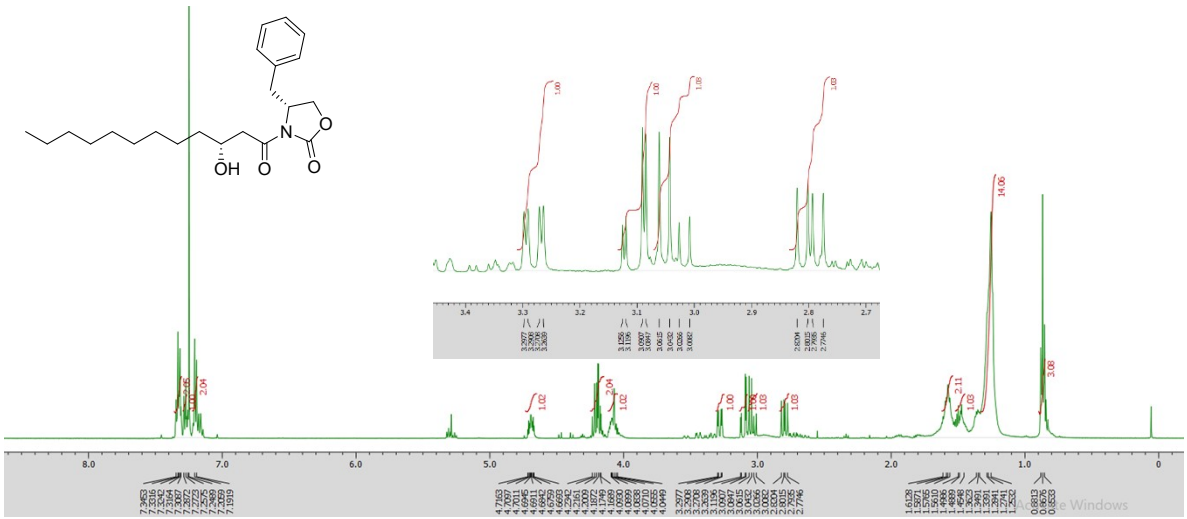


^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.34-7.32 (m, 2H), 7.29-7.25 (m, 1H), 7.20-7.18 (m, 2H), 4.71-4.66 (m, 1H), 4.23-4.16 (m, 2H), 4.15-4.10 (m, 1H), 3.30 (dd, *J* = 13.5, 3.2 Hz, 1H), 3.17 (dd, *J* = 17.4, 2.5 Hz, 1H), 2.97 (dd, *J* = 17.4, 9.5 Hz, 1H), 2.77 (dd, *J* = 13.5, 9.6 Hz, 1H), 1.62-1.56 (m, 1H), 1.53-1.44 (m, 2H), 1.38-1.26 (m, 14H), 0.87 (t, *J* = 7.0 Hz, 3H).

