Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Green transformation of CO_2 into γ-amino alcohols with continuous stereocenters

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1. General experimental information

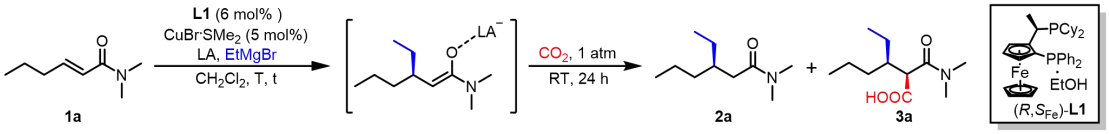
All reactions using oxygen- and/or moisture-sensitive materials were carried out with anhydrous solvents under a argon atmosphere using oven-dried glassware and standard Schlenk techniques. Flash column chromatography was performed using Merck 60 Å 230-400 mesh silica gel. Thin layer chromatography was performed using 0.25 mm E. Merck silica plates (60F-254). Components were visualized by bromocresol green and $KMnO_4$ staining. NMR data was collected on Varian VXR400 (^1H at 400.0 MHz; ^{13}C at 100.58 MHz) equipped with a 5 mm *z*-gradient broadband probe. Chemical shifts are reported in parts per million (ppm) relative to residual solvent peak ($CDCl_3$, ^1H: 7.26 ppm, ^{13}C: 77.16 ppm; DMSO-d_6, ^1H: 2.50 ppm, ^{13}C: 39.52 ppm). Coupling constants are reported in Hertz. Multiplicity is reported with the usual abbreviations (s: singlet, d: doublet, t: triplet, q: quartet, m: multiplet). Exact mass spectra were recorded on a LTQ Orbitrap XL apparatus with ESI ionization. Enantiomeric ratio (er) were determined by chiral HPLC analysis of the CA product isolated from the trapping reaction mixture using a Shimadzu LC-10AD*VP* HPLC equipped with a Shimadzu SPD-M10A*VP* diode array detector. Diastereomeric ratio (dr) were determined by ^1H NMR and ^{13}C NMR of pure trapping products.

2. Chemicals

Unless otherwise indicated, reagents and substrates were purchased from commercial sources and used as received. Solvents not required to be dry were purchased as technical grade and used as received. Dry solvents were freshly collected from a dry solvent purification system prior to use. Inert atmosphere experiments were performed with standard Schlenk techniques with dried (P_2O_5) Ar gas. Dried (P_2O_5) CO_2 with the purity of 99.999% was used. Grignard reagents were purchased from Sigma-Aldrich: EtMgBr, MeMgBr (3.0 M in Et_2O), *i*-BuMgBr, *n*-HexMgBr (2.0 M in Et_2O). All other Grignard reagents were prepared from the corresponding alkyl bromides and Mg activated with I_2 in methyl *tert*-butyl ether (MTBE): *i*-PentMgBr (2.0 M in MTBE), PhEtMgBr (1.4 M in MTBE), pent-4-en-1-ylMgBr (1.7 M in MTBE). Chiral ligands (R,S_{Fe})-**L1** was purchased from Sigma-Aldrich. All reported compounds were characterized by ^1H NMR and compared with literature data. All new compounds were fully characterized by ^1H, ^{13}C NMR and HRMS techniques.

3. Optimization of reaction conditions

Table S1. Optimization of the copper-catalyzed ACA/CO_2-trapping tandem reaction[a]



Entry	T [°C]	t [h]	LA	EtMgBr	**1a**:**2a**:**3a**[b]	er[c]	dr[d]
1	−78	16	2.0 equiv. Me_3SiOTf	2.0 equiv.	12:88:0	99:1	–
2	0	2	2.0 equiv. Me_3SiOTf	2.0 equiv.	16:50:34	97:3	56:44
3	−40	2	2.0 equiv. Me_3SiOTf	2.0 equiv.	7:48:45	99:1	51:49
4[e]	−40	2	2.0 equiv. Me_3SiOTf	2.0 equiv.	22:6:72	99:1	54:46
5[f]	−40	2	2.0 equiv. Me_3SiOTf	2.0 equiv.	0:23:77	99:1	54:46
6[f]	−40	2	3.0 equiv. Me_3SiOTf	3.0 equiv.	0:37:63	95:5	54:46
7[f]	−40	2	4.0 equiv. Me_3SiOTf	4.0 equiv.	0:41:59	94:6	51:49
8[f]	−40	2	1.5 equiv. Me_3SiOTf	2.0 equiv.	7:23:70	96:4	59:41
9[f,g]	−40	2	2.0 equiv. Me_3SiOTf	2.0 equiv.	9:23:68	97:3	54:46
10[f]	−40	2	2.0 equiv. *t*-$BuMe_2SiOTf$	2.0 equiv.	80:20:0	–	–
11[f]	−40	2	2.0 equiv. *i*-Pr_3SiOTf	2.0 equiv.	22:20:58	88:12	50:50
12[f]	−40	2	2.0 equiv. Me_3SiCl	2.0 equiv.	81:4:15	–	–
13[f]	−40	2	2.0 equiv. Me_3SiBr	2.0 equiv.	24:6:70	97:3	50:50
14[f]	−40	2	2.0 equiv. $BF_3·Et_2O$	2.0 equiv.	1:99:0	–	–

[a]Reaction conditions: 0.5 mmol **1a** in 5 mL CH_2Cl_2, 5 mol% CuBr·SMe_2, 6 mol% **L1**, 2.0~4.0 equiv. of Me_3SiOTf and 2.0~4.0 equiv. of EtMgBr was used at −78~0 °C for 2~16 h, then stirred for 24 h at RT under 1 atm CO_2 atmosphere. [b]The ratio was determined by ^1H NMR of reaction crude. [c]Enantiomeric ratio was determined by chiral HPLC analysis of the CA product isolated from the trapping reaction mixture. [d]The ratio was determined by ^1H NMR and ^{13}C NMR of the trapping product. [e]10 mL CH_2Cl_2 was used for ACA reaction. [f]After the first step, 5 mL CH_2Cl_2 was added before the inflation of CO_2. [g]EtMgBr was added first, after which LA was added.

4. Synthesis of the substrates

α,*β*-Unsaturated amides **1a~1f** were prepared according to the literature method, and the ^{1}H NMR of each substrate is consistent with the literature data.[1]

5. ACA-CO_2 trapping reactions

5.1 General procedure for ACA-CO_2 trapping tandem reactions

To a flame-dried Schlenk tube equipped with septum and magnetic stirring bar was added CuBr·SMe_2 (0.025 mmol, 5 mol%), ligand **L1** (0.030 mmol, 6 mol%) and the substrate (0.5 mmol, 1.0 equiv., if solid). The tube was evacuated and filled with Ar for three times, after which the substrate (0.5 mmol, 1.0 equiv., if liquid) was added using a microsyringe. Dry CH_2Cl_2 (5 mL) was added, and this mixture was stirred for 20 min at RT. Then the mixture was cooled down (see the details per substrate), followed by addition of Me_3SiOTf (1.0 mmol, 2.0 equiv.). After 20 min., RMgBr (1.0 mmol, 2.0 equiv.) was added by hand in about 1 min. After stirring for 2 h, 5 mL dry CH_2Cl_2 was added again to dilute the mixture, and CO_2 (1 atm) was inflated into the reaction system. Then the reaction mixture was warmed to RT and stirred for 24 h. The resulting reaction mixture was quenched with HCl (5 mL, 1.0 M) and extracted with MTBE (20 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on a rotary evaporator. The crude was purified by flash chromatography on the silica gel (typical eluent CH_2Cl_2:CH_3OH = 10:1). Then the product was redissolved in MTBE (5 mL) and transferred to a separation funnel, which was extracted with saturated $NaHCO_3$ aqueous solution (5.0 mL × 3). The combined aqueous phase was acidified with HCl aqueous solution (5.0 mL, 12.0 M), and extracted with MTBE (20.0 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on rotary evaporator to afford the pure product.

5.2 The process of CO_2 inflation

After ACA reaction was completed, CH_2Cl_2 was added to diluted the reaction mixture. Then the terminal valve of the Shlenk line was open and blew with CO_2 for 10 minutes to replace the Ar in it, after which the valve was closed (Figure S1a). Then a needle was inserted into the septum of the Schlenk tube, which was blew with CO_2 for 10 minutes to replace the Ar in it (Figure S1b). Finally, the needle was removed and the Shlenk tube was warmed to RT. The mixture was stirred for 24 h to proceed the CO_2 trapping reaction (Figure S1c).

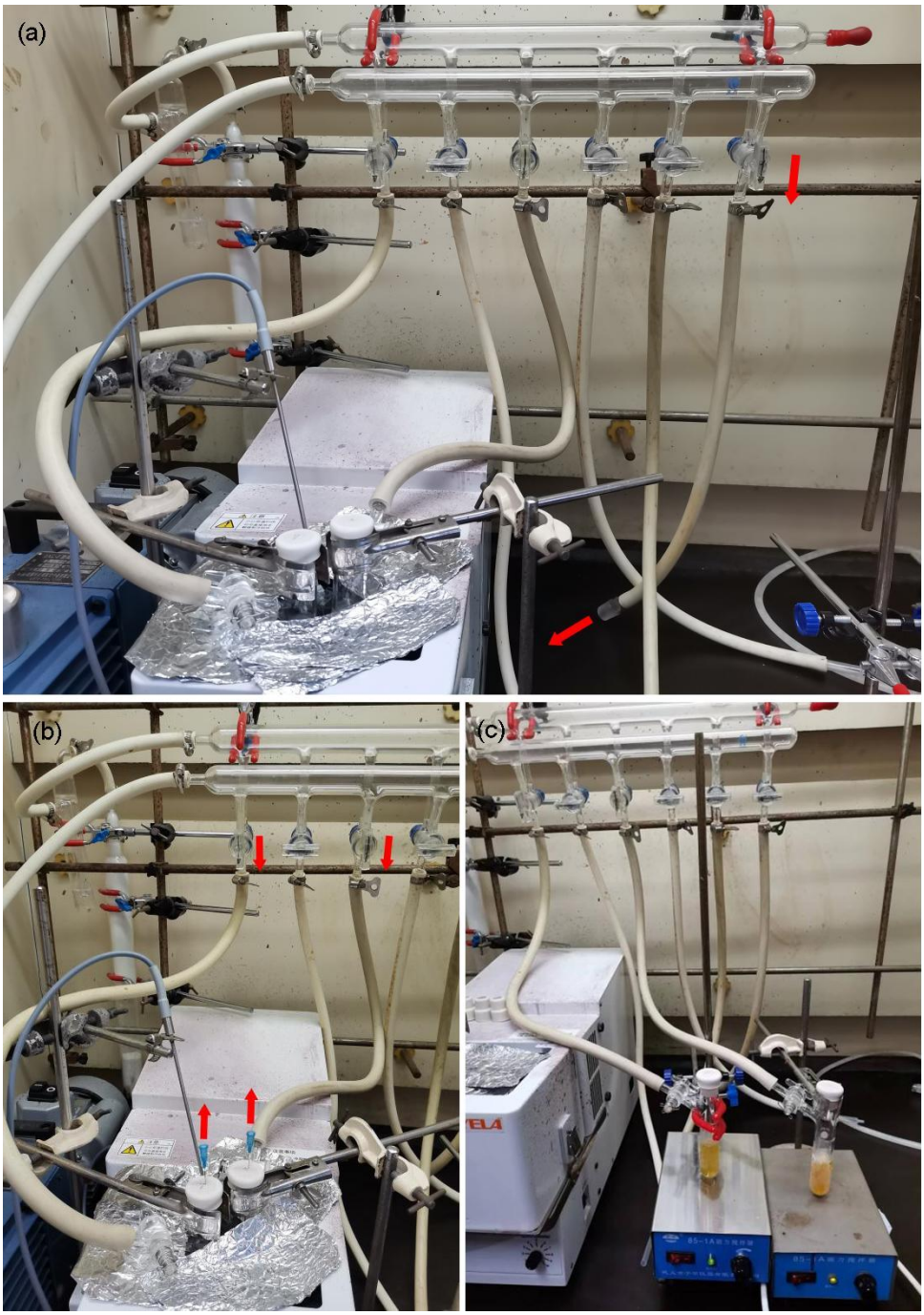


Figure S1. The process of CO_2 inflation.

5.3 Procedure for the ACA-CO_2 trapping reaction in preparative (1.0 g) scale

To a flame-dried two-necked flask (250 ml) equipped with septum and magnetic stirring bar was added CuBr·SMe_2 (72.79 mg, 0.355 mmol, 5 mol%) and ligand **L1** (272.12 mg, 0.426 mmol, 6 mol%). The tube was evacuated and filled with Ar for three times, after which substrate **1a** (1.13 mL, 7.1 mmol, 1.0 equiv.) was added. Dry CH_2Cl_2 (70 mL) was added, and this mixture was stirred for 20 min at RT. Then the mixture was cooled down to −40 °C, followed by addition of Me_3SiOTf (2.57 mL, 14.2 mmol, 2.0 equiv.). After 20 min., MeMgBr

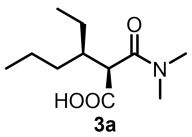
(14.2 mmol, 3.0 M in Et_2O, 2.0 equiv.) was added with syringe pump in 20 min. After stirring the mixutre at −40 °C for 2 h, 70 mL dry CH_2Cl_2 was added again to dilute the mixture, and CO_2 (1 atm) was inflated into the reaction system. Then the reaction mixture was warmed to RT and stirred for 24 h. The resulting reaction mixture was quenched with HCl (35 mL, 1.0 M) and extracted with MTBE (140 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on a rotary evaporator. The crude was purified by flash chromatography on the silica gel (SiO_2, CH_2Cl_2:CH_3OH = 10:1). Then the product was redissolved in MTBE (35 mL) and transferred to a separation funnel, which was extracted with saturated $NaHCO_3$ aqueous solution (35 mL × 3). The combined aqueous phase was acidified with HCl aqueous solution (35 mL, 12.0 M), and extracted with MTBE (140 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on rotary evaporator to afford the pure product **3a**.

5.4 General procedure for the synthesis of racemic ACA products

To a flame-dried Schlenk tube equipped with septum and magnetic stirring bar was added CuBr·SMe_2 (0.025 mmol, 5 mol%), racemic ligand **L1** (0.030 mmol, 6 mol%) and the substrate (0.5 mmol, 1.0 equiv., if solid). The tube was evacuated and filled with Ar for three times, after which the substrate (0.5 mmol, 1.0 equiv., if liquid) was added using a microsyringe. Dry tetrahydrofuran (THF, 5 mL) was added, and this mixture was stirred for 20 min at RT. Then the mixture was cooled down (see the details per substrate), followed by addition of Me_3SiOTf (1.0 mmol, 2.0 equiv.). After 20 min., RMgBr (1.0 mmol, 2.0 equiv.) was added by hand in about 1 min. After stirring for 16 h, the reaction was quenched with saturated aqueous NH_4Cl solution and extracted with MTBE (20 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on a rotary evaporator. The crude was purified by flash chromatography on the silica gel.

5.5 Specific experimental details and product characterization

(2*S*,3*R*)-*N*,*N*-Dimethyl-2-carboxyl-3-ethyl-hexanamide (3a)



3a

The ACA reaction was performed with **1a** (0.5 mmol, 1.0 equiv.), CuBr·SMe_2 (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), EtMgBr (1.0 mmol, 3.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −40 °C for 2 h, followed by trapping of CO_2. Product **3a** was obtained as a colorless oil [66% yield, er 99:1, dr 54:46].

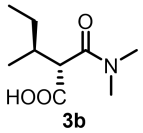
^{1}H NMR (400 MHz, DMSO-d_6): δ 3.53 (minor) and 3.52 (major) (d, J = 9.1 Hz, 1H), 3.03 (s, 3H), 2.83 (minor) and 2.83 (major) (s, 3H), 2.04-1.93 (m, 1H), 1.50-1.14 (m, 6H), 0.89-0.73 (m, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.75, 167.91 (minor) and 167.88 (major), 51.60, 38.24 (major) and 38.16 (minor), 37.20 (minor) and 37.18 (major), 35.38, 31.94 (major) and 31.85 (minor), 22.57 (major) and 22.51 (minor), 19.28 (minor) and 19.15 (major), 14.45 (major) and 14.39 (minor), 10.52 (major) and 10.31 (minor).

HRMS (ESI+, m/Z): calcd. for $C_{11}H_{22}NO_3^+$ $[M+H]^+$: 216.1594, found: 216.1590.

HPLC: Chiracel-OBH, *n*-hexane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 207 nm. Retention time (min): 10.0 (minor) and 10.7 (major).

(2*R*,3*S*)-*N*,*N*-Dimethyl-2-carboxyl-3-methyl-pentanamide (3b)



3b

The reaction was performed with **1b** (0.5 mmol, 1.0 equiv.), CuBr·SMe_2 (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), EtMgBr (1.0 mmol, 3.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −40 °C for 2 h, followed by trapping of CO_2. Product **3b** was obtained as a colorless oil [58% yield, er 98:2, dr 64:36].

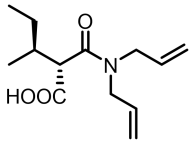
^{1}H NMR (400 MHz, DMSO-d_6): δ 3.44 (minor) and 3.42 (major) (d, J = 9.1 Hz, 1H), 3.04 (minor) and 3.03 (major) (s, 3H), 2.83 (s, 3H), 2.07-1.95 (m, 1H), 1.54-1.41 (minor) and 1.38-1.26 (major) (m, 1H), 1.17-0.97 (m, 1H), 0.92-0.77 (m, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.72 (minor) and 170.62 (major), 168.00 (major) and 167.97 (minor), 53.96 (major) and 53.85 (minor), 37.35 (minor) and 37.23 (major), 35.34 (major) and 35.33 (minor), 34.47 (minor) and 34.40 (major), 26.43, 16.35 (major) and 16.20 (minor), 11.34 (major) and 11.29 (minor).

HRMS (ESI+, m/Z): calcd. for $C_9H_{18}NO_3^+$ $[M+H]^+$: 188.1281, found: 188.1280.

HPLC: Chiracel-OBH, *n*-hexane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 207 nm. Retention time (min): 10.2 (major) and 11.5 (minor).

(2*R*,3*S*)-*N*,*N*-Diallyl-2-carboxyl-3-methyl-pentanamide (3c)



3c

The reaction was performed with **1c** (0.5 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), EtMgBr (1.0 mmol, 3.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −20 °C for 2 h, followed by trapping of CO_2. Product **3c** was obtained as a colorless oil [62% yield, er 82:18, dr 65:35].

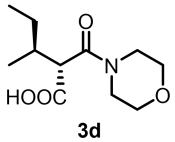
^{1}H NMR (400 MHz, DMSO-d_6): δ 5.89-5.76 (m, 1H), 5.76-5.63 (m, 1H), 5.22-5.04 (m, 4H), 4.17-4.05 (m, 1H), 4.04-3.94 (m, 1H), 3.93-3.84 (m, 1H), 3.80-3.70 (m, 1H), 3.33 (minor) and 3.31 (major) (d, J = 9.4 Hz, 1H), 2.14-2.00 (m, 1H), 1.52-1.40 (minor) and 1.40-1.29 (major) (m, 1H), 1.17-1.06 (minor) and 1.06-0.93 (major) (m, 1H), 0.92-0.75 (m, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.60 (minor) and 170.57 (major), 167.71 (minor) and 167.69 (major), 133.77 (minor) and 133.72 (major), 133.31, 116.66 (major) and 116.62 (minor), 116.47, 54.45 (major) and 54.10 (minor), 49.29 (minor) and 49.17 (major), 47.53 (minor) and 47.46 (major), 34.51 (major) and 34.39 (minor), 26.52 (major) and 26.31 (minor), 16.23 (minor) and 16.19 (major), 11.39 (major) and 11.05 (minor).

HRMS (ESI+, m/Z): calcd. for $C_{13}H_{22}NO_3^+$ $[M+H]^+$: 240.1594, found: 240.1589.

HPLC: Chiracel-ASH, *n*-hexane/*i*-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 13.0 (major) and 13.6 (minor).

