Supporting Information

A Stereoselective Sequential Organocascade and Multicomponent Approach for the preparation of Tetrahydropyridines and Chimeric Derivatives

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General Aspects and Materials

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at 400 MHz for ^{1}H and 100 MHz for ^{13}C, respectively. Chemical shifts (δ) are reported in parts per million relatives to the residual solvent signals, and coupling constants (*J*) are reported in hertz. High resolution mass spectra (HRMS) were recorded using electron spray ionization (ESI) (Hybrid linear ion trap–orbitrap FT-MS /MS – and QqTOF Microtof – QII models). Reagents and materials were of the highest commercially available grade and used without further purification. Flash column chromatography was carried out using silica gel 60 (230-400 mesh) and analytical thin layer chromatography (TLC) was performed using silica gel aluminum sheets. Visualization of the compounds was achieved by UV or $KMnO_4$. HPLC chromatograms were obtained on an apparatus with an LC-10AT Pump, SPD-10AUV-Vis Detector, SCL-10A System Controller, using a Chiralpak AD-H (4,6 mmØ · 250 mmL, particle size 5 μm), Chiralpak OD-H (4,6 mmØ · 250 mmL, particle size 5 μm), Chiralpak OJ-H (4,6 mmØ · 250 mmL, particle size 5 μm), Chiralpak AS-H (4,6 mmØ · 250 mmL, particle size 5 μm) columns as chiral stationary phases Optical rotations were measured with a Polarimeterat 589 nm, 20 °C.

Experimental Section

General one-pot reaction procedure A: To a solution of Jørgensen catalyst (0.01 mmol, 0.1 equiv.), 3,5-dinitrobenzoicacid (0.02 mmol, 0.2 equiv.), and α,β-unsaturated aldehyde **2** (0.10 mmol, 1.0 equiv.) in toluene (1.0 mL) was added α-cyanoketones **1** (0.15 mmol, 1.5 equiv.) at $0^{o}C$ [1]. The resulting solution was stirred for 48h. 2,2,2-trifluoroethanol (1.0 mL), the amine (0.15 mmol, 1.5 equiv.) and the isocyanide (0.15 mmol, 1.5 equiv.) were added in a 10 mL glass tube and introduced in the microwave reactor. NEt_3 (0.15 mmol, 1.5 equiv.) was added when α-amino acid and peptide methyl ester hydrochlorides were employed as amino components. The flask was irradiated for 20 min (300 W) under high-speed magnetic stirring, while the temperature was raised up to 70 °C. The reaction course was monitored by TLC, and additional cycles of 5 min were applied in cases of poor consumption of the starting material. The volatiles was concentrated under reduced pressure and the resulting crude product was purified by flash column chromatography.

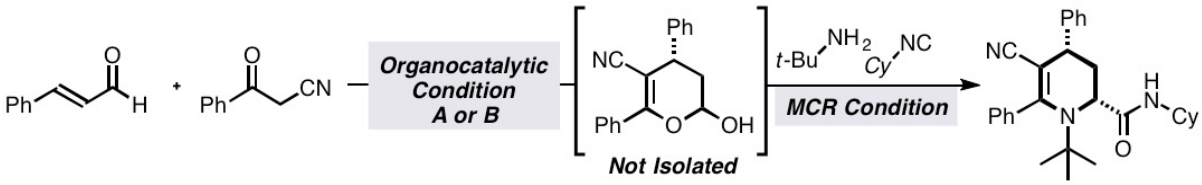
General one-pot reaction procedure B: To a solution of Jørgensen catalyst (0.01 mmol, 0.1 equiv.), 3,5-dinitrobenzoicacid (0.02 mmol, 0.2 equiv.), and α,β-unsaturated aldehyde **2** (0.10 mmol, 1.0 equiv.) in toluene (1.0 mL) was added α-cyanoketones **1** (0.15 mmol, 1.5 equiv.) and

[1] Niu, Z.; He, X.; Shang, Y. *Tetrahedron Asymm.* **2014**, *25*, 796

was irradiated for 30 min (300 W) under high-speed magnetic stirring at -20 ^{o}C. 2,2,2-trifluoroethanol (1.0 mL), the amine (0.15 mmol, 1.5 equiv.) and the isocyanide (0.15 mmol, 1.5 equiv.) were added and the glass tube was sealed. NEt_3 (0.15 mmol, 1.5 equiv.) was added when α-amino acid and peptide methyl ester hydrochlorides were employed as amino components. The flask was irradiated for 20 min (300 W) under high-speed magnetic stirring, while the temperature was raised up to 70 °C. The reaction course was monitored by TLC, and additional cycles of 5 min were applied in cases of poor consumption of the starting material. The volatiles was concentrated under reduced pressure and the resulting crude product was purified by flash column chromatography.

Optimization Studies for the organocatalytic and multicomponent reaction.

Table 1. Optimization Studies for the One-Pot Organocatalytic Conjugate Addition/4-Center 3-Component Reaction

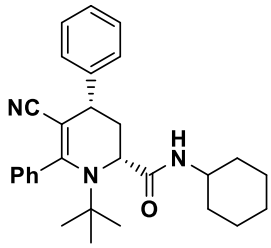


Entry[c]	Solvent	Temp(°C)	Time (min)	Yield (%)[d]	*dr* [e]	ee (%)[f]
1[a]	TFE	70	5	40	20:1	96
2[a]	TFE	70	10	60	20:1	96
3[a]	TFE	70	15	65	20:1	96
4[a]	TFE	70	20	71	20:1	96
5[a]	TFE	70	40	76	10:1	96
6[a]	TFE	60	20	65	20:1	96
7[a]	TFE	85	20	61	9:1	96
8[a]	EtOH	70	20	35	9:1	96
10[a]	THF	70	20	23	9:1	96
11[a]	Toluene	70	20	36	9:1	96
12[b]	TFE	70	20	69	20:1	96

[a] **Condition A**: Reaction performed with Jørgensen catalyst (10 mol%), 3,5- dinitrobenzoic acid (20 mol%), cinnamaldehyde (0.10 mmol; 1 eq), benzoacetonitrile (0.15 mmol; 1.5 eq) in tolulene at -20^{0} C for 20h. [b] **Condition B**: Reaction performed with Jørgensen catalyst (10 mol%), 3,5- dinitrobenzoic acid (20 mol%), cinnamaldehyde (0.10 mmol; 1 eq), benzoacetonitrile (0.15 mmol; 1.5 eq) in tolulene under microwave irradiated (300 W) at -20 ^{0}C for 30 min. [c] Reactions performed on 0.15 mmol scale and 2.0 mL total volume of solvent under microwave irradiation [d] Isolated yields after purification. [e] d.r. was determined by ^{1}H NMR analysis of the crude product. [f] e.e was determined by HPLC analysis on a chiral stationary phase column.

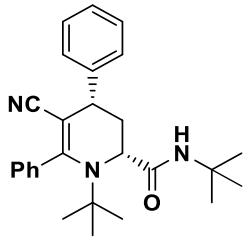
Analytical data of tetrahydropyridine compounds

Compound 5a



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), *tert*-butylamine (15.7 μL, 0.15 mmol), and cyclohexylisocyanide (18.7 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 4:1) afforded compound **5a** (30.5 mg, 69%, isomer *cis*) as a yellow oil. $[\alpha]_D^{20}$ −2.4 (*c* 0.5, acetone, 20°C). R_f = 0.38 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74-7.42 (m, 6H); 7.39-7.28 (m, 4H); 5.43 (d, *J* = 8.1 Hz, 1H); 4.00 (d, *J* = 8.9 Hz, 1H); 3.97-3.90 (m, 1H,); 3.79 (dd, *J* = 10.1, 7.0 Hz, 1H); 2.36 (dd, *J* = 12.3, 7.0 Hz, 1H); 2.16-2.10 (m, 2H); 1.96-1.85 (m, 1H); 1.82-1.72 (m, 2H); 1.56-1.45 (m, 2H); 1.35-1.22 (m, 4H); 1.10 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.3, 25.7, 30.5, 33.3, 33.8, 44.6, 47.3, 50.7, 51.3, 57.2, 69.7, 115.5, 116.1, 121.1, 123.7, 126.5, 126.9, 127.5, 128.7, 129.1, 129.3, 131.5, 133.3, 144.5, 149.8, 156.5, 160.9. HRMS (ESI-FT-QQTOF) *m/z*: 442.2869 $[M+H]^+$; calcd. for $C_{29}H_{36}N_3O$: 442.2858. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (major)= 5.6 min, t_R (minor)= 6.6 min, 96% ee.

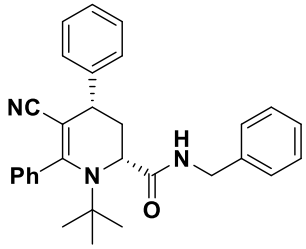
Compound 5b



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), *tert*-butylamine (15.7 μL, 0.15 mmol), and *tert*-butyl isocyanide (16.9 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 5:1) afforded compound **5b** (23.0 mg, 55%, isomer *cis*) as a yellow oil. $[\alpha]_D^{20}$ −6.8 (*c* 0.4, acetone, 20°C). R_f = 0.40 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35-

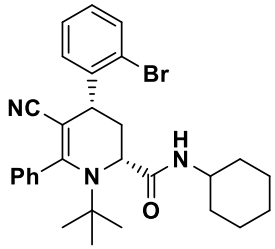
7.28 (m, 6H); 7.24-7.14 (m, 4H); 5.05 (brs, 1H); 4.74 (ddd, *J* = 7.9, 7.0, 0.8 Hz, 1H); 4.13-4.06 (m, 1H,); 2.69 (dt, *J* = 12.0, 7.0 Hz, 1H); 1.49 (s, 9H), 1.47 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3, 30.4, 41.8, 43.2, 47.2, 48.3, 52.3, 117.4, 21.7, 126.8, 126.9, 127.2, 127.7, 128.5, 128.8, 129.2, 131.3, 143.7, 147.8, 156.9, 162.9. HRMS (ESI-FT-QQTOF) *m/z*: 416.2711 $[M+H]^+$; calcd. for $C_{27}H_{34}N_3O$: 416.2702. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*-PrOH 95:5) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (major)= 18.7 min, t_R (minor)= 33.7 min, 98% ee.

Compound 5c



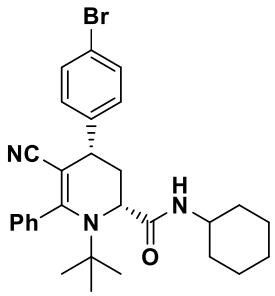
Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), *tert*-butylamine (15.7 μL, 0.15 mmol), and benzyl isocyanide (18.3 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/ EtOAc 5:1) afforded compound **5c** (35.1 mg, 78%, isomer *cis*) as a dark yellow oil. $[\alpha]_D^{20}$ −6.7 (*c* 0.5, acetone, 20°C). R_f = 0.40 (*n*-hexane/CH_2Cl_2 1:6). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37-7.29 (m, 12H); 7.24-7.16 (m, 3H); 5.71 (brs, 1H); 3.99 (d, *J* = 8.8 Hz, 1H); 3.75 (dd, *J* = 12.4, 5.0 Hz, 1H); 3.70 (d, *J* = 5.0 Hz, 1H); 3.63 (d, *J* = 10.9 Hz, 2H); 2.14 (m, 1H); 1.93 (m, 1H); 1.42 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.3, 39.4, 48.1, 48.6, 50.9, 51.7, 63.6, 63.9, 71.5, 122.7, 126.6, 126.9, 127.4, 127.5, 127.7, 127.8, 128.1, 128.2, 128.7, 139.9, 143.8, 144.3, 156.7. HRMS (ESI-FT-QQTOF) *m/z*: 450.2551 $[M+H]^+$; calcd. for $C_{30}H_{32}N_3O$: 450.2545. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.5 mL/min, UV-detection at λ= 254 nm: t_R (major)= 15.6 min, t_R (minor)= 17.3 min, 95% ee.

Compound 5d



Benzoylacetontrile (21.8 mg, 0.15 mmol), *o*-bromo-cinnamaldehyde (19.9 mg, 0.10 mmol), *tert*-butylamine (15.7 µL, 0.15 mmol), and cyclohexylisocyanide (18.7 µL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 3:1) afforded compound **5d** (28.1 mg, 54%, isomer *cis*) as a pale yellow solid. $[\alpha]_D^{20}$ −2.2 (*c* 0.6, acetone, 20°C). R_f = 0.36 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.83-7.76 (m, 1H); 7.66-7.52 (m, 2H); 7.50-7.41 (m, 2H); 7.37-7.11 (m, 3H); 7.05-6.96 (m, 1H); 5.42 (d, *J* = 8.5 Hz, 1H); 4.21 (d, *J* = 9.0 Hz, 1H); 3.92-3.78 (m, 1H); 3.46 (dd, *J* = 10.2, 7.1 Hz, 1H); 2.19-2.11 (m, 1H); 2.10-1.97 (m, 2H); 1.84-1.73 (m, 1H); 1.72-1.61 (m, 2H); 1.47-1.32 (m, 2H); 1.27-1.09 (m, 4H); 0.95 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2, 24.4, 25.7, 30.5, 33.2, 33.9, 43.2, 47.0, 50.7, 51.4, 56.5, 67.5, 112.7, 120.9, 125.9, 127.5, 128.1, 128.9, 128.8, 129.2, 132.2, 133.3, 133.5, 133.8, 142.7, 147.3, 155.8. HRMS (ESI-FT-QQTOF) *m/z*: 520.1971 $[M+H]^+$; calcd. for $C_{29}H_{35}BrN_3O$: 520.1964. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.5 mL/min, UV-detection at λ= 254 nm: t_R (major)= 13.1 min, t_R (minor)= 14.5 min, 96% ee.

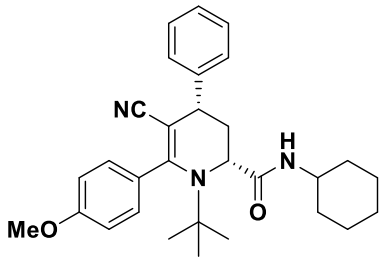
Compound 5e



Benzoylacetontrile (21.8 mg, 0.15 mmol), *trans*-4-bromocinnamaldehyde (19.9 mg, 0.10 mmol), *tert*-butylamine (15.7 µL, 0.15 mmol), and cyclohexylisocyanide (18.7 µL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 3:1) afforded compound **5e** (29.1 mg, 56%, isomer *cis*) as a pale yellow solid. $[\alpha]_D^{20}$ −1.3 (*c* 0.4, acetone, 20°C). R_f = 0.38 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.94-7.85 (m, 1H); 7.65-7.47 (m, 3H); 7.45-7.35 (m, 3H); 7.11-7.05 (m, 2H); 5.42 (d, *J* = 8.6

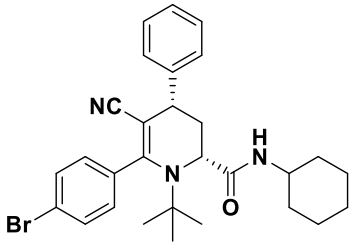
Hz, 1H); 3.94-3.83 (m, 2H); 3.69 (dd, *J* = 10.2, 7.1 Hz, 1H); 2.29-2.21 (m, 1H); 1.91-1.79 (m, 1H); 1.77-1.67 (m, 2H); 1.66-1.59 (m, 2H); 1.54-1.38 (m, 2H); 1.32- 1.16 (m, 4H); 1.05 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2, 24.3, 25.7, 30.5, 33.3, 33.8, 44.5, 46.9 , 50.8, 51.4, 57.2, 69.2, 120.3, 120.9, 124.3, 128.7, 128.8, 129.2, 129.9, 131.8, 132.6, 133.5, 143.6, 148.0, 155.9, 161.1. HRMS (ESI-FT-QQTOF) *m/z*: 520.1970 $[M+H]^+$; calcd. for $C_{29}H_{35}BrN_3O$: 520.1964. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AS-H column (*n*-hexane/*i*-PrOH 90:10) at 0.5 mL/min, UV-detection at λ= 254 nm: t_R (major)= 6.1 min, t_R (minor)= 6.9 min, 91% ee.

Compound 5f



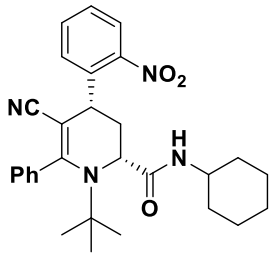
4-Methoxybenzoylacetontrile (26.4 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), *tert*-butylamine (15.7 μL, 0.15 mmol), and cyclohexylisocyanide (18.7 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 3:1) afforded compound **5f** (27.4 mg, 58%) as a yellow solid. $[\alpha]_D^{20}$ −2.6 (*c* 0.6, acetone, 20°C). R_f = 0.34 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91-7.84 (m, 1H); 7.38-7.33 (m, 1H); 7.25-7.19 (m, 2H); 7.17-7.10 (m, 4H); 6.94-6.90 (m, 1H); 5.30 (d, *J* = 8.4 Hz, 1H); 3.89 (d, *J* = 8.9 Hz, 1H); 3.82 (s, 3H); 3.67 (dd, *J* = 10.1/ 7.1 Hz, 1H); 2.27-2.21 (m, 1H); 2.07-1.98 (m, 2H); 1.83-1.75 (m, 1H); 1.70-1.61 (m, 2H); 1.44-1.34 (m, 2H); 1.23-1.11 (m, 4H); 0.98 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.2, 24.3, 25.8, 30.6, 33.4, 33.8, 44.6, 47.4, 50.8, 51.3, 57.3, 69.8, 114.1, 121.1, 123.8, 123.7, 126.5, 126.9, 128.5, 128.7, 129.3, 131.3, 131.8, 133.3, 144.6, 149.1, 155.9, 160.9. HRMS (ESI-FT-QQTOF) *m/z*: 472.2971 $[M+H]^+$; calcd. for $C_{30}H_{38}N_3O_2$: 472.2964. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AD-H column (n-hexane/i-PrOH 80:20) at 1.0 mL/min, UV-detection at λ= 254 nm: t_R (minor)= 31.7 min, t_R (major)= 37.1 min, 89% ee.

Compound 5g



4-Bromobenzoyacetontrile (33.6 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), *tert*-butylamine (15.7 μL, 0.15 mmol), and cyclohexylisocyanide (18.7 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 4:1) afforded compound **5g** (29.7 mg, 57%) as a pale yellow solid. $[\alpha]_D^{20}$ −1.6 (*c* 0.5, acetone, 20°C). R_f = 0.35 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.52-7.27 (m, 4H); 7.25-6.97 (m, 5H); 5.29 (d, *J* = 8.1 Hz, 1H); 3.77 (d, *J* = 9-0 Hz, 1H); 3.74-3.60 (m, 1H); 3.54 (dd, *J* = 10.1, 7.1 Hz, 1H); 2.31-2.23 (m, 1H); 2.05-1.80 (m, 3H); 1.75-1.62 (m, 5H); 1.60-1.48 (m, 1H); 1.37-1.26 (m, 2H); 1,15 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.9, 24.0, 25.5, 30.2, 33.1, 33.5, 44.3, 47.1, 50.5, 51.0, 57.0, 69.5, 120.8, 125.1, 126.2, 126.6, 127.5, 127.9, 128.4, 128.9, 129.2, 129.9, 131.8, 132.4, 144.2, 160.7. HRMS (ESI-FT-QQTOF) *m/z*: 520.1978 $[M+H]^+$; calcd. for $C_{29}H_{35}BrN_3O$: 520.1964. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (n-hexane/i-PrOH 97:3) at 1.0 mL/min, UV-detection at λ= 254 nm: t_R (major)= 12.6 min, t_R (minor)= 16.6 min, 80% ee.

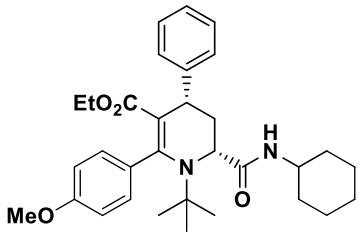
Compound 5h



Benzoylacetontrile (21.8 mg, 0.15 mmol), *trans*-2-nitrocinnamaldehyde (17.7 mg, 0.10 mmol), *tert*-butylamine (15.7 μL, 0.15 mmol), and cyclohexylisocyanide (18.7 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 5:1) afforded compound **5h** (28.7 mg, 59%) as a yellow solid. $[\alpha]_D^{20}$ −2.3 (*c* 0.5, acetone, 20°C). R_f = 0.32 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.08-8.04 (m, 2H); 7.91 (dd, *J* = 8.1, 1.3 Hz, 1H); 7.68-7.59 (m, 2H); 7.53-7.46 (m, 3H); 3.45-7.38 (m, 1H); 5.91 (dd, *J* = 7.6, 3.2 Hz, 1H); 5.39 (d, *J* = 8.7 Hz, 1H); 4.84 (dd, *J* = 7.9, 5.8 Hz, 1H); 3.93-3.79

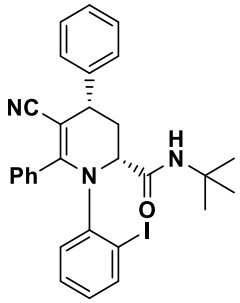
(m, 1H); 2.84-2.75 (m, 1H); 2.16-2.12 (m, 1H); 1.79-1.58 (m, 4H); 1.50-1.32 (m, 3H); 1,25 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2, 24.2, 25.5, 30.5, 33.4, 33.7, 39.3, 44.9, 52.3, 56.5, 60.5, 78.4, 119.2, 124.9, 128.1, 128.5, 128.75, 129.1, 130.0, 133.8, 133.9, 136.1, 138.2, 144.7, 149.8, 156.8, 167.6. HRMS (ESI-FT-QQTOF) *m/z*: 487.2721 $[M+H]^+$; calcd. for $C_{29}H_{35}N_4O_3$: 487.2709. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (n-hexane/i-PrOH 90:10) at 1.0 mL/min, UV-detection at λ= 254 nm: t_R (major)= 45.5 min, t_R (minor)= 53.2 min, >99% ee.

Compound 5i



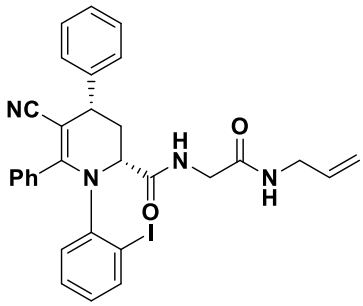
To a solution of Jørgensen catalyst (9.0 mg, 0.015 mmol), benzoic acid (4 mg, 0.03 mmol), and cinnamaldehyde (12.6 μL, 0.10 mmol) in dichloromethane (1.0 mL) was added ethyl 3-(4-methoxyphenyl)-3-oxopropionate (28.7 μL, 0.15 mmol) and was irradiated for 30 min (300 W) under high-speed magnetic stirring at -20 °C. 2,2,2-trifluoroethanol (1.0 mL), *tert*-butylamine (15.7 μL, 0.15 mmol), and cyclohexylisocyanide (18.7 μL, 0.15 mmol) were added and the glass tube was sealed. The flask was irradiated for 20 min (300 W) under high-speed magnetic stirring, while the temperature was raised up to 70 °C. Flash column chromatography purification (*n*-hexane/EtOAc 3:1) afforded compound **5i** (38.1 mg, 49%, isomer *cis*) as a yellowish oil. $[\alpha]_D^{20}$ −17.4 (*c* 0.5, EtOH, 20°C). R_f = 0.38 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69-7.60 (m, 2H); 7.53-7.41 (m, 5H); 7.25-7.10 (m, 2H); 6.24 (d, *J* = 6.9 Hz 1H); 4.52-4.48 (m, 1H); 4.18 (q, *J* = 7.8 Hz, 2H); 3.72 (s, 3H); 3.58-3.50 (m, 1H); 3.23-3.15 (m, 1H); 2.60-2.50 (m, 1H); 2.32-2.10 (m, 6H); 1.88-1.76 (m, 2H); 1.73-1.56 (m, 3H);1.47 (t, *J* = 7.5 Hz, 3H); 1.292 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.3, 22.8, 27.2, 29.5, 29.8, 31.1, 32.1, 32.9, 37.2, 45.1, 54.3, 56.7, 63.3, 77.5, 85.2, 105.9, 110.1, 115.3, 116.9, 118.6, 120.6, 125.1, 129.2, 129.6, 139.0, 140.3, 148.3, 155.1, 169.4, 174.0. HRMS (ESI-FT-QQTOF) *m/z*: 519.3229 $[M+H]^+$; calcd. for $C_{32}H_{43}N_2O_4$: 519.3223. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 95:5) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (major)= 15.5 min, t_R (minor)= 17.2 min, 90% ee.

Compound 5j



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), 2-iodoaniline (32.8 mg, 0.15 mmol), and *tert*-butyl isocyanide (16.9 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 4:1) afforded compound **5j** (33.7 mg, 60%, isomer *cis*) as amorphous white solid. $[\alpha]_D^{20}$ −6.2 (*c* 0.5, acetone, 20°C). R_f = 0.39 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74-7.52(m, 5H); 7.49-7.21 (m, 7H); 7.20-6.98 (m, 2H); 5.57 (s, 1H); 4.68 (dd, *J* = 6.9, 5.2 Hz, 1H); 4.39-4.25 (m, 1H); 4.10 (dd, *J* = 7.0, 4.5 Hz, 1H); 2.60 (m, 1H); 1.48 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.1, 41.6, 43.0; 47.1, 52.1, 73.7, 121.6, 122.7, 124.1, 126.7, 126.9, 127.1, 127.2, 127.6, 128.7, 129.9, 130.1, 131.4, 134.1, 140.3, 141.7, 143.6, 148.1, 157.0, 157.7, 180.5. HRMS (ESI-FT-QQTOF) *m/z*: 562.1369 $[M+H]^+$; calcd. for $C_{29}H_{29}IN_3O$: 562.1355. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*-PrOH 90:10) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (major)= 28.3 min, t_R (minor)= 41.9 min, 99% ee.

Compound 5k

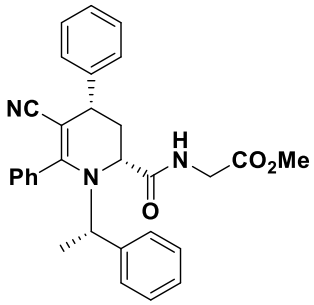


Benzoylacetontrile (**1**, 21.8 mg, 0.15 mmol), cinnamaldehyde (**2**, 12.6 μL, 0.10 mmol), 2-iodoaniline (32.8 mg, 0.15 mmol), and N-allyl-2-isocyanoacetamide[2] (18.6 mg, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 5:1) afforded compound **5k** (31.9 mg, 53%, isomer *cis*) as amorphous yellow

[2] Dömling, A.; Beck, B.; Fuchs, T.; Yazbak, A. *J. Comb. Chem*. **2006**, 8, 872.

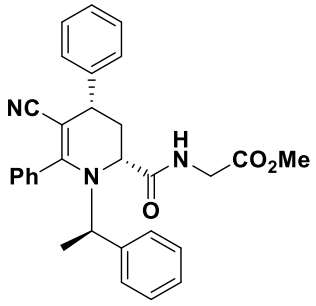
solid. $[\alpha]_D^{20}$ −10.6 (*c* 0.5, acetone, 20°C). R_f = 0.41 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (ddd, *J* = 7.6, 3.6, 1.3 Hz, 1H); 7.42-7.38 (m, 1H); 7.35-7.31 (m, 4H); 7.20-7.07 (m, 6H); 6.54 (dd, *J* = 6.9, 5.5 Hz, 1H); 6.47-6.42 (m, 1H); 6.28 (t, *J* = 6.3 Hz, 1H); 5.81-5.77 (m, 1H); 5.76-5.68 (m, 1H); 5.15-5.03 (m, 2H); 4.69 (t, *J* = 7.6 Hz, 1H); 4.21 (dd, *J* = 5.2, 2.4 Hz, 2H); 4.03 (t, *J* = 5.8 Hz, 1H); 3.87-3.80 (m, 2H); 2.21 (dd, *J* = 7.7, 5.9 Hz, 2H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 39.5, 42.2, 46.3, 47.7, 59.6, 78.3, 87.2, 112.3, 117.0, 120.5, 126.8, 127.0, 127.2, 127.4, 128.4, 128.6, 128.8, 129.2, 129.5, 129.9, 130.1, 133.4, 139.5, 143.2, 145.5, 156.5, 159.3, 167.7, 170.6. HRMS (ESI-FT-QQTOF) *m/z*: 603.1268 $[M+H]^+$; calcd. for $C_{30}H_{28}IN_4O_2$: 603.1257. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.7 mL/min, UV-detection at λ= 254 nm: t_R (major)= 19.2 min, t_R (minor)= 24.4 min, 95% ee.

Compound 5l



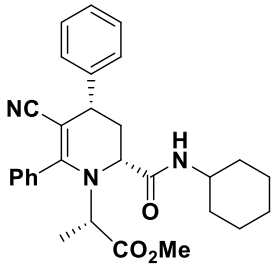
Benzoaylcetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 µL, 0.10 mmol), (*S*)-α-methylbenzylamine (19.4 µL, 0.15 mmol), and methyl isocyanoacetate (13.6 µL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 3:1) afforded compound **5l** (32.6 mg, 68%, isomer *cis*) as a pale yellow oil. $[\alpha]_D^{20}$ −2.9 (*c* 0.6, acetone, 20°C). R_f = 0.35 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25-7.23 (m, 5H); 7.21-7.13 (m, 6H); 7.12-6.98 (m, 4H); 5.68 (t, *J* = 6.1 Hz, 1H); 4.32 (m, 1H); 4.22 (m, 2H); 3.95 (d, *J* = 8.8 Hz, 1H); 3.76 (s, 3H); 3.57 (t, *J* = 8.0 Hz, 1H); 2.25 (m, 1H); 1.94 (m, 1H); 1.28 (d, *J* = 6.5 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.6, 40.9, 45.1, 47.8, 52.8, 53.6, 56.1, 60.3, 74.9, 119.7, 124.3, 125.4, 126.5, 126.7, 126.8, 126.9, 127.6, 128.7, 128.8, 143.8, 144.5, 145.9, 160.6, 170.5. HRMS (ESI-FT-QQTOF) *m/z*: 480.2288 $[M+H]^+$; calcd. for $C_{30}H_{30}N_3O_3$: 480.2282. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 1.0 mL/min, UV-detection at λ= 254 nm: t_R (major)= 20.7 min, t_R (minor)= 44.5 min, 91:9 *dr*.

Compound 5m



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), (*R*)-α-methylbenzylamine (37.3 μL, 0.15 mmol), and methyl isocyanoacetate (13.6 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 3:1) afforded compound **5m** (28.8 mg, 60%, isomer *cis*) as a pale yellow oil. $[\alpha]_D^{20}$ −2.1 (*c* 0.6, acetone, 20°C). R_f = 0.40 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42-7.21 (m, 12H); 7.18-7.04 (m, 3H); 5.93 (brs, 1H); 4.36 (m, 2H); 3.97 (m, 2H); 3.84 (brs, 4H); 2.04 (m, 1H); 1.83 (m, 1H); 1.39 (d, *J* = 6.5 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 23.4, 41.4, 44.9, 47.6, 48.6, 52.8, 56.8, 61.1, 74.6, 119.8, 126.4, 126.6, 126.8, 127.4, 127.9, 128.7, 129.1, 143.6, 144.3, 145.7, 160.6, 170.4. HRMS (ESI-FT-QQTOF) *m/z*: 480.2290 $[M+H]^+$; calcd. for $C_{30}H_{30}N_3O_3$: 480.2287. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (minor)= 22.8 min, t_R (major)= 30.8 min, 87:13 *dr*.

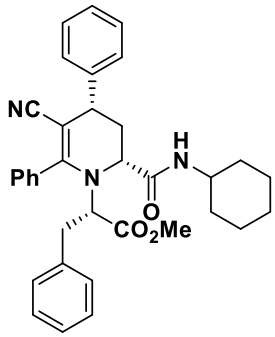
Compound 5n



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), alanine methyl ester hydrochloride (20.9 mg, 0.15 mmol), Et_3N (21 μL, 0.15 mmol) and cyclohexylisocyanide (18.7 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 2:1) afforded compound **5n** (28.8 mg, 61%, isomer *cis*) as a pale yellow oil. $[\alpha]_D^{20}$ −14.4 (*c* 5.0, acetone, 20°C). R_f = 0.32 (*n*-hexane/EtOAc 2:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56-7.24 (m, 6H); 7.21-7.13 (m, 3H); 5.59 (d, *J*= 8.2 Hz, 1H); 4.01 (dd, *J*= 8.6, 1.4 Hz, 1H); 3.86 (m, 1H); 3.72 (s, 3H); 3.37 (q, *J* = 7.0 Hz, 1H); 2.18-2.03

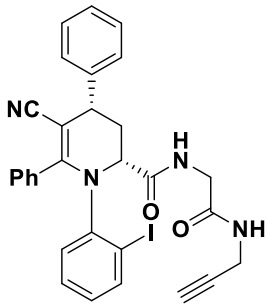
(m, 2H); 2.01-1.90 (m, 1H); 1.81-1.71 (m, 2H); 1.68-1.55 (m, 2H); 1.46 (d, *J* = 12.0 Hz 1H); 1.30 (d, *J* = 7.0 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.0, 24.2, 25.6, 25.9, 33.5, 33.6, 40.4, 47.6, 51.5, 52.2, 54.2, 61.7, 71.2, 102.5, 113.7, 120.6, 125.0, 126.6, 126.9, 127.9, 128.6, 129.8, 130.5, 132.5, 134.6, 144.0, 159.1, 176.4. HRMS (ESI-FT-QQTOF) *m/z*: 472.2618 $[M+H]^+$; calcd. for $C_{29}H_{34}N_3O_3$: 472.2601. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (major)= 8.8 min, >99:1 *dr*.

Compound 5o



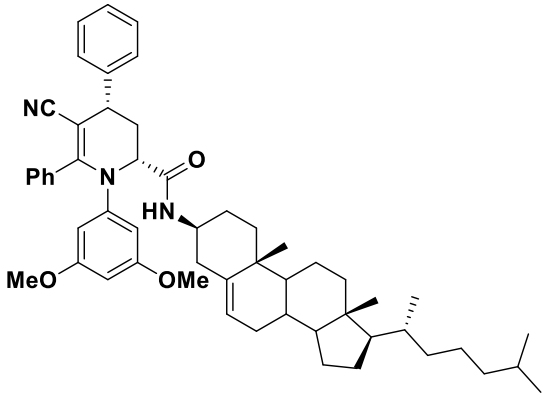
Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), HCl Phe-OMe (32.3 mg, 0.15 mmol), Et_3N (21.0 μL, 0.15 mmol) and cyclohexylisocyanide (18.7 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 4:1) afforded compound **5o** (28.5 mg, 52%, isomer *cis*) as a pale yellow solid. $[\alpha]_D^{20}$ −5.3 (*c* 0.5, acetone, 20°C). R_f = 0.33 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60-7.35 (m, 7H); 7.29-7.12 (m, 8H); 4.81 (d, *J* = 7.9 Hz, 1H); 4.47 (t, *J* = 7.1 Hz, 1H); 4.15 (d, *J* = 4.9 Hz, 1H); 3.70 (s, 3H); 3.60 (m, 1H); 3.48 (t, *J* = 7.6 Hz, 1H); 3.12 (dd, *J* = 13.9, 6.8 Hz, 1H); 2.58 (dd, *J* = 14.0, 6.8 Hz, 1H); 2.35-2.27 (m, 2H); 2.22-2.12 (m, 2H); 1.82-1.60 (m, 6H); 1.56-1.50 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 24.4, 24.5, 25.7, 33.4, 36.1, 39.7, 39.9, 45.6, 47.4, 51.6, 52.4, 60.1, 61.5; 67.5, 111.4, 116.2, 123.8, 126.9, 127.3, 128.6, 128.7, 128.8, 128.9, 129.2, 129.3; 131.5, 133.4, 144.4, 149.8, 149.7, 156.5, 158.9, 175.6. HRMS (ESI-FT-QQTOF) *m/z*: 548.2910 $[M+H]^+$; calcd. for $C_{35}H_{38}N_3O_3$: 548.2913. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (major)= 19.2 min, t_R (minor)= 23.4 min, 99:1 *dr*.

Compound 5p



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), 2-iodoaniline (32.8 mg, 0.15 mmol), and 2-Isocyano-*N*-(prop-2-yn-1-yl)acetamide[2] (18.3 mg, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 4:1) afforded compound **5p** (34.8 mg, 58%, isomer *cis*) as yellow solid. $[\alpha]_D^{20}$−10.1 (*c* 0.5, acetone, 20°C). R_f = 0.32 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76-7.67 (m, 3H); 7.63-7.24 (m, 9H); 7.10-6.94 (m, 2H); 6.12-5.80 (m, 1H); 5.30-5.13 (m, 1H); 4.46 (d, *J* = 5.8 Hz, 2H); 4.24 (dd, *J* = 5.4, 2.6 Hz, 2H); 4.00 (dd, *J* = 7.1, 2.9 Hz, 1H); 3.65-3.59 (m, 1H); 3.52-3.48 (m, 1H); 2.65-2.54 (m, 1H); 2.31 (t, *J* = 2.6 Hz, 1H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4, 39.4, 46.2, 47.6, 59.6, 68.4, 71.9, 78.9, 79.0, 87.1, 112.3, 118.5, 120.5, 126.2, 126.9, 127.0, 128.8, 128.9, 128.2, 129.6, 130.1, 139.5, 143.2, 145.6, 159.6, 167.9, 170.7. HRMS (ESI-FT-QQTOF) *m/z*: 601.1128 $[M+H]^+$; calcd. for $C_{30}H_{26}IN_4O_2$: 601.1100. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (n-hexane/i-PrOH 90:10) at 1.0 mL/min, UV-detection at λ= 300 nm: t_R (minor)= 20.4 min, t_R (major)= 21.7 min, 92% ee.

