Supporting Information

Exploring The Synthesis of Aminal Guanidine-Based Molecules: Synthesis of Cernumidine and Analogues and Survey of its Anti-inflammatory Activity

Rafael Rippel,[a] Flávia Leitão,[a] Miglena K. Georgieva,[a] Rafael Mamede,[a] Clara S. B. Gomes,[a] Catarina Roma-Rodrigues,[b,c] Alexandra R. Fernandes,[b,c] Ana Lourenço,[a] Luísa M. Ferreira,*[,a] and Paula S. Branco,*[,a]

1. General Information

All used reagents were commercially acquired and used without further purification, unless mentioned. All the mentioned solvents were, when necessary, dried using typical methods. Molecular sieves were activated by heating in the microwave for 10 minutes and placing in vacuum.[1] Cooling baths at 25 °C were prepared by mixing MeCN and liquid N_2. Thin-layer chromatography was performed on Merck Kieselgel GF 254 0.2mm plates supported on aluminum and revealed under UV light (254 nm) and by staining with ninhydrin or dragendorff solutions.[2] Preparative thin-layer chromatography was performed on Merck Kieselgel GF 0.5mm or 1mm plates supported on glass. Column chromatography was performed with stationary phase Kieselgel 60A (Carlo Erba) with granulometry 40-63 μm in normal phase flash chromatography and LiChroprep RP-18 (Merck) with granulometry 40-63 μm in reverse phase chromatography.

Infrared (IR) spectra were acquired using a Perkin-Elmer Spectrum Two FTIR spectrophotometer equipped with a UATR module. Transmittance of the sample was acquired on between 4000 and 600 cm^{-1}.

NMR spectra were acquired with Bruker ARX 400 or Bruker Avance III spectrometers. ^{1}H NMR and ^{13}C NMR spectra were measured either at 400 and 101 MHz respectively. Samples were prepared on 5 mm NMR tubes using $CDCl_3$, D_2O, MeOD or CD_3CN as solvents and NMR data was recorded as follows: chemical shift in ppm, multiplicity, coupling constant(s) in Hz and integration. Chemical shifts are reported in ppm with the corresponding trace deuterated solvent used as reference signals. Signal multiplicity of NMR signals are described as singlet (s), doublet (d), doublet of doublets (dd), doublet of triplets (dt), doublet of quartets (dq), triplet (t), triplet of doublets (td), quartet (q) and multiplet (m) with coupling constants (*J*) being given in Hz.

Mass spectra were obtained with a HPLC Thermo Vanquish coupled to a diode array ultraviolet detector and a Thermo Orbitrap QExactive Focus mass spectrometer. High-resolution mass spectra (HRMS) were obtained at the University of Salamanca (Spain), Elemental Analysis, Chromatography and Mass Spectrometry Service (NUCLEUS), using a High-Performance Liquid Chromatography (HPLC) Agilent 1100 coupled to a QSTARXL Hybrid qTOF (AB Sciex, Framingham, MA, USA) mass spectrometer.

Enantiomeric excesses (*ee*) were determined by HPLC analysis in a Waters Alliance system with a 2695 separation module coupled to a 2996 Photodiode Array detector array and Empower 3 software. The separation was performed on a Phenomenex Lux 5 μm Cellulose-2 column.

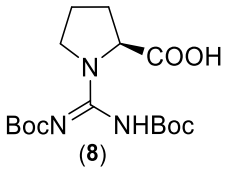
Specific optical rotations were measured in a Belligham + Stanley ADP410.

ICP-AES analyses were performed in a Horiba Jobin-Yvon Ultima model equipped with a 40.68 MHz RF generator, a Czerny–Turner monochromator with 1.00 m (sequential), and an autosampler AS500 (Horiba, Kyoto, Japan).

Selected crystals were covered with Fomblin (polyfluoroether oil) and mounted on a nylon loop. The X-ray diffraction data were collected at 296(2) K on a Bruker D8 Venture diffractometer equipped with a Photon 100 CMOS detector, using graphite monochromated Mo-Kα radiation (λ = 0.71073 Å) or Cu-Kα radiation (λ = 1.54178 Å). Data were processed using APEX3 suite software package, which includes integration and scaling (SAINT), absorption corrections[3] and space group determination (XPREP). Structure solution and refinement were done using direct methods with the programs SHELXT 2014/5 and SHELXL-2018/3[4,5] inbuilt in APEX and WinGX-Version 2021.3[6] software packages. All non-hydrogen atoms were refined anisotropically. Except for the NHs that were located in the electron density map, all hydrogen atoms were inserted in idealized positions and allowed to refine riding on the parent carbon atom with C–H distances of 0.96 Å, 0.97 Å, 0.98 Å, and 0.93 Å for methyl, methylene, methine and aromatic H atoms, respectively. The crystals of **15e** were of low quality and showed poor diffracting power, with diffraction spots from high angles very weak, which, consequently, led to low quality data and a high R_{int}. Several attempts on different crystals were performed, although unsuccessful in getting better crystal data. Nevertheless, the structure refined to convergence and the results are in agreement with the remaining analytical data. Due to the existence of residual solvent in **15e**, for which a reasonable model was impossible to obtain, the SQUEEZE routine of PLATON7 was applied. Although **19** displays a pseudo centre of symmetry element ($P2_1/c$) with 92% fit, tests with PLATON/ADDSYM[7] revealed the existence of pseudo-translations but no obvious need for a space group change. The molecular diagrams were drawn with Mercury.[8] The data was deposited in CCDC under the deposit numbers 2306654 for **15e** and 2306655 for **19**.

S.1. Experimental Section

S.1.1. Synthesis of *N,N'*-bis(*tert*-butoxycarbonyl)carbamimidoyl)-L-proline (8)



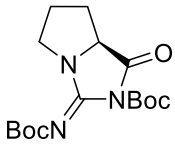
(**8**)

N,N'-bis(*tert*-Butoxycarbonyl)carbamimidoyl)-L-proline (**8**) was prepared by adapting the previously described literature procedure:[9] To a stirred solution of *N,N'*-Di-Boc-1*H*-pyrazole-1-carboxamidine (**GR3** – 1.1 equiv.) and *i*-Pr_2NEt (1.1 equiv) in MeCN/H_2O (95:5, volume to make a 0.2 M solution of substrate), L-proline (2 g, 17.4 mmol) was added and the mixture was stirred at 80 °C for 16h. The reactional mixture was evaporated until dryness and the residue dissolved in AcOEt. The organic phase was washed with a HCl 1M solution (2 x 10 mL), brine (1 x 10 mL), dried over Na_2SO_4, filtered, and evaporated under reduced pressure to afford **8** as a white solid (6g, 96%). The spectral data are in agreement with the literature.[9]

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.70-4.53 (m, 1H), 3.80-3.66 (m, 1H), 3.57-3.45 (m, 1H), 2.66-2.44 (m, 1H), 2.09-1.95 (m, 2H), 1.95-1.83 (m, 1H), 1.48 (s, 18H).

IR (ATR) ν_{max} (cm^{-1}): 3192, 2976, 2936, 1790, 1749, 1729, 1615, 1460, 1394, 1366, 1288, 1248, 1133, 1101, 1048.

S.1.2. *tert*-Butyl (S)-3-((tert-butoxycarbonyl)imino)-1-oxotetrahydro-1H-pyrrolo[1,2-c]imidazole-2(3H)-carboxylate (9)



(**9**)

White solid (320 mg, 92%). Obtained from 970 mg of 8 when subjected to the general procedure for the synthesis of acyl azides.

^{1}H NMR (400 MHz, CDCl3) δ 4.14 (dd, J = 8.50 and 3.11 Hz, 1H), 3.52-3.39 (m, 2H), 2.32-2.23 (m, 1H), 2.22-2.11 (m, 2H), 2.11-2.06 (m, 1H), 1.56 (s, 9H), 1.49 (s, 9H).

^{13}C NMR (101 MHz, CDCl3) δ 169.31, 158.94, 153.97, 146.09, 86.06, 80.33, 63.61, 48.06, 30.95, 28.23, 27.92, 27.63.

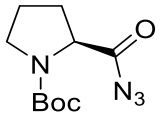
IR (ATR) νmax (cm^{-1}): 3400, 2980, 2931, 2878, 1794, 1765, 1688, 1639, 1468, 1398, 1374, 1301, 1252, 1121.

ESI-MS: m/z calculated for C16H26N3O5 [M+H]+: 340.1872, found: 340.2.

S.1.3. General procedure for the synthesis of acyl azides

Acyl azides were synthesized by employing the modified conditions of a previously reported procedure:[10] In a rounded bottom flask, the correspondent *N*-protected amino acid (1 equiv.) was dissolved in dry THF (volume to make a 0.2 M solution of substrate), placed under inert atmosphere, and cooled to -15 °C. Then, *N*-methylmorpholine (1.1 equiv.) and isobutyl chloroformate (1.1 equiv.) were added dropwise, to the mixture, allowing it to stir for 20 minutes. An aqueous solution of sodium azide (2.4 equiv, 5M) was added, and the mixture was stirred for an hour at -15°C (formation of two distinct phases). The progress of the reaction was monitored by observing the emergence of the acyl azide band at 2200 cm-1, and upon complete consumption of the starting material the two phases were separated, and the organic layer was concentrated under vacuum. The residue was dissolved in ethyl acetate and the organic phase washed with a solution of HCl 1 M, a saturated solution of $NaHCO_3$, dried under Na_2SO_4, filtered, and concentrated under vacuum to afford the correspondent acyl azide.

S.1.3.1. *tert*-Butyl (*S*)-2-(azidocarbonyl)pyrrolidine-1-carboxylate (2)



(**2**)

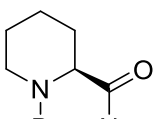
Colorless oil (1.01 g, 91%). Obtained from 1g of *N*-Boc-L-proline when subjected to the general procedure for the synthesis of acyl azides.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.30-4.15 (m, 1H), 3.59-3.33 (m, 2H), 2.31-2.11 (m, 1H), 2.02-1.76 (m, 3H), 1.46-1.40 (m, 9H).

IR (ATR) ν_{max} (cm^{-1}): 2948, 2872, 2138, 1720, 1575, 1520, 1451.

$[\alpha]_D^{26}$-88 (*c* 0.43, THF)

S.1.3.2 *tert*-Butyl 2-(azidocarbonyl)piperidine-1-carboxylate (12a)

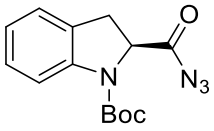


(**12a**)

Colorless oil (1.05 g, 95%). Obtained from 1g of (*S*)-1-(*tert*-butoxycarbonyl)piperidine-2-carboxylic when subjected to the general procedure for the synthesis of acyl azides.

IR (ATR) ν_{max} (cm^{-1}): 2941, 2871, 2134, 1697, 1475, 1459, 1393, 1364.

S.1.3.3. *tert*-Butyl (*S*)-2-(azidocarbonyl)indoline-1-carboxylate (**13a**)



(**13a**)

Light reddish solid (1.07 g, 98%). Obtained from 1g of (*S*)-1-(*tert*-butoxycarbonyl)indoline-2-carboxylic acid when subjected to the general procedure for the synthesis of acyl azides.

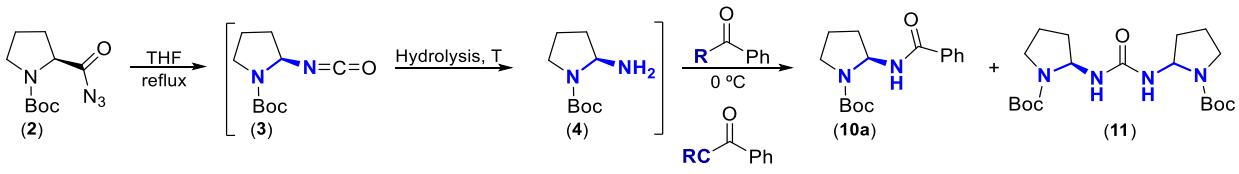
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97-7.80 (m, 0.6H), 7.57-7.43 (m, 0.4H), 7.24-7.17 (m, 1H), 7.12 (d, *J* = 7.4 Hz, 1H), 6.96 (t, *J* = 7.4 Hz, 1H), 4.97-4.76 (m, 1H), 3.58-3.45 (m, 1H), 3.20-3.09 (m, 1H), 1.64-1.50 (m, 9H).

IR (ATR) ν_{max} (cm^{-1}): 2979, 2936, 2140, 1714, 1598, 1490, 1386, 1316, 1161, 1084

S.1.4 General procedure for isocyanate (**3**) hydrolysis and amide formation.

In a rounded bottom flask, acyl azide (**2**) was dissolved in THF (volume to make a 0.2 M solution of substrate). The mixture was left to reflux under nitrogen atmosphere for 2 hours. The evolution of the reaction was monitored by IR (FTIR) by following the disappearance of the azide band at 2140 cm^{-1} and the appearance of the isocyanate band at 2240 cm^{-1}. After full consumption of acyl azide, the mixture was allowed to reach room temperature. Water or NaOH solution were then added. Conditions for the hydrolysis reaction of the isocyanate are presented in Table S1. The evolution of the reaction was monitored by IR until the disappearance of the isocyanate band at 2240 cm^{-1}. The mixture was then concentrated under vacuum. The obtained residue was dissolved in DCM (volume to make a 0.2 M solution of substrate) and placed under an inert atmosphere at 0 °C. Then, triethylamine (1.1 equiv.) and benzoyl chloride (1.1 equiv.) or the pre-activated benzoic acid with the correspondent carbodiimide (1.1equiv) were added. The mixture was left to react at room temperature for 18 hours. The reactional mixture was washed with water (1 x 10 mL), brine (1 x 5 mL), dried under Na_2SO_4, filtered, and concentrated under vacuum. The crude mixture was purified by flash chromatography (silica gel, hexane:EtOAc, 100:0 → 60:40).

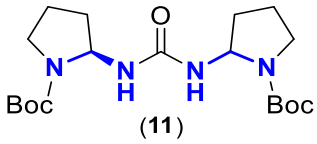
Table S1. Screened conditions to access the free aminal (**4**) followed by trapping with benzoyl chloride or pre-activated benzoic acid.



Entry	Rearrangement conditions	Hydrolysis reagent	R/CR	Hydrolysis temperature (°C)	Time (h)	Results
1	[a]	-	Cl[c]	70	3	11/Benzoic acid
2[b]	THF rfx	NaOH (1M) (0.4M solution)	Cl[c]	Rt	20	11/Benzoic acid
3[b]	THF rfx	H_2O (0.2 M solution)	Cl[c]	70	3	11/Benzoic acid
4[b]	THF rfx	H_2O (0.2M solution)	Cl[c]	Rt	5	11/Benzoic acid
5[b]	THF rfx	H_2O (0.1M solution)	Cl[c]	70	3	11/Benzoic acid
6[b]	THF rfx	H_2O (0.1M solution)	Cl[c]	Rt	5	11/Benzoic acid
7[b]	THF rfx	H_2O (0.02 M solution)	Cl[c]	70	3	11/Benzoic acid
8[b]	THF rfx	H_2O (0.02 M solution)	Cl[c]	Rt	7	11/Benzoic acid
9[b]	THF rfx	H_2O (20equiv)	Cl[c]	70	5	11/Benzoic acid
10[b]	THF rfx	H_2O (20equiv)	Cl[c]	Rt	7	11/Benzoic acid/**10a** (15%)
11	THF rfx	H_2O (20 equiv.)	OH/DCC	Rt	16	11/Benzoic acid
12	THF rfx	H_2O (20 equiv.)	OH/EDC	Rt	16	11/Benzoic acid
13	THF rfx	H_2O (20 equiv.)	OH/CDI	Rt	16	11/Benzoic acid

[a]Rearrangement and hydrolysis performed one-pot in a (1:1) mixture of water and THF (0.2 M solution), [b]Rearrangement performed in 0.2M solution of substrate, [c] added in the presence of an equivalent amount of TEA (1.1 equiv.)

S.1.4.1 *tert*-Butyl 2-(3-((*S*)-1-(tert-butoxycarbonyl)pyrrolidin-2-yl)ureido)pyrrolidine-1-carboxylate (**11**)



(**11**)

White Solid. Isolated as the major compound throughout the attempts of isocyanate hydrolysis.

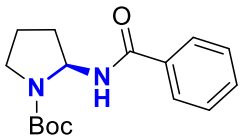
^{1}H NMR (500 MHz, $CDCl_3$) δ 5.52-5.34 (m, 2H), 3.58-3.43 (m, 2H), 3.35-3.20 (m, 2H), 2.03-1.77 (m, 8H), 1.49-1.40 (m, 18H).

LC-MS: *m/z* calculated for $C_{19}H_{35}N_4O_5$ $[M+H]^+$ 399.2607, found 399.3.

S.1.5. General procedure for the trapping of isocyanate (3) by organometallic reagents

The round-bottom flask charged with the corresponding isocyanate (prepared as described in IV.2.10) was cooled at 25 °C under a N_2 atmosphere. The organometallic reagent (1.2 equiv.) was added dropwise over 5 min. After complete consumption of the isocyanate (monitored by IR (FTIR)), the mixture was quenched with MeOH (at 25 °C) and stirred for 5 minutes. The reactional mixture was then concentrated under vacuum and purified by flash chromatography (silica gel, hexane:EtOAc, 70:30 → 10:90).

S.1.5.1. *tert*-Butyl (S)-2-benzamidopyrrolidine-1-carboxylate (**10a**)



(**10a**)

White solid (263 mg, 87%). Prepared from 250 mg of **2**.

^{1}H NMR (400 MHz, CD_3OD) δ 7.84 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 5.98-5.79 (m, 1H, H-2), 3.63-3.55 (m, 1H), 3.40-3.35 (m, 1H), 2.32-2.20 (m, 1H), 2.16-2.03 (m, 1H), 2.02-1.91 (m, 2H), 1.52-1.38 (m, 9H).

^{13}C NMR (125 MHz, CD_3OD) δ 169.19, 155.88, 135.69, 132.71, 129.51, 128.44 (3C), 81.39, 65.62, 47.10, 34.84, 28.70, 23.26.

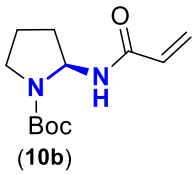
IR (ATR) ν_{max} (cm^{-1}): 3304, 3060, 2979, 1699, 1637, 1533, 1486, 1390, 1362, 1161.

ESI-HRMS: *m/z* calculated for $C_{16}H_{23}N_2O_3$ $[M+H]^+$ 291.1709, found 291.1699.

$[\alpha]_D^{26}$-10 (*c* 0.39, MeOH).

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 233 nm) t_R = 10.82 min (major), t_R = 11.83 min (minor), 30% *ee*.

S.1.5.2. *tert*-Butyl (*S*)-2-acrylamidopyrrolidine-1-carboxylate (10b)



(**10b**)

White solid (165 mg, 66%). Prepared from 250 mg of **2**.

^{1}H NMR (400 MHz, CD_3OD) δ 6.29-6.16 (m, 2H), 5.75-5.62 (m, 2H), 3.54-3.46 (m, 1H), 3.31-3.23 (m, 1H), 2.15-2.07 (m, 1H), 2.06-1.89 (m, 2H), 1.89-1.78 (m, 1H), 1.51-1.34 (m, 9H).

^{13}C NMR (101 MHz, CD_3OD) δ 166.60, 155.78, 131.98, 127.02, 81.43, 64.89, 46.90, 34.75, 28.68, 23.16.

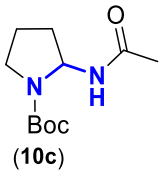
IR (ATR) ν_{max} (cm^{-1}): 3277, 3056, 2979, 1703, 1660, 1625, 1536, 1390, 1390, 1366, 1161.

ESI-HRMS: *m/z* calculated for $C_{12}H_{21}N_2O$ for $[M+H]^+$ 241.1552, found 241.1543.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 222 nm) t_R = 7.77 min (major), t_R = 8.58 min (minor), 64% *ee.*

$[\alpha]_D^{23}$+35.9 (*c* 1.17, MeOH).

S1.5.3. *tert*-Butyl 2-acetamidopyrrolidine-1-carboxylate (10c)



(**10c**)

White solid (99.8 mg, 42%). Prepared from 250 mg of **2**.

^{1}H NMR (400 MHz, CD_3OD) δ 5.72-5.55 (m, 1H), 3.53-3.45 (m, 1H), 3.32-3.22 (m, 1H), 2.16-2.04 (m, 1H), 2.04-1.95 (m, 2H), 1.94 (s, 3H), 1.86-1.77 (m, 1H), 1.47 (s, 9H).

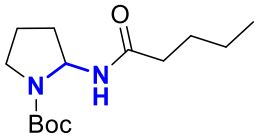
^{13}C NMR (101 MHz, CD_3OD) δ 171.71, 155.77, 81.33, 64.78, 46.82, 34.67, 28.72, 23.07, 22.52.

IR (ATR) ν_{max} (cm^{-1}): 3445, 3278, 3066, 2976, 2936, 1684, 1651, 1545, 1476, 1447, 1390, 1370, 1248, 1162, 1129, 1105.

ESI-HRMS: *m/z* calculated for $C_{11}H_{20}N_2O_3Na$ for $[M+Na]^+$ 251.1372, found 251.1362.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 220 nm) t_R = 15.65 min, t_R = 17.20 min, racemic.

S.1.5.4. tert-Butyl 2-pentanamidopyrrolidine-1-carboxylate (10d)



(**10d**)

White solid (50,6 mg, 18%). Prepared from 250 mg of **2**.

^{1}H NMR (500 MHz, CD_3OD) δ 5.67-5.56 (m, 1H), 3.52-3.45 (m, 1H), 3.29-3.22 (m, 1H), 2.22-2.13 (m, 2H), 2.11-2.01 (m, 1H), 2.01-1.95 (m, 1H), 1.95-1.86 (m, 2H), 1.60 (quint., *J* = 7.3 Hz, 2H), 1.45 (s, 9H), 1.38 (sext., *J*=7.3 Hz, 2H), 0.95 (t, *J*=7.3 Hz, 3H).

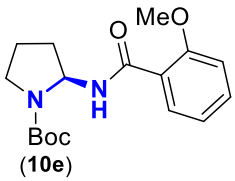
^{13}C NMR (125 MHz, CD_3OD) δ 174.76, 155.78, 81.41, 64.82, 46.86, 36.78, 34.80, 29.26, 28.72, 23.37, 23.03, 14.14.

IR (ATR) ν_{max} (cm^{-1}): 3412, 2963, 2932, 2874, 1703, 1633, 1444, 1386, 1366, 1250, 1165, 1111.

ESI-HRMS: *m/z* calculated for $C_{14}H_{27}N_2O_3$ $[M+H]^+$ 271.2022, found 271.2012.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 213 nm) t_R = 8.34 min, t_R = 8.81 min, racemic.

S.1.5.5. *tert*-Butyl (S)-2-(2-methoxybenzamido)pyrrolidine-1-carboxylate (10e)



(**10e**)

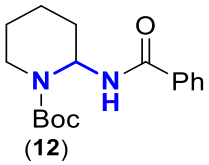
Light brownish solid (28.8 mg, 72%). Preparem from 30 mg of **2**.

^{1}H NMR (400 MHz, MeOD) δ 7.81 (d, *J* = 7.6 Hz, 1H), 7.55 – 7.46 (m, 1H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.11 – 7.03 (m, 1H), 5.85 (s, 1H), 3.95 (s, 3H), 3.61 – 3.51 (m, 1H), 3.40 – 3.34 (m, 1H), 2.27 – 2.12 (m, 1H), 2.09 – 1.93 (m, 3H), 1.50 – 1.40 (m, 9H).

^{13}C NMR (101 MHz, MeOD) δ 167.34, 158.88, 155.90, 133.96, 131.64, 123.75, 121.89, 112.91, 81.49, 65.45, 56.52, 47.00, 34.75, 28.68.

ESI-HRMS: *m/z* calculated for $C_{17}H_{24}N_2O_4Na$ $[M+Na]^+$ 346.1628, found 346.1620.

S.1.5.6 *tert*-Butyl 2-benzamidopiperidine-1-carboxylate (12)



(**12**)

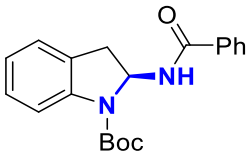
Clear crystalline solid (171 mg,54%). Prepared from 250 mg of **12a**.

^{1}H NMR 7.80 (d, 1H), 7.60 – 7.53 (m, 1H), 7.52 – 7.43 (m, 1H), 6.22 (d, *J* = 3.6 Hz, 0H), 4.00 – 3.91 (dd, *J* = 14.0, 3.5 Hz, 1H), 3.13 (td, *J* = 13.2, 2.9 Hz, 1H), 2.04 – 1.91 (m, 1H), 1.86 – 1.67 (m, 4H), 1.61 – 1.40 (m, 10H).

^{13}C NMR (101 MHz, MeOD) δ 170.22, 156.45, 136.01, 132.61, 129.46, 128.59, 81.57, 59.91, 40.66, 30.56, 28.63, 25.92, 19.47.

ESI-HRMS: *m/z* calculated for $C_{17}H_{24}N_2O_3Na$ $[M+Na]^+$ 327.1679, found 327.1672.

S.1.5.7. *tert*-Butyl (*S*)-2-benzamidoindoline-1-carboxylate (13)



(**13**)

White solid (241 mg, 82%). Prepared from 250 mg of **13a**.

^{1}H NMR ^{1}H NMR (500 MHz, MeOD) δ 7.87 – 7.69 (m, 3H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.25 – 7.17 (m, 2H), 7.00 (t, *J* = 7.4 Hz, 1H), 6.46 (dd, *J* = 9.2, 2.5 Hz, 1H), 3.64 (dd, *J* = 17.0, 9.2 Hz, 1H), 3.00 (dd, *J* = 17.1, 2.5 Hz, 1H), 1.50 (s, 9H).

^{13}C NMR (125 MHz, CD_3OD) δ 169.12, 153.46, 143.04, 135.41, 132.82, 130.03, 129.52, 128.55, 128.39, 125.82, 123.91, 115.80, 82.60, 66.75, 37.56, 28.66.

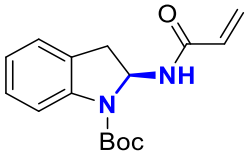
IR (ATR) ν_{max} (cm^{-1}): 3304, 3056, 2975, 2928, 1703, 1633, 1482, 1420, 1386, 1285, 1165, 1146

ESI-HRMS: *m/z* calculated for $C_{20}H_{23}N_2O_3$ $[M+H]^+$ 338.1630, found 339.1700

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 220 nm) t_R = 8.92 min, 100% *ee*.

$[\alpha]_D^{26}$+10 (*c* 0.40, MeOH).

S.1.5.8. *te*rt-Butyl (S)-2-acrylamidoindoline -1-carboxylate (16)



(**16**)

White solid (613 mg, 73%). Prepared from 840 mg of **13a**.

IR (ATR)ν_{max} (cm^{-1}): 3280, 2979, 2932, 1710, 1656, 1482, 1420, 1444, 1390, 1366, 1285, 1165.

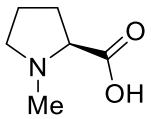
^{1}H NMR (500 MHz, CD_3OD) δ 7.83-7.69 (m, 1H), 7.23-7.18 (m, 2H), 7.03-6.98 (m, 1H), 6.33-6.25 (m, 2H, H-2), 6.24-6.16 (m, 1H), 5.72-5.6 (dd, *J*=1.9 Hz and *J*=10.1 Hz, 1H), 3.59-3.52 (m, 1H), 2.92-2.86 (m, 1H), 1.52 (s, 9H)

^{13}C NMR (125 MHz, CD_3OD) δ 166.62, 153.33, 142.77, 131.85, 129.90, 128.46, 127.43, 125.93, 123.99, 115.82, 82.67, 66.19, 37.55, 28.63

ESI-HRMS: calculated 288.1474, found [M+Na]+ 311.1362

S.1.6. Synthesis of *N*-protected L-proline Derivatives

S.1.6.1. *N*-methyl-L-Proline (14a)



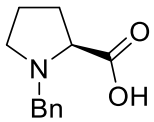
(**14a**)

White solid (501 mg, 91%) prepared from 490 mg of L-proline by following a previously described procedure.[11]

Spectral data is consistent with previous reports.[11]

^{1}H NMR (400 MHz, D2O) δ 3.89 (t, *J* = 6.9 Hz, 1H), 3.79 – 3.68 (m, 1H), 3.22 – 3.10 (m, 1H), 2.93 (s, 3H), 2.58 – 2.43 (m, 1H), 2.25 – 1.91 (m, 3H).

S.1.6.2. *N*-benzyl-L-proline (**14b**)



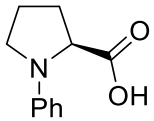
(**14b**)

White solid (880 mg, 88%) prepared from 560 mg of L-proline by following a previously described procedure.[12]

Spectral data is consistent with previous reports.[12]

^{1}H NMR (400 MHz, D_2O) δ 7.50 (s, 5H), 4.51 – 4.30 (m, 2H), 3.99 (t, *J* = 8.2 Hz, 1H), 3.72 – 3.55 (m, 1H), 3.39 – 3.23 (m, 1H), 2.62 – 2.40 (m, 1H), 2.26 – 1.85 (m, 3H).

S.1.6.3. N-Phenyl-L-proline (14c)



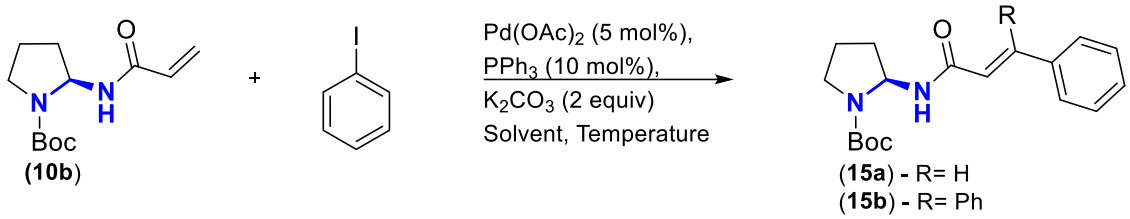
(**14c**)

White solid (740 mg, 76%) prepared from 500 mg of L-proline by adapting a previously described literature procedure.[13] Spectral data is consistent with previous reports.[13]

^{1}H NMR (400 MHz, CDCl3) δ 7.29 – 7.21 (m, 2H), 6.78 (t, *J* = 7.4 Hz, 1H), 6.62 (d, *J* = 8.0 Hz, 2H), 4.20 (dd, *J* = 8.9, 2.9 Hz, 1H), 3.67 – 3.58 (m, 1H), 3.37 – 3.27 (m, 1H), 2.36 – 2.24 (m, 2H), 2.15 – 1.99 (m, 2H).

S.1.7. General procedure for the Heck reaction of 10b with haloarenes

***Table S2**. Solvent and temperature effect on the Palladium-Catalyzed Heck Coupling of **10b** and iodobenzene.*

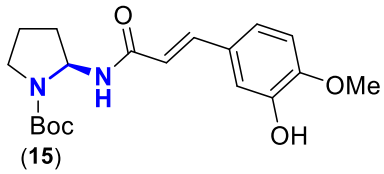


Entry	Solvent	T (°C)	time (h)	Yield (15a) (%)
1	MeCN	rfx	48	25[a,c]
2	MeCN	80 °C sealed tube	48	50[a,b]
3	Dioxane	rfx	18	60[c]
4	Dioxane	110 °C sealed tube	5	84[c]

[a]Incomplete reaction. [b]Formation of 15b. [c]Complete conversion

To a 15 mL sealed tube charged with triphenyl phosphine (10 mol %) and palladium diacetate (5 mol %) a dry solvent (volume to make a 0.2 M solution of substrate) was added. The mixture was stirred under inert atmosphere for 10 min at rt. Then, potassium carbonate (2 equiv.), **10b** (1.0 equiv.) and the corresponding haloarene (1.05 equiv.) were added and the mixture was stirred at 110 °C. After complete consumption of the starting material, the mixture was diluted with ethyl acetate and filtered under a celite pad. The filtrate was concentrated under vacuum and the resulting residue purified by flash chromatography (silica gel, hexane:EtOAc, 80:20 → 60:40).

S.1.7.1. *tert*-Butyl (*S,E*)-2-(3-(3-hydroxy-4-methoxyphenyl) acrylamido) pyrrolidine-1-carboxylate (15)



(**15**)

Starting from **10b** (300 mg, 1.25 mmol) and 3-hydroxy-4-methoxy bromobenzene (266 mg, 1.3 mmol) **15** was obtained as a white solid (280 mg, 62% yield).

^{1}H NMR (400 MHz, CD_3OD) δ 7.46 (d, *J* = 15.7 Hz, 1H), 7.09-7.06 (m, 1H), 7.06-7.00 (m, 1H), 6.98-6.93 (m, 1H), 6.41 (d, *J* = 15.7 Hz, 1H), 5.79-5.72 (m, 1H), 3.91 (s, 3H), 3.57-3.51 (m, 1H), 3.33-3.26 (m, 1H), 2.18-2.10 (m, 1H), 2.10-2.01 (m, 1H), 1.98-1.86 (m, 2H), 1.45 (s, 9H).

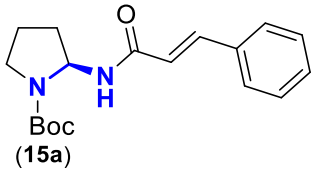
^{13}C NMR (125 MHz, CD_3OD) δ 167.57, 155.86, 150.91, 147.96, 142.27, 129.45, 122.17, 119.18, 114.46, 112.52, 81.47, 65.00, 56.37, 46.89, 34.88, 28.71, 23.18.

IR (ATR) ν_{max} (cm^{-1}): 3288, 2979, 2932, 2882, 1699, 1656, 1606, 1540, 1432, 1390, 1362, 1165, 1111, 983.

ESI-HRMS: *m/z* calculated for $C_{19}H_{27}N_2O_5$ $[M+H]^+$ 363.1920, found 363.1909.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 239 nm) t_R = 9.03 min (major), t_R = 9.92 min (minor), 82% *ee*

S.1.7.2. *tert*-Butyl (*S*)-2-cinnamamamidopyrrolidine-1-carboxylate (15a)



(**15a**)

Starting from **10b** (300 mg, 1.25 mmol) and iodobenzene (0.15 mL, 1.3 mmol), **15a** was obtained as a White solid (331.8 mg, 84%).

^{1}H NMR (500 MHz, CD_3CN) δ 7.52-7.48 (m, 2H), 7.44 (d, *J* = 15.8 Hz, 1H), 7.37-7.31 (m, 3H), 6.43 (d, *J* = 15.8 Hz, 1H), 5.63-5.58 (m, 1H), 3.40-3.35 (m, 1H), 3.20-3.13 (m, 1H), 2.04-1.94 (m, 1H), 1.86-1.80 (m, 2H), 1.80-1.73 (m, 1H), 1.38-1.28 (m, 9H).

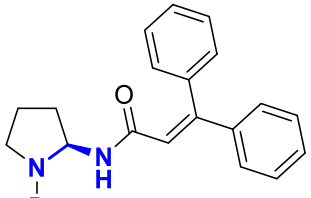
^{13}C NMR (125 MHz, CD_3OD) δ 167.14, 161.45, 155.87, 142.14, 136.24, 130.88, 129.96, 128.81, 121.69, 81.51, 65.04, 46.92, 34.83, 28.71, 23.18.

IR (ATR) ν_{max} (cm^{-1}): 3277, 3060, 2979, 2928, 2878, 1699, 1656, 1622, 1536, 1386, 1362, 1161, 1107.

ESI-HRMS: *m/z* calculated for $C_{18}H_{25}N_2O_3$ $[M+H]^+$ 317.1865, found 317.1857.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 275 nm) t_R = 18.79 min, t_R = 19.88 min, 44% *ee*.

S.1.7.3. *tert*-Butyl (*S*)-2-(3,3-diphenylacrylamido)pyrrolidine-1-carboxylate (15b)



(**15b**)

A crude mixture of **10a** (300 mg, 1.25 mmol), previously filtered under a celite pad, was resubjected to the general procedure for the Heck reaction using iodobenzene (0.15 mL, 1.3 mmol) to afford **15b** as a white solid (216 mg, 58%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.40-7.36 (m, 3H), 7.36-7.30 (m, 3H), 7.29-7.21 (m, 4H), 6.40 (s, 1H), 5.61-5.51 (m, 1H, H-2), 3.33-3.31 (m, 1H), 3.20-3.12 (m, 1H), 1.97-1.82 (m, 1H), 1.82-1.69 (m, 1H), 1.70-1.50 (m, 2H), 1.46 (s, 9H).

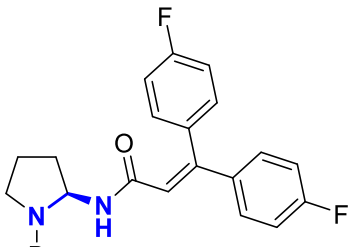
^{13}C NMR (101 MHz, CD_3OD) δ 167.69, 155.71, 142.48, 140.35, 130.73, 129.93, 129.44, 129.21, 129.14, 129.07, 122.12, 81.48, 64.81, 46.64, 34.25, 28.76, 22.91.

IR (ATR) ν_{max} cm^{-1}): 3312, 3288, 3060, 2975, 2932, 2882, 1695, 1645, 1525, 1386, 1366, 1161, 1115.

ESI-HRMS: *m/z* calculated for $C_{24}H_{29}N_2O_3$ $[M+H]^+$ 393.2178, found 393.2166.

$[\alpha]_D^{26}$+6 (*c* 1.0, MeOH).

S.1.7.4. *tert*-Butyl (*S*)-2-(3,3-bis(4-fluorophenyl)acrylamido)pyrrolidine-1-carboxylate (15c)



(**15c**)

A crude mixture, previously filtered under a celite pad, of **15e** (50 mg, 0.15 mmol), was resubjected to the general procedure for the Heck reaction using 1-fluor-4-bromobenzene (17.24 µL, 0.16 mmol) to afford **15c** as a white solid (45.5 mg, 71%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.34-7.29 (m, 2H), 7.29-7.21 (m, 2H), 7.17-7.06 (m, 4H), 6.38 (s, 1H), 5.62-5.53 (m, 1H), 3.44-3.38 (m, 1H), 3.25-3.18 (m, 1H), 1.87-1.79 (m, 1H), 1.79-1.55 (m, 3H), 1.47 (s, 9H).

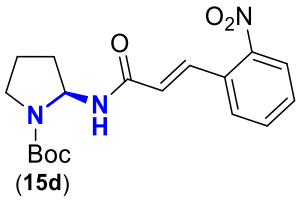
^{13}C NMR (101 MHz, CD_3OD) δ 167.30, 164.13 (d, *J*=246.3 Hz, 1C), 155.75, 138.79, 136.32, 132.76, 131.14 (d, *J*=8.5 Hz, 4C), 122.25, 116.32 (d, *J*=21.8 Hz, 2C), 115.92 (d, *J*=21.9 Hz, 2C), 81.52, 64.86, 46.74, 34.39, 28.74, 24.23.

IR (ATR) ν_{max} (cm^{-1}): 34067, 2981, 2924, 2875, 1686, 1637, 1597, 1508, 1382, 1366, 1341, 1224, 1191, 1163, 1106, 1057.

ESI-HRMS: *m/z* calculated for $C_{24}H_{27}F_2N_2O_3$ $[M+H]^+$ 429.1990, found 429.1978.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 266 nm) t_R = 22.27 min (major), t_R = 23.95 min (minor), 46% *ee*.

S.1.7.5. *tert*-Butyl (*S,E*)-2-(3-(2-nitrophenyl)acrylamido)pyrrolidine-2-carboxylate (15d)



(**15d**)

Starting from **10b** (300 mg, 1.25 mmol) and 1-Bromo-4-nitrobenzene iodobenzene (265 mg, 1.3 mmol), **15d** was obtained as a yellow solid (457 mg, 76%).

^{1}H NMR (400 MHz, CD_3OD) δ 8.02 (d, *J* = 7.7 Hz, 1H), 7.92 (d, *J* = 15.6 Hz, 1H), 7.78-7.68 (m, 2H), 7.60 (t, *J* = 7.7 Hz, 1H), 6.54 (d, *J* = 15.6 Hz, 1H), 5.84-5.70 (m, 1H), 3.57-3.49 (m, 1H), 3.37-3.27 (m, 1H), 2.24-2.10 (m, 1H), 2.10-2.00 (m, 1H), 2.00-1.86 (m, 2H), 1.45 (s, 9H).

^{13}C NMR (101 MHz, CD_3OD) δ 165.85, 155.71, 149.97, 137.20, 134.53, 131.66, 131.24, 129.91, 126.64, 125.65, 81.51, 64.93, 46.88, 34.73, 28.73, 23.18.

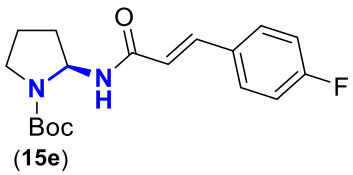
IR (ATR) ν_{max} (cm^{-1}): 3435, 2932, 2878, 1695, 1652, 1618, 1521, 1432, 1359, 1339, 1161, 1107.

ESI-HRMS: *m/z* calculated for $C_{18}H_{24}N_3O_5$ $[M+H]^+$ 362.1716, found 362.1703.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 246 nm) t_R = 13.11 min, enantiomers co-eluted (single peak).

$[\alpha]_D^{26}$ 0.0 (*c* 0.43, MeOH) – confirmed as a racemate

S.1.7.6. *tert*-Butyl (*S,E*)-2-(3-(4-fluorophenyl)acrylamido)pyrrolidine-1-carboxylate (**15e**)



(**15e**)

Starting from **10b** (300 mg, 1.25 mmol) and 1-Bromo-4-fluorobenzene (144 µL, 1.3 mmol), **15e** was obtained as white solid (457 mg, 71%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.64-7.57 (m, 2H), 7.53 (d, *J* = 15.7 Hz, 1H), 7.19-7.10 (m, 2H), 6.52 (d, *J* = 15.7 Hz, 1H), 5.79-5.67 (m, 1H), 3.57-3.48 (m, 1H), 3.31-3.24 (m, 1H), 2.16-2.08 (m, 1H), 2.07-1.93 (m, 2H), 1.92-1.82 (m, 1H), 1.42 (m, 9H).

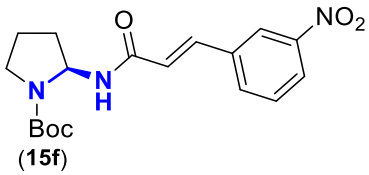
^{13}C NMR (101 MHz, CD_3OD) δ 166.27, 165.03 (d, *J* = 248.9 Hz, 1C), 155.83, 140.80, 132.71, 132.71, 130.88 (d, *J* = 8.5 Hz, 2C), 121.62, 116.84 (d, *J* = 21.9 Hz, 2C), 81.48, 65.05, 46.92, 34.85, 28.71 (3C), 23.20.

IR (ATR) ν_{max} (cm^{-1}): 3447, 3288, 2979, 2932, 2882, 1699, 1652, 1602, 1517, 1440, 1386, 1362, 1231, 1161, 1107.

ESI-HRMS: *m/z* calculated for $C_{18}H_{24}FN_2O_3$ $[M+H]^+$ 335.1771, found 335.1762.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 272 nm) t_R = 9.55 min (minor), t_R = 11.03 min (major), 20% *ee*.

S.1.7.7. *tert*-Butyl (S,E)-2-(3-(3-nitrophenyl)acrylamido)pyrolidine-1-carboxylate (**15f**)



(**15f**)

Starting from **10b** (300 mg, 1.25 mmol) and 1-Bromo-3-nitrobenzene (264.8mg, 1.3 mmol), **15f** was obtained as yellow solid (311.3 mg, 69%).

^{1}H NMR (400 MHz, CD_3OD) δ 8.43 (s, 1H), 8.27 (d, *J* = 8.5 Hz, 1H), 7.80 (d, *J* = 8.5 Hz, 1H), 7.74-7.54 (m, 2H), 6.74 (d, *J* = 15.6 Hz, 1H), 5.81-5.71 (m, 1H, H-2), 3.58-3.49 (m, 1H), 3.37-3.32 (m, 1H), 2.25-2.10 (m, 1H), 2.10-2.01 (m, 1H), 2.00-1.86 (m, 2H), 1.52-1.38 (m, 9H).

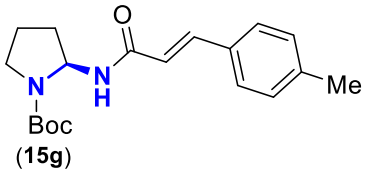
^{13}C NMR (101 MHz, CD_3OD) δ 166.00, 155.79, 150.16, 149.61, 134.65, 131.29, 129.68, 125.07, 123.00, 81.51, 65.10, 46.94, 34.80, 28.70, 23.20.

IR (ATR) ν_{max} (cm^{-1}): 3292, 2979, 2932, 2886, 1699, 1660, 1618, 1525, 1440, 1390, 1347, 1161, 1111.

ESI-HRMS: *m/z* calculated $C_{18}H_{23}N_3O_5$ $[M+H]^+$ 362.1716, found 362.1708.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 311 nm) t_R = 19.51 min (minor), t_R = 20.32 min (major), 64% *ee*.

S.1.7.8. *tert*-Butyl (S,E)-2-(3-(*p*-tolyl)acrylamido)pyrrolidine-1-carboxylate (**15g**)



(**15g**)

Starting from **10b** (300 mg, 1.25 mmol) and 4-iodotoluene (286 mg, 1.3 mmol), **15g** was obtained as White solid (321.8 mg ,78%).

^{1}H NMR (400 MHz, CD_3OD) δ 7.52 (d, *J* = 15.8 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 2H), 7.21 (d, *J* = 7.7 Hz, 2H), 6.52 (d, *J* = 15.7 Hz, 1H), 5.80 – 5.67 (m, 1H), 3.57 – 3.47 (m, 1H), 3.31 – 3.21 (m, 1H), 2.36 (s, 3H), 2.23 – 1.81 (m, 4H), 1.52 – 1.34 (m, 9H)..

^{13}C NMR (101 MHz, CD_3OD) δ 165.91, 154.44, 140.74, 139.99, 132.10, 129.21, 127.44, 119.20, 80.08, 63.61, 45.51, 33.47, 27.31, 21.79, 19.99.

IR (ATR) ν_{max} (cm^{-1}): 3509, 3280, 2975, 2932, 2882, 2840, 1680, 1652, 1606, 1513, 1440, 1393, 1266, 1161, 1127.

ESI-HRMS: *m/z* calculated for $C_{19}H_{27}N_2O_3$ $[M+H]^+$ 331.2022, found 331.2013.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 277 nm) t_R = 18.80 min (minor), t_R = 19.85 min (major), 58% *ee*.

S.1.8. General procedure for the Boc removal under Brønsted and Lewis acid conditions.

Method A

In a rounded bottom flask, the Boc protected starting material was dissolved in dichloromethane (volume to make a 0.2 M solution of substrate). The mixture was placed at 0 °C and under nitrogen atmosphere TFA was added dropwise, and the mixture was left to react at 0 °C. The evolution of the reaction was monitored by TLC and after total consumption of starting material, the mixture was concentrated under vacuum.

Method B

In a rounded bottom flask, the Boc protected starting material was dissolved in ethyl acetate (volume to make a 0.2 M solution of substrate). The mixture was placed at 0 °C and under nitrogen atmosphere. Acetyl chloride and the methanol were added dropwise, and the mixture was left to react at room temperature. The evolution of the reaction was monitored by TLC and after total consumption of starting material, the mixture was concentrated under vacuum.

Method C

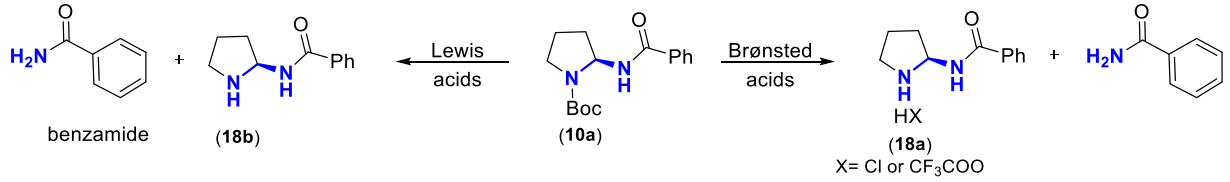
In a rounded bottom flask, the Boc protected starting material was dissolved in dichloromethane (volume to make a 0.2 M solution of substrate). The mixture was placed at 0 °C and under nitrogen atmosphere. A solution of HCl (4M in dioxane) was added dropwise, and the mixture was left to react at 0 °C. The evolution of the reaction was monitored by TLC and after total consumption of starting material, the mixture was concentrated under vacuum.

Method D

In a rounded bottom flask, the respective Boc-protected substrate was dissolved in dichloromethane (volume to make a 0.2 M solution of substrate). The mixture was cooled down to -78 °C under an inert atmosphere of N_2, and a solution of $AlMe_3$ (2 M in heptane - 4.5 equiv.) was added dropwise, after which the mixture was stirred at room temperature. After total consumption of starting material, the mixture was cooled to 0 °C and quenched with saturated aqueous solution of potassium sodium tartrate (a white solid precipitates). The mixture was stirred for 5 minutes at 0 °C and the two phases separated. The

aqueous phase was extracted with dichloromethane several times. The combined organic layers were washed with water, dried under Na_2SO_4, filtered, and concentrated under vacuum.

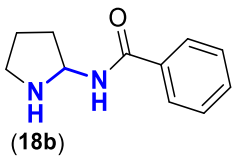
Table S3. Screening of the reactional conditions for the Boc removal of **10a**.



Entry	Acid (equiv)	Temperature (°C)	Solvent	Time (h)	Observations[a]
1	TFA (10)	0	DCM	1	Complete degradation. Only benzamide
2[b]	TFA (10)	0	DCM	6	Mix. of benzamide (35%) and **18a**
3[c]	HCl (8)	0 to rt	DCM	72	Mix. of benzamide (62%) and **18a**
4[d]	HCl (20)	0 to rt	DCM	1	Mix. of benzamide (40%) and **18a**
5[d]	HCl (20)	0	DCM	3	Mix. of benzamide (38%) and **18a**
6	I_2 (0.08)	rt	DCM	6	Unreacted starting material
7	$FeCl_3$ (2)	rt	MeCN	3	Only benzamide was observed
8	TMSOTf	0	MeCN	5	Only benzamide was observed
9	$Sn(OTf)_2$ (1.1)	0 to rt	DCM	1	Only benzamide was observed
10	$AlMe_3$ (4.5)	-78 to rt	DCM	4	Mix. of benzamide (11%) and **18b**

[a]Determined by ^{1}H NMR. [b]2equiv. were added every hour. [c] HCl generated in situ by the addition of acetyl chloride and MeOH. [d] 4N solution in dioxane.

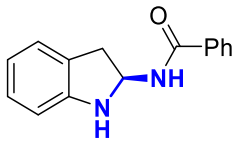
S.1.8.1. (*R*)-*N*-(pyrrolidin-2-yl)benzamide (18b)


(**18b**)

Following the general procedure D, from **10a** (100 mg, 0.34 mmol), **18b** was obtained as a white solid (62.24 mg, 95%).

^{1}H NMR (500 MHz, MeOD) δ 7.84 (d, *J* = 1.4 Hz, 2H), 7.54 (t, *J* = 1.4 Hz, 1H), 7.49 – 7.44 (m, 2H), 5.29 (dd, *J* = 7.1, 4.5 Hz, 1H), 3.09 – 2.90 (m, 2H), 2.23 – 2.11 (m, 1H), 2.05 – 1.93 (m, 1H), 1.92 – 1.72 (m, 1H).

S.1.8.2. (*R*)-*N*-(Indolin-2-yl)benzamide (19)



(**19**)

Following the general procedure D, from **13** (100 mg, 0.29 mmol), **19** was obtained as white solid (64 mg, 91%).

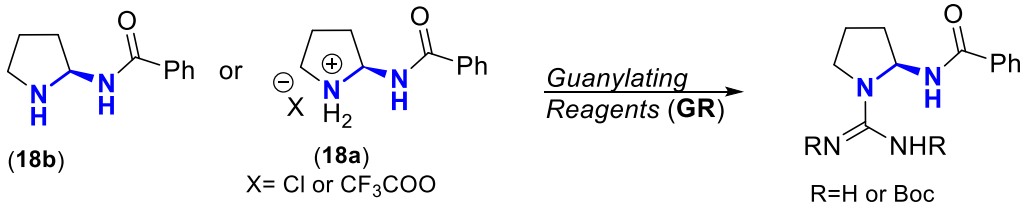
^{1}H NMR (400 MHz, MeOD) δ 7.84 (d, 2H), 7.58 – 7.50 (m, 1H), 7.49 – 7.40 (m, 2H), 7.11 (d, *J* = 7.3 Hz, 1H), 6.99 (t, *J* = 7.7 Hz, 1H), 6.73 – 6.62 (m, 2H), 5.85 (dd, *J* = 8.4, 4.7 Hz, 1H), 3.44 – 3.32 (m, 1H), 3.07 (dd, *J* = 16.3, 4.8 Hz, 1H).

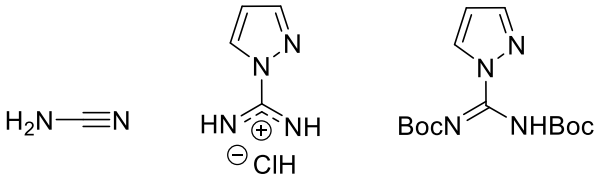
^{13}C NMR (101 MHz, MeOD) δ 170.52, 150.73, 135.45, 132.79, 129.48, 128.52 (d, *J* = 1.3 Hz), 127.94, 125.50, 119.83, 110.37, 67.33, 37.03.

S.1.9. General procedure for the Boc-removal and guanylation reaction

In a rounded bottom flask, the respective Boc-protected substrate was dissolved in dichloromethane (volume to make a 0.2 M solution of substrate). The mixture was placed under inert atmosphere and cooled down to -78 °C, and a solution of $AlMe_3$ (2 M in heptane) (4.5 equiv.) was added dropwise, after which the mixture was stirred at room temperature. After total consumption of starting material, the mixture was cooled to 0 °C and quenched with sat. aq. potassium sodium tartrate (a white solid precipitates). The mixture was stirred for 5 minutes at 0 °C and the two phases separated. The aqueous phase was extracted with dichloromethane several times. The combined organic layers were washed with water, dried under Na_2SO_4, filtered, and concentrated under vacuum. The formed residue was dissolved in the solvent indicated in table below (volume to make a 0.2 M solution of substrate) and placed under inert atmosphere. The guanylating reagent in the reaction solvent (volume to make 0.2 M solution) was added to the previous solution and left to react for 18-20h. The obtained mixture was concentrated under vacuum and the attained residue was purified by RP-18 with water/methanol starting with 100% of water and decreasing the polarity by 10% until 100% methanol.

***Table S44**. Optimization of reaction conditions for the guanylation reaction of **18a-b**.*



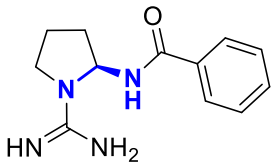


(**GR1**) (**GR2**) (**GR3**)

Entry	Starting material	GR (equiv.)	Base (equiv.)	Conditions	Yield	Obs
1	18a	GR1 (2)	-	MeCN/H_2O, rt, 16h	-	Unreacted SM
2	18a	GR1 (10)	-	MeCN/H_2O, rt, 16h	-	Unreacted SM
3	18a	GR1 (10)	-	MeCN/H_2O, 50 °C, 16h	-	Benzamide
4	18a	GR1 (2)	-	DMA, rt, 16h	-	Unreacted SM
5	18a	GR1 (2)	-	MeOH, rt, 16h	-	Unreacted SM
6	18a	GR1 (2)	-	DMF, rt, 16h	-	No reaction
7	18a	GR1 (2)	$NaHCO_3$ (1.1)	MeCN/H_2O, rt, 16h		Benzamide
8	18a	GR1 (2)	DABCO (1.1)	MeCN/H_2O, rt, 16h	-	Benzamide
9	18a	GR1 (2)	DIPEA (1.1)	MeCN/H_2O, rt, 16h		Benzamide
10	18a	GR1 (3)	-	MeCN/H_2O, rt, 16h		Benzamide
11	18b	GR1 (2)	-	MeCN, rt, 16h	-	Unreacted SM
12	18b	GR3 (1.1)	-	MeCN, rt, 18h	57%	-
13[a]	18b	GR2 (1.1)	DIPEA (1.1)	MeCN, rt, 18h	46%	-

[a]Prior to the addition of **II.32b**, DIPEA was pre-mixed with GR2 until a homogeneous solution was obtained. SM – starting material.

S.1.9.1. (*S*)-*N*-(1-carbamimidoylpyrrolidin-2-yl)benzamide (20a)



(**20a**)

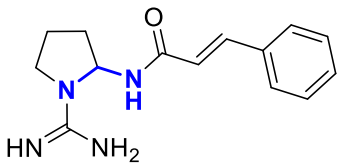
Following the general procedure, from 150 mg (0.52 mmol) tert-Butyl (S)-2-benzamidopyrrolidine-1-carboxylate (**10a**), the mixture was left to react with $AlMe_3$ for 3 hours. After guanylation and purification compound **20a** was obtained as a white solid in 46%. Spectroscopic data is in agreement with the literature.[14]

^{1}H NMR (400 MHz, CD3OD) δ 7.88 (d, J = 7.6 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.49 (t, J = 7.6 Hz, 2H), 5.98-5.93 (m, 1H), 3.66-3.60 (m, 1H), 3.51-3.43 (m, 1H), 2.45-2.34 (m, 2H), 2.20-2.10 (m, 1H).

^{13}C NMR (101 MHz, CD3OD) δ 171.57, 156.83, 134.22, 133.57, 129.65, 128.87, 66.03, 48.50, 33.41, 23.71.

IR (ATR) ν_{max} (cm^{-1}): 3327, 3219, 2990, 2886, 1645, 1606, 1533, 1490, 1359, 1188.

S.1.9.2. (*S*)-*N*-(1-carbamimidoylpyrrolidin-2-yl)cinnamamide (20c)



(**20c**)

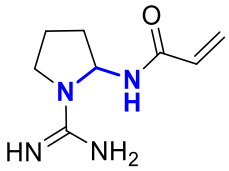
Following the general procedure, from 200 mg (0.63 mmol) of *tert*-Butyl (*S*)-2-cinnamamidopyrrolidine-1-carboxylate (**15a**), the mixture was left to react with $AlMe_3$ for 4 hours. After guanylation and purification compound **20c** was obtained as a white solid in 41% yield. Spectroscopic data is in agreement with the literature.[14]

^{1}H NMR (500 MHz, CD_3OD) δ 7.69 (d, *J* = 15.8 Hz, 1H), 7.63-7.57 (m, 2H), 7.46-7.39 (m, 3H), 6.69 (d, *J* = 15.8 Hz, 1H), 5.86-5.81 (m, 1H), 3.66-3.57 (m, 1H), 3.50-3.42 (m, 1H), 2.41-2.30 (m, 2H), 2.24-2.15 (m, 1H), 2.11-2.03 (m, 1H);

^{13}C NMR (125 MHz, CD_3OD) δ 160.56, 156.78, 144.29, 135.84, 133.41, 130.06, 129.10, 120.23, 65.41, 48.24, 33.37, 23.80.

IR (ATR) ν_{max} (cm^{-1}): 3327, 3207, 3029, 2890, 2754, 1660, 1618, 1544, 1409, 1362, 1219, 1115.

S.1.9.3. *N*-(1-carbamimidoylpyrrolidin-2-yl)acrylamide (20f)



(**20f**)

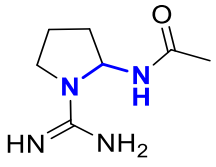
Following the general procedure, from 382 mg (1.58 mmol) of *tert*-Butyl (*S*)-2-acrylamidopyrrolidine-1-carboxylate (**10b**), the mixture was left to react with $AlMe_3$ for 4 hours. After guanylation and purification compound **20f** was obtained as a white solid in 52% yield. Spectroscopic data is in agreement with the literature.[14]

^{1}H NMR (400 MHz, D_2O) δ 6.36–6.29 (m, 2H), 5.80 (d, *J* = 2.6 Hz, 1H), 5.79–5.75 (m, 1H), 3.62–3.54 (m, 1H), 3.46–3.38 (m, 1H), 2.33–2.26 (m, 2H), 2.17–2.10 (m, 1H), 2.04–1.98 (m, 1H).

^{13}C NMR (101 MHz, D_2O) δ 167.55, 129.37, 127.98, 63.83, 46.81, 31.93, 22.30.

HRMS (ESI) m/z calculated $C_8H_{15}N_4O$ [M+H]+: 183.1240; Found: 183.1236

S.1.9.4. *N*-(1-carbamimidoylpyrrolidin-2-yl)acrylamide (20i)



(**20i**)

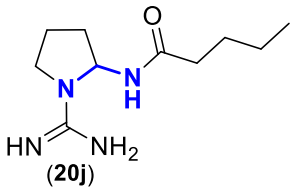
Following the general procedure, from 355 mg (1.56 mmol) of *tert*-Butyl 2-acetamidopyrrolidine-1-carboxylate (**10c**), the mixture was left to react with $AlMe_3$ for 4 hours. After guanylation and purification compound **20i** was obtained as a white solid in 52% yield. The analytical data are consistent with previous reports.[14]

^{1}H NMR (400 MHz, D_2O) δ 5.66 (d, *J* = 5.3 Hz, 1H), 3.63 – 3.51 (m, 1H), 3.48 – 3.38 (m, 1H), 2.36 – 2.05 (m, 4H), 2.01 (s, 3H).

^{13}C NMR (101 MHz, D_2O) δ 173.37, 155.36, 63.69, 46.72, 31.84, 22.27, 21.01.

HRMS (ESI) *m/z* calculated for $C_7H_{16}N_4O$ [M+H]+: 171.1240; Found: 171.1241.

S.1.9.5. (*S*)-*N*-(1-carbamimidoylpyrrolidi-2-yl)pentanamide (20j)


(**20j**)

Following the general procedure, from 82 mg (0.30 mmol) of *tert*-Butyl (*S*)-2-pentanamidopyrrolidine-1-carboxylate (**10d**), the mixture was left to react with $AlMe_3$ for 3 hours. After guanylation and purification compound **20j** was obtained as a white solid in 20% yield.

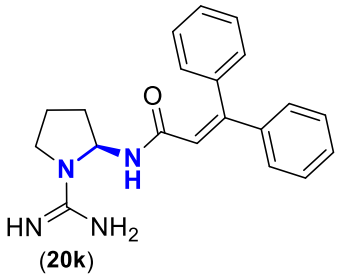
^{1}H NMR (500 MHz, CD_3OD) δ 5.69-5.64 (m, 1H), 3.56-3.50 (m, 1H), 3.41-3.34 (m, 1H), 2.29-2.20 (m, 4H), 2.14-2.06 (m, 1H), 1.97-1.93 (m, 1H), 1.57 (q, *J* = 7.4 Hz, 2H), 1.33 (sext., *J* = 7.4 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H).

^{13}C NMR (125 MHz, CD_3OD) δ 177.80, 156.75, 65.05, 36.29, 33.24, 28.74, 23.70, 23.29, 14.09.

IR (ATR) ν_{max} (cm^{-1}): 3331, 3222, 2959, 2928, 2878, 2660, 1591, 1552, 1451, 1405, 1362, 1123.

ESI-HRMS: m/z calculated for $C_{10}H_{21}N_4O$ $[M+H]^+$ 213.1715, found 213.1705.

S.1.9.6. (*S*)-*N*-(1-carbamimidoylpyrrolidin-2-yl)-3,3-diphenylacrylamide (20k)


(**20k**)

(*S*)-N-(1-carbamimidoylpyrrolidin-2-yl)-3,3-diphenylacrylamide (13.4): Following the general procedure, from 280 mg (0.71 mmol) of *tert*-Butyl (*S*)-2-(3,3-diphenylacrylamido) pyrrolidine-1-carboxylate (**15b**), the mixture was left to react with $AlMe_3$ for 6 hours. After guanylation and purification compound **20k** was obtained as a white solid in 42% yield.

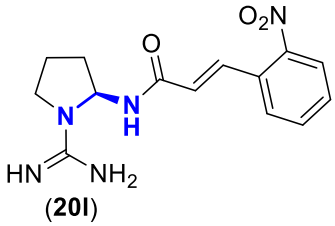
^{1}H NMR (500 MHz, CD^3OD) δ 7.43-7.34 (m, 6H), 7.33-7.29 (m, 2H), 7.24-7.19 (m, 2H), 6.48 (s, 1H), 5.62-5.58 (m, 1H), 3.37-3.34 (m, 1H), 3.31-3.28 (m, 1H), 2.20-2.09 (m, 1H), 2.06-1.98 (m, 2H), 1.76-1.69 (m, 1H).

^{13}C NMR (125 MHz, CD3OD) δ 170.64, 156.56, 154.52, 141.91, 140.18, 130.62, 130.42, 129.57, 129.49, 129.23, 120.92, 65.00, 47.90, 32.85, 23.55

IR (ATR) ν_{max} (cm^{-1}): 3327, 3199, 3021, 2983, 2886, 2751, 1652, 1606, 1536, 1444, 1366, 1215, 1196, 1119.

ESI-HRMS: m/z calculated for $C_{20}H_{23}N_4O$ $[M+H]^+$ 335.1872, found 335.1860.

S.1.9.7. (*S,E*)-*N*-(1-carbamimidoylpyrrolidin-2-yl)-3-(2-nitrophenyl)acryl-amide (**20l**)



(**20l**)

Following the general procedure, from 335 mg (0.93 mmol) of *tert*-Butyl (*S,E*)-2-(3-(2-nitrophenyl)acrylamido) pyrrolidine-1-carboxylate (**15d**), the mixture was left to react with $AlMe_3$ for 6 hours. After guanylation and purification compound **20l** was obtained as a yellow solid in 14% yield.

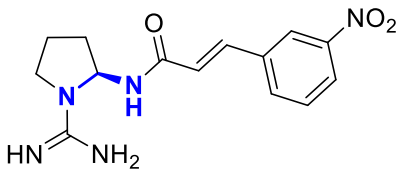
^{1}H NMR (400 MHz, CD_3OD) δ 7.88 (d, *J* = 15.4 Hz, 1H), 7.38 (d, *J* = 7.9 Hz, 1H), 6.74-6.61 (m, 2H), 6.49 (d, *J* = 15.4 Hz, 1H), 5.89-5.78 (m, 1H), 3.63-3.54 (m, 1H), 3.47-3.38 (m, 1H), 2.40-2.26 (m, 2H), 2.20-2.12 (m, 1H), 2.09-2.01 (m, 1H).

^{13}C NMR (101 MHz, CD_3OD) δ 170.17, 156.82, 149.83, 140.15, 132.69, 128.46, 120.86, 119.14, 117.70, 111.96, 65.31, 48.16, 33.38, 23.80.

ESI-HRMS: m/z calculated for $C_{14}H_{18}N_5O_3$ $[M+H]^+$ 304.1410, found 304.1397.

IR (ATR) ν_{max} (cm^{-1}): 3210, 2925, 1651, 1599, 1571, 1405, 1359, 1215, 1190, 1168, 1118.

S.1.9.8. (*S,E*)-*N*-(1-carbamimidoylpyrrolidin-2-yl)-3-(3-nitrophenyl) acrylamide (**20m**)



(**20m**)

Following the general procedure, from 289 mg (0.80 mmol) of *tert*-Butyl (*S,E*)-2-(3-(3-nitrophenyl)acrylamido) pyrrolidine-1-carboxylate (**15f**), the mixture was left to react with $AlMe_3$ for 6 hours. After guanidinylation and purification compound **20m** was obtained as a yellow solid in 11% yield.

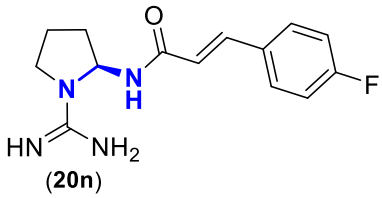
^{1}H NMR (400 MHz, CD_3OD) δ 8.42 (s, 1H), 8.28-8.20 (m, 1H), 7.96 (d, *J* = 7.7 Hz, 1H), 7.82-7.62 (m, 2H), 6.78 (d, *J* = 15.7, 1H), 5.86-5.75 (m, 1H), 3.62-3.52 (m, 1H), 3.48-3.36 (m, 1H), 2.37-2.22 (m, 2H), 2.20-2.12 (m, 1H), 2.09-2.00 (m, 1H).

^{13}C NMR (101 MHz, CD_3OD) δ 168.67, 156.93, 150.16, 141.41, 137.78, 134.85, 131.40, 129.96, 125.43, 123.29, 65.42, 48.21, 33.41, 23.76.

IR (ATR) ν_{max} (cm^{-1}): 3191, 2924, 2854, 1660, 1595, 1526, 1348, 1304, 1222, 1188, 1113, 1077;

ESI-HRMS: m/z calculated for $C_{14}H_{18}N_5O_3$ $[M+H]^+$ 304.1410, found 304.1402.

S.1.9.9. (S,E)-*N*-(1-carbamimidoylpyrrolidin-2-yl)-3-(4-fluorophenyl) acrylamide (20n)



(**20n**)

Following the general procedure, from 279 mg (0.83 mmol) of *tert*-Butyl (*S,E*)-2-(3-(4-fluorophenyl)acrylamido) pyrrolidine-1-carboxylate (**15e**), the mixture was left to react with $AlMe_3$ for 2 hours. After guanidinylation and purification compound **20n** was obtained as a white solid in 49% yield.

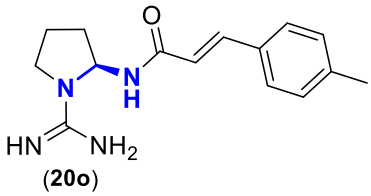
^{1}H NMR (400 MHz, CD_3OD) δ 7.64-7.59 (m, 2H), 7.51 (d, *J* = 15.9 Hz, 1H), 7.22-7.11 (m, 2H), 6.44 (d, J=15.9 Hz, 1H), 5.81-5.76 (m, 1H), 3.64-3.56 (m, 1H), 3.47-3.38 (m, 1H), 2.35-2.25 (m, 1H), 2.25-2.13 (m, 2H), 2.09-2.02 (m, 1H)

^{13}C NMR (101 MHz, CD_3OD) δ 169.79, 164.77 (d, *J* = 249.2 Hz, 1C), 155.89, 143.05, 131.37 (d, *J* = 3.36 Hz, 1C), 131.23 (d, J=8.8 Hz, 2C), 119.28, 116.87 (d, J=22.1 Hz, 2C), 65.14, 47.96, 32.99, 23.33.

IR (ATR) ν_{max} (cm^{-1}): 3215, 3025, 2956, 2890, 1660, 1622, 1598, 1544, 1509, 1417, 1359, 1212, 1161, 1088, 1057

ESI-HRMS: m/z calculated for $C_{14}H_{18}FN_4O$ $[M+H]^+$ 277.1465, found 277.1456.

S.1.9.10. (*S,E*)-*N*-(1-carbamimidoylpyrrolidin-2-yl)-3-(p-tolyl) acrylamide (20o)



(**20o**)

Following the general procedure, from 305 mg (0.92 mmol) of *tert*-Butyl (*S,E*)-2-(3-(p-tolyl)acrylamido)pyrrolidine-1-carboxylate (**15g**), the mixture was left to react with $AlMe_3$ for 3 hours. After guanylation and purification compound **20o** was obtained as a white solid in 55% yield.

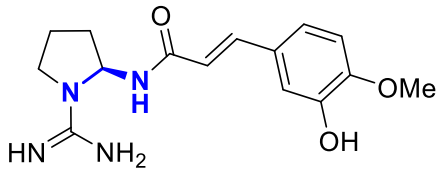
^{1}H NMR (400 MHz, CD_3OD) δ 7.64 (d, *J* = 15.6 Hz, 1H), 7.48 (d, *J* = 7.8 Hz, 2H), 7.24 (d, *J* = 7.8 Hz, 2H), 6.63 (d, *J* = 15.6 Hz, 1H), 5.87-5.79 (m, 1H), 3.65-3.56 (m, 1H), 3.51-3.39 (m, 1H), 2.37 (s, 3H), 2.36-2.27 (m, 2H), 2.24-2.13 (m, 1H), 2.11-2.01 (m, 1H).

^{13}C NMR (101 MHz, CD_3OD) δ 169.77, 156.75, 144.25, 142.00, 133.09, 130.68, 129.14, 119.14, 65.38, 48.24, 33.26, 23.81, 21.44.

IR (ATR) ν_{max} (cm^{-1}): 3365, 3238, 3029, 2983, 2886, 1652, 1606, 1575, 1513, 1420, 1362, 1185, 1115, 983;

ESI-HRMS: m/z calculated for $C_{15}H_{21}N_4O$ [M+H]+ 273.1715, found 273.1704.

