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Supporting Information

Catalytic Enantioselective Synthesis of α-Aryl α-Hydrazino Esters and Amides

Marta Velázquez,[a] Saúl Alberca,[a] Javier Iglesias-Sigüenza,[a] Rosario Fernández *,[a] José M. Lassaletta*,[b] and David Monge*,[a]

[a]Departamento de Química Orgánica, Universidad de Sevilla, C/Prof. García González, 1, 41012 Sevilla, Spain; Fax: +34 954624960; Tel: +34 954551518; E-mail: dmonge@us.es, ffernaan@us.es

[b]Instituto de Investigaciones Químicas (CSIC-US, Américo Vespucio 49, E-41092 Sevilla, Spain; Fax: +34 954460565; Tel: +34 954489563; E-mail: jmlassa@iiq.csic.es

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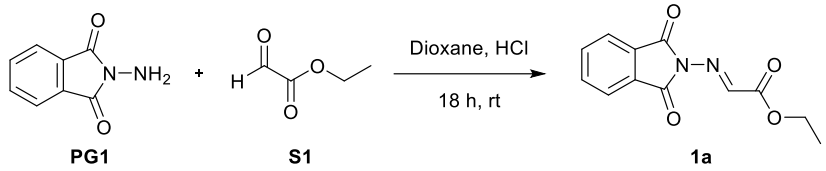
1. General information

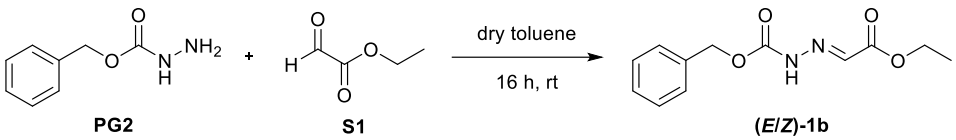
^{1}H NMR spectra were recorded at 300 MHz, 500 MHz or 700 MHz (internal reference; $CDCl_3$ = 7.26; CD_2Cl_2 = 5.32; Acetone-d^6 = 2.05; DMSO-d^6 = 2.50); ^{13}C NMR spectra were recorded at 75.5 MHz, 126 MHz or 176 MHz (internal reference; $CDCl_3$ = 77.16; CD_2Cl_2 = 54.00; Acetone-d^6 = 29.84; DMSO-d^6 = 39.52). Column chromatography was performed on silica gel (Merck Kieselgel 40-60). Analytical TLC was performed on aluminum backed plates (1.5 × 5 cm) pre-coated (0.25 mm) with silica gel (Merck, Silica Gel 60 F_{254}). Semipreparative TLC was performed on glass backed plates (5 x 10 cm) pre-coated (0.25 mm) with silica gel (Merck, Silica Gel 60 F_{254}). Compounds were visualized by exposure to UV light or/and by dipping the plates in solutions of ninhydrin, vainilline or phosphomolibdic acid stains following by heating. Melting points were recorded in a metal block and are uncorrected. Optical rotations were measured on a Perkin-Elmer 341 MC polarimeter. The enantiomeric excess (ee) of the products was determined by chiral stationary phase HPLC (Daicel Chiralpack IA, IB, IE). Dichloroethane was purchased from Acros Organics (99.5% Extra Dry, Over Molecular Sieves, <0.005% H_2O). Unless otherwise noted, commercially available reagents were used without further purification. Pyridine bis-hydrazone **IIa**,[1] Bis-hydrazone **IIb**,[2] Bis-hydrazone **IIc**,[3] Phosphino-hydrazone **IId**,[4] Pyridine-hydrazones (**L2-5**; **L7-9**),[5] Pyridine-hydrazone **L6**,[6] hydrazone **(*E*)-1h**,[7] hydrazone **(*E*)-1j**,[8] were synthesized according to literature procedures.

2. Synthesis of ethyl 2-[(1,3-dioxoisoindolin-2-yl)imino]acetate 1a



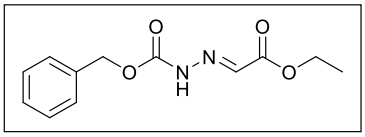
To a stirred solution of *N*-aminophthalimide **(PG1)** (0.72 g, 4 mmol) and ethyl glyoxalate (50% in toluene) **(S1)** (2.5 mL, 12 mmol) in 1,4-dioxane (64 mL) was added concentrated hydrochloric acid (2 drops) at room temperature. After the mixture was stirred for 18 hours, the solvent was evaporated under reduced pressure and the residue purified by flash chromatography on silica gel (*n*-hexane/EtOAc 3/2) to give **1a** as a white solid (0.73 g, 74%). **Mp**: 119-121 °C, **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 9.06 (s, 1H), 7.98 – 7.94 (m, 2H), 7.86 – 7.81 (m, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 1.39 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 164.1, 162.9, 145.8, 135.3, 129.9, 124.4, 62.1, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{12}H_{10}O_4N_2Na$ [M^++Na] 269.0533, found 269.0535.

3. General procedure for the synthesis of hydrazones 1b

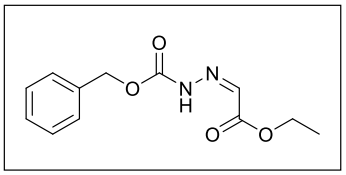


Ethyl glyoxalate (50% in toluene) **(S1)** (2.5 mL, 12 mmol) was added to a stirred solution of benzyl carbazate **(PG2)** (0.68 g, 4 mmol) in dry toluene (8 mL). The reaction mixture was stirred under Ar at room temperature for 16 hours. The solvent was removed under reduced pressure and the residue purified by flash chromatography on silica gel (*n*-hexane/EtOAc 3/2) to afford the products.

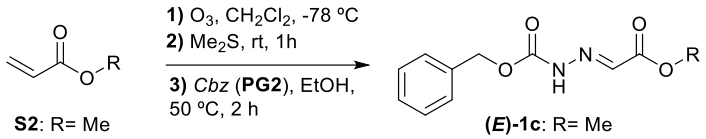
Benzyl (*E*)-2-(2-ethoxy-2-oxoethylidene)hydrazine-1-carboxylate (*E*)-1b: white solid (0.71 g, 71%). **Mp**: 63-65 °C, **^{1}H-NMR** (500 MHz, Acetone-d^6): δ 10.62 (br s, 1H), 7.54 (s, 1H), 7.43 – 7.32 (m, 5H), 5.24 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, Acetone-d^6): δ 163.7, 153.7, 137.2, 135.5, 129.3, 129.08, 129.06, 67.9, 61.5, 14.5. **HRMS** (ESI): *m/z* calcd for $C_{12}H_{14}O_4N_2Na$ [M^++Na] 273.0846, found 273.0849.



Benzyl (*Z*)-2-(2-ethoxy-2-oxoethylidene)hydrazine-1-carboxylate (*Z*)-1b: colourless oil (0.17 g, 17%).**^{1}H-NMR** (500 MHz, Acetone-d^6): δ11.99 (br s, 1H), 7.49 – 7.33 (m, 5H), 6.86 (s, 1H), 5.27 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 1.31 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, Acetone-d^6): δ 162.9, 153.4, 137.0, 129.4, 129.17, 129.15, 128.3, 68.2, 62.2, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{12}H_{14}O_4N_2Na$ [M^++Na] 273.0846, found 273.0846.



4. General procedure for the synthesis of hydrazones (*E*)-1c, (*E*)-1e and (*E*)-1f

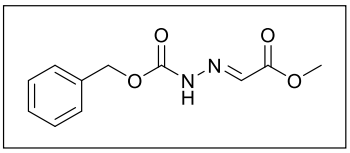


S2: R= Me
S3: R= ^{i}Pr
S4: R= ^{t}Bu

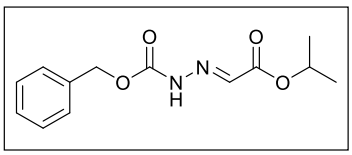
(*E*)-**1c**: R= Me
(*E*)-**1e**: R= ^{i}Pr
(*E*)-**1f**: R= ^{t}Bu

To a solution of the corresponding acrylate **(S2-4)** (2 mmol) in CH_2Cl_2 (3 mL) was bubbled ozone at -78 ºC for 20 min. After this time, Me_2S (176 µL, 2.4 mmol) was added and the reaction mixture was stirred for 1 hour at room temperature. The solvent was removed under reduced pressure and the residue was dissolved in EtOH (5 mL). Benzyl carbazate **(PG2)** (0.27 g, 1.6 mmol) was added and the resulting mixture was stirred under Ar at 50 °C for 2 hours. The solvent was removed under reduced pressure and the residue purified by flash chromatography on silica gel to afford the corresponding products **(*E*)-1c**, **(*E*)-1e** and **(*E*)-1f**.

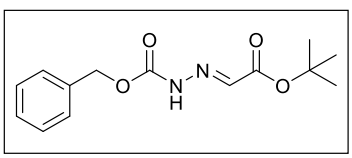
Benzyl (*E*)-2-(2-methoxy-2-oxoethylidene)hydrazine-1-carboxylate (*E*)-1c: Following the general procedure **4**, starting from methyl acrylate **S2** (184 µL, 2 mmol), **(*E*)-1c** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/2) as a white solid (0.3 g, 79%). **Mp**: 127-129 °C, **^{1}H-NMR** (300 MHz, Acetone-d^6): δ 10.67 (br s, 1H), 7.53 (s, 1H), 7.44 – 7.32 (m, 5H), 5.24 (s, 2H), 3.76 (s, 3H). **^{13}C-NMR** (75.5 MHz, Acetone-d^6): δ 164.6, 164.2, 153.7, 137.1, 135.1, 129.3, 129.1, 67.9, 52.2. **HRMS** (ESI): *m/z* calcd for $C_{11}H_{12}O_4N_2Na$ [M^++Na] 259.0689, found 259.0691.



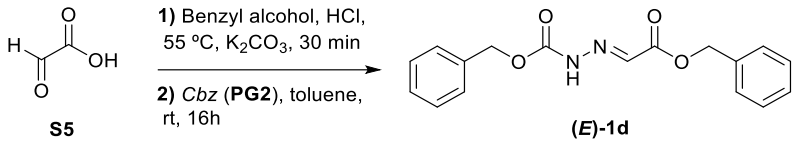
Benzyl (*E*)-2-(2-isopropoxy-2-oxoethylidene)hydrazine-1-carboxylate (*E*)-1e: Following the general procedure **4**, starting from isopropyl acrylate **S3** (256 µL, 2 mmol), **(*E*)-1e** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 4/1) as a white solid (0.27 g, 65%). **Mp**: 85-87 °C, **^{1}H-NMR** (300 MHz, Acetone-d^6): δ 10.64 (br s, 1H), 7.52 (s, 1H), 7.44 – 7.30 (m, 5H), 5.23 (s, 2H), 5.13 – 5.05 (m, 1H), 1.27 (d, *J* = 6.3 Hz, 6H). **^{13}C-NMR** (75.5 MHz, Acetone-d^6): δ 163.2, 153.7, 137.1, 135.9, 129.3, 129.0, 69.2, 67.8, 21.9. **HRMS** (ESI): *m/z* calcd for $C_{13}H_{16}O_4N_2Na$ [M^++Na] 287.1002, found 287.1004.



Benzyl (*E*)-2-(2-(*tert*-butoxy)-2-oxoethylidene)hydrazine-1-carboxylate (*E*)-1f: Following the general procedure **4**, starting from *tert*-butyl acrylate **S4** (290 µL, 2 mmol), **(*E*)-1f** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 4/1) as a white solid (0.27 g, 61%). **Mp**: 89-91 °C, **^{1}H-NMR** (300 MHz, Acetone-d^6): δ 10.57 (br s, 1H), 7.46 – 7.30 (m, 6H), 5.22 (s, 2H), 1.5 (s, 9H). **^{13}C-NMR** (75.5 MHz, Acetone-d^6): δ 162.8, 153.7, 137.2, 136.9, 129.3, 129.0, 82.0, 67.7, 28.2. **HRMS** (ESI): *m/z* calcd for $C_{14}H_{18}O_4N_2Na$ [M^++Na] 301.1159, found 301.1159.

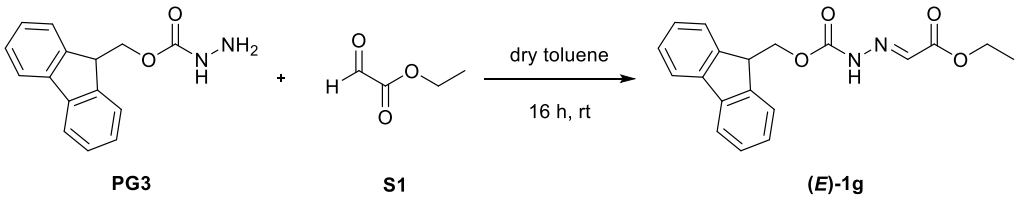


5. Synthesis of benzyl (*E*)-2-[2-(benzyloxy)-2-oxoethylidene]hydrazine-1-carboxylate (*E*)-1d



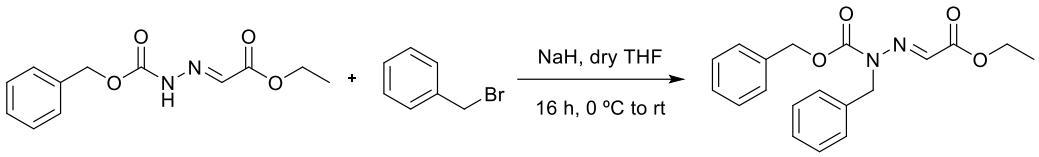
Benzyl alcohol (3.4 mL, 32.8 mmol) was added to a stirred solution of glyoxylic acid (50% in H_2O) **(S5)** (1.4 mL, 12.9 mmol) and HCl (37%) (0.1 mL, 1.3 mmol). The reaction mixture was stirred at 50 °C for 30 minutes. After this time, the reaction crude was neutralized with K_2CO_3 and extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was dissolved in toluene (8 mL) and was added benzyl carbazate **(PG2)** (0.68 g, 4 mmol). The reaction mixture was stirred at room temperature for 16 hours. Then, the solvent was removed under reduced pressure and the residue purified by flash chromatography (*n*-hexane/EtOAc 3/1) to give **(*E*)-1d** as a white solid (0.88 g, 71%). **Mp**: 102-104 °C, **^{1}H-NMR** (700 MHz, Acetone-d^6): δ 10.72 (br s, 1H), 7.59 (s, 1H), 7.46 – 7.32 (m, 10 H), 5.27 (s, 2H), 5.23 (s, 2H). **^{13}C-NMR** (176 MHz, Acetone-d^6): δ 163.6, 153.6, 137.1, 136.9, 135.1, 129.30, 129.29, 129.2, 129.05, 129.03, 67.9, 67.1. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{16}O_4N_2Na$ [M^++Na] 335.1002, found 335.1002.

6. Synthesis of (9*H*-Fluoren-9-yl)methyl (*E*)-2-(2-ethoxy-2-oxoethylidene)hydrazine-1-carboxylate (*E*)-1g



Ethyl glyoxalate (50% in toluene) **(S1)** (0.5 mL, 2.4 mmol) was added to a stirred solution of fluorenyl carbazate **(PG3)** (0.62 g, 2.4 mmol) in dry toluene (15 mL). The reaction mixture was stirred under Ar at room temperature for 16 hours. The solvent was removed under reduced pressure and the residue washed with Et_2O (3 x 5 mL) and dried in *vacuo* to give **(*E*)-1g** as a white solid (0.82 g, 99%). **Mp**: 144-146 °C, **^{1}H-NMR** (300 MHz, DMSO-d^6): δ 11.72 (s, 1H), 7.90 (d, *J* = 7.4 Hz, 2H), 7.73 (d, *J* = 7.3 Hz, 2H), 7.45 – 7.31 (m, 5H), 4.57 (d, *J* = 5.1 Hz, 2H), 4.32 (t, *J* = 6.4 Hz, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 1.25 (s, 3H). **^{13}C-NMR** (75.5 MHz, DMSO-d^6): δ 162.8, 152.9, 143.5, 140.8, 134.5, 127.7, 127.1, 125.1, 120.2, 66.2, 60.7, 46.5, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{18}O_4N_2Na$ [M^++Na] 361.1159, found 361.1155.

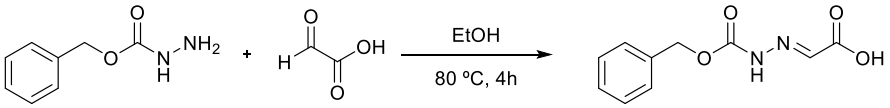
7. Synthesis of benzyl (*E*)-1-benzyl-2-(2-ethoxy-2-oxoethylidene)hydrazine-1-carboxylate (*E*)-1i



(*E*)-1b (*E*)-1i

Sodium hydride (0.96 g, 4 mmol) was added to a stirred solution of **(*E*)-1b** (0.4 g, 1.6 mmol) in dry THF (15 mL). The reaction mixture was stirred under Ar at room temperature for 1 hour. After this time, benzyl bromide (0.36 mL, 3 mmol) was slowly added at 0 °C. The mixture was allowed to warm to room temperature and stirred overnight. Then, was diluted with H_2O (25 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were washed with brine (2 x 20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography (Toluene/EtOAc 20/1) to give **(*E*)-1i** as a white solid (0.12 g, 22%). **Mp**: 116-118 °C, **^{1}H-NMR** (300 MHz, Acetone-d^6): δ 7.51 – 7.47 (m, 2H), 7.43 – 7.24 (m, 8H), 7.13 (s, 1H), 5.39 (s, 2H), 5.27 (s, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.23 (t, *J* = 7.1 Hz, 3H).**^{13}C-NMR** (75.5 MHz, Acetone-d^6): δ 163.4, 155.1, 137.2, 135.4, 131.9, 129.8, 129.3, 129.0, 128.8, 128.4, 127.3, 69.3, 61.5, 14.4. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{20}O_4N_2Na$ [M^++Na] 363.1315, found 363.1311.

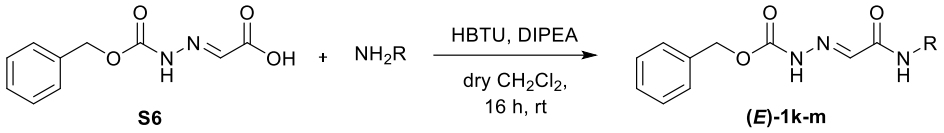
8. Synthesis of hydrazone S6



PG2 S5 S6

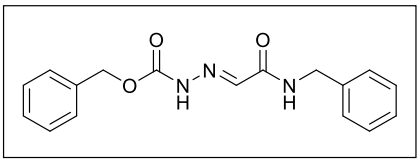
Glyoxylic acid (50% in H_2O) **(S5)** (1.1 mL, 10 mmol) was added to a stirred solution of benzyl carbazate **(PG2)** (1.7 g, 10 mmol) in EtOH (14 mL). The reaction mixture was stirred at 80 °C for 4 hours. The solvent was removed under reduced pressure and the residue washed with Et_2O (3 x 5 mL) and dried in *vacuo* to give **S6** as a white solid (2.2 g, 98%). **Mp**: 196-198 °C, **^{1}H-NMR** (500 MHz, DMSO-d^6): δ 12.98 (br s, 1H), 11.67 (br s, 1H), 7.42 – 7.33 (m, 6H), 5.20 (s, 2H). **^{13}C-NMR** (126 MHz, DMSO-d^6): δ 164.4, 153.0, 136.0, 135.5, 128.5, 128.24, 128.19, 66.6. **HRMS** (ESI): *m/z* calcd for $C_{10}H_{10}O_4N_2Na$ [M^++Na] 245.0533, found 245.0532.

9. General procedure for the synthesis of hydrazones (*E*)-1k, (*E*)-1l and (*E*)-1m

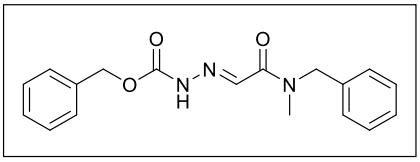


Primary or secondary amine (3.3 mmol) was added to a solution of HBTU (1.28 g, 3.3 mmol), hydrazone **S6** (0.66 g, 3 mmol) and diisopropylethylamine (1.3 mL, 7.2 mmol) in dry CH_2Cl_2 (45 mL). The resulting mixture was stirred under Ar at room temperature for 16 hours. The reaction was diluted with EtOAc (65 mL) and washed with HCl (0.5 M, 2 x 55 mL), saturated aqueous $NaHCO_3$ (2 x 55 mL) and brine (2 x 55 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel to afford the corresponding products **(*E*)-1k, (*E*)-1l and (*E*)-1m**.

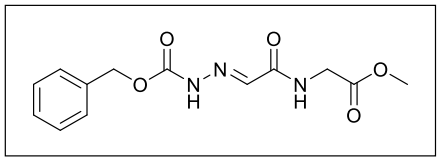
Benzyl (*E*)-2-[2-(benzylamino)-2-oxoethylidene]hydrazine-1-carboxylate (*E*)-1k: Following the general procedure **9**, starting from benzylamine (0.4 mL, 3.3 mmol), **(*E*)-1k** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 1/1) as a white solid (0.50 g, 54%). **Mp**: 154-156 °C, **^{1}H-NMR** (500 MHz, DMSO-d^6): δ 11.58 (br s, 1H), 8.67 (t, *J* = 6.2 Hz, 1H), 7.44 – 7.22 (m, 11H), 5.20 (s, 2H), 4.36 (d, *J* = 6.2 Hz, 2H). **^{13}C-NMR** (126 MHz, DMSO-d^6): δ 162.5, 153.1, 139.2, 138.5, 136.1, 128.4, 128.21, 128.15, 128.1, 127.3, 126.8, 66.4, 42.1. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{17}O_3N_3Na$ [M^++Na] 334.1162 found 334.1161.



Benzyl (*E*)-2-[2-(benzyl(methyl)amino]-2-oxoethylidene)hydrazine-1-carboxylate (*E*)-1l: Following the general procedure **9**, starting from *N*-benzylmethylamine (0.45 mL, 3.3 mmol), **(*E*)-1l** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 1/2) as a white solid (0.52 g, 53%). **Mp**: 102-104 °C, **^{1}H-NMR** (500 MHz, DMSO-d^6; the compound exists as 1,3:1 mixture of amide rotamers). *Signals corresponding to the major rotamer*: δ 13.02 (br s, 1H), 7.48 (d, *J* = 9.2 Hz, 1H), 7.42 – 7.13 (m, 10H), 5.21 (d, *J* = 4.0 Hz, 2H), 4.56 (s, 2H), 3.12 (s, 3H). *Representative signals to the corresponding minor rotamer*: δ 4.81 (s, 2H), 2.90 (s, 3H). **^{13}C-NMR** (126 MHz, DMSO-d^6): δ 162.6, 162.1, 152.7, 136.6, 136.4, 135.9, 128.7, 128.5, 128.4, 128.1, 128.04, 128.02, 127.7, 127.5, 127.3, 126.7, 66.7, 52.4, 50.0, 35.0, 33.5. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{19}O_3N_3Na$ [M^++Na] 348.1317 found 348.1319.

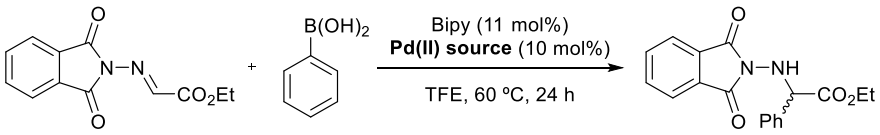


Benzyl (*E*)-2-{2-[(2-methoxy-2-oxoethyl)amino]-2-oxoethylidene}hydrazine-1-carboxylate



(*E*)-1m: Following the general procedure **9**, starting from glycine methyl ester hydrochloride (0.42 g, 3.3 mmol), **(*E*)-1l** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 1/1) as a white solid (0.59 g, 67%). **Mp**: 152-154 °C. **^{1}H-NMR** (500 MHz, DMSO-d^{6}; the compound exists as 16:1 mixture of amide rotamers). *Signals corresponding to the major rotamer*: δ 11.62 (br s, 1H), 8.43 (t, *J* = 6.0 Hz, 1H), 7.35 – 7.32 (m, 6H), 5.21 (s, 2H), 3.94 (d, *J* = 6.1 Hz, 2H), 3.64 (s, 3H). *Representative signals to the corresponding minor rotamer*: δ 12.98 (br s, 1H), 9.40 (t, *J* = 5.8 Hz, 1H), 7.03 (s, 1H), 5.20 (s, 2H), 4.00 (d, *J* = 5.9 Hz, 2H), 3.66 (s, 3H). **^{13}C-NMR** (126 MHz, DMSO-d^{6}; *signals corresponding to both rotamers*): δ 170.0, 169.4, 163.1, 163.0, 153.0, 152.6, 137.7, 136.1, 135.9, 128.5, 128.2, 128.1, 66.8, 66.5, 51.9, 51.7, 40.6. **HRMS** (ESI): *m/z* calcd for $C_{13}H_{15}O_5N_3Na$ [M^++Na] 316.0904, found 316.0904.

10. Optimization of Pd(II) source for 1,2-addition of phenyl boronic acid (2a) to hydrazone 1a



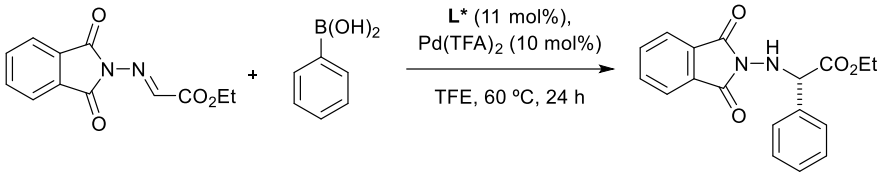
1a **2a** **3aa (rac)**

A test tube was charged with Pd(II) source (0.02 mmol), bipyridine (3 mg, 0.022 mmol), hydrazone **1a** (49 mg, 0.2 mmol), phenylboronic acid **2a** (37 mg, 0.3 mmol) and TFE (0.5 mL). The mixture was stirred at 60 °C for 24 h. Yields were determined by the ^{1}H-NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard.

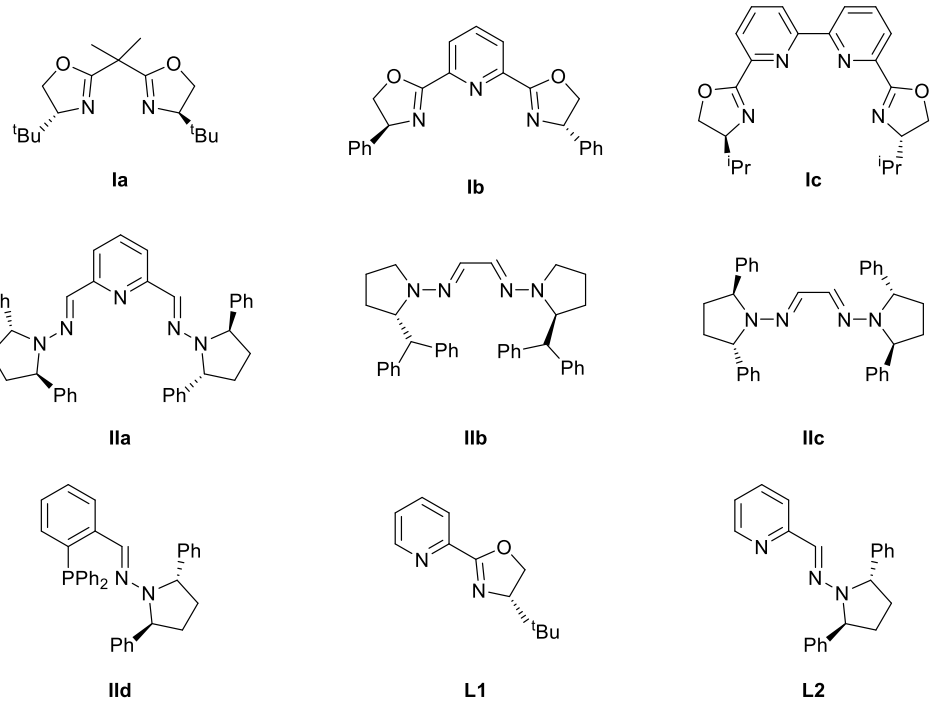
Table S1

Entry	Pd(II) source	Yield (%)
1	$PdCl_2$	24
2	$Pd(OAc)_2$	19
3	**$Pd(TFA)_2$**	**87**

11. Screening of chiral ligands for 1,2-addition of phenyl boronic acid (2a) to hydrazone 1a



Ligands

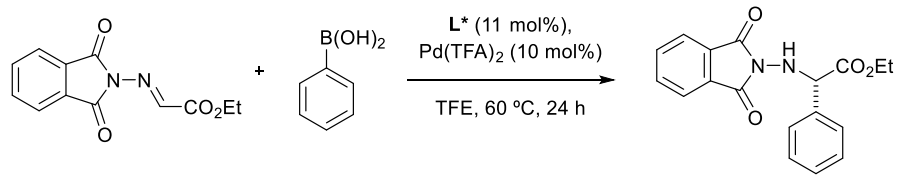


A test tube was charged with $Pd(TFA)_2$ (7 mg, 0.02 mmol), **L*** (0.022 mmol), hydrazone **1a** (49 mg, 0.2 mmol), phenylboronic acid **2a** (37 mg, 0.3 mmol) and TFE (0.5 mL). The mixture was stirred at 60 °C for 24 h. Yields were determined by the ^{1}H-NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. Enantiomeric excess (ee) was determined by HPLC analysis.

Table S2

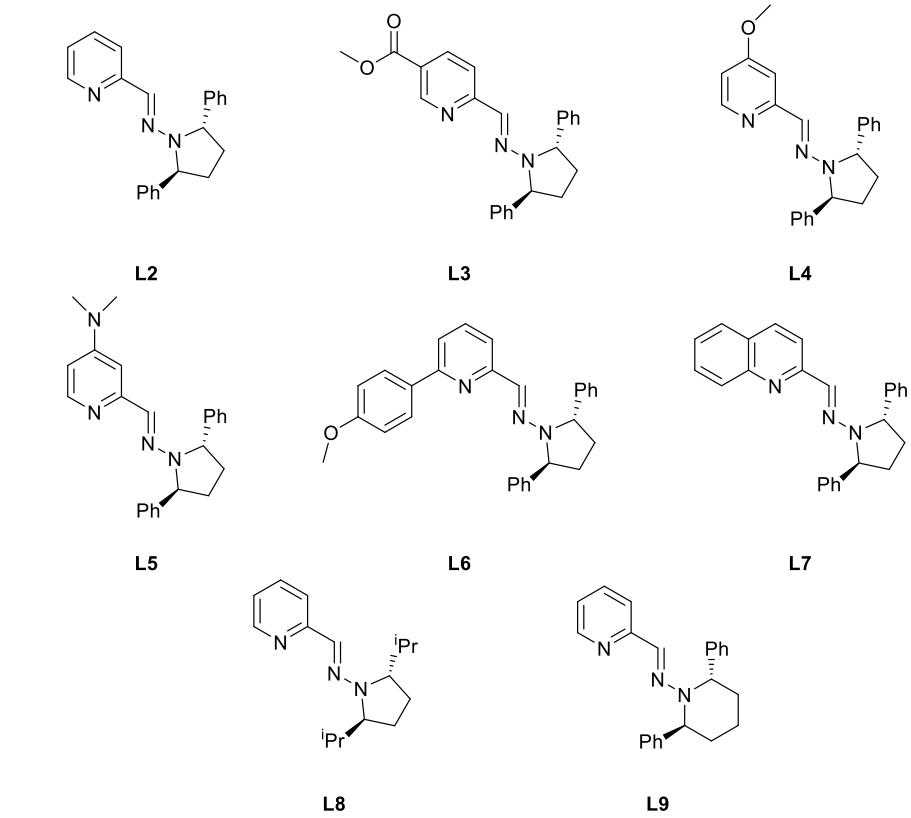
Entry	Ligand	Yield (%)	ee (%)
1	Ia	n.r	-
2	Ib	n.r	-
3	Ic	n.r	-
4	IIa	<10	-
5	IIb	17	-
6	IIc	12	-
7	IId	<10	-
8	L1	52	55
9	**L2**	**82**	**58**

12. Optimization of the structure of pyridine-hydrazone ligands for 1,2-addition of phenyl boronic acid (2a) to hydrazone 1a



1a **2a** **3aa**

Ligands



L2 **L3** **L4**

L5 **L6** **L7**

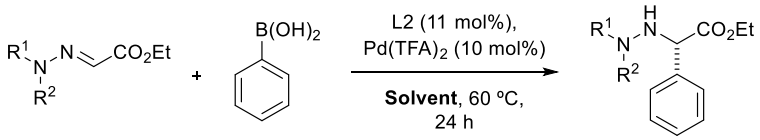
L8 **L9**

A test tube was charged with $Pd(TFA)_2$ (7 mg, 0.02 mmol), **L*** (0.022 mmol), hydrazone **1a** (49 mg, 0.2 mmol), phenylboronic acid **2a** (37 mg, 0.3 mmol) and TFE (0.5 mL). The mixture was stirred at 60 °C for 24 h. Yields were determined by the ^{1}H-NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. Enantiomeric excess (ee) was determined by HPLC analysis.

Table S3

Entry	Ligand	Yield (%)	ee (%)
1	**L2**	**82**	**58**
2	**L3**	**86**	**62**
3	L4	73	50
4	L5	33	38
5	L6	n.r	-
6	L7	17	Rac
7	L8	<10	-
8	L9	75	25

13. General procedure for optimization of 1,2-addition of phenyl boronic acid (2a) to hydrazones 1a and 1b



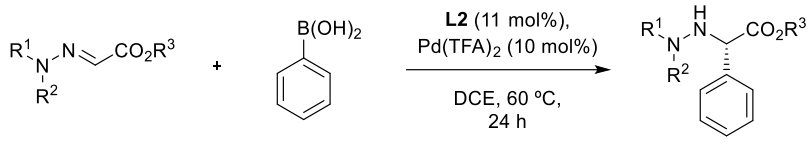
A test tube was charged with $Pd(TFA)_2$ (7 mg, 0.02 mmol), **L2** (7 mg, 0.022 mmol), hydrazone **1a,b** (0.2 mmol), phenylboronic acid **2a** (37 mg, 0.3 mmol) and the corresponding solvent (0.5 mL). The mixture was stirred at 60 °C for 24 h. Yields were determined by the ^{1}H-NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. Enantiomeric excess (ee) was determined by HPLC analysis.

Racemic products were synthesized in an analogous manner using $Pd(TFA)_2$ (10 mol%) and bipyridine (11 mol%) at 60 °C.

Table S4

Entry	1	Solvent	Yield (%)	ee (%)
1	**1a**	**TFE**	**82**	**58**
2	1a	DCE	49	48
3	1a	Toluene	29	56
4	1a	Trifluorotoluene	44	55
5	1a	Dioxane	n.r	-
6	(*E*)-1b	TFE	56	75
7	**(*E*)-1b**	**DCE**	**83**	**93**

14. Screening for optimal hydrazone structure



(*E*)-**1b**: R^1 = Cbz, R^2 = H, R^3 = Et
(*E*)-**1c**: R^1 = Cbz, R^2 = H, R^3 = Me
(*E*)-**1d**: R^1 = Cbz, R^2 = H, R^3 = Bn
(*E*)-**1e**: R^1 = Cbz, R^2 = H, R^3 = ^{i}Pr
(*E*)-**1f**: R^1 = Cbz, R^2 = H, R^3 = ^{t}Bu
(*E*)-**1g**: R^1 = Fmoc, R^2 = H, R^3 = Et
(*E*)-**1h**: R^1 = Boc, R^2 = H, R^3 = Et
(*E*)-**1i**: R^1 = Cbz, R^2 = Bn, R^3 = Et
(*E*)-**1j**: R^1 = PMP, R^2 = H, R^3 = Et

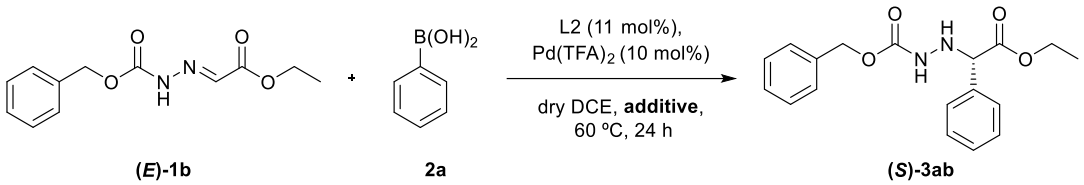
2a

(*S*)-**3**

A test tube was charged with $Pd(TFA)_2$ (7 mg, 0.02 mmol), **L2** (7 mg, 0.022 mmol), hydrazone **1b-j** (0.2 mmol), phenylboronic acid **2a** (37 mg, 0.3 mmol) and DCE (0.5 mL). The mixture was stirred at 60 °C for 24 h. Then, the solvent was removed under reduced pressure and the residue purified by flash chromatography to afford the corresponding products **(*S*)-3**.

Racemic products were synthesized in an analogous manner using $Pd(TFA)_2$ (10 mol%) and bipyridine (11 mol%) at 60 °C.

15. Study of the influence of water in the 1,2-addition of phenyl boronic acid (2a) to hydrazone (*E*)-1b



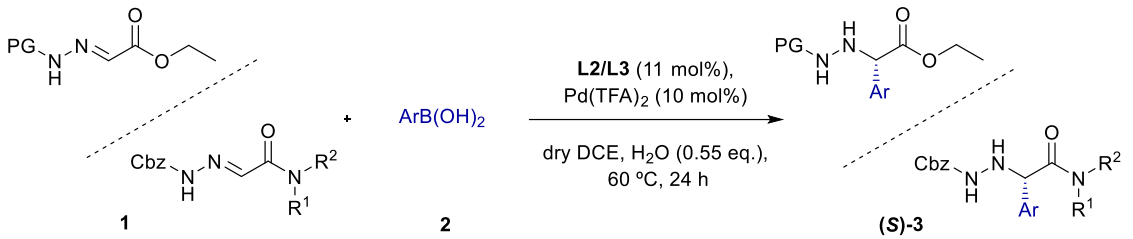
(*E*)-1b 2a (*S*)-3ab

A test tube was charged with $Pd(TFA)_2$ (13 mg, 0.04 mmol), **L2** (14 mg, 0.044 mmol), hydrazone **(*E*)-1b** (100 mg, 0.4 mmol), phenylboronic acid **2a** (73 mg, 0.6 mmol) and dry DCE (1 mL). The mixture was stirred at 60 °C for 24 h. Yields were determined by the ^{1}H-NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as an internal standard. Enantiomeric excess (ee) was determined by HPLC analysis.

Table S5

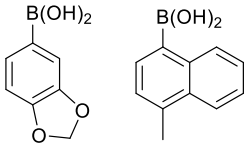
Entry	Additive	Yield (%)	ee (%)
1	-	84	88
2	2 µl H_2O	83	89
3	**4 µl H_2O**	**75**	**93**
4	10 µl H_2O	73	90
5	4 µl H_2O with O_2 atm	80	87
6	^{i}PrOH (0.5 eq)	77	88
7	TFE (0.5 eq)	92	87

16. General procedure for Pd(II)-catalyzed asymmetric 1,2-addition of arylboronic acids 2 to hydrazones (*E*)-1b, (*E*)-1g and (*E*)-1k-m.



(*E*)-**1b**: PG = Cbz
(*E*)-**1g**: PG = Fmoc
(*E*)-**1k**: R^1 = H, R^2 = Bn
(*E*)-**1l**: R^1 = Me, R^2 = Bn
(*E*)-**1m**: R^1 = H, R^2 = Gly

Ar = Ph (**2a**)
Ar = 4-MeO-C_6H_4 (**2b**)
Ar = 4-Me-C_6H_4 (**2c**)
Ar = 2-Me-C_6H_4 (**2d**)
Ar = 4-Cl-C_6H_4 (**2e**)
Ar = 3,5-$(Me)_2$-C_6H_4 (**2f**)



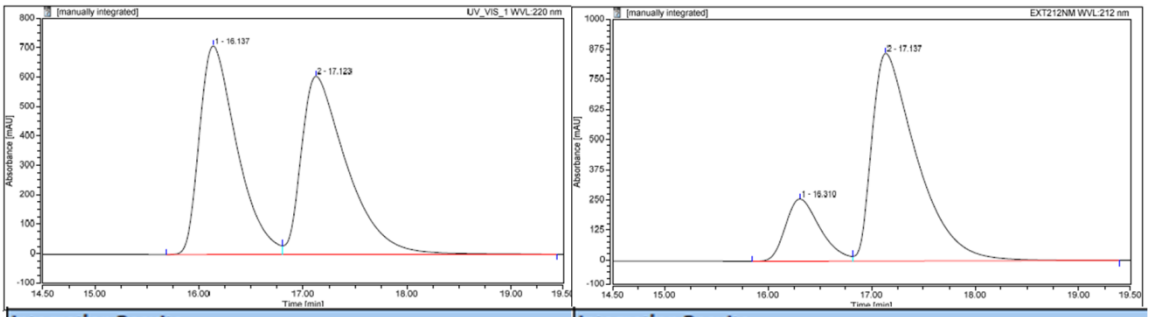
(**2g**) (**2h**)

A test tube was charged with $Pd(TFA)_2$ (13 mg, 0.04 mmol), **L2** or **L3** (0.044 mmol), hydrazone **(*E*)-1b, g, k-m** (0.4 mmol), arylboronic acid **2** (0.6 mmol), dry DCE (1 mL) and H_2O (4 µL, 0.22 mmol). The mixture was stirred at 60 °C for 24 h. The solvent was removed under reduced pressure and the residue purified by flash chromatography. Enantiomeric excess (ee) was determined by HPLC analysis.

Racemic products were synthesized in an analogous manner using $Pd(TFA)_2$ (10 mol%) and bipyridine (11 mol%) at 60 °C.

17. Characterization data

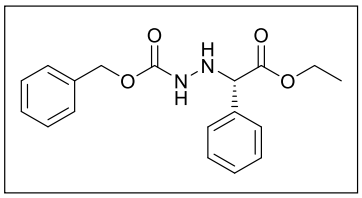
Ethyl (*S*)-2-[(1,3-dioxoisoindolin-2-yl)amino]-2-phenylacetate 3aa: Following the general procedure **13**, a solution of $Pd(TFA)_2$ (7 mg, 0.02 mmol), **L3** (9 mg, 0.022 mmol), **1a** (49 mg, 0.2 mmol) and phenylboronic acid **2a** (37 mg, 0.3 mmol) in TFE (0.5 mL) was stirred 24 h at 60 °C. Then, the solvent was removed under reduced pressure and the residue purified by flash chromatography (*n*-pentane/Et_2O 1/2) to give **3aa** as a yellow solid (52 mg, 80%, 62% ee). $[\alpha]_D^{20}$ = +153.8 (*c* 0.5, $CHCl_3$). **Mp**: 95-97 °C, **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.6 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.59 (dd, *J* = 5.4, 3.1 Hz, 2H), 7.40 (dd, *J* = 7.7, 1.6 Hz, 2H), 7.25 –7.19 (m, 3H), 5.04 (s, 1H), 4.19 – 4.07 (m, 2H), 1.13 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 170.2, 166.0, 134.9, 134.3, 130.1, 129.0, 128.7, 128.6, 123.5, 65.6, 61.8, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{16}O_4N_2Na$ [M^++Na] 347.1002, found 347.0000. **HPLC** (Chiralpak IB, *n*-hexane/2-propanol 93:7, flow 1 mL/min) t_R 16.3 min (minor) and 17.1 min (major).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	16.137	295.350	48.99
2	17.123	307.481	51.01

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	16.310	100.510	18.79
2	17.137	434.470	81.21

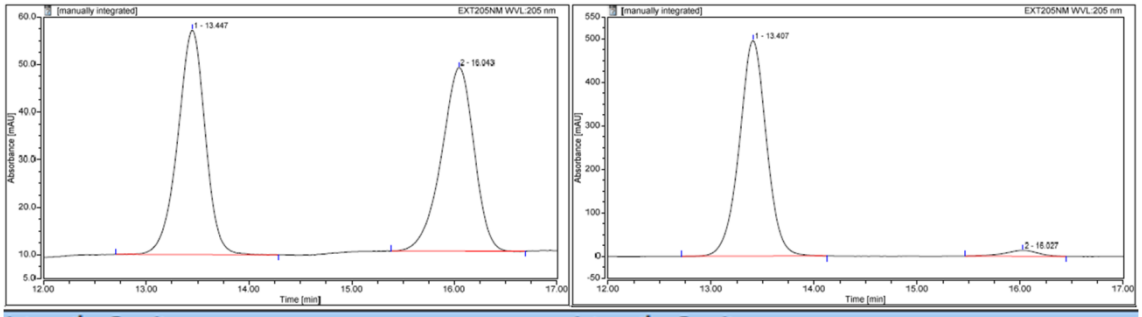
Benzyl (*S*)-2-(2-ethoxy-2-oxo-1-phenylethyl)hydrazine-1-carboxylate (*S*)-3ab:



0.4 mmol scale: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and phenylboronic acid **2a** (73 mg, 0.6 mmol), **(*S*)-3ab** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/1) as a white solid (91 mg, 69%, 94% ee).

1 mmol scale: A 10 mL round-bottom flask was charged with $Pd(TFA)_2$ (33 mg, 0.1 mmol), **L3** (42 mg, 0.11 mmol), **(*E*)-1b** (250 mg, 1 mmol), phenylboronic acid **2a** (183 mg, 1.5 mmol), dry DCE (2.5 mL) and H_2O (5 µL, 0.27 mmol). Subsequently, addition of **2a** (0.75 mmol/12 h) was performed. The mixture was stirred at 60 °C for 24 h and the solvent was removed under reduced pressure. Flash chromatography (*n*-hexane/EtOAc 3/1) afforded **(*S*)-3ab** as a white solid (270 mg, 82%, 92% ee). $[\alpha]_D^{20}$ = +72.4 (*c* 0.5, $CHCl_3$). **Mp**: 56-58 °C. **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.38 – 7.33 (m, 10H), 6.61 (br s, 1H), 5.16 – 5.11 (m, 2H), 4.83 (br s, 1H), 4.24 – 4.11 (m, 3H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 171.3, 157.0, 136.1, 135.4, 128.9, 128.8, 128.7, 128.45, 128.42, 128.3, 67.4, 67.1, 61.5, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{20}O_4N_2Na$ [M^++Na] 351.1314, found 351.1313. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 13.4 min (major) and 16.0 min (minor).

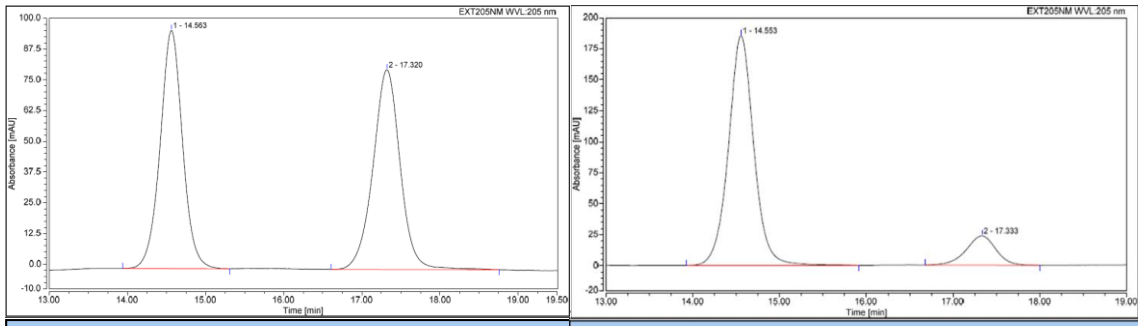
Crystallization of **(*S*)-3ab** by slow diffusion of *n*-pentane in a solution of **(*S*)-3ab** in DCM afforded crystals which are suitable of X-ray.



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	13.447	14.694	50.83
2	16.043	14.212	49.17

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	13.407	151.558	96.82
2	16.027	4.971	3.18

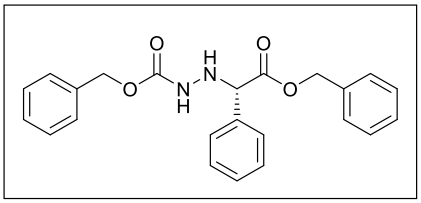
Benzyl (*S*)-2-(2-methoxy-2-oxo-1-phenylethyl)hydrazine-1-carboxylate (*S*)-3ac: Following the general procedure **14**, starting from **(*E*)-1c** (47 mg, 0.2 mmol), **(*S*)-3ac** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/2) as a colourless oil (47 mg, 74%, 74% ee). $[\alpha]_D^{20}$ = +71.2 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.44 – 7.30 (m, 10 H), 6.56 (br s, 1H), 5.14 (s, 2H), 4.84 (br s, 1H), 4.52 (br s, 1H), 3.70 (s, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.9, 157.1, 136.0, 135.2, 129.0, 128.7, 128.47, 128.45, 128.3, 67.4, 67.1, 52.5. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{18}O_4N_2Na$ [M^++Na] 337.1159, found 337.1161. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 14.5 min (major) and 17.3 min (minor).



