Supporting Information

Synthesis of the Antimalarial Peptide Aldehyde, a Precursor of Kozupeptin A, Utilizing a Designed Hydrophobic Anchor Molecule

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General remarks

Infrared (IR) spectra were recorded on a Horiba FT-210 spectrometer. UV spectra were measured with a Beckman DU640 spectrophotometer. NMR spectra were measured on a JEOL JNM-ECA-500 spectrometer with ^{1}H NMR at 500 MHz and ^{13}C NMR at 125 MHz. Chemical shifts were reported in ppm from the internal solvent peaks for chloroform-d_1 ($CDCl_3$) (^{1}H; δ = 7.26 ppm, ^{13}C; δ = 77.16 ppm) or dimethylsulfoxide-d_6 ($(CD_3)_2SO$, DMSO-d_6) (^{1}H; δ = 2.50 ppm, ^{13}C; δ = 39.52 ppm). ^{1}H NMR data were reported as follows: chemical shift (integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, app = apparent), coupling constants (Hz)). Liquid chromatography-electrospray ionization mass spectrometry (LC/MS) was performed on a Waters AQUITY UPLC H-Class using acetonitrile (MeCN) solvent system containing 0.05% formic acid. The high-resolution mass spectra (HRMS) were performed on a JEOL JMS-AX505 HA, a JEOL JMS-700 MStation, or a JEOL JMS-T100LP. Optical rotations were measured on a JASCO P-1010 polarimeter.

For thin layer chromatography (TLC) analysis, Merck precoated TLC plates (silica gel 60 GF_{254}, 0.25 mm) were used. Flash chromatography was carried out with Kanto Chemical silica gel (silica gel 60N, spherical neutral, 0.040–0.050 mm) or Fuji Silysia silica gel (FL60D, avg. 0.060 mm). For purification with preparative thin layer chromatography (PLC), Merck precoated PLC plates (silica gel 60 GF_{254}, 0.5 mm) were used.

Unless otherwise noted, reagents and solvents were commercially available and used without further purification. In experiments requiring dry solvents, dichloromethane (DCM) and tetrahydrofuran (THF) were purchased from Kanto Chemical Co. Inc. as "Dehydrated." For Fmoc-protected amino acids, Fmoc-Ala-OH, Fmoc-Asn-OH, Fmoc-Val-OH, and Fmoc-Thr-OH·H_2O were purchased from Watanabe Chemical Industries, Ltd. Fmoc-(2*S*, 4*R*)-4-MePro-OH was prepared by the procedure described in the literature.[1]

Screening of condensation reagents to suppress the epimerization in our previous report[2] (not shown in the previous paper)

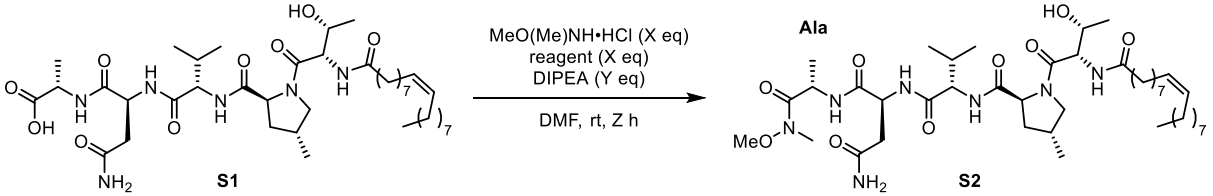
Experimental procedure and determination of the stereochemistry of α-position of Ala unit (L or D)

To a solution of **S1** (5.0 mg, 0.01 mmol, 1.0 eq.), MeO(Me)NH·HCl, and condensation reagent in dimethylformamide (DMF) (0.036 M) was added *N*,*N*-diisopropylethylamine (DIPEA) at room temperature. After stirring at room temperature until **S1** was completely consumed, the reaction mixture was then treated with aqueous 1 N HCl in an ice bath to quench the excess amine reagent, poured into a separatory funnel containing ethyl acetate (EtOAc) (20 mL), and washed with aqueous 1 N HCl (2 x 10 mL) and sat. NaCl aq. (10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo to afford the crude product **S2**.

The diastereoselective ratio (L/D) of α-position of Ala unit was determined by advanced Marfey's analysis.[3] A sample (100 µg) of the above crude product **S2** was dissolved in 6 N HCl (500 µL) and heated for 3 h at 100 °C. After cooling to room temperature, the hydrolysate was evaporated to dryness in vacuo, and the residue was dissolved in 100 µL of water. 50 µL of the hydrolysate aq. was treated with 25 µL of 1 M $NaHCO_3$ and 50 µL of 1% 1-fluoro-2,4-dinitrophenyl-5-D-leucinamide (D-FDLA) in acetone. The mixture was heated for 1 h at 37 °C. After cooling to room temperature, the reaction mixture was neutralized with 1 N HCl, and concentrated in vacuo. The residue was dissolved with 200 µL of MeCN, filtered to remove salt and analyzed by UPLC-MS (Waters Co., USA) on reversed-phase column (BEH C18 column; 2.1 x 50 mm, 1.7 µm, 0.5 mL/min) with a linear gradient from 50% to 100% aqueous MeCN containing formic acid (mobile phase A; 100% MeCN + 0.05% formic acid and mobile phase B; 90% H_2O / 10% MeCN + 0.05% formic acid) for 10 min.

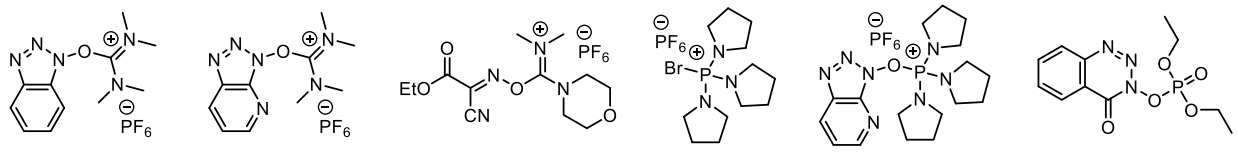
Commercial L-Ala-OH and D-Ala-OH standards were adjusted to 1 mM with water and were subjected to advanced Marfey's analysis as described above. The ESI positive mode was used for the detection of L- or D-Ala-D-FDLA derivative, and the L/D ratio of α-position of Ala unit was determined by a comparison of retention time between the Ala-D-FDLA derivatives from the hydrolysate of crude product **S2** and standards. The results were summarized in **Table S1**.

Table S1. Screening of condensation reagents in the transformation of carboxylic acid **S1** to Weinreb amide **S2**.



entry	reagent	X eq	Y eq	Z h[a]	L/D of **Ala** unit[b]	yield (isolated)
1	HBTU	1.2	2.4	3	62/38	–
2	HATU	1.2	2.4	4.5	82/18	–
3	COMU	1.2	2.4	4.5	86/14	–
4	PyBroP	1.8	4.8	5	61/39	–
5	PyAOP	1.2	2.4	6	89/11	–
6	DEPBT	3.2	6.4	16	97/3	quant.[c]

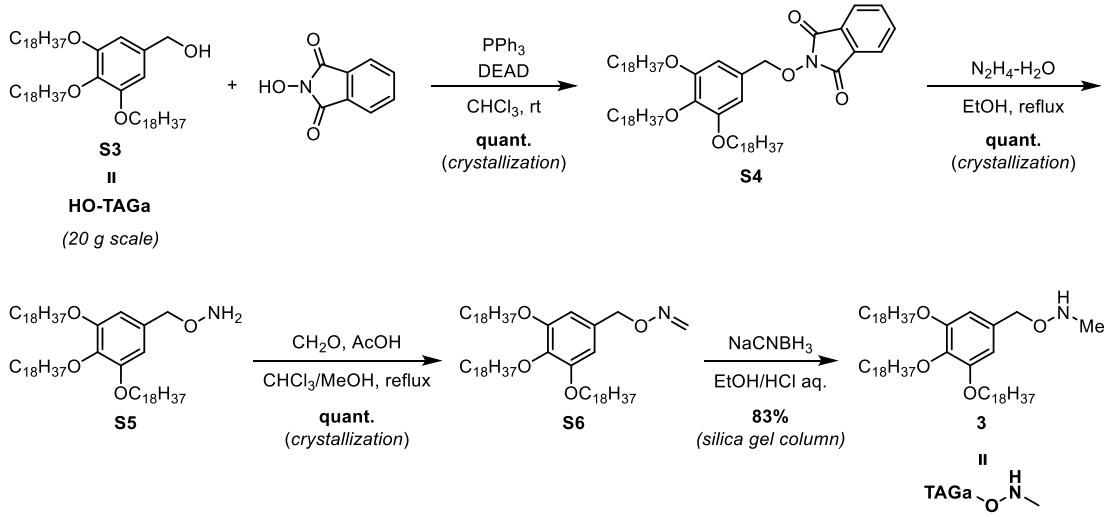
[a]In all entries, full conv. [b]Determined by advanced Marfey's analysis after complete hydrolysis.
[c]120 mg scale of **S1** (0.15 mmol). The crude was purified by flash column chromatography on silica gel ($CHCl_3$/MeOH).



Experimental procedures and compounds characterization

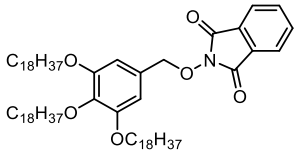
Preparation of TAGa-type anchor molecule

Scheme S1. Synthesis of a new designed hydrophobic anchor molecule (TAGa-type anchor molecule)



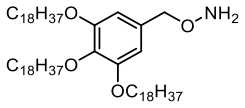
*3,4,5-Tris(octadecyloxy)benzyl alcohol (**S3**) (HO-TAGa)*

HO-TAGa (**S3**) was prepared by the procedure described in the literature as a white powder.[4] mp 68–69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.56 (2H, s), 4.59 (2H, s), 3.98-3.92 (6H, m, overlapped), 1.82-1.71 (6H, m, overlapped), 1.50-1.43 (6H, br m, overlapped), 1.35-1.22 (84H, br m, overlapped), 0.88 (9H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 137.7, 136.2, 105.5, 73.6, 69.3, 65.8, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.29, 26.26, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 3541, 2916, 2848, 1594, 1462, 1439, 1118, 719; HRMS (FAB, NBA matrix) Calcd. for $C_{61}H_{116}O_4$: 912.8874 ([M]$^+$), Found: 912.8876.



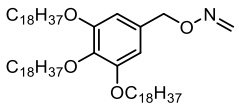
*Phthalimide-O-TAGa (**S4**)*

To a solution of **S3** (20.0 g, 21.9 mmol, 1.0 eq), triphenylphosphine (PPh_3) (11.5 g, 43.8 mmol, 2.0 eq) and *N*-hydroxyphthalimide (7.14 g, 43.8 mmol, 2.0 eq) in $CHCl_3$ (274 mL, 0.08 M) was added dropwise diethyl azodicarboxylate (DEAD) (40% toluene solution, 19.1 g, 43.8 mmol, 2.0 eq) at 0 ºC for 20 min. The mixture was heated to room temperature and stirred for 5 h. Methanol (MeOH) (1370 mL, 5-fold excess of $CHCl_3$) was added to the reaction mixture and the resulting heterogeneodus solution was stirred for a further 30 min at room temperature. The precipitate was filtered and washed with additional MeOH to afford phthalimide-O-TAGa (**S4**) (23.2 g, quant.) as a white powder. mp 81 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82-7.78 (2H, m), 7.74-7.71 (2H, m), 6.72 (2H, s), 5.13 (2H, s), 3.97-3.92 (6H, m, overlapped), 1.80-1.68 (6H, m, overlapped), 1.48-1.42 (6H, br m, overlapped), 1.35-1.22 (84H, br m, overlapped), 0.88 (9H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, peaks were complex because of rotamers) δ 163.6, 153.3, 139.1, 134.5, 129.0, 128.6, 123.6 108.4, 80.3, 73.5, 69.3, 32.1, 30.4, 29.9-29.5 (many signals overlapped), 26.2, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2916, 2849, 1739, 1466, 1440, 1112, 700; HRMS (FAB, NBA + Na matrix) Calcd. for $C_{69}H_{119}NO_6Na$: 1080.8935 ([M+Na]$^+$), Found: 1080.8942.



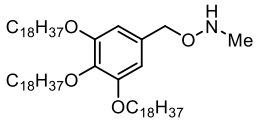
*NH_2-O-TAGa (**S5**)*

To a solution of **S4** (23.2 g, 21.9 mmol, 1.0 eq) in ethanol (EtOH) (730 mL, 0.03 M) was added dropwise $N_2H_4 \cdot H_2O$ (11.0 g, 219 mmol, 10 eq) at room temperature. The mixture was heated to reflux and stirred for 8 h. After cooling to room temperature, the resulting heterogeneous solution was stirred for a further 30 min at room temperature. The precipitate was filtered and washed with additional EtOH to afford NH_2-O-TAGa (**S5**) (20.3 g, quant.) as a white powder. mp 69–70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.55 (2H, s), 5.39 (2H, br s), 4.59 (2H, s), 3.98-3.92 (6H, m, overlapped), 1.82-1.71 (6H, m, overlapped), 1.50-1.43 (6H, br m, overlapped), 1.37-1.22 (84H, br m, overlapped), 0.88 (9H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 138.1, 132.4, 106.8, 78.5, 73.5, 69.2, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.29, 26.26, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2914, 2848, 1596, 1469, 1243, 1128, 718; HRMS (ESI$^+$) Calcd. for $C_{61}H_{118}NO_4$: 928.9061 ([M+H]$^+$), Found: 928.9056.



*CH_2=N-O-TAGa (**S6**)*

A mixture of **S5** (20.3 g, 21.9 mmol, 1.0 eq) and paraformaldehyde ($(CH_2O)_n$) (6.56 g, 219 mmol, 10 eq) in $CHCl_3$/MeOH = 5/1 (375 mL, 0.06 M) was heated to reflux and stirred for 3 h. After cooling to room temperature, MeOH (1560 mL, 5-fold excess of $CHCl_3$) was added to the reaction mixture and was stirred for a further 30 min at room temperature. The precipitate was filtered and washed with additional MeOH to afford CH_2=N-O-TAGa (**S6**) (20.6 g, quant.) as a white powder. mp 71–72 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.09 (1H, d, J = 8.5 Hz), 6.55 (2H, s), 6.48 (1H, d, J = 8.5 Hz), 5.02 (2H, s), 3.98-3.92 (6H, m, overlapped), 1.82-1.70 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.35-1.22 (84H, br m, overlapped), 0.88 (9H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 138.1, 137.8, 132.4, 106.9, 76.6, 73.5, 69.2, 32.1, 30.5, 29.9-29.2 (many signals overlapped), 26.29, 26.26, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2914, 2847, 1596, 1469, 1243, 1129, 717; HRMS data is not available because the parent peak was not detected by ESI nor FAB. Only hydrolyzed peaks (928.9 ([**S5** + H]$^+$) and 959.9 ([**S5** + Na]$^+$)) were observed.

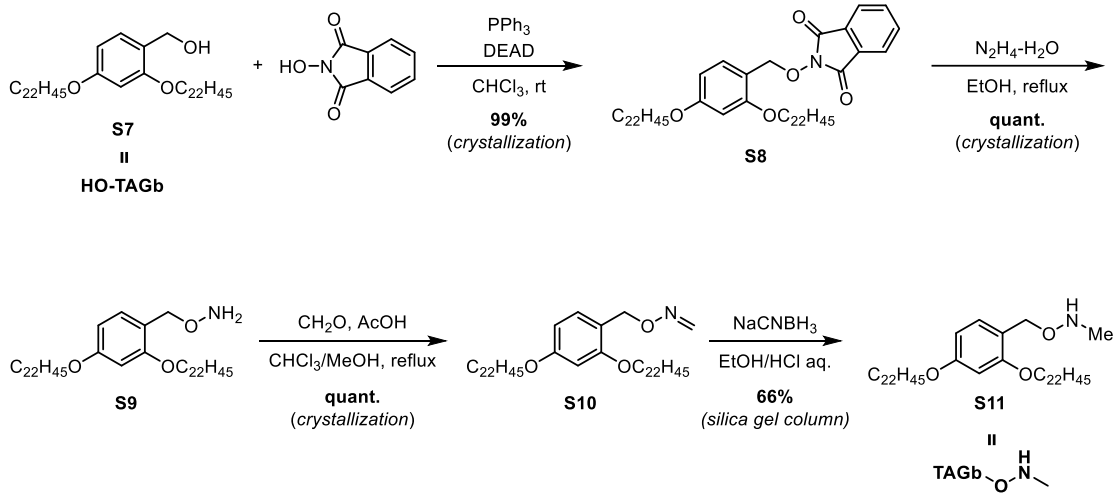


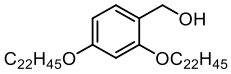
*Me-HN-O-TAGa (**3**)*

To a solution of **S6** (17.6 g, 18.7 mmol, 1.0 eq) and $NaBH_3CN$ (3.53 g, 56.1 mmol, 3.0 eq) in EtOH/THF = 1/1 (535 mL, 0.035 M) was added dropwise conc. HCl (4.29 g) at room temperature until the pH reached around 3. After stirring for 2 h, MeOH (1338 mL, 5-fold excess of THF) was added to the mixture and the resulting heterogeneous solution was stirred for a further 30 min at room temperature. The precipitate was filtered and washed with additional MeOH to afford Me-HN-O-TAGa (**3**) (17.7 g, app. quant.) as a white powder. Additional purification was performed by column chromatography on silica gel ($CHCl_3$/*n*-hexane = 1/1 to 5/1 as eluent) to give highly pure **3** (14.7 g, 83%) as a white powder. mp 53–54 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.55 (2H, s), 5.54 (1H, br s), 4.61 (2H, s), 3.98-3.91 (6H, m, overlapped), 2.75 (3H, s), 1.82-1.70 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.37-1.22 (84H, br m, overlapped), 0.88 (9H, t, J = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.3, 137.9, 133.1, 106.8, 76.1, 73.5, 69.2, 39.4, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.29, 26.26, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2916, 2849, 1588, 1468, 1234, 1116, 720; HRMS (ESI$^+$) Calcd. for $C_{62}H_{120}NO_4$: 942.9217 ([M+H]$^+$), Found: 942.9241.

Preparation of TAGb-type anchor molecule

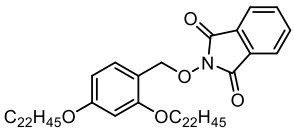
Scheme S2. Synthesis of TAGb-type anchor molecule





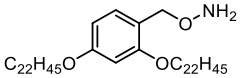
*2,4-Bis(docosyloxy)benzyl alcohol (**S7**) (HO-TAGb)*[5]

HO-TAGb (**S7**) (11.4 g, 15.1 mmol) was prepared by the same procedure as HO-TAGa (**S3**) described above as a white powder. mp 69–70 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.13 (1H, d, J = 8.5 Hz), 6.45 (1H, d, J = 2.5 Hz), 6.42 (1H, dd, J = 8.0, 2.0 Hz), 4.61 (2H, d, J = 6.5 Hz), 3.98 (2H, t, J = 6.5 Hz), 3.93 (2H, t, J = 6.5 Hz), 2.27 (1H, t, J = 6.5 Hz), 1.83-1.74 (4H, m, overlapped), 1.48-1.41 (4H, br m, overlapped), 1.37-1.22 (72H, br m, overlapped), 0.88 (6H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, peaks were complex because of rotamers) δ 160.3, 158.2, 129.7, 121.8, 104.6, 99.9, 68.3, 68.1, 62.2, 32.1, 29.9-29.4 (many signals overlapped), 26.3, 26.2, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2916, 2848, 1614, 1470, 1180, 1121, 718; HRMS (FAB, NBA + Na matrix) Calcd. for $C_{51}H_{96}O_3Na$: 779.7257 ($[M+Na]^+$), Found: 779.7258.



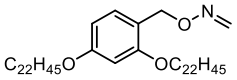
*Phthalimide-O-TAGb (**S8**)*

Following the same procedure described for phthalimide-O-TAGa (**S4**), HO-TAGb (**S7**) (6.30 g, 8.3 mmol) was converted to phthalimide-O-TAGa (**S4**) (7.40 g, 99%) as a white powder. mp 85–86 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80-7.76 (2H, m), 7.72-7.68 (2H, m), 7.32 (1H, d, J = 8.5 Hz), 6.43 (1H, dd, J = 8.5, 2.5 Hz), 6.37 (1H, d, J = 2.0 Hz), 5.20 (2H, s), 3.92 (2H, t, J = 6.5 Hz), 3.82 (2H, t, J = 6.5 Hz), 1.75 (2H, m), 1.68 (2H, m), 1.46-1.22 (76H, br m, overlapped), 0.88 (6H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 161.7, 159.4, 134.2, 133.5, 129.2, 123.4, 115.1, 105.0, 99.7, 74.5, 68.5, 68.1, 32.1, 29.9-29.4 (many signals overlapped), 29.1, 26.2, 26.1, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2913, 2849, 1745, 1471, 1187, 969, 695; HRMS (FAB, NBA + Na matrix) Calcd. for $C_{59}H_{99}NO_5Na$: 924.7421 ($[M+Na]^+$), Found: 924.7426.



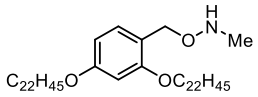
*NH_2-O-TAGb (**S9**)*

Following the same procedure described for NH_2-O-TAGa (**S5**), phthalimide-O-TAGb (**S8**) (7.30 g, 8.1 mmol) was converted to NH_2-O-TAGb (**S9**) (6.25 g, quant.) as a white powder. mp 71–73 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (1H, m), 6.46-6.43 (2H, m, overlapped), 5.33 (2H, s), 4.69 (2H, s), 3.96-3.93 (4H, m, overlapped), 1.82-1.74 (4H, m, overlapped), 1.48-1.41 (4H, br m, overlapped), 1.37-1.22 (72H, br m, overlapped), 0.88 (6H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, peaks were complex because of rotamers) δ 160.6, 158.7, 131.4, 117.9, 104.7, 100.0, 73.1, 68.4, 68.2, 32.1, 29.9-29.3 (many signals overlapped), 26.23, 26.21, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2915, 2848, 1618, 1471, 1200, 1178, 1041, 717; HRMS (ESI^+) Calcd. for $C_{51}H_{98}NO_3$: 772.7547 ($[M+H]^+$), Found: 772.7550.



*CH_2=N-O-TAGb (**S10**)*

Following the same procedure described for CH_2=N-O-TAGa (**S6**), NH_2-O-TAGb (**S9**) (3.94 g, 5.1 mmol) was converted to CH_2=N-O-TAGb (**S10**) (4.00 g, quant.) as a white powder. mp 64–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (1H, m), 7.05 (1H, d, J = 8.5 Hz), 6.45-6.42 (3H, m, overlapped), 5.12 (2H, s), 3.96-3.92 (4H, m, overlapped), 1.81-1.74 (4H, m, overlapped), 1.48-1.41 (4H, br m, overlapped), 1.37-1.22 (72H, br m, overlapped), 0.88 (6H, t, J = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, peaks were complex because of rotamers) δ 160.6, 158.4, 137.1, 131.1, 118.1, 104.7, 100.0, 71.2, 68.3, 68.2, 32.1, 29.9-29.3 (many signals overlapped), 26.2, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2916, 2848, 1613, 1465, 1289, 1183, 1004, 817, 718; HRMS (ESI^+) Calcd. for $C_{52}H_{97}NO_3Na$: 806.7366 ($[M+Na]^+$), Found: 806.7352.



*Me-HN-O-TAGb (**S11**)*

Following the same procedure described for Me-HN-O-TAGa (**3**), CH_2=N-O-TAGb (**S10**) (3.95 g, 5.0 mmol) was converted to Me-HN-O-TAGb (**S11**) (2.61 g after purification by column chromatography on silica gel ($CHCl_3$/*n*-hexane = 1/1 to 5/1 as eluent), 66%) as a white powder. mp 60–61 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (1H, m), 6.44-6.42 (2H, m, overlapped), 5.49 (1H, br s), 4.70 (2H, s), 3.96-3.91 (4H, m, overlapped), 2.75 (3H, s), 1.81-1.73 (4H, m, overlapped), 1.48-1.41 (4H, br m, overlapped), 1.37-1.22 (72H, br m, overlapped), 0.88 (6H, t, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, peaks were complex because of rotamers) δ 160.4, 158.5, 131.2, 118.5, 104.7, 100.0, 70.3, 68.3, 68.2, 39.3, 32.1, 29.9-29.4 (many signals overlapped), 26.3, 26.2, 22.8, 14.3; IR (KBr) ν (cm^{-1}) 2915, 2848, 1613, 1466, 1287, 1178, 718; HRMS (ESI$^+$) Calcd. for $C_{52}H_{100}NO_3$: 786.7703 ([M+H]$^+$), Found: 786.7685.

Peptide elongations

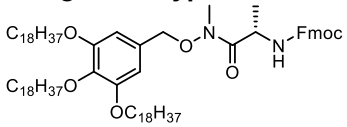
General procedure for elongation of peptide chain (condensation with Fmoc-protected amino acid)

To a solution of free amine (1.0 eq) in DCM (0.05 M for substrate) was added Fmoc protected amino acid (1.1 eq), 1-hydroxybenzotriazole (HOBt) (1.2 eq), and *N*,*N*'-diisopropylcarbodiimide (DIC) (1.2 eq (2.3 eq when Fmoc protected amino acid was monohydrate)) at room temperature to 40 °C and stirred until the reaction completed (1.5 to 5 h). The reaction mixture was subsequently cooled to 0 °C and MeOH (generally 5-fold excess of DCM) was added. The resulting heterogeneous solution was stirred for a further 30 min at 0 °C, and the precipitate was filtered and washed with additional MeOH to afford the corresponding Fmoc protected peptide with an anchor molecule as a white to off-white powder.

General procedure for Fmoc deprotection

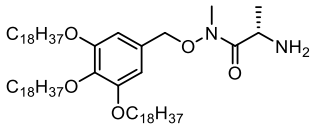
The Fmoc protected amino acid or peptide was dissolved into or 10% piperidine/DCM or 1% piperidine/1% 1,8-diazabicyclo[5.4.0]-7-undecene (DBU)/$CHCl_3$ (0.036 M for substrate) at room temperature, and the solution was stirred until the reaction was completed (generally 0.5 h to 2 h). The reaction mixture was subsequently cooled to 0 °C and MeOH (generally 5-fold excess of DCM or $CHCl_3$) was added. The resulting heterogeneous solution was stirred for a further 30 min at 0 °C, and the precipitate was filtered and washed with additional MeOH to afford the corresponding amine as a white to off-white powder.

Using TAGa-type anchor molecule



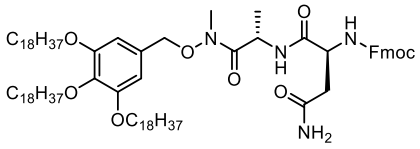
*Fmoc-Ala-(Me)N-O-TAGa (**S12**)*

Following the general procedure described for condensation, Me-HN-O-TAGa (**3**) (5.00 g, 5.3 mmol) was converted to Fmoc-Ala-(Me)N-O-TAGa (**S12**) (6.56 g, quant.) as a white powder. $[\alpha]_D^{24.3}$ = +12.1 (*c* 0.1, $CHCl_3$); mp 56–59 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (2H, d, *J* = 7.5 Hz), 7.62 (2H, t, *J* = 7.5 Hz), 7.40 (2H, t, *J* = 7.5 Hz), 7.32 (2H, t, *J* = 7.5 Hz), 6.63 (2H, s), 5.62 (1H, br d, *J* = 8.5 Hz), 4.88 (1H, br m), 4.86 (2H, s), 4.40-4.34 (2H, m, overlapped), 4.24 (1H, t, *J* = 7.5 Hz), 4.00-3.94 (6H, m, overlapped), 3.24 (3H, s), 1.83-1.71 (6H, m, overlapped), 1.50-1.44 (6H, br m, overlapped), 1.37-1.22 (87H, br m, overlapped), 0.89 (9H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 155.9, 153.5, 144.1, 143.9, 141.40, 141.38, 138.9, 129.1, 127.8, 127.2, 125.29, 125.25, 120.1, 107.8, 77.7, 73.5, 69.3, 67.1, 47.4, 47.3, 33.9, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.2, 22.8, 18.6, 14.2; IR (KBr) ν (cm^{-1}) 2916, 2849, 1658, 1467, 1243, 1119, 740, 720; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{80}H_{134}O_7N_2Na$: 1258.0089 ([M + Na]$^+$), Found: 1258.0090.



*Ala-(Me)N-O-TAGa (**4**)*

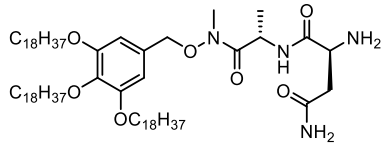
Following the general procedure described for Fmoc deprotection, Fmoc-Ala-(Me)N-O-TAGa (**S12**) (3.90 g, 3.2 mmol) was converted to Ala-(Me)N-O-TAGa (**4**) (3.20 g, quant.) as a white powder. $[\alpha]_D^{24.3}$ = +5.6 (*c* 0.1, $CHCl_3$); mp 64–65 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.53 (2H, s), 4.74 (2H, app dd, *J* = 18.5, 10.5 Hz), 3.97-3.93 (6H, m, overlapped), 3.85 (1H, br d, *J* = 6.0 Hz), 3.22 (3H, s), 1.82-1.70 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.37-1.22 (87H, br m, overlapped), 0.87 (9H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.2, 153.5, 139.0, 129.3, 107.7, 77.0, 73.6, 69.4, 47.3, 34.0, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.2, 22.8, 20.8, 14.3; IR (KBr) ν (cm^{-1}) 2915, 2848, 1641, 1469, 1335, 1240, 1123, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{65}H_{124}O_5N_2Na$: 1035.9408 ([M + Na]$^+$), Found: 1035.9396.



*Fmoc-Asn-Ala-(Me)N-O-TAGa (**S13**)*

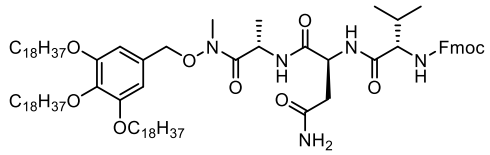
Following the general procedure described for condensation, Ala-(Me)N-O-TAGa (**4**) (5.00 g, 4.9 mmol) was converted to Fmoc-Asn-Ala-(Me)N-O-TAGa (**S13**) (6.54 g, 98%) as a white powder. $[\alpha]_D^{24.4}$ = +11.9 (*c* 0.1, $CHCl_3$); mp 134–135 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (2H, d, *J* = 7.5 Hz), 7.60 (2H, br dd, *J* = 7.0, 4.5 Hz), 7.54 (1H, br d, *J* = 7.5 Hz), 7.39 (2H, t, *J* = 7.5 Hz), 7.31 (2H, td, *J* = 7.5, 1.0 Hz), 6.58 (2H, s), 6.36 (1H, br d, *J* = 7.5 Hz), 6.09 (1H, br s), 5.63 (1H, br s), 4.93 (1H, br m), 4.84 (2H, app dd, *J* = 19.5,

10.0 Hz), 4.60 (1H, br m), 4.41-4.35 (2H, m, overlapped), 4.22 (1H, t, *J* = 7.5 Hz), 3.98-3.93 (6H, m, overlapped), 3.20 (3H, s), 2.91 (1H, br m), 2.63 (1H br m), 1.82-1.71 (6H, m, overlapped), 1.49-1.44 (6H, br m, overlapped), 1.34-1.22 (87H, br m, overlapped), 0.88 (9H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 173.4 (two signals), 170.5, 156.2, 153.5, 144.0, 143.8, 141.4, 138.7, 129.3, 127.8, 127.2, 125.3, 120.1, 107.7, 73.6, 69.3, 67.4, 51.3, 47.2, 46.5, 37.7, 34.0, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 17.7, 14.3; IR (KBr) ν (cm^{-1}) 3403, 3298, 2916, 2848, 1668, 1655, 1468, 1262, 1125, 990, 740, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{84}H_{140}O_9N_4Na$: 1372.0518 ([M + Na]$^+$), Found: 1372.0538.



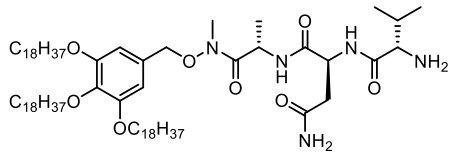
*Asn-Ala-(Me)N-O-TAGa (**5**)*

Following the general procedure described for Fmoc deprotection, Fmoc-Asn-Ala-(Me)N-O-TAGa (**S13**) (5.00 g, 3.7 mmol) was converted to Asn-Ala-(Me)N-O-TAGa (**5**) (4.18 g, quant.) as a white powder. $[\alpha]_D^{24.5}$ = –4.2 (*c* 0.1, $CHCl_3$); mp 67–69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.92 (1H, br d, *J* = 7.5 Hz), 6.59 (2H, s), 6.35 (1H, br s), 5.62 (1H, br s), 4.97 (1H, br m), 4.84 (2H, app dd, *J* = 21.5, 10.5 Hz), 3.98-3.92 (6H, m, overlapped), 3.70 (1H, m), 3.20 (3H, s), 2.67 (1H, br m), 2.53 (1H, br m), 1.82-1.70 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.37-1.21 (87H, br m, overlapped), 0.87 (9H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex due to the rotamers.) *δ* 173.75, 173.69, 173.55, 173.50, 173.45, 153.4, 138.8, 129.3, 107.8, 77.4, 73.6, 69.3, 52.4, 45.8, 45.6, 40.6, 34.0, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 18.08, 18.05, 14.3; IR (KBr) ν (cm^{-1}) 3366, 2916, 2848, 1659, 1468, 1334, 1122, 719; HRMS (FAB, NBA matrix) Calcd. for $C_{69}H_{131}O_7N_4$: 1128.0018 ([M + H]$^+$), Found: 1128.0023.



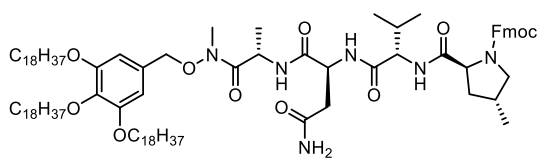
*Fmoc-Val-Asn-Ala-(Me)N-O-TAGa (**S14**)*

Following the general procedure described for condensation, Asn-Ala-(Me)N-O-TAGa (**5**) (4.10 g, 3.6 mmol) was converted to Fmoc-Val-Asn-Ala-(Me)N-O-TAGa (**S14**) (5.27 g, quant.) as a white powder. $[\alpha]_D^{24.5}$ = –0.1 (*c* 0.1, $CHCl_3$); mp 174–179 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were complex due to rotamers of the peptide bonds.) *δ* 7.75 (1H, br s), 7.73 (2H, dd, *J* = 7.5, 4.0 Hz), 7.63 (1H, br d, *J* = 7.0 Hz), 7.58 (2H, br d, *J* = 7.5 Hz), 7.36 (2H, app q, *J* = 7.0 Hz), 7.28 (2H, br t, *J* = 7.5 Hz), 6.55 (2H, s), 6.30 (1H, br s), 5.85 (1H, br s), 5.75 (1H, br d, *J* = 8.0 Hz), 4.93-4.77 (4H, br m, overlapped), 4.40 (1H, br dd, *J* = 10.5, 8.0 Hz), 4.31 (1H, br dd, *J* = 10.5, 7.5 Hz), 4.19 (1H, br t, *J* = 7.0 Hz), 4.14 (1H, br t, *J* = 7.0 Hz), 3.97-3.92 (6H, br m, overlapped), 3.17 (3H, s), 2.83 (1H, br m), 2.62 (1H, br m), 2.16 (1H, br m), 1.81-1.71 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.35-1.22 (87H, br m, overlapped), 0.99 (3H, d, *J* = 6.0 Hz), 0.94 (3H, d, *J* = 7.0 Hz), 0.88 (9H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex due to the rotamers.) *δ* 173.6, 173.4, 171.6, 170.2, 156.7, 153.4, 144.0, 143.9, 141.4, 138.8, 129.3, 127.8, 127.22, 127.18, 125.30, 125.25, 120.07, 120.05, 107.7, 73.6, 69.3, 67.3, 60.4, 49.8, 47.3, 46.4, 37.1, 34.0, 32.1, 31.5, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 19.4, 17.9, 17.6, 14.3; IR (KBr) ν (cm^{-1}) 3272, 2917, 2849, 1639, 1468, 1247,1120, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{89}H_{149}O_{10}N_5Na$: 1471.1202 ([M + Na]$^+$), Found: 1471.0200.



*Val-Asn-Ala-(Me)N-O-TAGa (**6**)*

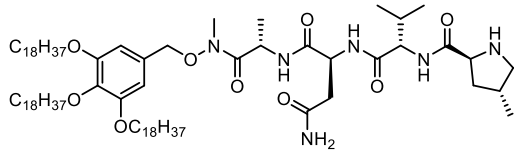
Following the general procedure described for Fmoc deprotection, Fmoc-Val-Asn-Ala-(Me)N-O-TAGa (**S14**) (5.21 g, 3.6 mmol) was converted to Val-Asn-Ala-(Me)N-O-TAGa (**6**) (4.41 g, quant.) as a white powder. $[\alpha]_D^{24.6}$ = –2.8 (*c* 0.1, $CHCl_3$); mp 81–83 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were complex due to rotamers of the peptide bonds.) *δ* 8.40 (1H, d, *J* = 8.0 Hz), 7.66 (1H, d, *J* = 7.0 Hz), 6.57 (2H, s), 6.47 (1H, br s), 5.75 (1H, br s), 4.92-4.77 (4H, br m, overlapped), 3.99-3.92 (6H, br m, overlapped), 3.26 (1H, br d, *J* = 3.0 Hz), 3.18 (3H, s), 2.83 (1H, m), 2.63 (1H, m), 2.24 (1H, m), 1.82-1.70 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.37-1.22 (87H, br m, overlapped), 0.98 (3H, d, *J* = 7.0 Hz), 0.87 (9H, t, *J* = 7.5 Hz), 0.83 (3H, d, *J* = 6.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex due to the rotamers.) *δ* 175.11, 175.05, 173.5, 173.41, 173.36, 170.6, 170.5, 153.4, 138.7, 129.3, 107.7, 73.6, 69.3, 60.3, 49.5, 49.4, 46.45, 46.35, 37.8, 34.0, 32.1, 31.2, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 19.8, 17.6, 16.3, 14.2; IR (KBr) ν (cm^{-1}) 3277, 2916, 2849, 1637, 1468, 1236, 1121, 720; HRMS (FAB, NBA matrix) Calcd. for $C_{74}H_{140}O_8N_5$: 1227.0702 ([M + H]$^+$), Found: 1227.0693.



*Fmoc-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S15**)*

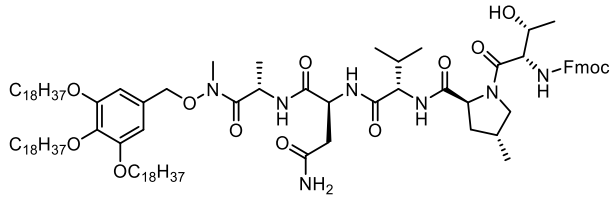
Following the general procedure described for condensation, Val-Asn-Ala-(Me)N-O-TAGa (**6**) (4.40 g, 3.6 mmol) was converted to Fmoc-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S15**) (5.60 g, quant.) as a white powder. $[\alpha]_D^{24.8}$ = –17.7 (*c* 0.1, $CHCl_3$); mp 169–171 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 7.76 (2H, br d, *J* = 7.5 Hz), 7.70 (1H, br d, *J* = 7.5 Hz), 7.58 (2H, br d, *J* = 7.0 Hz), 7.56 (1H, br m), 7.39 (2H, br t, *J*

= 7.5 Hz), 7.31 (2H, td, *J* = 7.5, 1.5 Hz), 6.57 (2H, br s), 6.45 (1H, br s), 5.93 (1H, br s), 5.51 (1H, ap p br d, *J* = 48 Hz), 4.92 (1H, br s), 4.86-4.78 (3H, m, overlapped), 4.46-4.33 (3H, br m, overlapped), 4.22 (1H, br t, *J* = 7.0 Hz), 3.97-3.92 (6H, m, overlapped), 3.65 (1H, br t, *J* = 8.5 Hz), 3.17 (3H, s), 2.95 (1H, br t, *J* = 10.0 Hz), 2.77 (1H, br m), 2.66 (1H, br m), 2.50-2.06 (4H, br m, overlapped), 1.81-1.70 (6H, m, overlapped), 1.65 (1H, br m), 1.49-1.43 (6H, br m, overlapped), 1.37-1.22 (87H, br m, overlapped), 1.06 (3H, br d, *J* = 6.5 Hz), 0.93 (3H, d, *J* = 7.0 Hz), 0.87 (12H, app t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 173.4 (two signals), 172.4, 171.3, 170.2, 156.3, 153.4, 144.0, 143.8, 141.4, 138.7, 129.4, 127.9, 127.2, 125.1, 120.1, 107.7, 73.6, 69.3, 68.1, 61.3, 58.7, 54.0, 49.9, 47.2, 46.3, 37.2, 36.7, 34.1, 32.7, 32.0, 30.9, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 19.5, 17.8, 17.7, 17.3, 14.2; IR (KBr) ν (cm^{-1}) 3272, 2916, 2849, 1661, 1638, 1468, 1236, 1122, 739, 720; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{95}H_{158}O_{11}N_6Na$: 1582.1886 ([M + Na]$^+$), Found: 1582.1896.



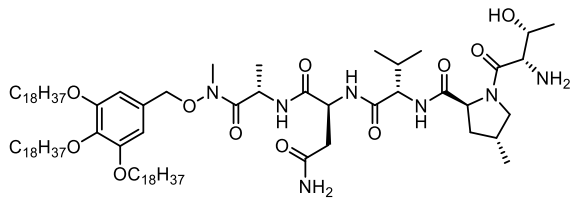
*4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**7**)*

Following the general procedure described for Fmoc deprotection, Fmoc-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S15**) (5.55 g, 3.6 mmol) was converted to 4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**7**) (4.76 g, quant.) as a white powder. $[\alpha]_D^{24.9}$ = –9.1 (*c* 0.1, $CHCl_3$); mp 100–102 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 8.31 (1H, d, *J* = 8.5 Hz), 7.81 (1H, br s), 7.61 (1H, d, *J* = 6.5 Hz), 6.60 (1H, br s), 6.57 (2H, s), 5.88 (1H, br s), 4.91-4.74 (4H, br m, overlapped), 4.26 (1H, br m), 4.00-3.91 (6H, m, overlapped), 3.81 (1H, br d, *J* = 9.0 Hz), 3.39 (1H, br m), 3.17 (3H, s), 3.08 (1H, br m), 2.81-2.55 (3H, br m, overlapped), 2.30-2.03 (3H, br m, overlapped), 1.81-1.63 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.35-1.22 (87H, br m, overlapped), 0.99 (3H, d, *J* = 6.0 Hz), 0.95 (3H, d, *J* = 6.5 Hz), 0.91 (3H, d, *J* = 7.0 Hz), 0.87 (9H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 176.4, 173.6, 173.5, 171.6, 170.4, 153.4, 138.7, 129.4, 107.7, 73.6, 69.3, 60.4, 58.1, 54.7, 54.2, 49.9, 48.7, 46.3, 39.0, 36.9, 34.1, 33.3, 32.1, 30.8, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 19.6, 17.9, 17.58, 17.56, 14.2; IR (KBr) ν (cm^{-1}) 3270, 2916, 2849, 1635, 1468, 1236, 1121, 720; HRMS (FAB, NBA matrix) Calcd. for $C_{80}H_{149}O_9N_6$: 1338.1386 ([M + H]$^+$), Found: 1338.1384.



*Fmoc-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S16**)*

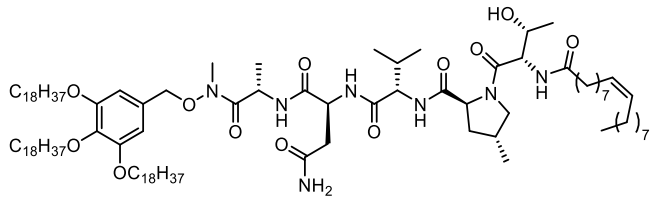
Following the general procedure described for condensation, 4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**7**) (4.70 g, 3.5 mmol) was converted to Fmoc-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S16**) (5.84 g, quant.) as a white powder. $[\alpha]_D^{25.0}$ = –22.8 (*c* 0.1, $CHCl_3$); mp 151–154 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 7.80-7.71 (3H, br m, overlapped), 7.59 (2H, br d, *J* = 7.0 Hz), 7.37 (2H, br t, *J* = 7.5 Hz), 7.32-7.28 (3H, br m, overlapped), 7.13 (1H, br d, *J* = 9.5 Hz), 6.95 (1H, br s), 6.57 (2H, s), 6.31-6.22 (2H, br m, overlapped), 5.01-4.95 (2H, br m, overlapped), 4.84 (1H, d, *J* = 10.5 Hz), 4.79 (1H, d, *J* = 10.5 Hz), 4.70 (1H, dd, *J* = 9.5, 3.5 Hz), 4.63 (1H, dd, *J* = 9.5, 4.0 Hz), 4.56 (1H, br m), 4.46 (1H, dd, *J* = 11.0, 7.5 Hz), 4.35 (1H, dd, *J* = 10.5, 7.0 Hz), 4.30 (1H, br m), 4.19 (1H, t, *J* = 6.5 Hz), 4.03 (1H, br t, *J* = 8.0 Hz), 3.97-3.92 (6H, m, overlapped), 3.32 (1H, br t, *J* = 9.0 Hz), 3.17 (3H, s), 2.81-2.69 (2H, br m, overlapped), 2.47 (1H, br m), 2.24-2.16 (2H, br m, overlapped), 1.93 (1H, m), 1.80-1.70 (6H, m, overlapped), 1.49-1.42 (6H, br m, overlapped), 1.35-1.22 (90H, br m, overlapped), 1.09 (3H, d, *J* = 6.0 Hz), 0.94 (3H, d, *J* = 6.5 Hz), 0.87 (12H, app t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 173.9, 173.3, 172.2, 171.7, 171.3, 169.9, 156.4, 153.4, 143.9, 143.8, 141.4, 138.7, 129.5, 127.9, 127.2, 125.21, 125.16, 120.1, 107.7, 73.6, 69.3, 68.0, 67.0, 61.5, 58.1, 57.0, 54.6, 50.5, 47.3, 46.2, 42.3, 37.8, 37.1, 34.2, 33.0, 32.1, 31.0, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 23.6, 22.8, 19.5, 18.8, 18.0, 17.9, 17.4, 14.3; IR (KBr) ν (cm^{-1}) 3286, 2917, 2849, 1638, 1467, 1439, 1236, 1119, 720; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{99}H_{165}O_{13}N_7Na$: 1683.2363 ([M + Na]$^+$), Found: 1683.2360.



*Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**8**)*

Following the general procedure described for Fmoc deprotection, Fmoc-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S16**) (5.78 g, 3.5 mmol) was converted to Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**8**) (5.01 g, quant.) as a white powder. $[\alpha]_D^{25.1}$ = –35.3 (*c* 0.1, $CHCl_3$); mp ca. 190 °C (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 7.34-7.30 (3H, br m, overlapped), 7.17 (1H, br s), 6.81 (1H, br s), 6.58 (2H, s), 4.97 (1H, br m), 4.93 (1H, dd *J* = 9.5, 4.5 Hz), 4.85 (1H, d, *J* = 10.0 Hz), 4.79 (1H, d, *J* = 10.5 Hz), 4.66-4.58 (2H, br m), 4.11 (1H, br m), 3.98-3.92 (6H, m, overlapped), 3.80 (1H, br m), 3.30 (1H, br m), 3.17 (3H, s), 3.16 (1H, br m), 2.78-2.63 (2H, br m, overlapped), 2.46 (1H, br m), 2.22 (1H, m), 2.12 (2H, m), 1.83 (1H, m, overlapped), 1.81-1.70 (6H, m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.37-1.22 (90H, br m, overlapped), 1.09 (3H, d, *J* = 6.0 Hz), 0.94 (3H, d, *J* = 7.0 Hz), 0.87 (12H, app t, *J* = 7.0 Hz); ^{13}C NMR (125

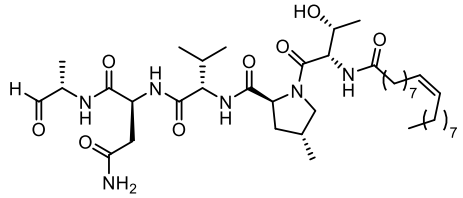
MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) δ 174.2, 173.3 (two signals), 172.4, 171.5, 170.1, 153.4, 138.8, 129.4, 107.7, 73.6, 70.1, 69.3, 61.7, 57.7, 56.4, 54.5, 50.5, 46.0, 37.6, 37.2, 34.1, 32.9, 32.1, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 19.5, 18.0, 17.9, 17.5, 17.3, 14.2; IR (KBr) ν (cm^{-1}) 3292, 2917, 2849, 1644, 1468, 1237, 1117, 720; HRMS (FAB, NBA matrix) Calcd. for $C_{84}H_{155}O_{11}N_7$: 1439.1863 ([M + H]$^+$), Found: 1439.1868.



*Oleic acid-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**9**)*

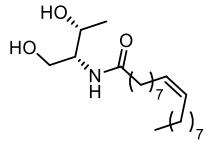
Following the general procedure described for condensation using oleic acid instead of Fmoc protected amino acid, Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**8**) (2.97 g, 2.1 mmol) was converted to oleic acid-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**9**) (3.52 g, quant.) as a white powder. Advanced Marfey's method for all the amino acid residues after complete acid hydrolysis in the same way as described above in "Screening of condensation reagents to suppress the epimerization in our previous report" section confirmed that no epimerization occurred. $[\alpha]_D^{25.1}$ = –11.9 (*c* 0.1, $CHCl_3$); mp 151–152 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (1H, br d, *J* = 8.0 Hz), 7.30 (1H, br d, *J* = 7.5 Hz), 7.09 (1H, d, *J* = 9.5 Hz), 7.03 (1H, br s), 6.77 (1H, br d, *J* = 8.5 Hz), 6.57 (2H, s), 6.37 (1H, br s), 5.37-5.29 (2H, m, overlapped), 4.98 (1H, dd, *J* = 7.5, 4.0 Hz), 4.95-4.89 (2H, br m, overlapped), 4.85 (1H, d, *J* = 10.5 Hz), 4.80 (1H, d, *J* = 10.5 Hz), 4.59 (1H, dd, *J* = 9.0, 4.0 Hz), 4.55 (1H, dd, *J* = 9.0, 6.5 Hz), 4.46 (1H, d, *J* = 6.0 Hz), 4.29 (1H, m), 4.03 (1H, dd, *J* = 9.5, 7.5 Hz), 3.98-3.92 (6H, m, overlapped), 3.36 (1H, br t, *J* = 9.5 Hz), 3.18 (3H, s), 2.79 (1H, m), 2.70 (1H, m), 2.46 (1H, m), 2.34 (2H, t, *J* = 8.0 Hz), 2.20-2.15 (2H, br m, overlapped), 2.20-1.98 (3H, m, overlapped), 1.90 (1H, m), 1.82-1.72 (6H, m, overlapped), 1.66-1.58 (2H, br m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.37-1.22 (110H, br m, overlapped), 1.09 (3H, d, *J* = 7.0 Hz), 0.94 (3H, d, *J* = 6.5 Hz), 0.89-0.86 (15H, m, overlapped); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 173.4 (two signals), 172.2, 171.7, 171.5, 169.9, 153.5, 138.8, 130.1, 129.9, 129.4, 107.7, 73.6, 69.4, 67.9, 61.5, 58.0, 54.7, 50.6, 46.2, 37.7, 37.1, 36.6, 34.1, 33.0, 32.1, 31.3, 30.5, 29.9-29.3 (many signals overlapped), 27.4, 27.3, 26.3, 25.7, 22.8, 19.5, 18.9, 17.93, 17.86, 17.3, 14.3; IR (KBr) ν (cm^{-1}) 3279, 2917, 2849, 1640, 1438, 1238, 1121, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{102}H_{187}O_{12}N_7Na$: 1725.4135 ([M + Na]$^+$), Found: 1725.4131.

Reduction to afford the aldehyde



*Oleic acid-Thr-4-MePro-Val-Asn-Ala-H (**2**)*

To a solution of **9** (850 mg, 0.50 mmol, 1.0 eq) in dehydrated THF (50 mL, 0.01 M) was added dropwise 1.0 M $LiAlH(O\textit{t}\text{-}Bu)_3$ in dehydrated THF (4.99 mL, 10 eq, prepared by the procedure described in the literature.[6]) at room temperature. After stirring for 1 h at room temperature, the reaction mixture was then treated with aqueous 1 N HCl (25 mL) at 0 °C to quench the excess $LiAlH(O\textit{t}\text{-}Bu)_3$. After stirring for 10 min at room temperature, MeOH (250 mL) was added. The resulting heterogeneous solution was stirred for a further 30 min at room temperature, and the precipitate was filtered and washed with additional MeOH. The filtrate was roughly concentrated in vacuo, poured into a separatory funnel containing aqueous 1 N HCl (20 mL), and extracted with $CHCl_3$ (3 × 20 mL). The combined organic extracts were dried with Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel ($CHCl_3$/MeOH = 50/1 to 10/1 as eluent) to afford aldehyde **2** (240.0 mg, 63%) as a white powder and MePro-Thr amide bond-cleaved alcohol **S17** (37.5 mg, 20% yield) as a colorless oil (the structure is shown below).
$[\alpha]_D^{24.6}$ = –33.8 (*c* 0.1, DMSO), $[\alpha]_D^{24.6}$ = –29.6 (*c* 0.1, $CHCl_3$); mp 170–175 °C; ^{1}H NMR (500 MHz, DMSO-d_6, Signals derived from the diastereomer of the α-position of alaninal moiety were not observed at all.) δ 9.34 (1H, s), 8.14 (1H, d, *J* = 6.5 Hz), 8.11 (1H, d, *J* = 7.5 Hz), 7.87 (2H, app dd, *J* = 8.0, 1.5 Hz), 7.37 (1H, br s), 6.93 (1H, br s), 5.35-5.29 (2H, m, overlapped), 4.67 (1H, d, *J* = 6.0 Hz), 4.55-4.47 (2H, m, overlapped), 4.41 (1H, t, *J* = 7.5 Hz), 4.09-3.98 (2H, m, overlapped), 3.83-3.76 (2H, m, overlapped), 3.27 (1H, t, *J* = 9.5 Hz), 2.55-2.46 (2H, m, overlapped with solvent residual signals), 2.34 (1H, m), 2.17-2.06 (2H, m, overlapped), 2.01-1.94 (6H, m, overlapped), 1.65 (1H, m), 1.48-1.42 (2H, m, overlapped), 1.32-1.19 (20H, br m, overlapped), 1.14 (3H, d, *J* = 7.5 Hz), 1.08 (3H, d, *J* = 6.0 Hz), 0.97 (3H, d, *J* = 7.0 Hz), 0.86-0.82 (9H, m, overlapped); ^{13}C NMR (125 MHz, DMSO-d_6) δ 201.4, 172.2, 171.9, 171.4, 171.3, 170.6, 169.5, 129.7, 66.9, 59.2, 58.0, 56.2, 54.0, 53.9, 49.5, 36.8, 36.5, 34.9, 32.0, 31.3, 30.4, 29.2-28.6 (many signals overlapped), 26.64, 26.60, 25.3, 22.1, 19.4, 19.1, 18.0, 17.2, 14.0, 13.6; IR (KBr) ν (cm^{-1}) 3285, 2924, 2853, 1736, 1639, 1542, 1426, 1235; HRMS (ESI$^+$) Calcd. for $C_{40}H_{70}N_6O_8Na$: 785.5153 ([M + Na]$^+$), Found: 785.5151.

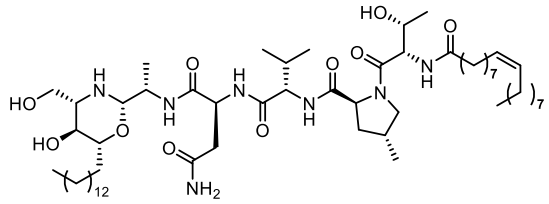


*MePro-Thr amide bond-cleaved alcohol **S17***

$[\alpha]_D^{25.2}$ = –25.7 (*c* 0.1, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.24 (1H, br d, *J* = 9.0 Hz), 5.35-5.28 (2H, m, overlapped), 4.55-4.51 (2H, br m, overlapped), 3.85 (1H, br m), 3.62 (1H, m), 3.42 (1H, br m), 3.29 (1H, br m), 2.15-2.04 (2H, m, overlapped), 2.02-1.93 (4H, br m, overlapped), 1.51-1.43 (2H, br m, overlapped), 1.30-1.20 (20H, br m, overlapped), 0.97 (3H, d, *J* = 6.0 Hz), 0.85 (3H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.4, 129.6, 64.2, 60.6, 55.4, 35.4, 31.3, 29.2-28.6 (many signals overlapped), 26.64, 26.60, 25.5, 22.1, 20.1, 14.0; IR (KBr) ν (cm^{-1}) 3294, 2923, 2853, 1632, 1541, 1458, 1065; HRMS (ESI$^+$) Calcd. for $C_{22}H_{43}NO_3Na$: 392.3141 ([M + Na]$^+$), Found: 392.3139.

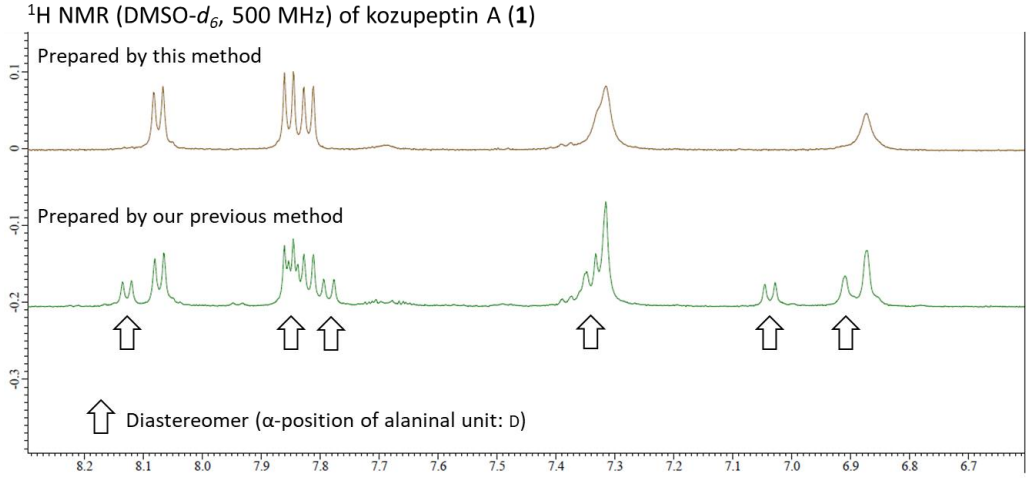
Recovery of benzyloxy methyl amine anchor molecule 3

To a solution of **9** (50.0 mg, 0.029 mmol, 1.0 eq) in dehydrated THF (2.9 mL, 0.01 M) was added dropwise 1.0 M LiAlH(*t*-BuO)$_3$ in dehydrated THF (0.293 mL, 10 eq, prepared by the procedure described in the literature.[6]) at room temperature. After stirring for 1 h at room temperature, the reaction mixture was then treated with aqueous 1 N HCl (1.5 mL) at 0 °C to quench the excess LiAlH(*t*-BuO)$_3$. After stirring for 10 min at room temperature, MeOH (14.7 mL) was added. The resulting heterogeneous solution was stirred for a further 30 min at room temperature, and the precipitate was filtered and washed with additional MeOH to recover benzyloxy methyl amine anchor molecule **3** as its hydrogen chloride salt form (28.8 mg, quant.). Aldehyde **2** was obtained from the filtrate by the same procedure described above (13.7 mg, 61%). The ^{1}H NMR spectrum of this recovered **3** showed clear match with the data of newly prepared **3** in $CDCl_3$ + small amount of conc. HCl (see NMR spectra section below).



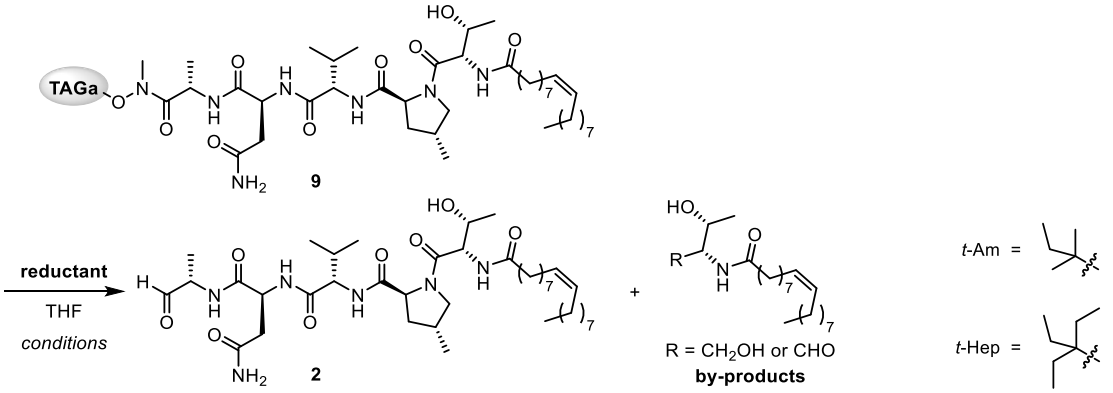
*Kozupeptin A (**1**)*

To a solution of **2** (17.5 mg, 0.023 mmol, 1.0 eq) in $CHCl_3$ (1.2 mL) was added phytosphingosine (8.7 mg, 0.028 mmol, 1.2 eq) at room temperature. After stirring for 6 h at room temperature, the reaction mixture was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel ($CHCl_3$/MeOH) to afford kozupeptin A (**1**) (23.1 mg, 95%) as a white powder. All physical data for **1** obtained here matched with the data in our previous paper. [2] In ^{1}H NMR spectrum, signals derived from the diastereomer of the α-position of alaninal moiety were not observed at all. The amide-H region was shown below (upper: derived from this method, lower: derived from the previous report method using HBTU as a condensation reagent to get Weinreb amide **S2**).



Use of the reductants having bulkier alkoxy group

Table S2. Screening of the reductant

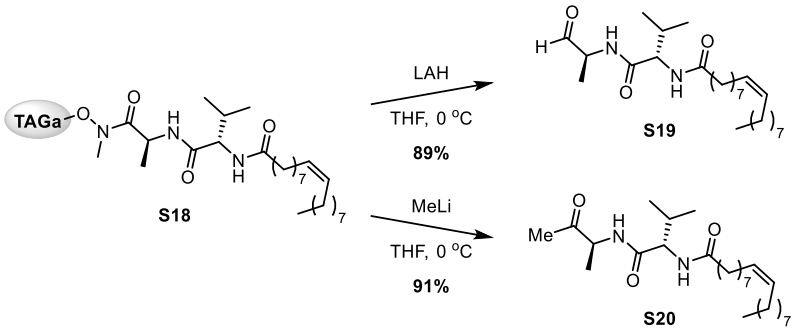


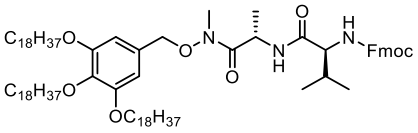
entry	reductant	temperature	isolated yield of **2** (%)	note
1	$LiAlH_4$ (1.8 eq)	0 °C	42	Full conversion. **By-products** were obtained together in 20-30% yield.
2	Red-Al® (9.0 eq)	0 °C	37	Full conversion. **By-products** were obtained together in 20-30% yield.
3	$LiAlH(Ot\text{-}Bu)_3$ (10 eq)	rt	63	850 mg of substrate **9** was used. Full conversion. **By-product** alcohol was obtained in 20% yield.
S3-1*	$LiAlH(Ot\text{-}Am)_3$ (10 eq)	rt	62	Full conversion. **By-product** alcohol was obtained in around 20% yield.
S3-2*	$LiAlH(Ot\text{-}Hep)_3$ (10 eq)	rt	58	Full conversion. **By-product** alcohol was obtained in around 20% yield.
4	DIBAL (10 eq)	–78 °C to rt	not obtained	No reaction to decomposition.
5	$LiBH_4$ (4.0 eq)	rt	trace	**By-product** alcohol was observed as a major product in TLC analysis.
6	K-selectride® (30 eq)	rt to 40 °C	not obtained	No reaction to decomposition.
7	$LiBHEt_3$ (7.0 eq)	0 °C	38	Full conversion. **By-products** were obtained together in 20-30% yield.

Unless noted, 40.0 or 50.0 mg of **9** in THF (0.01 M) was used. *Prepared by the procedure described in the literature.[6]

Use of a model substrate

Scheme S3. Use of a model substrate without Thr-Pro amide bond

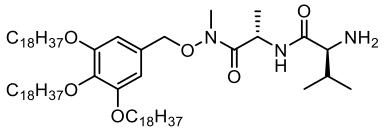




*Fmoc-Val-Ala-(Me)N-O-TAGa (**S21**)*

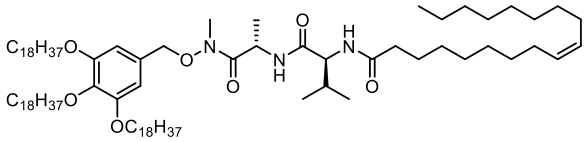
Following the general procedure described for condensation, Ala-(Me)N-O-TAGa (**4**) (817 mg, 0.81 mmol) was converted to Fmoc-Val-Ala-(Me)N-O-TAGa (**S21**) (1.08 g, quant.) as a white powder. $[\alpha]_D^{24.3}$ = –13.8 (*c* 0.1, $CHCl_3$); mp 65–69 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.76 (2H, d, *J* = 7.5 Hz), 7.61 (2H, br dd, *J* = 7.5, 4.0 Hz), 7.39 (2H, br td, *J* = 7.5, 2.0 Hz), 7.31 (2H, m), 6.63 (1H, br s, overlapped), 6.60 (2H, s), 5.43 (1H, br d, *J* = 9.0 Hz), 5.05 (1H, br m), 4.85 (2H, br s), 4.45 (1H, dd, *J* = 10.5, 7.5 Hz), 4.36 (1H, dd, *J* = 11.0, 6.5 Hz), 4.23 (1H, t, *J* = 7.0 Hz), 4.07 (1H, br dd, *J* = 8.5, 6.5 Hz), 3.99-3.94 (6H, m, overlapped), 3.21 (3H, s), 2.13 (1H, m), 1.82-1.71 (6H, m, overlapped), 1.50-1.44 (6H, br m, overlapped), 1.36-1.22 (87H, br m, overlapped), 0.97 (3H, d, *J* = 6.5 Hz), 0.94 (3H, d, *J* = 7.0 Hz), 0.88 (9H, t, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex due to the rotamers.) *δ* 173.4, 170.8, 156.4, 153.5, 144.1, 143.9, 141.4, 138.9, 129.1, 127.8, 127.2, 125.3, 125.2, 120.11, 120.09, 107.8, 77.6, 73.6, 69.3, 67.2, 60.3, 47.3, 46.0, 34.1, 32.1, 31.7, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 19.3, 18.3, 17.9, 14.3; IR (KBr) ν (cm^{-1}) 3290, 2916,

2849, 1644, 1468, 1237, 1119, 739, 721; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{85}H_{143}N_3O_8Na$: 1357.0773 ([M + Na]$^+$), Found: 1357.0785.



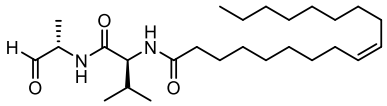
*Val-Ala-(Me)N-O-TAGa (**S22**)*

Following the general procedure described for Fmoc deprotection, Fmoc-Val-Ala-(Me)N-O-TAGa (**S21**) (965 mg, 0.72 mmol) was converted to Val-Ala-(Me)N-O-TAGa (**S22**) (804 mg, quant.) as a white powder. $[\alpha]_D^{24.4}$ = –10.0 (*c* 0.1, $CHCl_3$); mp 58–59 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.82 (1H, br d, *J* = 8.0 Hz), 6.62 (2H, s), 5.10 (1H, br m), 4.89 (1H, d, *J* = 10.0 Hz), 4.84 (1H, d, *J* = 10.5 Hz), 4.01-3.91 (6H, m, overlapped), 3.25 (1H, d, *J* = 4.0 Hz), 3.20 (3H, s), 2.26 (1H, m), 1.82-1.70 (6H, br m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.36-1.22 (87H, br m, overlapped), 1.00 (3H, d, *J* = 7.0 Hz), 0.89-0.85 (12H, m, overlapped); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex due to the rotamers.) *δ* 173.94, 173.87, 153.5, 138.8, 129.3, 107.9, 77.7, 73.6, 69.3, 60.3, 45.3, 34.0, 32.1, 31.2, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 22.8, 19.8, 18.5, 16.4, 14.3; IR (KBr) ν (cm^{-1}) 2916, 2849, 1659, 1467, 1236, 1119, 720; HRMS (FAB, NBA matrix) Calcd. for $C_{70}H_{134}O_6N_3$: 1113.0273 ([M + H]$^+$), Found: 1113.0282.



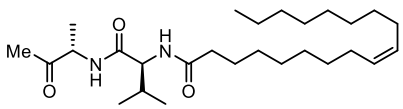
*Oleic acid-Val-Ala-(Me)N-O-TAGa (**S18**)*

Following the general procedure described for condensation using oleic acid instead of Fmoc protected amino acid, Val-Ala-(Me)N-O-TAGa (**S22**) (770 mg, 0.72 mmol) was converted to oleic acid-Val-Ala-(Me)N-O-TAGa (**S18**) (933 mg, 98%) as a white powder. $[\alpha]_D^{24.4}$ = –11.6 (*c* 0.1, $CHCl_3$); mp 54–55 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 6.70 (1H, br d, *J* = 7.0 Hz), 6.59 (2H, s), 6.11 (1H, br d, *J* = 7.5 Hz), 5.36-5.29 (2H, m, overlapped), 5.01 (1H, br m), 4.83 (2H, s), 4.36 (1H, dd, *J* = 8.5, 6.5 Hz), 3.99-3.93 (6H, m, overlapped), 3.20 (3H, s), 2.22 (2H, m), 2.07 (1H, m), 2.01-1.98 (3H, br m, overlapped), 1.82-1.70 (6H, m, overlapped), 1.68-1.59 (2H, br m, overlapped), 1.49-1.43 (6H, br m, overlapped), 1.36-1.22 (107H, br m, overlapped), 0.94 (3H, d, *J* = 7.0 Hz), 0.92 (3H, d, *J* = 6.5 Hz), 0.87 (12H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex because of the rotamers.) *δ* 173.4, 173.2, 170.8, 153.5, 138.9, 130.1, 129.9, 129.2, 107.8, 77.6, 73.6, 69.3, 58.0, 45.9, 36.9, 34.1, 32.1, 32.0, 31.7, 30.5, 29.9-29.3 (many signals overlapped), 27.34, 27.30, 26.3, 25.9, 22.8, 19.3, 18.19, 18.16, 14.2; IR (KBr) ν (cm^{-1}) 3303, 2917, 2849, 1638, 1467, 1235, 1118, 721; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{88}H_{165}N_3O_7Na$: 1399.2545 ([M + Na]$^+$), Found: 1399.2542.



*Oleic acid-Val-Ala-H (**S19**)*

To a solution of **S18** (20.0 mg, 0.015 mmol, 1.0 eq) in dehydrated THF (1.8 mL, 0.008 M) was added dropwise 2.0 M $LiAlH_4$ in dehydrated THF (8.7 µL, 1.2 eq) at 0 °C. After stirring for 15 min at 0 °C, the reaction mixture was then treated with aqueous 1 N HCl (0.9 mL) at 0 °C to quench the excess $LiAlH_4$. After stirring for 10 min at room temperature, MeOH (9.0 mL) was added. The resulting heterogeneous solution was stirred for a further 30 min at room temperature, and the precipitate was filtered and washed with additional MeOH. The filtrate was roughly concentrated in vacuo, poured into a separatory funnel containing aqueous 1 N HCl (10 mL), and extracted with $CHCl_3$ (3 × 10 mL). The combined organic extracts were dried with Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel ($CHCl_3$/MeOH = 200/1 to 20/1 as eluent) to afford aldehyde **S19** (5.6 mg, 89%) as a white powder. $[\alpha]_D^{24.5}$ = –12.5 (*c* 0.1, $CHCl_3$); mp 96–99 °C; ^{1}H NMR (500 MHz, 500 MHz, DMSO-d_6, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 9.37 (1H, s), 8.45 (1H, d, *J* = 6.0 Hz), 7.83 (1H, d, *J* = 7.5 Hz), 5.35-5.29 (2H, m, overlapped), 4.19 (1H, m), 4.07 (1H, m), 2.21-2.07 (2H, m, overlapped), 1.99-1.91 (5H, m, overlapped), 1.53-1.42 (2H, m, overlapped), 1.30-1.22 (20H, br m, overlapped), 1.16 (3H, d, *J* = 7.5 Hz), 0.88-0.84 (9H, m, overlapped); ^{13}C NMR (125 MHz, DMSO-d_6, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 201.9, 173.2, 172.5, 130.5, 58.2, 54.7, 36.1, 32.2, 31.3, 30.0-29.5 (many signals overlapped), 27.53, 27.49, 26.3, 23.0, 20.1, 19.1, 14.9, 14.4; IR (KBr) ν (cm^{-1}) 3284, 2919, 2850, 1733, 1633, 1541, 1466, 1386, 693; HRMS (FAB, NBA matrix) Calcd. for $C_{26}H_{49}O_3N_2$: 437.3743 ([M + H]$^+$), Found: 437.3747.

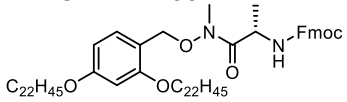


*Oleic acid-Val-Ala-Me (**S20**)*

To a solution of **S18** (20.0 mg, 0.015 mmol, 1.0 eq) in dehydrated THF (1.8 mL, 0.008 M) was added dropwise 1.11 M MeLi in dehydrated diethyl ether (Et_2O) (131 µL, 10 eq) at 0 °C. After stirring for 20 min at 0 °C, the reaction mixture was then treated with aqueous 1 N HCl (0.9 mL) at 0 °C to quench the excess MeLi. After stirring for 10 min at room temperature, MeOH (9.0 mL) was added. The resulting heterogeneous solution was stirred for a further 30 min at room temperature, and the precipitate was filtered and washed with additional MeOH. The filtrate was roughly concentrated in vacuo, poured into a separatory funnel containing aqueous 1 N HCl (10 mL), and extracted with $CHCl_3$ (3 × 10 mL). The combined organic extracts were dried with Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by PLC on silica gel ($CHCl_3$/MeOH = 10/1) to afford methyl ketone **S20** (5.9 mg, 91%) as a white powder. $[\alpha]_D^{24.5}$ = –9.0 (*c* 0.1, $CHCl_3$); mp 93–97 °C; ^{1}H NMR (500 MHz, DMSO-d_6, Signals were broad and complex due to the rotamers.) *δ* 8.34-8.30 (1H, m), 7.84-7.79 (1H, m), 5.35-5.29 (2H, m, overlapped), 4.23-4.11 (2H, m, overlapped), 2.20-2.07 (2H, m, overlapped), 2.06 & 2.04 (3H, two s) 1.99-1.90 (5H, m, overlapped), 1.51-1.42 (2H, br m, overlapped), 1.30-1.22 (20H, br m, overlapped), 1.15 (3H, t, *J* = 7.0 Hz), 0.87-0.83 (9H, m, overlapped); ^{13}C NMR (125 MHz, DMSO-d_6, Signals were complex due

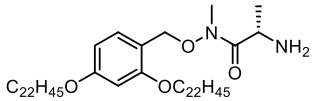
to the rotamers) δ 208.0, 207.4, 172.3, 172.2, 171.3, 171.1, 129.6, 57.7, 57.3, 54.1, 54.0, 35.1, 31.3, 30.4, 30.2, 29.1-28.6 (many signals overlapped), 26.61, 26.57, 26.1, 25.7, 25.41, 25.38, 22.1, 19.24, 19.19, 18.4, 18.1, 15.8, 15.6, 14.0; IR (KBr) ν (cm^{-1}) 3284, 2921, 2851, 1720, 1633, 1540, 1467, 1386, 719; HRMS (ESI^+) Calcd. for $C_{27}H_{50}N_2O_3Na$: 473.3719 ([M + Na]$^+$), Found:473.3720.

Using TAGb-type anchor molecule



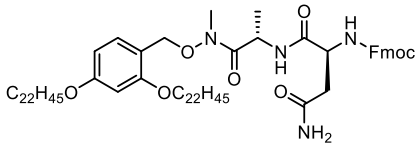
*Fmoc-Ala-(Me)N-O-TAGb (**S23**)*

Following the general procedure described for condensation, Me-HN-O-TAGb (**S11**) (1.50 g, 1.9 mmol) was converted to Fmoc-Ala-(Me)N-O-TAGb (**S23**) (2.03 g, 99%) as a white powder. $[\alpha]_D^{24.3}$ = 23.6 (*c* 0.1, $CHCl_3$); mp 53–54 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (2H, d, *J* = 7.5 Hz), 7.62 (2H, d, *J* = 7.0 Hz), 7.40 (2H, t, *J* = 7.5 Hz), 7.32 (2H, t, *J* = 7.5 Hz), 7.24 (1H, br d, *J* = 8.0 Hz), 6.45-6.43 (2H, br m, overlapped), 5.59 (1H, br d, *J* = 8.5 Hz), 4.97 (1H, d, *J* = 9.5 Hz), 4.88-4.84 (2H, br m, overlapped), 4.39-4.31 (2H, m, overlapped), 4.23 (1H, t, *J* = 7.5 Hz), 4.04-3.95 (2H, br m, overlapped), 3.91 (2H, t, *J* = 7.0 Hz), 3.27 (3H, s), 1.82 (2H, m), 1.73 (2H, m), 1.48-1.38 (4H, br m, overlapped), 1.34-1.22 (75H, br m, overlapped), 0.88 (6H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex due to the rotamers) δ 173.7, 161.7, 159.1, 155.7, 144.2, 144.0, 141.43, 141.40, 133.0, 127.8, 127.2, 125.4, 125.3, 120.1, 114.6, 104.9, 99.9, 71.6, 68.33, 68.27, 67.0, 47.4, 47.3, 33.5, 32.1, 29.9-29.3 (many signals overlapped), 26.23, 26.17, 22.8, 18.8, 14.3; IR (KBr) ν (cm^{-1}) 3315, 2916, 2849, 1717, 1669, 1468, 1253, 1178, 1131, 1034, 739; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{70}H_{114}N_2O_6Na$: 1101.8575 ([M + Na]$^+$), Found: 1101.8588.



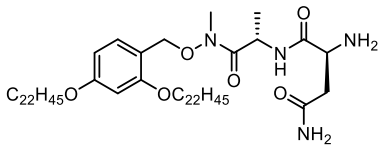
*Ala-(Me)N-O-TAGb (**S24**)*

Following the general procedure described for Fmoc deprotection, Fmoc-Ala-(Me)N-O-TAGb (**S23**) (1.67 g, 1.6 mmol) was converted to Ala-(Me)N-O-TAGb (**S24**) (1.30 g, 98%) as a white powder. $[\alpha]_D^{24.4}$ = 15.2 (*c* 0.1, $CHCl_3$); mp 55 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.16 (1H, d, *J* = 8.0 Hz), 6.45-6.42 (2H, m, overlapped), 4.86 (1H, d, *J* = 10.0 Hz), 4.77 (1H, d, *J* = 9.5 Hz), 3.98-3.92 (5H, m, overlapped), 3.25 (3H, s), 1.84-1.73 (4H, m, overlapped), 1.48-1.41 (4H, br m, overlapped), 1.35-1.20 (75H, br m, overlapped), 0.87 (6H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.6, 161.7, 159.1, 132.9, 114.8, 104.9, 99.8, 71.0, 68.34, 68.30, 46.8, 33.4, 32.1, 29.9-29.3 (many signals overlapped), 26.24, 26.17, 22.8, 20.4, 14.3; IR (KBr) ν (cm^{-1}) 2915, 2849, 1658, 1614, 1470, 1181, 1131, 718; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{55}H_{104}N_2O_4Na$: 879.7894 ([M + Na]$^+$), Found: 879.7898.



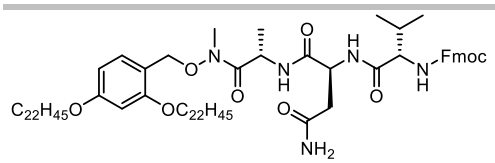
*Fmoc-Asn-Ala-(Me)N-O-TAGb (**S25**)*

Following the general procedure described for condensation, Ala-(Me)N-O-TAGb (**S24**) (1.25 g, 1.5 mmol) was converted to Fmoc-Asn-Ala-(Me)N-O-TAGb (**S25**) (1.74 g, quant.) as a white powder. $[\alpha]_D^{24.4}$ = 20.5 (*c* 0.1, $CHCl_3$); mp 75–79 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (2H, d, *J* = 7.5 Hz), 7.60 (2H, br dd, *J* = 7.0, 4.5 Hz), 7.53 (1H, br d, *J* = 5.0 Hz), 7.39 (2H, t, *J* = 7.5 Hz), 7.31 (2H, t, *J* = 7.5 Hz), 7.23 (1H, br d, *J* = 8.0 Hz), 6.44-6.42 (2H, overlapped), 6.38 (1H, br d, *J* = 7.5 Hz), 6.13 (1H, br s), 5.65 (1H, br s), 5.01-4.96 (2H, br m, overlapped), 4.85 (1H, d, *J* = 9.0 Hz), 4.61 (1H, br m), 4.41-4.34 (2H, br m, overlapped), 4.22 (1H, t, *J* = 7.5 Hz), 4.02-3.92 (4H, m, overlapped), 3.24 (3H, s), 2.92 (1H, br m), 2.65 (1H, br m), 1.81-1.74 (4H, br m, overlapped), 1.47-1.41 (4H, br m, overlapped), 1.35-1.22 (75H, br m, overlapped), 0.88 (6H, t, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were complex due to the rotamers) δ 173.4, 173.3, 170.3, 161.7, 159.1, 156.2, 144.0, 143.9, 141.4, 133.0, 127.8, 127.2, 125.3, 120.1, 114.7, 104.9, 99.9, 71.6, 68.3, 67.4, 51.3, 47.2, 46.5, 37.8, 33.5, 32.1, 29.9-29.3 (many signals overlapped), 26.2, 22.8, 17.8, 14.3; IR (KBr) ν (cm^{-1}) 3421, 2917, 2849, 1661, 1469, 1265, 1178, 1130, 1040, 737; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{74}H_{120}N_4O_8Na$: 1215.9004 ([M + Na]$^+$), Found: 1215.8998.



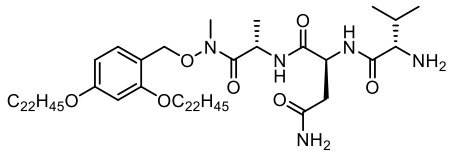
*Asn-Ala-(Me)N-O-TAGb (**S26**)*

Following the general procedure described for Fmoc deprotection, Fmoc-Asn-Ala-(Me)N-O-TAGb (**S25**) (1.70 g, 1.4 mmol) was converted to Asn-Ala-(Me)N-O-TAGb (**S26**) (1.38 g, quant.) as a white powder. $[\alpha]_D^{24.5}$ = 17.5 (*c* 0.1, $CHCl_3$); mp ca. 190 °C (decomp.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (1H, br d, *J* = 8.0 Hz), 7.24 (1H, d, *J* = 8.0 Hz), 6.44-6.43 (2H, m, overlapped), 6.18 (1H, br s), 5.35 (1H, br s), 5.03-4.97 (2H, br m, overlapped), 4.83 (1H, d, *J* = 9.5 Hz), 4.04-3.93 (4H, m, overlapped), 3.69 (1H, br m), 3.24 (3H, s), 2.68 (1H, m), 2.57 (1H, m), 1.83-1.74 (4H, m, overlapped), 1.48-1.41 (4H, br m, overlapped), 1.35-1.22 (75H, br m, overlapped), 0.88 (6H, t, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD = 10/1, Signals were complex due to the rotamers.) δ 174.1, 173.5 (two signals), 161.6, 160.5, 159.0, 158.5, 132.9, 131.2, 118.0, 114.6, 104.9, 104.7, 99.9, 99.8, 71.6, 70.2, 68.23, 68.18, 52.1, 45.7, 39.89, 39.87, 38.9, 33.4, 32.0, 29.8-29.2 (many signals overlapped), 26.15, 26.10, 22.7, 17.6, 14.2; IR (KBr) ν (cm^{-1}) 3360, 2916, 2849, 1660, 1468, 1177, 1130, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{59}H_{110}N_4O_6Na$: 993.8323 ([M + Na]$^+$), Found: 993.8315.



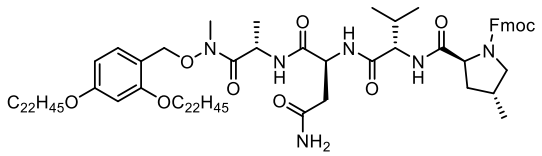
*Fmoc-Val-Asn-Ala-(Me)N-O-TAGb (**S27**)*

Following the general procedure described for condensation, Asn-Ala-(Me)N-O-TAGb (**S26**) (1.34 g, 1.4 mmol) was converted to Fmoc-Val-Asn-Ala-(Me)N-O-TAGb (**S27**) (1.66 g, 93%) as a white powder. $[\alpha]_D^{24.5}$ = 9.6 (*c* 0.1, $CHCl_3$); mp 185–190 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers.) *δ* 7.76-7.72 (3H, br m, overlapped), 7.60-7.57 (3H, br m, overlapped), 7.38-7.35 (2H, br m), 7.28 (2H, t, *J* = 7.5 Hz), 7.20 (1H, d, *J* = 8.5 Hz), 6.43-6.40 (2H, overlapped), 6.30 (1H, br s), 5.86 (1H, br s), 5.76 (1H, br d, *J* = 8.5 Hz), 5.00-4.92 (2H, br m, overlapped), 4.86-4.77 (2H, br m, overlapped), 4.41-4.29 (2H, br m, overlapped), 4.21-4.14 (2H, br m, overlapped), 4.00-3.91 (4H, br m, overlapped), 3.20 (3H, br s), 2.83 (1H, br m), 2.63 (1H, br m), 2.16 (1H, br m), 1.81-1.73 (4H, br m, overlapped), 1.47-1.40 (4H, br m, overlapped), 1.35-1.22 (75H, br m, overlapped), 0.99 (3H, d, *J* = 6.5 Hz), 0.95 (3H, d, *J* = 7.0 Hz), 0.88 (6H, t, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers.) *δ* 173.5, 173.3, 171.6, 170.1, 161.6, 159.0, 156.7, 144.1, 143.9, 141.4, 132.9, 127.8, 127.22, 127.18, 125.32, 125.29, 120.1, 114.7, 104.8, 99.8, 71.6, 68.3, 67.2, 60.3, 49.8, 47.3, 46.4, 37.2, 33.5, 32.1, 31.5, 29.8-29.2 (many signals overlapped), 26.18, 26.16, 22.8, 19.4, 17.8, 17.7, 14.3; IR (KBr) *ν* (cm^{-1}) 3288, 2917, 2849, 1642, 1535, 1468, 1292, 1248, 1180, 1131, 1032, 740, 718; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{79}H_{129}N_5O_9Na$: 1314.9688 ([M + Na]$^+$), Found: 1314.9697.



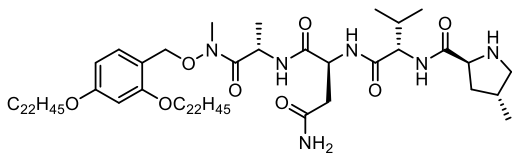
*Val-Asn-Ala-(Me)N-O-TAGb (**S28**)*

Following the general procedure described for Fmoc deprotection, Fmoc-Val-Asn-Ala-(Me)N-O-TAGb (**S27**) (1.61 g, 1.2 mmol) was converted to Val-Asn-Ala-(Me)N-O-TAGb (**S28**) (1.33 g, quant.) as a white powder. $[\alpha]_D^{24.5}$ = 7.7 (*c* 0.1, $CHCl_3$); mp 101–102 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 8.39 (1H, br d, *J* = 7.5 Hz), 7.61 (1H, br d, *J* = 7.5 Hz), 7.22 (1H, d, *J* = 9.0 Hz), 6.50 (1H, br s), 6.44-6.42 (2H, m, overlapped), 5.78 (1H, br s), 4.97-4.91 (2H, br m, overlapped), 4.84-4.78 (2H, br m, overlapped), 4.01-3.92 (4H, m, overlapped), 3.28 (1H, d, *J* = 4.0 Hz), 3.22 (3H, s), 2.84 (1H, m), 2.64 (1H, m), 2.24 (1H, m), 1.82-1.73 (4H, m, overlapped), 1.47-1.41 (4H, br m, overlapped), 1.35-1.22 (75H, br m, overlapped), 0.98 (3H, d, *J* = 7.0 Hz), 0.89-0.83 (9H, m, overlapped); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 174.9, 173.4, 173.3, 170.4, 161.6, 159.0, 132.9, 114.7, 104.8, 99.8, 71.6, 68.2, 60.3, 49.6, 46.4, 37.9, 33.5, 32.0, 31.2, 29.8-29.2 (many signals overlapped), 26.1, 22.8, 19.7, 17.7, 16.4, 14.2; IR (KBr) *ν* (cm^{-1}) 3286, 2916, 2849, 1654, 1469, 1179, 1131, 719; HRMS (FAB, NBA matrix) Calcd. for $C_{64}H_{120}N_5O_7$: 1070.9188 ([M + Na]$^+$), Found: 1070.9191.



*Fmoc-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S29**)*

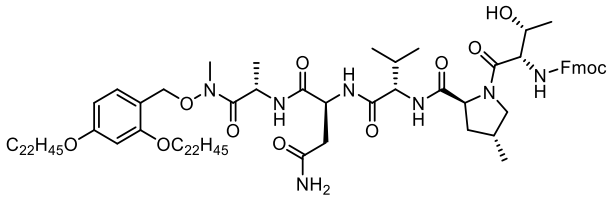
Following the general procedure described for condensation, Val-Asn-Ala-(Me)N-O-TAGb (**S28**) (1.28 g, 1.2 mmol) was converted to Fmoc-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S29**) (1.68 g, quant.) as a white powder. $[\alpha]_D^{24.6}$ = –9.7 (*c* 0.1, $CHCl_3$); mp 160–161 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 7.76 (2H, br d, *J* = 6.5 Hz), 7.63 (1H, br d, *J* = 7.0 Hz), 7.59 (2H, br d, *J* = 7.5 Hz), 7.49 (1H, br d, *J* = 7.0 Hz), 7.40 (2H, br t, *J* = 7.5 Hz), 7.32 (2H, td, *J* = 7.5, 1.0 Hz), 7.23 (1H, br d, *J* = 8.0 Hz), 6.43-6.42 (2H, br m, overlapped), 6.34 (1H, br s), 5.85 (1H, br s), 5.39 (1H, br s), 4.97-4.92 (2H, br m, overlapped), 4.81 (2H, br m, overlapped), 4.48-4.34 (4H, br m, overlapped), 4.25 (1H, br t, *J* = 6.5 Hz), 4.01-3.92 (4H, br m, overlapped), 3.66 (1H, br t, *J* = 7.0 Hz), 3.21 (3H, br s), 2.96 (1H, br t, *J* = 10.0 Hz), 2.78 (1H, br m), 2.65 (1H, br m), 2.28-2.07 (3H, br m, overlapped), 1.80-1.73 (4H, br m), 1.65 (1H, br m), 1.47-1.41 (4H, br m, overlapped), 1.35-1.22 (75H, br m, overlapped), 1.06 (3H, br d, *J* = 6.0 Hz), 0.93 (3H, d, *J* = 6.5 Hz), 0.90-0.86 (9H, m, overlapped); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers.) *δ* 173.4, 173.2, 172.3, 171.2, 170.0, 161.6, 159.0, 156.3, 144.1, 143.8, 141.4, 133.0, 127.9, 127.5, 127.3, 125.2, 120.1, 114.8, 104.8, 99.8, 71.6, 68.3, 68.0, 61.3, 58.7, 54.0, 49.9, 47.3, 46.3, 37.3, 36.7, 33.5, 32.7, 32.1, 30.9, 29.8-29.3 (many signals overlapped), 26.2, 22.8, 19.5, 17.9, 17.8, 17.3, 14.3; IR (KBr) *ν* (cm^{-1}) 3286, 2917, 2849, 1642, 1468, 1418, 1178, 1129, 739, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{85}H_{138}N_6O_{10}Na$: 1426.0372 ([M + Na]$^+$), Found: 1426.0363.



*4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S30**)*

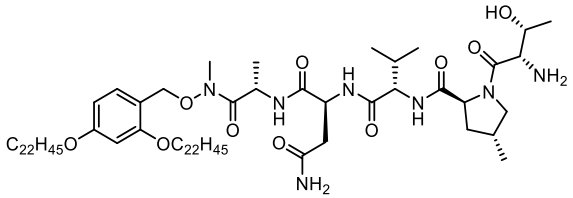
Following the general procedure described for Fmoc deprotection, Fmoc-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S29**) (1.64 g, 1.2 mmol) was converted to 4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S30**) (1.38 g, quant.) as a white powder. $[\alpha]_D^{24.6}$ = –2.3 (*c* 0.1, $CHCl_3$); mp 93–95 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 8.31 (1H, br d, *J* = 8.5 Hz), 7.78 (1H, br d, *J* = 7.5 Hz), 7.58 (1H, br d, *J* = 7.0 Hz), 7.23 (1H, br m), 6.54 (1H, br s), 6.43-6.42 (2H, br m, overlapped), 5.94 (1H, br s), 4.97-4.92 (2H, br m, overlapped), 4.83-4.75 (2H, m, overlapped), 4.28 (1H, dd, *J* = 9.5, 6.5 Hz), 4.01-3.92 (4H, m, overlapped), 3.82 (1H, m), 3.21 (3H, s), 3.08 (1H, dd, *J* = 10.0, 6.5 Hz), 2.80 (1H, m), 2.65-2.56 (2H, m, overlapped), 2.21 (1H, m), 2.13-2.04 (2H, m, overlapped),1.82-1.68 (5H, m, overlapped), 1.46-1.41 (4H, br m, overlapped), 1.35-1.22 (75H, br m, overlapped), 0.99 (3H, d, *J* = 6.5 Hz), 0.96 (3H, d, *J* = 6.5 Hz), 0.91 (3H, d, *J* = 7.0 Hz),

0.87 (6H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 176.2, 173.6, 173.3, 171.7, 170.2, 161.6, 159.0, 133.0, 114.8, 104.9, 99.8, 71.6, 68.3, 60.4, 58.1, 54.7, 50.0, 46.3, 39.0, 37.2, 33.5, 33.3, 32.1, 30.9, 29.8-29.3 (many signals overlapped), 26.19, 26.17, 22.8, 19.7, 17.9, 17.7, 17.6, 14.3; IR (KBr) ν (cm^{-1}) 3271, 2916, 2849, 1643, 1508, 1468, 1179, 1131, 719; HRMS (FAB, NBA matrix) Calcd. for $C_{70}H_{128}N_6O_8$: 1181.9872 ([M + H]$^+$), Found: 1181.9851.