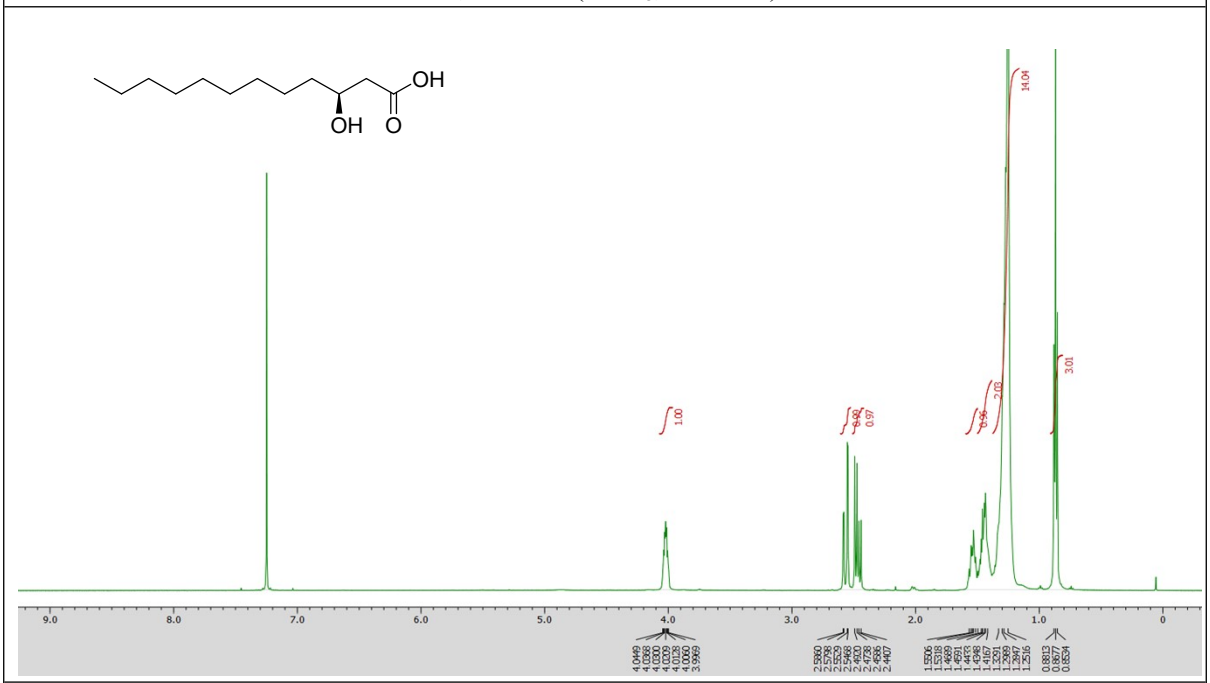
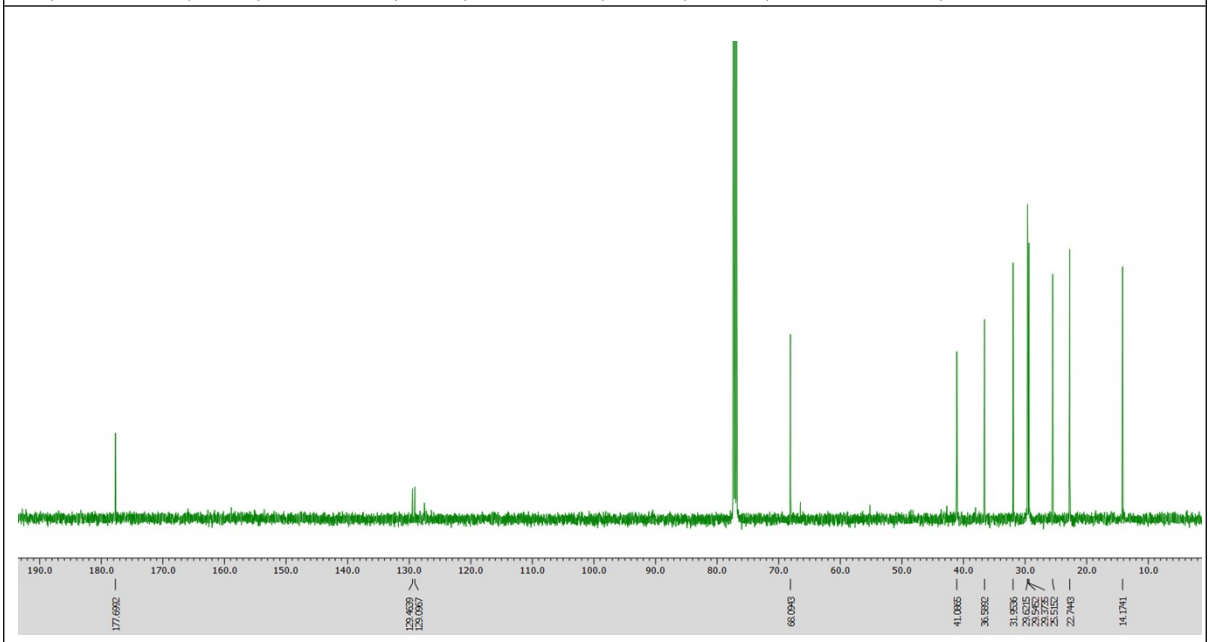


^{13}C-NMR (126 MHz, $CDCl_3$) δ173.0, 153.5, 135.2, 129.5, 129.1, 127.5, 68.0, 66.4, 55.2, 42.8, 38.0, 36.7, 32.0, 29.7, 29.4, 25.6, 22.8, 14.2.

(R)-4-benzyl-3-((R)-3-hydroxydodecanoyl)oxazolidine-2-one (9cc)