(2*R*,3*S*)-3-Methyl-2-(4-morpholinylcarbonyl)-pentanoic acid (3d)



3d

The reaction was performed with **1d** (0.5 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), EtMgBr (1.0 mmol, 3.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −40 °C for 2 h, followed by trapping of CO_2. Product **3d** was obtained as a white solid [50% yield, er 86:14, dr 72:28].

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.62-3.44 (m, 9H), 2.11-1.98 (m, 1H), 1.53-1.41 (minor)

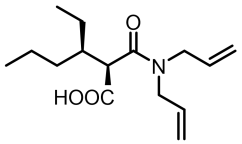
and 1.41-1.28 (major) (m, 1H), 1.17-1.00 (m, 1H), 0.94-0.77 (m, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.70 (minor) and 170.60 (major), 166.68, 66.22, 53.48 (major) and 53.39 (minor), 46.19 (minor) and 46.10 (major), 42.09, 34.31 (minor) and 34.18 (major), 26.47 (major) and 26.37 (minor), 16.28, 11.33.

HRMS (ESI+, m/Z): calcd. for $C_{11}H_{20}NO_4^+$ $[M+H]^+$: 230.1387, found: 230.1386.

HPLC: Chiracel-OBH, *n*-hexane/*i*-PrOH 95:5, 0.5 mL/min, 40 °C, detection at 207 nm. Retention time (min): 16.8 (minor) and 17.6 (major).

(2*S*,3*R*)-*N*,*N*-Diallyl-2-carboxyl-3-ethyl-hexanamide (3e)



3e

The reaction was performed with **1e** (0.5 mmol, 1.0 equiv.), CuBr·SMe_2 (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), EtMgBr (1.0 mmol, 3.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −40 °C for 2 h, followed by trapping of CO_2. Product **3e** was obtained as a colorless oil [55% yield, er 88:12, dr 57:43].

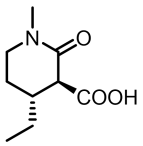
^{1}H NMR (400 MHz, DMSO-d_6): δ 5.88-5.76 (m, 1H), 5.75-5.63 (m, 1H), 5.23-5.04 (m, 4H), 4.15-4.05 (m, 1H), 4.04-3.96 (m, 1H), 3.91-3.81 (m, 1H), 3.80-3.70 (m, 1H), 3.44 (major) and 3.43 (minor) (d, J = 9.3 Hz, 1H), 2.13-2.02 (m, 1H), 1.51-1.10 (m, 6H), 0.88-0.74 (m, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.73 (minor) and 170.68 (major), 167.65 (major) and 167.61 (minor), 133.71 (major) and 133.68 (minor), 133.29, 116.61 (minor) and 116.56 (major), 116.41, 52.04 (minor) and 51.93 (major), 49.23 (major) and 49.18 (minor), 47.55 (major) and 47.52 (minor), 38.43 (minor) and 38.11 (major), 31.85 (major) and 31.72 (minor), 22.73 (minor) and 22.27 (major), 19.27 (major) and 18.83 (minor), 14.39 (minor) and 14.20 (major), 10.72 (minor) and 10.00 (major).

HRMS (ESI+, m/Z): calcd. for $C_{15}H_{26}NO_3^+$ $[M+H]^+$: 268.1907, found: 268.1901.

HPLC: Chiracel-ADH, *n*-hexane/*i*-PrOH 99.2:0.8, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 16.6 (major) and 18.5 (minor).

(3*S*,4*R*)-3-Carboxyl-4-ethyl-1-methylpiperidin-2-one (3f)



3f

The reaction was performed with **1f** (0.5 mmol, 1.0 equiv.), CuBr·SMe_2 (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), EtMgBr (1.0 mmol, 3.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −50 °C for 16 h, followed by trapping of CO_2. Product **3f** was obtained as a colorless oil [45% yield, er 94:6, dr 57:43].

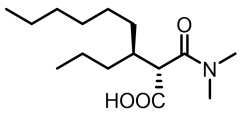
^{1}H NMR (400 MHz, DMSO-d_6): δ 3.31-3.25 (m, 1H), 2.92-2.79 (m, 5H), 1.93-1.85 (m, 1H), 1.51-1.31 (major) and 1.30-1.12 (minor) (m, 4H), 0.87 (t, J = 7.4 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 172.06, 168.30, 48.29, 38.05, 34.20 (major) and 33.66 (minor), 28.08, 27.77, 21.09, 11.01.

HRMS (ESI+, m/Z): calcd. for $C_9H_{16}NO_3^+$ $[M+H]^+$: 186.1125, found: 186.1119.

HPLC: Chiracel-OBH, *n*-hexane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 35.8 (major) and 37.0 (minor).

(2*R*,3*S*)-*N*,*N*-Dimethyl-2-carboxyl-3-propyl-nonanamide (3g)



3g

The reaction was performed with **1a** (0.5 mmol, 1.0 equiv.), CuBr·SMe_2 (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), *n*-HexMgBr (1.0 mmol, 2.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −40 °C for 2 h, followed by trapping of CO_2. Product **3g** was obtained as a colorless oil [57% yield, er 97:3, dr 55:45].

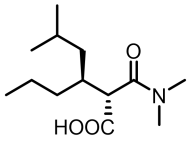
^{1}H NMR (400 MHz, DMSO-d_6): δ 3.52 (d, J = 8.9 Hz, 1H), 3.02 (s, 3H), 2.83 (s, 3H), 2.10-2.01 (m, 1H), 1.41-1.13 (m, 14H), 0.89-0.78 (m, 6H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.65, 167.90, 51.90, 37.12, 37.05 (major) and 37.02 (minor), 35.30, 32.66 (minor) and 32.62 (major), 31.20, 30.13, 29.14 (minor) and 29.06 (major), 25.80 (major) and 25.66 (minor), 22.10 (major) and 22.06 (minor), 19.25 (major) and 19.11 (minor), 14.37 (major) and 14.33 (minor), 13.93.

HRMS (ESI+, m/Z): calcd. for $C_{15}H_{30}NO_3^+$ $[M+H]^+$: 272.2220, found: 272.2201.

HPLC: Chiracel-OBH, *n*-hexane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 207 nm. Retention time (min): 11.2 (major) and 11.6 (minor).

(2*R*,3*S*)-*N*,*N*-Dimethyl-2-carboxyl-5-methy-3-propyl-hexanamide (3h)



3h

The reaction was performed with **1a** (0.5 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (10.28 mg, 0.050 mmol, 10 mol%), ligand (R,S_{Fe})-**L1** (38.44 mg, 0.060 mmol, 12 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), *i*-BuMgBr (1.0 mmol, 2.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −20 °C for 2 h, followed by trapping of CO_2. Product **3h** was obtained as a white solid [58% yield, er 94:6, dr 70:30].

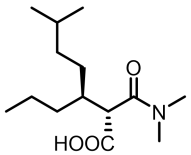
^{1}H NMR (400 MHz, DMSO-d_6): δ 3.53 (d, J = 8.0 Hz, 1H), 3.02 (major) and 3.01 (minor) (s, 3H), 2.83 (s, 3H), 2.18-2.04 (m, 1H), 1.62-1.49 (m, 1H), 1.34-1.12 (m, 6H), 0.88-0.79 (m, 9H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.71, 168.04 (major) and 167.99 (minor), 51.99 (minor) and 51.97 (major), 40.36, 37.13 (minor) and 37.10 (major), 35.31 (minor) and 35.29 (major), 35.13 (major) and 35.07 (minor), 33.44 (major) and 33.02 (minor), 25.12 (major) and 24.88 (minor), 23.66 (major) and 23.56 (minor), 21.95 (minor) and 21.91 (major), 18.94 (major) and 18.72 (minor), 14.47.

HRMS (ESI+, m/Z): calcd. for $C_{13}H_{26}NO_3^+$ $[M+H]^+$: 244.1907, found: 244.1900.

HPLC: Chiracel-ASH, *n*-hexane/*i*-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 206 nm. Retention time (min): 14.8 (major) and 15.9 (minor).

(2*R*,3*S*)-*N*,*N*-Dimethyl-2-carboxyl-6-methy-3-propyl-heptanamide (3i)



3i

The reaction was performed with **1a** (0.5 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), *i*-PentMgBr (1.0 mmol, 2.0 M in MTBE, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −20 °C for 2 h, followed by trapping of CO_2. Product **3i** was obtained as a colorless oil

[55% yield, er 97:3, dr 50:50].

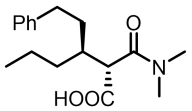
^{1}H NMR (400 MHz, DMSO-d_6): δ 3.53 (d, J = 8.9 Hz, 1H), 3.03 and 3.03 (s, 3H), 2.83 and 2.83 (s, 3H), 2.10-2.00 (m, 1H), 1.51-0.96 (m, 9H), 0.88-0.73 (m, 9H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.66 and 170.63, 167.89, 51.91 and 51.85, 37.16 and 37.14, 37.11 and 37.05, 35.33 and 35.30, 34.99 and 34.82, 32.54, 27.82 and 27.74, 27.68 and 27.65, 22.70 and 22.68, 22.30 and 22.24, 19.22 and 19.11, 14.39 and 14.35.

HRMS (ESI+, m/Z): calcd. for $C_{14}H_{28}NO_3^+$ $[M+H]^+$: 268.2064, found: 268.2057.

HPLC: Chiracel-ODH, *n*-hexane/*i*-PrOH 98:2, 0.5 mL/min, 40 °C, detection at 205 nm. Retention time (min): 10.8 (major) and 11.2 (minor).

(2*R*,3*S*)-*N*,*N*-Dimethyl-2-carboxyl-3-phenylethyl-hexanamide (3j)



3j

The reaction was performed with **1a** (0.5 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), PhEtMgBr (1.0 mmol, 1.4 M in MTBE, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −20 °C for 2 h, followed by trapping of CO_2. Product **3j** was obtained as a white solid [59% yield, er 97:3, dr 53:47].

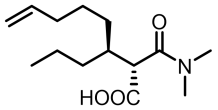
^{1}H NMR (400 MHz, DMSO-d_6): δ 7.30-7.22 (m, 2H), 7.19-7.11 (m, 3H), 3.63 (minor) and 3.62 (major) (d, J = 8.7 Hz, 1H), 3.02 (major) and 3.01 (minor) (s, 3H), 2.84 (major) and 2.83 (minor) (s, 3H), 2.68-2.51 (m, 2H), 2.18-2.06 (m, 1H), 1.77-1.20 (m, 6H), 0.90-0.80 (m, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.65, 167.86 (minor) and 167.83 (major), 142.38 (minor) and 142.31 (major), 128.26, 128.12 (minor) and 128.09 (major), 125.61, 51.78 (major) and 51.75 (minor), 37.13 (major) and 37.08 (minor), 36.92 (major) and 36.80 (minor), 35.33 (major) and 35.31 (minor), 32.65 (minor) and 32.54 (major), 32.43, 32.32 (major) and 32.13 (minor), 19.24 (minor) and 19.07 (major), 14.36 (major) and 14.31 (minor).

HRMS (ESI+, m/Z): calcd. for $C_{17}H_{26}NO_3^+$ $[M+H]^+$: 292.1907, found: 292.1898.

HPLC: Chiracel-ASH, *n*-hexane/*i*-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 205 nm. Retention time (min): 32.0 (major) and 37.6 (minor).

(2*R*,3*S*)-*N*,*N*-Dimethyl-2-carboxyl-3-propyl-oct-7-enamide (3k)



3k

The reaction was performed with **1a** (0.5 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), pent-4-en-1-ylMgBr (1.0 mmol, 1.7 M in MTBE, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −20 °C for 2 h, followed by trapping of CO_2. Product **3k** was obtained as a colorless oil [56% yield, er 97:3, dr 57:43].

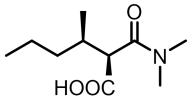
^{1}H NMR (400 MHz, DMSO-d_6): δ 5.84-5.70 (m, 1H), 5.03-4.88 (m, 2H), 3.53 (d, J = 8.8 Hz, 1H), 3.02 (s, 3H), 2.83 (major) and 2.83 (minor) (s, 3H), 2.12-2.02 (m, 1H), 2.02-1.91 (m, 2H), 1.43-1.14 (m, 8H), 0.87-0.77 (m, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.67 (major) and 170.65 (minor), 167.90, 138.66, 114.75 (major) and 114.72 (minor), 51.89, 37.15, 37.04 (major) and 36.99 (minor), 35.33, 33.63 (minor) and 33.54 (major), 32.68, 29.76 (minor) and 29.74 (major), 25.31 (major) and 25.11 (minor), 19.26 (major) and 19.15 (minor), 14.38 (minor) and 14.34 (major).

HRMS (ESI+, m/Z): calcd. for $C_{14}H_{26}NO_3^+$ $[M+H]^+$: 256.1907, found: 256.1902.

HPLC: Chiracel-ASH, *n*-hexane/*i*-PrOH 99:1, 0.5 mL/min, 40 °C, detection at 205 nm. Retention time (min): 17.1 (minor) and 17.9 (major).

(2*S*,3*R*)-*N*,*N*-Dimethyl-2-carboxyl-3-methyl-hexanamide (3l)



3l

The reaction was performed with **1a** (0.5 mmol, 1.0 equiv.), $CuBr{\cdot}SMe_2$ (5.14 mg, 0.025 mmol, 5 mol%), ligand (R,S_{Fe})-**L1** (19.22 mg, 0.030 mmol, 6 mol%), Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.), MeMgBr (1.0 mmol, 3.0 M in Et_2O, 2.0 equiv.) in CH_2Cl_2 (5 mL) at −40 °C for 2 h, followed by trapping of CO_2. Product **3l** was obtained as a white solid [56% yield, er 99:1, dr 62:38].

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.43 (minor) and 3.41 (major) (d, J = 9.0 Hz, 1H), 3.04 (minor) and 3.03 (major) (s, 3H), 2.84 (s, 3H), 2.16-2.04 (m, 1H), 1.44-0.99 (m, 4H), 0.92-0.77 (m, 6H).

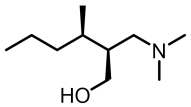
^{13}C NMR (100 MHz, DMSO-d_6): δ 170.62 (minor) and 170.55 (major), 167.96 (major) and 167.95 (minor), 54.25 (major) and 54.12 (minor), 37.29 (minor) and 37.18 (major), 36.01, 35.30 (major) and 35.28 (minor), 32.70 (minor) and 32.59 (major), 19.63 (major) and 19.57 (minor), 16.77 (major) and 16.71 (minor), 14.16 (minor) and 14.10 (major).

HRMS (ESI+, m/Z): calcd. for $C_{10}H_{20}NO_3^+$ $[M+H]^+$: 202.1438, found: 202.1434.

HPLC: Chiracel-OBH, *n*-hexane/*i*-PrOH 90:10, 0.5 mL/min, 40 °C, detection at 207 nm. Retention time (min): 8.8 (minor) and 9.6 (major).

6. Transformation of *α*-carboxyl amide into chiral *γ*-amino alcohol

(2*S*,3*R*)-*N*,*N*-dimethyl-2-hydroxymethyl-3-methyl-1-hexanamine (4l)



4l

To a flame-dried Schlenk tube equipped with septum and magnetic stirring bar was added **3l** (100.64 mg, 0.5 mmol). The tube was evacuated and filled Ar for three times, after which dry THF (5 mL) was added. This mixture was stirred for 20 min at RT, followed by addition of BH_3·THF (1.0 M in THF, 2.0 mmol, 4.0 equiv.). After stirring for 16 h at RT, the solvent was evaporated on rotary evaporator. The crude was purified by flash chromatography on the silica gel (SiO_2, CH_2Cl_2:CH_3OH = 5:1). The product **4l** was obtained as a colorless oil. [68% yield, er 99:1, dr 62:38].

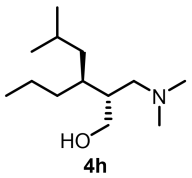
^{1}H NMR (400 MHz, DMSO-d_6): δ 3.49-3.41 (m, 1H), 3.38-3.31 (dd, J = 10.5, 6.6 Hz, 1H), 2.33-2.07 (m, 8H), 1.67-1.52 (m, 2H), 1.38-1.03 (m, 4H), 0.86 (t, J = 7.0 Hz, 3H), 0.78 (major) and 0.77 (minor) (d, J = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 62.65 (minor) and 61.57 (major), 60.44 (major) and 59.03 (minor), 45.59 (minor) and 45.51 (major), 41.64 (major) and 41.56 (minor), 36.00, 31.54 (major) and 31.15 (minor), 20.32 (major) and 20.29 (minor), 15.89 (major) and 15.57 (minor), 14.27 (major) and 14.23 (minor).

HRMS (ESI+, m/Z): calcd. for $C_{10}H_{24}NO^+$ $[M+H]^+$: 174.1852, found: 174.1841.

7. Synthesis of the chiral *γ*-amino alcohol by one-pot method

(2*R*,3*S*)-*N*,*N*-dimethyl-2-hydroxymethyl-5-methyl-3-propyl-1-hexanamine (4h)



4h

To a flame-dried Schlenk tube equipped with septum and magnetic stirring bar was added CuBr·SMe_2 (10.28 mg, 0.050 mmol, 10 mol%) and ligand (R,S_{Fe})-**L1** (38.44 mg, 0.060 mmol, 12 mol%). The tube was evacuated and filled Ar for three times, after which substrate **1a** (0.5 mmol, 1.0 equiv.) was added using a microsyringe. Dry CH_2Cl_2 (5 mL) was added and this mixture was stirred for 20 min at RT. Then the mixture was cooled down to −20 °C, followed by addition of Me_3SiOTf (0.181 mL, 1.0 mmol, 2.0 equiv.). After 20 min., *i*-BuMgBr (1.0 mmol, 2.0 M in Et_2O, 2.0 equiv.) was added by hand in about 1 min. After stirring the mixutre at −20 °C for 2 h, 5 mL dry CH_2Cl_2 was added again to dilute the mixture, and CO_2 (1 atm) was inflated into the reaction system. Then the reaction mixture was warmed to RT and stirred for 24 h. After completion, CO_2 was replaced by Ar again, and BH_3·THF (1.0 M in THF, 2.0 mmol, 4.0 equiv.) was added. After stirring for 16 h at RT, the reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and stirred for 10 min. Then the mixture was extracted with MTBE (20 mL × 3). The combined organic phases were dried over $MgSO_4$, filtered and evaporated on a rotary evaporator. The crude was purified by flash chromatography on the silica gel (SiO_2, CH_2Cl_2 : MeOH=5:1). Then the product was redissolved in MTBE (5 mL) and transferred to a separation funnel, which was extracted with HCl solution (2.0 mL × 3, 1.0 M). The combined aqueous phase was acidified with saturated aqueous $NaHCO_3$ (10 mL), and extracted with MTBE (20.0 mL × 3). The combined organic phase was dried over $MgSO_4$, filtered and evaporated on rotary evaporator to afford the pure product **4h** as a colorless oil. [34% yield, er 94:6, dr 70:30].

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.42-3.31 (m, 2H), 2.25-1.93 (m, 8H), 1.72-1.49 (m, 3H), 1.31-1.18 (m, 4H), 1.12-1.03 (m, 8H), 0.88-0.80 (m, 9H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 62.19 (minor) and 62.14 (major), 59.95 (minor) and 59.61 (major), 45.69 (minor) and 45.65 (major), 40.04, 33.95 (minor) and 33.92 (major), 32.86 (major) and 32.84 (minor), 25.35, 22.98 (minor) and 22.92 (major), 22.71 (major) and 22.68 (minor), 20.54 (major) and 20.42 (minor), 14.32 (major) and 14.28 (minor).

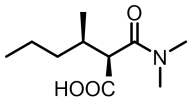
HRMS (ESI+, m/Z): calcd. for $C_{10}H_{24}NO^+$ $[M+H]^+$: 216.2322, found: 216.2317.

8. Determination of absolute configuration

The absolute configuration of **3l** was determined by X-ray single crystallography of the major diastereomer **3la** separated by a Waters Prep SFC 80 preparative system equiped with a Chirapak-IG/SFC column (see Figure S2). The absolute configurations of other compounds were assigned by analogy. As the er of **3l** is 99:1, we omitted the two minor isomers of 1% and only collected the two major isomers of 99% (**3la** and **3lb**). For the NMR spectra of **3la** and **3lb**, as well as the comparision of them with **3l**, see Figures S16~S18.