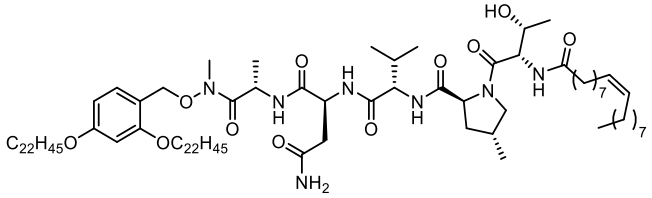
*Fmoc-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S31**)*

Following the general procedure described for condensation, 4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S30**) (657 mg, 0.56 mmol) was converted to Fmoc-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S31**) (818 mg, 98%) as a white powder. $[\alpha]_D^{24.6}$ = –11.9 (*c* 0.1, $CHCl_3$); mp 115–125 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 7.78 (1H, br d, *J* = 8.0 Hz), 7.74 (2H, br d, *J* = 7.5 Hz), 7.59 (2H, br d, *J* = 7.5 Hz), 7.38 (2H, br t, *J* = 7.5 Hz), 7.30 (2H, br td, *J* = 7.5, 2.0 Hz), 7.30 (1H, br d, *J* = 8.5 Hz), 7.15 (1H, br d, *J* = 9.0 Hz), 6.95 (1H, br s), 6.44-6.40 (2H, br m, overlapped), 6.36 (1H, br s), 6.23 (1H, br d, *J* = 8.0 Hz), 5.05-4.96 (3H, br m, overlapped), 4.80 (1H, br d, *J* = 10.0 Hz), 4.71 (1H, br dd, *J* = 9.5, 4.0 Hz), 4.66-4.49 (3H, br m, overlapped), 4.45 (1H, dd, *J* = 11.0, 7.5 Hz), 4.35 (1H, dd, *J* = 10.5, 7.0 Hz), 4.30 (1H, br m), 4.20 (1H, t, *J* = 7.0 Hz), 4.05 (1H, br t, *J* = 8.0 Hz), 4.01-3.90 (4H, br m, overlapped), 3.31 (1H, br t, *J* = 9.5 Hz), 3.21 (3H, s), 2.79 (1H, br m), 2.70 (1H, br m), 2.47 (1H, br m), 2.25-2.17 (2H, br m, overlapped), 1.93 (1H, br m), 1.82-1.73 (4H, br m, overlapped), 1.47-1.41 (4H, br m, overlapped), 1.35-1.22 (78H, br m, overlapped), 1.09 (3H, d, *J* = 6.5 Hz), 0.95 (3H, d, *J* = 7.0 Hz), 0.88 (9H, t, *J* = 7.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers.) *δ* 173.8, 173.1, 172.2, 171.6, 171.2, 169.8, 161.6, 159.0, 156.4, 143.9, 143.8, 141.4, 133.0, 127.9, 127.2, 125.23, 125.19, 120.10, 120.08, 114.8, 104.8, 99.8, 71.6, 68.3, 68.1, 67.1, 61.6, 58.0, 56.8, 54.6, 50.5, 47.3, 46.1, 37.8, 37.2, 33.5, 32.9, 32.1, 31.2, 29.8-29.3 (many signals overlapped), 26.2, 22.8, 19.6, 18.6, 18.1, 18.0, 17.4, 14.3; IR (KBr) ν (cm^{-1}) 3302, 2917, 2849, 1644, 1508, 1467, 1264, 1179, 740, 721; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{89}H_{145}N_7O_{12}Na$: 1527.0849 ([M + Na]$^+$), Found: 1527.0854.



*Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S32**)*

Following the general procedure described for Fmoc deprotection, Fmoc-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S31**) (768 mg, 0.51 mmol) was converted to Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S32**) (664 mg, quant.) as a white powder. $[\alpha]_D^{24.6}$ = –9.7 (*c* 0.1, $CHCl_3$); mp 70–78 °C; ^{1}H NMR (500 MHz, $CDCl_3$, Signals were broad and complex due to the rotamers. Those derived from minor rotamers were not described here.) *δ* 7.97 (1H, br d, *J* = 8.0 Hz), 7.35 (1H, br d, *J* = 9.5 Hz), 7.25 (1H, br m), 7.16 (1H, br s), 6.96 (1H, br s), 6.43-6.41 (2H, br m, overlapped), 5.04-4.91 (3H, br m, overlapped), 4.80 (1H, br m), 4.69-4.60 (2H, br m, overlapped), 4.15-4.09 (2H, br m, overlapped), 4.01-3.92 (4H, br m, overlapped), 3.84 (1H, br d, *J* = 5.0 Hz), 3.21 (3H, s), 3.15 (1H, br t, *J* = 9.5 Hz), 2.75 (1H, br m), 2.65 (1H, br m), 2.47 (1H, br m), 2.24-2.08 (3H, br m, overlapped), 1.87-1.73 (5H, br m, overlapped), 1.47-1.40 (4H, br m, overlapped), 1.35-1.22 (78H, br m, overlapped), 1.09 (3H, d, *J* = 6.5 Hz), 0.95 (3H, d, *J* = 6.0 Hz), 0.87 (9H, t, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 174.0, 173.3, 173.2, 172.4, 171.5, 169.9, 161.6, 159.0, 133.0, 114.8, 104.9, 99.8, 71.6, 70.2, 68.3, 61.7, 57.6, 56.3, 54.5, 50.5, 46.0, 37.6, 37.3, 33.5, 32.8, 32.3, 32.1, 29.8-29.3 (many signals overlapped), 26.2, 22.8, 19.5, 18.2, 17.9, 17.4, 14.3; IR (KBr) ν (cm^{-1}) 3297, 2917, 2849, 1645, 1508, 1468, 1178, 1131, 719; HRMS (FAB, NBA matrix) Calcd. for $C_{74}H_{136}N_7O_{10}$: 1283.0349 ([M + H]$^+$), Found: 1283.0349.



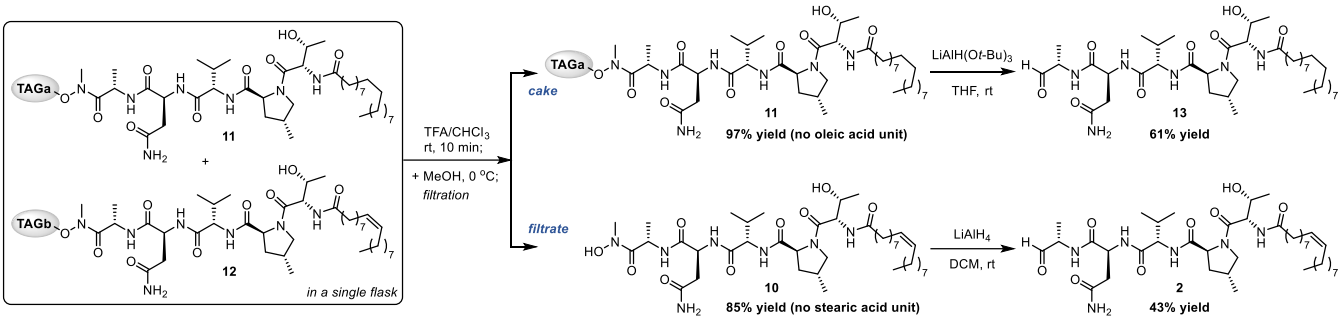
*Oleic acid-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**12**)*

Following the general procedure described for condensation using oleic acid instead of Fmoc protected amino acid, Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S32**) (610 mg, 0.48 mmol) was converted to oleic acid-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGb (**12**) (707 mg, 96%) as a white powder. $[\alpha]_D^{24.6}$ = –8.5 (*c* 0.1, $CHCl_3$); mp 155–163 °C; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.84 (1H, br d, *J* = 9.0 Hz), 7.28 (1H, br d, *J* = 7.5 Hz), 7.24 (1H, br d, *J* = 8.5 Hz), 7.16 (1H, br d, *J* = 9.0 Hz), 7.11 (1H, br s), 6.76 (1H, br d, *J* = 8.0 Hz), 6.58 (1H, br s), 6.44-6.42 (2H, br m, overlapped), 5.36-5.29 (2H, m, overlapped), 5.01-4.92 (4H, br m, overlapped), 4.80 (1H, br d, *J* = 9.5 Hz), 4.61-4.58 (2H, br m, overlapped), 4.29 (1H, br m), 4.06 (1H, br m), 4.02-3.92 (4H, br m, overlapped), 3.35 (1H, br t, *J* = 9.5 Hz), 3.21 (3H, s), 2.81-2.76 (1H, br m), 2.70-2.66 (1H, br m), 2.46 (1H, br m), 2.25-2.15 (6H, br m, overlapped), 1.99 (3H, br m), 1.89 (1H, br m), 1.82-1.73 (4H, br m), 1.62 (2H, br m), 1.44 (4H, br m), 1.35-1.22 (98H, br m, overlapped), 1.09 (3H, d, *J* = 6.5 Hz), 0.94 (3H, d, *J* = 6.5 Hz), 0.88-0.86 (12H, m, overlapped); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 173.7, 173.4, 173.2, 172.2, 171.6, 171.3, 169.8, 161.7, 159.0, 133.0, 130.1, 129.9, 114.7, 104.9, 99.8, 71.7, 68.3, 67.9, 61.6, 57.8, 54.6, 54.5, 50.3, 46.1, 37.8, 37.2, 36.6, 33.6, 32.9, 32.1, 31.6, 29.9-29.3 (many signals overlapped), 27.3, 26.2, 25.7, 22.8, 19.5, 18.8, 18.0, 17.9, 17.3, 14.3; IR (KBr) ν (cm^{-1}) 3284,

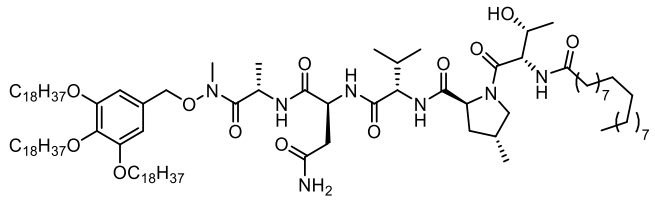
2915, 2849, 1645, 1536, 1468, 1180, 1130, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{92}H_{167}N_7O_{11}Na$: 1569.2621 ([M + Na]$^+$), Found: 1569.2625.

Selective deprotection of TAG benzyl group under acid conditions and reduction to the aldehydes

Scheme 3c.

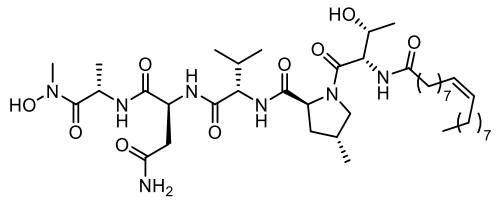


11 (55.1 mg, 0.032 mmol, 1.0 eq) and **12** (50.0 mg, 0.032 mmol, 1.0 eq) was dissolved into 30% TFA/$CHCl_3$ (3.2 mL, 0.01 M for each substrate) at room temperature, and the solution was stirred for 10 min. The reaction mixture was subsequently cooled to 0 °C and MeOH (19 mL, 6-fold excess of TFA/$CHCl_3$) was added. The resulting heterogeneous solution was stirred for a further 30 min at 0 °C. The precipitate was filtered and washed with additional MeOH to afford the crude cake **11**. On the other hand, the filtrate was concentrated in vacuo to afford the crude **10**. The crude products were purified by PLC on silica gel ($CHCl_3$/MeOH = 5/1 as eluent) to give **11** (53.5 mg, 97%) as a white powder and hydroxamic acid **10** (22.2 mg, 85%) as a white powder respectively.



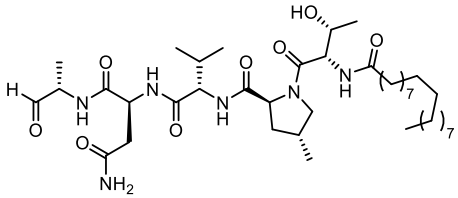
*Stearic acid-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**11**)*

Following the general procedure described for condensation using stearic acid instead of Fmoc protected amino acid, Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**8**) (0.300 g, 0.21 mmol) was converted to stearic acid-Thr-4-MePro-Val-Asn-Ala-(Me)N-O-TAGa (**11**) (0.356 g, quant.) as a white powder. $[\alpha]_D^{24.6}$ = –15.5 (*c* 0.1, $CHCl_3$); mp 153–154 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (1H, br d, *J* = 8.5 Hz), 7.33 (1H, br d, *J* = 7.5 Hz), 7.11-7.08 (2H, br m, overlapped), 6.81 (1H, br d, *J* = 8.5 Hz), 6.57 (2H, s), 6.39 (1H, br s), 4.98 (1H, dd, *J* = 8.5, 4.0 Hz), 4.96-4.90 (2H, m, overlapped), 4.85 (1H, br d, *J* = 10.0 Hz), 4.79 (1H, br d, *J* = 10.5 Hz), 4.59 (1H, dd, *J* = 9.0, 4.0 Hz), 4.55 (1H, dd, *J* = 9.0, 6.5 Hz), 4.49 (1H, br s), 4.29 (1H, br m), 4.03 (1H, br dd, *J* = 9.5, 7.5 Hz), 3.98-3.92 (6H, m, overlapped), 3.36 (1H, t, *J* = 9.5 Hz), 3.18 (3H, s), 2.80 (1H, m), 2.70 (1H, m), 2.46 (1H, m), 2.25-2.15 (4H, m, overlapped), 1.90 (1H, m), 1.82-1.70 (6H, m, overlapped), 1.65-1.56 (2H, m), 1.49-1.43 (6H, br m, overlapped), 1.36-1.22 (89H, br m, overlapped), 1.09 (3H, t, *J* = 7.0 Hz), 0.94 (3H, t, *J* = 6.5 Hz), 0.89-0.86 (15H, m, overlapped); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 173.5, 173.4, 172.2, 171.7, 171.5, 170.0, 153.5, 138.8, 129.4, 107.7, 73.6, 69.3, 67.8, 61.5, 58.0, 54.7, 54.6, 50.6, 46.2, 37.8, 37.1, 36.7, 34.1, 33.0, 32.1, 31.3, 30.5, 29.9-29.5 (many signals overlapped), 26.3, 25.8, 22.8, 19.5, 18.9, 17.9, 17.8, 17.3, 14.3; IR (KBr) ν (cm^{-1}) 3281, 2916, 2849, 1638, 1543, 1468, 1439, 1239, 1121, 719; HRMS (FAB, NBA + NaI matrix) Calcd. for $C_{102}H_{189}N_7O_{12}Na$: 1727.4292 ([M + Na]$^+$), Found: 1727.4307.



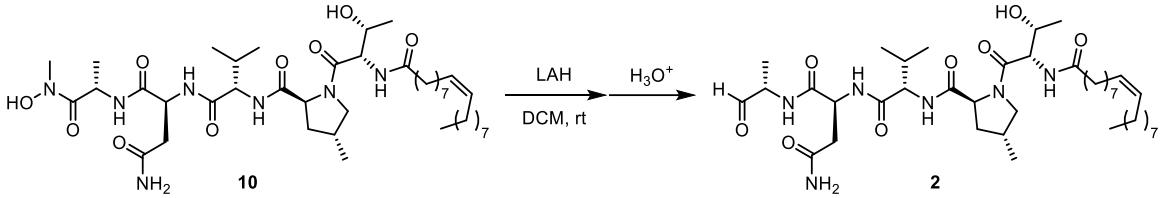
Oleic acid-Thr-4-MePro-Val-Asn-Ala-(Me)N-OH (**10**)

12 (350 mg, 0.23 mmol) was dissolved into 30% trifluoroacetic acid (TFA)/$CHCl_3$ (11 mL, 0.02 M for substrate) at room temperature, and the solution was stirred for 20 min. The reaction mixture was subsequently cooled to 0 °C and MeOH (66 mL, 6-fold excess of TFA/$CHCl_3$) was added, and the resulting heterogeneous solution was stirred for a further 30 min at 0 °C. The precipitate was filtered and washed with additional MeOH, and the filtrate was concentrated in vacuo. The residue was purified by flash column chromatography on silica gel ($CHCl_3$/MeOH = 50/1 to 10/1 as eluent) to afford hydroxamic acid **10** (160 mg, 88%) as a white powder. $[\alpha]_D^{24.6}$ = –32.1 (*c* 0.1, DMSO); mp 193–196 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.05 (1H, s), 8.15 (1H, d, *J* = 8.0 Hz), 7.86 (1H, d, *J* = 7.5 Hz), 7.82 (1H, d, *J* = 8.5 Hz), 7.59 (1H, br d, *J* = 7.5 Hz), 7.33 (1H, br s), 6.89 (1H, br s), 5.35-5.29 (2H, m, overlapped), 4.76 (1H, br m), 4.65 (1H, d, *J* = 6.0 Hz), 4.55-4.48 (2H, m, overlapped), 4.42 (1H, t, *J* = 7.5 Hz), 4.12 (1H, dd, *J* = 8.0, 6.0 Hz), 3.83-3.76 (2H, m, overlapped), 3.25 (1H, t, *J* = 9.0 Hz), 3.08 (3H, s), 2.56 (1H, dd, *J* =11.0, 6.5 Hz), 2.39-2.30 (2H, m, overlapped), 2.17-2.06 (2H, m, overlapped), 2.01-1.91 (6H, m, overlapped), 1.64 (1H, m), 1.45 (2H, br m), 1.30-1.20 (20H, br m, overlapped), 1.16 (3H, d, *J* = 7.0 Hz), 1.08 (3H, d, *J* = 6.0 Hz), 0.97 (3H, d, *J* = 6.5 Hz), 0.86-0.80 (9H, m, overlapped); ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.2, 171.7, 171.5, 171.4, 170.8, 170.1, 169.4, 129.7, 67.0, 59.2, 57.5, 56.1, 54.0, 49.3, 45.0, 36.7, 36.6, 35.9, 34.9, 32.0, 31.3, 30.7, 29.2-28.6 (many signals overlapped), 26.64, 26.60, 25.3, 22.1, 19.3, 19.2, 17.9, 17.3, 17.2, 14.0; IR (KBr) ν (cm^{-1}) 3283, 2924, 2854, 1636, 1540, 1435, 1199; HRMS (ESI$^+$) Calcd. for $C_{41}H_{73}N_7O_9Na$: 830.5367 ([M + Na]$^+$), Found: 830.5358.



Stearic acid-Thr-4-MePro-Val-Asn-Ala-H (**13**)

To a solution of **11** (50 mg, 0.029 mmol, 1.0 eq) in dehydrated THF (2.9 mL, 0.01 M) was added dropwise 1.0 M $LiAlH(t\text{-}BuO)_3$ in dehydrated THF (293 mL, 10 eq) at room temperature. After stirring for 1 h at room temperature, the reaction mixture was then treated with aqueous 1 N HCl (1.5 mL) at 0 °C to quench the excess $LiAlH(t\text{-}BuO)_3$. After stirring for 10 min at room temperature, MeOH (15 mL) was added. The resulting heterogeneous solution was stirred for a further 30 min at room temperature, and the precipitate was filtered and washed with additional MeOH. The filtrate was roughly concentrated in vacuo, poured into a separatory funnel containing aqueous 1 N HCl (10 mL), and extracted with $CHCl_3$ (3 × 10 mL). The combined organic extracts were dried with Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by PLC on silica gel ($CHCl_3$/MeOH = 5/1 as eluent) to afford aldehyde **13** (13.7 mg, 61%) as a white powder. $[\alpha]_D^{24.6}$ = –35.6 (*c* 0.1, $CHCl_3$); mp 176–177 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.34 (1H, s), 8.13 (1H, d, *J* = 6.5 Hz), 8.10 (1H, d, *J* = 8.5 Hz), 7.87 (2H, app d, *J* = 8.5 Hz, overlapped), 7.37 (1H, br s), 6.92 (1H, br s), 4.67 (1H, br m), 4.55-4.47 (2H, m, overlapped), 4.41 (1H, br m), 4.03 (1H, m), 3.83-3.77 (2H, m, overlapped), 3.27 (1H, br m), 2.52 (1H, m, overlapped with solvent residual signals), 2.34 (1H, m), 2.12 (2H, m), 2.01-1.92 (2H, m, overlapped), 1.65 (1H, m), 1.45 (2H, br m), 1.29-1.18 (30H, br m, overlapped), 1.14 (3H, d, *J* = 7.5 Hz), 1.08 (3H, d, *J* = 6.0 Hz), 0.97 (3H, d, *J* = 6.5 Hz), 0.86-0.82 (9H, m, overlapped); ^{13}C NMR (125 MHz, DMSO-d_6) δ 201.3, 172.2, 171.8, 171.4, 171.3, 170.6, 169.4, 66.9, 59.2, 56.2, 53.9, 49.5, 36.7, 36.5, 34.8, 32.0, 31.3, 30.3, 29.0-28.7 (many signals overlapped), 25.2, 22.1, 19.3, 19.1, 18.0, 17.2, 14.0, 13.5; IR (KBr) ν (cm^{-1}) 3286, 2920, 2851, 1639, 1541, 1419, 1239, 1066; HRMS (ESI^+) Calcd. for $C_{40}H_{72}N_6O_8Na$: 787.5309 ($[M + Na]^+$), Found: 787.5315.



10 **2**

To a solution of **10** (20.0 mg, 0.025 mmol, 1.0 eq) in dehydrated DCM (2.5 mL, 0.01 M) was added dropwise 0.2 M $LiAlH_4$ in dehydrated THF (pre-prepared, 0.272 mL, 2.2 eq) at 0 °C. After stirring for 40 min at room temperature, the reaction mixture was then treated with aqueous 1 N HCl (1.2 mL) at 0 °C to quench the excess $LiAlH_4$. After stirring for 10 min at room temperature, MeOH (13 mL) was added. The resulting heterogeneous solution was stirred for a further 30 min at room temperature, and the precipitate was filtered and washed with additional MeOH. The filtrate was roughly concentrated in vacuo, poured into a separatory funnel containing aqueous 1 N HCl (10 mL), and extracted with $CHCl_3$ (3 × 10 mL). The combined organic extracts were dried with Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by PLC on silica gel ($CHCl_3$/MeOH = 5/1 as eluent) to afford aldehyde **2** (8.1 mg, 43%) as a white powder.

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[1] a) J. R. D. Valle, M. Goodman, *J. Org. Chem.* **2003**, *68*, 3923–3931; b) M. D. Shoulders, J. A. Hodges, R. T. Raines, *J. Am. Chem. Soc.* **2006**, *128*, 8112–8113.

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[4] a) H. Tamiaki, T. Obata, Y. Azefu, K. Toma, *Bull. Chem. Soc. Jpn.* **2001**, *74*, 733–738; b) T. Hirose, T. Kasai, T. Akimoto, A. Endo, A. Sugawara, K. Nagasawa, K. Shiomi, S. Ōmura, T. Sunazuka, *Tetrahedron* **2011**, *67*, 6633–6643.

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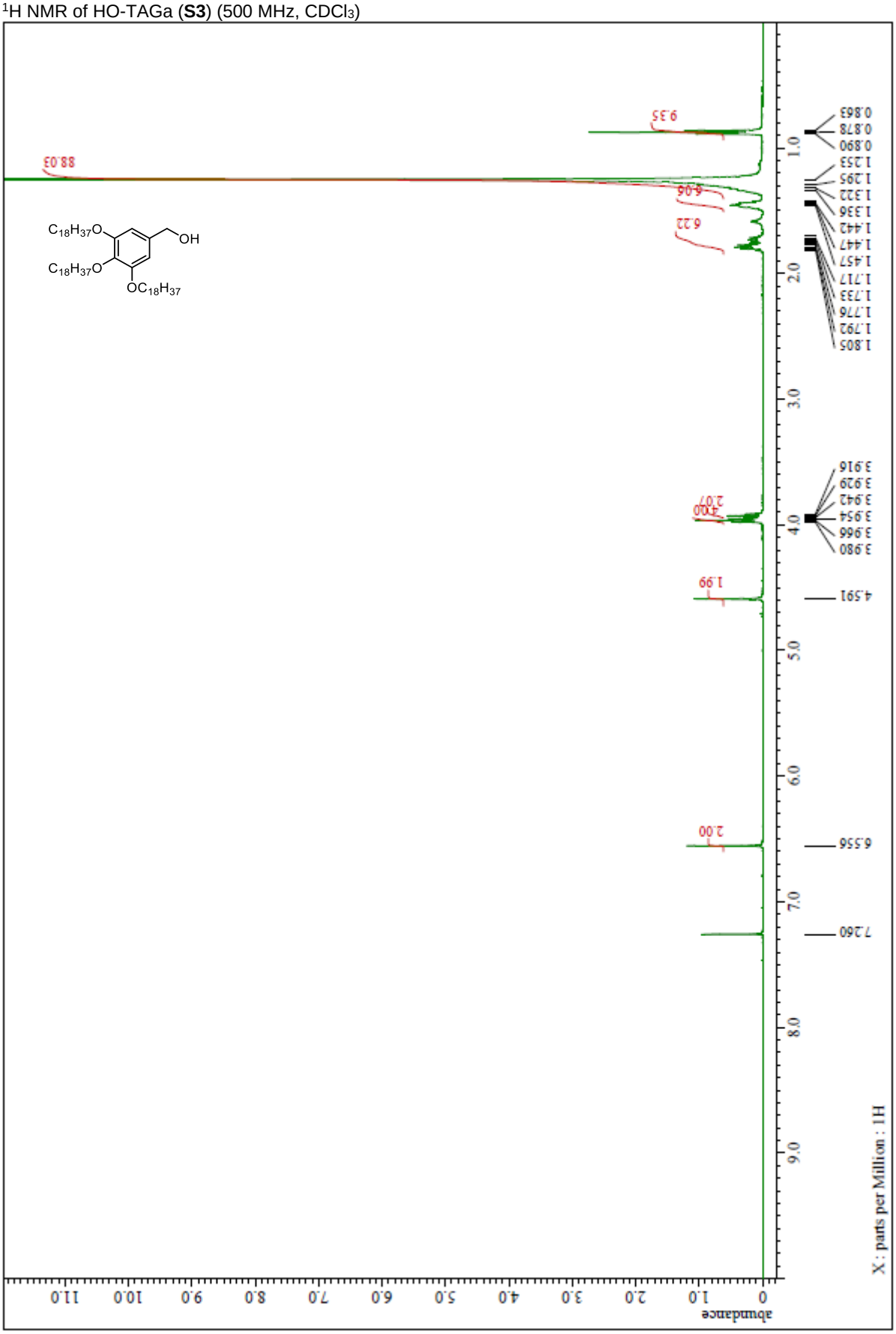
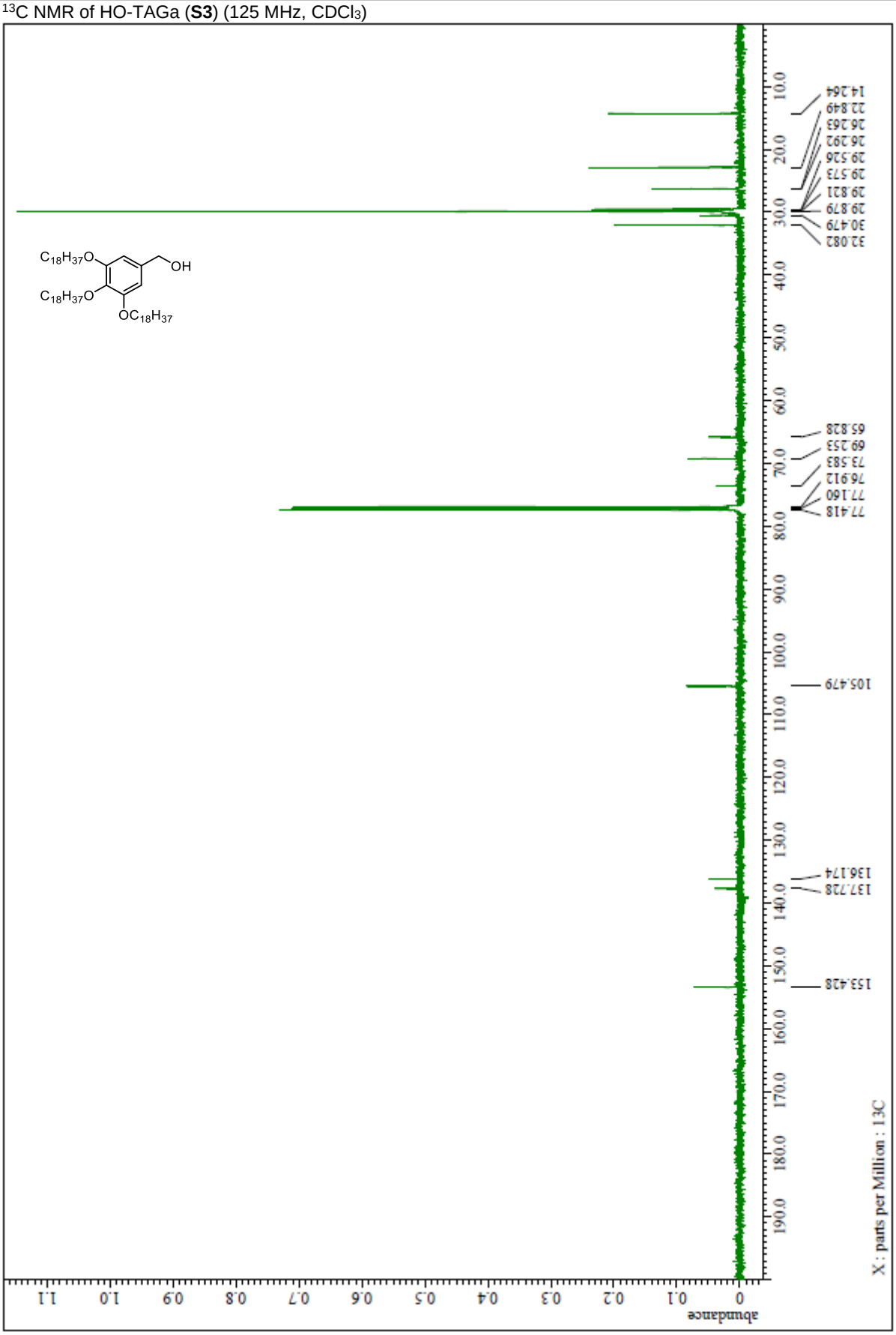
NMR spectra of the products

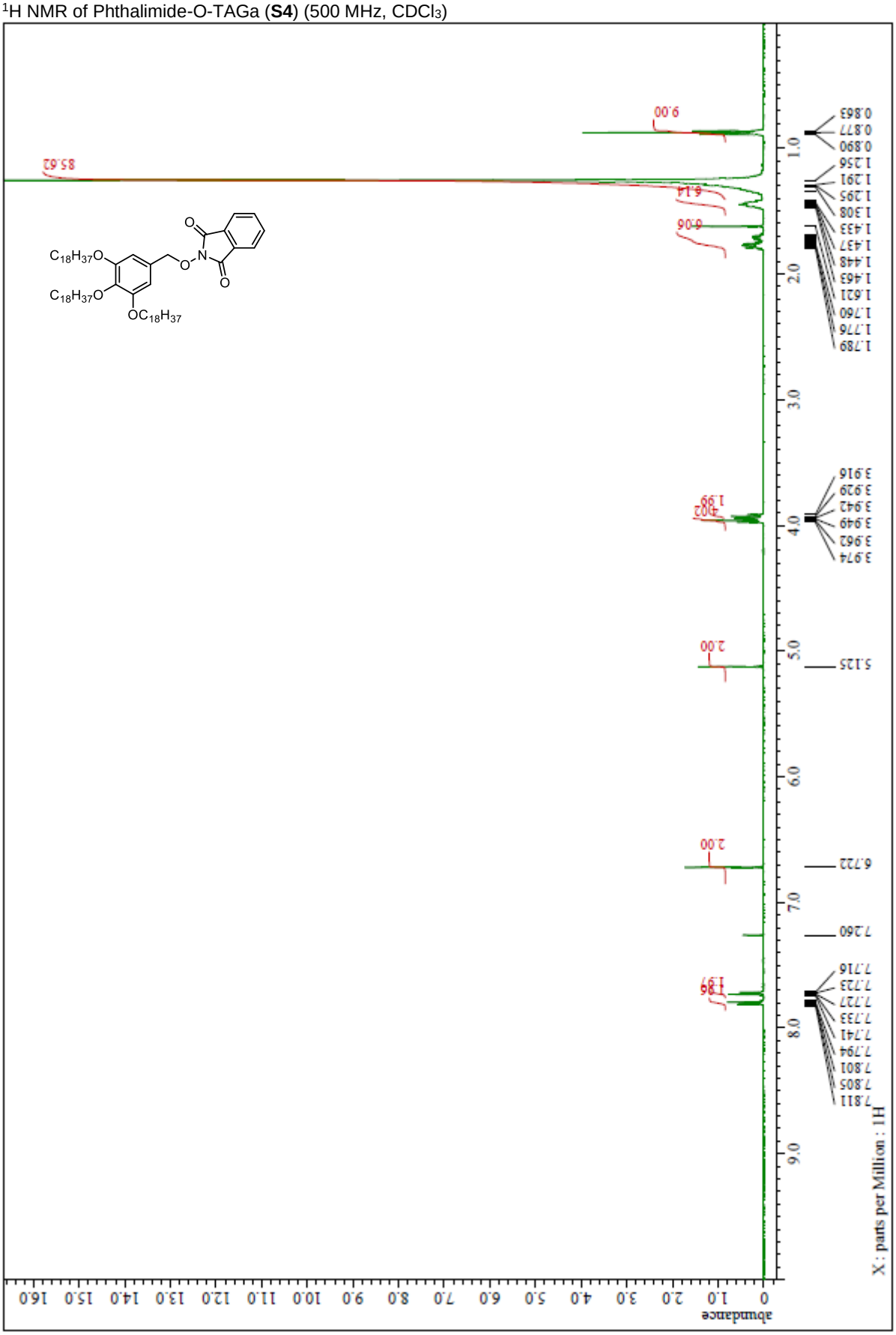
^{1}H NMR of HO-TAGa (**S3**) (500 MHz, $CDCl_3$)



^{13}C NMR of HO-TAGa (**S3**) (125 MHz, $CDCl_3$)



^{1}H NMR of Phthalimide-O-TAGa (**S4**) (500 MHz, $CDCl_3$)



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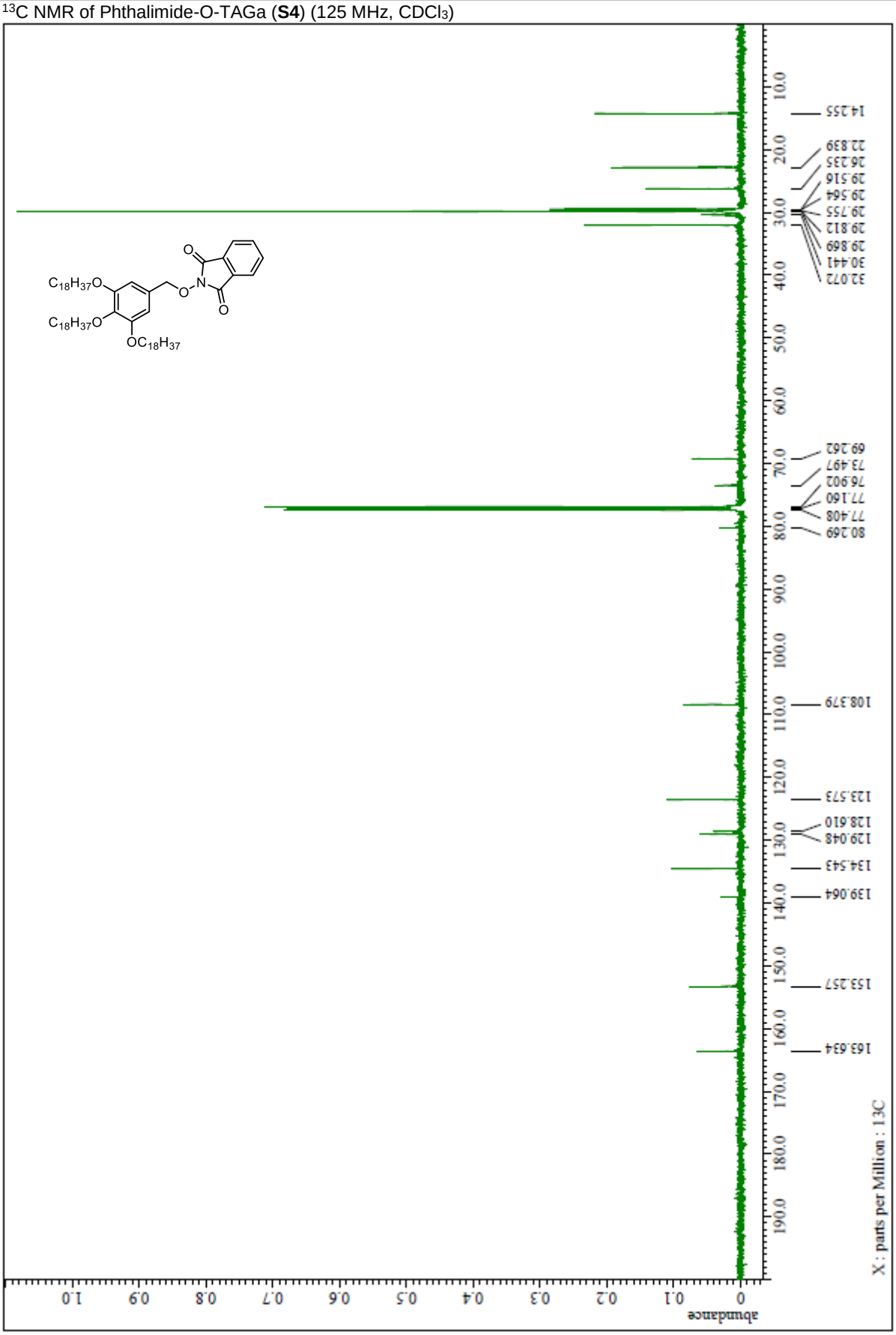
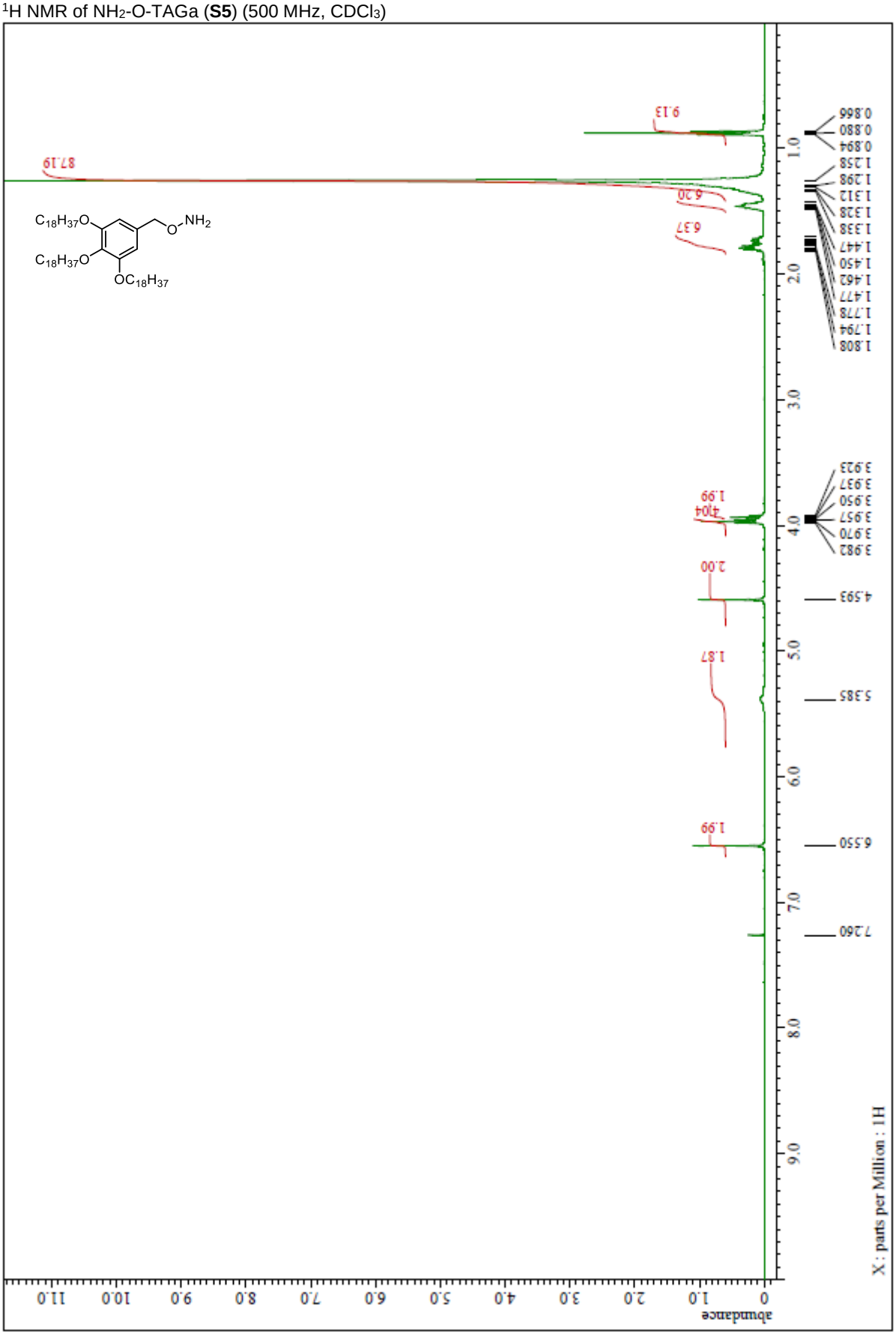


^{1}H NMR of NH_2-O-TAGa (**S5**) (500 MHz, $CDCl_3$)



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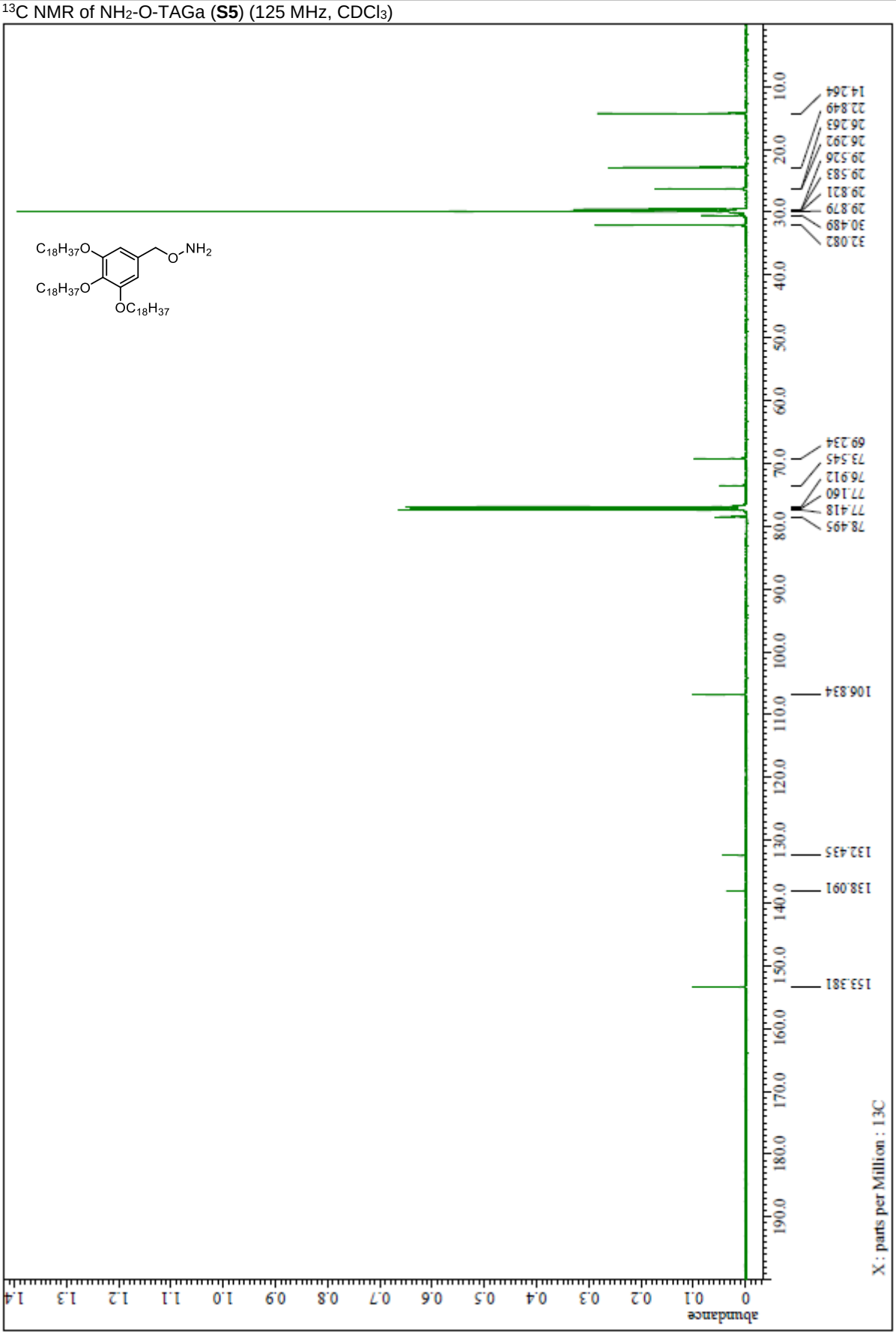

