Supporting Information

"Customizable" Units in Di- and tripeptides: Selective Conversion into Substituted Dehydroamino Acids

Carlos J. Saavedra, Alicia Boto,* and Rosendo Hernández*

Instituto de Productos Naturales y Agrobiología CSIC, Avda. Astrofísico Fco. Sánchez 3, 38206-La Laguna, Tenerife, Spain

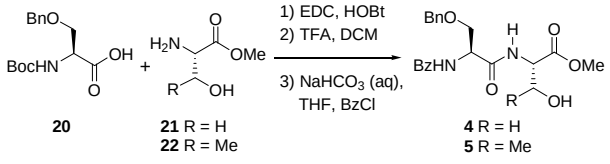
alicia@ipna.csic.es; rhernandez@ipna.csic.es

Supporting Information. Procedures for the synthesis of the substrates for the scission-phosphorylation process **4**, **5** and **17** (pp 1–2), study of the scission–oxidation reaction and formation of the α-methoxyglycine derivatives **4**, **5** and **11** (pp 2–3), procedure for the phosphorylation reaction and synthesis of phosphorylated compounds **7**, **12** and **18** (pp 2–4), procedures for the Horner-Wadsworth-Emmons Reaction and preparation of dehydroamino acid-containing peptides **8**, **9**, **13**–**16** and **19** (pp 4–7). ^{1}H and ^{13}C NMR spectra of compounds **4–9** and **11–19** and NOE experiments for compounds **8**, **13**, **14**, **16** and **19**. (pp 8–27). This material is available free of charge via the Internet at http://pubs.acs.org.

General Methods. Melting points were determined with a hot-stage apparatus and are uncorrected. Optical rotations were measured at the sodium line at ambient temperature (26 °C) in $CHCl_3$ solutions. NMR spectra were determined at 500 MHz for ^{1}H and 125.7 or 100 MHz for ^{13}C in the presence of TMS as internal standard, unless otherwise stated. Mass spectra were determined at 70 eV. Merck silica gel 60 PF_{254} and 60 (0.063–0.2 mm) were used for preparative thin layer chromatography and column chromatography, respectively. All reactions involving air- or moisture-sensitive materials were carried out under a nitrogen atmosphere. The reagent for TLC analysis was $KMnO_4$ in $NaOH/K_2CO_3$ aqueous solution and the TLC was heated until development of color.

Preparation of Substrates 4, 5 and 17.

Scheme 1. Preparation of substrates **4** and **5**



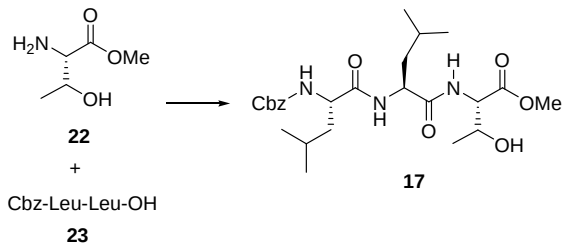
20 **21** R = H, **22** R = Me → **4** R = H, **5** R = Me

***N*-(*O*-Benzyl-*N*-benzoyl-L-seryl)-L-serine Methyl Ester (4).** To a solution of Boc-Ser(OBn)-OH (**20**) (2.96 g, 10 mmol) and and H-Ser-OMe•HCl (**21**) (1.56 g, 10 mmol) in dry CH_2Cl_2 (100 mL) at 0 °C, was added diisopropylethylamine (3.4 mL, 2.59 g, 20 mmol), 1-hydroxybenzotriazol hydrate (HOBt) (1.49 g, 11 mmol), and N-(3-dimethylaminopropyl)-N-ethylcarbodiimide hydrochloride (EDC, 2.1 g, 11 mmol). The reaction mixture was stirred for 2 h at 0 °C, then was allowed to reach room temperature (26 °C) and stirred for 18 h. Then it was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried on sodium sulfate, filtered and evaporated under vaccum. The residue was dissolved in 1:1 TFA:CH_2Cl_2 (25 mL) and the solution was stirred at 26 °C for 1.5 h. Then the solvent was removed under vaccum and the residue was dissolved in THF (15 mL). Then saturated aqueous $NaHCO_3$ (15 mL) was added, the mixture was cooled to 0 °C, and benzoyl chloride was added dropwise (1.51 mL, 1.83 g, 13 mmol). After stirring for 16 h, the mixture was poured into 5% aqueous HCl at 0°C and extracted with EtOAc. The residue was purified by column chromatography (hexanes/EtOAc, 30:70), to give compound **4** (2.68 g, 67%) as a syrup; $[\alpha]_D$ +51 (*c* 0.34, $CHCl_3$); IR ($CHCl_3$) ν_{max}. 3418, 1747, 1679, 1660, 1512 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.05 (1H, brb),

3.70 (1H, dd, *J* = 6.9, 9.5 Hz), 3.75 (3H, s), 3.90–3.98 (2H, m), 3.99 (1H, dd, *J* = 4.4, 9.2 Hz), 4.60 (2H, s), 4.66 (1H, ddd, *J* = 3.8, 3.8, 7.3 Hz), 4.84 (1H, ddd, *J* = 4.7, 6.6, 6.9 Hz), 7.17 (1H, brd, *J* = 6.6 Hz), 7.28 (1H, m), 7.31–7.35 (4H, m), 7.42 (2H, dd, *J* = 7.3, 7.9 Hz), 7.51 (1H, dd, *J* = 7.8, 7.9 Hz), 7.53 (1H, d, *J* = 7.6 Hz), 7.77 (2H, d, *J* = 7.3 Hz); ^{13}C NMR (100.6 MHz, $CDCl_3$): δ_C 52.7 (CH_3), 53.2 (CH), 55.1 (CH), 62.8 (CH_2), 69.5 (CH_2), 73.6 (CH_2), 127.2 (2 × CH), 127.9 (2 × CH), 128.0 (CH), 128.5 (2 × CH), 128.6 (2 × CH), 131.9 (CH), 133.5 (C), 137.3 (C), 167.6 (C), 170.3 (C), 170.5 (C); HRMS calcd for $C_{20}H_{22}N_2O_5$ (M^+ + H −OMe), 370.1529; found, 370.1513. Anal. calcd for $C_{21}H_{24}N_2O_6$ C 62.99, H 6.04, N 7.00; found C 62.73, H 6.13, N 7.10.

***N*-(*O*-Benzyl-*N*-benzoyl-L-seryl)-L-threonine Methyl Ester (5).** Obtained from commercial Boc-Ser(OBn)-OH (**20**) (2.95 g, 10 mmol) and H-Thr-OMe•HCl (**27**) (1.70 g, 10 mmol) as described before for the synthesis of dipeptide **4**. After purification by column chromatography (hexanes/EtOAc, 30:70), dipeptide **5** was isolated (3.31 g, 80%) as a syrup; $[\alpha]_D$ +34 (*c* 0.23, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3419, 1747, 1680, 1660, 1653, 1511 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.19 (3H, d, *J* = 6.3 Hz), 3.70 (1H, m), 3.72 (3H, s), 3.99 (1H, dd, *J* = 4.4, 9.1 Hz), 4.34 (1H, m), 4.59-4.62 (3H, m), 4.91 (1H, m), 7.22 (1H, brb), 7.28 (1H, m), 7.29-7.38 (4H, m), 7.41 (2H, dd, *J* = 7.6, 7.9 Hz), 7.48 (1H, brb), 7.50 (1H, dd, *J* = 7.3, 7.6 Hz), 7.79 (2H, d, *J* = 6.9 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 19.9 (CH_3), 52.5 (CH_3), 53.0 (CH), 57.7 (CH), 67.9 (CH), 69.6 (CH_2), 73.5 (CH_2), 127.1 (2 × CH), 127.9 (3 × CH), 128.4 (2 × CH), 128.6 (2 × CH), 131.9 (CH), 133.5 (C), 137.3 (C), 167.5 (C), 170.7 (C), 171.0 (C); HRMS calcd for $C_{21}H_{22}N_2O_5$ (M^+ −HOMe), 382.1529; found, 382.1512. Anal. calcd for $C_{22}H_{26}N_2O_6$ C 63.76, H 6.32, N 6.76; found C 63.67, H 6.27, N 6.73.

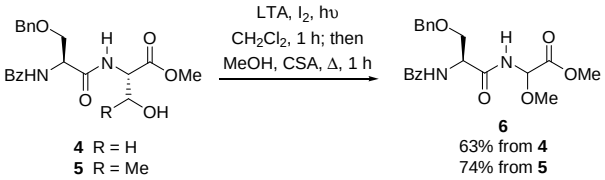
Scheme 2. Preparation of substrate **17**



***N*-(*N*-Benzyloxycarbonyl-L-leucyl-L-leucyl)-L-threonine Methyl Ester (17).** Obtained from commercial H-Thr-OMe•HCl (**22**) (1.70 g, 10 mmol) and Cbz-Leu-Leu-OH (**23**) (3.78 g, 10 mmol) as described before for the synthesis of dipeptide **4**. After purification by column chromatography (hexanes/EtOAc, 40:60), tripeptide **17** was isolated (3.95 g, 80%) as a syrup; $[\alpha]_D$ −48 (*c* 0.23, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3425, 1731, 1673, 1508 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.89–0.93 (12H, m), 1.17 (3H, d, *J* = 6.3 Hz), 1.49–1.75 (6H, m), 3.75 (3H, s), 4.19 (1H, m), 4.29 (1H, m), 4.52 (1H, ddd, *J* = 6.3, 7.9, 8.2 Hz), 4.58 (1H, br d, *J* = 7.5 Hz), 5.06 (1H, d, *J* = 13.0 Hz), 5.11 (1H, d, *J* = 12.0 Hz), 5.46 (1H, d, *J* = 6.6 Hz), 6.59 (1H, br b), 7.13 (1H, br b), 7.30–7.40 (5H, m); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 19.7 (CH_3), 22.0 (CH_3), 22.3 (CH_3), 22.5 (CH_3), 22.8 (CH_3), 24.5 (CH), 24.6 (CH), 40.7 (CH_2), 41.1 (CH_2), 52.2 (CH), 52.5 (CH_3), 53.5 (CH), 57.6 (CH), 67.0 (CH_2), 68.3 (CH); 128.0 (2 × CH), 128.1 (CH), 128.5 (2 × CH), 136.1 (C), 156.4 (C), 171.2 (C), 172.4 (C), 173.0 (C); HRMS calcd for $C_{22}H_{31}N_3O_7$ (M^+ − H − $CHMe_2$), 449.2162; found, 449.2173. Anal. calcd for $C_{25}H_{39}N_3O_7$ C 60.83, H 7.96, N 8.51; found C 60.74, H 7.75, N 8.61.

Study of the scission–oxidation reaction.

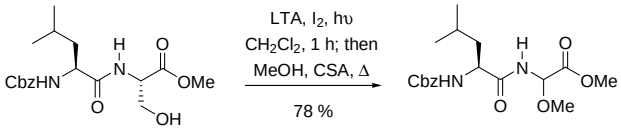
Scheme 3. Preparation of the α-methoxyglycine derivative **6**



Procedure for the Radical Scission–Oxidation –Addition of *O*-Nucleophiles Process: Synthesis of *N*-(*O*-Benzyl-*N*-benzoyl-L-seryl)-2-(methoxy)glycine Methyl Ester (6). To a solution of Bz-Ser(Bn)-Ser-OMe (**4**) (80 mg, 0.2 mmol) or Bz-Ser(Bn)-Thr-OMe (**5**) (83 mg, 0.2 mmol) in dry dichloromethane (8 mL) was added iodine (51 mg, 0.2 mmol) and lead tetraacetate (LTA, 178 mg, 0.4 mmol). The reaction mixture was stirred for 1 h at room temperature (26 °C) under irradiation with visible light (80-W tungsten-filament lamp). Then the reaction mixture was poured into 10% aqueous $Na_2S_2O_3$ and extracted with CH_2Cl_2. The organic layer was dried over sodium sulfate, filtered, and the solvent was removed under vacuum. The residue was dissolved in dry methanol (8 mL), and camphorsulfonic acid (CSA) was added (139 mg, 0.6 mmol). The mixture was stirred for 1 h at reflux temperature; then was cooled to 26 °C, poured into water and extracted with dichloromethane. The organic layer was dried and filtered as before. The solvent was removed under vacuum and the residue was purified by chromatography on silica gel (hexanes/EtOAc 60:40), to afford product **6** (50 mg, 63% from substrate **4**; 59 mg, 74% from substrate **5**) as a 1:1 diastereomer mixture. Syrup; IR ($CHCl_3$) ν_{max} 3420, 1753, 1691, 1660, 1508, 1482 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 3.41/3.42 (3H, s/s), 3.65/3.71 (1H, m), 3.75 (3H, s), 4.02/4.04 (1H, [dd, *J* = 4.1, 6.3 Hz/ dd, *J* = 4.1, 6.3 Hz]), 4.57/4.59 (1H, [d, *J* = 12 Hz/ d, *J* = 11.3 Hz]), 4.62/4.64 (1H, [d, *J* = 12 Hz/ d, *J* = 11.9 Hz]), 4.89 (1H, m), 5.57/5.59 (1H, [d, *J* = 5.7 Hz/ d, *J* = 5.9 Hz]), 7.15 (1H, d, *J* = 6.6 Hz), 7.28

(1H, m), 7.30–7.35 (4H, m), 7.42 (2H, dd, *J* = 7.3, 7.9 Hz), 7.51 (1H, dd, *J* = 7.3, 7.6 Hz), 7.58/7.70 (1H, [d, *J* = 9.1 Hz/ d, *J* = 8.8 Hz]), 7.79 (2H, d, *J* = 8.0 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 52.8 (CH_3), 52.96/53.03 (CH), 56.4/56.5 (CH_3), 69.16/69.21 (CH_2), 73.6 (CH_2), 78.3/78.4 (CH), 127.1 (2 × CH), 127.8 (2 × CH), 128.0 (CH), 128.5 (2 × CH), 128.6 (2 × CH), 131.9 (CH), 133.4 (C), 137.08/137.12 (C), 167.3 (C), 167.8 (C), 170.9/171.0 (C); HRMS (EI) calcd for $C_{21}H_{24}N_2O_6$ (M^+) 400.1634; found, 400.1622. Anal. calcd for $C_{21}H_{24}N_2O_6$ C 62.99, H 6.04, N 7.00; found C 62.64, H 6.06, N 6.92.

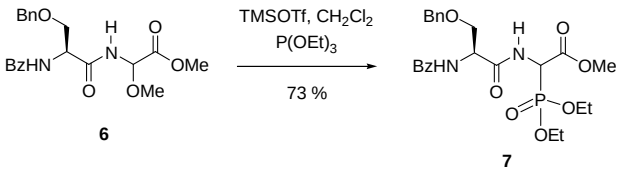
Scheme 4. Preparation of α-methoxyglycine Derivative **11**



***N*-(*N*-Benzyloxycarbonyl-L-leucyl)-2-(methoxy) glycine Methyl Ester (11).** Obtained from commercial Cbz-Leu-Ser-OMe (**10**) (73 mg, 0.2 mmol) as described for the α-methoxyglycine derivative **6**. Usual work-up and purification by column chromatography (hexanes-EtoAc 60:40) gave the methoxy derivative **11** (57 mg, 78%) as a 10:7 diastereomer mixture. White solid; m.p. 109-110 °C (EtOAc/hexane). IR ($CHCl_3$) ν_{max} 3423, 1751, 1719, 1697, 1504 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 0.92 (3H, d, *J* = 6.3 Hz), 0.93 (3H, d, *J* = 6.4 Hz), 1.53 (1H, m), 1.60–1.74 (2H, m), 3.38/3.40 (3H, s/s), 3.76/3.77 (3H, s/s), 4.31 (1H, m), 5.08 (1H, d, *J* = 14 Hz), 5.12 (1H, d, *J* = 14.5 Hz), 5.44/5.47 (1H, [d, *J* = 7.9 Hz /d, *J* = 8.2 Hz]), 5.52/5.53 (1H, [d, *J* = 8.8 Hz/ d, *J* = 9.1 Hz]), 7.26–7.32 (6H, m); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ_C 21.7/21.8 (CH_3), 22.8/22.9 (CH_3), 24.6/24.7 (CH), 41.3/41.4 (CH_2), 52.8 (CH_3), 53.7 (CH), 56.4/56.5 (CH_3), 67.1 (CH_2), 78.3 (CH), 128.0 (2 × CH), 128.1 (CH), 128.5 (2 × CH), 136.1 (C), 156.2 (C), 168.2 (C), 173.2 (C). HRMS (EI) calcd for $C_{16}H_{23}N_2O_4$ (M^+ – CO_2Me) 307.1664; found, 307.1658. Anal. calcd for $C_{18}H_{26}N_2O_6$ C 59.00, H 7.15, N 7.65; found C 58.71, H 7.07, N 7.86.

Study of the Phosphorylation Reaction.

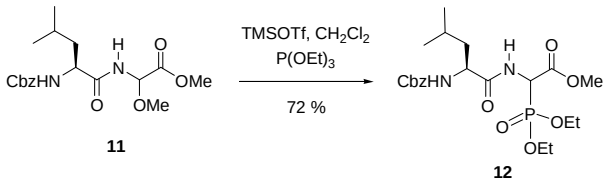
Scheme 5. Synthesis of the phosphorylation product **7**



General Procedure for the Phosphorylation Reaction. To a solution of the methoxyderivative (0.2 mmol) in CH_2Cl_2 (8 mL) at 0 °C was added triethylphosphite (174 μL, 166 mg, 1 mmol) and TMSOTf (109 μL, 133 mg, 0.6 mmol). The reaction mixture was stirred for 3 h, then it was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried and evaporated as usual, and the residue was purified by chromatography on silica gel (hexanes/EtOAc), to afford the α-aminophosphonate derivatives.

