Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is (c) The Royal Society of Chemistry 2010

Stereoselective palladium-catalyzed allylic alkylations of peptide amide enolates

Swarup Datta and Uli Kazmaier*

Institut für Organische Chemie, Universität des Saarlandes,
D-66123 Saarbrücken, Germany.
Fax: +49 681 302 2409; Tel: +49 681 302 3409;
E-mail: u.kazmaier@mx.uni-saarland.de

Supplementary Information

Table of Content

General Remarks **S2**

Experimental procedures and analytical Data of Compounds 1 to 16 **S2-S14**

^{1}H and ^{13}C spectra of compounds 1 to 16 **S15-S61**

General remarks

All reactions were carried out in oven-dried glassware (70 °C) under an atmosphere of nitrogen. THF and Et_2O were dried with sodium and benzophenone and distilled before use. Dichloromethane was dried over CaH_2 and distilled before use. The products were purified by column chromatography on silica gel columns (Macherey-Nagel 60, 0.063-0.2 mm). Mixtures of ethyl acetate and hexanes were generally used as eluents. Analytical TLC was performed on precoated silica gel plates (Macherey-Nagel, Polygram® SIL G/UV254). Visualization was accomplished with UV-light, $KMnO_4$ solution or Iodine. ^1H and ^{13}C NMR spectra were recorded with a Bruker AC-400 [400 MHz (^1H) and 100 MHz (^{13}C)] spectrometer in $CDCl_3$. Compound which shows mixture of rotamers at room temperature were recorded with Brucker DRX-500 [500 Mz (^1H) and 125 MHz (^{13}C)] spectrometer at 80 ^oC (353 K) in DMSO-d_6. Mass spectra were recorded with a Finnigan MAT 95 spectrometer using the CI technique. Elemental analyses were performed at the Saarland University.

Experimental procedures and analytical data:

Benzyl 2-oxo-2-(piperidin-1-yl)ethylcarbamate (1). TBTU (2.76 g, 8.7 mmol) was added to a solution of Z-glycine (1.50 g, 7.2 mmol) in dichloromethane (15 mL) at 0 ^oC. To this solution diisopropylethylamine (3.6 mL, 21.5 mmol) was slowly added at 0 ^oC and stirred for 15 min before piperidine (0.85 mL, 8.6 mmol) was added at 0 ^oC. After stirring for 10 min the cooling bath was removed and stirred for overnight at room temperature. Water (10 mL) was added to the reaction mixture, the aqueous layer was extracted twice with dichloromethane and the combined organic layer were successively washed with 1M $KHSO_4$, saturated $NaHCO_3$ solution and water. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (hexanes/EtOAc 85 : 15) to give **1** in 72% yield (1.42 mg, 5.2 mmol) as white solid. m.p. 105-107 °C; ^1H-NMR (400 MHz, $CDCl_3$): δ 7.35-7.29 (m, 5H), 5.87 (bs, 1H), 5.11 (s, 2H), 3.99 (d, J = 4.4 Hz, 1H), 3.54 (t, J = 5.2 Hz, 2H), 3.29 (t, J = 5.2 Hz, 2H), 1.64-1.61 (m, 2H), 1.56-1.51 (m, 4H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 165.8, 156.1, 136.4, 128.4 (2 C), 128.0, 127.9 (2 C), 66.6, 45.3, 43.1, 42.5, 26.1, 25.3, 24.3. HRMS (CI) *m/z* calcd for $C_{15}H_{21}N_2O_3$ $[M+H]^+$ 277.1552. Found 277.1523. Elemental analysis calcd (%) for $C_{15}H_{20}N_2O_3$: C 65.20, H 7.30, N 10.15 and found: C 65.29, H 6.88, N 10.08.

Benzyl 1-oxo-1-(piperidin-1-yl)propan-2-ylcarbamate (2). According to the general procedure for methylation of dipeptides (see main text) **2** (102 mg, 0.35 mmol, 98%) was obtained from **1** (100 mg, 0.36 mmol) as a white foam after column chromatography (hexanes/EtOAc 85 : 15). ^1H-NMR (400 MHz, $CDCl_3$): δ 7.35-7.28 (m, 5H), 5.92 (d, J = 6.8 Hz, 1H), 5.09 (s, 2H), 4.65 (quin, J = 6.8 Hz, 1H), 3.62-3.39 (m, 4H), 1.66-1.54 (m, 6H), 1.32 (d, J = 6.8 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.3, 155.4, 136.4, 128.3 (2 C), 127.9, 127.8 (2 C), 66.4, 46.6, 46.3, 43.1, 26.2, 25.3, 24.3, 19.3. HRMS (CI) *m/z* calcd for $C_{16}H_{23}N_2O_3$ $[M+H]^+$ 291.1709. Found 291.1703. Elemental analysis calcd (%) for $C_{16}H_{22}N_2O_3$: C 66.18, H 7.64, N 9.65 and found: C 65.69, H 7.28, N 9.37.

Benzyl 3-ethyl-3-hydroxy-1-oxo-1-(piperidin-1-yl)pentan-2-ylcarbamate (3). According to the general procedure for aldol reactions of dipeptides (see main text) **3** (123.8 mg, 0.34 mmol, 95%) was obtained from **1** (100 mg, 0.36 mmol) as a white foam after column chromatography (hexanes/EtOAc 9 : 1). ^1H-NMR (400 MHz, $CDCl_3$): δ 7.37-7.30 (m, 5H), 5.74 (d, J = 9.6 Hz, 1H), 5.12 (d, J = 12.0 Hz, 1H), 5.08 (d, J = 12.0 Hz, 1H), 4.62 (d, J = 9.6 Hz, 1H), 3.73-3.49 (m, 4H), 1.68-1.37 (m, 10H), 0.88 (t, J = 7.6 Hz, 3H), 0.83 (t, J = 7.6 Hz, 3H); ^{13}C-NMR (100 MHz, $CDCl_3$): δ 171.1, 156.1, 136.2, 128.3 (2 C), 127.9, 127.8 (2 C), 76.3, 66.9, 50.9, 47.4, 42.9, 27.8, 26.6, 25.5, 24.3, 7.5, 7.4. HRMS (CI) *m/z* calcd for $C_{20}H_{31}N_2O_4$ $[M+H]^+$ 363.2284. Found 363.2268.

Benzyl (1*S*,2*S*)-1-[2-oxo-2-(piperidin-1-yl)ethylcarbamoyl]-2-methylbutylcarbamate (4a). Pd/C (300 mg, 10% w/w)) was dried in *vacuo* before MeOH (3 mL) was added. The vessel was purged with H_2 and charged with a solution of **1** (3.0 g, 10.8 mmol) in MeOH (30 mL). The reaction mixture was stirred overnight under H_2 atmosphere. The solution was filtered through a plug of celite and concentrated to afford 2-amino-1-(piperidin-1-yl)ethanone (1.44 g, 10.1 mmol, 93%) as a viscous oil.
TBTU (3.24 g, 10.1 mmol) was added to a solution of Cbz-L-Isoleucine (2.23 g, 8.4 mmol) in dichloromethane (10 mL) at 0 ^oC. To this solution diisopropylethylamine (4.3 mL, 25.2 mmol) was slowly added at 0 ^oC and stirred for 15 min before 2-amino-1-(piperidin-1-yl)ethanone (1.44 g, 10.1 mmol) in dichloromethane (7 mL) was added at 0 ^oC. After stirring for 10 min the cooling bath was removed and the mixture was stirred overnight at room temperature. Water (10 mL) was added to the reaction mixture and the aqueous layer was extracted twice with dichloromethane. The combined organic layers were washed with 1M $KHSO_4$, saturated $NaHCO_3$ solution and water. The solvent was removed under reduced pressure and the crude product was purified by column chromatography (hexanes/EtOAc 4 : 1) to give **4a** in 73% yield (2.38 g, 6.1 mmol) as white solid. $[\alpha]_D^{20}$ = -3.0° (c = 1.0, $CHCl_3$);m.p. 127-129 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.34-7.27 (m, 5H), 7.05 (bs, 1H), 5.52 (d, *J* = 8.4 Hz, 1H), 5.12 (d, *J* = 12.0 Hz, 1H), 5.06 (d, *J* = 12.0 Hz, 1H), 4.18-4.15 (m, 1H), 4.03-4.01 (m, 2H), 3.55 (t, *J* = 5.6 Hz, 2H), 3.29 (t, *J* = 5.6 Hz, 2H), 1.96-1.81 (m, 1H), 1.66-1.62 (m, 2H), 1.55-1.44 (m, 5H), 1.17-1.09 (m, 1H), 0.93-0.87 (m, 6H).^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.9, 165.6, 156.1, 136.3, 128.4 (2 C), 128.0, 127.9 (2 C), 66.8, 59.5, 45.3, 43.1, 41.1, 37.7, 26.1, 25.3, 24.7, 24.2, 15.4, 11.4. HRMS (CI) *m/z* calcd for $C_{21}H_{32}N_3O_4$ $[M+H]^+$ 390.2393. Found 390.2394. Elemental analysis calcd (%) for $C_{21}H_{31}N_3O_4$: C 64.76, H 8.02, N 10.79. Found C 64.61 H 7.69, N 10.82.

(2*S*,3*S*)-2-(2,2,2-Trifluoroacetamido)-3-methyl-N-[2-oxo-2-(piperidin-1-yl)ethyl]pentanamide (4b). Pd/C (70 mg, 10% w/w)) was dried in *vacuo* before MeOH (2 mL) was added. The vessel was purged with H_2 and charged with a solution of **4a** (0.70 g, 1.8 mmol) in MeOH (30 mL). The reaction mixture was stirred overnight under H_2 atmosphere. The solution was filtered through a plug of celite and concentrated to afford afford (2*S*,3*S*)-2-amino-3-methyl-*N*-(2-oxo-2-(piperidin-1-yl)ethyl)pentanamide (0.42 g, 1.64 mmol, 91%) as a viscous oil.
Triethylamine (0.3 mL, 2.3 mmol) was added to a solution of (2*S*,3*S*)-2-amino-3-methyl-*N*-[2-oxo-2-(piperidin-1-yl)ethyl]pentanamide (300 mg, 1.2 mmol) in methanol and the reaction mixture was cooled to 0 ^{o} C before trifloroacetic acid ethyl ester (0.27 ml, 2.3 mmol) was slowly added. The ice bath was removed and the reaction mixture was stirred for 6h. Methanol was removed under reduced pressure and the crude product was dissolved in ethyl acetate before the addition of 1M $KHSO_4$. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with water, dried over Na_2SO_4. The solvent was removed in vacuo and the crude product was purified by flash chromatography (hexanes/EtOAc 7 : 3) to afford **4b** (0.37 g, 1.07 mmol, 91%) as a white solid. $[\alpha]_D^{20}$ = -0.7° (c = 1.0, $CHCl_3$); m.p. 205-207 °C. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.23 (bs, 1H), 7.04 (bs, 1H), 4.47 (dd, *J* = 8.4 Hz, *J* = 6.0 Hz, 1H), 4.10 (dd, *J* = 17.2 Hz, *J* = 4.0 Hz, 1H), 4.04 (dd, *J* = 17.2 Hz, *J* = 3.6 Hz, 1H), 3.60-3.56 (m, 2H), 3.35-3.32 (m, 2H), 1.94-1.86 (m, 1H), 1.70-1.49 (m, 7H), 1.25-1.15 (m, 1H), 0.95-0.92 (m, 6H) ^{13}C-NMR (100 MHz, $CDCl_3$): δ 169.7, 165.4, 156.8 (q, $^2J_{C,F}$ = 36.9 Hz), 115.8 (q, $^1J_{C,F}$ = 286.0 Hz), 57.6, 45.4, 43.1, 41.4, 37.9, 26.0, 25.3, 24.8, 24.2, 15.1, 11.1. HRMS (CI) *m/z* calcd for $C_{15}H_{25}F_3N_3O_3$ $[M+H]^+$ 352.1848. Found 352.1852. Elemental analysis calcd (%) for $C_{15}H_{24}F_3N_3O_3$: C 51.27, H 6.28, N 11.96. Found: C 51.93 H 6.54, N 11.67.

Benzyl (1*S*,2*S*)-1-[1-oxo-1-(piperidin-1-yl)propan-2-ylcarbamoyl]-2-methylbutylcarbamate (5a). According to the general procedure for methylation of dipeptides (see main text) **5a** (93.1 mg, 0.23 mmol, 90%) was obtained from **4a** (100 mg, 0.26 mmol) as a mixture of two diastereomers after column chromatography (hexanes/EtOAc 4 : 1). HPLC (Silicagel, hexanes/EtOAc 50 : 50,

1mL/min, 260 nm): t_R (60%) = 12.02 min, t_R (40%) = 14.05 min. Major diastereomer: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.32-7.27 (m, 5H), 7.20 (d, *J* = 6.4 Hz, 1H), 5.59 (d, *J* = 8.8 Hz, 1H), 5.09 (d, *J* = 12.0 Hz, 1H), 5.05 (d, *J* = 12.0 Hz, 1H), 4.88-4.80 (m, 1H), 4.13-4.08 (m, 1H), 3.57-3.47 (m, 2H), 3.42-3.34 (m, 2H), 1.92-1.77 (m, 1H), 1.64-1.44 (m, 7H), 1.28 (d, *J* = 6.4 Hz, 3H), 1.65-1.06 (m, 1H), 0.92-0.87 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.0, 169.9, 156.0, 136.3, 128.3 (2 C), 127.9, 127.9 (2 C), 66.7, 59.3, 46.2, 45.1, 43.1, 37.9, 26.2, 25.3, 24.7, 24.3, 18.7, 15.3, 11.3.
Minor diastereomer (selected peaks): ^{1}H-NMR (400 MHz, $CDCl_3$): δ 5.60 (d, *J* = 8.8 Hz, 1H), 5.10 (d, *J* = 12.0 Hz, 1H), 5.04 (d, *J* = 12.0 Hz, 1H). ^{13}C-NMR (400 MHz, $CDCl_3$): δ 170.2, 169.9,156.1, 66.7, 59.5, 46.3, 45.2, 37.7, 26.3, 24.5, 18.8, 15.4, 11.4. HRMS (CI) *m/z* calcd for $C_{22}H_{34}N_3O_4$ $[M+H]^+$ 404.2549. Found 404.2549. Elemental analysis calcd (%) for $C_{15}H_{24}F_3N_3O_3$: C 51.27, H 6.28, N 11.96. Found: C 51.93 H 6.54, N 11.67.

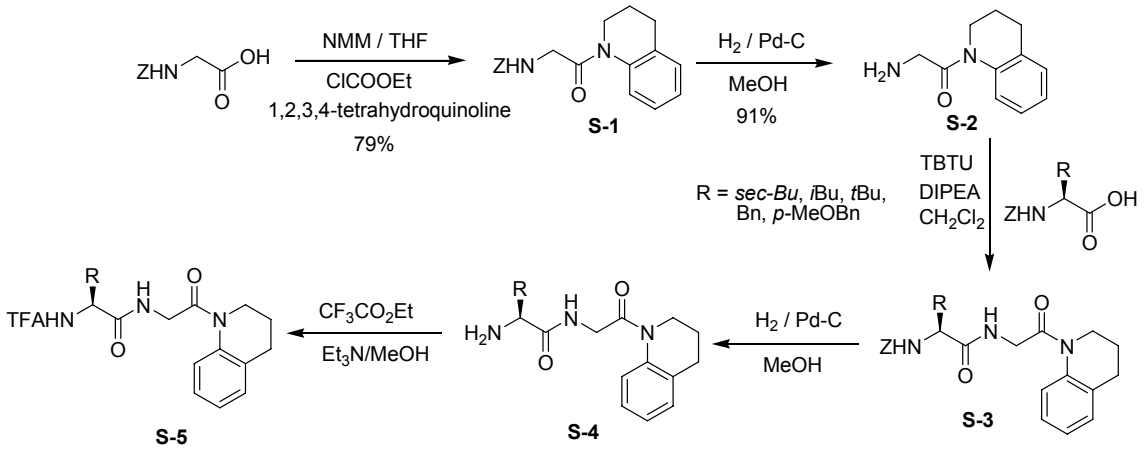
(2*S*,3*S*)-2-(2,2,2-Trifluoroacetamido)-3-methyl-N-[1-oxo-1-(piperidin-1-yl)propan-2-yl]pentanamide (5b). According to the general procedure for methylation of dipeptides (see main text) **5b** (85.2 mg, 0.23 mmol, 90%) was obtained from **4b** (100 mg, 0.28 mmol) as a mixture of two diastereomers after column chromatography (hexanes/EtOAc 7 : 3). Peaks of two diastereomers are overlapped; ^{1}H-NMR (400 MHz, $CDCl_3$) (two diastereomers): δ 7.68 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 1H), 7.63 (d, *J* = 7.6 Hz, 1H), 7.56 (d, *J* = 6.8 Hz, 1H), 4.96-4.86 (m, 1H), 4.51-4.43 (m, 1H), 3.61-3.51 (m, 2H), 3.46-3.40 (m, 2H), 1.93-1.83 (m, 1H), 1.67-1.49 (m, 7H), 1.32 (d, *J* = 6.4 Hz, 3H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.18-1.11 (m, 1H), 0.94-0.85 (m, 6H). ^{13}C-NMR (100 MHz, $CDCl_3$), diastereomer 1 : δ 169.7, 168.7, 156.8 (q, *J* = 37.1 Hz), 115.8 (q, *J* = 286.0 Hz), 57.6, 46.4, 45.6, 43.4, 38.0, 26.2, 25.3, 24.9, 24.2, 18.6, 14.9, 11.2; diastereomer 2: δ 169.7, 168.9, 156.8 (q, $^2J_{C,F}$ = 37.1 Hz), 115.8 (q, $^1J_{C,F}$ = 286.2 Hz), 57.8, 46.5, 45.3, 43.3, 37.8, 26.3, 25.4, 24.7, 24.3, 18.9, 15.1, 11.1. HRMS (CI) *m/z* calcd for $C_{16}H_{27}F_3N_3O_3$ $[M+H]^+$ 336.2005. Found 336.1994.

Benzyl (1*S*,2*S*)-1-[3-ethyl-3-hydroxy-1-oxo-1-(piperidin-1-yl)pentan-2-ylcarbamoyl]-2-methylbutylcarbamate (6a). According to the general procedure for methylation of dipeptides (see main text) **6a** (103.6 mg, 0.22 mmol, 85%) was obtained from **4a** (100 mg, 0.26 mmol) as a mixture of two diastereomers after column chromatography (hexanes/EtOAc 85 : 15). HPLC (Silicagel, hexanes/EtOAc 80 : 20, 1mL/min): t_R (55%) = 21.80 min, t_R (45%) = 24.67 min. Peaks of two diastereomers are overlapped; ^{1}H-NMR (400 MHz, $CDCl_3$) (two diastereomers): δ 7.34-7.26 (m, 5H), 7.95 (d, *J* = 8.4 Hz, 1H), 5.48 (d, *J* = 9.2 Hz, 1H), 5.12-5.03 (m, 2H), 4.89 (d, *J* = 9.2 Hz, 1H), 4.20-4.13 (m, 1H), 3.76-3.36 (m, 4H), 1.91-1.78 (m, 1H), 1.69-1.36 (m, 11H), 1.13-1.05 (m, 1H), 0.94-0.76 (m, 12H). ^{13}C-NMR (100 MHz, $CDCl_3$), major diastereomer: δ 170.7, 170.6, 156.1, 136.2, 128.4 (2 C), 128.0, 127.9 (2 C), 76.2, 66.9, 59.6, 49.2, 47.5, 43.1, 38.1, 27.8, 26.7, 25.7, 25.6, 24.3 (2 C), 15.4, 11.4, 7.4 (2 C). Minor diastereomer (selected peaks): δ 170.9, 170.6, 76.3, 59.3, 43.0, 37.9, 27.8, 26.6, 25.7, 25.6, 24.7, 24.3, 15.6, 11.4, 7.5,7.3. HRMS (CI) *m/z* calcd for $C_{26}H_{42}N_3O_5$ $[M+H]^+$ 476.3124. Found 476.3109.

(2*S*,3*S*)-2-(2,2,2-Trifluoroacetamido)-N-(3-ethyl-3-hydroxy-1-oxo-1-(piperidin-1-yl)pentan-2-yl)-3-methylpentanamide (6b). According to the general procedure for aldol reactions of dipeptides (see main text) **6b** (91.7 mg, 0.21 mmol, 85%) was obtained from **4b** (100 mg, 0.28 mmol) as a mixture of two diastereomers after column chromatography (hexanes/EtOAc 7:3).White solid; m.p.149-151°C; Major diastereomer: ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.05 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 9.2 Hz, 1H), 4.91 (d, *J* = 9.2 Hz, 1H), 4.63 (s, 1H), 4.43 (dd, *J* = 8.0 Hz, *J* = 4.8 Hz, 1H), 3.81-3.41 (m, 4H), 1.95-1.84 (m, 1H), 1.67-1.55 (m, 7H), 1.47-1.39 (m, 4H), 1.23-1.14 (m, 1H), 0.98-0.88 (m, 9H), 0.82 (d, *J* = 7.2 Hz, 3H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.2, 169.3, 156.7 (q, $^2J_{C,F}$ = 37.2 Hz), 115.7 (q, $^1J_{C,F}$ = 286.1 Hz), 76.4, 57.7, 49.5, 47.5, 43.2, 38.5, 27.7, 26.6, 25.8, 25.5, 24.3, 24.2, 15.3, 11.2, 7.5, 7.2. Minor diastereomer (selected peaks): ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.09 (d, *J* = 8.4 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 1H), 4.88 (d, *J* = 8.0 Hz, 1H), 4.64 (s, 1H). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 170.4, 169.5, 156.8 (q, $^2J_{C,F}$ = 36.9 Hz), 76.3, 57.3, 43.0, 38.1,

27.8, 26.7, 25.7, 25.6, 24.3, 15.0, 11.1, 7.4, 7.3. HRMS (CI) *m/z* calcd for $C_{20}H_{35}F_3N_3O_4$ $[M+H]^+$ 438.2580. Found 438.2509

General procedure for synthesis of dipeptide amides:



Scheme 1: Synthesis of dipeptide amides

Step 1: *N*-Methylmorpholine (11.8 mL, 107.6 mmol) was added to a solution of Z-glycine (15 g, 71.7 mmol) in THF (120 mL) at room temperature. The reaction mixture was cooled to -20 ^oC before ethylchloroformate (9.5 mL, 100.4 mmol) was slowly added and the solution was stirred for 10 min at -20 ^oC. To this reaction mixture 1,2,3,4-tetrahydroquinoline (9.9 mL, 78.8 mmol) was added and stirring was continued for 15 min at -20 ^oC before the cooling bath was removed and the mixture was stirred overnight at room temperature. H_2O (50 mL) was added and the aqueous layer was extracted three times with ethyl acetate (3 x 25 mL). The combined organic layers were washed with 1M HCl, saturated Na_2HCO_3 solution and H_2O. The solvent was dried over Na_2SO_4, evaporated in vacuo and the crude product was purified by column chromatography (hexane/EtOAc 4 : 1) to afford benzyl 2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethylcarbamate (**S-1**) in 79% yield (18.3 g, 56.6 mmol).

Step 2: Pd/C (1.83 g, 10% w/w) was dried in vacuo before MeOH (7 mL) was added. This vessel was purged with H_2 and charged with a solution of **S-1** (18.3 g, 56.6 mmol) in MeOH (150 mL). The reaction mixture was stirred overnight under H_2 atmosphere. The solution was filtered through a plug of celite, and concentrated to afford 2-amino-1-(3,4-dihydroquinolin-1(2*H*)-yl)ethanone **(S-2)** (10.7 g, 51.5 mmol, 91%) as a viscous oil.

Step 3: TBTU (1.15 g, 3.6 mmol) was added to a solution of Z-protected amino acid (3.0 mmol) in dichloromethane (10 mL) at 0 ^oC. To this solution diisopropylethylamine (1.5 mL, 9.0 mmol) was slowly added at 0 ^oC and the mixture was stirred for 15 min before 2-amino-1-(3,4-dihydroquinolin-1(2H)-yl)ethanone (**S-2**) (0.68 g, 3.6 mmol) in dichloromethane (5 mL) was added at 0 ^oC. After stirring for 10 min the cooling bath was removed and the mixture was stirred overnight at room temperature. H_2O (10 mL) was added to the reaction mixture, the aqueous layer was extracted twice with dichloromethane and the combined organic layers were successively washed with 1M $KHSO_4$, saturated $NaHCO_3$ solution and water. The solvent was removed under reduced pressure and the crude product was purified by column chromatography to give Z-protected dipeptide amide **S-3**.

Step 4: Pd/C (100 mg, 10% w/w) was dried in vacuo before MeOH (2 mL) was added. This vessel was purged with H_2 and charged with a solution of **S-3** (1.0 g) in MeOH (7 mL). The reaction mixture was stirred overnight under H_2 atmosphere. The solution was filtered through a plug of celite, and concentrated to afford **S-4**.

Step 5: Triethylamine (3.0 mmol) was added to a solution of **S-4** (1.5 mmol) in MeOH (7mL) and the reaction mixture was cooled 0 ^{o} C before trifloroacetic acid ethyl ester (3.0 mmol) was slowly added. The ice bath was removed and the reaction mixture was stirred for 6h. The methanol was removed under reduced pressure and the crude product was dissolved in ethyl acetate before the addition of 1M $KHSO_4$. The aqueous layer was extracted twice with ethyl acetate and the combined organic layers were washed with water and dried over Na_2SO_4. The solvent was removed in vacuo and the crude product was purified by flash chromatography to afford TFA-protected dipeptide amide **S-5.**

Benzyl (1*S*,2*S*)-1-[2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethylcarbamoyl]-2-methylbutylcarbamate (7a). Following the general procedure for the synthesis of dipeptide amides (scheme 1, step 3) **7a** (1.0 g, 2.28 mmol, 76%) was obtained from Z-L-Isoleucine (0.79 g, 3.0 mmol) as a white solid after column chromatography (hexanes/EtOAc 4 : 1). $[\alpha]_D^{20}$ = -8.7° (c = 1.0, $CHCl_3$): m.p. 123-125 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 7.77 (bs, 1H), 7.54 (d, *J* = 8.0 Hz, 1H), 7.35-7.34 (m, 4H), 7.31-7.27 (m, 1H), 7.19-7.16 (m, 2H), 7.11 (td, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H), 6.84 (bs, 1H), 5.07 (d, *J* = 13.0 Hz, 1H), 5.04 (d, *J* = 13.0 Hz, 1H), 4.11 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 4.05 (dd, *J* = 16.5 Hz, *J* = 5.0 Hz, 1H), 3.98 (dd, *J* = 8.5 Hz, *J* = 7.0 Hz, 1H), 3.70 (t, *J* = 6.5 Hz, 2H), 2.72 (t, *J* = 6.5 Hz, 2H), 1.91 (quin, *J* = 6.5 Hz, 2H), 1.83-1.75 (m, 1H), 1.52-1.44 (m, 1H), 1.20-1.11 (m, 1H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.84 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.6, 167.4, 155.3, 137.8, 136.6, 131.7, 127.9, 127.6 (2 C), 127.0, 126.9 (2 C), 125.2, 124.2, 123.6, 65.0, 59.0, 42.6, 41.1, 36.2, 25.6, 23.9, 22.8, 14.8, 10.3. HRMS (CI) *m/z* calcd for $C_{25}H_{32}N_3O_4$ $[M+H]^+$ 338.2393. Found 338.2402

(2*S*,3*S*)-2-(2,2,2-Trifluoroacetamido)-N-[2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethyl]-3-methylpentanamide (7b). Following the general procedure for the synthesis of dipeptide amides (scheme 1, step 4 and step 5) **7b** (0.75 g, 1.87 mmol) was obtained from **7a** (1.0 g, 2.28 mmol) as a white solid in 82% yield over two steps after column chromatography (hexane/EtOAc 7 : 3). $[\alpha]_D^{20}$ = -5.1° (c = 1.0, $CHCl_3$); m.p. 152-154 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.98 (bs, 1H), 8.05 (bs, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.19-7.16 (m, 2H), 7.10 (td, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H), 4.29 (d, *J* = 7.5 Hz, 1H), 4.14 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 4.08 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 3.70 (td, *J* = 6.0 Hz, *J* = 1.5 Hz, 1H), 2.72 (t, *J* = 6.5 Hz, 2H), 1.97-1.89 (m, 3H), 1.52-1.44 (m, 1H), 1.21-1.12 (m, 1H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.85 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 169.0, 167.2, 155.7 (q, $^2J_{C\text{-}F}$ = 36.2), 137.8, 131.7, 127.9, 125.2, 124.3, 123.6, 115.4 (q, $^1J_{C\text{-}F}$ = 286.3), 57.3, 42.6, 41.2, 35.4, 25.6, 23.9, 22.8, 14.5, 9.8. HRMS (CI) *m/z* calcd for $C_{19}H_{25}F_3N_3O_3$ $[M+H]^+$ 400.1848. Found 400.1853

Benzyl (S)-1-(2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethylcarbamoyl)-2 phenylethylcarbamate (8a). Following the general procedure for the synthesis of dipeptide amides (scheme 1, step 3) **8a** (1.0 g, 2.13 mmol, 71%) was obtained from Z-L-Phenylalanine (0.79 g, 3.0 mmol) as a white solid after column chromatography (hexanes/EtOAc 4 : 1). $[\alpha]_D^{20}$ = -9.8° (c = 1.0, $CHCl_3$); m.p. 120-122 °C; ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.85 (bs, 1H), 7.52 (d, *J* = 8.0 Hz, 1H), 7.29-7.19 (m, 9H), 7.17-7.14 (m, 3H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.03 (bs, 1H), 4.96 (d, *J* = 16.5 Hz, 1H), 4.93 (d, *J* = 16.5 Hz, 1H), 4.34-4.29 (m, 1H), 4.09 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 4.05 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 3.69-3.66 (m, 2H), 3.05 (dd, *J* = 14.0 Hz, *J* = 4.5 Hz, 1H), 2.80 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.69 (t, *J* = 6.5 Hz, 2H), 1.87 (quintet, *J* = 6.5 Hz, 2H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.8, 167.4, 155.1, 137.7, 137.5, 136.5, 131.7, 128.5 (2 C), 127.9, 127.6, 127.4 (2 C), 126.9 (2 C), 126.7 (2 C), 125.6, 125.2, 124.3, 123.6, 64.9, 55.7, 42.7, 41.4, 37.1, 25.6, 22.8. HRMS (CI) *m/z* calcd for $C_{28}H_{30}N_3O_4$ $[M+H]^+$: 472.2236. Found 472.2258. Elemental analysis calcd (%) for $C_{28}H_{29}N_3O_4$: C 71.32, H 6.20, N 8.91. Found: C 71.18, H 6.16, N 8.94.

(*S*)-2-(2,2,2-Trifluoroacetamido)-N-[2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethyl]-3-phenylpropanamide (8b). Following the general procedure for the synthesis of dipeptide amides (scheme

1, step 4 and step 5) **8b** (0.78 g, 1.80 mmol) was obtained from **8a** (1.0 g, 2.28 mmol) as a white solid in 79% yield over two steps after column chromatography (hexane/EtOAc 7 : 3). $[\alpha]_D^{20}$ = +15.5° (c = 1.0, $CHCl_3$); m.p. 124-126 °C; ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 9.23 (d, *J* = 6.0 Hz, 1H), 8.14 (bs, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.29-7.24 (m, 4H), 7.21-7.17 (m, 3H), 7.11 (t, *J* = 7.0 Hz, 1H), 4.70-4.66 (m, 1H), 4.15 (dd, *J* = 16.5 Hz, *J* = 5.0 Hz, 1H), 4.11 (dd, *J* = 16.5 Hz, *J* = 5.0 Hz, 1H), 3.76-3.67 (m, 2H), 3.18 (dd, *J* = 14.0 Hz, *J* = 4.5 Hz, 1H), 2.98 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.73 (t, *J* = 6.5 Hz, 2H), 1.93 (quintet, *J* = 6.5 Hz, 2H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ169.1, 167.3, 155.6 (q, $^2J_{C,F}$ = 36.5 Hz), 137.8, 136.8, 131.7, 128.4 (2 C), 127.9, 127.4 (2 C), 125.8, 125.2, 124.3, 123.6, 115.1 (q, $^1J_{C,F}$ = 286.6 Hz), 54.2, 42.7, 41.4, 36.3, 25.7, 22.8. HRMS (CI) *m/z* calcd for $C_{22}H_{23}F_3N_3O_3$ $[M+H]^+$: 434.1692. Found 434.1615. Elemental analysis calcd (%) for $C_{22}H_{22}F_3N_3O_3$: C 60.96, H 5.12, N 9.69. Found: C 61.13, H 5.06, N 9.47.

***tert*-Butyl (*S*)-1-[2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethylcarbamoyl]-2-phenylethylcarbamate (8c).** Following the general procedure for the synthesis of dipeptide amides (scheme 1, step 4) **S-4** (R=Bn) was obtained from **8a** (1.0 g, 2.28 mmol) as a viscous oil in 92% yield (0.71 g, 2.1 mmol).

Triethylamine (0.6 mL, 4.2 mmol) was added to a THF solution (7mL) of **S-4** (0.71 g, 2.1 mmol) and the reaction mixture was cooled 0 ^{o} C before di-tert-butyl dicarbonate (687 mg, 3.1 mmol) was slowly added. The ice bath was removed and the reaction mixture was stirred overnight. A 1M $KHSO_4$ was added and the aqueous layer was extracted twice with ethyl acetate and the combined organic layers were washed with water and dried over Na_2SO_4. The solvent was removed in vacuo and the crude product was purified by flash chromatography (hexane/EtOAc 85 : 15) to afford **8c** (0.735 g, 1.7 mmol, 80%) as a white solid. $[\alpha]_D^{20}$ = -12.3° (c = 1.0, $CHCl_3$); m.p. 149-151 °C; ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.77 (bs, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.25-7.24 (m, 4H), 7.20-7.17 (m, 3H), 7.11 (dt, *J* = 7.5 Hz, 1.0 Hz, 1H), 6.44 (bs, 1H), 4.28-4.23 (m, 1H), 4.13 (dd, *J* = 16.5 Hz, *J* = 5.0 Hz, 1H), 4.08 (dd, *J* = 16.5 Hz, *J* = 5.0 Hz, 1H), 3.71-3.69 (m, 2H), 3.06 (dd, *J* = 14.0 Hz, *J* = 4.5 Hz, 1H), 2.80 (dd, *J* = 14.0 Hz, *J* = 9.5 Hz, 1H), 2.74-2.72 (m, 2H), 1.92 (quintet, *J* = 6.5 Hz, 2H), 1.26 (s, 9H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ170.9, 167.4, 154.4, 137.8, 137.6, 131.7, 128.6 (2 C), 127.9, 127.3 (2 C), 125.5, 125.3, .124.3, 123.6, 77.7, 55.3, 42.6, 41.3, 37.2, 27.6 (3 C), 25.6, 22.8. HRMS (CI) *m/z* calcd for $C_{25}H_{32}N_3O_4$ $[M+H]^+$: 438.2393. Found 438.2397. Elemental analysis calcd (%) for $C_{25}H_{31}N_3O_4$: C 68.03, H 7.14, N 9.60. Found: C 67.66, H 7.03, N 9.37.

(*S*)-N-[2-(3,4-Dihydroquinolin-1(2*H*)-yl)-2-oxoethyl]-3-phenyl-2-(tosylamino)propanamide (8d). *p*-Toluenesulfonyl chloride (520 mg, 2.7 mmol) was added to a solution of **S-4** (0.71 g, 2.1 mmol) in CH_2Cl_2 (7 mL) and the reaction mixture was cooled 0 ^{o} C before triethylamine (0.4 mL, 2.7 mmol) was slowly added. The ice bath was removed and the reaction mixture was stirred for overnight at room temperature. 1M $KHSO_4$ solution was added and the aqueous layer was extracted twice with ethyl acetate and the combined organic layers were washed with water and dried over Na_2SO_4. The solvent was removed in vacuo and the crude product was purified by flash chromatography (hexane/EtOAc 3 : 2) to afford **8d** (0.835 g, 1.7 mmol, 82%) as a white solid. $[\alpha]_D^{20}$ = -57.7° (c = 1.0, $CHCl_3$); m.p. 144-146 °C; ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.84 (bs, 1H), 7.52-7.47 (m, 4H), 7.21-7.10 (m, 10H), 4.05 (bs, 1H), 3.93 (d, *J* = 5.5 Hz, 2H), 3.65 (d, *J* = 6.5 Hz, 2H), 2.93 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 2.73-2.69 (m, 3H), 2.32 (s, 3H) 1.91 (quintet, *J* = 6.5 Hz, 2H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 169.8, 167.1, 141.6, 137.8, 137.7, 136.6, 131.7, 128.6 (2 C), 128.5 (2 C), 127.9, 127.3 (2 C), 125.8 (2 C), 125.5, 125.2, 124.3, 123.6, 57.4, 42.6, 41.3, 37.9, 25.6, 22.8, 20.2. HRMS (CI) *m/z* calcd for $C_{27}H_{30}N_3O_4S$ $[M+H]^+$: 492.1957. Found 492.1967. Elemental analysis calcd (%) for $C_{27}H_{29}N_3O_4S$: C 64.97, H 5.95, N 8.55. Found: C 65.29, H 5.91, N 8.48.

(*S*)-2-(2,2,2-Trifluoroacetamido)-N-(2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethyl)-4-methylpentanamide (11). Following the general procedure for steps 3 to 5, dipeptide amide **11** was

obtained from Z-L-Leucine (0.79 g, 3.0 mmol) as a white solid in 56% overall yield (0.67 g, 1.7 mmol). $[\alpha]_D^{20}$ = -20.2° (c = 1.0, $CHCl_3$); m.p. 68-70 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.19 (d, *J* = 3.0 Hz, 1H), 7.96 (bs, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.19-7.16 (m, 2H), 7.11 (t, *J* = 8.0 Hz, 1H), 4.46-4.42 (m, 1H), 4.12 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 4.05 (dd, *J* = 16.5 Hz, *J* = 5.0 Hz, 1H), 3.74-3.69 (m, 2H), 2.72 (t, *J* = 7.0 Hz, 2H), 1.94-1.89 (m, 2H), 1.70-1.59 (m, 3H), 0.92 (d, *J* = 6.0 Hz, 3H), 0.88 (d, *J* = 6.0 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 169.9, 167.3, 155.7 (q, $^2J_{C,F}$ = 36.4 Hz), 137.8, 131.7, 127.9, 127.4, 125.2, 124.3, 123.6, 118.3, 115.4 (q, $^1J_{C,F}$ = 286.7 Hz), 51.6, 42.6, 41.3, 25.6, 23.8, 22.8, 22.1, 20.8. HRMS (CI) *m/z* calcd for $C_{19}H_{25}F_3N_3O_3$ $[M+H]^+$ 400.1848. Found 400.1868. Elemental analysis calcd (%) for $C_{19}H_{24}F_3N_3O_3$: C 57.14, H 6.06, N 10.52 and found: C 57.37, H 6.02, N 10.48.

(*S*)-2-(2,2,2-Trifluoroacetamido)-N-[2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethyl]-3,3-dimethylbutanamide (13). Following the general procedure for steps 3 to 5, dipeptide amide **12** was obtained from Z-L-*tert*-Leucine (0.79 g, 3.0 mmol) as a white solid in 60% overall yield (0.72 g, 1.8 mmol). $[\alpha]_D^{20}$ = -9.6° (c = 1.0, $CHCl_3$); m.p. 138-140 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.53 (d, *J* = 9.0 Hz, 1H), 8.12 (bs, 1H), 7.53 (d, *J* = 8.0 Hz, 1H), 7.19-7.16 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 4.41 (d, *J* = 9.5 Hz, 1H), 4.16 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 4.07 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 3.72-3.69 (m, 2H), 2.72 (t, *J* = 6.5 Hz, 2H), 1.92 (quin, *J* = 6.5, 2H), 1.00 (s, 9H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 168.0, 167.2, 155.7 (q, $^2J_{C,F}$ = 36.5 Hz), 137.8, 131.7, 127.9, 125.2, 124.3, 123.6, 115.4 (q, $^1J_{C,F}$ = 287.0 Hz), 60.6, 42.7, 41.2, 33.9, 25.9 (3 C), 25.6, 22.8. HRMS (CI) *m/z* calcd for $C_{19}H_{25}F_3N_3O_3$ $[M+H]^+$ 400.1848. Found 400.1837. Elemental analysis calcd (%) for $C_{19}H_{24}F_3N_3O_3$: C 57.14, H 6.06, N 10.52. Found: C 57.37, H 6.02, N 10.48.

(*S*)-2-(2,2,2-Trifluoroacetamido)-N-[2-(3,4-dihydroquinolin-1(2*H*)-yl)-2-oxoethyl]-3-(4-methoxyphenyl)propanamide (15). Following the general procedure for steps 3 to 5, dipeptide amide **15** was obtained from Z-L-OMe-Tyrosine (0.98 g, 3.0 mmol) as a white solid in 50% overall yield (0.69 g, 1.8 mmol). $[\alpha]_D^{20}$ = +20.7° (c = 1.0, $CHCl_3$); m.p. 149-151 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.14 (d, *J* = 6.5 Hz, 1H), 8.08 (bs, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.20-7.17 (m, 4H), 7.11 (t, *J* = 8.0 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.64-4.59 (m, 1H), 4.14 (dd, *J* = 16.5 Hz, *J* = 5.0 Hz, 1H), 4.10 (dd, *J* = 16.5 Hz, *J* = 5.5 Hz, 1H), 3.73 (s, 3H), 3.72-3.68 (m, 2H), 3.10 (dd, *J* = 14.0 Hz, *J* = 4.5 Hz, 1H), 2.92 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.73 (t, *J* = 6.5 Hz, 2H), 1.92 (quin, *J* = 6.5, 2H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 169.1, 167.3, 157.6, 155.6 (q, $^2J_{C,F}$ = 36.2 Hz), 137.8, 131.7, 129.5 (2 C), 128.7, 127.9, 125.2, 124.3, 123.6, 115.3 (q, $^1J_{C,F}$ = 286.7 Hz), 113.2 (2 C), 54.5, 54.4, 42.7, 41.4, 35.5, 25.6, 22.8. HRMS (CI) *m/z* calcd for $C_{23}H_{25}F_3N_3O_4$ $[M+H]^+$ 464.1797. Found 464.1787. Elemental analysis calcd (%) for $C_{23}H_{24}F_3N_3O_4$: C 59.61, H 5.22, N 9.07. Found: C 59.41, H 5.18, N 8.77.

Products **9a**, **9b**, **10a**, **10c** and **10d** were obtained following the general procedure for methylation of dipeptide amides (see main text). Analytical data of these compounds are given below.