S.1.9.11. Cernumidine (1)



(**1**)

Following the general procedure, from 100 mg (0.28 mmol) of *tert*-Butyl (*S,E*)-2-(3-(3-hydroxy-4-methoxyphenyl)acrylamido) pyrrolidine-1-carboxylate (**15**), the mixture was left to react with $AlMe_3$ for 3 hours. After guanidinylation and purification compound **1** was obtained as a white solid in 23% yield and 70% *ee*. Spectroscopic data is in agreement with literature.[13]

^{1}H NMR (500 MHz, CD_3OD) δ 7.56 (d, J=15.7 Hz, 1H), 7.09-7.06 (m, 1H), 7.06-7.02 (m, 1H), 6.96 (d, J=8.3 Hz, 1H), 6.47 (d, J=15.7 Hz, 1H), 5-85-5.79 (m, 1H), 3.90 (s, 3H), 3.62-3.57 (m, 1H), 3.47-3.41 (m, 1H), 2.38-2.29 (m, 2H), 2.21-2.15 (m, 1H), 2.08-2.02 (m, 1H).

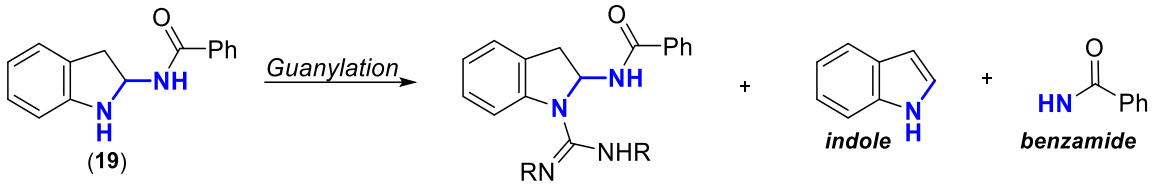
^{13}C NMR (125 MHz, CD_3OD) δ 170.01, 156.76, 151.38, 148.02, 144.51, 128.98, 122.71, 117.57, 114.62, 112.53, 65.38, 56.41, 48.21, 33.37, 23.80.

IR (ATR) ν_{max} (cm^{-1}): 3331, 3219, 2979, 2894, 2843, 1656, 1606, 1509, 1432, 1362, 1266, 1212, 1127, 1022.

HPLC (water/methanol = 60/40, flow rate 1.0 mL/min, λ = 240 nm) tR = 9.07 min (minor), tR = 9.89 min (major), 70% *ee.*

S.1.9.12. Guanylation of compound 19

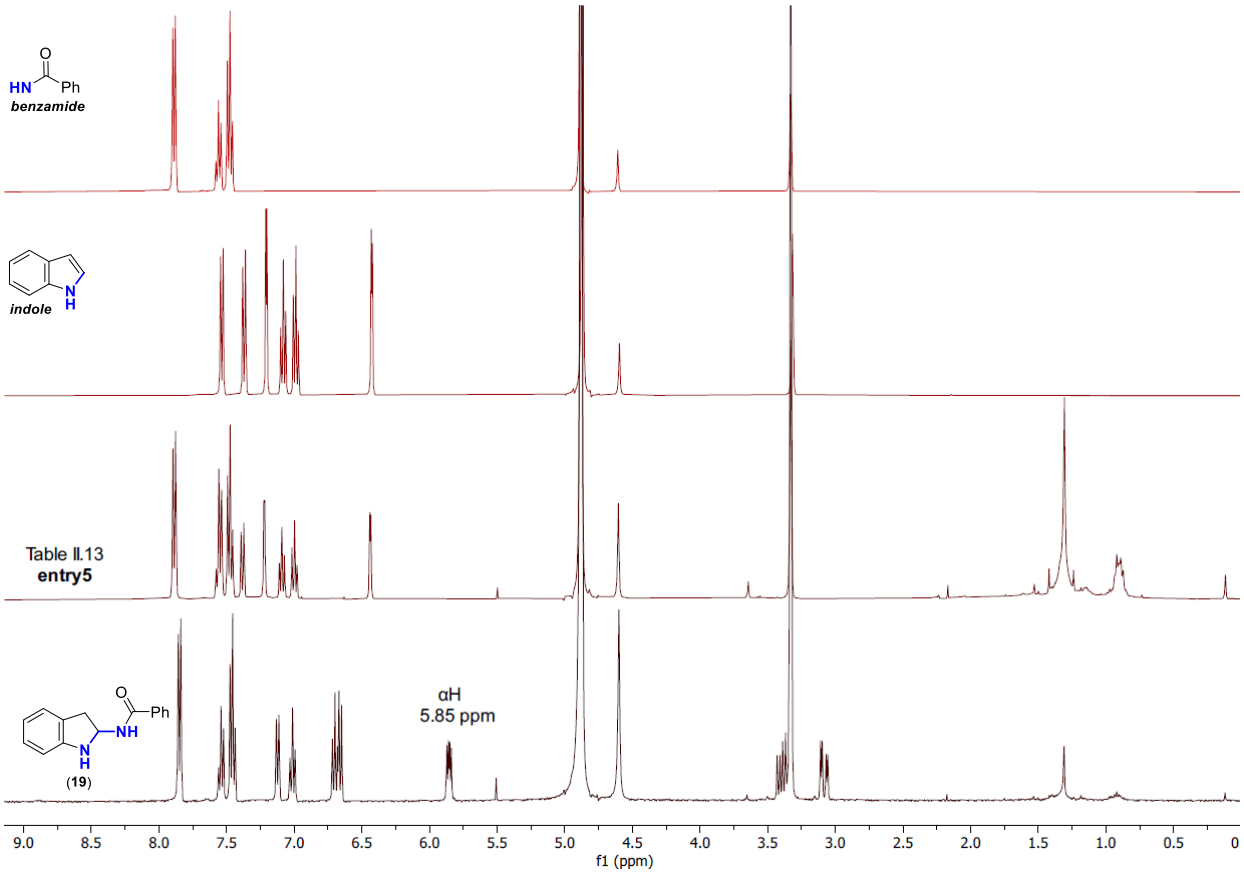
Table S5 Screening of conditions for the guanylation of **19**.



Entry	Electrophile (equiv.)	Base (equiv.)	Observations
1	GR1 (1.1)	-	Unreacted SM
2	GR1 (5)	-	Unreacted SM
3	GR3 (1.1)	-	Unreacted SM
4	GR2 (1.1)	DIPEA (1.1)	Unreacted SM
5	GR2 (1.1)	NaH (2.1)	Indole and benzamide
6	Boc_2O	TEA (1.1)	SM (86%) and 19 (14%)
7	Boc_2O	TEA (1.1)	SM (70%) and 19 (30%)

SM – starting material.

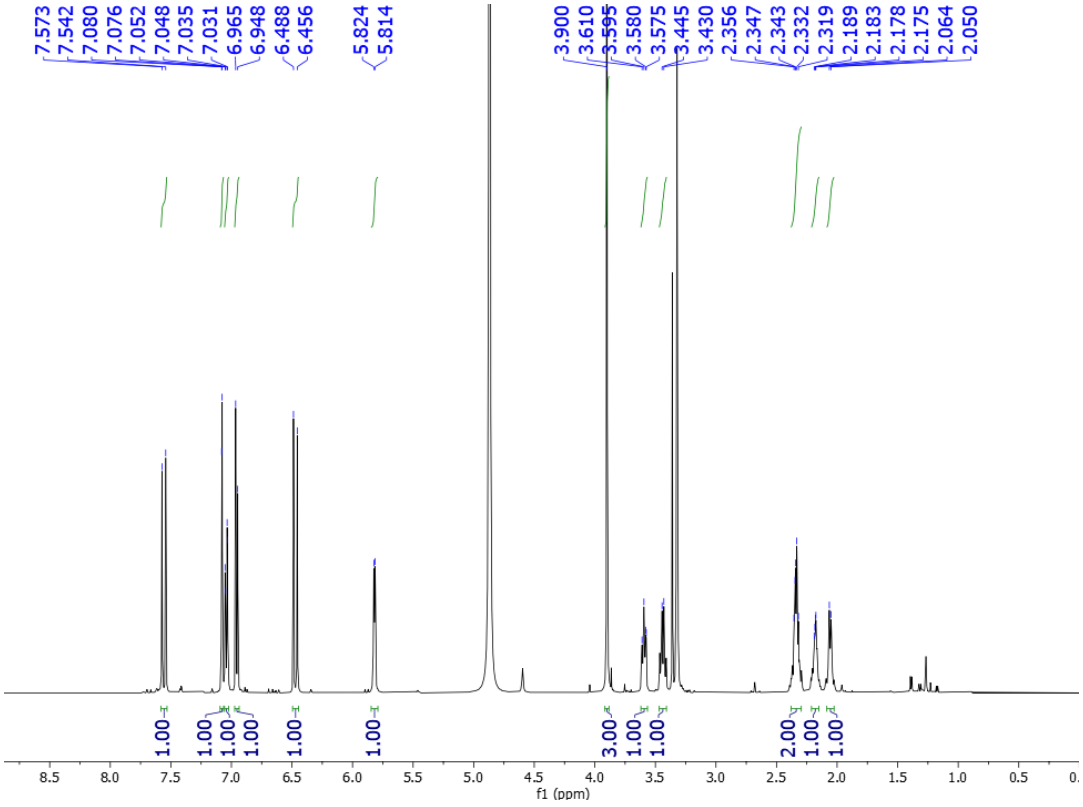
S.1.9.13. ^{1}H-NMR (400MHz, MeOD) spectra of **19**, indole, benzamide and reactional mixture of entry 5 from table *S5*.


HN
Ph
benzamide
N
H
indole
Table II.13
entry5
O
Ph
NH
N
H
(19)
αH
5.85 ppm
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
f1 (ppm)

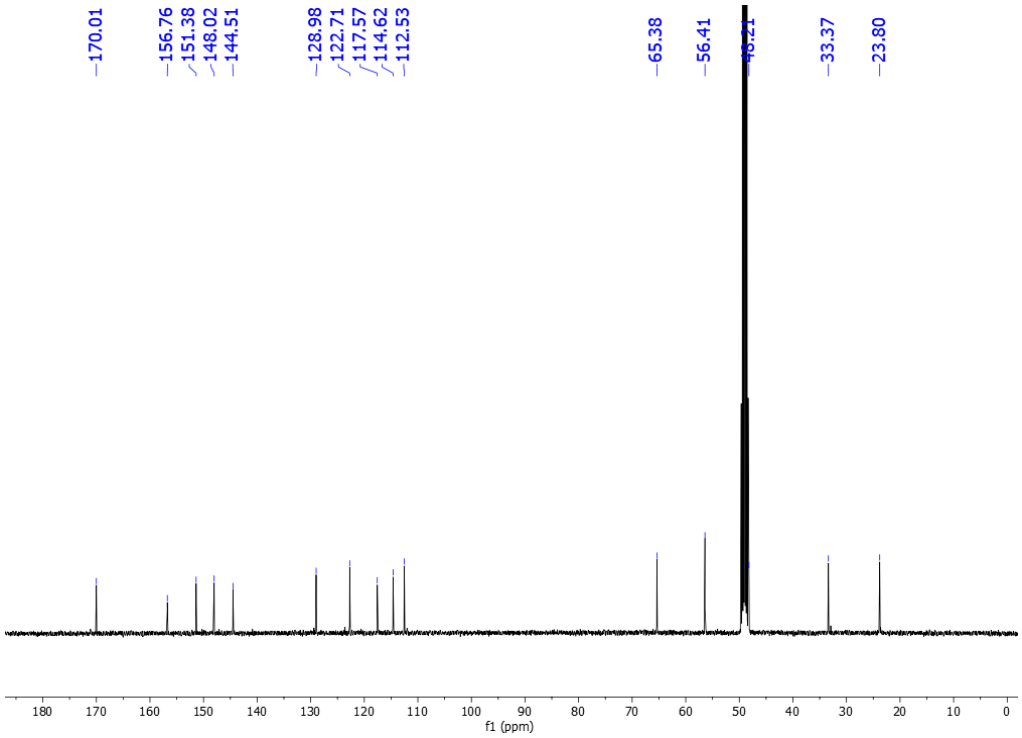
S.2. Spectral and Analytical data of Compounds

S.2.1. Cernumidine (1)

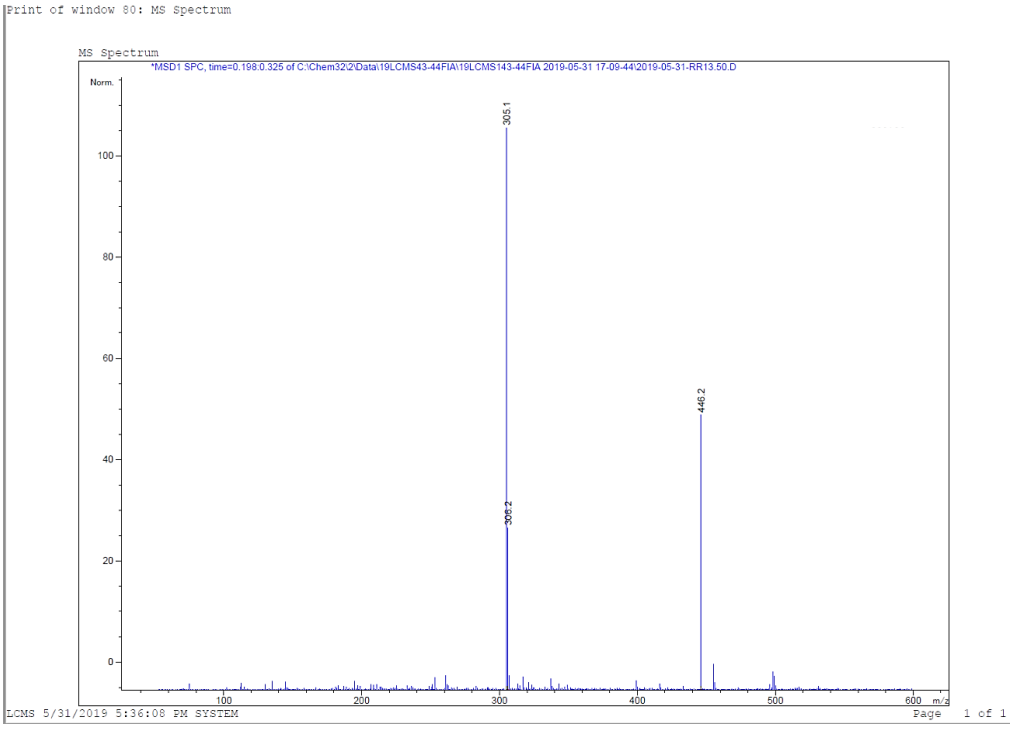
S.2.1.1 ^{1}H NMR (CD_3OD, 500 MHz) spectrum of compound 1



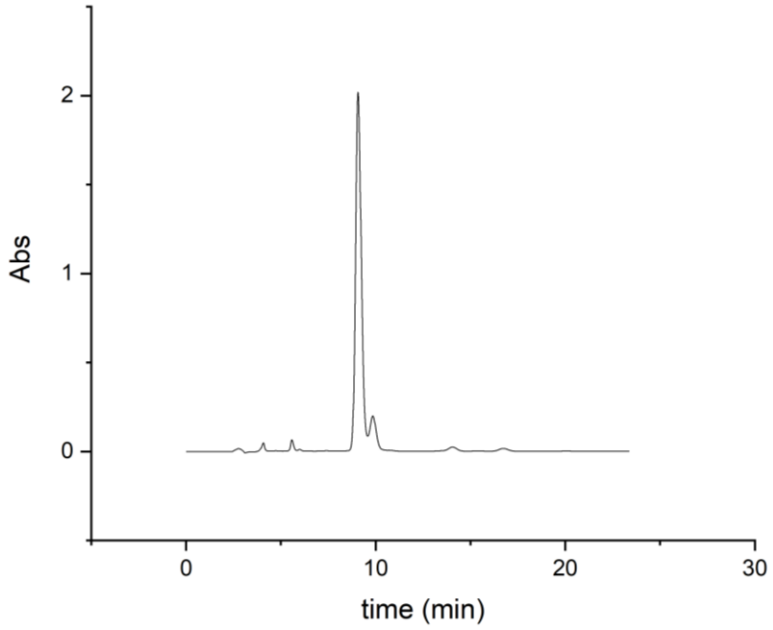
S.2.1.2 ^{13}C NMR (CD_3OD, 125 MHz) spectrum of compound 1



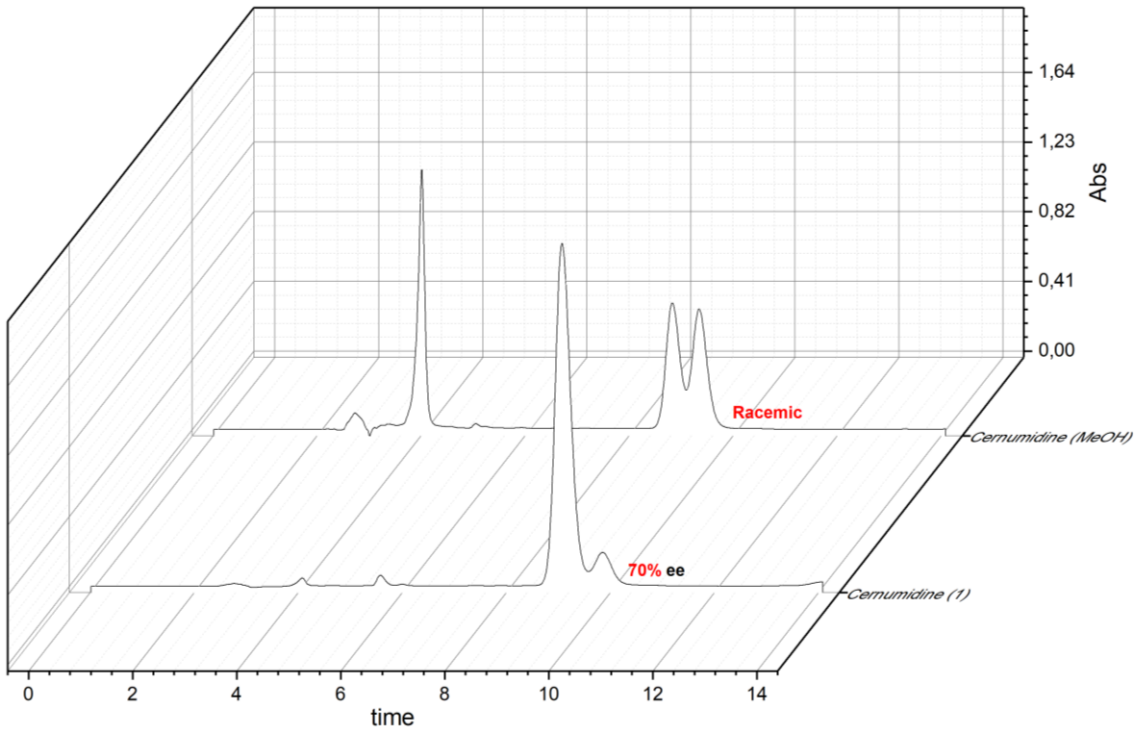
S.2.1.3. ESI-MS of compound 1



S.2.1.4. Chiral HPLC chromatogram of compound 1

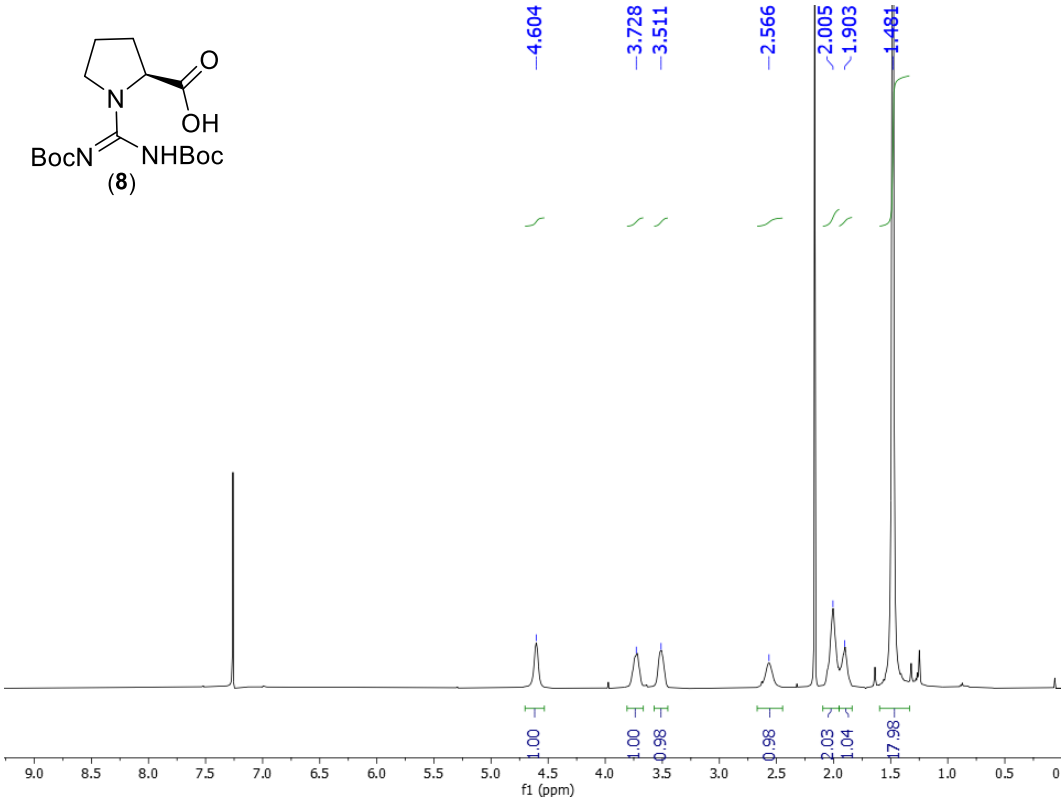


S.2.1.5. Chiral HPLC chromatogram of compound **1** after isolation (Apeak1= 0.85 – Apeak2= 0.15, 70% *ee*) and after one week in MeOH (racemic).



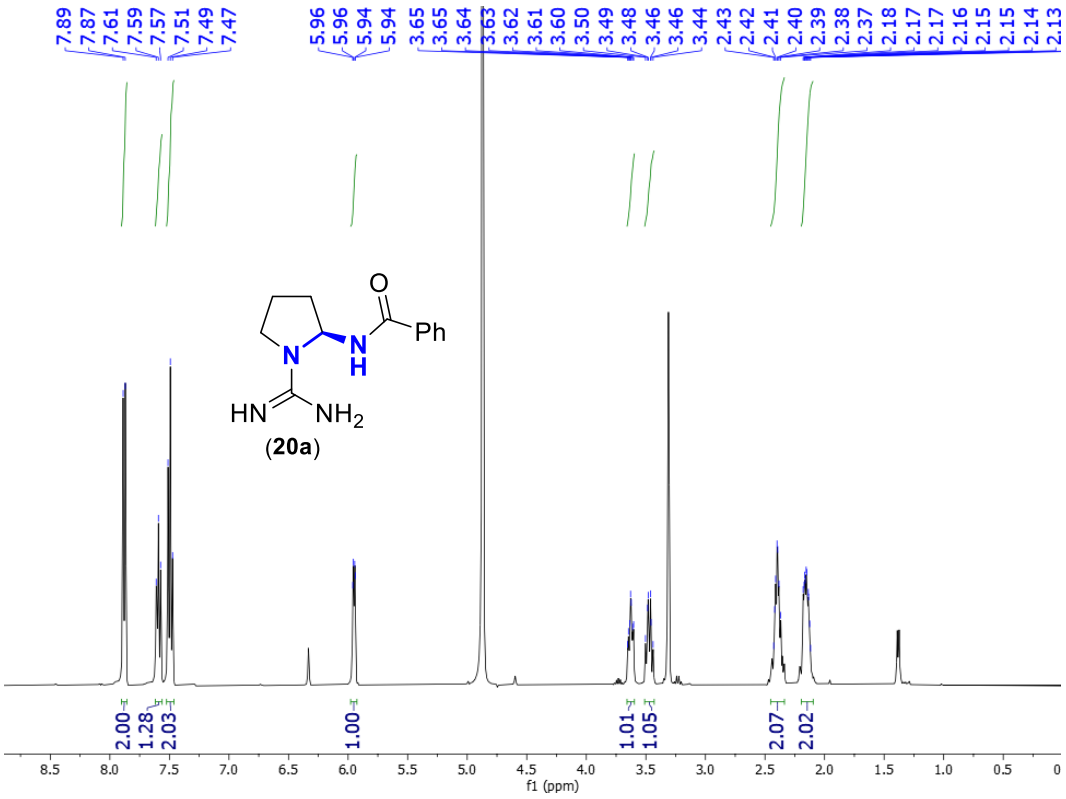
S.2.2. (1*R*)-2-((Z)-*N,N'*-bis(*tert*-butoxycarbonyl)carbamimidoyl)cyclopentane-1-carboxylic acid (**8**)

S.2.2.1. ^{1}H NMR ($CDCl_3$, 500 MHz) spectrum of compound **8**

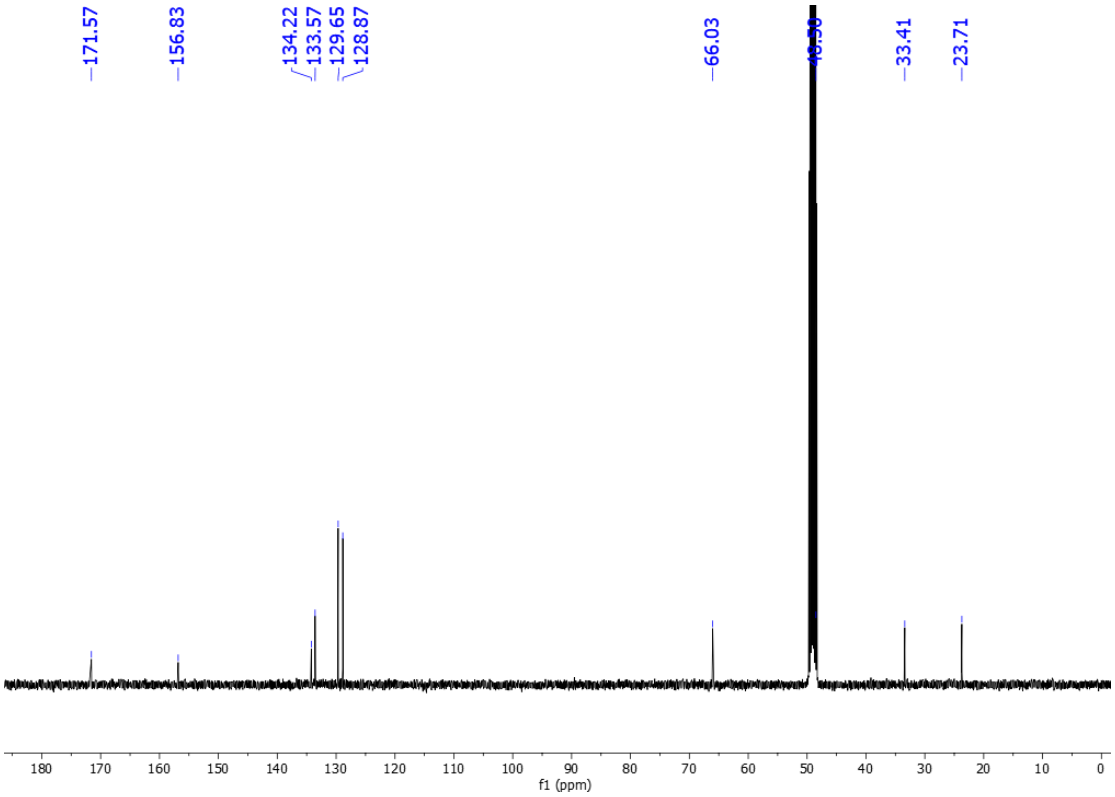


S.2.3. *N*-(1-carbamimidoylpyrrolidin-2-yl)benzamide (**20a**)

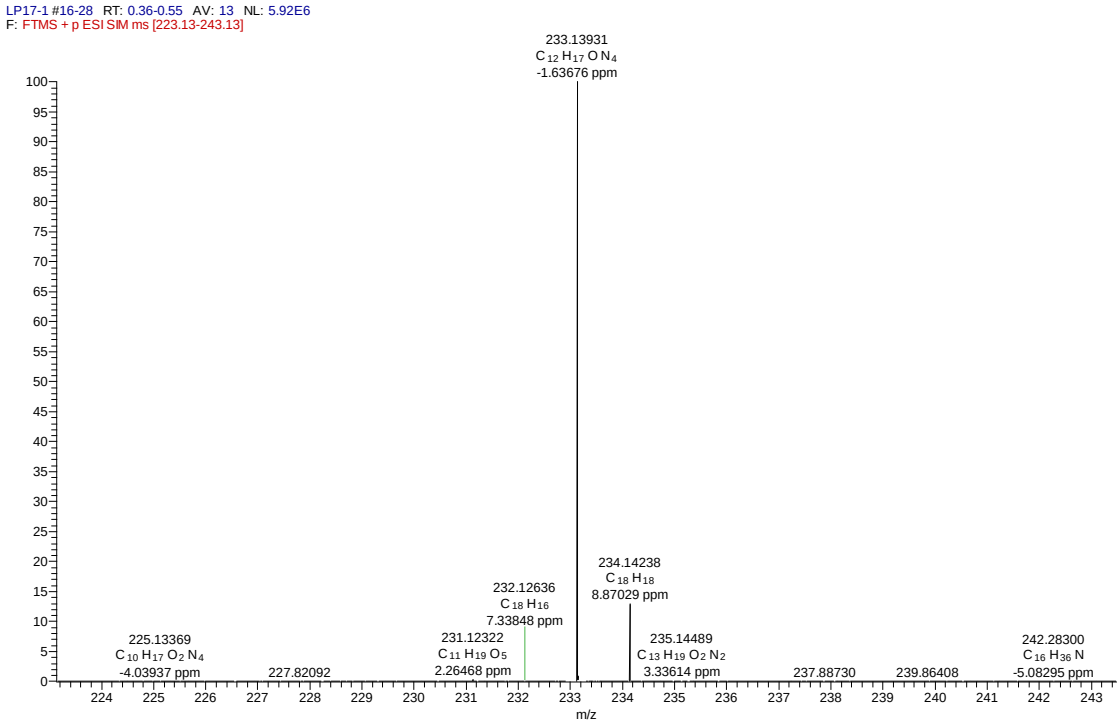
S.2.3.1. ^{1}H NMR (CD_3OD, 400 MHz) spectrum of compound **20a**



S.2.3.2. ^{13}C NMR (CD_3OD, 101 MHz) spectrum of compound **20a**

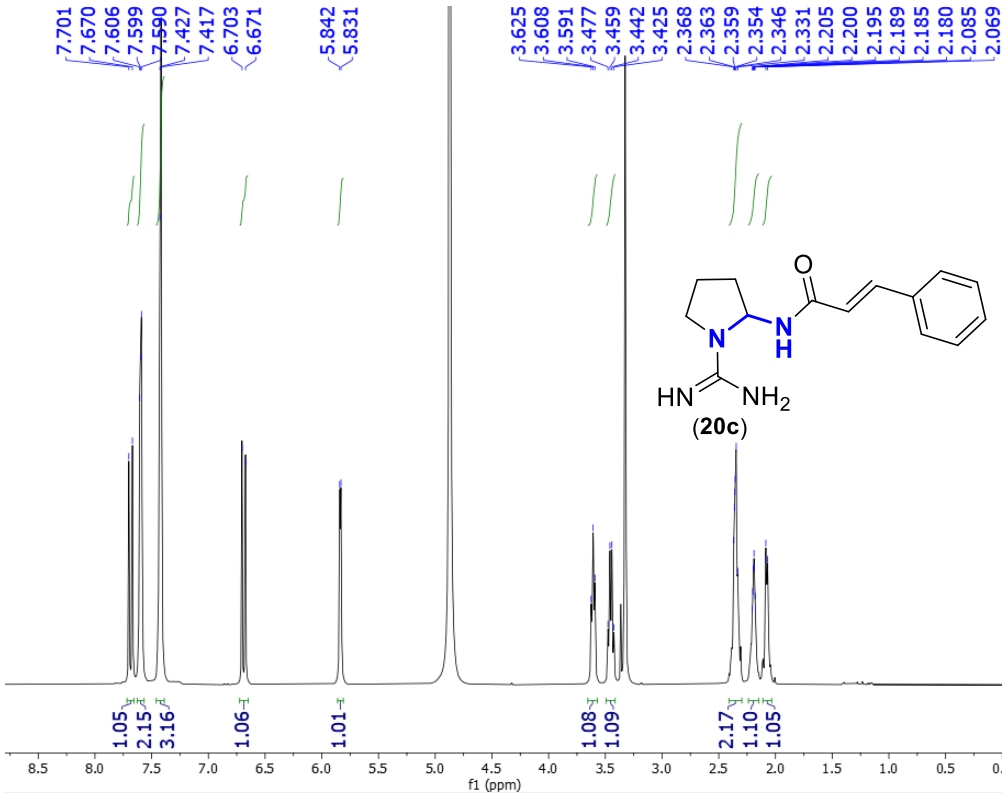


S.2.3.3. ESI-HRMS spectrum of compound **20a**

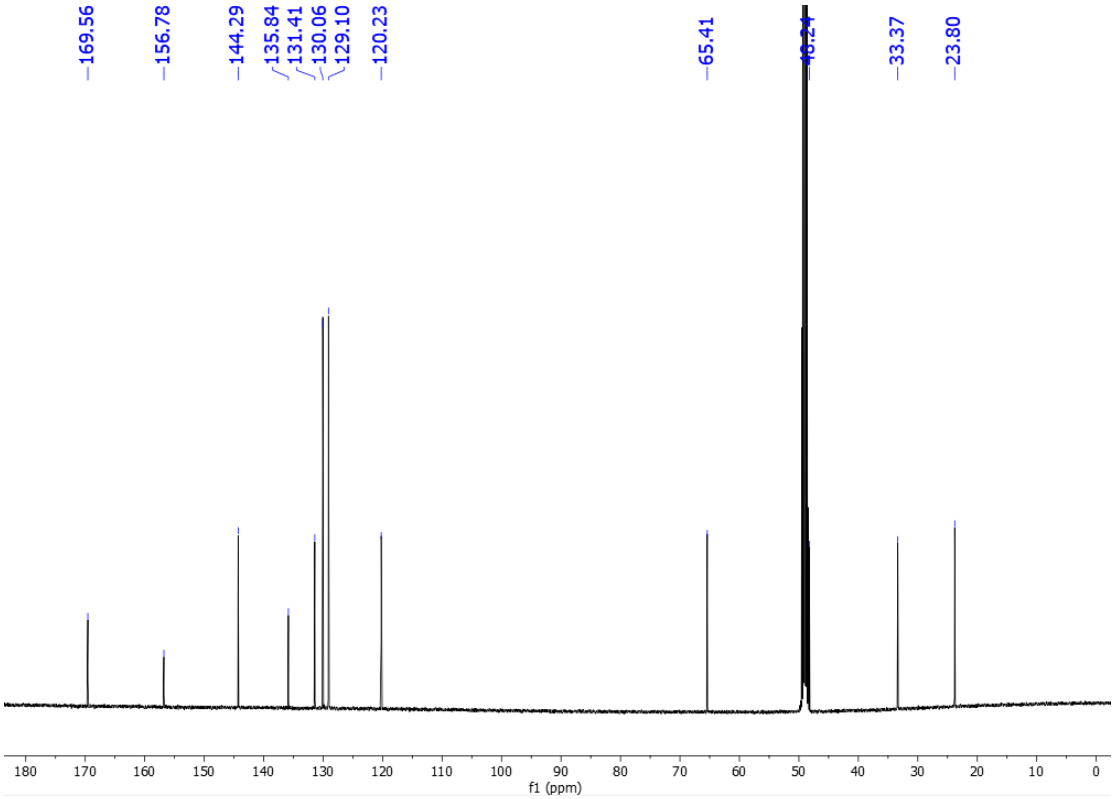


S.2.4. *N*-(1-Carbamimidoylpyrrolidin-2-yl)cinnamamide (**20c**)

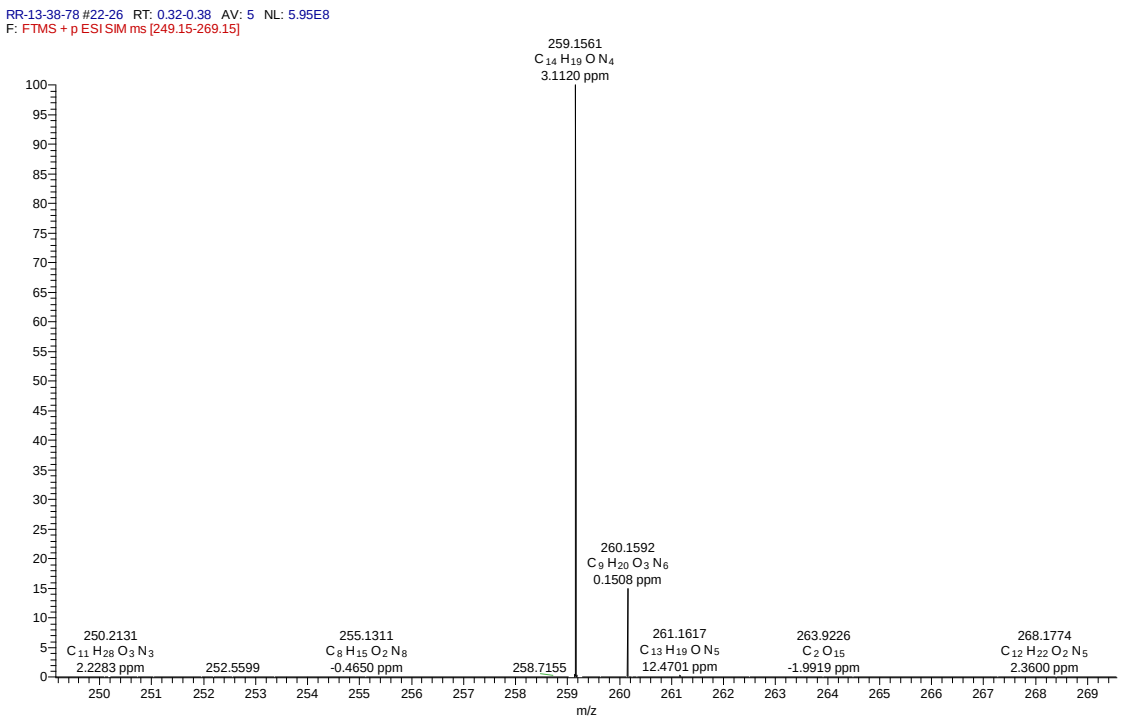
S.2.4.1. ^{1}H NMR (CD_3OD, 500 MHz) spectrum of compound **20c**



S.2.4.2. ^{13}C NMR (CD_3OD, 125 MHz) spectrum of compound **20c**

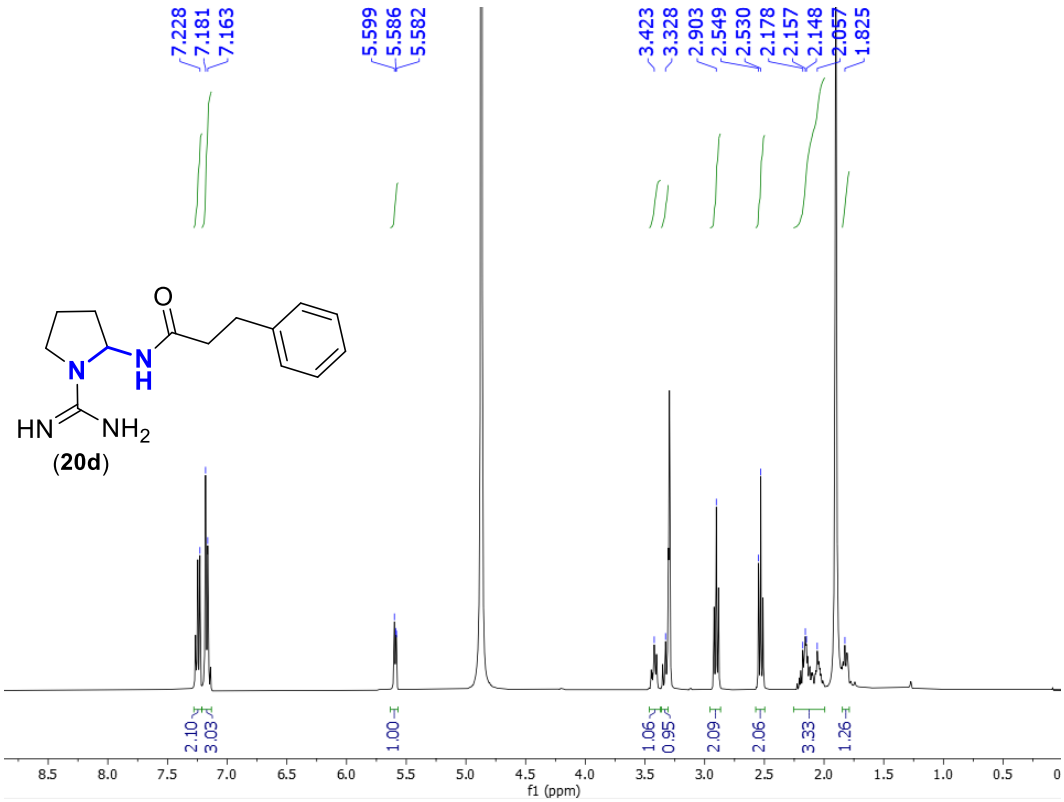


S.2.4.3. ESI-HRMS spectrum of compound **20c**

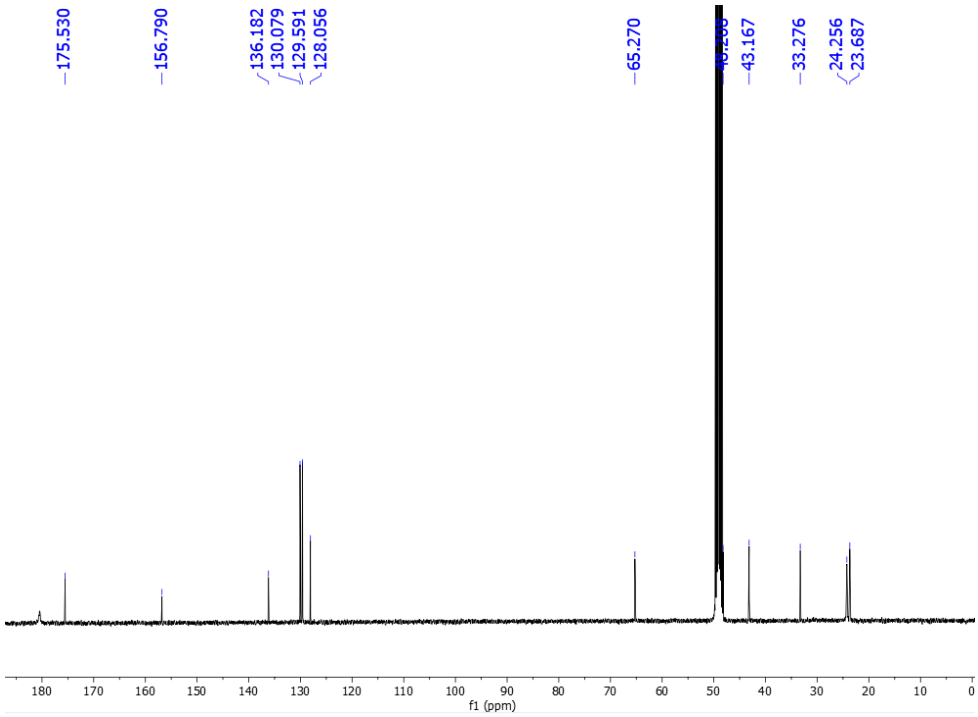


S.2.5. 1H NMR *N*-(1-Carbamimidoylpyrrolidin-2-yl)-3-phenylpropanamide (**20d**)

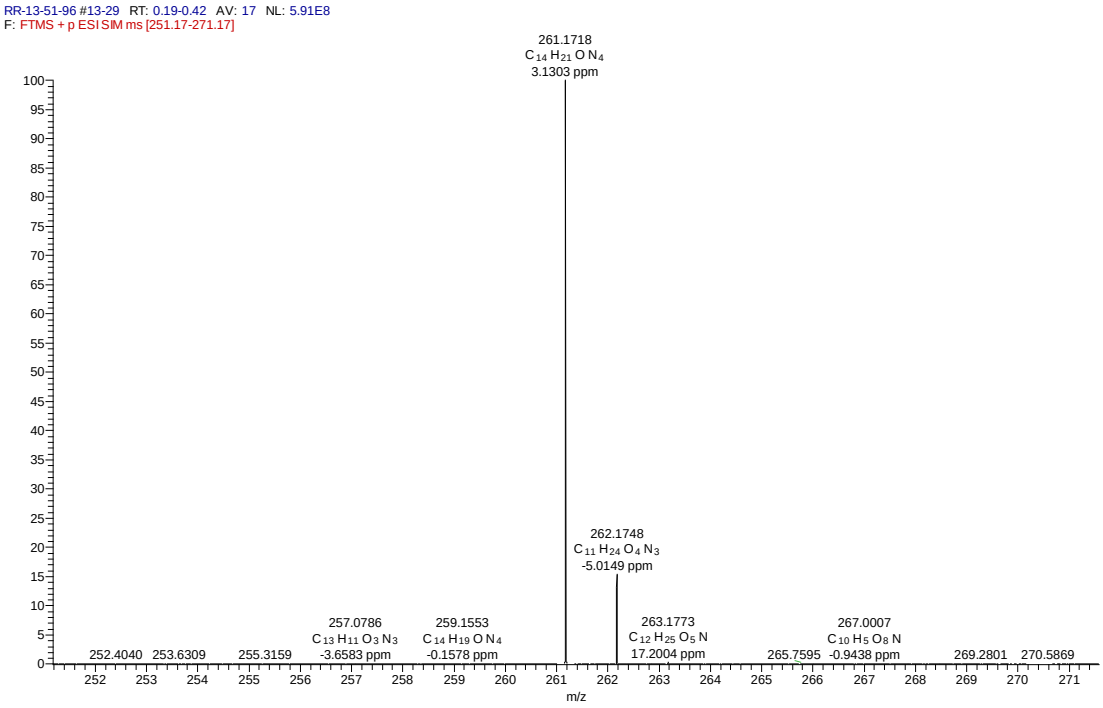
S.2.5.1. ^{1}H NMR (CD_3OD, 400 MHz) spectrum of compound **20d**



S.2.5.2. ^{1}H NMR (CD_3OD, 101 MHz) spectrum of compound **20d**

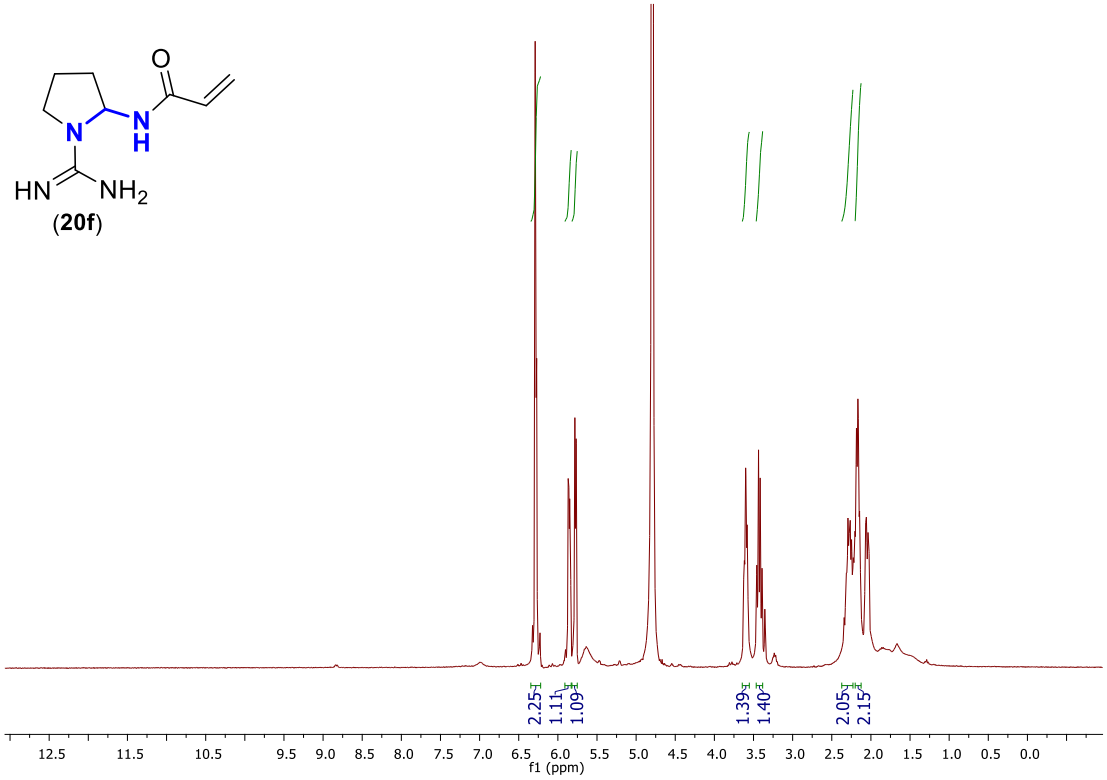


S.2.5.3. ESI-HRMS spectrum of compound **20d**

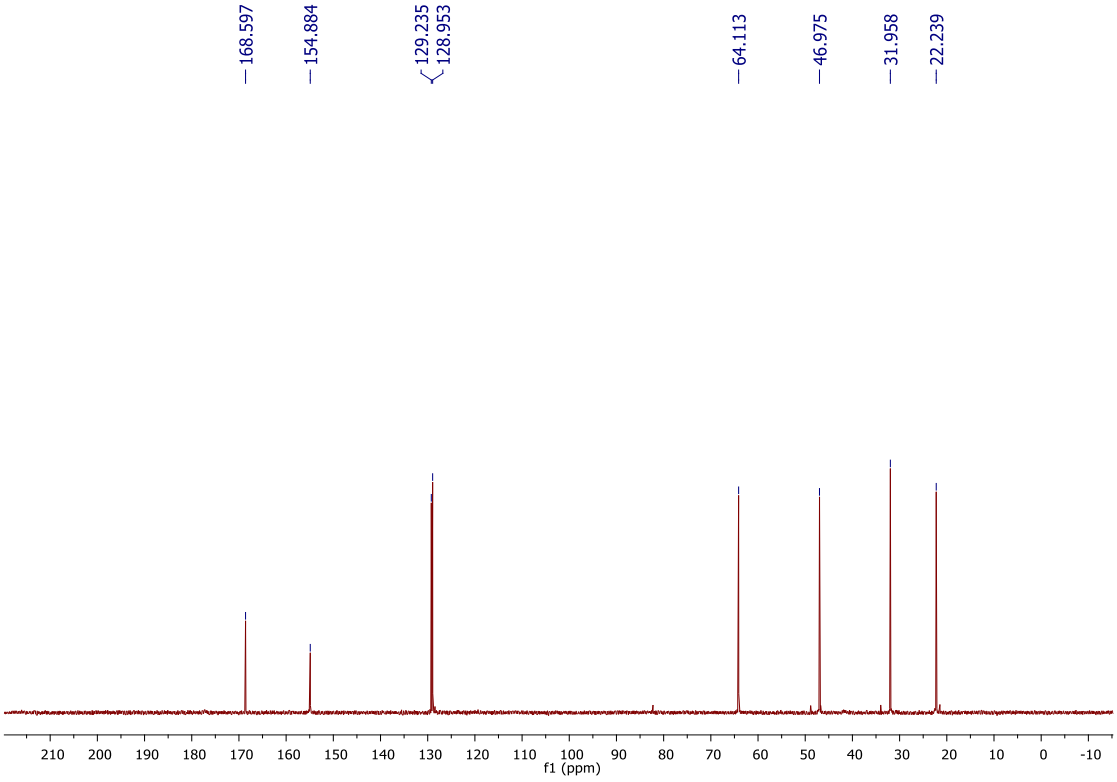


S.2.6. *N*-(1-Carbamimidoylpyrrolidin-2-yl)acrylamide (**20f**)

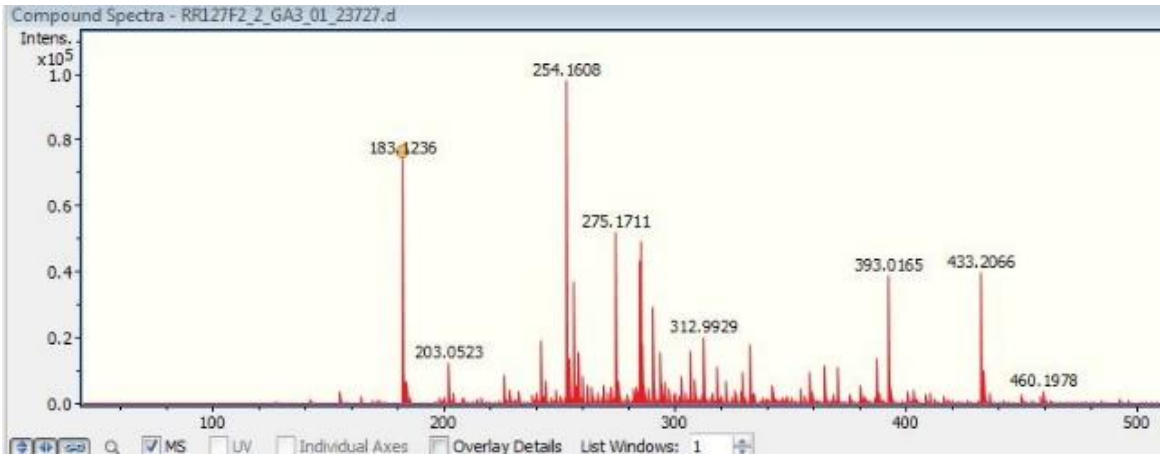
S.2.6.1. ^{1}H NMR (D_2O, 400 MHz) spectrum of compound **20f**



S.2.6.2. ^{13}C NMR (D_2O, 101 MHz) spectrum of compound **20f**



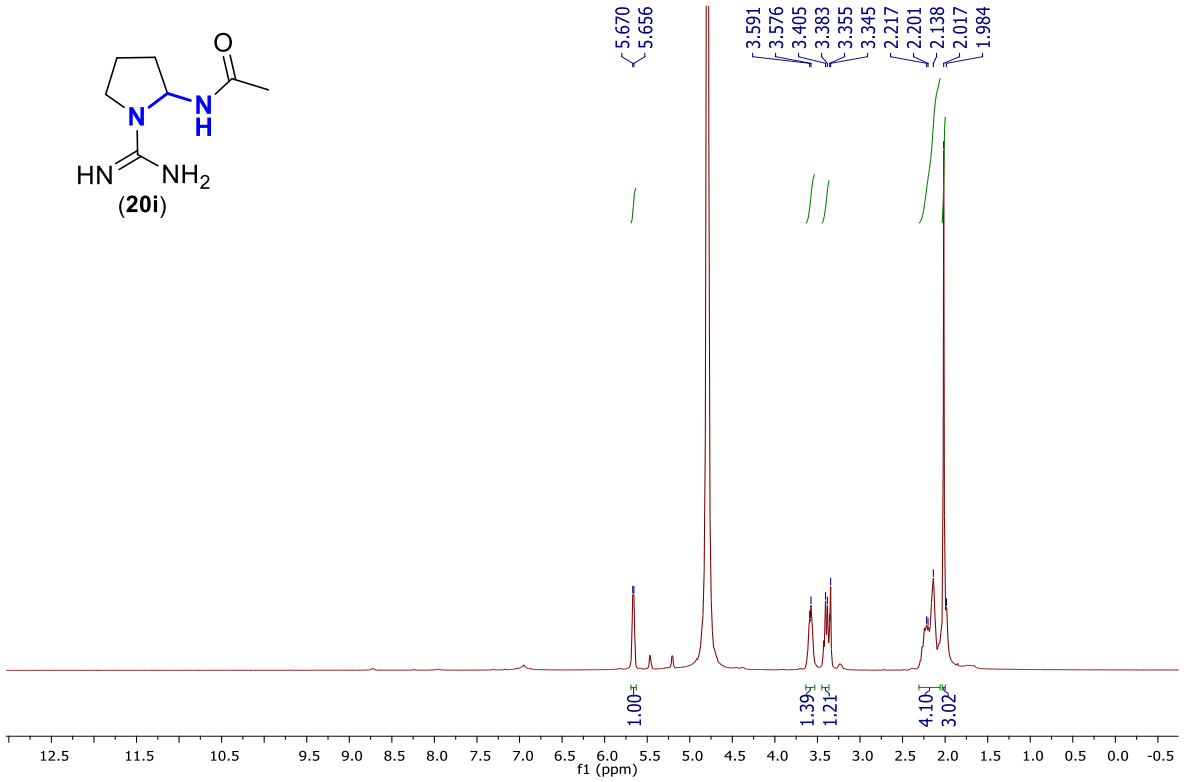
S.2.6.3. ESI-HRMS spectrum of compound **20f**



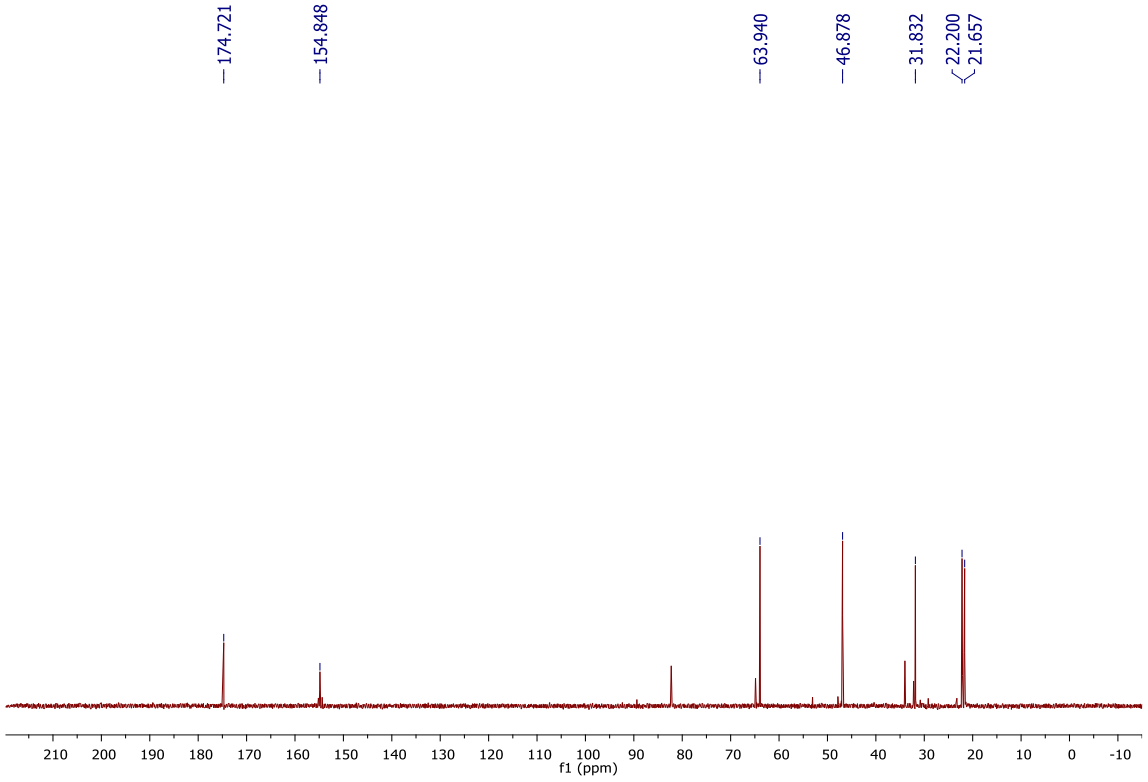
accurate mass	ion formula	exact mass	err (ppm)
183.1236	$C_8H_{15}N_4O$	183.1240	2.2

S.2.7. *N*-(1-Carbamimidoylpyrrolidin-2-yl)acrylamide (**20i**)

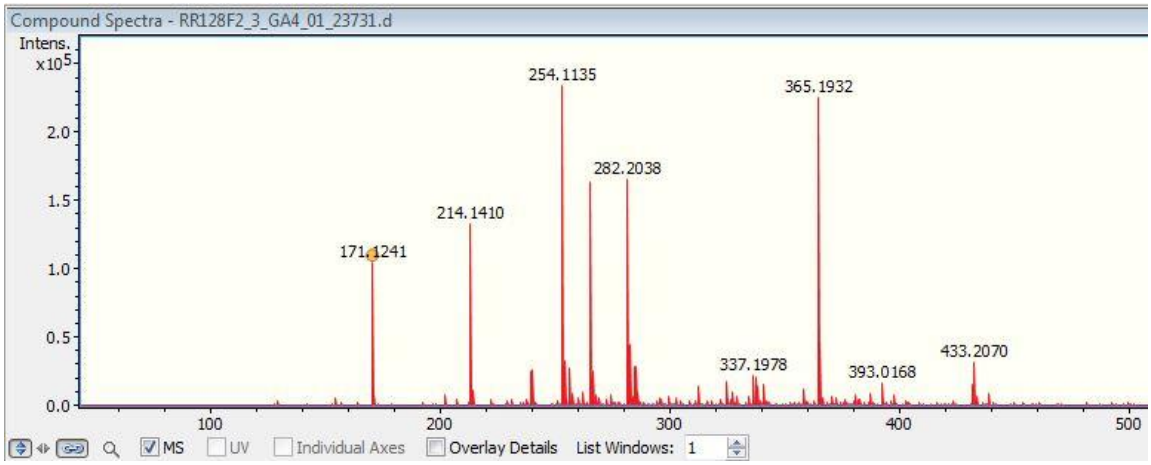
S.2.7.1. ^{1}H NMR (D_2O, 400 MHz) spectrum of compound **20i**



S.2.7.2. ^{13}C NMR (D_2O, 101 MHz) spectrum of compound **20i**



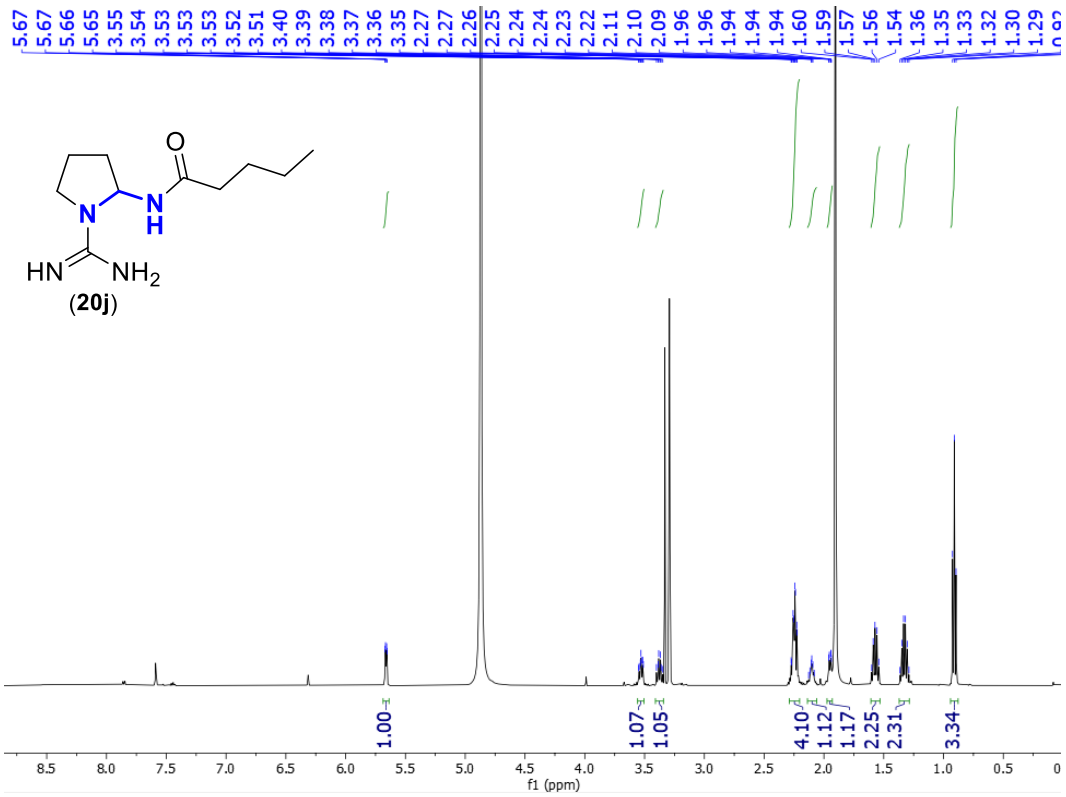
S.2.7.3. ESI-HRMS spectrum of compound **20i**



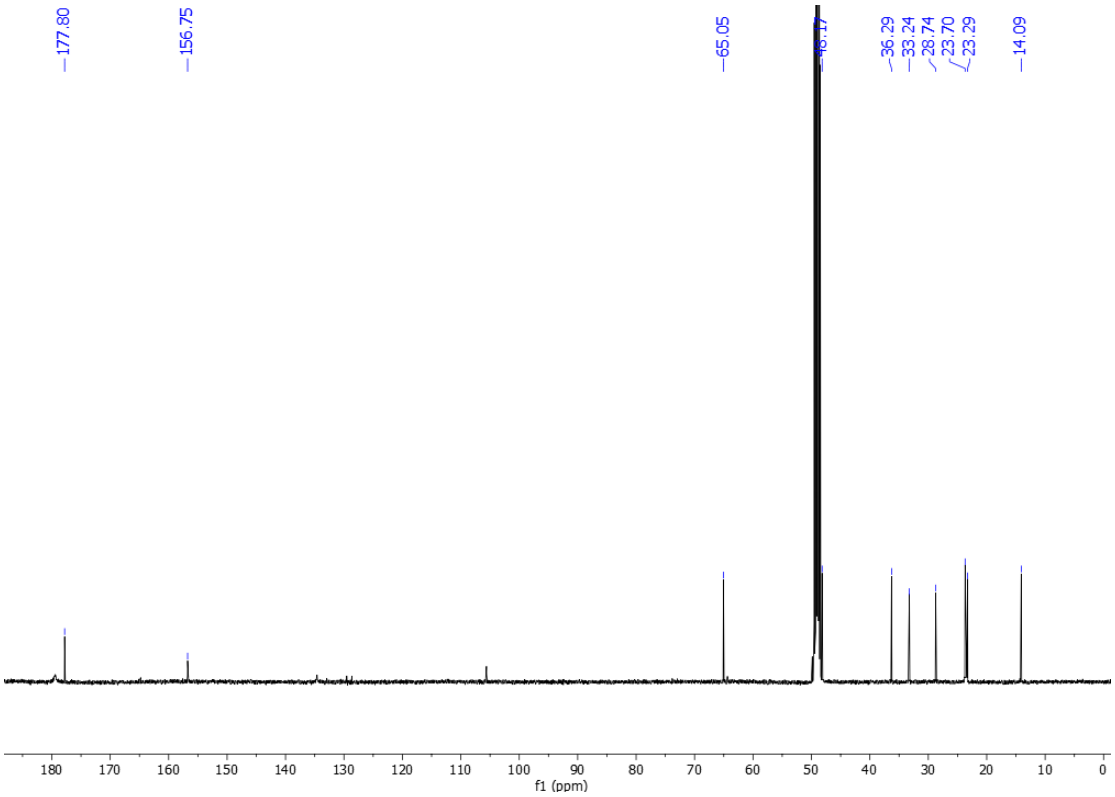
accurate mass	ion formula	exact mass	err (ppm)
171.1241	$C_7H_{15}N_4O$	171.1240	-0.4

S.2.8. (*S*)-*N*-(1-carbamimidoylpyrrolidi-2-yl)pentanamide (**20j**)

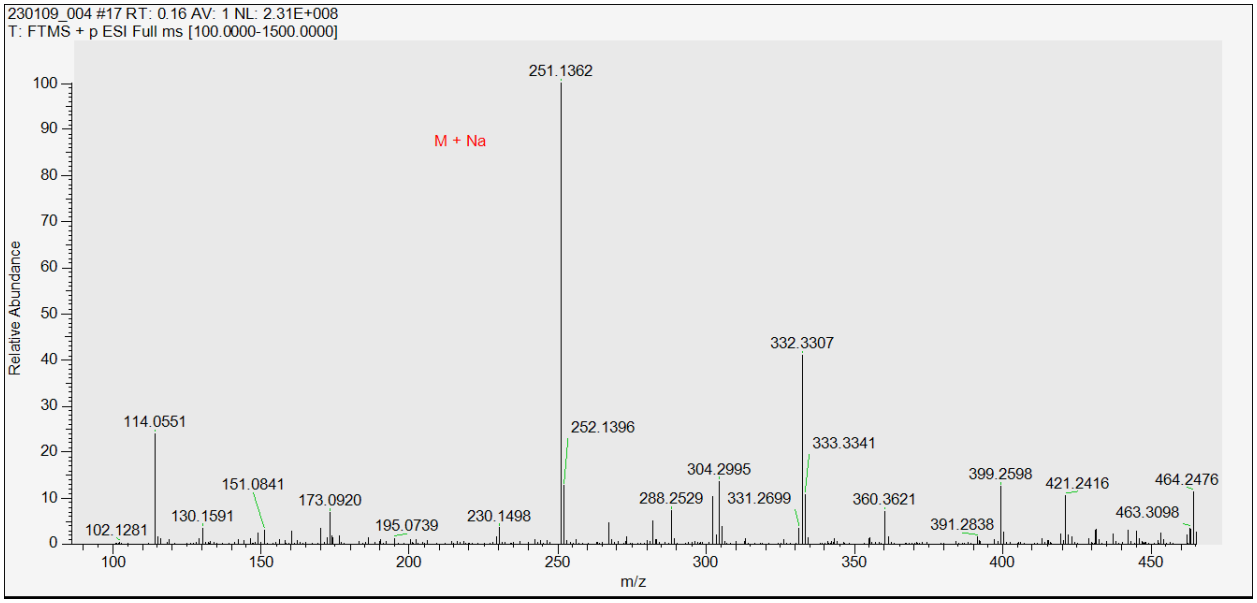
S.2.8.1. ^{1}H NMR (MeOD, 500 MHz) spectrum of compound **20j**



S.2.8.2. ^{13}C NMR (MeOD, 125 MHz) spectrum of compound **20j**

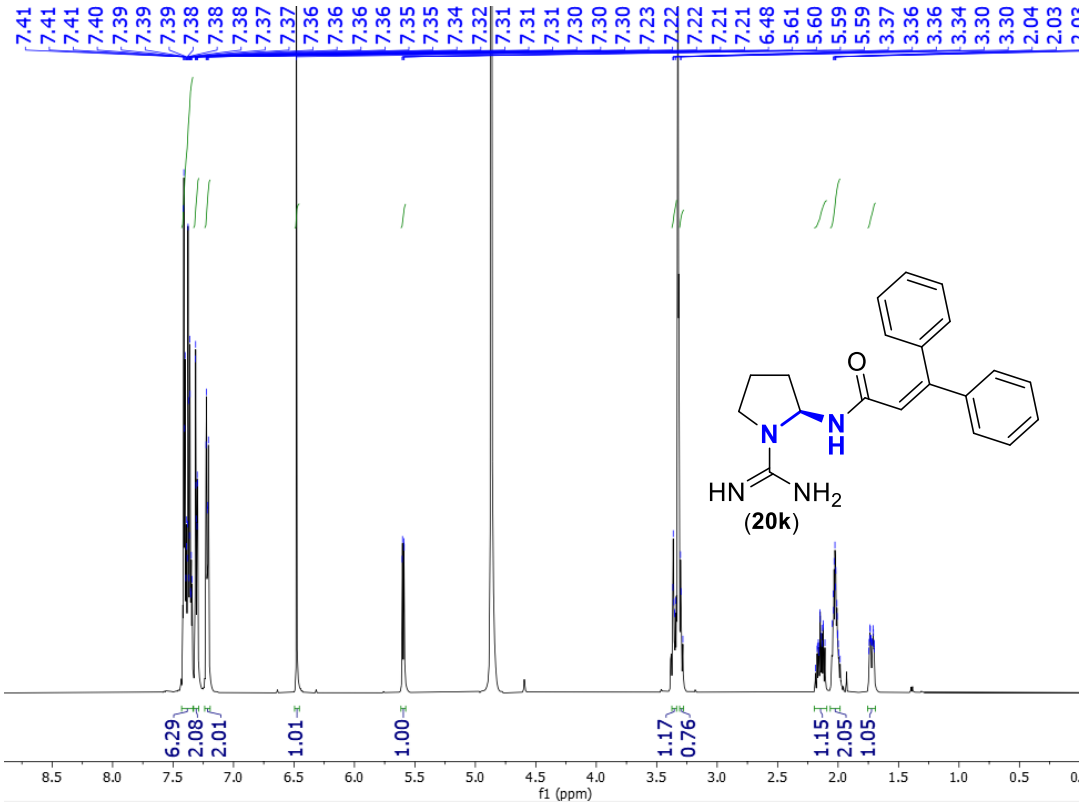


S.2.8.3. ESI-HRMS spectrum of compound **20j**

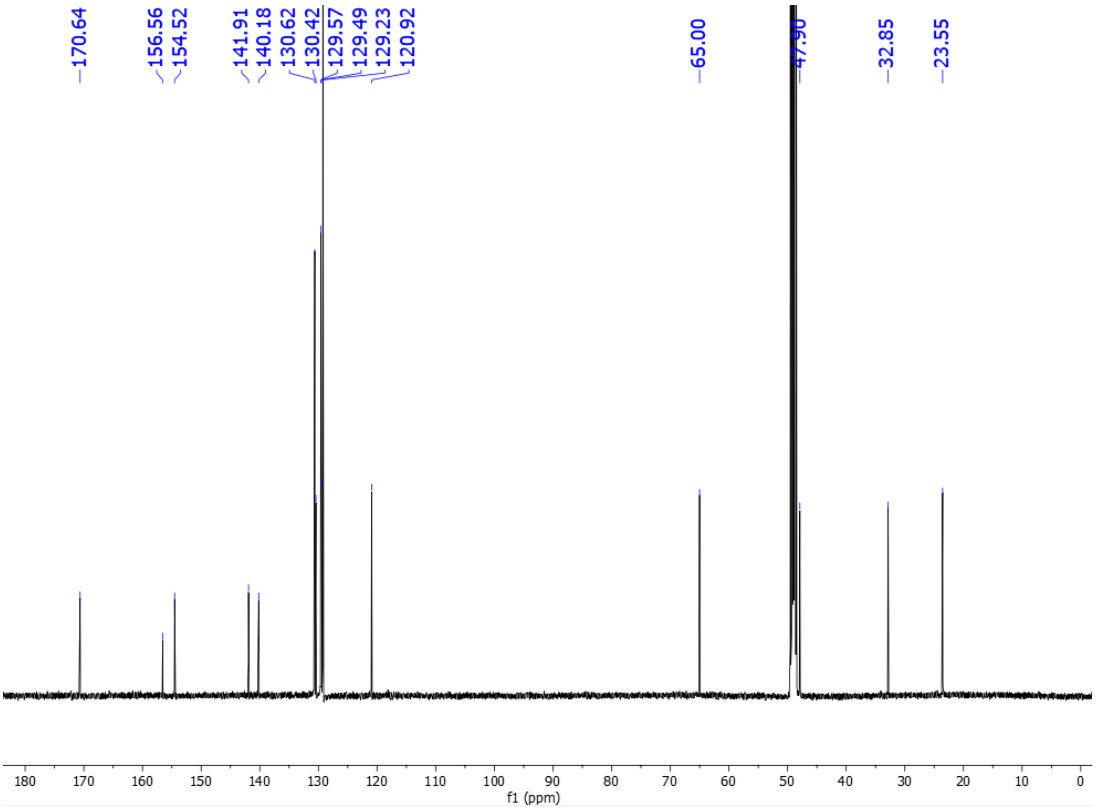


S.2.9. (*S*)-N-(1-carbamimidoylpyrrolidin-2-yl)-3,3-diphenylacrylamide (**20k**)