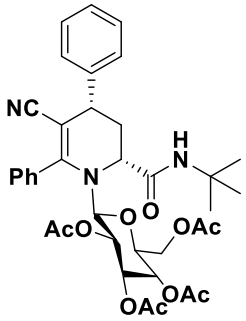
Compound 6



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), 3,5dimethoxy aniline (22.7 mg, 0.15 mmol), and cholesterol isocyanide[3] (59.3 mg, 0.15 mmol) were reacted according to the general procedure B. The reaction was concentrated *in vacuo*. The resulting residue was dissolved in CH_2Cl_2 (3 mL). The product was recrystallized by addition of MeOH and collected by vacuum filtration to afforded compound **6** (49.3 mg, 61%, isomer *cis*) as a yellow solid. $[\alpha]_D^{20}$ −2.9 (*c* 0.5, acetone, 20°C). R_f = 0.40 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49-7.32 (m, 2H); 7.31-7.21 (m, 5H); 7.19-7.06 (m, 6H); 5.87 (s, 1H); 5.75 (d, *J* = 2.7 Hz, 1H); 5.33 (s, 1H); 4.77 (d, *J* = 8.2 Hz, 1H); 4.49 (t, *J* = 7.2 Hz, 1H); 4.02-3.95 (m, 1H); 3.84-3.75 (m, 3H); 3.66 (s, 6H); 2.43-2.30 (m, 1H); 2.18-2.10 (m, 1H); 2.09-1.98 (m, 3H); 1.96-1.84 (m, 3H), 1.82-1.71 (m, 3H), 0.84 (d, *J* = 6.4 Hz, 6H), 0.80 (s, 3H), 0.78 (s, 3H), 0.6 (s, 3H) .^{13}C NMR (100 MHz, $CDCl_3$): δ = 10.8, 17.6, 18.4, 19.9, 21.5, 21.8, 22.8, 23.3, 27.0, 27.2, 28.5, 28.7, 29.0, 30.8, 34.8, 35.2, 35.6, 36.0, 38.3, 38.5, 38.7, 38.9, 41.3, 46.6, 48.8, 52.3 54.2, 55.0, 55.6, 58.2, 59.7, 60.1, 89.9, 92.1, 118.9, 121.6, 124.7, 125.8, 126.1, 126.4, 127.6, 127.7, 128.9, 129.0, 132.9, 138.5 142.7, 147.2, 157.5, 160.8. HRMS (ESI-FT-QQTOF) *m/z*: 808.5429 $[M+H]^+$; calcd. for $C_{54}H_{70}N_3O_3$: 808.5417. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.8 mL/min, UV-detection at λ= 254 nm: t_R (minor)= 9.7 min, t_R (major)= 12.0 min, 96:4 *dr*.

[3] Rivera, D. G.; Pérez-Labrada, K.; Lambert, L.; Dörner, S.; Westermann, B.; Wessjohann, L. A. C*arbohydr. Res.* **2012**, 359, 102-110.

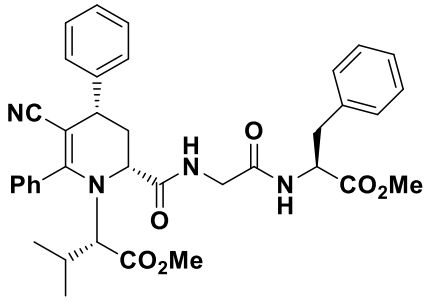
Compound 7



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), 2,3,4,6-tetra-O-acetyl-β -D-glucopyranosylamine[4] (52.1 mg, 0.15 mmol), and *tert*-butyl isocyanide (16.9 μL, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 2:1) afforded compound **7** (21.8 mg, 63%, isomer *cis*) as a yellow solid. $[\alpha]_D^{20}$ −3.9 (*c* 0.4, acetone, 20°C). R_f = 0.37 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68-7.57 (m, 1H); 7.51-7.35 (m, 6H); 7.30- 7.12 (m, 3H); 5.90 (s, 1H); 5,45 (t, *J* = 7.5 Hz, 1H); 5.30 (t, *J* = 7.5 Hz, 1H); 5.15 (dd, *J* = 10.0, 9.5 Hz, 1H); 4.98 (dd, *J* = 9.4, 9.5 Hz, 1H); 4.60 (dd, *J* = 9.0, 9.5 Hz, 1H); 4.28 (d, *J* = 9.0 Hz, 1H); 4.24 (dd, *J* = 12.0, 4.9 Hz, 1H); 4.10 (dd, 1H); 3.80-3.60 (m, 1H); 3.48 (t, *J* = 7.0 Hz, 1H); 2.78-2.46 (m, 1H), 2.14, 2.12, 2.01, 1.97 (4·s, 12H); 1.48 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.9, 22.7, 26.2, 27.3, 30.2, 35.4, 41.6, 43.0, 47.0, 48.1, 52.2, 62.0, 69.4, 71.2, 72.5, 73.6, 82.8, 84.8, 121.7, 126.1, 126.8, 126.9, 127.1, 127.6, 128.1, 128.7, 129.9, 143.7, 156.9, 167.9, 168.5, 169.3, 170.3, 171.1. HRMS (ESI-FT-QQTOF) *m/z*: 690.3039 $[M+H]^+$; calcd. for $C_{37}H_{44}N_3O_{10}$: 690.3026. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel AS-H column (*n*-hexane/*i*-PrOH 90:10) at 1.0 mL/min, UV-detection at λ= 290 nm: t_R (major)= 13.5 min, t_R (minor)= 18.3 min, 98:2 *dr*.

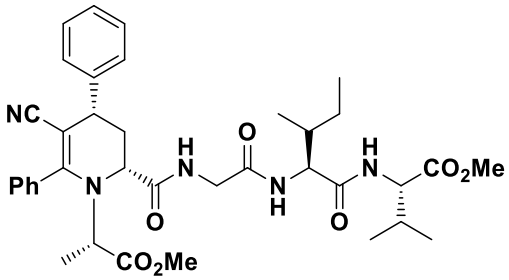
[4] Badia, C.; Souard, F.; Vicent, C. *J. Org. Chem*. **2012**, 77, 10870-10881.

Compound 8



Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), HCl Val-OMe (25.1 mg, 0.15 mmol), Et_3N (21 μL, 0.15 mmol), and CN-Gly-Phe-OMe (36.9 mg, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 1:1) afforded compound **8** (33.1 mg, 52%, isomer *cis*) as a pale brown oil. $[\alpha]_D^{20}$ −1.3 (*c* 0.5, acetone, 20°C). R_f = 0.33 (*n*-hexane/ EtOAc 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35-7.27 (m, 6H, Ph); 7.25-7.19 (m, 3H, Ph); 7.18-7.08 (m, 6H, Ph); 6.37 (d, *J* = 7.7 Hz, 1H); 6.17 (t, *J* = 5.8 Hz, 1H); 4.95 (dd, *J* = 13.7, 6.0 Hz, 1H); 4.28 (d, *J* = 5.8 Hz, 2H); 4.12 (m, 1H); 4.02 (dd, *J* = 7.8, 4.0 Hz, 1H) 3.77 (m, 1H); 3.73 (s, 3H); 3.72 (s, 3H); 3.16 (m, 2H); 3.07 (d, *J* = 5.2 Hz, 1H); 2.04 (m, 3H); 1.99 (m, 2H); 1.26 (t, *J* = 7.1 Hz, 1H); 0.95 (d, *J* = 6.8 Hz, 3H); 0.90 (d, *J* = 6.9 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 18.2, 19.4, 31.6, 37.9, 39.9, 46.3, 47.8, 52.0, 52.4, 53.4, 61.8, 64.4, 75.4, 119.9, 120.1, 126.7, 126.9, 127.2, 127.5, 128.1, 128.3, 128.7, 128.9, 129.0, 129.1, 129.2, 135.6, 142.2, 143.3, 160.3, 167.8, 171.6, 175.8. HRMS (ESI-FT-QQTOF) *m/z*: 637.3031 $[M+H]^+$; calcd. for $C_{37}H_{41}N_4O_6$: 637.3026. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 1.0 mL/min, UV-detection at λ= 254 nm: t_R (major)= 22.6 min, 99:1 *dr*.

Compound 9

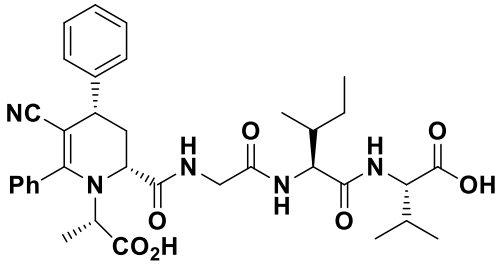


Benzoylacetontrile (21.8 mg, 0.15 mmol), cinnamaldehyde (12.6 μL, 0.10 mmol), HCl Ala-OMe (20.9 mg, 0.15 mmol), Et_3N (21.0 μL, 0.15 mmol), and CN-Gly-Ile-Val-OMe (46.7 mg, 0.15 mmol) were reacted according to the general procedure B. Flash column chromatography purification (*n*-hexane/EtOAc 1:3) afforded compound **9** (39.1 mg, 58%, isomer *cis*) as a pale

yellow solid. $[\alpha]_D^{20}$ −5.2 (*c* 0.5, acetone, 20°C). R_f = 0.29 (*n*-hexane/ EtOAc 1:3). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76-7.60 (m, 2H); 7.55-7.46 (m, 5H); 7.23-7.02 (m, 3H); 6.33 (d, *J* = 6.8 Hz, 1H); 6.16 (t, *J* = 5.7 Hz, 1H); 6.12 (t, *J* = 5.8 Hz, 1H); 5.76 (t *J* = 5.8 Hz, 1H); 4.70-4.62 (m, 1H); 4.55-4.60 (m, 2H); 4.52-4.47 (m, 1H); 4.28 (d, *J* = 7.1 Hz, 1H); 4.12 (d, *J* = 8.2 Hz, 1H); 3.74 (2xs, 6H); 3.49 (q, *J* = 7.0 Hz, 1H); 2.51 (m, 1H); 2.26-2.12 (m, 2H); 2.09-1.97 (m, 1H); 1.60-1.55 (m, 1H); 1.51(d, *J* = 7.0 Hz, 3H); 1.46-1.30 (m, 1H); 1.09 (d, *J* = 7.0 Hz, 6H); 0.90 (d, *J* = 6.8 Hz, 6H); 0.80 (t, *J* = 2.5 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.3, 15.3, 17.9, 18.9, 19.8, 37.5, 46.4, 47.1, 52.1, 52.2 54.1, 56.2, 57.3, 57.9, 58.0, 61.7, 62.3, 75.2, 119.7, 120.1, 126.7, 126.8, 126.9, 127.5, 128.3, 128.6, 128.7, 130.1, 143.0, 143.5, 161.0, 168.6, 170.9, 172.2, 176.1. HRMS (ESI-FT-QQTOF) *m/z*: 674.3565 $[M+H]^+$; calcd. for $C_{37}H_{48}N_5O_7$: 674.3554. The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.7 mL/min, UV-detection at λ= 254 nm: t_R (major)= 13.8 min, t_R (minor)= 21.8 min, 96:4 *dr*.

Methyl ester removal procedure for compound 9

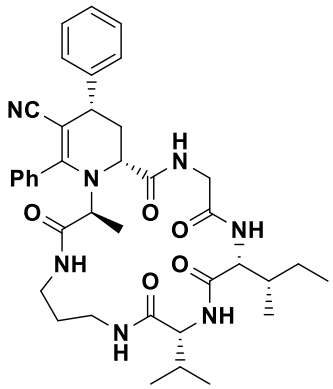
Compound 9a



The THP-peptide chimeric **9** (30.0 mg, 0.04 mmol) was dissolved in THF/H_2O (2:1, 5 mL) and LiOH (5.7 mg, 0.24 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 2 h and then acidified with aquouse 10% $NaHSO_4$ to pH 3. The resulting phases were separated and the aqueous phase was additionally extracted with EtOAc (2·10 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to yield the ***C*-deprotected THP-peptide 9a** (22.7 mg, 88%) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.82-7.75 (m, 1H); 7.70-7.57 (m, 1H); 7.49-7.21 (m, 8H); 5.58 (d, *J* = 6.8 Hz, 1H); 4.64 (d, *J* = 6.0 Hz, 1H); 4.56 (t, *J* = 5.9 Hz, 1H); 4.51-4.47 (m, 2H); 4.43-4.39 (m, 1H); 4.33-4.29 (m, 1H); 4.20 (dd, *J* = 6.9, 5.7 Hz, 1H) 4.11(m, 1H); 4.00 (d, *J* = 8.2 Hz, 1H); 3.48 (m, 1H); 2.65 (m, 1H); 2.15-2.06 (m, 4H); 1.35 (d, *J* = 7.0 Hz, 3H); 1.25 (d, *J* = 7.0 Hz, 3H); 1.18 (t, *J* = 7.1 Hz, 1H); 0.96 (d, *J* = 6.8 Hz, 6H); 0.85 (t, *J* = 2.5 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.4, 15.6, 17.9, 18.4, 19.4, 25.9, 30.2, 38.0, 41.4, 42.3, 46.4, 47.8, 56.6, 57.3, 57.8, 62.1, 75.2, 119.7, 120.1,

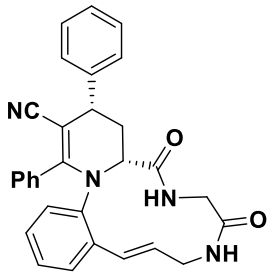
126.7, 126.8, 126.9, 127.5, 128.4, 128.6, 128.7, 130.4, 143.0, 143.8, 161.0, 168.6, 171.9, 172.2, 176.1. HRMS (ESI-FT-QQTOF) *m/z*: 646.3235 $[M+H]^+$; calcd. for $C_{35}H_{44}N_5O_7$: 646.3240.

Synthesis of cyclic compound 10



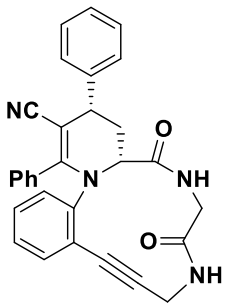
The ***C*-deprotected THP-peptide 9a** (22.6 mg, 0.035 mmol), PyBOP (41.6 mg, 0.070 mmol) and DIEA (41.8 μL, 0.210 mmol) are suspended in CH_2Cl_2/DMF (100 mL). 1,3-Diaminopropane (3.4 μL, 0.035 mmol) is syringed in portion wise and the resulting solution is stirred at room temperature for 12h. The reaction mixture is concentrated and then diluted with 20 mL EtOAc, transferred to a separatory funnel and sequentially washed with 5% aqueous solution of $KHSO_4$ (2·10 mL) and 5% aqueous suspension $NaHCO_3$ (2·10 mL) and brine (3x10 mL). The organic phase is dried over Na_2SO_4, filtered and concentrated under reduced pressure. Flash column chromatography purification (CH_2Cl_2/MeOH 15:1) furnished the chimeric THP-peptide macrocycle **10** (11.2 mg, 41%). ^{1}H NMR (400 MHz, CD_3OD): δ = 7.78-7.61 (m, 1H); 7.57-7.33 (m, 9H); 6.21 (m, 1H); 5.86 (d, *J* = 6.8 Hz, 1H); 5.42 (d, *J* = 6.0 Hz, 1H); 4.64 (t, *J* = 5.9 Hz, 1H); 4.57 (m, 1H); 4.47-4.42 (m, 2H); 4.39-4.26 (m, 1H); 4.20-4.00 (m, 1H); 4.02 (dd, *J* = 6.9, 5.7 Hz, 1H) 3.53(m, 2H); 3.25 (m, 2H); 3.18 (m, 1H); 2.85-2.80 (m, 1H); 2.59-2.43 (m, 4H); 1.82 (t, *J* = 7.0 Hz, 3H); 1.20 (d, *J* = 7.0 Hz, 3H); 0.96 (d, *J* = 6.8 Hz, 6H); 0.85 (t, *J* = 3.0 Hz, 3H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.5, 15.8, 17.6, 18.6, 19.9, 25.9, 27.3, 30.7, 32.4, 37.7, 40.2, 41.2, 42.6, 43.3, 44.1, 56.7, 58.3, 59.8, 62.2, 74.2, 111.6, 118.6, 126.7, 127.1, 127.5, 127.8, 128.1, 128.9, 129.8, 131.7, 144.5, 146.8, 165.9, 168.4, 171.7, 173.8, 177.4. HRMS (ESI-FT-QQTOF) *m/z*: 684.3869 $[M+H]^+$; calcd. for $C_{38}H_{50}N_7O_5$: 684.3873.

Compound 11



A mixture of **5g** (60.2 mg, 0.100 mmol), palladium(II) acetate (1.1 mg, 0.005 mmol), triphenyl phosphine (2.6 mg, 0.010 mmol) and triethylamine (34.7 μL, 0.250 mmol) in acetonitrile (2mL) was heated to 120 °C for 45 min (300W). Flash column chromatography purification (*n*-hexane/EtOAc 6:1) afforded compound **11** (21.4 mg, 45%) as amorphous white solid. R_f = 0.50 (*n*-hexane/ EtOAc 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (dd, *J* = 7.2, 4.6 Hz, 1H); 7.48-7.39 (m, 1H); 7.38-7.29 (m, 4H); 7.28-7.15 (m, 6H); 6.82 (dd, *J* = 6.7, 5.1 Hz,1H); 6.77-6.72 (m, 1H); 6.62 (d, *J* = 15.1 Hz, 1H); 6.36 (brs, 1H); 5.93-5.70 (m, 2H); 4.76 (t, *J* = 7.7 Hz,1H); 4.28 (dd, *J* = 5.4, 2.5 Hz, 2H); 4.11 (t, *J* = 6.0 Hz, 1H); 3.95-3.86 (m, 2H); 2.31-2.25 (m, 2H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 42.3, 46.4, 47.1, 47.8, 59.7, 87.3, 112.4, 117.1,120.0, 120.6, 126.9, 127.1, 127.3, 127.5, 128.5, 128.7, 128.9, 129.0, 129.3, 129.7, 130.1, 133.2, 133.5, 139.6, 143.3, 145.6, 156.6, 159.4, 167.8, 170.7. HRMS (ESI-FT-QQTOF) *m/z*: 475.2139 $[M+H]^+$; calcd. for $C_{30}H_{27}N_4O_2$: 475.2134. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*-PrOH 90:10) at 1.0 mL/min, UV-detection at λ= 254 nm: t_R (major)= 8.8 min, t_R (minor)= 17.0 min, 94% ee.

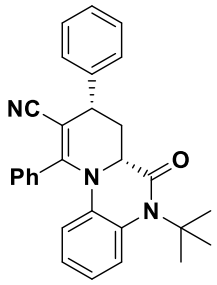
Compound 12



A solution of **5l** (121 mg, 0.20 mmol), $Pd(PPh_3)_2Cl_2$ (1.4 mg, 0.002 mmol) and CuI (1.0 mg, 0.004 mmol) in Et_3N/CH_3CN (1:1, 4.0 mL) was heated at 100 °C for 3h under N_2 atmosphere. The reaction mixture was poured into water and extracted with DCM, then the combined organic phases were concentrated *in vacuo* and purified by column chromatography (*n*-hexane/EtOAc 5:1) to afford compound **12** (49.1 mg, 52%) as brown oil. R_f= 0.37 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91-7.52 (m, 4H); 7.49 -7.21 (m, 7H); 7.169-6.69 (m, 3H); 6.13 (t, *J* = 7.0 Hz, 1H); 5.62 (m, 1H); 5.03 (d, *J* = 5.8 Hz, 2H); 4.70 (d, *J* = 6.1 Hz, 2H), 4.17(d, *J* = 6.9

Hz, 1H); 3.85 (t, *J* = 7.0 Hz, 1H); 3.78 (d, *J* =6.9 Hz, 1H); 2.65-2.50 (m, 1H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.5, 37.5, 39.5, 46.3, 47.7, 59.6, 72.0, 87.1, 90.1, 91.0, 112.4, 118.6, 119.9, 120.6 126.3, 126.9, 127.1, 128.5, 128.9, 129.1, 129.3, 129.6, 133.5, 139.6, 143.3, 145.6, 159.6, 167.9, 169.9. HRMS (ESI-FT-QQTOF) *m/z*: 473.1989 $[M+H]^+$; calcd. for $C_{30}H_{25}N_4O_2$: 473.1978. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel IA column (*i*-PrOH) at 1.0 mL/min, UV-detection at λ= 254 nm: t_R (minor)= 3.6 min, t_R (major)= 3.7 min, 87% ee.

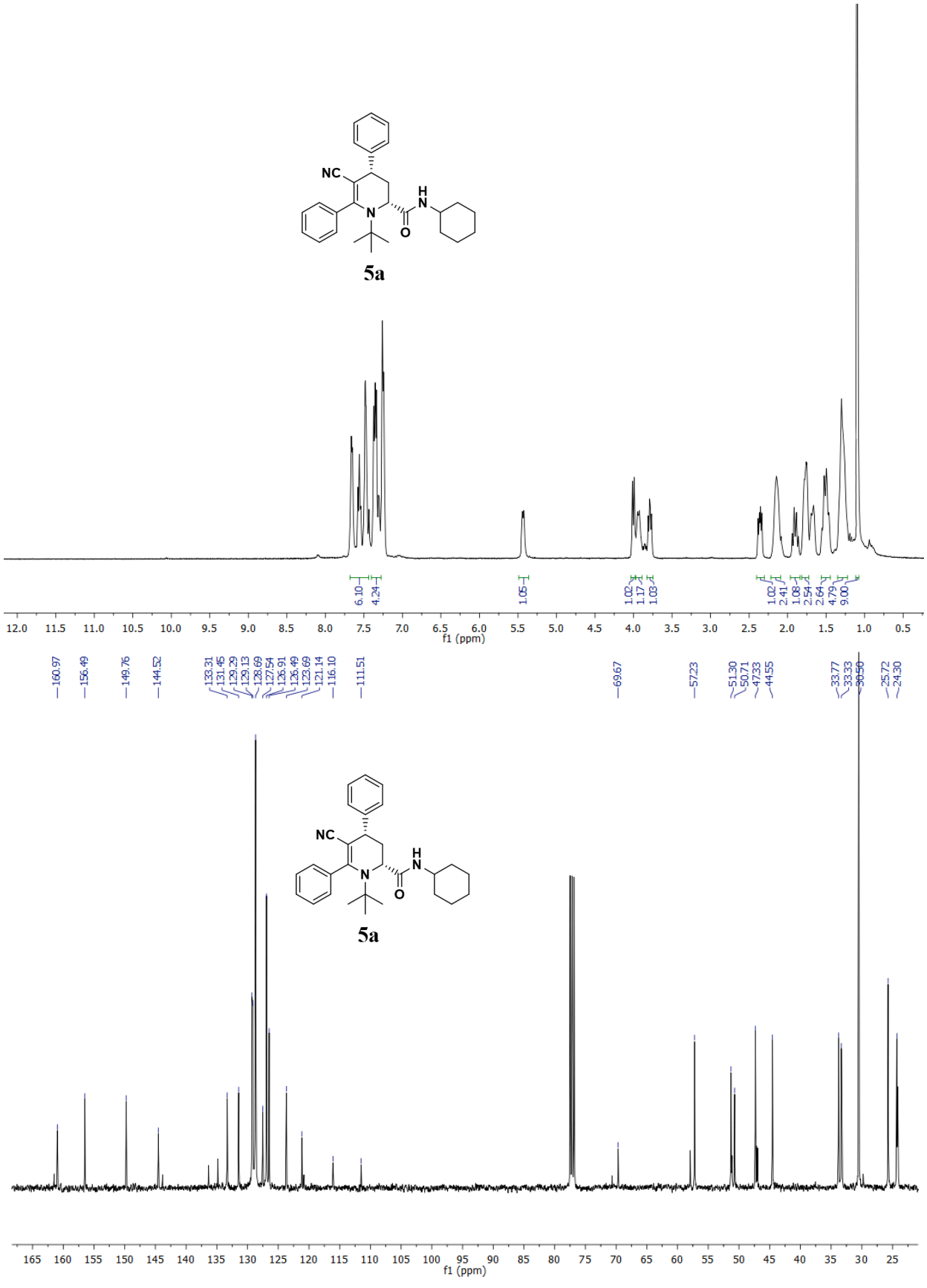
Compound 13



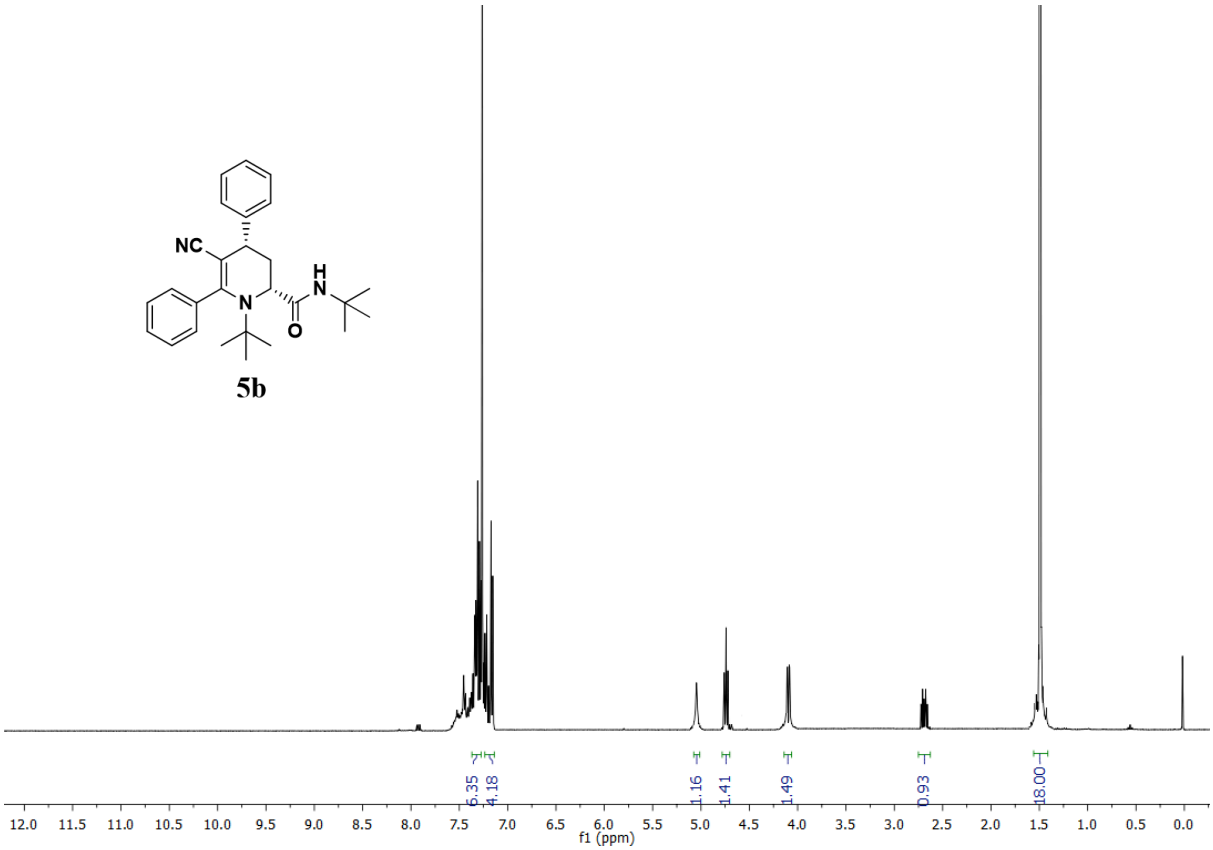
To a solution of **5f** (56.1 mg, 0.1 mmol), in toluene/acetonitrile (*v*/*v* = 3/1 c= 50 mM, ca 2mL), was added K_2CO_3 (27.7 mg, 0.2 mmol), $Pd(dba)_2$ (2.7 mg, 0.005 mmol) and XantPhos (2.9, 0.005 mmol) in a teflon-capped vial. The sealed vial is then subjected to micro-wave heating (150W, 100°C) for 1 h. After cooling to room temperature, the catalyst and salt were removed by filtration through a short pad of Celite. The filtrate was concentrated to dryness and purified by flash column chromatography (*n*-hexane/EtOAc 4:1) to afford compound **13** (26.4 mg, 61%) as an amorphous white solid. R_f = 0.35 (*n*-hexane/ EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48-7.07 (m, 11H); 6.97-6.68 (m, 3H); 4.15 (t, *J* = 7.3 Hz, 1H); 3.90 (t, *J* = 7.0 Hz, 1H); 2.89 (dd, *J* = 7.5, 2.8 Hz, 1H); 2.16 (dd, *J* = 7.0, 2.9 Hz, 1H); 1.39 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.9, 42.0, 43.4, 49.7, 51.8, 94.5, 116.6, 119.8, 121.5, 125.4, 126.9, 127.6, 128.4, 129.0, 129.1, 130.5, 134.8, 139.4, 141.7, 143.4, 145.3, 147.9, 151.3, 152.9, 157.6, 158.5, 169.1. HRMS (ESI-FT-QQTOF) *m/z*: 456.2069 $[M+Na]^+$; calcd. for $C_{29}H_{27}N_3NaO$: 456.2052. The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*-PrOH 80:20) at 0.7 mL/min, UV-detection at λ= 254 nm: t_R (minor)= 10.6 min, t_R (major)= 14.6 min, 97% ee.

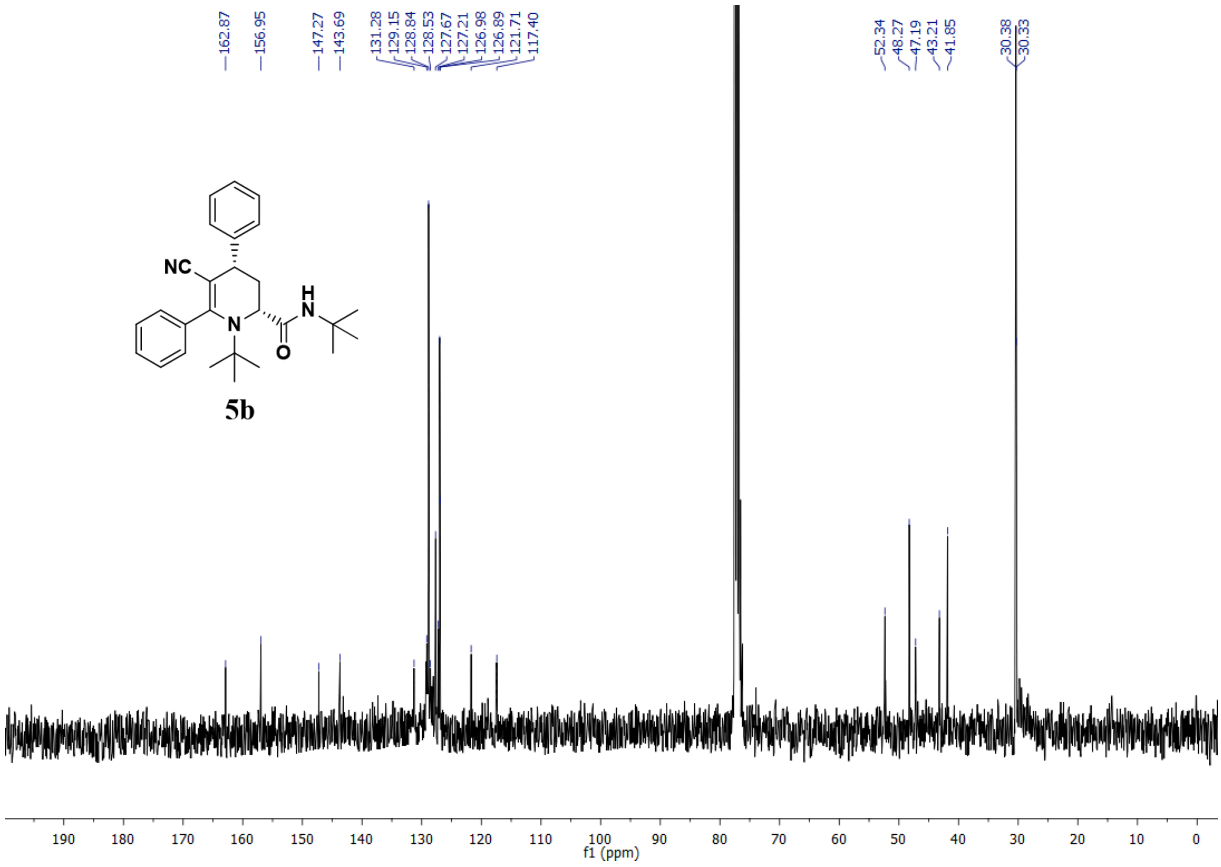
^{1}H and ^{13}C NMR Spectra of Tetrahydropyridines and Chimeric Derivatives

^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5a**

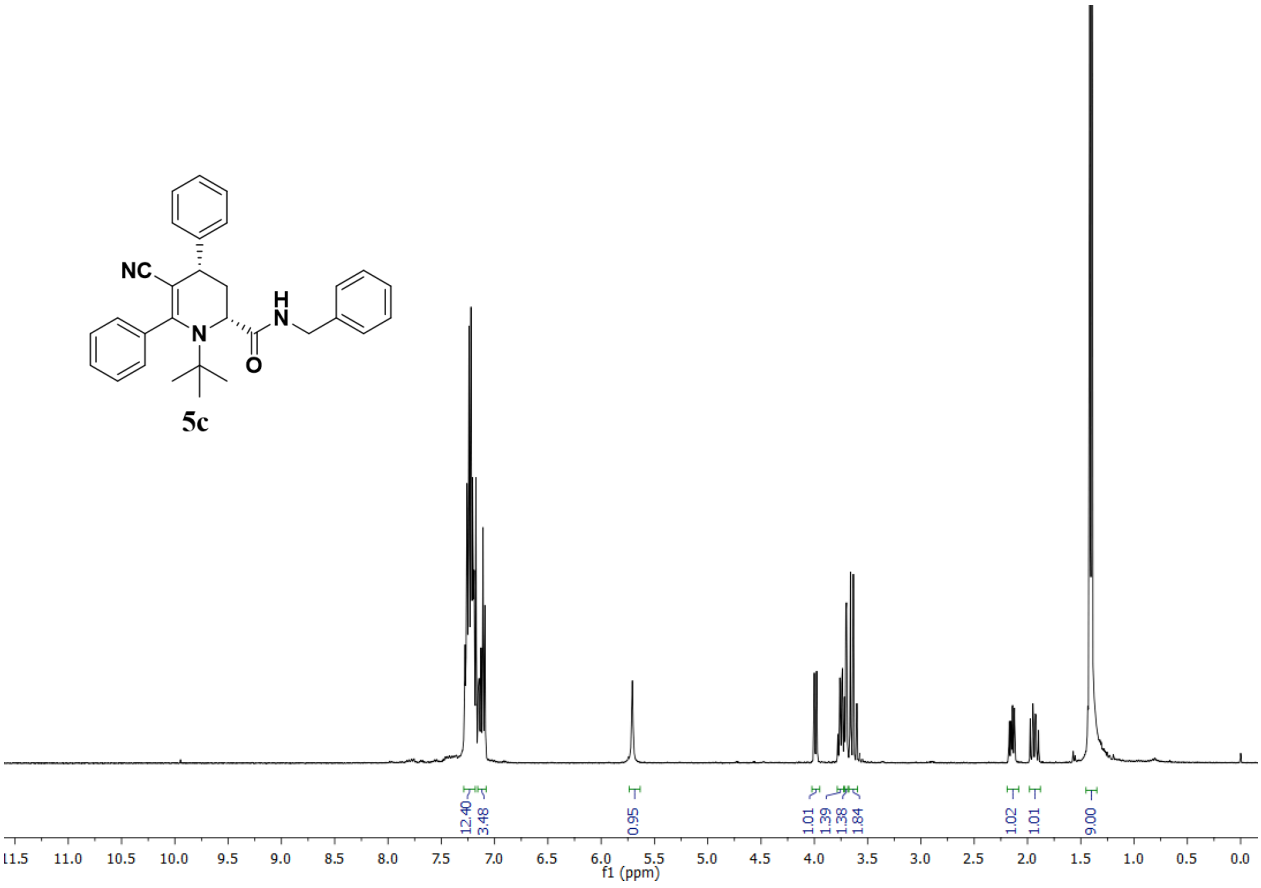


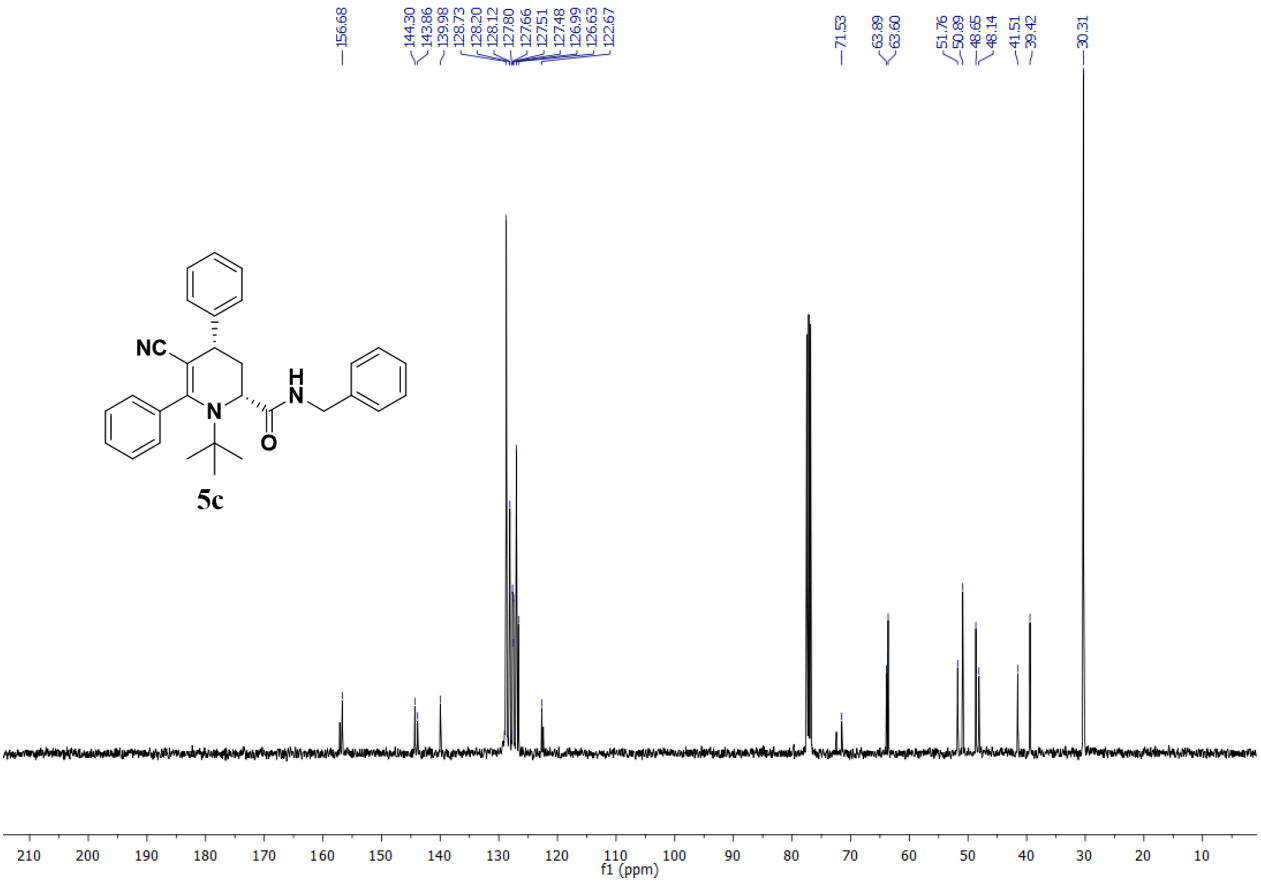
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5b**