Prep SFC：Chiralpak-IG/SFC, CO_2/MeOH (0.1% V/V of 7M NH_3 in MeOH was added) = 85:15, 70 mL/min., 40 °C, detection at 207 nm.

Major diastereomer: **(2*S*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-hexanamide**

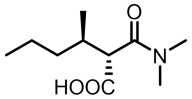


3la

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.42 (d, J = 9.0 Hz, 1H), 3.03 (s, 3H), 2.84 (s, 3H), 2.16-2.04 (m, 1H), 1.40-1.11 (m, 3H), 1.09-0.99 (m, 1H), 0.89 (d, J = 6.7 Hz, 3H), 0.82 (t, J = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.50, 167.93, 54.21, 37.14, 35.98, 35.27, 32.55, 19.59, 16.74, 14.07.

Minor diastereomer: **(2*R*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-hexanamide**



3lb

^{1}H NMR (400 MHz, DMSO-d_6): δ 3.43 (d, J = 9.3 Hz, 1H), 3.04 (s, 3H), 2.84 (s, 3H), 2.16-2.04 (m, 1H), 1.44-1.31 (m, 2H), 1.26-1.04 (m, 2H), 0.85 (t, J = 6.9 Hz, 3H), 0.80 (d, J = 6.7 Hz, 3H).

^{13}C NMR (100 MHz, DMSO-d_6): δ 170.57, 167.91, 54.09, 37.25, 35.97, 35.24, 32.67, 19.53, 16.68, 14.12.

9. X-ray crystallographic analysis

3la was dissolved in THF and the resulting solution was filtered. The filtrate was left for slow evaporation at room temperature in air. Colorless needleshaped crystals was formed when the solvent was completely evaporated.

A single crystal of compound **3la** was mounted on top of a cryoloop and transferred into the cold nitrogen stream (100 K) of a Bruker-AXS D8 Venture diffractometer. Data collection and reduction was done using the Bruker software suite APEX3.[2] The final unit cell was obtained from the xyz centroids of 6259 reflections after integration. A multiscan absorption correction was applied, based on the intensities of symmetry-related reflections measured at different angular settings (SADABS). The structures were solved by direct methods using SHELXT[3] and refinement of the structure was performed using SHLELXL.[4] The hydrogen atoms were generated by geometrical considerations, constrained to idealized geometries and allowed to ride on their carrier atoms with an isotropic displacement parameter related to the equivalent displacement parameter of their carrier atoms. The absolute configuration of the model was chosen based on anomalous dispersion. Refinement of the Flack x parameter converged -0.020(16).

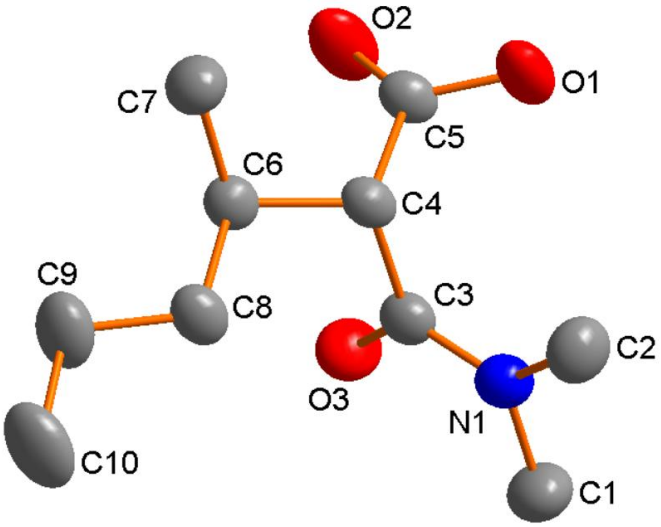


Figure S2. Molecular structure of compound **3la**, showing 50% probability ellipsoids. Hydrogen atoms are omitted for clarity.

Table S2. Crystallographic data for compound **3la**

Chem. formula	$C_{10}H_{19}NO_3$
M_r	201.26
Cryst syst.	Monoclinic
Color, habit	colorless, needle
Size (mm)	0.12 × 0.10 × 0.09
Space group	P 1 21 1
a (Å)	5.4153(5)
b (Å)	11.2753(12)
c (Å)	9.4479(10)
α, deg	90
β, deg	98.633(7)
γ, deg	90
V (Å^3)	570.34(10)
Z	2
ρ_{calc}, g·cm^{-3}	1.172
μ(Mo Kα), cm^{-1}	0.700
F(000)	220
Temp (K)	193.00
θ range (deg)	6.152 – 79.660
Data collected (h,k,l)	-6:6, -14:13, -11:11
No. of rflns collected	9916
No. of indpndt reflns	2324
Observed reflns	2124 ($F_o \geq 2(F_o)$)
R(F) (%)	4.53
wR(F^2) (%)	12.39
GooF	1.065
Weighting a,b	0.0701, 0.0614
Params refined	132
Restraints	1
Min, max resid dens	-0.158, 0.218
Flack x	-0.02(16)

10. Mechanistic studies

10.1 Study on the interaction between Me_3SiOTf and CO_2

To a flame-dried Schlenk tube equipped with septum and magnetic stirring bar was added CH_2Cl_2 (2 mL) and Me_3SiOTf (0.036 mL, 0.2 mmol) under CO_2 atmosphere. After stirring for 2 h, the mixture was transferred into a NMR tube under Ar protection. 0.2 mL $CDCl_3$ was added to the NMR tube and ^1H NMR was measure immediately. For comparision, the same solution under Ar atmosphere was also prepared for the ^1H NMR measurement.

As shown in Figure S3, we initially assumed that CO_2 can be activated by Me_3SiOTf through coordination with the Me_3Si^+ to form a silyl complex, resulting in the shift of the ^1H NMR peak of trimethyl silyl. However, no shift of the peak was observed, indicating that activation of CO_2 by Me_3SiOTf can be excluded.

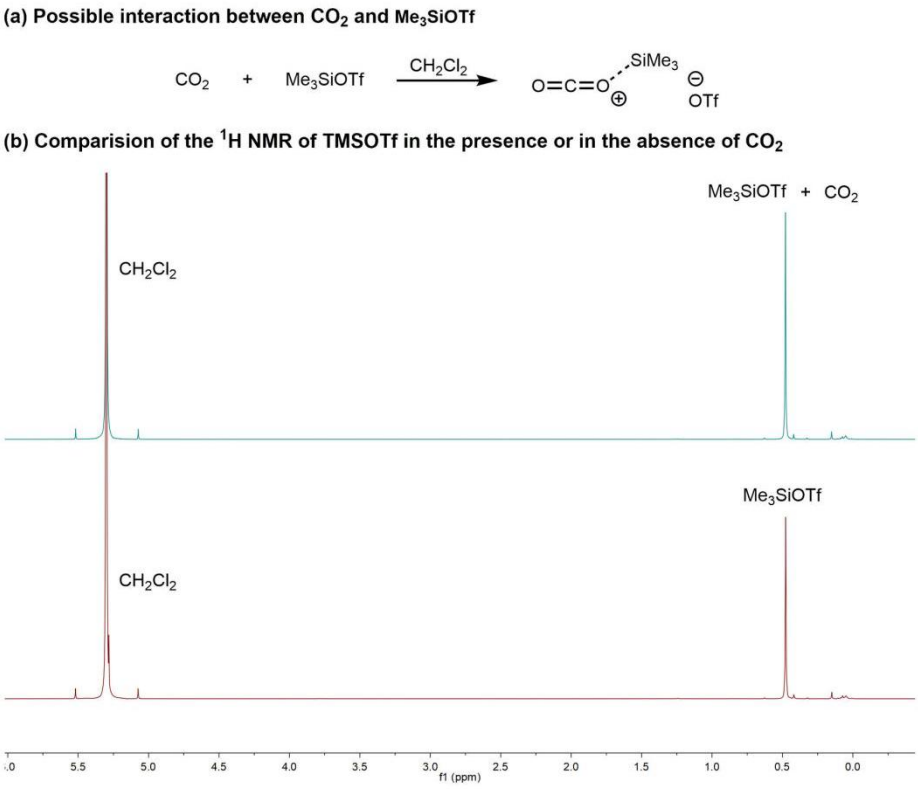
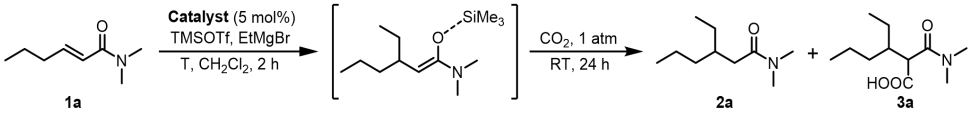


Figure S3. ^1H NMR study on the interaction between Me_3SiOTf and CO_2.

10.2 Study on the function of the copper catalyst

Table S3. Comparision of the ACA-CO_2 trapping reactions with different copper catalyst[a]



Entry	T [°C]	Catalyst	Me_3SiOTf	EtMgBr	**1a**:**2a**:**3a**[b]	er[c]	dr[d]
1	−40	**L1**/CuBr	2.0 equiv.	2.0 equiv.	0:23:77	99:1	56:44
2	−20	–	3.0 equiv.	3.0 equiv.	74:26:0	50:50	–
3	−40	rac. **L1**/CuBr	2.0 equiv.	2.0 equiv.	0:23:77	50:50	56:44

[a]Reaction conditions: 0.5 mmol **1a** in 5 mL CH_2Cl_2, 5 mol% catalyst, 2.0~3.0 equiv. of Me_3SiOTf and 2.0~3.0 equiv. of EtMgBr was used at −40~−20 °C for 2 h, then 5 mL CH_2Cl_2 was added and stirred for 24 h at RT under 1 atm CO_2 atmosphere. [b]The ratio was determined by ^{1}H NMR of reaction crude. [c]Enantiomeric ratio was determined by chiral HPLC analysis of the CA product isolated from the trapping reaction mixture. [d]The ratio was determined by ^{1}H NMR and ^{13}C NMR of the trapping product.

11. NMR spectra

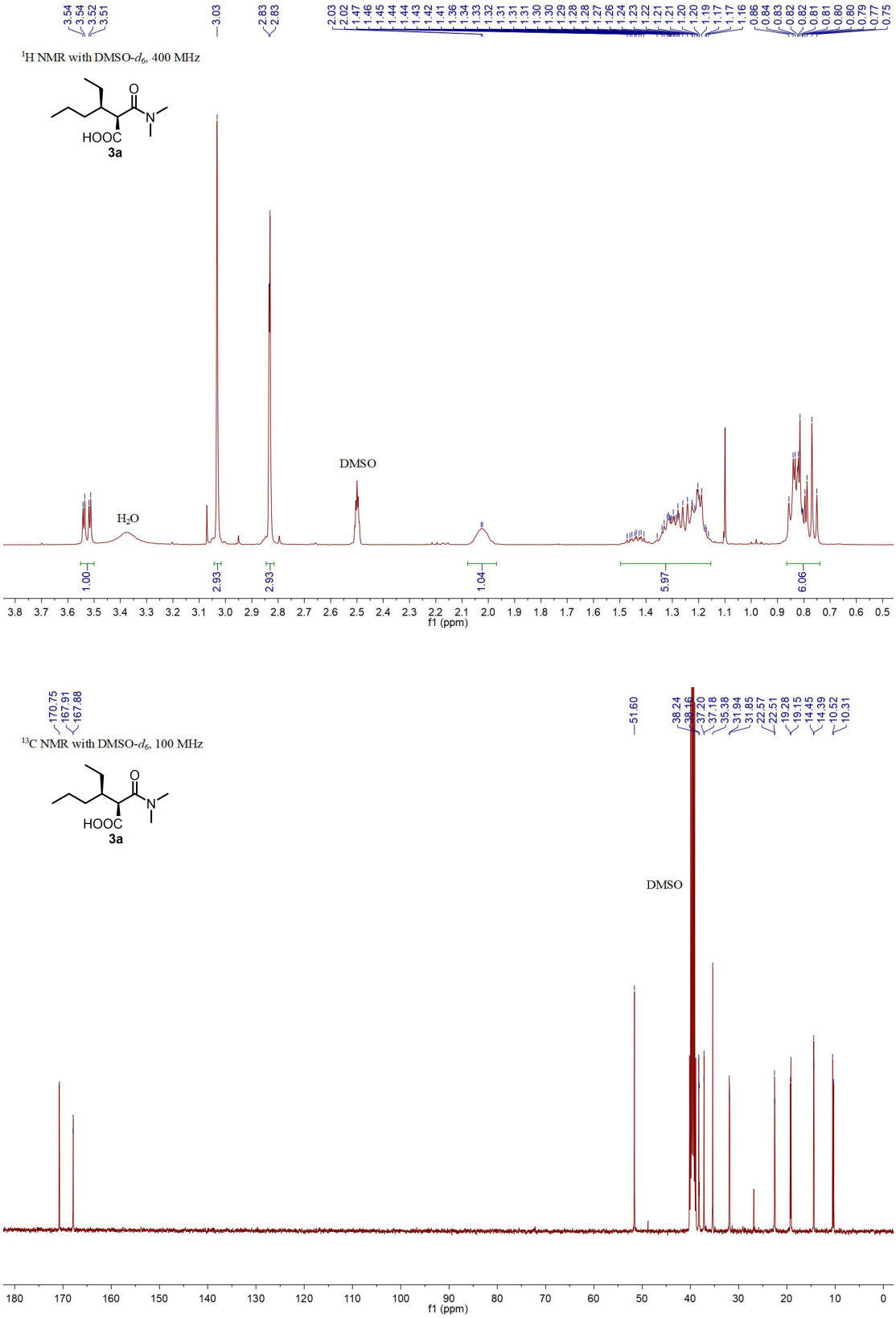


Figure S4. NMR spectra of (2*S*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-ethyl-hexanamide (**3a**)

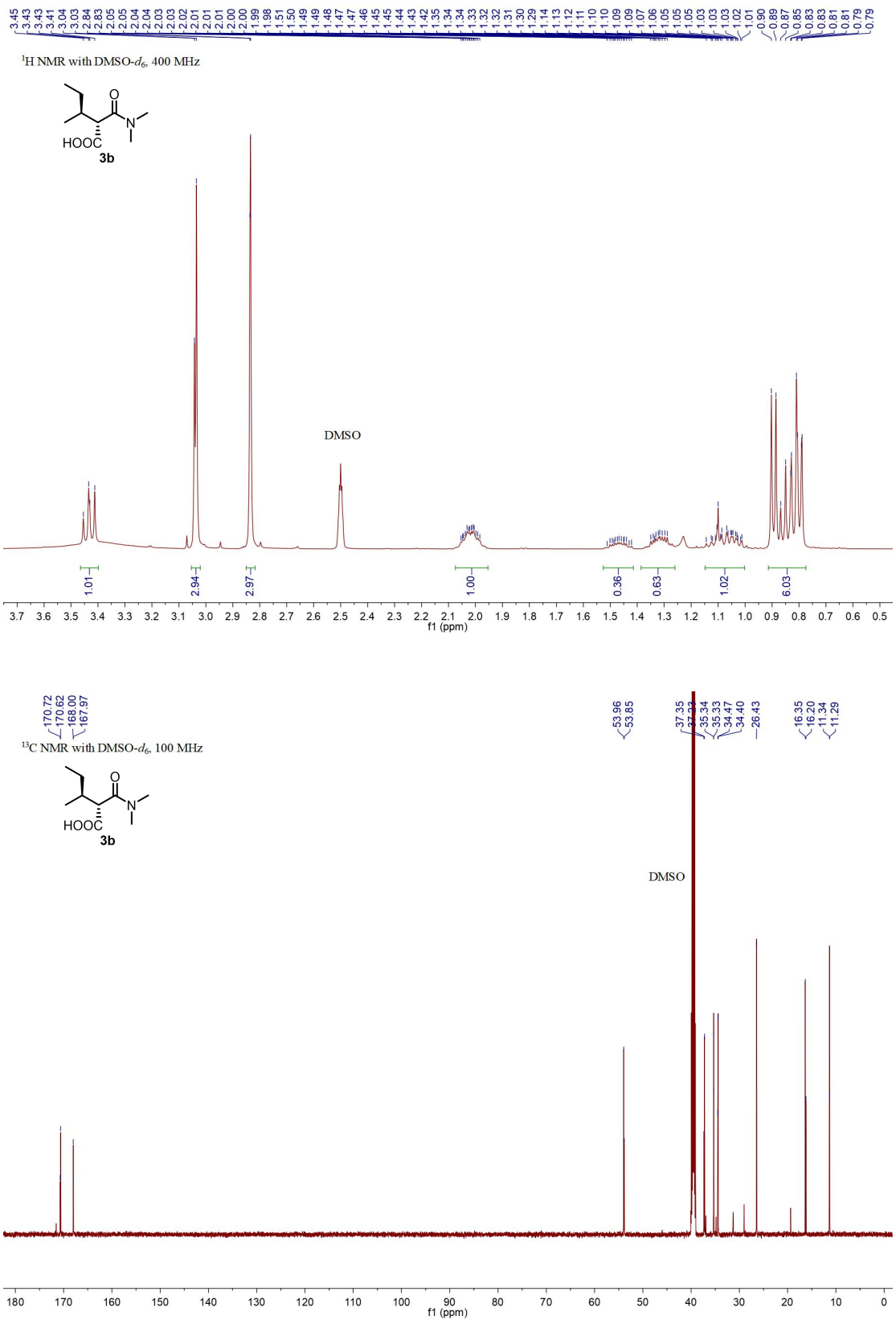


Figure S5. NMR spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-pentanamide (**3b**)

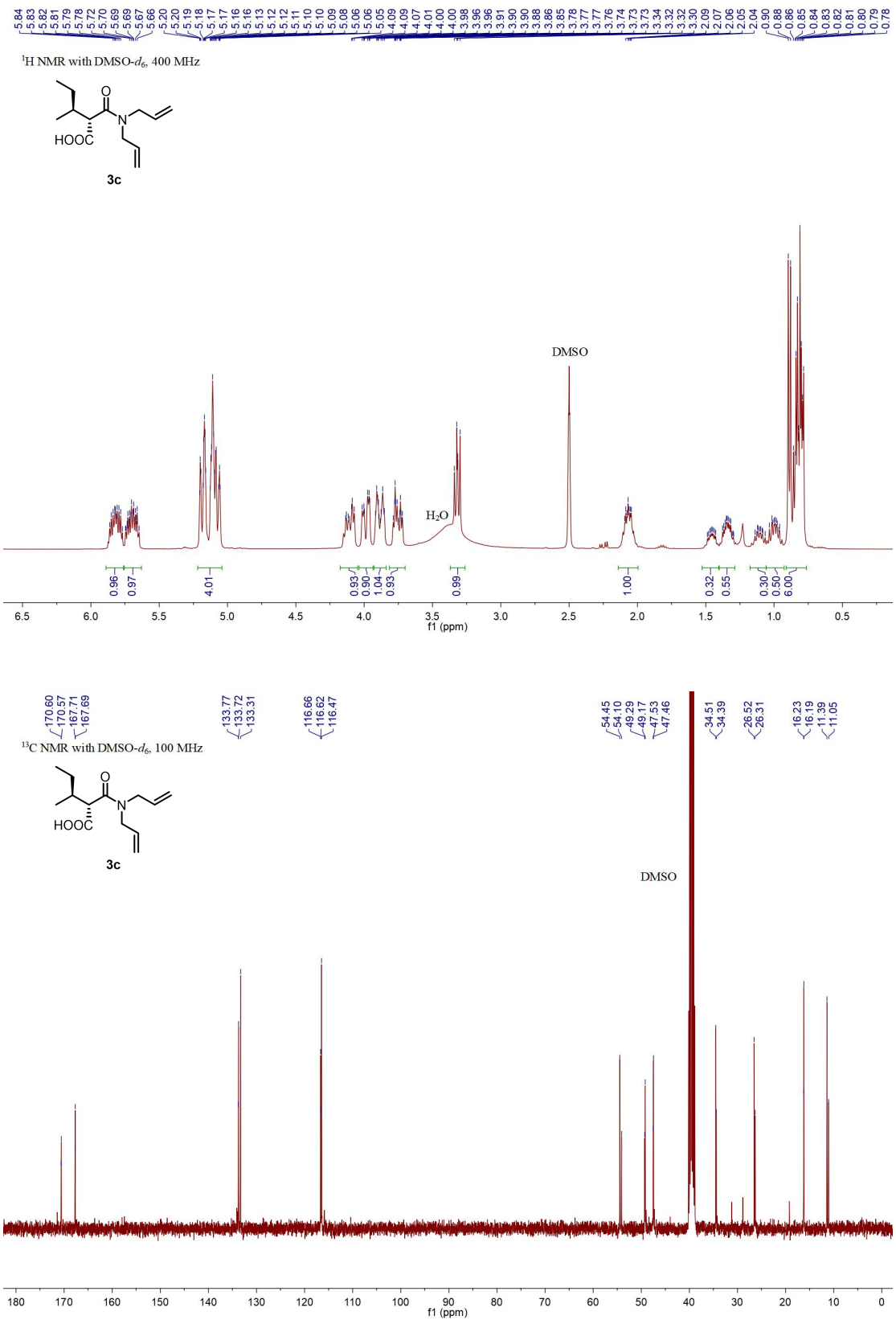


Figure S6. NMR spectra of (2*R*,3*S*)-*N*,*N*-diallyl-2-carboxyl-3-methyl-pentanamide (**3c**)