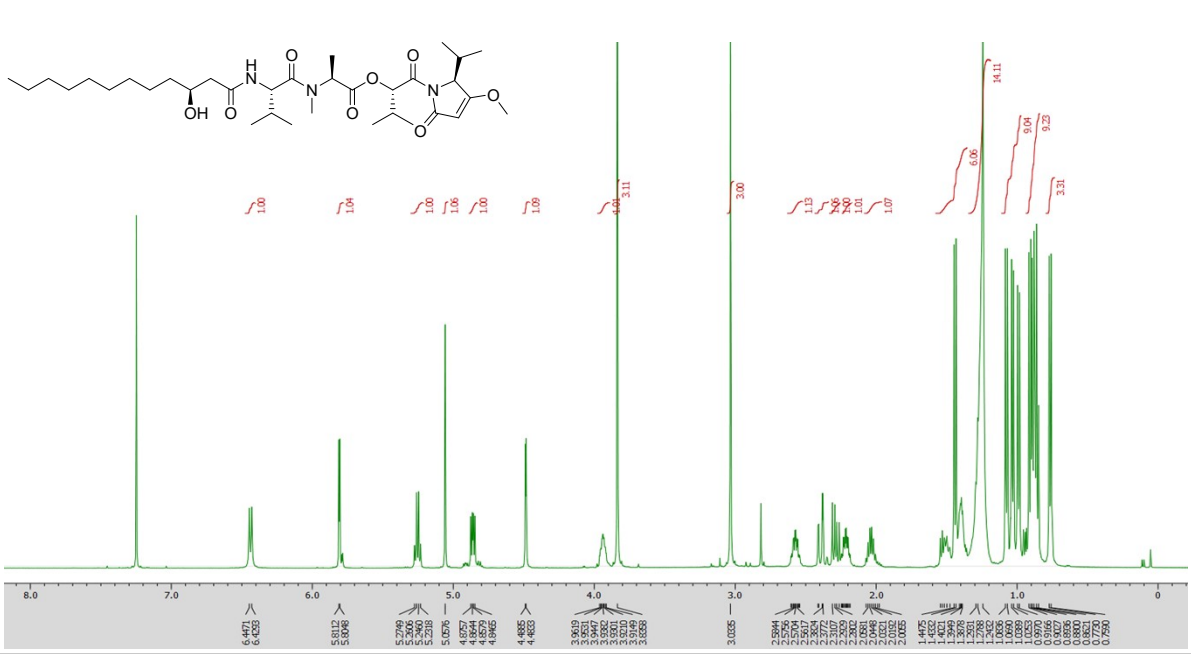
^{1}H, ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.35-7.30 (m, 2H), 7.29-7.26 (m, 1H), 7.21-7.19 (m, 2H), 4.71-4.66 (m, 1H), 4.24-4.16 (m, 2H), 4.10-4.04 (m, 1H), 3.28 (dd, *J* = 13.4, 3.4 Hz, 1H), 3.10 (dd, *J* = 17.4, 3.0 Hz, 1H), 3.03 (dd, *J* = 17.4, 9.2 Hz, 1H), 2.80 (dd, *J* = 13.5, 9.4 Hz, 1H), 1.62-1.55 (m, 2H), 1.50-1.45 (m, 1H), 1.37-1.24 (m, 14H), 0.87 (t, *J* = 7.0 Hz, 3H).

(S)-3-hydroxydodecanoic acid (2c)

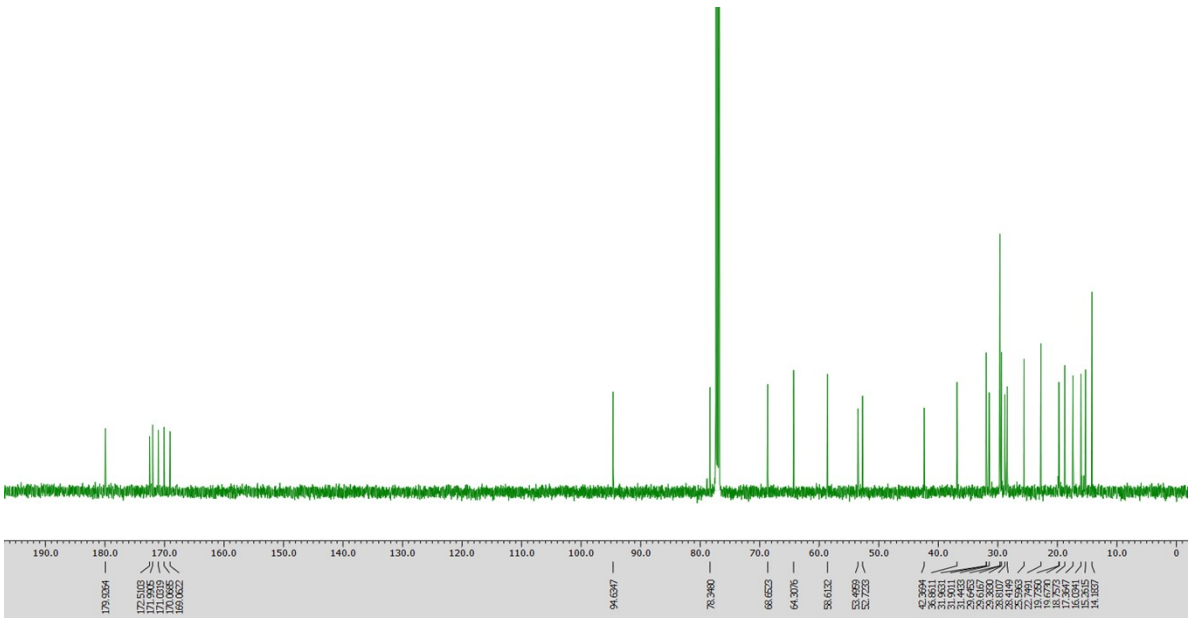
$^{1}H,^{13}C$ NMR ($CDCl_3$, 500 MHz)

