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Supporting Information

Cyclization of *N*-Boc-(*E*)-α,β-Unsaturated γ-Amino Acid Active Esters into *N*-Boc-*(Z)*-α,β-Unsaturated γ-Lactams through *E*→*Z* Isomerization

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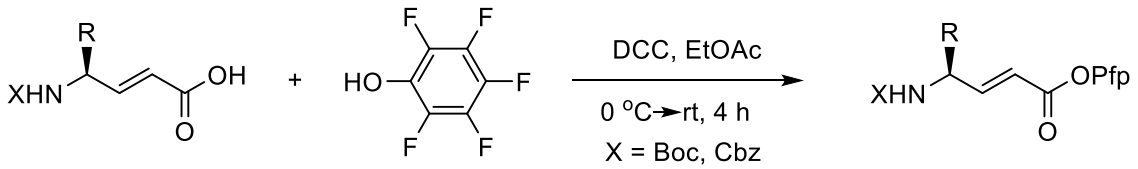
1. Materials and methods

All the cyclization reactions were performed under N_2 conditions. All the amino acids, Boc anhydride, Benzyl chloroformate, N-hydroxysuccinimide, $NaBH_4$, Oxone, HBTU, HOBt, Ethyl bromoacetate, Triphenyl Phosphine (PPh_3), Trifluoroacetic acid (TFA), N,N-Diisopropylethylamine (DIPEA), DMF, EtOAc, Hexane, were purchased from different commercial sources. Ethyl acetate, Hexane, and THF (over sodium) were distilled before use. Column chromatography was performed on silica gel (60-120). Reactions were monitored by analytical thin layer chromatography (TLC) and confirmed by UV light chamber and $KMnO_4$ or ninhydrin staining. ^{1}H NMR, ^{13}C NMR, and ^{19}F NMR spectra were recorded in deuterated solvents on 400 MHz, 101 MHz, and 377 MHz NMR machines respectively using the residual solvent signal as the internal standard ($CDCl_3$). Chemical shifts are reported in parts per million (ppm, δ) relative to tetramethyl silane (δ 0.00). ^{1}H NMR splitting patterns are assigned as singlet (s), doublet (d), broad singlet (bs), triplet (t), doublet of doublets (dd), and quintet (qn). Coupling constants (*J*) are reported in Hertz (Hz). Mass spectra were recorded using HRMS Electron Spray Ionization (ESI). IR spectra were recorded on an IR spectrometer. HPLC was done using a Chiralpak®-IC column (4.6 mmϕ x 250 mmL) of particle size 5 µm. The X-ray data were collected at low temperatures (100, 120 K and 150 K) on a Bruker APEX (II) DUO CCD diffractometer using Mo K_α (λ = 0.71073 Å) and Cu K_α radiation (λ = 1.54178 Å) graphite monochromated radiation.

2. Synthetic procedures for OPfp/ONp esters of (*E*)-vinylogous amino acids.

The *N*-protected α,β-unsaturated γ-amino esters (Boc/CbzHN-(*S*,*E*)d^{2,3}γXxx-OEt) were prepared by the previously reported procedures.[1] Boc/Cbz and ethyl ester protecting groups were used to protect the N- terminus and C- terminus of the (*E*)-vinylogous amino acids, respectively and the ethyl ester was deprotected by base hydrolysis using 1*N* NaOH, to obtain **1a-1g**.[1] The synthetic details of OPfp esters synthesis is given below. The purification of final OPfp esters was carried out through silica gel column chromatography using ethyl acetate and hexane solvent gradient as eluent.

A) General procedure for the synthesis of OPfp esters of (*E*)-vinylogous amino acids (2a-2g).

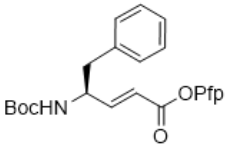


Scheme S1: Synthesis of active esters Boc/CbzHN-(*S,E*)-d^{2,3}γXxx-OPfp (**2a-2g**).

Boc/CbzHN-d^{2,3}γXxx-OH (2 mmol) was dissolved in 50 mL of EtOAc, to this solution DCC (459 mg, 2.2 mmol) was added under ice-cold conditions, after stirring the reaction mixture for about 5 min, pentafluorophenol (368 mg, 2 mmol) was added.[2] The reaction mixture was allowed to be stirred for 4 h at room temperature. After completion of the reaction (progress of the reaction monitored by TLC), filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The obtained crude product was purified through a silica gel (60-120 mesh) column by ethyl acetate and hexane mixture as eluent.

Boc-(*S,E*)-d^{2,3}γPhe-OPfp (2a) A mixture of Boc-(*S,E*)-d^{2,3}γPhe-OH (**1a,** 582 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, pentafluorophenol (368 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–10% EtOAc in hexane) to provide an active ester as a white solid in 94% yield.

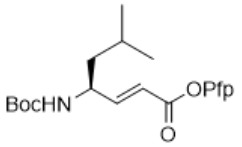
R_f = 0.85 (20% EtOAc in hexane). M.p. 102-104 °C. $[\alpha]_D^{25}$ = +6 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.31 (m, 2H), 7.31 – 7.26 (m, 1H), 7.26 – 7.21 (m, 1H), 7.19 (dd, *J* = 8.3, 1.5 Hz, 2H), 6.10 (dd, *J* = 15.7, 1.7 Hz, 1H), 4.73 (s, 1H), 4.61 (s, 1H), 2.96 (d, *J* = 6.9 Hz, 2H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.82, 155.09, 153.40, 142.56, 140.87, 140.11, 139.28, 138.34, 136.74, 135.98, 129.48, 128.89, 127.30, 117.83, 80.44, 52.74, 40.70, 28.40. ^{19}F NMR



(377 MHz, Chloroform-*d*) δ -152.50, -158.07, -162.40. HRMS (ESI) calculated for $C_{22}H_{20}F_5NO_4Na$ $[M+Na]^+$ *m/z* 480.1209 found 480.1206. IR: 1765 cm^{-1}.

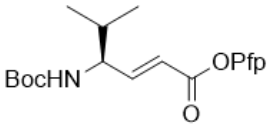
Boc-(*S*,*E*)-d^{2,3}γLeu-OPfp (2b) A mixture of Boc-(*S*,*E*)-d^{2,3}γLeu-OH (**1b,** 514 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, pentafluorophenol (368 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–10% EtOAc in hexane) to provide an active ester as a white solid in 90% yield.

R_f = 0.85 (20% EtOAc in hexane). M.p. 97-99 °C. $[\alpha]_D^{25}$ = -22 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.16 (dd, *J* = 15.6, 5.1 Hz, 1H), 6.16 (dd, *J* = 15.6, 1.6 Hz, 1H), 4.53 (d, *J* = 8.4 Hz, 1H), 4.46 (s, 1H), 1.77 – 1.72 (m, 1H), 1.46 (s, 9H), 1.44 (d, *J* = 7.1 Hz, 2H), 0.97 (dd, *J* = 6.6, 0.9 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.06, 155.24, 154.80, 142.60, 140.86, 140.06, 139.29, 138.34, 136.75, 117.07, 80.24, 50.28, 43.61, 28.47, 24.94, 22.95, 22.12. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -152.40, -158.20, -162.42. HRMS (ESI) calculated for $C_{19}H_{22}F_5NO_4Na$ $[M+Na]^+$ *m/z* 446.1366 found 446.1361. IR: 1765 cm^{-1}.



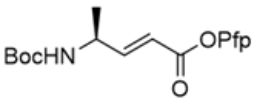
Boc-(*S*,*E*)-d^{2,3}γVal-OPfp (2c) A mixture of Boc-(*S*,*E*)-d^{2,3}γVal-OH (**1c,** 482 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, pentafluorophenol (368 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–10% EtOAc in hexane) to provide an active ester as a white solid in 91% yield.

R_f = 0.86 (20% EtOAc in hexane). M.p. 129-131 °C. $[\alpha]_D^{25}$ = -25 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (dd, *J* = 15.6, 5.1 Hz, 1H), 6.17 (dd, *J* = 15.6, 1.8 Hz, 1H), 4.64 (d, *J* = 9.2 Hz, 1H), 4.30 (s, 1H), 1.99 – 1.89 (m, 1H), 1.47 (s, 9H), 0.98 (dd, *J* = 12.5, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.92, 155.48, 153.38, 142.71, 141.09, 140.11, 139.33, 138.36, 136.77, 118.23, 80.27, 57.15, 32.37, 28.49, 19.14, 18.19. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -152.46, -158.15, -162.44. HRMS (ESI) calculated for $C_{18}H_{20}F_5NO_4Na$ $[M+Na]^+$ *m/z* 432.1209 found 432.1215. IR: 1759 cm^{-1}.



Boc-(*S,E*)-d^{2,3}γAla-OPfp (2d) A mixture of Boc-(*S,E*)-d^{2,3}γAla-OH (**1d**, 430 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, pentafluorophenol (368, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–10% hexane in EtOAc) to provide an active ester as a white solid in 92% yield.

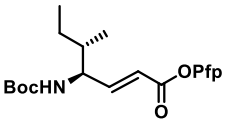
R_f = 0.80 (20% EtOAc in hexane). M.p. 91-93 °C. $[\alpha]_D^{25}$ = -29 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.19 (dd, *J* = 15.7, 4.8 Hz, 1H), 6.14 (dd, *J* = 15.7, 1.7 Hz, 1H), 4.63 (s, 1H), 4.51 (s, 1H), 1.46 (s, 9H), 1.34 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.04, 155.11, 155.04, 142.59, 140.86, 140.17, 139.28, 138.35, 136.75, 116.91, 80.30, 28.45, 20.12. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -152.50, -158.16, -162.46. HRMS (ESI) calculated for $C_{16}H_{16}F_5NO_4Na$ $[M+Na]^+$ *m/z* 404.0896 found 404.0889. IR: 1764 cm^{-1}.



Boc-(*S,E*)-d^{2,3}γIle-OPfp (2e) A mixture of Boc-(*S,E*)-d^{2,3}γIle-OH (**1e,** 514 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, pentafluorophenol (368 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for

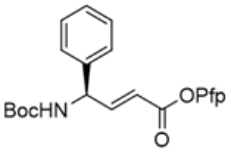
removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–10% EtOAc in hexane) to provide an active ester as a white solid in 90% yield.

R_f = 0.85 (20% EtOAc in hexane). M.p. 100-102 °C. $[\alpha]_D^{25}$ = -18.5 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.18 (dd, *J* = 15.7, 5.2 Hz, 1H), 6.17 (dd, *J* = 15.7, 1.8 Hz, 1H), 4.66 (d, *J* = 9.1 Hz, 1H), 4.39 (s, 1H), 1.73 – 1.66 (m, 1H), 1.54 – 1.48 (m, 1H), 1.47 (s, 9H), 1.19 (ddd, *J* = 11.8, 8.3, 6.2 Hz, 1H), 0.98 – 0.93 (m, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.90, 155.41, 153.20, 140.09, 118.29, 80.24, 56.24, 39.14, 28.48, 25.49, 15.59, 11.75. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -152.44, -158.17, -162.46. HRMS (ESI) calculated for $C_{19}H_{22}F_5NO_4Na$ $[M+Na]^+$ *m/z* 446.1366 found 446.1375. IR: 1764 cm^{-1}.



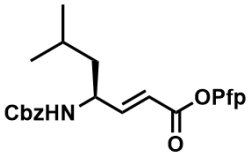
Boc-(*S*,*E*)-d^{2,3}γPhg-OPfp (2f) A mixture of Boc-(*S*,*E*)-d^{2,3}γPhg-OH (**1f,** 554 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, pentafluorophenol (368 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–10% EtOAc in hexane) to provide an active ester as a white solid in 88% yield.

R_f = 0.88 (20% EtOAc in hexane). M.p. 136-138 °C. $[\alpha]_D^{25}$ = +9 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.33 (m, 4H), 7.32 – 7.28 (m, 2H), 6.24 (dd, *J* = 15.6, 1.9 Hz, 1H), 5.54 (s, 1H), 4.95 (s, 1H), 1.47 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.87, 154.91, 152.76, 140.07, 139.32, 138.42, 136.73, 129.44, 128.75, 127.46, 125.13, 118.15, 80.76, 55.99, 28.47. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -152.34, -157.99, -162.34. HRMS (ESI) calculated for $C_{21}H_{18}F_5NO_4Na$ $[M+Na]^+$ *m/z* 466.1053 found 466.1053. IR: 1764 cm^{-1}.

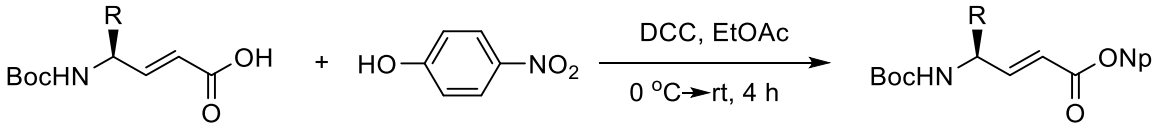


Cbz-(*S*,*E*)-d^{2,3}γLeu-OPfp (2g) A mixture of Cbz-(*S*,*E*)-d^{2,3}γLeu-OH (**1g,** 582 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, pentafluorophenol (368 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–15% EtOAc in hexane) to provide an active ester as a white solid in 91% yield.

R_f = 0.82 (20% EtOAc in hexane). $[\alpha]_D^{25}$ = -42 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.31 (m, 5H), 7.16 (dd, *J* = 15.6, 5.3 Hz, 1H), 6.17 (d, *J* = 15.6 Hz, 1H), 5.14 (s, 2H), 4.83 (d, *J* = 8.4 Hz, 1H), 4.53 (p, *J* = 7.2 Hz, 1H), 1.74 (m, 1H), 1.48 (t, *J* = 7.3 Hz, 2H), 0.97 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.95, 155.84, 154.04, 142.69, 140.87, 140.06, 139.28, 138.36, 136.75, 136.20, 128.74, 128.48, 128.32, 117.38, 67.35, 50.80, 43.46, 24.89, 22.91, 22.08. ^{19}F NMR (377 MHz, Chloroform-*d*) δ -152.39, -158.08, -162.40. HRMS (ESI) calculated for $C_{22}H_{20}F_5NO_4Na$ $[M+Na]^+$ *m/z* 480.1210 found 480.1209. IR: 1765 cm^{-1}.



B) General procedure for the synthesis of ONp esters of (*E*)-vinylogous amino acids (4a-4c).



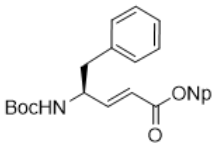
Scheme S2: Synthesis of active esters (**4a-4c)**.

BocHN-d^{2,3}γXxx-OH (2 mmol) was dissolved in 50 mL of EtOAc, to this solution DCC (454 mg, 2.2 mmol) was added under ice-cold conditions, after stirring the reaction mixture for about 5 min, *p*-nitrophenol (278 mg, 2 mmol) was added.[3] The reaction mixture was allowed to be stirred for 4 h at room temperature. After completion of the reaction (progress of the reaction monitored by TLC), filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated

under reduced pressure. The obtained crude product was purified through a silica gel (60-120 mesh) column by ethyl acetate and petroleum ethers mixture as eluent.

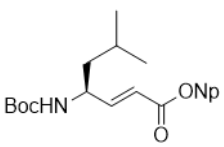
Boc-(*S*,*E*)-d^{2,3}γPhe-ONp (4a) A mixture of Boc-(*S*,*E*)-d^{2,3}γPhe-OH (**1a**, 582 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, *p*-nitrophenol (278 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–15% EtOAc in hexane) to provide an active ester as a white solid in 93% yield.

R_f = 0.86 (20% EtOAc in hexane). M.p. 143-146 °C. $[\alpha]_D^{25}$ = -2 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 – 8.25 (m, 2H), 7.36 – 7.27 (m, 5H), 7.22 – 7.14 (m, 3H), 6.07 (dd, *J* = 15.6, 1.7 Hz, 1H), 4.70 (bs, 1H), 4.61 (s, 1H), 2.96 (d, *J* = 6.8 Hz, 2H), 1.42 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.59, 155.51, 155.11, 151.78, 145.45, 136.13, 129.47, 128.89, 127.27, 125.34, 122.56, 119.66, 80.35, 52.75, 40.75, 28.44. HRMS (ESI) calculated for $C_{22}H_{24}N_2O_6Na$ $[M+Na]^+$ *m/z* 435.1531 found 435.1522. IR: 1743 cm^{-1}.



Boc-(*S*,*E*)-d^{2,3}γLeu-ONp (4b) A mixture of Boc-(*S*,*E*)-d^{2,3}γLeu-OH (**1b**, 514 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, *p*-nitrophenol (278 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–15% EtOAc in hexane) to provide an active ester as a white solid in 91% yield.

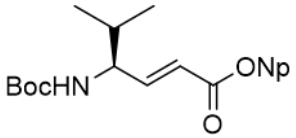
R_f = 0.81 (20% EtOAc in hexane). M.p. 67-69 °C. $[\alpha]_D^{25}$ = -40 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 9.2 Hz, 2H), 7.31 (d, *J* = 9.1 Hz, 2H), 7.09 (dd, *J* = 15.6, 5.4 Hz, 1H), 6.13 (dd, *J* = 15.6, 1.5 Hz, 1H), 4.55 (d, *J* = 8.2 Hz, 1H), 4.44 (t, *J* = 6.5, 1H), 1.73 (dq, *J* = 13.5, 6.8 Hz, 1H), 1.47 (s,



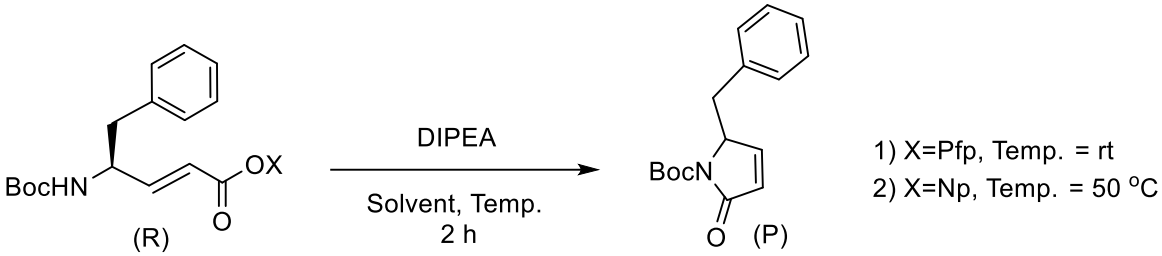
9H), 1.45 – 1.42 (m, 2H), 0.97 (dd, *J* = 6.6, 1.3 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.83, 155.34, 153.04, 145.45, 126.32, 125.35, 122.59, 118.96, 115.77, 80.31, 50.30, 43.67, 28.51, 24.94, 22.89, 22.22. HRMS (ESI) calculated for $C_{19}H_{26}N_2O_6Na$ $[M+Na]^+$ *m/z* 401.1688 found 401.1682. IR: 1740 cm^{-1}.

Boc-(*S*,*E*)-d^{2,3}γVal-ONp (4c) A mixture of Boc-(*S*,*E*)-d^{2,3}γVal-OH (**1c**, 482 mg, 2 mmol), DCC (454 mg, 2.2 mmol), EtOAc (50 mL) in 100 ml round bottom flask with a magnetic stirring bar was stirred vigorously for 5 min. at 0 ºC under N_2 atmosphere. Then, *p*-nitrophenol (278 mg, 2 mmol) was added to the above reaction mixture. The progress of the reaction is monitored by TLC, after the completion of the reaction, filtration was done by using a sintered funnel for removing urea (DCU) from the reaction mixture in form of residue. The filtrate part containing the product was concentrated under reduced pressure. The reaction mixture was purified by column chromatography (1–15% EtOAc in hexane) to provide an active ester as a white solid in 90% yield.

R_f = 0.80 (20% EtOAc in hexane). M.p. 102-104 °C. $[\alpha]_D^{25}$ = -44 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.28 (d, *J* = 9.2 Hz, 2H), 7.32 (d, *J* = 9.2 Hz, 2H), 7.12 (dd, *J* = 15.6, 5.4 Hz, 1H), 6.14 (dd, *J* = 15.7, 1.7 Hz, 1H), 4.65 (d, *J* = 9.0 Hz, 1H), 4.27 (s, 1H), 1.93 (dt, *J* = 12.8, 6.3 Hz, 1H), 1.47 (s, 9H), 0.98 (dd, *J* = 11.2, 6.8 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.68, 155.53, 151.64, 145.45, 126.36, 125.34, 122.59, 120.06, 115.92, 80.21, 57.16, 32.32, 28.50, 19.11, 18.23. HRMS (ESI) calculated for $C_{18}H_{24}N_2O_6Na$ $[M+Na]^+$ *m/z* 387.1531 found 387.1531. IR: 1740 cm^{-1}.



3. Reaction condition optimization

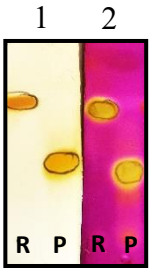


Scheme S3: Transformation of OPfp/ONp ester of α,β-unsaturated amino acid into α,β-unsaturated γ-lactam under various reaction conditions.

Table S1: List of solvents and reaction conditions used for lactamization.

Entry	Solvent	Base (eq.)	Yield[a] (%)
1	DMF	DiPEA (1)	35
2	Dry DMF	DiPEA (5)	88
3	EtOAc	DiPEA (5)	27
4	THF	DiPEA (5)	56
5	DCM	DiPEA (5)	42

[a]Isolated yield.



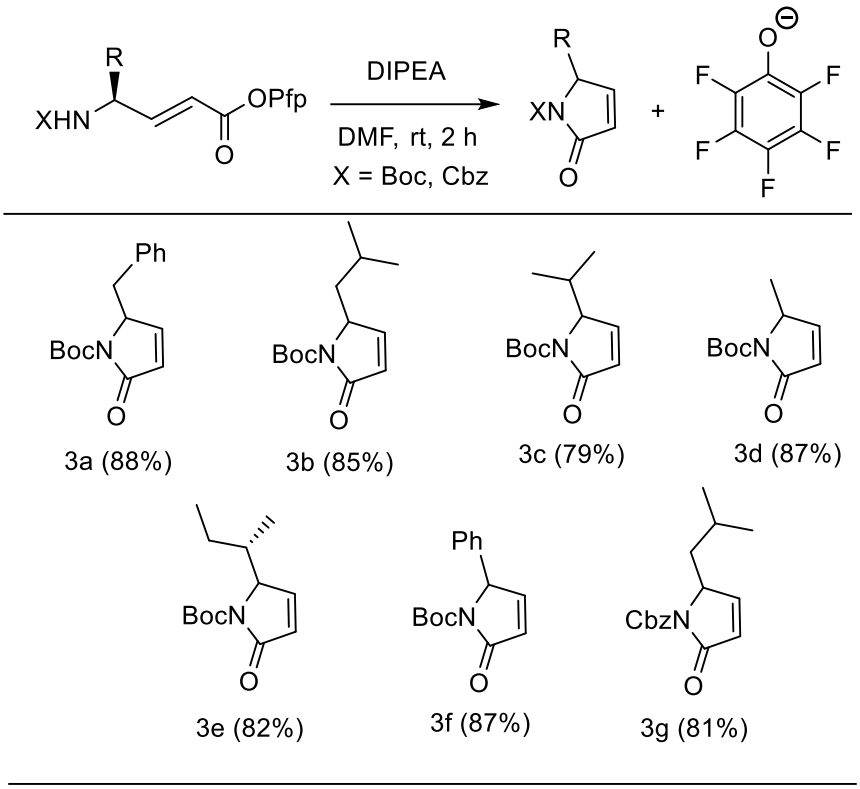
TLC in 20% EtOAc in Pet Ether.

1. Ninhydrin 2. KMnO4 staining.

Fig. S1. TLC analysis of lactamization reaction.

4. Transformation of active esters into α,β-unsaturated γ-lactam.

A) Synthesis of α,β-unsaturated γ-lactam from OPfp esters.



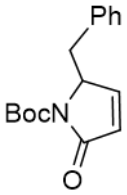
Scheme S4: Synthesis of *N*-protected-(*Z*)-α,β-unsaturated γ-lactam from OPfp esters of (*E*)-vinylogous amino acids.

Boc-d^{2,3}γXxx-OPfp (1 mmol) was dissolved in 10 mL of DMF, to this solution DIPEA (0.87 mL, 5 mmol) was added. The reaction mixture was stirred for 2 h at room temperature. After completion of the reaction (monitored by TLC), workup was done by diluting the reaction mixture with ethyl acetate (2 × 50 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3 × 40 mL) and brine solution (3 × 25 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The obtained crude product was purified through a silica gel (60-120 mesh) column by ethyl acetate and petroleum ethers mixture as eluent.

***tert*-butyl-2-benzyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3a)** Boc-d^{2,3}γPhe-OPfp (457 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of a round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the

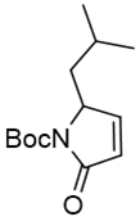
resulting mixture was stirred vigorously at room temperature under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3a** as a white solid in 88% yield.

R_f = 0.55 (20% EtOAc in hexane). M.p. 99-102 °C. $[\alpha]_D^{25}$ = +6 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 3H), 7.17 – 7.13 (m, 2H), 7.02 (dd, *J* = 6.1, 2.0 Hz, 1H), 6.02 (dd, *J* = 6.1, 1.6 Hz, 1H), 4.75 (ddt, *J* = 9.5, 3.8, 1.8 Hz, 1H), 3.55 (dd, *J* = 13.1, 3.9 Hz, 1H), 2.74 (dd, *J* = 13.1, 9.5 Hz, 1H), 1.63 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.20, 150.05, 149.64, 135.76, 129.51, 128.84, 127.30, 126.79, 83.34, 63.51, 38.74, 28.37. HRMS (ESI) calculated for $C_{16}H_{19}NO_3Na$ $[M+Na]^+$ *m/z* 296.1262, found 296.1262.



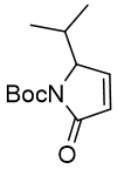
***tert*-butyl-2-isobutyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3b)** Boc-d^{2,3}γLeu-OPfp (423 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at room temperature under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3b** as an oily liquid with an 85% yield.

R_f = 0.60 (20% EtOAc in hexane). $[\alpha]_D^{25}$ = +2 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (dd, *J* = 6.1, 2.0 Hz, 1H), 6.08 (dd, *J* = 6.1, 1.6 Hz, 1H), 4.60 (ddt, *J* = 9.9, 3.7, 1.8 Hz, 1H), 1.67 (td, *J* = 4.5, 2.3 Hz, 1H), 1.56 (s, 9H), 1.47 – 1.41 (m, 2H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.43, 150.69, 149.45, 126.46, 83.01, 61.54, 41.27, 28.28, 25.29, 24.05, 22.29. HRMS (ESI) calculated for $C_{13}H_{21}NO_3Na$ $[M+Na]^+$ *m/z* 262.1418, found 262.1418.



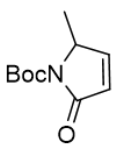
***tert*-butyl-2-isopropyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3c)** Boc-d^{2,3}γVal-OPfp (409 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at room temperature under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3c** as an oily liquid in 79% yield.

R_f = 0.58 (20% EtOAc in hexane). $[\alpha]_D^{25}$ = +4 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.12 (dd, *J* = 6.2, 2.0 Hz, 1H), 6.14 (dd, *J* = 6.2, 1.7 Hz, 1H), 4.55 (dt, *J* = 3.9, 1.8 Hz, 1H), 2.59 (qt, *J* = 6.9, 3.5 Hz, 1H), 1.54 (s, 9H), 1.09 (d, *J* = 7.1 Hz, 3H), 0.66 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.70, 149.73, 147.94, 127.92, 83.00, 67.41, 28.99, 28.23, 19.63, 14.98. HRMS (ESI) calculated for $C_{12}H_{19}NO_3Na$ $[M+Na]^+$ *m/z* 248.1262, found 248.1261.



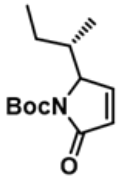
***tert*-butyl-2-methyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3d)** Boc-d^{2,3}γAla-OPfp (381 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at room temperature under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3d** as an oily liquid in 87% yield.

R_f = 0.52 (20% EtOAc in hexane). $[\alpha]_D^{25}$ = +6 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.09 (dd, *J* = 6.1, 2.0 Hz, 1H), 6.06 (dd, *J* = 6.1, 1.7 Hz, 1H), 4.61 (dt, *J* = 6.7, 1.8 Hz, 1H), 1.56 (s, 9H), 1.43 (d, *J* = 6.7 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.30, 151.90, 149.53, 126.07, 83.04, 58.53, 28.28, 18.30. HRMS (ESI) calculated for $C_{11}H_{18}NO_3Na$ $[M+Na]^+$ *m/z* 220.0949, found 220.0955.



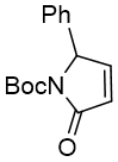
***tert*-butyl-2-((*S*)-sec-butyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3e)** Boc-d^{2,3}γIle-OPfp (423 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at room temperature under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3e** as an oily liquid in 82% yield.

R_f = 0.60 (20% EtOAc in hexane). $[\alpha]_D^{25}$ = -6 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*, mixture of two isomers in ratio of 1:1) δ 7.12 (dd, *J* = 6.2, 2.0 Hz, 1H), 7.07 (dd, *J* = 6.1, 2.1 Hz, 1H), 6.12 (dd, *J* = 6.2, 1.7 Hz, 1H), 6.09 (dd, *J* = 6.2, 1.8 Hz, 1H), 4.64 (dt, *J* = 4.0, 1.9 Hz, 1H), 4.55 (dt, *J* = 3.9, 1.9 Hz, 1H), 2.30 (dddt, *J* = 20.7, 10.5, 7.0, 3.2 Hz, 2H), 1.53 (s, 18H), 1.44 – 1.23 (m, 4H), 1.06 (d, *J* = 7.1 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.82 (t, *J* = 7.4 Hz, 3H), 0.61 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.79, 169.77, 149.66, 149.57, 148.31, 148.12, 127.86, 127.40, 82.94, 67.60, 66.10, 35.87, 35.81, 28.22, 28.20, 27.31, 22.59, 16.59, 12.66, 12.37, 12.26. HRMS (ESI) calculated for $C_{13}H_{21}NO_3Na$ $[M+Na]^+$ *m/z* 262.1418, found 262.1418.



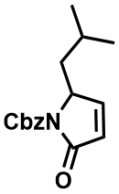
***tert*-butyl-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3f)** Boc-d^{2,3}γPhg-OPfp (443 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at room temperature under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3f** as a white solid with an 87% yield.

R_f = 0.59 (20% EtOAc in hexane). M.p. 102-104 °C. $[\alpha]_D^{25}$ = 0 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.31 (m, 3H), 7.21 – 7.18 (m, 2H), 7.06 (dd, *J* = 6.0, 2.2 Hz, 1H), 6.16 (dd, *J* = 6.0, 1.7 Hz, 1H), 5.53 (t, *J* = 2.0 Hz, 1H), 1.27 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.00, 150.31, 148.78, 135.85, 129.00, 128.62, 126.62, 125.44, 83.09, 66.39, 27.89. HRMS (ESI) calculated for $C_{15}H_{17}NO_3Na$ $[M+Na]^+$ *m/z* 282.1105, found 282.1103.

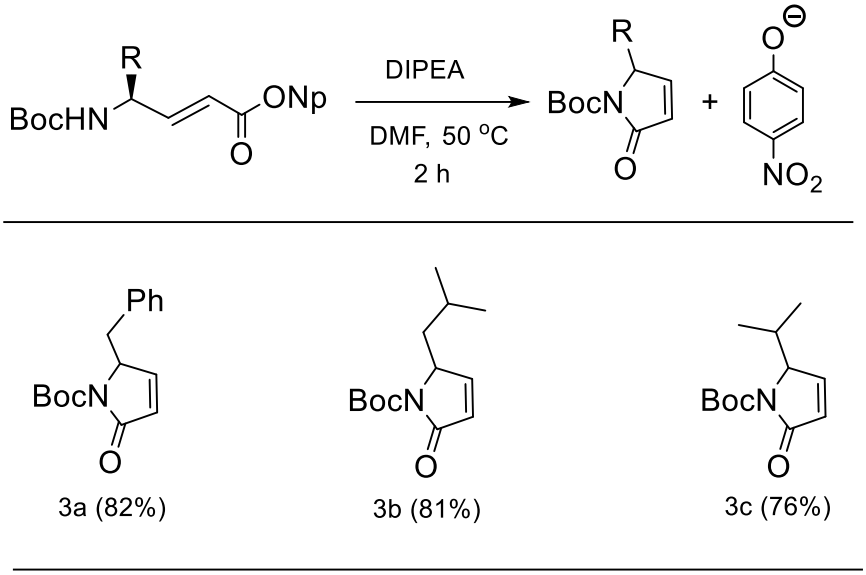


benzyl 2-isobutyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3g) Cbz-d^{2,3}γLeu-OPfp (457 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at room temperature under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3g** as an oily liquid with an 81% yield.

R_f = 0.55 (30% EtOAc in hexane). $[\alpha]_D^{25}$ = +4 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.42 (m, 2H), 7.39 – 7.32 (m, 3H), 7.27 (dd, *J* = 6.1, 2.0 Hz 1H), 6.10 (dd, *J* = 6.1, 1.7 Hz, 1H), 5.36 (d, *J* = 12.3 Hz, 1H), 5.27 (d, *J* = 12.3 Hz, 1H), 4.66 (ddd, *J* = 7.5, 3.8, 1.9 Hz, 1H), 2.0 – 1.94 (m, 1H), 1.69 – 1.62 (m, 1H), 1.45 – 1.38 (m, 1H), 0.93 (d, *J* = 6.6 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 168.92, 151.42, 150.93, 135.42, 128.71, 128.52, 128.34, 126.17, 68.07, 61.60, 40.96, 25.24, 23.85, 22.14. HRMS (ESI) calculated for $C_{16}H_{20}NO_3$ $[M+H]^+$ *m/z* 274.1443, found 274.1439.



B) Synthesis of α,β-unsaturated gamma lactam from ONp esters.



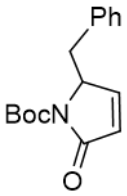
Scheme S5: Synthesis of *N*-Boc-(*Z*)-α,β-unsaturated γ-lactam from ONp esters of (*E*)-vinylogous amino acids.

BocHN-d^{2,3}γXxx-ONp (1 mmol) was dissolved in 10 mL of DMF, to this solution DIPEA (0.87 mL, 5 mmol) was added. The reaction mixture was stirred 2 h at 50 ºC. After completion of the reaction (monitored by TLC), workup was done by diluting the reaction mixture with ethyl acetate (50 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The obtained crude product was purified through a silica gel (60-120 mesh) column by ethyl acetate and petroleum ethers mixture as eluent.

***tert*-butyl-2-benzyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3a)** Boc-d^{2,3}γPhe-ONp (428 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of a round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at 50 ºC under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The

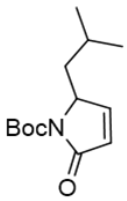
reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3a** as an oily liquid in 82% yield.

R_f = 0.59 (20% EtOAc in hexane). M.p. 99-102 °C. $[\alpha]_D^{25}$ = +6 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 3H), 7.17 – 7.13 (m, 2H), 7.02 (dd, *J* = 6.1, 2.0 Hz, 1H), 6.02 (dd, *J* = 6.1, 1.6 Hz, 1H), 4.75 (ddt, *J* = 9.5, 3.8, 1.8 Hz, 1H), 3.55 (dd, *J* = 13.1, 3.9 Hz, 1H), 2.74 (dd, *J* = 13.1, 9.5 Hz, 1H), 1.63 (s, 9H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.20, 150.05, 149.64, 135.76, 129.51, 128.84, 127.30, 126.79, 83.34, 63.51, 38.74, 28.37. HRMS (ESI) calculated for $C_{16}H_{19}NO_3Na$ $[M+Na]^+$ *m/z* 296.1262, found 296.1262.



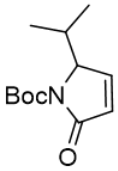
***tert*-butyl-2-isobutyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3b)** Boc-d^{2,3}γLeu-ONp (394 mg, 2 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (1.74 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at 50 ºC under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3b** as an oily liquid in 81% yield.

R_f = 0.60 (20% EtOAc in hexane). $[\alpha]_D^{25}$ = +2 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (dd, *J* = 6.1, 2.0 Hz, 1H), 6.08 (dd, *J* = 6.1, 1.6 Hz, 1H), 4.59 (ddt, *J* = 9.9, 3.7, 1.8 Hz, 1H), 1.69 (ddd, *J* = 9.3, 4.7, 2.5 Hz, 1H), 1.55 (s, 9H), 1.47 – 1.40 (m, 2H), 0.99 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.43, 150.69, 149.45, 126.46, 83.01, 61.54, 41.27, 28.28, 25.29, 24.05, 22.29. HRMS (ESI) calculated for $C_{13}H_{21}NO_3Na$ $[M+Na]^+$ *m/z* 262.1418, found 262.1418.