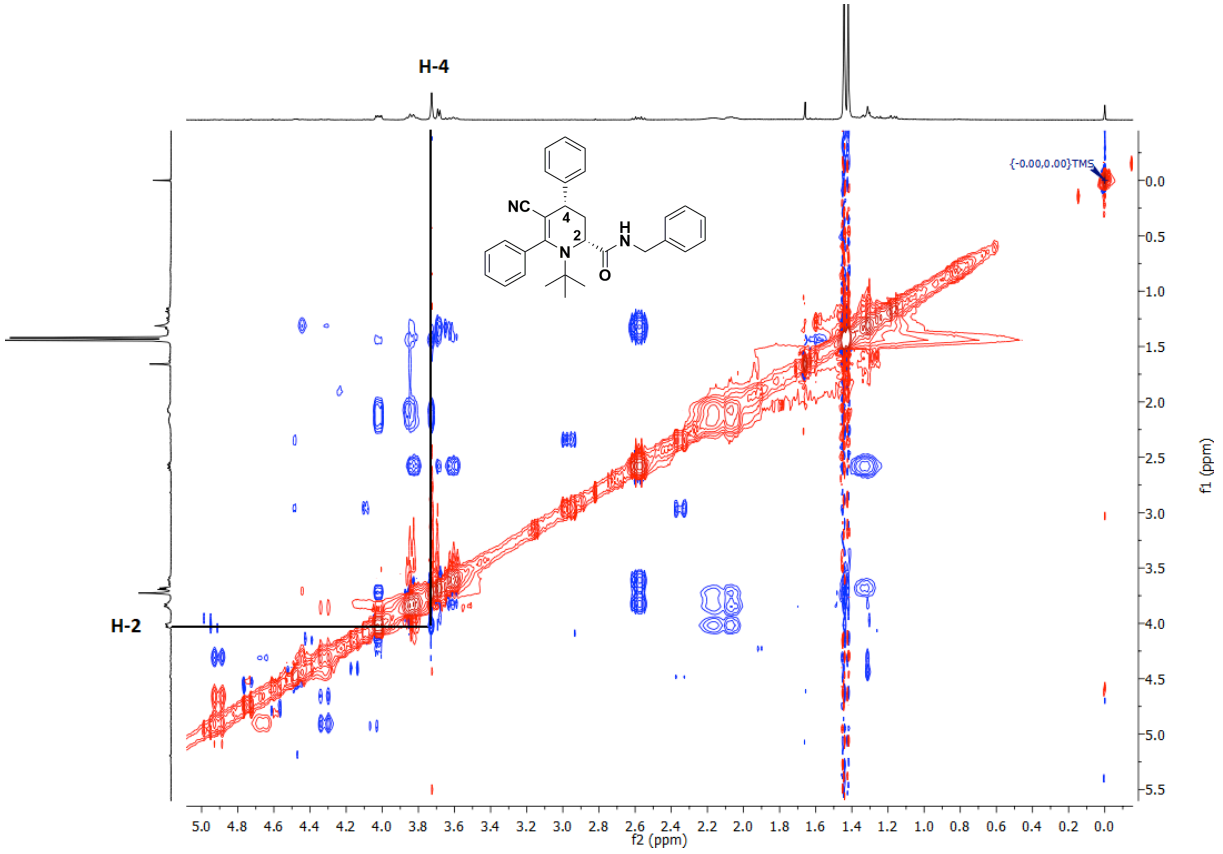


^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5c**

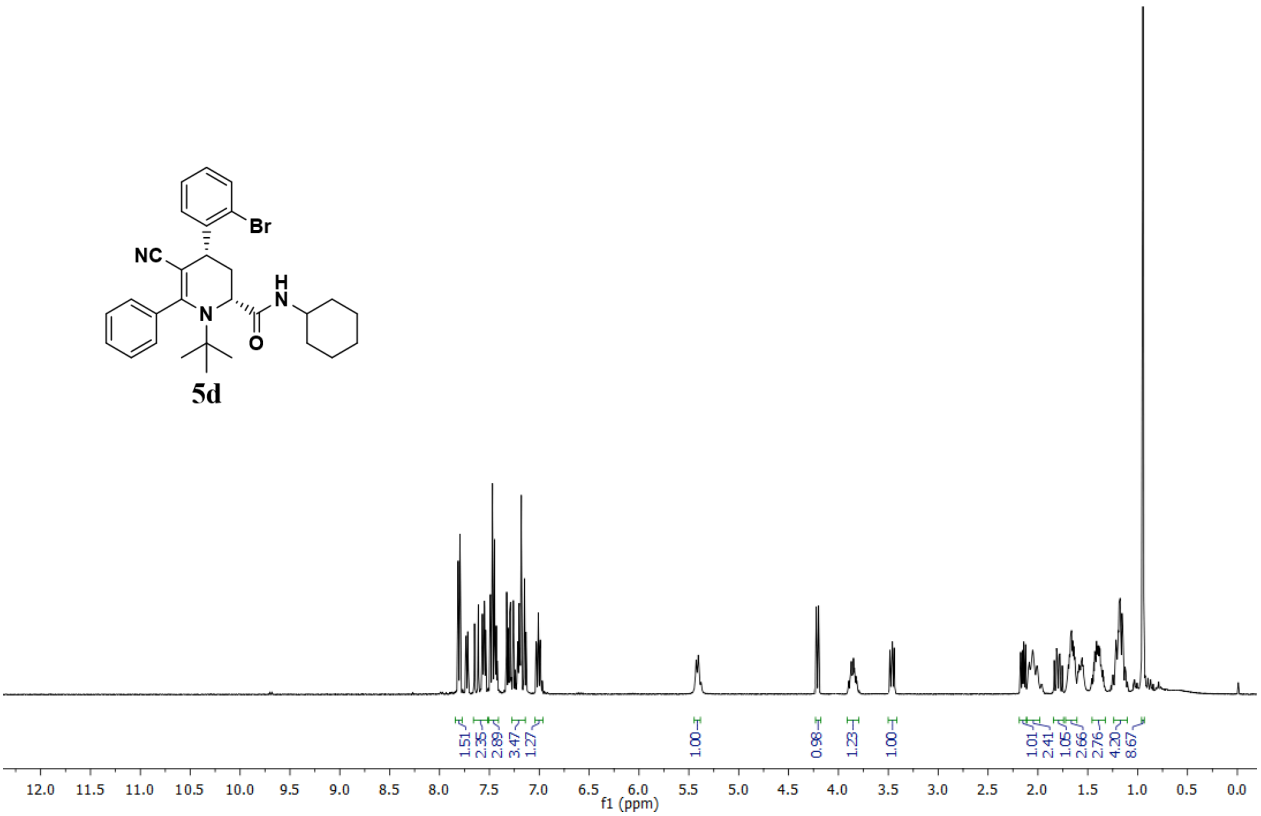


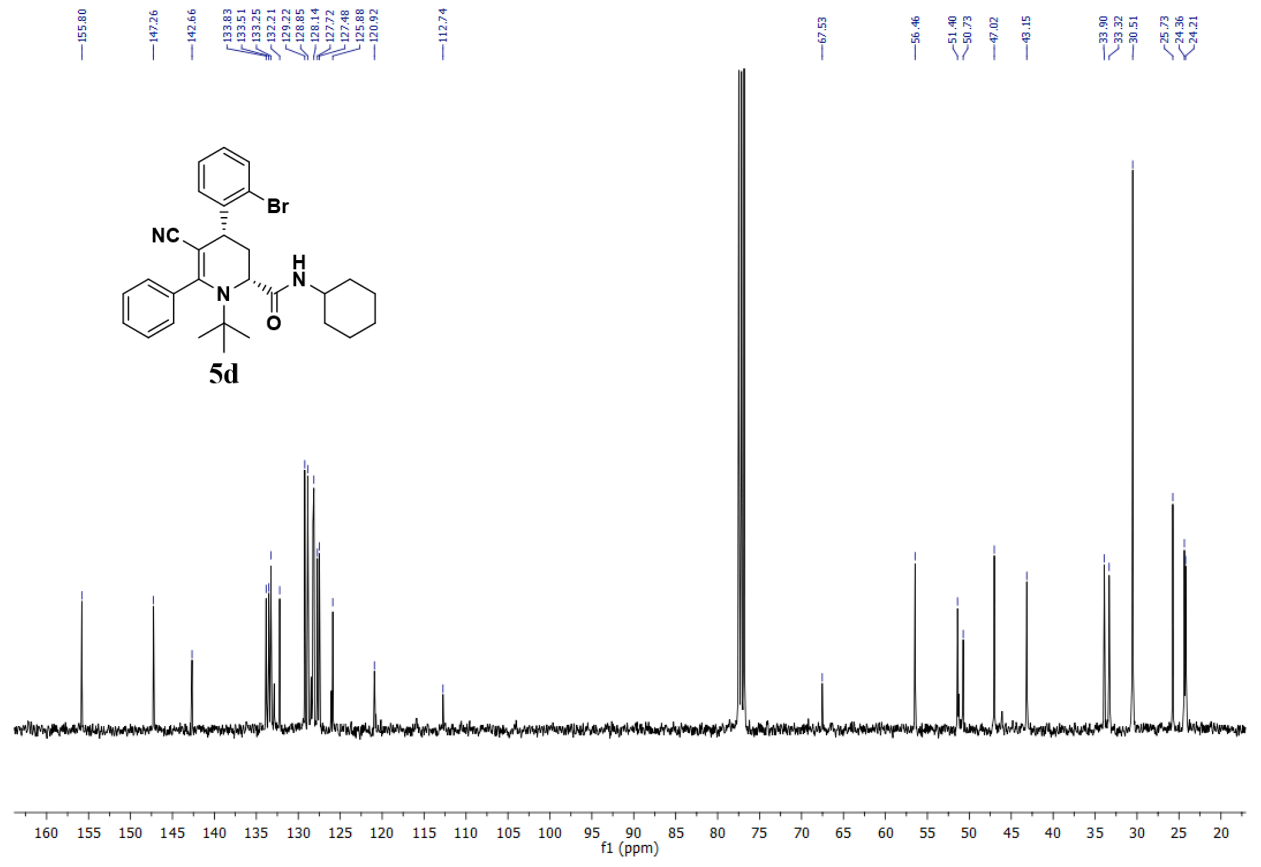


Expanded region of NOESY spectra for compound **5c**

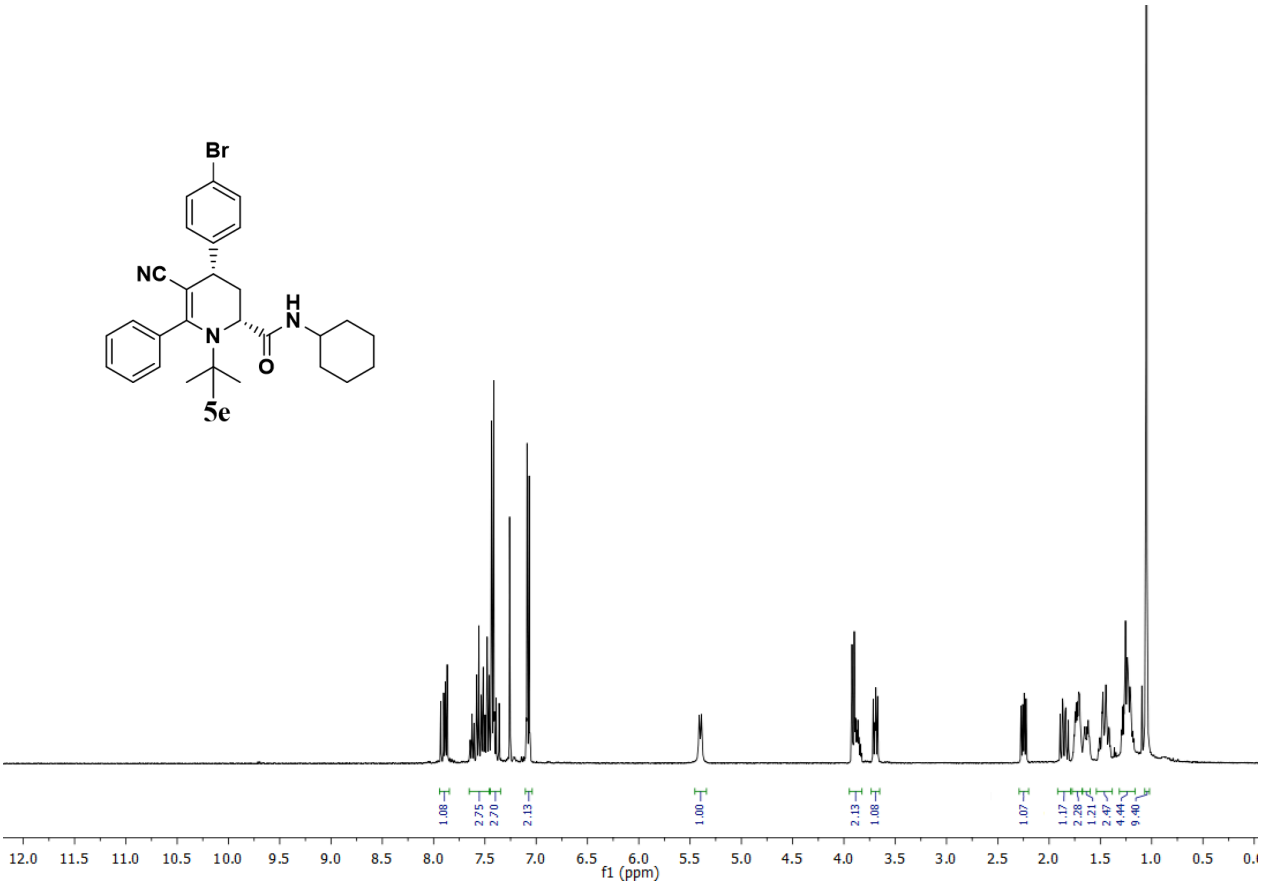


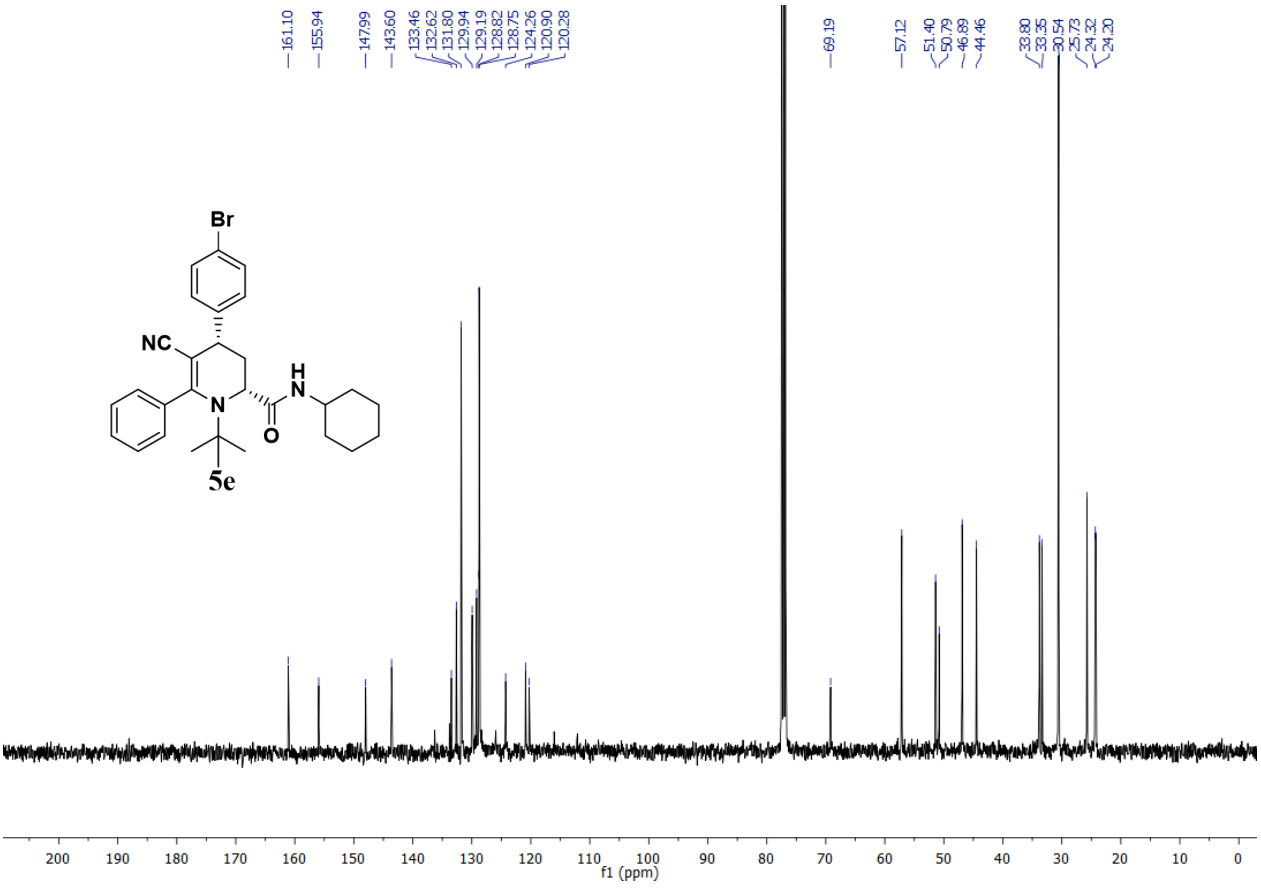
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5d**



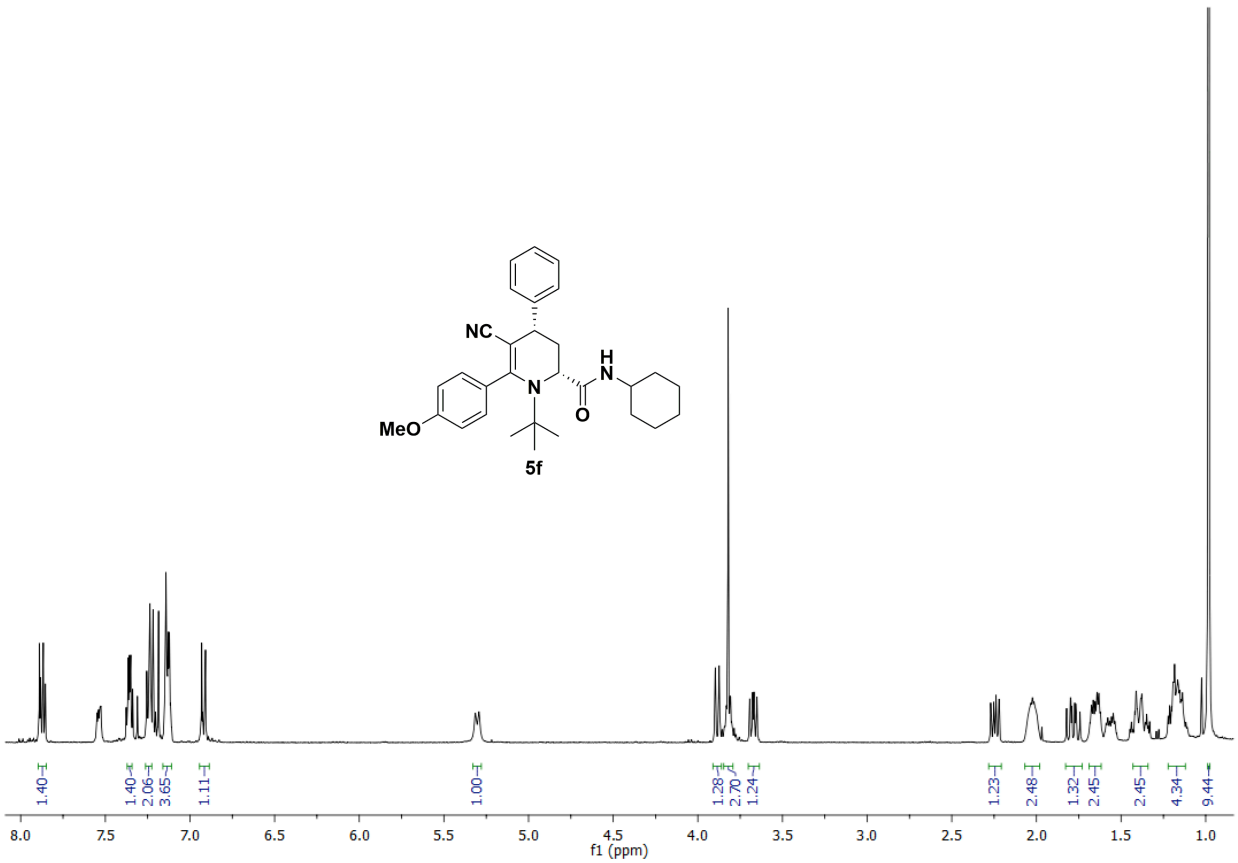


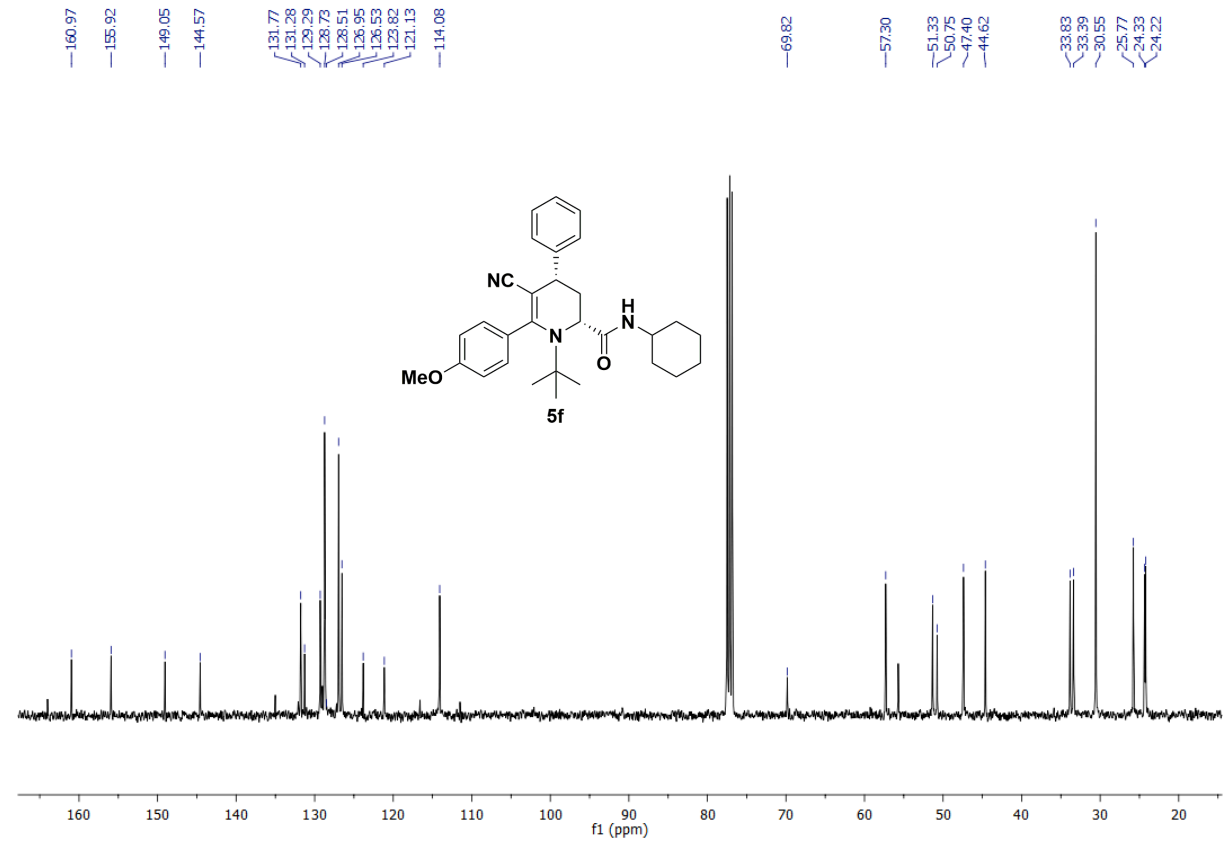
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5e**



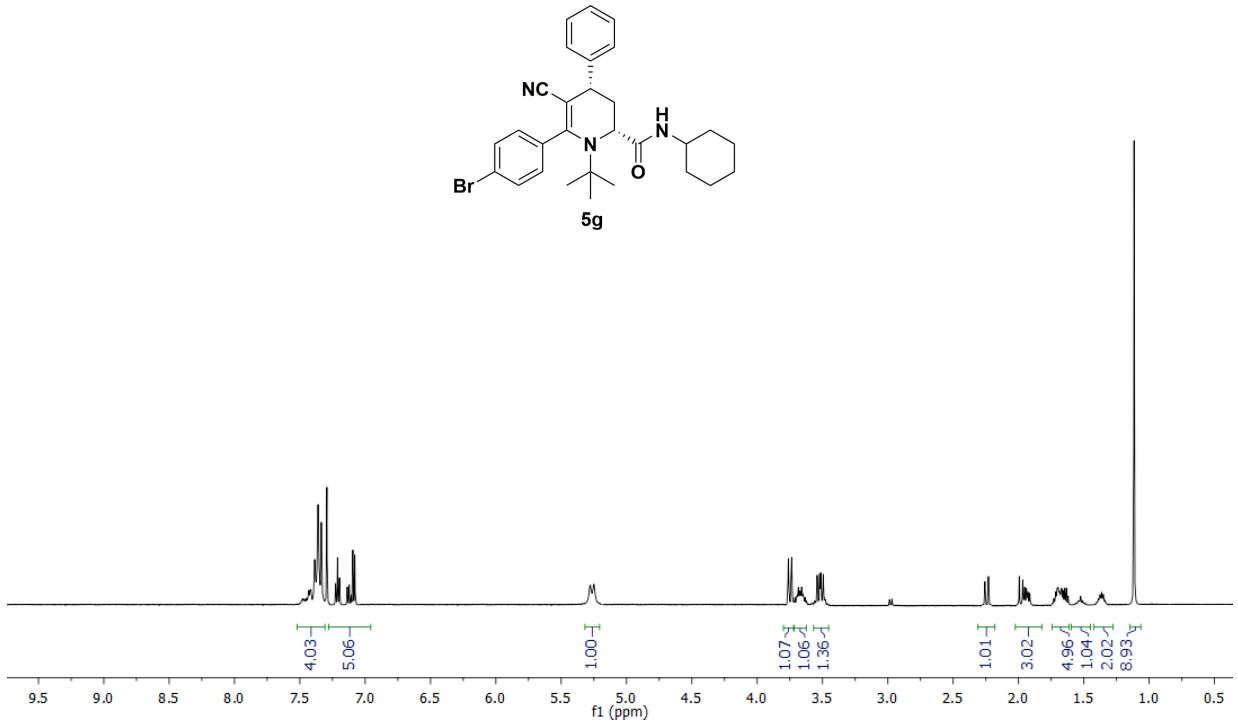


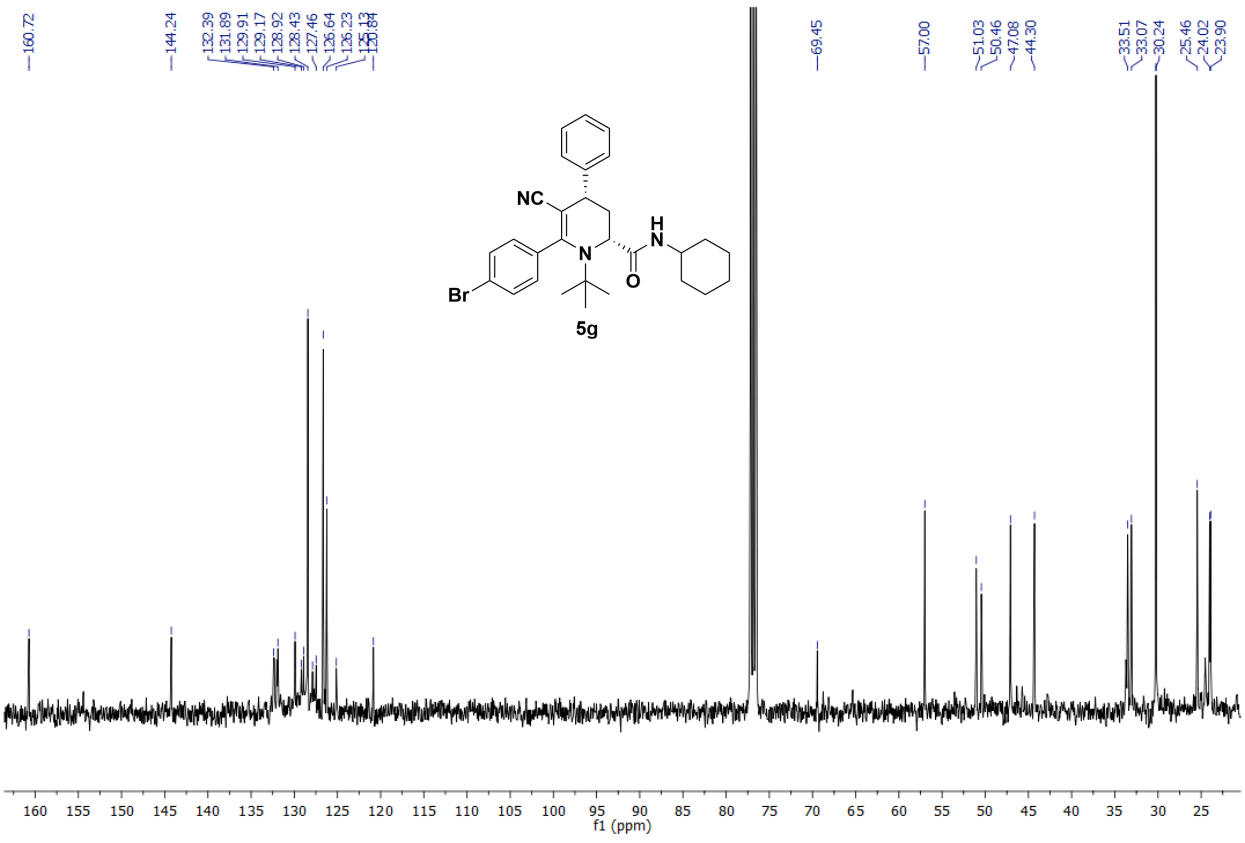
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5f**



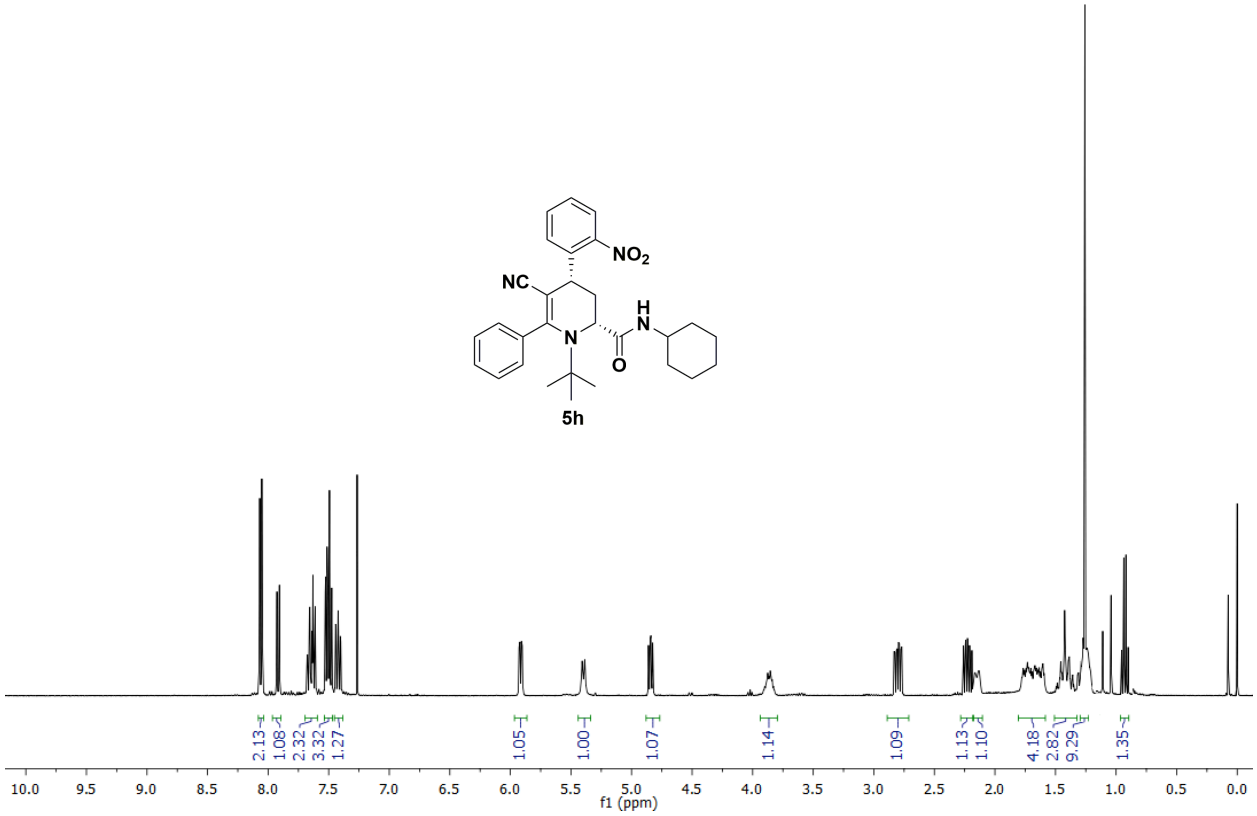


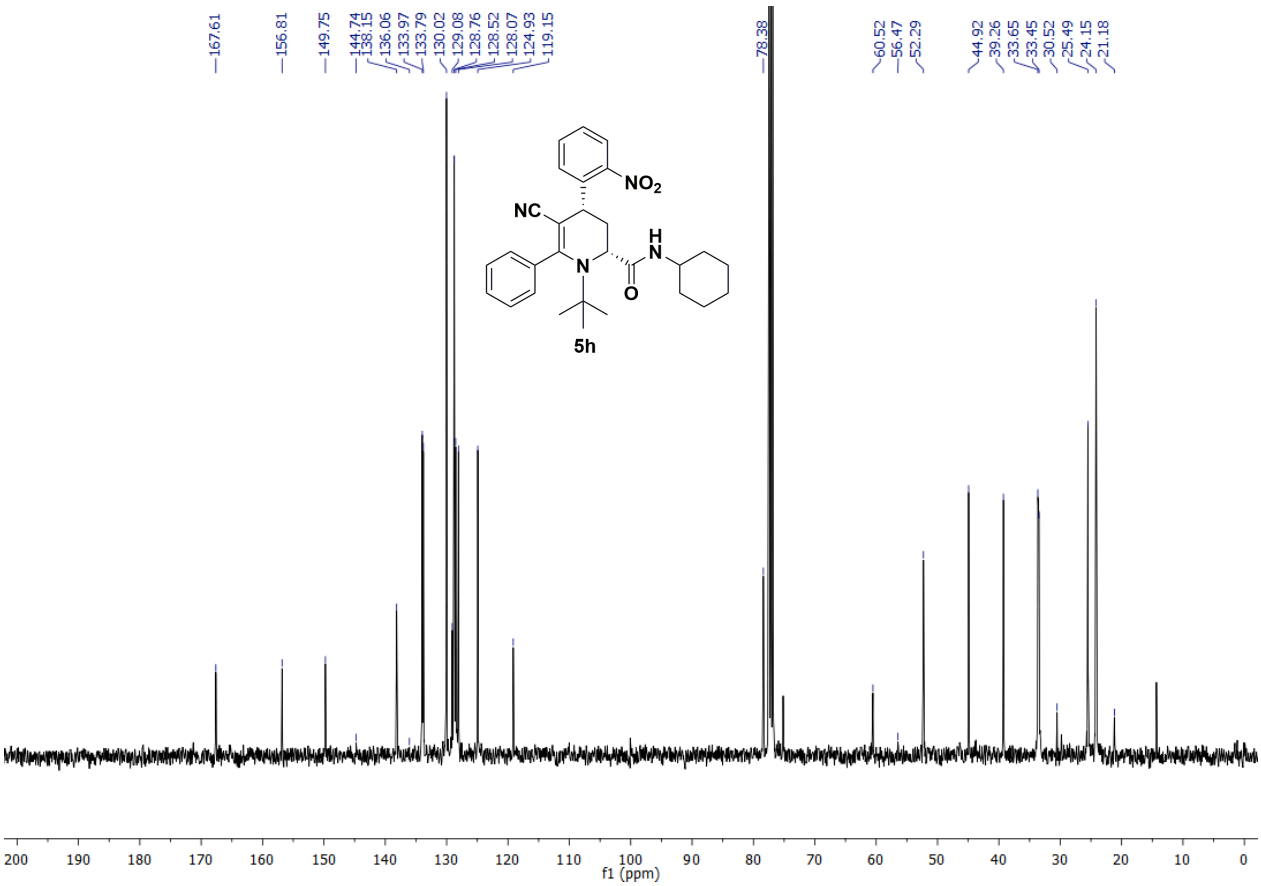
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5g**