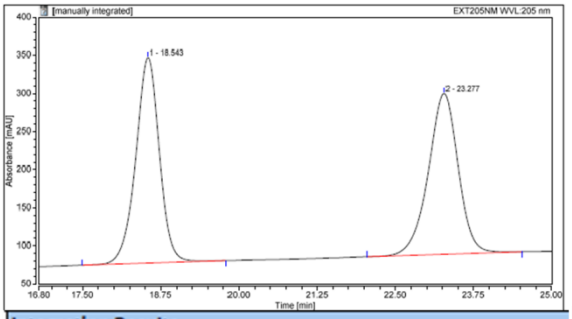
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.563	32.287	49.71
2	17.320	32.658	50.29

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.553	63.010	86.99
2	17.333	9.422	13.01

Benzyl (*S*)-2-[2-(benzyloxy)-2-oxo-1-phenylethyl]hydrazine-1-carboxylate (*S*)-3ad:

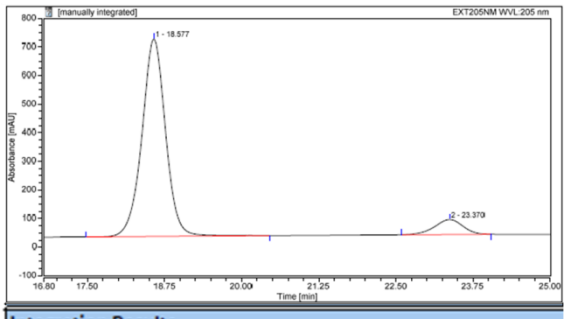


Following the general procedure **14**, starting from **(*E*)-1d** (63 mg, 0.2 mmol), **(*S*)-3ad** was obtained after purification by flash chromatography (Toluene/EtOAc 10/1) as a yellow oil (53 mg, 67%, 83% ee). **$[\alpha]_D^{20}$** = +42.5 (*c* 1, $CHCl_3$). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.45 – 7.38 (m, 2H), 7.37 – 7.33 (m, 8H), 7.30 – 7.28 (m, 3H), 7.21 – 7.18 (m, 2H), 6.72 (br s, 1H), 5.19 – 5.11 (m, 4H), 4.93 (br s, 1H), 4.57 (br s, 1H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 171.2, 157.1, 136.0, 135.5, 135.2, 128.8, 128.6, 128.5, 128.4, 128.35, 128.26, 128.2, 127.9, 67.3, 67.1, 66.9. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{22}O_4N_2Na$ [M^++Na] 413.1472, found 413.1466. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 18.5 min (major) and 23.3 min (minor).



Integration Results

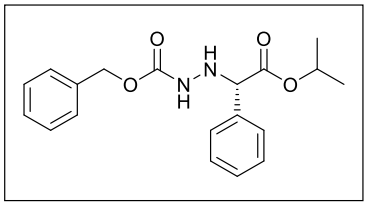
No.	Retention Time min	Area mAU*min	Relative Area %
1	18.543	117.998	50.24
2	23.277	116.862	49.76



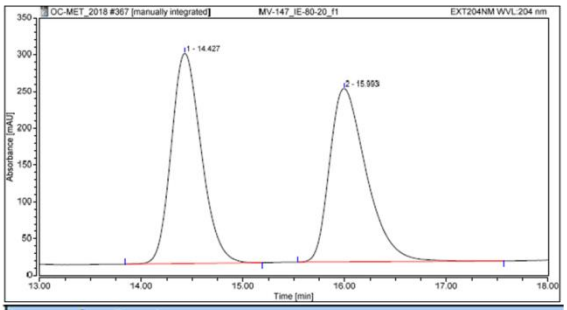
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	18.577	306.264	91.68
2	23.370	27.776	8.32

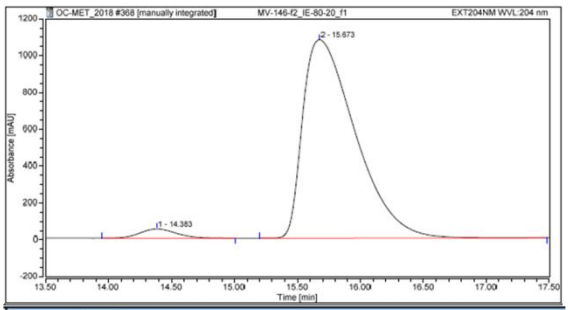
Benzyl (*S*)-2-(2-isopropoxy-2-oxo-1-phenylethyl)hydrazine-1-carboxylate (*S*)-3ae:



Following the general procedure **14**, starting from **(*E*)-1e** (51 mg, 0.2 mmol), **(*S*)-3ae** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/1) as a colourless oil (28 mg, 44%, 94% ee). **$[\alpha]_D^{20}$** = +61.8 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.38 – 7.29 (m, 10 H), 6.58 (br s, 1H), 5.14 (s, 2H), 5.09 – 4.99 (m, 1H), 4.78 (br s, 1H), 4.51 (br s, 1H), 1.23 (d, *J* = 6.3 Hz, 3H), 1.09 (d, *J* = 6.2 Hz, 3H).**^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 170.9, 157.0, 136.1, 135.4, 128.8, 128.72, 128.67, 128.41, 128.38, 128.2, 69.1, 67.3, 67.2, 21.8, 21.5. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{22}O_4N_2Na$ [M^++Na] 365.1472, found 365.1467. **HPLC** (Chiralpak IE, *n*-hexane/2-propanol 80:20, flow 1 mL/min) t_R 14.4 min (minor) and 15.7 min (major).

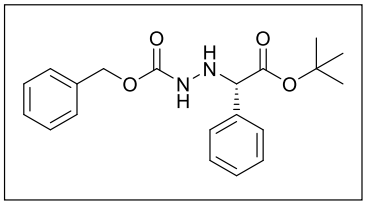


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.427	97.745	49.80
2	15.993	98.532	50.20

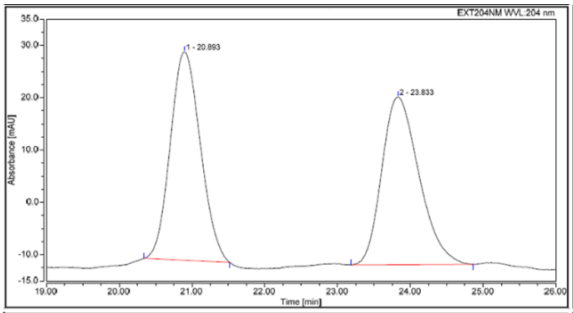


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.383	16.882	3.14
2	15.673	521.404	96.86

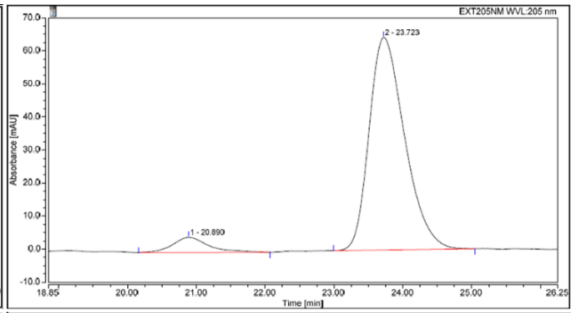
Benzyl (*S*)-2-[2-(*tert*-butoxy)-2-oxo-1-phenylethyl]hydrazine-1-carboxylate (*S*)-3af:



Following the general procedure **14**, starting from **(*E*)-1f** (56 mg, 0.2 mmol), **(*S*)-3af** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/1) as a colourless oil (28 mg, 38%, 86% ee). $[\alpha]_D^{20}$ = +73.3 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.44 – 7.28 (m, 10 H), 6.67 (br s, 1H), 5.13 (s, 2H), 4.71 (br s, 1H), 4.08 (br s, 1H), 1.38 (s, 9H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): 170.5, 157.0, 136.1, 135.9, 128.7, 128.6, 128.5, 128.30, 128.29, 128.2, 82.1, 67.5, 67.2, 27.9. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{24}O_4N_2Na$ [M^++Na] 379.1628, found 379.1625. **HPLC** (Chiralpak IE, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 20.9 min (minor) and 23.7 min (major).

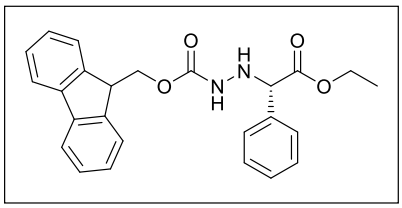


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	20.893	19.062	50.09
2	23.833	18.993	49.91



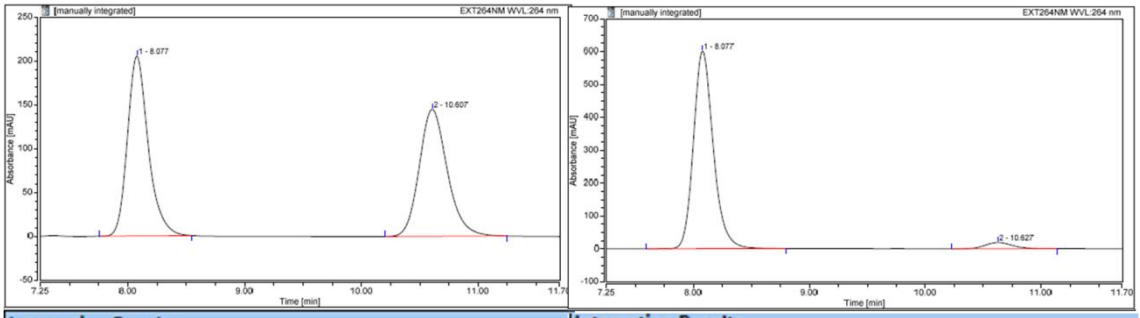
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	20.890	2.826	6.85
2	23.723	38.440	93.15

(9*H*-Fluoren-9-yl)methyl (*S*)-2-(2-ethoxy-2-oxo-1-phenylethyl)hydrazine-1-carboxylate (*S*)-3ag:



0.4 mmol scale: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and phenylboronic acid **2a** (73 mg, 0.6 mmol), **(*S*)-3ag** was obtained after purification by flash chromatography (Toluene/EtOAc 4/1) as a white solid (130 mg, 81%, 92% ee).

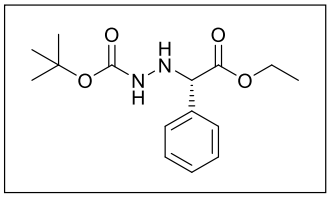
1 mmol scale: A 10 mL round-bottom flask was charged with $Pd(TFA)_2$ (33 mg, 0.1 mmol), **L3** (42 mg, 0.11 mmol), **(*E*)-1g** (339 mg, 1 mmol), phenylboronic acid **2a** (183 mg, 1.5 mmol), dry DCE (2.5 mL) and H_2O (5 µL, 0.27 mmol). Subsequently, addition of **2a** (0.5 mmol/12 h) was performed. The mixture was stirred at 60 °C for 36 h and the solvent was removed under reduced pressure. Flash chromatography (Toluene/EtOAc 4/1) afforded **(*S*)-3ag** as a white solid (354 mg, 85%, 92% ee). $[\alpha]_D^{25}$ = +72.4 (*c* 1, $CHCl_3$). **Mp**: 69-71 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.5 Hz, 2H), 7.46 (s, 2H), 7.34 – 7.17 (m, 9H), 6.49 (br s, 1H), 4.72 (br s, 1H), 4.37 (br s, 2H), 4.19 – 4.02 (m, 3H), 3.58 (br s, 1H), 1.12 (t, *J* = 7.1 Hz, 3H).**^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.4, 157.0, 143.74, 143.72, 141.4, 135.4, 128.92, 128.88, 128.5, 127.9, 127.2, 125.1, 120.2, 67.3, 67.1, 61.5, 47.3, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{25}H_{24}O_4N_2Na$ [M^++Na] 439.1628, found 439.1622. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 80:20, flow 1 mL/min) t_R 8.0 min (major) and 10.6 min (minor).

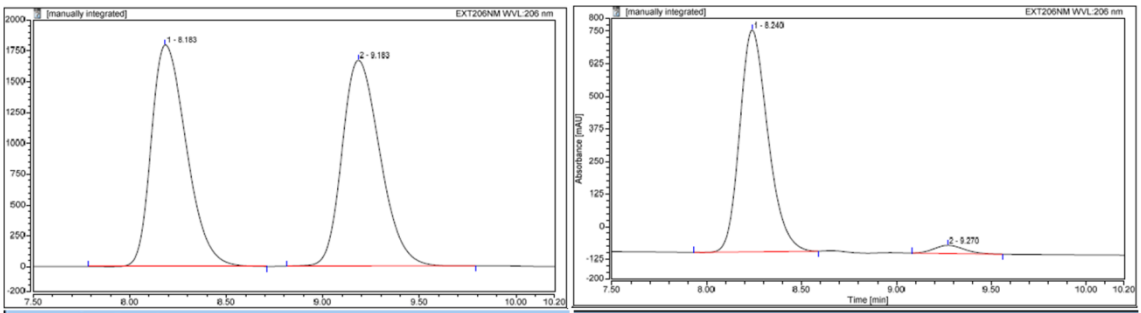


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.077	42.501	51.31
2	10.607	40.336	48.69

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.077	119.379	95.80
2	10.627	5.233	4.20

***tert*-Butyl (*S*)-2-(2-ethoxy-2-oxo-1-phenylethyl)hydrazine-1-carboxylate (*S*)-3ah:** Following the general procedure **14**, starting from **(*E*)-1h** (43 mg, 0.2 mmol), **(*S*)-3ah** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/1) as a colourless oil (15 mg, 26%, 92% ee). $[\alpha]_D^{25}$ = +74.1 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.42 – 7.32 (m, 5H), 6.32 (br s, 1H), 4.79 (s, 1H), 4.26 – 4.08 (m, 2H), 3.38 (br s, 1H), 1.44 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.5, 156.5, 135.6, 128.84, 128.75, 128.5, 81.0, 67.2, 61.4, 28.4, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{15}H_{22}O_4N_2Na$ [M^++Na] 317.1472, found 317.1471. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 93:7, flow 1 mL/min) t_R 8.2 min (major) and 9.3 min (minor).



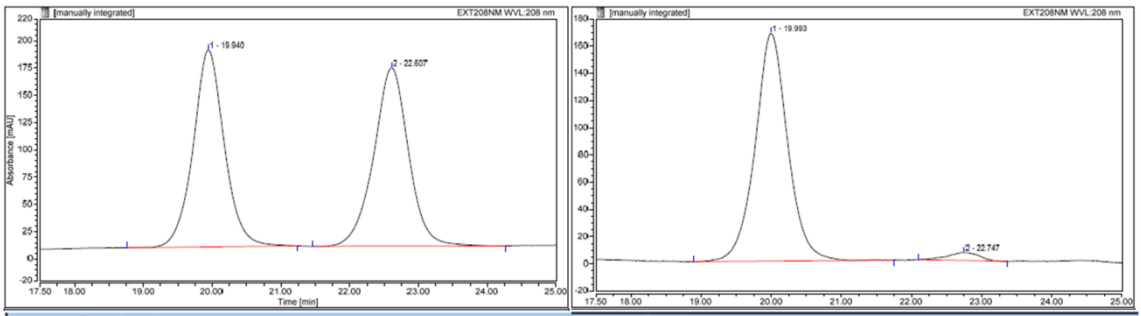


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.183	378.162	49.86
2	9.183	380.218	50.14

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	8.240	146.780	96.23
2	9.270	5.746	3.77

Ethyl (*E*)-2-[2-(4-methoxyphenyl)hydrazineylidene]-2-phenylacetate 3aj´: Following the general procedure **14**, starting from **(*E*)-1j** (45 mg, 0.2 mmol), **3aj´** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 4/1) as a yellow oil (20 mg, 33%). **^{1}H-NMR** (300 MHz, CD_2Cl_2): δ 12.41 (br s, 1H), 7.67 –7.63 (m, 2H), 7.40 – 7.28 (m, 3H), 7.23 (d, *J* = 15.8 Hz, 2H), 6.89 (d, *J* = 15.8 Hz, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 3.79 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, CD_2Cl_2): δ 164.3, 156.2, 137.7, 137.5, 129.1, 128.3, 127.8, 127.5, 115.8, 115.2, 61.5, 56.1, 14.5. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{18}O_3N_2Na$ [M^++Na] 321.1210, found 321.1208.

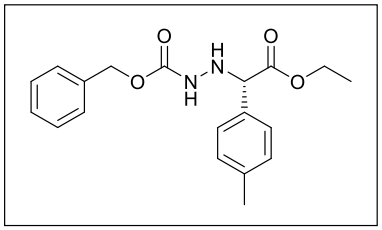
Benzyl (*S*)-2-[2-ethoxy-1-(4-methoxyphenyl)-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3bb: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and boronic acid **2b** (91 mg, 0.6 mmol), **(*S*)-3bb** was obtained after purification by flash chromatography (Toluene/EtOAc 5/1) as a yellow oil (132 mg, 92%, 94% ee). **$[\alpha]_D^{25}$** = +68.6 (*c* 1, $CHCl_3$).**^{1}H-NMR** (500 MHz, $CDCl_3$): δ 7.36 – 7.27 (m, 7H), 6.85 (d, *J* = 8.6 Hz, 2H), 6.70 (br s, 1H), 5.13 (q, *J* = 12.2 Hz, 2H), 4.79 (br s, 1H), 4.22 – 4.10 (m, 2H), 4.03 (br s, 1H), 3.78 (s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H).**^{13}C-NMR** (126 MHz, $CDCl_3$): δ 171.6, 160.0, 157.0, 136.1, 129.7, 128.6, 128.4, 128.2, 127.3, 114.3, 67.3, 66.5, 61.4, 55.3, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{22}O_5N_2Na$ [M^++Na] 381.1421, found 381.1417. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 19.9 min (major) and 22.7 min (minor).



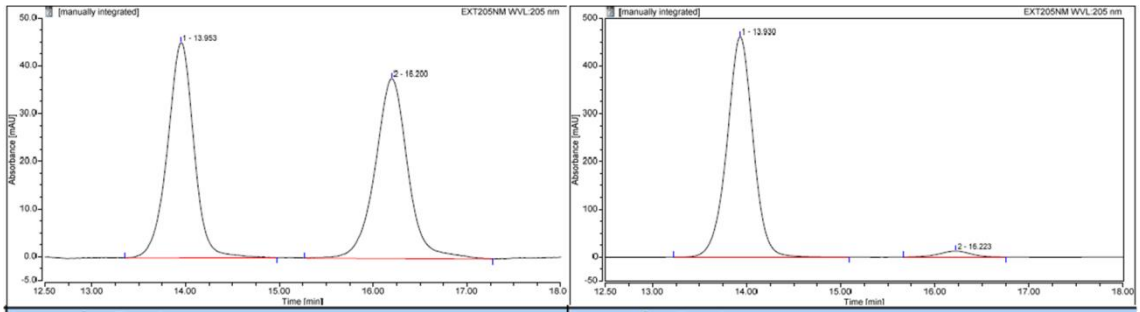
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	19.940	94.982	49.65
2	22.607	96.320	50.35

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	19.993	90.228	96.83
2	22.747	2.957	3.17

Benzyl (*S*)-2-[2-ethoxy-2-oxo-1-(*p*-tolyl)ethyl]hydrazine-1-carboxylate (*S*)-3cb: Following



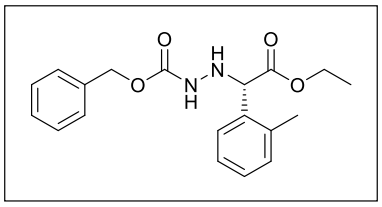
the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and boronic acid **2c** (82 mg, 0.6 mmol), **(*S*)-3cb** was obtained after purification by flash chromatography (*n*-hexane /EtOAc 3/1) as a white solid (119 mg, 87%, 94% ee). $[\alpha]_D^{20}$ = +79.8 (*c* 0.5, $CHCl_3$). **Mp**: 55-57 °C. **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.27 – 7.16 (m, 7H), 7.04 (d, *J* = 7.9 Hz, 2H), 6.60 (br s, 1H), 5.07 – 5.01 (m, 2H), 4.70 (br s, 1H), 4.12 – 3.99 (m, 3H), 2.23 (s, 3H), 1.09 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 171.5, 157.0, 138.6, 136.1, 132.4, 128.6, 128.33, 128.29, 128.2, 67.3, 66.8, 61.4, 21.2, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{22}O_4N_2Na$ [M^++Na] 365.1472, found 365.1468. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 13.9 min (major) and 16.2 min (minor).



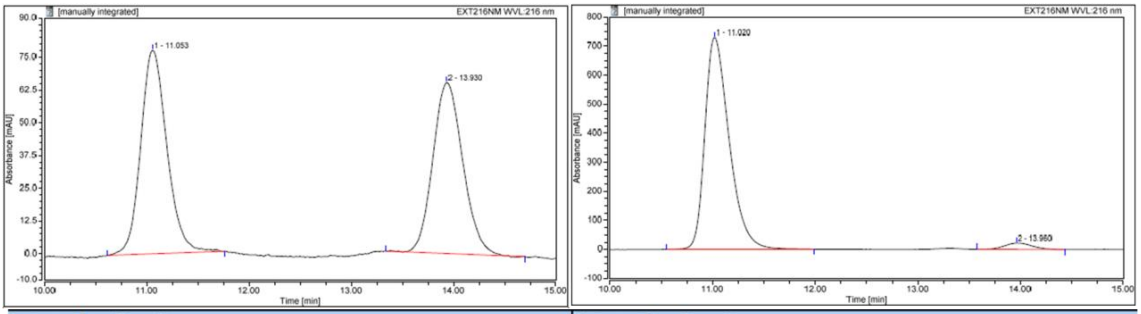
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	13.953	14.802	49.19
2	16.200	15.289	50.81

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	13.930	148.502	96.84
2	16.223	4.848	3.16

Benzyl (*S*)-2-[2-ethoxy-2-oxo-1-(*o*-tolyl)ethyl]hydrazine-1-carboxylate (*S*)-3db: Following



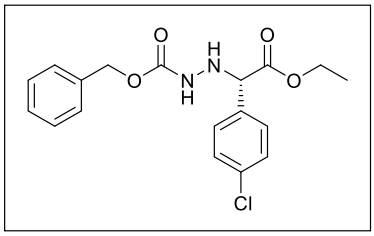
the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and boronic acid **2d** (82 mg, 0.6 mmol), **(*S*)-3db** was obtained after purification by flash chromatography (*n*-hexane /EtOAc 3/1) as a colourless oil (95 mg, 69%, 93% ee). $[\alpha]_D^{25}$ = +68.7 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 7.39 – 7.11 (m, 9H), 6.76 (br s, 1H), 5.20 – 5.05 (m, 3H), 4.26 – 4.09 (m, 2H), 3.88 (br s, 1H), 2.47 (br s, 3H), 1.19 (t, *J* = 7.1 Hz, 3H).**^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 172.0, 157.0, 137.7, 136.0, 133.6, 130.9, 128.64, 128.60, 128.4, 128.3, 127.6, 126.3, 67.2, 63.7, 61.4, 19.4, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{22}O_4N_2Na$ [M^++Na] 365.1472, found 365.1468. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 11.0 min (major) and 13.9 min (minor).



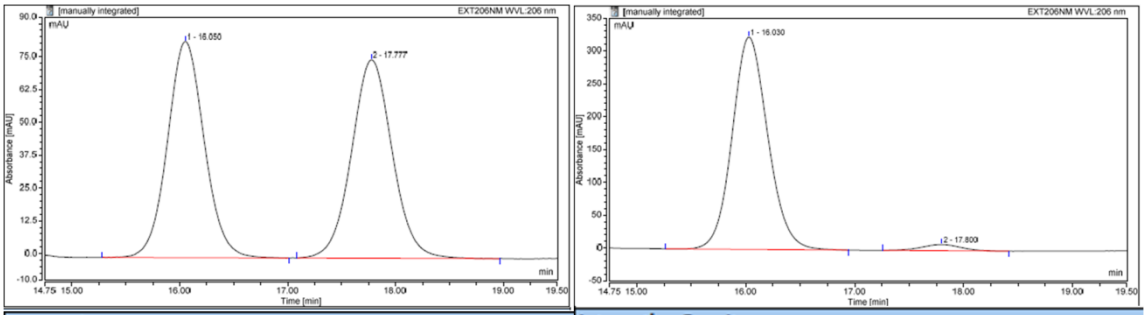
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	11.053	23.107	51.06
2	13.930	22.150	48.94

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	11.020	199.767	96.74
2	13.960	6.724	3.26

Benzyl (*S*)-2-[1-(4-chlorophenyl)-2-ethoxy-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3eb:



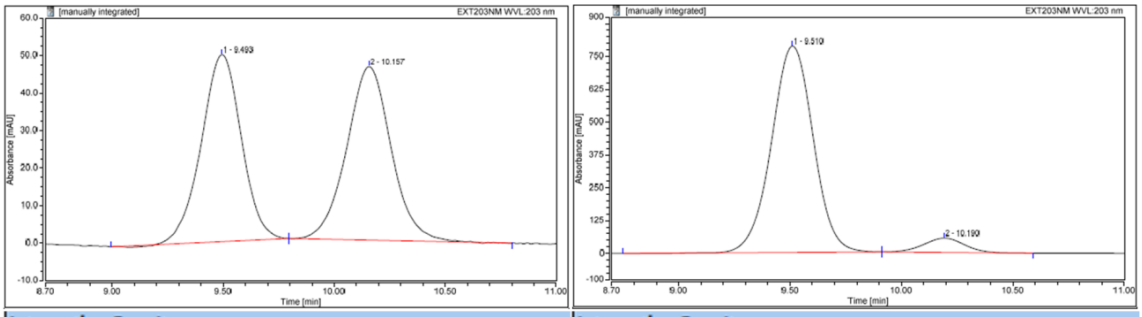
Following the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and boronic acid **2e** (97 mg, 0.6 mmol), **(*S*)-3eb** was obtained after purification by flash chromatography (Toluene/EtOAc 5/1) as a yellow oil. Subsequently, addition of **2e** (0.3 mmol/12 h) was performed. Reaction run for 24 h: (37 mg, 25%, 94% ee). Reaction run for 48 h: (70 mg, 48%, 82% ee). $[\alpha]_D^{25}$ = +84.2 (*c* 1, $CHCl_3$, 94 % ee). **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.48 – 7.29 (m, 9H), 6.54 (br s, 1H), 5.15 – 5.10 (m, 2H), 4.80 (br s, 1H), 4.22 – 4.10 (m, 2H), 3.91 (br s, 1H), 1.19 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 170.9, 157.1, 136.0, 134.8, 134.1, 129.8, 129.1, 128.7, 128.5, 128.3, 67.5, 66.3, 61.7, 14.7. **HRMS** (ESI): *m/z* calcd for $C_{18}H_{19}O_4N_2ClNa$ [M^++Na] 385.0926, found 385.0921. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 16.0 min (major) and 17.8 min (minor).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	16.050	32.617	49.68
2	17.777	33.036	50.32

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	16.030	122.722	96.91
2	17.800	3.909	3.09

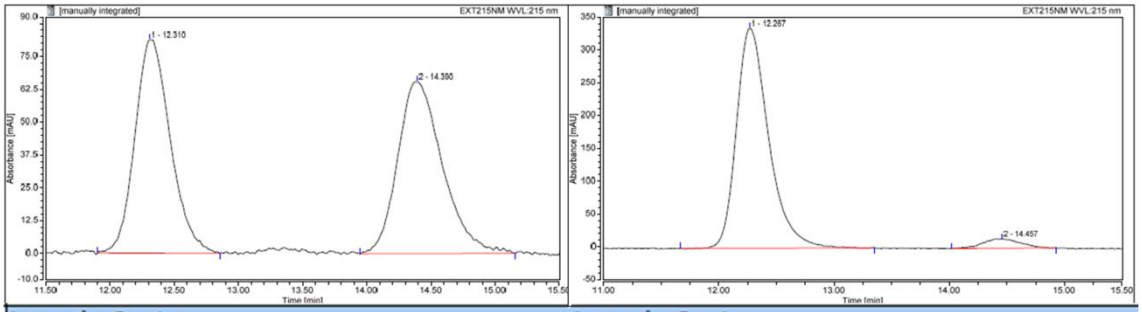
Benzyl (*S*)-2-[1-(3,5-dimethylphenyl)-2-ethoxy-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3fb: Following the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and boronic acid **2f** (90 mg, 0.6 mmol), **(*S*)-3fb** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/1) as a yellow oil (110 mg, 77%, 87% ee). **$[\alpha]_D^{20}$** = +73.5 (*c* 0.5, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 7.40 – 7.30 (m, 5H), 6.97 (d, *J* = 5.8 Hz, 3H), 6.50 (br s, 1H), 5.15 – 5.14 (m, 2H), 4.74 (br s, 1H), 4.28 – 4.08 (m, 2H), 3.53 (br s, 1H), 2.29 (s, 6H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.5, 157.1, 138.6, 136.1, 135.0, 130.6, 128.7, 128.5, 128.3, 126.2, 67.4, 67.2, 61.5, 21.3, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{24}O_4N_2Na$ [M^++Na] 379.1628, found 379.1629. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 9.5 min (major) and 10.2 min (minor).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.493	10.414	49.15
2	10.157	10.775	50.85

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.510	170.723	93.64
2	10.190	11.589	6.36

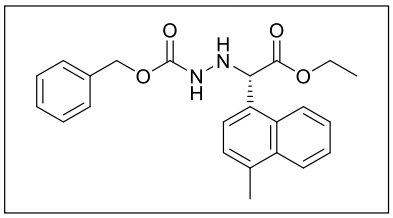
Benzyl (*S*)-2-[1-(benzo[d][1,3]dioxol-5-yl)-2-ethoxy-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3gb: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and boronic acid **2g** (100 mg, 0.6 mmol), **(*S*)-3gb** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 3/1) as a white solid (105 mg, 70%, 91% ee). **$[\alpha]_D^{25}$** = +87.9 (*c* 1, $CHCl_3$). **Mp**: 74-76 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 7.39 – 7.29 (m, 5H), 6.88 – 6.83 (m, 2H), 6.75 (d, *J* = 7.9 Hz, 1H), 6.57 (br s, 1H), 5.94 (s, 2H), 5.13 (s, 2H), 4.73 (br s, 1H), 4.25 – 4.07 (m, 2H), 3.69 (br s, 1H), 1.20 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.3, 157.0, 148.07, 148.05, 136.0, 129.0, 128.7, 128.4, 128.3, 122.3, 108.6, 108.5, 101.4, 67.4, 66.7, 61.5, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{19}H_{20}O_6N_2Na$ [M^++Na] 395.1214, found 395.1212. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 80:20, flow 1 mL/min) t_R 12.3 min (major) and 14.4 min (minor).



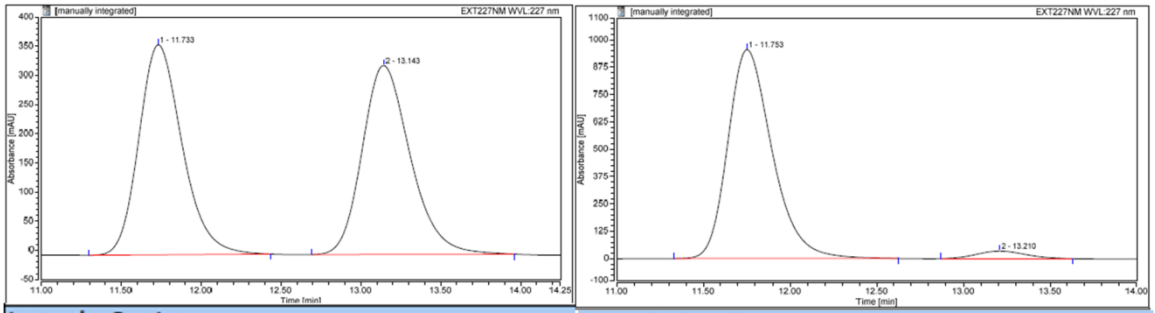
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	12.310	26.050	49.59
2	14.390	26.478	50.41

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	12.267	108.329	95.37
2	14.457	5.261	4.63

Benzyl (*S*)-2-[2-ethoxy-1-(4-methylnaphthalen-1-yl)-2-oxoethyl]hydrazine-1-carboxylate



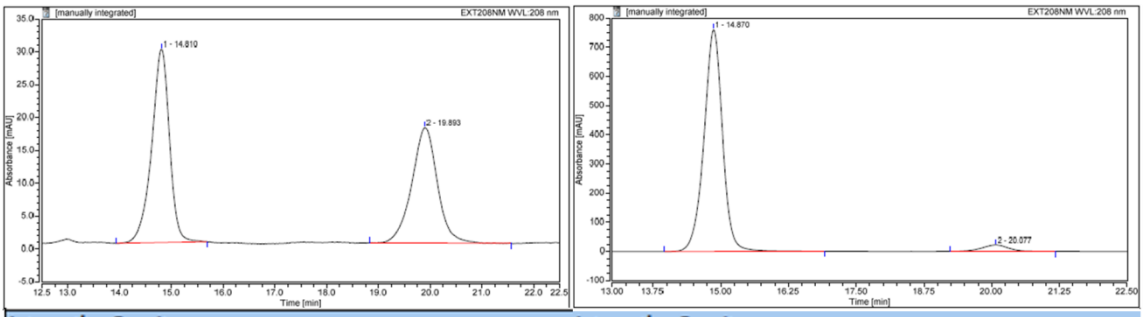
(*S*)-3hb: Following the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1b** (100 mg, 0.4 mmol) and boronic acid **2h** (112 mg, 0.6 mmol), **(*S*)-3hb** was obtained after purification by flash chromatography (Toluene/EtOAc 8/1) as a colourless oil (99 mg, 63%, 92% ee). $[\alpha]_D^{25}$ = +76.5 (*c* 1, $CHCl_3$). **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.89 (d, *J* = 9.4 Hz, 1H), 7.43 – 7.40 (m, 2H), 7.22 (s, 6H), 7.13 – 7.11 (m, 1H), 6.66 (br s, 1H), 5.42 (br s, 1H), 5.09 – 4.99 (m, 2H), 4.18 (br s, 1H), 4.41 – 3.99 (m, 2H), 2.55 (s, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 172.2, 157.1, 136.1, 135.8, 133.2, 131.8, 129.5, 128.6, 128.3, 128.2, 126.6, 126.4, 126.1, 125.9, 124.7, 124.5, 67.2, 64.4, 61.4, 19.7, 14.0. **HRMS** (ESI): *m/z* calcd for $C_{23}H_{24}O_4N_2Na$ [M^++Na] 415.1628, found 415.1625. **HPLC** (Chiralpak IB, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 11.7 min (major) and 13.2 min (minor).



Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	11.733	113.365	50.04
2	13.143	113.168	49.96

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	11.753	282.468	96.16
2	13.210	11.292	3.84

(9*H*-Fluoren-9-yl)methyl (*S*)-2-[2-ethoxy-1-(4-methoxyphenyl)-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3bg: Following the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and boronic acid **2b** (91 mg, 0.6 mmol), **(*S*)-3bg** was obtained after purification by flash chromatography (Toluene/EtOAc 4/1) as a yellow oil (139 mg, 78%, 92% ee). **$[\alpha]_D^{25}$** = +54.1 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.58 – 7.56 (m, 2H), 7.43 – 7.28 (m, 6H), 6.87 (d, *J* = 8.7 Hz, 2H), 4.80 (br s, 1H), 4.45 (br s, 2H), 4.28 – 4.10 (m, 3H), 3.96 (br s, 1H), 3.78 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.6, 159.9, 157.0, 143.7, 141.4, 129.6, 127.8, 127.3, 127.1, 125.11, 125.09, 120.1, 114.2, 67.2, 66.4, 61.4, 55.3, 47.2, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{26}H_{26}O_5N_2Na$ [M^++Na] 469.1734, found 469.1725. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 14.8 min (major) and 20.0 min (minor).



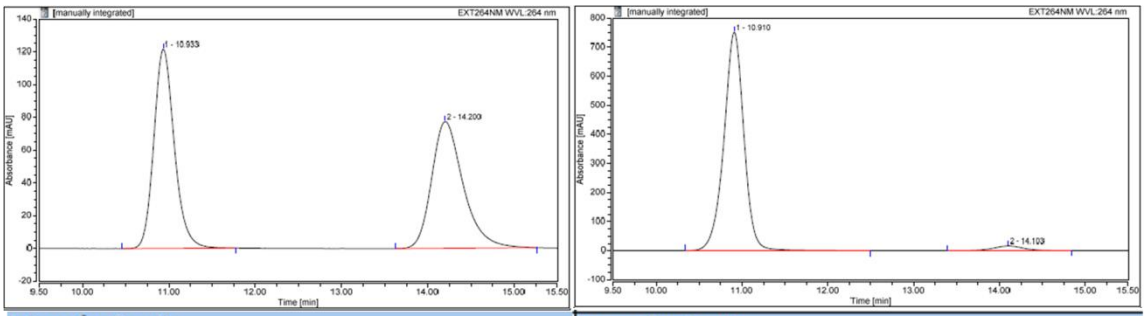
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	14.810	11.744	53.81
2	19.893	10.080	46.19

Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	14.870	301.761	95.98
2	20.077	12.650	4.02

(9*H*-Fluoren-9-yl)methyl (*S*)-2-[2-ethoxy-2-oxo-1-(*p*-tolyl)ethyl]hydrazine-1-carboxylate (*S*)-3cg: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and boronic acid **2c** (82 mg, 0.6 mmol), **(*S*)-3cg** was obtained after purification by flash chromatography (Toluene/EtOAc 5/1) as a yellow oil (157 mg, 91%, 94% ee). **$[\alpha]_D^{25}$** = +54.4 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.5 Hz, 2H), 7.58 (s, 2H), 7.44 – 7.26 (m, 6H), 7.17 (d, *J* = 7.8 Hz, 2H), 6.88 (br s, 1H), 4.84 (br s, 1H), 4.46 (br s, 2H), 4.29 – 4.11 (m, 4H), 2.35 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.5, 157.0, 143.7, 141.3, 138.6, 132.3, 129.5, 128.3, 127.8, 127.1, 125.1, 120.0, 67.2, 66.7, 61.4, 47.2, 21.2, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{26}H_{26}O_4N_2Na$ [M^++Na] 453.1785, found 453.1778. **HPLC** (Chiralpak IB, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 10.9 min (major) and 14.1 min (minor).



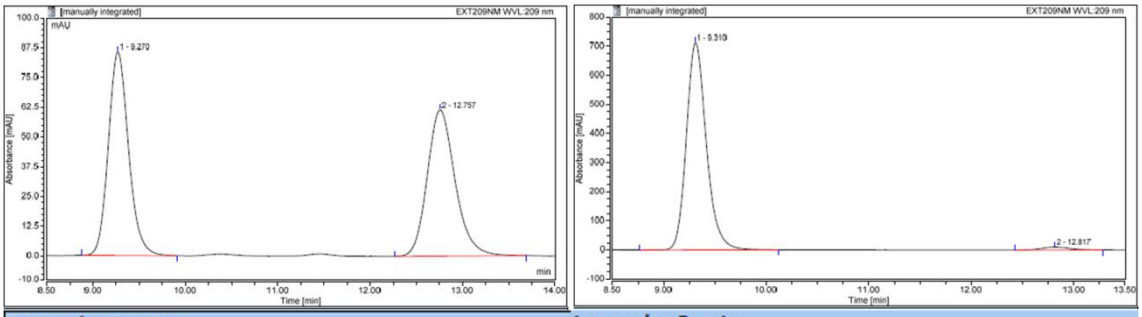
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	10.933	33.458	50.55
2	14.200	32.725	49.45

Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	10.910	202.881	96.89
2	14.103	6.508	3.11

(9*H*-Fluoren-9-yl)methyl (*S*)-2-[2-ethoxy-2-oxo-1-(*o*-tolyl)ethyl]hydrazine-1-carboxylate (*S*)-3dg: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and boronic acid **2d** (82 mg, 0.6 mmol), **(*S*)-3cg** was obtained after purification by flash chromatography (Toluene/EtOAc 5/1) as a white solid (133 mg, 77%, 96% ee). $[\alpha]_D^{25}$ = +43.8 (*c* 1, $CHCl_3$). **Mp**: 45-47 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.64 – 7.49 (m, 2H), 7.41 (t, *J* = 7.3 Hz, 2H), 7.33 – 7.15 (m, 6H), 6.72 (br s, 1H), 5.05 (br s, 1H), 4.52 – 4.38 (m, 2H), 4.30 – 4.11 (m, 3H), 3.81 (br s, 1H), 2.49 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 172.1, 157.0, 143.8, 143.7, 141.4, 137.7, 133.6, 131.0, 128.7, 127.9, 127.7, 127.2, 126.4, 125.2, 125.1, 120.1, 67.3, 63.8, 61.5, 47.2, 19.5, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{26}H_{26}O_4N_2Na$ [M^++Na] 453.1785, found 453.1776. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 9.3 min (major) and 12.8 min (minor).



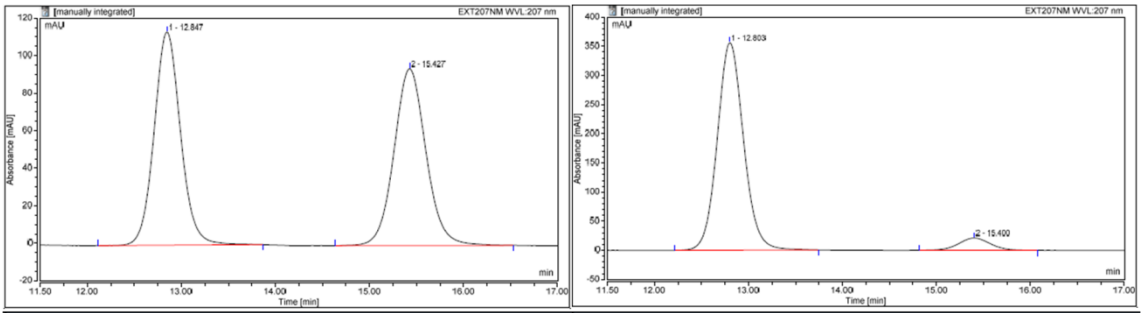
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	9.270	21.697	50.23
2	12.757	21.500	49.77

Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	9.310	160.826	98.03
2	12.817	3.239	1.97

(9H-fluoren-9-yl)methyl (*S*)-2-[1-(4-chlorophenyl)-2-ethoxy-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3eg: Following the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and boronic acid **2e** (94 mg, 0.6 mmol), **(*S*)-3eg** was obtained after purification by flash chromatography (Toluene/EtOAc 6/1) as a yellow solid. Subsequently, addition of **2e** (0.2 mmol/12 h) was performed. Reaction run for 36 h: (84 mg, 47%, 87% ee). $[\alpha]_D^{25}$ = +45.8 (*c* 1, $CHCl_3$). **Mp**: 84-86 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.5 Hz, 2H), 7.51 – 7.39 (m, 2H), 7.34 – 7.17 (m, 8H), 6.48 (br s, 1H), 4.71 (br s, 1H), 4.38 (br s, 3H), 4.17 – 4.00 (m, 3H), 1.11 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 170.9, 157.1, 143.6, 141.4, 134.8, 134.0, 129.9, 129.1, 127.9, 127.2, 125.0, 120.2, 67.2, 66.2, 61.7, 47.2, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{25}H_{23}O_4N_2ClNa$ [M^++Na] 473.1239, found 473.1230. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 12.8 min (major) and 15.4 min (minor).



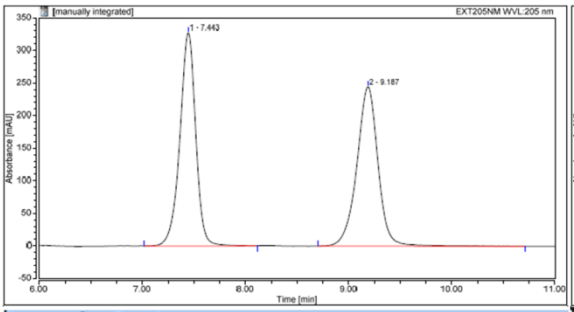
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	12.847	36.986	49.91
2	15.427	37.118	50.09

Integration Results

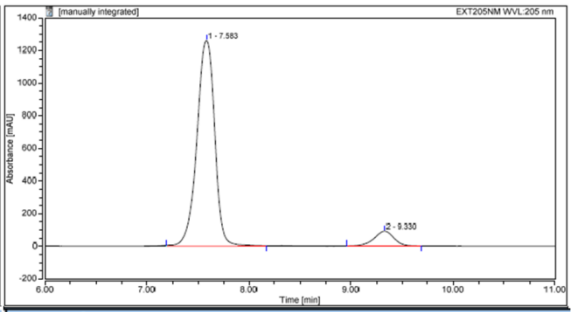
No.	Retention Time min	Area mAU*min	Relative Area %
1	12.803	115.405	93.35
2	15.400	8.225	6.65

(9*H*-Fluoren-9-yl)methyl (*S*)-2-[1-(3,5-dimethylphenyl)-2-ethoxy-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3fg: Following the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and boronic acid **2f** (90 mg, 0.6 mmol), **(*S*)-3fg** was obtained after purification by flash chromatography (Toluene/EtOAc 5/1) as a yellow oil (158 mg, 89%, 85% ee). $[\alpha]_D^{25}$ = +48.3 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 2H), 7.59 – 7.55 (m, 2H), 7.41 (t, *J* = 7.5 Hz, 2H), 7.31 (tdd, *J* = 7.5, 2.4, 1.1 Hz, 2H), 6.99 (d, *J* = 7.4 Hz, 3H), 6.60 (br s, 1H), 4.73 (br s, 1H), 4.51 – 4.37 (m, 2H), 4.31 – 4.10 (m, 3H), 3.76 (br s, 1H), 2.31 (s, 6H), 1.23 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.6, 157.0, 143.7, 141.4, 138.6, 135.0, 130.6, 127.9, 127.2, 126.1, 125.2, 120.1, 67.3, 67.2, 61.5, 47.3, 21.3, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{27}H_{29}O_4N_2$ [M^++H] 445.2122, found 445.2114. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 7.6 min (major) and 9.3 min (minor).



Integration Results

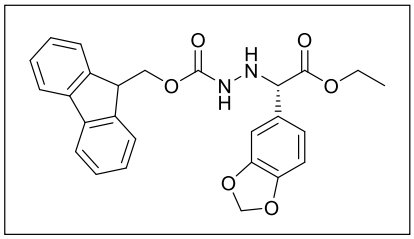
No.	Retention Time min	Area mAU*min	Relative Area %
1	7.443	58.291	50.00
2	9.187	58.301	50.00



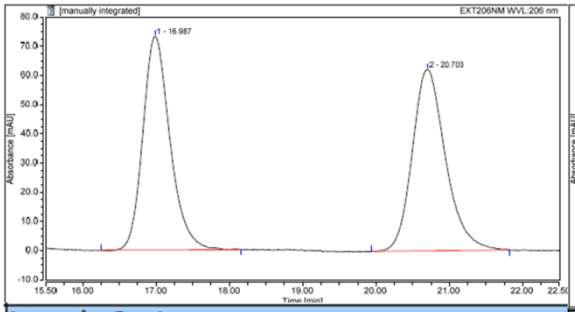
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	7.583	255.573	92.53
2	9.330	20.640	7.47

(9*H*-Fluoren-9-yl)methyl

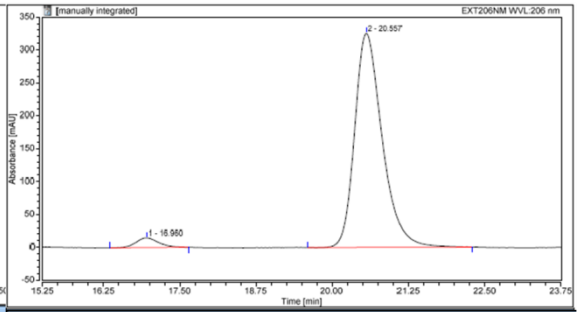


(*S*)-2-[1-(benzo[d][1,3]dioxol-5-yl)-2-ethoxy-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3gg: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and boronic acid **2g** (100 mg, 0.6 mmol), **(*S*)-3fg** was obtained after purification by flash chromatography (Toluene/EtOAc 4/1) as a white solid (129 mg, 70%, 93% ee). $[\alpha]_D^{25}$ = +57.6 (*c* 1, $CHCl_3$). **Mp**: 53-55 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 7.76 (d, *J* = 7.5 Hz, 2H), 7.57 (d, *J* = 7.2 Hz, 2H), 7.40 (t, *J* = 7.3 Hz, 2H), 7.32 – 7.27 (m, 2H), 6.93 (s, 2H), 6.76 (d, *J* = 7.9 Hz, 1H), 5.91 (s, 2H), 4.77 (br s, 1H), 4.45 (br s, 2H), 4.29 – 4.10 (m, 4H), 1.22 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.3, 157.1, 148.0, 143.7, 141.3, 129.0, 127.8, 127.1, 125.1, 125.0, 122.2, 120.0, 108.5, 108.4, 101.3, 67.1, 66.5, 61.4, 47.2, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{26}H_{24}O_6N_2Na$ [M^++Na] 483.1527, found 483.1523. **HPLC** (Chiralpak IB, *n*-hexane/2-propanol 80:20, flow 1 mL/min) t_R 16.9 min (minor) and 20.5 min (major).