Benzyl (1*S*,2*S*)-1-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxopropan-2-ylcarbamoyl]-2-methylbutylcarbamate (9a). HPLC (Silicagel, hexane/EtOAc 7 : 3, 1mL/min): t_R (40%) = 16.89 min, t_R (60%) = 20.09 min. Minor diastereomer: $[\alpha]_D^{20}$ = -72.9° (c = 1.0, $CHCl_3$); m.p. 143-145 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 7.87 (d, *J* = 7.0 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 7.35-7.34 (m, 4H), 7.31-7.28 (m, 1H), 7.20-7.15 (m, 2H), 7.11 (td, *J* = 7.5 Hz, *J* = 1.5 Hz, 1H), 6.82 (bs, 1H), 5.07 (d, *J* = 13.0 Hz, 1H), 5.04 (d, *J* = 13.0 Hz, 1H), 4.98-4.91 (m, 1H), 3.96 (dd, *J* = 9.0 Hz, *J* = 7.5 Hz, 1H), 3.89-3.84 (m, 1H), 3.54-3.49 (m, 1H), 2.72 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.66 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 1.98-1.91 (m, 1H), 1.89-1.81 (m, 1H), 1.78-1.70 (m, 1H), 1.51-1.42 (m, 1H), 1.15 (d, *J* = 7.0 Hz, 3H), 1.13-1.08 (m, 1H), 0.85 (d, *J* = 7.0 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 171.2, 170.0, 155.2, 138.2, 136.6, 132.1, 127.9, 127.6 (2 C), 127.0, 126.8 (2 C), 125.2, 124.4, 123.7, 64.9, 58.8, 45.0, 42.7, 36.6, 25.4, 23.9, 22.9, 17.1, 14.7,

10.3. HRMS (CI) *m/z* calcd for $C_{26}H_{34}N_3O_4$ $[M+H]^+$ 452.2549. Found 452.2546. Elemental analysis calcd (%) for $C_{26}H_{33}N_3O_4$: C 69.16, H 7.37, N 9.31. Found: C 69.11, H 7.22, N 9.10.
Major diastereomer: $[\alpha]_D^{20}$ = +27.3° (c = 1.0, $CHCl_3$); m.p. 103-105 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 7.84 (d, *J* = 7.0 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.35-7.33 (m, 4H), 7.30-7.27 (m, 1H), 7.20-7.16 (m, 2H), 7.12 (td, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H), 6.81 (bs, 1H), 5.05 (s, 2H), 4.98-4.92 (m, 1H), 3.96 (dd, *J* = 9.0 Hz, *J* = 7.0 Hz, 1H), 3.86-3.81 (m, 1H), 3.57-3.52 (m, 1H), 2.74 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 2.66 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 1.98-1.91 (m, 1H), 1.89-1.83 (m, 1H), 1.79-1.71 (m, 1H), 1.49-1.41 (m, 1H), 1.17 (d, *J* = 7.0 Hz, 3H), 1.14-1.11 (m, 1H), 0.87 (d, *J* = 6.5 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 171.3, 170.0, 155.2, 138.3, 136.6, 132.2, 127.9, 127.6 (2 C), 127.0, 126.8 (2 C), 125.2, 124.5, 123.7, 64.9, 58.7, 45.0, 42.7, 36.3, 25.4, 23.8, 22.9, 17.0, 14.7, 10.3. HRMS (CI) *m/z* calcd for $C_{26}H_{34}N_3O_4$ $[M+H]^+$ 452.2549. Found 452.2557.

(2*S*,3*S*)-2-(2,2,2-Trifluoroacetamido)-N-(1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxopropan-2-yl)-3-methylpentanamide (9b). Minor diastereomer; $[\alpha]_D^{20}$ = -99.0° (c = 1.0, $CHCl_3$); m.p. 169-171 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.96 (d, *J* = 7.0 Hz, 1H), 8.19 (d, *J* = 7.5 Hz, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.19-7.15 (m, 2H), 7.11 (td, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H), 4.98 (quin, *J* = 7.5 Hz, 1H), 4.28 (t, *J* = 8.0 Hz, 1H), 3.88-3.83 (m, 1H), 3.55-3.50 (m, 1H), 2.74 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 2.67 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 1.98-1.82 (m, 3H), 1.49-1.41 (m, 1H), 1.18 (d, *J* = 7.0 Hz, 3H), 1.15-1.09 (m, 1H), 0.87(d, *J* = 6.5 Hz, 3H), 0.84 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 171.0, 168.3, 155.6 (q, $^2J_{C,F}$ = 36.4 Hz), 138.2, 132.1, 127.9, 125.2, 124.5, 123.7, 115.4 (q, $^1J_{C,F}$ = 286.8 Hz), 57.3, 45.1, 42.7, 35.4, 25.3, 24.0, 22.9, 17.0, 14.5, 9.8.
Major diastereomer; $[\alpha]_D^{20}$ = +46.0° (c = 1.0, $CHCl_3$); m.p. 143-145 °C; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.93 (bs, 1H), 8.13 (d, *J* = 6.5 Hz, 1H), 7.46 (d, *J* = 8.0 Hz, 1H), 7.20-7.16 (m, 2H), 7.12 (td, *J* = 7.5 Hz, *J* = 1.0 Hz, 1H), 4.98-4.82 (m, 1H), 4.28-4.25 (m, 1H), 3.84-3.79 (m, 1H), 3.61-3.55 (m, 1H), 2.77-2.64 (m, 2H), 1.96-1.87 (m, 3H), 1.49-1.41 (m, 1H), 1.20 (d, *J* = 7.0 Hz, 3H), 1.13-1.10 (m, 1H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.84 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 172.2, 169.5, 155.7 (q, $^2J_{C,F}$ = 36.2 Hz), 139.3, 133.3, 128.9, 126.3, 125.5, 124.7, 116.4 (q, $^1J_{C,F}$ = 286.8 Hz), 58.2, 46.2, 43.7, 36.5, 26.4, 24.9, 24.0, 17.8, 15.5, 10.9. HRMS (CI) *m/z* calcd for $C_{20}H_{27}F_3N_3O_3$ $[M+H]^+$ 414.2005. Found 414.2025. HPLC (Silicagel, hexane/EtOAc 7 : 3, 1mL/min): t_R (36%) = 18.06 min, t_R (64%) = 23.18 min.

Benzyl (*S*)-1-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxopropan-2-ylcarbamoyl]-2-phenylethyl-carbamate (10a). HPLC (Silicagel, hexane/EtOAc 6 : 4, 1mL/min): t_R (41%) = 13.01 min, t_R (59%) = 14.84 min. Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.96 (d, *J* = 7.0 Hz, 1H), 7.49 (d, *J* = 8.0 Hz, 1H), 7.34-7.10 (m, 13H), 6.99 (bs, 1H), 4.98-4.93 (m, 3H), 4.37-4.31 (m, 1H), 3.91-3.82 (m, 1H), 3.57-3.49 (m, 1H), 3.06-2.98 (m, 1H) , 2.85-2.63 (m, 3H), 1.99-1.84 (m, 2H), 1.18 (d, *J* = 7.0 Hz, 3H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 171.3, 170.2, 154.9, 138.2, 137.3, 136.5, 132.2, 128.6 (2 C), 127.9, 127.6 (2 C), 127.4 (2 C), 126.9, 126.7 (2 C), 125.5, 125.3, .124.5, 123.7, 64.8, 55.4, 45.2, 42.7, 37.1, 25.3, 23.0. 17.1. Minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.92 (d, *J* = 7.5 Hz, 1H), 7.50 (d, *J* = 8.0 Hz, 1H), 1.11 (d, *J* = 7.0 Hz, 3H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ = 171.2, 170.1, 155.0,138.2, 137.2, 136.6, 132.1, 125.6, 125.2, 124.4, 123.8, 55.6, 45.1, 37.4, 22.9, 17.2. HRMS (CI) *m/z* calcd for $C_{29}H_{32}N_3O_4$ $[M+H]^+$: 486.2393. Found 486.2375. Elemental analysis calcd (%) for $C_{29}H_{31}N_3O_4$: C 71.73, H 6.43, N 8.65. Found: C 71.20, H 6.63, N 8.15.

***tert*-Butyl (*S*)-1-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxopropan-2-ylcarbamoyl]-2-phenylethyl-carbamate (10c).** HPLC (Silicagel, hexane/EtOAc 7 : 3, 1mL/min): t_R (40%) = 17.79 min, t_R (60%) = 19.85 min. Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.85 (d, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 7.5 Hz, 1H), 7.25-7.11 (m, 8H), 6.42 (bs, 1H), 5.00-4.92 (m, 1H), 4.26-4.21 (m, 1H), 3.90-3.82 (m, 1H), 3.57-3.50 (m, 1H), 3.03-2.96 (m, 1H), 2.82-2.50 (m, 3H), 1.98-1.93 (m,

1H), 1.91-1.85 (m, 1H), 1.32 (s, 9H), 1.19 (d, *J* = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ = 171.3, 170.3, 154.3,138.2, 137.4, 132.2, 128.6 (2 C), 127.9, 127.3 (2 C), 125.5, 125.3, .124.5, 123.7, 77.7. 55.1, 45.1, 42.7, 37.1, 27.5 (3 C), 25.4, 22.9, 17.2. Minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 1.33 (s, 9H), 1.27 (d, *J* = 7.0 Hz, 3H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ = 171.2, 170.2, 154.4,137.3, 124.5, 55.3, 45.0, 37.4, 17.2. HRMS (CI) *m/z* calcd for $C_{26}H_{34}N_3O_4$ $[M+H]^+$: 452.2549Found 452.2555.

(2*S*)-N-[1-(3,4-Dihydroquinolin-1(2*H*)-yl)-1-oxopropan-2-yl]-3-phenyl-2-(tosylamino)propanamide (10d). White solid; m.p. 67-70 °C; Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.88 (d, *J* = 7.0 Hz, 1H),), 7.54-7.46 (m, 3H), 7.37 (t, *J* = 7.0 Hz, 1H), 7.19-7.11 (m, 10H), 4.79 (quintet, *J* = 7.0 Hz, 1H), 4.11-4.03 (m, 1H), 3.89-3.84 (m, 1H), 3.51-3.44 (m, 1H), 2.90-2.85 (m, 1H),), 2.76-2.61 (m, 3H),), 2.28 (s, 3H), 1.87-1.82 (m, 2H), 0.97 (d, *J* = 6.5 Hz, 3H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.9, 169.2, 141.6, 138.0, 137.8, 136.4, 132.2, 128.7 (2 C), 128.6 (2 C), 127.9, 127.3 (2 C), 125.8 (2 C), 125.6, 125.3, 124.5, 123.7, 57.4, 44.8, 42.6, 38.3, 25.2, 22.9, 20.2, 17.1. Minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.95 (d, *J* = 7.0 Hz, 1H), 4.75-4.69 (m, 1H), 3.82-3.77 (m, 1H), 2.31 (s, 3H), 1.04 (d, *J* = 7.0 Hz, 3H) ; ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 171.0, 169.1, 138.1, 138.0, 136.5, 132.1, 128.7 (2 C), 128.5 (2 C), 127.8, 127.2 (2 C), 125.9, 125.5, 123.6, 55.8, 45.0, 42.7, 37.9, 25.3, 16.9. HRMS (CI) *m/z* calcd for $C_{28}H_{32}N_3O_4S$ $[M+H]^+$: 506.2114. Found 506.2101. Diastereomeric ratio (53:47) was determined from crude nmr.

Products **10e**, **10g-10p**, **12**, **14** and **16** were obtained following the general procedure for palladium-catalyzed allylic alkylation of dipeptide amide (see main text). Analytical data of these compounds are given below.

(2*S*)-N-[1-(3,4-Dihydroquinolin-1(2*H*)-yl)-4-methyl-1-oxopent-4-en-2-yl]-3-phenyl-2-(tosylamino)propanamide (10e). HPLC (Silicagel, hexane/EtOAc 7 : 3, 1mL/min, 254 nm): t_R (24%) = 12.26 min, t_R (76%) = 13.63 min. Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 8.02 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.26 (bs, 1H), 7.21-7.11 (m, 11H), 5.04 (q, *J* = 8.0 Hz, 1H), 4.63 (s, 1H), 4.55 (s, 1H), 4.17-4.13 (m, 1H), 4.08-4.03 (m, 1H), 3.35-3.30 (m, 1H), 2.88 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 2.69 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.76-2.71 (m, 1H), 2.62-2.57 (m, 1H), 2.25 (s, 3H), 2.18 (dd, *J* = 9.0 Hz, *J* = 6.5 Hz, 1H), 2.00-1.95 (m, 2H), 1.83-1.76 (m, 1H), 1.35 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.2, 169.4, 141.5, 140.1, 138.1, 137.9, 136.6, 132.6, 128.8 (2 C), 128.6 (2 C), 127.7, 127.2 (2 C), 125.8 (2 C), 125.6, 125.3, 124.6, 123.9, 112.5, 57.1, 47.9, 42.5, 40.4, 38.4, 25.4, 23.0, 20.9, 20.2. Minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 7.99 (d, *J* = 7.5 Hz, 1H), 4.96 (q, *J* = 7.5 Hz, 1H), 4.65 (s, 1H), 4.00-3.95 (m, 1H), 2.30 9s, 3H), 1.38 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.2, 169.5, 141.6, 137.9, 137.8, 136.5, 128.67(2 C), 127.3 (2 C), 125.9 (2 C), 112.4, 56.9, 47.9, 40.1, 38.2, 23.0, 21.0. 20.3. HRMS (CI) *m/z* calcd for $C_{31}H_{36}N_3O_4S$ $[M+H]^+$: 546.2348. Found 546.2424.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxopent-4-en-2-yl]-3-phenylpropanamide (10g). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (15%) = 14.45 min, t_R (85%) = 19.04 min. Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 9.21 (d, *J* = 8.5 Hz, 1H), 8.28 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.29-7.11 (m, 8H), 5.64-5.54 (m, 1H), 5.01-4.96 (m, 3H), 4.72-4.69 (m, 1H), 3.97-3.92 (m, 1H), 3.49-3.44 (m, 1H), 3.10 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 2.96 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.77-2.72 (m, 1H), 2.68-2.62 (m, 1H), 2.39-2.33 (m, 1H), 2.26-2.21 (m, 1H), 2.00-1.92 (m, 1H), 1.88-1.80 (m, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 169.8, 168.6, 155.5 (q, $^2J_{C,F}$ = 36.2 Hz), 138.0, 136.6, 132.9, 132.3, 128.5 (2 C), 127.9, 127.4 (2 C), 125.8, 125.2, 123.8, 116.9, 115.2 (q, $^1J_{C,F}$ = 286.5 Hz), 54.1, 49.1, 42.8, 36.6, 35.6, 25.4, 23.0. Minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6 ,

353 K): δ 9.18 (d, *J* = 8.5 Hz, 1H), 8.22 (d, *J* = 7.5 Hz, 1H), 7.46 (d, *J* = 8.5 Hz, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 169.9, 168.7, 136.7, 128.4 (2 C), 127.8, 125.3, 123.7, 53.9, 49.3, 36.2, 35.5, 23.0. HRMS (CI) *m/z* calcd for $C_{25}H_{27}F_3N_3O_3$ $[M+H]^+$: 474.2005. Found 474.2035.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[(*E*)-1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxo-5-phenyl-pent-4-en-2-yl]-3-phenylpropanamide (10h). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (14%) = 24.63 min, t_R (86%) = 31.90 min. Major diastereomer; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.22 (d, *J* = 8.5 Hz, 1H), 8.39 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 8.0 Hz, 1H), 7.30-7.16 (m, 12H), 7.12 (t, *J* = 7.5 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 6.02-5.96 (m, 1H), 5.16-5.12 (m, 1H), 4.75-4.70 (m, 1H), 4.02-3.95 (m, 1H), 3.50-3.43 (m, 1H), 3.09 (dd, *J* = 15.0 Hz, *J* = 5.0 Hz, 1H), 2.93 (dd, *J* = 15.0 Hz, *J* = 10.0 Hz, 1H), 2.71-2.65 (m, 1H), 2.59-2.52 (m, 2H), 2.43-2.38 (m, 1H), 1.95-1.90 (m, 1H), 1.85-1.78 (m, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 169.9, 168.7, 155.5 (q, $^2J_{C,F}$ = 36.7 Hz), 115.2 (q, $^1J_{C,F}$ = 287.2 Hz), 138.0, 136.6, 136.4, 131.9, 128.5 (2 C), 127.9, 127.8 (2 C), 127.4, (2 C), 126.6, 125.5, 125.4, 125.4 (2 C), 125.3, 124.7, 124.6, 123.8, 54.1, 49.2, 42.8, 36.6, 35.1, 25.3, 22.9. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.33 (d, *J* = 8.5 Hz, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 6.38 (d, *J* = 16.0 Hz, 1H), 3.96-3.93 (m, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 169.9, 168.8, 131.7, 127.4(2 C), 123.7, 54.0, 49.6, 36.2, 35.0, 23.0. HRMS (CI) *m/z* calcd for $C_{31}H_{31}F_3N_3O_3$ $[M+H]^+$ 550.2318. Found 550.2266.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[(*E*)-1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxooct-4-en-2-yl]-3-phenylpropanamide (10i). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (9%) = 13.79 min, t_R (91%) = 18.57 min. Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6, 353 K): δ 9.20 (d, *J* = 8.0 Hz, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.29-7.20 (m, 4H), 7.18-7.11 (m, 4H), 5.41 (dt, *J* = 15.5 Hz, *J* = 6.5 Hz 1H), 5.19 (dt, *J* = 15.5 Hz, *J* = 7.0 Hz 1H), 5.02-4.97 (m, 1H), 4.73-4.68 (m, 1H), 4.00-3.96 (m, 1H), 3.47-3.42 (m, 1H), 3.10 (dd, *J* = 13.5 Hz, *J* = 5.0 Hz, 1H), 2.96 (dd, *J* = 13.5 Hz, *J* = 10.0 Hz, 1H), 2.78-2.72 (m, 1H), 2.67-2.61 (m, 1H), 2.33-2.28 (m, 1H), 2.20-2.14 (m, 1H), 2.00-1.94 (m, 1H), 1.90-1.80 (m, 3H), 1.29 (sex, *J* = 7.5 Hz, 2H), 0.82 (t, *J* = 7.5 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.0, 168.6, 155.5 (q, $^2J_{C,F}$ = 36.2 Hz),138.1, 136.6, 132.6, 132.3, 128.5 (2 C), 127.8, 127.4 (2 C), 125.8, 125.2, 124.5, 124.2, 123.8, 115.2 (q, $^1J_{C,F}$ = 287.1 Hz), 54.1, 49.5, 42.7, 36.6, 34.6, 33.3, 25.4, 23.0, 21.1, 12.6. minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6, 353 K): δ 9.14 (d, *J* = 8.5 Hz, 1H), 8.17 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.1, 168.7,136.6, 132.5, 123.7, 53.9, 49.7, 36.3, 34.5. HRMS (CI) *m/z* calcd for $C_{28}H_{33}F_3N_3O_3$ $[M+H]^+$: 516.2474. Found 516.2436.

Analytical data of compound **10k**. HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (17%) = 9.88 min, t_R (87%) = 12.49 min. Major diastereomer; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.19 (d, *J* = 8.5 Hz, 1H), 8.27 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.29-7.24 (m, 4H), 7.20-7.15 (m, 3H), 7.12 (t, *J* = 7.5 Hz, 1H), 5.58-5.49 (m, 1H), 5.45-5.36 (m, 1H), 5.04-4.98 (m, 1H), 4.74-4.69 (m, 1H), 4.03 (dd, *J* = 4.5 Hz, *J* = 1.0 Hz, 1H), 3.99-3.94 (m, 1H), 3.84 (dd, *J* = 5.0 Hz, *J* = 1.0 Hz, 1H), 3.48-3.43 (m, 1H), 3.13-3.08 (m, 1H), 2.99-2.94 (m, 1H), 2.77-2.62 (m, 2H), 2.41-2.32 (m, 1H), 2.23-2.18 (m, 1H), 2.01-1.92 (m, 1H), 1.88-1.81 (m, 1H), 0.87 (s, 9H), -0.01 (s, 6H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.0, 168.6, 155.5 (q, $^2J_{C,F}$ = 36.3 Hz), 138.1, 136.7, 133.3, 132.0, 128.5 (2 C), 127.8, 127.4 (2 C), 125.8, 125.2, 124.5, 124.2, 123.8, 115.2 (q, $^1J_{C,F}$ = 287.0 Hz), 62.3, 60.7, 54.1, 49.4, 42.8, 36.7, 34.1, 25.2 (3 C), 23.0, 17.3, -3.8, -5.8. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.15 (d, *J* = 8.5 Hz, 1H), 8.22 (d, *J* = 7.0 Hz, 1H), 7.45 (d, *J* = 6.0 Hz, 1H), 3.94-3.91 (m, 1H), 0.86 (s, 9H), 0.01 (s, 6H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 132.3, 128.5 (2 C), 124.2, 54.0, 36.3, 25.4. HRMS (CI) *m/z* calcd for $C_{32}H_{43}F_3N_3O_4Si$ $[M+H]^+$ 618.2975. Found 618.2963.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[(*E*)-1-(3,4-dihydroquinolin-1(2*H*)-yl)-5-((S)-2,2-dimethyl-1,3-dioxolan-4-yl)-1-oxopent-4-en-2-yl]-3-phenylpropanamide (10l). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (10%) = 24.52 min, t_R (90%) = 34.25 min. Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 9.17 (d, *J* = 8.5 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 7.27-7.21 (m, 4H), 7.16 (d, *J* = 7.5 Hz, 2H), 7.13 (td, *J* = 7.5 Hz, *J* = 1.5 Hz, 1H), 7.09 (td, *J* = 7.5 Hz, *J* = 1.5 Hz 1H), 5.51 (dt, *J* = 15.5 Hz, *J* = 7.0 Hz, 1H), 5.42 (dd, *J* = 15.5 Hz, *J* = 6.5 Hz, 1H), 5.02-4.98 (m, 1H), 4.71-4.66 (m, 1H), 4.36-4.32 (m, 1H), 3.95-3.89 (m, 2H), 3.47-3.42 (m, 1H), 3.39-3.58 (m, 1H), 3.09 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 2.94 (dd, *J* = 14.0 Hz, *J* = 10.5Hz, 1H), 2.70-2.60 (m, 2H), 2.36-2.31 (m, 1H), 2.25-2.19 (m, 1H), 1.97-1.87 (m, 1H), 1.85-1.77 (m, 1H), 1.24 (s, 3H), 1.23 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 169.7, 168.7, 155.5 (q, $^2J_{C,F}$ = 36.3 Hz), 138.0, 136.7, 130.9,128.5 (2 C), 127.9, 127.6, 127.4 (2 C), 125.8, 125.2, 124.6, 124.6, 123.8, 115.4 (q, $^1J_{C,F}$ = 287.0 Hz), 107.7, 75.3, 68.1, 54.1, 49.2, 42.8, 36.7, 34.1, 25.9, 25.4, 25.1, 23.0. Minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 9.12 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 7.5 Hz, 1H), 7.42 (d, *J* = 8.5 Hz, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 169.9, 168.7, 136.6, 128.5 (2 C), 127.4 (2 C), 125.8, 125.3, 123.7, 75.4, 73.9, 79.4, 72.7, 36.3, 34.1, 25.9, 23.0. HRMS (CI) *m/z* calcd for $C_{27}H_{29}F_3N_3O_4$ $[M-C_3H_6O+H]^+$: 516.2110. Found 516.2124.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-5-methyl-1-oxohex-4-en-2-yl]-3-phenylpropanamide (10m$_l$). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (15%) = 9.53 min, t_R (85%) = 16.68 min. Major diastereomer; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.20 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 1H), 7.28-7.24 (m, 4H), 7.21-7.11 (m, 4H), 5.02-5.97 (m, 1H), 4.91-4.88 (m, 1H), 4.72-4.68 (m, 1H), 4.05-4.00 (m, 1H), 3.40-3.35 (m, 1H), 3.09 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 2.96 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 2.77-2.72 (m, 1H), 2.65-2.59 (m, 1H), 2.31-2.25 (m, 1H), 2.17-2.11 (m, 1H), 2.01-1.93 (m,1H), 1.86-1.78 (m, 1H), 1.58 (s, 3H), 1.44 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.3, 168.7, 138.1, 136.6, 133.5, 132.5, 128.5 (2 C), 127.8, 127.4 (2 C), 125.8, 125.3, 124.6, 123.9, 118.3, 54.1, 49.4, 42.7, 36.6, 30.4, 25.4, 24.7, 23.0, 16.7. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.19 (d, *J* = 8.5 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 3.97-3.92 (m, 1H), 3.49-3.42 (m, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 123.8, 53.9, 49.3. HRMS (CI) *m/z* calcd for $C_{27}H_{31}F_3N_3O_3$ $[M+H]^+$ 502.2318. Found 502.2335.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-3,3-dimethyl-1-oxopent-4-en-2-yl]-3-phenylpropanamide (10m$_b$). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (10%) = 14.69 min, t_R (90%) = 19.94 min. Major diastereomer; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.30 (d, *J* = 8.0 Hz, 1H), 7.96 (d, *J* = 8.5 Hz, 1H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.31 (d, *J* = 7.5 Hz, 2H), 7.27-7.23 (m, 2H), 7.21-7.11 (m, 4H), 5.72 (dd, *J* = 17.5 Hz, *J* = 10.5 Hz, 1H), 5.20 (d, *J* = 8.5 Hz, 1H), 4.89 (dd, *J* = 17.5 Hz, *J* = 1.5 Hz, 1H), 4.88 (dd, *J* = 10.5 Hz, *J* = 1.5 Hz, 1H), 4.86-4.82 (m, 1H), 4.20-4.12 (m, 1H), 3.28-3.25 (m, 1H), 3.16 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 3.01 (dd, *J* = 14.0 Hz, *J* = 5.5 Hz, 1H), 2.75 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 2.60 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.08-2.00 (m, 1H), 1.81-1.74 (m, 1H), 0.93 (s, 3H), 0.91 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 169.1, 169.1, 155.6 (q, $^2J_{C,F}$ = 36.2 Hz), 143.5, 138.2, 136.6, 132.6, 128.6 (2 C), 127.7, 127.4 (2 C), 125.8, 125.3, 124.6, 124.2, 111.8, 54.8, 54.3, 43.0, 40.7, 36.6, 25.5, 23.4, 23.0, 22.2. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.25 (d, *J* = 8.0 Hz, 1H), 7.74 (d, *J* = 9.0 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 4.81-4.78 (m, 1H), 0.98 (m, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 169.1, 168.9, 143.5, 136.6, 128.5 (2 C), 127.8, 124.0, 111.8, 54.8, 54.1, 40.7, 35.9, 23.6, 22.1. HRMS (CI) *m/z* calcd for $C_{27}H_{31}F_3N_3O_3$ $[M+H]^+$ 502.2318. Found 502.2331

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[(*E*)-1-(3,4-dihydroquinolin-1(2*H*)-yl)-5,9-dimethyl-1-oxodeca-4,8-dien-2-yl]-3-phenylpropanamide (10n). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (8%) = 12.34 min, t_R (92%) = 16.51 min. Major diastereomer; ^{1}H-NMR (500 MHz,

DMSO-d_6, 353K): δ 9.17 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.29-7.24 (m, 4H), 7.20-7.15 (m, 3H), 7.12 (dt, *J* = 7.5 Hz, *J* = 1.5 Hz, 1H), 5.06-5.03 (m, 1H), 5.02-4.98 (m, 1H), 4.96-4.93 (m, 1H), 4.73-4.69 (m, 1H), 4.05-3.99 (m, 1H), 3.43-3.38 (m, 1H), 3.20 (dd, *J* = 14.0 Hz, *J* = 1.0 Hz, 1H), 2.97 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.75 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 2.63 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.75 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 2.35-2.29 (m, 1H), 2.20-2.13 (m, 1H), 2.20-1.95 (m, 3H), 1.91-1.87 (m, 2H), 1.85-1.80 (m, 1H), 1.62 (s, 3H), 1.53 (s, 3H), 1.46 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.3, 168.7, 155.5 (q, $^2J_{C,F}$ = 36.2 Hz), 138.1, 137.2, 136.6, 132.3, 130.1, 128.5 (2 C), 127.8, 127.4 (2 C), 125.8, 125.2, 124.5, 123.8, 123.4, 118.0, 54.1, 49.5, 42.8, 38.6, 36.6, 30.3, 25.6, 25.4, 24.6, 23.0, 16.7, 15.2. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.12 (d, *J* = 8.5 Hz, 1H), 8.19 (d, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.5 Hz, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 136.6, 128.5 (2 C), 23.0, 16.7. HRMS (CI) *m/z* calcd for $C_{32}H_{39}F_3N_3O_3$ $[M+H]^+$ 570.2944; Found 570.2914.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-1-oxo-4-phenylpent-4-en-2-yl]-3-phenylpropanamide (10o). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (6%) = 14.33 min, t_R (94%) = 21.82 min. Major diastereomer: ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 9.16 (d, *J* = 8.5 Hz, 1H), 8.33 (d, *J* = 8.0 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.26-7.15 (m, 11H), 7.10 (td, *J* = 8.0 Hz, *J* = 1.0 Hz, 1H), 7.03 (td, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H), 5.30 (d, *J* = 1.5 Hz, 1H), 5.14-5.10 (m, 1H), 5.07 (d, *J* = 1.5 Hz, 1H), 4.73-4.66 (m, 1H), 4.01-3.96 (m, 1H), 3.35-3.28 (m, 1H), 3.07 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H), 2.92 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.84 (dd, *J* = 14.5 Hz, *J* = 6.0 Hz, 1H), 2.76-2.59 (m, 3H), 1.99-1.91 (m, 1H), 1.83-1.72 (m, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.3, 168.7, 155.5 (q, $^2J_{C,F}$ = 36.3 Hz), 142.7, 138.9, 137.9, 136.6, 132.5, 128.5 (2 C), 127.7, 127.6 (2 C), 127.4 (2 C), 126.8, 125.8, 125.3, 125.0 (2 C), 124.6, 123.8, 115.2 (q, $^1J_{C,F}$ = 286.6 Hz), 114.5, 54.1, 48.4, 42.6, 37.2, 36.7, 25.3, 23.0. Minor diastereomer (selected peaks): ^{1}H-NMR (500 MHz, DMSO-d_6 , 353 K): δ 9.12 (d, *J* = 8.5 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 5.31 (d, *J* = 1.5 Hz, 1H), 5.08 (d, *J* = 1.5 Hz, 1H), 3.94-3.89 (m, 1H), 3.13 (dd, *J* = 14.0 Hz, *J* = 5.0 Hz, 1H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353 K): δ 170.2, 168.6,142.6, 139.0, 137.8, 136.6, 128.4 (2 C),127.4 (2 C),125.3, 125.0 (2 C), 124.6, 123.6,53.8, 48.6, 42.7,25.3. HRMS (CI) *m/z* calcd for $C_{31}H_{31}F_3N_3O_3$ $[M+H]^+$: 550.2318. Found 550.2275.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-4-methyl-1-oxopent-4-en-2-yl]-4-methylpentanamide (12). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (14%) = 8.72 min, t_R (86%) = 11.63 min. Major diastereomer; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.10 (d, *J* = 7.5 Hz, 1H), 8.06 (d, *J* = 7.5 Hz, 1H), 7.49 (d, *J* = 7.5 Hz, 1H), 7.21-7.13 (m, 2H), 7.12 (d, *J* = 7.5 Hz, 1H), 5.17-5.13 (m, 1H), 4.68 (s, 1H), 4.62 (s, 1H), 4.48-4.44 (m, 1H), 4.03-3.98 (m, 1H), 3.43-3.38 (m, 1H), 2.74 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.64 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.29 (dd, *J* = 13.5 Hz, *J* = 5.0 Hz, 1H), 2.22 (dd, *J* = 13.5 Hz, *J* = 9.0 Hz, 1H), 2.01-1.93 (m, 1H), 1.86-1.78 (m, 1H), 1.67-1.54 (m, 3H), 1.45 (s, 3H), 0.90 (d, *J* = 6.0 Hz, 3H), 0.88 (d, *J* = 6.0 Hz, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.4, 169.6, 155.6 (q, $^2J_{C,F}$ = 36.2 Hz), 140.2, 138.1, 132.6, 127.8, 125.3, 124.7, 123.9, 115.4 (q, $^1J_{C,F}$ = 286.4 Hz), 112.5, 51.7, 47.9, 42.6, 25.4, 23.9, 22.9, 22.1, 20.9, 20.8. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 7.15 (d, *J* = 7.5 Hz, 1H), 7.47 (d, *J* = 7.5 Hz, 1H), 1.46 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.4, 169.5, 123.8, 112.4, 51.5, 48.1, 23.8, 22.1, 21.1. HRMS (CI) *m/z* calcd for $C_{23}H_{31}F_3N_3O_3$ $[M+H]^+$ 454.2318. Found 454.2319.

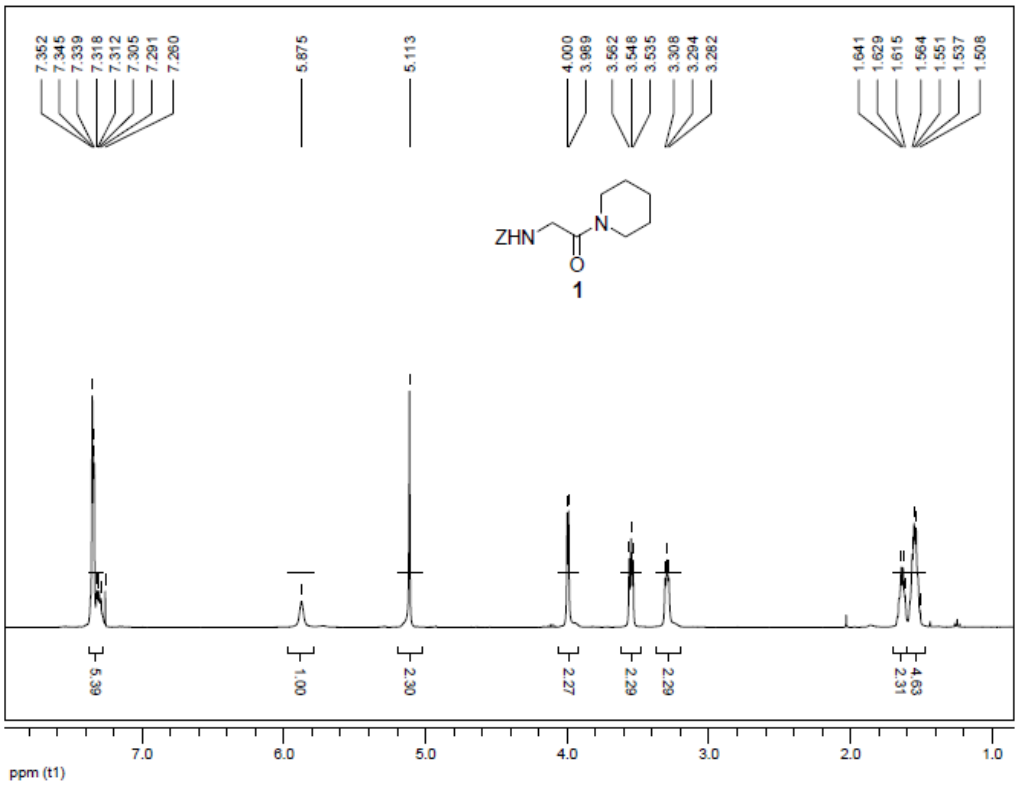
(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-4-methyl-1-oxopent-4-en-2-yl]-3,3-dimethylbutanamide (14). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (9%) = 8.51 min, t_R (91%) = 11.25 min. Major diastereomer; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.62 (d, *J* = 9.0 Hz, 1H), 8.23 (d, *J* = 8.0 Hz, 1H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.21-7.15 (m, 2H), 7.13 (t, *J* = 7.5 Hz, 1H), 5.22-5.17 (m, 1H), 4.68 (s, 1H), 4.64 (s, 1H), 4.43 (d, *J* = 9.0 Hz, 1H),

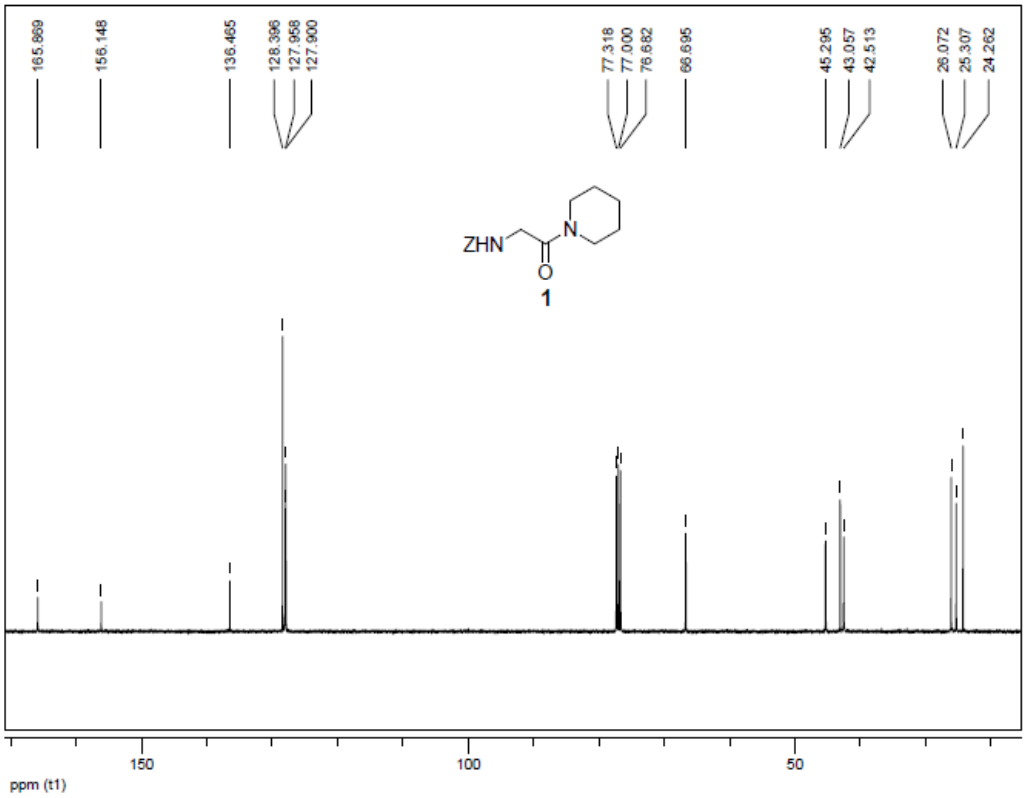
4.01-3.96 (m, 1H), 3.46-3.39 (m, 1H), 2.73 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 2.63 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.32-2.15 (m, 2H), 2.00-1.92 (m, 1H), 1.86-1.77 (m, 1H), 1.44 (s, 3H), 0.96 (s, 9H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.4, 167.6, 155.7 (q, $^{2}J_{C,F}$ = 36.6 Hz), 140.1, 138.1, 132.6, 127.9, 125.3, 124.7, 123.8, 115.4 (q, $^{1}J_{C,F}$ = 287.8 Hz), 112.6, 60.6, 48.0, 42.6, 33.7, 28.3, 26.0 (3 C), 25.3, 23.0, 20.8. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 8.54 (d, *J* = 8.5 Hz, 1H), 8.12 (d, *J* = 7.5 Hz, 1H), 3.96-3.92 (m, 1H), 3.49-3.45 (m, 1H), 1.45 (s, 3H), 0.98 (s, 9H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.5, 167.7, 140.2, 137.9, 127.9, 125.3, 124.8, 123.8, 112.4, 60.6, 42.7, 33.9, 25.9 (3 C), 25.4, 21.1. HRMS (CI) *m/z* calcd for $C_{23}H_{31}F_3N_3O_3$ $[M+H]^+$ 454.2318. Found 454.2341.

(2*S*)-2-(2,2,2-Trifluoroacetamido)-N-[1-(3,4-dihydroquinolin-1(2*H*)-yl)-4-methyl-1-oxopent-4-en-2-yl)-3-(4-methoxyphenyl]propanamide (16). HPLC (Reprosil, hexane/*i*PrOH 95 : 5, 1mL/min): t_R (8%) = 17.95 min, t_R (92%) = 22.80 min. Major diastereomer; ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.14 (d, *J* = 8.5 Hz, 1H), 8.24 (d, *J* = 8.5 Hz, 1H), 7.25 (d, *J* = 7.5 Hz, 1H), 7.21-7.12 (m, 5H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.18-5.14 (m, 1H), 4.68 (s, 1H), 4.63 (s, 1H), 4.65-4.61 (m, 2H), 4.04-3.98 (m, 1H), 3.72 (s, 3H), 3.43-3.38 (m, 1H), 3.03 (dd, *J* = 14.0 Hz, *J* = 5.5 Hz, 1H), 2.87 (dd, *J* = 14.0 Hz, *J* = 10.0 Hz, 1H), 2.74 (dt, *J* = 16.0 Hz, *J* = 6.5 Hz, 1H), 2.63 (dt, *J* = 16.0 Hz, *J* = 7.0 Hz, 1H), 2.28 (dd, *J* = 14.0 Hz, *J* = 5.5 Hz, 1H), 2.19 (dd, *J* = 14.0 Hz, *J* = 8.5 Hz, 1H), 2.01-1.94 (m, 1H), 1.86-1.79 (m, 1H), 1.44 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 170.4, 168.8, 157.6, 140.3, 138.0, 129.5 (2 C), 128.5, 127.8, 125.3, 124.7, 123.9, 113.2 (2 C), 112.6, 54.4, 47.9, 42.7, 35.9, 25.4, 23.0, 20.9. Minor diastereomer (selected peaks); ^{1}H-NMR (500 MHz, DMSO-d_6, 353K): δ 9.10 (d, *J* = 8.5 Hz, 1H), 8.14 (d, *J* = 8.5 Hz, 1H), 7.45 (d, *J* = 8.0 Hz, 1H), 3.98-3.95 (m, 1H), 3.72 (s, 3H), 1.46 (s, 3H); ^{13}C-NMR (125 MHz, DMSO-d_6, 353K): δ 140.2, 129.5, 128.6, 127.9, 125.4, 123.8, 112.5, 54.2, 48.2, 24.5, 23.0, 21.0. HRMS (CI) *m/z* calcd for $C_{26}H_{31}F_3N_3O_4$ $[M+H]^+$ 518.2267. Found 518.2307.

