Supplementary Information

BODNs as biocompatible brominating reagents: visible-light photocatalytic tyrosine modification under physiologically favorable conditions

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Contents

Instrumentation and Chemicals

^{1}H and ^{13}C Nuclear magnetic resonance spectra were taken on a JEOL ECZ-600R (^{1}H, 600 MHz; ^{13}C, 150 MHz) spectrometer using tetramethylsilane as an internal standard for ^{1}H NMR ($\delta = 0$ ppm) and $CDCl_3$ as an internal standard for ^{13}C NMR ($\delta = 77.0$ ppm). ^{1}H NMR data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sext = sextet, sept = septet, br = broad, m = multiplet), coupling constants (Hz), integration. Mass spectra were recorded on a Thermo Scientific Exactive (ESI, APCI) spectrometer (analyzer type: TOF). Infrared (IR) spectra were determined on an Affinity-1S spectrometer with QATR 10. Melting points were determined using a Stanford Research Systems MPA100. UV-Vis absorption spectra were determined using a SHIMADZU UV-1900i spectrophotometer. Fluorescence spectra were determined using a SHIMADZU RF-6000 fluorospectrophotometer. ASAHI SPECTRA CL-1503/CL-H1-525-7-1-B (525 nm), CL-H1-430-9-1-B (430 nm) were used for light irradiation. TLC analyses were performed by means of Merck Kieselgel 60 F_{254} (0.25 mm) Plates. Visualization was accomplished with UV light (254 nm) and/or such as an aqueous alkaline $KMnO_4$ solution followed by heating. Flash column chromatography was carried out using Kanto Chemical silica gel (spherical, 40–50 μm). Unless otherwise noted, commercially available reagents were used without purification.

Experimental Procedure

General procedure for photocatalytic tyrosine bromination

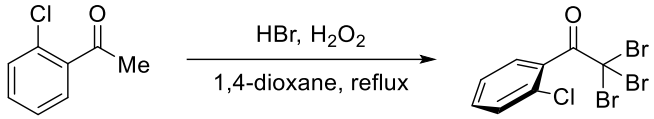
To a 10-mL round-bottom flask were sequentially added tyrosine derivative **2** (30 mg, 0.10 mmol), a solution of a photocatalyst (0.0010 mmol) in MeCN (0.50 mL), and H_2O (0.50 mL) without any special care for excluding air and moisture. The reaction mixture was stirred at 37 °C for 30 min. To the resulting solution was added brominating reagent **1** (0.12 mmol), and the mixture was irradiated with LEDs (525 nm). After being stirred for 3 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (1.5 mL) and H_2O (15 mL), and the aqueous layer was extracted with CH_2Cl_2 (15 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification of the crude product by flash silica gel column chromatography using hexane/EtOAc (v/v = 9:1) as an eluent gave the product **3**.

Procedure for photochemical tyrosine bromination

To a 10-mL round-bottom flask were sequentially added tyrosine derivative **2** (30 mg, 0.10 mmol), MeCN (0.50 mL), and H_2O (0.50 mL) without any special care for excluding air and moisture. The reaction mixture was stirred at 37 °C for 30 min. To the resulting solution was added brominating reagent **1e** (39 mg, 0.12 mmol), and the mixture was irradiated with LEDs (430 nm). After being stirred for 3 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ (1.5 mL) and H_2O (15 mL), and the aqueous layer was extracted with CH_2Cl_2 (15 mL × 3). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. Purification of the crude product by flash silica gel column chromatography using hexane/EtOAc (v/v = 2:1) as an eluent gave the product **3**.

Brominating reagents **1a** and **1b** were commercially available.

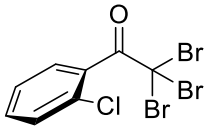
Procedure for preparation of 1c[1]



S1 **1c**

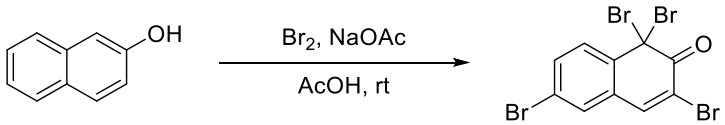
To a solution of 1-(2-chlorophenyl)ethan-1-one (**S1**, 0.77 g, 5.0 mmol) in 1,4-dioxane (14 mL) was added 48% aqueous HBr (13 mL, 0.12 mol), and the mixture was refluxed. To the mixture was slowly added a solution of 30% aqueous H_2O_2 (2.1 mL, 21 mmol) in 1,4-dioxane (1.4 mL). After being stirred for 2 h, the reaction mixture was cooled to ambient temparature, diluted with H_2O (30 mL), and extracted with CH_2Cl_2 (30 mL × 4). The combined organic layers were washed with H_2O (15 mL × 4), dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using hexane/EtOAc (v/v = 94:6) as an eluent gave **1c**.

2,2,2-Tribromo-1-(2-chlorophenyl)ethan-1-one (1c): CAS RN [296281-78-2].



Slightly yellow solid; 58% yield (1.1 g). ^{1}H NMR ($CDCl_3$) δ 7.88 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.50 (dd, *J* = 8.4, 1.2 Hz, 1H), 7.45 (ddd, *J* = 8.4, 7.8, 1.2 Hz, 1H), 7.34 (ddd, *J* = 7.8, 7.8, 1.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 185.7, 133.4, 132.1, 131.8, 130.1, 129.0, 126.3, 41.7. TLC: R_f 0.40 (hexane/EtOAc = 94:6).

Procedure for preparation of 1d[2]

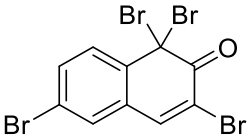


S2 **1d**

To a solution of sodium acetate (11 g, 0.14 mol) and 2-naphthol (**S2**, 2.9 g, 20 mmol) in acetic acid (80 mL) was added bromine (26 g, 0.16 mol) portionwise over 10 min at 0 °C. The reaction mixture was stirred at ambient temperature for 2 h. Ice was added

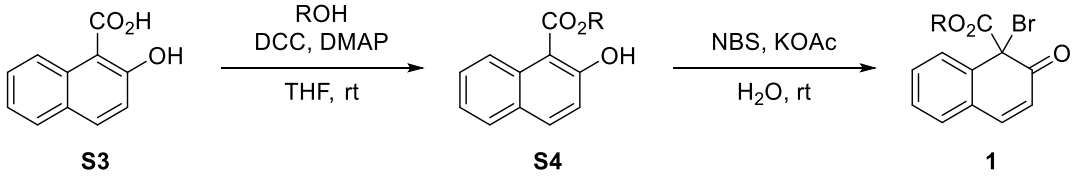
to the reaction mixture, forming slight yellow precipitates, which were collected by filtration with EtOAc and washed with cold water followed by EtOAc. A solution of the crude solid in CH_2Cl_2 was washed with H_2O, dried over Na_2SO_4, and concentrated in vacuo. Purification by recrystallization from toluene gave **1d**.

1,3,3,6-Tetrabromonaphthalen-2-(1*H*)-one (1d): CAS RN [858023-30-0].



Slightly yellow solid; 29% yield (2.6 g). ^{1}H NMR ($CDCl_3$) δ 7.99 (d, *J* = 8.8, 1H), 7.78 (s, 1H), 7.65 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.40 (d, *J* = 2.4 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 179.7, 143.9, 140.3, 134.2, 133.4, 131.2, 127.4, 124.8, 119.2, 57.4. TLC: R_f 0.35 (hexane/EtOAc = 50:1).

General procedure for preparation of BODN 1e–1g

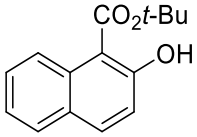


S3 **S4** **1**

General procedure for preparation of **S4e**–**S4g**[3]

To a solution of 2-hydroxy-1-naphthoicacid (**S3**, 9.4 g, 50 mmol) in THF (50 mL) was sequentially added an alcohol (0.50 mol), 4-dimethylaminopyridine (0.61 g, 5.0 mmol), and *N*,*N*'-dicyclohexylcarbodiimide (15 g, 75 mmol), and the mixture was stirred at ambient temperature overnight. The mixture was filtered through a celite pad, which was washed with CH_2Cl_2, and the combined filtrate was concentrated in vacuo. Purification by flash silica gel column chromatography using hexane/EtOAc (v/v = 20/1) as an eluent gave **S4**.

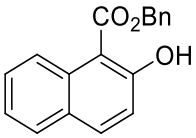
***tert*-Butyl 2-hydroxy-1-naphthoate (S4e)**: CAS RN [2222802-20-0].



Colorless oil; 99% yield (13 g). ^{1}H NMR ($CDCl_3$) δ 12.47 (s, 1H), 8.80 (dd, *J* = 8.8, 1.2 Hz, 1H), 7.86 (d, *J* = 9.2 Hz, 1H), 7.74 (d, *J* = 9.2 Hz, 1H), 7.53 (ddd, *J* = 8.8, 6.8, 1.6

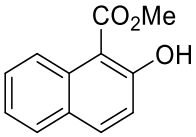
Hz, 1H), 7.35 (ddd, *J* = 8.4, 6.8, 1.2 Hz, 1H), 7.15 (dd, *J* = 8.4, 1.6 Hz, 1H), 1.74 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 171.7, 164.1, 136.2, 132.0, 129.0, 128.7, 128.1, 125.2, 123.4, 119.4, 105.9, 84.1, 28.5. TLC: R_f 0.35 (hexane/EtOAc = 20:1).

Benzyl 2-hydroxy-1-naphthoate (S4f): CAS RN [86170-47-0].



White solid; 36% yield (5.0 g). ^{1}H NMR ($CDCl_3$) δ 12.26 (s, 1H), 8.79 (d, *J* = 9.0 Hz, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.75 (d, *J* = 9.0 Hz, 1H), 7.54–7.49 (m, 3H), 7.44–7.34 (m, 4H), 7.17 (d, *J* = 9.0 Hz, 1H), 5.58 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 172.2, 164.6, 137.0, 135.2, 131.8, 129.1, 128.8, 128.65, 128.57, 128.5, 128.4, 125.3, 123.6, 119.3, 104.6, 67.5. TLC: R_f 0.35 (hexane/EtOAc = 20:1).

Methyl 2-hydroxy-1-naphthoate (S4g): CAS RN [947-65-9].

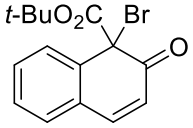


White solid; 43% yield (4.3 g). ^{1}H NMR ($CDCl_3$) δ 12.27 (s, 1H), 8.75 (d, *J* = 8.5 Hz, 1H), 7.90 (d, *J* = 9.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.56 (dd, *J* = 8.5, 8.0 Hz, 1H), 7.38 (dd, *J* = 8.0, 8.0 Hz, 1H), 7.17 (d, *J* = 9.0 Hz, 1H), 4.12 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 172.8, 164.4, 136.9, 131.7, 129.1, 128.6, 128.5, 125.3, 123.6, 119.3, 104.7, 52.4. TLC: R_f 0.45 (hexane/EtOAc = 20:1).

General procedure for preparation of **1e**–**1g**[4]

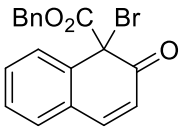
To a solution of **S4** (1.0 equiv) and potassium acetate (1.5 equiv) in H_2O (0.13 M) was added *N*-bromosuccinimide (1.2 equiv), and the mixture was stirred at ambient temperature for 1 h. The mixture was extracted with CH_2Cl_2 (0.15 L × 3), and the organic layers were washed with H_2O, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using hexane or hexane/EtOAc (v/v = 5:1) as an eluent gave **1**.

***tert*-Butyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1e)**.



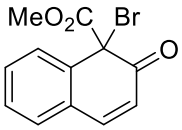
Yellow solid; 77% yield (12 g). ^{1}H NMR ($CDCl_3$) δ 7.50–7.35 (m, 5H), 6.28 (d, *J* = 9.5 Hz, 1H), 1.40 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 190.3, 164.6, 144.7, 138.7, 130.8, 129.9, 129.5 128.8, 127.9, 123.3, 84.9, 61.2, 27.6. TLC: R_f 0.33 (hexane/EtOAc = 5:1). Mp. 60.5–61.5 °C. IR (neat): 2983, 1750, 1662, 1367, 1239, 1146, 994, 745, 620, 514 cm^{-1}. HRMS (ESI) Calcd for $C_{15}H_{15}BrO_3Na$: $[M+Na]^+$, 345.0097, 347.0076. Found: *m*/*z* 345.0097, 347.0072.

Benzyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1f).



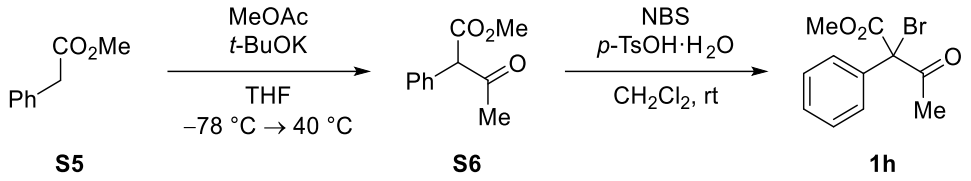
Yellow solid; 84% yield (5.4 g). ^{1}H NMR ($CDCl_3$) δ 7.46 (d, *J* = 10.0 Hz, 1H), 7.40–7.34 (m, 4H), 7.30–7.28 (m, 3H), 7.22–7.19 (m, 2H), 6.30 (d, *J* = 10.0 Hz, 1H), 5.25 (s, 2H). ^{13}C NMR ($CDCl_3$) δ 189.7, 165.9, 144.9, 137.9, 134.7, 130.8, 130.0, 129.8, 129.1, 128.5, 128.4, 128.1, 127.9, 123.2, 69.1, 60.3. TLC: R_f 0.25 (hexane/EtOAc = 5:1). Mp. 87.5–88.5 °C. IR (neat): 2928, 1753, 1659, 1229, 1204, 945, 752, 698, 623, 500 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{13}BrO_3Na$: $[M+Na]^+$, 378.9940, 380.9920. Found: *m*/*z* 378.9945, 380.9912.

Methyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1g): CAS RN [1799904-02-1].



Yellow solid; 76% yield (4.8 g). ^{1}H NMR ($CDCl_3$) δ 7.49–7.37 (m, 5H), 6.31 (d, *J* = 10.0 Hz, 1H), 3.81 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 189.8, 166.6, 144.9, 138.0, 131.0, 130.1, 129.9, 129.1, 127.9, 123.2, 60.1, 54.4. TLC: R_f 0.25 (hexane/EtOAc = 5:1).

Procedure for preparation of 1h



S5 **S6** **1h**

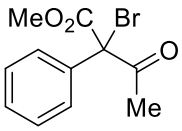
Procedure for preparation of **S6**[5]

To a solution of methyl phenylacetate (**S5**, 3.8 g, 25 mmol) and methyl acetate (7.3 mL, 75 mmol) in THF (25 mL) were slowly added a suspension of *t*-BuOK (4.2 g, 38 mmol) in THF (25 mL) at –78 °C under argon atmosphere. After being stirred for 4 h, the reaction mixture was warmed to 40 °C. After being stirred for additional 11 h, the reaction was quenched with 1.0 M HCl (ca. 50 mL). The aqueous layer was extracted with EtOAc (50 mL × 3), and the combined organic layers were washed with brine (50 mL × 2), dried over Na_2SO_4, and concentrated in vacuo. Purification by distillation gave methyl 2-phenylaetoacetate (**S6**) as a colorless oil in 74% yield (2.9 g).

Procedure for preparation of **1h**[6]

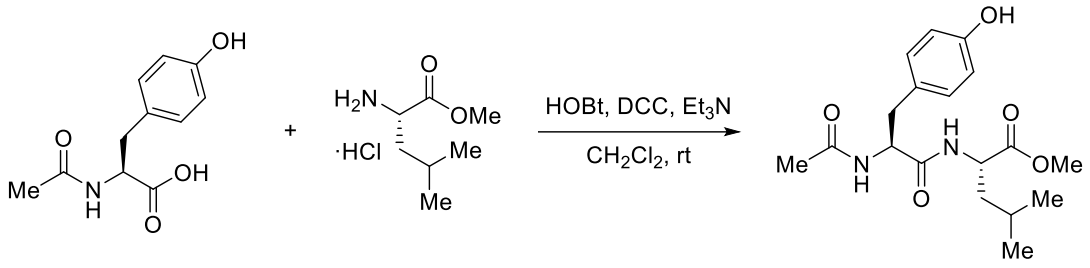
To a solution of **S6** (1.5 g, 8.0 mmol) in CH_2Cl_2 (40 mL) was sequentially added *p*-toruenesulfonic acid monohydrate (0.30 g, 1.6 mmol) and *N*-bromosuccinimide (1.6 g, 8.8 mmol), and the mixture was stirred at ambient temperature for 2 h. H_2O (30 mL) was added to the reaction mixture, and the aqueous layer was extracted with CH_2Cl_2 (40 mL × 3). The combined organic layers were washed with H_2O (40 mL × 2), dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using hexane/EtOAc (v/v = 10:1) as an eluent gave **1h**.

Methyl 2-bromo-3-oxo-2-phenylbutanoate (1h).



Colorless oil; 67% yield (1.8 g). ^{1}H NMR ($CDCl_3$) δ 7.51–7.49 (m, 2H), 7.41–7.37 (m, 3H), 3.86 (s, 3H), 2.40 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 196.8, 167.8, 134.1, 129.2, 128.6, 128.5, 70.9, 54.0, 26.3. TLC: R_f 0.35 (hexane/EtOAc = 10:1). IR (neat): 2955, 1724, 1433, 1356, 1240, 1180, 1030, 739, 692, 556 cm^{-1}. HRMS (ESI) Calcd for $C_{11}H_{11}BrO_3Na$: $[M+Na]^+$, 292.9784, 294.9769. Found: *m*/*z* 292.9777, 294.9756.

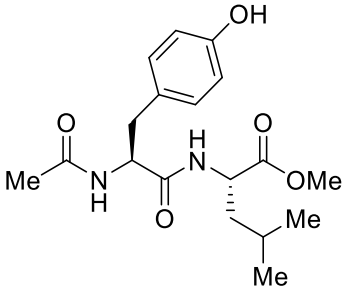
Procedure for preparation of 6a



S7 **S8** **6a**

To a 200-mL round-bottom flask were sequentially added *N*-acetyl-L-tyrosine **S7** (2.2 g, 10 mmol), L-leucine methyl ester hydrochloride **S8** (1.8 g, 10 mmol), DMF (50 mL), 1-hydroxybenzotriazole (1.4 g, 10 mmol), *N*,*N*'-dicyclohexylcarbodiimide (2.3 g, 11 mmol), and triethylamine (3.5 mL, 25 mmol). After being stirred at 25 °C overnight, the reaction was quenched with H_2O (30 mL). After white precipitates were removed by filtration, the aqueous layer was extracted with CH_2Cl_2 (50 mL × 3). The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using CH_2Cl_2/MeOH (v/v = 10:1) as an eluent gave **6a**.

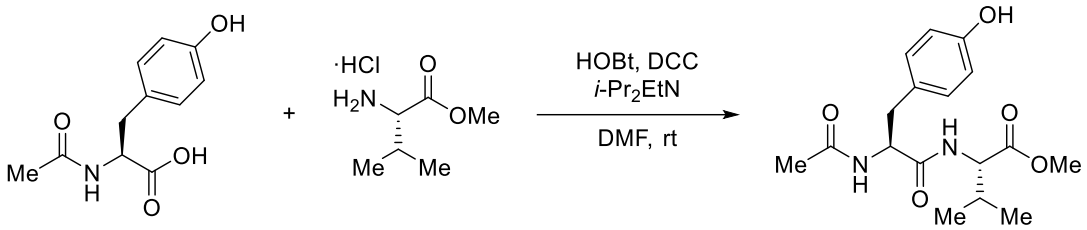
***N*-Acetyl-L-tyrosyl-L-leucin methyl ester (6a)**: CAS RN [33049-03-5].



White solid; 47% yield (1.6 g).

^{1}H NMR (CD_3OD) δ 7.03 (d, *J* = 8.4 Hz, 2H), 6.66 (d, *J* = 8.4 Hz, 2H), 4.53 (dd, *J* = 8.4, 6.0 Hz, 1H), 4.42 (dd, *J* = 9.6, 5.4 Hz, 1H), 3.64 (s, 3H), 2.98 (dd, *J* = 13.8, 6.0 Hz, 1H), 2.73 (dd, *J* = 13.8, 8.4 Hz, 1H), 1.87 (s, 3H), 1.66–1.52 (m, 3H), 0.91 (d, *J* = 6.6 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (CD_3OD) δ 172.9, 172.6, 155.9, 130.2, 129.7, 127.6, 114.8, 54.9, 54.7, 50.8, 48.2, 40.2, 24.4, 21.9, 20.9, 20.5. TLC: R_f 0.58 (CH_2Cl_2/MeOH = 10:1).

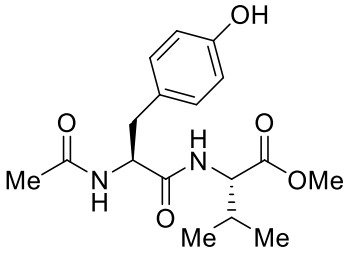
Procedure for preparation of 6b



S7 **S9** **6b**

To a 100-mL round-bottom flask were sequentially added *N*-acetyl-L-tyrosine **S7** (1.6 g, 6.0 mmol), L-valine methyl ester hydrochloride **S9** (1.0 g, 6.0 mmol), DMF (20 mL), 1-hydroxybenzotriazole (1.0 g, 6.6 mmol), *N*,*N*'-dicyclohexylcarbodiimide (1.2 g, 6.0 mmol), and *N*,*N*-diisopropylethylamine (2.2 mL, 13 mmol). After being stirred at 25 °C overnight, the reaction was quenched with H_2O (30 mL). After white precipitates were removed by filtration, the aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using CH_2Cl_2/MeOH (v/v = 10:1) as an eluent gave **6b**.

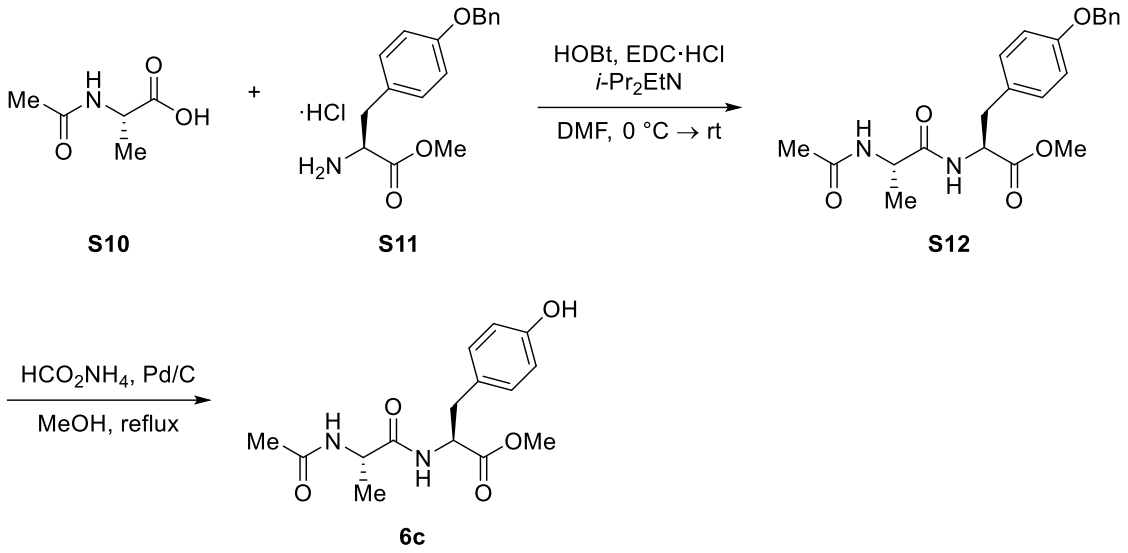
***N*-Acetyl-L-tyrosyl-L-valine methyl ester (6b)**: CAS RN [573968-42-0].



White solid; 56% yield (1.1 g).

^{1}H NMR ($CDCl_3$) δ 7.04 (d, *J* = 8.4 Hz, 2H), 6.72 (d, *J* = 8.4 Hz, 2H), 6.62 (s, 1H), 6.39 (d, *J* = 8.4 Hz, 1 H), 6.35 (d, *J* = 7.8 Hz, 1H), 4.68 (dt, *J* = 7.8, 7.2 Hz, 1H), 4.42 (dd, *J* = 8.4, 5.4 Hz, 1H), 3.71 (s, 3H), 2.97 (d, *J* = 7.2 Hz, 2H), 2.09 (m, 1H), 1.98 (s, 3H), 0.87 (d, *J* = 6.6 Hz, 3H), 0.84 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 171.8, 171.2, 170.5, 155.3, 130.5, 127.8, 115.7, 57.6, 54.9, 52.3, 37.8, 31.2, 23.2, 18.9, 17.9. TLC: R_f 0.38 (CH_2Cl_2/MeOH = 10:1).

Procedure for preparation of 6c

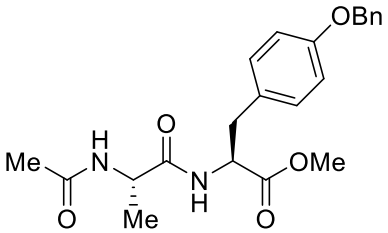


S10 **S11** **S12** **6c**

Procedure for preparation of **S12**

To a 50-mL round-bottom flask were sequentially added *N*-acetyl-L-alanine **S10** (0.60 g, 4.6 mmol), *O*-(phenylmethyl)-L-tyrosine methyl ester hydrochloride **S11** (1.5 g, 4.6 mmol), DMF (23 mL), and *N*,*N*-diisopropylethylamine (2.4 mL, 14 mmol) at 25 °C. Subsequently, 1-hydroxybenzotriazole (0.74 g, 5.5 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.1 g, 5.5 mmol) were added at 0 °C. After being stirred at 25 °C overnight, the reaction was quenched with H_2O (30 mL), and the aqueous layer was extracted with EtOAc (30 mL × 4). The combined organic layers were washed with 1.0 M aqueous HCl, saturated aqueous $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using hexane/EtOAc (v/v = 1:3) as an eluent gave **S12**.

Methyl (*S*)-2-((*S*)-2-acetamidopropanamido)-3-(4-(benzyloxy)phenyl)propanoate (S12): CAS RN [18828-16-5].



White solid; 56% yield (1.1 g).

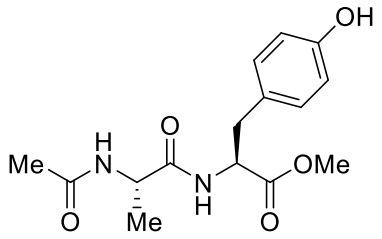
^{1}H NMR ($CDCl_3$) δ 7.42 (d, *J* = 7.2 Hz, 2H), 7.38 (dd, *J* = 7.2, 7.2 Hz, 2H), 7.33 (d, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 8.4 Hz, 2H), 6.89 (d, *J* = 8.4 Hz, 2H), 6.43 (m, 1H), 5.99 (m,

1H), 5.03 (s, 2H), 4.79 (m, 1H), 4.45 (dq, *J* = 7.2, 7.2 Hz, 1H), 3.73 (s, 3H), 3.09 (dd, *J* = 14.4, 6.0 Hz, 1H), 3.01 (dd, *J* = 14.4, 6.0 Hz, 1H), 1.96 (s, 3H), 1.33 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 171.83, 171.78, 169.9, 158.0, 137.0, 130.4, 128.7, 128.1, 127.9, 127.6, 115.0, 70.0, 53.4, 52.5, 48.8, 37.0, 23.2, 18.2. TLC: R_f 0.29 (hexane/EtOAc = 1:3).

Procedure for preparation of **6c**

To a 100 mL round-bottom flask were sequentially added palladium-activated carbon (0.13 g, 0.11 mmol), MeOH (4.0 mL), **S12** (0.88 g, 2.2 mmol), and ammonium formate (2.8 g, 44 mmol) under argon atmosphere. After being refluxed overnight, the mixture was filtered through a celite pad and concentrated in vauo. H_2O (25 mL) was added, and the aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using EtOAc as an eluent gave **6c**.

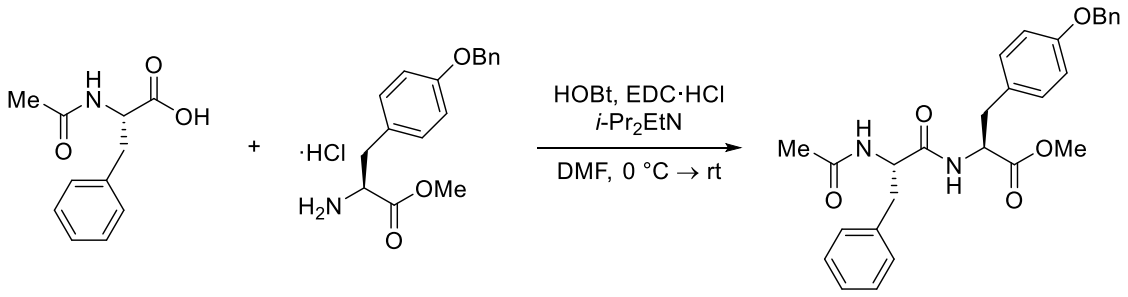
***N*-Acetyl-L-alanyl-L-tyrosine methyl ester (6c)**: CAS RN [57328-71-9].



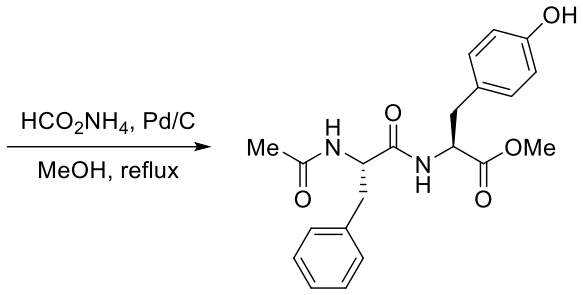
White solid; 50% yield (0.34 g).