Integration Results

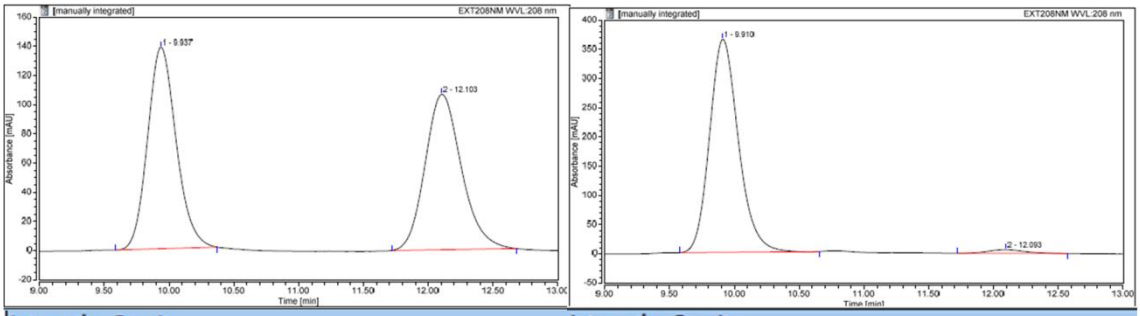
No.	Retention Time min	Area mAU*min	Relative Area %
1	16.987	31.389	49.05
2	20.703	32.609	50.95



Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	16.960	6.178	3.51
2	20.557	170.079	96.49

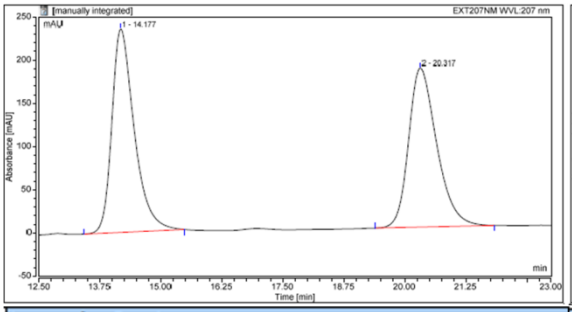
(9*H*-Fluoren-9-yl)methyl (*S*)-2-[2-ethoxy-1-(4-methylnaphthalen-1-yl)-2-oxoethyl]hydrazine-1-carboxylate (*S*)-3hg: Following the general procedure **16**, employing **L2** (14 mg, 0.044 mmol) and starting from **(*E*)-1g** (135 mg, 0.4 mmol) and boronic acid **2h** (112 mg, 0.6 mmol), **(*S*)-3fg** was obtained after purification by flash chromatography (Toluene/EtOAc 9/1) as a white solid (116 mg, 52%, 96% ee). **$[\alpha]_D^{25}$** = +62.0 (*c* 1, $CHCl_3$). **Mp**: 96-98 °C. **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 8.44 (d, *J* = 7.2 Hz, 1H), 8.04 (d, *J* = 9.6 Hz, 1H), 7.77 (d, *J* = 7.5 Hz, 2H), 7.61 – 7.53 (m, 4H), 7.43 – 7.27 (m, 6H), 6.72 (br s, 1H), 5.52 (br s, 1H), 4.54 – 4.39 (m, 2H), 4.30 – 4.13 (m, 4H), 2.70 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 172.2, 157.1, 148.3, 143.7, 141.43, 141.40, 136.0, 133.3, 131.8, 129.4, 127.89, 127.87, 127.20, 127.17, 126.8, 126.6, 126.2, 126.0, 125.22, 125.16, 124.9, 124.6, 120.1, 67.4, 64.5, 61.6, 47.2, 19.8, 14.2. **HRMS** (ESI): *m/z* calcd for $C_{30}H_{29}O_4N_2$ [M^++H] 481.2122, found 481.2118. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 9.9 min (major) and 12.1 min (minor).



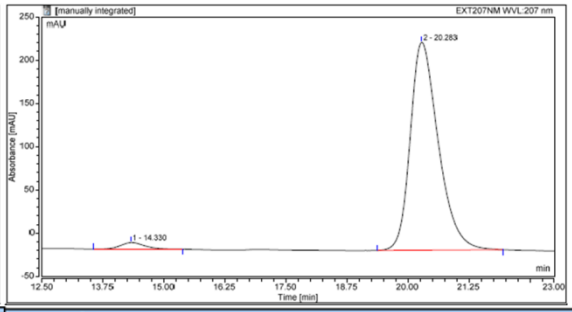
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.937	35.319	50.51
2	12.103	34.612	49.49

Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	9.910	94.105	97.92
2	12.093	1.995	2.08

Benzyl (*S*)-2-[2-(benzylamino)-2-oxo-1-(*p*-tolyl)ethyl]hydrazine-1-carboxylate (*S*)-3ck: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1k** (124 mg, 0.4 mmol) and boronic acid **2c** (86 mg, 0.6 mmol), **(*S*)-3ck** was obtained after purification by flash chromatography (*n*-hexane/EtOAc 1/1) as a light yellow solid (83 mg, 52%, 95% ee). **$[\alpha]_D^{25}$** = +37.6 (*c* 1, $CHCl_3$). **Mp**: 114-116 °C. **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.36 (br s, 1H), 7.27 – 7.10 (m, 12H), 7.02 (d, *J* = 7.8 Hz, 2H), 6.61 (br s, 1H), 4.96 (s, 2H), 4.56 (br s, 1H), 4.32 (ddd, *J* = 35.5, 14.9, 5.9 Hz, 2H), 3.94 (br s, 1H), 2.23 (s, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 170.7, 157.0, 138.8, 138.4, 136.0, 133.0, 129.7, 128.71, 128.69, 128.5, 128.3, 128.1, 127.8, 127.5, 69.0, 67.5, 43.4, 21.3. **HRMS** (ESI): *m/z* calcd for $C_{24}H_{25}O_3N_3Na$ [M^++Na] 426.1785, found 426.1788. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 80:20, flow 1 mL/min) t_R 14.3 min (minor) and 20.3 min (major).

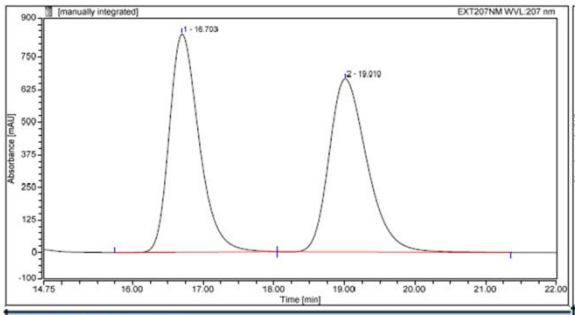


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.177	125.291	50.48
2	20.317	122.914	49.52

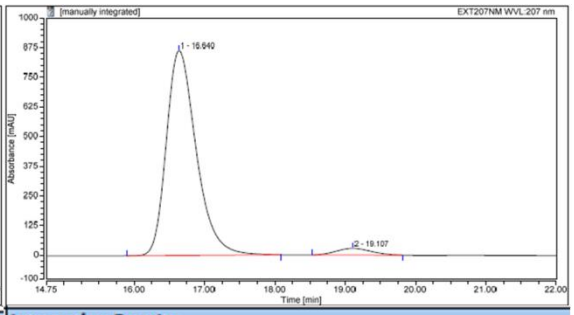


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	14.330	4.348	2.64
2	20.283	160.415	97.36

Benzyl (*S*)-2-{2-[benzyl(methyl)amino]-2-oxo-1-(*p*-tolyl)ethyl}hydrazine-1-carboxylate (*S*)-3cl: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1l** (130 mg, 0.4 mmol) and boronic acid **2c** (86 mg, 0.6 mmol), **(*S*)-3cl** was obtained after purification by flash chromatography (Toluene/EtOAc 3/1) as a yellow oil (143 mg, 86%, 93% ee). $[\alpha]_D^{25}$ = +25.4 (*c* 1, $CHCl_3$). **^{1}H-NMR** (500 MHz, $CDCl_3$; the compound exists as 1,8:1 mixture of amide rotamers). *Signals corresponding to the major rotamer*: δ 7.30 – 7.12 (m, 11H), 7.08 – 7.04 (m, 3H), 6.86 (br s, 1H), 5.08 – 5.04 (m, 2H), 4.83 (br s, 1H), 4.66 – 4.39 (m, 2H), 3.82 (br s, 1H), 2.59 (s, 3H), 2.24 (s, 3H). *Representative signals to the corresponding minor rotamer*: δ 5.01 – 4.97 (m, 2H), 4.41 – 4.03 (m, 2H), 2.84 (s, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 171.2, 171.0, 156.7, 156.6, 138.9, 138.8, 136.8, 136.42, 136.39, 135.8, 131.8, 131.4, 129.91, 129.85, 129.0, 128.74, 128.71, 128.6, 128.3, 128.2, 128.1, 127.8, 127.6, 126.5, 67.0, 65.8, 52.5, 51.5, 34.3, 34.0, 21.3. **HRMS** (ESI): *m/z* calcd for $C_{25}H_{28}O_3N_3$ $[M^+ + H]$ 418.2122, found 418.2125. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 80:20, flow 1 mL/min) t_R 16.6 min (major) and 19.1 min (minor).

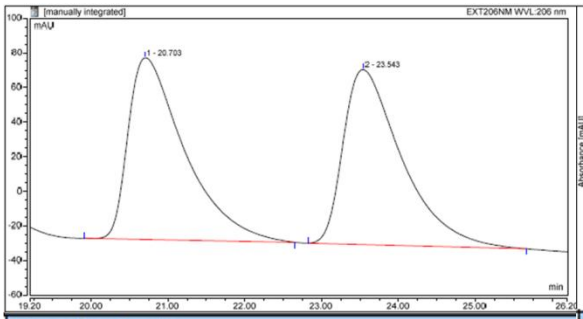


Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	16.703	408.437	49.67
2	19.010	413.843	50.33



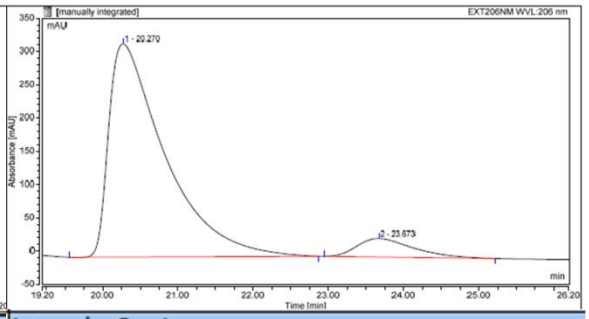
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	16.640	424.864	96.37
2	19.107	16.024	3.63

Benzyl (*S*)-2-{2-[(2-methoxy-2-oxoethyl)amino]-2-oxo-1-(*p*-tolyl)ethyl}hydrazine-1-carboxylate (*S*)-3cm: Following the general procedure **16**, employing **L3** (17 mg, 0.044 mmol) and starting from **(*E*)-1m** (117 mg, 0.4 mmol) and boronic acid **2c** (86 mg, 0.6 mmol), **(*S*)-3cm** was obtained after purification by flash chromatography (*n*-hexane /EtOAc 1/2) as a colorless oil (112 mg, 73%, 84% ee). $[\alpha]_D^{25}$ = +7.3 (*c* 1, $CHCl_3$). **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.70 (br s, 1H), 7.37 – 7.23 (m, 7H), 7.11 (d, *J* = 7.7 Hz, 2H), 6.96 (br s, 1H), 5.11 (s, 2H), 4.61 (br s, 1H), 4.34 (br s, 1H), 3.99 (br s, 2H), 3.69 (s, 3H), 2.30 (s, 3H). **^{13}C-NMR** (126 MHz, $CDCl_3$): δ 171.6, 170.4, 157.3, 138.7, 136.0, 132.8, 129.6, 128.6, 128.4, 128.2, 128.1, 69.0, 67.3, 52.3, 40.8, 21.2. **HRMS** (ESI): *m/z* calcd for $C_{20}H_{23}O_5N_3Na$ [M^++Na] 408.1530, found 408.1525. **HPLC** (Chiralpak IB, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 20.3 min (major) and 23.7 min (minor).



Integration Results

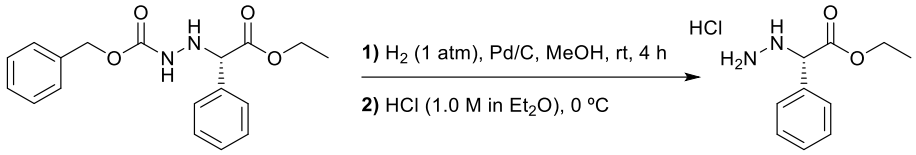
No.	Retention Time min	Area mAU*min	Relative Area %
1	20.703	89.224	50.00
2	23.543	89.229	50.00



Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	20.270	277.198	92.01
2	23.673	24.063	7.99

18. Deprotection of (*S*)-3ab

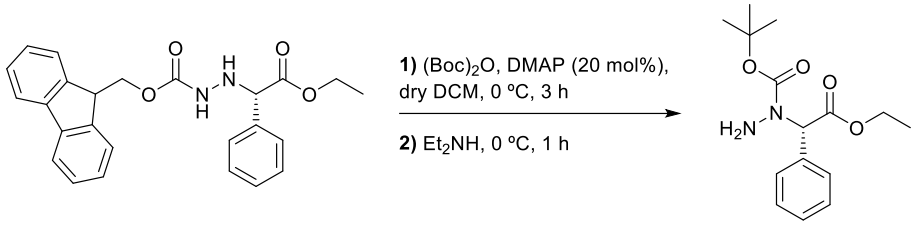


(*S*)-3ab (*S*)-4a

A 25-mL round bottomed flask was charged with Pd/C (10% w/w) (33 mg, 0.031 mmol), methanol (10 mL), **(*S*)-3ab** (328 mg, 1 mmol, 94% ee) and sealed with a rubber septum. The head-space was evacuated and back-filled with hydrogen three times and then stirred under a ballon of hydrogen for 4 h at room temperature. After this time, the mixture was filtered through a celite pad and the solvent was concentrated under reduced pressure. The crude was dissolved in dry Et_2O (1 mL) and cooled at 0 °C. Then 1.0 M HCl (in Et_2O, 1 mL, 1 mmol) was added drop-wise. After the mixture was stirred at 0 °C for 30 min, the solid was filtrated and washed with Et_2O (5 mL) and dried under vacuum to obtain the pure hydrochloride salt **(*S*)-4a** as a white solid (163 mg, 71%, 93% ee). $\mathbf{[\alpha]_D^{25}}$ = +68.2 (*c* 1, H_2O). **Mp**: 140-142 °C. **^{1}H-NMR** (300 MHz, DMSO-d^6) δ 9.44 (br s, 3H), 7.46 – 7.35 (m, 5H), 6.17 (br s, 1H), 4.91 (s, 1H), 4.21 – 4.04 (m, 2H), 1.13 (t, *J* = 7.1 Hz, 3H). **^{13}C-NMR** (75.5 MHz, DMSO-d^6): δ 170.1, 134.8, 128.8, 128.1, 64.3, 61.2, 13.9. **HRMS** (ESI): *m/z* calcd for $C_{10}H_{15}O_2N_2$ [M^+] 195.1128, found 195.1128.

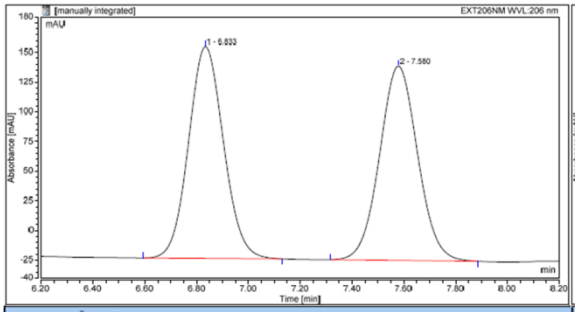
*The enantiomeric excess was determined after protection of the hydrochloride salt **(S)-4a** (12 mg, 0.05 mmol, 93% ee), with benzyl chloroformate (8 µL, 0.055 mmol), diisopropylethylamine (17 µL, 0.1 mmol) in dry CH_2Cl_2 (750 µL). The product **(*S*)-3ab** was purified by preparative TLC (n-hexane/EtOAc 1/2) and the enantiomeric excess (ee) was determined by HPLC analysis (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 13.4 min (major) and 16.0 min (minor).

19. Deprotection of (*S*)-3ag



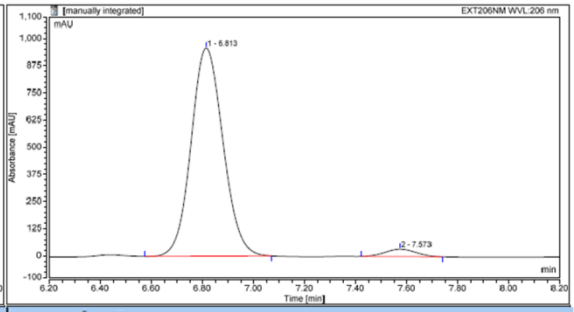
(*S*)-3ag (*S*)-5a

A 25-mL round bottomed flask was charged with **(*S*)-3ag** (416 mg, 1 mmol, 93% ee), dry CH_2Cl_2 (10 mL) and di-*tert*-butyl dicarbonate (337 mg, 1.5 mmol) and the resulting solution was cooled to 0 °C. 4-Dimethylaminopyridine (24 mg, 0.2 mmol) was added and the resulting mixture was stirred at 0 °C for 3 hours. After this time, diethylamine (525 µL, 5 mmol) was added and the reaction mixture was stirred for 1 hour at 0 °C. The solvent was removed under reduced pressure and the residue purified by flash chromatography (*n*-hexane/EtOAc 3/1) to give **(*S*)-5a** as a colourless oil (229 mg, 78%, 93% ee). $[\alpha]_D^{25}$ = +73.5 (*c* 1, $CHCl_3$). **^{1}H-NMR** (300 MHz, $CDCl_3$) δ 7.44 – 7.29 (m, 5H), 6.31 (br s, 1H), 4.79 (s, 1H), 4.44 (br s, 1H), 4.25 – 4.07 (m, 2H), 1.44 (s, 9H), 1.19 (t, *J* = 7.1 Hz, 3H).**^{13}C-NMR** (75.5 MHz, $CDCl_3$): δ 171.5, 156.5, 135.7, 128.8, 128.7, 128.5, 80.9, 67.2, 61.4, 28.4, 14.1. **HRMS** (ESI): *m/z* calcd for $C_{15}H_{23}O_4N_2$ [M^++H] 295.1652, found 295.1651. **HPLC** (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 6.8 min (major) and 7.6 min (minor).



Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	6.833	27.960	50.06
2	7.580	27.893	49.94



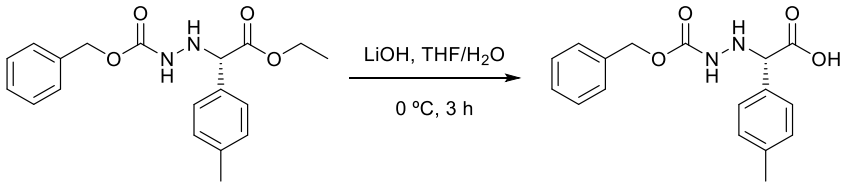
Integration Results

No.	Retention Time min	Area mAU*min	Relative Area %
1	6.813	139.026	96.67
2	7.573	4.790	3.33

*The absolute configuration of the products **(*S*)-3ag** and **(*S*)-5a** were determine by the deprotection of **(*S*)-5a** (44 mg, 0.15 mmol) with 4 M HCl (in dioxane, 0.5 mL, 2 mmol) at 0 °C for 4 hours. After this time, the solvent was removed under reduced pressure and the residue dried under vacuum to obtain the pure hydrochloride salt **(*S*)-4a** (33 mg, 95%, 93% ee).

The enantiomeric excess was determined after protection of the hydrochloride salt **(S)-4a** (12 mg, 0.05 mmol, 93% ee), with benzyl chloroformate (8 µL, 0.055 mmol), diisopropylethylamine (17 µL, 0.1 mmol) in dry CH_2Cl_2 (750 µL). The product **(*S*)-3ab** was purified by preparative TLC (n-hexane /EtOAc 1/2) and the enantiomeric excess (ee) was determined by HPLC analysis (Chiralpak IA, *n*-hexane/2-propanol 90:10, flow 1 mL/min) t_R 13.4 min (major) and 16.0 min (minor).

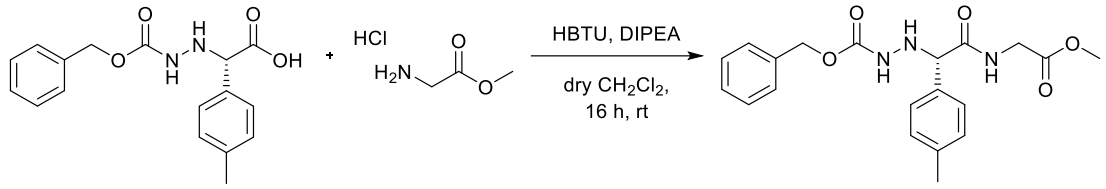
20. Hydrolysis of ester (*S*)-3cb



(*S*)-3cb **(S)-6a**

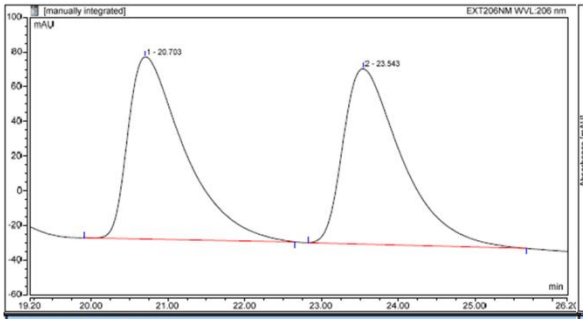
A 50-mL round bottomed flask was charged with LiOH (245 mg, 10 mmol) and distilled H_2O (10 mL) and the resulting solution was cooled to 0 °C. A solution of **(*S*)-3cb** (342 mg, 1 mmol, 94% ee) in THF (10 mL) was added and the reaction mixture was stirred for 3 hour at 0 °C. The reaction mixture was then concentrated to remove the THF and the residue was diluted with H_2O (15 mL) and Et_2O (15 mL). The aqueous layer was separated and neutralized with saturated $NaHSO_4$ solution to pH ~2. The acidic aqueous layer was extracted with Et_2O (3 x 15 mL), and the combined organic layers were washed with brine (3 x 15 mL), dried over $MgSO_4$, concentrated under reduced pressure and dried under vacuum to obtain the pure acid **(*S*)-6a** as a white solid (267 mg, 85%, 93% ee). **$[\alpha]_D^{25}$ =** +96.3 (*c* 1, $CHCl_3$). **Mp**: 58-60 °C. **^{1}H-NMR** (500 MHz, DMSO-d^6) δ 8.63 (br s, 1H), 7.42 – 7.27 (m, 7H), 7.15 (d, *J* = 7.4 Hz, 2H), 5.05 (s, 2H), 4.65 (br s, 1H), 2.29 (s, 3H). **^{13}C-NMR** (126 MHz, DMSO-d^6): δ172.4, 156.9, 137.1, 136.9, 134.1, 128.8, 128.3, 128.1, 127.8, 127.6, 65.8, 66.5, 20.7. **HRMS** (ESI): *m/z* calcd for $C_{17}H_{18}O_4N_2Na$ [M^++Na] 337.1159, found 337.1157.

21. Peptide coupling reaction with (*S*)-6a

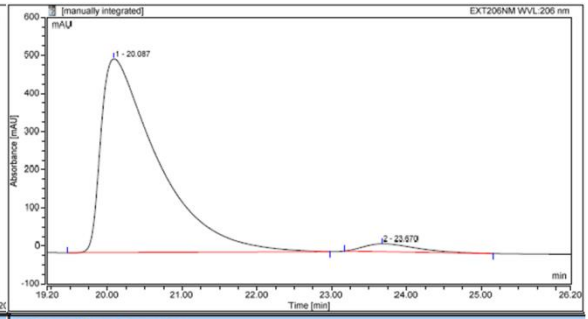


(*S*)-6a **(*S*)-3cm**

Glycine methyl ester hydrochloride (117 mg, 0.94 mmol) was added to a solution of HBTU (362 mg, 0.94 mmol), acid **(*S*)-6a** (267 mg, 0.85 mmol, 93% ee) and diisopropylethylamine (350 µL, 2.0 mmol) in dry CH_2Cl_2 (12 mL). The resulting mixture was stirred under Ar at room temperature for 16 hours. The reaction was diluted with EtOAc (30 mL) and washed with HCl (0.5 M, 2 x 15 mL), saturated aqueous $NaHCO_3$ (2 x 15 mL) and brine (2 x 15 mL), dried over $MgSO_4$ and concentrated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel (*n*-hexane/EtOAc 3/1) to give **(*S*)-3cm** as a colourless oil (266 mg, 81%, 93% ee). $[\alpha]_D^{25}$ = +14.0 (*c* 1, $CHCl_3$). **HPLC** (Chiralpak IB, *n*-hexane/2-propanol 85:15, flow 1 mL/min) t_R 20.1 min (major) and 23.7 min (minor).



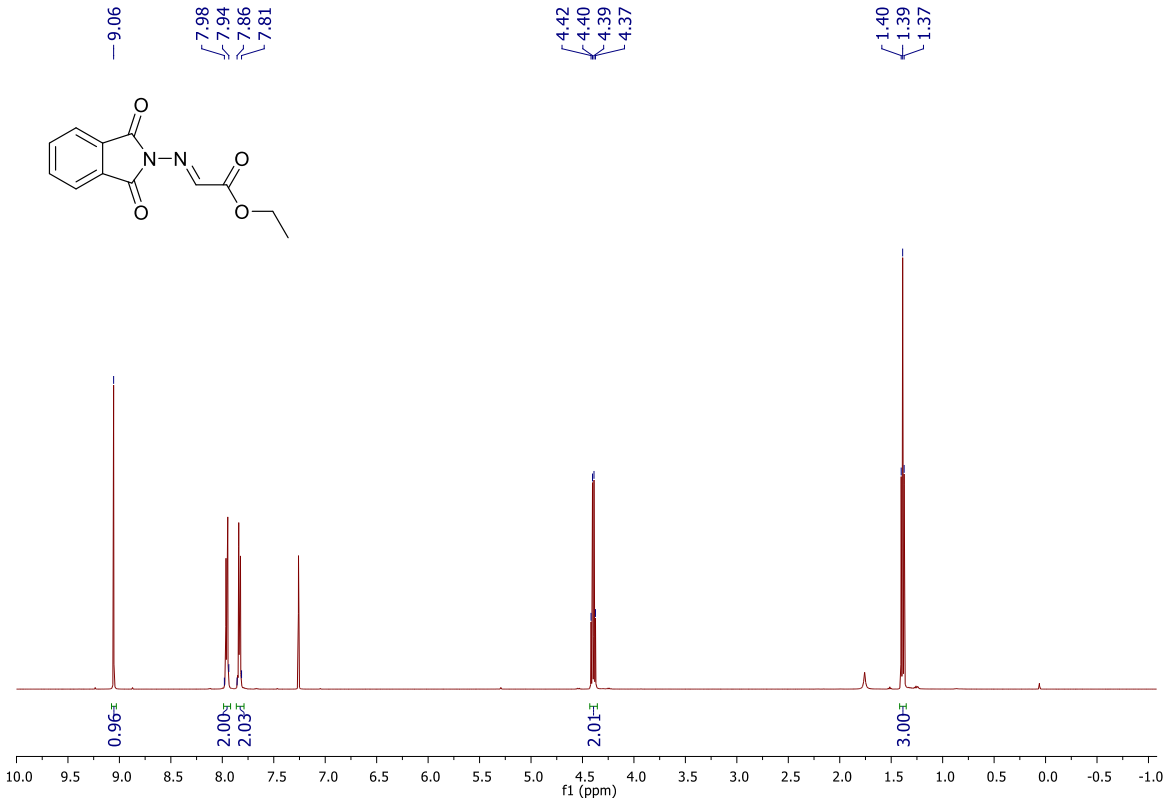
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	20.703	89.224	50.00
2	23.543	89.229	50.00



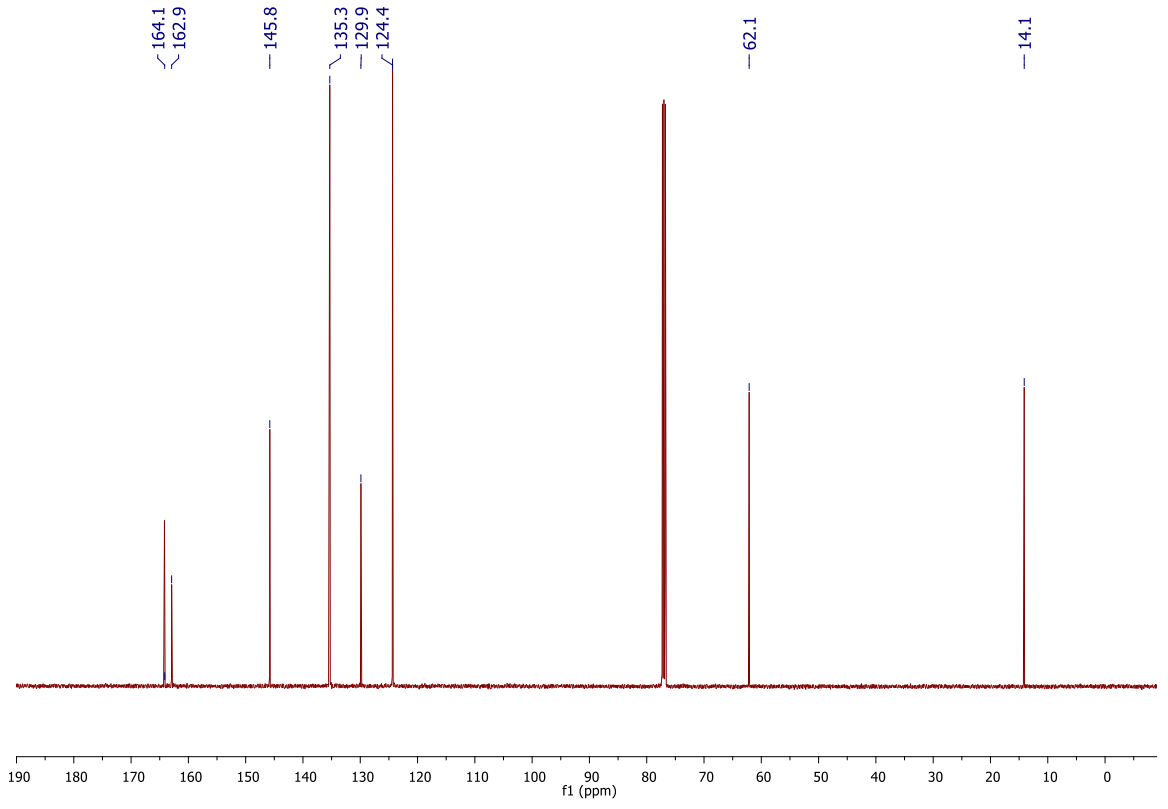
Integration Results			
No.	Retention Time min	Area mAU*min	Relative Area %
1	20.087	447.485	96.43
2	23.670	16.567	3.57

22. NMR spectra of new compounds

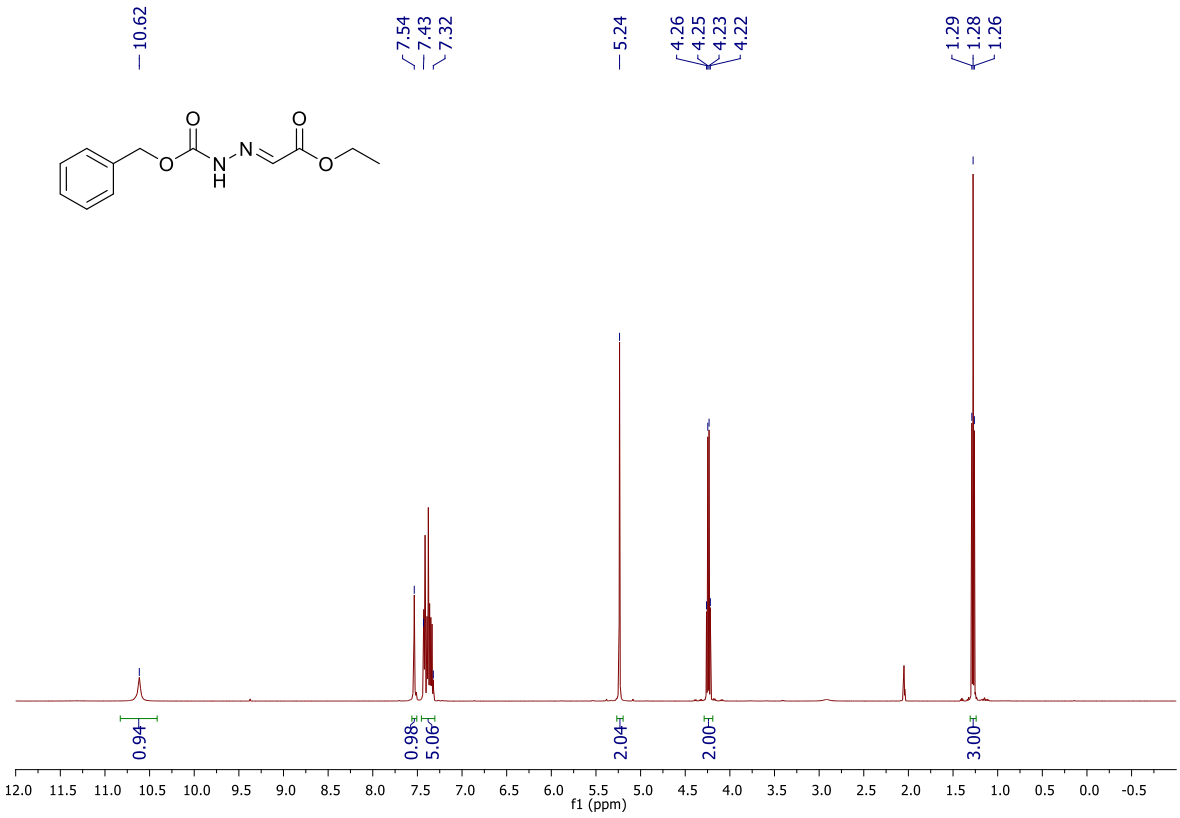
^{1}H NMR ($CDCl_3$, 500 MHz) of **1a**



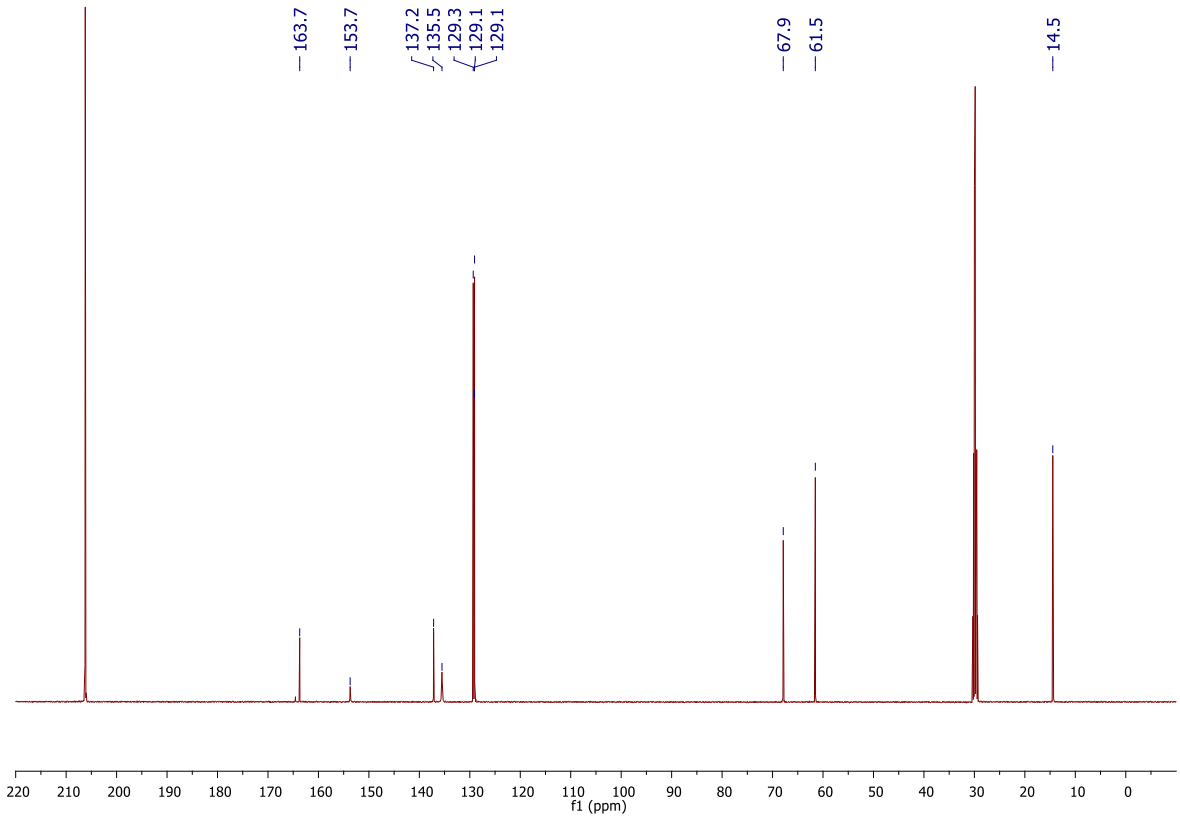
^{13}C NMR ($CDCl_3$, 126 MHz) of **1a**



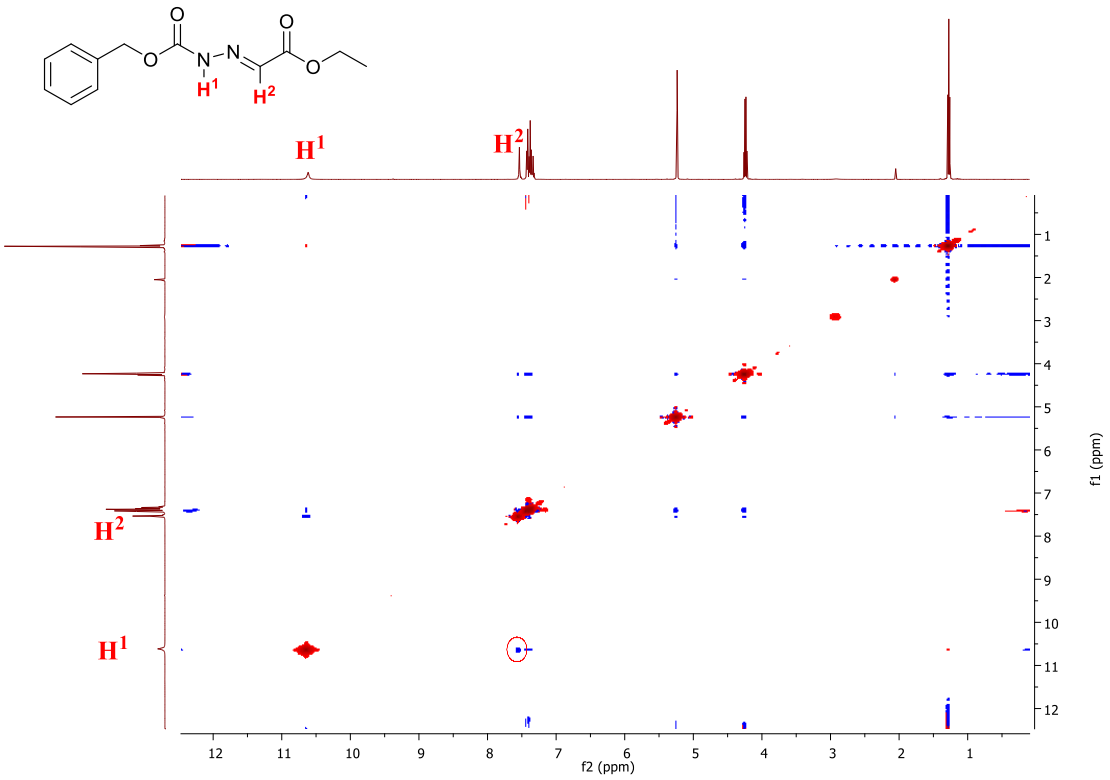
^{1}H NMR (Acetone-d^{6}, 500 MHz) of ***(E)*-1b**



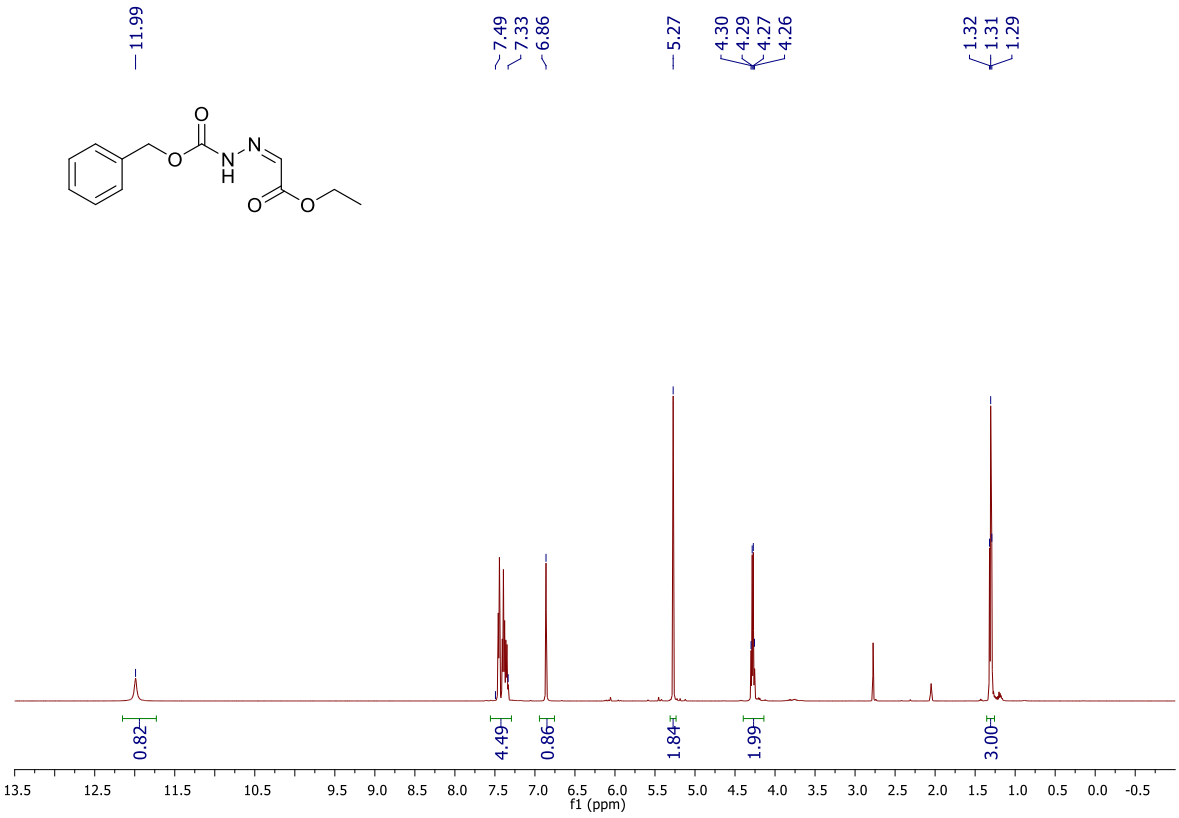
^{13}C NMR (Acetone-d^{6}, 126 MHz) of ***(E)*-1b**



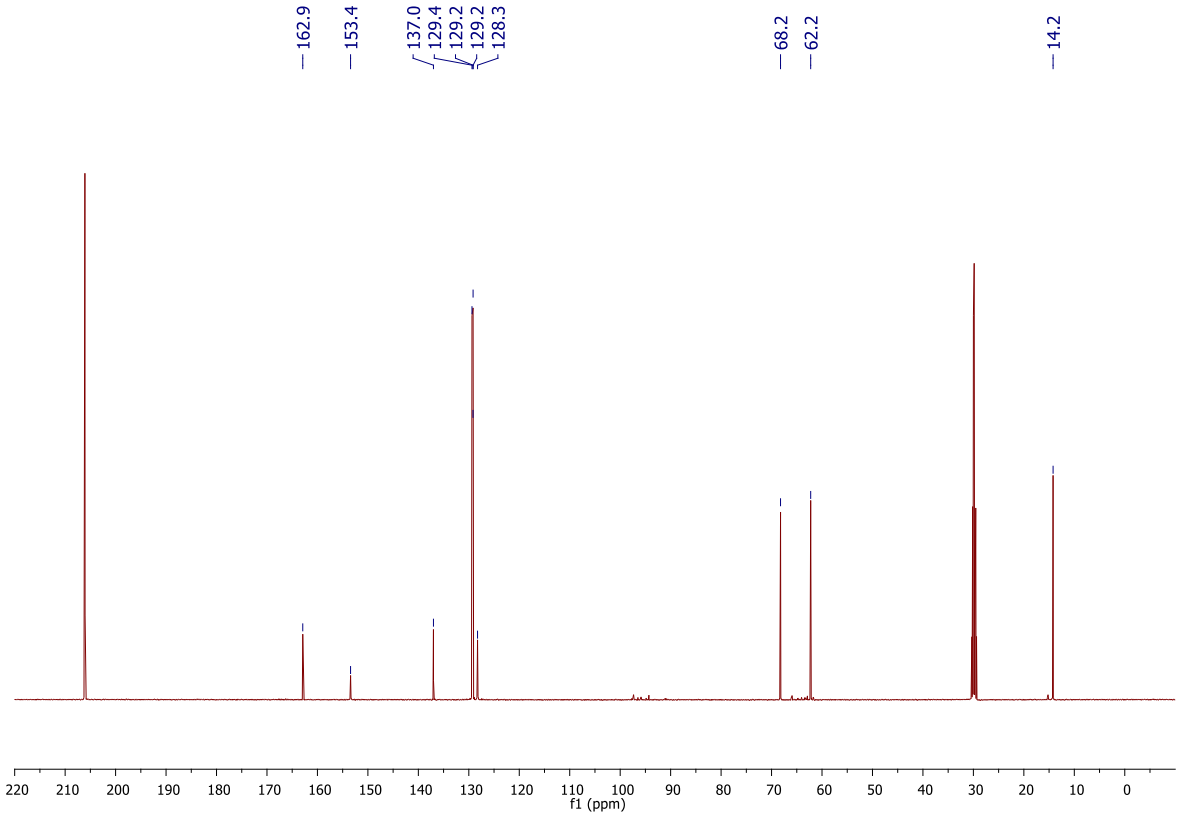
NOESY (Acetone-d^6, 500 MHz) of ***(E)*-1b**



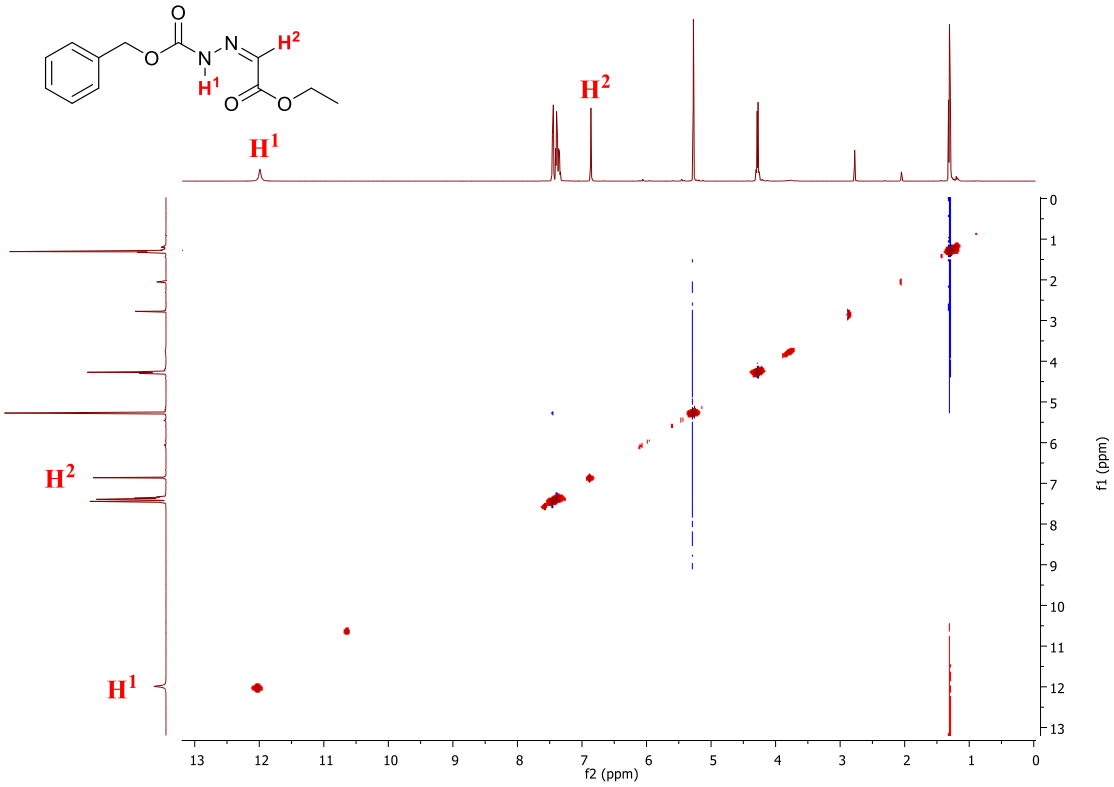
^{1}H NMR (Acetone-d^{6}, 500 MHz) of ***(Z)*-1b**