***N*-(*N*-Benzoyl-*O*-benzyl-L-seryl)-2-(diethoxyphosphoryl)glycine Methyl Ester (7).** Obtained from compound **6** (80 mg, 0.2 mmol) according to the General Procedure for the phosphorylation reaction. After purification by rotatory chromatography (hexanes/EtOAc 50:50), compound **7** was isolated as a 1:1 diastereomer mixture (74 mg, 73%): Syrup; IR ($CHCl_3$) ν_{max} 3419, 1748, 1684, 1660, 1508 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 1.20–1.35 (6H, m), 3.64/3.68 (1H, dd, *J* = 7.9, 9.5 Hz/dd, *J* = 7.3, 9.8 Hz), 3.79/3.80 (3H, s/s), 4.04/4.05 (1H, dd, *J* = 4.0, 9.3 Hz/dd, *J* = 4.0, 9.5 Hz), 4.08-4.20 (4H, m), 4.60 (1H, d, *J* = 11.9 Hz), 4.65 (1H, d, *J* = 11.9 Hz), 4.88 (1H, m), 5.16/5.20 (1H, dd, *J* = 8.0, 21.8 Hz/ dd, *J* = 7.3, 20.5 Hz), 7.14/7.15 (1H, d, *J* = 7.0, 7.3 Hz), 7.30–7.40 (5H, m), 7.42 (2H, dd, *J* = 7.6, 7.9 Hz), 7.51 (1H, dd, *J* = 7.6, 7.9 Hz), 7.63/7.64 (1H, d, *J* = 8.8 Hz/d, *J* = 8.9 Hz), 7.80/7.81 (2H, brd, *J* = 8.0 Hz/brd, *J* = 8.5 Hz); ^{13}C NMR (125.7 MHz, $CDCl_3$, 26 °C): δ_C 16.2 (2 × CH_3, d, $J_{C,P}$ = 5.7 Hz), 50.95/51.00 (CH, d, $J_{C,P}$ = 147.2 Hz), 52.5/52.8 (CH), 53.2 (CH_3), 63.8 (CH_2, d, $J_{C,P}$ = 7.4 Hz), 63.9 (CH_2, d, $J_{C,P}$ = 7.4 Hz), 69.2 (CH_2), 73.5/73.6 (CH_2), 127.1 (2 × CH), 127.8 (CH), 127.9 (2 × CH), 128.5 (2 × CH), 128.6 (2 × CH), 131.9 (CH), 133.5 (C), 137.1/137.2 (C), 166.8 (C), 167.2/167.3 (C), 169.8/170.2 (C, d, $J_{C,P}$ = 6.4 Hz); HRMS calcd for $C_{24}H_{31}N_2O_8P$ [M^+], 506.1818; found, 506.1831.

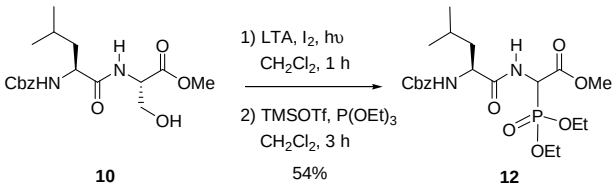
Scheme 6. Synthesis of the phosphorylation product **12**



***N*-(*N*-Benzyloxycarbonyl-L-leucyl)-2-(diethoxyphosphoryl)glycine Methyl Ester (20).** Obtained from compound **11** (73 mg, 0.2 mmol) according to the General Procedure for the phosphorylation reaction. After purification by rotatory chromatography (hexanes/EtOAc 50:50), compound **12** (68 mg, 72%) was isolated as a 1:1 diastereomer mixture: Syrup; IR ($CHCl_3$) ν_{max} 3429, 1746, 1719, 1688, 1507 cm^{-1};^{1}H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 0.92 (6H, d, *J* = 6.3 Hz), 1.25–1.32 (6H, m), 1.51 (1H, m), 1.60–1.73 (2H, m), 3.77 (3H, s), 4.05–4.20 (4H, m), 4.34 (1H, m),

5.09 (2H, s), 5.15/5.17 (1H, [dd, J = 8.8 Hz, $J_{H,P}$ = 22.4 Hz/ dd, J = 8.9 Hz, $J_{H,P}$ = 22.3 Hz]), 5.47 (1H, br b), 7.20 (1H, br d, J = 7.9 Hz), 7.28–7.35 (5H, m). ^{13}C NMR (100.6 MHz, $CDCl_3$, 26 °C): δ_C 16.2 (2 × CH_3, d, $J_{C,P}$ = 5.7 Hz), 21.8 (CH_3), 22.8 (CH_3), 24.6 (CH), 41.5 (CH_2), 50.6 (CH, d, $J_{C,P}$ = 147.9 Hz), 52.97/53.03 (CH_3), 53.44/53.51 (CH), 63.7 (CH_2, d, $J_{C,P}$ = 7.0 Hz), 63.9 (CH_2, d, $J_{C,P}$ = 5.2 Hz), 67.0 (CH_2), 127.9 (CH), 128.1 (2 × CH), 128.5 (2 × CH), 136.2 (C), 156.0 (C), 166.9 (C), 172.1 (C); HRMS calcd for $C_{21}H_{33}N_2O_8P$ [M^+], 472.1975; found, 472.1978.

Scheme 7. Simplified procedure for the preparation of the scission-phosphorylation product **12**

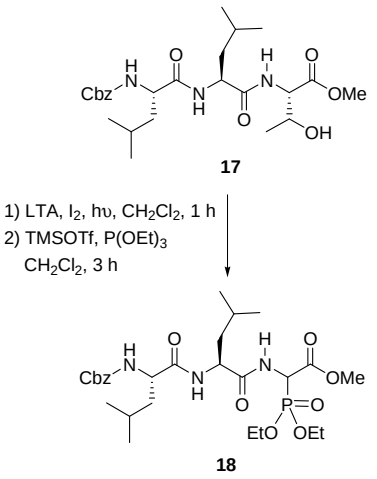


10 **12**

General Procedure for the Simplified Scission –Phosphorylation Process. To a solution of the starting material (0.2 mmol) in dry dichloromethane (8 mL) was added iodine (51 mg, 0.2 mmol) and lead tetraacetate (LTA, 178 mg, 0.4 mmol). The reaction mixture was stirred for 1 h at room temperature (26 °C) under irradiation with visible light (80-W tungsten-filament lamp). Then the reaction mixture was poured into 10% aqueous $Na_2S_2O_3$ and extracted with CH_2Cl_2, and the solvent was dried and evaporated as usual. The unpurified residue was dissolved in dry CH_2Cl_2 (8 mL), the solution was cooled to 0 °C and triethylphosphite (174 μL, 166 mg, 1 mmol) and TMSOTf (109 μL, 133 mg, 0.6 mmol) were added. The reaction mixture was stirred for 3 h, then it was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. After usual solvent drying and evaporation, the residue was purified by chromatography on silica gel (hexanes/EtOAc), to afford the α-aminophosphonate derivatives.

***N*-(*N*-Benzyloxycarbonyl-L-leucyl)-2-(diethoxy phosphoryl)glycine Methyl Ester (12).** Obtained from Cbz-Leu-Ser-OMe (**10**) (73 mg, 0.2 mmol) according to the General Procedure for the scission-phosphorylation reaction. After purification by rotatory chromatography (hexanes/EtOAc 50:50), compound **12** (67 mg, 71%) was isolated as a 1:1 diastereomer mixture.

Scheme 8. Synthesis of the scission–phosphorylation **18**

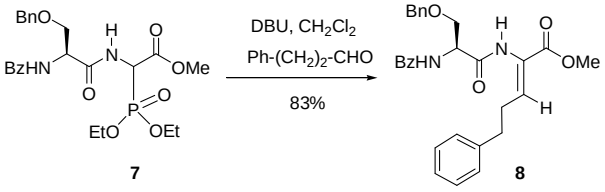


17 **18**

***N*-(*N*-Benzyloxycarbonyl-L-leucyl-L-leucyl)-2-(diethoxy phosphoryl)glycine Methyl Ester (18).** Obtained from compound **17** (80 mg, 0.2 mmol) according to the Simplified Scission–Phosphorylation Procedure. After purification by rotatory chromatography (hexanes/EtOAc 40:60), compound **18** was isolated as a 1:1 diastereomer mixture (71 mg, 61%): Syrup; IR ($CHCl_3$) ν_{max} 3426, 3318, 1747, 1712, 1678, 1506 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 0.85–0.92 (12H, m), 1.24–1.35 (6H, m), 1.50–1.70 (6H, m), 3.75/3.77 (3H, s/s), 4.11–4.25 (5H, m), 4.61/4.69 (1H, m/m), 5.09 (2H, s), 5.13/5.16 (1H, m/m), 5.49/5.68 (1H, [d, J = 7.9 Hz/ d, J = 7.9 Hz]), 6.66/6.76 (1H, [d, J = 8.2 Hz/ d, J = 7.6 Hz], 7.26-7.35 (5H, m), 7.34/7.56 (1H, [m/ d, J = 8.5 Hz]); ^{13}C NMR (125.7 MHz, $CDCl_3$, 26 °C): δ_C 16.2 (2 × CH_3, d, $J_{C,P}$ = 5.8 Hz), 21.8 (CH_3), 22.0/22.1 (CH_3), 22.7/22.8 (CH_3), 22.9 (CH_3), 24.5 (CH), 24.6 (CH), 41.1 (CH_2), 41.2 (CH_2), 50.5/50.6 (CH, [d, $J_{C,P}$ = 146 Hz/ d, $J_{C,P}$ = 147.2 Hz), 51.4/51.5 (CH), 53.0/53.1 (CH_3), 53.4/53.5 (CH), 63.6 (CH_2, d, $J_{C,P}$ = 7.4 Hz), 63.9 (CH_2, d, $J_{C,P}$ = 6.4 Hz), 67.0 (CH_2), 128.0 (2 × CH), 128.1 (CH), 128.4 (2 × CH), 136.2 (C), 156.3 (C), 166.8/166.9 (C), 171.8 (C), 172.3/172.5 (C); HRMS calcd for $C_{27}H_{44}N_3O_9P$ [M^+], 585.2815; found, 585.2804.

Preparation of Dehydroamino Acids.

Scheme 9. Preparation of the HWE product **8**



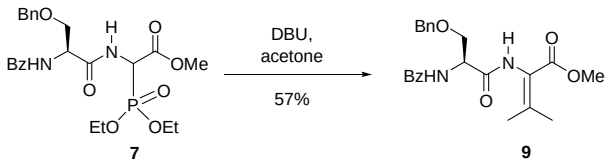
7 **8**

General Procedures for the Horner-Wadsworth-Emmons Reaction. Method A. To a solution of the α-phosphonate (0.2 mmol) in dry CH_2Cl_2 (2 mL) was added a solution of DBU (151 µL, 76 mg, 0.5 mmol) in dry CH_2Cl_2 (1 mL). The reaction mixture was stirred for 10 min, and then was added the aldehyde (0.4 mmol) in dry CH_2Cl_2 (1 mL). After stirring for 16 h, the solution was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over sodium sulfate, filtered and evaporated under vacuum. The residue was purified by chromatography on silica gel (hexanes/EtOAc) affording the dehydroamino acid derivatives.

Method B. To a solution of the amino phosphonate (0.2 mmol) in dry acetone (4 mL) was added DBU (302 µL, 152 mg, 1.0 mmol). The reaction mixture was stirred for 24 h, followed by work-up and purification as described for Method A, giving the dehydroamino acid derivatives.

(*Z*)-(*N*-Benzoyl-*O*-benzyl-L-seryl)-α,β-dehydro-5-(phenyl)norvaline Methyl Ester (8). Obtained from the amino phosphonate **7** (101 mg, 0.2 mmol) and hydrocinnamaldehyde (53 µL, 54 mg, 0.4 mmol), according to the General HWE Procedure, Method A. After purification by column chromatography (hexanes/EtOAc 65:35), compound **8** (81 mg, 83%) was isolated as a syrup; $[\alpha]_D$ = +12 (*c* 0.52, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3409, 1722, 1695, 1659, 1506 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 2.39 (2H, ddd, *J* = 6.6, 7.6, 7.6 Hz), 2.69 (2H, dd, *J* = 7.6, 7.6 Hz), 3.63 (1H, dd, *J* = 7.6, 9.1 Hz), 3.66 (3H, s), 4.00 (1H, dd, *J* = 4.1, 9.2 Hz), 4.54 (1H, d, *J* = 11.7 Hz), 4.58 (1H, d, *J* = 11.8 Hz), 4.83 (1H, m), 6.67 (1H, dd, *J* = 7.3, 7.6 Hz), 7.09 (1H, br b), 7.10 (2H, dd, *J* = 7.8, 7.9 Hz), 7.11 (1H, dd, *J* = 7.4, 7.8 Hz), 7.19 (2H, dd, *J* = 7.6, 7.8 Hz), 7.24 (1H, m), 7.25–7.28 (4H, m), 7.37 (2H, dd, *J* = 7.8, 7.9 Hz), 7.46 (1H, dd, *J* = 7.6, 7.8 Hz), 7.74 (2H, d, *J* = 7.5 Hz), 7.88 (1H, br b); ^{13}C NMR (125.7 MHz, $CDCl_3$, 26 °C): δ_C 30.3 (CH_2), 34.1 (CH_2), 52.3 (CH_3), 52.9 (CH), 69.3 (CH_2), 73.6 (CH_2), 125.2 (C), 126.1 (CH), 127.1 (2 × CH), 127.9 (2 × CH), 128.0 (CH), 128.3 (2 × CH), 128.4 (2 × CH), 128.5 (2 × CH), 128.6 (2 × CH), 131.9 (CH), 133.5 (C), 137.2 (C), 137.8 (CH), 140.8 (C), 164.5 (C), 167.3 (C), 168.7 (C); HRMS calcd for $C_{29}H_{30}N_2O_5$ [M^+], 486.2155; found, 486.2147.

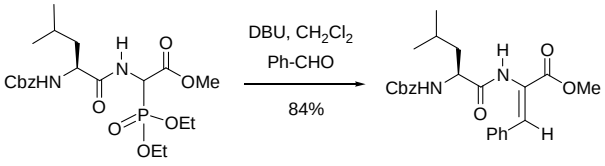
Scheme 10. Preparation of the HWE product **9**



7 **9**

(Z)-(*N*-Benzoyl-*O*-benzyl-L-seryl)-α,β-dehydro valine Methyl Ester (9). Obtained from the amino phosphonate **7** (101 mg, 0.2 mmol), according to the General HWE Procedure, Method B. After purification by column chromatography (hexanes/EtOAc 60:40), compound **9** (47 mg, 57%) was isolated as a syrup; $[\alpha]_D$ = +16 (*c* 0.56, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3414, 1723, 1687, 1658, 1507 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 1.78 (3H, s), 2.15 (3H, s), 3.68 (1H, m), 3.69 (3H, s), 4.08 (1H, dd, *J* = 4.4, 9.5 Hz), 4.61 (1H, d, *J* = 11.7 Hz), 4.68 (1H, d, *J* = 11.8 Hz), 4.87 (1H, m), 7.19 (1H, d, *J* = 6.0 Hz), 7.32 (1H, m), 7.33–7.36 (4H, m), 7.44 (2H, dd, *J* = 7.6, 7.8 Hz), 7.52 (1H, dd, *J* = 7.0, 7.8 Hz), 7.81 (2H, d, *J* = 7.9 Hz), 7.86 (1H, brb); ^{13}C NMR (125.7 MHz, $CDCl_3$, 26 °C): δ_C 21.2 (CH_3), 22.3 (CH_3), 51.7 (CH_3), 52.6 (CH), 69.3 (CH_2), 73.7 (CH_2), 120.7 (C), 127.1 (2 × CH), 127.9 (2 × CH), 128.1 (CH), 128.5 (2 × CH), 128.6 (2 × CH), 131.9 (CH), 133.6 (C), 137.2 (C), 145.9 (C), 164.9 (C), 167.3 (C), 168.9 (C); HRMS calcd for $C_{23}H_{26}N_2O_5$ [M^+] 410.1842, found 410.1829.

Scheme 11. Preparation of the HWE product **13**

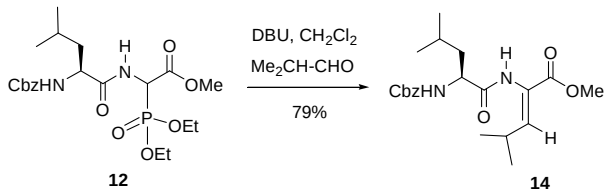


12 **13**

(Z)-(*N*-Benzyloxycarbonyl-L-leucyl)-α,β-dehydrophenylalanine Methyl Ester (13).[1] Obtained from the amino phosphonate **12** (94 mg, 0.2 mmol) and benzaldehyde (41 µL, 42 mg, 0.4mmol) according to the General HWE Procedure, Method A. After purification by rotatory chromatography (hexanes/EtOAc 80:20), compound **13** (71 mg, 84%) was isolated as a syrup; $[\alpha]_D$ = –11 (*c* 0.30, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3430, 1716, 1705, 1504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 0.94 (3H, d, *J* = 7.3 Hz), 0.95 (3H, d, *J* = 6.3 Hz), 1.54 (1H, m), 1.70–1.78 (2H, m), 3.80 (3H, s), 4.35 (1H, m), 5.09 (1H, d, *J* = 12.6 Hz), 5.13 (1H, d, *J* = 12.0 Hz), 5.26 (1H, d, *J* = 8.2 Hz), 7.29–7.34 (8H, m), 7.41 (1H, s), 7.45 (2H, m), 7.74 (1H, br b); ^{13}C NMR (125.7 MHz, $CDCl_3$, 26 °C): δ_C 22.0 (CH_3), 22.8 (CH_3), 24.6 (CH), 40.6 (CH_2), 52.6 (CH_3), 53.7 (CH), 67.2 (CH_2), 123.8 (C), 128.0 (2 × CH), 128.2 (2 × CH), 128.5 (4 × CH), 129.5 (CH), 129.7 (CH), 132.9 (CH), 133.5 (C), 136.0 (C), 156.4 (C), 165.4 (C), 170.8 (C); HRMS calcd for $C_{24}H_{28}N_2O_5$ [M^+], 424.1998; found, 424.1982.

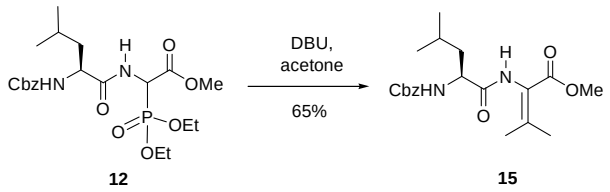
[1] Buck, R. T.; Clarke, P. A.; Coe, D. M.; Drysdale, M. J.; Ferris, L.; Haigh, D.; Moody, C. J.; Pearson, N. D.; Swann, E. *Chem. Eur. J.* **2000**, *6*, 2160–2167.

