Catalytic asymmetric aza-Michael addition of fumaric monoacids with multifunctional thiourea/boronic acids

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Supporting Information

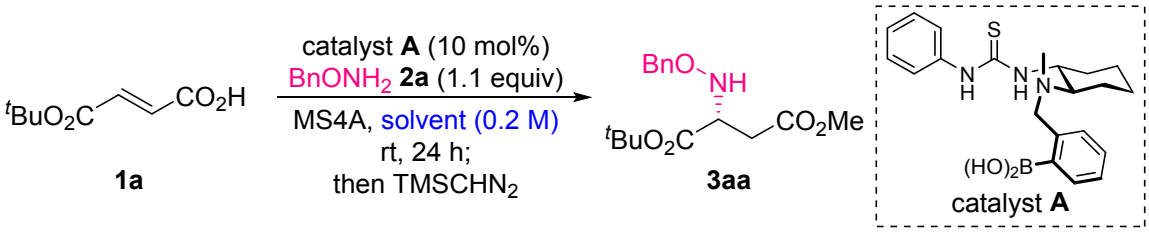
Table of Contents

(A) Supplemental Data

(A-1) Optimisation Details: Tables S1-S8

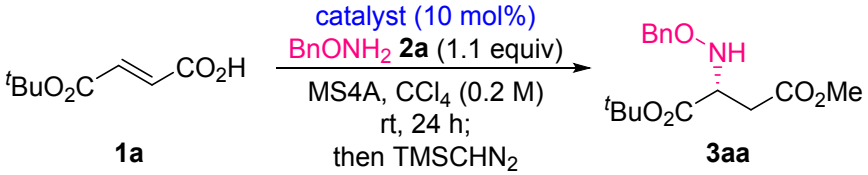
Several reaction parameters of the enantioselective aza-Michael addition were investigated. In each tables are described isolated yields.

Table S1. Investigation of Solvent Effect



entry	solvent	**3aa** (%)	ee (%)	entry	solvent	**3aa** (%)	ee (%)
1	DMF	0	-	7	hexane	35	38
2	MeCN	0	-	***8***	***CCl_4***	***70***	***88***
3	EtOAc	0	-	9	C_2Cl_4	70	81
4	Et_2O	22	28	10	4-$F_3CC_6H_4Cl$	55	73
5	CH_2Cl_2	10	47	11	PhF	15	62
6	toluene	60	69	12	PhCl	29	7

Table S2. Deviation of Thioureas of Multifunctional Organoboron Catalysts



entry	catalyst	**3aa** (%)	ee (%)
1	***A***	***80***	***88***
2	**B**	66	80
3	**C**	72	76
4	**D**	59	90
5	**E**	62	80
6	**F**	54	51

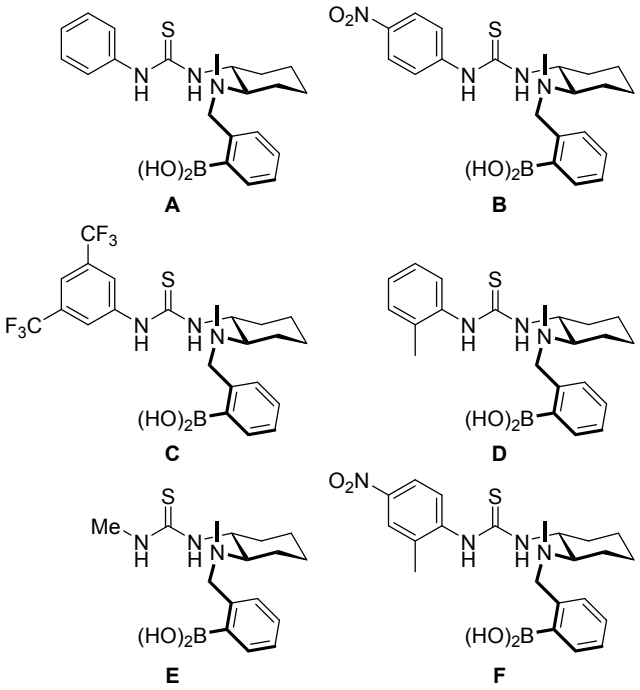
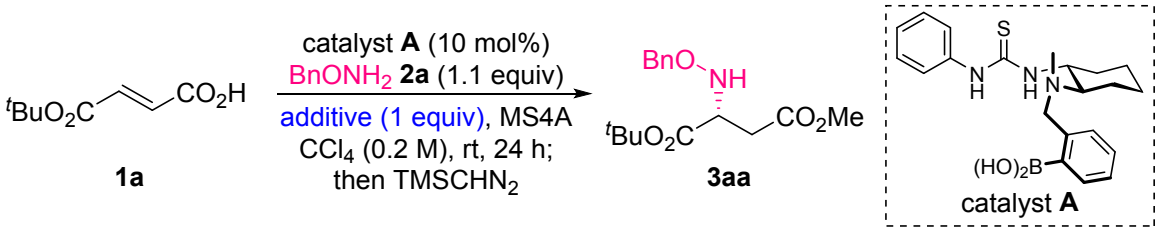
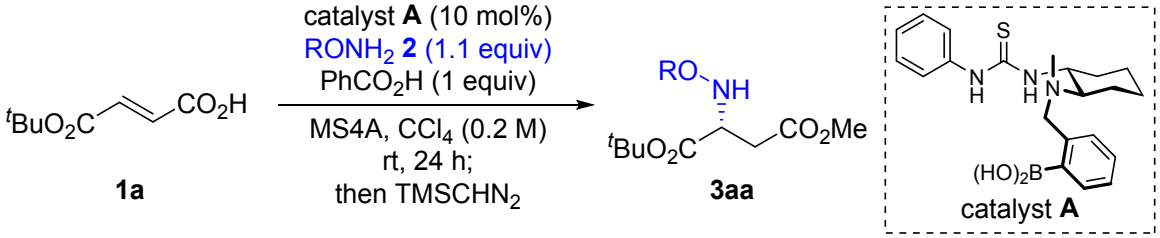


Table S3. Screening of Acid Additives

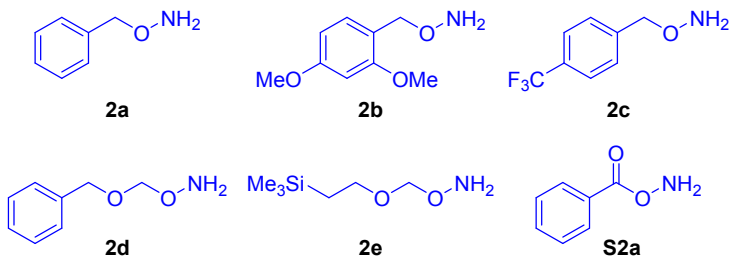


entry	additive	**3aa** (%)	ee (%)
1	none	80	88
2	HCO_2H	0	-
3	$MeCO_2H$	57	91
4	$^tBuCO_2H$	77	87
5	***$PhCO_2H$***	***76***	***93***
6	$TsOH{\cdot}H_2O$	0	-

Table S4. Investigation of Nucleophiles



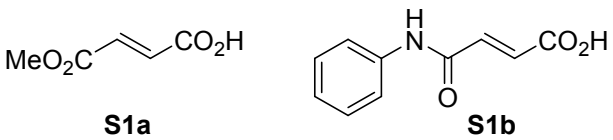
entry	nucleophile	**3aa** (%)	ee (%)
1	**2a**	76	93
2	**2b**	50	74
3	**2c**	64	96
4	**2d**	60	87
5[a]	**2e**	70	85
6	**S2a**	0	-



[a]Ee was determined after *N*-benzoylation.

Figure S1. Unsuccessful Substrates

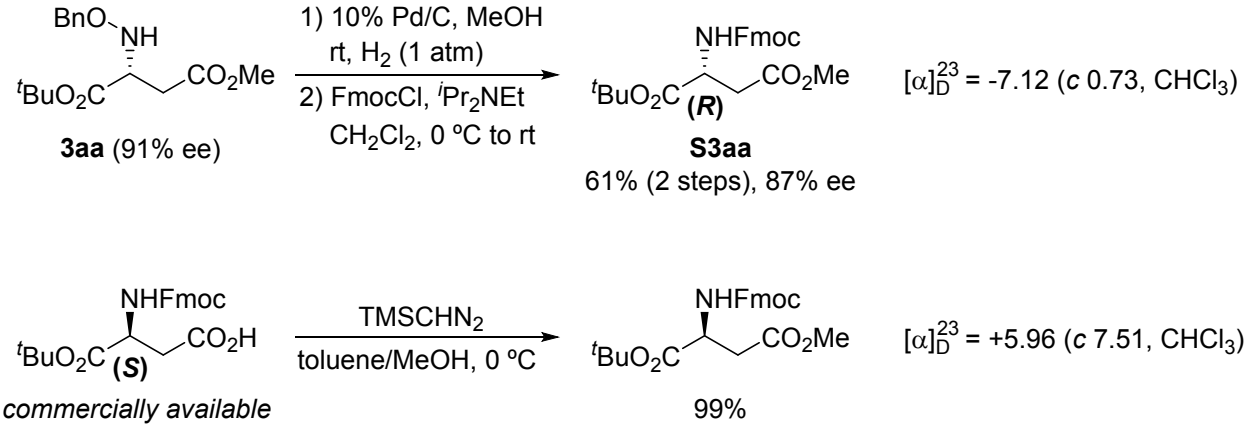
Monomethyl fumarate (**S1a**) and fumaryl monoanilide (**S1b**) did not undergo the aza-Michael addition, probably due to low solubility in CCl_4.



(A-2) Determination of Stereochemistry

The aza-Michael adduct **3aa** was converted into *N*-Fmoc-aspartic diester **S3aa** and the stereochemistry was determined as *R* configuration by comparison of HPLC charts and optical rotations with (*S*)-*N*-Fmoc-aspartic diester derived from the commercially available mono-*tert*-butyl-L-aspartate (Scheme S1).

Scheme S1



(B) General

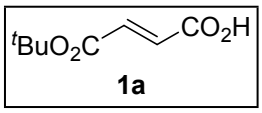
All manipulations were carried out under argon atmosphere unless otherwise noted. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 Fourier transform infrared spectrophotometer. NMR spectra were recorded on a JEOL ECP-400 spectrometer and JEOL ECA-500 spectrometer, operating at 400 MHz (^{1}H) or 100 MHz (^{13}C) and 500 MHz (^{1}H) or 125 MHz (^{13}C), respectively. Chemical shifts in $CDCl_3$, DMSO-d_6, and CD_3OD were reported in the scale relative to $CHCl_3$ (7.26 ppm), DMSO (2.50 ppm), and MeOH (3.31 ppm) for ^{1}H NMR, and to $CDCl_3$ (77.0 ppm) for ^{13}C NMR as internal references, respectively. NMR data are reported as follows: chemical shifts, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, quin: quintet, m: multiplet, br: broad signal), coupling constant (Hz), and integration. ESI-HRMS spectra were measured on a Shimadzu LCMS-IT-TOF fitted with an ESI. Optical rotations were measured on a JASCO P-2200 digital polarimeter with a path length of 1 cm; concentrations are quoted in grams per 100 mL. $[\alpha]_D$values are measured in 10^{-1} deg cm^2/g. Chiral HPLC analyses were carried out using a SHIMADZU DGU-20A$_5$. Column chromatography was performed with Cica silica gel 60N (40-100 μm, spherical, neutral). Dry solvents were purchased from Wako Pure Chemical Industries, Ltd. and used as received. Organocatalysts **A**-**F** were prepared according to our developed procedures.[1]

(C) Materials and Methods

(C-1) Preparation of Substrates

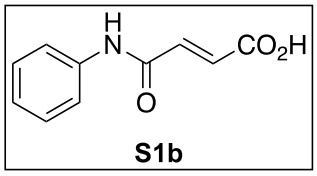
Monoethyl fumarate (**1c**) was purchased from Tokyo Chemical Industry Co., Ltd. Monomethyl fumarate (**S1a**) was purchased from Sigma-Aldrich Co. LLC. mono-*tert*-butyl fumarate (**1a**)[2] and (*E*)-4-oxo-4-(phenylamino)but-2-enoic acid (**S1b**)[3] were prepared according to the reported procedures.

Mono-*tert*-butyl fumarate (1a)[2]: White solids.



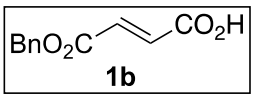
^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.87 (d, J = 15.6 Hz, 1H), 6.76 (d, J = 15.6 Hz, 1H), 1.52 (s, 9H) ppm.

(*E*)-4-Oxo-4-(phenylamino)but-2-enoic acid (S1b)[3]: White solids.



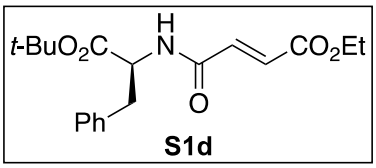
IR (neat) $\tilde{\nu}$: 1696, 1654 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ: 12.99 (br s, 1H), 10.51 (s, 1H), 7.67 (d, J = 8.0 Hz, 2H), 7.34 (t, J = 7.6 Hz, 2H), 7.14 (d, J = 15.2 Hz, 1H), 7.09 (t, J = 7.6 Hz, 1H), 6.65 (d, J = 15.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ: 166.4, 161.6, 138.6, 137.2, 130.8, 128.9, 124.0, 119.4 ppm; HRMS (ESI) *m/z* calcd. for $[M-H]^-$: 190.0510, found: 190.0521.

Monobenzyl fumarate (1b)[4]: To a solution of benzyl *tert*-butyl fumarate[5] (262.1 mg, 1.0 mmol, 1 equiv) in CH_2Cl_2 (4.0 mL) was added TFA (1.8 mL) and stirred at room temperature for 7 h. The mixture was concentrated, and the resulting solids were recrystallised from CH_2Cl_2 and hexane to afford **1b** as white solids (138.4 mg, 0.67 mmol, 67%).



IR (neat) $\tilde{\nu}$: 2940, 1719, 1694 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.39-7.34 (m, 5H), 6.99 (d, J = 16.0 Hz, 1H), 6.88 (d, J = 16.0 Hz, 1H), 5.25 (s, 2H) ppm.

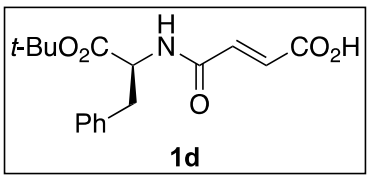
Ethyl (*S*,*E*)-4-((1-(*tert*-butoxy)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobut-2-enoate (S1d):



A mixture of L-phenylalanine *tert*-butyl ester hydrochloride[6] (1.32 g, 6.0 mmol, 1.0 equiv), monoethyl fumarate (944.0 mg, 6.6 mmol, 1.1 equiv), HOBt (972.0 mg, 7.2 mmol, 1.2 equiv), Et_3N (1.82 g, 18.0 mmol, 3.0 equiv) and EDCI (1.38 g, 7.2 mmol, 1.2 equiv) in DMF (30 mL) was stirred at room temperature for 20 h. The solution was diluted with brine (20 mL) and extracted with Et_2O (20 mL, 2 times). The combined organic phase was dried over Na_2SO_4 followed by filtration and concentration under reduced pressure. The residue was then purified by silica-gel column chromatography (eluent: hexane/EtOAc, 3:1) to afford **S1d** as white solids (1.43 g, 4.12 mmol, 67%).

m.p. 139.3-140.0 °C; $[\alpha]_D^{19}$ 106.9 (*c* 0.89, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3312, 1734, 1716, 1637 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.29-7.22 (m, 3H), 7.14 (d, J = 6.0 Hz, 2H), 6.92 (d, J = 15.5 Hz, 1H), 6.80 (d, J = 15.5 Hz, 1H), 6.45 (d, J = 7.5 Hz, 1H), 4.84 (dt, J = 7.0, 6.0 Hz, 1H), 4.22 (q, J = 7.5 Hz, 2H), 3.14 (d, J = 6.0 Hz, 2H), 1.42 (s, 9H), 1.30 (t, J = 7.5 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.2, 165.5, 163.0, 135.9, 130.9, 129.6, 128.5, 127.2, 82.9, 61.3, 53.9, 37.9, 28.0, 14.2 ppm; HRMS (ESI) *m/z* calcd. for $C_{19}H_{25}NO_5$ $[M+Na]^+$: 370.1625, found: 370.1588.

(*S*,*E*)-4-((1-(*tert*-Butoxy)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobut-2-enoic acid (1d): To a solution

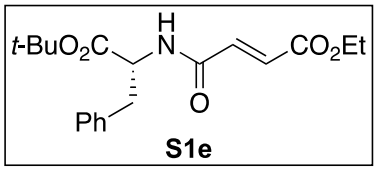


1d

of **S1d** (1.43 g, 4.12 mmol, 1.0 equiv) in THF (20 mL) and water (8.0 mL) was added LiOH (172.8 mg, 4.12 mmol, 1.0 equiv) and stirred at room temperature for 12 h. The mixture was washed with Et_2O, and the aqueous phase was acidified with 1 M HCl aq. The solution was extracted with EtOAc (20 mL, 2 times) and the combined organic layer was washed with brine. After drying over Na_2SO_4 followed by filtration, the solvent wasremoved under reduced pressure to afford **1d** as white solids (565.3 mg, 1.77 mmol, 43%).

m.p. 118.7-119.1°C; $[\alpha]_D^{20}$ 105.8 (*c* 0.68, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3350, 1726, 1659, 1642cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.29-7.24 (m, 3 H), 7.15-7.14 (m, 2 H), 7.00 (d, *J* = 15.5 Hz, 1H), 6.83 (d, *J* = 7.5 Hz, 1H), 6.82 (d, *J* = 15.0 Hz, 1H), 4.89 (dt, *J* = 8.0, 7.0 Hz, 1H), 3.13 (d, *J* = 6.0 Hz, 2H), 1.42 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.9, 169.4, 163.1, 137.6, 135.7, 130.3, 129.6, 128.6, 127.3, 83.4, 54.0, 38.1, 28.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{17}H_{21}NO_5$ $[M+Na]^+$: 342.1312, found: 342.1295.

Ethyl (*R*,*E*)-4-((1-(*tert*-butoxy)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobut-2-enoate (S1e):

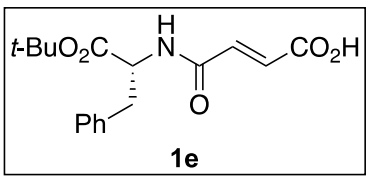


S1e

A mixture of D-phenylalanine *t*-butyl ester hydrochloride[6] (1.32 g, 6.0 mmol, 1.0 equiv), monoethyl fumarate (944.0 mg, 6.6 mmol, 1.1 equiv), HOBt (972.0 mg, 7.2 mmol, 1.2 equiv), Et_3N (1.82 g, 18.0 mmol, 3.0 equiv) and EDCI (1.38 g, 7.2 mmol, 1.2 equiv) in DMF (30 mL) was stirred at room temperature for 20 h. The solution was diluted with brine (20 mL) and extracted with Et_2O (20 mL, 2 times). The combined organic phase was dried over Na_2SO_4 followed by filtration and concentration under reduced pressure. The residue was then purified by silica-gel column chromatography (eluent: hexane/EtOAc, 3:1) to afford **S1d** as white solids (1.46 g, 4.23 mmol, 70%).

m.p. 135.5-137.8 °C; $[\alpha]_D^{18}$ - 91.3 (*c* 0.94, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3310, 1734, 1716, 1636 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.27-7.22 (m, 3H), 7.15-7.13 (m, 2H), 6.94 (d, *J* = 15.5 Hz, 1H), 6.81 (d, *J* = 14.5 Hz, 1H), 6.54 (d, *J* = 7.5 Hz, 1H), 4.85 (dt, *J* = 7.5, 6.0 Hz, 1H), 4.21 (q, *J* = 7.0 Hz, 2H), 3.14 (d, *J* = 6.0 Hz, 2H), 1.41 (s, 9H), 1.29 (t, *J* = 7.5 Hz, 3H), ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.3, 165.5, 163.0, 135.95, 135.91, 130.9, 129.5, 128.5, 127.1, 82.8, 61.3, 53.9, 37.9, 28.0, 14.2 ppm; HRMS (ESI) *m/z* calcd. for $C_{19}H_{25}NO_5$ $[M+Na]^+$: 370.1625, found: 370.1576.

(*R*,*E*)-4-((1-(*tert*-Butoxy)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobut-2-enoic acid (1e): To a solution



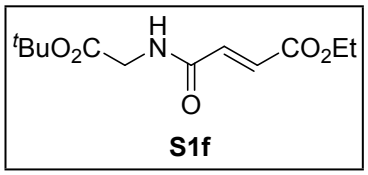
1e

of **S1e** (1.46 g, 4.23 mmol, 1.0 equiv) in THF (20 mL) and water (8.0 mL) was added LiOH. (177.4 mg, 4.23 mmol, 1.0 equiv) and stirred at room temperature for 12 h. The mixture was washed with Et_2O, and the aqueous phase was acidified with 1 M HCl aq. The solution was extracted with EtOAc (20 mL, 2 times) and the combined organic layer was washed with brine. After drying over Na_2SO_4 followed by filtration, the solvent was removed under reduced pressure to afford **1e** as white solids (855.0 mg, 2.67 mmol, 65 %).

m.p. 118.6-119.2°C; $[\alpha]_D^{21}$ - 95.0 (*c* 0.48, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3351, 1726, 1660, 1642cm^{-1}; ^{1}H NMR (500

MHz, $CDCl_3$) δ: 7.29-7.24 (m, 3 H), 7.14 (d, J = 7.0 Hz, 2 H), 6.99 (d, J = 15.5 Hz, 1H), 6.81 (d, J = 15.0 Hz, 1H), 6.74 (d, J = 8.0 Hz, 1H), 4.88 (dt, J = 8.0, 6.0 Hz, 1H), 3.14 (d, J = 6.5 Hz, 2H), 1.42 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 170.9, 169.4, 163.0, 137.6, 130.2, 129.6, 128.6, 127.3, 83.4, 54.0, 38.0, 28.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{17}H_{21}NO_5$ $[M+Na]^+$: 342.1312, found: 342.1291.

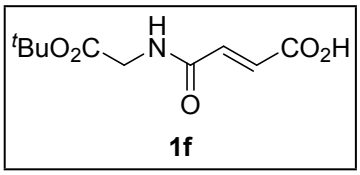
Ethyl (*E*)-4-((*tert*-butoxycarbonylmethyl)amino)-4-oxobut-2-enoate (S1f): A mixture of glycine *tert*-butyl ester hydrochloride (835.0 mg, 4.98 mmol, 1.0 equiv), monoethyl fumarate (788.4 mg, 5.47 mmol, 1.1 equiv), HOBt (1.01 g, 7.47 mmol, 1.5 equiv), and EDCI (1.43 g, 7.47 mmol, 1.5 equiv) in DMF (13.5 mL) was stirred at room temperature for 20 h. The solution was diluted with brine (30 mL) and extracted with Et_2O (50 mL, 3 times). The combined organic phase was dried over Na_2SO_4 followed by filtration and concentration under reduced pressure. The residue was then purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:1) to afford **S1f** as yellow oil (716.7 mg, 2.78 mmol, 56%).



S1f

IR (neat) $\tilde{\nu}$: 3301, 2980, 1724, 1668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.94 (d, J = 15.0 Hz, 1H), 6.82 (d, J =15.0 Hz, 1H), 4.24 (q, J = 7.0 Hz, 2H), 4.03 (d, J = 4.5 Hz, 2H), 1.47 (s, 9H), 1.31 (t, J = 6.5 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 168.6, 165.5, 163.6, 135.5, 131.1, 82.9, 61.3, 42.4, 28.1, 14.2 ppm; HRMS (ESI) *m/z* calcd. for $[M+Na]^+$: 280.1155, found: 280.1157.

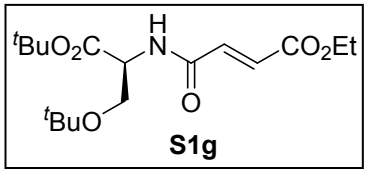
(*E*)-4-((*tert*-Butoxycarbonylmethyl)amino)-4-oxobut-2-enoic acid (1f): A solution of **S1f** (716.0 mg, 2.78 mmol, 1 equiv) in THF (14 mL) was treated with 1 M LiOH aq. (2.78 mL, 2.78 mmol, 1.0 equiv) and stirred at ambient temperature for 4 h. The mixture was acidified with 1 M HCl aq. and extracted with $CHCl_3$ (30 mL, 3 times). After drying over Na_2SO_4 followed by filtration, the solvent was removed under reduce pressure to afford **1f** as white solids (366.7 mg, 1.60 mmol, 60%).



1f

m.p. 229.4 ˚C (decomp.); IR (neat) $\tilde{\nu}$: 3339, 2868, 1732, 1689, 1658, 1637 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.02 (d, J = 15.5 Hz, 1H), 6.84 (d, J = 15.5 Hz, 1H), 6.54 (br s, 1H), 4.06 (d, J = 4.5 Hz, 2H), 1.48 (s, 9H) ppm; ^{13}C NMR (125 MHz, CD_3OD) δ: 168.6, 166.9, 165.3, 135.6, 130.5, 81.7, 41.6, 26.9 ppm; HRMS (ESI) *m/z* calcd. for $[M-H]^-$: 228.0877, found: 228.0868.

Ethyl (*S*,*E*)-4-((1,3-bis(*tert*-butoxy)-1-oxopropan-2yl)amino)-4-oxobut-2-enoate (S1g): A mixture of *O*-*tert*-butyl-L-serine *tert*-butyl ester hydrochloride (2.53 g, 10.0 mmol, 1.0 equiv), monoethyl fumarate (1.72 g, 12.0 mmol, 1.2 equiv), HOBt (1.62 g, 12.0 mmol, 1.2 equiv), and EDCI (2.87 g, 15.0 mmol, 1.5 equiv) in DMF (27 mL) was stirred at room temperature for 12 h. The solution was diluted with brine (50 mL) and extracted with Et_2O (50 mL, 3 times). The combined organic phase was dried over Na_2SO_4 followed by filtration and concentration under reduced pressure. The residue was then purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:1) to afford **S1g** as white solids (3.06 g, 8.91 mmol, 89%).

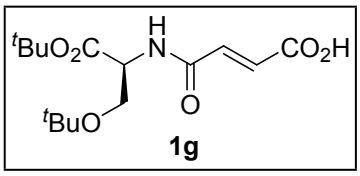


S1g

m.p. 79.4- 80.5 ˚C; $[\alpha]_D^{25}$ 43.2 (*c* 0.45, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3309, 2981, 1741, 1715, 1656 cm^{-1}; ^{1}H NMR (125

MHz, $CDCl_3$) δ: 6.99 (d, J = 15.5 Hz, 1H), 6.96 (d, J = 8.5 Hz, 1H), 4.60 (dt, J = 8.0, 3.0 Hz, 1H), 4.13 (q, J = 7.0 Hz, 2H), 3.69 (dd, J = 8.0, 3.0 Hz, 1H), 3.46 (dd, J = 8.0, 3.0 Hz, 1H), 1.35 (s, 9H), 1.18 (t, J = 7.0 Hz, 3H), 1.01 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 169.0, 165.5, 163.2, 136.3, 130.5, 81.9, 73.0, 62.1, 61.1, 53.5, 27.9, 27.2, 14.1 ppm; HRMS (ESI) *m/z* calcd. for $C_{17}H_{29}NO_6$ $[M+Na]^+$: 366.1887, found: 366.1861.

(*S*,*E*)-4-((1,3-Bis(*tert*-butoxy)-1-oxopropan-2-yl)amino)-4-oxobut-2-enoic acid (1g): A solution of **S1g** (1.03 g, 3.0 mmol, 1.0 equiv) in THF (15 mL) was treated with 1 M LiOH aq. (3.0 mL, 3.0 mmol, 1.0 equiv) and stirred at ambient temperature for 4 h. The mixture was acidified with 1 M HCl aq. and extracted with $CHCl_3$ (20 mL, 3 times). After drying over Na_2SO_4 followed by filtration, the solvent was removed to afford **1g** as white solids (836.9 mg, 2.65 mmol, 88%).



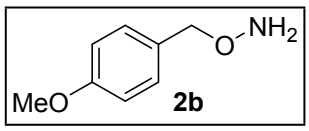
1g

m.p. 165.5-167.9°C; $[\alpha]_D^{23}$ 25.6 (*c* 0.42, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3331, 3074, 1720, 1706, 1631 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.19 (d, J = 8.5 Hz, 1H), 7.07 (d, J = 15.5 Hz, 1H), 6.88 (d, J = 15.5 Hz, 1H), 4.73 (dt, J = 9.0, 3.0 Hz, 1H), 3.80 (dd, J = 9.0, 3.0 Hz, 1H), 3.56 (dd, J = 9.0, 3.0 Hz, 1H), 1.45 (s, 9H), 1.12 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 169.7, 168.8, 137.3, 130.5, 82.8, 73.5, 62.2, 53.6, 28.0, 27.3 ppm; HRMS (ESI) *m/z* calcd. for $C_{15}H_{25}NO_6$[M+Na]$^+$: 338.1574, found: 338.1554.

(C-2) Preparation of Nucleophiles

O-benzylhydroxylamine (**2a**) was prepared by neutralization of $BnONH_2$·HCl by 4 M NaOH aq. After extraction with $CHCl_3$, general work up and dried under vacuum to afford **2a**. *O*-Benzoylhydroxylamine (**S2a**) was prepared according to the reported procedure.[8]

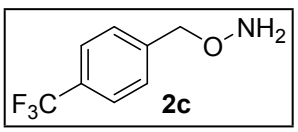
***O*-(4-Methoxybenzyl)hydroxylamine (2b)**: A mixture of *N*-hydroxyphthalimide (1.80 g, 11.0 mmol, 1.1 equiv), 4-methoxybenzyl chloride (1.86 g, 10.0 mmol, 1.0 equiv), and Et_3N (1.22 g, 12.1 mmol, 1.1 equiv) in CH_2Cl_2 (25 mL) was stirred at room temperature for 4 h. The suspension was washed with brine (20 mL, 3 times) and the combined organic phase was dried over Na_2SO_4. After the solvent was removed under reduced pressure, the residue was dissolved in $CHCl_3$/MeOH = 3:1 (50 mL). To the solution was added to N_2H_4·H_2O (750.9 mg, 15.0 mmol, 1.5 equiv) and stirred at room temperature for 2 h. The mixture was filtered through a pad of Celite® and the filtrate was concentrated under reduced pressure. The residue was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:1) to afford **2b** as colorless oil (1.10 g, 6.2 mmol, 62%).



2b

IR (neat) $\tilde{\nu}$: 2977, 2917 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.29 (d, J = 9.0 Hz, 2H), 6.89 (d, J = 9.0 Hz, 2H), 5.33 (br s, 2H), 4.61 (s, 2H), 3.80 (s, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 159.5, 130.1, 129.4, 113.9,113.7, 77.7, 53.3 ppm; HRMS (ESI) *m/z* calcd. for C_8H_9NO, $[M]^+$: 176.0682, found: 176.0556.

***O*-(4-Trifluoromethylbenzyl)hydroxylamine (2c)**: **2c** was prepared through the procedure analogous to that of **2b**. Alkylation was performed using *N*-hydroxyphthalimide (1.35 g, 7.0 mmol, 1.4 equiv), 4-(trifluoromethyl)benzyl chloride (815.0 mg, 5.0 mmol, 1.0

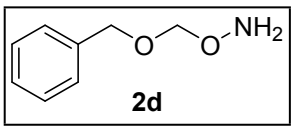


2c

equiv), and Et_3N (708.3 mg, 7.0 mmol, 1.4 equiv) in CH_2Cl_2 (20 mL). Deprotection of phthalimide was conducted with $N_2H_4 \cdot H_2O$ (525.6 mg, 10.5 mmol, 1.5 equiv) in CH_3Cl/MeOH = 3:1 (15 mL), which afforded **2c** as colorless oil (810.0 mg, 4.2 mmol, 84%).

IR (neat) $\tilde{\nu}$: 2940, 1323 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.63 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 5.48 (br s, 2H), 4.75 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 141.7, 130.0 (q, J = 32.5 Hz), 128.3, 125.4 (q, J = 3.9 Hz), 76.9 ppm; HRMS (ESI) *m/z* calcd. for C_8H_8FNO, $[M+H]^+$: 192.0631, found: 192.0579.

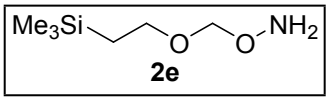
***O*-(Benzyloxymethyl)hydroxylamine (2d)**: **2d** was prepared through the procedure analogous to that of **2b**. Alkylation was performed using *N*-hydroxyphthalimide (322.6 mg. 2.0 mmol, 1.0 equiv), chloromethyl benzyl ether (439.1 mg, 2.8 mmol, 1.4 equiv), and Et_3N (286.0 mg, 2.8 mmol, 1.4 equiv) in CH_2Cl_2 (4.5 mL). Deprotection of phthalimide was conducted with $N_2H_4 \cdot H_2O$ (150.2 mg, 3.0 mmol, 1.5 equiv) in CH_3Cl/MeOH = 3:1 (5 mL), which afforded **2d** as colorless oil (213.4 mg, 1.4 mmol, 70%).



2d

IR (neat) $\tilde{\nu}$: 2871 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.38-7.34 (m, 4H), 7.32-7.29 (m, 1H), 5.51 (br s, 2H), 4.85 (s, 2H), 4.67 (s, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 137.1, 128.4, 127.7, 98.5, 69.9 ppm; HRMS (ESI) *m/z* calcd. for $C_8H_{12}NO_2$, $[M]^+$: 154.0865, found: 154.0805.

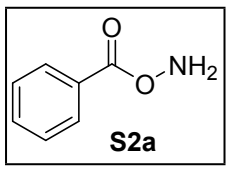
***O*-((2-Trimethylsilylethoxy)methyl)hydroxylamine (2e)**: **2e** was prepared through the procedure analogous to that of **2b**. Alkylation was performed using *N*-hydroxyphthalimide (815.5 mg. 5.0 mmol, 1.0 equiv), chloromethyl 2-(trimethylsilyl)ethyl ether (1.16 g, 7.0 mmol, 1.4 equiv), and Et_3N (708.3 mg, 7.0 mmol, 1.4 equiv) in CH_2Cl_2 (11.4 mL). Deprotection of phthalimide was conducted with $N_2H_4 \cdot H_2O$ (375.5 mg, 7.5 mmol, 1.5 equiv) in CH_3Cl/MeOH = 3:1 (10 mL), which afforded **2e** as colorless oil (550.5 mg, 3.1 mmol, 62%).



2e

IR (neat) $\tilde{\nu}$: 2953 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 5.47 (br s, 2H), 4.73 (s, 2H), 3.64 (t, J = 8.0 Hz, 2H), 0.96 (t, J = 8.0 Hz, 2H), 0.01 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 98.8, 65.7, 18.3 ppm; HRMS (ESI) *m/z* calcd. for $C_6H_{17}NO_2Si$, $[M+H]^+$: 164.1107, found: 164.1018.

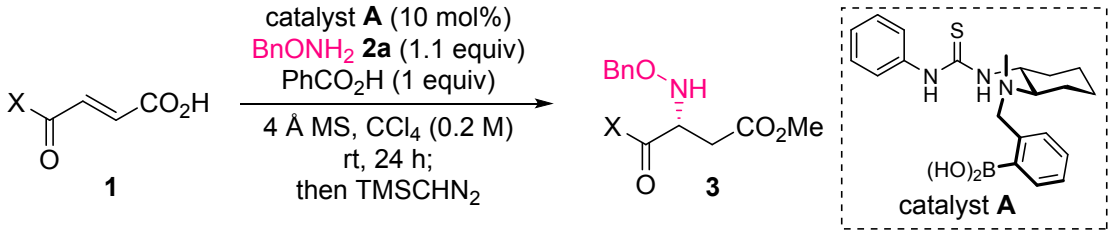
***O*-Benzoylhydroxylamine (S2a)**[7]: Colorless oil.



S2a

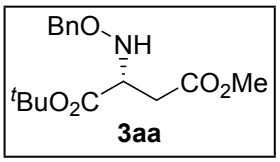
^1H NMR (400 MHz, $CDCl_3$) δ: 8.00 (d, J = 2.0 Hz, 2H), 7.58 (t, J = 7.6 Hz, 1H), 7.45 (t, J = 7.6 Hz, 2H), 6.60 (br s, 2H) ppm.

(C-3) General Procedure for Catalytic Aza-Michael Addition



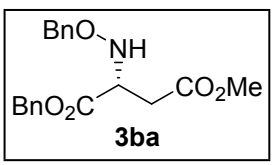
Prior to the reaction, 4 Å MS was dried by heat-gun (>300 ºC, 15 min) under vacuum (*ca*. 2 Torr). To an oven-dried 10 mL screw tube were placed an organocatalyst (10 mol%), substrate **1** (1.0 equiv), and benzoic acid (1.0 equiv), which were suspended in CCl_4 (0.2 M) and sealed with a Teflon-coated screw cap. After stirring at room temperature for 10 min, pre-heated 4 Å MS (500 mg/mmol) was added and the tube was capped and further stirred for 5 min. Hydroxylamine **2** (1.1 equiv) was then added and the system was closed again followed by stirring at ambient temperature for the indicated time. After the reaction progress was monitored by ^{1}H NMR analysis (a small amount of the mixture was transferred into an NMR tube). The reaction mixture was diluted in toluene/MeOH (3:1, 1 mL) and treated with $TMSCHN_2$ (10% in hexane, 1 mL) and stirred for 30 min. The excess $TMSCHN_2$ was quenched with AcOH, then the mixture was filtered through Celite® and the cake was washed with MeOH. After the solvent was removed under reduced pressure, the residue was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:1) to afford the product **3**. The ee of **3** was estimated by chiral HPLC analysis.

1-*tert*-Butyl 4-methyl *N*-benzyloxy-D-aspartate (3aa): The reaction was carried out using **1a** (34.4 mg, 200 µmol, 1.0 equiv) and **2a** (27.0 mg, 220 µmol, 1.1 equiv) in the presence of catalyst **A** (7.9 mg, 20 µmol, 10 mol%), benzoic acid (24.4 mg, 200 µmol, 1.0 equiv) and 4 Å MS (100.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 3:1) afforded **3aa** as colorless oil (40.5 mg, 164 µmol, 80%, 93% ee).



$[\alpha]_D^{24}$ +5.4 (*c* 1.00, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3275, 1731 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31 (m, 5H), 6.18 (br s, 1H), 4.69 (s, 2H), 3.92 (br s, 1H), 3.68 (s, 3H), 2.76 (dd, J = 16.0, 6.4 Hz, 1H), 2.63 (dd, J = 16.0, 6.4 Hz, 1H), 1.47 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.3, 170.6, 137.5, 128.3, 128.2 127.7, 76.3, 64.2, 60.1, 51.8, 34.3, 27.9 ppm; HRMS (ESI) *m/z* calcd. for $C_{16}H_{23}NO_5$, $[M+Na]^+$: 332.1468, found: 332.1470. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 99/1, flow rate: 1.0 mL/min. detector: UV at 220 nm), t_R = 12.0 min (minor), 10.5 min (major).

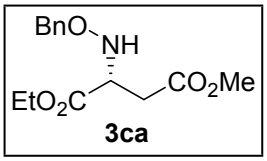
1-Benzyl 4-methyl *N*-benzyloxy-D-aspartate (3ba): The reaction was carried out using **1b** (82.4 mg, 400 µmol, 1.0 equiv) and **2a** (54.2 mg, 440 µmol, 1.1 equiv) in the presence of catalyst **A** (15.9 mg, 40 µmol, 10 mol%), benzoic acid (48.8 mg, 400 µmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 2:1) afforded **3ba** as colorless oil (69.6 mg, 201 µmol, 50%, 91% ee).