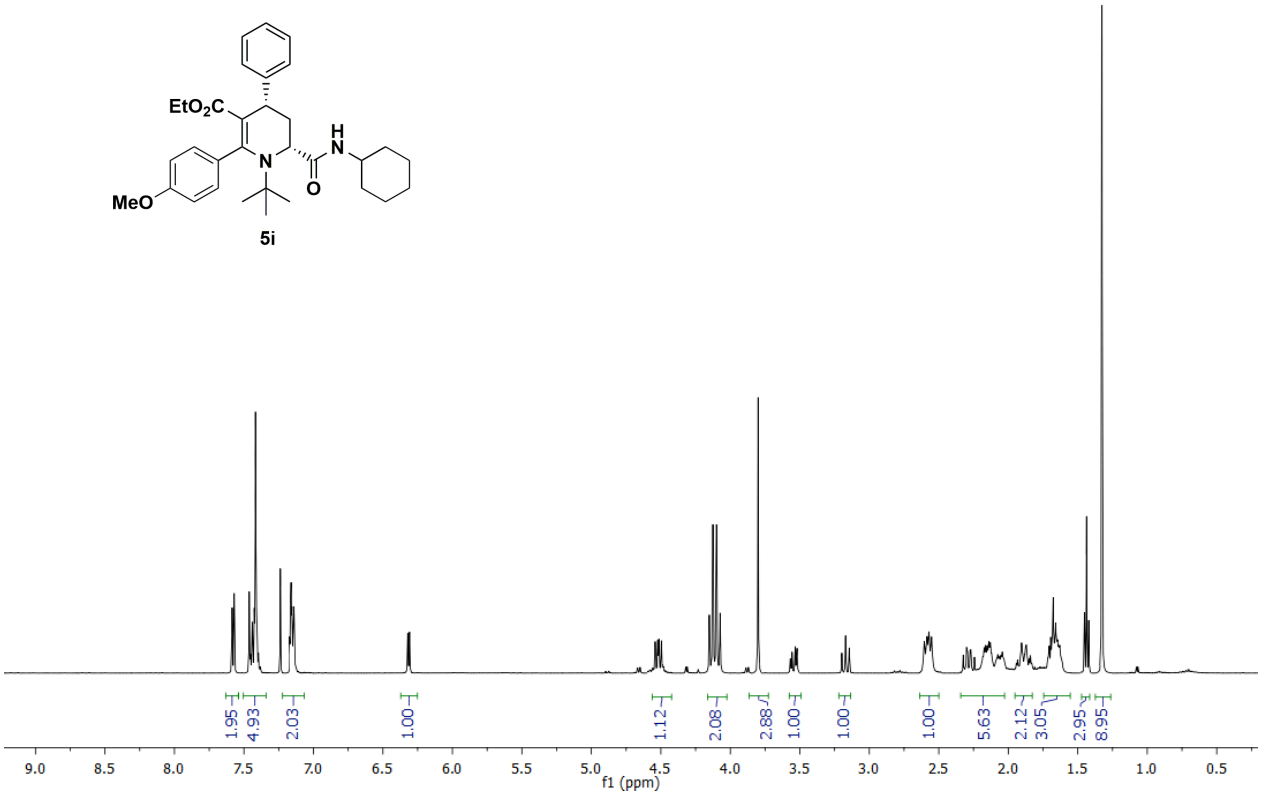


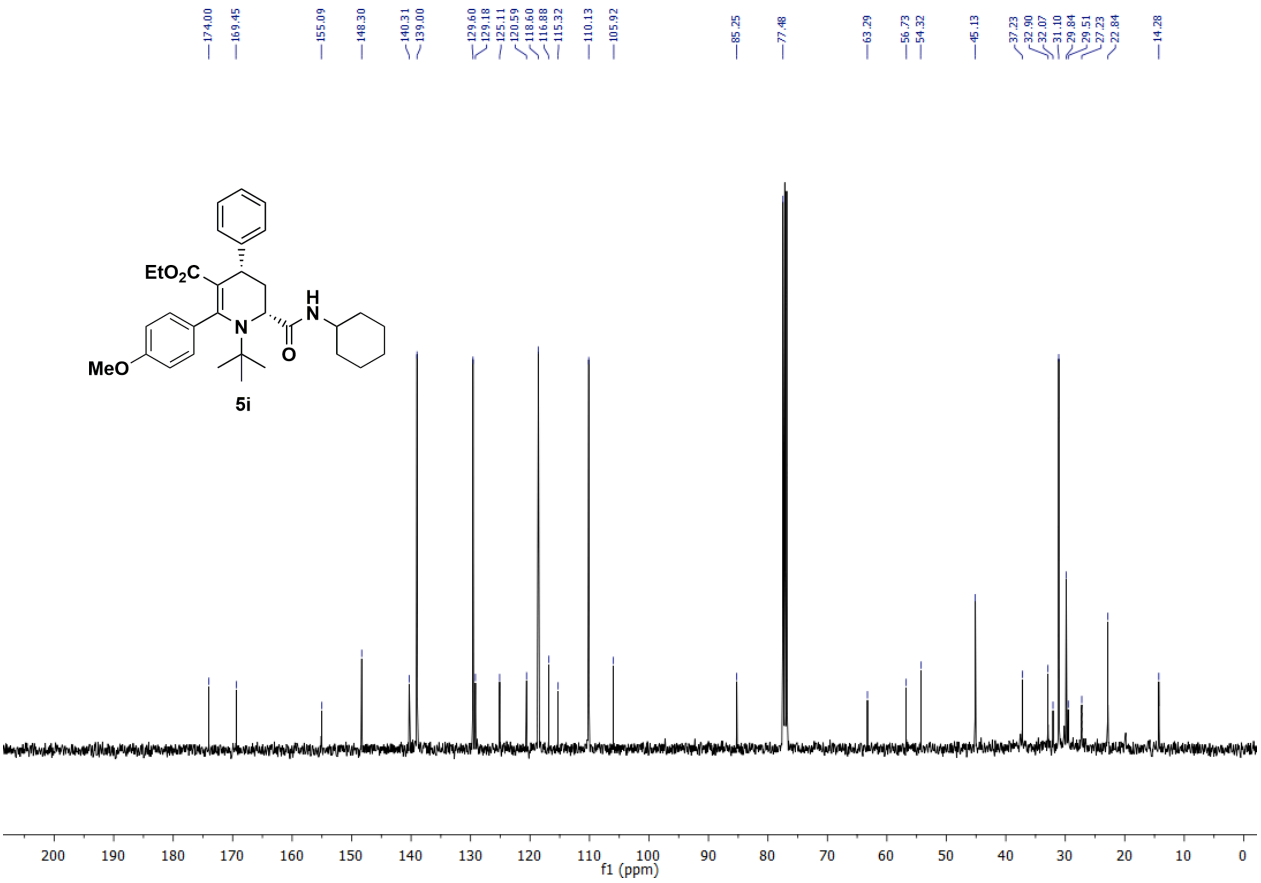
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5h**



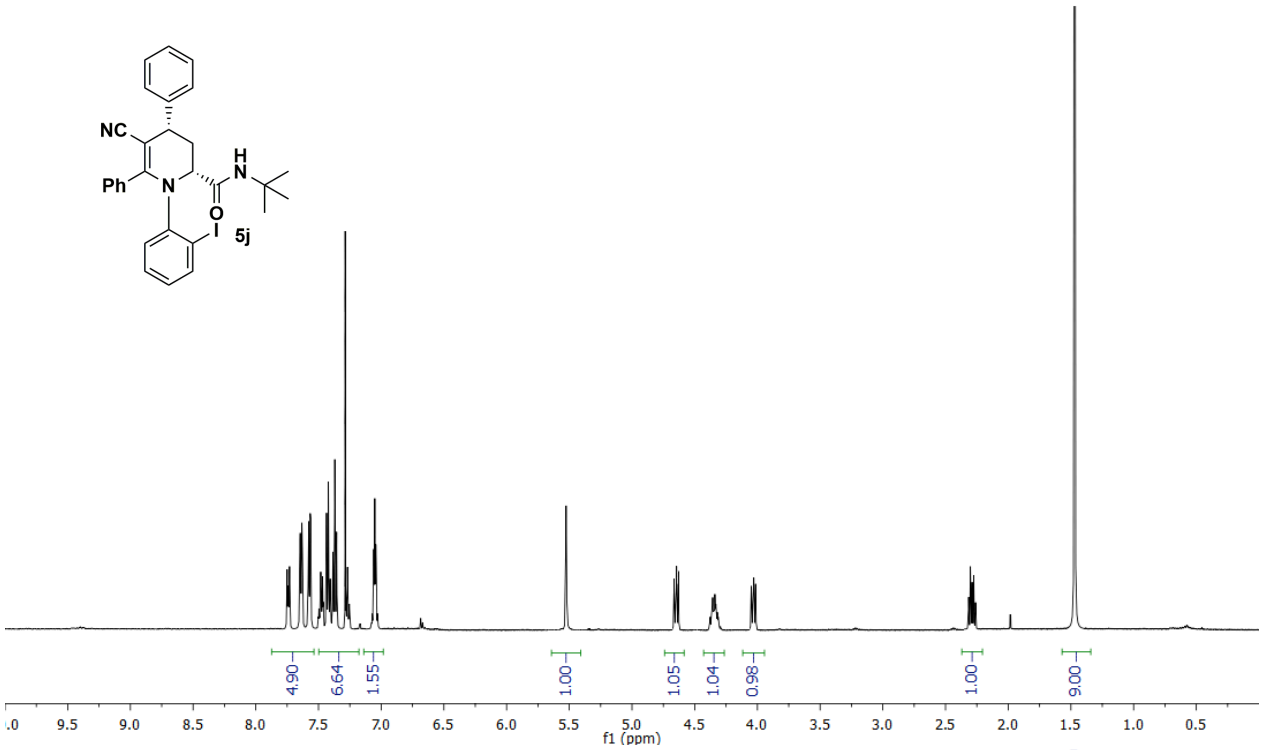


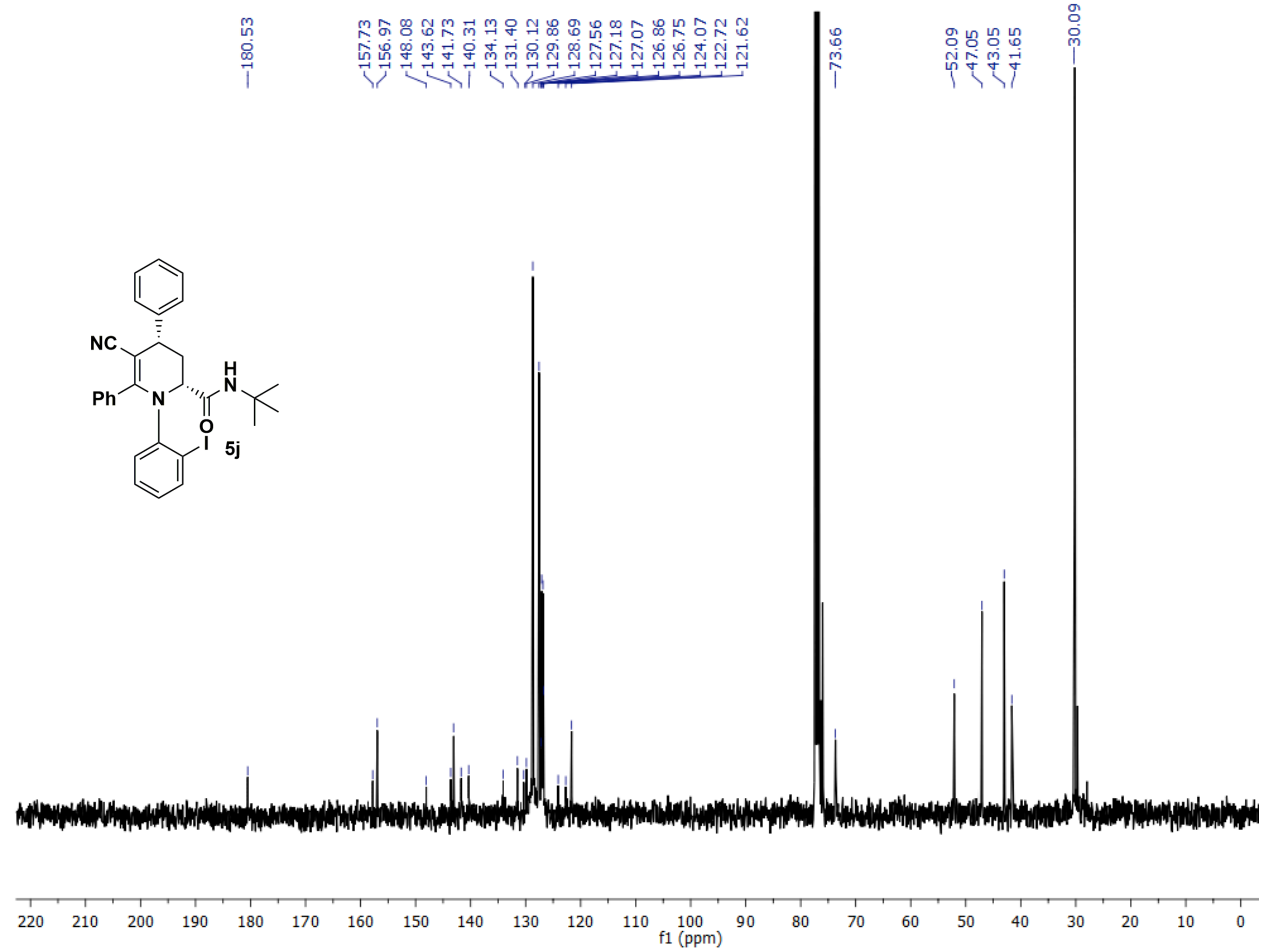
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5i**



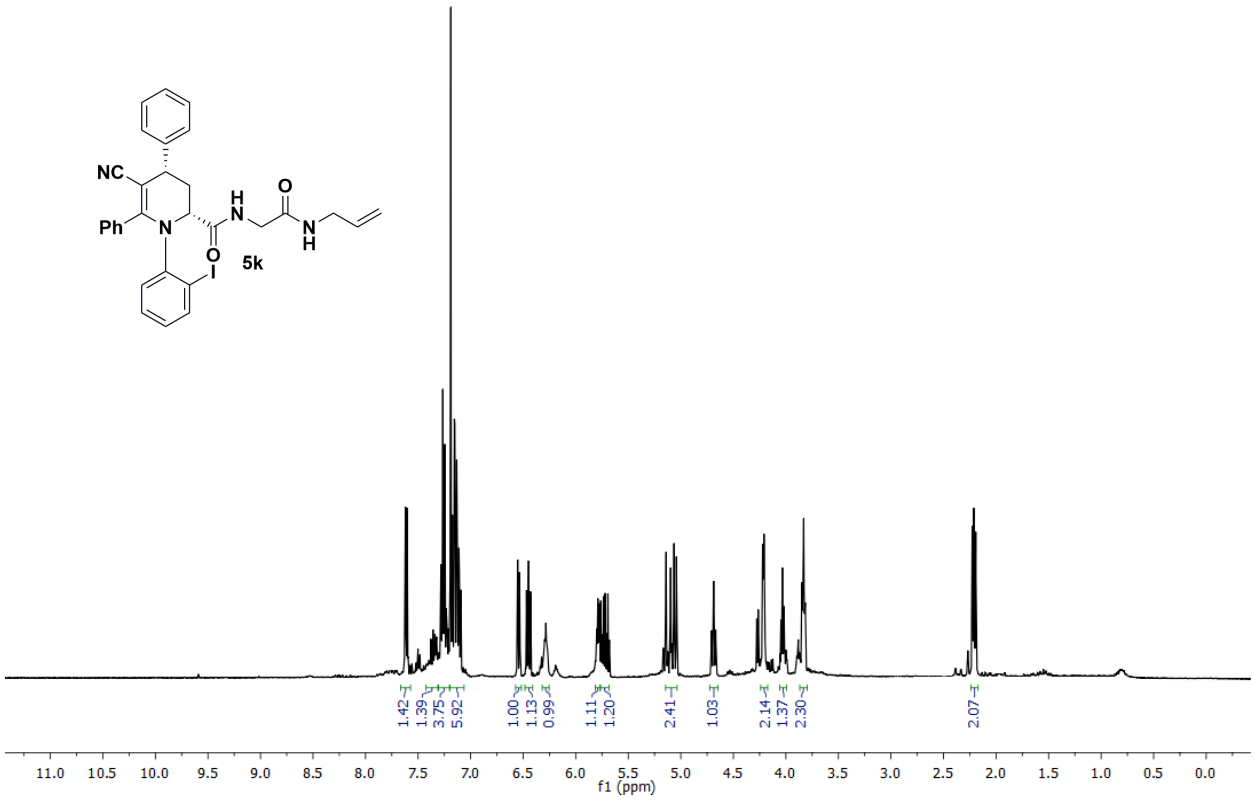


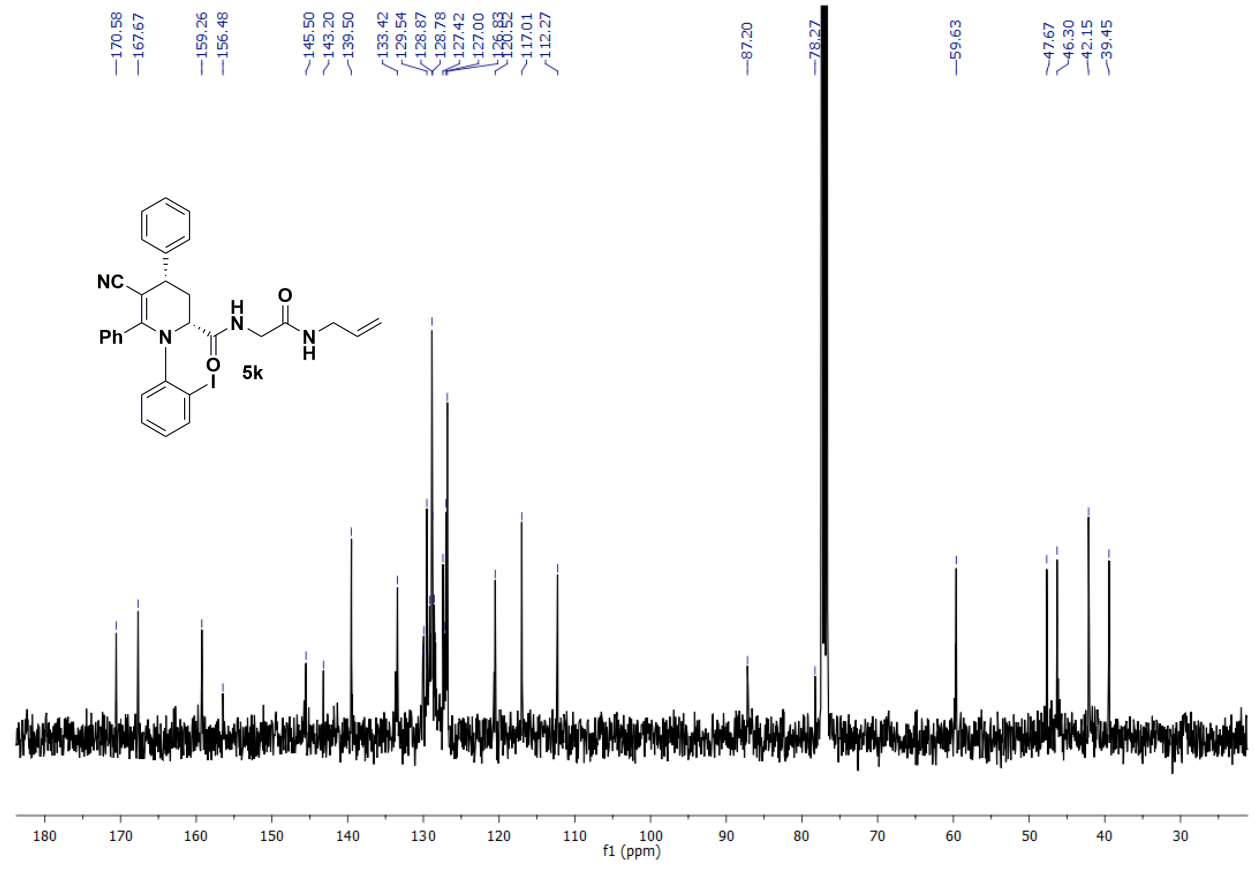
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5j**



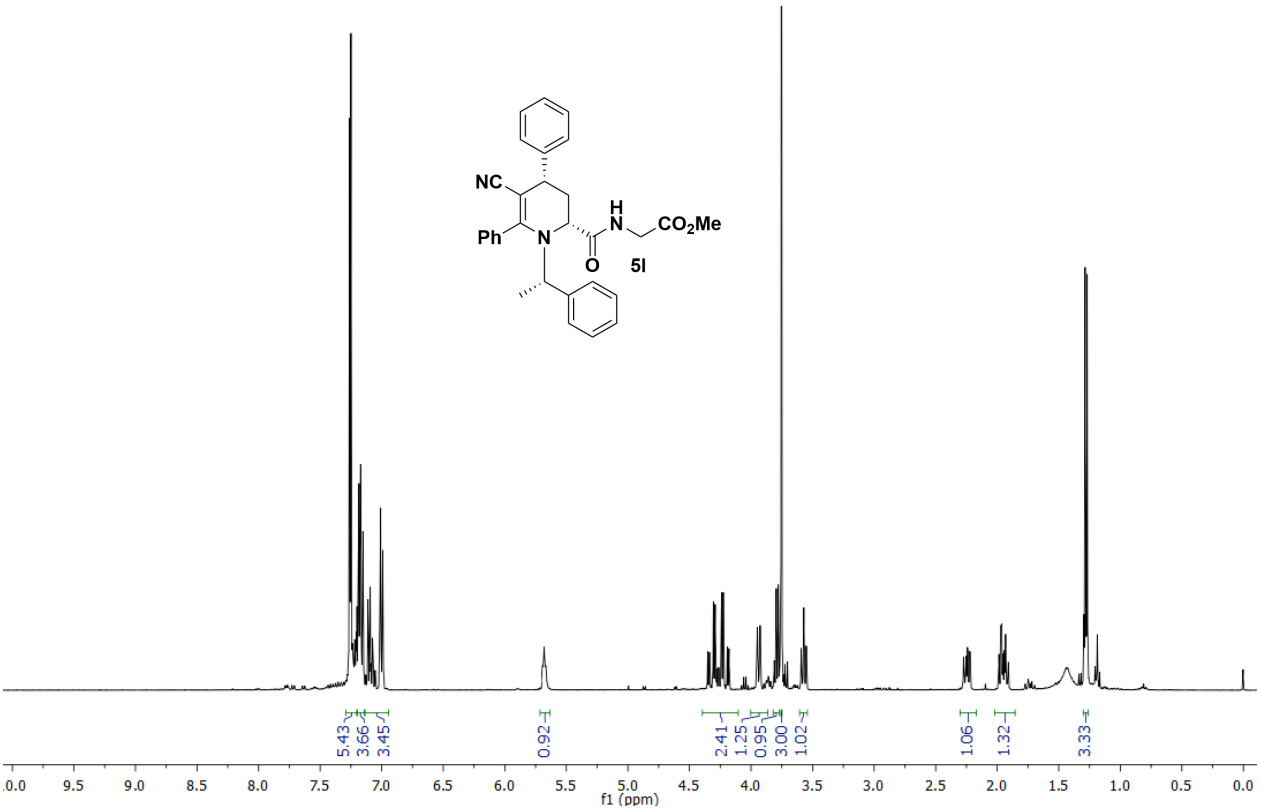


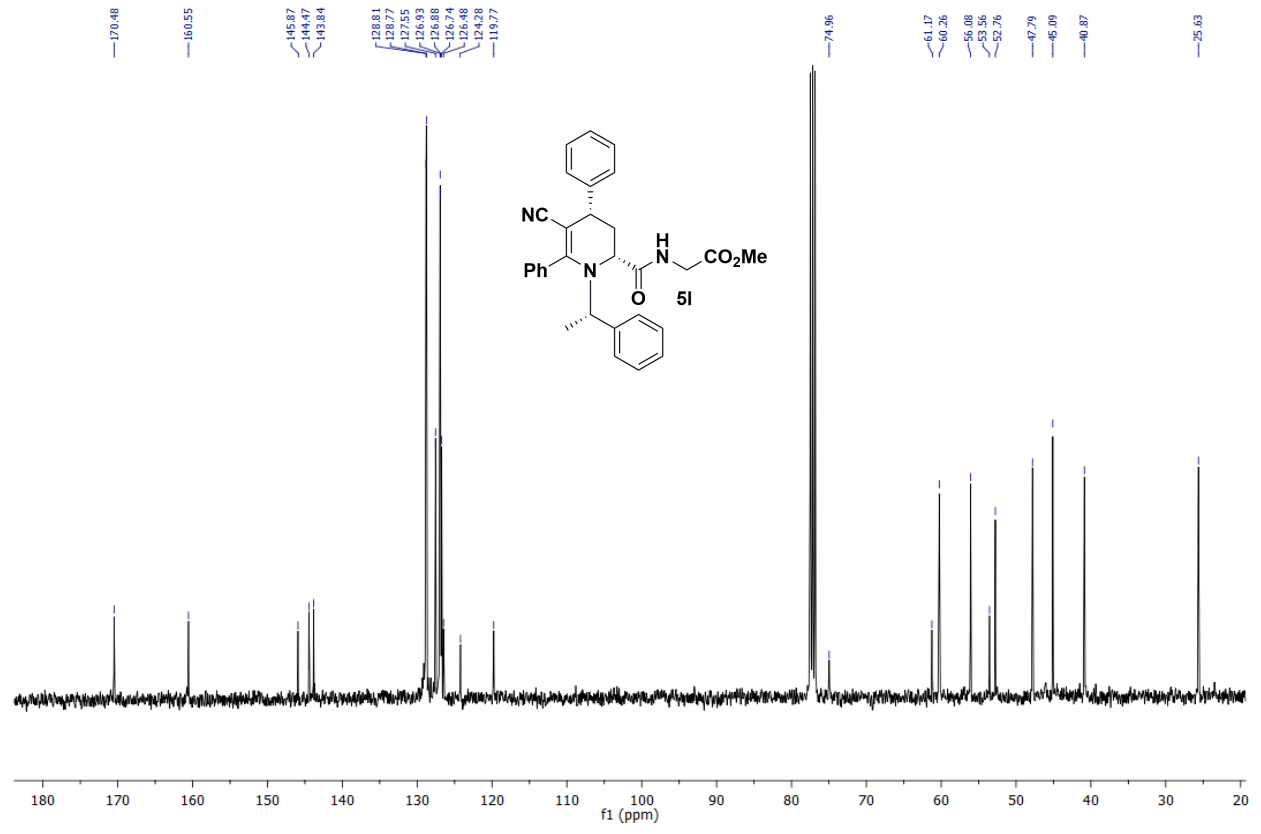
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5k**



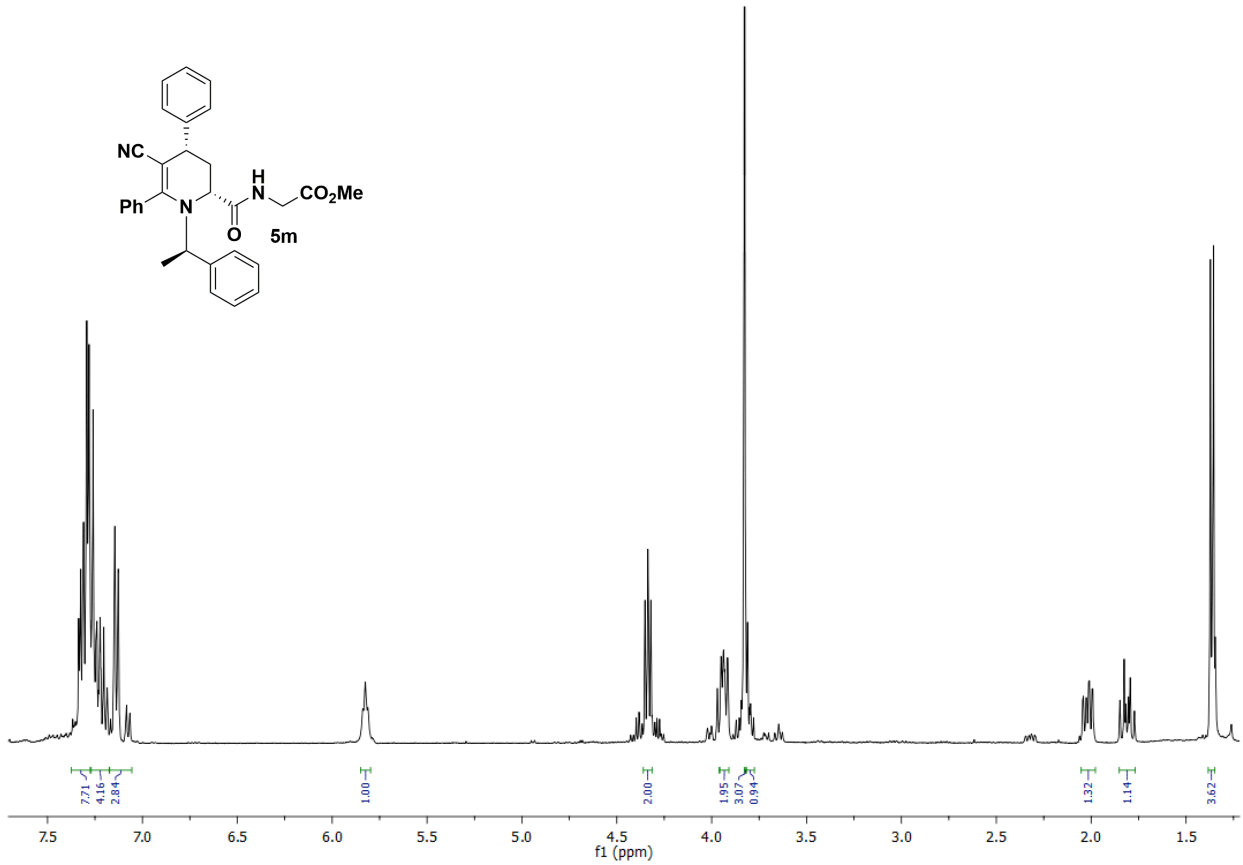


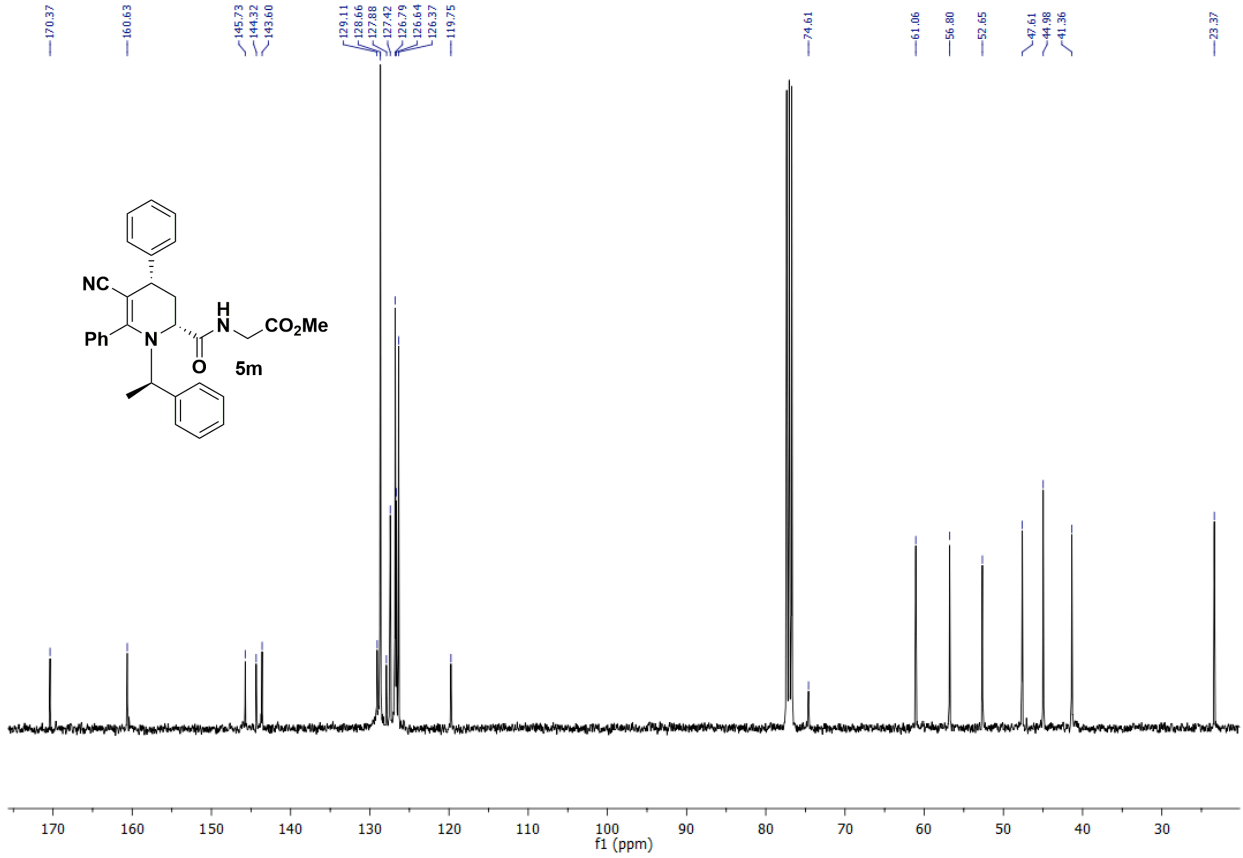
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5l**



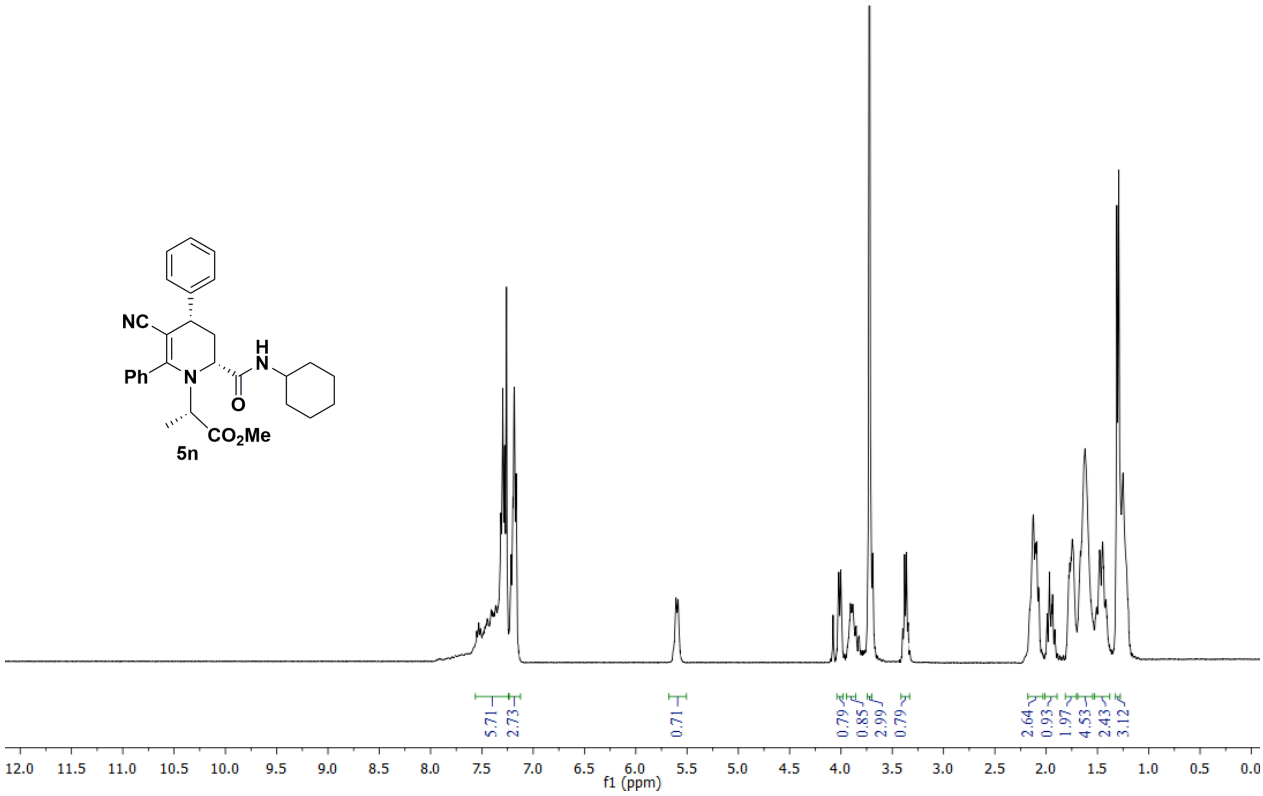


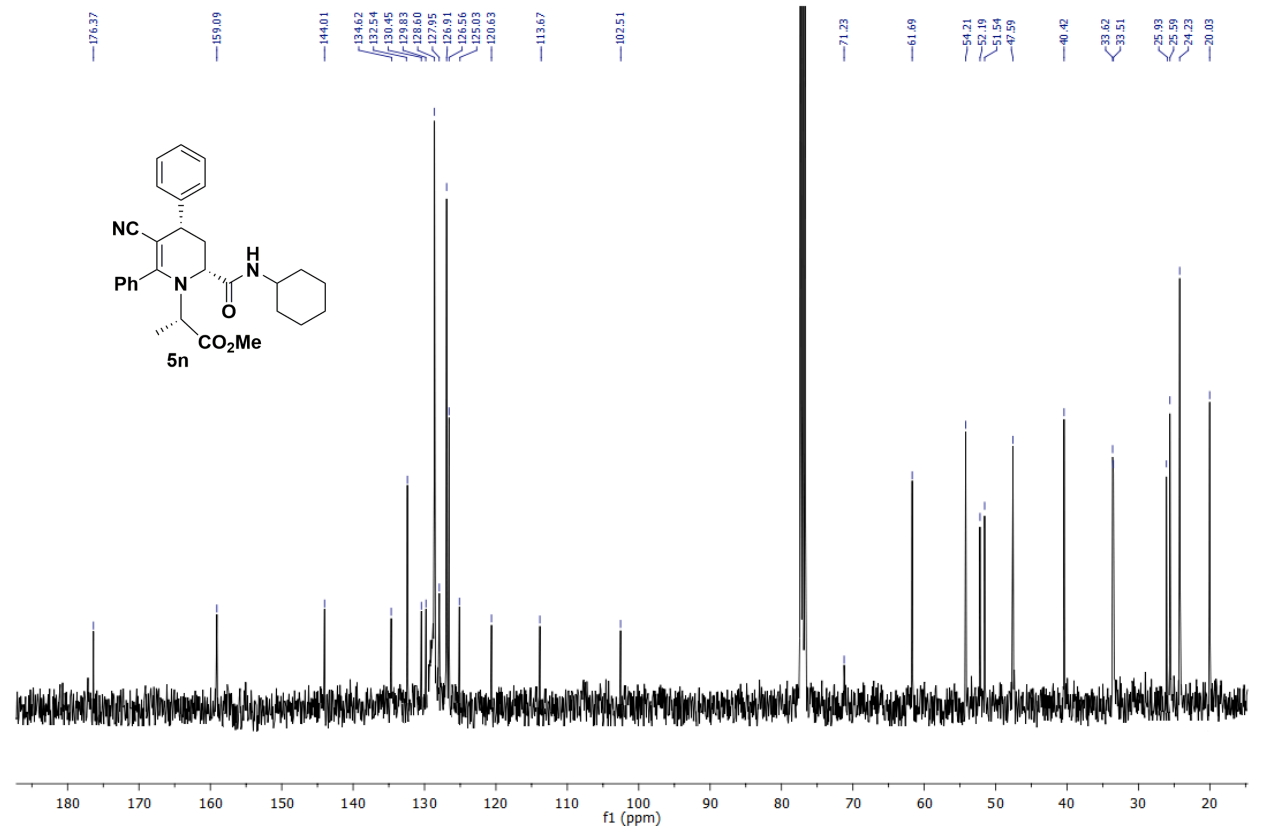
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5m**