Scheme 12. Preparation of the HWE product **14**



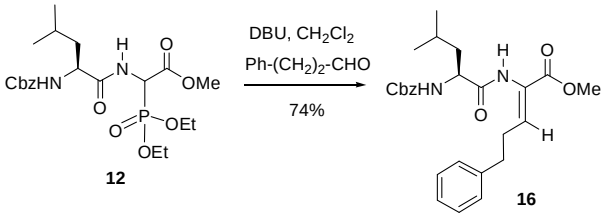
(Z)-(*N*-Benzyloxycarbonyl-L-leucyl)-α,β-dehydro leucine Methyl Ester (14). Obtained from the amino phosphonate **12** (94 mg, 0.2 mmol) and isobutyraldehyde (37 µL, 29 mg, 0.4 mmol), according to the General HWE Procedure, Method A. After purification by column chromatography (hexanes/EtOAc 85:15), compound **15** (62 mg, 79%) was isolated as a syrup; $[\alpha]_D$ = –25 (*c* 0.19, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3430, 1717, 1701, 1508 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 0.95 (6H, d, *J* = 6.3 Hz), 1.00 (3H, d, *J* = 6.6 Hz), 1.02 (3H, d, *J* = 6.3 Hz), 1.56 (1H, m), 1.69–1.78 (2H, m), 2.54 (1H, m), 3.72 (3H, s), 4.34 (1H, m), 5.11 (2H, s), 5.38 (1H, d, *J* = 7.3 Hz), 6.51 (1H, d, *J* = 10.4 Hz), 7.28–7.37 (5H, m), 7.51 (1H, br b). ^{13}C NMR (100.6 MHz, $CDCl_3$, 26 °C): δ_C 21.5 (CH_3), 21.6 (CH_3), 21.9 (CH_3), 22.9 (CH_3), 24.7 (CH), 27.9 (CH), 41.1 (CH_2), 52.2 (CH_3), 53.6 (CH), 67.1 (CH_2), 122.9 (C), 127.9 (2 × CH), 128.1 (CH), 128.5 (2 × CH), 136.1 (C), 146.0 (CH), 156.3 (C), 165.0 (C), 171.2 (C); HRMS calcd for $C_{21}H_{30}N_2O_5$ [M^+], 390.2155; found, 390.2163.

Scheme 13. Preparation of the HWE product **15**



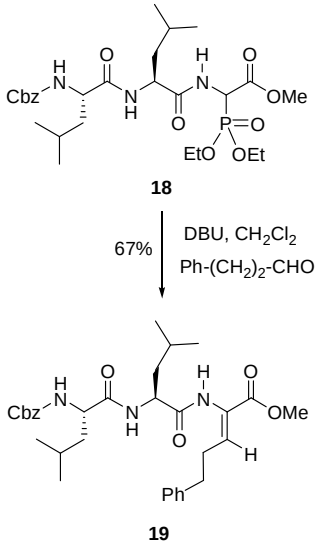
(Z)-(*N*-Benzyloxycarbonyl-L-leucyl)-α,β-dehydrovaline Methyl Ester (15). Obtained from the amino phosphonate **12** (94 mg, 0.2 mmol), according to the General HWE Procedure, Method B. After purification by column chromatography (hexanes/EtOAc 75:25), compound **15** (49 mg, 65%) was isolated as a syrup; $[\alpha]_D$ = –39 (*c* 0.13, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3428, 1718, 1507 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 0.93 (3H, d, *J* = 6.0 Hz), 0.94 (3H, d, *J* = 6.3 Hz), 1.54 (1H, m), 1.67–1.73 (2H, m), 1.76 (3H, s), 2.12 (3H, s), 3.67 (3H, s), 4.30 (1H, m), 5.09 (2H, brs), 5.39 (1H, brb), 7.26–7.38 (5H, m), 7.50 (1H, brb); ^{13}C NMR (125.7 MHz, $CDCl_3$, 26 °C): δ_C 21.2 (CH_3), 22.1 (CH_3), 22.4 (CH_3), 22.8 (CH_3), 24.7 (CH), 40.9 (CH_2), 51.6 (CH_3), 53.5 (CH), 67.1 (CH_2), 120.7 (C), 128.0 (2 × CH), 128.2 (CH), 128.5 (2 × CH), 136.1 (C), 146.3 (C), 156.3 (C), 164.9 (C), 170.9 (C); HRMS calcd for $C_{20}H_{28}N_2O_5$ [M^+], 376.1998; found, 376.2004.

Scheme 14. Preparation of the HWE product **16**



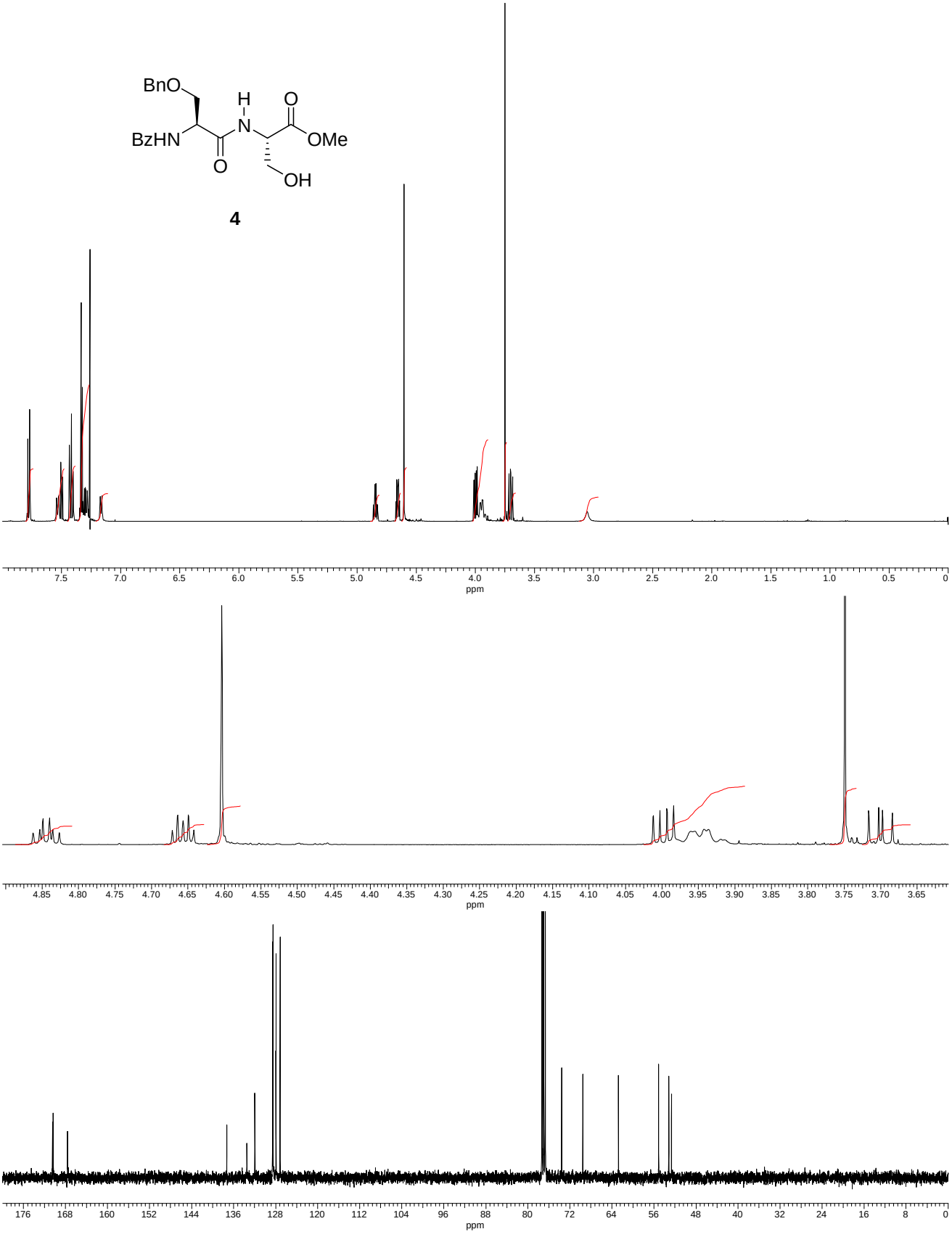
(Z)-(*N*-Benzyloxycarbonyl-L-leucyl)-α,β-dehydro-5-(phenyl)norvaline Methyl Ester (16). Obtained from the amino phosphonate **12** (94 mg, 0.2 mmol) and hydrocinnamaldehyde (53 µL, 54 mg, 0.4mmol), according to the General HWE Procedure, Method A. After purification by column chromatography (hexanes/EtOAc 75:25), compound **16** (67 mg, 74%) was isolated as a syrup; $[\alpha]_D$ = –27 (*c* 0.24, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3420, 1716, 1703, 1504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 0.95 (6H, d, *J* = 6.6 Hz), 1.53 (1H, m), 1.65–1.75 (2H, m), 2.45 (2H, m), 2.77 (2H, dd, *J* = 7.2, 7.6 Hz), 3.73 (3H, s), 4.25 (1H, m), 5.08 (1H, d, *J* = 12.6 Hz), 5.12 (1H, d, *J* = 12.0 Hz), 5.17 (1H, br b), 6.72 (1H, dd, *J* = 7.6, 7.6 Hz), 7.17–7.21 (4H, m), 7.28 (2H, dd, *J* = 7.3, 7.3 Hz), 7.33–7.40 (5H, m); ^{13}C NMR (100.6 MHz, $CDCl_3$, 26 °C): δ_C. 21.9 (CH_3), 22.9 (CH_3), 24.7 (CH), 30.3 (CH_2), 34.1 (CH_2), 41.2 (CH_2), 52.3 (CH_3), 53.7 (CH), 67.1 (CH_2), 125.2 (C), 126.1 (CH), 128.0 (2 × CH), 128.2 (CH), 128.4 (2 × CH), 128.44 (2 × CH), 128.49 (2 × CH), 136.1 (C), 137.8 (CH), 140.9 (C), 156.2 (C), 164.6 (C), 170.8 (C); HRMS calcd for $C_{26}H_{32}N_2O_5$ [M^+], 452.2311; found, 452.2297.

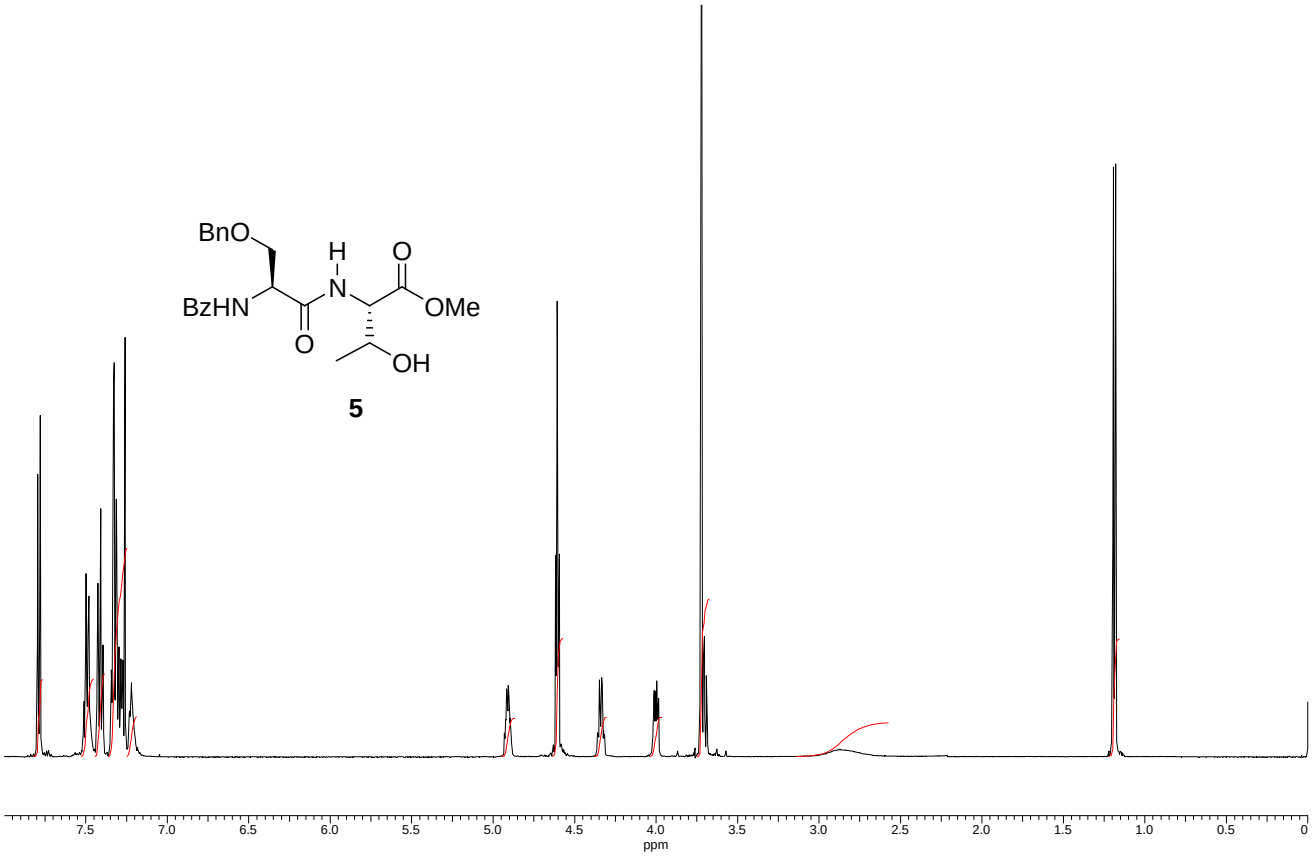
Scheme 15. Preparation of the HWE product **19**

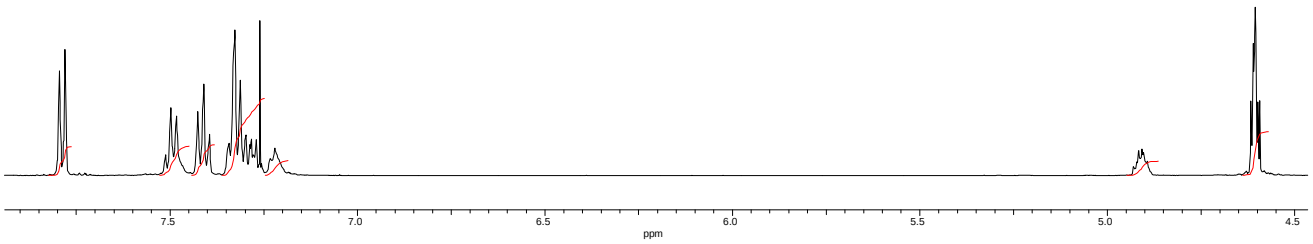


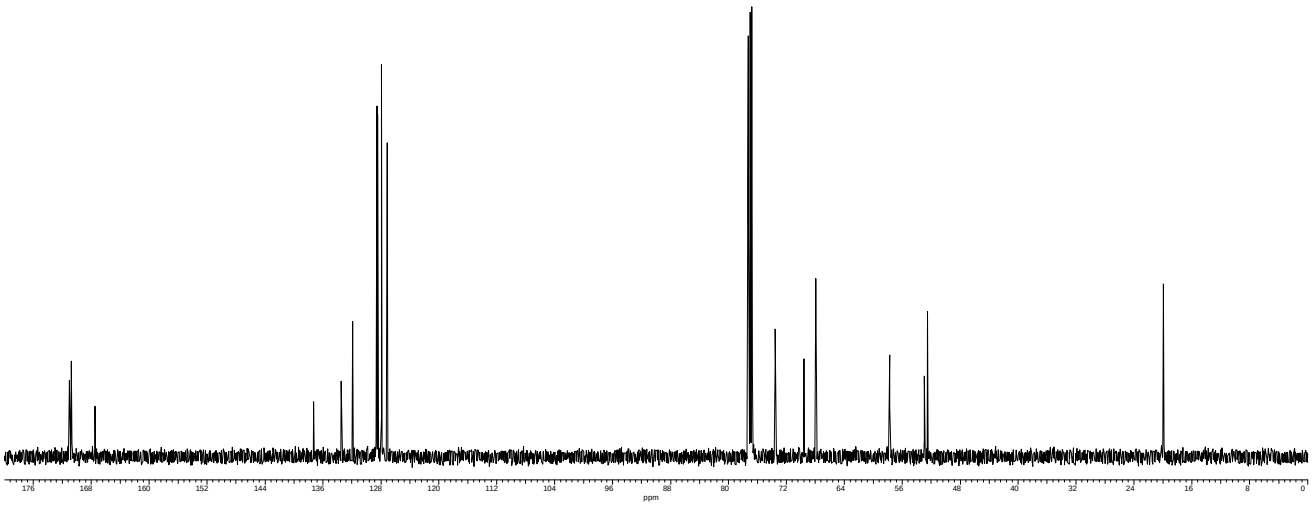
(*Z*)-(*N*-Benzyloxycarbonyl-L-leucyl-L-leucyl)-α,β-dehydro-5-(phenyl)norvaline Methyl Ester (19). Obtained from the amino phosphonate **18** (117 mg, 0.2 mmol) and hydrocinnamaldehyde (53 μL, 54 mg, 0.4 mmol), according to the General HWE Procedure, Method A. After purification by column chromatography (hexanes/EtOAc 40:60), compound **19** (76 mg, 67%) was isolated as a syrup; $[\alpha]_D$ = −50 (*c* 0.26, $CHCl_3$); IR ($CHCl_3$) ν_{max} 3422, 1716, 1504 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 26 °C): δ_H 0.81–0.87 (12H, m), 1.38–1.71 (6H, m), 2.35–2.40 (2H, m), 2.65–2.72 (2H, m), 3.64 (3H, s), 4.13 (1H, m), 4.45 (1H, ddd, *J* = 6.0, 8.2, 8.2 Hz), 4.98 (1H, d, *J* = 11 Hz), 5.03 (1H, d, *J* = 12.0 Hz), 5.24 (1H, br d, *J* = 7.6 Hz), 6.58 (1H, br d, *J* = 8.2 Hz), 6.62 (1H, dd, *J* = 7.3, 7.3 Hz), 7.10–7.14 (3H, m), 7.19–7.30 (7H, m), 7.50 (1H, br b); ^{13}C NMR (125.7 MHz, $CDCl_3$, 26 °C): δ_C 21.8 (CH_3), 22.0 (CH_3), 22.8 (CH_3), 22.9 (CH_3), 24.7 (2 × CH), 30.2 (CH_2), 34.1 (CH_2), 40.6 (CH_2), 41.1 (CH_2),. 51.8 (CH), 52.3 (CH_3), 53.6 (CH), 67.2 (CH_2), 125.3 (C), 126.1 (CH), 128.1 (2 × CH), 128.2 (CH), 128.4 (2 × CH), 128.5 (4 × CH), 136.0 (C), 137.8 (CH), 140.9 (C), 156.4 (C), 164.6 (C), 170.4 (C), 172.5 (C); HRMS calcd for $C_{32}H_{43}N_3O_6$ [M^+], 565.3152; found, 565.3165.