^{1}H NMR ($CDCl_3$) δ 8.01 (s, 1H), 6.91 (d, *J* = 8.4 Hz, 1H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.69 (d, *J* = 8.4 Hz, 2H), 6.67 (d, *J* = 7.8 Hz, 1H), 4.79 (m, 1H), 4.51 (dq, *J* = 7.8, 7.2 Hz, 1H), 3.72 (s, 3H), 3.05 (dd, *J* = 13.8, 4.8 Hz, 1H), 2.93 (dd, *J* = 13.8, 6.0 Hz), 1.93 (s, 3H), 1.30 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 172.4, 171.9, 170.9, 155.7, 130.4, 126.8, 115.7, 53.6, 52.5, 48.8, 37.0, 23.0, 18.2. TLC: R_f 0.17 (EtOAc).

Procedure for preparation of 6d



S13 **S11** **S14**

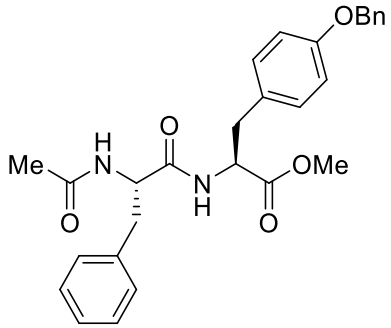


6d

Procedure for preparation of **S14**

To a 50-mL round-bottom flask were sequentially added *N*-acetyl-L-phenylalanine **S13** (1.6 g, 5.0 mmol), *O*-(phenylmethyl)-L-tyrosine methyl ester hydrochloride **S11** (1.6 g, 5.0 mmol), DMF (15 mL), and *N*,*N*-diisopropylethylamine (1.26 mL, 7.5 mmol) at 25 °C. Subsequently, 1-hydroxybenzotriazole (0.81 g, 6.0 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.2 g, 6.0 mmol) were added at 0 °C. After being stirred at 25 °C overnight, the reaction was quenched with H_2O (45 mL), and the aqueous layer was extracted with EtOAc (30 mL × 4). The combined organic layers were washed with 1.0 M aqueous HCl, saturated aqueous $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using hexane/EtOAc (v/v = 1:3) as an eluent gave **S14**.

Methyl (*S*)-2-((*S*)-2-acetamido-3-phenylpropanamido)-3-(4-(benzyloxy)phenyl)propanoate (S14).



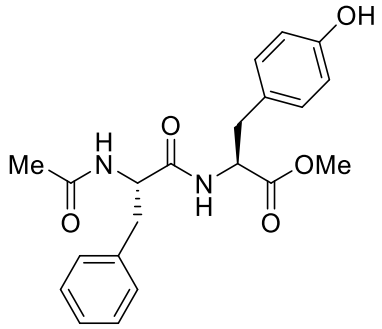
White solid; 86% yield (2.0 g).

^{1}H NMR (CD_3OD) δ 7.39–7.15 (m, 10H), 7.06 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.01 (s, 2H), 4.57–4.56 (m, 2H), 3.62 (s, 3H), 3.06–3.02 (m, 2H), 2.89 (dd, *J* = 13.8, 8.6 Hz, 1H), 2.77 (dd, *J* = 13.8, 8.6 Hz, 1H), 1.82 (s, 3H). ^{13}C NMR (CD_3OD) δ 173.4, 173.1, 173.0, 159.2, 138.8, 138.4, 131.4, 130.3, 130.1, 129.5, 129.4, 128.8, 128.5, 127.7, 115.9, 70.9, 55.8, 55.3, 52.7, 38.8, 37.6, 22.3. Mp. 172.3–172.7 °C. TLC: R_f 0.68 (hexane/EtOAc = 1:3). IR (neat): 1738, 1635, 1512, 1454, 1246, 1176, 1024, 741, 696, 517 cm^{-1}. HRMS (ESI) Calcd for $C_{28}H_{30}N_2O_5Na$: $[M+Na]^+$, 497.20469. Found: *m*/*z* 497.20502.

Procedure for preparation of **6d**

To a 100 mL round-bottom flask were sequentially added palladium-activated carbon (0.20 g, 0.19 mmol), MeOH (10 mL), **S14** (2.0 g, 4.3 mmol), and ammonium formate (6.3 g, 0.10 mol) under argon atmosphere. After being refluxed overnight, the mixture was filtered through a celite pad and concentrated in vauo. H_2O (50 mL) was added, and the aqueous layer was extracted with EtOAc (30 mL × 3). The combined organic layers were washed with H_2O and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using Hexane/EtOAc (v/v = 1:3) as an eluent gave **6d**.

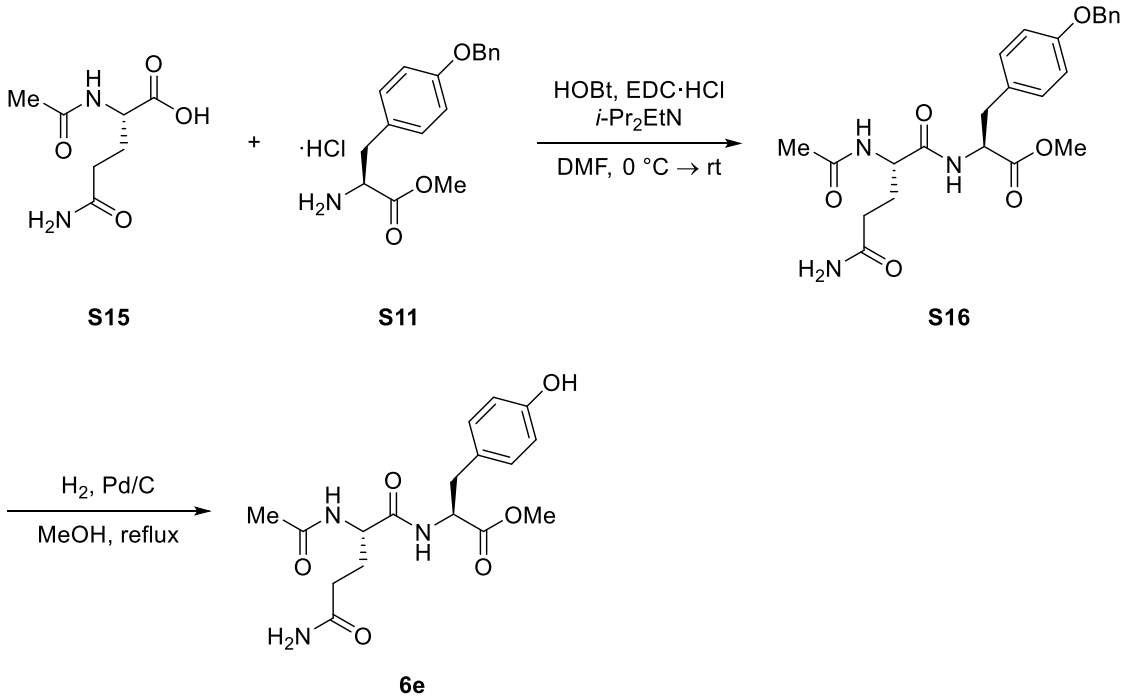
***N*-Acetyl-L-phenylalanyl-L-tyrosine methyl ester (6d)**: CAS RN [15852-46-7].



White solid; 85% yield (1.4 g).

^{1}H NMR (CD_3OD) δ 7.25–7.15 (m, 5H), 6.96 (d, *J* = 6.6 Hz, 2H), 6.66 (d, *J* = 6.6 Hz, 2H), 4.62–4.55 (m, 2H), 3.63 (s, 3H), 3.07–2.98 (m, 2H), 2.88–2.75 (m, 2H), 1.84 (s, 3H). ^{13}C NMR ($CDCl_3$) δ 171.4, 170.73, 170.66, 155.5, 136.1, 130.3, 129.2, 128.6, 127.0, 126.7, 115.5, 54.3, 53.5, 52.4, 38.1, 37.0, 22.9. TLC: R_f 0.48 (Hexane/EtOAc = 1:3).

Procedure for preparation of 6e



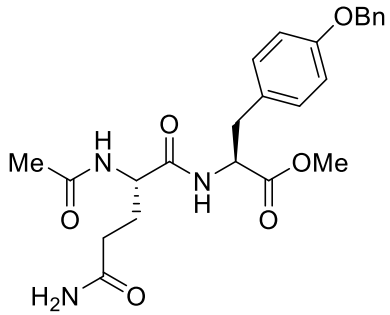
S15 **S11** **S16** **6e**

Procedure for preparation of **S16**

To a 100-mL round-bottom flask were sequentially added *N*-acetyl-L-glutamine **S15** (1.3 g, 7.0 mmol), *O*-(phenylmethyl)-L-tyrosine methyl ester hydrochloride **S11** (2.2 g, 7.0 mmol), DMF (35 mL), and *N*,*N*-diisopropylethylamine (3.7 mL, 22 mmol) at 25 °C.

Subsequently, 1-hydroxybenzotriazole (1.1 g, 8.4 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (1.6 g, 8.4 mmol) were added at 0 °C. After being stirred at 25 °C overnight, the reaction was quenched with H_2O (45 mL), and the aqueous layer was extracted with EtOAc (40 mL × 5). The combined organic layers were washed with 1.0 M aqueous HCl, saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated in vacuo. Purification by flash silica gel column chromatography using CH_2Cl_2/MeOH (v/v = 10:1) as an eluent gave **S16**.

Methyl (*S*)-2-((*S*)-2-acetamido-5-amino-5-oxopentanamido)-3-(4-(benzyloxy)phenyl)propanoate (S16).



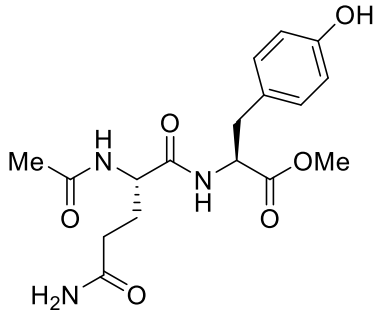
White solid; 16% yield (0.50 g).

^{1}H NMR (DMSO-d_6) δ 8.27 (d, J = 6.0 Hz, 1H), 7.92 (d, J = 8.4 Hz, 1H), 7.41–7.27 (m, 5H), 7.23 (s, 1H), 7.09 (d, J = 6.0 Hz, 2H), 6.87 (d, J = 6.0 Hz, 2H), 6.73 (s, 1H), 5.02 (s, 2H), 4.35 (m, 1H), 4.22 (dd, J = 14.1, 8.4 Hz, 1H), 3.54 (s, 3H), 2.90 (dd, J = 13.2, 6.0 Hz, 1H), 2.82 (dd, J = 13.2, 9.0 Hz, 1H), 2.02 (dd, J = 15.0, 8.4 Hz, 2H), 1.81 (m, 1H), 1.78 (s, 3H), 1.59 (m, 1H). ^{13}C NMR (DMSO-d_6) δ 174.2, 172.4, 172.2, 169.7, 157.6, 138.7, 130.8, 130.6, 129.6, 129.0, 128.2, 114.9, 69.6, 54.3, 52.2, 40.5, 36.3, 31.9, 23.1, 22.9. Mp. 234.0–235.0 °C. TLC: R_f 0.23 (CH_2Cl_2/MeOH = 10:1). IR (neat): 3283, 1659, 1638, 1545, 1514, 1246, 1219, 1178, 729, 598 cm^{-1}. HRMS (ESI) Calcd for $C_{24}H_{29}N_3O_6Na$: $[M+Na]^+$, 478.19486. Found: *m*/*z* 478.19448.

Procedure for preparation of **6e**

To a 50 mL round-bottom flask were sequentially added palladium-activated carbon (0.17 g, 0.17 mmol), dry MeOH (20 mL), and **S16** (0.50 g, 1.1 mmol) under argon atmosphere, which was then replaced with hydrogen gas, and the mixture was stirred at 60 °C. After being refluxed for 3 h, the solution was filtered through a celite pad and concentrated in vacuo. Purification by flash silica gel column chromatography using CH_2Cl_2/MeOH (v/v = 10:1) as an eluent gave **6e**.

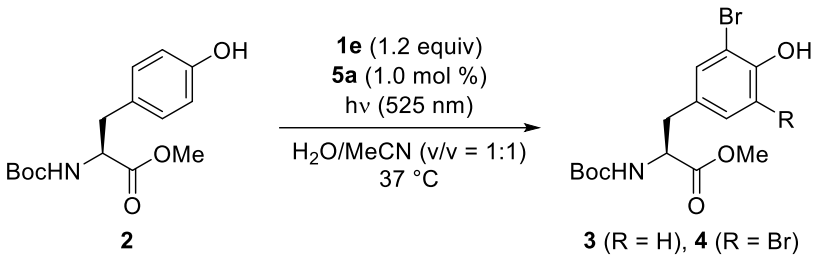
***N*-Acetyl-L-glutaminyl-L-tyrosine methyl ester (6e)**.



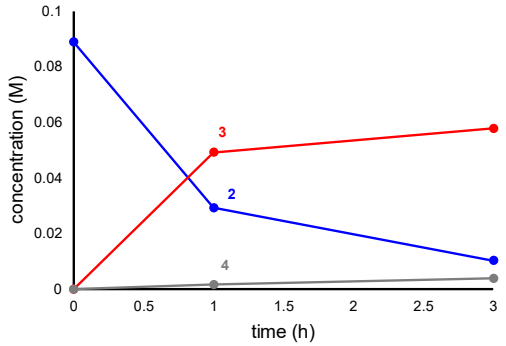
White solid; 94% yield (0.38 g).

^{1}H NMR (DMSO-d_6) δ 9.20 (s, 1H), 8.23 (d, J = 7.2 Hz, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.22 (s, 1H), 6.94 (d, J = 7.2 Hz, 2H), 6.72 (s, 1H), 6.60 (d, J = 7.2 Hz, 2H), 4.31 (m, 1H), 4.22 (m, 1H), 3.54 (s, 3H), 2.84 (dd, J = 13.8, 6.0 Hz, 1H), 2.77 (dd, J = 13.8, 7.8 Hz, 1H), 2.03 (m, 2H), 1.82 (m, 1H), 1.78 (s, 3H), 1.60 (m, 1H). ^{13}C NMR (DMSO-d_6) δ 173.7, 171.9, 171.6, 169.1, 156.0, 130.2, 127.0, 115.0, 53.9, 52.0, 51.7, 35.9, 31.3, 27.9, 22.5. Mp. 213.8–214.3 °C. TLC: R_f 0.080 (CH_2Cl_2/MeOH = 10:1). IR (neat): 1724, 1662, 1630, 1544, 1516, 1236, 1223, 604, 592, 530 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{23}N_3O_6Na$: $[M+Na]^+$, 388.14791. Found: *m*/*z* 388.14710.

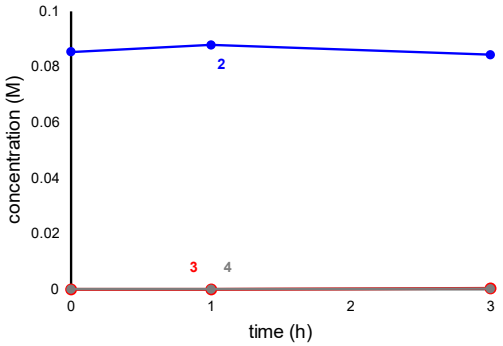
Scheme S1. Photocatalytic Tyrosine Bromination with Green Light



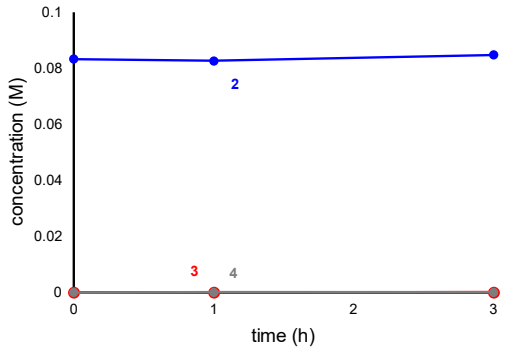
(a) with light and **5a**, 0.10 M



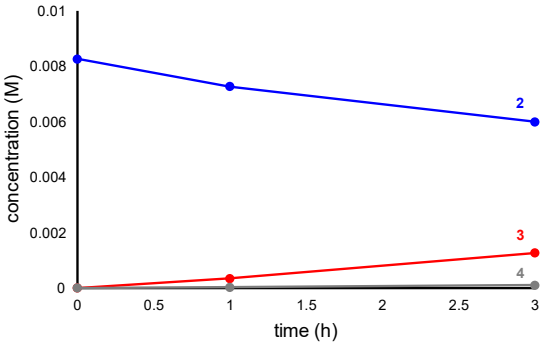
(b) with light, without **5a**, 0.10 M



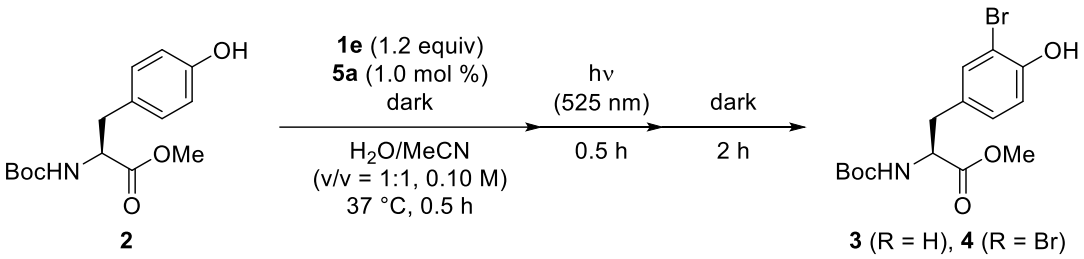
(c) without light, with **5a**, 0.10 M

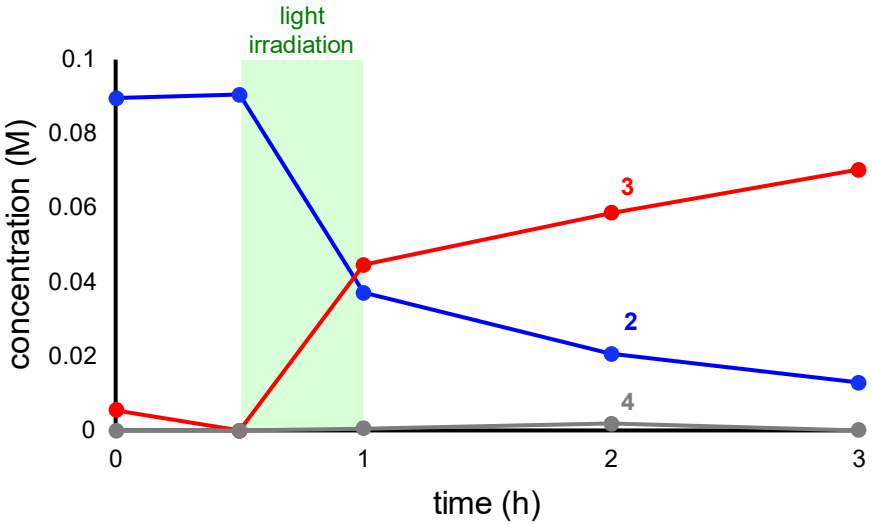


(d) with light and **5a**, 0.010 M

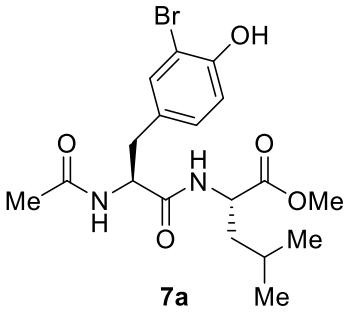


Scheme S2. Temporal Control of Tyrosine Bromination with Light

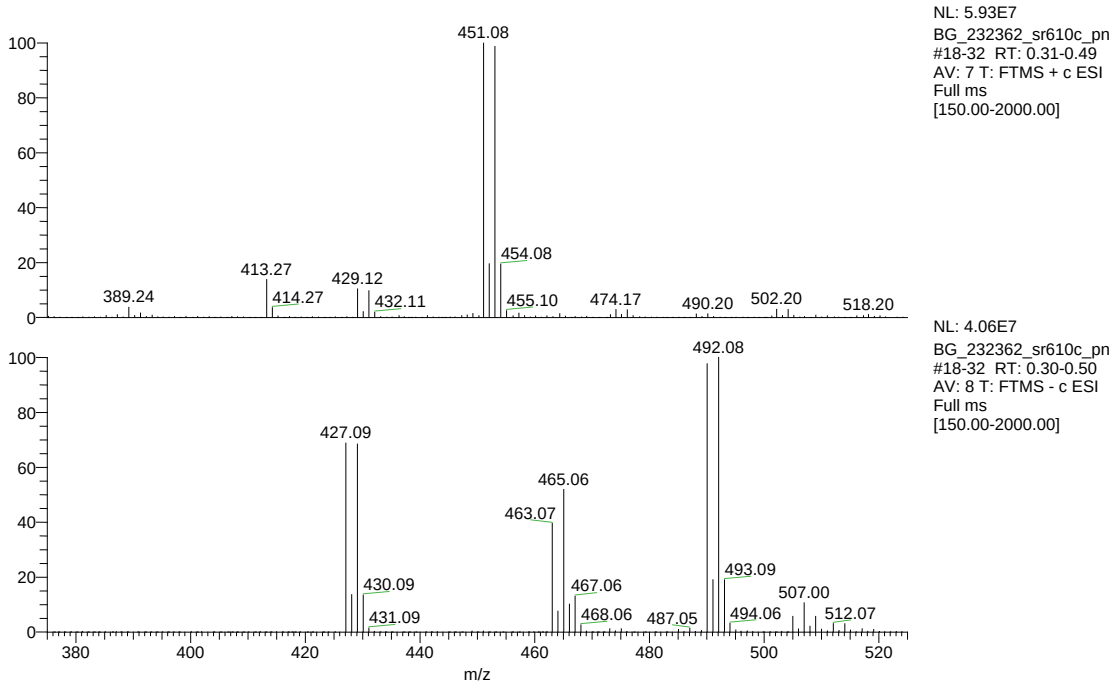


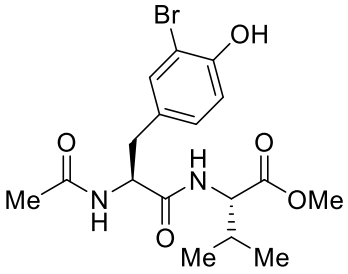


Scheme S3. Mass Spectra Analyses of **7**

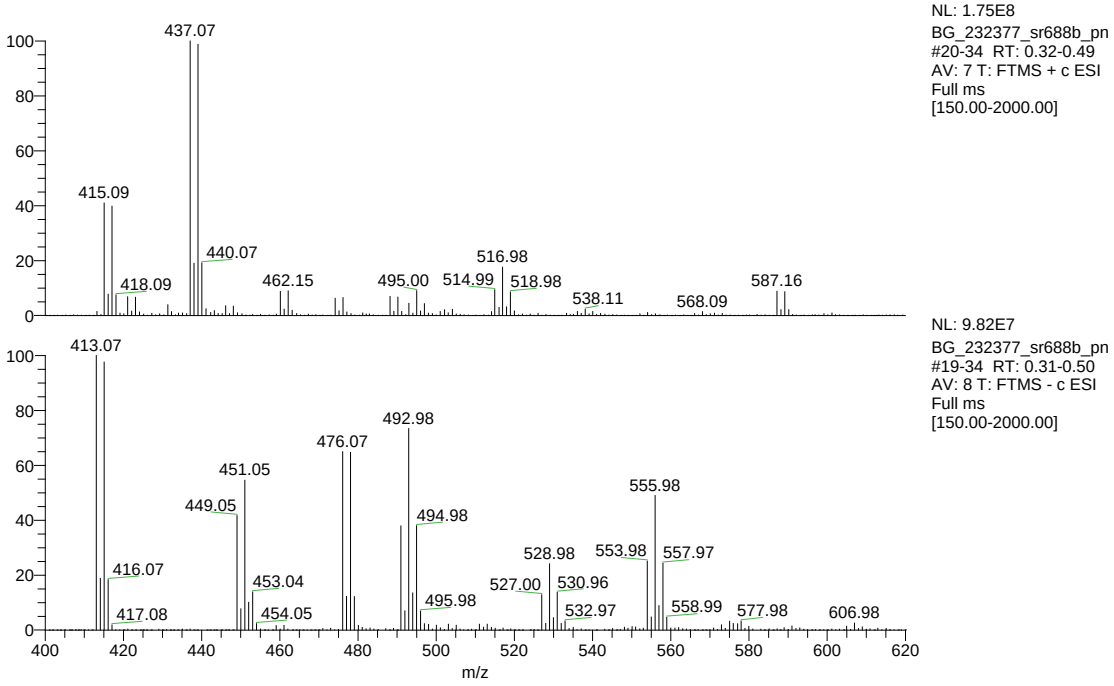


7a




Br
OH
O
Me
N
H
H
N
O
O
OMe
O
Me
Me

7b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AV: 7 T: FTMS + c ESI
Full ms
[150.00-2000.00]
437.07
415.09
440.07
516.98
418.09
462.15
495.00
514.99
518.98
538.11
568.09
587.16
NL: 9.82E7
BG_232377_sr688b_pn
#19-34 RT: 0.31-0.50
AV: 8 T: FTMS - c ESI
Full ms
[150.00-2000.00]
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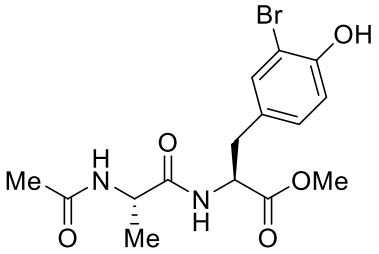
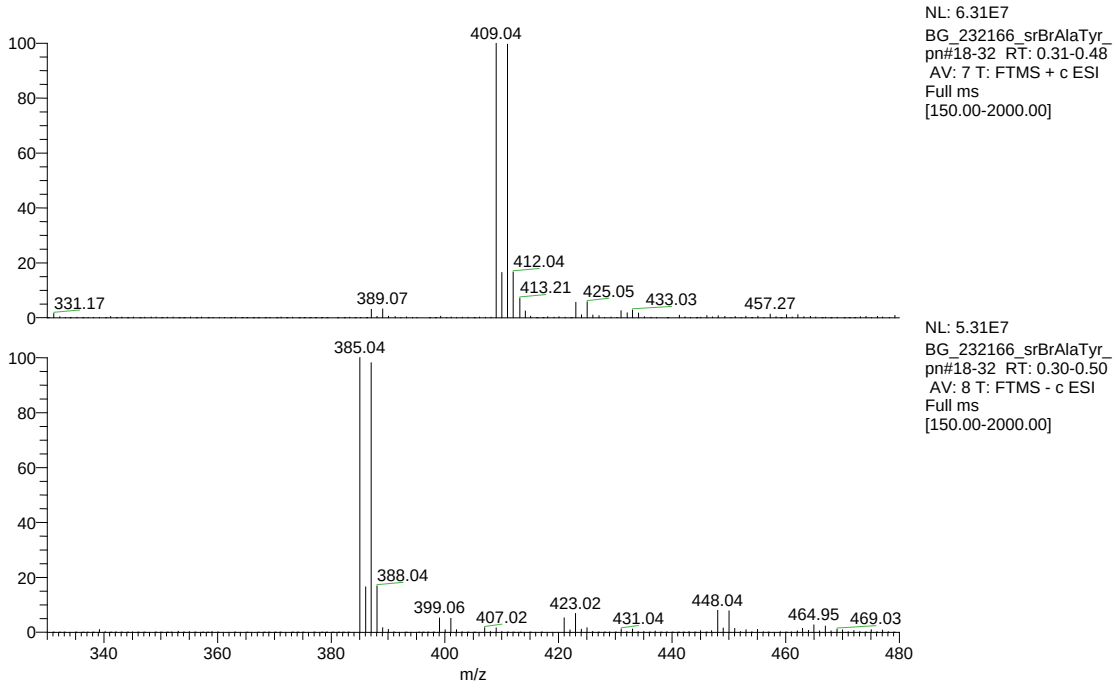
492.98
476.07
451.05
555.98
449.05
494.98
528.98
553.98
557.97
416.07
527.00
530.96
453.04
495.98
532.97
558.99
577.98
606.98
417.08
454.05
m/z


Br
OH
Me
H
N
O
N
H
OMe
O
Me
O

7c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AV: 7 T: FTMS + c ESI
Full ms
[150.00-2000.00]
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412.04
413.21
425.05
433.03
331.17
389.07
457.27
NL: 5.31E7
BG_232166_srBrAlaTyr_
pn#18-32 RT: 0.30-0.50
AV: 8 T: FTMS - c ESI
Full ms
[150.00-2000.00]
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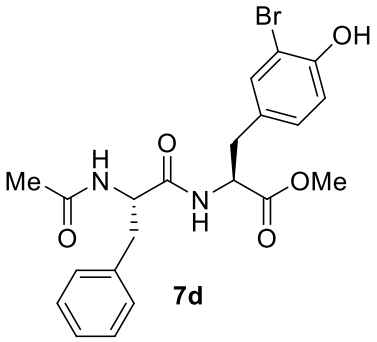
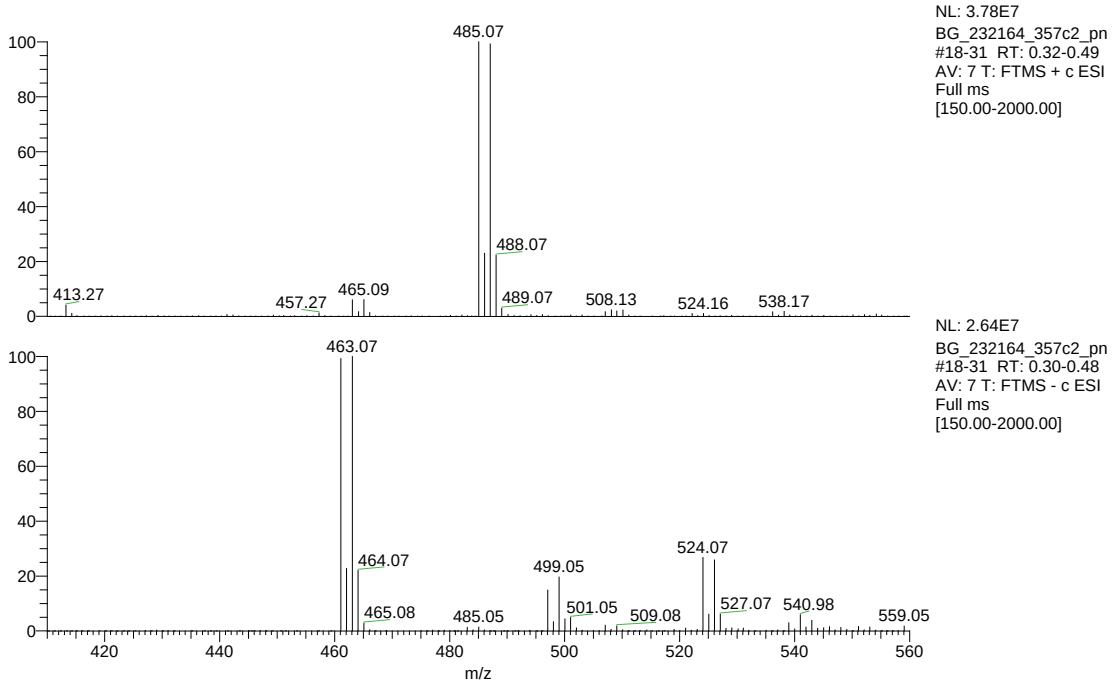
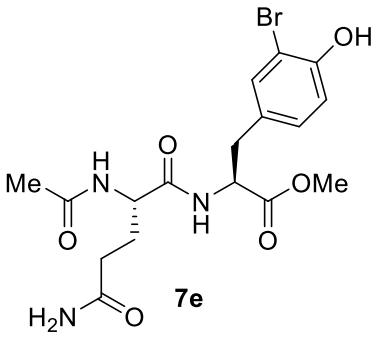
388.04
399.06
407.02
423.02
431.04
448.04
464.95
469.03
m/z