***tert*-butyl-2-isopropyl-5-oxo-2,5-dihydro-1*H*-pyrrole-1-carboxylate (3c)** Boc-d^{2,3}γVal-ONp (380 mg, 1 mmol) was dissolved in 10 mL of dry DMF, in a 25 ml of round bottom flask with a magnetic stirring bar. Then DIPEA (0.87 mL, 5 mmol) was added to the above solution, the resulting mixture was stirred vigorously at 50 ºC under an N_2 atmosphere for 2 h. The progress of the reaction is monitored by TLC, after completion of the reaction workup was done by diluting the reaction mixture with ethyl acetate (100 mL), followed by successive washings with 10% HCl (3 × 40 mL), 10% Na_2CO_3 (3× 40 mL) and brine solution (2 × 30 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The reaction mixture was purified by column chromatography (5–25% EtOAc in hexane) to provide a **3c** as an oily liquid with a 76% yield.

R_f = 0.58 (20% EtOAc in hexane). $[\alpha]_D^{25}$ = +4 (*c* 0.1, MeOH). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.12 (dd, *J* = 6.2, 2.0 Hz, 1H), 6.14 (dd, *J* = 6.2, 1.7 Hz, 1H), 4.55 (dt, *J* = 3.9, 1.8 Hz, 1H), 2.59 (qt, *J* = 6.9, 3.5 Hz, 1H), 1.54 (s, 9H), 1.09 (d, *J* = 7.1 Hz, 3H), 0.66 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 169.70, 149.73, 147.94, 127.92, 83.00, 67.41, 28.99, 28.23, 19.63, 14.98. HRMS (ESI) calculated for $C_{12}H_{19}NO_3Na$ $[M+Na]^+$ *m/z* 248.1262, found 248.1261.



5. Determining the kinetic parameters of lactamization reaction by UV experiment.

The samples of various concentrations are prepared by dissolving (**4a-4c**) in DMF solvent. All spectra were recorded in presence of 5 eq. of DIPEA. The molar extinction coefficient (ε) for the 4-nitrophenolate ion was obtained 4110 M^{-1} cm^{-1} by plotting the absorbance against concentration, under the reaction condition. As shown in Fig. S2, the 4-nitrophenolate ion uniquely absorbs at 431 nm, which was used to spectrophotometrically monitor the formation of the product, as the 4-nitrophenolate ion releases from the substrate as the reaction proceeds shown in Scheme 5. To measure the kinetic parameter of the lactamization reaction, we use (29.42 μM solutions of **4a**/**4b**/**4c** and 5 eq. of DIPEA), where the first-order equation reduces to $\ln[A]_t = \ln[A]_0 - kt$ ($[A]_t$: concentration of a reactant at time t; $[A]_0$: initial concentration of reactant; *k*: rate constant). The standard curve was first generated to determine the product concentration at a given time from the observed absorbance at 431 nm. The observed absorbance was used to determine the value of $[A]_t$. Plotting $\ln[A]_t$ against time yielded the rate constant, using linear fit method. All the kinetic experiments were performed at 50 ºC.

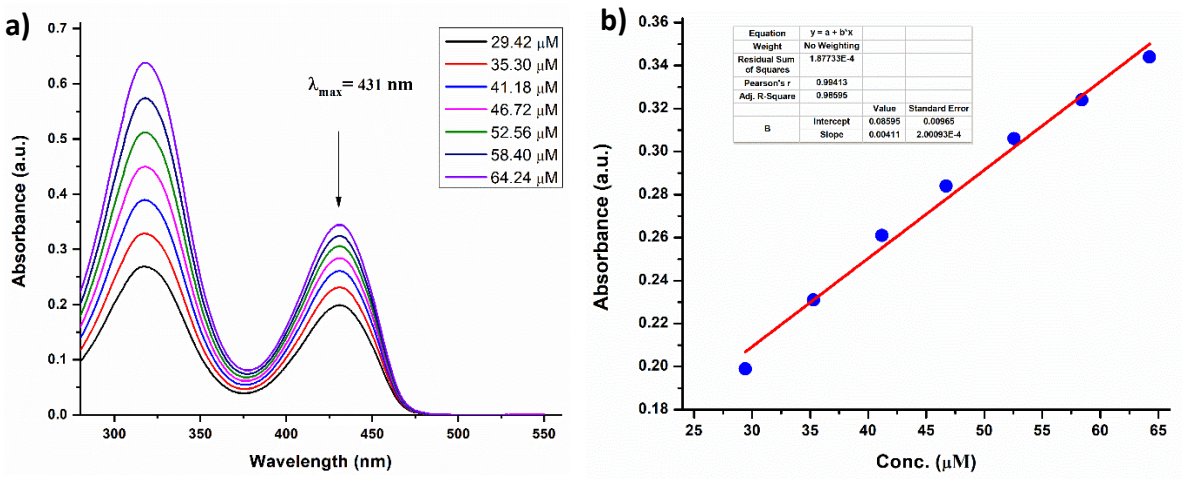


Fig. S2: **a)** λ_{max} 431 nm of 4-nitrophenolate ion under reaction conditions. **b)** Plot of absorbance against concentration.

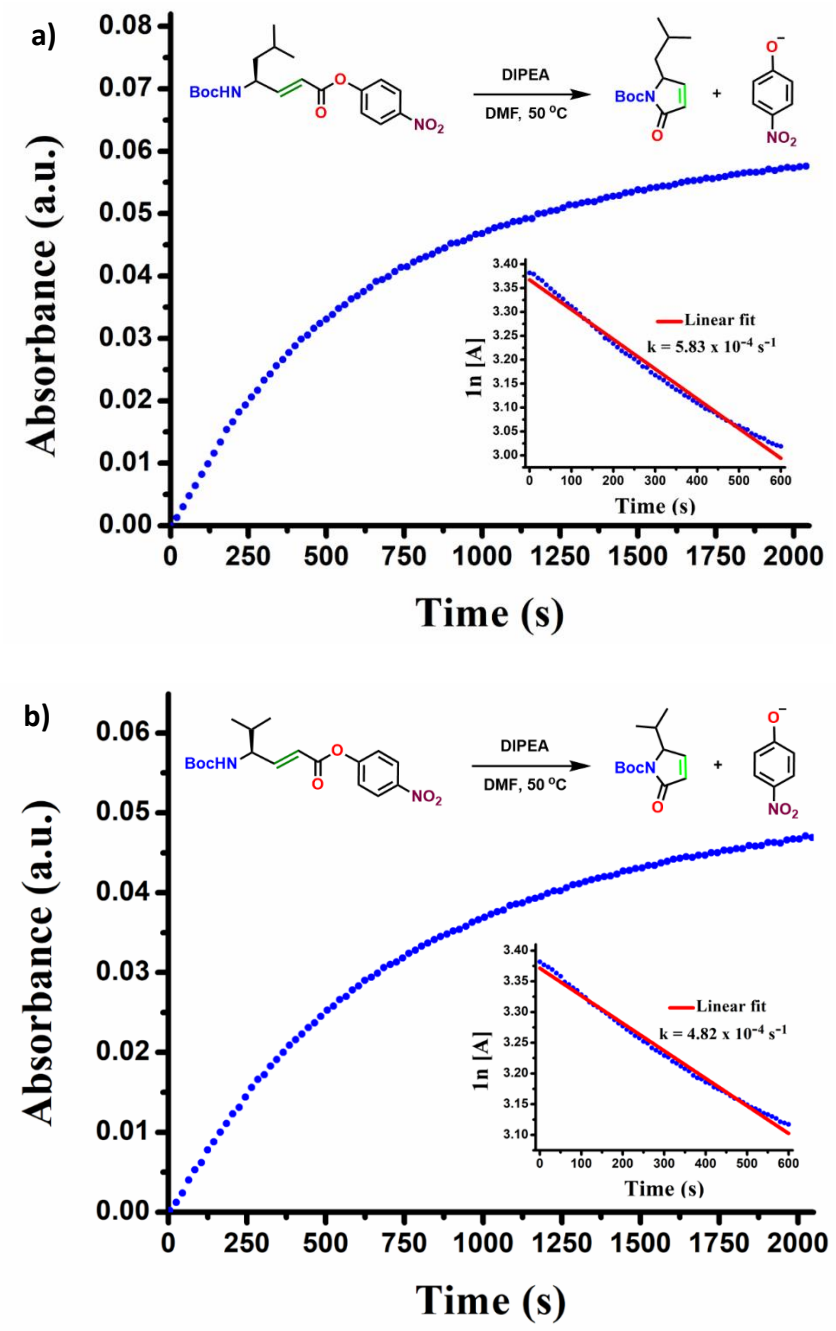


Fig. S3: Kinetic analysis for the transformation of ONp esters into the corresponding α,β-unsaturated γ-lactams (a) **4b** to **3b** and (b) **4c** to **3c**.

6. Determination of the extent of activation by ^{1}H NMR and IR Experiment

The comparison of ^{1}H NMR spectra of Boc-dg-Leu-OPfp (**2b**), Boc-dg-Leu-ONp (**4b**), and Boc-dg-Leu-OH (**1b**) shows that a significant increase in chemical shift of protons H1 and H2 in active esters due to the strong electron-withdrawing nature of -ONp and -OPfp groups shown in Fig. S4. The difference in chemical shifts shown in **Table S2** is more for H2 protons compared to H1 protons for both the active esters, this is because H2 is present near the electron-withdrawing groups.

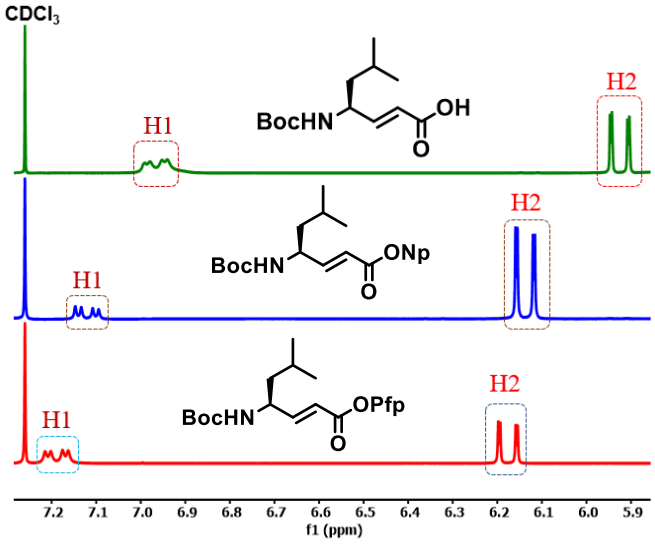
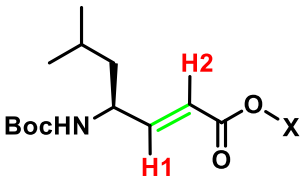


Fig. S4: Combined Partial ^{1}H NMR spectra of OPfp, ONp esters of α,β-unsaturated γ-amino acid and α,β-unsaturated γ-amino acid.

Table S2: Comparison of chemical shifts of active esters with α,β-unsaturated γ-amino acid.

Active Ester	$\Delta\delta = (\delta_{\text{active ester}} - \delta_{\text{acid}})$ in ppm	
	H1	H2
4b	0.15	0.21
2b	0.22	0.25



(Structure of Active Ester)

The active esters can be arranged for their activating properties in approximately the order: ONp < OPfp. One of the pieces of evidence of this reactivity order was obtained from the comparison IR stretching frequency of the active ester Boc-dg-Phe-OPfp (**2a**) 1766 cm^{-1} and Boc-dg-Phe-ONp (**4a**) 1743 cm^{-1} with their parent molecule Boc-dg-Phe-OH (**1a**) 1699 cm^{-1} shown in Fig. S5. It has been observed that Boc-dg-Phe-OPfp (**2a**) undergoes lactamization reaction at room temperature due to the more activating nature of the -OPfp group confirmed by the IR stretching frequency. However, Boc-dg-Phe-ONp (**4a**) undergoes the same reaction at elevated temperature (50 ºC) due to the less activating nature of the -ONp group confirmed by the IR stretching frequency.

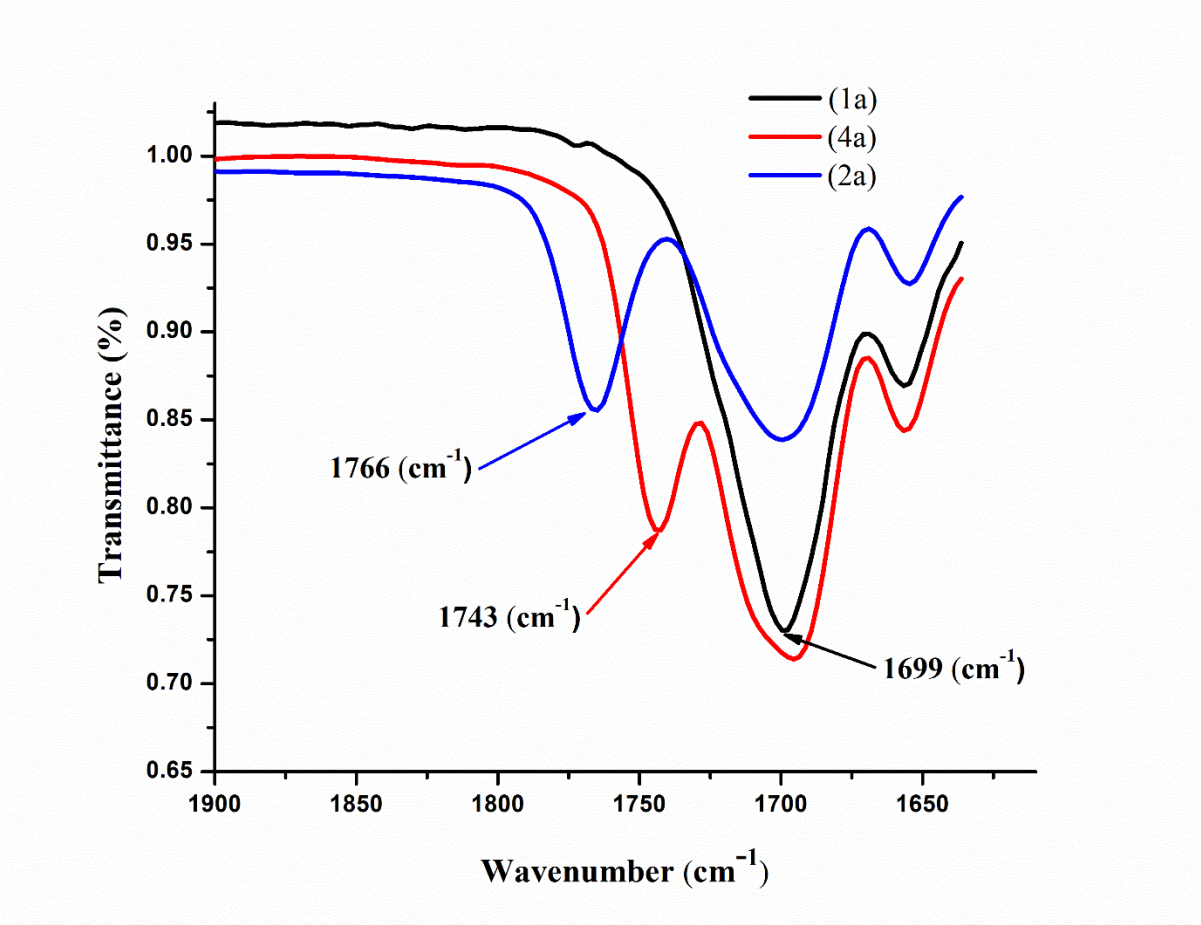


Fig. S5: Combined Partial IR spectra of active esters and α,β-unsaturated γ-amino acid.

7. ORTEP Diagrams

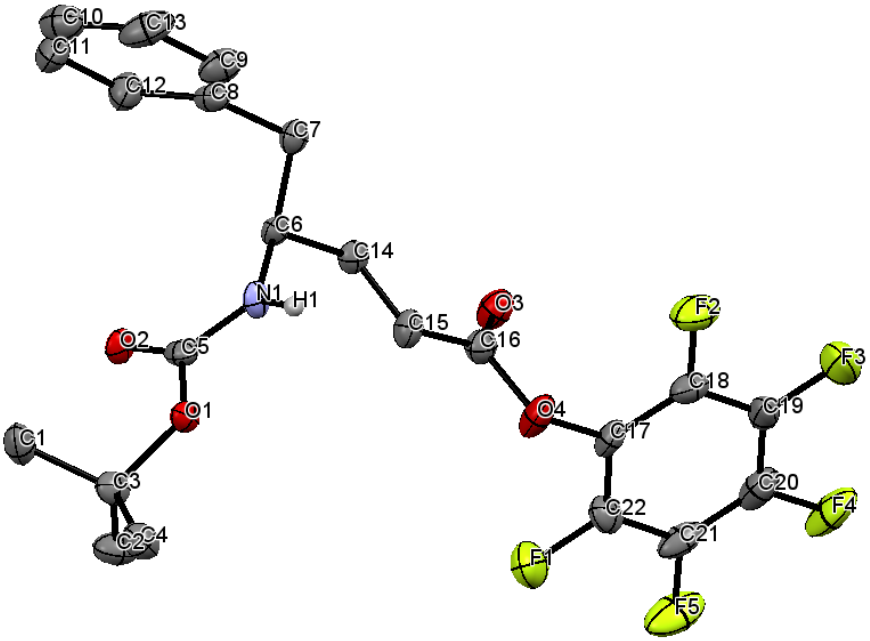


Fig. S6: ORTEP diagram of compound **2a.** H-atoms are omitted for clarity. Ellipsoids are drawn at 50% probability (CCDC no 2212219).

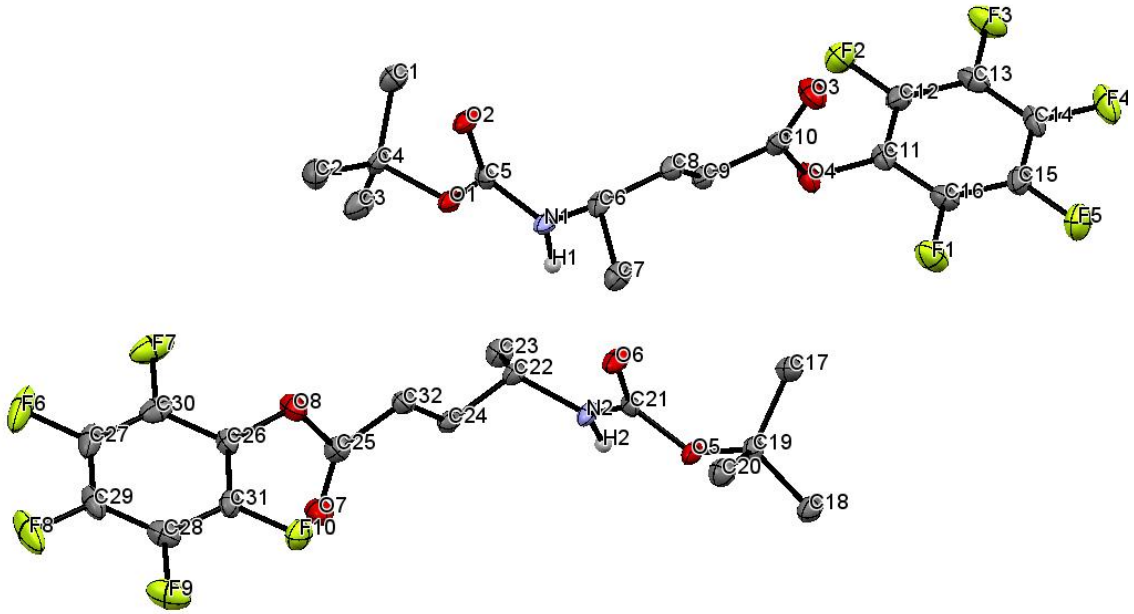


Fig. S7: ORTEP diagram of compound **2d.** H-atoms are omitted for clarity. Ellipsoids are drawn at 50% probability (CCDC no 2212205).

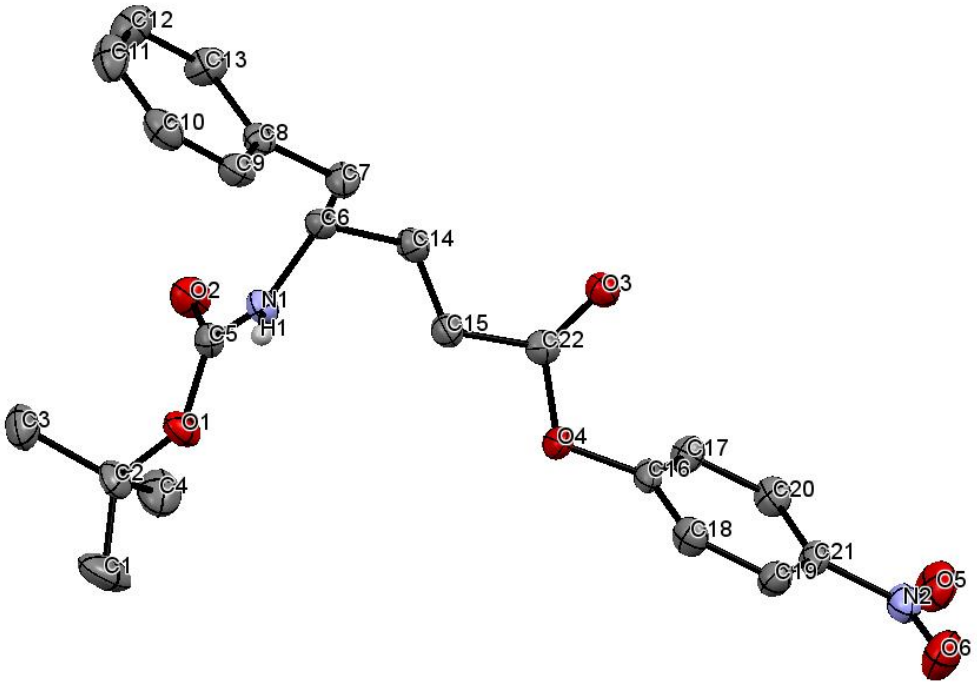


Fig. S8: ORTEP diagram of compound **4a.** H-atoms are omitted for clarity. Ellipsoids are drawn at 50% probability (CCDC no 2212221).

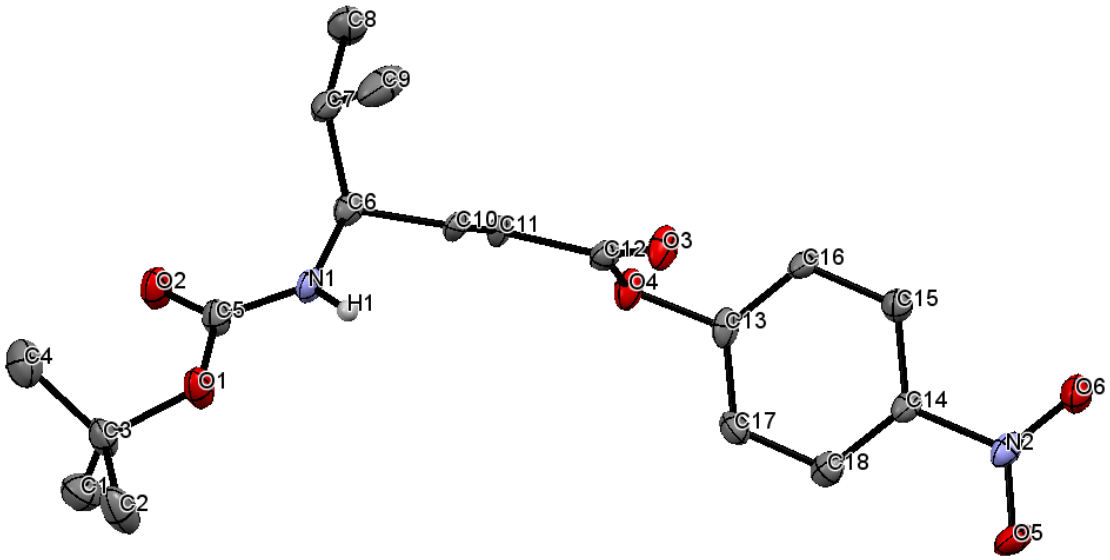


Fig. S9: ORTEP diagram of compound **4c.** H-atoms are omitted for clarity. Ellipsoids are drawn at 50% probability (CCDC no 2212220).

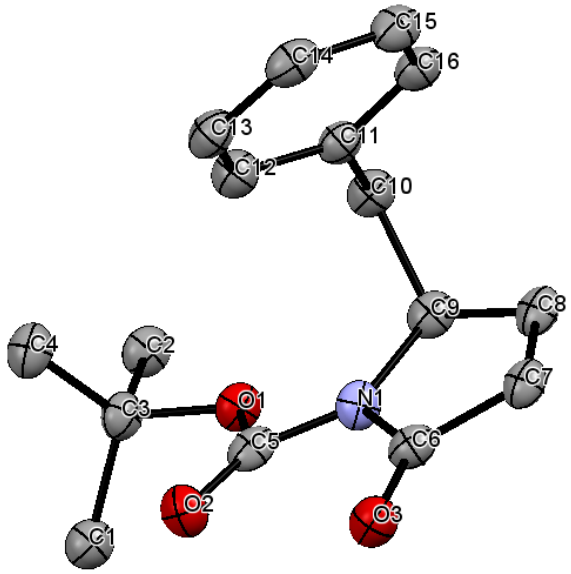


Fig. S10: ORTEP diagram of compound **3a.** H-atoms are omitted for clarity. Ellipsoids are drawn at 50% probability (CCDC no 2225785).

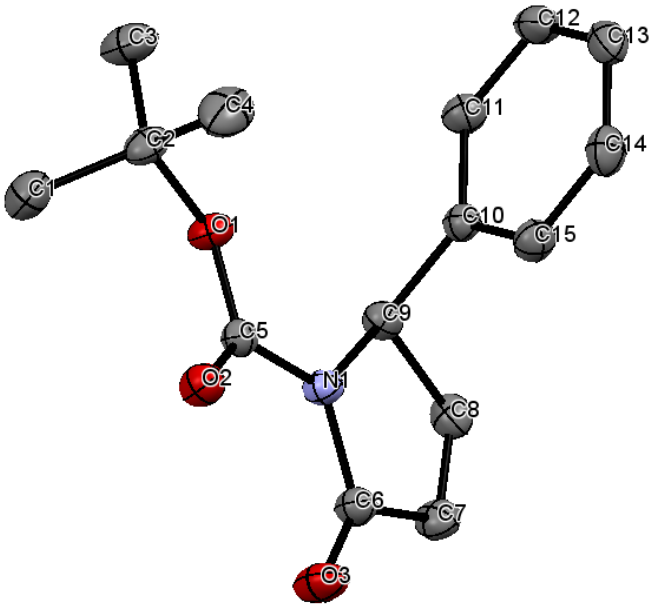


Fig. S11: ORTEP diagram of compound **3f.** H-atoms are omitted for clarity. Ellipsoids are drawn at 50% probability (CCDC no 2212223).

Crystallographic Information:

Boc-dg-Phe-OPfp 2a: Crystals of **2a** were grown by slow evaporation from a solution of aqueous methanol at room temperature. A single crystal (0.16 × 0.05 × 0.12 mm) was mounted on a loop with a small amount of paraffin oil. The X-ray data were collected at 120K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 56.896), for a total of 15970 independent reflections. Space group P 21, a = 10.469 (6), b = 9.455 (6), c = 11.567 (6), α = 90, β = 110.556 (14), γ = 90, V = 1072.1(10) $Å^3$, Monoclinic, Z = 2 for chemical formula C22 H20 F5 N O4, with one molecule in asymmetric unit; ρ calcd = 1.417 gcm^{-3}, μ = 0.125 mm^{-1}, F (000) = 472, R_{int}= 0.1422. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0687 (wR2 = 0.1476) 4988 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 293 variables, S = 0.893.

Boc-dg-Ala-OPfp 2d: Crystals of **2d** were grown by slow evaporation from a solution of aqueous methanol at room temperature. A single crystal (0.14 × 0.1 × 0.06 mm) was mounted on a loop with a small amount of paraffin oil. The X-ray data were collected at 150K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 49.654), for a total of 16604 independent reflections. Space group P 1, a = 6.2002 (9), b = 9.3687 (12), c = 15.799 (2), α = 101.093 (4), β = 99.079 (4), γ = 105.428 (4), V = 846.7 (2) $Å^3$, Triclinic, Z = 2 for chemical formula C16 H16 F5 N O4, with two molecules in asymmetric unit; ρ calcd = 1.496 gcm^{-3}, μ = 0.142 mm^{-1}, F (000) = 392, R_{int}= 0.0407. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0326 (wR2 = 0.0631) 5740 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 478 variables, S = 1.023.

Boc-dg-Phe-ONp 4a: Crystals of **4a** were grown by slow evaporation from a solution of aqueous methanol at room temperature. A single crystal (0.15 × 0.07 × 0.06 mm) was mounted on a loop with a small amount of paraffin oil. The X-ray data were collected at 150K temperature on a Bruker APEX(II) DUO CCD diffractometer using Cu K_α radiation (λ = 1.54178 Å), ω-scans (2θ = 66.768), for a total of 26912 independent reflections. Space group P 21 21 21, a = 6.1910 (7), b = 14.7184 (16), c = 22.774 (3), α = 90, β = 90, γ = 90, V = 2075.2 (4) $Å^3$, Orthorhombic, Z = 4 for chemical formula C22 H24 N2 O6, with one molecule in

asymmetric unit; ρ calcd = 1.32 gcm^{-3}, μ = 0.803 mm^{-1}, F (000) = 872, R_{int}= 0.1486. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0408 (wR2 = 0.0922) 3681 observed reflections ($F_0 \geq 4\sigma$ (|F_0|)) and 275 variables, S = 1.037.

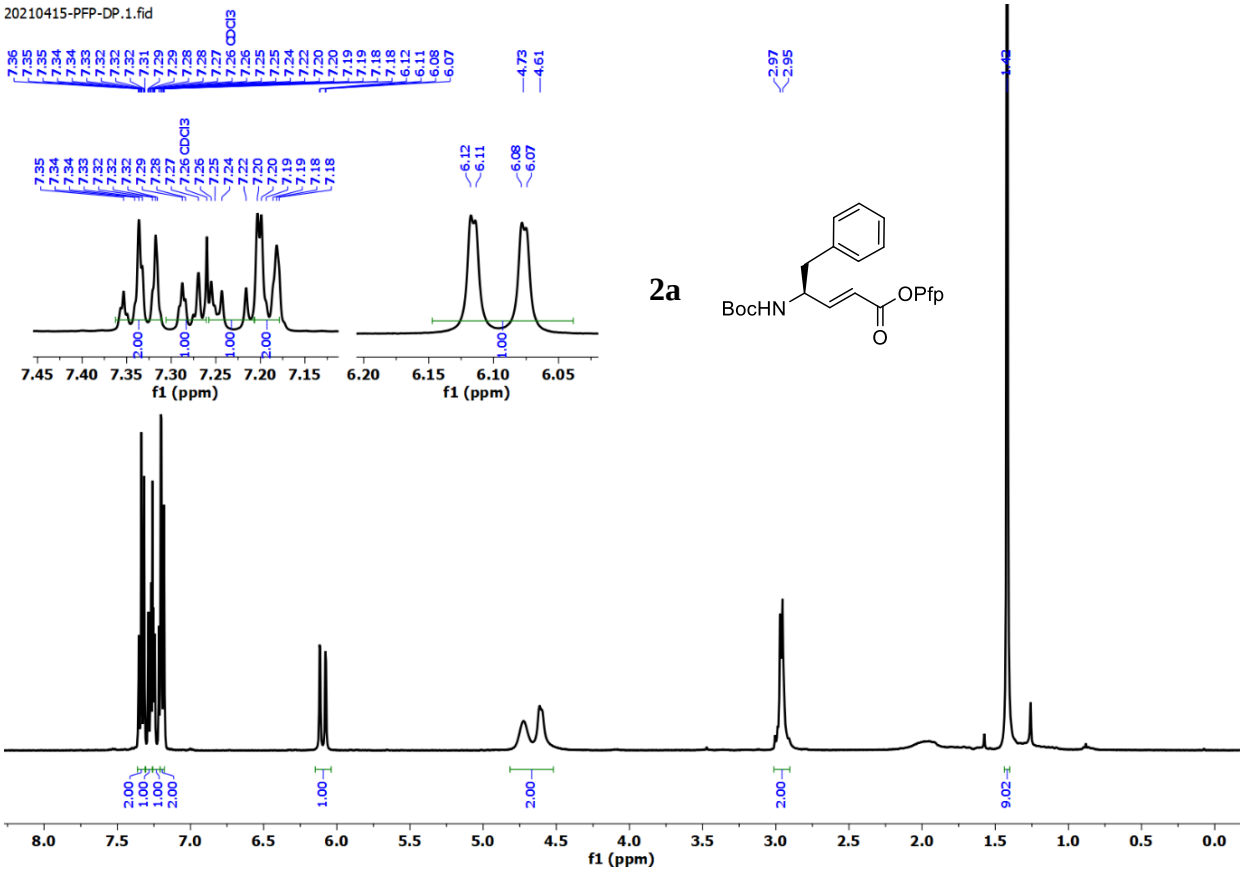
Boc-dg-Val-ONp 4c: Crystals of **4c** were grown by slow evaporation from a solution of aqueous methanol at room temperature. A single crystal (0.12 × 0.07 × 0.05 mm) was mounted on a loop with a small amount of paraffin oil. The X-ray data were collected at 150K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 57.602), for a total of 26912 independent reflections. Space group P 21, a = 6.216 (3), b = 5.362 (3), c = 28.415 (13), α = 90, β = 95.424(12), γ = 90, V = 942.8(8) Å^3, Monoclinic, Z = 2 for chemical formula C18 H24 N2 O6, with one molecule in asymmetric unit; ρ calcd = 1.284 gcm^{-3}, μ = 0.097 mm^{-1}, F (000) = 388, R_{int}= 0.1842. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0899 (wR2 = 0.2110) 4704 observed reflections ($F_0 \geq 4\sigma$ (|F_0|)) and 241 variables, S = 1.085.

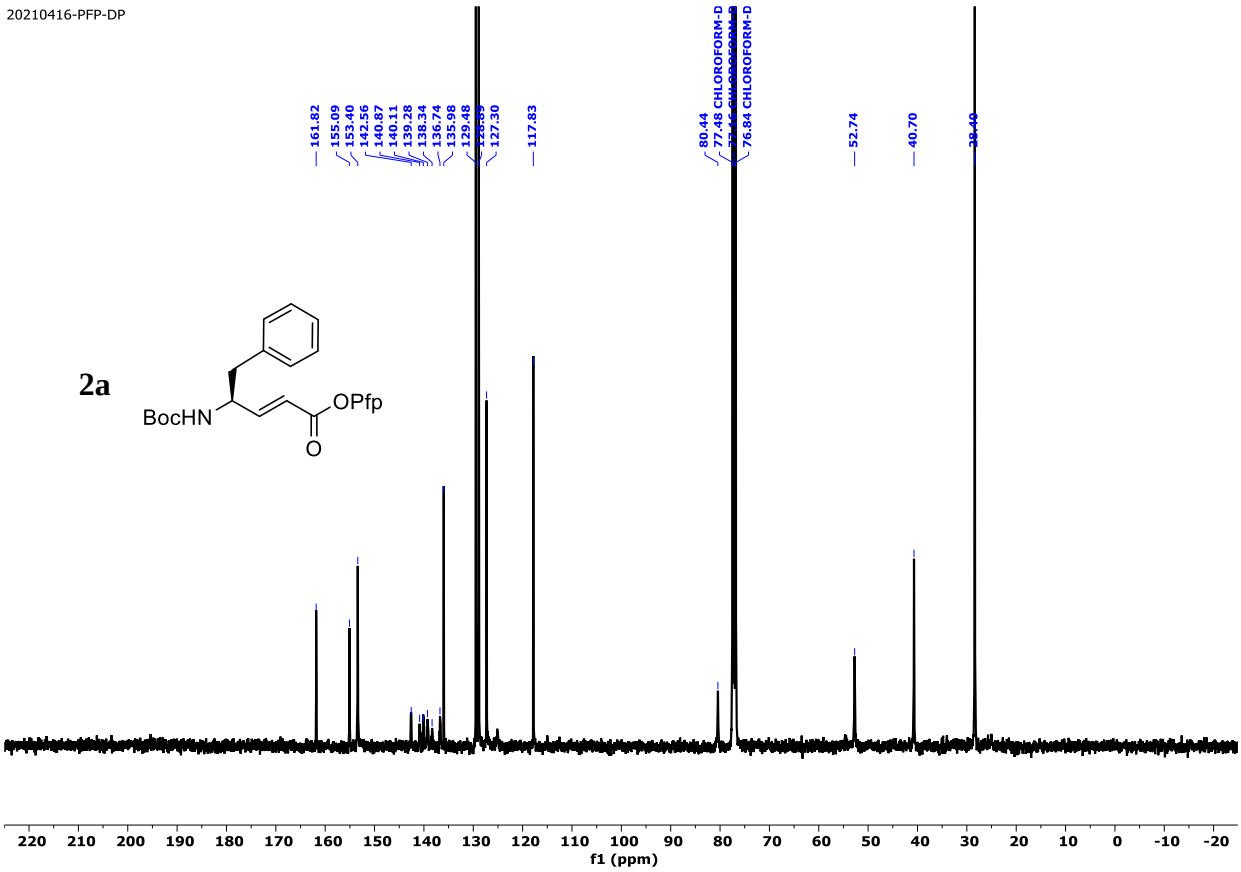
***tert*-butyl 2-benzyl-5-oxo-2,5-dihydro-1H-pyrrole-1-carboxylate 3a:** Crystals of **3a** were grown by slow evaporation from a solution of ethyl acetate-pet ether at room temperature. A single crystal (0.11 × 0.6 × 0.08 mm) was mounted on a loop with a small amount of paraffin oil. The X-ray data were collected at 100K temperature on a Bruker APEX(II) DUO CCD diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 56.76), for a total of 20509 independent reflections. Space group P 21/n, a = 6.146 (3), b = 14.129 (7), c = 16.674 (8), α = 90, β = 99.499 (14), γ = 90, V = 1427.9 (12) Å^3, Monoclinic, Z = 4 for chemical formula C16 H19 N O3, with one molecule in the asymmetric unit; ρ calcd = 1.271 gcm^{-3}, μ = 0.088 mm^{-1}, F (000) = 5, R_{int}= 0.0525. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0723 (wR2 = 0.1772) 3576 observed reflections ($F_0 \geq 4\sigma$ (|F_0|)) and 185 variables, S = 0.790.