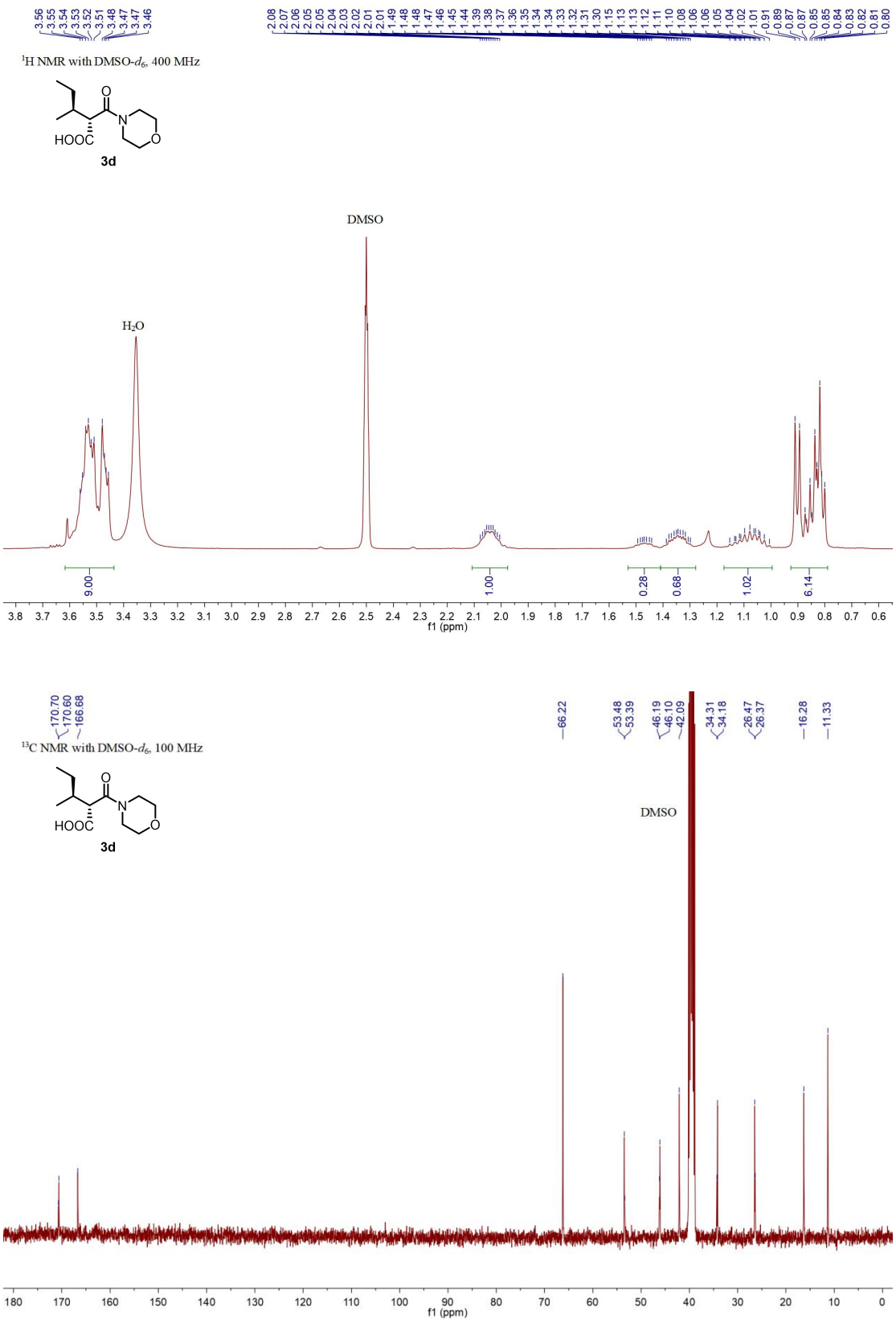


Figure S7. NMR spectra of (2*R*,3*S*)-3-methyl-2-(4-morpholinylcarbonyl)-pentanoic acid (**3d**)

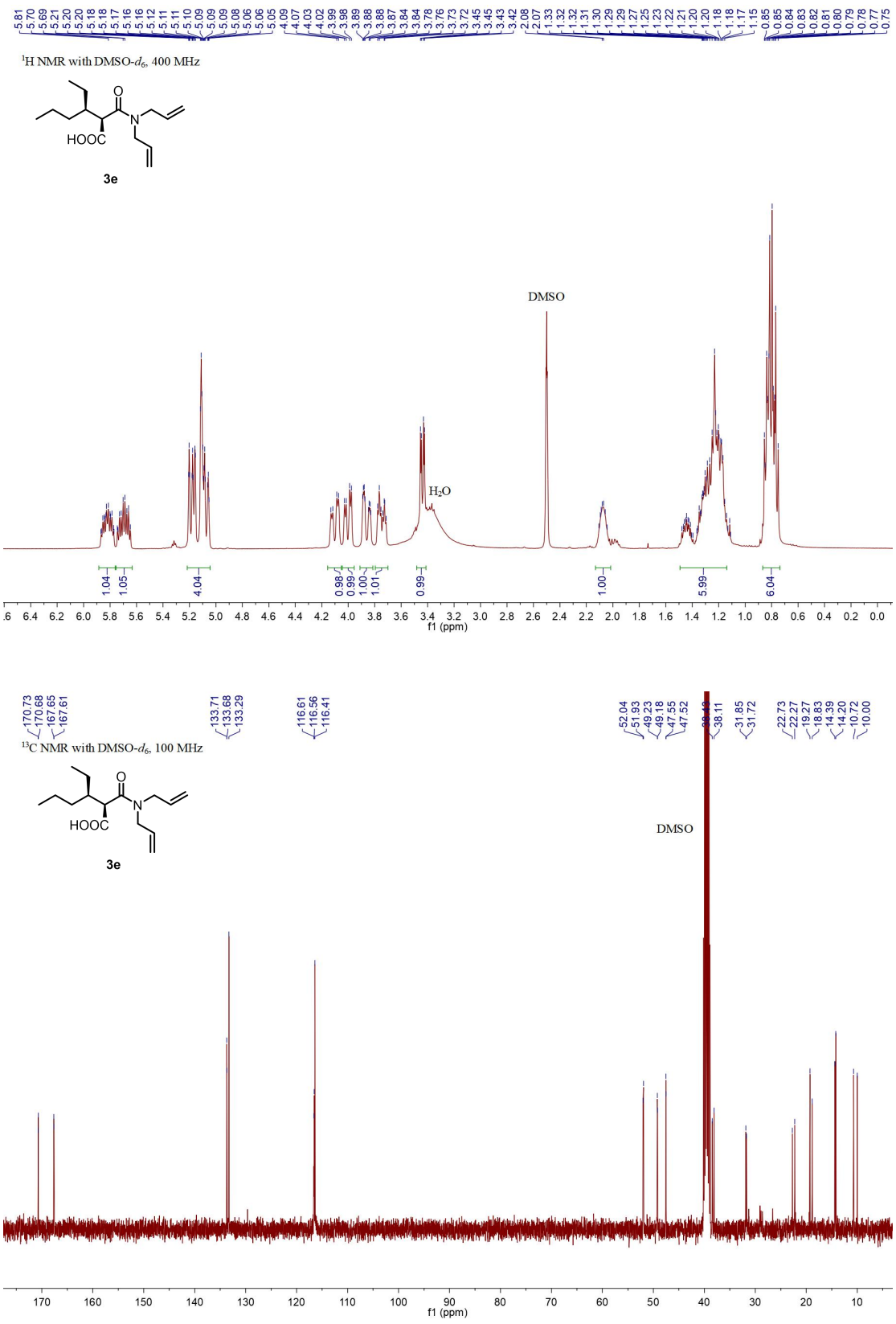


Figure S8. NMR spectra of (2*S*,3*R*)-*N*,*N*-diallyl-2-carboxyl-3-ethyl-hexanamide (**3e**)

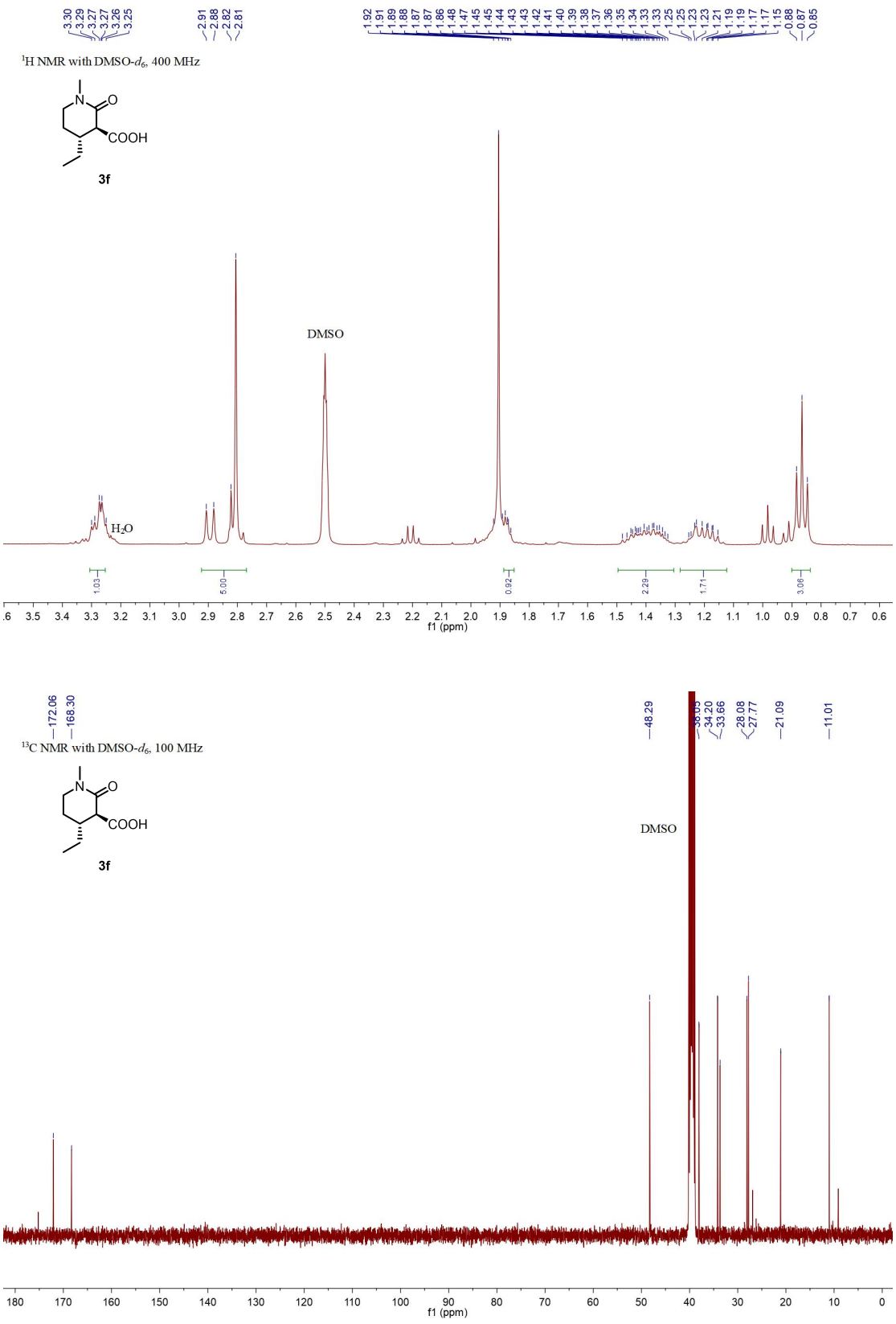


Figure S9. NMR spectra of (3*S*,4*R*)-3-carboxyl-4-ethyl-1-methylpiperidin-2-one (**3f**)

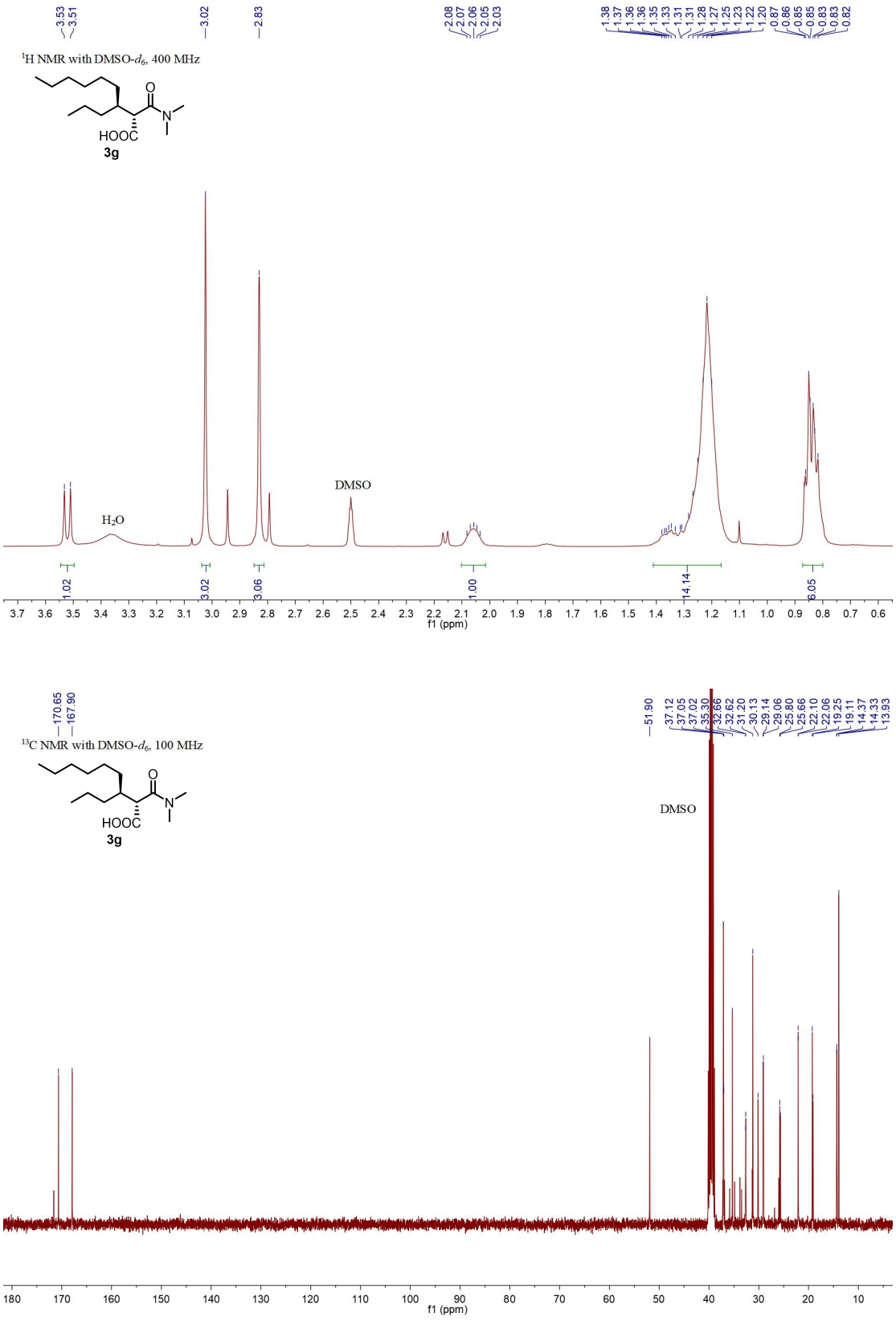


Figure S10. NMR spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-propyl-nonanamide (**3g**)

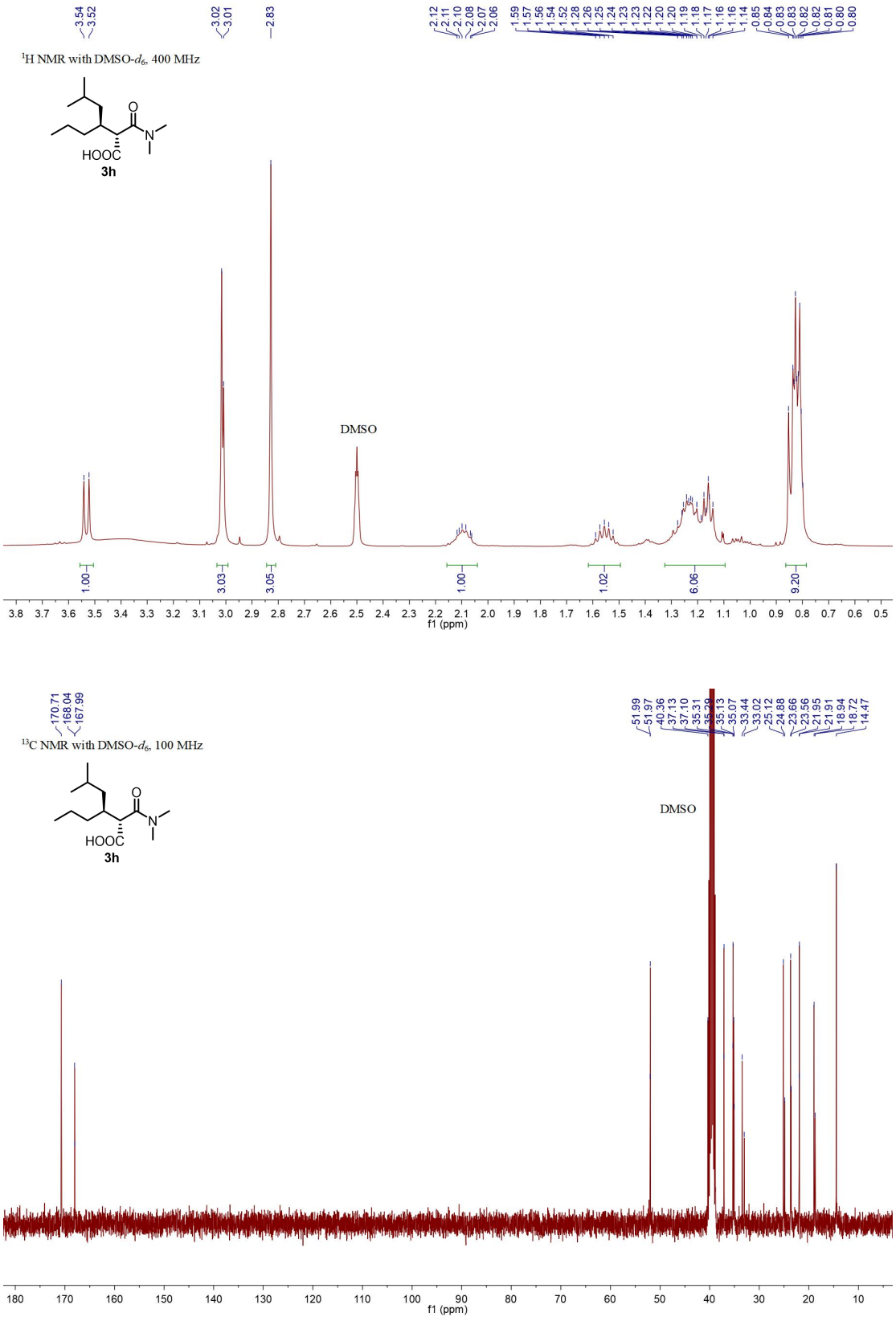


Figure S11. NMR spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-5-methy-3-propyl-hexanamide (**3h**)