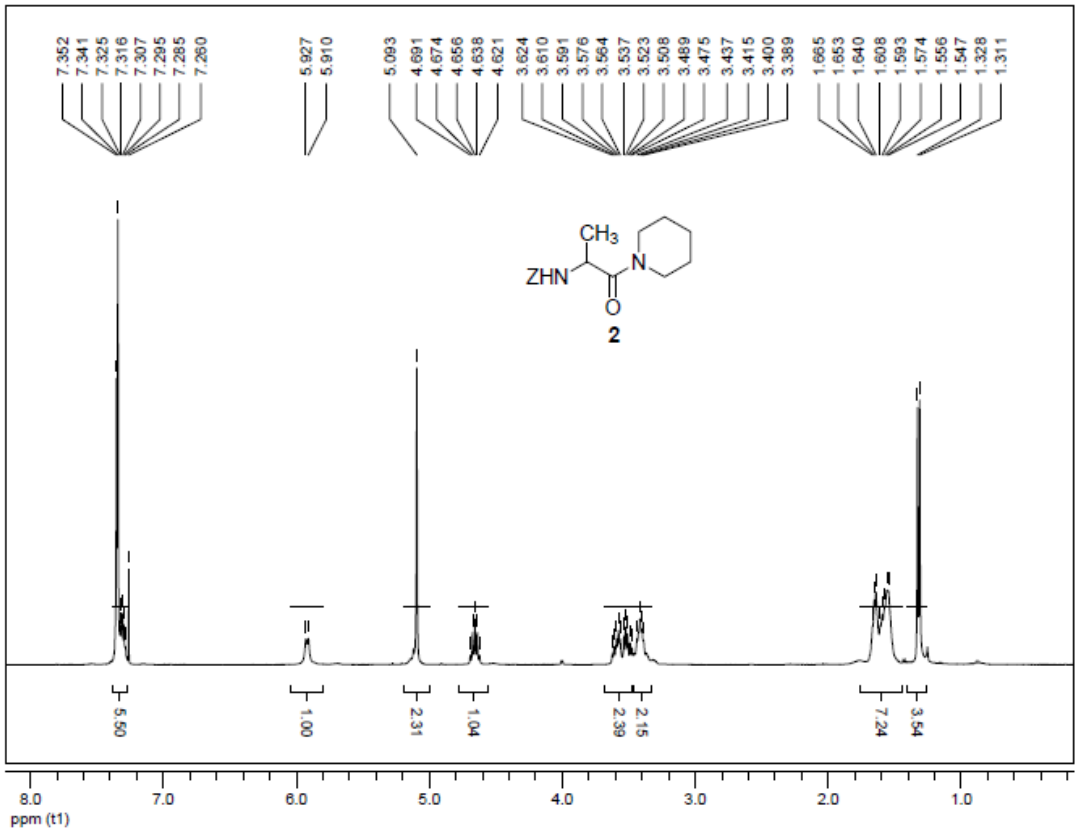
^{1}H and ^{13}C spectra of compounds 1 to 16

