Supporting information

for

Photochemical formation of quinone methides from peptides containing modified tyrosine

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Content:

1. Synthetic procedures for the preparation of known compounds

BOC-(L)-Tyr(OH)-OH

In a flask, K_2CO_3 (9.12 g, 66.6 mmol) was dissolved in a mixture of H_2O and dioxane (1:1, 100 mL). The solution was cooled to 0°C and then L-tyrosine (4.00 g, 22.0 mmol) and a solution of BOC_2O (4.80 g, 22.0 mmol) in dioxane (30 mL) were added. The reaction mixture was stirred at rt over night. The next day, H_2O (100 mL) was added, followed by saturated solution of $KHSO_4$ until pH = 4. The product was extracted by ethyl acetate (3×100 mL), the organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was removed on a rotary evaporator. The product was isolated in a form of yellow oil (5.83 g, 94 %) which was used in the next step without further purification. Characterization is in accord with the precedent literature.[1]

Yellow oil; ^{1}H NMR (CD_3OD, 300 MHz) δ/ppm: 7.03 (d, J= 8.4 Hz, 2H), 6.70 (d, J= 8.4 Hz, 2H), 4.32-4.23 (m, 1H), 3.04 (dd, J= 13.8, 5.2 Hz, 1H), 2.81 (dd, J= 13.8, 5.2 Hz, 1H),1.39 (s, 9H).

BOC-(L)-Tyr(OH)-OBn

A round bottom flask was charged with L-BOC-Tyr(OH)-OH (5.83 g, 20.7 mmol) and a mixture of dioxane and DMF (1:1, 150 mL). To the suspension, benzyl bromide (2.46 mL, 20.7 mmol) and $NaHCO_3$ (1.74 g, 20.7 mmol) were added with continuous stirring. The reaction mixture was stirred overnight at 90 °C. The reaction mixture was cooled to rt and the solvent was removed on a rotary evaporator. The crude product was dissolved in ethyl acetate (100 mL) and the solution was washed with brine (100 mL) and water (100 mL). The organic layer was dried over the

anhydrous $MgSO_4$, filtered and the solvent was removed on a rotary evaporator. The product was isolated in a form of yellow oil (6.87 g, 89%). Characterization is in accord with the precedent literature.[2]

Yellow oil; ^{1}H NMR (CD_3OD, 600 MHz) δ/ppm: 7.37-7.24 (m, 5H), 6.96 (d, J= 8.0 Hz, 2H), 6.67 (d, J= 8.0 Hz, 2H), 5.10 (d, J= 12.8 Hz, 1H), 5.07 (d, J= 12.8 Hz, 1H), 4.34-4.23 (m, 1H), 2.97 (dd, J= 13.3, 6.4 Hz, 1H), 2.84 (dd, J= 13.3, 6.4 Hz, 1H), 1.38 (s, 9H); ^{13}C NMR (CD_3OD, 150 MHz) δ/ppm: 173.8 (s, 1C), 157.8 (s, 1C), 157.3 (s, 1C), 137.1 (s, 1C), 131.3 (d, 2C), 129.5 (d, 2C), 129.3 (d, 1C), 129.2 (d, 2C), 128.8 (s, 1C), 116.2 (d, 2C), 80.7 (s, 1C), 67.8 (t, 1C), 57.0 (d, 1C), 37.9 (t, 1C), 28.7 (q, 3C).

General procedure for the preparation of succinimide activated amino acids

A flask was filled with BOC-protected amino acid (10 mmol), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (EDC, 11 mmol), *N*-hydroxysuccinimide (NHS, 11 mmol) and CH_2Cl_2 (25 mL). The reaction mixture was stirred at -5 °C for 2 h, and left in refrigerator overnight. The next day, the solution was washed with 0.5 M Na_2CO_3 (30 mL), H_2O (30 mL), 0.5 M HCl (30 mL), and H_2O (30 mL), dried over anhydrous $MgSO_4$, filtered and the solvent was removed on a rotary evaporator. The crude succinimido-activated amino acid was used in the coupling step without additional purification.

BOC-(L)-Phe-OSu

Prepared according to the general procedure from BOC-(L)-Phe-OH (3.00 g, 11.3 mmol), NHS (1.43 g, 12.4 mmol) and EDC (1.93 g, 12.4 mmol). The product was isolated in a form of colorless solid (2.38 g, 58 %). Characterization is in accord with the precedent literature.[3]

Colorless solid; ^{1}H NMR (CD_3OD, 300 MHz) δ/ppm: 7.34-7.19 (m, 5H), 4.74 (dd, J= 4.8, 9.8 Hz, 1H), 3.02 (dd, J= 9,8, 14 Hz, 1H), 2.85 (s, 4H), 1.36 (s, 9H); ^{13}C NMR (DMSO-d_6, 75 MHz) δ/ppm: 171.3 (s, 2C), 169.9 (s, 1C), 157.5 (s, 1C), 137.6 (s, 1C), 130.5 (d, 2C), 129.5 (d, 2C), 128.0 (d, 1C), 80.9 (s, 1C), 54.8 (d, 1C), 38.6 (t, 1C), 28.6 (q, 3C), 26.5 (t, 2C).

General procedure for the peptide coupling from succinimide esters

A flask was charged with amino acid (2.5 mmol), $NaHCO_3$ (5 mmol, or 10 mmol in case of using TFA salt of amino acid) and THF-H_2O (1:1, 20 mL). To the mixture, a solution of succinimide-activated amino acid (2.75 mmol) in THF (15 mL) was added dropwise, and the reaction was stirred at rt for 2 days. THF was removed on a rotary evaporator, and the residue was acidified with 0.5 M HCl to pH 2, and the product was extracted with ethyl acetate (3×30 mL). The organic layers were washed with water and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvent, the product was purified by column chromatography on silica gel.

BOC-(L)-Phe-(L)-Tyr(OH)-OBn

Prepared according to the general procedure from TFA×H-Tyr-OBn (0.57 g, 2.1 mmol) and **BOC-(L)-Phe-OSu** (0.84 g, 2.3 mmol). The product was purified by column chromatography on

silica gel with using 2→5% CH_3OH in CH_2Cl_2 as eluent to afford the pure product (0.55 g, 50%) in a form of colorless solid. Characterization is in accord with the precedent literature.[4]

Colorless amorphous solid; ^{1}H NMR (CD_3OD, 300 MHz) δ/ppm: 7.36-7.26 (m, 5H), 7.24-7.15 (m, 5H), 6.94 (d, J= 8.0 Hz, 2H), 6.66 (d, J= 8.0 Hz, 1H), 4.70-4.60 (m, 1H), 4.34-4.23 (m, 1H), 3.06-2.65 (m, 4H), 1.34 (s, 9H); ^{13}C NMR (CD_3OD, 150 MHz) δ/ppm: 174.2 (s, 1C), 172.5 (s, 1C), 157.5 (s, 1C), 157.4 (s, 1C), 138.5 (s, 1C), 137.0 (s, 1C), 131.4 (d, 2C), 130.3 (d, 2C), 129.5 (d, 2C), 129.4 (d, 2C), 129.3 (d, 2C), 128.3 (s, 1C), 127.7 (d, 1C), 127.6 (d, 1C), 116.3 (d, 2C), 80.7 (s, 1C), 68.0 (t, 1C), 57.1 (d, 1C), 55.5 (d, 1C), 39.2 (t, 1C), 37.7 (t, 1C), 28.6 (q, 3C).

BOC-Phe-Tyr(OH)-OH

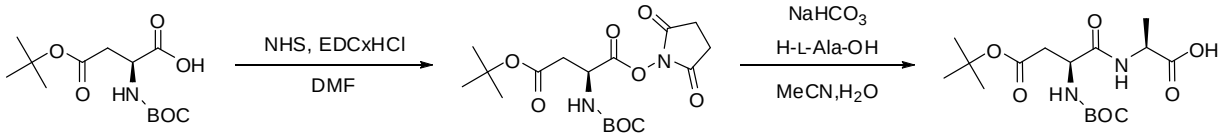
Prepared according to the general procedure from L-tyrosine (0.45 g, 2.5 mmol) and **BOC-(L)-Phe-OSu** (1.0 g, 2.7 mmol). The product was purified by column chromatography on silica gel using 2→5% CH_3OH in CH_2Cl_2 as eluent to yield the pure product (0.81 g, 81%) in the form of colorless solid. Characterization is in accord with the precedent literature.[4]

Colorless amorphous solid; ^{1}H NMR (CD_3OD, 300 MHz) δ/ppm: 7.28-7.14 (m, 5H), 7.02 (d, J= 8.0 Hz, 2H), 6.69 (d, J= 8.0 Hz, 2H), 4.64-4.50 (m, 1H), 4.31-4.19 (m, 1H), 3.13-3.00 (m, 2H), 2.92 (dd, J= 7.6 Hz, 1H), 2.79-2.68 (m, 1H), 1.34 (s, 9H); ^{13}C NMR ($(CD_3)_2SO$, 75 MHz) δ/ppm: 172.9 (s, 1C), 171.7 (s, 1C), 156.1 (s, 1C), 155.2 (s, 1C), 138.2 (s, 1C), 130.2 (d, 2C), 129.2 (d, 2C), 128.1 (d, 2C), 127.4 (s, 1C), 126.2 (d, 1C), 115.1 (d, 2C), 78.2 (s, 1C), 55.8 (d, 1C), 53.7 (d, 1C), 37.6 (t, 1C), 36.2 (t, 1C), 28.2 (q, 3C).

General procedure for the BOC deprotection

A three neck round bottom flask was filled with BOC protected amino acid or peptide (10 mmol) and dry CH_2Cl_2 (60 mL). Under inert N_2 atmosphere the reaction mixture was stirred, cooled by ice-bath at 0 °C, and TFA (100 mL) was added dropwise during 1 h. The stirring was continued over 1 h at 0 °C, and 2 h at rt. After the reaction was completed, the solvent and TFA were removed by evaporation under reduced pressure. To the residue, cold ether or hexane was added whereupon the product precipitated. The product was filtered off by a sinter funnel and dried in a dessicator over P_2O_5 and KOH for two days.

BOC-Asp(^{t}Bu)-Ala-OH



To a solution of BOC-Asp(^{t}Bu)-OH (100.0 mg, 345.6 μmol.) in DMF (2 mL), NHS (47.7 mg, 414.7 μmol) and EDC×HCl (79.5 mg, 414.7 μmol, 1.2 eq.) were added under stirring. The stirring was continued at rt for 21 h before H_2O (10 mL) was added to quench the reaction. The reaction mixture was extracted with EtOAc (3 × 10 mL), the combined organic phases were dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure to yield the activated ester (124 mg, 93 %). The product was used without any further purification for the next step.

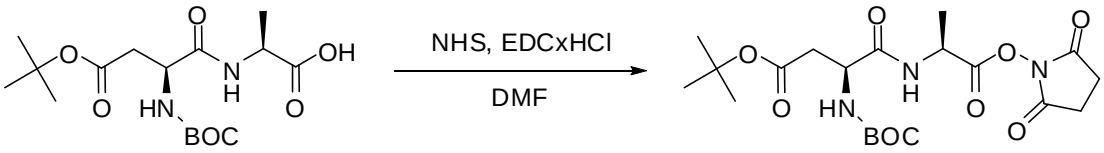
ESI-MS: *m/z* = 387.17630 $[M+H]^+$; calcd for $[C_{17}H_{26}N_2O_8 + H]^+$: 387.17619

To a solution of the activated ester BOC-Asp(^{t}Bu)-OSu (124 mg, 320.9 μmol) in CH_3CN (2 mL), a solution of $NaHCO_3$ (80.9 mg, 962.7 μmol) and H-Ala-OH (38.6 mg, 320.9 mmol) in H_2O (2

mL) was added. The reaction mixture was stirred for 22 h at rt before it was diluted with H_2O (2 mL). The pH was adjusted to 4.0 with 1 M HCl and the aqueous phase was extracted with EtOAc (3×20 mL). The combined organic phases were washed with 1 M HCl (2 mL) and brine (10 mL), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure to yield the desired product (109 mg, 93%). The product was used without any further purification for the next step. Characterization is in accord with the precedent literature.[5]

^{1}H NMR (CD_3CN, 500 MHz) δ/ppm: 6.99-7.01 (m, 1NH), 5.68-5.70 (m, 1NH), 4.20-4.30 (m, 2H), 2.58 (dd, J= 16.5, 5.5 Hz, 1H), 2.42-2.47 (m, 1H), 1.33 (s, 18H), 1.25 (d, J= 7.2 Hz, 3H); ^{13}C NMR (CD_3CN, 126 MHz) δ/ppm: 175.0 (s, 1C), 172.3 (s, 1C), 171.5 (s, 1C), 156.9 (s, 1C), 82.2 (s, 1C), 80.9 (s, 1C), 52.5 (s, 1C), 49.6 (s, 1C), 38.7 (s, 1C), 28.9 (s, 3C), 28.6 (s, 3C), 18.3 (s, 1C); ESI-MS *m/z* $[M+H]^+$ calcd for $C_{16}H_{28}N_2O_7 + H^+$: 361.19693 found: 361.19772.

BOC-Asp(^{t}Bu)-Ala-OSu

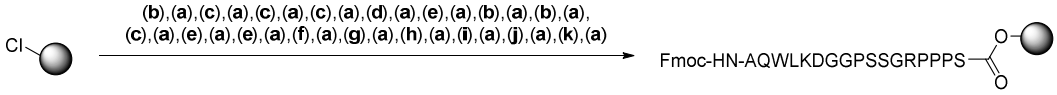


To a solution of BOC-Asp(^{t}Bu)-Ala-OH (109 mg, 302.4 μmol) in DMF (2 mL) NHS (41.8 mg, 362.9 μmol, 1.2 eq.) and EDC×HCl (69.6 mg, 362.9 μmol, 1.2 eq.) were added under stirring. The stirring was continued at rt for 22 h before H_2O (10 mL) was added to quench the reaction. The reaction mixture was extracted with EtOAc (3 × 10 mL), the combined organic phases were

washed with H_2O (2×15 mL) and brine (2×10 mL), dried over Na_2SO_4 and filtered. The solvent was removed under reduced pressure to yield the activated ester (130.8 mg, 95%). The product was used without any further purification for the next step.

^{1}H NMR ($CDCl_3$, 500 MHz) δ/ppm: 7.13-7.15 (m, 1H), 5.65-5.67 (m, 1H), 4.81-4.90 (m, 2H), 4.42-4.43 (m, 1H), 2.82 (dd, *J*= 17.2, 4.4 Hz, 1H), 2.76 (s, 4H), 2.53 (dd, *J*= 17.2, 6.6 Hz, 1H), 1.52 (d, *J*= 7.2 Hz, 3H), 1.37-1.38 (m, 18H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ/ppm: 170.7 (s, 1 C), 168.4 (s, 1 C), 168.4 (s, 1 C), 168.3 (s, 2 C), 155.5 (s, 1 C), 81.9 (s, 1 C), 80.4 (s, 1C), 46.5 (s, 2 C), 37.2 (s, 1 C) 28.3 (s, 3 C) 28.0 (s, 3 C) 25.5 (s, 2 C) 18.2 (s, 1 C). ESI-MS: *m/z* $[M+H]^+$ calcd for $C_{20}H_{31}N_3O_9 + H^+$ 458.21331, found 458.21222.

Synthesis of the intermediate 5 via SPPS

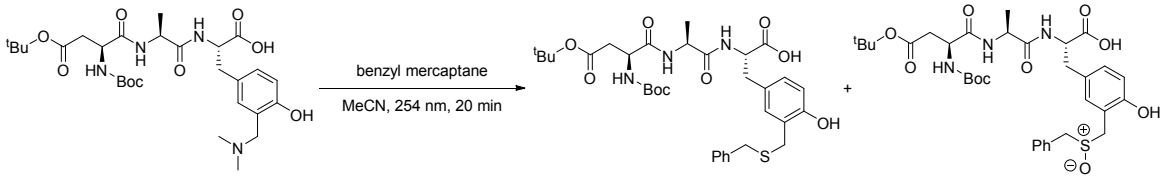


Scheme S1: Synthesis of the intermediate **5**;

Coupling conditions: (a) 20 % piperidine/DMF, 20 min. (b) Fmoc-Ser(^{t}Bu)-OH, TBTU, DIPEA, DMF 1 h. (c) Fmoc-Pro-OH, TBTU, DIPEA, DMF 1 h. (d) Fmoc-Arg(Pbf)-OH, TBTU, DIPEA, DMF 1 h. (e) Fmoc-Gly-OH, TBTU, DIPEA, DMF 1 h. (f) Fmoc-Asp(O^{t}Bu)-OH, TBTU, DIPEA, DMF 1 h. (g) Fmoc-Lys(BOC)-OH, TBTU, DIPEA, DMF 1 h. (h) Fmoc-Leu-OH, TBTU, DIPEA, DMF 1 h. (i) Fmoc-Trp(BOC)-OH, TBTU, DIPEA, DMF 1 h. (j) Fmoc-Gln(Trt)-OH, TBTU, DIPEA, DMF 1 h. (k) Fmoc-Ala-OH, TBTU, DIPEA, DMF 1 h.

General SPPS Procedure is given in the paper.

Irradiation of BOC-Asp(^{t}Bu)-Ala-1-OH (4) in the presence of benzyl mercaptan:



A solution of BOC-Asp(tBu)-Ala-**1**-OH (**4**) (2.0 mg, 3.44 µmol, 1.0 eq.) in CH_3CN (334 µL) in a quartz cuvette was purged with Ar for 10 min. To this solution was added an excess of benzyl mercaptan (4.0 µL, 34.44 µmol, 10.0 eq.) and was then irradiated at 254 nm (8 Watt) for 20 min. The solvent was removed afterwards to yield 2.2 mg of a crude product. The analytical HPLC-MS run showed a conversion of 23% to the oxidized product (R_t = 13.04). ESI-MS: *m/z* = 660.29492 ($M+H^+$); calculated for ($C_{33}H_{45}N_3O_9S + H^+$): 660.29493; *m/z* = 676.28943 ($M+H^+$); calculated for ($C_{33}H_{45}N_3O_{10}S+ H^+$): 676.28984.

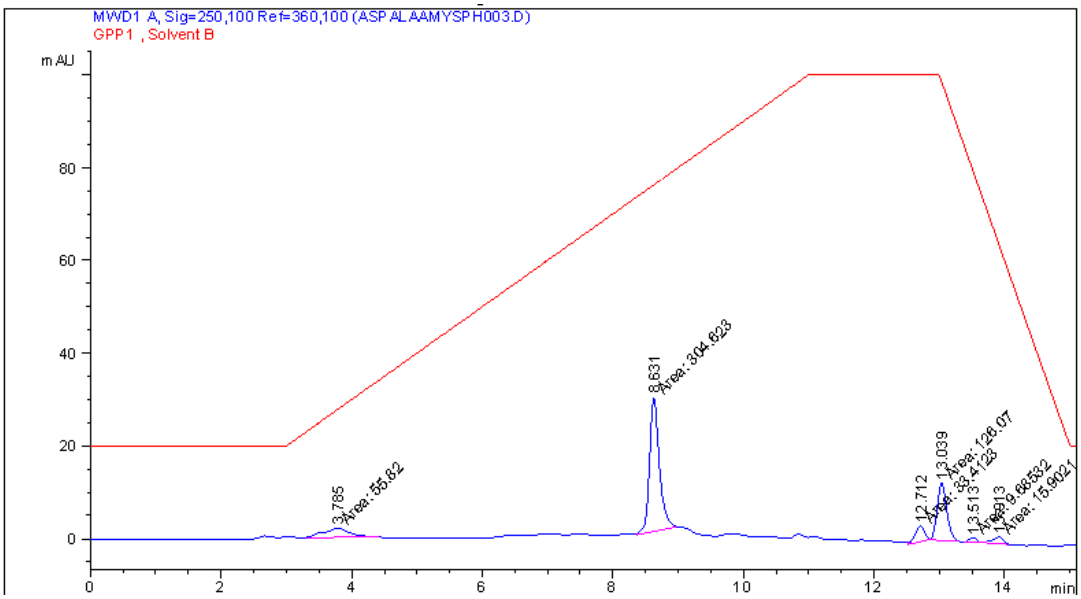
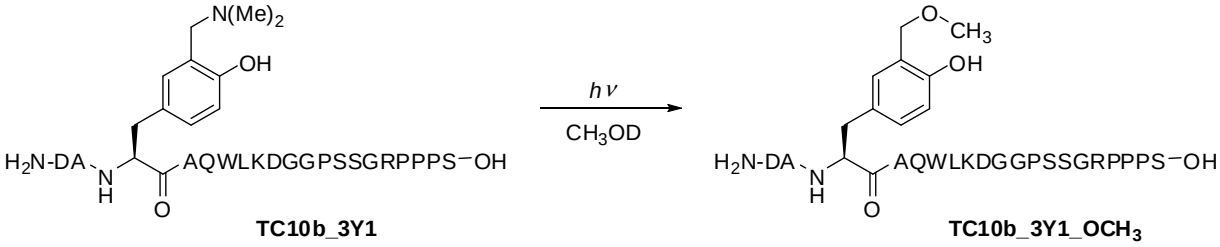


Fig S1: HPLC of the photolysis reaction mixture.