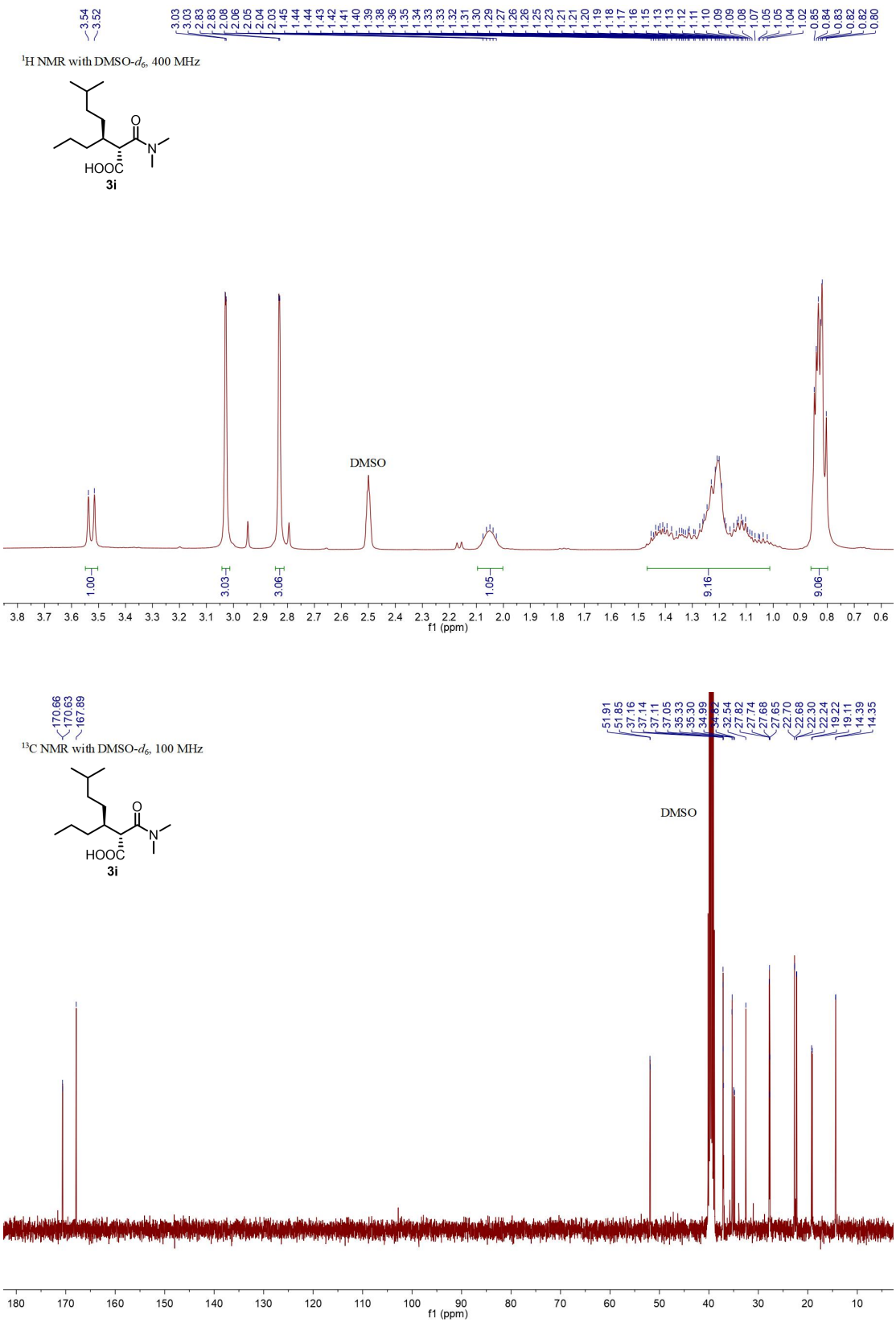


Figure S12. NMR spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-6-methy-3-propyl-heptanamide (**3i**)

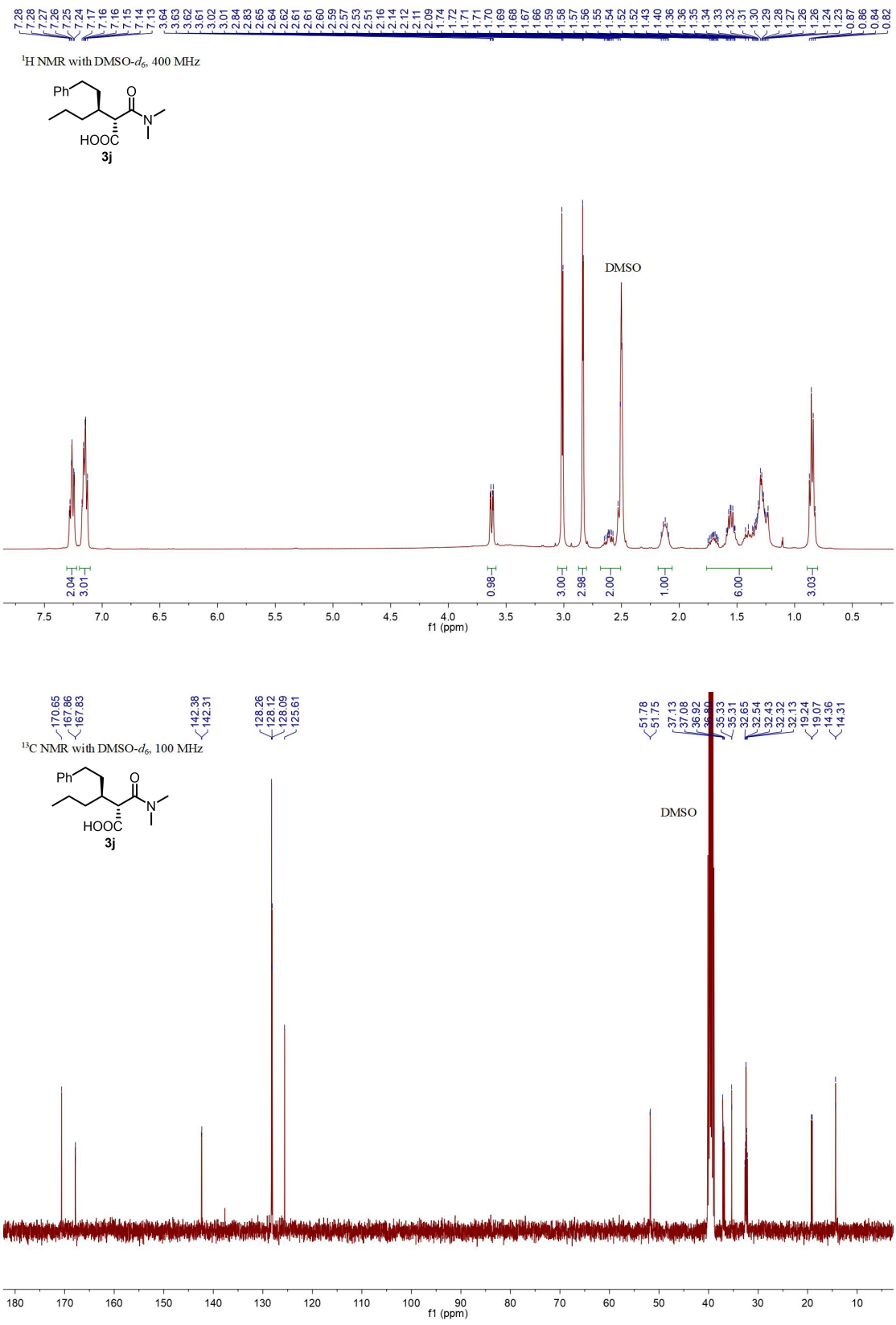


Figure S13. NMR spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-phenylethyl-hexanamide (**3j**)

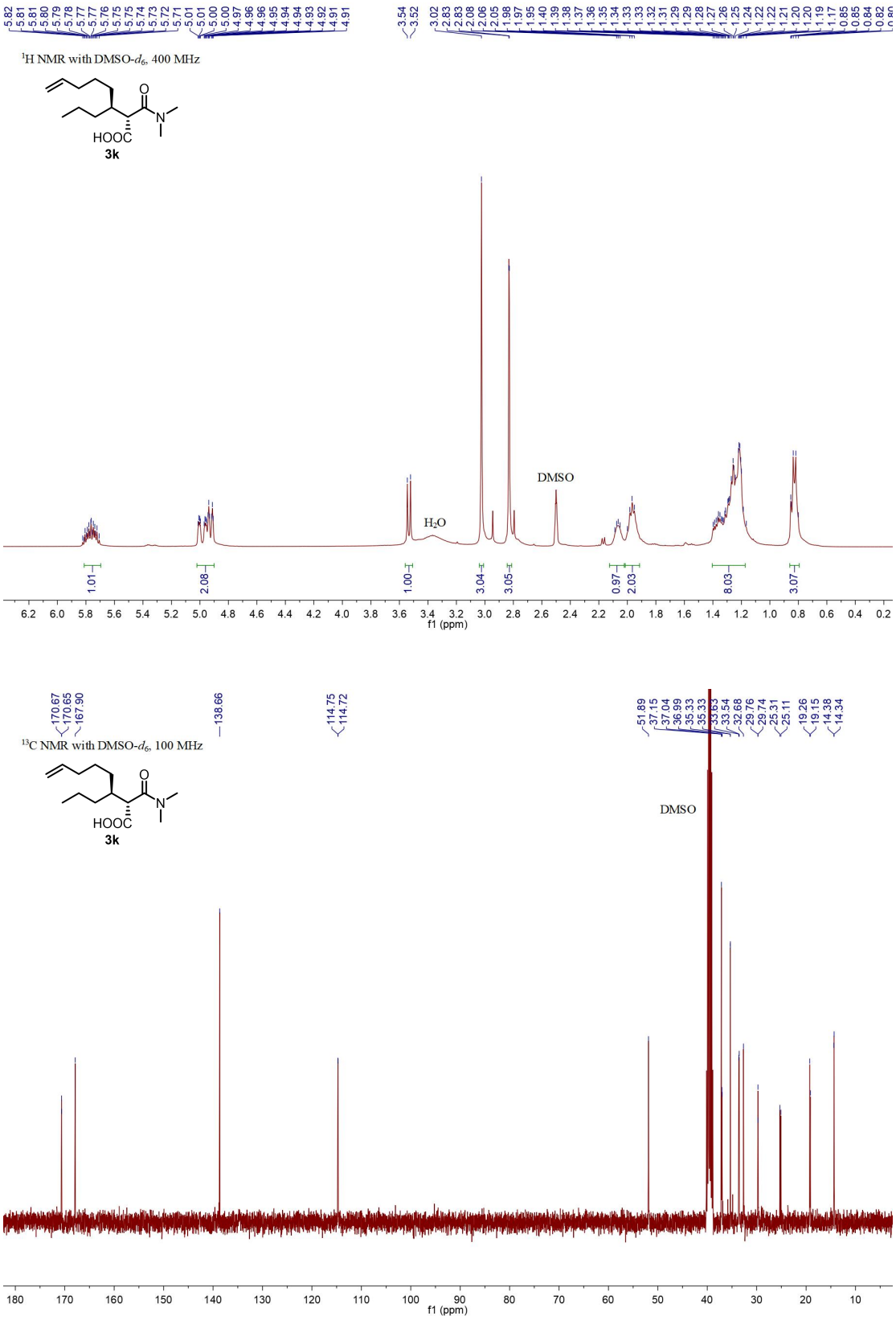


Figure S14. NMR spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-propyl-oct-7-enamide (**3k**)

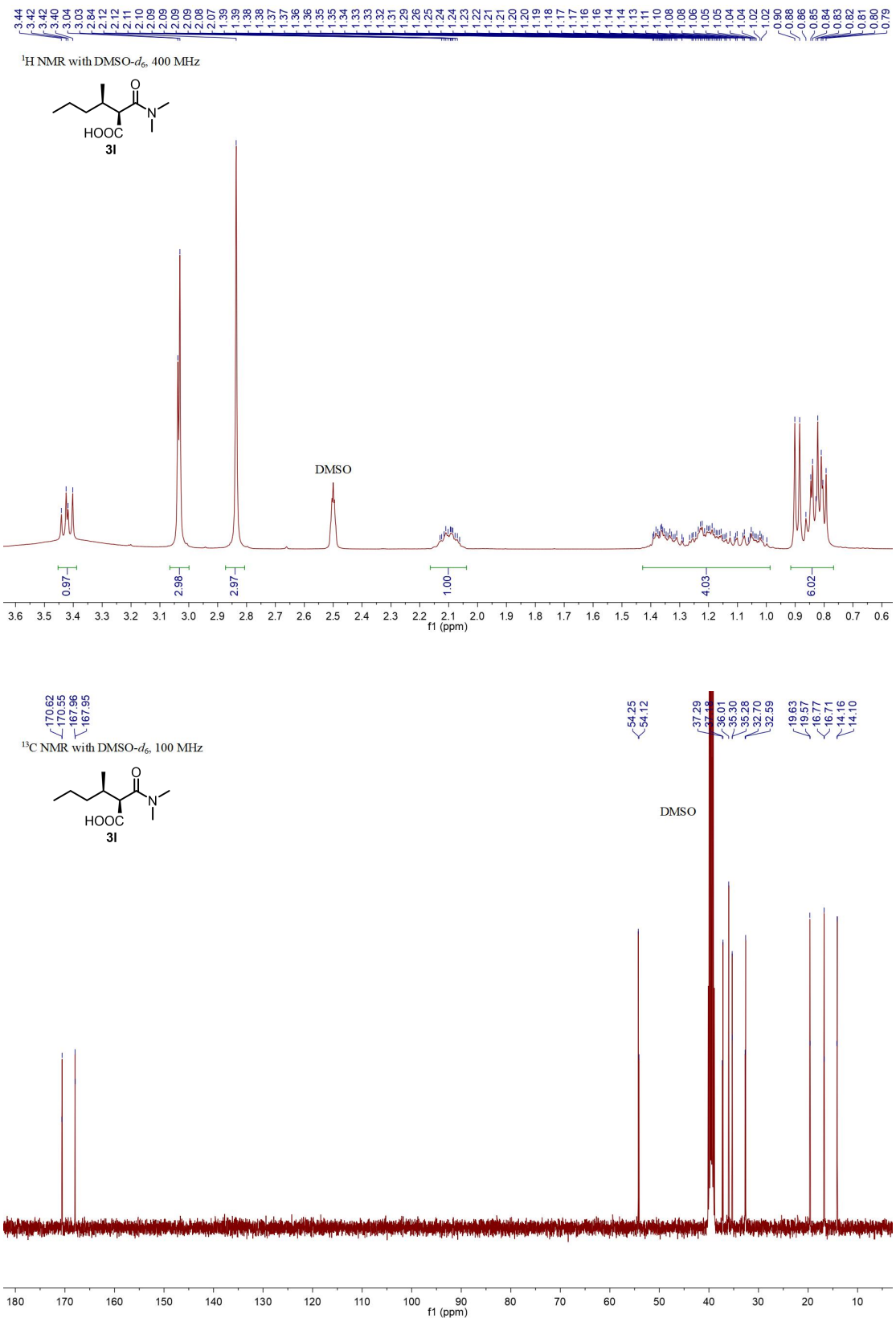


Figure S15. NMR spectra of (2*S*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-hexanamide (**3l**)

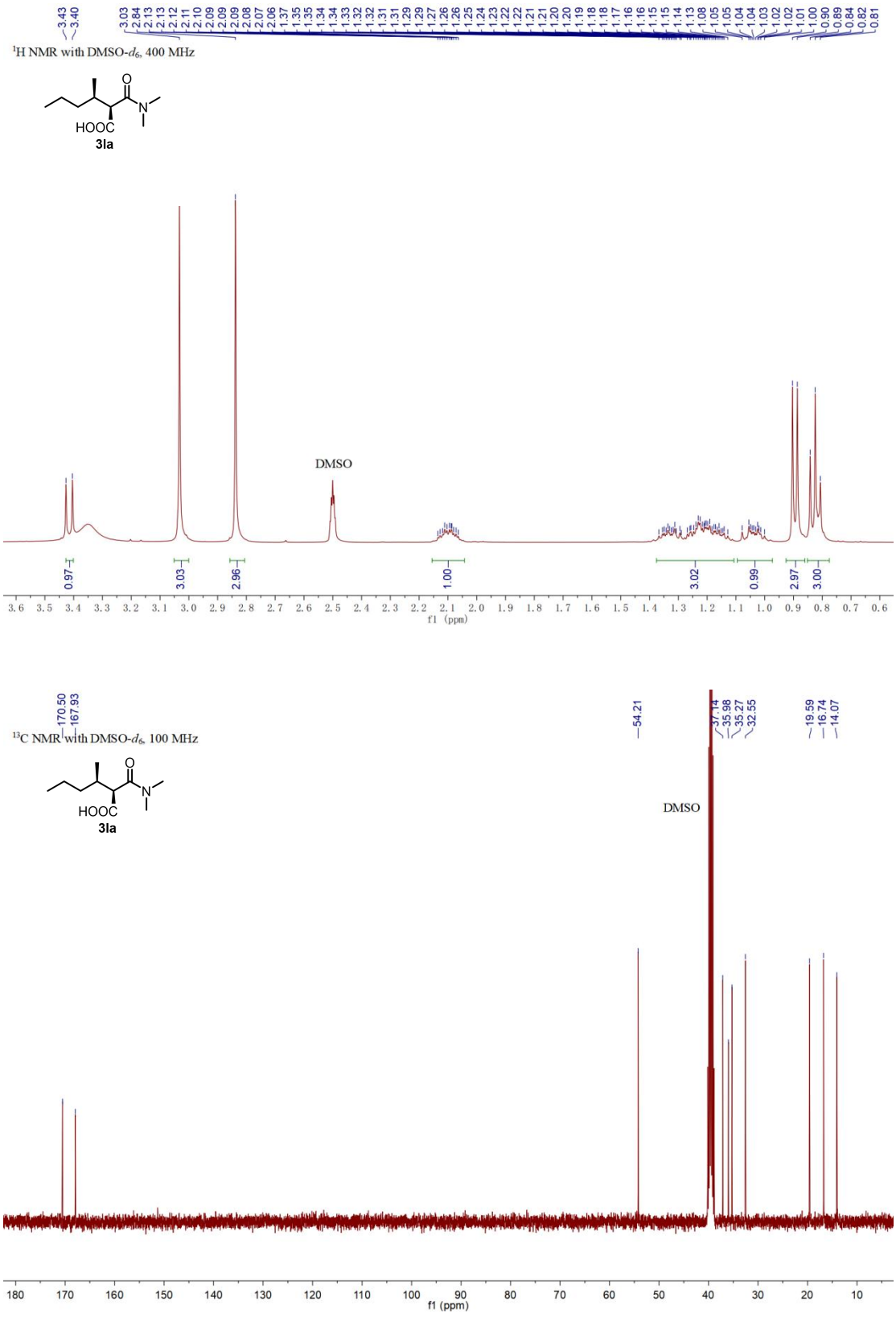


Figure S16. NMR spectra of (2*S*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-hexanamide (**3la**)