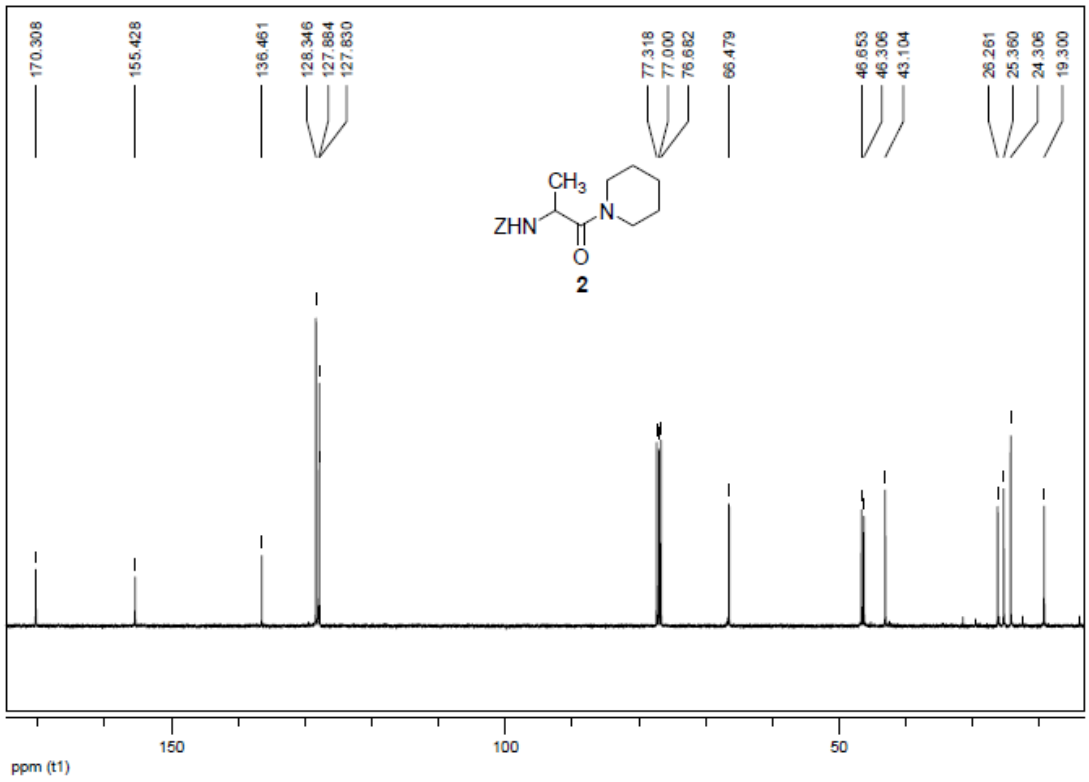
NMR spectra of compound **1**



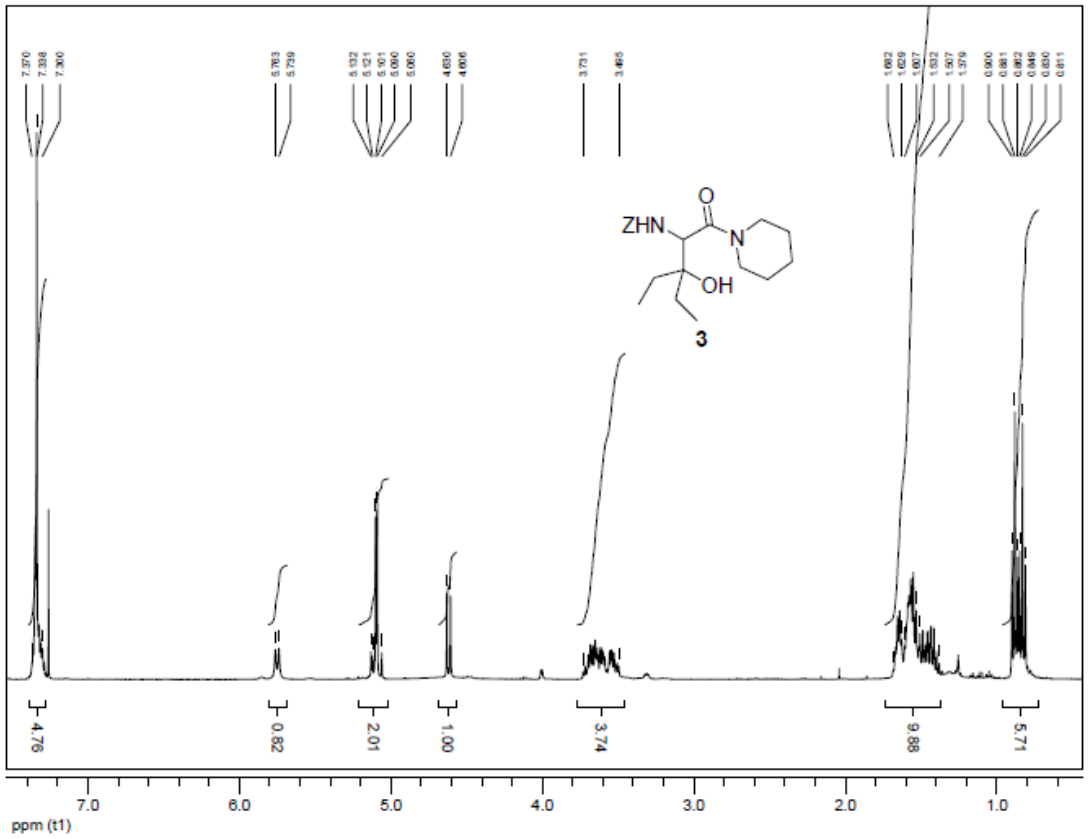


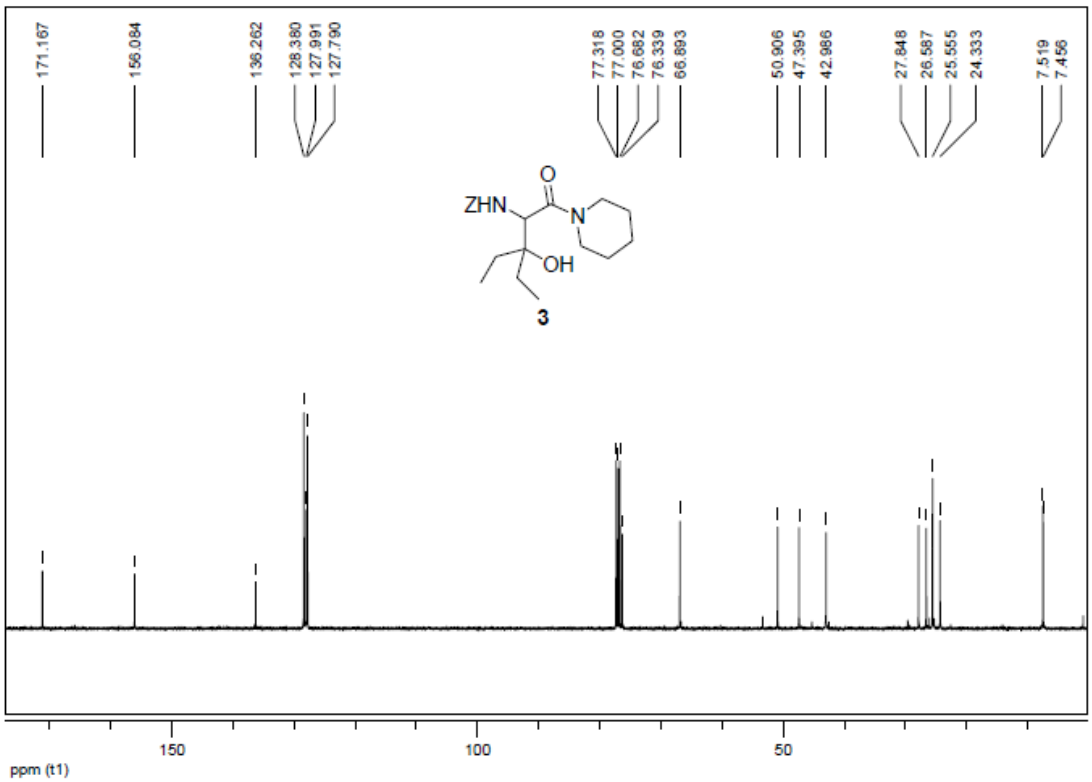
NMR spectra of compound **2**



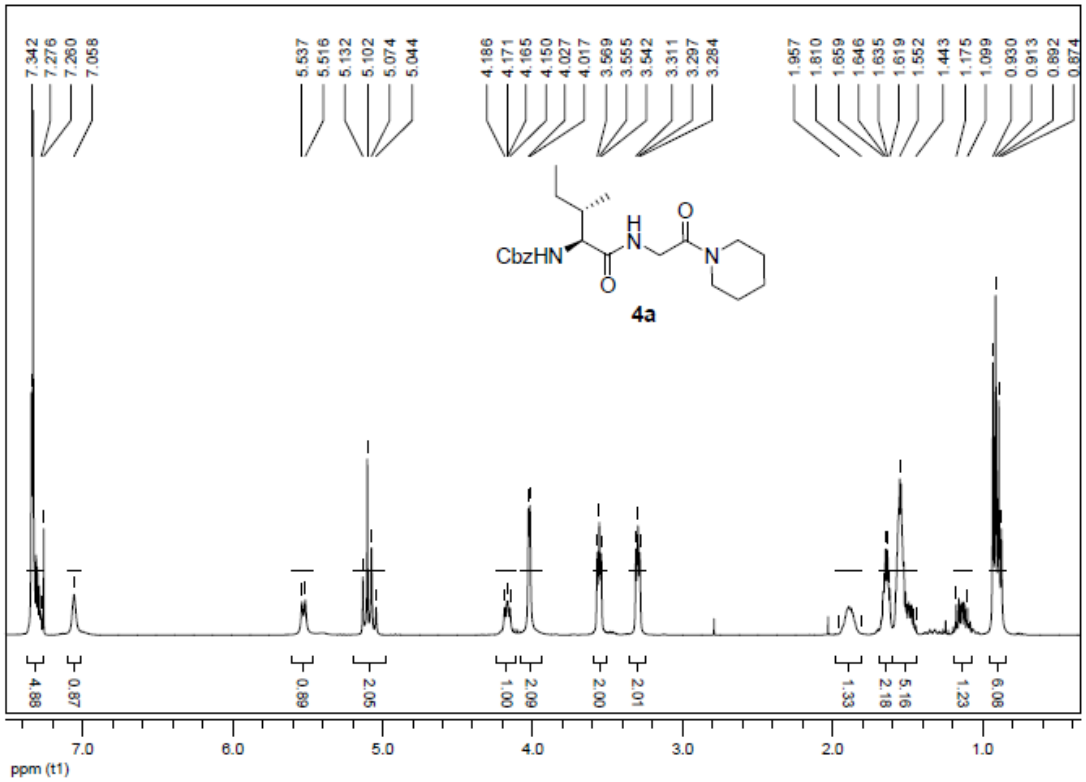


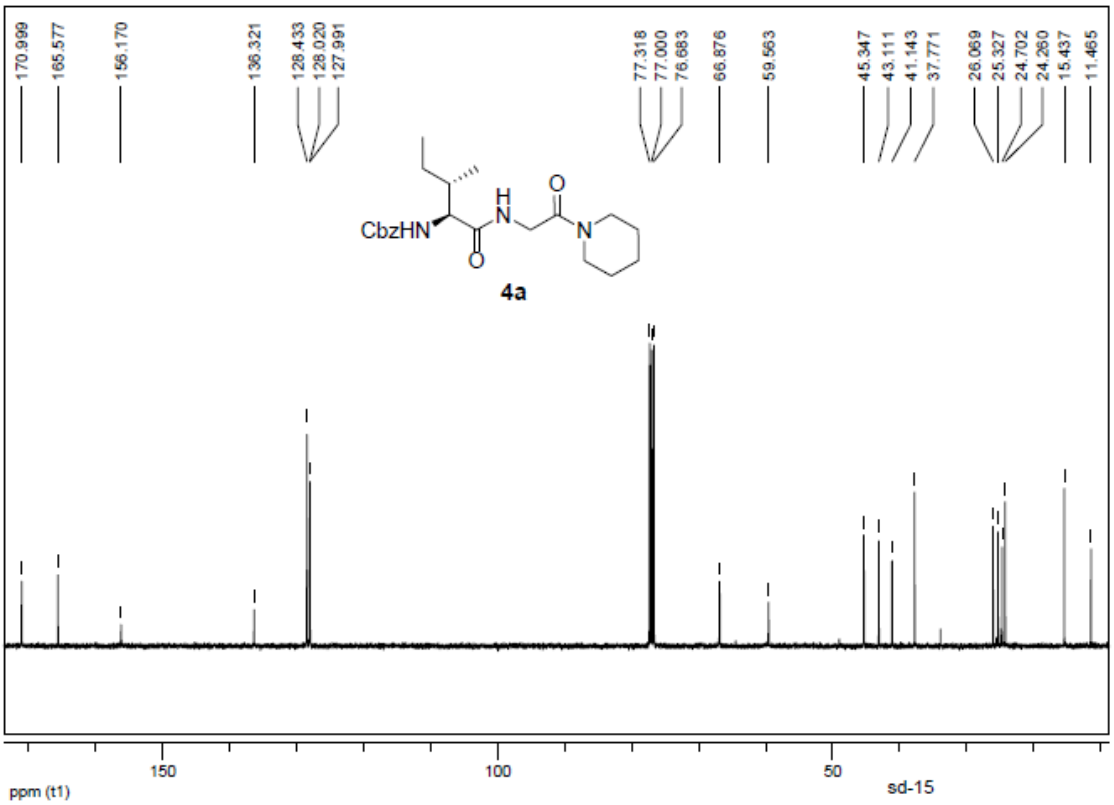
NMR spectra of compound **3**



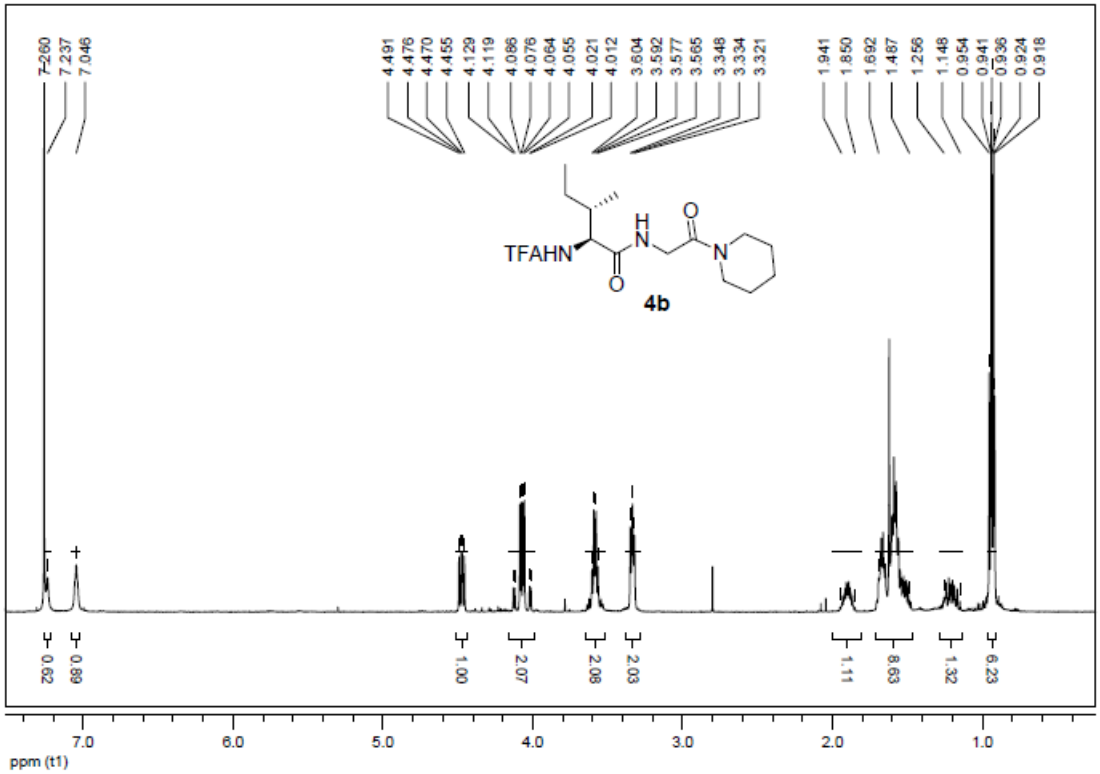


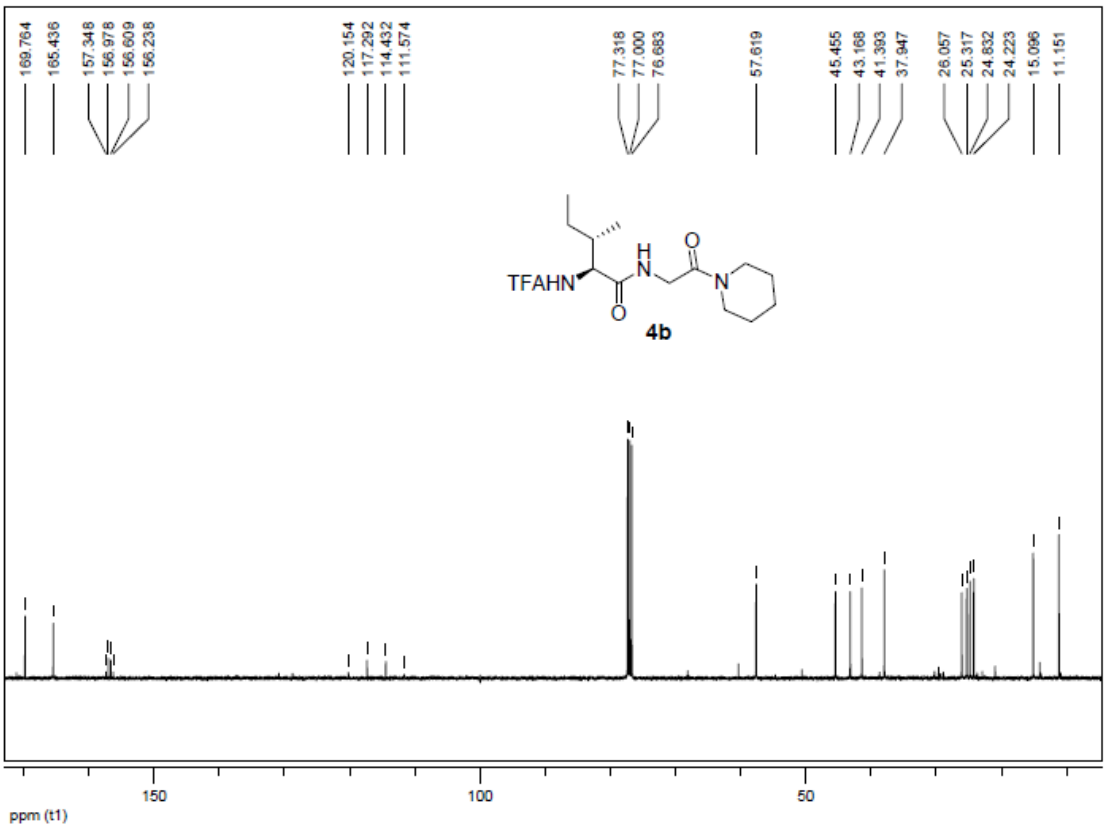
NMR spectra of compound **4a**



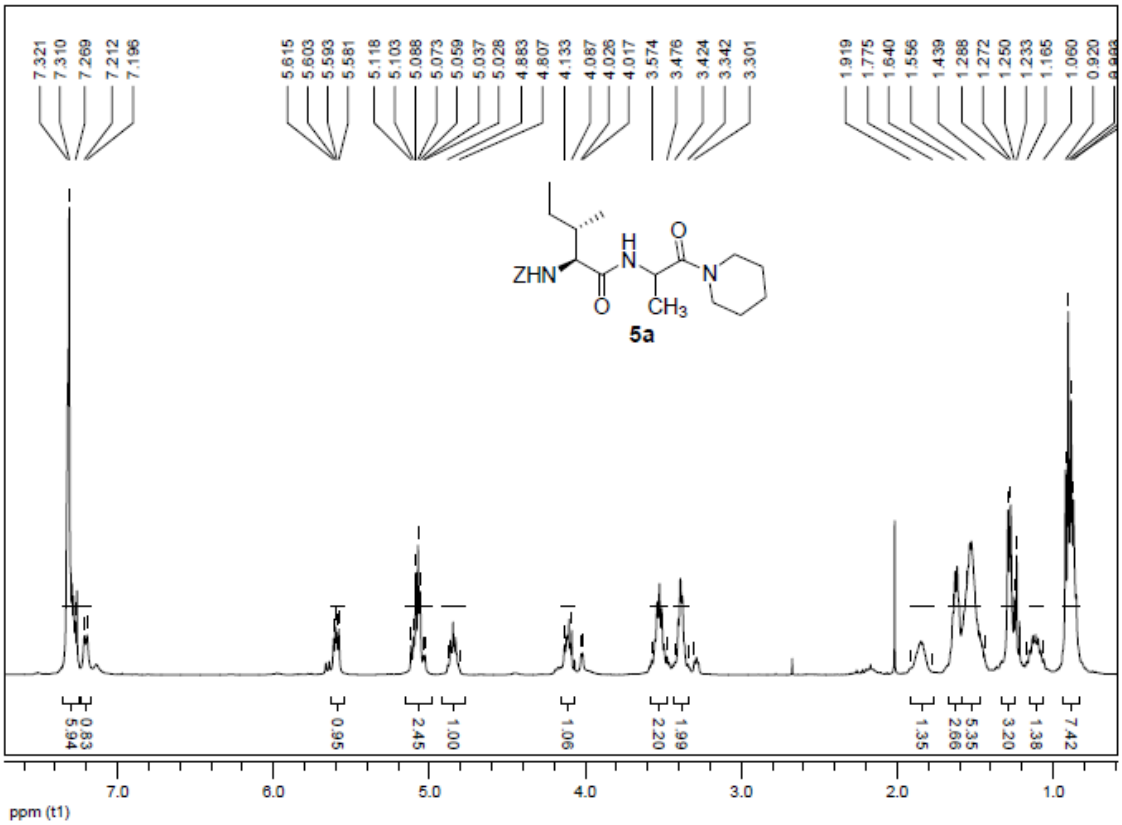


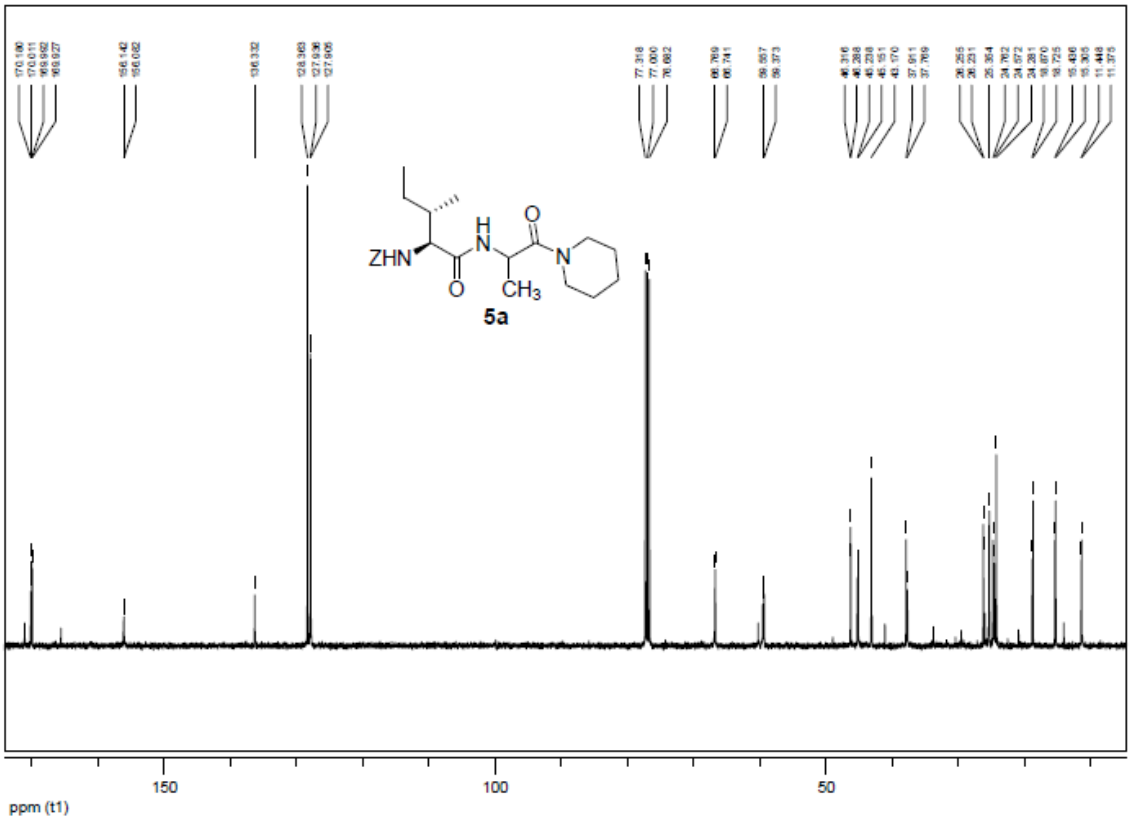
NMR spectra of compound **4b**



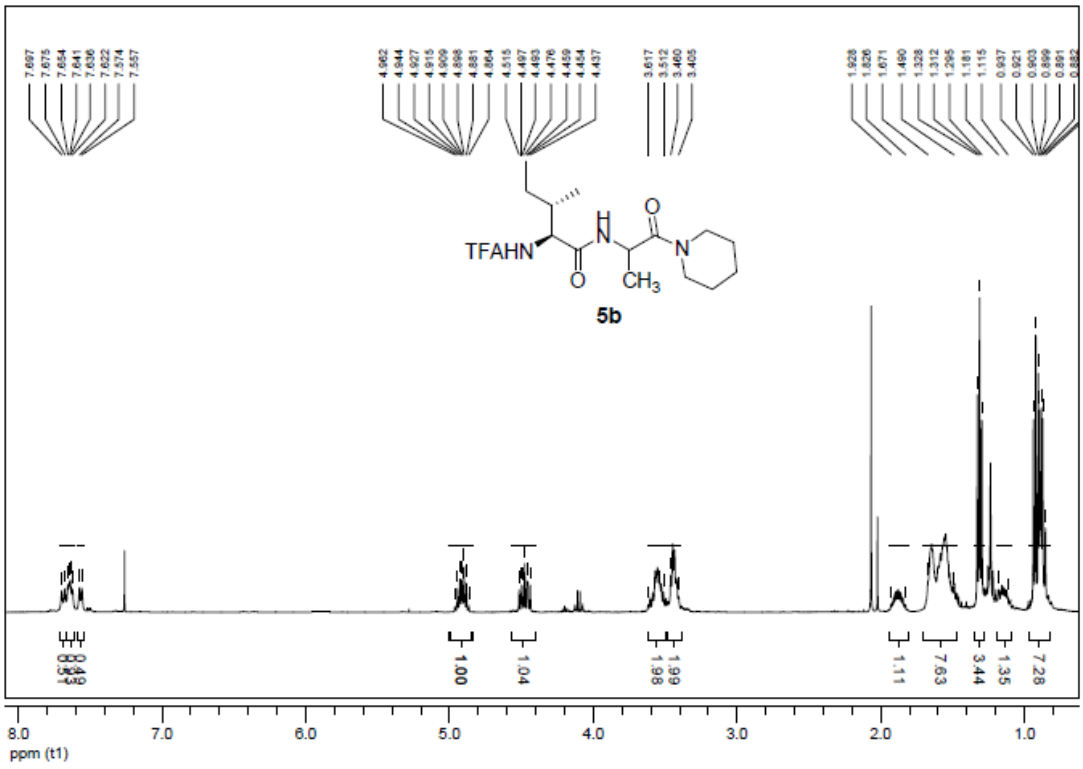


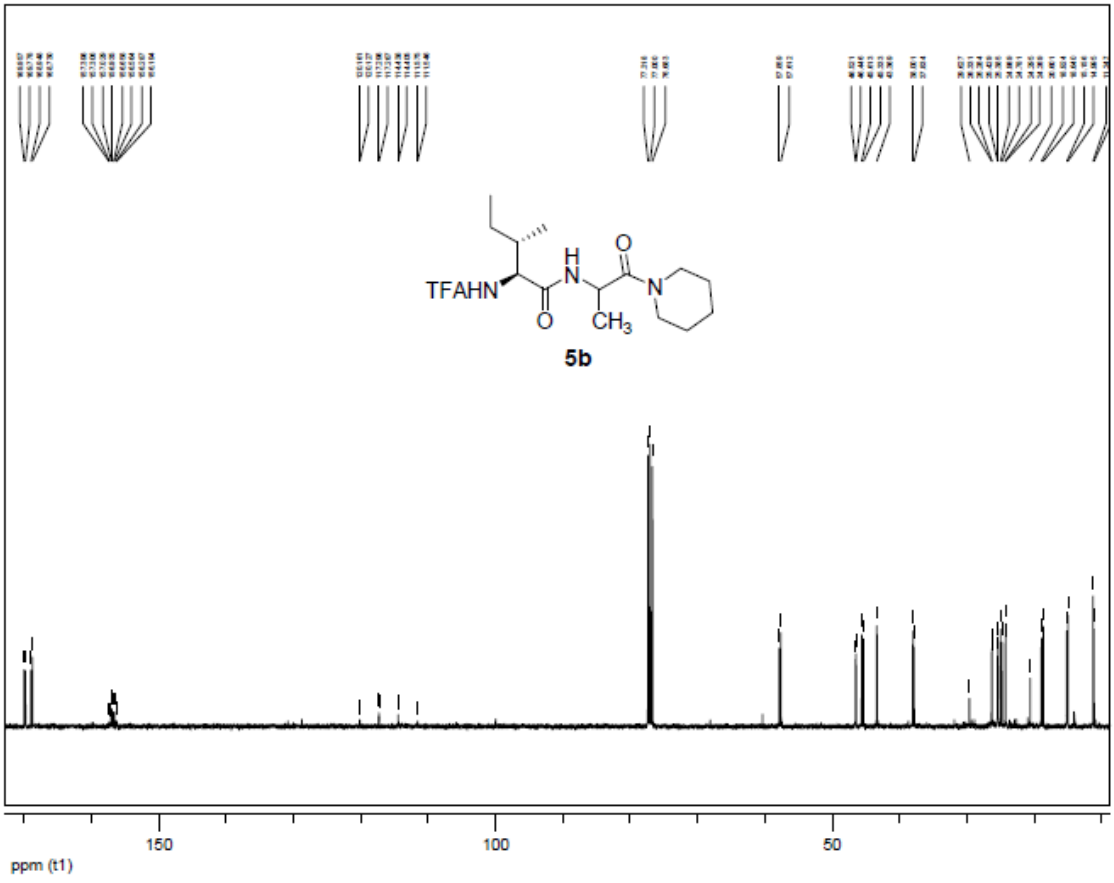
NMR spectra of compound **5a**



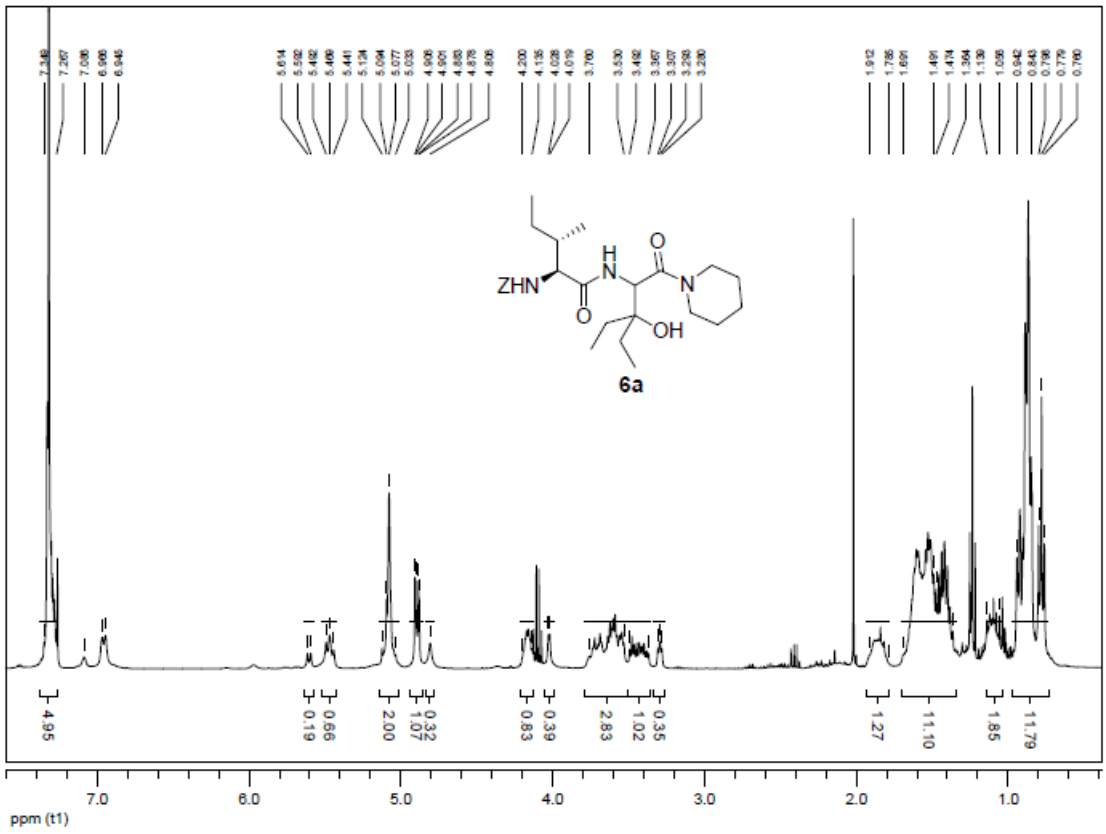


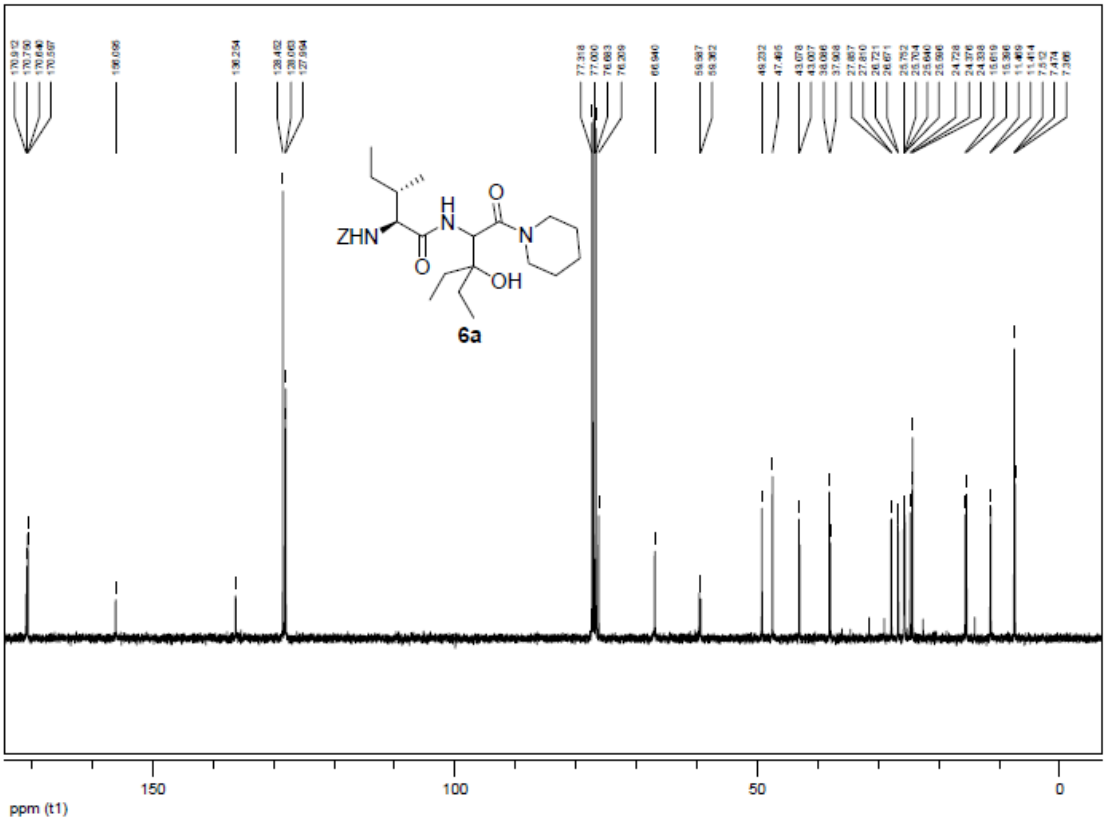
NMR spectra of compound **5b**



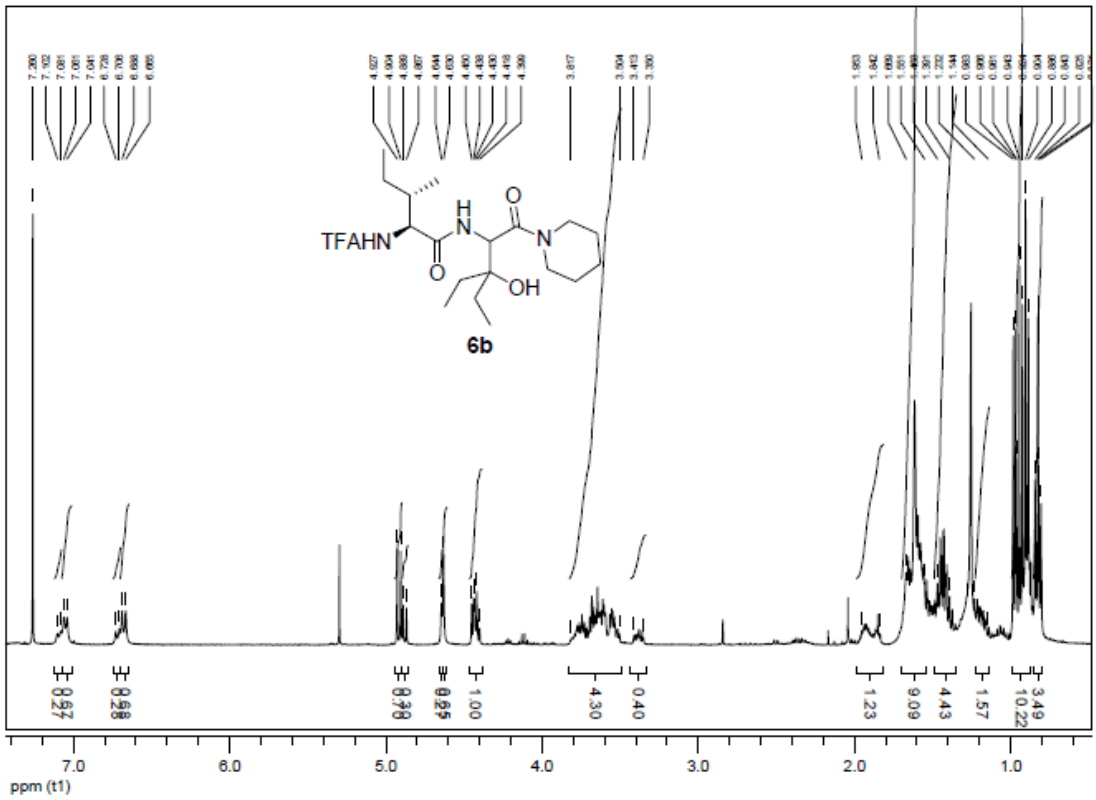


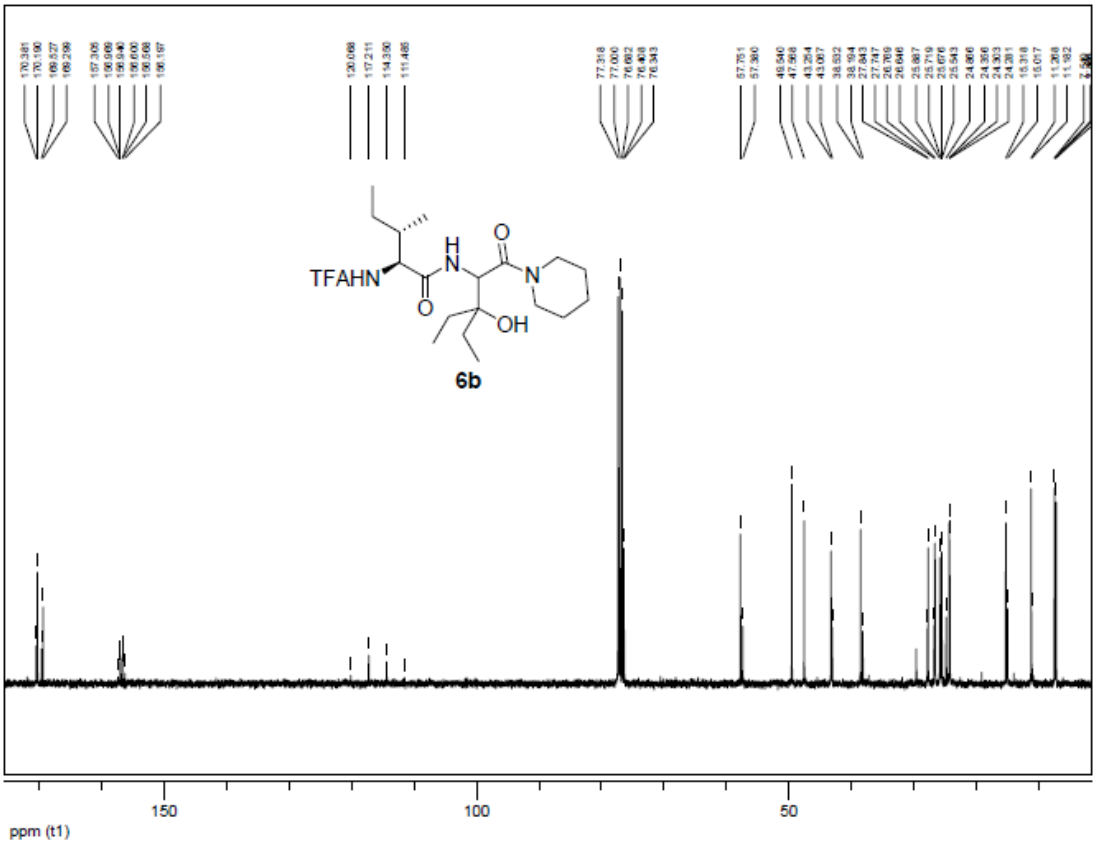
NMR spectra of compound **6a**



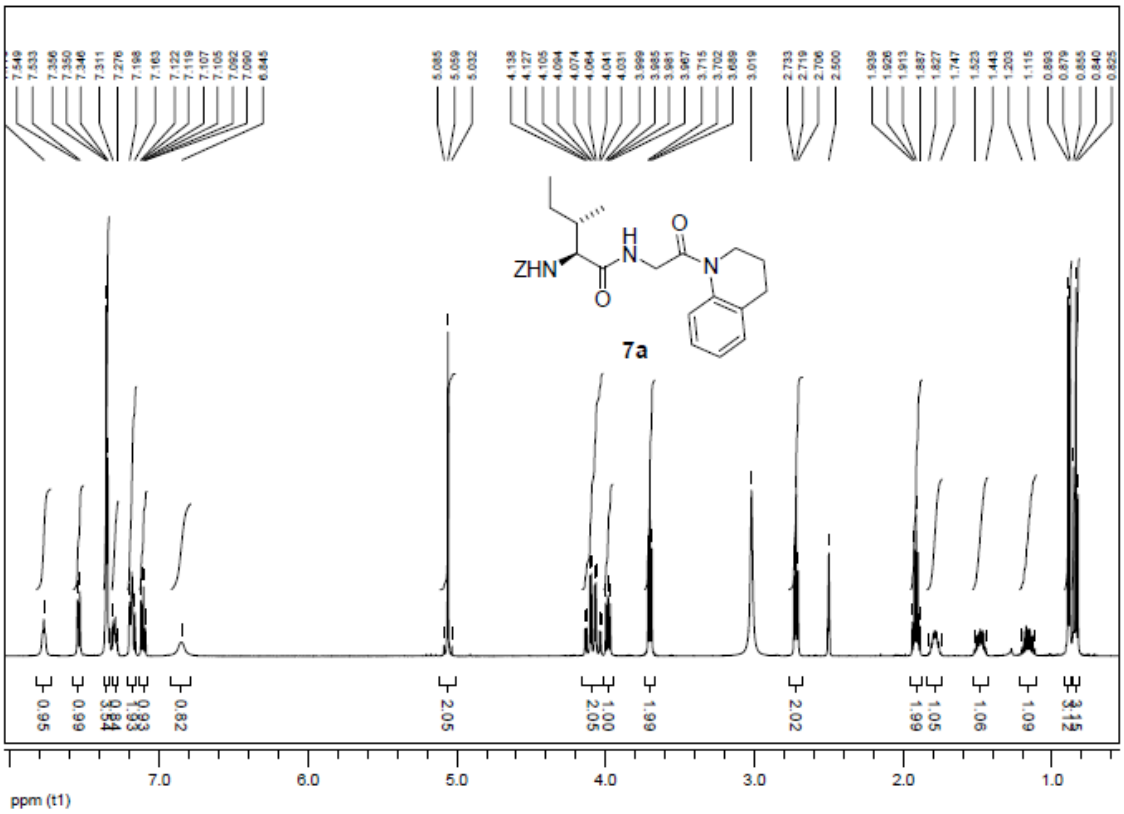


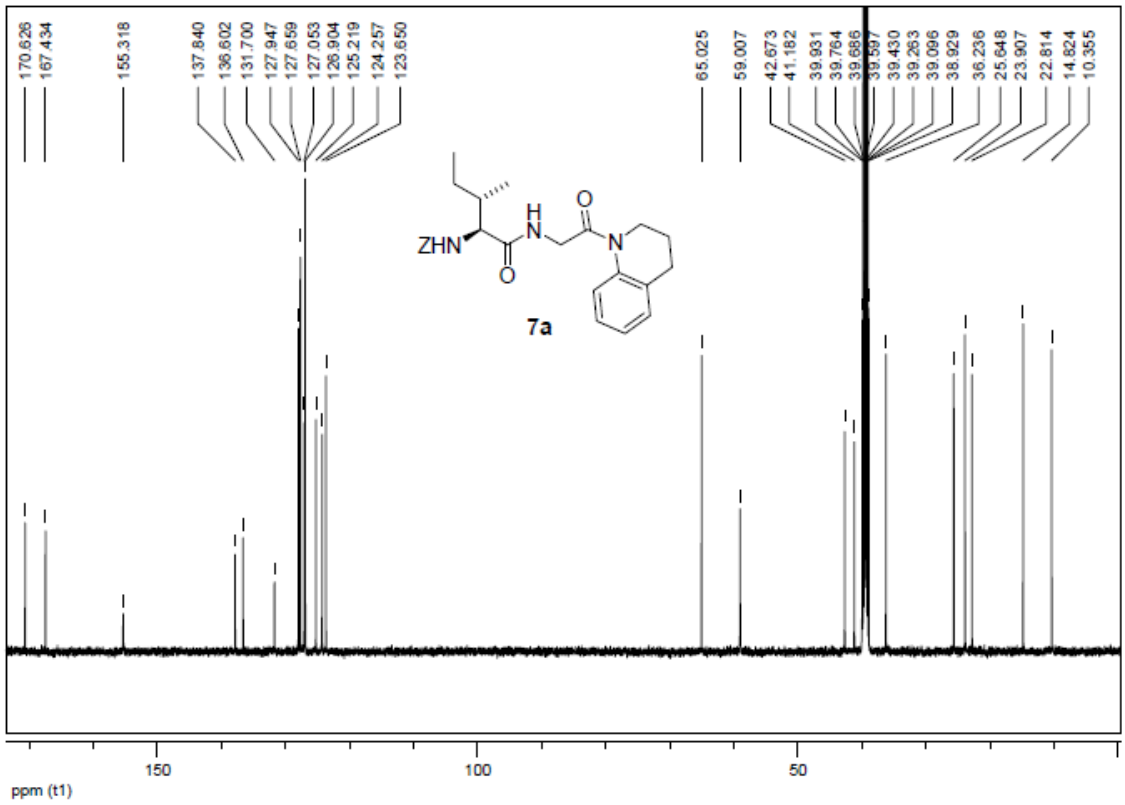
NMR spectra of compound **6b**



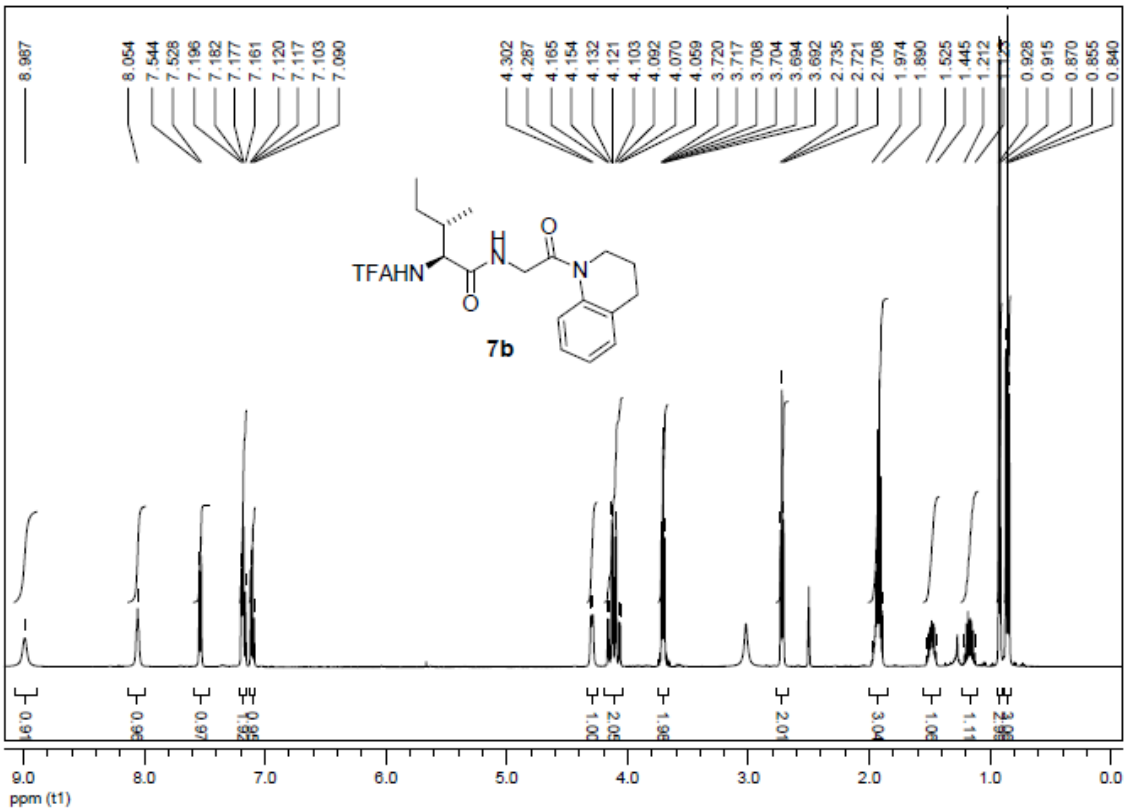


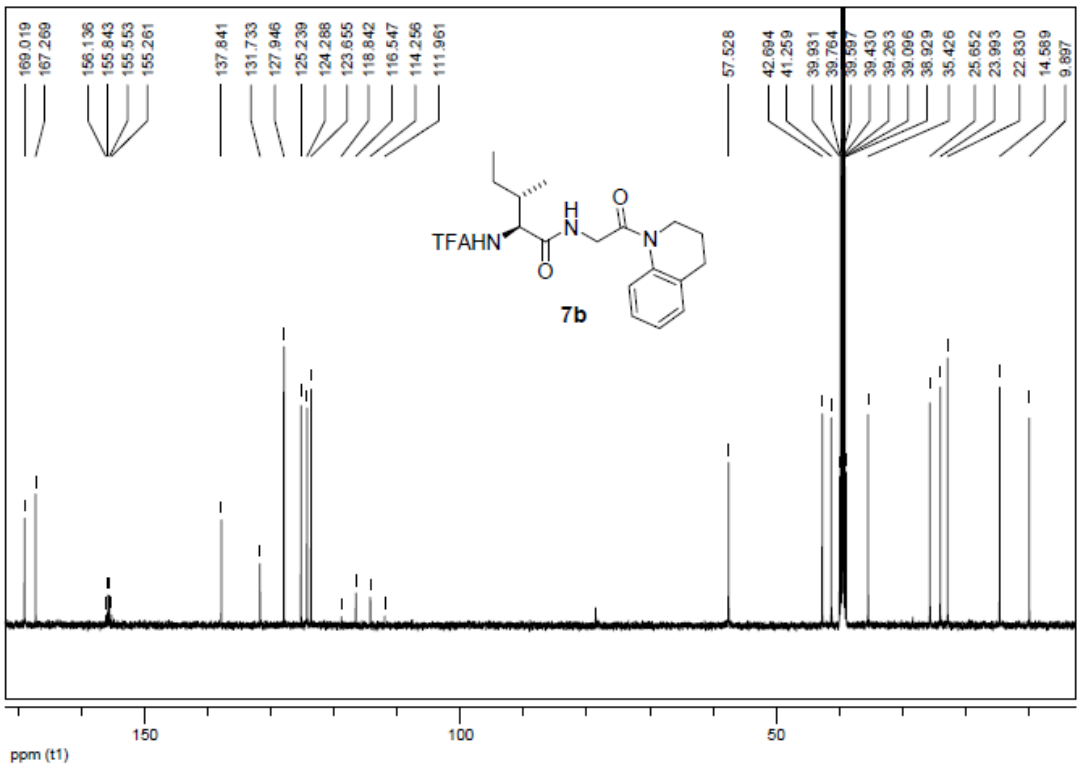
NMR spectra of compound **7a**



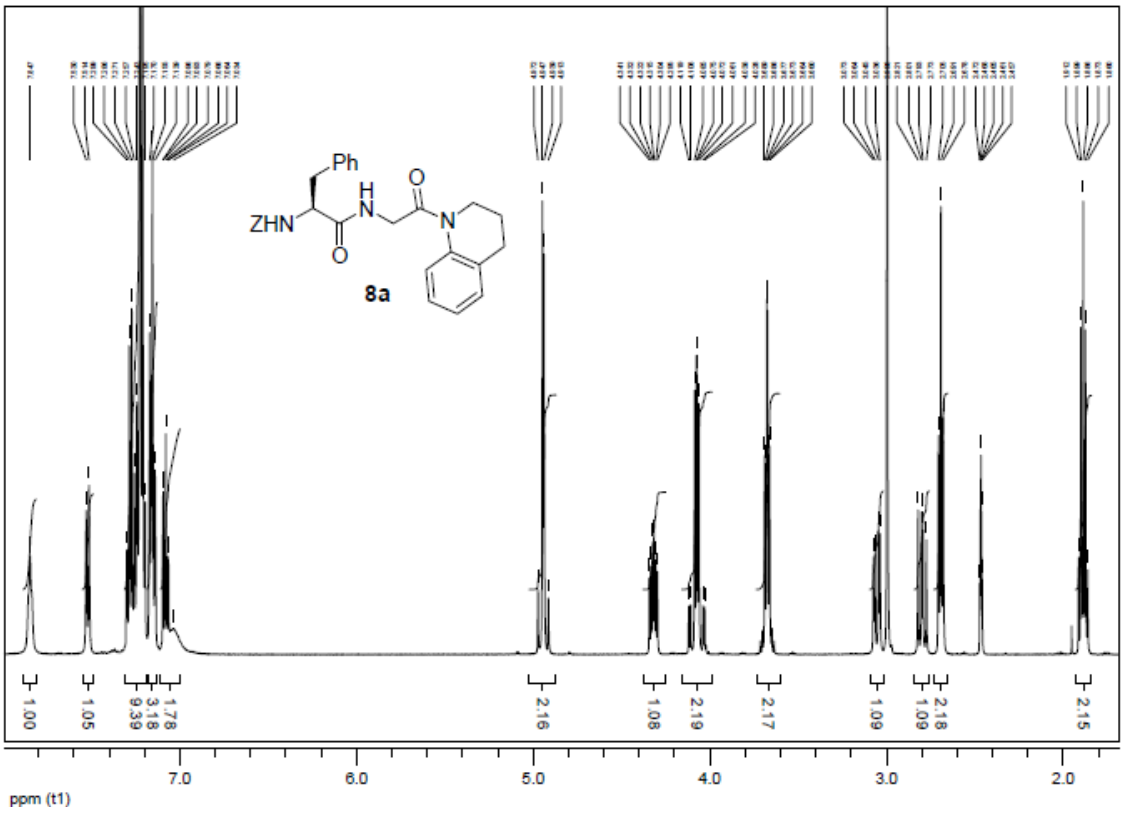


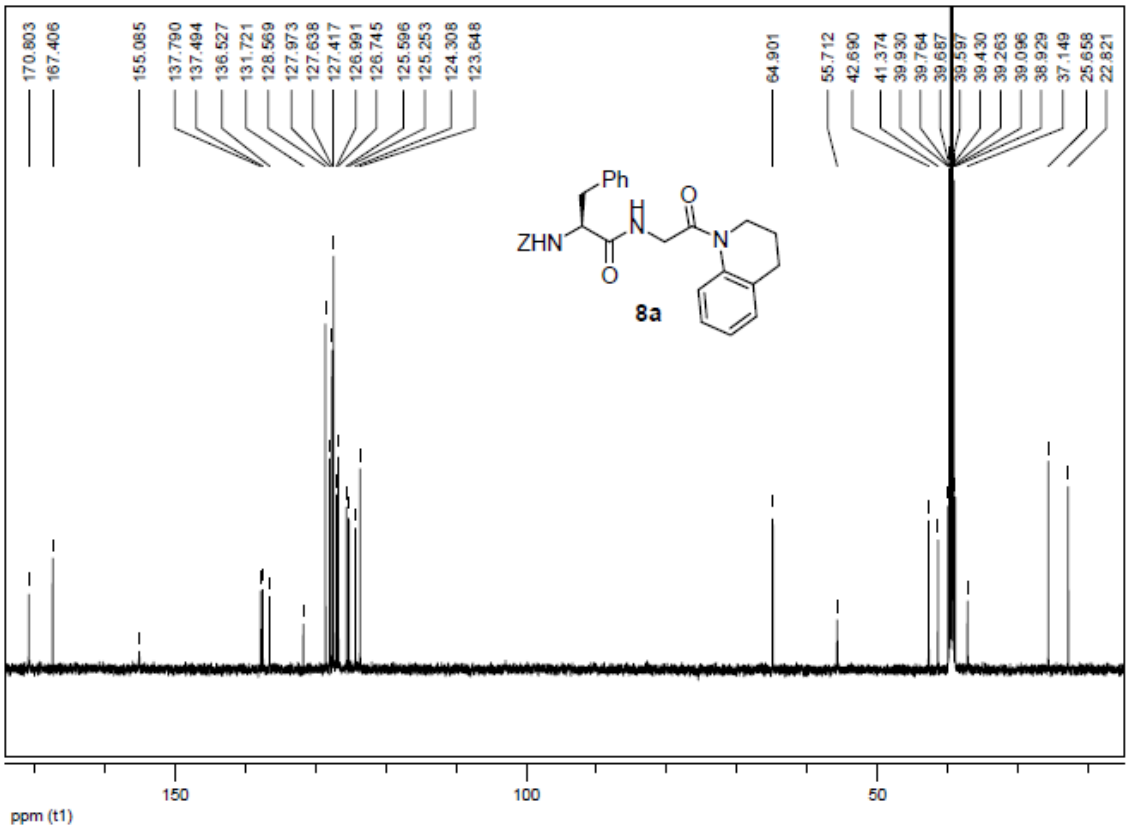
NMR spectra of compound **7b**



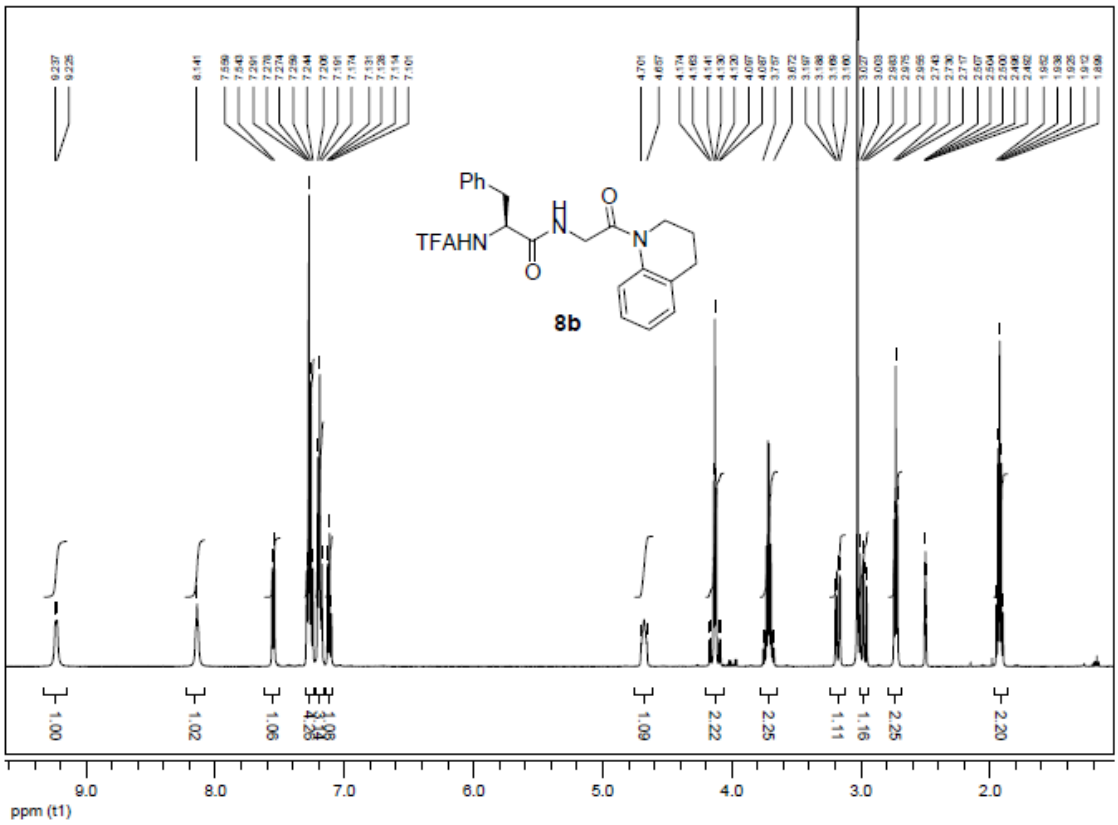


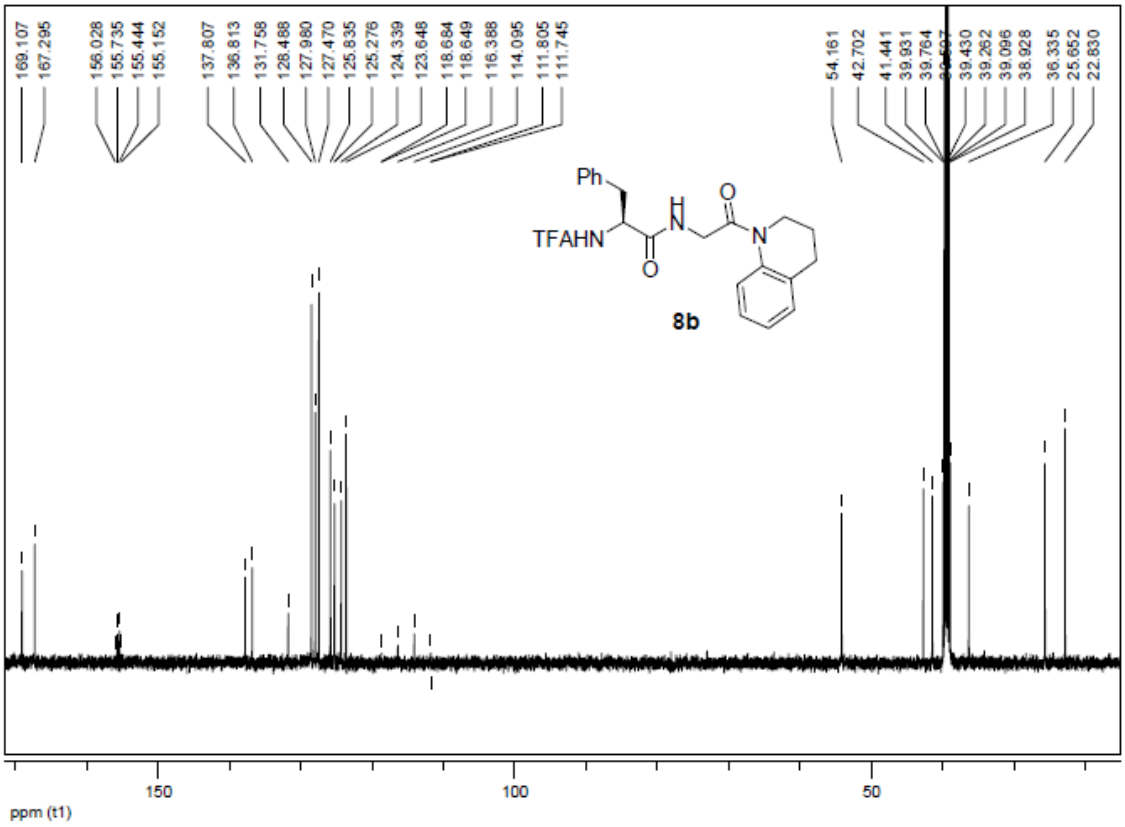
NMR spectra of compound **8a**



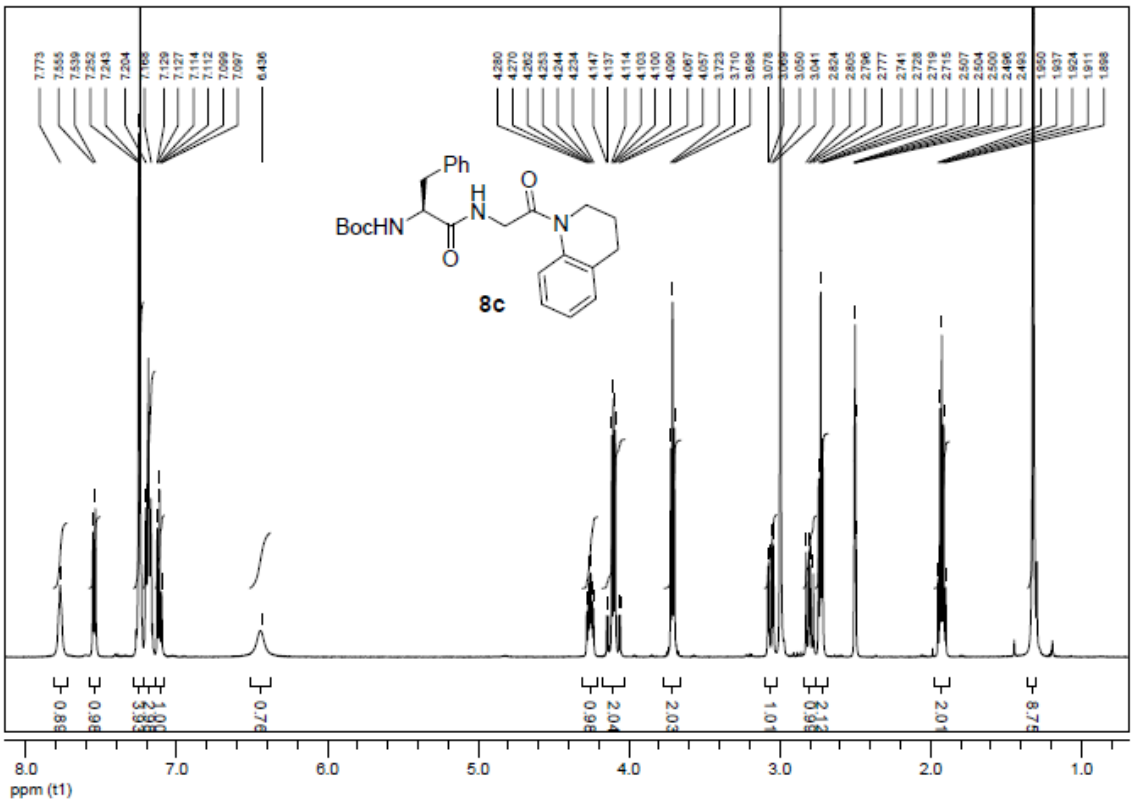


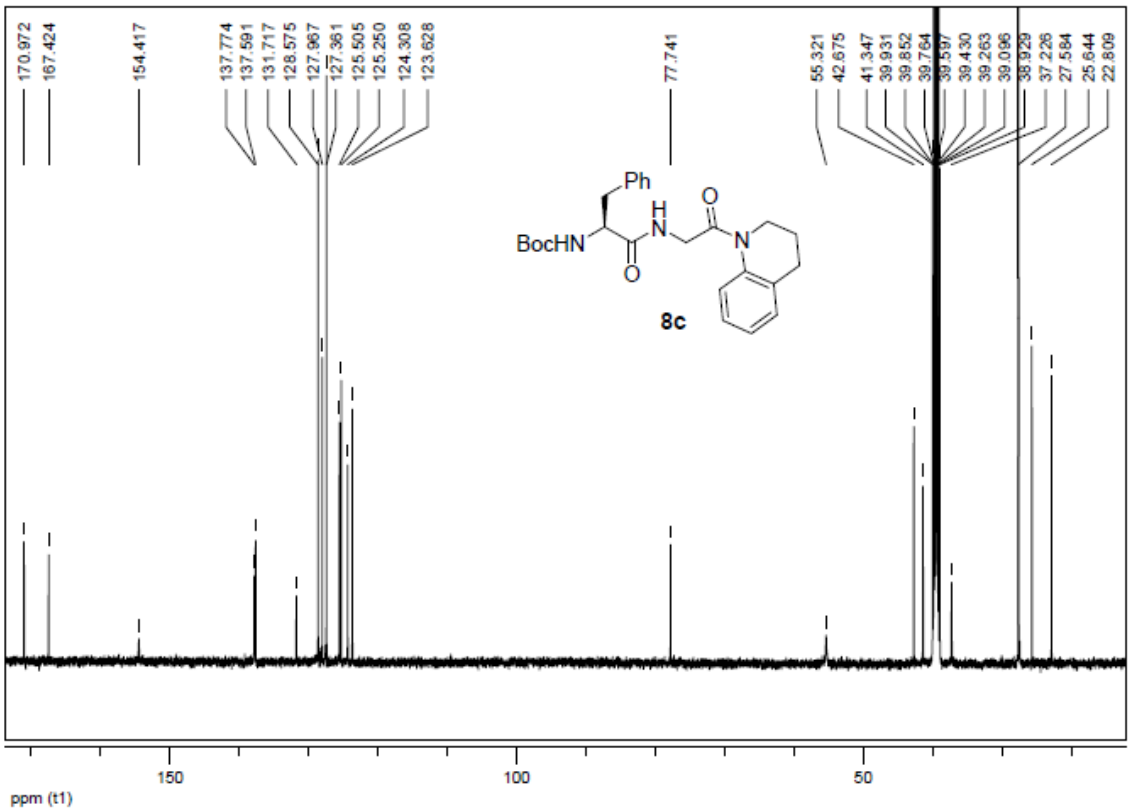
NMR spectra of compound **8b**



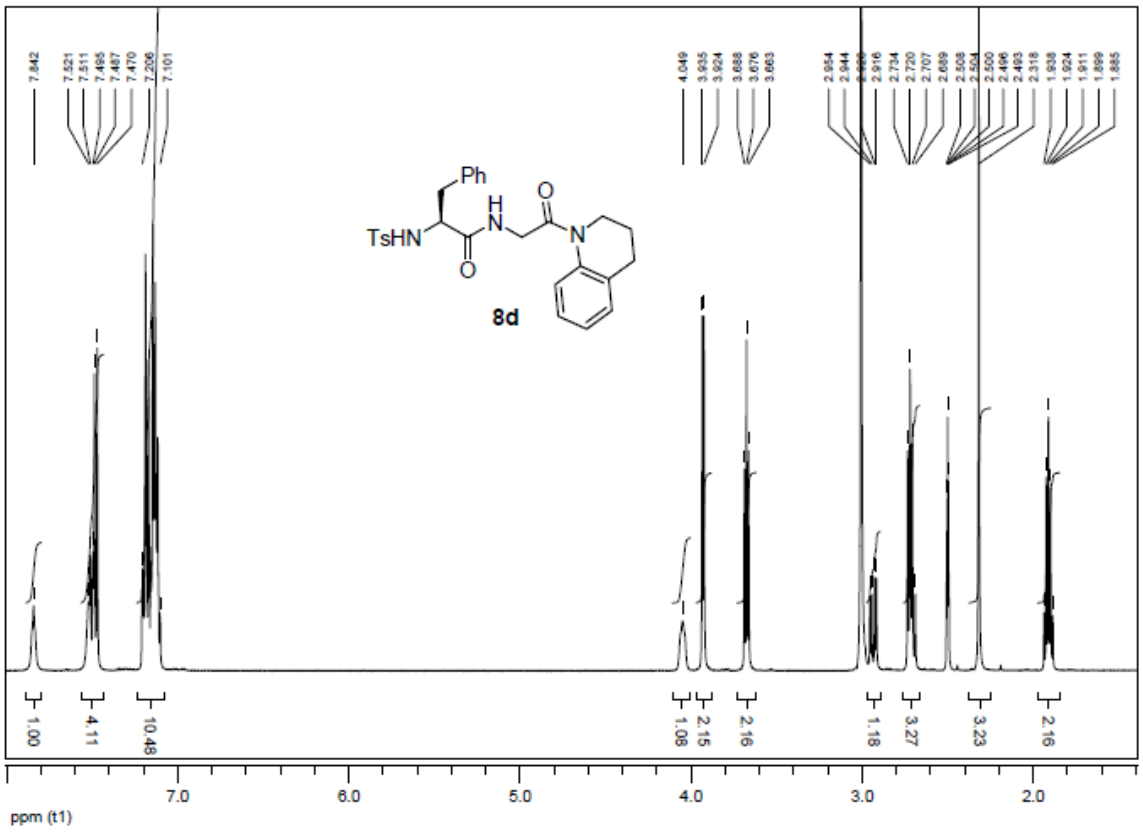


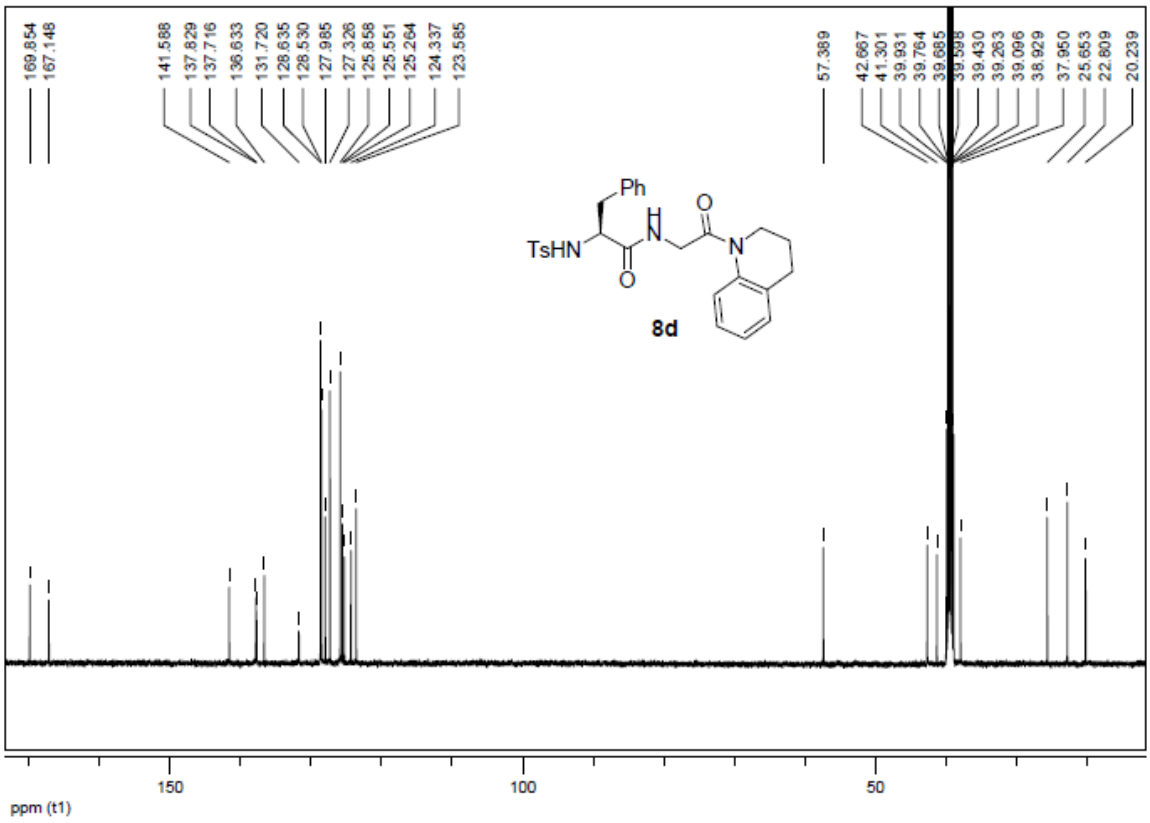
NMR spectra of compound **8c**



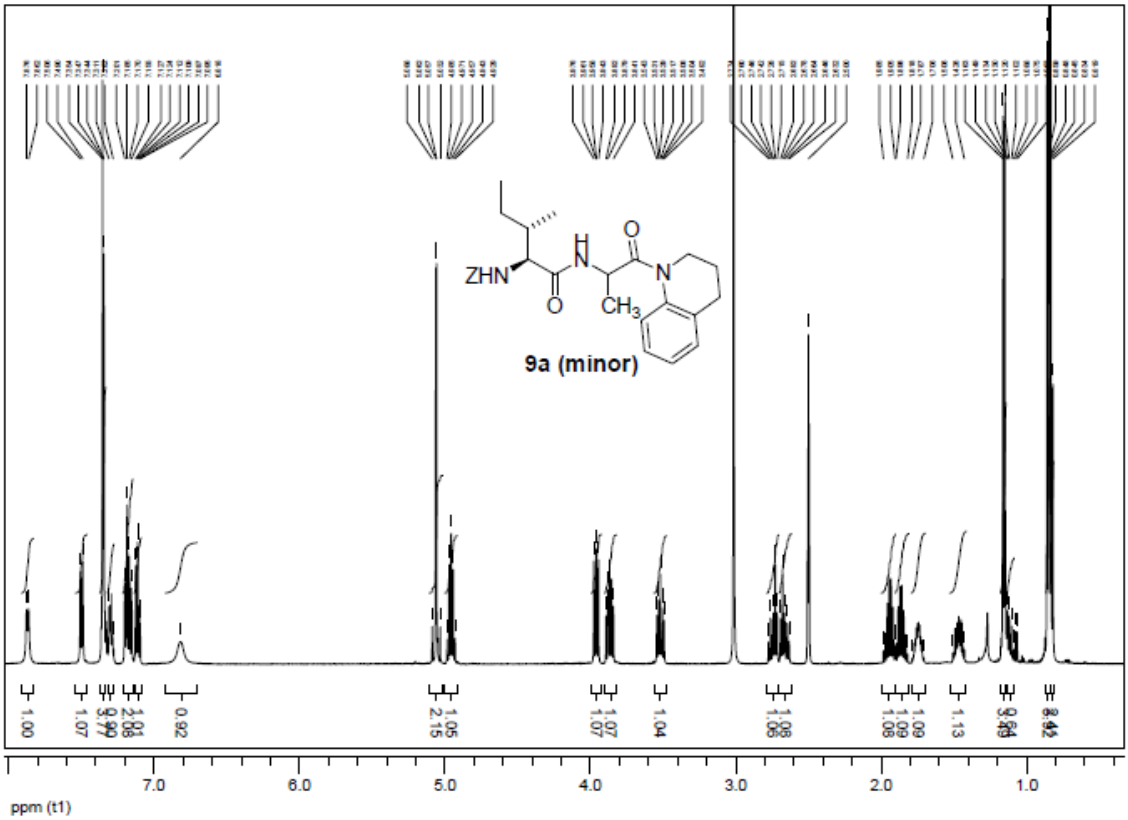


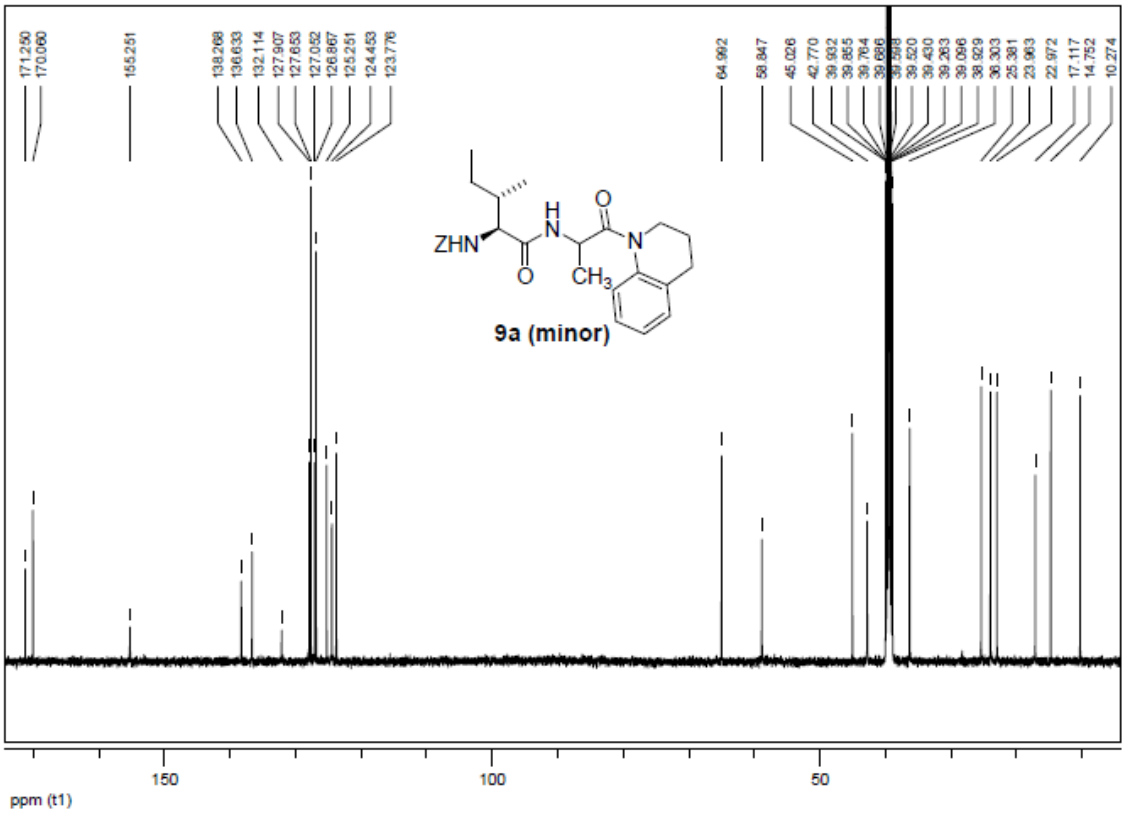
NMR spectra of compound **8d**



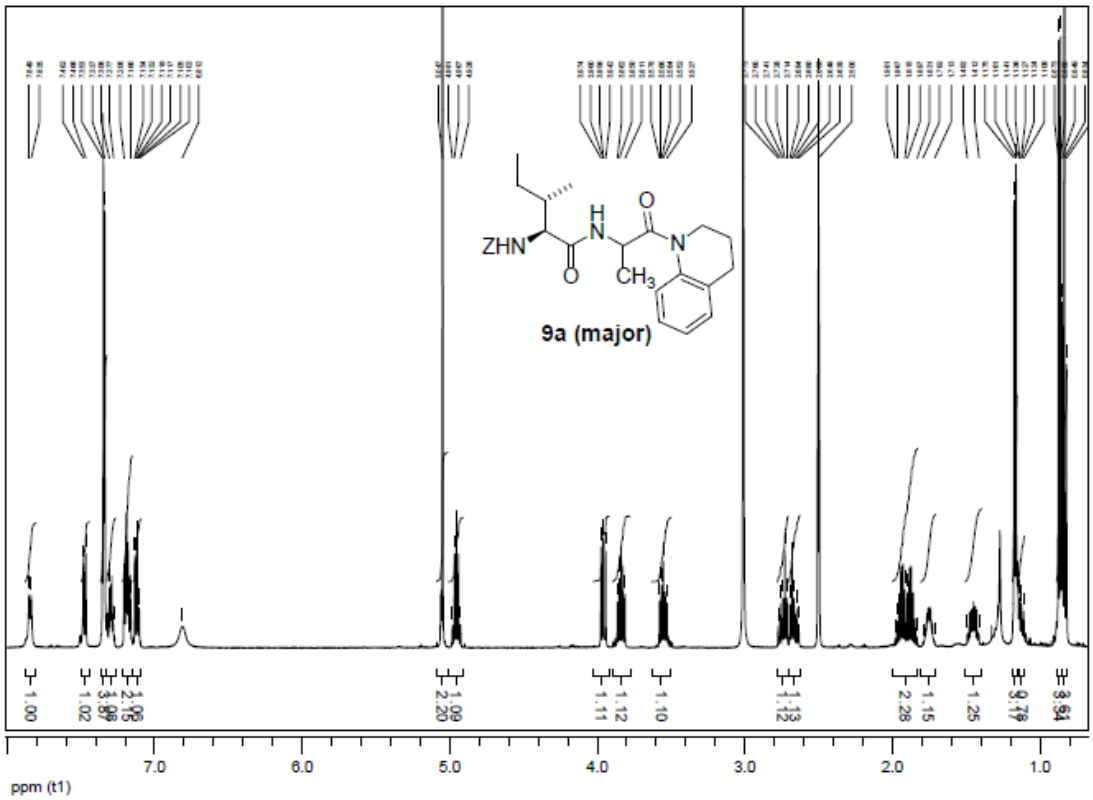


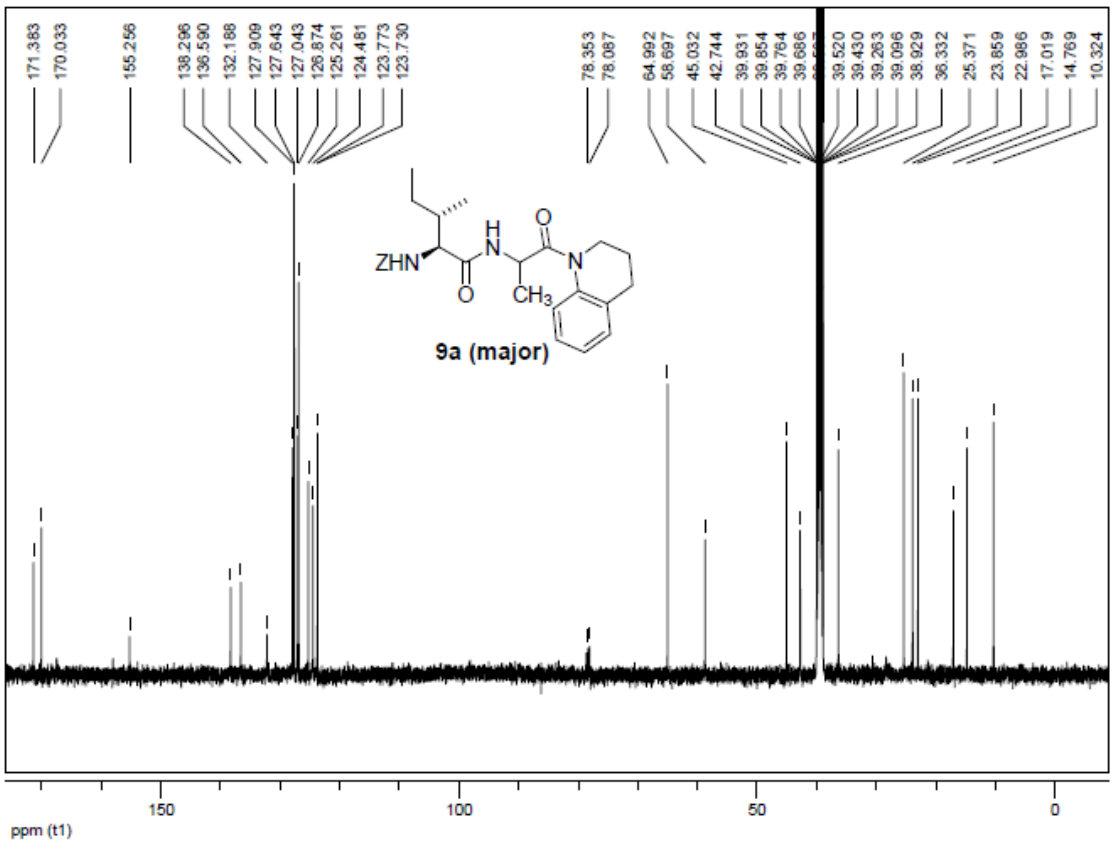
NMR spectra of compound **9a** (minor diastereomer)