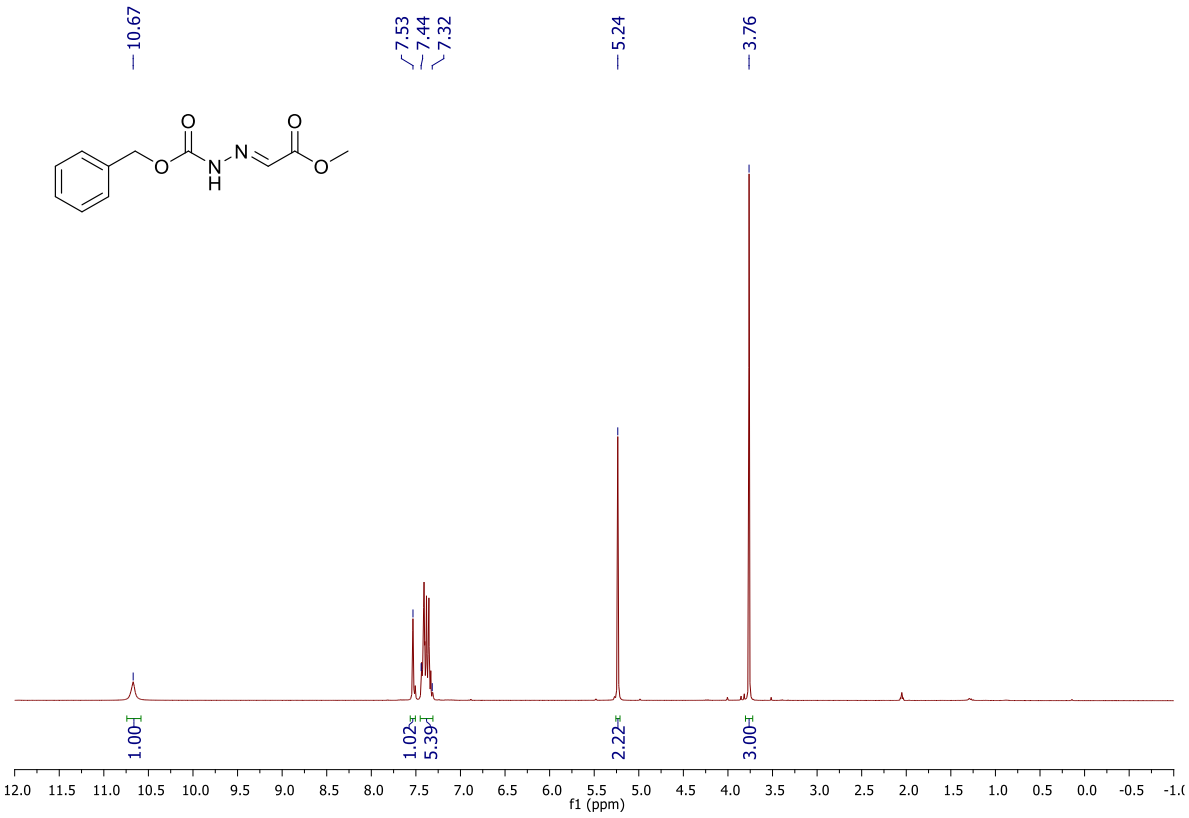
^{13}C NMR (Acetone-d^{6}, 126 MHz) of ***(Z)*-1b**



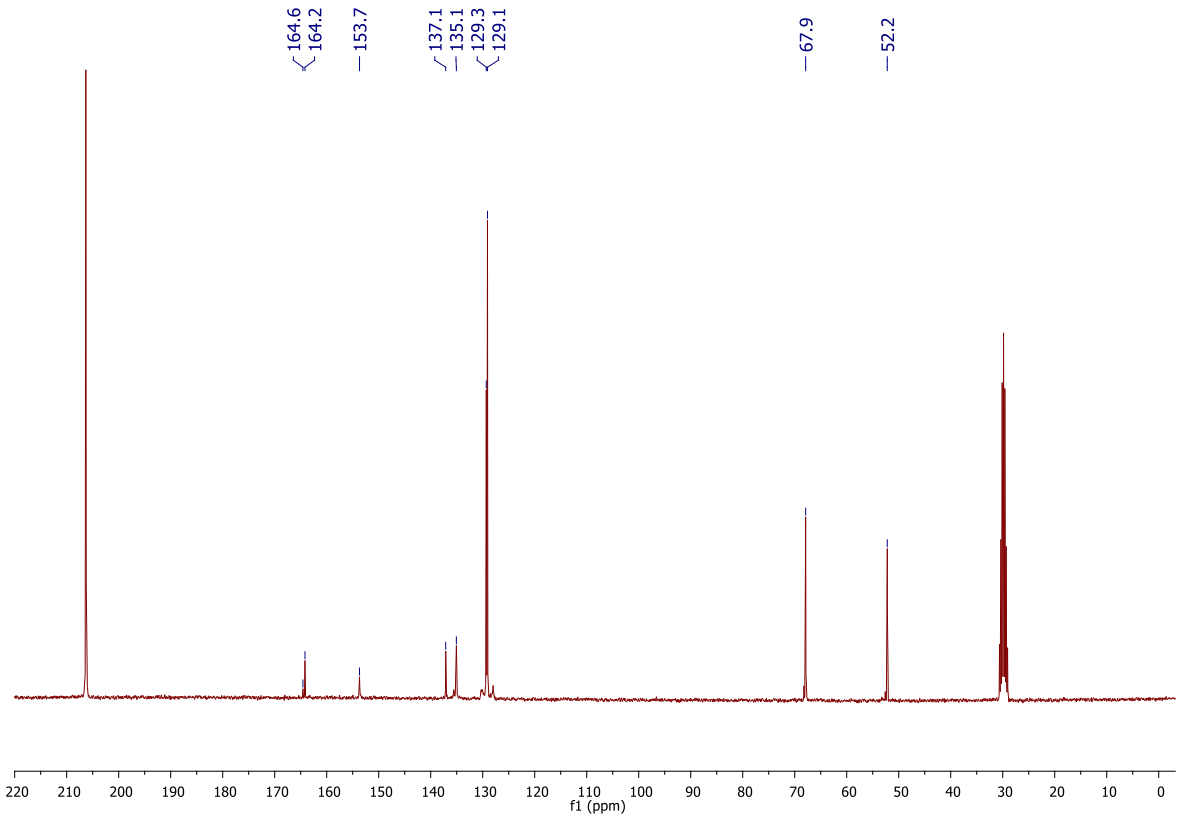
NOESY (Acetone-d^6, 500 MHz) of **(*Z*)-1b**



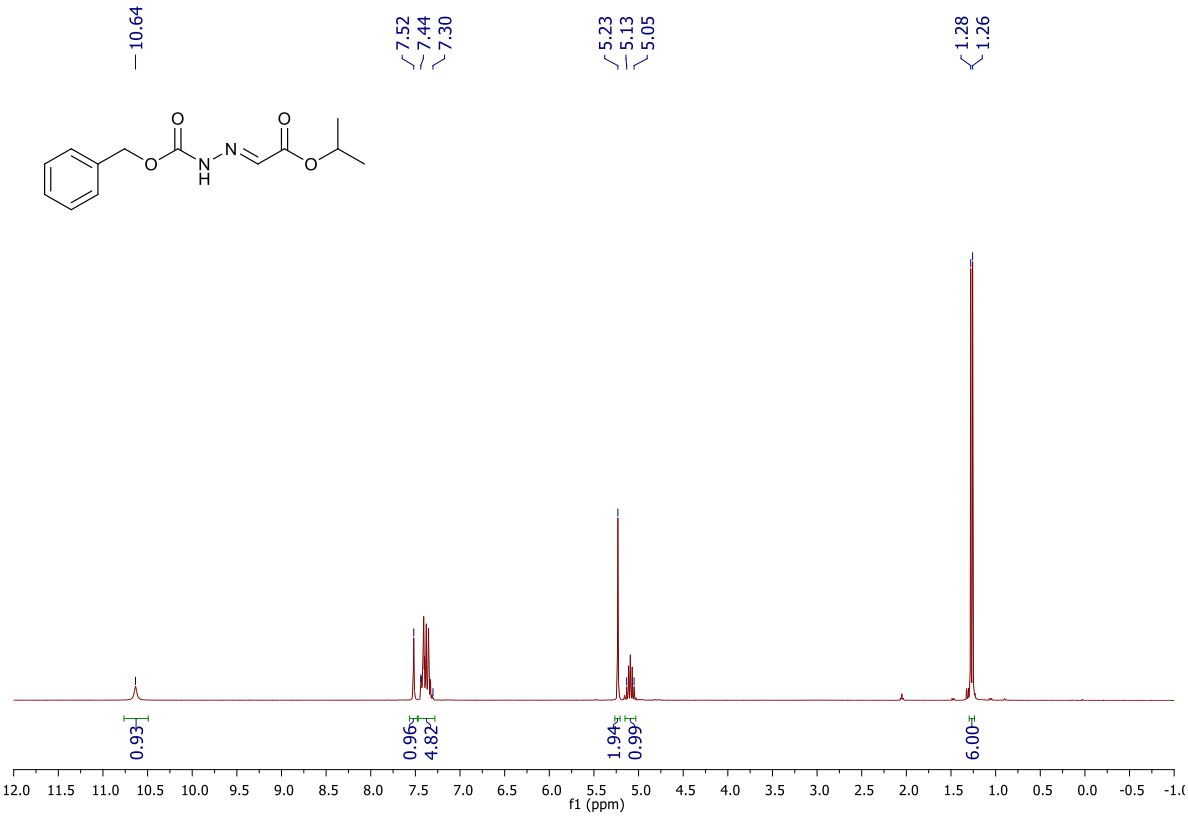
^{1}H NMR (Acetone-d^{6}, 300 MHz) of ***(E)*-1c**



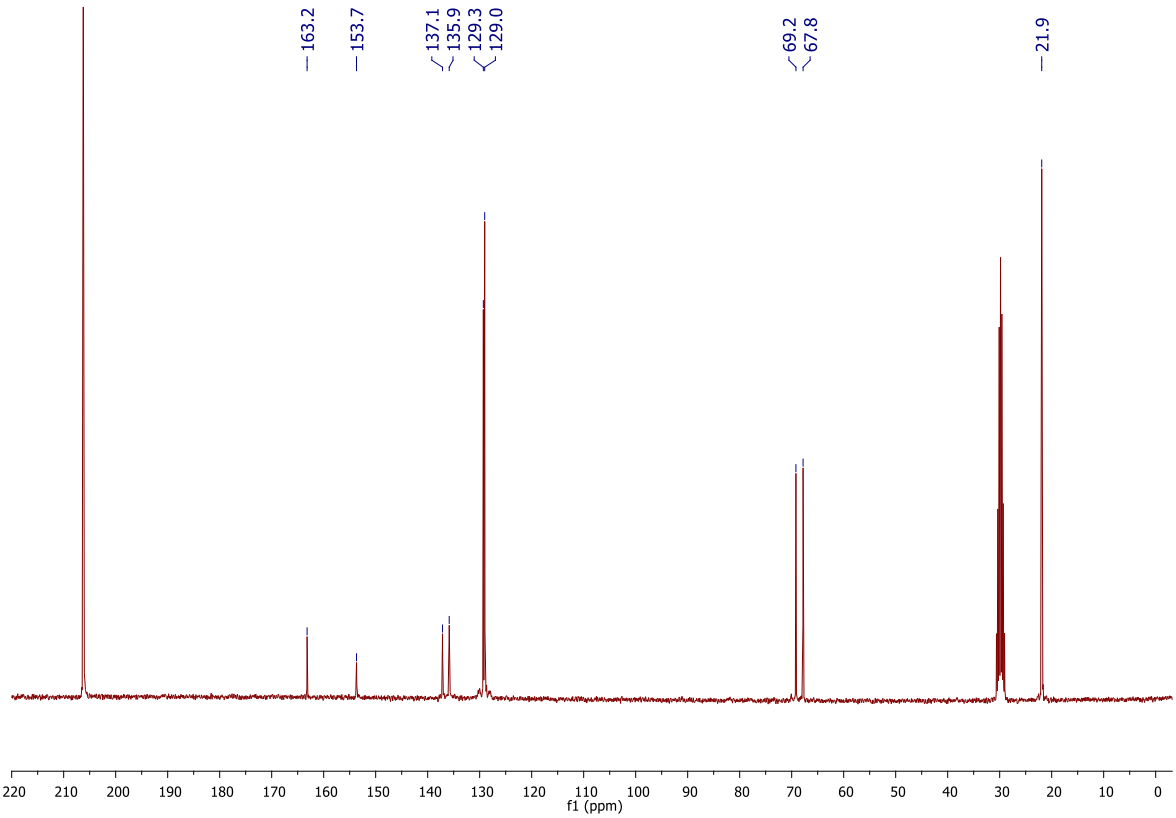
^{13}C NMR (Acetone-d^{6}, 75.5 MHz) of ***(E)*-1c**



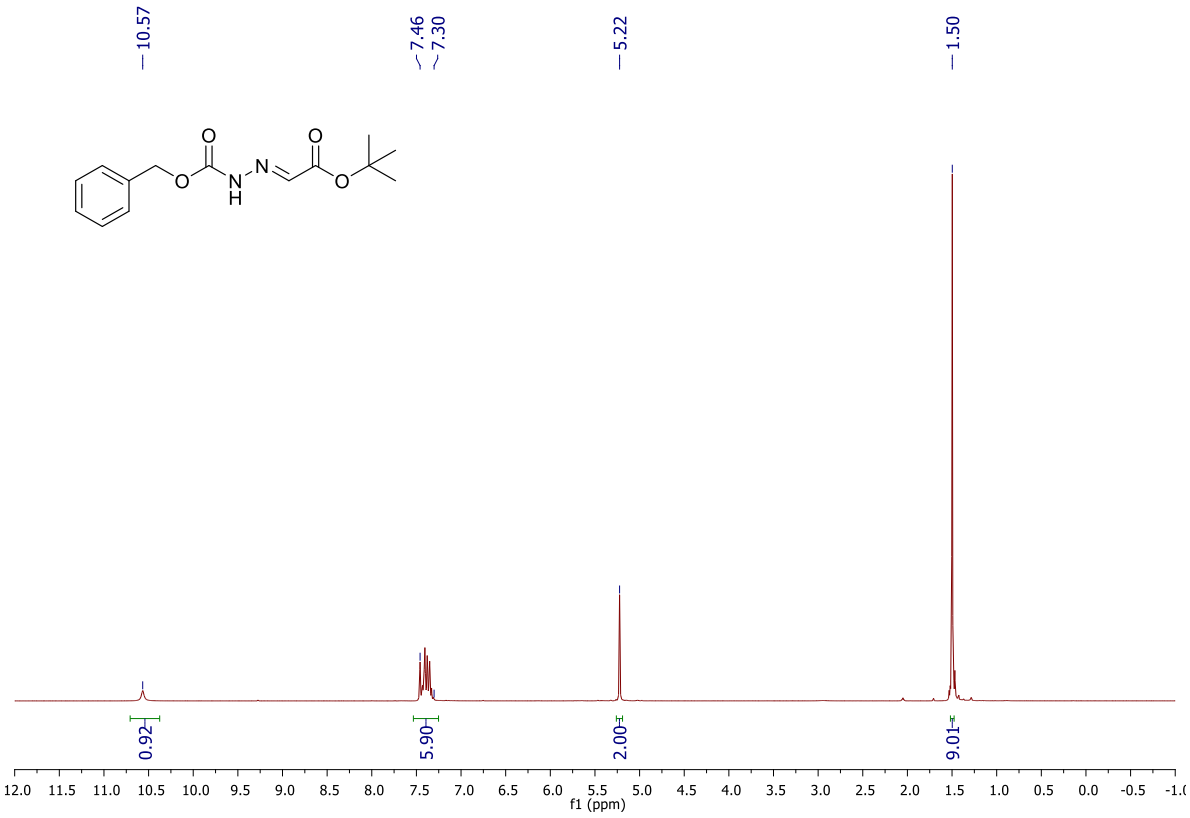
^{1}H NMR (Acetone-d^{6}, 300 MHz) of ***(E)*-1e**



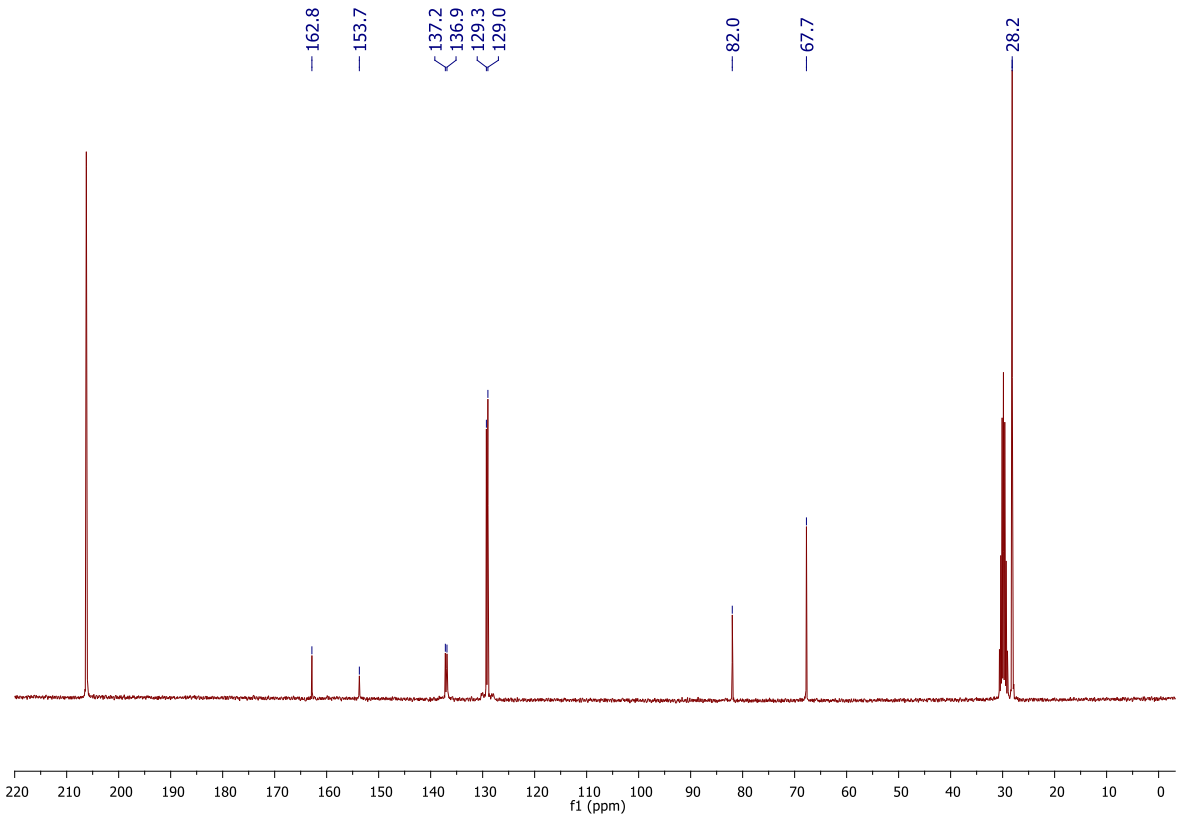
^{13}C NMR (Acetone-d^{6}, 75.5 MHz) of ***(E)*-1e**



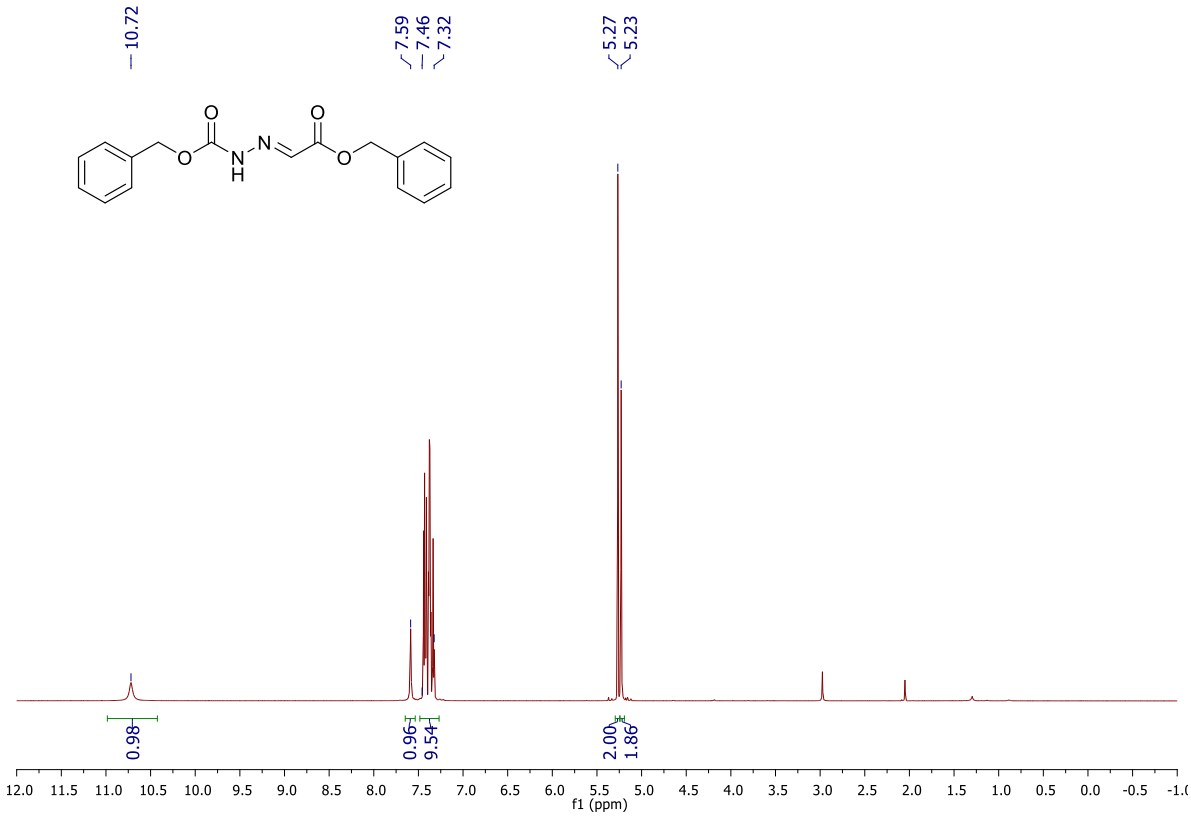
^{1}H NMR (Acetone-d^{6}, 300 MHz) of ***(E)*-1f**



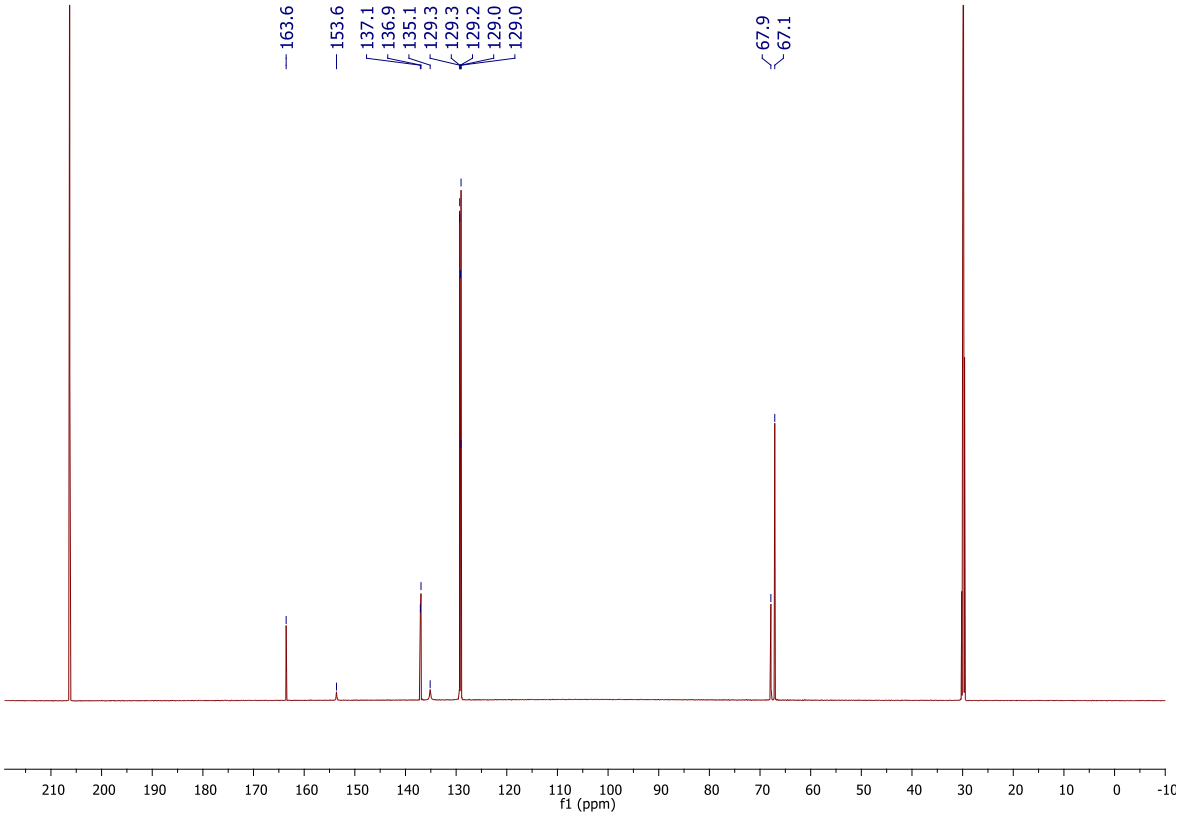
^{13}C NMR (Acetone-d^{6}, 75.5 MHz) of ***(E)*-1f**



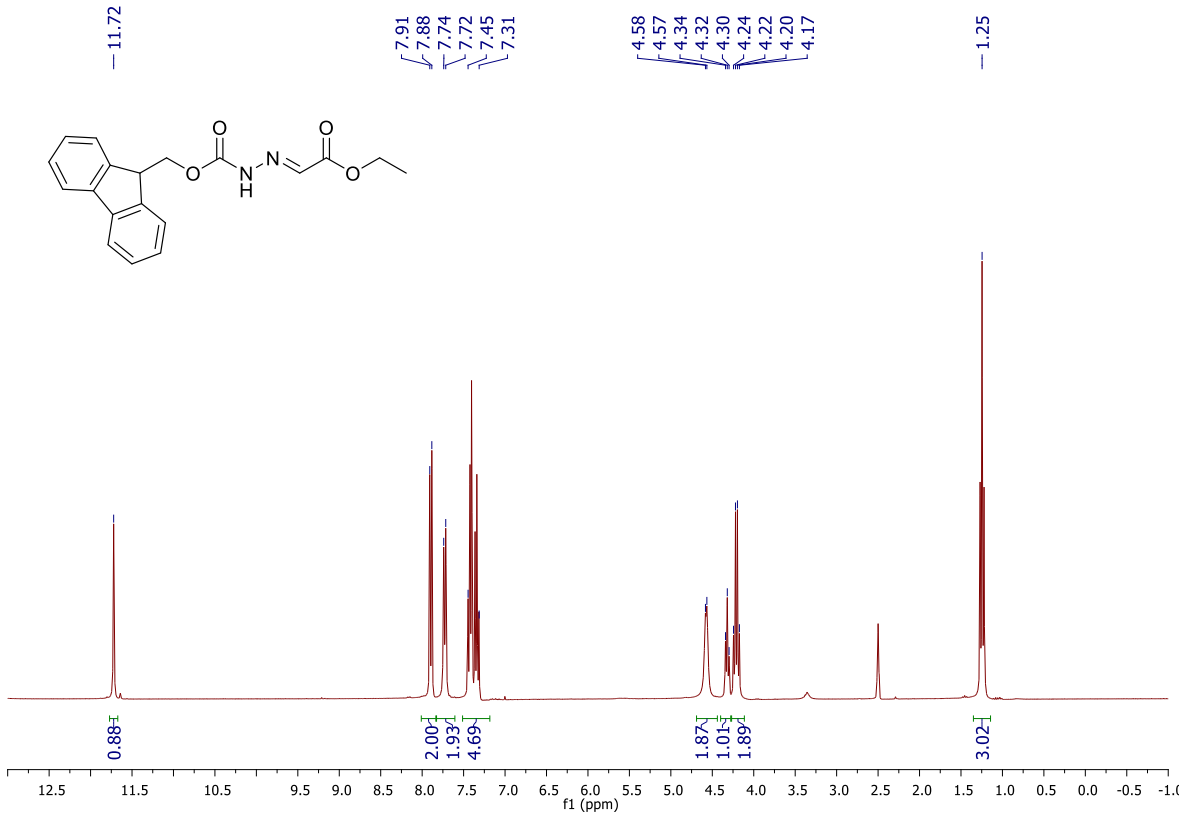
^{1}H NMR (Acetone-d^{6}, 700 MHz) of ***(E)*-1d**



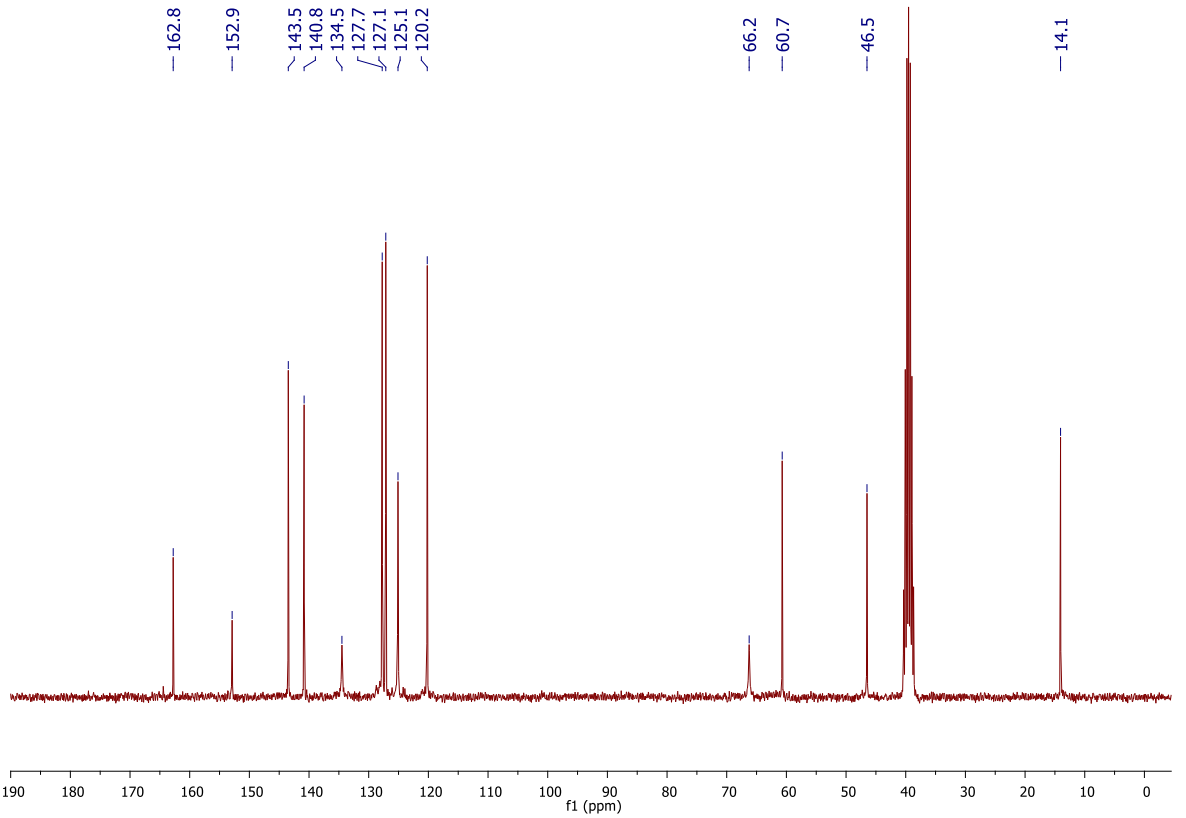
^{13}C NMR (Acetone-d^{6}, 176 MHz) of ***(E)*-1d**



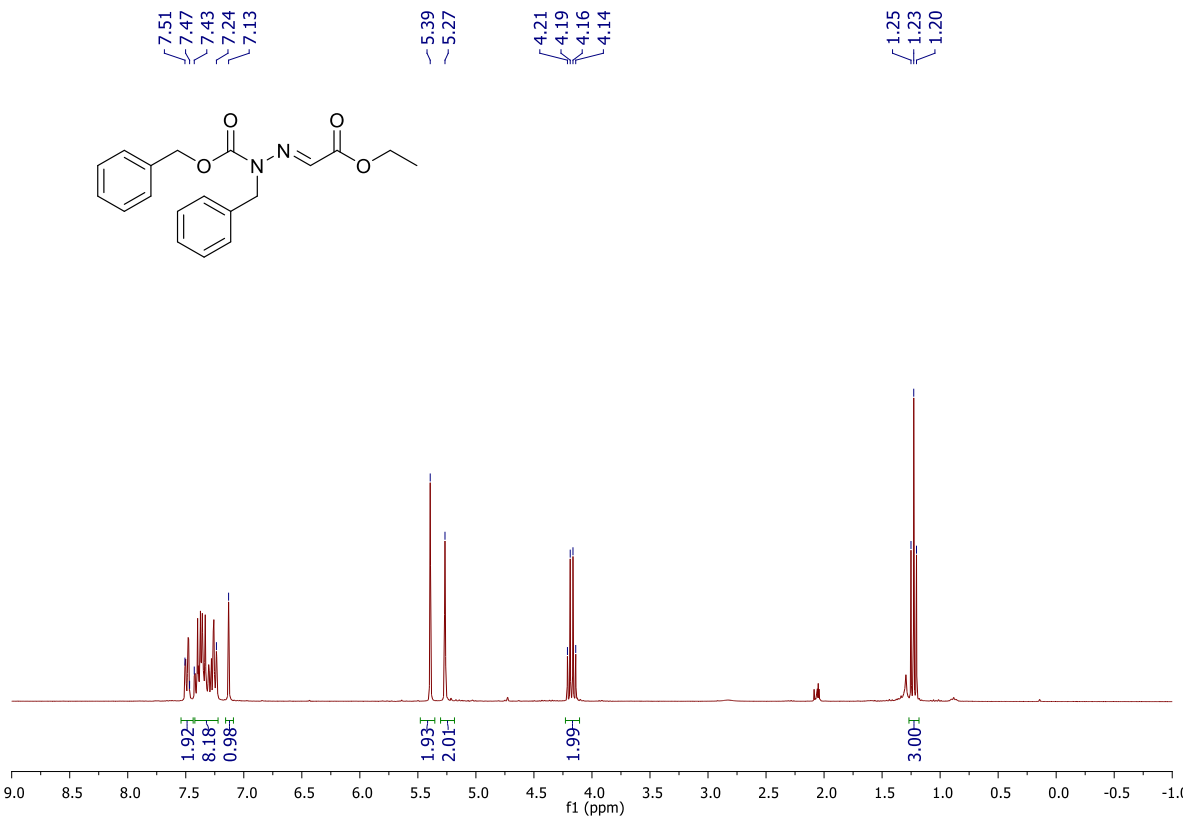
^{1}H NMR (DMSO-d^{6}, 300 MHz) of ***(E)*-1g**



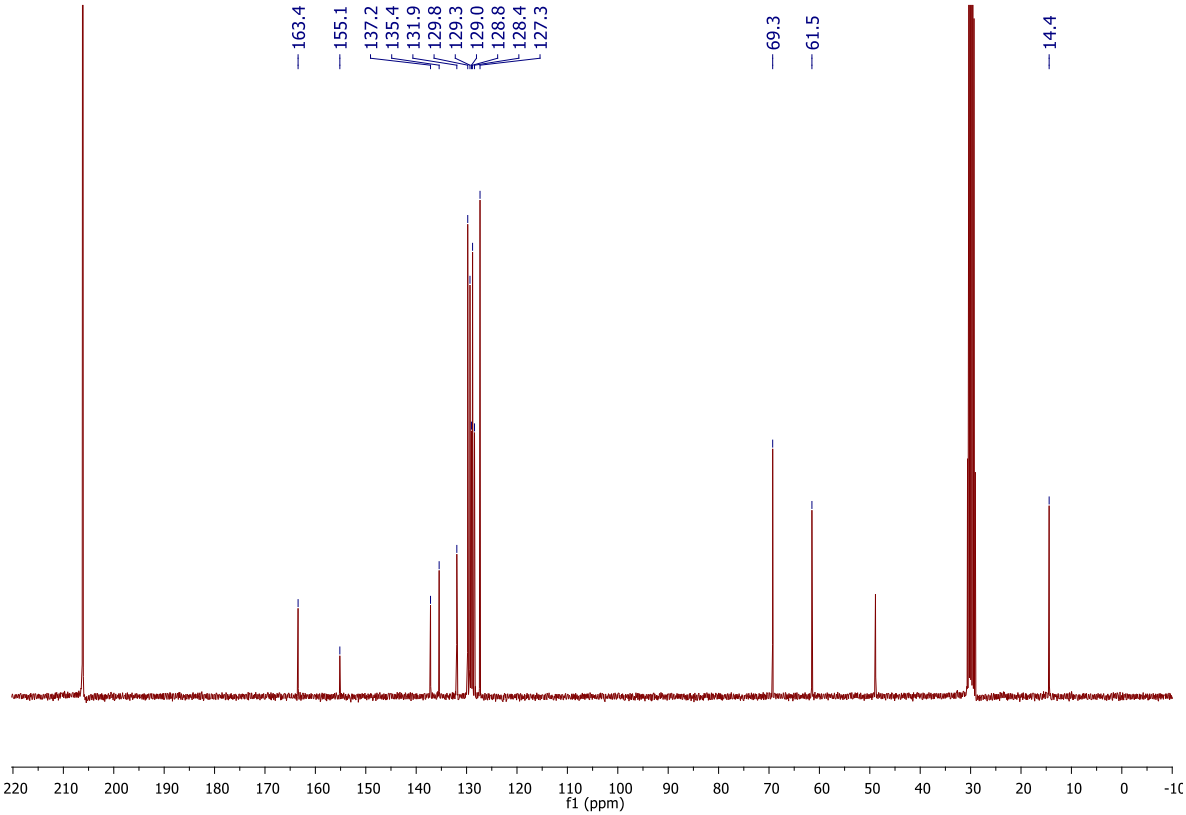
^{13}C NMR (DMSO-d^{6}, 75.5 MHz) of ***(E)*-1g**



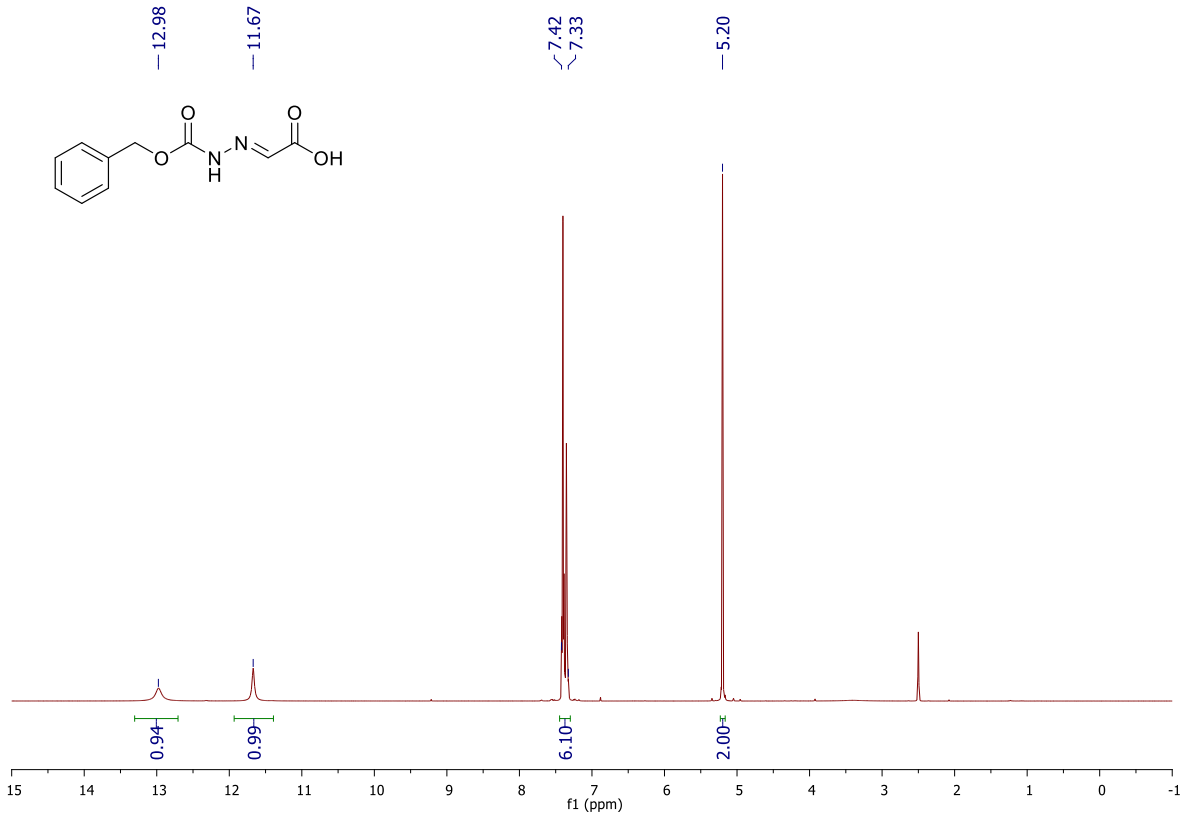
^{1}H NMR (Acetone-d^{6}, 300 MHz) of ***(E)*-1i**



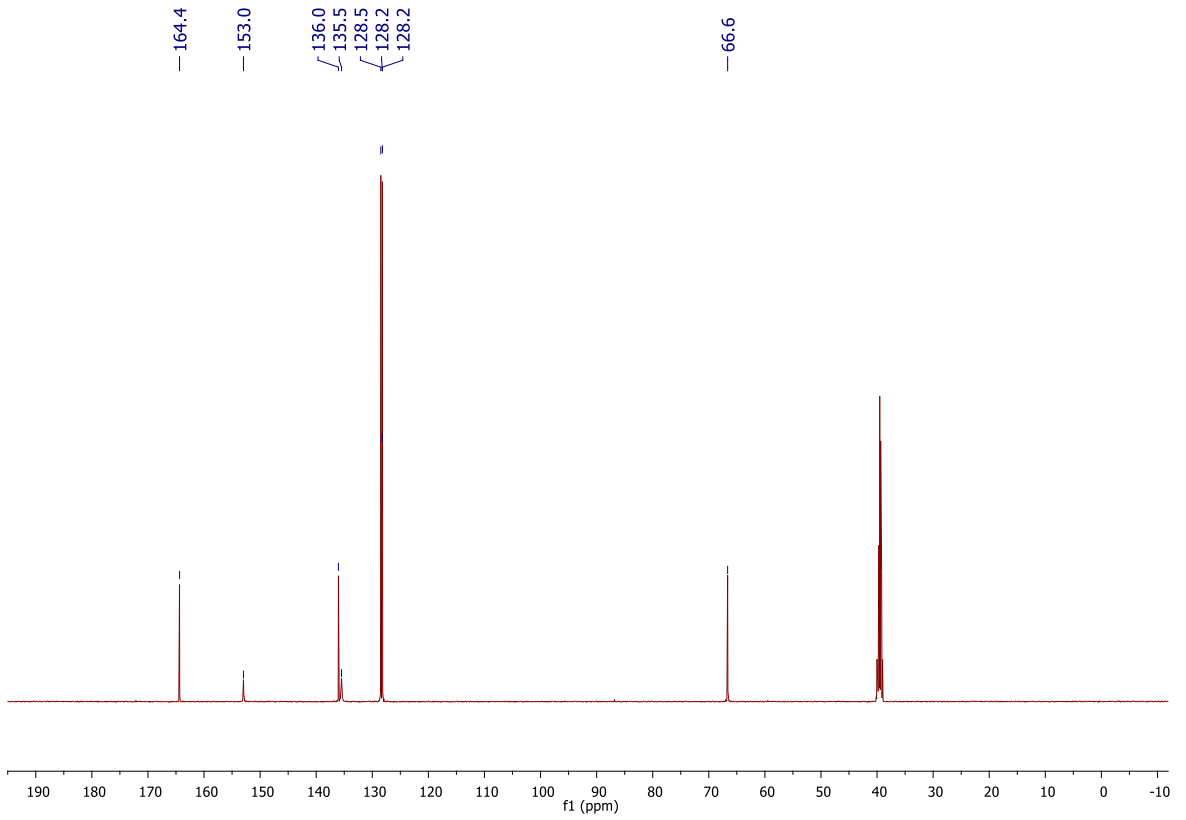
^{13}C NMR (Acetone-d^{6}, 75.5 MHz) of ***(E)*-1i**



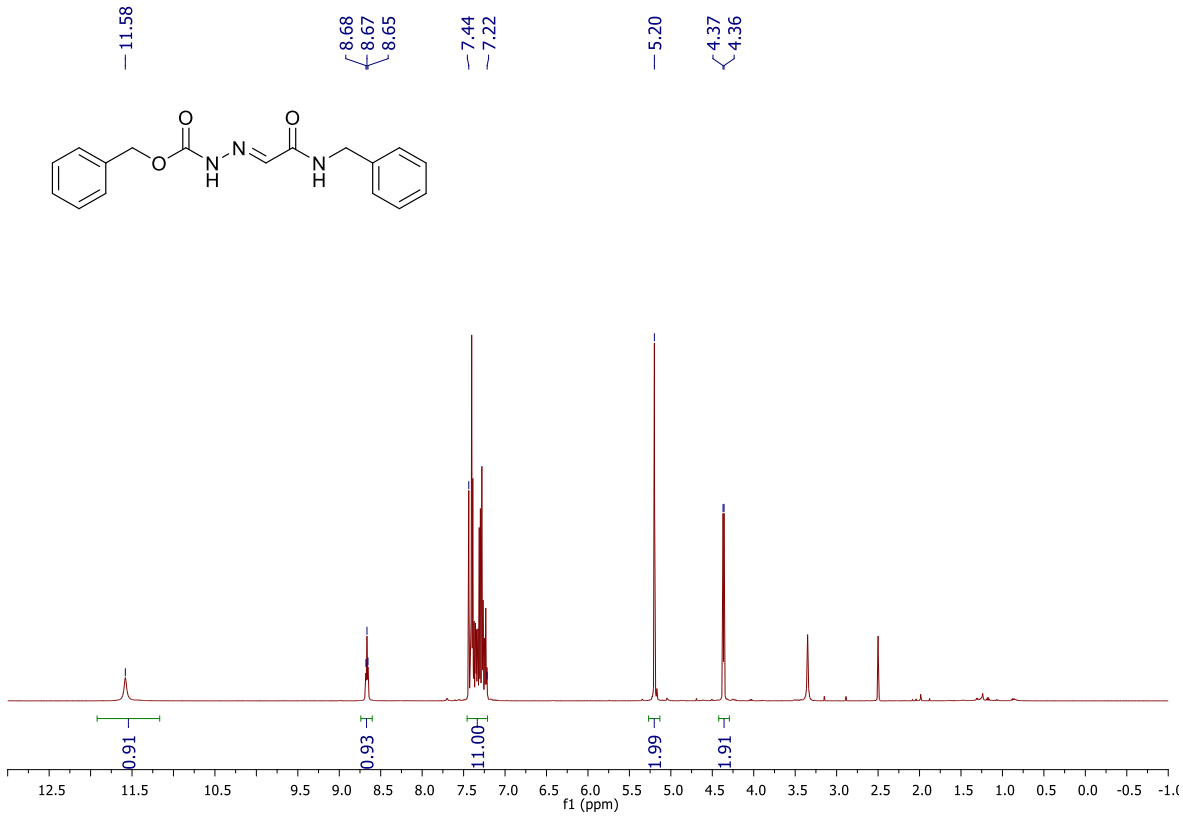
^{1}H NMR (DMSO-d^{6}, 500 MHz) of **S6**



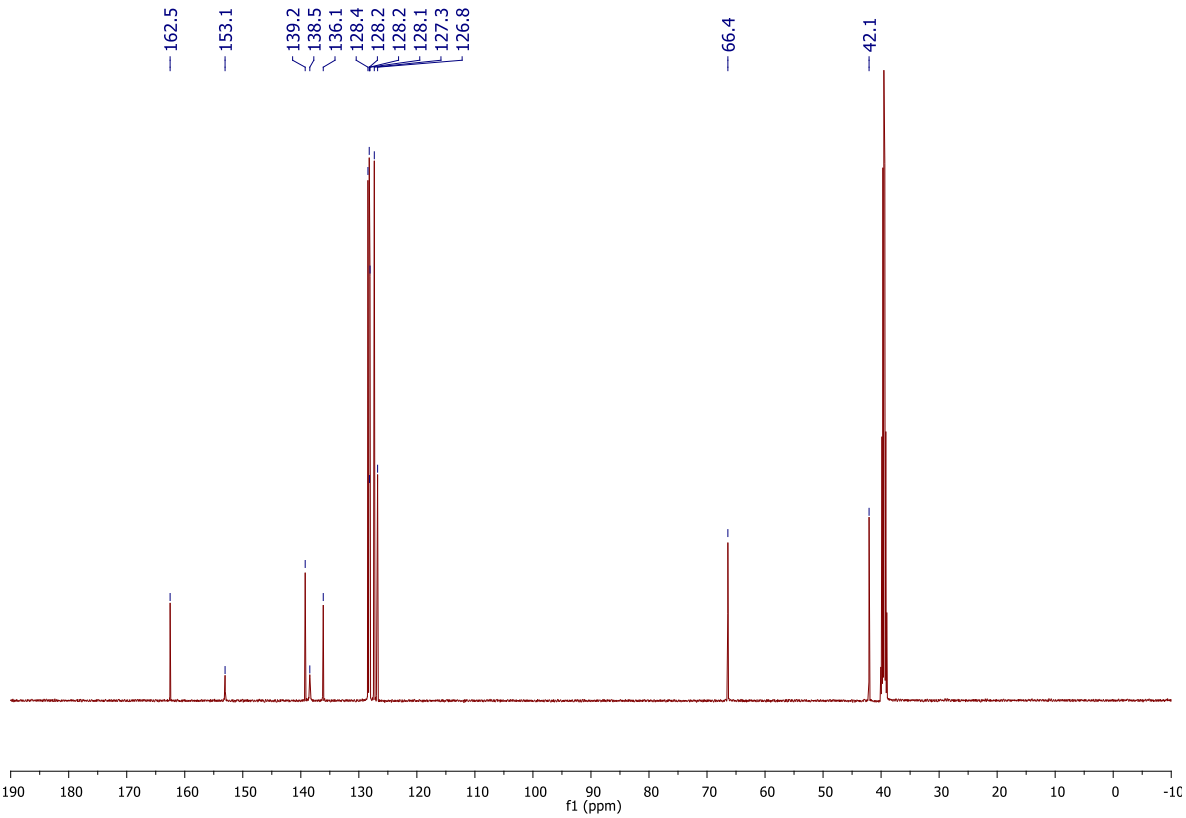
^{13}C NMR (DMSO-d^{6}, 126 MHz) of **S6**