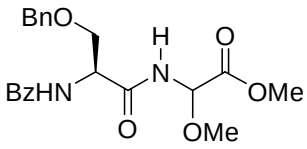
^{1}H and ^{13}C NMR spectra for compounds 4–9 and 11–19; NOE experiments for products 8, 13, 14, 16 and 19




BnO
H
N
O
BzHN
OMe
O
OH
5
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
ppm

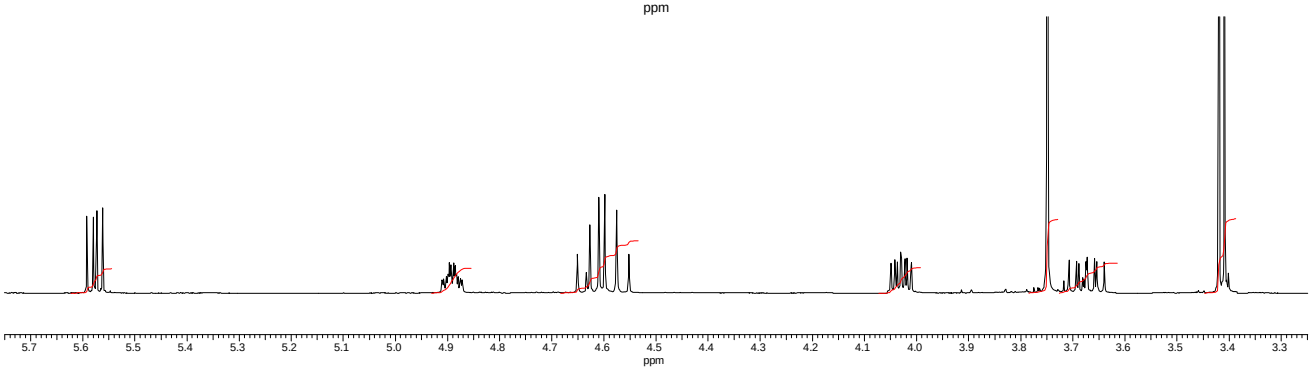

7.5
7.0
6.5
6.0
5.5
5.0
4.5
ppm

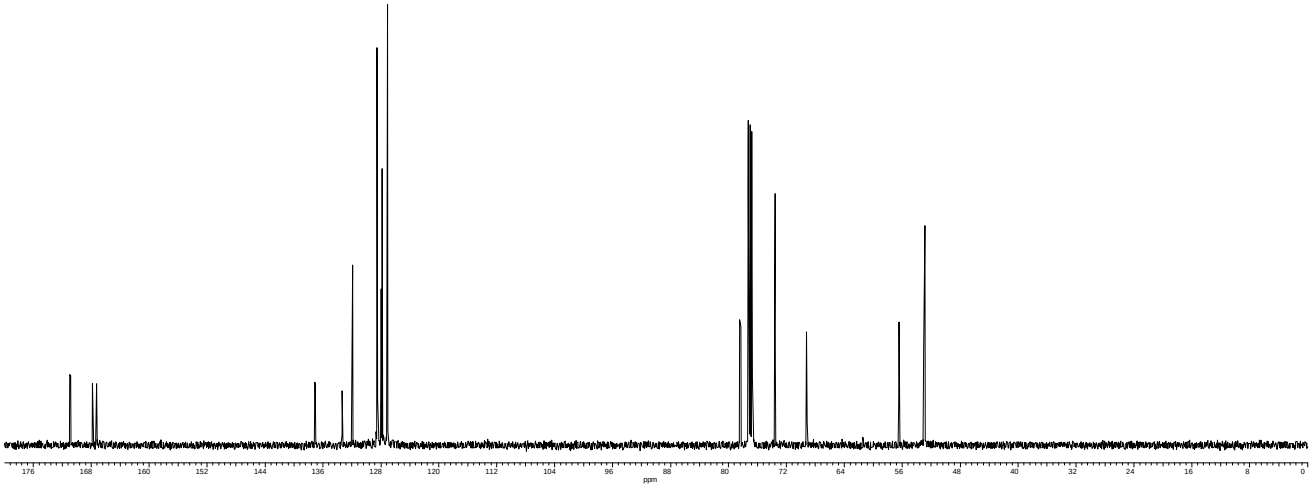

176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm

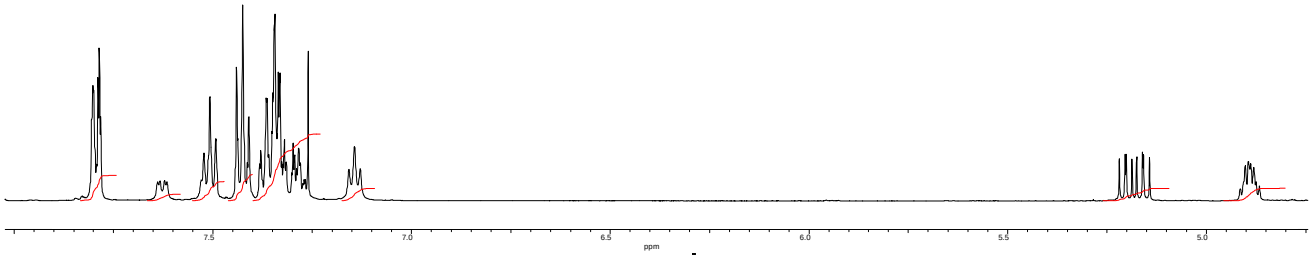

BnO
H
N
O
BzHN
OMe
O
OMe

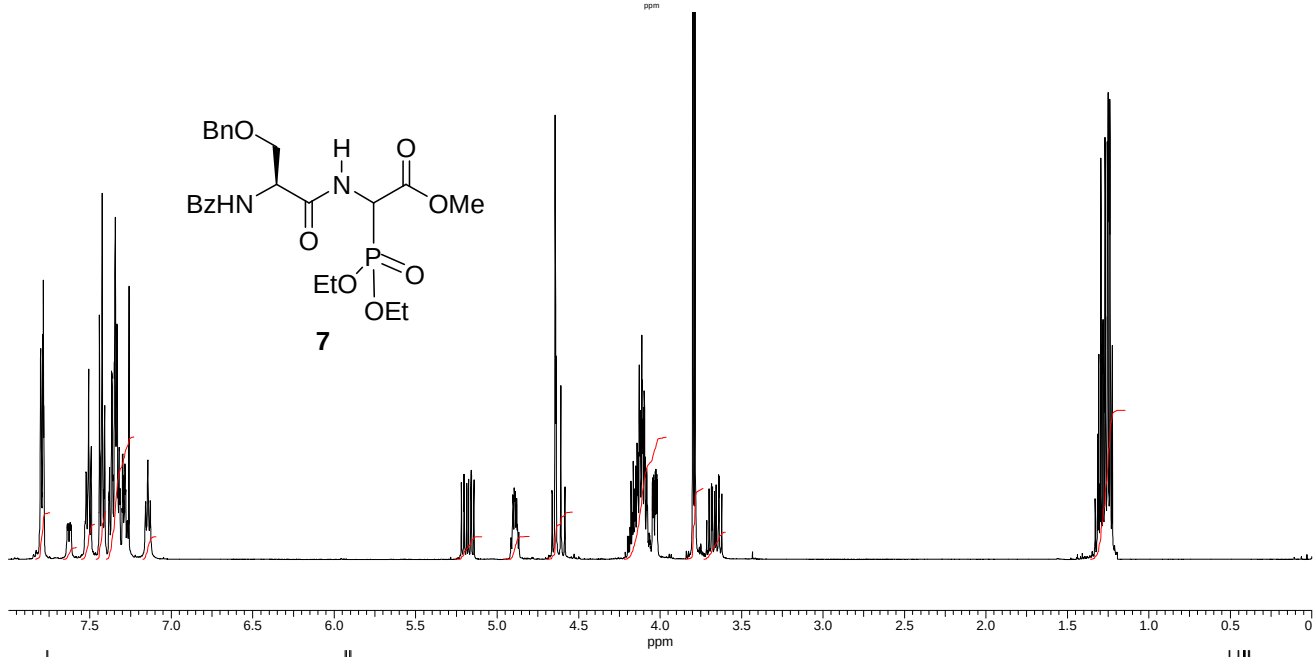
6

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
ppm


5.7 5.6 5.5 5.4 5.3 5.2 5.1 5.0 4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3
ppm