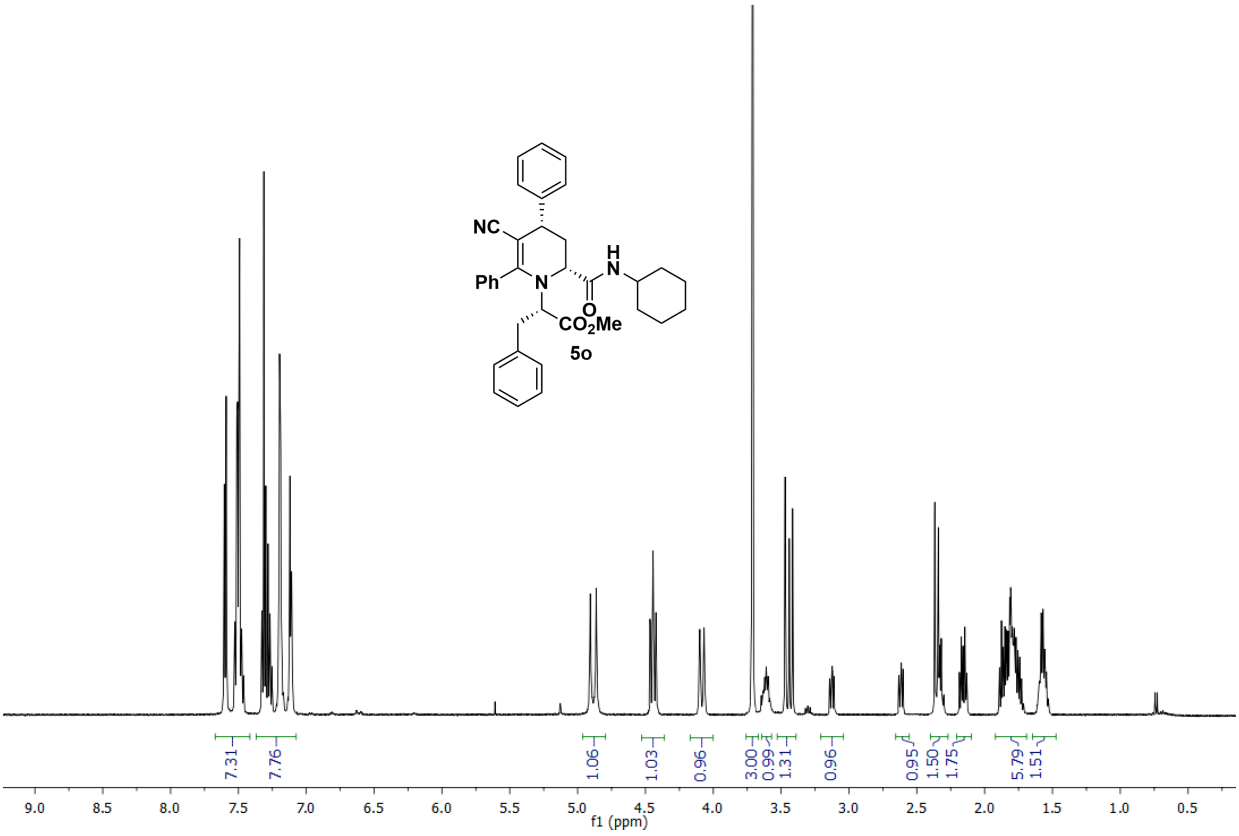


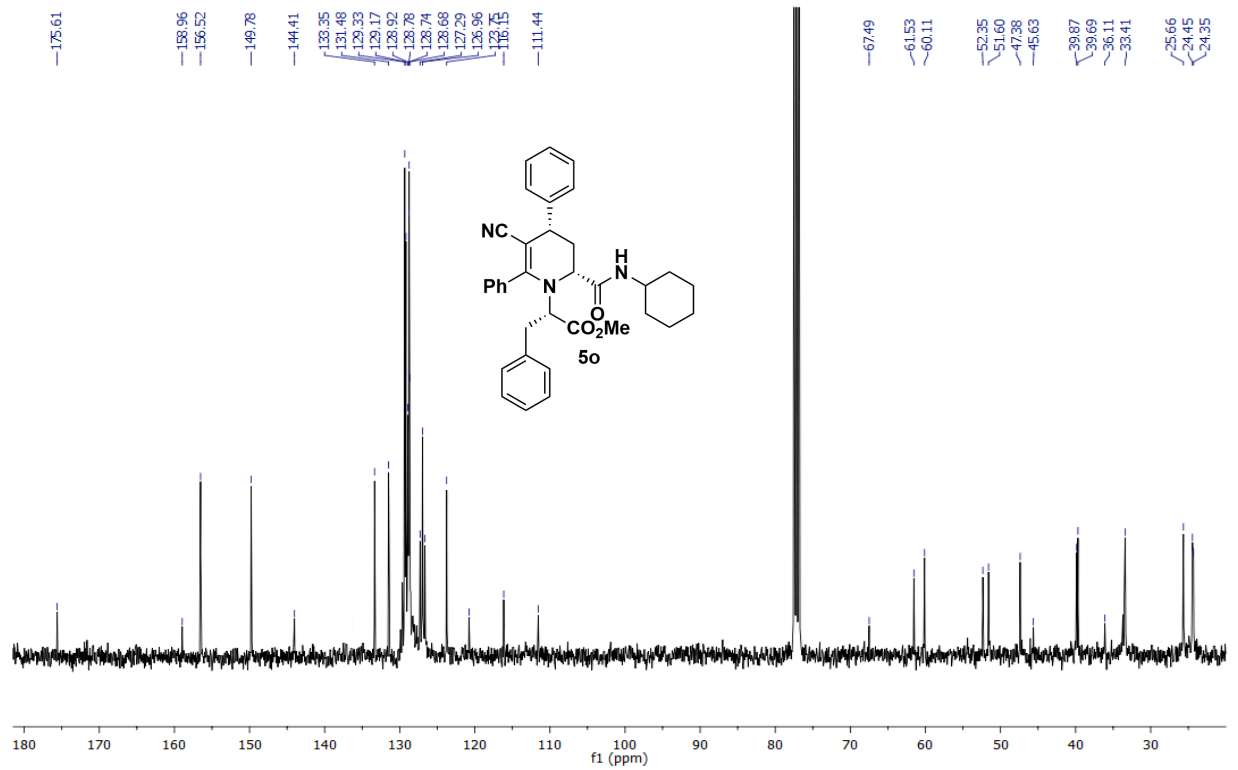
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5n**



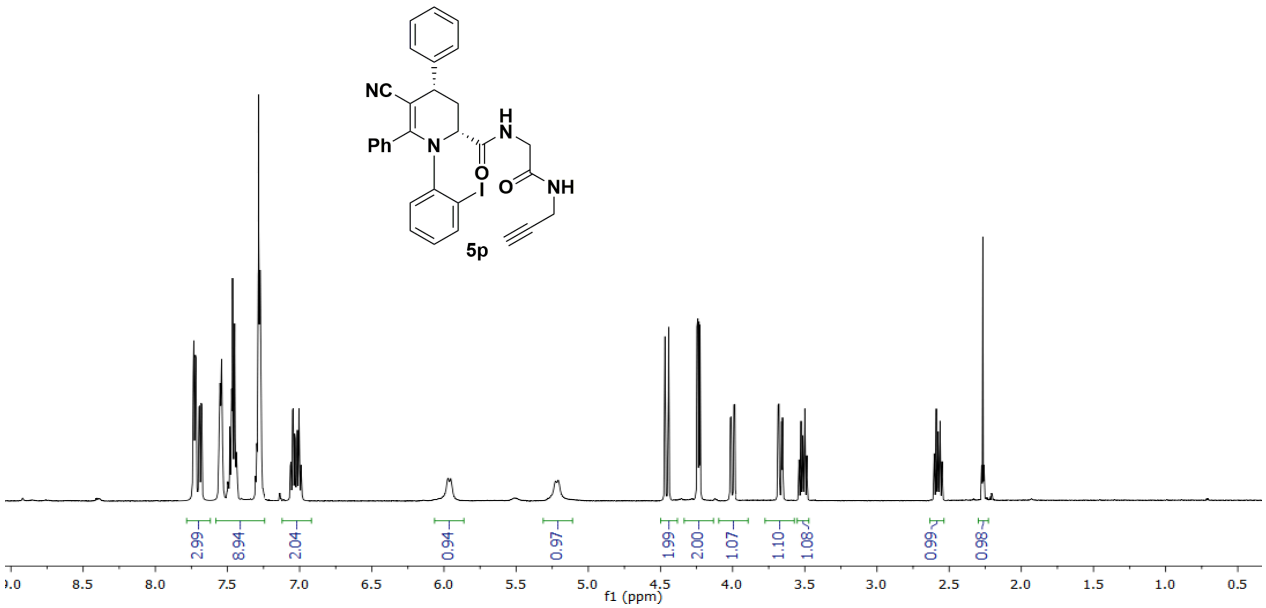


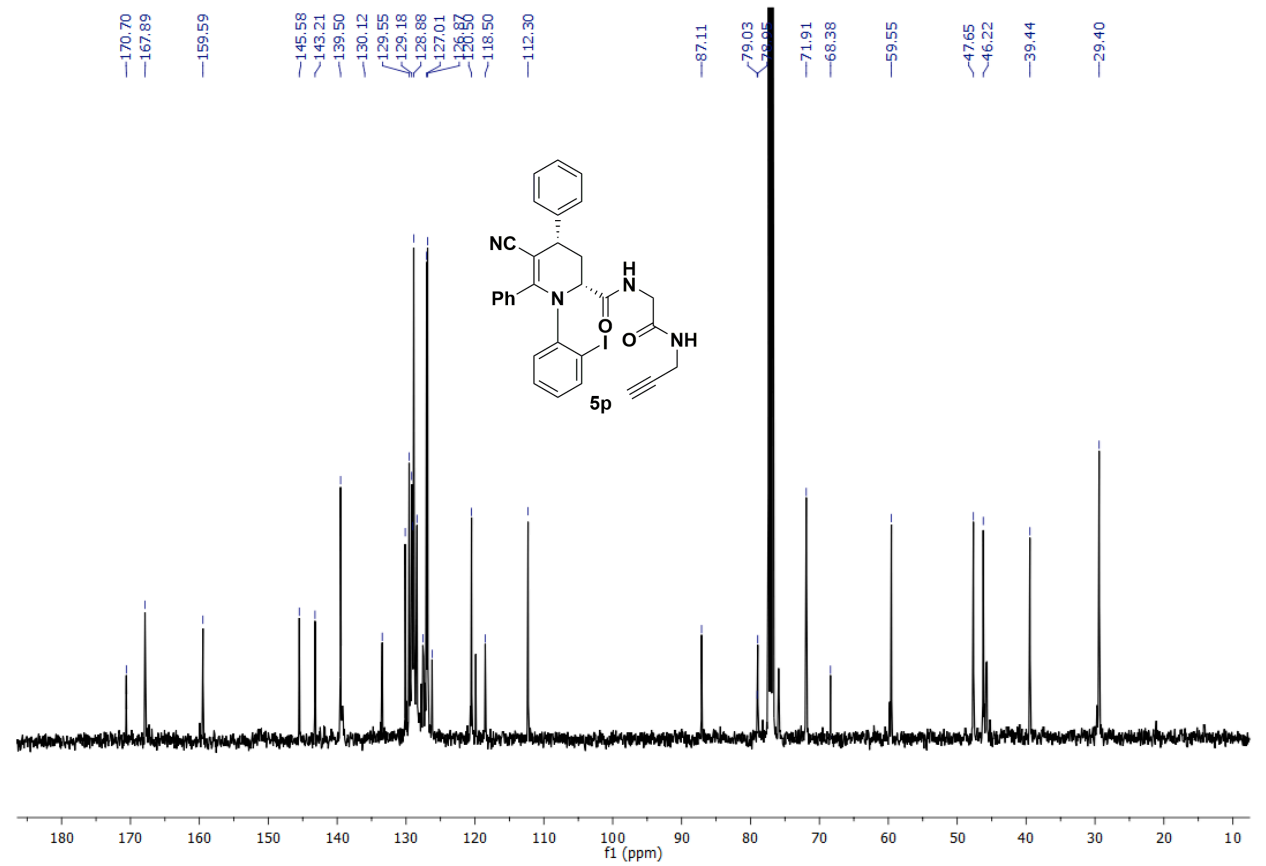
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5o**



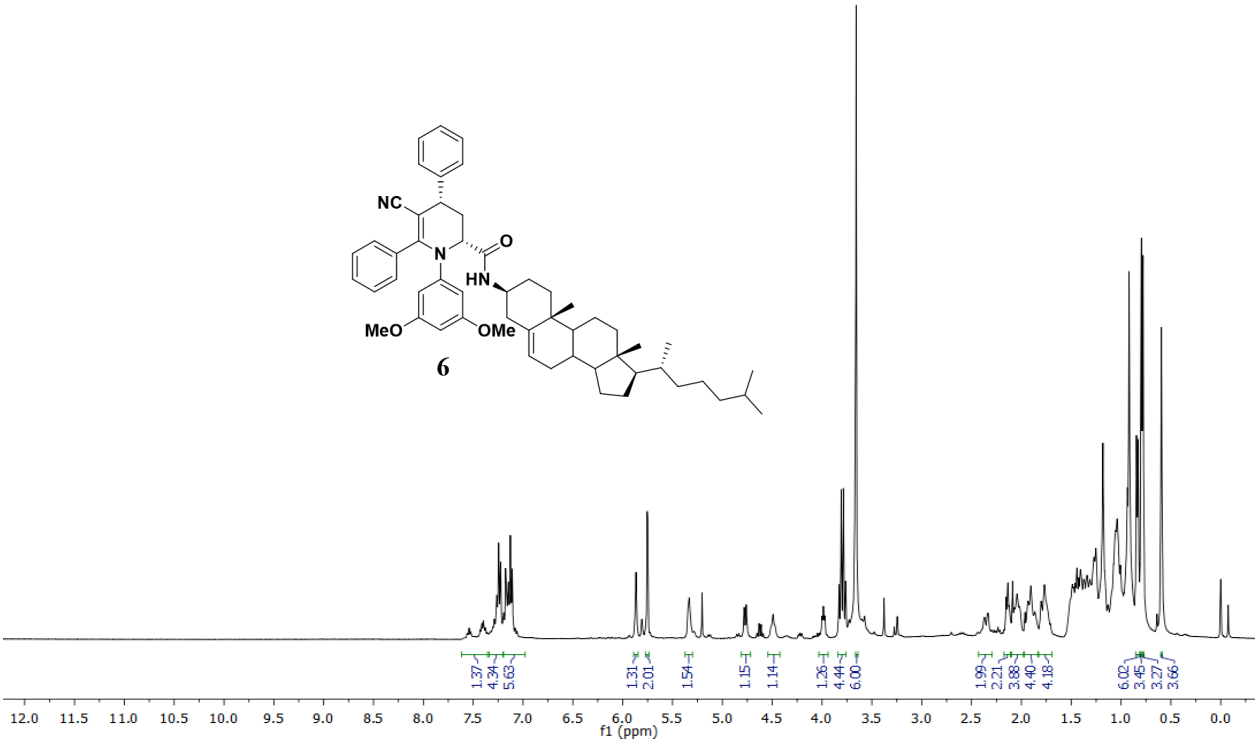


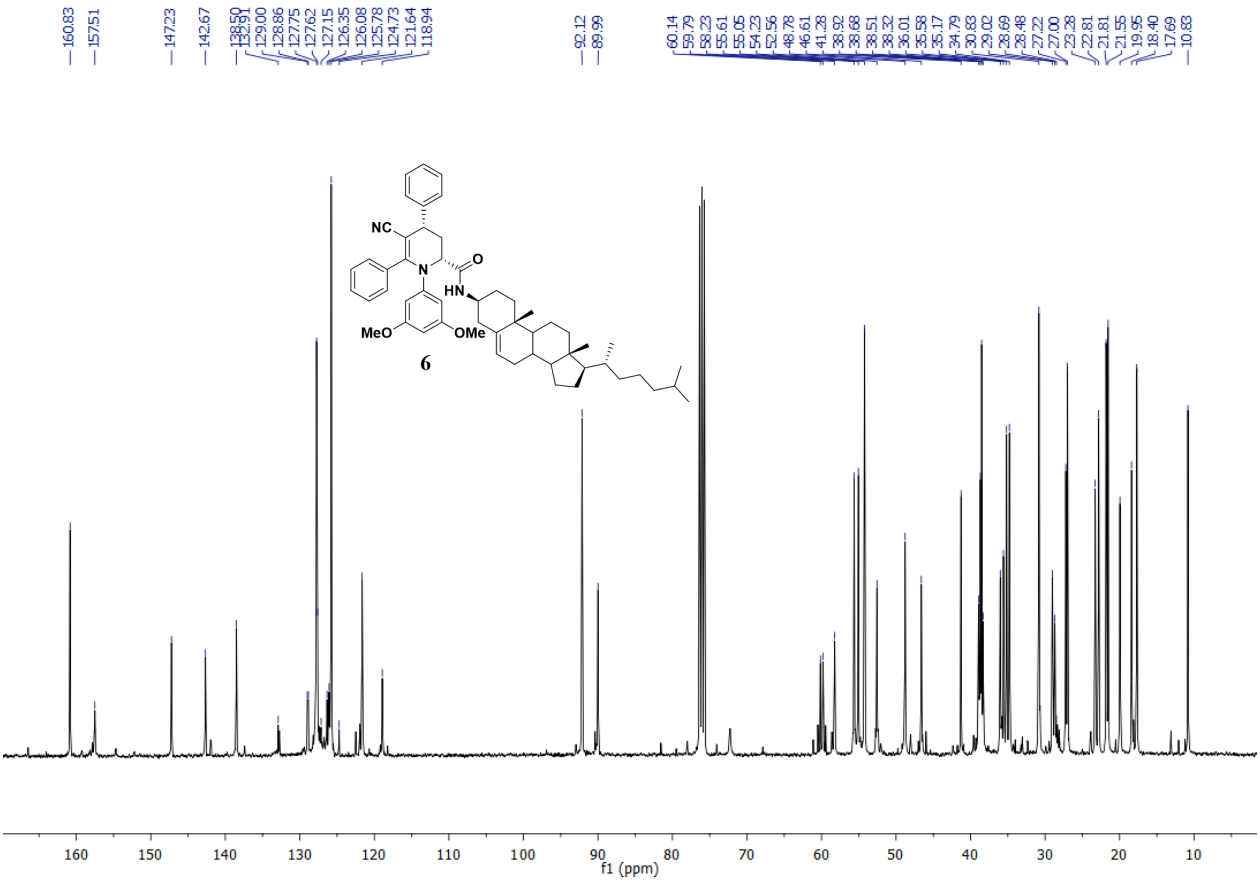
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **5p**



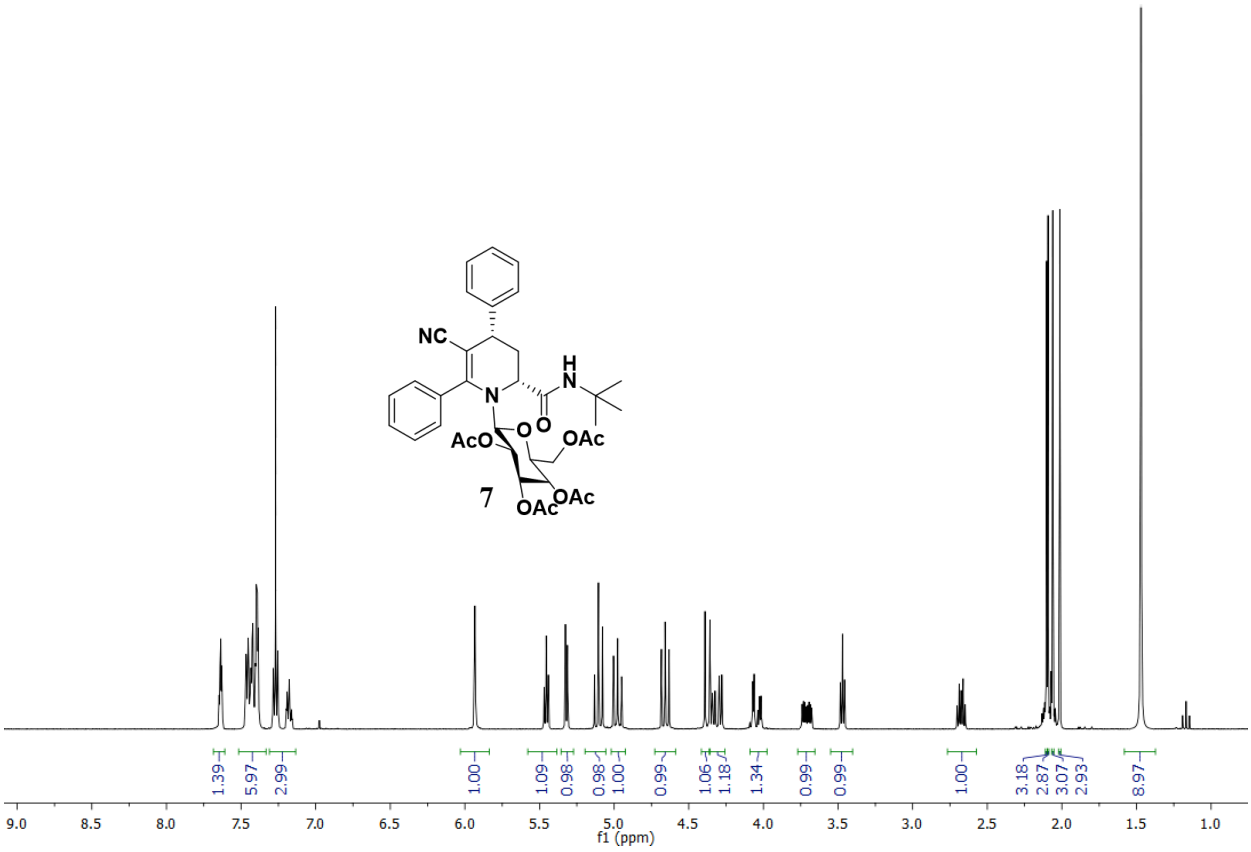


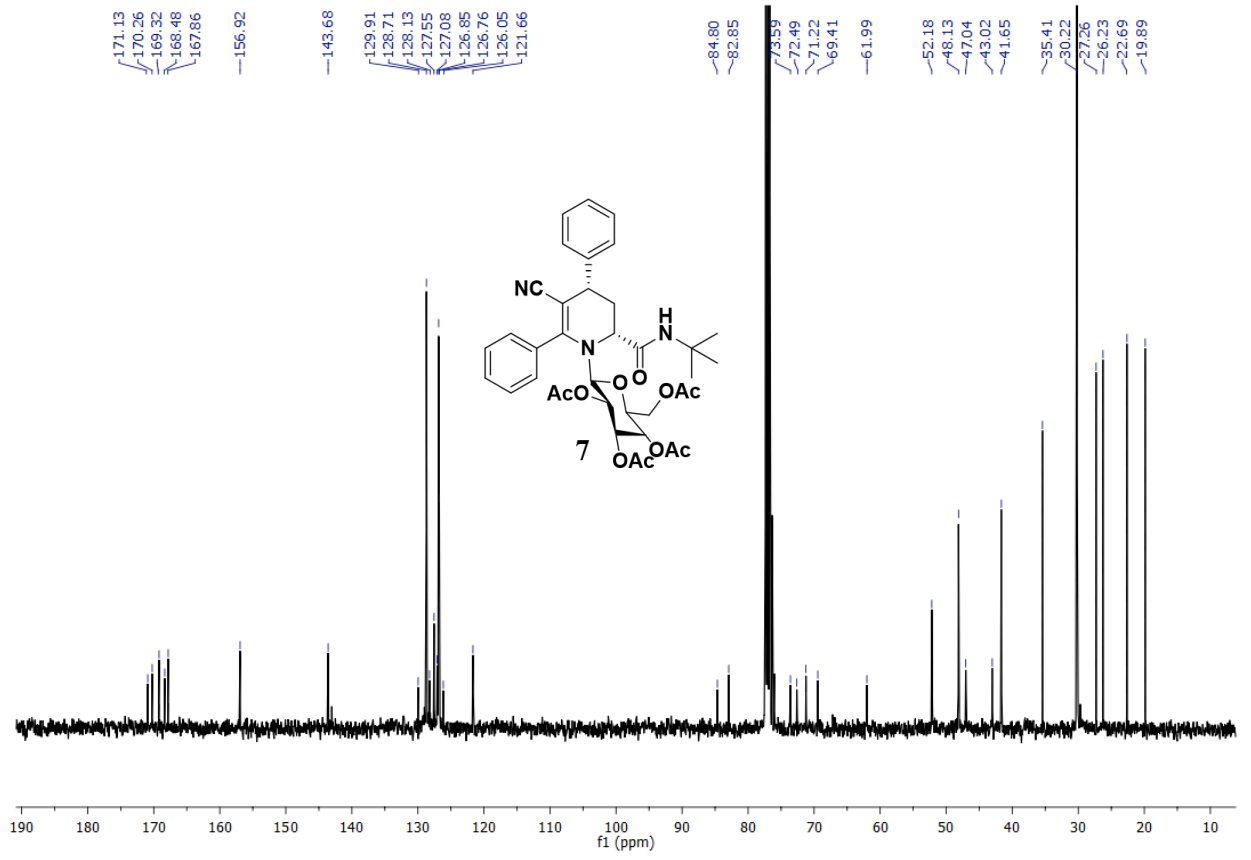
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **6**



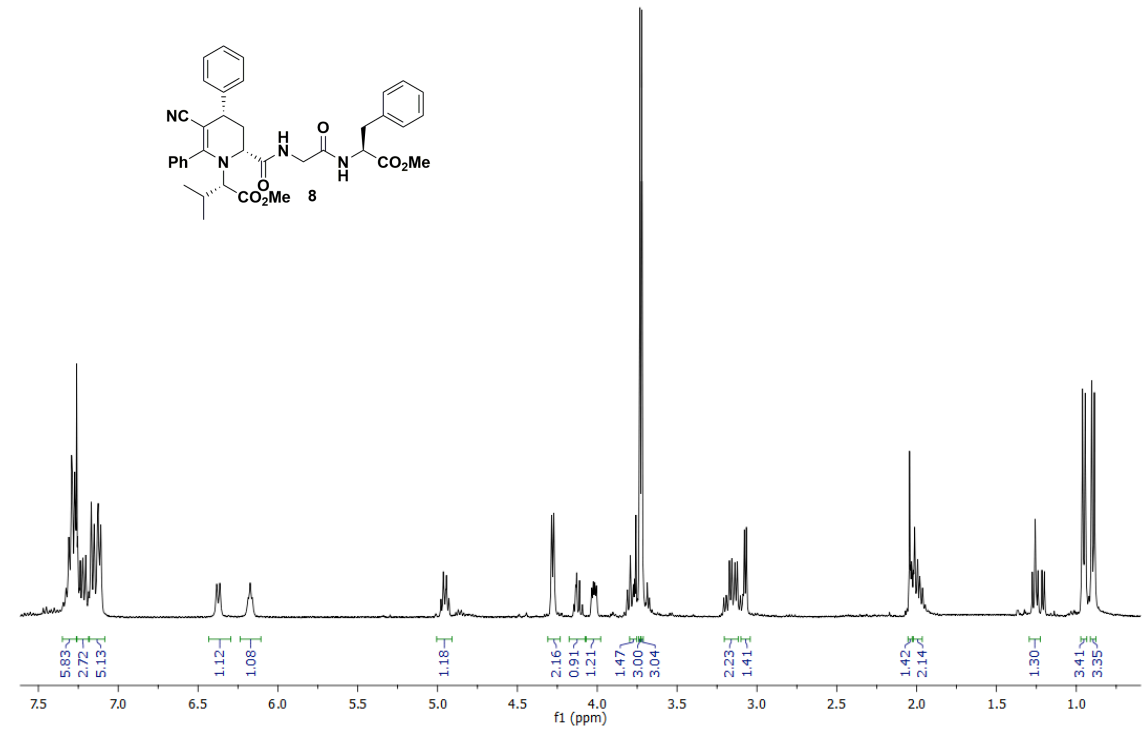


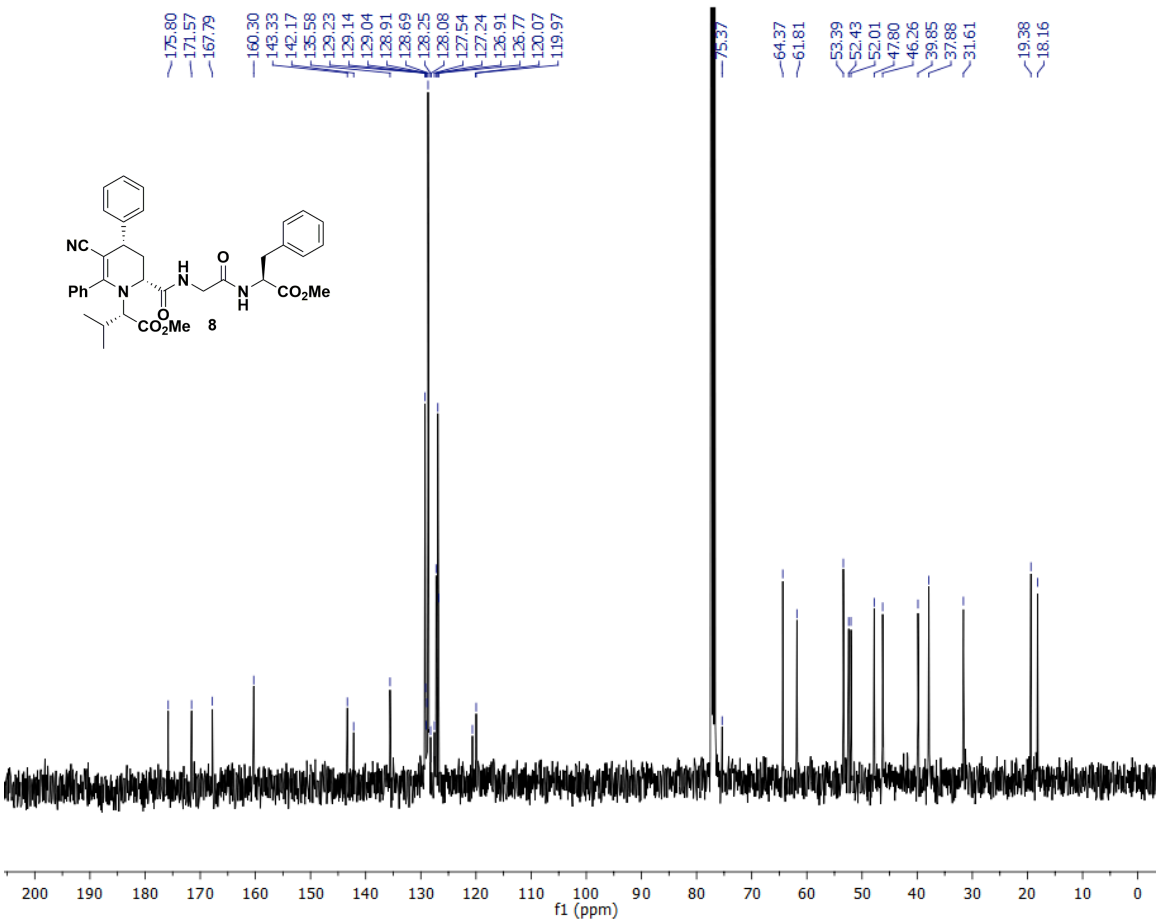
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **7**



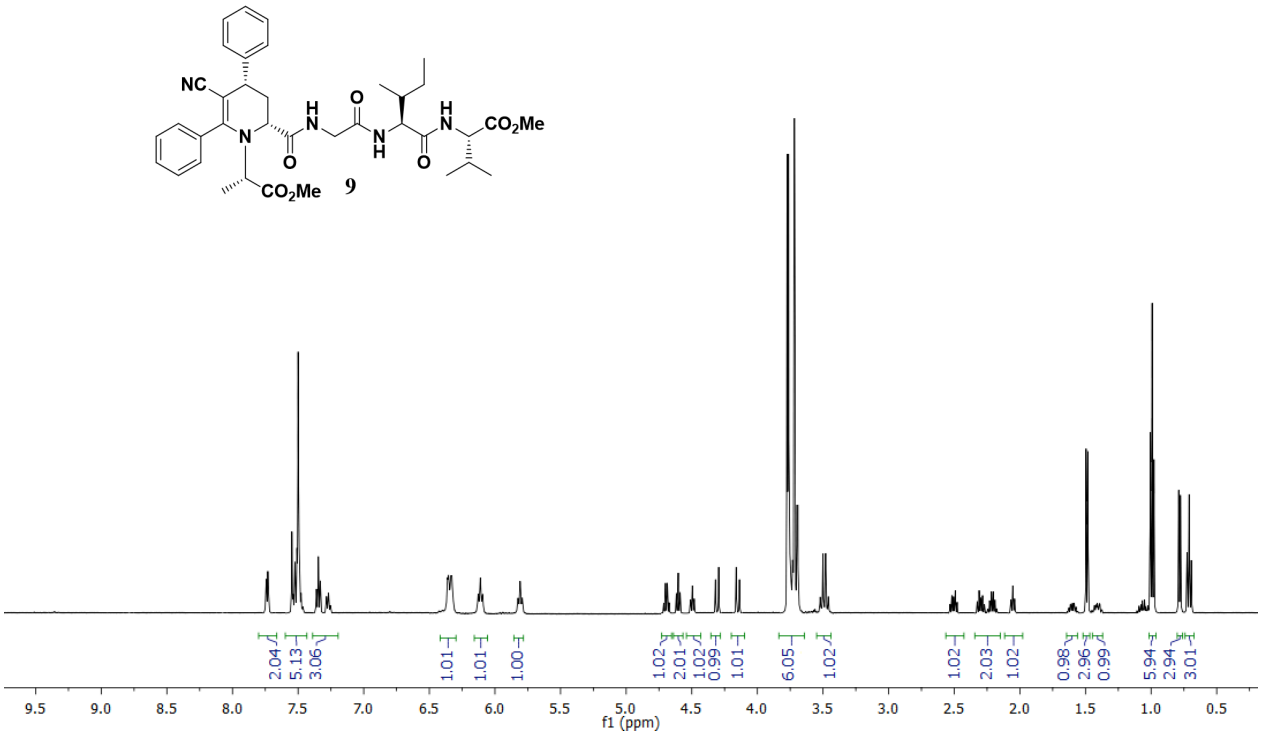


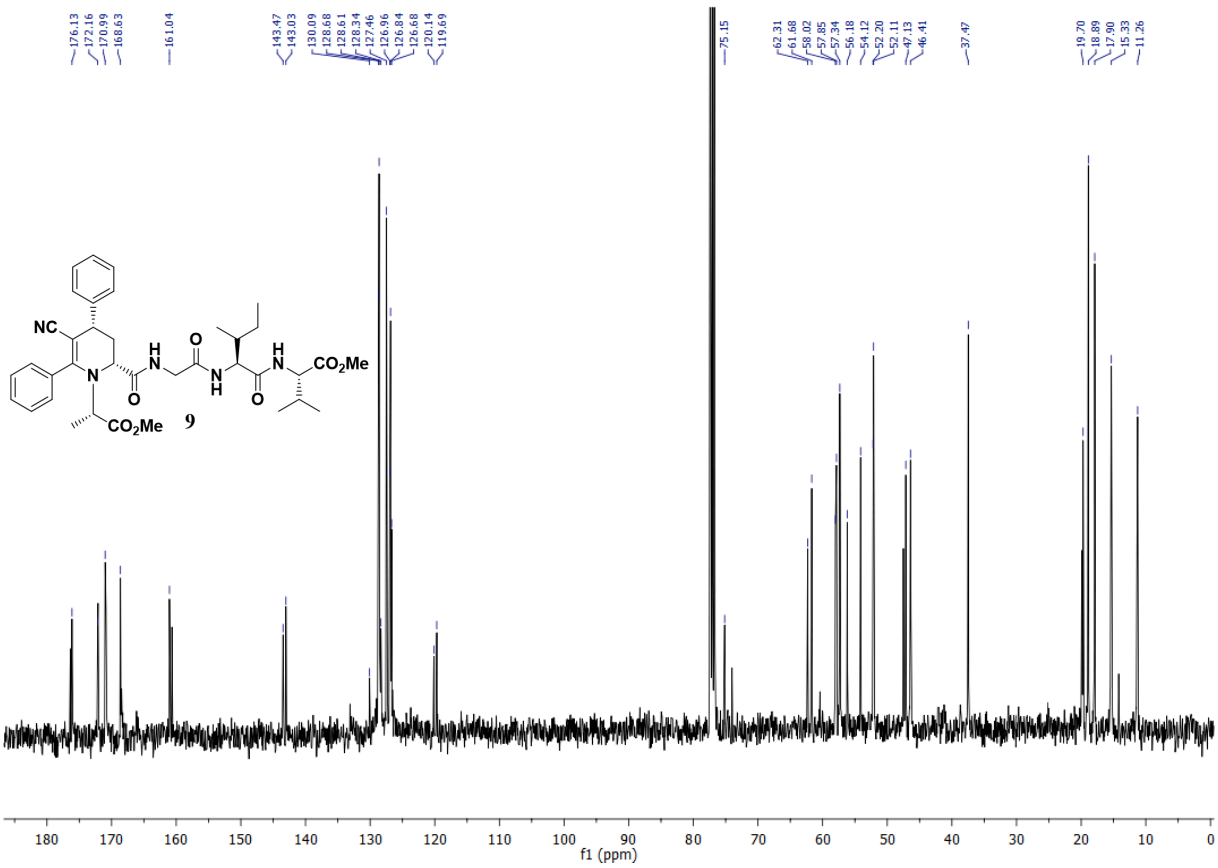
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **8**