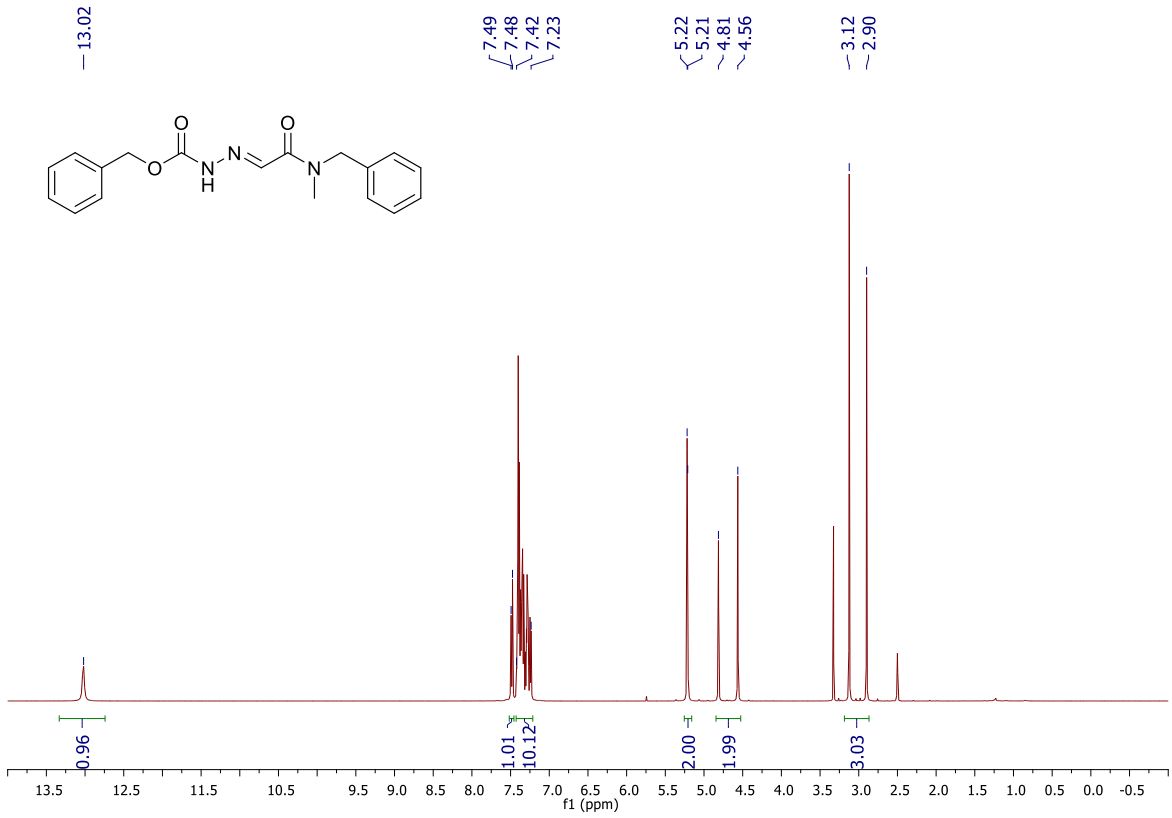
^{1}H NMR (DMSO-d^{6}, 500 MHz) of ***(E)*-1k**



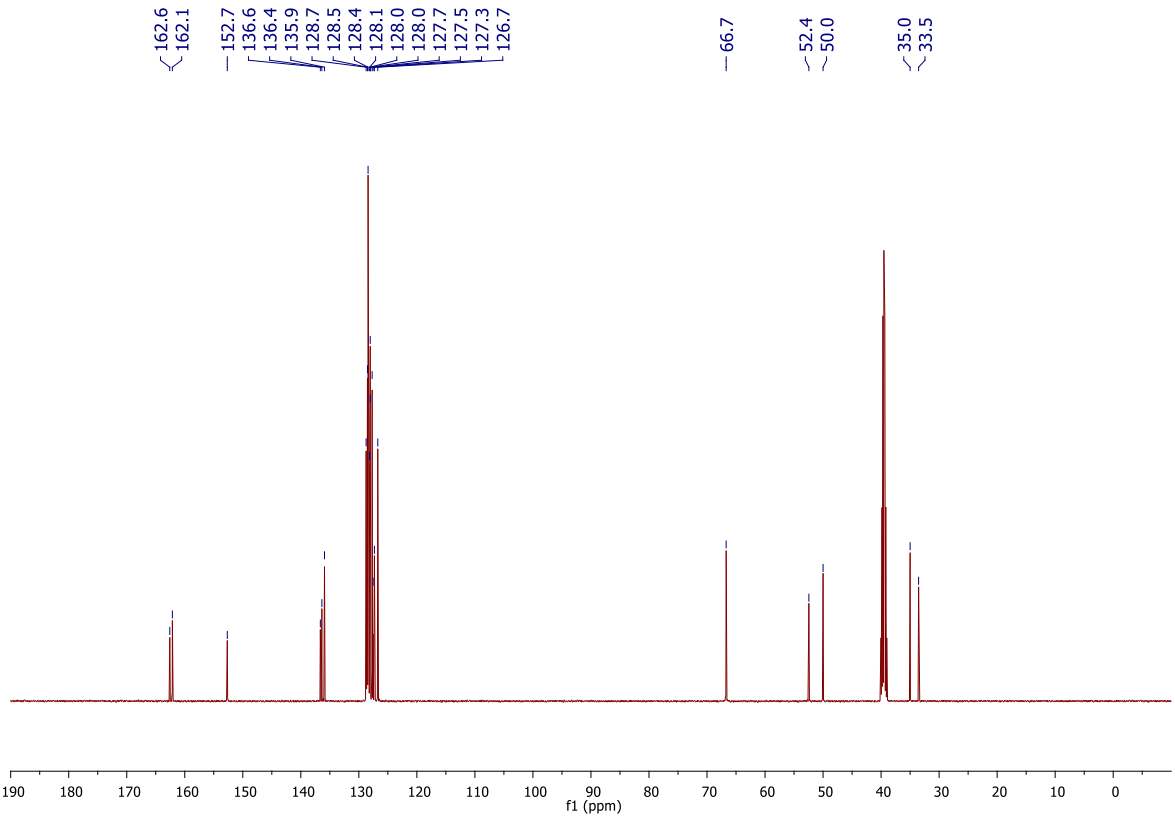
^{13}C NMR (DMSO-d^{6}, 126 MHz) of ***(E)*-1k**



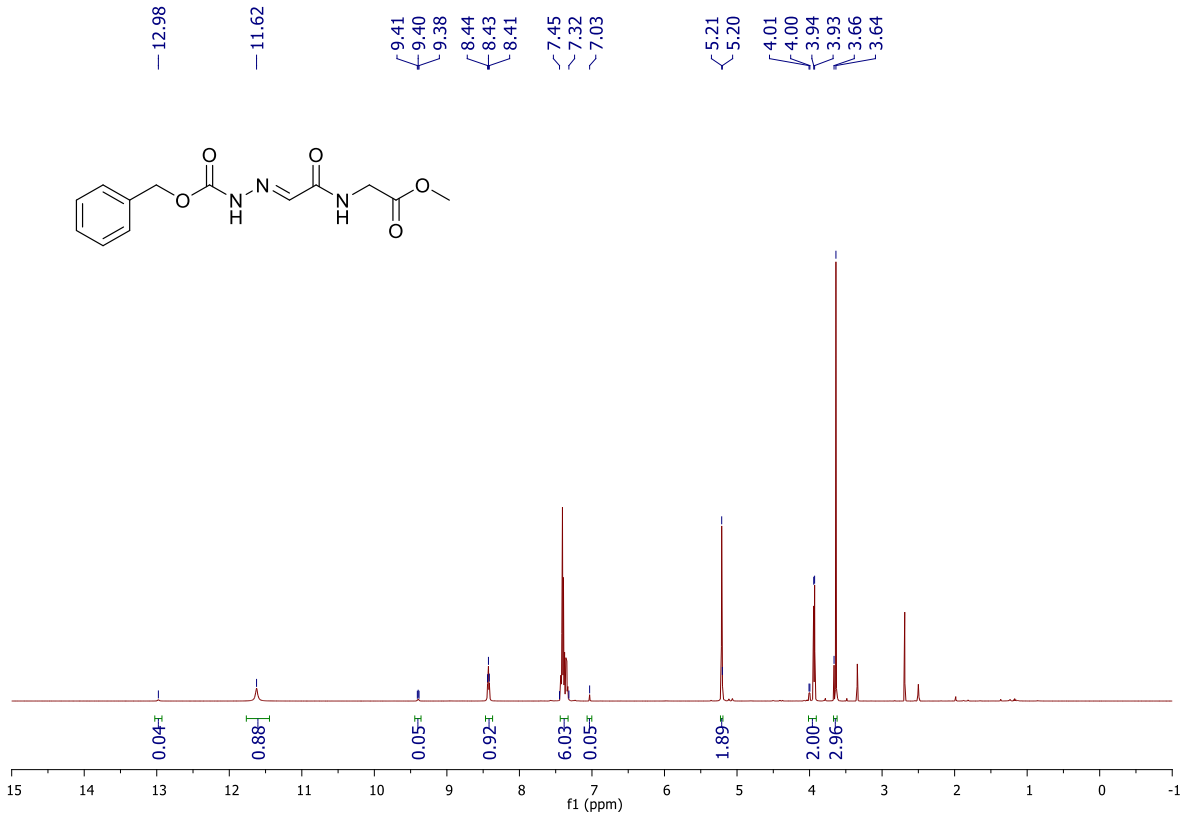
^{1}H NMR (DMSO-d^{6}, 500 MHz) of ***(E)*-1l**



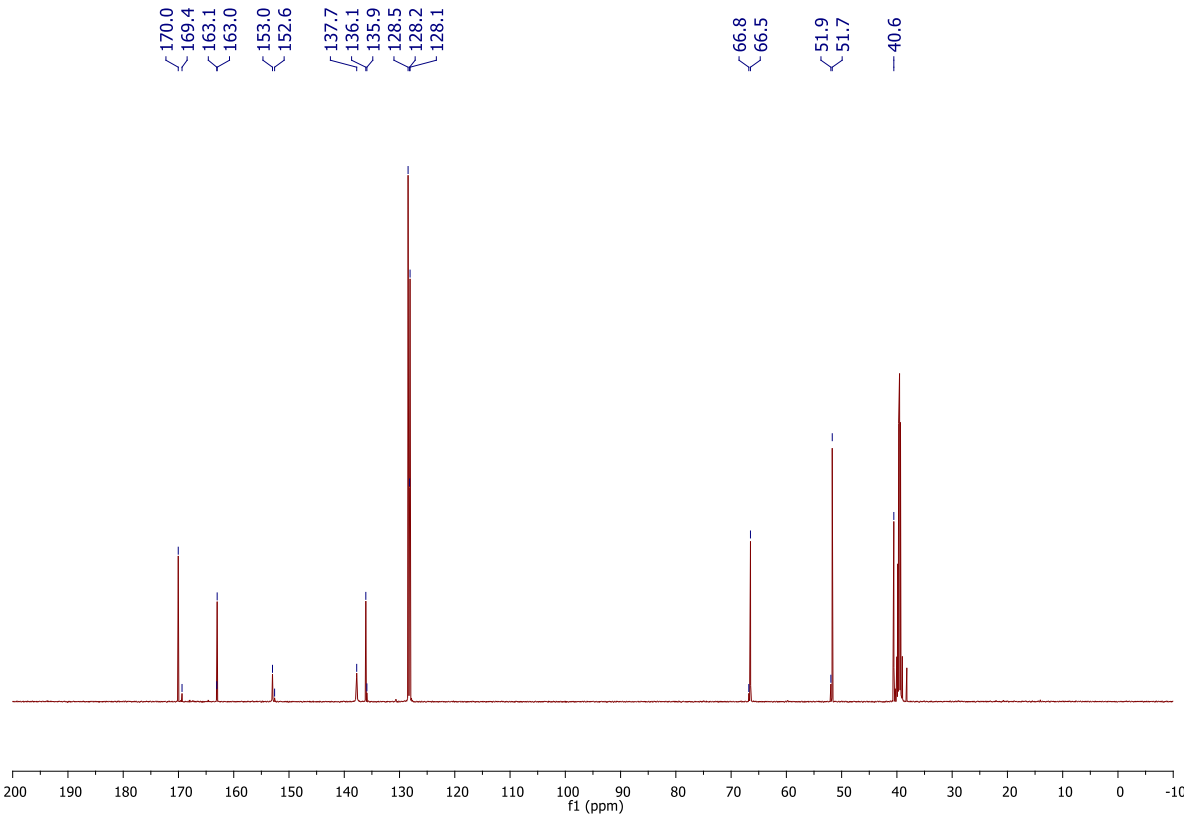
^{13}C NMR (DMSO-d^{6}, 126 MHz) of ***(E)*-1m**



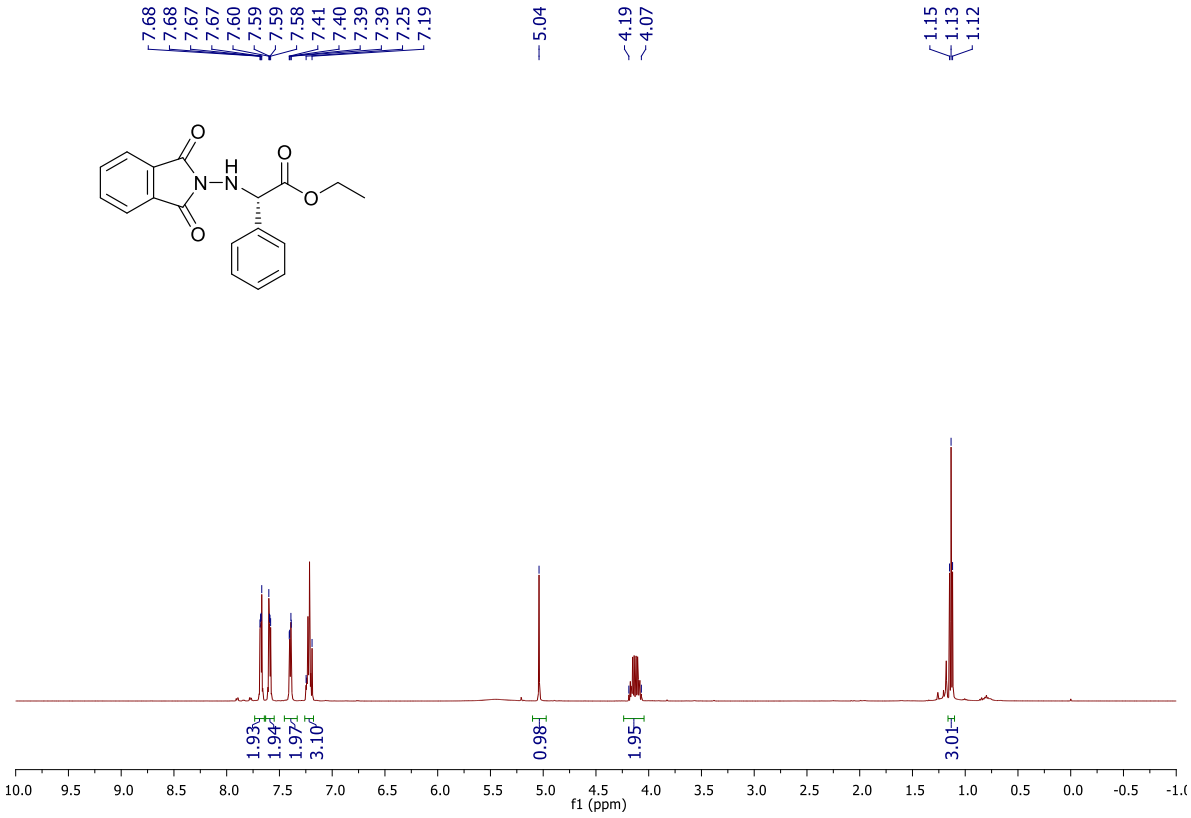
^{1}H NMR (DMSO-d^{6}, 500 MHz) of ***(E)*-1m**



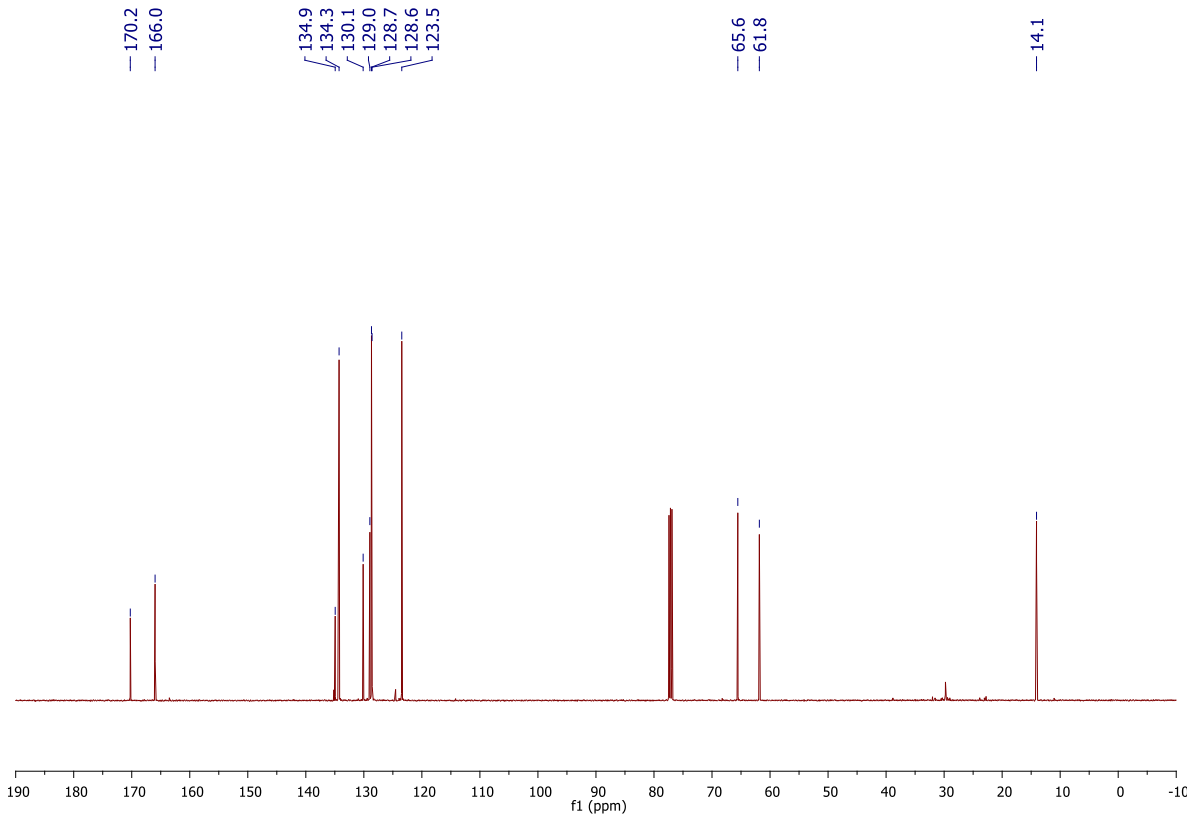
^{13}C NMR (DMSO-d^{6}, 126 MHz) of ***(E)*-1m**



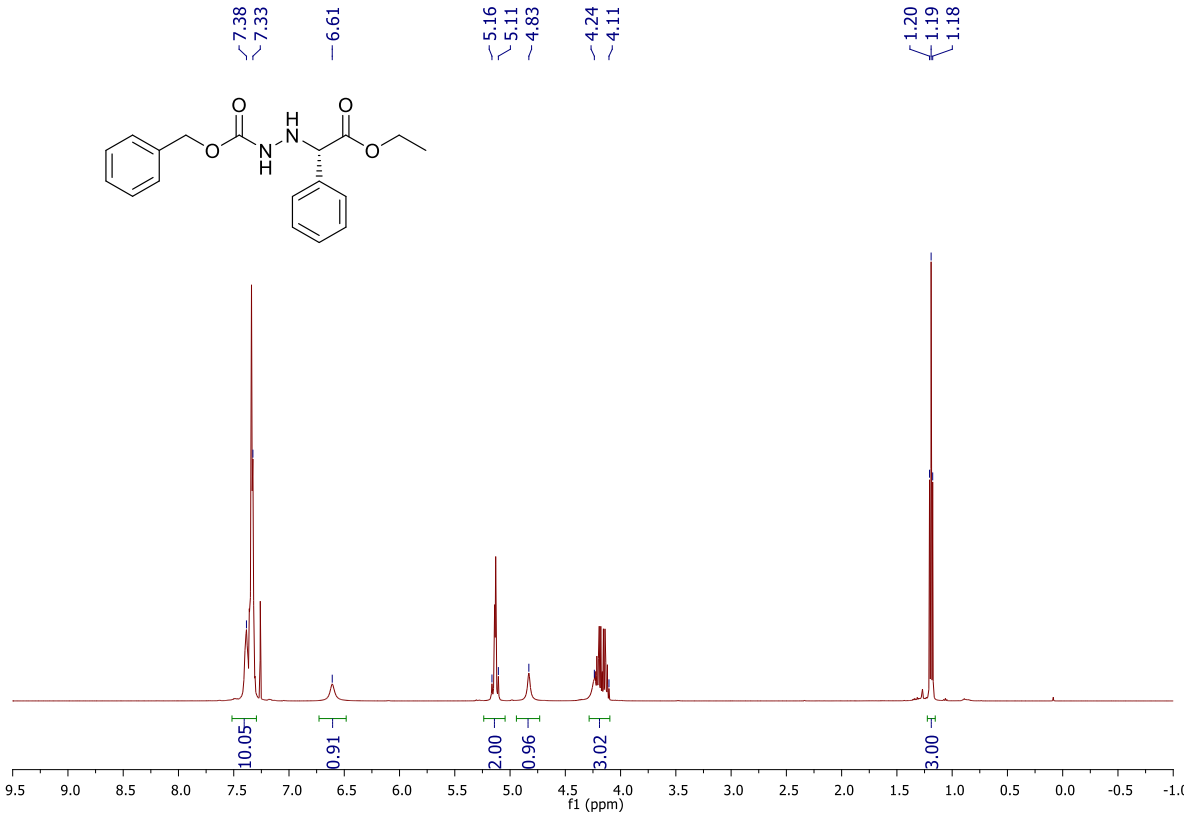
^{1}H NMR ($CDCl_3$, 500 MHz) of **3aa**



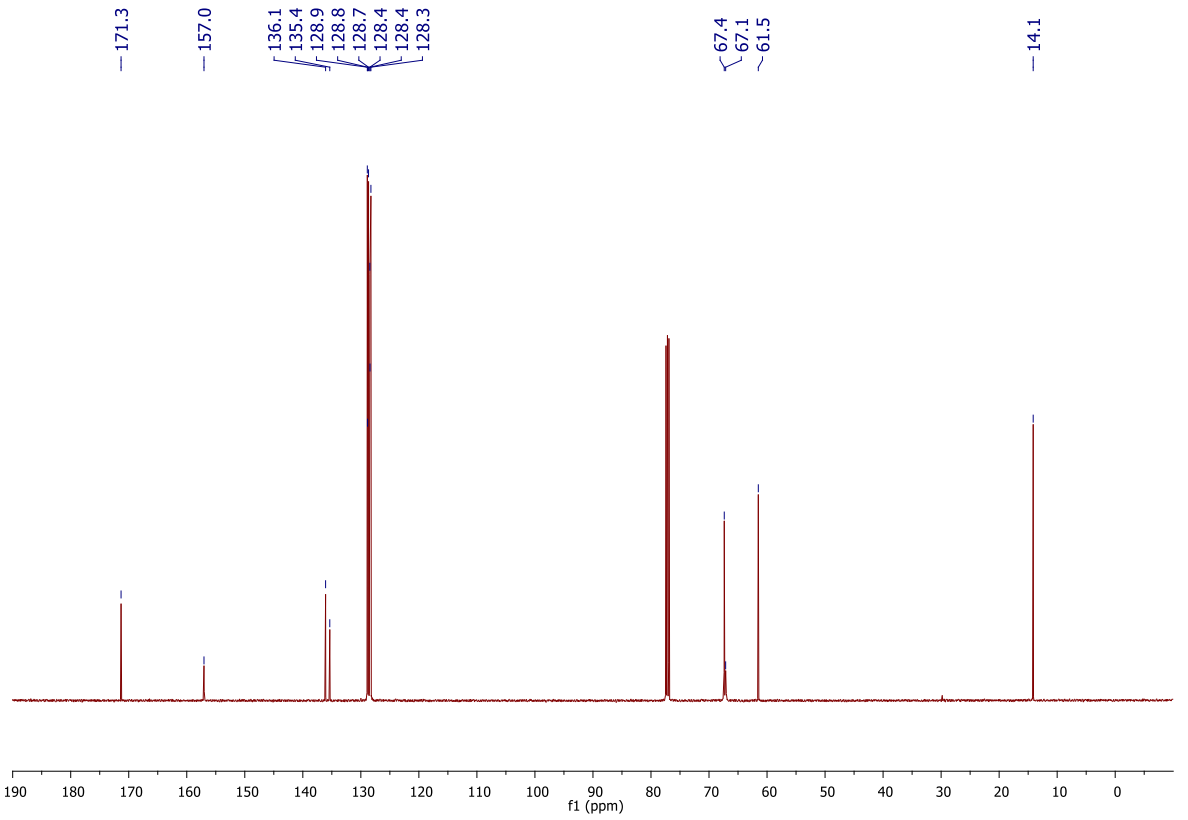
^{13}C NMR ($CDCl_3$, 126 MHz) of **3aa**



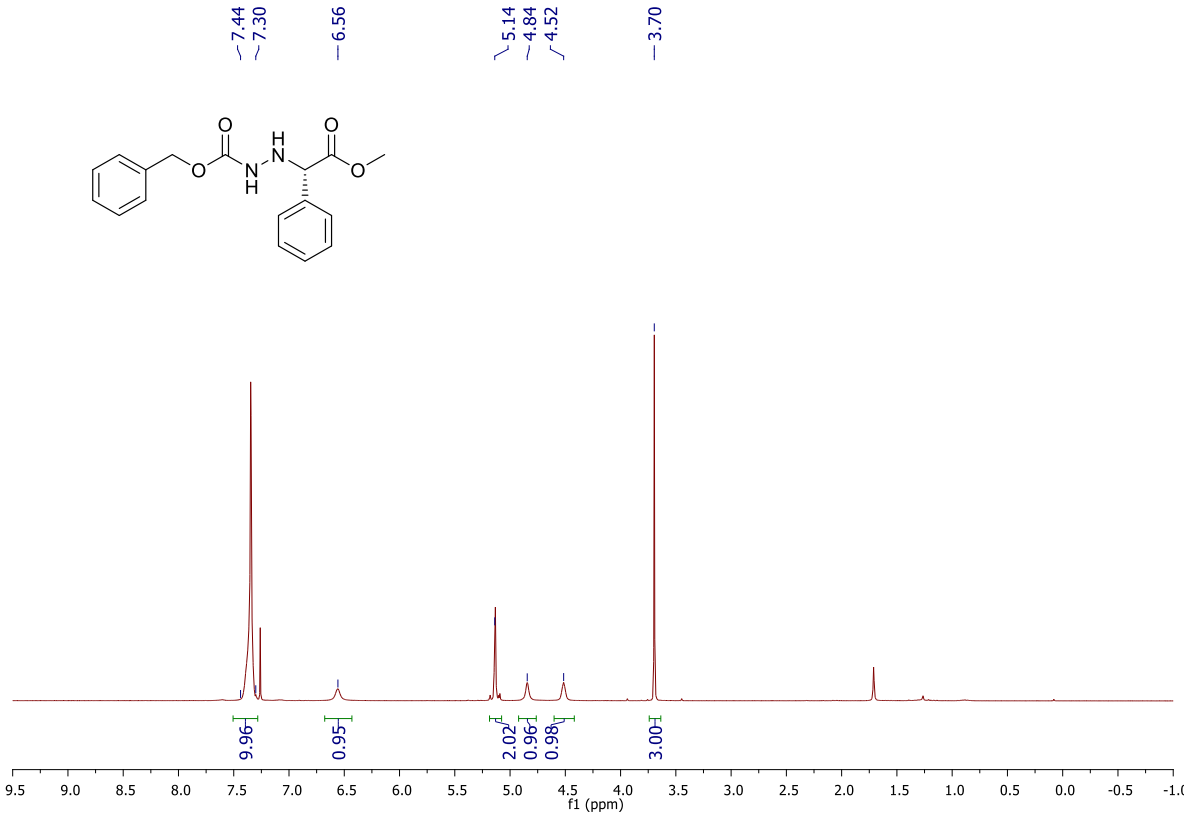
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3ab**



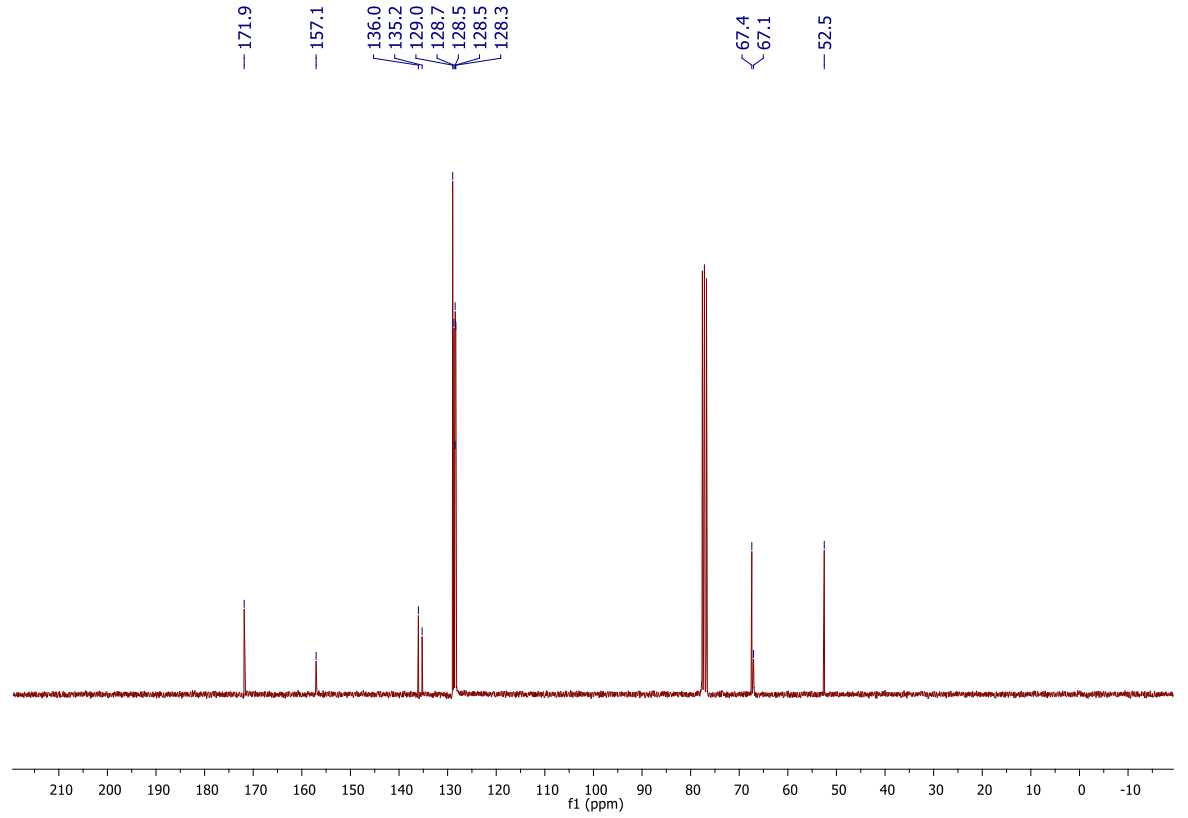
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3ab**



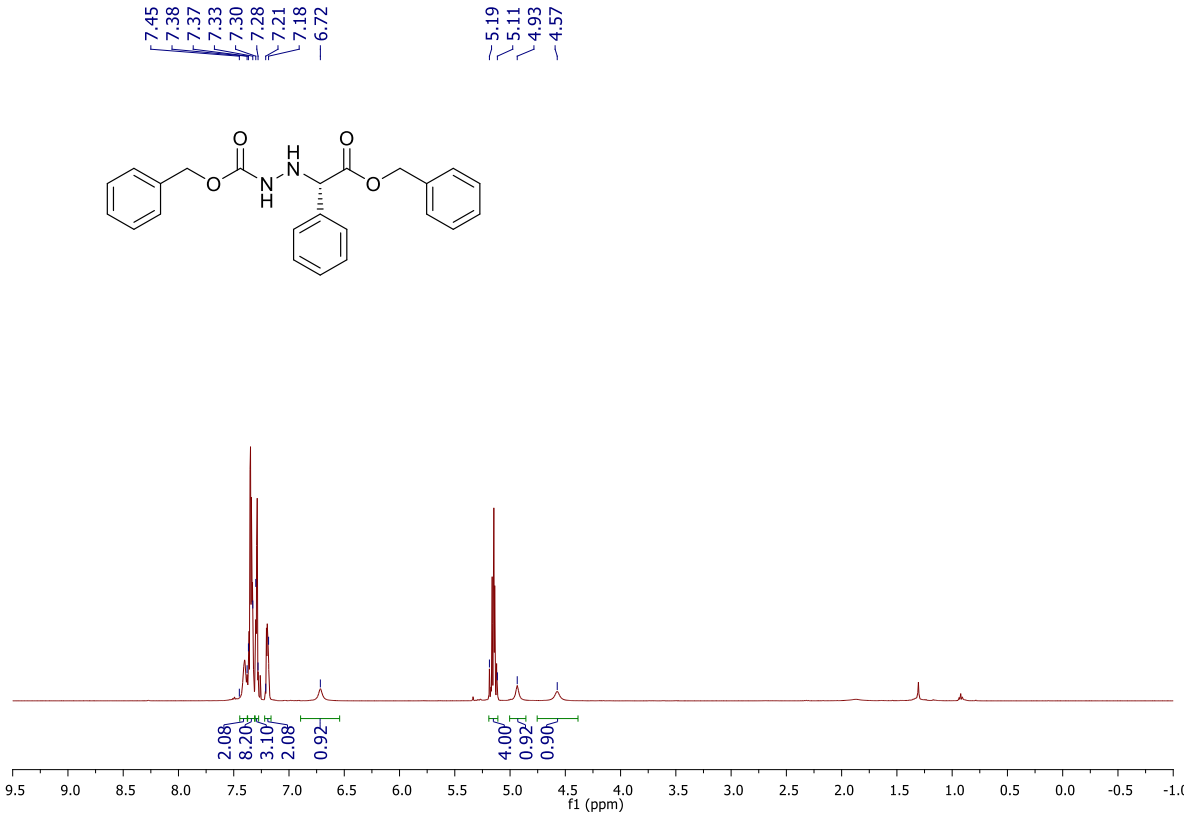
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3ac**



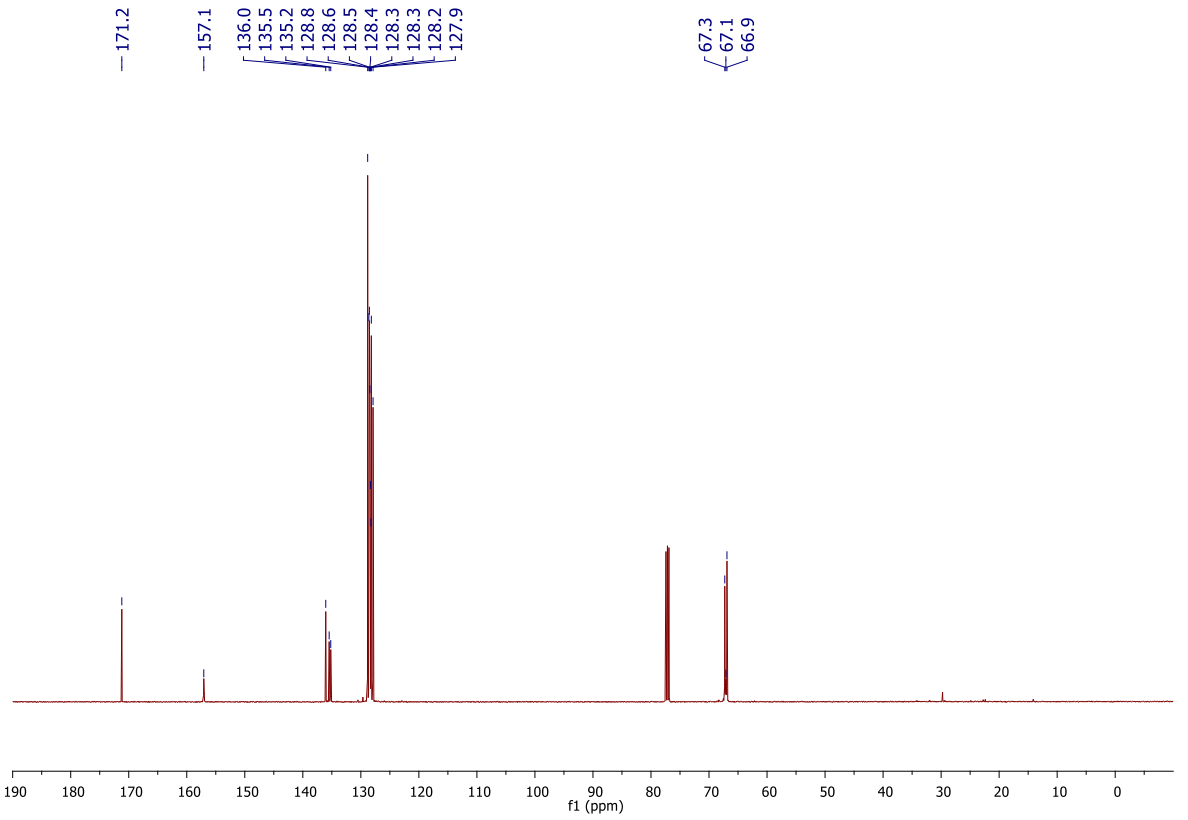
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3ac**



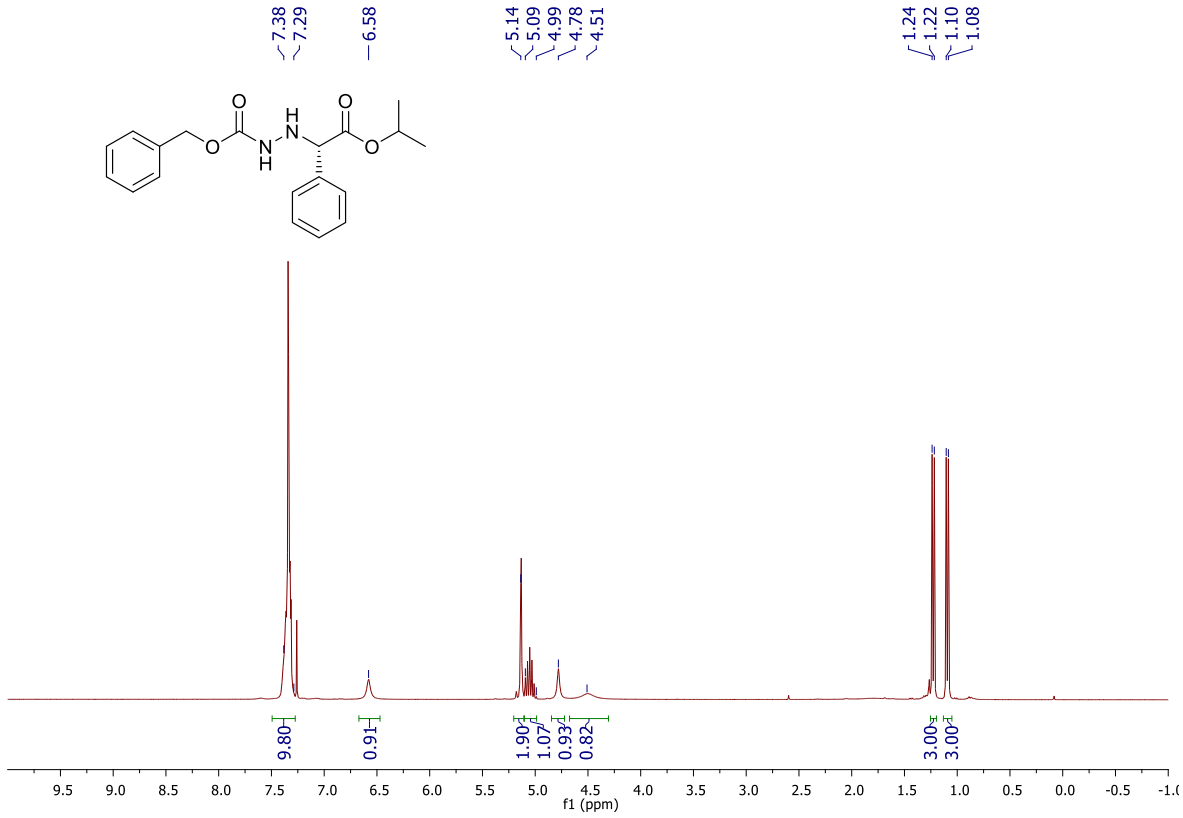
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3ad**



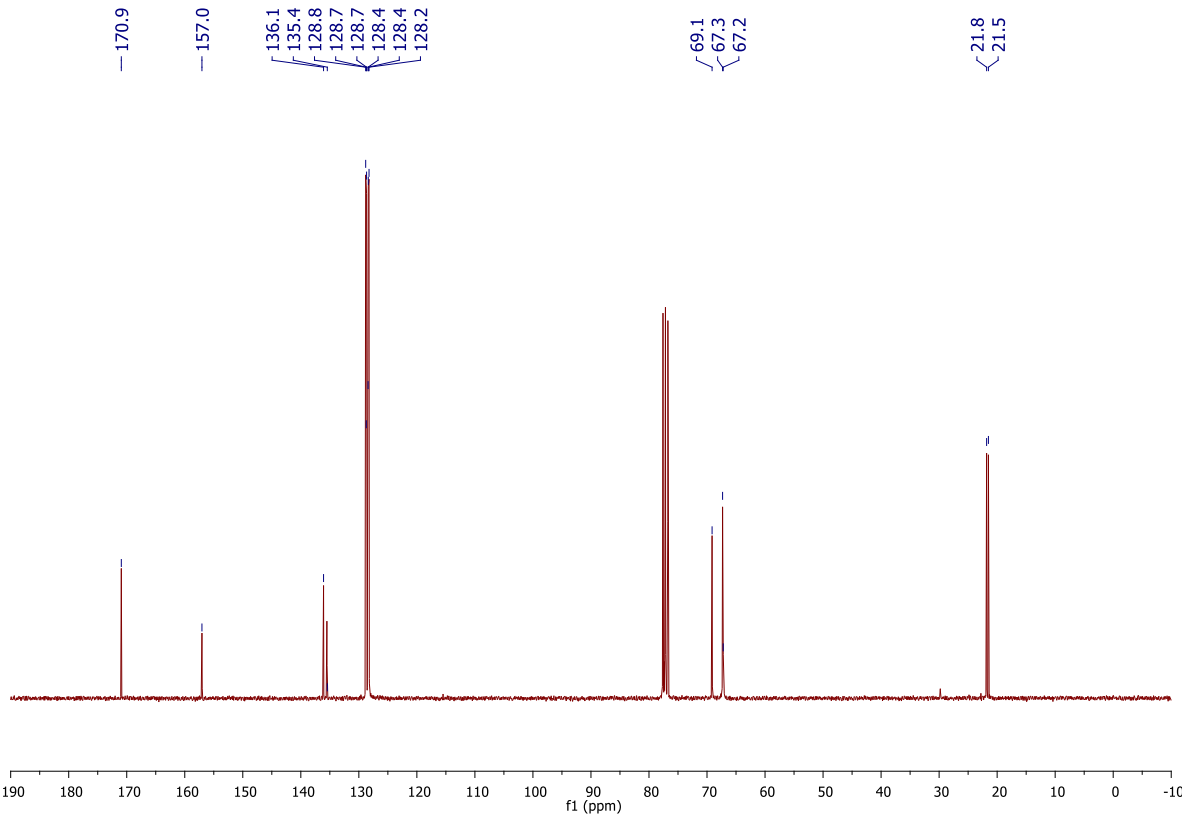
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3ad**



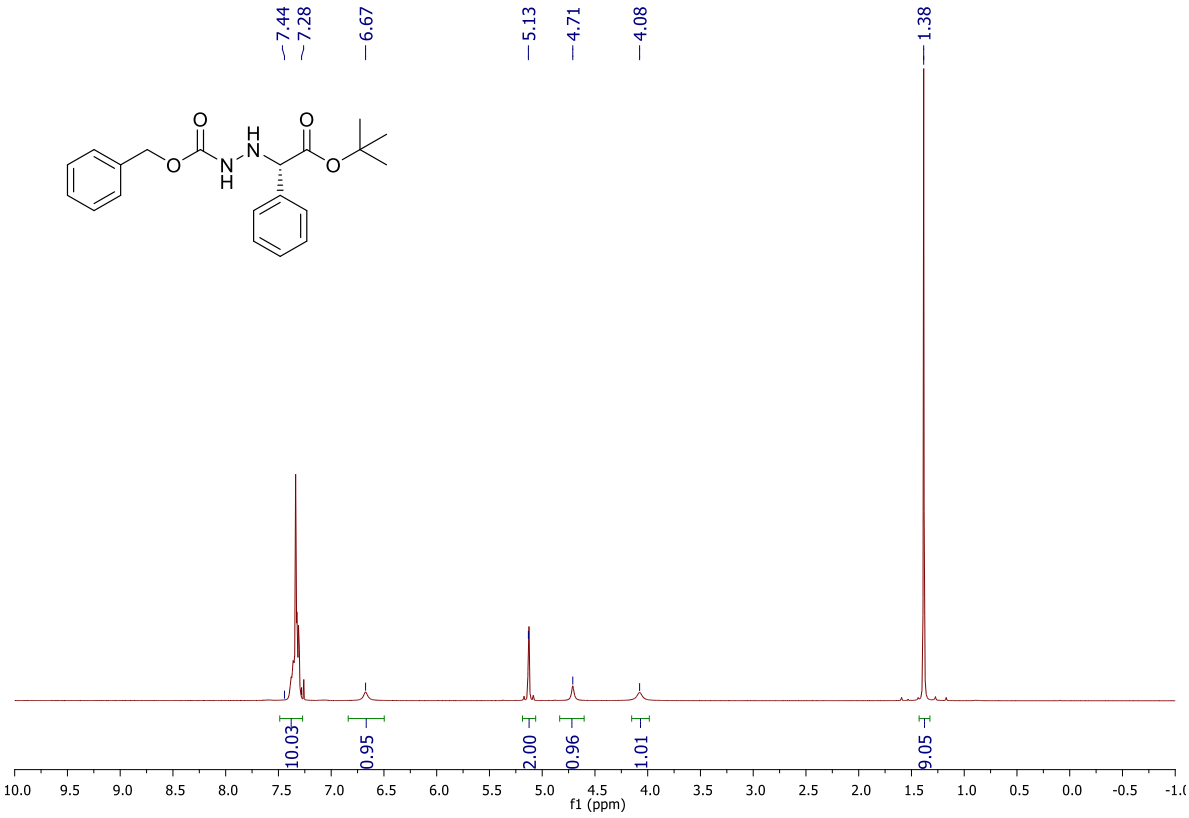
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3ae**