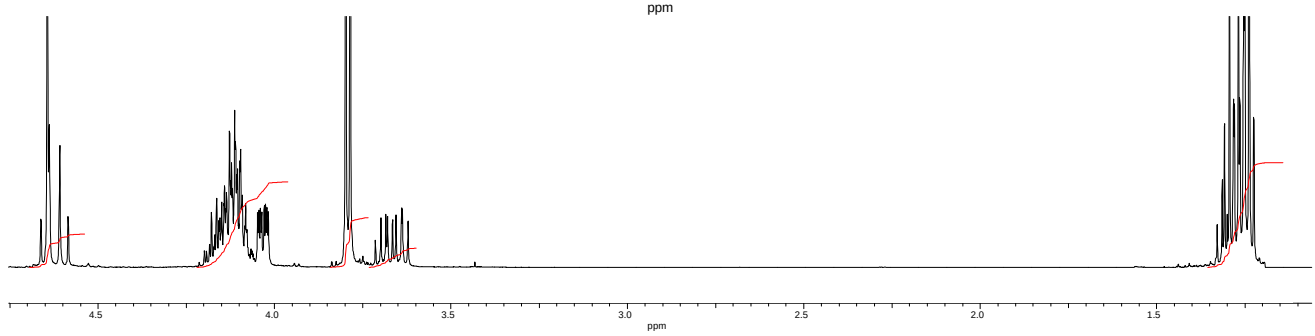

176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
ppm

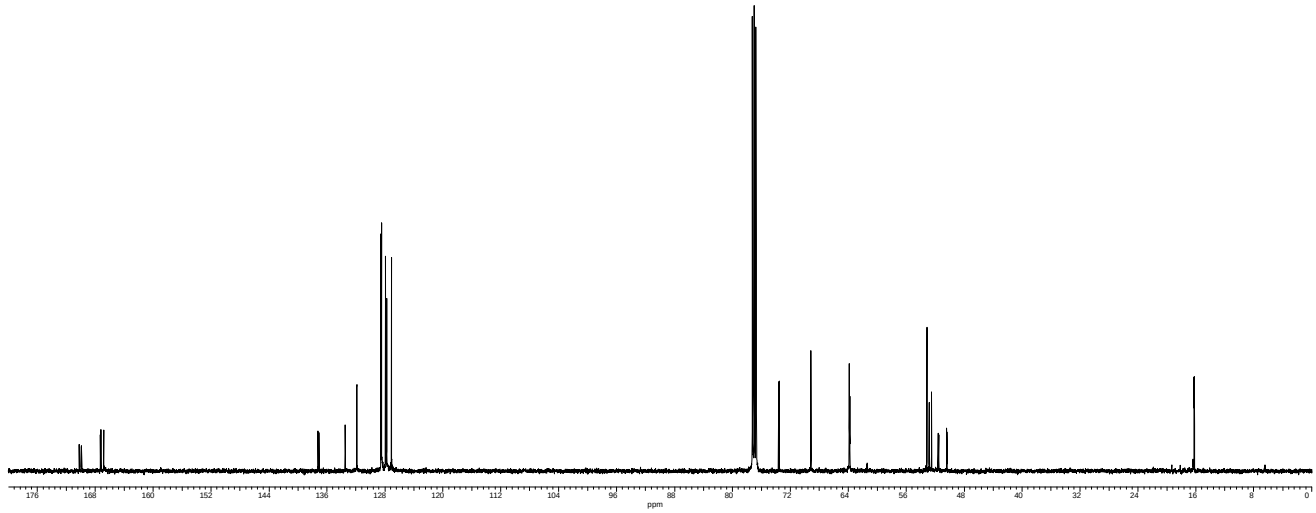


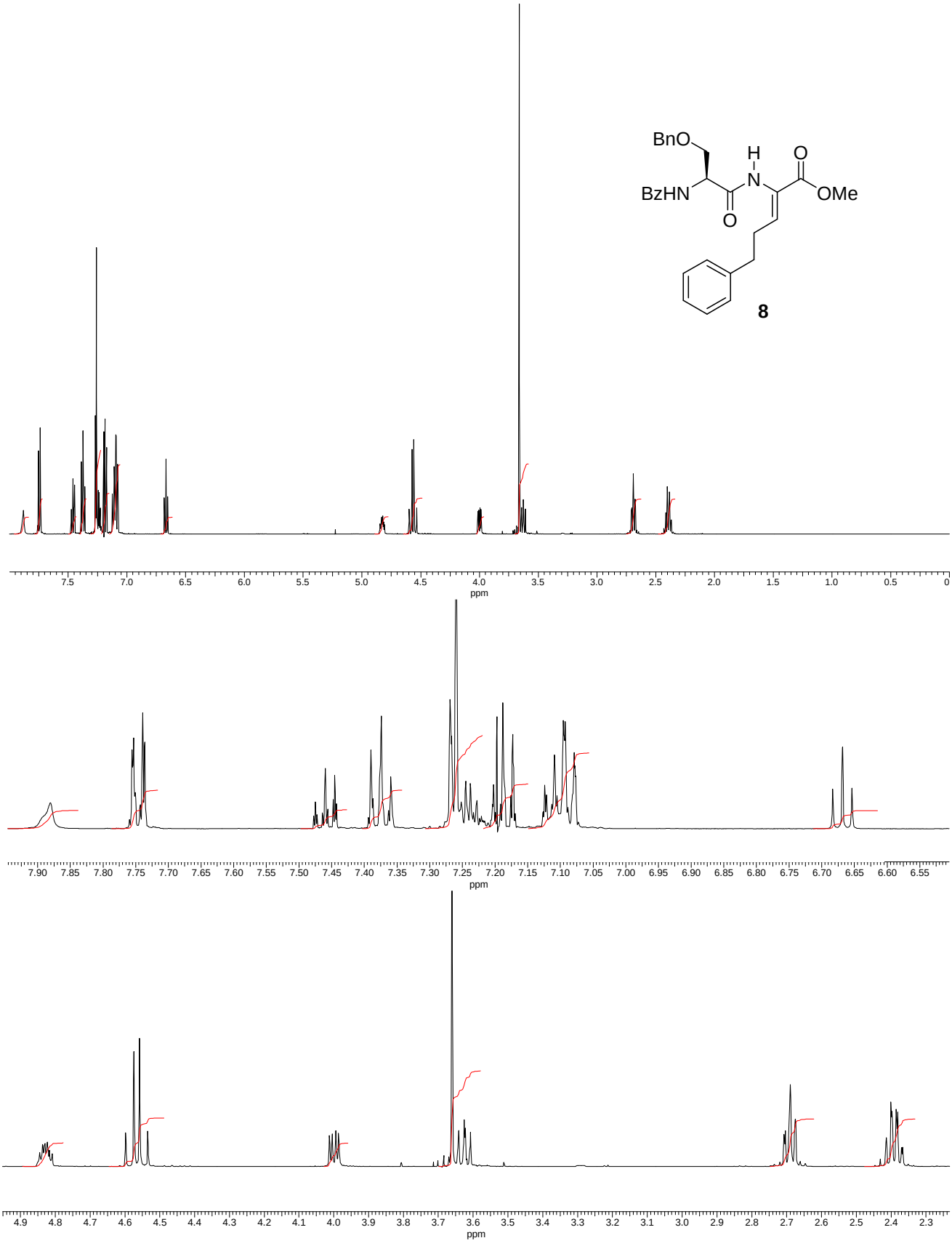

BnO
H
O
N
BzHN
OMe
O
P
O
EtO
OEt

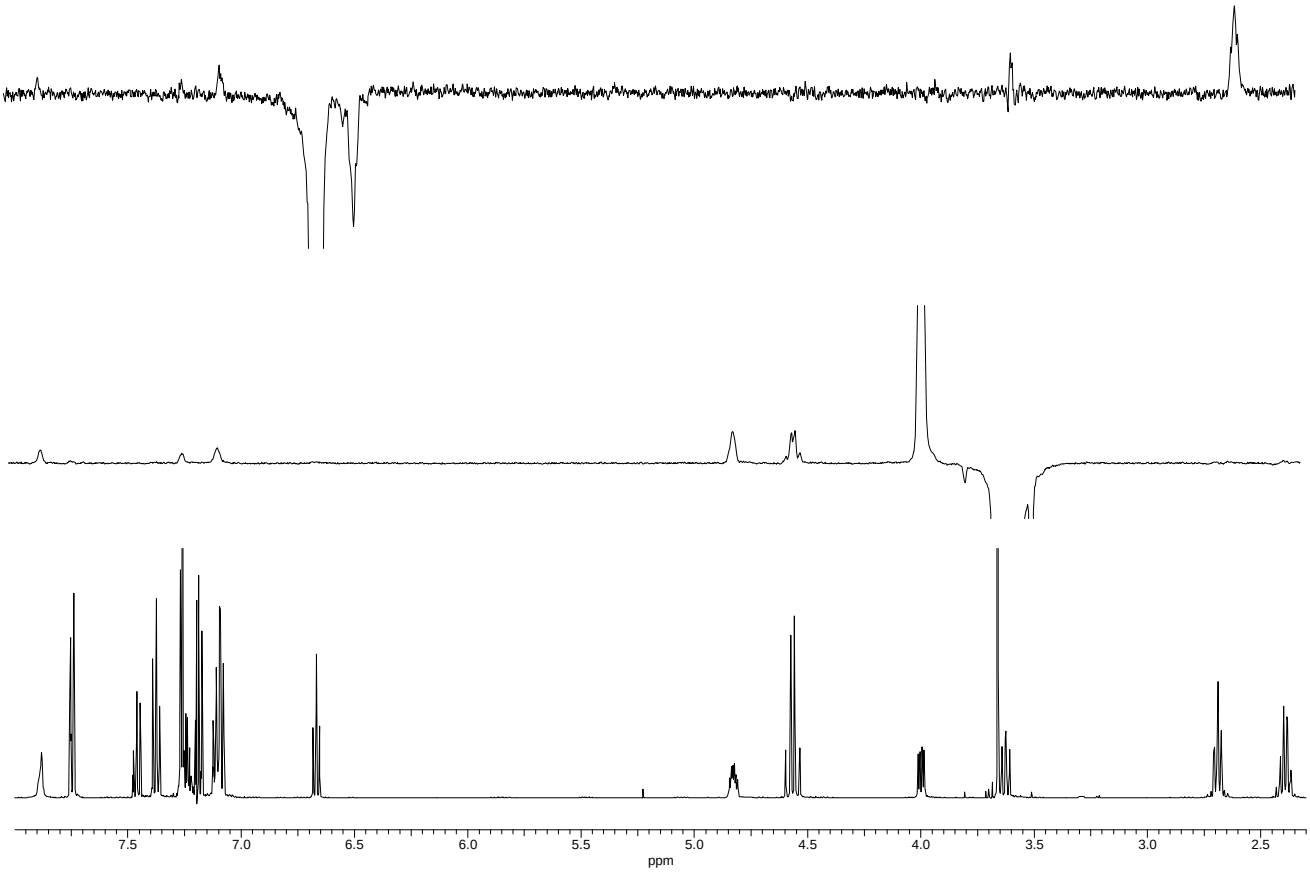
7

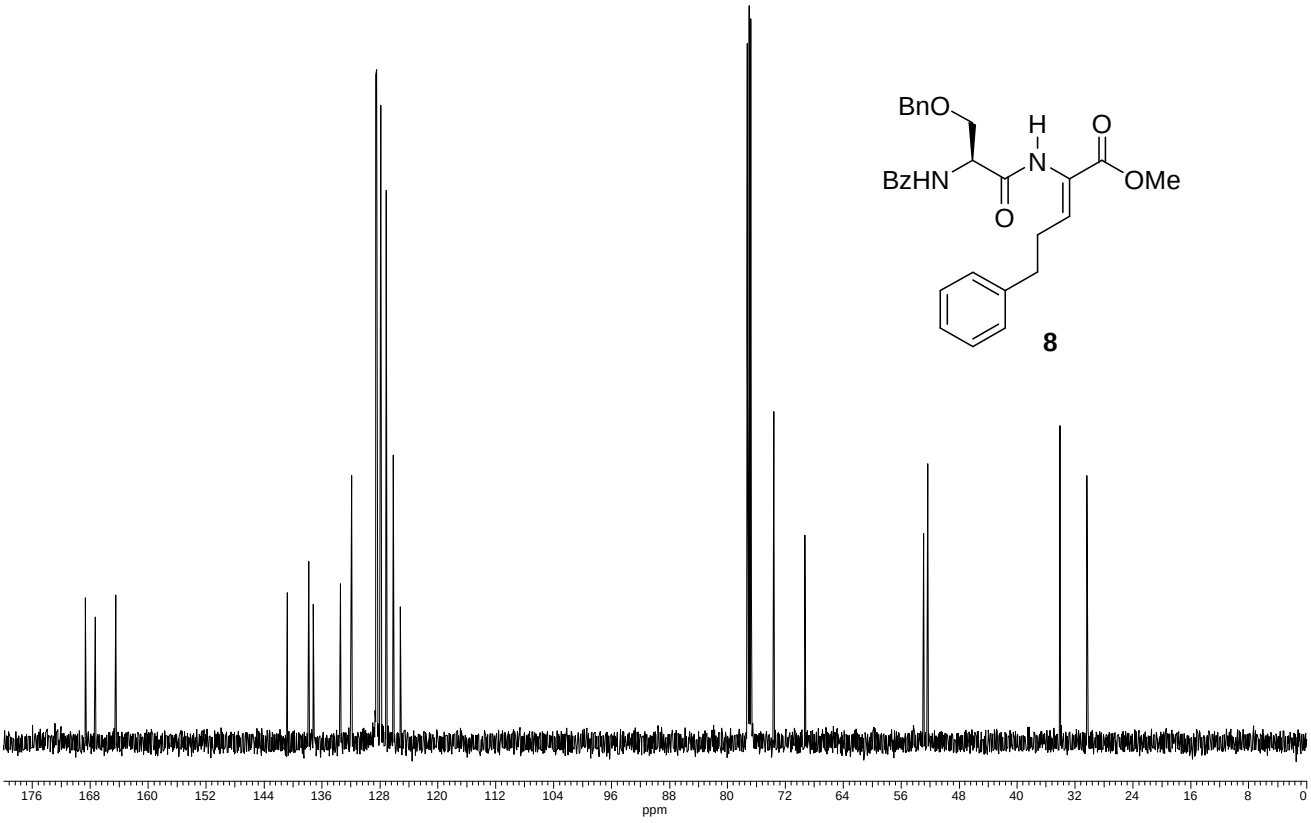
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
ppm


4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm


176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm

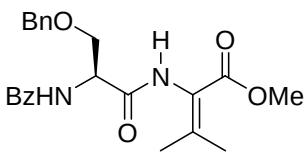

BnO
H
N
O
BzHN
O
OMe
8
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
ppm
7.90 7.85 7.80 7.75 7.70 7.65 7.60 7.55 7.50 7.45 7.40 7.35 7.30 7.25 7.20 7.15 7.10 7.05 7.00 6.95 6.90 6.85 6.80 6.75 6.70 6.65 6.60 6.55
ppm
4.9 4.8 4.7 4.6 4.5 4.4 4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3
ppm


7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
ppm


176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm

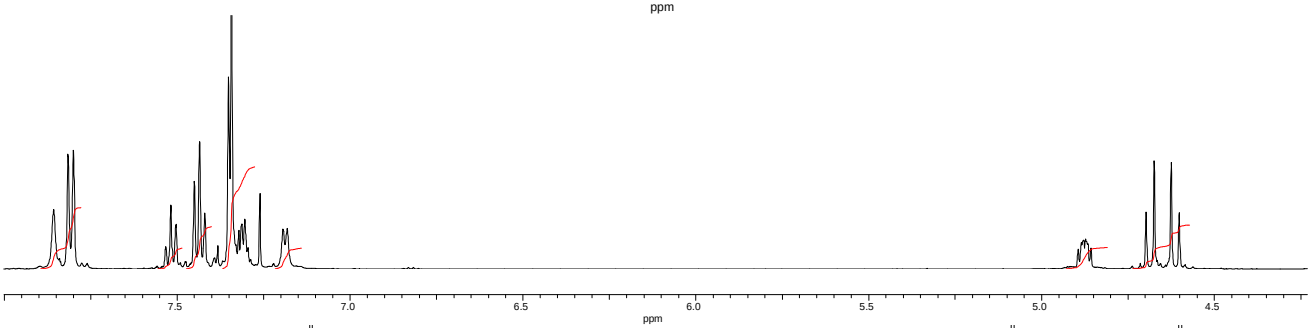
BnO
H
O
N
BzHN
OMe
O

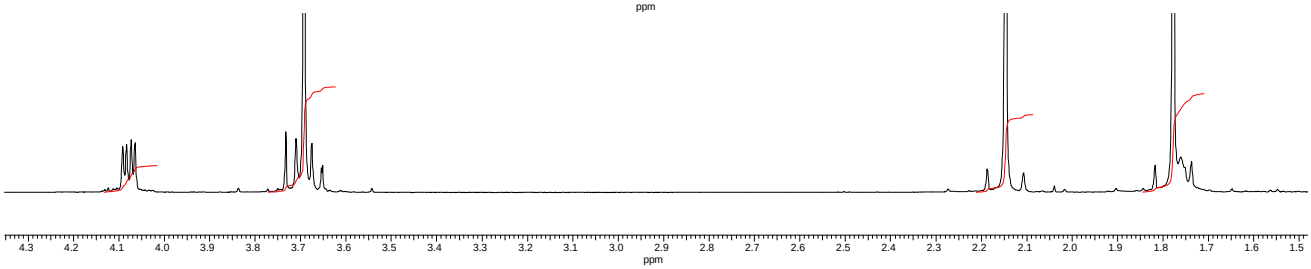
8

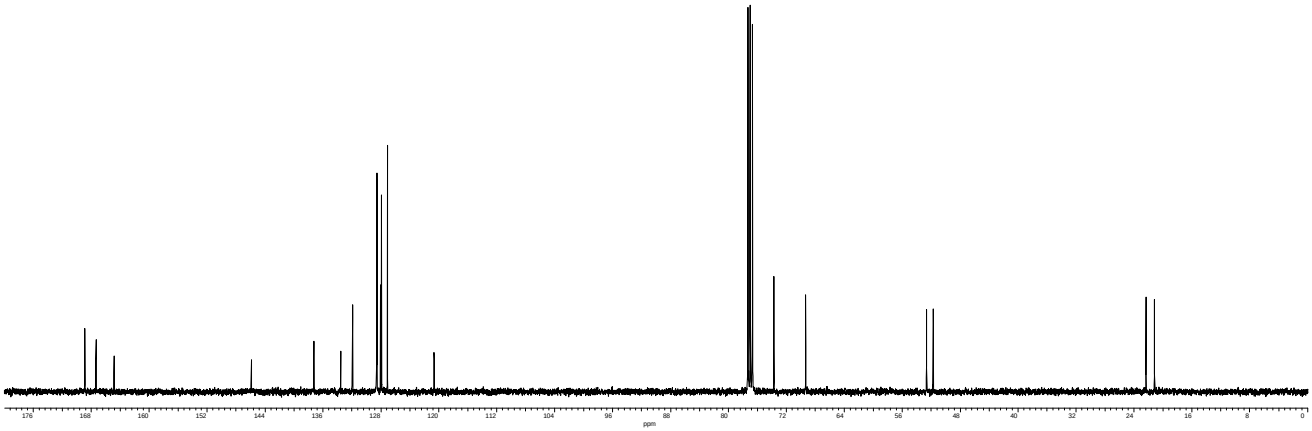

BnO
H
N
O
BzHN
O
OMe

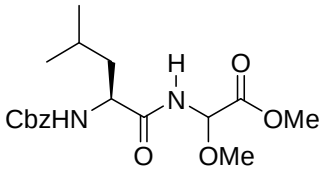
9

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
ppm


7.5 7.0 6.5 6.0 5.5 5.0 4.5
ppm

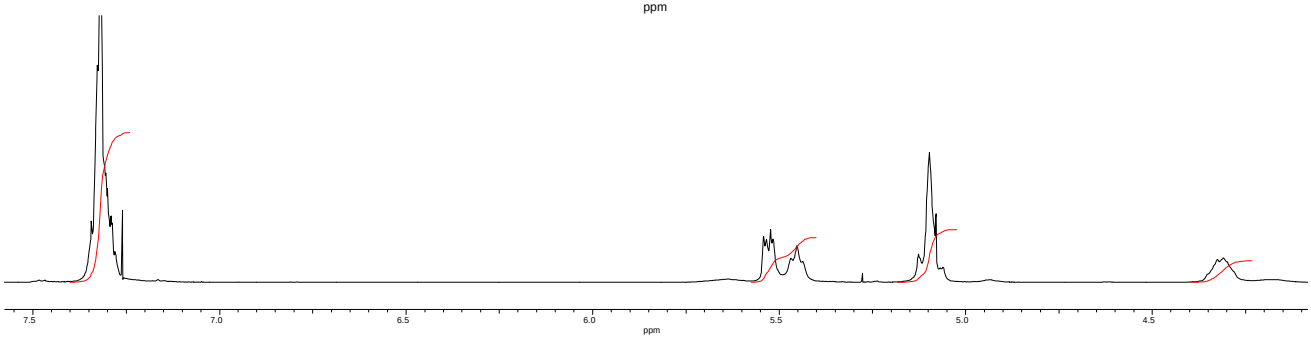

4.3 4.2 4.1 4.0 3.9 3.8 3.7 3.6 3.5 3.4 3.3 3.2 3.1 3.0 2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5
ppm

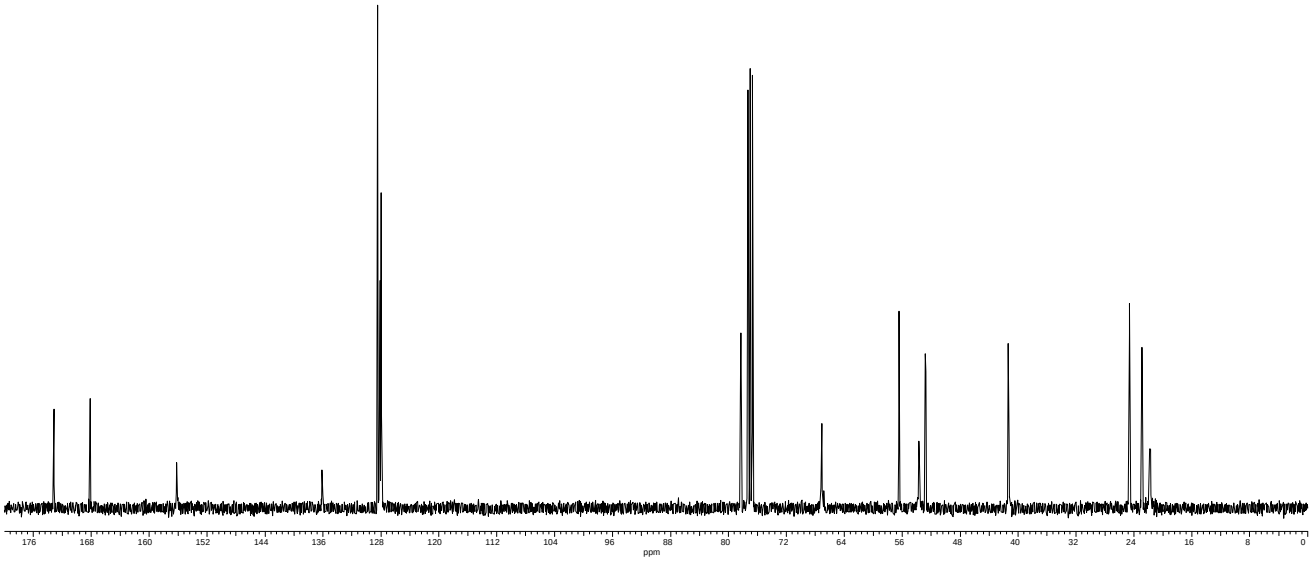

176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
ppm

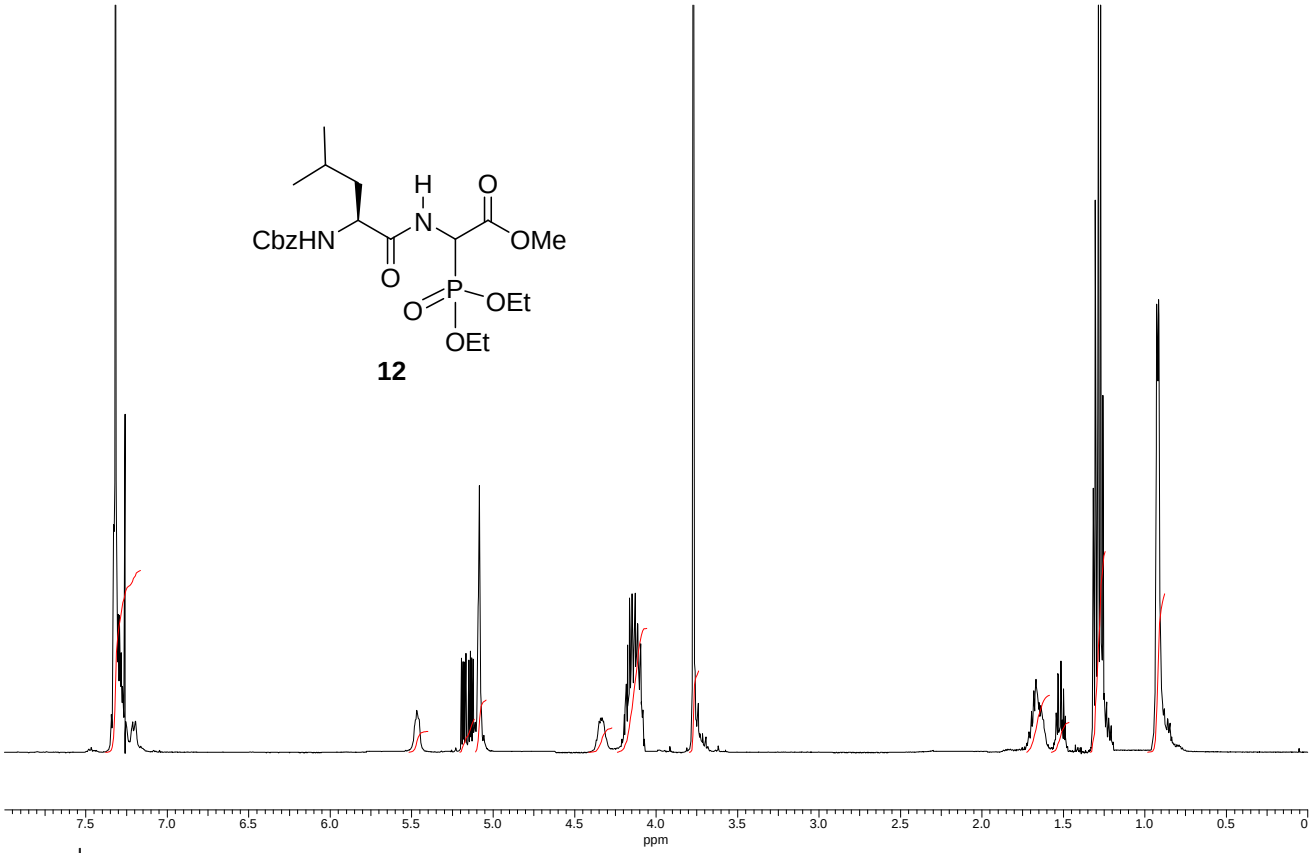

H
O
N
CbzHN
OMe
O
OMe

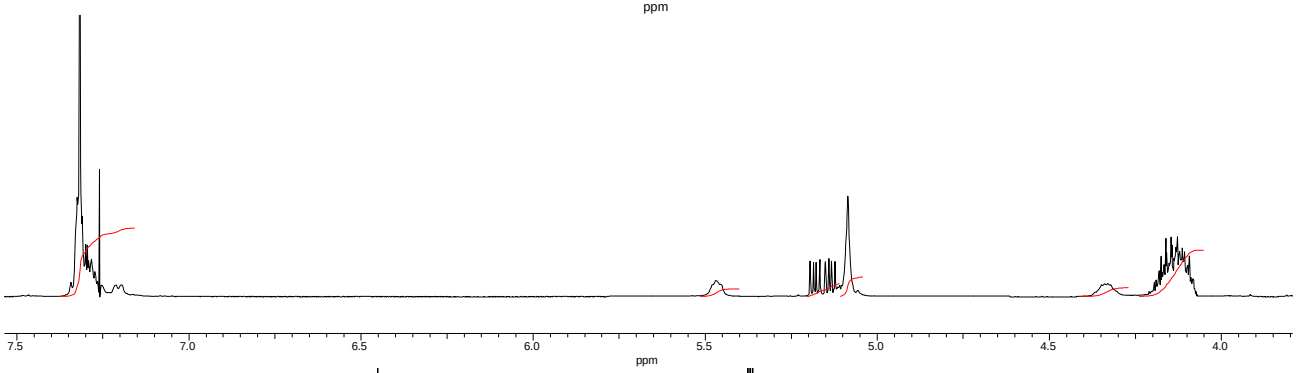
10

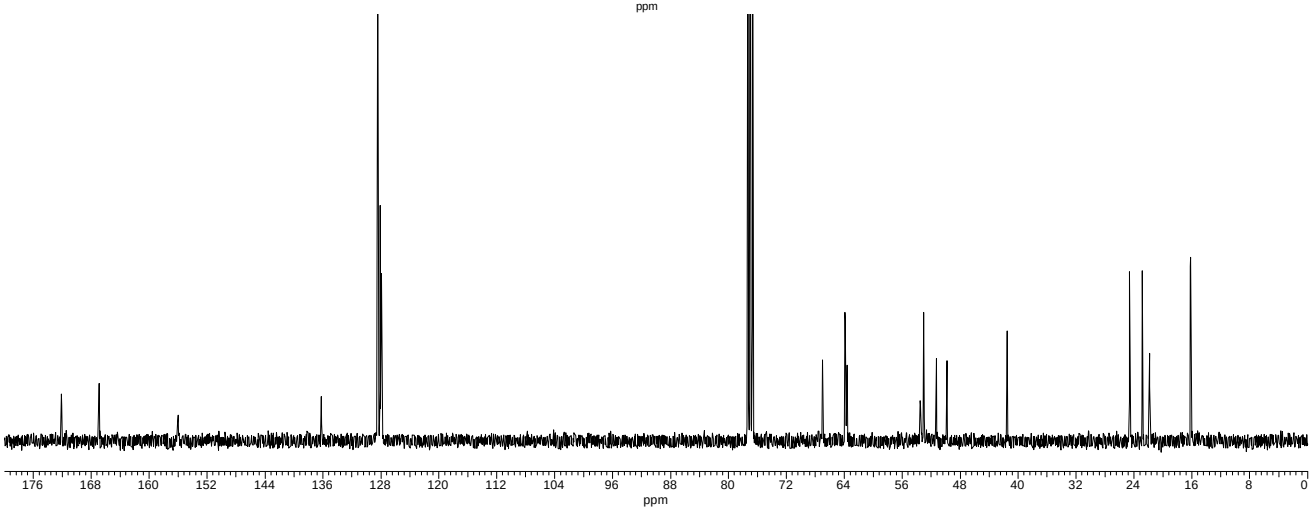
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
ppm