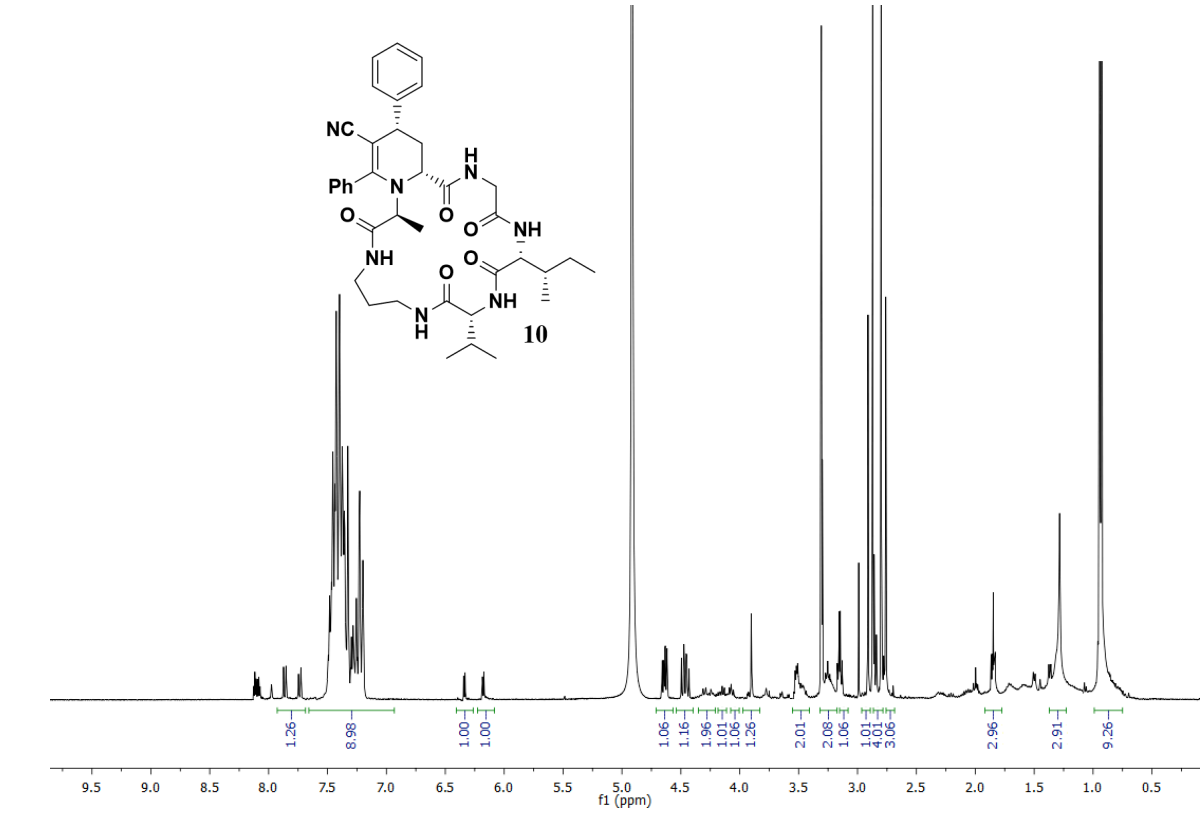


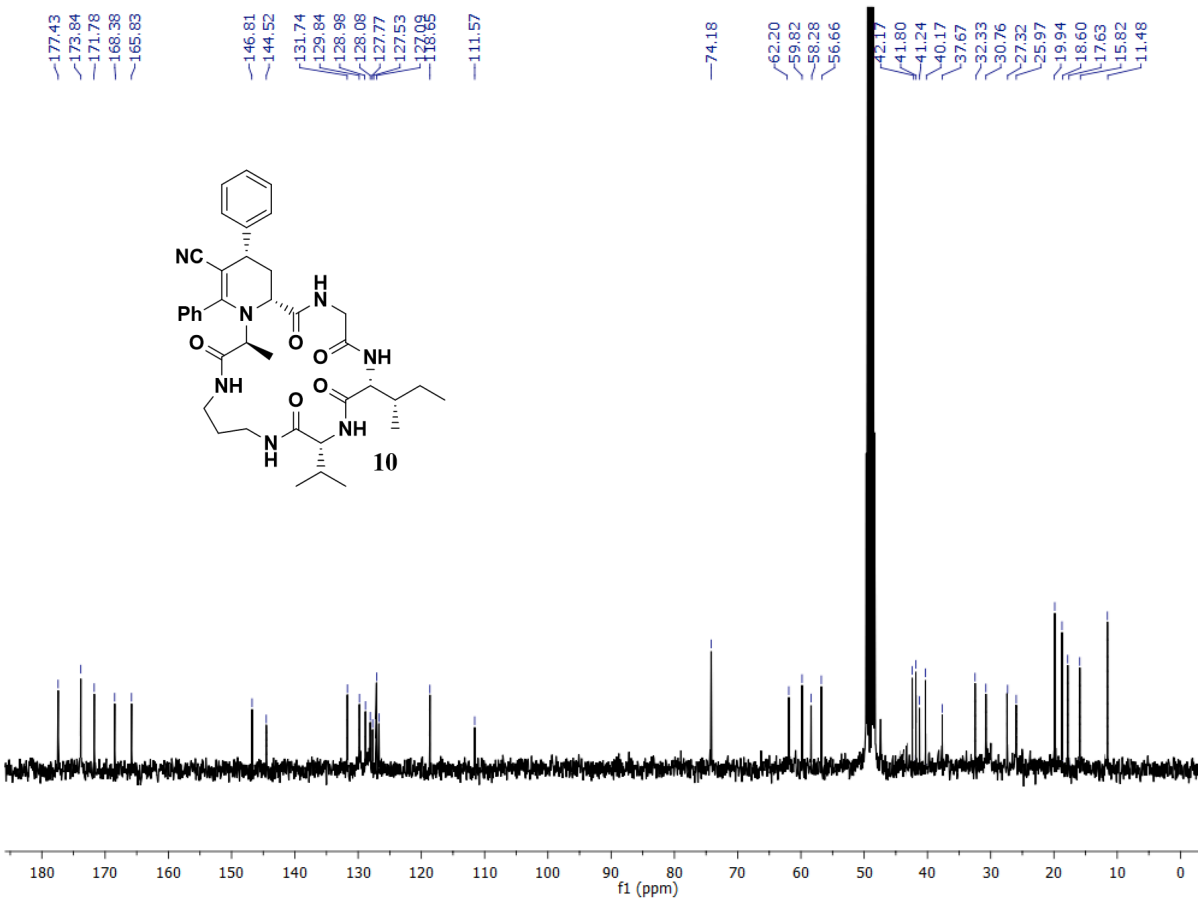
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **9**



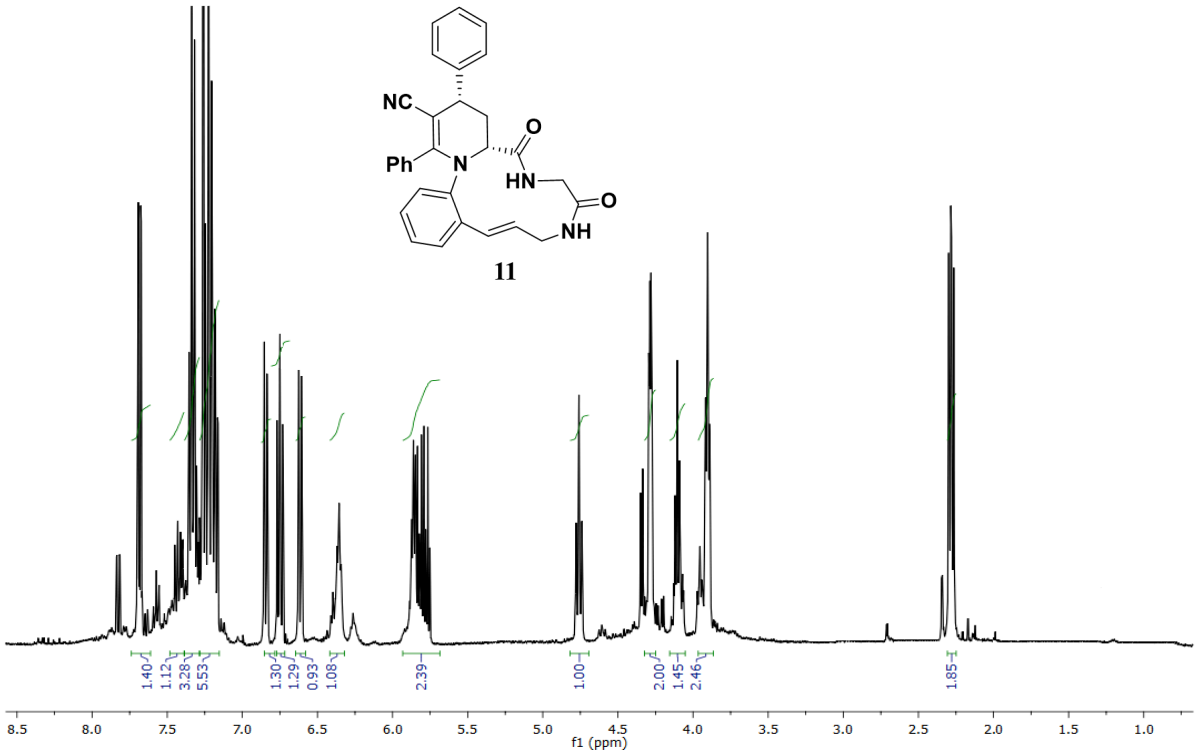


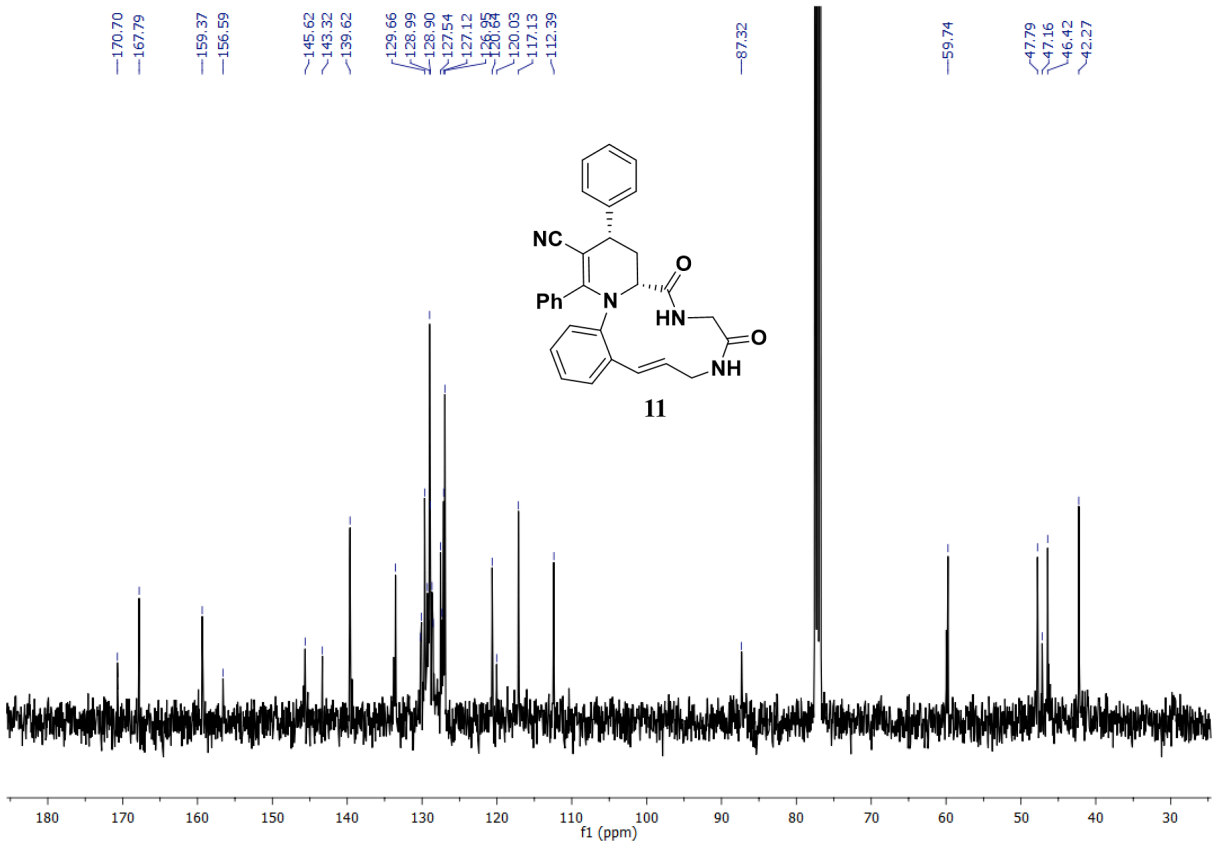
^{1}H and ^{13}C NMR spectra in CD_3OD of compound **10**



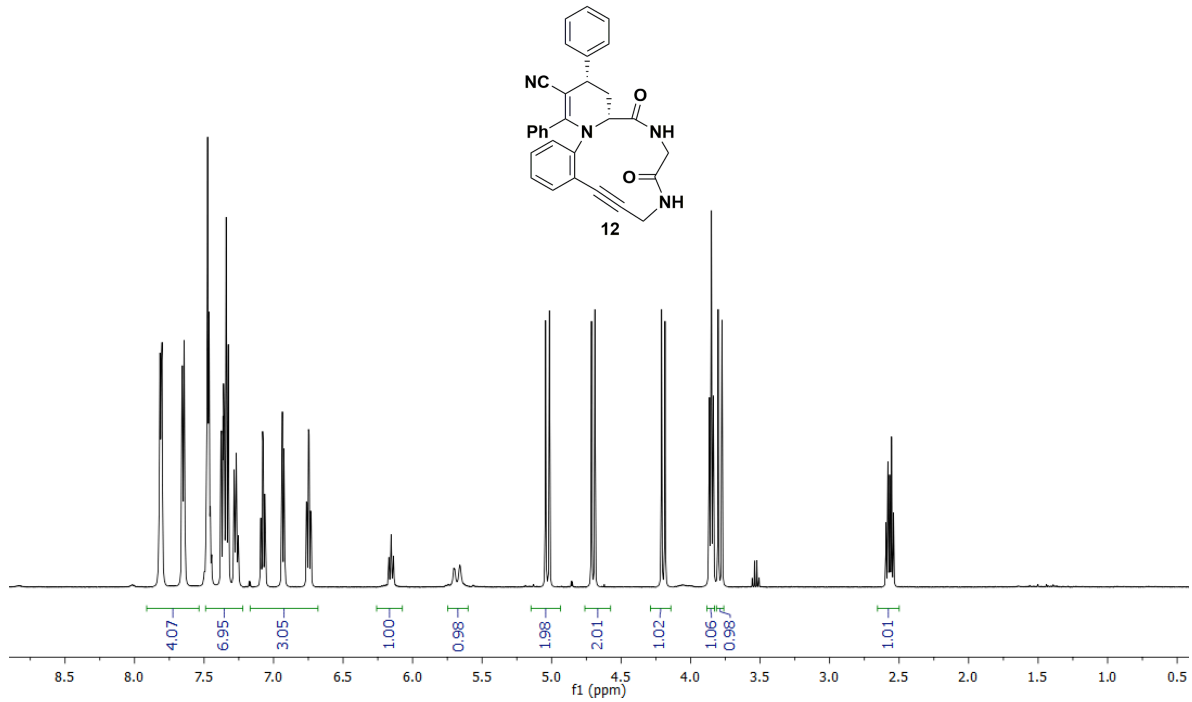


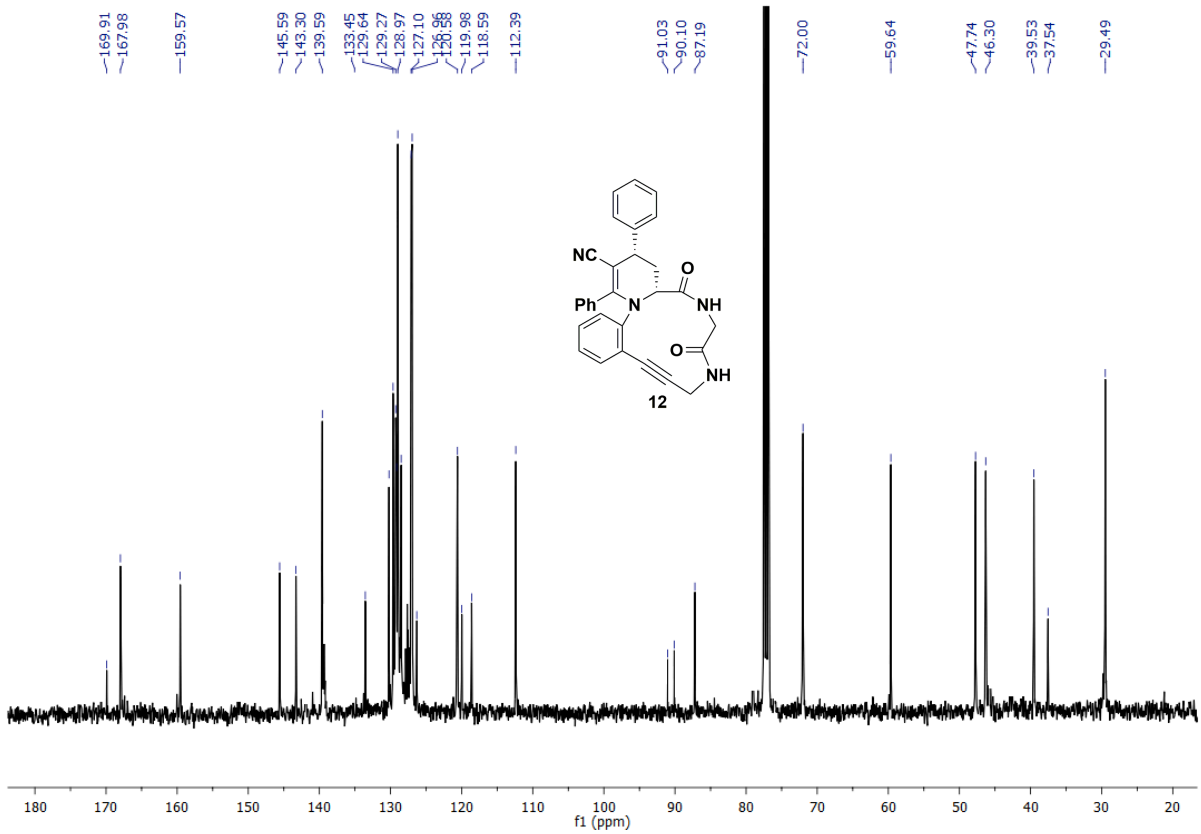
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **11**



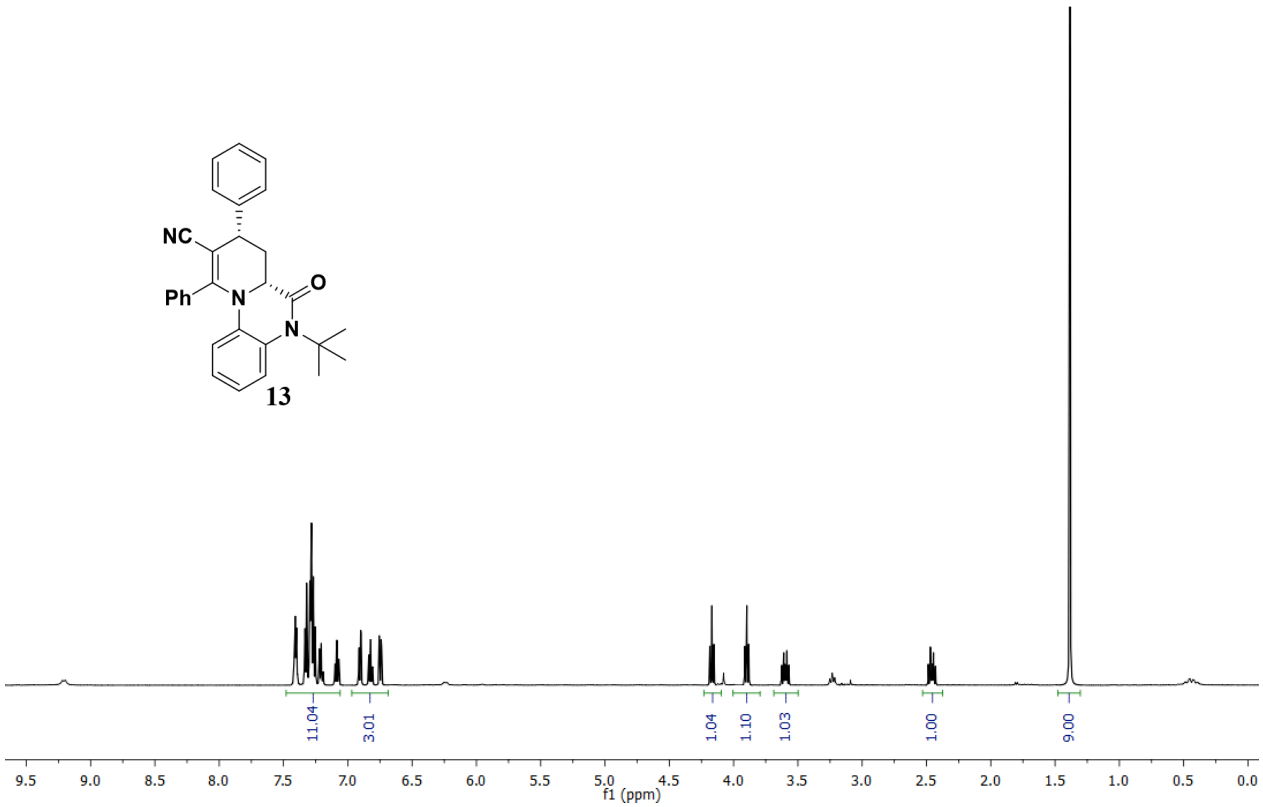


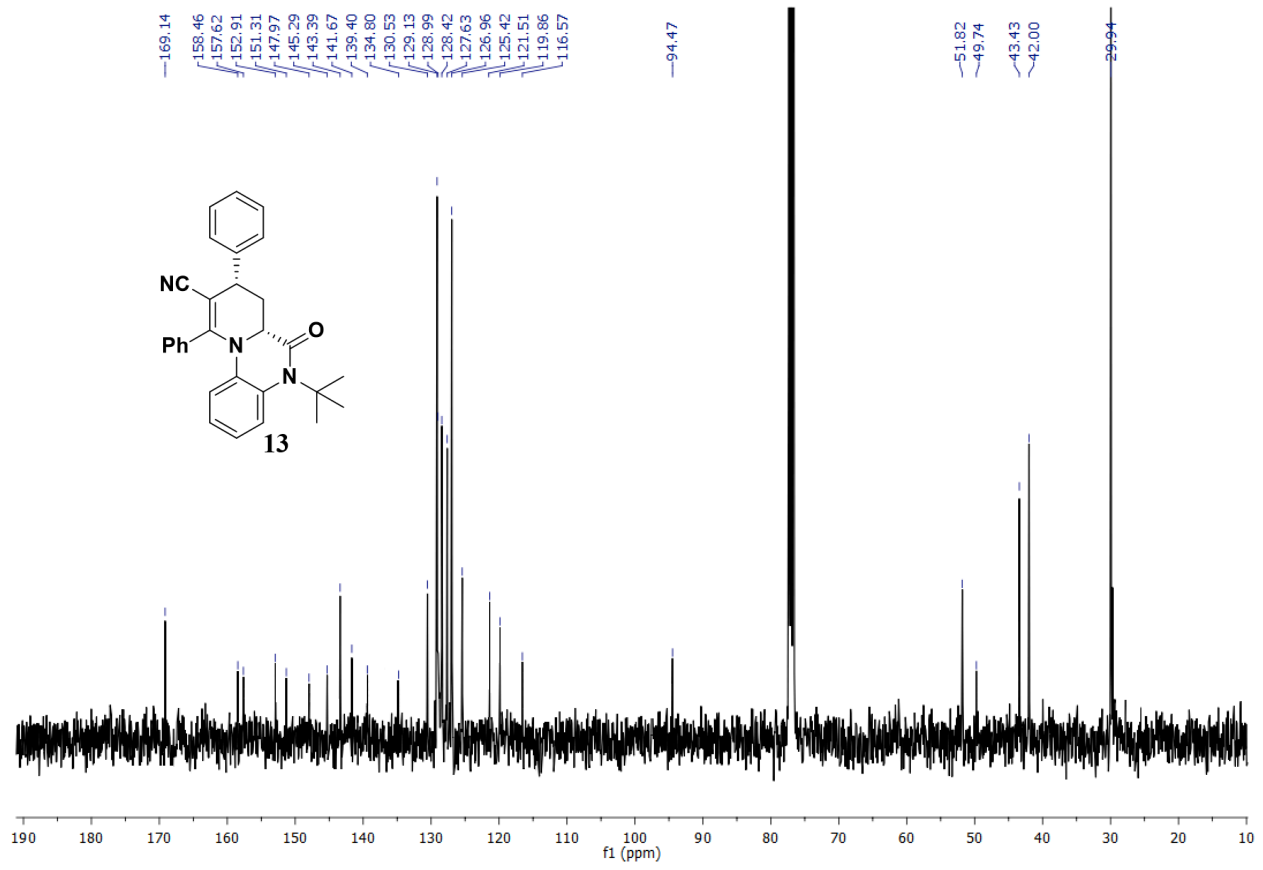
^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **12**





^{1}H and ^{13}C NMR spectra in $CDCl_3$ of compound **13**

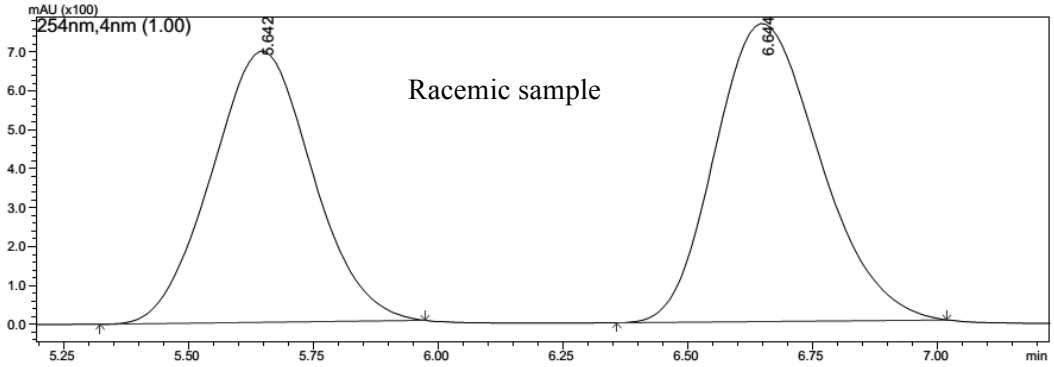


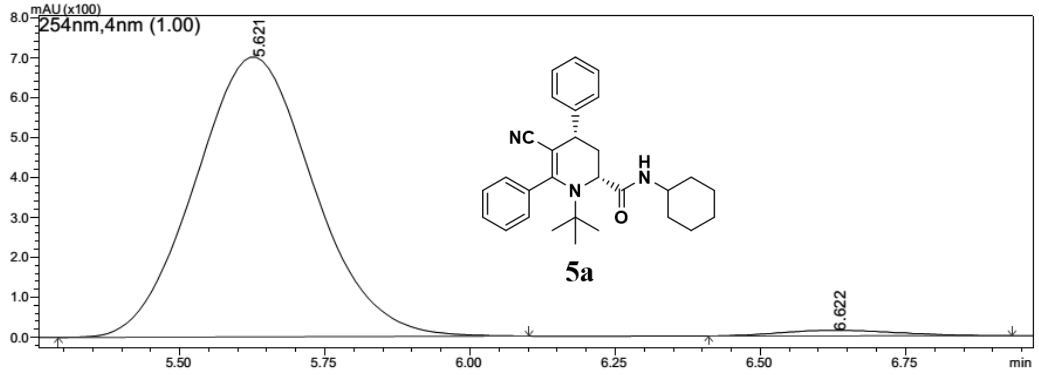


Chiral Stationary Phase HPLC Chromatograms

Chromatogram of Compound 5a

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 0.8 mL/min, UV-detection at λ = 254 nm:





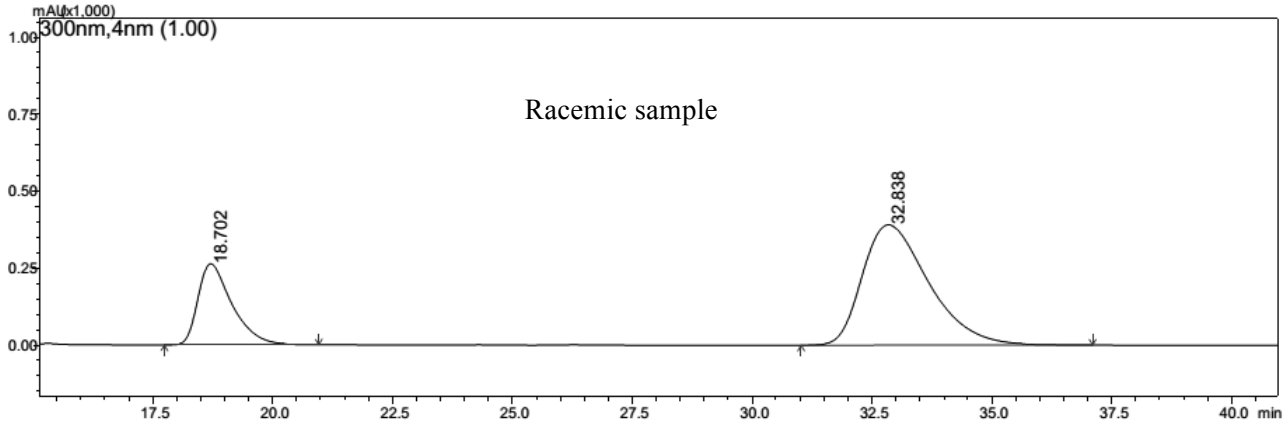
5a

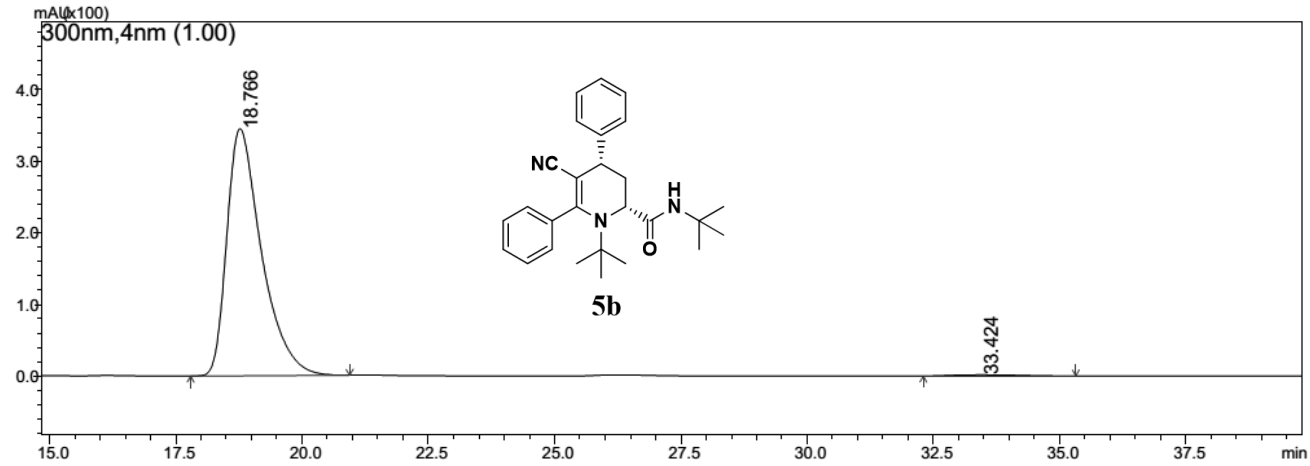
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	5.621	9945319	700393	98.041	98.049
2	6.622	198761	13933	1.959	1.951
Total		10144081	714326	100.000	100.000

Chromatogram of Compound 5b

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*PrOH 95:5) at 0.8 mL/min, UV-detection at λ = 254 nm:



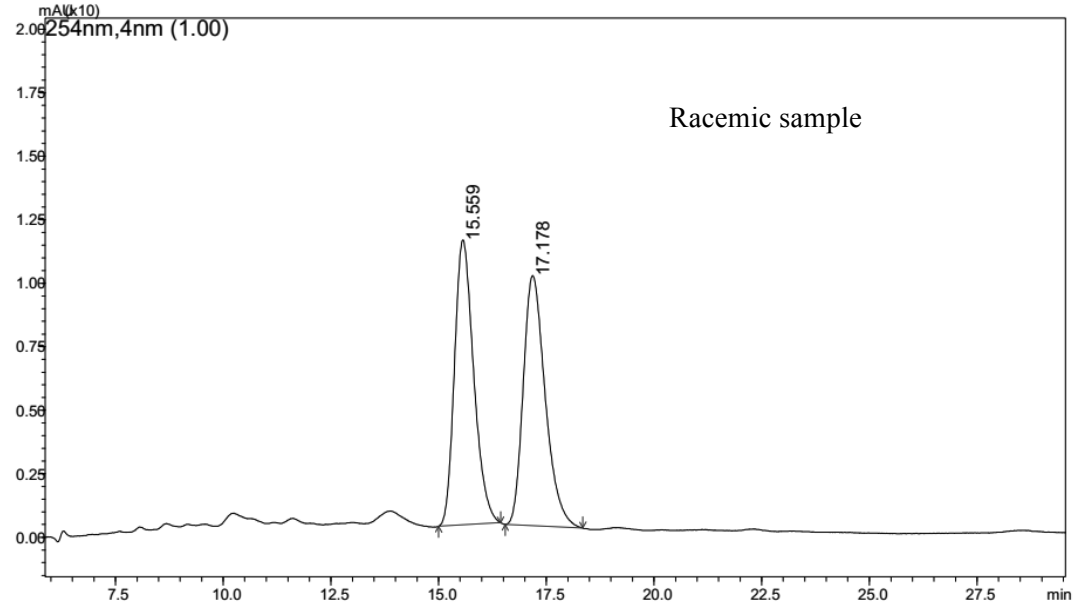


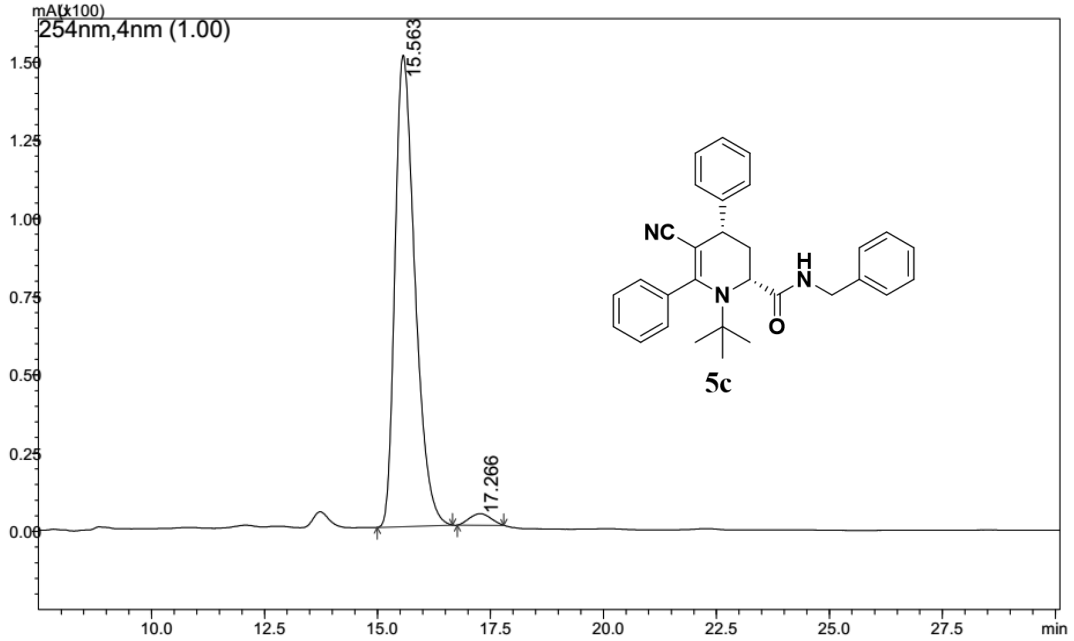
5b

Peak#	Ret. Time	Area	Height	Area %	Height %
1	18.766	16500835	344984	99.219	99.558
2	33.424	129861	1531	0.781	0.442
Total		16630696	346516	100.000	100.000

Chromatogram of Compound 5c

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AD-H column (*n*-hexane/*i*PrOH 90:10) at 0.5 mL/min, UV-detection at λ = 254 nm:





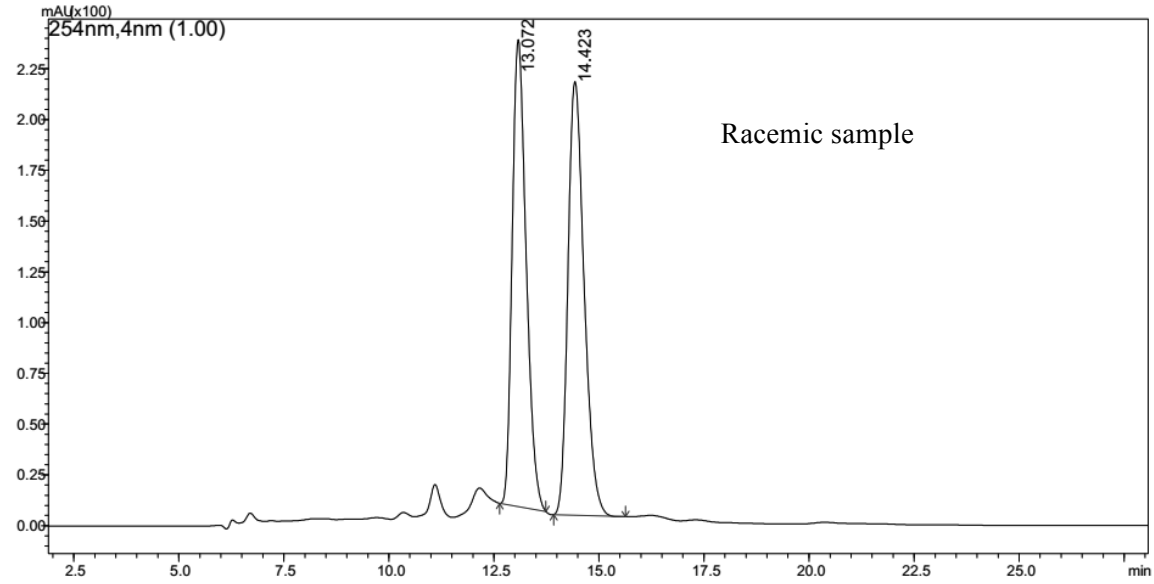
5c

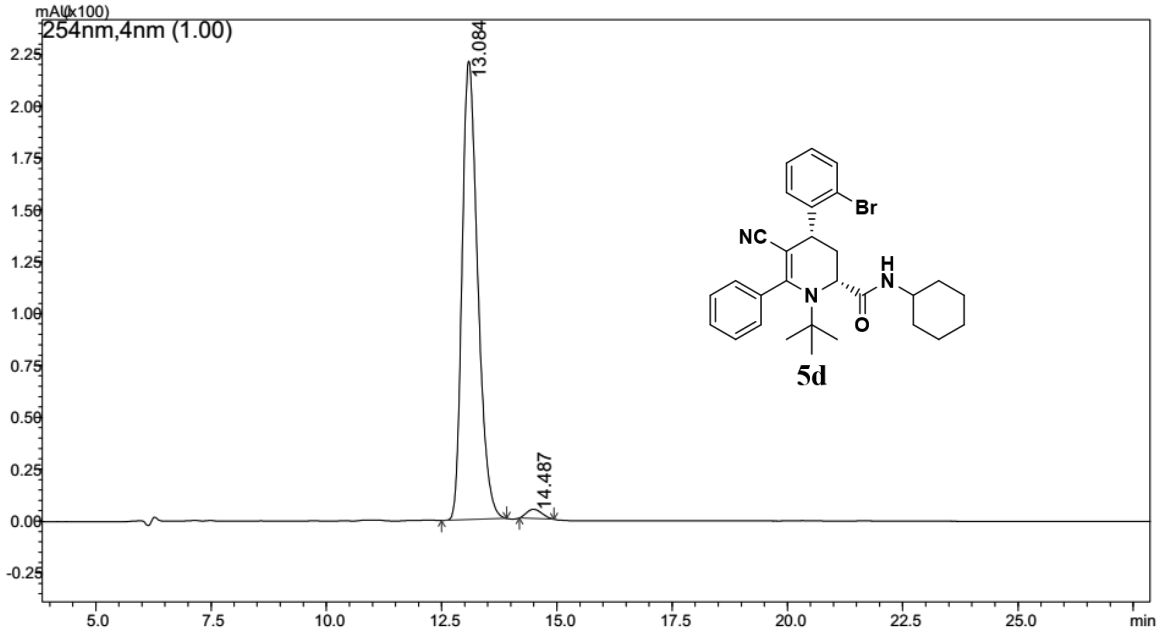
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.563	4639313	150582	97.476	97.629
2	17.266	120141	3656	2.524	2.371
Total		4759453	154239	100.000	100.000