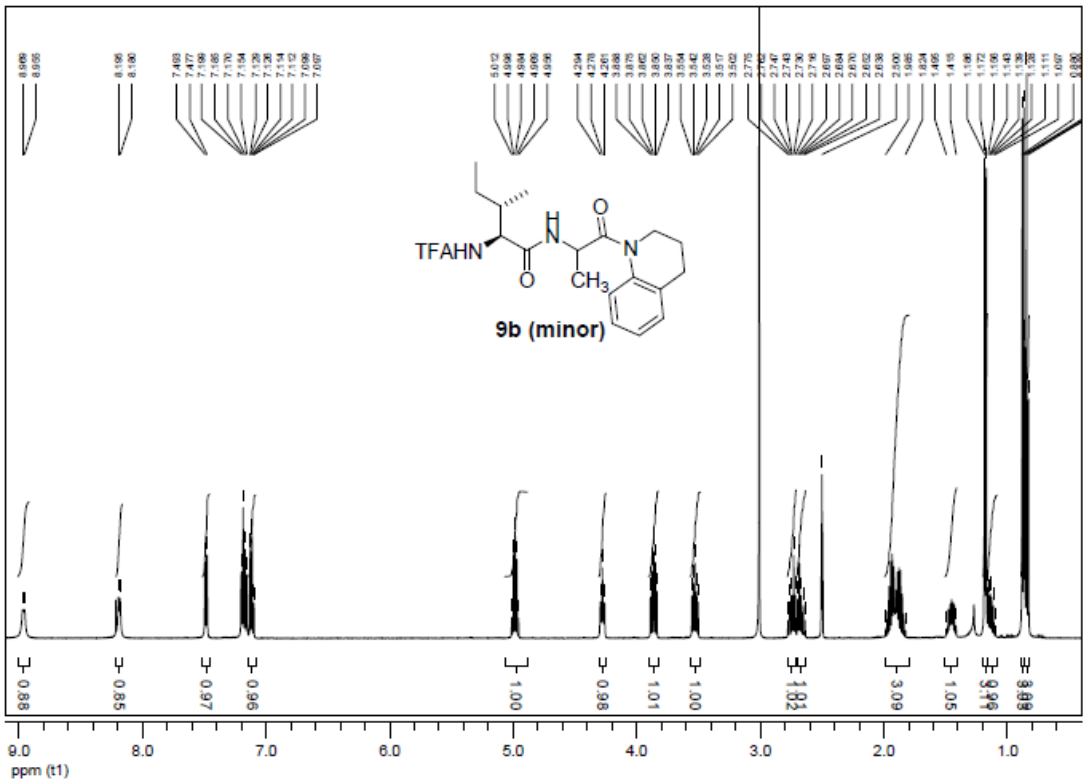


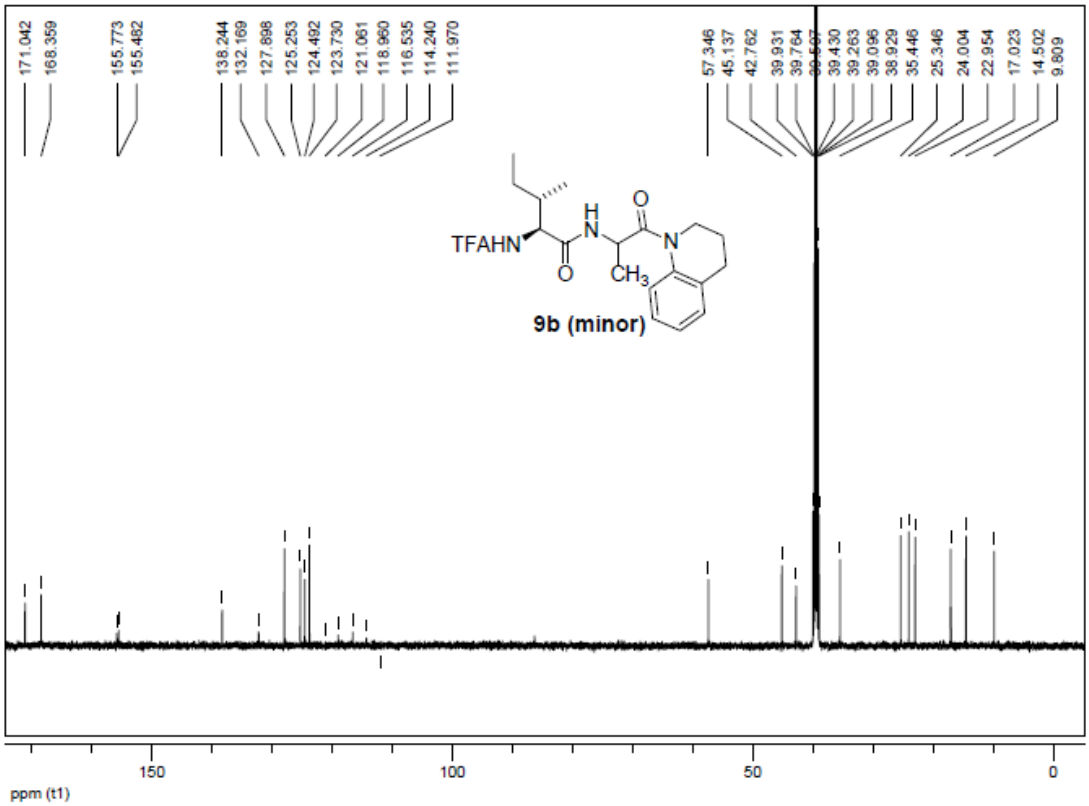
NMR spectra of compound **9a** (major diastereomer)



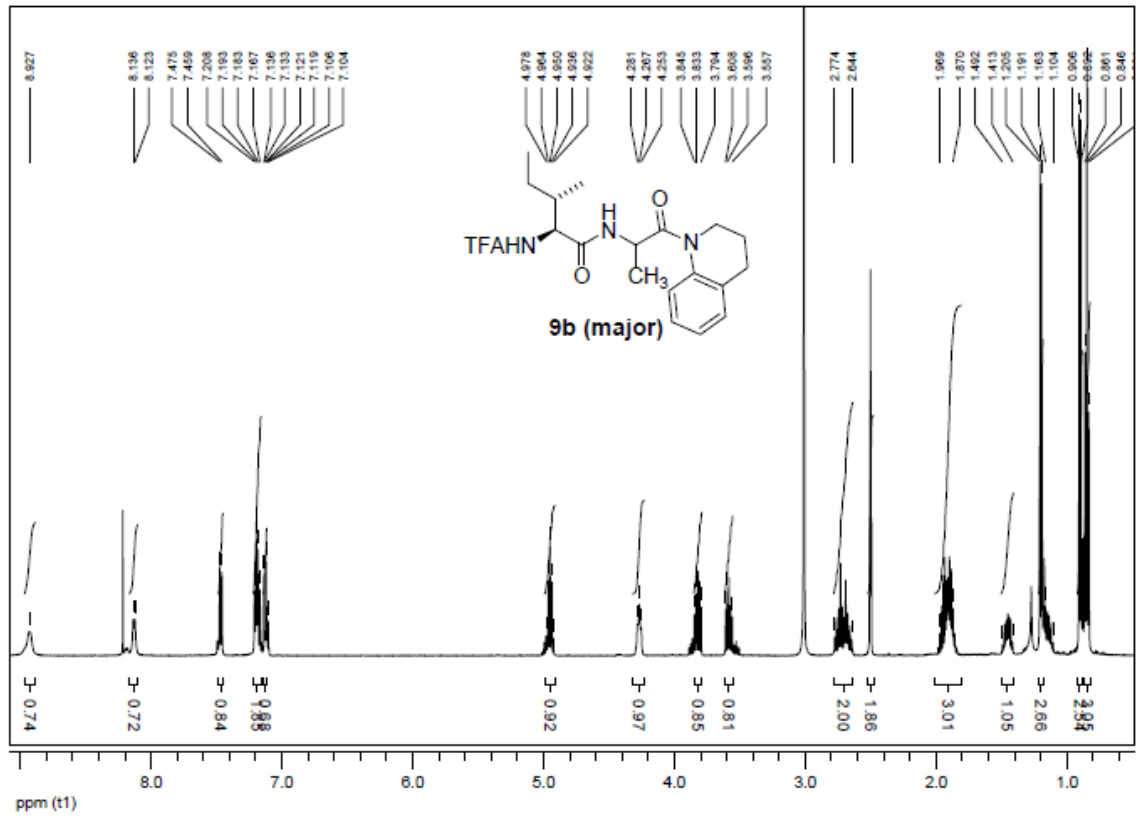


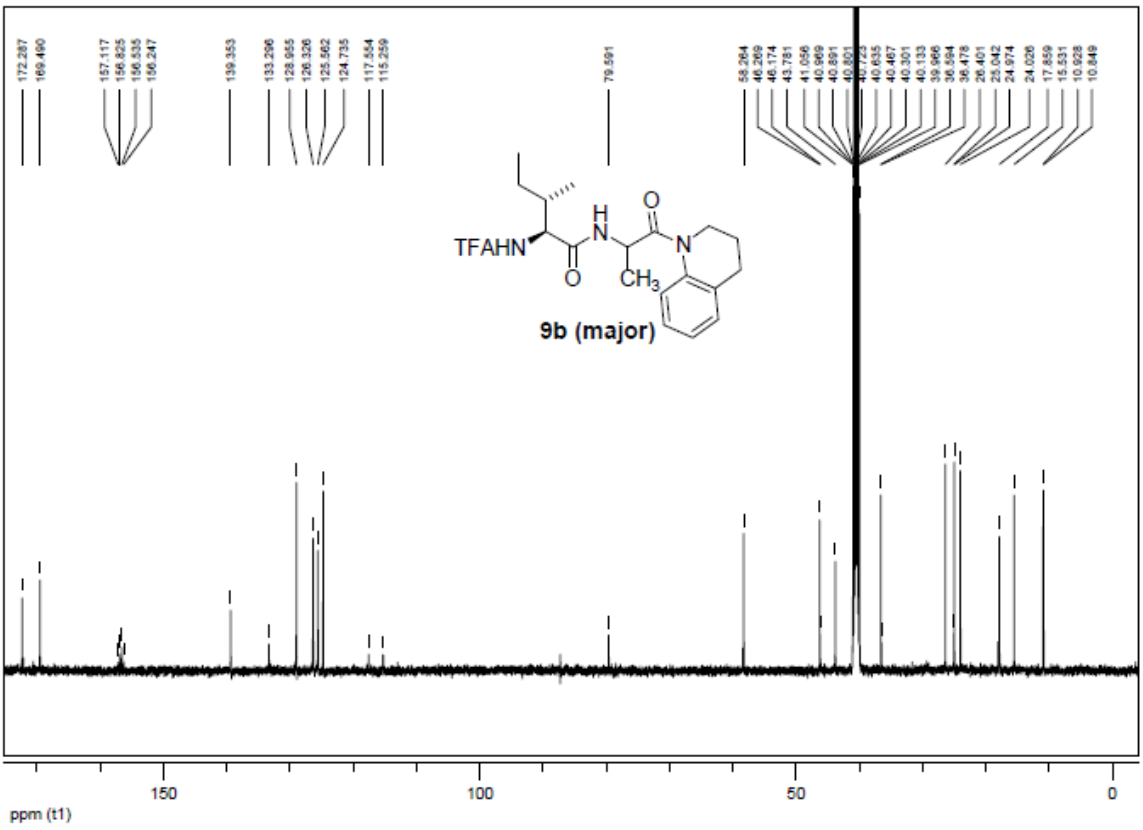
NMR spectra of compound **9b** (minor diastereomer)



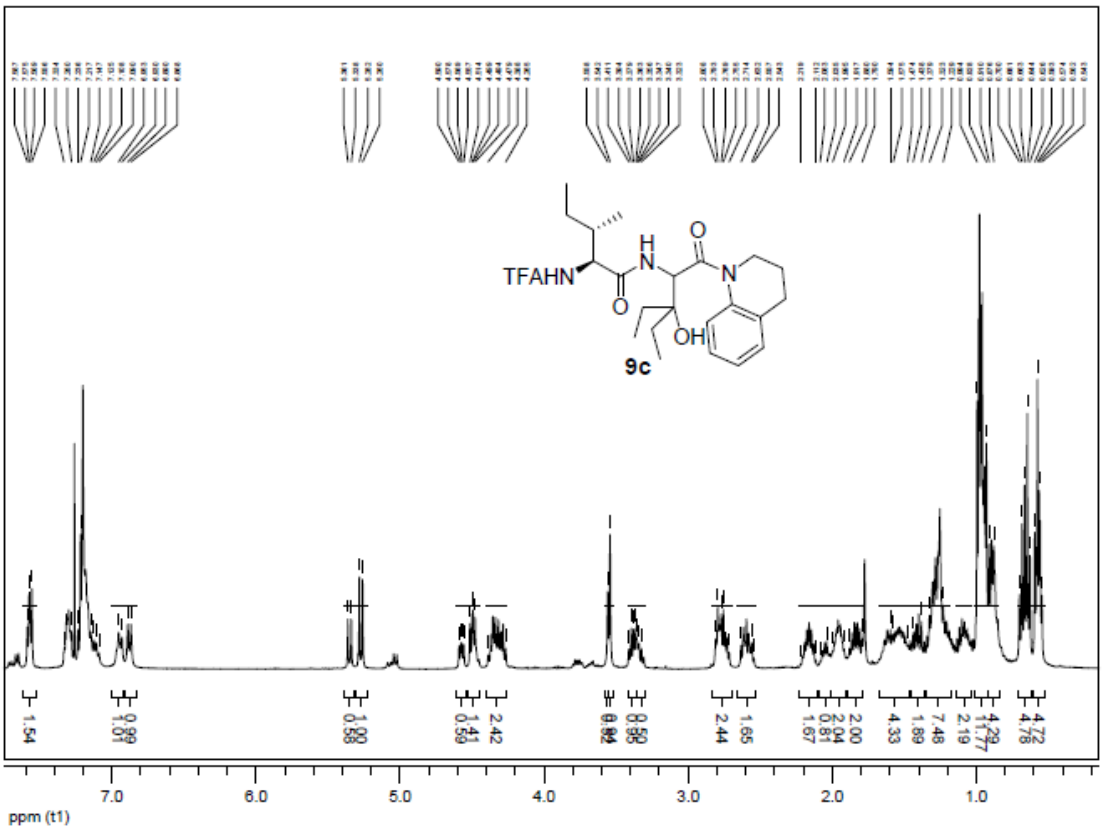


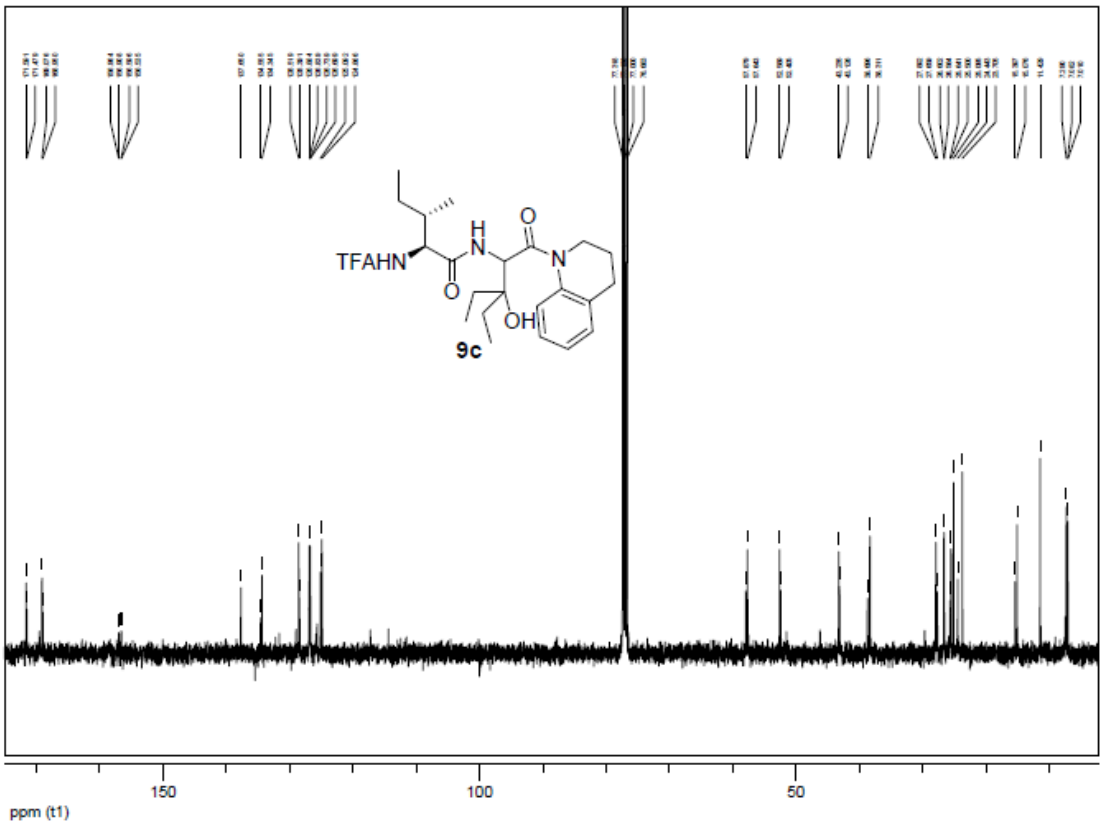
NMR spectra of compound **9b** (major diastereomer)



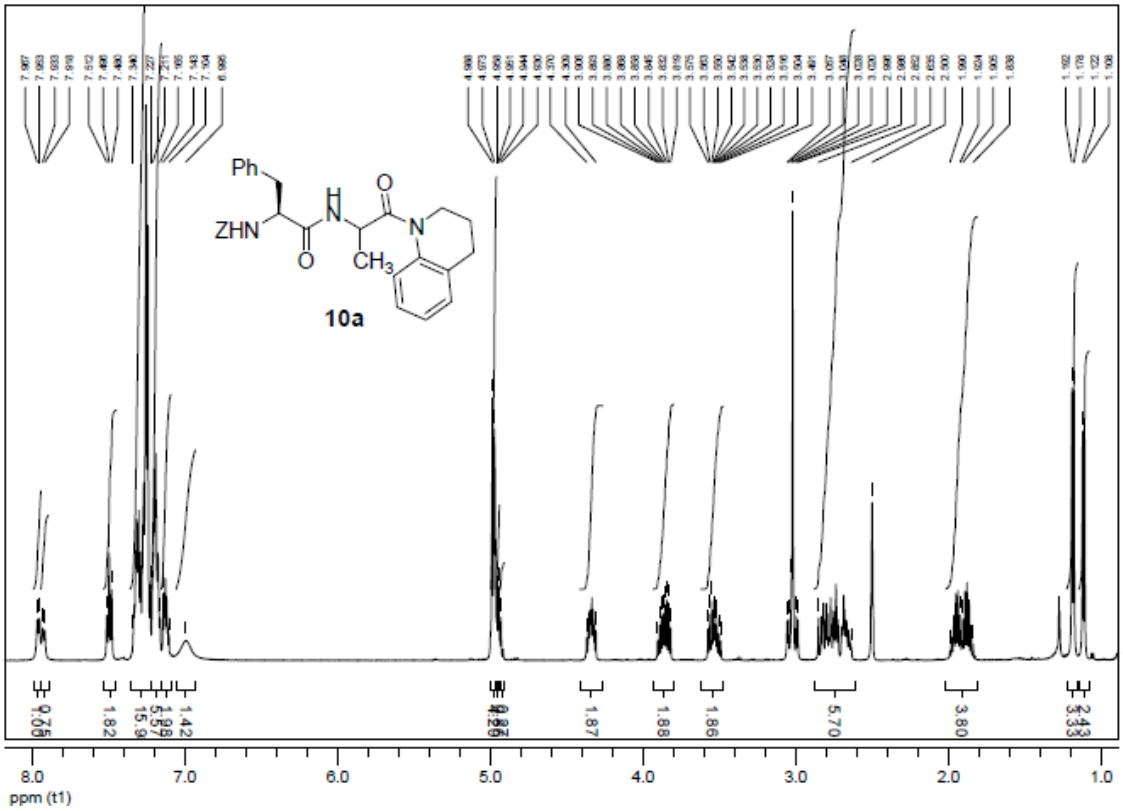


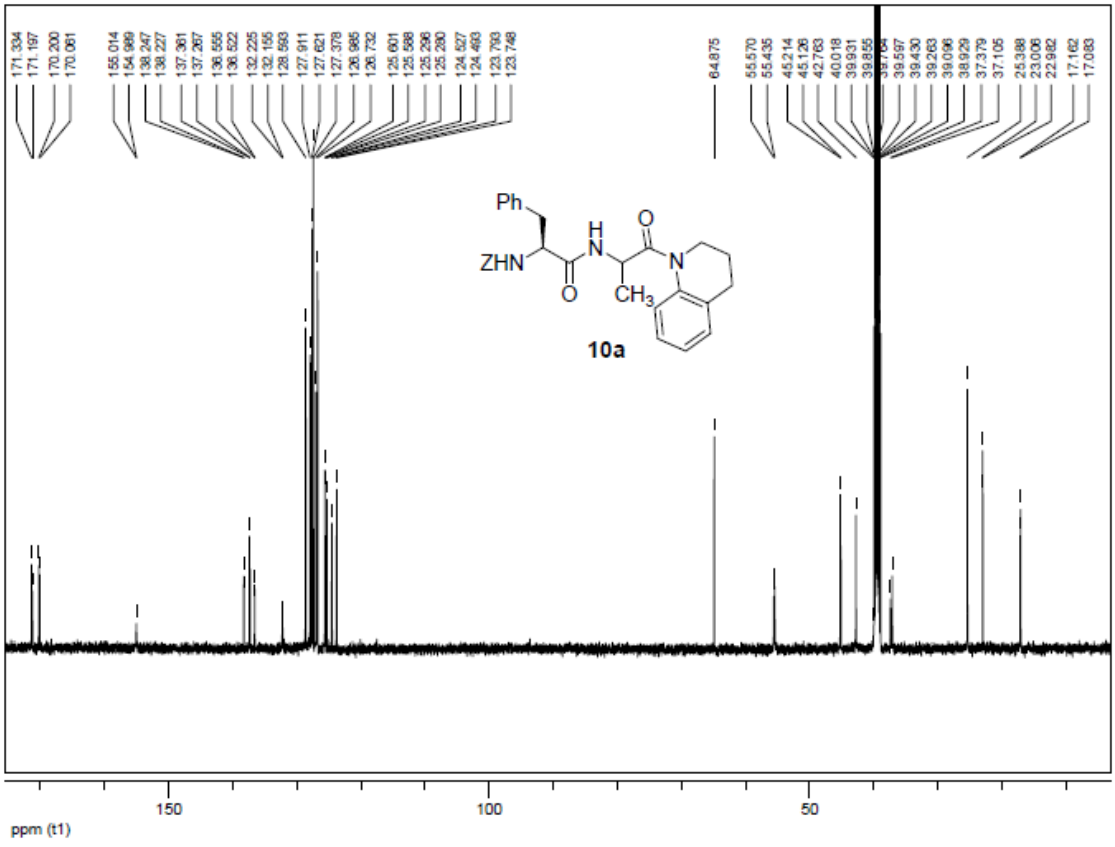
NMR spectra of compound **9c**



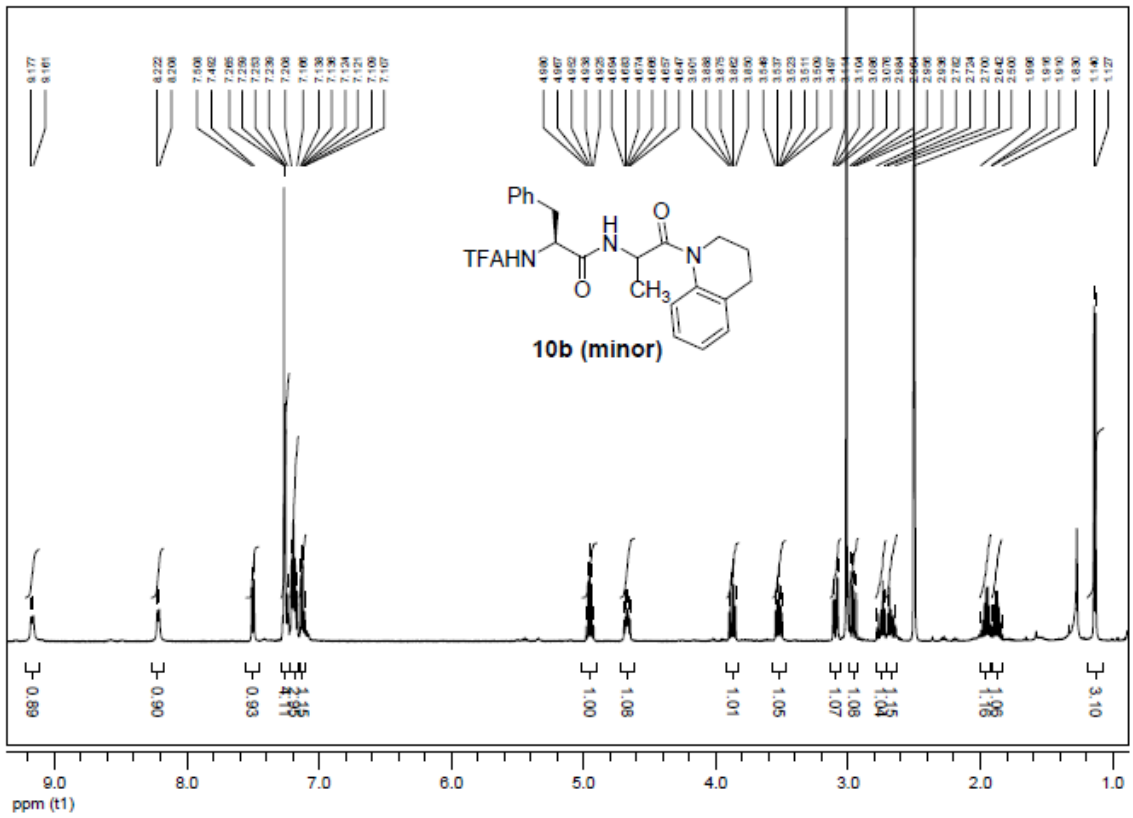


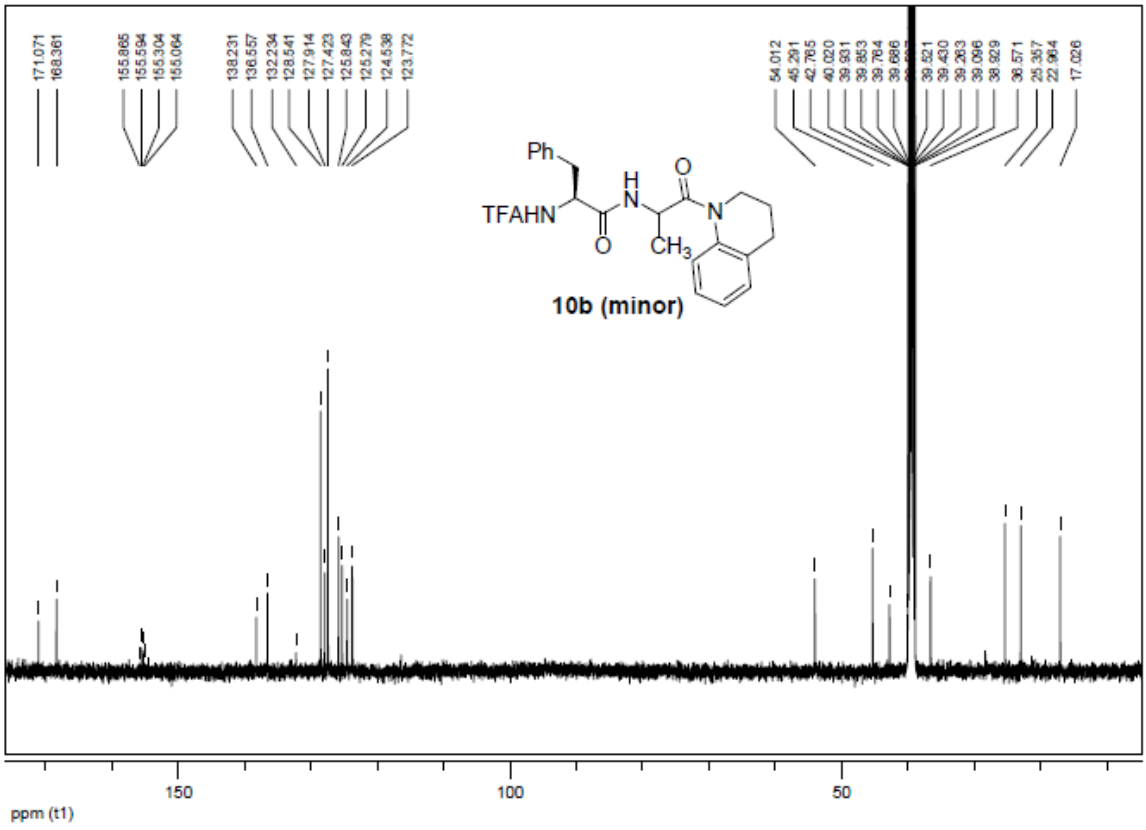
NMR spectra of compound **10a**



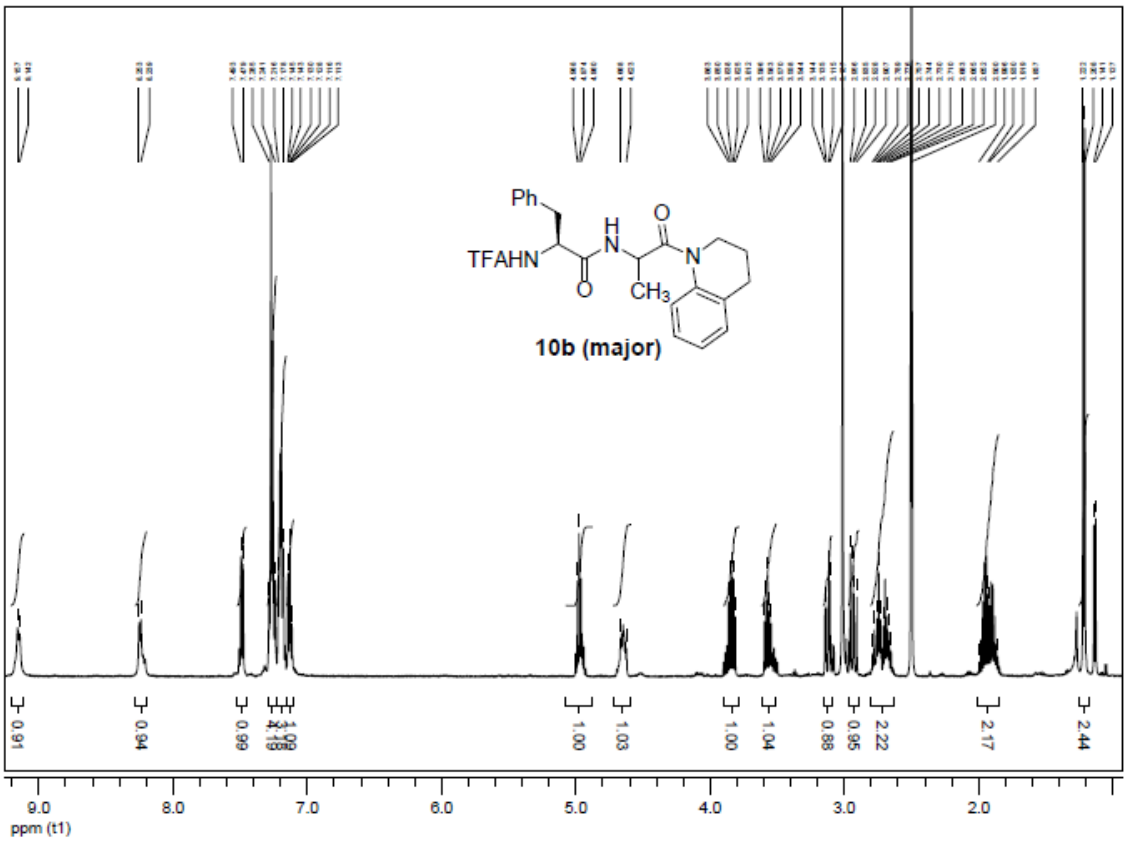


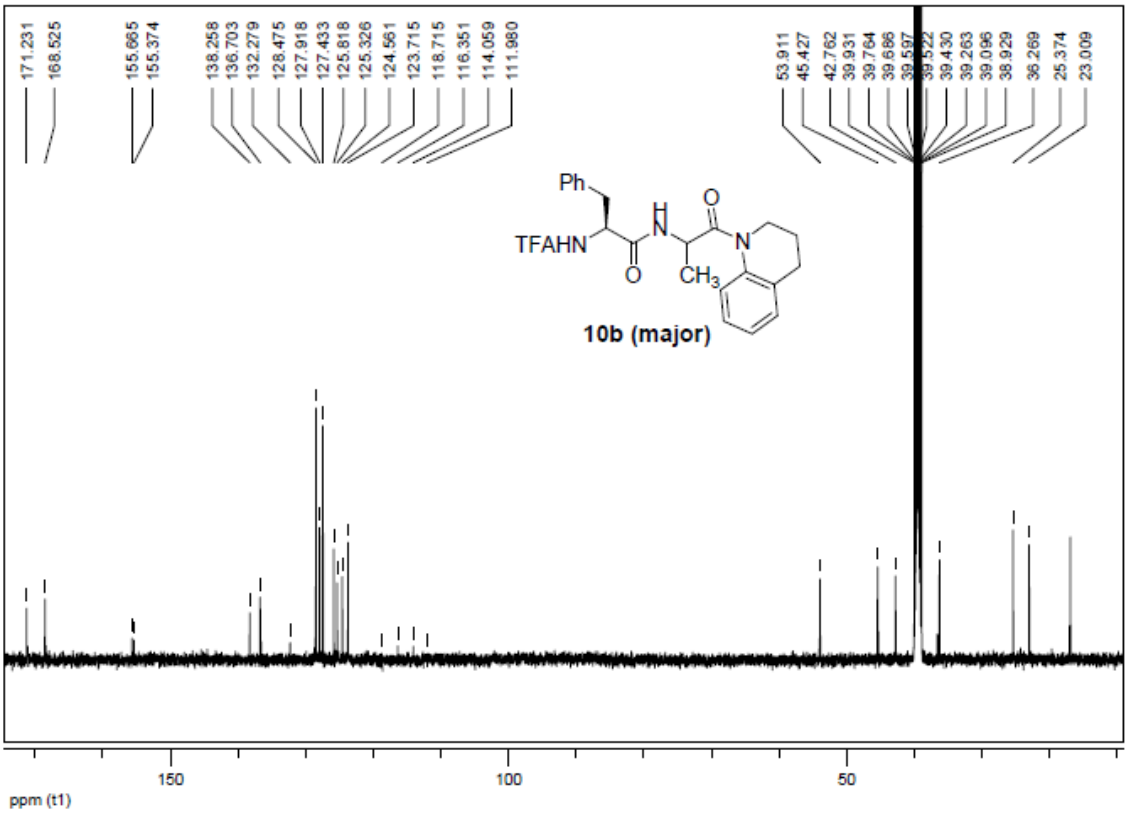
NMR spectra of compound **10b** (minor diastereomer)