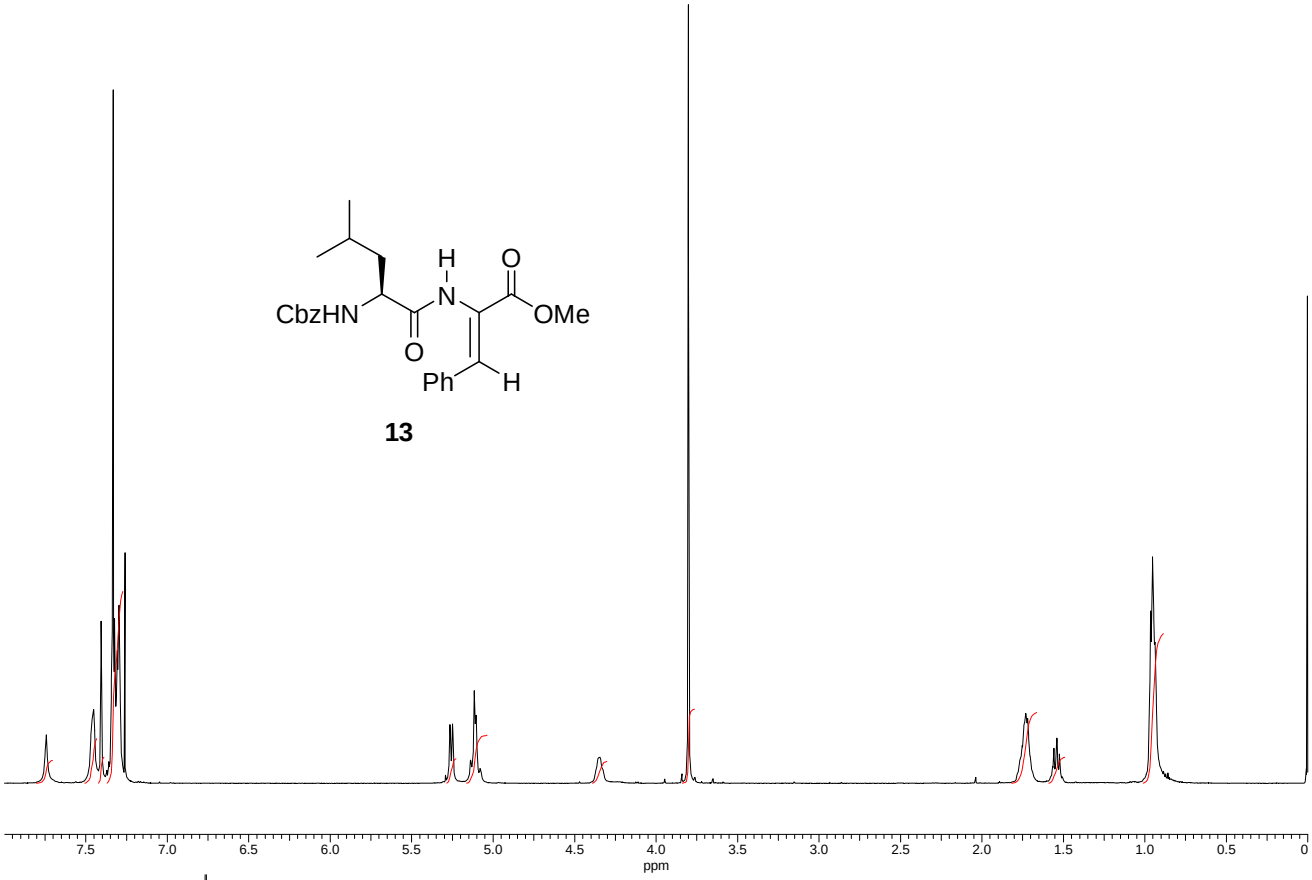

7.5
7.0
6.5
6.0
5.5
5.0
4.5
ppm


176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm

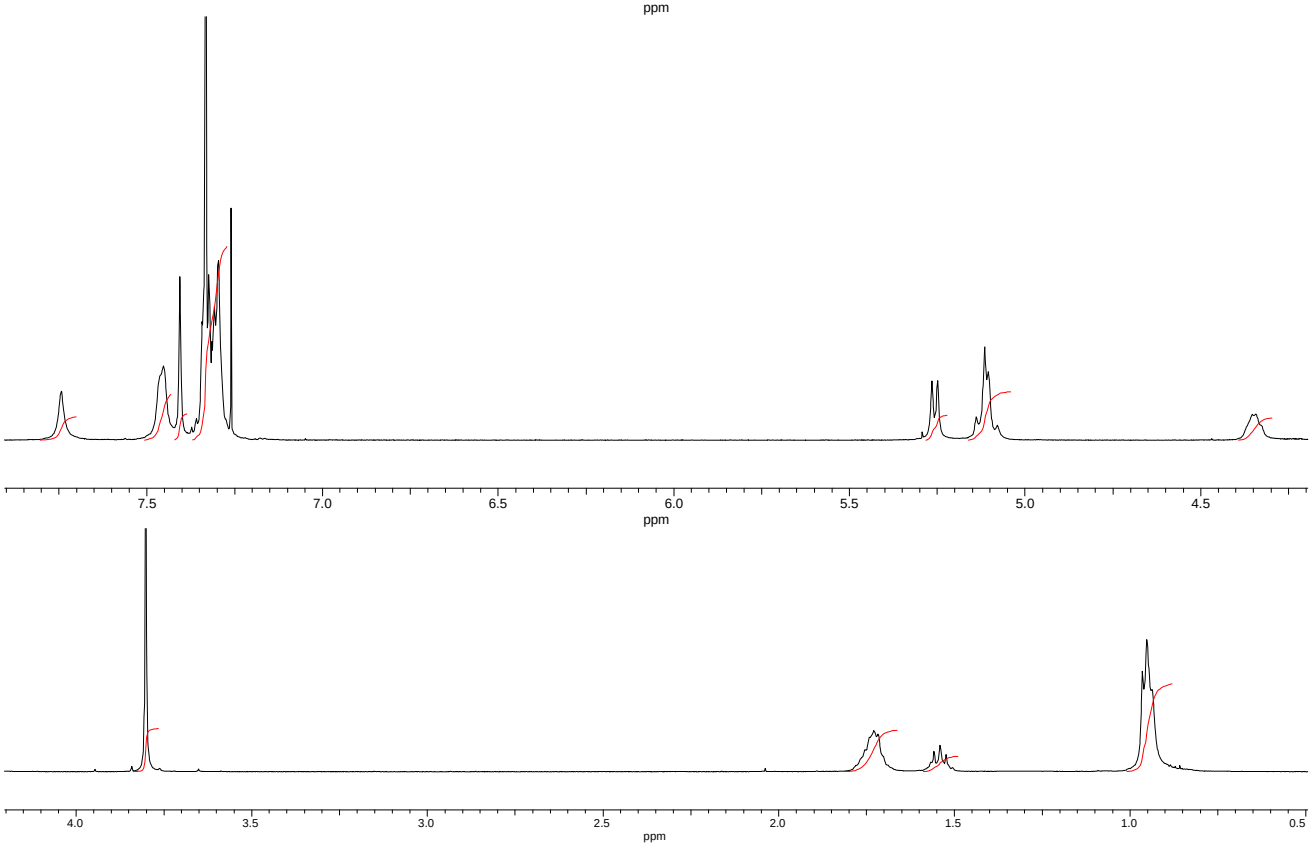

H
O
N
CbzHN
OMe
O
P
O
OEt
OEt
12
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
ppm

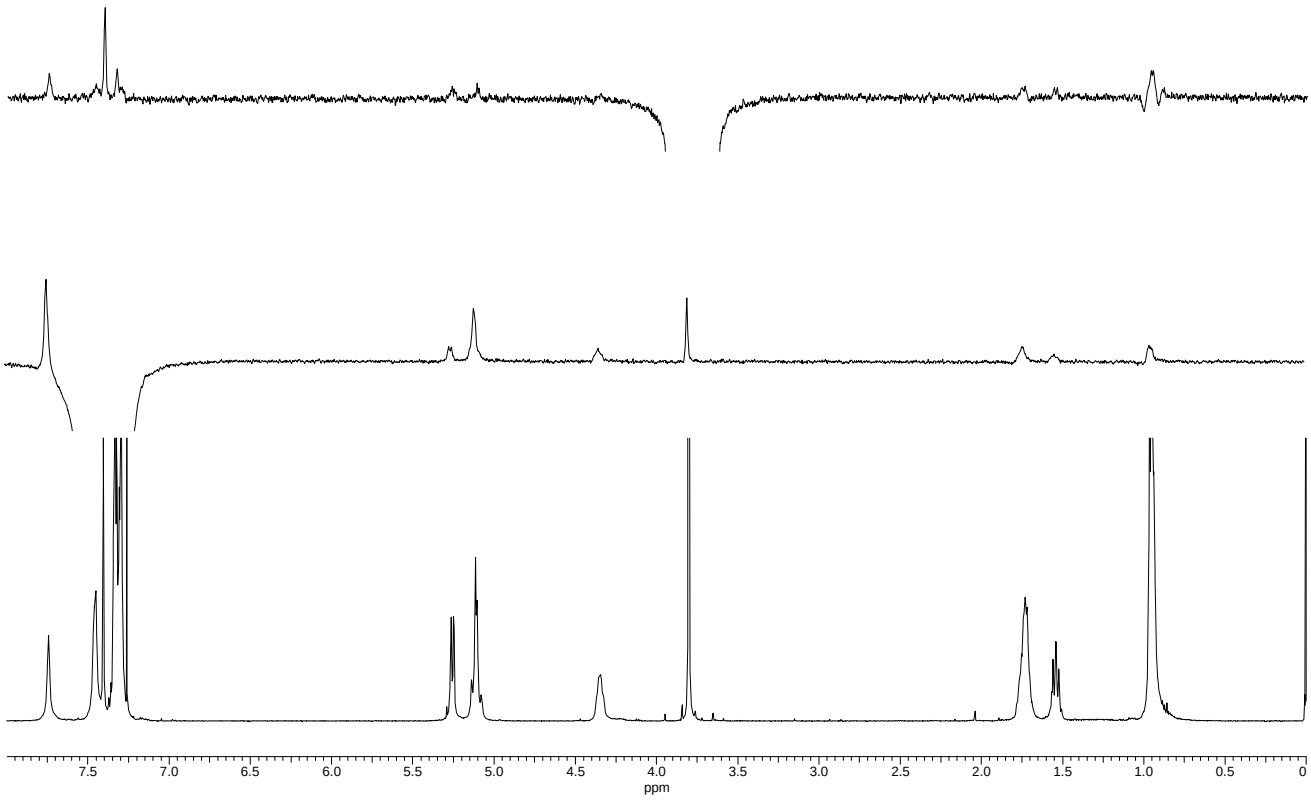

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0
ppm

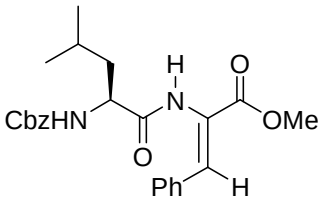

176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
ppm


H
O
N
CbzHN
OMe
O
Ph
H
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
ppm

13

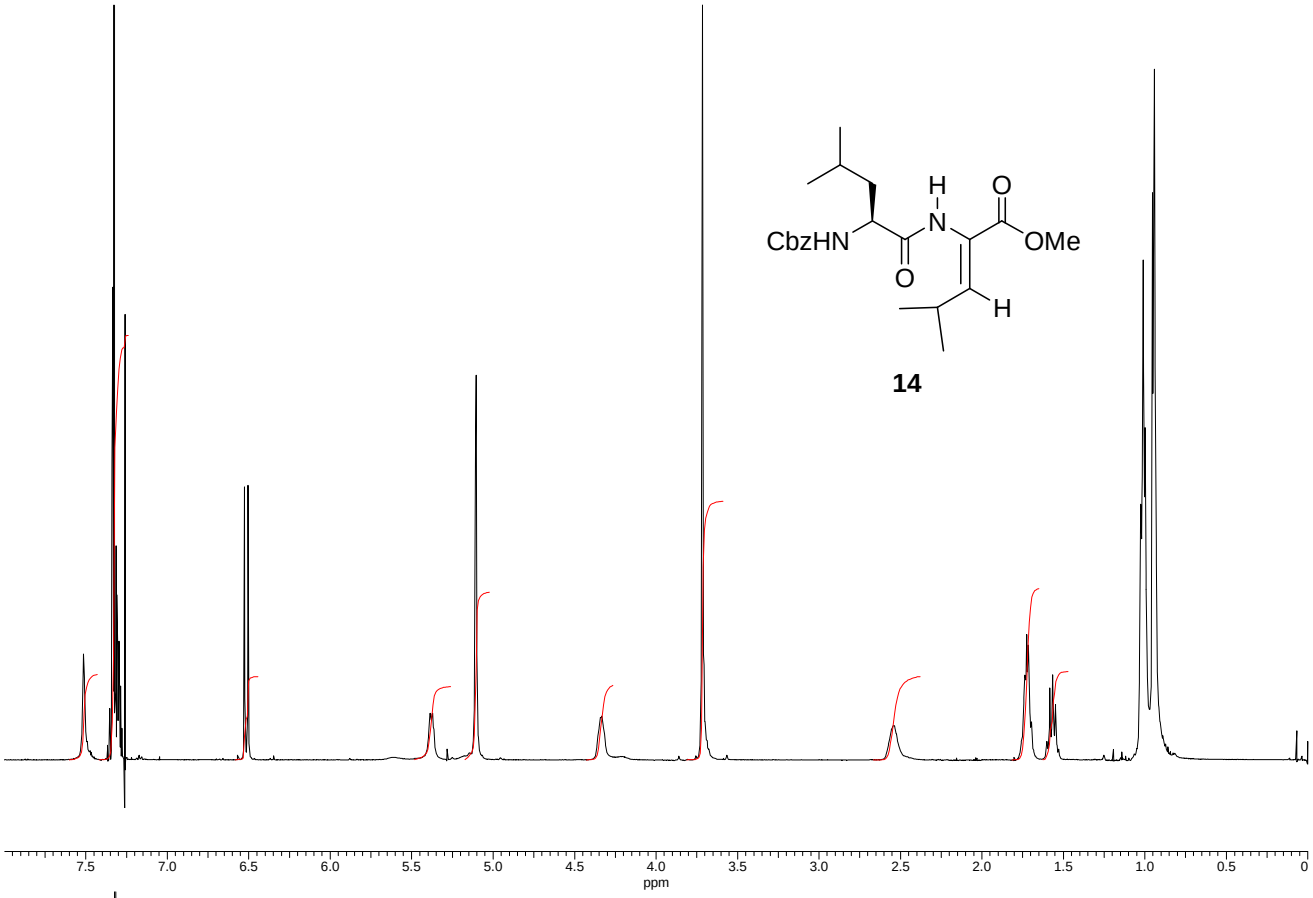

7.5
7.0
6.5
6.0
5.5
5.0
4.5
ppm
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm

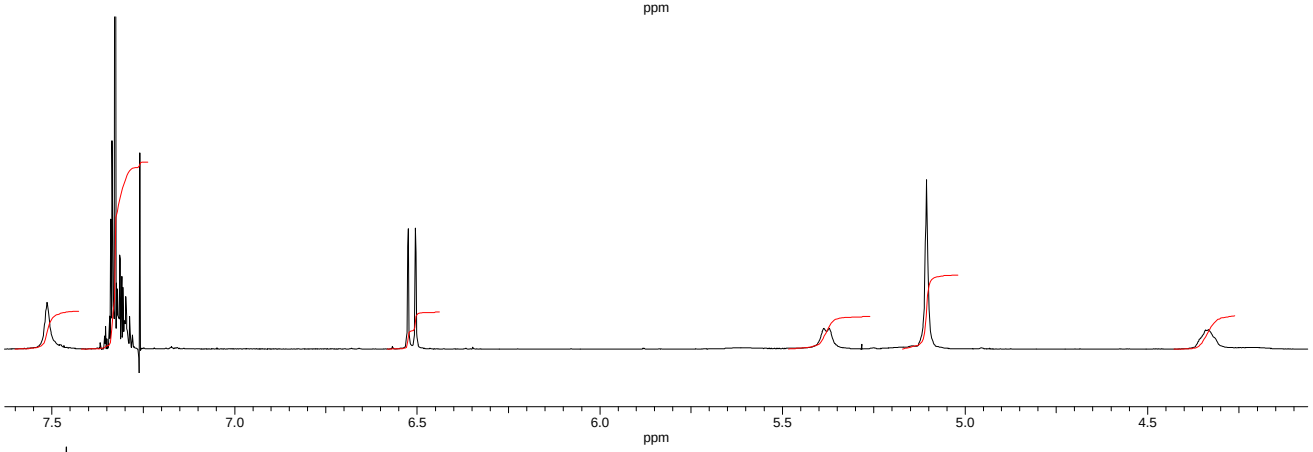

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
ppm

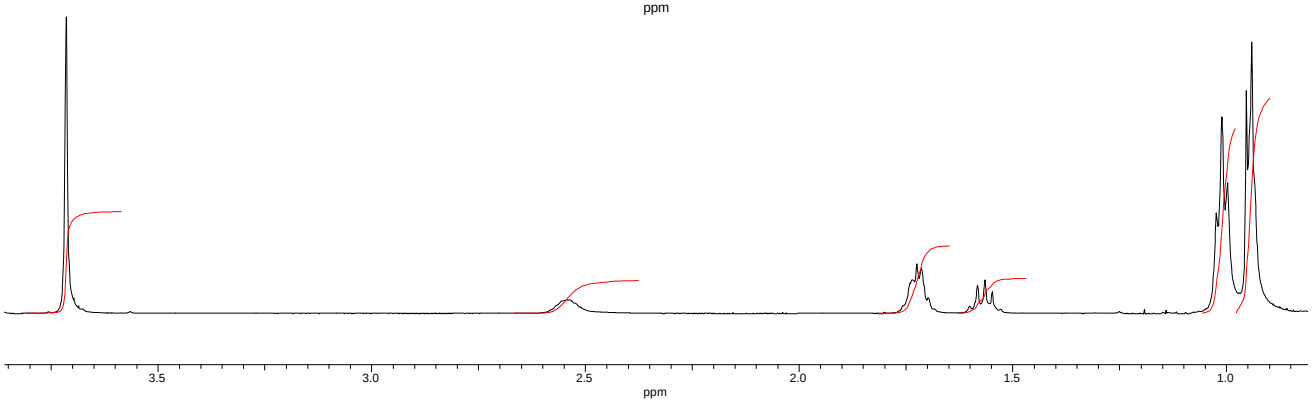

H
O
N
CbzHN
OMe
O
Ph
H

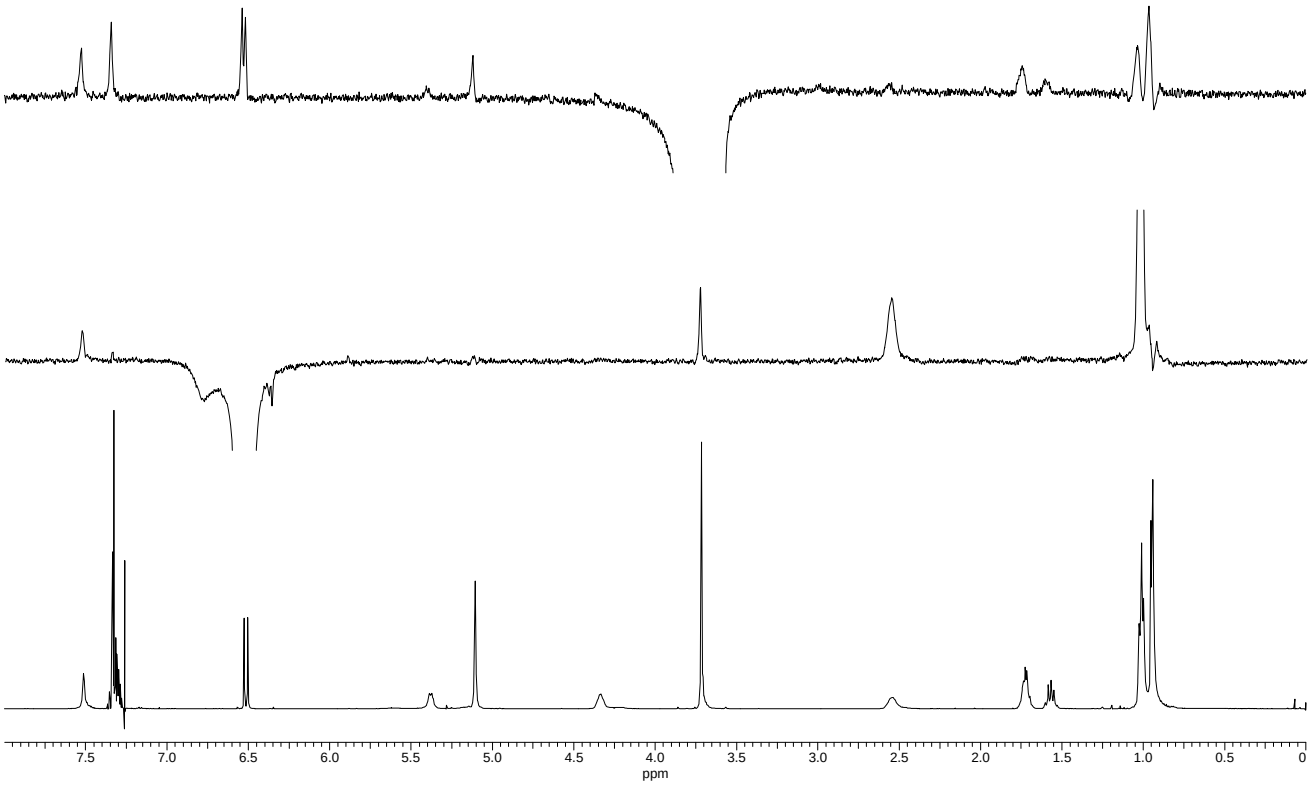
13

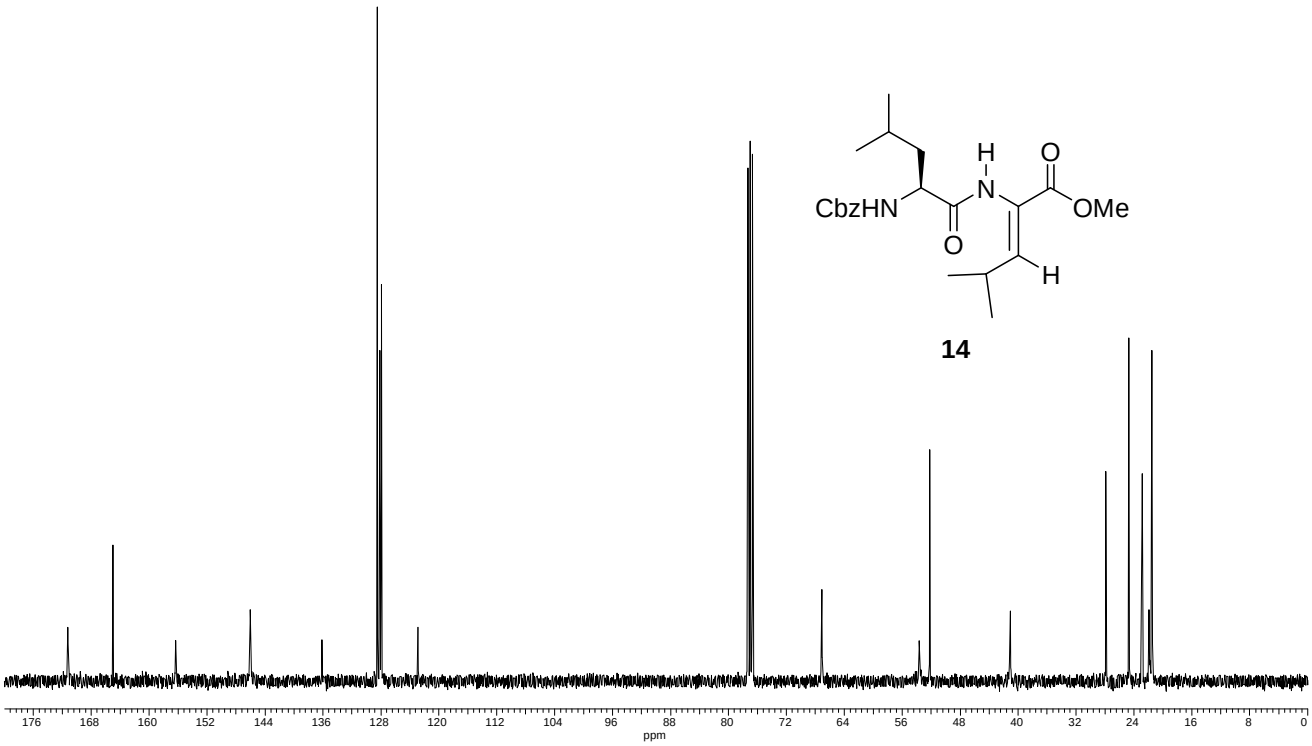
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm


CbzHN
H
N
O
O
OMe
O
H
14
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
ppm