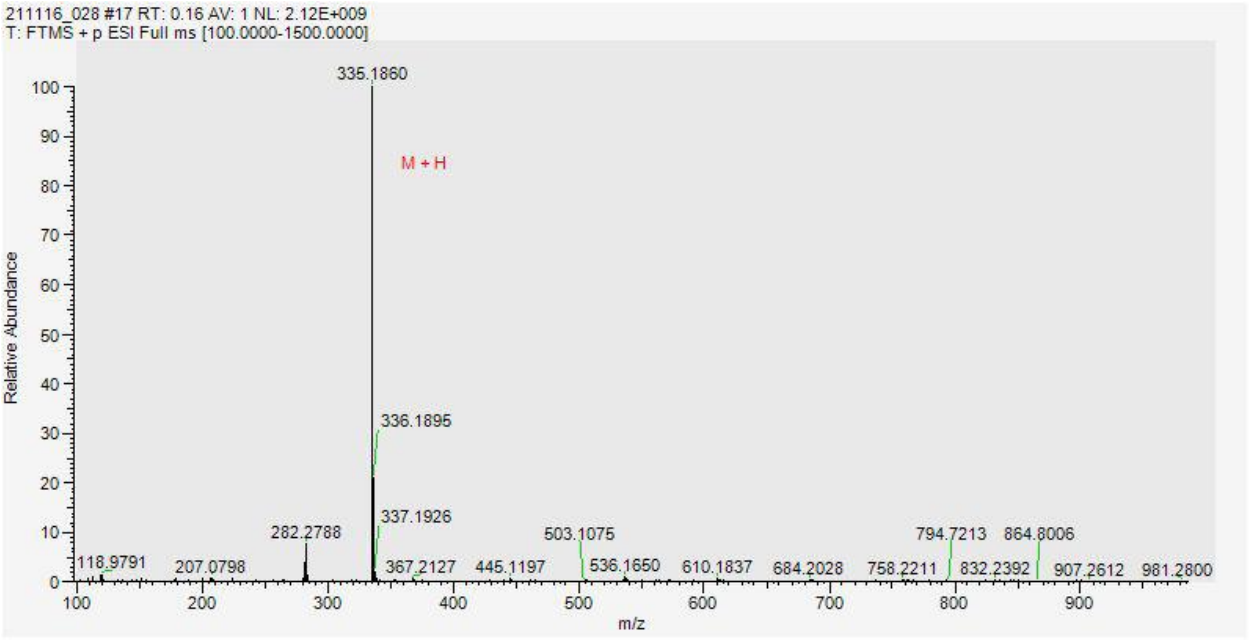
S.2.9.1. ^{1}H NMR (MeOD, 500 MHz) spectrum of compound **20k**



S.2.9.2. ^{13}C NMR (MeOD, 125 MHz) spectrum of compound **20k**

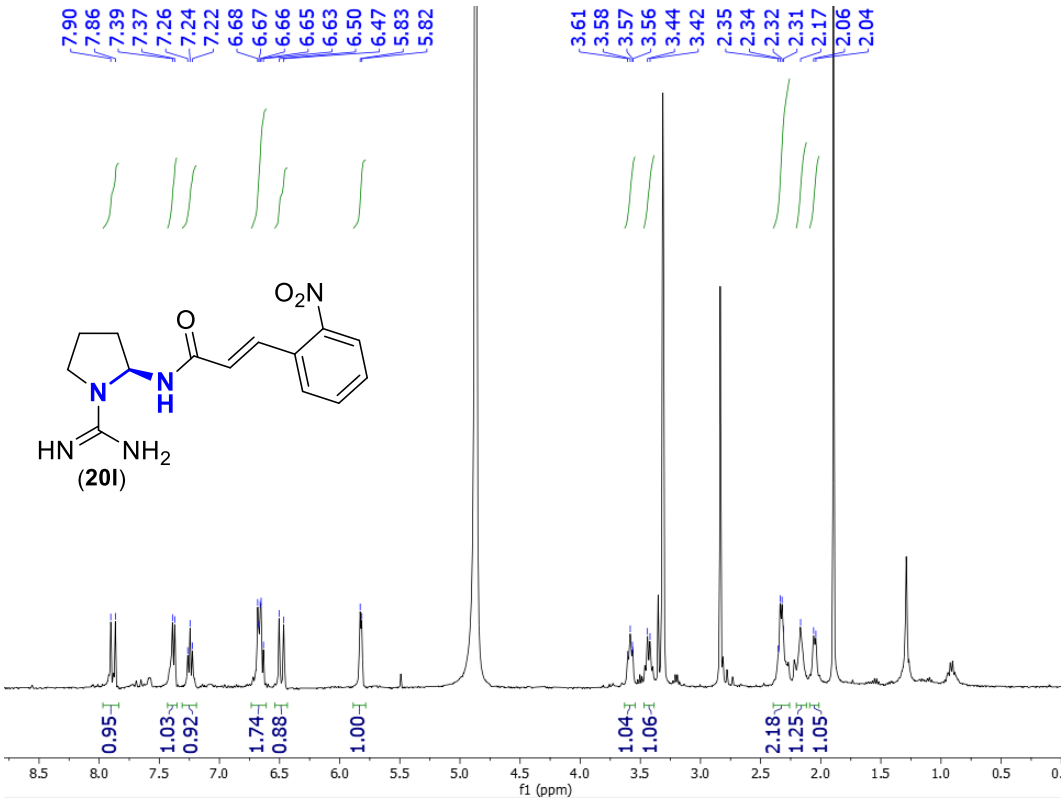


S.2.9.3. ESI-HRMS spectrum of compound **20k**

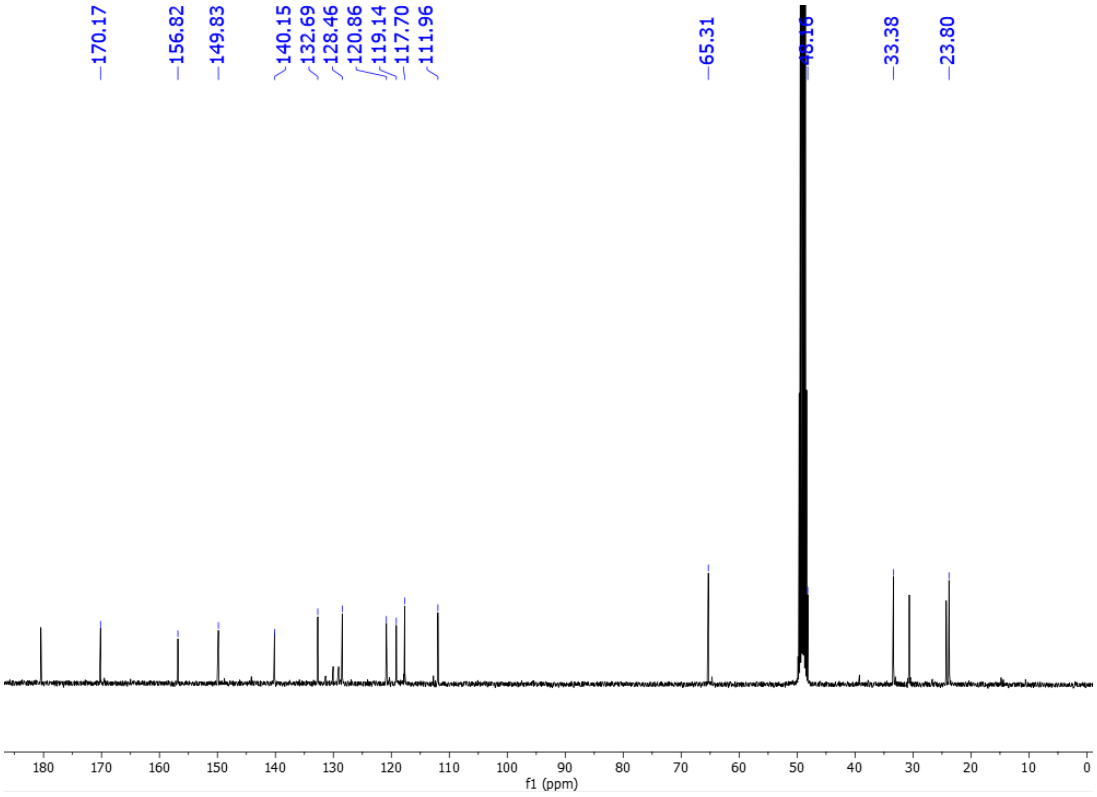


S.2.10. (*S,E*)-N-(1-carbamimidoylpyrrolidin-2-yl)-3-(2-nitrophenyl)acryl-amide (**20l**)

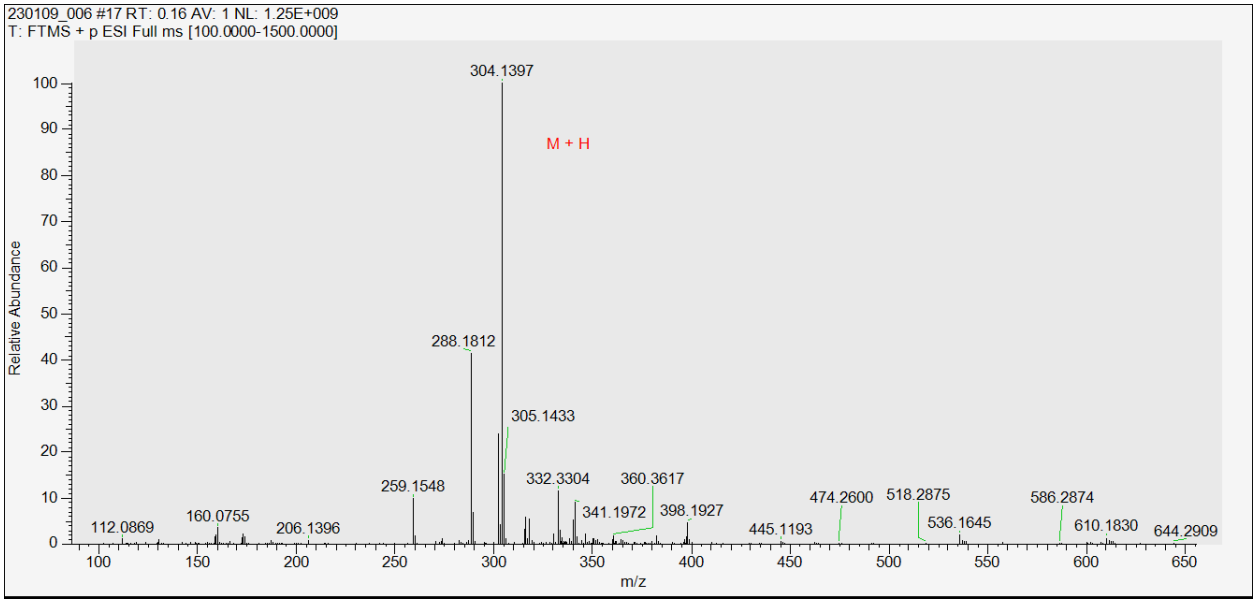
S.2.10.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **20l**



S.2.10.2. ^{12}C NMR (MeOD, 101 MHz) spectrum of compound **20l**

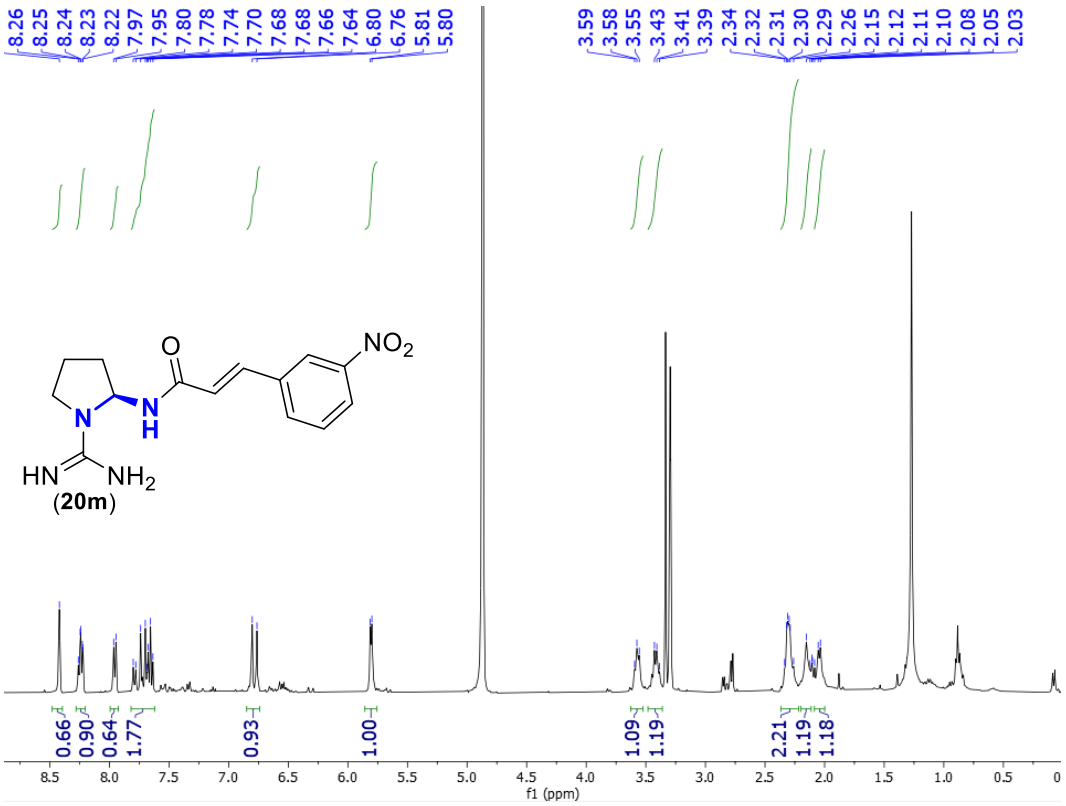


S.2.10.3 ESI-HRMS spectrum of compound **20l**

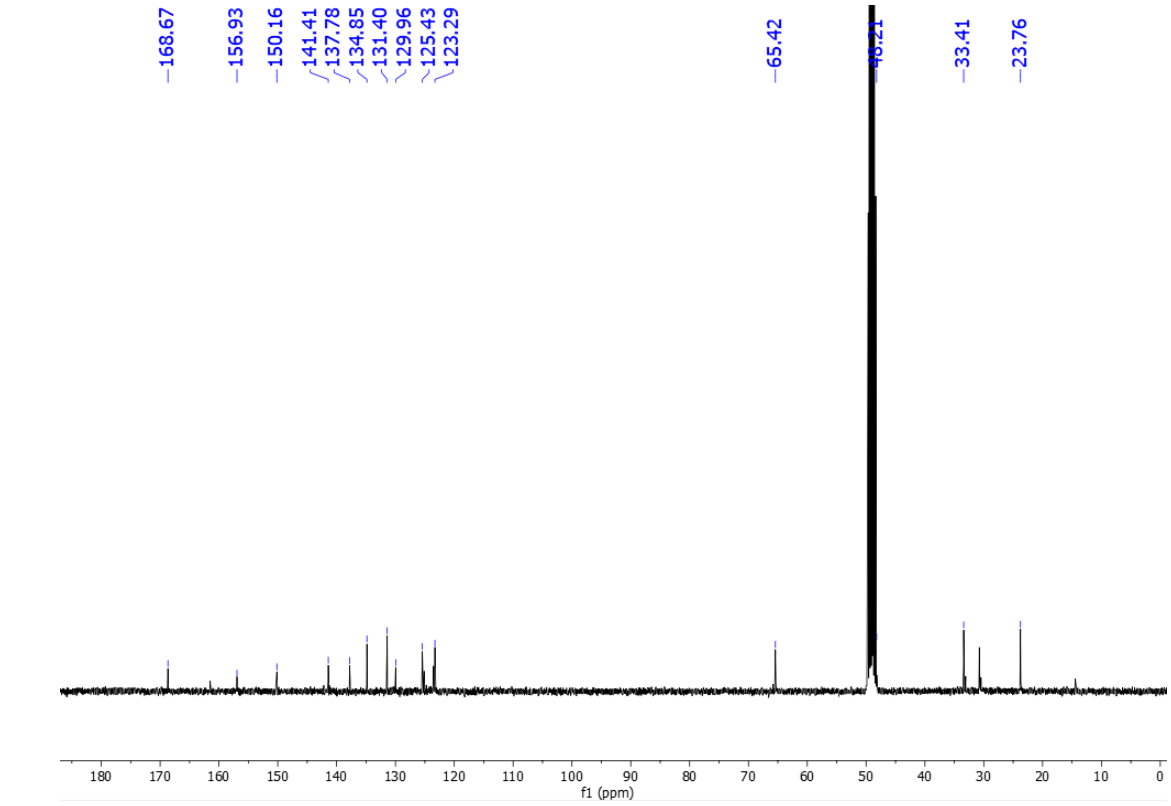


S.2.11. (*S,E*)-N-(1-carbamimidoylpyrrolidin-2-yl)-3-(3-nitrophenyl) acrylamide (20m)

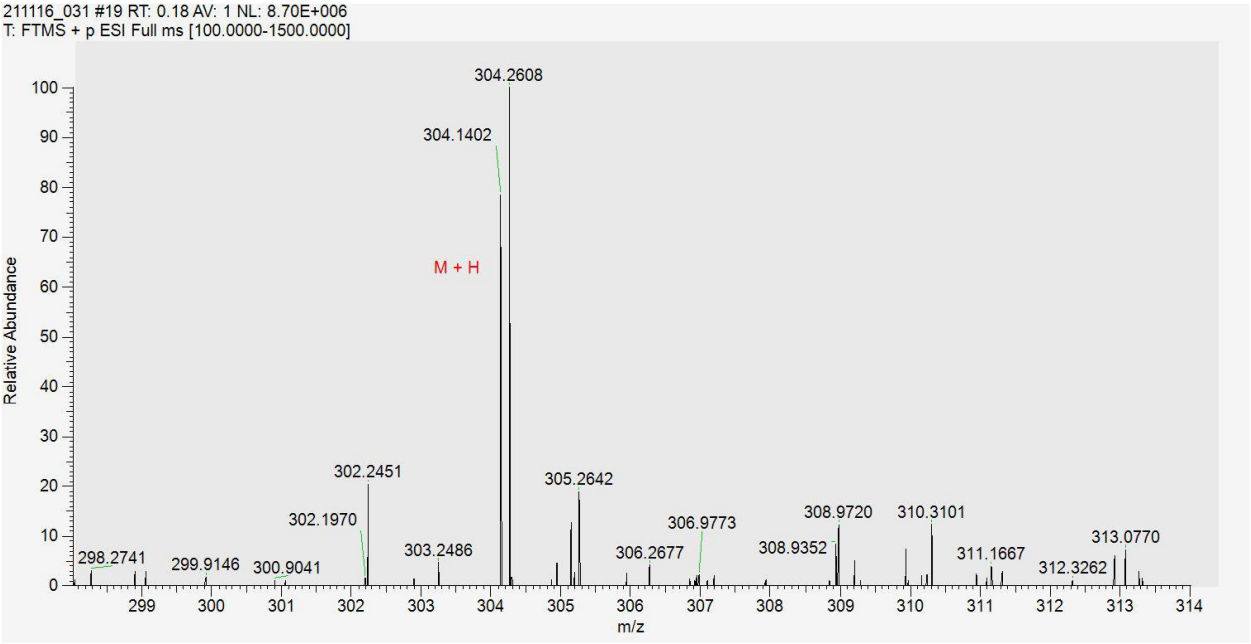
S.2.11.1 ^{1}H NMR (MeOD, 400 MHz) spectrum of compound 20m



S.2.11.2. ^{13}C NMR (MeOD, 100 MHz) spectrum of compound **20m**

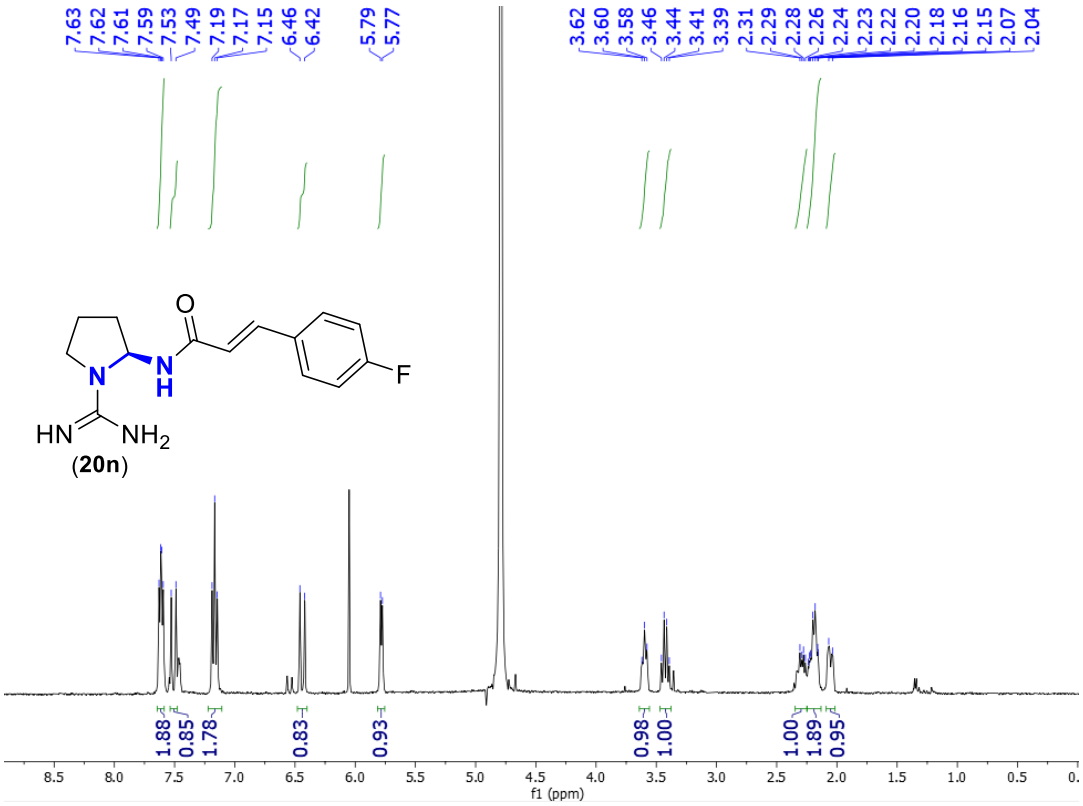


S.2.11.3. ESI-HRMS spectrum of compound **20m**

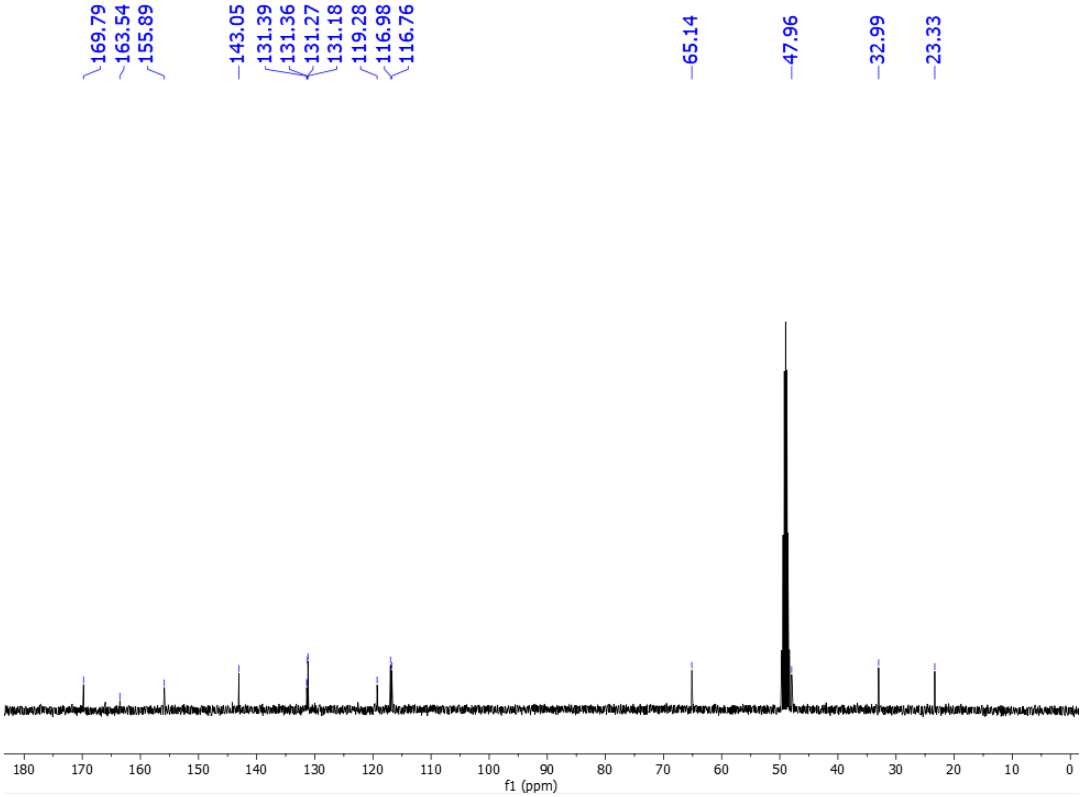


S.2.12. (*S,E*)-N-(1-carbamimidoylpyrrolidin-2-yl)-3-(4-fluorophenyl) acrylamide (**20n**)

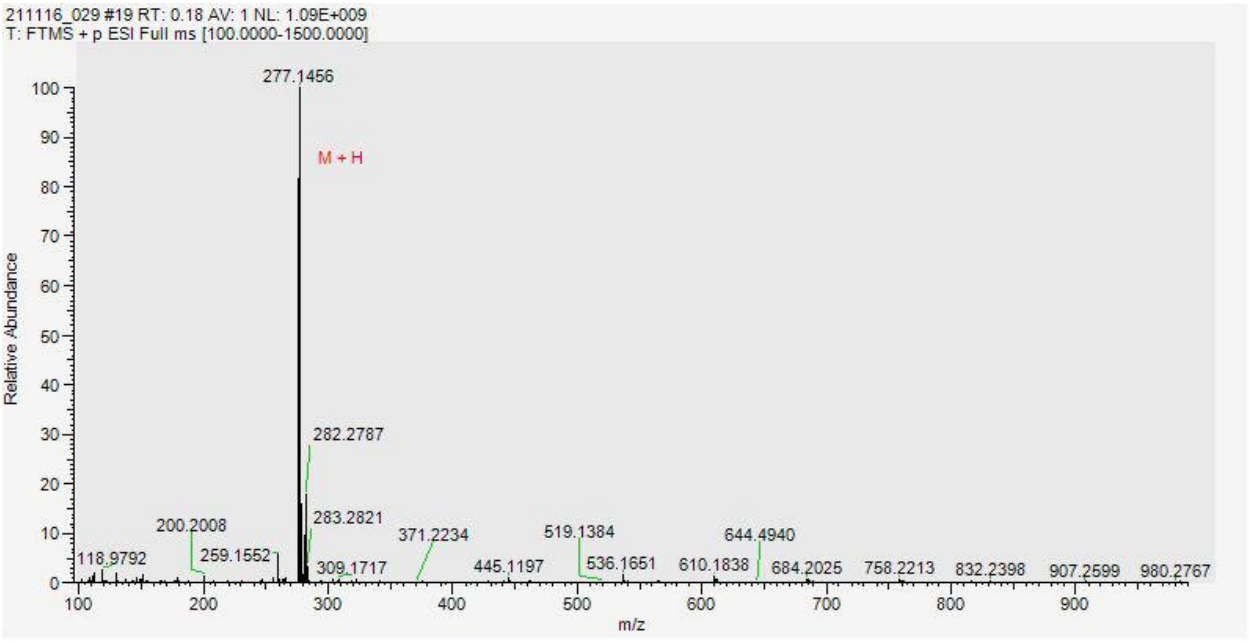
S.2.12.1. ^{1}H NMR (D_2O, 400 MHz) spectrum of compound **20n**



S.2.12.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **20n**

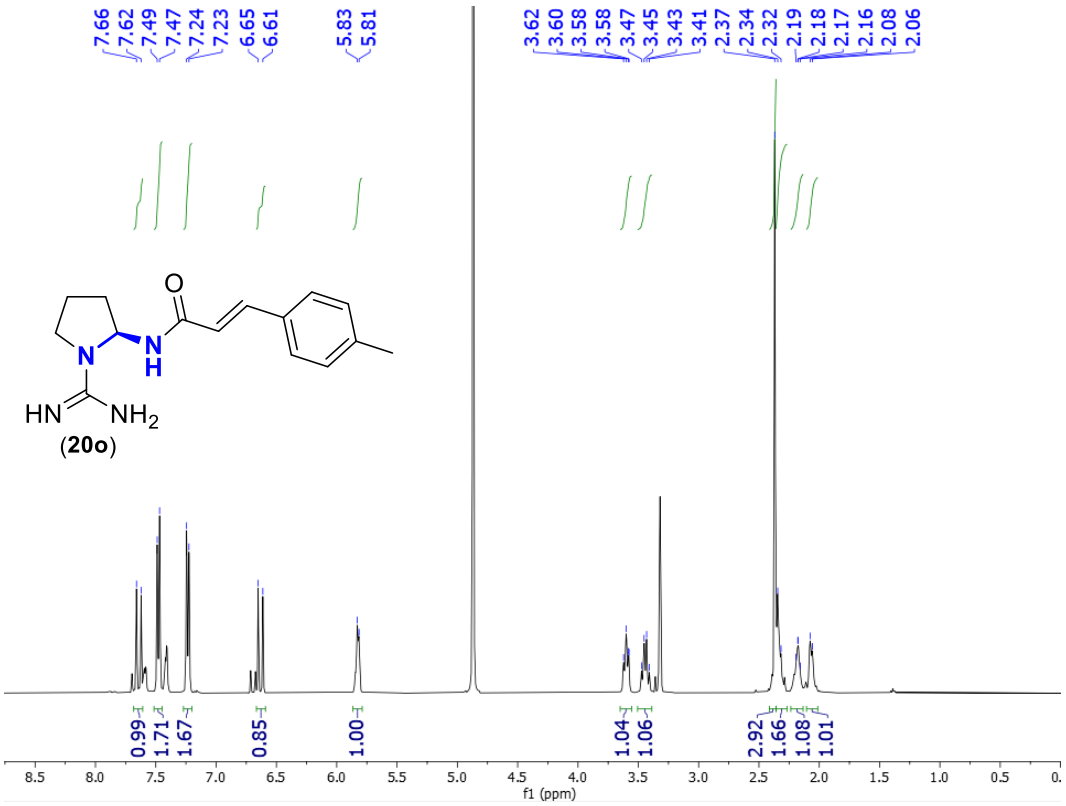


S.2.12.3. ESI-HRMS spectrum of compound **20n**

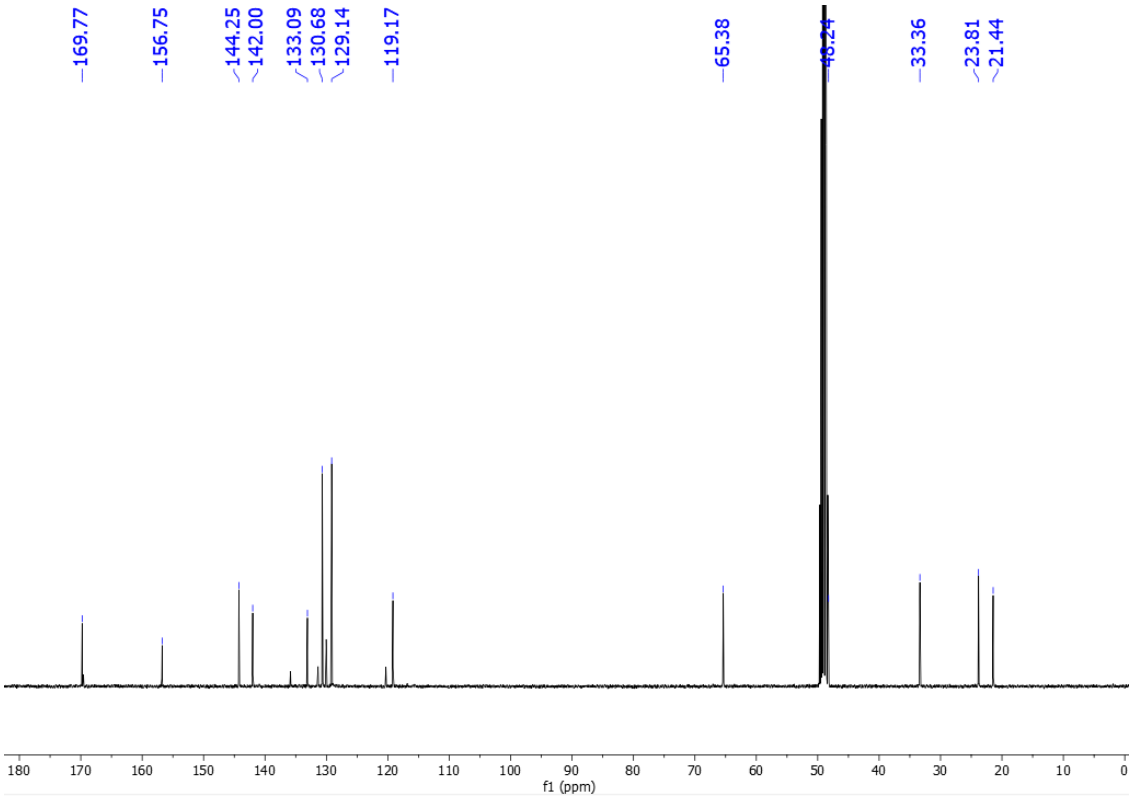


S.2.13. (*S,E*)-N-(1-carbamimidoylpyrrolidin-2-yl)-3-(p-tolyl) acrylamide (**20o**)

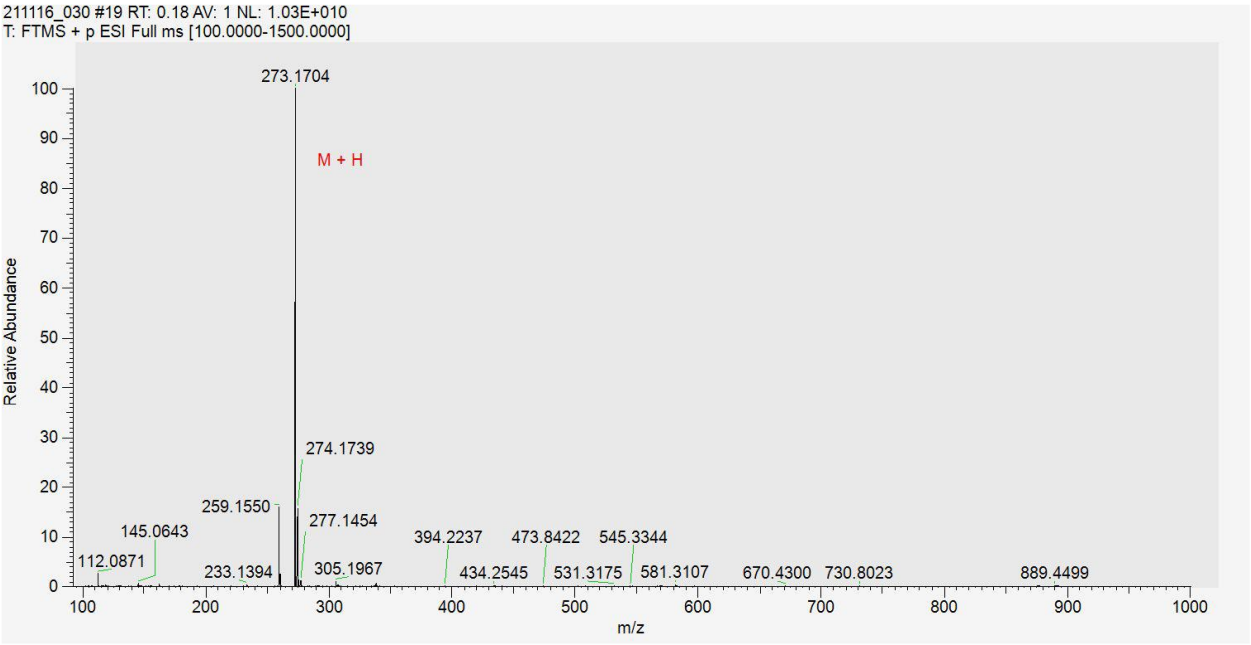
S.2.13.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **20o**



S.2.13.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **20o**

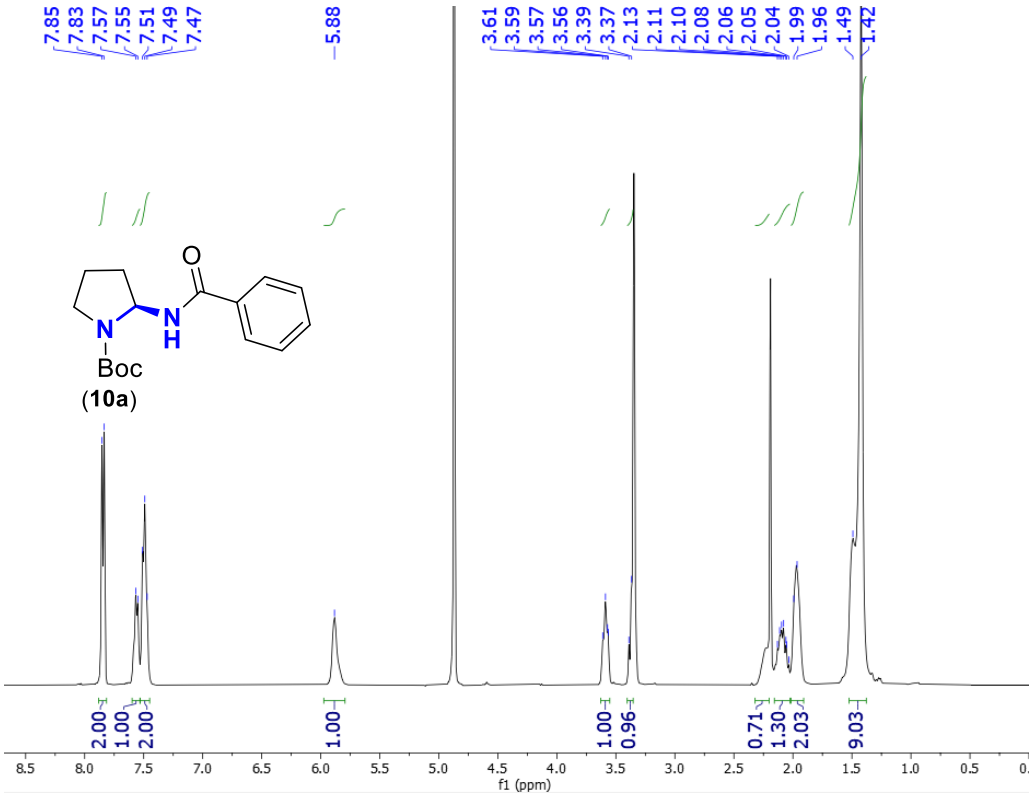


S.2.13.3. ESI-HRMS spectrum of compound **20o**

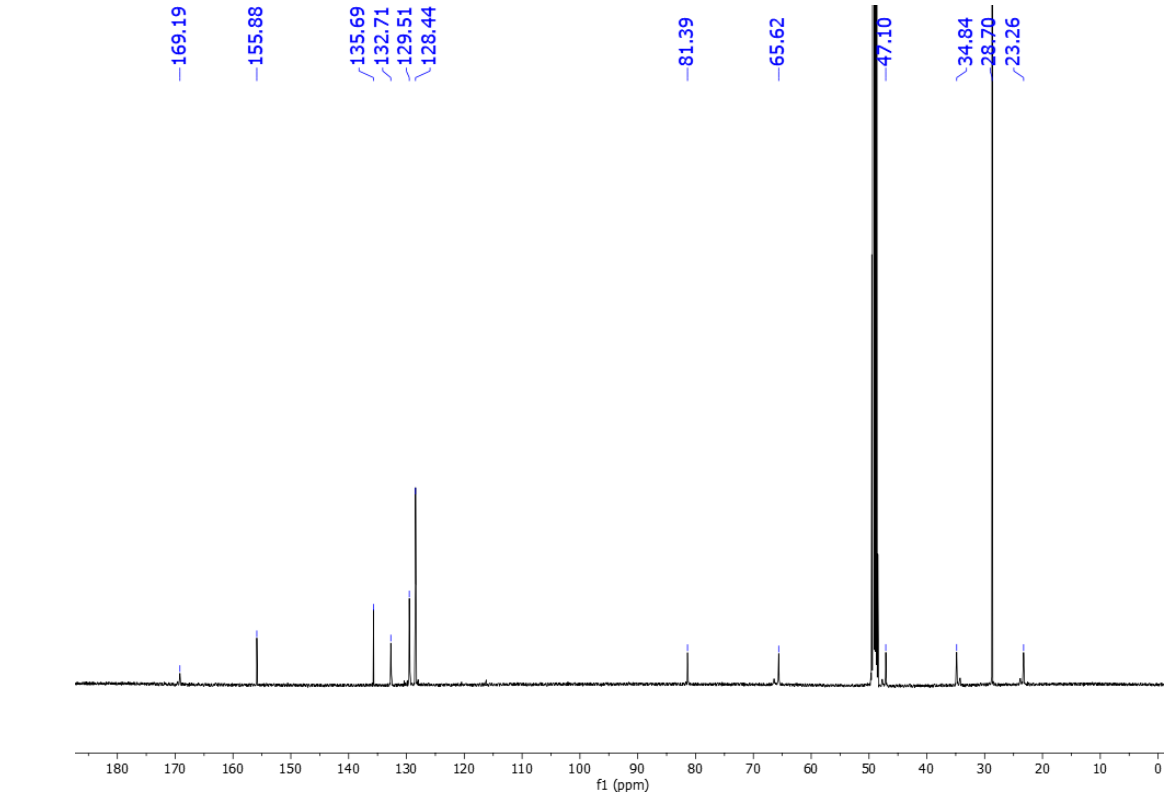


S.2.14. *tert*-Butyl (*S*)-2-benzamidopyrrolidine-1-carboxylate (**10a**)

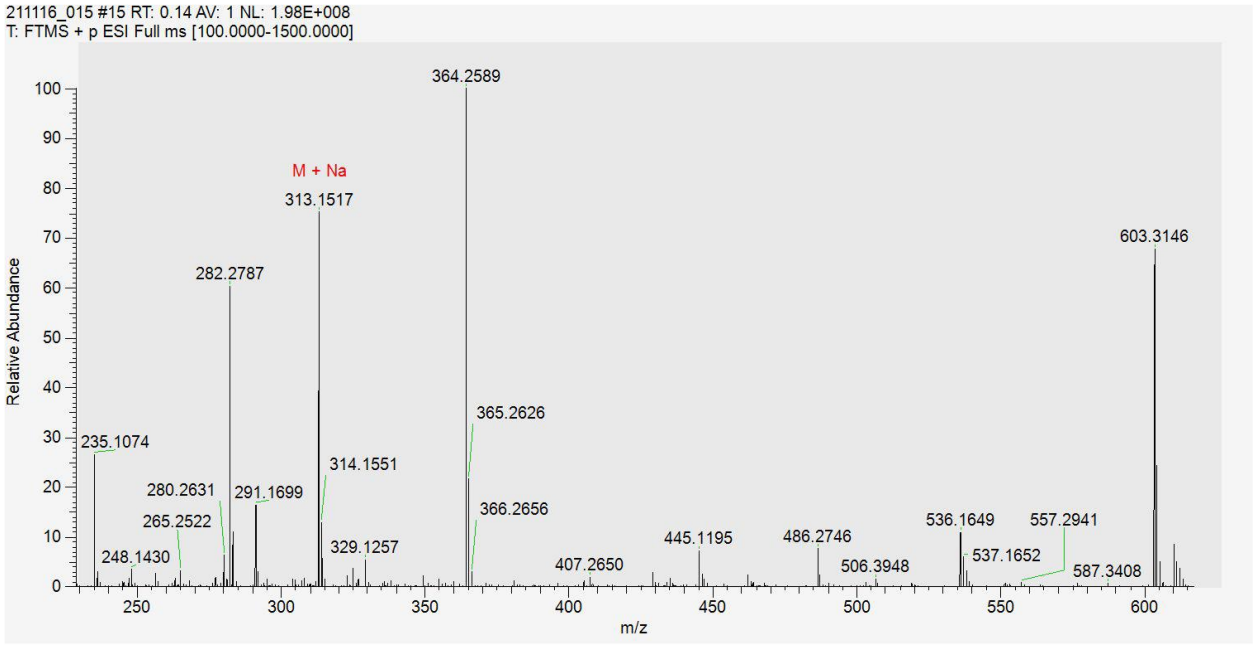
S.2.14.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **10a**



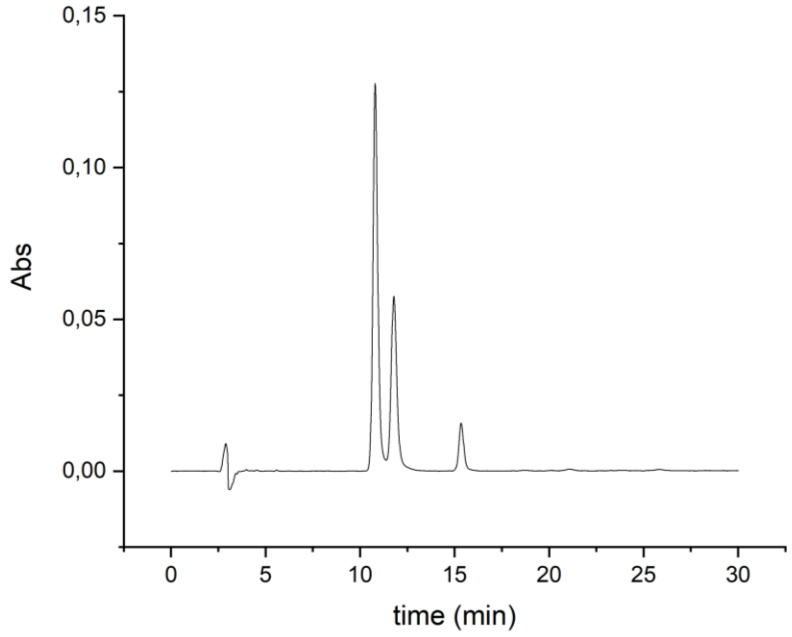
S.2.14.2. ^{13}C NMR (MeOD, 101MHz) spectrum of compound **10a**



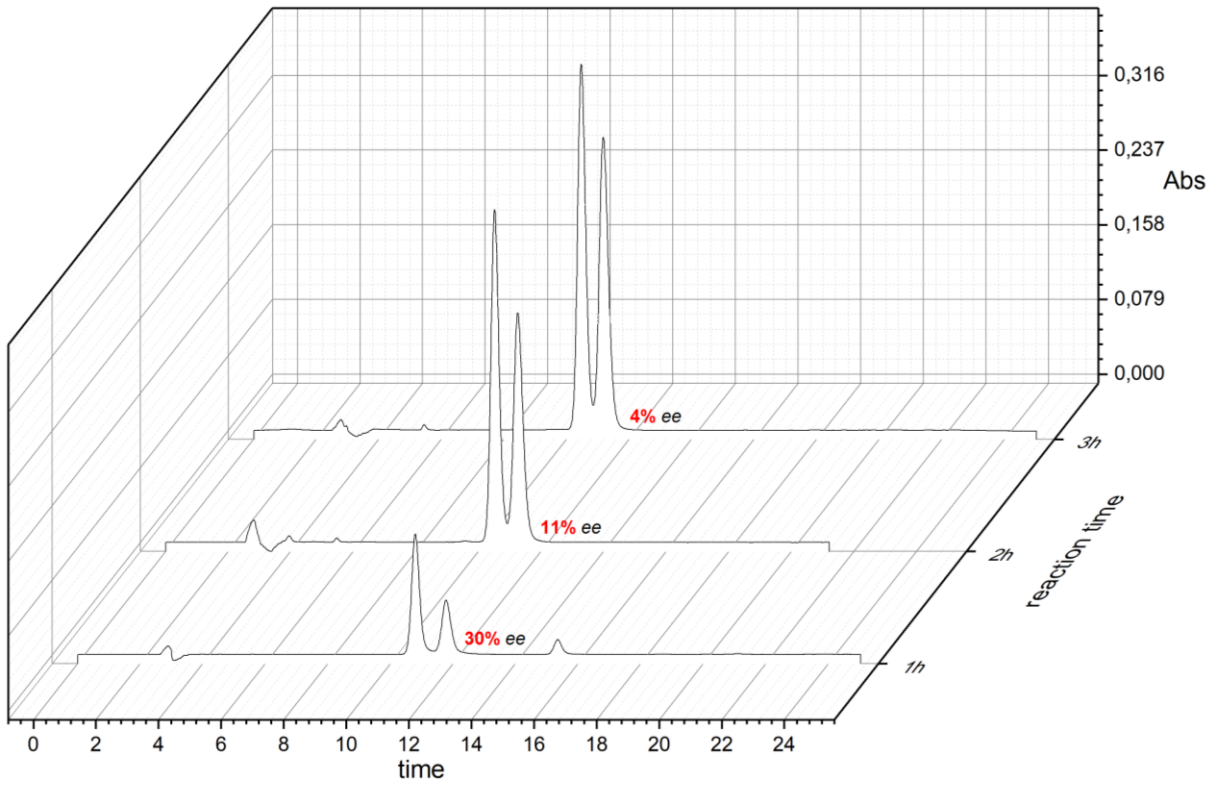
S.2.14.3. ESI-HRMS spectrum of compound **10a**



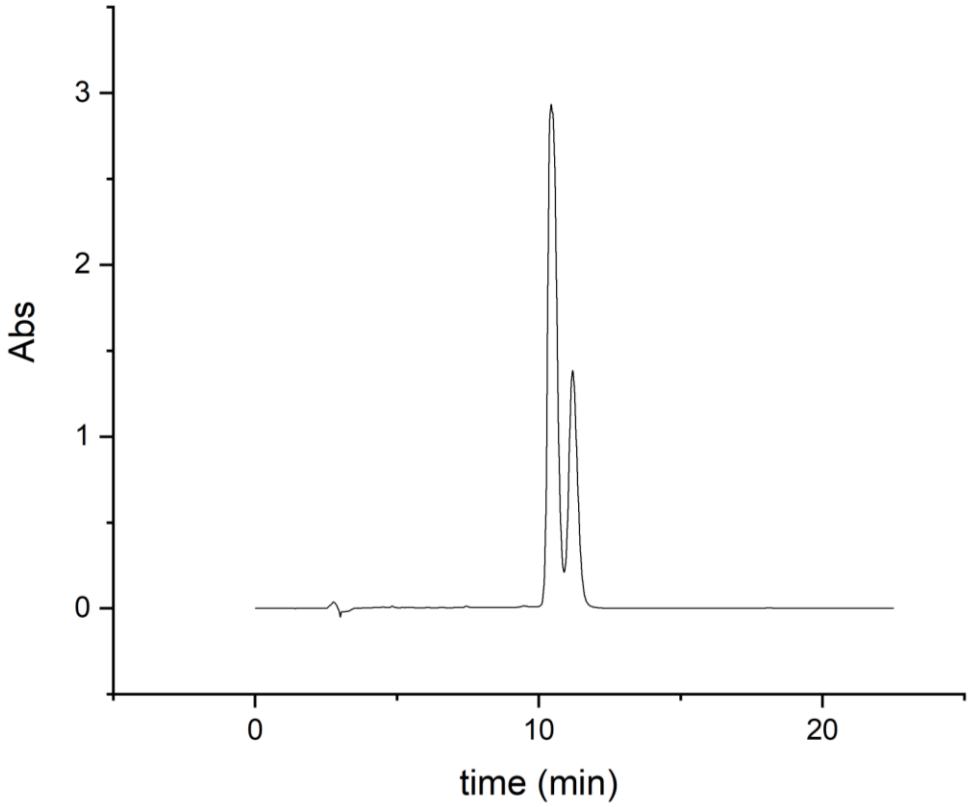
S.2.14.4. Chiral HPLC chromatogram of compound **10a** via PhMgBr



S.2.14.5. Chromatogram of the enantiomeric excess changes at different reaction times for the synthesis of **10a**. The separation was performed on a Phenomenex Lux 5 µm Cellulose-2 column.

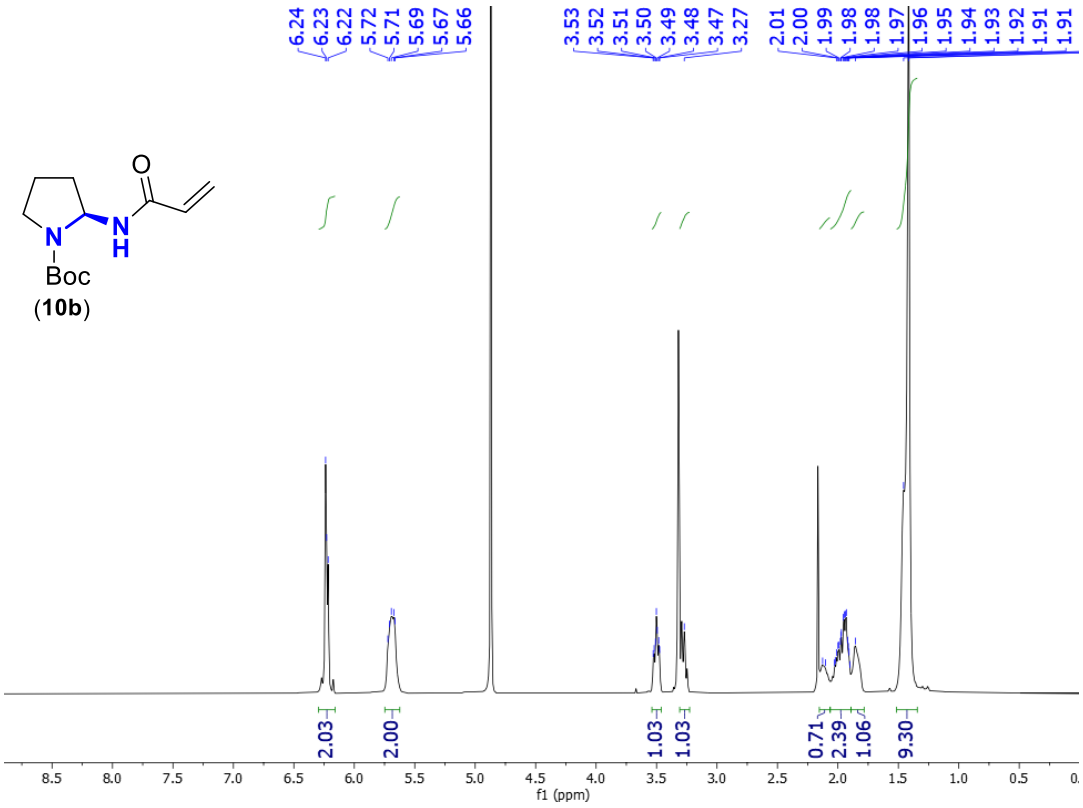


S.2.14.6. Chiral HPLC chromatogram of compound **10a** via PhLi

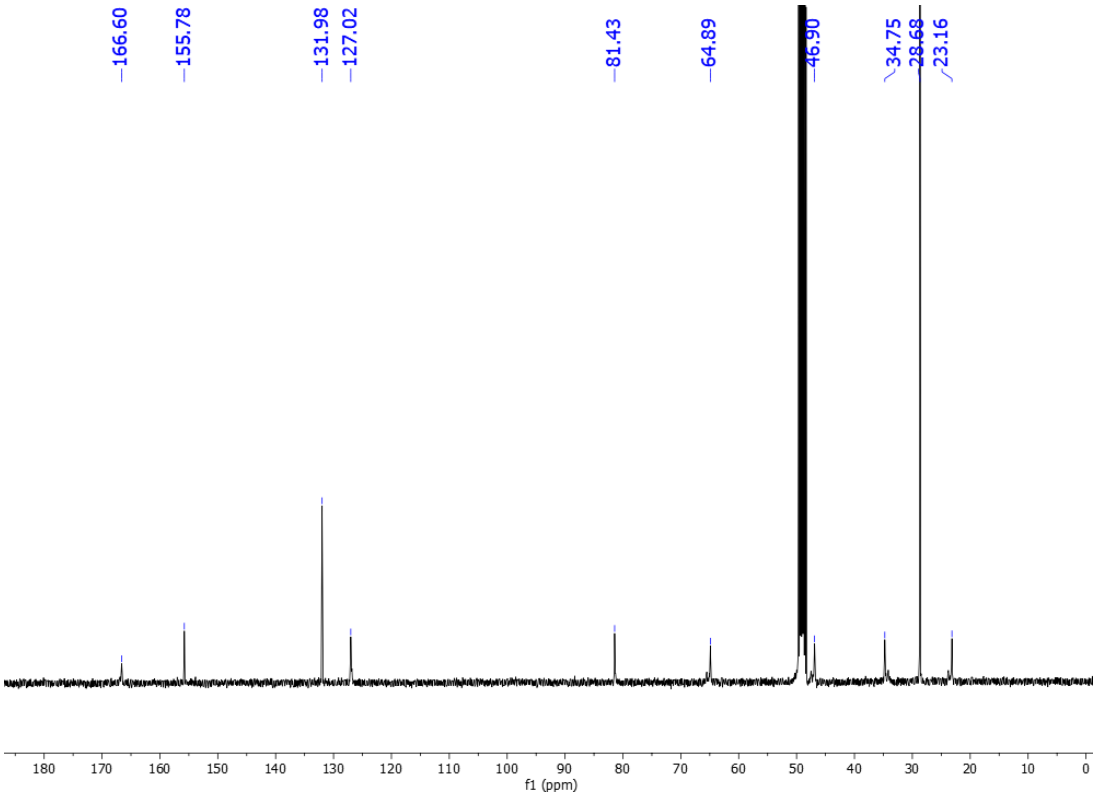


S.2.15. *tert*-Butyl (*S*)-2-acrylamidopyrrolidine-1-carboxylate (**10b**)

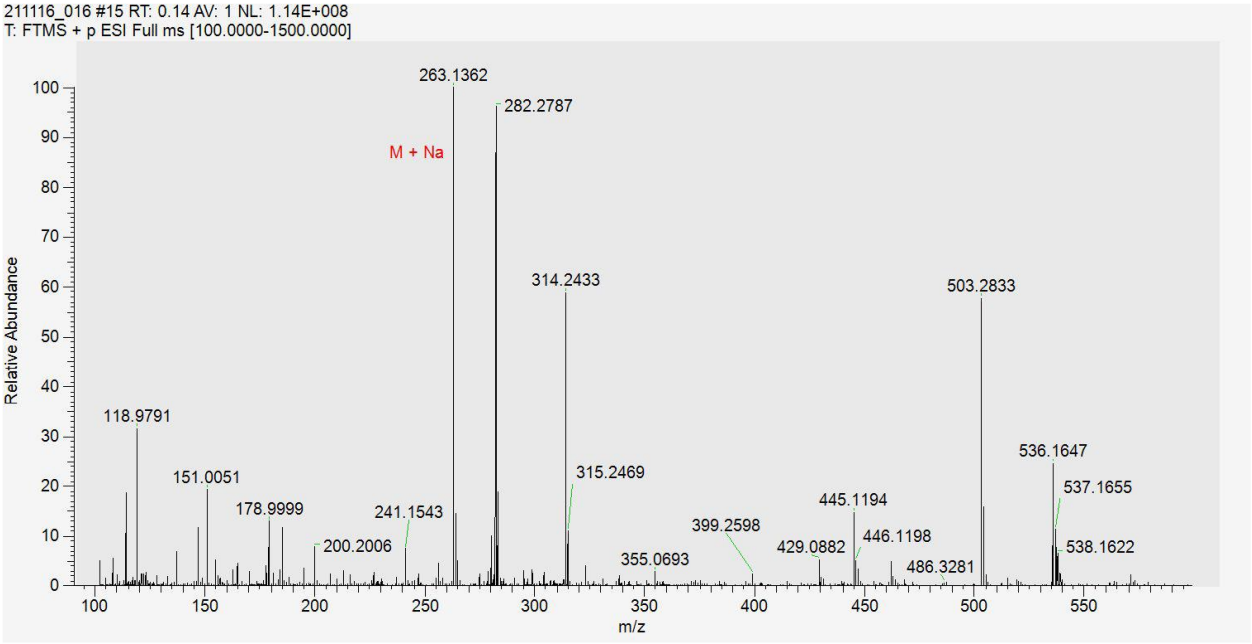
S.2.15.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **10b**



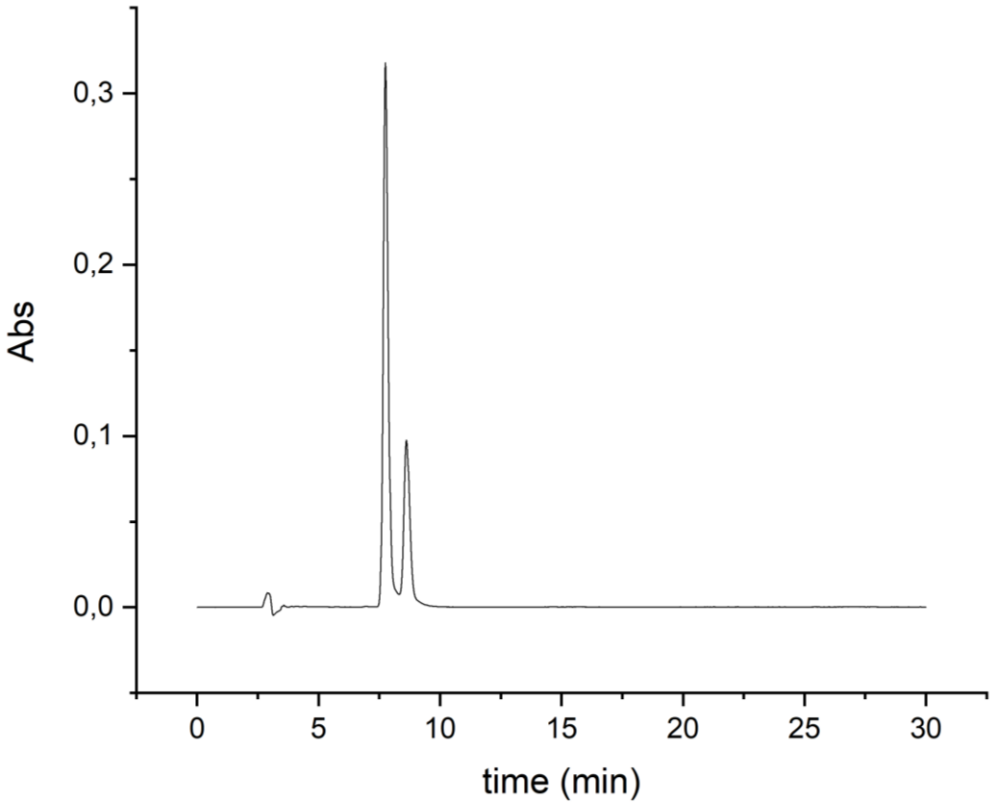
S.2.15.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **10b**



S.2.15.3. ESI-HRMS spectrum of compound **10b**

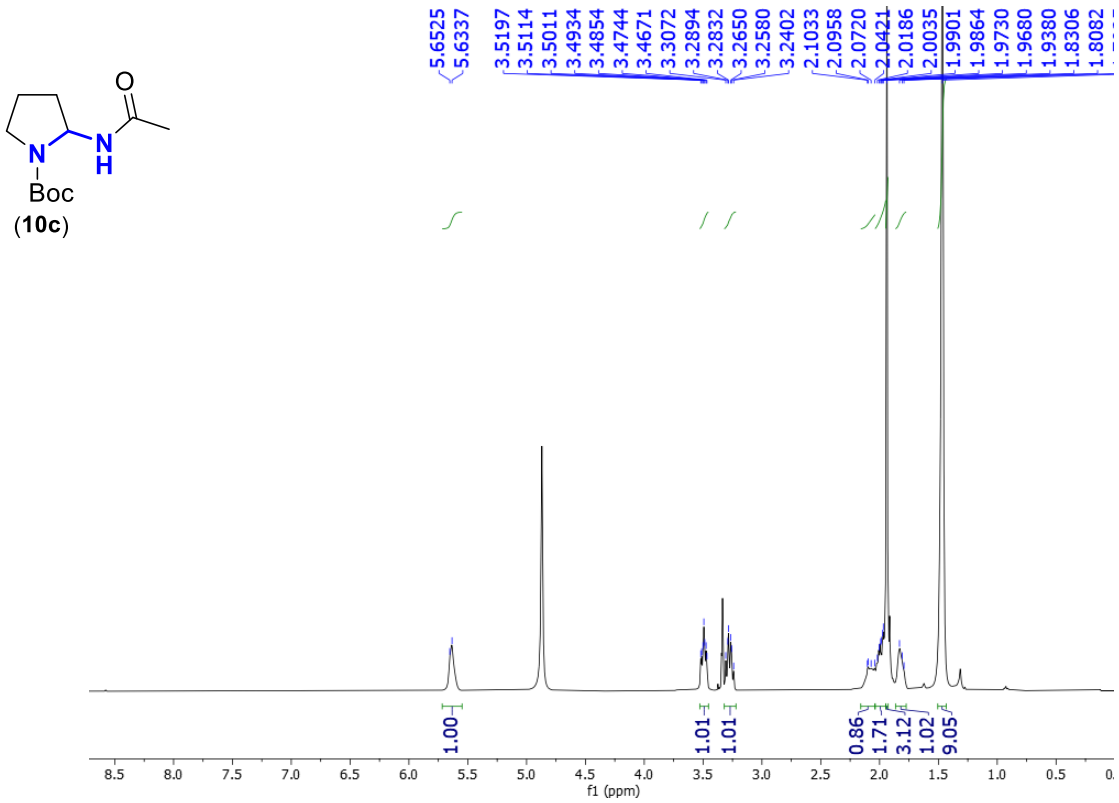


S.2.15.4. Chiral HPLC chromatogram of compound 10b

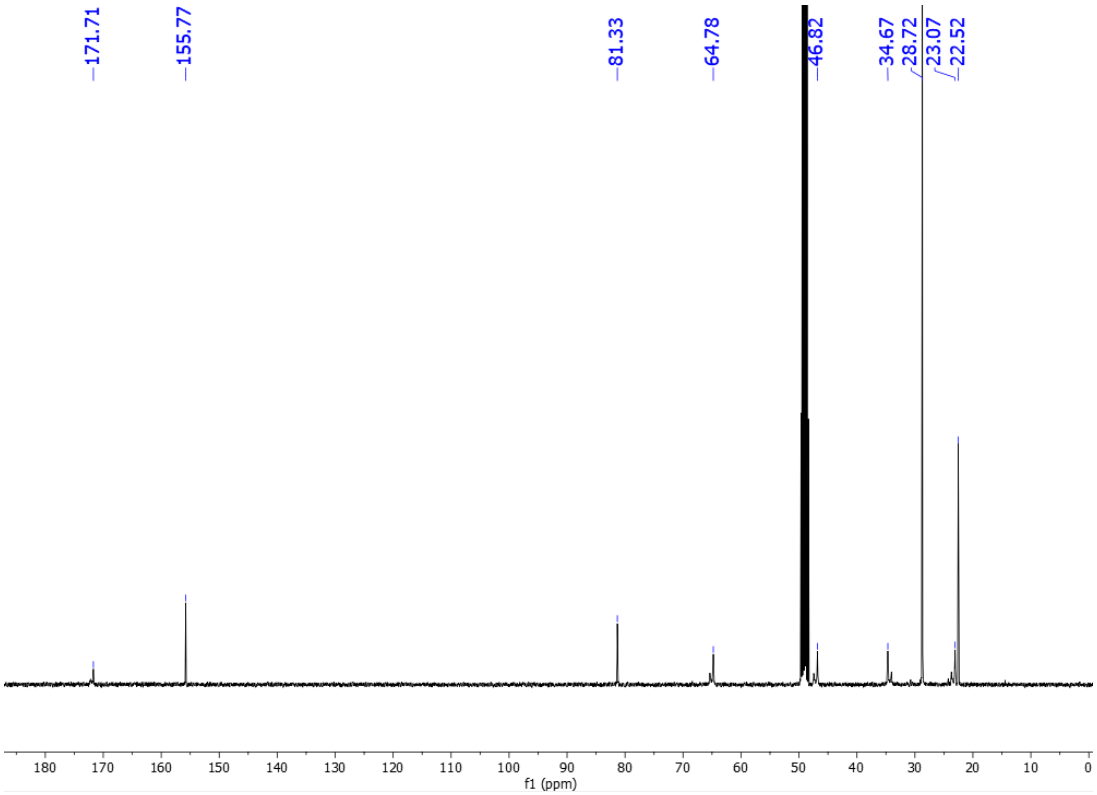


S.2.16. *tert*-Butyl 2-acetamidopyrrolidine-1-carboxylate (10c)

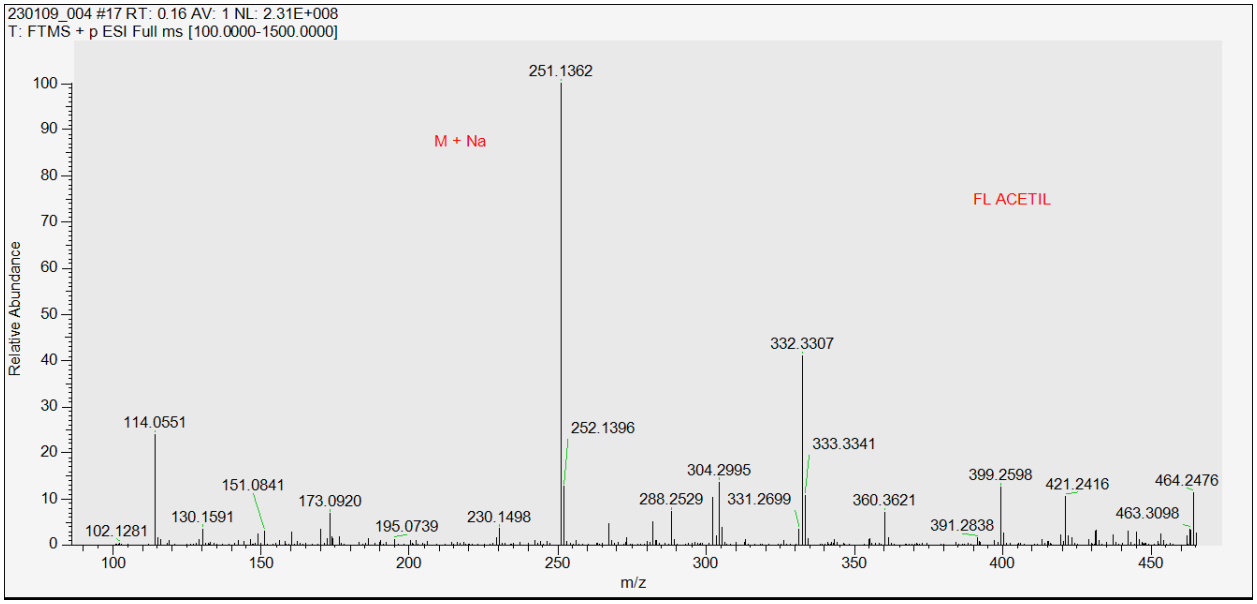
S.2.16.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound 10c



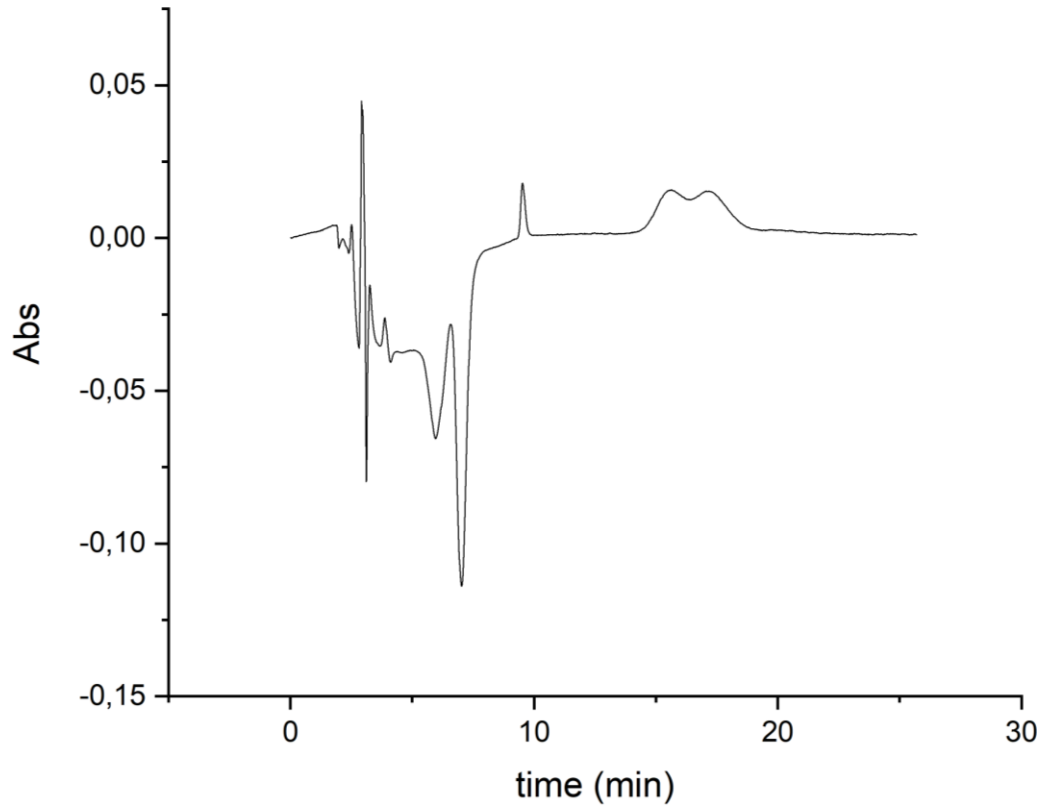
S.2.16.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **10c**



S.2.16.3. ESI-HRMS spectrum of compound **10c**



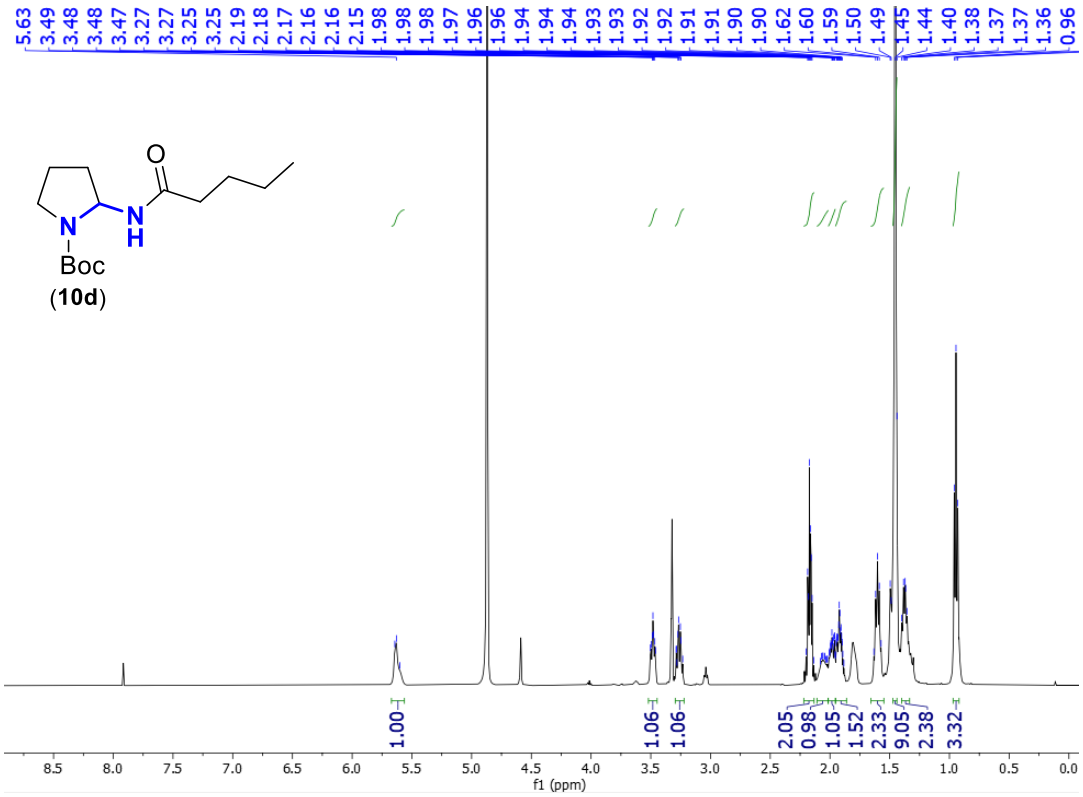
S.2.16.4. Chiral HPLC chromatogram of compound **10c**



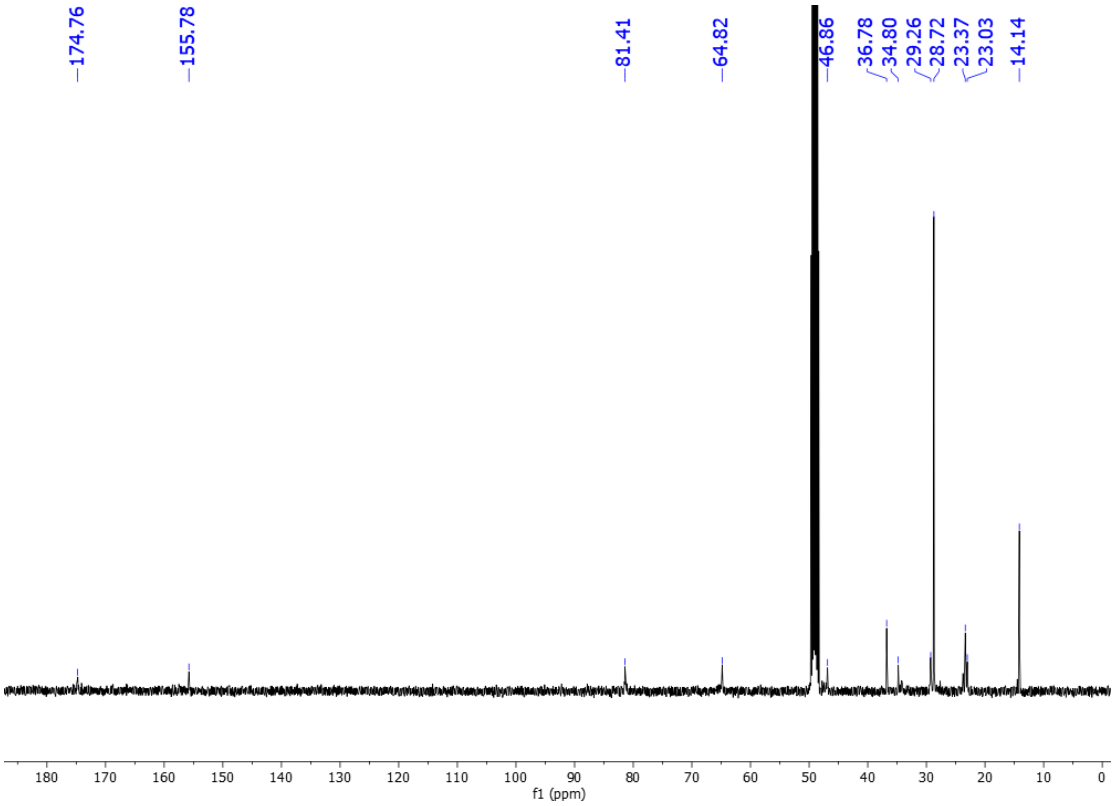
The poor definition of the chromatogram spectra is related to the instability and highly polar nature of compound **10c**, categorized as an aliphatic aminal.