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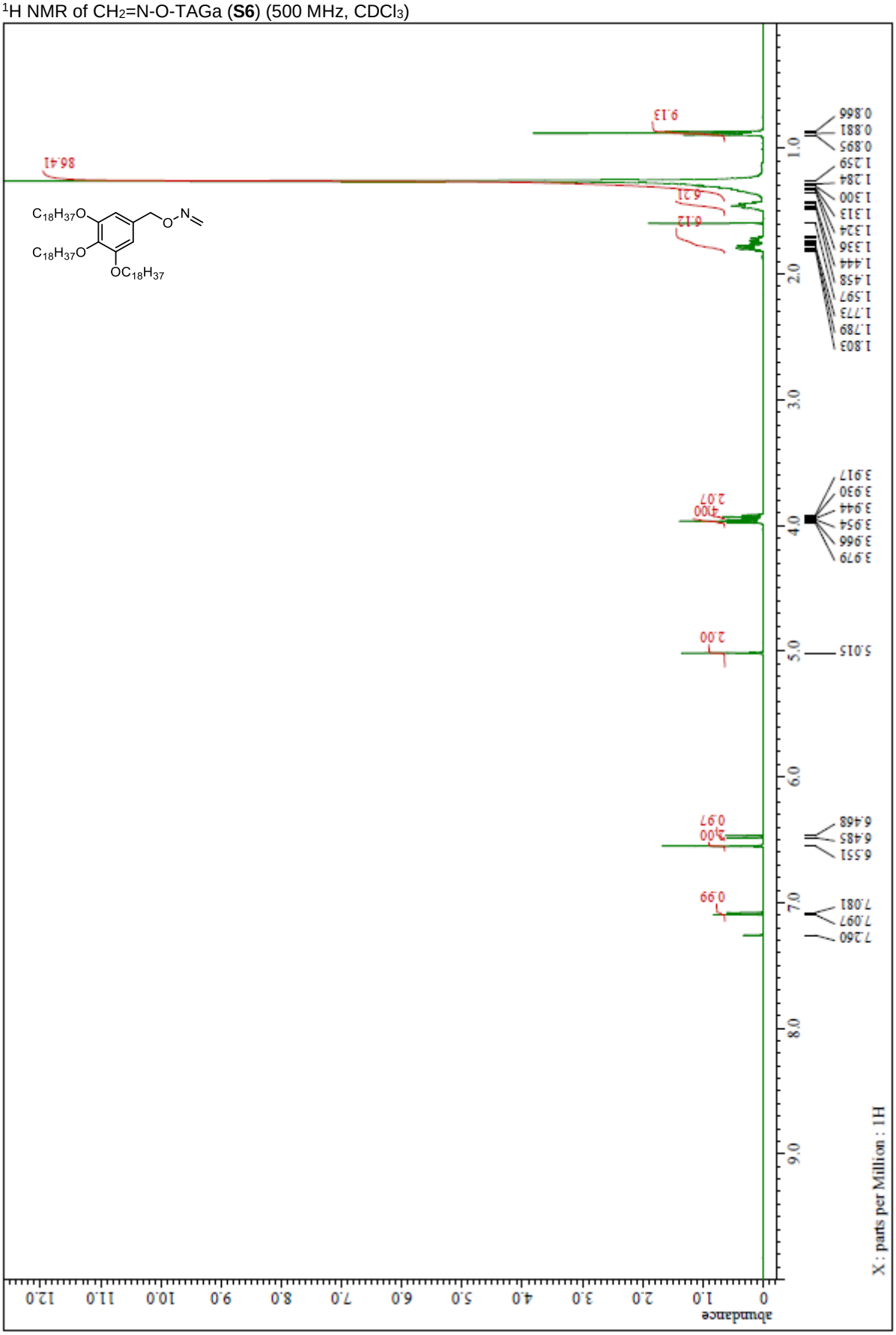

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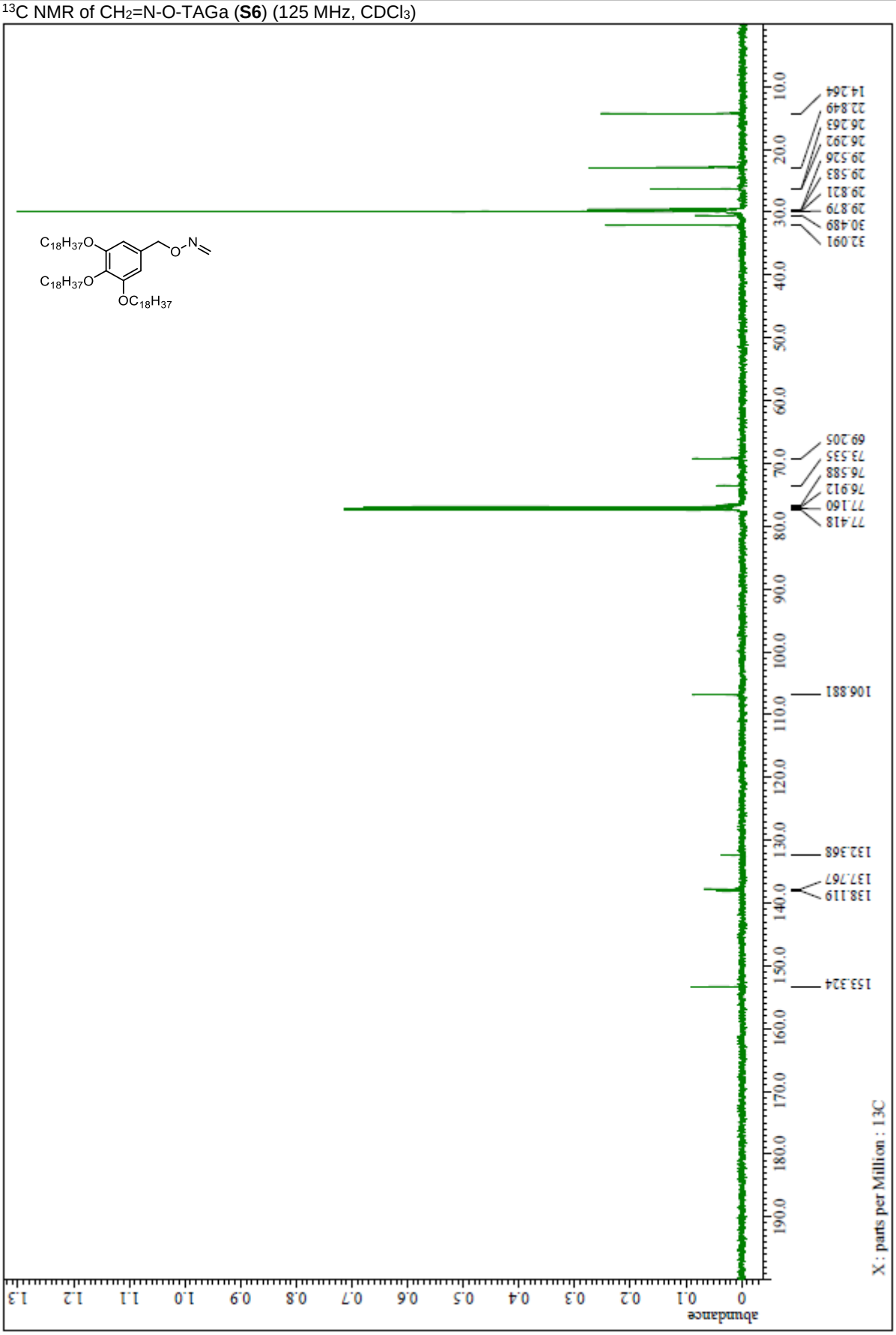

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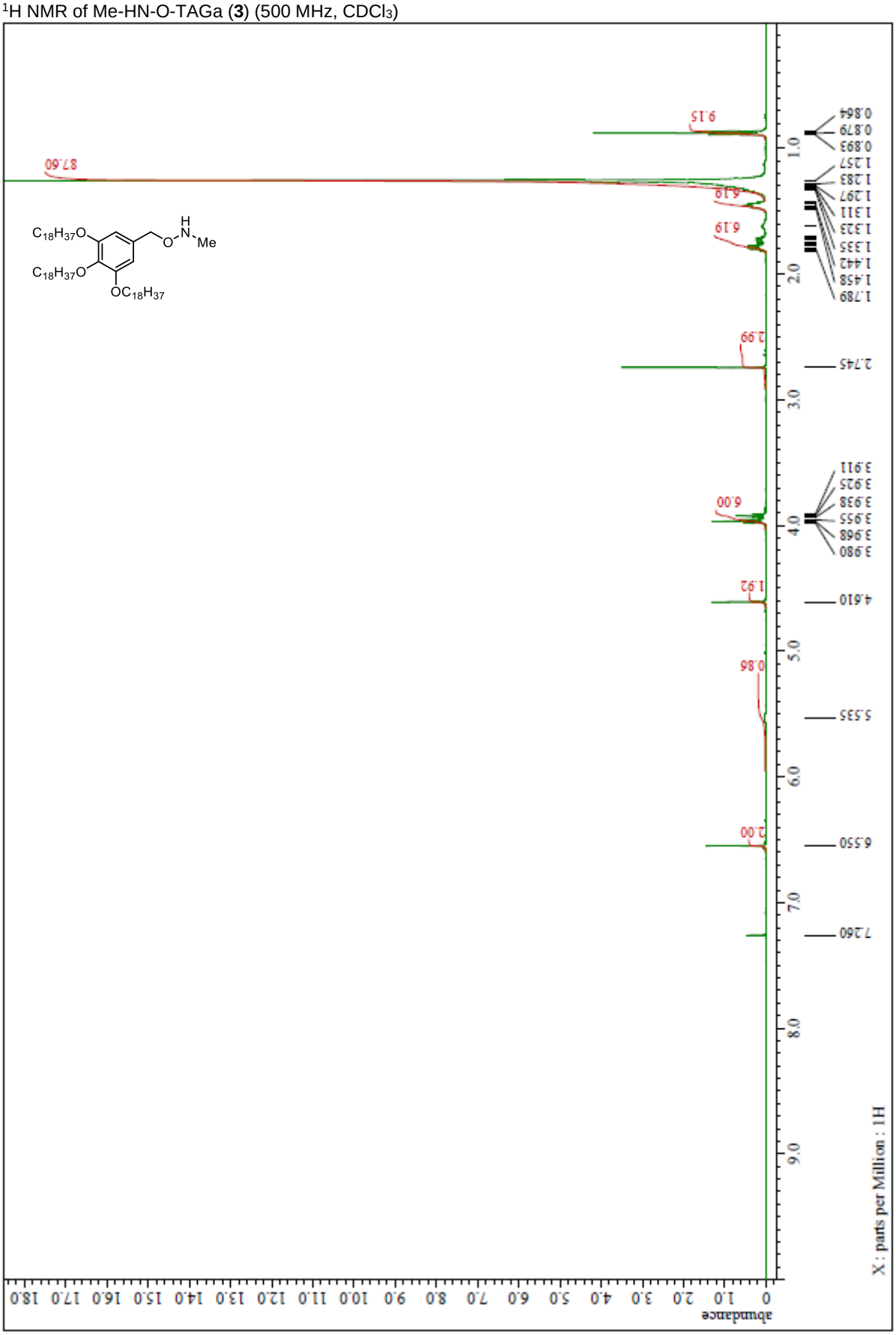

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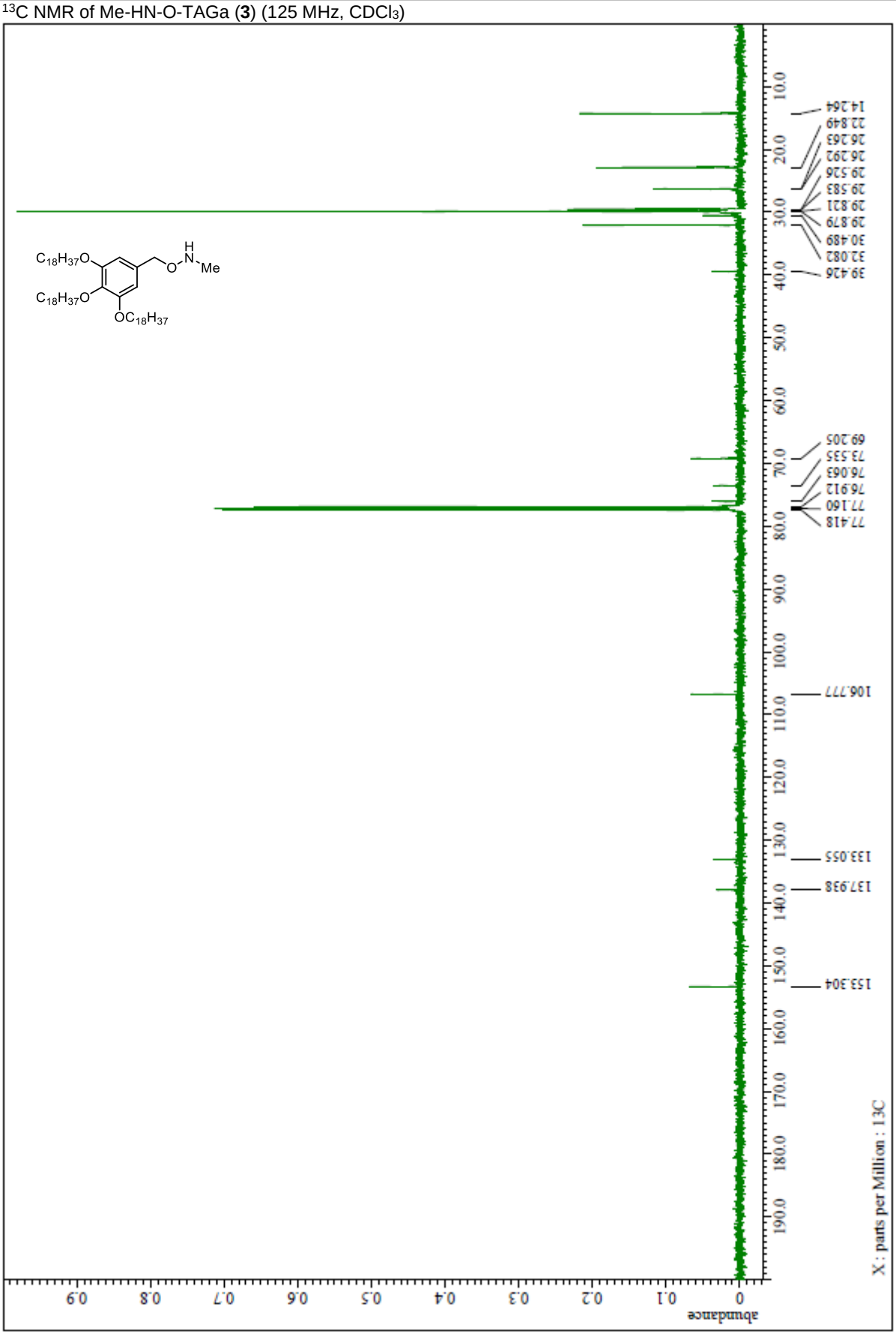
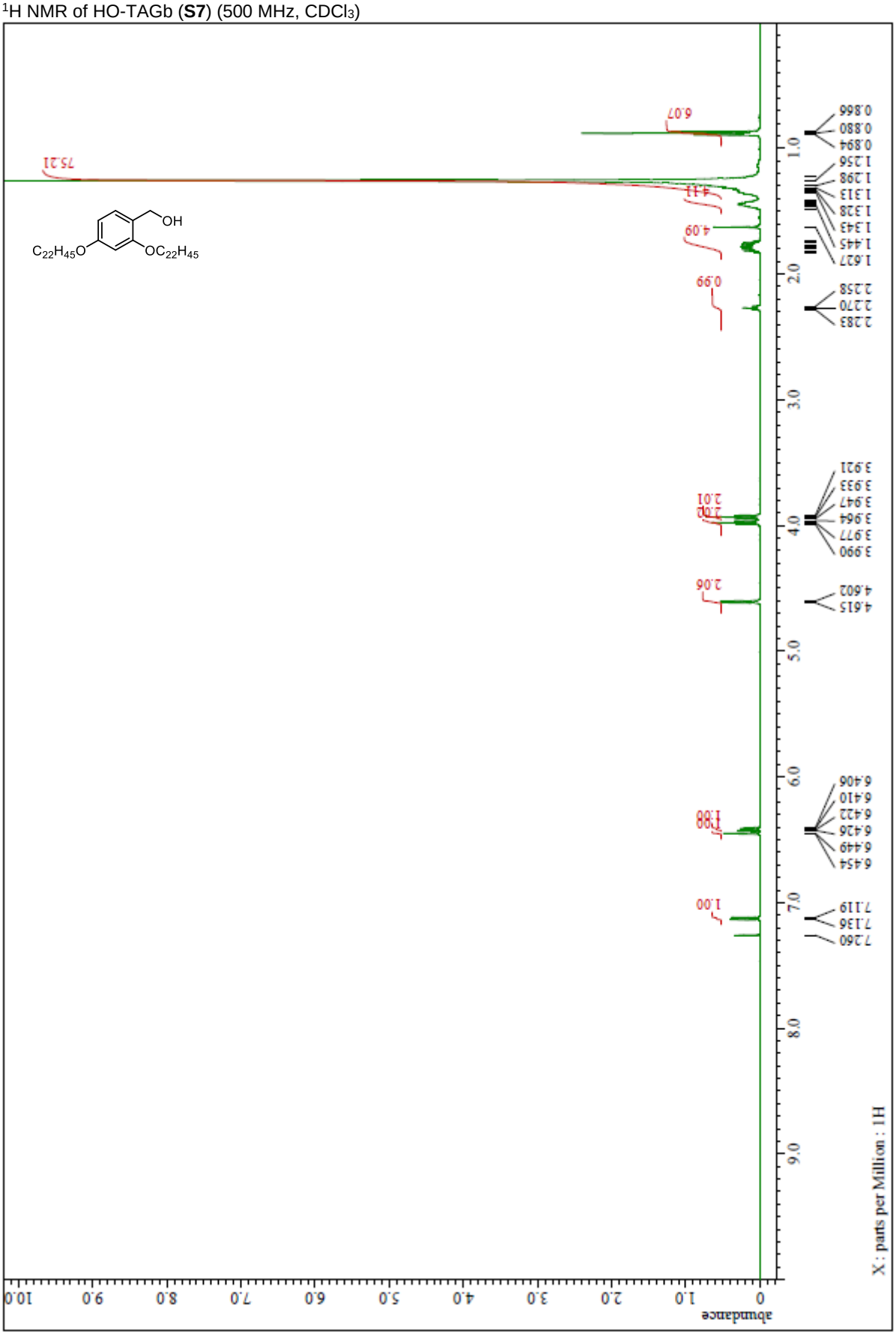


^{1}H NMR of HO-TAGb (**S7**) (500 MHz, $CDCl_3$)



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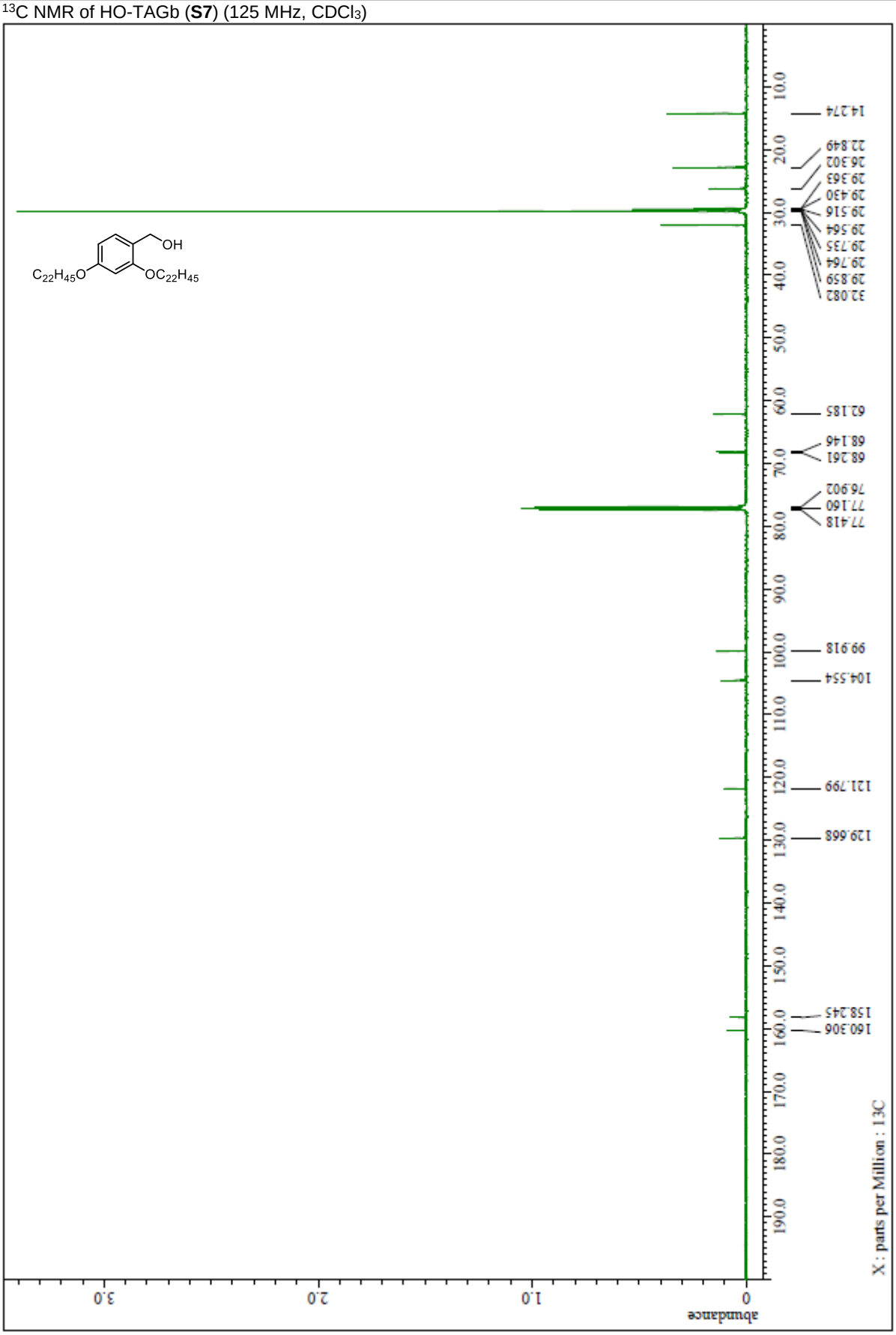
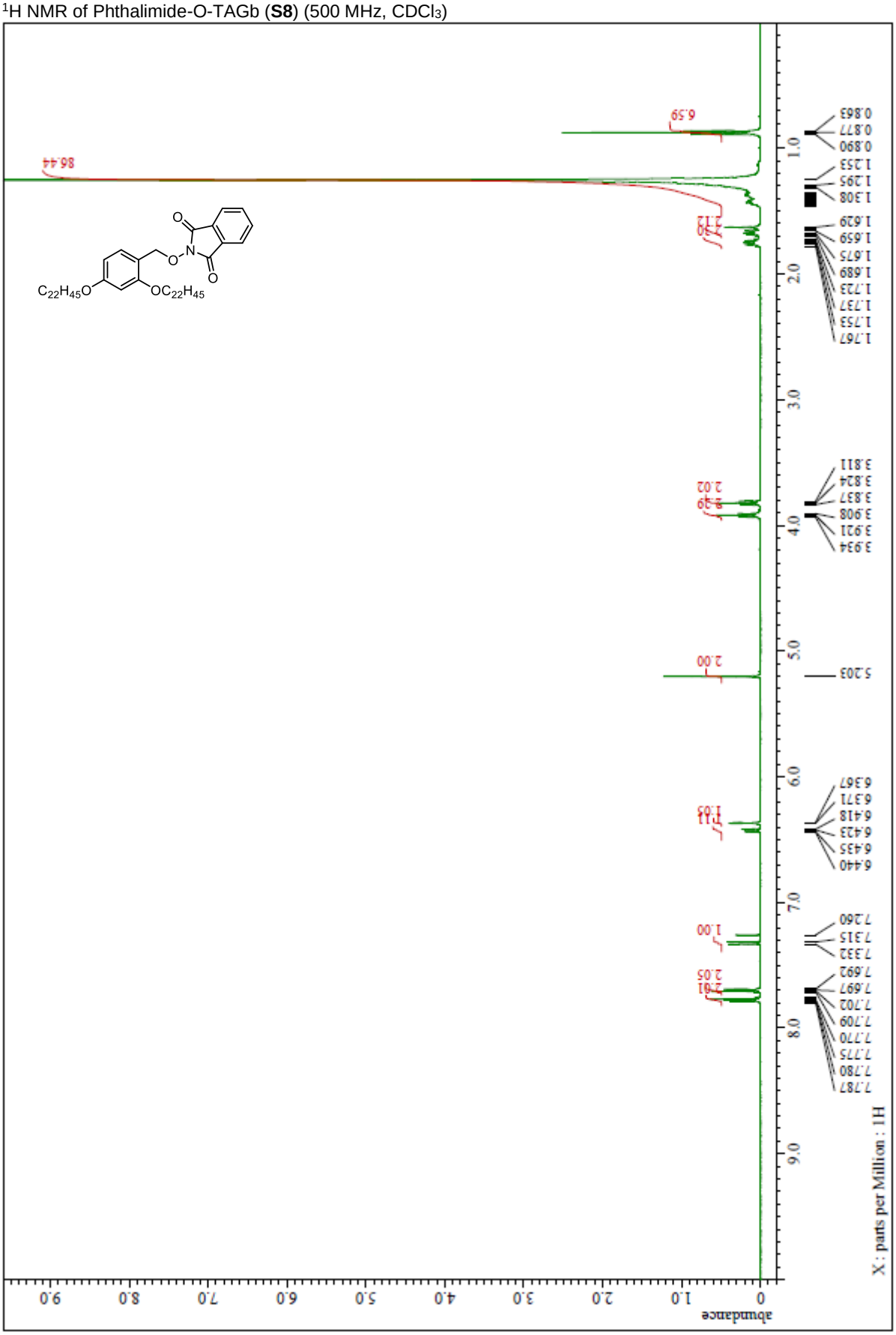


^{1}H NMR of Phthalimide-O-TAGb (**S8**) (500 MHz, $CDCl_3$)



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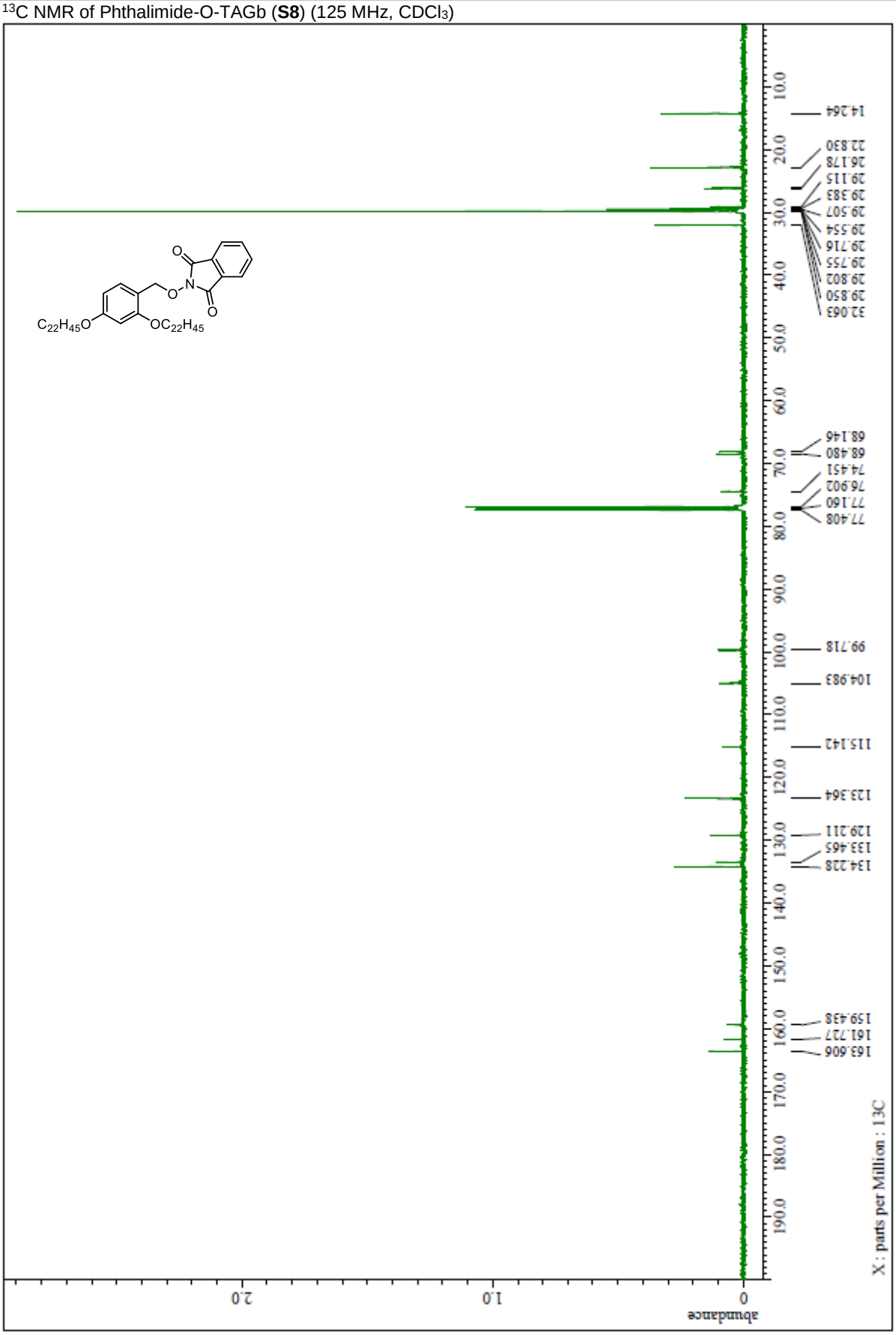

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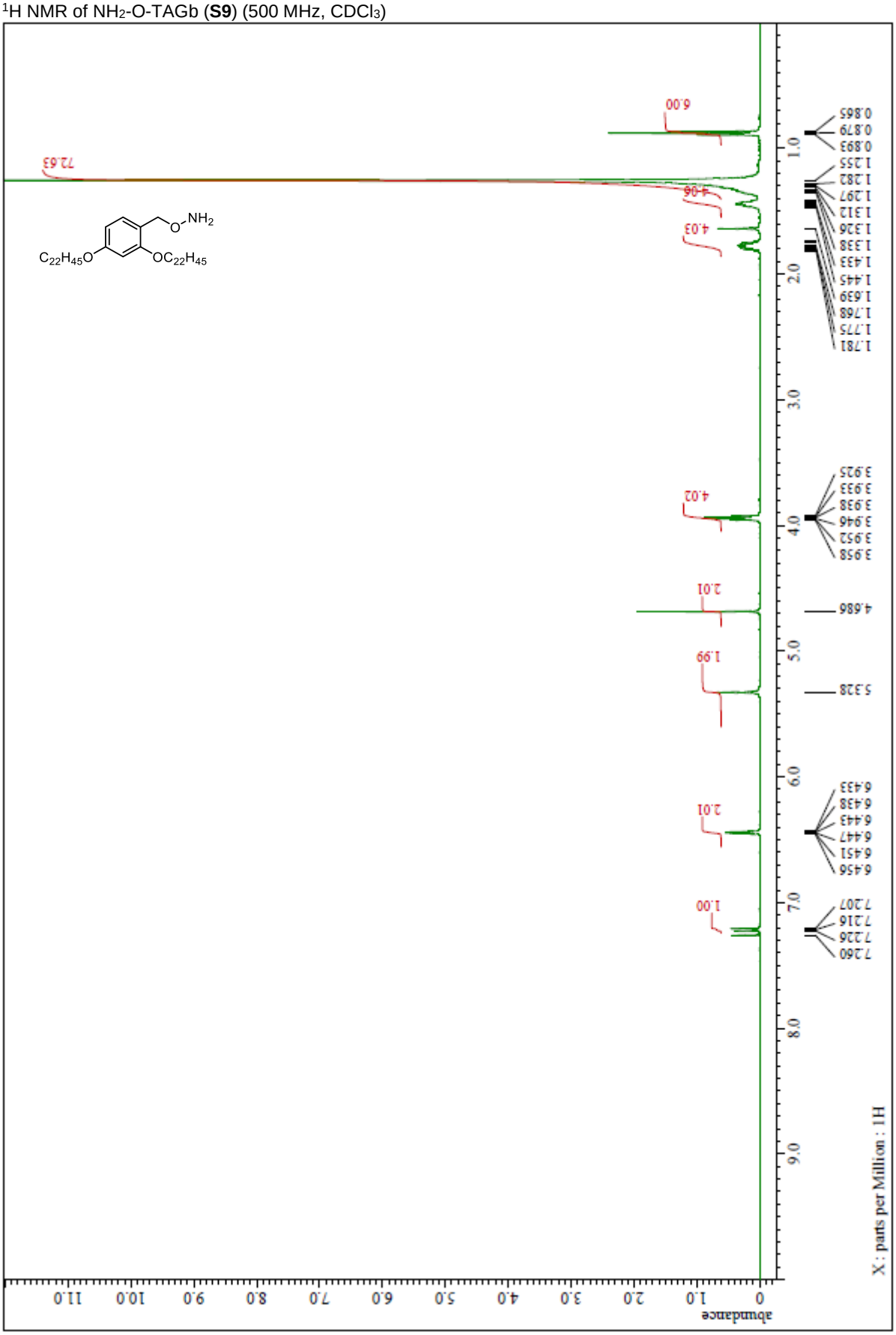

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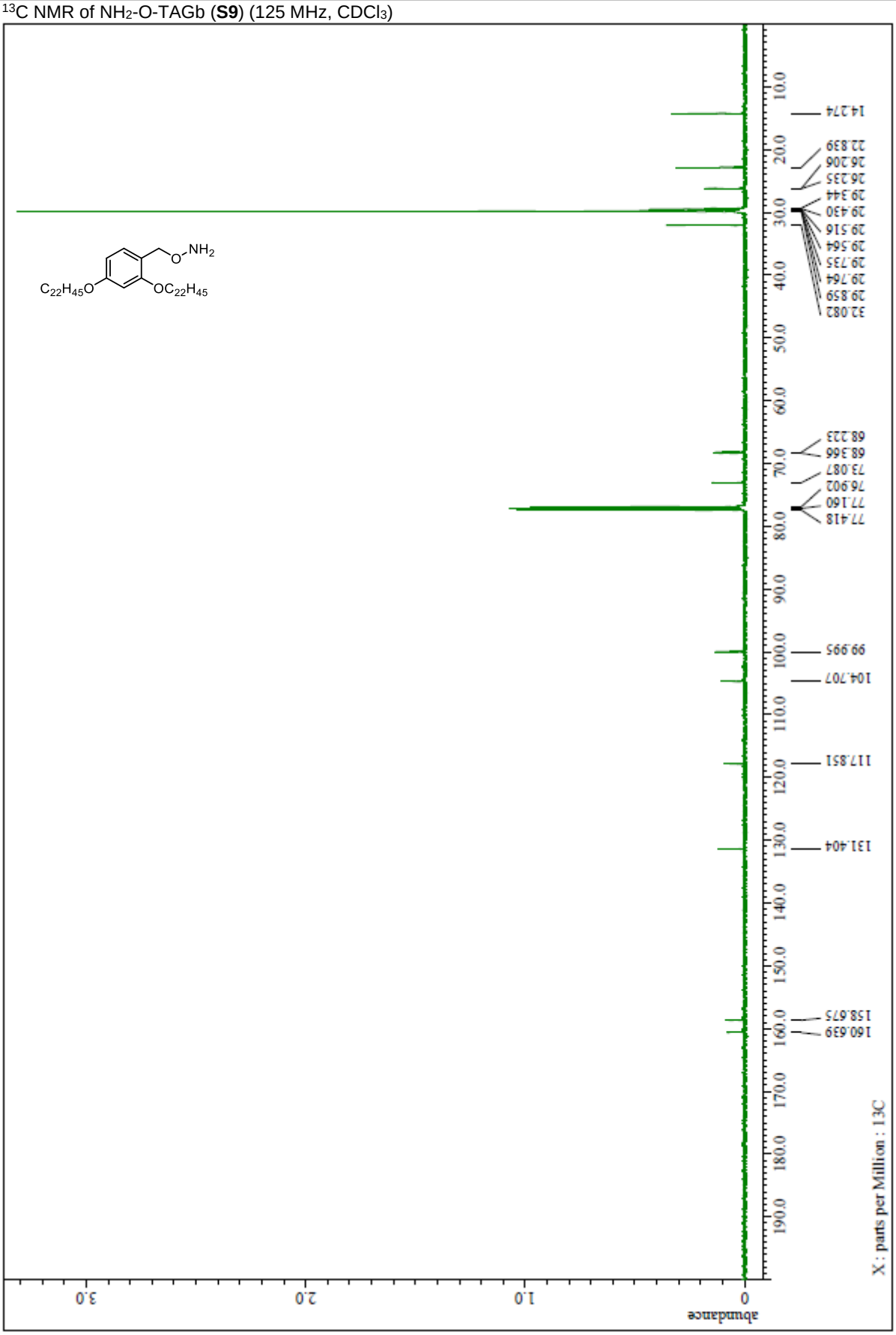

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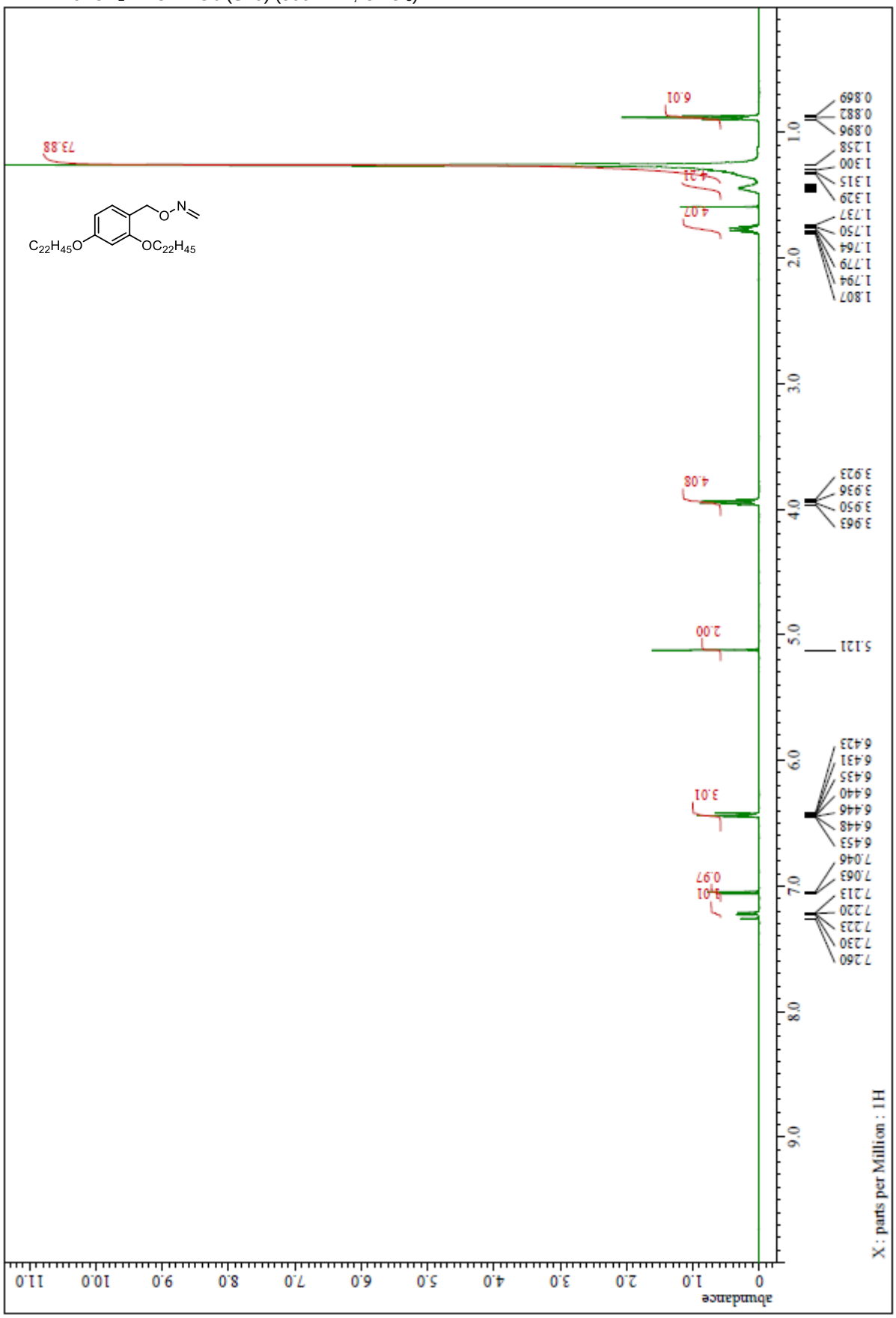

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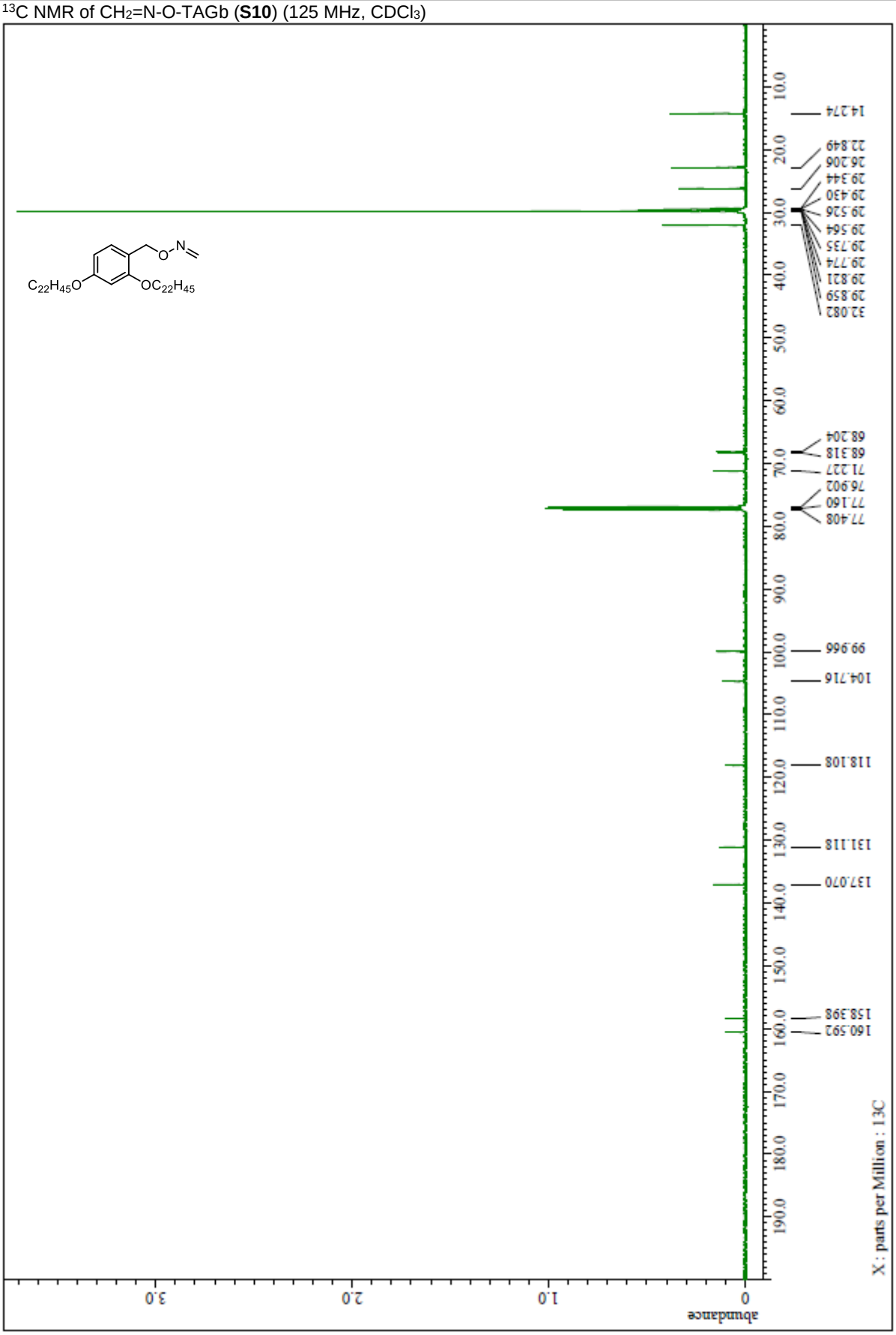

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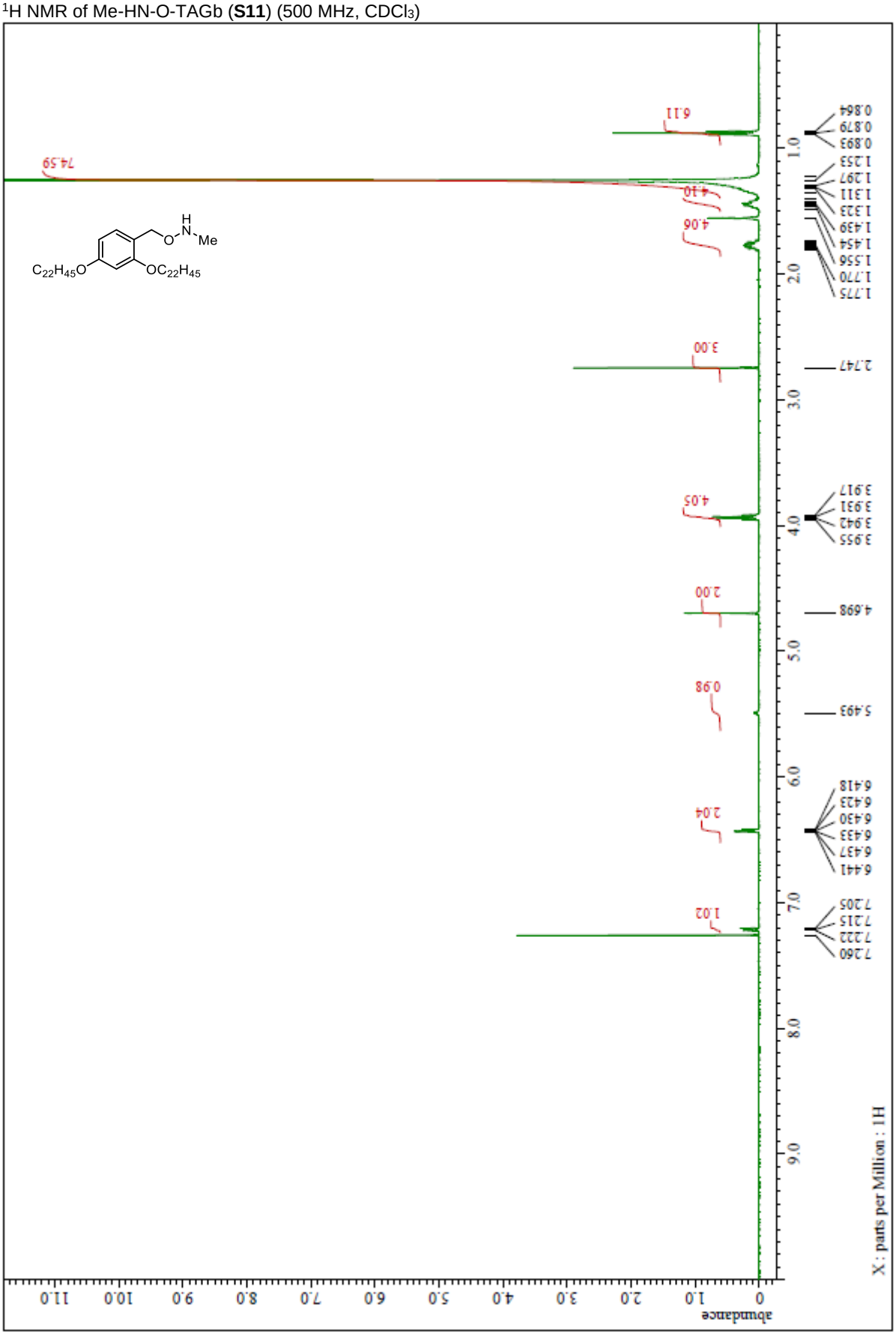