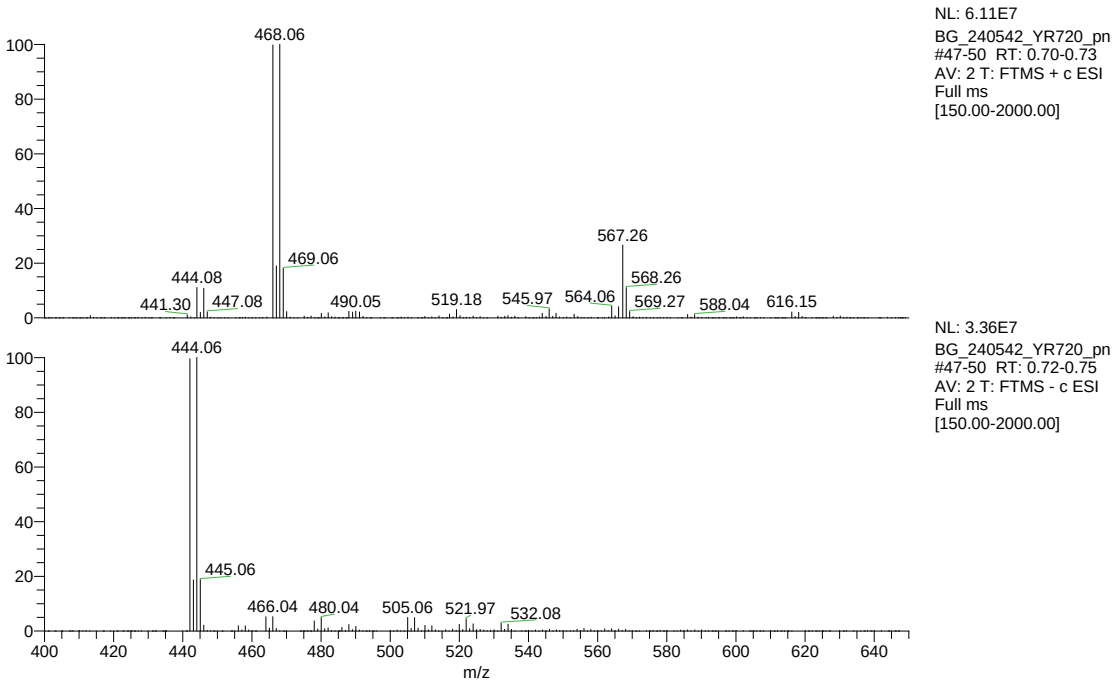

Br
OH
Me
H
N
O
N
H
O
OMe
O

7d

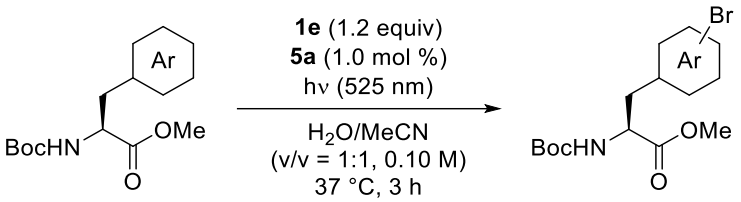

NL: 3.78E7
BG_232164_357c2_pn
#18-31 RT: 0.32-0.49
AV: 7 T: FTMS + c ESI
Full ms
[150.00-2000.00]
485.07
488.07
413.27
457.27
465.09
489.07
508.13
524.16
538.17
NL: 2.64E7
BG_232164_357c2_pn
#18-31 RT: 0.30-0.48
AV: 7 T: FTMS - c ESI
Full ms
[150.00-2000.00]
463.07
464.07
465.08
485.05
499.05
501.05
509.08
524.07
527.07
540.98
559.05
m/z


Br
OH
Me
H
N
O
N
H
OMe
O
O
O
H_2N
O

7e


NL: 6.11E7
BG_240542_YR720_pn
#47-50 RT: 0.70-0.73
AV: 2 T: FTMS + c ESI
Full ms
[150.00-2000.00]
468.06
469.06
444.08
441.30
447.08
490.05
519.18
545.97
564.06
567.26
568.26
569.27
588.04
616.15
NL: 3.36E7
BG_240542_YR720_pn
#47-50 RT: 0.72-0.75
AV: 2 T: FTMS - c ESI
Full ms
[150.00-2000.00]
444.06
445.06
466.04
480.04
505.06
521.97
532.08
m/z

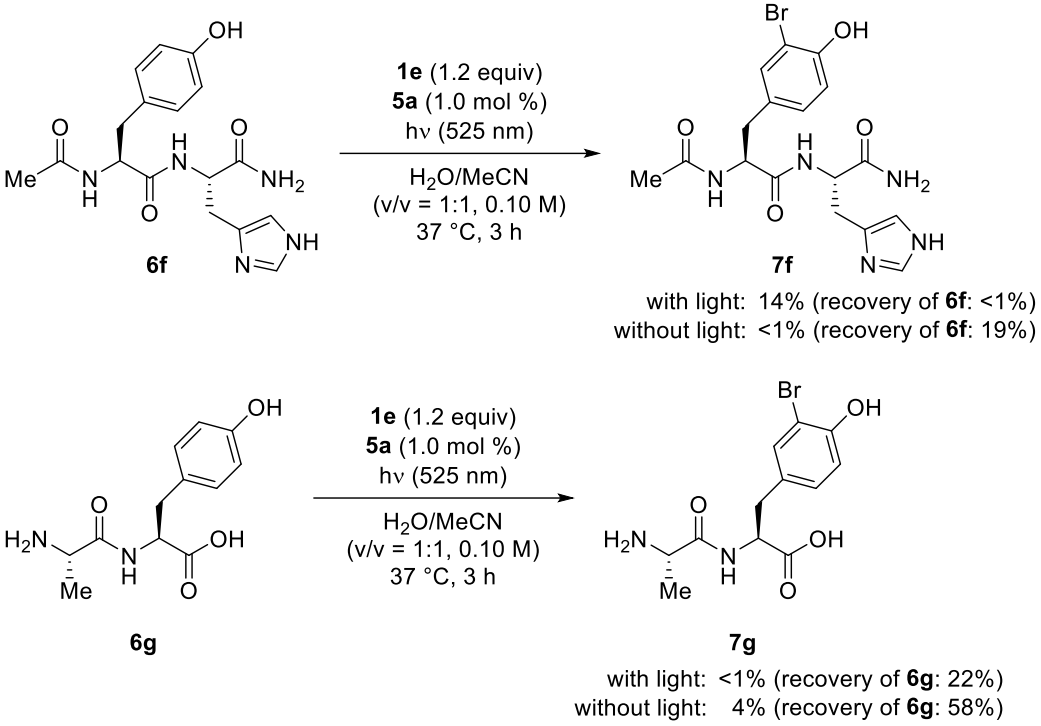
Scheme S4. Bromination of Aromatic Amino Acids[a]



entry	amino acid	yields without light [**S17** (recovery), **S18**] (%)		yields with light [**S17** (recovery), **S18**] (%)	
		S17	**S18**	**S17**	**S18**
1	Phe	90	<1	92	<1
2	Trp	19	<1	<1	<1
3	His	70	<1	72	<1

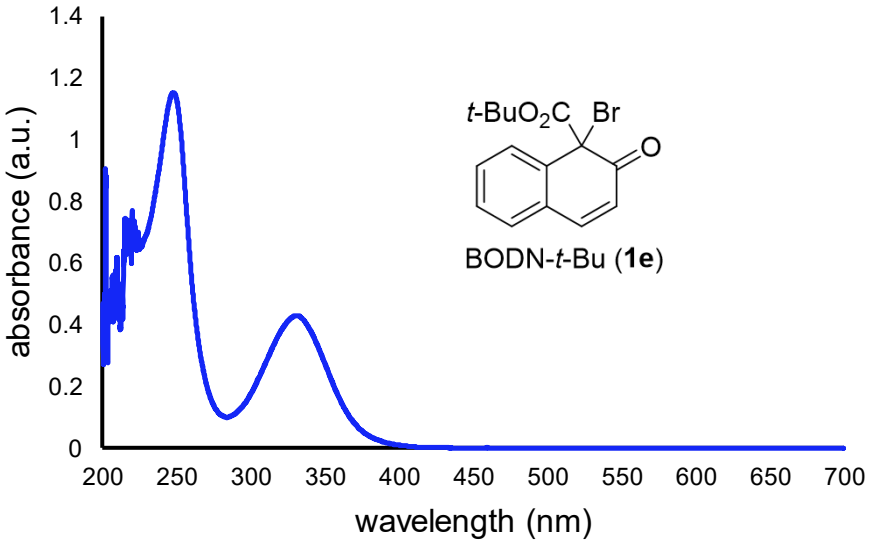
[a] Reactions were run using **S17** (0.10 mmol), **1e** (0.12 mmol), and **5a** (0.0010 mmol) in H_2O/MeCN (v/v =1:1, 1.0 mL). ASAHI SPECTRA CL-1503/CL-H1-450-9-1-B (525 nm) was used as a light source.

Scheme S5. Bromination of Tyrosine-Containing Peptides with Histidine and Unprotected Termini

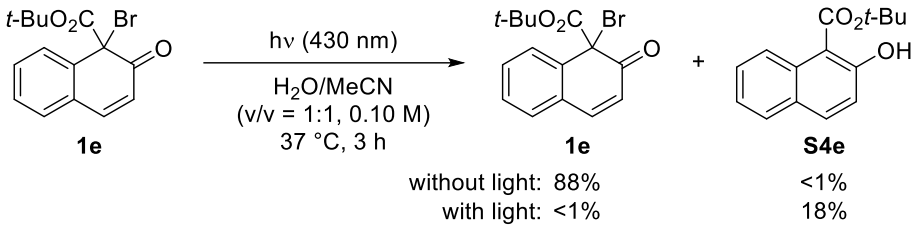


The reactions of **6f** and **6g** resulted in low mass balances while no byproduct was detected. It is probably because the high hydrophilicity of **6**/**7f** and **6**/**7g** decreased the efficiency of the extraction during the workup. The reaction of **6g** did not work probably because the substrate was not soluble in the present solvent system containing acetonitrile, which is at this stage necessary as **1e** is not soluble in more water-rich solvents.

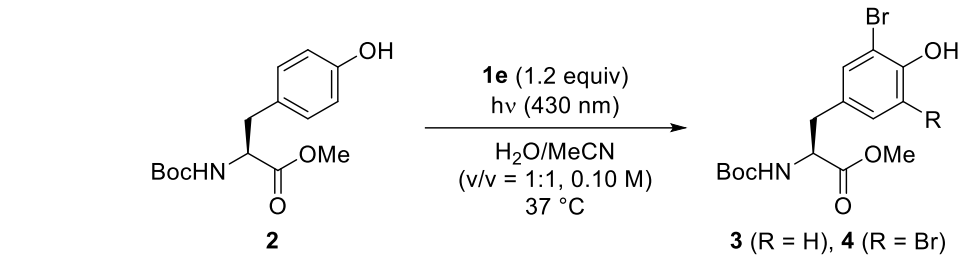
Scheme S6. UV-Vis Absorption of **1e**

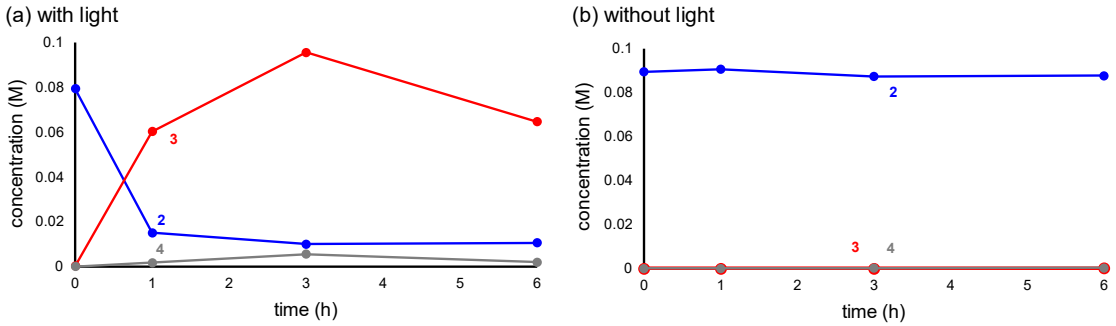


Scheme S7. Irradiation of 430 nm light to **1e**

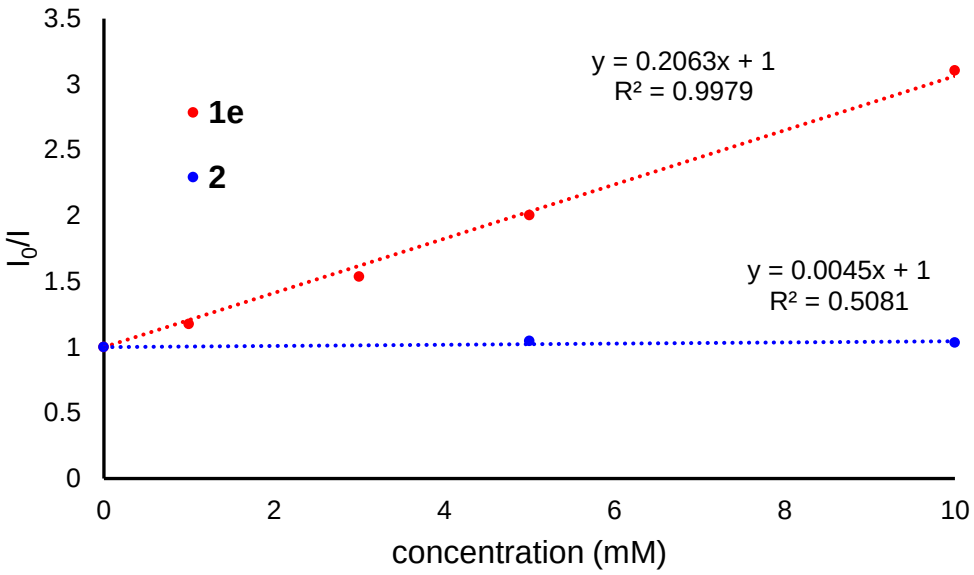


Scheme S8. Photochemical Tyrosine Bromination with Blue Light

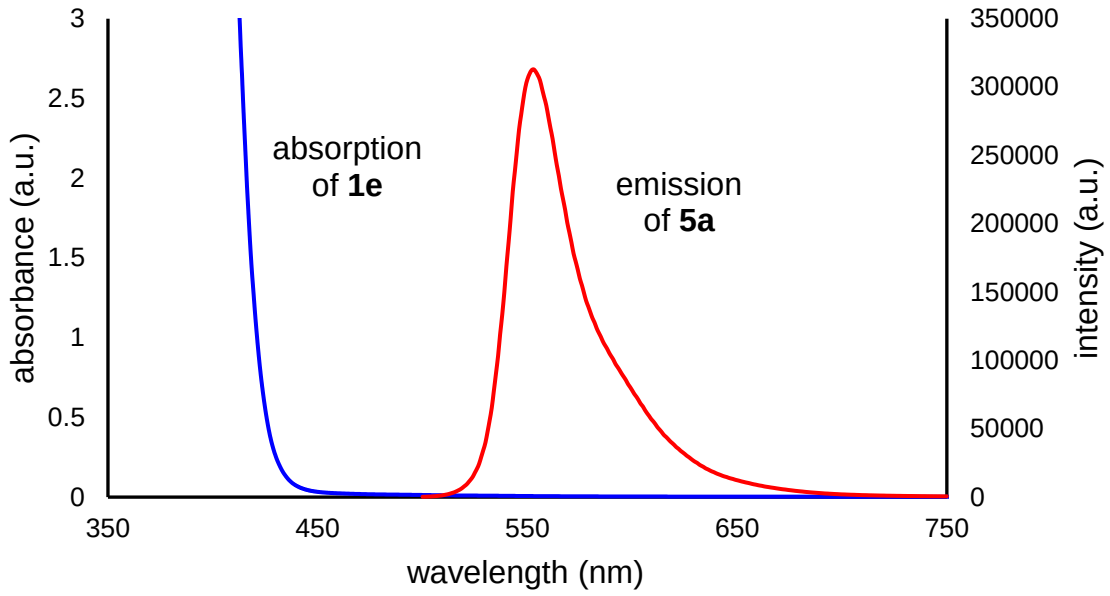




Scheme S9. Fluorescence-Quenching Experiments

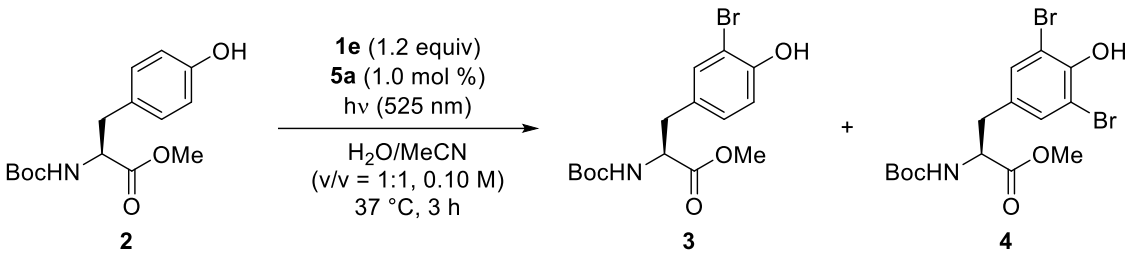


Scheme S10. Absorption of **1e** and Emission of **5a**



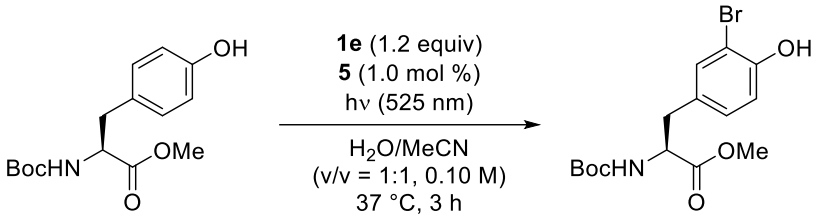
No overlap observed between the absorbance of **1e** and the emission of **5a**. The mechanism of Dexter energy transfer does not require their overlap, which is crucial for Förster energy transfer. Therefore, we believe that the present reaction proceeds through the mechanism of Dexter energy transfer.

Scheme S11. Reaction in the presence of O_2



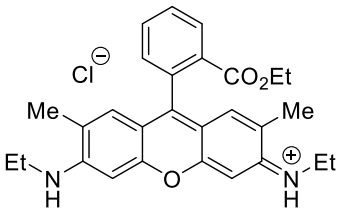
	3	4
under Ar:	73%	9%
open air (in the presence of O_2):	79%	4%

Scheme S12. Investigations of Photocatalysts[a]

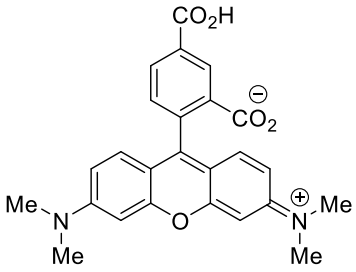


entry	**5**	yields without light (%)	yields with light (%)
1	**5a**	<1	76
2	**5b**	<1	47
3	**5c**	<1	54
4	**5d**	<1	64
5	**5e**	<1	57

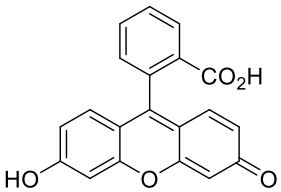
[a] Reactions were run using **2** (0.10 mmol), **1e** (0.12 mmol), and **5** (0.0010 mmol) in H_2O/MeCN (v/v = 1:1, 1.0 mL). ASAHI SPECTRA CL-1503/CL-H1-450-9-1-B (525 nm) was used as a light source. In all cases, yields of **4** were <5%.



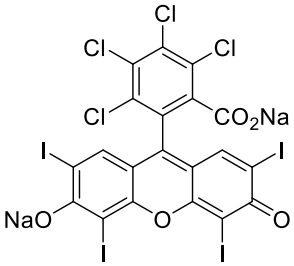
rhodamine 6G (**5a**)



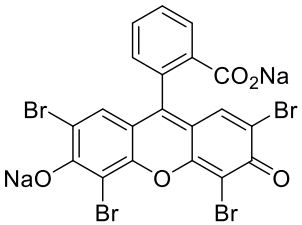
5-TAMRA (**5b**)



fluorescein (**5c**)



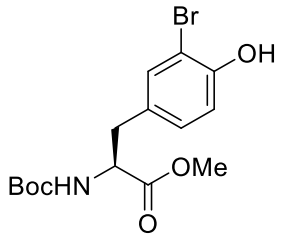
rose bengal (**5d**)



eosin Y (**5e**)

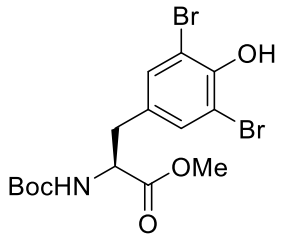
Characterization Data of Products

Methyl (*S*)-3-(3-bromo-4-hydroxyphenyl)-2-((*tert*-butoxycarbonyl)amino)propanoate (3): CAS RN [139517-74-1].



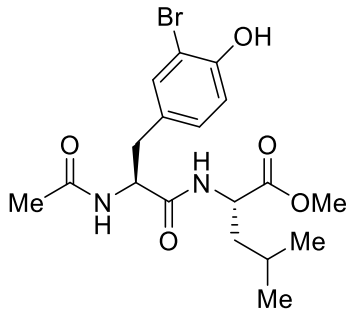
Yield: 76% (HPLC), white solid. ^{1}H NMR ($CDCl_3$) δ 7.22 (s, 1H), 6.97 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 8.4 Hz, 1H), 5.57 (s, 1H), 5.00 (m, 1H), 4.52 (dd, *J* = 13.6, 6.0 Hz, 1H), 3.72 (s, 3H), 3.05 (m, 1H), 2.95 (m, 1H), 1.43 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 172.1, 155.0, 151.4, 132.6, 130.0, 129.6, 116.1, 110.1, 80.1, 54.4, 52.3, 37.2, 28.3. TLC: R_f 0.32 (hexane/EtOAc = 3:1).

Methyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(3,5-dibromo-4-hydroxyphenyl)propanoate (4): CAS RN [355857-30-6].



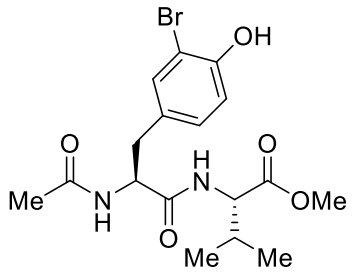
Yield: 27% (HPLC), white solid. ^{1}H NMR ($CDCl_3$) δ 7.22 (s, 2H), 5.82 (s, 1H), 5.03 (d, *J* = 7.2 Hz, 1H), 4.51 (m, 1H), 3.74 (s, 3H), 3.06 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.92 (dd, *J* = 14.0, 6.0 Hz, 1H), 1.44 (s, 9H). ^{13}C NMR ($CDCl_3$) δ 171.8, 154.9, 148.4, 132.7, 130.8, 109.7, 80.2, 54.3, 52.4, 36.9, 28.3. TLC: R_f 0.38 ($CHCl_3$/EtOAc = 20:1).

Methyl ((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-leucinate (7a).



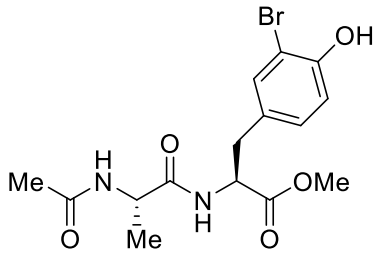
Yield: 75% (HPLC), white solid. ^{1}H NMR ($CDCl_3$) δ 7.28 (d, *J* = 2.4 Hz, 1H), 7.00 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.83–6.800 (m, 2H), 6.73 (s, 1H), 6.67 (d, *J* = 8.4 Hz, 1H), 4.72 (dd, *J* = 15.0, 6.6 Hz, 1H), 4.51 (m, 1H), 3.70 (s, 3H), 2.97–2.88 (m, 2H), 1.97 (s, 3H), 1.61–1.47 (m, 3H), 0.87 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR ($CDCl_3$) δ 172.9, 171.1, 170.5, 151.8, 133.2, 130.0, 129.7, 116.2, 110.1, 54.4, 52.5, 51.4, 41.3, 37.5, 24.8, 23.2, 22.8, 21.9. Mp. 72.0–72.2 °C. TLC: R_f 0.60 (CH_2Cl_2/MeOH = 10:1). IR (neat): 1743, 1645, 1539, 1508, 1499, 1209, 1153, 671, 594, 439 cm^{-1}. HRMS (ESI) Calcd for $C_{18}H_{25}BrN_2O_5Na$: $[M+Na]^+$, 451.08445, 453.08241. Found: *m*/*z* 451.08342, 453.08111.

Methyl ((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-valinate (7b).



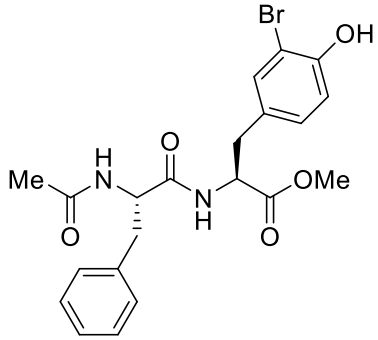
Yield: 73% (HPLC), white solid. ^{1}H NMR ($CDCl_3$) δ 7.35 (d, *J* = 1.8 Hz, 1H), 7.02 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.78 (d, *J* = 8.4 Hz, 1H), 4.59 (dd, *J* = 8.4, 6.6 Hz, 1H), 4.29 (d, *J* = 6.0 Hz, 1H), 3.67 (s, 3H), 2.95 (dd, *J* = 13.8, 6.6 Hz, 1H), 2.76 (dd, *J* = 13.8, 8.4 Hz, 1H), 2.09 (m, 1H), 1.91 (s, 3H), 0.92 (d, *J* = 7.2 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 171.8, 171.2, 170.5, 151.8, 133.1, 129.9, 129.7, 116.3, 110.1, 57.5, 54.6, 52.4, 37.6, 31.2, 23.1, 19.0, 17.8. Mp. 118.5–120.4 °C. TLC: R_f 0.26 (CH_2Cl_2/MeOH = 10:1). IR (neat): 1641, 1539, 1533, 1508, 1487, 1278, 1209, 1182, 1150, 752 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{23}BrN_2O_5Na$: $[M+Na]^+$, 437.06880, 439.06679. Found: *m/z* 437.06820, 4439.06609.

Methyl (*S*)-2-((*S*)-2-acetamidopropanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7c).



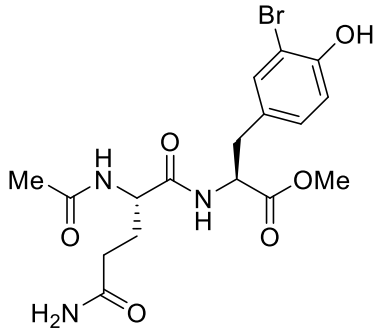
Yield: 51% (HPLC), white solid. ^{1}H NMR ($CDCl_3$) δ 7.26 (d, *J* = 1.8 Hz, 1H), 6.98 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 4.56 (dd, *J* = 8.4, 6.0 Hz, 1H), 4.31 (q, *J* = 7.2 Hz, 1H), 3.66 (s, 3H), 3.02 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.88 (dd, *J* = 14.4, 8.4 Hz, 1H), 1.93 (s, 3H), 1.26 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$) δ 173.6, 171.8, 171.7, 153.0, 133.3, 129.3, 129.1, 115.8, 109.2, 53.8, 51.3, 48.9, 35.7, 21.1, 16.5. Mp. 170.3–170.5 °C. TLC: R_f 0.30 (EtOAc). IR (neat): 1737, 1625, 1604, 1465, 1444, 1296, 1225, 1188, 835, 513 cm^{-1}. HRMS (ESI) Calcd for $C_{15}H_{19}BrN_2O_5Na$: $[M+Na]^+$, 409.0369, 411.03491. Found: *m*/*z* 409.03682, 411.03444.

Methyl (*S*)-2-((*S*)-2-acetamido-3-phenylpropanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7d).