7.5
7.0
6.5
6.0
5.5
5.0
4.5
ppm

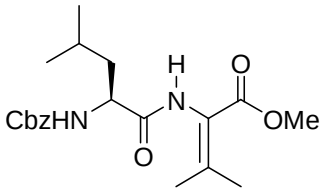

3.5
3.0
2.5
2.0
1.5
1.0
ppm


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
ppm


176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm

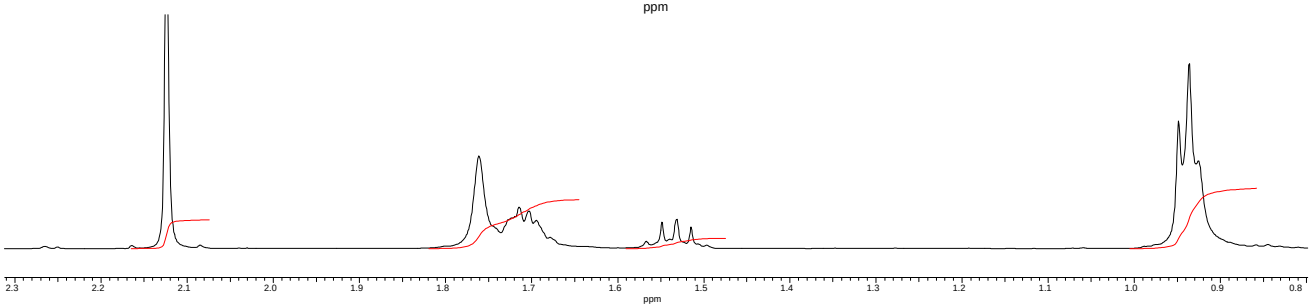
H
O
N
CbzHN
OMe
O
H

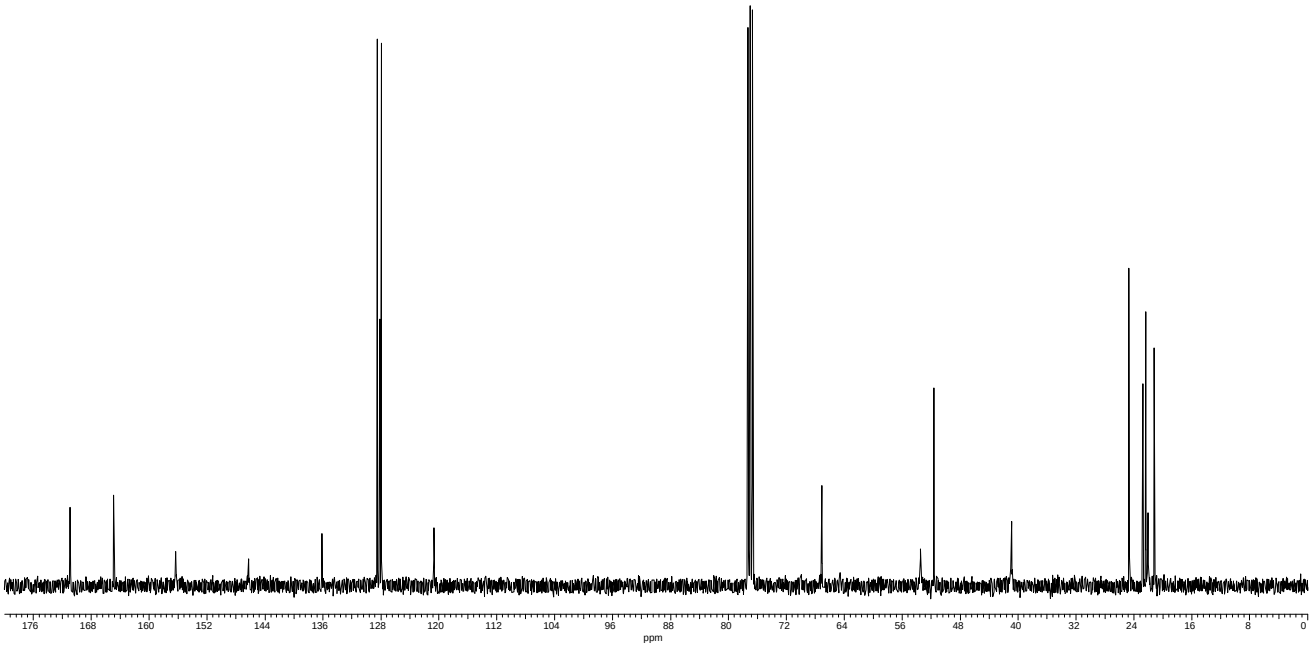
14

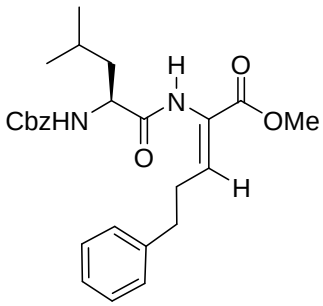

H
O
N
CbzHN
OMe
O

15

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
ppm

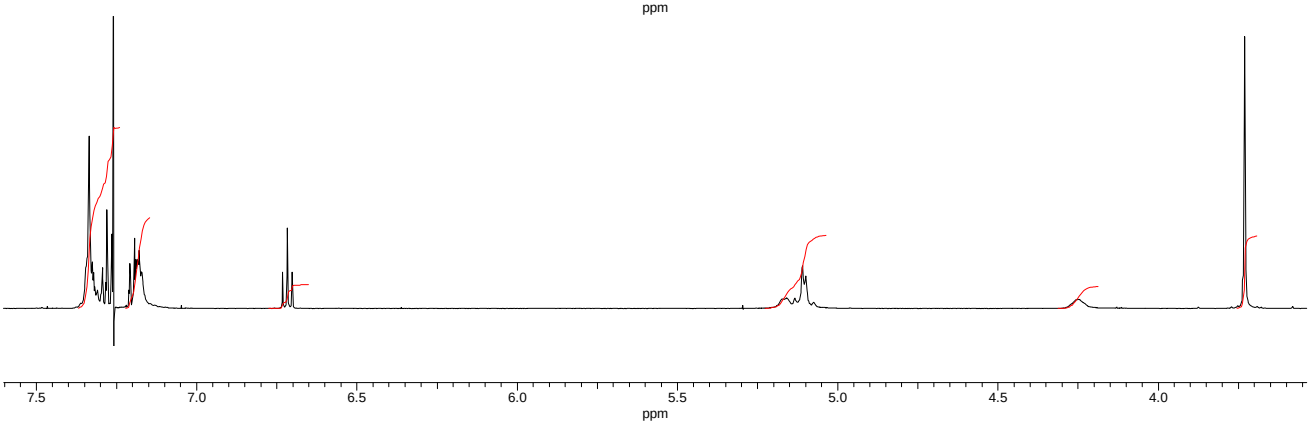

2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
ppm

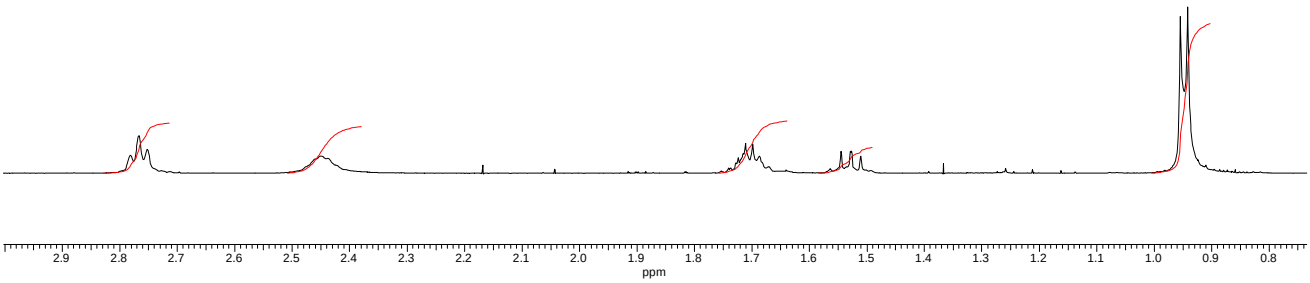

176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm

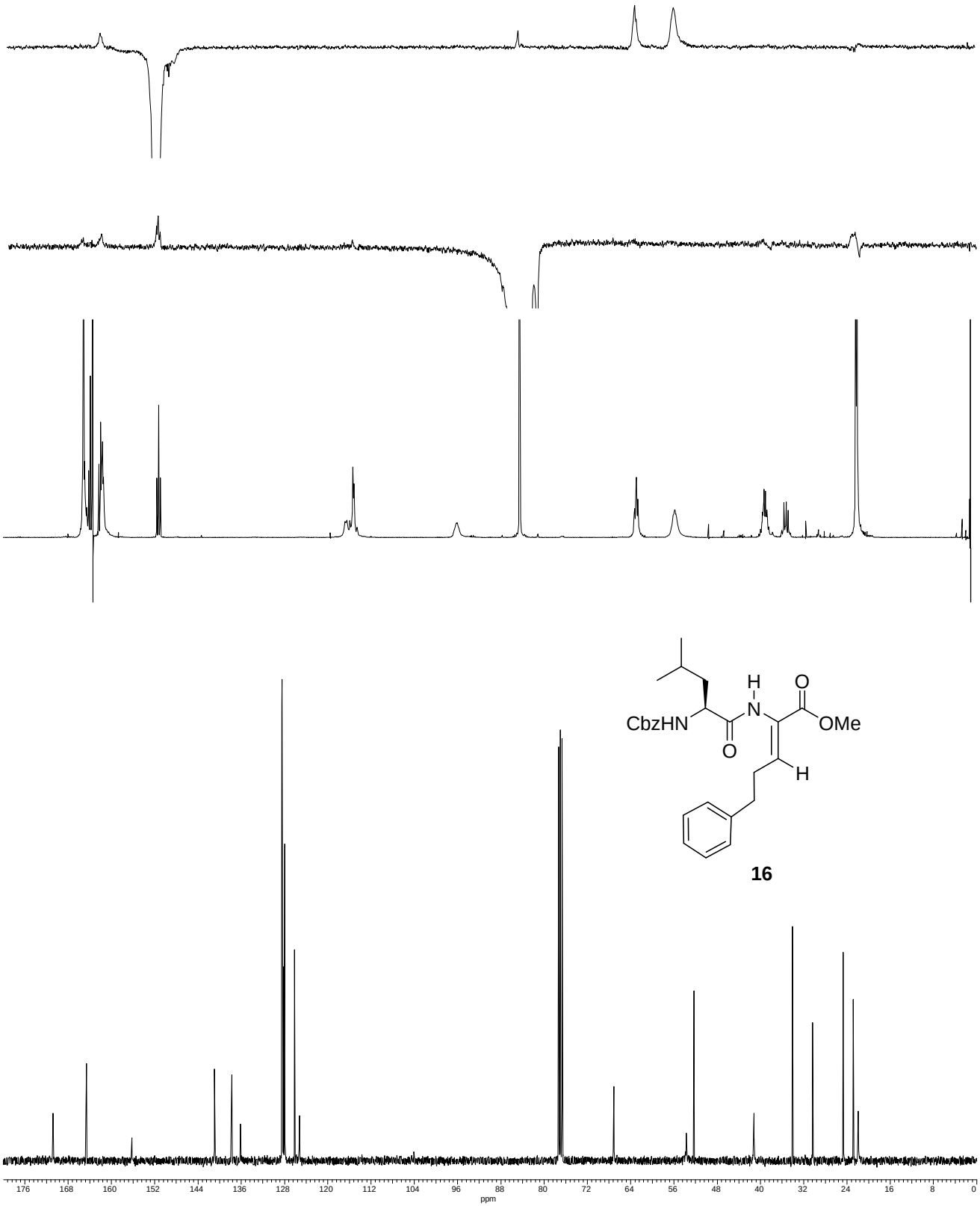

H
O
N
CbzHN
OMe
O
H

16

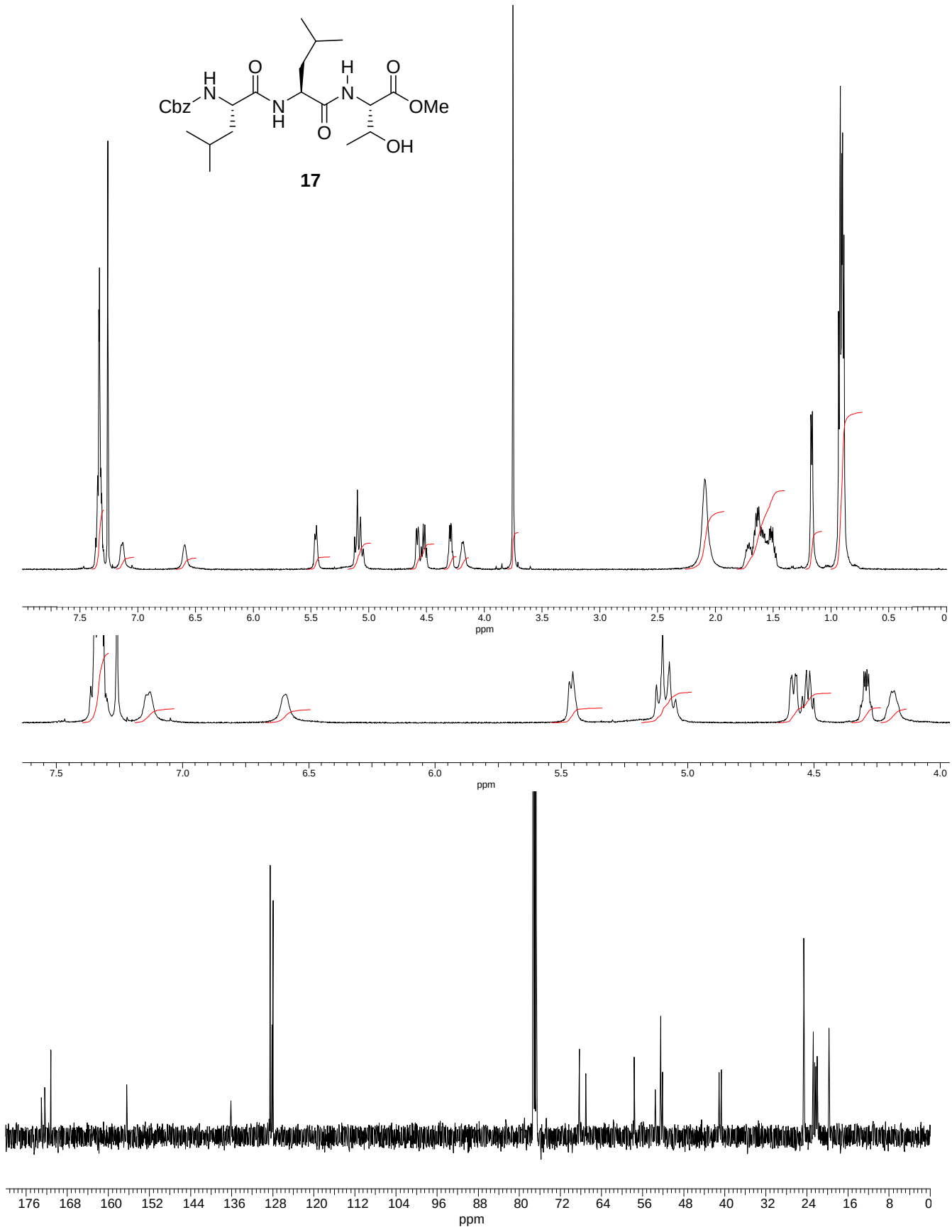
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
ppm

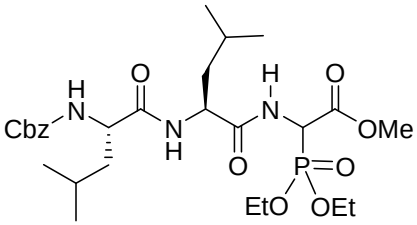

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
ppm


2.9
2.8
2.7
2.6
2.5
2.4
2.3
2.2
2.1
2.0
1.9
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
ppm


CbzHN
H
N
O
O
OMe
H
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
ppm

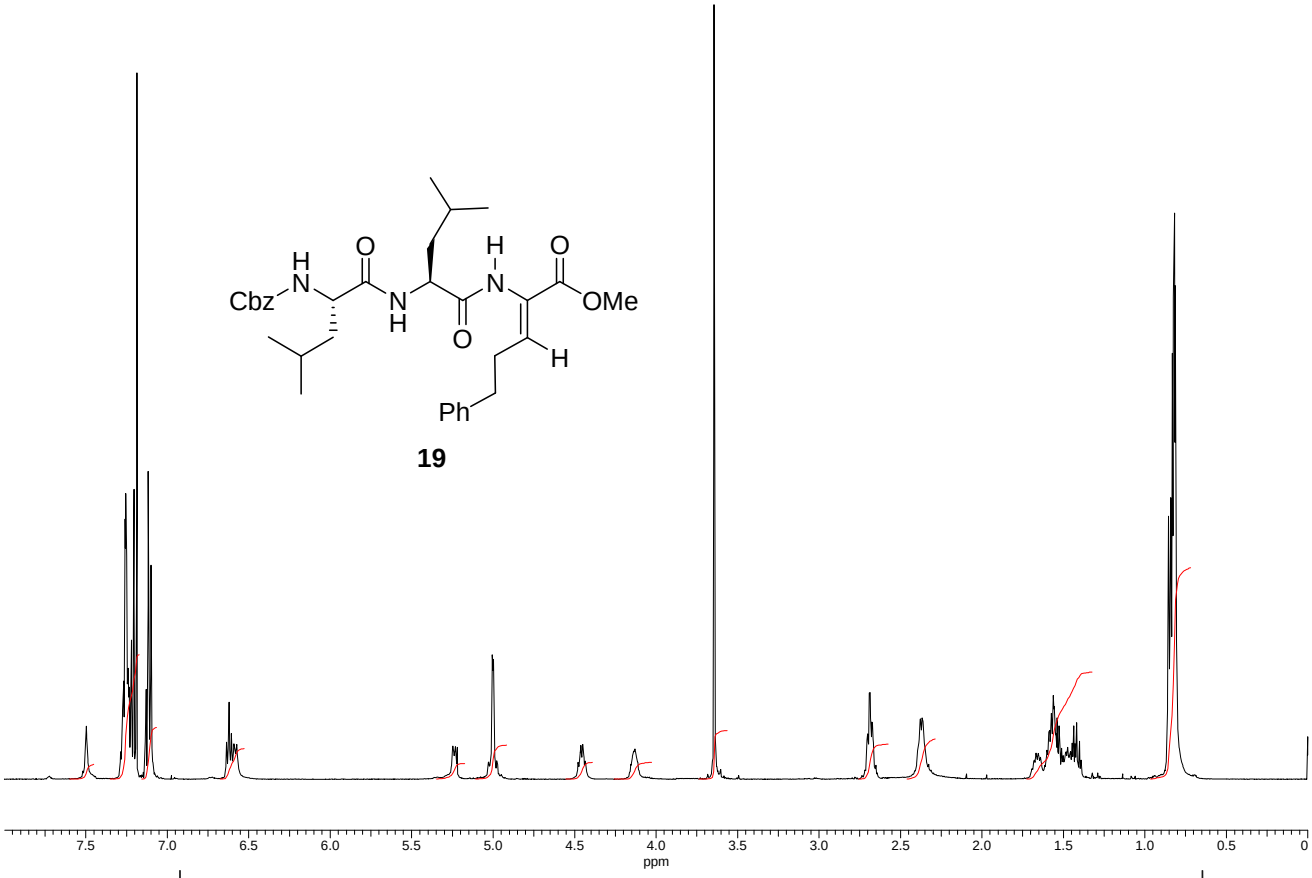
16

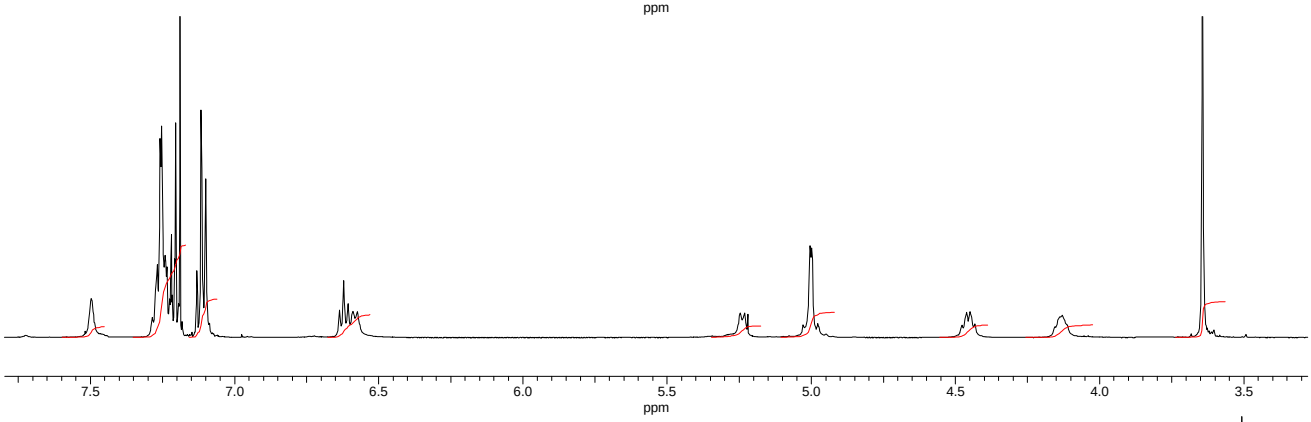

Cbz
H
N
O
N
H
H
N
O
O
OMe
OH
17
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
ppm
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0
ppm
176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
ppm

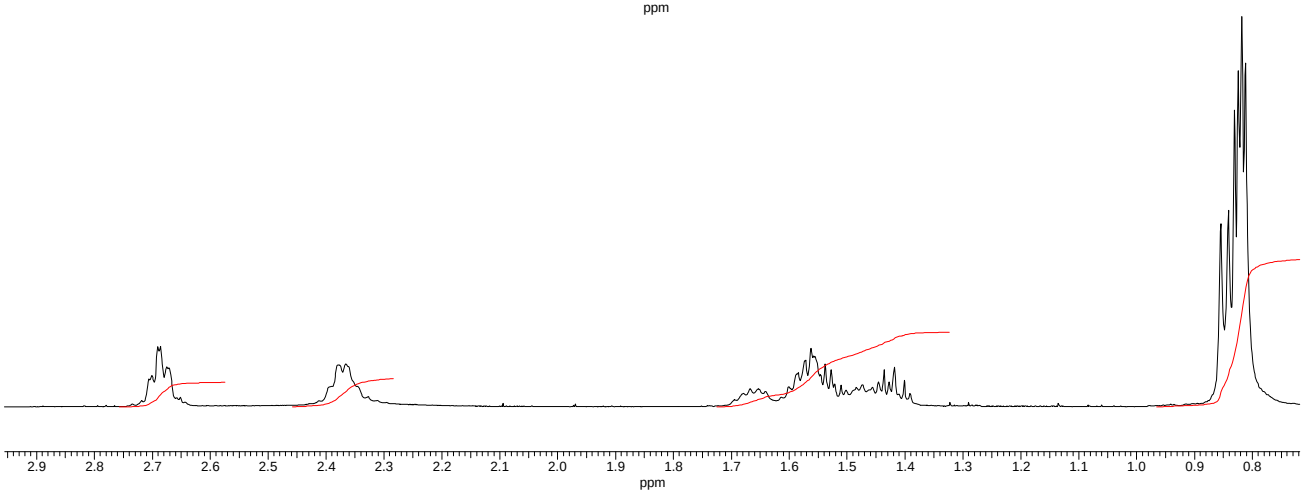

Cbz
H
N
O
N
H
O
H
N
O
OMe
O
P
O
EtO
OEt

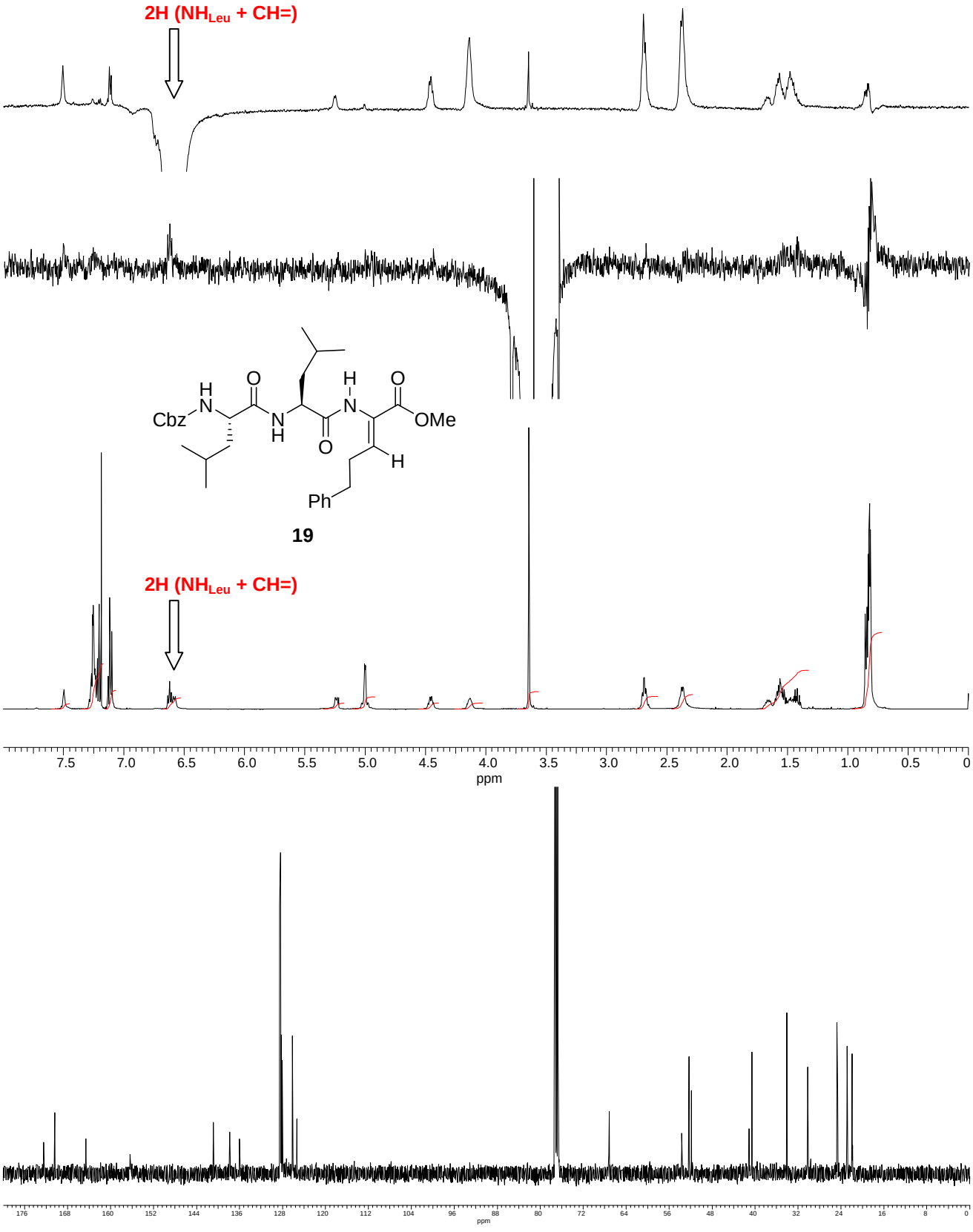
18

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
ppm


Cbz
H
N
O
N
H
H
N
O
OMe
O
H
Ph
19
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
ppm


7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5
ppm


2.9 2.8 2.7 2.6 2.5 2.4 2.3 2.2 2.1 2.0 1.9 1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0 0.9 0.8
ppm


2H (NHLeu + CH=)
Cbz
OMe
Ph
19
2H (NHLeu + CH=)
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
ppm
176 168 160 152 144 136 128 120 112 104 96 88 80 72 64 56 48 40 32 24 16 8 0
ppm