HPLC conditions:

Time [min]	System B [%]
0	20
3	20
11	100
13	100
15	20

Photomethanolysis of TC10b_3Y1



TC10b_3Y1 **TC10b_3Y1_OCH$_3$**

A solution of **TC10b_3Y1** in CH_3OD (1.0 mM, 200 µL) was purged with Ar for 10 min in a quartz cuvette and irradiated with one lamp at 254 nm for 1 h. After the irradiation composition of the solution was analyzed by ESI-MS.

m/z = 1070.54724 $(M + 2\ H)^{2+}$; calculated for $(C_{94}H_{132}D_9N_{26}O_{31} + 2\ H)^{2+}$: 1070.54609.

m/z = 714.03406 $(M + 3\ H)^{3+}$; calculated for $(C_{94}H_{131}D_9N_{26}O_{31} + 3\ H)^{3+}$: 714.03315.

2. UV-vis and fluorescence spectra

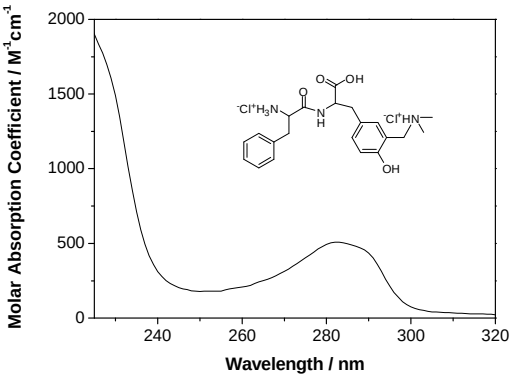


Fig S2. Absorption spectrum of **2** in CH_3CN.

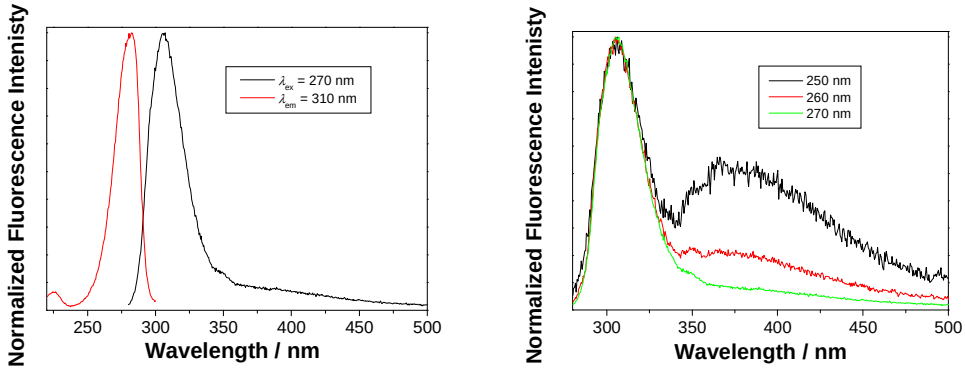


Fig S3. Normalized excitation and emission spectra of **2** in CH_3CN.

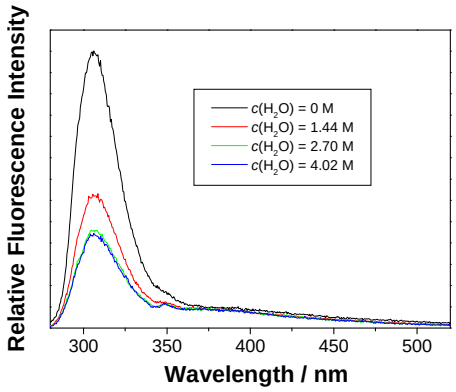


Fig S4. Fluorescence spectra of **2** in CH_3CN (λ_{ex} = 270 nm) at different H_2O concentration.

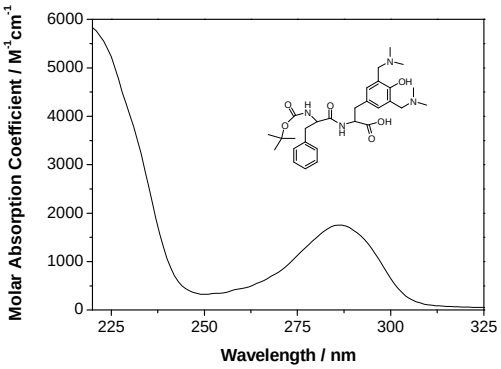


Fig S5. Absorption spectrum of **3A** in CH_3CN.

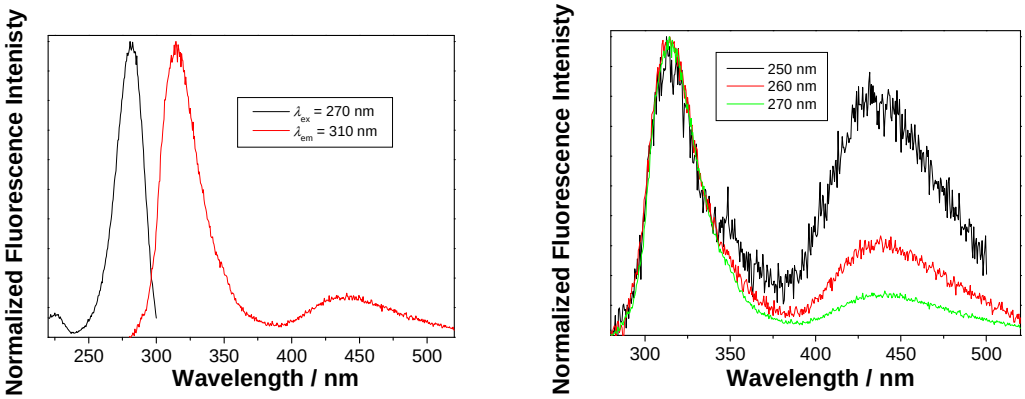


Fig S6. Normalized excitation and emission spectra of **3A** in CH_3CN.

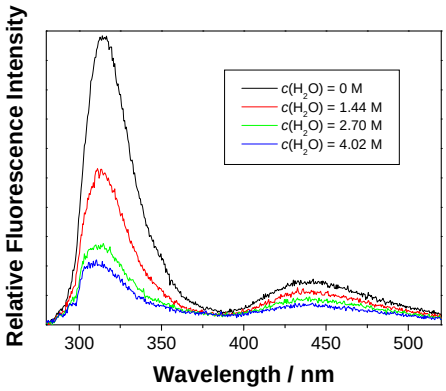


Fig S7. Fluorescence spectra of **3A** in CH_3CN (λ_{ex} = 270 nm) at different H_2O concentration.

3. Quantum yields of fluorescence and photomethanolysis quantum efficiency

The following equation was used for the determination of fluorescence quantum yields:

$$\Phi = \Phi_R \frac{I}{I_R} \frac{A_R}{A} \left(\frac{n_D}{n_D^R}\right)^2 \quad \text{(S1)}$$

wherein

Φ - quantum yield of fluorescence

Φ_R - quantum yield of fluorescence of reference compound, anisole in cyclohexane

I - intensity of fluorescence (integral of the corrected emission spectrum)

I_R - intensity of fluorescence (integral of the corrected emission spectrum) for the reference compound

A - absorbance of the solution at the excitation wavelength

A_R - absorbance of the solution of the reference compound at the excitation wavelength

n_D - refractive index of the solvent (acetonitrile)

n_D^R - refractive index of the solvent use to dissolve the reference compound (cyclohexane)

The **number of the absorbed photons for the KIO_3/KI** was calculated from:

$$n(\text{absorbed photons}) = \frac{\Delta A_{352} \times V_{irr}}{\varepsilon_{352} \times \ell \times \Phi_{\text{lit.}}}$$

where:

ΔA_{352}	absorbance difference at 352 nm for the irradiated and non-irradiated
.....	sample
V_{irr}	volume of the solution which was irradiated
ε_{352}	molar absorption coefficient for I_3^- in solution which contains iodides and iodates, 27600 M^{-1} cm^{-1}
l	length of the optical path (1 cm in all experiments)
$\Phi_{lit.}$	quantum yield (Φ_{254} = 0.74), the precise value was calculated from:

$$c(\Gamma^-) = A_{300} / 1.061 \qquad [M]$$

$$\Phi = 0.75 \times [1 + 0.02(T - 20.7)] \times [1+0.23(c(\Gamma^-) - 0.577)]$$

The quantum yield of the photomethanolysis was calculated according to:

$$\Phi = \frac{A_{254} \cdot V_{irr} \cdot x(\text{photoproduct})_{HPLC}}{\varepsilon_{254} \cdot \ell \cdot n(\text{total photons}) \cdot (1 - T_{254})}$$

For the absorbances in the range 0.4-0.8 the number of absorbed photons was calculated according to:

$$n(\text{absorbed photons}) = n(\text{total photons}) \times (1-T)$$

4. LFP data

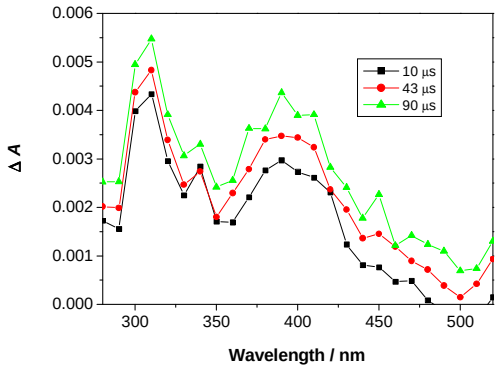


Fig S8. Transient absorption spectra of **2** in N_2-purged CH_3CN (compound not well soluble A_{355} = 0.08).

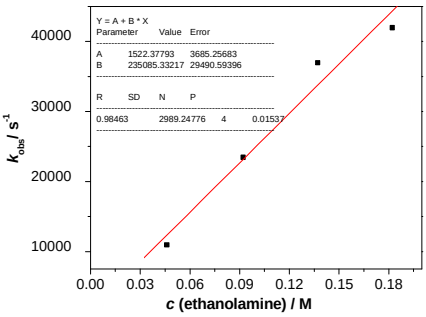


Fig S9. Dependance of the k_{obs} on ethanolamine concentration for CH_3CN-H_2O (1:1) solution of **2**. The slope corresponds to the k_q (2.3×10^5 M^{-1} s^{-1}).

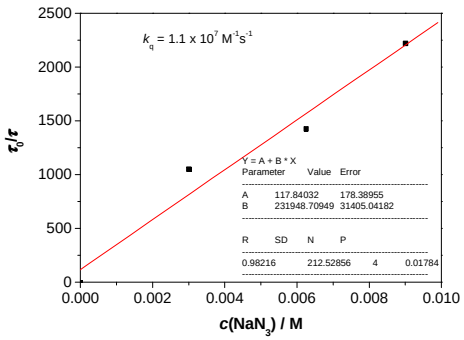


Fig S10. Stern-Volmer plot for the quenching of the transient absorbtion of **2** in CH_3CN-H_2O (1:1) with sodium azide. (Lifetime τ = 20 ± 2 ms).

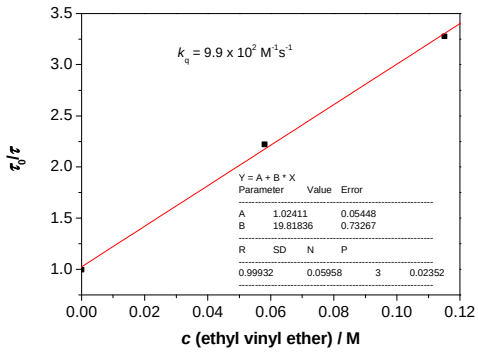


Fig S11. Stern-Volmer plot for the quenching of the transient absorbtion of **2** in CH_3CN-H_2O (1:1) with ethyl vinyl ether. (Lifetime τ = 20 ± 2 ms).

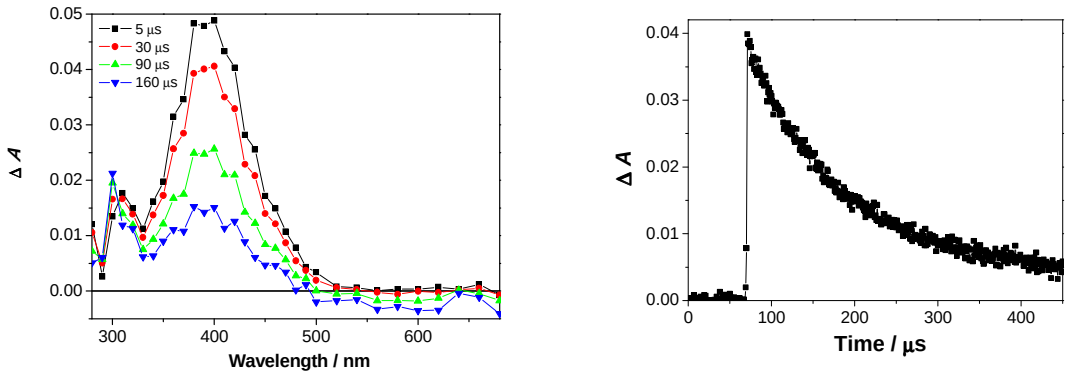


Fig S12. Transient absorption spectra of **3A** in N_2-purged CH_3CN (left), decay of transient absorbance at 400 nm (right).

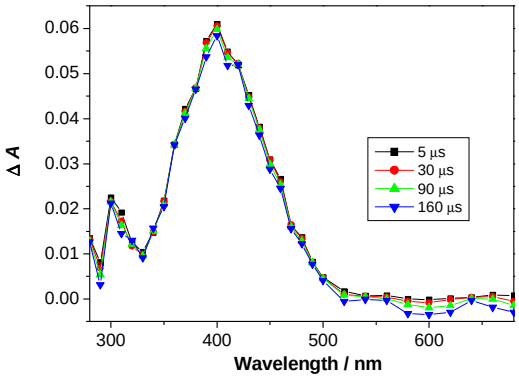


Fig S13. Transient absorption spectra in O_2-purged CH_3CN-H_2O (1:1) solution of **3A**.

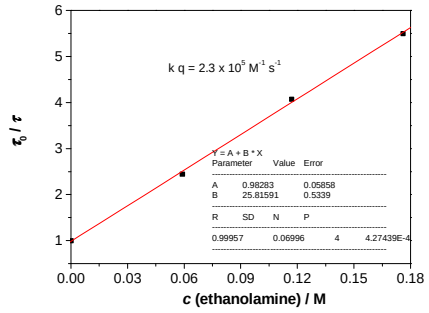


Fig S14. Stern-Volmer plot for the quenching of the transient in CH_3CN solution of **3A**. (Lifetime τ = 110 ± 10 μs).

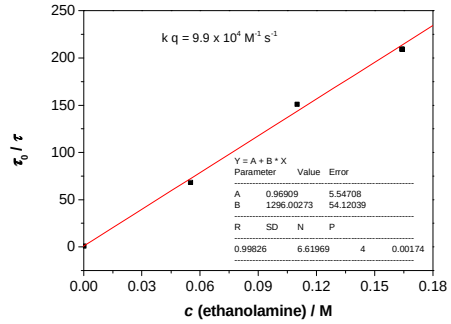


Fig S15. Stern-Volmer plot for the quenching of the transient in CH_3CN-H_2O solution of **3A**. (Lifetime τ = 13 ± 3 ms).

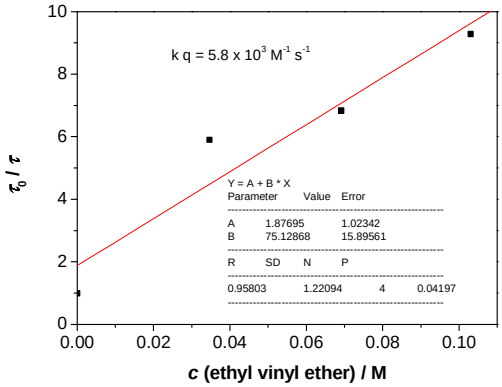
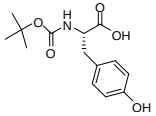
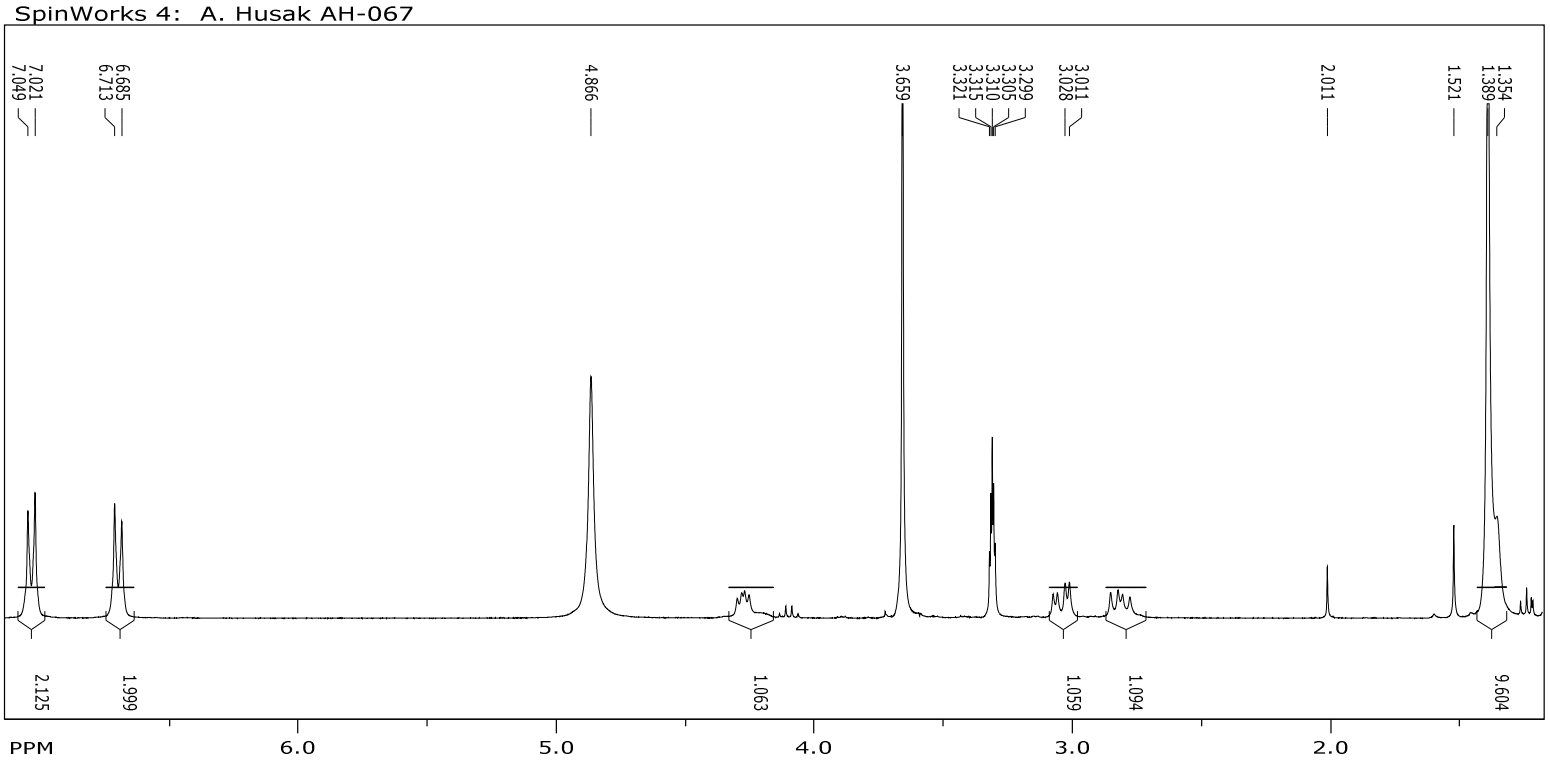


Fig S16. Stern-Volmer plot for the quenching of the in CH_3CN-H_2O solution of **3A**. (Lifetime τ = 13 ± 3 ms).