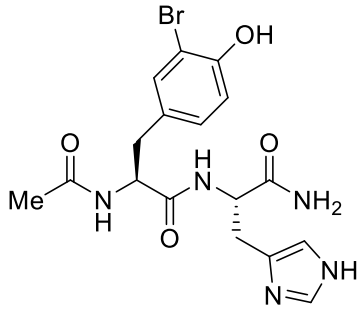
Yield: 69% (HPLC), pink solid. ^{1}H NMR (CD_3OD) δ 7.27–7.17 (m, 6H), 6.96 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 4.61–4.55 (m, 2H), 3.64 (s, 3H), 3.07–2.99 (m, 2H), 2.87–276 (m, 2H), 1.85 (s, 3H). ^{13}C NMR (CD_3OD) δ 172.1, 171.7, 171.6, 153.0, 137.0, 133.4, 129.2, 129.1, 128.9, 128.0, 126.4, 115.8, 109.2, 54.5, 53.8, 51.4, 37.5, 35.8, 21.1. Mp. 163.3–163.7 °C. TLC: R_f 0.48 (hexane/EtOAc = 1:3). IR (neat): 1653, 1647, 1533, 1420, 1179, 748, 698, 488, 422, 417 cm^{-1}. HRMS (ESI) Calcd for $C_{21}H_{23}BrN_2O_5Na$: $[M+Na]^+$, 485.06880, 487.06676. Found: *m*/*z* 485.06859, 487.06637.

Methyl (*S*)-2-((*S*)-2-acetamido-5-amino-5-oxopentanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7e).



Yield: 36% (HPLC, the mass balance was low probably because of the high hydrophilicity of **7e**, which decreased the efficiency of the extraction during the workup, while no byproduct was detected), white solid. ^{1}H NMR (CD_3OD) δ 7.29 (d, *J* = 2.4 Hz, 1H), 6.99 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 4.59 (dd, *J* = 8.4, 5.4 Hz, 1H), 4.35 (dd, *J* = 8.4, 6.0 Hz, 1H), 3.69 (s, 3H), 3.04 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.88 (dd, *J* = 14.4, 8.4 Hz, 1H), 2.26 (t, *J* = 7.8 Hz, 2H), 2.01 (ddt, *J* = 14.4, 8.4, 7.8 Hz, 1H), 1.96 (s, 3H), 1.86 (ddt, *J* = 14.4, 5.4, 7.8 Hz, 1H). ^{13}C NMR (CD_3OD) δ 177.8, 173.7, 173.3, 173.2, 154.3, 134.8, 130.8, 130.4, 117.3, 110.6, 55.4, 53.9, 52.7, 37.2, 32.4, 28.9, 22.5. Mp. 184.5–185.5 °C. TLC: R_f 0.23 (CH_2Cl_2/MeOH = 10:1). IR (neat): 1734, 1653, 1541, 1437, 1290, 1221, 1084, 1043, 583 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{22}BrN_3O_6Na$: $[M+Na]^+$, 466.05842, 468.05660. Found: *m/z* 466.05789, 468.05550.

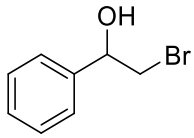
(*S*)-2-Acetamido-*N*-((*S*)-1-amino-3-(1*H*-imidazol-4-yl)-1-oxopropan-2-yl)-3-(3-bromo-4-hydroxyphenyl)propanamide (7f).



Yield: 14% (HPLC, the mass balance was low probably because of the high hydrophilicity of **7f**, which decreased the efficiency of the extraction during the workup, while no byproduct was detected), white solid. ^{1}H NMR (CD_3OD) δ 7.67 (s, 1H), 7.36 (s, 1H), 7.34 (d, *J* = 2.4 Hz, 1H), 7.01 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.89 (s, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 4.55 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.46 (dd, *J* = 9.6, 6.0 Hz, 1H), 3.09 (dd, *J* =

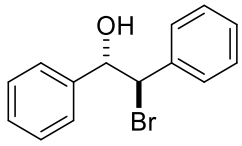
15.0, 4.8 Hz, 1H), 2.98 (dd, *J* = 14.4, 6.0 Hz, 1H), 2.97 (dd, *J* = 15.0, 7.8 Hz, 1H), 2.73 (dd, *J* = 14.4, 9.6 Hz, 2H), 1.91 (s, 3H). ^{13}C NMR (CD_3OD) δ 175.5, 173.6, 173.5, 154.2, 136.2, 134.7, 134.1, 130.9, 130.3, 117.2, 112.1, 110.6, 56.6, 54.4, 37.2, 30.1, 22.4. Mp. 147.5–148.5 °C. TLC: R_f 0.28 (CH_2Cl_2/MeOH = 5:1). IR (neat): 3254, 2924, 2853, 1636, 1646, 1539, 1429, 1373, 1288, 1203, 1134, 995, 588 cm^{-1}. HRMS (ESI) Calcd for $C_{17}H_{21}BrN_5O_4$: $[M+H]^+$, 438.07714, 440.07565. Found: *m/z* 438.07635, 440.07379.

2-Bromo-1-phenylethan-1-ol (9a): CAS RN [2425-28-7].



Yield: 46%, yellow liquid. ^{1}H NMR ($CDCl_3$) δ 7.39–7.32 (m, 5H), 4.94 (ddd, *J* = 8.8, 3.2, 3.2 Hz, 1H), 3.65 (dd, *J* = 10.8, 3.2 Hz, 1H), 3.55 (dd, *J* = 10.8, 8.8 Hz, 1H), 2.63 (d, *J* = 3.2 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 140.2, 128.7, 128.5, 126.0, 73.8, 40.3. TLC: R_f 0.23 (hexane/EtOAc = 9:1).

(1*S,2*R**)-2-Bromo-1,2-diphenylethan-1-ol (9b)**: CAS RN [10368-43-1].



Yield: 9%, yellow liquid. ^{1}H NMR ($CDCl_3$) δ 7.40–7.29 (m, 10H), 5.21 (dd, *J* = 6.6, 3.0 Hz, 1H), 5.09 (d, *J* = 6.6 Hz, 1H), 2.40 (d, *J* = 3.0 Hz, 1H). ^{13}C NMR ($CDCl_3$) δ 139.7, 137.6, 128.9, 128.8, 128.5, 128.4, 128.2, 127.0, 78.1, 58.9. TLC: R_f 0.38 (hexane/EtOAc = 10:1).

References

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3. Zhou, Y.-M.; Ping, Y.-J.; Xu, Z.-J.; Che, C.-M. *Asian J. Org. Chem.* **2021**, *10*, 674.
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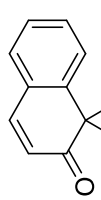
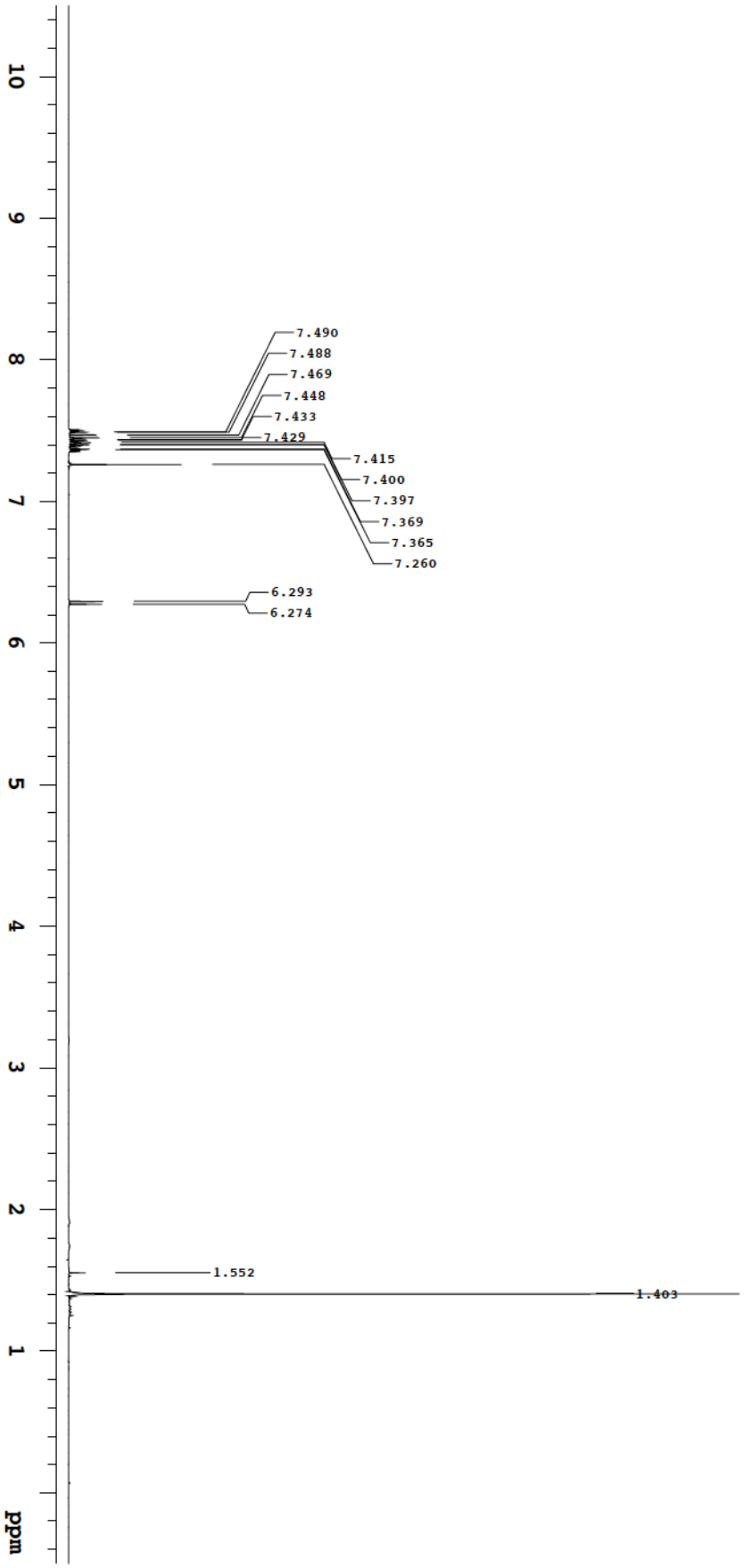
5. Ashida, Y.; Sato, Y.; Suzuki, T.; Ueno, K.; Kai, K.; Nakatsuji, H.; Tanabe, Y. *Chem. Eur. J.* **2015**, *21*, 5934.
6. Fang, L.-Z.; Shen, J.-M.; Lv, Q.-H.; Yan, F.-L. *Asian J. Chem.* **2011**, *23*, 3425.

NMR Spectra (^{1}H, ^{13}C) of BODNs

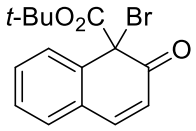


^{1}H NMR

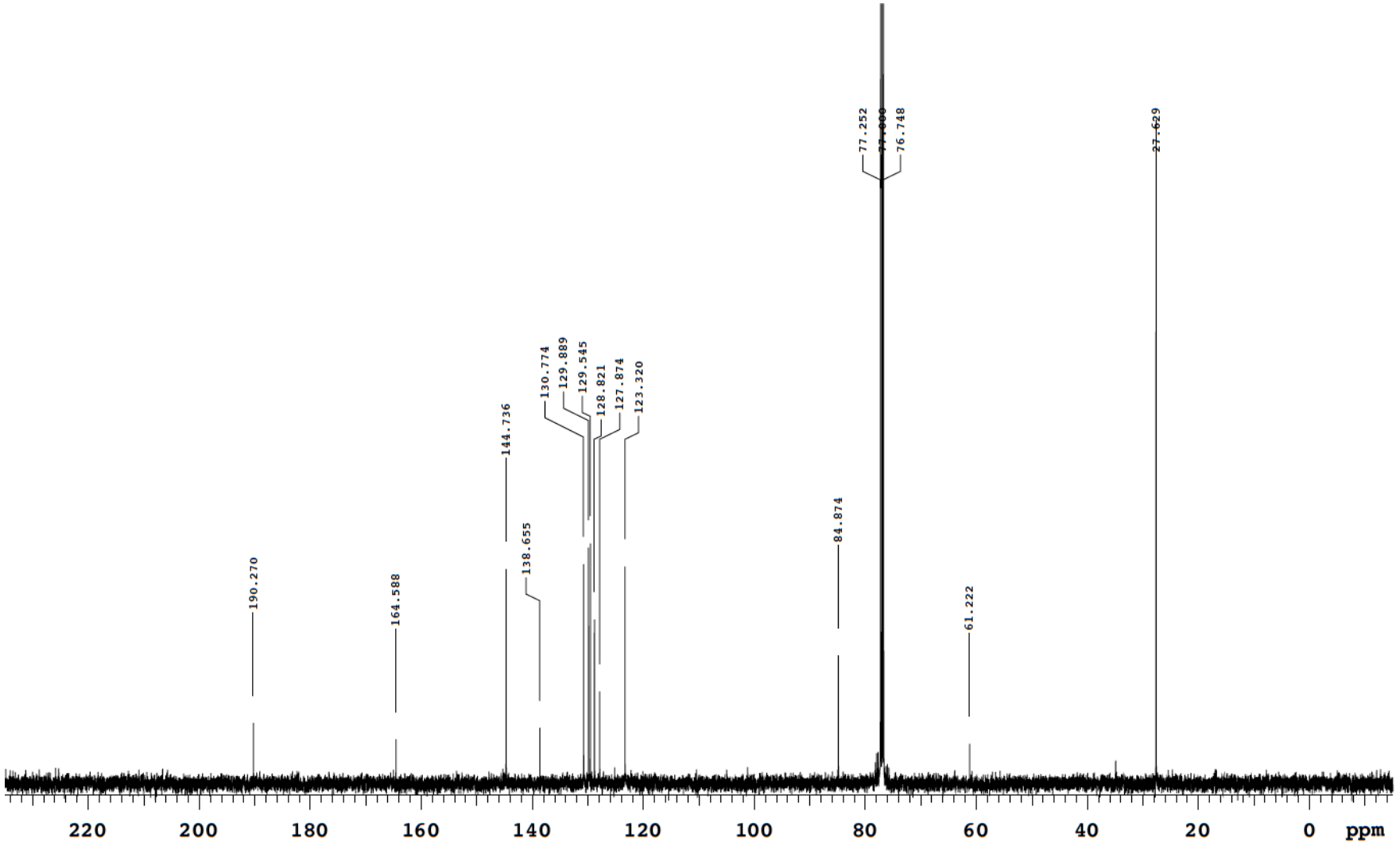
tert-Butyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1e)



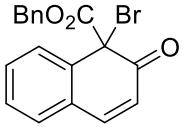
***tert*-Butyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1e)**



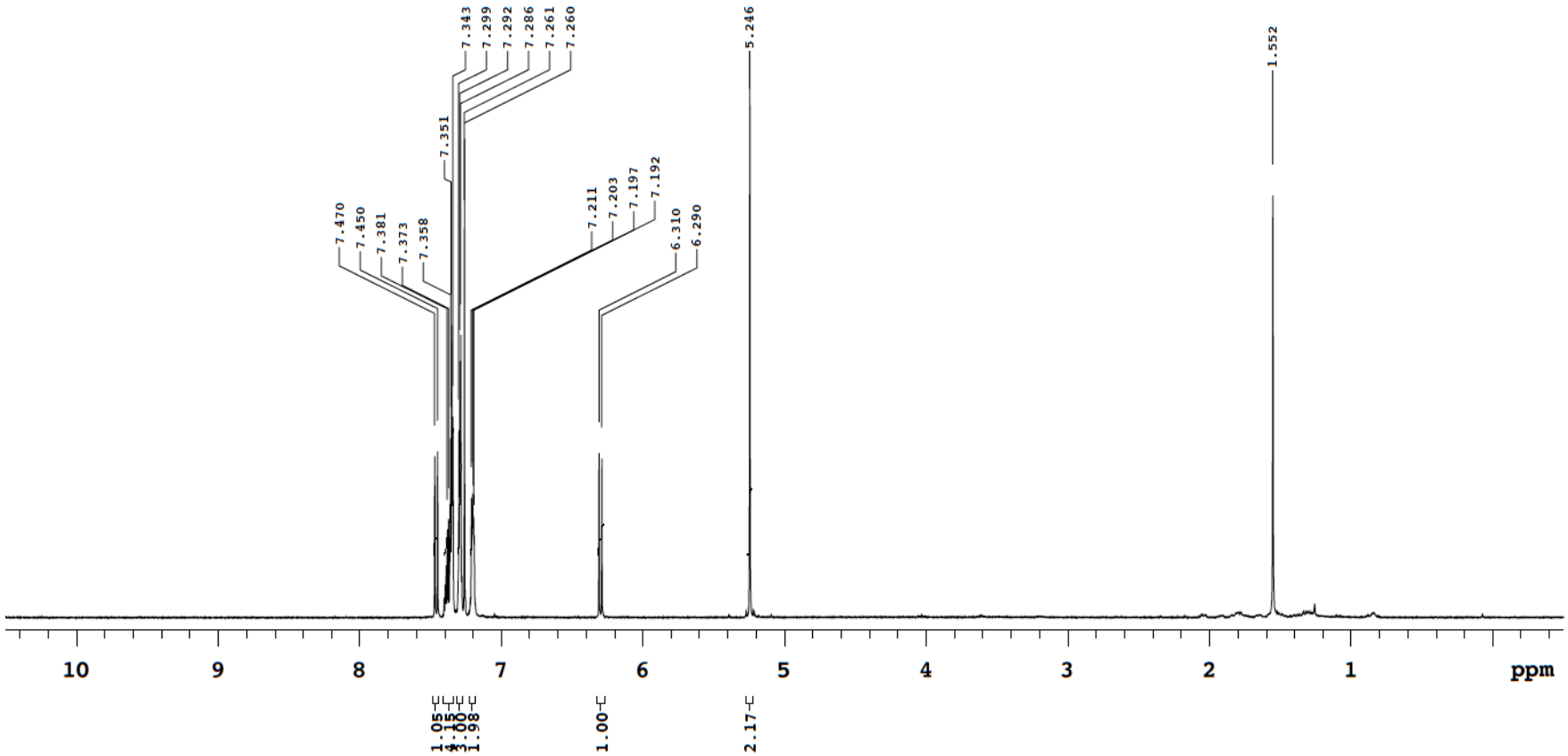
^{13}C NMR



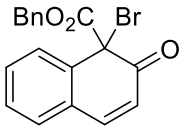
Benzyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1f)



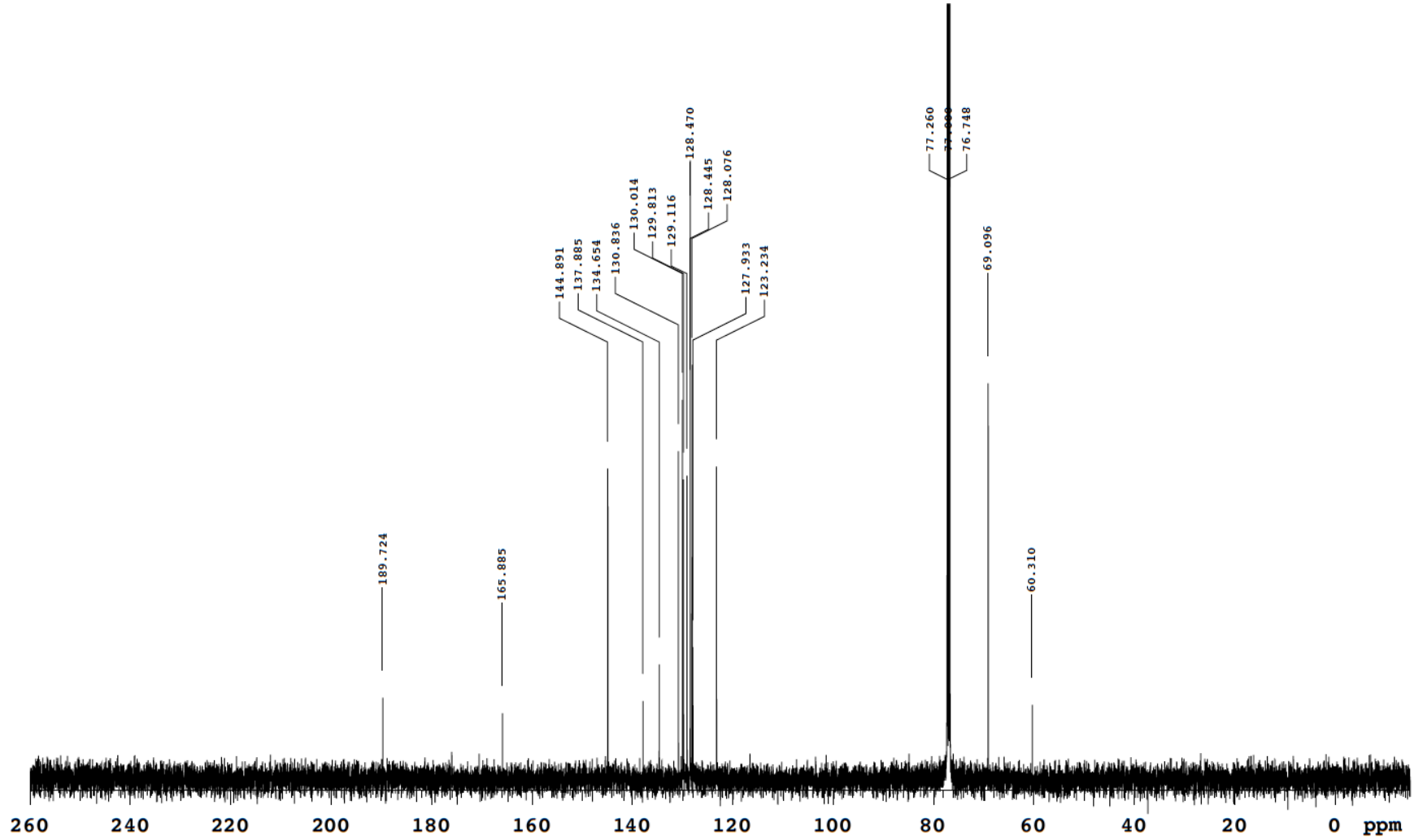
^{1}H NMR



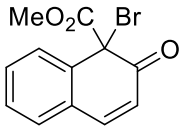
Benzyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1f)



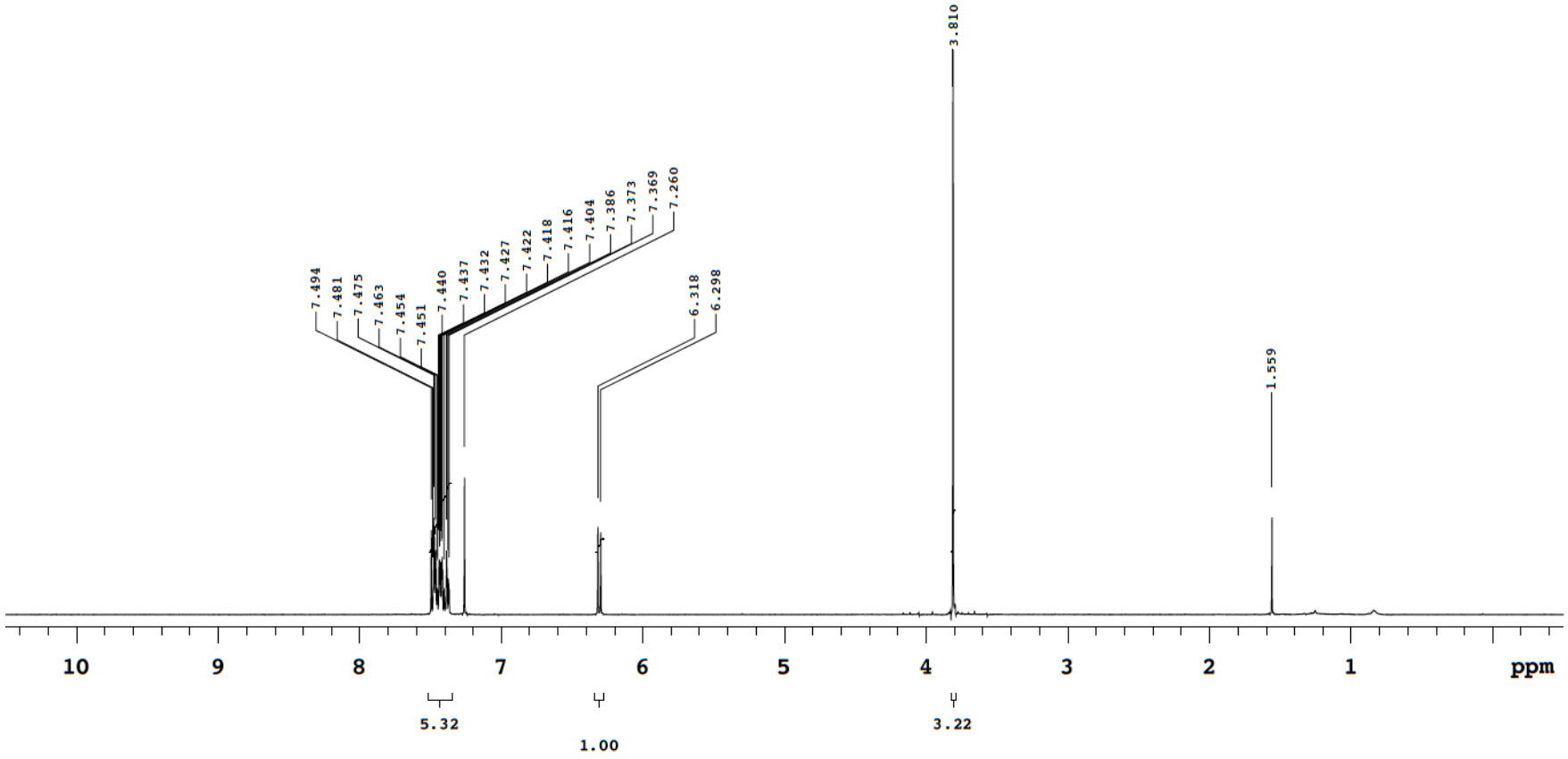
^{13}C NMR



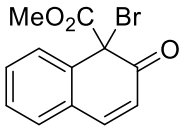
Methyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1g)



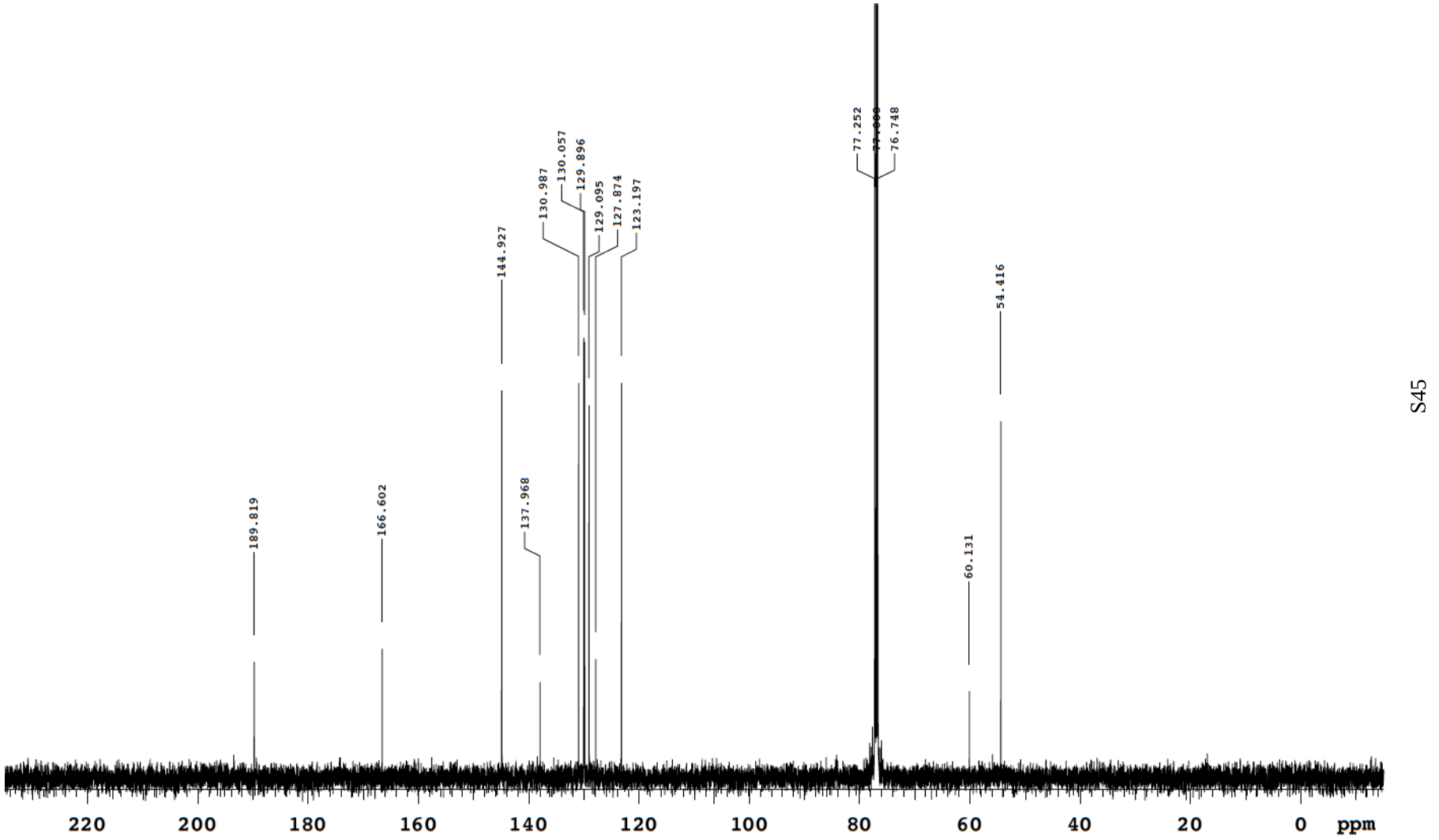
^{1}H NMR



Methyl 1-bromo-2-oxo-1,2-dihydronaphthalene-1-carboxylate (1g)