S.2.17. *tert*-Butyl 2-pentanamidopyrrolidine-1-carboxylate (10d)

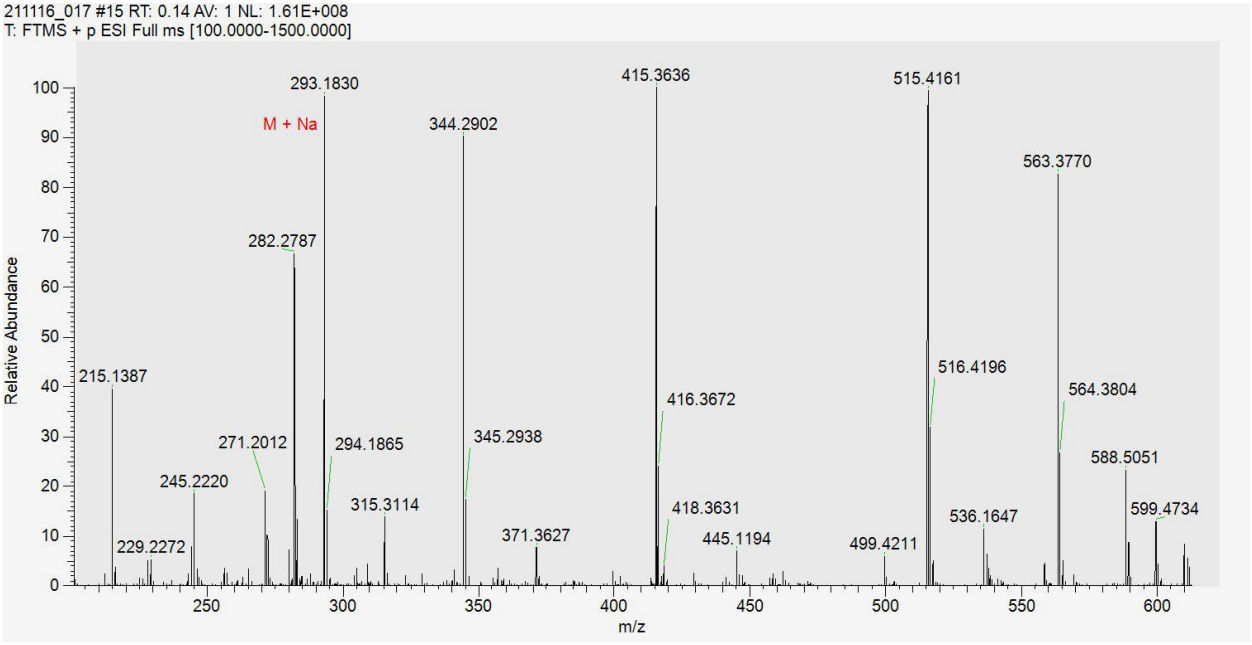
S.2.17.1. ^{1}H NMR (MeOD, 500 MHz) spectrum of compound 10d



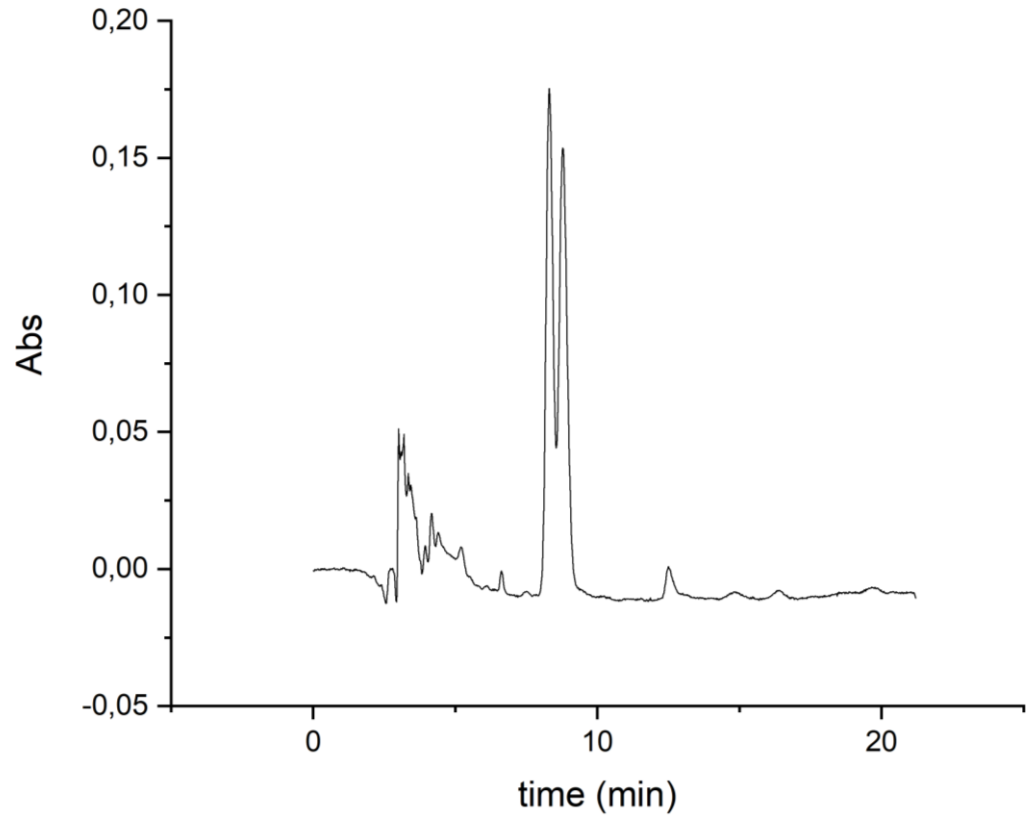
S.2.17.2. ^{13}C NMR (MeOD, 125 MHz) spectrum of compound **10d**



S.2.17.3. ESI-HRMS spectrum of compound **10d**

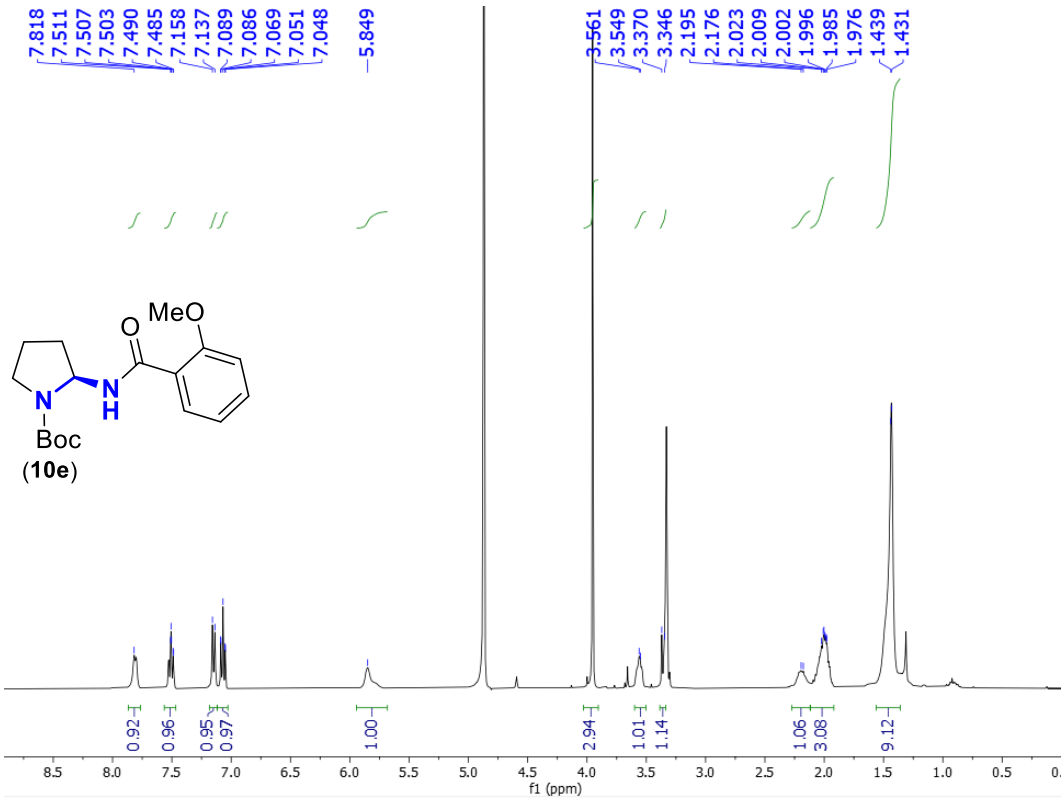


S.2.17.4. Chiral HPLC chromatogram of compound **10d**

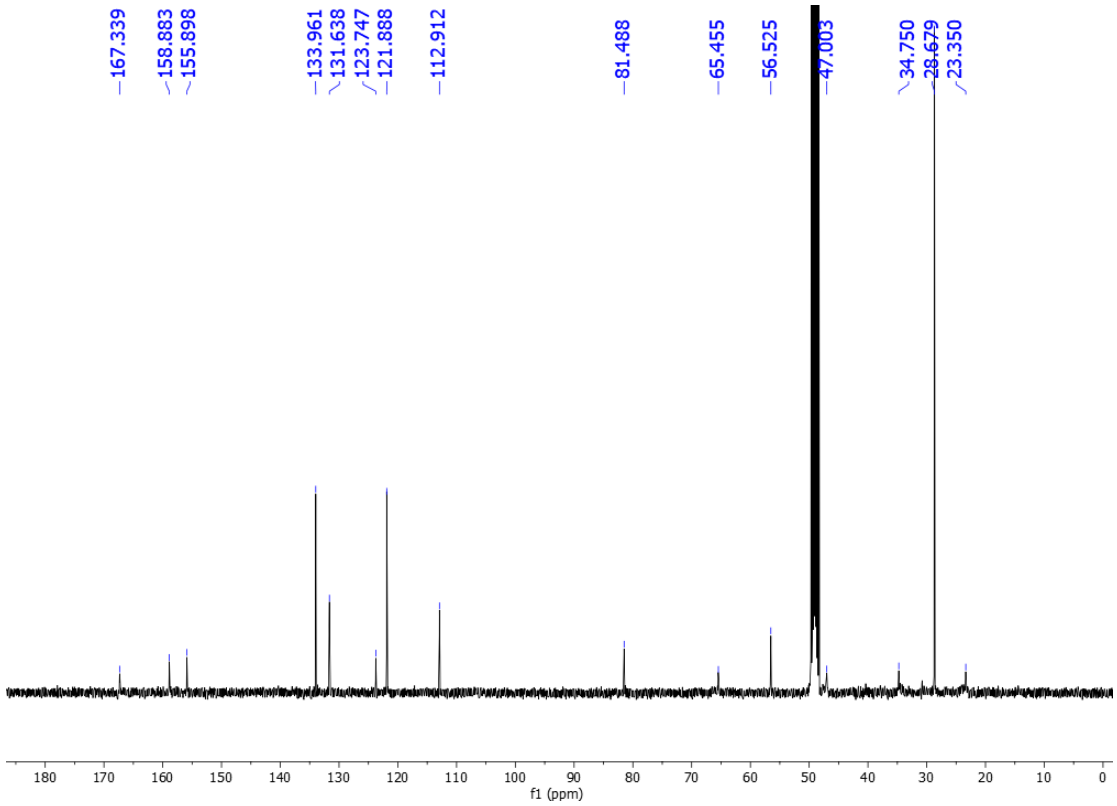


S.2.18. *tert*-Butyl (*S*)-2-(2-methoxybenzamido)pyrrolidine-1-carboxylate (**10e**)

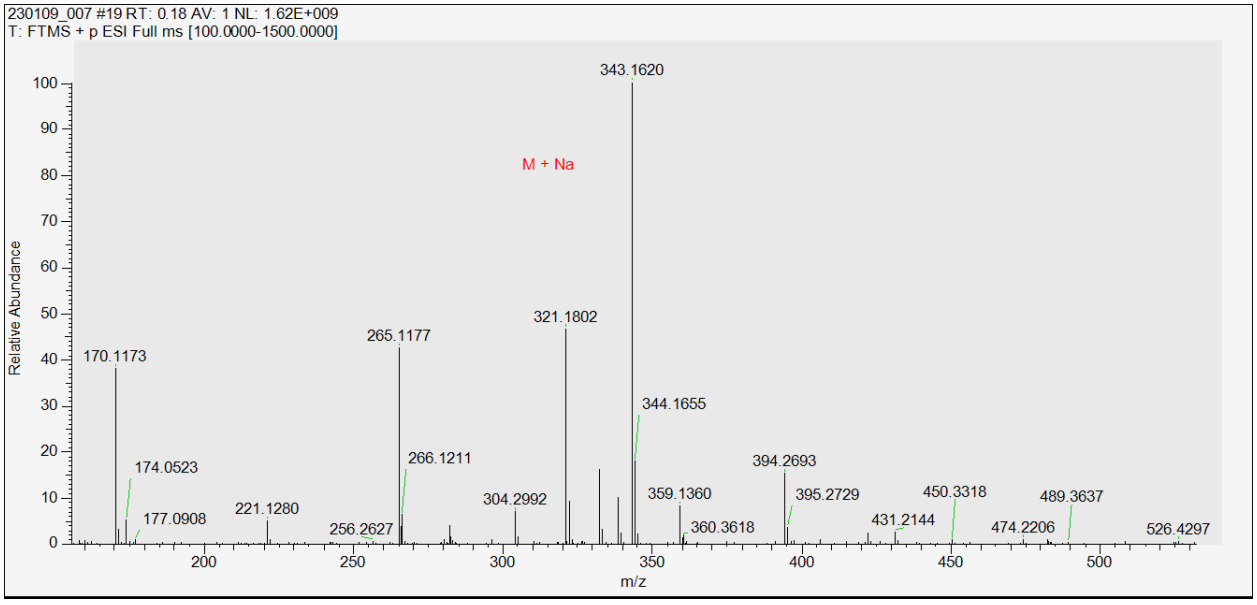
S.2.18.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **10e**



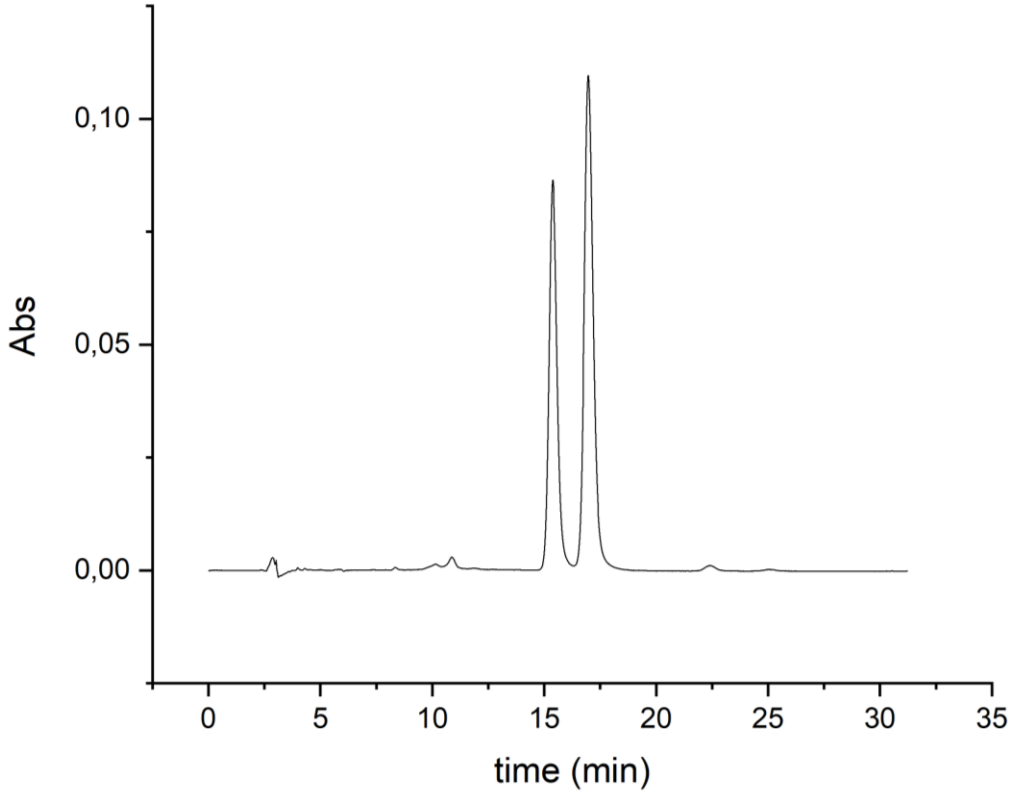
S.2.18.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **10e**



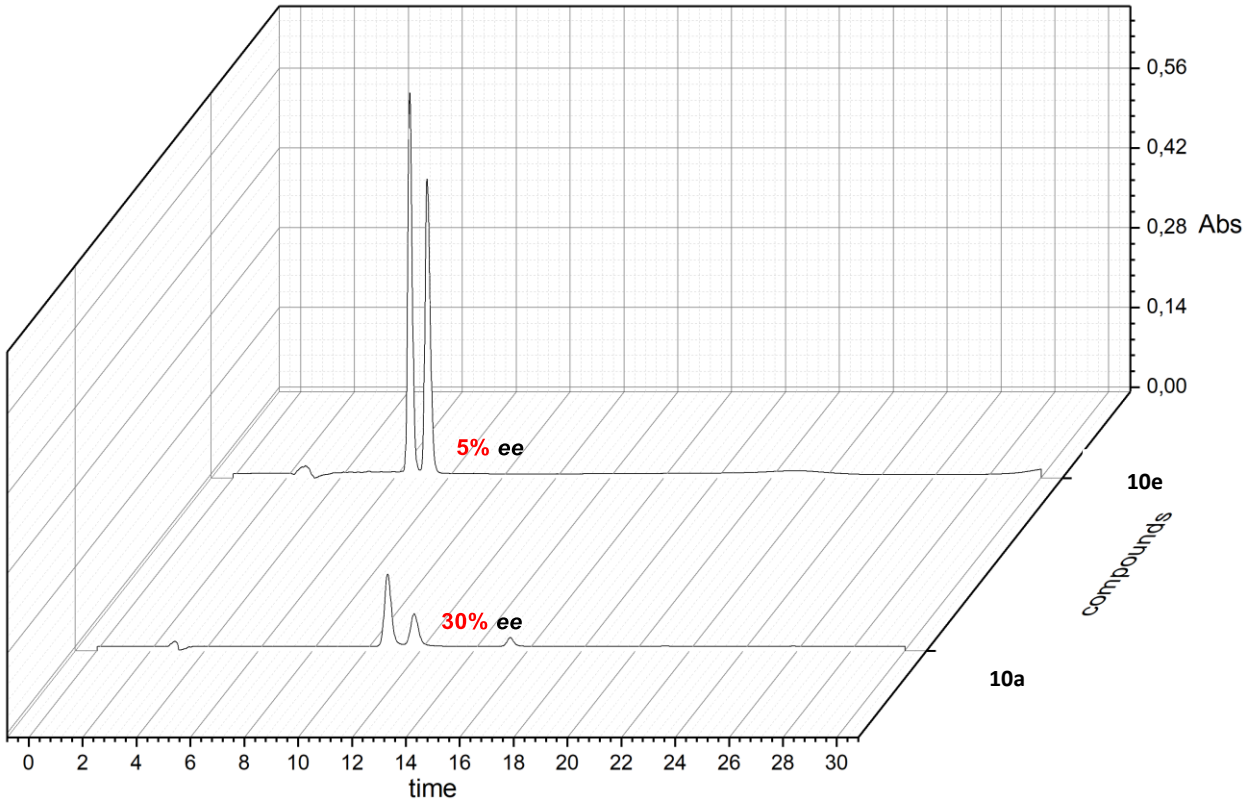
S.2.18.3. ESI-HRMS spectrum of compound **10e**



S.2.18.4. Chiral HPLC spectrum of compound 10e

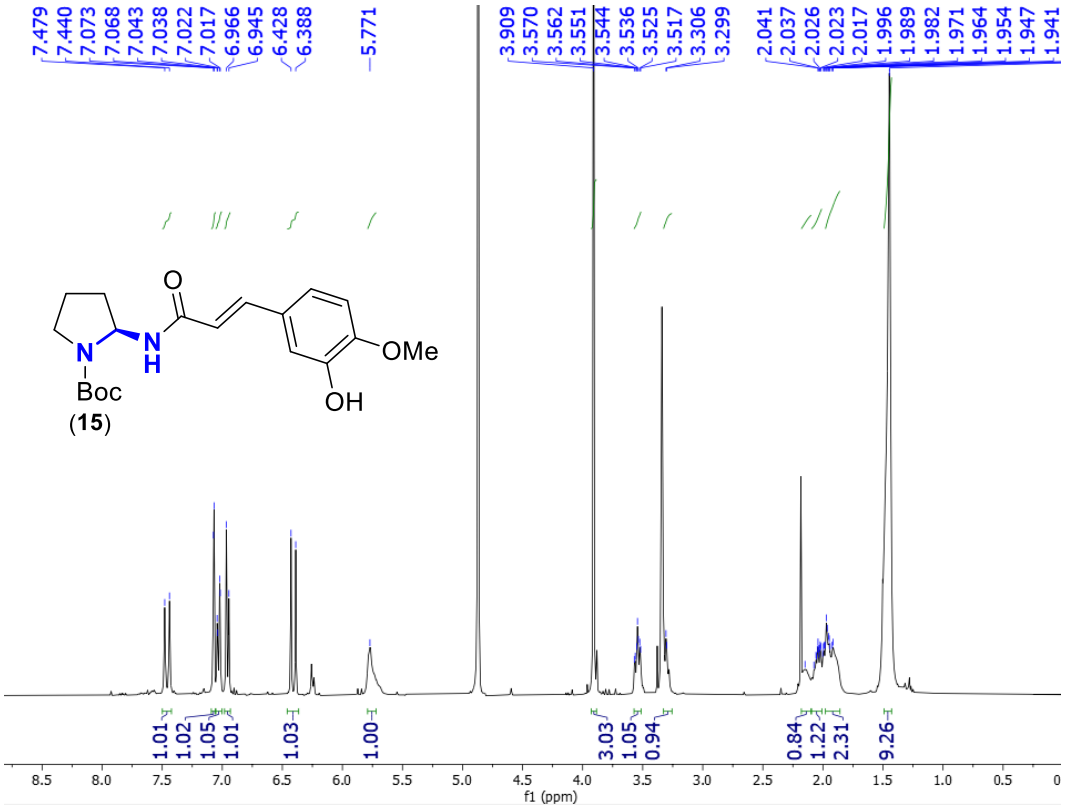


S.2.18.5. Influence of ortho-directing groups: Chromatogram of the enantiomeric excess of compounds at **10a** and **10e**. The separation was performed on a Phenomenex Lux 5 µm Cellulose-2 column.

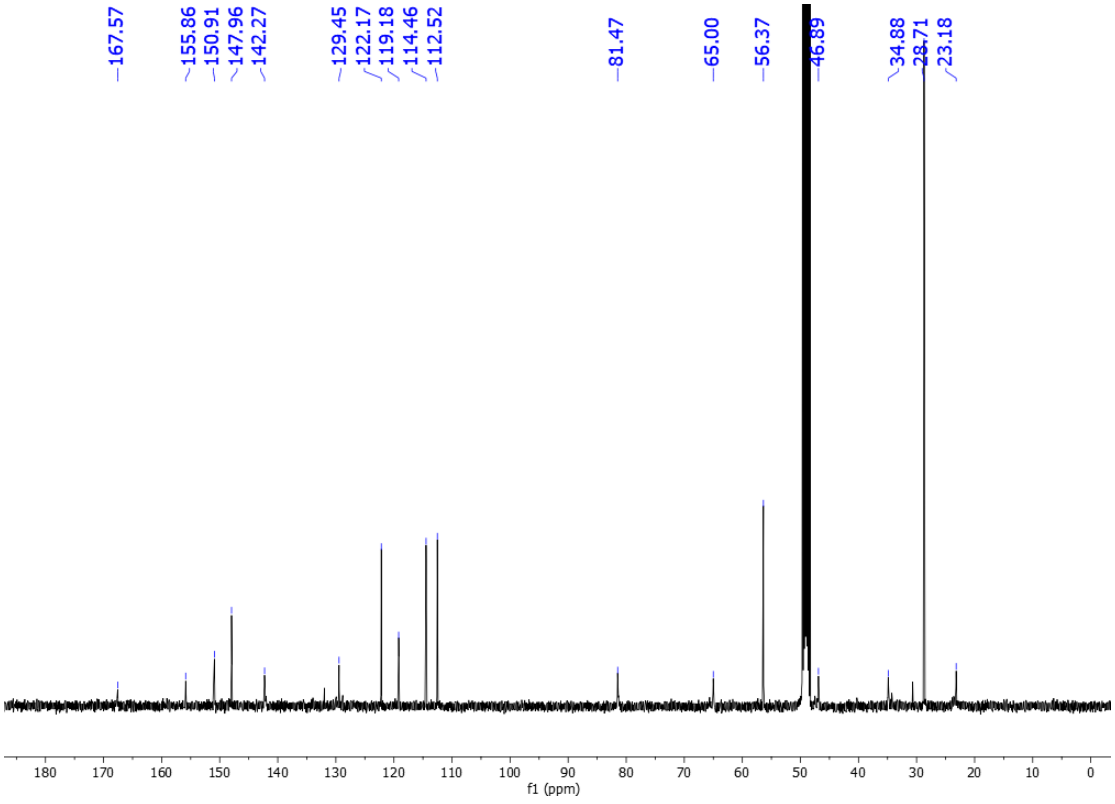


S.2.19. *tert*-Butyl (*S,E*)-2-(3-(3-hydroxy-4-methoxyphenyl) acrylamido) pyrrolidine-1-carboxylate (**15**)

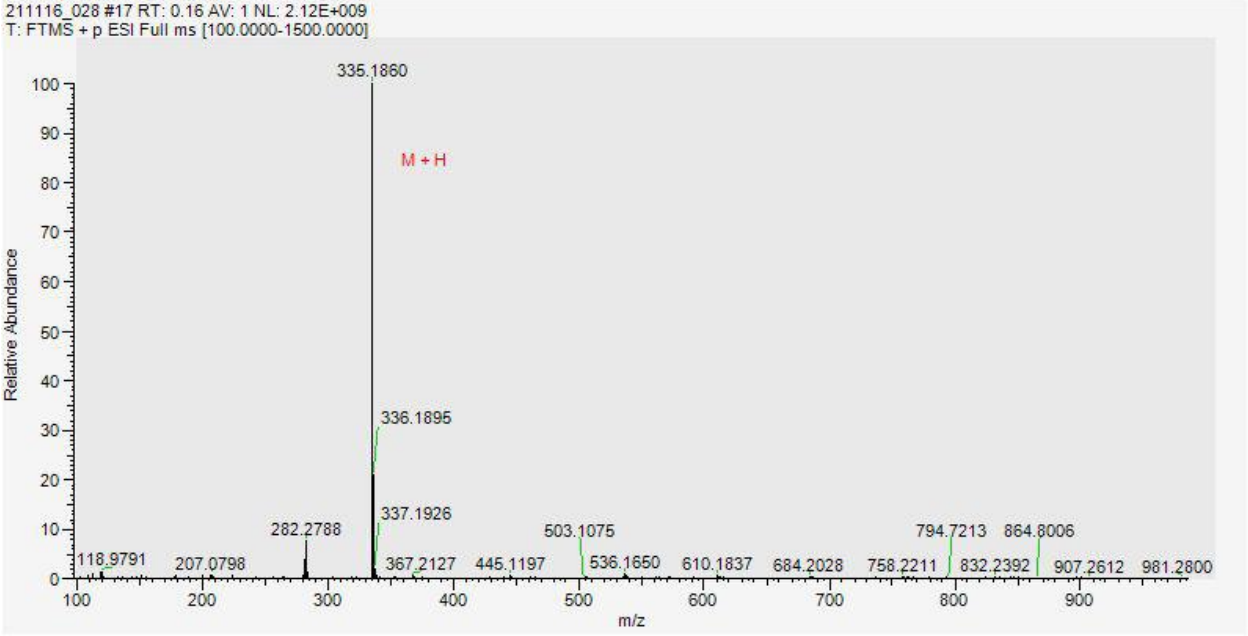
S.2.19.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **15**



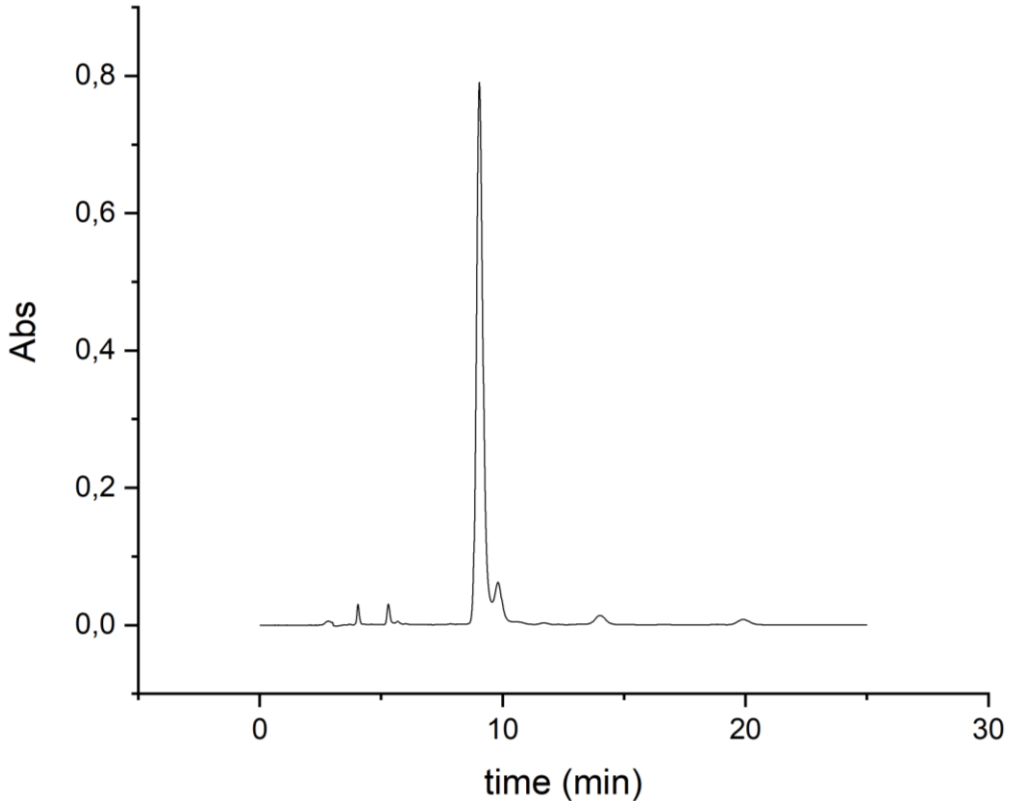
S.2.19.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **15**



S.19.3. ESI-HRMS spectrum of compound **15**

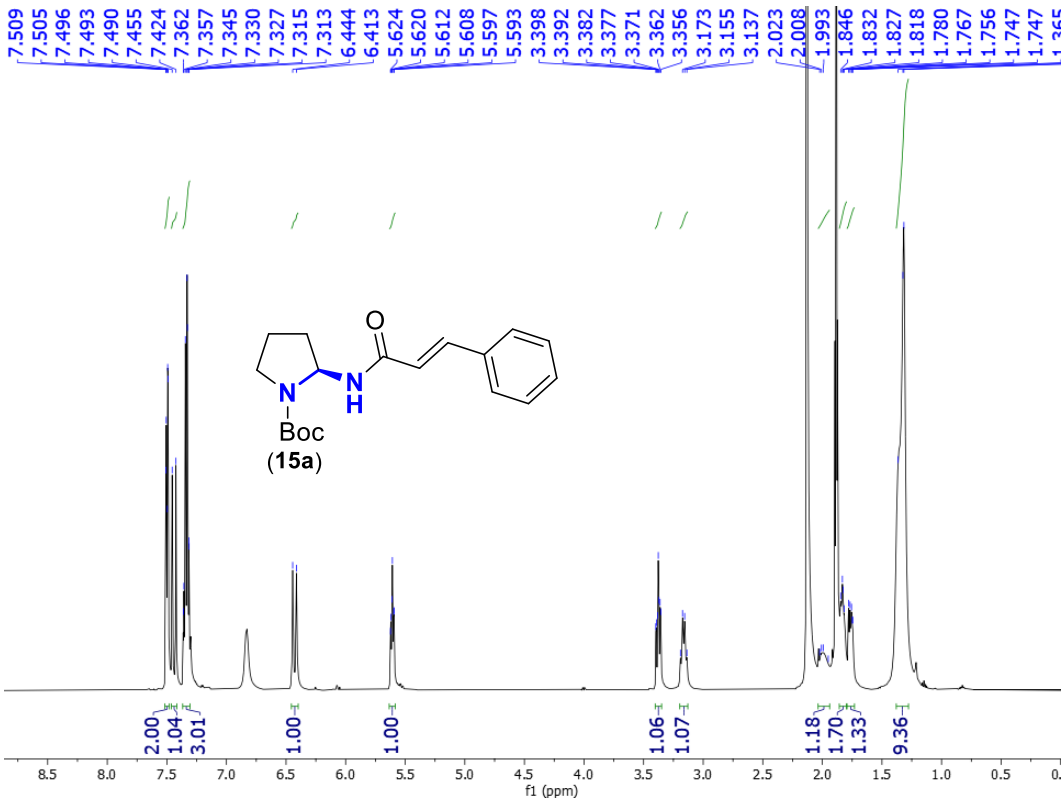


S.2.19.4. Chiral HPLC chromatogram of compound **15**

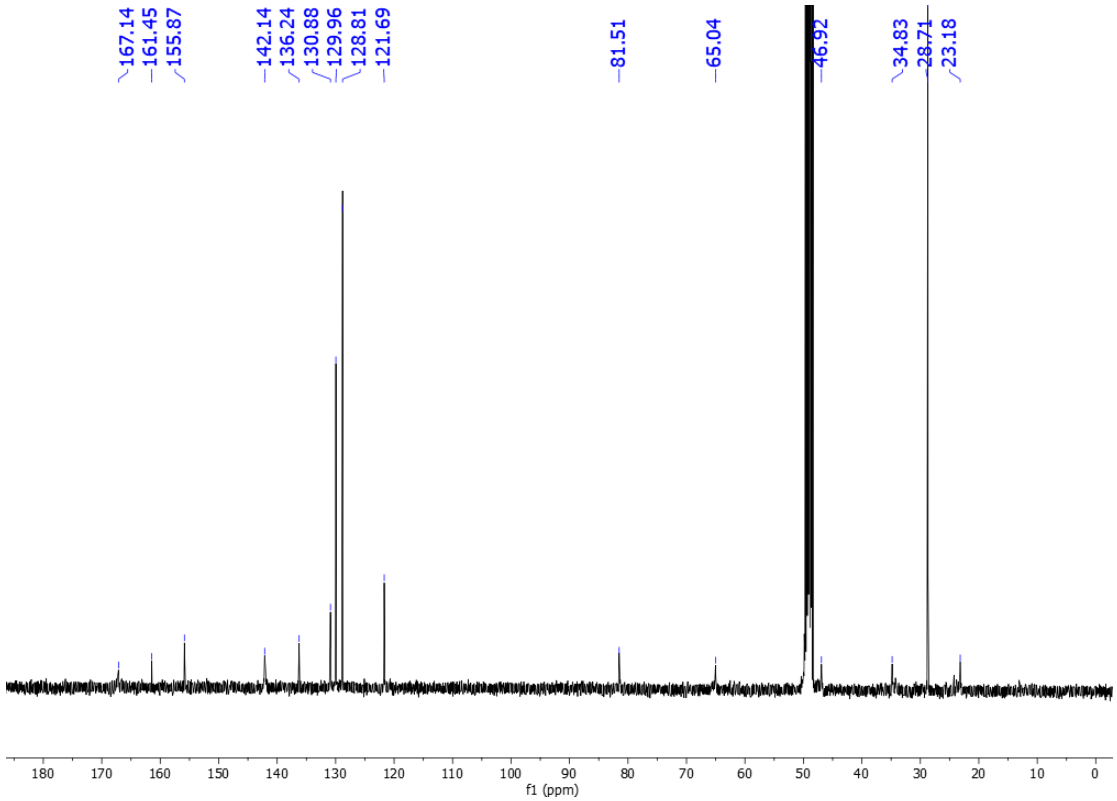


S.2.20. *tert*-Butyl (*S*)-2-cinnamamamidopyrrolidine-1-carboxylate (**15a**)

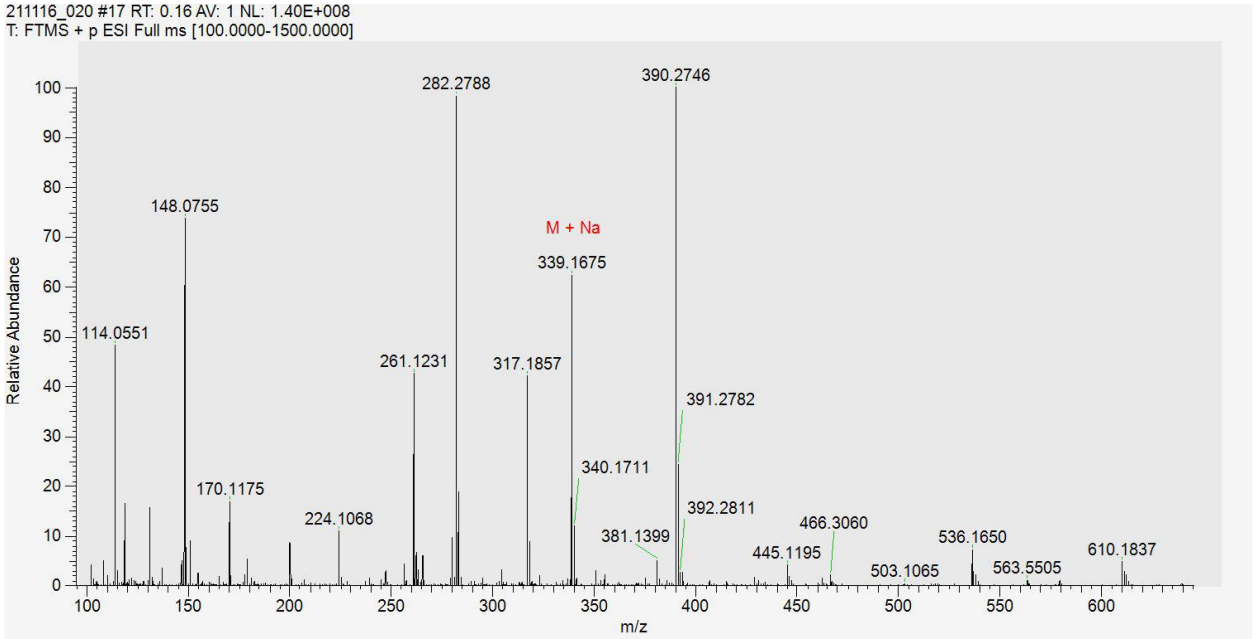
S.2.20.1. ^{1}H NMR (MeOD, 500 MHz) spectrum of compound **15a**



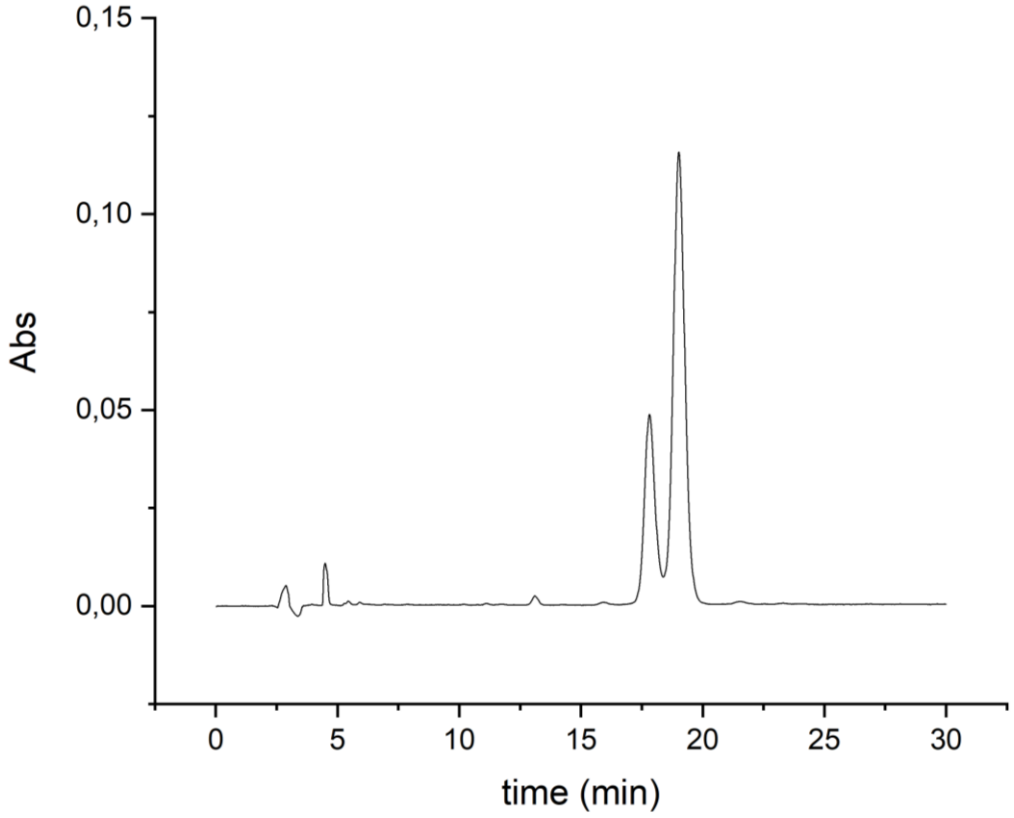
S.2.20.2. ^{13}C NMR (MeOD, 125 MHz) spectrum of compound **15a**



S.2.20.3. ESI-HRMS spectrum of compound **15a**

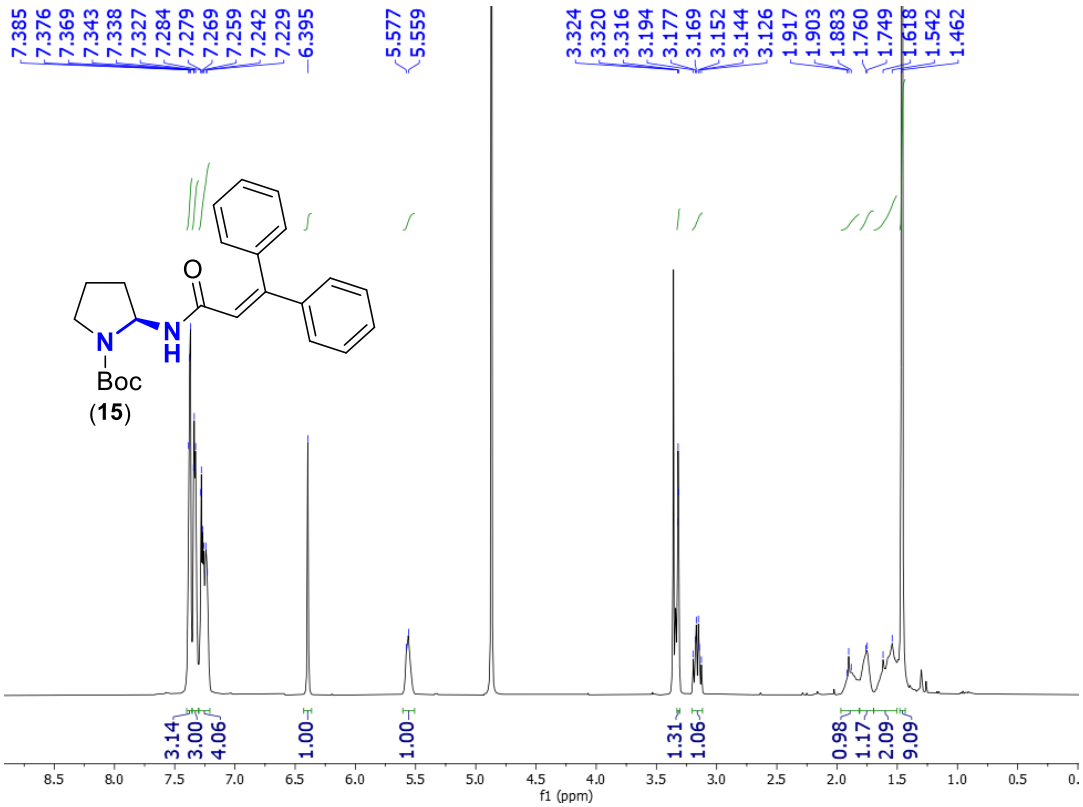


S.2.20.4. Chiral HPLC chromatogram of compound **15a**

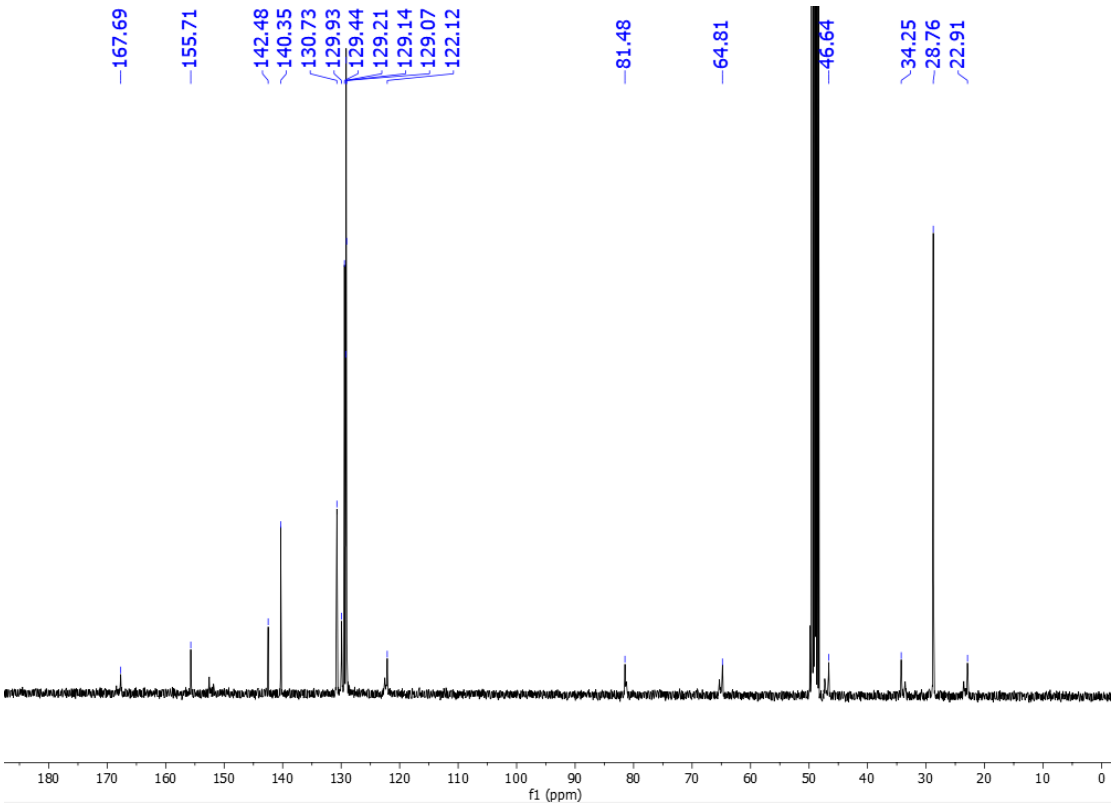


S.2.21. *tert*-Butyl (*S*)-2-(3,3-diphenylacrylamido)pyrrolidine-1-carboxylate (**15b**)

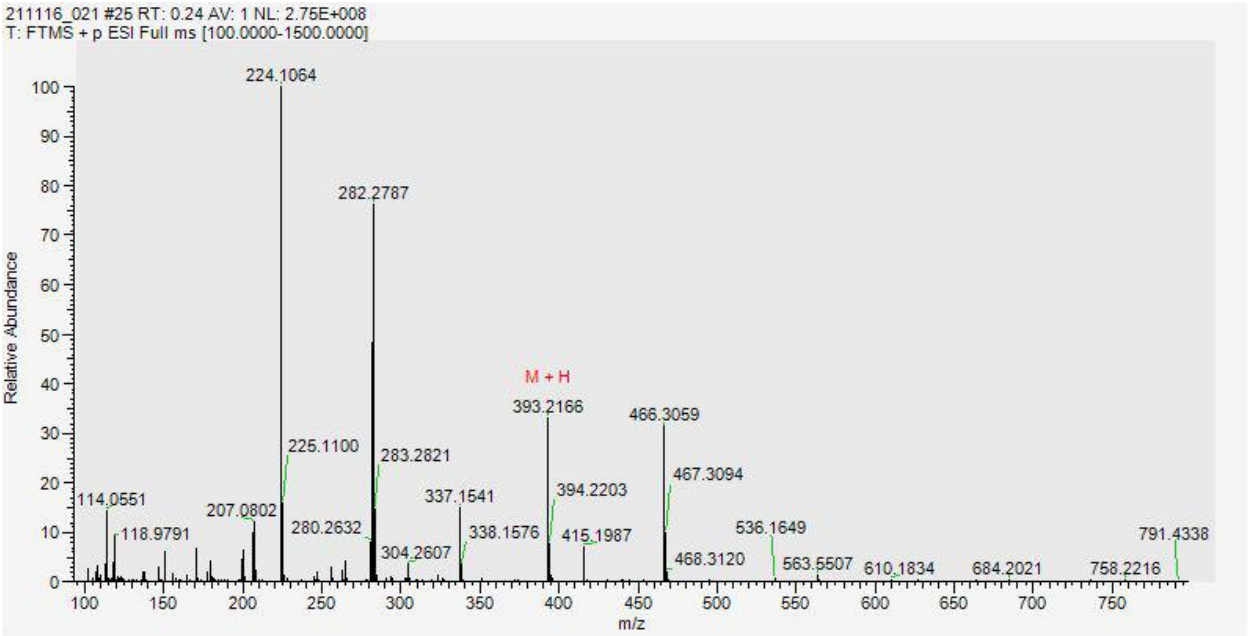
S.2.21.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **15b**



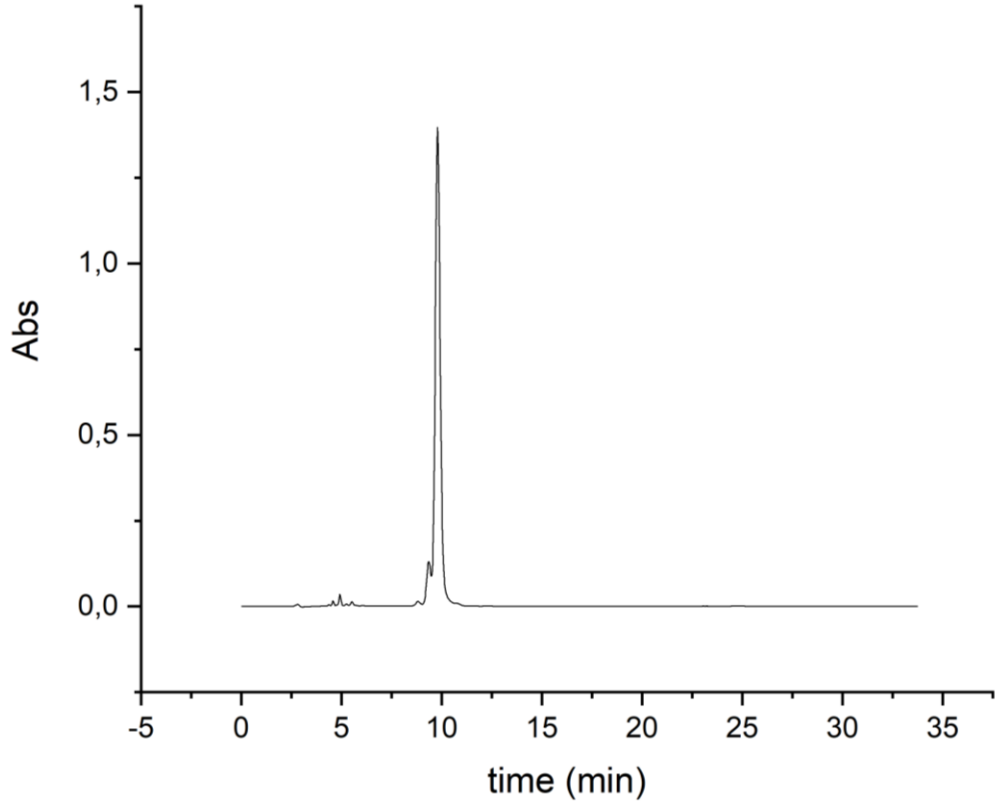
S.2.21.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **15b**



S.2.21.3. ESI-HRMS spectrum of compound **15b**

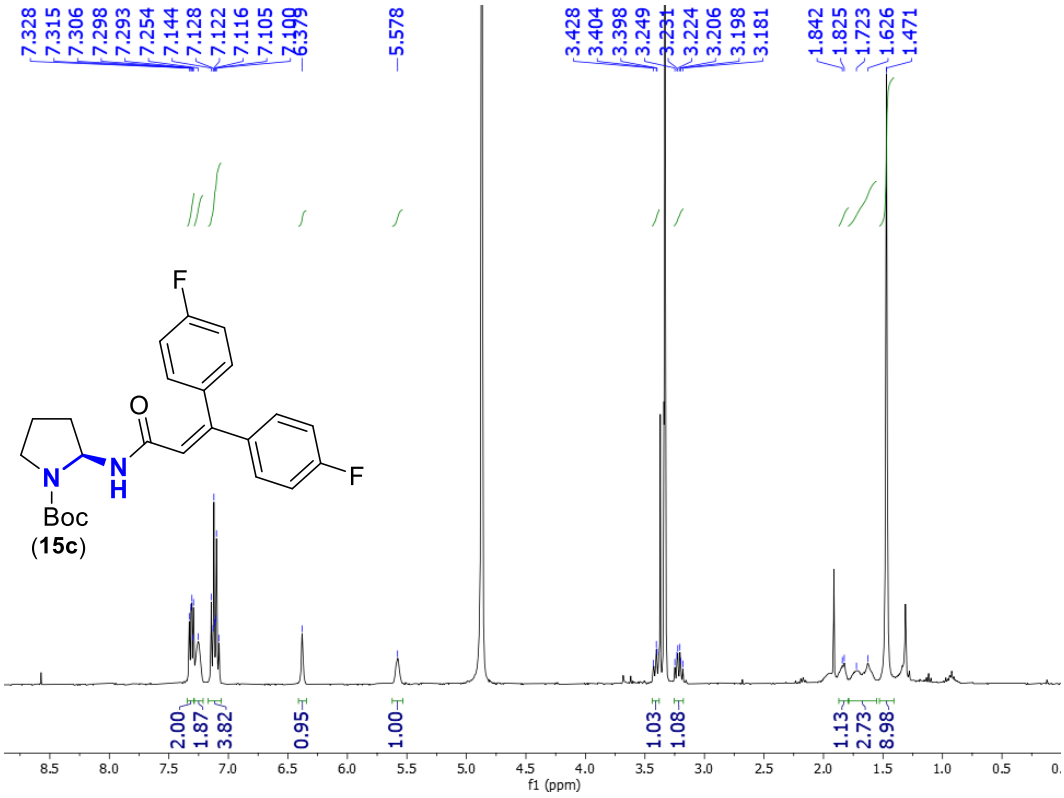


S.2.21.4. Chiral HPLC chromatogram of compound **15b**

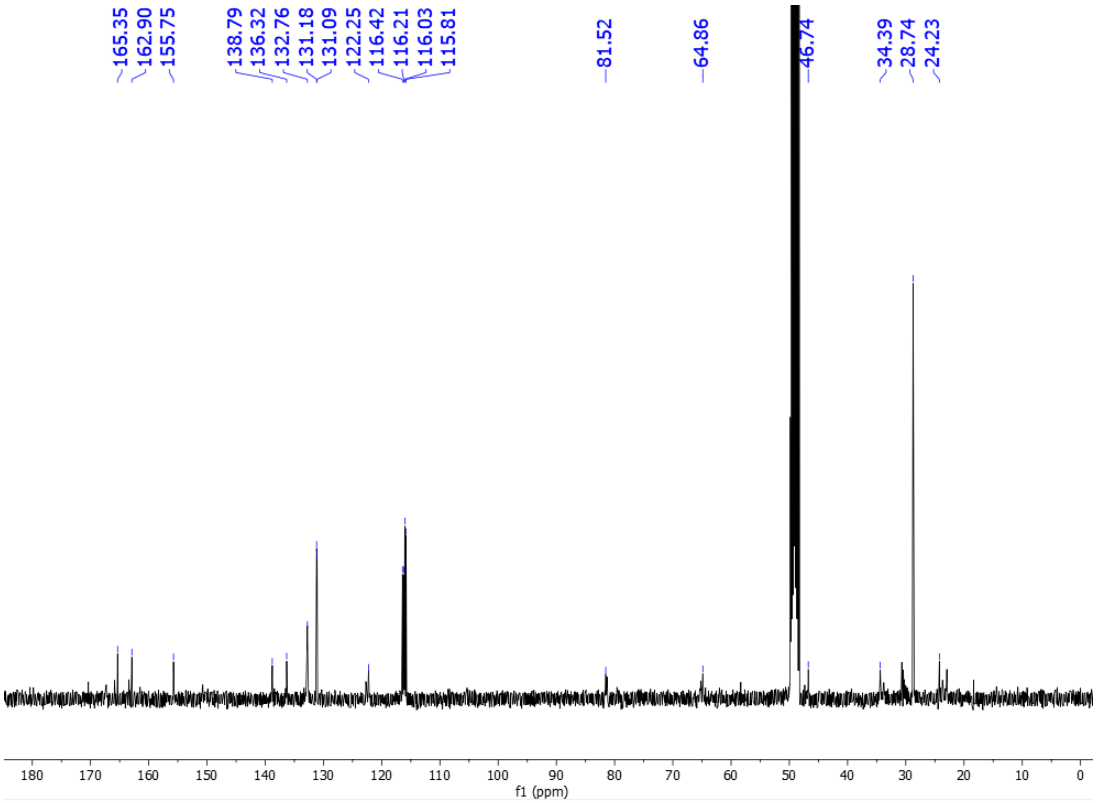


S.2.22. *tert*-Butyl (*S*)-2-(3,3-bis(4-fluorophenyl)acrylamido)pyrrolidine-1-carboxylate (**15c**)

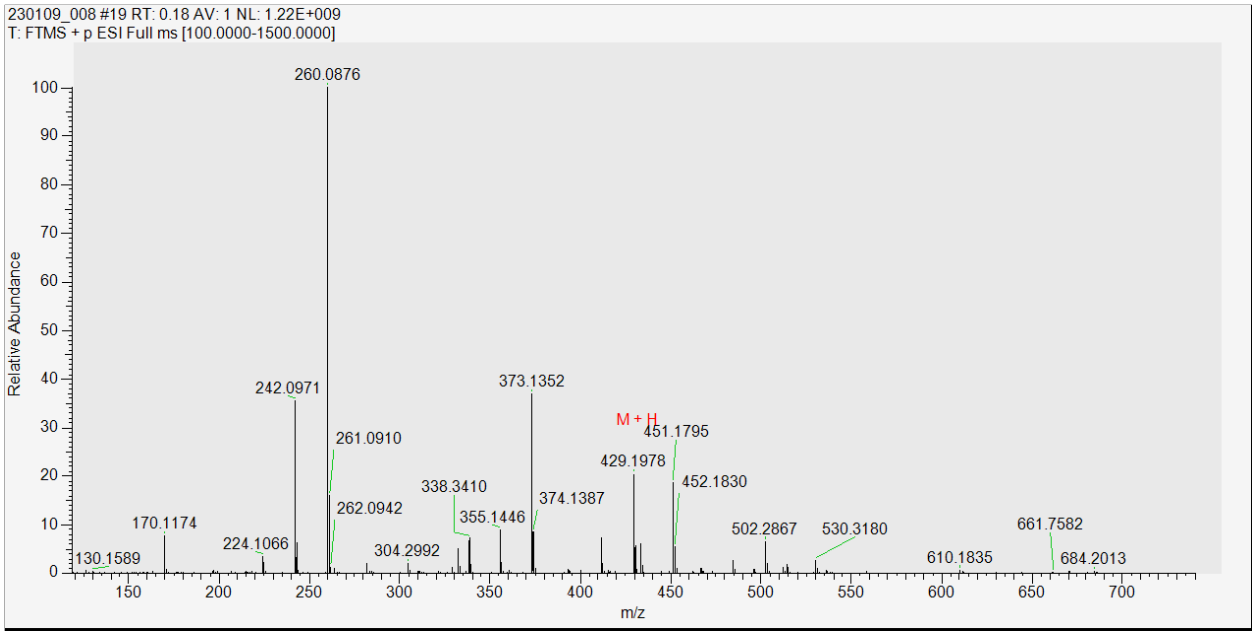
S.2.22.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **15c**



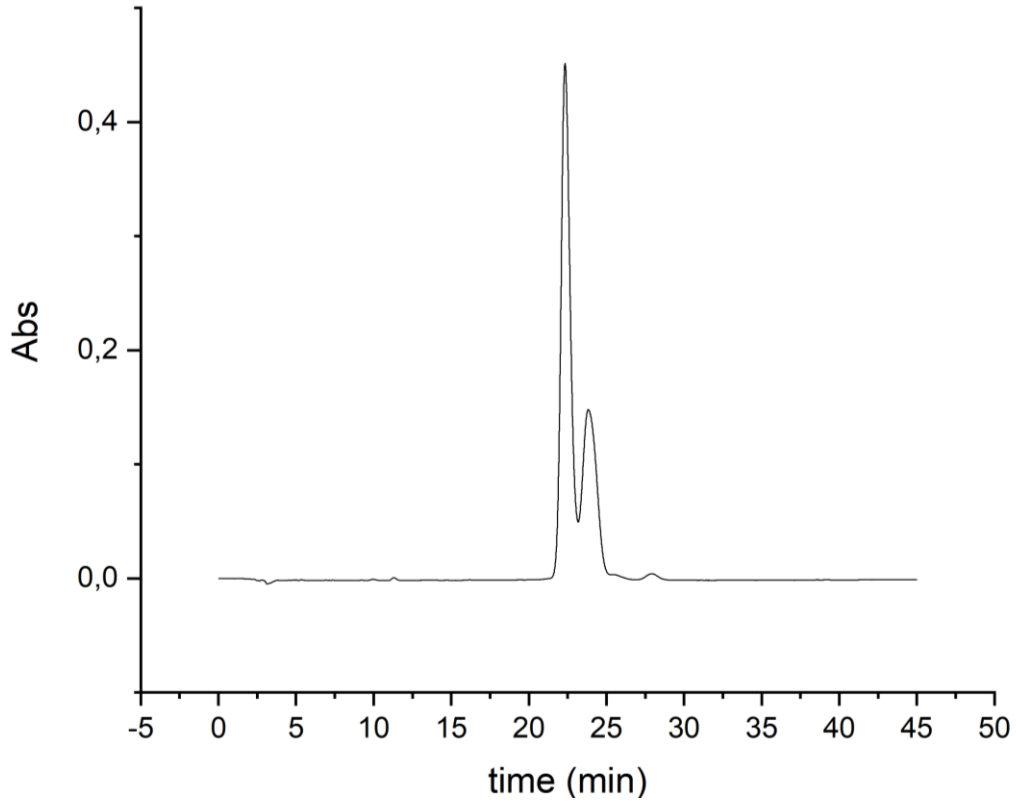
S.2.22.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **15c**