$[\alpha]_D^{26}$ +4.2 (*c* 0.94, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1738 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34 (m, 10H), 6.26 (br

s, 1H), 5.23 (d, J = 12.0 Hz, 1H), 5.19 (d, J = 12.0 Hz, 1H), 4.71 (d, J = 12.0 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.09 (t, J = 7.0 Hz, 1H), 3.64 (s, 3H), 2.85 (dd, J = 16.0, 6.0 Hz, 1H), 2.70 (dd, J =16.0, 6.0 Hz, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.5, 171.2, 137.4, 135.4, 128.68, 128.60, 128.4, 128.3, 128.0, 76.6, 67.2, 60.2, 52.0, 34.2 ppm; HRMS (ESI) *m/z* calcd. for $C_{19}H_{21}NO_5$, $[M+Na]^+$: 366.1312, found: 366.1290. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 98/2, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 16.1 min (major), 17.4 min (minor).

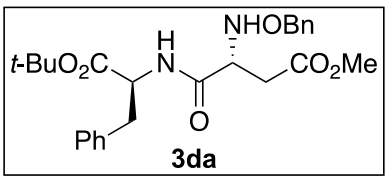
1-Ethyl 4-methyl *N*-benzyloxy-D-aspartate (3ca): The reaction was carried out using **1c** (57.6 mg, 400 μmol, 1.0 equiv) and **2a** (54.2 mg, 440 μmol, 1.1 equiv) in the presence of catalyst **A** (15.9 mg, 40 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 2:1) afforded **3ca** as colorless oil (55.2 mg, 197.6 μmol, 49%, 94% ee).



3ca

$[\alpha]_D^{26}$ 6.1 (c 1.04, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3265, 1732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.31 (m, 5H), 6.22 (br s, 1H), 4.69 (s, 2H), 4.23 (q, J = 6.8 Hz, 2H), 4.01 (t, J = 6.4 Hz, 1H), 3.68 (s, 3H), 2.81 (dd, J = 16.4, 6.4 Hz, 1H), 1.28 (t, J = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.5, 171.2, 137.4, 128.4, 128.3, 127.8, 76.5, 61.4, 60.0, 51.9, 34.1, 14.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{14}H_{19}NO_5$, $[M+Na]^+$: 304.1155, found: 304.1140. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK @, eluent: hexane/2-propanol = 99/1, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 16.9 min (major), 20.1 min (minor).

Methyl (*R*)-3-((benzyloxy)amino)-4-(((*S*)-1-(*tert*-butoxy)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobutanoate (3da): The reaction was carried out using **1d** (133.2 mg, 400 μmol, 1.0 equiv) and **2a** (54.2 mg, 440 μmol, 1.1 equiv) in the presence of catalyst **A** (15.9 mg, 40 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 2:1) afforded **3da** as colorless oil (120.0 mg, 263 μmol, 66%, 67:33 dr).

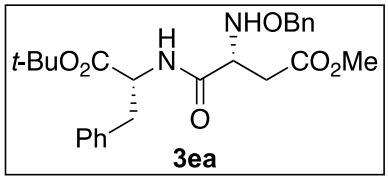


3da

For major diastereomer: $[\alpha]_D^{21}$ 39.8 (c 0.51, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3381, 1730, 1675 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34-7.14 (m, 10H), 6.19 (d, J = 5.5 Hz, 1H), 4.73 (dt, J = 7.5, 6.0 Hz, 1H), 4.68 (d, J = 12.0 Hz, 1H), 4.61 (d, J = 12.0 Hz, 1H), 3.81 (m, 1H), 3.66 (s, 3H), 3.11 (dd, J = 15.0, 6.0 Hz, 1H), 3.07 (dd, J = 15.0, 6.0 Hz, 1H), 2.87 (dd, J = 17.5, 9.0 Hz, 1H), 2.77 (dd, J = 17.0, 9.0 Hz, 1H), 1.40 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 172.5, 170.4, 170.2, 137.2, 136.3, 129.6, 128.57, 128.52, 128.4, 128.1, 127.0, 82.4, 76.3, 60.5, 53.6, 52.0, 38.2, 32.2, 28.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{25}H_{32}N_2O_6$, $[M+H]^+$: 457.2333, found: 457.2353.

For minor diastereomer: $[\alpha]_D^{21}$ 19.7 (c 0.60, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3388, 1732, 1674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.33-7.17 (m, 10H), 6.18 (d, J = 6.0 Hz, 1H), 4.73 (dt, J = 7.5, 6.0 Hz, 1H), 4.62 (d, J =

11.5 Hz, 1H), 4.59 (d, *J* = 11.5 Hz, 1H),3.82 (ddd, *J* = 8.0, 7.0, 4.5 Hz, 1H), 3.65 (s, 3H), 3.11 (dd, *J* = 14.0, 6.5 Hz, 1H), 3.08 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.83 (dd, *J* = 12.0, 4.5 Hz, 1H), 2.71 (dd, *J* = 12.0, 8.0 Hz, 1H), 1.44 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 172.3, 170.47, 170.42, 137.1, 136.2, 129.7, 128.4, 128.1, 127.0, 82.4, 76.2, 60.6, 53.6, 52.0, 38.1, 32.5, 28.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{25}H_{32}N_2O_6$, $[M+H]^+$: 457.2333, found: 457.2354.

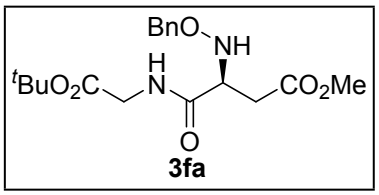


3ea

Methyl (*R*)-3-((benzyloxy)amino)-4-(((*R*)-1-(*tert*-butoxy)-1-oxo-3-phenylpropan-2-yl)amino)-4-oxobutanoate (3ea): The reaction was carried out using **1e** (133.2 mg, 400 μmol, 1.0 equiv) and **2a** (54.2 mg, 440 μmol, 1.1 equiv) in the presence of catalyst **A** (15.9 mg, 40 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 2:1) afforded **3ea** as colorless oil (128.2 mg, 280 μmol, 70%, 75:25 dr).

For major diastereomer: $[\alpha]_D^{21}$ - 15.0 (*c* 0.66, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3381, 1731, 1674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.34-7.16 (m, 10H), 6.19 (br s, 1H), 4.73 (dt, *J* = 7.5, 6.0 Hz, 1H), 4.61 (d, *J* = 11.5 Hz, 1H), 4.59 (d, *J* = 11.5 Hz, 1H), 3.82 (m, 1H), 3.66 (s, 3H), 3.11 (dd, *J* = 14.0, 6.5 Hz, 1H), 3.08 (dd, *J* = 14.0, 6.5 Hz, 1H), 2.83 (dd, *J* = 12.0, 4.5 Hz, 1H), 2.71 (dd, *J* = 17.0, 8.0 Hz, 1H), 1.41 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 172.3, 170.47, 170.42, 137.1, 136.2, 129.7, 128.5, 128.4, 128.1, 127.0, 82.4, 76.2, 60.6, 53.6, 52.0, 38.1, 32.5, 28.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{25}H_{32}N_2O_6$, $[M+H]^+$: 457.2333, found: 457.2328.

For minor diastereomer: $[\alpha]_D^{22}$ - 43.9 (*c* 0.57, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3383, 1729, 1674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.32-7.14 (m, 10H), 6.19 (d, *J* = 6.0 Hz, 1H), 4.74 (dt, *J* = 7.5, 6.5 Hz, 1H), 4.65 (d, *J* = 11.5 Hz, 1H), 4.59 (d, *J* = 11.5 Hz, 1H), 3.81 (m, 1H), 3.66 (s, 3H), 3.12 (dd, *J* = 14.0, 6.0 Hz, 1H), 3.07 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.87 (dd, *J* = 17.0, 5.0 Hz, 1H), 2.77 (dd, *J* = 17.5, 8.0 Hz, 1H), 1.40 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) *δ*: 172.5, 170.4, 170.2, 137.1, 136.3, 129.5, 128.5, 128.49, 128.46, 128.0, 127.0, 82.3, 76.2, 60.4, 53.6, 51.9, 38.1, 32.2, 28.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{25}H_{32}N_2O_6$, $[M+H]^+$: 457.2333, found: 457.2355.



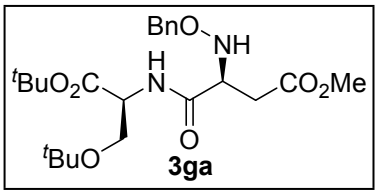
3fa

Methyl (*S*)-3-((benzyloxy)amino)-4-((*tert*-butoxycarbonylmethyl)amino)-4-oxobutanoate (3fa): The reaction was carried out using **1f** (91.6 mg, 400 μmol, 1.0 equiv) and **2a** (54.2 mg, 440 μmol, 1.1 equiv) in the presence of catalyst **ent-A** (15.9 mg, 40 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 2:1) afforded **3fa** as colorless oil (241.4 mg, 266 μmol, 66%, 63% ee).

$[\alpha]_D^{24}$ 4.6 (*c* 1.46, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1733, 1669 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.34-7.28 (m, 4H), 7.19 (m, 1H), 6.46 (br s, 1H), 4.73 (s, 2H), 4.03 (d, *J* = 5.5 Hz, 1H), 3.88 (dd, *J* = 5.0, 2.0 Hz, 1H), 3.85 (dd, *J* = 5.0, 2.0 Hz, 1H), 3.66 (s, 3H), 2.89 (dd, *J* = 17.0, 8.0 Hz), 2.78 (dd, *J* = 17.0, 8.0 Hz), 1.46 (s, 9H)

ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 172.5, 170.8, 168.7, 130.6, 128.7, 128.5, 128.1, 82.3, 76.2, 60.4, 52.0, 42.0, 32.3, 28.1 ppm; HRMS (ESI) *m/z* calcd. for $C_{18}H_{26}N_2O_6$, $[M+H]^+$: 367.1864, found: 367.1789. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 96/4, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 29.6 min (major), 27.7 min (minor).

Methyl (*R*)-3-((benzyloxy)amino)-4-(((*S*)-1,3-di-*tert*-butoxy-1-oxopropan-2-yl)amino)-4-oxobutanoate (3ga): The reaction was carried out using **1g** (126 mg, 400 μmol, 1.0 equiv) and **2a** (54.2 mg, 440 μmol, 1.1 equiv) in the presence of catalyst **ent-A** (15.9 mg, 40 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 2:1) afforded **3da** as colorless oil (366.6 mg, 322 μmol, 81%, 73:27 dr).

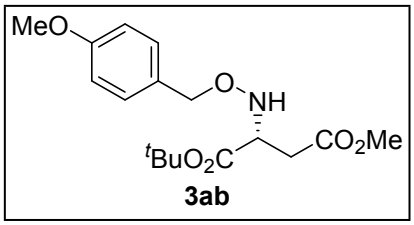


3ga

For major diastereomer: $[\alpha]_D^{21}$ 33.2 (*c* 1.02, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3403, 1735, 1679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.66 (d, *J* = 8.0 Hz, 1H), 7.37-7.31 (m, 5H), 6.26 (d, *J* = 10.0 Hz, 1H), 4.80 (dd, *J* = 15.0, 11.5 Hz, 2H), 4.60 (dt, *J* = 9.0, 2.5 Hz, 1H), 3.90 (dt, *J* = 7.5, 4.5 Hz, 1H), 3.81 (dd, *J* = 17.0, 4.5 Hz, 1H), 3.67 (s, 3H), 3.54 (dd, *J* = 8.5, 3.0 Hz, 1H), 2.91 (dd, *J* = 17.0, 4.5 Hz, 1H), 2.76 (dd, *J* = 17.0, 9.0 Hz, 1H), 1.47 (s, 9H), 1.13 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 172.4, 170.5, 169.2, 137.3, 128.6, 128.5, 128.0, 81.8, 76.4, 73.1, 60.7, 53.2, 52.0, 32.6, 28.1, 27.4 ppm; HRMS (ESI) *m/z* calcd. for $C_{25}H_{32}N_2O_6$, $[M+H]^+$: 453.2595, found: 453.2570.

For minor diastereomer: $[\alpha]_D^{21}$ 1.0 (*c* 0.96, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3405, 1737, 1679 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.61 (d, *J* = 8.5 Hz, 1H), 7.34-7.26 (m, 5H), 6.26 (d, *J* = 6.5 Hz, 1H), 4.78 (dd, *J* = 17.0, 11.0 Hz, 2H), 4.61 (dt, *J* = 8.5, 2.5 Hz, 1H), 3.91 (ddd, *J* = 9.0, 6.5, 3.0 Hz, 1H), 3.81 (dd, *J* = 9.0, 3.0 Hz, 1H), 3.67 (s, 3H), 3.54 (dd, *J* = 9.0, 3.0 Hz, 1H), 2.93 (dd, *J* = 17.5, 5.0 Hz, 1H), 2.80 (dd, *J* = 17.5, 9.0 Hz, 1H), 1.47 (s, 9H), 1.12 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 172.4, 170.5, 169.3, 137.3, 128.58, 128.51, 128.0, 81.9, 76.4, 73.1, 62.2, 60.5, 53.2, 51.9, 32.3, 28.1, 27.4 ppm; HRMS (ESI) *m/z* calcd. for $C_{25}H_{32}N_2O_6$, $[M+H]^+$: 453.2595, found: 453.2524.

1-*tert*-Butyl 4-methyl *N*-(4-methoxybenzyl)oxy-D-aspartate (3ab): The reaction was carried out using **1a** (68.8 mg, 400 μmol, 1.0 equiv) and **2b** (67.4 mg, 440 μmol, 1.1 equiv) in the presence of catalyst **A** (15.9 mg, 40 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 2:1) afforded **3ab** as colorless oil (101.8 mg, 300 μmol, 75%, 89% ee).

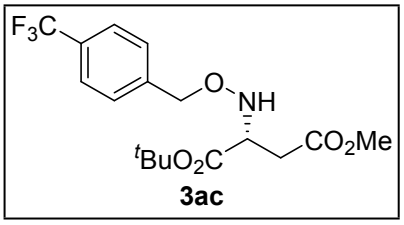


3ab

$[\alpha]_D^{23}$ 8.2 (*c* 0.68, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1732 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.26 (t, *J* = 7.0 Hz, 2H), 6.86 (d, *J* = 7.0 Hz, 2H), 6.12 (br s, 1H), 4.61 (s, 2H), 3.80 (s, 3H), 3.68 (s, 3H), 2.75 (dd, *J* = 16.0, 7.5 Hz, 1H), 2.62 (dd, *J* = 16.0, 7.5 Hz, 1H), 1.46 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.4, 170.7, 159.4,

130.1, 129.7, 113.7, 82.1, 76.1, 60.7, 55.3, 51.9, 34.4, 28.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{17}H_{25}NO_6$, $[M+H]^+$: 340.1755, found: 340.1744. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 98/2, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 13.3 min (major), 14.1 min (minor).

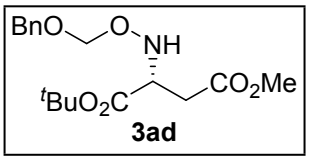
1-*tert*-Butyl 4-methyl *N*-(4-trifluoromethyl)benzyloxy-D-aspartate (3ac): The reaction was carried out using **1a** (34.4 mg, 200 μmol, 1.0 equiv) and **2c** (42.0 mg, 220 μmol, 1.1 equiv) in the presence of catalyst **A** (7.9 mg, 20 μmol, 10 mol%) and benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 3:1) afforded **3ac** as colorless oil (48.2 mg, 128 μmol, 64%, 96% ee).



3ac

$[\alpha]_D^{25}$ 6.6 (*c* 1.90, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1732, 1324 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.60 (d, J = 8.0 Hz, 1H), 7.44 (d, J = 8.0 Hz, 1H), 6.25 (d, J = 6.0 Hz, 1H), 4.75 (s, 2H), 3.93 (dt, J = 6.0 Hz, 1H), 3.67 (s, 3H), 2.75 (dd, J = 16.0, 6.5 Hz, 1H), 2.61 (dd, J = 16.0, 6.5 Hz, 1H), 1.48 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.1, 170.5, 141.7, 129.9 (q, J = 32.6 Hz), 128.2, 125.2 (q, J = 3.7 Hz), 124.1 (q, J = 270 Hz), 82.2, 75.4, 60.7, 51.8, 51.7, 34.2, 27.9 ppm; HRMS (ESI) *m/z* calcd. for $C_{17}H_{22}NO_5F_3$, $[M+Na]^+$: 400.1342, found: 400.1333. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 99/1, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 15.8 min (minor), 20.2 min (major).

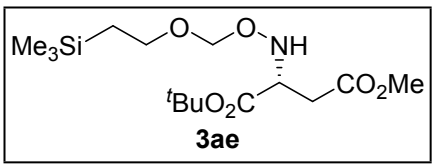
1-*tert*-Butyl 4-methyl *N*-(benzyloxy)methoxy-D-aspartate (3ad): The reaction was carried out using **1a** (34.4 mg, 200 μmol, 1.0 equiv) and **2d** (36.7 mg, 220 μmol, 1.1 equiv) in the presence of catalyst **A** (7.9 mg, 20 μmol, 10 mol%) and benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 3:1) afforded **3ad** as colorless oil (40.0 mg, 122 μmol, 60%, 87% ee).



3ad

$[\alpha]_D^{25}$ 4.4 (*c* 1.06, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.31 (m, 5H), 6.43 (d, J = 6.4 Hz, 1H), 4.86 (s, 2H), 4.65 (s, 2H), 3.98 (dt, J = 10.0, 6.4 Hz, 1H), 3.69 (s, 3H), 2.77 (dd, J = 16.4, 6.4 Hz, 1H), 2.67 (dd, J = 16.4, 6.4 Hz, 1H), 1.48 (s, 9H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ: 171.2, 170.6, 137.7, 128.4, 127.79, 127.67, 82.1, 69.9, 60.8, 51.8, 34.4, 27.9 ppm; HRMS (ESI) *m/z* calcd. for $C_{17}H_{25}NO_6$, $[M+Na]^+$: 362.1574, found: 362.1588. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 98/2, flow rate: 1.0 mL/min. detector: UV at 220 nm), t_R = 16.1 min (major), 17.4 min (minor).

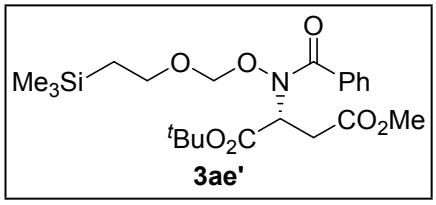
1-*tert*-Butyl 4-methyl *N*-(2-trimethylsilylethoxy)methoxy-D-aspartate (3ae): The reaction was carried out using **1a** (34.4 mg, 200 μmol, 1.0 equiv) and **2e** (33.6 mg, 220 μmol, 1.1 equiv) in the presence of catalyst **A** (7.9 mg, 20 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg)



3ae

for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 3:1) afforded **3ae** as colorless oil (48.9 mg, 142 μmol, 70%). Since **3ae** was not detectable on HPLC, *N*-benzoylation was conducted to estimate the ee of **3ae**.

$[\alpha]_D^{25}$ +4.3 (*c* 1.00, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1738 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ: 6.36 (d, J = 6.4 Hz, 1H), 4.75 (s, 2H), 3.94 (dt, J = 12.8 Hz, 6.4 Hz), 3.68 (s, 3H), 3.62 (t, J = 8.4 Hz, 2H), 1.45 (s, 9H), 0.94 (t, J = 8.4 Hz, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.2, 170.6, 97.7, 82.0, 65.7, 60.8, 51.8, 34.4, 27.9, 18.1 ppm; HRMS (ESI) *m/z* calcd. for $C_{15}H_{31}NO_6Si$, $[M+Na]^+$: 372.1813, found: 372.1820.

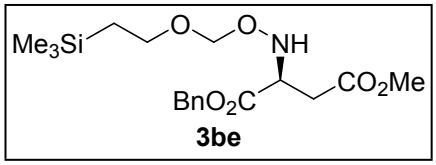


3ae'

1-*tert*-Butyl 4-methyl *N*-benzoyl-*N*-(2-trimethylsilylethoxy)methoxy-D-aspartate (3ae'): To a solution of **3ae** (34.9 mg, 100 μmol, 1.0 equiv) in EtOAc (1mL) were added BzCl (21.1 mg, 150 μmol, 1.5 equiv) and sat. $NaHCO_3$ aq. (1 mL) at 0 ºC. The mixture was allowed to warm to room temperature and stirred for 3 h. Added brine (2 mL) and extracted with EtOAc (5 mL, 2 times).
The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 5:1) afforded **3ae'** as colorless oil (38.8 mg, 85 μmol, 85%).

$[\alpha]_D^{25}$ 0.71 (*c* 5.84, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1736, 1648 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.67 (d, J = 7.0 Hz, 2H), 7.46 (t, J = 7.0 Hz, 1H), 7.41 (t, J = 7.0 Hz, 2H) 5.06 (br, 1H), 4.85 (br, 2H), 3.73 (s, 3H), 3.49 (s, 2H), 3.21 (dd, J = 17.0, 7.0 Hz, 1H), 2.97 (dd, J = 17.0, 7.0 Hz, 1H), 1.48 (s, 9H), 0.85 (t, J = 8.0 Hz, 2H), 0.018 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 198.7, 171.3, 167.6, 134.2, 130.9, 128.3, 128.2, 99.6, 82.9, 67.7, 61.1, 52.0, 34.0, 27.9, 17.9 ppm; HRMS (ESI) *m/z* calcd. for $C_{22}H_{35}NO_7Si$, $[M+H]^+$: 453.2111, found: 453.2183. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 1, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 18.9 min (major), 23.7 min (minor).

1-Benzyl 4-methyl *N*-(2-trimethylsilylethoxy)methoxy-L-aspartate (3be): The reaction was carried out using **1b** (82.5 mg, 400 μmol, 1.0 equiv) and **2e** (67.3 mg, 440 μmol, 1.1 equiv) in the presence of catalyst **ent-A** (15.9 mg, 40 μmol, 10 mol%), benzoic acid (48.8 mg, 400 μmol, 1.0 equiv) and 4 Å MS (200.0 mg) for 24 h. The crude product was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 3:1) afforded **3be** as colorless oil (268.4 mg, 284 μmol, 70%, 86% ee).

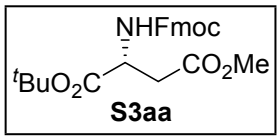


3be

$[\alpha]_D^{26}$ +4.7 (*c* 1.00, $CHCl_3$); IR (neat) $\tilde{\nu}$: 1739 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.35 (m, 5H), 6.42 (d J = 7.0 Hz, 1H), 5.21 (s, 2H), 4.76 (s, 2H), 4.12 (dt, J = 7.0, 6.0Hz, 1H), 3.65 (s, 3H), 3.62 (dt, J = 8.5, 1.0 Hz, 1H), 2.85 (dd, J = 16.0, 6.0Hz, 1H) 2.74 (dd, J = 16.0, 6.0 Hz, 1H), 0.94 (dt, J = 8.5, 1.2 Hz, 2H), 0.01 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.4, 170.9, 135.2, 128.5, 128.3, 128.2, 97.8, 67.1, 65.8, 60.2, 51.9, 34.1, 18.0 ppm; HRMS (ESI) *m/z* calcd. for $C_{18}H_{29}NO_6Si$, $[M+Na]^+$: 406.1656, found: 406.1643.

The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 99/1, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 16.4 min (major), 18.2 min (minor).

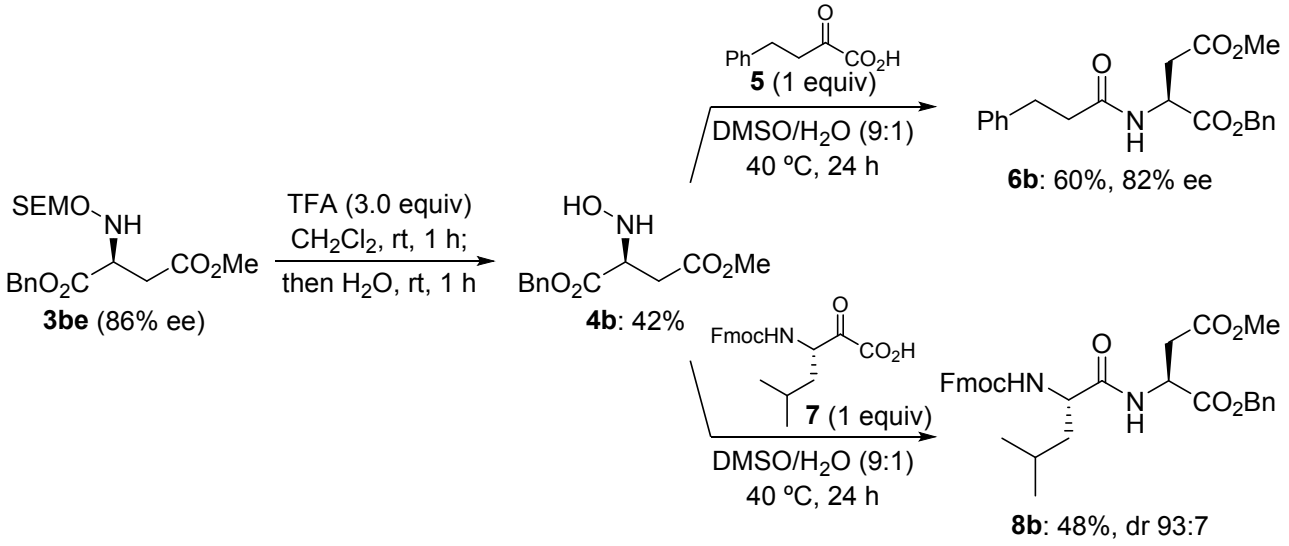
1-*tert*-Butyl 4-methyl 9*H*-fluoren-9-ylmethoxycarbonyl-D-aspartate (S3aa): **3aa** (25.3 mg 100 μmol, 1.0 equiv) was dissolved in MeOH (30 mL) and added to 10% Pd/C (80 mg) under an atmosphere of argon. The reaction was carefully flushed with hydrogen gas and stirred at room temperature for 5 h. The atmosphere was replaced with argon before filtration through a pad of Celite®□. The filtrate was concentrated under reduced pressure and the residue was dissolved in CH_2Cl_2 (1.0 mL). To the solution were added $^iPr_2NEt$ (64.6 mg, 500 μmol, 5.0 equiv) and FmocCl (25.8 mg, 120 μmol, 1.2 equiv). The resulting mixture was stirred at ambient temperature for 17 h, then the solvent was evaporated. The residue was purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:1) to afford **S3aa** as colorless oil (26.0 mg, 61 μmol, 61%).



S3aa

$[\alpha]_D^{23}$ - 7.1 (*c* 0.73, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3368, 1721 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ: 7.75 (d, *J* = 7.5 Hz, 2H), 7.60 (d, *J* = 7.5 Hz, 2H), 7.40 (t, *J* = 7.5 Hz, 2H), 5.80 (d, *J* = 8.5 Hz, 1H), 4.54 (dt, *J* = 8.5, 4.5 Hz, 1H), 4.38 (dt, *J* = 17.0, 7.0 Hz, 2H), 4.23 (t, *J* = 7.0 Hz, 1H), 3.71 (s, 3H), 3.00 (dd, *J* = 17.0, 4.0 Hz, 1H), 2.84 (dd, *J* = 17.0, 4.0 Hz, 1H), 1.48 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.3, 169.6, 156.0, 143.9, 143.8, 141.3, 127.8, 127.1, 125.2, 120.0, 82.7, 67.2, 52.0, 51.0, 47.2, 36.8, 27.9 ppm; HRMS (ESI) *m/z* calcd. for 448.1731, $[M+Na]^+$ found: 448.1757. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IA, eluent: hexane/2-propanol = 96/4, flow rate: 1.0 mL/min. detector: UV at 254 nm), t_R = 20.3 min (major), 26.6 min (minor).

(D) *O*-Deprotection and KAHA Ligation

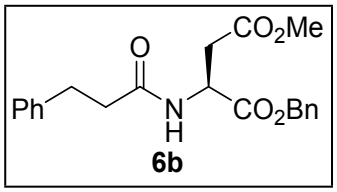


1-Benzyl 4-methyl *N*-hydroxy-L-aspartate (4b): To a solution of **3be** (192.7 mg, 500 μmol, 1.0 equiv) in CH_2Cl_2 (5 mL) was added TFA (172.5 mg, 1.5 mmol, 3.0 equiv) at room temperature and stirred for 1 h. H_2O (5 mL) was added and further stirred at ambient temperature for 1 h, and the mixture was dried over Na_2SO_4. The solids were filtered off and the solvent was removed under reduced presssure. The residue

was then purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:2) to afford **4b** as colorless oil (53.1 mg, 210 μmol, 42%). Since **4b** was gradually degraded on standing, **4b** was used for KAHA ligation soon after purification.

^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.32 (m, 5H), 5.22 (s, 2H), 4.06 (dt, J = 8.0, 5.0 Hz, 1H), 3.66 (s, 3H), 2.87 (dd, J = 16.0, 5.0 Hz, 1H), 2.80 (dd, J = 16.0, 5.0 Hz, 1H) ppm.

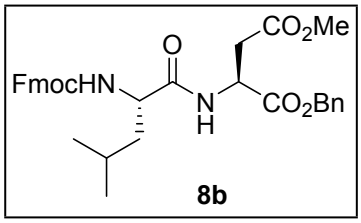
1-Benzyl 4-methyl (3-phenylpropanoyl)-L-aspartate (6b): A mixture of **4b** (23.3 mg, 92 μmol, 1.0 equiv) and 2-oxo-4-phenylbutanoic acid (**5**) (16.3 mg, 92 μmol, 1.0 equiv) in DMSO/H_2O (9:1, 200 μL) was stirred at 40 ºC for 24 h. The crude mixture was extracted with EtOAc (2 mL, 3 times) and then purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:2) to afford to **6b** as yellow oil (26.1 mg, 70 μmol, 60%, 82% ee).



6b

$[\alpha]_D^{24}$ - 13.2 (*c* 1.75, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3311, 1732, 1652 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38-7.30 (m, 6H), 7.27-7.24 (m, 1H), 7.19-7.17 (m, 3H), 6.42 (d, J = 8.0 Hz, 1H), 5.17 (dd, J = 28.0, 12.5 Hz, 2H), 4.88 (dt, J = 8.0, 4.0 Hz, 1H), 3.00 (dd, J = 17.5, 4.0 Hz, 1H), 2.95 (t, J = 8.0 Hz, 2H), 2.75 (dd, J = 17.5, 4.0 Hz, 1H), 2.59 (ddd, J = 18.0, 15.0, 8.0 Hz, 1H), 2.49 (ddd, J = 18.0 Hz, 15.0, 8.0 Hz) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 171.8, 171.4, 170.5, 140.5, 135.1, 128.55, 128.45, 128.26, 126.1, 67.5, 51.9, 48.3, 38.0, 36.0, 31.4 ppm; HRMS (ESI) *m/z* calcd. For $C_{21}H_{23}NO_5$, $[M+H]^+$: 370.1649, found: 370.1676. The enantiomeric excess was estimated by chiral HPLC analysis (DAICEL CHIRALPAK IB, eluent: hexane/2-propanol = 99/1, flow rate: 1 mL/min. detector: UV at 254 nm), t_R = 18.2 min (minor), 16.4 min (major).

1-Benzyl 4-methyl 9*H*-fluoren-9-ylmethoxycarbonyl-L-leucyl-L-aspartate (8b): A mixture of **4b** (60.1 mg, 156 μmol, 1.0 equiv) and (*S*)-3-(9*H*-fluoren-9-ylmethoxycarbonyl)amino)-5-methyl-2-oxohexanoic acid (**7**) (57.1 mg, 150 μmol, 1.0 equiv) in DMSO/H_2O (9:1, 15 mL) was stirred at 40 ºC for 15 h. The crude mixture was extracted with EtOAc (2 mL, 3 times) and then purified by silica-gel column chromatography (eluent: hexane/EtOAc, 1:2) to afford to **8b** as yellow oil (41.2 mg, 72 μmol, 50%, 93:7 dr).



8b

$[\alpha]_D^{23}$ - 3.20 (*c* 1.20, $CHCl_3$); IR (neat) $\tilde{\nu}$: 3314, 1738, 1661 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.75 (d, J = 7.0 Hz, 2H), 7.57 (d, J = 5.5 Hz, 2H), 7.39-7.29 (m, 9H), 6.95 (d, J = 8.0 Hz, 1H), 5.34 (d, J = 8.0 Hz, 1H), 5.15 (dd, J = 21.0, 12.0 Hz, 2H), 4.91 (t, J = 4.0 Hz, 1H), 4.36 (m, 2H) 4.21 (m, 2H), 3.58 (s, 3H), 3.05 (dd, J = 17.0, 3.5 Hz, 1H), 2.81 (dd, J = 17.0, 3.5 Hz, 1H), 1.63 (m, 2H), 1.50 (m, 1H), 0.89 (s, 6H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ: 172.2, 171.5, 170.3, 156.1, 143.9, 143.8, 141.3, 135.1, 128.69, 128.60, 128.4, 127.8, 127.1, 125.1, 120.0, 67.7, 67.1, 53.4, 52.1, 48.5, 41.9, 36.0, 24.6, 22.9, 22.0 ppm; HRMS (ESI) *m/z* calcd. For $C_{33}H_{36}N_2O_7$, $[M+Na]^+$: 595.2415, found: 595.2396.

(E) References

[1] N. Hayama, T. Azuma, Y. Kobayashi, Y. Takemoto, *Chem. Pharm. Bull.*, 2016, **64**, 704.

[2] S. E. Denmark, A. Thorarensen, D. S. Middleton, *J. Am. Chem. Soc.*, 1996, **118**, 8266.

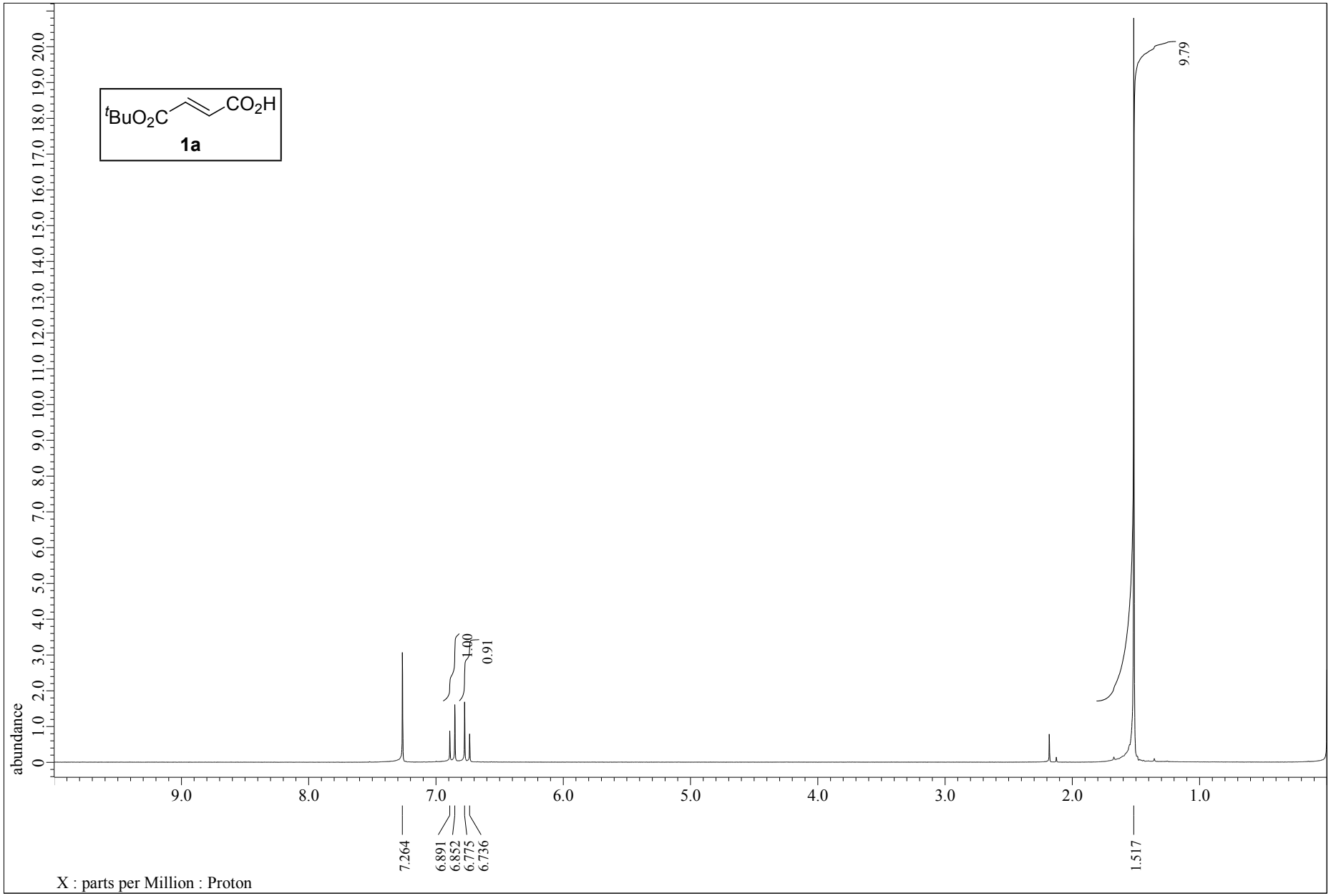
[3] D. Hadjipavlou-Litina, G. E. Magoulas, M. Krokidis, D. Papaioannou, *Eur. J. Med. Chem.*, 2010, **45**, 298.

[4] J. P. D. van Veldhoven, C. C. Blad, A. C. Klopman, D. R. Wolfram, M. J. Abdelkadir, J. R. Lane, J. Brussee, A. P. IJzerman, *Bioorg. Med. Chem. Lett.*, 2011, **21**, 2736.

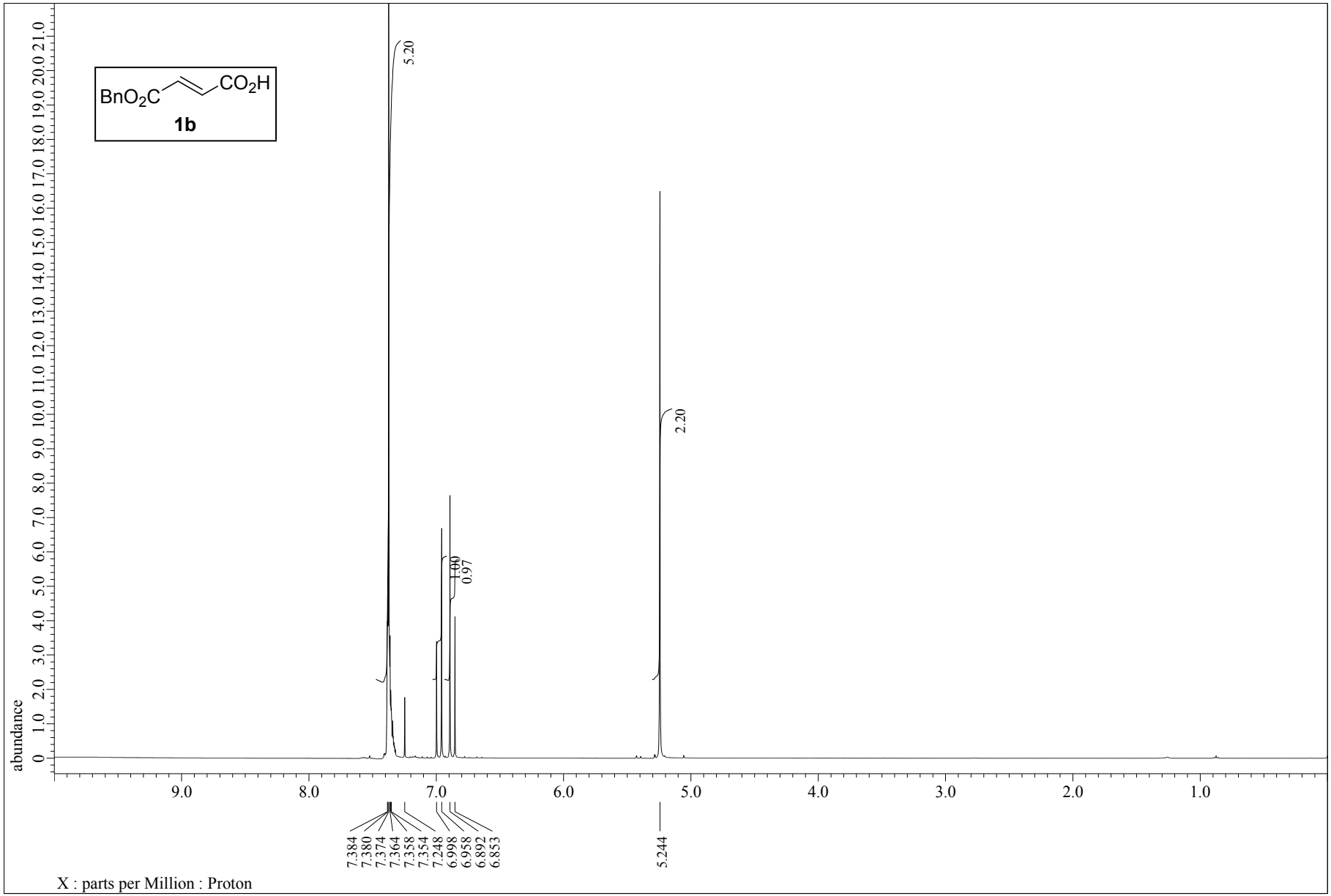
[5] Ö. D. Ekici, Z. Z. Li, A. J. Campbell, K. E. James, J. L. Asgian, J. Mikolajczyk, G. S. Salvesen, R. Ganesan, S. Jelakovic, M. G. Grütter, J. C. Powers, *J. Med. Chem.*, 2006, **49**, 5728.