***tert*-butyl-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-1-carboxylate 3f:** Crystals of **3f** were grown by slow evaporation from a solution of ethyl acetate-pet ether at room temperature. A single crystal (0.13 × 0.8 × 0.05 mm) was mounted on a loop with a small amount of paraffin oil. The X-ray data were collected at 150K temperature on a Bruker APEX(II) DUO CCD

diffractometer using Mo K_α radiation (λ = 0.71073 Å), ω-scans (2θ = 56.76), for a total of 20800 independent reflections. Space group P 21/c, a = 6.2063 (11), b = 13.323 (3), c = 16.945 (3), α = 90, β = 91.668 (6), γ = 90, V = 1400.6 (4) $Å^3$, Monoclinic, Z = 4 for chemical formula C15 H17 N O3, with one molecule in the asymmetric unit; ρ calcd = 1.23 gcm^{-3}, μ = 0.086 mm^{-1}, F (000) = 552, R_{int}= 0.0525. The structure was obtained by direct methods using SHELXS-97. The final R value was 0.0416 (wR2 = 0.0915) 3509 observed reflections ($F_0 \geq 4\sigma$ ($|F_0|$)) and 176 variables, S = 1.022.

8. ^{1}H, ^{13}C, and ^{19}F NMR of all compounds

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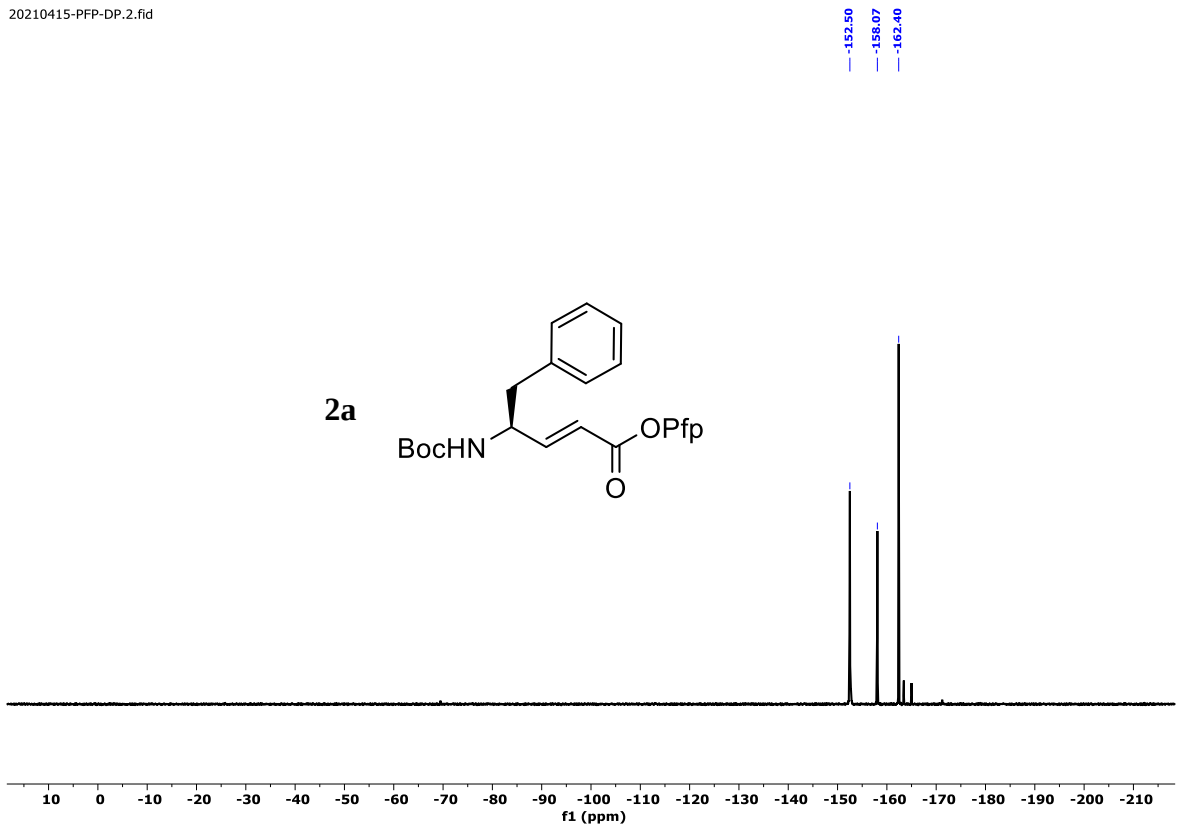
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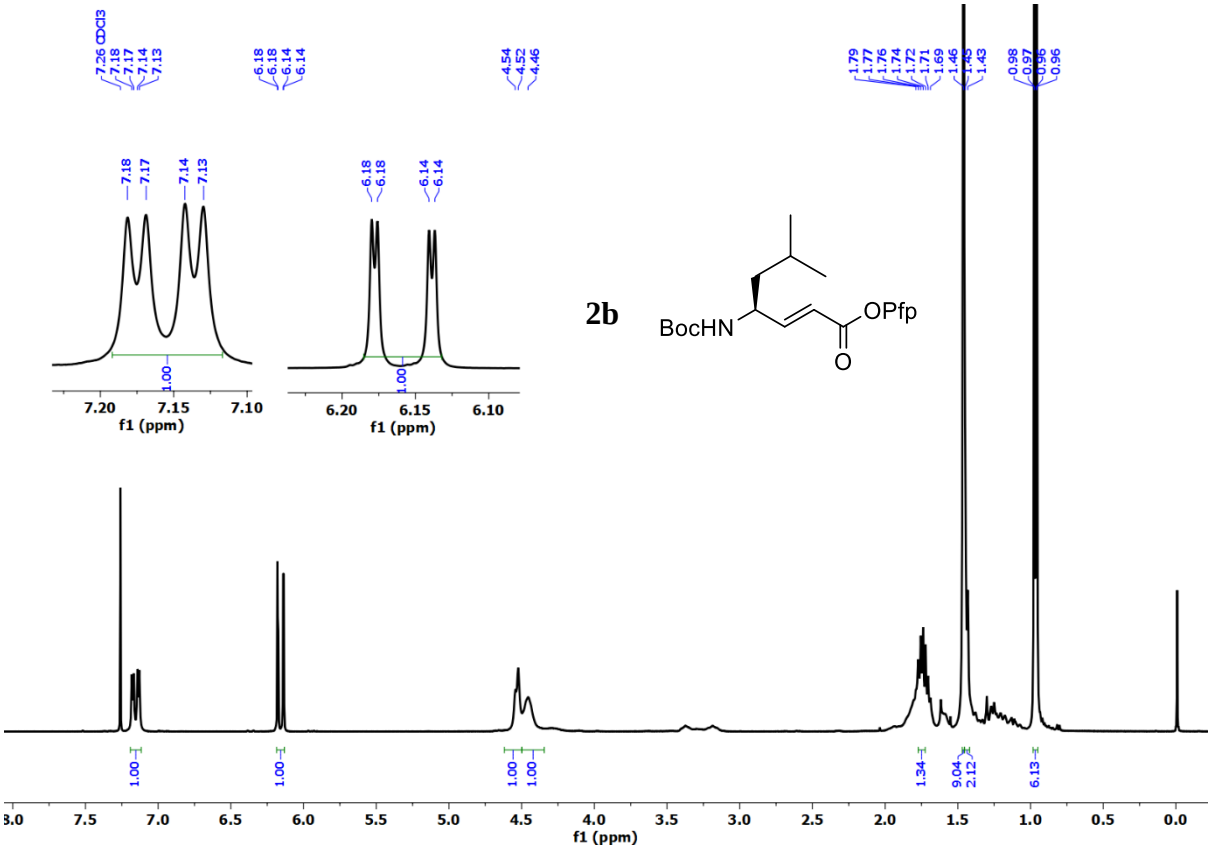
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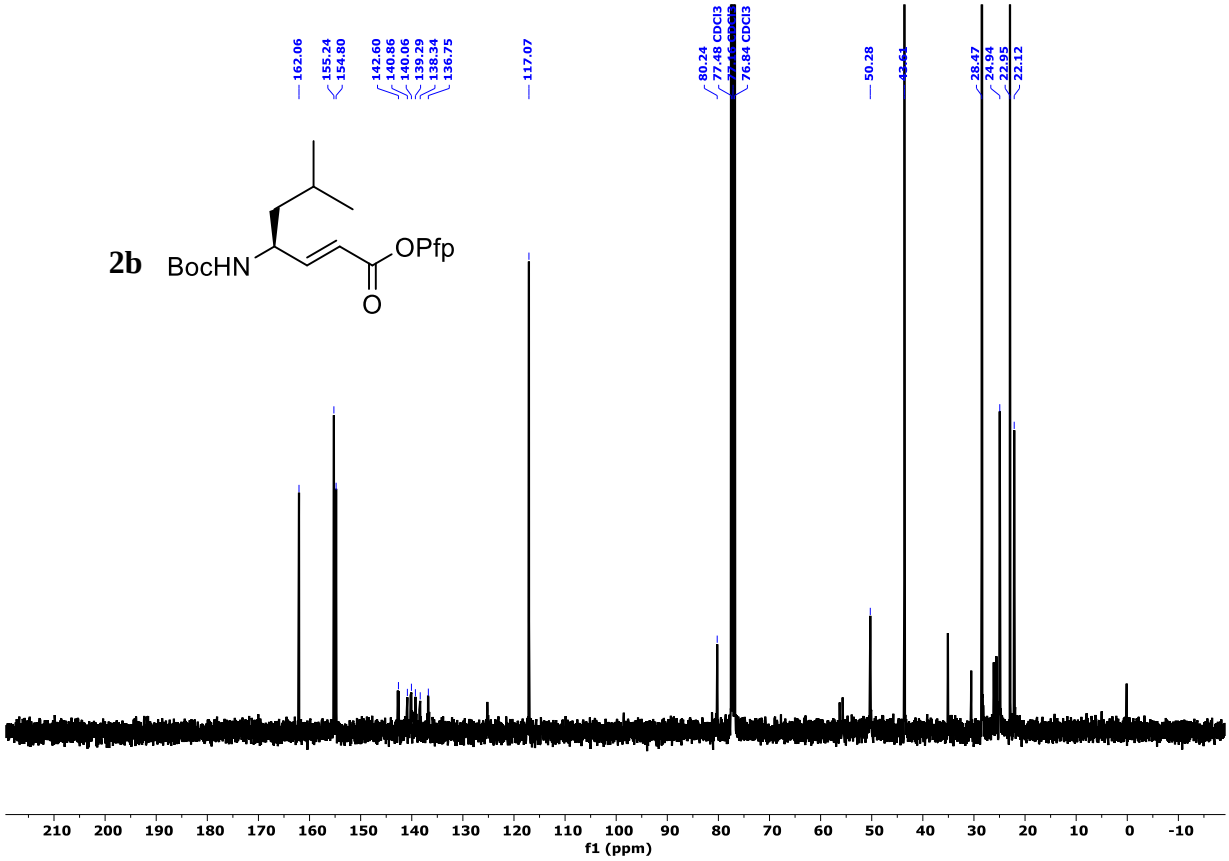
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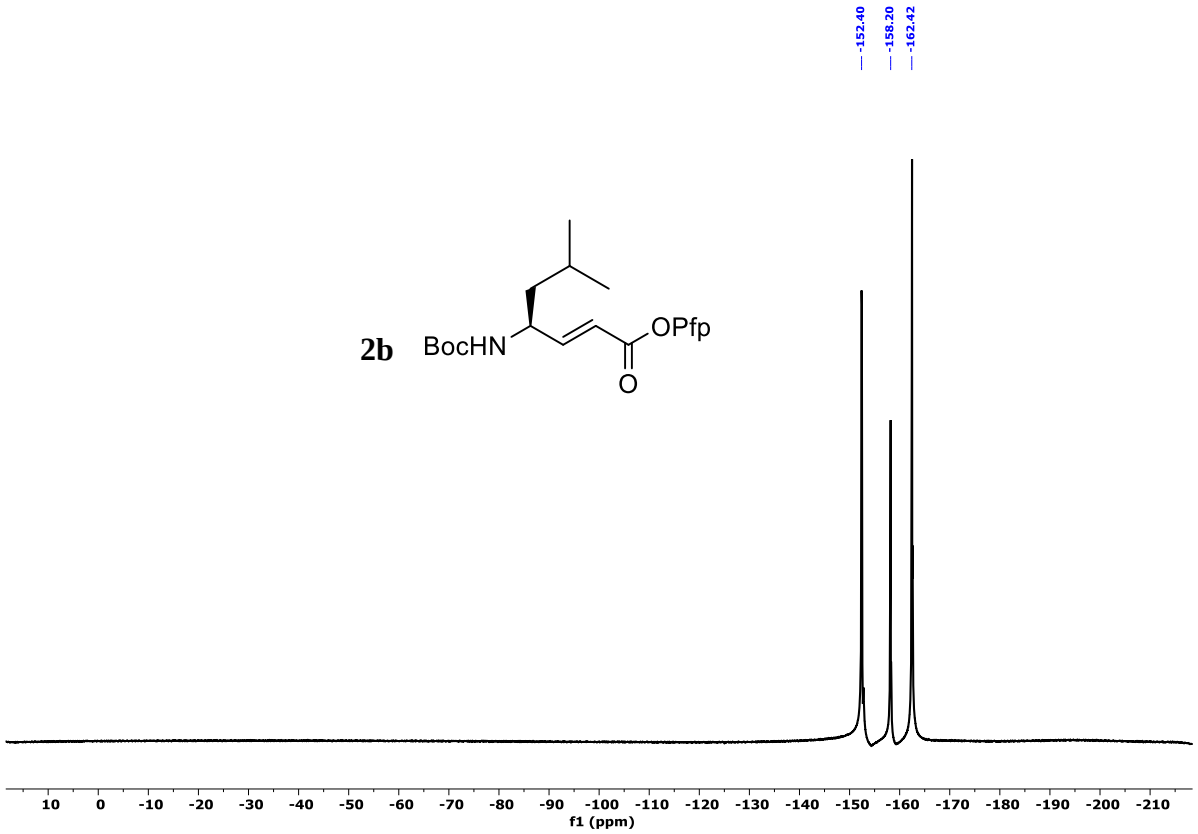
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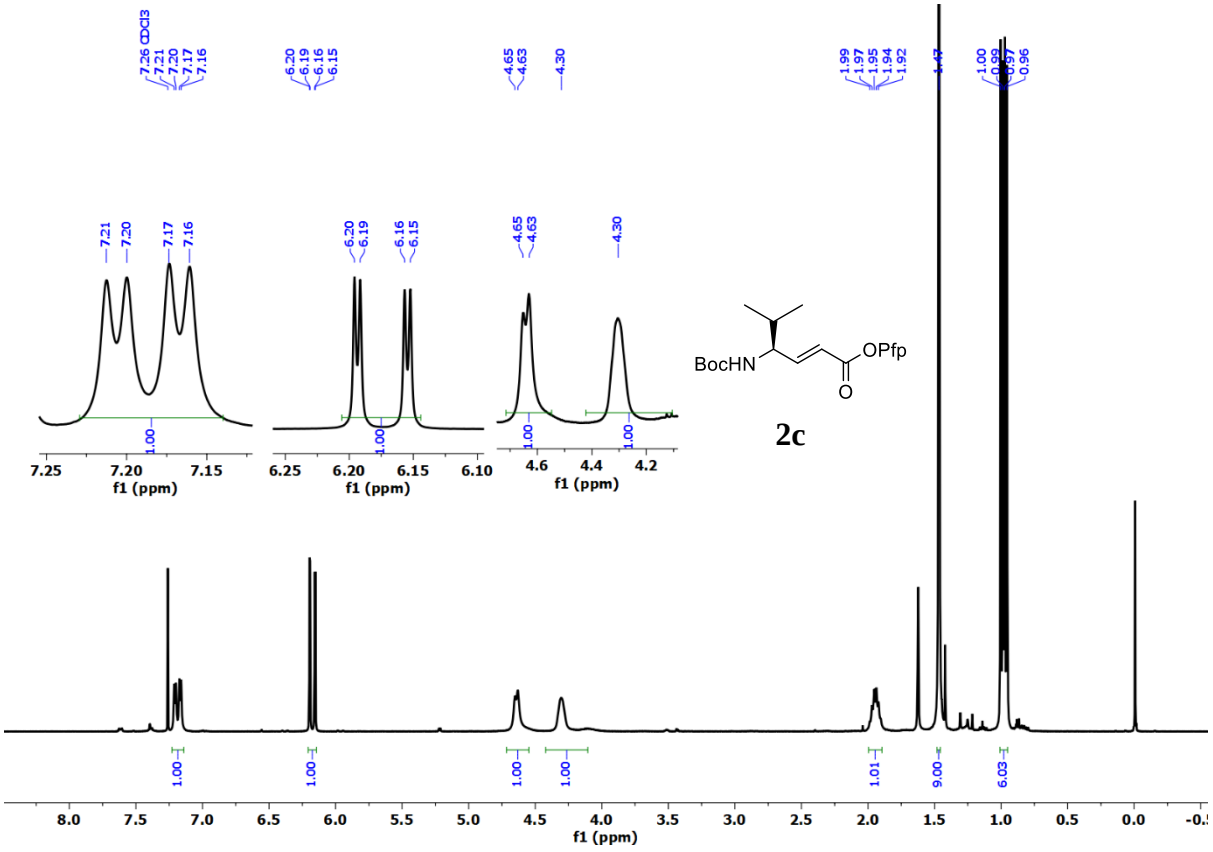
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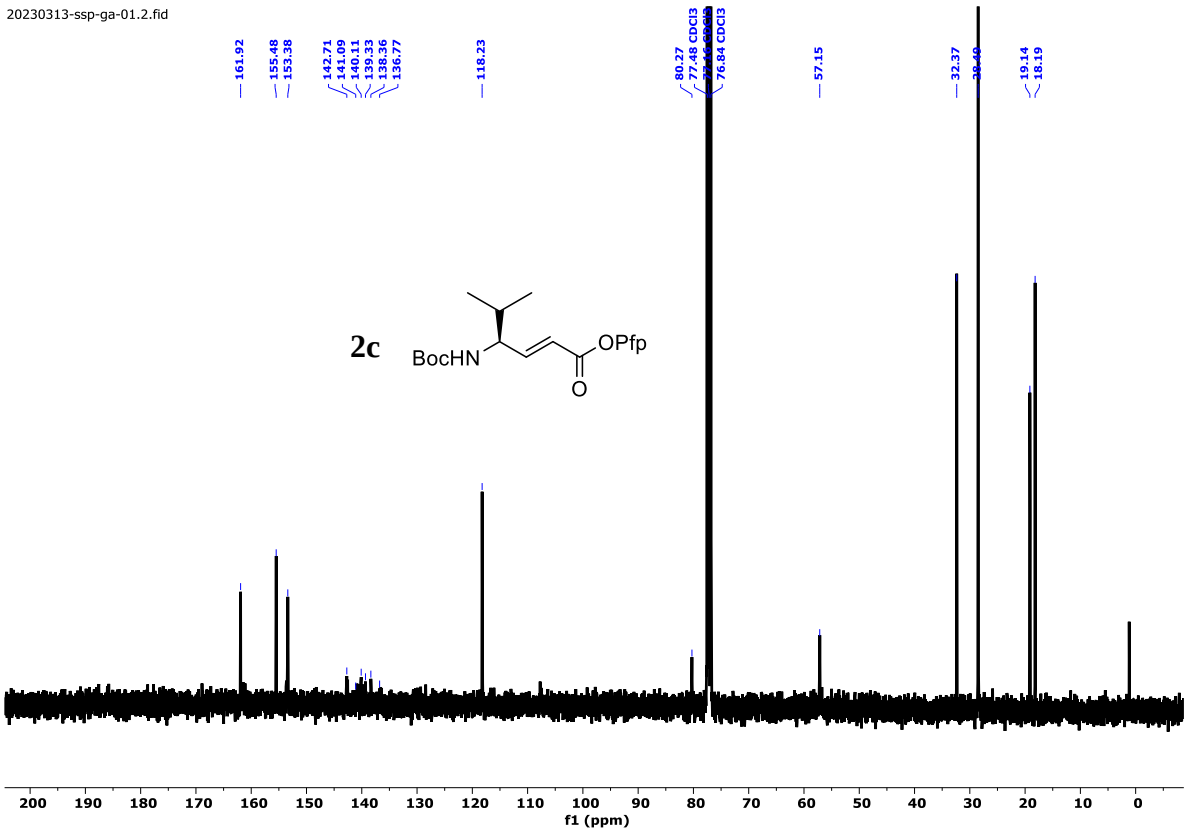
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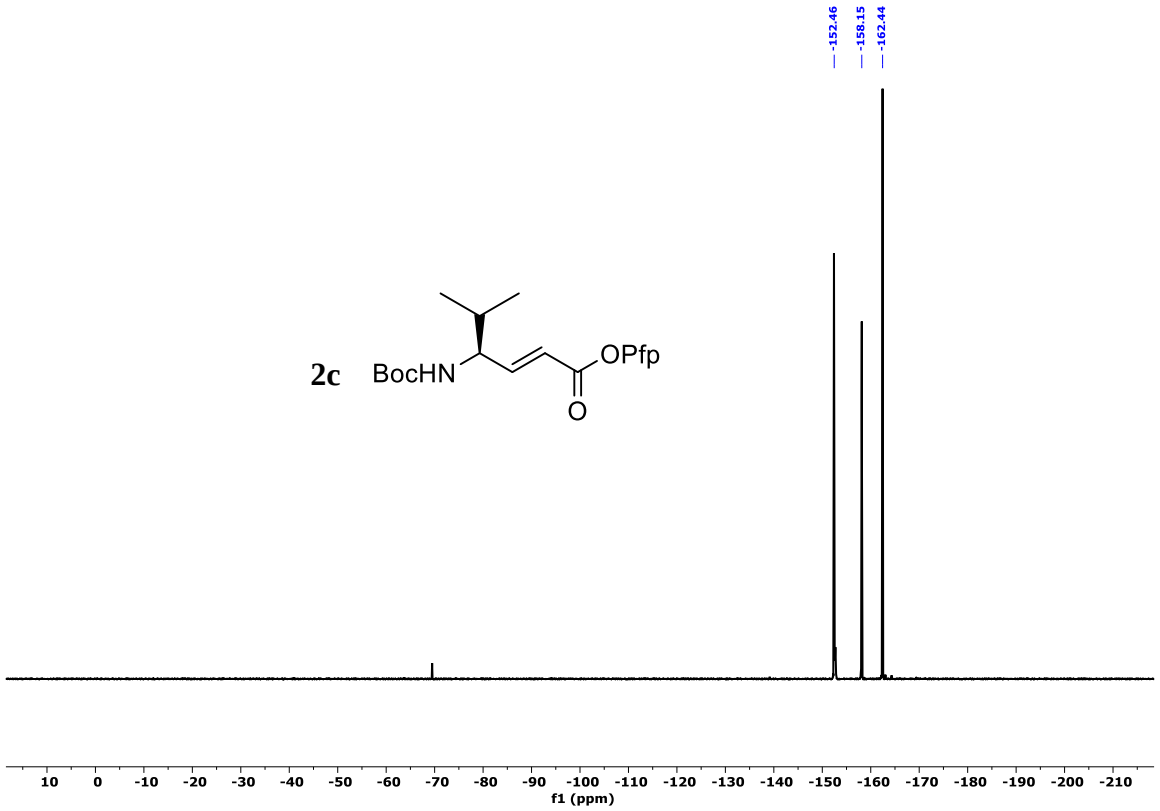
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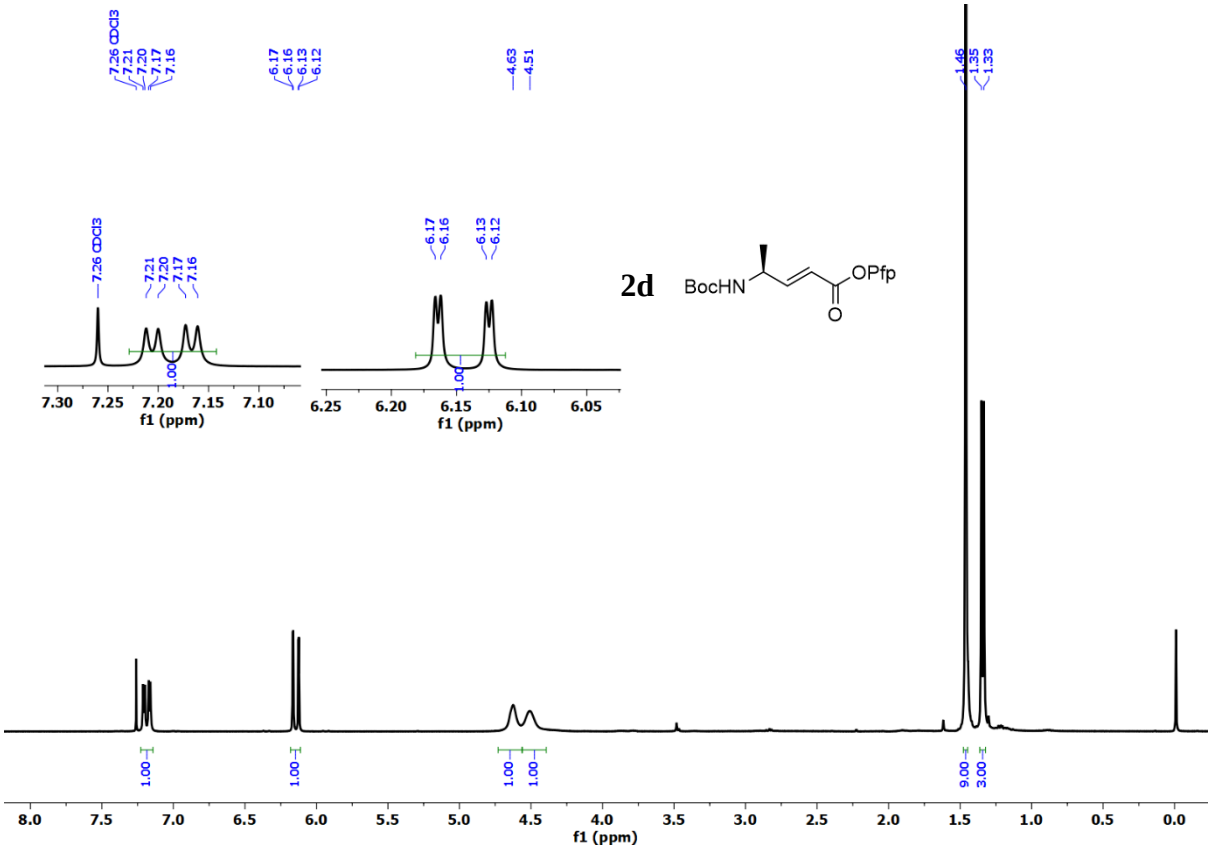
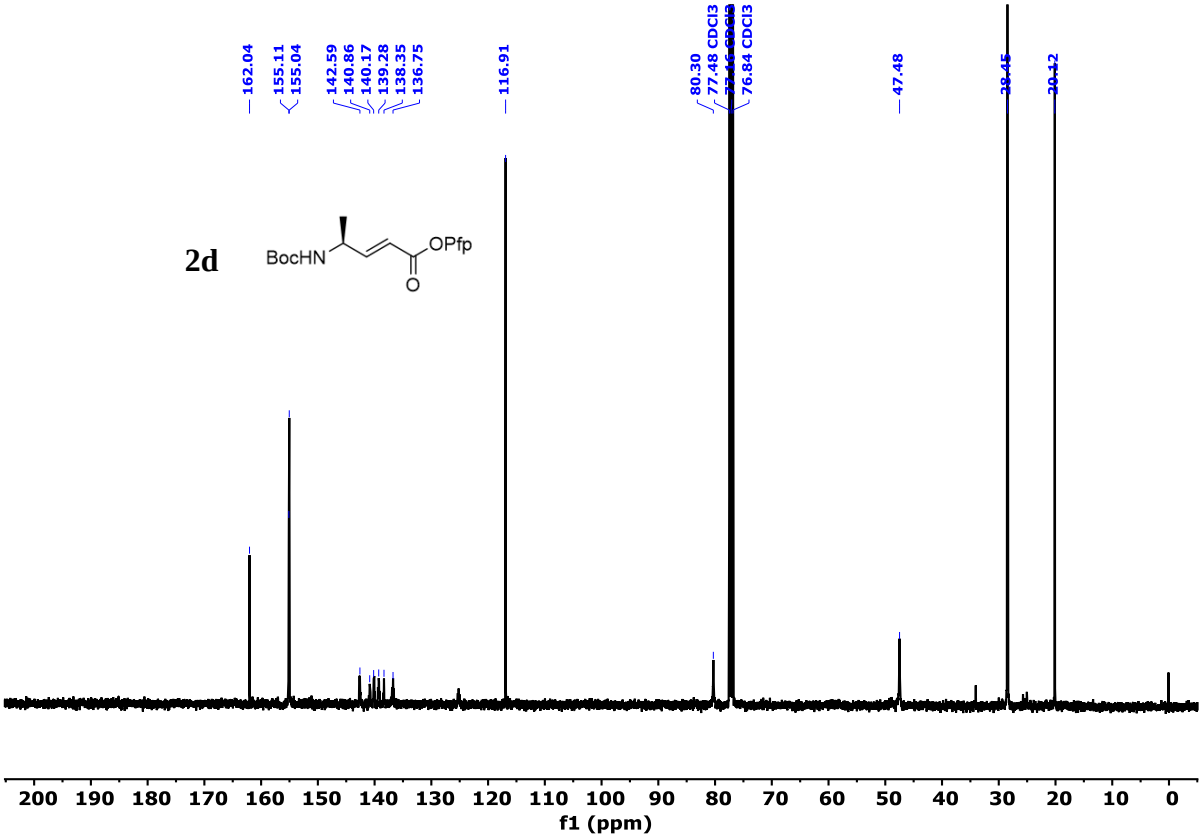
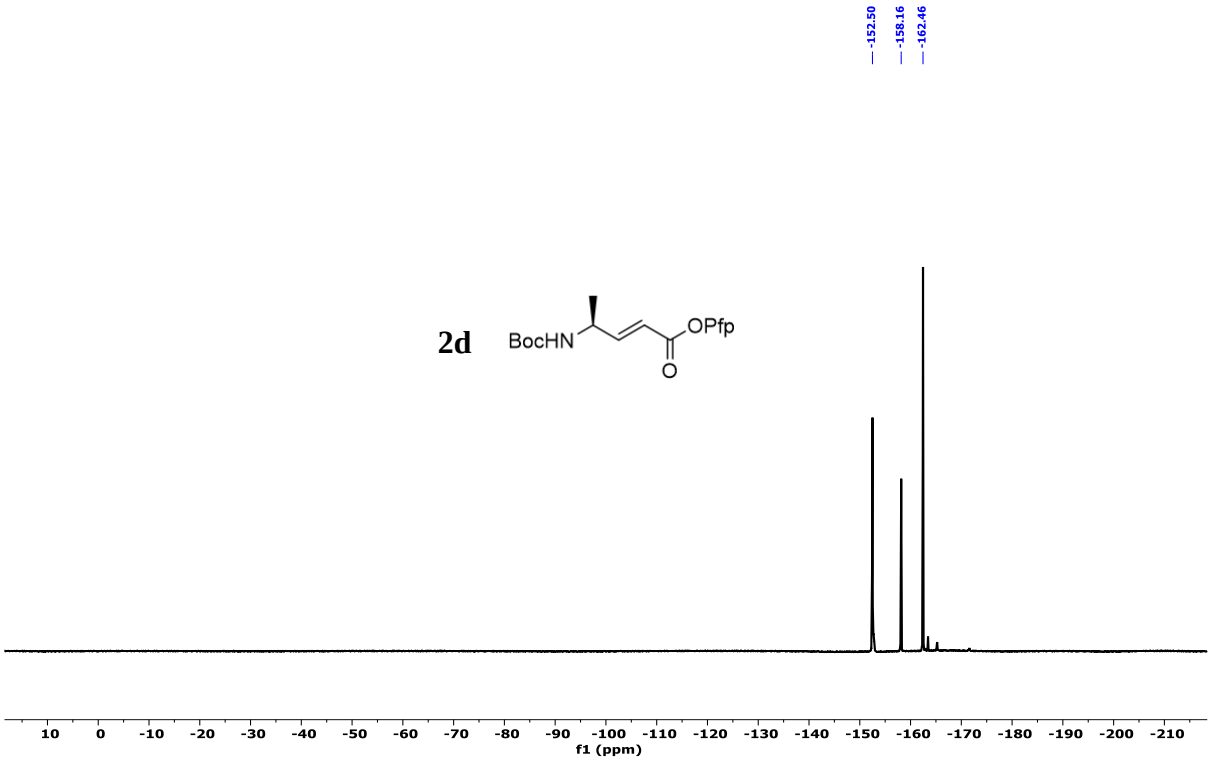
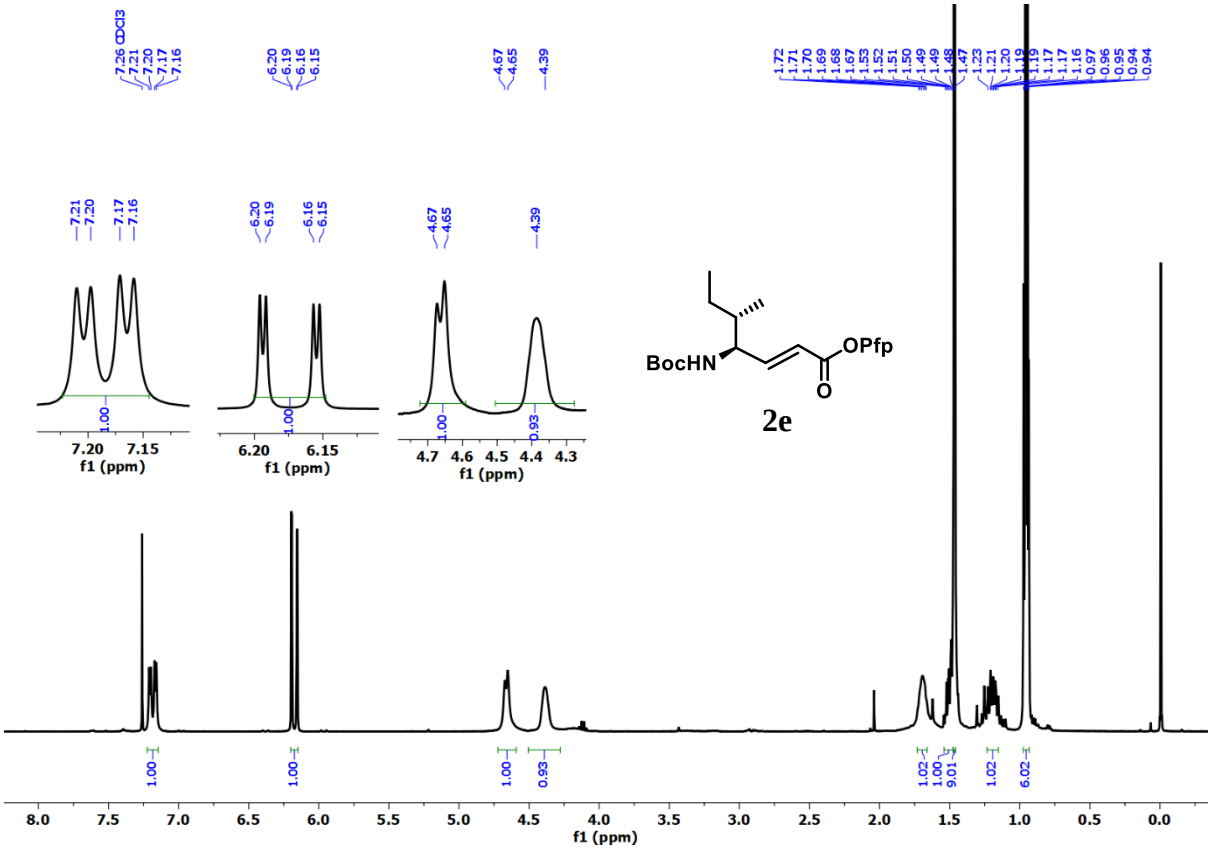
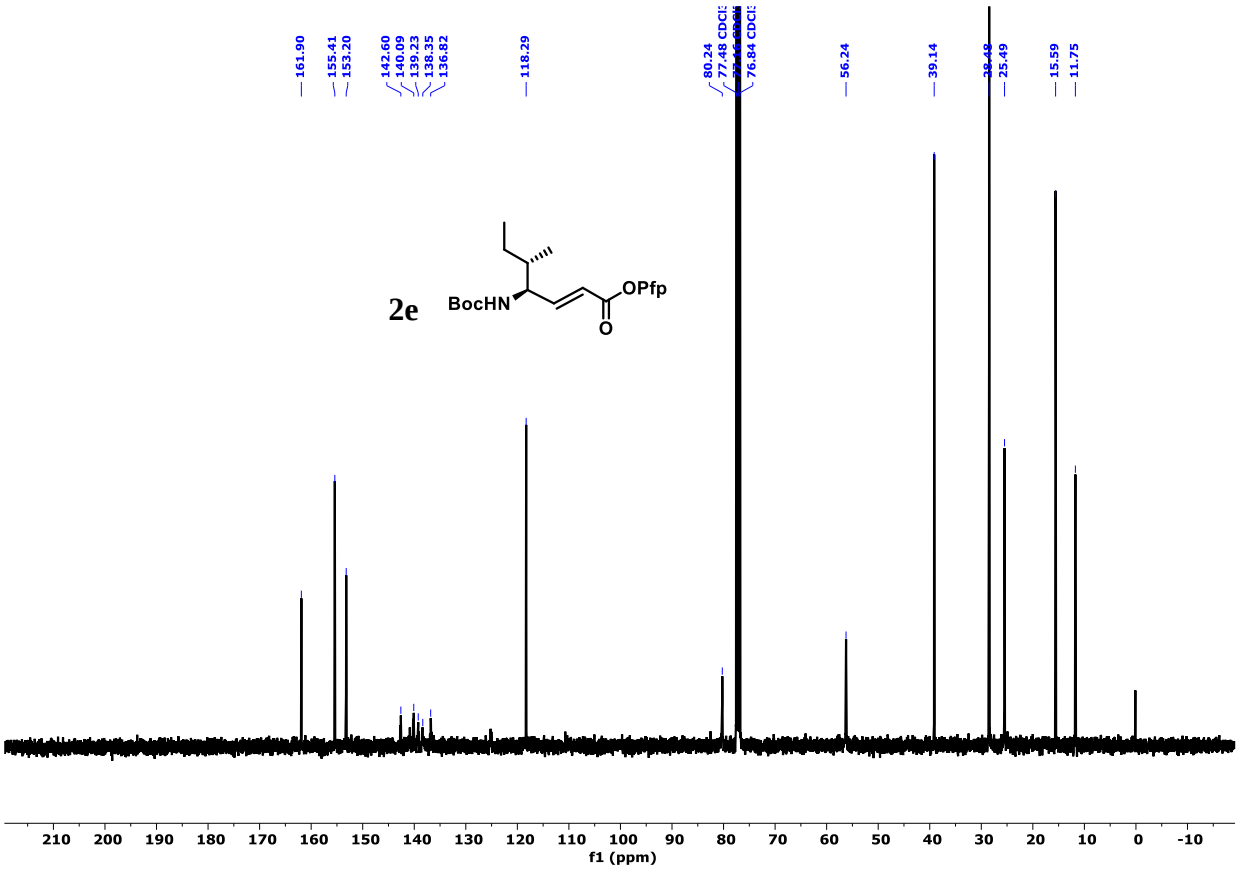
f1 (ppm)