S.2.22.3. ESI-HRMS spectrum of compound **15c**

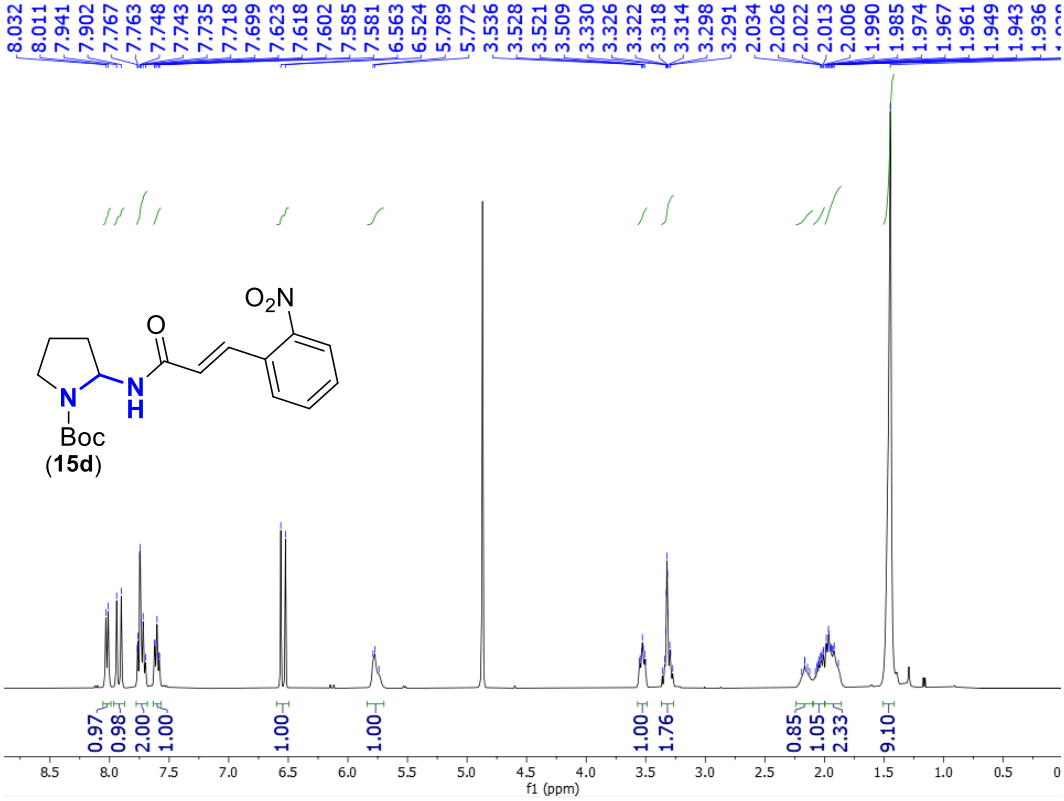


S.2.22.4. Chiral HPLC chromatogram of compound 15c

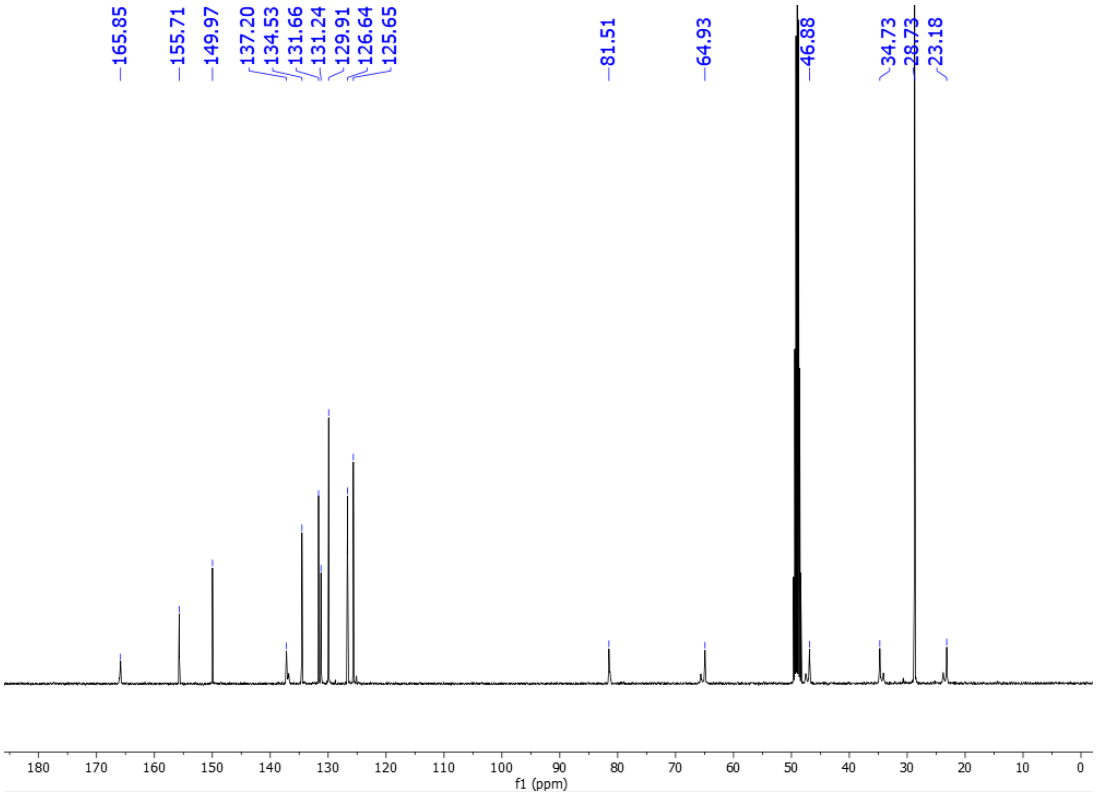


S.2.23. *tert*-Butyl (*S,E*)-2-(3-(2-nitrophenyl)acrylamido)pyrrolidine-2-carboxylate (**15d**)

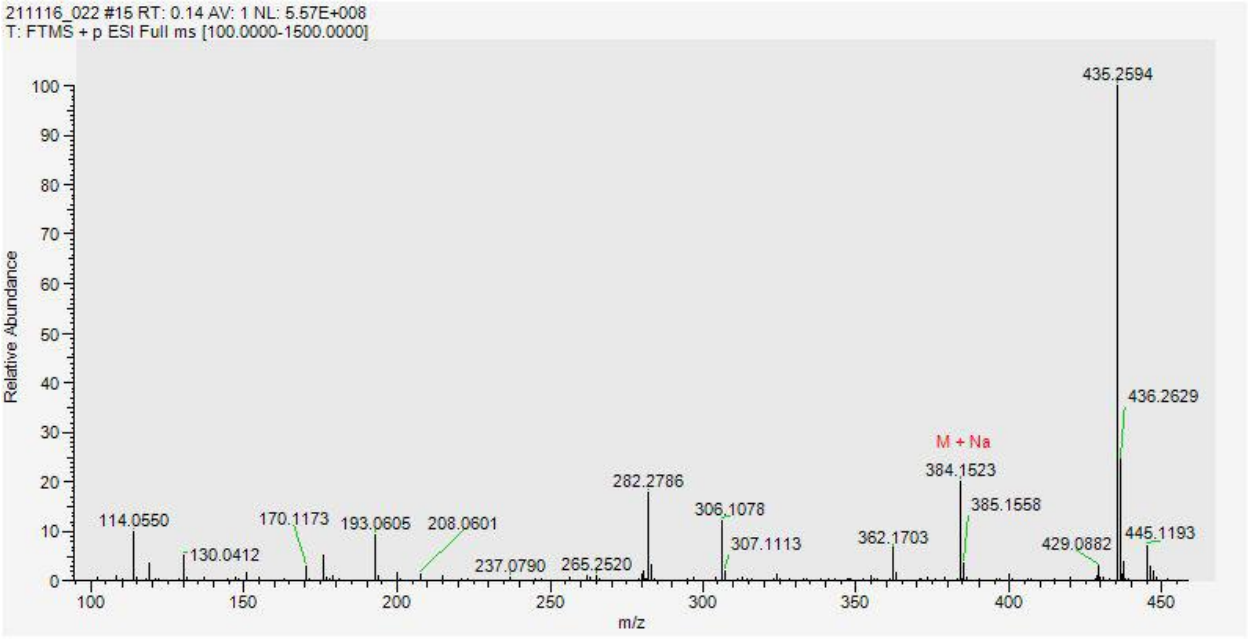
S.2.23.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **15d**



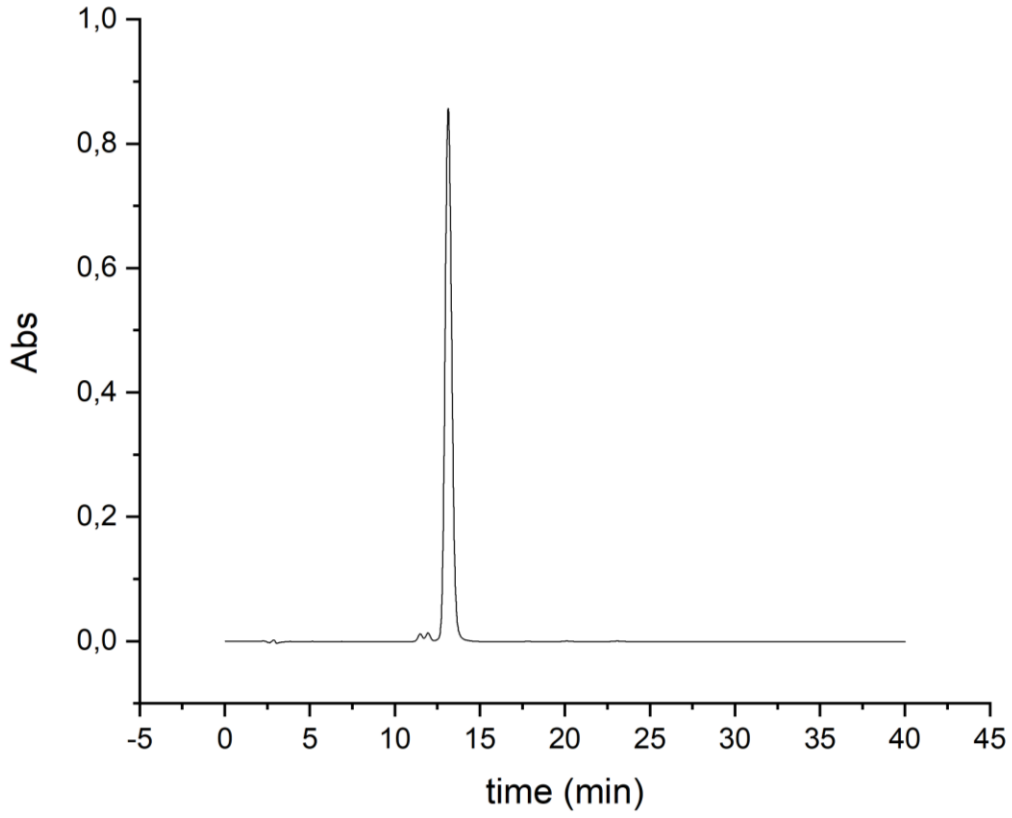
S.2.23.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **15d**



S.2.23.3. ESI-HRMS spectrum of compound **15d**

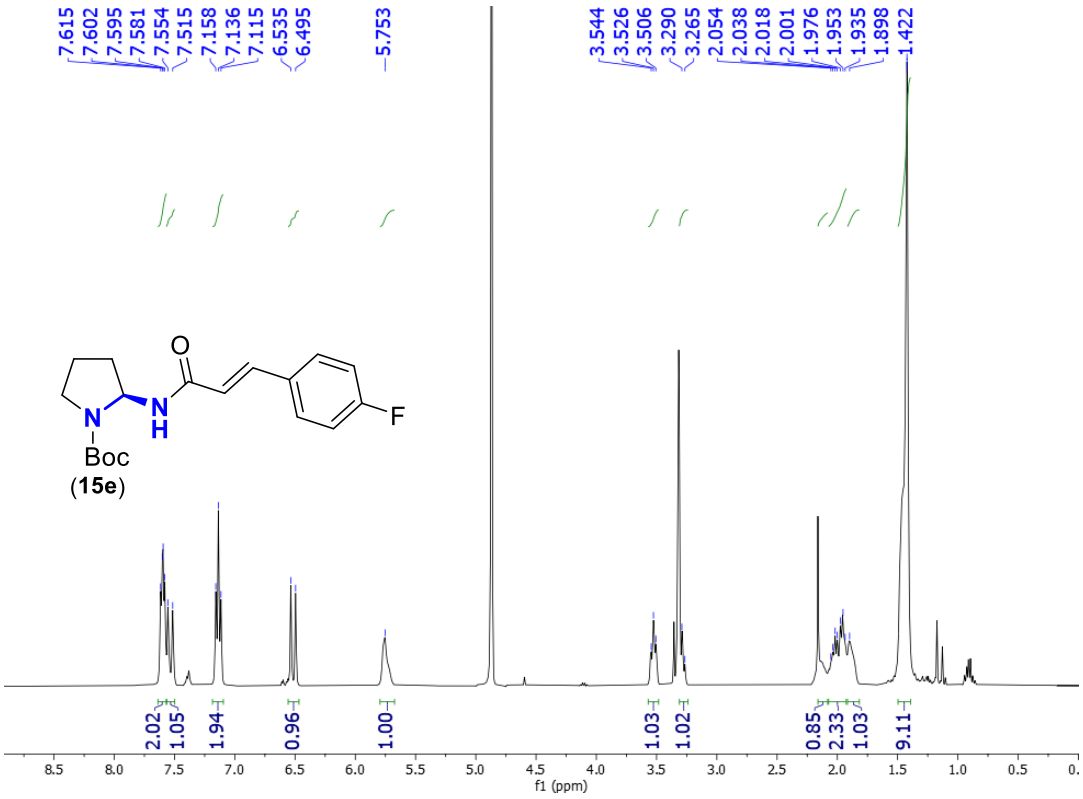


S.2.23.4. Chiral HPLC chromatogram of compound 15d

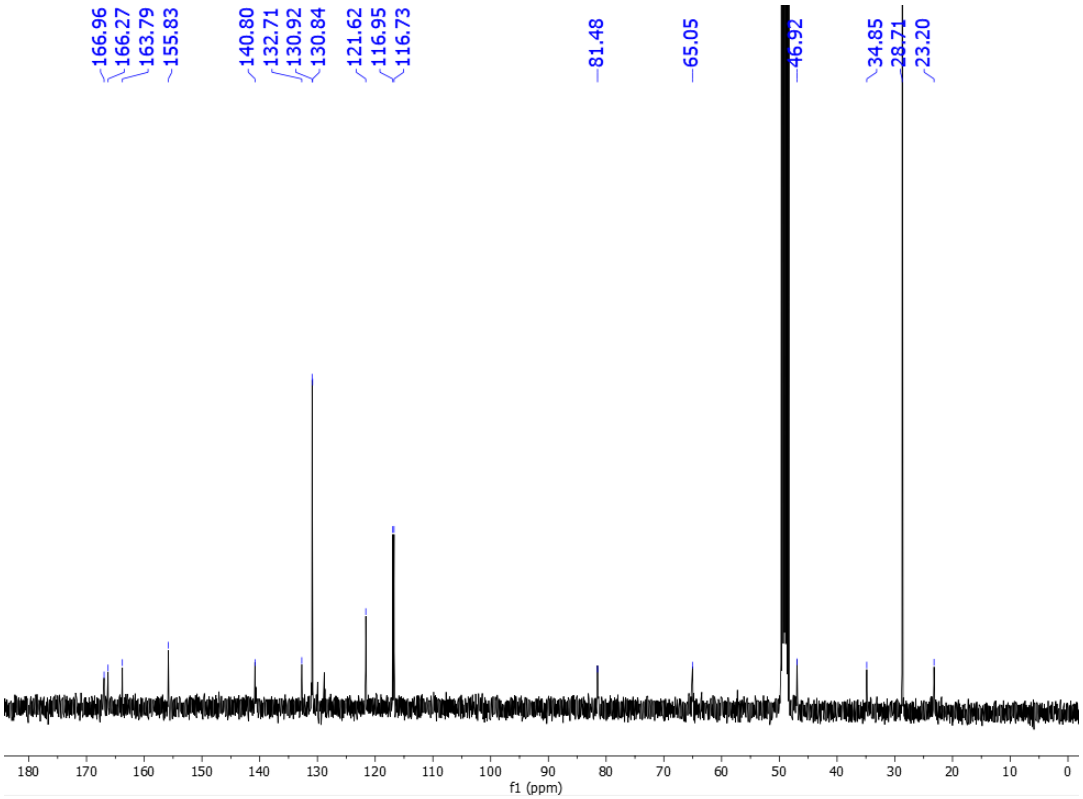


S.2.24. *tert*-Butyl (*S,E*)-2-(3-(4-fluorophenyl)acrylamido)pyrrolidine-1-carboxylate (**15e**)

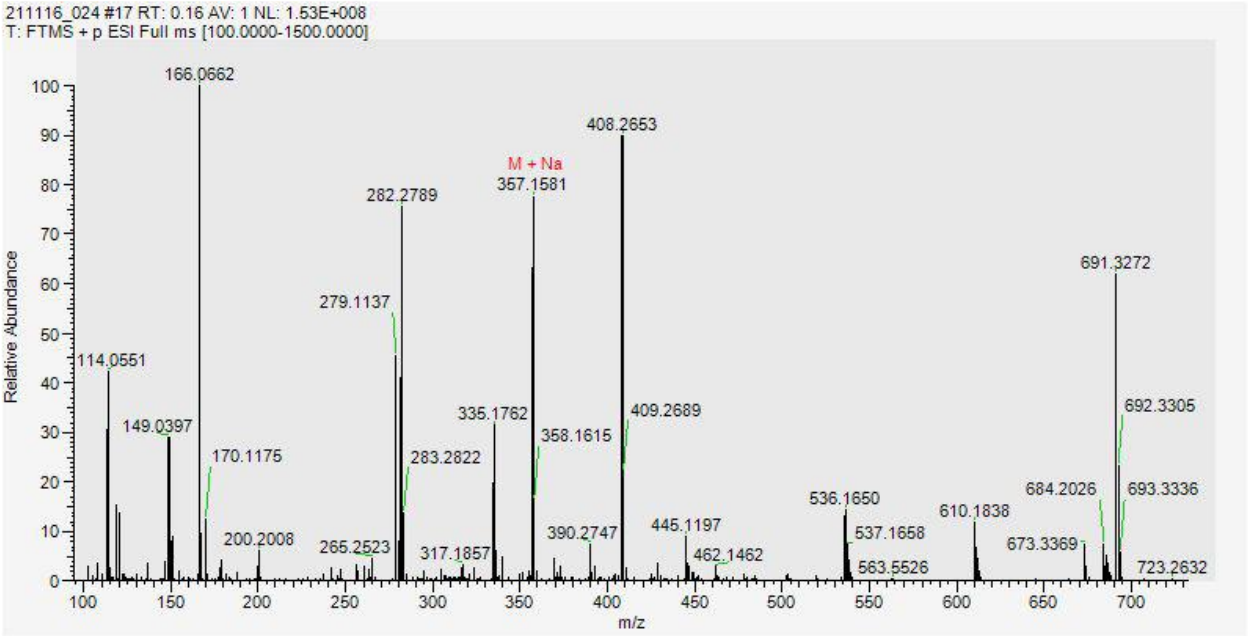
S.2.24.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **15e**



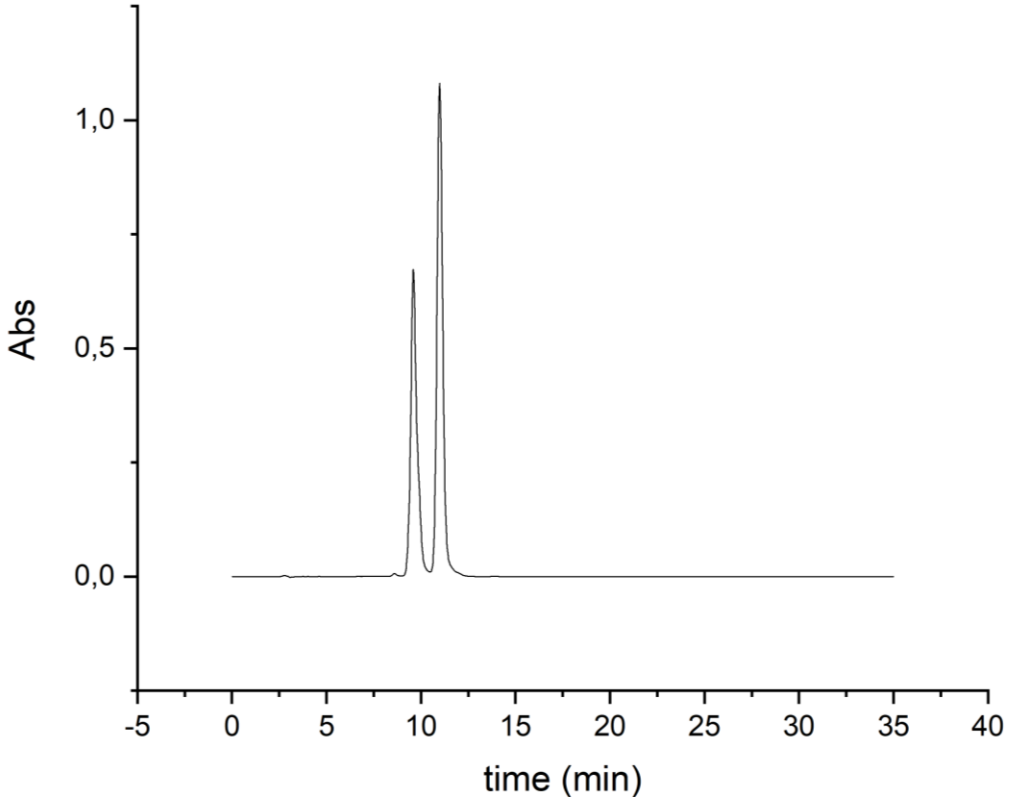
S.2.24.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **15e**



S.2.24.3. ESI-HRMS spectrum of compound **15e**

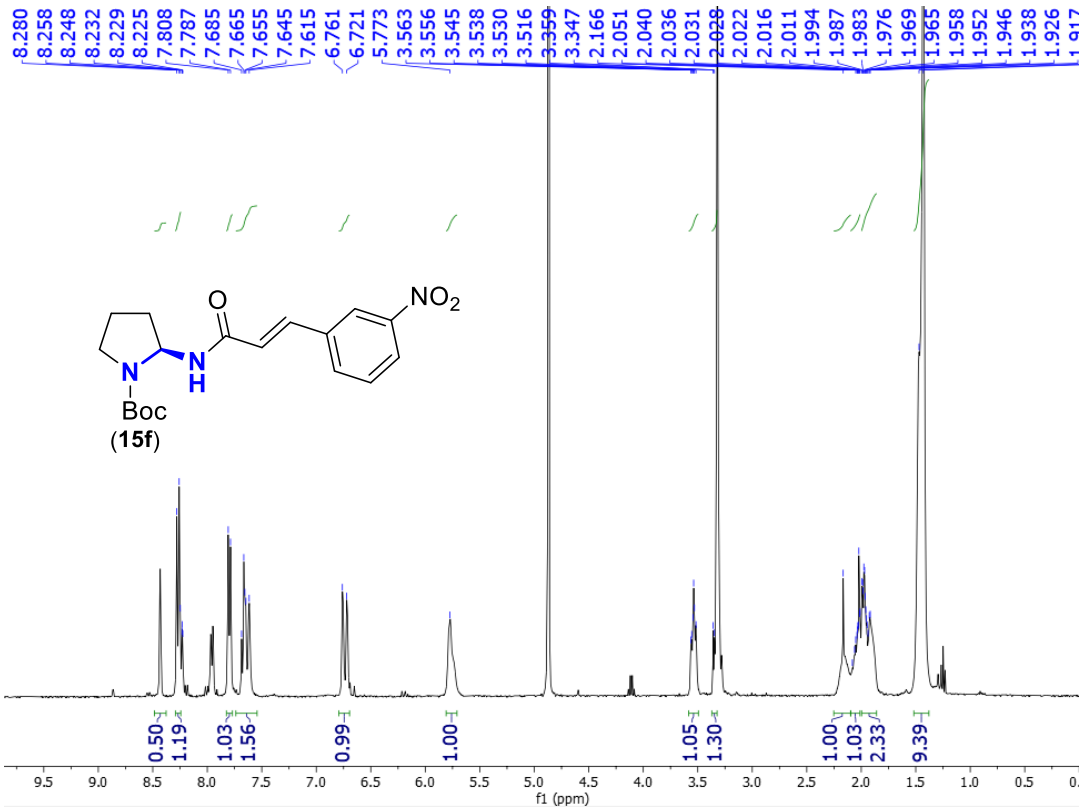


S.2.24.4. Chiral HPLC chromatogram of compound **15e**

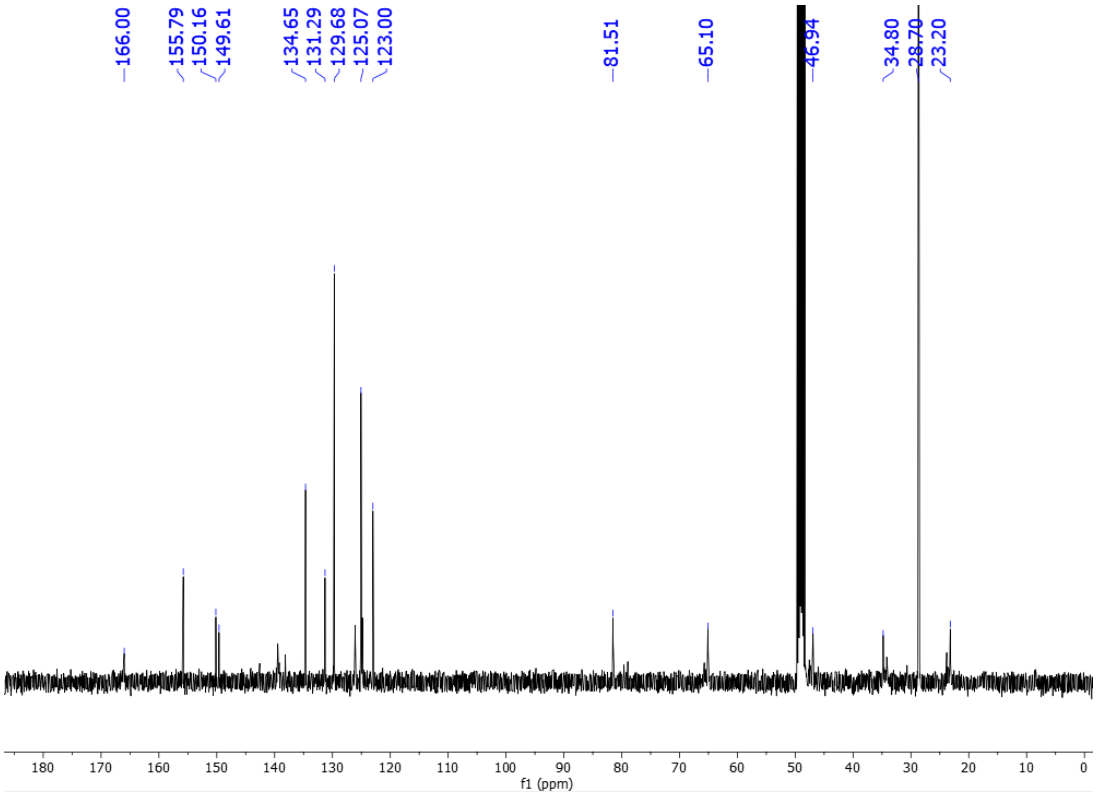


S.2.25. *tert*-Butyl (*S,E*)-2-(3-(3-nitrophenyl)acrylamido)pyrolidine-1-carboxylate (**15f**)

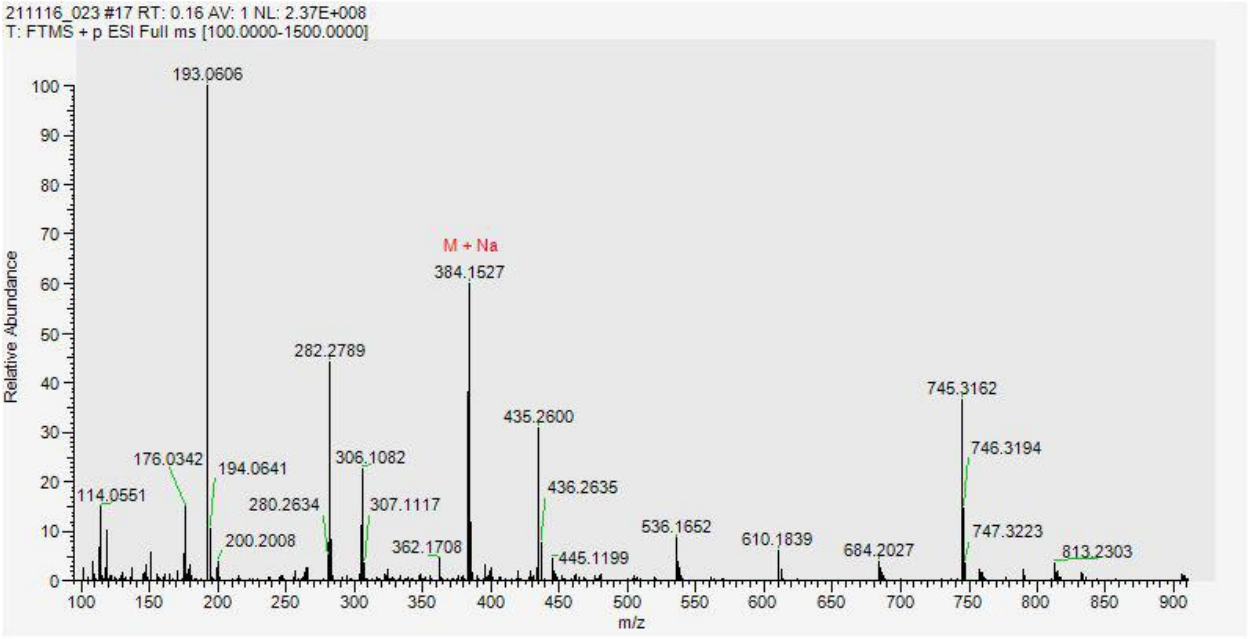
S.2.25.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **15f**



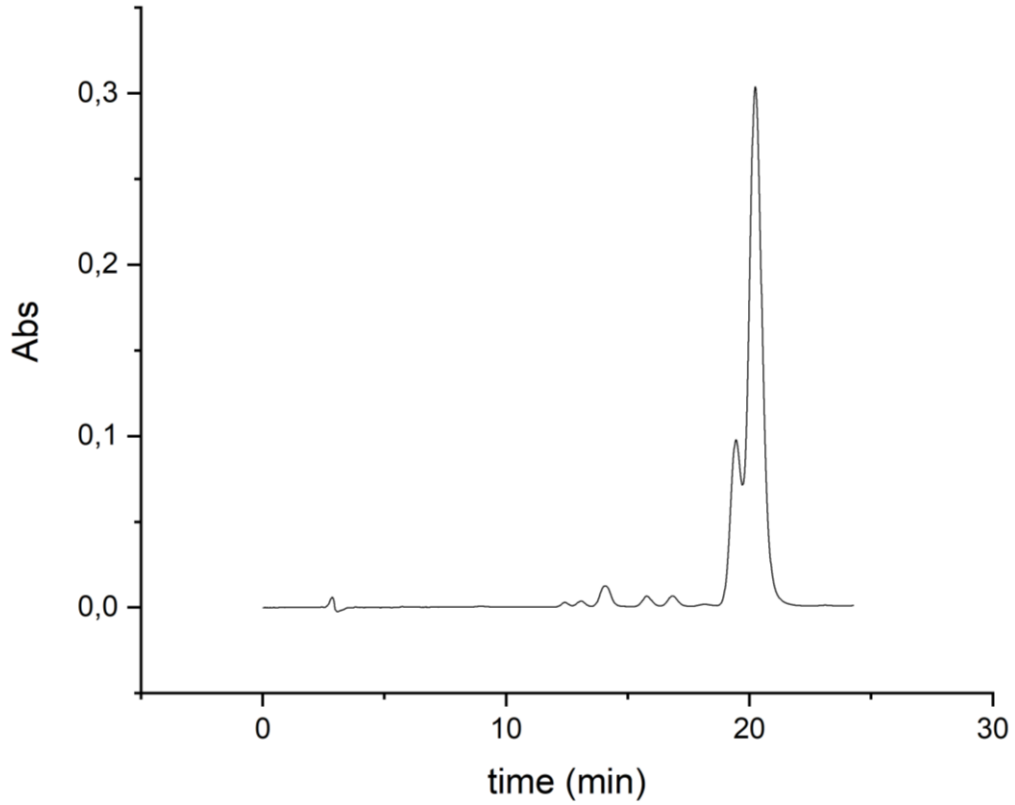
S.2.25.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **15f**



S.2.25.3. ESI-HRMS spectrum of compound **15f**

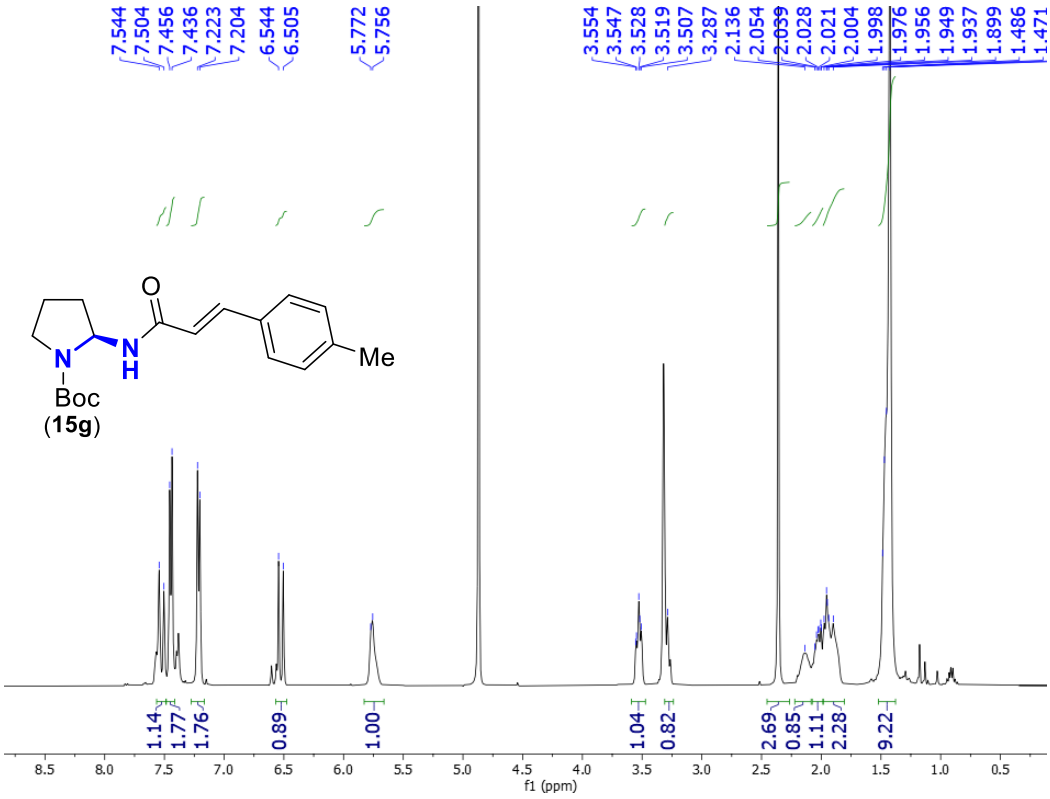


S.2.25.4. Chiral HPLC chromatogram of compound **15f**

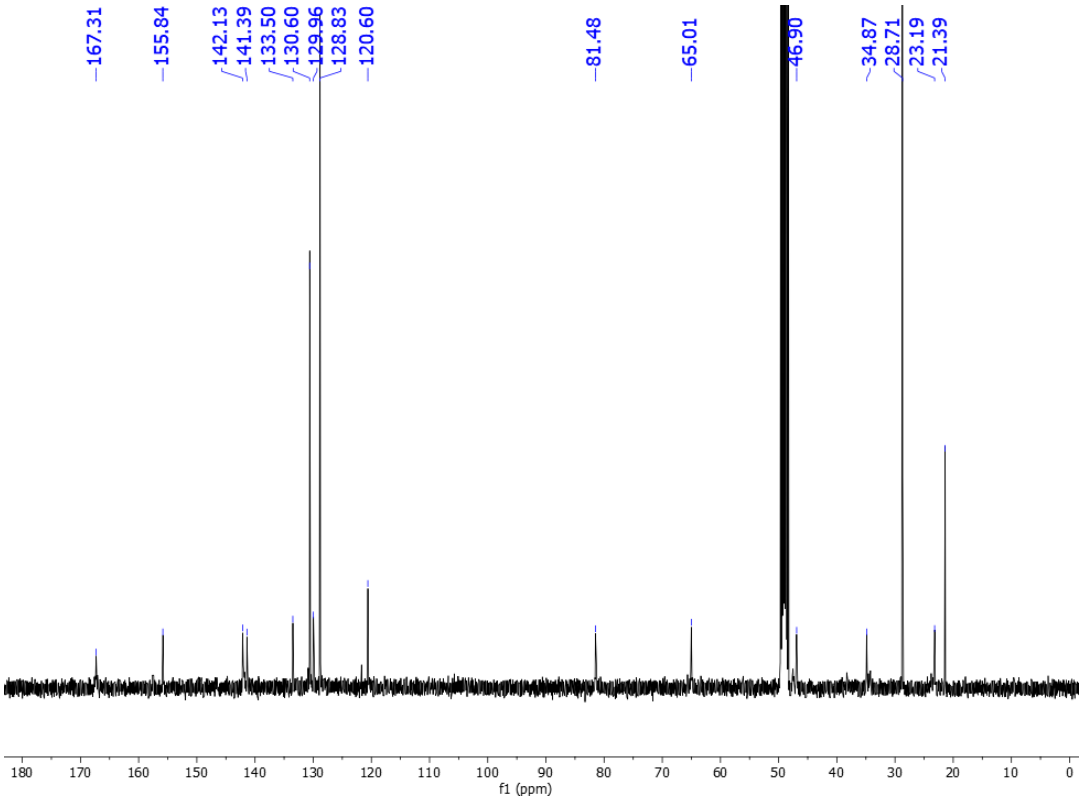


S.2.26. *tert*-Butyl (*S,E*)-2-(3-(p-tolyl)acrylamido)pyrrolidine-1-carboxylate (**15g**)

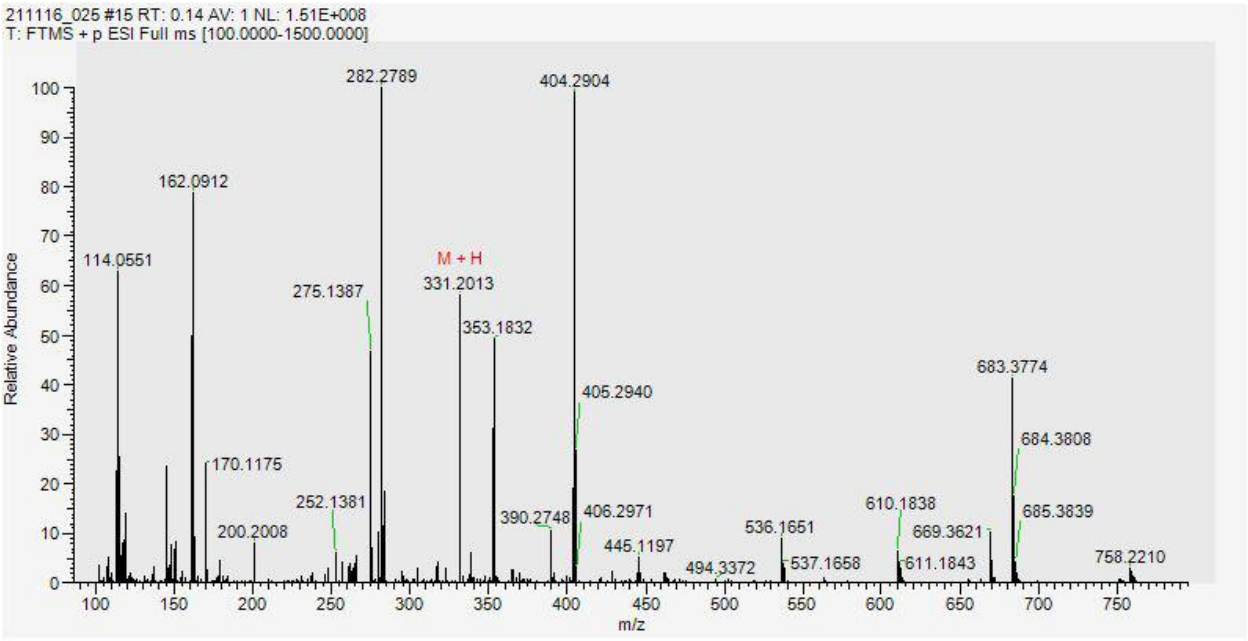
S.2.26.1. 1H NMR (MeOD, 400 MHz) spectrum of compound **15g**



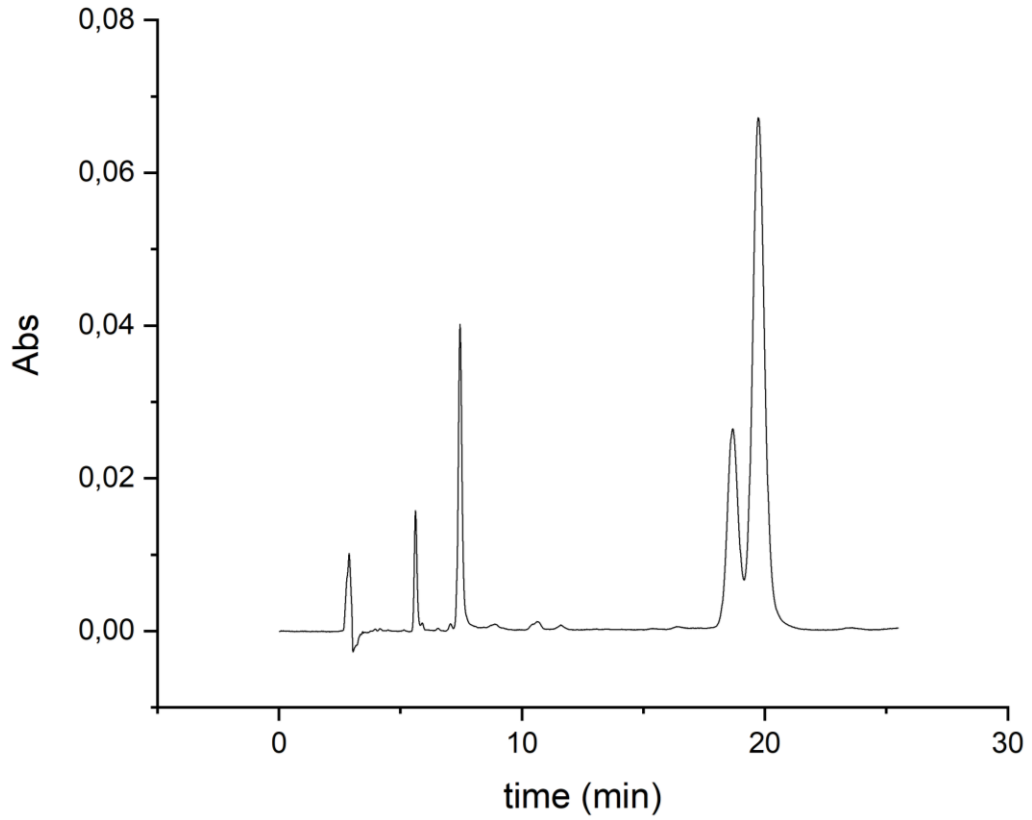
S.2.26.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **15g**



S.2.26.3. ESI-HRMS spectrum of compound **15g**

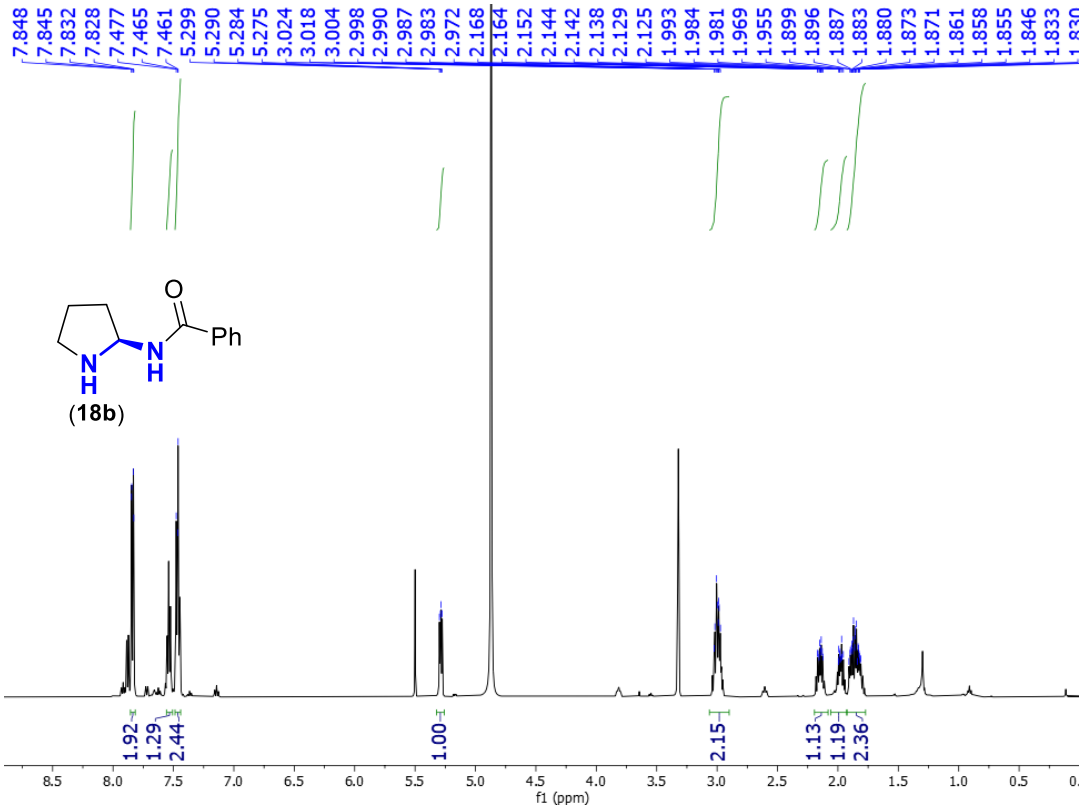


S.2.26.4. Chiral HPLC chromatogram of compound **15g**

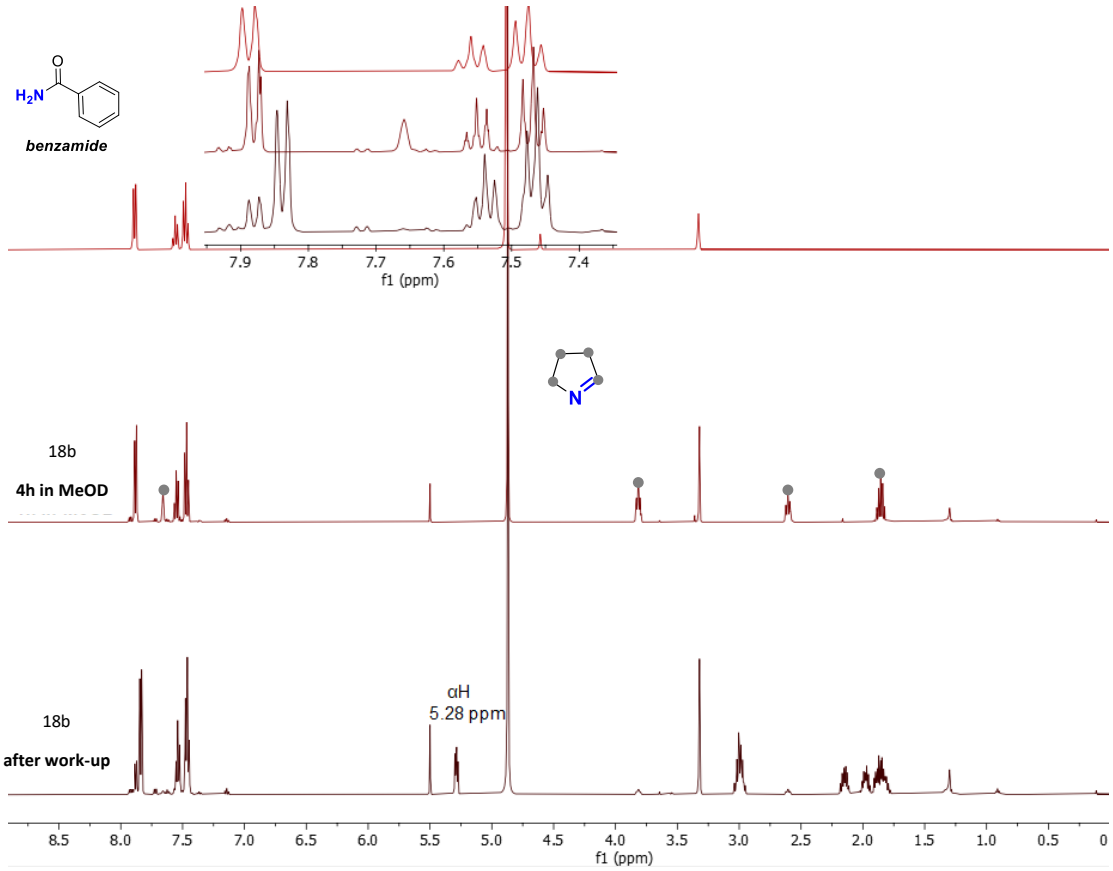


S.2.27. (R)-N-(pyrrolidin-2-yl)benzamide (**18b**)

S.2.27.1. ^{1}H NMR (MeOD, 500 MHz) spectrum of compound **18b**

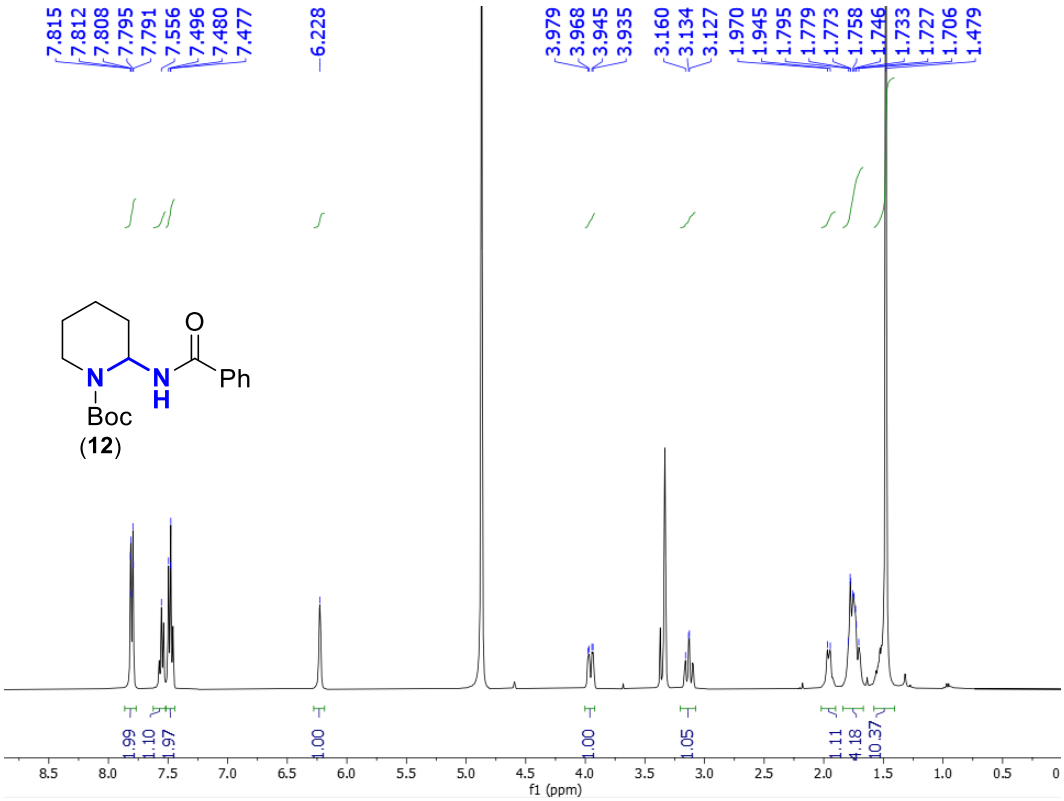


S.2.27.2. ^{1}H NMR (400MHz, MeOD) stability study of compound **18b** in MeOD. Expansion highlighting the formation of benzamide (decomposition product) after 4h in MeOD

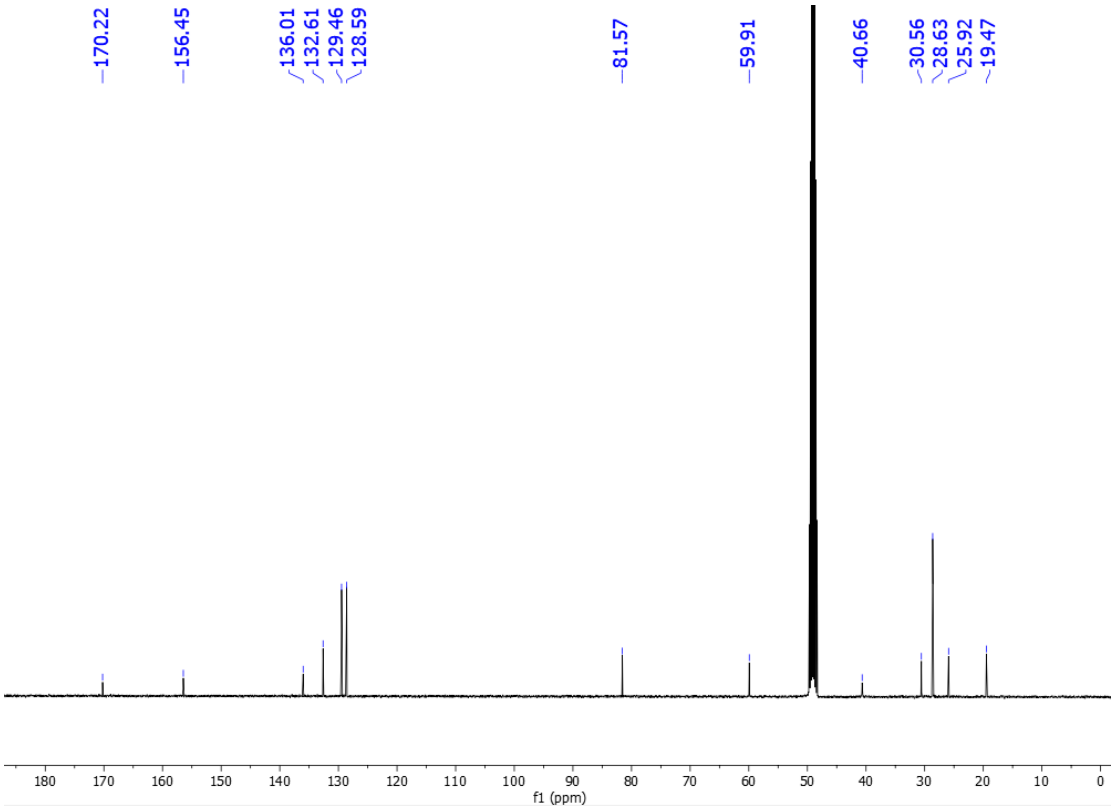


S.2.28. *tert*-Butyl 2-benzamidopiperidine-1-carboxylate (12)

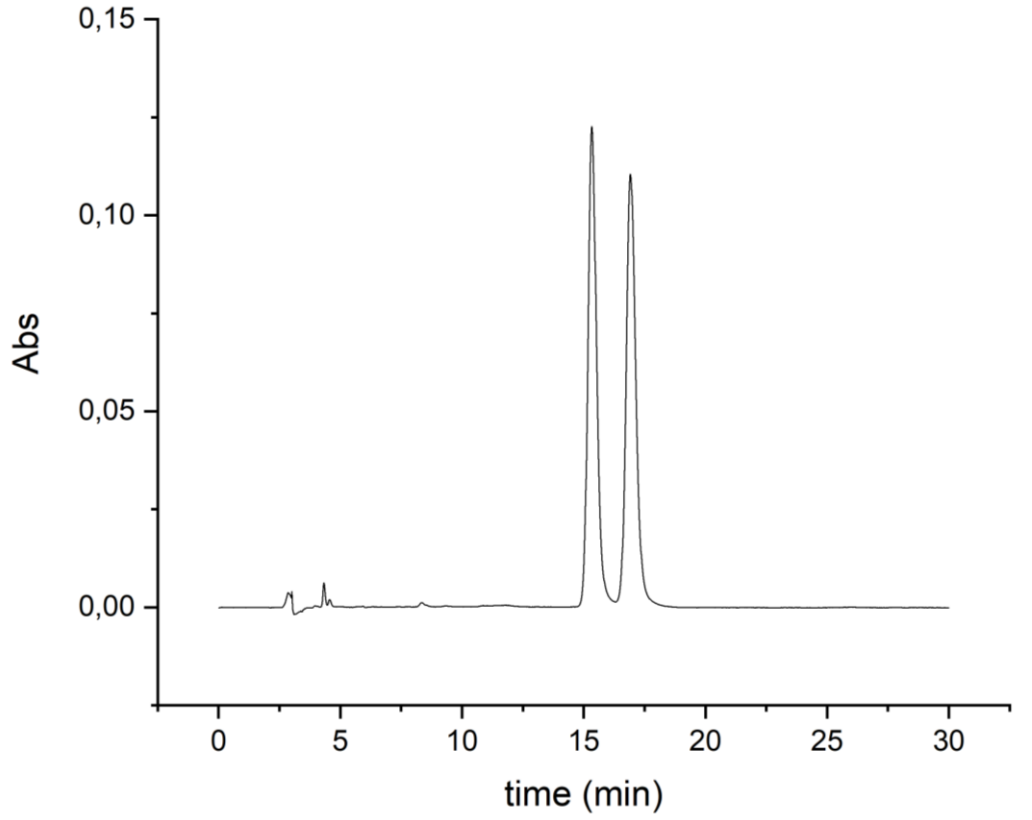
S.2.28.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound 12



S.2.28.2. ^{13}C NMR (MeOD, 101 MHz) spectrum of compound **12**

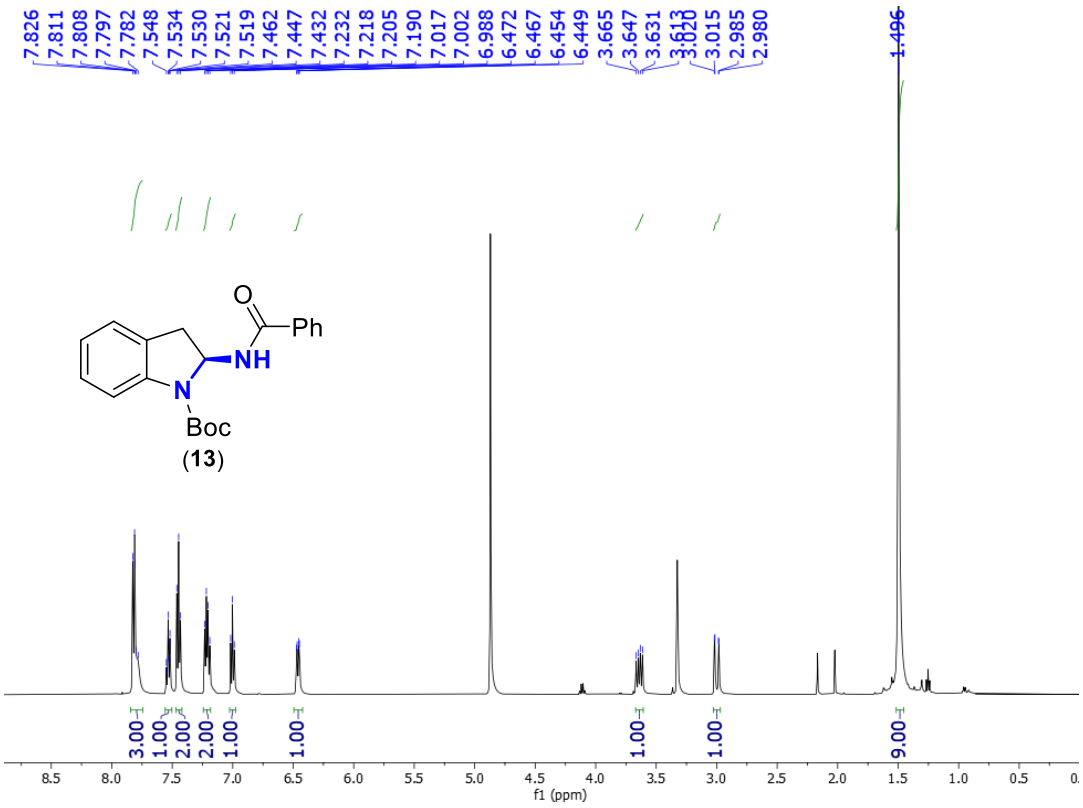


S.2.28.3. Chiral HPLC chromatogram of compound 12.

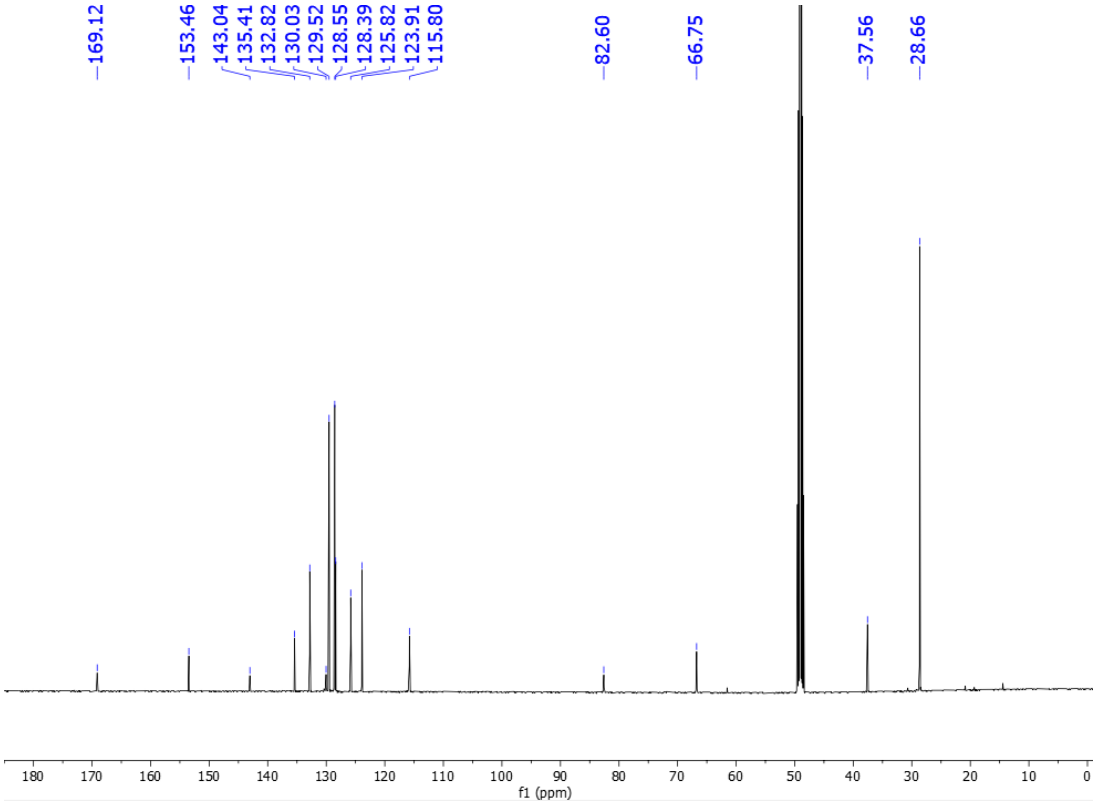


S.2.29. *tert*-Butyl (*S*)-2-benzamidoindoline-1-carboxylate (**13**)

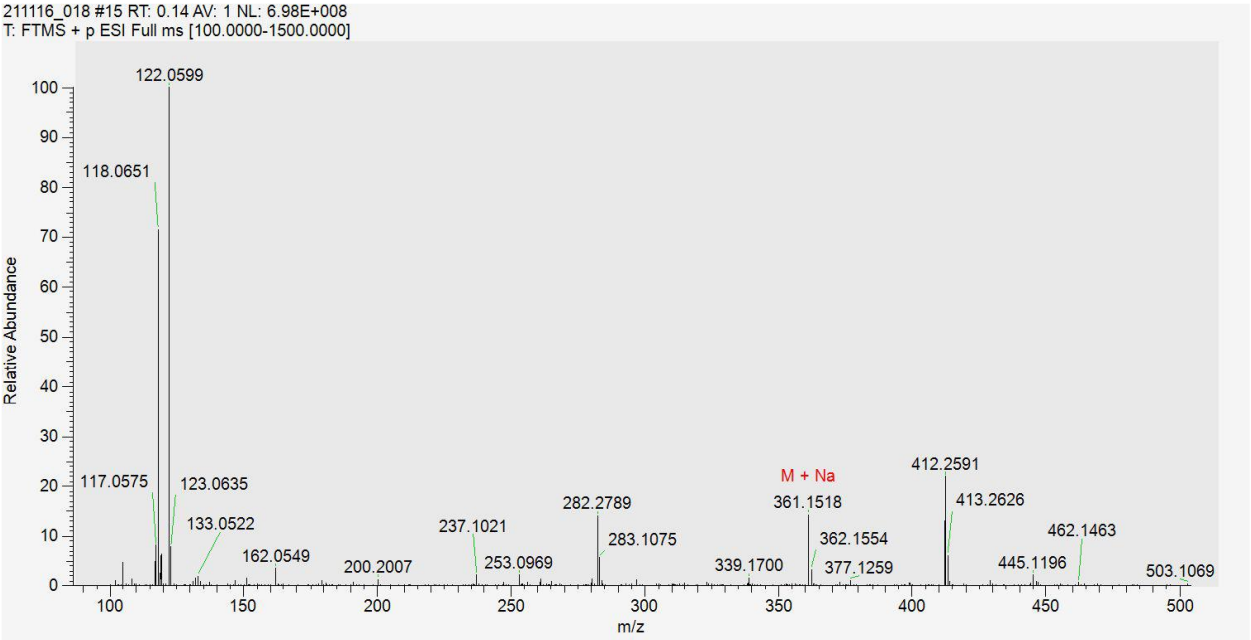
S.2.29.1. ^{1}H NMR (MeOD, 500 MHz) spectrum of compound **13**



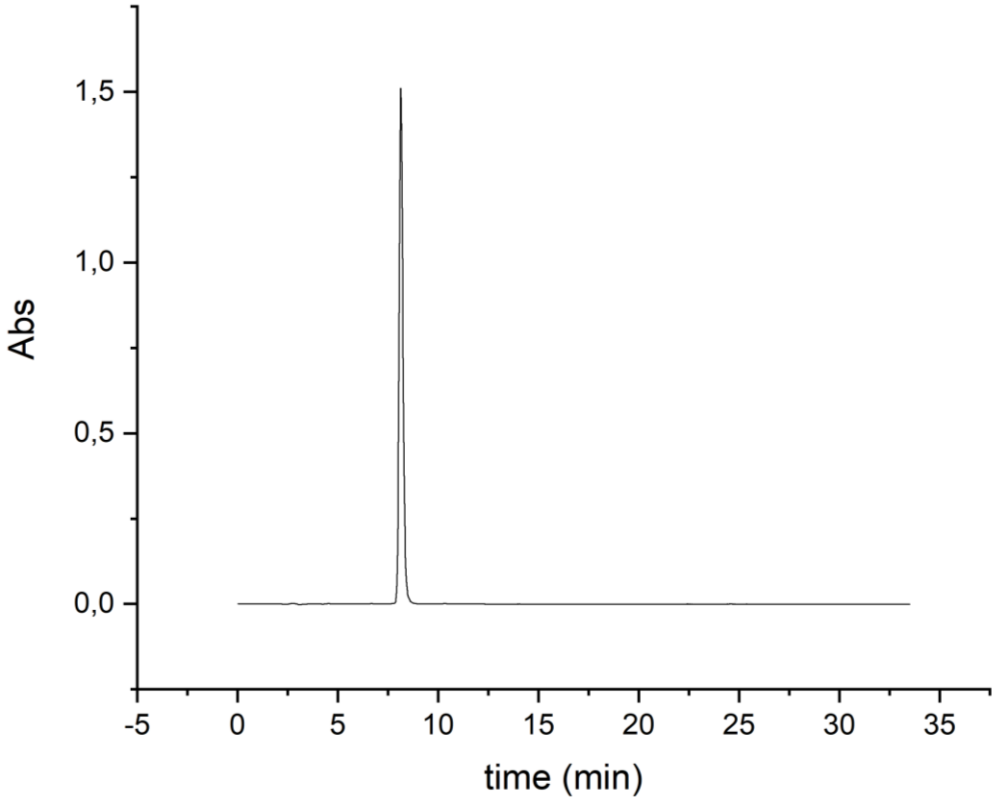
S.2.29.2. ^{13}C NMR (MeOD, 125 MHz) spectrum of compound **13**



S.2.29.3. ESI-HRMS spectrum of compound 13

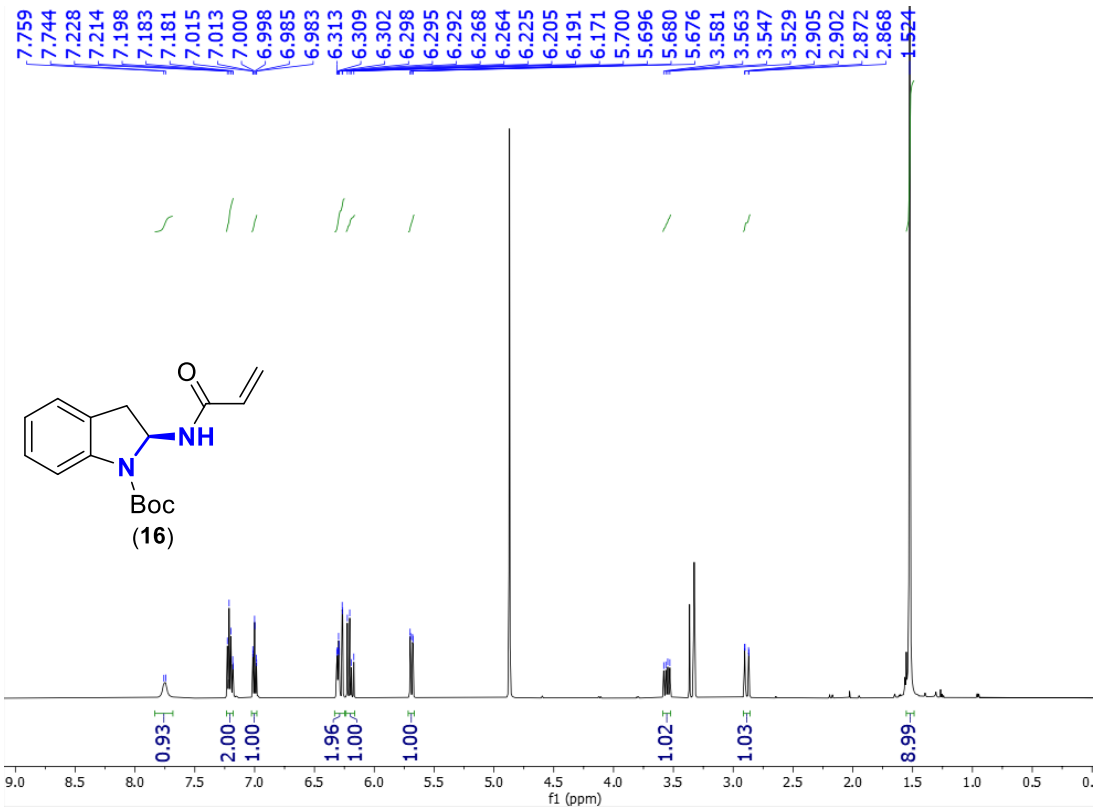


S.2.29.4. Chiral HPLC chromatogram of compound 13

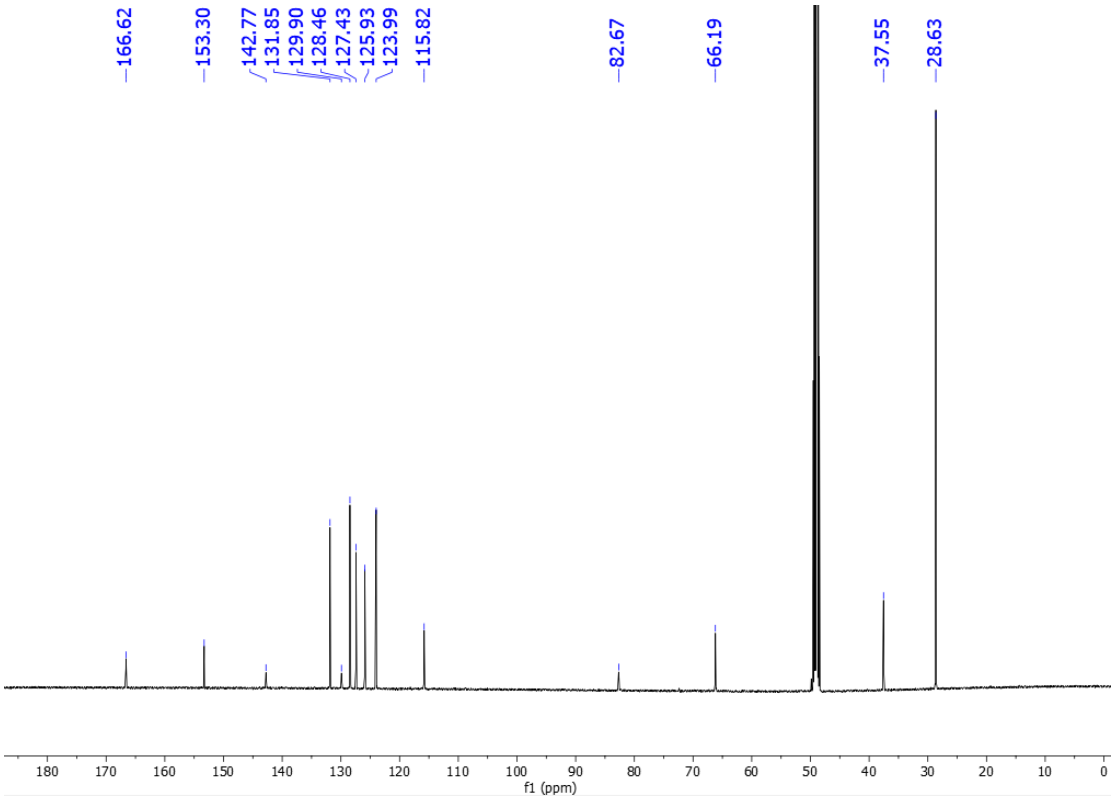


S.2.30. *tert*-Butyl (S)-2-acrylamidoindoline-1-carboxylate (**16**)