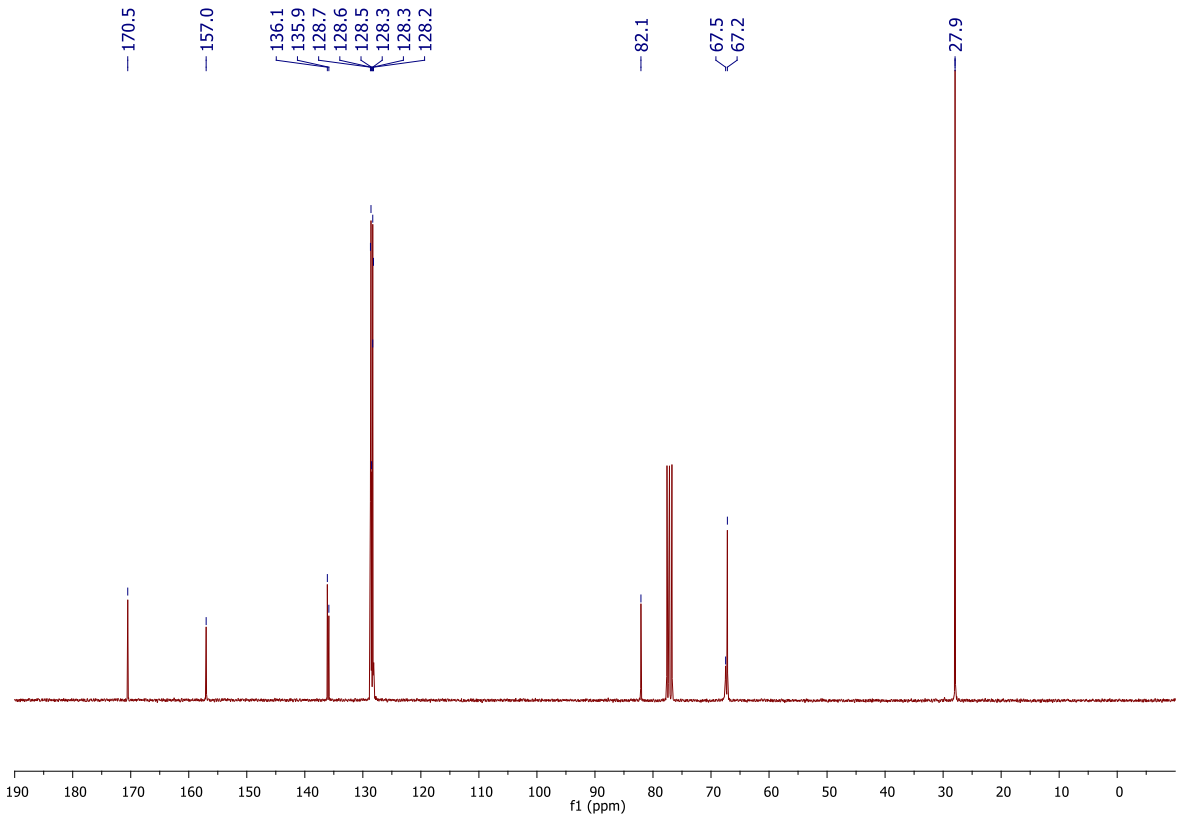
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3ae**



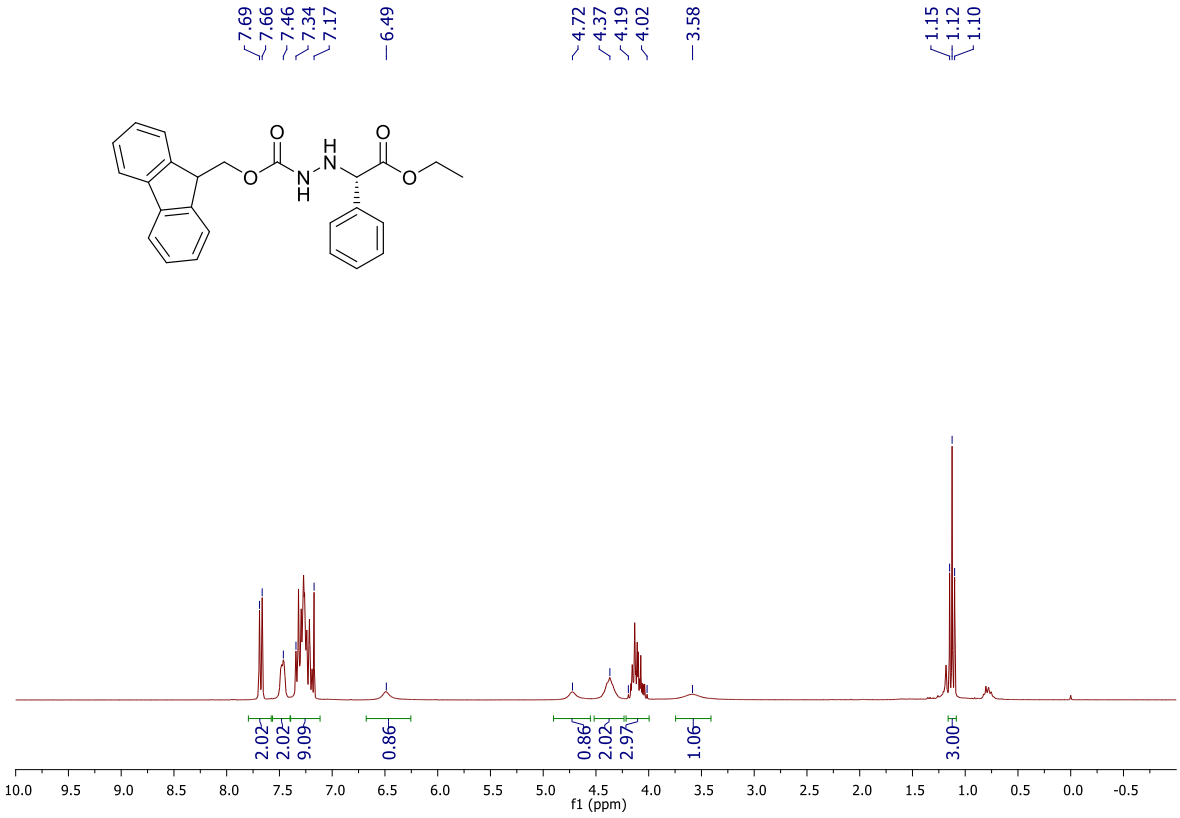
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3af**



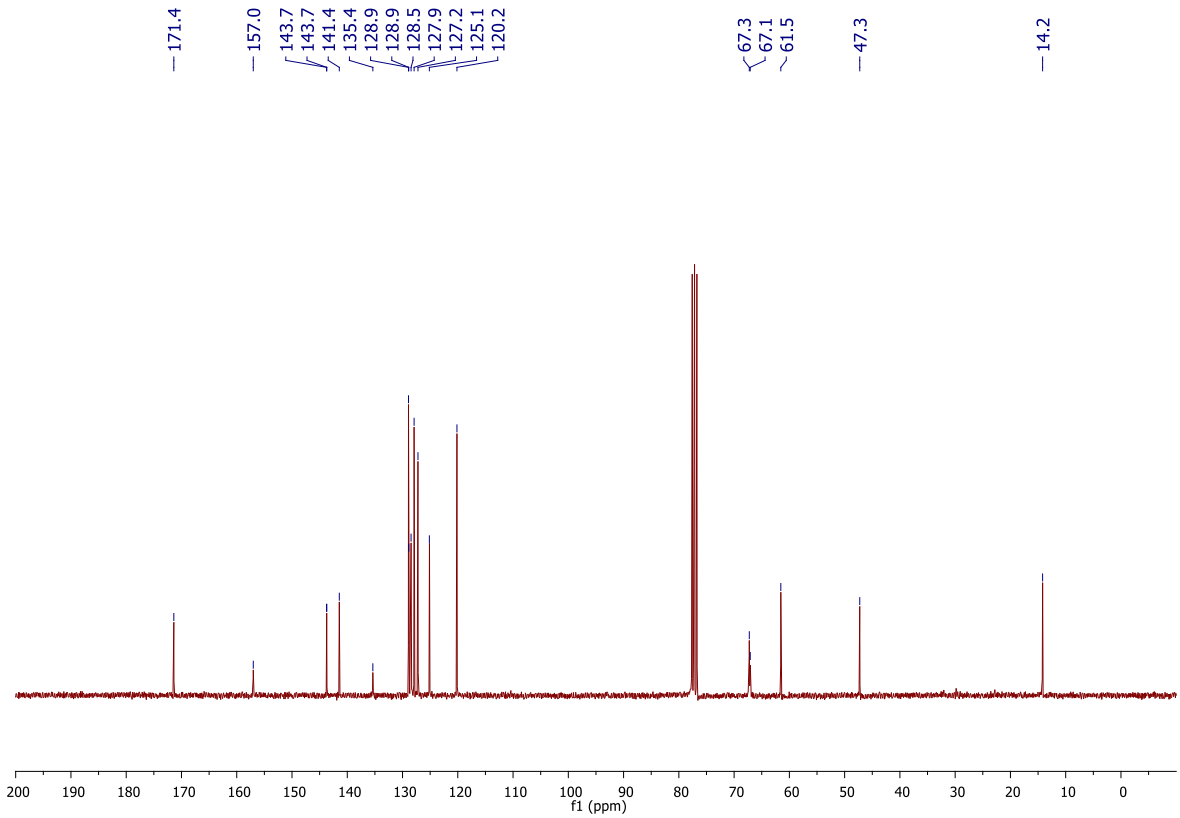
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3af**



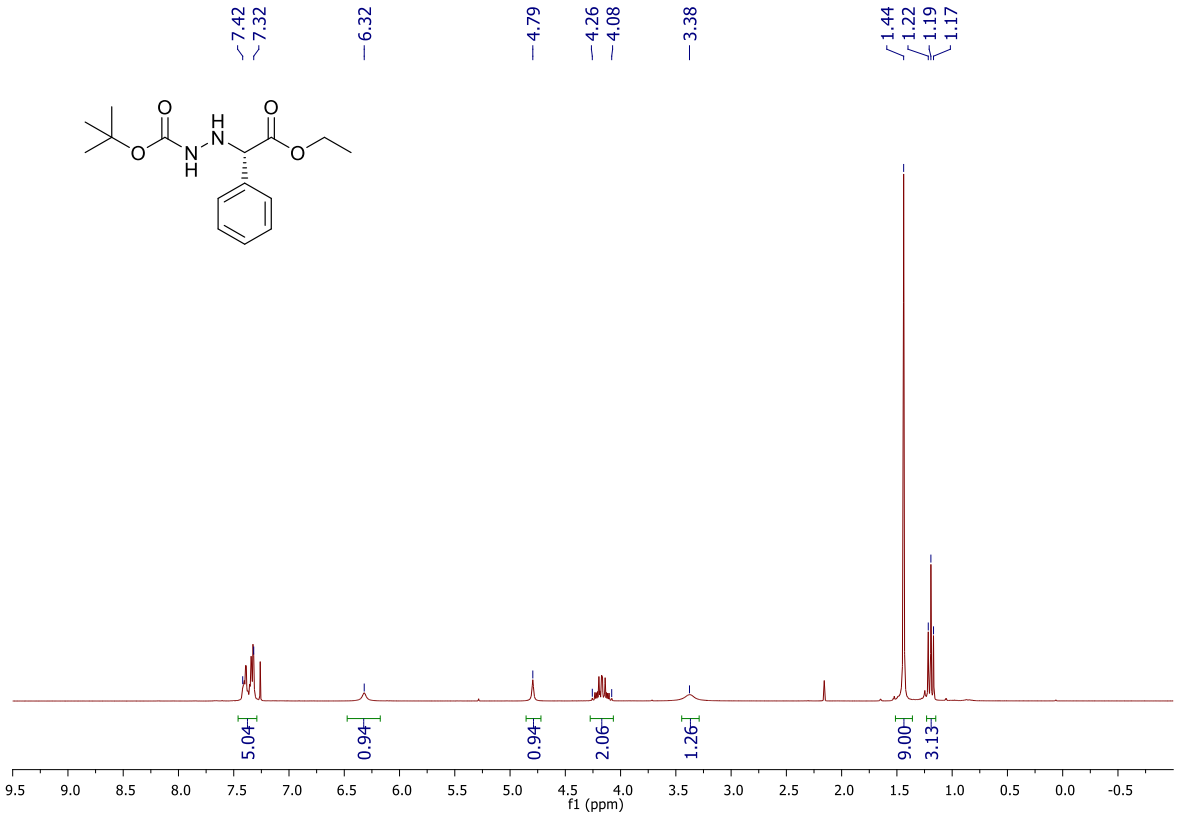
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3ag**



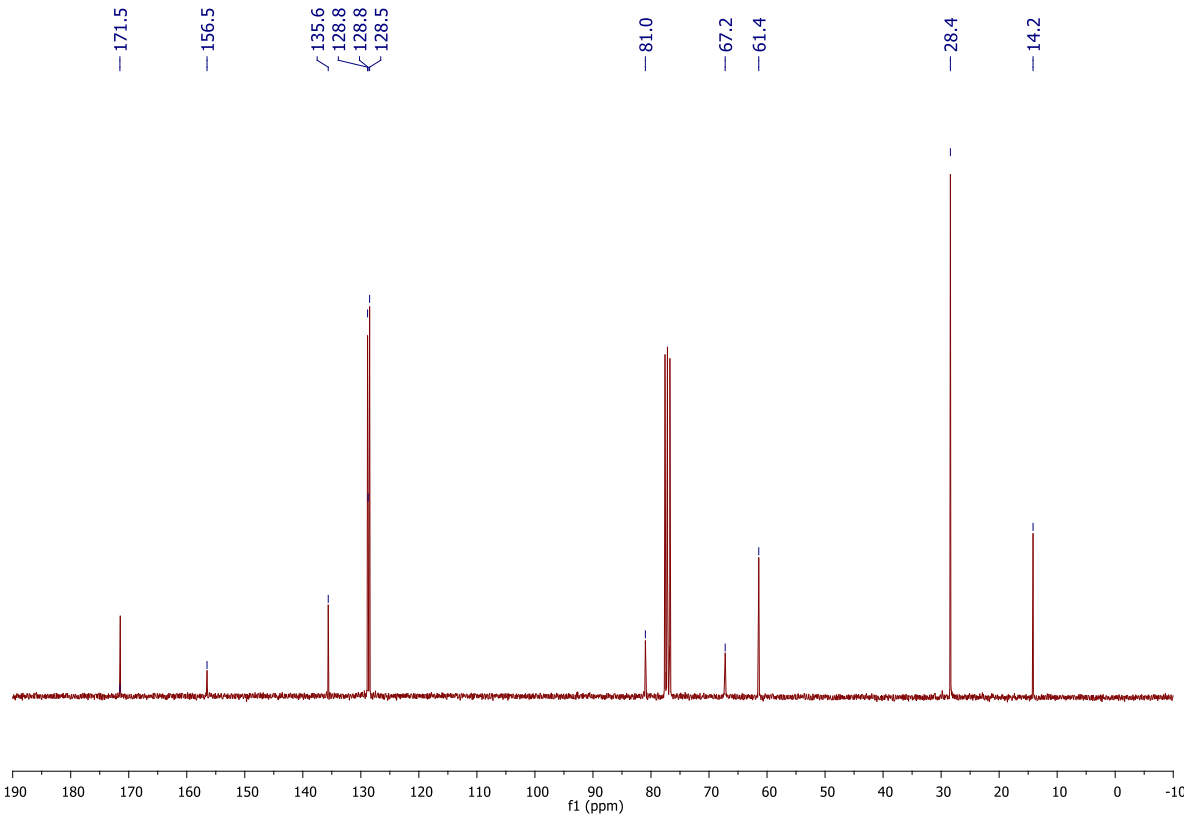
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3ag**



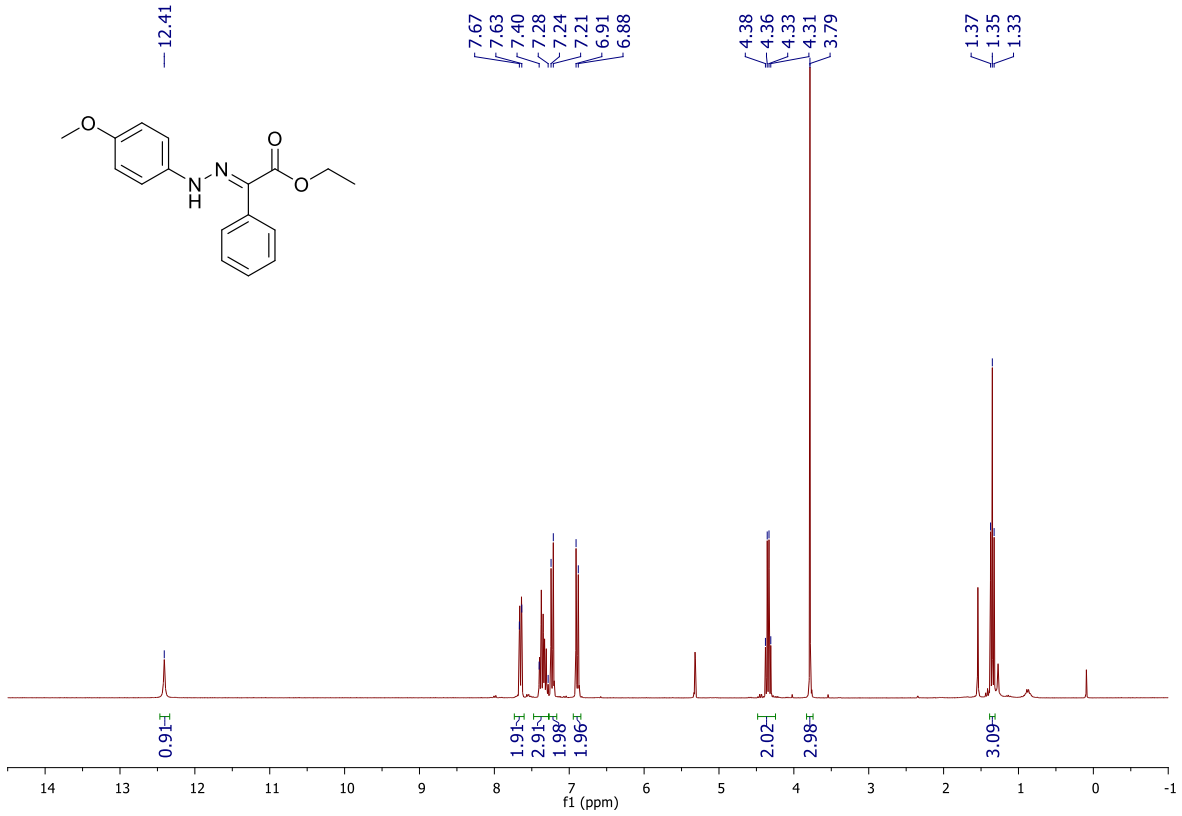
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3ah**



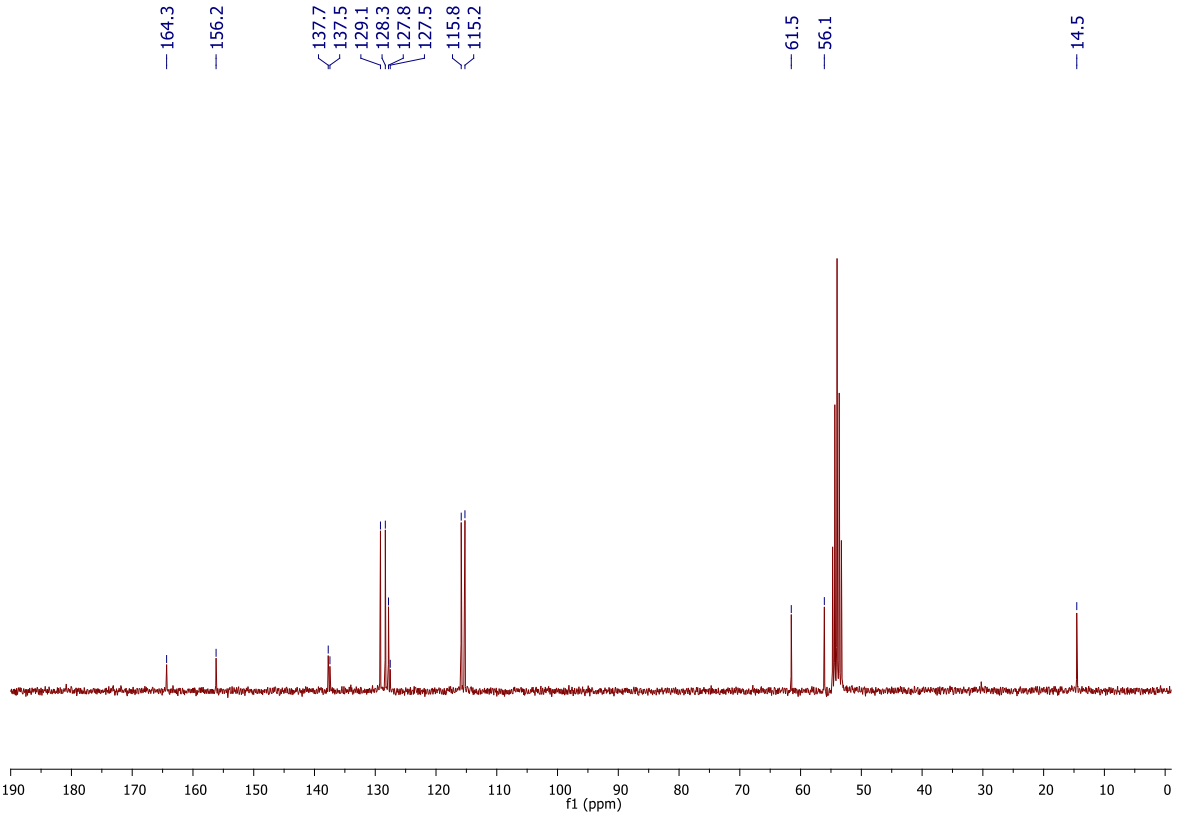
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3ah**



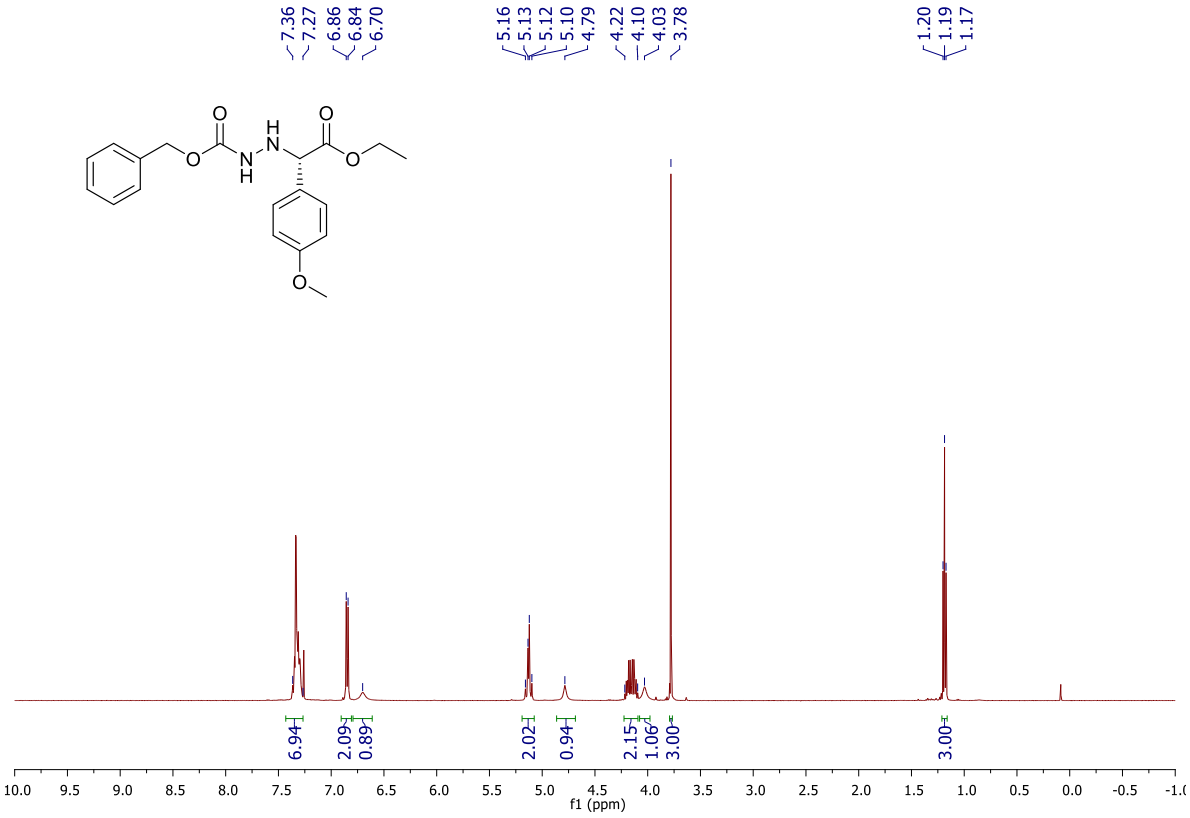
^{1}H NMR (CD_2Cl_2, 300 MHz) of **3aj´**



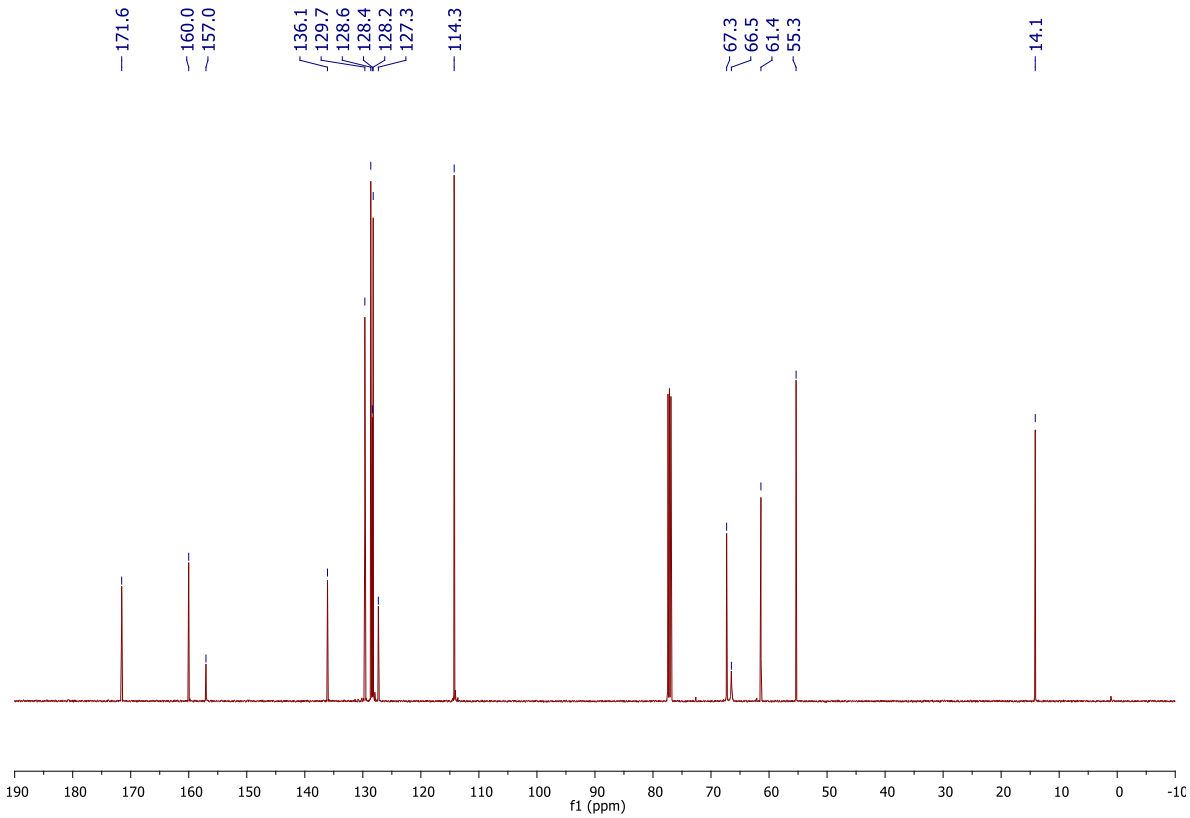
^{13}C NMR (CD_2Cl_2, 75.5 MHz) of **3aj´**



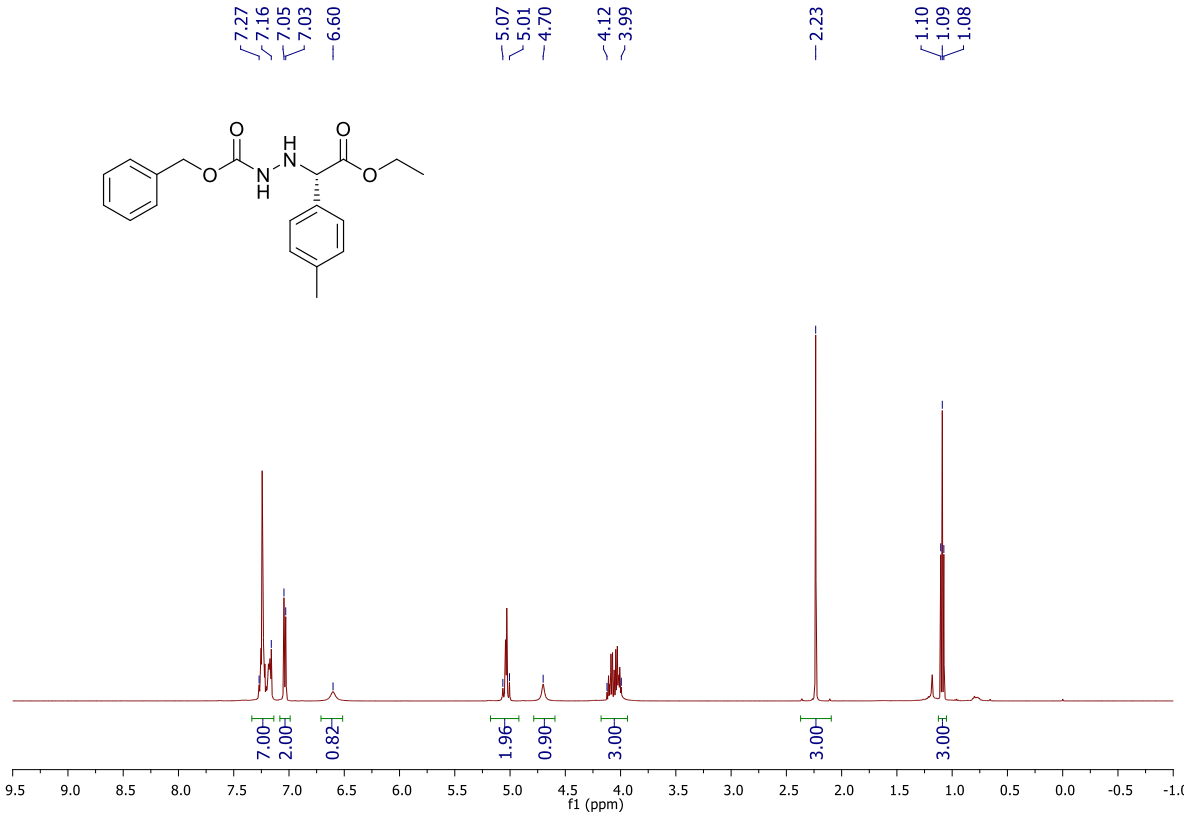
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3bb**



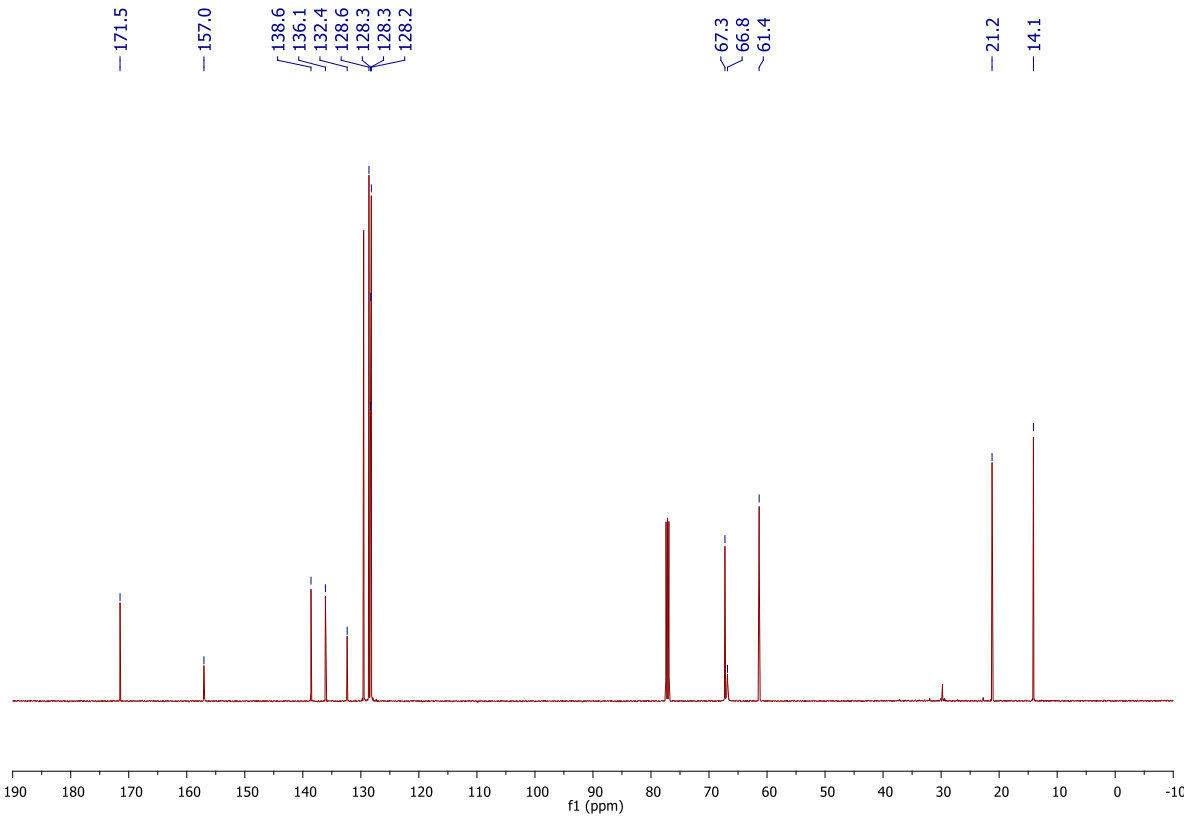
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3bb**



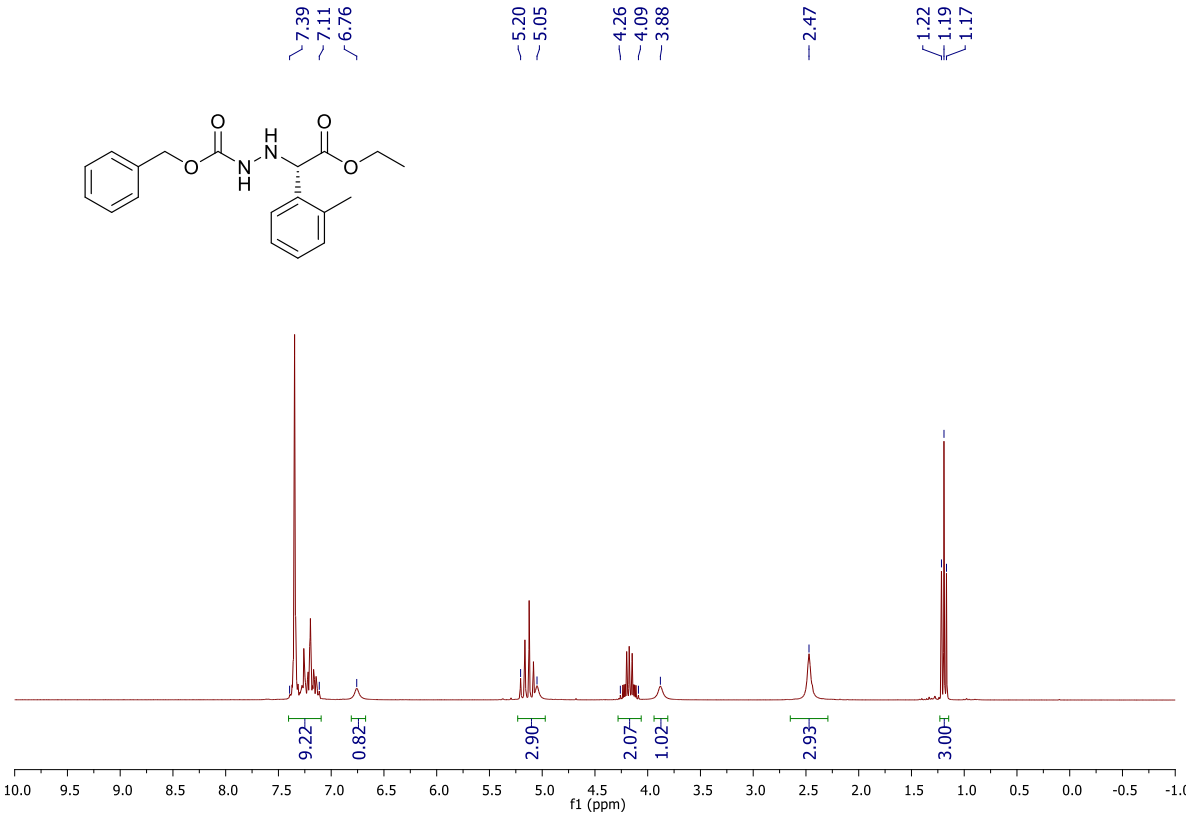
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3cb**



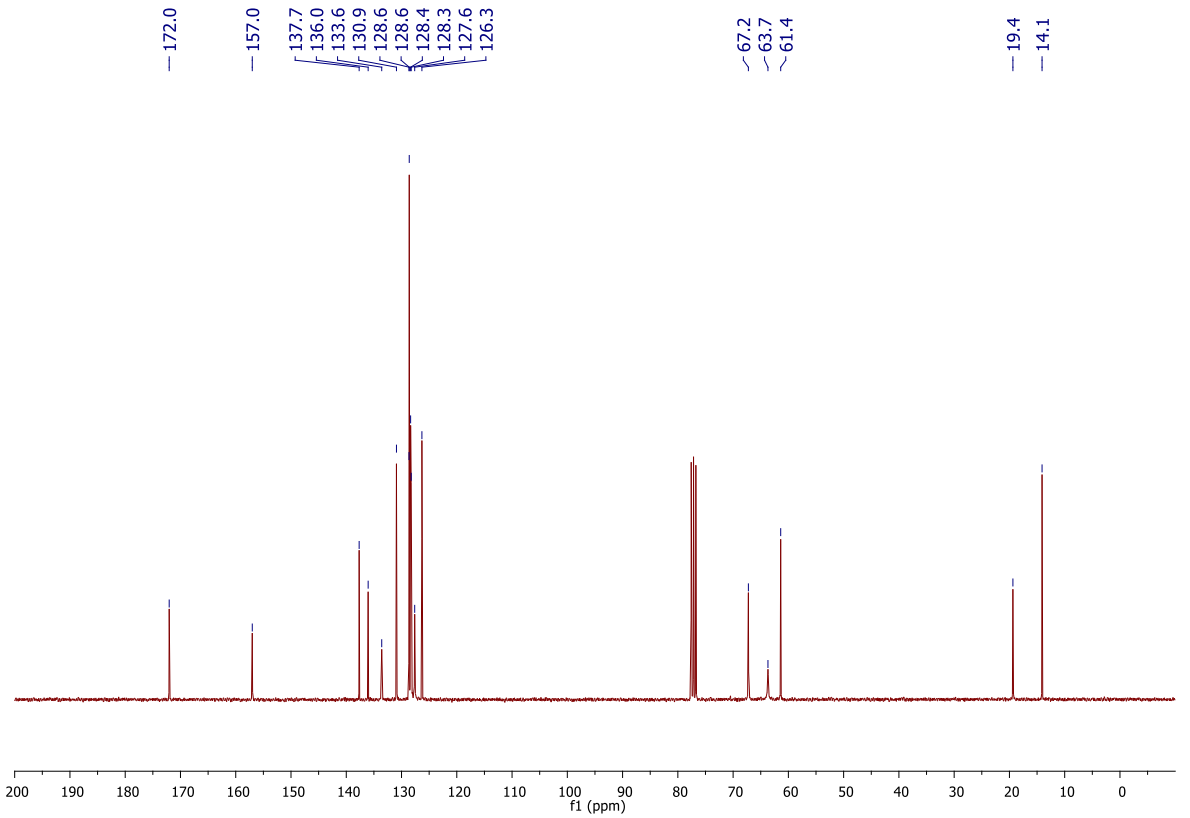
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3cb**



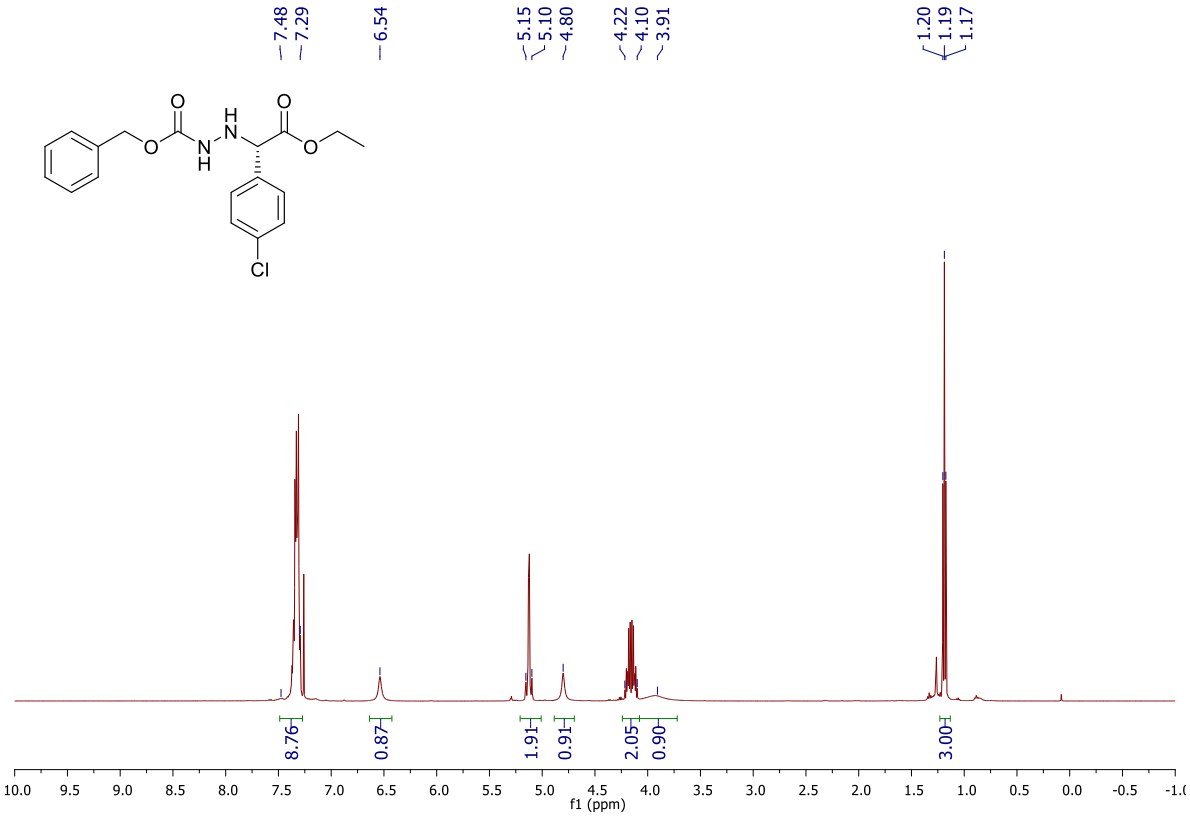
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3db**



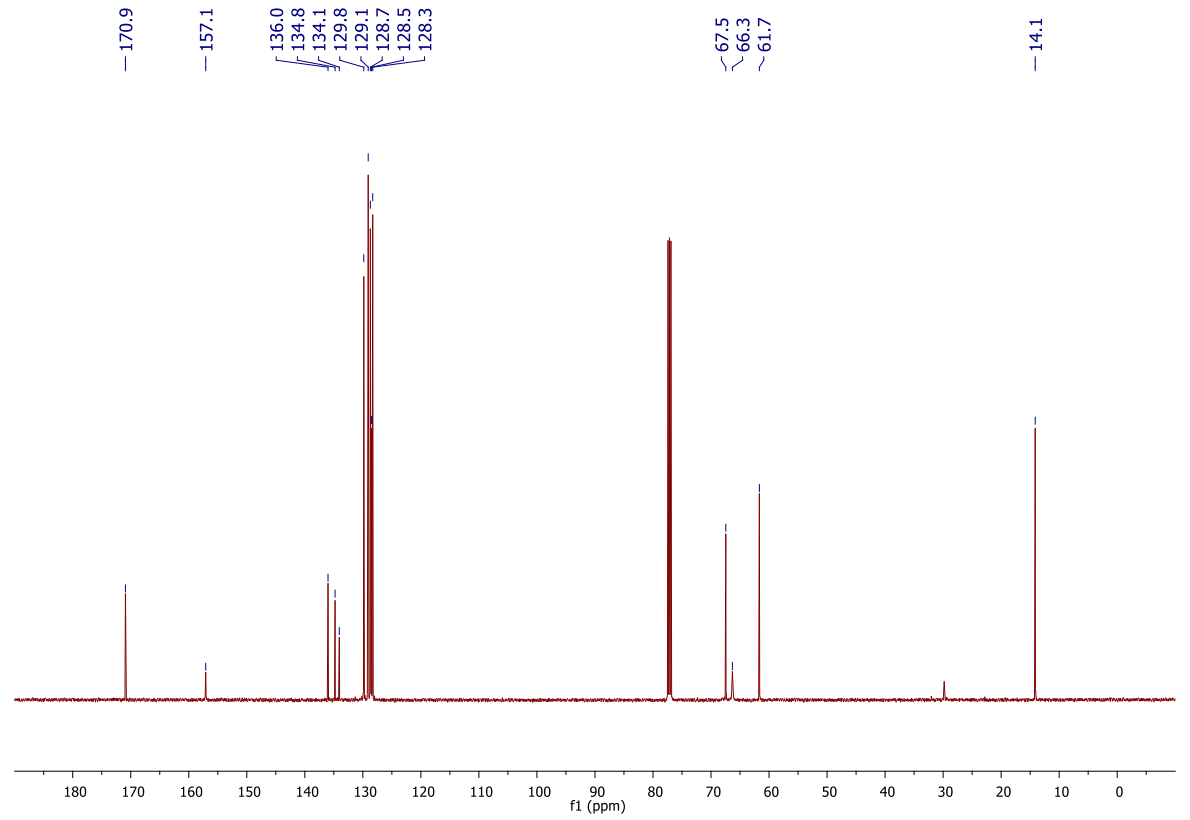
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3db**



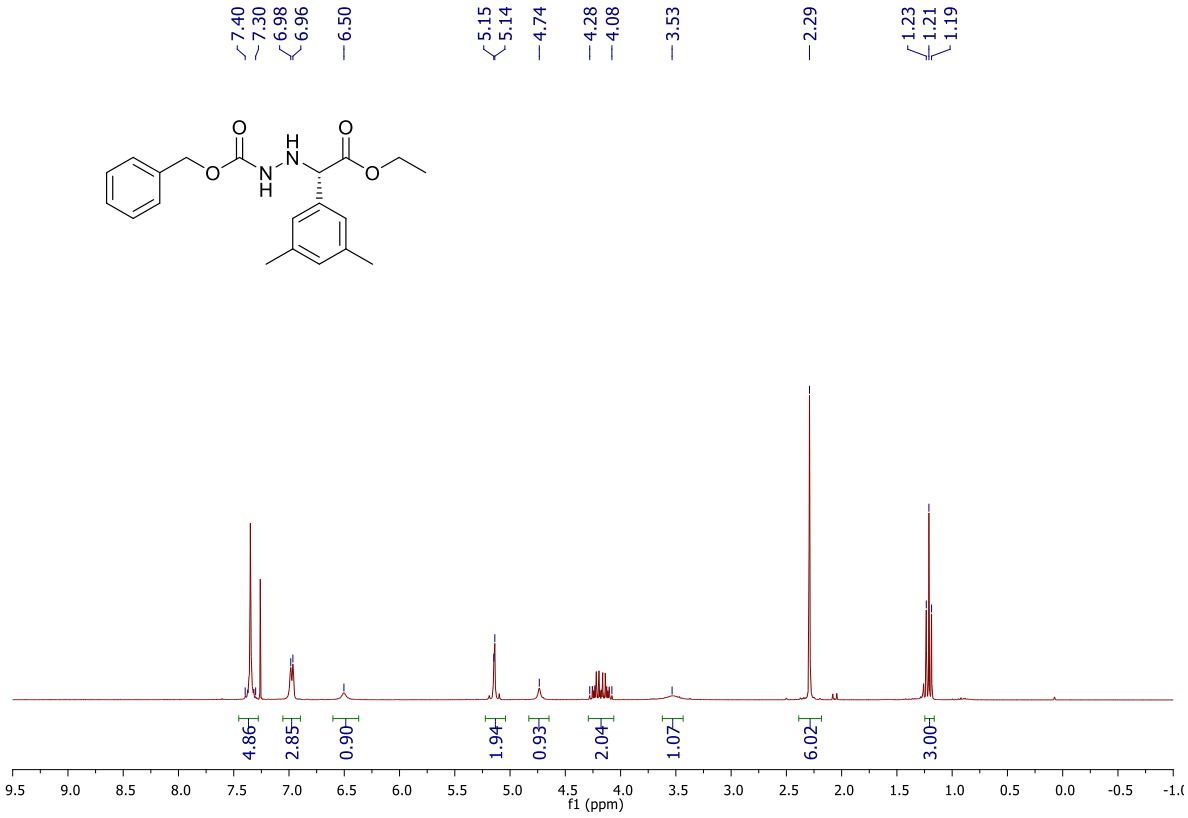
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3eb**