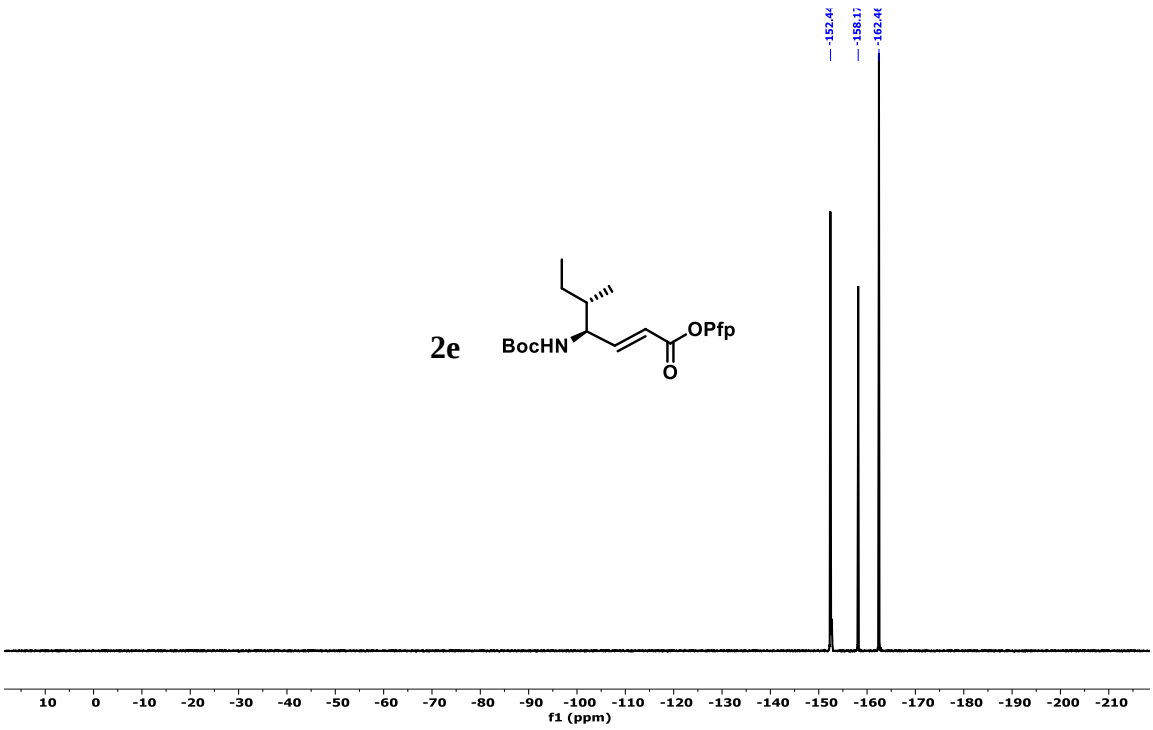

7.26 CDCl3
7.21
7.20
7.17
7.16
6.17
6.16
6.13
6.12
4.63
4.51
1.46
1.35
1.33
2d
BocHN
OPfp
O
f1 (ppm)
1.00
9.00
3.00

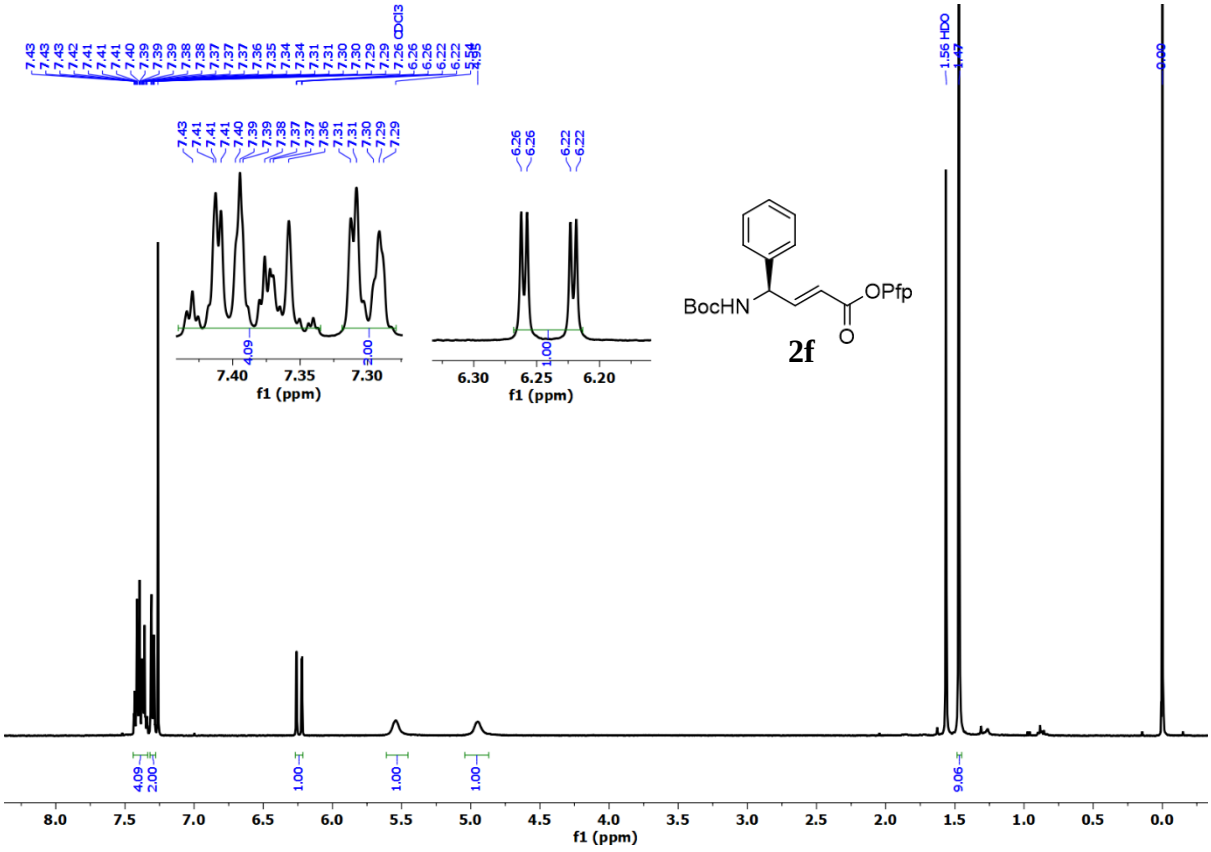

2d
BocHN
OPfp
O
162.04
155.11
155.04
142.59
140.86
140.17
139.28
138.35
136.75
116.91
80.30
77.48 CDCl3
76.84 CDCl3
47.48
28.45
20.12
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

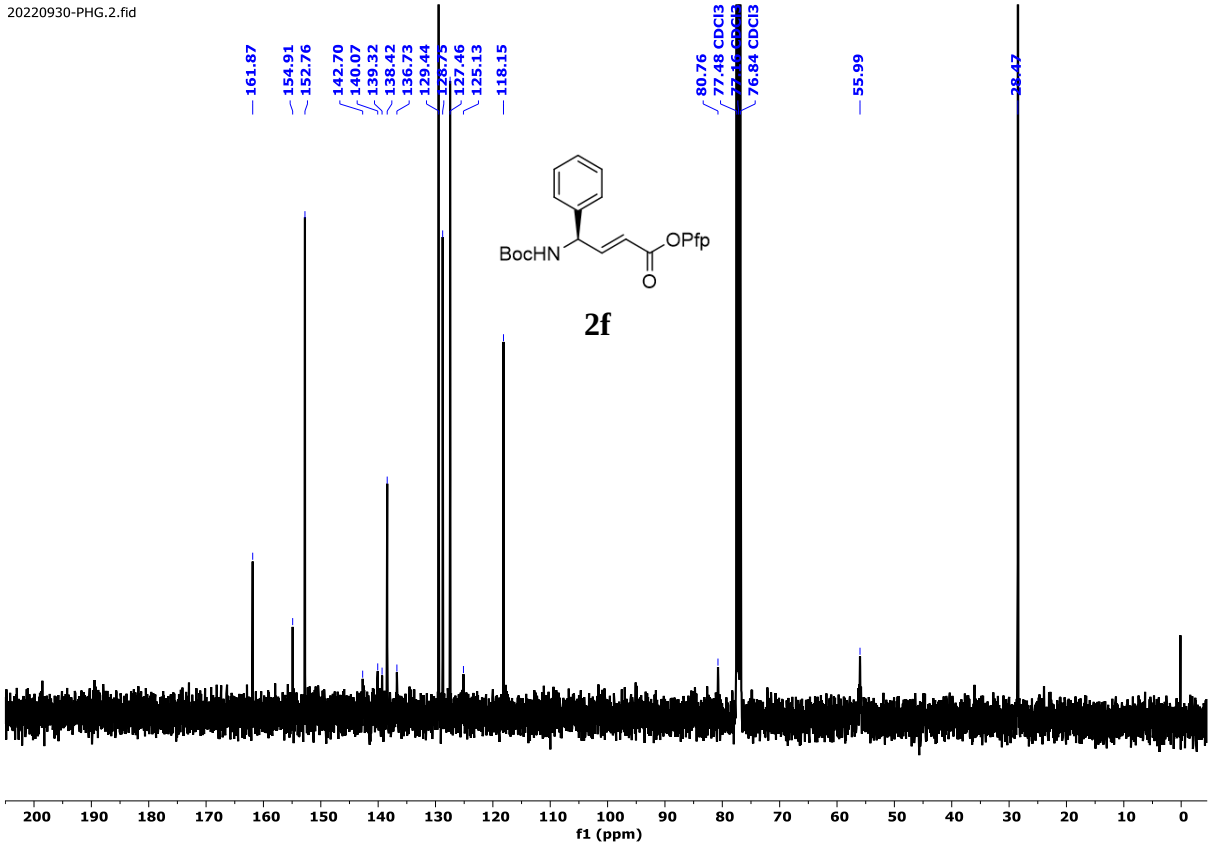

-152.50
-158.16
-162.46
2d
BocHN
OPfp
O
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


BocHN
OPfp
O
2e
f1 (ppm)

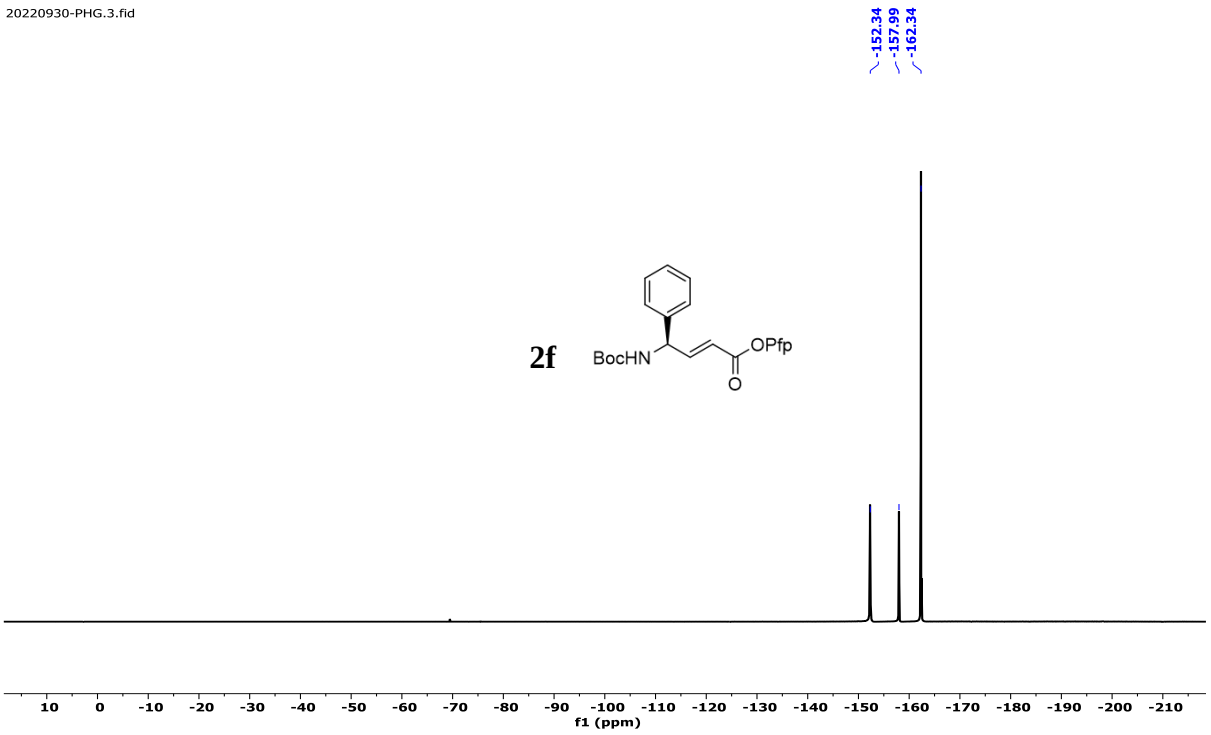

161.90
155.41
153.20
142.60
140.09
139.23
138.35
136.82
118.29
80.24
77.48 CDCl3
76.84 CDCl3
56.24
39.14
28.48
25.49
15.59
11.75
2e
BocHN
OPfp
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


-152.44
-158.17
-162.48
2e
BocHN
OPfp
O
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

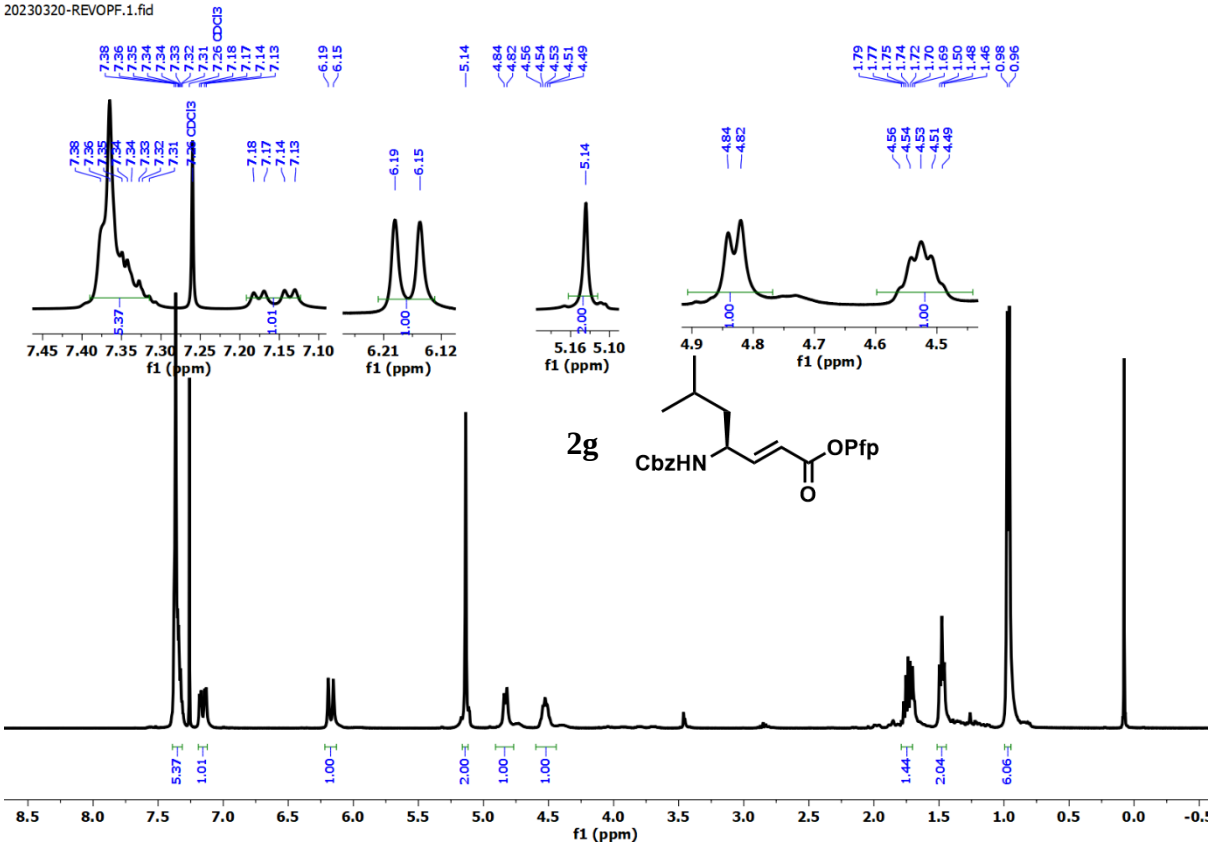

BocHN
OPfp
O
2f
f1 (ppm)

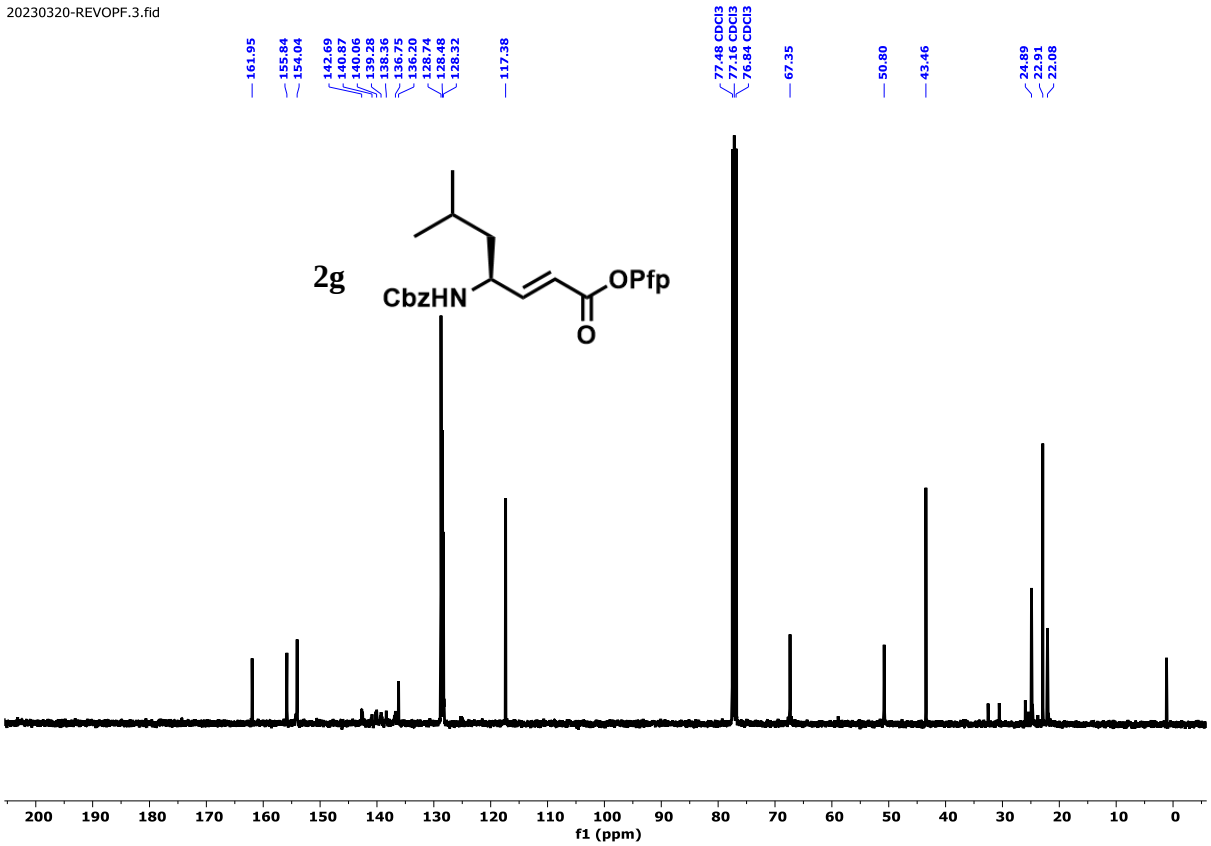

20220930-PHG.2.fid
161.87
154.91
152.76
142.70
140.07
139.32
138.42
136.73
129.44
128.75
127.46
125.13
118.15
80.76
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.99
28.47
BocHN
OPfp
O
2f
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

20220930-PHG.3.fid

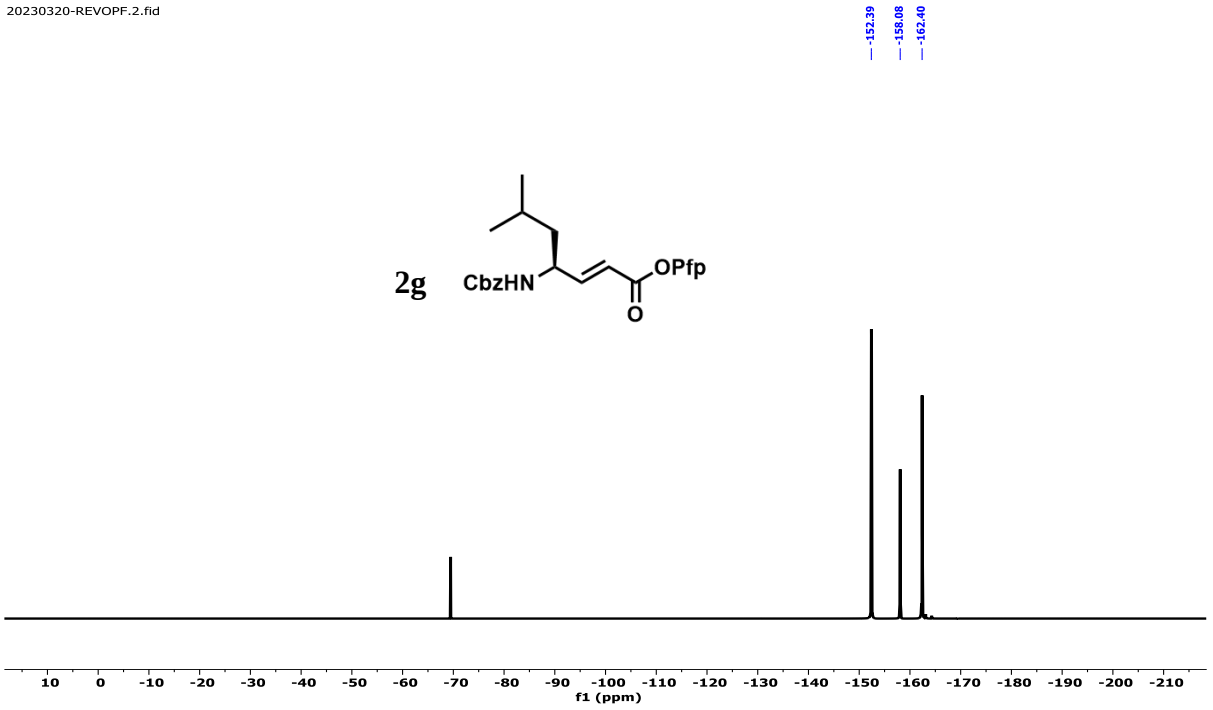


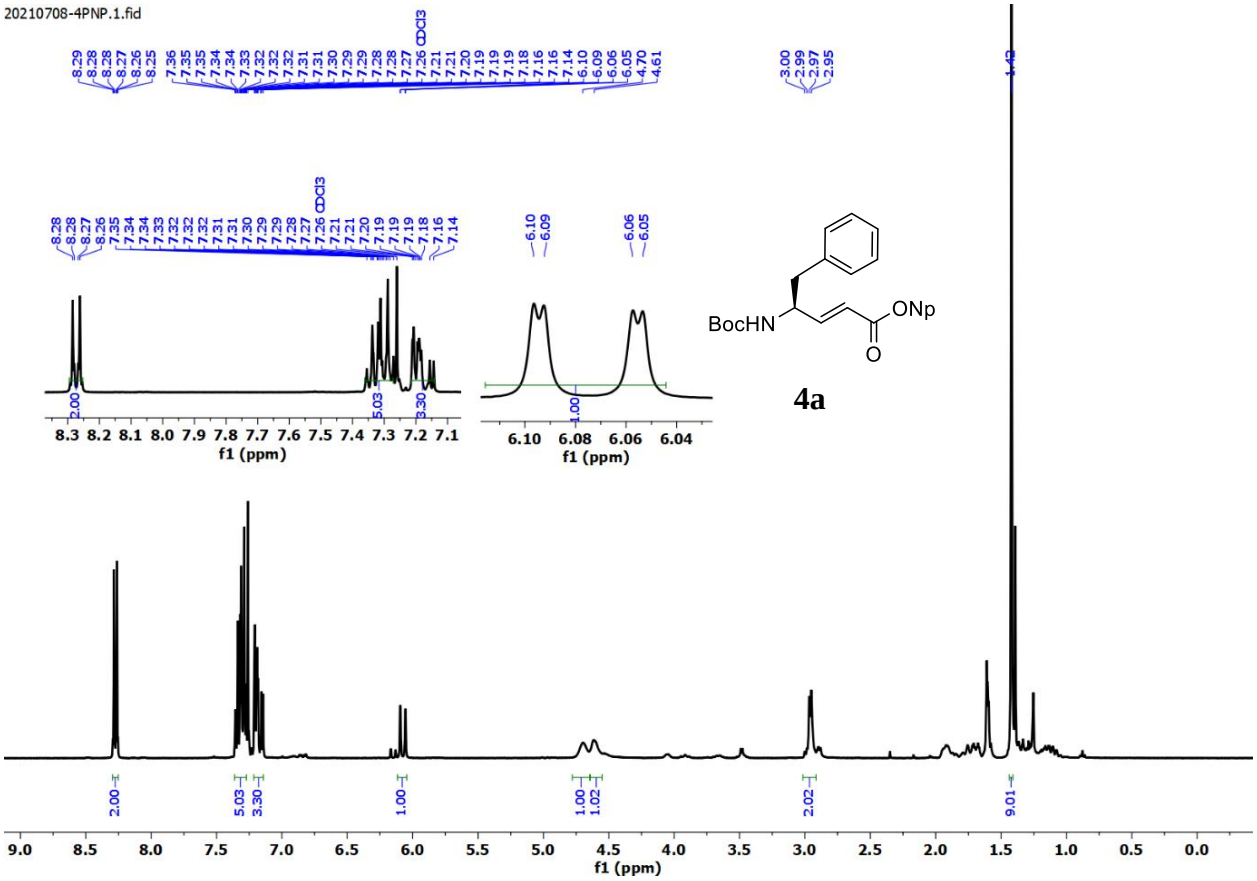
2f

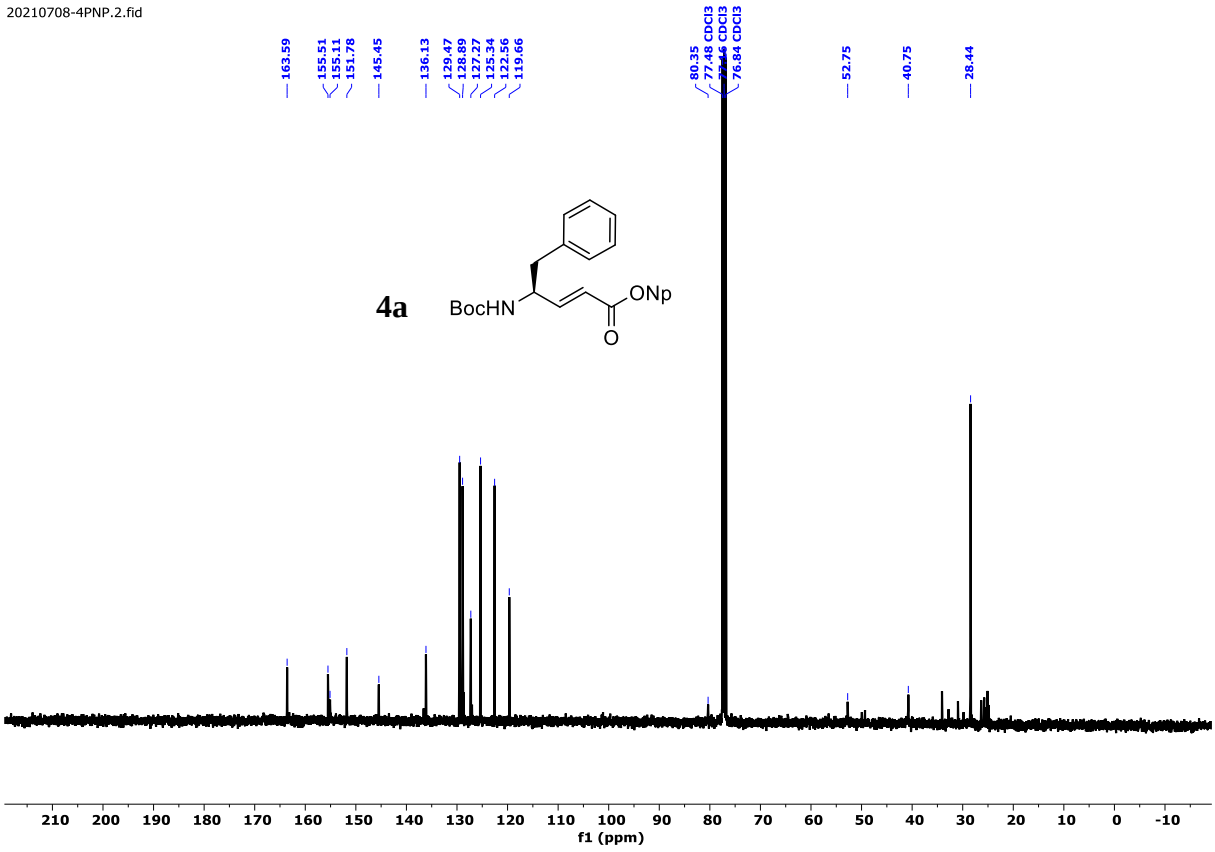

20230320-REVOPF.1.fid
2g
CbzHN
OPfp
O
f1 (ppm)