^{1}H-NMR (500 MHz, $CDCl_3$) δ 4.04-4.00 (m, 1H), 2.57 (dd, *J* = 16.5, 3.1 Hz, 1H), 2.47 (dd, *J* = 16.6, 9.0 Hz, 1H), 1.57-1.52 (m, 1H), 1.50-1.42 (m, 2H), 1.33-1.25 (m, 14H), 0.87 (t, *J* =7.0 Hz, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ 177.7, 68.1, 41.1, 36.6, 32.0, 29.6, 29.5, 29.4, 25.5, 22.7, 14.2.

(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxydodecanamido)-N,3-dimethylbutanamido)propanoate (1c)

^{1}H,^{13}C NMR ($CDCl_3$, 500 MHz)



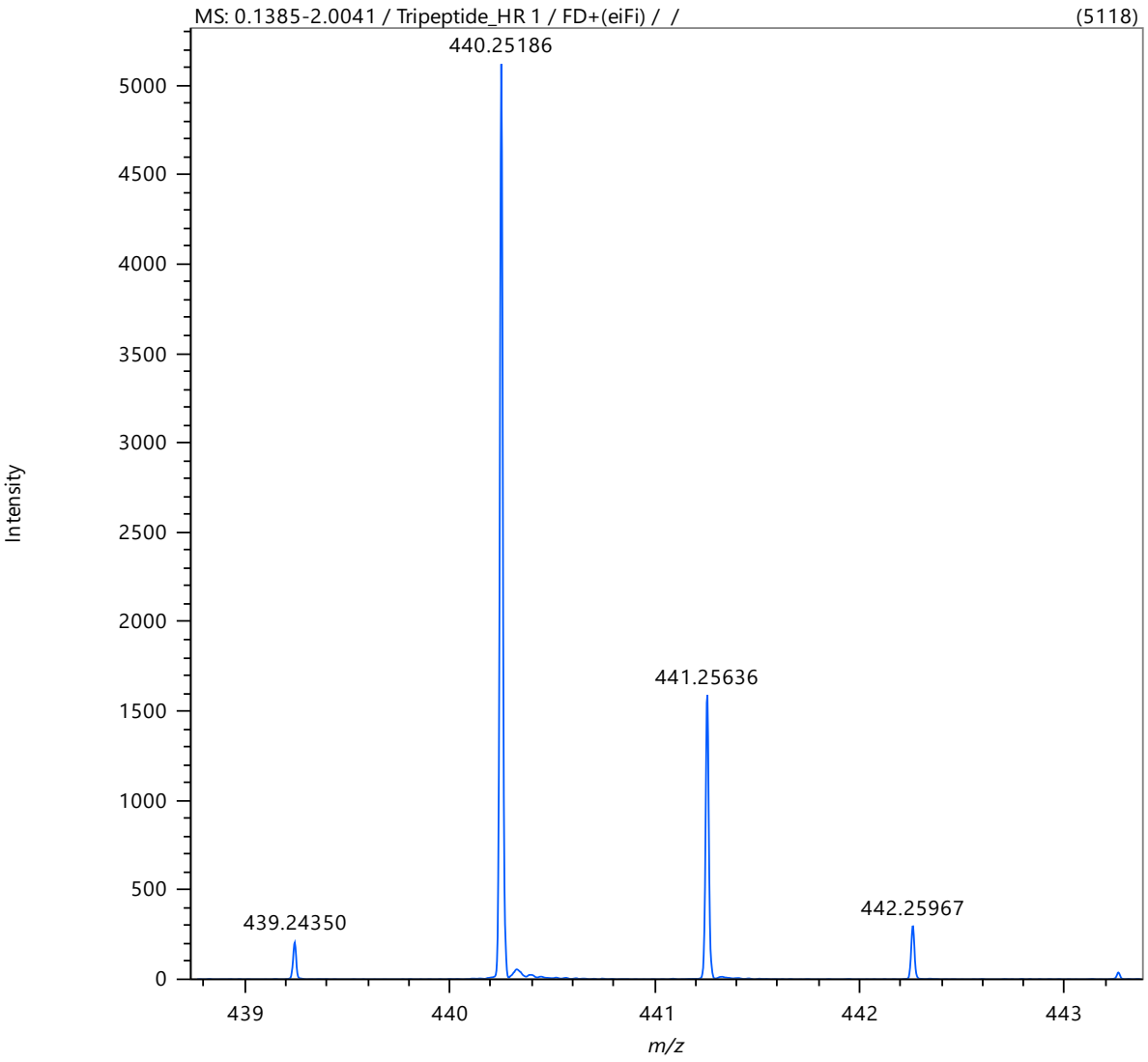
^{1}H-NMR (500 MHz, $CDCl_3$) δ 6.44 (d, *J* = 8.9 Hz, 1H), 5.81 (d, *J* = 3.2 Hz, 1H), 5.25 (q, *J* = 7.2 Hz, 1H), 5.06 (s, 1H), 4.86 (dd, *J* = 8.9, 5.7 Hz, 1H), 4.49 (d, *J* = 2.6 Hz, 1H), 3.96-3.91 (m, 1H), 3.84 (s, 3H), 3.03 (s, 3H), 2.56 (tt, *J* = 7.1, 2.7 Hz, 1H), 2.40 (dd, *J* = 15.3, 2.7 Hz, 1H), 2.29 (d, *J* = 8.9 Hz, 1H), 2.25-2.19 (m, 1H), 2.04 (dt, *J* = 12.5, 6.5 Hz, 1H), 1.53 (dd, *J* = 8.8, 7.8 Hz, 1H), 1.44 (d, *J* = 7.1 Hz, 3H), 1.42-1.38 (m, 1H), 1.25 (m, 14H), 1.07 (d, *J* = 7.3 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.90 (d, *J* = 6.5 Hz, 3H), 0.88 (d, *J* = 6.3 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H), 0.76 (d, *J* = 7.0 Hz, 3H).