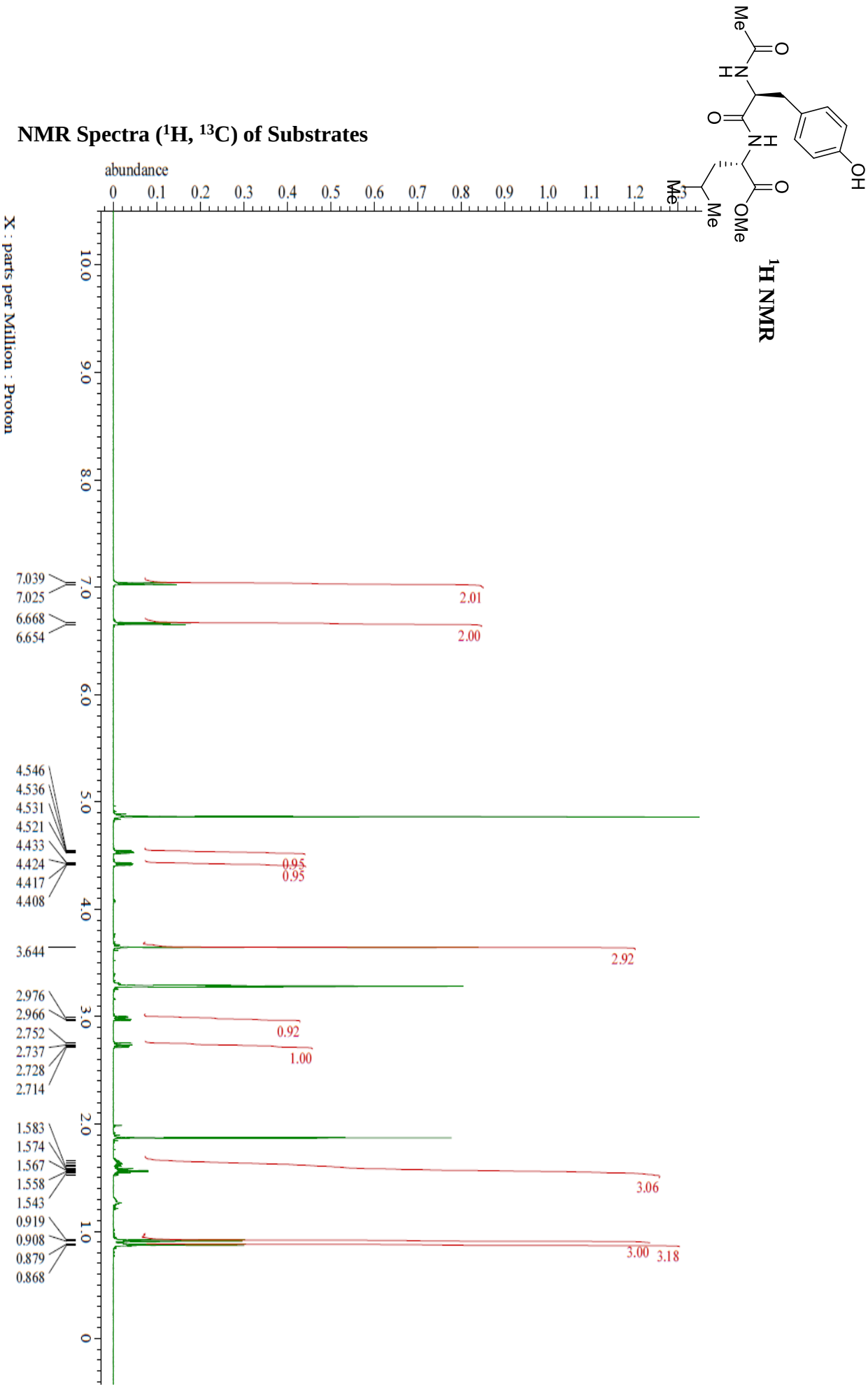


^{13}C NMR

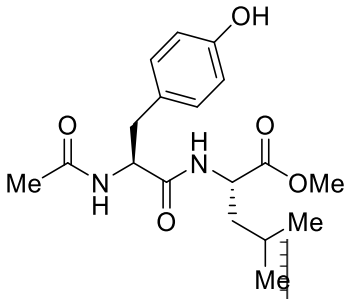


NMR Spectra (^{1}H, ^{13}C) of Substrates

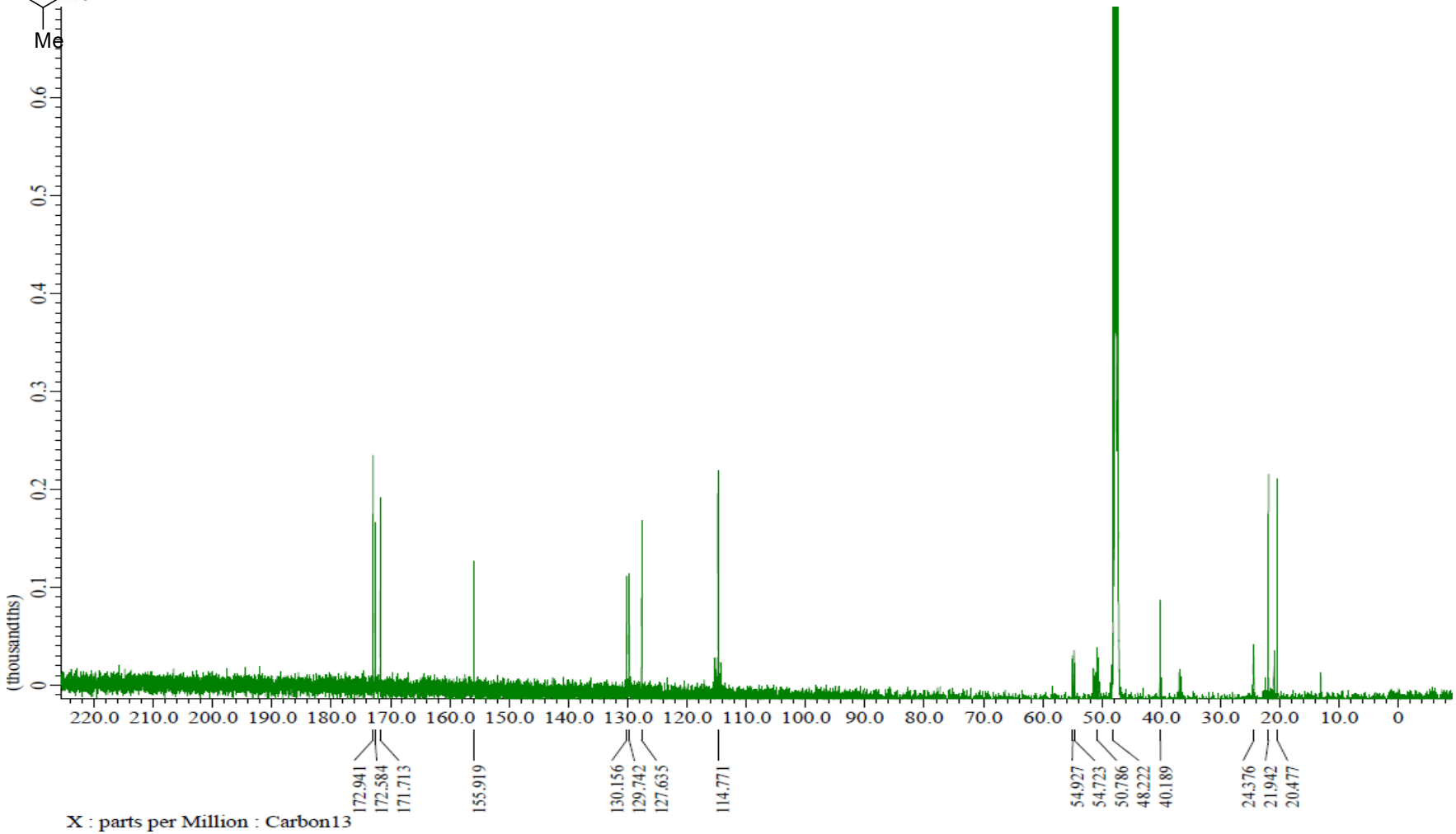
N-Acetyl-L-tyrosyl-L-leucin methyl ester (6a)



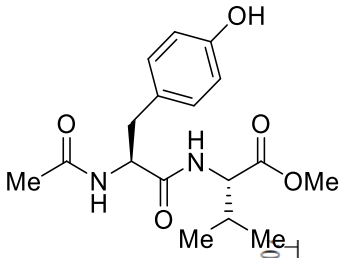
_N_-Acetyl-L-tyrosyl-L-leucin methyl ester (6a)



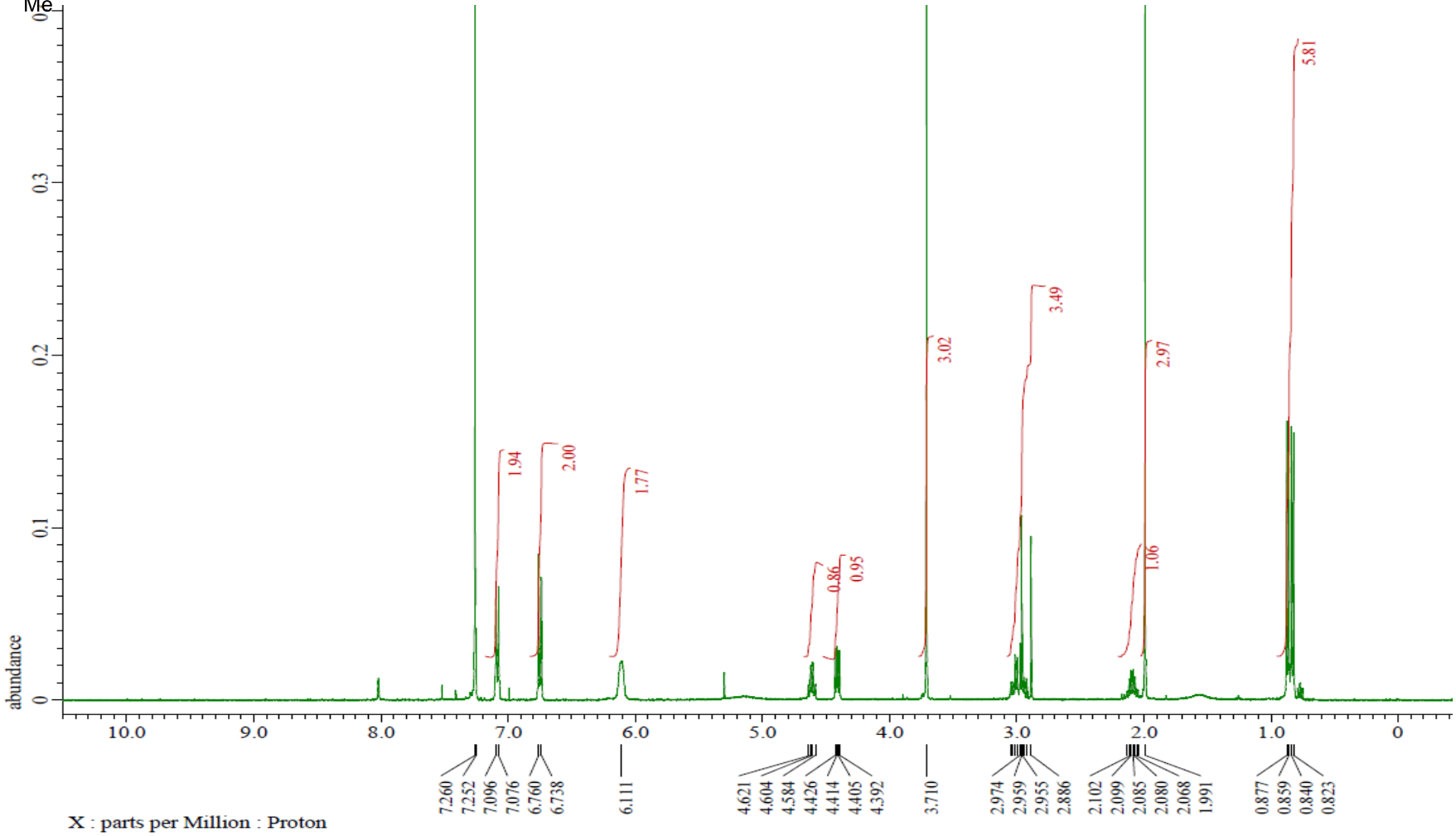
^{13}C NMR



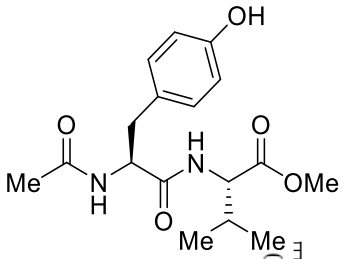
_N_-Acetyl-L-tyrosyl-L-valine methyl ester (6b)



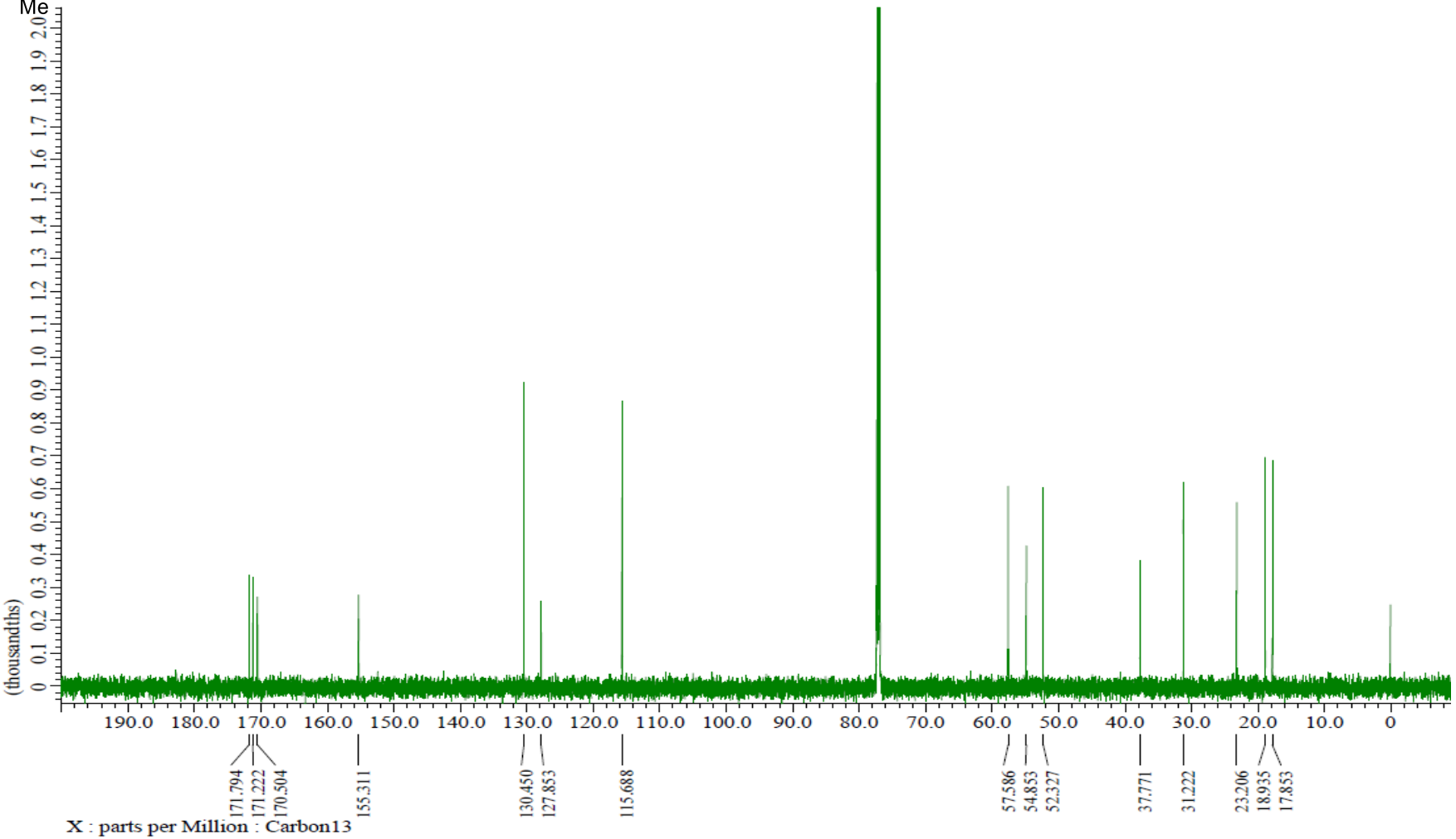
^{1}H NMR



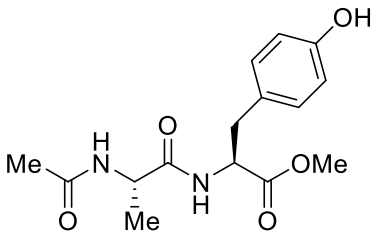
_N_-Acetyl-L-tyrosyl-L-valine methyl ester (6b)



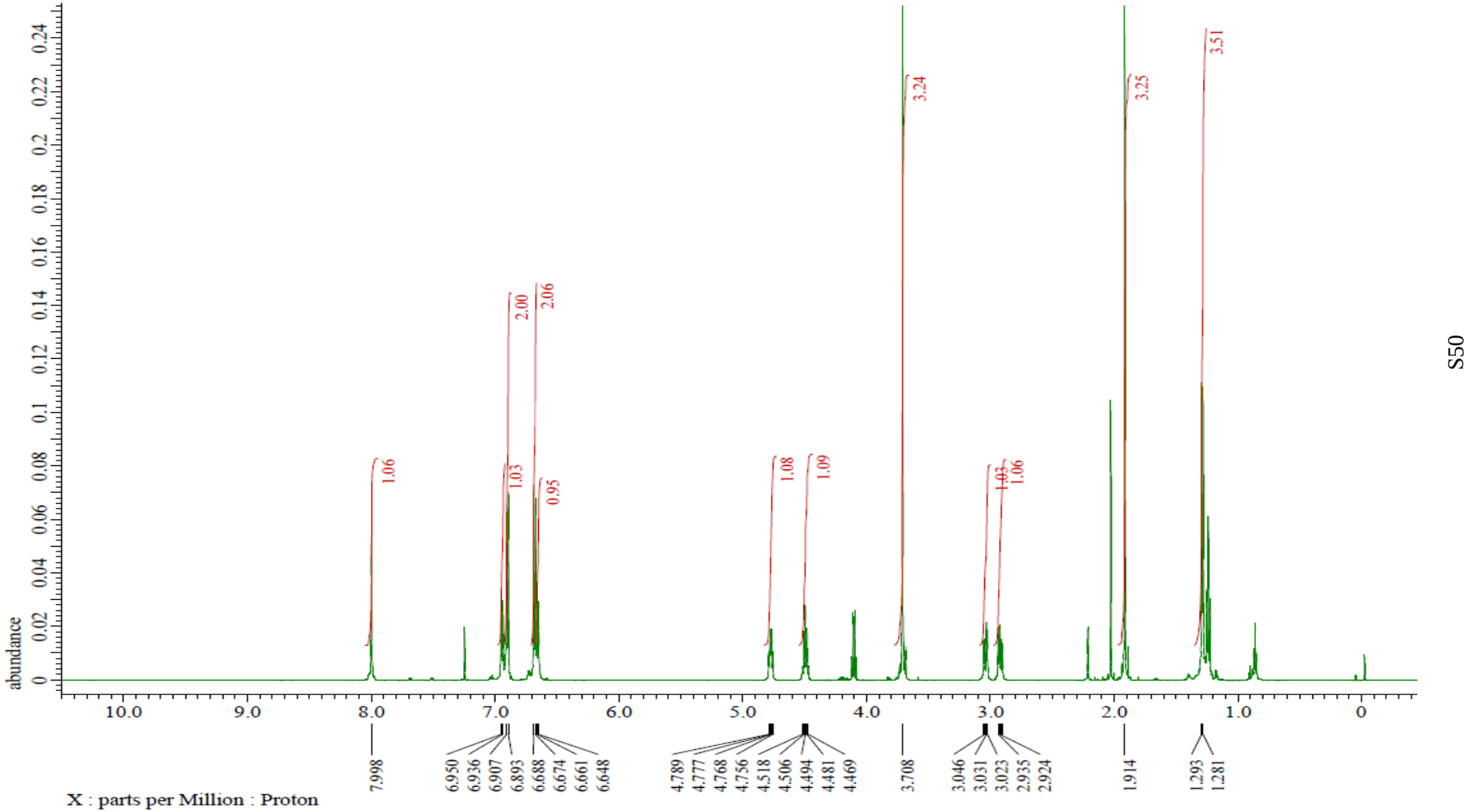
^{13}C NMR



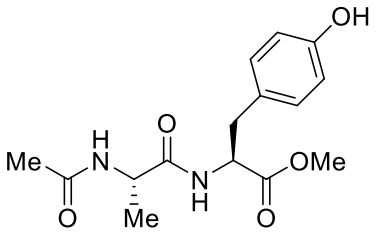
_N_-Acetyl-L-alanyl-L-tyrosine methyl ester (6c)



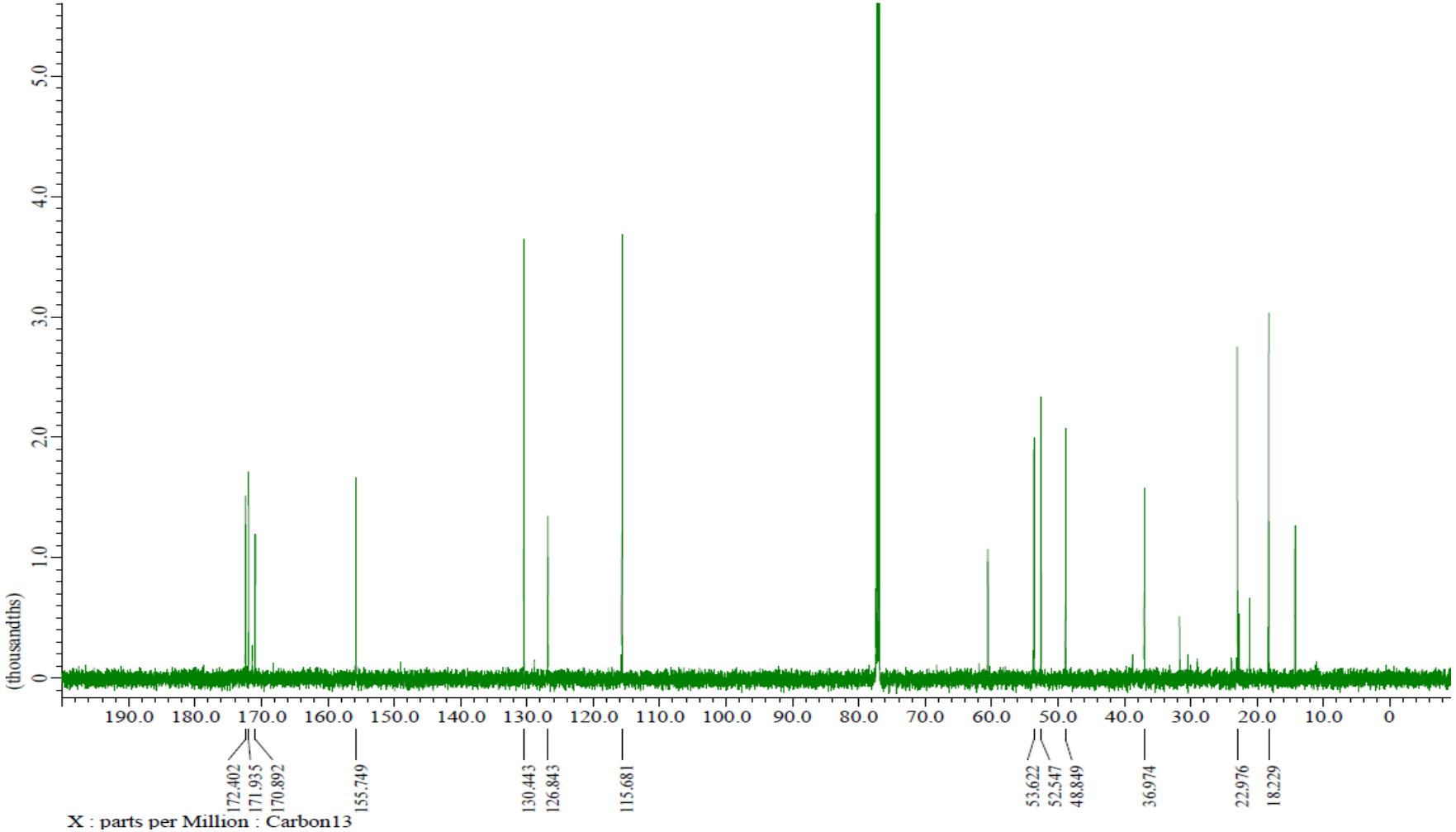
^{1}H NMR



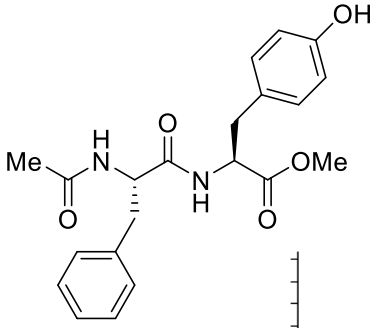
_N_-Acetyl-L-alanyl-L-tyrosine methyl ester (6c)



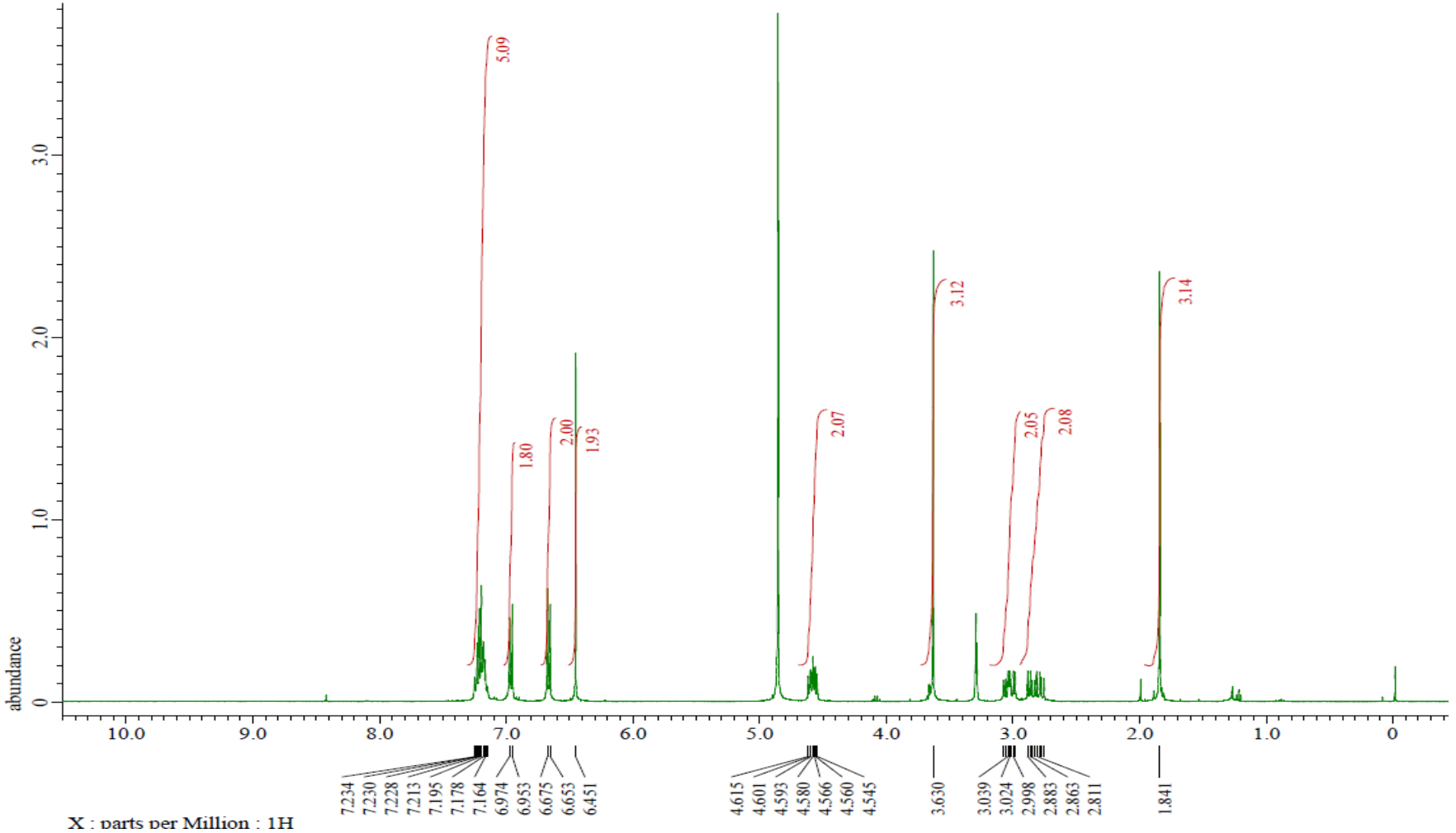
^{13}C NMR



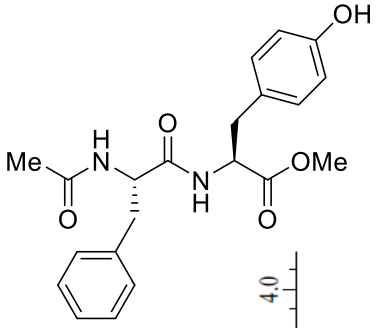
_N_-Acetyl-L-phenylalanyl-L-tyrosine methyl ester (6d)