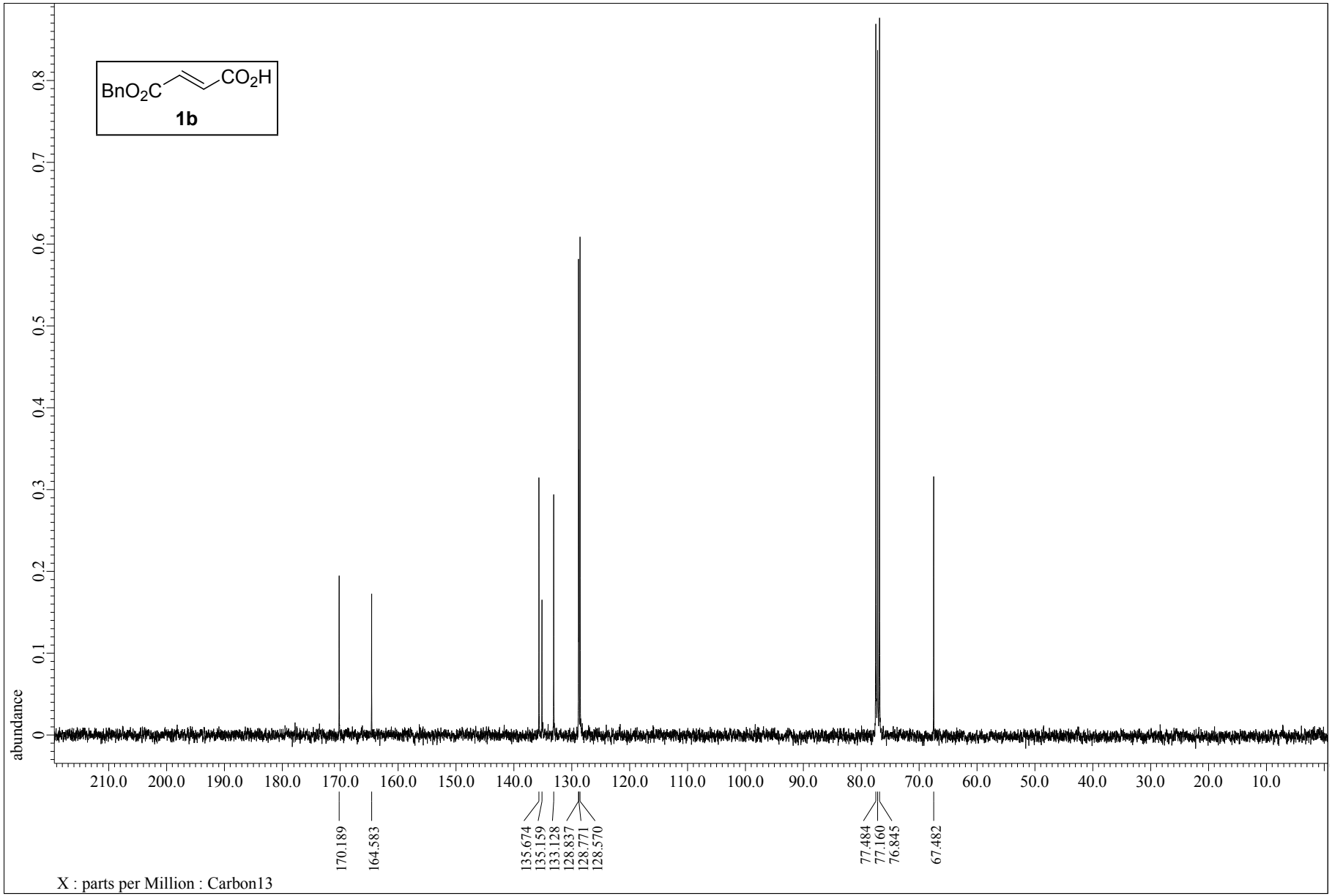
[6] A. Odriozola, M. Oiarbide, C. Palomo, *Chem. Eur. J.*, 2017, **23**, 12758.

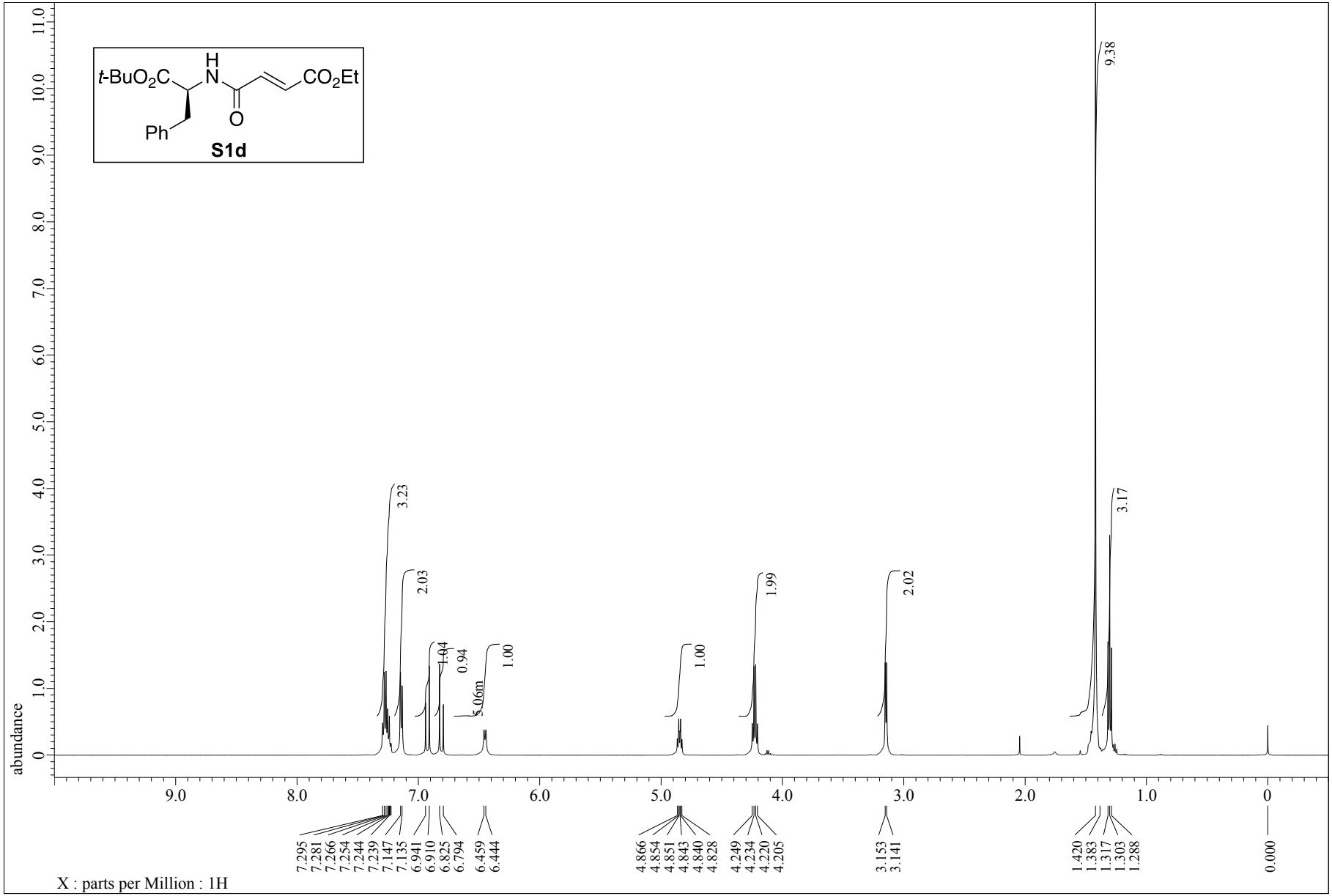
[7] L. A. Carpino, C. A. Giza, B. A. Carpino, *J. Am. Chem. Soc.*, 1959, **81**, 955.



(F) ^{1}H NMR and ^{13}C NMR Spectra


BnO2C
CO2H
1b
5.20
2.20
1.00
0.97
abundance
X : parts per Million : Proton
7.384
7.380
7.374
7.364
7.358
7.354
7.248
6.998
6.958
6.892
6.853
5.244


BnO2C
CO2H
1b
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
170.189
164.583
135.674
135.159
133.128
128.837
128.771
128.570
77.484
77.160
76.845
67.482
X : parts per Million : Carbon13


t-BuO2C
H
N
CO2Et
O
Ph
S1d
abundance
X : parts per Million : 1H
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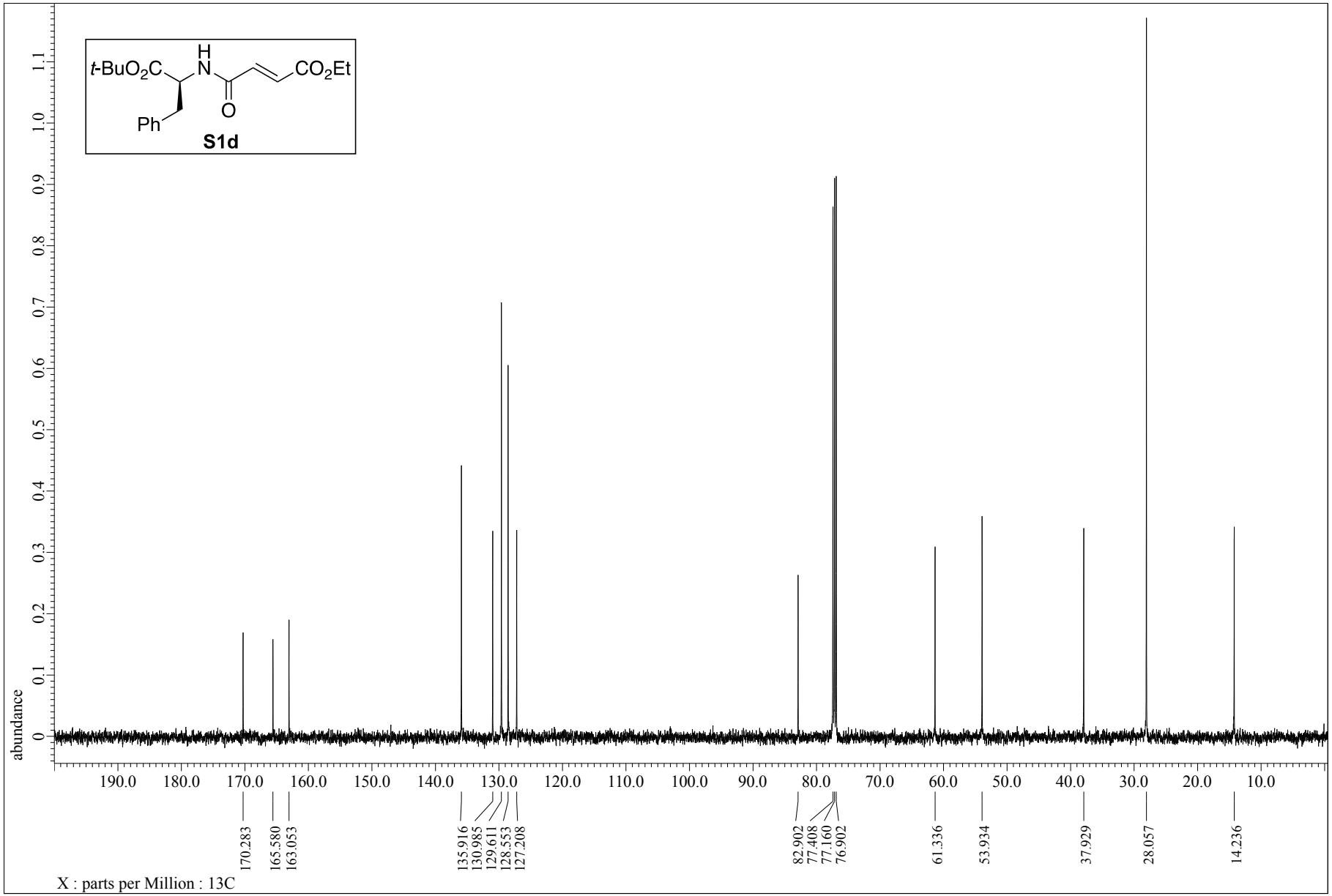
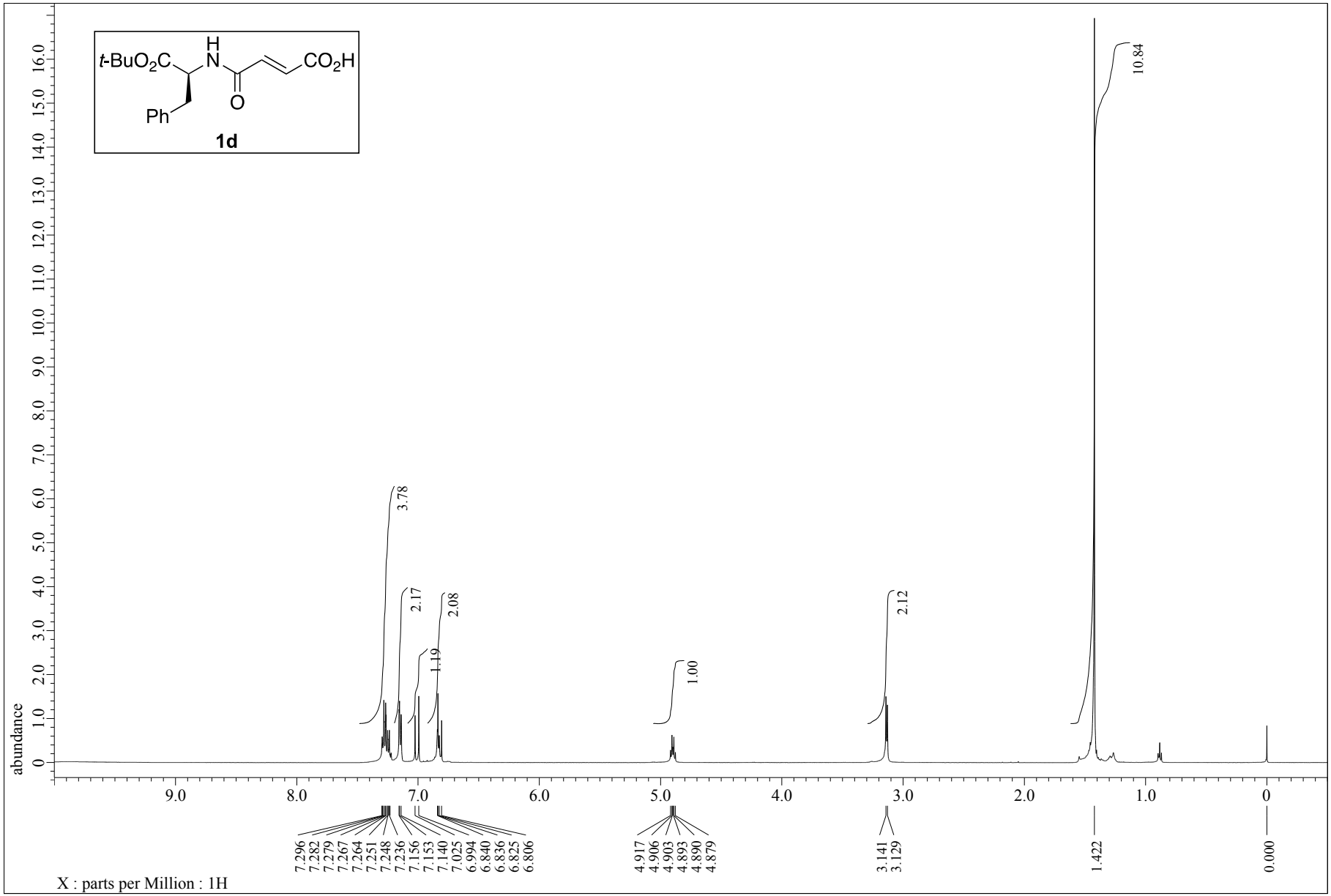
3.23
2.03
1.04
0.94
5.06m
1.00
1.00
1.99
2.02
3.17
7.295
7.281
7.266
7.254
7.244
7.239
7.147
7.135
6.941
6.910
6.825
6.794
6.459
6.444
4.866
4.854
4.851
4.843
4.840
4.828
4.249
4.234
4.220
4.205
3.153
3.141
1.420
1.383
1.317
1.303
1.288
0.000


t-BuO2C
H
N
CO2Et
O
Ph
S1d
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
170.283
165.580
163.053
135.916
130.985
129.611
128.553
127.208
82.902
77.408
77.160
76.902
61.336
53.934
37.929
28.057
14.236
X : parts per Million : 13C


t-BuO2C
H
N
O
CO2H
Ph
1d
abundance
X : parts per Million : 1H
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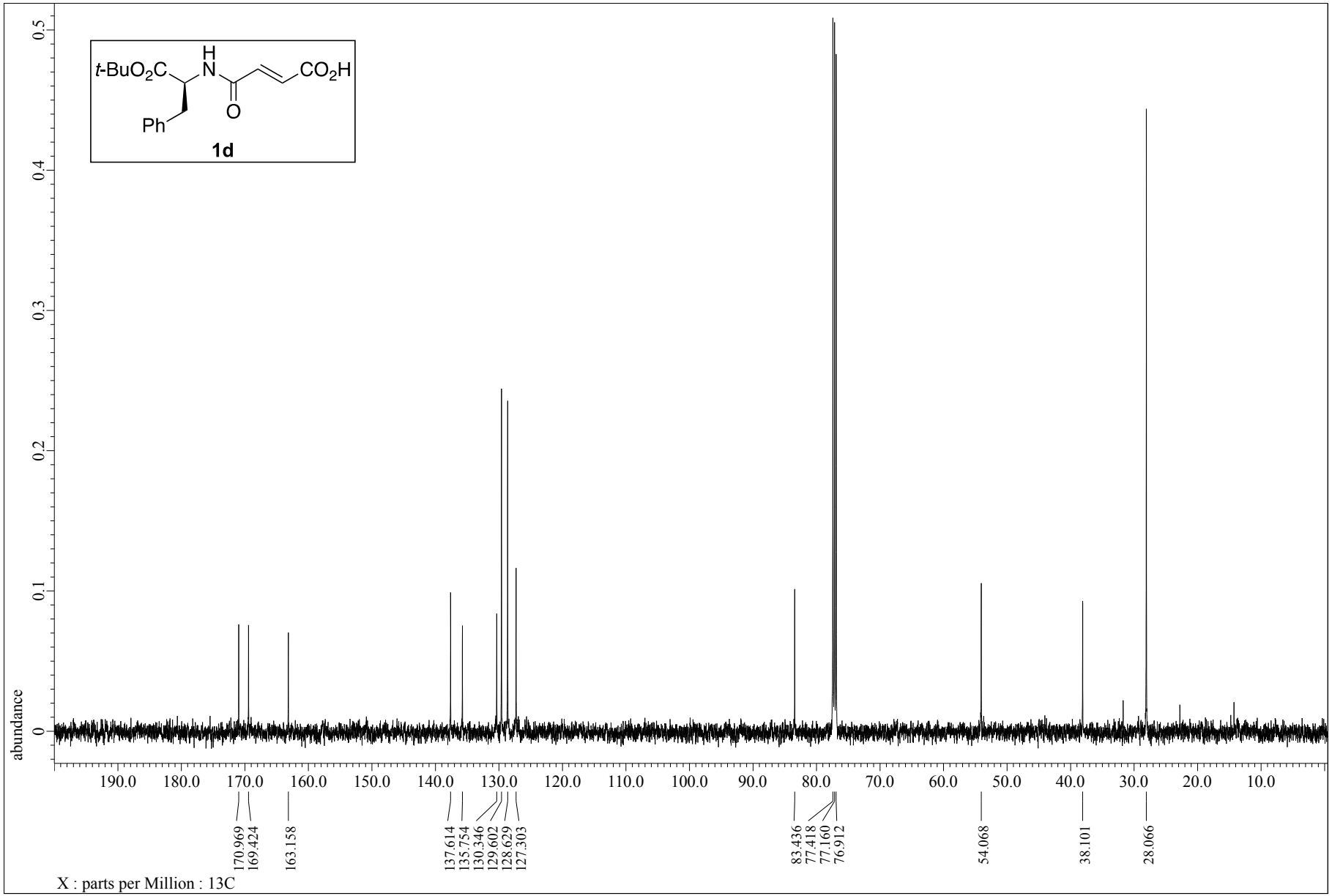
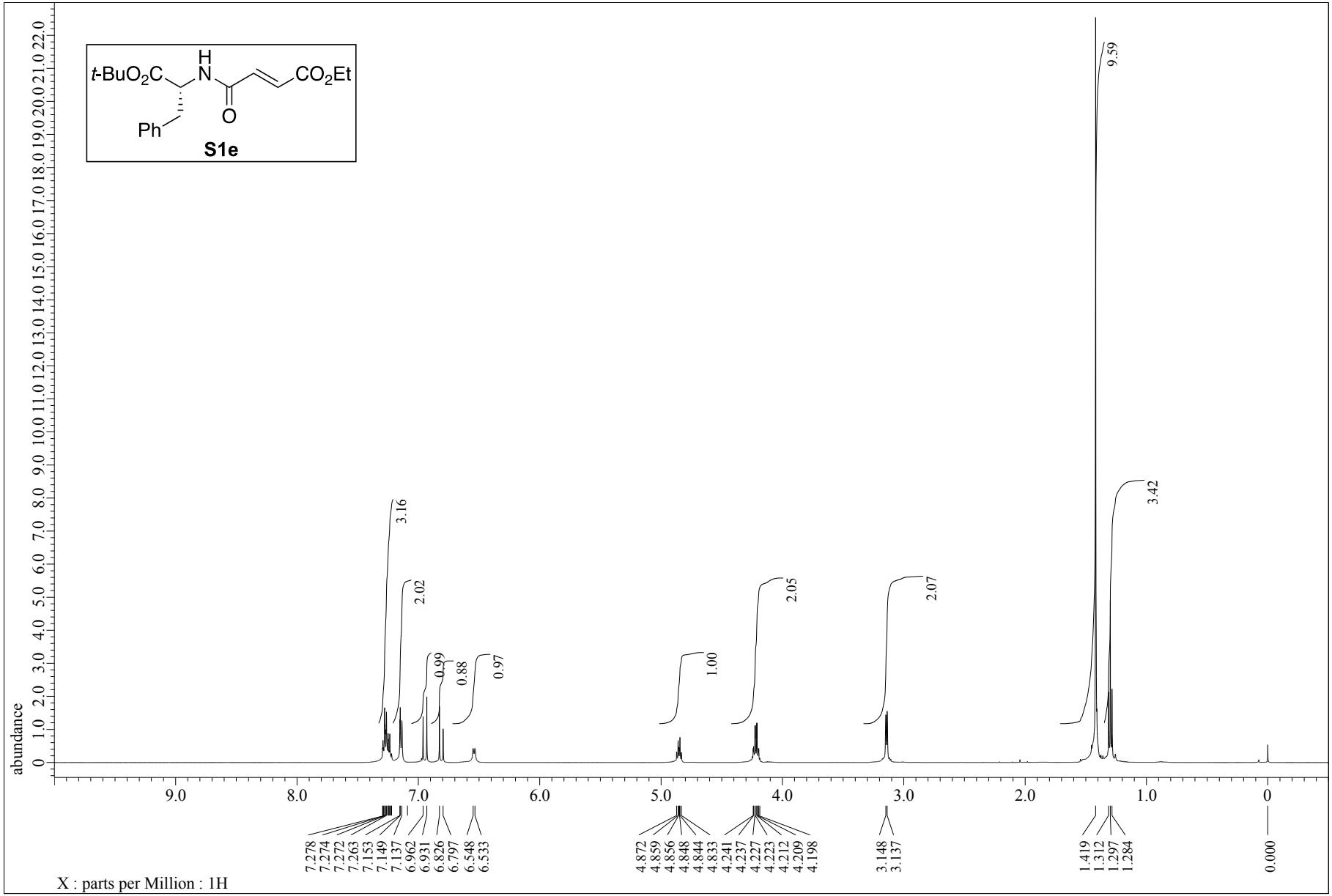
2.17
2.08
1.19
1.00
2.12
10.84
7.296
7.282
7.279
7.267
7.264
7.251
7.248
7.236
7.156
7.153
7.140
7.025
6.994
6.840
6.836
6.825
6.806
4.917
4.906
4.903
4.893
4.890
4.879
3.141
3.129
1.422
0.000


t-BuO2C
H
N
CO2H
O
Ph
1d
abundance
0.5
0.4
0.3
0.2
0.1
0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
170.969
169.424
163.158
137.614
135.754
130.346
129.602
128.629
127.303
83.436
77.418
77.160
76.912
54.068
38.101
28.066
X : parts per Million : 13C


t-BuO2C
H
N
CO2Et
O
Ph
S1e
abundance
X : parts per Million : 1H
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3.42
3.16
2.02
0.99
0.88
0.97
1.00
2.05
2.07
7.278
7.274
7.272
7.263
7.153
7.149
7.137
6.962
6.931
6.826
6.797
6.548
6.533
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4.856
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4.237
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4.209
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1.419
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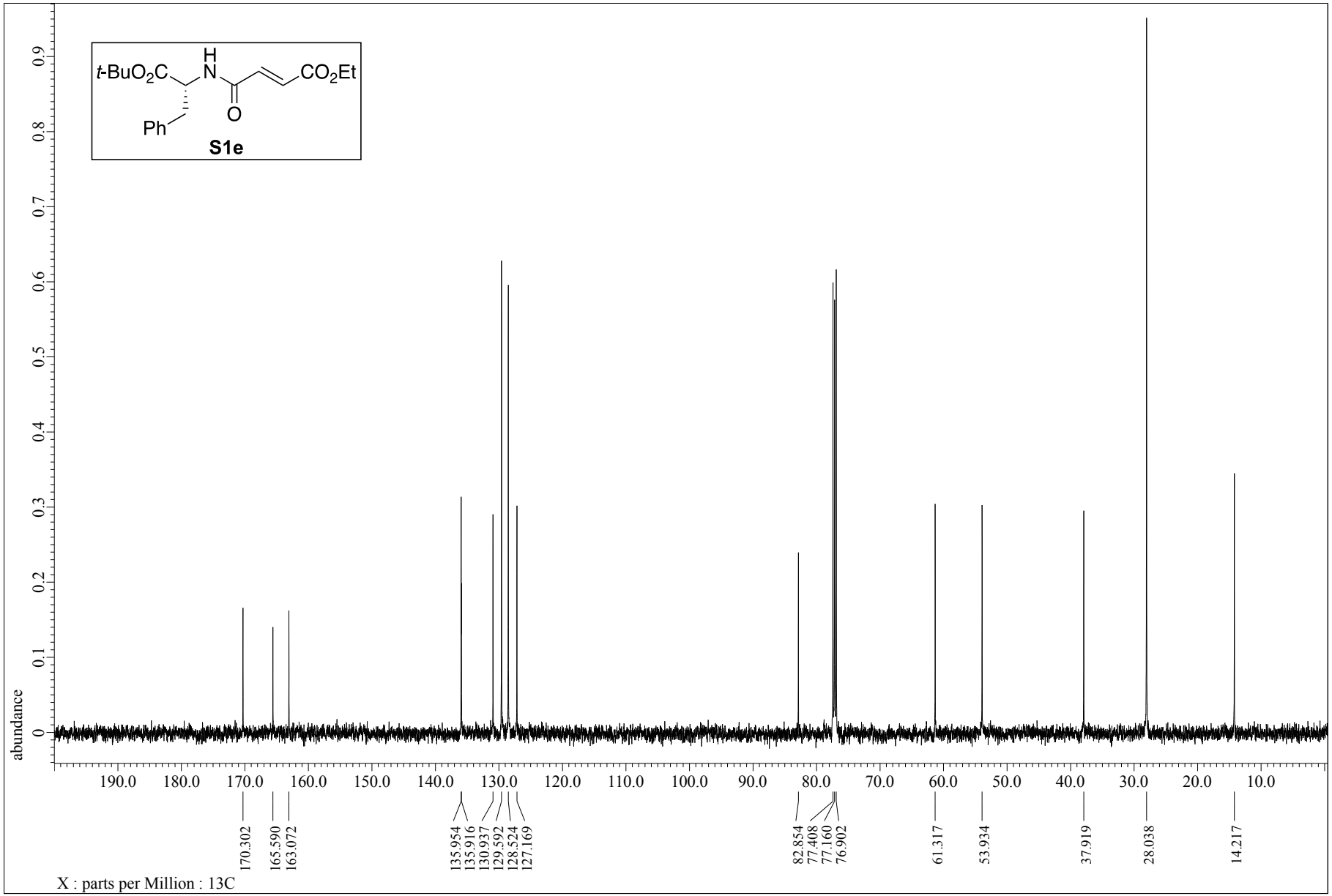
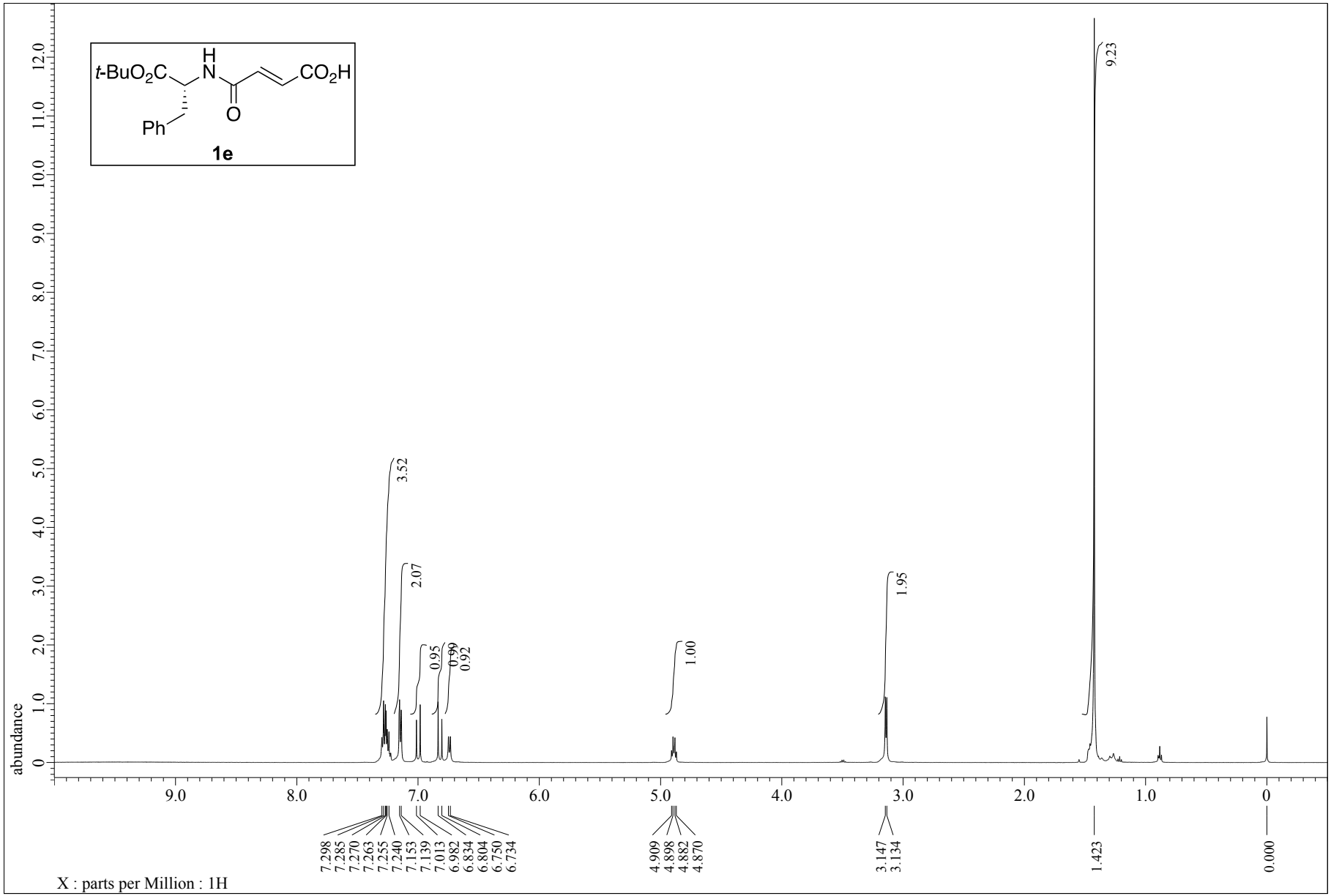

t-BuO2C
H
N
CO2Et
O
Ph
S1e
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
170.302
165.590
163.072
135.954
135.916
130.937
129.592
128.524
127.169
82.854
77.408
77.160
76.902
61.317
53.934
37.919
28.038
14.217
X : parts per Million : 13C


t-BuO2C
H
N
CO2H
O
Ph
1e
abundance
X : parts per Million : 1H
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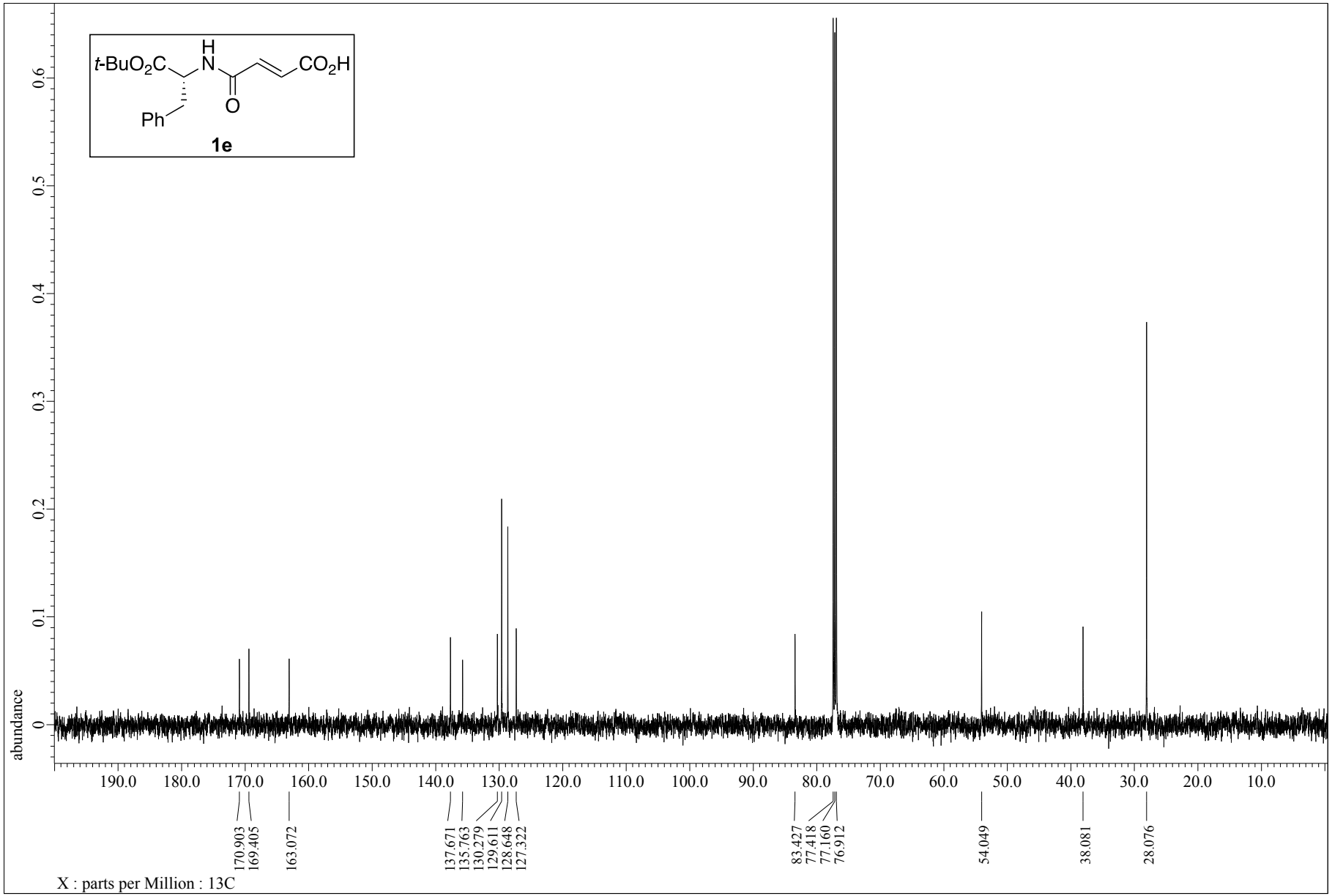
3.52
2.07
1.95
1.00
0.95
0.99
0.92
7.298
7.285
7.270
7.263
7.255
7.240
7.153
7.139
7.013
6.982
6.834
6.804
6.750
6.734
4.909
4.898
4.882
4.870
3.147
3.134
1.423
0.000