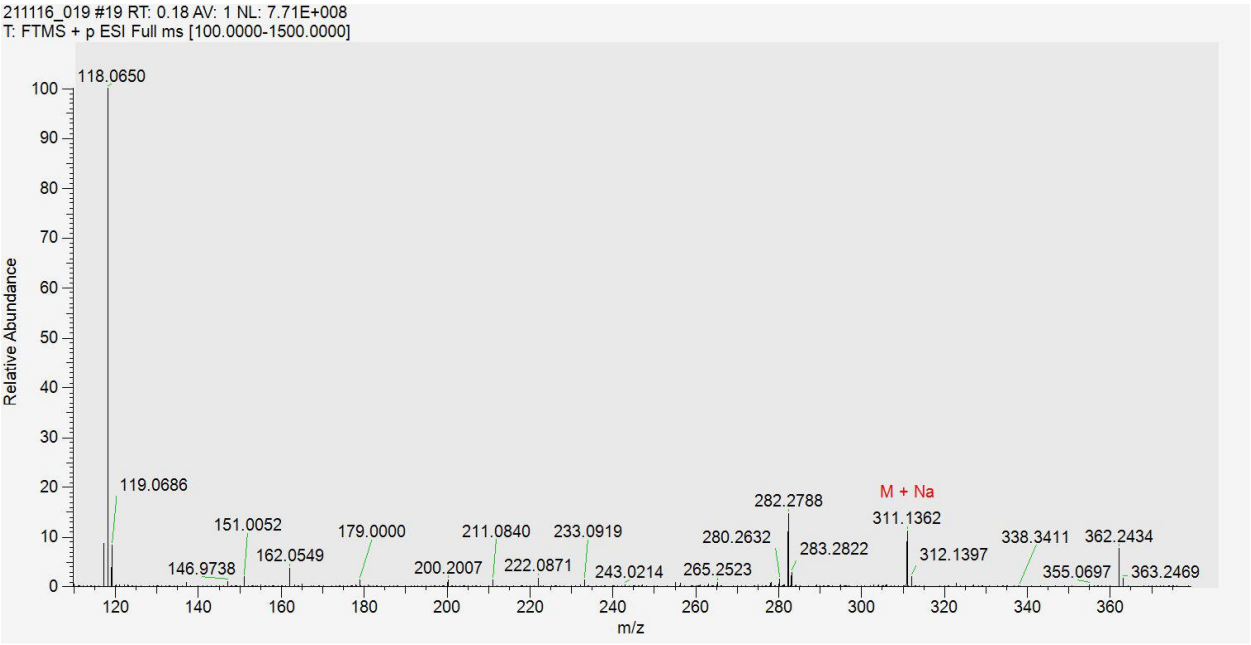
S.2.30.1. ^{1}H NMR (MeOD, 500 MHz) spectrum of compound **16**



S.2.30.2. ^{13}C NMR (MeOD, 125 MHz) spectrum of compound **16**

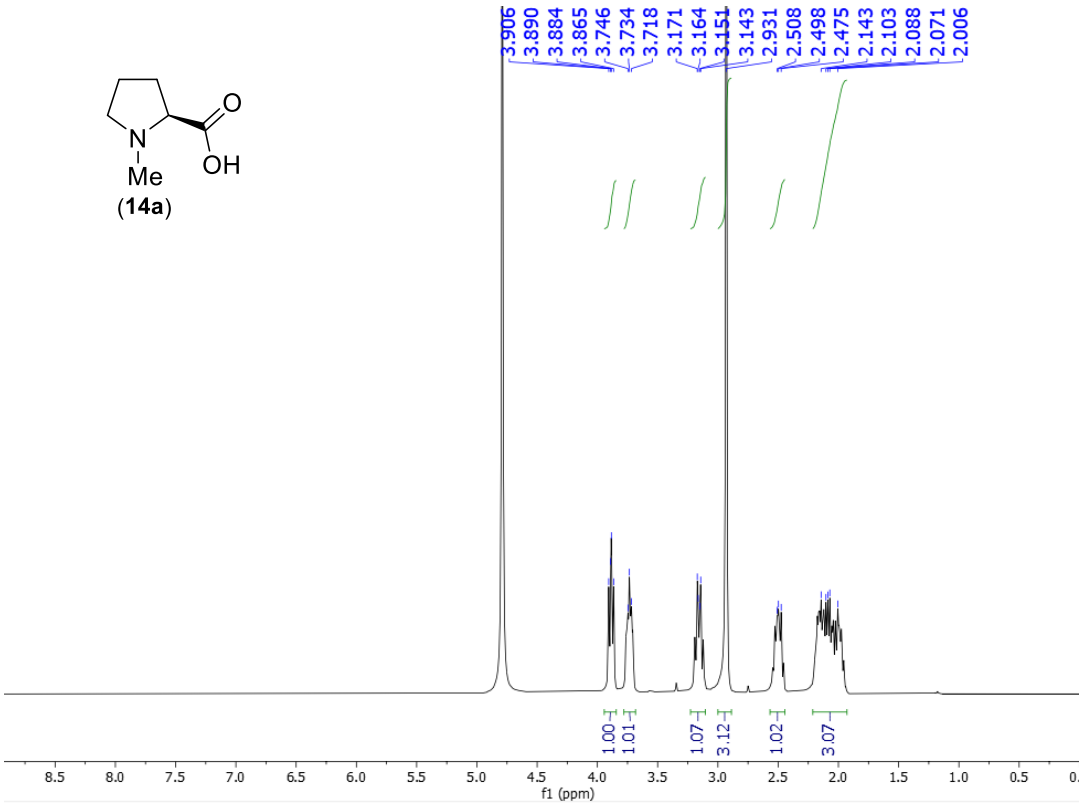


S.2.30.3. ESI-HRMS spectrum of compound **16**



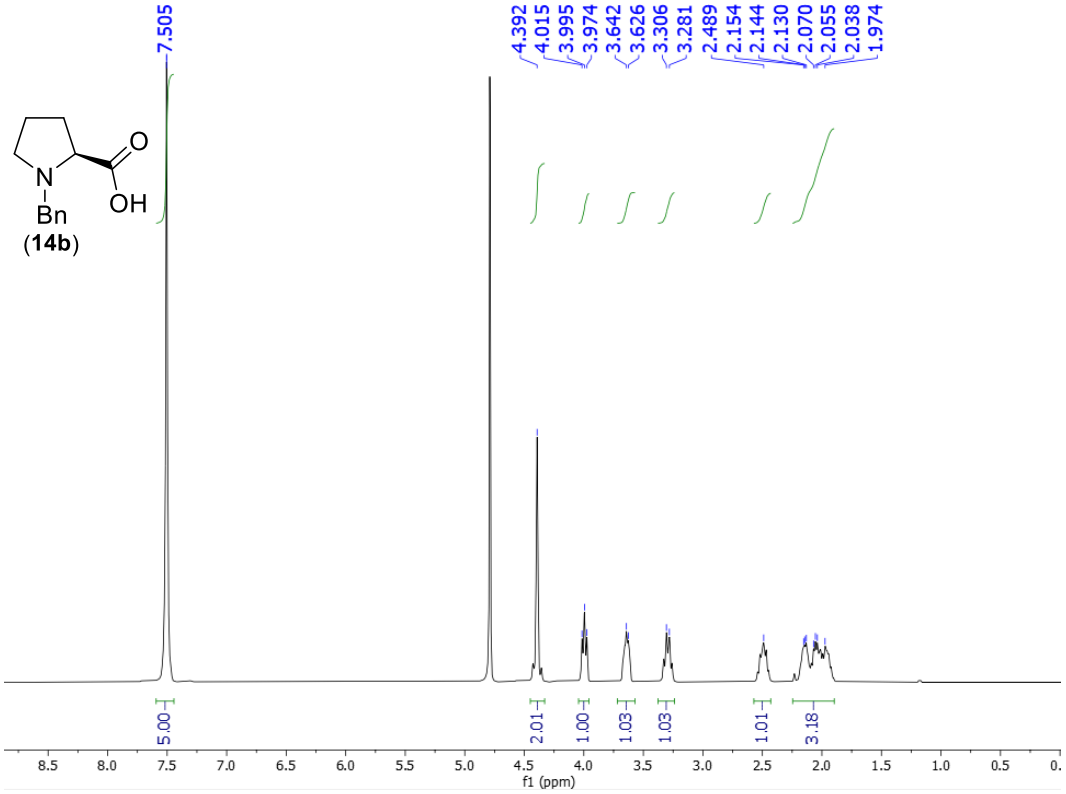
S.2.31. *N*-Methyl-L-Proline (**14a**)

S.2.31.1. ^{1}H NMR (D_2O, 400 MHz) spectrum of compound **14a**



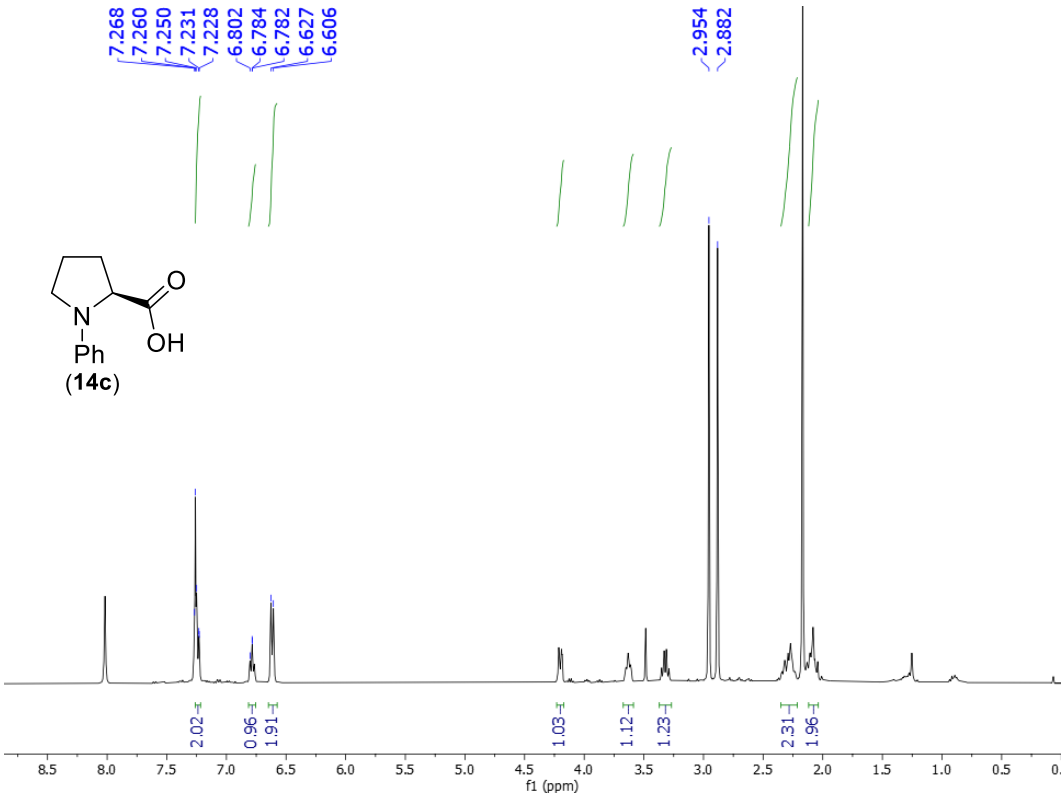
S.2.32. *N*-Benzyl-L-proline (**14b**)

S.2.32.1 ^{1}H NMR (D_2O, 400 MHz) spectrum of compound **14b**



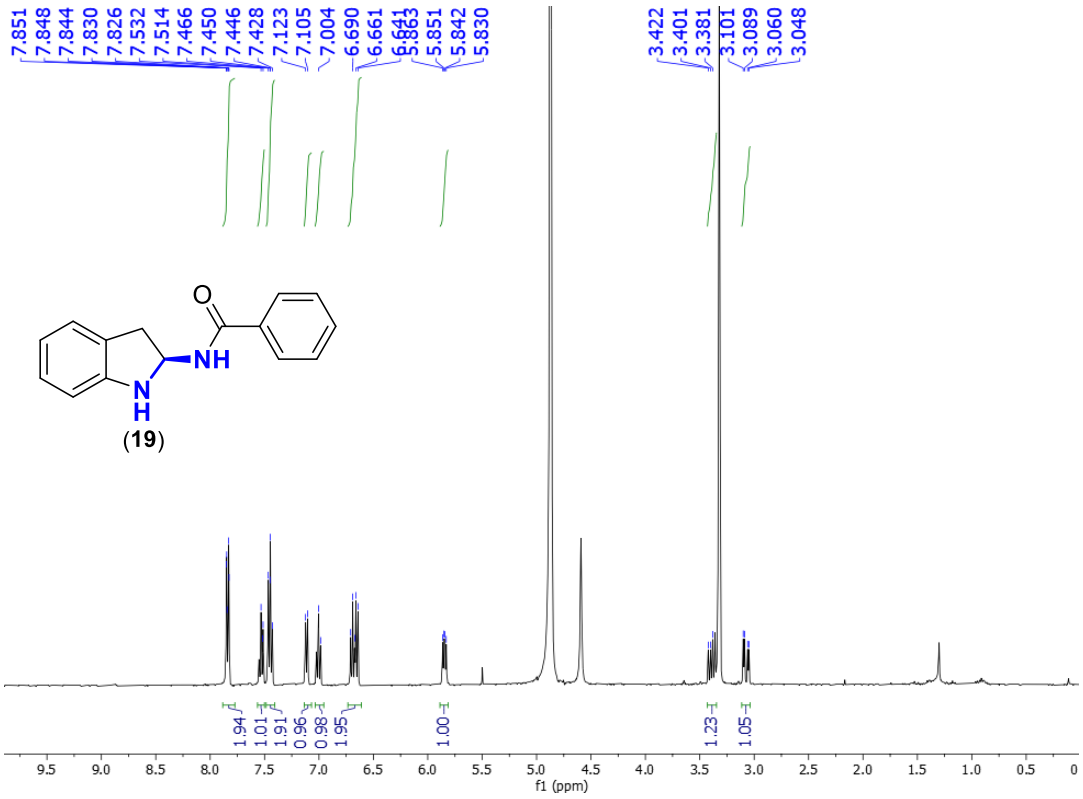
S.2.33. *N*-Phenyl-L-Proline (**14c**)

A.2.33.1. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **14c**

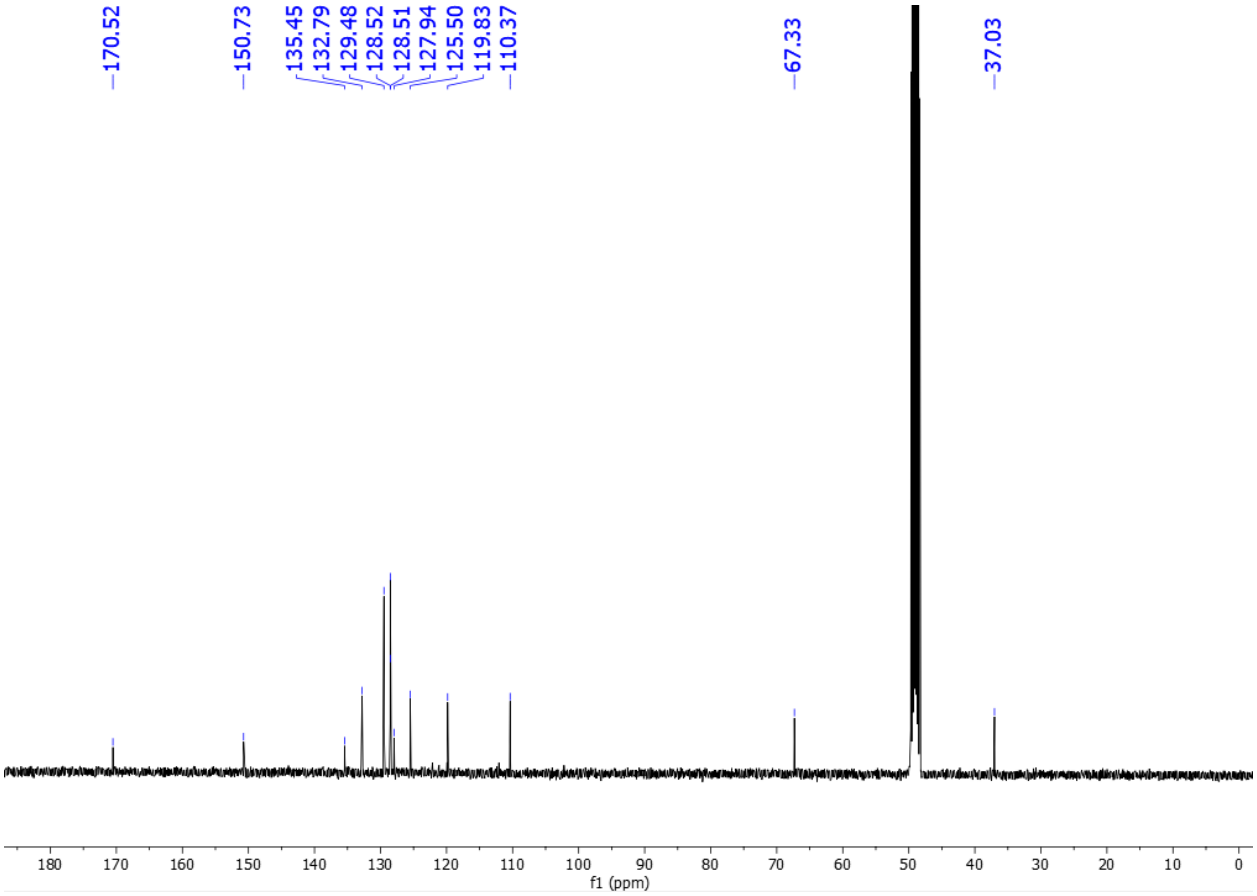


S.2.34. (*R*)-*N*-(Indolin-2-yl)benzamide (**19**)

S.2.34.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **19**

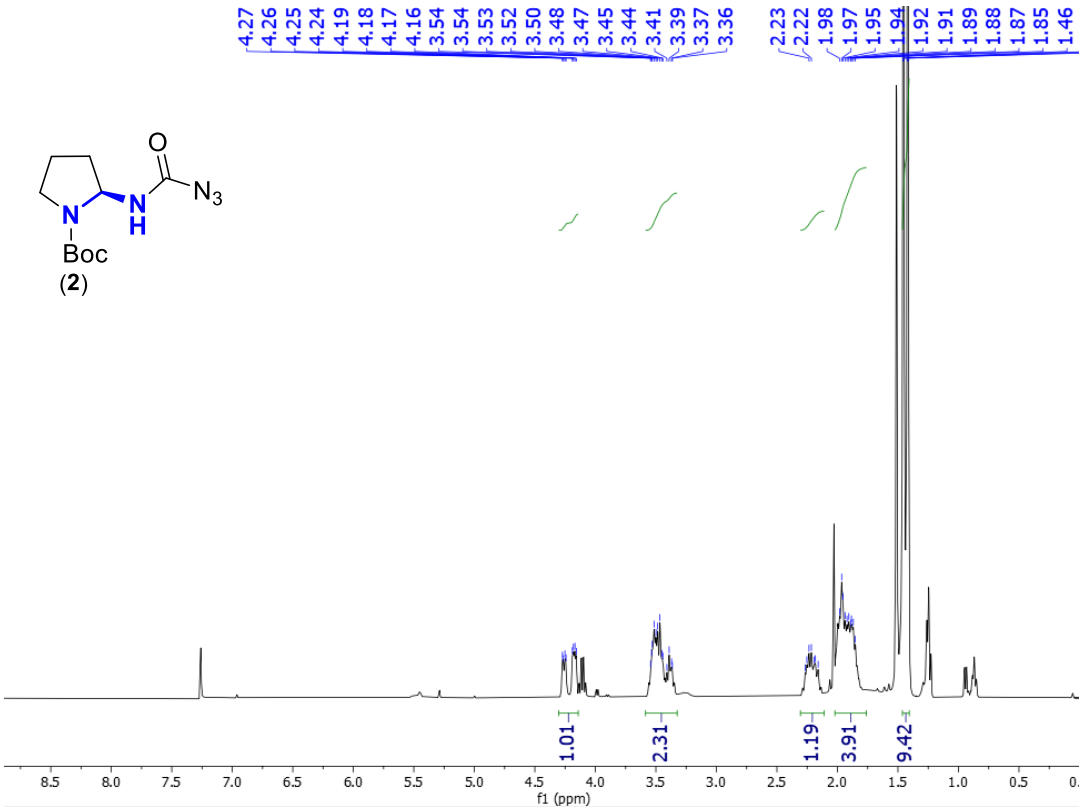


S.2.34.2. ^{13}C NMR (MeOD, 400 MHz) spectrum of compound **19**

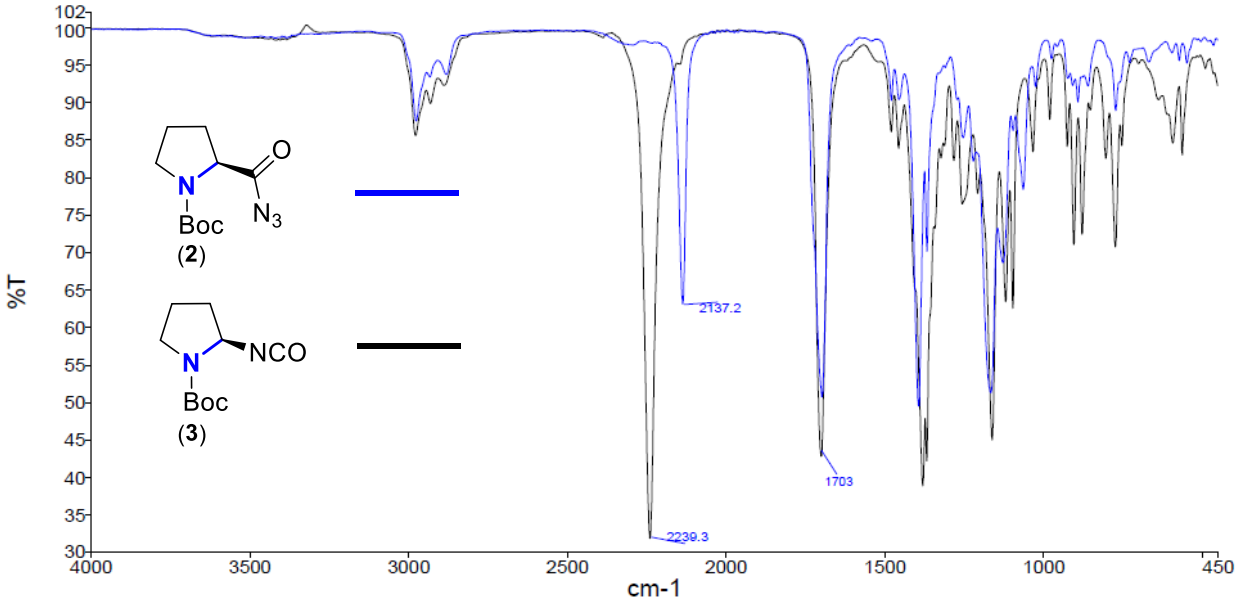


S.2.35. Acyl azides and isocyanates

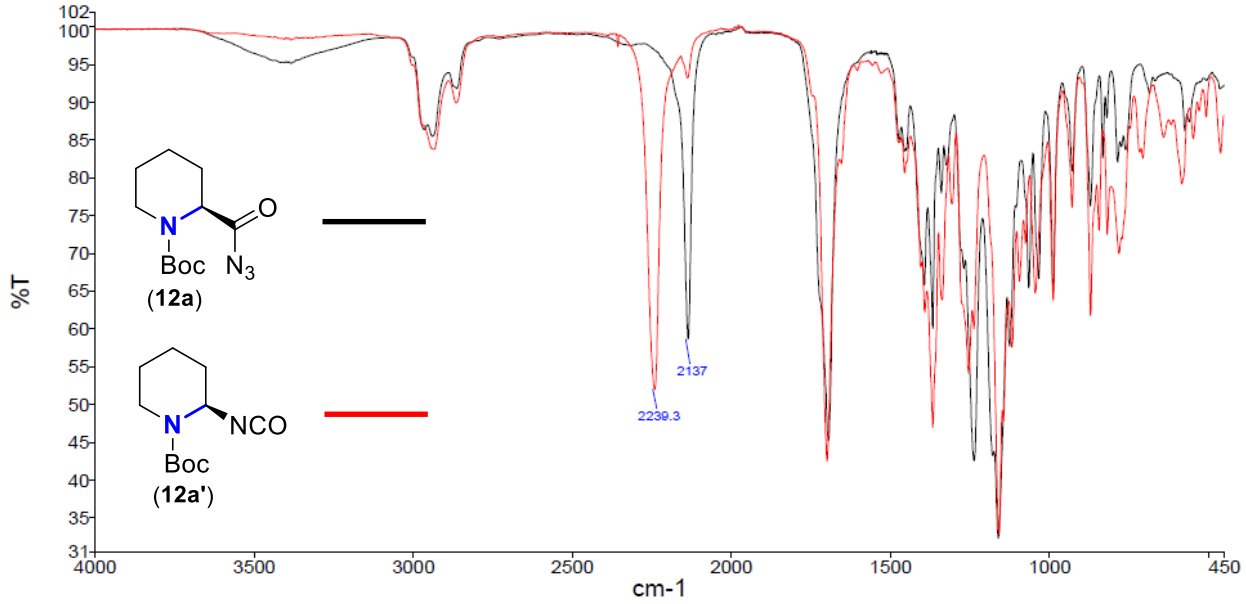
S.2.35.1. ^{1}H NMR (MeOD, 400 MHz) spectrum of compound **2**



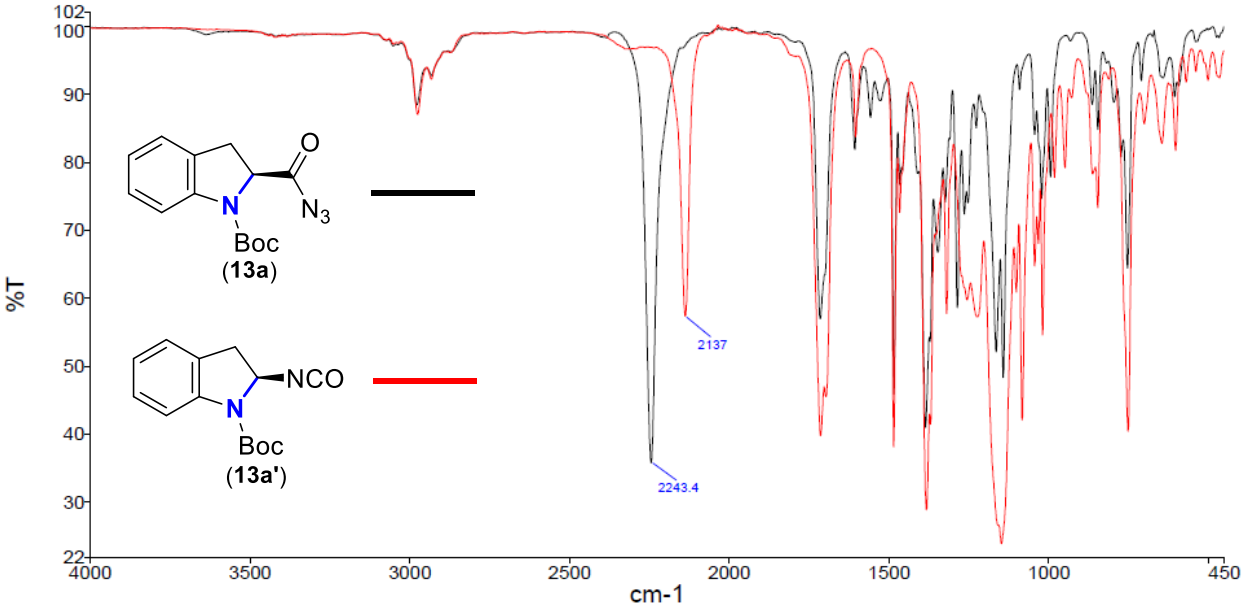
S.2.35.2. Stacked ATR-FTIR spectrum of compound acyl azide **2** (blue) isocyanate **3** (black)



S.2.35.3. Stacked ATR-FTIR spectrum of acyl azide from L-pipecolic carboxylic acid (12a-black) and isocyanate (12a'-red)

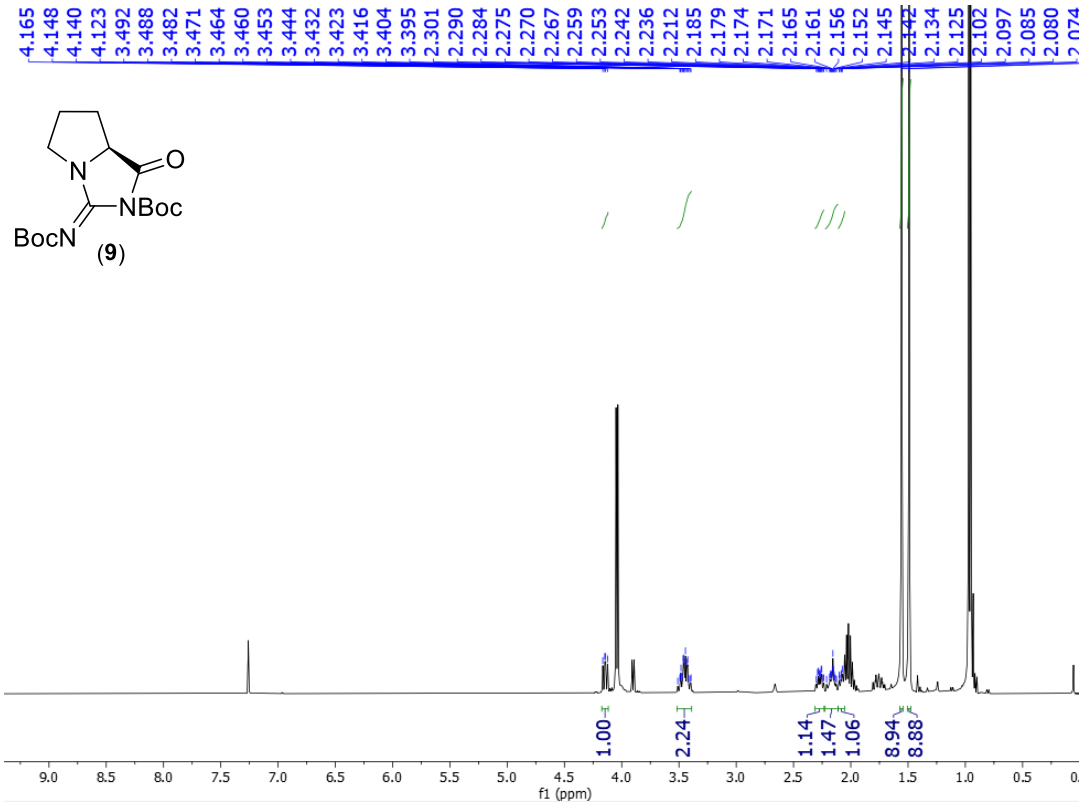


S.2.35.4. Stacked ATR-FTIR spectrum of acyl azide from (*S*)-(-)-indoline-2-carboxylic acid (13a-red) and isocyanate (13a'-black)

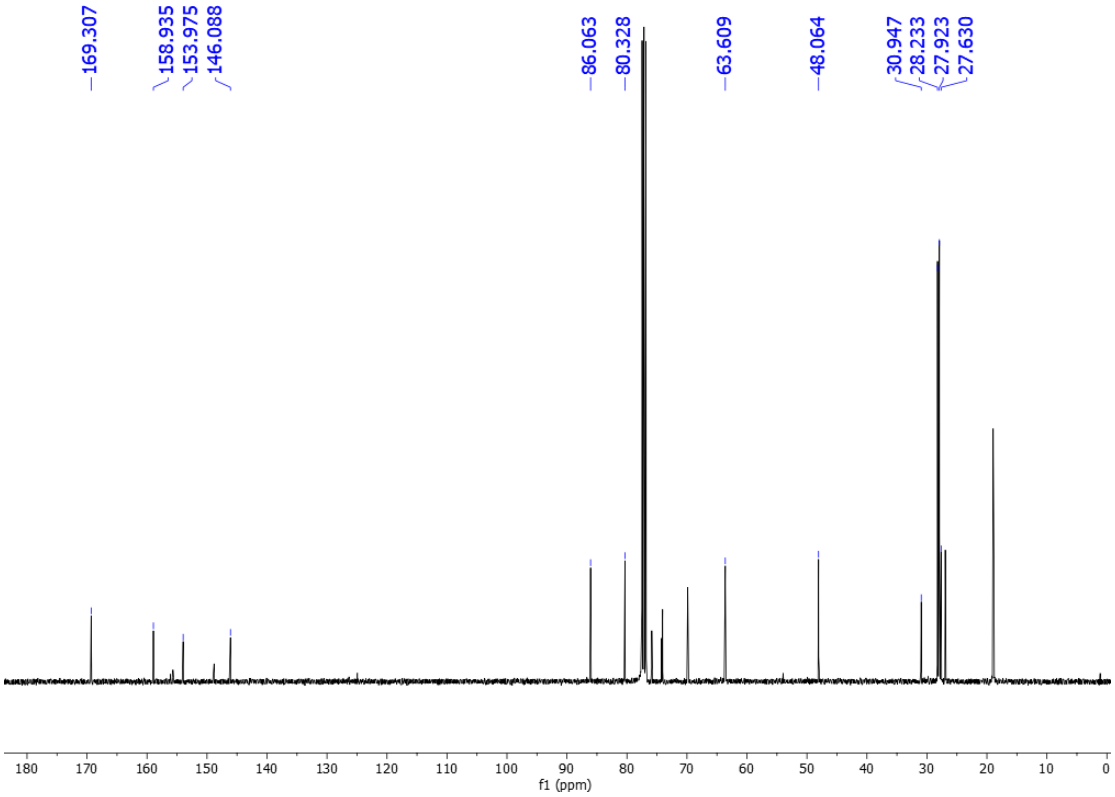


S.2.36. *tert*-Butyl (*S*)-3-((tert-butoxycarbonyl)imino)-1-oxotetrahydro-1*H*-pyrrolo[1,2-c]imidazole-2(3*H*)-carboxylate (**9**)

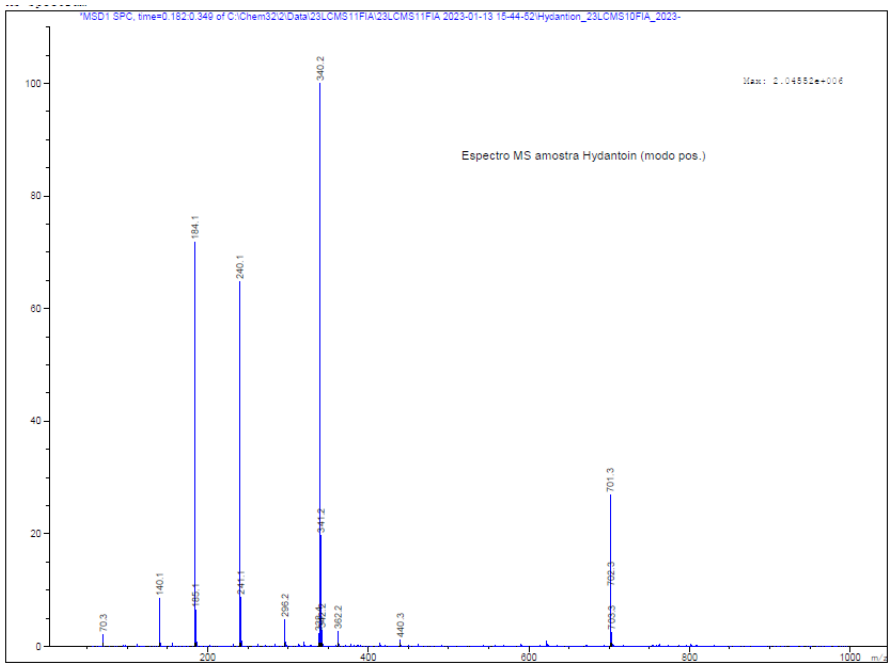
S.2.36.1. ^{1}H NMR ($CDCl_3$, 400 MHz) spectrum of compound **9**



S.2.36.**2.** ^{13}C NMR ($CDCl_3$, 101 MHz) spectrum of compound **9**



S.2.36.3. LCMS spectrum of compound **9**



S.3. Biological studies

Biological evaluation was performed by the postdoc researcher Catarina Roma-Rodrigues under the supervision of Professor Alexandra Fernandes at UCIBIO – Applied Molecular Biosciences Unit, Department of Life Sciences, NOVA School of Science and Technology, NOVA University Lisbon, 2819-516 Caparica, Portugal,

The procedure for evaluation of anti-inflammatory potential of the compounds followed a previously described protocol.[15] In a 6-well plate, 2x106 THP1 cells were exposed for 2 h to 700 ng/mL lipopolysaccharide (LPS, Sigma Aldrich, St Louis, MO, USA) in RPMI 1640 medium (ThermoFisher Scientific, Waltham, MA, USA) supplemented with 10% (IV/IV) fetal bovine serum and a mixture of 100 U/mL Penicillin and 100 µg/mL Streptomycin (ThermoFisher Scientific), and then exposed for 3 h to 0.1 % (IV/IV) DMSO (control) or 50 µM of each compound (LPS treated cells). In parallel, cells were submitted to the same procedure but without exposure to LPS (Normal cells). Samples were collected for mRNA and protein analysis, by centrifugation at 500 xg for 5 min, when cells were submitted to compounds (T=0) or after 3 h of compound exposure. The concentration of 50 µM of compounds did not induce any cytotoxicity, as evaluated by the MTS assay. Briefly, cell viability was determined using Cell Titer 96® Aqueous One solution cell proliferation assay (Promega, USA). In this method, an inner salt, 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) is bio-reduced into a colored formazan product that is soluble in culture medium. This conversion is achieved by mitochondrial dehydrogenases (NADPH or NADH) present in metabolically active cells in the presence of the phenazine methosulfate (PMS) that is used as electron coupling reagent. Formazan production, measured by absorbance at 490 nm, is directly proportional to the number of living cells in culture medium.[16]

The analysis of the tumor necrosis factor alpha (TNFa) expression was performed by reverse transcriptase - quantitative polymerase chain reaction (RT-qPCR). The total RNA was extracted using NZYol reagent (NZYtech, Lisbon, Portugal) according to manufacturer's instructions and then was reverse transcribed using the NZY MullV First Strand cDNA synthesis kit (NZYtech) according to manufacturer's instructions. The expression of TNFa and of the housekeeping gene, RNA18S, was determined by qPCR in a Rotor-Gene Q (Qiagen) using NZYSupreme qPCR Green Master Mix (NZYtech) using the conditions described in [Fernandes et al, 2020]. The relative expression of TNFa in LPS treated cells was calculated using the 2-DDCt method,[17] normalizing for RNA18S and for the expression of TNFa in the Normal cells condition.

The analysis of expression of the nuclear factor kappa B (NF-kB) was performed by western-blot. Pelleted cells were washed twice with Phosphate buffer saline (PBS) using centrifugations of 500 xg for 5 min, and

then solubilized in lysis buffer composed by 50 mM Tris-HCl (Sigma Aldrich), pH 8.5, 150 mM NaCl (Sigma Aldrich), 2% (IV/IV) NP-40 (ThermoFisher Scientific), 5 mM ethylenediaminetetraacetic acid (EDTA, Sigma Aldrich), 1× Phosphatase inhibitor (PhosStop, Roche, Basel, Switzerland), 1× Proteases inhibitors (complete Mini, Roche), 0.1% (w/IV) 1,4-Dithiothreitol (DTT, Sigma Aldrich), and 1 mM Phenylmethylsulfonyl fluoride (PMSF, Sigma Aldrich). After 2 h incubation at -80 °C, cells were submitted to 5 cycles of 2 min 30 sec of ultrasounds, centrifuged at 1500 xg for 5 min and the total amount of protein in the supernatant was quantified with Pierce 660nm protein assay kit (ThermoFisher Scientific) according to manufacturer's instructions. For western-blot analysis of NF-kB, 20 µg protein were first separated by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) using a 10% (w/IV) polyacrylamide gel and then semi-dry transferred to a polyvinylidene fluoride (PIVDF) membrane. The membranes were then blocked for 2 h with 5% (w/IV) low fat milk in TBST (50 mM Tris-HCl, pH 7.5, 150 mM NaCl, 0.1% (IV/IV) Tween-20 (Sigma Aldrich)), incubated o.n. with 1.3 µg/mL of anti-NF-kB p65 antibody (ab16502, Abcam, Cambridge, UK), washed three times with TBST, incubated for 1 h with 1 : 2 000 dilution of anti-IgG rabbit HRP-linked antibody (ref. 7074, Cell Signalling, DanIVers, MA, USA), washed three times with TBST, incubated for 5 min with ECL Prime Western Blotting System (CytiIVa, Marlborough, MA, USA) and signal was acquired in a Hyperfilm ECL (GE Healthcare). The membrane was then incubated with acidic stripping solution (0.1 M glycine, 20 mM magnesium acetate, 50 mM KCl, pH 2.2) and washed 3 times with TBST. After blocking with 5% (w/IV) low fat milk in TBST for 1 h, membranes were incubated for 1 h with a 1:5 000 dilution of β-actin antibody (ref. A5441, Sigma Aldrich), washed 3 times with TBST, incubated for 1 h with 1:3 000 dilution of anti-IgG mouse HRP-linked antibody (ref. 7076, Cell Signalling) and the signal of β-actin bands was acquired using the same procedure as for NF-kB. The percentage of area of the protein band on each sample (**Figure S1**), was measured using FIJI software.[18] The percentage of NF-kB in each sample incubated with LPS was calculated by normalizing to the internal control (β-actin) and to the expression in the corresponding sample in Normal cells. GraphPad Software (GraphPad Prism version 8.01 for Windows, GraphPad Software, La Jolla, CA, USA, www.graphpad.com) was used to perform the statistical analysis of the data performing a comparison using one-way ANOVA with a confidence interval of 95 % (* $p<0.05$).

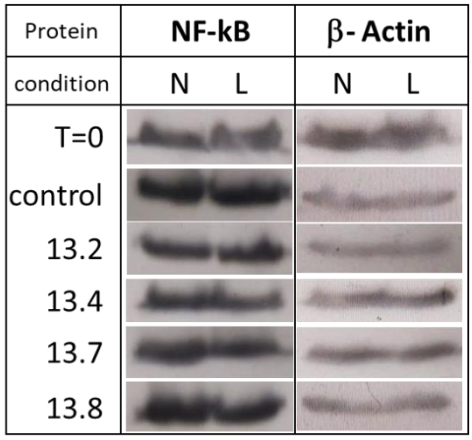


Figure S1*. Western Blot analysis of NF-kB (64 KDa) and b-Actin (45 KDa) proteins. THP1 cells were exposed for 2 h to LPS, and then exposed for 3 h to 0.1 % (IV/IV) DMSO (control) or 50 µM of each compound (L). In parallel, cells were submitted to the same procedure but without exposure to LPS (N). Samples were collected when cells were submitted to compounds (T=0) or after 3 h of compound exposure*

S.4. Aluminum ICP-AES analysis of deprotected 15d and 13

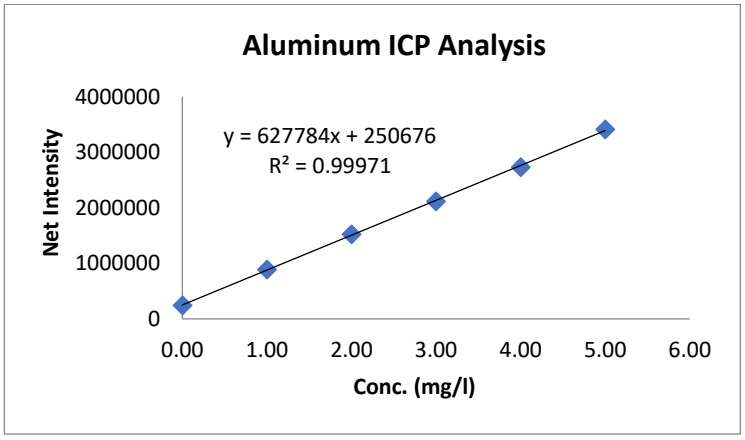
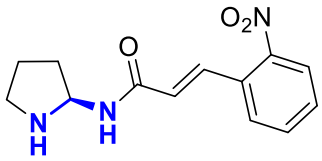
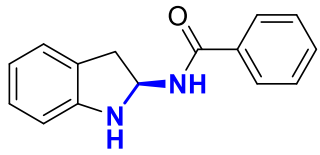


Figure S2*. Standard curve of Aluminum ICP assay.*



Deprotected 15d
(**Dep.15d**)



(**19**)

Sample	Conc. (ppm)	Conc. (g/ml)	Conc. (mg/l)	Net Intensity
Standard			0.00	244468
			1.00	887209
			2.00	1525686
			3.00	2116224
			4.00	2735150
			5.00	3412086
Blank			0.39	492713
19	517	0.002	1.42	1142217
Dep.15d	1253	0.002	2.89	2066133

MF	MW	MW + $AlMe_3$	%Al if complexed	Found (% of Al)
Dep.15d $C_{13}H_{15}N_3O_3$	261.11	333.16	8.09821107	0.12531539
19 $C_{15}H14N2O$	238,29	310,34	8,69369079	0,05172984

Although the analysis revealed the presence of aluminum, the percentage present in the sample (0.125%) is not in agreement with the expected percentage of 8.098% in case of aluminum coordination.

S.5. Computational Results

Full geometry optimizations have been performed with the Gaussian 16 software package[19] employing density functional theory (DFT) with the hybrid functional PBE1PBE[20-22] and the 6-31+G** basis set. Solvent effects in THF were included in the optimizations by using the Polarizable Continuum Model (PCM).[23] Harmonic vibrational frequencies have been calculated for all located stationary structures to verify whether they are minima or transition states. Thermal corrections have been taken from unscaled vibrational frequencies. Single-point PCM energy calculations in THF, were performed at the PBE1PBE/6-

311++G** levels of theory. All energies are in kcal.mol $^{-1}$ and were calculated at 25 °C. All bond distances are in Å.

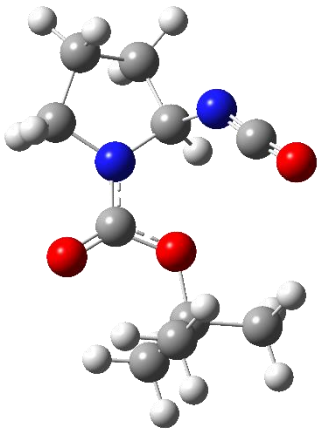
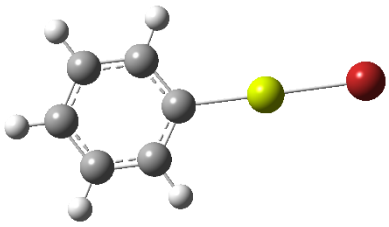
A – complex stablished by the coordination of magnesium with the amide carbonyl.

B – complex stablished by the coordination of magnesium with the amide nitrogen.

C – complex stablished by the coordination of magnesium with the amide and Boc carbonyl (8-membered ring).

D = IM1 – complex stablished by the coordination of magnesium with the amide nitrogen and Boc carbonyl (6-membered ring).

S.5.1 Cartesian coordinates and computed total energies for the reaction of 3 and PhMgBr: 3, PhMgBr, C-IM1, TS1, IM2, TSrot, IM2', TS2 and IM1'.

	
Isocyanate (3), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -725.142790945 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.216579 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -725.295250302 a.u	PhMgBr, optimization in solv. THF PBE1PBE/6-31G(d,p) E= -3002.84542151a.u. thermal correction to Gibbs Free energy at 25 °C = 0.056875 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3005.32501099 a.u
0, 1	0, 1

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O,0,-1.4627052227,-1.1107734498,0.3206776394	C,0,1.2608935423,-4.3912335173,-2.8219482789
O,0,-0.8451268697,1.0689976289,-0.0114169728	C,0,0.6053061151,-3.1431686909,-2.8218320292
C,0,-2.1983227135,1.6279824814,0.0882943631	C,0,-0.8034807021,-3.1941826984,-2.8211965064
C,0,-3.0740531847,1.0727677114,-1.0276849336	C,0,-1.5129772702,-4.3985287395,-2.8206859808
C,0,-2.7759318556,1.3560564327,1.4713106195	H,0,-1.3718774835,-6.5529029979,-2.8204090187
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H,0,-3.2531661953,0.0044131015,-0.896788854	H,0,-1.3812647237,-2.2699103364,-2.8210876251
H,0,-4.0368727852,1.5932580355,-1.0212753326	H,0,-2.6010478028,-4.3900224791,-2.820191693
H,0,-2.0960349441,1.7216887441,2.24749226	Mg,0,1.663499433,-1.3097728744,-2.822253788
H,0,-3.7262941245,1.8891829337,1.5740671526	Br,0,2.8675427018,0.8098695934,-2.8224755372
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H,0,2.8276639938,-1.8069059416,-1.3578004632	
H,0,3.3222160855,-2.4833532602,0.2019598819	
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H,0,3.1365684966,-0.2776671329,1.278954313	
H,0,3.8988400916,0.128512658,-0.2729629939	
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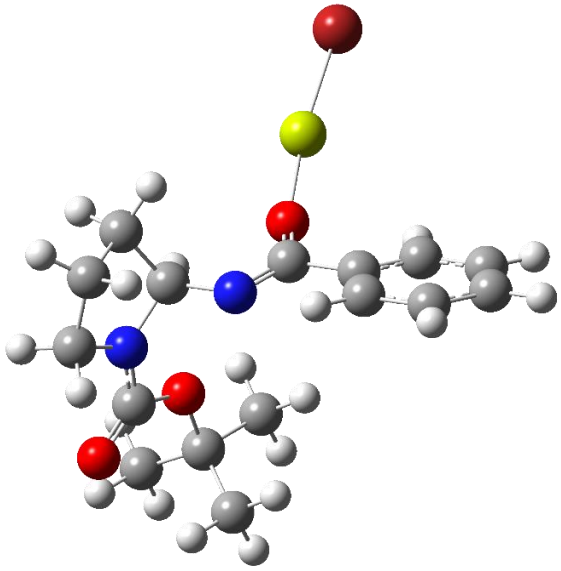
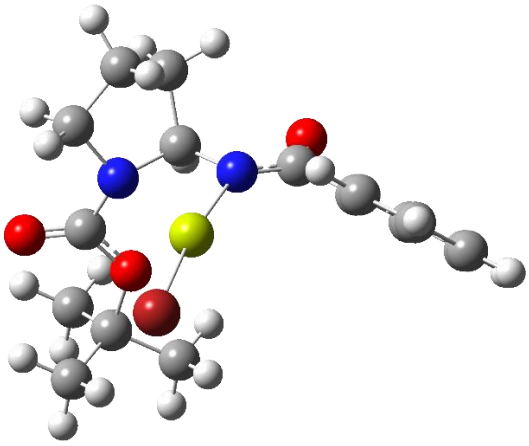
N,0,1.81980806,0.9421152268,-1.5480990291	

	
C (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3728.05731411 a.u. thermal correction to Gibbs Free energy at 25 °C = 0. 0.297301 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -- 3730.68431908 a.u	**D** (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-31G(d,p) E= -3728.06753889 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.302737 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3730.69098668 a.u
0, 1 N,0,0.7303782881,-0.4626072898,-0.0760630311 C,0,-0.5651225522,-0.1109625899,0.066650927 O,0,-1.4852965946,-0.9243300171,0.1140344521 O,0,-0.7032589622,1.2260834076,0.1660052069 C,0,-2.018355447,1.8503441613,0.2640628726 C,0,-2.8445577109,1.5399511189,-0.9788997833 C,0,-2.7192115141,1.4188884327,1.5474075065 C,0,-1.6788519948,3.3347660362,0.3181165077 H,0,-2.2917107407,1.8199933418,-1.8813103289 H,0,-3.0966830129,0.4796506681,-1.030717057 H,0,-3.7716574175,2.1215142406,-0.9521966109 H,0,-2.0801945128,1.6172471199,2.4141911788 H,0,-3.64268675,1.9946501109,1.6673312594 H,0,-2.9665332051,0.3566000294,1.5237683981 H,0,-2.5977903815,3.9247703847,0.3837681661	0, 1 N,0,0.5847343185,-0.5405338612,-0.478678462 C,0,-0.7093073223,-0.2727712322,-0.0030371628 O,0,-1.4190047627,-1.113257855,0.5075347767 O,0,-1.0315664264,0.9919967211,-0.2759129352 C,0,-2.3459329473,1.5577566635,0.089598986 C,0,-3.4487024602,0.8167260801,-0.6532110603 C,0,-2.5205386557,1.5089046439,1.6006900627 C,0,-2.2309440049,2.9940761361,-0.3980003211 H,0,-3.261440849,0.8249210377,-1.7314236 H,0,-3.5353874309,-0.2166271426,-0.3137660527 H,0,-4.401099949,1.3239870328,-0.4717915303 H,0,-1.6809620053,2.002802295,2.0995021145 H,0,-3.4368617789,2.0429956106,1.8696323917 H,0,-2.6000620428,0.4822398917,1.962097293 H,0,-3.1590606178,3.5298963317,-0.1806394481

H,0,-1.060932917,3.5572597277,1.1935953068	H,0,-1.4065432519,3.5094538036,0.1031787624
H,0,-1.1328896359,3.6372815934,-0.5805311902	H,0,-2.0601400546,3.0253115925,-1.4781900853
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H,0,0.8959929497,-2.3868345454,0.7623189415	H,0,0.8431781474,-2.1597120367,0.8586207592
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H,0,2.794330648,-1.7863273517,-1.5424479327	H,0,2.8887621137,-1.7611121244,-1.3910380711
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C,0,2.5271694826,4.7084465773,-4.5011401199	C,0,2.9577777382,2.2352788641,-4.050290395
H,0,2.3703825038,4.8330308828,-2.3568999354	C,0,2.840300102,5.0160668218,-4.1552152021
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H,0,2.4853004566,0.8731263741,-3.9773516142	C,0,3.1364141771,2.8948571518,-5.2658228805
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H,0,2.5256115805,5.7863231086,-4.6387208057	C,0,3.0668835622,4.2860953058,-5.3230091294
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H,0,2.6754834294,4.2771613598,-6.6078126379	H,0,3.3362926745,2.3215778599,-6.166828485
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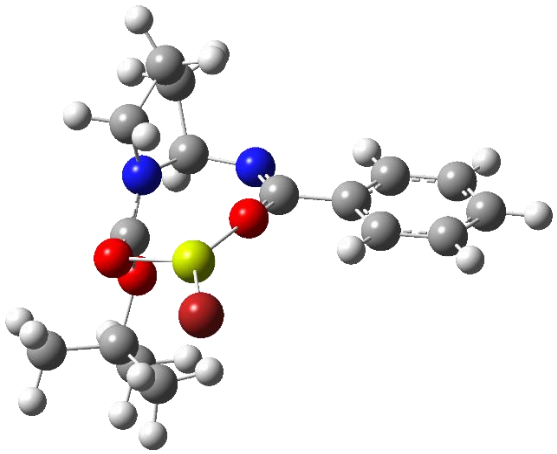

E (**3 + PhMgBr**), optimization in solv. THF

PBE1PBE/6-31+G(d,p) E= -3728.07179824 a.u.

thermal correction to Gibbs Free energy at 25 °C = 0.304796 a.u.

SP at PBE1PBE/6-311++G(d,p) in THF, E= --3730.69484408 a.u

0, 1

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C,0,2.3048361149,1.9410768947,-4.3015954505
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H,0,2.9554665887,2.2065883914,-3.4748404761
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H,0,-0.0458457694,0.943249161,-7.2103449566
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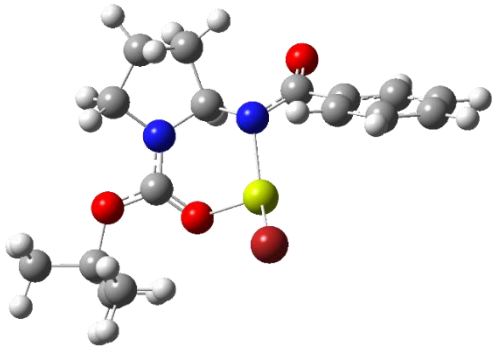	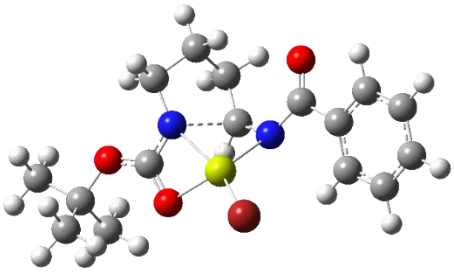
F (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3728.08137703 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.302826 SP at PBE1PBE/6-311++G(d,p) in THF, E= -3730.70469045 a.u	**TS1** (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3728.03897317 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.300759 a.u. 1 imaginary frequency = -122.68 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3730.66082454 a.u
0, 1 N,0,0.6005013898,-0.408023703,-0.1319281199 C,0,-0.6945848544,-0.1002475695,-0.2204290924 O,0,-1.4996823094,-1.0678071851,0.1758555779 O,0,-1.099704549,1.0124999992,-0.6488047686 C,0,1.0904269662,-1.7509902744,0.190398021 H,0,0.5094046714,-2.5015332582,-0.3487419946 H,0,0.9911951992,-1.9439498766,1.266406585 C,0,1.6763559141,0.6082027227,-0.1803844909 H,0,1.4943388499,1.3396909917,0.619817868 C,0,2.5481430391,-1.6680809719,-0.2316585993 H,0,2.6326367135,-1.8197982647,-1.3131787272 H,0,3.1661466465,-2.4180208873,0.2679988419 C,0,2.9261392239,-0.2375248634,0.1417515983 H,0,3.1358757478,-0.1701787223,1.2150611963 H,0,3.7980198241,0.1418940641,-0.3897207789 C,0,2.6779339841,2.2092404252,-1.5755438227 O,0,3.4413353361,2.5684132777,-0.6574764505 N,0,1.7099839171,1.2770216715,-1.4713846759 C,0,2.81356076,2.8494928435,-2.9334793657	0, 1 N,0,0.3693251564,-0.6140304119,-1.1112732479 C,0,-0.9470766987,-0.472222678,-0.8979364174 O,0,-1.5591427765,-1.3078793631,-0.0778493788 O,0,-1.5278422142,0.4812743038,-1.4970415219 C,0,1.1491067015,-1.648140543,-0.4592299354 H,0,1.2937182211,-2.5024262377,-1.1330318365 H,0,0.6336414909,-2.0143390548,0.4362271078 C,0,1.3615096371,1.1577391691,-0.2984443347 H,0,0.3968317403,1.4464747638,0.1213771498 C,0,2.4961489282,-1.0388605885,-0.0827007567 H,0,3.1119493296,-0.8832528213,-0.9734691641 H,0,3.0492868971,-1.6971963679,0.594452364 C,0,2.2344676748,0.3208503452,0.5825046493 H,0,1.7165296787,0.1745991867,1.5359756493 H,0,3.1836771167,0.8361800863,0.7554563214 C,0,3.0025025966,1.9598878834,-1.8304825508 O,0,3.9624650278,1.3785580295,-1.3301603767 N,0,1.6826010551,1.8603608829,-1.3878444161 C,0,-3.0066239104,-1.2402759175,0.2016125569

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H,0,-3.1574349877,0.0668137697,1.9118303587
H,0,-3.2245845156,1.1160100238,0.4745967567
Mg,0,-0.135186369,1.7361584159,-2.2471770645
Br,0,-1.1746847378,1.2411753169,-4.398881352
C,0,-3.2084944403,-2.4065530274,1.1577939949
H,0,-2.6045603211,-2.2765641827,2.0607030971
H,0,-4.2605720308,-2.4638772132,1.4505588211
H,0,-2.9293727048,-3.3509536404,0.6814295058
C,0,-3.7922889509,-1.4525209492,-1.0847255343
H,0,-3.6590828754,-0.619936786,-1.7770068812
H,0,-3.4809737178,-2.3806496245,-1.5741078235
H,0,-4.8557630549,-1.5378232724,-0.841473876
C,0,-3.3379412567,0.0808423099,0.8814189455
H,0,-4.3853490804,0.0664854177,1.1981233423
H,0,-2.7165644148,0.2186586075,1.7719946208
H,0,-3.1900384141,0.9244022668,0.2054380586
Mg,0,0.1539888494,0.9349454438,-2.6282147378
Br,0,-0.349453774,1.6748160837,-4.8848811012
C,0,3.2047178528,2.9051263466,-2.9697013925
C,0,4.4478153158,2.8961969822,-3.6170605534
C,0,2.2255260251,3.8172712085,-3.3800283888
C,0,4.7065776905,3.7813529196,-4.6567019825
H,0,5.2016323377,2.1877158398,-3.2882206044
C,0,2.493866971,4.7187670101,-4.4071215936
H,0,1.2639882705,3.8382082887,-2.8802056856
C,0,3.7293897401,4.6979678928,-5.051373078
H,0,5.6696447886,3.7616629792,-5.1586772147
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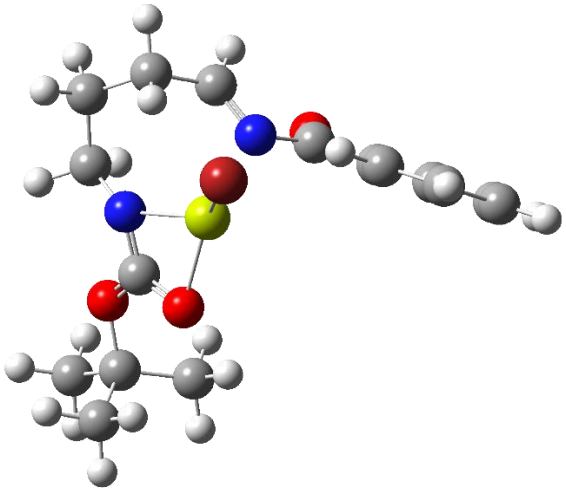
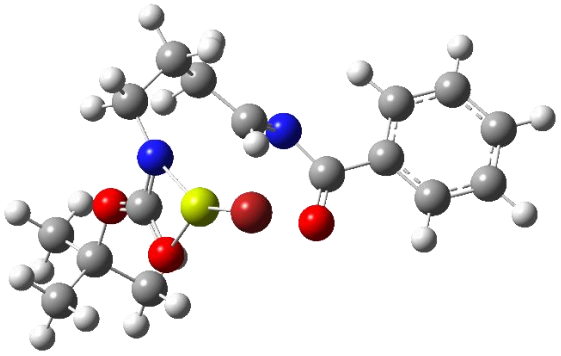
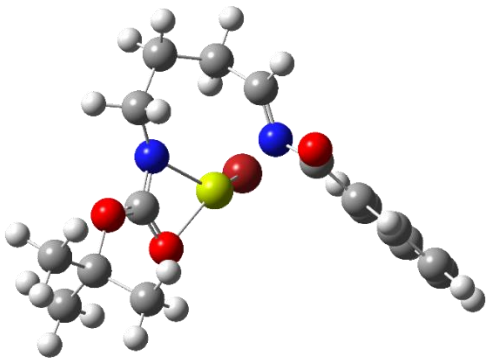
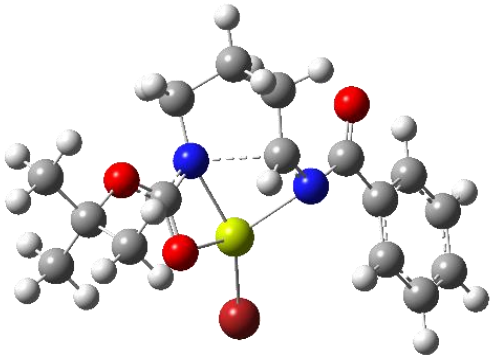
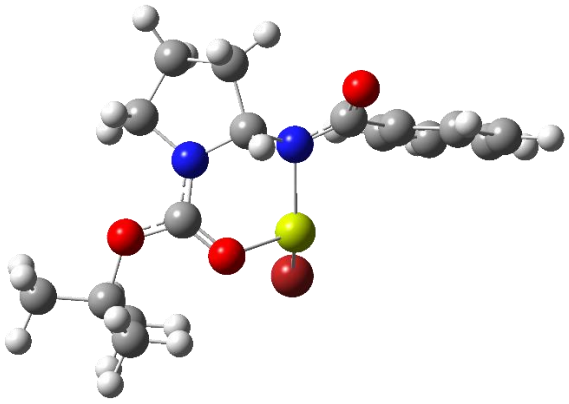
H,0,3.9335055913,5.3963327773,-5.8582692036

	
IM2 (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3728.08221191a.u. thermal correction to Gibbs Free energy at 25 °C = 0.302031 SP at PBE1PBE/6-311++G(d,p) in THF, E= -3730.67552509 a.u	**TSrot** (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3728.04182179 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.295977a.u. 1 imaginary frequency = -26.53 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3730.66712455 a.u
0, 1 N,0,0.8684280321,-0.8141328943,-0.4544846305 C,0,-0.3876659968,-0.7629182808,-0.9006549149 O,0,-1.2737933107,-1.2555037096,-0.0550117773 O,0,-0.6873206235,-0.2972735779,-2.0306269266 C,0,1.2638585424,-1.5050028135,0.7760219619 H,0,0.7514464834,-2.4664227378,0.8478910879 H,0,0.9941471503,-0.9034920427,1.6535315533 C,0,1.9717197768,-0.0511523139,-1.0770795735 H,0,1.697754301,1.0131322817,-1.0775617256 C,0,2.7712981559,-1.6131956515,0.6113552284 H,0,3.0168433102,-2.471088948,-0.0241082157 H,0,3.2833775983,-1.7394208193,1.5683014896 C,0,3.1289665911,-0.3063898526,-0.0907232564 H,0,3.168031752,0.5141929528,0.6342577068 H,0,4.0851398086,-0.3327150825,-0.6119899842 C,0,3.2136784416,0.1811467535,-3.0530895528	0, 1 N,0,1.409040798,-0.3223152374,-0.1829596956 C,0,0.4900659327,-0.1178458053,0.7432916729 O,0,-0.0771722417,1.0301311506,0.7817280494 O,0,0.1883948514,-1.0980469298,1.5942073005 C,0,-0.8475992182,-0.974020779,2.6248750407 C,0,-0.4656274606,0.1113399279,3.6223809019 C,0,-2.2039160519,-0.7224745679,1.9788788158 C,0,-0.820212982,-2.3444562641,3.2883955551 H,0,0.5289014879,-0.0831485605,4.0356775782 H,0,-0.4678278813,1.0971830207,3.1552966787 H,0,-1.1838617257,0.1099132185,4.448418268 H,0,-2.419505008,-1.4934257398,1.2320131486 H,0,-2.9823150737,-0.7674176199,2.7470647307 H,0,-2.239011197,0.2581380691,1.5018197325 H,0,-1.5566045785,-2.3788153309,4.0963115382 H,0,-1.0621569878,-3.1295417137,2.5655566857

O,0,3.8272320716,1.1550112616,-2.5756923682	H,0,0.1676525745,-2.5494103748,3.7119156854
N,0,2.2229061824,-0.5013140735,-2.4395019148	C,0,2.0607271732,-1.6025940085,-0.3730664011
C,0,3.5706488115,-0.3006115604,-4.4348466969	H,0,2.0375691718,-1.8415759648,-1.4436502415
C,0,3.9445575085,0.6390769551,-5.4025739356	H,0,1.5064962123,-2.3955786827,0.1445306663
C,0,3.5855149922,-1.6615450867,-4.763388043	C,0,3.7301089783,-0.0346337415,2.0623223511
C,0,4.2954214602,0.2284484659,-6.6850035175	H,0,3.2999551896,0.7244594214,1.3960039907
H,0,3.9557683113,1.6913751916,-5.133681242	C,0,3.5194671662,-1.6323387446,0.0857397652
C,0,3.954284932,-2.0741005696,-6.043413044	H,0,4.0933869232,-0.8731719809,-0.462325192
H,0,3.3226517926,-2.3954836753,-4.0062145296	H,0,3.9369255644,-2.6023249776,-0.2083494107
C,0,4.3019911291,-1.1300067108,-7.007878199	C,0,3.7218366368,-1.4528346076,1.5921187845
H,0,4.5684701341,0.9665208843,-7.4341165903	H,0,2.9210953545,-1.9724047815,2.1392181307
H,0,3.9724873633,-3.1329852012,-6.2857566268	H,0,4.6566682296,-1.9193381875,1.9222862552
H,0,4.5826793945,-1.4505225942,-8.0072808966	C,0,4.083669132,1.6360931578,3.5968566285
C,0,-2.7073194592,-1.4001171504,-0.3882318382	O,0,3.024588481,2.2442309992,3.5047800294
C,0,-3.2600457672,-2.0633775904,0.8646998971	N,0,4.2184806243,0.3012535632,3.1925988616
H,0,-3.0855750966,-1.4361094336,1.7435992554	C,0,5.2989597023,2.240278122,4.2030422833
H,0,-4.3375594081,-2.2128504048,0.7541218243	C,0,5.2665606303,3.5919691541,4.5685941693
H,0,-2.7899310279,-3.0374488514,1.0284997801	C,0,6.4700970633,1.4972725459,4.3961141233
C,0,-2.8776765658,-2.3072311086,-1.5986032386	C,0,6.3920538706,4.1934737061,5.1193653613
H,0,-2.526897314,-1.8341180125,-2.5170187545	H,0,4.351747816,4.155169872,4.41219133
H,0,-2.3436349435,-3.2509417029,-1.4491345915	C,0,7.5964829325,2.1027749022,4.9471209929
H,0,-3.9405691083,-2.5382119181,-1.7176396627	H,0,6.4855600036,0.4475716569,4.1217049296
C,0,-3.3235752322,-0.0233161953,-0.5892866837	C,0,7.5587069811,3.4492496438,5.3087003466
H,0,-4.4060097921,-0.1321365946,-0.7063256698	H,0,6.3636128706,5.2418955484,5.4014320834
H,0,-3.1380938149,0.6091534279,0.2843039379	H,0,8.5026241148,1.5234500928,5.0982828372
H,0,-2.9257715787,0.4675655203,-1.4787073692	H,0,8.4376872101,3.9197815378,5.7403700478
Mg,0,0.5253028573,-0.7428473094,-3.5667854807	Mg,0,0.9952780485,1.5781706676,-0.8791151156
Br,0,-0.6704765344,-1.2431184565,-5.612824092	Br,0,1.3314546814,3.303103622,-2.553372294

	
IM2' (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3728.05612034 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.299220 SP at PBE1PBE/6-311++G(d,p) in THF, E= --3730.67552628 a.u	**TS2** (**3 + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3728.03897317a.u. thermal correction to Gibbs Free energy at 25 °C = 0.300759 a.u. 1 imaginary frequency = -122.68 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= --3730.66082454 a.u
0, 1 N,0,0.4446101551,-1.4287957261,1.0470422523 C,0,-0.7533856354,-0.9037929885,1.1900096822 O,0,-1.6336529285,-1.0120735629,0.1915795063 O,0,-1.015405985,-0.2842653558,2.2825546686 C,0,0.9513806214,-1.8323308188,-0.2434263603 H,0,0.3612401228,-2.647127429,-0.6849222333 H,0,0.885011069,-0.9906389003,-0.9512151391 C,0,3.1440316165,0.0032583574,0.7032825314 H,0,3.6702634767,0.4844605848,-0.1282871636 C,0,2.4129012904,-2.2799679242,-0.1381009888 H,0,2.4687664365,-3.3216519131,0.196152504 H,0,2.8662083991,-2.2427304069,-1.1343330724 C,0,3.2665123801,-1.4683786425,0.8636566123 H,0,4.3187375543,-1.7392602369,0.7176463134 H,0,3.0057567817,-1.7496820811,1.8882463195 C,0,2.3517698401,2.1202762956,1.175688992 O,0,2.2296589552,2.4821125759,0.0191779691 N,0,2.4436576702,0.729796436,1.5002985455 C,0,2.3705993715,3.0554658326,2.3216871602	0, 1 N,0,0.369325,-0.61403,1.111273 C,0,-0.947077,-0.472223,0.897936 O,0,-1.559143,-1.307879,0.077849 O,0,-1.527842,0.481274,1.497042 C,0,1.149107,-1.648141,0.45923 H,0,1.293718,-2.502426,1.133032 H,0,0.633641,-2.014339,-0.436227 C,0,1.36151,1.157739,0.298444 H,0,0.396832,1.446475,-0.121377 C,0,2.496149,-1.038861,0.082701 H,0,3.111949,-0.883253,0.973469 H,0,3.049287,-1.697196,-0.594452 C,0,2.234468,0.32085,-0.582505 H,0,1.71653,0.174599,-1.535976 H,0,3.183677,0.83618,-0.755456 C,0,3.002503,1.959888,1.830483 O,0,3.962465,1.378558,1.33016 N,0,1.682601,1.860361,1.387844 C,0,-3.006624,-1.240276,-0.201613

C,0,2.0816330863,4.4051254118,2.0736634511	C,0,-3.208494,-2.406553,-1.157794
C,0,2.7029446337,2.6394581541,3.6178993517	H,0,-2.60456,-2.276564,-2.060703
C,0,2.108878572,5.3254517992,3.1129413326	H,0,-4.260572,-2.463877,-1.450559
H,0,1.8327762129,4.7115507681,1.06253172	H,0,-2.929373,-3.350954,-0.68143
C,0,2.7370604453,3.5689246157,4.6539843048	C,0,-3.792289,-1.452521,1.084726
H,0,2.9417198319,1.5997132361,3.823558309	H,0,-3.659083,-0.619937,1.777007
C,0,2.4382366688,4.9075820732,4.4047104245	H,0,-3.480974,-2.38065,1.574108
H,0,1.8761020893,6.3684000642,2.9201594131	H,0,-4.855763,-1.537823,0.841474
H,0,2.997211673,3.2456638323,5.6573734405	C,0,-3.337941,0.080842,-0.881419
H,0,2.4611881158,5.6280840948,5.217364169	H,0,-4.385349,0.066485,-1.198123
C,0,-2.991292378,-0.4654662494,0.2656977631	H,0,-2.716564,0.218659,-1.771995
C,0,-3.5830017185,-0.8611577656,-1.0805613966	H,0,-3.190038,0.924402,-0.205438
H,0,-3.0064307095,-0.4225292761,-1.9005780627	Mg,0,0.153989,0.934945,2.628215
H,0,-4.6145356839,-0.5043141037,-1.1519306882	Br,0,-0.349454,1.674816,4.884881
H,0,-3.5838065278,-1.9491535336,-1.1966798225	C,0,3.204718,2.905126,2.969701
C,0,-3.7603984809,-1.1287764316,1.4015488378	C,0,4.447815,2.896197,3.617061
H,0,-3.3420163471,-0.8582859915,2.3722472518	C,0,2.225526,3.817271,3.380028
H,0,-3.7352283947,-2.2177906186,1.292258474	C,0,4.706578,3.781353,4.656702
H,0,-4.8062506892,-0.8076580351,1.3662992262	H,0,5.201632,2.187716,3.288221
C,0,-2.9419265562,1.0509072501,0.4040950461	C,0,2.493867,4.718767,4.407122
H,0,-3.9573859722,1.4534162611,0.3330221456	H,0,1.263988,3.838208,2.880206
H,0,-2.3459263348,1.487418469,-0.4039241542	C,0,3.72939,4.697968,5.051373
H,0,-2.5131343734,1.3452063159,1.3632564683	H,0,5.669645,3.761663,5.158677
Mg,0,0.9943342949,-0.4070473451,2.7690126596	H,0,1.732972,5.431931,4.710235
Br,0,2.3149513508,-1.0657160917,4.721587236	H,0,3.933506,5.396333,5.858269



IM1' (3 + PhMgBr), optimization in solv. THF

PBE1PBE/6-311+G(d,p) E= -3728.08137707 a.u.

thermal correction to Gibbs Free energy at 25 °C = 0.302817

SP at PBE1PBE/6-311++G(d,p) in THF, E= - -3730.70468816 a.u

0, 1

N,0,0.6004338971,-0.4081156363,0.1323172304

C,0,-0.6946811608,-0.1004139856,0.220716847

O,0,-1.4997019873,-1.068060239,-0.1755036849

O,0,-1.0998720055,1.0124180175,0.6489440443

C,0,1.0904010705,-1.7509996743,-0.1902241481

H,0,0.5098531327,-2.5016177593,0.3493285274

H,0,0.990534482,-1.9440649637,-1.2661502871

C,0,1.6760823596,0.6082570356,0.1805803677

H,0,1.4935622585,1.3399915358,-0.619290178

C,0,2.5483613336,-1.6678807722,0.2309821287

H,0,2.6335971707,-1.8199458034,1.312388861

H,0,3.1661975062,-2.4175232231,-0.269331562

C,0,2.9259442299,-0.2371235138,-0.1421698029

H,0,3.1354622626,-0.1694011025,-1.2154901754

H,0,3.7978686547,0.1422690815,0.389243202

C,0,2.6778295251,2.2092726242,1.5758422064

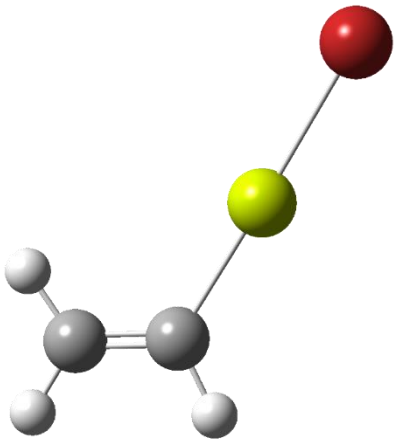
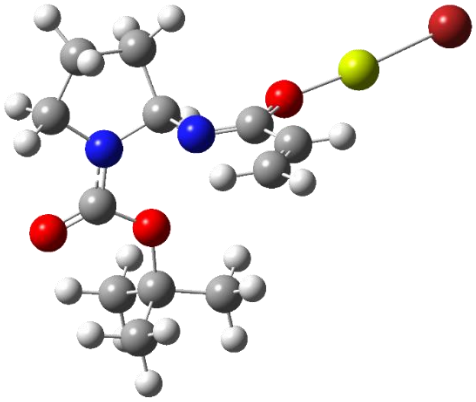
O,0,3.4410651733,2.5685918278,0.6576810636

N,0,1.7099110967,1.2769723982,1.4717135989

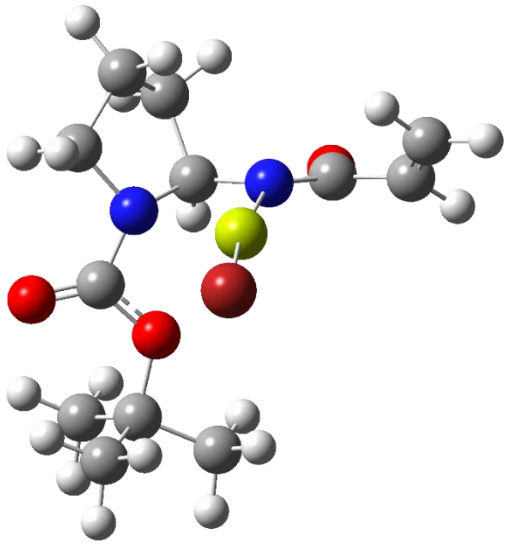
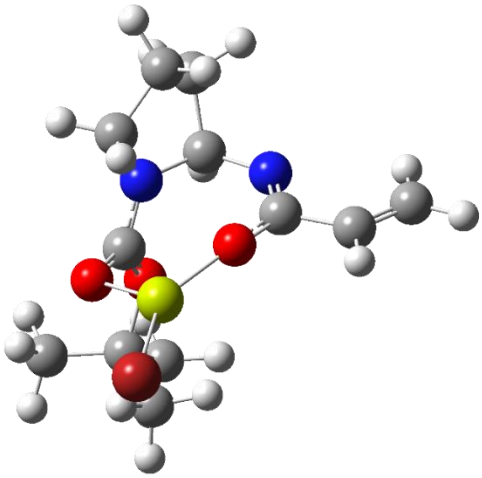
C,0,2.8136241143,2.8494780065,2.9337809715

C,0,3.27923483,4.1671414322,3.0178054518
C,0,2.5302861725,2.1499539603,4.1127489596
C,0,3.4358188413,4.7831698764,4.2554351289
H,0,3.5201200227,4.6941149456,2.0991908162
C,0,2.7031901409,2.7623236948,5.354166362
H,0,2.2044397528,1.1150905321,4.0610364098
C,0,3.1487449339,4.0803649782,5.4278909978
H,0,3.7878109306,5.8097351093,4.3091297593
H,0,2.4913715221,2.2065857059,6.2632111736
H,0,3.2794631988,4.5580252436,6.3949637098
C,0,-2.9708080883,-1.0001666671,-0.0399193009
C,0,-3.4046634269,-2.3417901269,-0.6117718064
H,0,-3.0881630415,-2.4392974803,-1.6543161626
H,0,-4.494468448,-2.4208983171,-0.5718350064
H,0,-2.9756768691,-3.1661633695,-0.034938955
C,0,-3.3500999824,-0.8899998104,1.4290136625
H,0,-3.0369475727,0.0607178326,1.8632841606
H,0,-2.9030620998,-1.7071095073,2.0034293747
H,0,-4.4377845701,-0.967887124,1.5199190169
C,0,-3.5147603306,0.1457159563,-0.8812870758
H,0,-4.6072938458,0.0855943561,-0.895944808
H,0,-3.1570564967,0.0657383389,-1.912479934
H,0,-3.2244514731,1.1156774845,-0.4758055965
Mg,0,-0.1352308593,1.736298097,2.2471895656
Br,0,-1.175274355,1.2406320051,4.3985018857

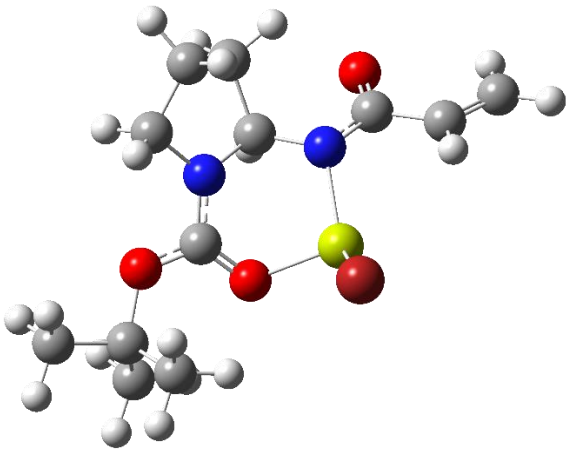
S.5.2. Cartesian coordinates and computed total energies for the reaction of **3** and **VinylMgBr**: 3, VinylMgBr, C-F, TS1, IM2, TSrot.