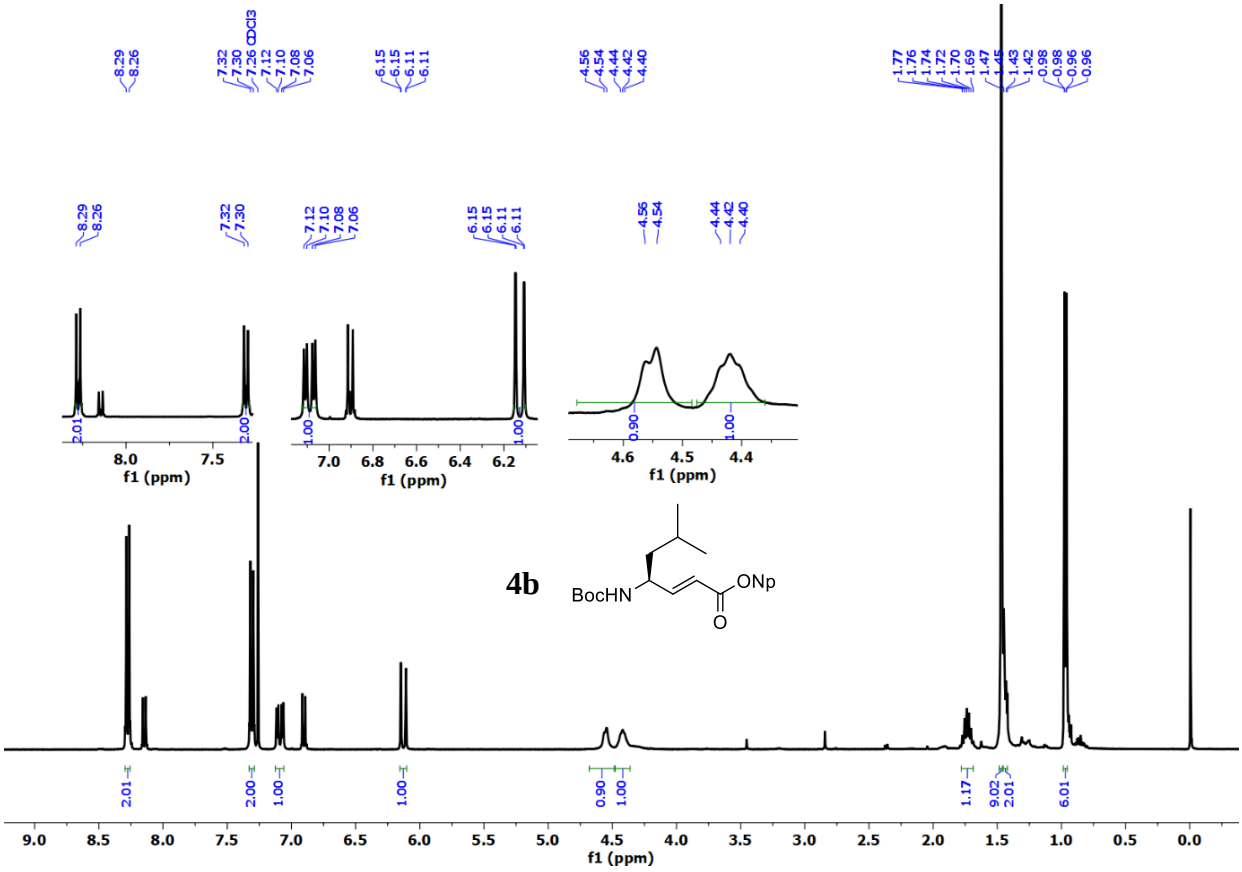

20230320-REVOPF.3.fid
161.95
155.84
154.04
142.69
140.87
140.06
139.28
138.36
136.75
136.20
128.74
128.48
128.32
117.38
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
67.35
50.80
43.46
24.89
22.91
22.08
2g
CbzHN
OPfp
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

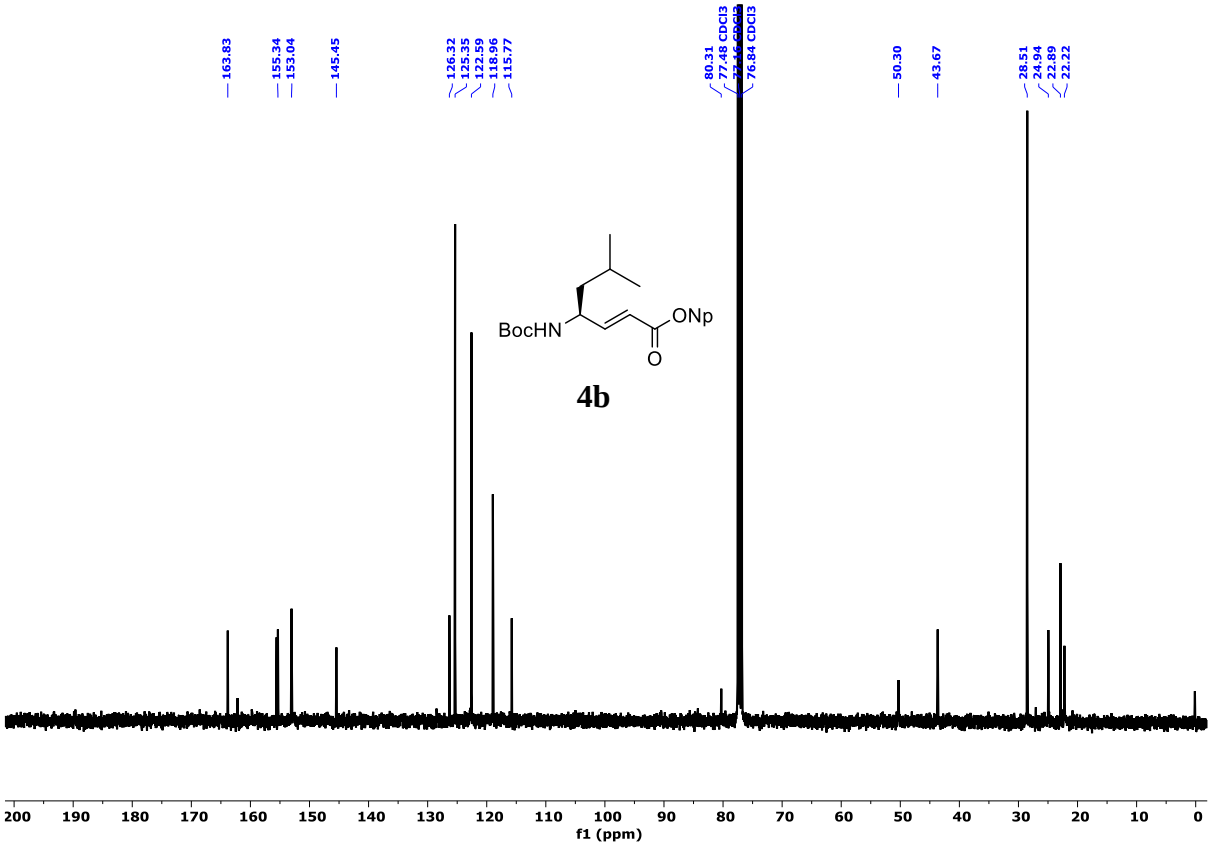
20230320-REVOPF.2.fid

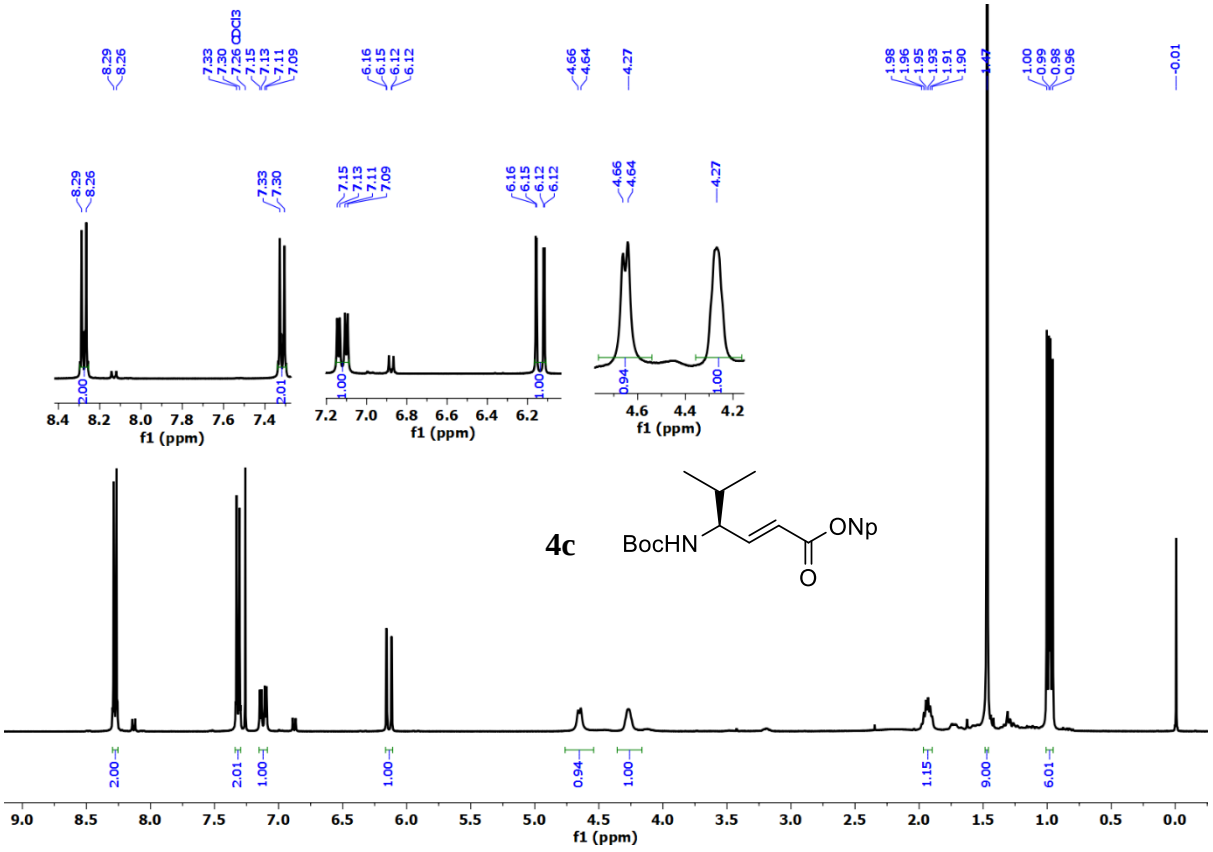


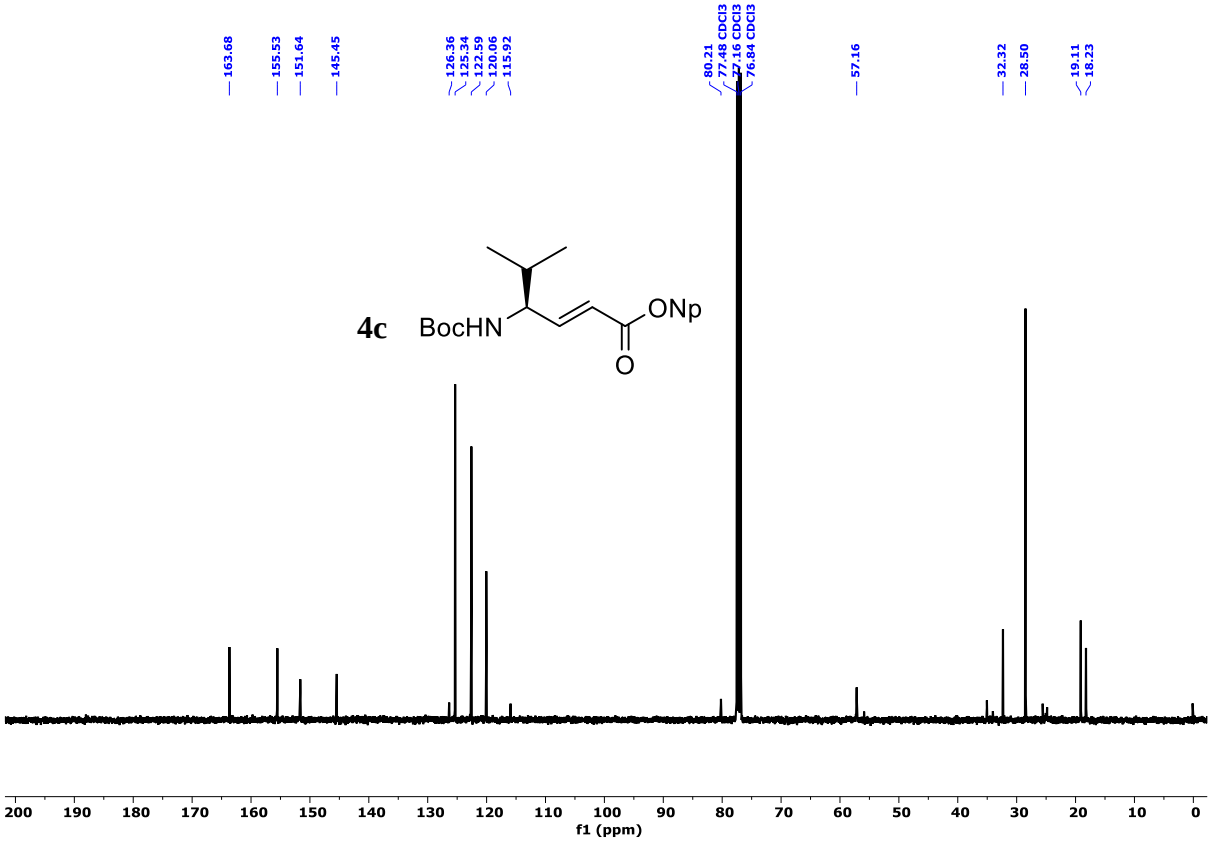

20210708-4PNP.1.fid
CDCl3
BocHN
ONp
O
4a
f1 (ppm)

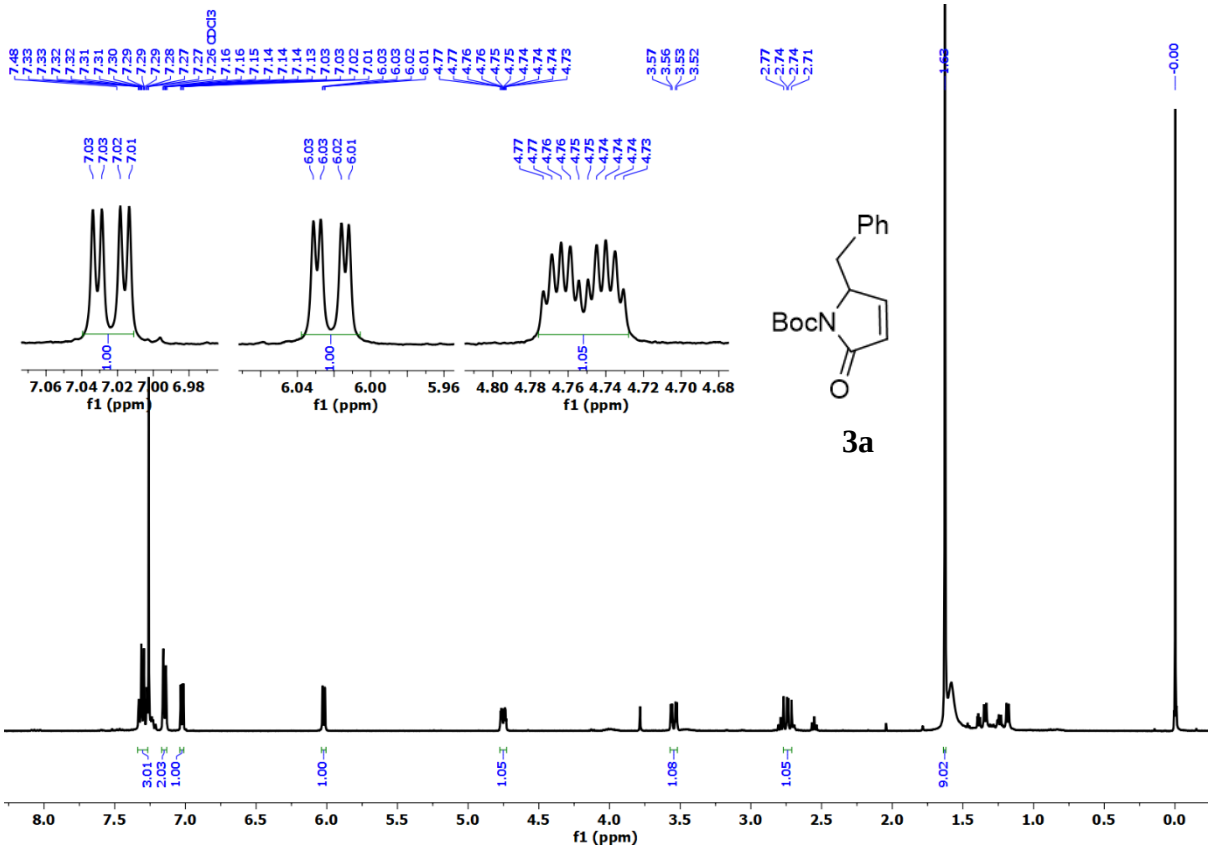

20210708-4PNP.2.fid
163.59
155.51
155.11
151.78
145.45
136.13
129.47
128.89
127.27
125.34
122.56
119.66
80.35
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
52.75
40.75
28.44
4a
BocHN
ONp
O
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

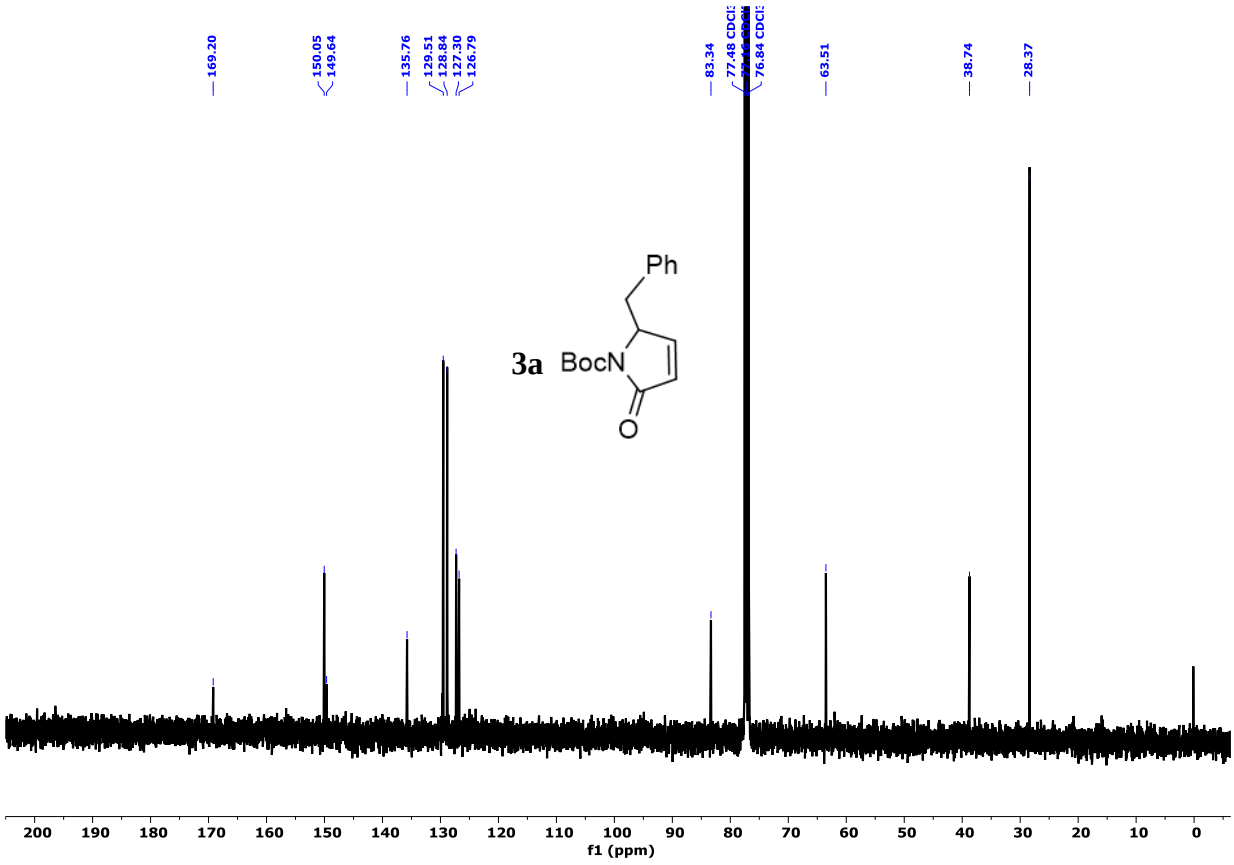

4b
BocHN
ONp
O
f1 (ppm)

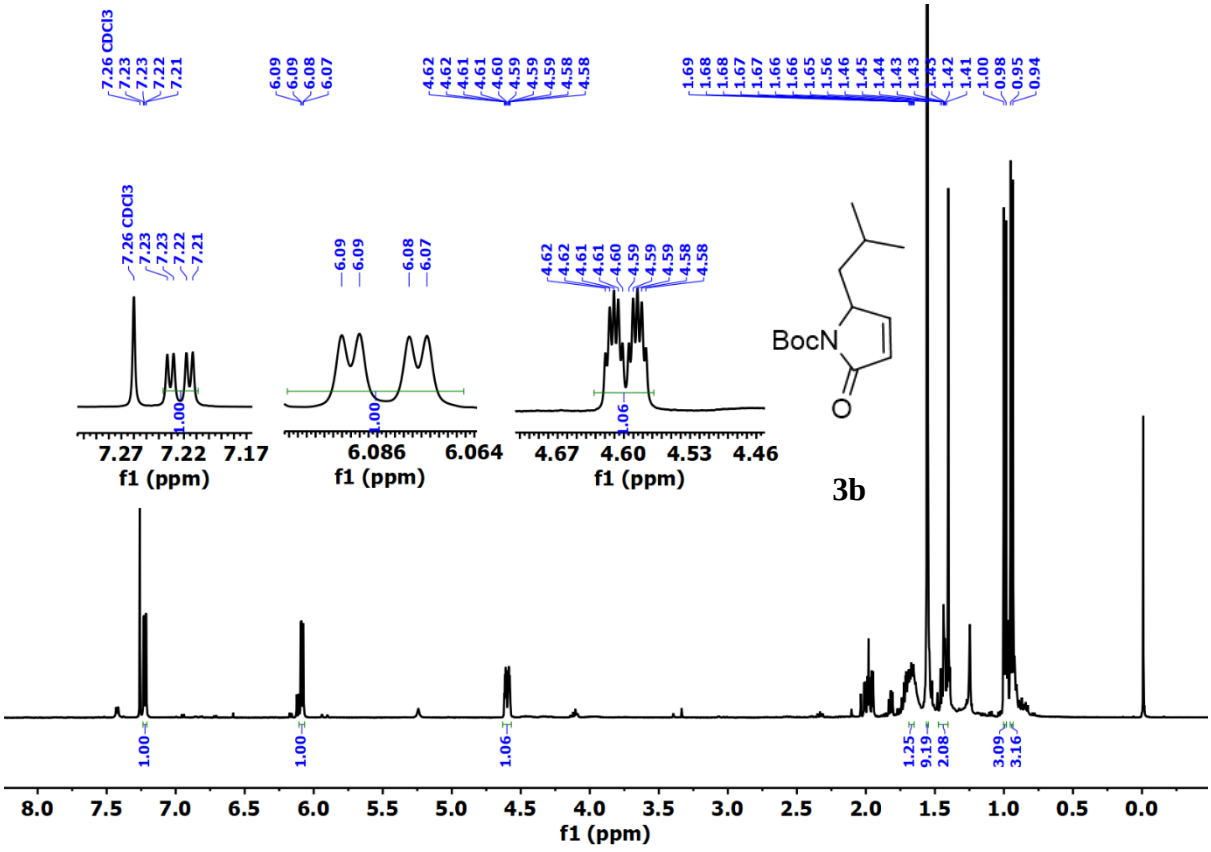

163.83
155.34
153.04
145.45
126.32
125.35
122.59
118.96
115.77
80.31
77.48 CDCl3
76.84 CDCl3
50.30
43.67
28.51
24.94
22.89
22.22
BocHN
ONp
O
4b
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

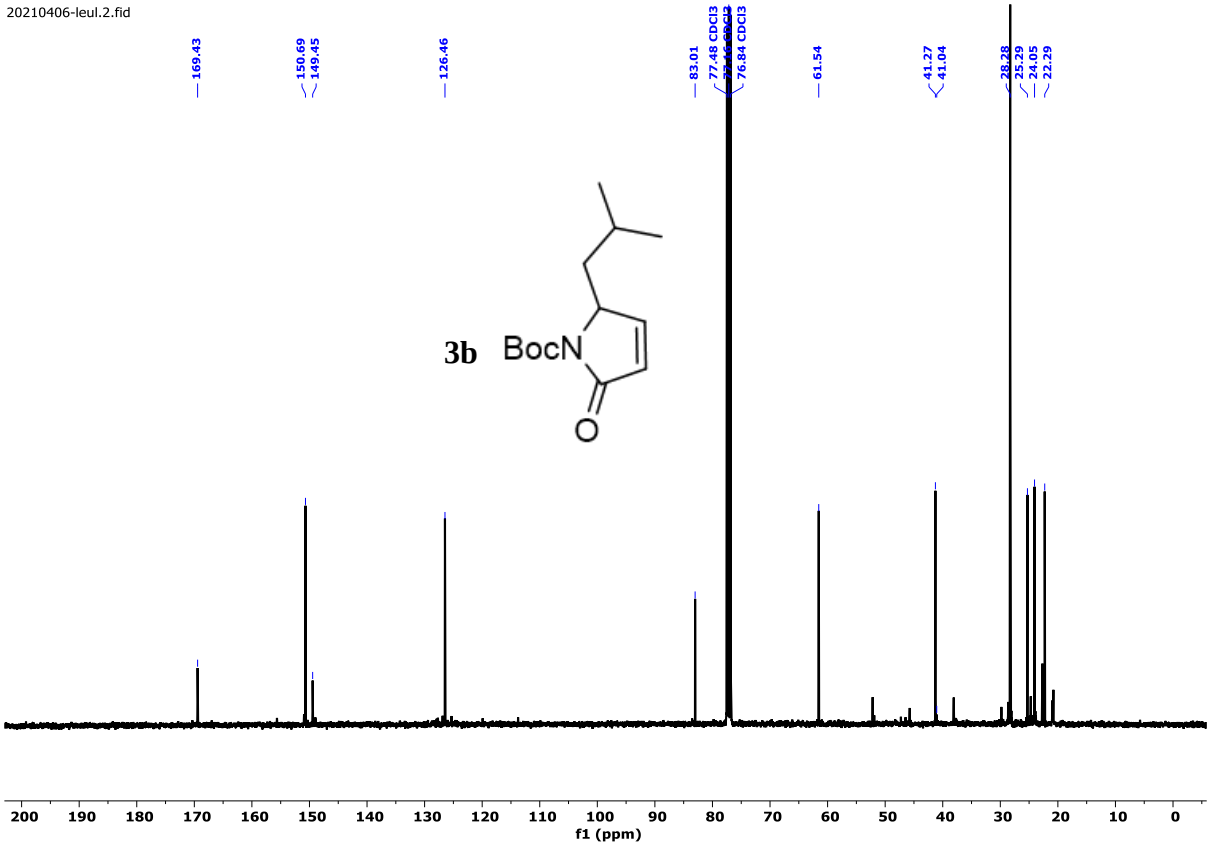

4c
BocHN
ONp
O
f1 (ppm)

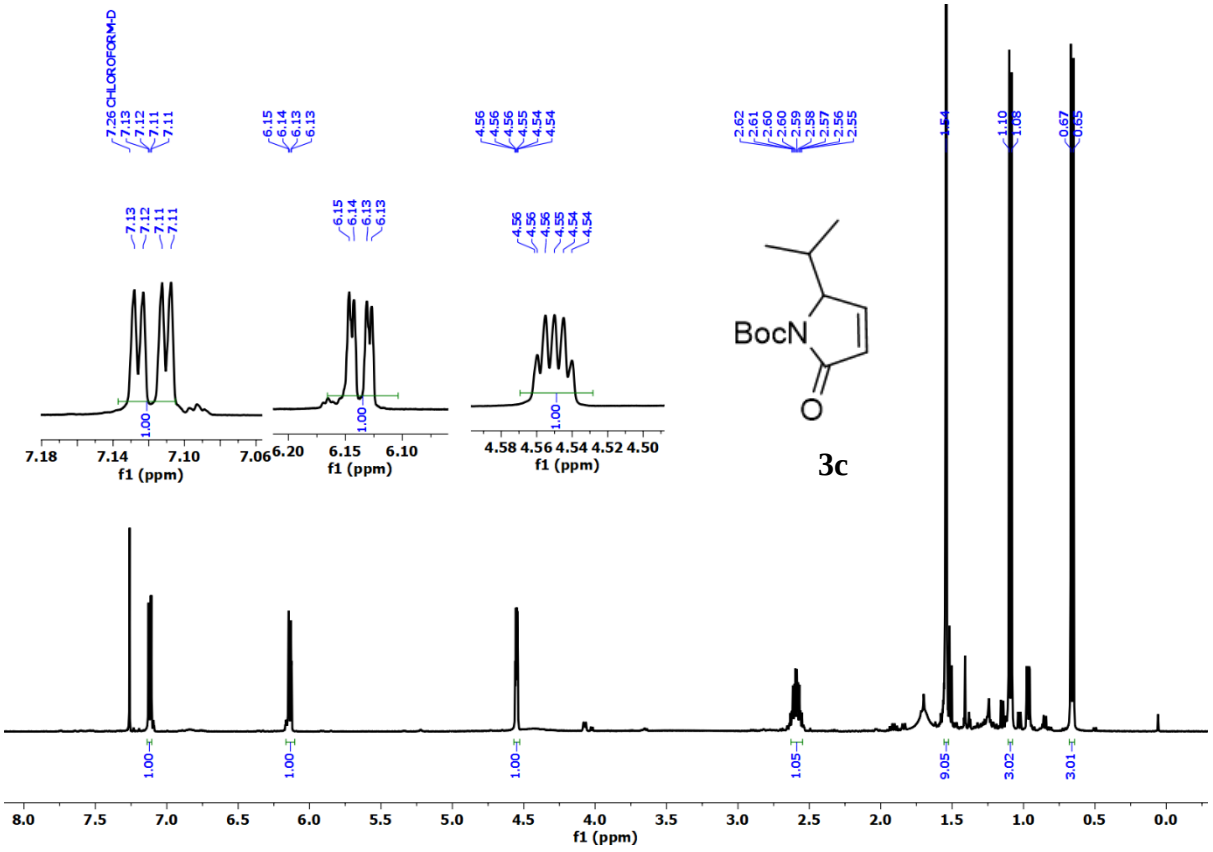

163.68
155.53
151.64
145.45
126.36
125.34
122.59
120.06
115.92
80.21
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
57.16
32.32
28.50
19.11
18.23
4c
BocHN
ONp
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

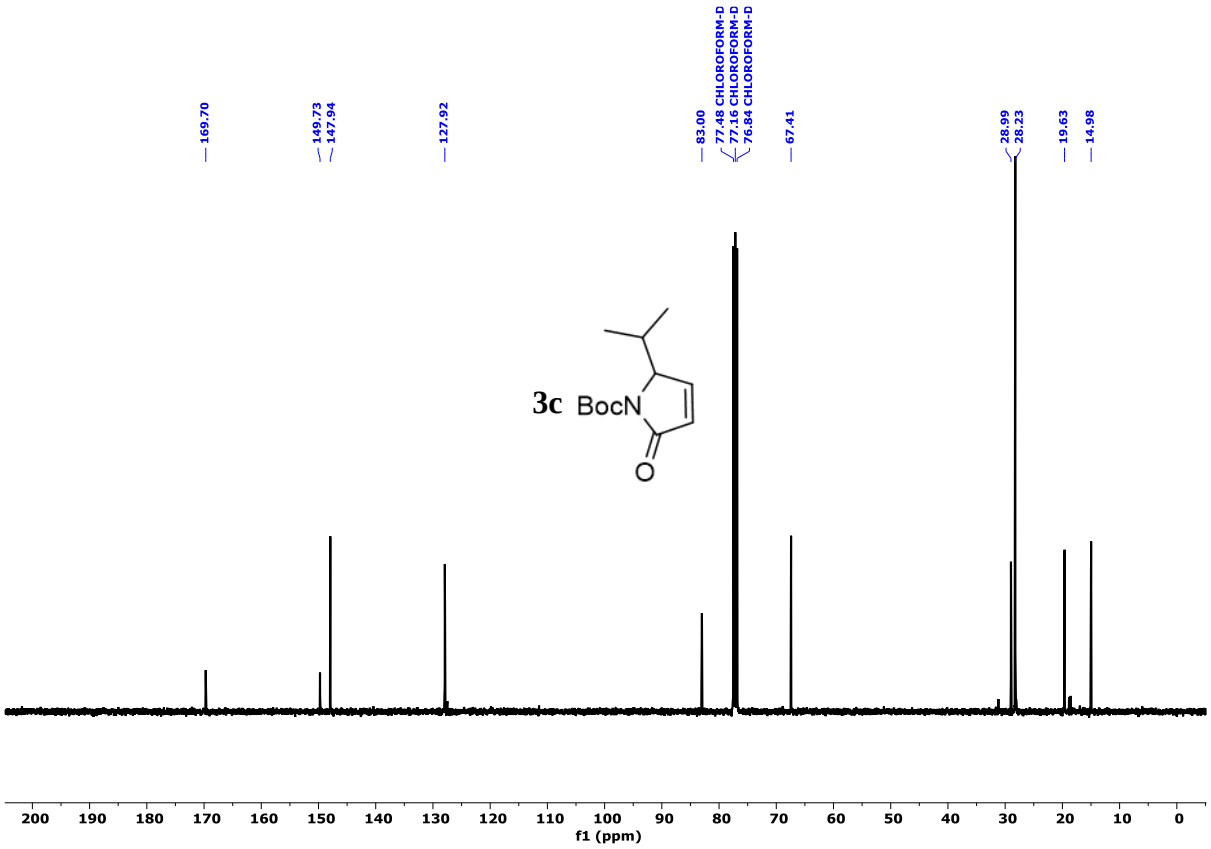

Ph
BocN
O
3a
f1 (ppm)

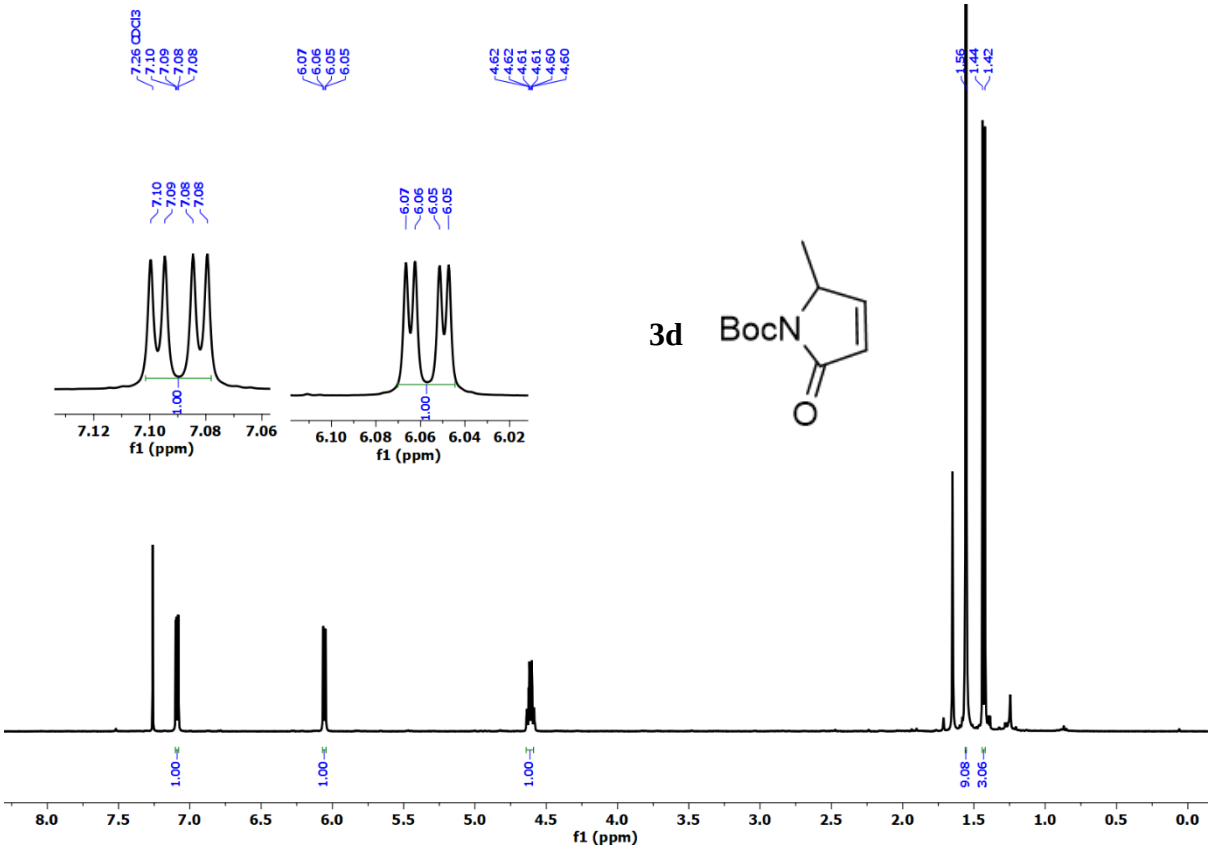

169.20
150.05
149.64
135.76
129.51
128.84
127.30
126.79
83.34
77.48 CDCl3
76.84 CDCl3
63.51
38.74
28.37
Ph
3a BocN
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