t-BuO2C
H
N
CO2H
O
Ph
1e
abundance
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0.1
0.2
0.3
0.4
0.5
0.6
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
170.903
169.405
163.072
137.671
135.763
130.279
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127.322
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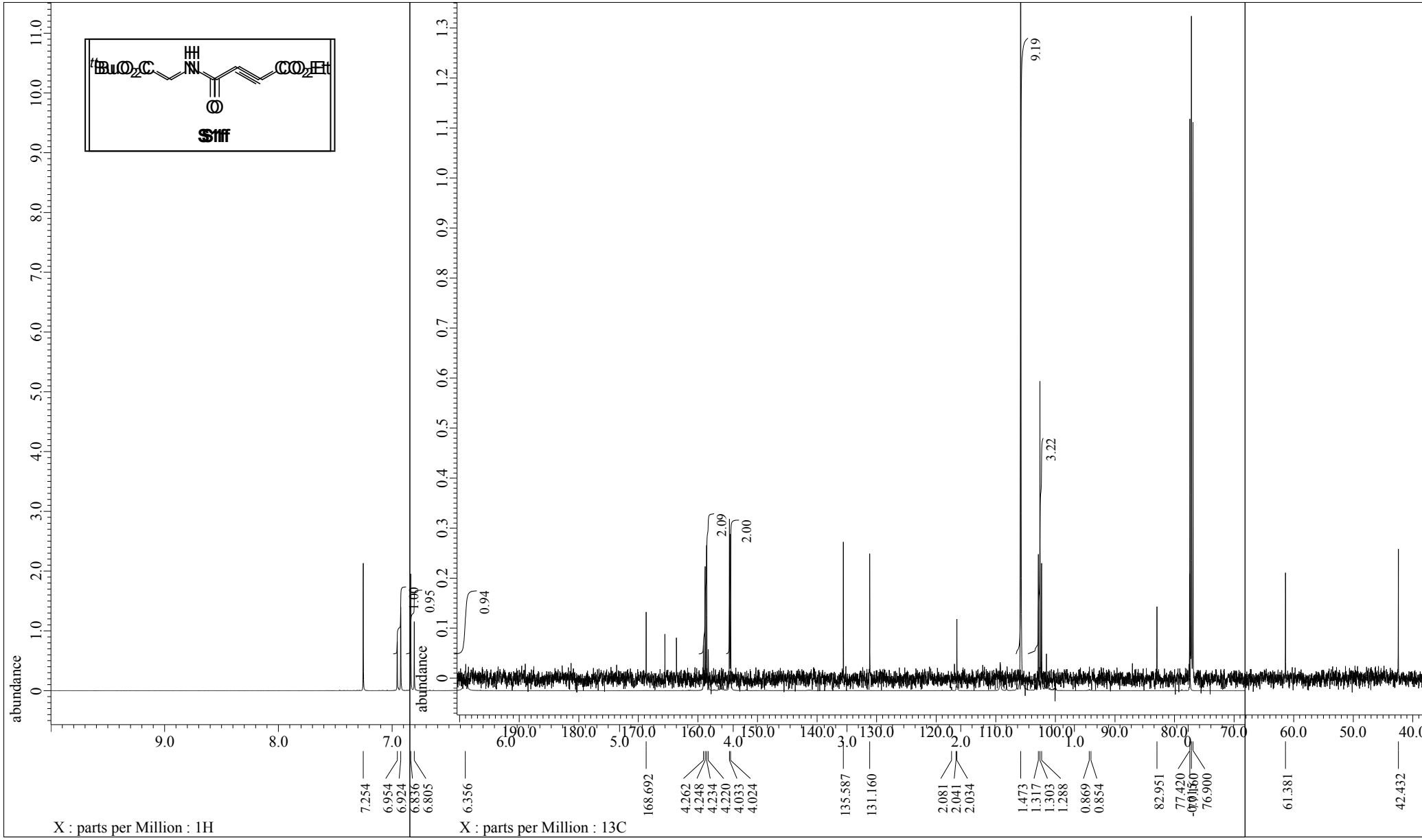
77.160
76.912
54.049
38.081
28.076
X : parts per Million : 13C


abundance
X : parts per Million : 1H
X : parts per Million : 13C
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6.924
6.836
6.805
6.356
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4.262
4.248
4.234
4.220
4.033
4.024
135.587
131.160
2.081
2.041
2.034
1.473
1.317
1.303
1.288
0.869
0.854
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61.381
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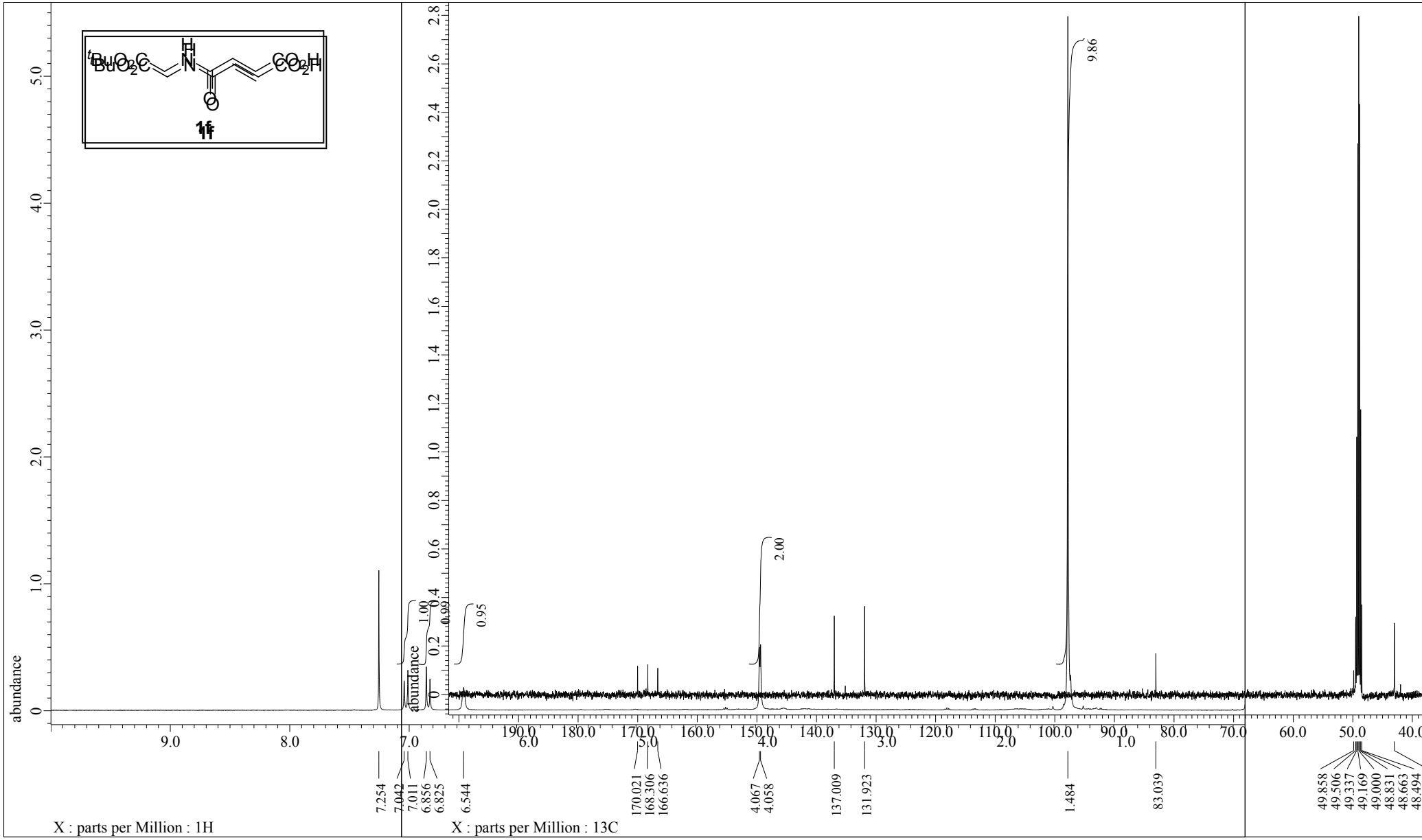
3.22
2.09
2.00
1.00
0.95
0.94


1f
abundance
X : parts per Million : 1H
X : parts per Million : 13C
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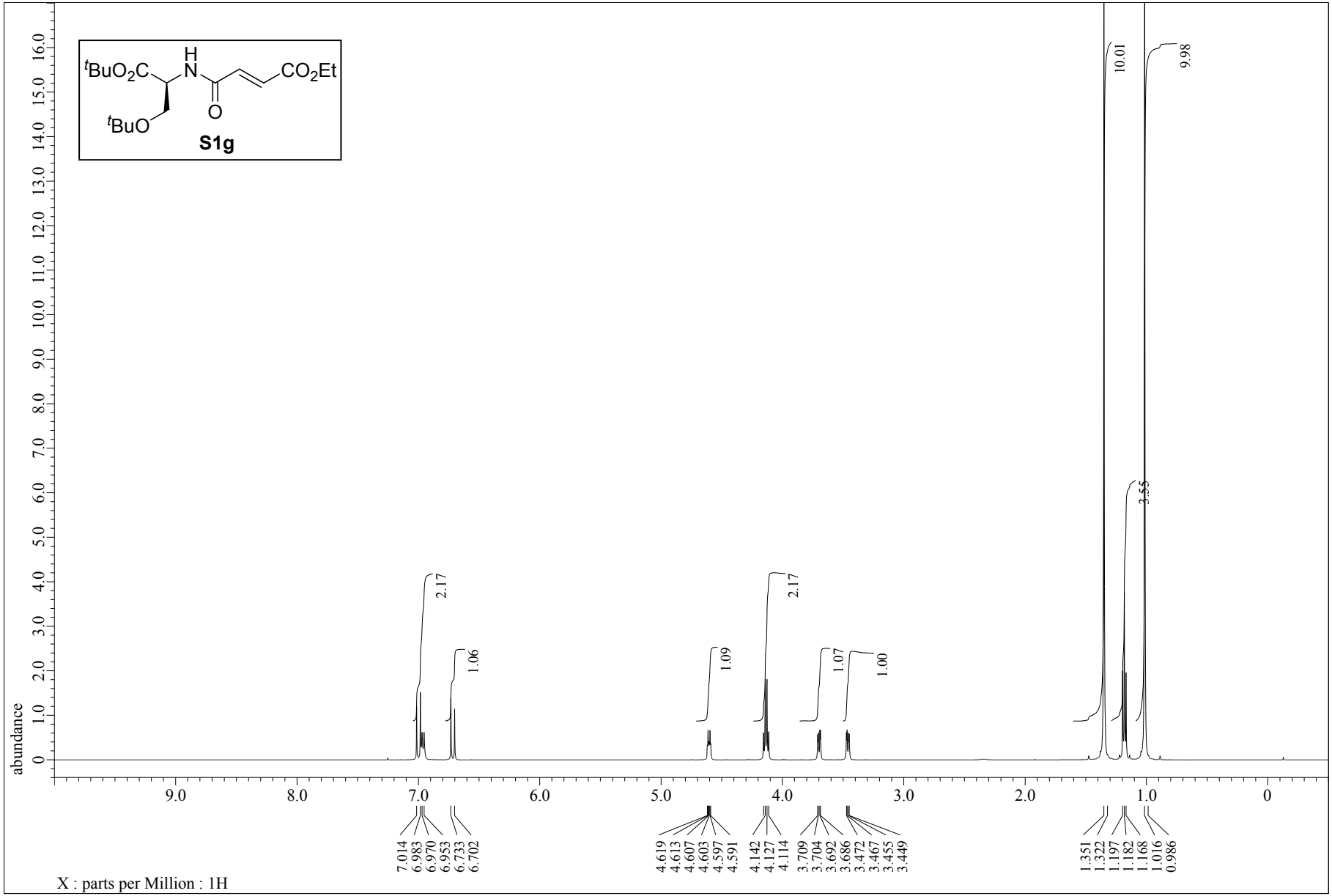
7.042
7.011
6.856
6.825
6.544
170.021
168.306
166.636
4.067
4.058
137.009
131.923
1.484
83.039
49.858
49.506
49.337
49.169
49.000
48.831
48.663
48.494
9.86
2.00
1.00
0.99
0.95


S1g
abundance
X : parts per Million : 1H
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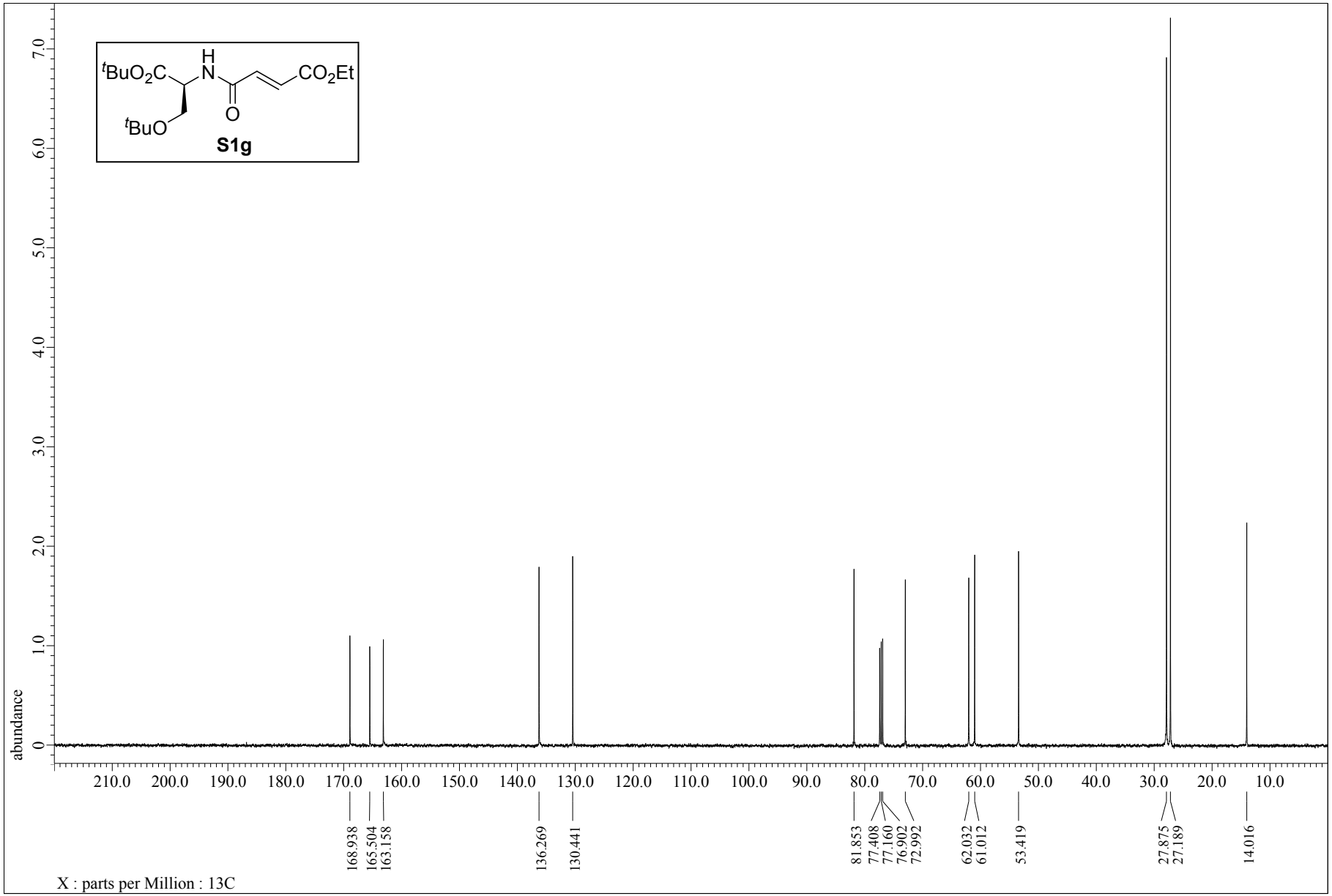
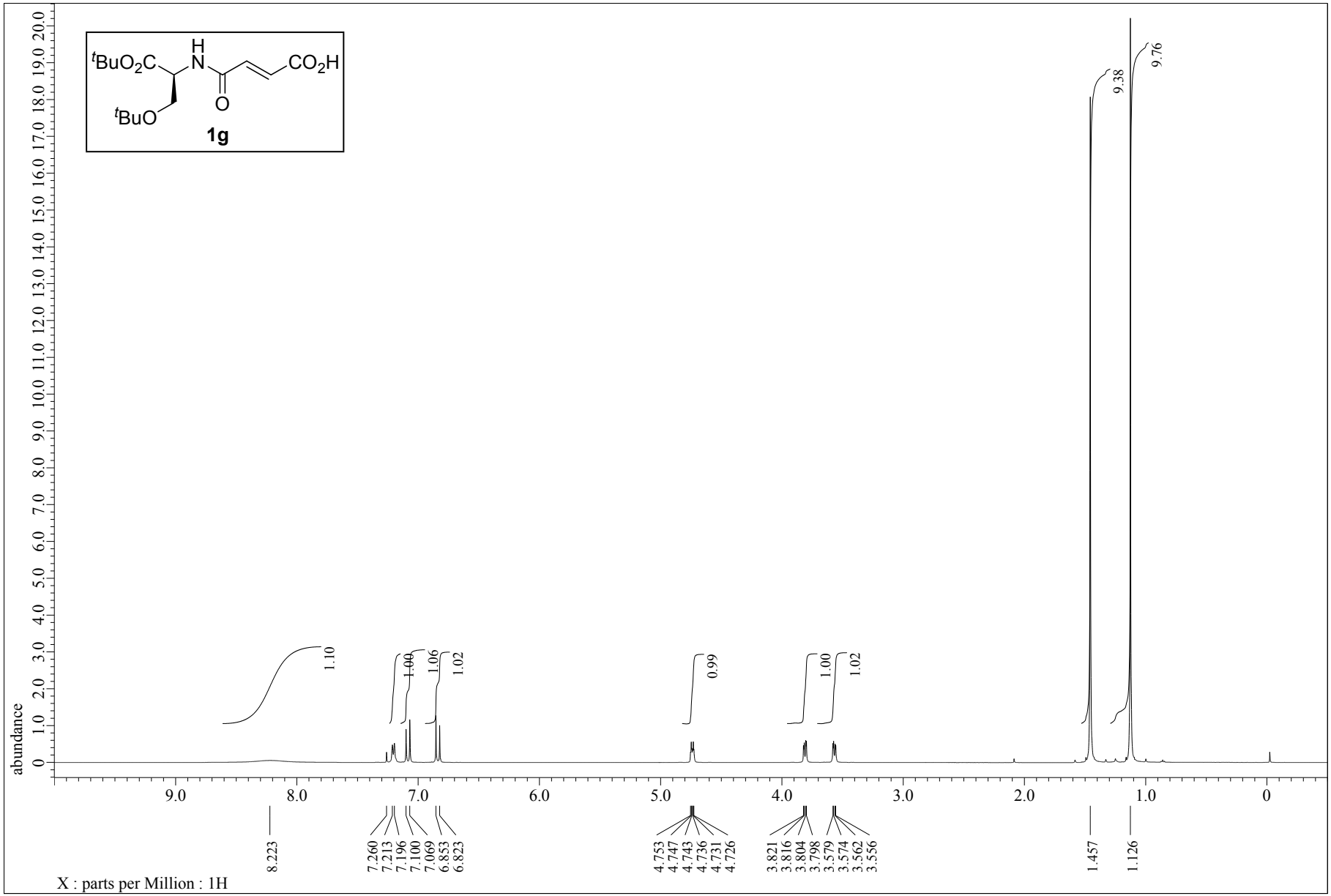
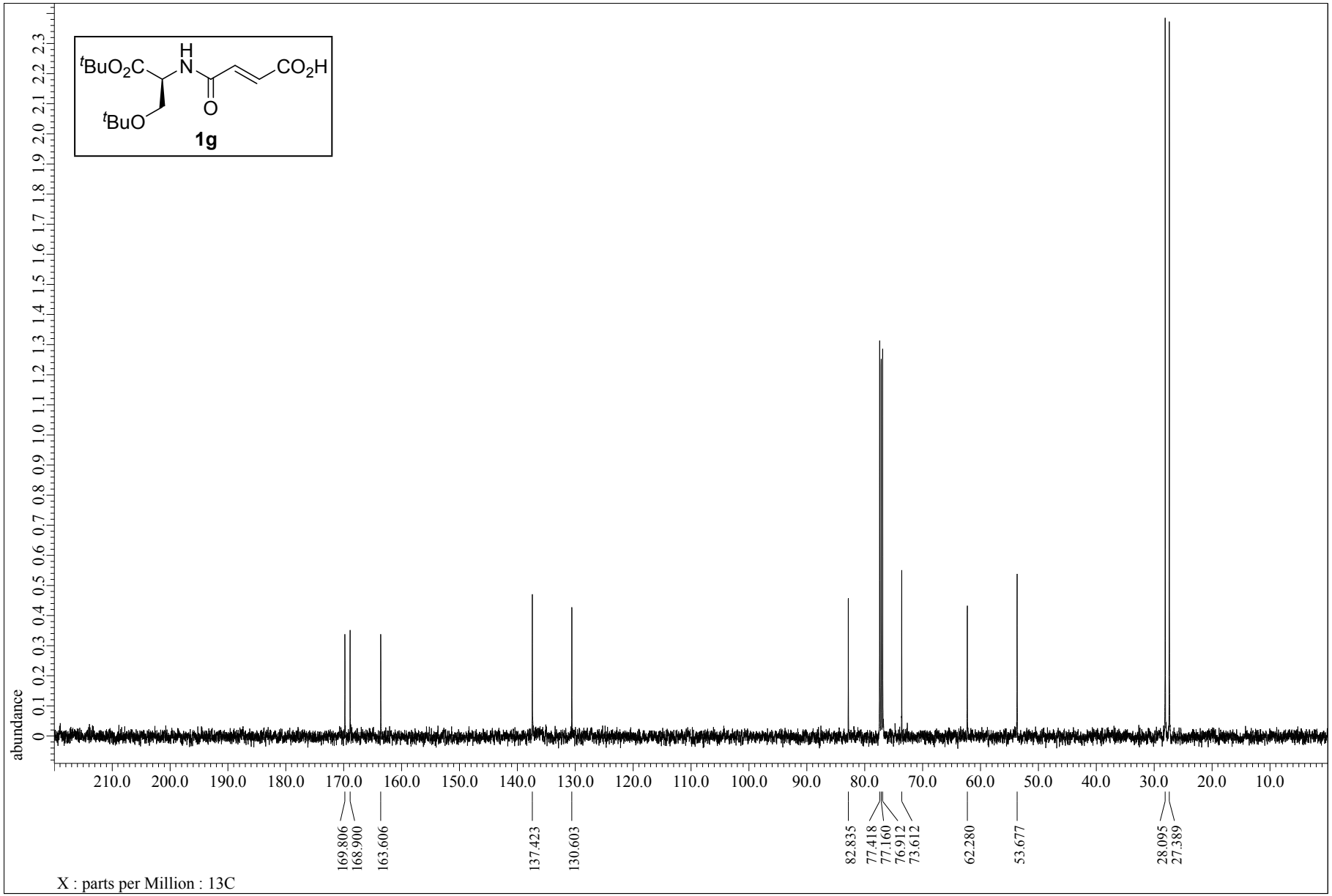
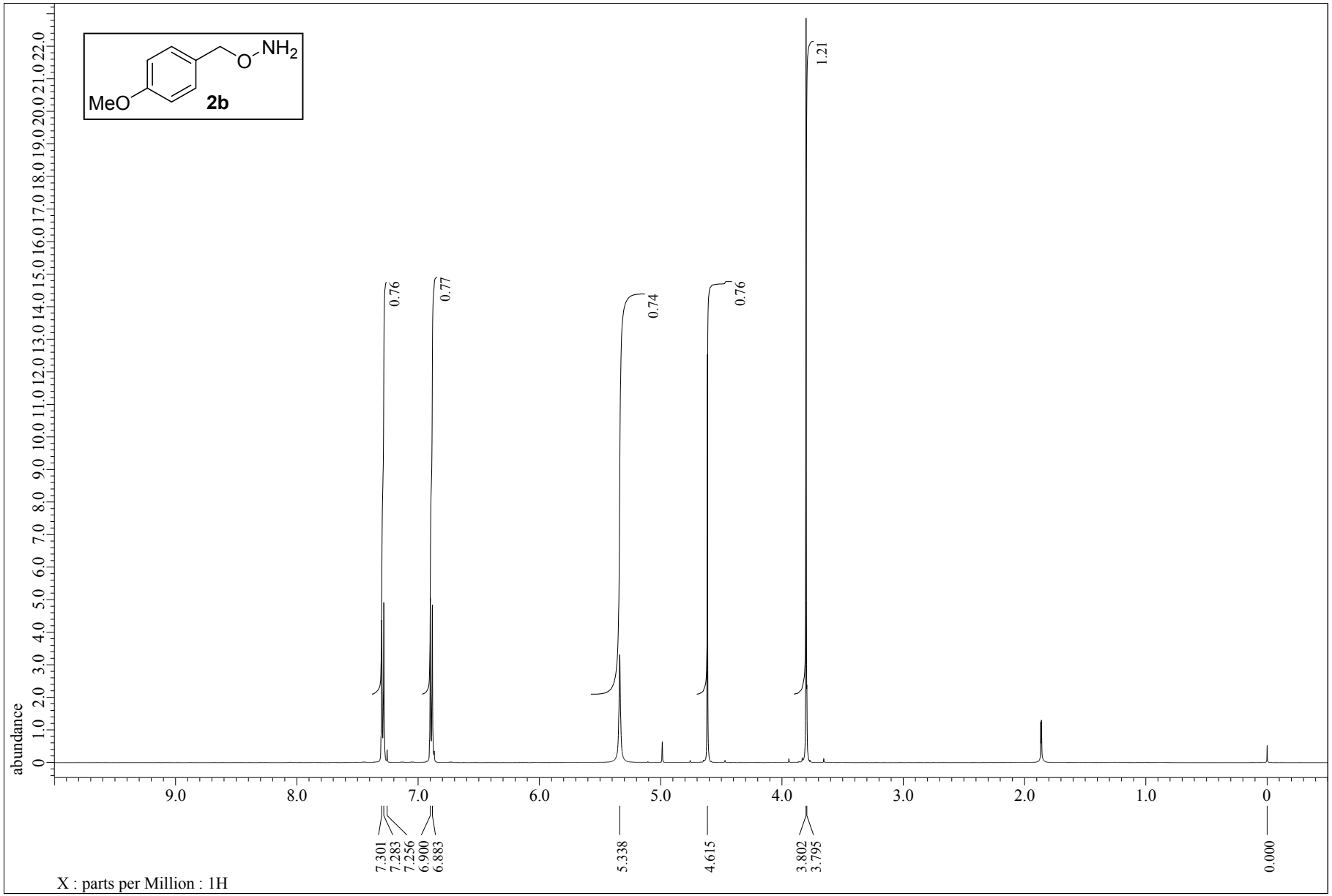
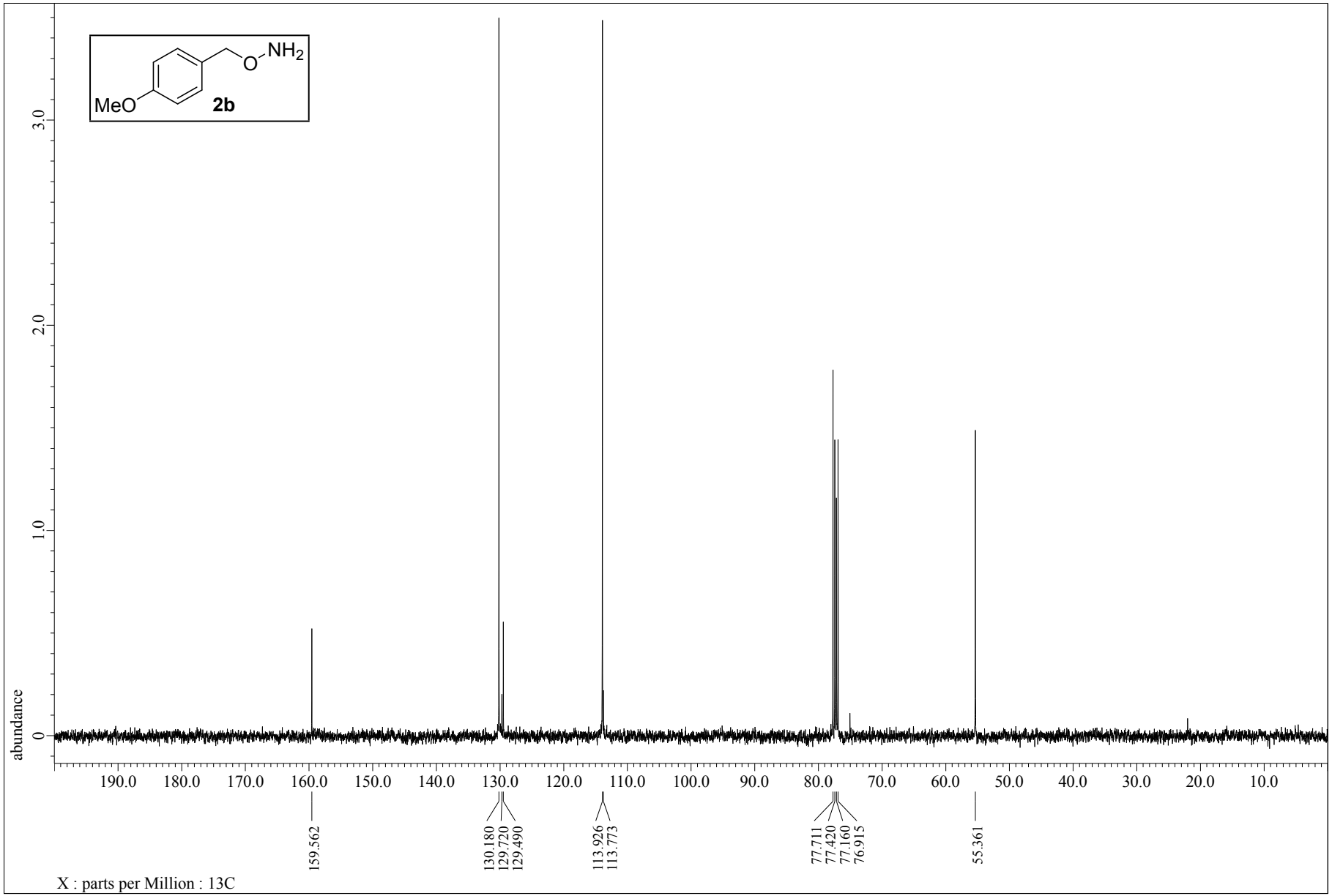
1.06
1.09
2.17
1.07
1.00
10.01
3.55
9.98
7.014
6.983
6.970
6.953
6.733
6.702
4.619
4.613
4.607
4.603
4.597
4.591
4.142
4.127
4.114
3.709
3.704
3.692
3.686
3.472
3.467
3.455
3.449
1.351
1.322
1.197
1.182
1.168
1.016
0.986

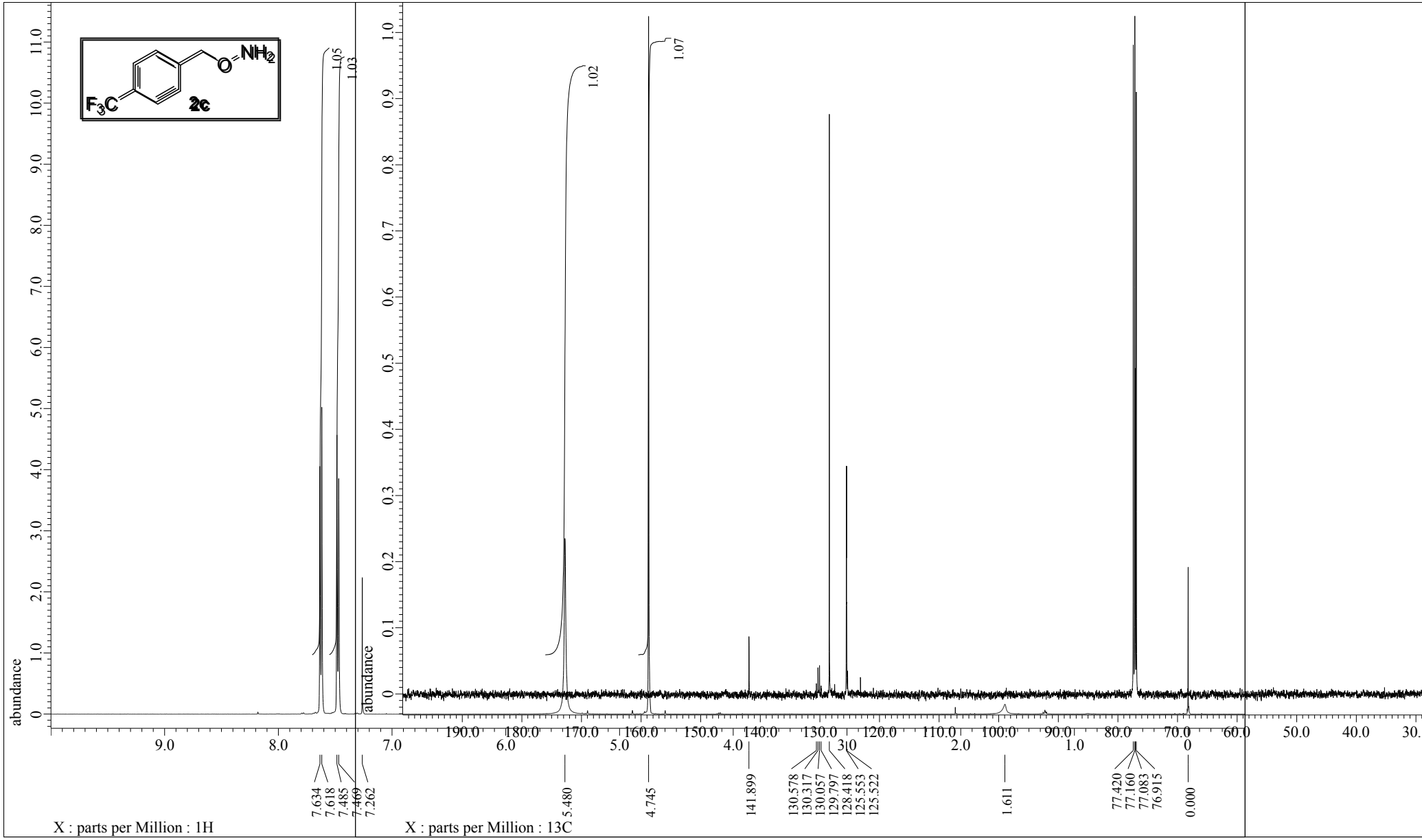

tBuO2C
H
N
CO2Et
O
tBuO
S1g
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
168.938
165.504
163.158
136.269
130.441
81.853
77.408
77.160
76.902
72.992
62.032
61.012
53.419
27.875
27.189
14.016
X : parts per Million : 13C

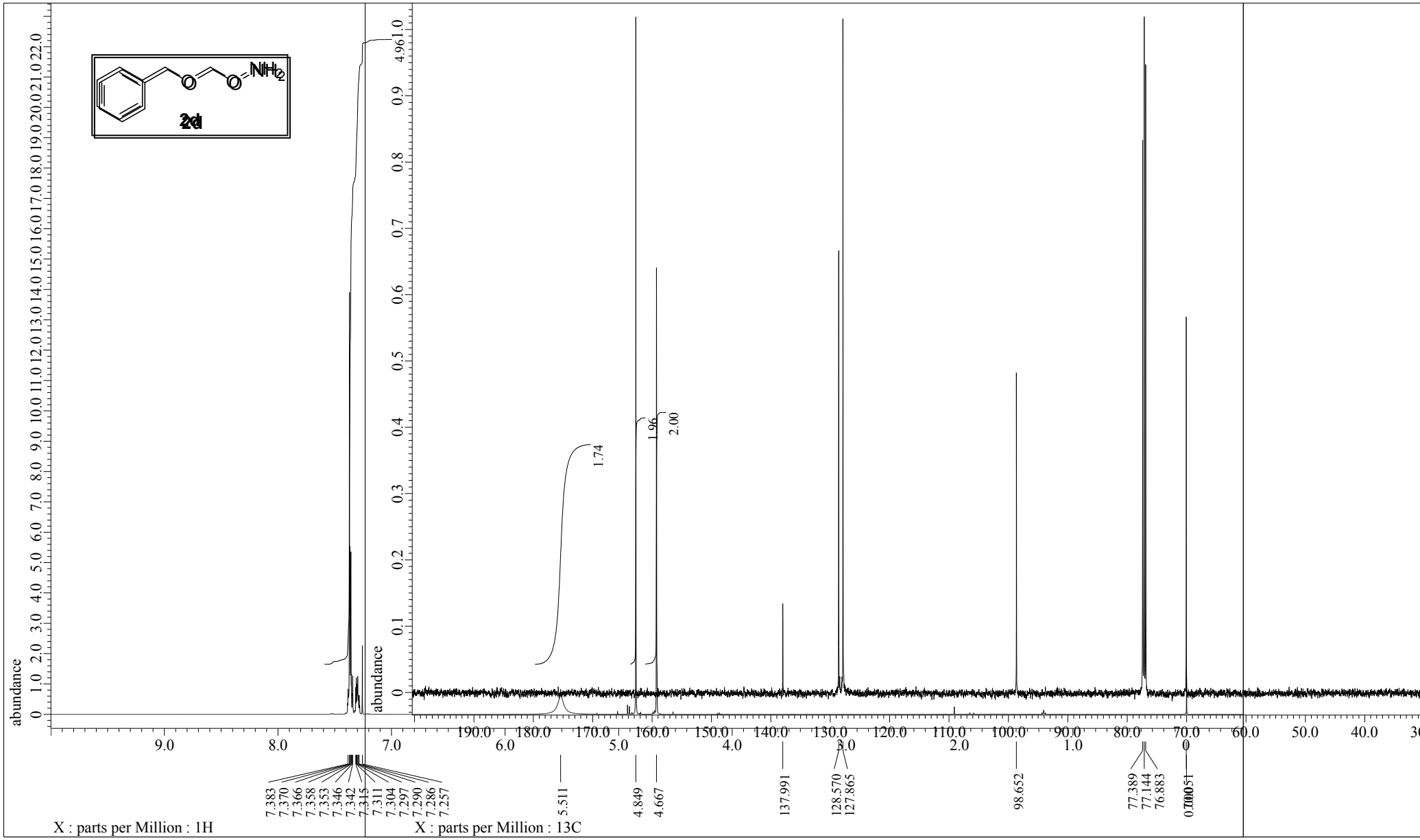

1g
abundance
X : parts per Million : 1H
1.10
1.00
1.06
1.02
0.99
1.00
1.02
9.38
9.76
8.223
7.260
7.213
7.196
7.100
7.069
6.853
6.823
4.753
4.747
4.743
4.736
4.731
4.726
3.821
3.816
3.804
3.798
3.579
3.574
3.562
3.556
1.457
1.126

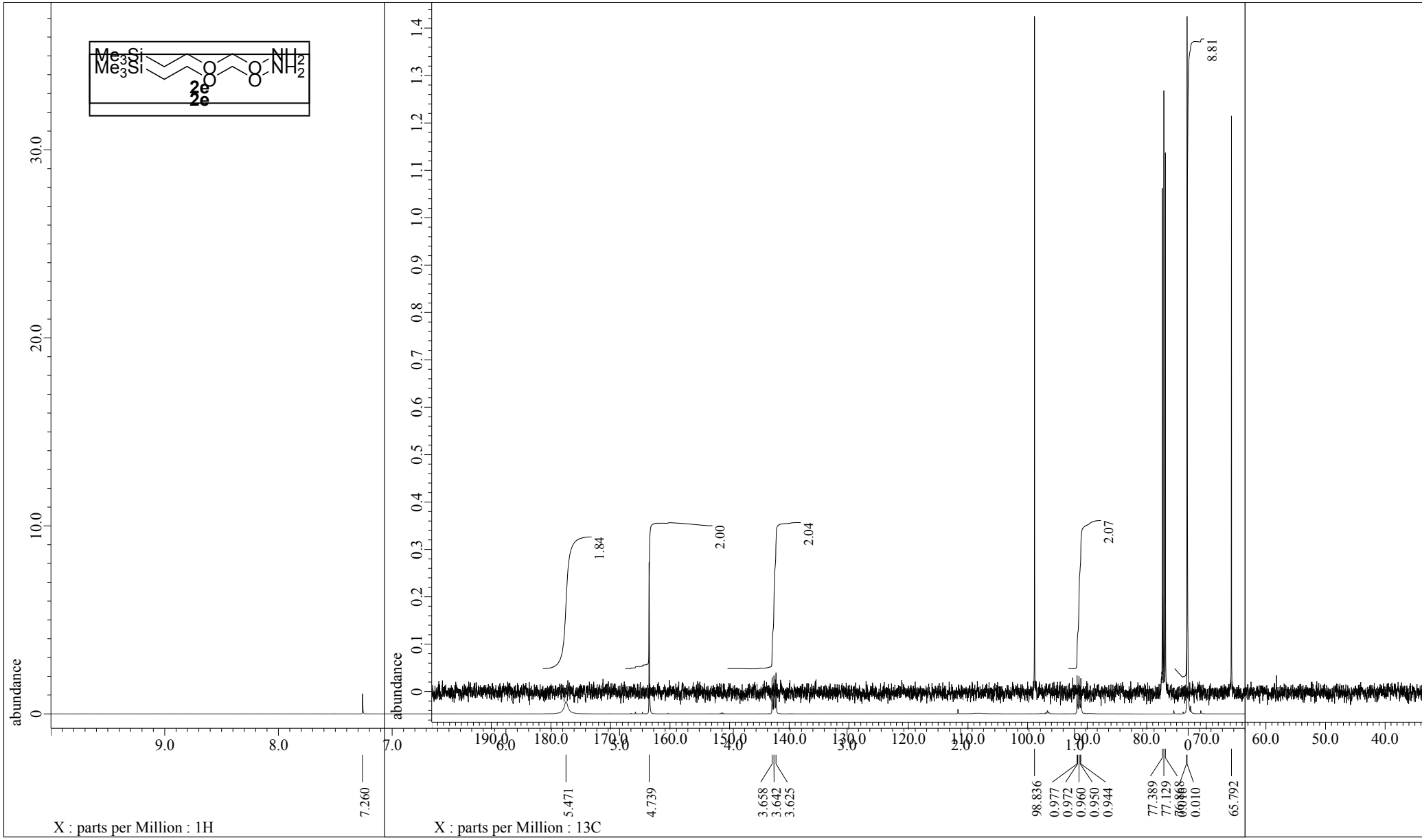

1g
abundance
X : parts per Million : 13C
169.806
168.900
163.606
137.423
130.603
82.835
77.418
77.160
76.912
73.612
62.280
53.677
28.095
27.389