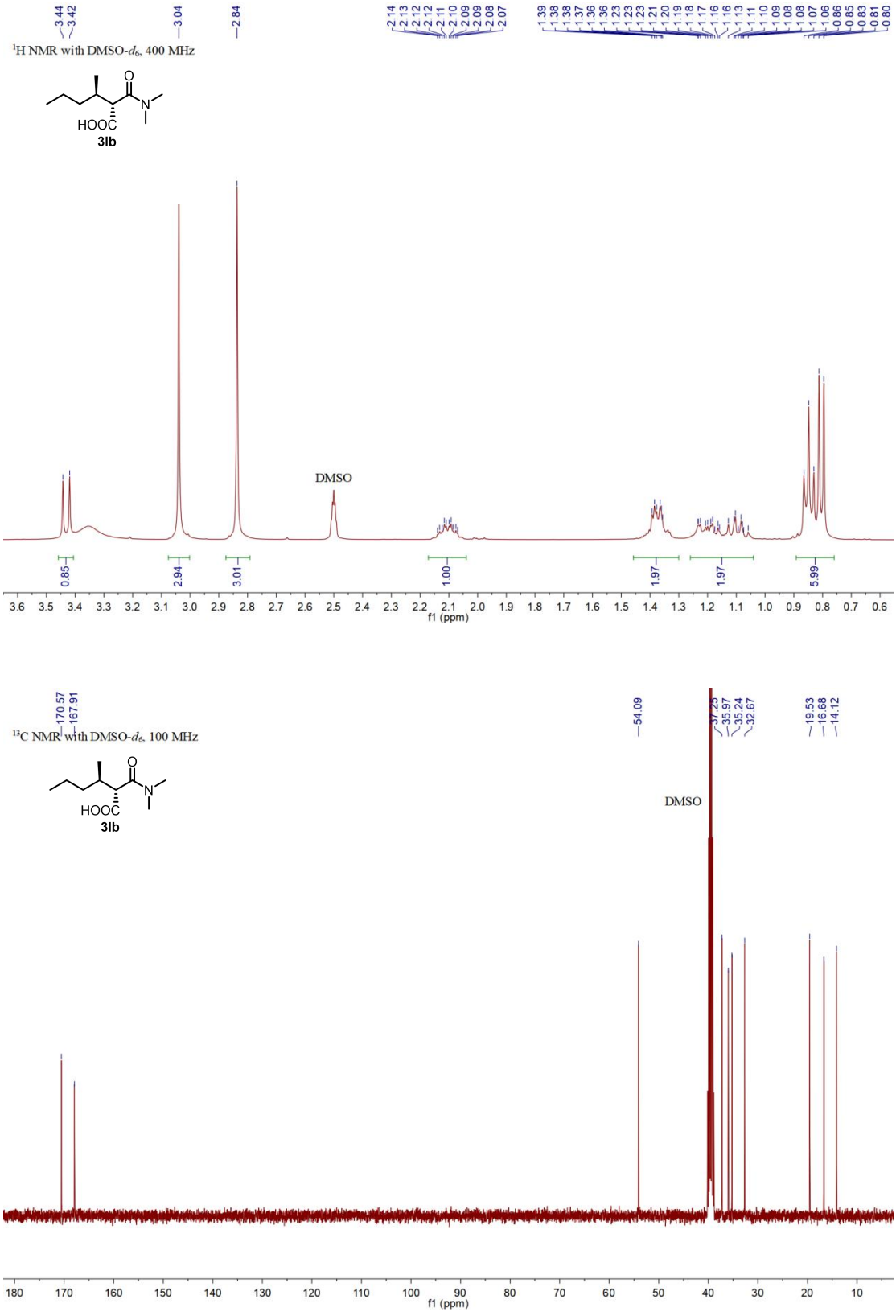


Figure S17. NMR spectra of (2*R*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-hexanamide (**3lb**)

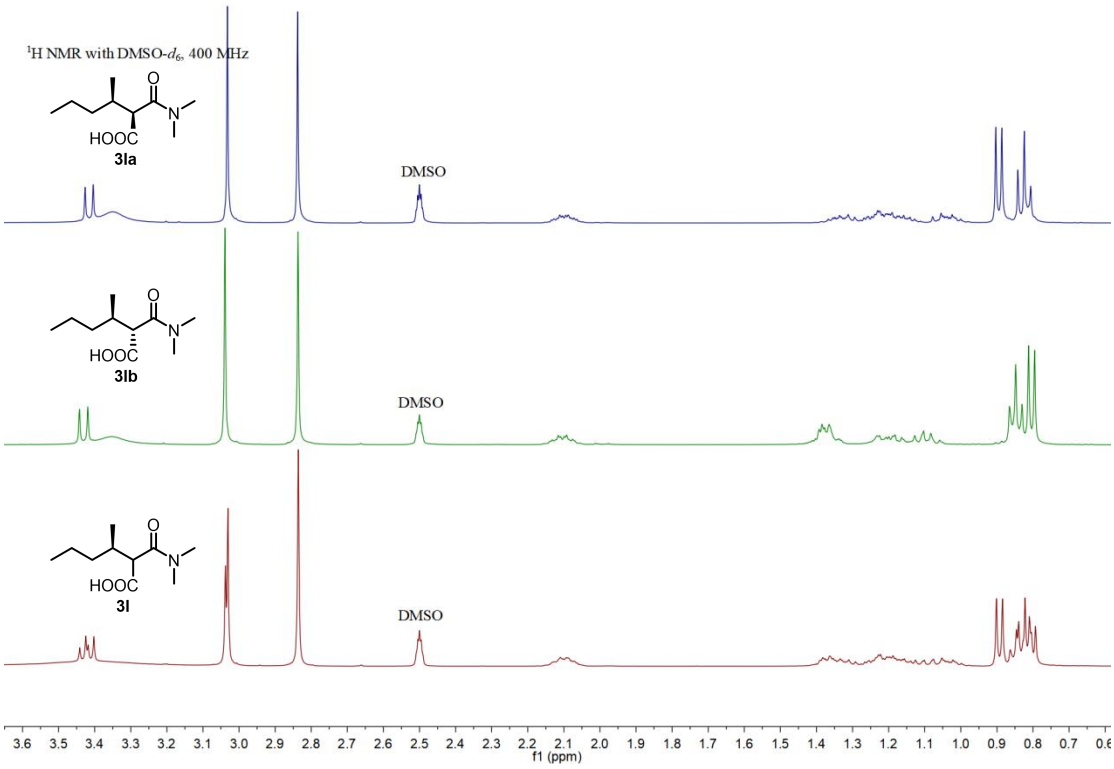


Figure S18. Comparison of the ^{1}H NMR spectra of **3l** with **3la** and **3lb**

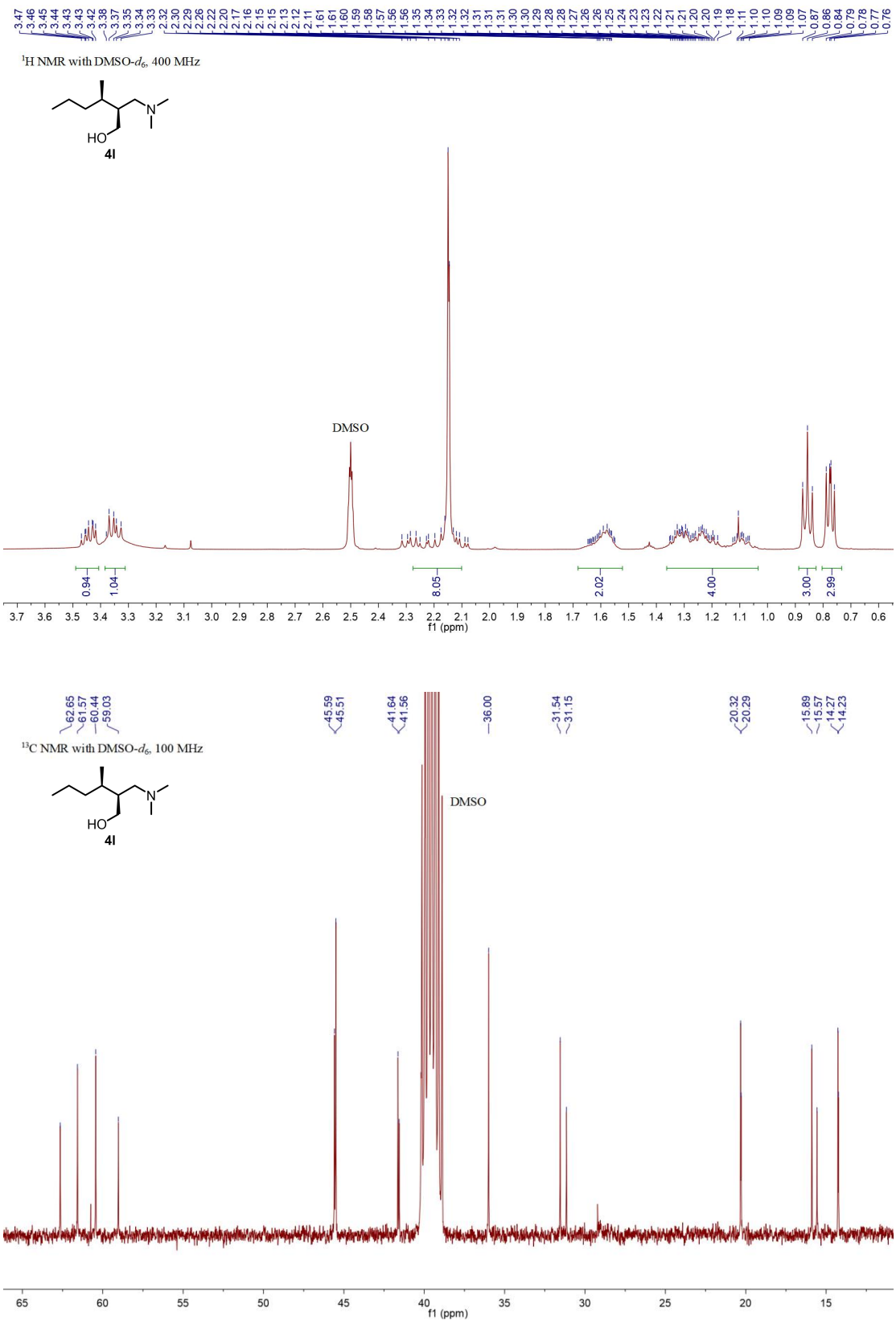


Figure S19. NMR spectra of (2*S*,3*R*)-*N*,*N*-dimethyl-2-hydroxymethyl-3-methyl-1-hexanamine (**4l**)

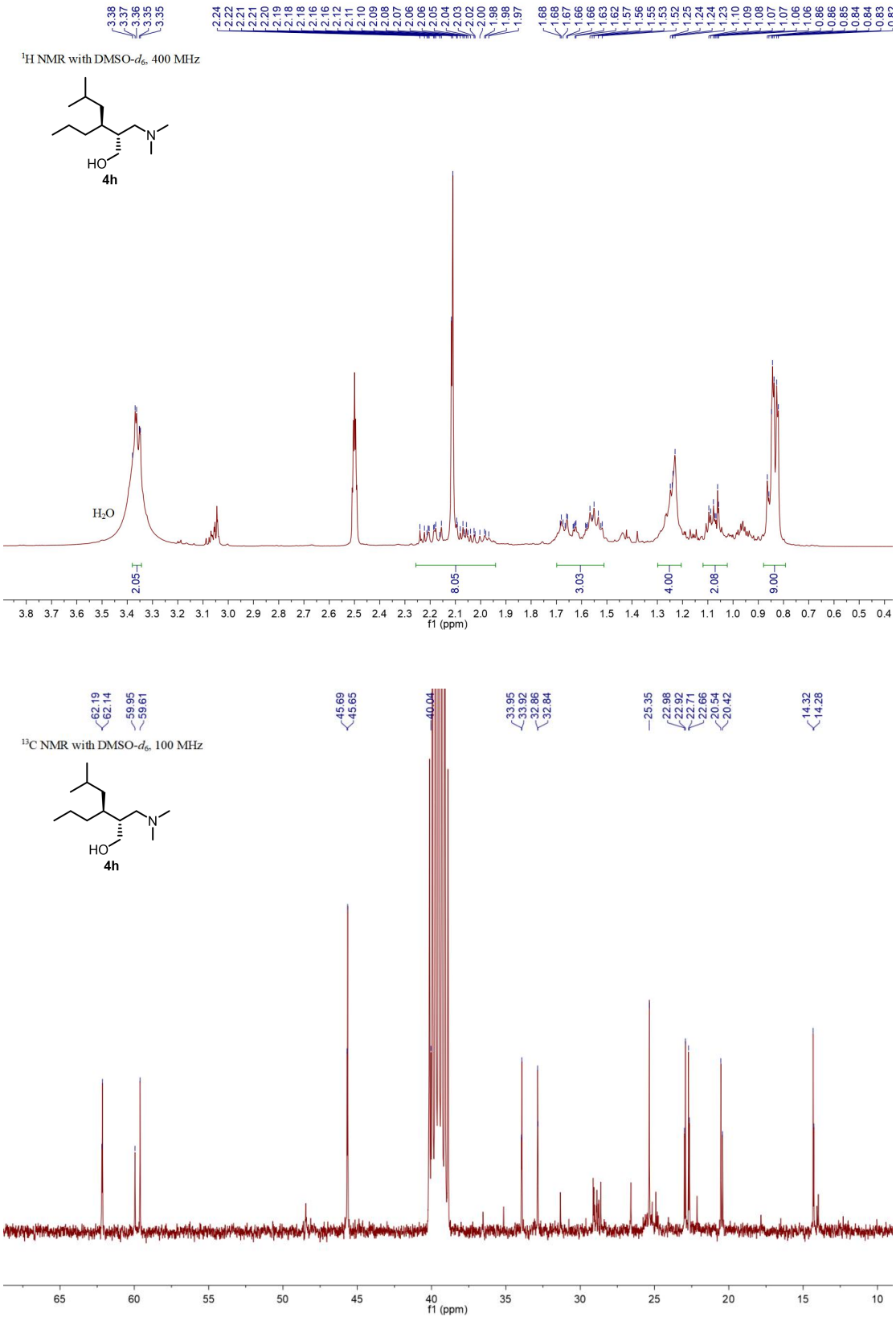
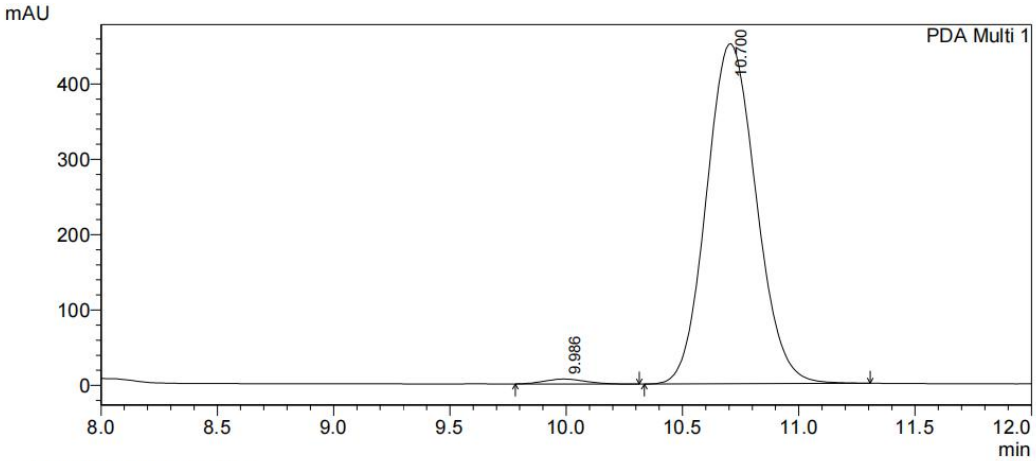


Figure S20. NMR spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-hydroxymethyl-5-methyl-3-propyl-1-hexanamine (**4h**)

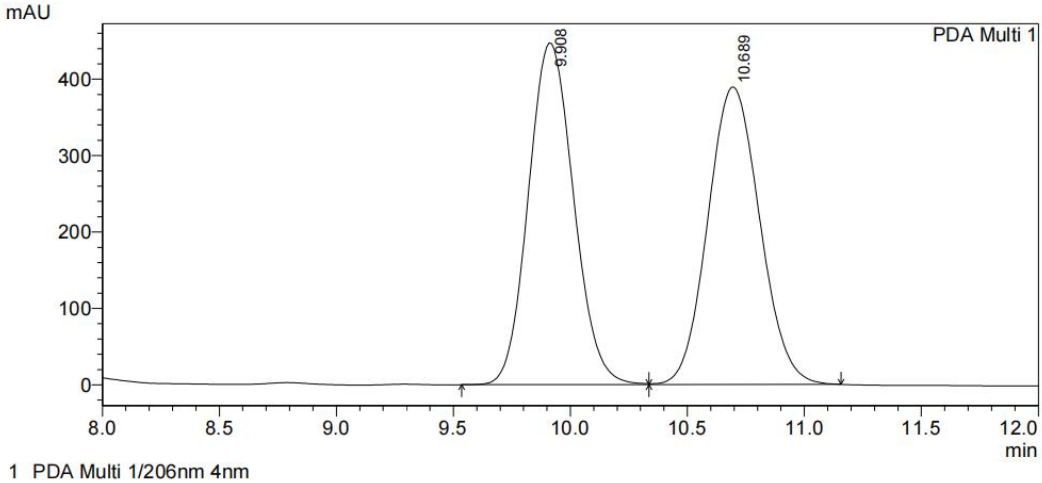
12. HPLC spectra



PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	9.986	79802	6488	1.417	1.176
2	10.700	6704454	451253	98.583	98.824
Total		6784256	457740	100.000	100.000

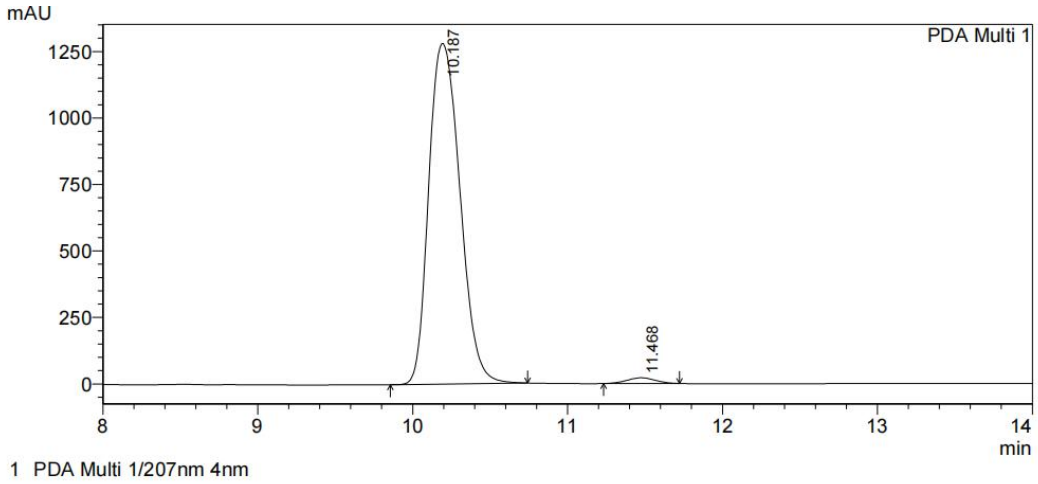


PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	9.908	6016509	447199	53.460	49.993
2	10.689	6018203	389305	46.540	50.007
Total		12034712	836504	100.000	100.000

Figure S21. HPLC spectra of (2*S*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-ethyl-hexanamide (**3a**)