Chromatogram of Compound 5d

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AD-H column (*n*-hexane/*i*PrOH 90:10) at 0.5 mL/min, UV-detection at λ = 254 nm:



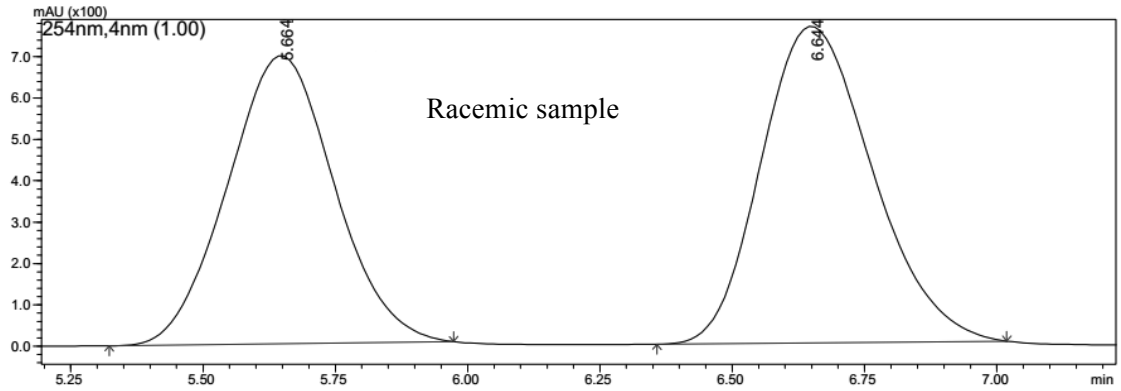


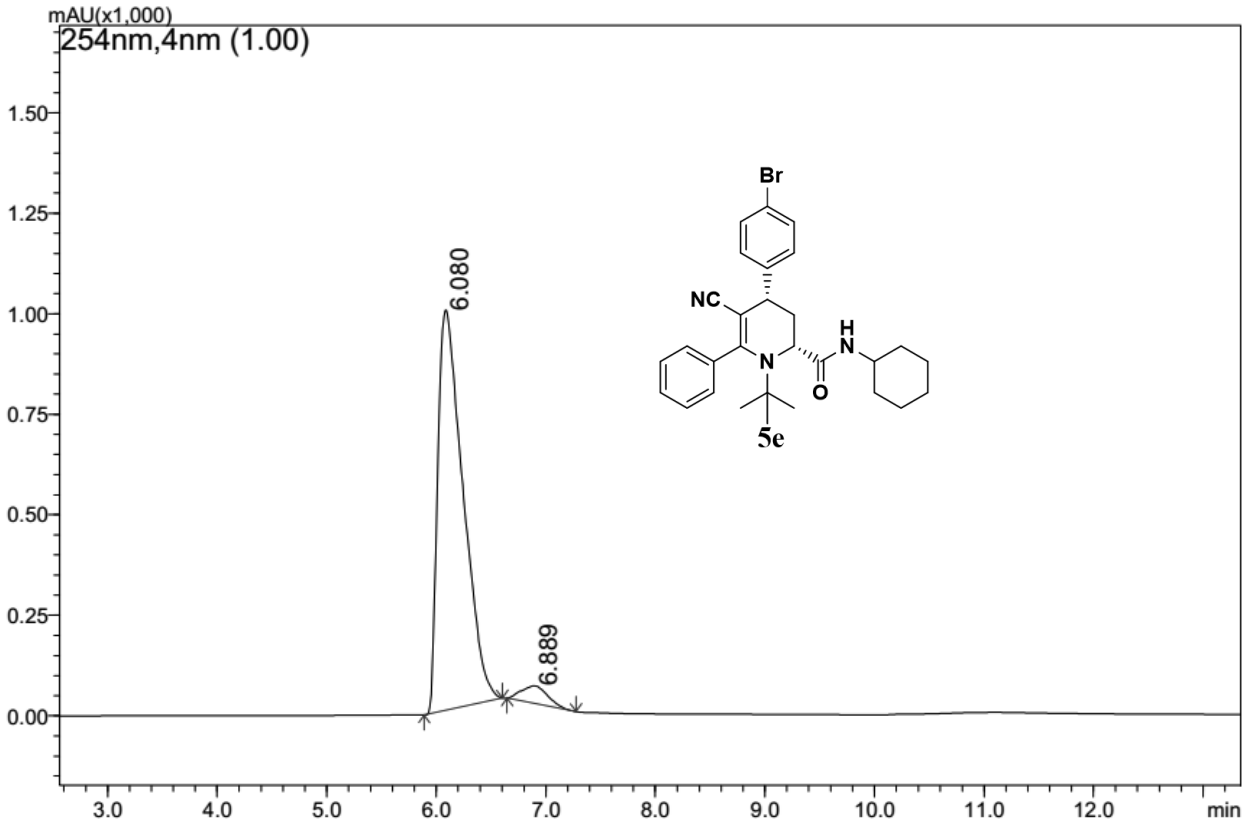
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.084	5222760	221151	98.087	98.032
2	14.487	101867	4440	1.913	1.968
Total		5324626	225591	100.000	100.000

Chromatogram of Compound 5e

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AS-H column (*n*-hexane/*i*PrOH 90:10) at 0.5 mL/min, UV-detection at λ = 254 nm:



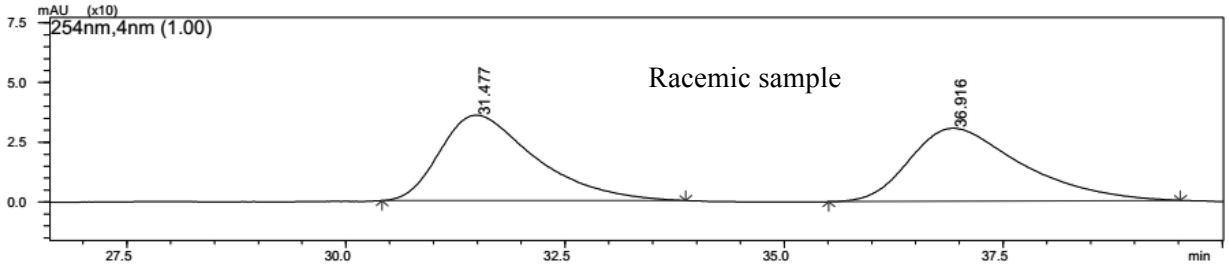


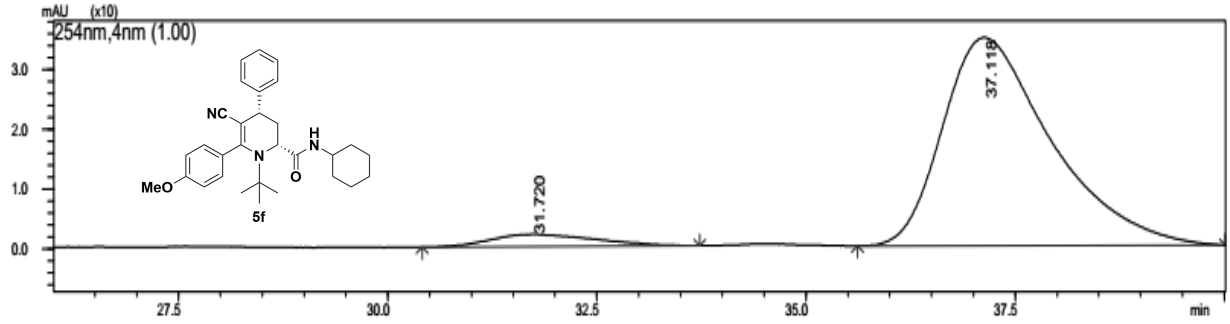
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	6.080	15967714	995212	95.651	95.782
2	6.889	726023	43826	4.349	4.218
Total		16693738	1039037	100.000	100.000

Chromatogram of Compound 5f

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AD-H column (*n*-hexane/*i*PrOH 90:10) at 1.0 mL/min, UV-detection at λ = 254 nm:



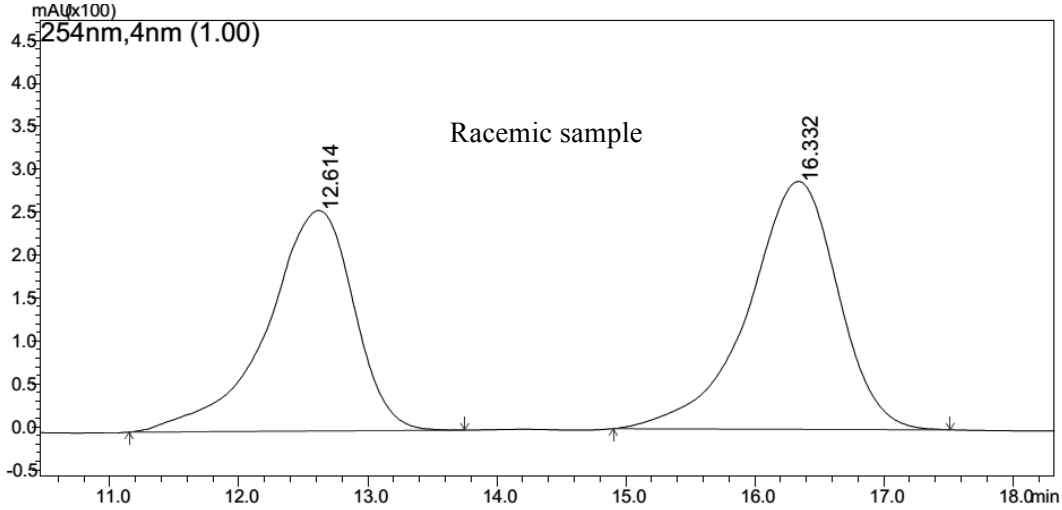


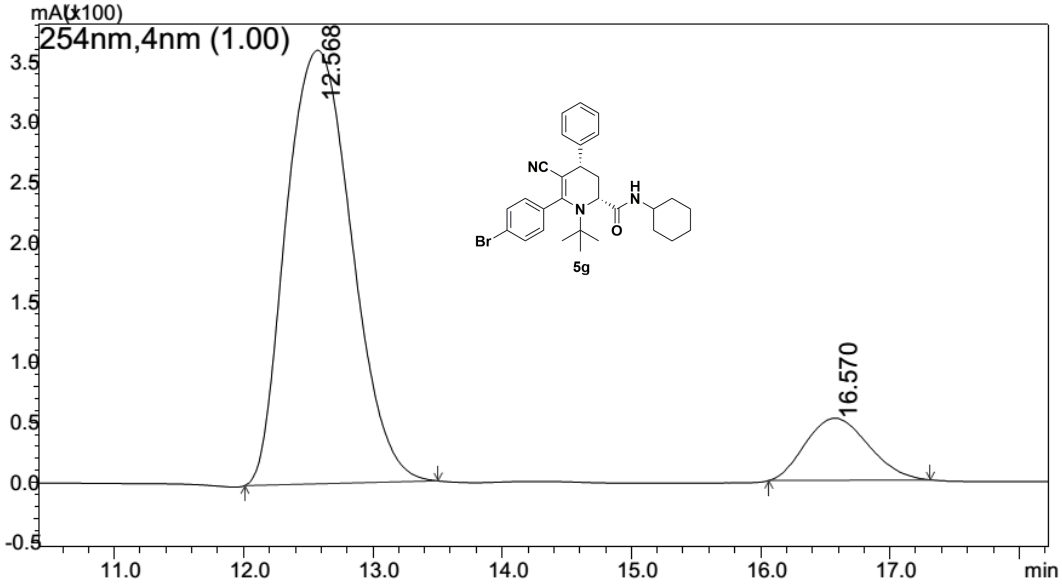
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.720	179125	2066	5.381	5.597
2	37.118	3149559	34857	94.619	94.403
Total		3328684	36923	100.000	100.000

Chromatogram of Compound 5g

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel AD-H column (*n*-hexane/*i*PrOH 97:3) at 0.5 mL/min, UV-detection at λ = 254 nm:



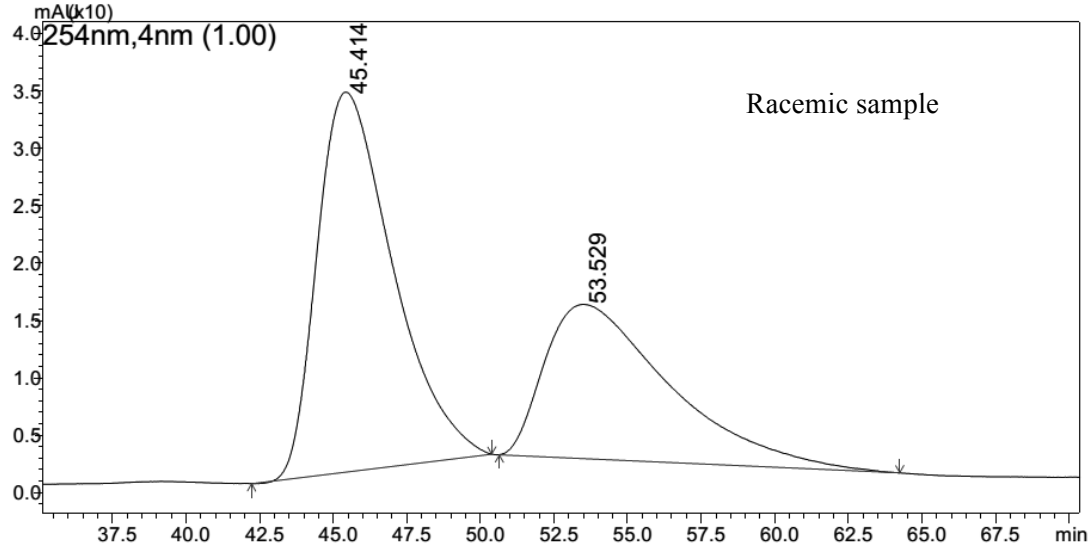


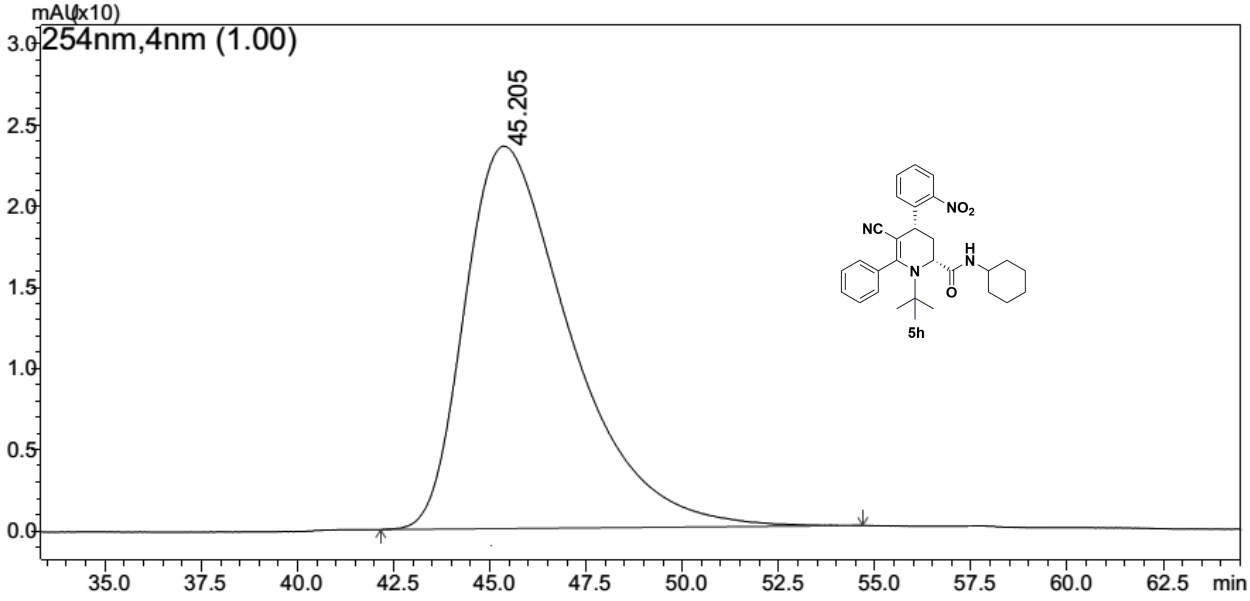
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.568	12742098	360860	89.915	89.516
2	16.570	1751576	51474	10.085	10.484
Total		14493674	412333	100.000	100.000

Chromatogram of Compound 5h

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (n-hexane/i-PrOH 90:10) at 1.0 mL/min, UV-detection at λ= 254 nm:



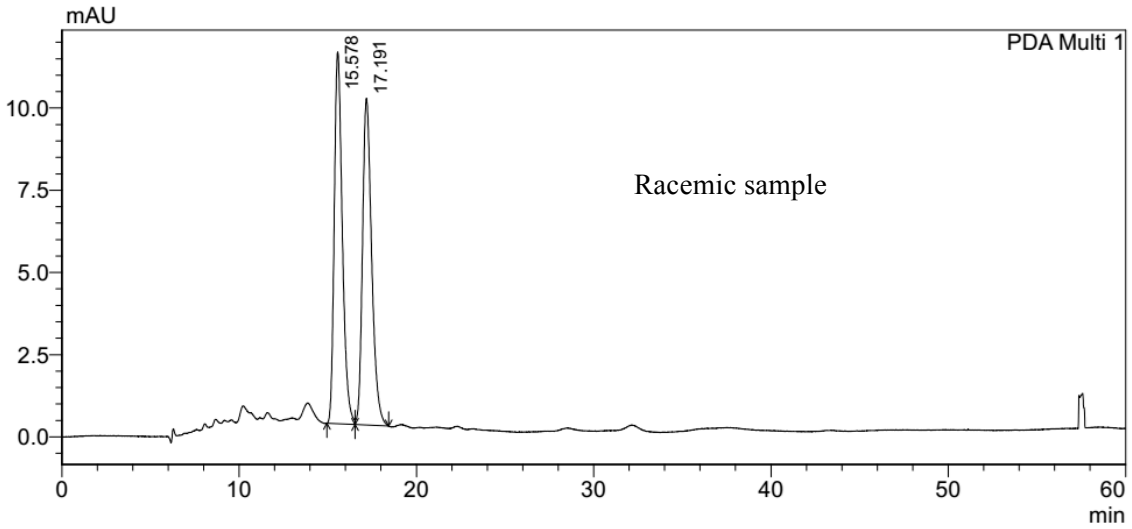


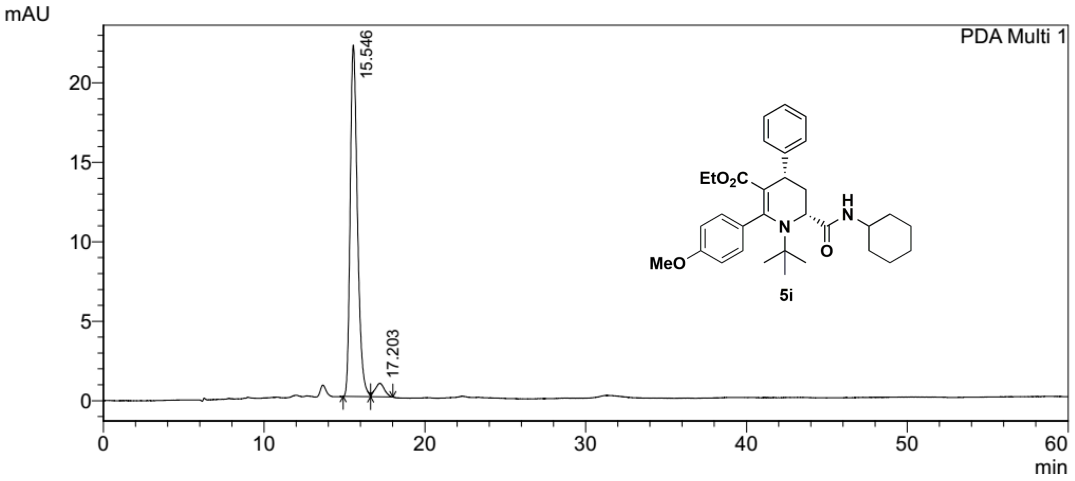
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	45.205	4523143	23535	100.000	100.000
Total		4523143	23535	100.000	100.000

Chromatogram of Compound 5i

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 95:5) at 0.8 mL/min, UV-detection at λ= 254 nm:



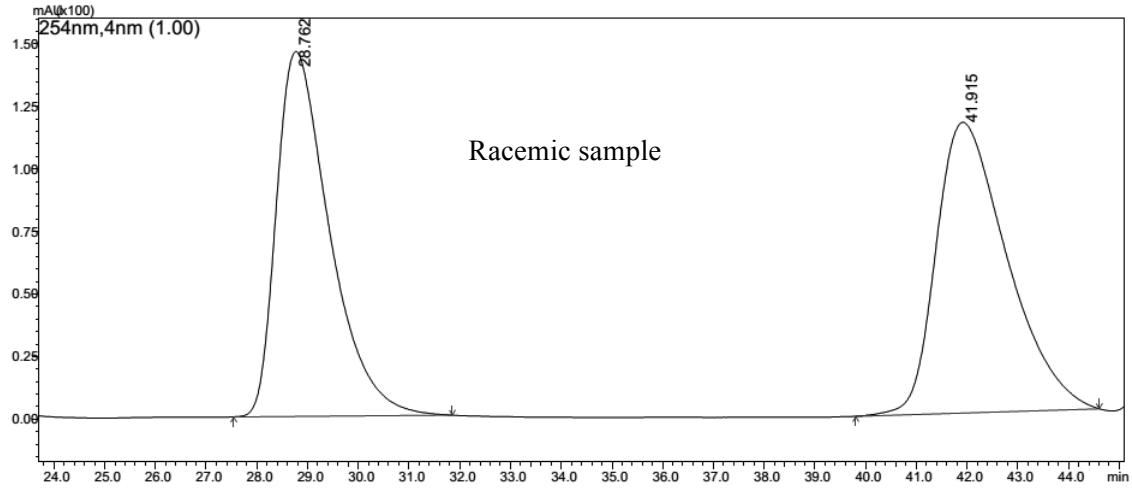


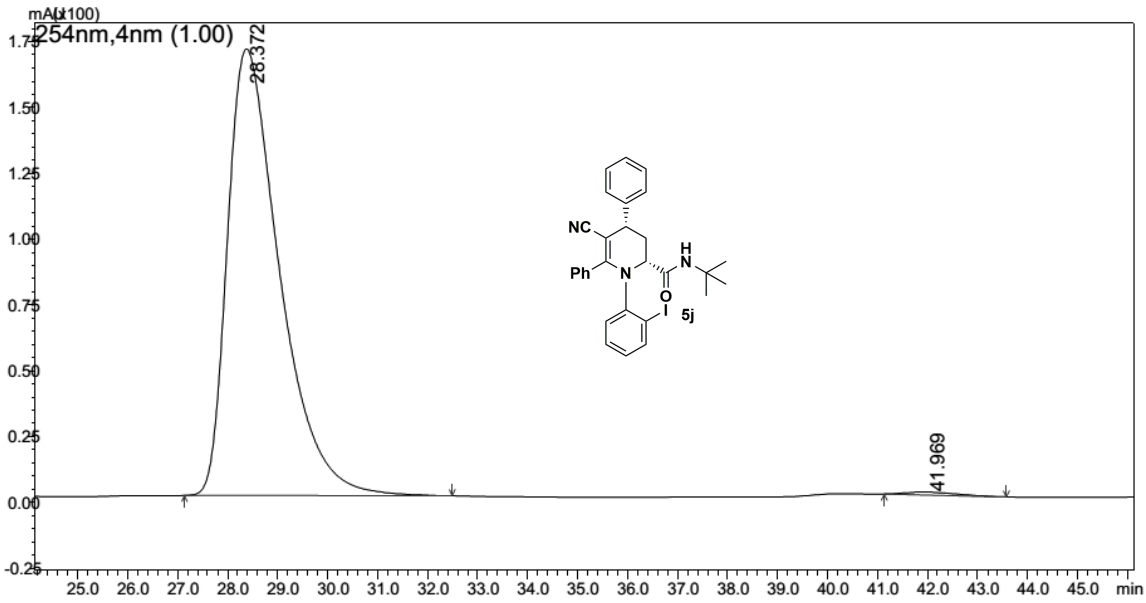
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.546	693555	22127	95.180	96.264
2	17.203	35120	859	4.820	3.736
Total		728674	22985	100.000	100.000

Chromatogram of Compound 5j

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*-PrOH 90:10) at 0.7 mL/min, UV-detection at λ= 254 nm:



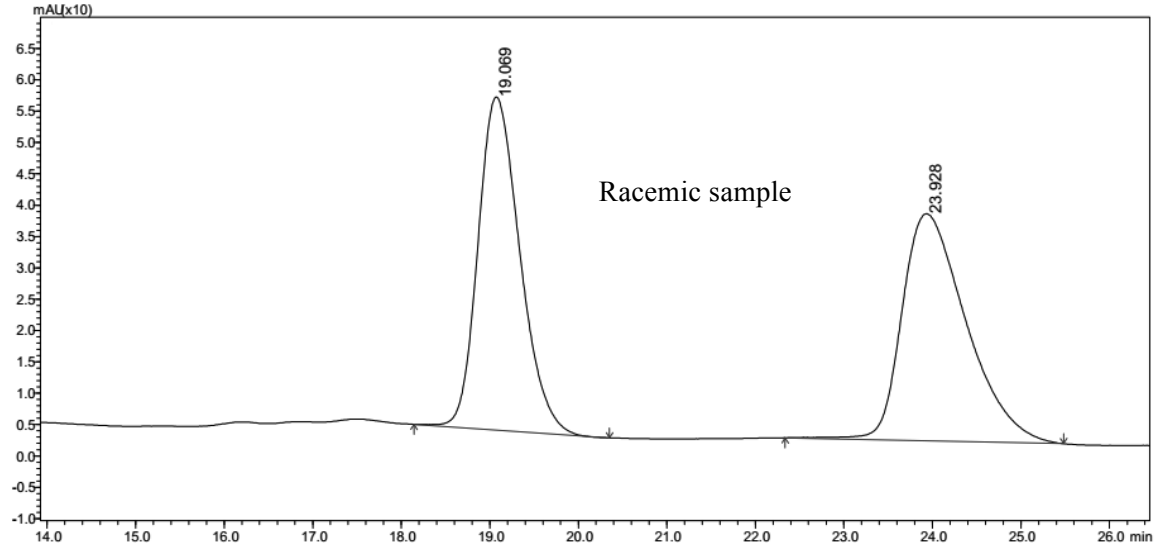


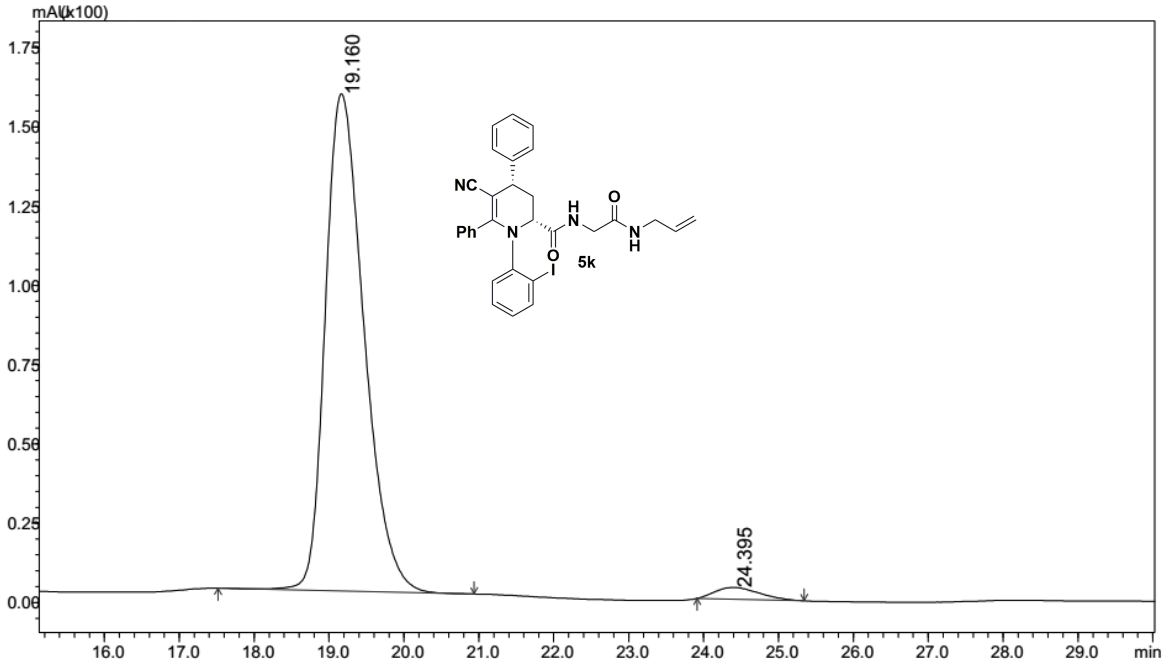
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	28.372	12279505	169664	99.348	99.358
2	41.969	80583	1096	0.652	0.642
Total		12360088	170760	100.000	100.000

Chromatogram of Compound 5k

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 0.7 mL/min, UV-detection at λ = 254 nm:



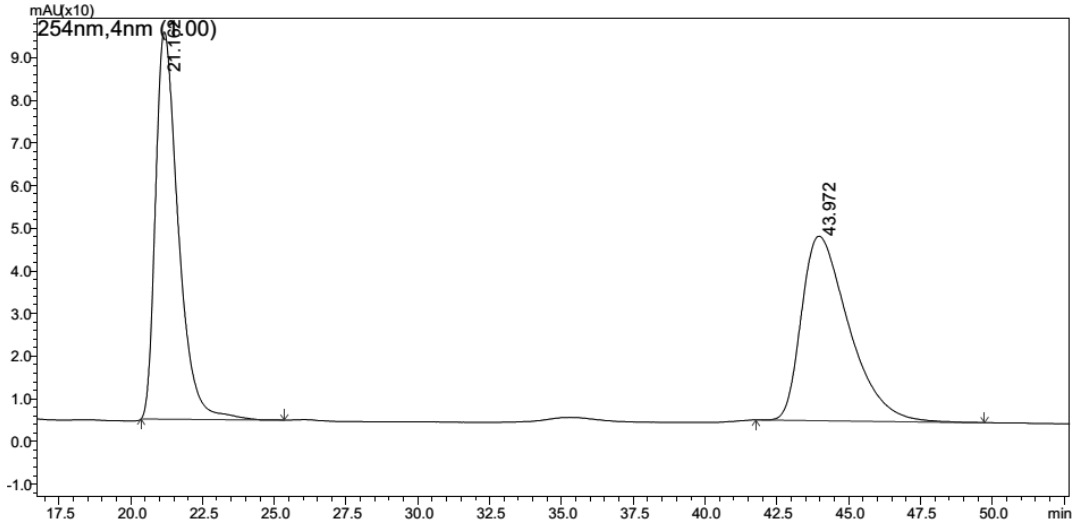


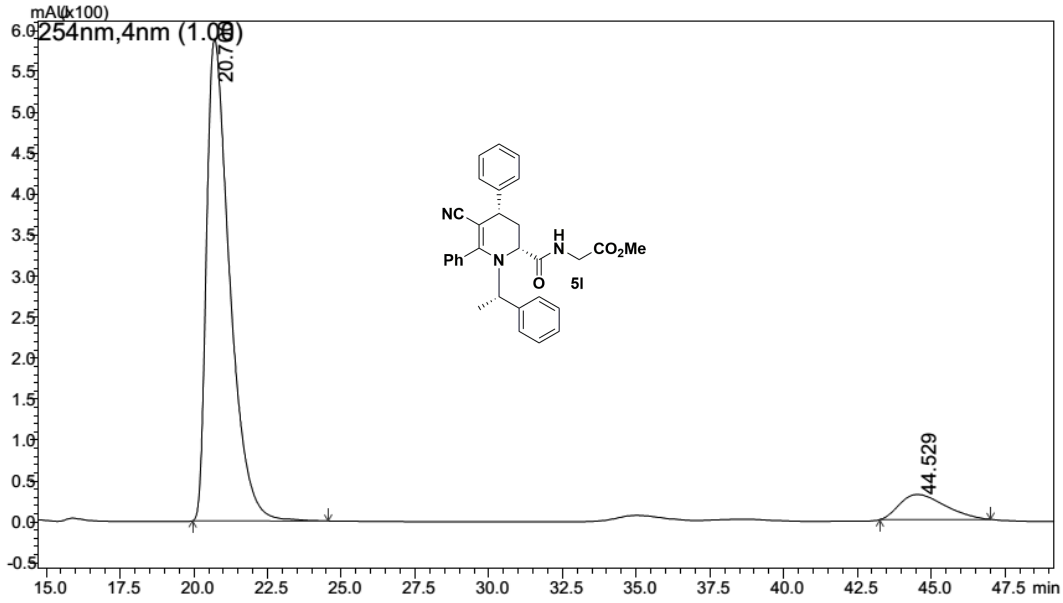
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.160	5628372	156805	97.370	97.682
2	24.395	152004	3720	2.630	2.318
Total		5780376	160525	100.000	100.000

Chromatogram of Compound 5l

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 1.0 mL/min, UV-detection at λ = 254 nm:



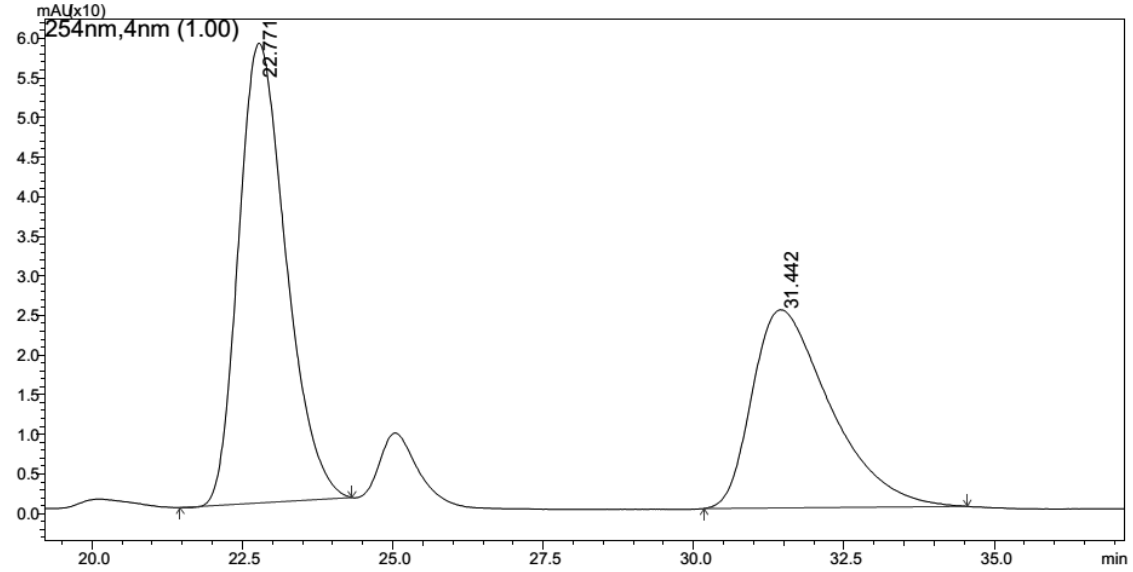


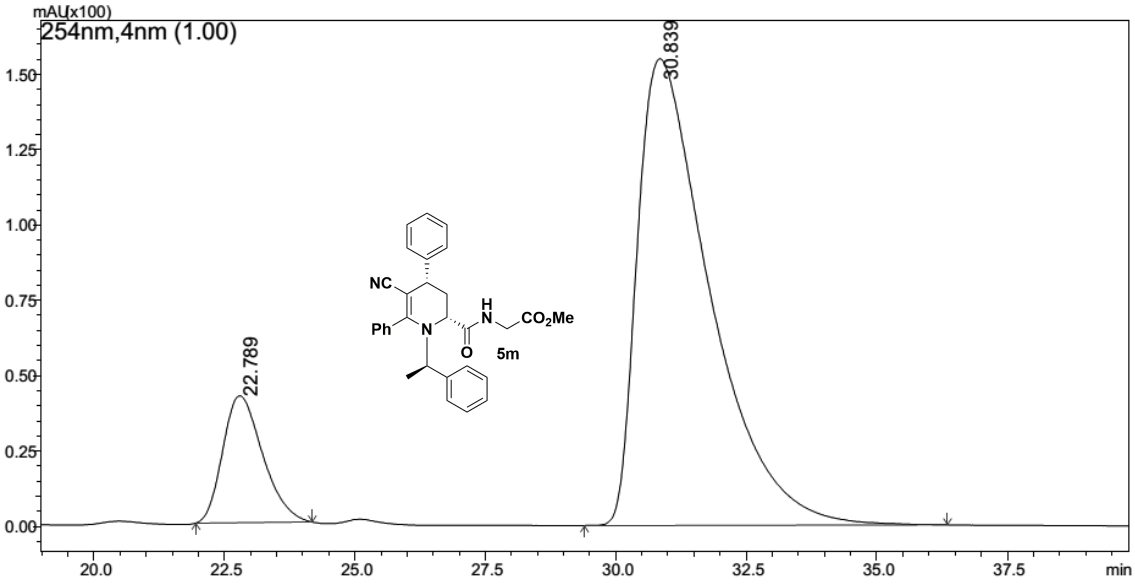
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.700	32092726	588171	90.659	95.027
2	44.529	3306840	30778	9.341	4.973
Total		35399566	618949	100.000	100.000

Chromatogram of Compound 5m

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 0.8 mL/min, UV-detection at λ = 254 nm:



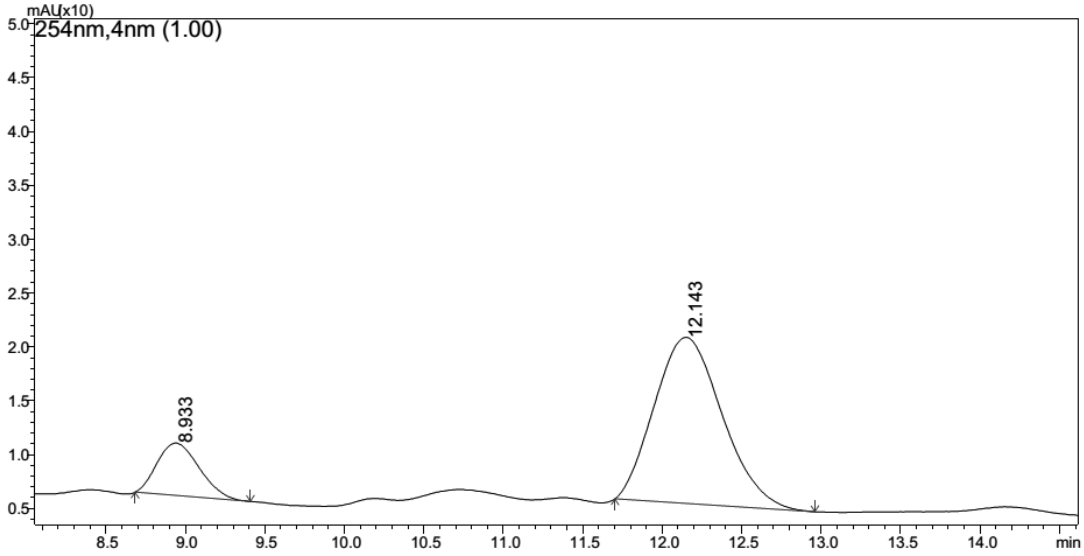


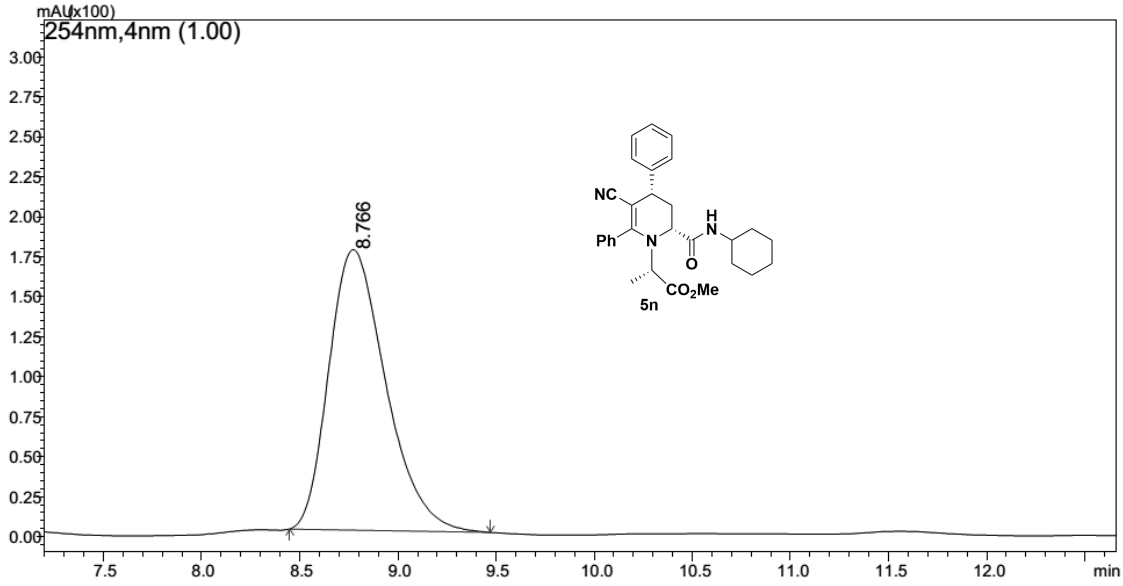
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.789	2246979	42156	13.021	21.392
2	30.839	15009969	154908	86.979	78.608
Total		17256948	197065	100.000	100.000

Chromatogram of Compound 5n

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 0.8 mL/min, UV-detection at λ = 254 nm:



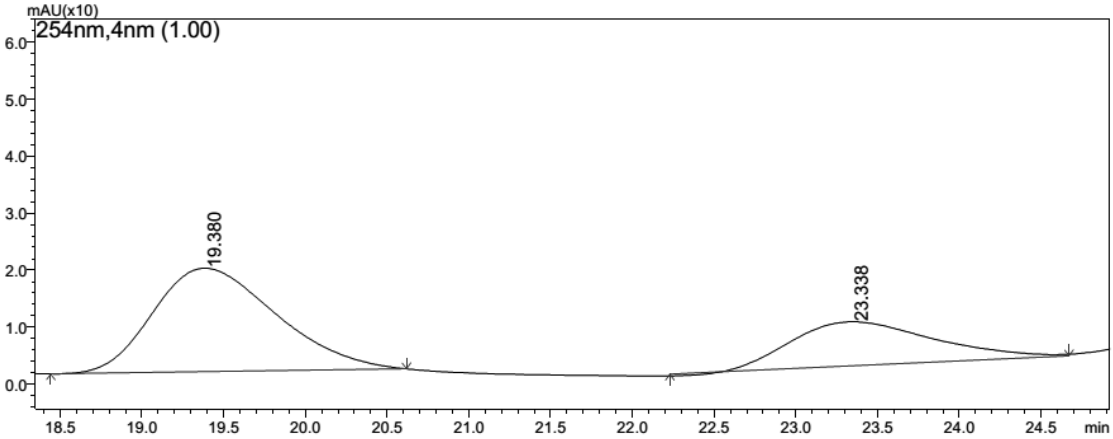


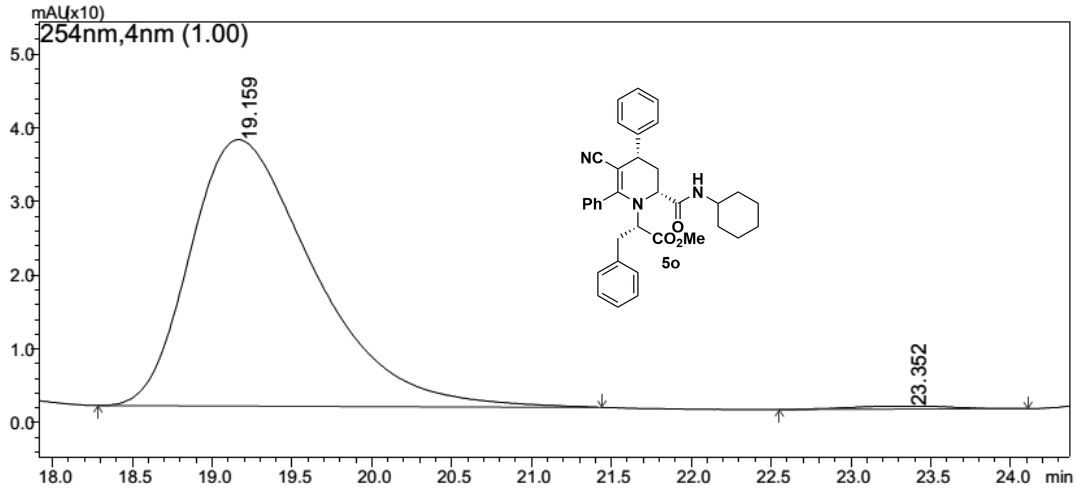
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.766	3539778	175302	100.000	100.000
Total		3539778	175302	100.000	100.000

Chromatogram of Compound 5o

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*PrOH 90:10) at 0.8 mL/min, UV-detection at λ = 254 nm:



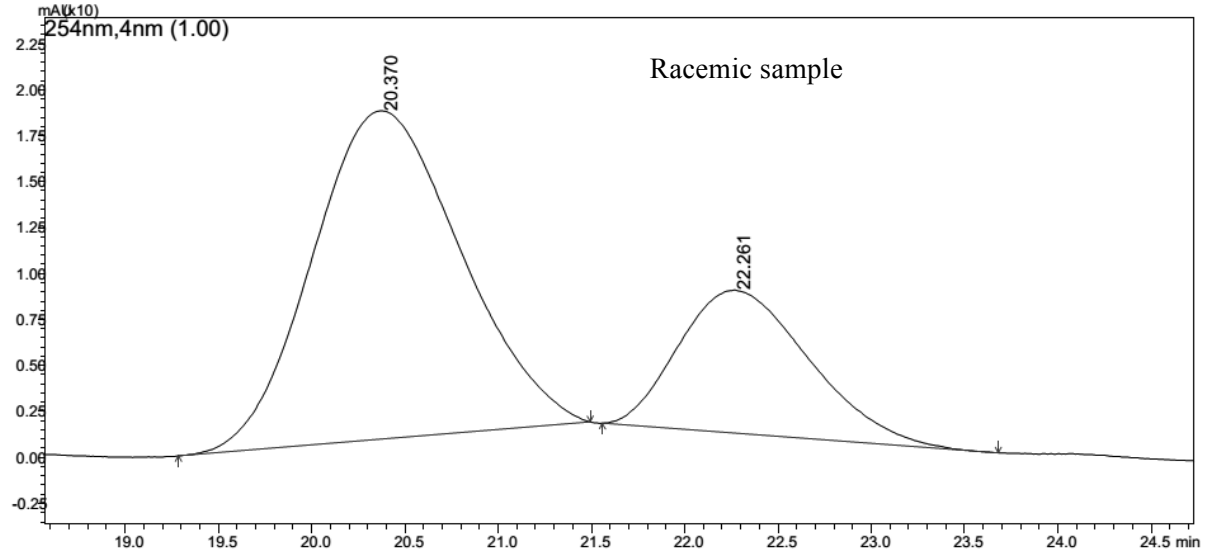


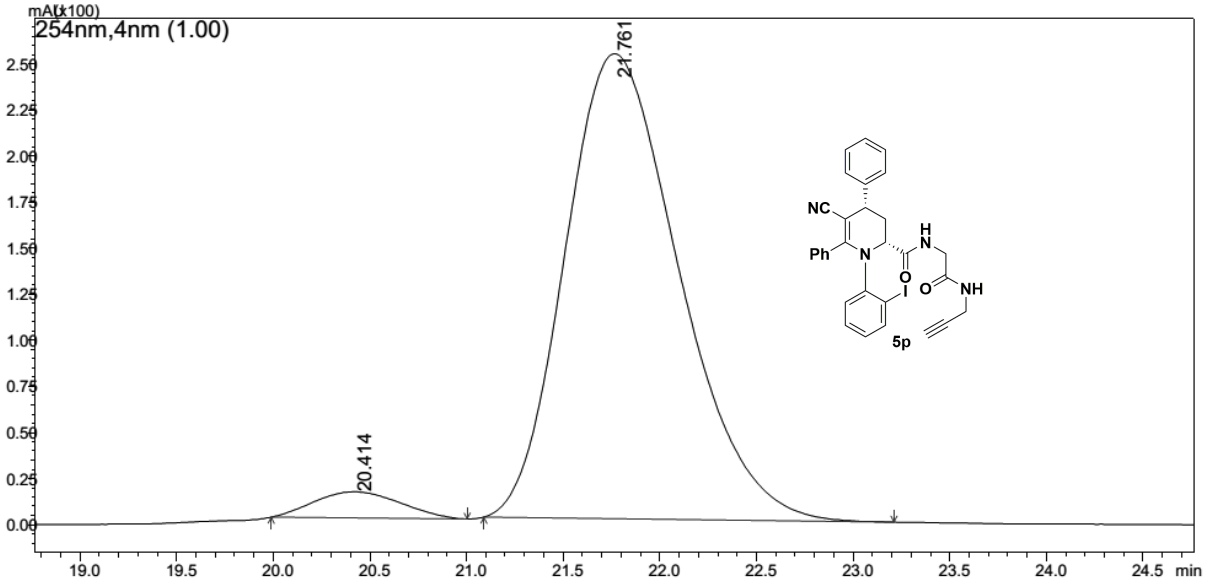
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.159	1959481	36161	99.137	98.974
2	23.352	17058	375	0.863	1.026
Total		1976539	36536	100.000	100.000

Chromatogram of Compound 5p

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*PrOH 90:10) at 1.0 mL/min, UV-detection at λ = 254 nm:





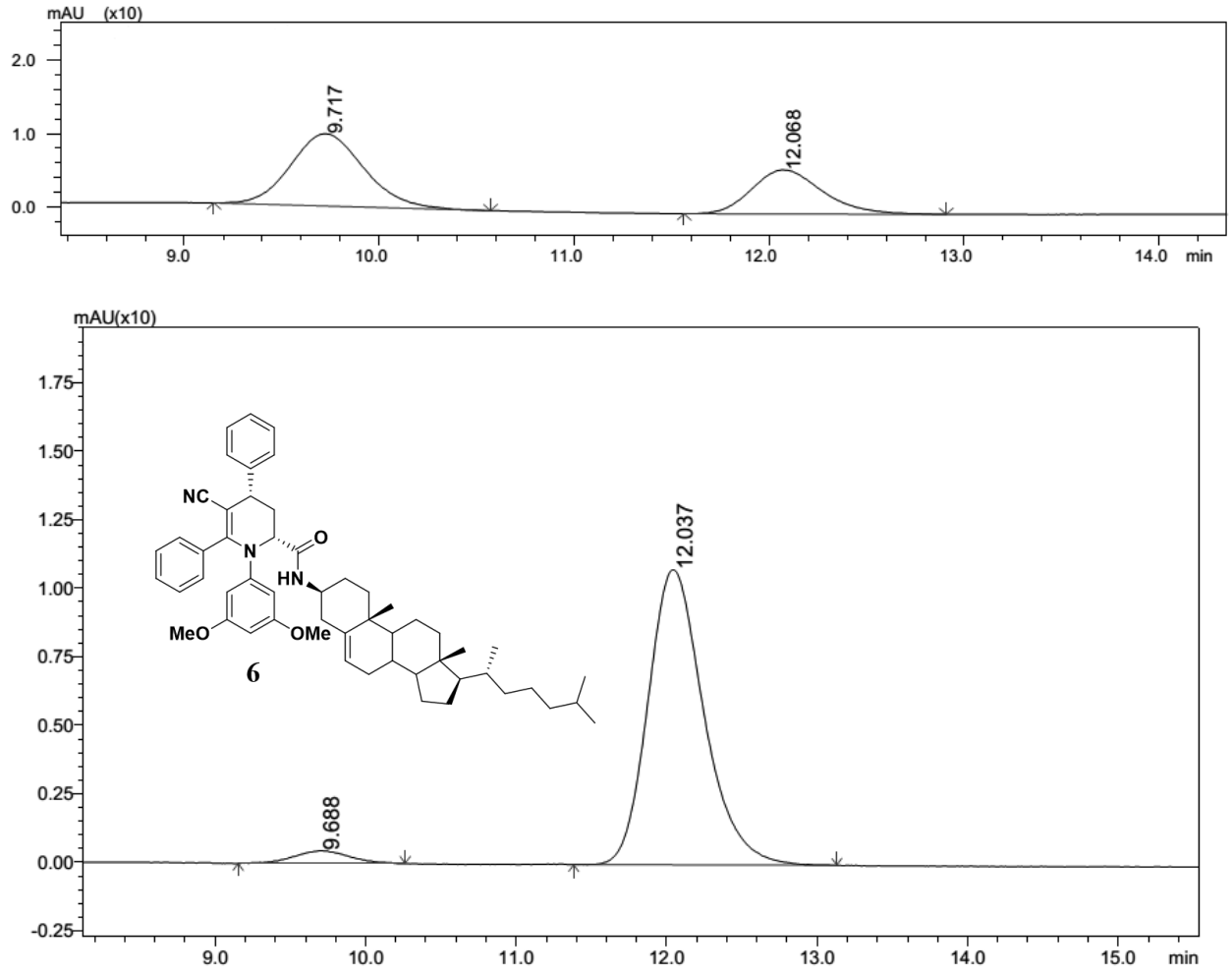
5p

PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.414	438930	14104	4.075	5.292
2	21.761	10332978	252395	95.925	94.708
Total		10771909	266499	100.000	100.000

Chromatogram of Compound 6

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 0.8 mL/min, UV-detection at λ = 254 nm:

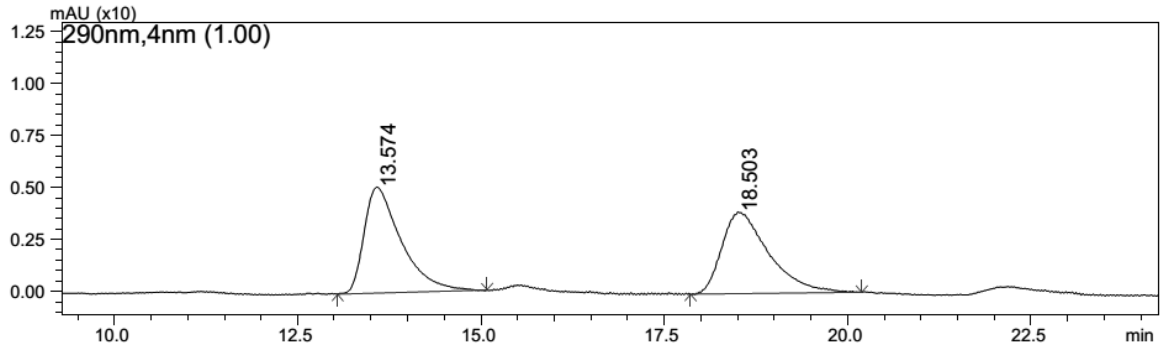


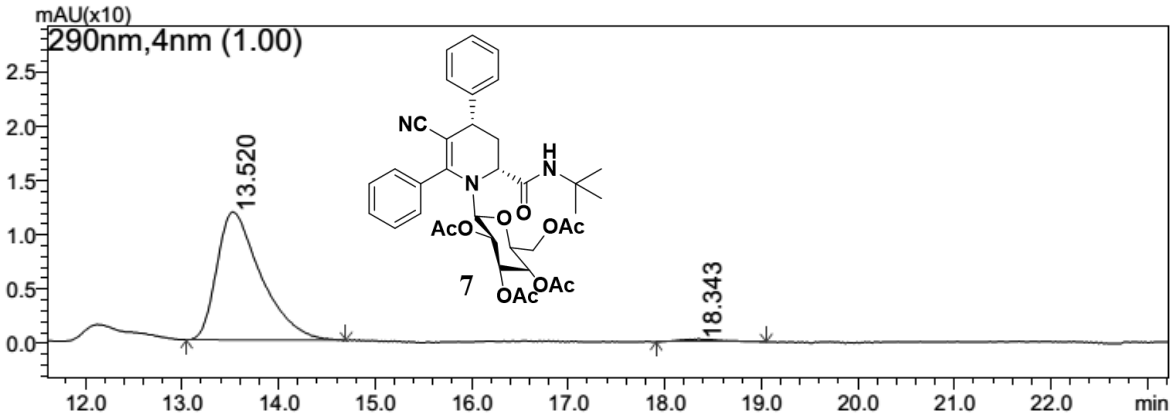
PDA Ch2 300nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.688	11613	454	4.027	4.048
2	12.037	276761	10759	95.973	95.952
Total		288374	11213	100.000	100.000

Chromatogram of Compound 7

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel AS-H column (*n*-hexane/*i*PrOH 90:10) at 1.0 mL/min, UV-detection at λ = 290 nm:

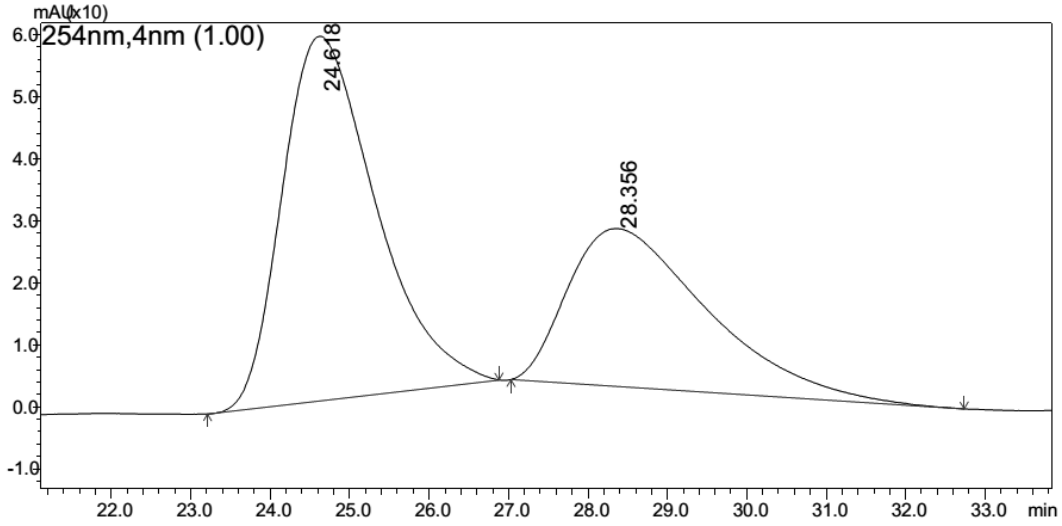


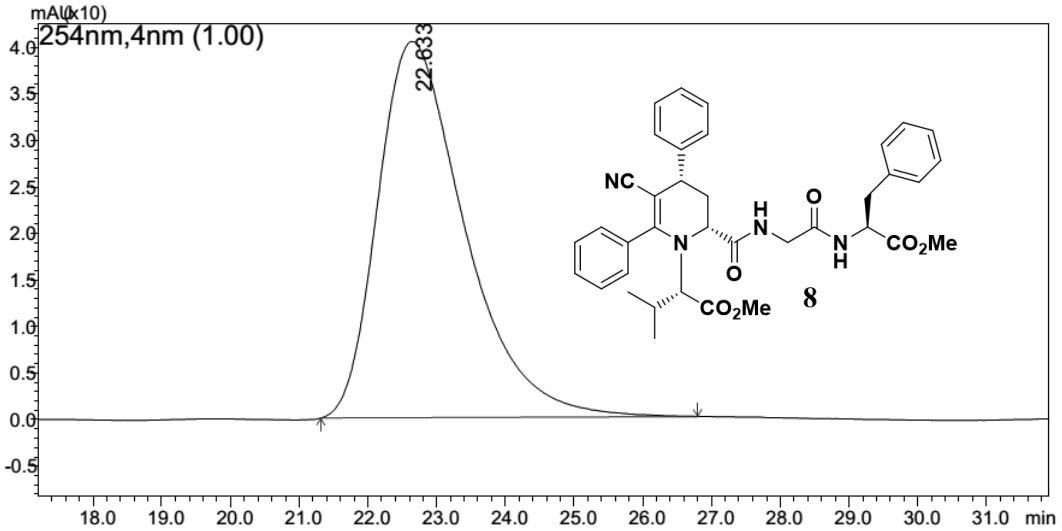


Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.520	375306	11800	97.902	97.390
2	18.343	8044	316	2.098	2.610
Total		383351	12116	100.000	100.000

Chromatogram of Compound 8

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 1.0 mL/min, UV-detection at λ = 254 nm:



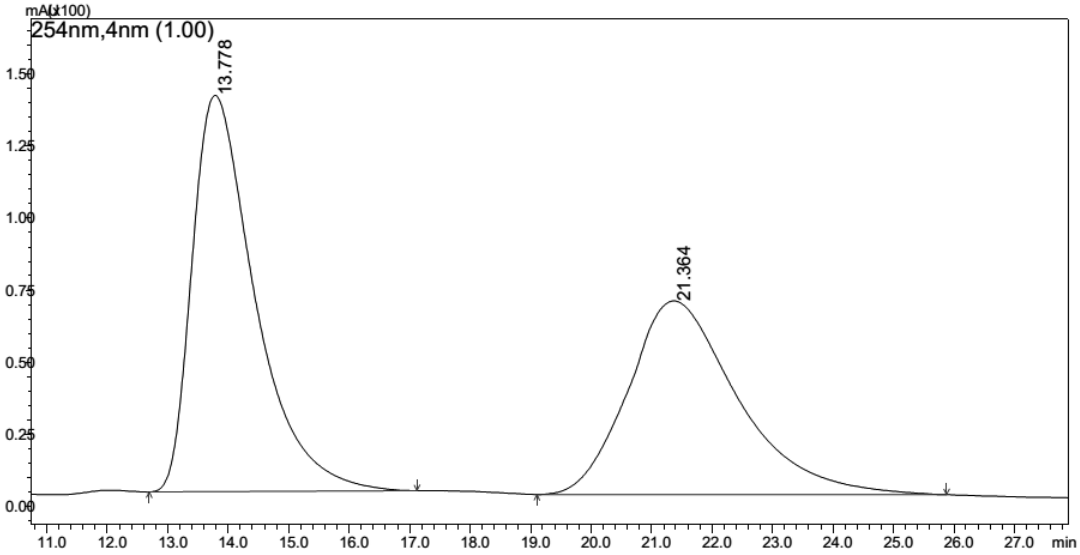


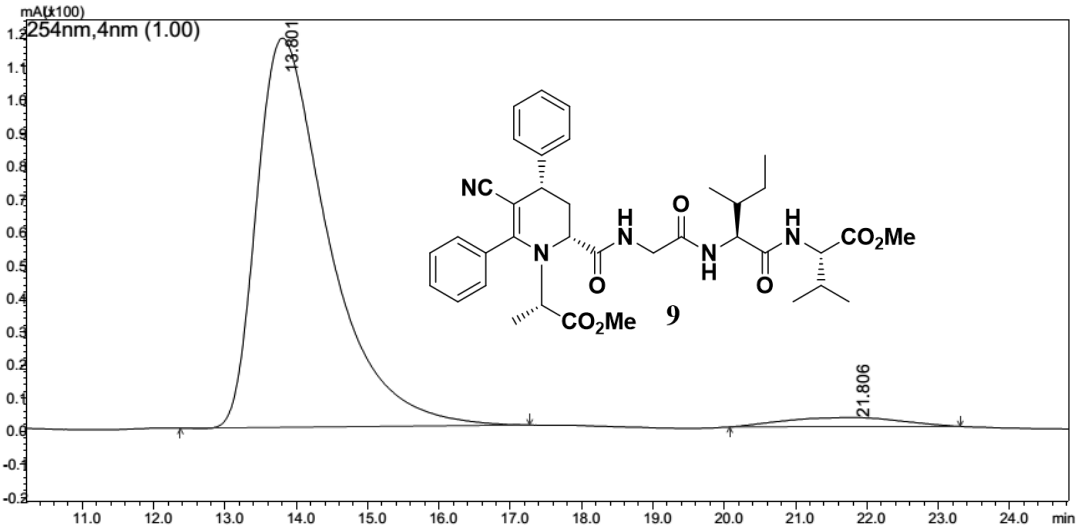
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	22.633	3562657	40413	100.000	100.000
Total		3562657	40413	100.000	100.000

Chromatogram of Compound 9

The diastereomeric ratio was determined by chiral stationary phase HPLC using a Chiralcel OD-H column (*n*-hexane/*i*PrOH 90:10) at 0.7 mL/min, UV-detection at λ = 254 nm:





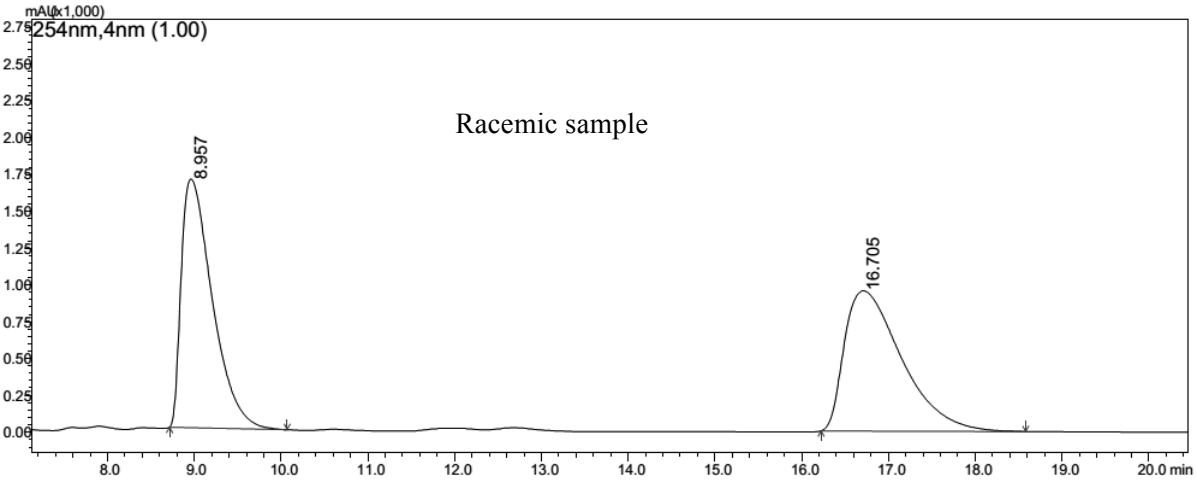
9

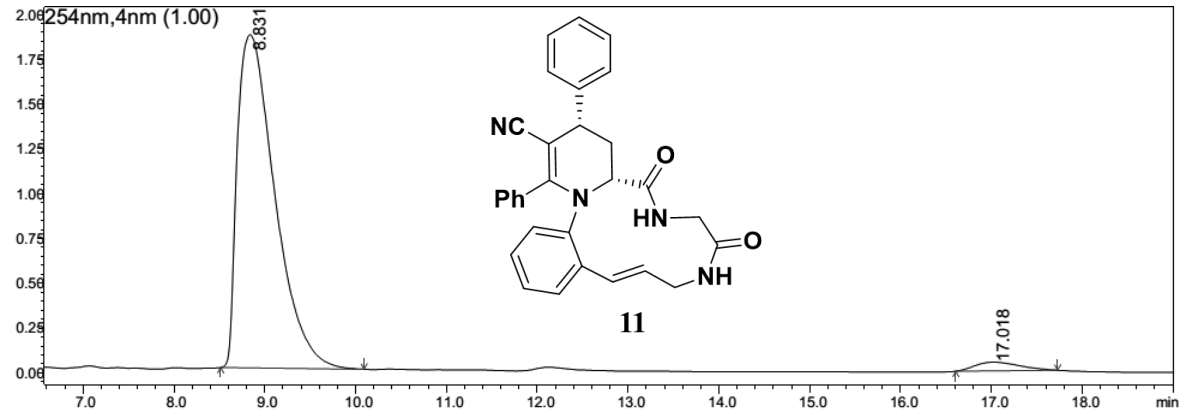
PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.801	8226330	117559	96.334	97.649
2	21.806	313044	2830	3.666	2.351
Total		8539374	120389	100.000	100.000

Chromatogram of Compound 11

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*PrOH 90:10) at 1.0 mL/min, UV-detection at λ = 254 nm:



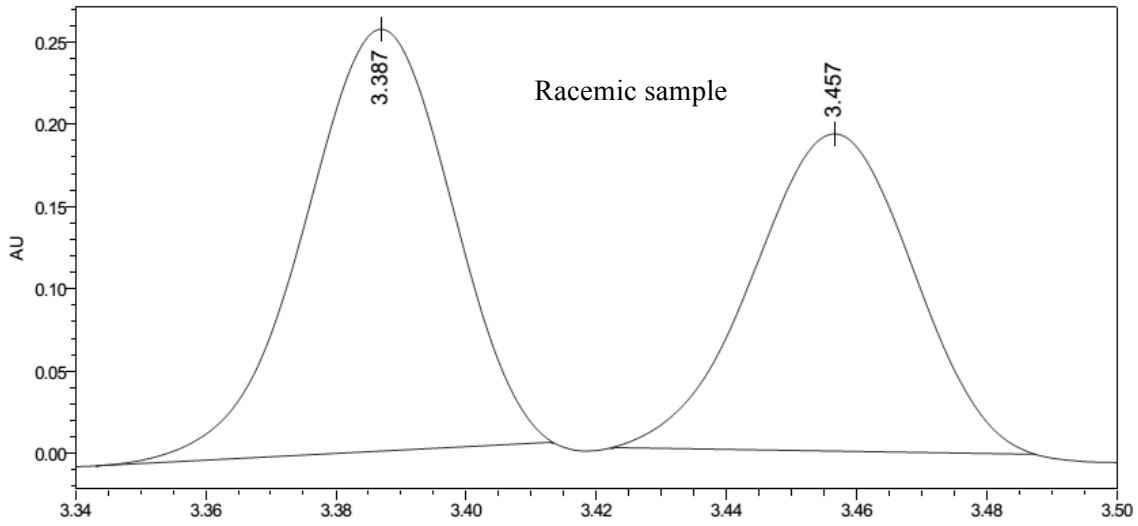


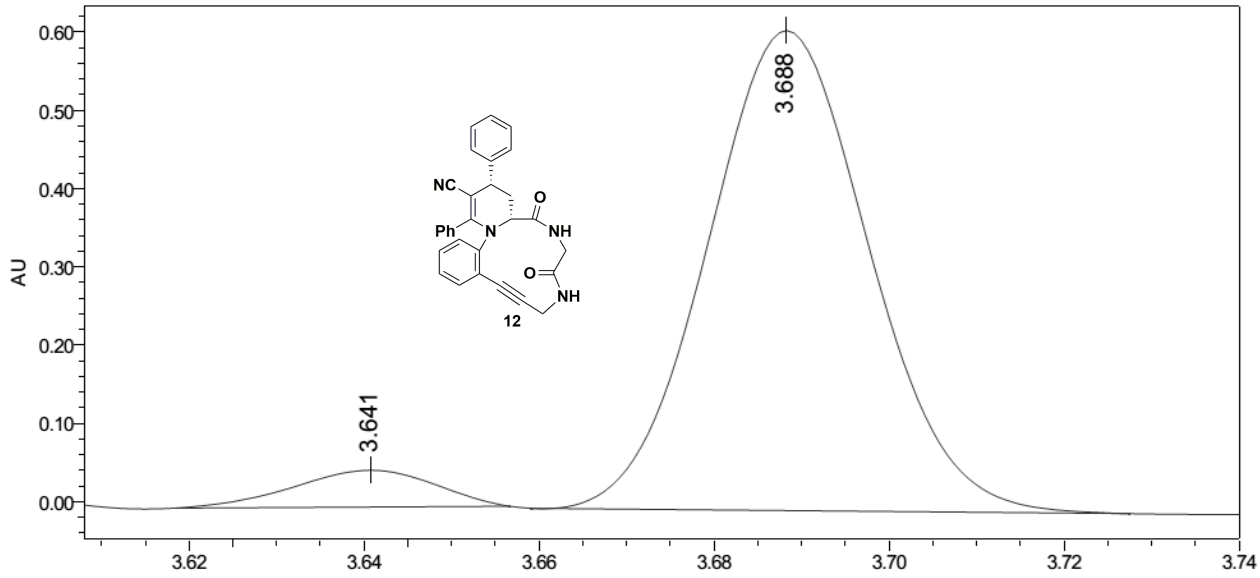
11

Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.831	5342503	185967	96.996	97.443
2	17.018	165464	4879	3.004	2.557
Total		5507967	190847	100.000	100.000

Chromatogram of Compound 12

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel IA column (*i*PrOH) at 1.0 mL/min, UV-detection at λ = 254 nm:



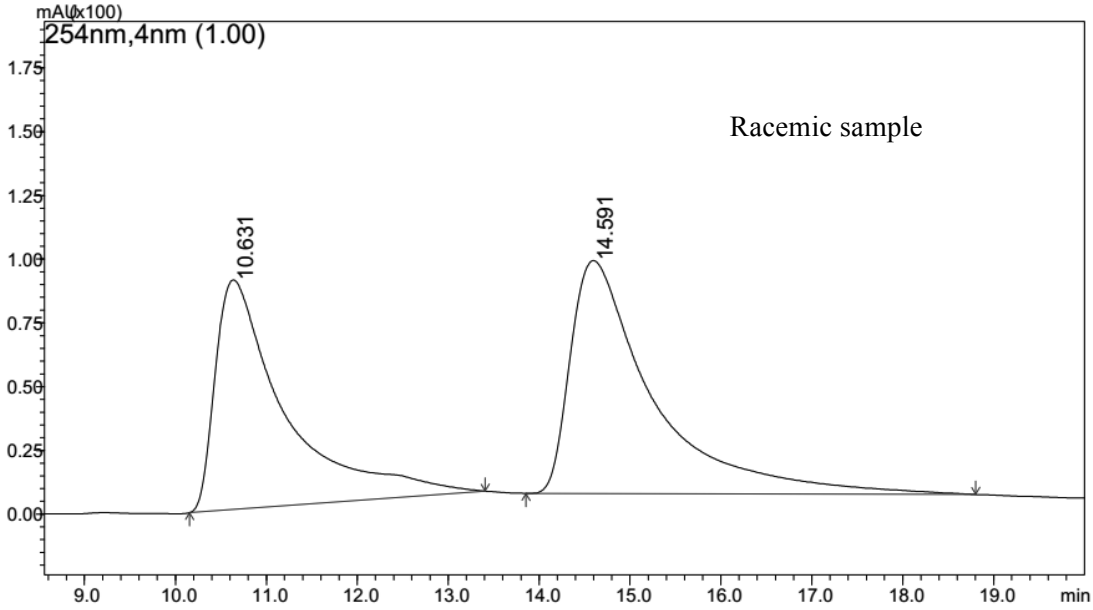


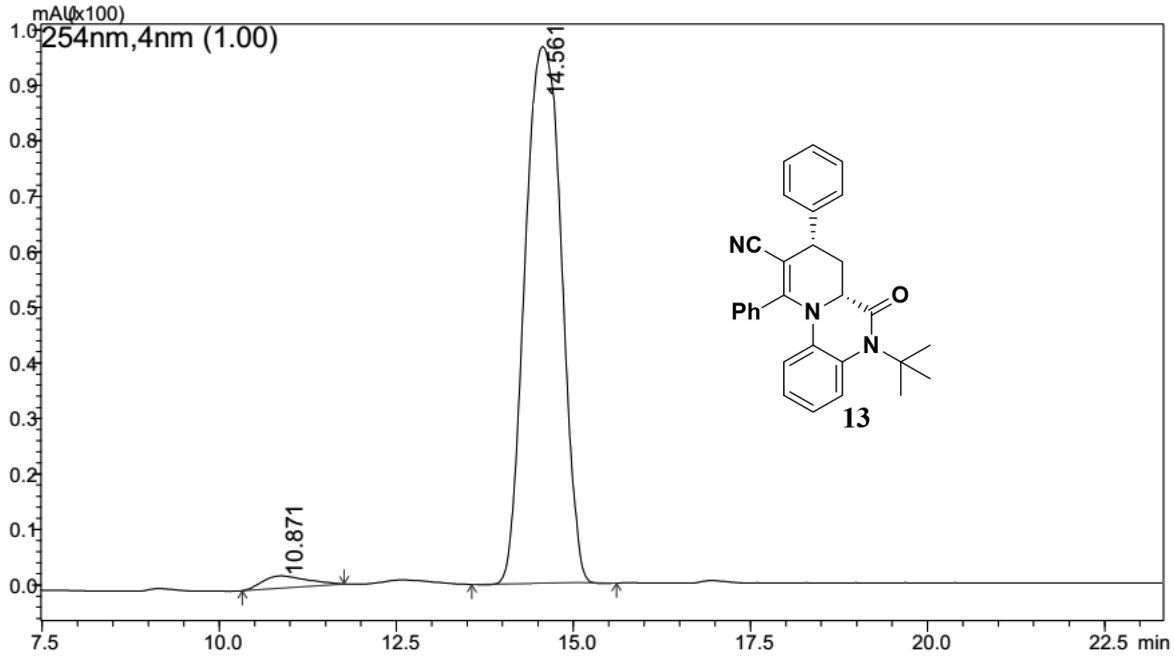
Peak Results

	RT	Area	Height	% Area
1	3.641	52635	46881	6.28
2	3.688	785515	613678	93.72

Chromatogram of Compound 13

The enantiomeric excess was determined by chiral stationary phase HPLC using a Chiralcel OJ-H column (*n*-hexane/*i*-PrOH 80:20) at 0.7 mL/min, UV-detection at λ= 254 nm: t_R (minor)= 10.6 min, t_R (major)= 14.6 min, ee=97%.





PDA Ch1 254nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.871	95227	2196	1.347	2.220
2	14.561	6972468	96704	98.653	97.780
Total		7067695	98900	100.000	100.000