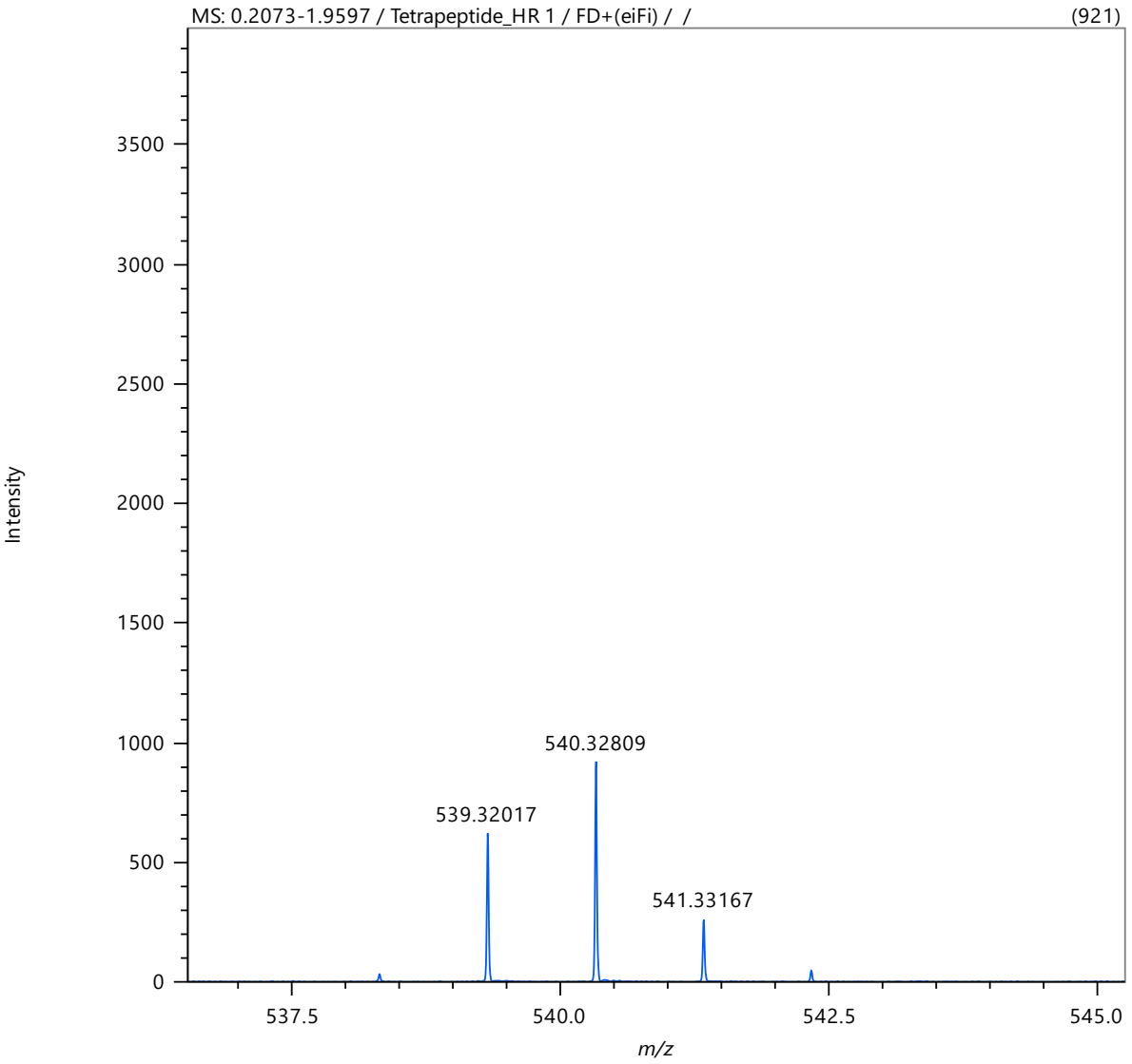
^{13}C-NMR (126 MHz, $CDCl_3$) δ 179.9, 172.5, 172.0, 171.0, 170.1, 169.1, 94.6, 78.3, 68.7, 64.3, 58.6, 53.5, 52.7, 42.4, 36.9, 32.0, 31.9, 31.4, 29.6, 29.6, 29.4, 28.8, 28.4, 25.6, 22.7, 19.7, 19.7, 18.8, 17.4, 16.0, 15.3, 14.2.