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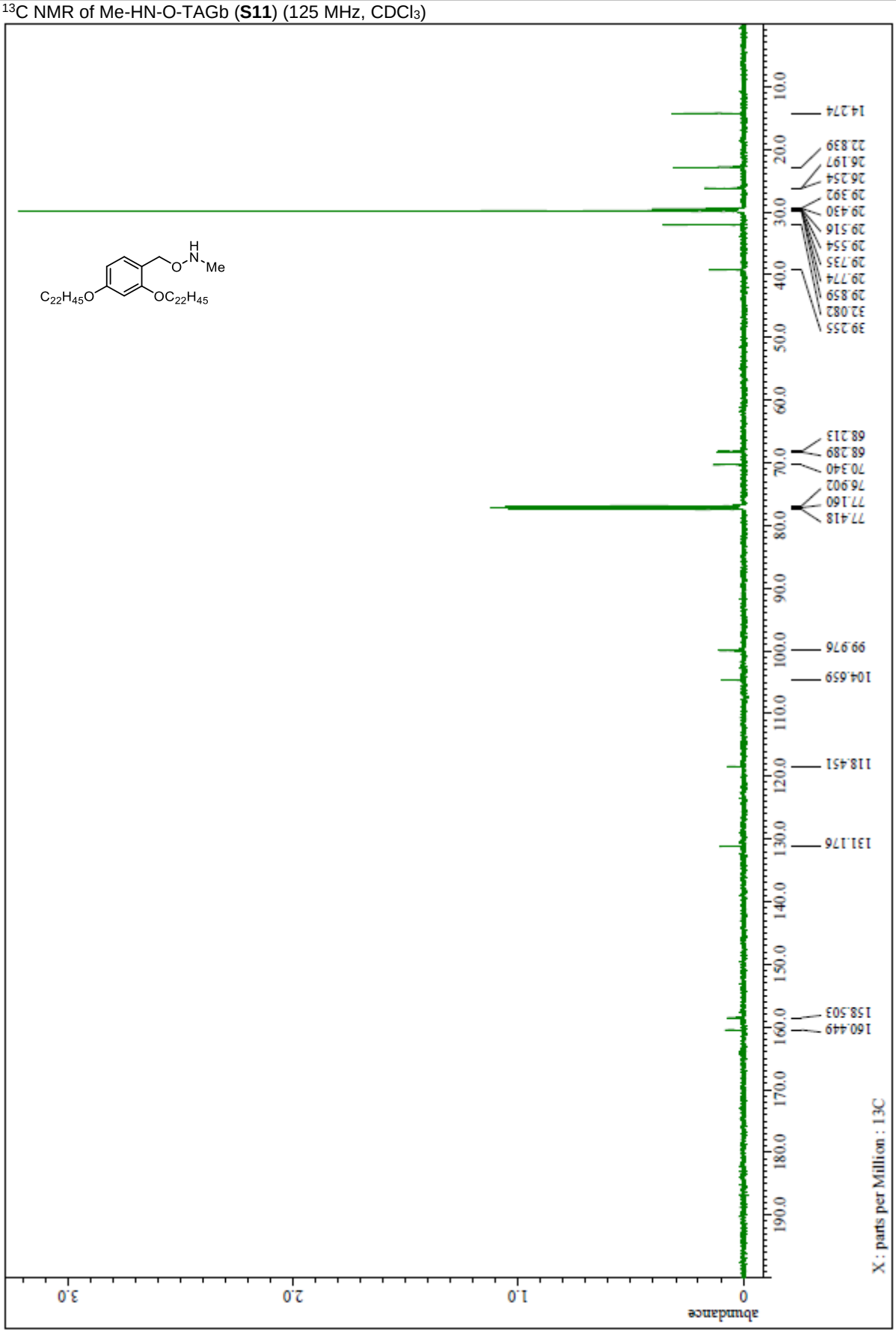

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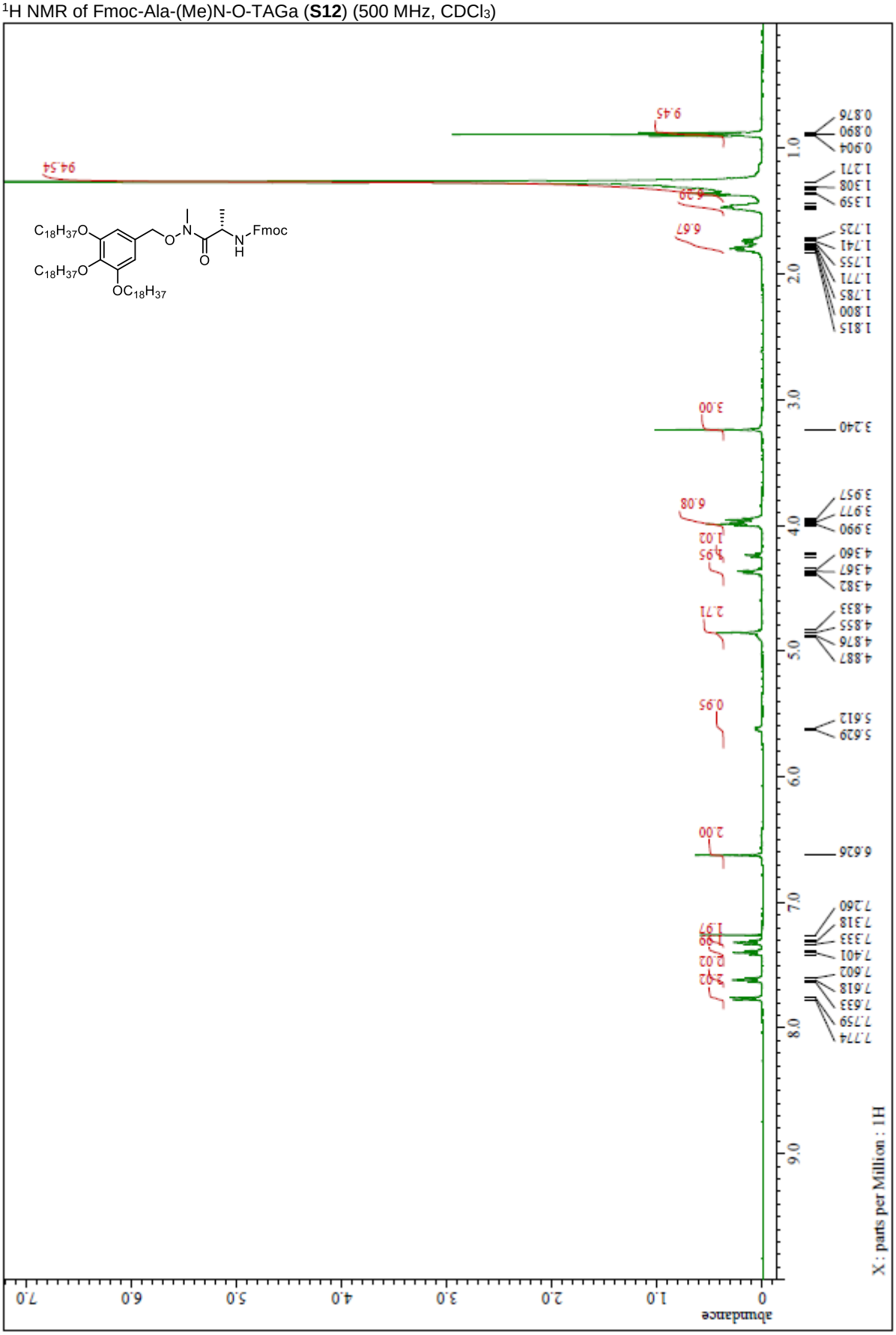

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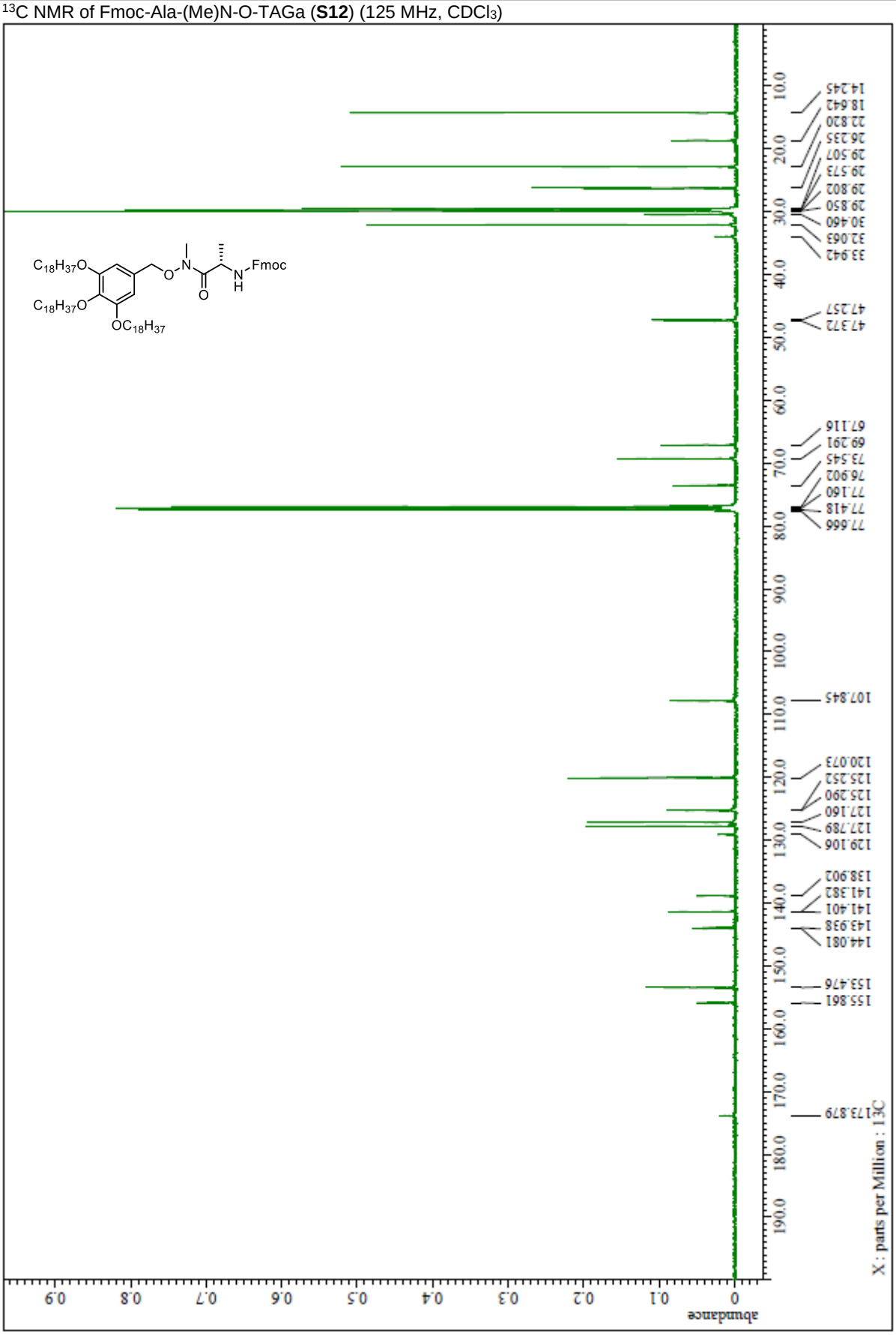
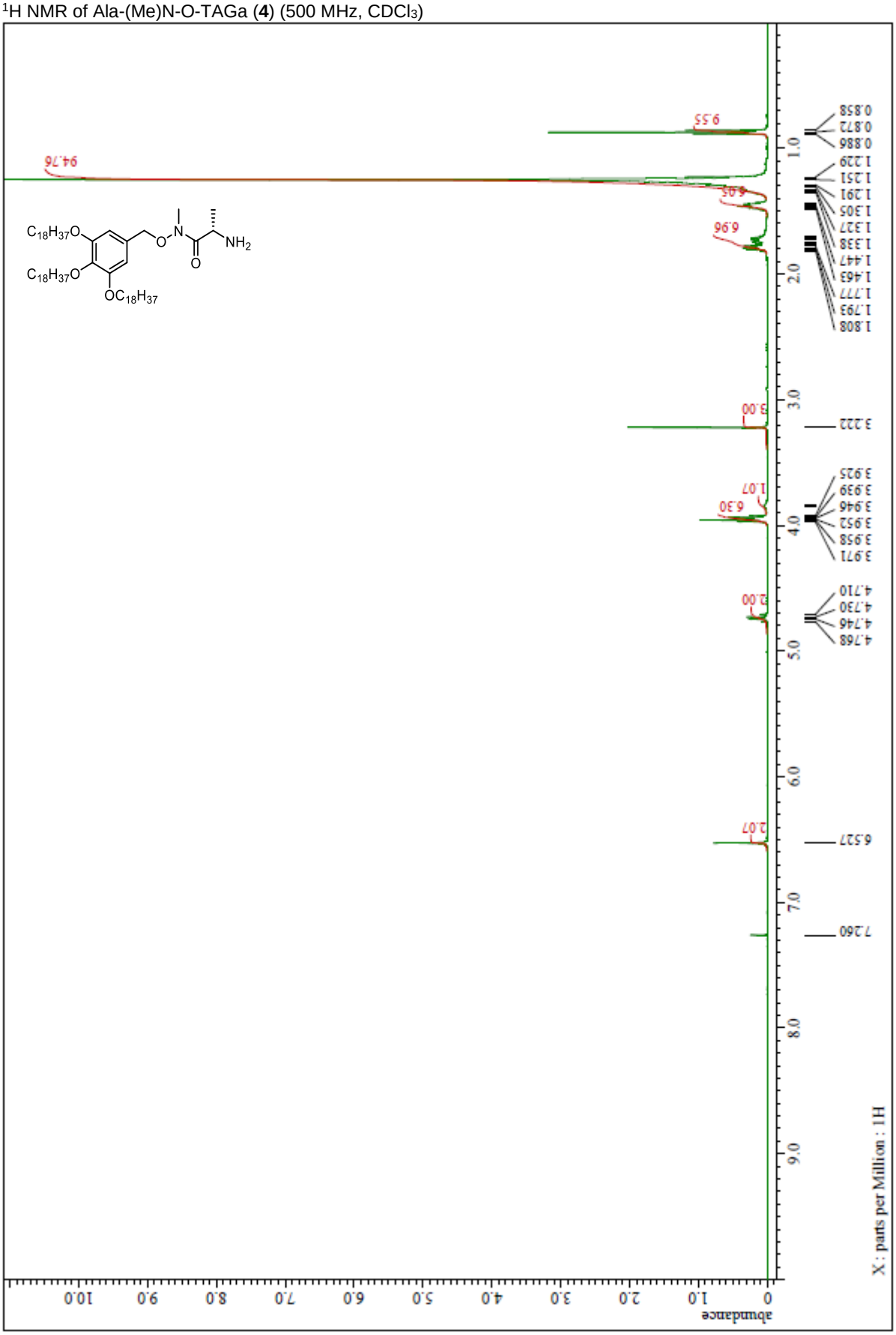


^{1}H NMR of Ala-(Me)N-O-TAGa (**4**) (500 MHz, $CDCl_3$)



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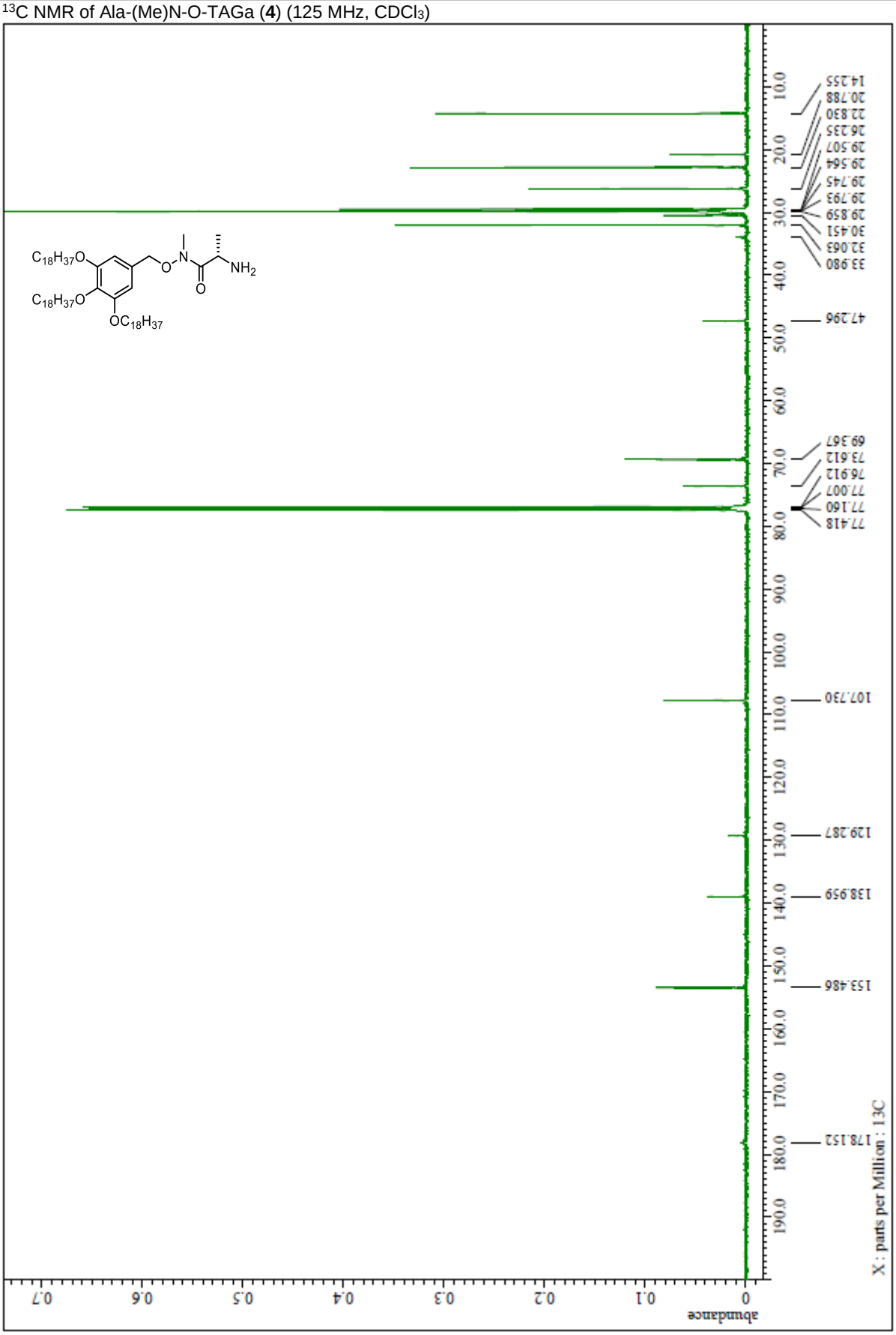

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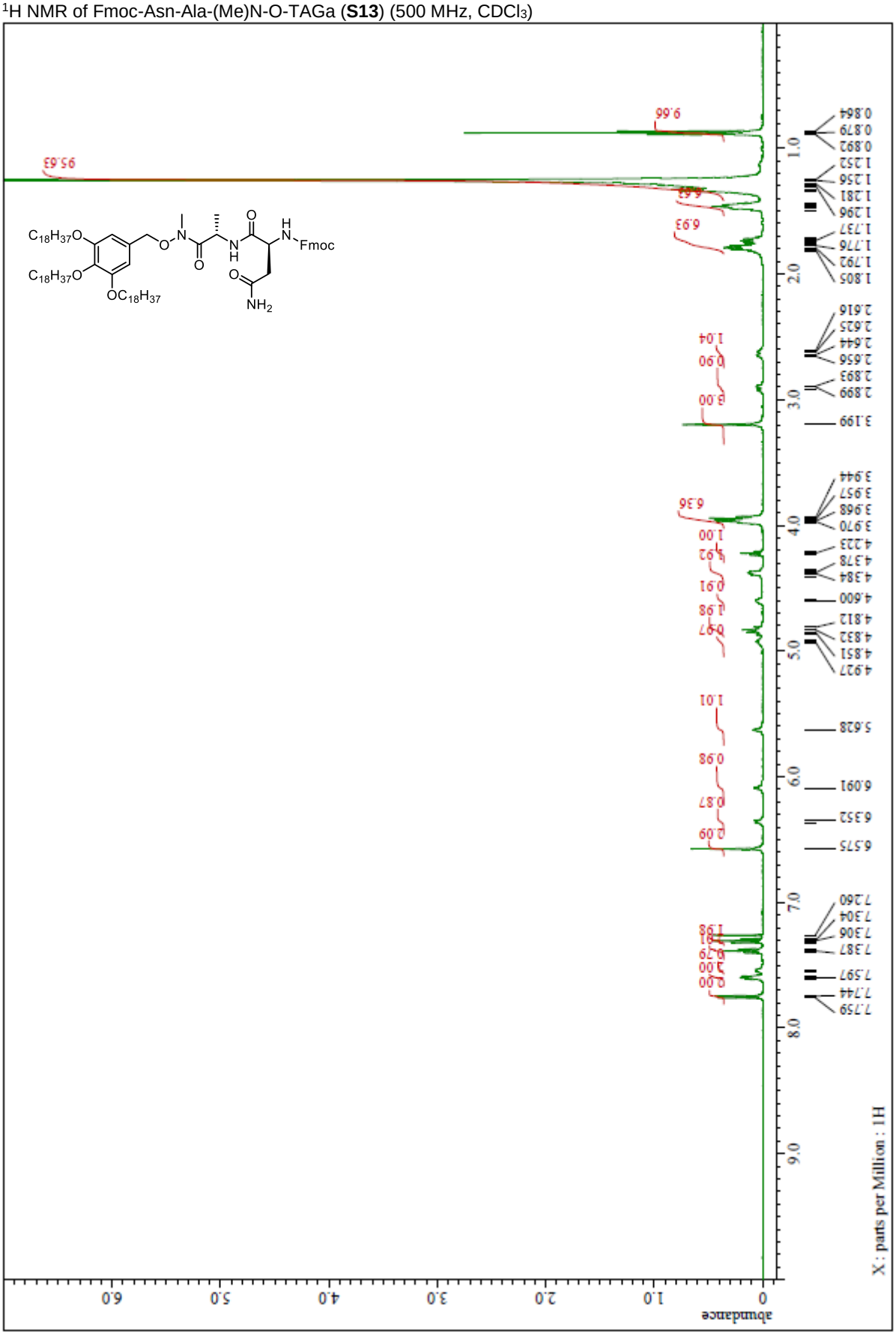

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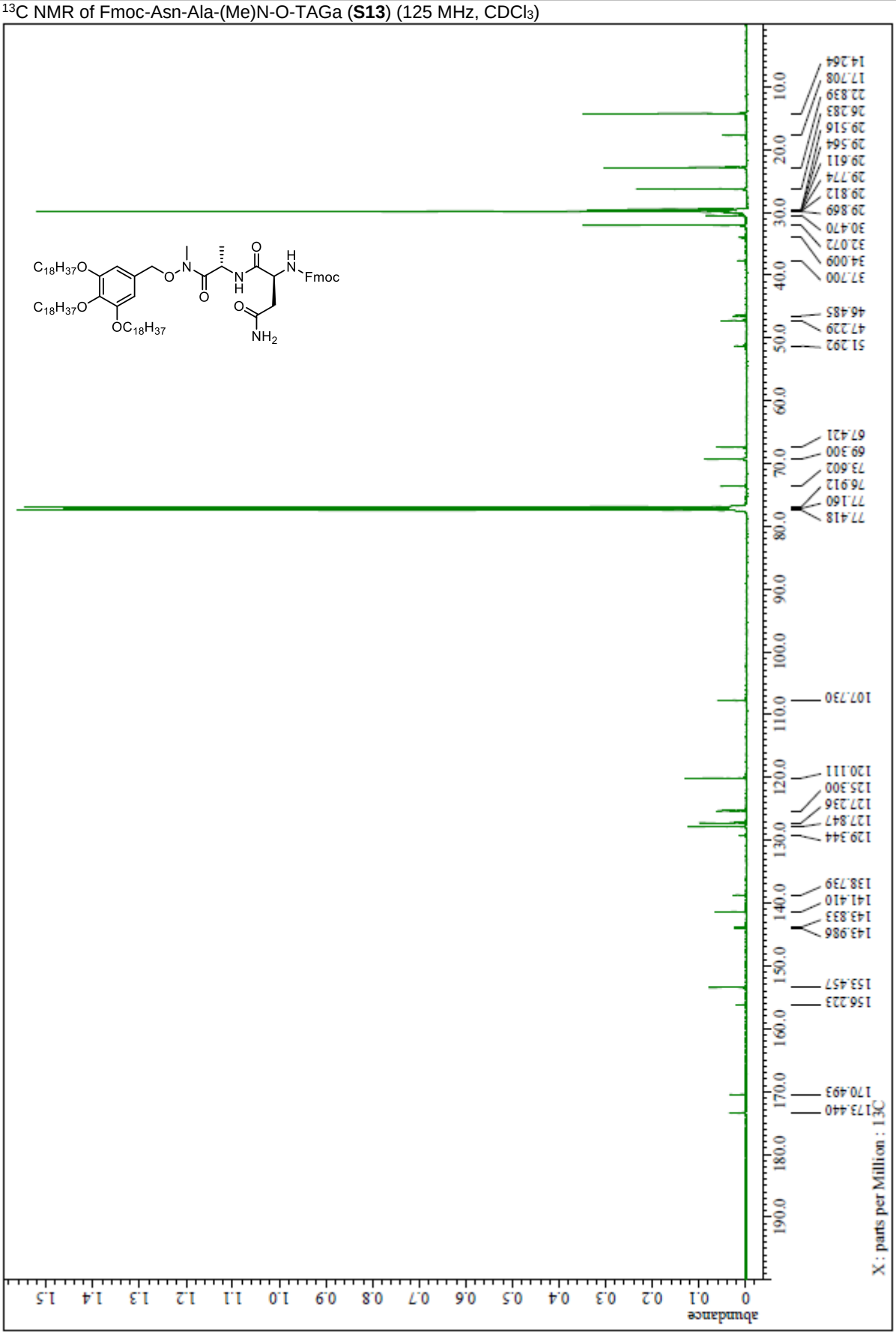

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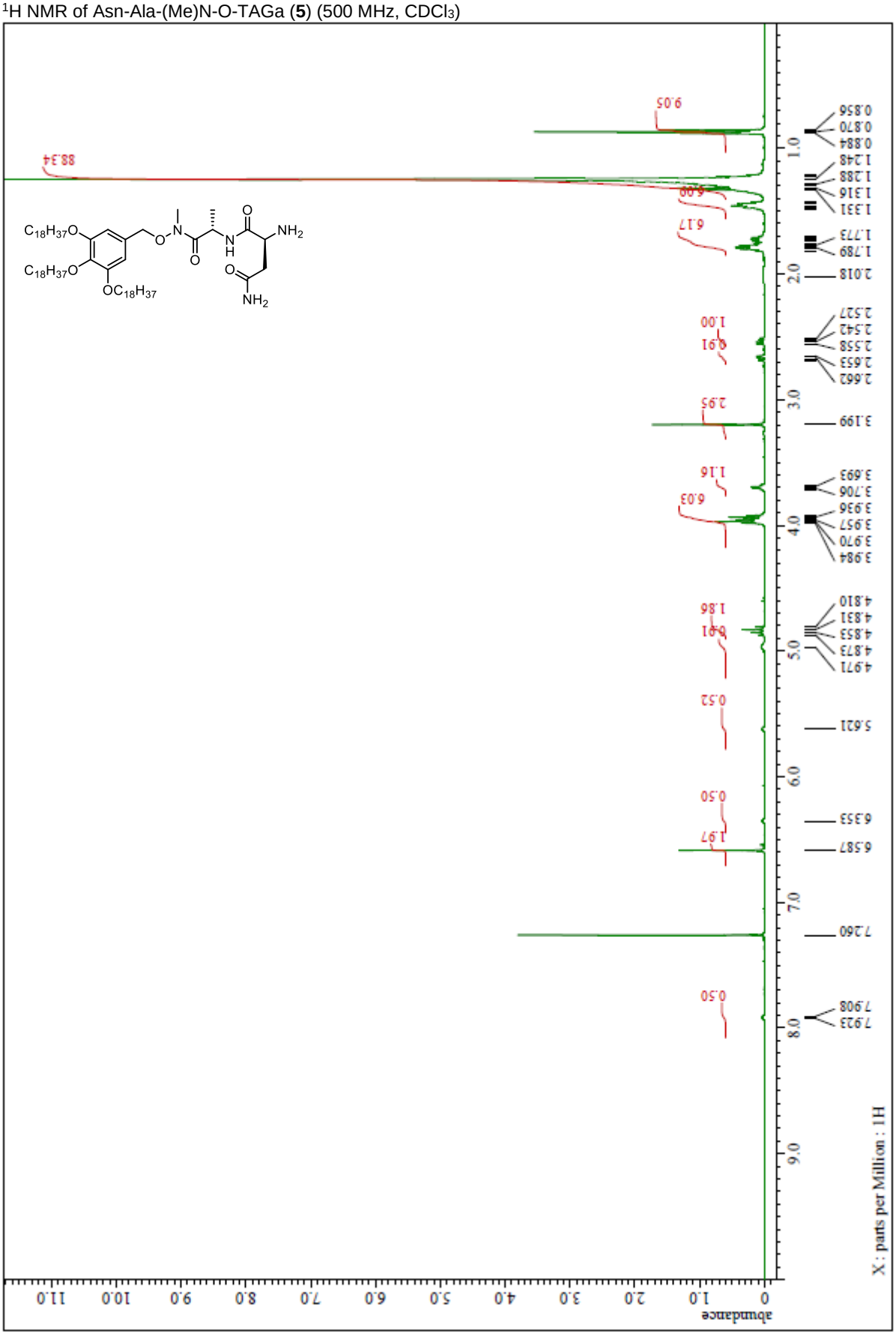

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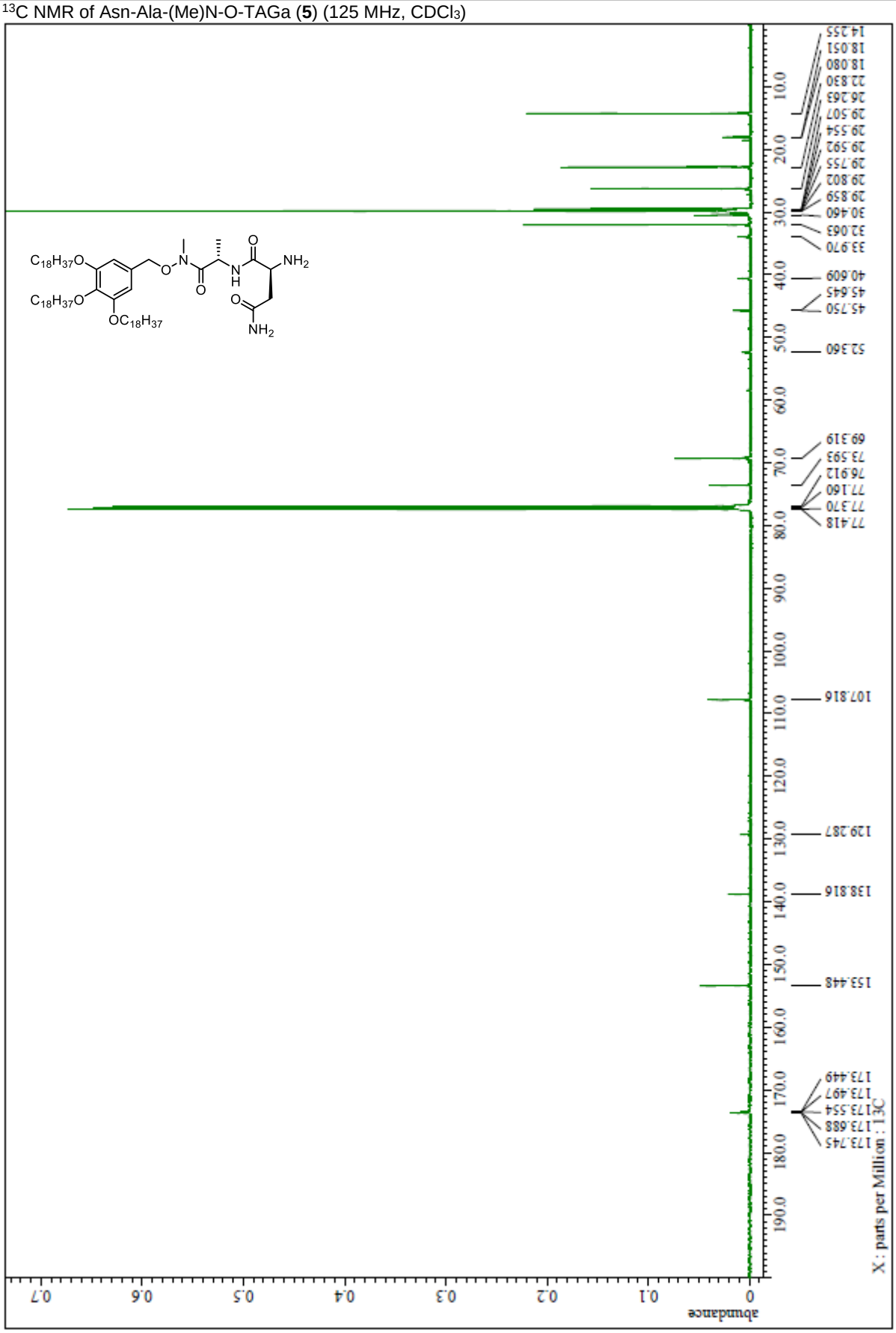
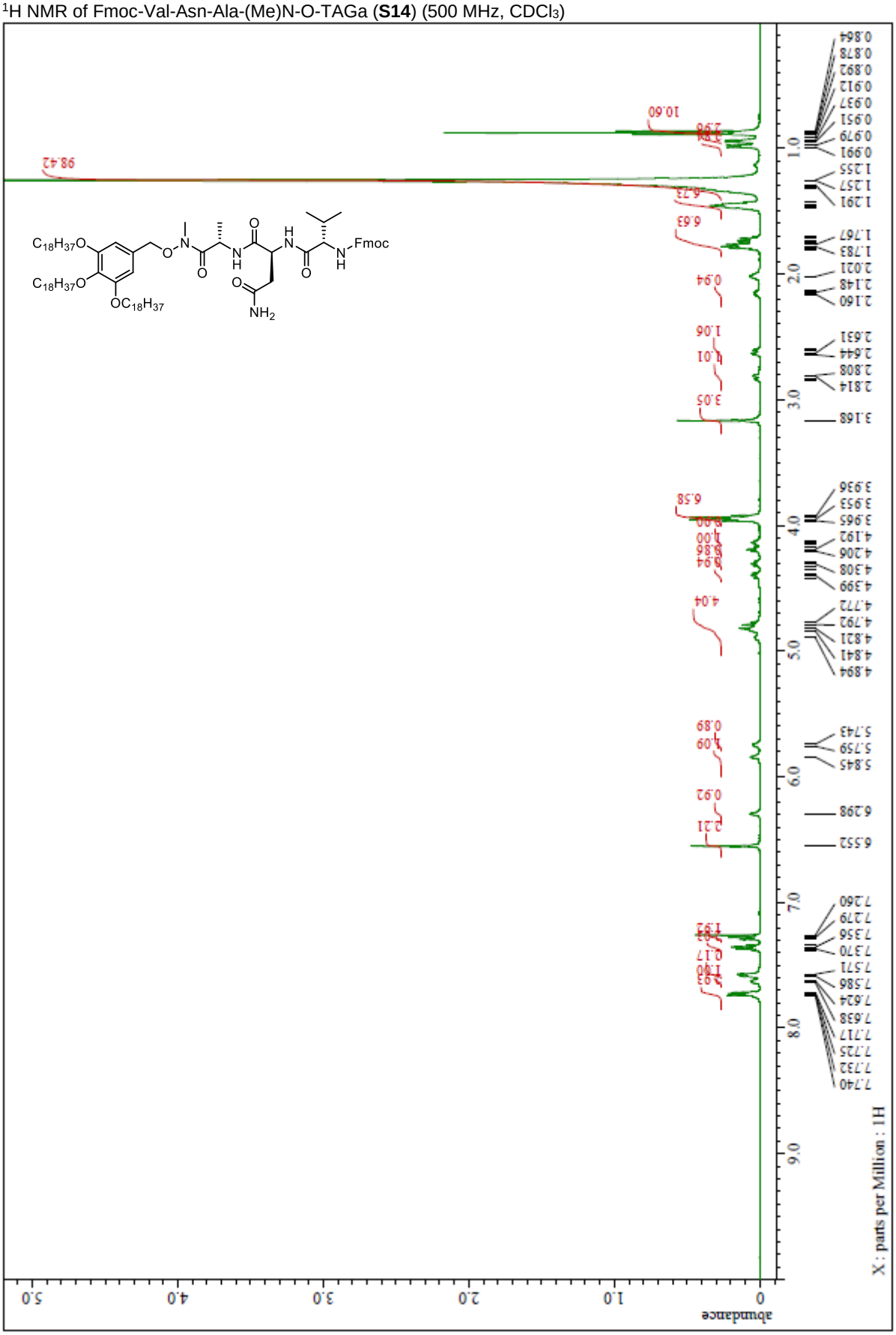


^{1}H NMR of Fmoc-Val-Asn-Ala-(Me)N-O-TAGa (**S14**) (500 MHz, $CDCl_3$)



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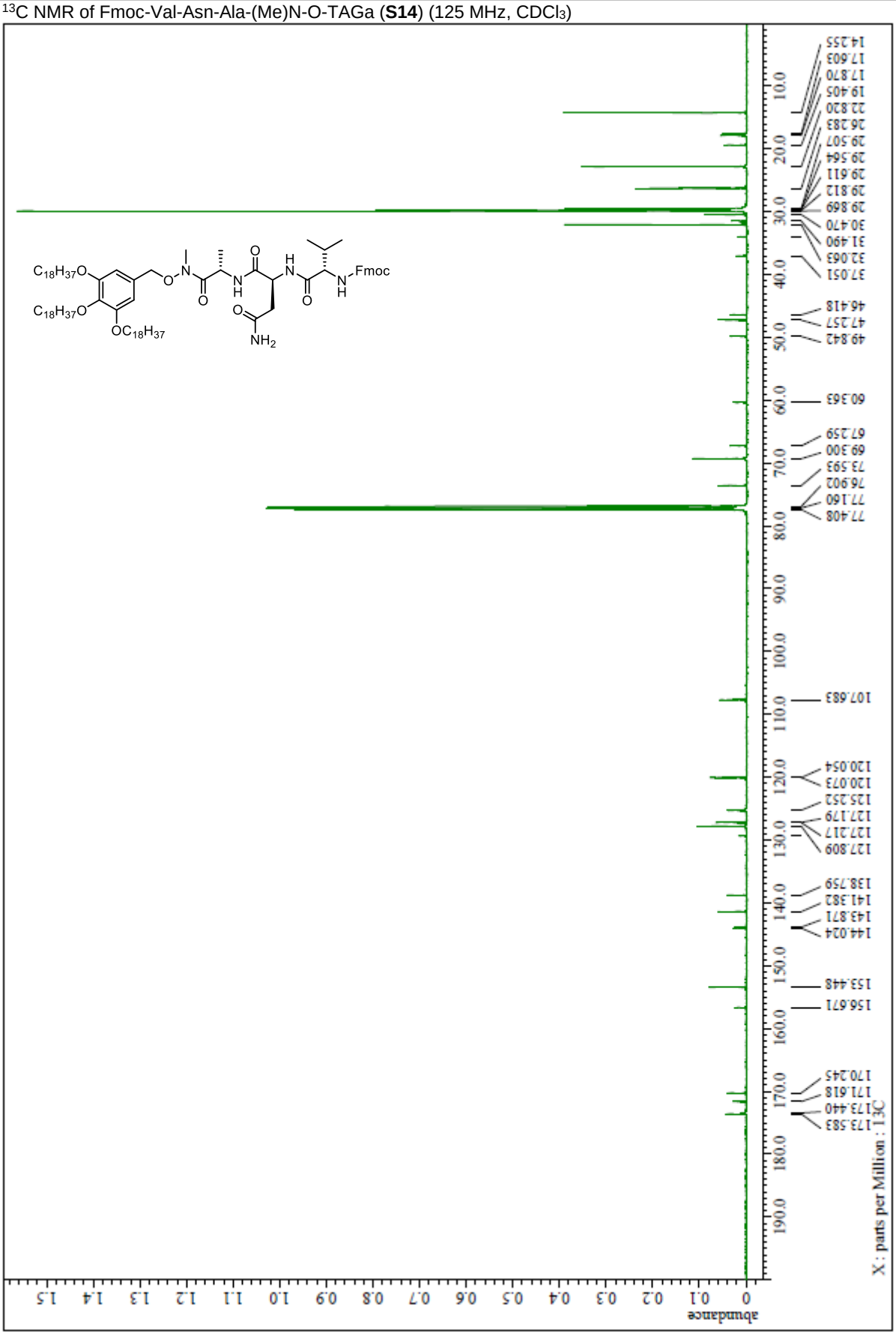

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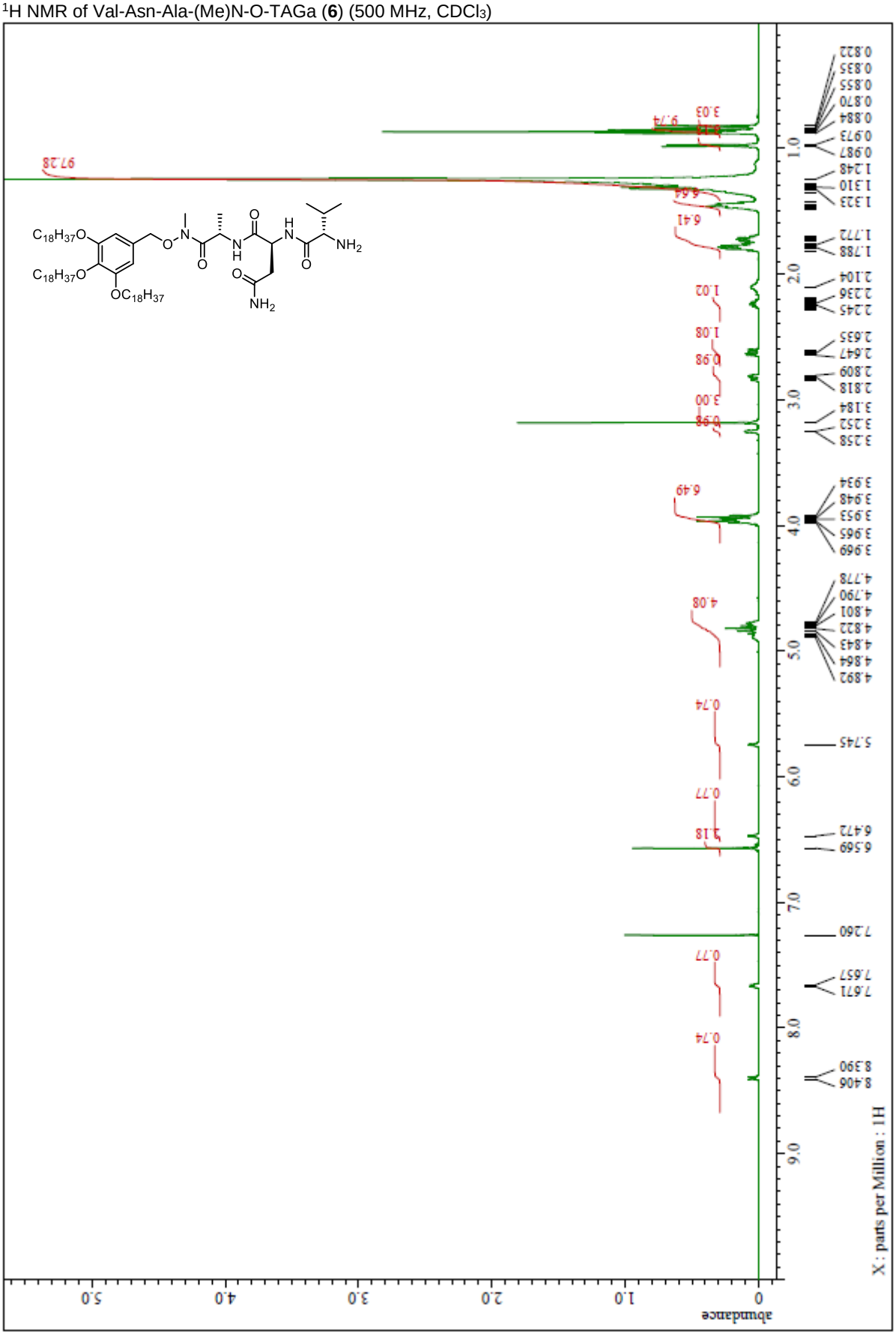
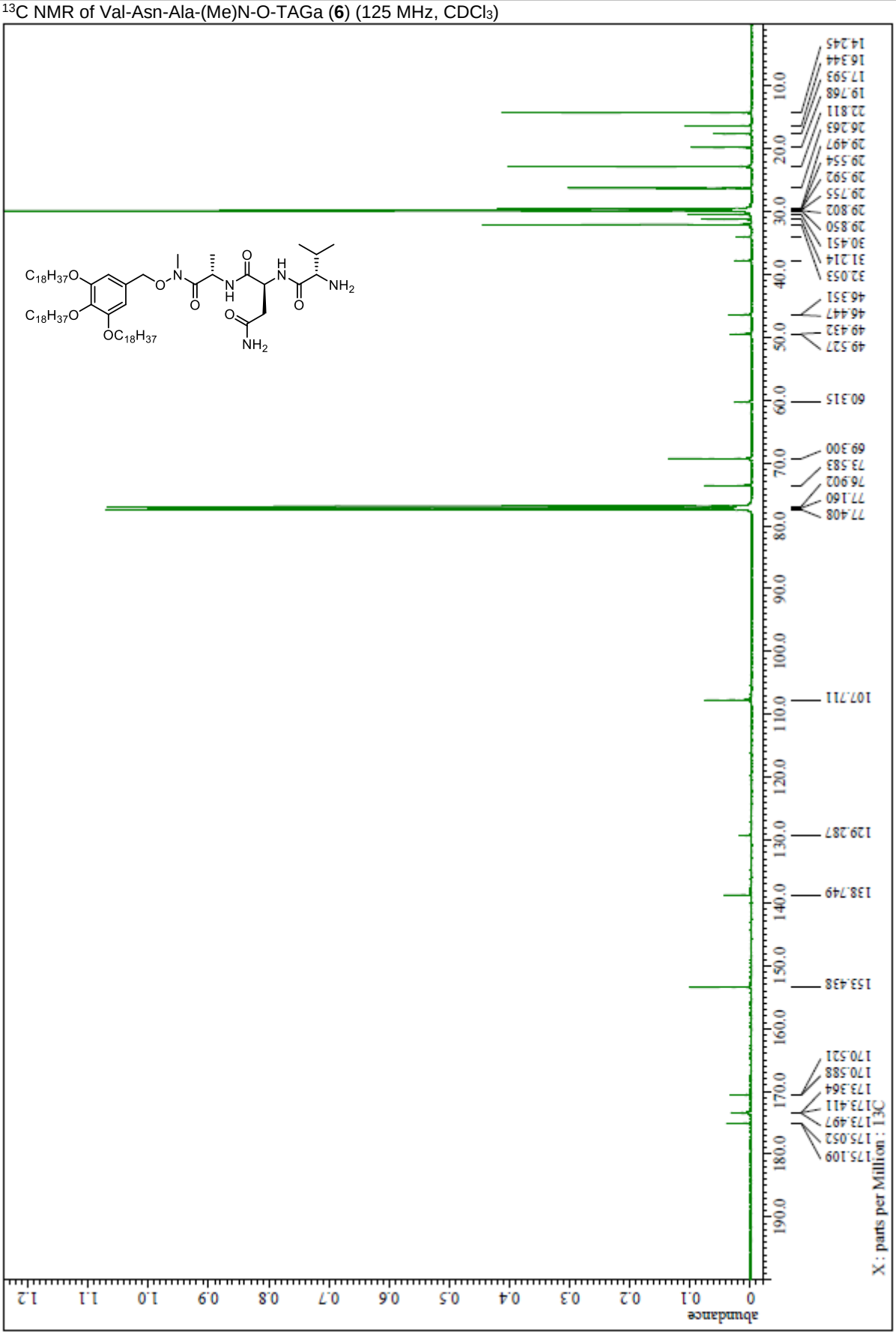
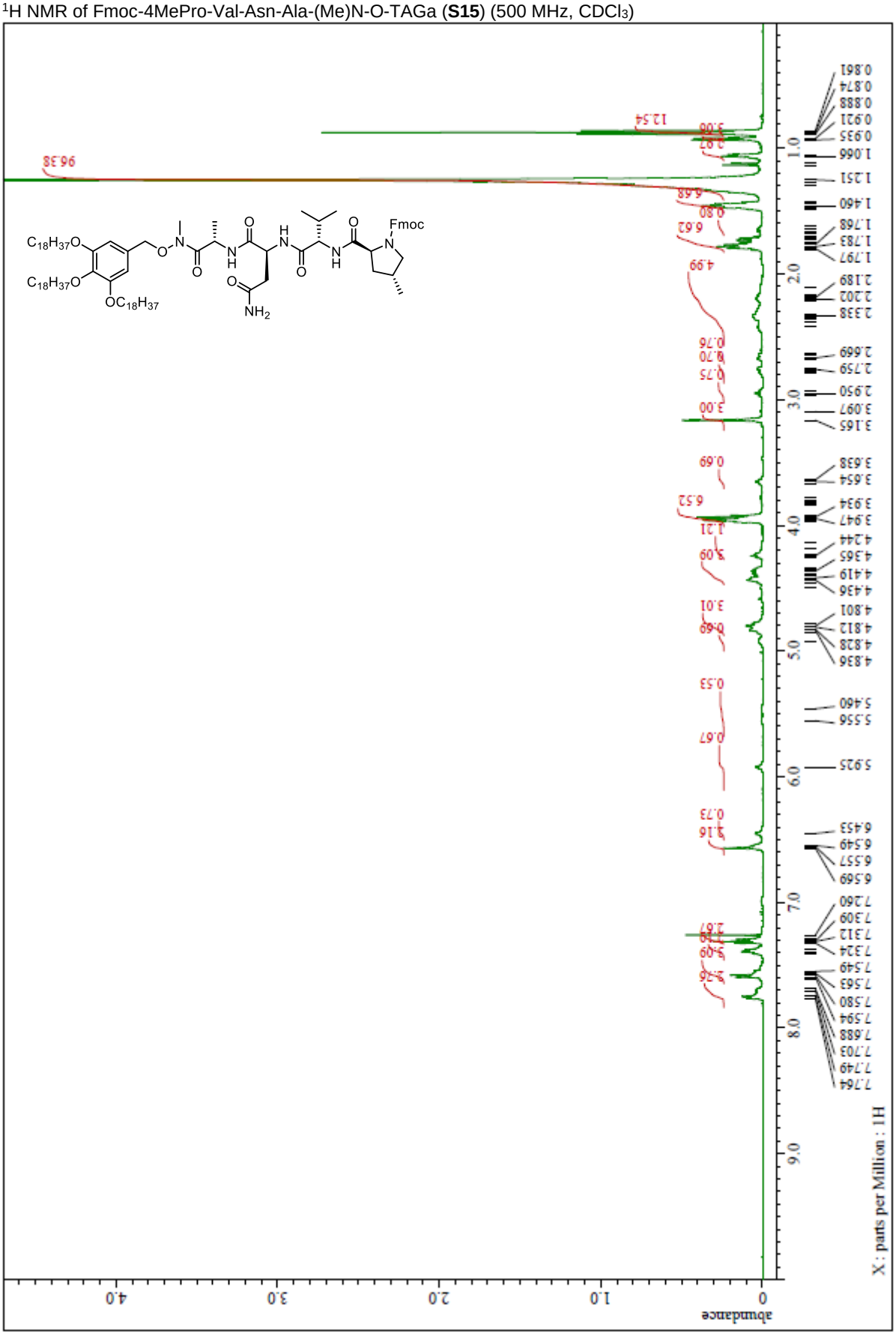