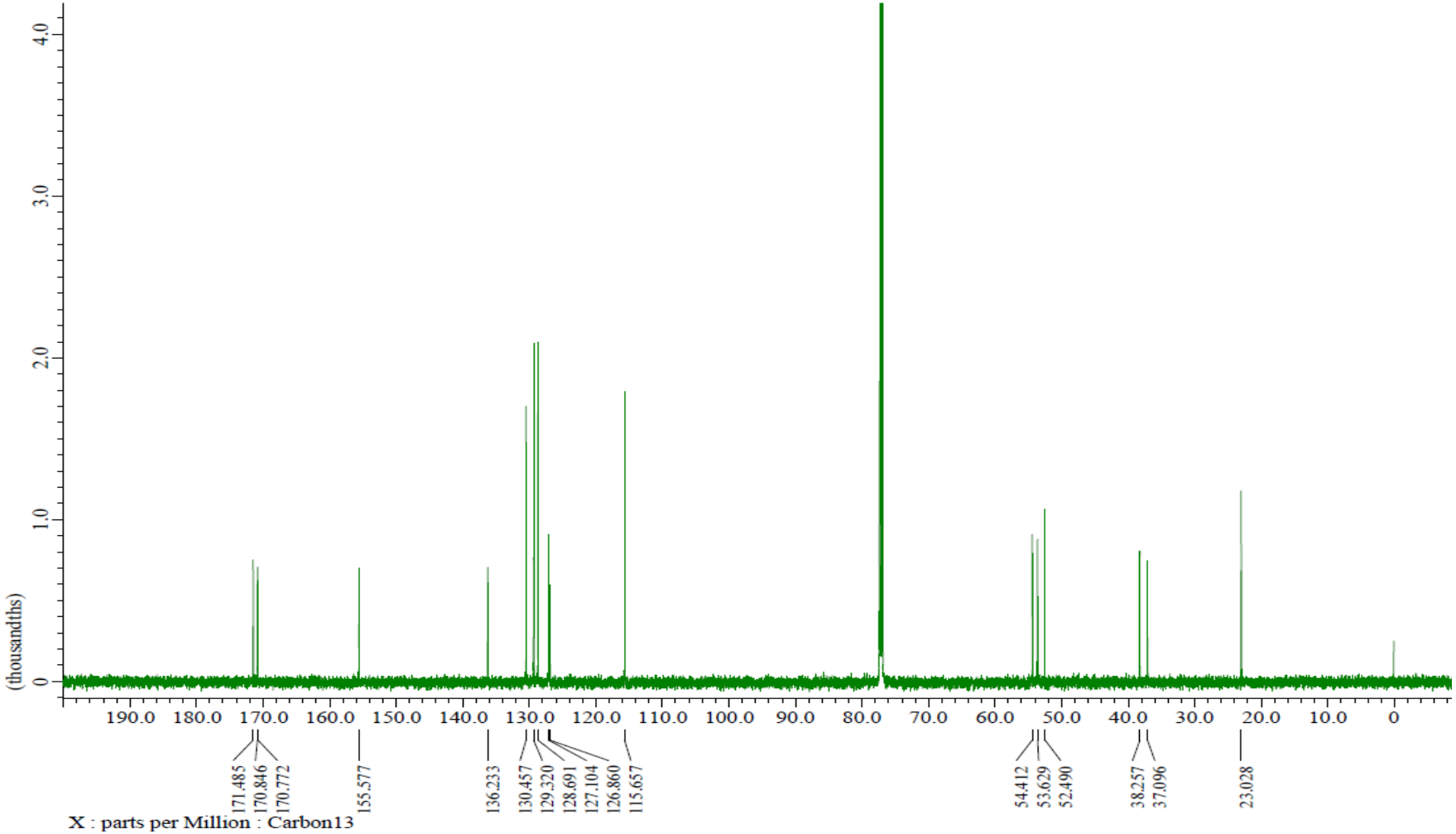
^{1}H NMR



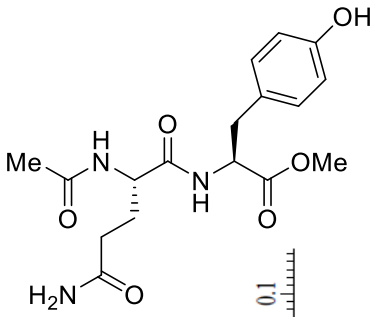
_N_-Acetyl-L-phenylalanyl-L-tyrosine methyl ester (6d)



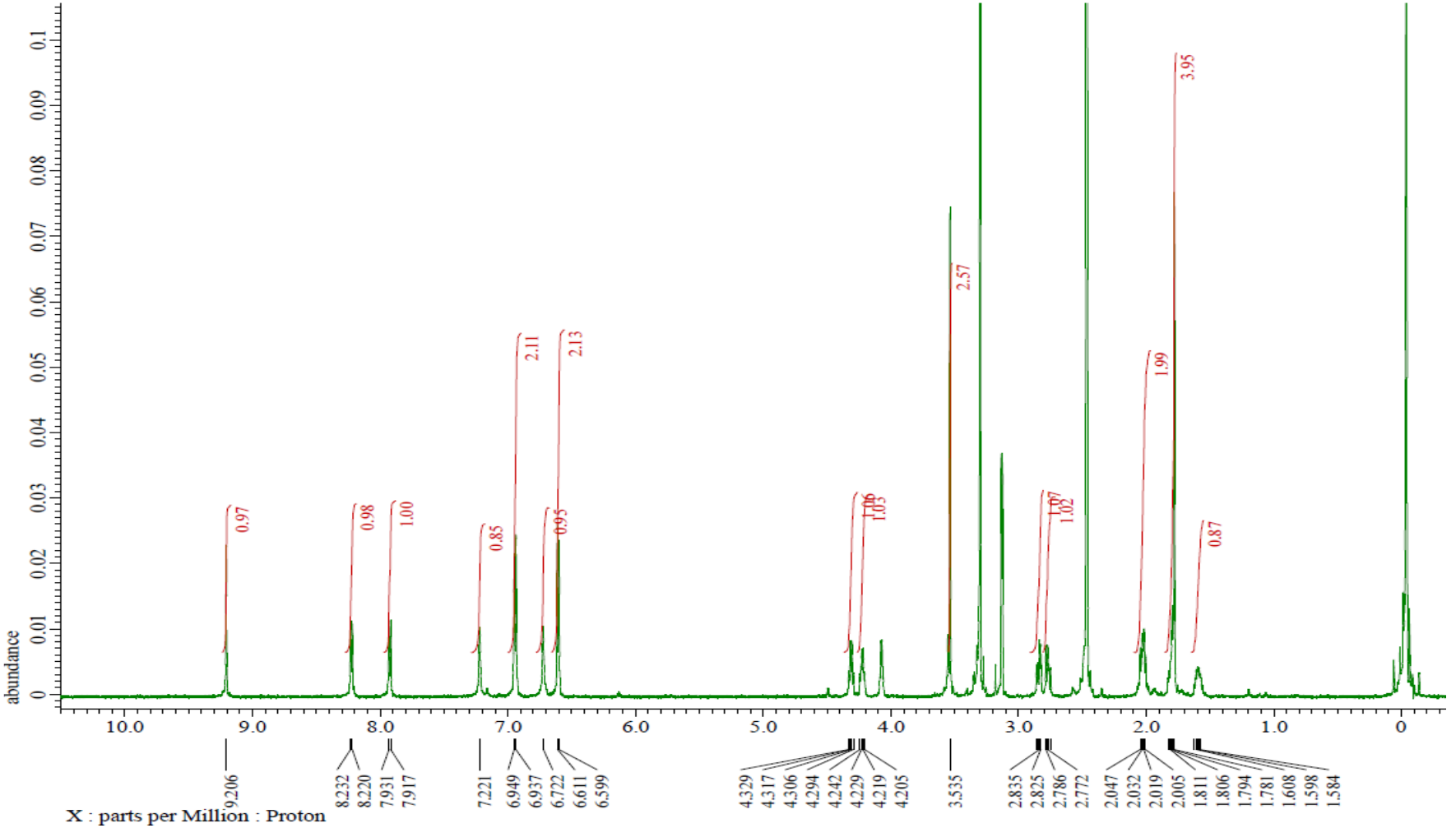
^{13}C NMR



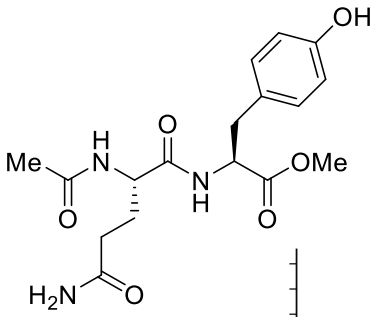
_N_-Acetyl-L-glutaminyl-L-tyrosine methyl ester (6e)



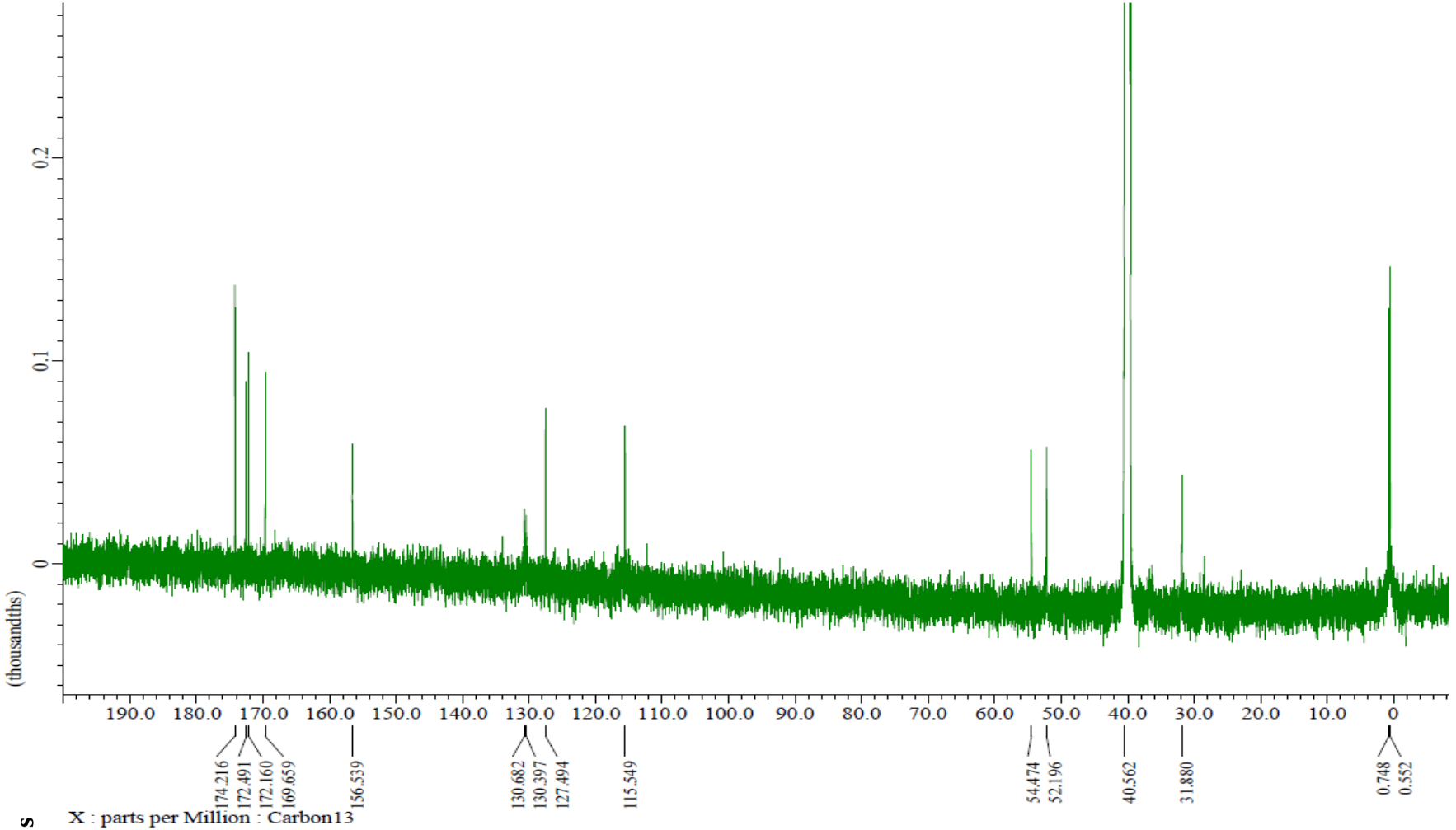
^{1}H NMR



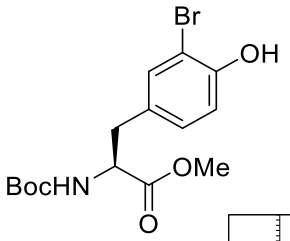
_N_-Acetyl-L-glutaminyl-L-tyrosine methyl ester (6e)



^{13}C NMR

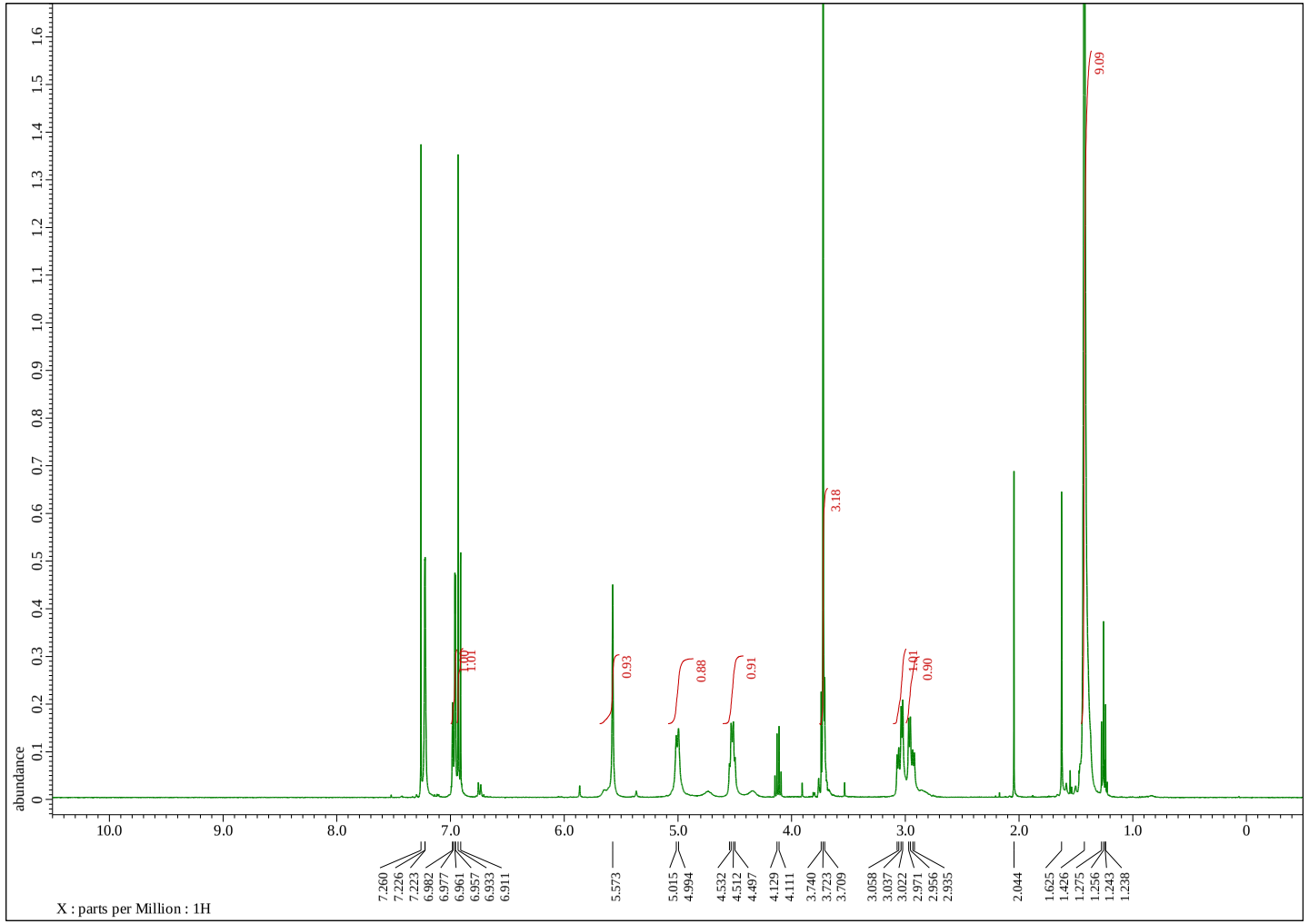


Methyl (*S*)-3-(3-bromo-4-hydroxyphenyl)-2-((*tert*-butoxycarbonyl)amino)propanoate (3)

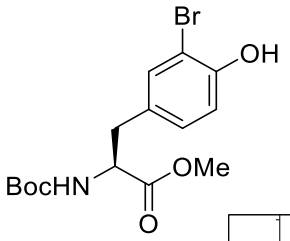


^{1}H NMR

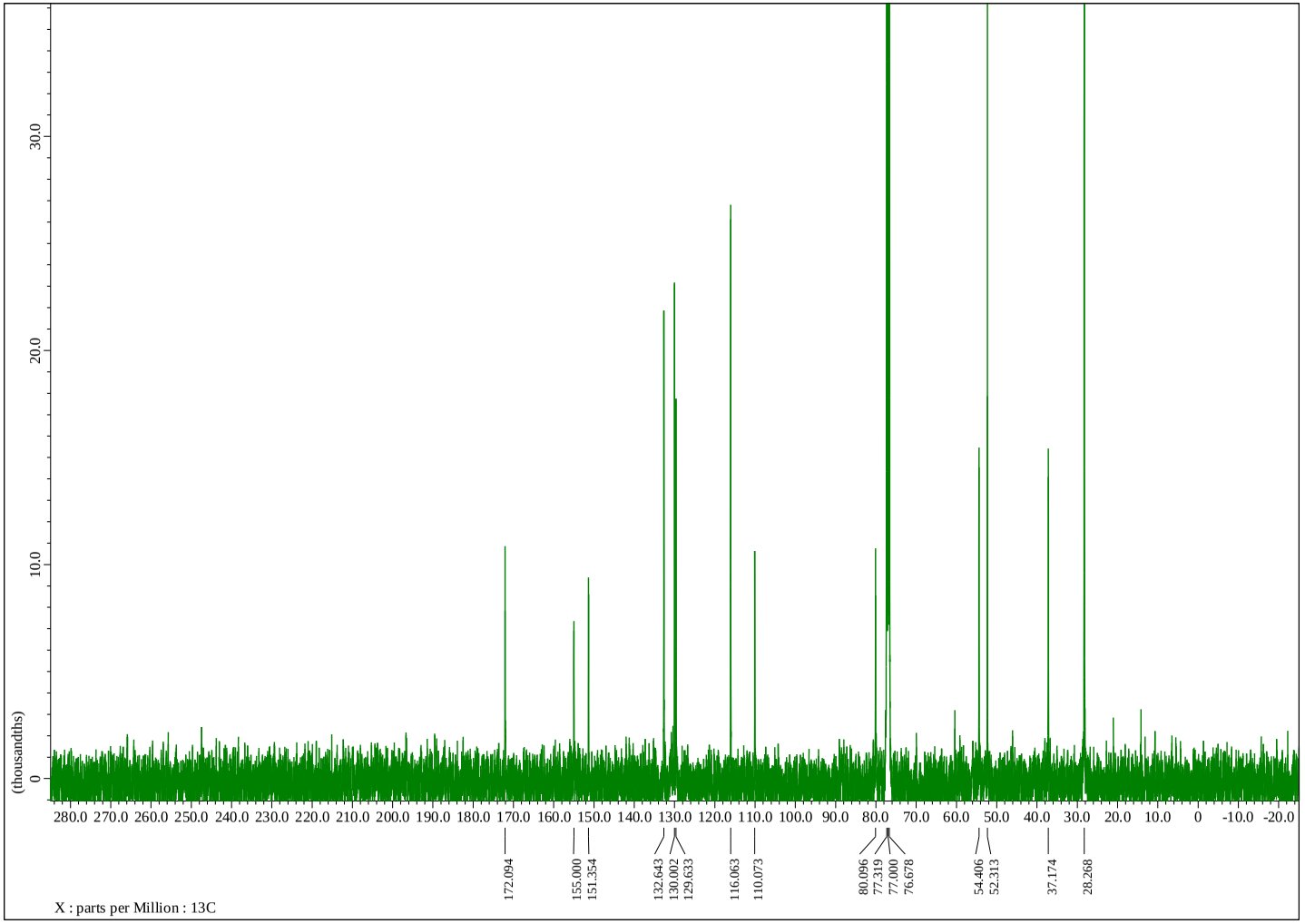
NMR Spectra (^{1}H, ^{13}C) of Products



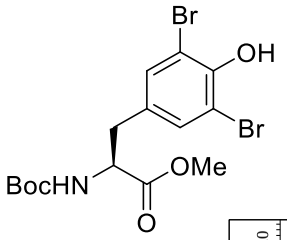
Methyl (*S*)-3-(3-bromo-4-hydroxyphenyl)-2-((*tert*-butoxycarbonyl)amino)propanoate (3)



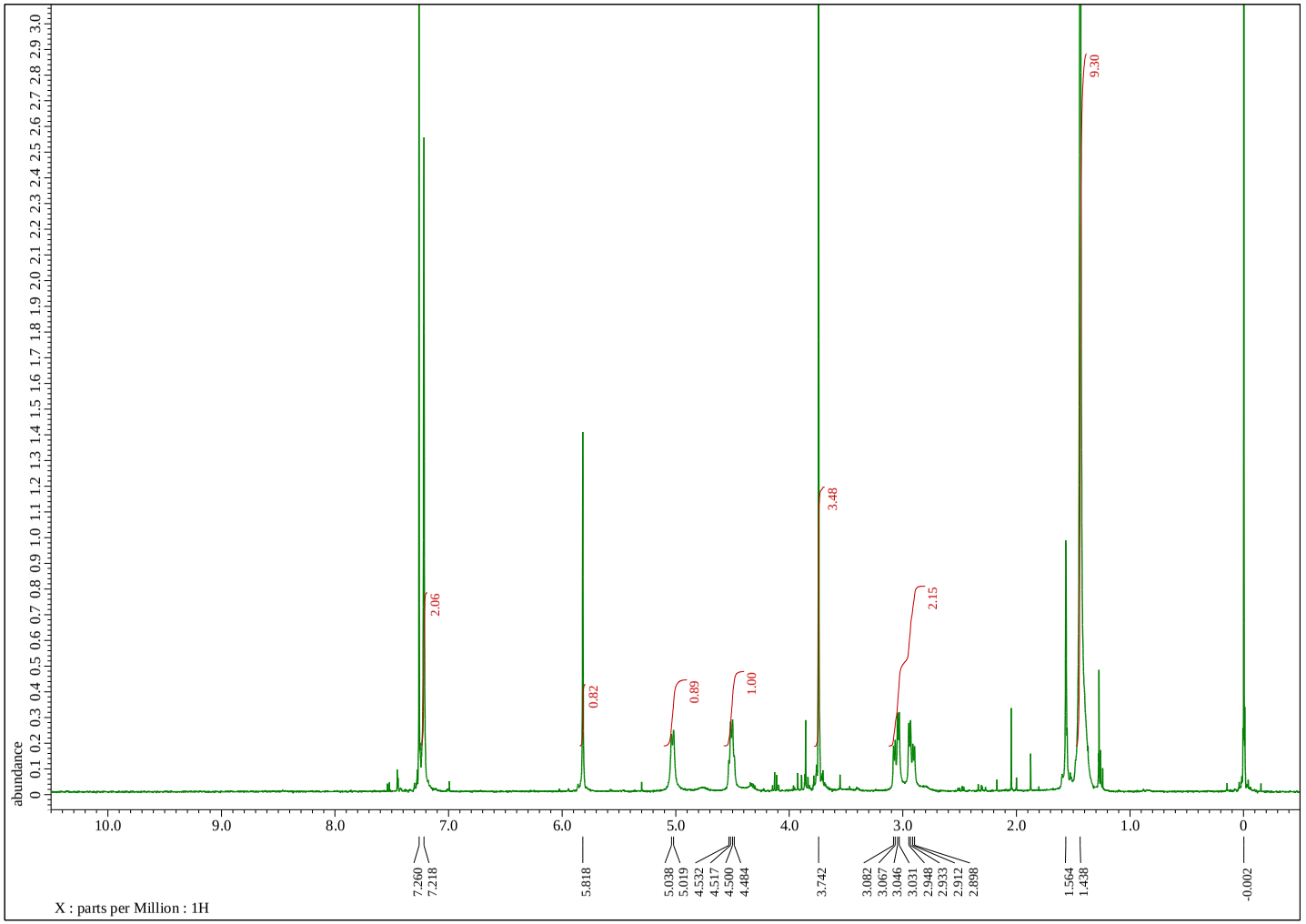
^{13}C NMR



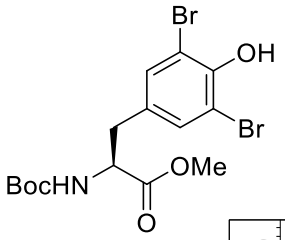
Methyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(3,5-dibromo-4-hydroxyphenyl)propanoate (4)



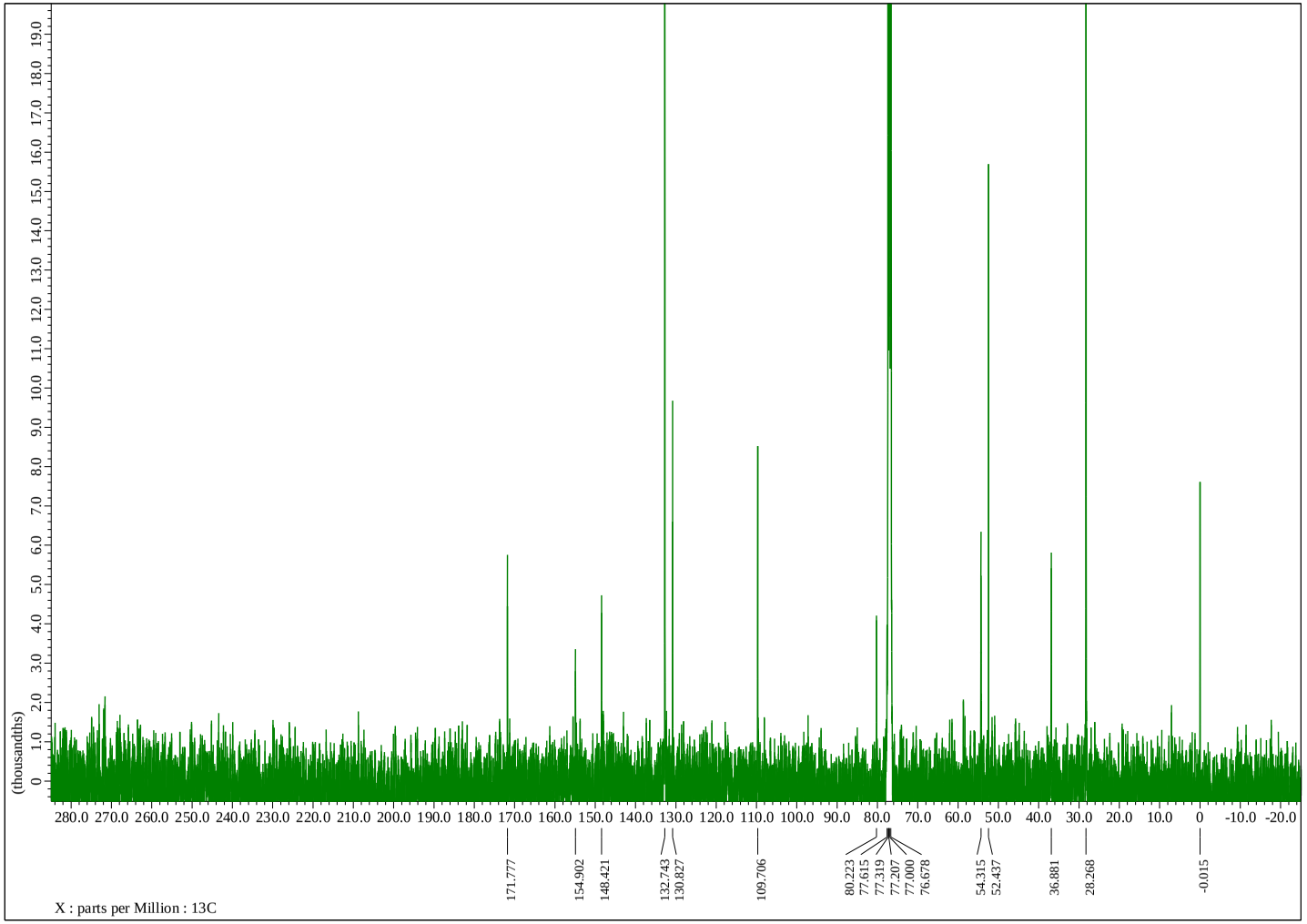
^{1}H NMR



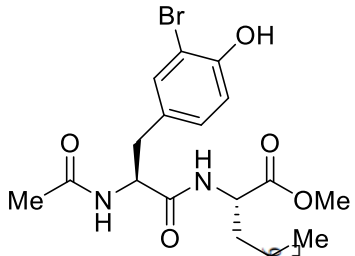
Methyl (*S*)-2-((*tert*-butoxycarbonyl)amino)-3-(3,5-dibromo-4-hydroxyphenyl)propanoate (4)