VII. The copies of HRMS spectra

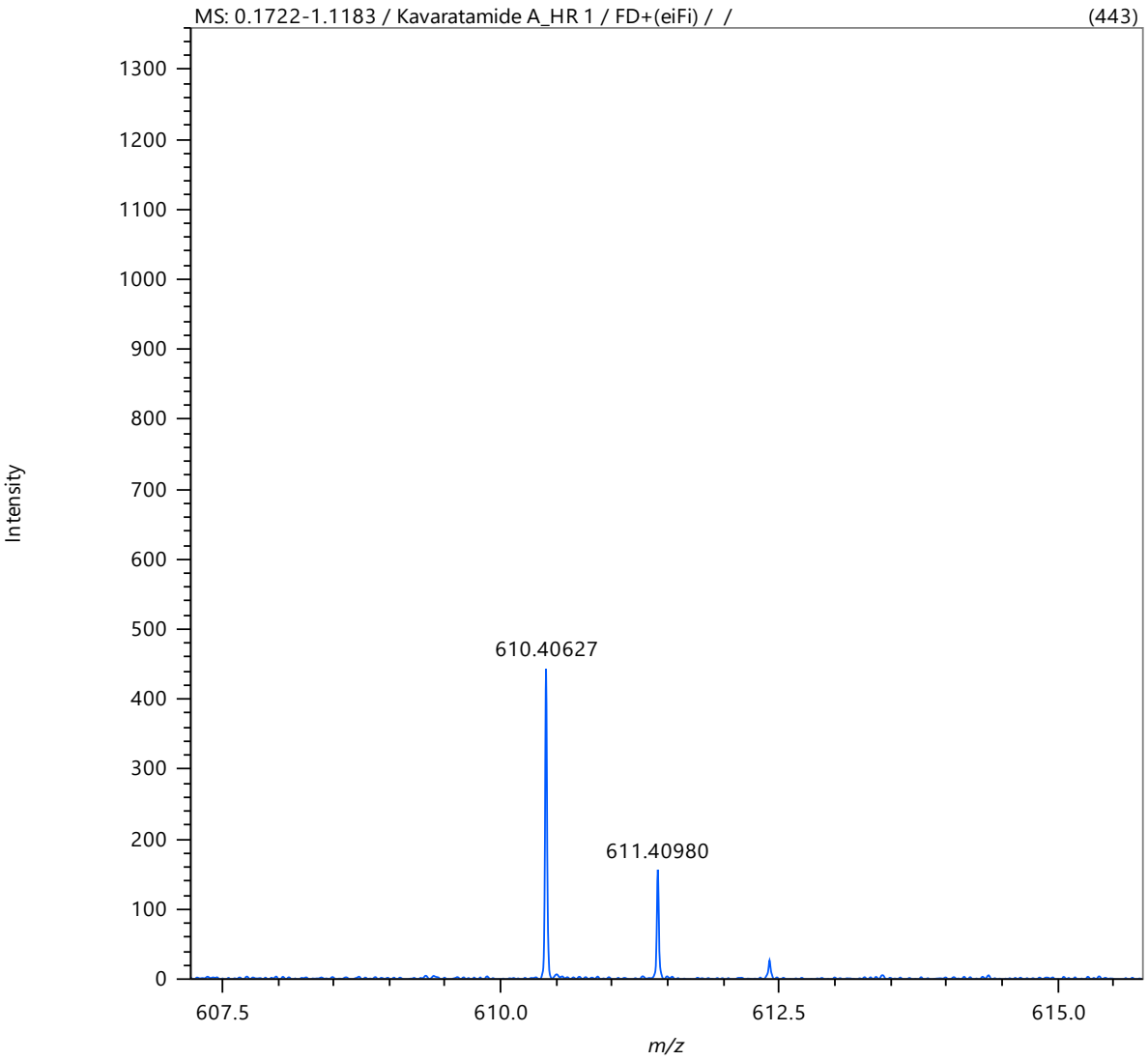
(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((tert-butoxycarbonyl)(methyl)amino)propanoate (18)