	
VinylMgBr, optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -2849.35255834 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.010705 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -2851.80963288 a.u	**C** (**3** + **VinylMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3574.56591775 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.264524 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= ---3577.16901287 a.u
0, 1 Mg,0,1.6611562969,-1.3522396202,-2.8224471238 Br,0,2.9101290645,0.7521621066,-2.8223880315 C,0,-0.8039265391,-3.1888859192,-2.8211254303 H,0,-1.3708259708,-4.1252403709,-2.8209231405 H,0,-1.4239829611,-2.2898330819,-2.8206280354 C,0,0.5414461057,-3.1357041595,-2.8218869079 H,0,1.022265154,-4.1227664049,-2.8222739606	0, 1 N,0,0.6971894348,-0.4808820001,-0.0880948018 C,0,-0.5992432961,-0.1314564207,0.0427450939 O,0,-1.5186625274,-0.9463644405,0.08542953 O,0,-0.7427449524,1.2062863759,0.135077919 C,0,-2.0602571114,1.8224396276,0.2480664688 C,0,-2.8985824407,1.5094951852,-0.9861956949 C,0,-2.7449586084,1.3853112819,1.5383145492 C,0,-1.7297849632,3.3090426635,0.3012233604 H,0,-2.3570008286,1.7935706549,-1.8942066301 H,0,-3.1452701297,0.4479209987,-1.0366456284 H,0,-3.8283875833,2.086159622,-0.9486261641 H,0,-2.0978476789,1.5861097783,2.3984928476 H,0,-3.6704415244,1.9554977699,1.6688320082 H,0,-2.9864632169,0.3216757539,1.5157185283 H,0,-2.6514643276,3.8928599813,0.3818222483 H,0,-1.1008657025,3.5333786015,1.1683811669 H,0,-1.1997892568,3.6178926075,-0.6049119636

	C,0,1.0819457876,-1.8867293432,-0.1751796151 H,0,0.5428369683,-2.3910422087,-0.983138114 H,0,0.8334120711,-2.4021826763,0.7617091333 C,0,1.8312075537,0.4405804785,-0.1600798072 H,0,1.6968524884,1.2369859798,0.5789482454 C,0,2.5921054496,-1.8261243705,-0.4096779013 H,0,2.8066067331,-1.8146724524,-1.4827299412 H,0,3.1103680128,-2.6815829856,0.0314391272 C,0,2.9957078861,-0.4897614557,0.2136518644 H,0,3.0523004295,-0.578615967,1.3055335599 H,0,3.9505925678,-0.1048117299,-0.1522127686 C,0,2.5760128663,2.104786735,-1.6059577119 N,0,1.9679844474,0.9740225778,-1.495946338 O,0,3.0721384033,2.7929083551,-0.6041733462 Mg,0,4.0418655871,4.2883717544,-0.035089333 Br,0,5.3424545966,6.1134601871,0.8578307751 C,0,2.750748267,2.7075019173,-2.9567712766 H,0,3.24554455,3.6777904384,-2.9697844318 C,0,2.36015303,2.1448575696,-4.1027968868 H,0,2.5215669945,2.6389953718,-5.056260498 H,0,1.8696272135,1.1754758238,-4.1032243532

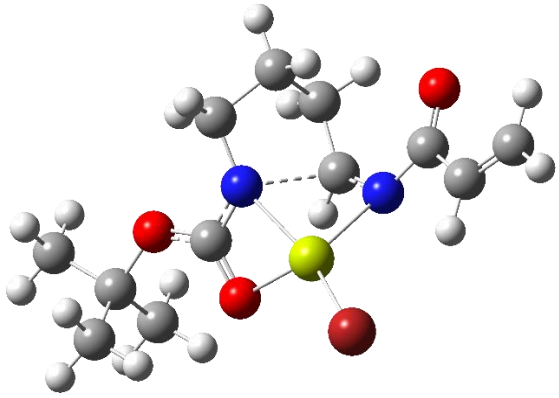
	
D (**3** + **VinylMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3574.57561949 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.258376 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= --3577.17567926 a.u	**E** (**3** + **VinylMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3574.57757770 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.259643 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3577.17801295 a.u
0, 1 N,0,0.5464709165,-0.5175326478,-0.5211584788 C,0,-0.747095985,-0.272831462,-0.0361830319 O,0,-1.4375050553,-1.1240015123,0.4835553139 O,0,-1.0961494805,0.9854618384,-0.3099971231 C,0,-2.3937861722,1.5400977007,0.1249368487 C,0,-3.5320115955,0.7826162463,-0.5442640222 C,0,-2.4770925339,1.5022550501,1.6443218947 C,0,-2.3244326118,2.9735324633,-0.3792225124 H,0,-3.4033727833,0.7751618649,-1.6309621858 H,0,-3.5942864449,-0.2457215801,-0.1854843379 H,0,-4.4752710677,1.2891293731,-0.3183071022 H,0,-1.6166053403,2.0126050519,2.0879908324 H,0,-3.383537874,2.0249490841,1.9641855959 H,0,-2.5197207894,0.477687215,2.0182090108 H,0,-3.24146926,3.5023427723,-0.1048421812 H,0,-1.4740818073,3.5002955627,0.0633110684 H,0,-2.2261318878,2.998145939,-1.4685910931	0, 1 N,0,0.6409964732,-0.3410973345,0.0767426316 C,0,-0.6376206493,0.0351954069,0.0943737654 O,0,-1.5867778105,-0.7617262779,-0.1420276252 O,0,-0.8067820448,1.3201599155,0.3575050958 C,0,-2.1255936992,1.9376892235,0.5928229189 C,0,-3.0136102332,1.8312979584,-0.6387403411 C,0,-2.7613662357,1.3028495001,1.820961595 C,0,-1.7541423561,3.3901474694,0.8544016632 H,0,-2.4612953676,2.1145452583,-1.5406129543 H,0,-3.4293246387,0.8290386917,-0.7560655522 H,0,-3.8523212747,2.525565287,-0.5305777886 H,0,-2.0972282939,1.3893382736,2.6861425023 H,0,-3.6936897097,1.8267939054,2.052405468 H,0,-2.993428272,0.2497468096,1.6486109691 H,0,-2.6564964903,3.9633036902,1.0844169374 H,0,-1.0676854193,3.4670898764,1.7021980382 H,0,-1.276978056,3.8315692913,-0.0254495151

C,0,1.0902718901,-1.866761169,-0.2342273854	C,0,1.0484137636,-1.7429322785,-0.0426628635
H,0,0.6669457086,-2.6008297101,-0.9234501886	H,0,0.4909351917,-2.2711331575,-0.8209234676
H,0,0.8155186712,-2.1599429074,0.7849331869	H,0,0.8572734098,-2.2494867256,0.9093622225
C,0,1.6151955282,0.5260560905,-0.308532766	C,0,1.730012521,0.5833686966,-0.3101024865
H,0,1.2659229009,1.2771676984,0.4066397286	H,0,1.6542527513,1.4845934568,0.3052356129
C,0,2.5928049974,-1.6730559716,-0.3656248612	C,0,2.5433202139,-1.6646879001,-0.3760474237
H,0,2.8946319506,-1.6820172045,-1.4190211509	H,0,2.6903816052,-1.7743447211,-1.4549205176
H,0,3.1510103684,-2.4569949353,0.1512737718	H,0,3.1121121561,-2.4528262873,0.122946889
C,0,2.7959761183,-0.2852403874,0.2348356953	C,0,2.9522950467,-0.259143229,0.0634091941
H,0,2.7367089546,-0.334456829,1.3283092013	H,0,3.0992665059,-0.2184409827,1.148924059
H,0,3.7423500668,0.1872225406,-0.0357908785	H,0,3.8546775064,0.1076185781,-0.4286481813
C,0,2.5250019468,2.2845508484,-1.6048881875	C,0,0.9747413528,0.5961625342,-2.6304550965
O,0,2.908943407,2.8910139133,-0.5834564736	N,0,1.7723258154,0.9801492653,-1.6895147188
N,0,1.8618945185,1.1197899476,-1.6061693601	O,0,-0.0469442643,-0.2178964593,-2.5671245805
Mg,0,0.5245812813,0.1845257586,-2.759575903	Mg,0,-1.6782768868,-1.0877885685,-2.1448984157
Br,0,-0.9179441382,-0.7685969499,-4.4484751018	Br,0,-3.5095394528,-2.1924563683,-3.2757677569
C,0,2.8282724942,2.8820558418,-2.9407585183	C,0,2.1871377084,1.9839945497,-4.3452369813
H,0,2.7935380036,3.9697152421,-2.9703778595	H,0,2.303385036,2.3230129234,-5.3705758376
C,0,3.2330364814,2.1889403753,-4.0084964265	H,0,2.8795250516,2.3627436093,-3.5983901906
H,0,3.502218218,2.68679026,-4.9359616014	C,0,1.222845321,1.1253228768,-4.0065269397
H,0,3.3366216247,1.1066003783,-3.9799787178	H,0,0.531942055,0.7483441929,-4.758400318



F (**3 + VinylMgBr**), optimization in solv. THF

PBE1PBE/6-311+G(d,p) E= -3574.59013047 a.u.

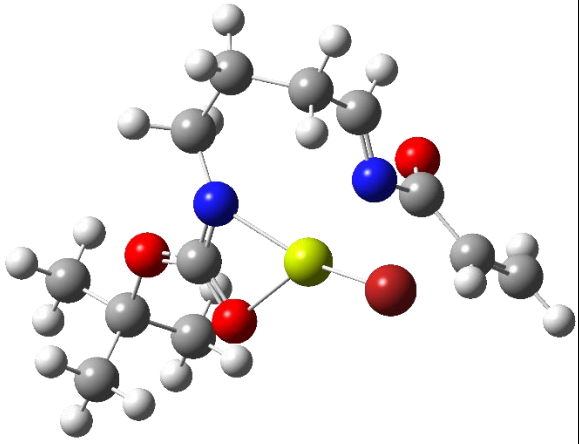
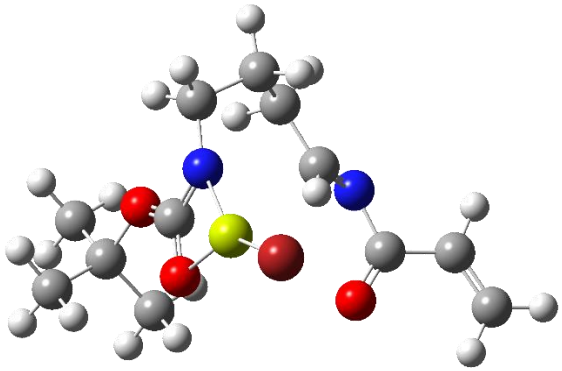


TS1 (**3 + VinylMgBr**), optimization in solv. THF

PBE1PBE/6-311+G(d,p) E= -3574.54890748 a.u.

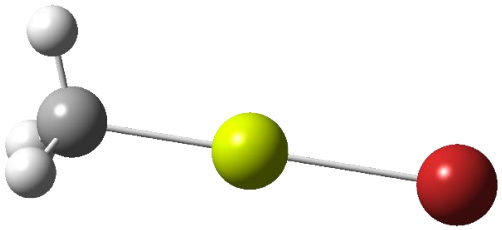
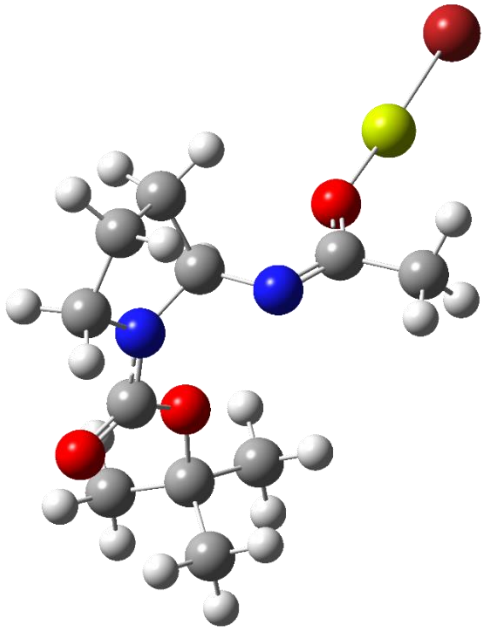
thermal correction to Gibbs Free energy at 25 °C = 0.259338 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3577.18870023 a.u	thermal correction to Gibbs Free energy at 25 °C = 0.254923a.u. 1 imaginary frequency = -128.25 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3577.14784887ca.u
0, 1	0, 1
N,0,1.1585883209,0.0237715394,0.5236774926	N,0,0.3885162259,-0.4671874308,-1.0957880042
C,0,-0.0897427076,0.4174383896,0.7957241345	C,0,-0.9293388615,-0.3663457478,-0.8750731903
O,0,-0.58132277,1.4770510877,0.3249477111	O,0,-1.5300830649,-1.2740159729,-0.1264583848
O,0,-0.7499383132,-0.4142060256,1.5771932776	O,0,-1.5240671895,0.6238609742,-1.3991194681
C,0,-2.1886057569,-0.2667417754,1.888732048	C,0,1.2002041104,-1.5215772349,-0.5222612923
C,0,-2.4148718756,1.0226696311,2.6647442035	H,0,1.3940553836,-2.3042398252,-1.2669011547
C,0,-3.0077351173,-0.3392943255,0.6094180552	H,0,0.6879557272,-1.989281311,0.3266365642
C,0,-2.4489373854,-1.4805752947,2.7685957037	C,0,1.3279973385,1.2733876859,-0.1060737368
H,0,-1.7622658982,1.0607466578,3.5423442729	H,0,0.3427537308,1.5246951929,0.2906973529
H,0,-2.2325635996,1.9012969322,2.0443961532	C,0,2.514641143,-0.8941434018,-0.061312635
H,0,-3.4522802214,1.0493760137,3.0118149003	H,0,3.1376037422,-0.6266103808,-0.9215946328
H,0,-2.7593070975,-1.2422089419,0.0435891923	H,0,3.088122566,-1.5937300097,0.5543965646
H,0,-4.0689137889,-0.3845466436,0.8723833576	C,0,2.1762130839,0.3754325258,0.7346872547
H,0,-2.8477484764,0.531637233,-0.027606509	H,0,1.6136149718,0.1096103139,1.6351358193
H,0,-3.4964997227,-1.4869215136,3.0820385163	H,0,3.0927103514,0.9011150098,1.0148089524
H,0,-2.244718434,-2.4062357899,2.2228590843	C,0,3.0157494263,2.2136791463,-1.5159317164
H,0,-1.8196752697,-1.4529517085,3.6628995315	O,0,3.9854049434,1.9437870558,-0.8108225286
C,0,1.665332353,-1.3099032651,0.8607607448	N,0,1.684211062,2.0101551056,-1.1564969418
H,0,0.9241998988,-2.0670779552,0.5972714642	C,0,-2.9827342208,-1.2642601987,0.1335572016
H,0,1.8686194179,-1.3821264902,1.9370090902	C,0,-3.171068177,-2.5137823371,0.9810824689
C,0,2.2239707777,0.9509000793,0.0700152585	H,0,-2.583529262,-2.4505609892,1.9017489144
H,0,2.3044446696,1.7649748994,0.8044046375	H,0,-4.2257420503,-2.6194167122,1.2500915948
C,0,2.9439887433,-1.3782670151,0.0430043265	H,0,-2.8634214985,-3.406428156,0.4285659456
H,0,2.7085168299,-1.637517575,-0.9949028809	C,0,-3.7442429376,-1.3827178166,-1.1792682311
H,0,3.6445142944,-2.1209765604,0.4324167818	H,0,-3.6247175284,-0.4893030621,-1.7937928291
C,0,3.4749820545,0.0489672984,0.132882457	H,0,-3.400863301,-2.2559058869,-1.7428314868
H,0,3.9797633868,0.2050988475,1.0927247926	H,0,-4.8082221844,-1.5170818703,-0.9619222802
H,0,4.1778421519,0.3098700843,-0.6571824372	C,0,-3.3555056525,-0.0146800792,0.9187583649
C,0,2.8788667125,2.3671481007,-1.6806038844	H,0,-4.4077198571,-0.0782243785,1.2127495256

O,0,3.8842955863,2.7206920059,-1.0323928839	H,0,-2.7528973525,0.0581656355,1.8296229109
N,0,1.9398145275,1.4998966137,-1.2462257402	H,0,-3.2147588567,0.8874598622,0.3213498593
Mg,0,-0.0601359522,1.7678408441,-1.6004707612	Mg,0,0.1555481087,1.1889134513,-2.4770265638
Br,0,-1.3978324546,0.4382570032,-3.1558033476	Br,0,-0.1691019094,2.1688924087,-4.6861171164
C,0,2.6499031395,2.8999903878,-3.060997535	C,0,3.1604937287,2.8892537725,-2.8315587022
H,0,1.8459309747,2.4602216742,-3.6495800578	C,0,4.3582218386,3.2578836227,-3.2943942671
C,0,3.4200803926,3.8524894556,-3.5910126394	H,0,2.2550012881,3.0650717253,-3.4077852571
H,0,4.2398243806,4.2741764551,-3.0152158679	H,0,4.4649940494,3.7475555593,-4.2572201739
H,0,3.2565465588,4.2219984963,-4.5987671133	H,0,5.2560339041,3.077272034,-2.7088832107

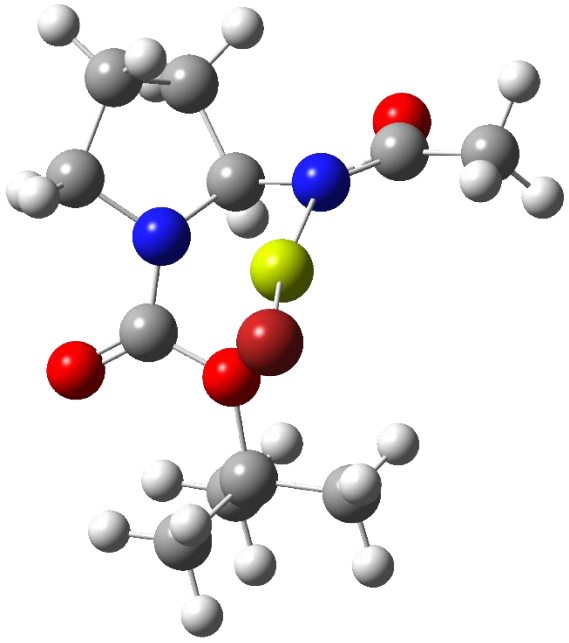
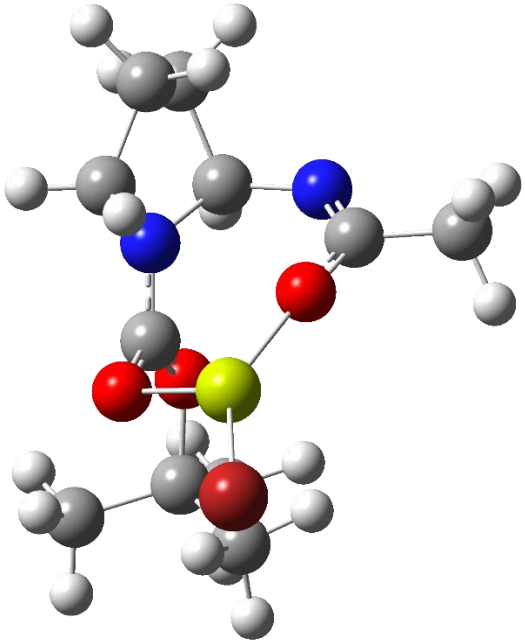
	
IM2 (**3 + VinylMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3574.56318696 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.254377 SP at PBE1PBE/6-311++G(d,p) in THF, E= -3577.16010417 a.u	**TSrot** (**3 + VinylMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3574.54989247 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.250661 a.u. 1 imaginary frequency = -35.52 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= --3577.14784887 a.u
0, 1 N,0,0.4257075308,-1.2429289329,-1.2058757219 C,0,-0.8174450073,-0.8070894068,-1.1950030952 O,0,-1.6361916806,-1.2104673738,-0.2202406638 O,0,-1.1816768186,0.0116343126,-2.1114244524 C,0,1.0077397297,-1.8630640224,-0.0369787688	0, 1 N,0,1.4077804628,-0.3028055439,-0.1700780178 C,0,0.4805168902,-0.1023466948,0.7487598044 O,0,-0.095343015,1.0415703771,0.7796236133 O,0,0.1796161394,-1.0817057729,1.6008442715 C,0,-0.8660697293,-0.9616803208,2.6222600682

H,0,0.5541722678,-2.8396435128,0.1819262671	C,0,-0.5010866992,0.1303647902,3.6189333163
H,0,0.8223519806,-1.2373473212,0.8501742382	C,0,-2.2186651623,-0.7228705977,1.9637090226
C,0,2.9169882297,0.4555729845,-0.4679108382	C,0,-0.8338195159,-2.3293298206,3.2912240353
H,0,3.4311989524,0.8262957175,0.4252603026	H,0,0.4925640589,-0.053109661,4.0394118993
C,0,2.5185470129,-2.0504414916,-0.2068832137	H,0,-0.5095747195,1.1146550053,3.1486815491
H,0,2.7275554482,-2.9643087631,-0.7737356569	H,0,-1.2248237787,0.124654866,4.440116166
H,0,2.9702404361,-2.1835487484,0.7817643859	H,0,-2.4222253203,-1.4984206898,1.2182387021
C,0,3.2332172807,-0.9095637248,-0.9648190694	H,0,-3.0032343872,-0.770356704,2.7254261579
H,0,4.314981019,-1.0598325117,-0.8737743798	H,0,-2.2569142943,0.2555184555,1.4823400978
H,0,2.998259574,-0.9693447133,-2.0316635491	H,0,-1.5771791668,-2.366534787,4.09260626
C,0,1.8642685619,2.5179738705,-0.503390922	H,0,-1.0629711816,-3.119059768,2.569283005
O,0,1.8558204488,2.6993084686,0.6996961714	H,0,0.151783603,-2.524772797,3.7243774691
N,0,2.076655774,1.220900007,-1.0680060803	C,0,2.0711361936,-1.5785186464,-0.3506636312
C,0,-3.0121866598,-0.7234751009,-0.0849228351	H,0,2.0544119215,-1.8238187691,-1.4199471056
C,0,-3.5009825437,-1.4511757738,1.1601917987	H,0,1.5217325824,-2.3732621795,0.1693084462
H,0,-2.8864007383,-1.1904448551,2.027111504	C,0,3.7178773711,0.0221775279,2.0787091137
H,0,-4.5366035711,-1.1696782723,1.3717564528	H,0,3.2818934343,0.7716190055,1.4052578139
H,0,-3.4590372598,-2.534778223,1.0147554871	C,0,3.5280921614,-1.5926962969,0.1144189602
C,0,-3.8357471601,-1.1322183955,-1.2997344237	H,0,4.098157386,-0.8330164464,-0.4369455553
H,0,-3.4876513093,-0.624783067,-2.2006133255	H,0,3.9548723649,-2.5613967823,-0.1702927292
H,0,-3.776340524,-2.2145202871,-1.4530571783	C,0,3.7218699011,-1.3998829107,1.620311516
H,0,-4.8847813487,-0.8698469614,-1.1296139551	H,0,2.9214184903,-1.9199123085,2.1674416535
C,0,-3.0162710634,0.7834359045,0.1398666627	H,0,4.6579595367,-1.8571630012,1.959287329
H,0,-4.0344861782,1.111242092,0.3721291421	C,0,4.0646462933,1.7065065073,3.6108249674
H,0,-2.3741404359,1.0437637855,0.987602013	O,0,2.9960233334,2.3021228976,3.5665362039
H,0,-2.6705052613,1.3159829019,-0.7474546088	N,0,4.2037202691,0.3731137814,3.2053862588
Mg,0,0.8123521577,0.2418810252,-2.613469422	Mg,0,0.9835887555,1.5933263665,-0.8754378939
Br,0,2.0279885709,0.8308877162,-4.647333594	Br,0,1.3241854879,3.321267116,-2.5458194188
C,0,1.644831886,3.5655682011,-1.5193994792	C,0,5.3102161732,2.2910943351,4.161321274
C,0,1.4420958142,4.8371126084,-1.1592987023	H,0,6.1822960836,1.64372331,4.1920980949
H,0,1.6870371983,3.2638411529,-2.5630281466	C,0,5.3595415137,3.5577781986,4.5830592965
H,0,1.2995634028,5.6164458617,-1.9008317026	H,0,4.4741538076,4.1869712463,4.5449376471
H,0,1.4161290437,5.1190192286,-0.1101000411	H,0,6.2756172553,3.9892557421,4.9737961188

S.5.3. Cartesian coordinates and computed total energies for the reaction of **3** and **MethylMgBr**: 3, MethylMgBr, C-F, TS1, IM2, TSrot.

	
MethylMgBr, optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -2811.32092555 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.006500 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= --2813.77139951 a.u	**C** (**3** + **MethylMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3536.53173149 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.248342 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3539.12862986 a.u
0, 1 Mg,0,1.6613237753,-1.3027846983,-2.8221183218 Br,0,2.8797764584,0.8256721684,-2.822333435 C,0,0.6133596641,-3.1304036608,-2.8221009705 H,0,1.2963043867,-3.9888917,-2.8636870238 H,0,0.0019454807,-3.2417225367,-1.9170069847 H,0,-0.0615890752,-3.2066724626,-3.6846200441	0, 1 N,0,0.67660044,-0.4547248774,-0.1203195298 C,0,-0.618765031,-0.1175423731,0.0461406785 O,0,-1.5291757235,-0.9411784058,0.113837021 O,0,-0.7736300594,1.2187782252,0.1418074852 C,0,-2.0950436466,1.8210747689,0.2798144011 C,0,-2.9612171666,1.4853852349,-0.9291033332 C,0,-2.7419218187,1.3905158988,1.5915658276 C,0,-1.781494536,3.3120323398,0.3078001441 H,0,-2.4446769151,1.7615055115,-1.8540063243 H,0,-3.2007429066,0.4215244785,-0.9598160803 H,0,-3.8941018948,2.0557914623,-0.8756611158

	H,0,-2.0773193556,1.6115848781,2.4332265773 H,0,-3.6725737243,1.9484394022,1.7376000392 H,0,-2.9679818229,0.3231898121,1.587470936 H,0,-2.7075261394,3.8854044265,0.4105582807 H,0,-1.1292145514,3.5533142657,1.1528447045 H,0,-1.2835646758,3.6178511728,-0.617376256 C,0,1.07000221,-1.8580629873,-0.2085001362 H,0,0.5093092348,-2.3727981293,-0.9946547401 H,0,0.856659502,-2.3686485412,0.7399768733 C,0,1.8037901015,0.4757209768,-0.1989632728 H,0,1.6794385353,1.2557443931,0.5591251425 C,0,2.5706843894,-1.7858464643,-0.4900902807 H,0,2.7504484615,-1.7643237143,-1.5694931715 H,0,3.1083537876,-2.6413038929,-0.0727193536 C,0,2.9827122203,-0.4518721753,0.1324705076 H,0,3.072631287,-0.5515636597,1.2212848214 H,0,3.9241194917,-0.0571463207,-0.2570278015 C,0,2.5282581848,2.168465473,-1.6169306768 N,0,1.9069087741,1.0429542964,-1.5274318947 O,0,3.0634290848,2.8072203726,-0.602870371 Mg,0,4.1041644849,4.22827233,0.0244036654 Br,0,5.481173072,6.0022333001,0.8993534604 C,0,2.6623855165,2.8194098349,-2.9682334378 H,0,2.2035291252,3.814582169,-2.9532548557 H,0,3.7200681674,2.9501636942,-3.2233787642 H,0,2.1818405468,2.2173818636,-3.7404940394

	
D (**3** + **MethylMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3536.54392185 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.254696 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3539.13631464 a.u	**E** (**3** + **MethylMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3574.57757770 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.255624 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3539.13727341 a.u
0, 1 N,0,0.7875025683,-0.5291750983,-0.3274631983 C,0,-0.5124314401,-0.207674977,0.0666583284 O,0,-1.2201021873,-0.8463381762,0.8050655676 O,0,-0.8732411713,0.9026694608,-0.6268285936 C,0,-2.145451222,1.6385506788,-0.3615495759 C,0,-3.3214335002,0.7444605817,-0.7189940503 C,0,-2.1508068784,2.0824315227,1.0919365486 C,0,-2.0532383727,2.8281032063,-1.3044705763 H,0,-3.2300313454,0.3851325301,-1.7482601218 H,0,-3.395578433,-0.1095152783,-0.0442518247 H,0,-4.2422646562,1.3305830461,-0.6425664356 H,0,-1.2606796293,2.6769759065,1.3182663605 H,0,-3.030959187,2.7082949436,1.2653179657 H,0,-2.1988697981,1.2304855797,1.772783872	0, 1 N,0,0.6393602687,-0.3379535013,0.0747292429 C,0,-0.6405332554,0.0323445568,0.0997562649 O,0,-1.5888684824,-0.7705971178,-0.1203114812 O,0,-0.8130679288,1.3198029704,0.3507908789 C,0,-2.1316701351,1.9335744726,0.5941996581 C,0,-3.0327635472,1.8116757692,-0.6265095 C,0,-2.7515140978,1.3087753167,1.8355661341 C,0,-1.7642907314,3.3903677603,0.8372548835 H,0,-2.4914148499,2.0895299818,-1.5367256744 H,0,-3.4450838043,0.8065590333,-0.7304405302 H,0,-3.8735240358,2.5030167482,-0.5156423546 H,0,-2.0782014235,1.406893548,2.692384303 H,0,-3.6833947998,1.8313007743,2.0719781603 H,0,-2.9808668369,0.252985693,1.6765753777

H,0,-2.9224941564,3.4734896376,-1.1526281852	H,0,-2.6668083433,3.9617429325,1.0710593235
H,0,-1.1516285133,3.4159578048,-1.1076018065	H,0,-1.0691342448,3.4790609665,1.6767575136
H,0,-2.0541146665,2.5018421218,-2.3496765613	H,0,-1.2984613479,3.8250985322,-0.0519627573
C,0,1.2587050006,-1.8873480077,-0.004670561	C,0,1.0524509142,-1.7385949777,-0.038423374
H,0,0.7506327272,-2.6160702586,-0.6407240463	H,0,0.482318875,-2.2784726114,-0.7992334069
H,0,1.0372106351,-2.1239450781,1.0428085106	H,0,0.8839122965,-2.2360640219,0.9227475954
C,0,1.8856332995,0.4841318701,-0.0513538848	C,0,1.7198266184,0.5901378656,-0.3294174396
H,0,1.5863245505,1.129397693,0.7842743867	H,0,1.6488427481,1.4911336584,0.2863178426
C,0,2.7552752922,-1.779995618,-0.2414724145	C,0,2.5396246641,-1.6551190916,-0.401895974
H,0,2.975440934,-1.8140852696,-1.3143461048	H,0,2.6649205706,-1.7659964147,-1.4834562772
H,0,3.3061914011,-2.589884023,0.2422620179	H,0,3.1218188186,-2.4399811266,0.0867985511
C,0,3.0779627033,-0.4047373137,0.3378654825	C,0,2.9503292216,-0.2467751319,0.0266364972
H,0,3.1451567708,-0.4643509323,1.429564495	H,0,3.1160886086,-0.2032263481,1.1093770633
H,0,4.0072195069,0.0296514792,-0.0341909812	H,0,3.8428554572,0.1221650342,-0.4815799625
C,0,2.8189498798,2.3516678342,-1.1530276551	C,0,0.9368389078,0.5951739517,-2.6408408508
O,0,3.3933457681,2.702528551,-0.1018716568	N,0,1.7430308355,0.991922553,-1.7112099945
N,0,2.0547547633,1.2548350511,-1.2637221273	O,0,-0.0678012053,-0.2368878339,-2.5561715268
Mg,0,0.5176733328,0.5584173954,-2.3485732849	Mg,0,-1.6945110589,-1.1073824628,-2.1216941217
Br,0,-0.8026998298,-0.1301614992,-4.2532355423	Br,0,-3.5305207518,-2.2136325274,-3.2450214797
C,0,2.981727739,3.1916439073,-2.4018668185	C,0,1.169020762,1.143264195,-4.028214729
H,0,2.4360705887,2.7987848139,-3.2629687268	H,0,1.3553146868,0.3161629638,-4.7219931429
H,0,2.643912756,4.2122311017,-2.1968700352	H,0,0.2670817401,1.6571753345,-4.3781593699
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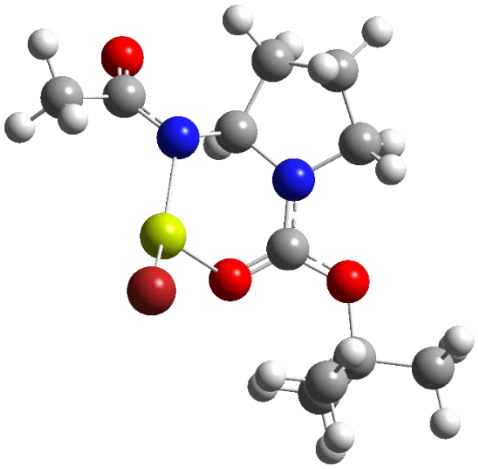	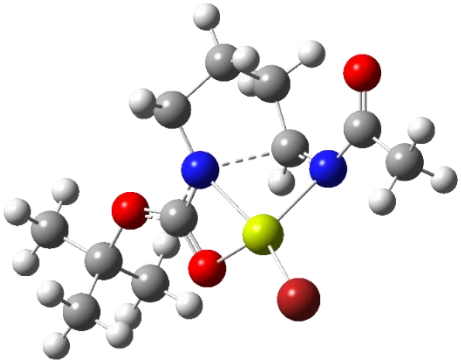
F (**3 + MethylMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3536.55341435 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.252867 SP at PBE1PBE/6-311++G(d,p) in THF, E= -3539.14802297 a.u	**TS1** (**3 + MethylMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3536.51291726 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.250546 a.u. 1 imaginary frequency = -142.79 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3539.10586942 a.u
0, 1 N,0,0.590978612,-0.4171240513,-0.1823212715 C,0,-0.7067778966,-0.1079340932,-0.2584151137 O,0,-1.5059097189,-1.0508171245,0.2017908937 O,0,-1.1165952127,0.9782371108,-0.7472504488 C,0,1.0727832688,-1.7527980053,0.1819904345 H,0,0.4841209444,-2.5156841696,-0.3309115349 H,0,0.9778736261,-1.9114388847,1.2640195604 C,0,1.675385704,0.5953785143,-0.2253940818 H,0,1.4927685065,1.3236654654,0.5770817337 C,0,2.52829319,-1.6912509969,-0.2481538982 H,0,2.6049218694,-1.8599312373,-1.3279249457 H,0,3.1419998127,-2.4392996911,0.2596028412 C,0,2.9190814999,-0.2585195117,0.1018024465 H,0,3.1386985554,-0.1772090665,1.1720823836 H,0,3.7890716636,0.1066204828,-0.4424677856 C,0,2.680742167,2.2361394269,-1.5585871772 O,0,3.4250512411,2.5434618671,-0.6062415271	0, 1 N,0,0.3952853359,-0.6077427704,-1.1243570386 C,0,-0.9207506404,-0.4562243292,-0.9195710061 O,0,-1.5485597556,-1.2935451448,-0.1137115176 O,0,-1.486317604,0.512620718,-1.5103119003 C,0,1.1623359112,-1.6662073658,-0.4966988252 H,0,1.3131162815,-2.4971635254,-1.1975907121 H,0,0.6349576955,-2.0609975373,0.3795283345 C,0,1.3778634615,1.124783514,-0.2349456362 H,0,0.4084920632,1.4148617788,0.1738355996 C,0,2.5054520898,-1.0722156087,-0.0805479183 H,0,3.1315002496,-0.8791449401,-0.9575295992 H,0,3.0528842377,-1.7578218402,0.5735904527 C,0,2.2262570288,0.2558208835,0.6381365062 H,0,1.6825853835,0.0666215005,1.5693845204 H,0,3.1674904069,0.7675730738,0.8573266931 C,0,3.0625100229,1.9844012343,-1.7001109589 O,0,4.0286700954,1.5058416594,-1.1154093777

N,0,1.7313568405,1.2774787008,-1.5115090054	N,0,1.7292449806,1.8391980854,-1.306891931
C,0,-2.9779118627,-1.0024620267,0.0619513719	C,0,-2.9937853631,-1.2021685639,0.1711747945
C,0,-3.3996437601,-2.3254343045,0.6841253381	C,0,-3.2162196509,-2.379287009,1.1093001669
H,0,-3.074002969,-2.3843384048,1.726691828	H,0,-2.6068770513,-2.2761667101,2.012028448
H,0,-4.4892739762,-2.4118314269,0.6560856027	H,0,-4.2682740003,-2.4198505237,1.404938133
H,0,-2.9707661081,-3.1675850053,0.1333667782	H,0,-2.9580716649,-3.321410458,0.616910234
C,0,-3.3599246373,-0.9510778786,-1.40973788	C,0,-3.78772927,-1.3780527533,-1.1154988561
H,0,-3.0781082656,-0.004862224,-1.8740092659	H,0,-3.6388041645,-0.5381062689,-1.7955447857
H,0,-2.8884137628,-1.7721546187,-1.9583906479	H,0,-3.4979996084,-2.3052358194,-1.6197227292
H,0,-4.4445766385,-1.0663771361,-1.4961018628	H,0,-4.8519880454,-1.4441927549,-0.8698210061
C,0,-3.5285557117,0.1710553708,0.859112147	C,0,-3.2954628542,0.1144542358,0.8731244366
H,0,-4.6212627592,0.1133732138,0.866377147	H,0,-4.3438347688,0.1200783847,1.1868934975
H,0,-3.1794686564,0.1262690062,1.8953489422	H,0,-2.673680255,0.2218993758,1.7675760292
H,0,-3.233054567,1.1260747249,0.4225117103	H,0,-3.1254849055,0.9659882381,0.2124437125
Mg,0,-0.0971466868,1.546012966,-2.382135167	Mg,0,0.2091291047,0.9820294524,-2.6080402522
Br,0,-1.1142646111,1.068946096,-4.5491042627	Br,0,0.0634642626,1.8603557944,-4.8775349561
C,0,2.8363056677,2.9820223969,-2.8707336635	C,0,3.2342486984,2.894557661,-2.8864407819
H,0,2.3870762574,2.4711980366,-3.7263181445	H,0,3.1056694945,3.9310080335,-2.5530029271
H,0,2.399023721,3.9828990531,-2.7815401754	H,0,4.2366508939,2.7799476784,-3.3004559871
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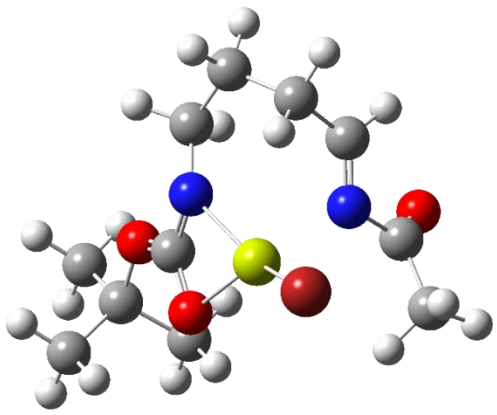
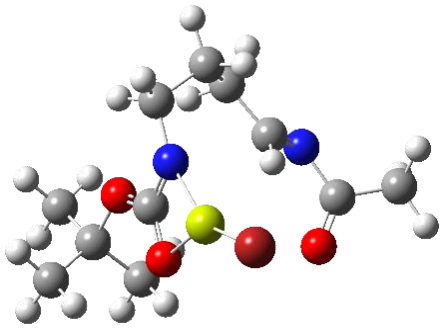
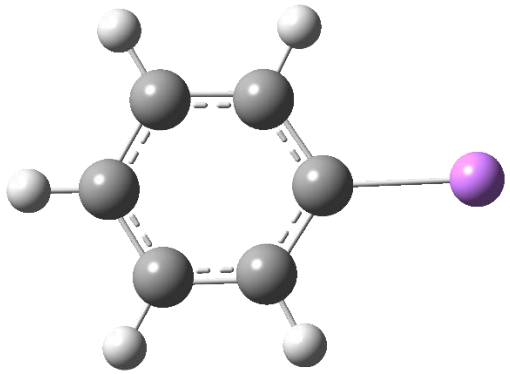
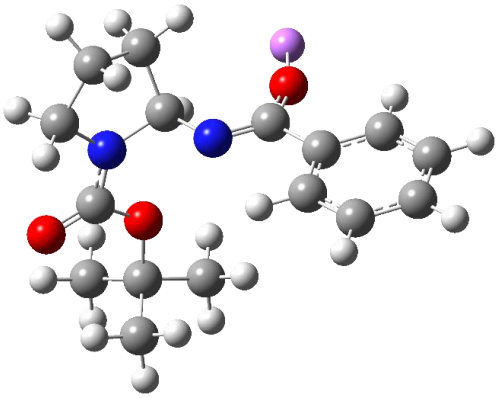
	
IM2 (**3 + MethylMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3536.52747292 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.249722	**TSrot** (**3 + MethylMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3536.51533510 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.246054 a.u.

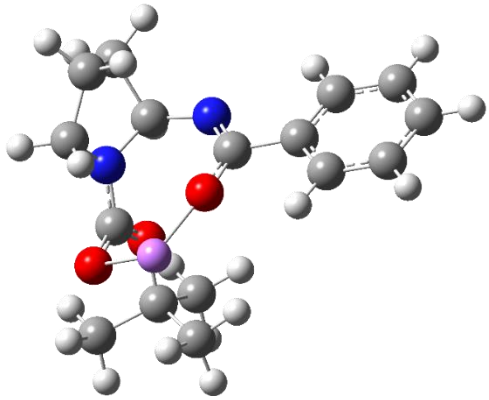
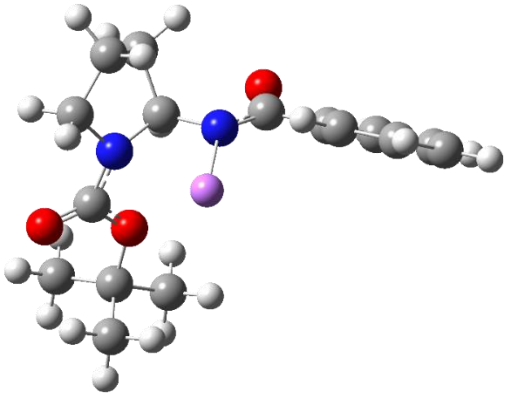
SP at PBE1PBE/6-311++G(d,p) in THF, E= -3539.11921755 a.u	1 imaginary frequency = -36.30 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3539.11000905 a.u
0, 1	0, 1
N,0,0.4476381603,-1.2948351219,-1.2384303294	N,0,1.4097890804,-0.3112213837,-0.1757740856
C,0,-0.7846326417,-0.8293546875,-1.223578715	C,0,0.4845833733,-0.115976289,0.7462150962
O,0,-1.6083588508,-1.2087836561,-0.243350267	O,0,-0.0907984172,1.0280639368,0.7854912491
O,0,-1.1337611106,-0.0040181704,-2.1401610524	O,0,0.1848060311,-1.1007768572,1.5923723826
C,0,1.0176714953,-1.9145713405,-0.0628974367	C,0,-0.8570072166,-0.9866685357,2.618267422
H,0,0.564823084,-2.8931302974,0.1491616908	C,0,-0.4866087354,0.0976283304,3.621411076
H,0,0.8189994362,-1.2912097278,0.8229679461	C,0,-2.2117524134,-0.7411071299,1.9666656437
C,0,2.9093857161,0.4163746858,-0.4367591275	C,0,-0.8242282632,-2.3592238954,3.2771098272
H,0,3.3964521034,0.7878697213,0.4711614055	H,0,0.508895019,-0.0895083734,4.0358886892
C,0,2.5303297483,-2.0977956729,-0.2130746455	H,0,-0.4965446324,1.0854211237,3.1585313145
H,0,2.7492851446,-2.9998766203,-0.7948377869	H,0,-1.206587925,0.0864328837,4.4458284757
H,0,2.964800209,-2.2508977261,0.7803630337	H,0,-2.4192696687,-1.5108649626,1.2162975517
C,0,3.2595135489,-0.9409547038,-0.9341511024	H,0,-2.9934430424,-0.793127708,2.7310460257
H,0,4.338769005,-1.0815804075,-0.8069188285	H,0,-2.2504265693,0.2408405024,1.4926424785
H,0,3.0633911635,-0.9932346883,-2.009512307	H,0,-1.5648772869,-2.4014265415,4.0807450911
C,0,1.8237843789,2.462344272,-0.4679834985	H,0,-1.0568910917,-3.143297604,2.5501419393
O,0,1.83172168,2.6317795757,0.7326100056	H,0,0.1626533131,-2.5591222316,3.7053029005
N,0,2.0669147405,1.171714901,-1.0464229646	C,0,2.0709365564,-1.5866558536,-0.366298461
C,0,-2.9647901038,-0.6736957202,-0.0921052839	H,0,2.058671685,-1.8203671185,-1.4382143953
C,0,-3.4659588715,-1.3876994708,1.155997515	H,0,1.5167086514,-2.3853302143,0.1424608098
H,0,-2.8330522672,-1.1523755029,2.0169651706	C,0,3.7200886567,-0.0113808013,2.0830187084
H,0,-4.4883810043,-1.0698073585,1.3797297121	H,0,3.2967536514,0.7456303813,1.4098163789
H,0,-3.4646398247,-2.4715974734,1.0066916916	C,0,3.5254901855,-1.610331947,0.105891568
C,0,-3.8156429309,-1.0476420372,-1.2992511584	H,0,4.100996992,-0.848004216,-0.4362033872
H,0,-3.4603067547,-0.5475744173,-2.2013787294	H,0,3.9498885484,-2.5780681825,-0.1856947554
H,0,-3.7952736795,-2.1304986145,-1.4585450594	C,0,3.7124649422,-1.4310920734,1.6144555004
H,0,-4.853029154,-0.7502832803,-1.1156702304	H,0,2.9040696681,-1.9478743472,2.1525905729
C,0,-2.9118970368,0.8316422923,0.1373394861	H,0,4.6426895318,-1.8995547333,1.9541627936
H,0,-3.9143636066,1.1949612355,0.3846953642	C,0,4.0901854716,1.6627458832,3.6219135924
H,0,-2.2493485708,1.0660757456,0.9769080086	O,0,3.0291009689,2.266745772,3.6045491613
H,0,-2.5601106428,1.3545498803,-0.7534092186	N,0,4.2001277485,0.3259163709,3.2157518576

Mg,0,0.8632187587,0.1895123911,-2.6434952835	Mg,0,0.983805018,1.5882617168,-0.8691888829
Br,0,2.0879110448,0.818281545,-4.6602267775	Br,0,1.324998818,3.3227000444,-2.5320138484
C,0,1.5281965599,3.5269383908,-1.475901796	C,0,5.3645118869,2.2421138219,4.1623770418
H,0,1.551803033,4.5070087647,-1.0002990833	H,0,5.2396367795,3.3055412028,4.3666249748
H,0,2.2349201894,3.4780313828,-2.3089916797	H,0,5.6326085316,1.7192374441,5.0863810719
H,0,0.5278638511,3.3573729117,-1.8926636683	H,0,6.1858382933,2.0831590944,3.456831191

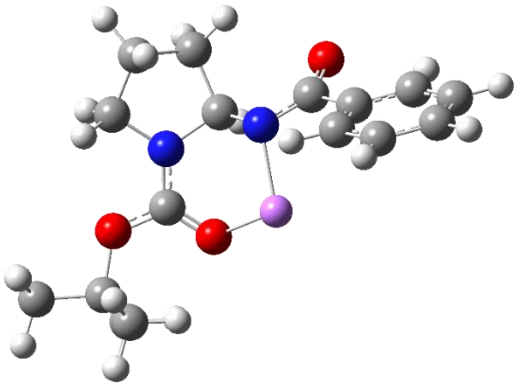
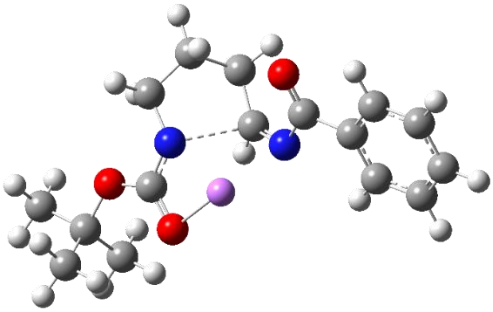
S.5.4. Cartesian coordinates and computed total energies for the reaction of **3** and **PhLi**: 3, PhLi, Int5-8, TS1, IM2, TSrot.

	
PhLi, optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -238.893028020a.u. thermal correction to Gibbs Free energy at 25 °C = 0.059445 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -238.933338059 a.u	**Int5** (**3** + **PhLi**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -964.131299955 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.248342 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -964.319463163
0, 1 C,0,-2.3888475227,1.0928743264,0.0002156387 C,0,-0.9753250842,1.0046193131,0.0007999702 C,0,-0.3370041259,2.269077162,0.0001148481 C,0,-1.0173343006,3.4933666407,-0.0010526833 C,0,-2.4127568527,3.5136477995,-0.0016123534 C,0,-3.1005006263,2.2992330416,-0.000960834 H,0,-2.983551349,0.1749413608,0.0006647265 H,0,0.7557766808,2.3182813138,0.000480471	0, 1 N,0,0.7888522527,-0.4816755597,-0.1130361214 C,0,-0.4986888838,-0.1175776659,0.0476251438 O,0,-1.4257528906,-0.9227096772,0.1245967139 O,0,-0.6298813493,1.2228818613,0.1331480872 C,0,-1.9415456892,1.8497277426,0.2484329194 C,0,-2.7937374388,1.5256080597,-0.9735307479 C,0,-2.618767301,1.4376304862,1.5510517776 C,0,-1.6016513102,3.3349303722,0.2761214814

H,0,-0.4621915361,4.4311401419,-0.0015317389 H,0,-2.9536934289,4.4575361976,-0.002521438 H,0,-4.1902607527,2.2947548388,-0.0013695355 Li,0,0.1082207683,-0.7835915263,0.0019385887	H,0,-2.2580316326,1.792042258,-1.8902873379 H,0,-3.0493688847,0.4654652597,-1.0061615755 H,0,-3.7184850909,2.1104157326,-0.9360915174 H,0,-1.9629363794,1.646835166,2.4027346753 H,0,-3.5388153768,2.0168593288,1.6807968349 H,0,-2.8677196598,0.3755198318,1.5467101815 H,0,-2.5191437781,3.9257893719,0.3533866281 H,0,-0.9662904258,3.5694951868,1.1360106971 H,0,-1.0752038484,3.6261890555,-0.6376606482 C,0,1.1527565681,-1.8935963169,-0.1828548262 H,0,0.5925103564,-2.4046896512,-0.9722068617 H,0,0.9131410218,-2.3899700647,0.7668628151 C,0,1.9369654413,0.4232952621,-0.2377666911 H,0,1.8218204554,1.2366895872,0.4897140117 C,0,2.6595151582,-1.8593049412,-0.4437641825 H,0,2.8561016149,-1.8693193455,-1.5201354064 H,0,3.1729018359,-2.7142940212,0.0043066226 C,0,3.0918725231,-0.5168431639,0.1458103166 H,0,3.163224504,-0.5873445379,1.2389329906 H,0,4.0462094373,-0.1540450617,-0.2432511849 C,0,2.730827769,2.0238619174,-1.7252520372 N,0,2.0506042097,0.9218071751,-1.5834520996 C,0,2.8449761366,2.5676467926,-3.1254087677 C,0,3.63320176,3.6959265849,-3.3730984847 C,0,2.1743326548,1.9681250566,-4.1989829798 C,0,3.7531916674,4.2147194567,-4.662243182 H,0,4.1514931829,4.1578524412,-2.5385353601 C,0,2.2898569237,2.4847455555,-5.4864006547 H,0,1.562928595,1.0938437903,-4.0005303343 C,0,3.0811372012,3.611026503,-5.7240664582 H,0,4.3721382969,5.0909625591,-4.8378800102 H,0,1.7611229838,2.0093527913,-6.3086434096 H,0,3.1720079002,4.0134701402,-6.7295084129 O,0,3.3186125176,2.6985738068,-0.7968111494 Li,0,3.6708279714,3.327154874,0.8226495449

	
Int6 (**3** + **PhLi**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -964.130176842 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.307134 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -964.317902601	**Int7** (**3** + **PhLi**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -964.129274953 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.304882 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -964.316868833 a.u
0, 1 N,0,0.6868020568,-0.3940764282,0.1148885693 C,0,-0.6128953746,-0.0623318576,0.1422861119 O,0,-1.5325584028,-0.8939388997,0.0245642401 O,0,-0.7972150661,1.2489247462,0.3121814908 C,0,-2.1252011901,1.8494588039,0.4532706961 C,0,-2.9662339877,1.6207211608,-0.7967985827 C,0,-2.8006154596,1.3146781769,1.7096087193 C,0,-1.7985873481,3.3294655568,0.6052683825 H,0,-2.3970612066,1.8837055626,-1.6936877453 H,0,-3.3025192948,0.5852553324,-0.8698288422 H,0,-3.8499908563,2.2651673632,-0.7542969568 H,0,-2.1654288413,1.4821604361,2.5851193246 H,0,-3.7446724753,1.8457418192,1.8670176882 H,0,-3.0115810834,0.2473773185,1.6200477211 H,0,-2.7209128799,3.8999486011,0.7471589211 H,0,-1.1514385819,3.493707857,1.4718515641 H,0,-1.2895448071,3.7057277286,-0.2870355916	0, 1 N,0,0.6039522693,-0.4581850076,-0.3547156764 C,0,-0.7126794721,-0.2580510707,-0.0563295936 O,0,-1.4929393606,-1.1721756935,0.1848079181 O,0,-1.0318765294,1.0459360318,-0.1084278709 C,0,-2.3807798389,1.520517262,0.2064397372 C,0,-3.3840667811,0.9657784683,-0.7977876191 C,0,-2.7423558645,1.1639877011,1.6431620735 C,0,-2.2462987185,3.0294425565,0.0492838354 H,0,-3.0730154242,1.2054039007,-1.8200995988 H,0,-3.4879850342,-0.1157747707,-0.6982907204 H,0,-4.3604057543,1.4299007134,-0.6261599587 H,0,-1.9748609111,1.5335771504,2.3306070629 H,0,-3.6912569121,1.6426973757,1.9049144375 H,0,-2.8476003572,0.0854946016,1.7713395007 H,0,-3.2045939949,3.5112970899,0.2637755041 H,0,-1.49559249,3.4242188162,0.7400066775 H,0,-1.9490278147,3.2882186149,-0.9714550859

C,0,1.1060977502,-1.7897171769,0.0037185933	C,0,1.1595832433,-1.8017809094,-0.1477262504
H,0,0.5190966453,-2.3274017652,-0.7466628506	H,0,0.7529416834,-2.5103164982,-0.8752055354
H,0,0.9589695598,-2.2911392199,0.9675162332	H,0,0.8918003032,-2.1652737045,0.8527531123
C,0,1.7490090108,0.5402093656,-0.3145614752	C,0,1.6427069401,0.6009186666,-0.2768774725
H,0,1.6824892503,1.4375563224,0.3095989715	H,0,1.3162298714,1.3803012872,0.4190374338
C,0,2.585805654,-1.7002418442,-0.3871831373	C,0,2.6626280799,-1.5830375364,-0.2781374087
H,0,2.6920404618,-1.8097245254,-1.4711604934	H,0,2.9653046275,-1.6158084592,-1.3307497616
H,0,3.1838906352,-2.4806817964,0.0904137662	H,0,3.233450374,-2.3438831816,0.2604745999
C,0,2.992557301,-0.2875331625,0.0308761569	C,0,2.847089011,-0.1738828469,0.2798481483
H,0,3.1718843844,-0.2411063889,1.1119111204	H,0,2.7963607949,-0.1942787594,1.3756869293
H,0,3.8767214346,0.0857377861,-0.4894612669	H,0,3.7858695883,0.3021807454,-0.0108010357
C,0,0.9541684313,0.5349253057,-2.6191505388	C,0,2.4579072016,2.335047338,-1.60591726
N,0,1.7643611976,0.9542486926,-1.6896594207	O,0,2.8143049252,2.9985100683,-0.5982677969
C,0,1.202178783,1.1257961219,-3.9912716563	N,0,1.8625383916,1.1449929244,-1.5978885531
C,0,0.4053334571,0.7290080631,-5.0699250681	C,0,2.705171597,2.9348462206,-2.9711852062
C,0,2.2164388134,2.064316425,-4.2195638616	C,0,2.7866666859,4.3263503098,-3.0918049869
C,0,0.6133891343,1.2531584902,-6.3457423937	C,0,2.8871282009,2.1523449394,-4.1174330055
H,0,-0.3792740053,0.0007454221,-4.8905810913	C,0,3.0129720747,4.9234722345,-4.3299764759
C,0,2.4267633795,2.5910237557,-5.4911092626	H,0,2.6721096844,4.9284483399,-2.1953550227
H,0,2.8324964517,2.3694978664,-3.3797870137	C,0,3.1287442029,2.7449361781,-5.3563031617
C,0,1.6256296127,2.1870005739,-6.5615050976	H,0,2.8693020091,1.0698282775,-4.0283585053
H,0,-0.0153551649,0.9316031234,-7.172284715	C,0,3.1849710186,4.1341845796,-5.4680103614
H,0,3.2181619919,3.3192379455,-5.6499643343	H,0,3.0624927339,6.0064489469,-4.4075202049
H,0,1.7903200529,2.5974660482,-7.554282935	H,0,3.2834949489,2.1217670397,-6.2334052753
O,0,-0.0219230039,-0.3037077063,-2.5470768634	H,0,3.3720982724,4.5978853202,-6.4327610742
Li,0,-1.4290948497,-1.2417501296,-1.9347620965	Li,0,0.6233110445,0.2525924294,-2.7806783023

	
Int8 (**3 + PhLi**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -964.139035219 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.305582 SP at PBE1PBE/6-311++G(d,p) in THF, E= -964.326273051 a.u	**TS1** (**3 + PhLi**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -964.092841858 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.302036 a.u. 1 imaginary frequency = -58.59 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -964.280391891 a.u
0, 1 N,0,0.9925463382,-0.7216529948,0.197924934 C,0,-0.2836751228,-0.3209008452,0.1910622899 O,0,-0.6456320176,0.8230839698,-0.1427385086 O,0,-1.122471569,-1.2860349012,0.5804049315 C,0,-2.5796934265,-1.1187775115,0.5464501071 C,0,-3.0052079163,-0.025588206,1.5181307444 C,0,-3.0462638071,-0.8476227542,-0.8783509328 C,0,-3.0767863105,-2.478298077,1.0193366336 H,0,-2.6137015563,-0.2330514205,2.5189373314 H,0,-2.6518103274,0.9540211046,1.1933326885 H,0,-4.0978942711,-0.0039790426,1.5784483204 H,0,-2.6633491011,-1.6155979208,-1.5580626064 H,0,-4.1396443868,-0.8817805693,-0.9106046381 H,0,-2.7203362371,0.1340840498,-1.2252467336 H,0,-4.1700994572,-2.4822901291,1.0483014639 H,0,-2.7447116035,-3.2697458252,0.3408631383 H,0,-2.7025915629,-2.698147302,2.0235438825 C,0,1.4187625014,-2.0943367918,0.4718949297	0, 1 N,0,0.3287461509,-0.7205362263,-0.9394024168 C,0,-0.9892781093,-0.5882385013,-0.8686581223 O,0,-1.6425901325,-1.3758452424,0.0136806404 O,0,-1.5880940921,0.2440959646,-1.6046952896 C,0,1.0430523324,-1.5867680033,-0.0302458651 H,0,1.0429652026,-2.6293193904,-0.3842430802 H,0,0.5863603121,-1.592357011,0.9706101557 C,0,1.4929549017,1.2080122089,-0.4342623123 H,0,0.5591264442,1.4719120803,0.061381611 C,0,2.4721201429,-1.0745321821,0.0479182298 H,0,2.9638559812,-1.1988132512,-0.9210330864 H,0,3.0494637313,-1.6270515541,0.7976838495 C,0,2.4716896836,0.4241367453,0.3961943448 H,0,2.1837806156,0.5505806985,1.4464074726 H,0,3.4798378445,0.8264720858,0.257655089 C,0,2.8945999604,1.7442499359,-2.2490187083 O,0,3.6458540081,0.7717424769,-2.1994186904 N,0,1.7028793253,1.8775131371,-1.5460505086

H,0,0.7672924593,-2.8057536407,-0.0406287056	C,0,-3.0903114666,-1.3301109397,0.1880994878
H,0,1.3687871707,-2.3027203937,1.5491488626	C,0,-3.3330690349,-2.3794475367,1.2662672256
C,0,2.1167977669,0.2134687147,-0.0234188939	H,0,-2.7993828113,-2.1190654098,2.1855203408
H,0,2.0468525112,1.0202376793,0.7226403097	H,0,-4.4017619543,-2.442825183,1.4920544655
C,0,2.8557428683,-2.1012446495,-0.030740305	H,0,-2.9901999077,-3.3632487097,0.9314233706
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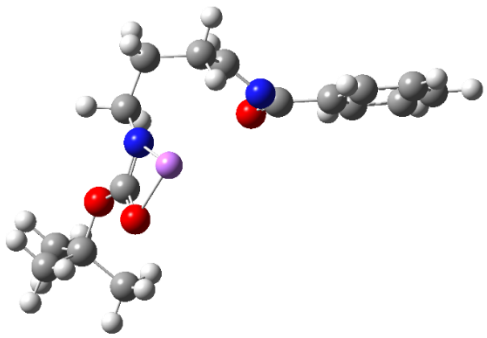
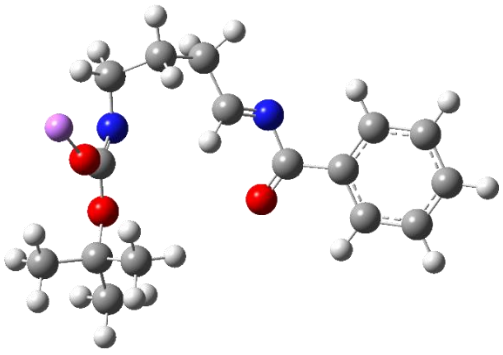
H,0,3.4576266539,-2.8757293064,0.4519537791	H,0,-3.628885633,-0.9836113617,-1.8851744856
C,0,3.3314118174,-0.6855624554,0.2823691246	H,0,-3.4311409911,-2.6990905531,-1.4519278229
H,0,3.5866149894,-0.6014153963,1.3456583452	H,0,-4.8711527446,-1.8128634233,-0.9198040167
H,0,4.1983822607,-0.3667536842,-0.295798907	C,0,-3.5242213311,0.0456481327,0.6818649769
C,0,3.033741553,1.6416493028,-1.6205484218	H,0,-4.5907341198,0.0243111128,0.9288795539
O,0,3.9087598185,2.0584838435,-0.818319599	H,0,-2.971338436,0.3152743658,1.5878324615
N,0,2.0707727699,0.7550858385,-1.3645343503	H,0,-3.3530206558,0.8074197572,-0.0801641268
C,0,3.0410158707,2.196137884,-3.030076611	C,0,3.2040586,2.8971881802,-3.1511595721
C,0,3.7484535125,3.3747987876,-3.2891930877	C,0,4.366418195,2.8438028951,-3.9306858707
C,0,2.3846313338,1.5584152752,-4.0905524951	C,0,2.3776481471,4.0252203586,-3.2269954968
C,0,3.7863459143,3.9160986212,-4.5724165501	C,0,4.6961810708,3.898193746,-4.7752876114
H,0,4.2697537427,3.8516364771,-2.4644927573	H,0,5.0002145365,1.9650881913,-3.8607035324
C,0,2.4272721892,2.0930435334,-5.3774592889	C,0,2.7098656734,5.0817555873,-4.0718434563
H,0,1.8550523339,0.6297197953,-3.8965846779	H,0,1.4798516656,4.0625064101,-2.6193578589
C,0,3.1253513648,3.2763001564,-5.6217591792	C,0,3.8676065763,5.0198926191,-4.8471807423
H,0,4.3356848636,4.8357710998,-4.7563780695	H,0,5.5988182192,3.848819775,-5.3776682592
H,0,1.9226623235,1.5813967223,-6.1930213135	H,0,2.0651158687,5.9544080177,-4.1254097149
H,0,3.1603415742,3.692855476,-6.624839794	H,0,4.1250766778,5.8442202477,-5.5065221969
Li,0,0.2668825764,1.5609716023,-1.6403491868	Li,0,0.1251789548,0.6788266304,-2.4773462244

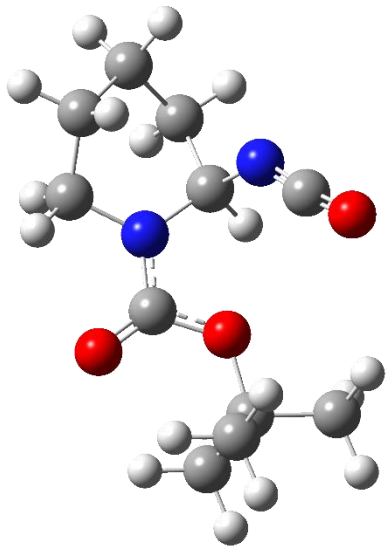
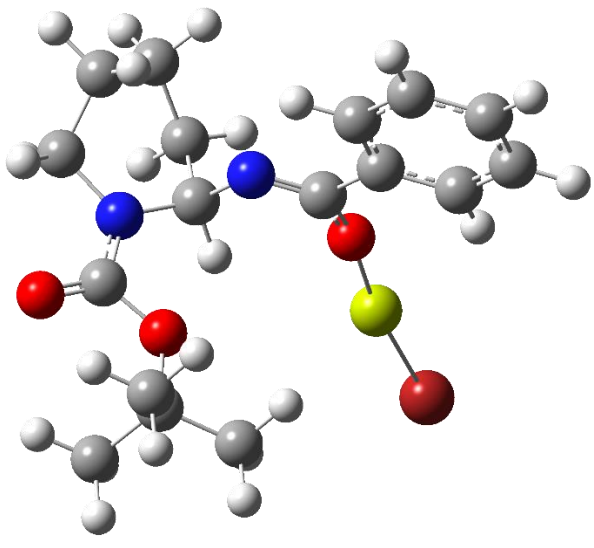




IM2 (3 + PhLi), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -964.097762531 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.296116 SP at PBE1PBE/6-311++G(d,p) in THF, E= -964.286142258a.u	TSrot (3 + PhLi), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -964.080621952 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.296969 a.u. 1 imaginary frequency = -47.02 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= --964.269375547 a.u
0, 1	0, 1
N,0,-0.225316656,-1.8913128512,-1.4449845083	N,0,0.4650367425,-0.4932797888,1.0107967635
C,0,-1.5213885554,-1.6886815297,-1.3536262928	C,0,-0.5587998833,-0.2550239734,0.2458014584
O,0,-2.0027750591,-1.254838111,-0.1568434187	O,0,-1.004843438,-0.9256243876,-0.7449630443
O,0,-2.2915416181,-1.8927144336,-2.3442401598	O,0,-1.2247451243,0.8912446338,0.6179159943
C,0,0.6104786318,-1.6507966445,-0.2921303082	C,0,-2.2944822694,1.4715040452,-0.1559828476
H,0,0.3071537246,-2.2750724043,0.5634955298	C,0,-1.8271436206,1.8277804353,-1.5659354042
H,0,0.5234287722,-0.6081711789,0.0588358149	C,0,-3.5250992913,0.5661495859,-0.1748551743
C,0,2.7641182568,0.3760804919,-1.2464973339	C,0,-2.6158269594,2.7497367693,0.6148086365
H,0,3.2107155527,0.5642552288,-0.2586670288	H,0,-0.9367168457,2.4635733199,-1.5165626313
C,0,2.0734858226,-1.9510038886,-0.6033105727	H,0,-1.588485632,0.9297572049,-2.1382567102
H,0,2.1660635511,-2.992464625,-0.9339110233	H,0,-2.6133395916,2.3833550451,-2.0884822882
H,0,2.6618076546,-1.8594452488,0.3193011579	H,0,-3.8113157447,0.3014827291,0.8485907738
C,0,2.6746705269,-1.0439341074,-1.682282168	H,0,-4.3664692127,1.0930798269,-0.6381775482
H,0,3.6990254383,-1.3811849814,-1.8992660763	H,0,-3.3292389522,-0.350452332,-0.7327482608
H,0,2.0993792825,-1.1013650798,-2.6104251029	H,0,-3.4236374144,3.29873506,0.1206108465
C,0,2.4290709234,2.6448362794,-1.4367507347	H,0,-2.930580288,2.5116507245,1.6355572393
O,0,1.9652096642,2.9196433055,-0.3373672877	H,0,-1.7341777855,3.3955254895,0.6681947363
N,0,2.3707906049,1.3512965077,-1.968907133	C,0,1.2296444417,-1.6788406109,0.7174855989
C,0,3.0299513198,3.6731186111,-2.3275052234	H,0,0.6260082644,-2.4764825741,0.2508772216
C,0,3.1799109147,4.9776875973,-1.8407715984	H,0,1.6036441771,-2.0909131263,1.6674853895
C,0,3.464866885,3.3614269455,-3.6214409945	C,0,3.0169175458,1.0410717217,0.2267237212
C,0,3.7591891988,5.9582203276,-2.637764689	H,0,2.0111071093,1.2418791303,-0.1603074855
H,0,2.8388159579,5.2038608657,-0.8352609693	C,0,2.4464495898,-1.4140390183,-0.176142827
C,0,4.04527729,4.3454880642,-4.4175505539	H,0,2.1102453842,-1.0839743022,-1.1689090134
H,0,3.3359743269,2.351913294,-3.99799488	H,0,2.982061817,-2.3602717149,-0.3265506934
C,0,4.1929551481,5.6428275844,-3.9272924038	C,0,3.4236152635,-0.3893686011,0.3980003144
H,0,3.8744685789,6.9687213928,-2.2567174346	H,0,3.5710307348,-0.5671219613,1.4729714155

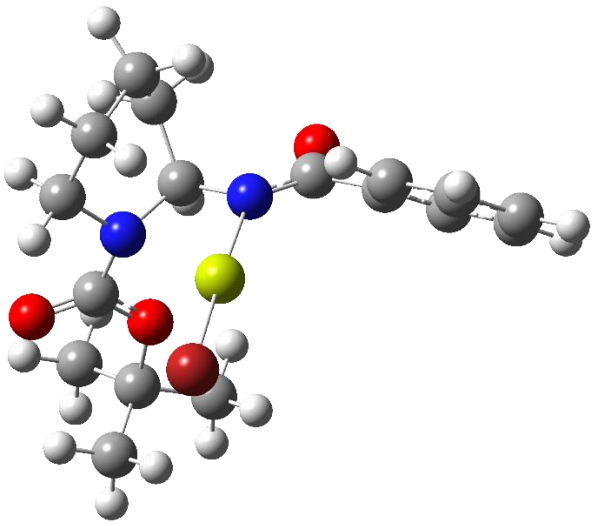
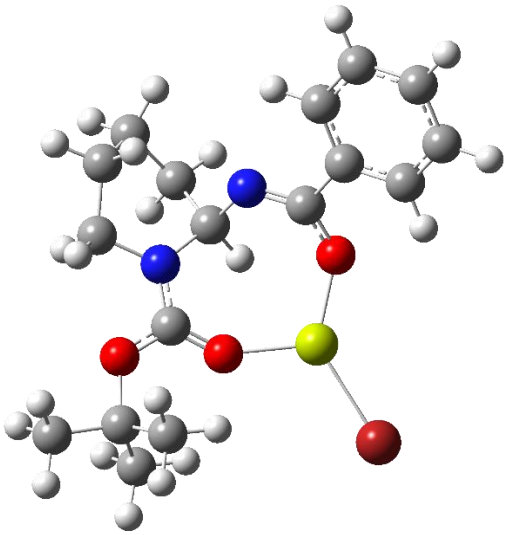
H,0,4.3790457488,4.1016623616,-5.4219211958	H,0,4.4154569918,-0.5023613424,-0.0572465531
H,0,4.6445209652,6.4099283061,-4.5501816281	C,0,3.3690708303,3.3137752725,0.395826022
C,0,-3.4110432471,-0.9769466733,0.0694992364	O,0,2.3294093655,3.7026068848,0.9132203771
C,0,-3.4391838968,-0.523447502,1.5250542418	N,0,3.818528315,1.9971112009,0.5015633599
H,0,-2.8156714119,0.3652470873,1.6635022399	C,0,4.281756141,4.237334069,-0.3357064955
H,0,-4.4635111993,-0.2787767496,1.8226403203	C,0,3.8763031689,5.5622576085,-0.5378076508
H,0,-3.066667467,-1.3150270637,2.1828253299	C,0,5.5154942011,3.8070761127,-0.8385976636
C,0,-4.243617385,-2.243798698,-0.1014887833	C,0,4.6929436384,6.4451380685,-1.235490456
H,0,-4.2245678717,-2.5840548462,-1.1379455856	H,0,2.9170605161,5.8814708924,-0.1420357199
H,0,-3.8560869828,-3.0404357581,0.5425599137	C,0,6.3317639602,4.69287443,-1.537678073
H,0,-5.2800991095,-2.0444213564,0.190749961	H,0,5.8303503399,2.7825924262,-0.6686346942
C,0,-3.8892936304,0.1506595806,-0.839772312	C,0,5.9220566133,6.011132421,-1.7367303736
H,0,-4.9120857545,0.4325001093,-0.5680140079	H,0,4.3741815317,7.4719396942,-1.3900573541
H,0,-3.249707277,1.0311694551,-0.7177422106	H,0,7.2897323866,4.3562510265,-1.9234533418
H,0,-3.8716199107,-0.1589214531,-1.8857974543	H,0,6.5607563656,6.7018803677,-2.2802375144
Li,0,-0.6718303884,-2.3812835017,-3.3317120016	Li,0,-1.211803382,-2.370834463,-1.7623210503

S.5.5. Cartesian coordinates and computed total energies for the reaction of **12a**' and PhMgBr: 12a', PhMgBr, C-4, TS1, IM2, TSrot.