5. NMR spectra

^{1}H NMR (CD_3OD, 300 MHz) of BOC-Tyr(OH)-OH





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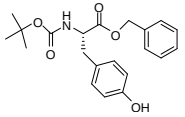
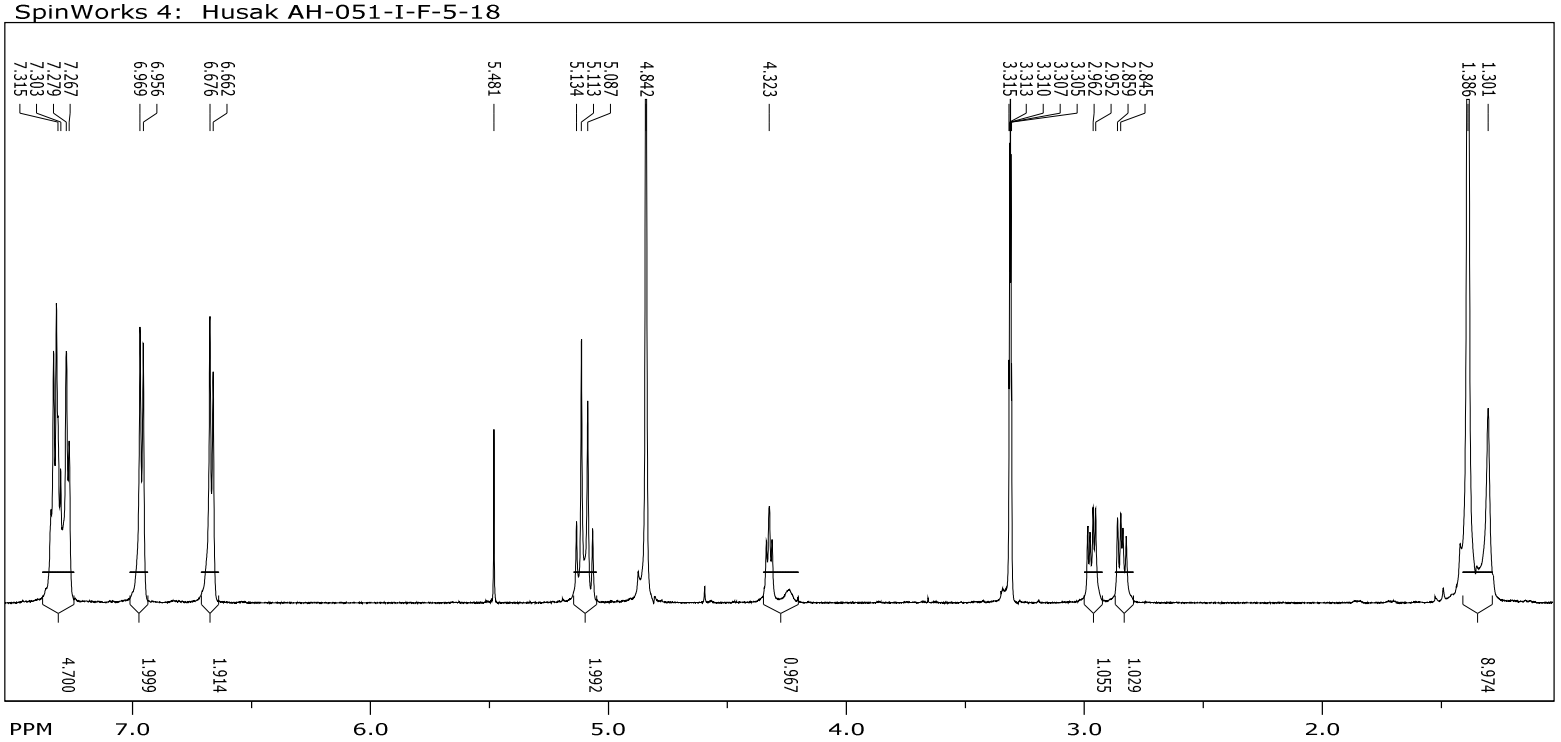
number of scans: 0

freq. of 0 ppm: 300.130005 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{1}H NMR (CD_3OD, 600 MHz) of BOC-Tyr(OH)-OBn





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number of scans: 0

freq. of 0 ppm: 600.130007 MHz
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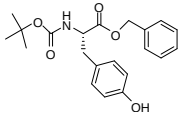
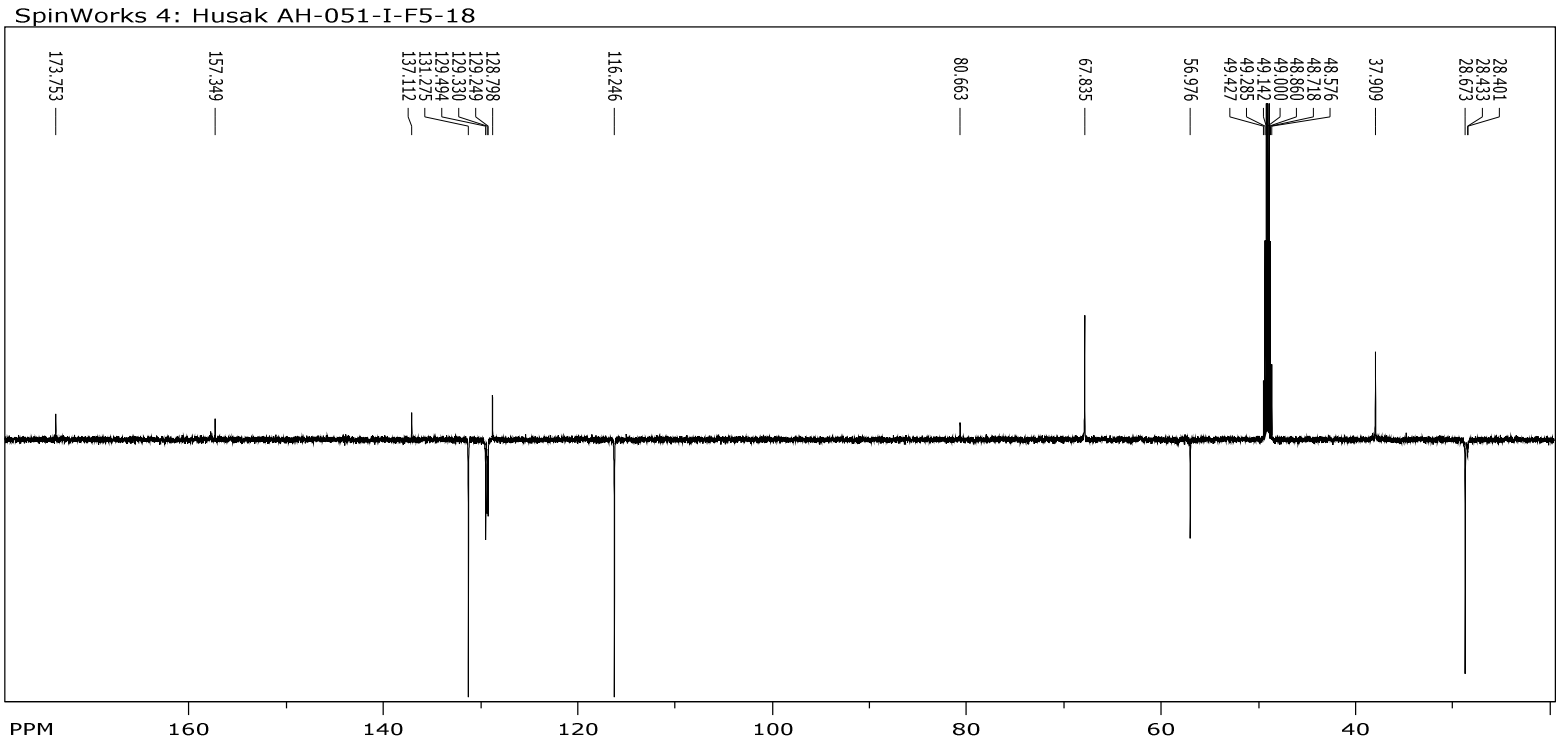
^{13}C NMR (CD_3OD, 150 MHz, APT) of BOC-Tyr(OH)-OBn





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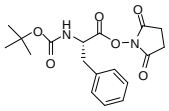
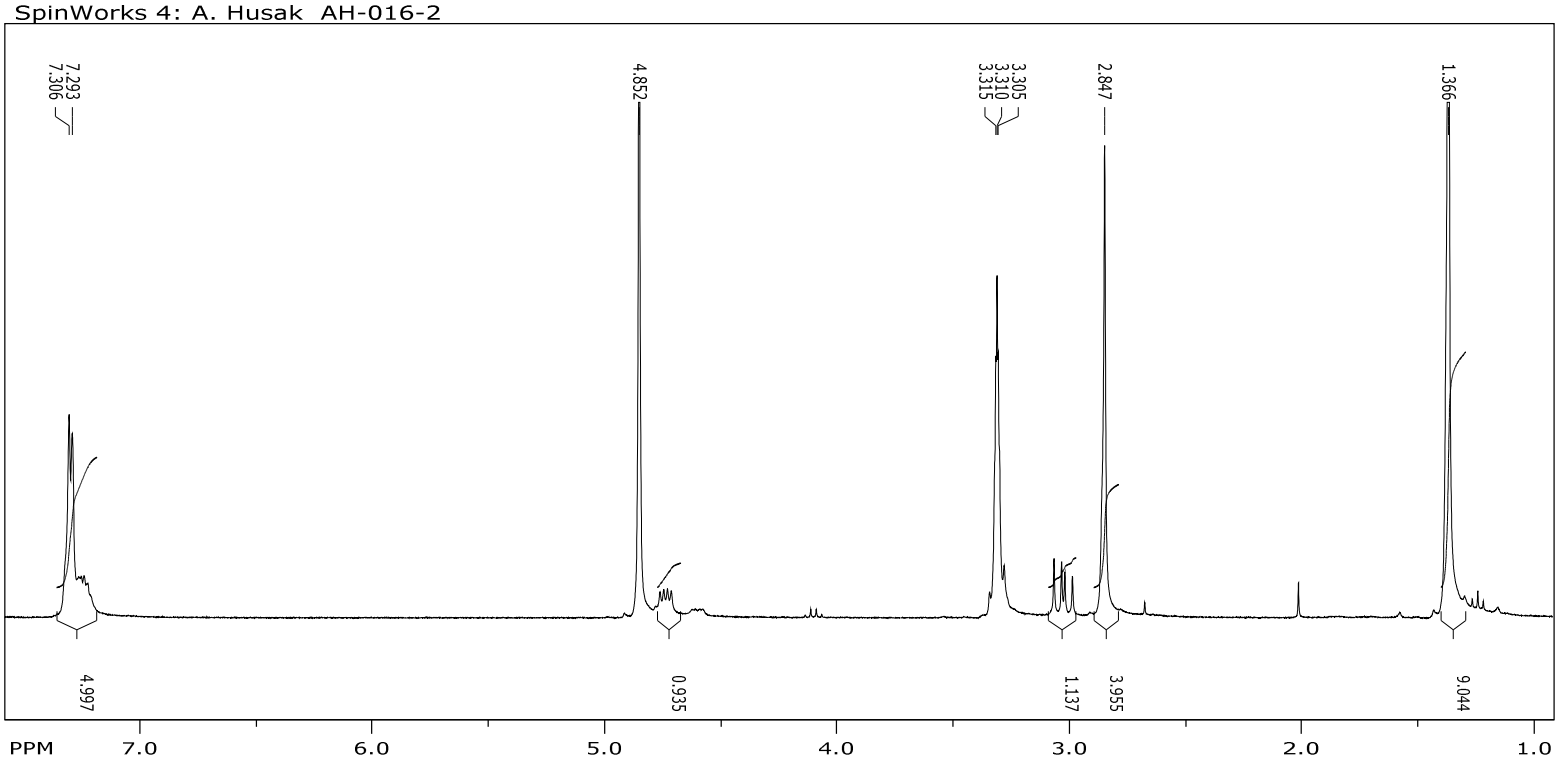
LB: 1.000 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of BOC-Phe-OSn





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number of scans: 16

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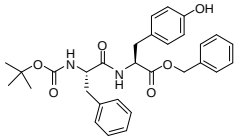
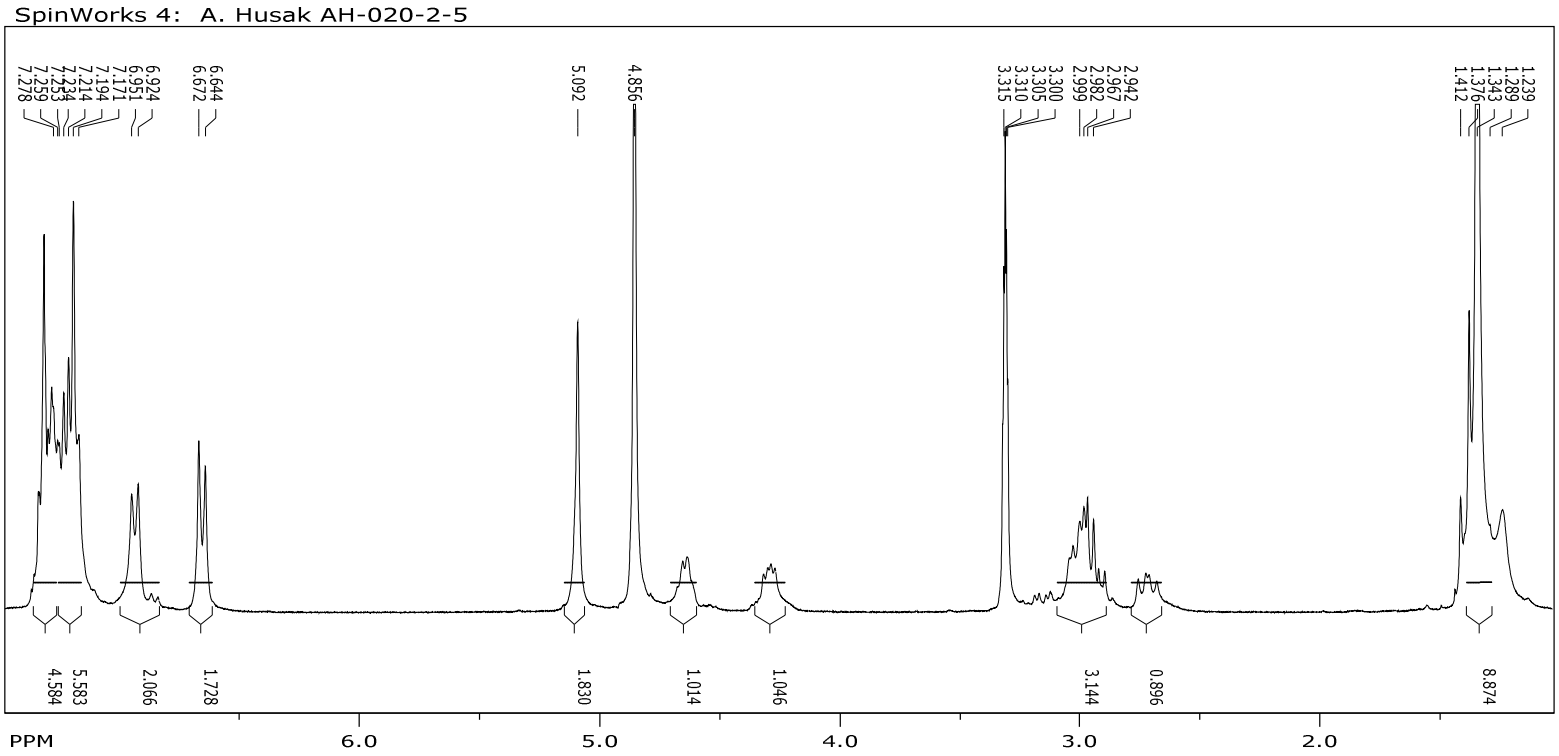
processed size: 32768 complex points
LB: 0.300 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of BOC-Phe-Tyr-OBn





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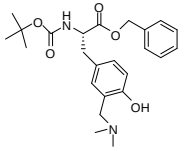
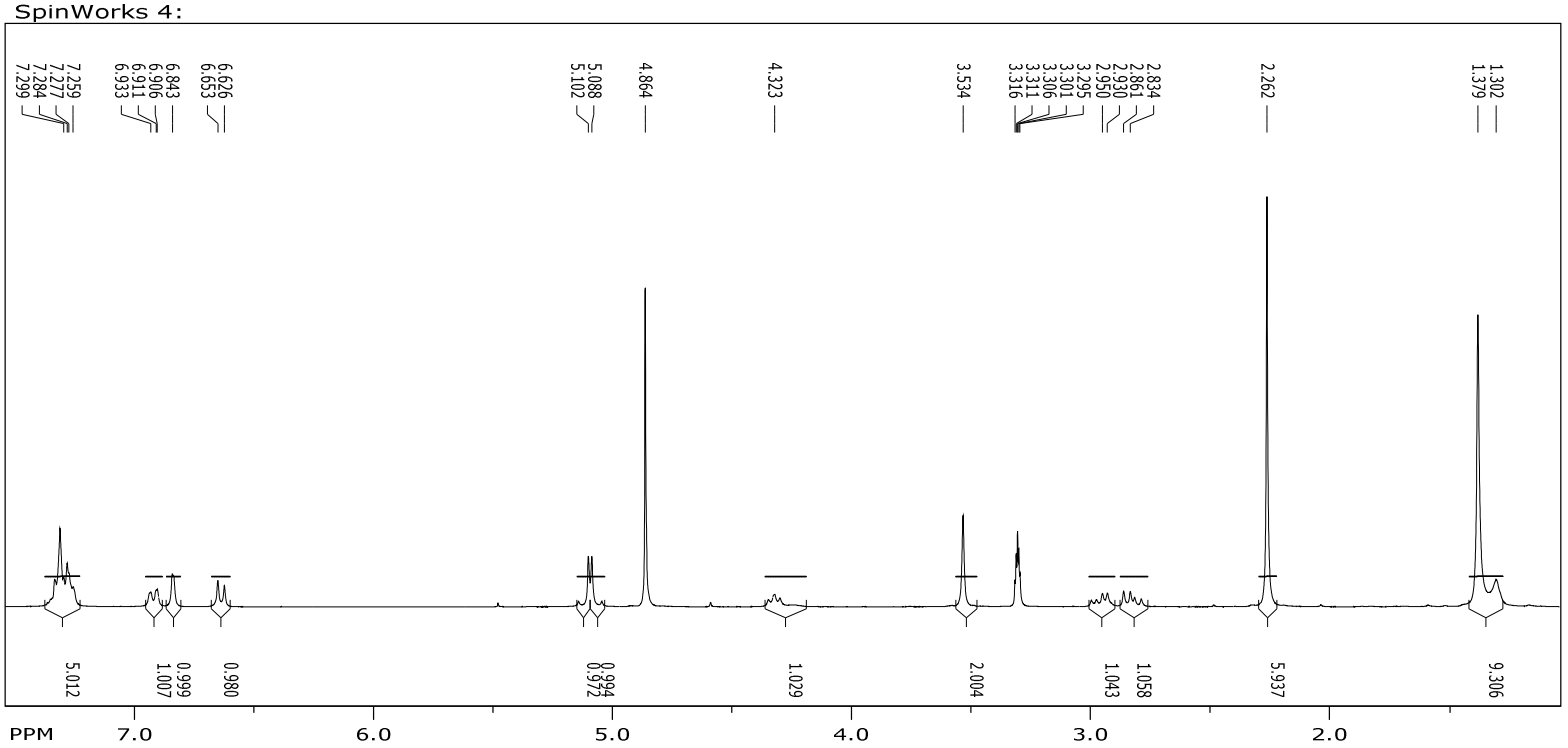
number of scans: 0

freq. of 0 ppm: 300.130005 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of BOC-Tyr[$CH_2N(CH_3)_2$]-OBn (**1B**)





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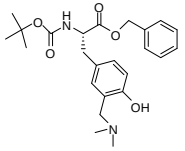
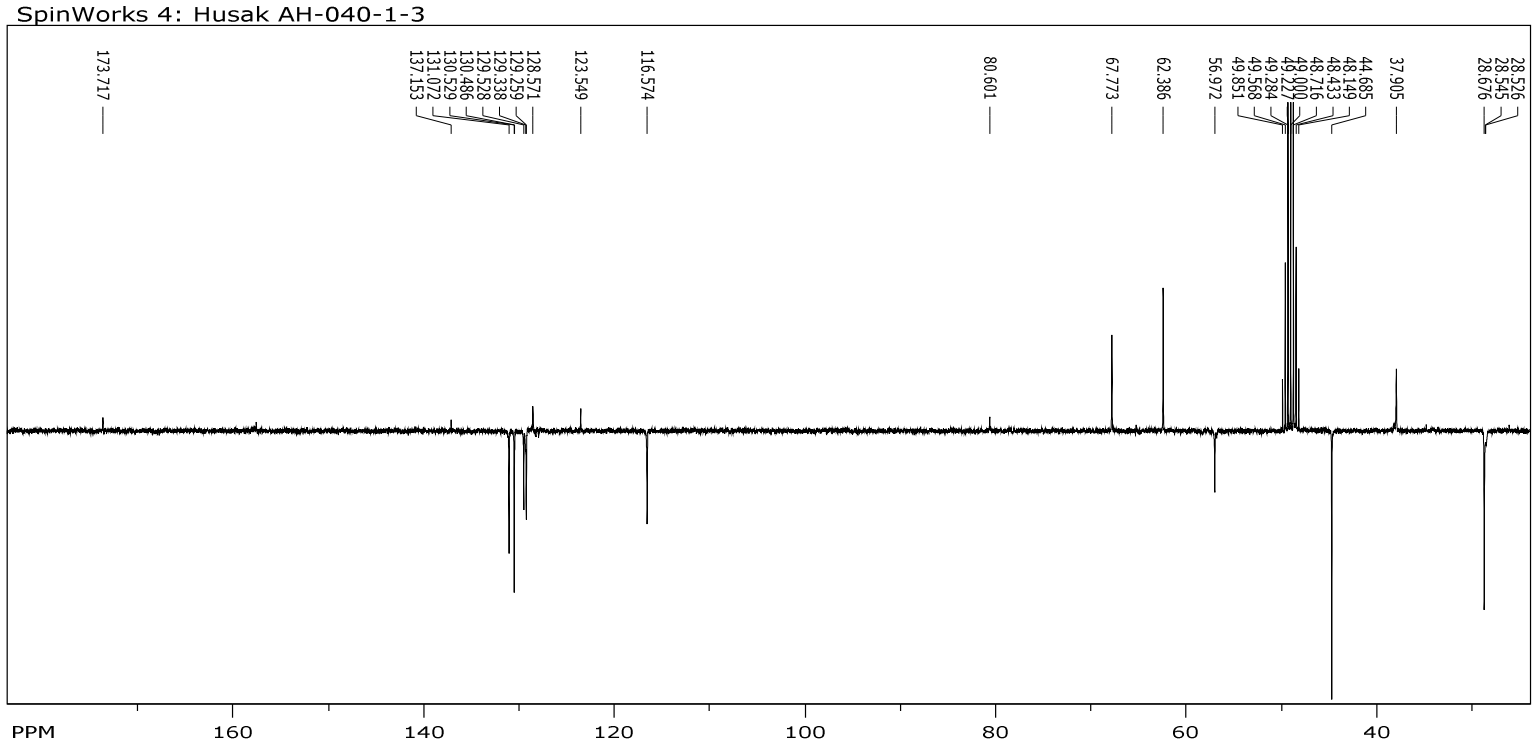
number of scans: 0