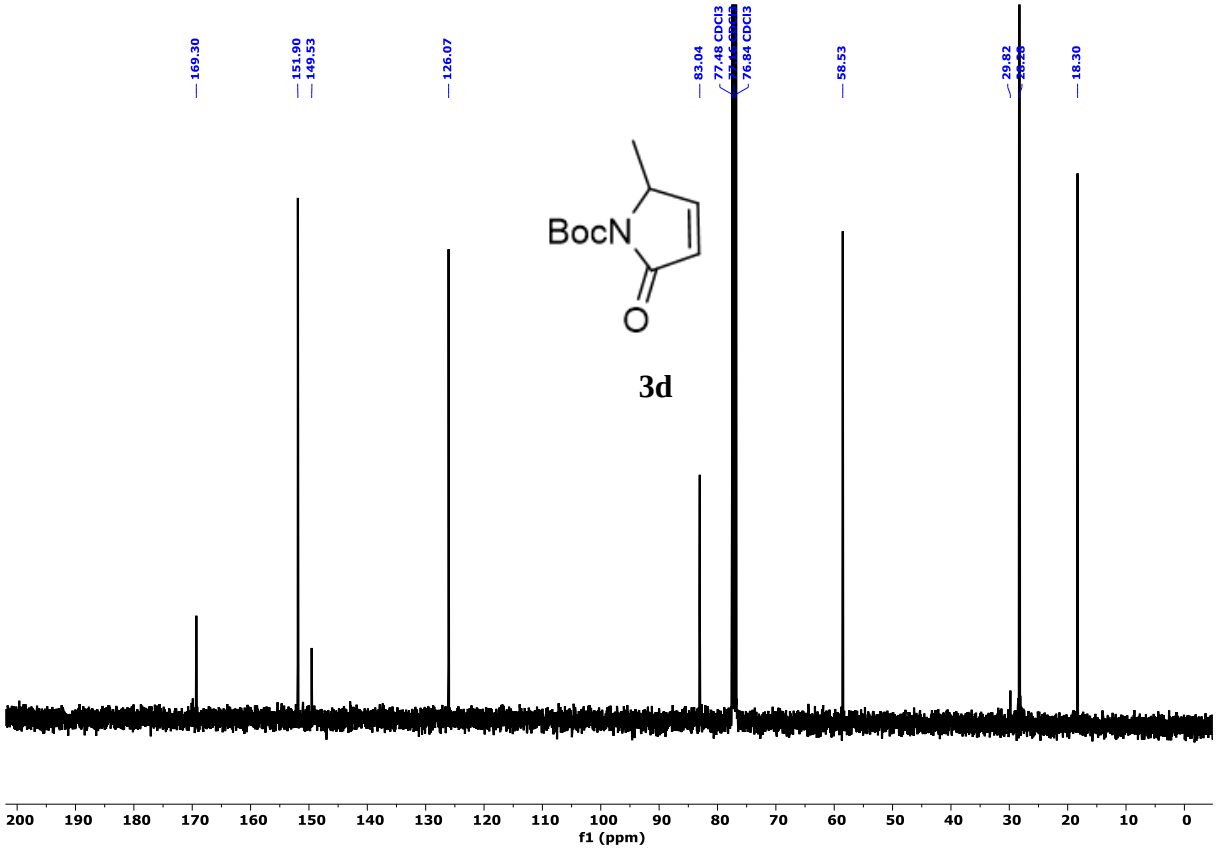

7.26 CDCl3
7.23
7.23
7.22
7.21
6.09
6.09
6.08
6.07
4.62
4.62
4.61
4.61
4.60
4.59
4.59
4.59
4.58
4.58
1.69
1.68
1.68
1.67
1.67
1.66
1.66
1.65
1.56
1.46
1.45
1.44
1.43
1.43
1.42
1.41
1.00
0.98
0.95
0.94
BocN
O
3b
1.00
1.00
1.06
1.25
9.19
2.08
3.09
3.16
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
7.27
7.22
7.17
6.086
6.064
4.67
4.60
4.53
4.46


20210406-leul.2.fid
169.43
150.69
149.45
126.46
83.01
77.48 CDCl3
76.84 CDCl3
61.54
41.27
41.04
28.28
25.29
24.05
22.29
3b
BocN
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

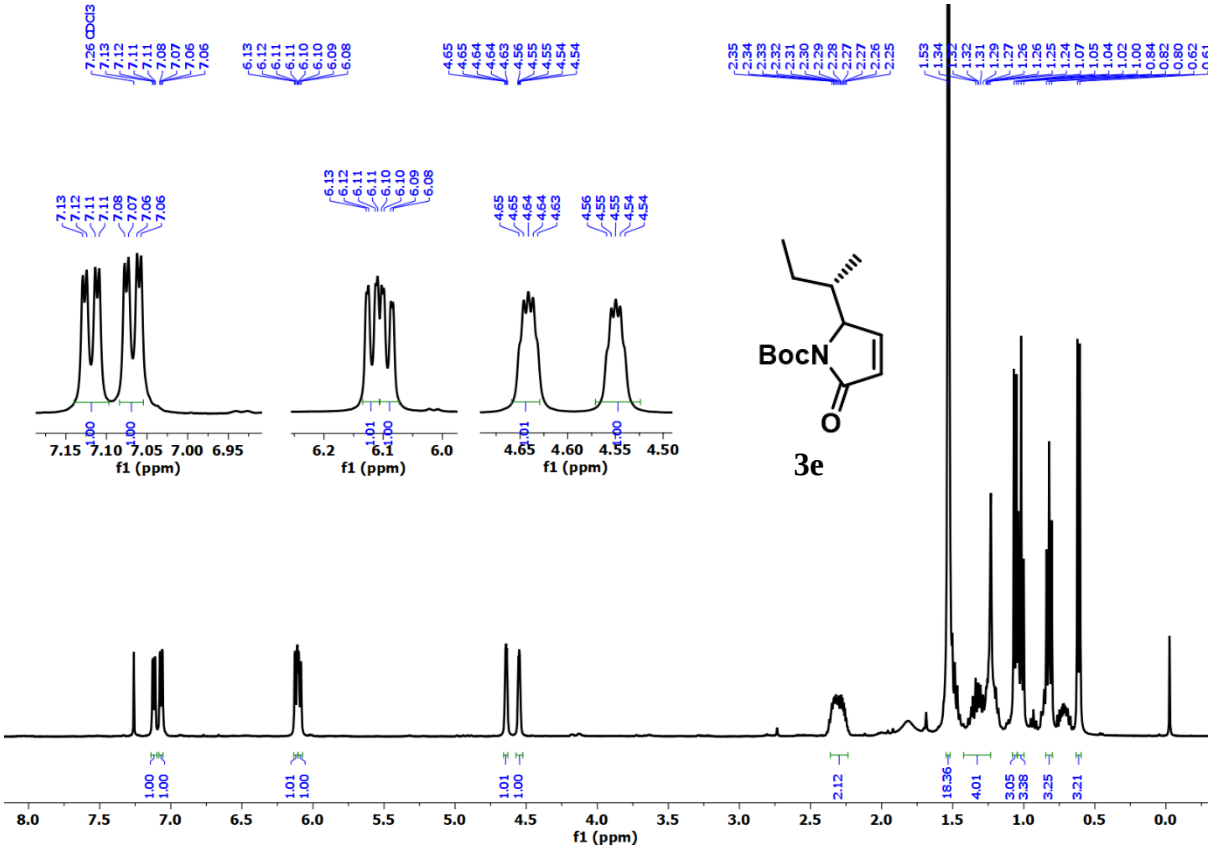

7.26 CHLOROFORM-D
7.13
7.12
7.11
7.11
6.15
6.14
6.13
6.13
4.56
4.56
4.56
4.55
4.54
4.54
2.62
2.61
2.60
2.60
2.59
2.58
2.57
2.56
2.55
1.54
1.10
1.08
0.67
0.65
BocN
O
3c
f1 (ppm)
1.00
1.00
1.00
1.05
9.05
3.02
3.01

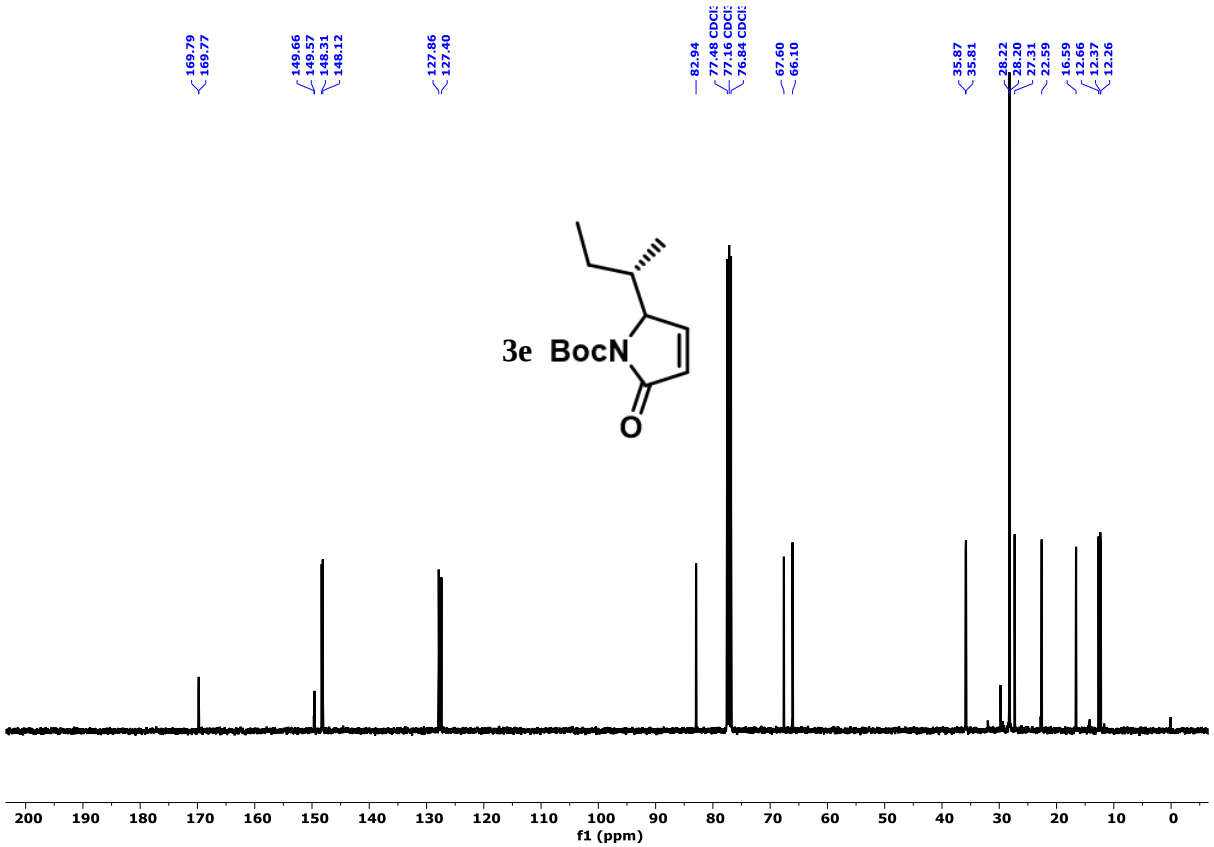

169.70
149.73
147.94
127.92
83.00
77.48 CHLOROFORM-D
77.16 CHLOROFORM-D
76.84 CHLOROFORM-D
67.41
28.99
28.23
19.63
14.98
3c
BocN
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

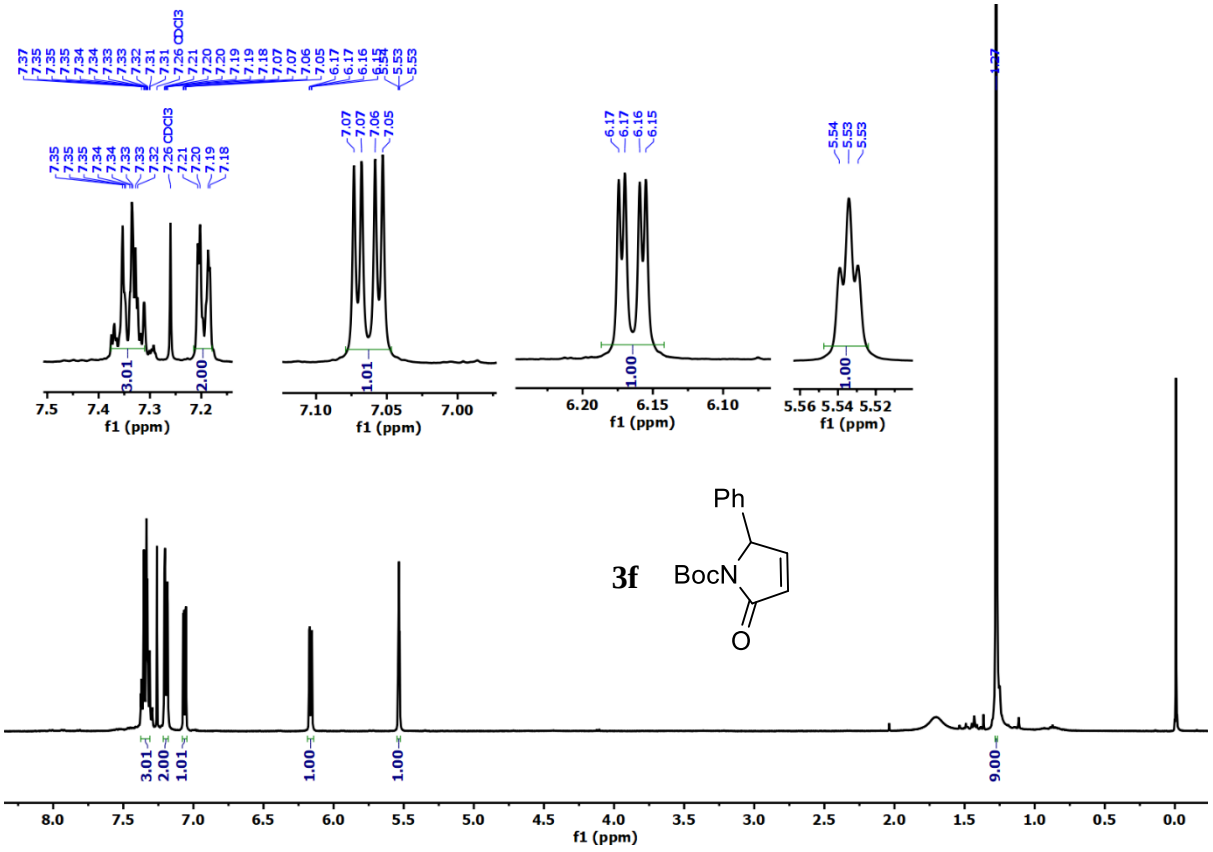

7.26 CDCl3
7.10
7.09
7.08
7.08
6.07
6.06
6.05
6.05
4.62
4.62
4.61
4.61
4.60
4.60
1.56
1.44
1.42
7.12
7.10
7.08
7.06
f1 (ppm)
6.10
6.08
6.06
6.04
6.02
f1 (ppm)
3d
BocN
O
1.00
1.00
1.00
9.08
3.06
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

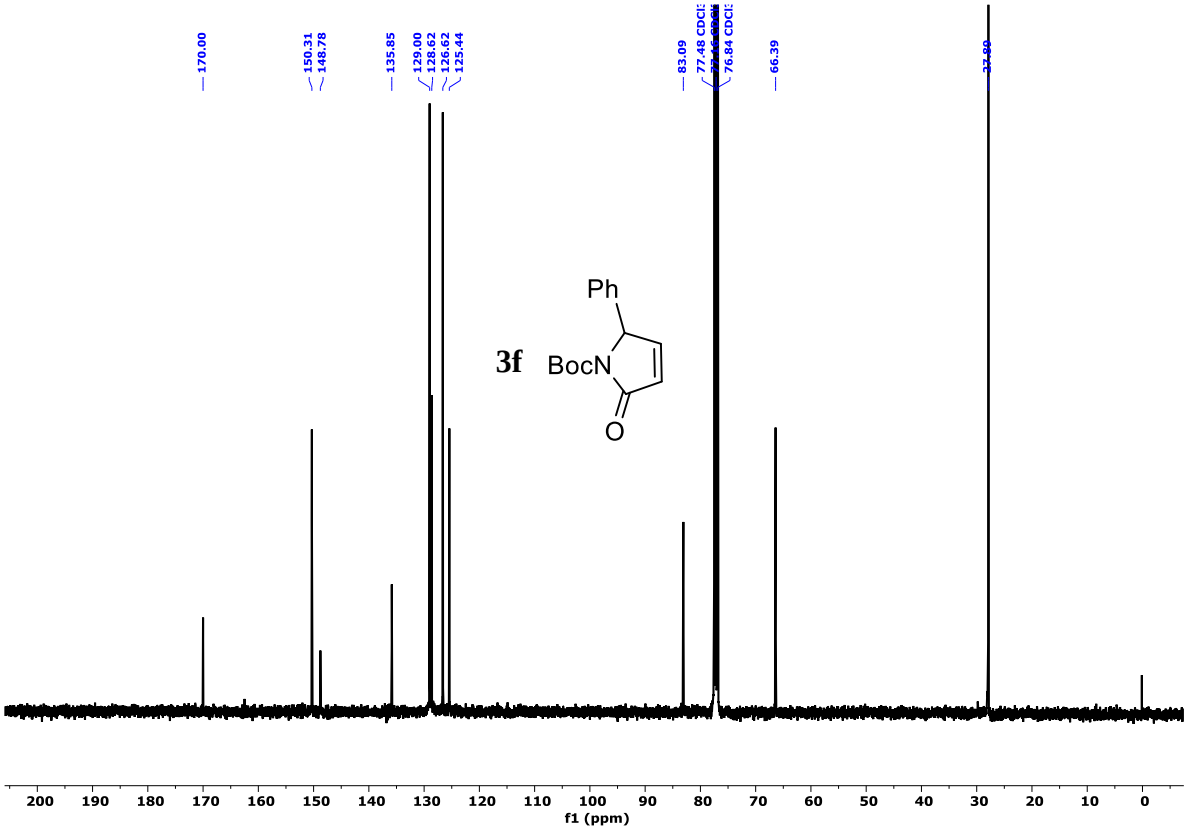

169.30
151.90
149.53
126.07
83.04
77.48 CDCl3
76.84 CDCl3
58.53
29.82
28.20
18.30
BocN
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

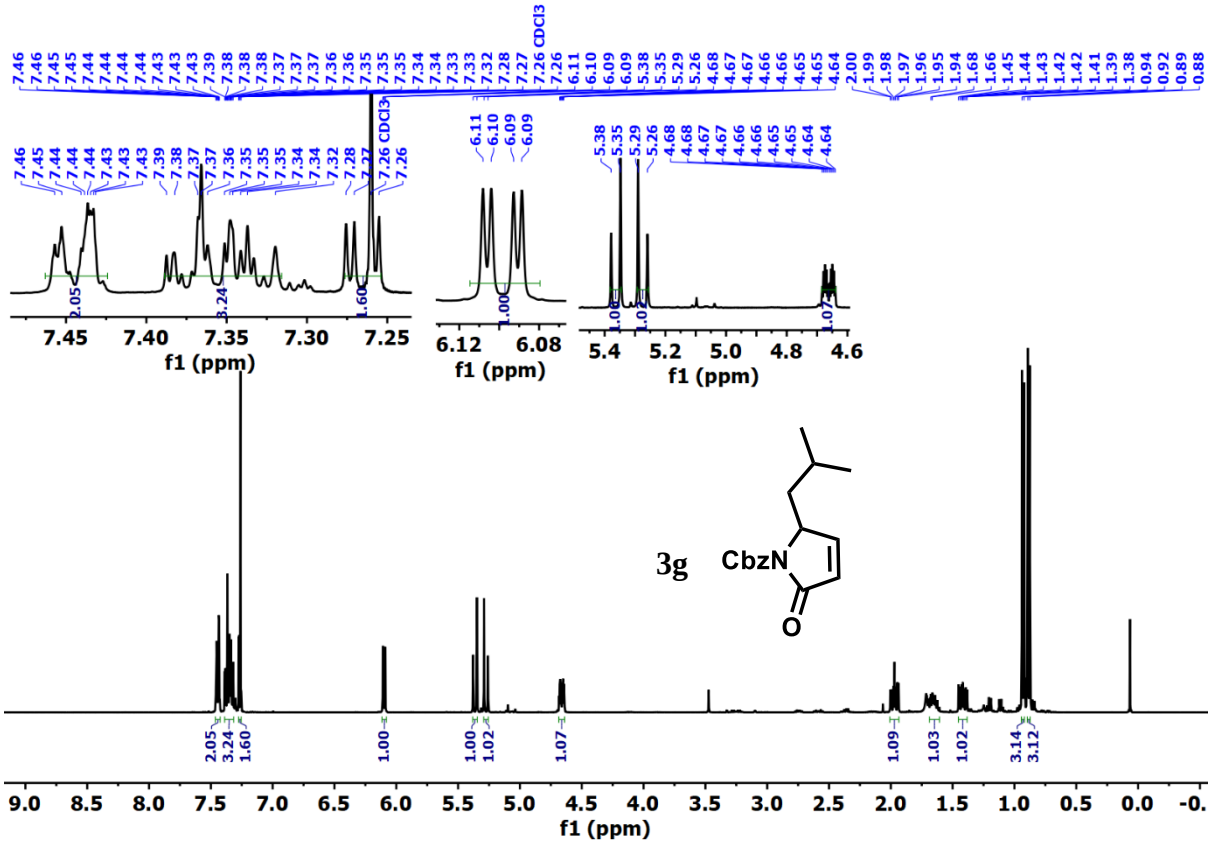
3d

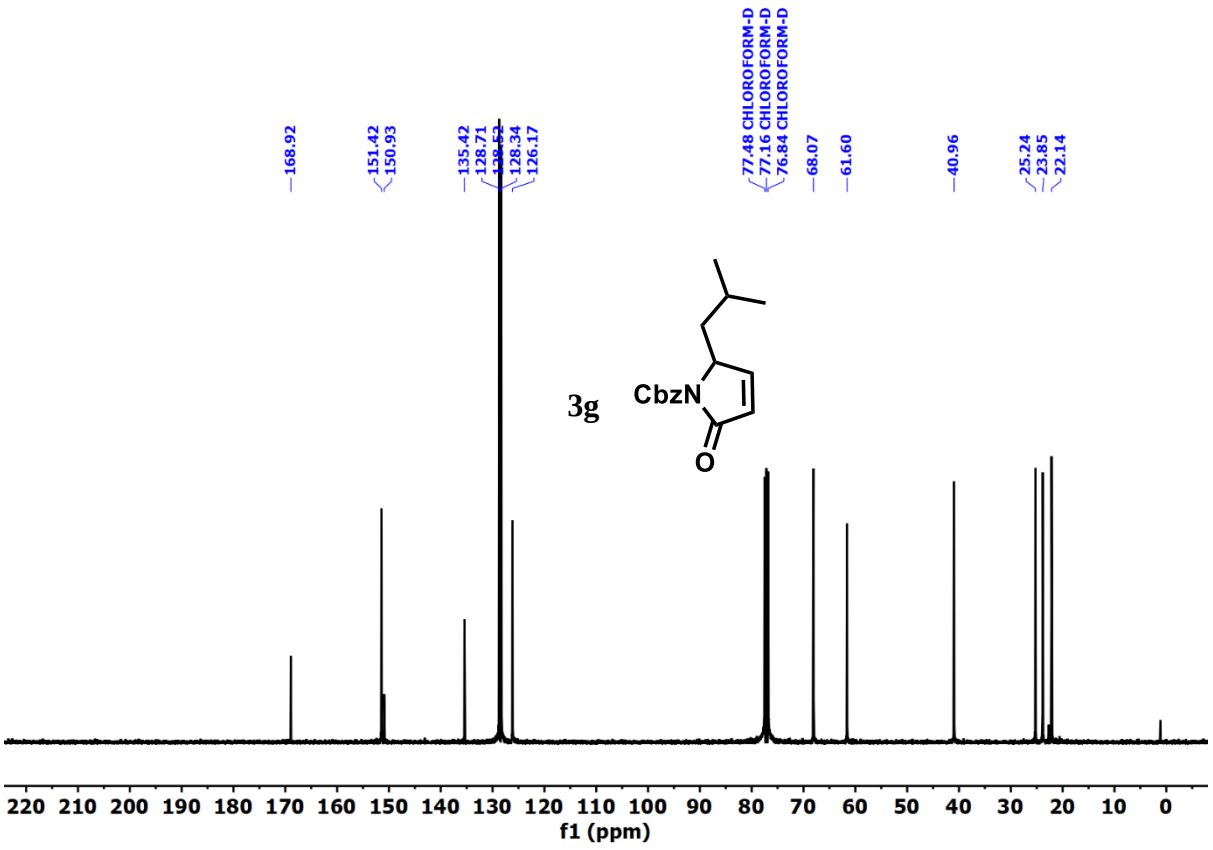

BocN
O
3e
f1 (ppm)

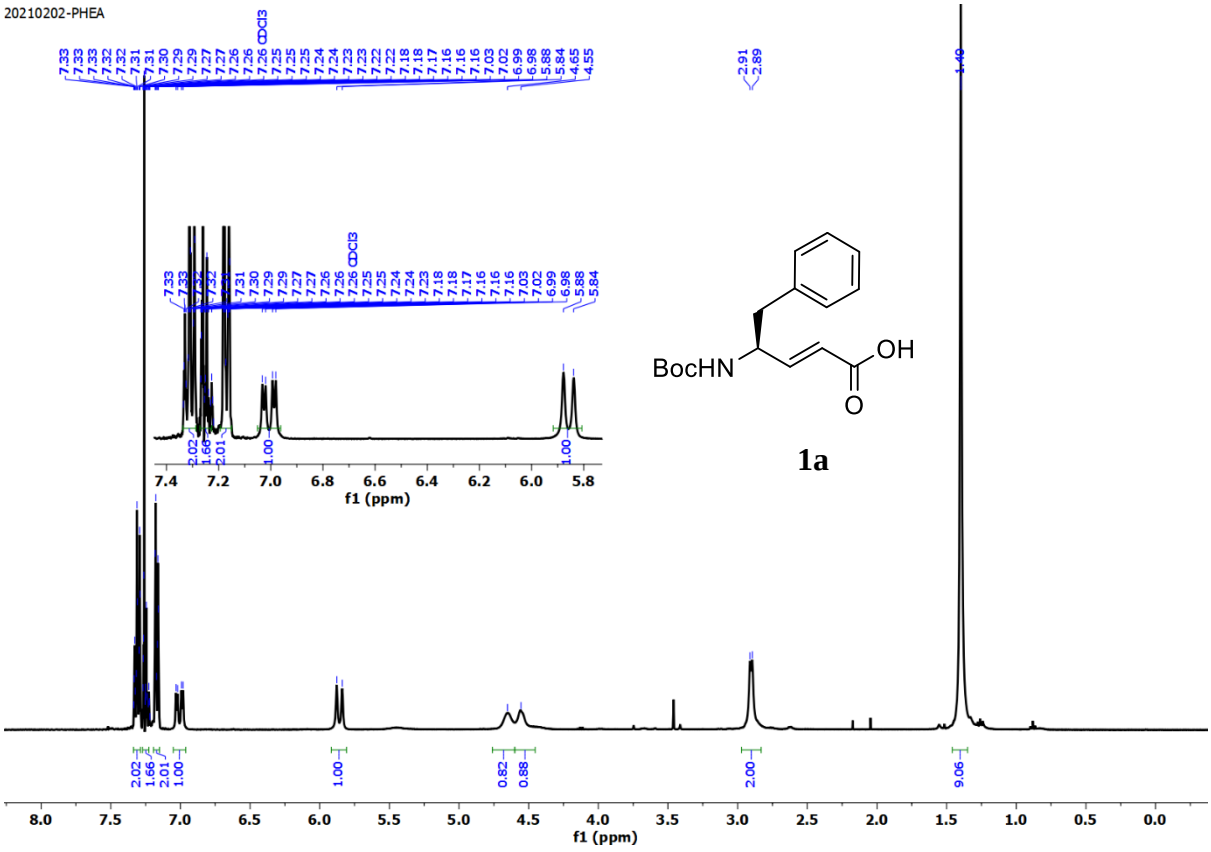

169.79
169.77
149.66
149.57
148.31
148.12
127.86
127.40
82.94
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
67.60
66.10
35.87
35.81
28.22
28.20
27.31
22.59
16.59
12.66
12.37
12.26
3e BocN
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

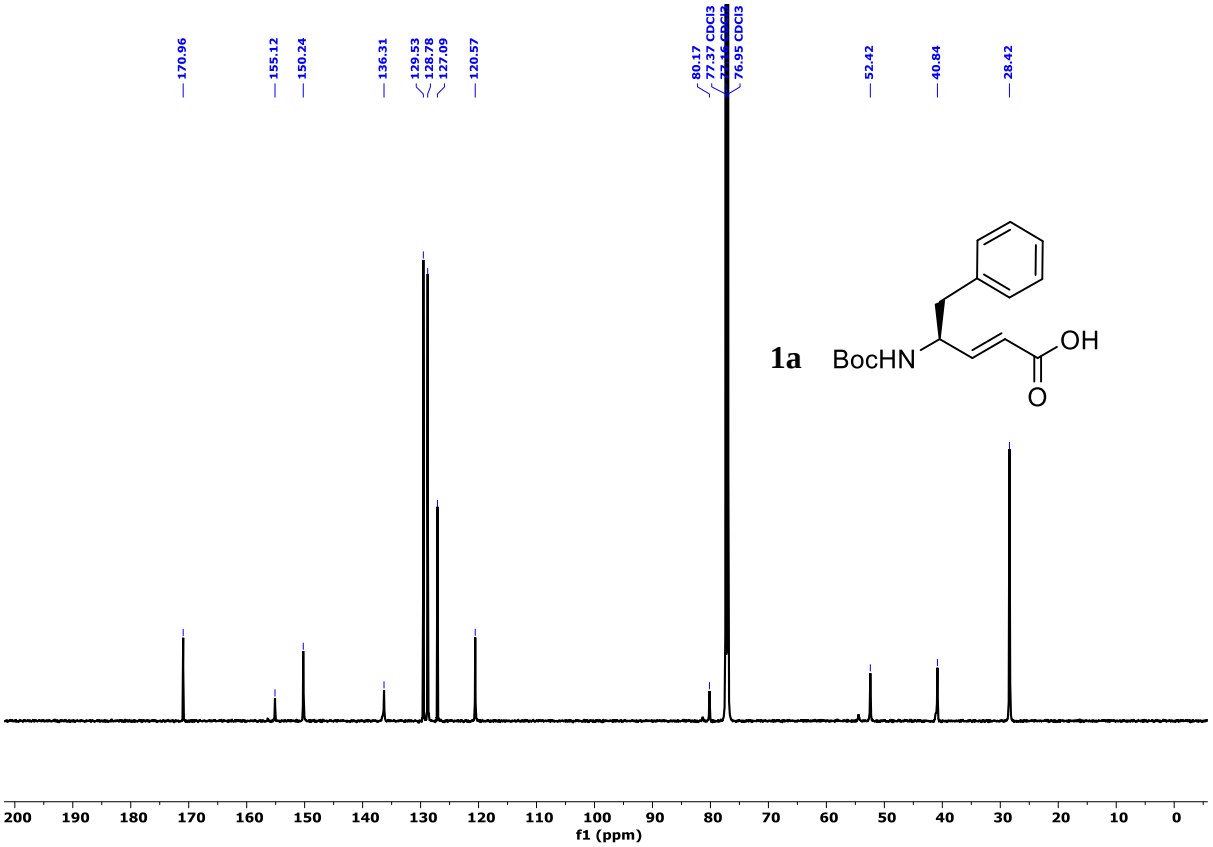

3f
Ph
BocN
O
f1 (ppm)

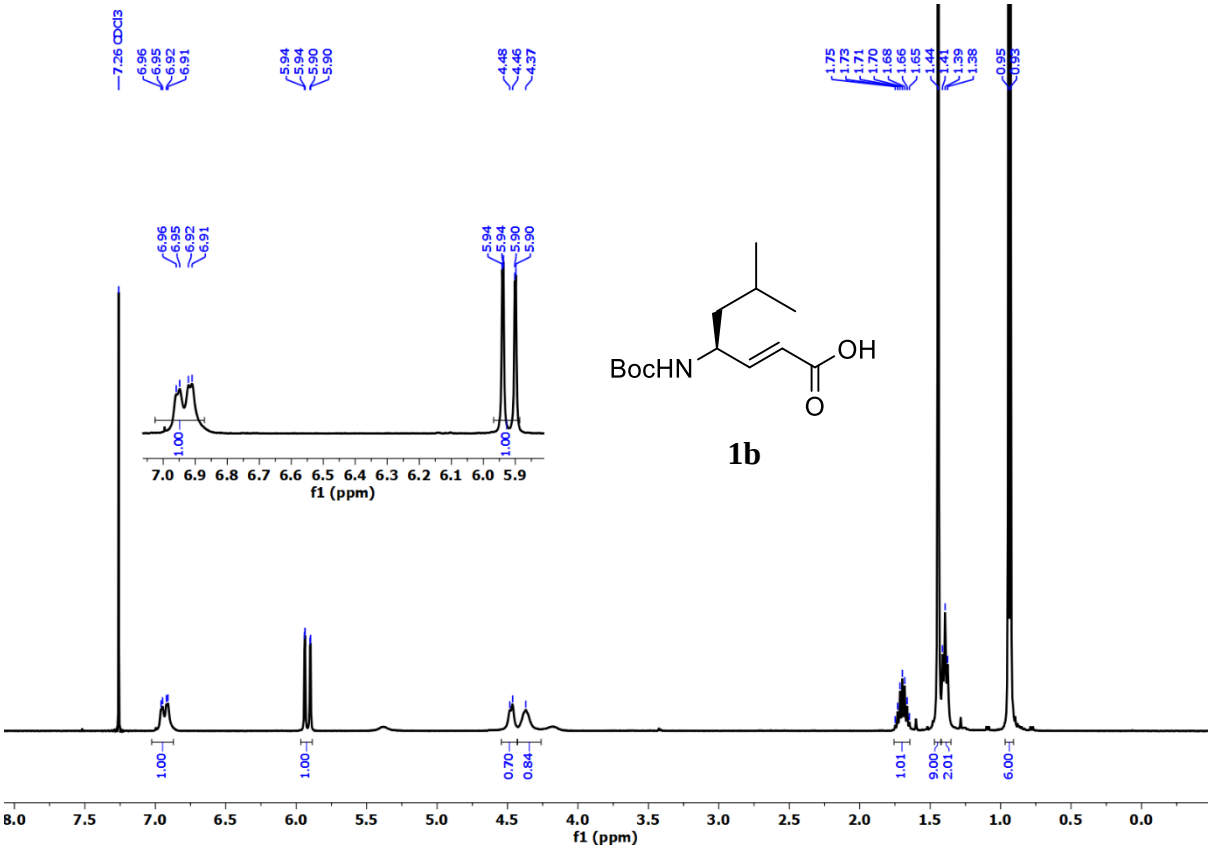

170.00
150.31
148.78
135.85
129.00
128.62
126.62
125.44
83.09
77.48 CDCl3
76.84 CDCl3
66.39
27.89
3f
Ph
BocN
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


3g
CbzN
O
f1 (ppm)