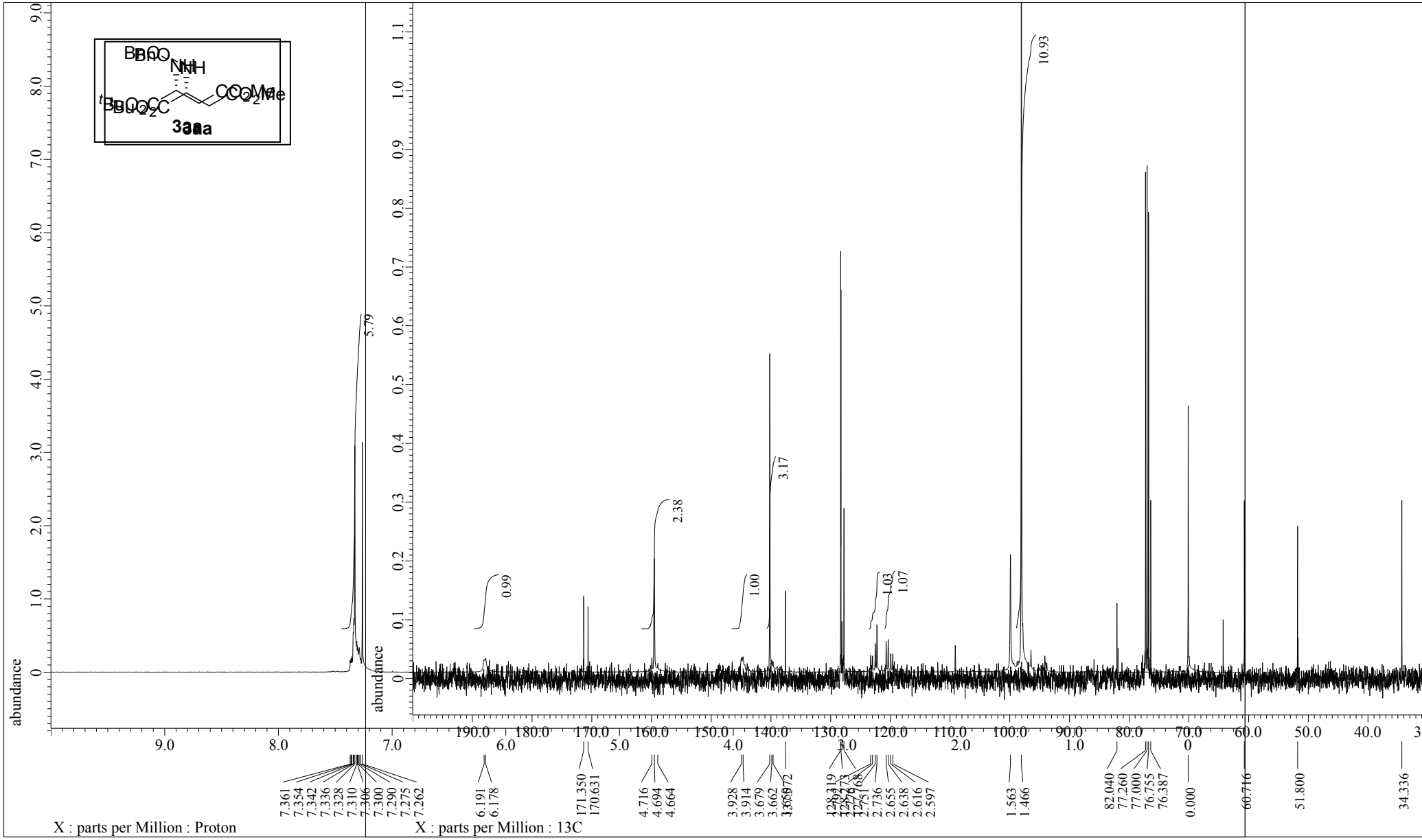

MeO
NH2
O
2b
abundance
X : parts per Million : 1H
0.76
0.77
0.74
0.76
1.21
7.301
7.283
7.256
6.900
6.883
5.338
4.615
3.802
3.795
0.000

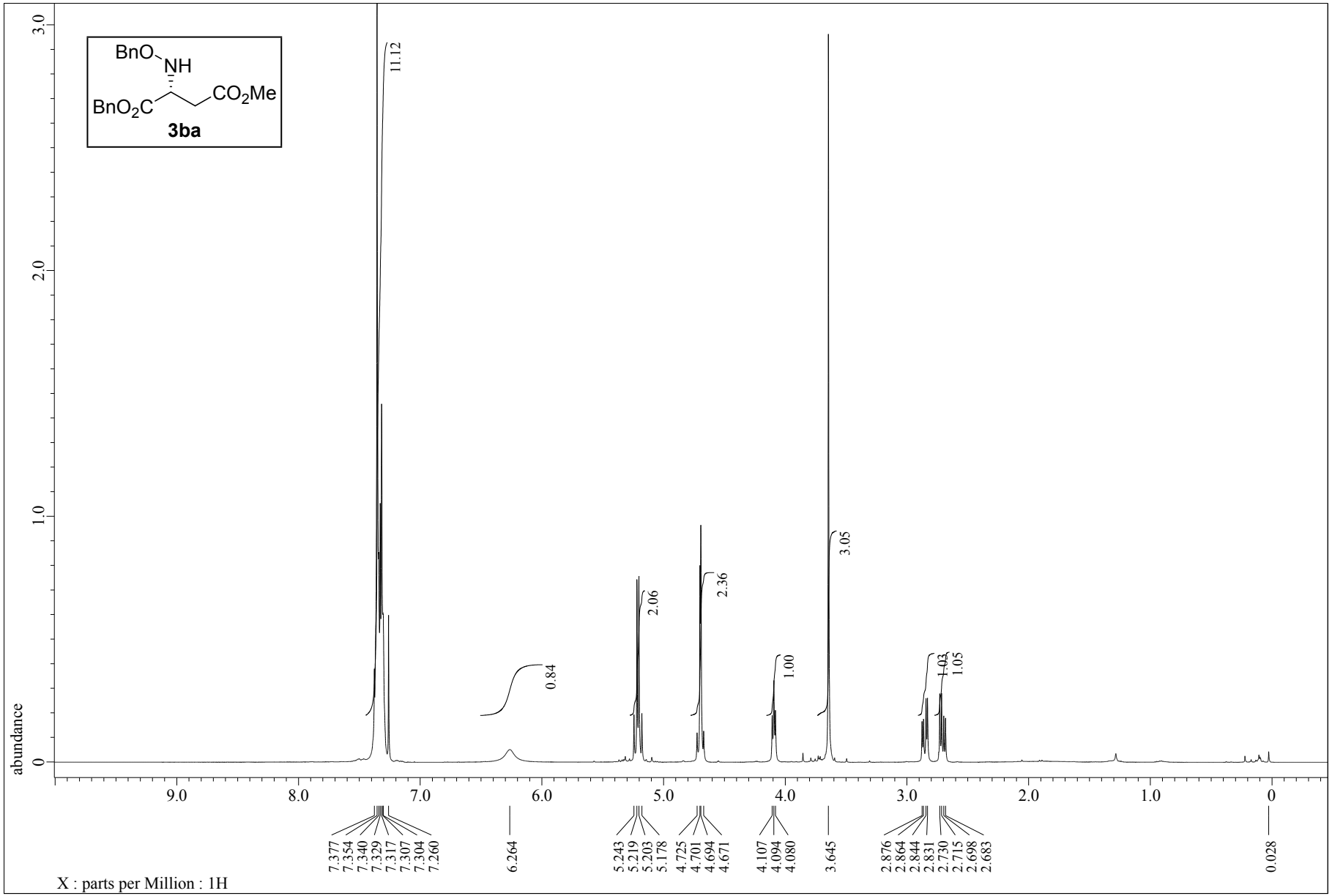

MeO
NH2
O
2b
abundance
3.0
2.0
1.0
0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
159.562
130.180
129.720
129.490
113.926
113.773
77.711
77.420
77.160
76.915
55.361
X : parts per Million : 13C

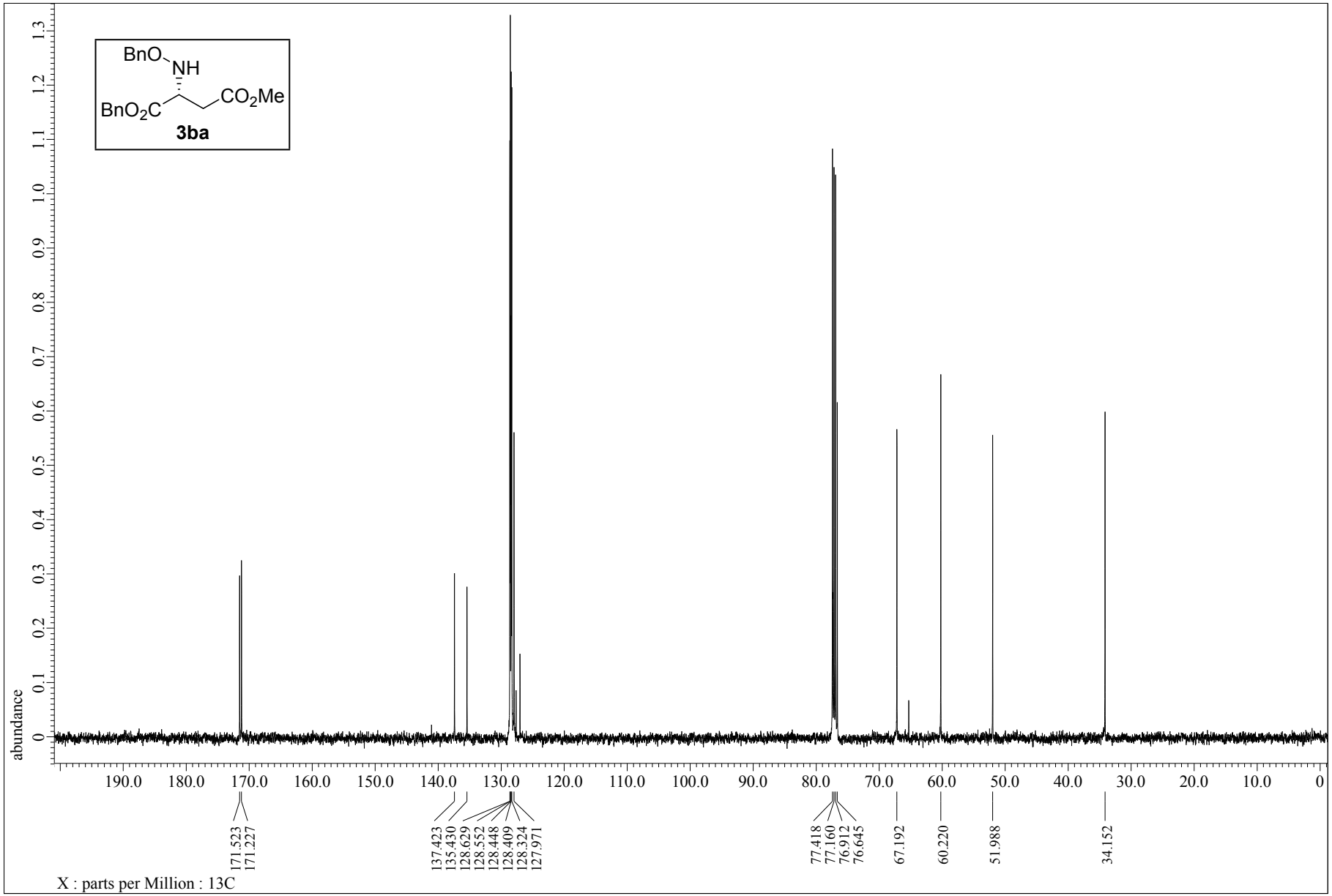

2c
abundance
X : parts per Million : 1H
X : parts per Million : 13C
7.634
7.618
7.485
7.469
7.262
5.480
4.745
141.899
130.578
130.317
130.057
129.797
128.418
125.553
125.522
1.611
77.420
77.160
77.083
76.915
0.000

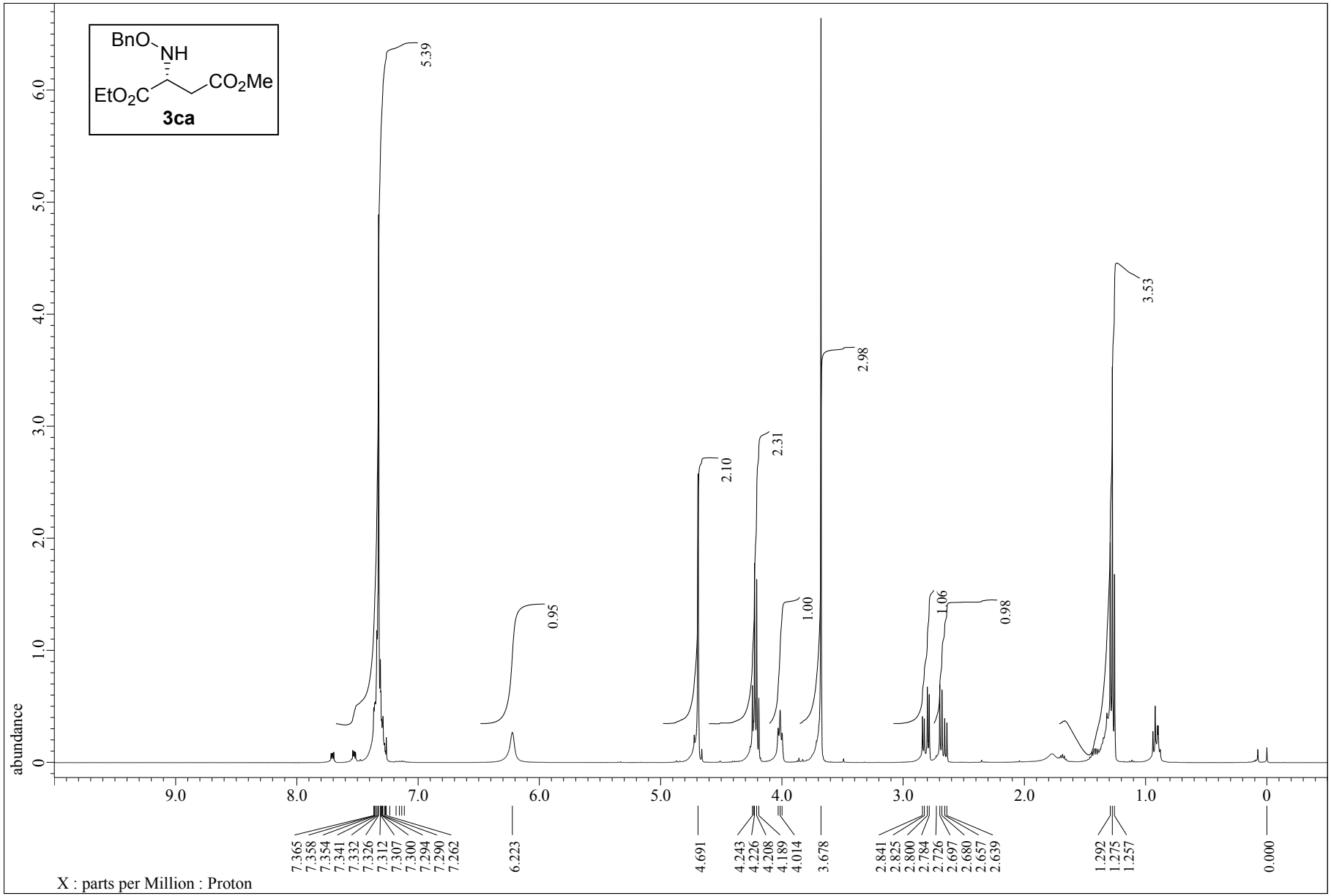

2cl
abundance
X : parts per Million : 1H
X : parts per Million : 13C
7.383
7.370
7.366
7.358
7.353
7.346
7.342
7.315
7.311
7.304
7.297
7.290
7.286
7.257
5.511
4.849
4.667
137.991
128.570
127.865
98.652
77.389
77.144
76.883
1.74
1.96
2.00
4.96

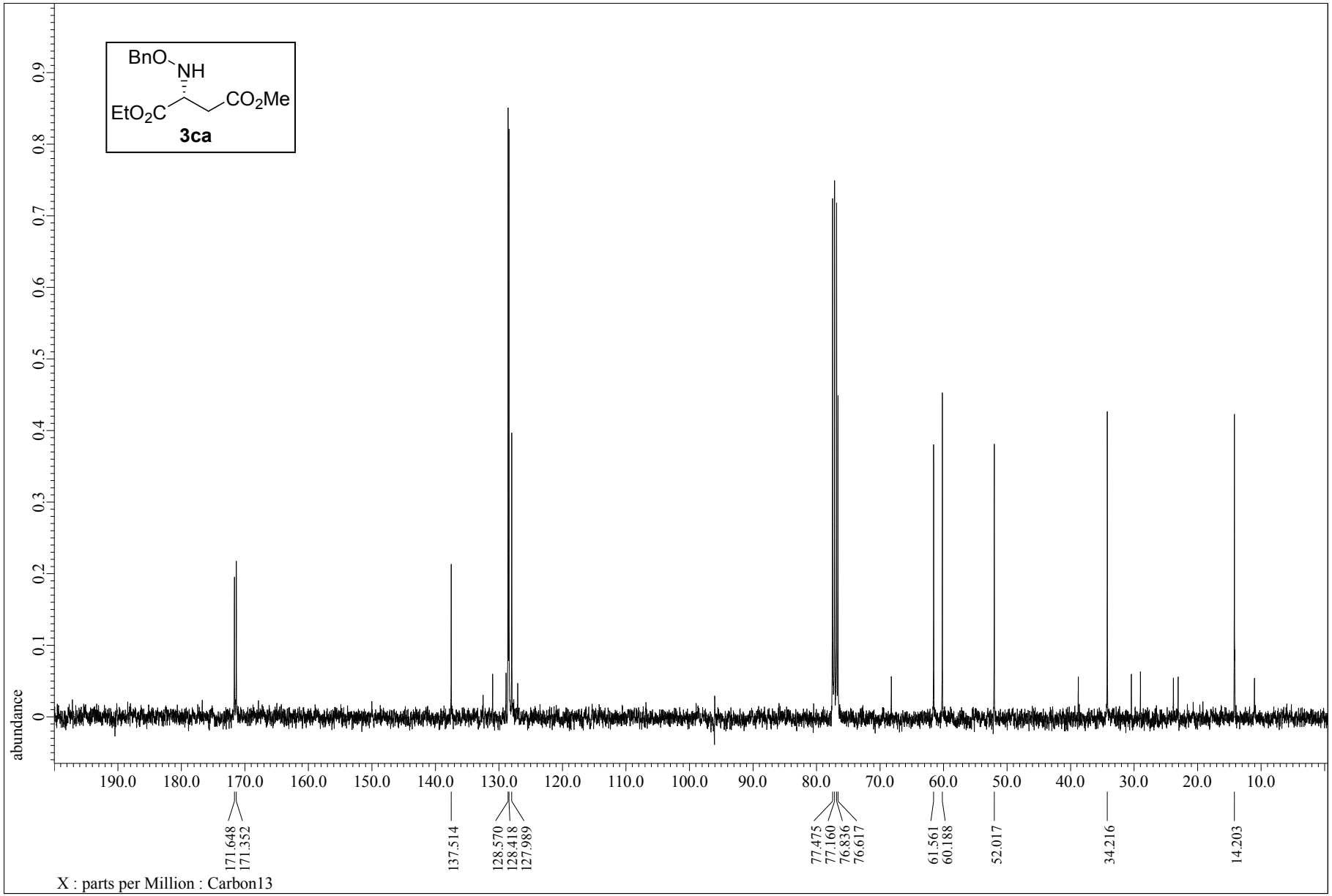

Me3Si
NH2
Me3Si
NH2
2e
2e
abundance
X : parts per Million : 1H
X : parts per Million : 13C
7.260
5.471
4.739
3.658
3.642
3.625
98.836
0.977
0.972
0.960
0.950
0.944
77.389
77.129
0.010
65.792
1.84
2.00
2.04
2.07
8.81

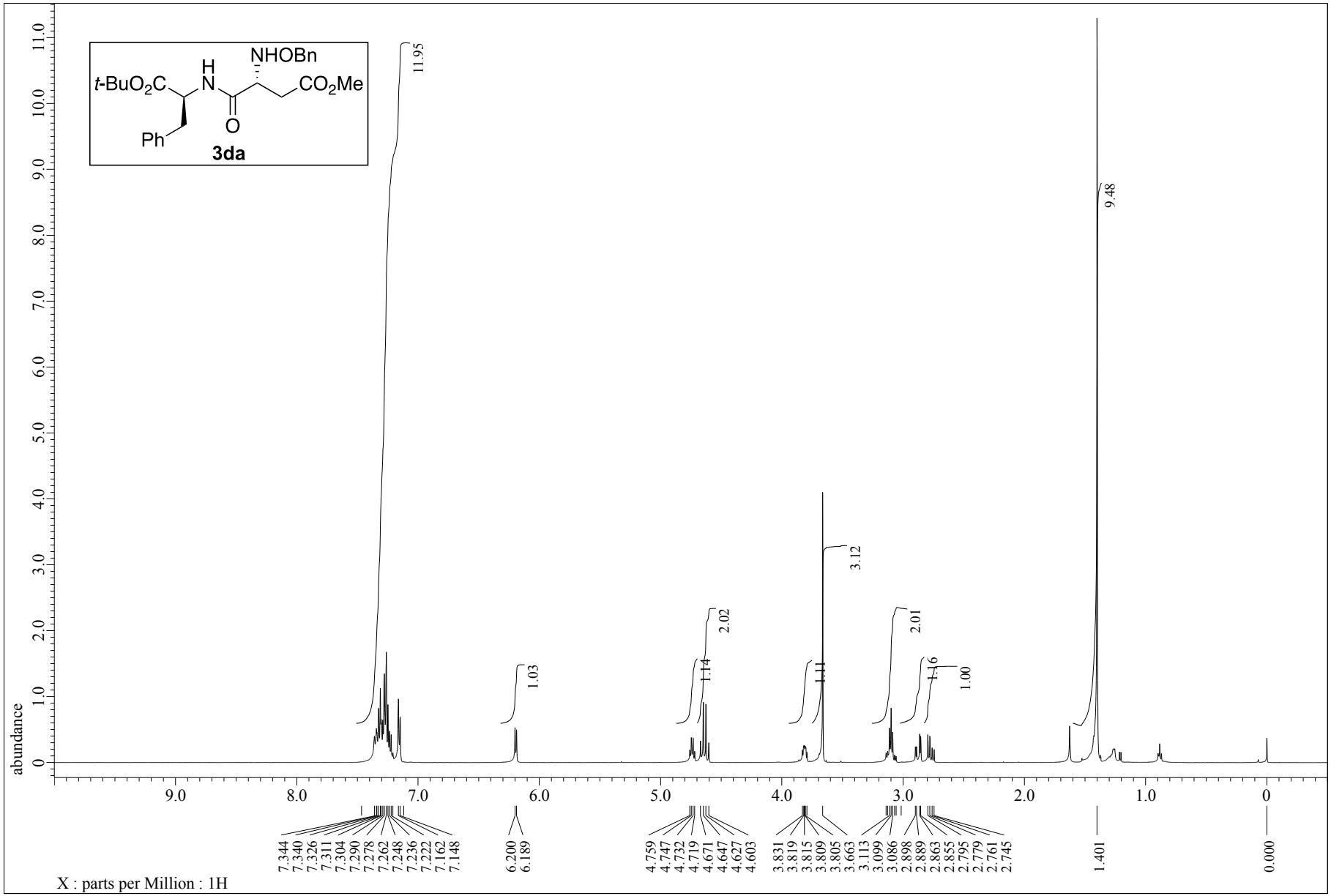

3aa
abundance
X : parts per Million : Proton
X : parts per Million : 13C
5.79
0.99
2.38
1.00
3.17
1.03
1.07
10.93

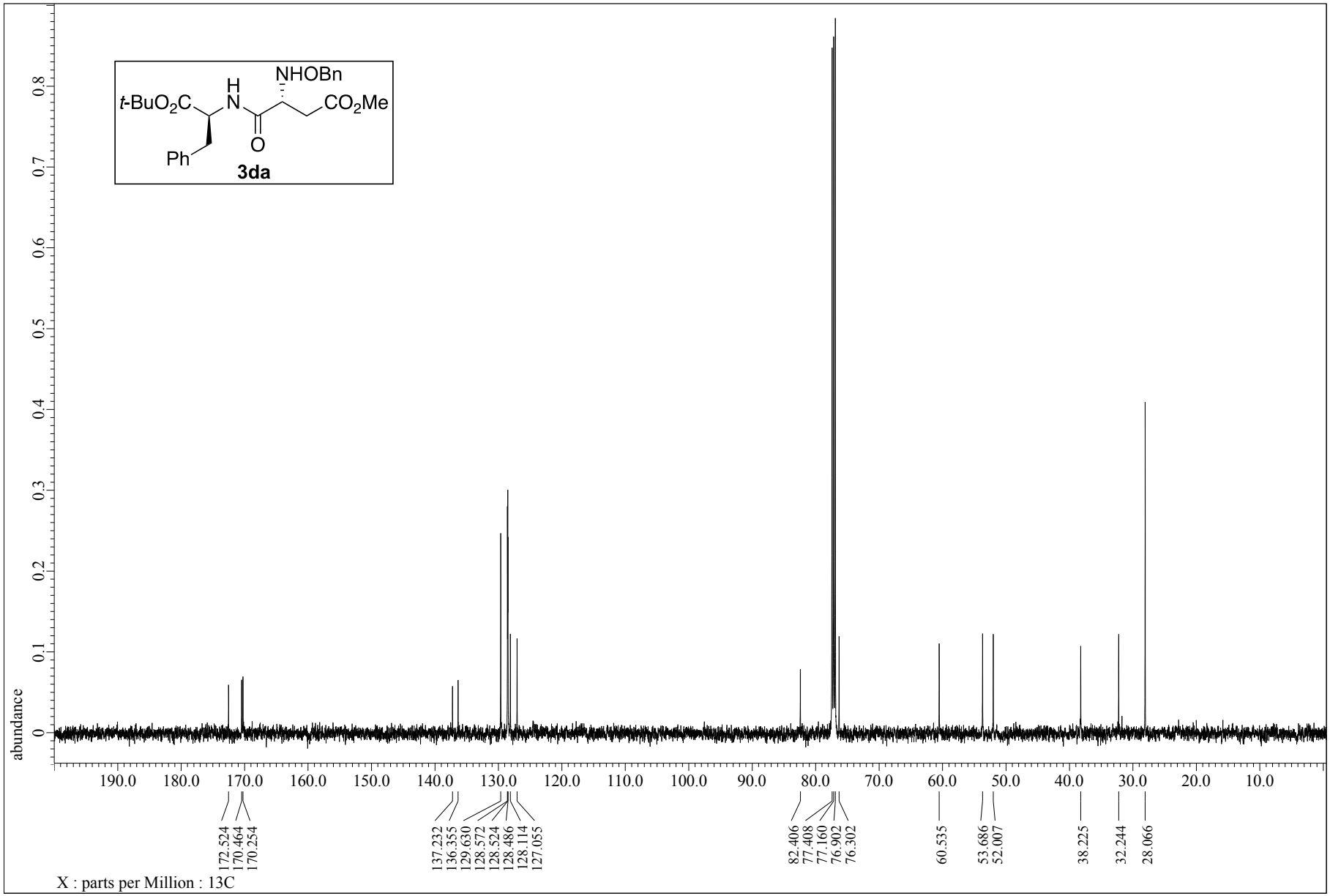

BnO
NH
BnO2C
CO2Me
3ba
abundance
X : parts per Million : 1H
11.12
0.84
2.06
2.36
3.05
1.00
1.03
1.05
7.377
7.354
7.340
7.329
7.317
7.307
7.304
7.260
6.264
5.243
5.219
5.203
5.178
4.725
4.701
4.694
4.671
4.107
4.094
4.080
3.645
2.876
2.864
2.844
2.831
2.730
2.715
2.698
2.683
0.028

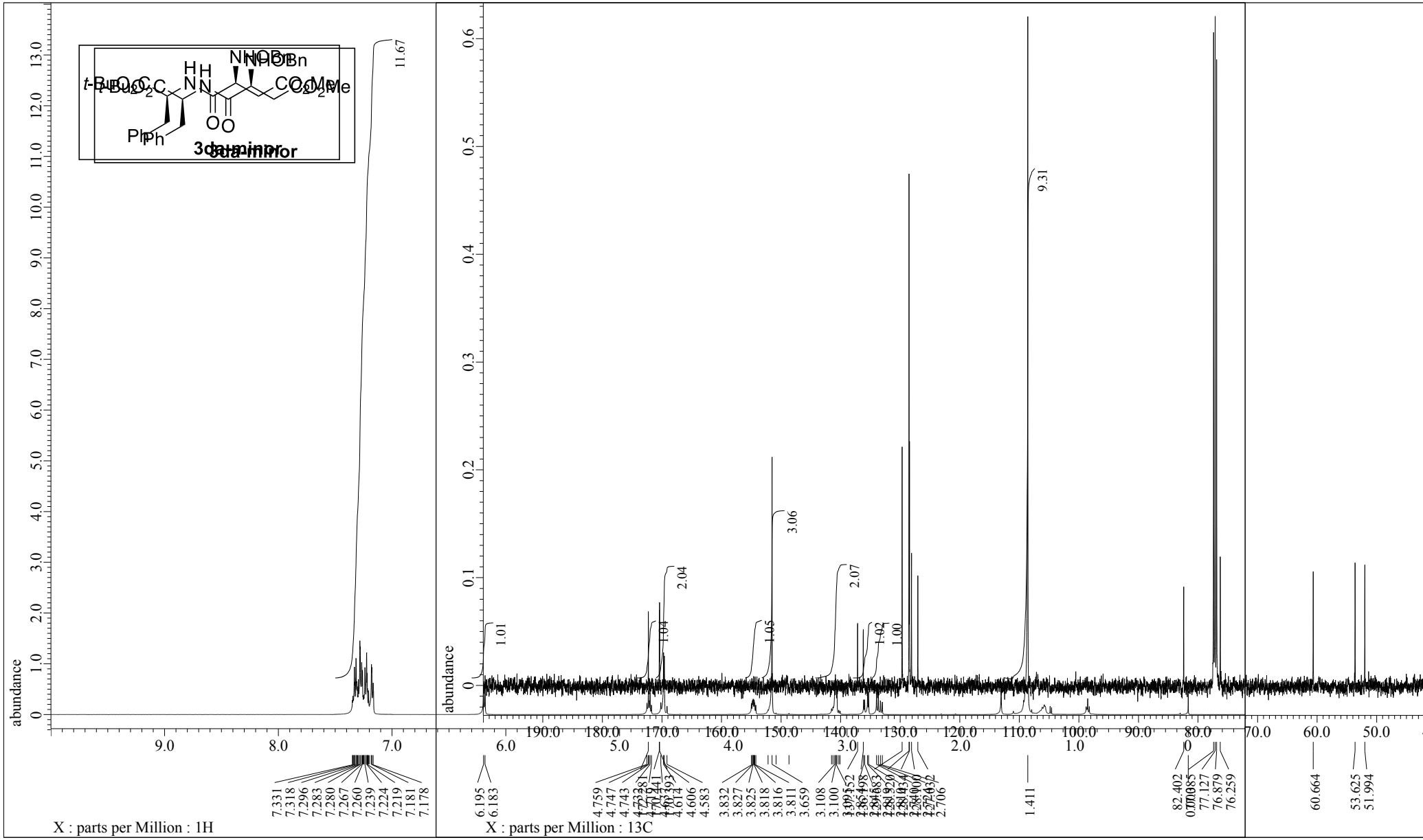

BnO
NH
BnO2C
CO2Me
3ba
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
171.523
171.227
137.423
135.430
128.629
128.552
128.448
128.409
128.324
127.971
77.418
77.160
76.912
76.645
67.192
60.220
51.988
34.152
X : parts per Million : 13C

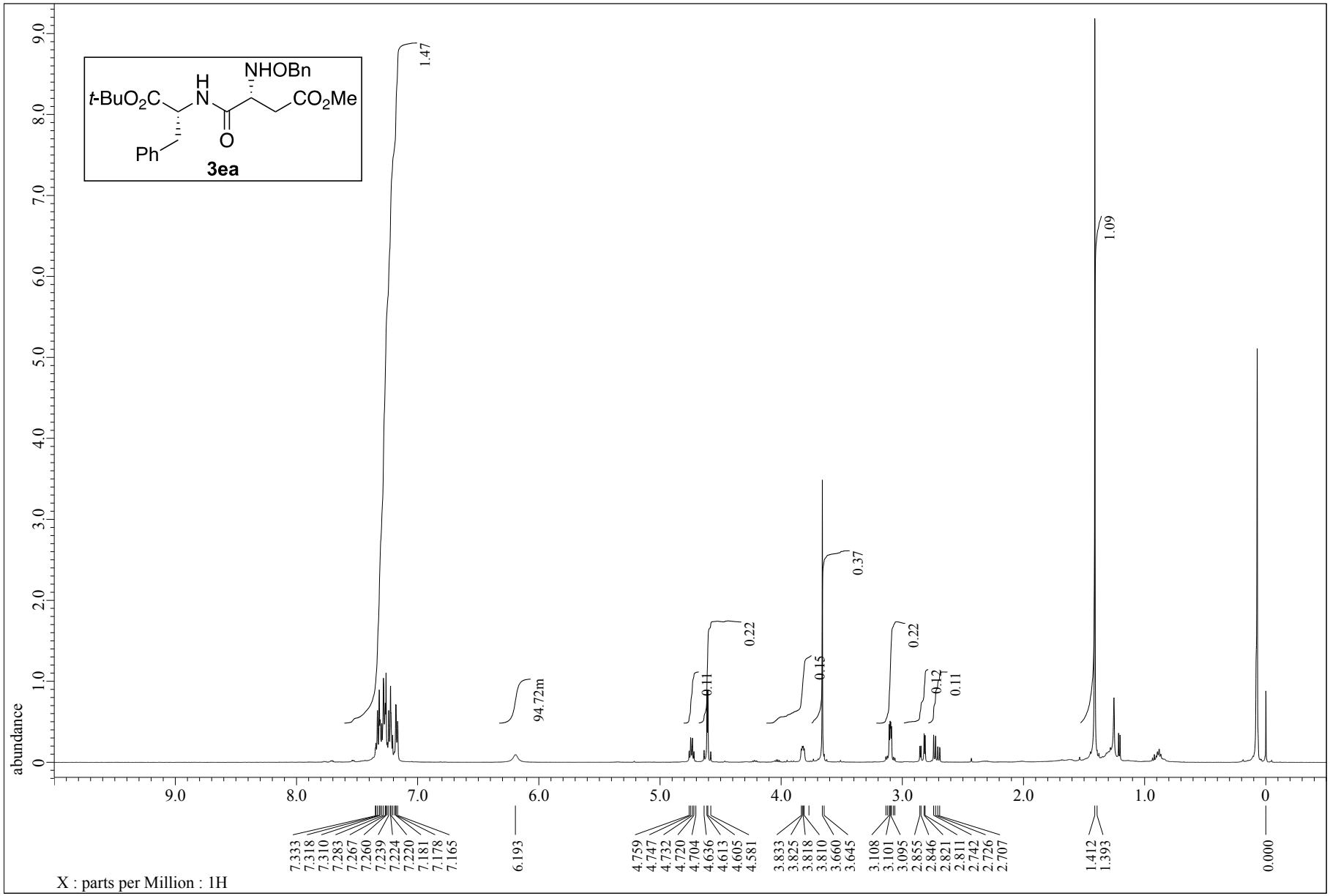

BnO
NH
EtO2C
CO2Me
3ca
abundance
X : parts per Million : Proton
5.39
2.10
2.31
1.00
2.98
0.95
1.06
0.98
3.53
7.365
7.358
7.354
7.341
7.332
7.326
7.312
7.307
7.300
7.294
7.290
7.262
6.223
4.691
4.243
4.226
4.208
4.189
4.014
3.678
2.841
2.825
2.800
2.784
2.726
2.697
2.680
2.657
2.639
1.292
1.275
1.257
0.000

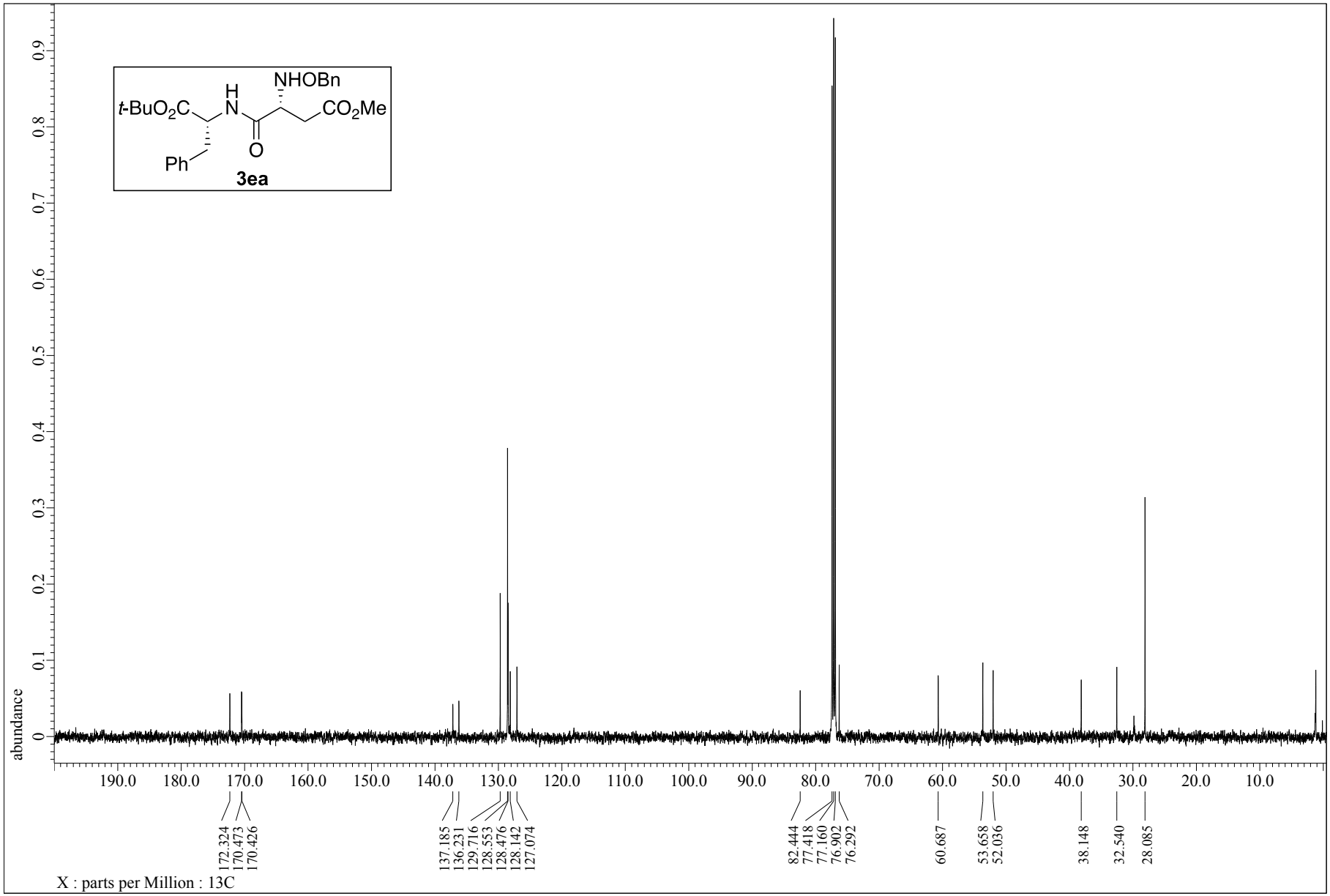

BnO
NH
EtO2C
CO2Me
3ca
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
171.648
171.352
137.514
128.570
128.418
127.989
77.475
77.160
76.836
76.617
61.561
60.188
52.017
34.216
14.203
X : parts per Million : Carbon13