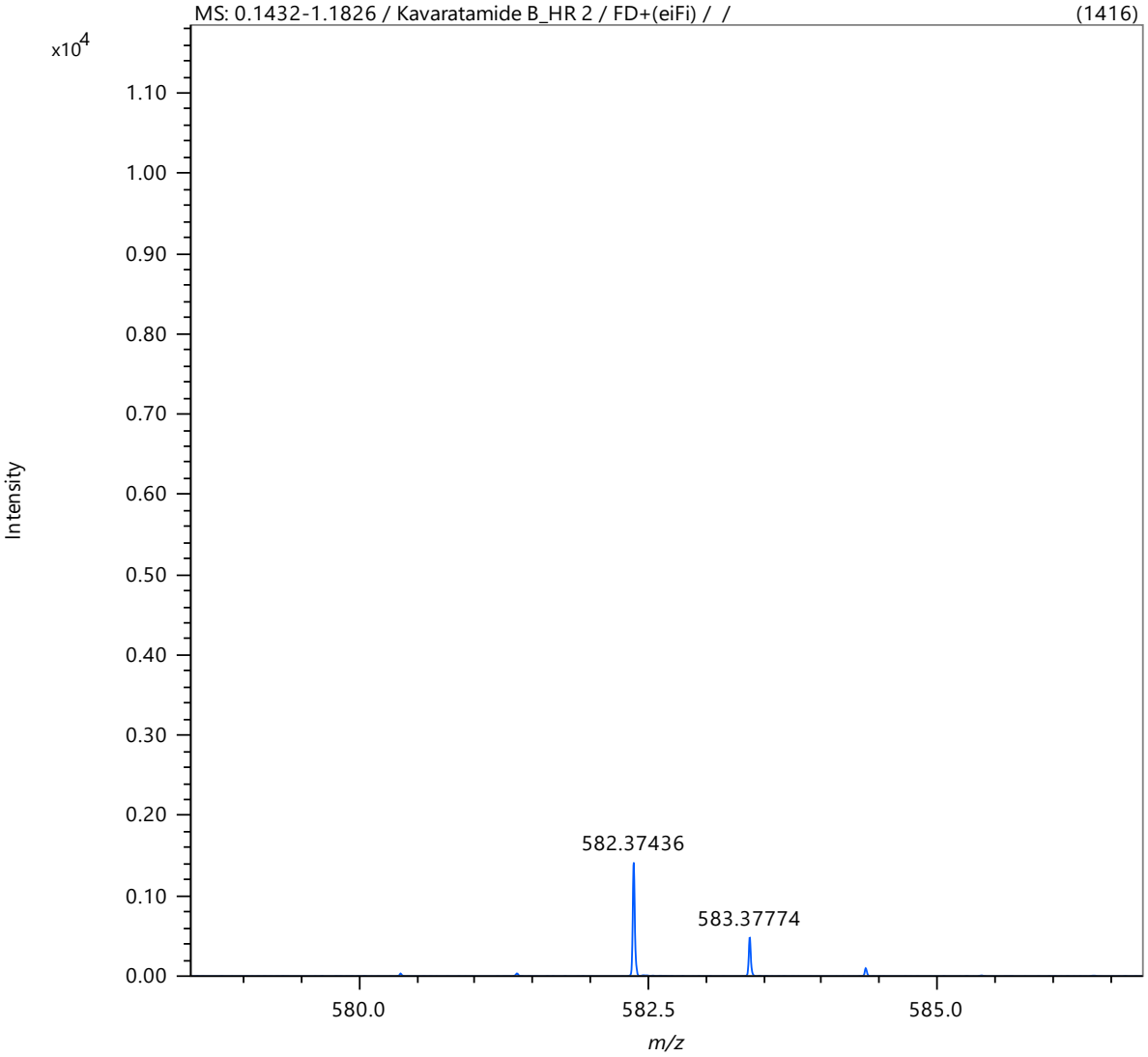
(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((tert-butoxycarbonyl)amino)-N,3-dimethylbutanamido)propanoate (3)