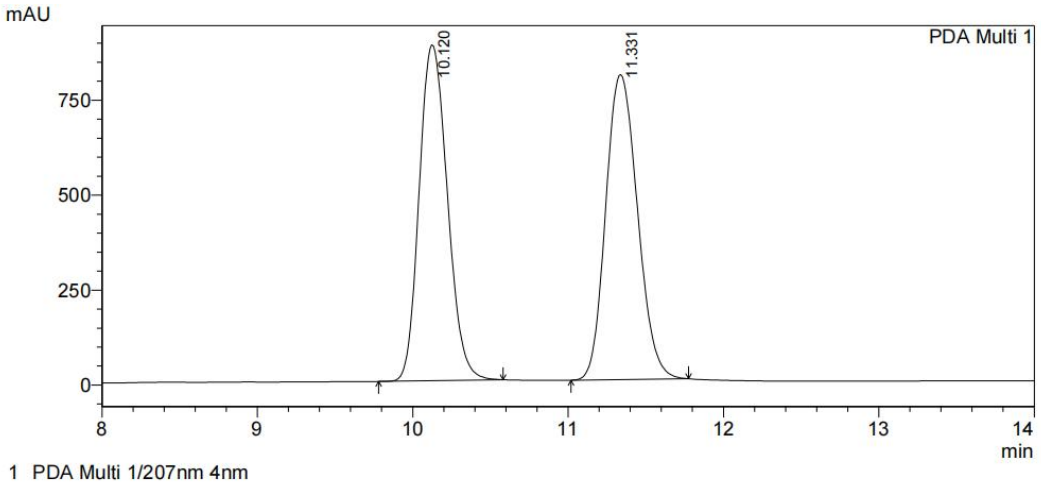


1 PDA Multi 1/207nm 4nm

PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	10.187	17953569	1280892	98.339	98.492
2	11.468	274874	21639	1.661	1.508
Total		18228443	1302531	100.000	100.000



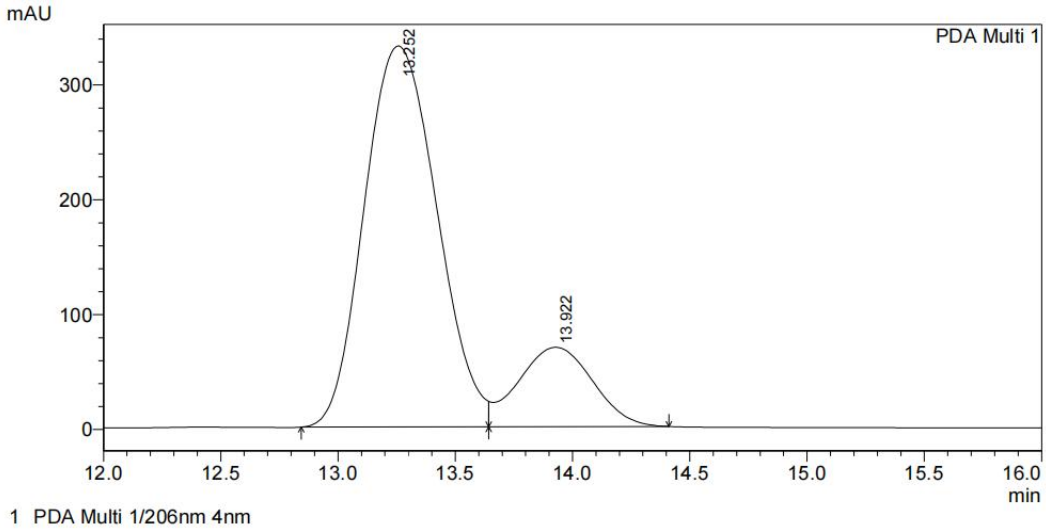
1 PDA Multi 1/207nm 4nm

PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	10.120	11170863	884444	52.402	49.427
2	11.331	11429993	803378	47.598	50.573
Total		22600856	1687822	100.000	100.000

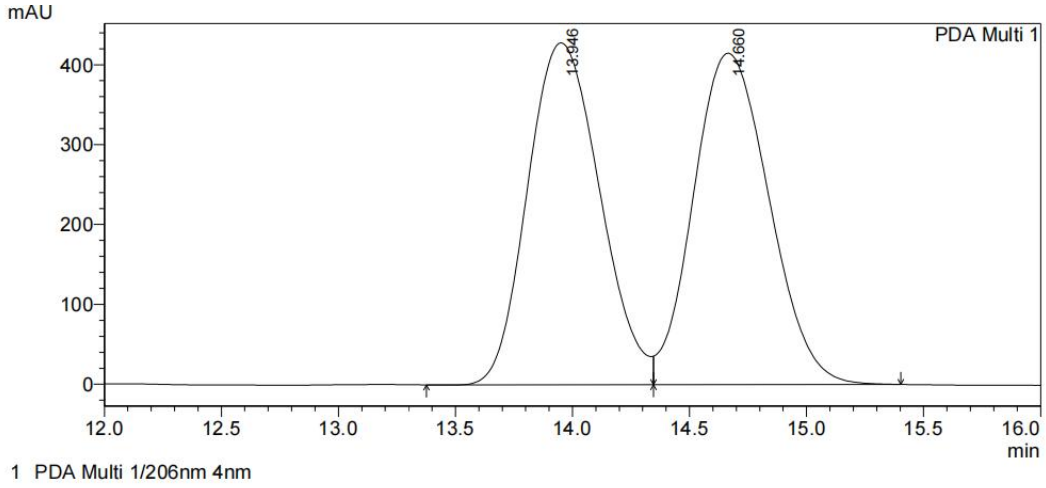
Figure S22. HPLC spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-pentanamide (**3b**)



PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	13.252	7148295	331832	82.743	82.436
2	13.922	1523019	69206	17.257	17.564
Total		8671314	401038	100.000	100.000

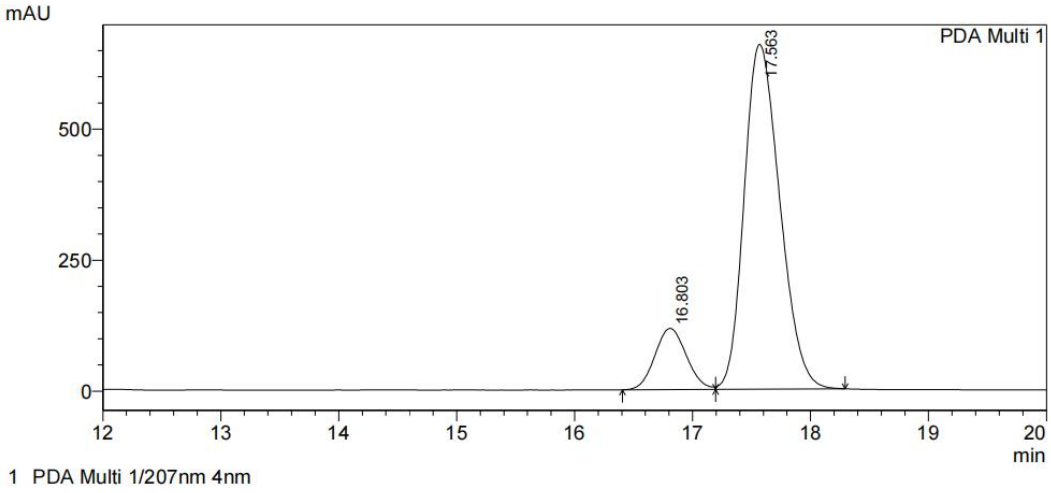


PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	13.946	9205609	428088	50.776	49.691
2	14.660	9320097	415006	49.224	50.309
Total		18525706	843093	100.000	100.000

Figure S23. HPLC spectra of (2*R*,3*S*)-*N*,*N*-diallyl-2-carboxyl-3-methyl-pentanamide (**3c**)

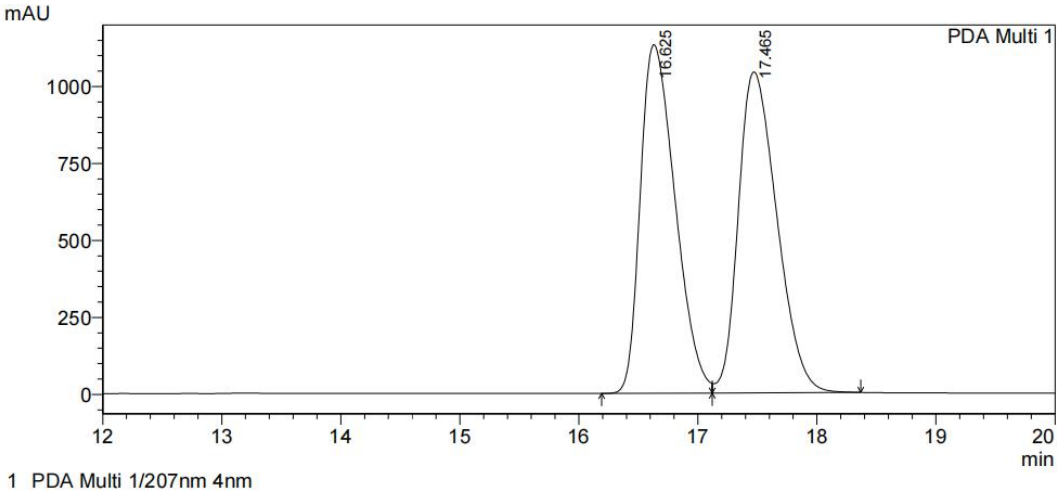


1 PDA Multi 1/207nm 4nm

PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	16.803	2170625	116850	15.072	13.559
2	17.563	13837803	658440	84.928	86.441
Total		16008428	775290	100.000	100.000



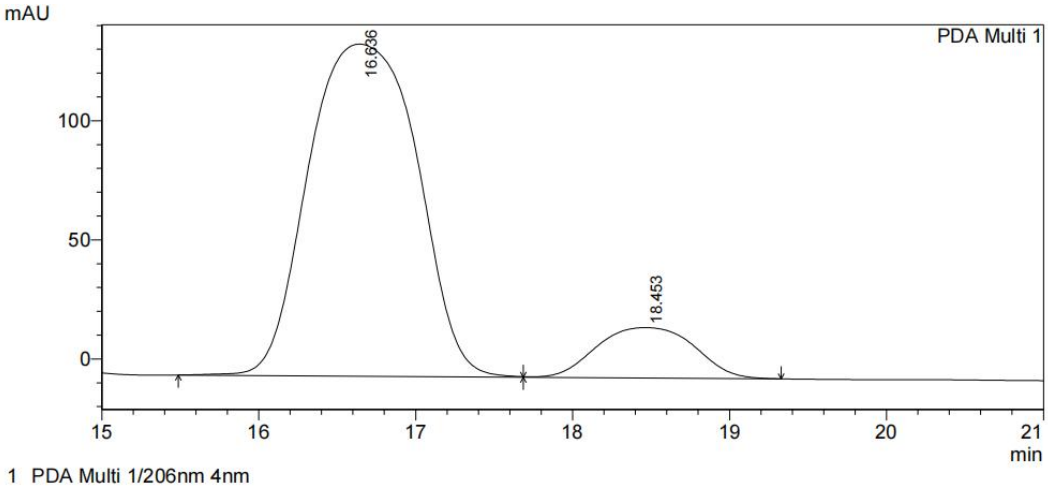
1 PDA Multi 1/207nm 4nm

PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	16.625	23051306	1132426	52.062	49.513
2	17.465	23504968	1042710	47.938	50.487
Total		46556274	2175136	100.000	100.000

Figure S24. HPLC spectra of (2*R*,3*S*)-3-methyl-2-(4-morpholinylcarbonyl)-pentanoic acid (**3d**)

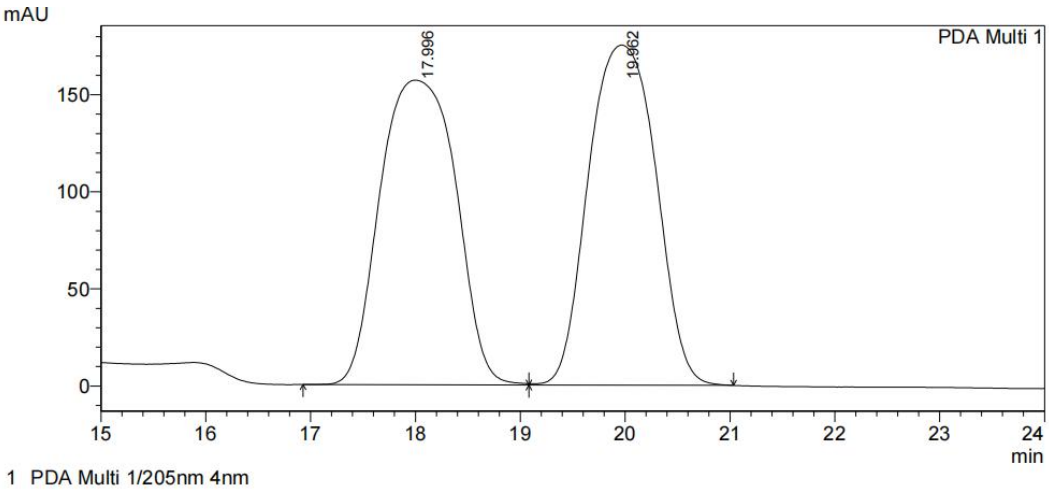


1 PDA Multi 1/206nm 4nm

PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	16.636	6730485	139391	86.836	88.028
2	18.453	915379	21132	13.164	11.972
Total		7645864	160523	100.000	100.000



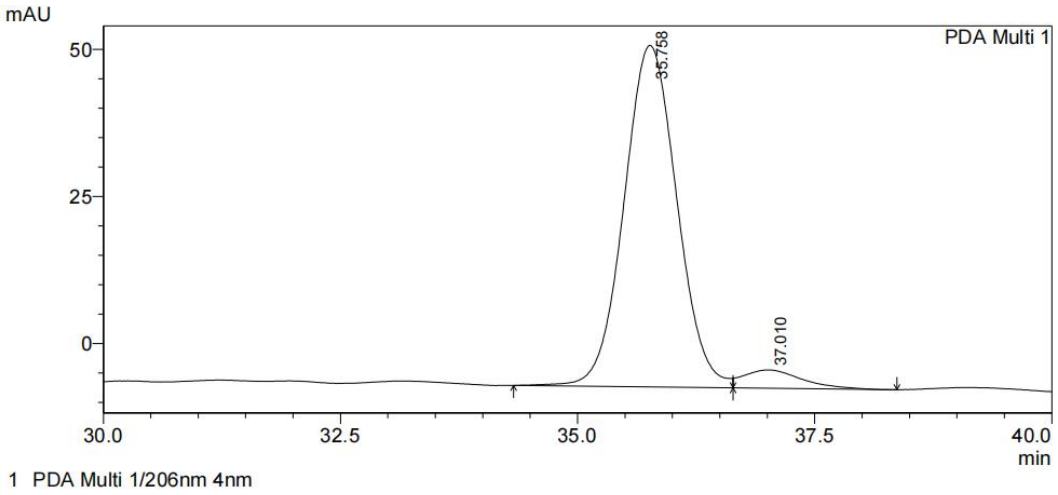
1 PDA Multi 1/205nm 4nm

PeakTable

PDA Ch1 205nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	17.996	7925367	156973	47.254	50.157
2	19.962	7875605	175220	52.746	49.843
Total		15800972	332193	100.000	100.000

Figure S25. HPLC spectra of (2*S*,3*R*)-*N*,*N*-diallyl-2-carboxyl-3-ethyl-hexanamide (**3e**)

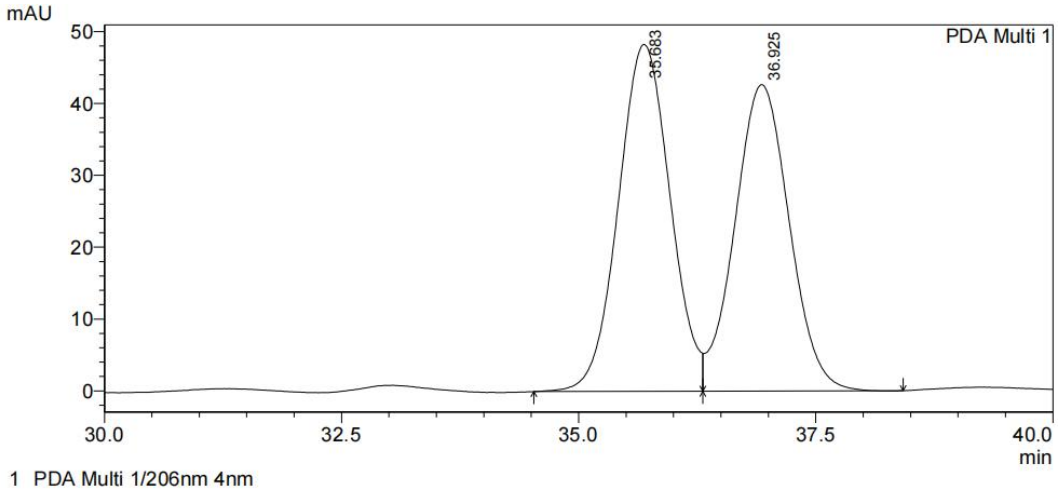


1 PDA Multi 1/206nm 4nm

PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	35.758	2250655	58046	94.900	94.458
2	37.010	132045	3119	5.100	5.542
Total		2382700	61165	100.000	100.000



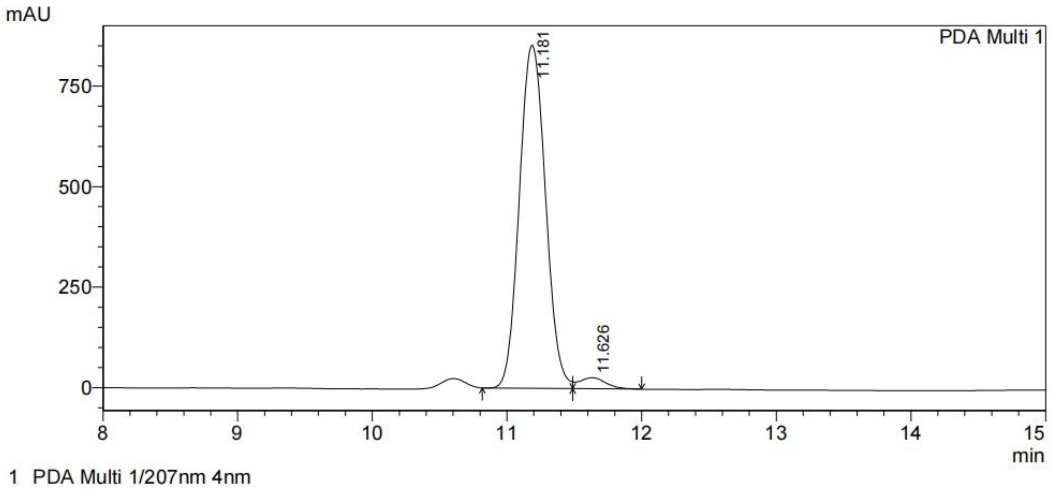
1 PDA Multi 1/206nm 4nm

PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	35.683	1834997	48286	53.103	51.864
2	36.925	1703078	42643	46.897	48.136
Total		3538075	90929	100.000	100.000

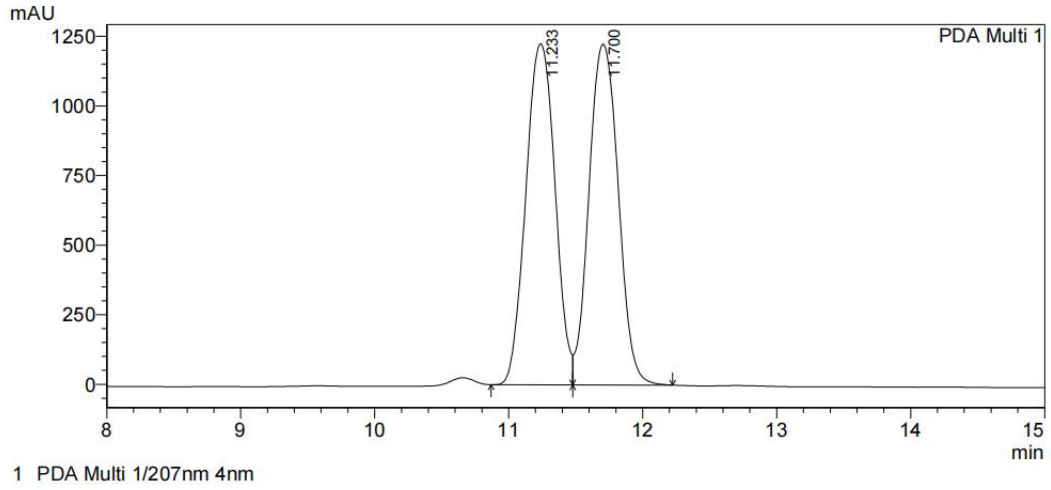
Figure S26. HPLC spectra of (3*S*,4*R*)-3-carboxyl-4-ethyl-1-methylpiperidin-2-one (**3f**)



PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	11.181	11521076	853234	96.872	96.801
2	11.626	380763	27551	3.128	3.199
Total		11901838	880784	100.000	100.000

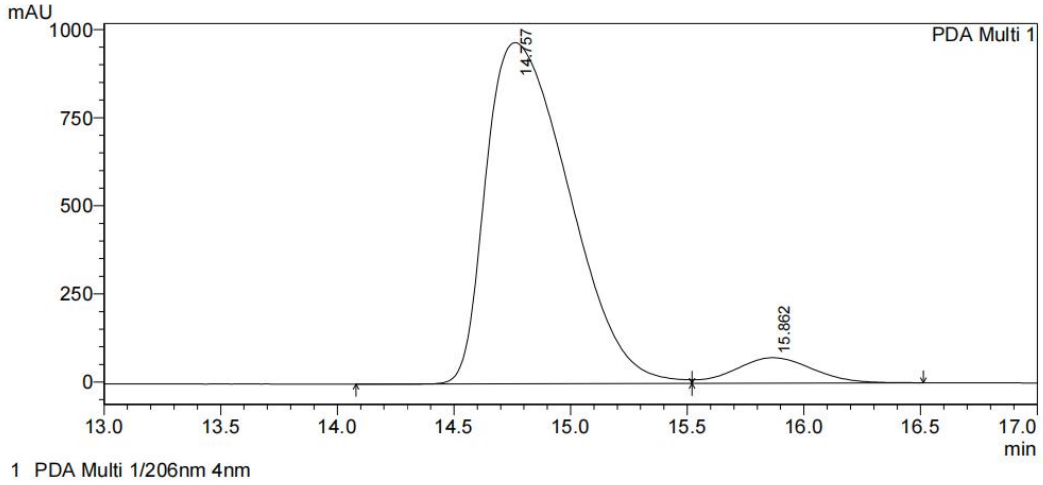


PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	11.233	18614784	1225288	50.016	50.000
2	11.700	18614890	1224522	49.984	50.000
Total		37229673	2449810	100.000	100.000

Figure S27. HPLC spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-propyl-nonanamide (**3g**)

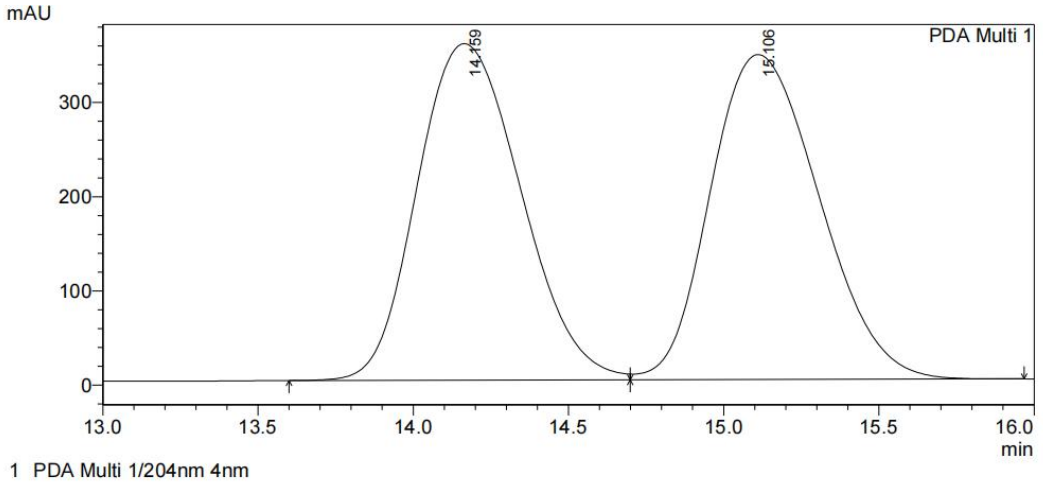


1 PDA Multi 1/206nm 4nm

PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	14.757	23917620	967621	93.061	93.518
2	15.862	1657813	72153	6.939	6.482
Total		25575433	1039774	100.000	100.000



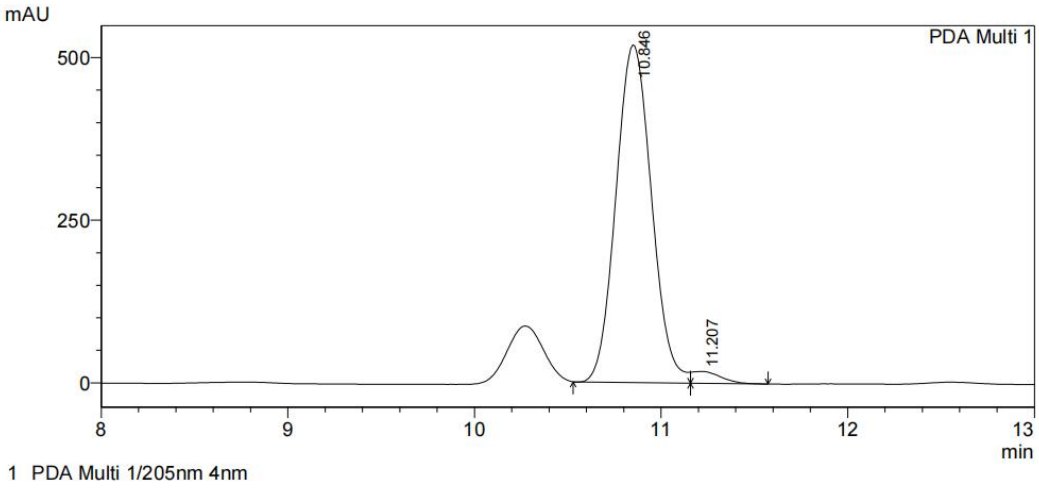
1 PDA Multi 1/204nm 4nm

PeakTable

PDA Ch1 204nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	14.159	8291240	357121	50.879	49.727
2	15.106	8382276	344778	49.121	50.273
Total		16673515	701899	100.000	100.000

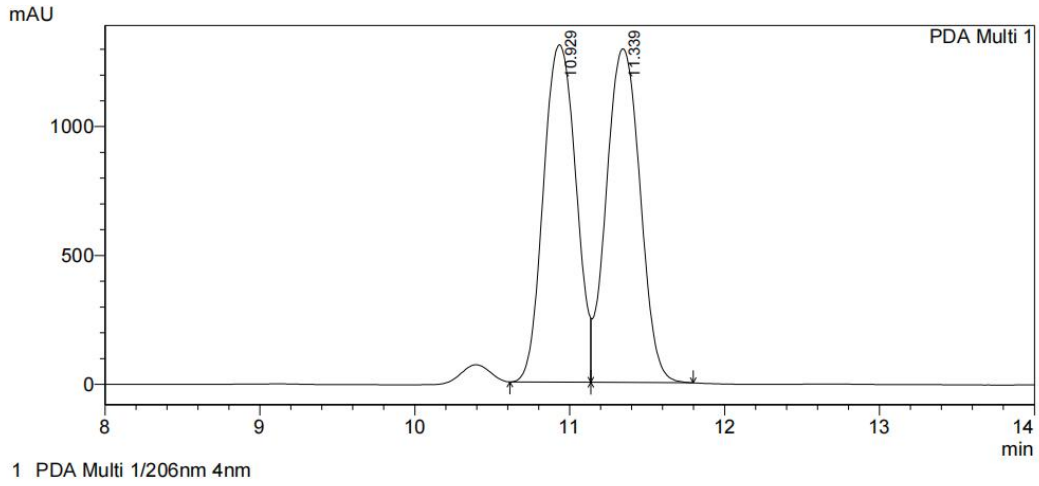
Figure S28. HPLC spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-5-methy-3-propyl-hexanamide (**3h**)



PeakTable

PDA Ch1 205nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	10.846	6896962	519093	96.608	97.351
2	11.207	187693	18224	3.392	2.649
Total		7084654	537317	100.000	100.000

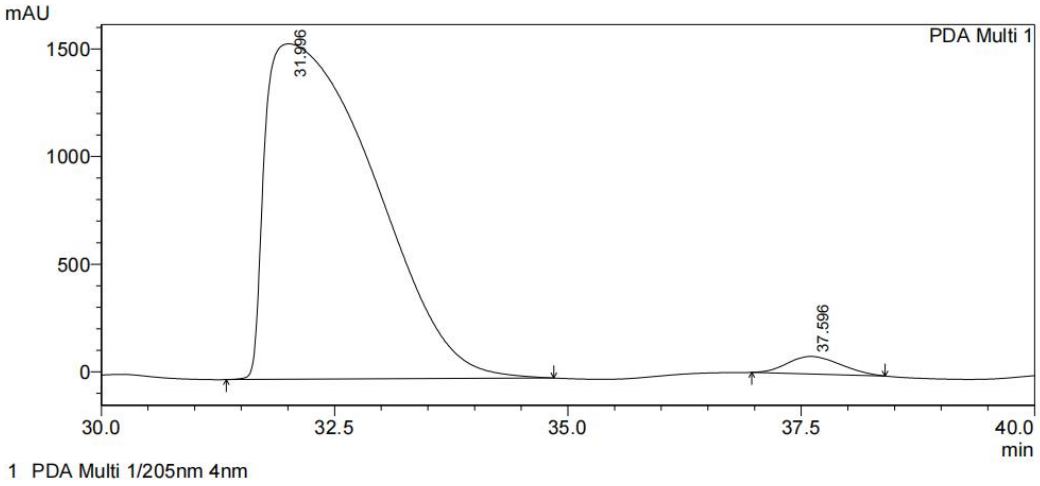


PeakTable

PDA Ch1 206nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	10.929	19175675	1309814	50.299	49.374
2	11.339	19661746	1294259	49.701	50.626
Total		38837421	2604072	100.000	100.000

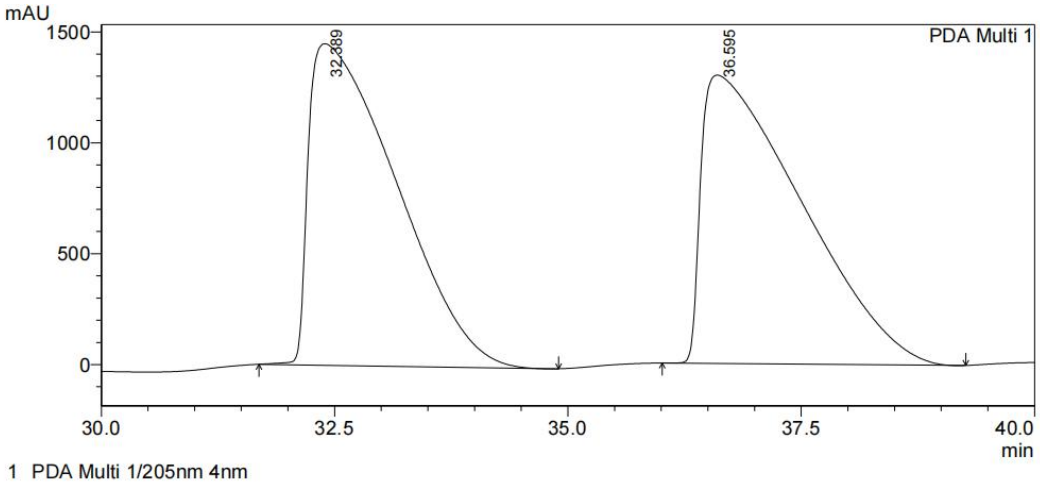
Figure S29. HPLC spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-6-methy-3-propyl-heptanamide (**3i**)



PeakTable

PDA Ch1 205nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	31.996	126485591	1559038	95.039	97.495
2	37.596	3249410	81389	4.961	2.505
Total		129735001	1640427	100.000	100.000

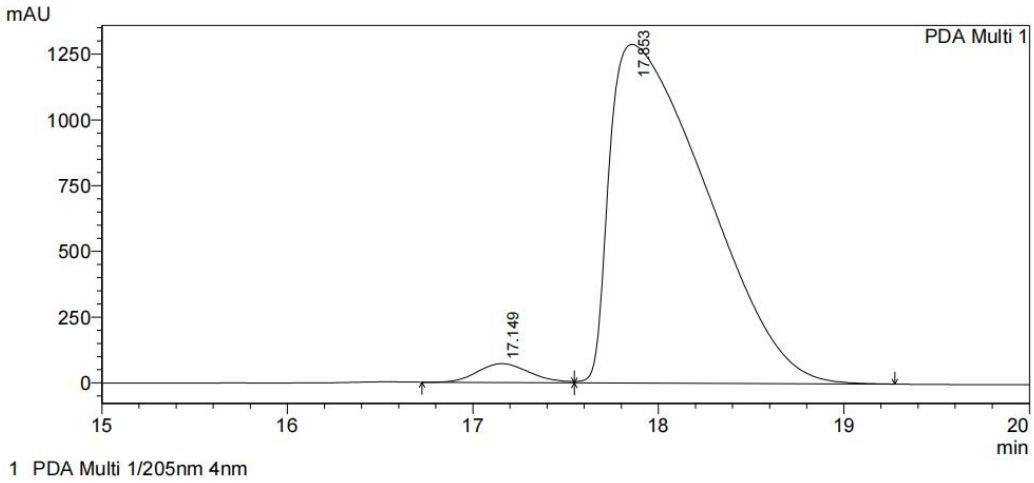


PeakTable

PDA Ch1 205nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	32.389	94527511	1449206	52.713	49.376
2	36.595	96918326	1300012	47.287	50.624
Total		191445837	2749218	100.000	100.000

Figure S30. HPLC spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-phenylethyl-hexanamide (**3j**)

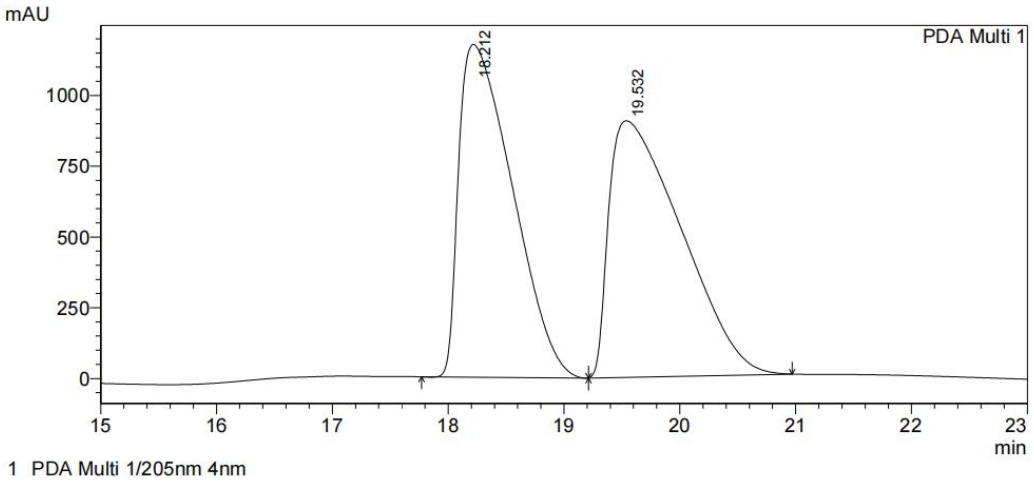


1 PDA Multi 1/205nm 4nm

PeakTable

PDA Ch1 205nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	17.149	1407882	71834	5.284	2.926
2	17.853	46715042	1287555	94.716	97.074
Total		48122924	1359389	100.000	100.000



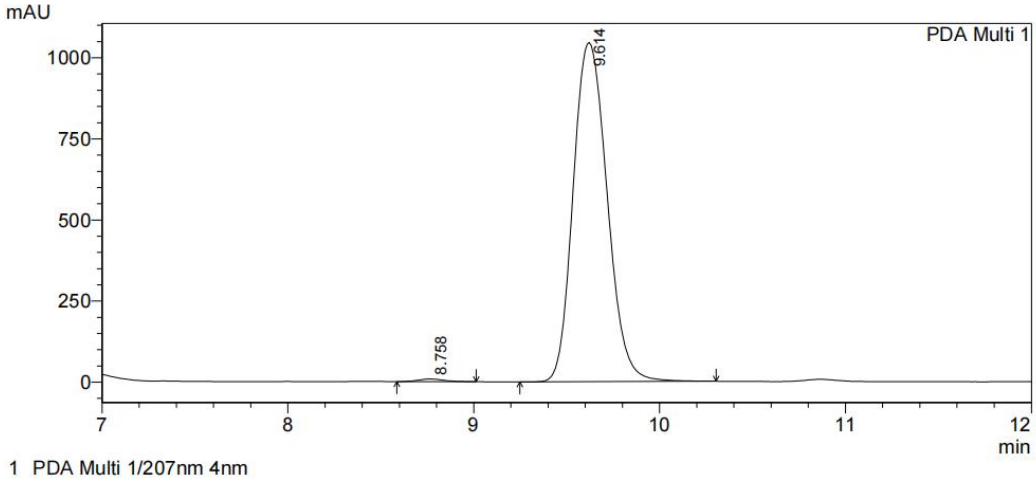
1 PDA Multi 1/205nm 4nm

PeakTable

PDA Ch1 205nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	18.212	37810860	1175720	56.475	48.995
2	19.532	39362643	906131	43.525	51.005
Total		77173503	2081851	100.000	100.000

Figure S31. HPLC spectra of (2*R*,3*S*)-*N*,*N*-dimethyl-2-carboxyl-3-propyl-oct-7-enamide (**3k**)

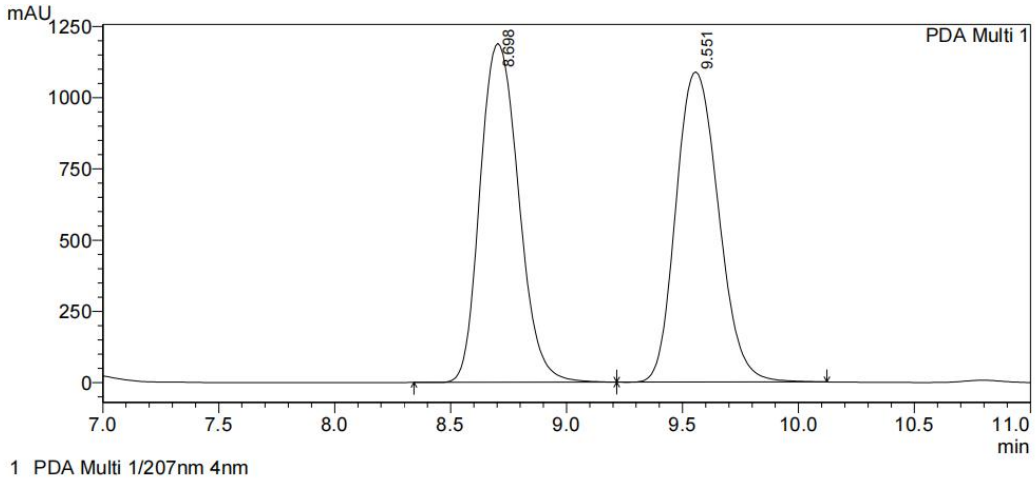


1 PDA Multi 1/207nm 4nm

PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	8.758	81233	8164	0.775	0.608
2	9.614	13272680	1045681	99.225	99.392
Total		13353913	1053845	100.000	100.000



1 PDA Multi 1/207nm 4nm

PeakTable

PDA Ch1 207nm 4nm

Peak#	Ret. Time	Area	Height	Height %	Area %
1	8.698	13767417	1189845	52.204	49.753
2	9.551	13903908	1089396	47.796	50.247
Total		27671325	2279241	100.000	100.000

Figure S32. HPLC spectra of (2*S*,3*R*)-*N*,*N*-dimethyl-2-carboxyl-3-methyl-hexanamide (**3l**)

13. References

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3 G. M. Sheldrick, Crystal Structure Refinement with SHELXL. *Acta Cryst. C*, 2015, **71**, 3–8.

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