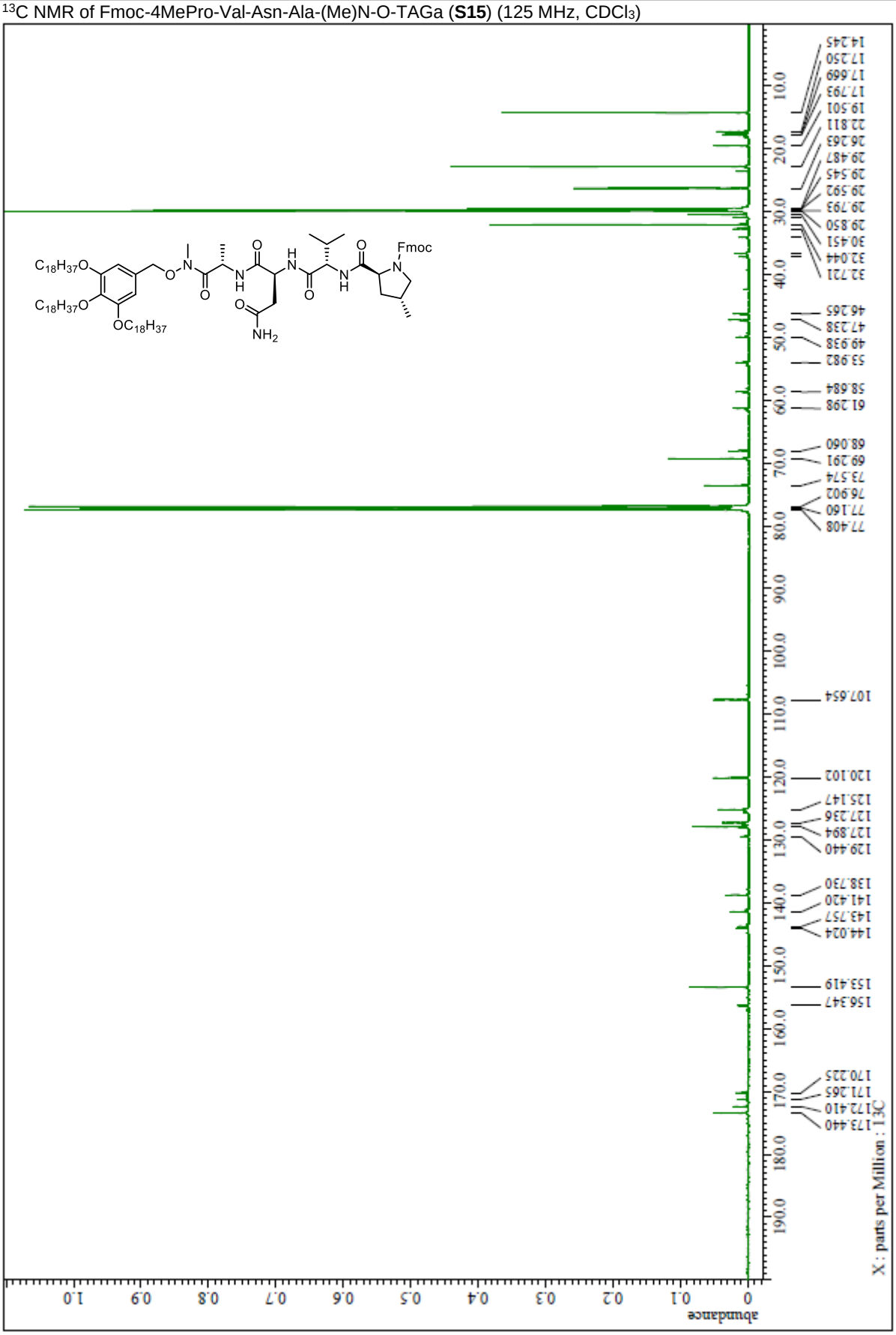
^{13}C NMR of Val-Asn-Ala-(Me)N-O-TAGa (**6**) (125 MHz, $CDCl_3$)



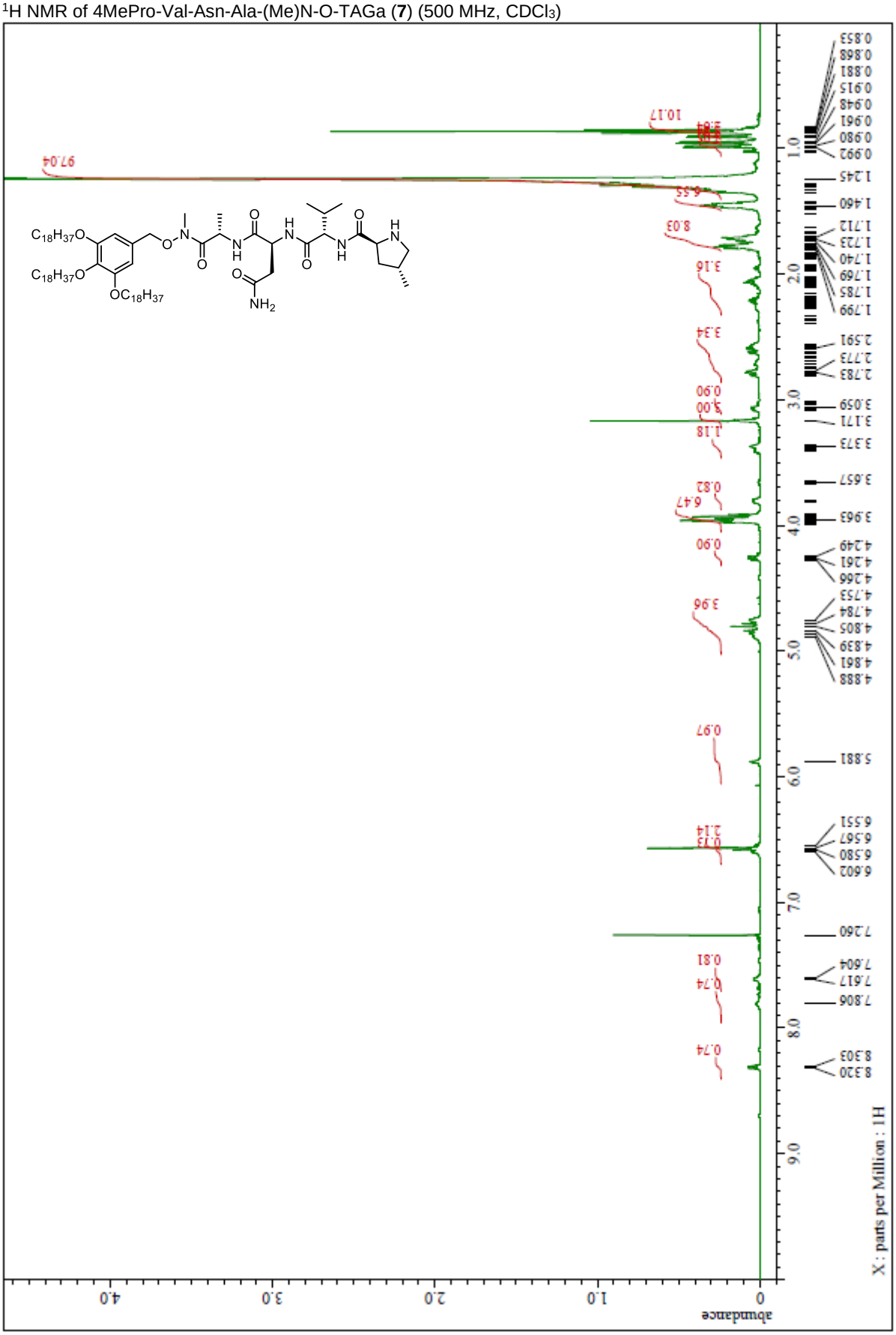
^{1}H NMR of Fmoc-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S15**) (500 MHz, $CDCl_3$)



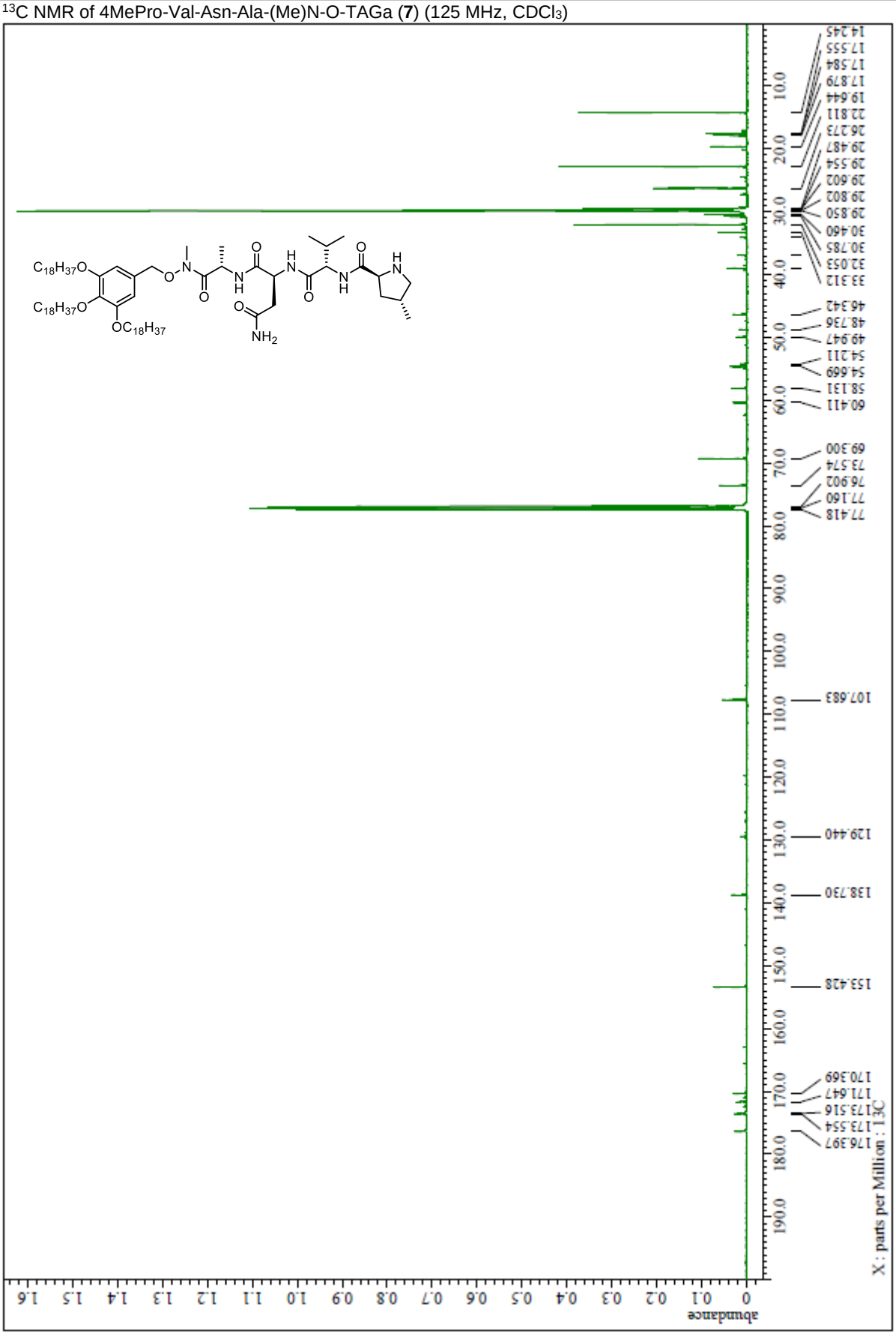
^{13}C NMR of Fmoc-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S15**) (125 MHz, $CDCl_3$)



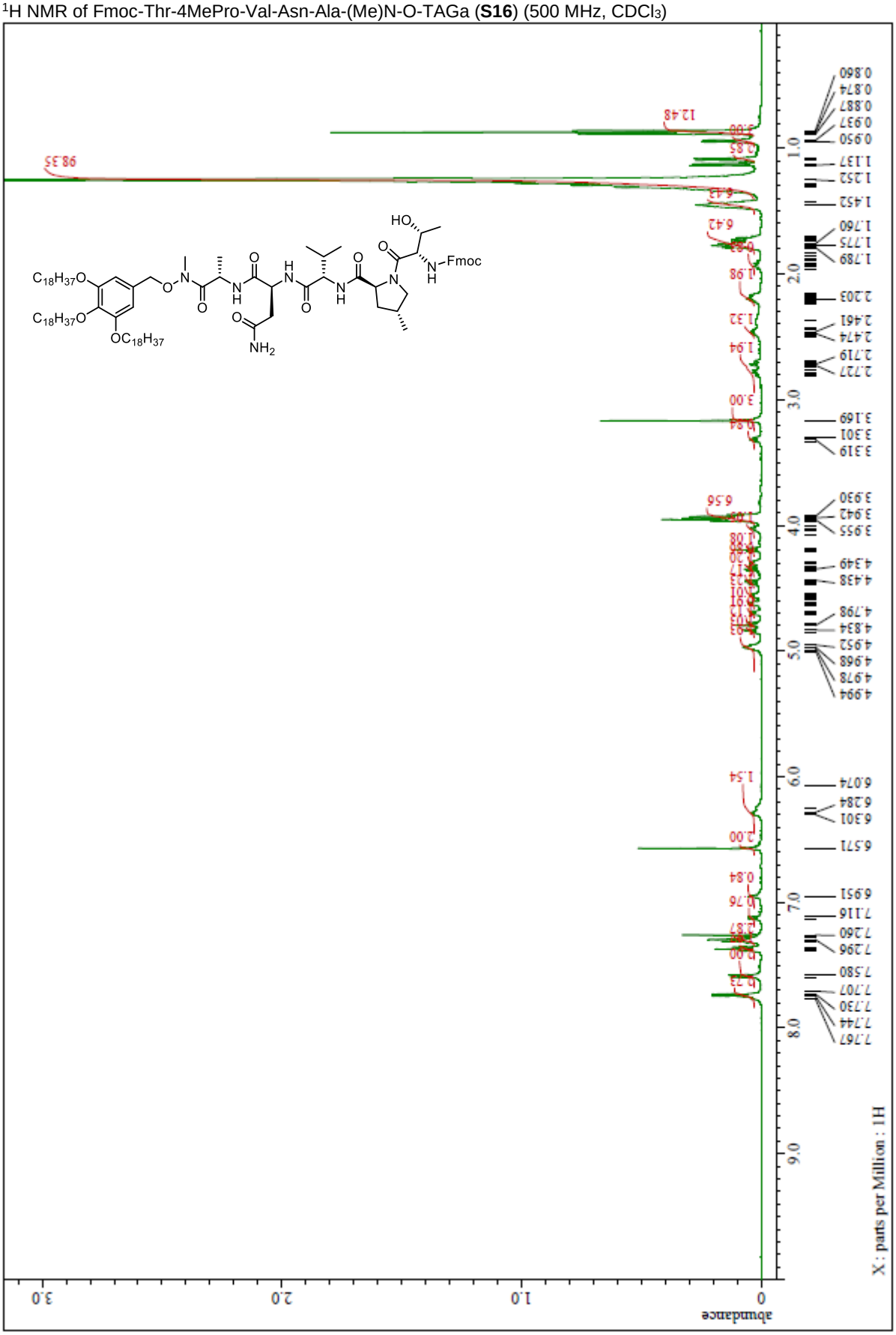
^{1}H NMR of 4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**7**) (500 MHz, $CDCl_3$)



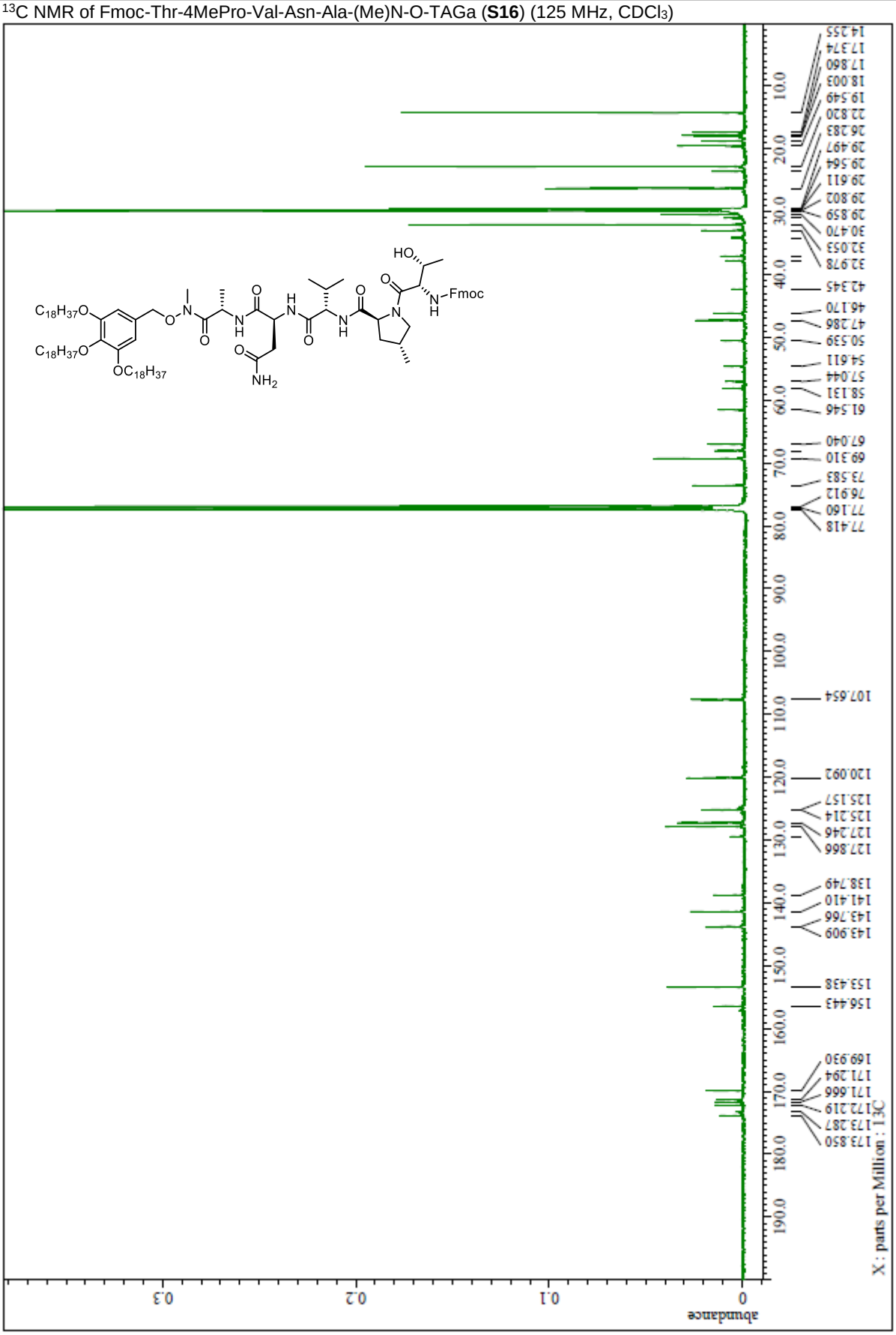
^{13}C NMR of 4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**7**) (125 MHz, $CDCl_3$)



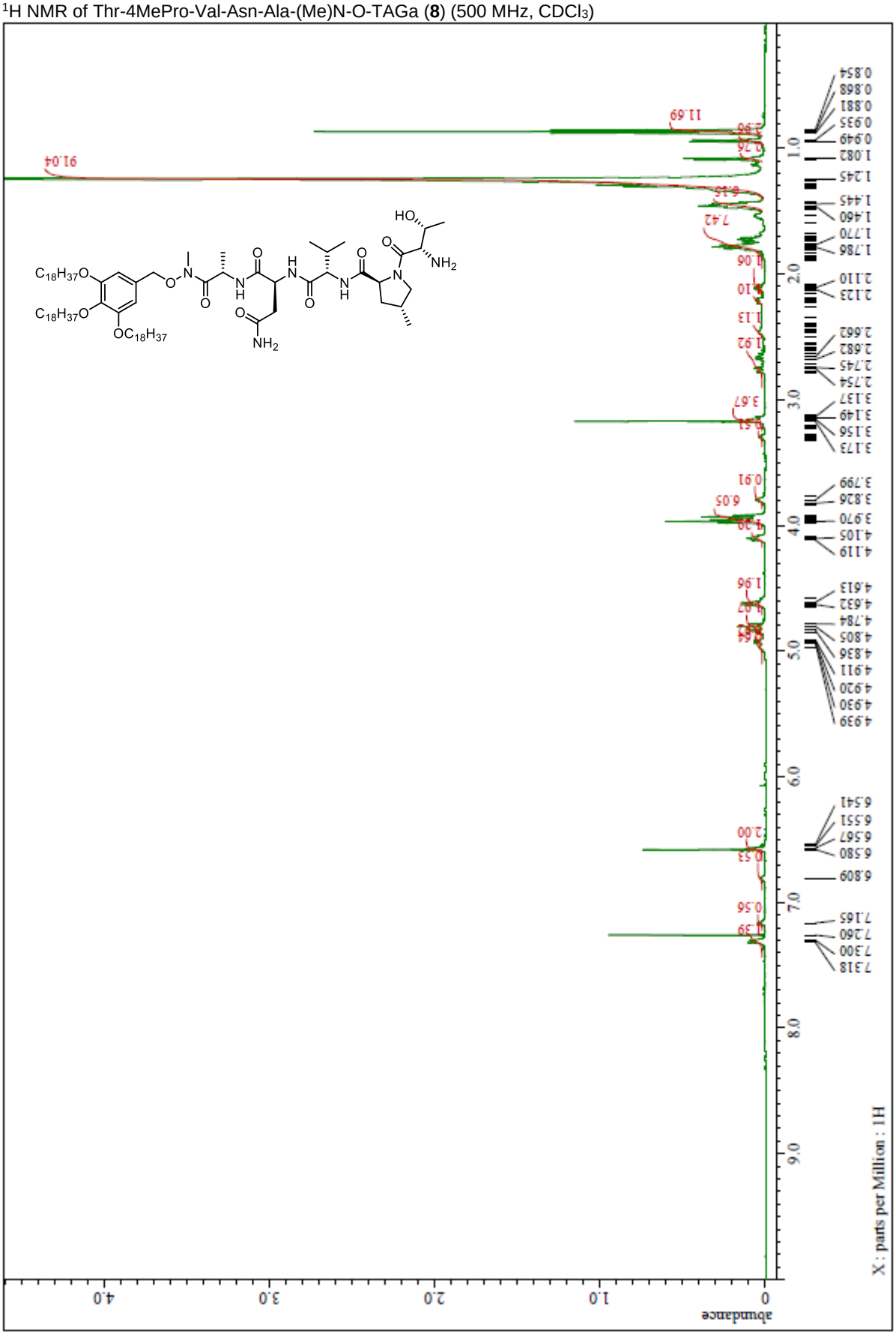
^{1}H NMR of Fmoc-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S16**) (500 MHz, $CDCl_3$)



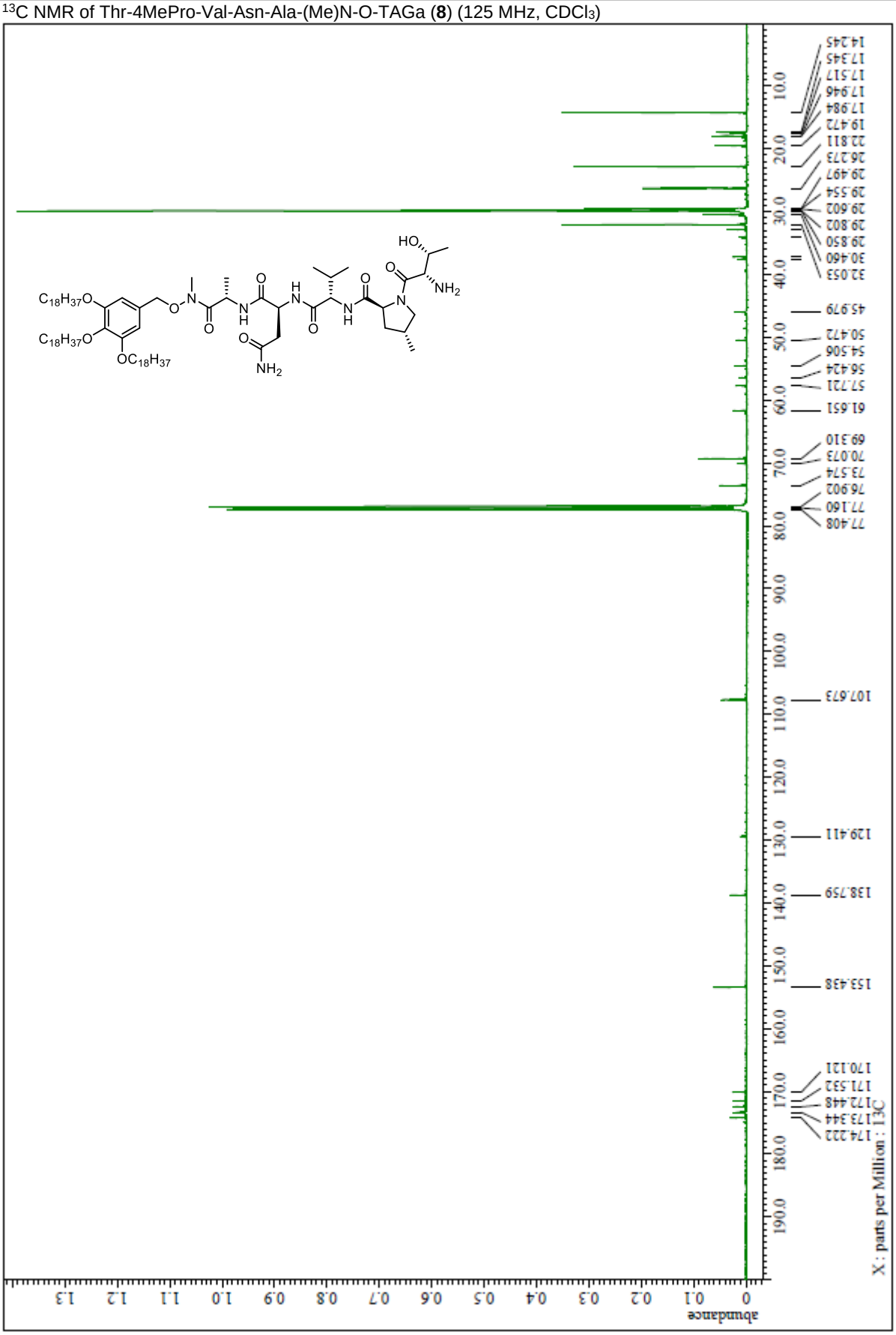
^{13}C NMR of Fmoc-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**S16**) (125 MHz, $CDCl_3$)



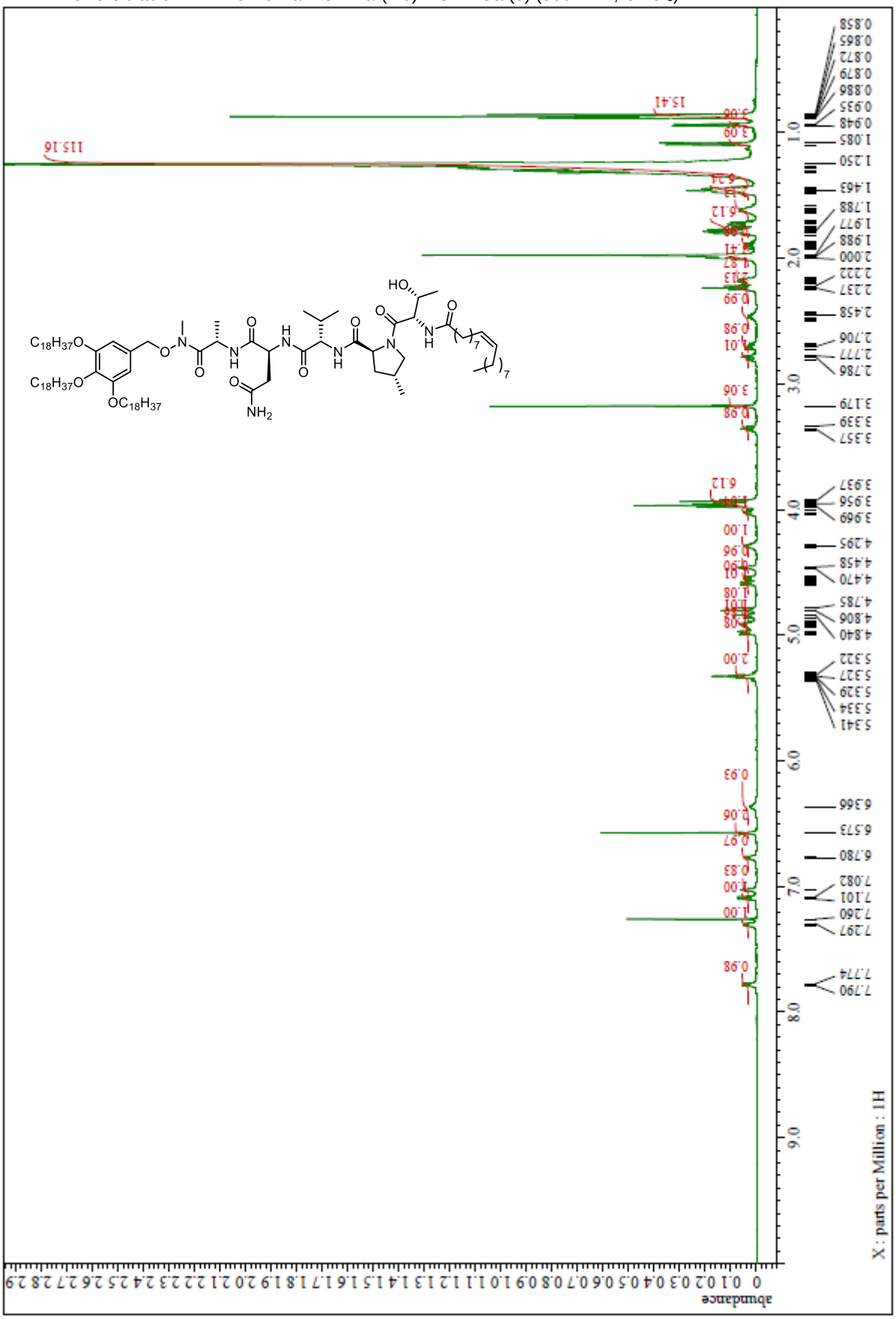
^{1}H NMR of Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**8**) (500 MHz, $CDCl_3$)



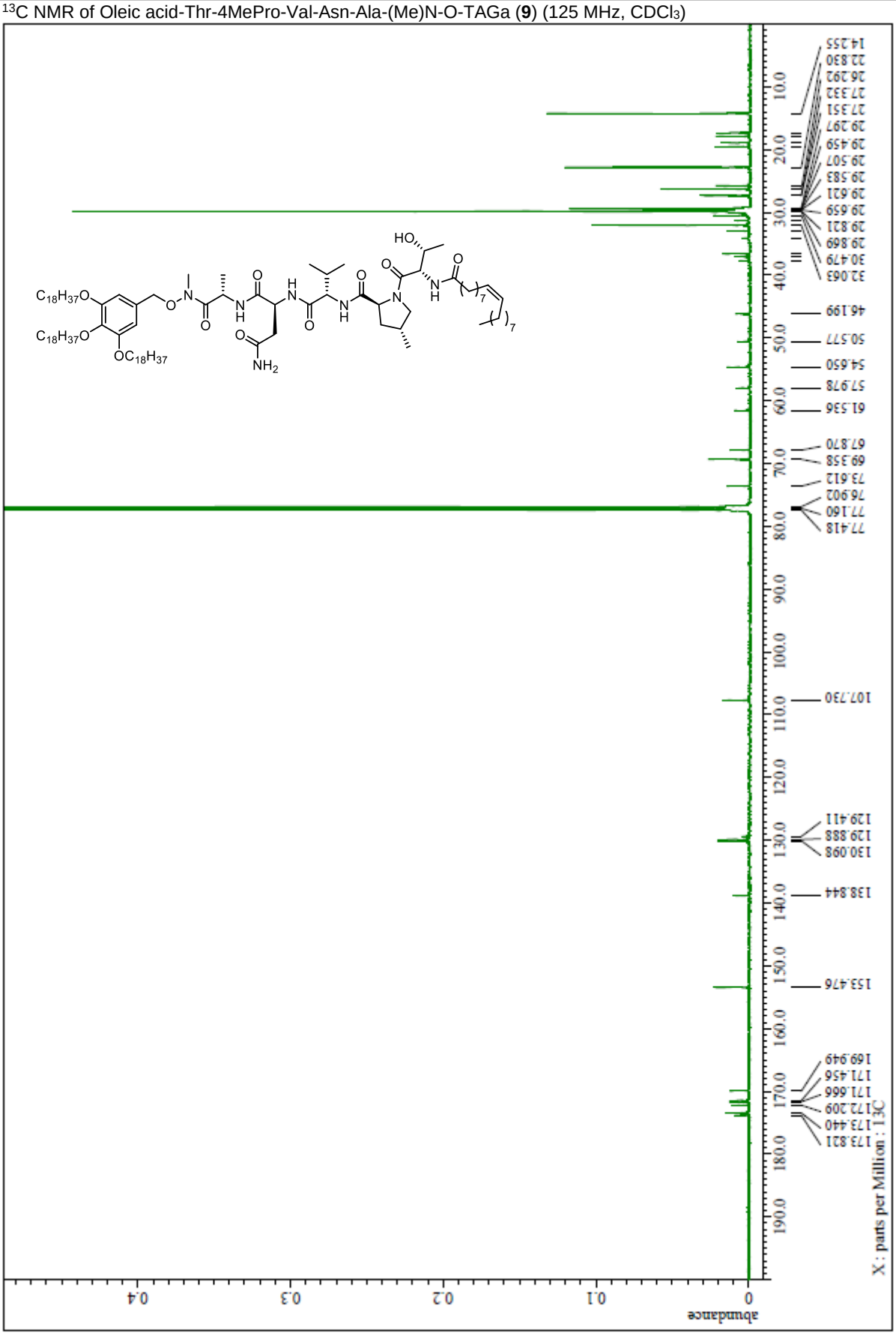
^{13}C NMR of Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**8**) (125 MHz, $CDCl_3$)



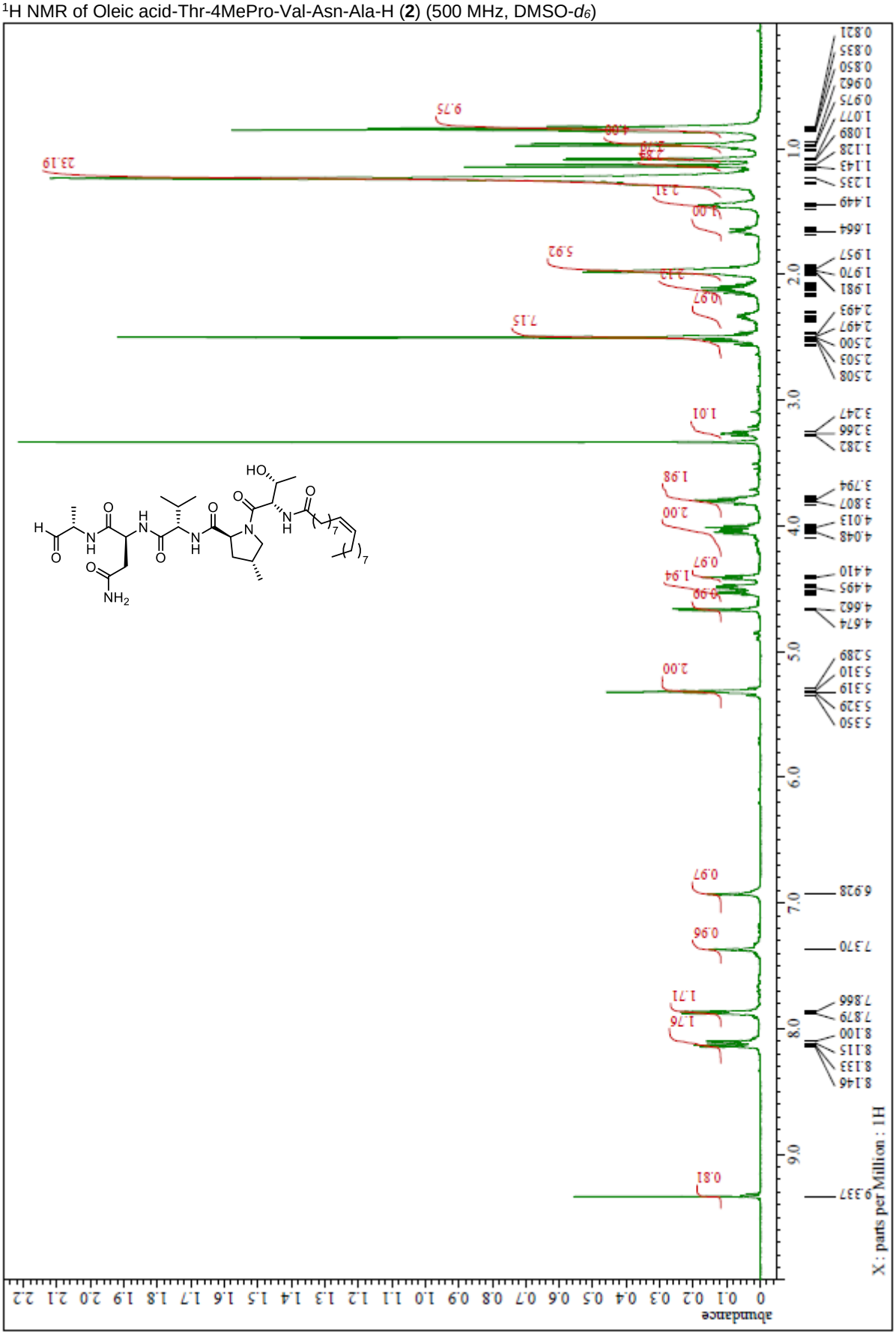
^{1}H NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**9**) (500 MHz, $CDCl_3$)



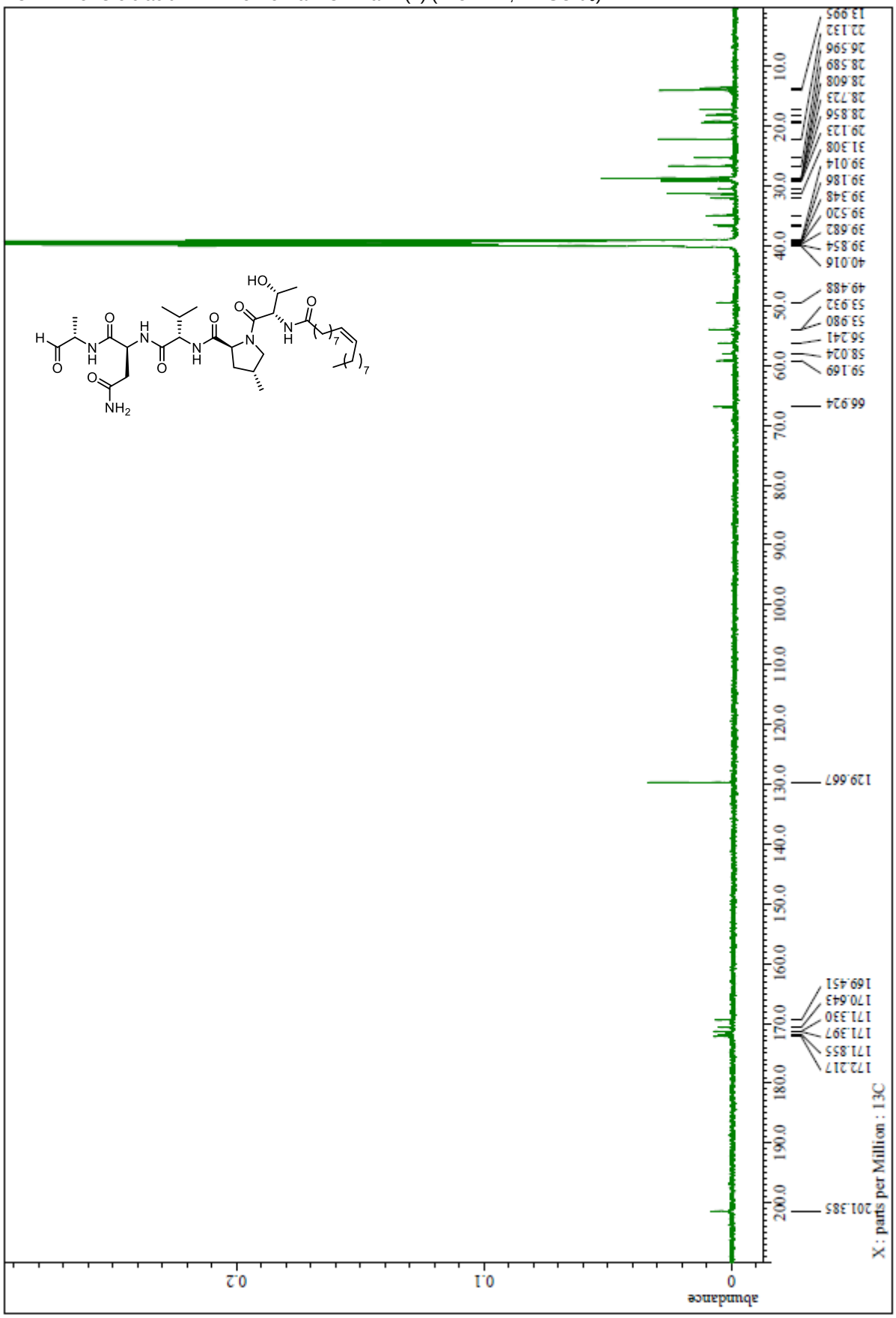
^{13}C NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**9**) (125 MHz, $CDCl_3$)