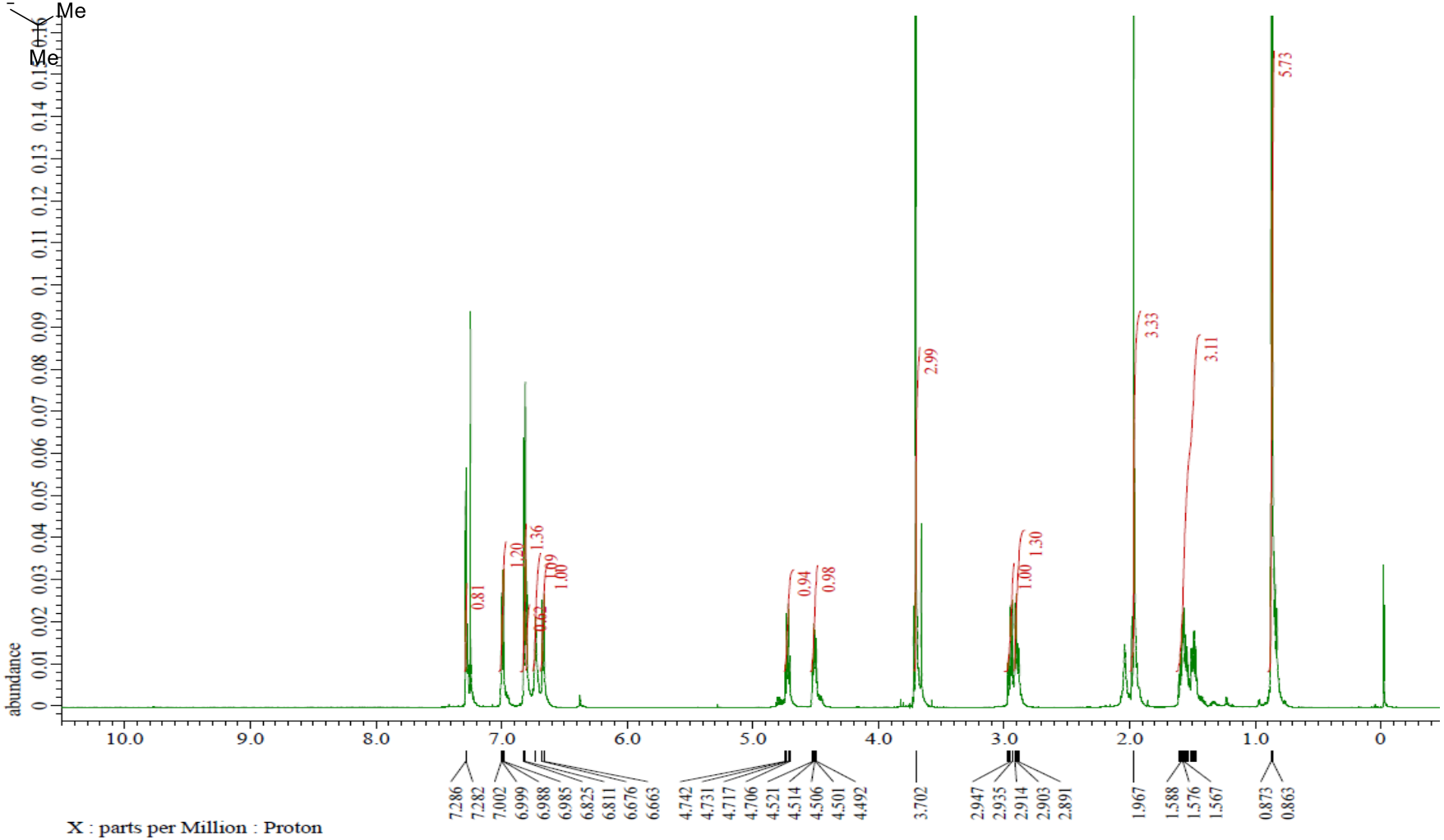
^{13}C NMR



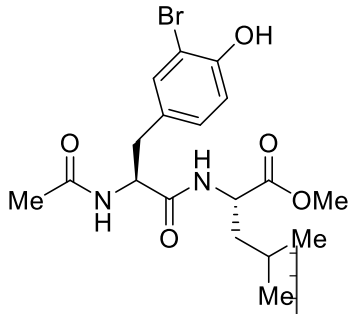
Methyl ((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-leucinate (7a)



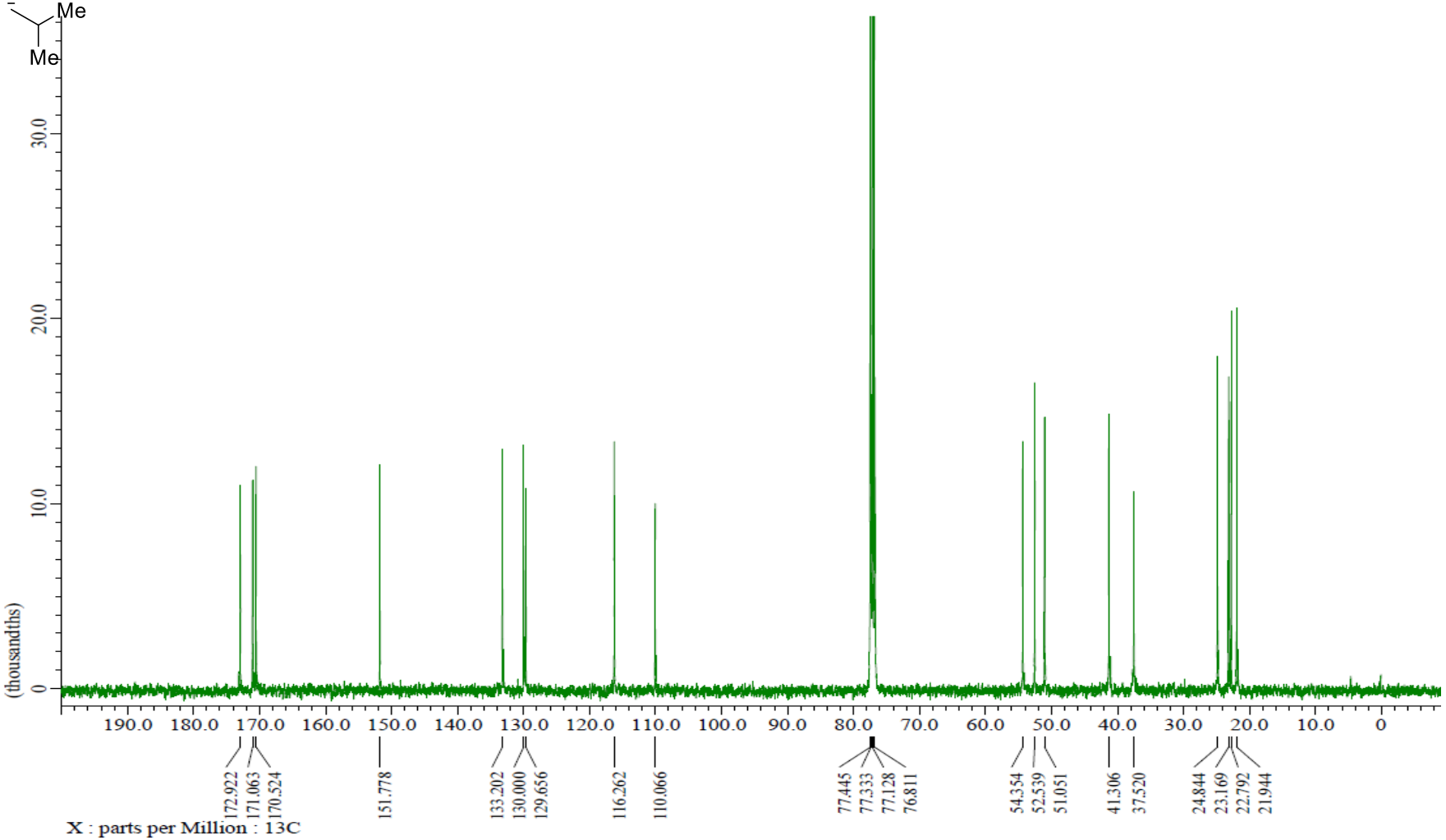
^{1}H NMR



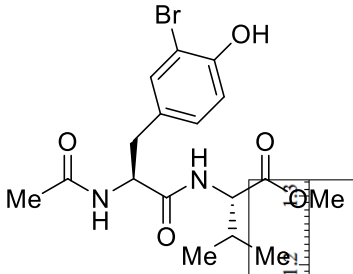
Methyl ((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-leucinate (7a)



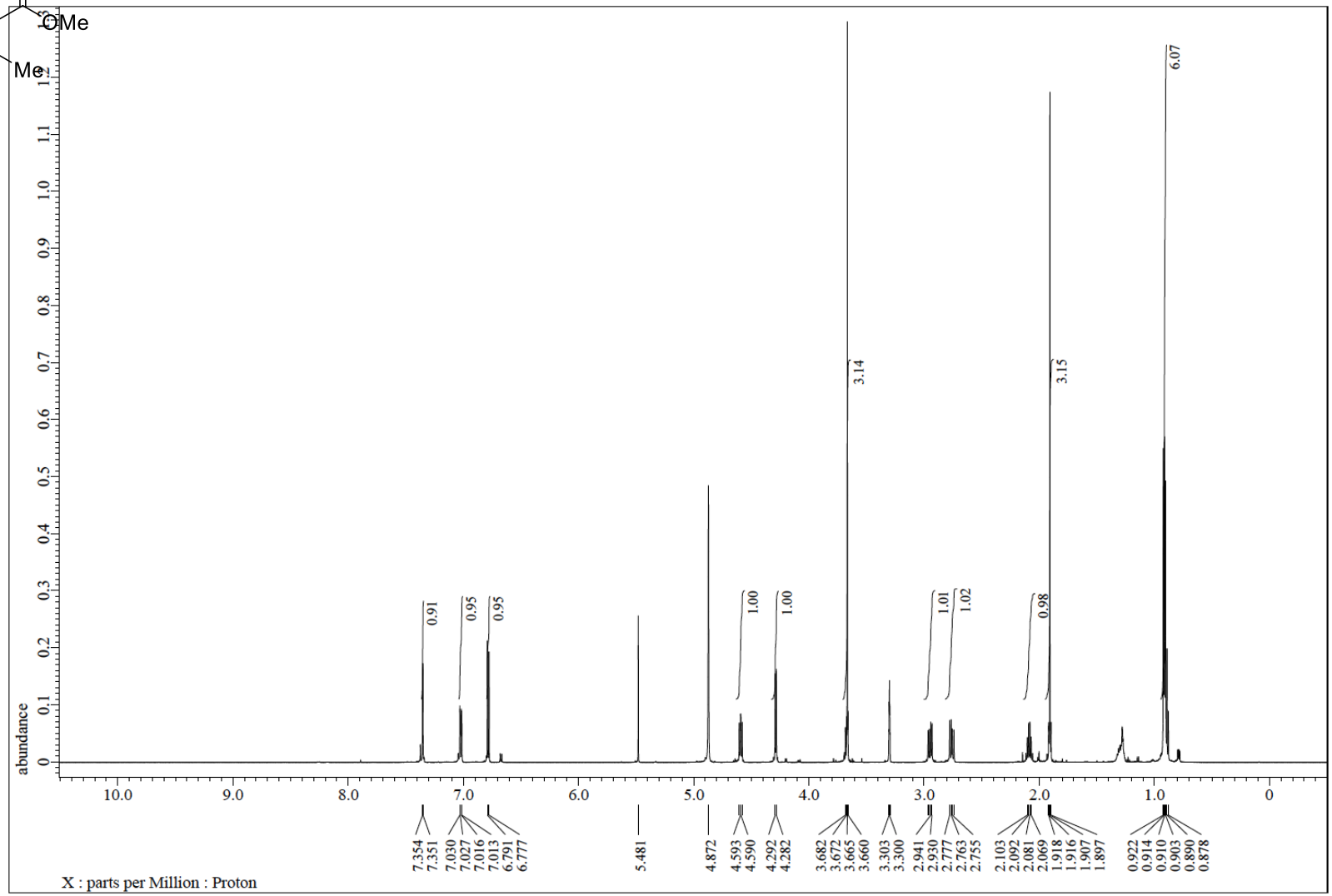
^{13}C NMR



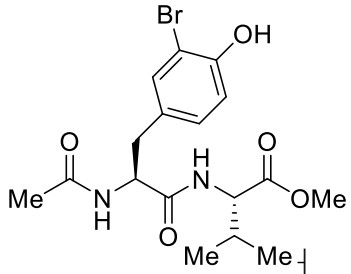
Methyl ((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-valinate (7b)



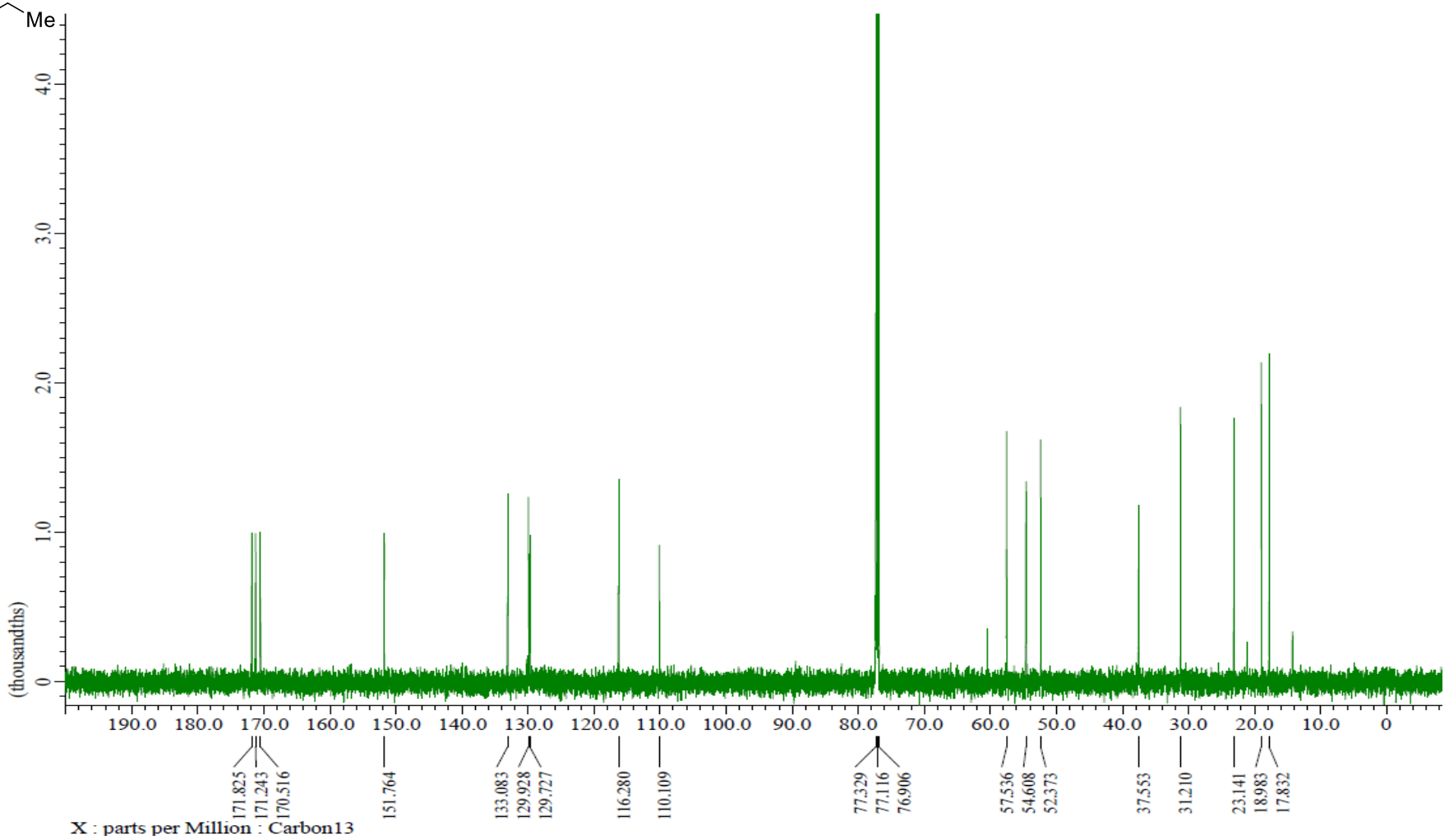
^{1}H NMR



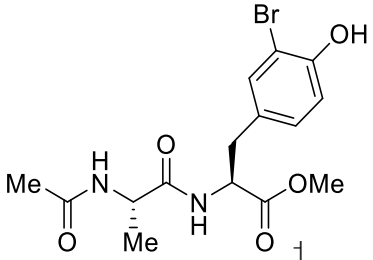
Methyl ((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-valinate (7b)



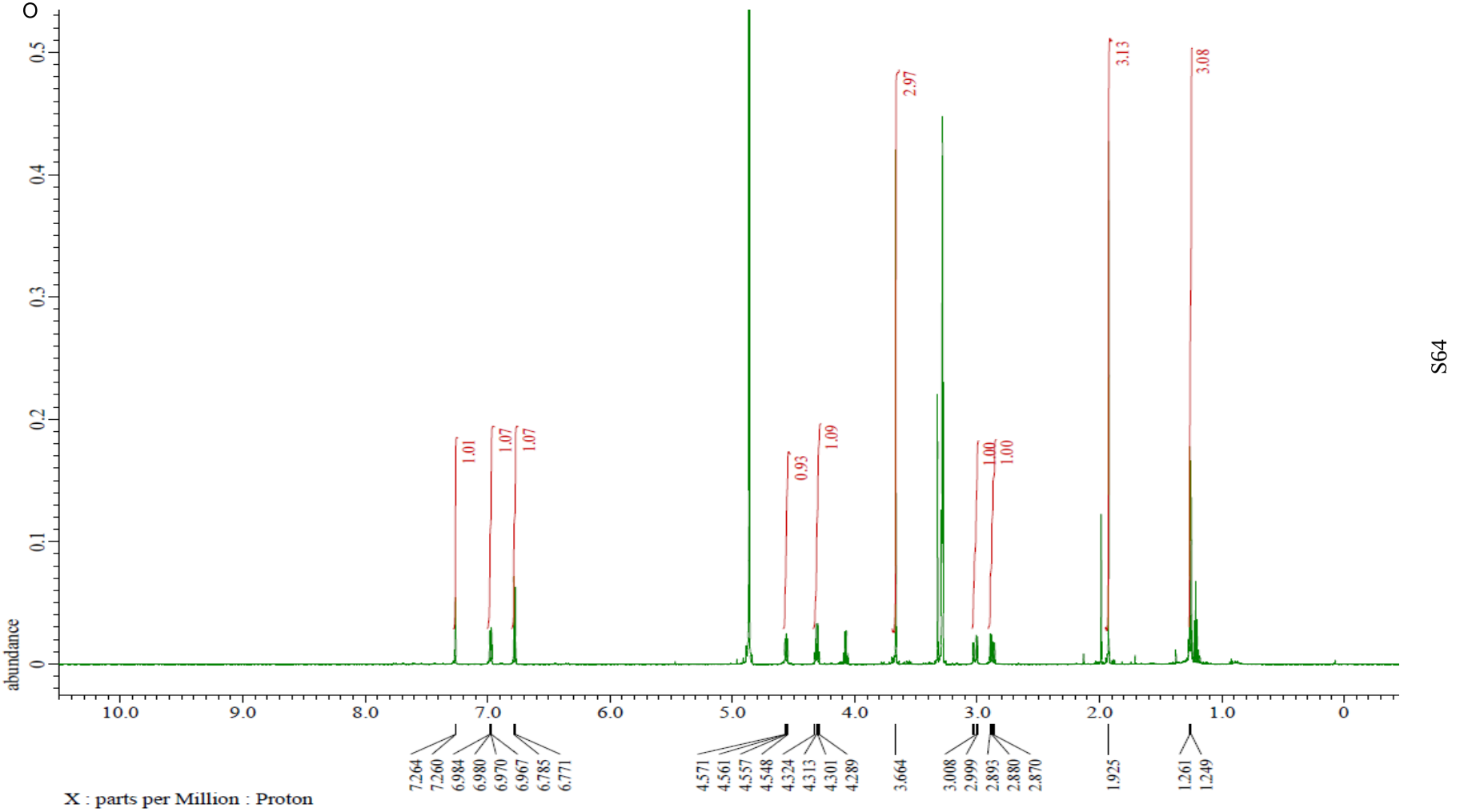
^{13}C NMR



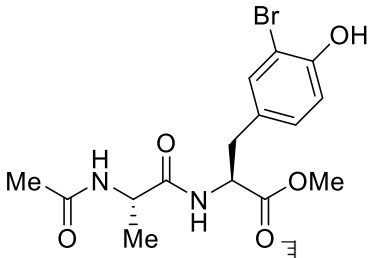
Methyl (*S*)-2-((*S*)-2-acetamidopropanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7c)



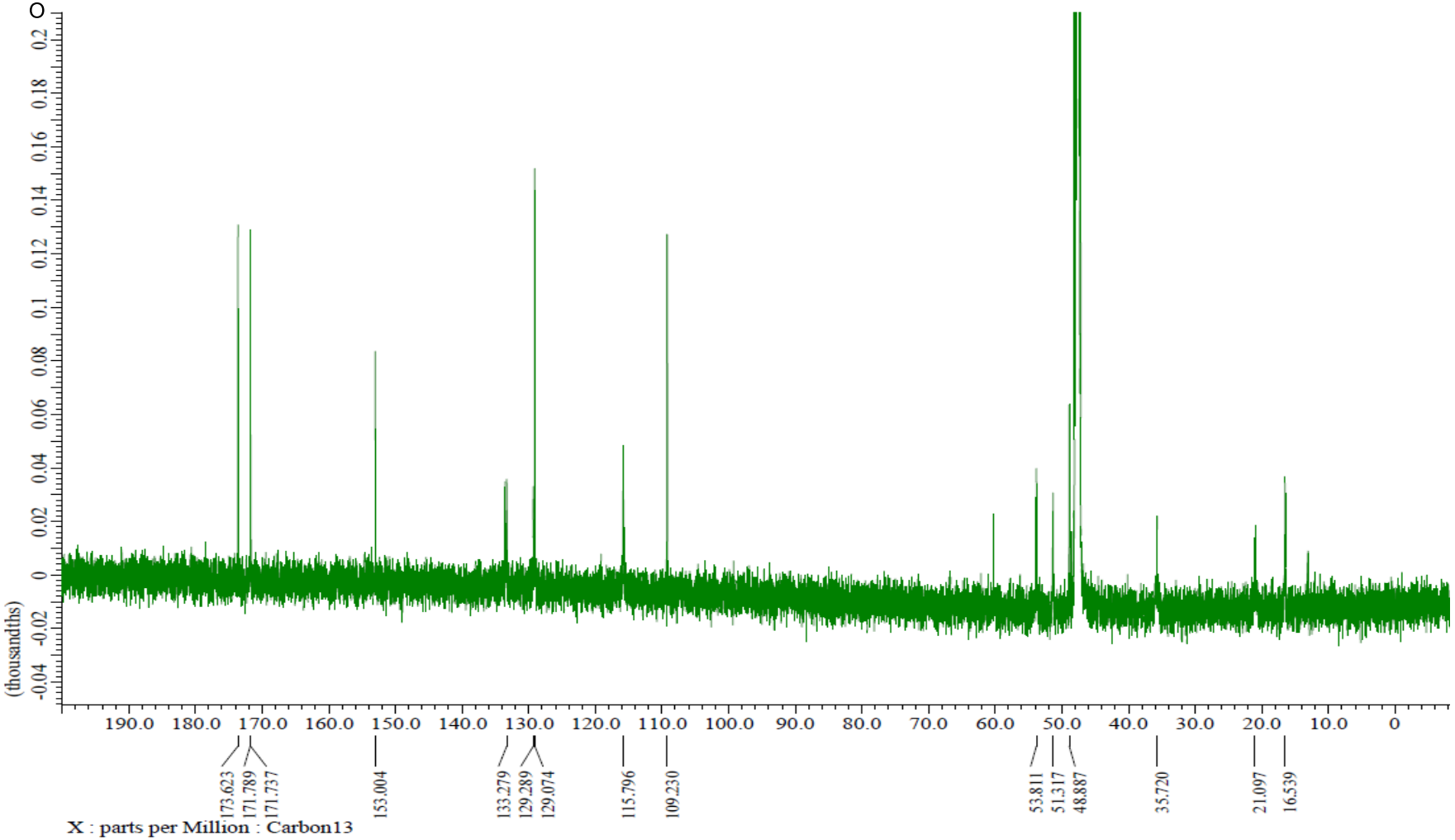
^{1}H NMR



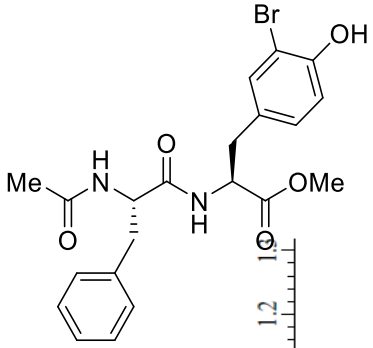
Methyl (*S*)-2-((*S*)-2-acetamidopropanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7c)



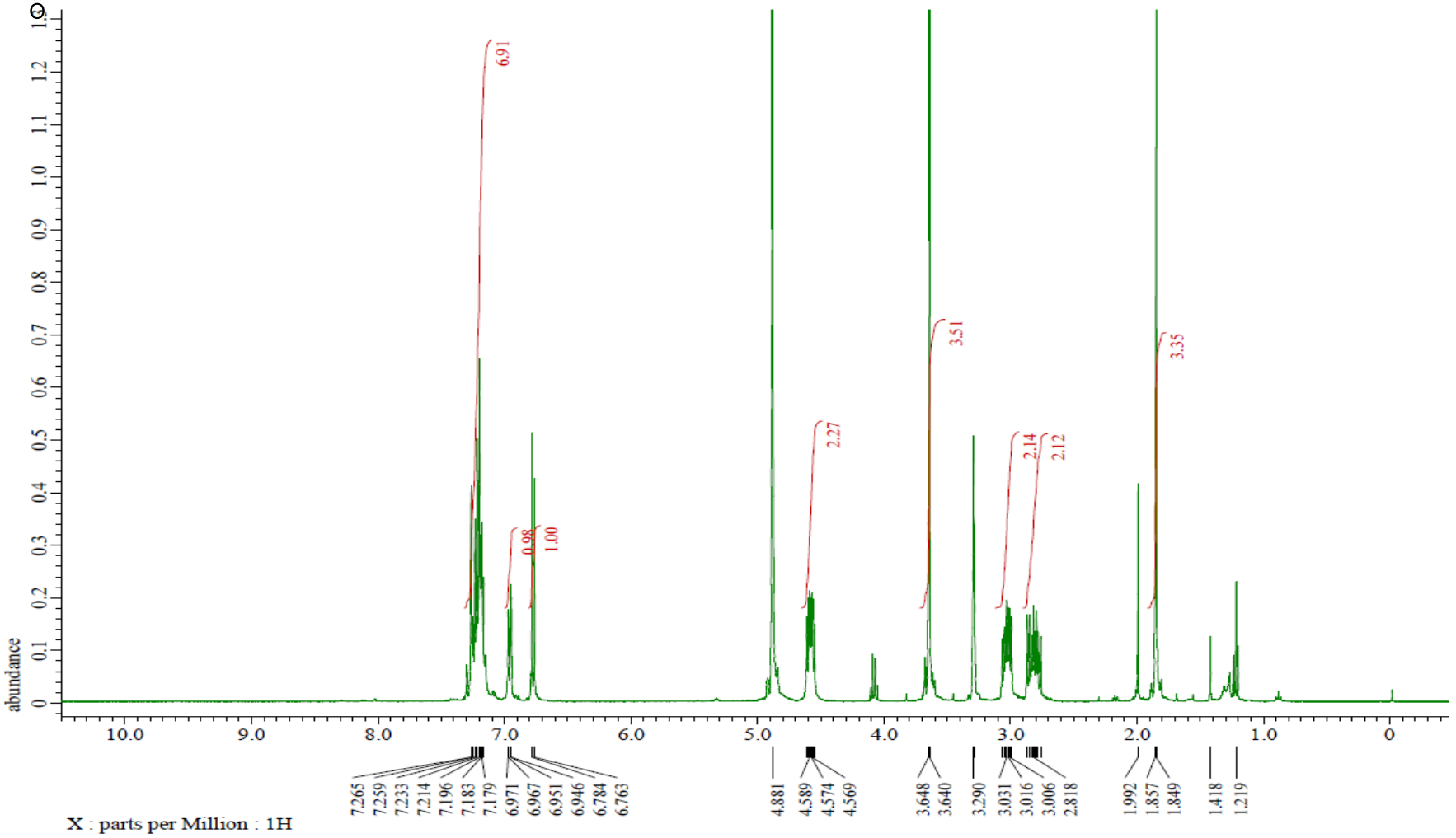
^{13}C NMR



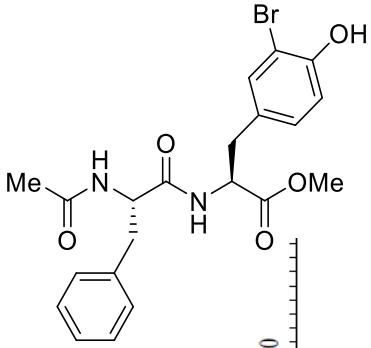
Methyl (*S*)-2-((*S*)-2-acetamido-3-phenylpropanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7d)



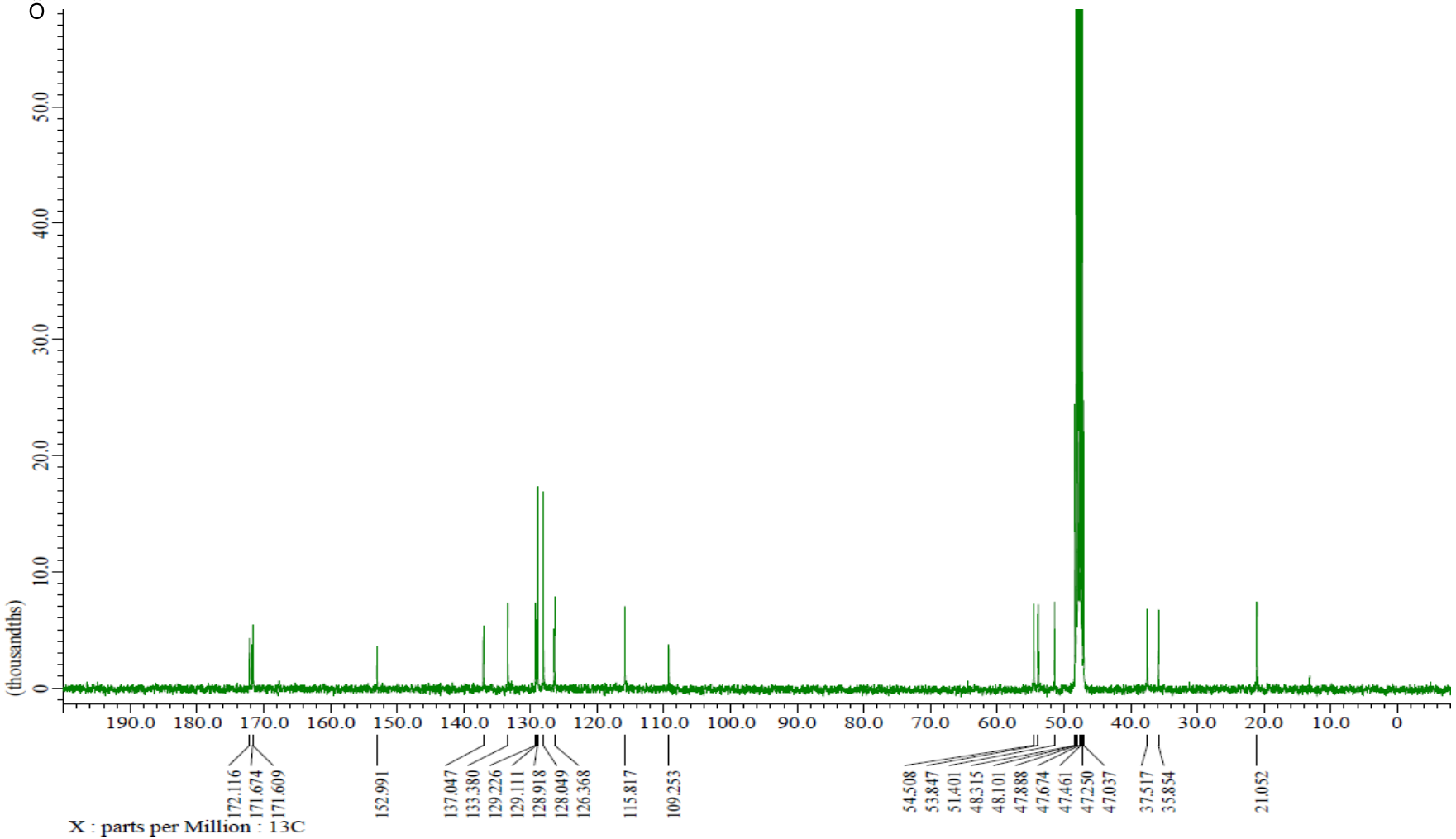
^{1}H NMR



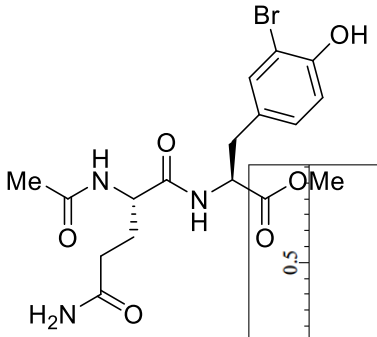
Methyl (*S*)-2-((*S*)-2-acetamido-3-phenylpropanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7d)