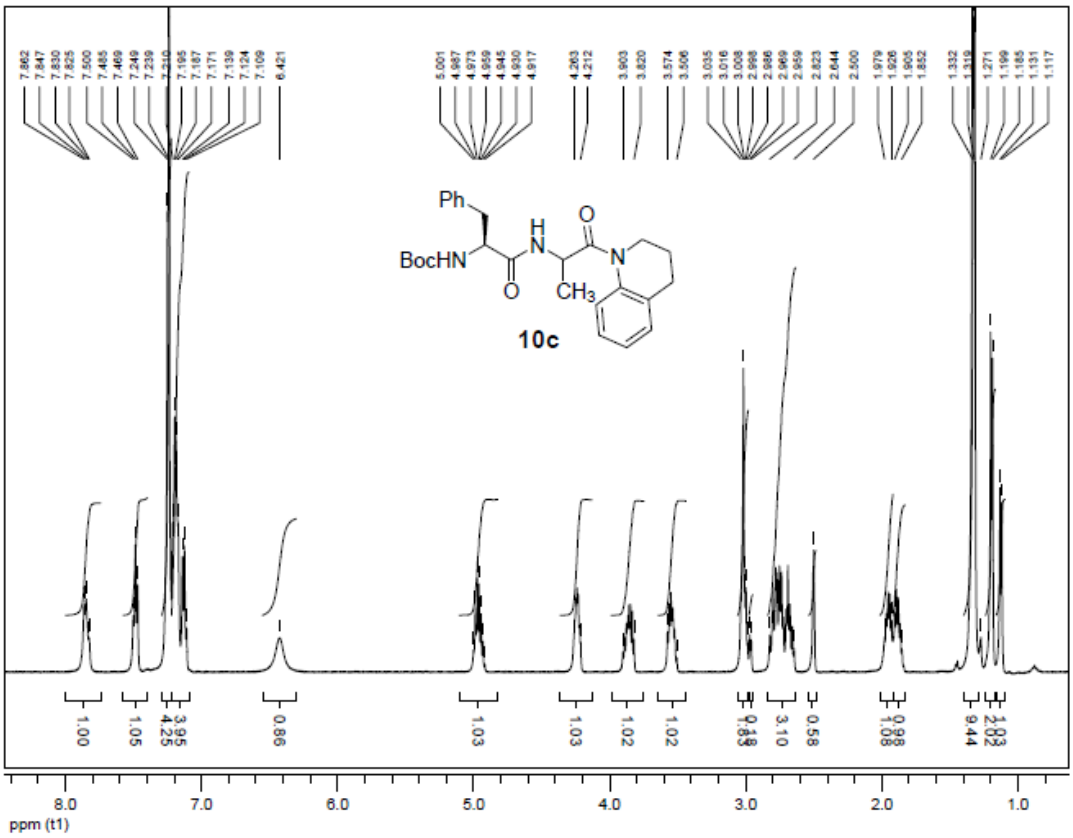


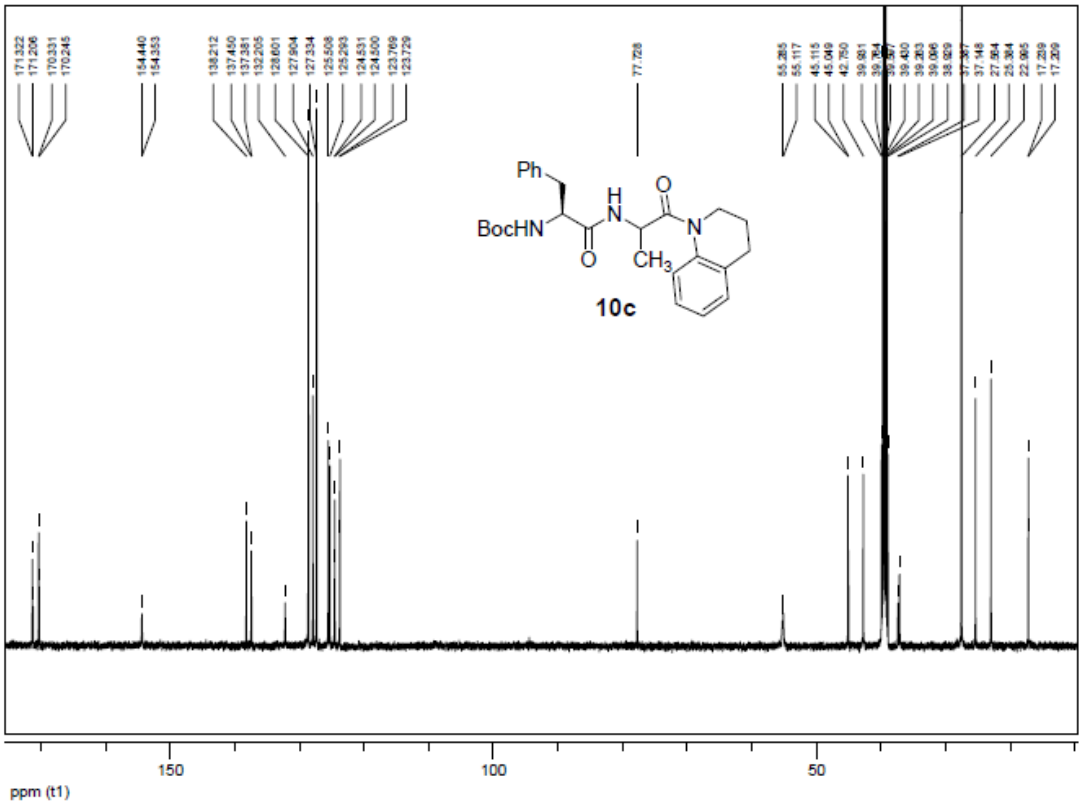
NMR spectra of compound **10b** (major diastereomer)