MS: 0.2073-1.9597 / Tetrapeptide_HR 1 / FD+(eiFi) / /
(921)
Intensity
3500
3000
2500
2000
1500
1000
500
0
540.32809
539.32017
541.33167
537.5
540.0
542.5
545.0
m/z

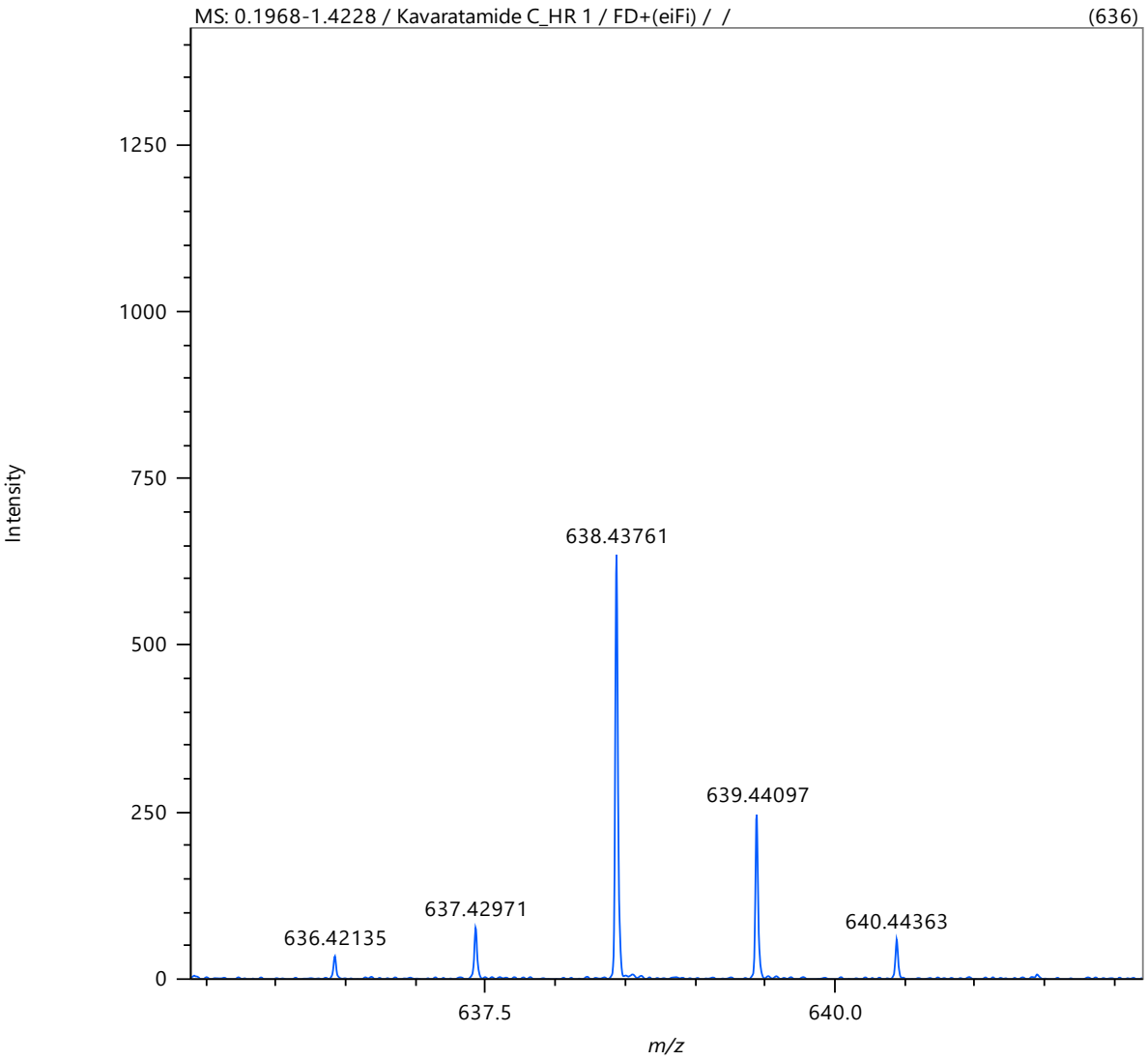
(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxydecanamido)-N,3-dimethylbutanamido)propanoate (1a)



(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxyoctanamido)-N,3-dimethylbutanamido)propanoate (1b)



(S)-(S)-1-((S)-2-isopropyl-3-methoxy-5-oxo-2,5-dihydro-1H-pyrrol-1-yl)-3-methyl-1-oxobutan-2-yl 2-((S)-2-((S)-3-hydroxydodecanamido)-N,3-dimethylbutanamido)propanoate (1c)



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