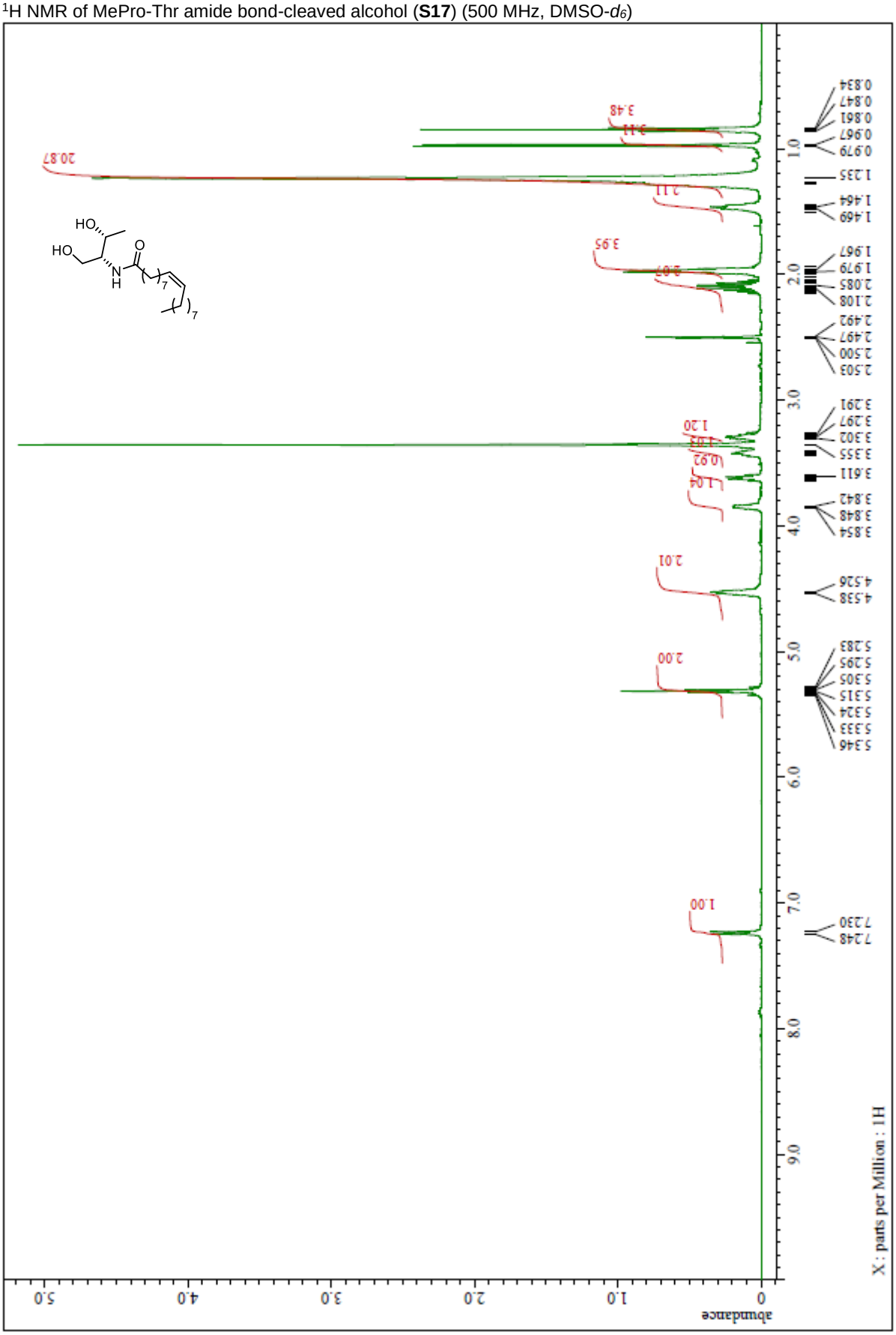
^{1}H NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-H (**2**) (500 MHz, DMSO-d_6)



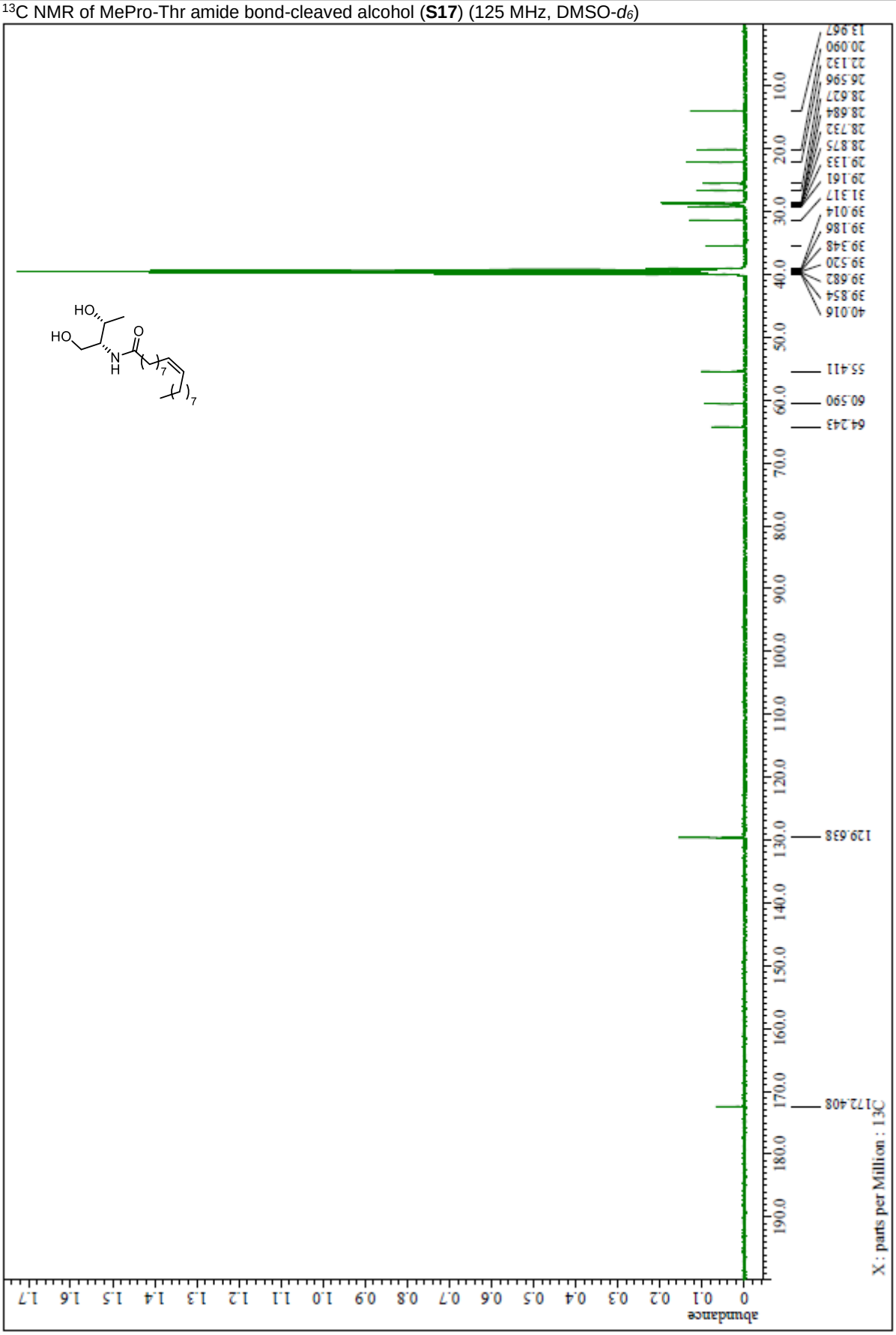
^{13}C NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-H (**2**) (125 MHz, DMSO-d_6)



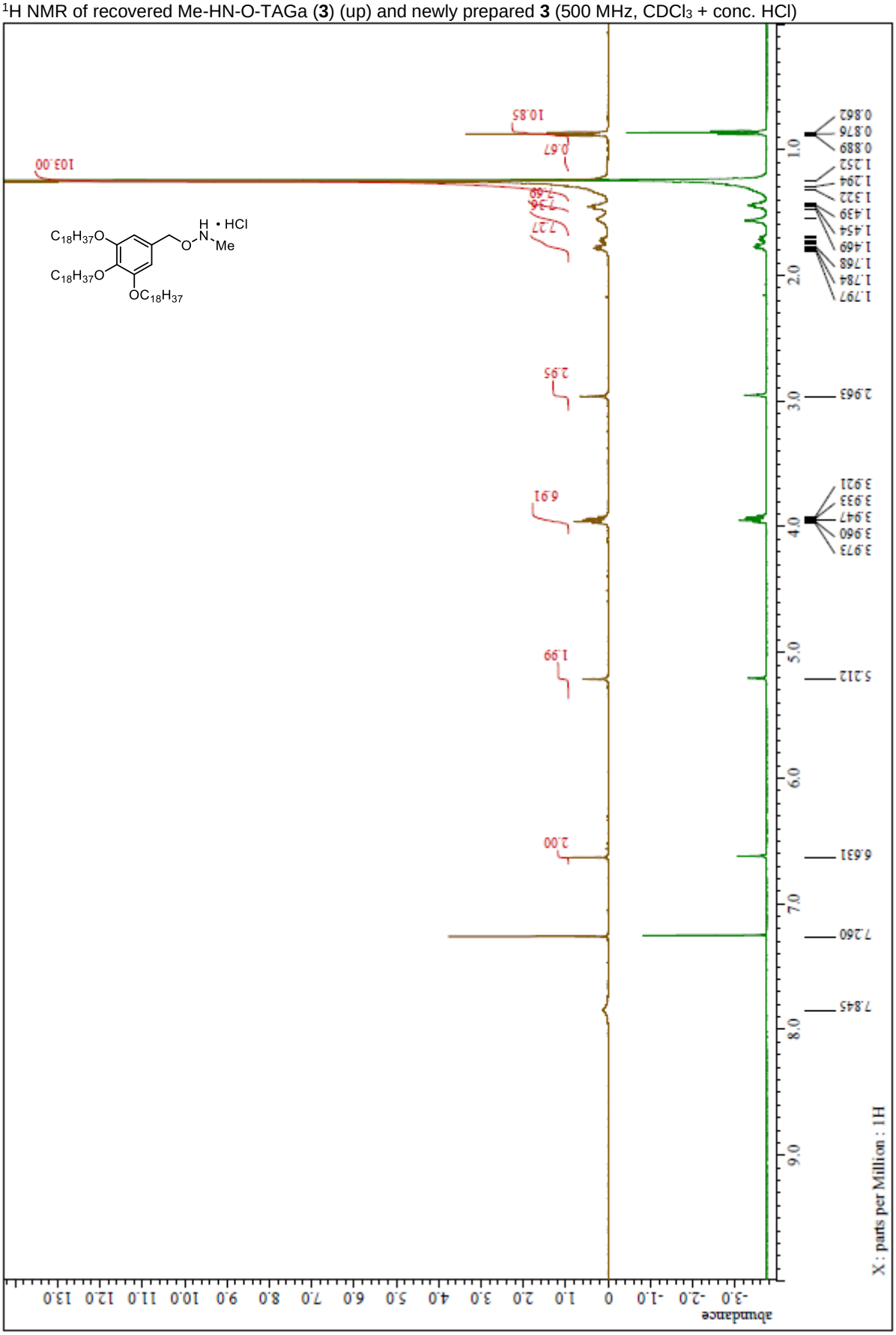
^{1}H NMR of MePro-Thr amide bond-cleaved alcohol (**S17**) (500 MHz, DMSO-d_6)



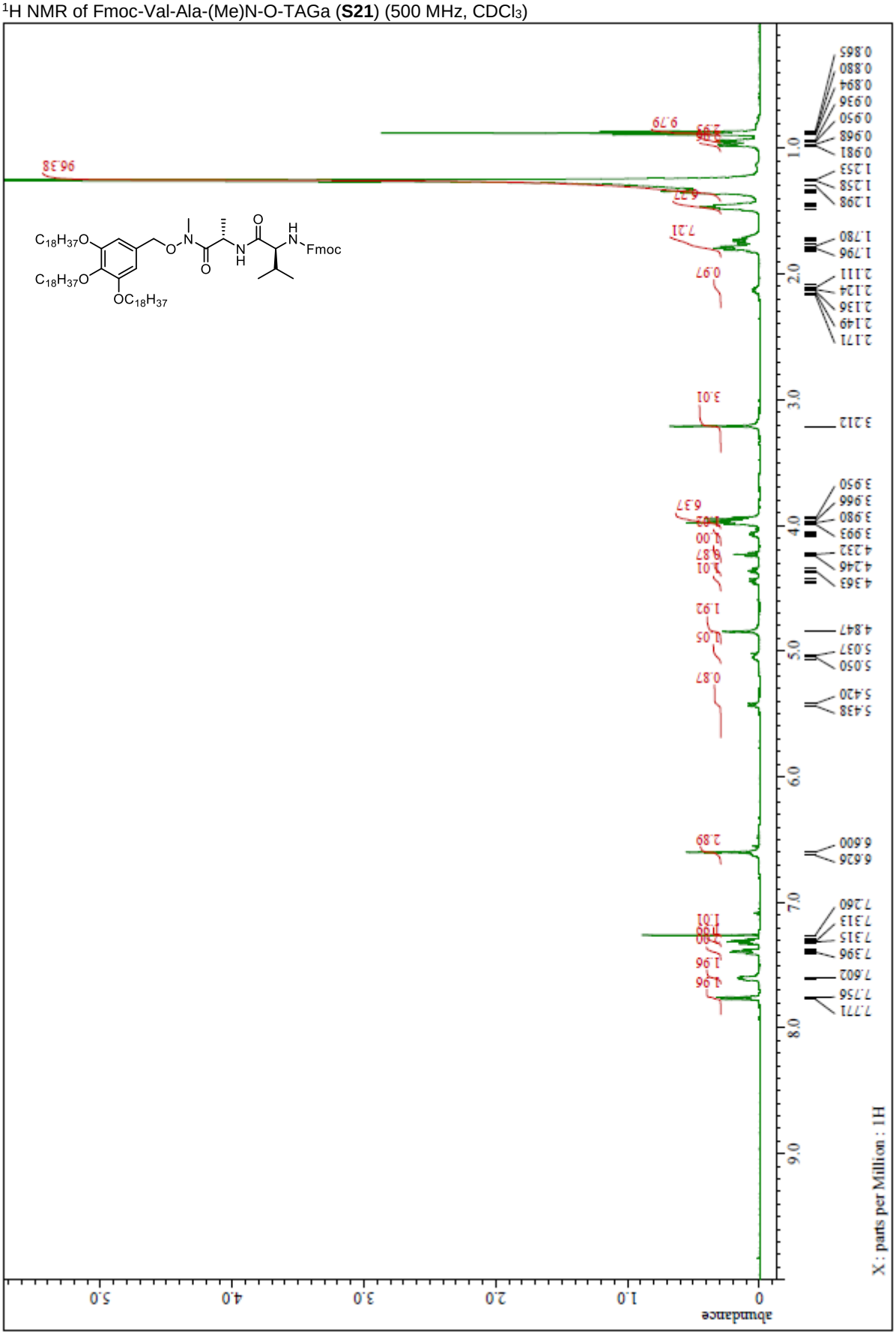
^{13}C NMR of MePro-Thr amide bond-cleaved alcohol (**S17**) (125 MHz, DMSO-d_6)



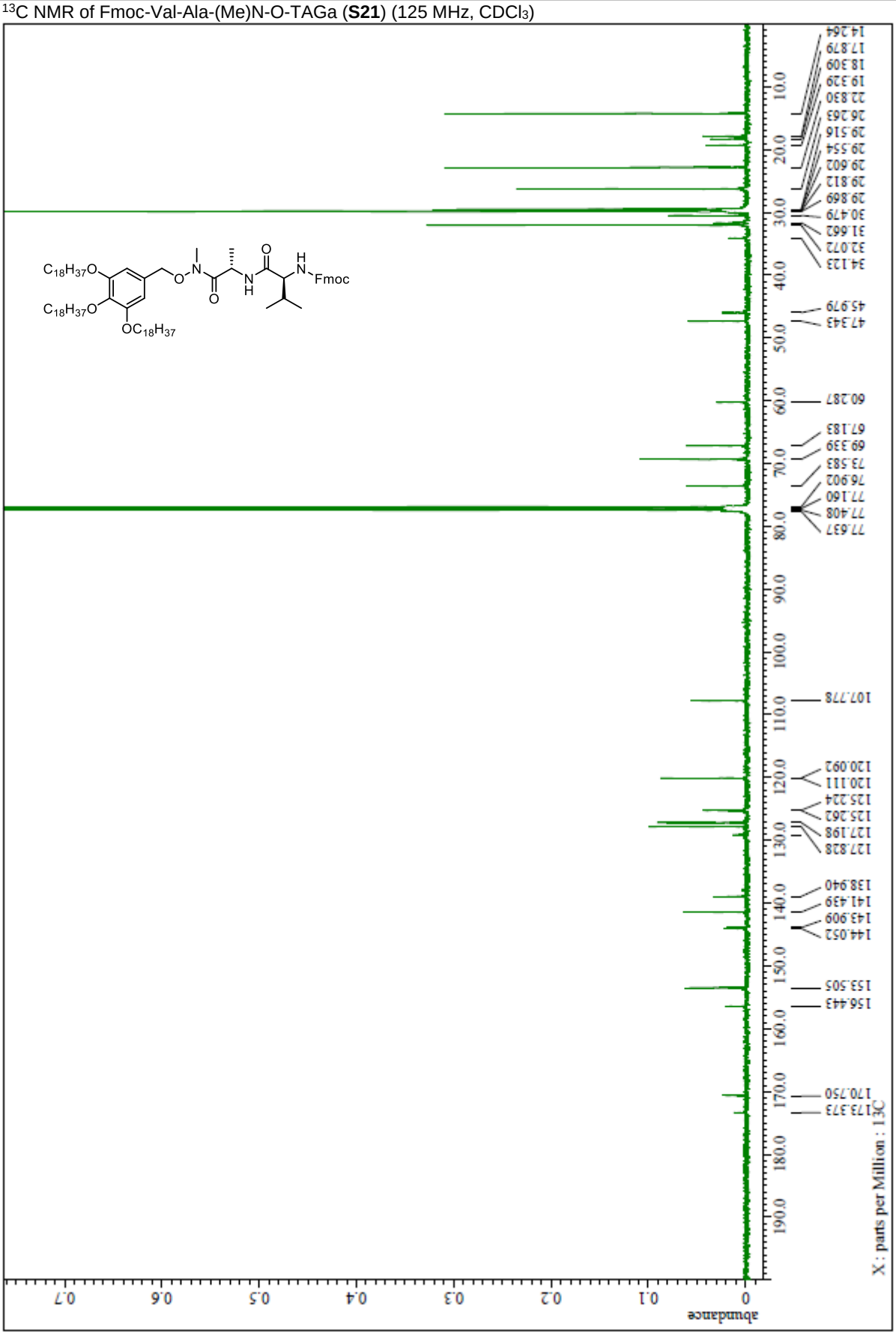
^{1}H NMR of recovered Me-HN-O-TAGa (**3**) (up) and newly prepared **3** (500 MHz, $CDCl_3$ + conc. HCl)



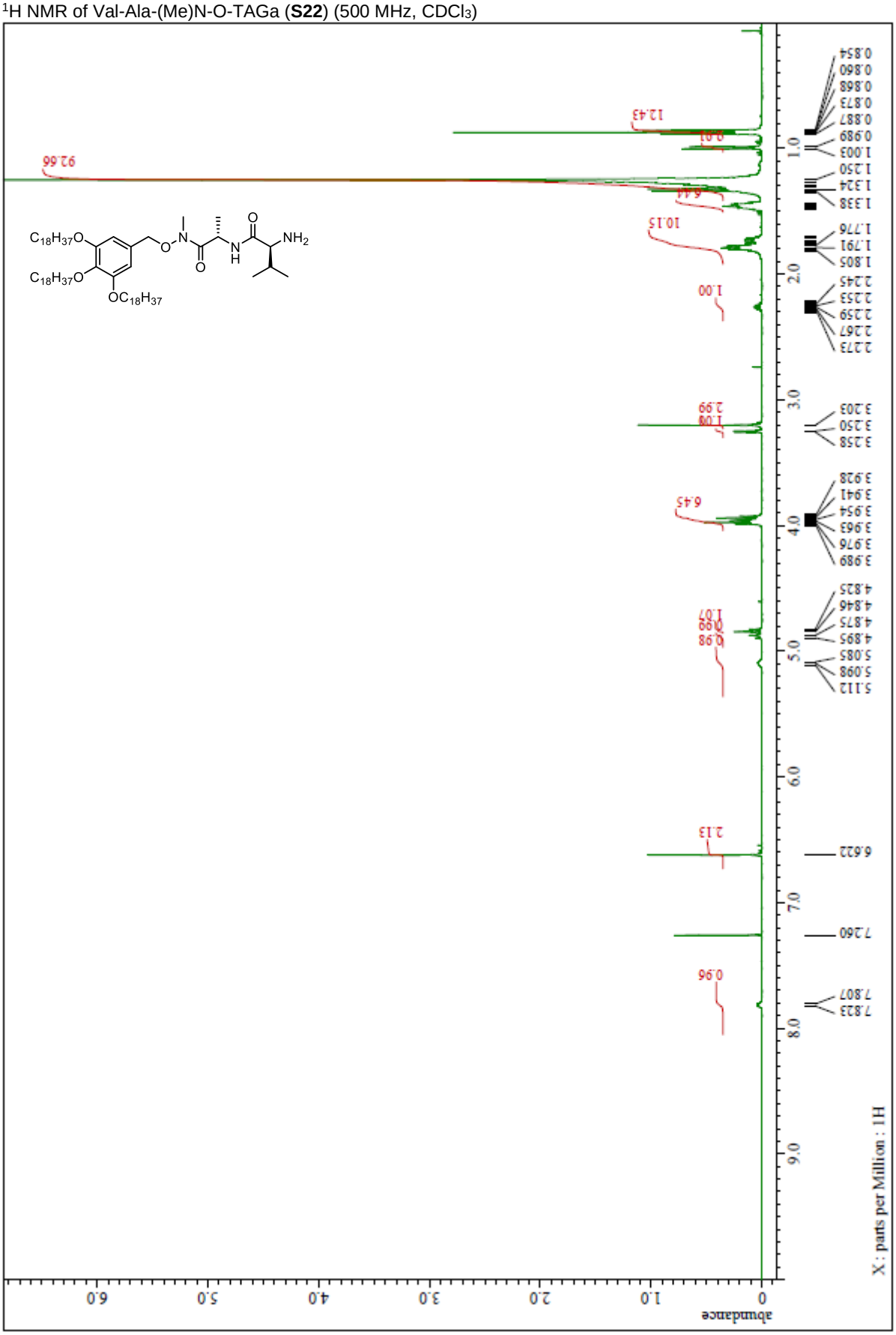
^{1}H NMR of Fmoc-Val-Ala-(Me)N-O-TAGa (**S21**) (500 MHz, $CDCl_3$)



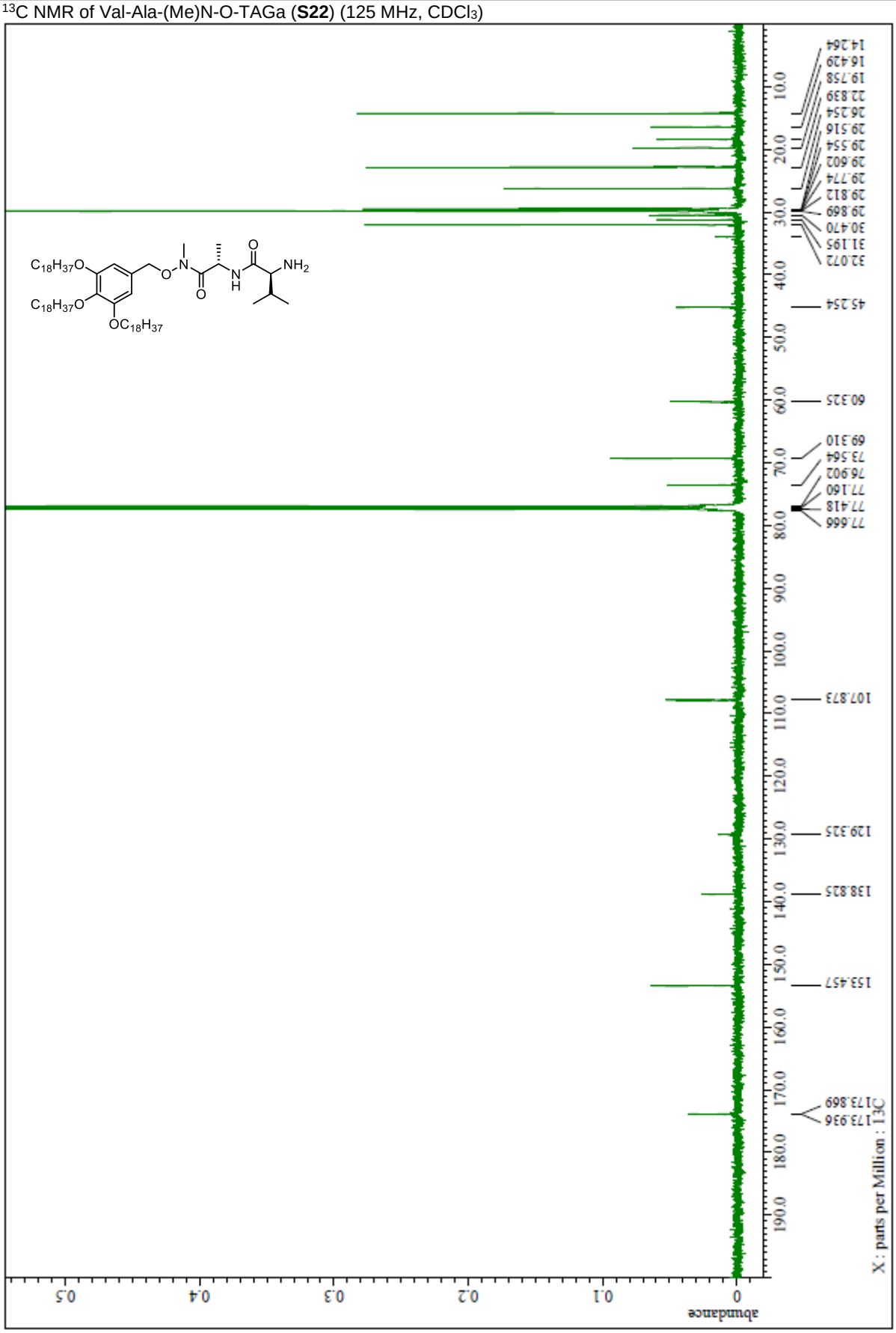
^{13}C NMR of Fmoc-Val-Ala-(Me)N-O-TAGa (**S21**) (125 MHz, $CDCl_3$)



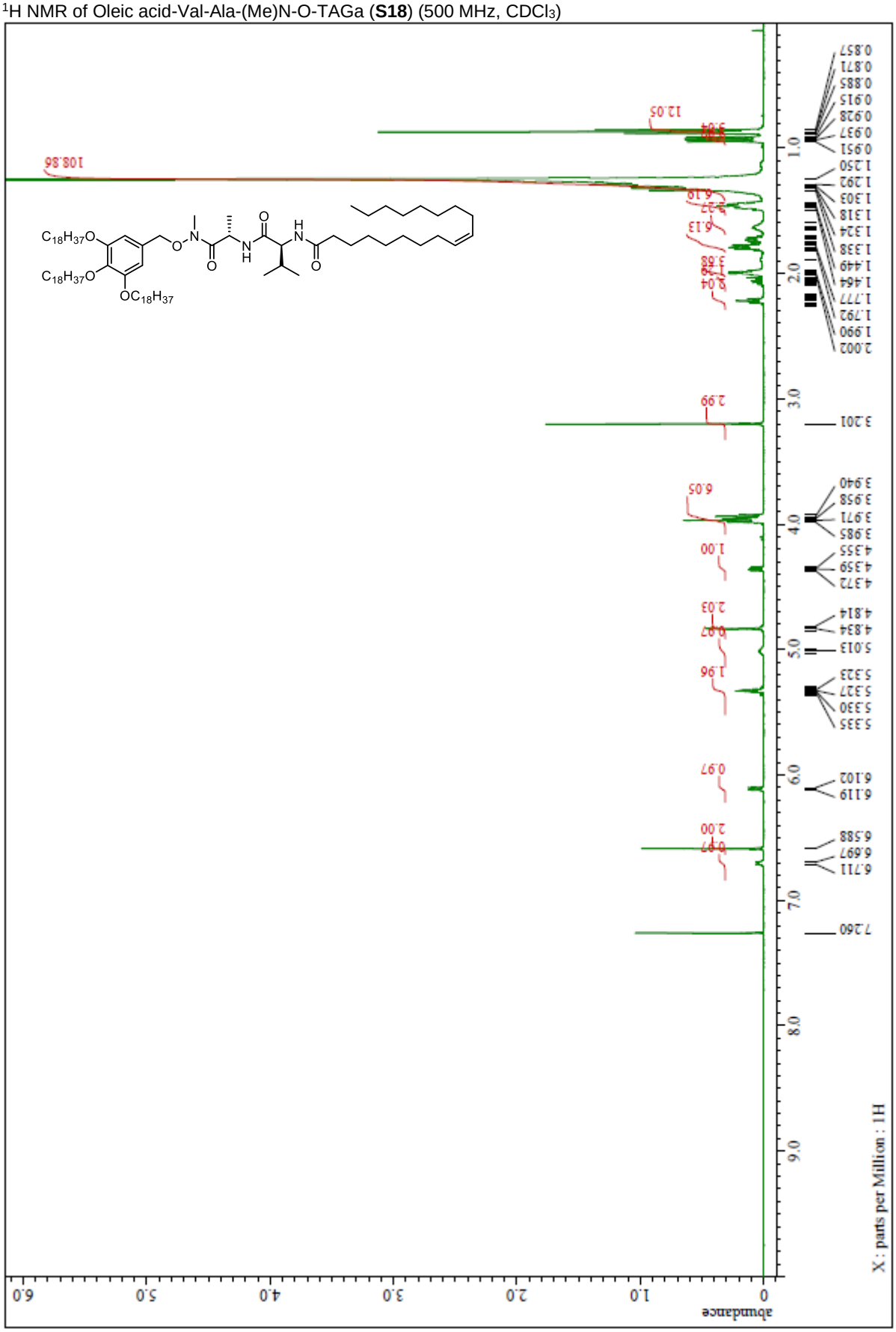
^{1}H NMR of Val-Ala-(Me)N-O-TAGa (**S22**) (500 MHz, $CDCl_3$)



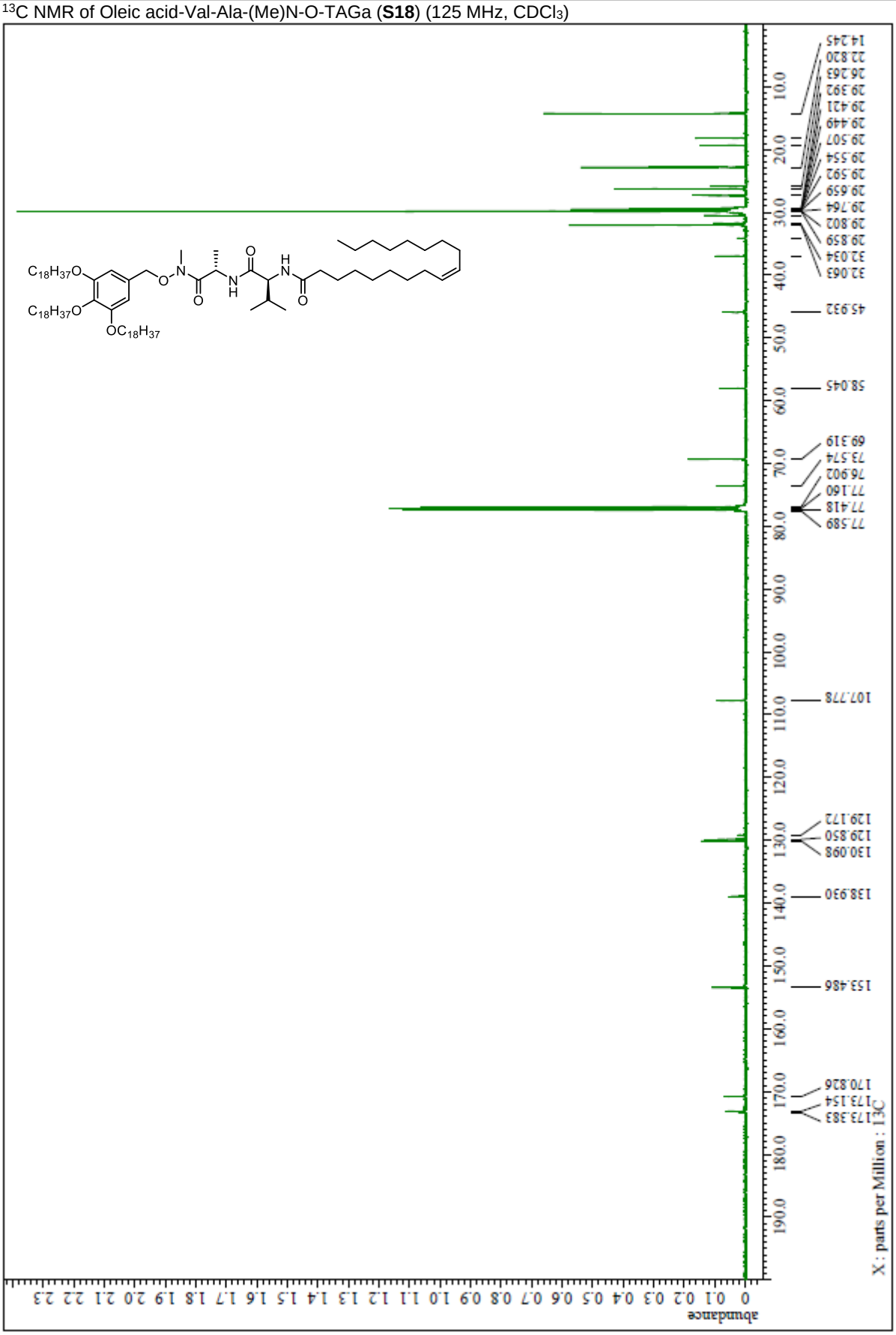
^{13}C NMR of Val-Ala-(Me)N-O-TAGa (**S22**) (125 MHz, $CDCl_3$)



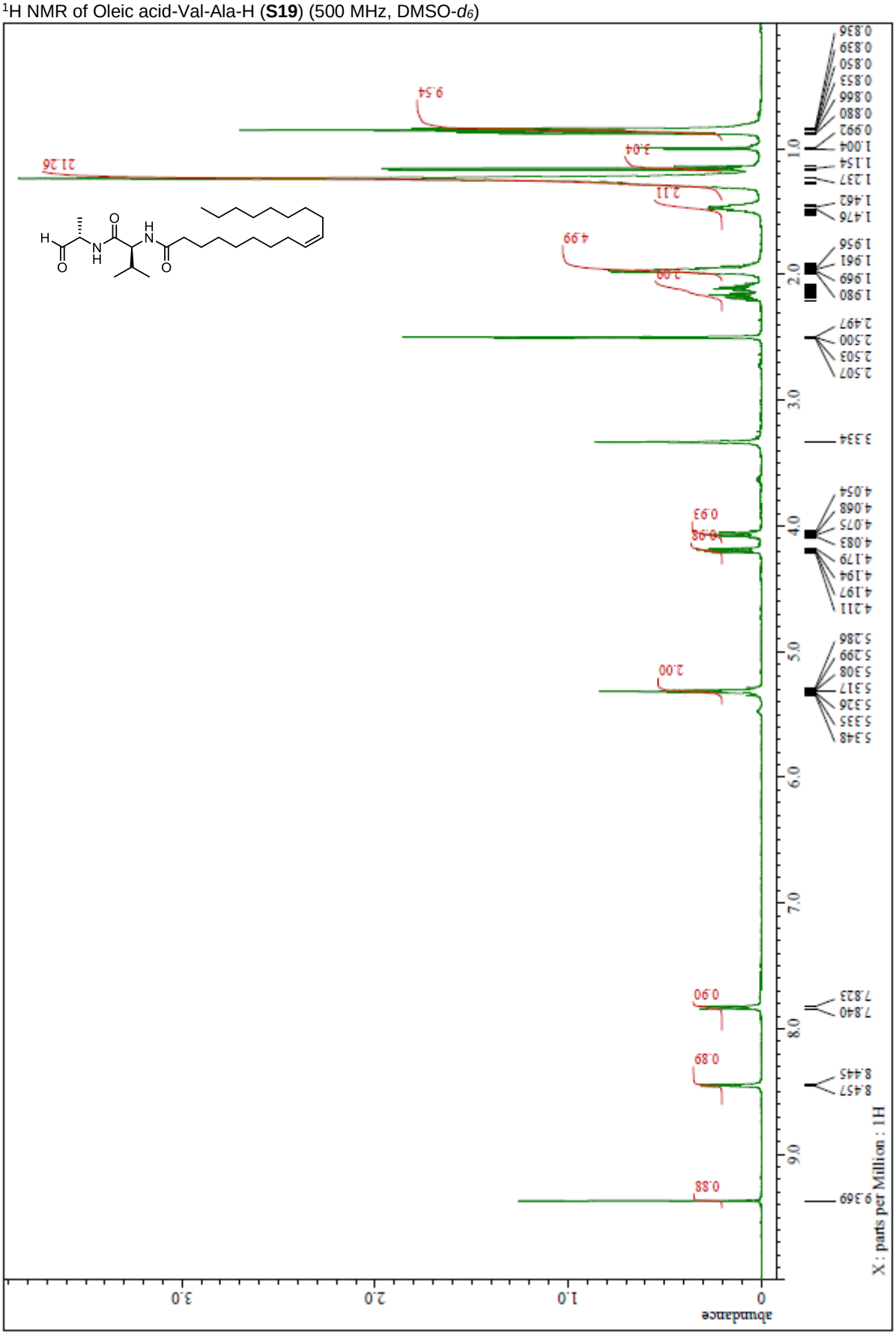
^{1}H NMR of Oleic acid-Val-Ala-(Me)N-O-TAGa (**S18**) (500 MHz, $CDCl_3$)



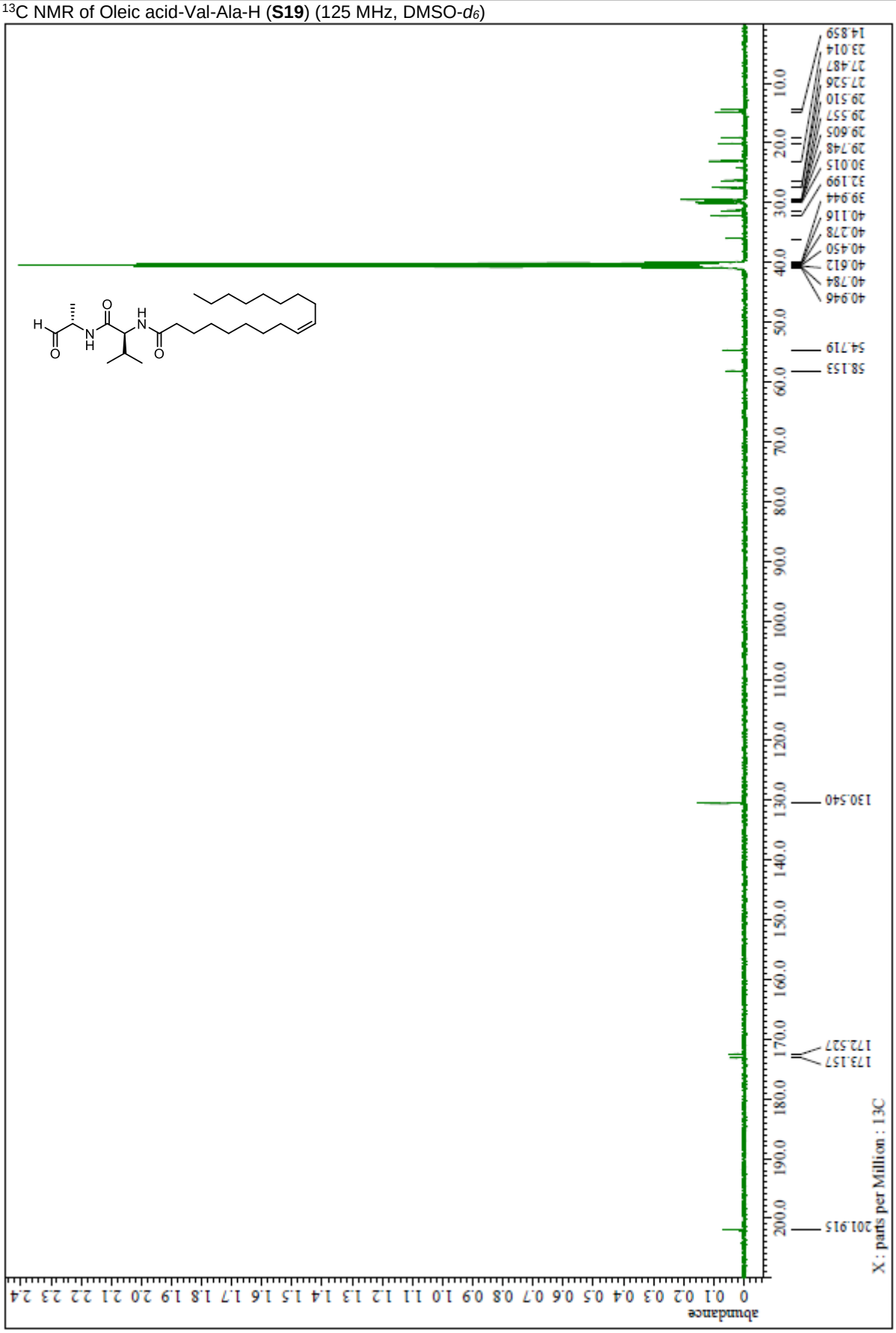
^{13}C NMR of Oleic acid-Val-Ala-(Me)N-O-TAGa (**S18**) (125 MHz, $CDCl_3$)



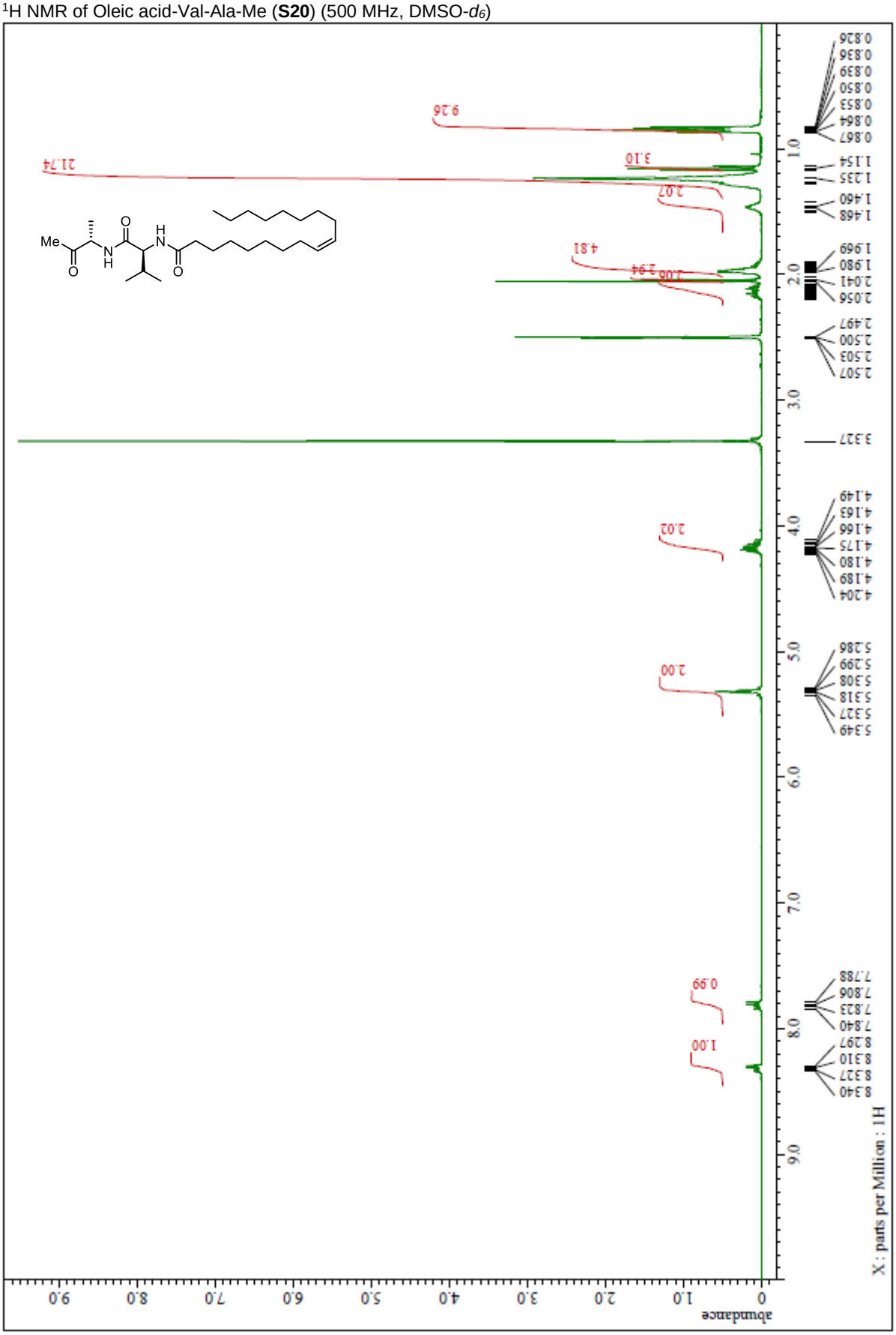
^{1}H NMR of Oleic acid-Val-Ala-H (**S19**) (500 MHz, DMSO-d_6)



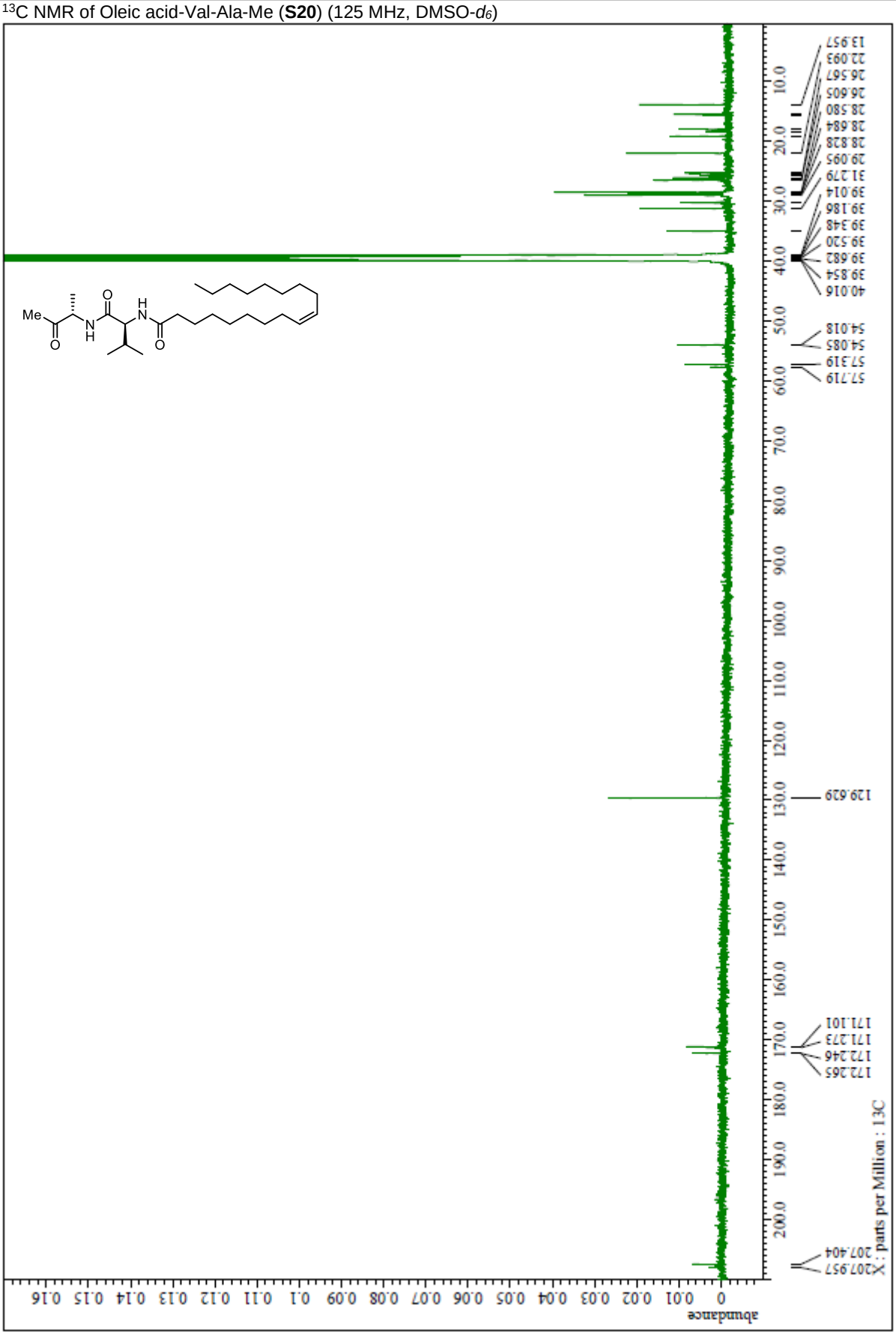
^{13}C NMR of Oleic acid-Val-Ala-H (**S19**) (125 MHz, DMSO-d_6)