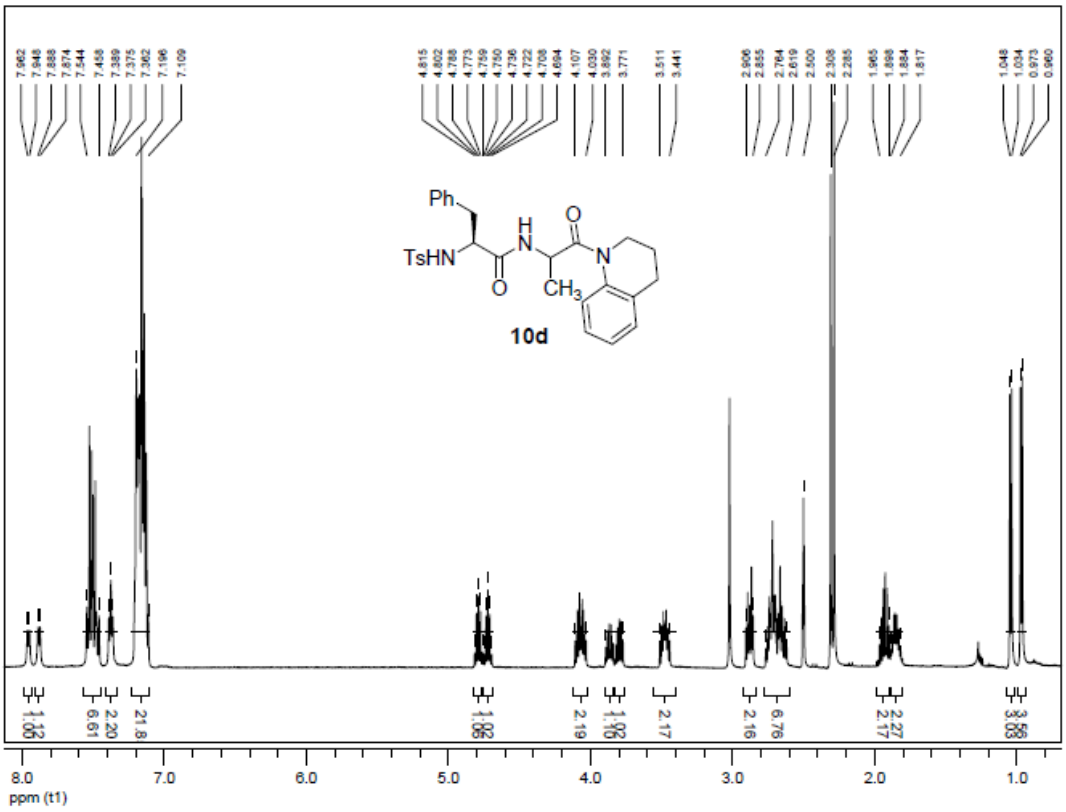


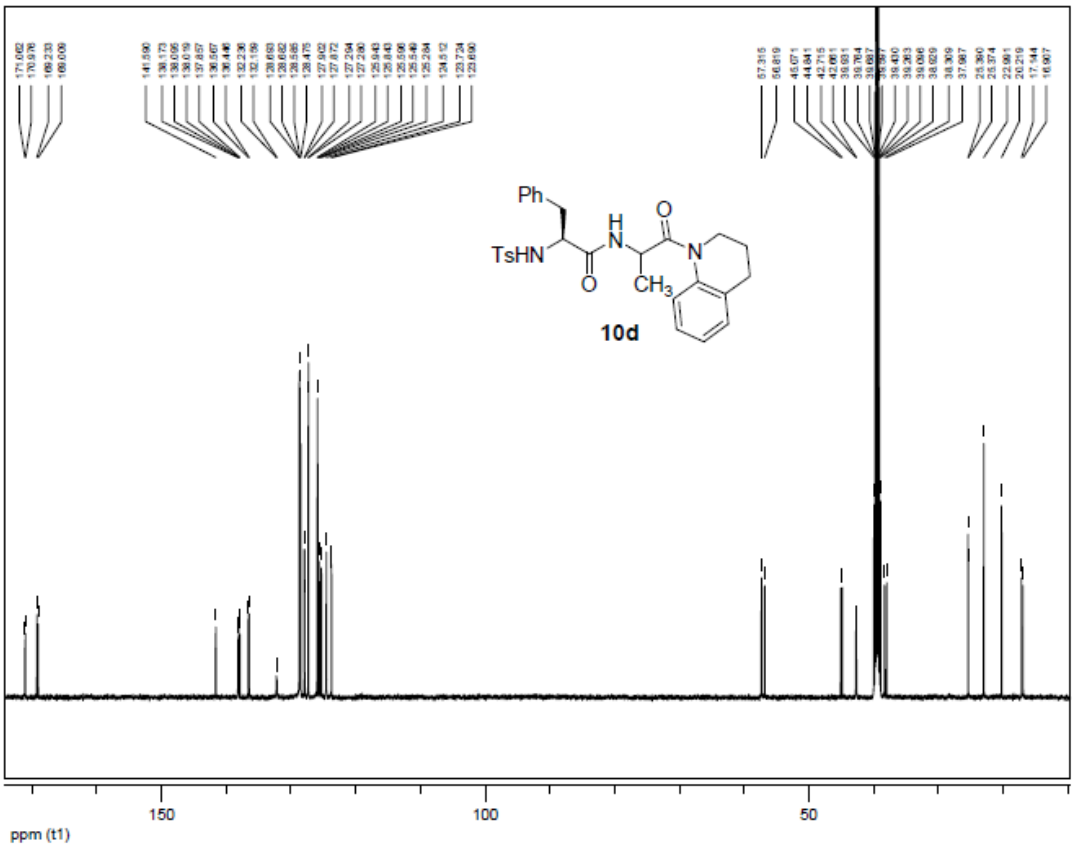
NMR spectra of compound **10c**



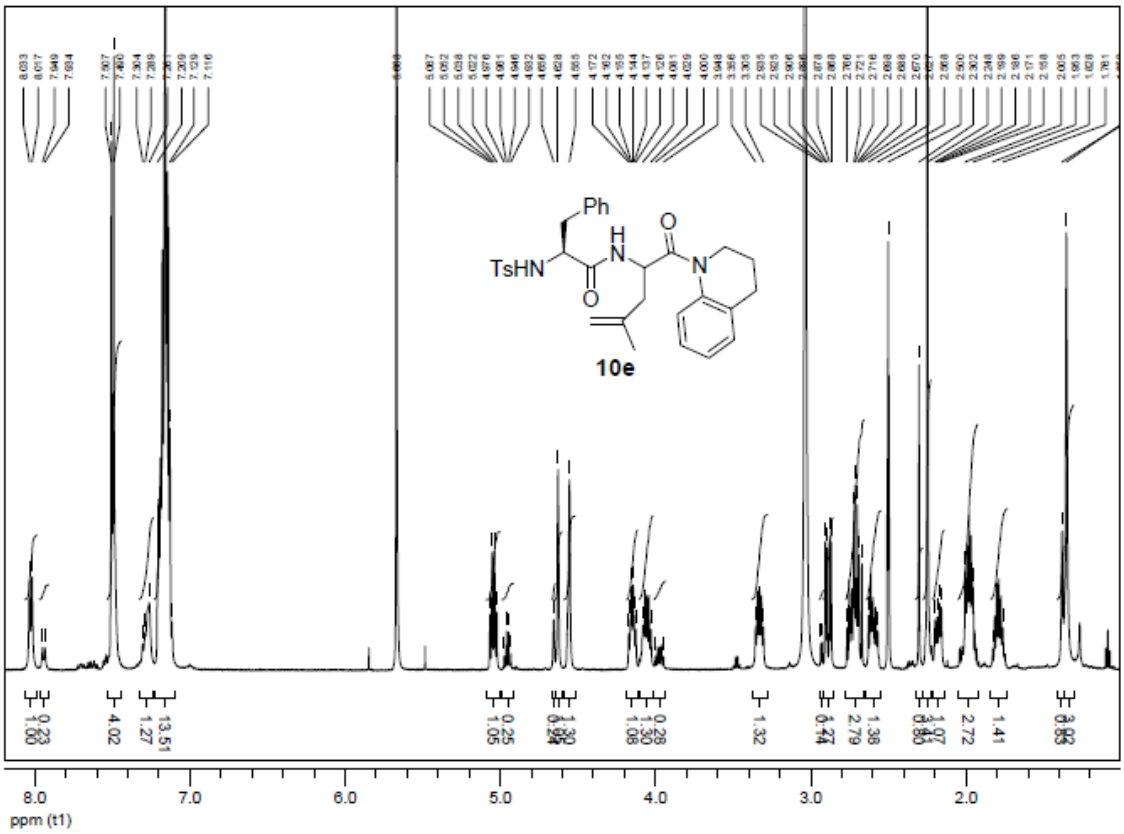


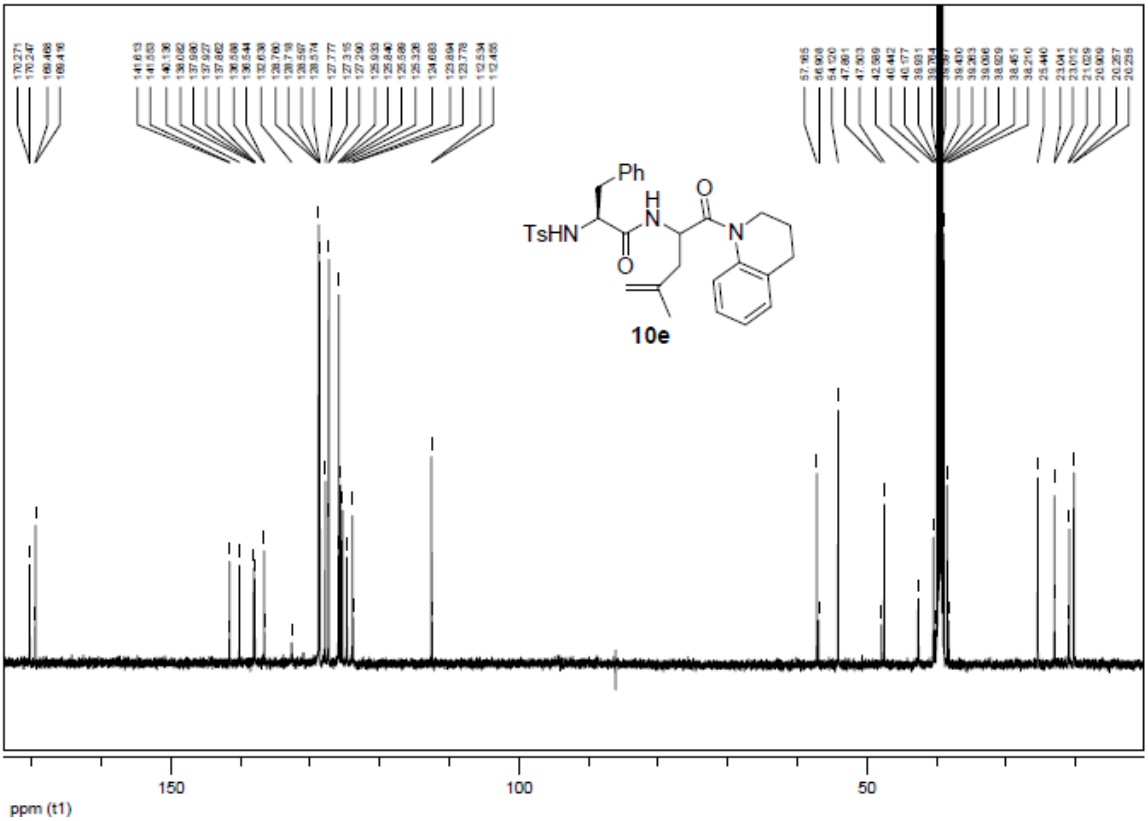
NMR spectra of compound **10d**



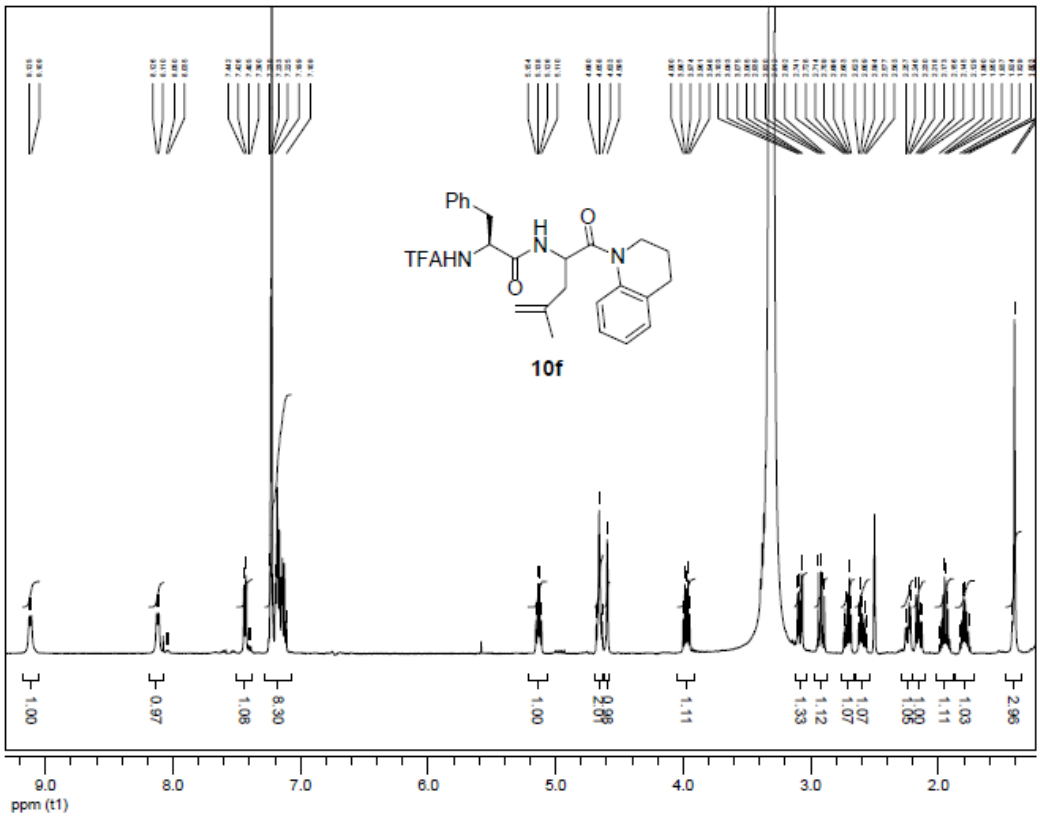


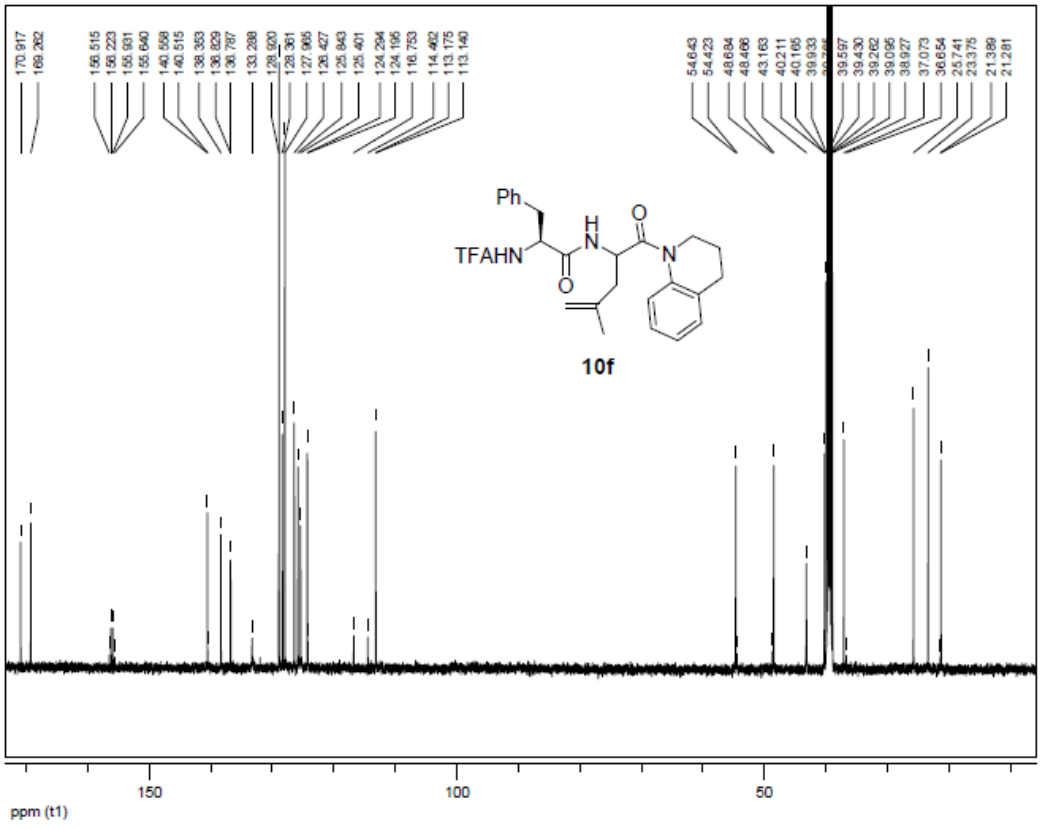
NMR spectra of compound **10e**



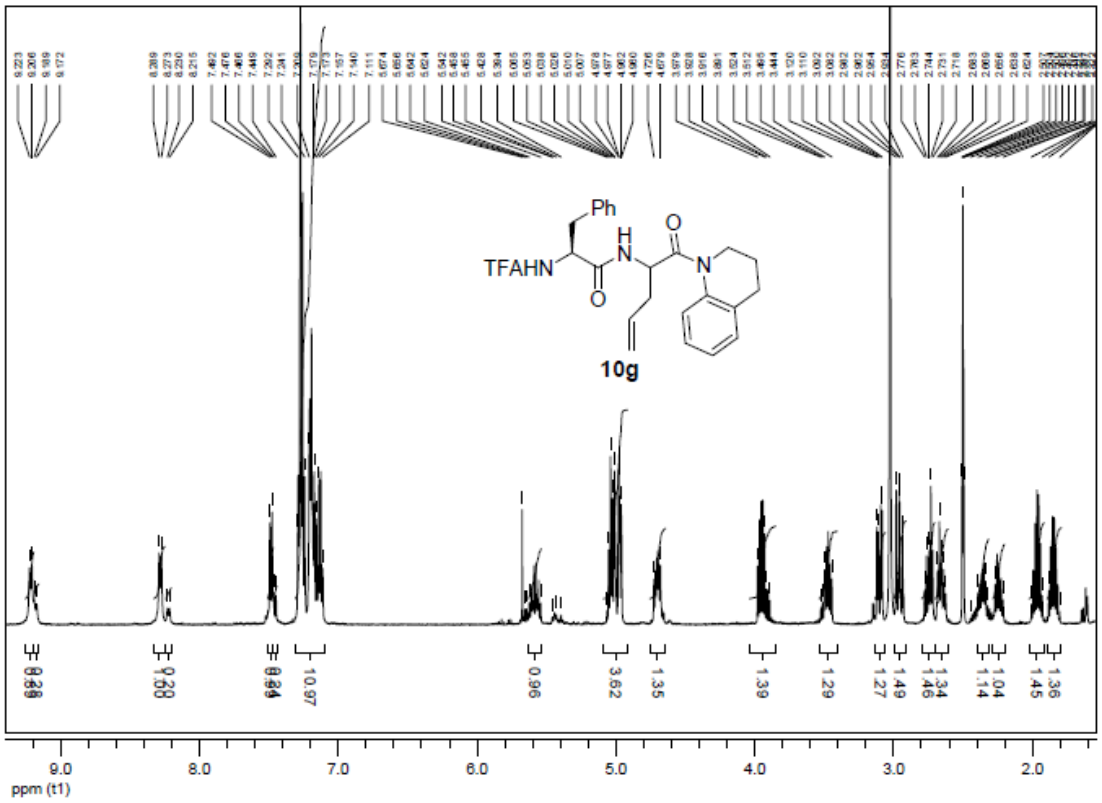


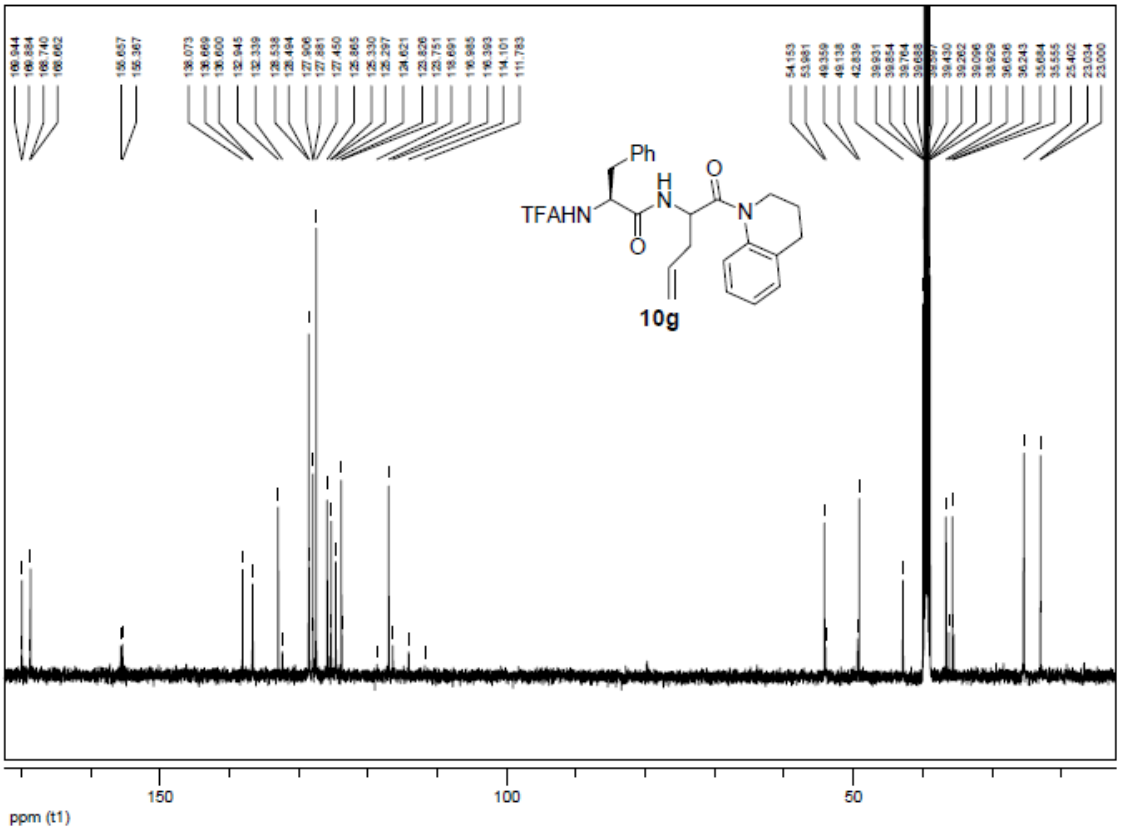
NMR spectra of compound **10f**



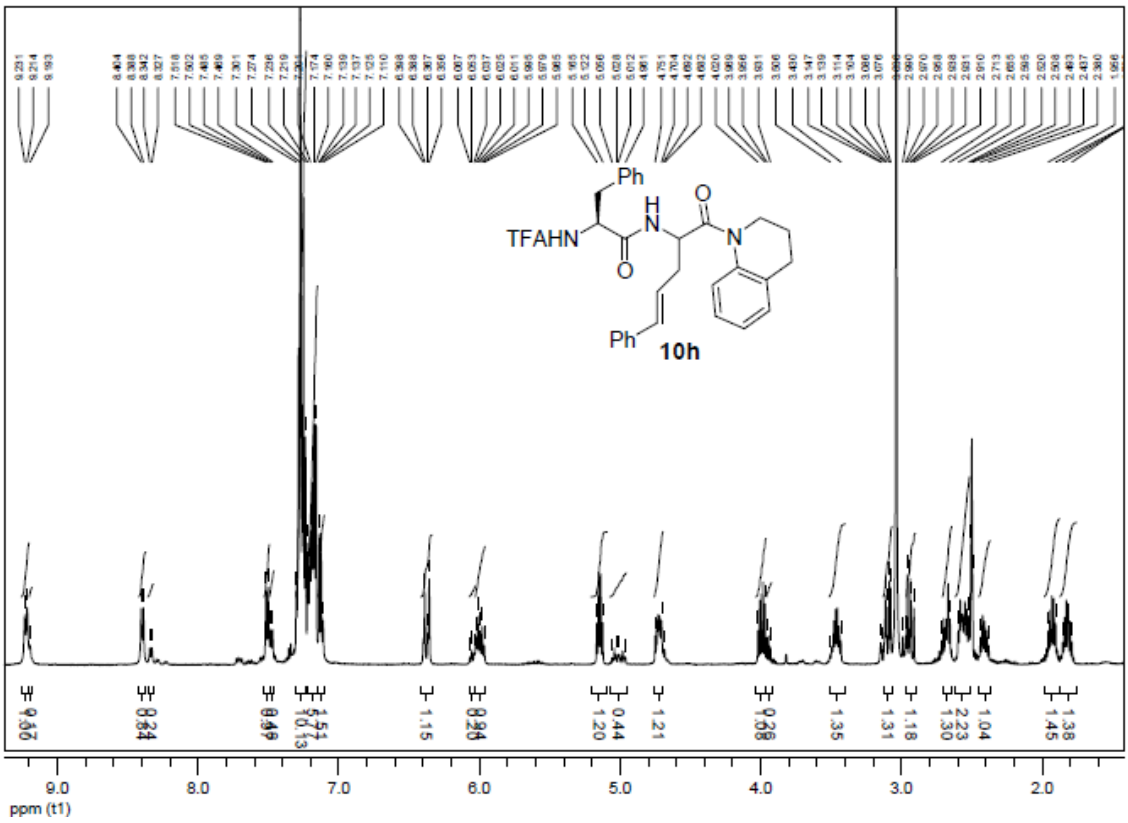


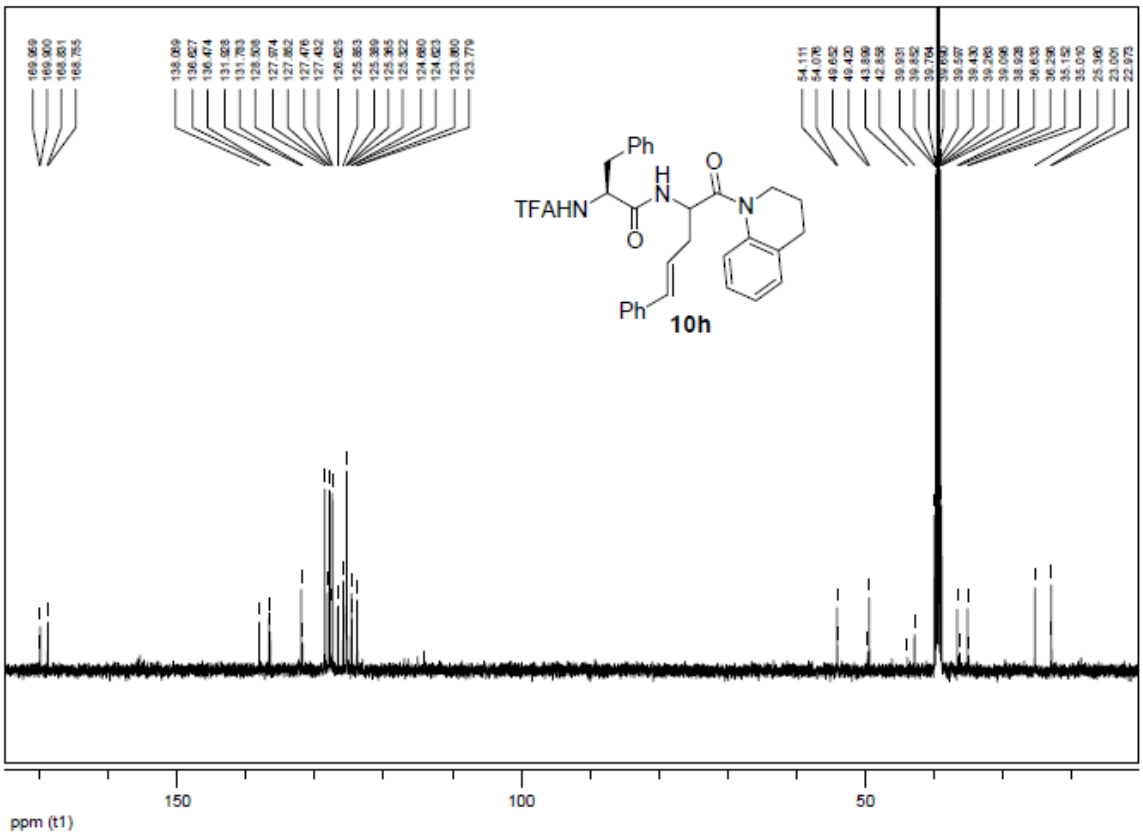
NMR spectra of compound **10g**



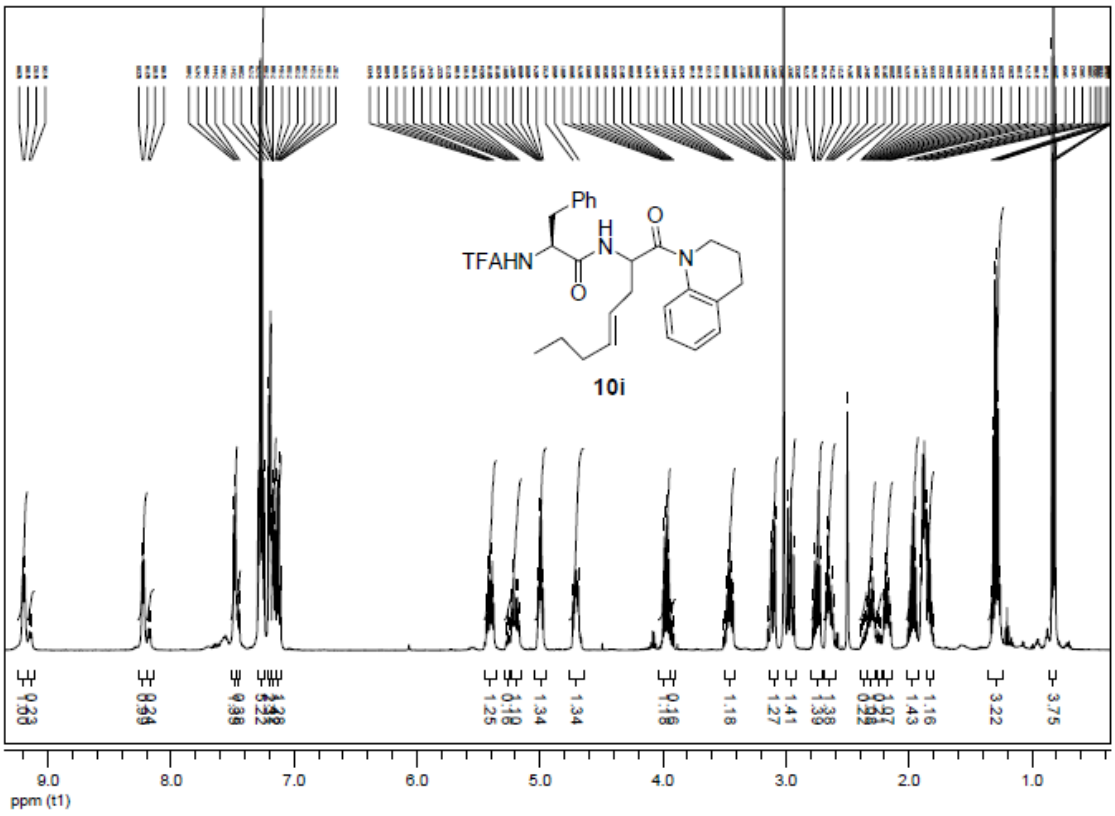


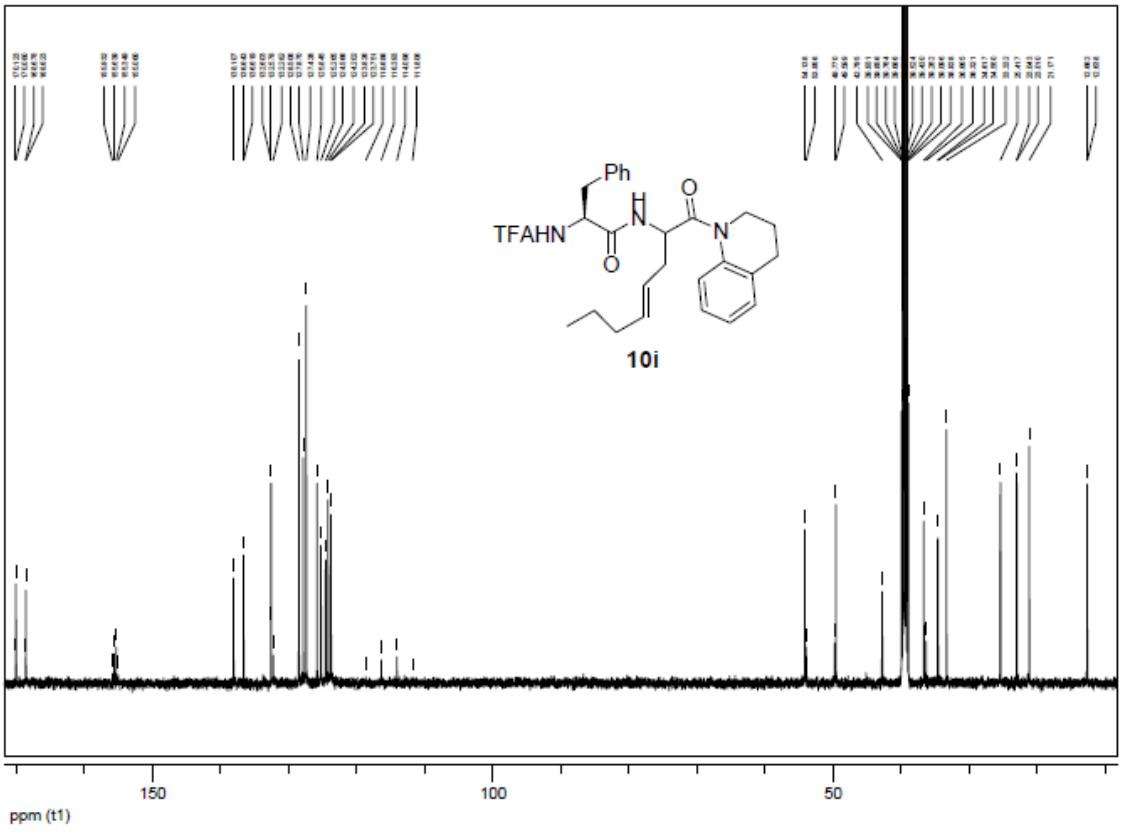
NMR spectra of compound **10h**



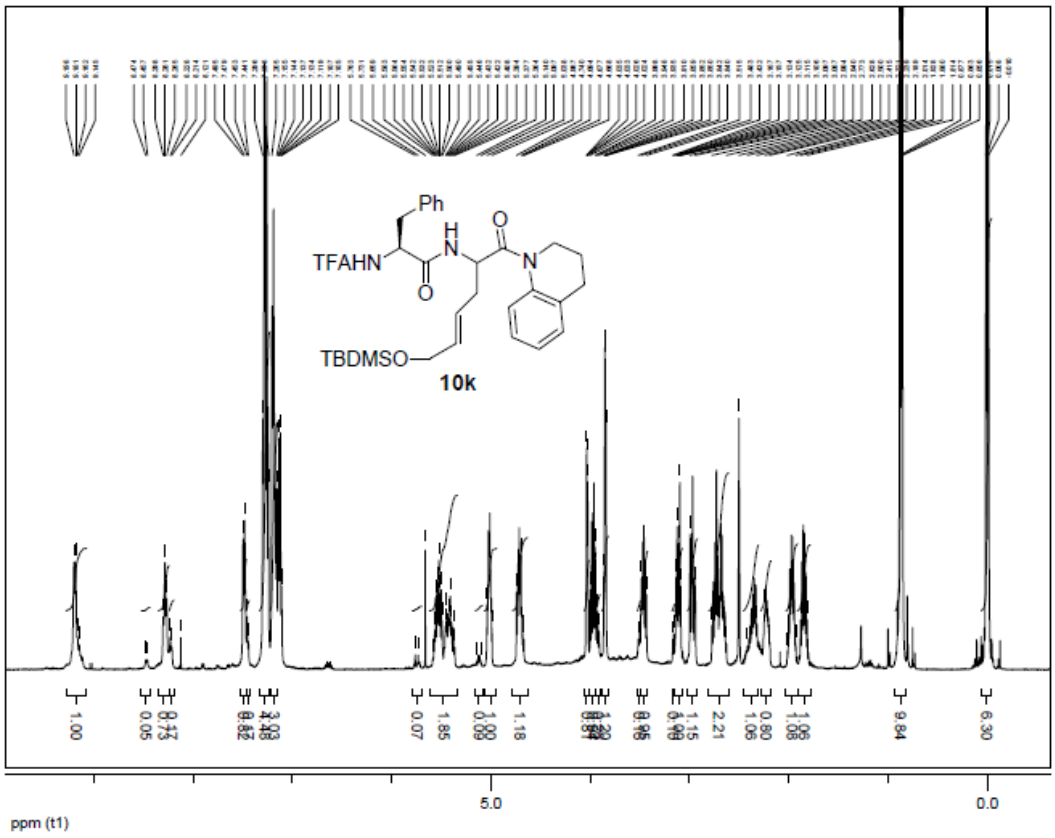


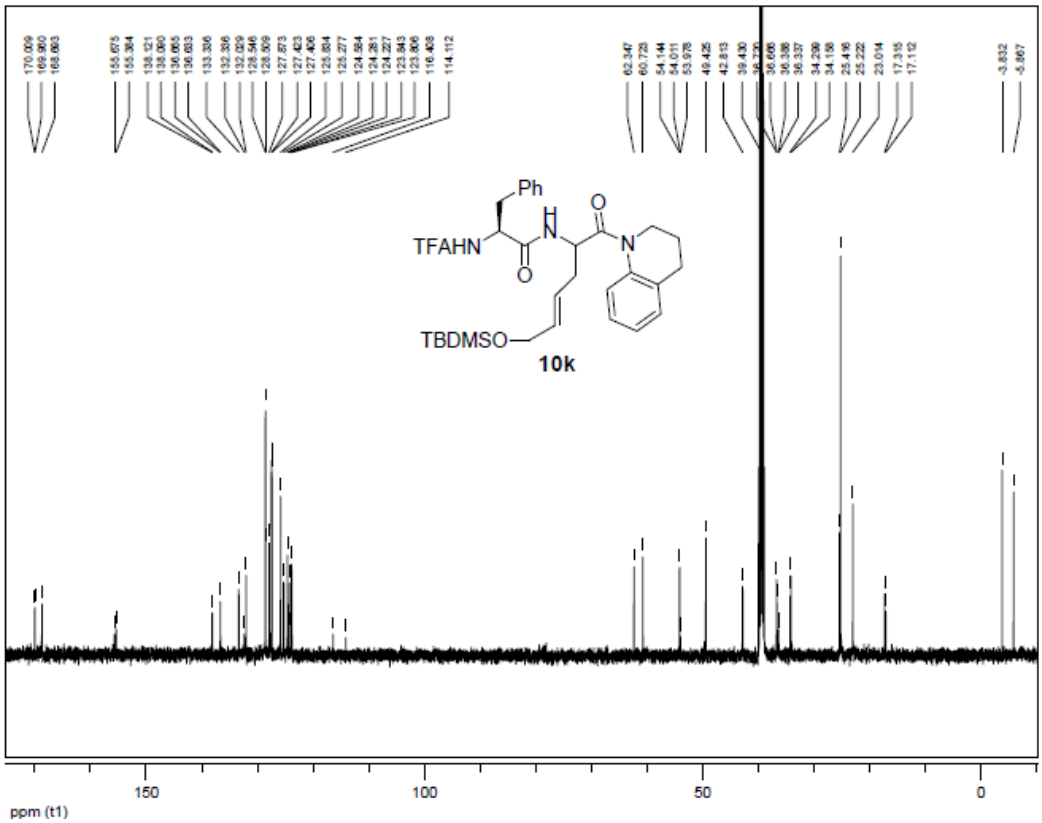
NMR spectra of compound **10i**



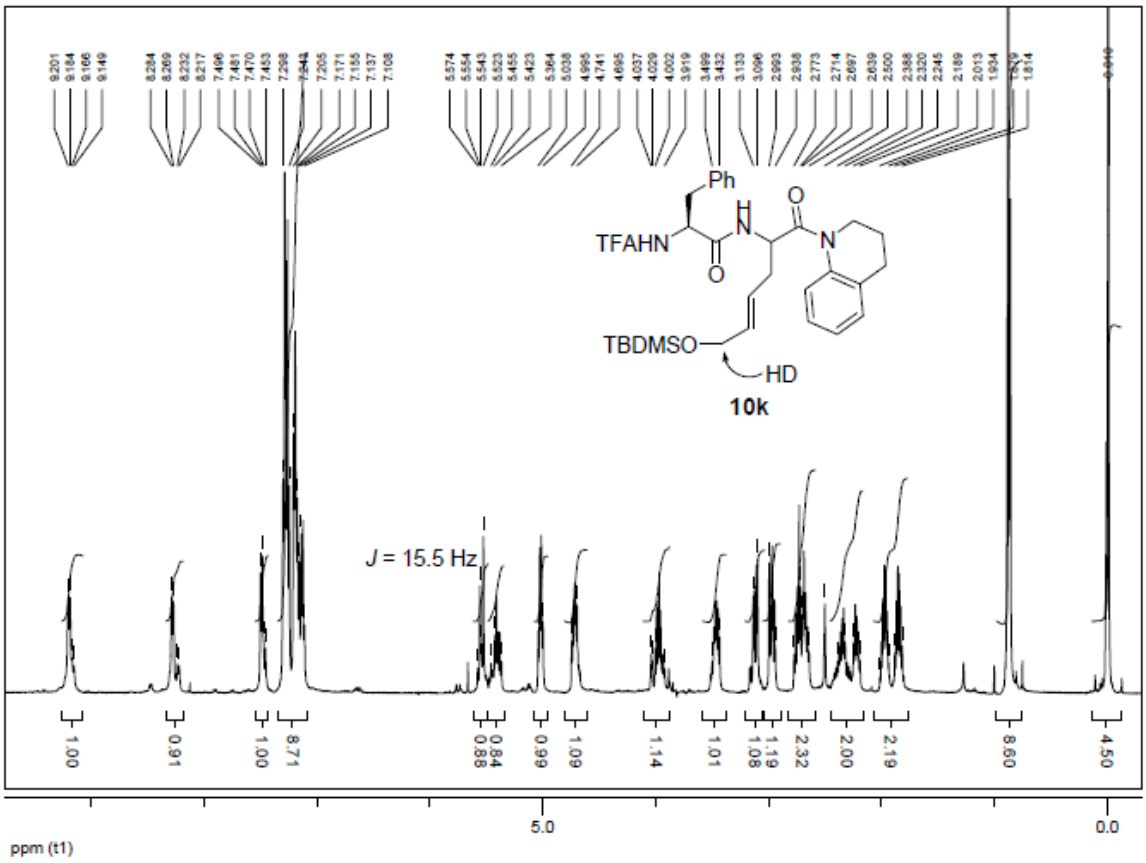


NMR spectra of compound **10k**

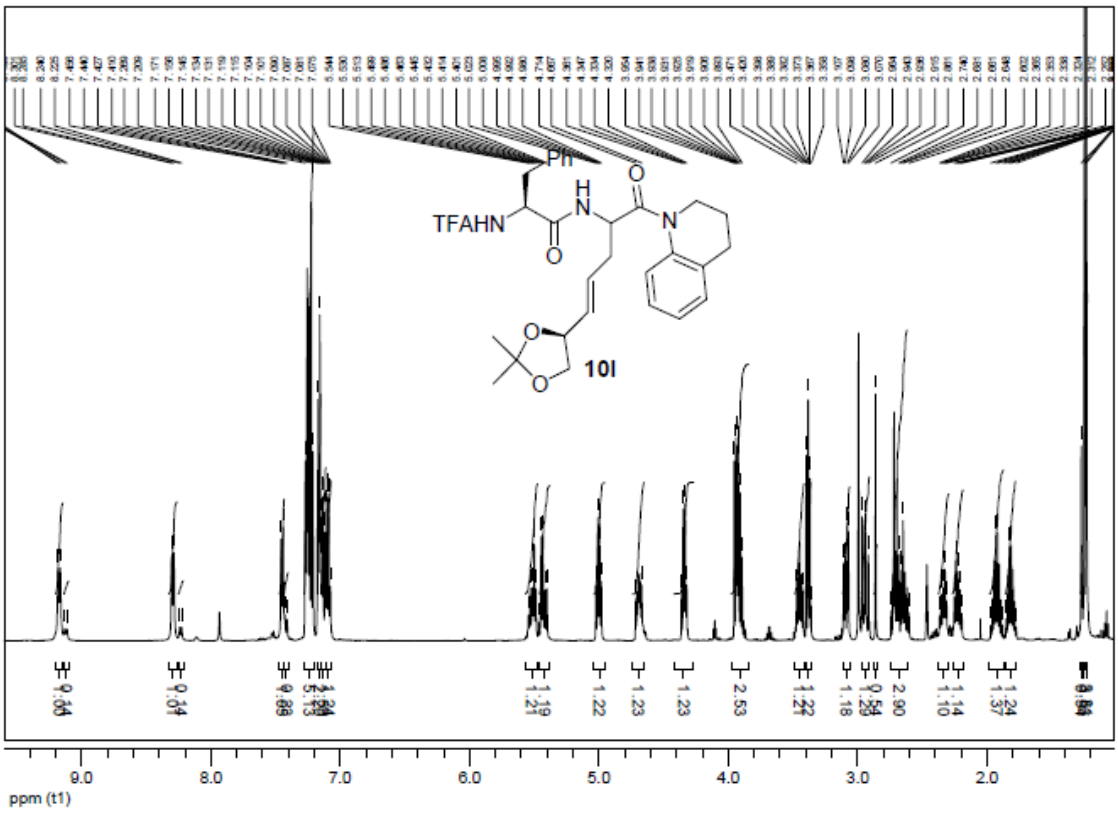


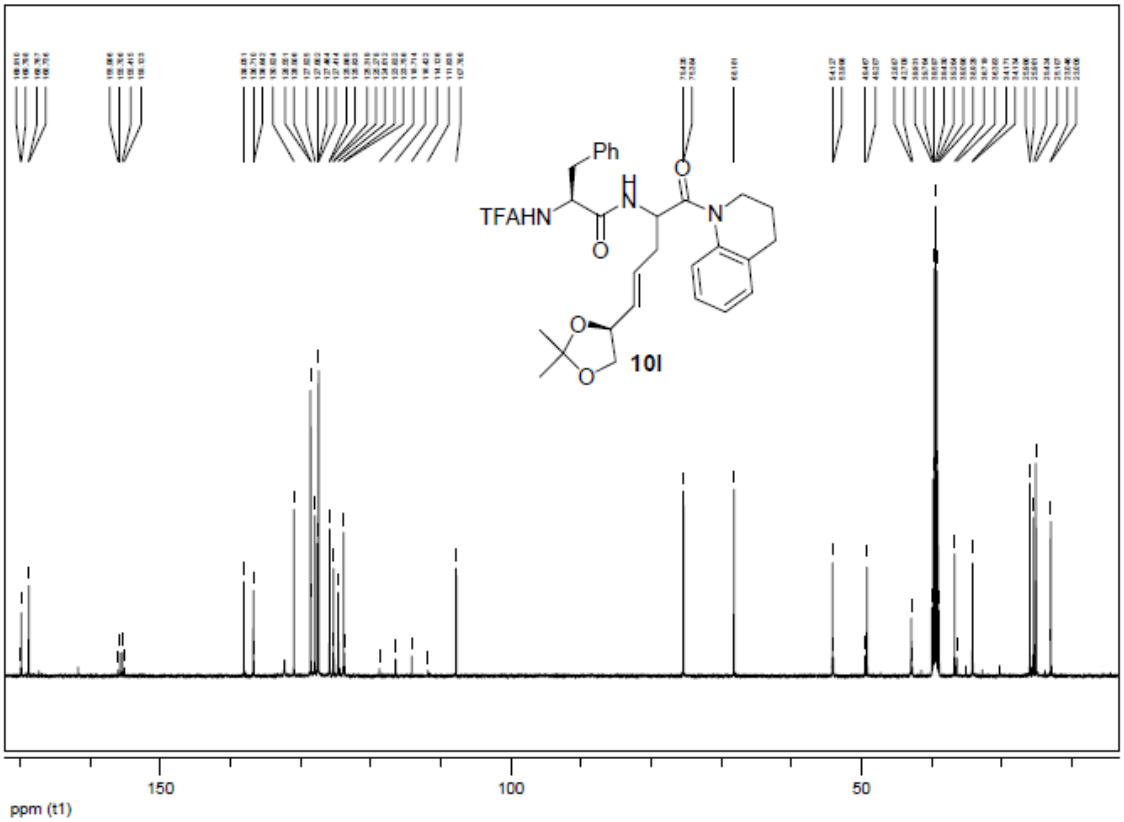


NMR spectra of compound **10k** (HD experiment)