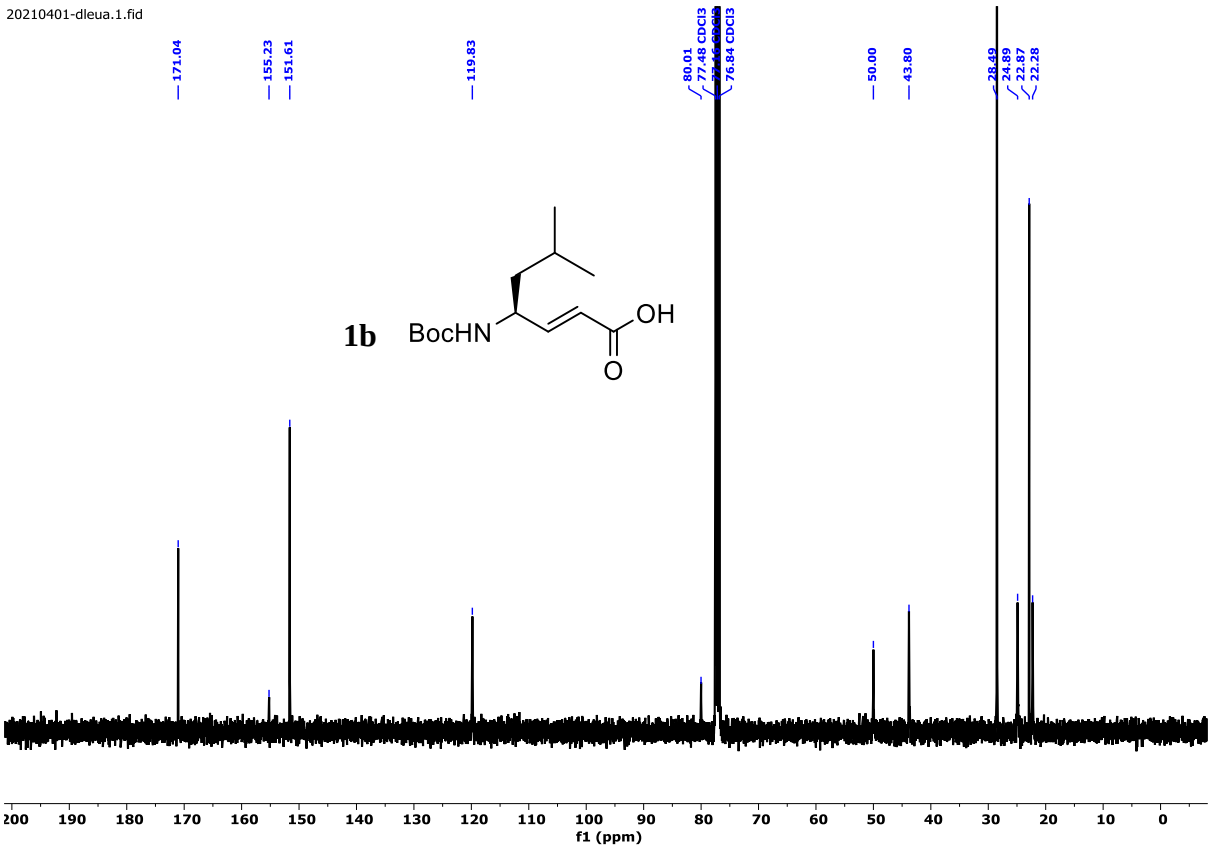

168.92
151.42
150.93
135.42
128.71
128.53
128.34
126.17
77.48 CHLOROFORM-D
77.16 CHLOROFORM-D
76.84 CHLOROFORM-D
68.07
61.60
40.96
25.24
23.85
22.14
3g
CbzN
O
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


20210202-PHEA
BocHN
OH
O
1a
f1 (ppm)

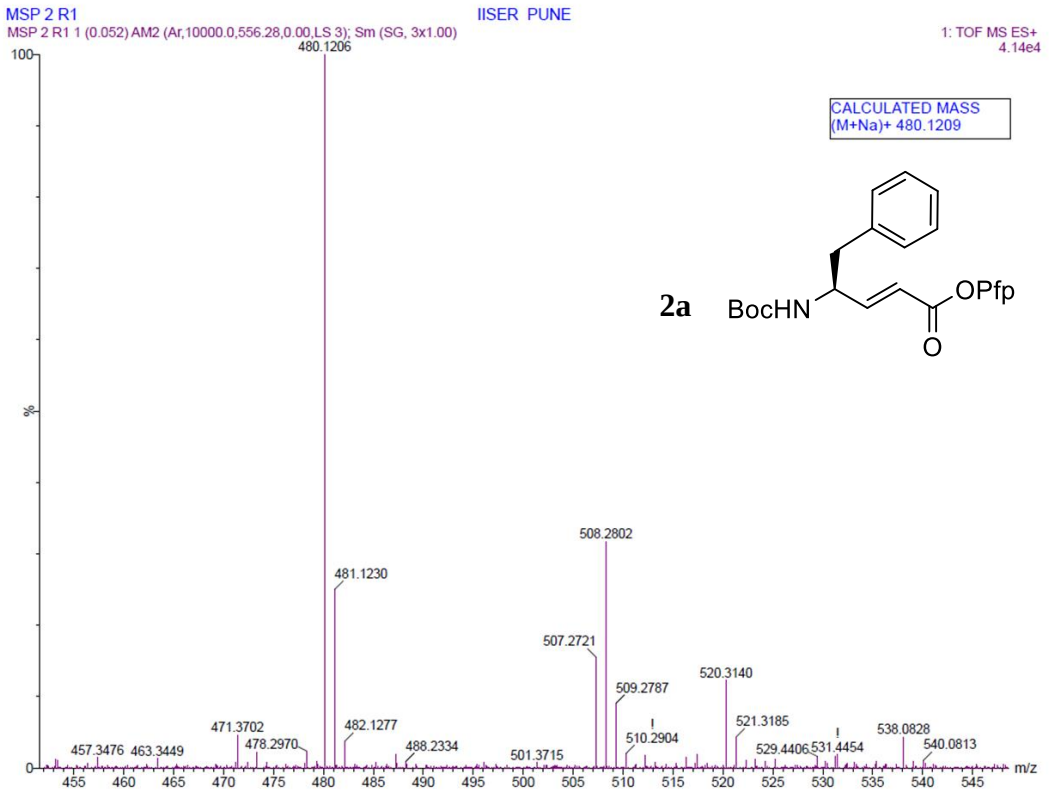

170.96
155.12
150.24
136.31
129.53
128.78
127.09
120.57
80.17
77.37 CDCl3
76.95 CDCl3
52.42
40.84
28.42
1a
BocHN
OH
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

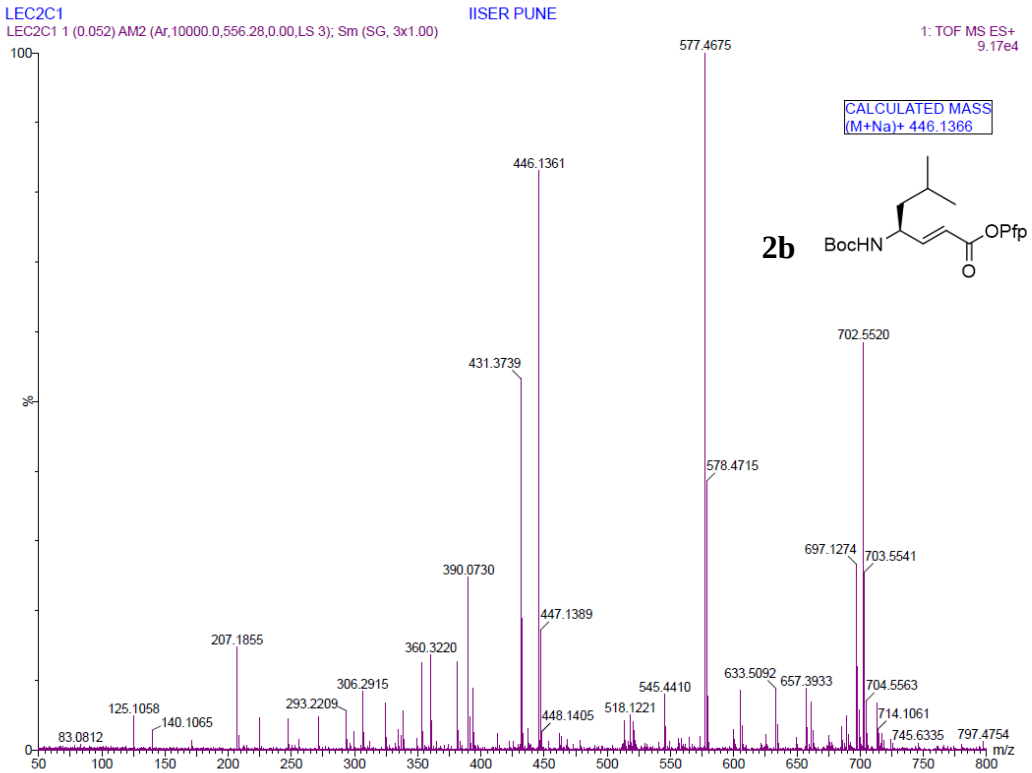

7.26 CDCl3
6.96
6.95
6.92
6.91
5.94
5.94
5.90
5.90
4.48
4.46
4.37
1.75
1.73
1.71
1.70
1.68
1.66
1.65
1.44
1.41
1.39
1.38
0.95
0.93
1.00
1.00
1.00
0.70
0.84
1.01
9.00
2.01
6.00
f1 (ppm)
BocHN
OH
O

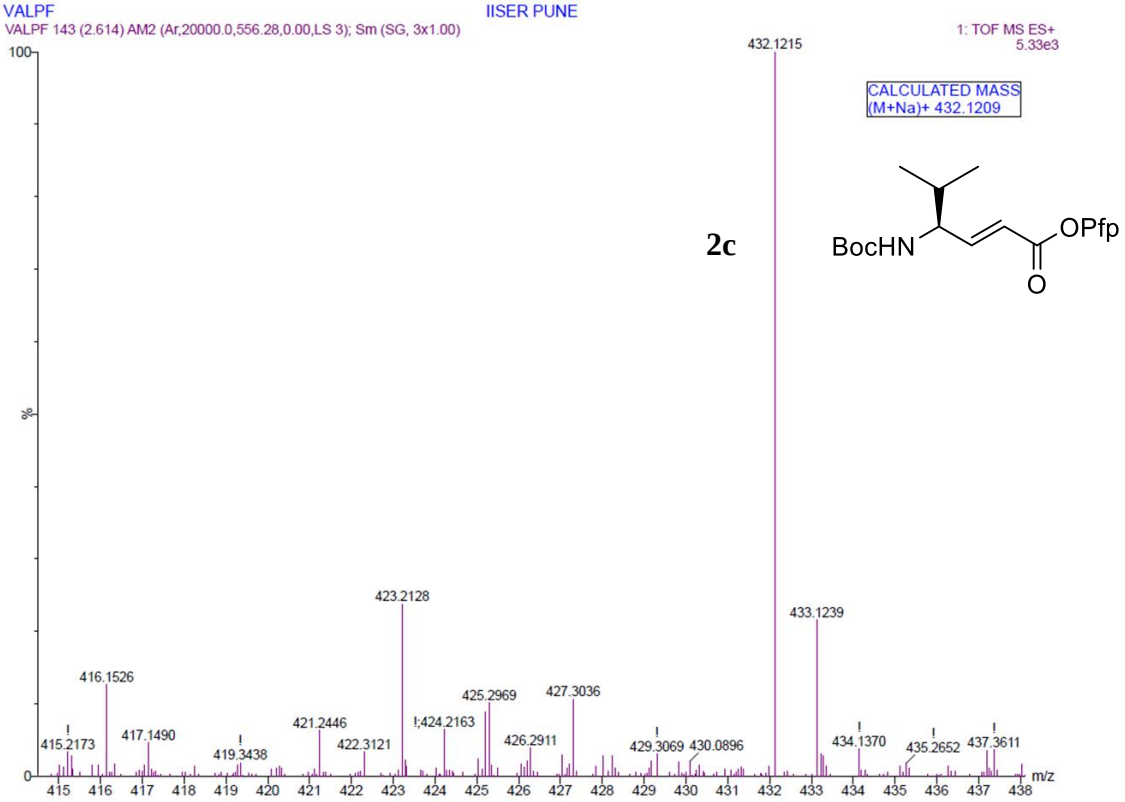
1b

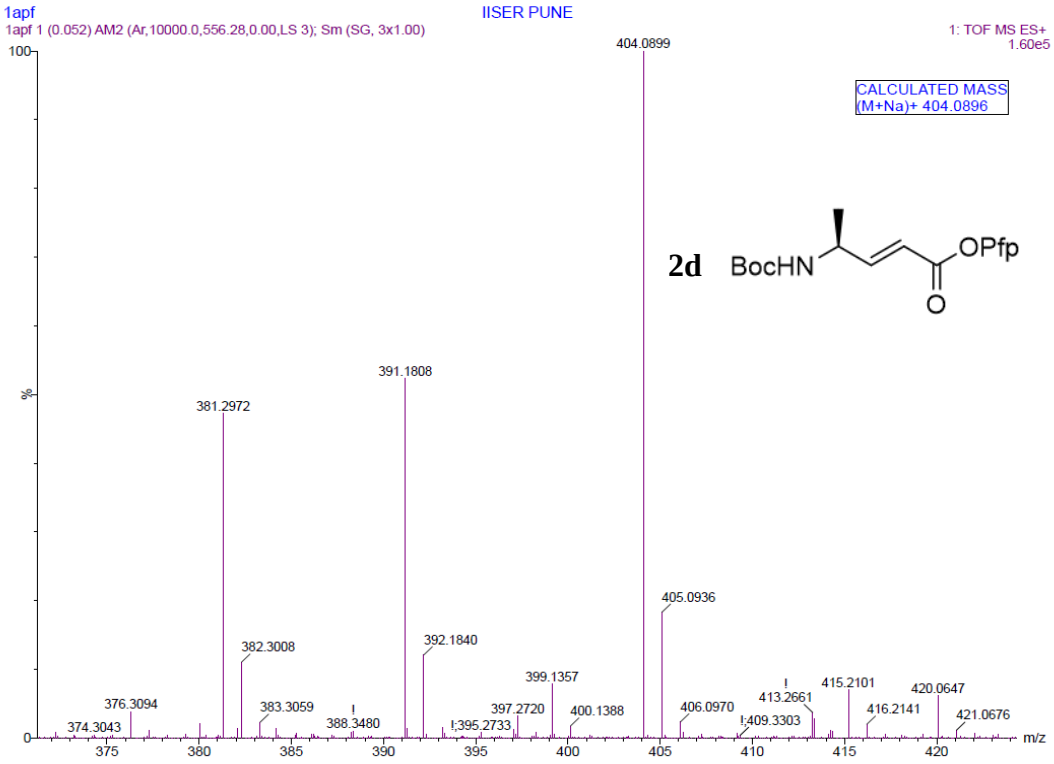

20210401-dleua.1.fid
171.04
155.23
151.61
119.83
80.01
77.48 CDCl3
76.84 CDCl3
50.00
43.80
28.49
24.89
22.87
22.28
1b
BocHN
OH
O
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

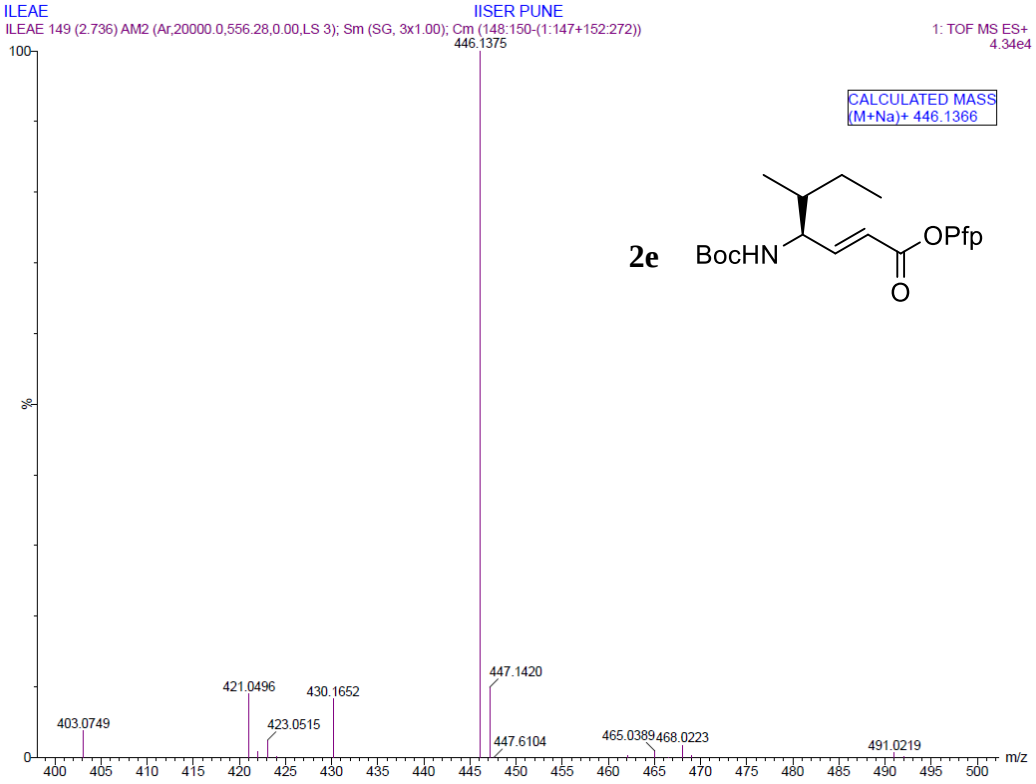
9.1. Mass Spectra of compounds

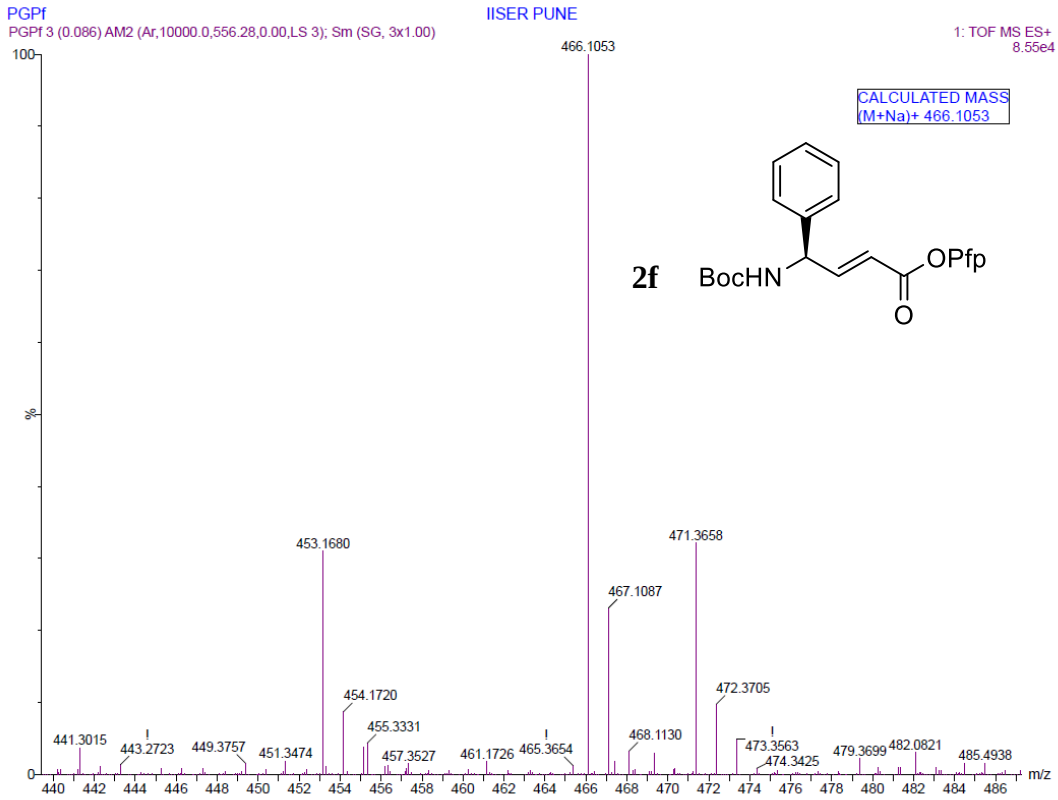


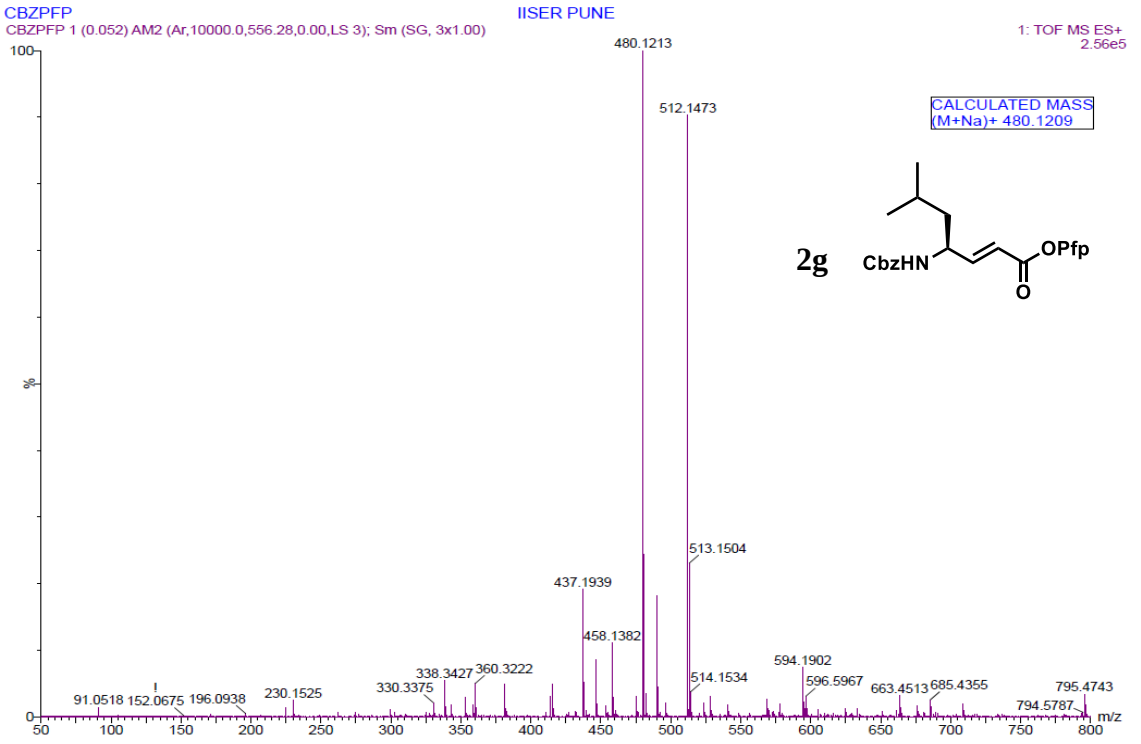


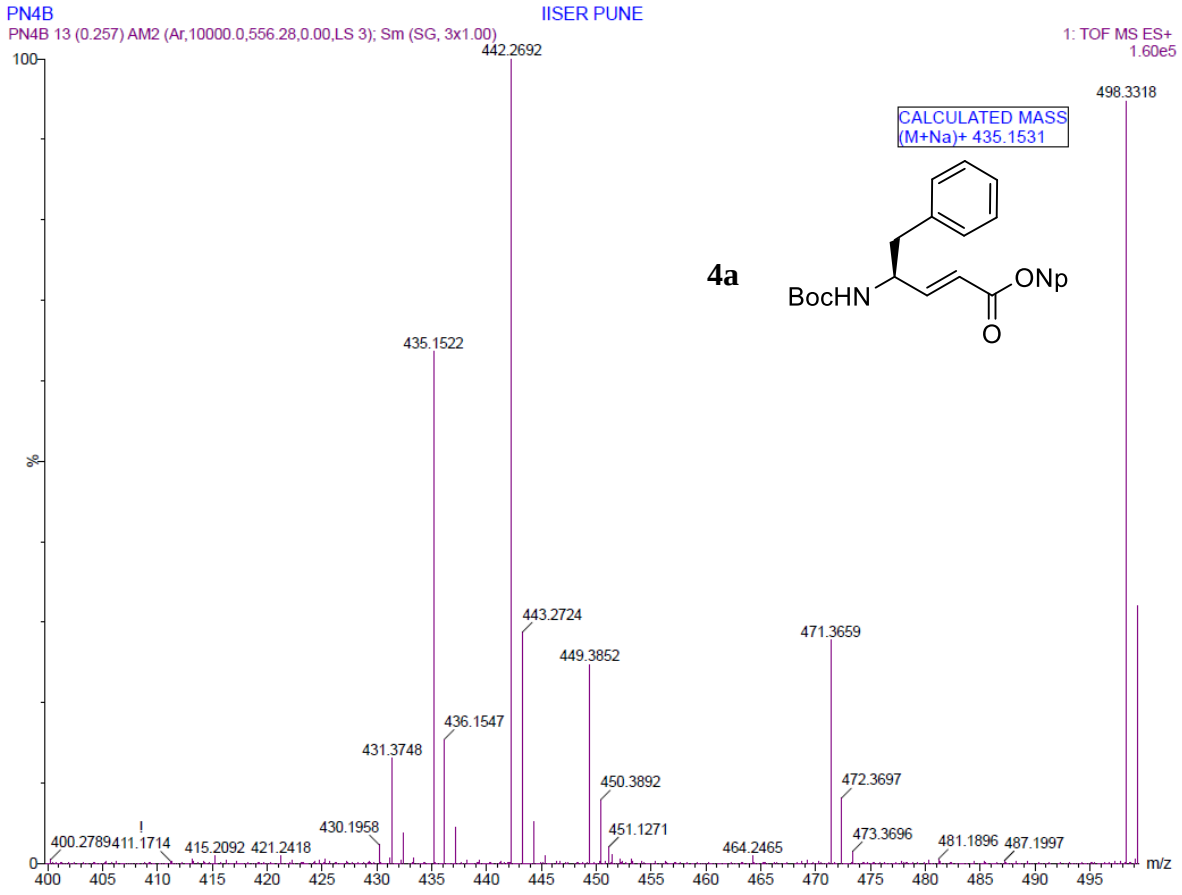

VALPF
IISER PUNE
VALPF 143 (2.614) AM2 (Ar,20000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
5.33e3
CALCULATED MASS
(M+Na)+ 432.1209
2c
BocHN
OPfp
O
432.1215
423.2128
433.1239
416.1526
425.2969
427.3036
421.2446
424.2163
415.2173
417.1490
419.3438
422.3121
426.2911
429.3069
430.0896
434.1370
435.2652
437.3611
%
m/z

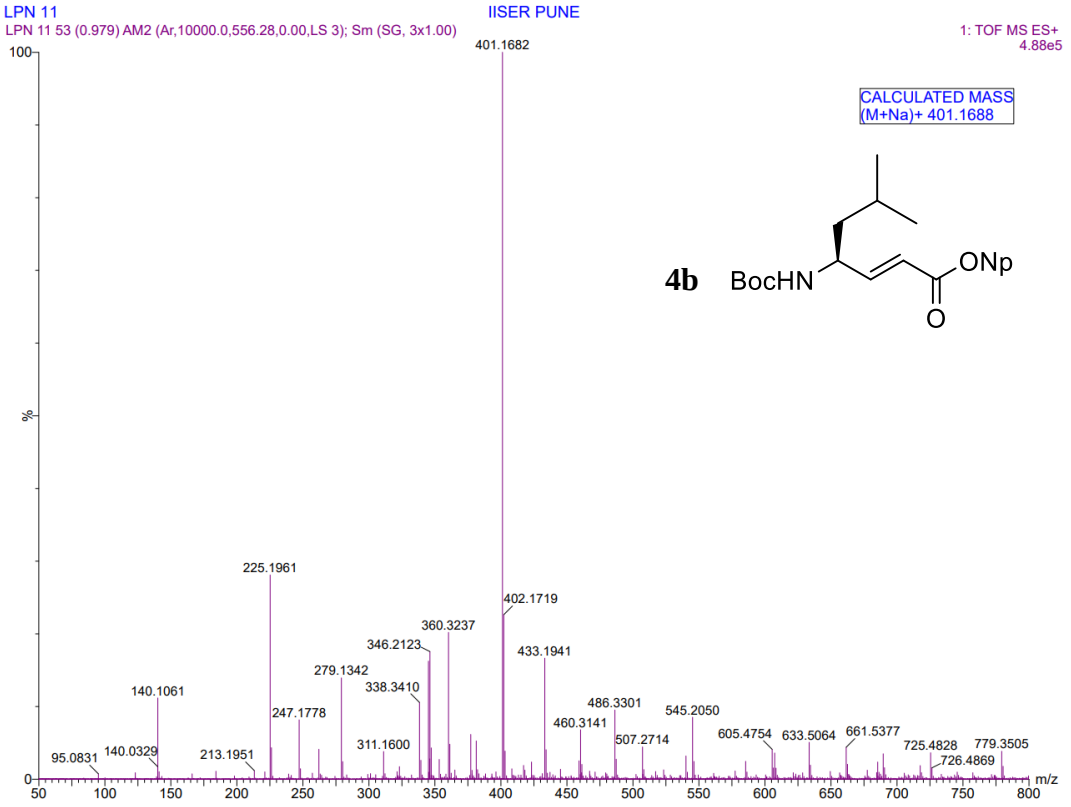

1apf
IISER PUNE
1apf 1 (0.052) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
1.60e5
CALCULATED MASS
(M+Na)+ 404.0896
2d
BocHN
OPfp
O
404.0899
391.1808
381.2972
405.0936
382.3008
392.1840
399.1357
376.3094
374.3043
383.3059
388.3480
397.2720
395.2733
400.1388
406.0970
409.3303
413.2661
415.2101
416.2141
420.0647
421.0676
%
m/z

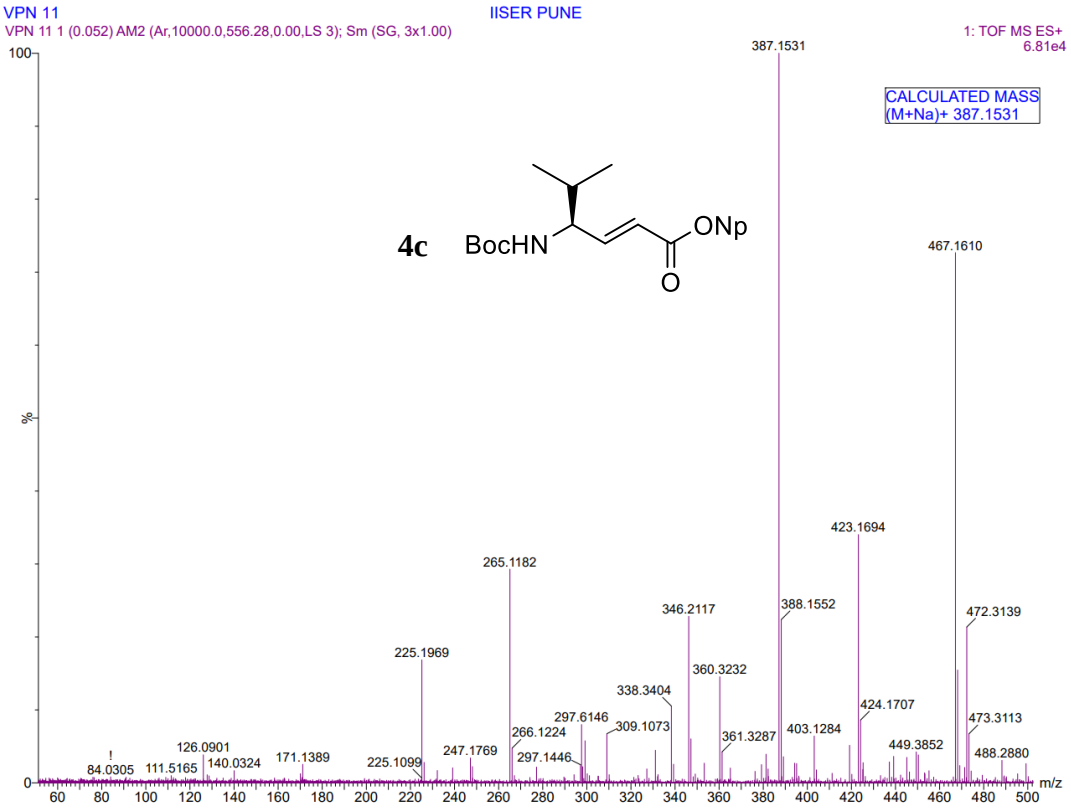

ILEAE
IISER PUNE
ILEAE 149 (2.736) AM2 (Ar,20000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00); Cm (148:150-(1:147+152:272))
1: TOF MS ES+
4.34e4
446.1375
CALCULATED MASS
(M+Na)+ 446.1366
2e
BocHN
OPfp
O
447.1420
421.0496
430.1652
403.0749
423.0515
447.6104
465.0389
468.0223
491.0219
%
m/z

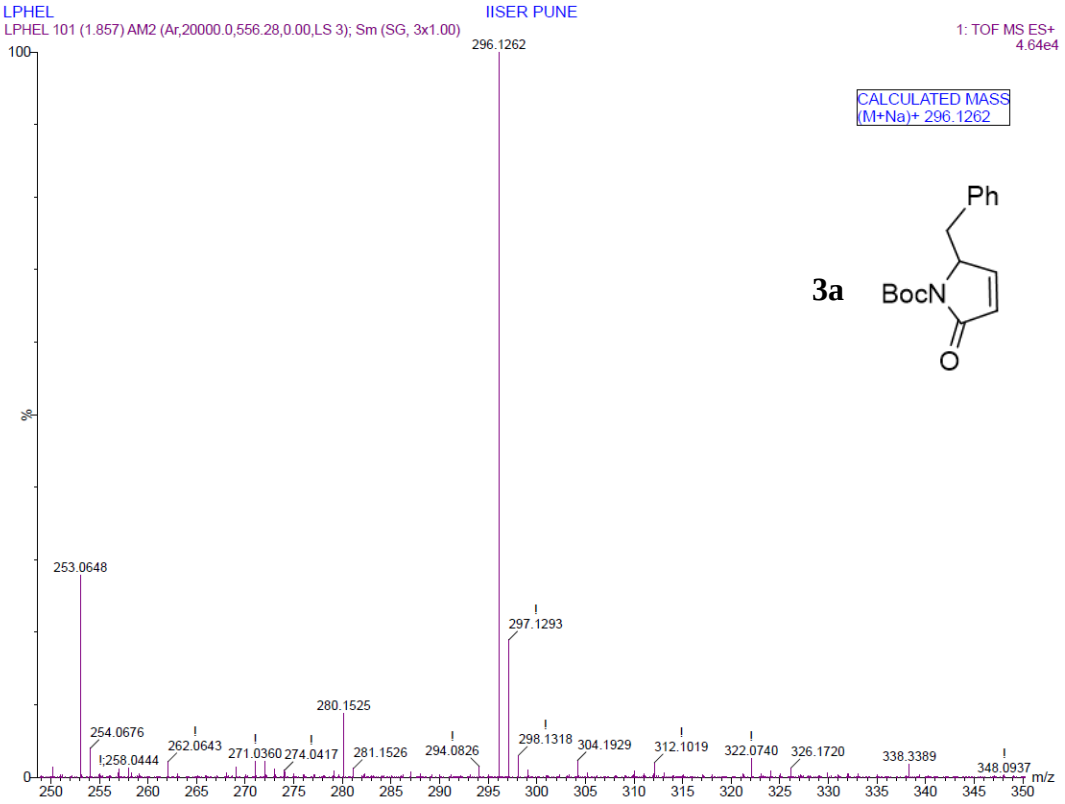

PGPf
IISER PUNE
PGPf 3 (0.086) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
8.55e4
466.1053
CALCULATED MASS
(M+Na)+ 466.1053
2f
BocHN
OPfp
O
453.1680
471.3658
467.1087
454.1720
472.3705
455.3331
441.3015
443.2723
449.3757
451.3474
457.3527
461.1726
465.3654
468.1130
473.3563
474.3425
479.3699
482.0821
485.4938
%
m/z

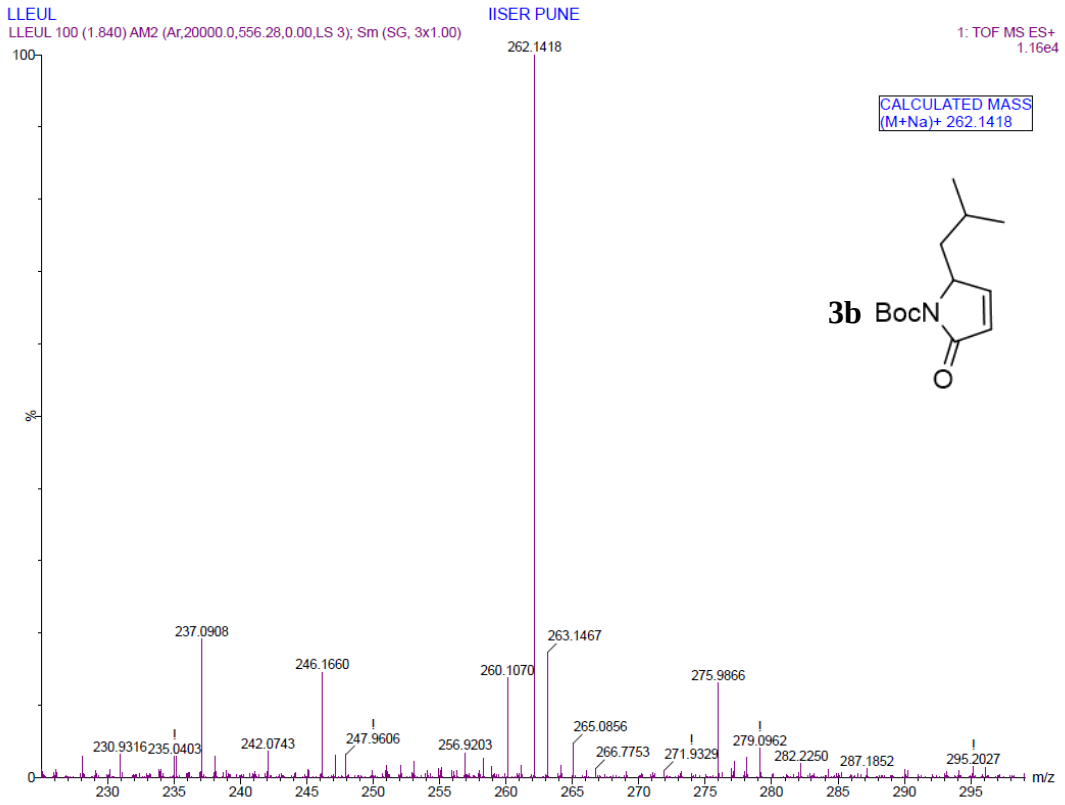

CBZPFP
IISER PUNE
CBZPFP 1 (0.052) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
2.56e5
CALCULATED MASS
(M+Na)+ 480.1209
2g
CbzHN
OPfp
O
480.1213
512.1473
513.1504
437.1939
458.1382
514.1534
594.1902
596.5967
663.4513
685.4355
795.4743
794.5787
338.3427
360.3222
330.3375
91.0518
152.0675
196.0938
230.1525
%
m/z