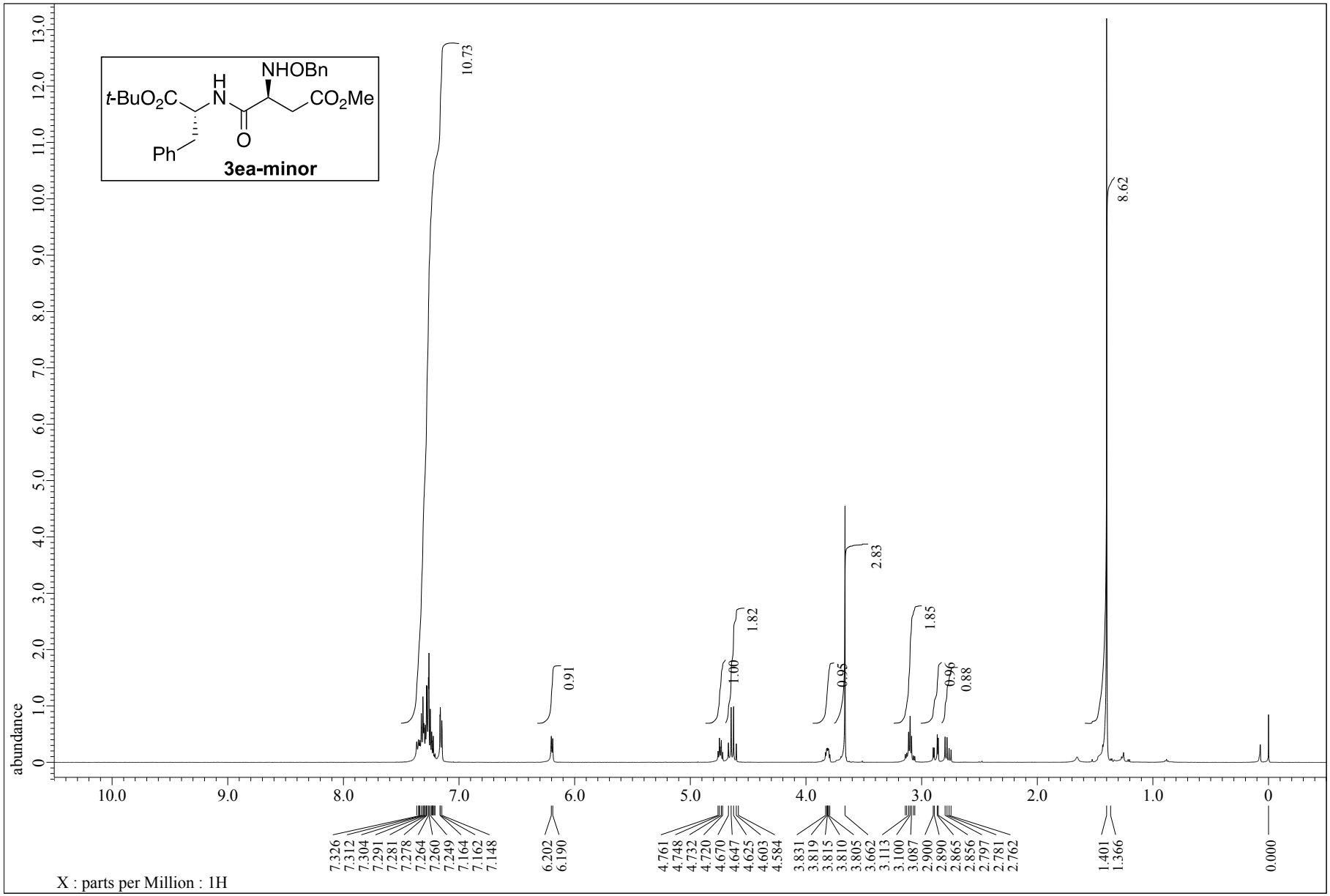

NHOBn
H
N
t-BuO2C
CO2Me
O
Ph
3da
11.95
9.48
3.12
2.02
2.01
1.03
1.14
1.11
1.16
1.00
abundance
X : parts per Million : 1H
7.344
7.340
7.326
7.311
7.304
7.290
7.278
7.262
7.248
7.236
7.222
7.162
7.148
6.200
6.189
4.759
4.747
4.732
4.719
4.671
4.647
4.627
4.603
3.831
3.819
3.815
3.809
3.805
3.663
3.113
3.099
3.086
2.898
2.889
2.863
2.855
2.795
2.779
2.761
2.745
1.401
0.000

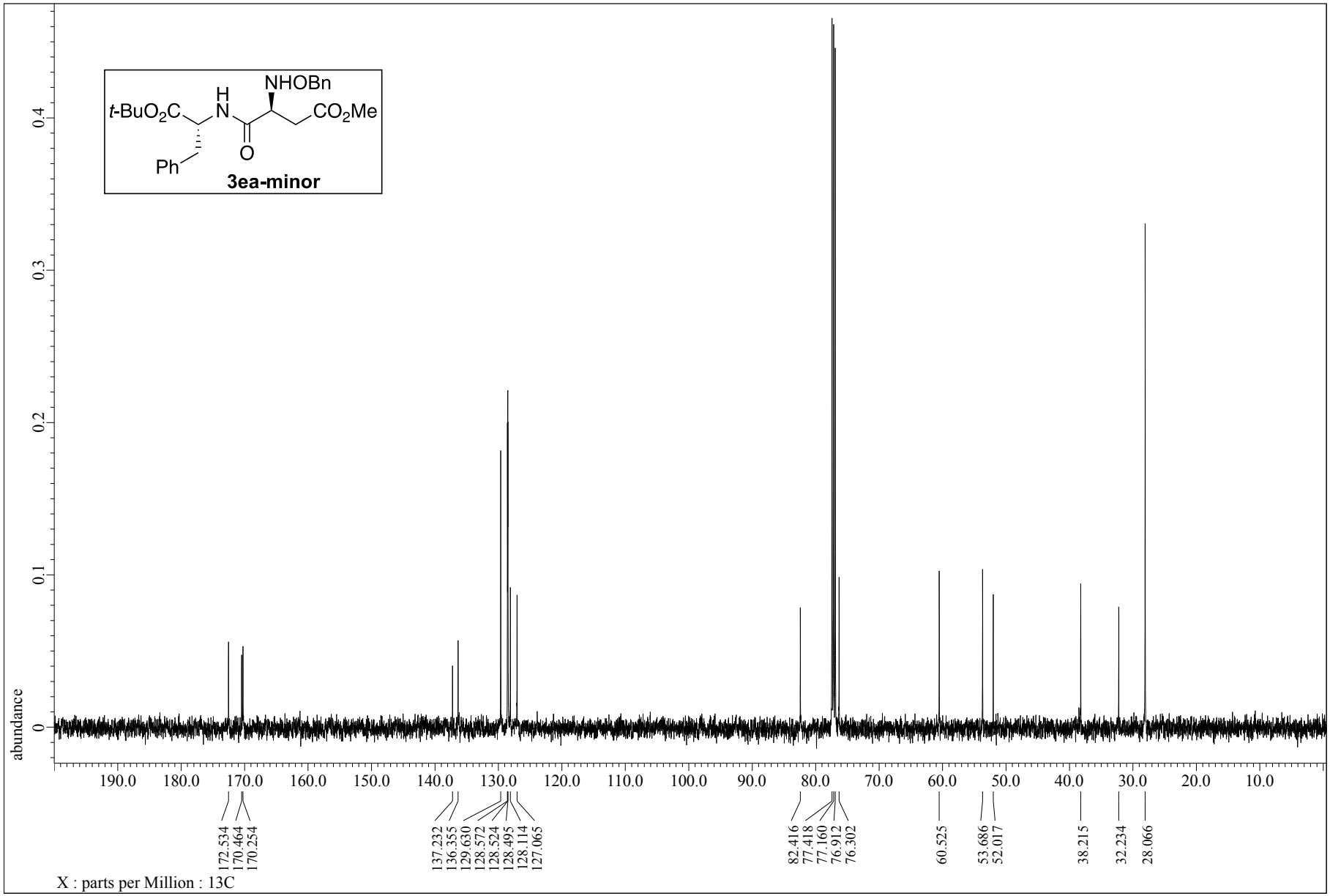

NHOBn
H
N
t-BuO2C
CO2Me
O
Ph
3da
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
172.524
170.464
170.254
137.232
136.355
129.630
128.572
128.524
128.486
128.114
127.055
82.406
77.408
77.160
76.902
76.302
60.535
53.686
52.007
38.225
32.244
28.066
X : parts per Million : 13C

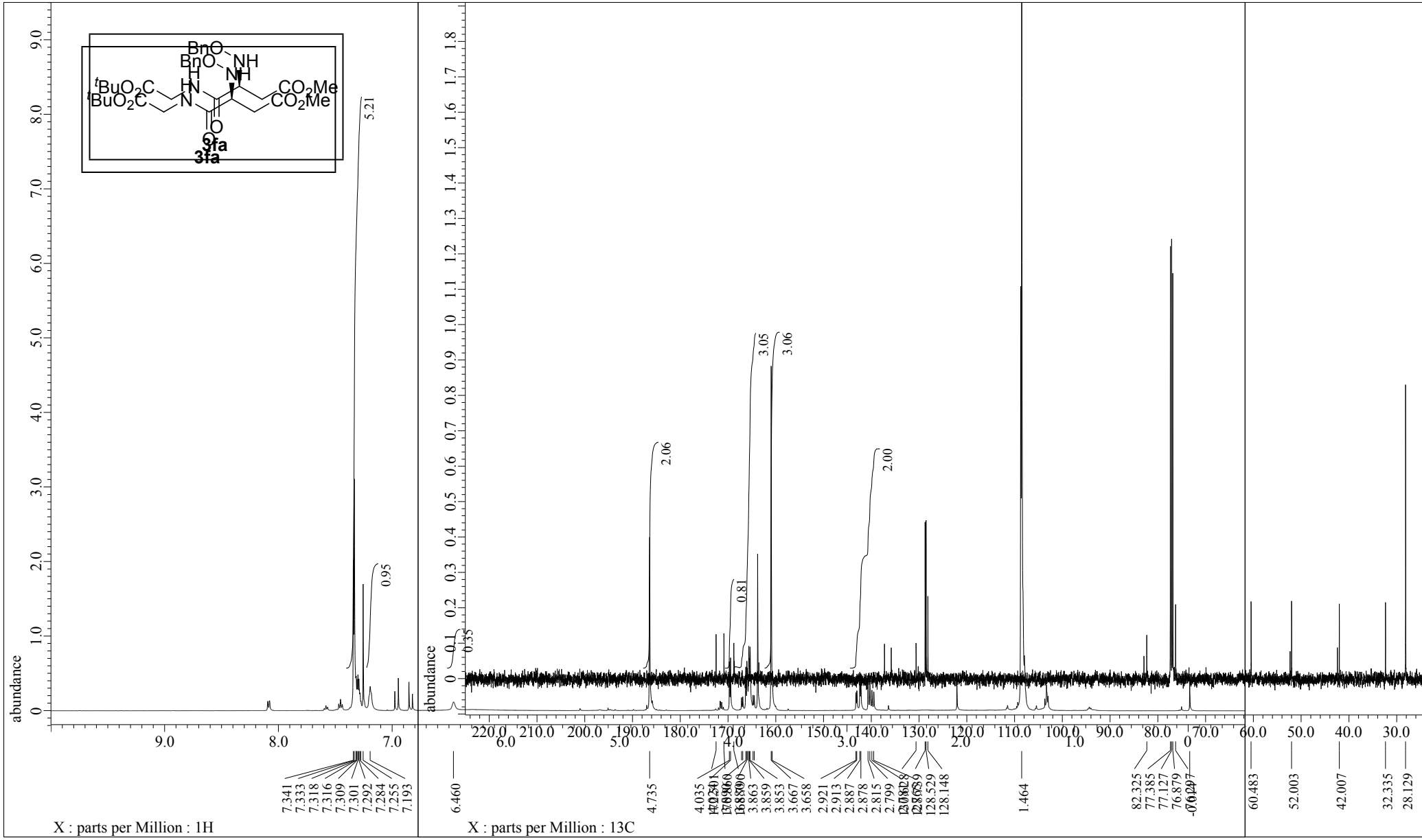

3da-minor
X : parts per Million : 1H
X : parts per Million : 13C

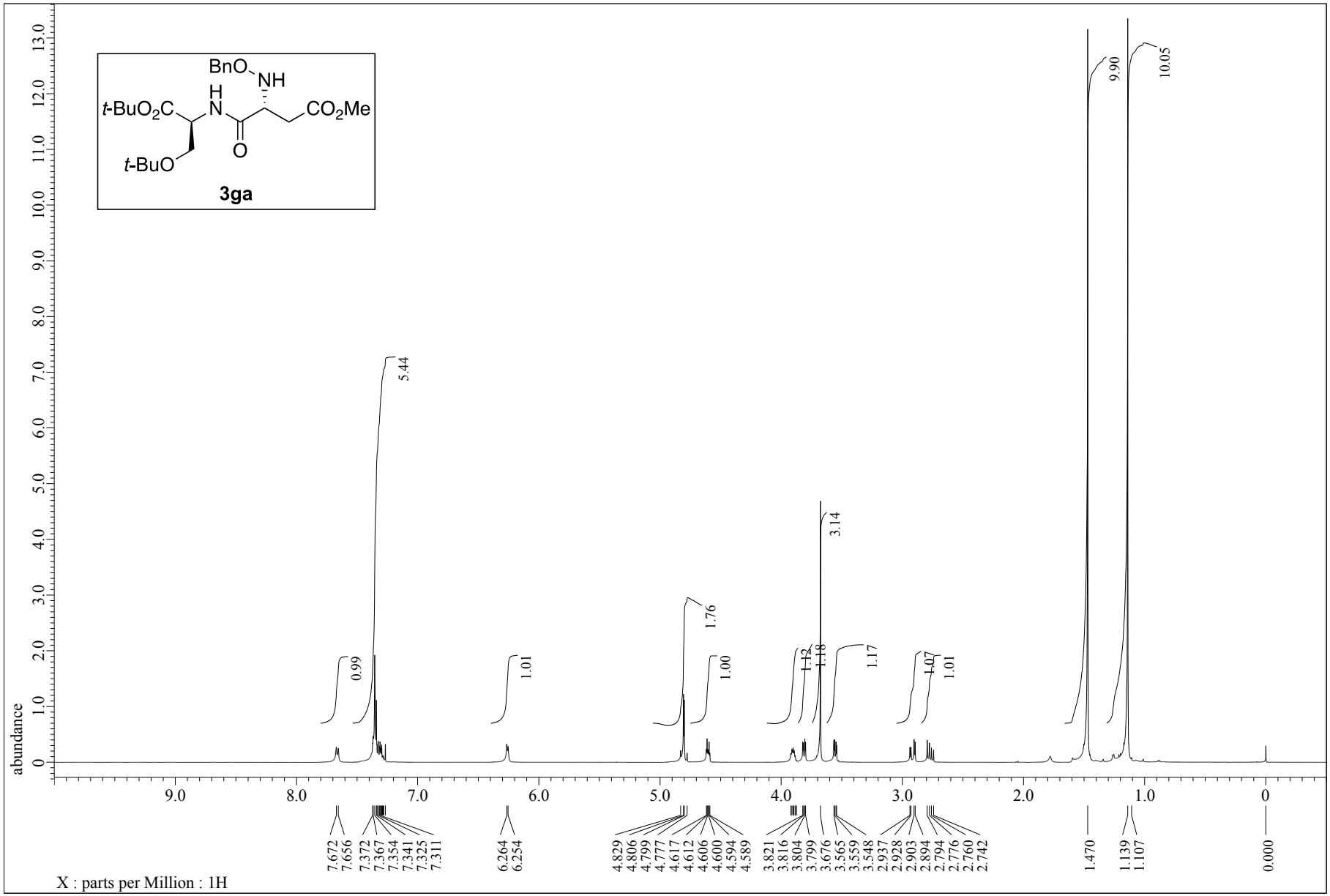

NHOBn
H
N
t-BuO2C
CO2Me
O
Ph
3ea
1.47
1.09
0.37
0.22
0.22
0.15
0.12
0.11
0.11
94.72m
abundance
X : parts per Million : 1H
7.333
7.318
7.310
7.283
7.267
7.260
7.239
7.224
7.220
7.181
7.178
7.165
6.193
4.759
4.747
4.732
4.720
4.704
4.636
4.613
4.605
4.581
3.833
3.825
3.818
3.810
3.660
3.645
3.108
3.101
3.095
2.855
2.846
2.821
2.811
2.742
2.726
2.707
1.412
1.393
0.000

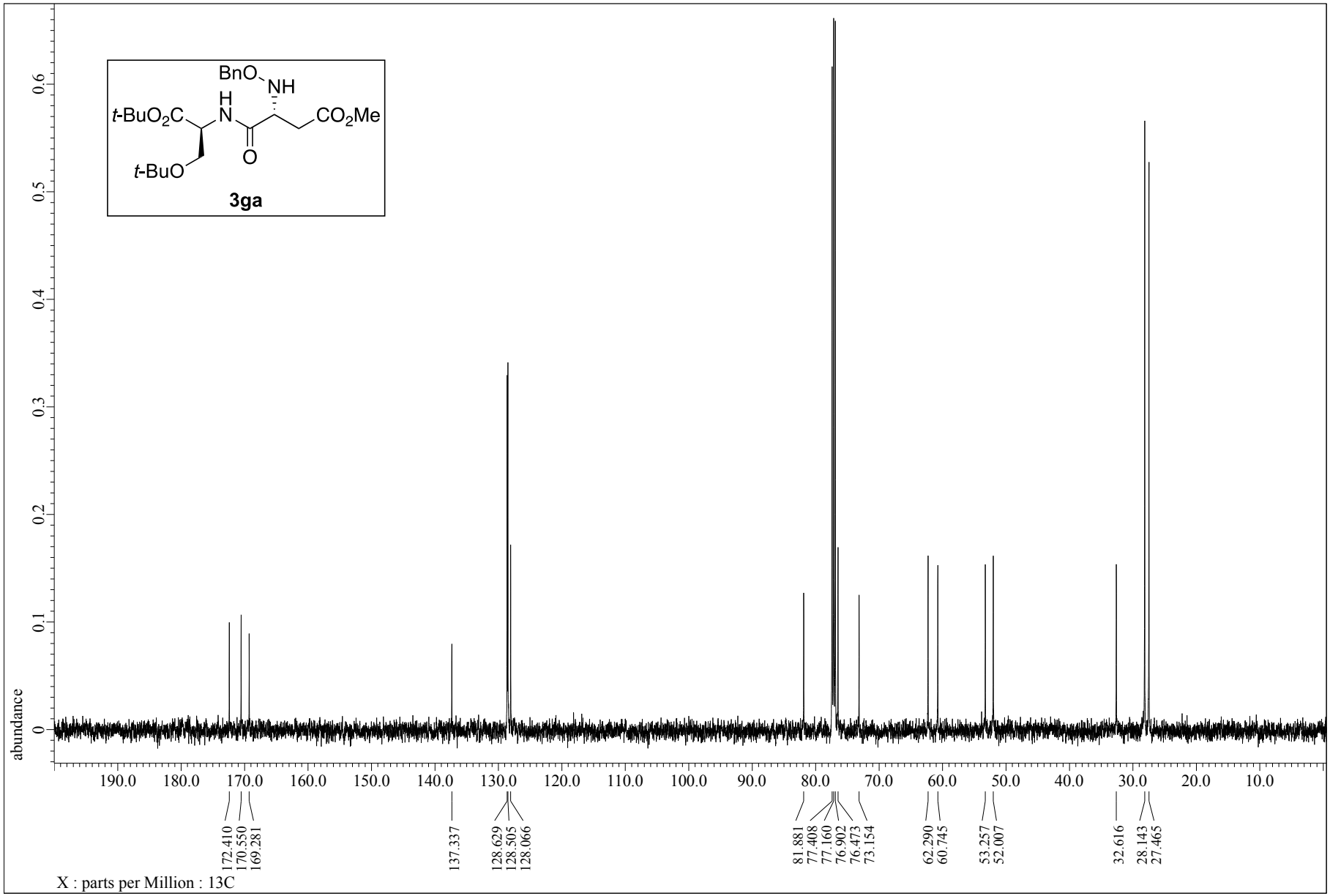

NHOBn
H
N
t-BuO2C
CO2Me
O
Ph
3ea
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
172.324
170.473
170.426
137.185
136.231
129.716
128.553
128.476
128.142
127.074
82.444
77.418
77.160
76.902
76.292
60.687
53.658
52.036
38.148
32.540
28.085
X : parts per Million : 13C

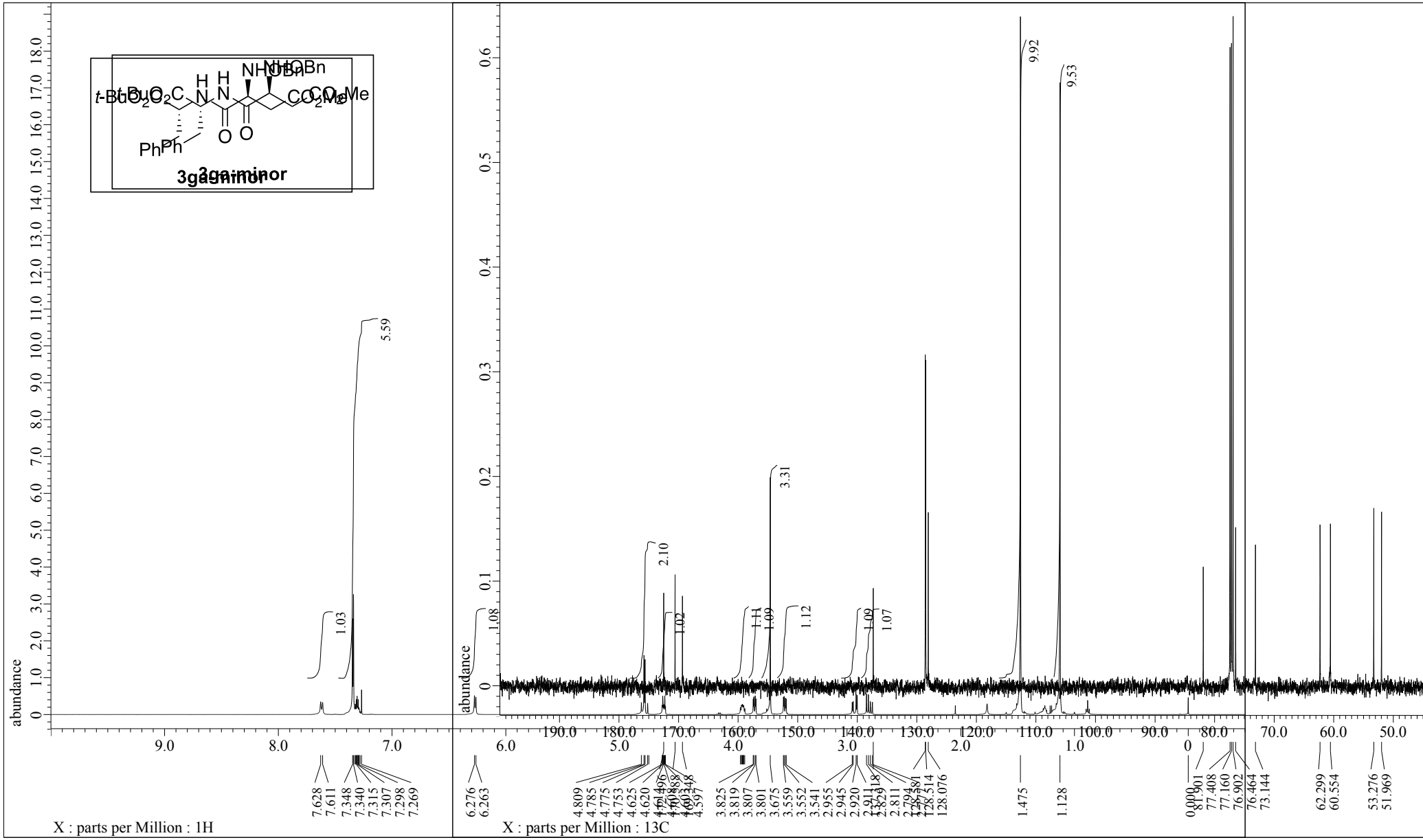

NHOBn
t-BuO2C
H
N
CO2Me
O
Ph
3ea-minor
10.73
8.62
2.83
1.82
1.85
0.91
1.00
0.95
0.96
0.88
abundance
X : parts per Million : 1H
7.326
7.312
7.304
7.291
7.281
7.278
7.264
7.260
7.249
7.164
7.162
7.148
6.202
6.190
4.761
4.748
4.732
4.720
4.670
4.647
4.625
4.603
4.584
3.831
3.819
3.815
3.810
3.805
3.662
3.113
3.100
3.087
2.900
2.890
2.865
2.856
2.797
2.781
2.762
1.401
1.366
0.000

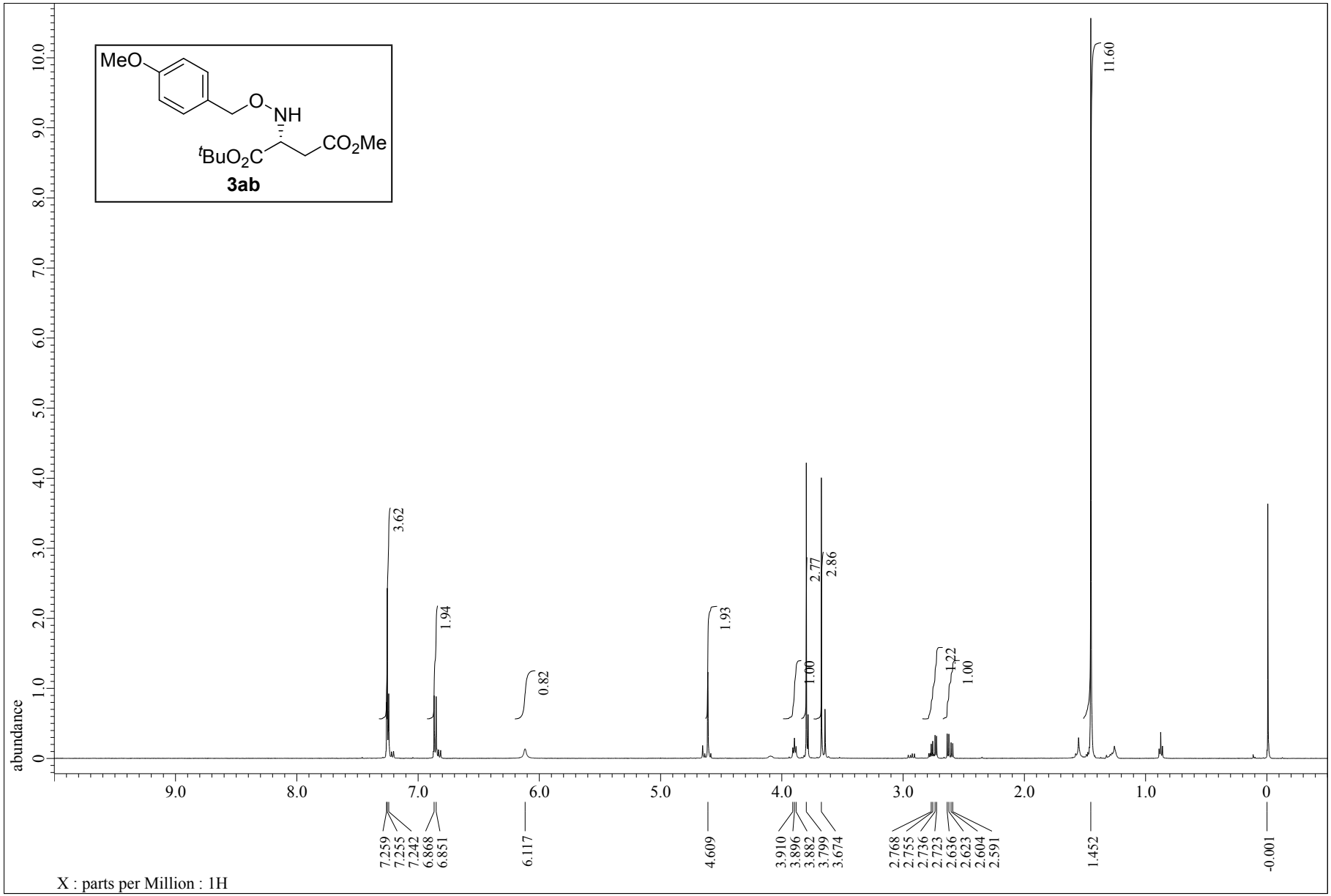

NHOBn
H
N
t-BuO2C
CO2Me
O
Ph
3ea-minor
abundance
0
0.1
0.2
0.3
0.4
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
172.534
170.464
170.254
137.232
136.355
129.630
128.572
128.524
128.495
128.114
127.065
82.416
77.418
77.160
76.912
76.302
60.525
53.686
52.017
38.215
32.234
28.066
X : parts per Million : 13C

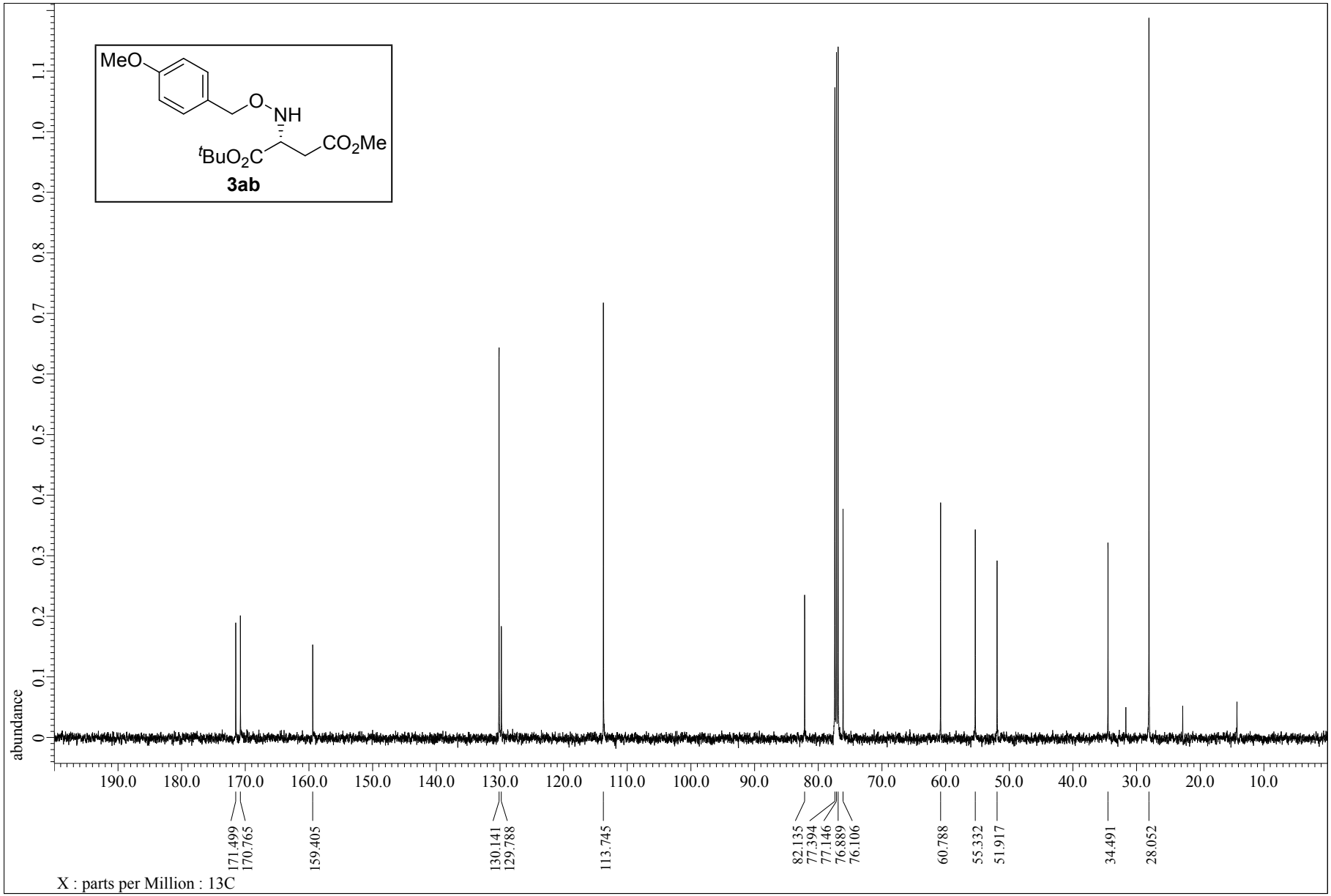

BnO
BnO
NH
H
N
NH
tBuO2C
tBuO2C
N
CO2Me
CO2Me
O
6fa
3fa
3fa
5.21
0.95
2.06
0.81
3.05
3.06
2.00
0.35
abundance
abundance
X : parts per Million : 1H
X : parts per Million : 13C

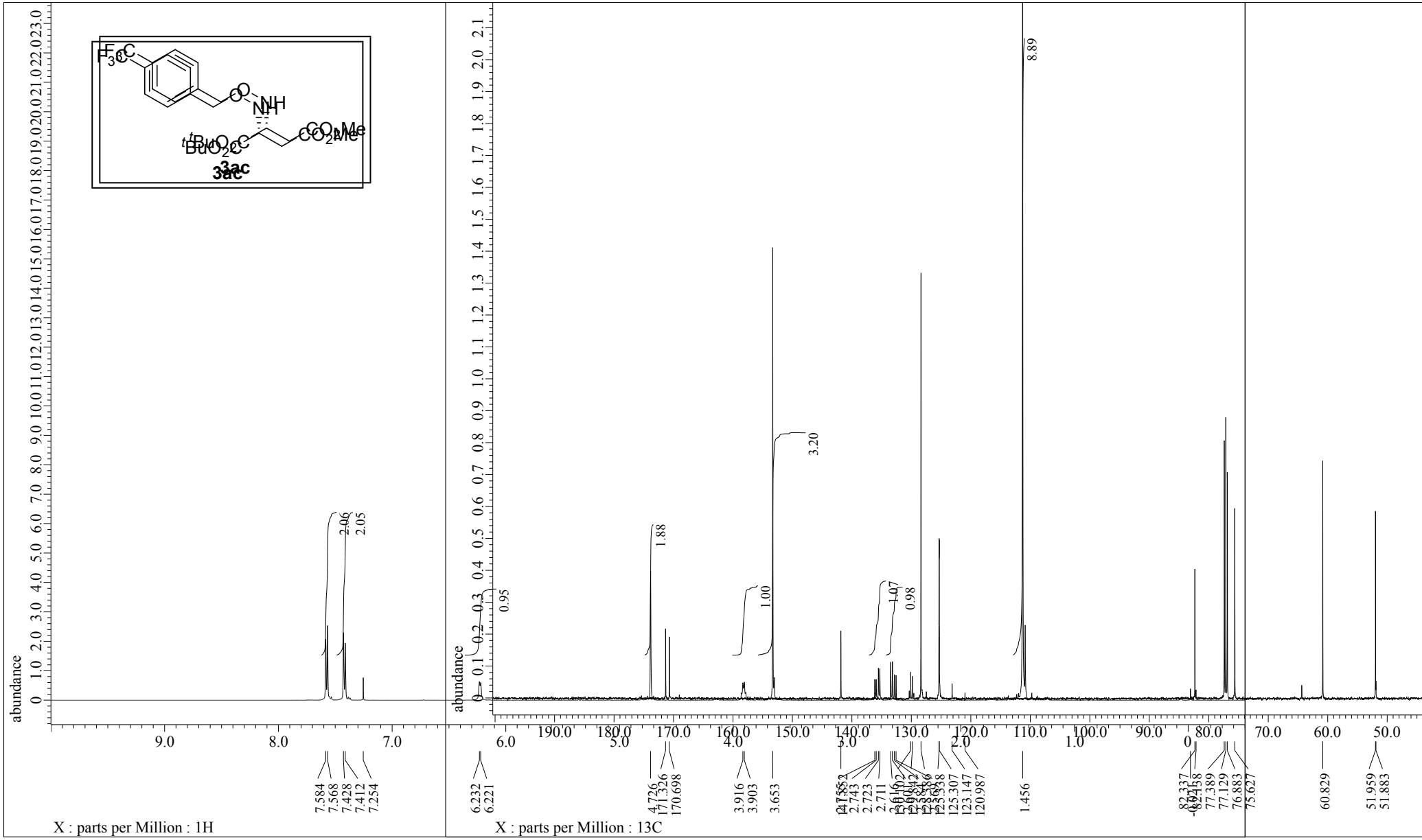

BnO
NH
H
N
t-BuO2C
CO2Me
O
t-BuO
3ga
abundance
9.90
10.05
5.44
0.99
1.01
1.76
1.00
1.12
1.18
3.14
1.17
1.07
1.01
7.672
7.656
7.372
7.367
7.354
7.341
7.325
7.311
6.264
6.254
4.829
4.806
4.799
4.777
4.617
4.612
4.606
4.600
4.594
4.589
3.821
3.816
3.804
3.799
3.676
3.565
3.559
3.548
2.937
2.928
2.903
2.894
2.794
2.776
2.760
2.742
1.470
1.139
1.107
0.000
X : parts per Million : 1H