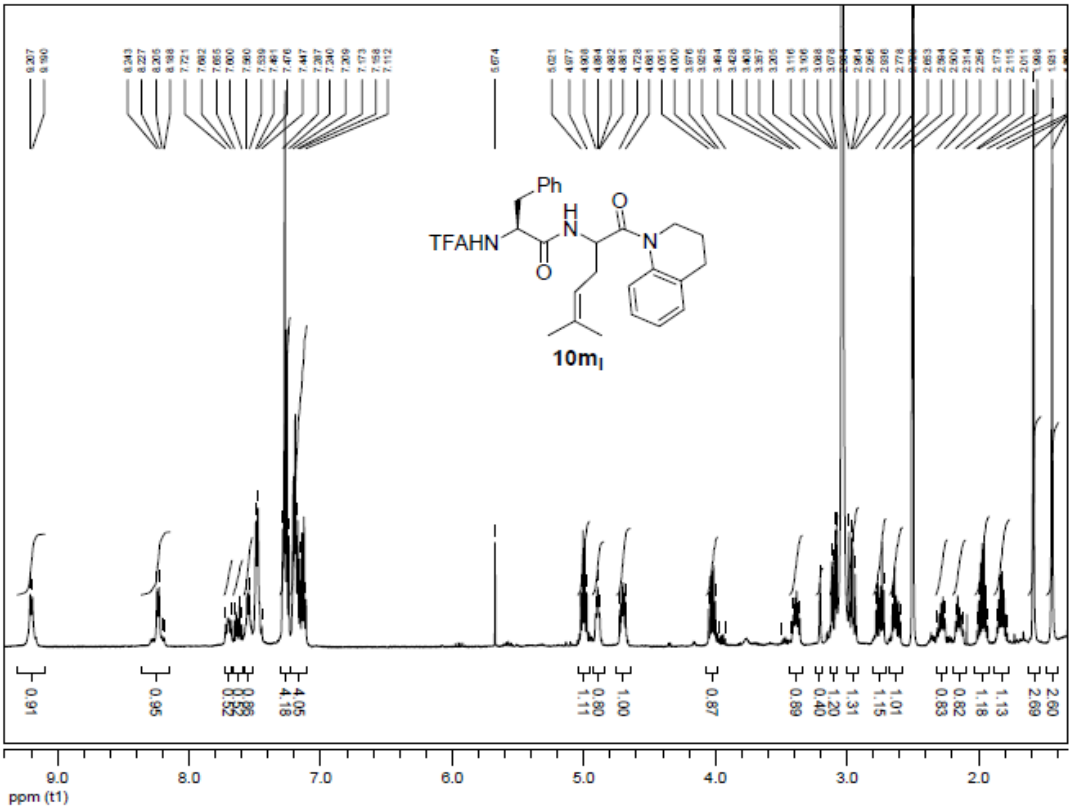


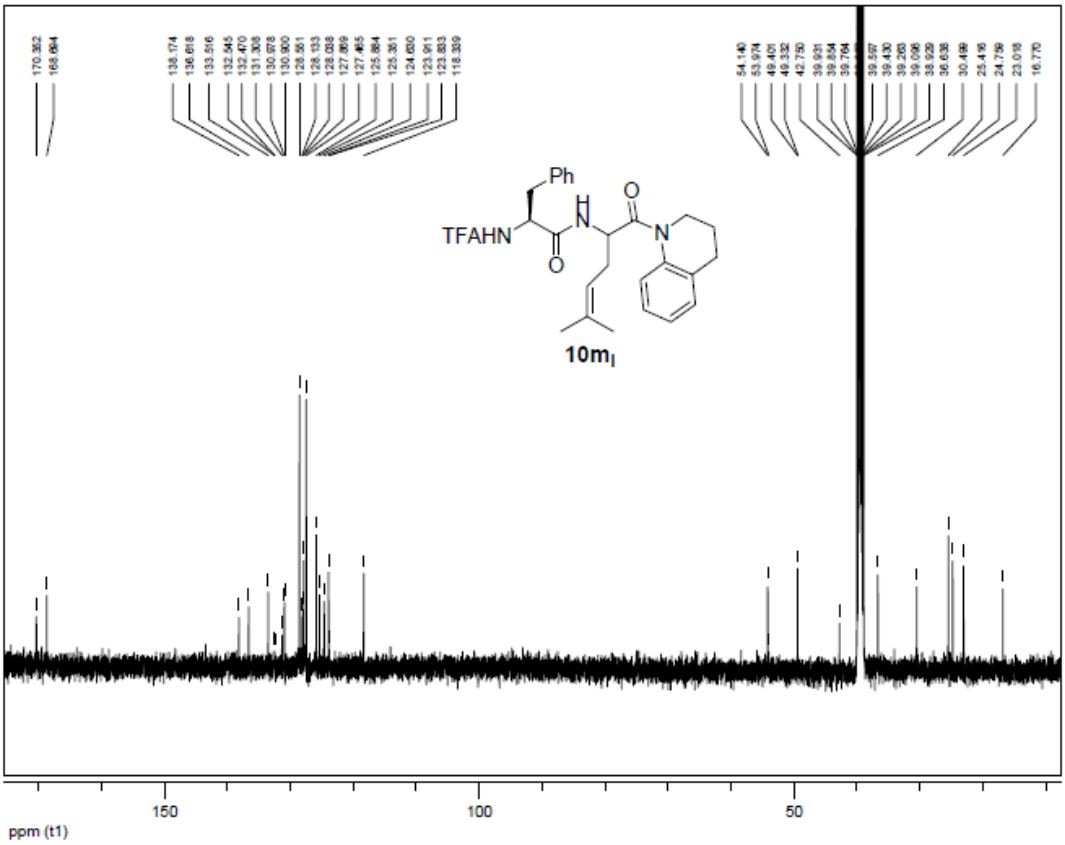
NMR spectra of compound **10l**



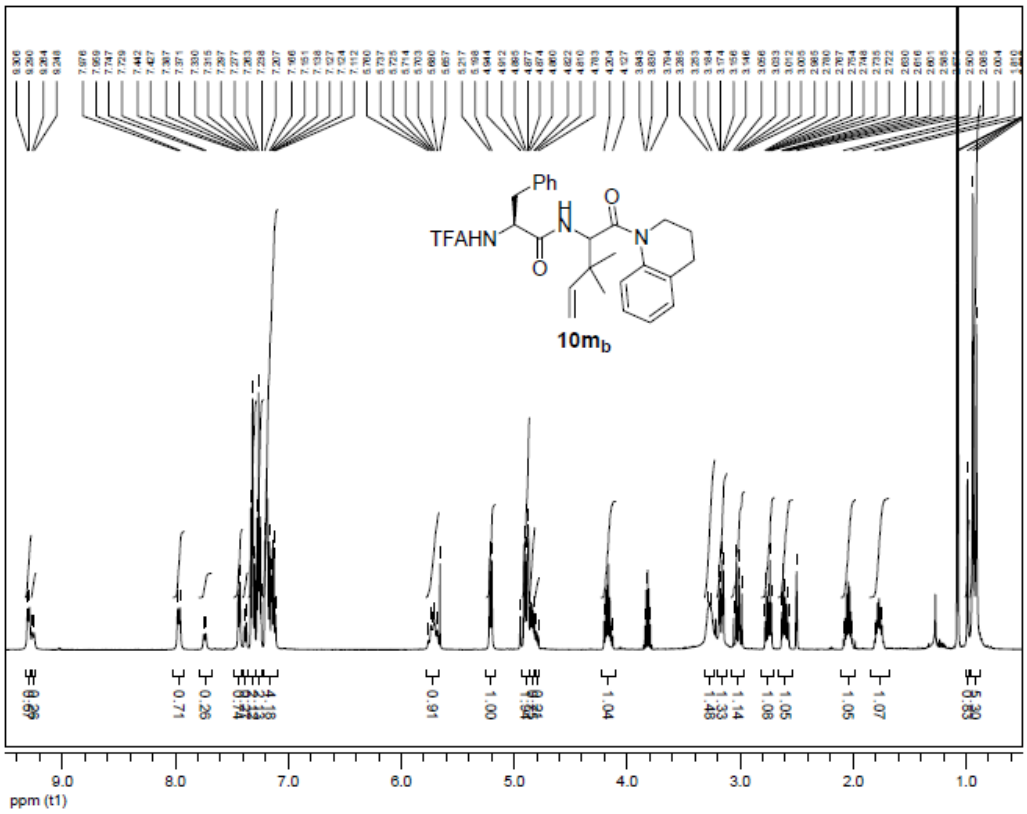


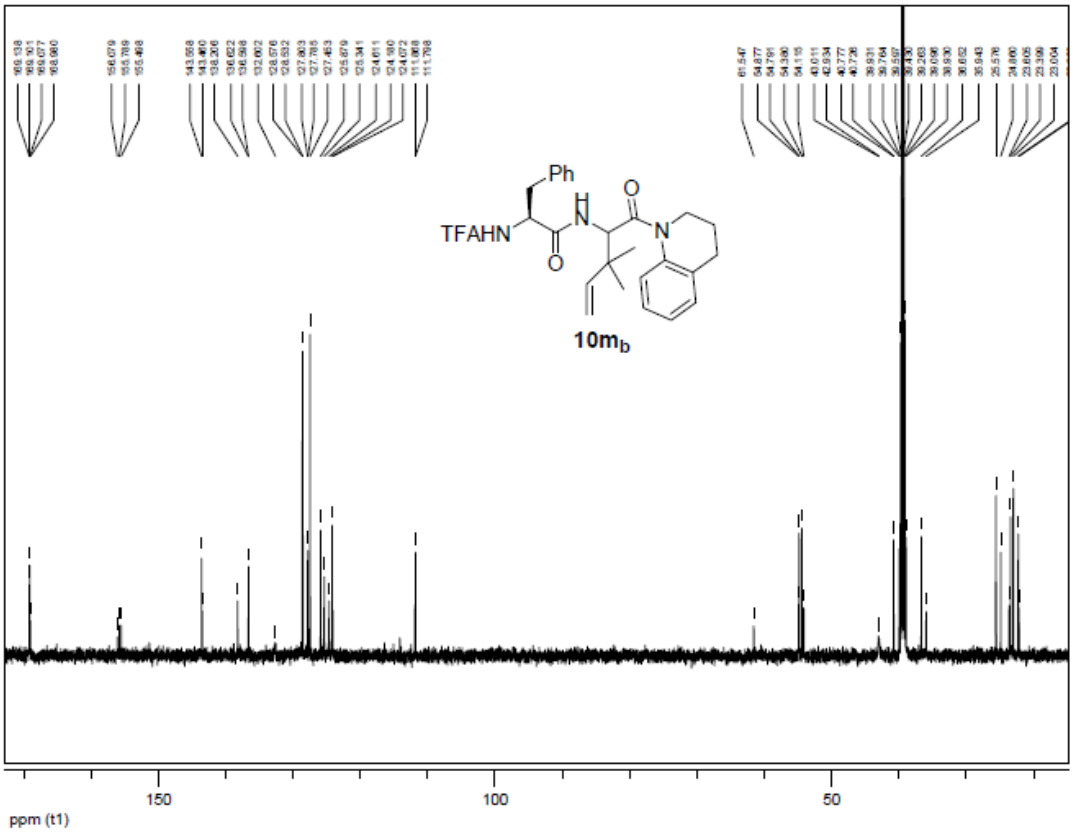
NMR spectra of compound **10m$_l$**



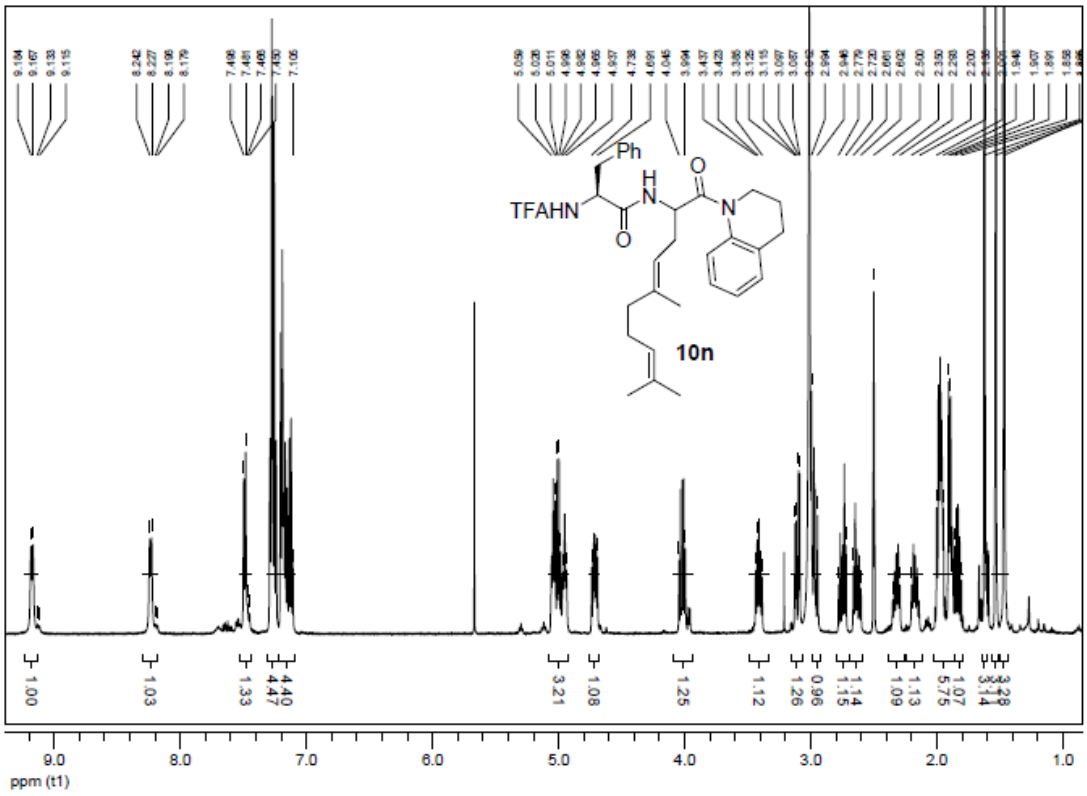


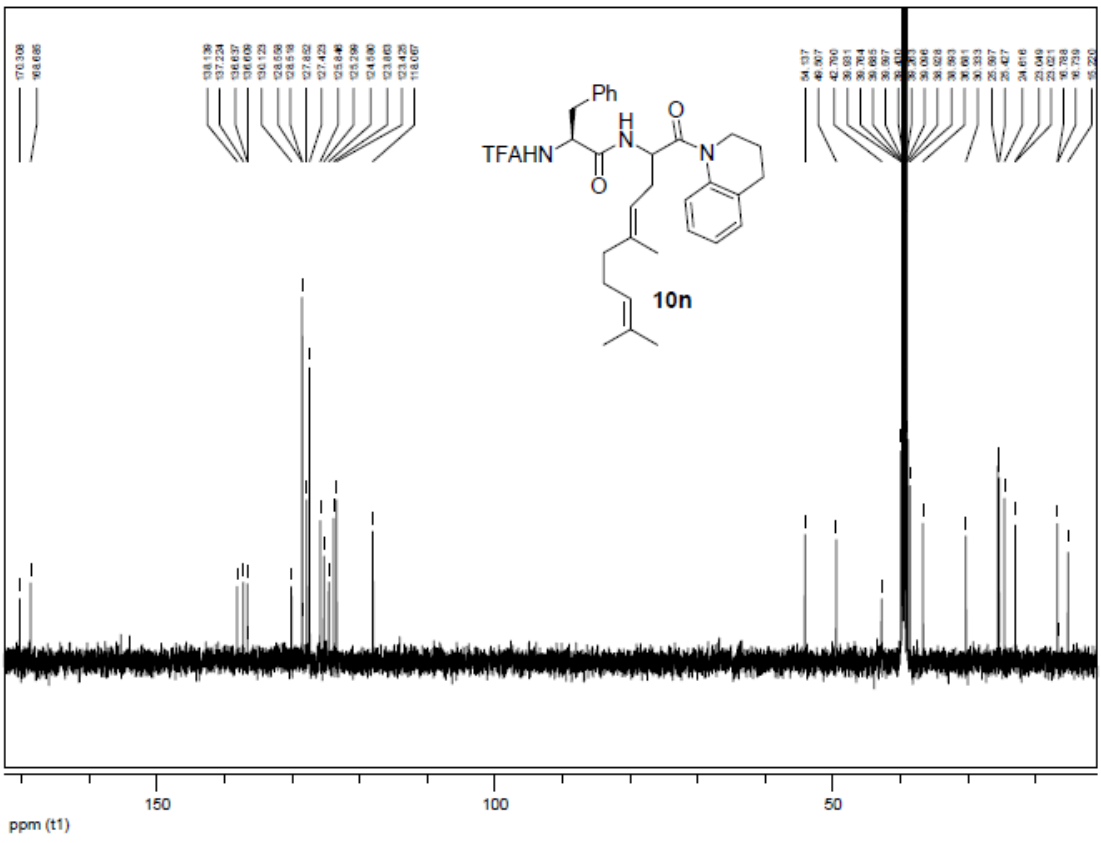
NMR spectra of compound **10m$_b$**



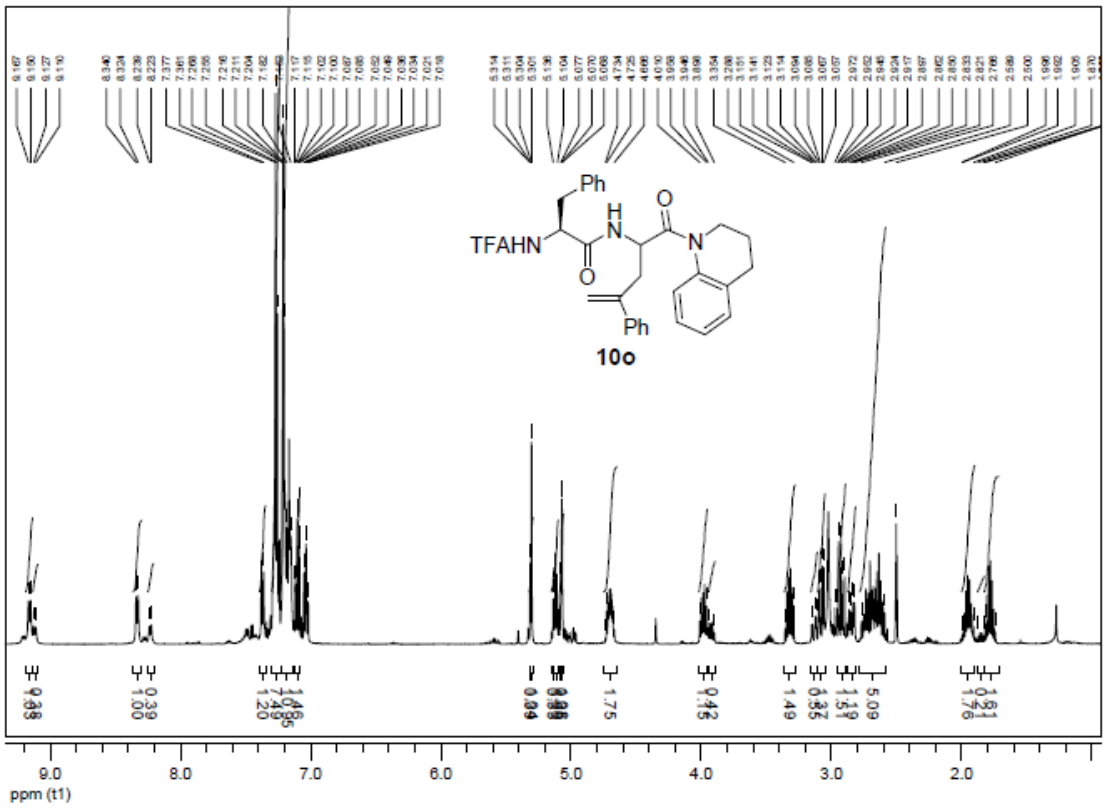


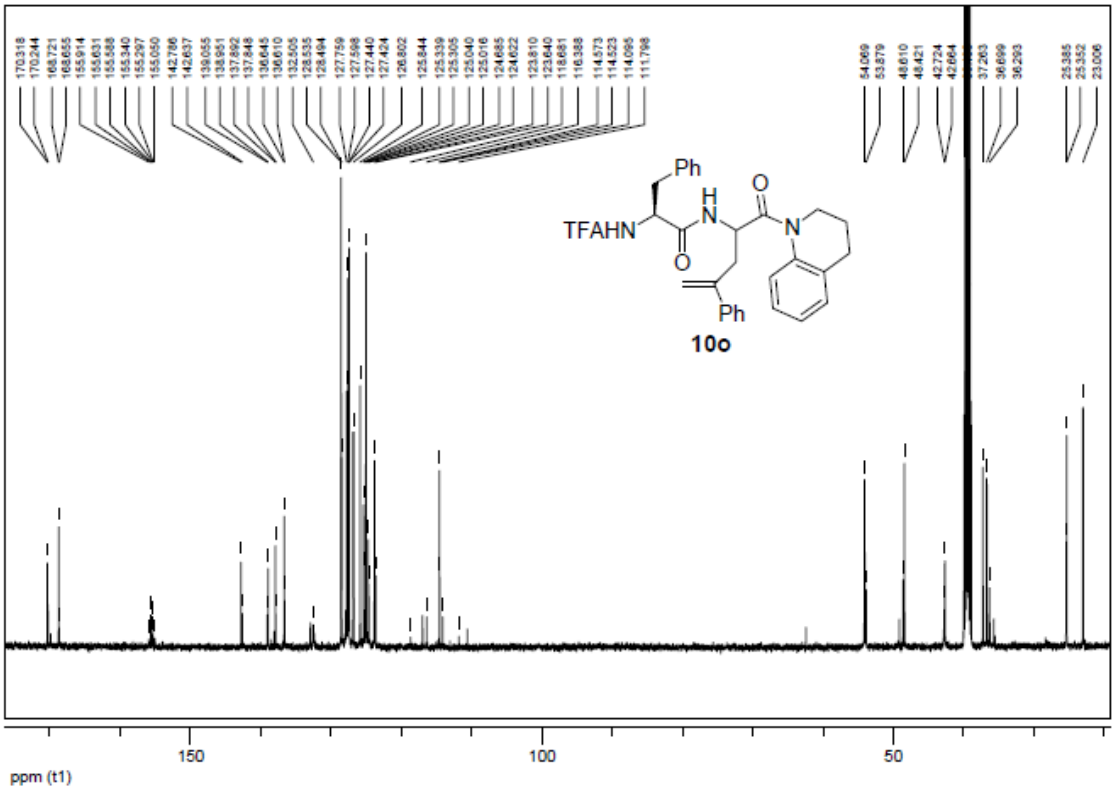
NMR spectra of compound **10n**



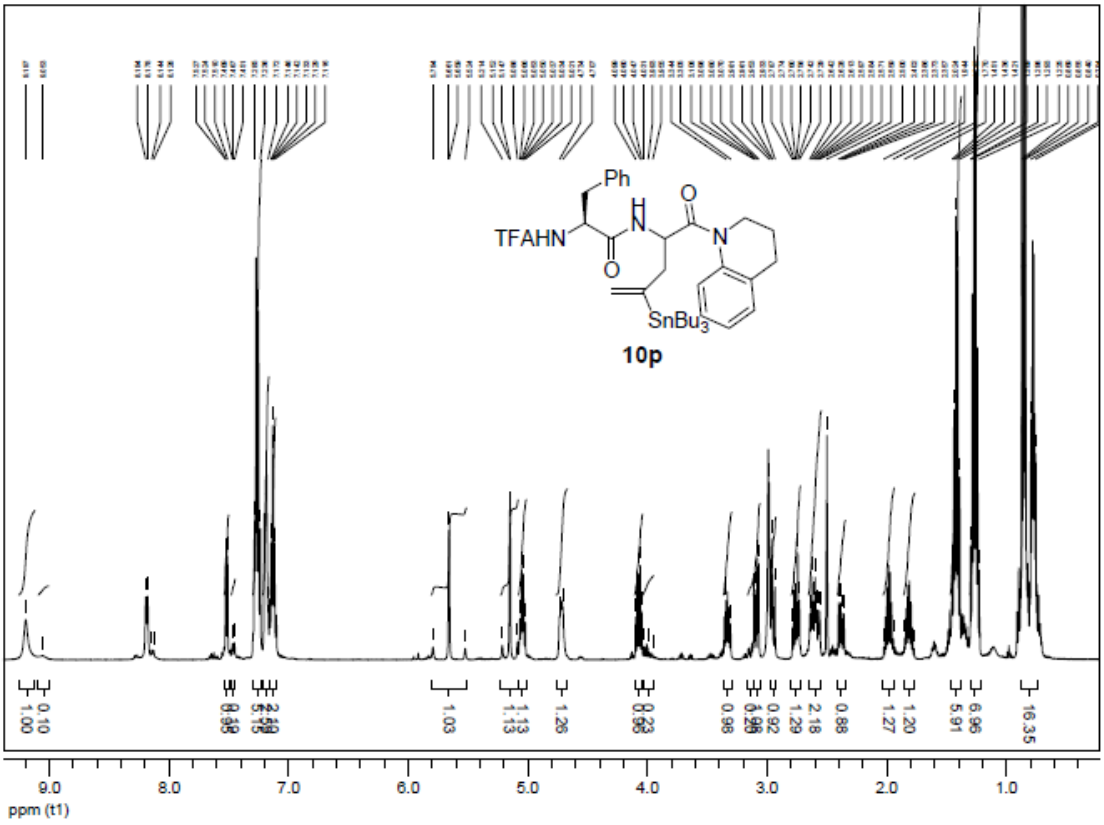


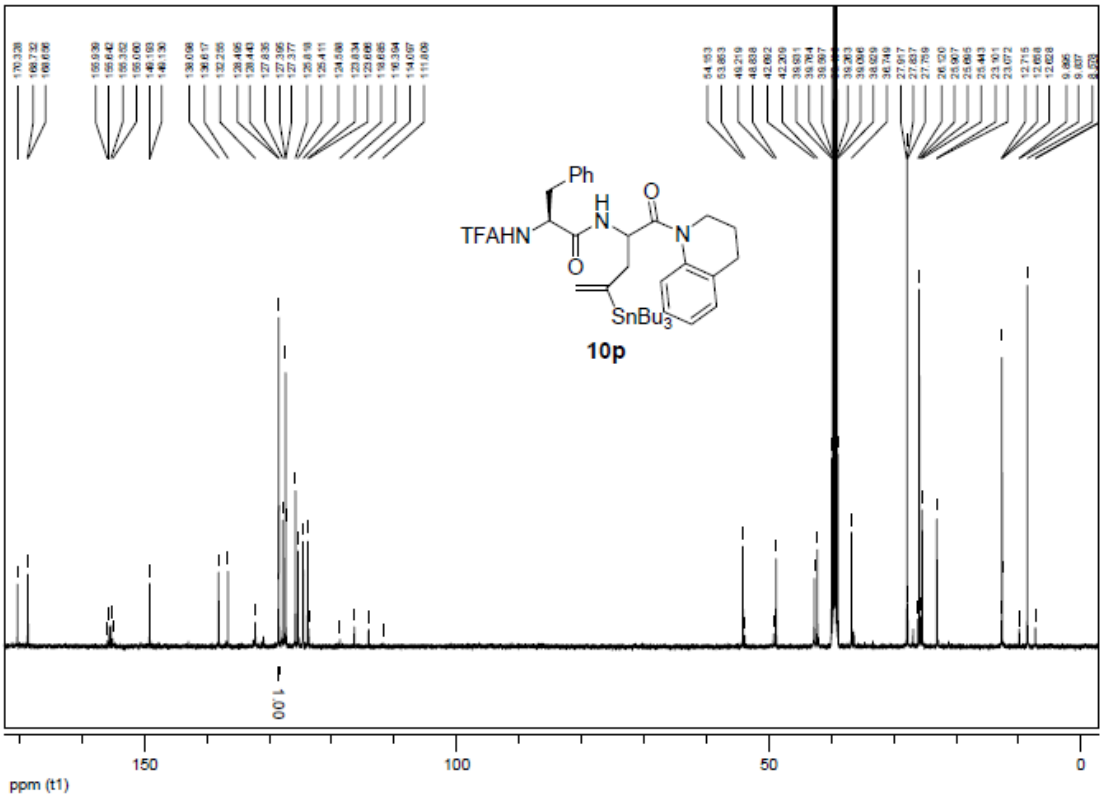
NMR spectra of compound **10o**



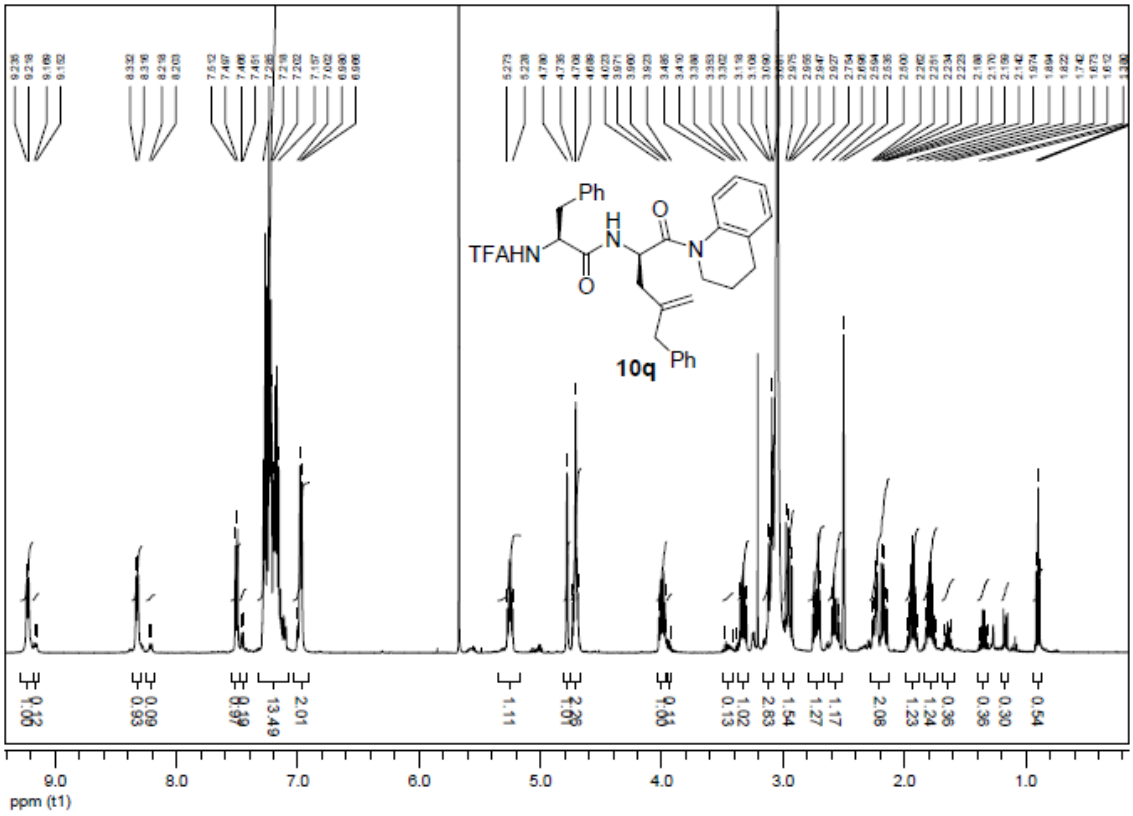


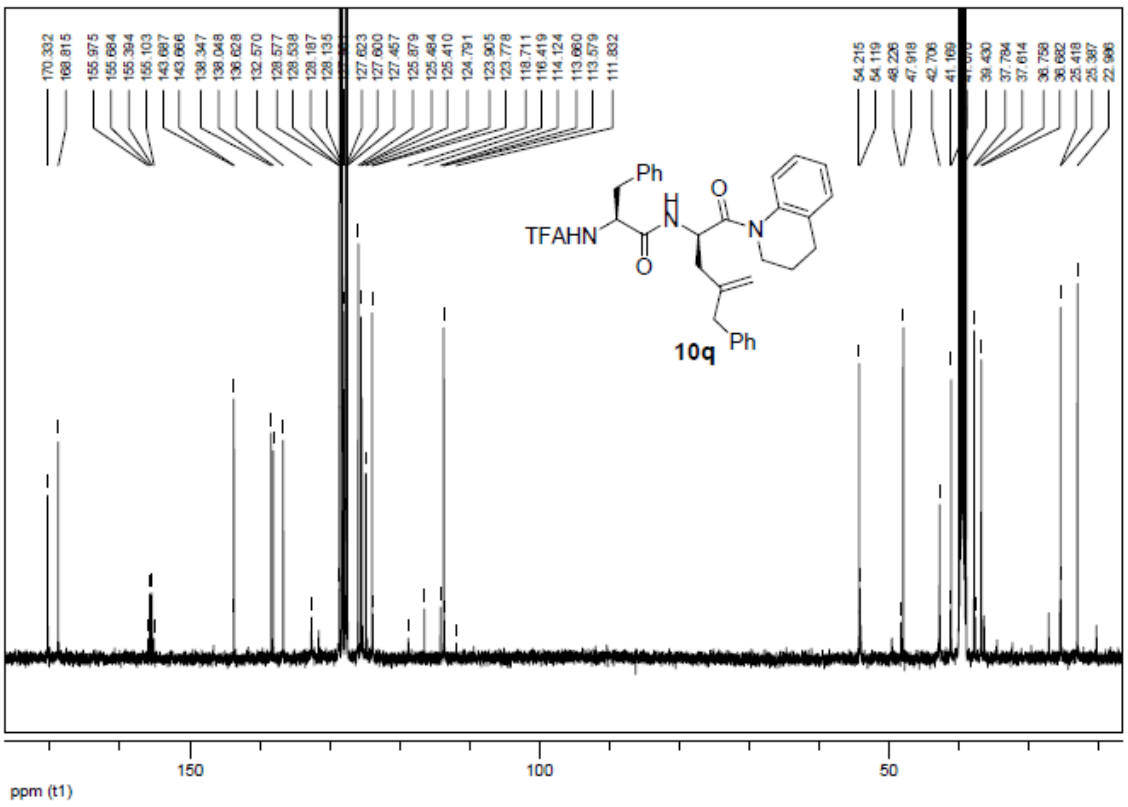
NMR spectra of compound **10p**



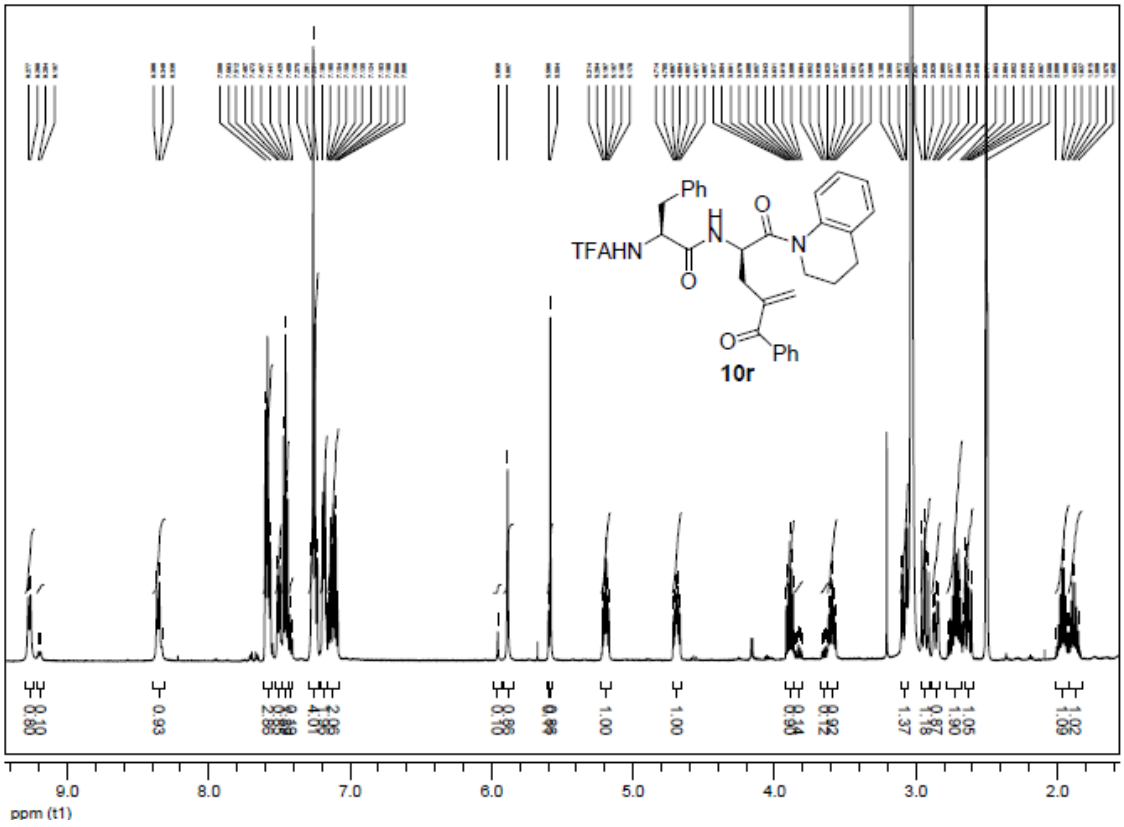


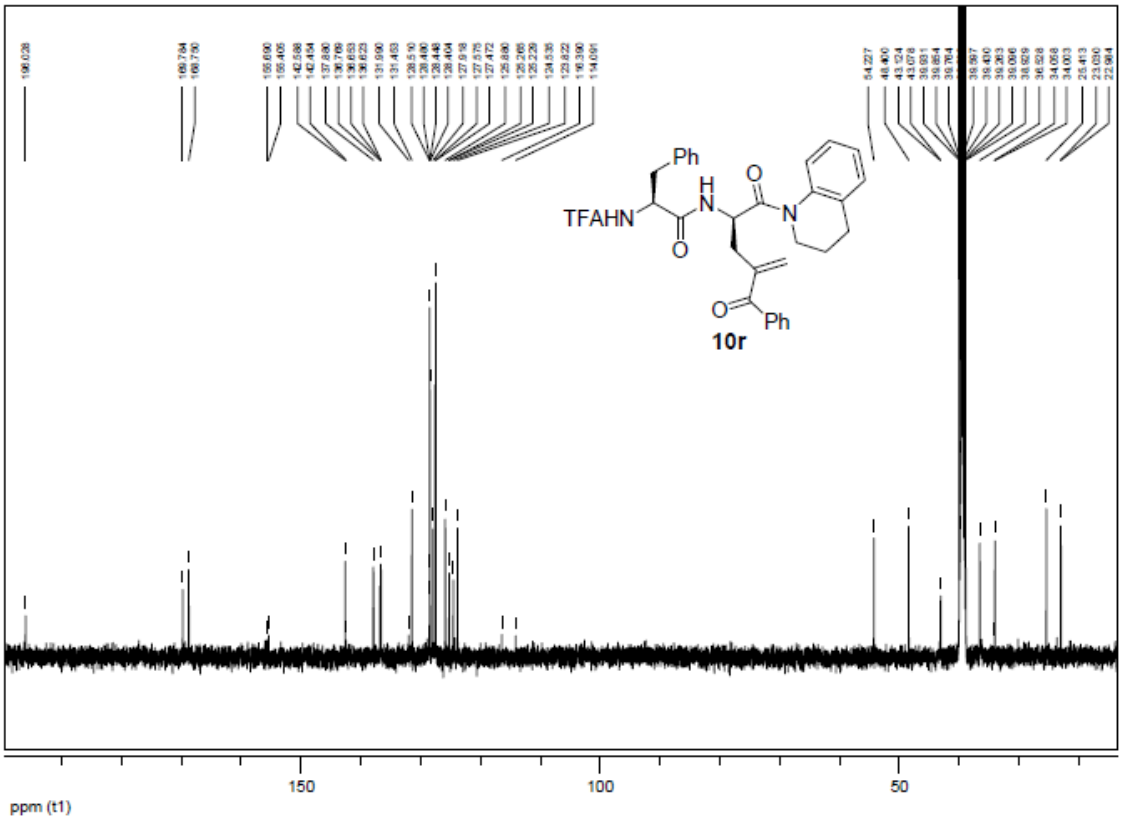
NMR spectra of compound **10q**



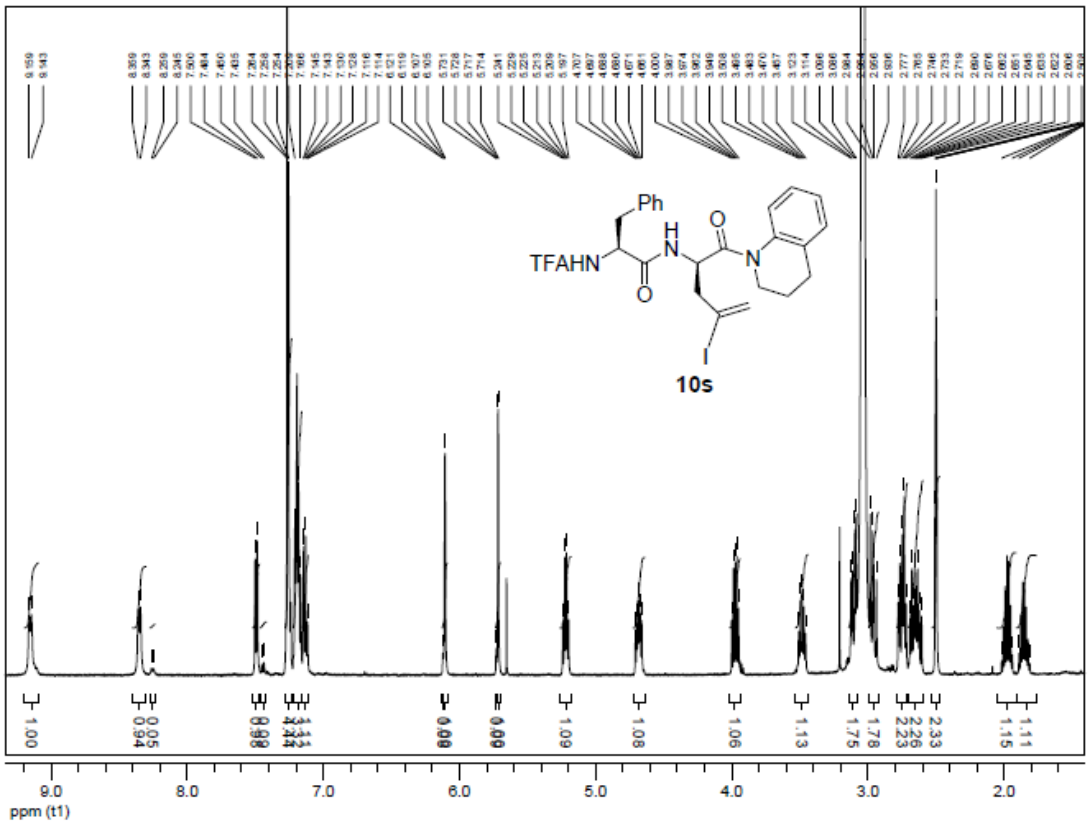


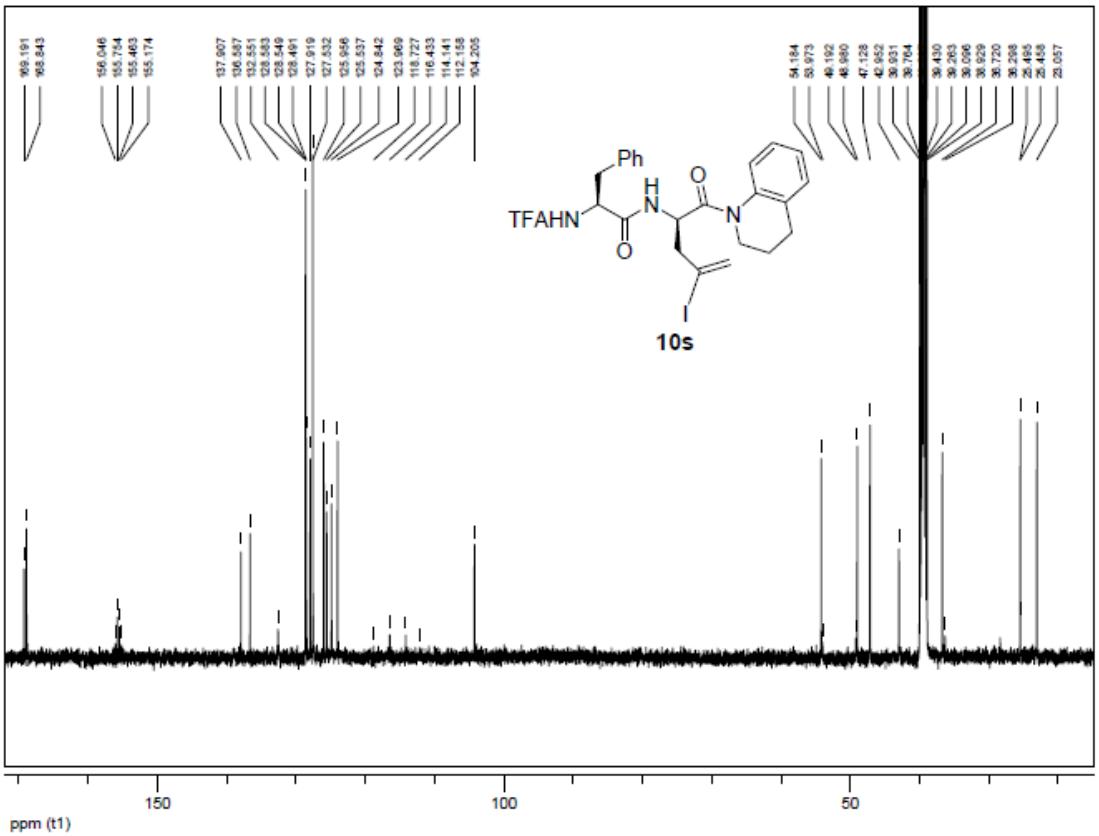
NMR spectra of compound **10r**



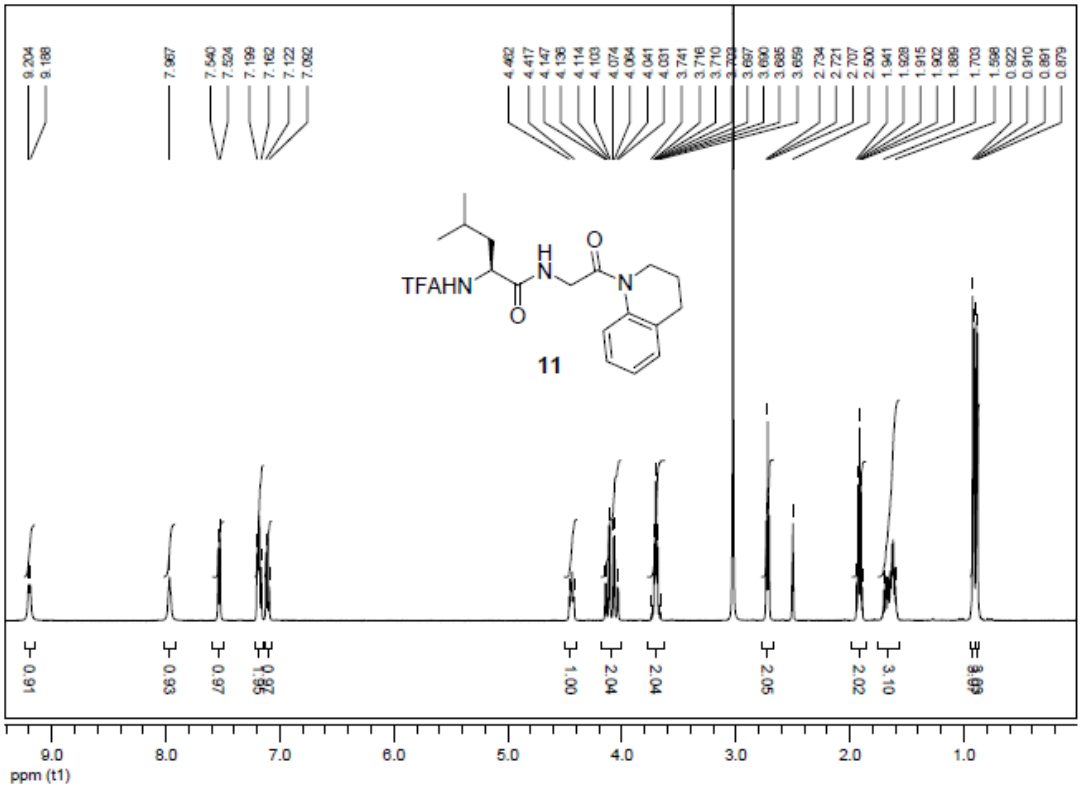


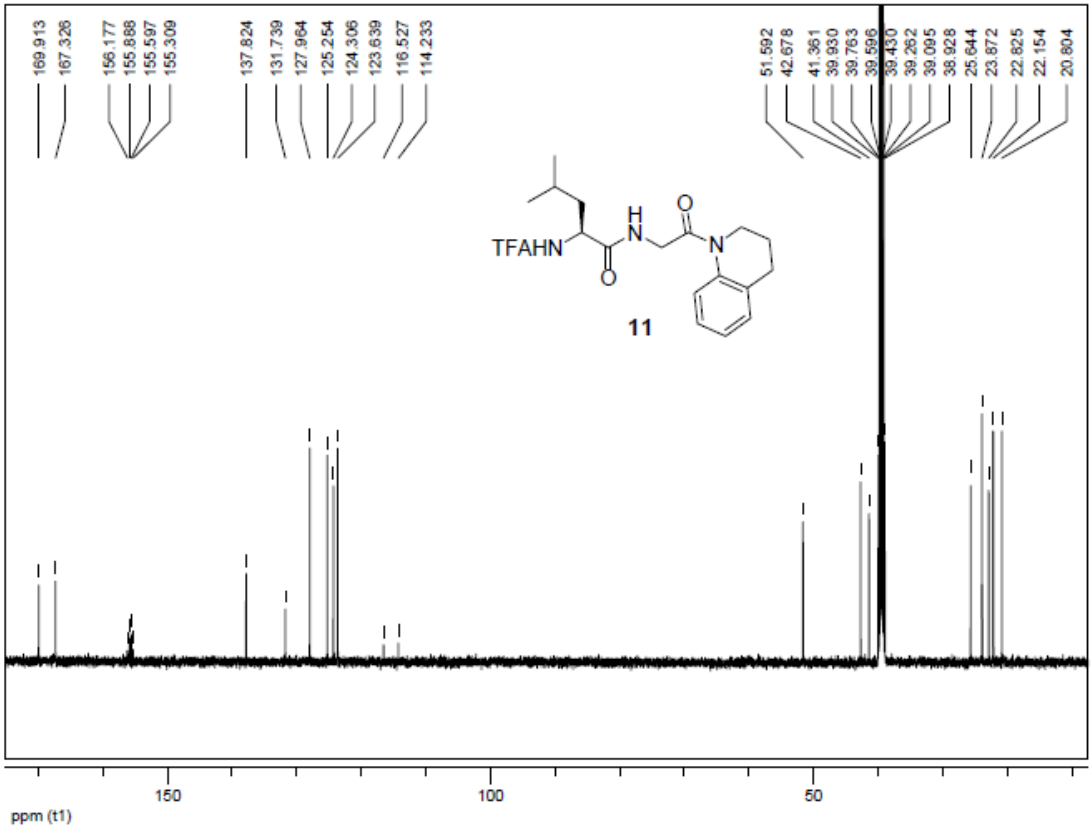
NMR spectra of compound **10s**



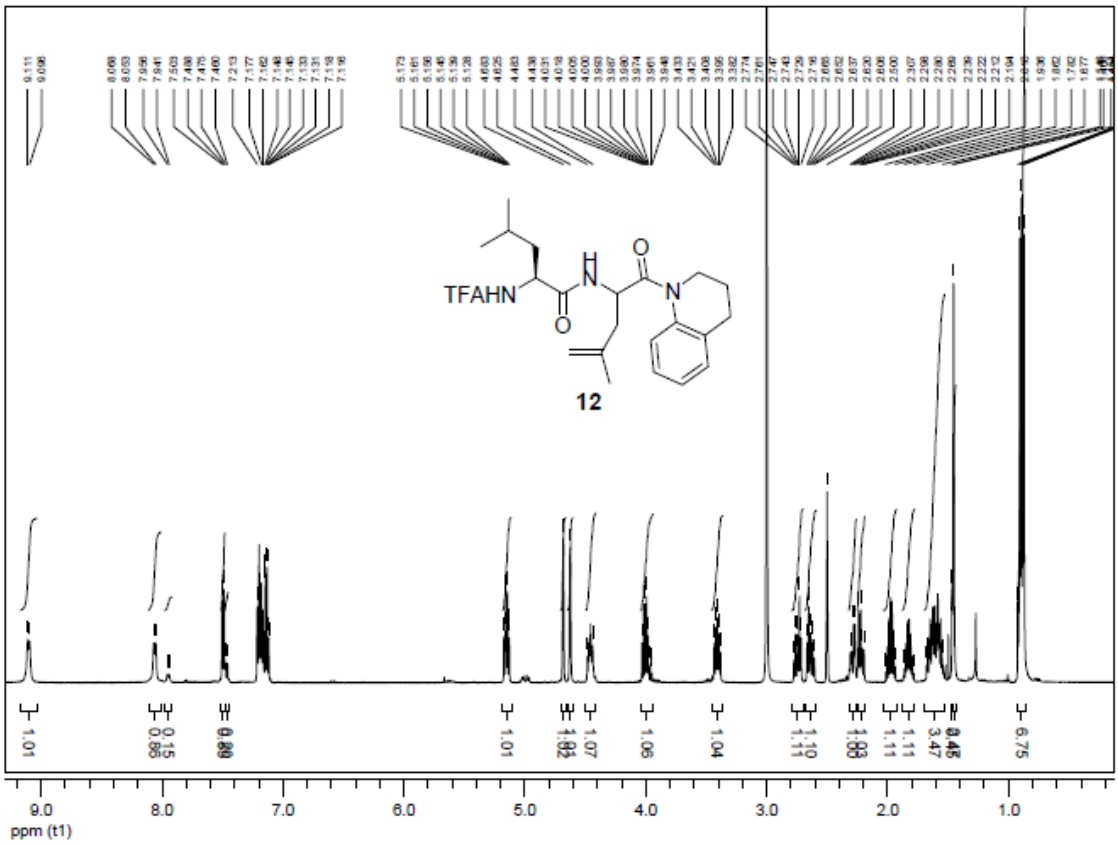


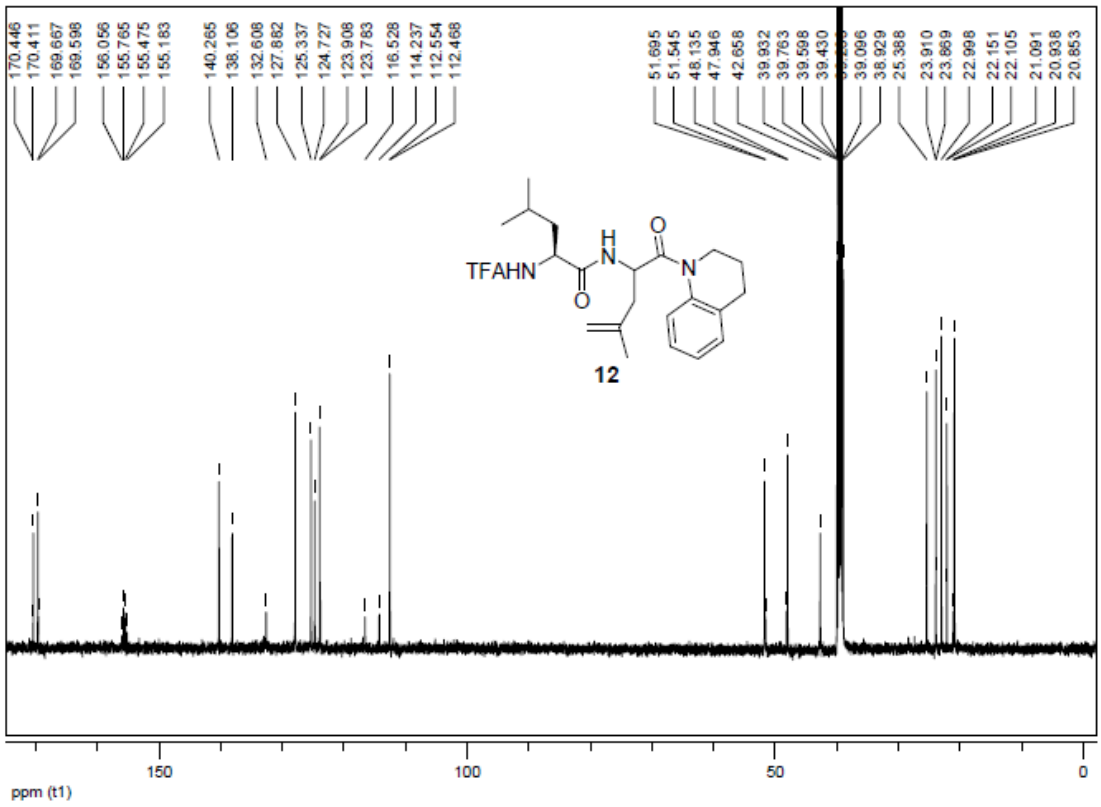
NMR spectra of compound **11**



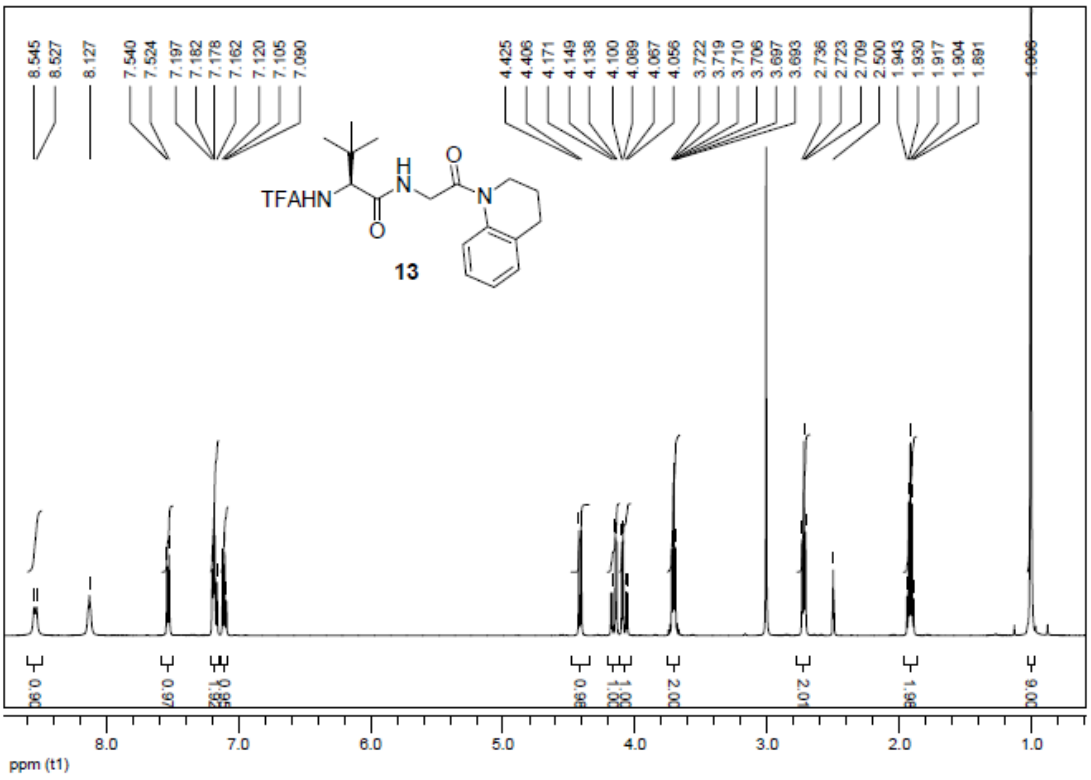


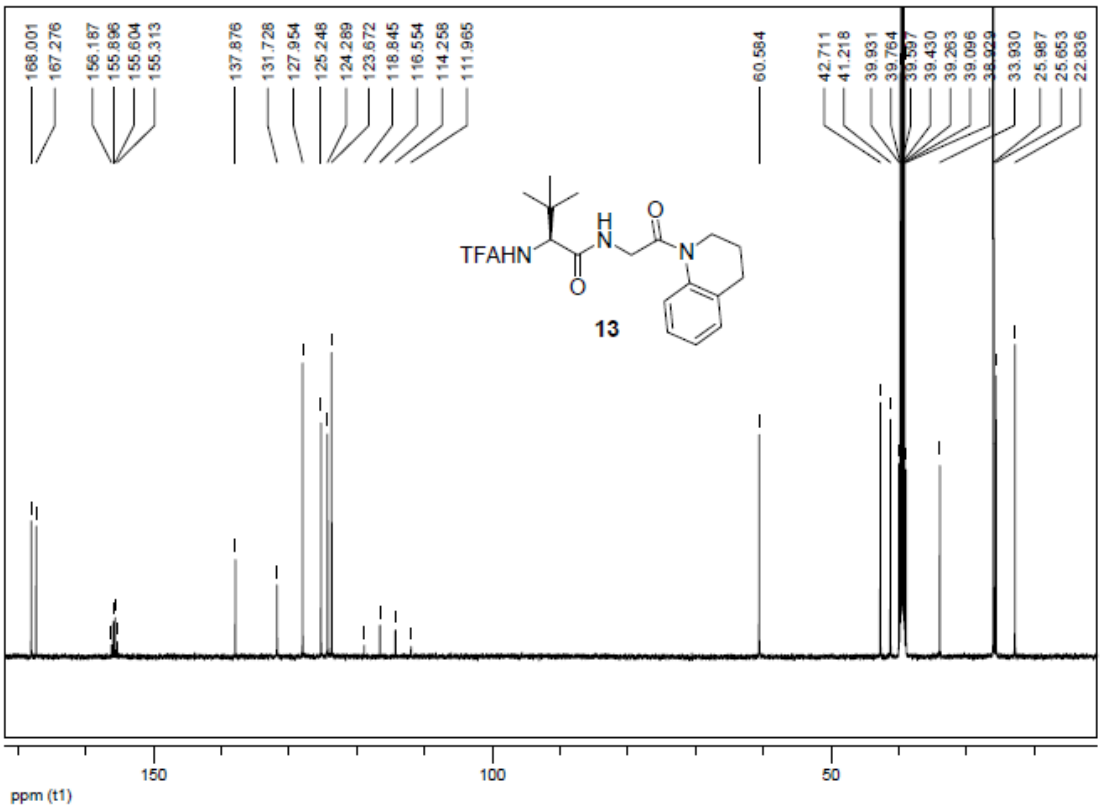
NMR spectra of compound **12**



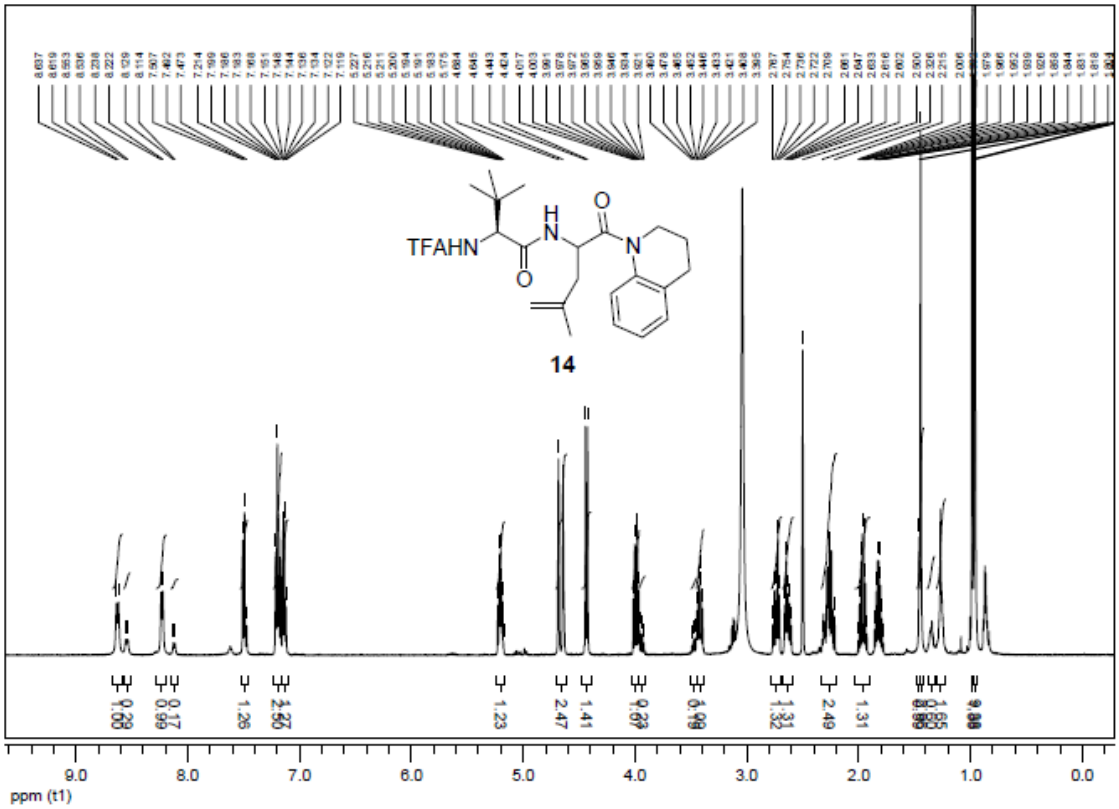


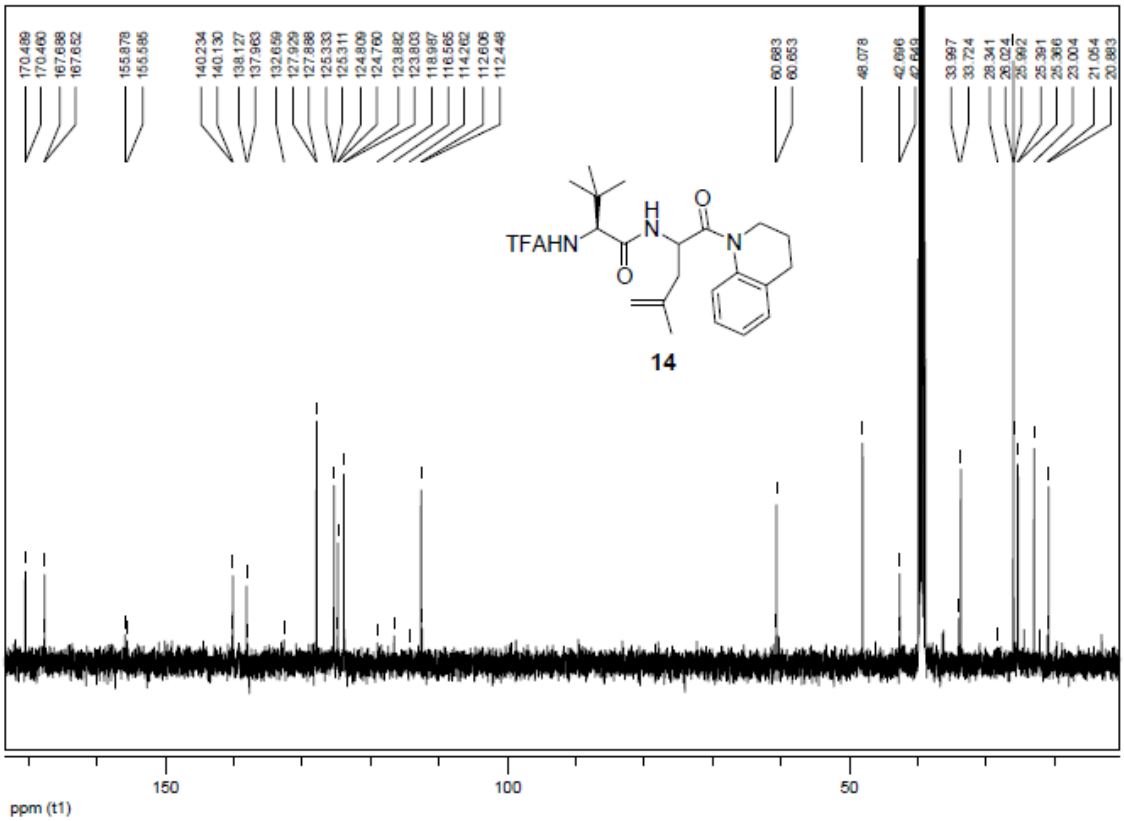
NMR spectra of compound **13**



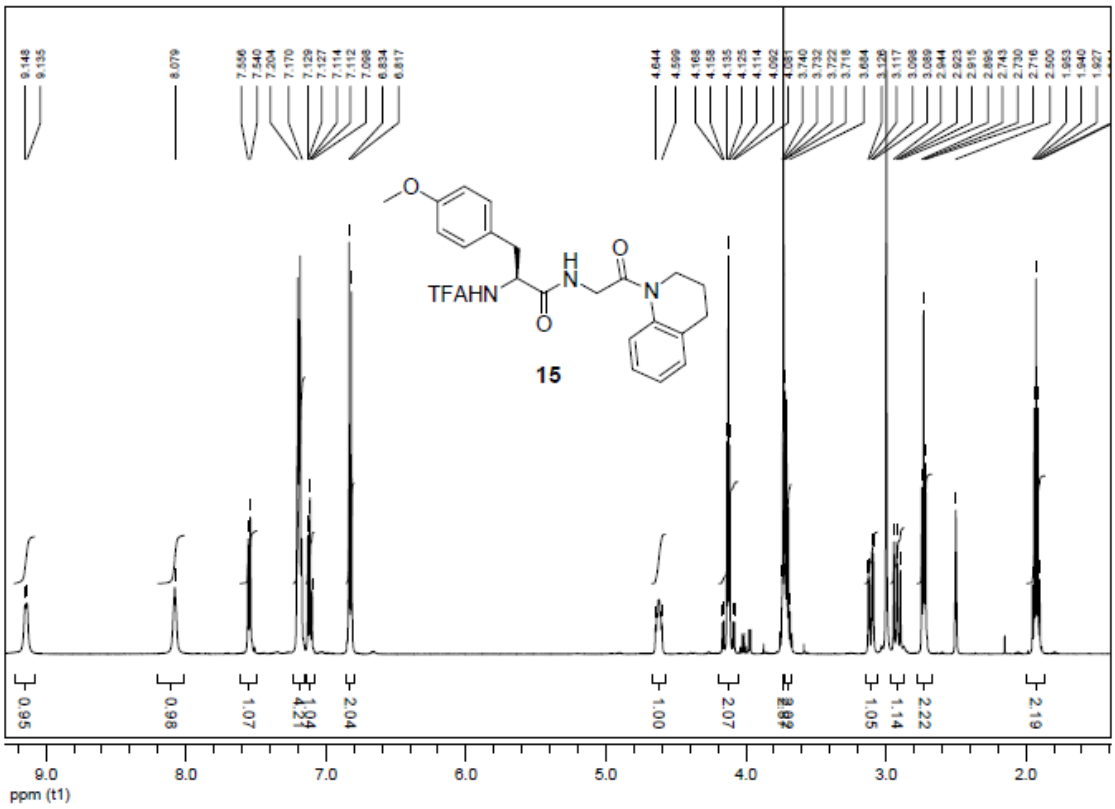


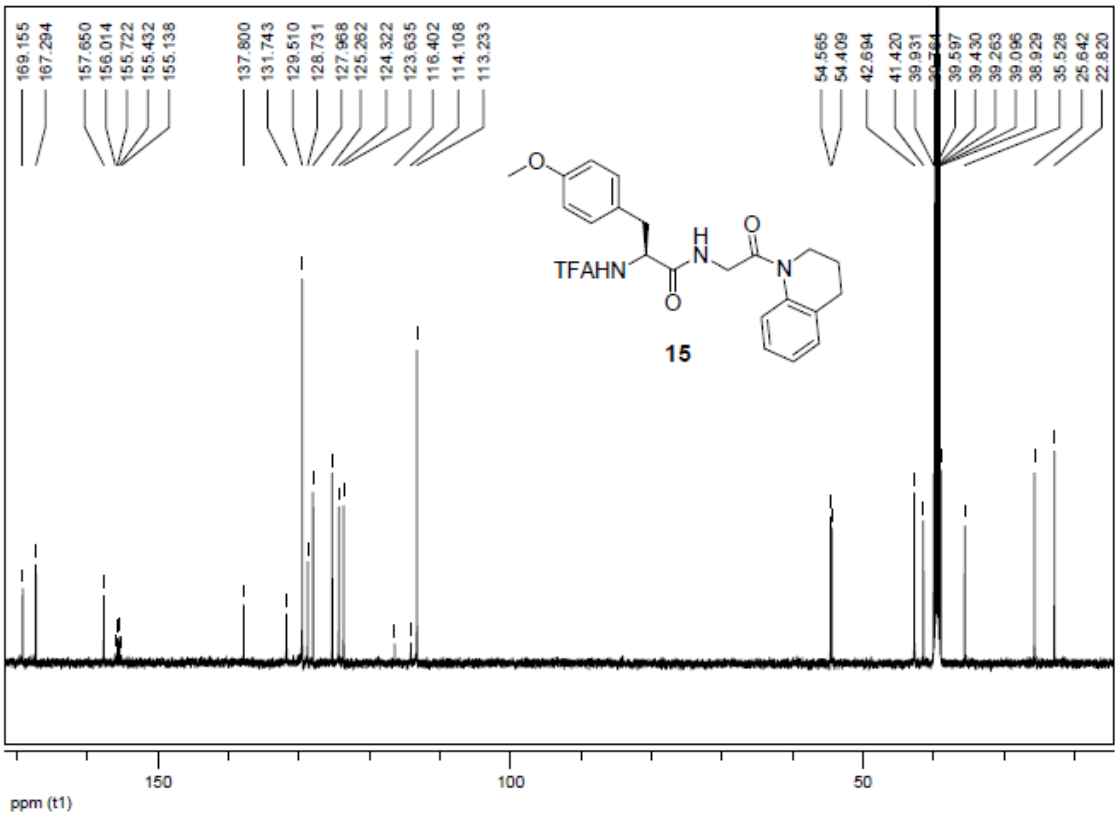
NMR spectra of compound **14**





NMR spectra of compound **15**





NMR spectra of compound **16**