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR (CD_3OD, 75 MHz, APT) of BOC-Tyr[$CH_2N(CH_3)_2$]-OBn (**1B**)





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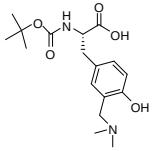
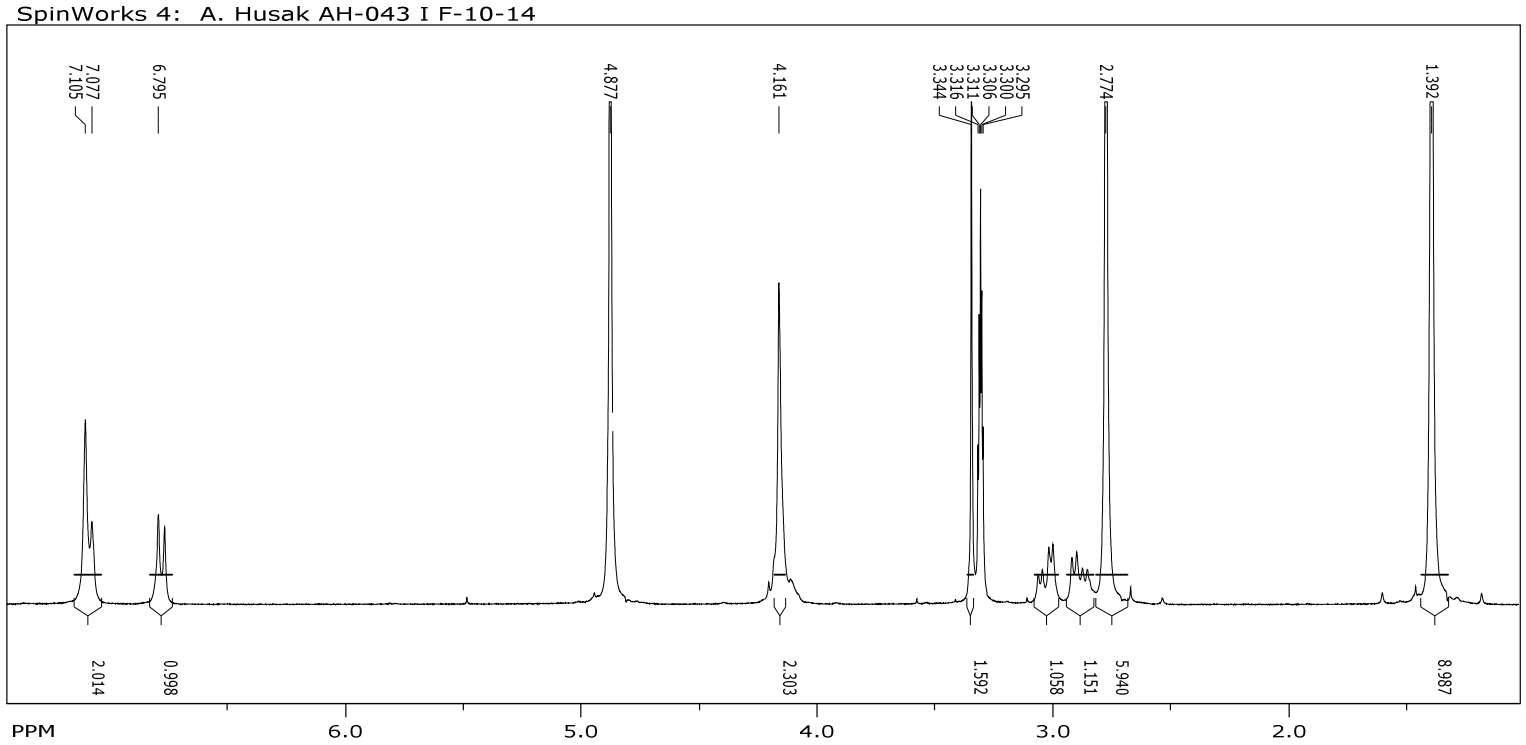
number of scans: 3798

freq. of 0 ppm: 75.467642 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of BOC-Tyr[$CH_2N(CH_3)_2$]-OH (**1A**)





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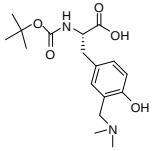
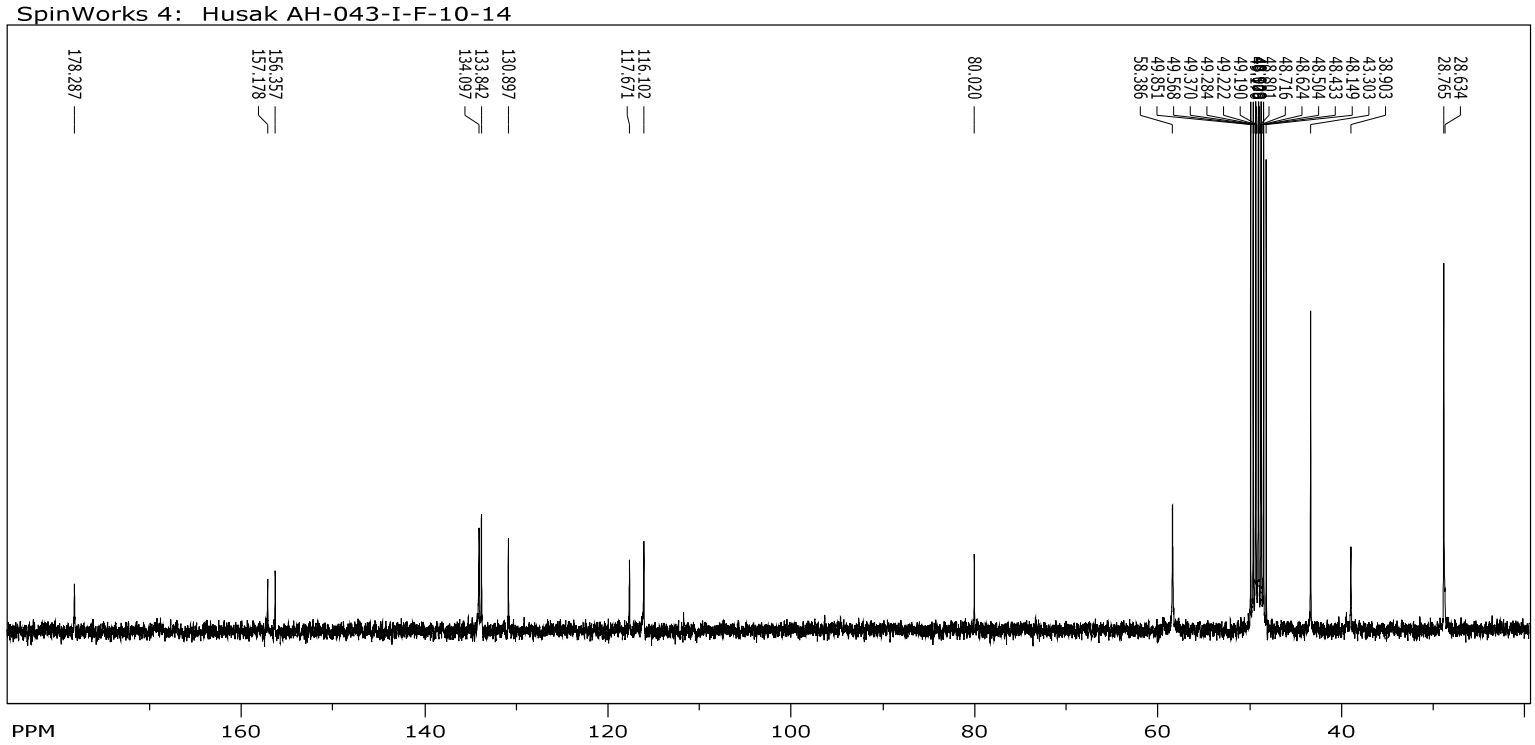
number of scans: 0

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR (CD_3OD, 75 MHz) of BOC-Tyr[$CH_2N(CH_3)_2$]-OH (**1A**)





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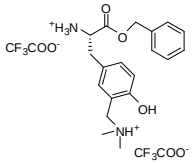
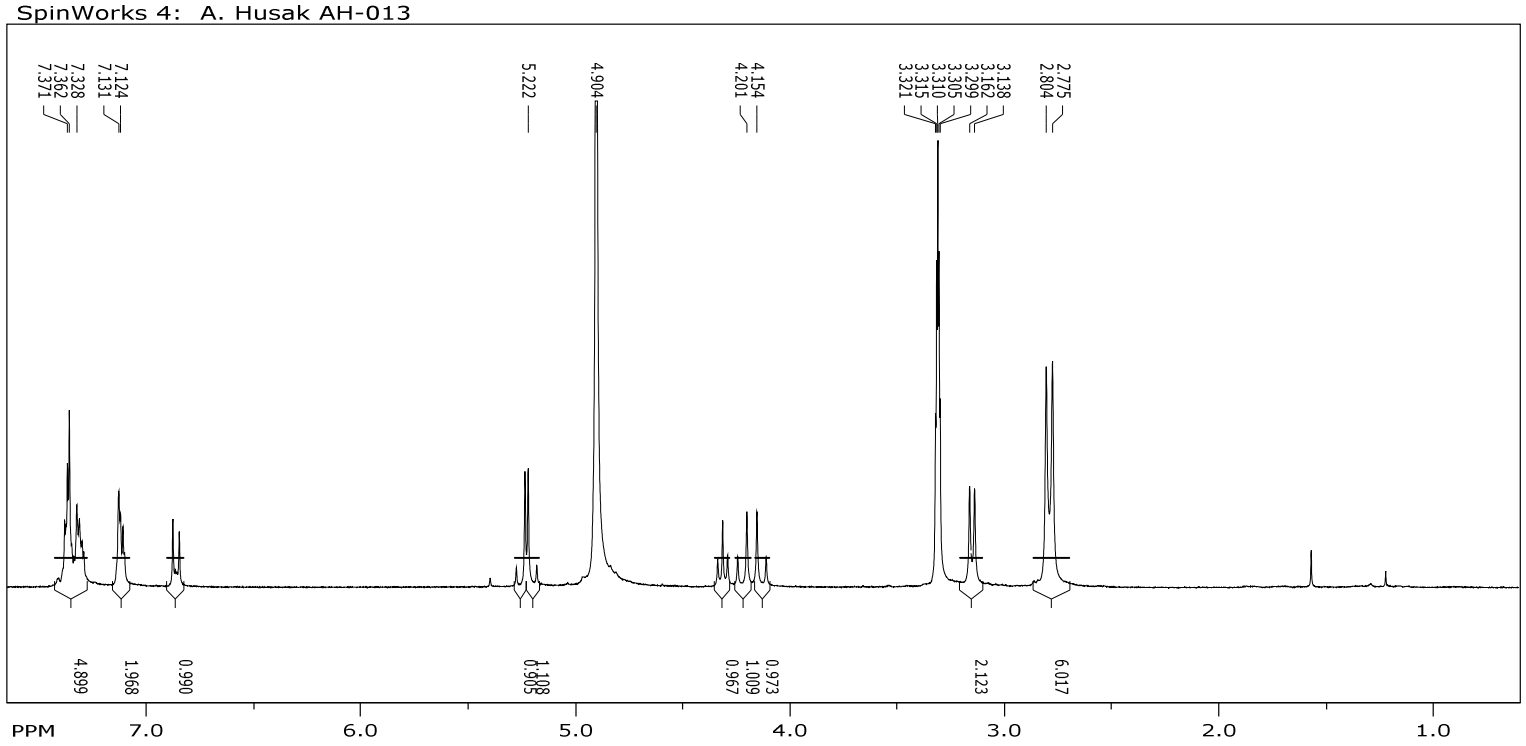
number of scans: 0

freq. of 0 ppm: 75.467642 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of TFA×H-Tyr[$CH_2N(CH_3)_2$×TFA]-OBn (**1C**)





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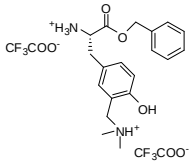
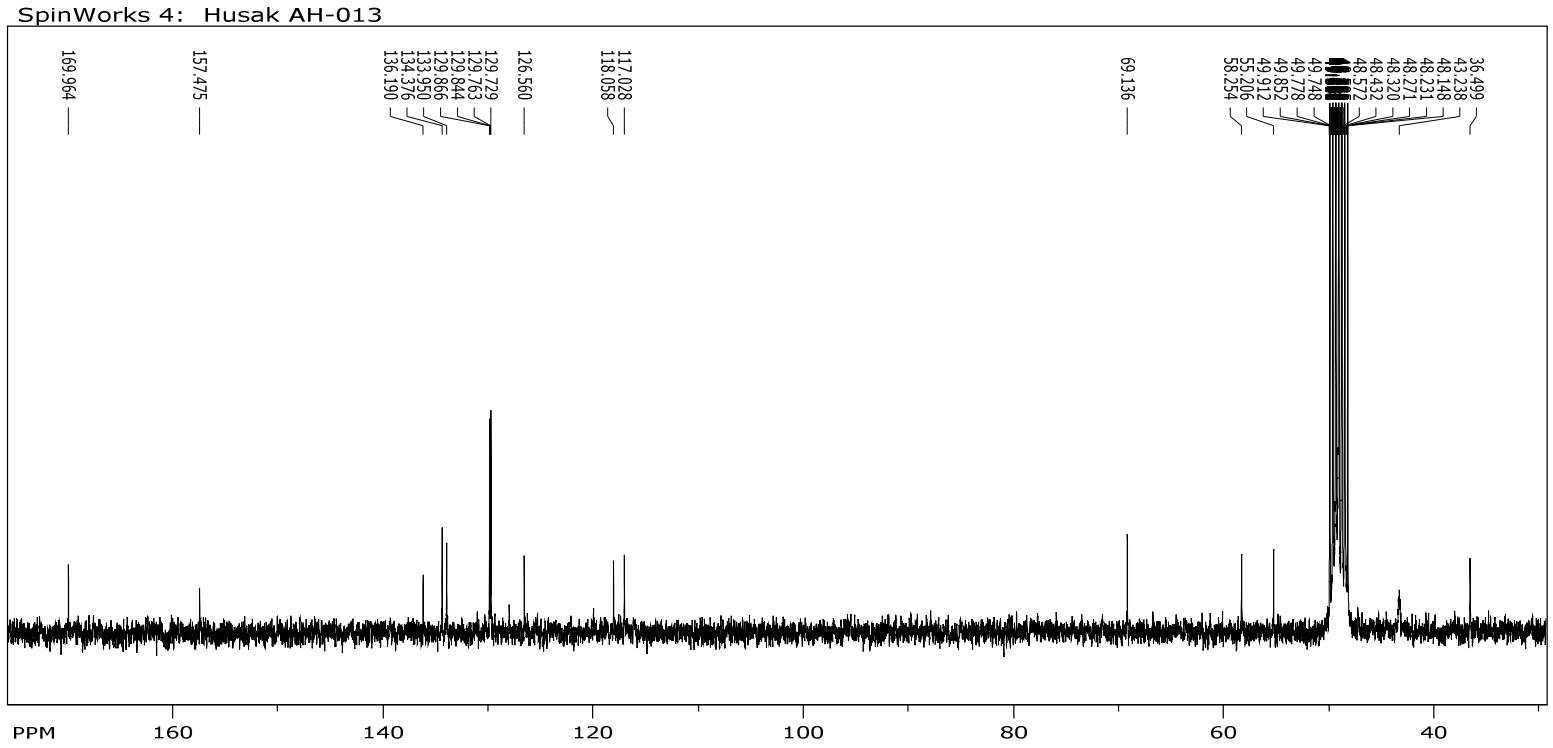
number of scans: 0

freq. of 0 ppm: 300.130005 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR (CD_3OD, 75 MHz) of TFA×H-Tyr[$CH_2N(CH_3)_2$×TFA]-OBn (**1C**)





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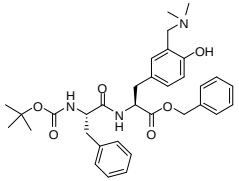
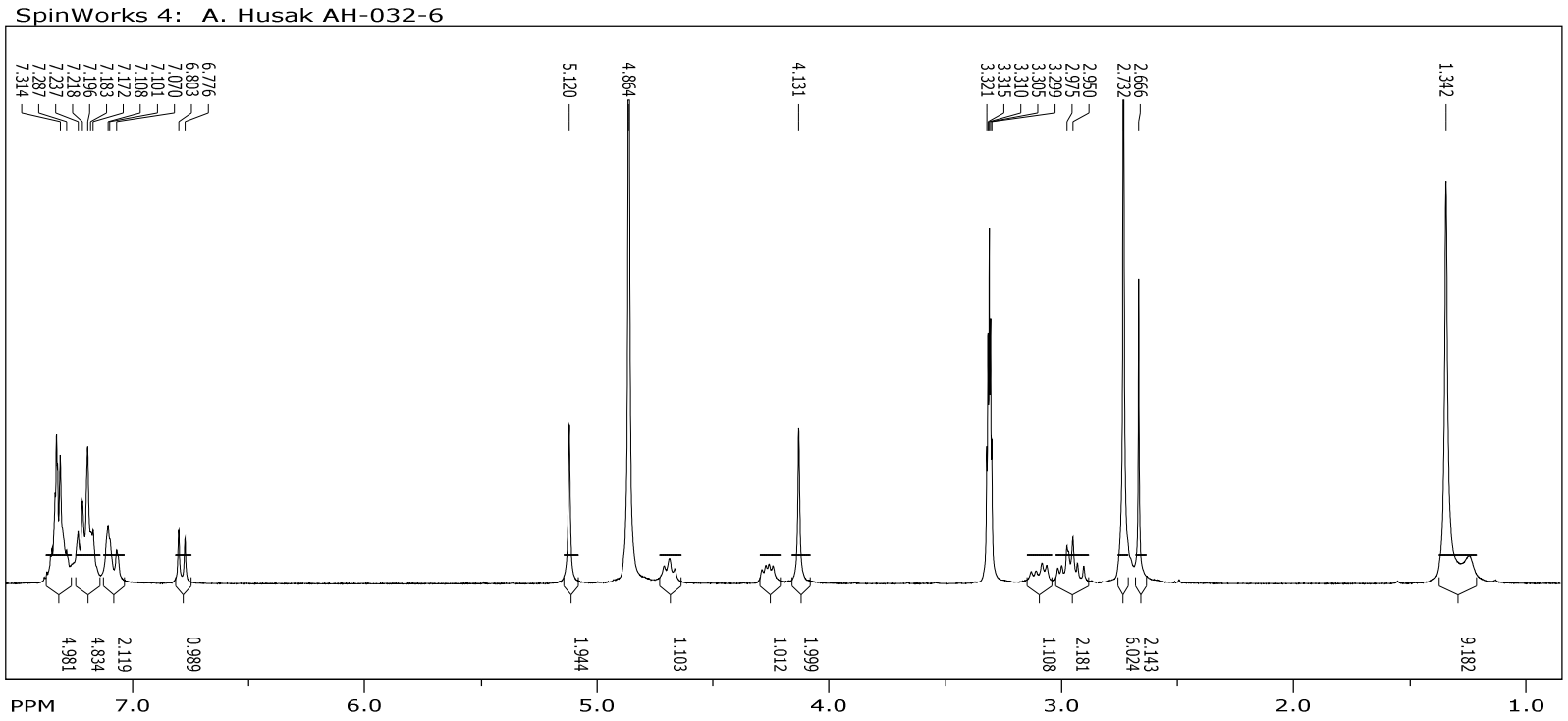
number of scans: 0

freq. of 0 ppm: 75.467643 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]-OBn (**2B**)