	
Isocyanate (12a'), optimization in solv. THF	**C** (**12a'** + **PhMgBr**), optimization in solv. THF

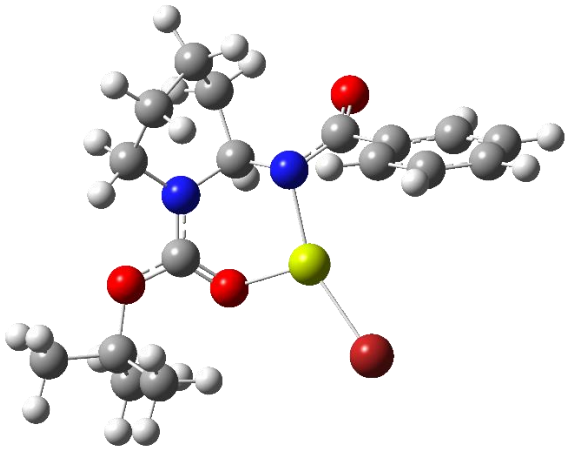
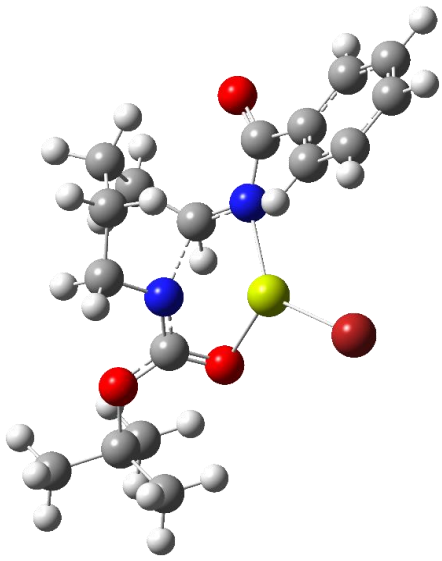
PBE1PBE/6-31+G(d,p) E= -764.407410047 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.245159 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -764.566415848 a.u	PBE1PBE/6-31G(d,p) E= -3767.32219592 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.327421 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3769.95501007a.u
0, 1 N,0,0.8873127638,-0.4489176197,0.1426087483 C,0,-0.4550727285,-0.1991438048,0.1081753332 O,0,-1.3058846037,-1.0767469602,0.0635452691 O,0,-0.6959199671,1.1224825886,0.1237341836 C,0,-2.0637745714,1.6535802548,0.1443226904 C,0,-2.7899591323,1.2684737493,-1.1382369543 C,0,-2.792967309,1.177365385,1.3941078772 C,0,-1.8341309221,3.1579180941,0.198766109 H,0,-2.2120009096,1.5849064312,-2.0122909498 H,0,-2.9580212964,0.1917532247,-1.1910646859 H,0,-3.7585040579,1.7774966851,-1.1692566795 H,0,-2.2155158144,1.4256919542,2.2904298388 H,0,-3.7589499838,1.687535881,1.4611468388 H,0,-2.9673468653,0.100706059,1.3680414747 H,0,-2.7965541755,3.6772809515,0.2148149886 H,0,-1.2780817546,3.4325967527,1.1003272004 H,0,-1.2727832501,3.4958544154,-0.677289582 C,0,1.356972509,-1.8295738777,0.0236250348 H,0,0.5671095938,-2.4023475747,-0.4645034398 H,0,1.5046651242,-2.2625491034,1.0231916886 C,0,1.8637084037,0.6161662316,0.2425861774	0, 1 N,0,1.6084999595,0.9758180142,1.1977855122 C,0,0.2665278158,1.0009856842,1.0033918597 O,0,-0.5259886453,0.2779719164,1.6024140722 O,0,-0.0866988736,1.9247600739,0.0864663545 C,0,-1.4782141362,2.0901602892,-0.3239662361 C,0,-1.9932681892,0.8088662762,-0.9694887808 C,0,-2.3381369344,2.5317410179,0.8548903114 C,0,-1.3911310838,3.2039774324,-1.3603382894 H,0,-1.3291318385,0.5008134112,-1.7834268015 H,0,-2.0621032238,0.0001753621,-0.2404721458 H,0,-2.9877410145,0.9898409774,-1.3899045351 H,0,-1.9094853259,3.4224658595,1.3260052046 H,0,-3.3401082525,2.7874080704,0.4953518029 H,0,-2.4217665504,1.7406186355,1.6010341284 H,0,-2.3839289579,3.4085709587,-1.771397493 H,0,-1.0136658111,4.1252642946,-0.9052734317 H,0,-0.7284806791,2.9140459022,-2.181491769 C,0,2.1564169015,-0.0076500129,2.1295666127 H,0,1.4333462664,-0.8203141083,2.2171322088 H,0,2.2625642972,0.4395148998,3.129758178 C,0,2.5341797931,1.8193623223,0.4346440361 H,0,2.0702763205,2.8078187742,0.3426522969 C,0,3.5009039048,-0.5199128399,1.633324573 H,0,3.3443742685,-1.0031027892,0.6634615488 H,0,3.8645864707,-1.2866952361,2.32584103 C,0,3.8241292095,1.963018819,1.2473444568 H,0,3.5621970953,2.428479513,2.2061064742 H,0,4.4863698737,2.6603274948,0.7244656929 C,0,2.9954827477,2.0425169612,-1.8474050812

H,0,1.4747292934,1.3821083377,0.9165375106 C,0,2.6498765689,-1.8738439321,-0.7780836561 H,0,2.4423708275,-1.4939840418,-1.7846725776 H,0,2.9620143254,-2.9170142756,-0.8898050498 C,0,3.1699708912,0.0564036969,0.7837413505 H,0,2.9517891262,-0.3421358738,1.7808129667 H,0,3.8749931121,0.8816765047,0.9173904937 C,0,1.4943980841,1.9922502428,-1.781129746 O,0,1.0095501644,2.7053534013,-2.5858162908 N,0,2.1103666288,1.2576592071,-1.0508824014 C,0,3.757636103,-1.0371124046,-0.1157580537 H,0,4.4102262414,-1.6745189533,0.4901559889 H,0,4.3888004708,-0.586016467,-0.8876279966	O,0,3.0024859616,3.3472410554,-1.7870859619 N,0,2.7927921995,1.236669098,-0.8619820902 C,0,3.2705486288,1.4464675661,-3.1944585227 C,0,3.4543567544,2.2673013646,-4.311650862 C,0,3.3456342414,0.0573483689,-3.3585331892 C,0,3.7037773106,1.7154591298,-5.5677610769 H,0,3.4023129835,3.3445891438,-4.1918382853 C,0,3.5944795255,-0.4950014569,-4.6107281274 H,0,3.202027158,-0.5736599941,-2.48741785 C,0,3.774342476,0.3323001202,-5.7216749267 H,0,3.8435971028,2.3673721292,-6.4258931536 H,0,3.6494332382,-1.5745082995,-4.722749872 H,0,3.9690936083,-0.099949609,-6.699352479 C,0,4.5224778984,0.6179915703,1.4857553781 H,0,5.1419689651,0.6959499505,2.3867424019 H,0,5.2004732561,0.3937364244,0.656306315 Mg,0,2.6789156895,5.1509131115,-1.5531584267 Br,0,2.4851098843,7.5454071832,-1.5074476819

	
D (**12a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3767.32943767 a.u.	**E** (**12a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-31G(d,p) E= -3767.35402140 a.u.

thermal correction to Gibbs Free energy at 25 °C = 0.331286 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3769.95964573 a.u	thermal correction to Gibbs Free energy at 25 °C = 0.330741 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3769.98470417 a.u
0, 1 N,0,1.233115121,0.6357392714,0.8695470064 C,0,-0.1149820353,1.0336071564,0.9953751129 O,0,-0.7375834841,0.9267696313,2.0320133127 O,0,-0.5875046121,1.4633799159,-0.1717064743 C,0,-1.9808938961,1.9232110171,-0.322367792 C,0,-2.9367386123,0.7755907604,-0.0271137772 C,0,-2.2205576398,3.133288648,0.569631315 C,0,-2.0384482678,2.3118351527,-1.7922346578 H,0,-2.7019260669,-0.0910350272,-0.6531003732 H,0,-2.8966014469,0.4799179629,1.0222896482 H,0,-3.9570986368,1.0942114393,-0.2614871397 H,0,-1.4771725909,3.9105698437,0.3671049618 H,0,-3.2103371396,3.5457832387,0.3517558607 H,0,-2.1817627173,2.8659911453,1.6269255675 H,0,-3.0377892195,2.6839072508,-2.0344160314 H,0,-1.3110760992,3.0979158716,-2.0146489122 H,0,-1.8276209169,1.4479990111,-2.4297545454 C,0,1.8360993146,0.2665182836,2.1722231304 H,0,1.2137478204,-0.5135826996,2.6134761066 H,0,1.8005924758,1.1276844826,2.8508849624 C,0,2.107757036,1.4396477854,-0.0579174358 H,0,1.5261733897,2.2929407907,-0.4176067045 C,0,3.2659639436,-0.2151042696,1.9930363442 H,0,3.2689425357,-1.1465777487,1.4131153434 H,0,3.6474607463,-0.4933170384,2.9804742903 C,0,3.3282928407,1.9598913296,0.6952586242 H,0,2.9797479524,2.6600591877,1.4648042354 H,0,3.9205807154,2.5433480467,-0.014801816 C,0,2.8397335654,1.1578613634,-2.2971587071 O,0,2.9355439481,2.3906140029,-2.4545605815	0, 1 N,0,1.3555110358,0.8576706541,0.7087146026 C,0,0.0205663104,0.826325992,0.7271753442 O,0,-0.7121588726,1.5044800777,-0.0326191612 O,0,-0.4796112556,0.0185171504,1.6488268716 C,0,-1.927366632,-0.226821301,1.8056732849 C,0,-2.6355272614,1.0608160258,2.2040734406 C,0,-2.4959775547,-0.8420131028,0.5346194772 C,0,-1.954542616,-1.2320894075,2.9483513632 H,0,-2.1442782574,1.5146798448,3.0703412842 H,0,-2.6576078005,1.7802483295,1.3845681122 H,0,-3.6664880228,0.8246912003,2.484868849 H,0,-1.9056522438,-1.7122659295,0.2316029147 H,0,-3.5184894092,-1.1782482681,0.7310878729 H,0,-2.5263265717,-0.1224623641,-0.2846653796 H,0,-2.9898074657,-1.5000150285,3.1763546652 H,0,-1.4123678232,-2.1425466413,2.6768237244 H,0,-1.5000716783,-0.8073741307,3.8481556228 C,0,2.1403798139,0.0340882871,1.6410110037 H,0,1.6579367602,-0.9408624163,1.7277859152 H,0,2.1234514919,0.498033949,2.6369809472 C,0,2.071077027,1.8358665883,-0.1457009826 H,0,1.3798343264,2.6718983491,-0.2984596227 C,0,3.5680420104,-0.1174804134,1.1415900315 H,0,3.5407549886,-0.6276067404,0.1740737882 H,0,4.1071442646,-0.7658768385,1.8400378934

N,0,2.4332947343,0.5568343049,-1.1670683496 C,0,3.1752344743,0.2422191162,-3.4433533854 C,0,2.8898708799,0.6686540049,-4.7451122464 C,0,3.7902860483,-1.0014296695,-3.2563371838 C,0,3.1762117457,-0.1471281746,-5.8362535199 H,0,2.4381980944,1.6460543011,-4.8869383246 C,0,4.0930153223,-1.8119849266,-4.3502326156 H,0,4.0695765807,-1.3250025172,-2.2570862242 C,0,3.7778363682,-1.3913844331,-5.6414233785 H,0,2.9349738271,0.1890593821,-6.8409395877 H,0,4.5829210854,-2.7690506953,-4.1935883853 H,0,4.008427986,-2.025452471,-6.4929461876 C,0,4.1621838761,0.8455389772,1.3266024251 H,0,4.8435543467,1.2863959101,2.0614634056 H,0,4.7903835381,0.3755378994,0.5638838225 Mg,0,1.3929862274,-1.0917220277,-0.7156076108 Br,0,0.3740718416,-3.2298467864,-0.2573705275	C,0,3.270441749,2.3484983493,0.6496418353 H,0,2.8879852016,2.8139490504,1.566888457 H,0,3.7482844388,3.1418616173,0.0668369464 C,0,1.8980064166,1.5672279901,-2.478872242 O,0,0.8552097428,2.33897419,-2.6054454495 N,0,2.5146333864,1.2461926432,-1.3840017215 C,0,2.4480779123,1.0171573426,-3.7615759091 C,0,1.750210203,1.2067930152,-4.9588825804 C,0,3.6674328389,0.3294023746,-3.7888169812 C,0,2.2564465078,0.7128927046,-6.160235784 H,0,0.8131477368,1.7536556967,-4.9376178985 C,0,4.1722675561,-0.1666263589,-4.9869886051 H,0,4.2076300918,0.1971619094,-2.8568755545 C,0,3.4673163352,0.0223788871,-6.17766825 H,0,1.704606736,0.8680651318,-7.08344277 H,0,5.1205444146,-0.697409727,-4.9955059318 H,0,3.8634647984,-0.3621632192,-7.1136178398 C,0,4.2715558568,1.2367206935,0.9921653064 H,0,4.7923235243,1.4999804466,1.9199718228 H,0,5.034357193,1.1612692278,0.2119818937 Mg,0,-0.8710243686,2.3548233051,-1.791640395 Br,0,-3.1016351761,3.0291450141,-2.4557151418

	
F (**12a'** + PhMgBr), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3767.34337914 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.330360 SP at PBE1PBE/6-311++G(d,p) in THF, E= -3769.97296494 a.u	**TS1** (**12a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3767.29653246 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.326036 a.u. 1 imaginary frequency = -179.12 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= --3769.92583415 a.u
0, 1 N,0,1.5756845138,1.2571142179,1.1060891782 C,0,0.2635758193,1.1381546373,0.8792644754 O,0,-0.231912155,1.2665060102,-0.2708557933 O,0,-0.4620450804,0.8809517269,1.9519622042 C,0,-1.908938466,0.5816268357,1.8904098818 C,0,-2.6639143846,1.816313117,1.4201228265 C,0,-2.1602141826,-0.6363498591,1.0127225622 C,0,-2.2310094795,0.2715430692,3.3450750625 H,0,-2.4232471403,2.6750945644,2.0542434741 H,0,-2.4281151876,2.0590798724,0.38302201 H,0,-3.7387331849,1.6266914395,1.4981696821 H,0,-1.5264061553,-1.4721026892,1.3260278818 H,0,-3.2033775086,-0.9446644656,1.1307507284 H,0,-1.9863375484,-0.425287872,-0.0435555655 H,0,-3.2972669559,0.0504798505,3.4443723544	0, 1 N,0,1.1356919832,0.3467962985,0.7152476402 C,0,-0.1394386591,0.7318366772,0.8372666242 O,0,-0.7940539655,0.9049860036,-0.2369603938 O,0,-0.6420352277,0.9171443428,2.0456252058 C,0,-2.0570629842,1.2694252918,2.2751904829 C,0,-2.3511788137,2.6369753381,1.6743802031 C,0,-2.9583835627,0.176708148,1.7173505029 C,0,-2.1401134289,1.3167364941,3.7936164655 H,0,-1.6486303688,3.3827486191,2.059632574 H,0,-2.2899448456,2.6147062838,0.5853055905 H,0,-3.3619521027,2.9429303759,1.9613963186 H,0,-2.6761758849,-0.7980666486,2.1273257273 H,0,-3.991508041,0.3825886179,2.0134236035 H,0,-2.9103882107,0.1348255234,0.6282039214 H,0,-3.1578505929,1.5769339391,4.0977444881

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H,0,-1.9931959052,1.1263629557,3.9846760915	H,0,-1.455462297,2.0692036629,4.1959618882
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H,0,1.4889181443,0.1707008143,2.8770961531	H,0,1.6620533763,-0.9274197475,2.292900468
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H,0,3.4644797906,-3.3864906146,-3.3881397231	H,0,3.62255752,-3.3691675168,-3.3318272846
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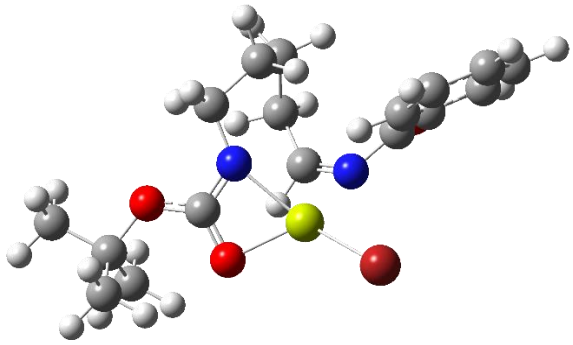	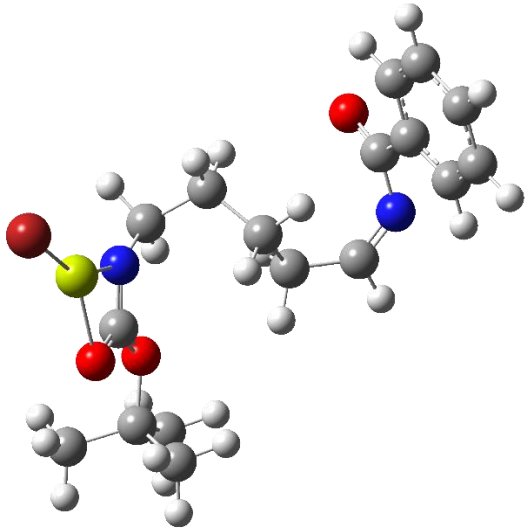
IM2 (**12a' + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3767.29877499 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.326964 SP at PBE1PBE/6-311++G(d,p) in THF, E= -3769.92597428 a.u	**TSrot** (**12a' + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3767.30383926 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.323288 a.u. 1 imaginary frequency = -49.69 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3769.93645321 a.u
0, 1 N,0,1.0897663677,-0.2203788313,0.5226571307 C,0,-0.1475276688,0.0988225812,0.8536477244 O,0,-0.9748261652,0.3256671183,-0.0985759754 O,0,-0.4778866752,0.2061062483,2.1388065857 C,0,-1.8275278638,0.5688818693,2.5905443146 C,0,-2.188047623,1.9661200821,2.1027596407 C,0,-2.8277810484,-0.4849383763,2.133970602 C,0,-1.6844295092,0.551494963,4.1062441342 H,0,-1.4235593871,2.6866634598,2.4112418809 H,0,-2.288876527,1.9928559101,1.0167948888 H,0,-3.1392017946,2.2692652544,2.5514762038 H,0,-2.5102503654,-1.4790818261,2.4643393497 H,0,-3.8036614773,-0.2738032143,2.582166783 H,0,-2.933878976,-0.4857426278,1.0480222035 H,0,-2.6408026771,0.8081365653,4.5707207951	0, 1 N,0,0.1602509157,1.7563534073,0.2497762343 C,0,-1.1196266574,1.7357630591,0.5651130169 O,0,-1.9513604575,2.2587570031,-0.2596850607 O,0,-1.5067221254,1.176679067,1.7130055975 C,0,-2.9141050713,1.0218704176,2.0899465626 C,0,-3.5656630229,2.3875279832,2.265603346 C,0,-3.639312726,0.1576448198,1.0661094611 C,0,-2.8223061019,0.2966611284,3.4260851977 H,0,-2.9889226443,2.9959133203,2.9699906066 H,0,-3.6366982246,2.9152280253,1.3134475138 H,0,-4.5727760248,2.2581625938,2.674312337 H,0,-3.1152301507,-0.7941048874,0.9318687107 H,0,-4.6494019491,-0.0593296637,1.4275692859 H,0,-3.7135463029,0.6642589025,0.1025898319 H,0,-3.8265749828,0.120639369,3.8219473731

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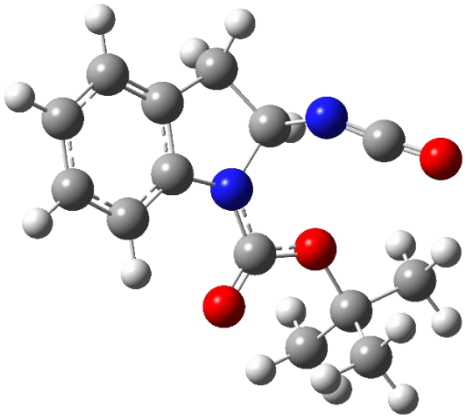
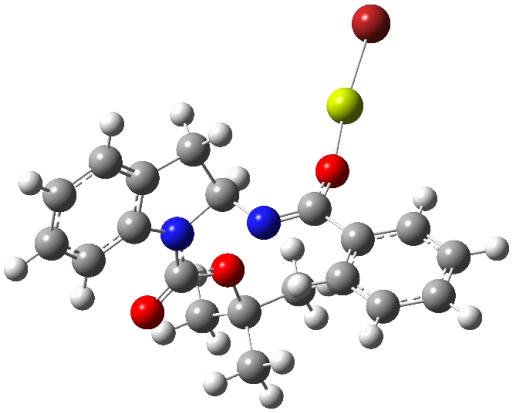
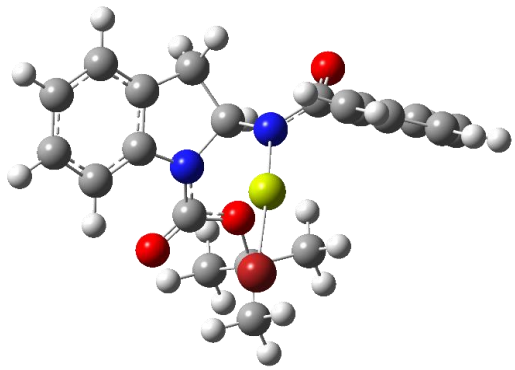
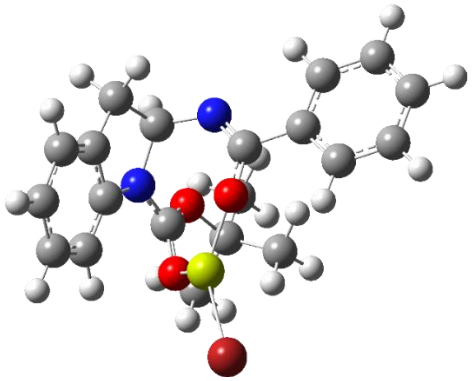
H,0,4.3255998868,1.742753169,1.7574128906	H,0,2.0632157481,4.1590242678,2.7747681146
H,0,4.6987996933,1.4946163518,0.0688132807	H,0,0.5350106567,3.7386697153,2.0569462934
Mg,0,0.4504006309,-0.100312811,-1.5182712428	Mg,0,-0.3736990384,2.6793059777,-1.5124100563
Br,0,0.1188478807,-1.0601631439,-3.7267193094	Br,0,0.1063572954,3.6319036497,-3.6900424396

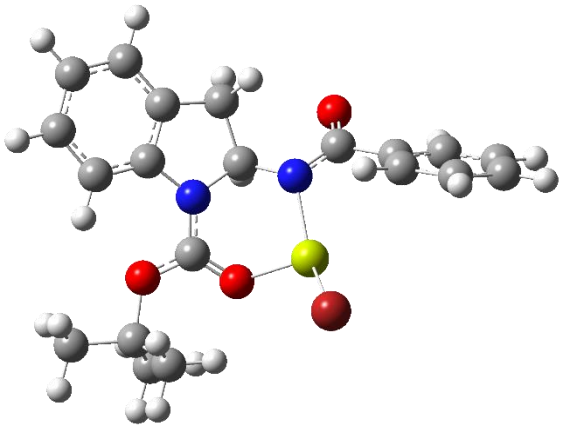
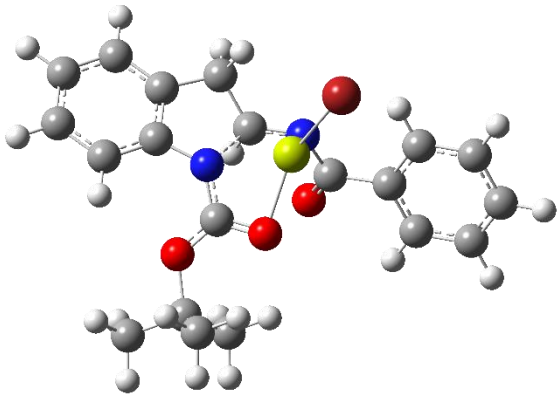
S.5.6. Cartesian coordinates and computed total energies for the reaction of **13a'** and **PhMgBr**: 13a', PhMgBr, C-F, TS1, IM2, TSrot.

	
Isocyanate (13a'), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -877.402245189 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.237746 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -877.579553621 a.u	**C** (**13a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-31G(d,p) E= -3880.32105475 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.319278 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3882.97204045 a.u
0, 1 C,0,0.5571044709,-1.7582108232,-0.1283735419 C,0,-0.777114125,-1.9974515712,-0.4758597315 C,0,-1.7364870376,-0.990862191,-0.4218594723 C,0,-1.3217076891,0.2750709428,0.002987716 C,0,0.0024931683,0.5250392514,0.3608092178 C,0,0.9532830502,-0.4989206353,0.2932433909 C,0,0.2865870232,-4.0985003977,-0.4928234478 H,0,-2.7637107606,-1.1867101716,-0.7002372704 H,0,-2.0537216137,1.0760269973,0.056698938 H,0,0.297332744,1.5164360104,0.6917085901 H,0,1.988381285,-0.3103236894,0.5653535991 H,0,0.5172521843,-4.8208954233,-1.2758931922 N,0,-0.9188195612,-3.350945764,-0.8454471554 N,0,0.111211899,-4.8066124949,0.7627725437 C,0,-2.059329461,-3.9337544939,-1.3406438704 O,0,-3.0766173537,-3.3158103899,-1.6016514337 O,0,-1.8692243886,-5.2509175326,-1.4876827416	0, 1 C,0,0.7200696849,-1.5125052434,-0.3094063144 C,0,-0.6274662997,-1.4769358234,-0.692737043 C,0,-1.3548555893,-0.2883581129,-0.664839921 C,0,-0.6978373505,0.8689534358,-0.2353183893 C,0,0.6402173829,0.8438719339,0.1553570128 C,0,1.356972748,-0.3575557986,0.1159998286 C,0,-0.0166095511,-3.7637623615,-0.6637815189 H,0,-2.3945635432,-0.2707664972,-0.9641143764 H,0,-1.2503009459,1.8041586319,-0.2027938608 H,0,1.1265968389,1.7554481555,0.4902835166 H,0,2.401835434,-0.3855945322,0.4149724082 H,0,0.0917235574,-4.4934523879,-1.4710165302 N,0,-1.0318082257,-2.7670421963,-1.0711993659 N,0,-0.4259494787,-4.3636923511,0.5753304052 C,0,-2.2666663645,-3.1010185077,-1.5509820406 O,0,-3.1710716177,-2.2988563397,-1.7350055064 O,0,-2.3230346476,-4.4152171659,-1.8147963619

C,0,-2.9211555008,-6.1212381592,-2.0380155471	C,0,-3.5683835097,-5.0538714741,-2.2433559351
C,0,-2.2514924485,-7.4881441841,-2.0385610776	C,0,-3.1631834913,-6.5169445168,-2.3690919961
H,0,-2.944738032,-8.2358475442,-2.4340045691	H,0,-4.0269362689,-7.1157517988,-2.6721270817
H,0,-1.3560940505,-7.4806724585,-2.6674387033	H,0,-2.3791737084,-6.6367633971,-3.1233989336
H,0,-1.9676687906,-7.7821375439,-1.0239264892	H,0,-2.7930164945,-6.8985074208,-1.4127545586
C,0,-4.1320288971,-6.1138411153,-1.1146477471	C,0,-4.6370375958,-4.8863958712,-1.1701641883
H,0,-4.6189243098,-5.1375088988,-1.1032618514	H,0,-4.9372806909,-3.8422951563,-1.0677556205
H,0,-4.8523889454,-6.8597302429,-1.4644732876	H,0,-5.5166193733,-5.477870947,-1.4430496574
H,0,-3.8361158768,-6.3799669217,-0.095101146	H,0,-4.267312238,-5.248352689,-0.2056625618
C,0,-3.263030991,-5.6890843407,-3.4577060774	C,0,-4.0096479203,-4.5048170698,-3.594791858
H,0,-3.9431598964,-6.4239259765,-3.8994685883	H,0,-4.8581520494,-5.0913347673,-3.9613521084
H,0,-3.7481052256,-4.711960668,-3.4730905137	H,0,-4.3114227036,-3.4593068234,-3.5190461419
H,0,-2.3589084834,-5.6509422571,-4.0735293655	H,0,-3.1975916367,-4.5900483248,-4.3241257916
C,0,-0.4192491136,-5.8353624712,1.1041764863	C,0,-0.1377765518,-5.6063925796,0.7710445
O,0,-0.8872457908,-6.8068121996,1.5760276042	C,0,-0.5944971208,-6.2326086667,2.0528062516
C,0,1.3594476965,-3.0104896541,-0.3429842357	C,0,-1.2342942334,-5.4651803898,3.034466995
H,0,1.9462261576,-2.9406120031,-1.2662289273	C,0,-0.3910140156,-7.5958595286,2.2882821402
H,0,2.0419644738,-3.2494405554,0.4749651473	C,0,-1.6570419644,-6.0492826617,4.2240923192
	H,0,-1.3891627715,-4.4079446583,2.8457940852
	C,0,-0.8182020037,-8.1836334429,3.4782401962
	H,0,0.1001575731,-8.1955708927,1.5293550756
	C,0,-1.4514646932,-7.4119982368,4.4506946208
	H,0,-2.1493769298,-5.4410941676,4.9780393298
	H,0,-0.6556163067,-9.2450433434,3.6449875014
	H,0,-1.7827778266,-7.8676445018,5.3797725183
	C,0,1.255619723,-2.9039729467,-0.4924135818
	H,0,1.8848257204,-2.9567544534,-1.3902520756
	H,0,1.8451161402,-3.2577121551,0.357554442
	O,0,0.5098414428,-6.3872879246,-0.0491595047
	Mg,0,1.7728061766,-7.1426471573,-1.1753245842
	Br,0,3.3592375399,-8.3319828361,-2.5150421887

	
D (**13a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-31+G(d,p) E= -3880.32495930 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.323800 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3882.97335076 a.u	**E** (**13a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-31G(d,p) E= -3880.33434017 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.322708 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3882.98153053 a.u
0, 1 C,0,0.4703727867,-1.6075460045,-0.0123796569 C,0,-0.8927648363,-1.502370651,-0.312812721 C,0,-1.5872086753,-0.3069704081,-0.1465135904 C,0,-0.8753255833,0.7955168245,0.3355536051 C,0,0.4810369668,0.7032684159,0.6467914001 C,0,1.1613747203,-0.5063410081,0.4716601235 C,0,-0.3537098912,-3.801288246,-0.4835585299 H,0,-2.6392263472,-0.235348384,-0.3913914648 H,0,-1.3961354892,1.7390641786,0.4723005922 H,0,1.0111063926,1.5727920581,1.0243296557 H,0,2.2203181866,-0.5822231512,0.7047365007 H,0,-0.3129752242,-4.4913092679,-1.3280008161 N,0,-1.3749656628,-2.7636485075,-0.7357681203 N,0,-0.7014520805,-4.5169990329,0.7310962879 C,0,-2.4953313216,-2.9418287124,-1.5163404841 O,0,-3.2562572776,-2.037013385,-1.8174232883 O,0,-2.6252136844,-4.2287720104,-1.8570643787 C,0,-3.7533035713,-4.6890186459,-2.6790495177 C,0,-3.481198903,-6.1811745611,-2.8082842166	0, 1 C,0,0.7224700744,-1.3484167789,-0.29271582 C,0,-0.5707927029,-1.3789992428,-0.8287708621 C,0,-1.3120635753,-0.2084168581,-1.0036999719 C,0,-0.7435412811,0.9972884962,-0.5695719875 C,0,0.5245534878,1.0310043692,0.0013183191 C,0,1.2690942811,-0.1481909468,0.1297052264 C,0,0.1293673968,-3.6580015888,-0.6257906891 H,0,-2.2782889997,-0.2091208093,-1.4973782395 H,0,-1.3082556846,1.9166268684,-0.6925466938 H,0,0.9437374209,1.9747879612,0.336394922 H,0,2.2698603747,-0.1220313502,0.5524366523 H,0,0.3644088429,-4.3685761161,-1.4206488435 N,0,-0.8984630358,-2.7026709088,-1.1769619827 N,0,-0.2549548656,-4.4122726567,0.5276531567 C,0,-2.1633388462,-3.1195532714,-1.4253360549 O,0,-3.1635916508,-2.4083103063,-1.1766428262 O,0,-2.2110447819,-4.3256517062,-1.9337535245 C,0,-3.4782339335,-5.0651498369,-2.1478379421 C,0,-2.978432524,-6.4054128364,-2.6643664811

H,0,-4.2649808758,-6.6470464937,-3.4123626541	H,0,-3.8319559447,-7.0534995137,-2.8808922213
H,0,-2.5170488666,-6.358346279,-3.2937338596	H,0,-2.4005614589,-6.2742290145,-3.5836409241
H,0,-3.4708360491,-6.661586345,-1.8253706606	H,0,-2.3480421848,-6.8974993785,-1.9183658252
C,0,-5.0645471482,-4.4418349864,-1.944262972	C,0,-4.2099675651,-5.2328053919,-0.8245432506
H,0,-5.2691112688,-3.3753917978,-1.8388712127	H,0,-4.6252283678,-4.289764494,-0.46563239
H,0,-5.882834031,-4.9003792651,-2.5080296624	H,0,-5.0376026952,-5.9337133526,-0.9682480636
H,0,-5.0408271503,-4.9030289591,-0.9517025362	H,0,-3.540900967,-5.6492228108,-0.0655405745
C,0,-3.7117256558,-4.0161544128,-4.0449261772	C,0,-4.3081202902,-4.3461247672,-3.2006030745
H,0,-4.4740213045,-4.4656318937,-4.6887665642	H,0,-5.1749154557,-4.9651177138,-3.4510448028
H,0,-3.9061670105,-2.9454176665,-3.9684149706	H,0,-4.6644004459,-3.3797264727,-2.8403113666
H,0,-2.7357314738,-4.1707248965,-4.5156781678	H,0,-3.7225349102,-4.1969399126,-4.1128082716
C,0,-0.0882509113,-5.7029378064,0.8969466723	C,0,-1.1120800448,-4.0309751765,1.4200586555
C,0,-0.4459184936,-6.4052942386,2.1806143618	C,0,-1.3046492258,-4.9417301002,2.5997758324
C,0,-0.4214123439,-5.7318407738,3.4104097342	C,0,-0.562296467,-6.1210392801,2.7384699844
C,0,-0.8073483925,-7.75687913,2.1504916925	C,0,-2.2389920367,-4.6113986383,3.5869933713
C,0,-0.7822620815,-6.3939529949,4.5866597428	C,0,-0.7521202129,-6.9508692346,3.8392471798
H,0,-0.0519627866,-4.7082742894,3.4633967881	H,0,0.1621763013,-6.3717757486,1.970397587
C,0,-1.1756099253,-8.4112315398,3.3217983857	C,0,-2.4300827221,-5.4417678688,4.6903397568
H,0,-0.8022265033,-8.2839414715,1.2007983959	H,0,-2.8102353499,-3.6946237416,3.484001804
C,0,-1.1696042857,-7.7303599969,4.5416769576	C,0,-1.6891741096,-6.6152700353,4.8188147881
H,0,-0.7456331656,-5.8666786506,5.5355206075	H,0,-0.1688549275,-7.8628215928,3.9347688411
H,0,-1.4693135555,-9.4565172952,3.2861148078	H,0,-3.1590504723,-5.1715946069,5.449564532
H,0,-1.4548912487,-8.2457557428,5.4540783471	H,0,-1.8374250188,-7.264061033,5.6778143516
C,0,0.9514437556,-2.9925171824,-0.3375889391	C,0,1.3259122307,-2.7211316095,-0.3398439784
H,0,1.5138683346,-2.9937046047,-1.2796031257	H,0,2.067609499,-2.7815099802,-1.1452924923
H,0,1.5908509694,-3.4318654957,0.4315015287	H,0,1.816623672,-3.0155482363,0.5905718364
O,0,0.6956140773,-6.2349549307,0.0921044322	O,0,-1.8327641939,-2.9494152649,1.4337027895
Mg,0,-2.2442441803,-3.9840335037,1.8941982015	Mg,0,-3.0927530867,-1.7082081592,0.7492606547
Br,0,-4.2260838641,-3.2447044184,3.045004636	Br,0,-4.8559000966,-0.3050128221,1.646527383

	
F (**13a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3767.34337914 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.330360 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3769.97296494 a.u	**TS1** (**13a'** + **PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3880.31306408 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.320124 a.u. 1 imaginary frequency = -218.37 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3882.95830608a.u
0, 1 C,0,0.6473272928,-0.8734039398,0.1231235641 C,0,-0.7124408411,-0.5321302062,0.0364547776 C,0,-1.1034195013,0.6393251285,-0.6129880912 C,0,-0.1250605539,1.4596254627,-1.1767182389 C,0,1.2255164033,1.1225050542,-1.0963347324 C,0,1.6118150862,-0.0499263734,-0.4430630502 C,0,-0.2510934984,-3.0879232609,0.6182096126 H,0,-2.152379828,0.9059958948,-0.6803022521 H,0,-0.4258892544,2.3706530393,-1.6865461432 H,0,1.9759761338,1.766277548,-1.5453035544 H,0,2.6621873434,-0.3236229726,-0.3838198379 H,0,-0.4412909661,-3.3379068907,-0.4312865377 N,0,-1.5360624792,-1.4447260186,0.7121257117 N,0,-0.6977927254,-3.9248941007,1.5505517679 C,0,-2.7934953952,-1.8071154757,0.3860157904 O,0,-3.3873395792,-2.5529483727,1.2136065702 O,0,-3.3059075472,-1.3997388007,-0.7527747862	0, 1 C,0,0.6473272928,-0.8734039398,0.1231235641 C,0,-0.7124408411,-0.5321302062,0.0364547776 C,0,-1.1034195013,0.6393251285,-0.6129880912 C,0,-0.1250605539,1.4596254627,-1.1767182389 C,0,1.2255164033,1.1225050542,-1.0963347324 C,0,1.6118150862,-0.0499263734,-0.4430630502 C,0,-0.2510934984,-3.0879232609,0.6182096126 H,0,-2.152379828,0.9059958948,-0.6803022521 H,0,-0.4258892544,2.3706530393,-1.6865461432 H,0,1.9759761338,1.766277548,-1.5453035544 H,0,2.6621873434,-0.3236229726,-0.3838198379 H,0,-0.4412909661,-3.3379068907,-0.4312865377 N,0,-1.5360624792,-1.4447260186,0.7121257117 N,0,-0.6977927254,-3.9248941007,1.5505517679 C,0,-2.7934953952,-1.8071154757,0.3860157904 O,0,-3.3873395792,-2.5529483727,1.2136065702 O,0,-3.3059075472,-1.3997388007,-0.7527747862

C,0,-4.6907767771,-1.7201468218,-1.1678575477	C,0,-4.6907767771,-1.7201468218,-1.1678575477
C,0,-4.8026611904,-1.0005795834,-2.5030987168	C,0,-4.8026611904,-1.0005795834,-2.5030987168
H,0,-5.7983485738,-1.1647449917,-2.9242467502	H,0,-5.7983485738,-1.1647449917,-2.9242467502
H,0,-4.6526118003,0.075789262,-2.3781293201	H,0,-4.6526118003,0.075789262,-2.3781293201
H,0,-4.059511629,-1.3793205701,-3.2105592769	H,0,-4.059511629,-1.3793205701,-3.2105592769
C,0,-4.8365393108,-3.2239943112,-1.3452094835	C,0,-4.8365393108,-3.2239943112,-1.3452094835
H,0,-4.7541642364,-3.7500043925,-0.392912992	H,0,-4.7541642364,-3.7500043925,-0.392912992
H,0,-5.8196596583,-3.4351809249,-1.776942294	H,0,-5.8196596583,-3.4351809249,-1.776942294
H,0,-4.0740280813,-3.6049480394,-2.0311651363	H,0,-4.0740280813,-3.6049480394,-2.0311651363
C,0,-5.6736162009,-1.1463233792,-0.1574554097	C,0,-5.6736162009,-1.1463233792,-0.1574554097
H,0,-6.6895482103,-1.2674021888,-0.5452053599	H,0,-6.6895482103,-1.2674021888,-0.5452053599
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C,0,-1.8712752426,-5.9821530401,2.117940898	C,0,-1.8712752426,-5.9821530401,2.117940898
C,0,-1.4268860519,-5.9181415095,3.444658951	C,0,-1.4268860519,-5.9181415095,3.444658951
C,0,-2.811674534,-6.9532396041,1.7506319569	C,0,-2.811674534,-6.9532396041,1.7506319569
C,0,-1.9289438685,-6.8079334864,4.3918582794	C,0,-1.9289438685,-6.8079334864,4.3918582794
H,0,-0.6845716197,-5.1797850361,3.7299241126	H,0,-0.6845716197,-5.1797850361,3.7299241126
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C,0,-2.8756806597,-7.7623279632,4.0226548805	C,0,-2.8756806597,-7.7623279632,4.0226548805
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H,0,-4.0564550137,-8.5760383196,2.4115070995	H,0,-4.0564550137,-8.5760383196,2.4115070995
H,0,-3.2688622417,-8.4522171007,4.7641736876	H,0,-3.2688622417,-8.4522171007,4.7641736876
C,0,0.8998449873,-2.1587760924,0.8600997558	C,0,0.8998449873,-2.1587760924,0.8600997558
H,0,1.801742606,-2.6612404699,0.4868118109	H,0,1.801742606,-2.6612404699,0.4868118109
H,0,1.044655797,-2.0002936085,1.9364196342	H,0,1.044655797,-2.0002936085,1.9364196342
O,0,-1.4736194987,-5.3329049729,-0.1276491031	O,0,-1.4736194987,-5.3329049729,-0.1276491031
Mg,0,-1.8898058265,-2.4780144512,2.644484814	Mg,0,-1.8898058265,-2.4780144512,2.644484814
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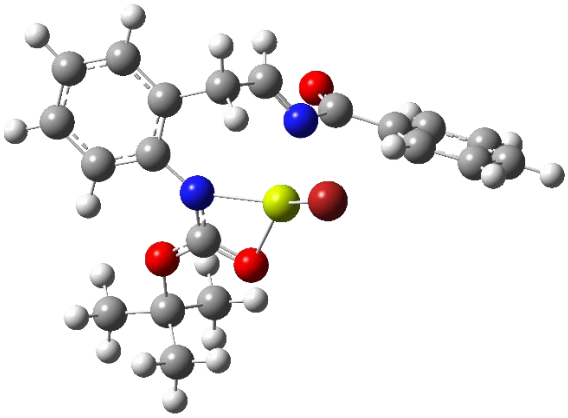	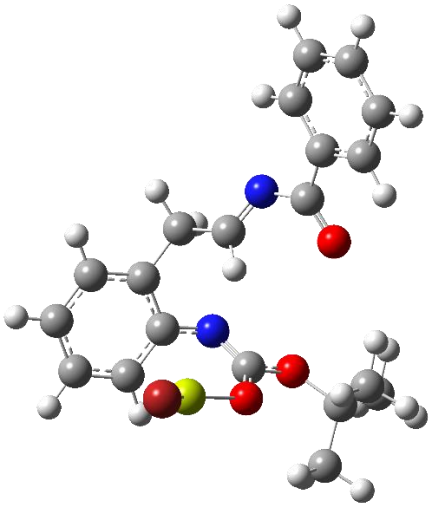
IM2 (**13a' + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3880.32756460 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.320565 a.u. SP at PBE1PBE/6-311++G(d,p) in THF, E= -3882.97069343 a.u	**TSrot** (**13a' + PhMgBr**), optimization in solv. THF PBE1PBE/6-311+G(d,p) E= -3880.28531400 a.u. thermal correction to Gibbs Free energy at 25 °C = 0.316972 a.u. 1 imaginary frequency = -39.11 i cm^{-1} SP at PBE1PBE/6-311++G(d,p) in THF, E= -3882.93548192 a.u
0, 1 C,0,0.4850691971,-1.1952225438,0.1898471106 C,0,-0.8157601258,-0.8560787778,-0.2626696421 C,0,-1.0046846331,0.4133562026,-0.8394058768 C,0,0.0594181771,1.2989676947,-0.9813770705 C,0,1.3399246455,0.9532585936,-0.5540789337 C,0,1.5375386949,-0.2933862054,0.0340565023 C,0,0.6788221398,-3.6299687698,-0.1610663055 H,0,-1.9922032404,0.6993185111,-1.1768661575 H,0,-0.1192956011,2.2713620613,-1.4329383541 H,0,2.1691607082,1.6453016767,-0.6650312526 H,0,2.5278349407,-0.574652779,0.3848006896 H,0,1.5341756917,-3.7434016786,-0.8347669649 N,0,-1.8024592156,-1.8134295716,-0.0674457375 N,0,-0.3306506192,-4.414545869,-0.2890293006 C,0,-2.9870739205,-1.9250798688,-0.6625431878 O,0,-3.650965091,-2.9880843741,-0.4203432896	0, 1 C,0,-0.5864941861,-2.0764759687,0.2058265658 C,0,-1.2036140616,-1.9510548302,-1.0667127863 C,0,-1.8869800053,-0.7400441387,-1.3539856759 C,0,-1.9177555719,0.3169634797,-0.4328744265 C,0,-1.292768877,0.1834061408,0.8008448227 C,0,-0.6364300614,-1.0124574328,1.1041241204 C,0,-0.8170518477,-4.5163775059,0.7453646383 H,0,-2.285787306,-0.5920847063,-2.3573200364 H,0,-2.4223764277,1.2416539709,-0.6990093124 H,0,-1.3127359073,0.9944638023,1.5214970887 H,0,-0.1513609097,-1.1230741713,2.0713548359 H,0,-1.8888625016,-4.3483993375,0.5658734695 N,0,-1.0617695517,-2.9643880597,-1.9913879371 N,0,-0.3969693718,-5.656005852,1.1296979711 C,0,-2.1311943796,-3.4524810226,-2.5633033693 O,0,-3.354426076,-3.2252746164,-2.2349408199

O,0,-3.4340517537,-0.9803110237,-1.4771256716	O,0,-1.8731461305,-4.2966719966,-3.5708083983
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H,0,-5.6542002825,-2.2467563086,-3.7089974685	H,0,-4.2698304903,-6.6755048983,-3.8584772671
H,0,-3.8843595389,-2.2252807636,-3.7913321429	H,0,-2.8841923595,-6.6140450006,-2.7536826895
C,0,-5.8614169926,-1.1145865445,-1.150904782	C,0,-3.8759910781,-4.1366706774,-4.9881206851
H,0,-6.8188495352,-1.038247996,-1.6756215014	H,0,-4.5350959673,-4.7336265233,-5.626603782
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H,0,-5.7845314058,-0.2686059593,-0.4605164998	H,0,-3.3267490309,-3.4378705817,-5.6275194494
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C,0,-0.814876784,-6.6965236494,-1.0929266646	C,0,-1.1600001914,-7.5905525192,2.3987109451
C,0,-1.1333482402,-7.1160270765,0.2055523445	C,0,-0.0608316232,-7.4644293907,3.2574977821
C,0,-0.9679460507,-7.5805750258,-2.1707570204	C,0,-2.1259386049,-8.5741490996,2.6473027862
C,0,-1.6092152882,-8.4074781344,0.4161760832	C,0,0.0679296151,-8.3139086669,4.3532769315
H,0,-1.006904327,-6.4478101581,1.0526344834	H,0,0.6900571739,-6.708813857,3.0521681398
C,0,-1.4534730166,-8.8633228102,-1.9551618939	C,0,-1.9948251471,-9.4199952176,3.7422149417
H,0,-0.7089494402,-7.2420051933,-3.169004433	H,0,-2.9727047848,-8.6599653433,1.9733705609
C,0,-1.773189195,-9.2782770249,-0.6599686154	C,0,-0.8975375878,-9.290309773,4.5968017954
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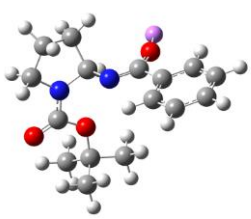
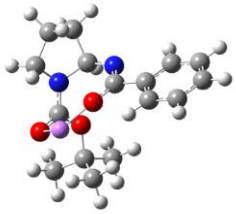
H,0,-1.5815300586,-9.5427643953,-2.7924201855	H,0,-2.7461727498,-10.180602924,3.9331756868
H,0,-2.1507623784,-10.2827545225,-0.4910946407	H,0,-0.7948976733,-9.9532106195,5.4514191704
C,0,0.7398227178,-2.5368602729,0.8510975619	C,0,0.1163958068,-3.3579763808,0.547964069
H,0,1.7461161324,-2.5336983957,1.2822593102	H,0,0.8088757501,-3.6359038097,-0.2577458453
H,0,0.0376781767,-2.7247061116,1.6718704728	H,0,0.7167788194,-3.2404570995,1.4566783629
O,0,0.1769616365,-5.0186210086,-2.4545191801	O,0,-2.2125099381,-6.8718217643,0.3893185326
Mg,0,-2.1349172657,-3.7223431732,0.7432699867	Mg,0,-3.9055021938,-2.0896130845,-0.7593100116
Br,0,-1.9382944595,-4.6362590828,3.0022030287	Br,0,-5.4081821143,-1.7848660822,1.1108662693

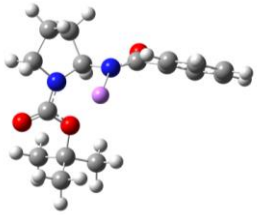
S.5.7. Optimized intermediates formed from the addition of phenyl lithium to isocyanate using PBE1PBE/6-311++G**//PBE1PBE/6-31+G**level of theory in solvent THF. Energies relative to the common reactants are indicated in kcalmol^{-1}.



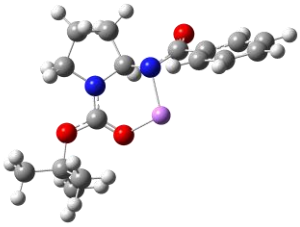
Int5
ΔG = - 40.32 kcalmol-1



Int6
ΔG = -36.5 kcalmol^{-1}



Int7
ΔG = -37.26 kcalmol^{-1}



Int8 = IM1
ΔG = -42.75 kcalmol^{-1}

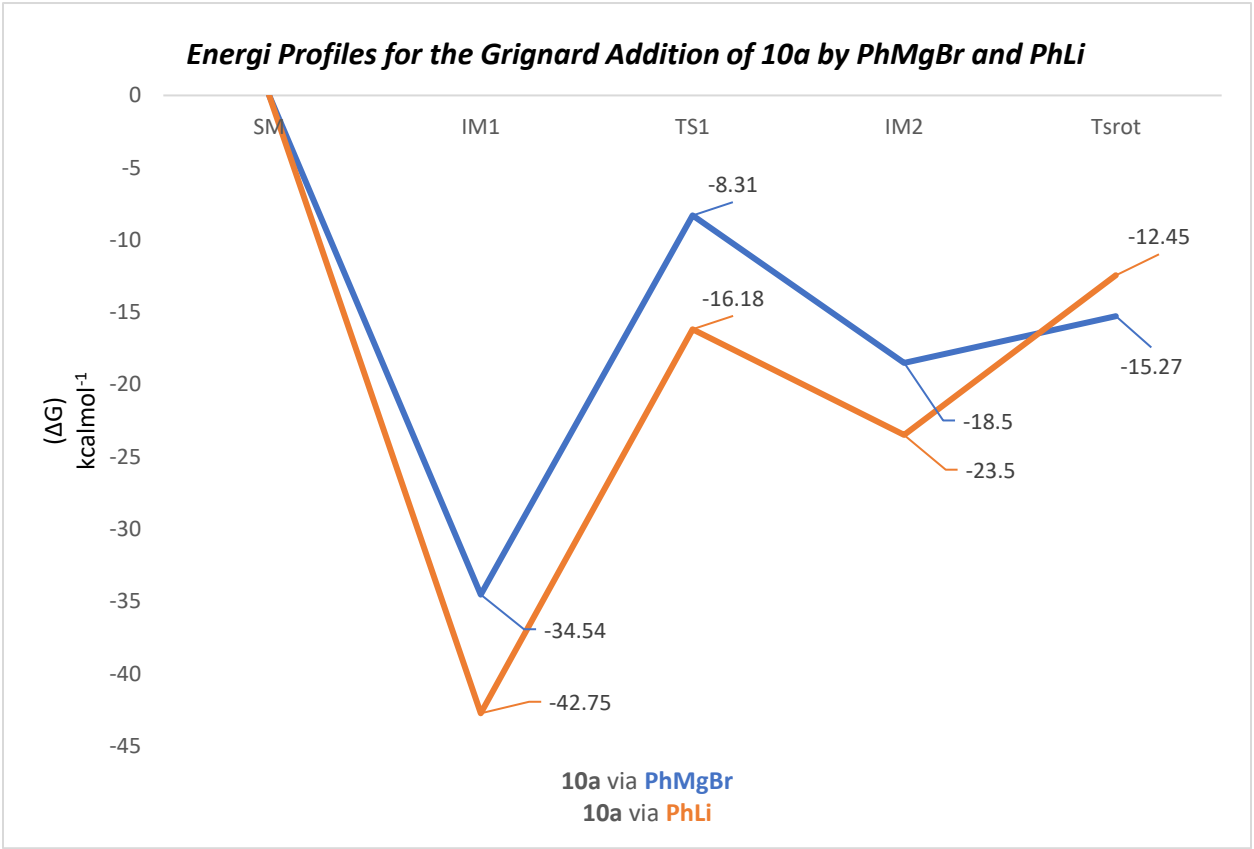


Figure S3*. Calculated energy profile for the reaction of isocyanate and phenyl magnesium bromide for the synthesis of 10a. Calculations performed using PBE1PBE/6-311++G**//PBE1PBE/6-31+G**level of theory in solvent THF. For 10a via PhLi, IM1=Int8.*

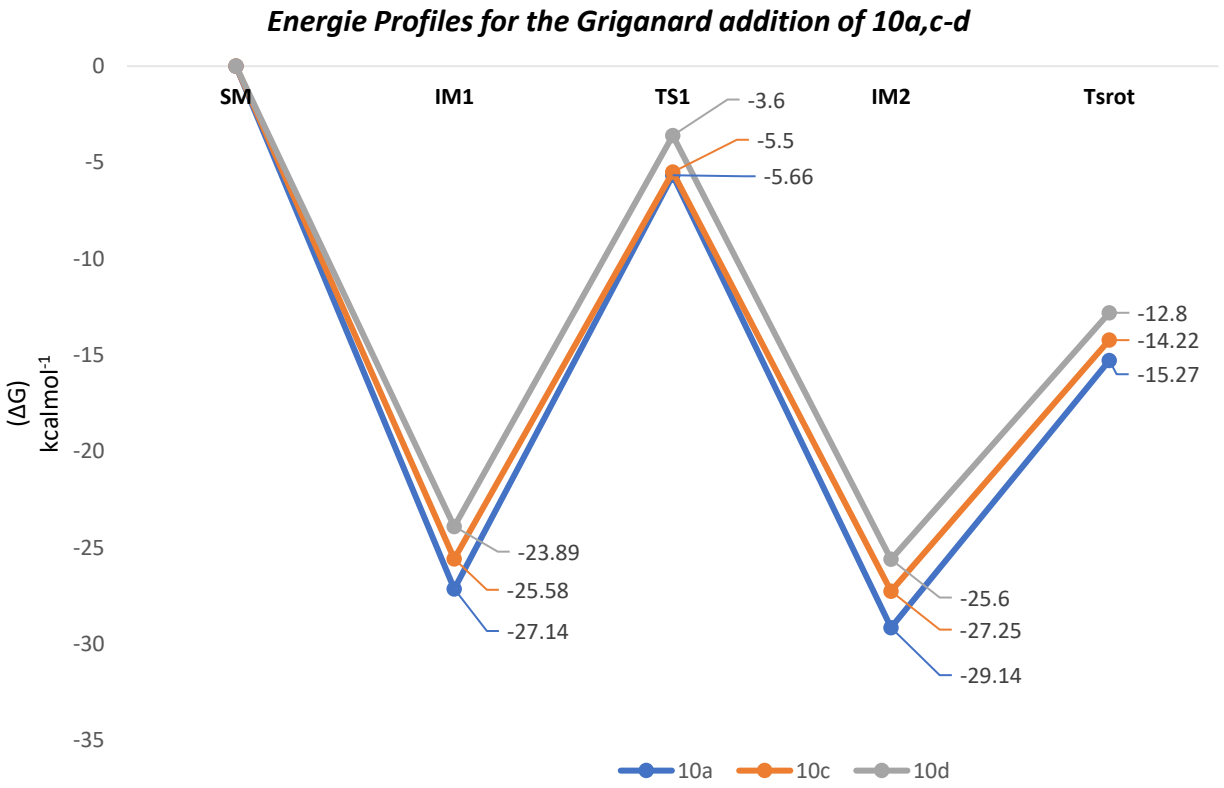


Figure S4*. Calculated energy profiles for the synthesis of 10a,c-d via Grignard addition using PBE1PBE/6-311++G**//PBE1PBE/6-31+G** level of theory in solvent THF.*

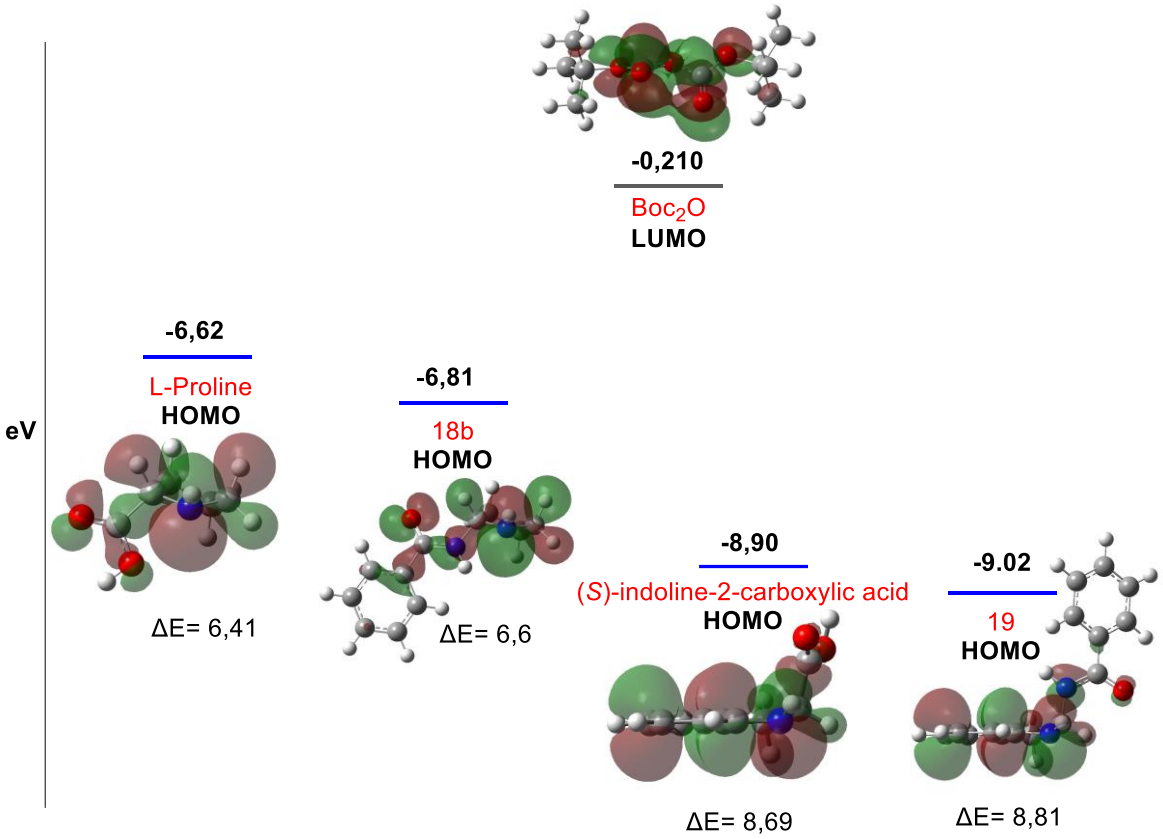
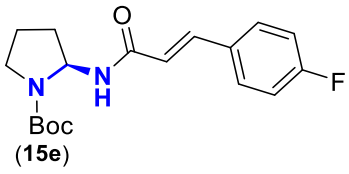
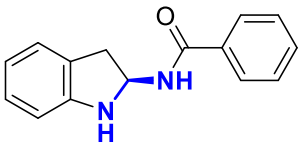


Figure S5. LUMO energy value of Boc_2O and HOMO energy values of L-Proline, (S)-inodline-2-caboxylix acid, ***18b*** and ***19***. Calculations performed using PBE1PBE/6-31+G** theoretical methods in solvent THF.

S.6. X-Ray Data of Compounds 15e and 19

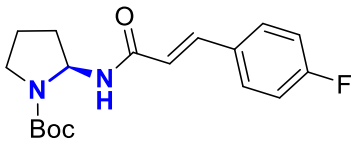
Crystallographic experimental data and structure refinement parameters are given in **Table S6**.

Table S6. *Crystallographic experimental data and structure refinement parameters*

	 (**15e**)	 (**19**)
Formula	$C_{18}H_{23}FN_2O_3$	$C_{15}H_{14}N_2O$
M	334.38	238.28
λ (Å)	0.71073	1.54178
T (K)	296(2)	296(2)
crystal system	Orthorhombic	Monoclinic
space group	*Pbca*	$P2_1$
Crystal description	Plate	Plate
Crystal color	Colourless	Colourless
Crystal Size	0.08 × 0.14 × 0.20	0.06 × 0.10 × 0.20
a (Å)	14.6133(11)	5.0552(3)
b (Å)	19.1979(13)	9.2248(5)
c (Å)	26.659(2)	25.6961(13)
α (deg)	90	90
β (deg)	90	90.499(3)
γ (deg)	90	90
V (Å^3)	7479.0(10)	1198.25(11)

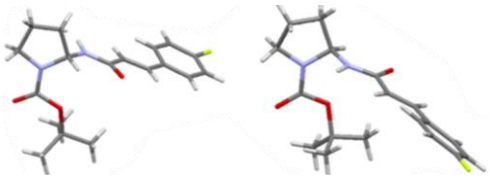
Z	16	4
ρ_{calc} (g cm^{-3})	1.188	1.321
μ (mm^{-1})	0.088	0.670
θ_{max} (deg)	20.945	70.317
total data	189962	22687
unique data	3947	4429
R_{int}	0.5294	0.1277
R [I>3σ(I)]	0.0916	0.0704
wR_2	0.2280	0.1780
Goodness of fit	1.066	1.015
ρ min	- 0.452	-0.359
ρ max	0.403	0.393

S.6.1. X-ray structure of compound **15**.



(**15e**)
ee 20%

≡



(*R*) and (*S*) enantiomer

S.7. References

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