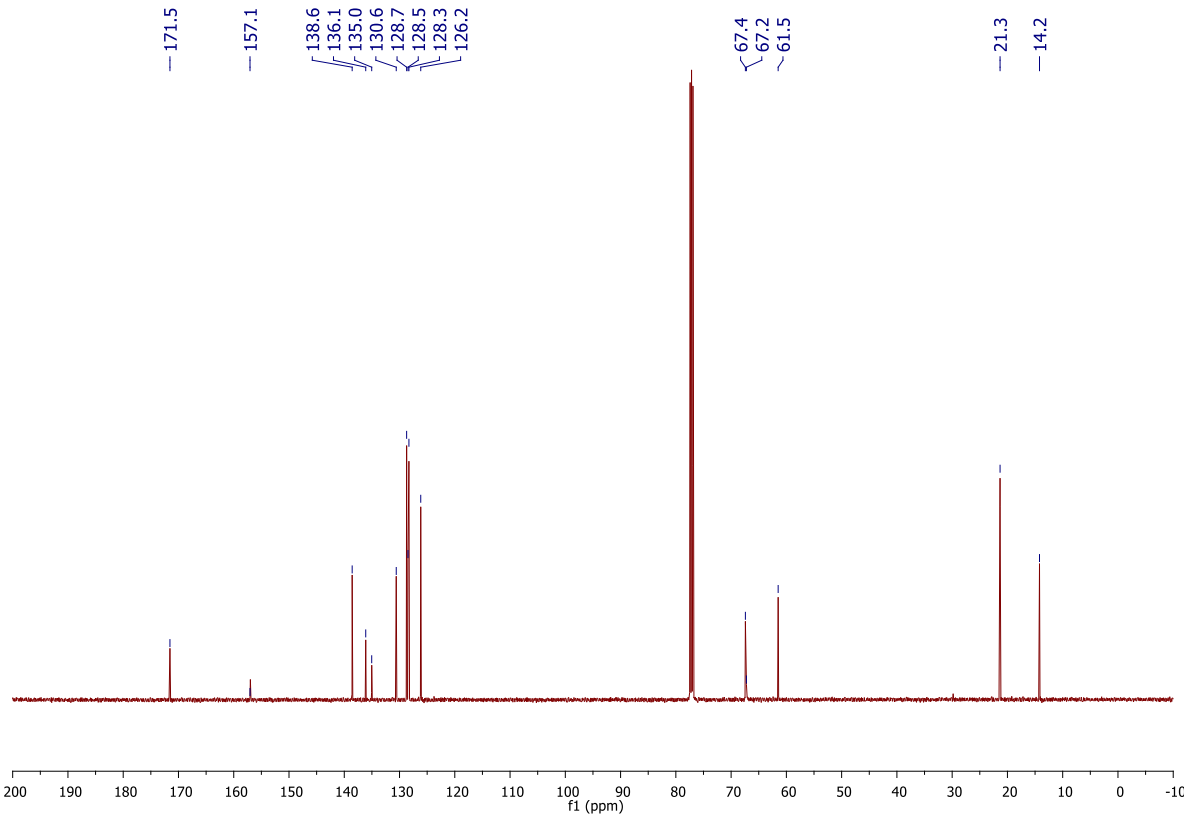
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3eb**



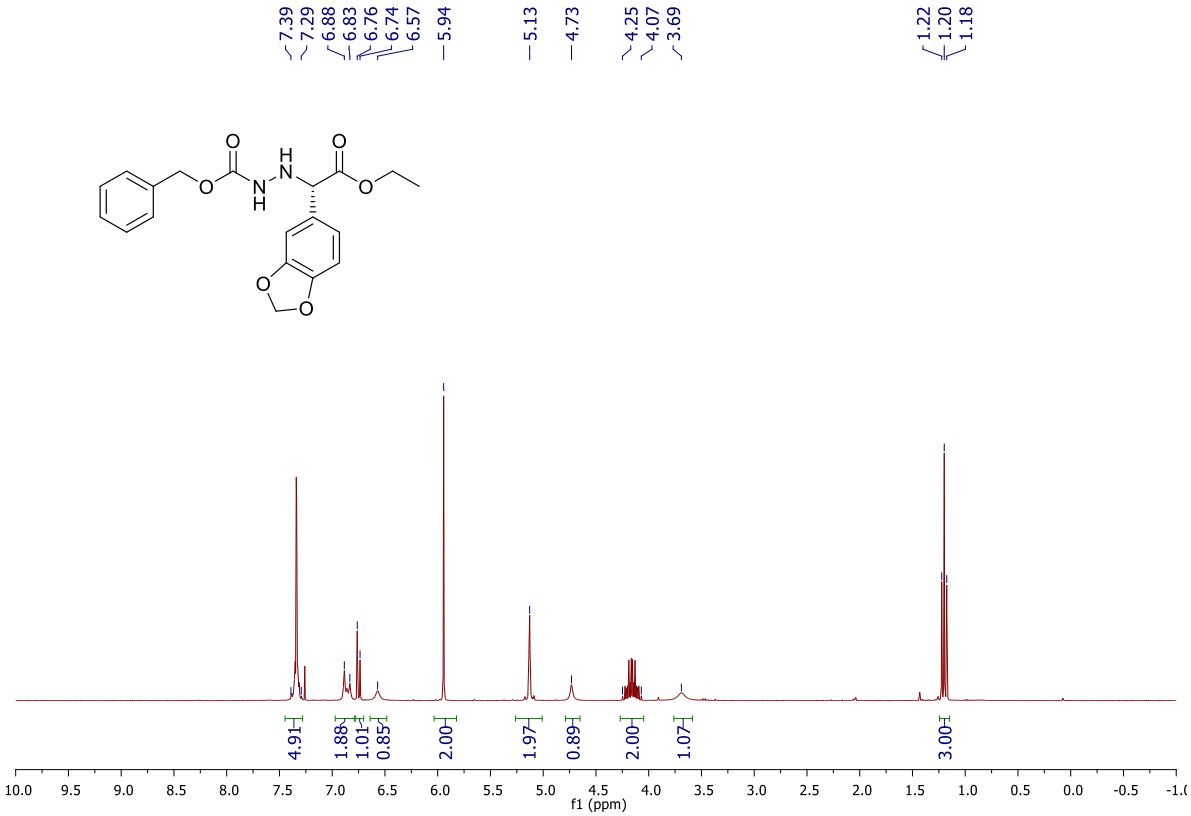
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3fb**



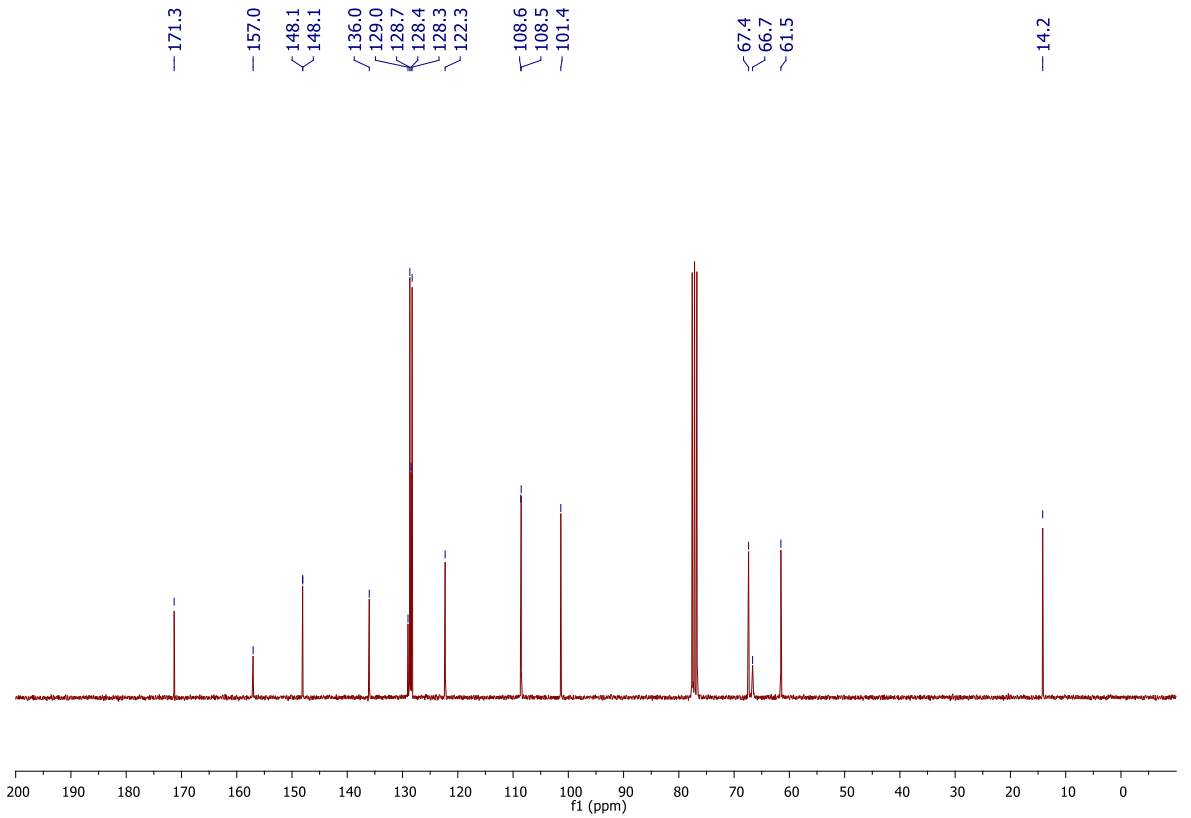
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3fb**



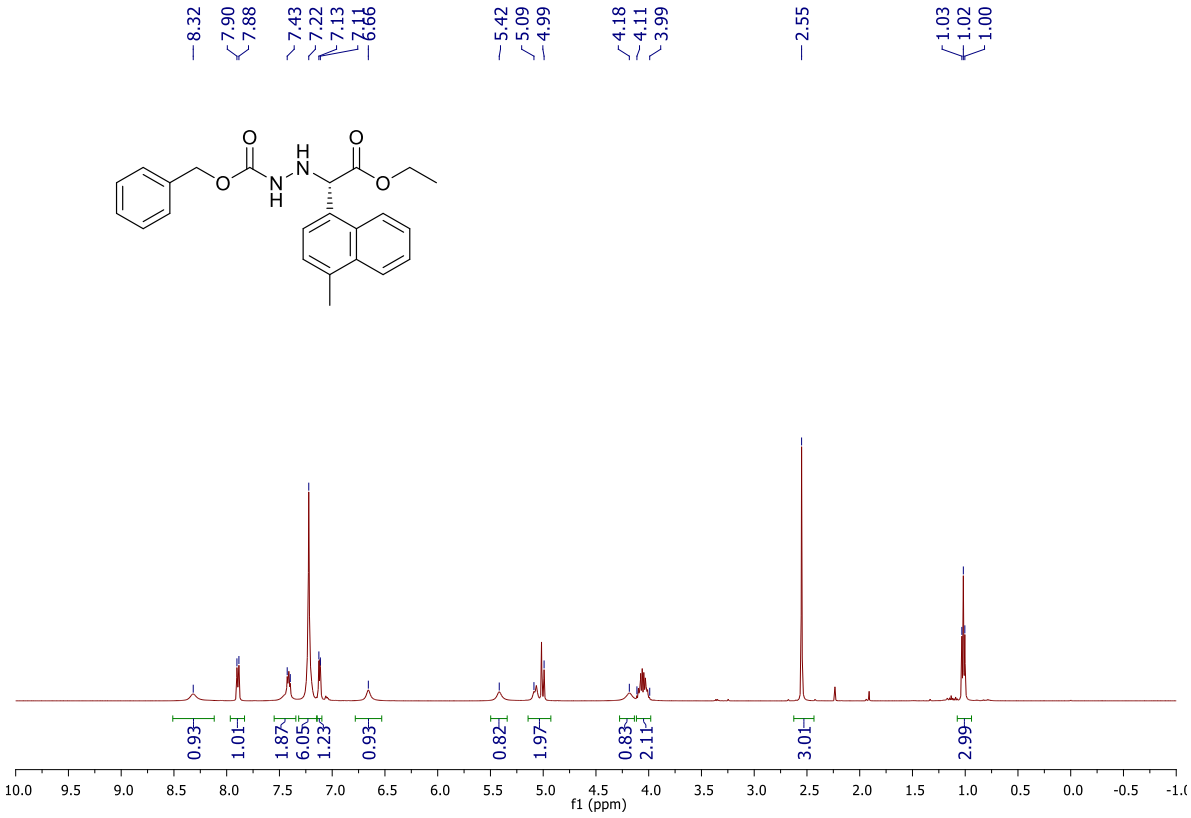
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3gb**



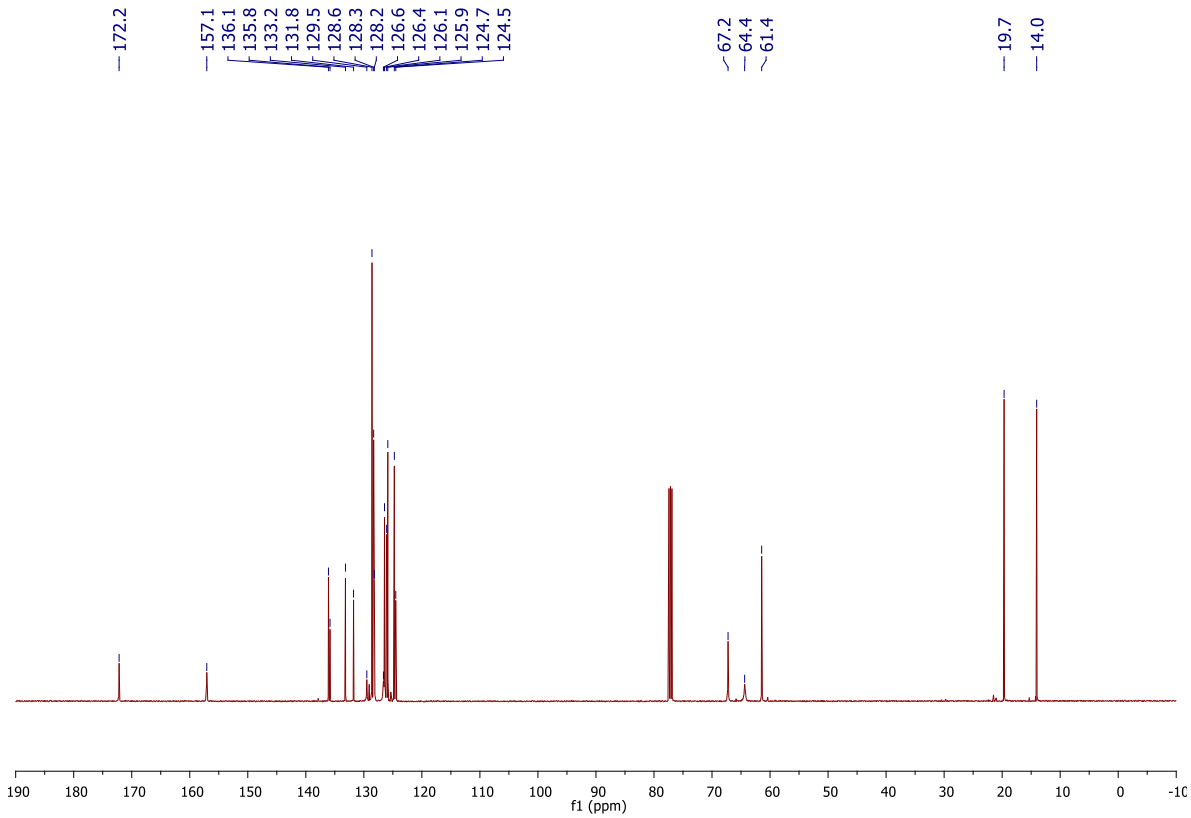
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3fb**



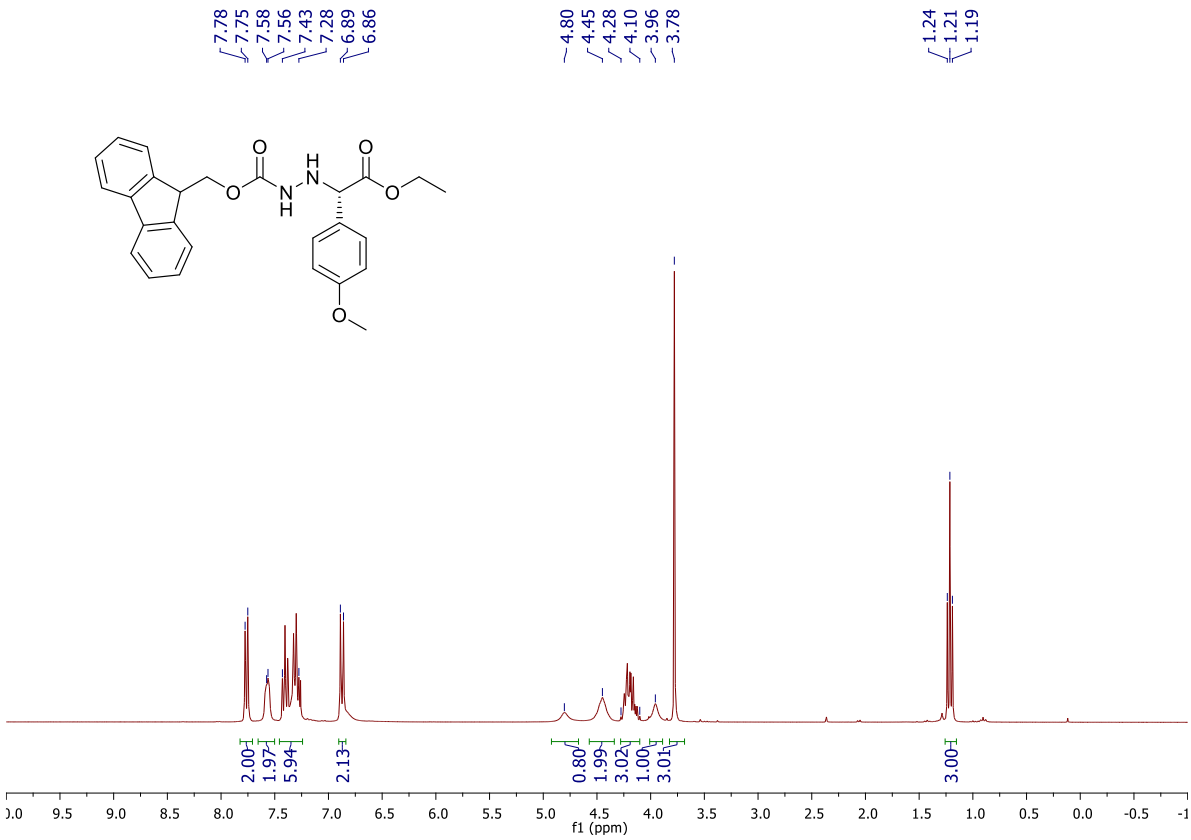
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3hb**



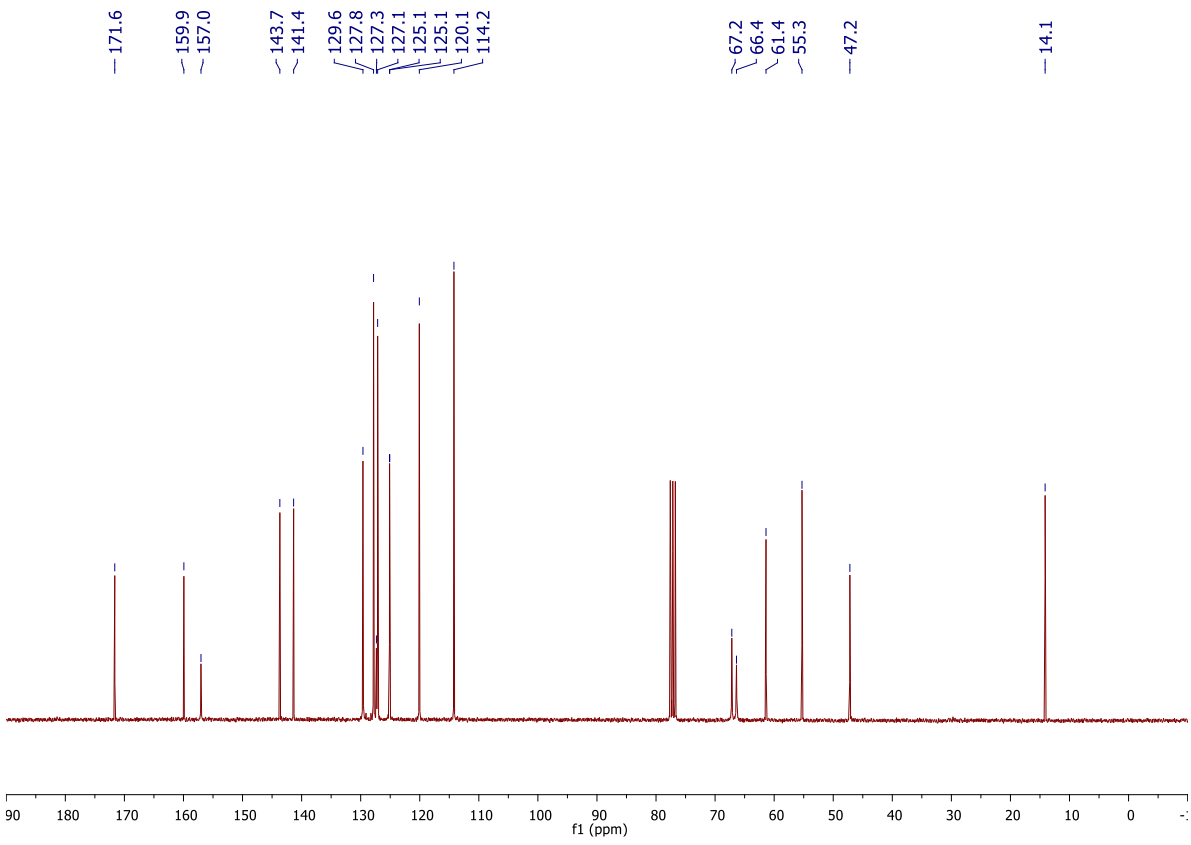
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3hb**



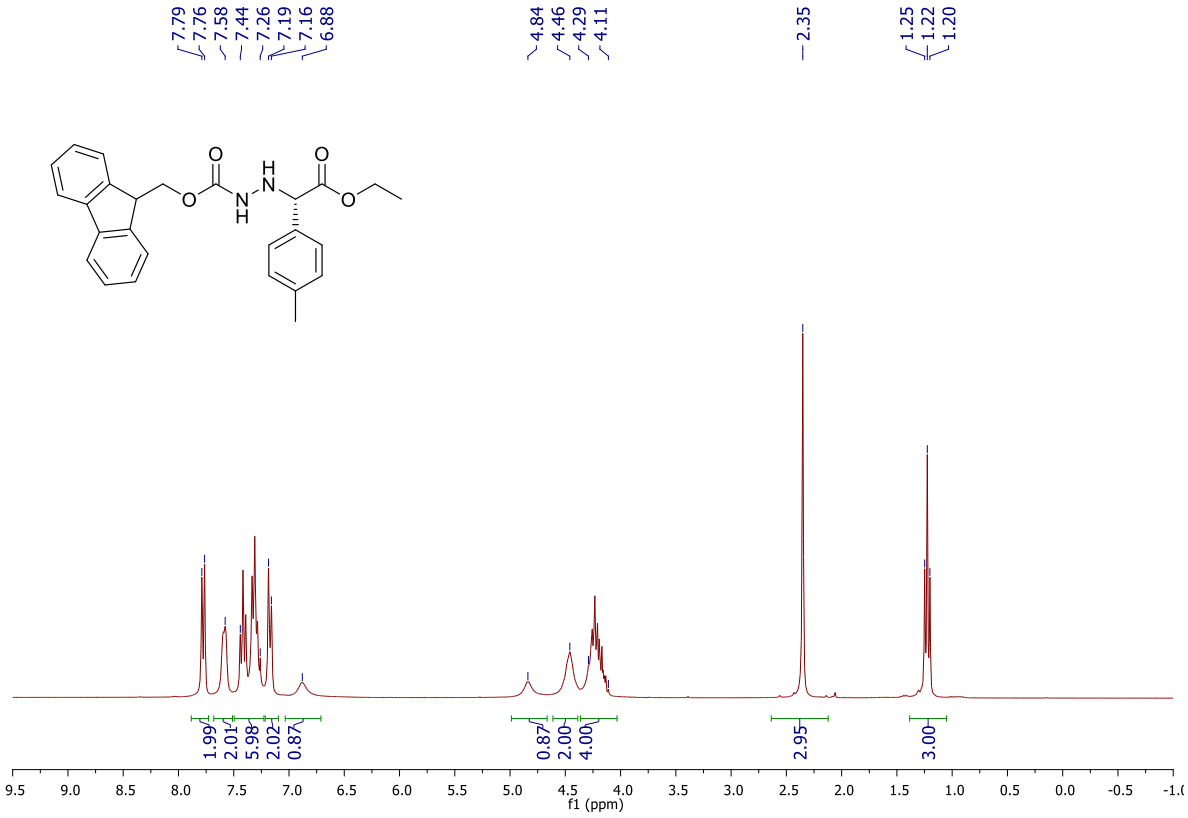
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3bg**



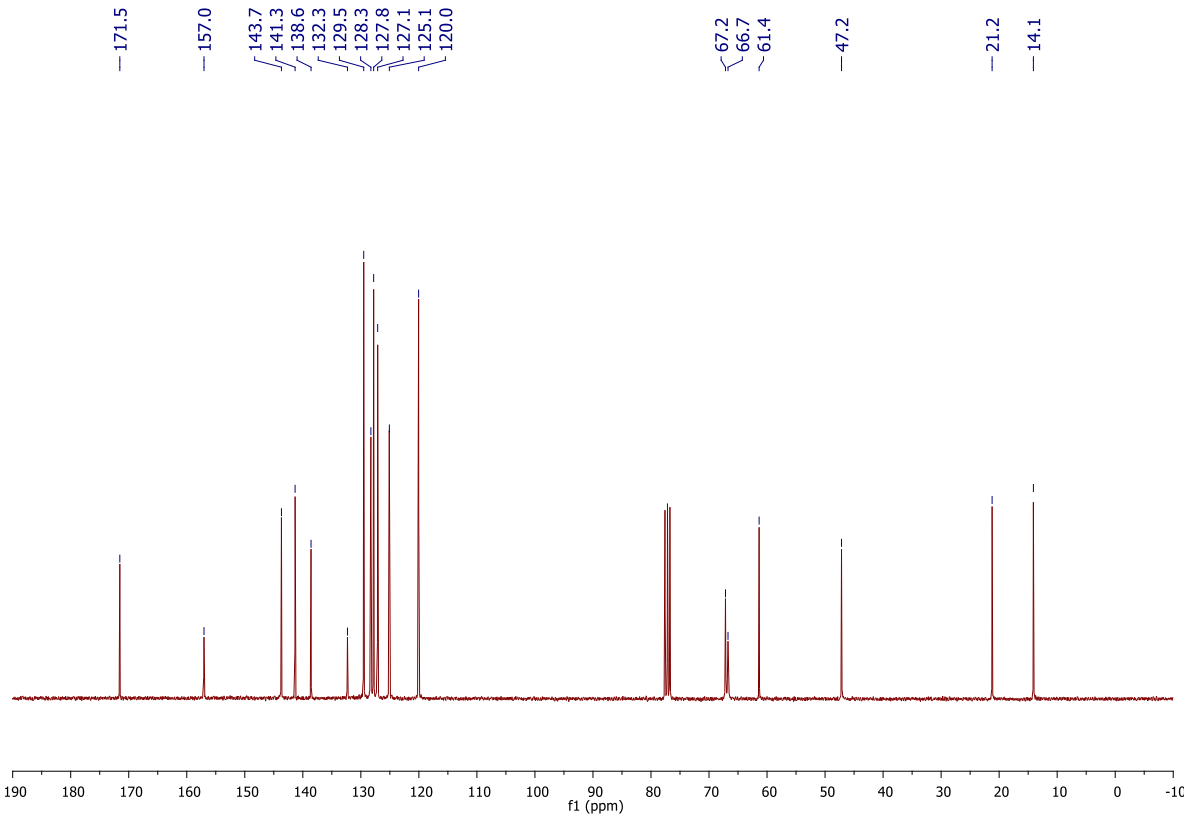
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3bg**



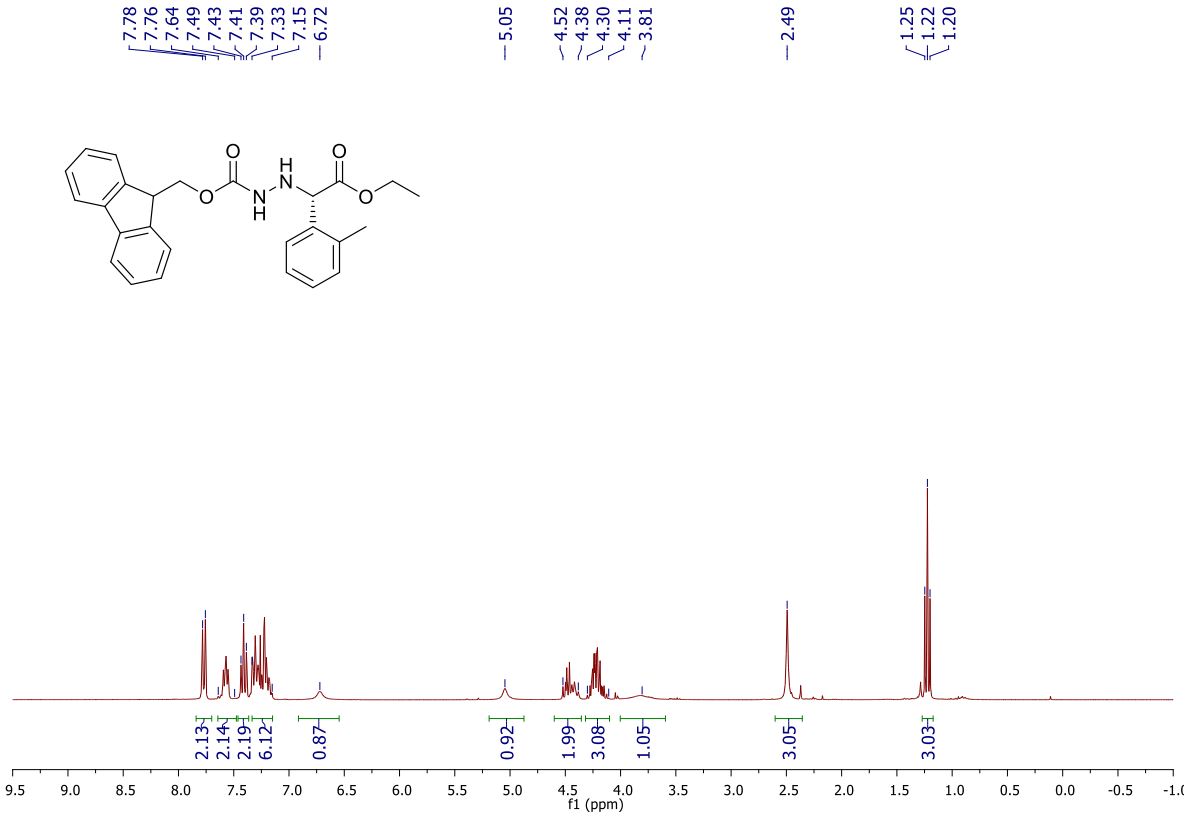
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3cg**



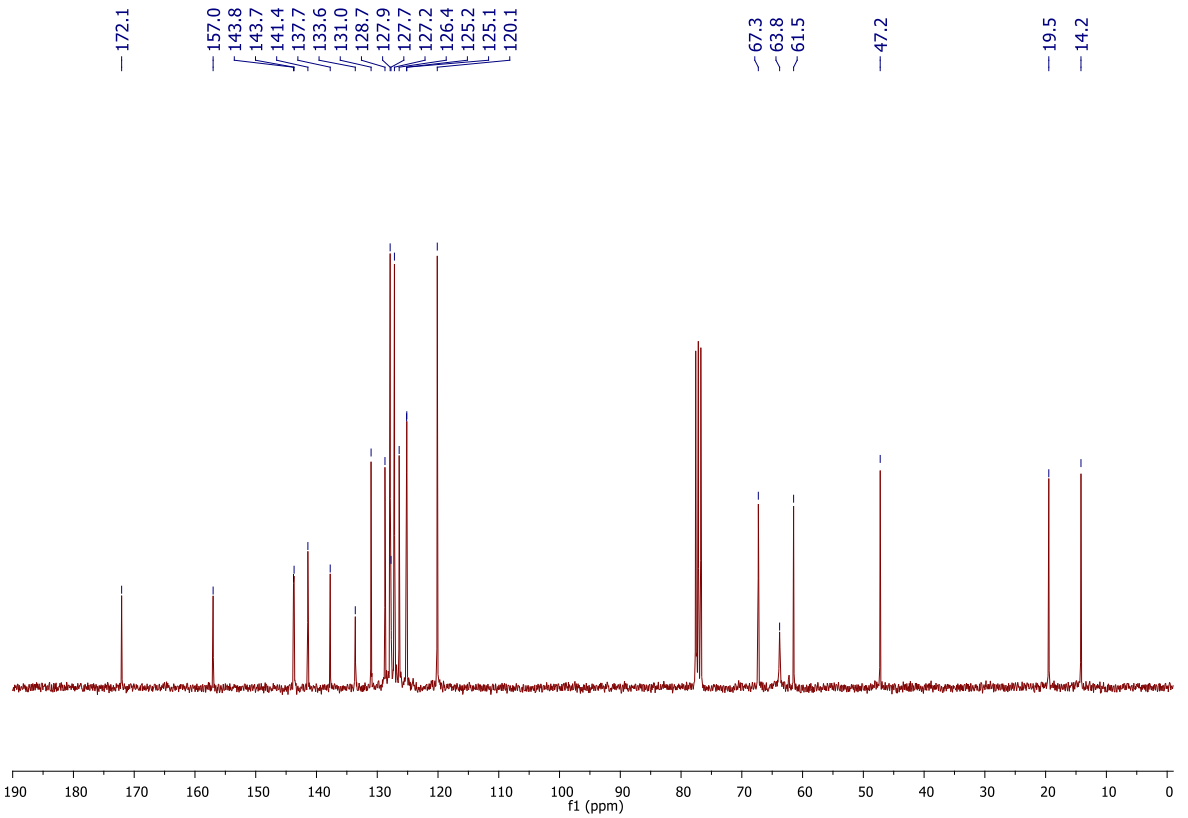
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3cg**



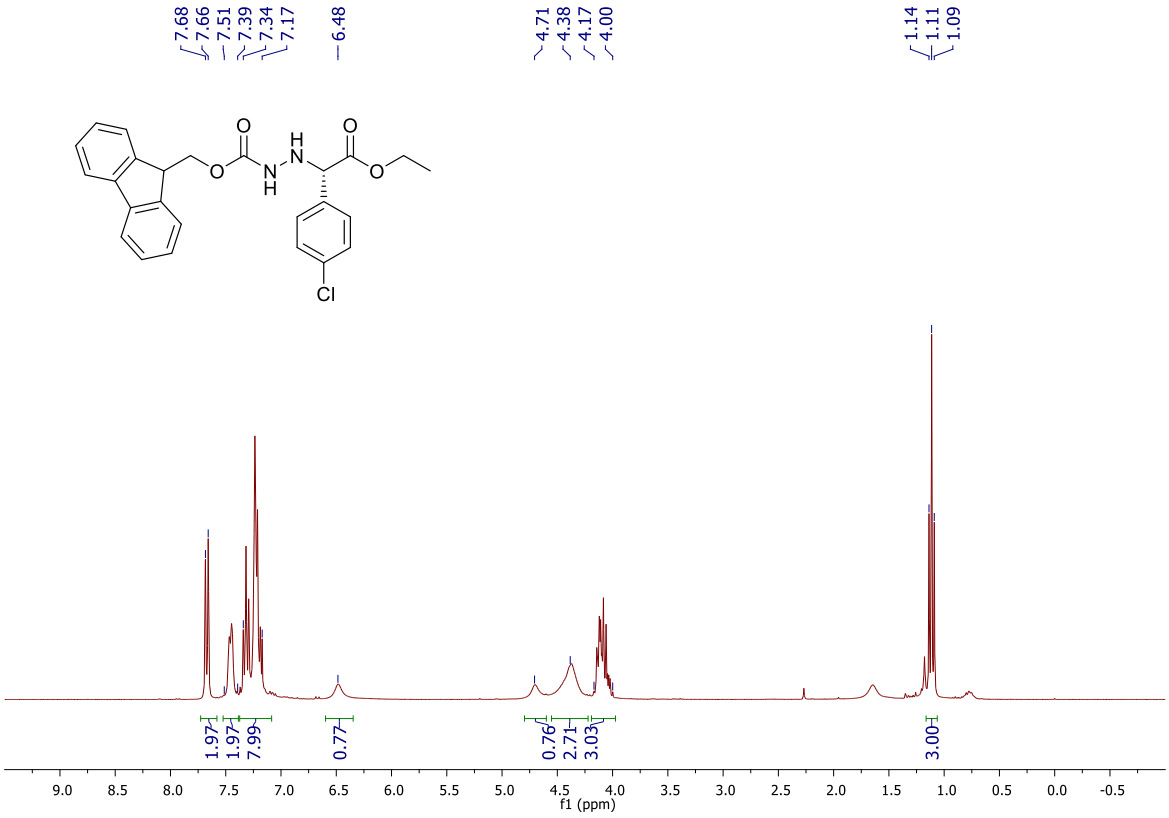
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3dg**



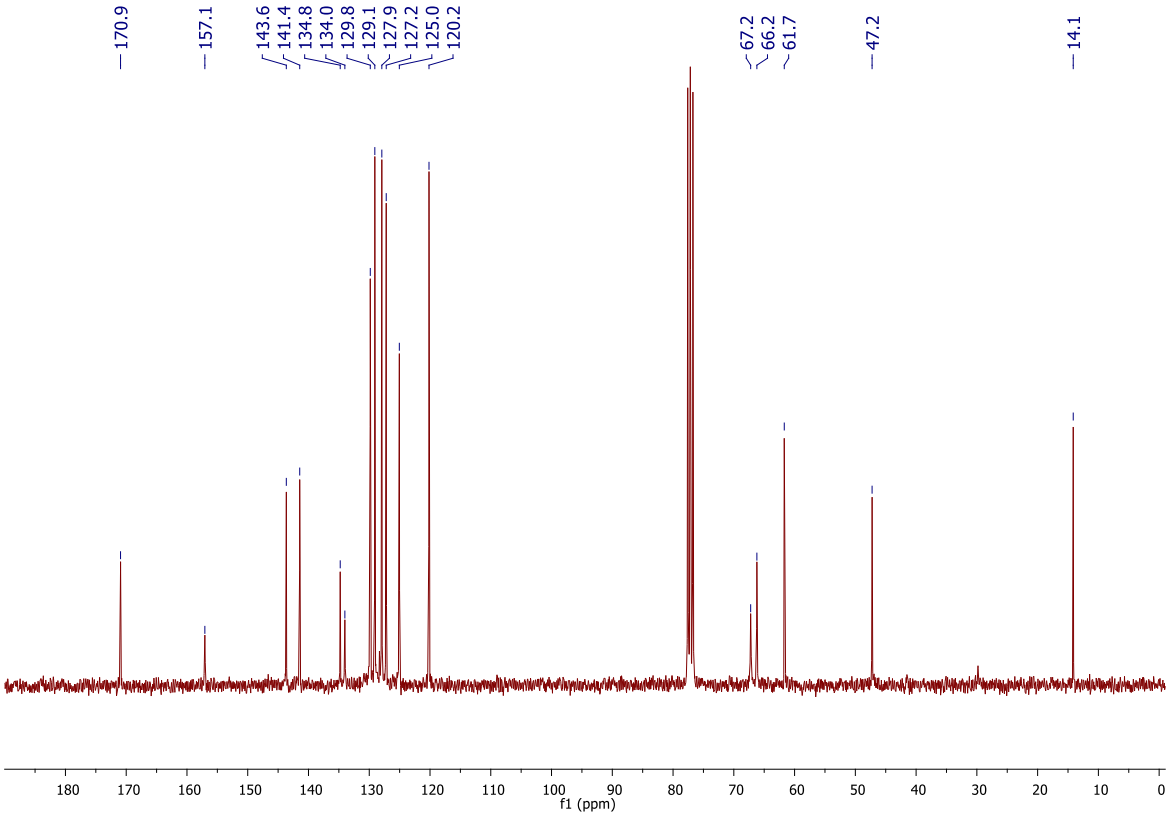
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3dg**



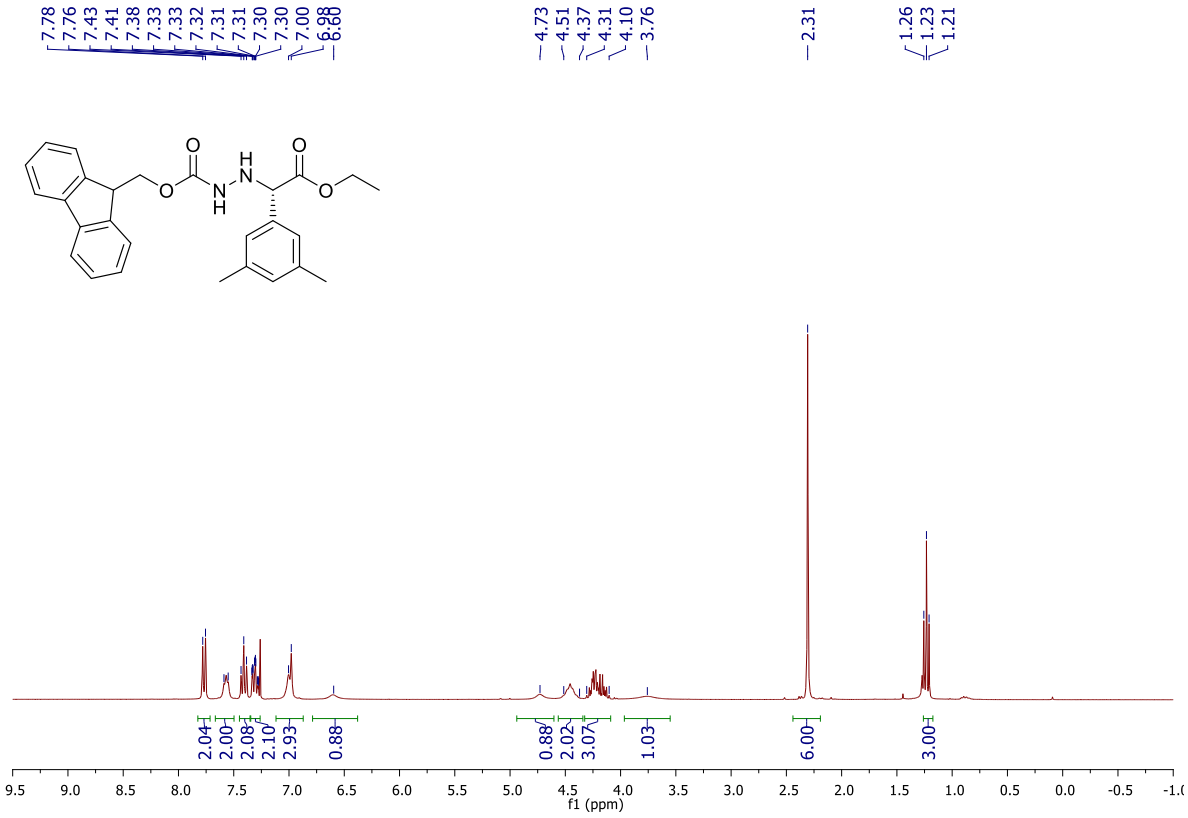
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3eg**



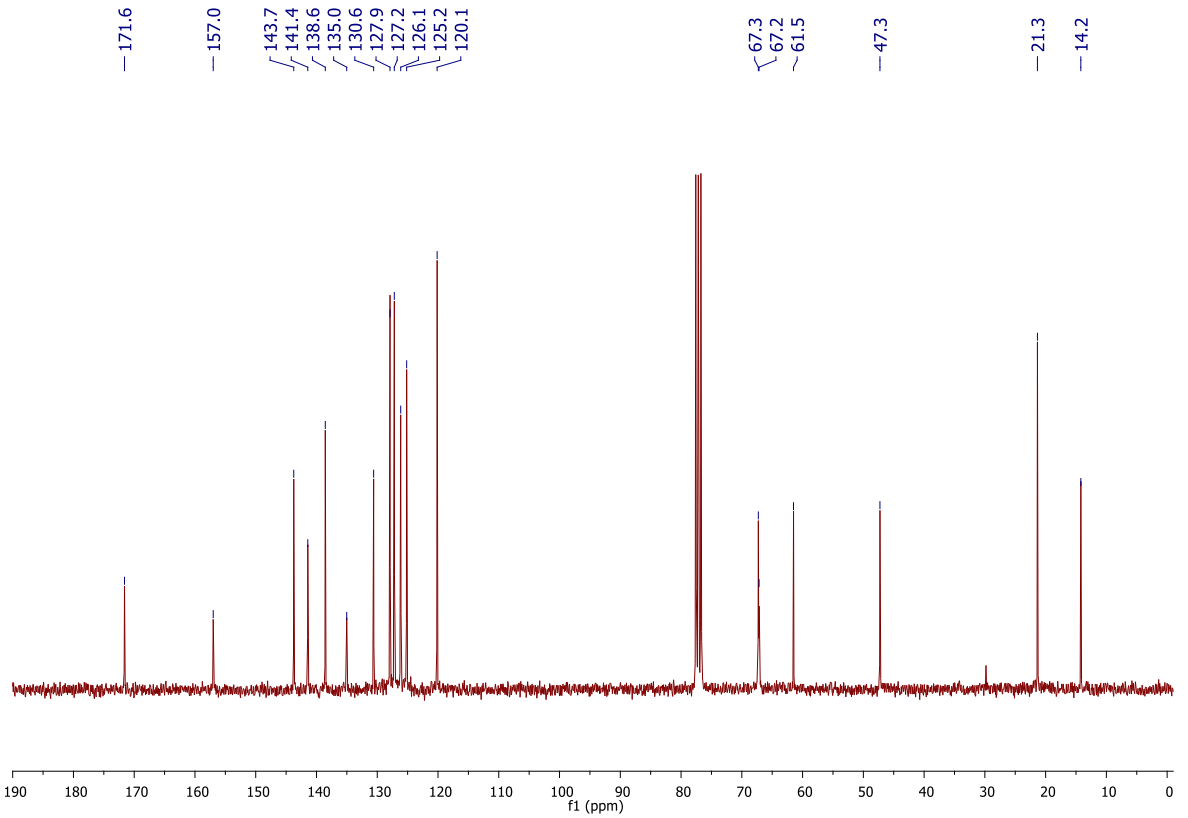
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3eg**



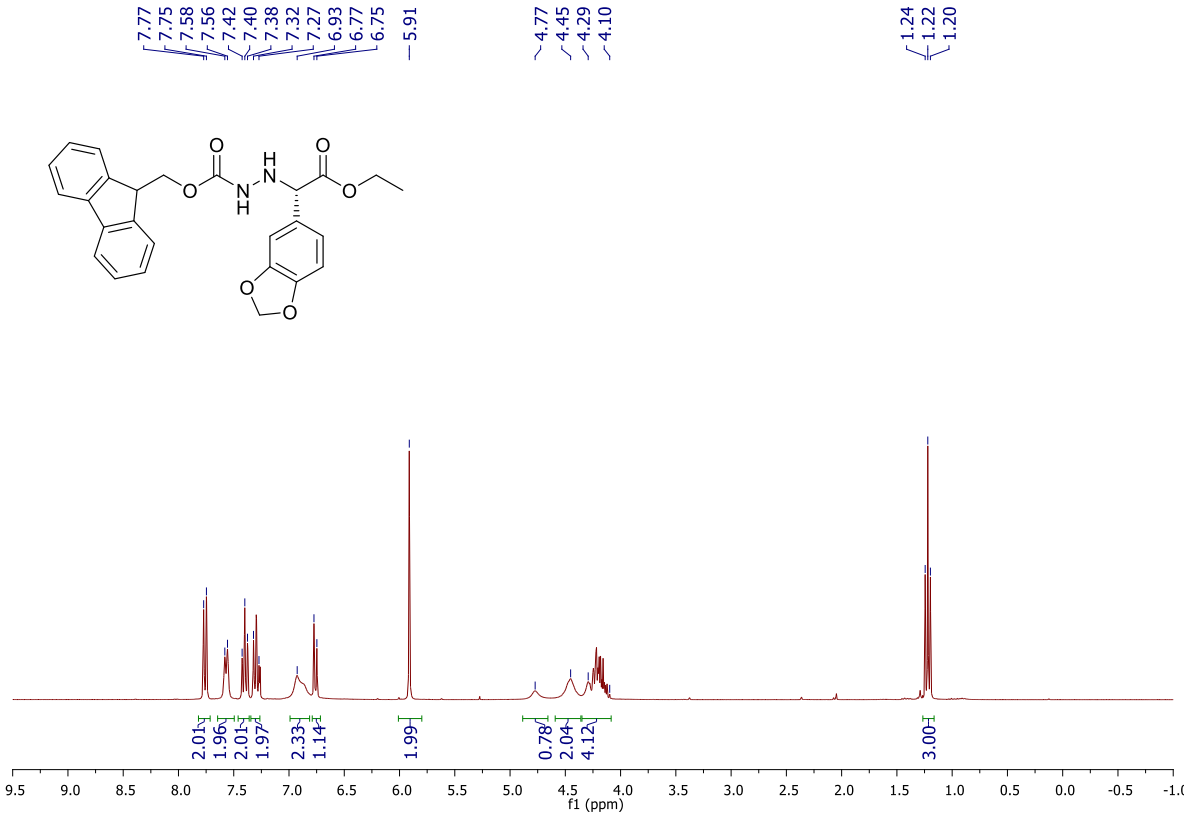
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3fg**