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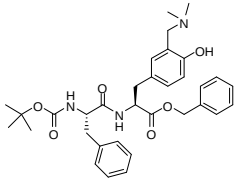
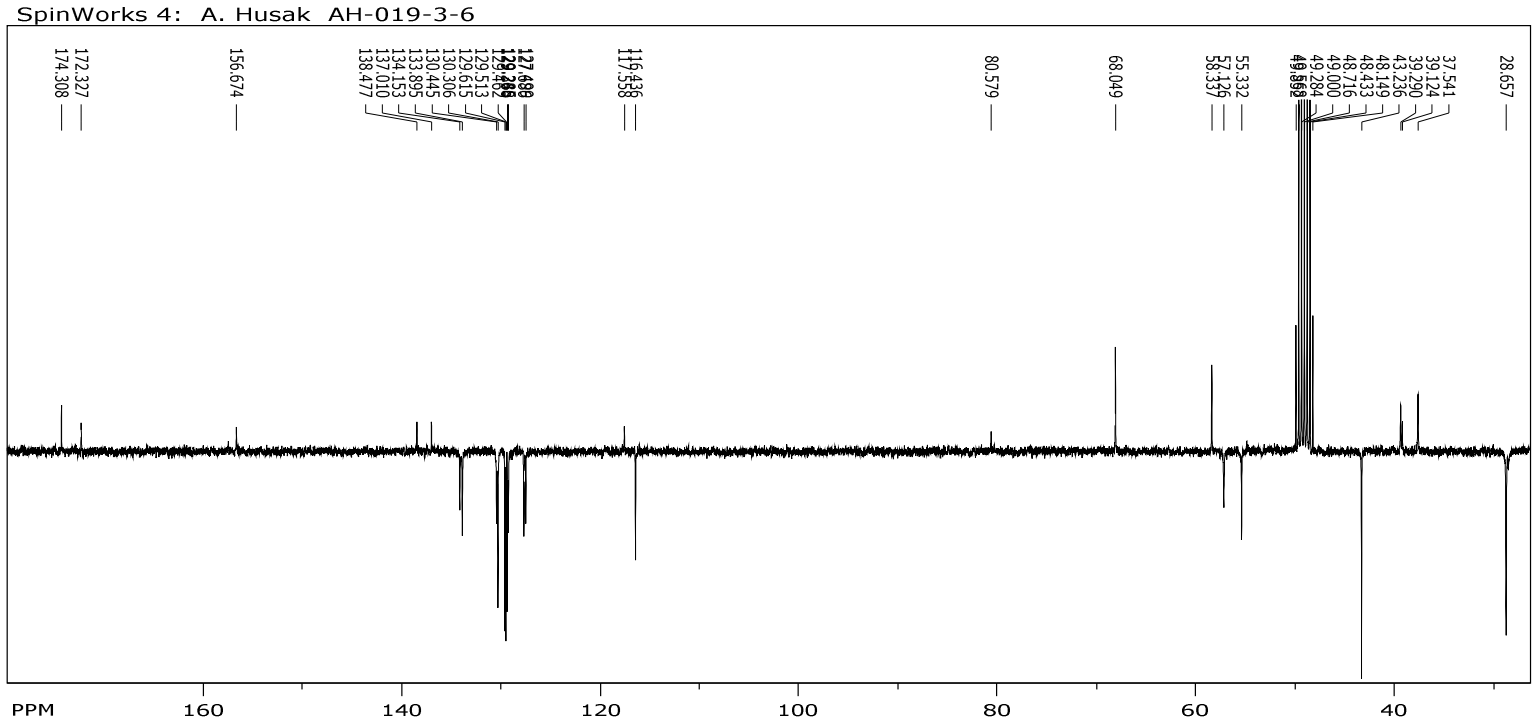
number of scans: 0

freq. of 0 ppm: 300.130005 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR (CD_3OD, 75 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]-OBn (**2B**)





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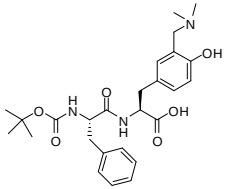
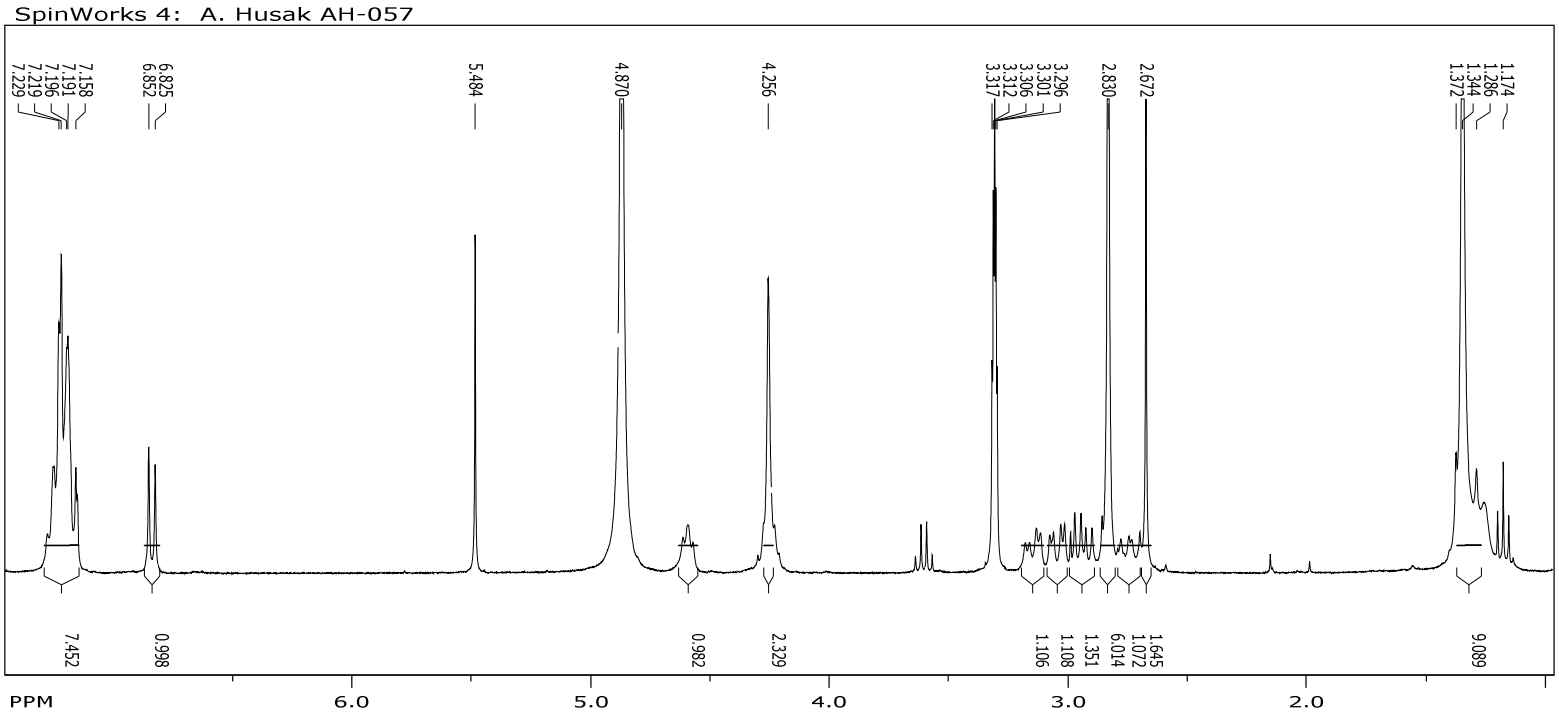
number of scans: 0

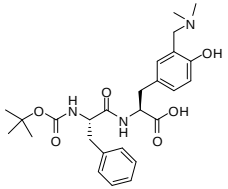
freq. of 0 ppm: 75.467525 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

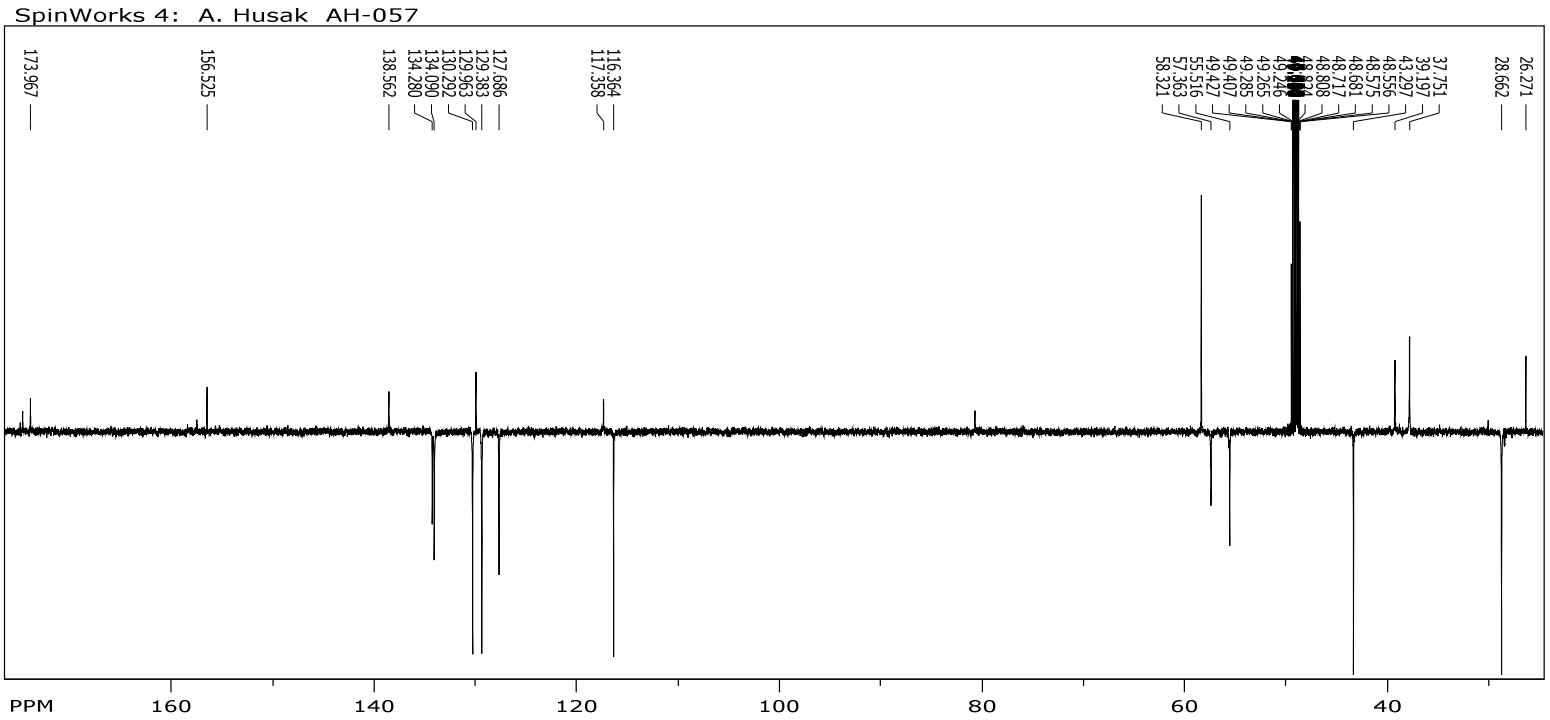
^{1}H NMR (CD_3OD, 300 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]-OH (**2A**)





^{13}C NMR (CD_3OD, 150 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]-OH (**2A**)





file: ...ektri\husak_ah057apt\1\spectrum.dx expt: <jmod>
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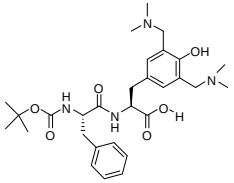
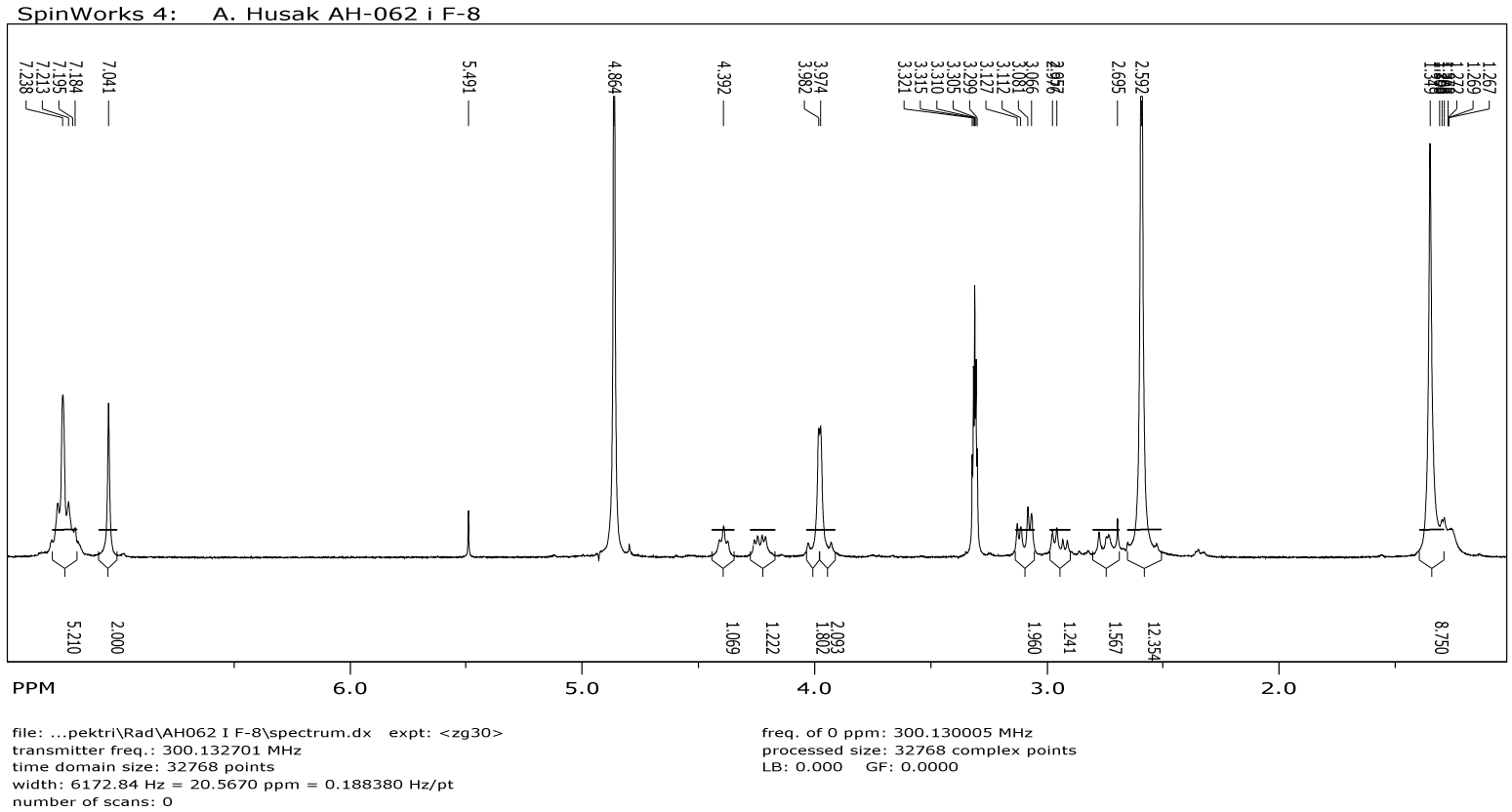
time domain size: 32768 points
width: 39370.08 Hz = 260.8708 ppm = 1.201479 Hz/pt
number of scans: 0

freq. of 0 ppm: 150.902598 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]$_2$-OH (**3A**)





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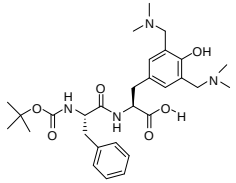
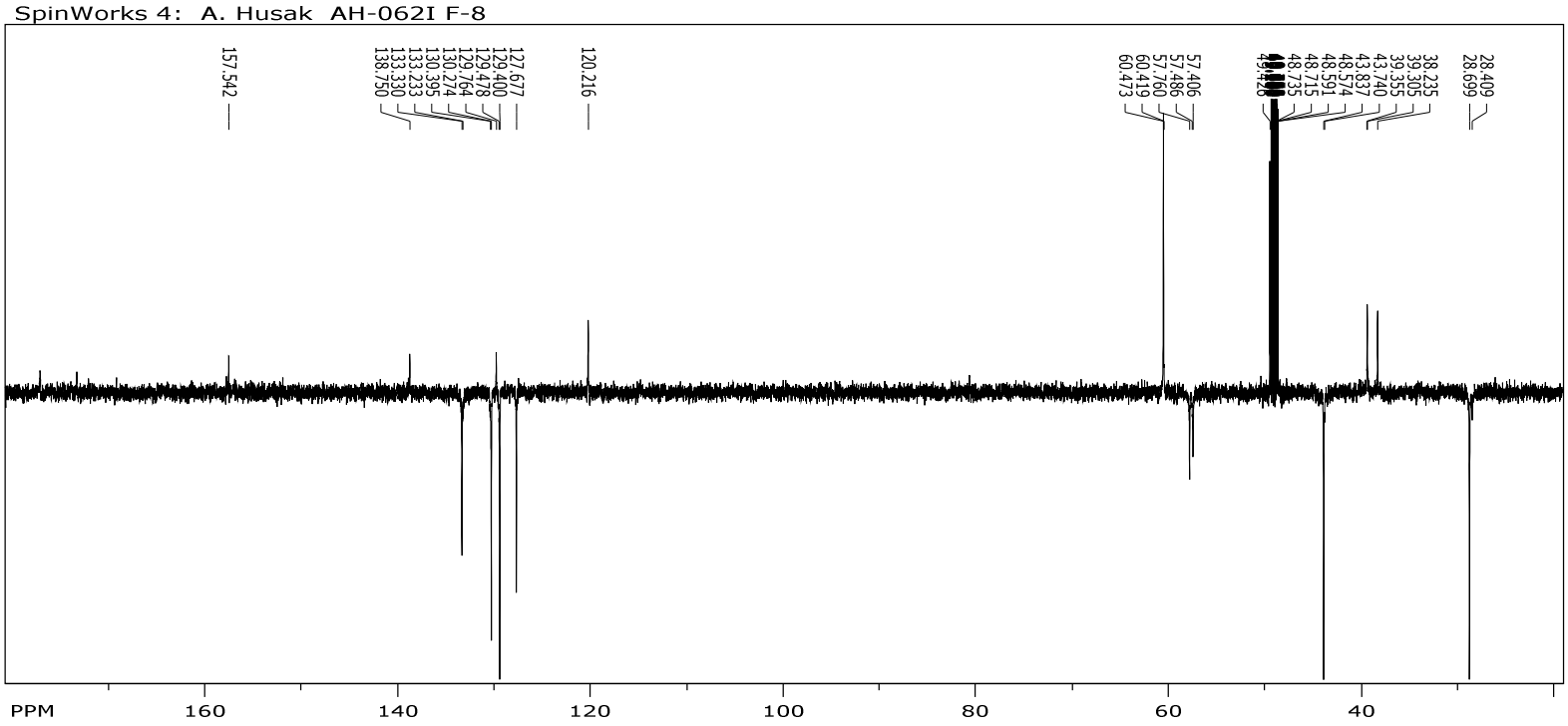
number of scans: 0

freq. of 0 ppm: 300.130005 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR (CD_3OD, 150 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]$_2$-OH (**3A**)