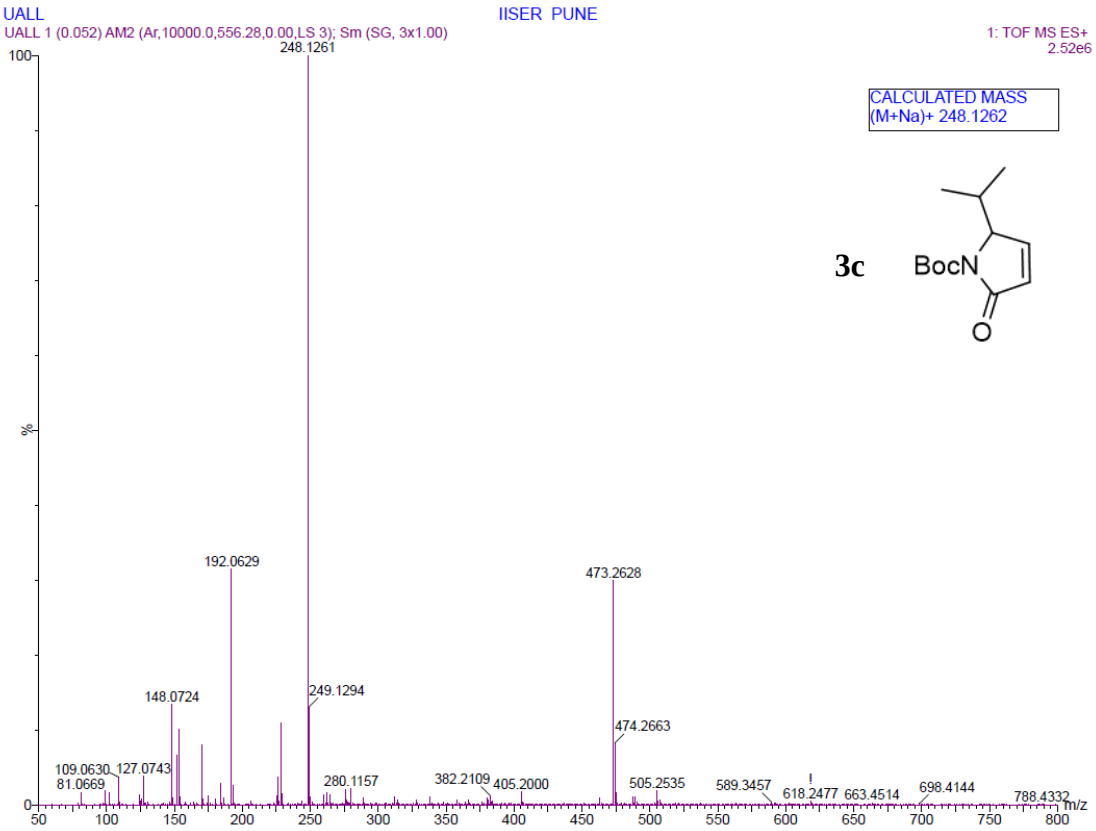

PN4B
IISER PUNE
PN4B 13 (0.257) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
1.60e5
CALCULATED MASS
(M+Na)+ 435.1531
4a
BocHN
ONp
O
442.2692
498.3318
435.1522
443.2724
471.3659
449.3852
436.1547
431.3748
450.3892
472.3697
430.1958
451.1271
473.3696
481.1896
487.1997
400.2789
411.1714
415.2092
421.2418
464.2465
%
m/z

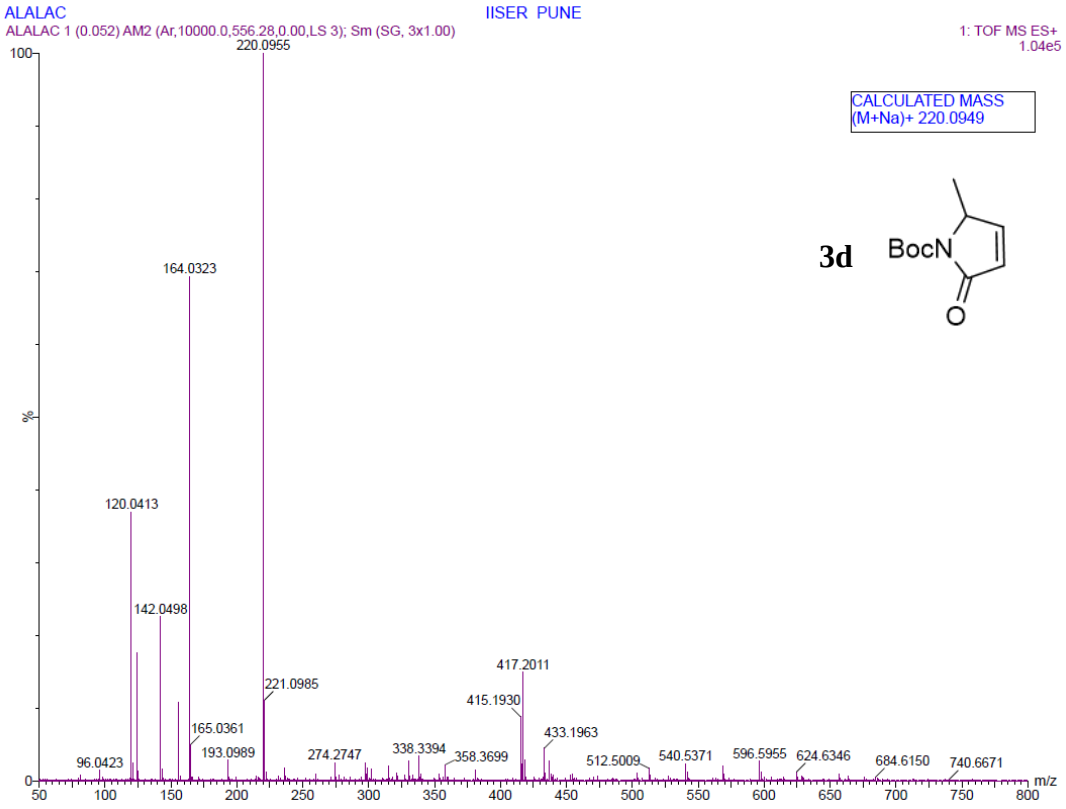

LPN 11
IISER PUNE
LPN 11 53 (0.979) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
4.88e5
CALCULATED MASS
(M+Na)+ 401.1688
4b
BocHN
ONp
O
401.1682
225.1961
402.1719
360.3237
346.2123
433.1941
279.1342
338.3410
140.1061
247.1778
486.3301
545.2050
460.3141
507.2714
605.4754
633.5064
661.5377
725.4828
779.3505
726.4869
95.0831
140.0329
213.1951
311.1600
m/z

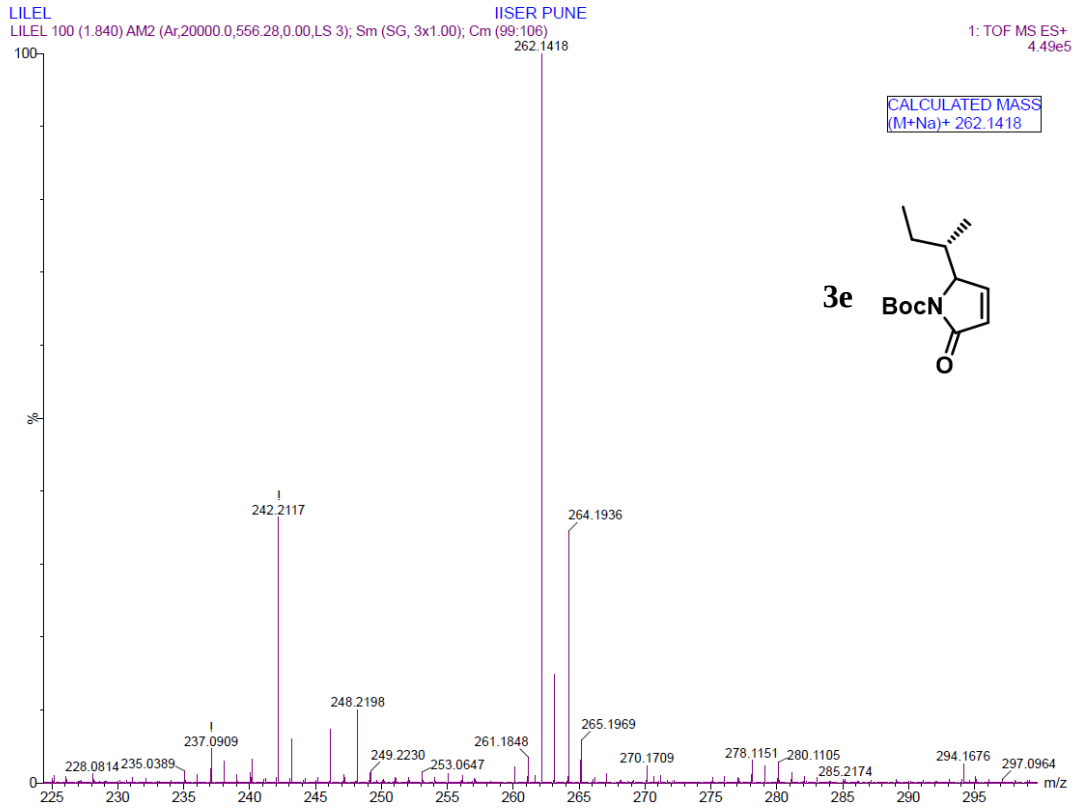

VPN 11
IISER PUNE
VPN 11 1 (0.052) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
6.81e4
CALCULATED MASS
(M+Na)+ 387.1531
4c
BocHN
ONp
O
387.1531
467.1610
423.1694
265.1182
346.2117
388.1552
472.3139
225.1969
360.3232
338.3404
424.1707
297.6146
309.1073
266.1224
361.3287
403.1284
473.3113
126.0901
247.1769
449.3852
140.0324
171.1389
297.1446
488.2880
84.0305
111.5165
225.1099
m/z

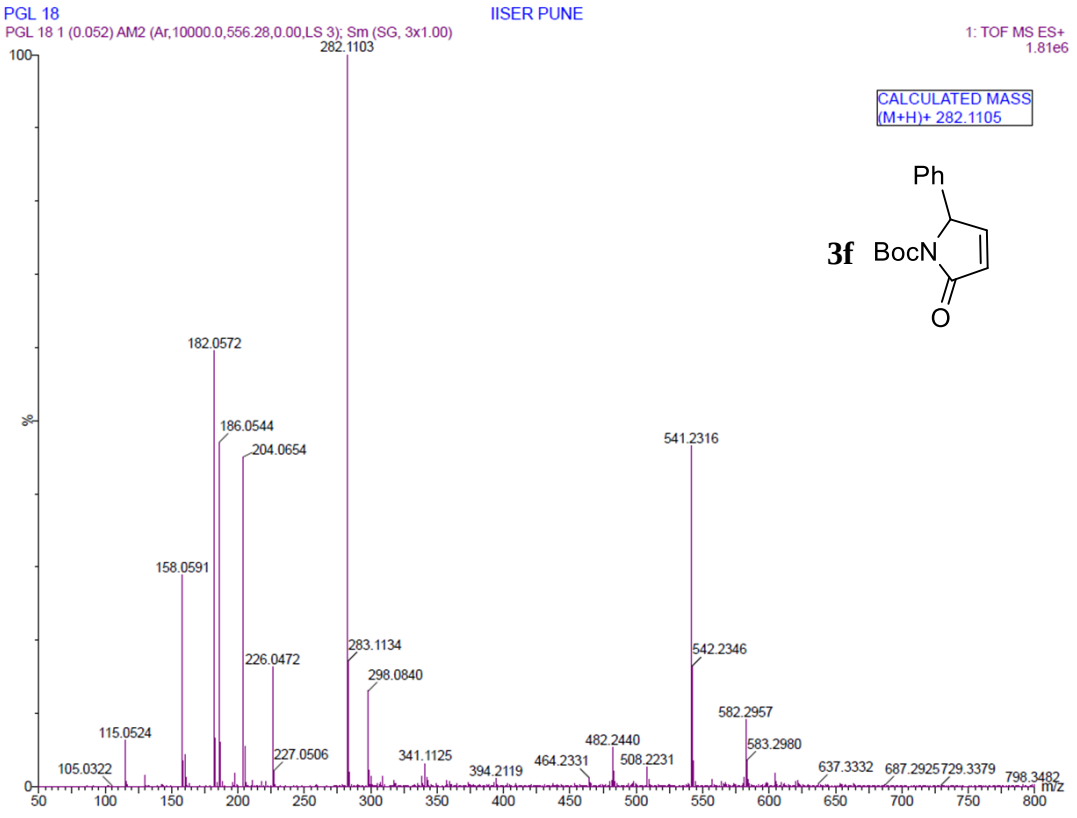

LPHEL
IISER PUNE
LPHEL 101 (1.857) AM2 (Ar,20000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
4.64e4
CALCULATED MASS
(M+Na)+ 296.1262
3a
Ph
BocN
O
296.1262
253.0648
297.1293
280.1525
254.0676
262.0643
258.0444
271.0360
274.0417
281.1526
294.0826
298.1318
304.1929
312.1019
322.0740
326.1720
338.3389
348.0937
m/z

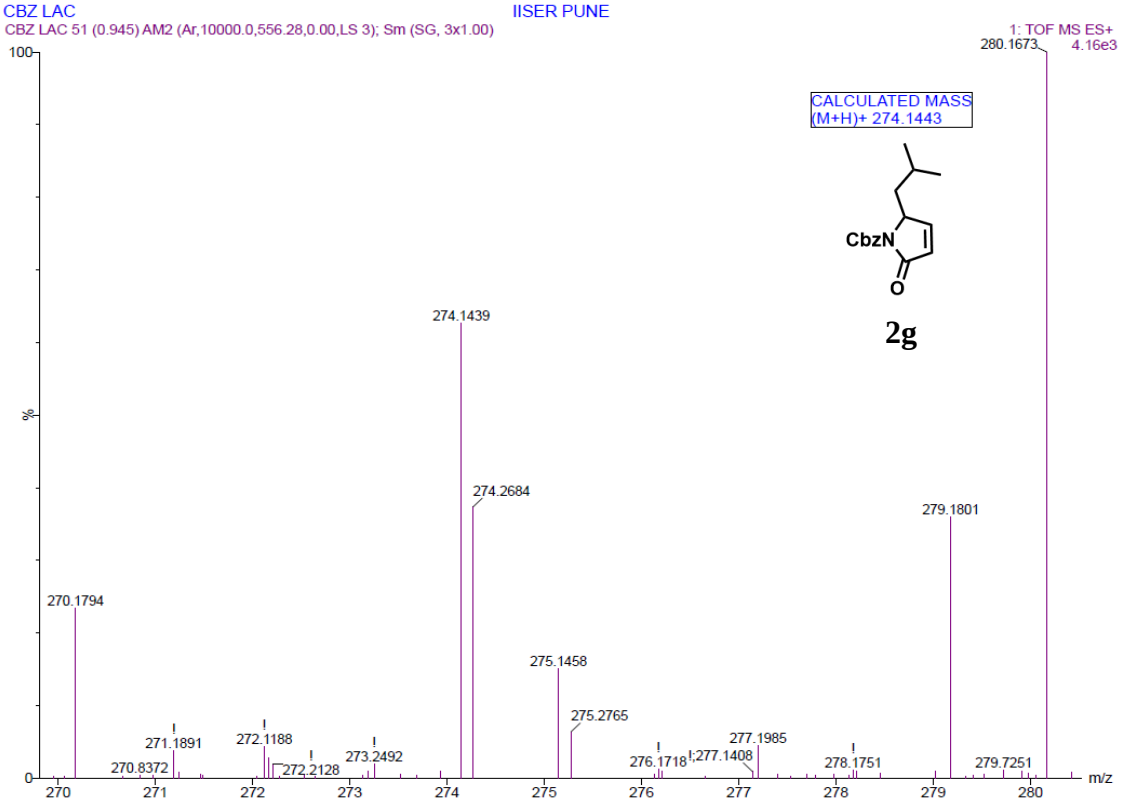

LLEUL
IISER PUNE
LLEUL 100 (1.840) AM2 (Ar,20000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
1.16e4
CALCULATED MASS
(M+Na)+ 262.1418
3b
BocN
O
262.1418
237.0908
246.1660
263.1467
260.1070
275.9866
230.9316
235.0403
242.0743
247.9606
256.9203
265.0856
266.7753
271.9329
279.0962
282.2250
287.1852
295.2027
m/z

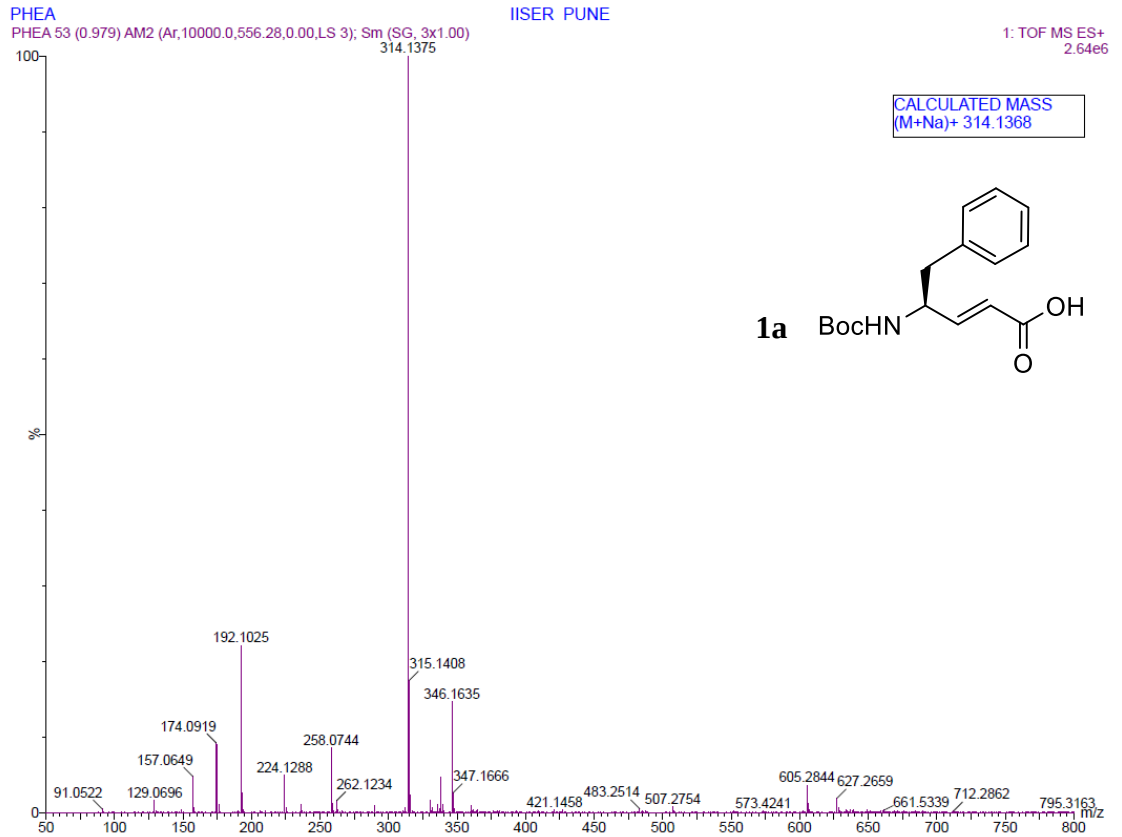

UALL
IISER PUNE
UALL 1 (0.052) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
2.52e6
CALCULATED MASS
(M+Na)+ 248.1262
3c
BocN
O
248.1261
192.0629
473.2628
148.0724
249.1294
474.2663
109.0630
127.0743
81.0669
280.1157
382.2109
405.2000
505.2535
589.3457
618.2477
663.4514
698.4144
788.4332
%
m/z

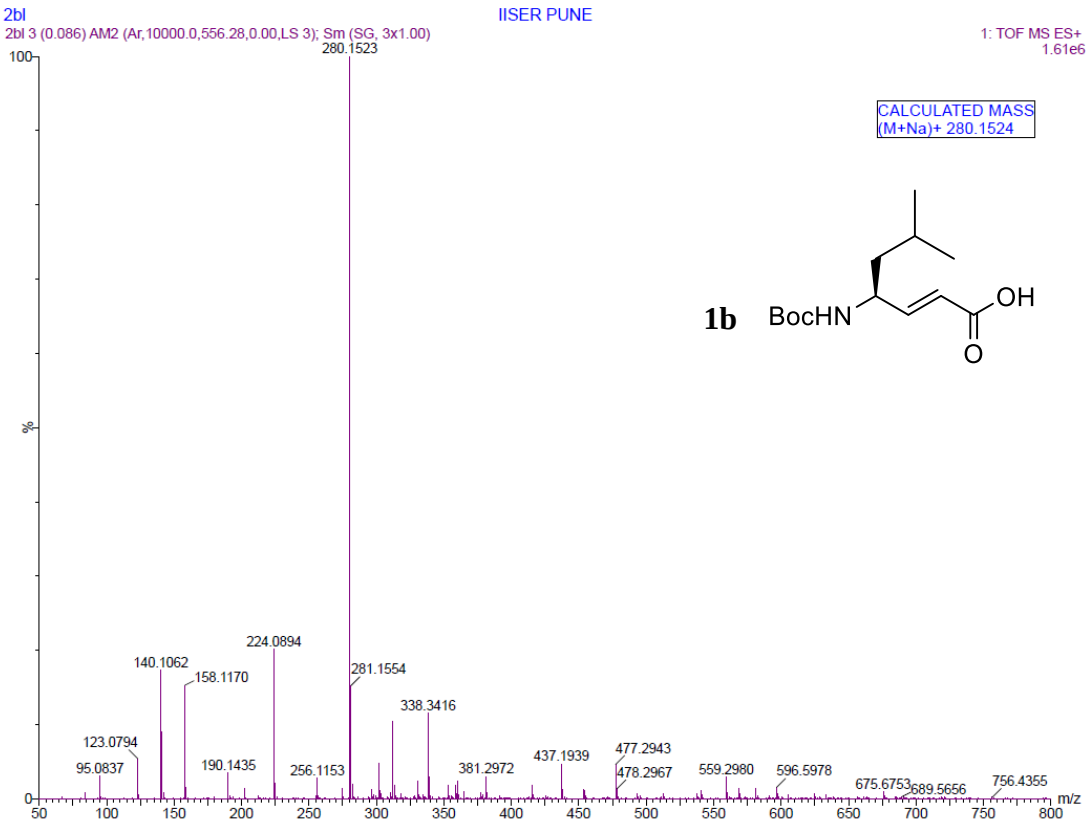

ALALAC
IISER PUNE
ALALAC 1 (0.052) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
1.04e5
CALCULATED MASS
(M+Na)+ 220.0949
3d
BocN
O
220.0955
164.0323
120.0413
142.0498
417.2011
221.0985
415.1930
165.0361
433.1963
96.0423
193.0989
274.2747
338.3394
358.3699
512.5009
540.5371
596.5955
624.6346
684.6150
740.6671
%
m/z


LILEL
IISER PUNE
LILEL 100 (1.840) AM2 (Ar,20000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00); Cm (99:106)
1: TOF MS ES+
4.49e5
CALCULATED MASS
(M+Na)+ 262.1418
3e
BocN
O
262.1418
242.2117
264.1936
248.2198
265.1969
237.0909
261.1848
249.2230
253.0647
270.1709
278.1151
280.1105
285.2174
294.1676
297.0964
228.0814
235.0389
m/z

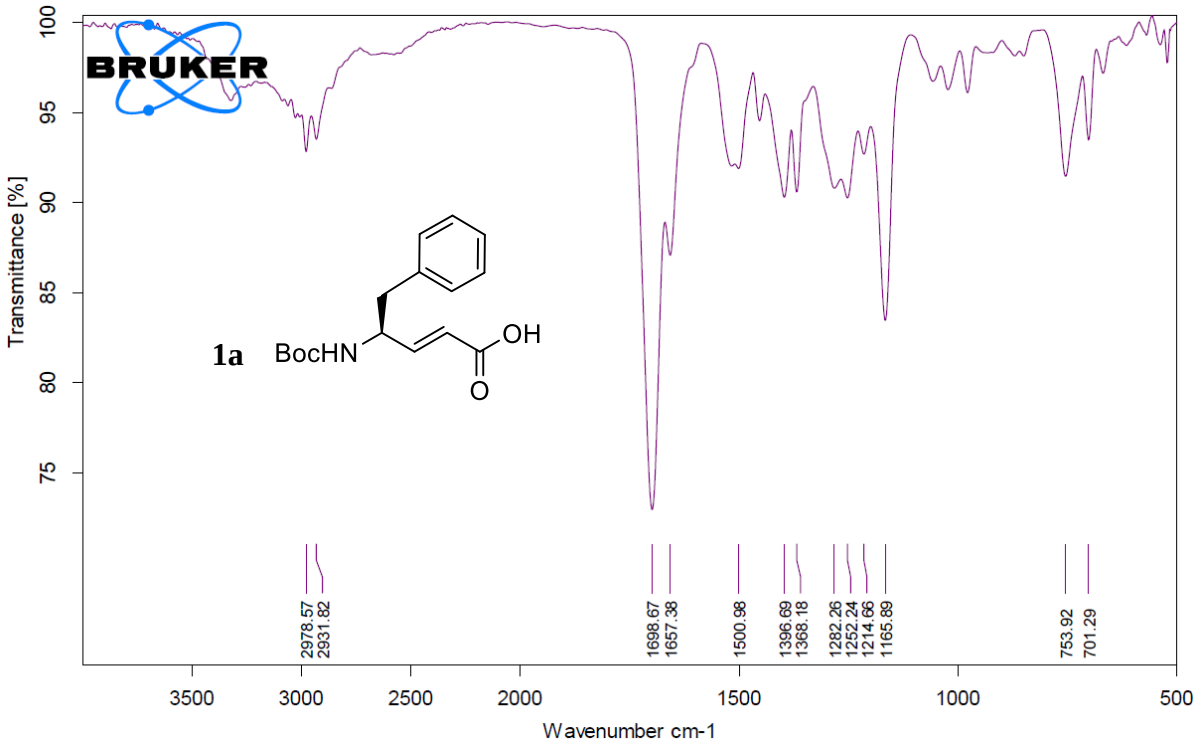

PGL 18
IISER PUNE
PGL 18 1 (0.052) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
1.81e6
CALCULATED MASS
(M+H)+ 282.1105
3f
Ph
BocN
O
282.1103
182.0572
186.0544
204.0654
541.2316
158.0591
283.1134
542.2346
226.0472
298.0840
582.2957
115.0524
583.2980
482.2440
227.0506
341.1125
508.2231
105.0322
394.2119
464.2331
637.3332
687.2925
729.3379
798.3482
m/z

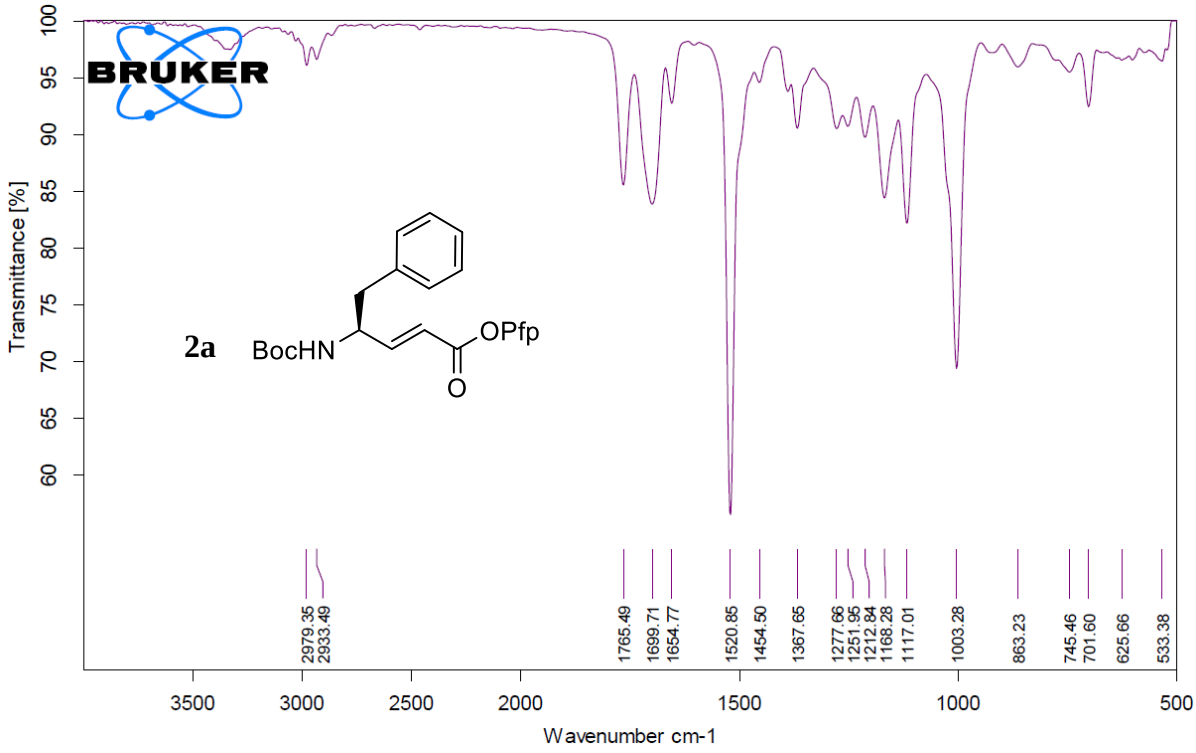

CBZ LAC
IISER PUNE
CBZ LAC 51 (0.945) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
4.16e3
280.1673
CALCULATED MASS
(M+H)+ 274.1443
CbzN
O
2g
274.1439
274.2684
279.1801
270.1794
275.1458
275.2765
271.1891
272.1188
273.2492
270.8372
272.2128
276.1718
277.1985
277.1408
278.1751
279.7251
%
m/z

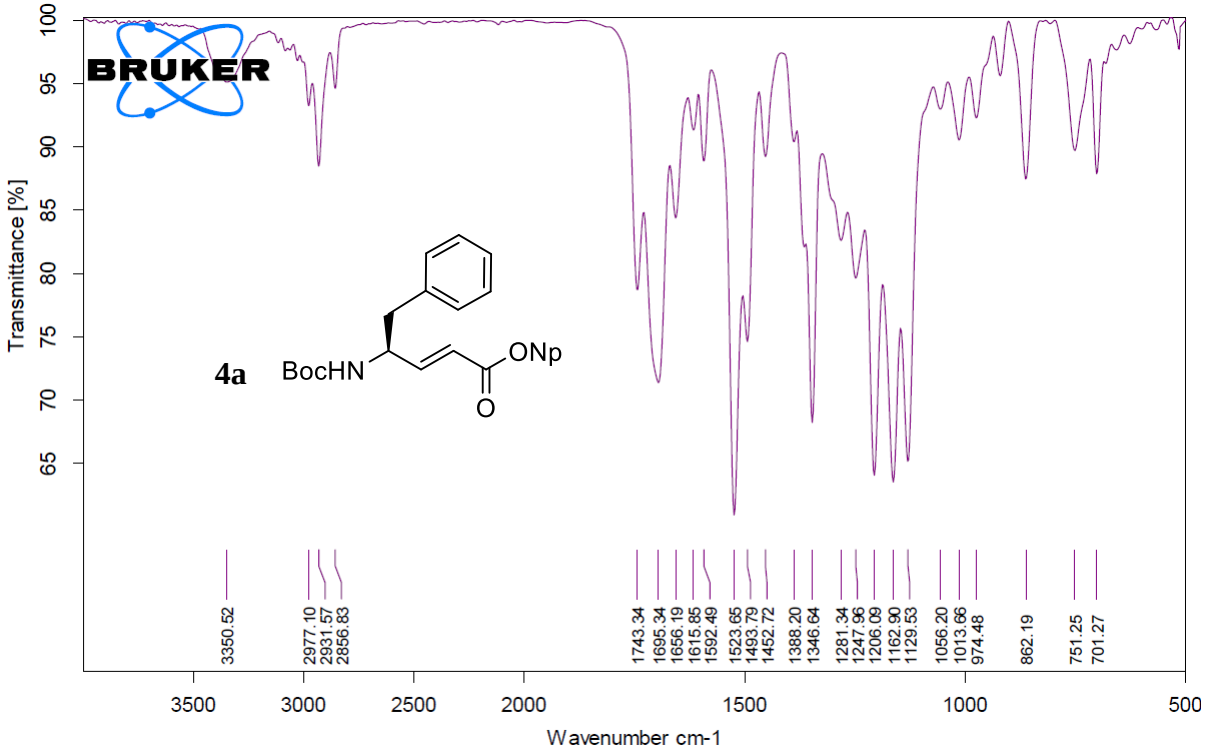

PHEA
IISER PUNE
PHEA 53 (0.979) AM2 (Ar,10000.0,556.28,0.00,LS 3); Sm (SG, 3x1.00)
1: TOF MS ES+
2.64e6
314.1375
CALCULATED MASS
(M+Na)+ 314.1368
1a
BocHN
OH
O
192.1025
315.1408
346.1635
174.0919
258.0744
157.0649
224.1288
347.1666
262.1234
91.0522
129.0696
421.1458
483.2514
507.2754
573.4241
605.2844
627.2659
661.5339
712.2862
795.3163
%
m/z



9.2. IR Spectra of compounds




BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
60
2a
BocHN
OPfp
O
2979.35
2933.49
1765.49
1699.71
1654.77
1520.85
1454.50
1367.65
1277.66
1251.95
1212.84
1168.28
1117.01
1003.28
863.23
745.46
701.60
625.66
533.38
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1


BRUKER
Transmittance [%]
100
95
90
85
80
75
70
65
4a
BocHN
ONp
O
3350.52
2977.10
2931.57
2856.83
1743.34
1695.34
1656.19
1615.85
1592.49
1523.65
1493.79
1452.72
1388.20
1346.64
1281.34
1247.96
1206.09
1162.90
1129.53
1056.20
1013.66
974.48
862.19
751.25
701.27
3500
3000
2500
2000
1500
1000
500
Wavenumber cm-1

10. HPLC Peaks (using chiral column)

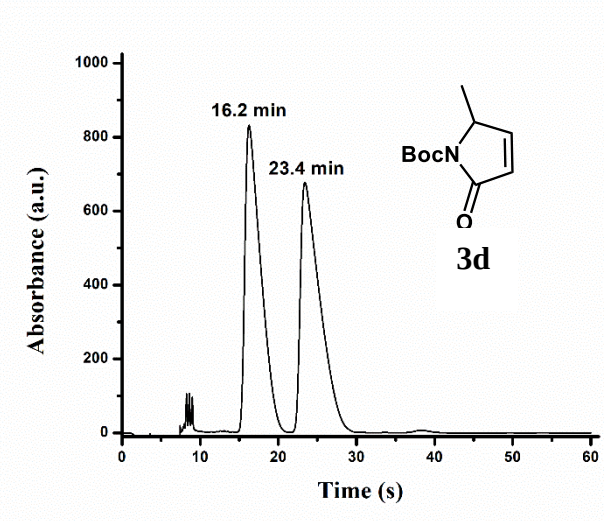


Fig. 12: HPLC traces of **3d** using chiral column.

11. References

1. S. M. Mali, A. Bandyopadhyay, S. V. Jadhav, M. G. Kumar and H. N. Gopi, *Org. Biomol. Chem*., 2011, **9**, 6566-6574.
2. H.-Q. Lan, J.-L. Ye, A.-E. Wang, Y.-P. Ruan and P.-Q. Huang, *Chem.—Eur. J*., 2011, **17**, 958–968.
3. M. Bodanszky, *Nature*, 1955, **175**, 685.