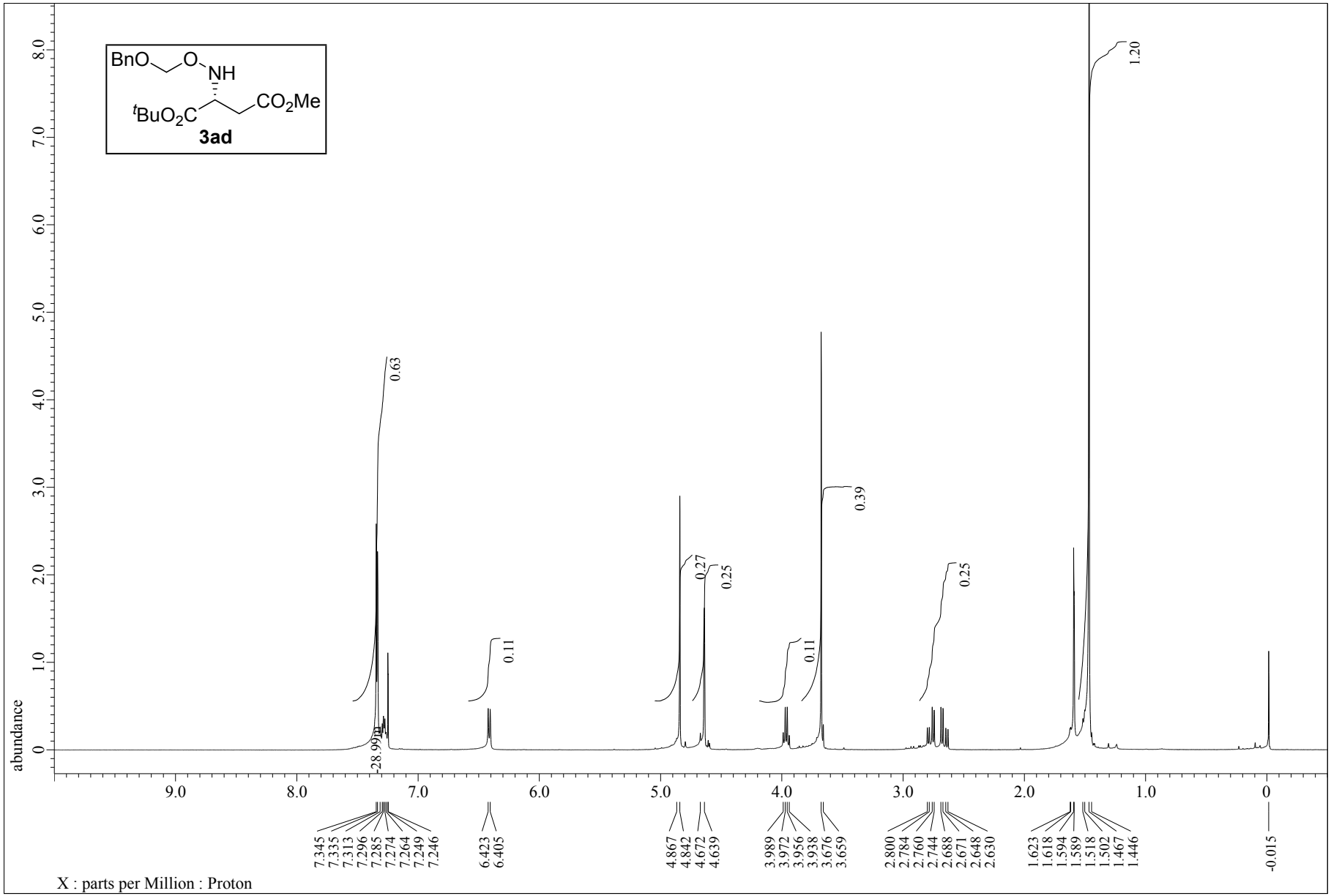

BnO
NH
H
N
t-BuO2C
CO2Me
O
t-BuO
3ga
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
172.410
170.550
169.281
137.337
128.629
128.505
128.066
81.881
77.408
77.160
76.902
76.473
73.154
62.290
60.745
53.257
52.007
32.616
28.143
27.465
X : parts per Million : 13C

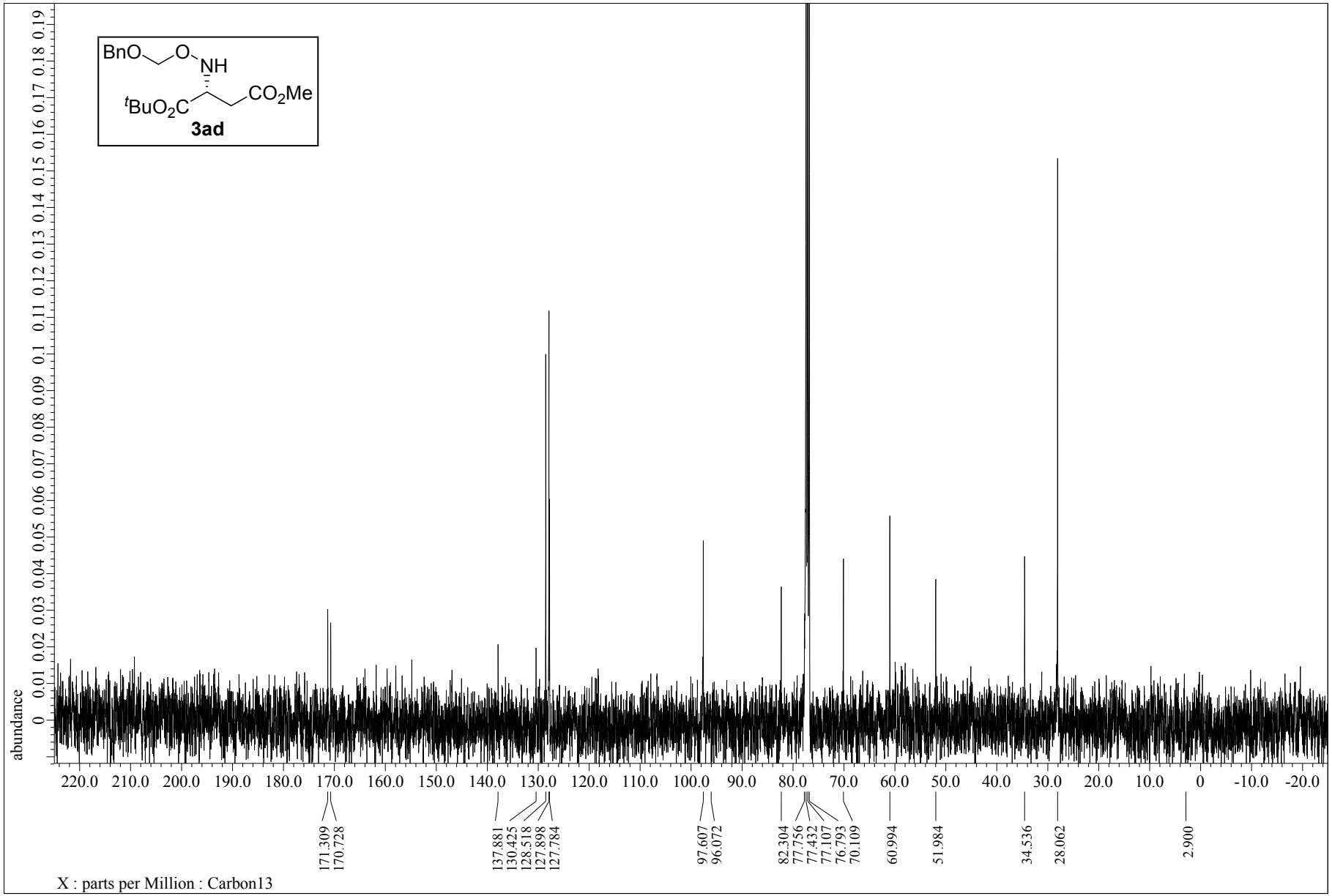

3ga-minor
X : parts per Million : 1H
X : parts per Million : 13C

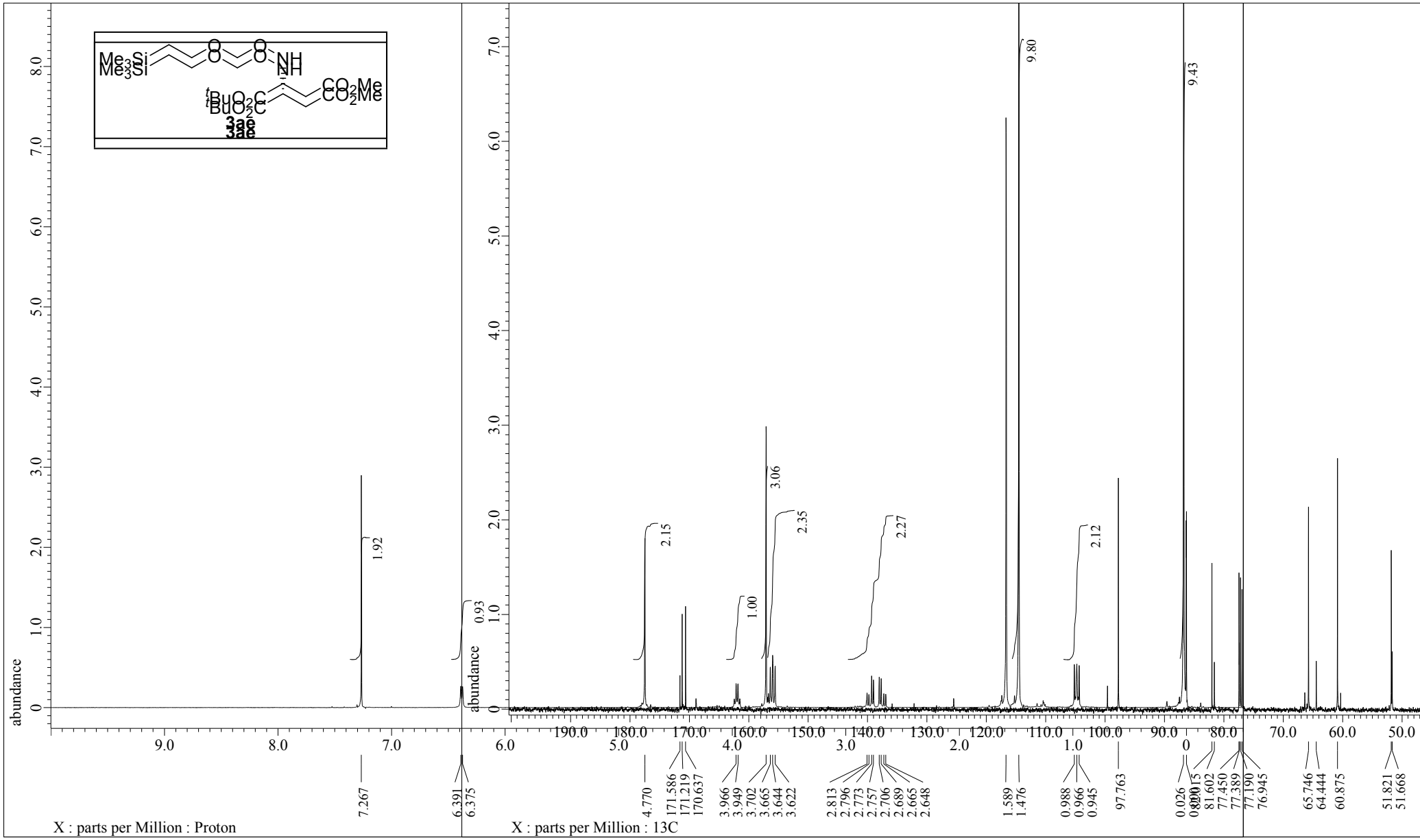

MeO
O
NH
^{t}BuO$_2$C
CO$_2$Me
3ab
abundance
X : parts per Million : 1H
3.62
1.94
0.82
1.93
2.77
2.86
1.00
1.22
1.00
11.60
7.259
7.255
7.242
6.868
6.851
6.117
4.609
3.910
3.896
3.882
3.799
3.674
2.768
2.755
2.736
2.723
2.636
2.623
2.604
2.591
1.452
-0.001

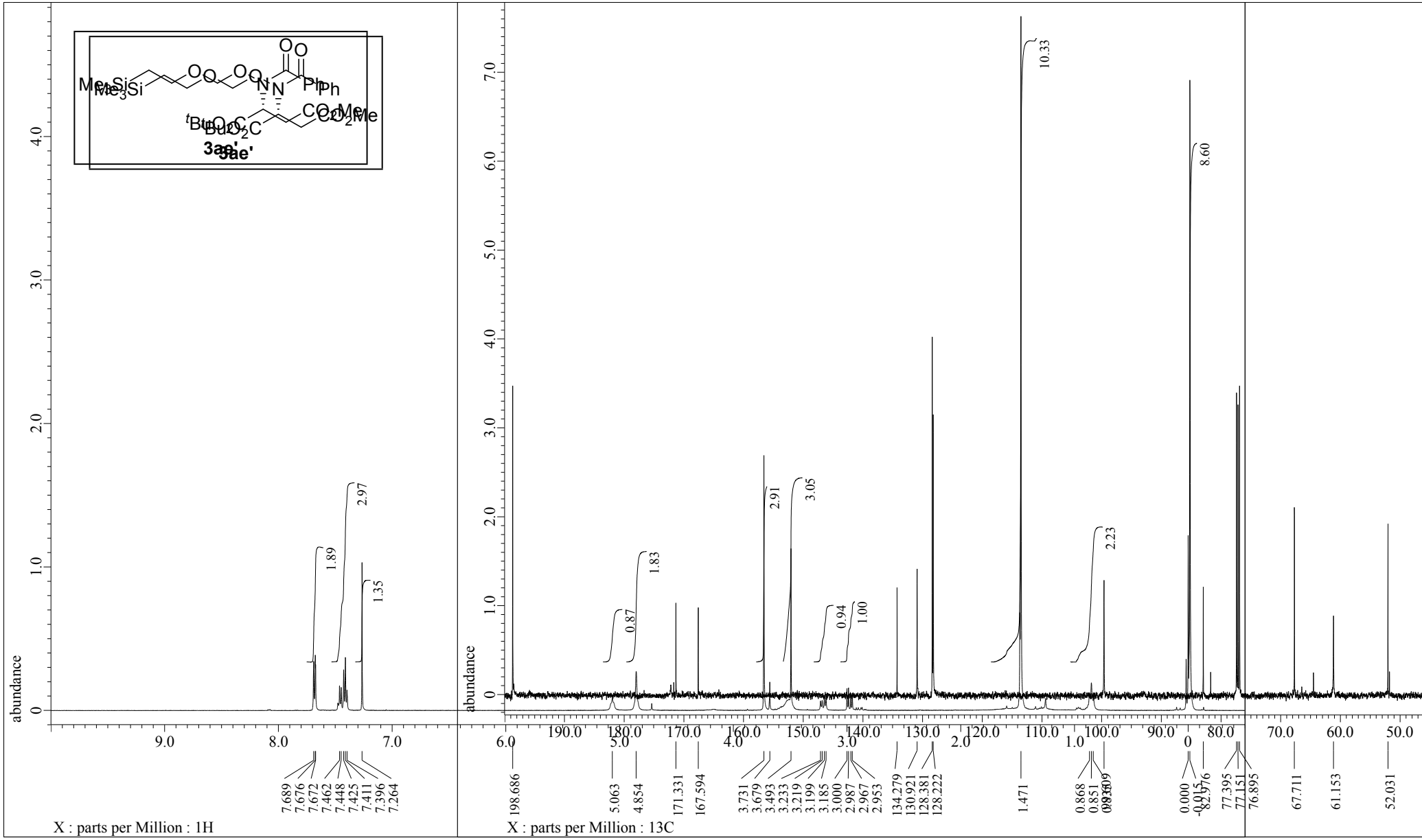

MeO
O
NH
^{t}BuO$_2$C
CO$_2$Me
3ab
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
171.499
170.765
159.405
130.141
129.788
113.745
82.135
77.394
77.146
76.889
76.106
60.788
55.332
51.917
34.491
28.052
X : parts per Million : 13C

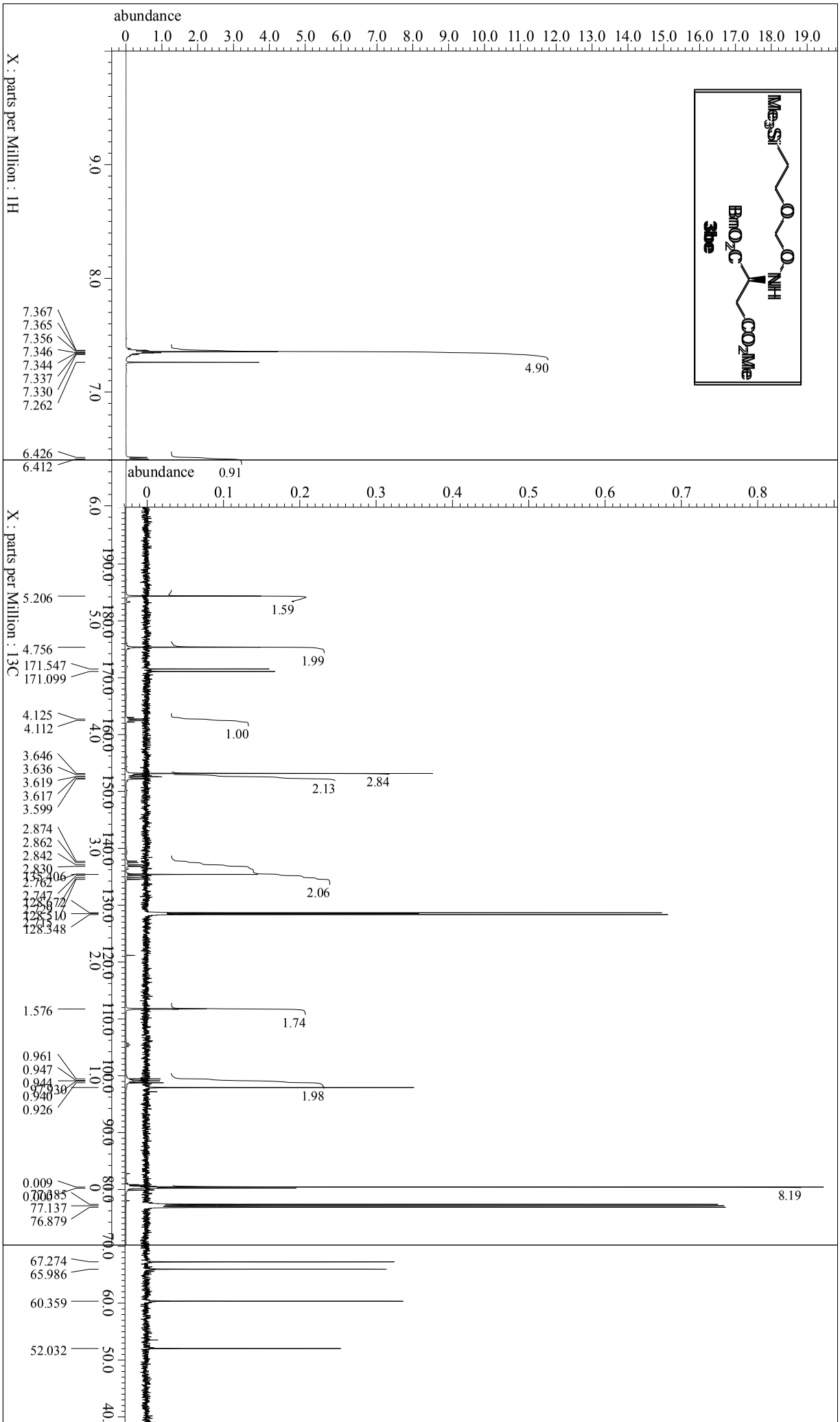

3ac
abundance
X : parts per Million : 1H
X : parts per Million : 13C
7.584
7.568
7.428
7.412
7.254
2.06
2.05
6.232
6.221
4.726
171.326
170.698
3.916
3.903
3.653
2.743
2.723
2.711
125.307
123.147
120.987
1.456
82.337
77.389
77.129
76.883
75.627
60.829
51.959
51.883
0.95
1.88
1.00
3.20
1.07
0.98
8.89

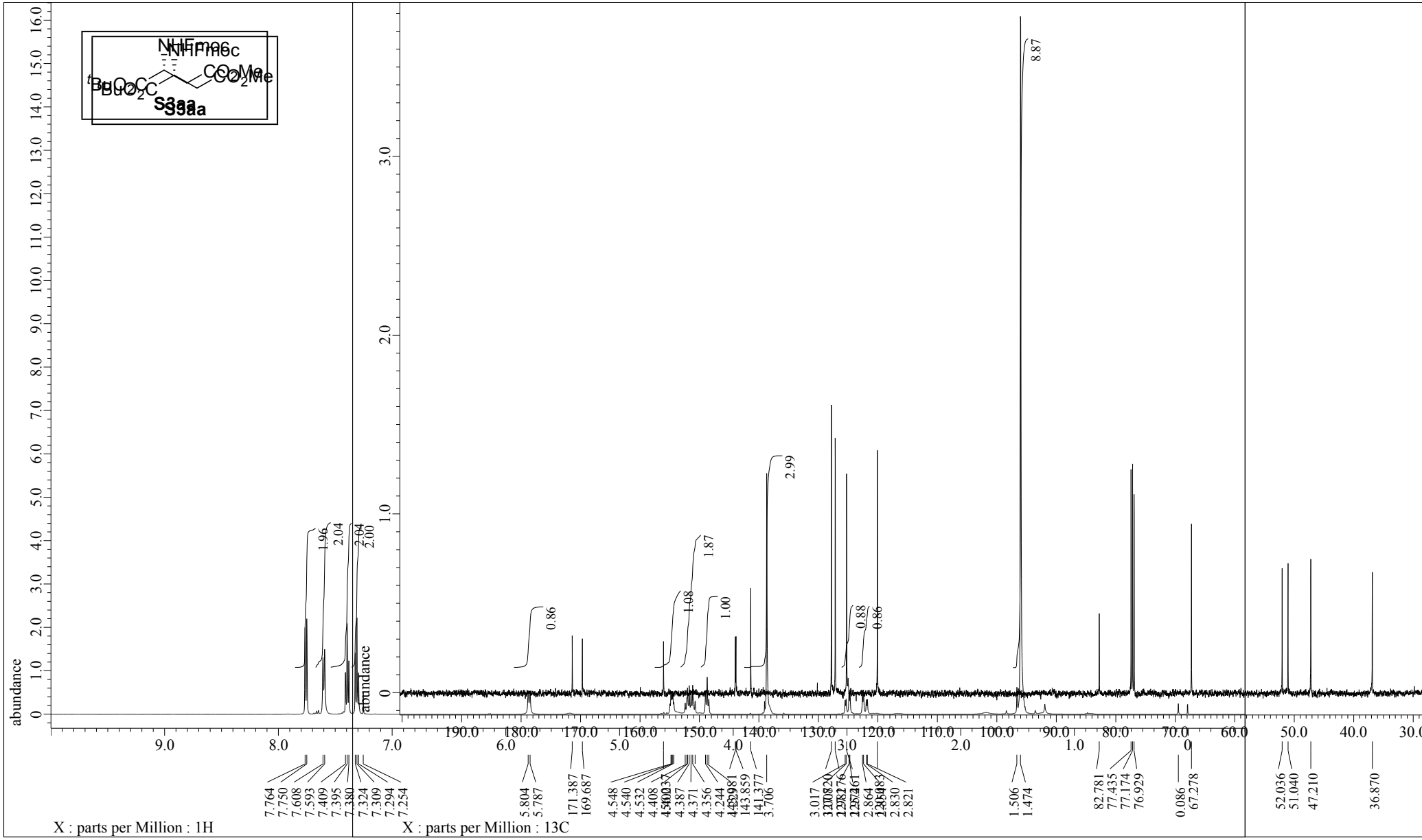

BnO
O
NH
tBuO2C
CO2Me
3ad
abundance
X : parts per Million : Proton
28.99
0.63
0.11
0.27
0.25
0.11
0.39
0.25
1.20
7.345
7.335
7.313
7.296
7.285
7.274
7.264
7.249
7.246
6.423
6.405
4.867
4.842
4.672
4.639
3.989
3.972
3.956
3.938
3.676
3.659
2.800
2.784
2.760
2.744
2.688
2.671
2.648
2.630
1.623
1.618
1.594
1.589
1.518
1.502
1.467
1.446
-0.015

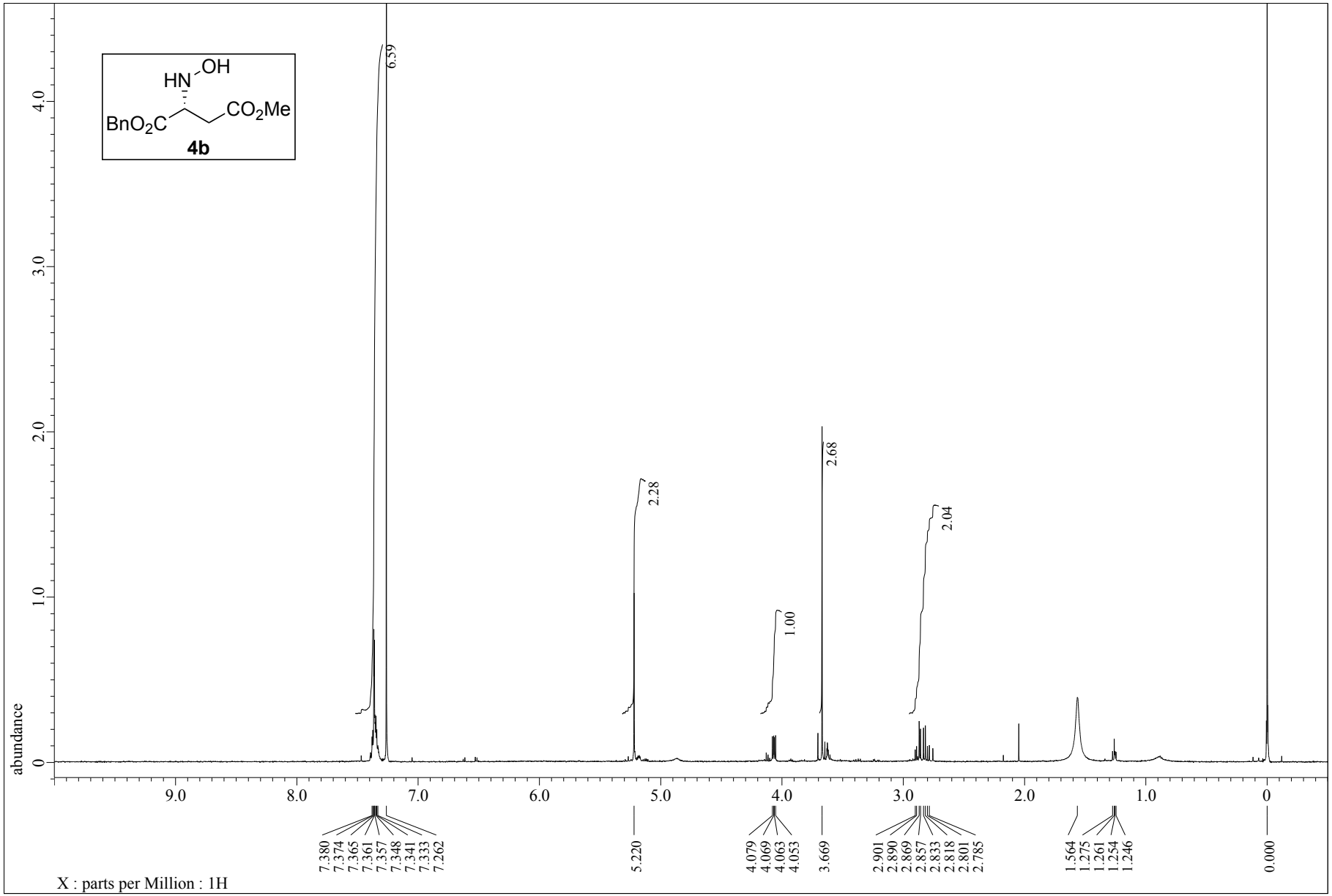

BnO
O
NH
^{t}BuO$_2$C
CO$_2$Me
3ad
abundance
0 0.01 0.02 0.03 0.04 0.05 0.06 0.07 0.08 0.09 0.1 0.11 0.12 0.13 0.14 0.15 0.16 0.17 0.18 0.19
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
171.309
170.728
137.881
130.425
128.518
127.898
127.784
97.607
96.072
82.304
77.756
77.432
77.107
76.793
70.109
60.994
51.984
34.536
28.062
2.900
X : parts per Million : Carbon13

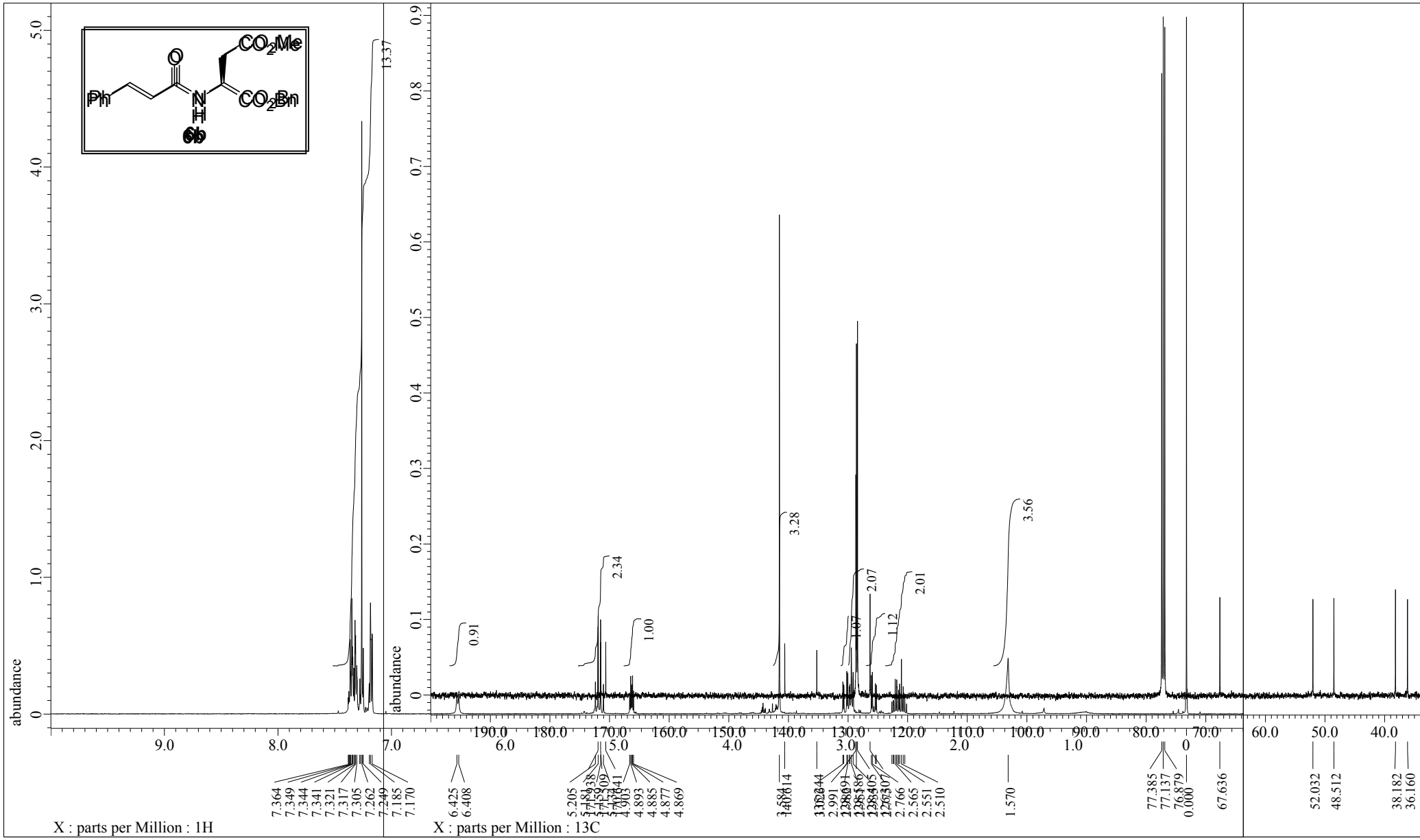

Me3Si
Me3Si
NH
tBuO2C
CO2Me
3ae
abundance
X : parts per Million : Proton
X : parts per Million : 13C
9.80
9.43
3.06
2.35
2.27
2.15
2.12
1.92
1.00
0.93
7.267
6.391
6.375
4.770
171.586
171.219
170.637
3.966
3.949
3.702
3.665
3.644
3.622
2.813
2.796
2.773
2.757
2.706
2.689
2.665
2.648
1.589
1.476
0.988
0.966
0.945
97.763
0.026
81.602
77.450
77.389
77.190
76.945
65.746
64.444
60.875
51.821
51.668

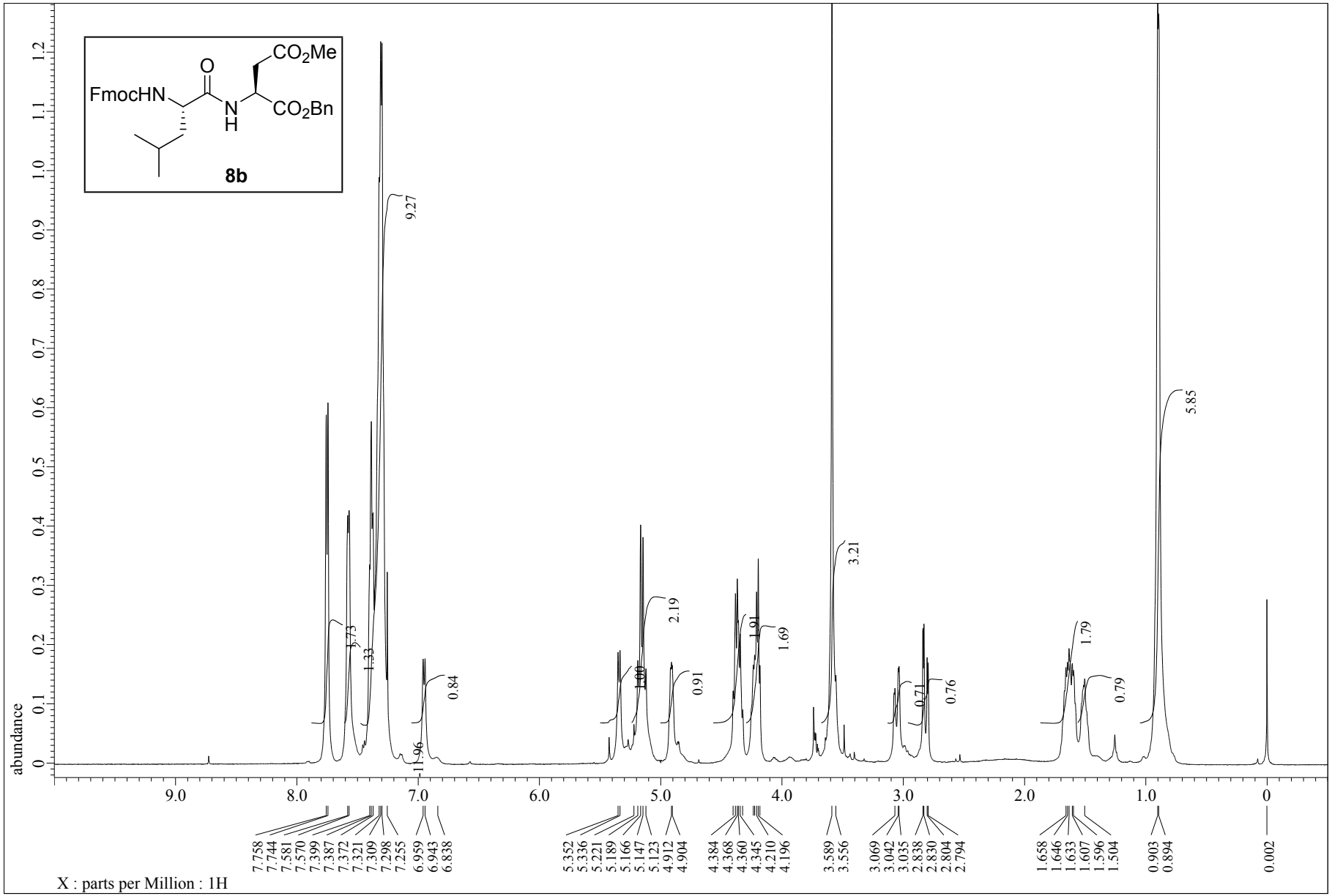

3ae'
abundance
X : parts per Million : 1H
X : parts per Million : 13C
7.689
7.676
7.672
7.462
7.448
7.425
7.411
7.396
7.264
1.89
2.97
1.35
198.686
5.063
4.854
171.331
167.594
3.731
3.679
3.493
3.233
3.219
3.199
3.185
3.000
2.987
2.967
2.953
134.279
130.921
128.381
128.222
1.471
0.868
0.851
0.000
77.395
77.151
76.895
67.711
61.153
52.031
0.87
1.83
2.91
3.05
0.94
1.00
10.33
2.23
8.60

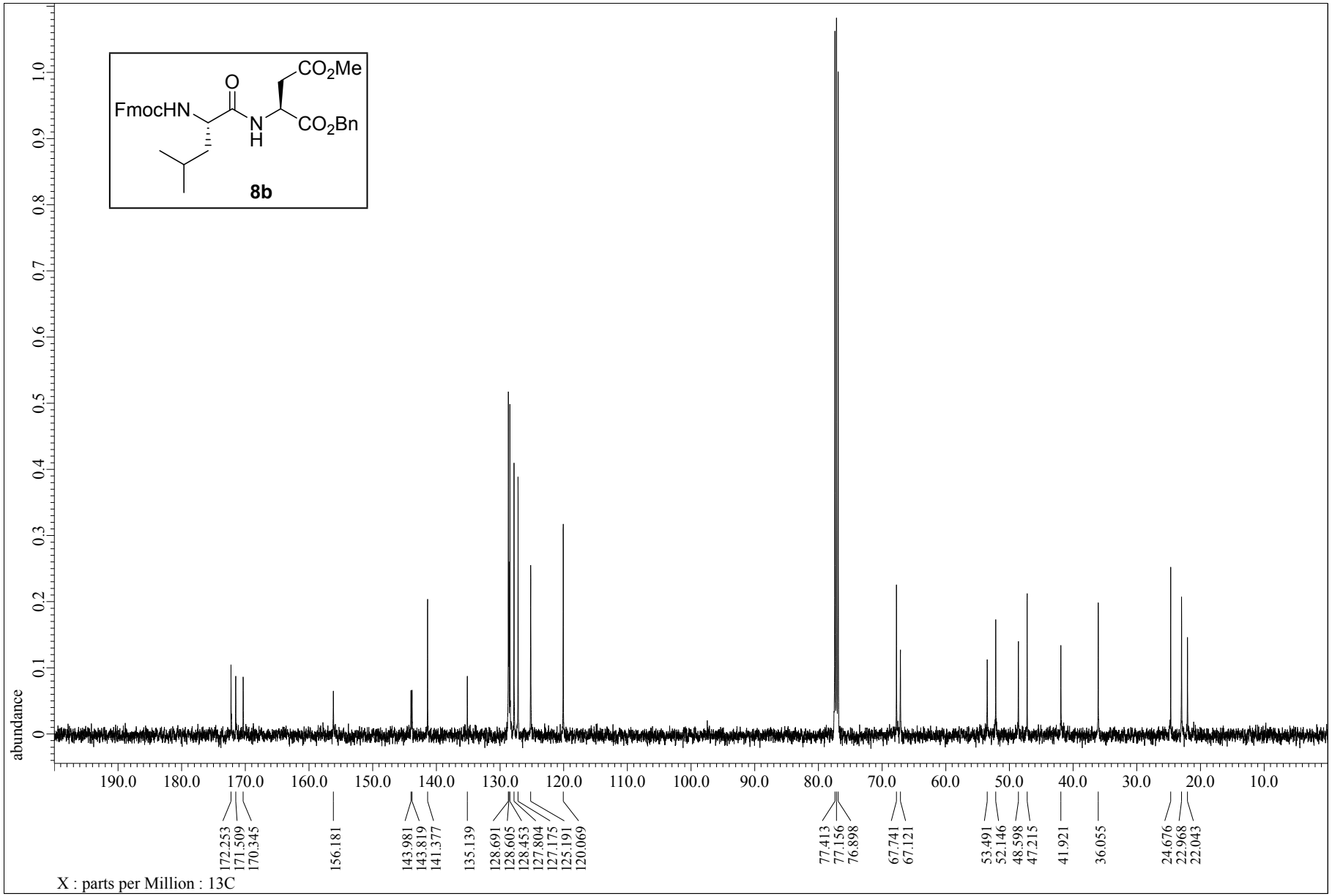

abundance
X : parts per Million : 1H
7.367
7.365
7.356
7.346
7.344
7.337
7.330
7.262
6.426
6.412
4.90
Me3Si
O
O
NH
BnO2C
CO2Me
3be
abundance
0.91
X : parts per Million : 13C
5.206
1.59
4.756
171.547
171.099
1.99
4.125
4.112
1.00
3.646
3.636
3.619
3.617
3.599
2.13
2.84
2.874
2.862
2.842
2.830
2.762
2.747
2.06
128.348
1.576
1.74
0.961
0.947
0.944
0.940
0.926
1.98
0.009
0.000
77.137
76.879
8.19
67.274
65.986
60.359
52.032