file: ...ri\husak_ah062if8apt\1\spectrum.dx expt: <jmod>
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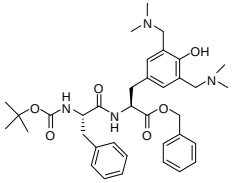
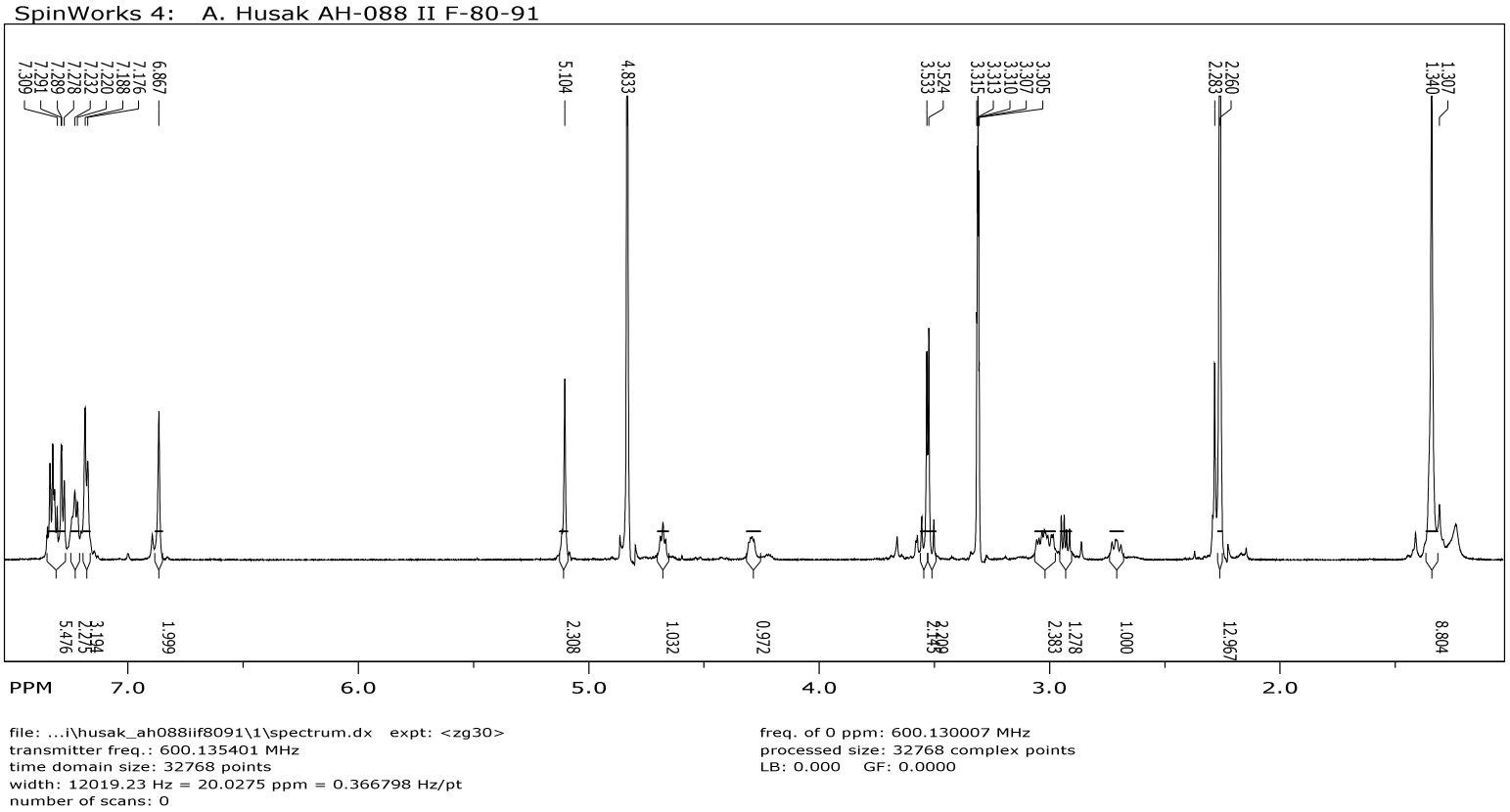
time domain size: 32768 points
width: 39370.08 Hz = 260.8708 ppm = 1.201479 Hz/pt
number of scans: 0

freq. of 0 ppm: 150.902600 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{1}H NMR (CD_3OD, 600 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]$_2$-OBn (**3B**)





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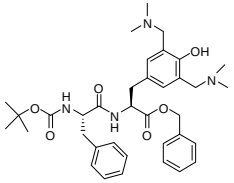
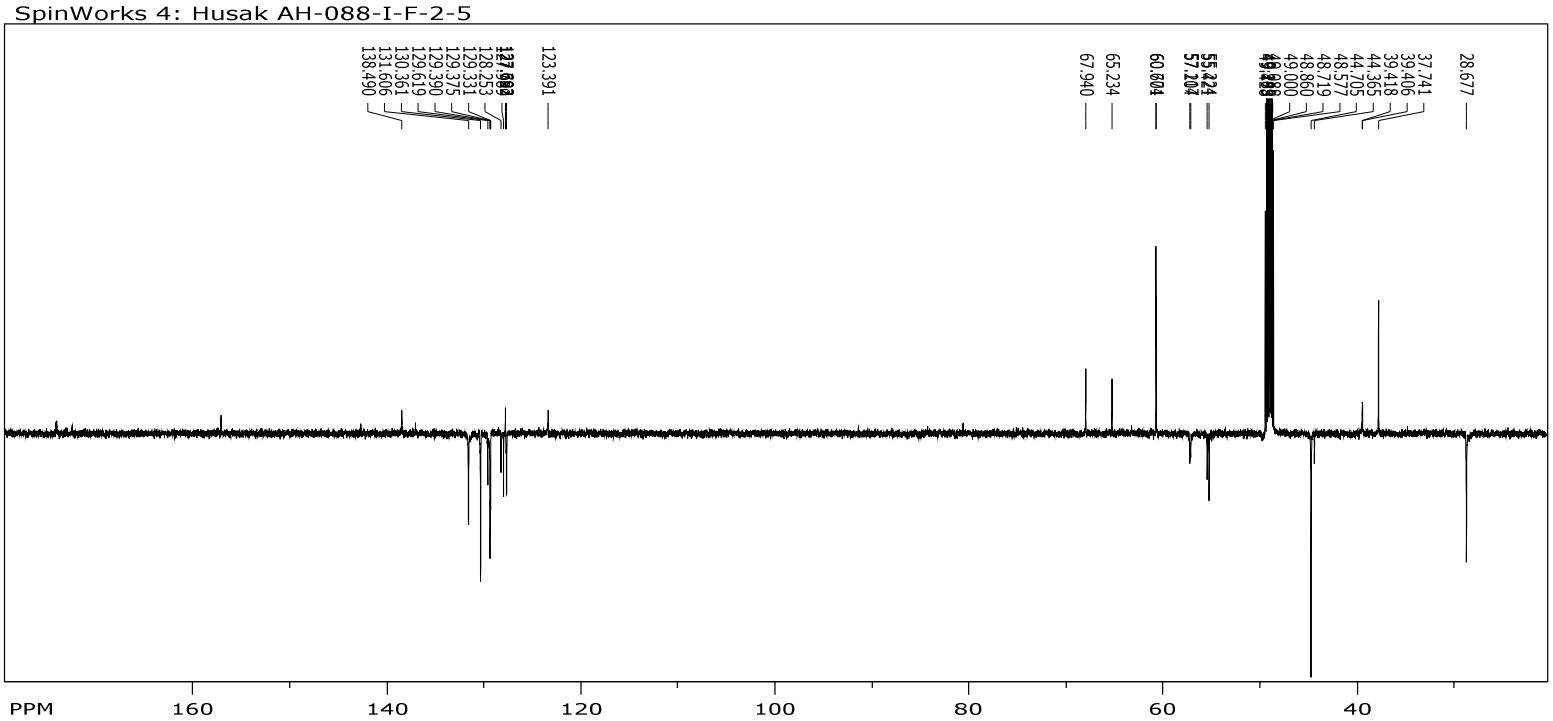
number of scans: 0

freq. of 0 ppm: 600.130007 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR (CD_3OD, 150 MHz) of BOC-Phe-Tyr[$CH_2N(CH_3)_2$]$_2$-OBn (**3B**)





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number of scans: 5000

freq. of 0 ppm: 150.902595 MHz
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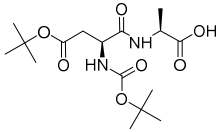
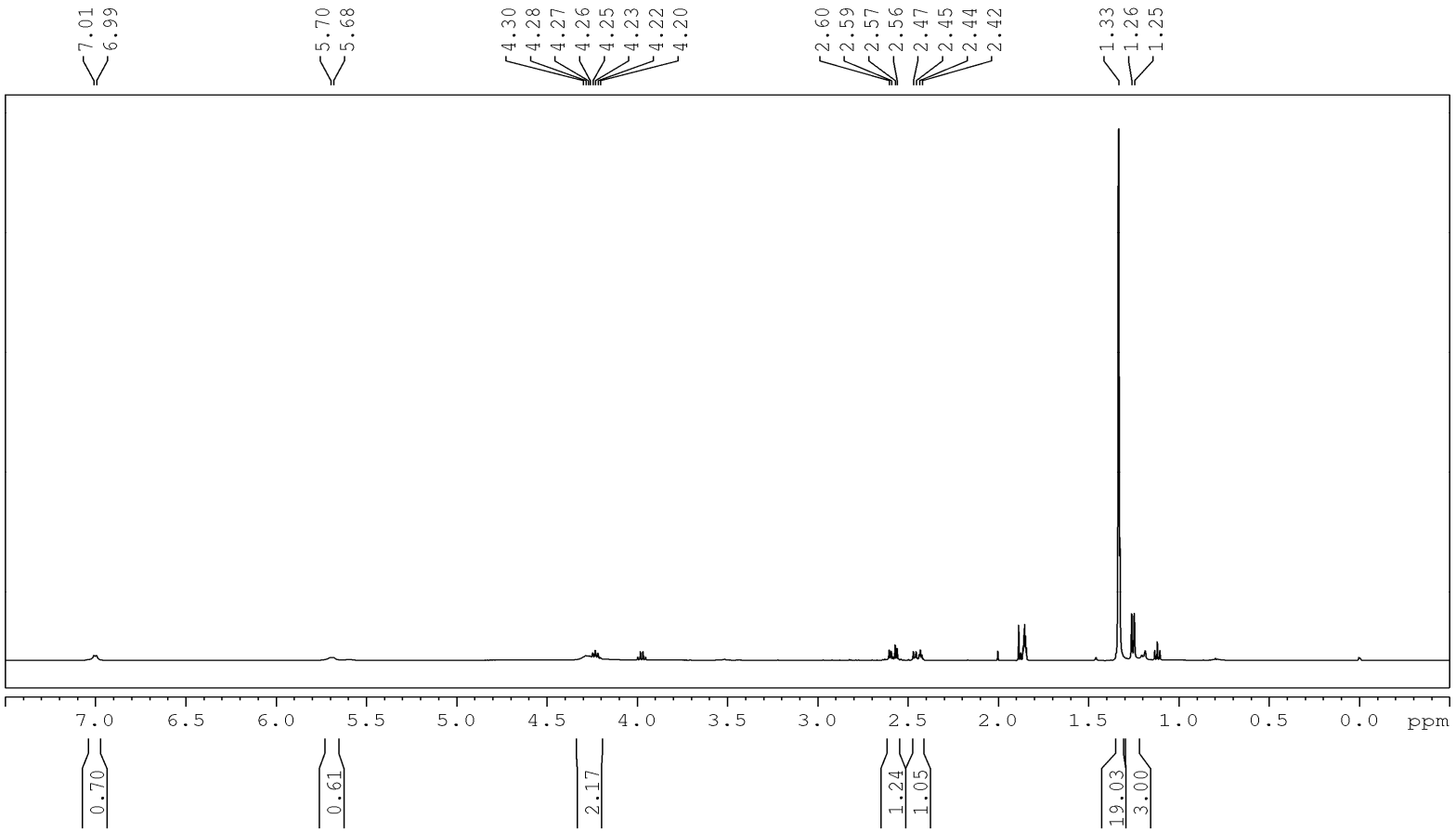
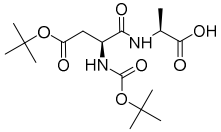
LB: 1.000 GF: 0.0000

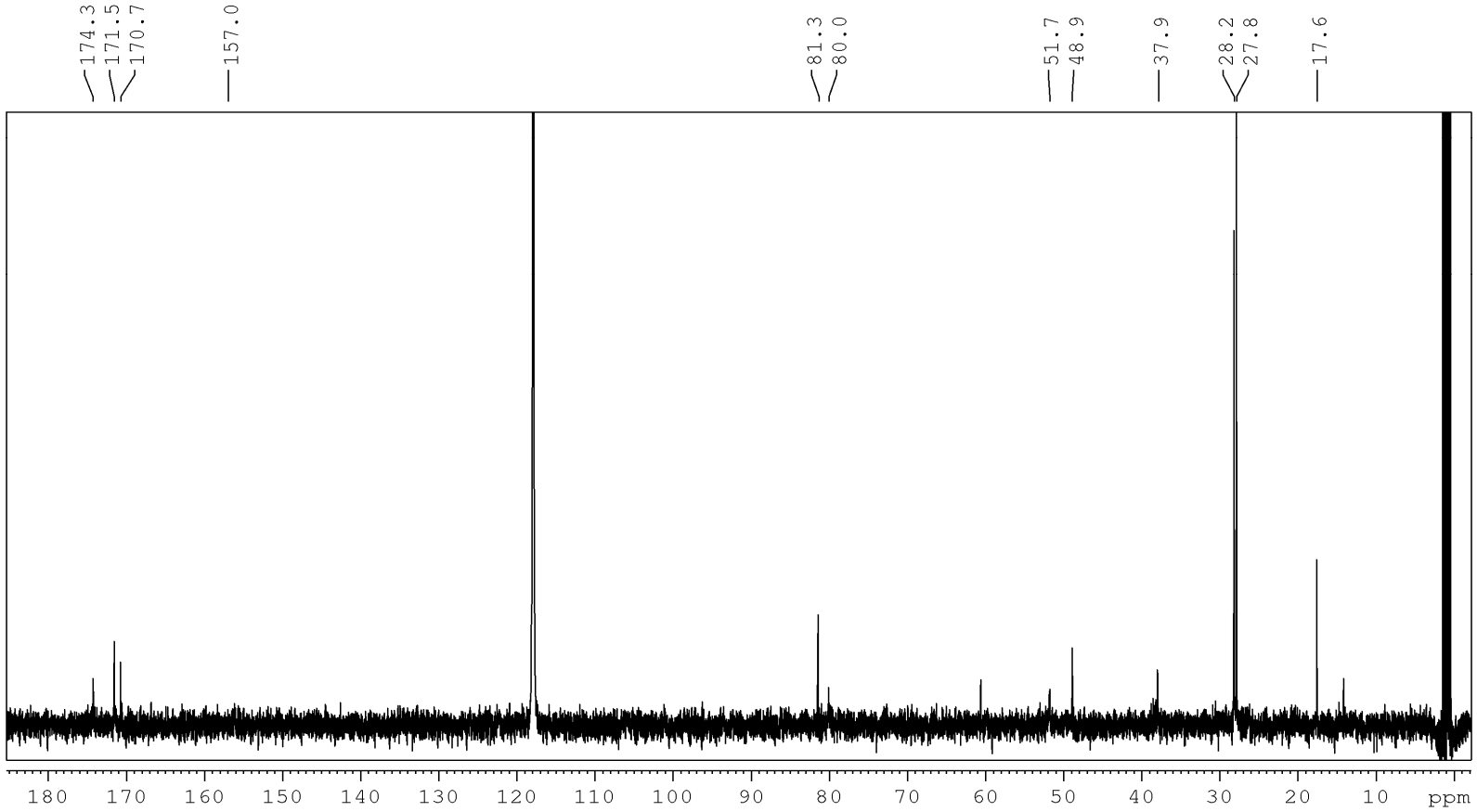
^{1}H NMR (CD_3CN, 500 MHz) of BOC-Asp(^{t}Bu)-Ala-OH



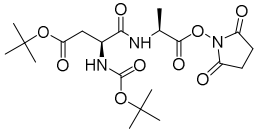


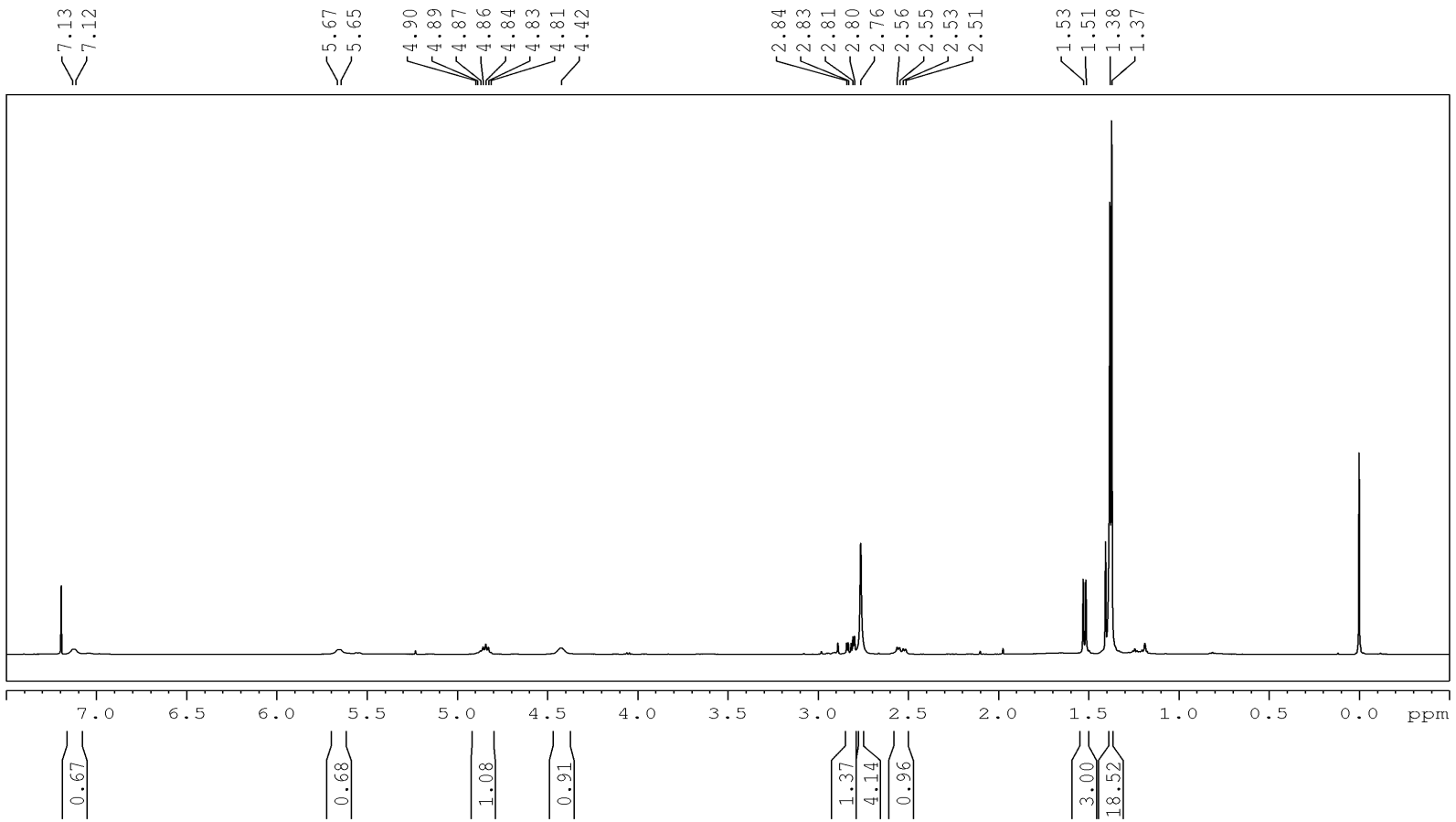
^{13}C NMR (CD_3CN, 126 MHz) of BOC-Asp(^{t}Bu)-Ala-OH