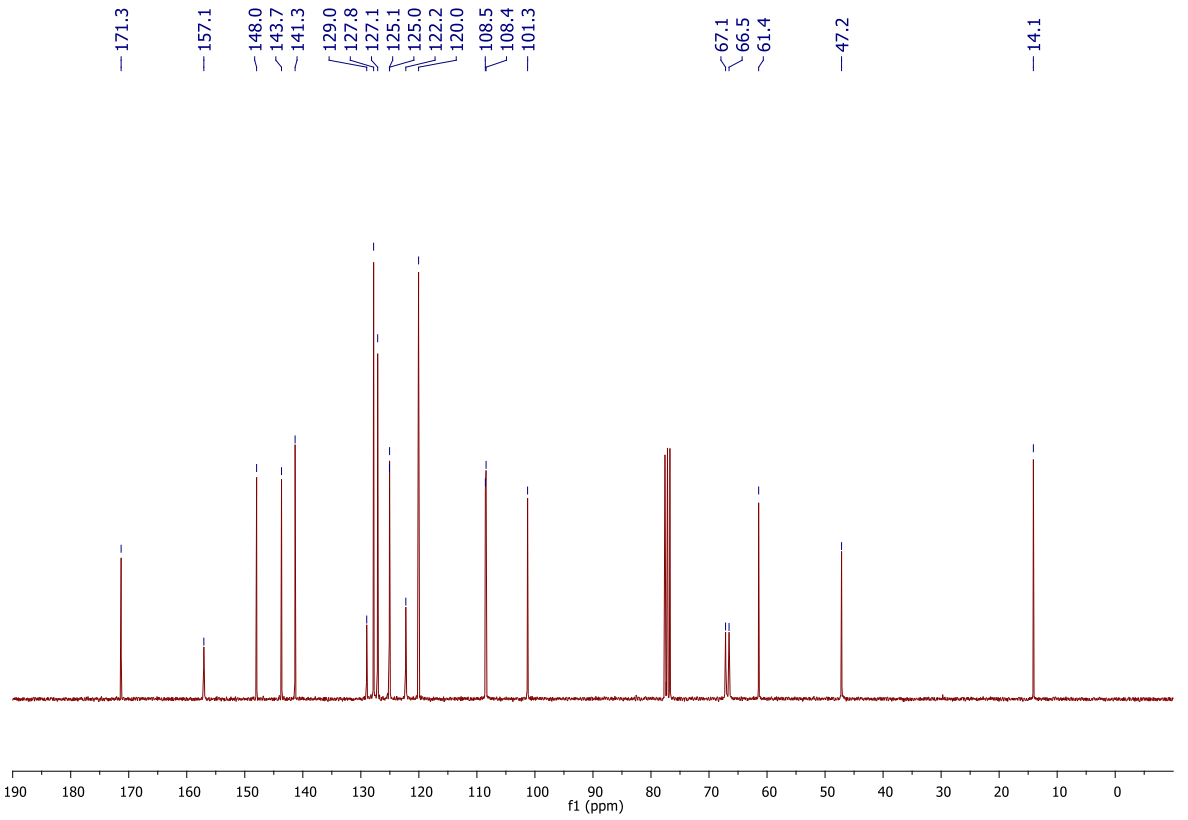
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3fg**



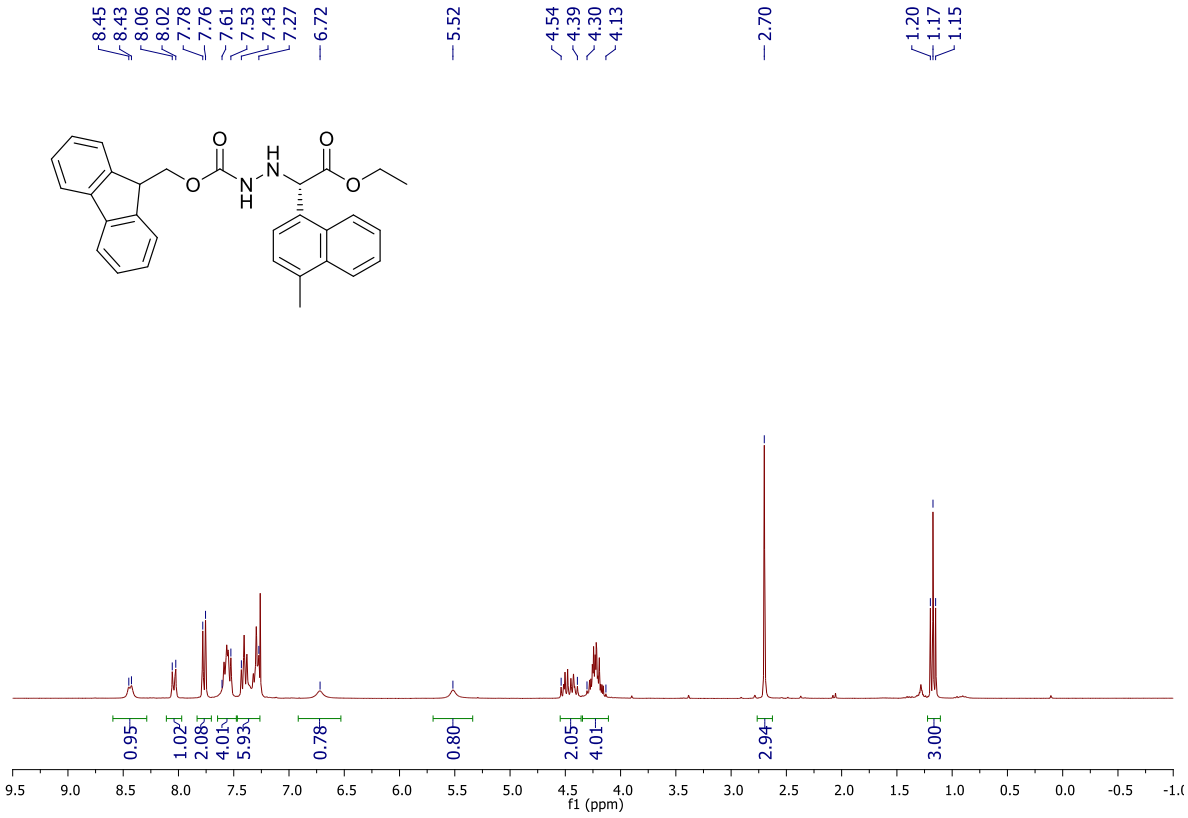
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3gg**



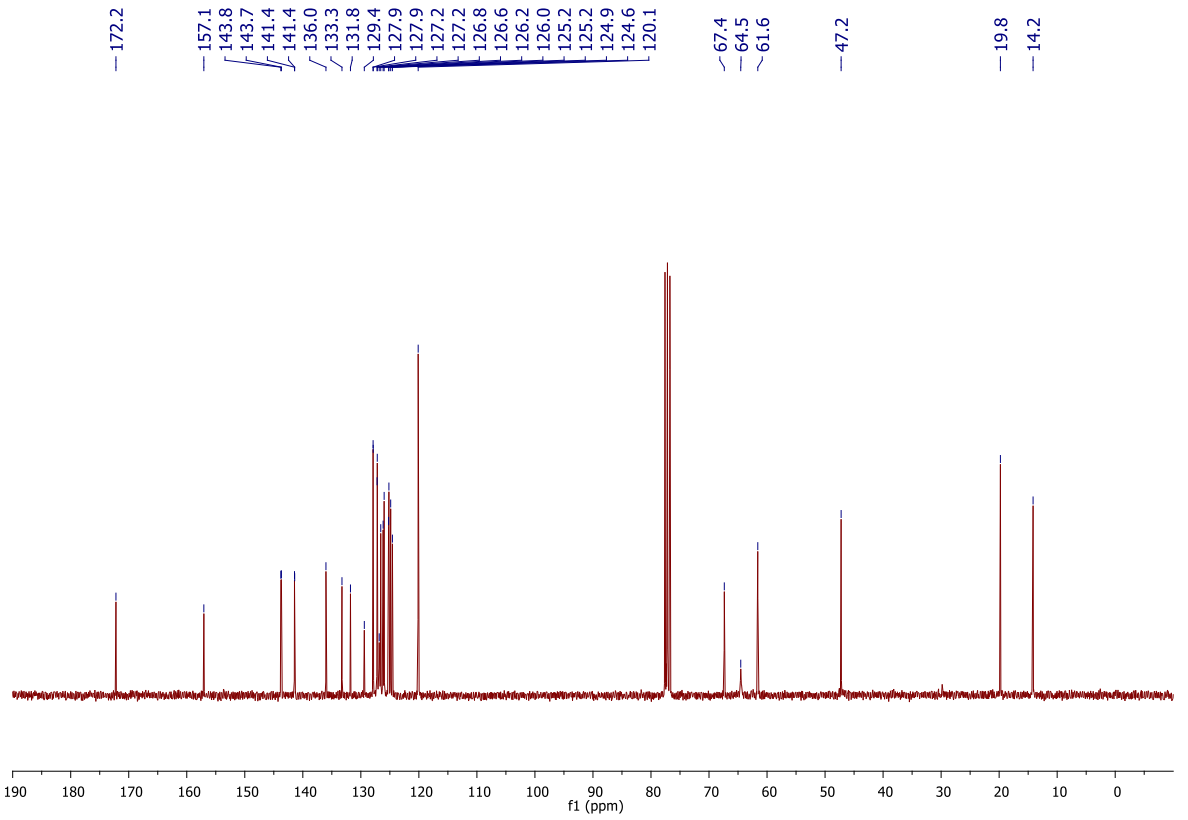
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3gg**



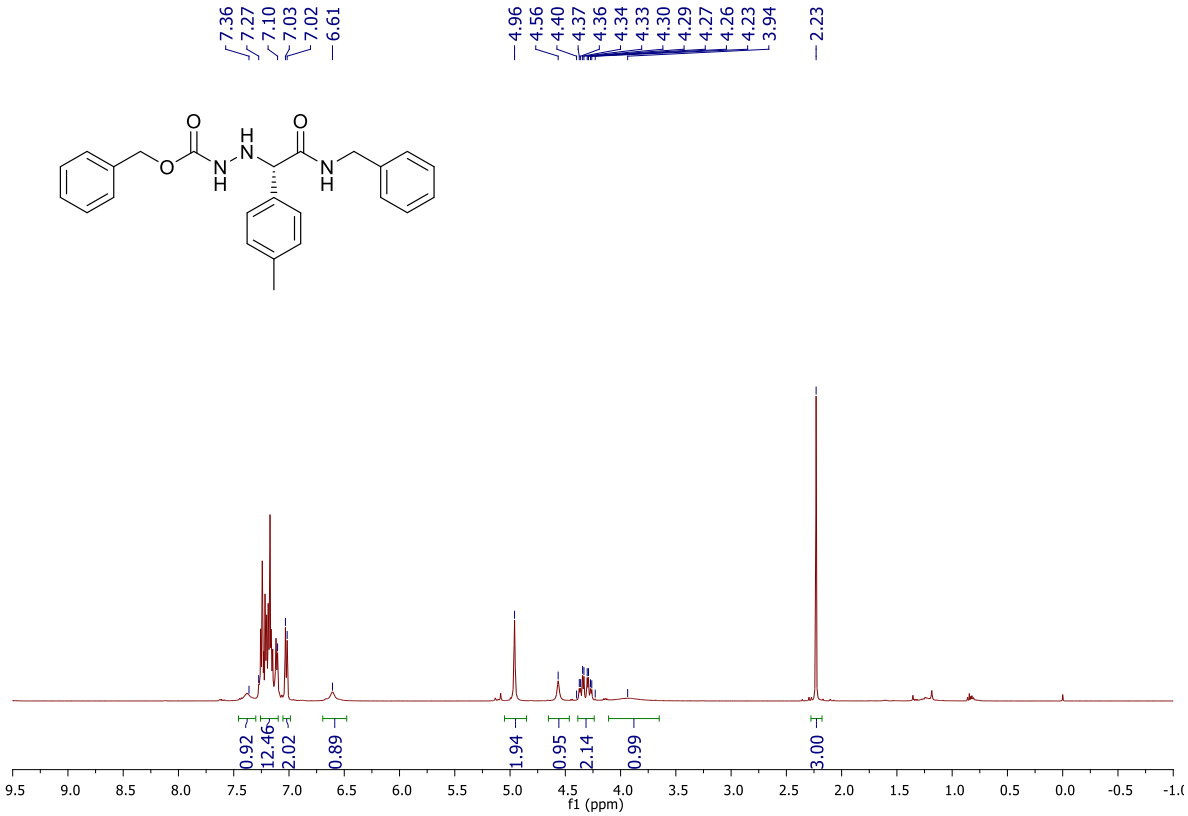
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-3hg**



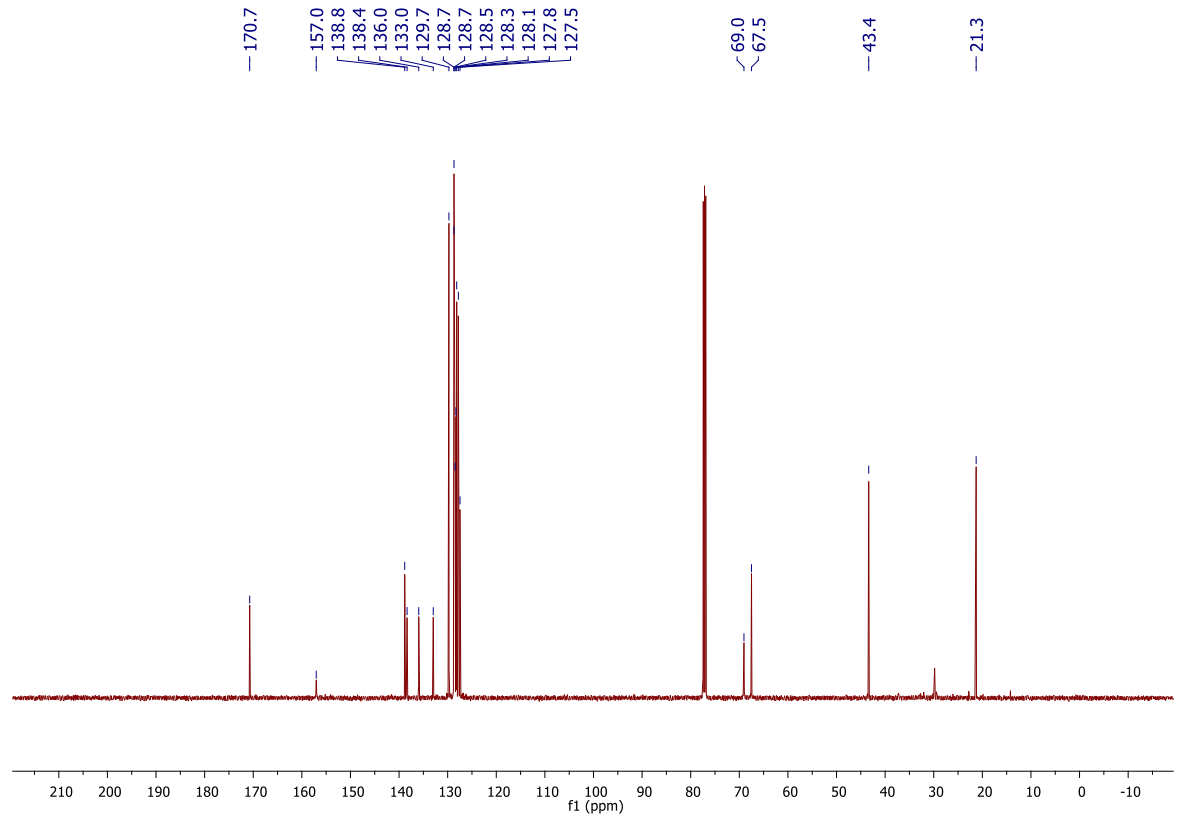
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-3hg**



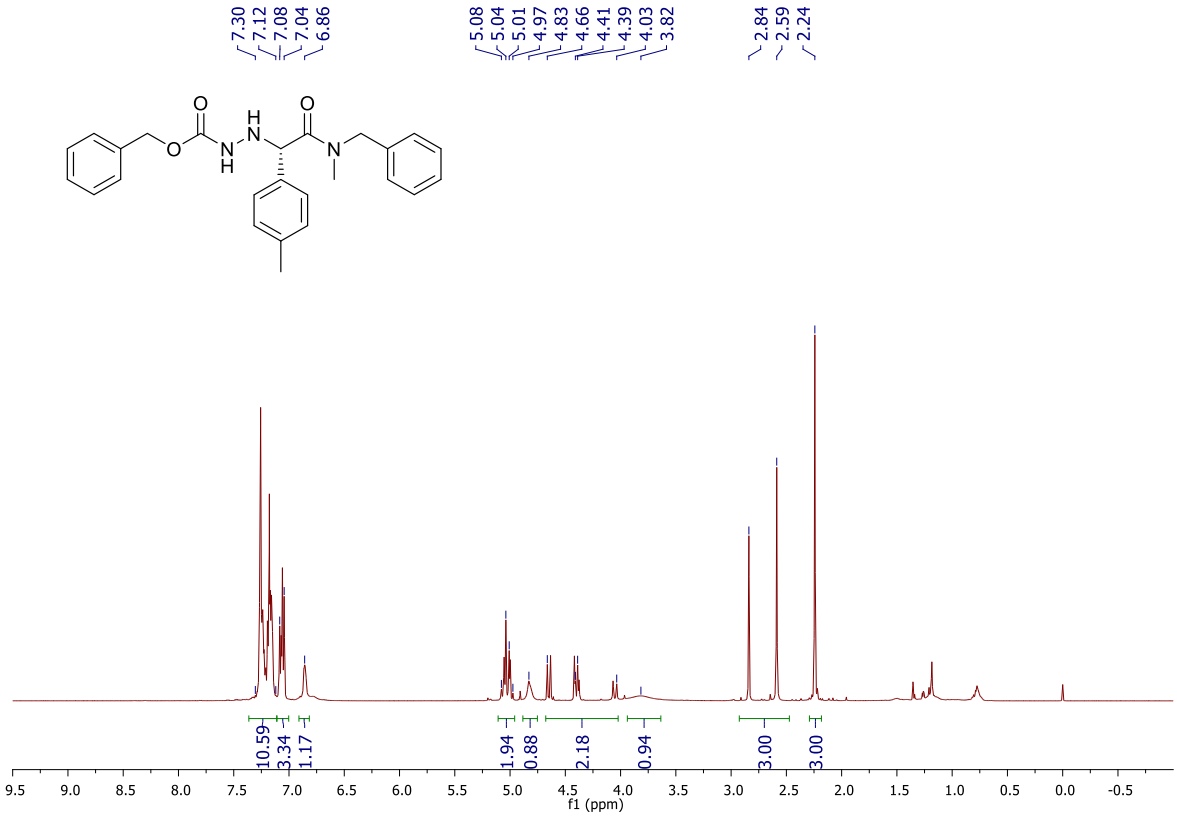
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3ck**



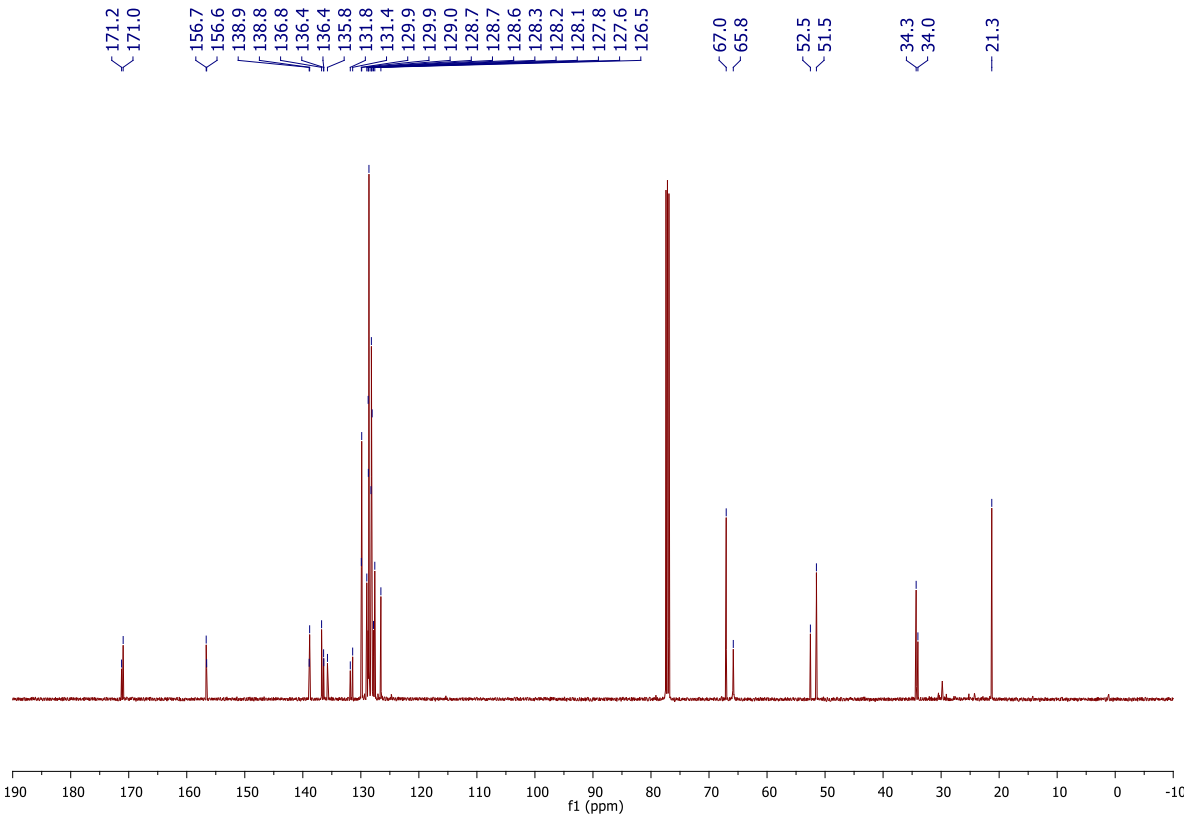
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3ck**



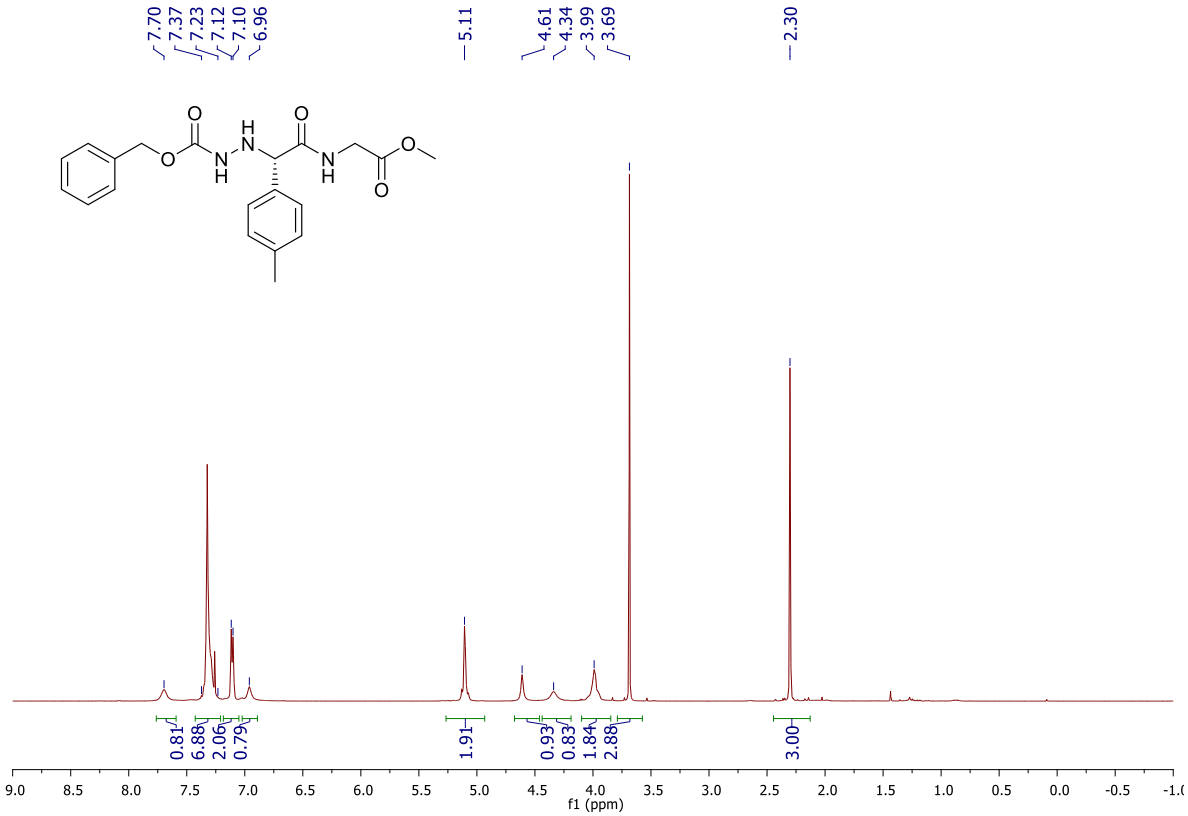
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3cl**



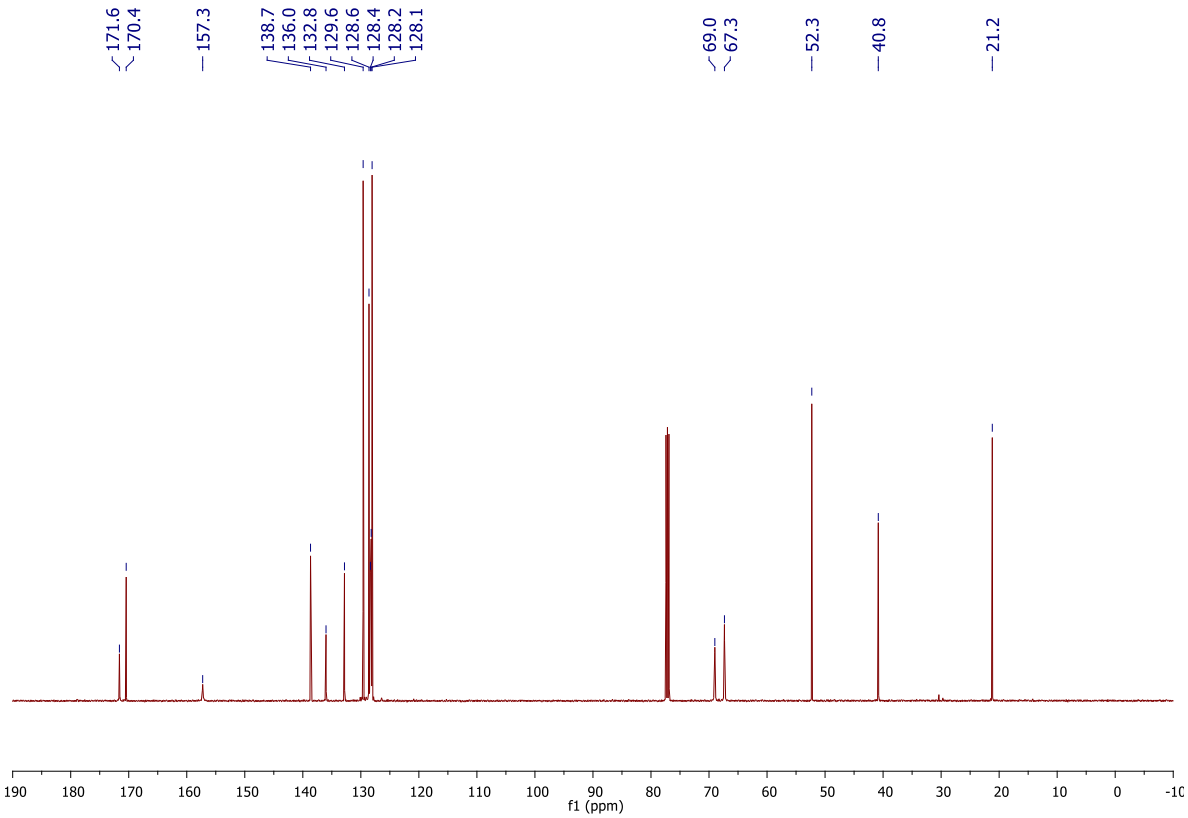
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3cl**



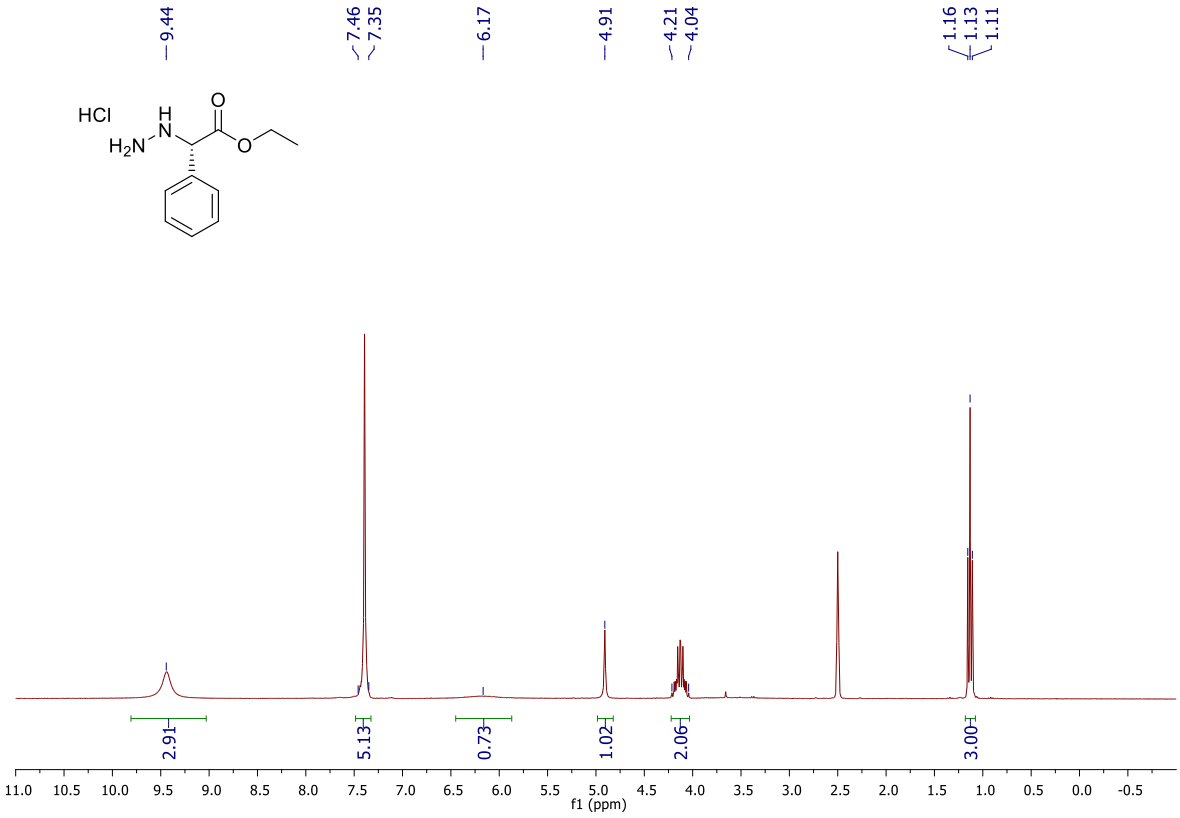
^{1}H NMR ($CDCl_3$, 500 MHz) of **(*S*)-3cm**



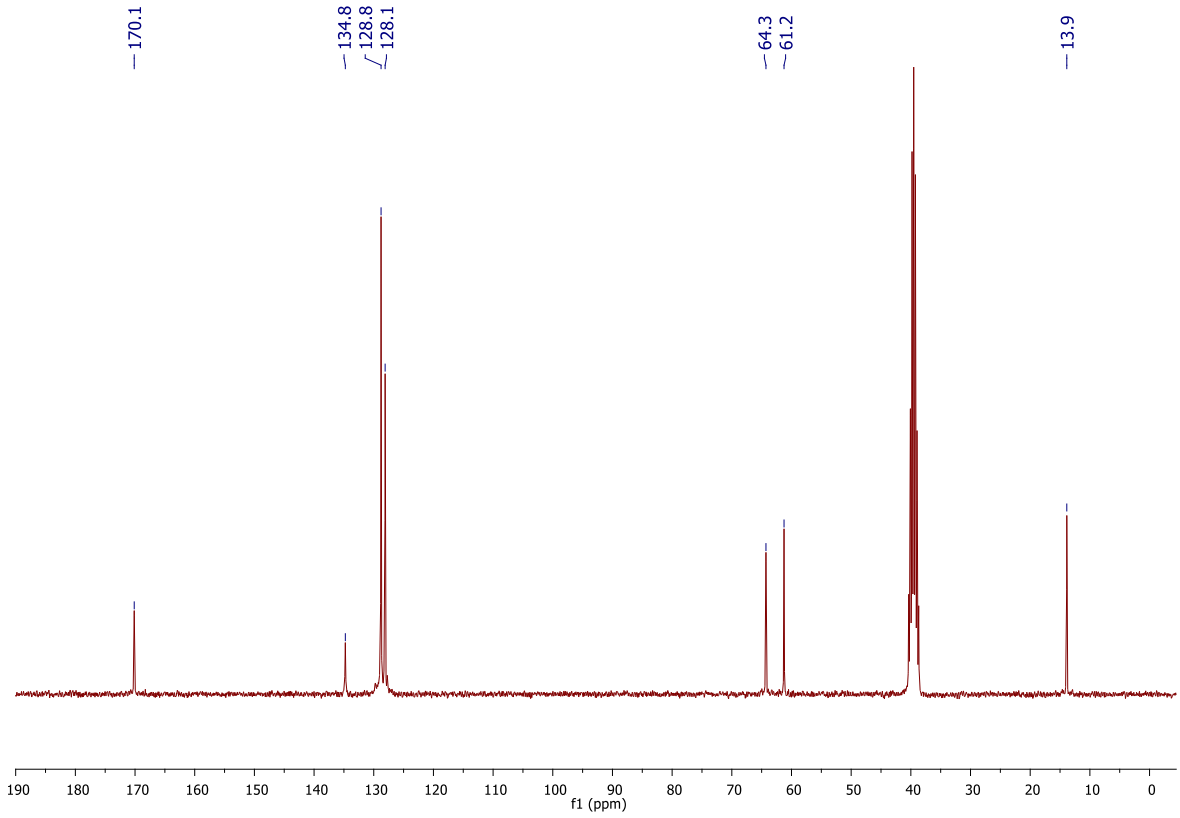
^{13}C NMR ($CDCl_3$, 126 MHz) of **(*S*)-3cm**



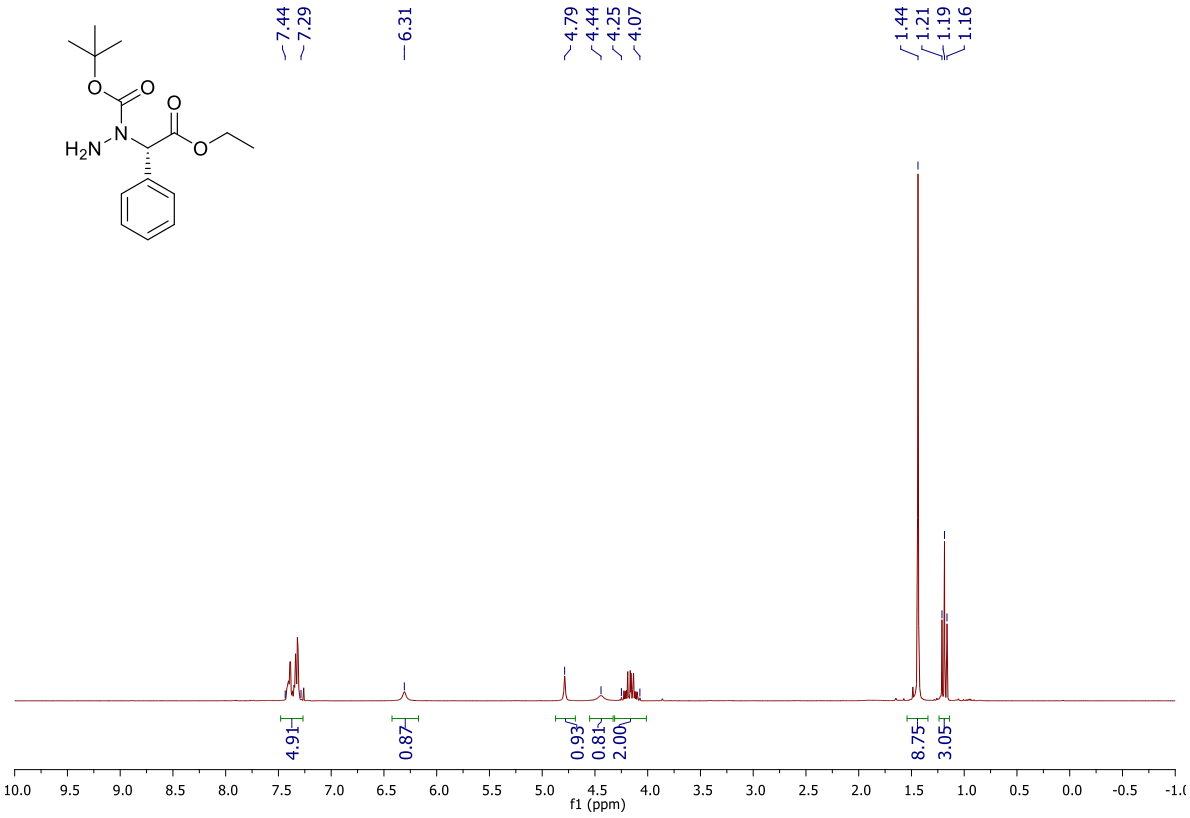
^{1}H NMR (DMSO-d^{6}, 300 MHz) of ***(S)*-4a**



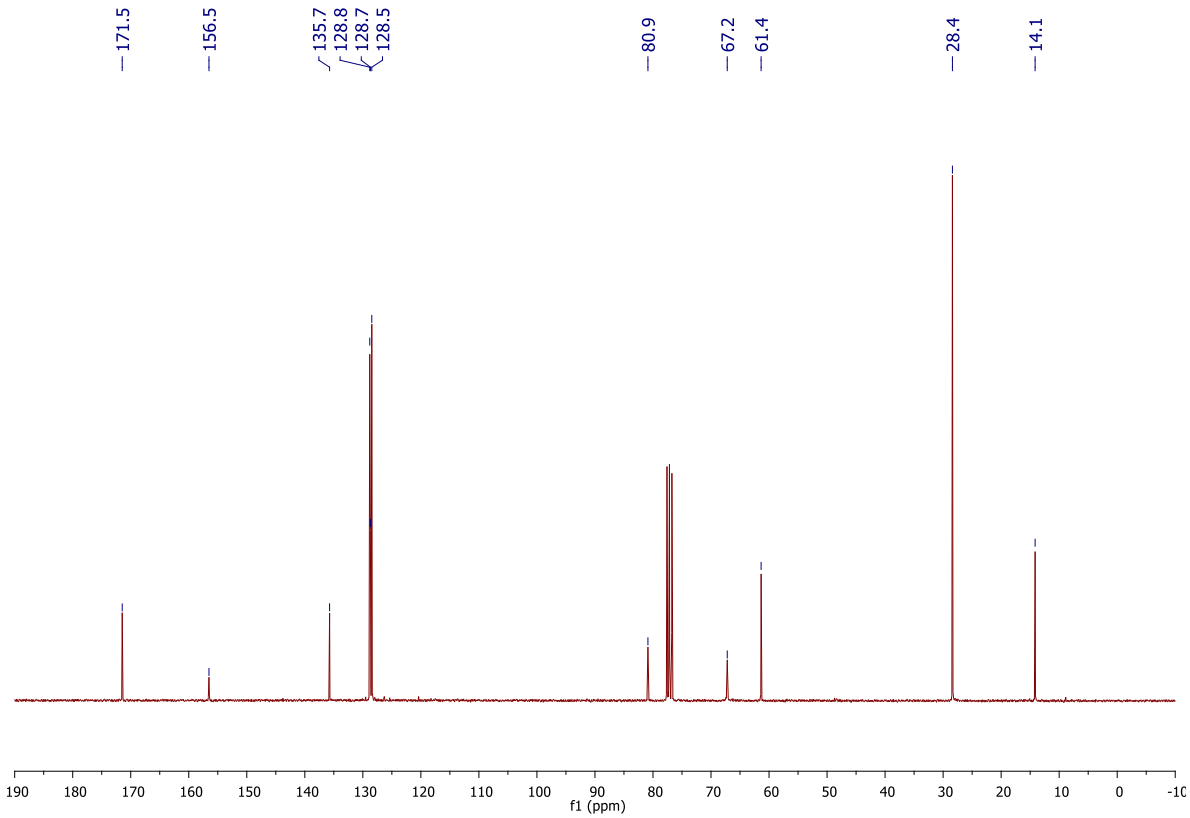
^{13}C NMR (DMSO-d^{6}, 75.5 MHz) of ***(S)*-4a**



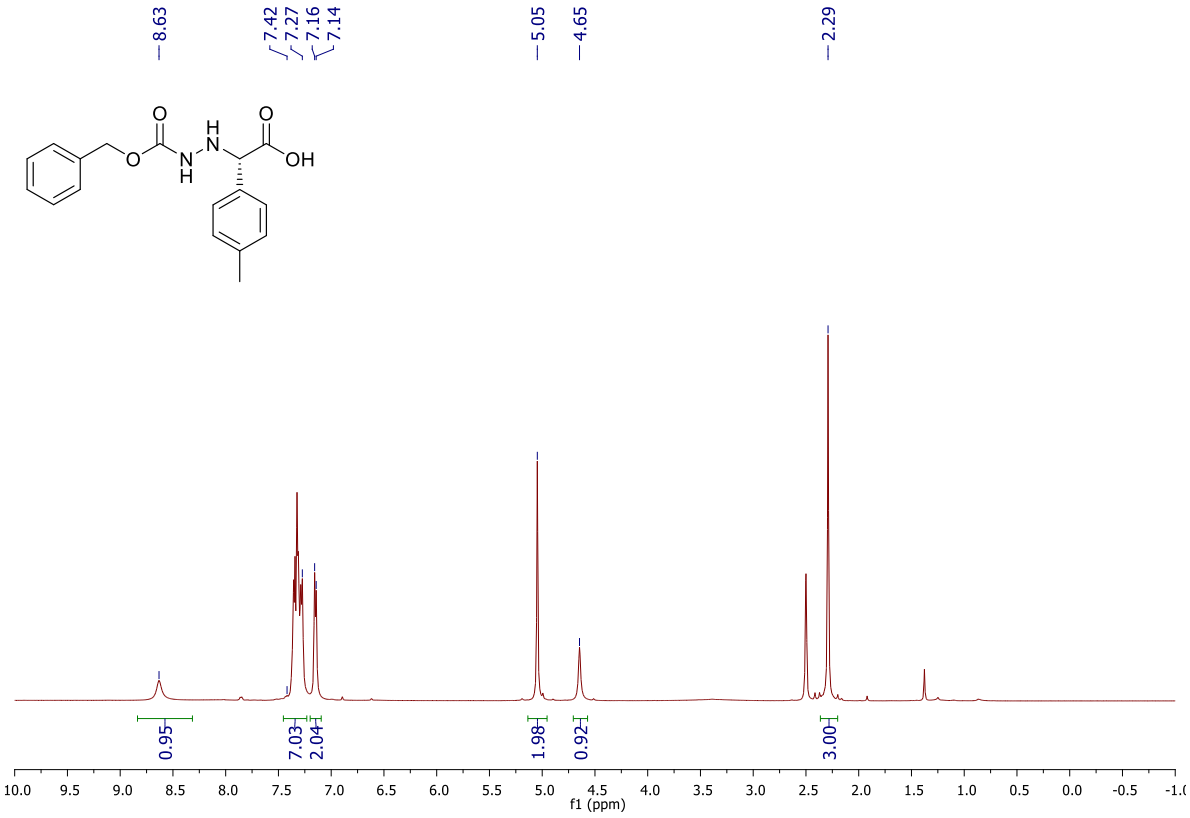
^{1}H NMR ($CDCl_3$, 300 MHz) of **(*S*)-5a**



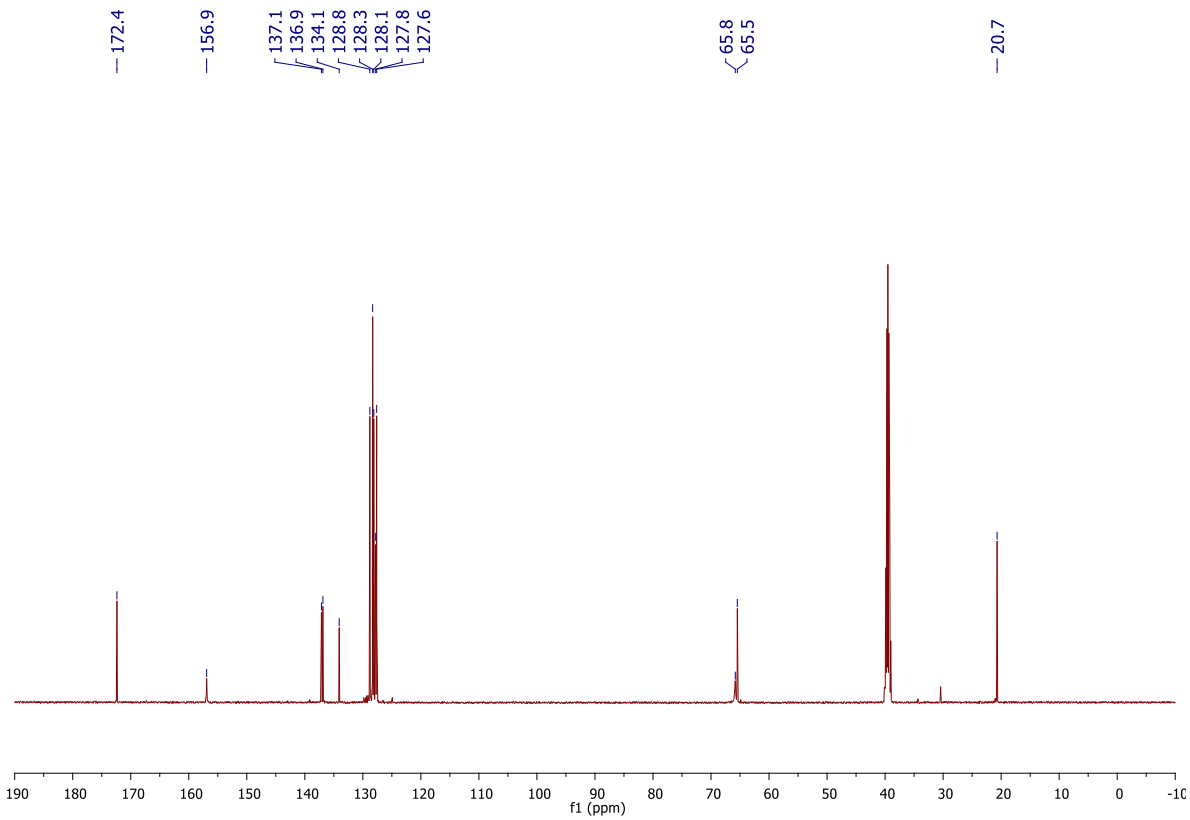
^{13}C NMR ($CDCl_3$, 75.5 MHz) of **(*S*)-5a**



^{1}H NMR (DMSO-d^{6}, 500 MHz) of ***(S)*-6a**



^{13}C NMR (DMSO-d^{6}, 126 MHz) of ***(S)*-6a**



23. References

(1) D. Monge, A. Bermejo, J. Vázquez, R. Fernández, J.M. Lassaletta. *ARKIVOC* 2013, **2**, 33-45.

(2) A. Bermejo, A. Ros, R. Fernández, J. M. Lassaletta. *J. Am. Chem. Soc.* 2008, **130**, 15798-15799.

(3) J.M. Lassaletta, M. Alcarazo, R. Fernández. *Chem. Commun*. 2004, 298-299.

(4) A. Ros, B. Estepa, A. Bermejo, E. Álvarez, R. Fernández, J. M. Lassaletta. *J. Org. Chem.* 2012, **77**, 4740-4750.

(5) Y. Álvarez-Casao, D. Monge, E. Álvarez, R. Fernández, J. M. Fernández, *Org. Lett*. 2015, **17**, 5104-5107.

(6) Y. Álvarez-Casao, B. Estepa, D. Monge, A. Ros, J. Iglesias-Sigüenza, E. Álvarez, R. Fernández, J. M. Fernández, *Tetrahedron* 2016, **72**, 5184-5190.

(7) P. S. Dragovich, J. K. Blazel, K. Dao, D. A. Ellis, L-S. Li, D. E. Murphy, F. Ruebsam, C. V. Tran, Y. Zhou, *Synthesis* 2008, **4**, 610-660.

(8) M. Fernández, U. Uria, J.L. Vicario, E. Reyes, L. Carrillo, *J. Am. Chem. Soc.* 2012, **134**, 11875-11875.