NHFmoc
CO2Me
tBuO2C
S3aa
S3aa
abundance
X : parts per Million : 1H
X : parts per Million : 13C

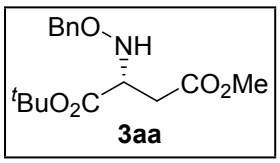

HN
OH
BnO2C
CO2Me
4b
6.59
2.28
2.68
2.04
1.00
abundance
4.0
3.0
2.0
1.0
0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.380
7.374
7.365
7.361
7.357
7.348
7.341
7.333
7.262
5.220
4.079
4.069
4.063
4.053
3.669
2.901
2.890
2.869
2.857
2.833
2.818
2.801
2.785
1.564
1.275
1.261
1.254
1.246
0.000
X : parts per Million : 1H


CO2Me
O
Ph
N
H
CO2Bn
6b
13.37
0.91
2.34
1.00
3.28
1.07
2.07
1.12
2.01
3.56
abundance
X : parts per Million : 1H
X : parts per Million : 13C


FmocHN
O
N
H
CO2Me
CO2Bn
8b
abundance
X : parts per Million : 1H
9.27
5.85
3.21
2.19
1.79
1.69
1.91
1.33
1.73
1.00
0.91
0.84
0.79
0.76
0.71
11.96
7.758
7.744
7.581
7.570
7.399
7.387
7.372
7.321
7.309
7.298
7.255
6.959
6.943
6.838
5.352
5.336
5.221
5.189
5.166
5.147
5.123
4.912
4.904
4.384
4.368
4.360
4.345
4.210
4.196
3.589
3.556
3.069
3.042
3.035
2.838
2.830
2.804
2.794
1.658
1.646
1.633
1.607
1.596
1.504
0.903
0.894
0.002

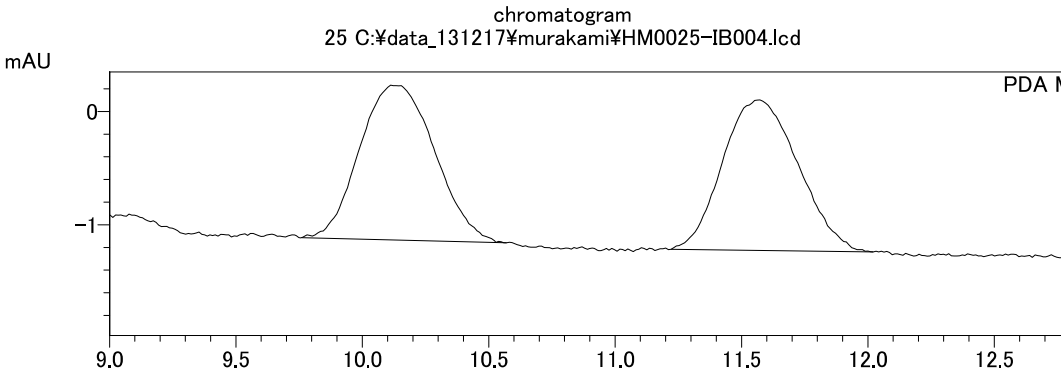

FmocHN
O
N
H
CO2Me
CO2Bn
8b
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
172.253
171.509
170.345
156.181
143.981
143.819
141.377
135.139
128.691
128.605
128.453
127.804
127.175
125.191
120.069
77.413
77.156
76.898
67.741
67.121
53.491
52.146
48.598
47.215
41.921
36.055
24.676
22.968
22.043
X : parts per Million : 13C

(G) HPLC Traces



3aa

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

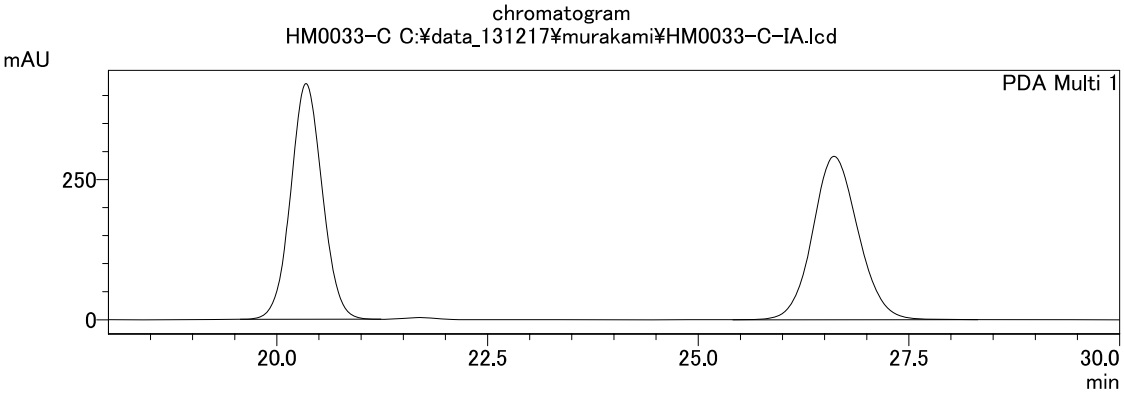
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0025-IB004.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	10.110	28220	50.566
2	11.563	27589	49.434

<Chromatogram>



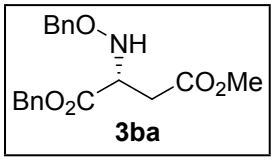
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0033-C-IA.lcd

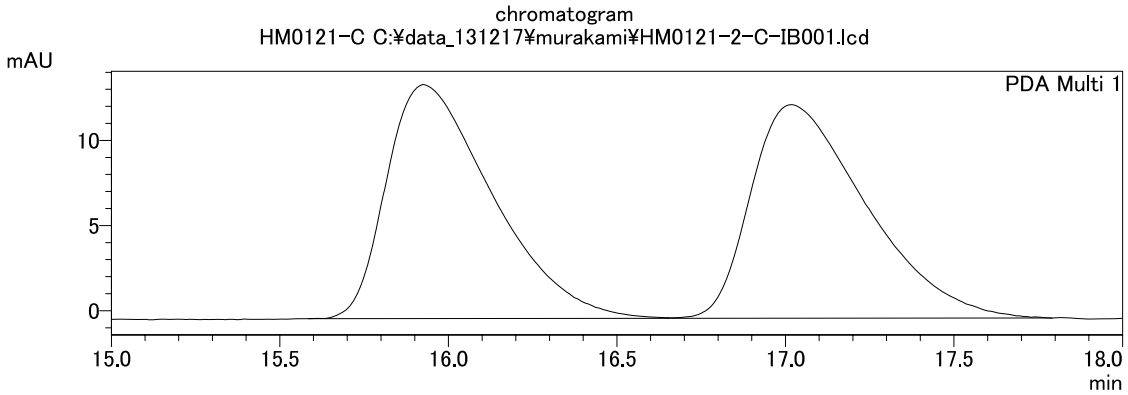
PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	20.340	11004240	50.134
2	26.606	10945554	49.866



3ba

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

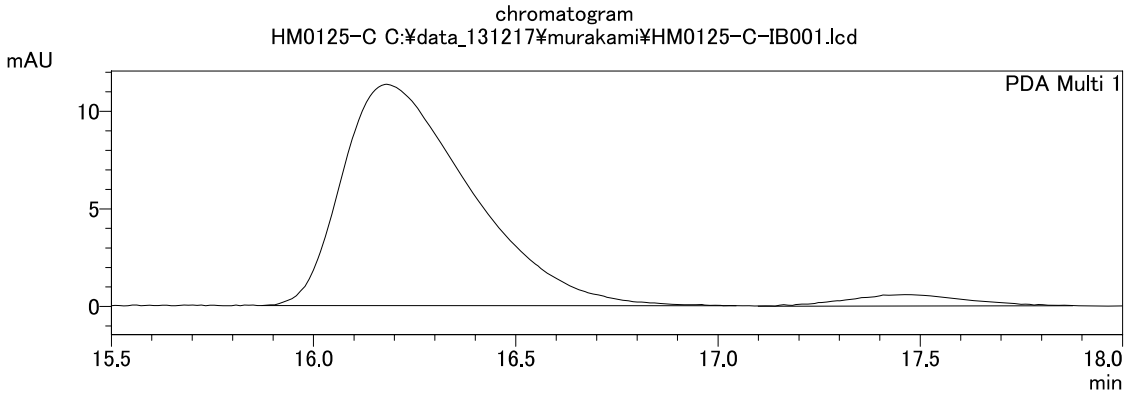
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0121-2-C-IB001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	15.920	300238	50.167
2	17.012	298243	49.833

<Chromatogram>



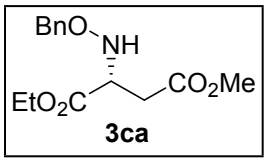
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0125-C-IB001.lcd

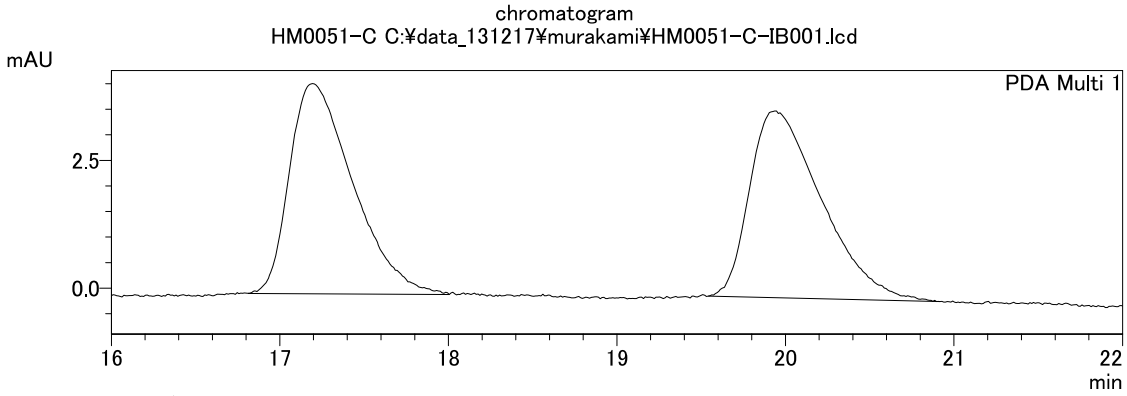
PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	16.175	249368	95.468
2	17.454	11837	4.532



3ca

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

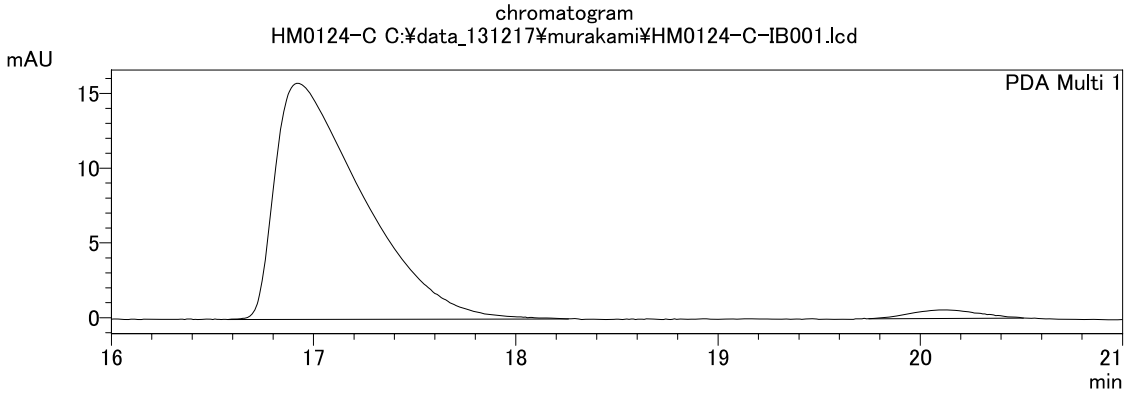
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0051-C-IB001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	17.190	107411	49.860
2	19.936	108013	50.140

<Chromatogram>



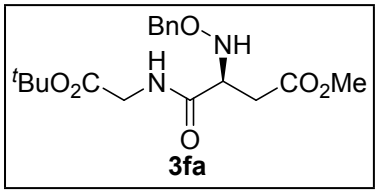
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0124-C-IB001.lcd

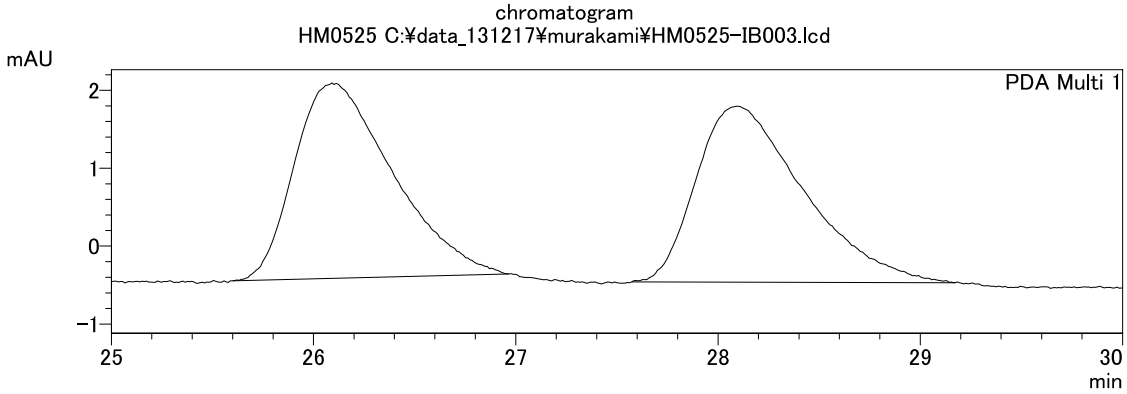
PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	16.916	476565	97.175
2	20.131	13852	2.825



3fa

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

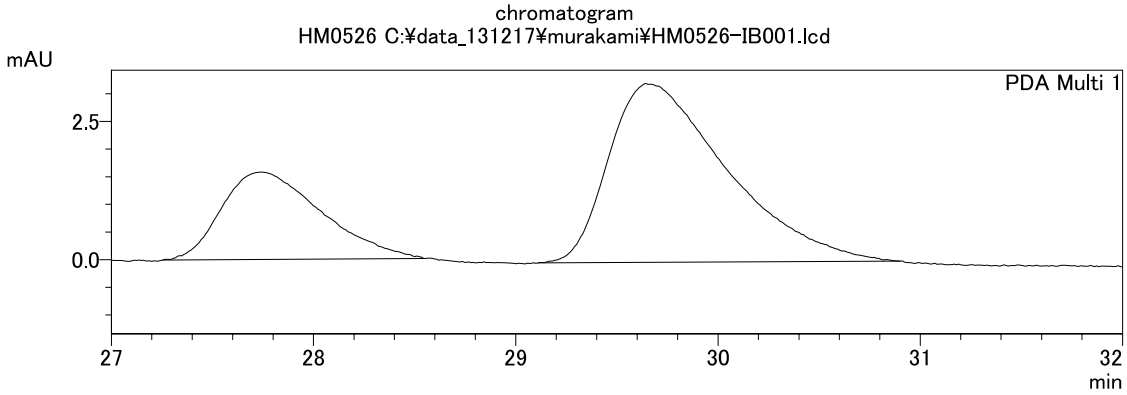
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0525-IB003.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	26.085	84655	50.344
2	28.090	83498	49.656

<Chromatogram>



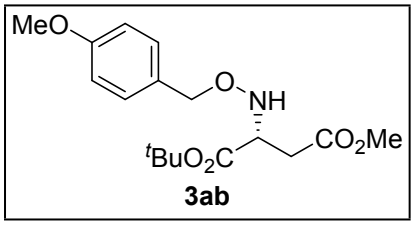
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0526-IB001.lcd

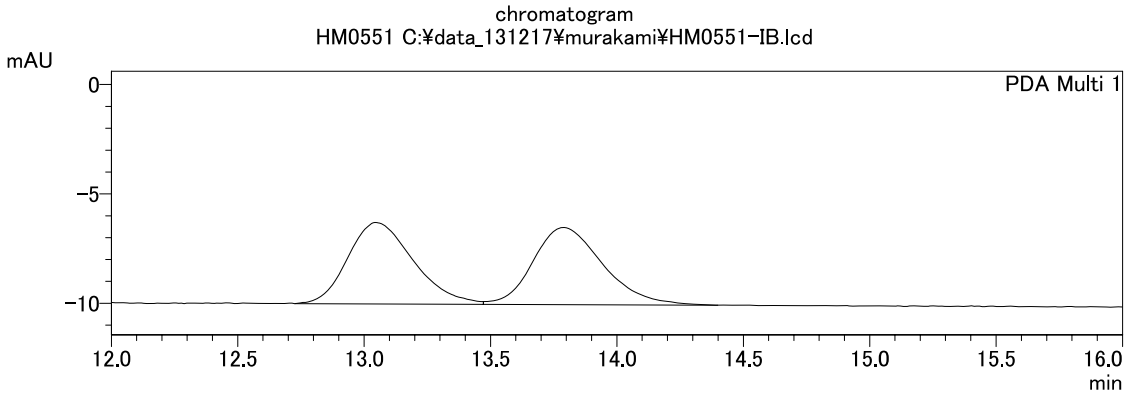
PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	27.732	54324	29.314
2	29.637	130993	70.686



3ab

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

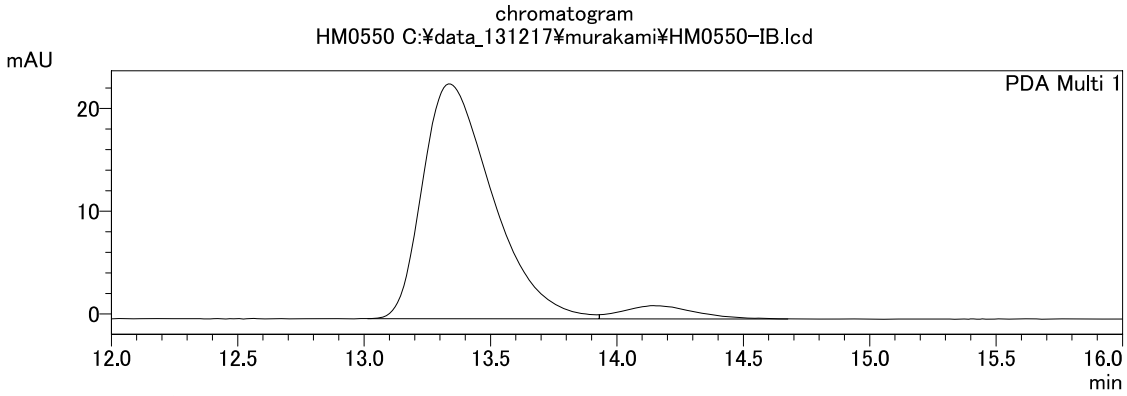
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0551-IB.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	13.040	67291	49.834
2	13.784	67740	50.166

<Chromatogram>



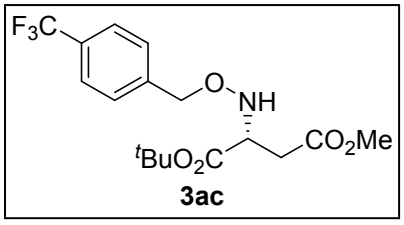
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0550-IB.lcd

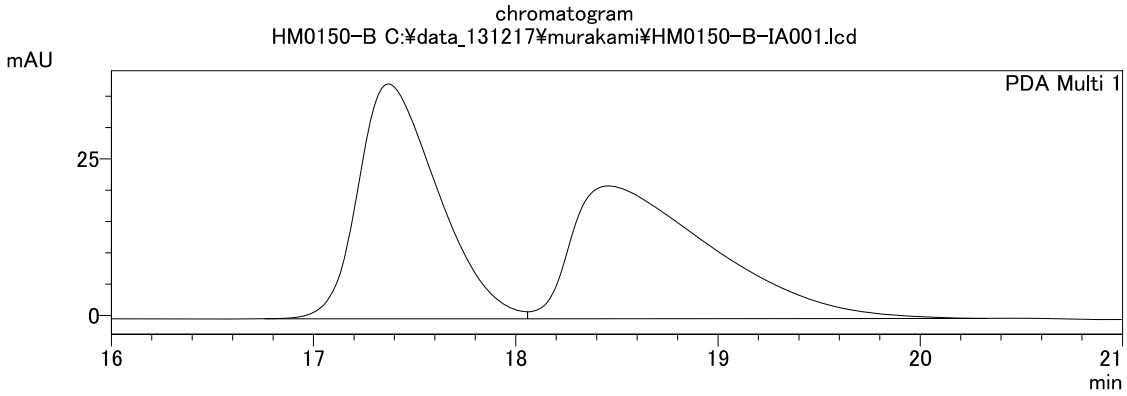
PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	13.332	440616	94.445
2	14.132	25918	5.555



3ac

<Chromatogram>



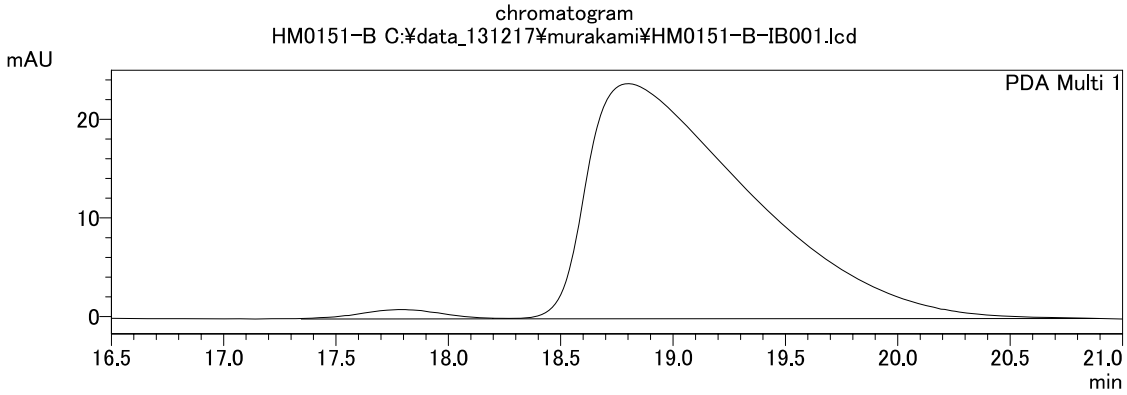
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0150-B-IA001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	17.363	1032118	50.070
2	18.456	1029236	49.930

<Chromatogram>



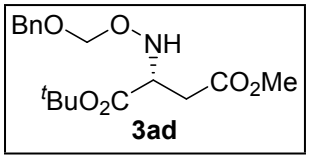
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0151-B-IB001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	17.799	24343	1.981
2	18.800	1204526	98.019



3ad

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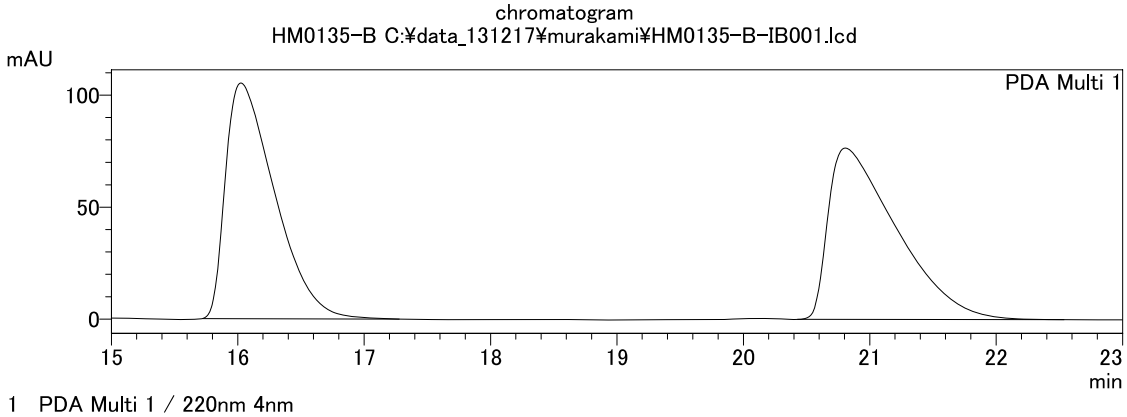


1 PDA Multi 1 / 220nm 4nm

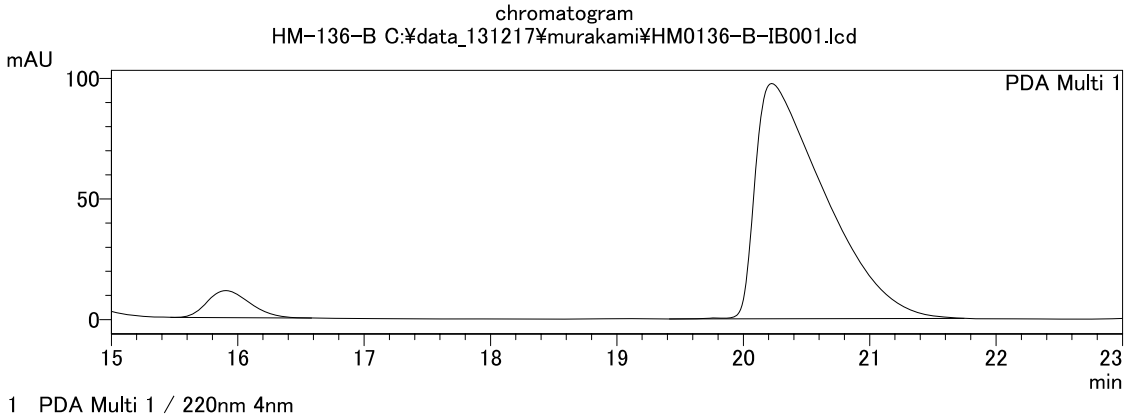
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0135-B-IB001.lcd

PDA Ch1 220nm 4nm

peak#	retention time (min)	area	area (%)
1	16.019	2851908	49.822
2	20.800	2872271	50.178

<Chromatogram>



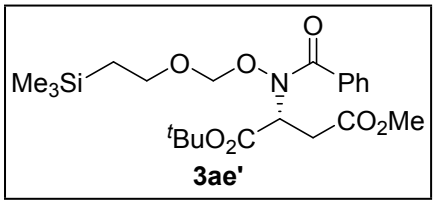
1 PDA Multi 1 / 220nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0136-B-IB001.lcd

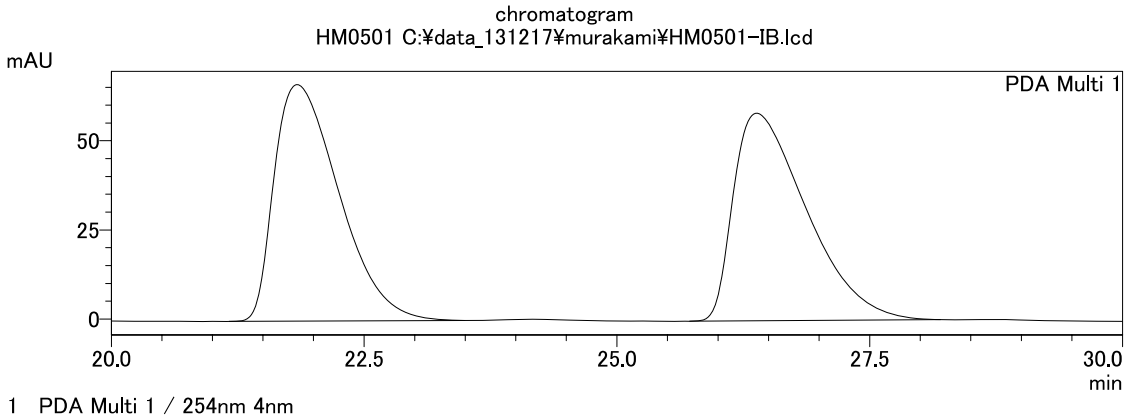
PDA Ch1 220nm 4nm

peak#	retention time (min)	area	area (%)
1	15.904	262510	6.579
2	20.219	3727434	93.421



3ae'

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

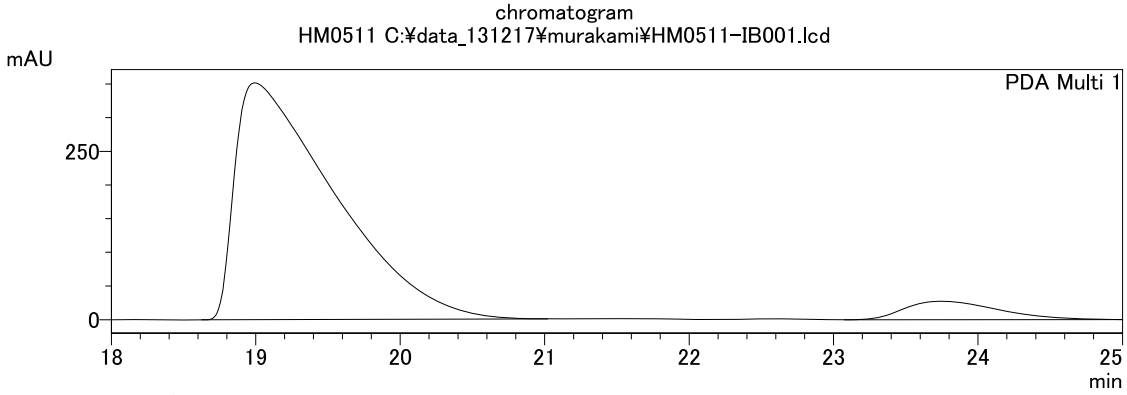
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0501-IB.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	21.830	2954870	50.255
2	26.375	2924865	49.745

<Chromatogram>



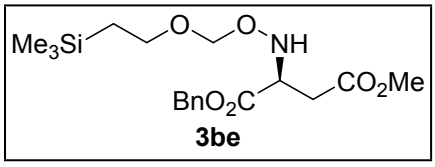
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0511-IB001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	18.988	16853273	93.145
2	23.742	1240399	6.855



3be

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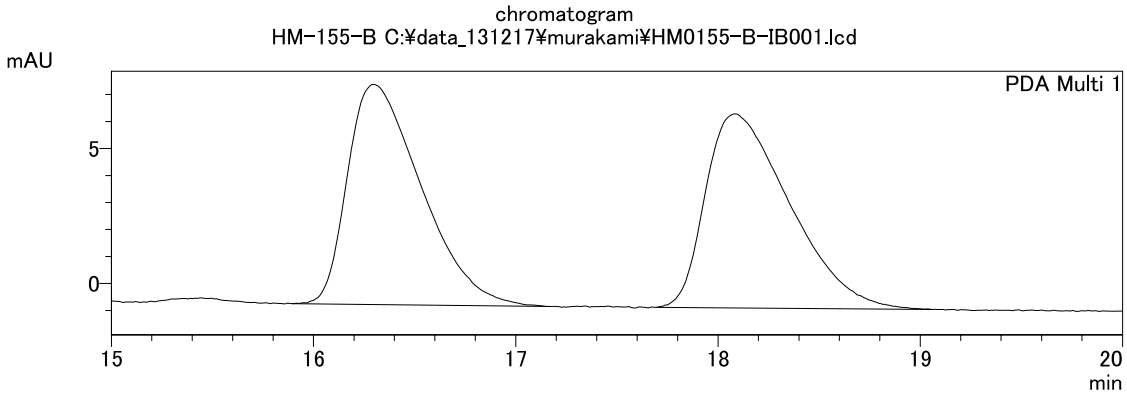


1 PDA Multi 1 / 254nm 4nm

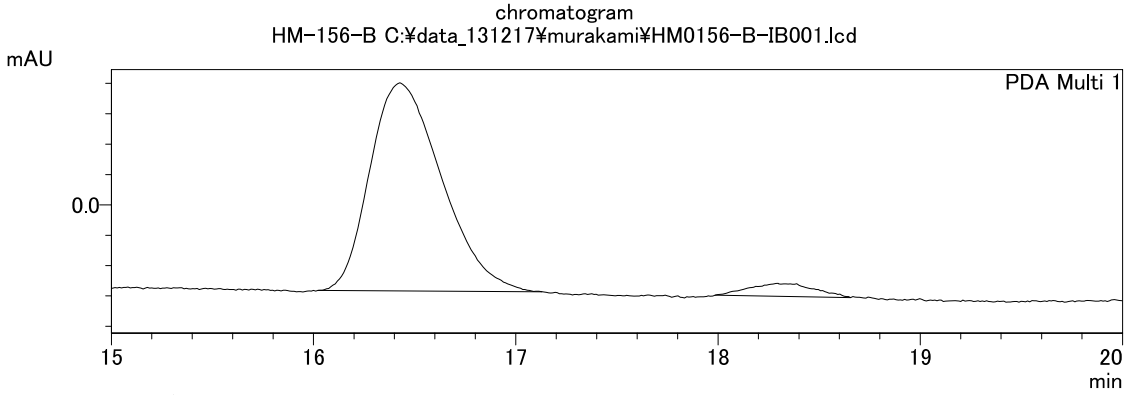
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0155-B-IB001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	16.289	206655	49.880
2	18.079	207647	50.120

<Chromatogram>



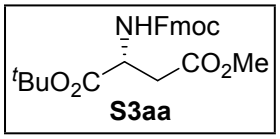
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0156-B-IB001.lcd

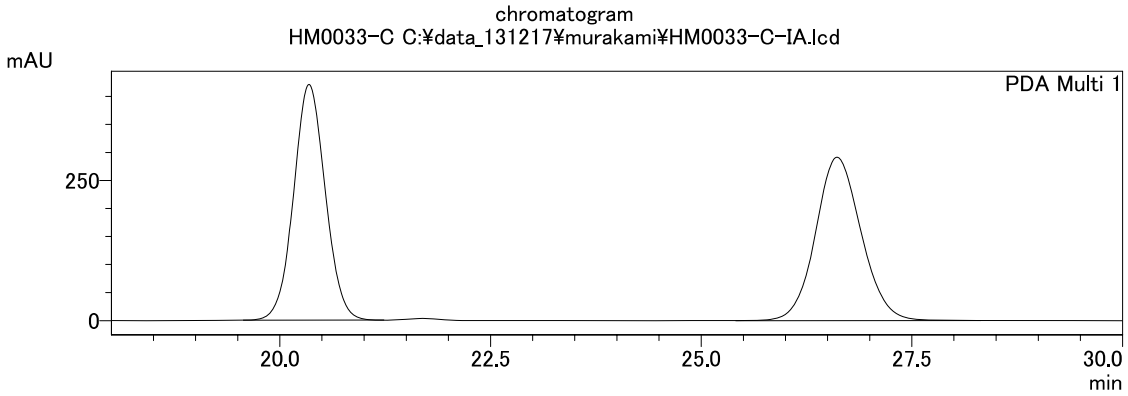
PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	16.421	84529	94.632
2	18.287	4795	5.368



S3aa

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

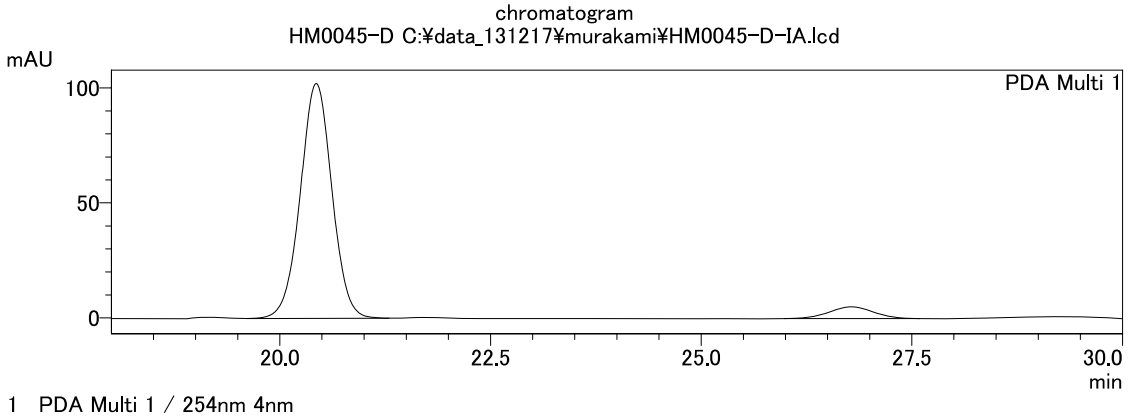
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0033-C-IA.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	20.340	11004240	50.134
2	26.606	10945554	49.866

<Chromatogram>



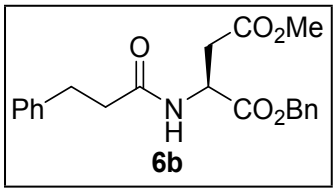
1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0045-D-IA.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	20.425	2667915	93.426
2	26.772	187744	6.574



6b

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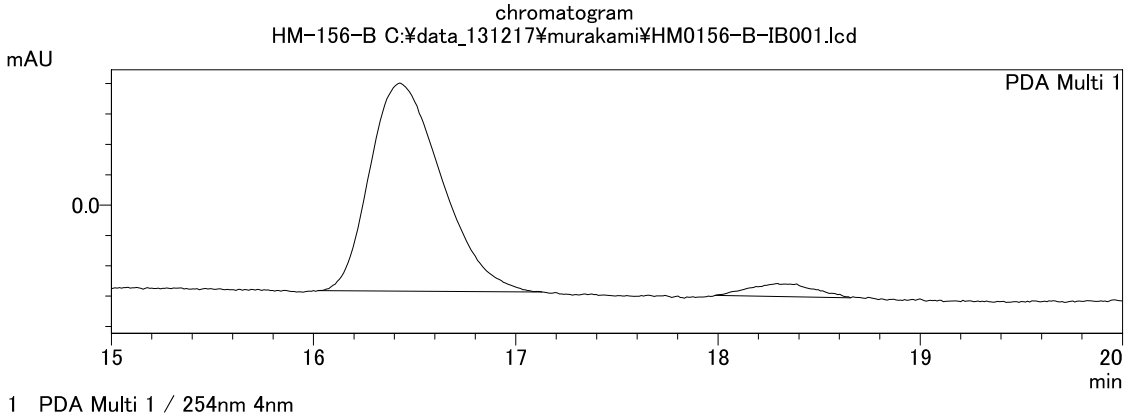


1 PDA Multi 1 / 254nm 4nm

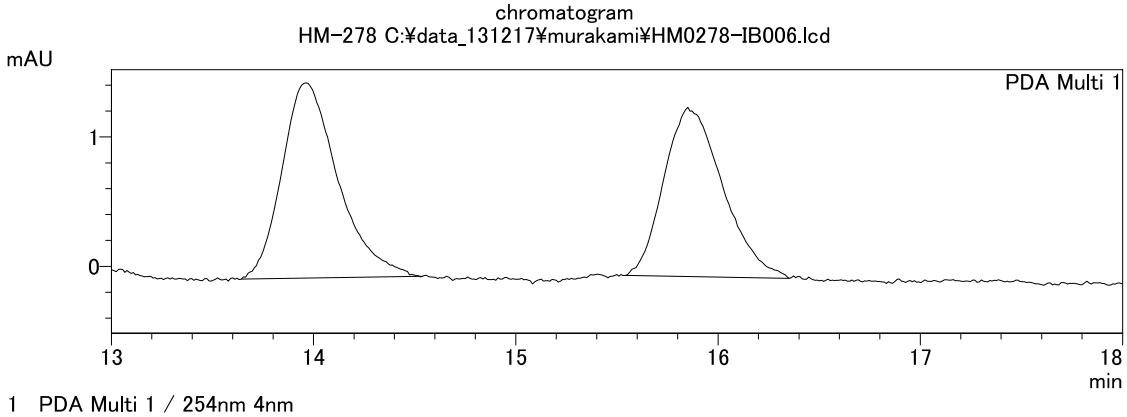
<Peak Report>

peak table C:¥data_131217¥murakami¥HM0156-B-IB001.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	16.421	84529	94.632
2	18.287	4795	5.368

<Chromatogram>



1 PDA Multi 1 / 254nm 4nm

<Peak Report>

peak table C:¥data_131217¥murakami¥HM0278-IB006.lcd

PDA Ch1 254nm 4nm

peak#	retention time (min)	area	area (%)
1	13.958	29089	52.465
2	15.844	26356	47.535