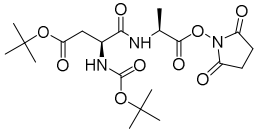


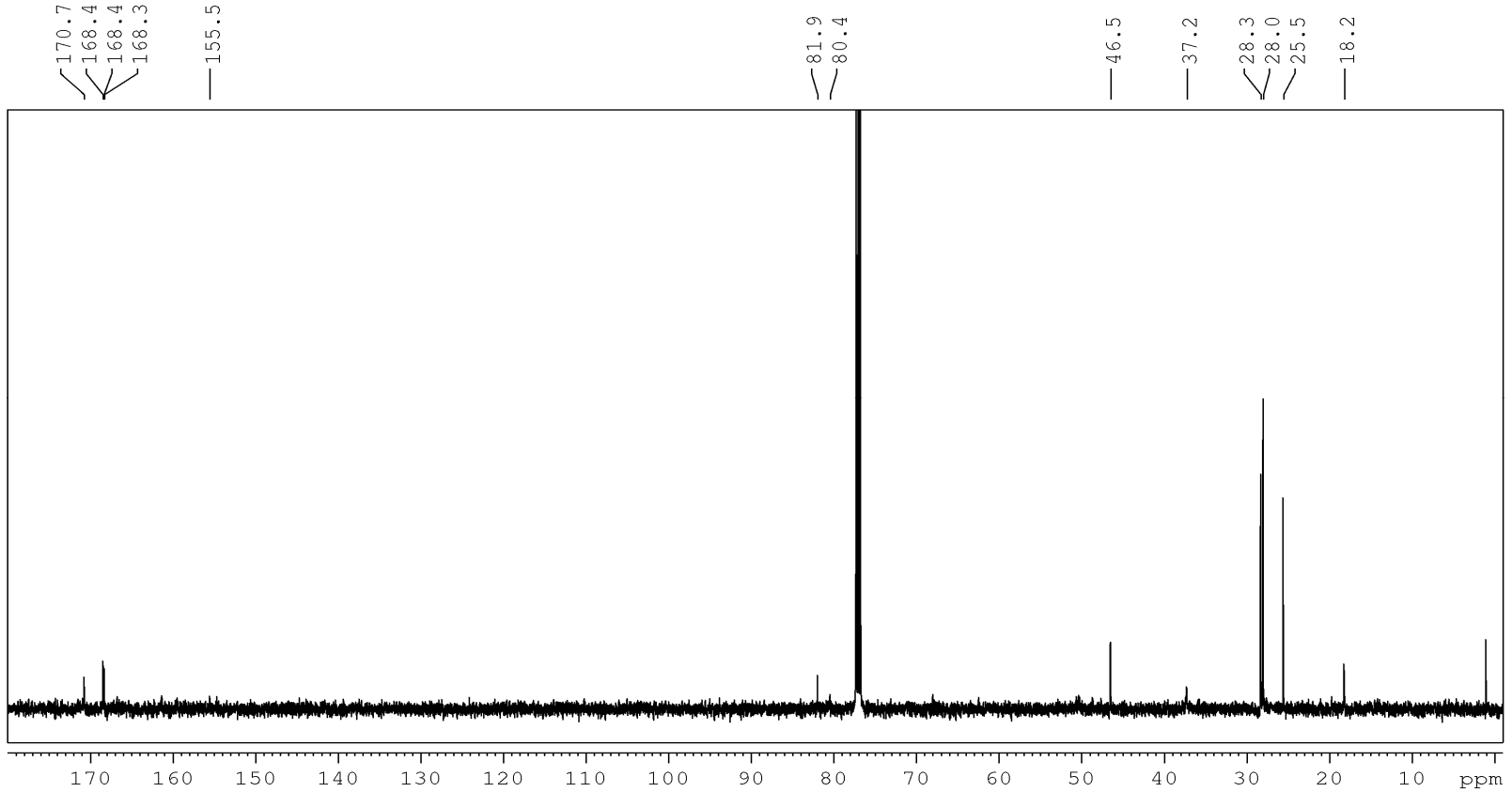
^{1}H NMR ($CDCl_3$, 500 MHz) of BOC-Asp(^{t}Bu)-Ala-OSu



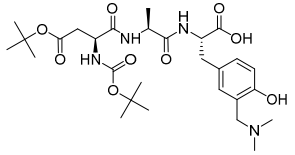


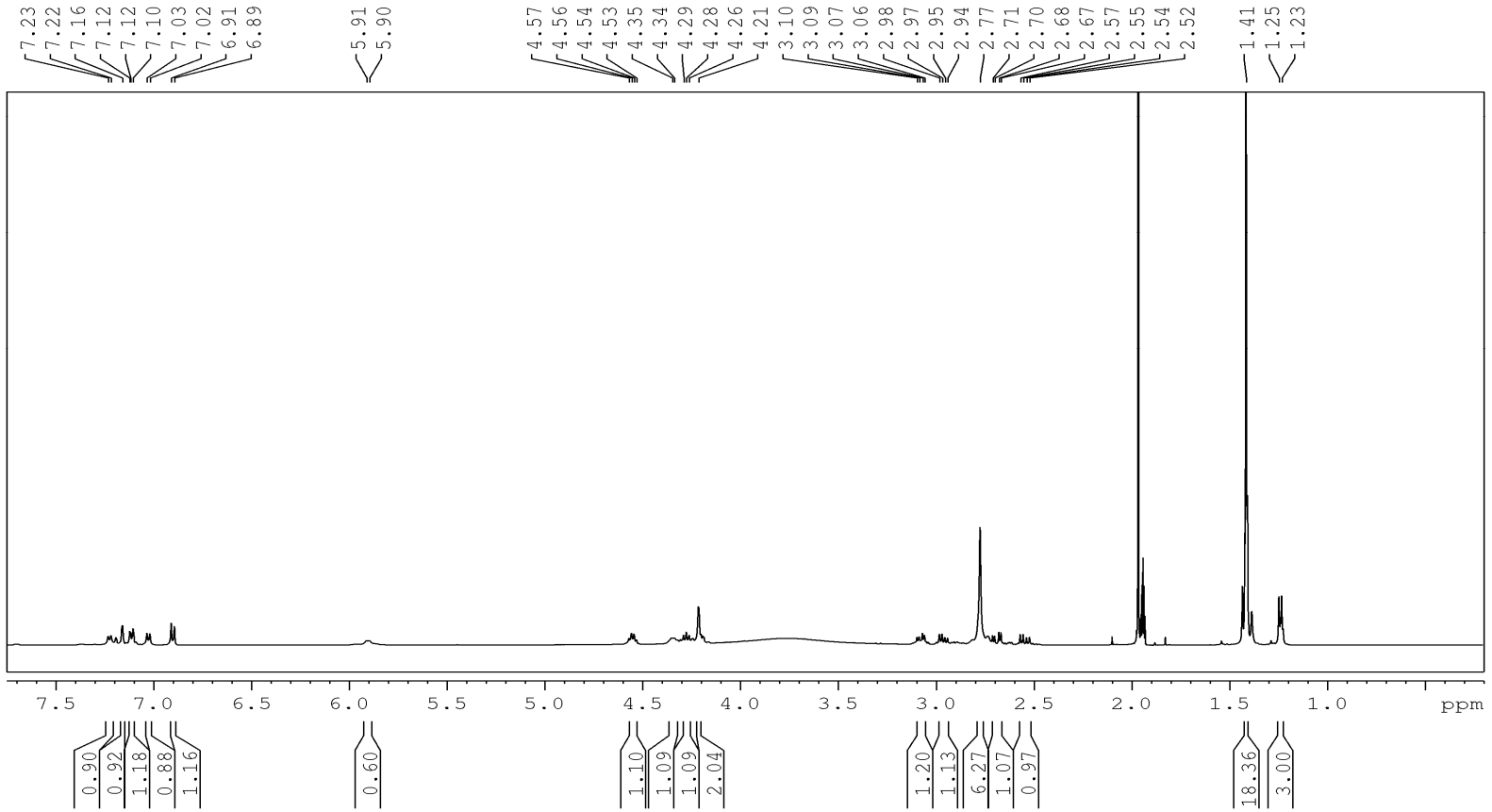
^{13}C NMR ($CDCl_3$, 126 MHz) of BOC-Asp(^{t}Bu)-Ala-OSu



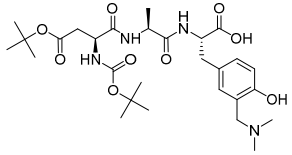


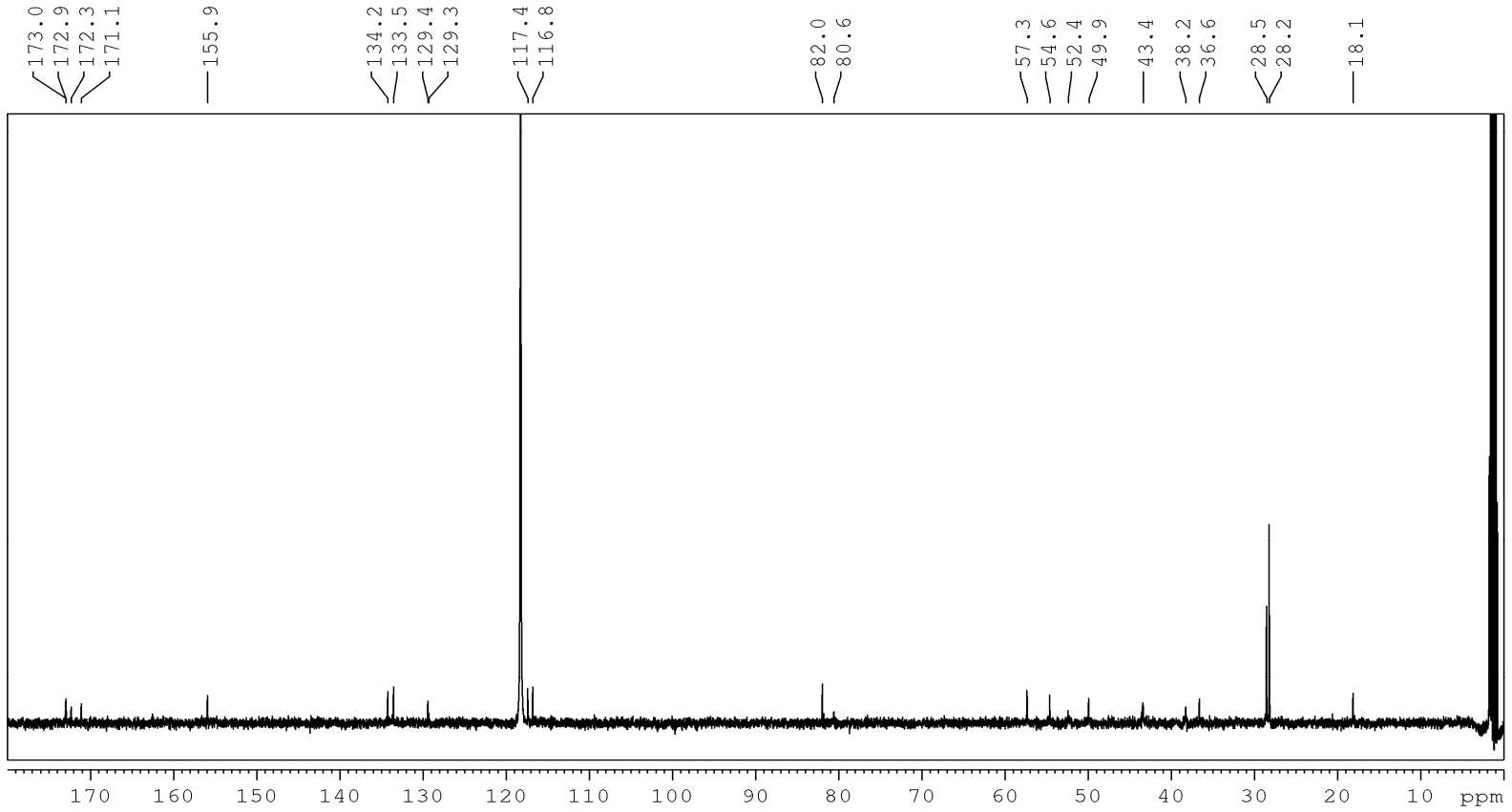
^{1}H NMR ($CDCl_3$, 500 MHz)of BOC-Asp(^{t}Bu)-Ala-**1**-OH (**4**):



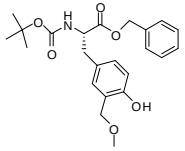


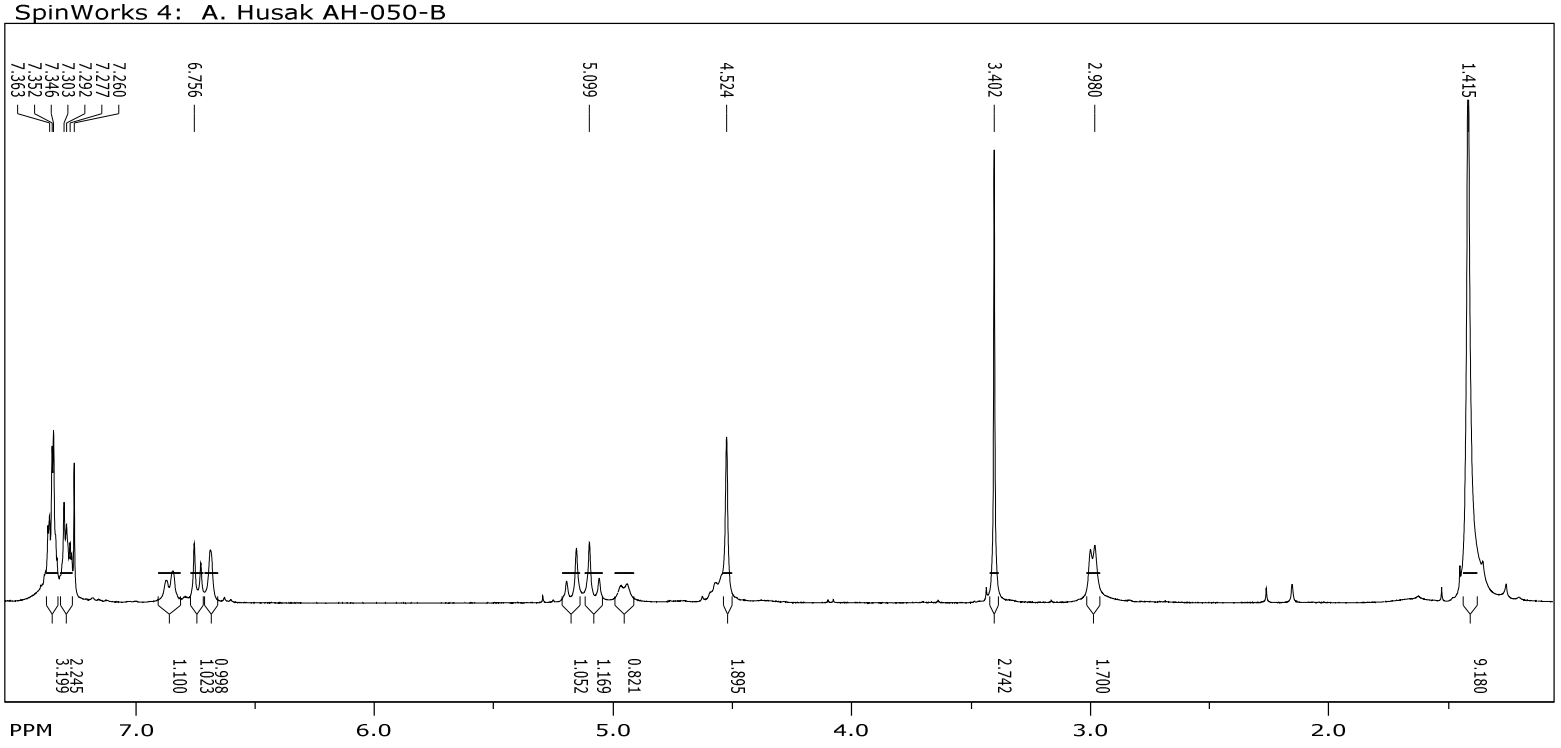
^{13}C NMR ($CDCl_3$, 126 MHz) of BOC-Asp(^{t}Bu)-Ala-**1**-OH (**4**):



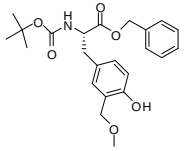


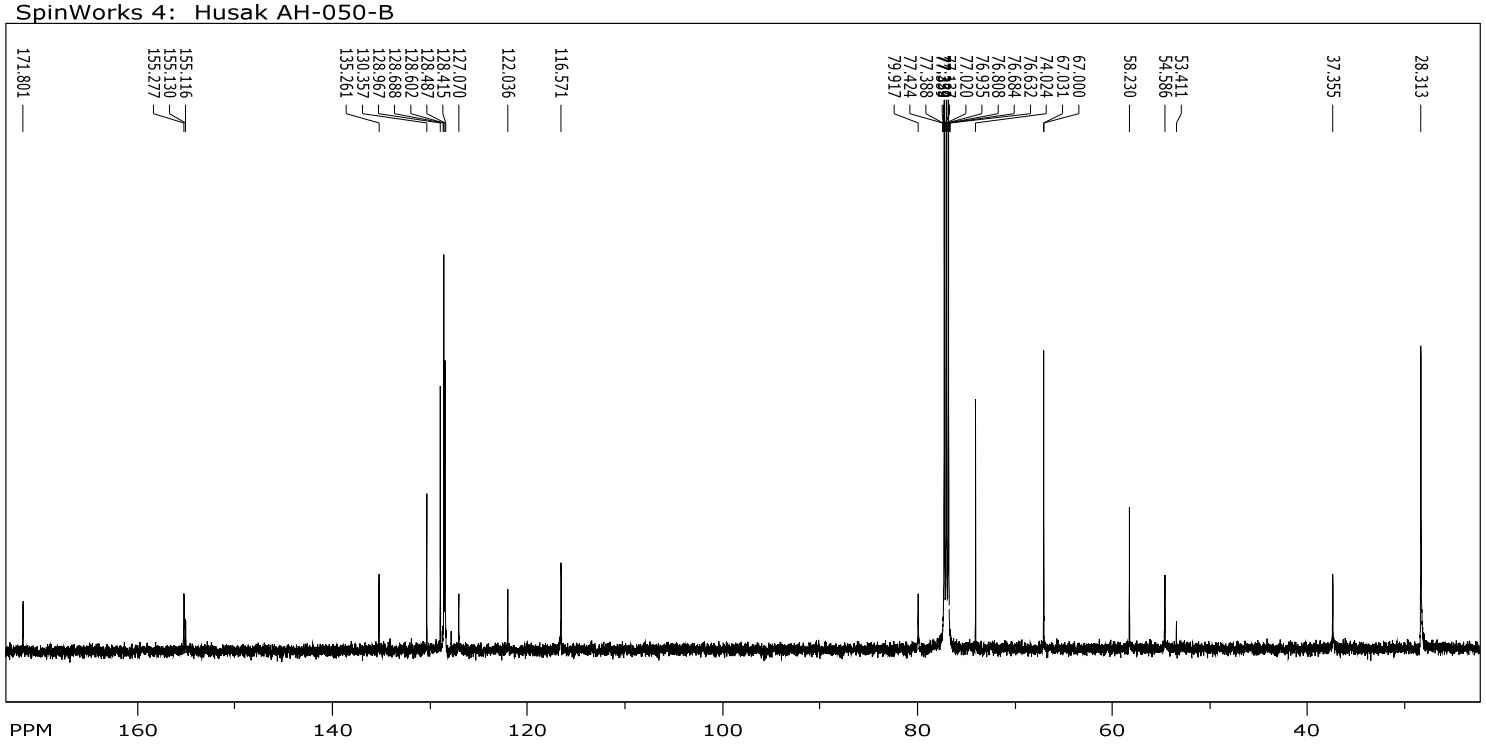
^{1}H NMR ($CDCl_3$, 300 MHz) of **6**





^{13}C NMR ($CDCl_3$, 150 MHz) of **6**





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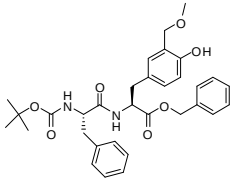
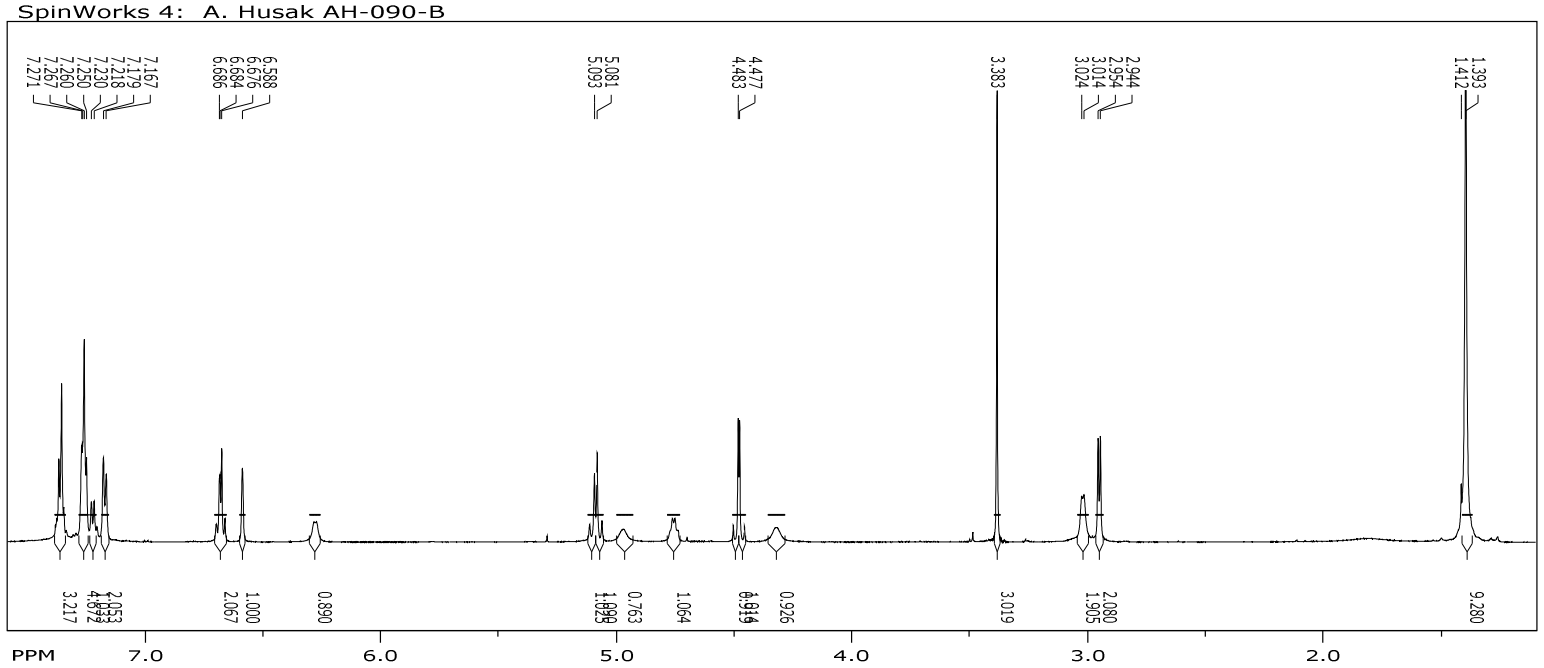
number of scans: 0

freq. of 0 ppm: 150.902806 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{1}H NMR ($CDCl_3$, 600 MHz) of **7**