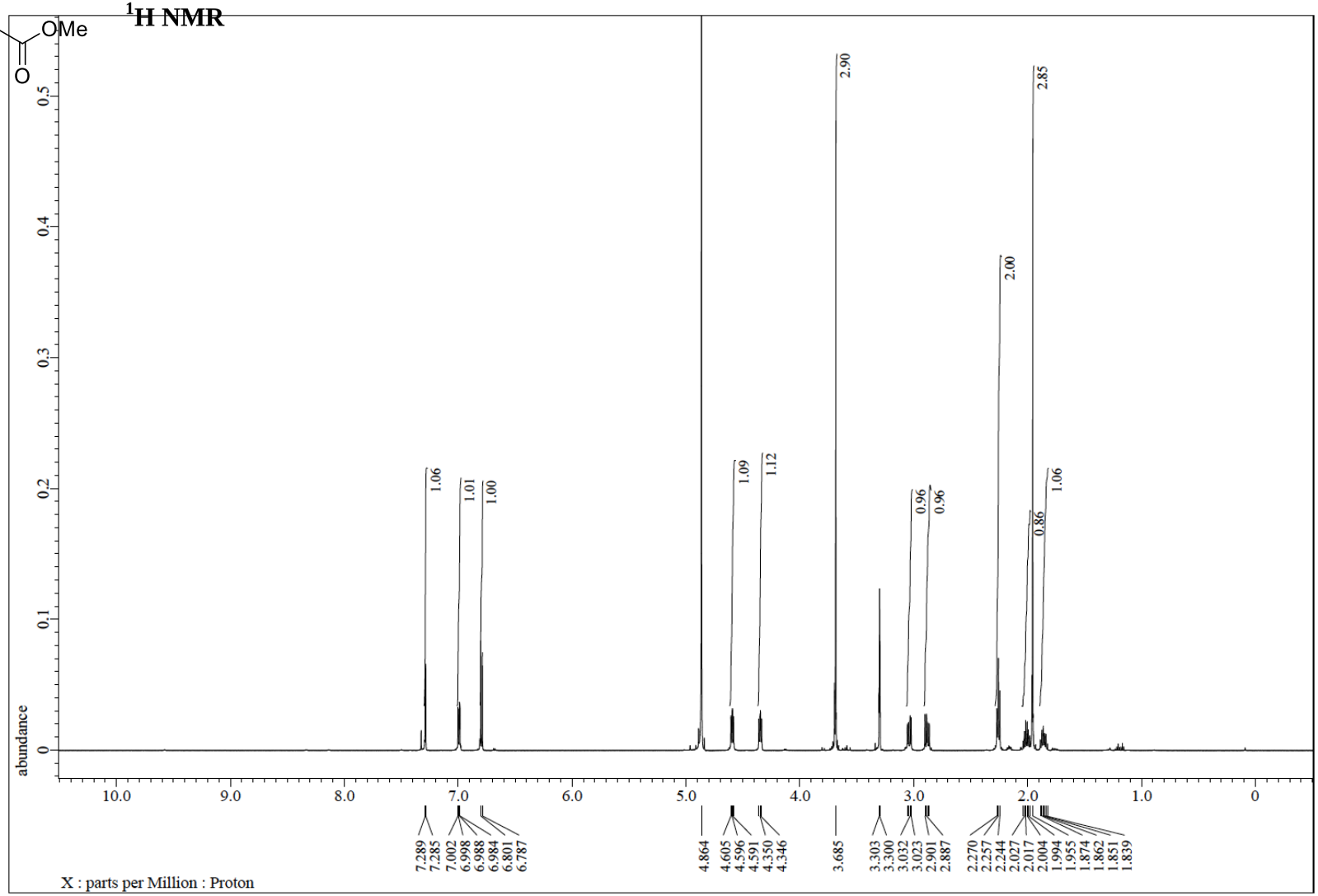
^{13}C NMR



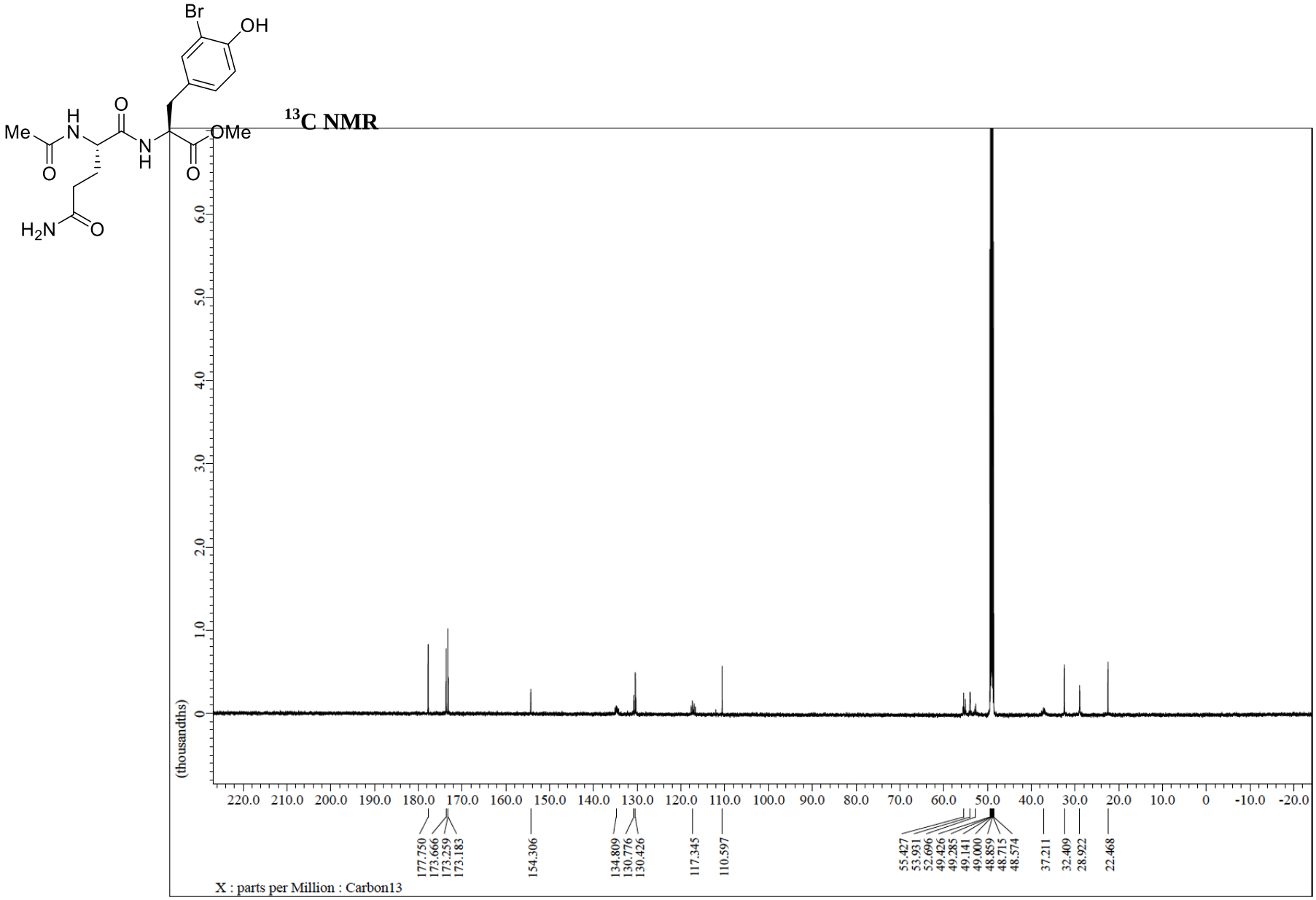
Methyl (*S*)-2-((*S*)-2-acetamido-5-amino-5-oxopentanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7e)



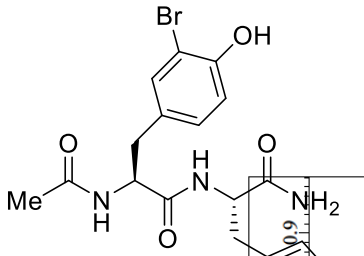
^{1}H NMR



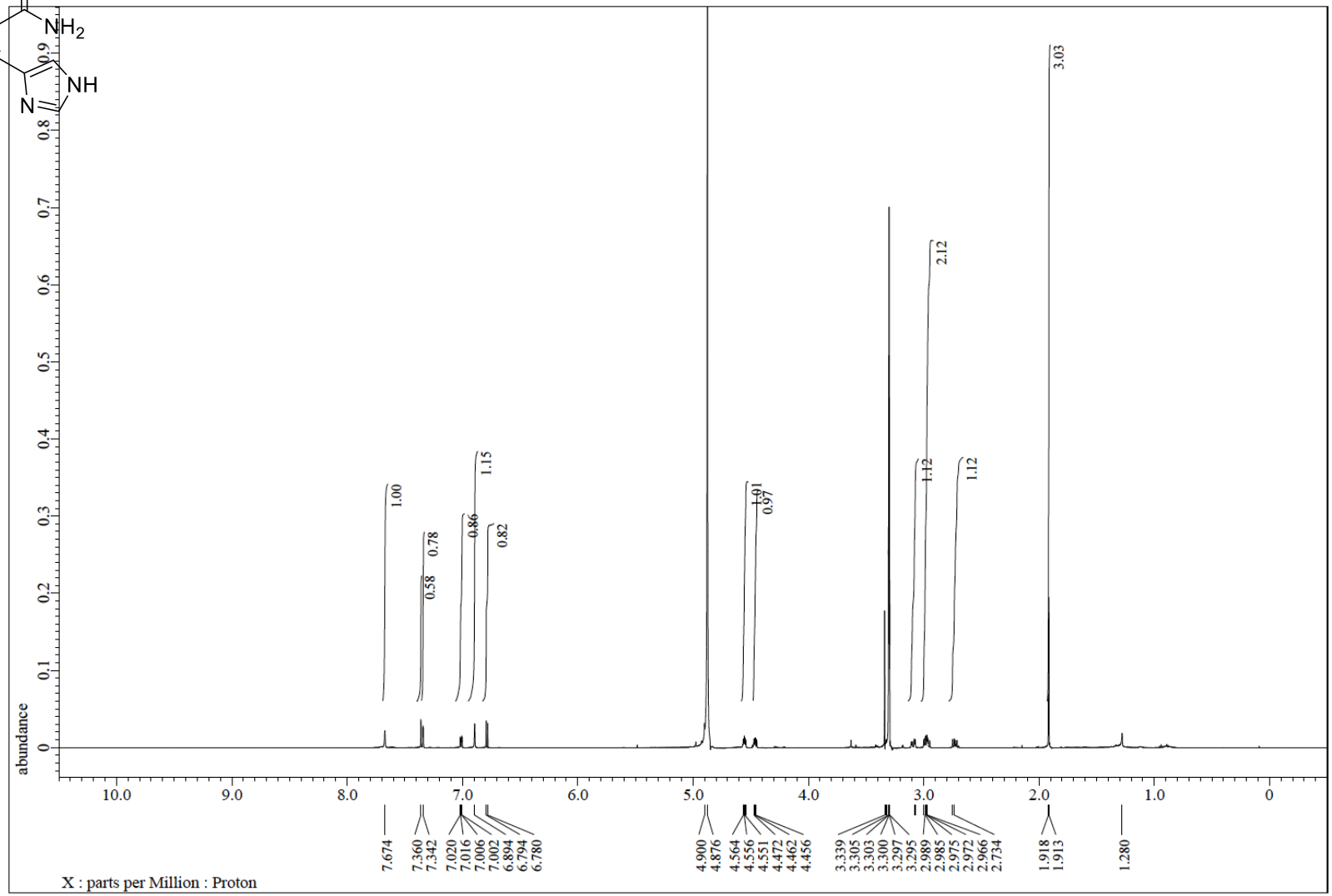
Methyl (*S*)-2-((*S*)-2-acetamido-5-amino-5-oxopentanamido)-3-(3-bromo-4-hydroxyphenyl)propanoate (7e)



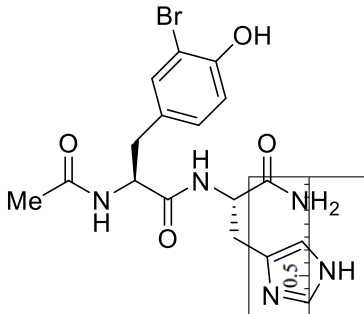
((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-histidinamide (7f)



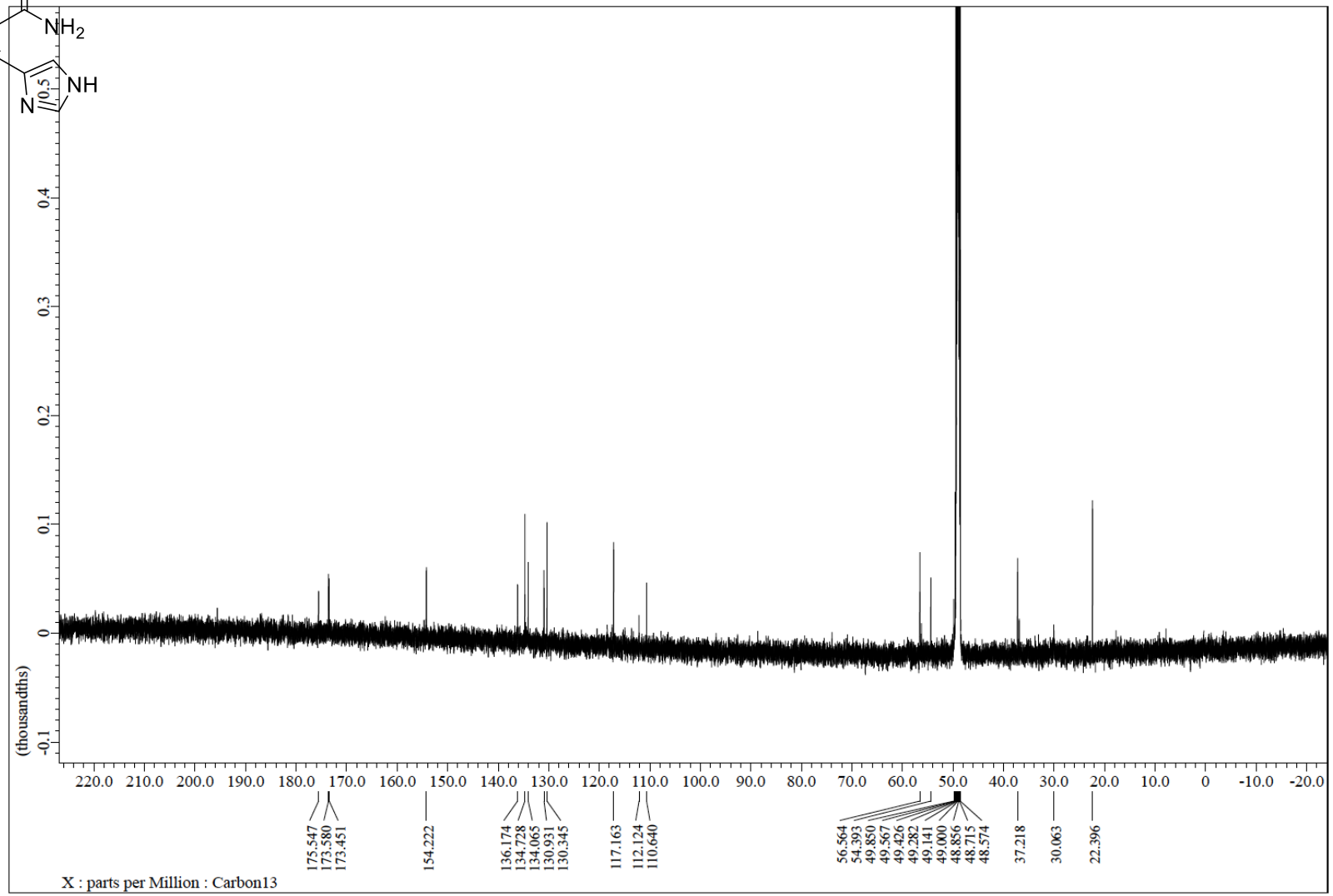
^{1}H NMR



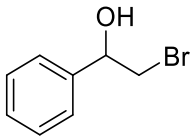
((*S*)-2-acetamido-3-(3-bromo-4-hydroxyphenyl)propanoyl)-L-histidinamide (7f)



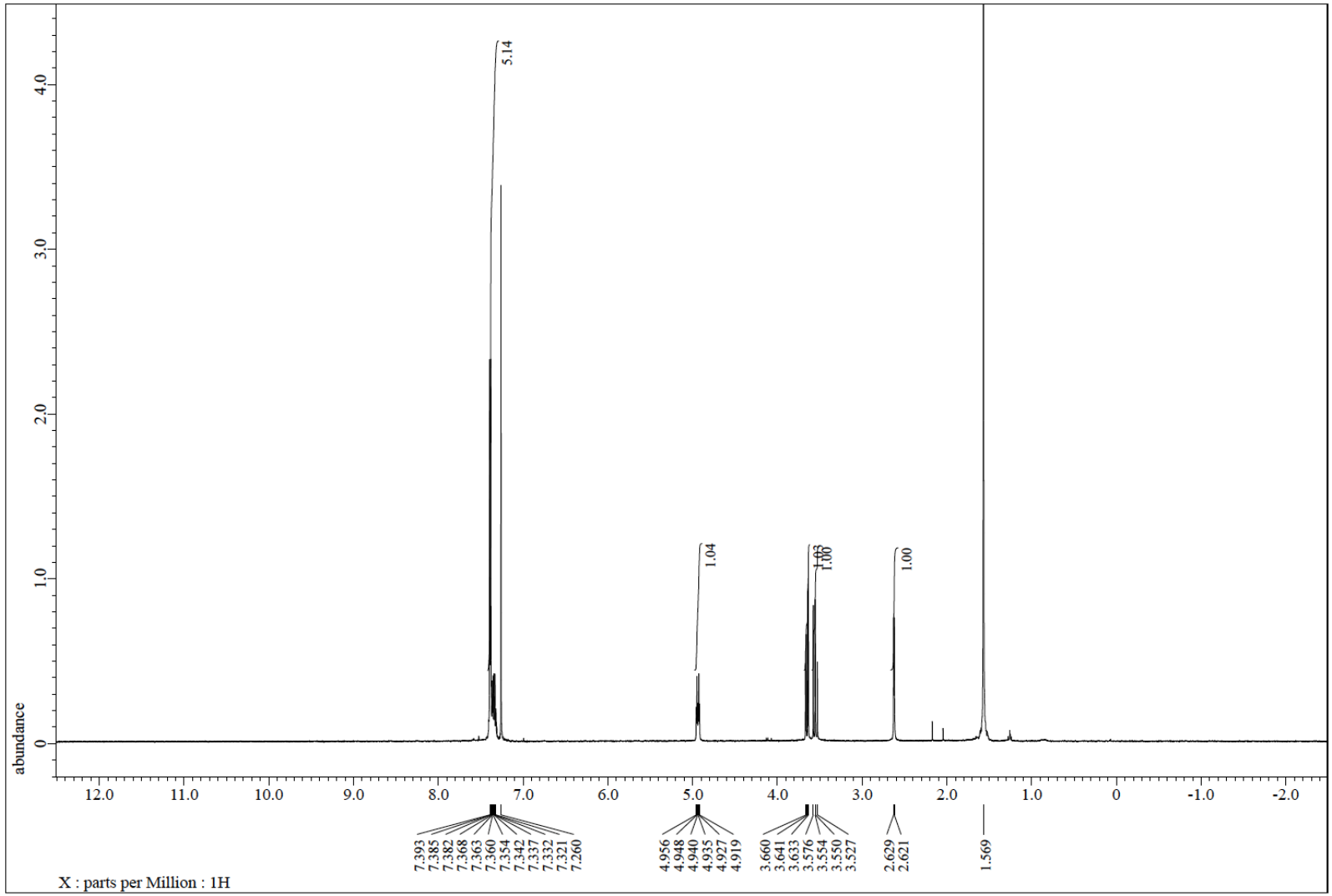
^{13}C NMR



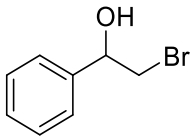
2-Bromo-1-phenylethan-1-ol (9a)



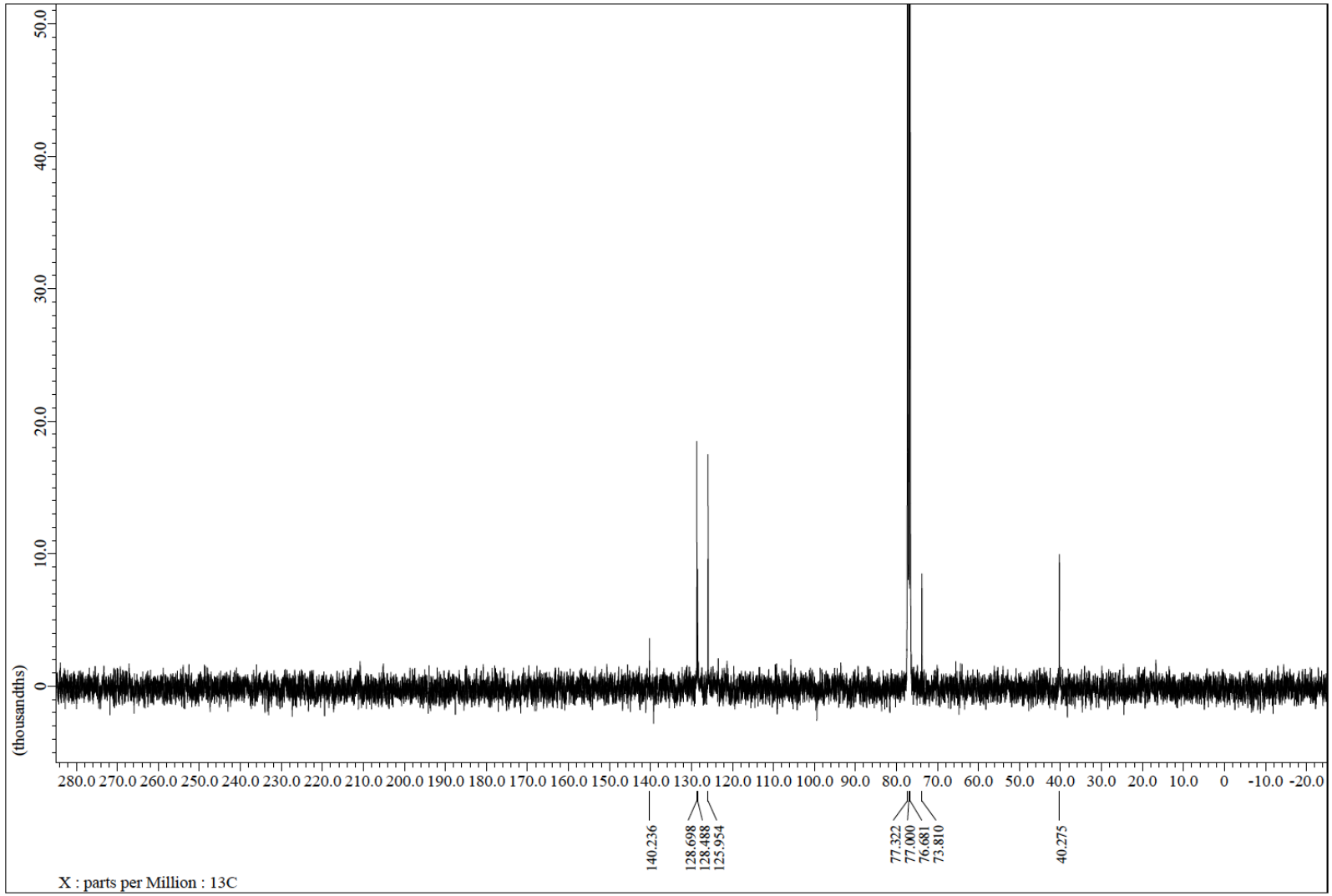
^{1}H NMR



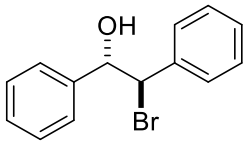
2-Bromo-1-phenylethan-1-ol (9a)



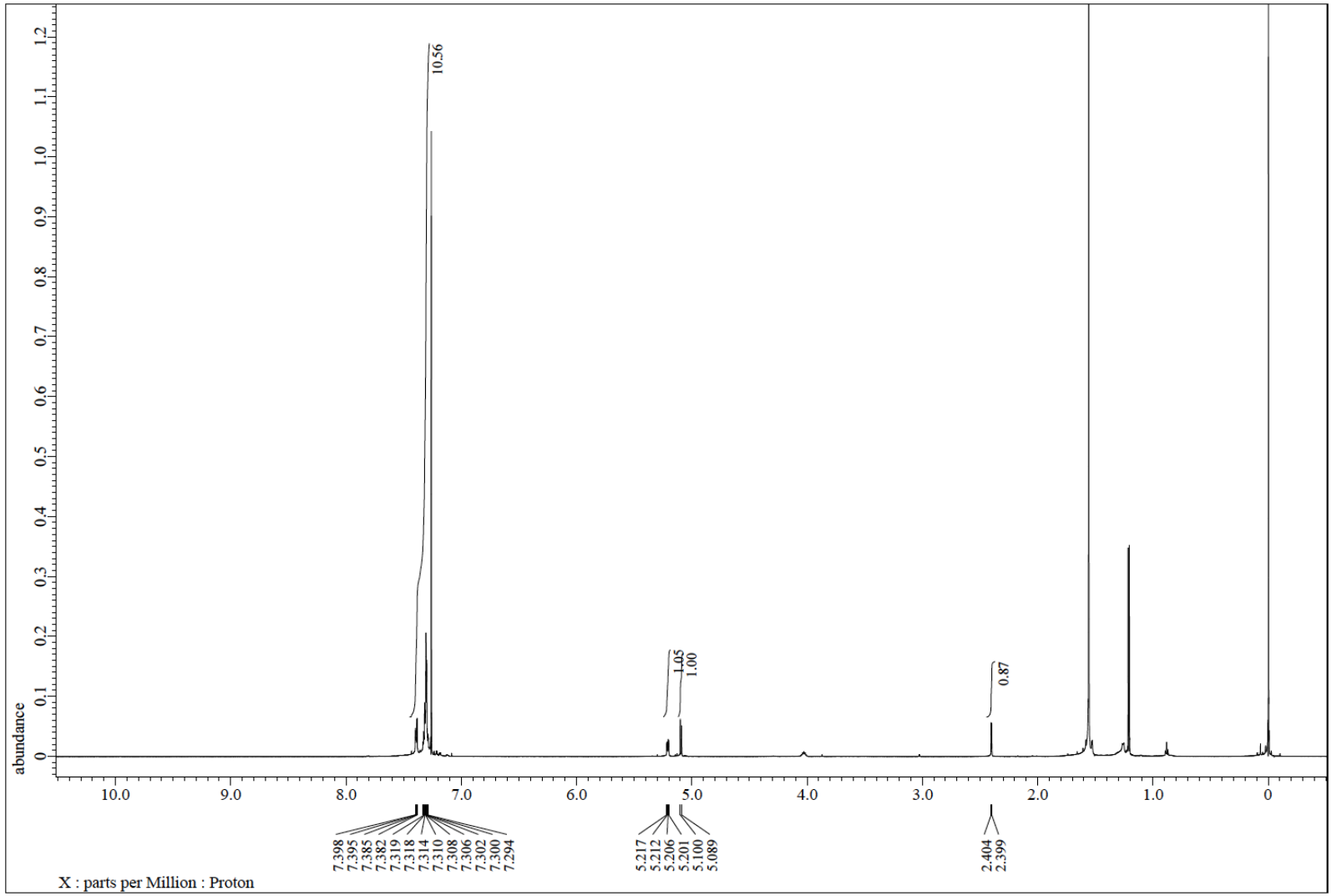
^{13}C NMR



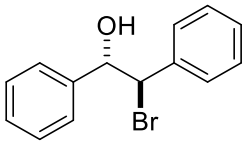
(1*S,2*R**)-2-Bromo-1,2-diphenylethan-1-ol (9b)**



^{1}H NMR



(1*S,2*R**)-2-Bromo-1,2-diphenylethan-1-ol (9b)**



^{13}C NMR