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number of scans: 0

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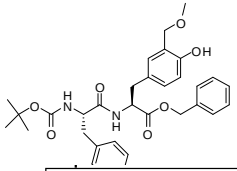
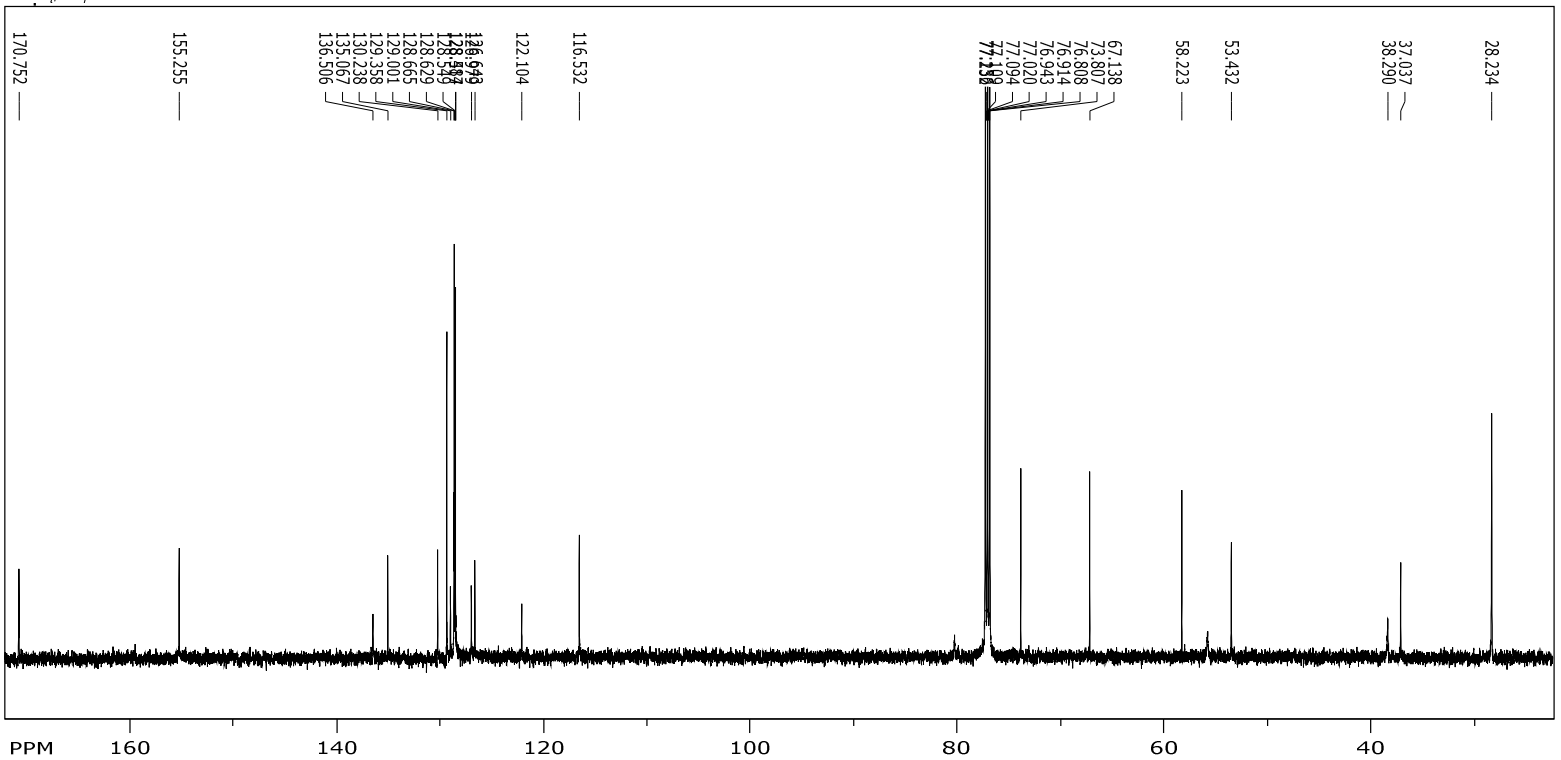
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR ($CDCl_3$, 150 MHz) of **7**





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number of scans: 0

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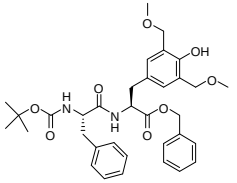
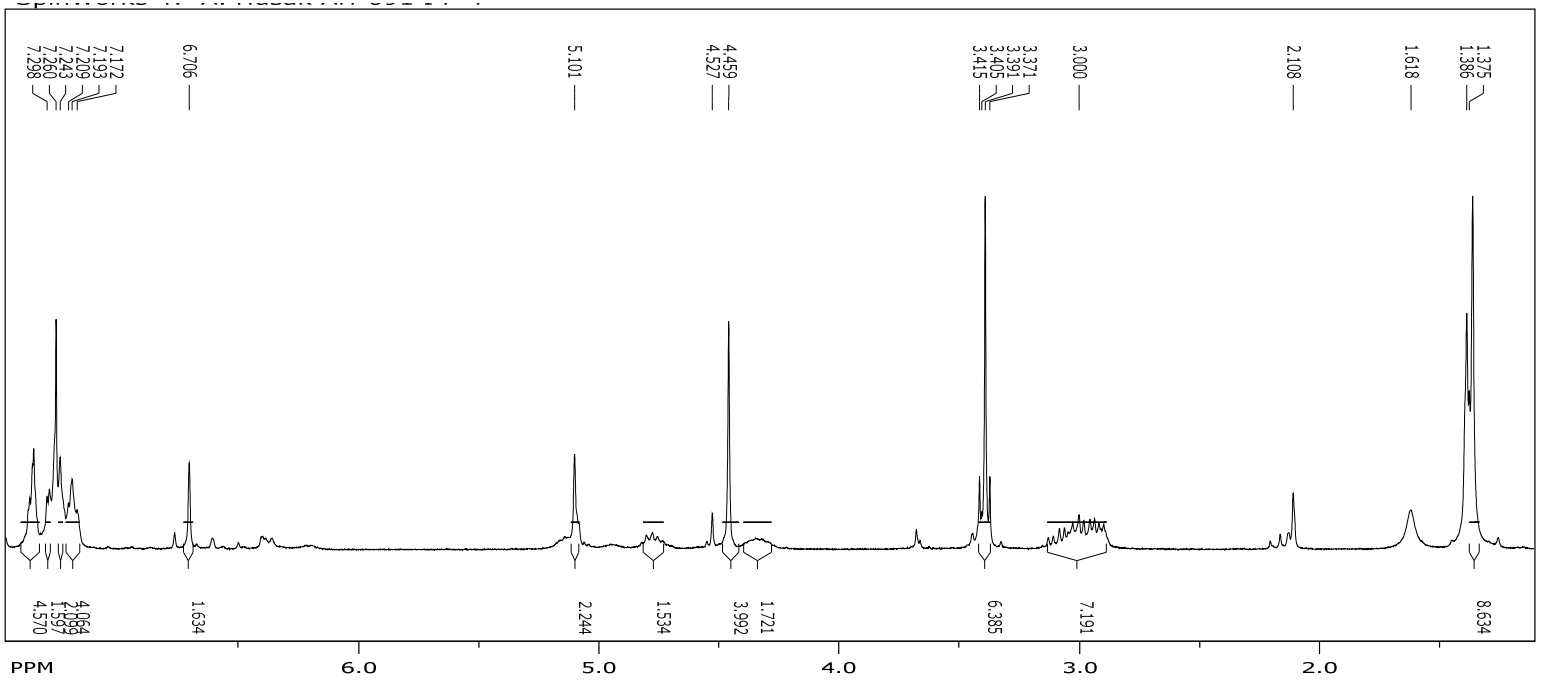
^{1}H NMR ($CDCl_3$, 300 MHz) of **9**





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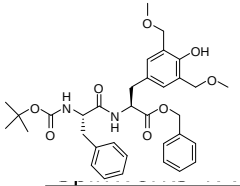
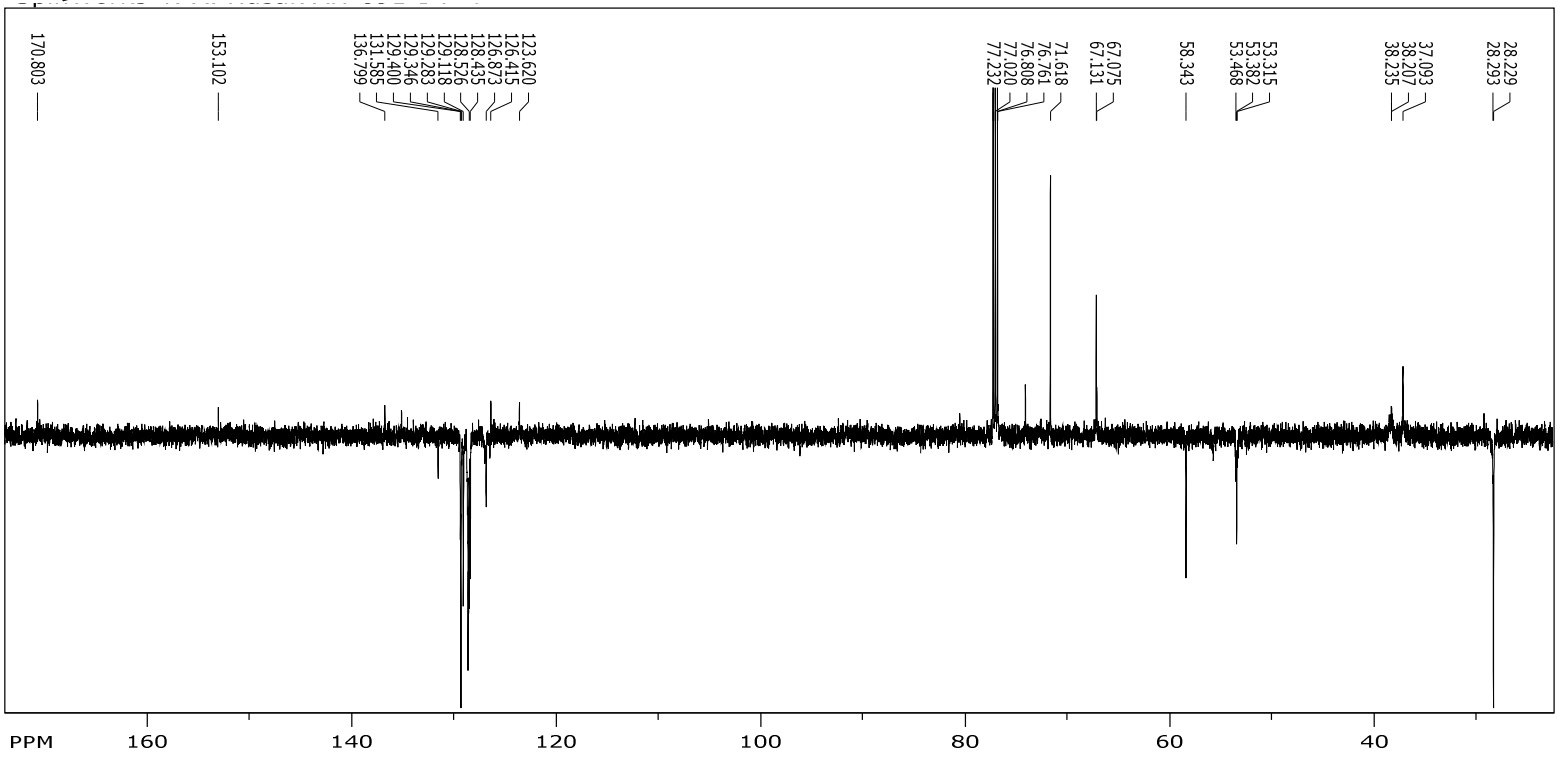
number of scans: 0

freq. of 0 ppm: 300.130006 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR ($CDCl_3$, 150 MHz) of **9**





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time domain size: 65536 points
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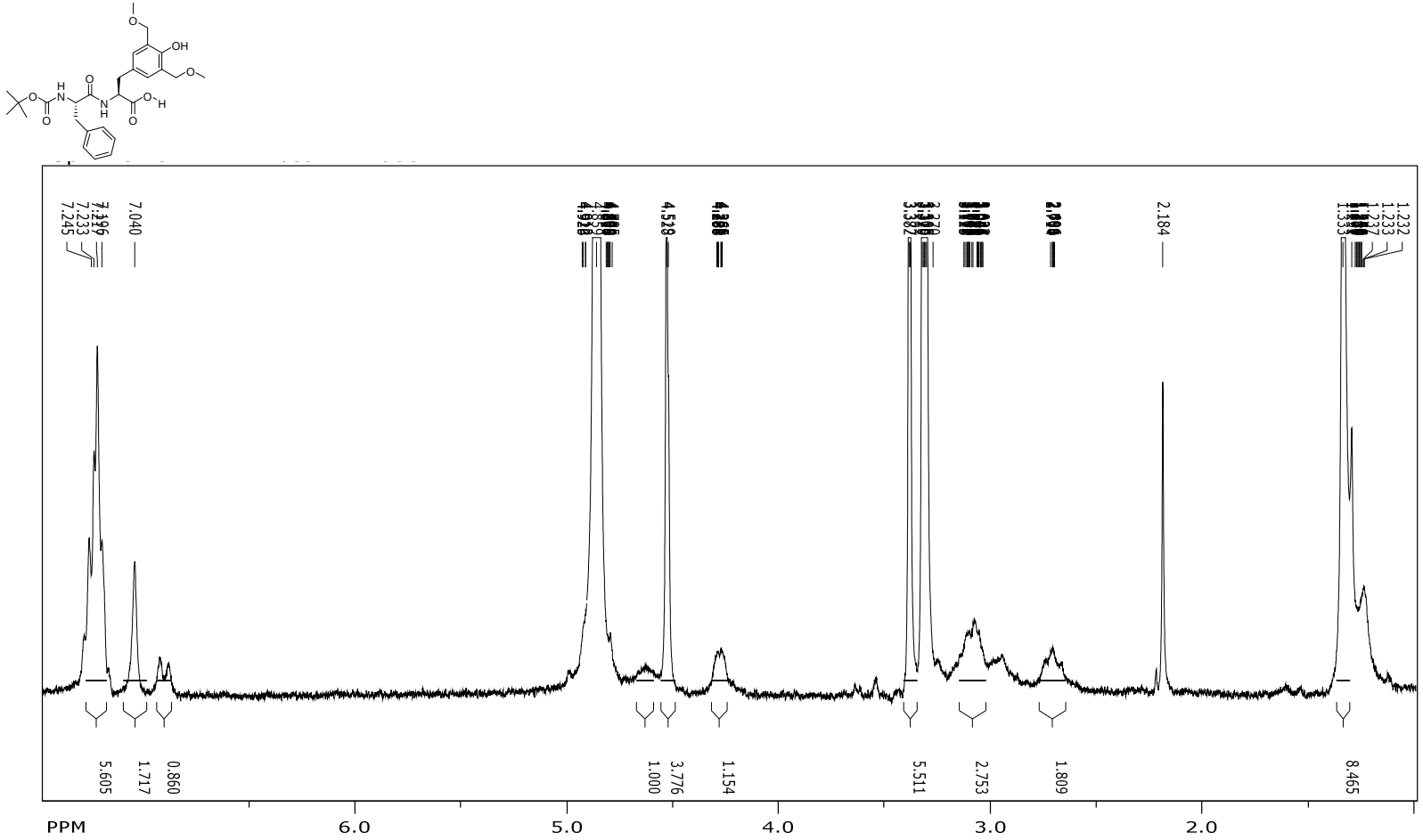
number of scans: 32250

freq. of 0 ppm: 150.902804 MHz
processed size: 32768 complex points
LB: 1.000 GF: 0.0000

^{1}H NMR (CD_3OD, 300 MHz) of **10**



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number of scans: 0

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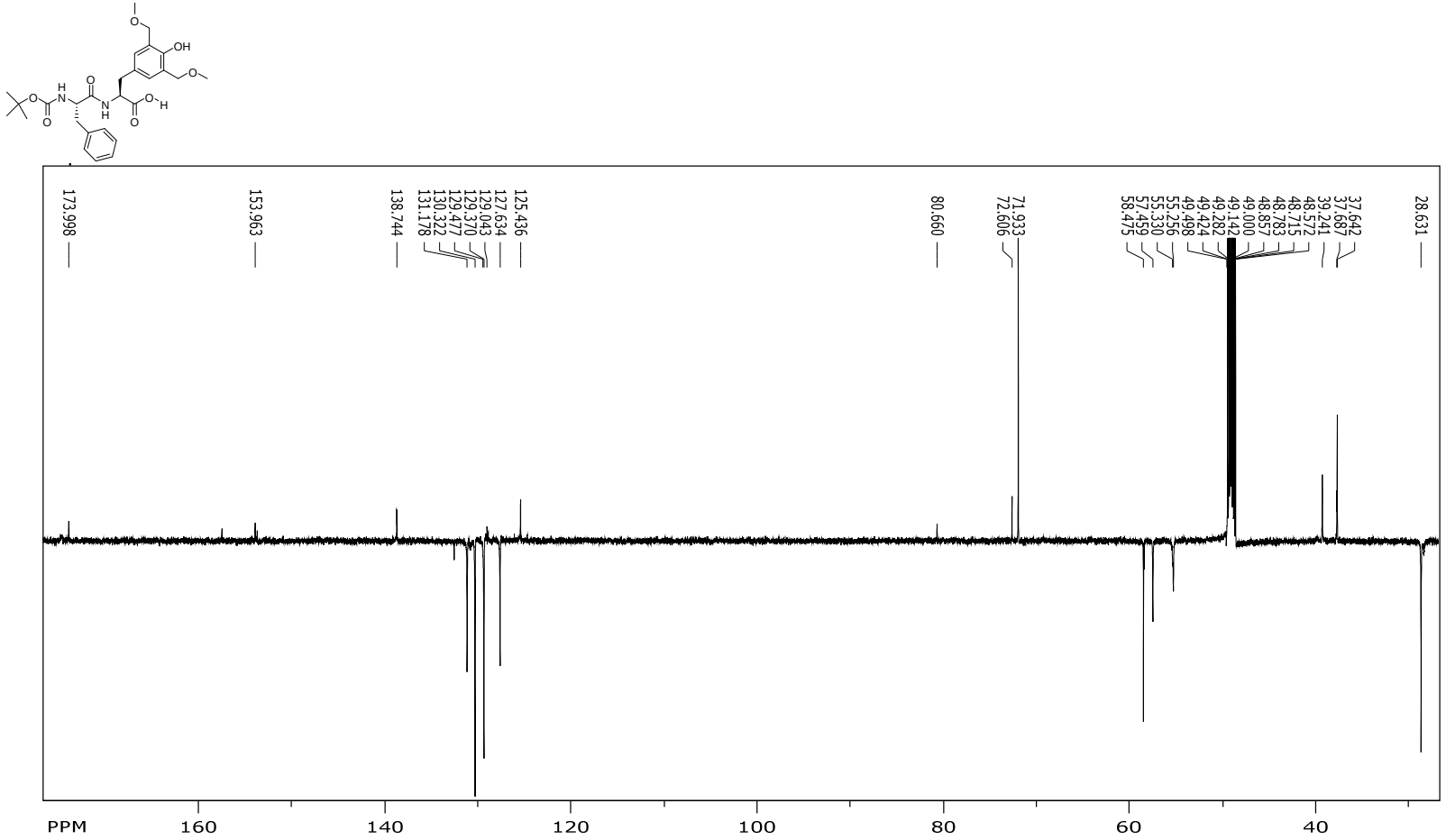
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

^{13}C NMR (CD_3OD, 150 MHz) of **10**



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number of scans: 37974

freq. of 0 ppm: 150.902593 MHz
processed size: 32768 complex points
LB: 0.000 GF: 0.0000

6. References

[1] O. Keller, W. E. Keller, G. van Look, G. Wersin, *Org. Synth.*, 1990, **7**, 70-78.

[2] A. Felix, L. Moroder, C. Toniolo (Eds.), *Synthesis of Peptides and Peptidomimetics*, Thieme, Stuttgart, 2004, Volume 22.

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