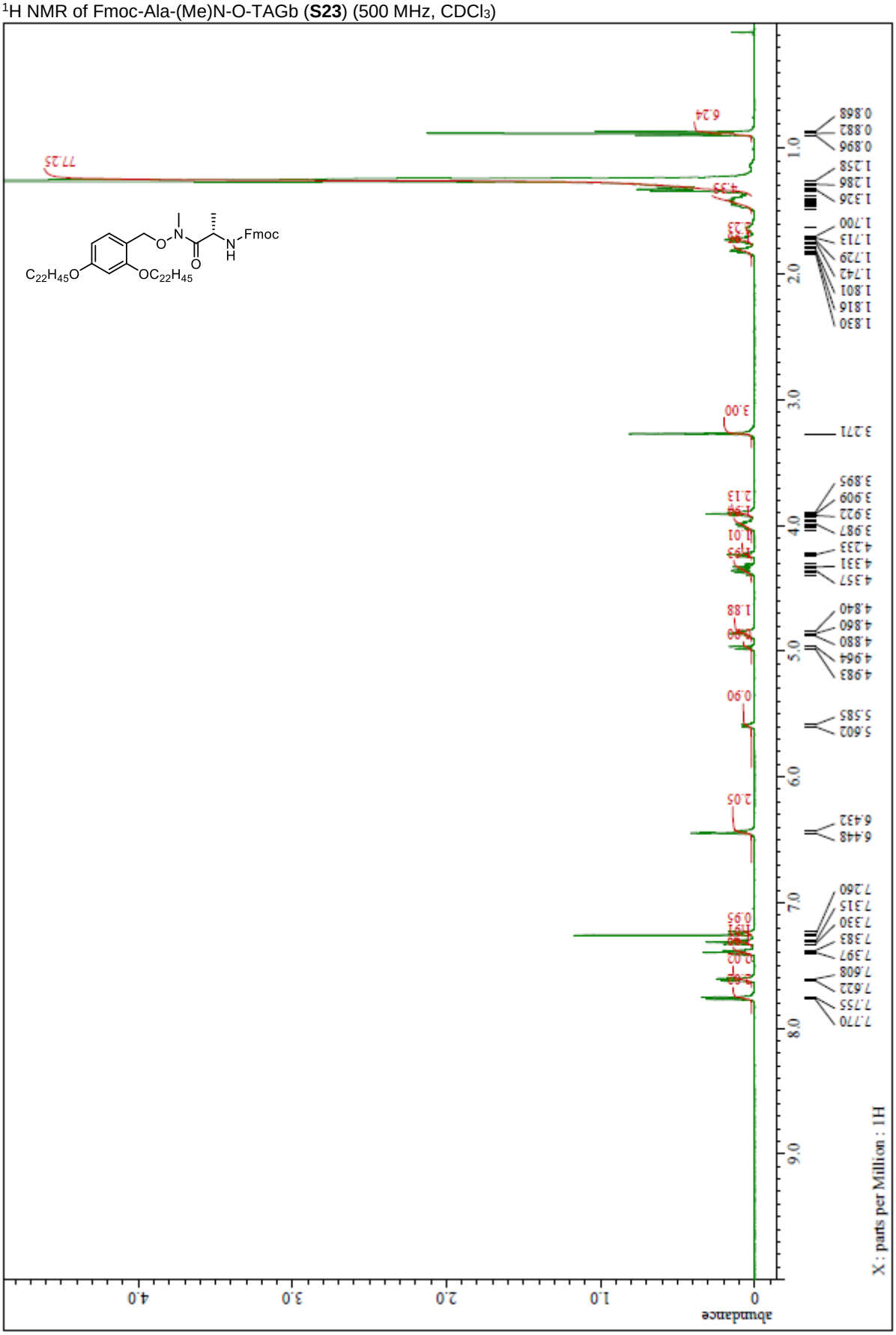
^{1}H NMR of Oleic acid-Val-Ala-Me (**S20**) (500 MHz, DMSO-d_6)



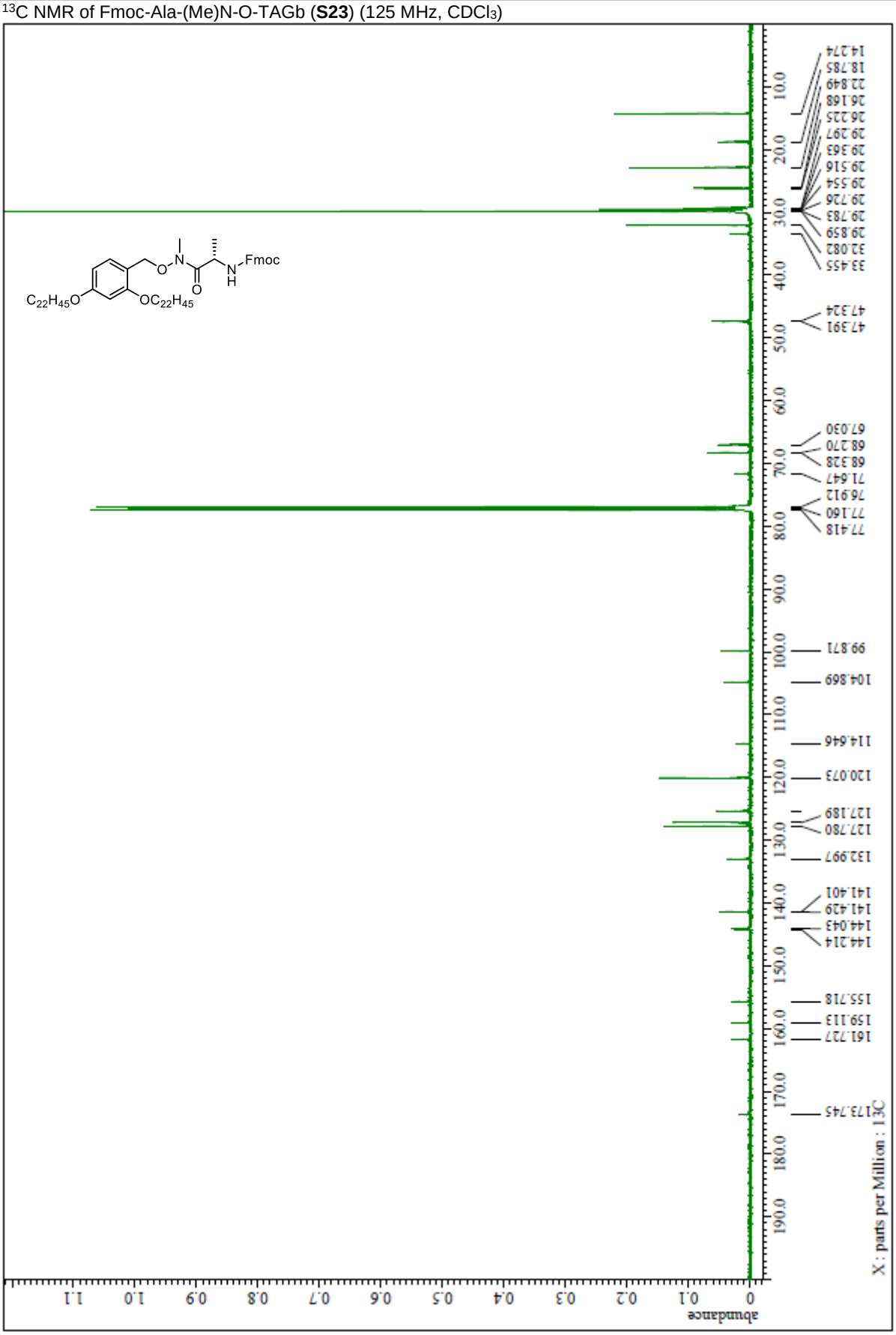
^{13}C NMR of Oleic acid-Val-Ala-Me (**S20**) (125 MHz, DMSO-d_6)



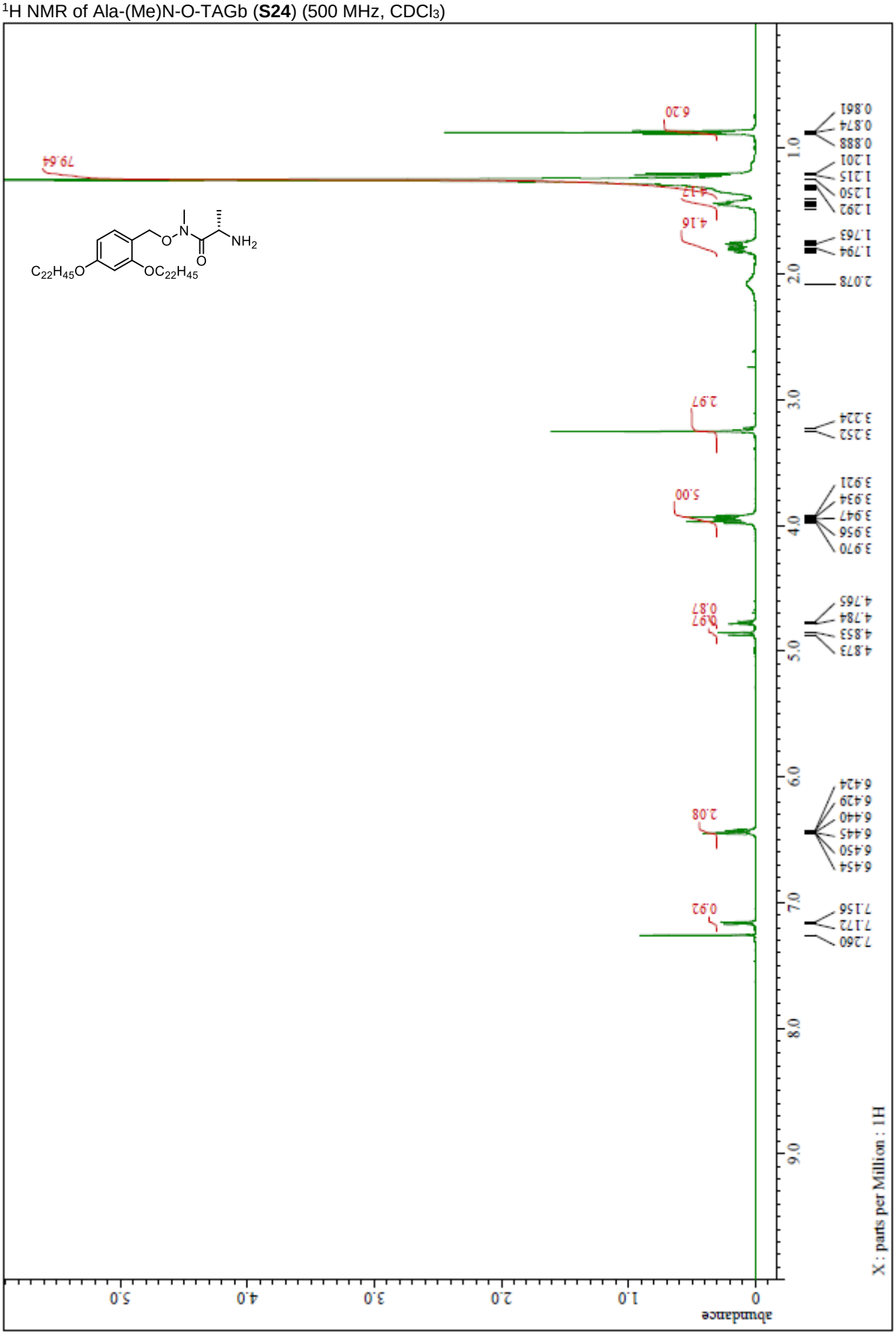
^{1}H NMR of Fmoc-Ala-(Me)N-O-TAGb (**S23**) (500 MHz, $CDCl_3$)



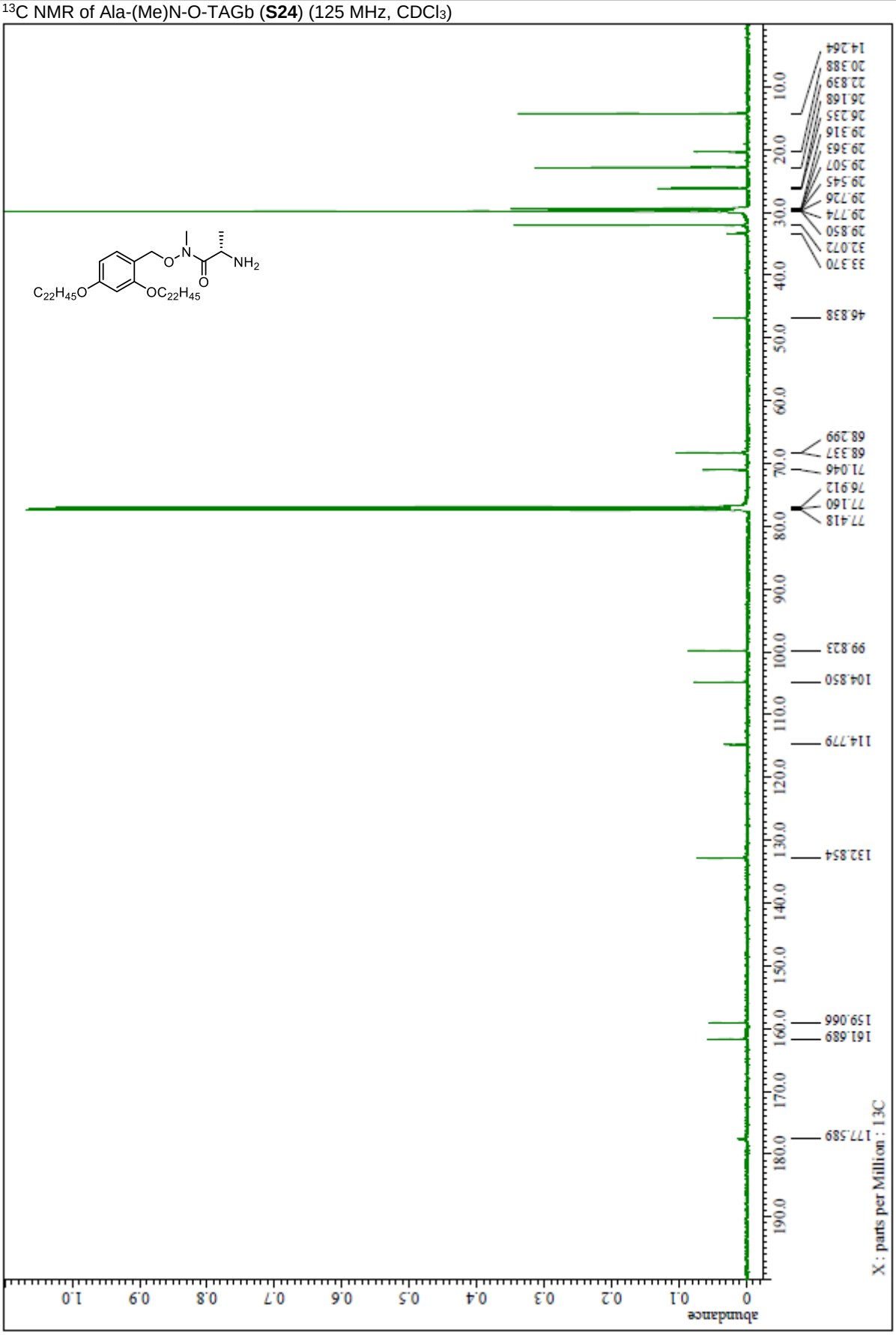
^{13}C NMR of Fmoc-Ala-(Me)N-O-TAGb (**S23**) (125 MHz, $CDCl_3$)



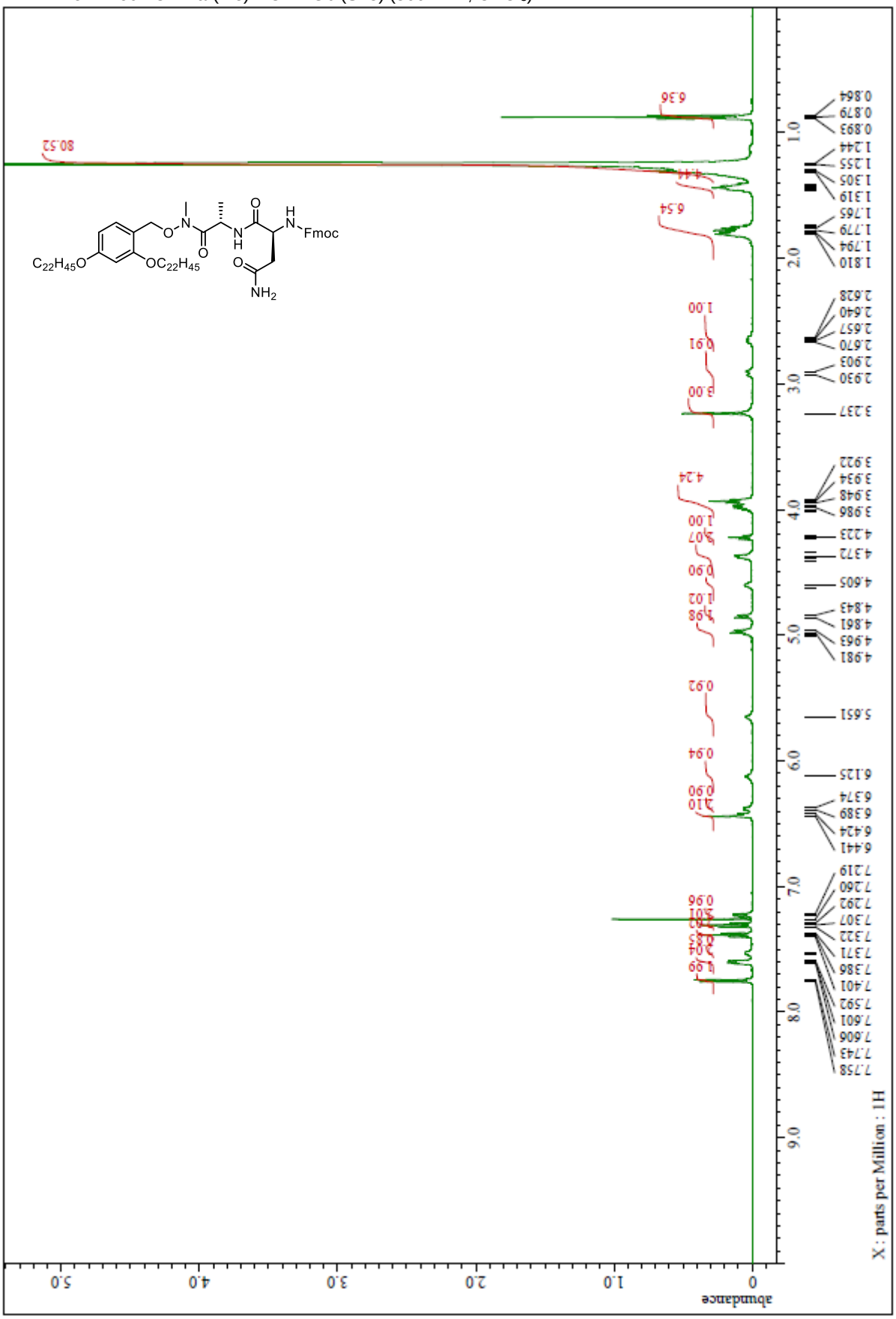
^{1}H NMR of Ala-(Me)N-O-TAGb (**S24**) (500 MHz, $CDCl_3$)



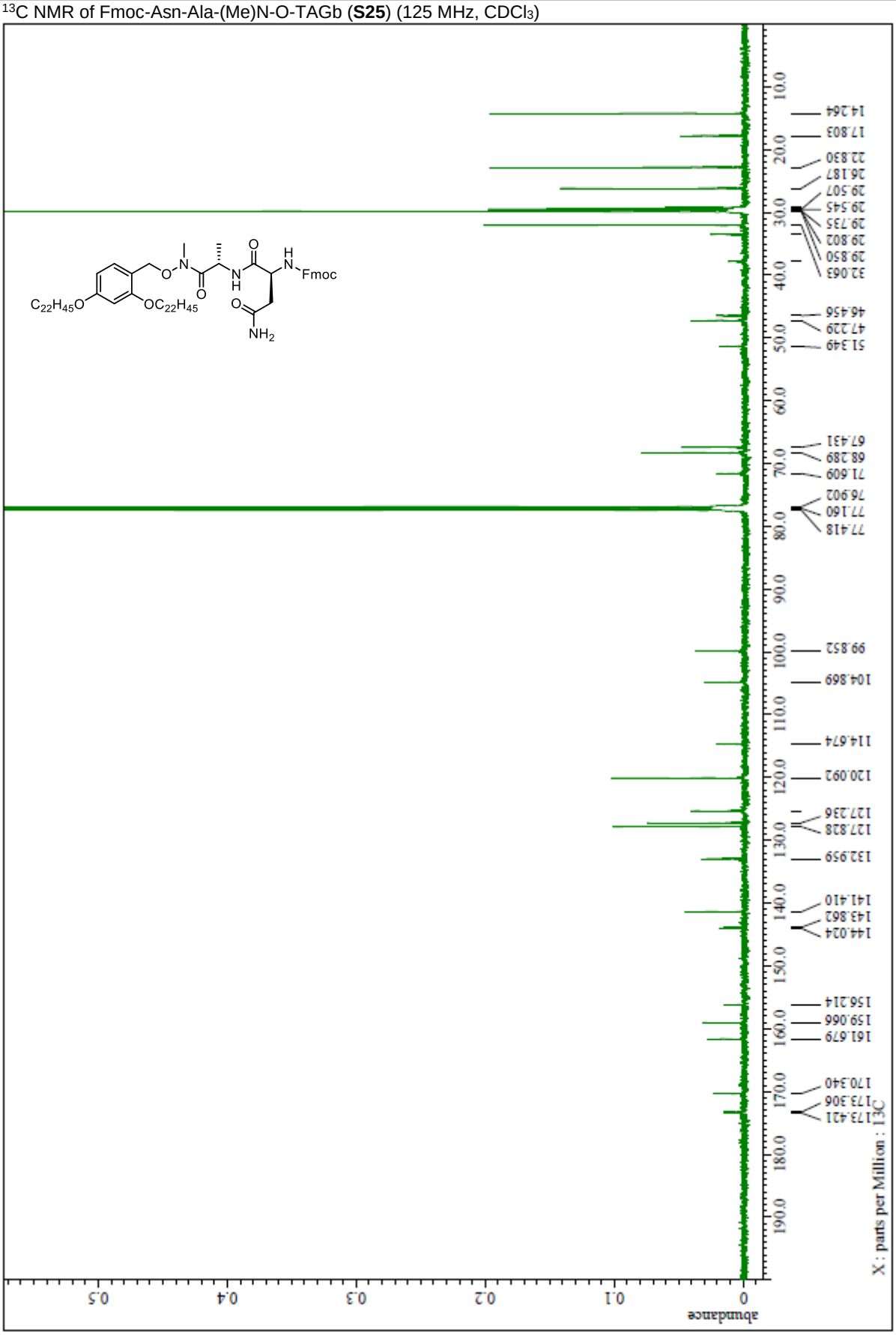
^{13}C NMR of Ala-(Me)N-O-TAGb (**S24**) (125 MHz, $CDCl_3$)



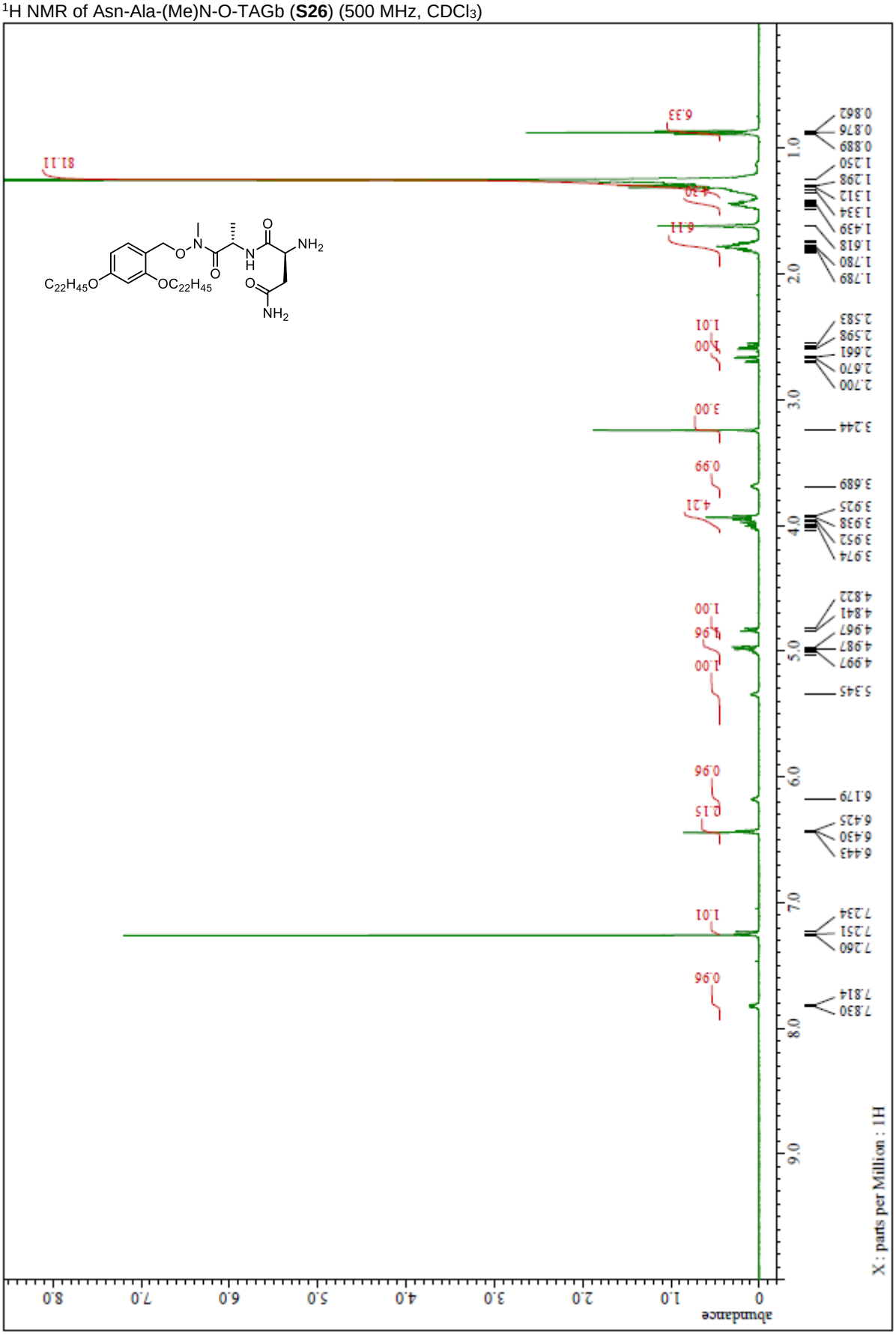
^{1}H NMR of Fmoc-Asn-Ala-(Me)N-O-TAGb (**S25**) (500 MHz, $CDCl_3$)



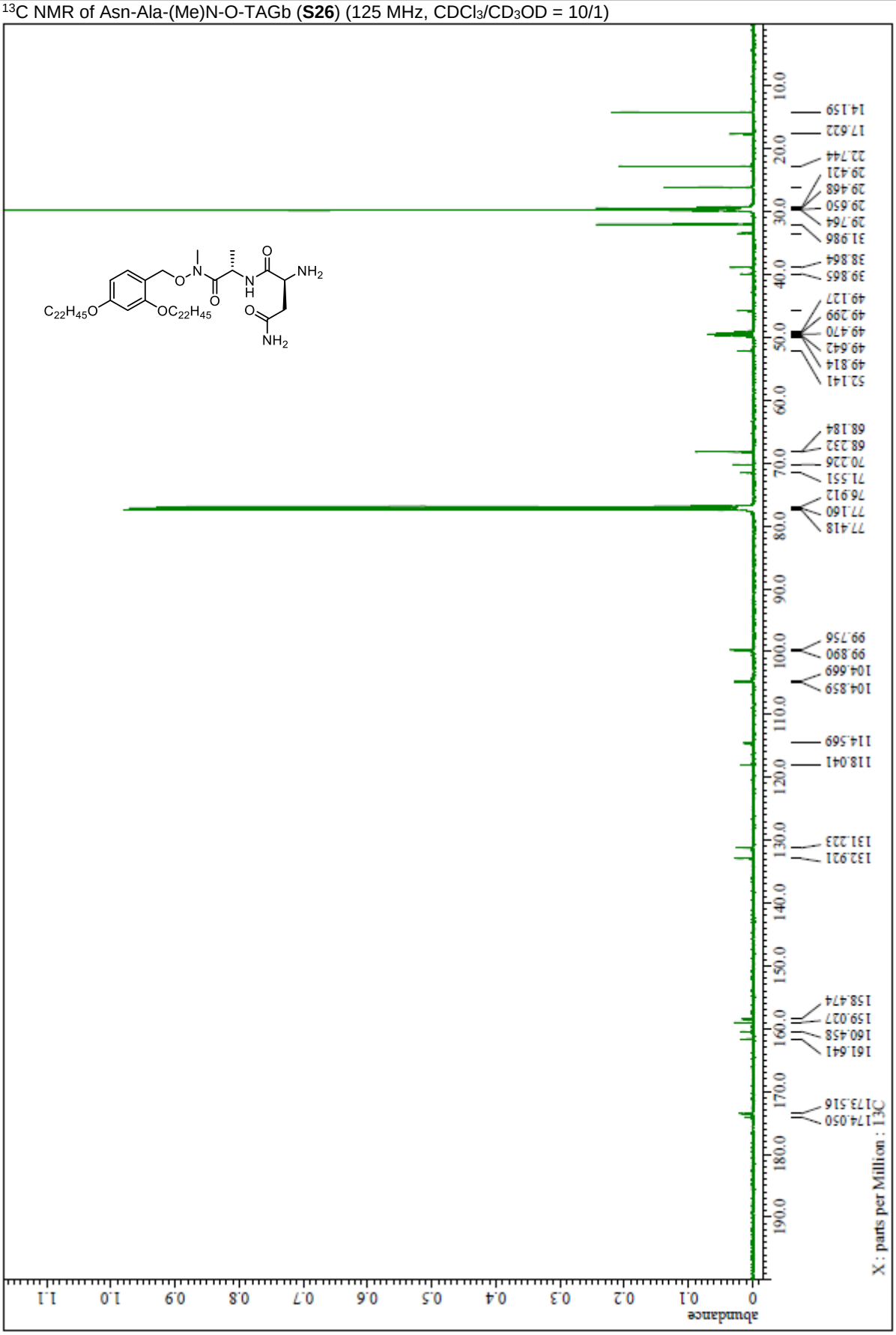
^{13}C NMR of Fmoc-Asn-Ala-(Me)N-O-TAGb (**S25**) (125 MHz, $CDCl_3$)



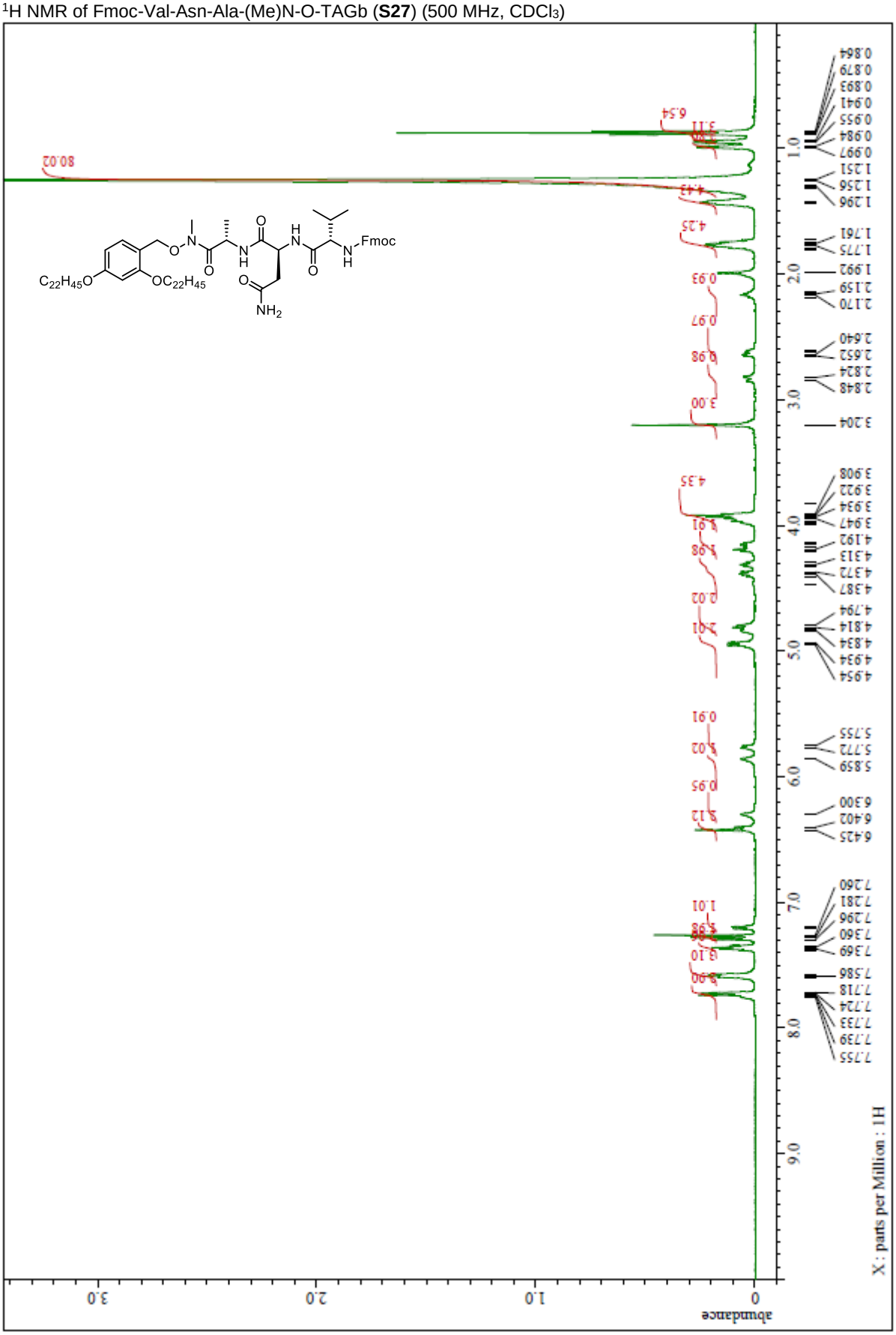
^{1}H NMR of Asn-Ala-(Me)N-O-TAGb (**S26**) (500 MHz, $CDCl_3$)



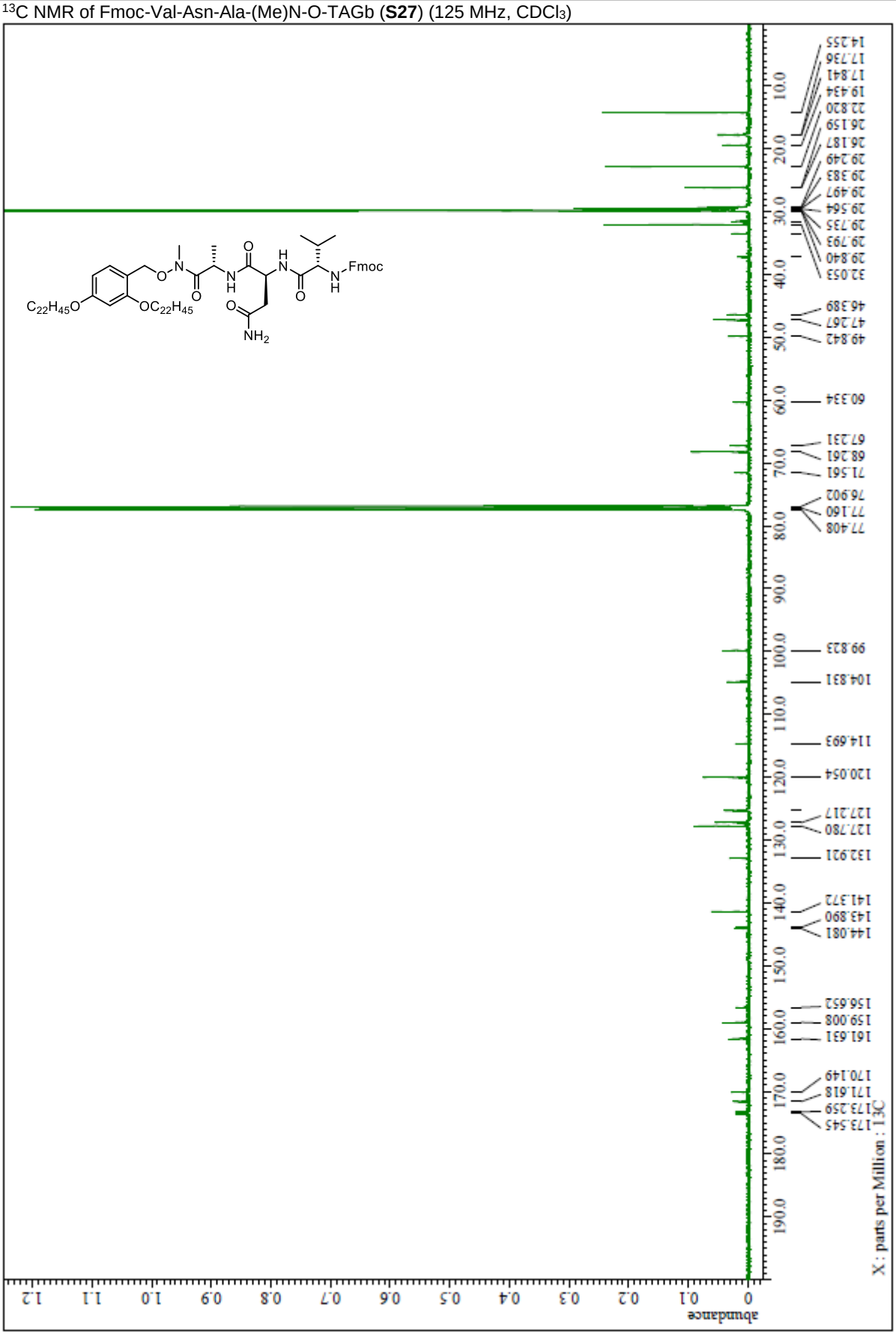
^{13}C NMR of Asn-Ala-(Me)N-O-TAGb (**S26**) (125 MHz, $CDCl_3/CD_3OD$ = 10/1)



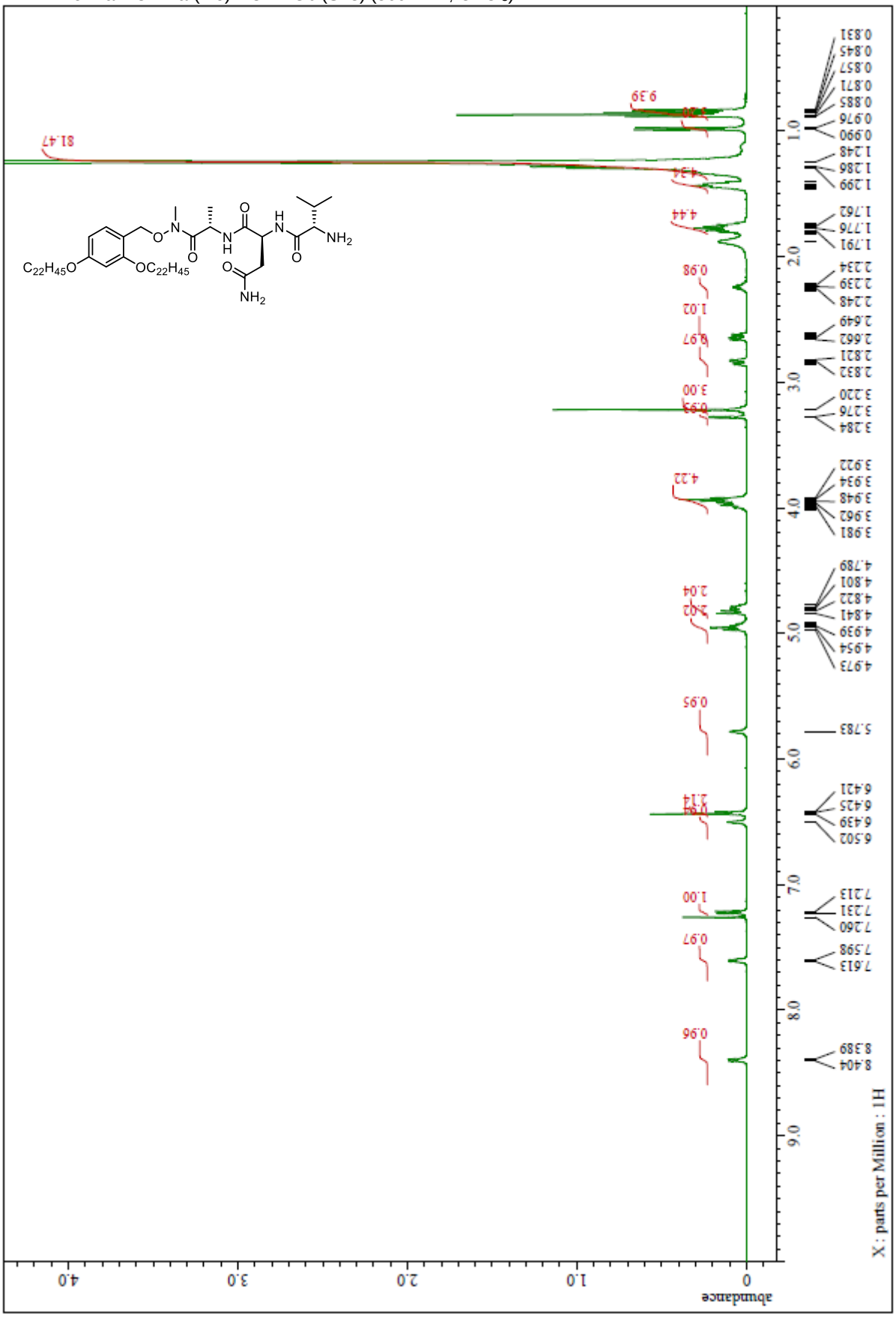
^{1}H NMR of Fmoc-Val-Asn-Ala-(Me)N-O-TAGb (**S27**) (500 MHz, $CDCl_3$)



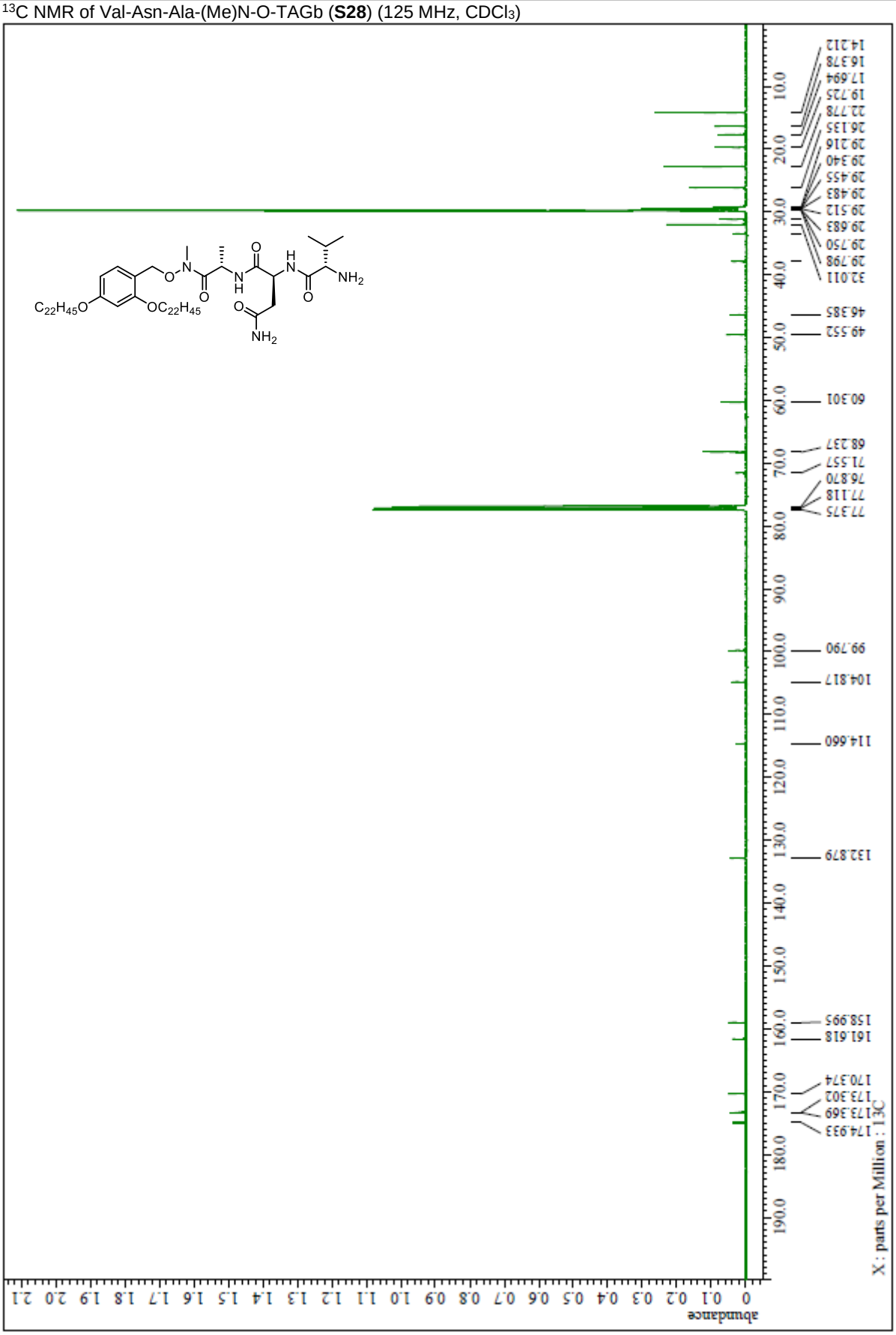
^{13}C NMR of Fmoc-Val-Asn-Ala-(Me)N-O-TAGb (**S27**) (125 MHz, $CDCl_3$)



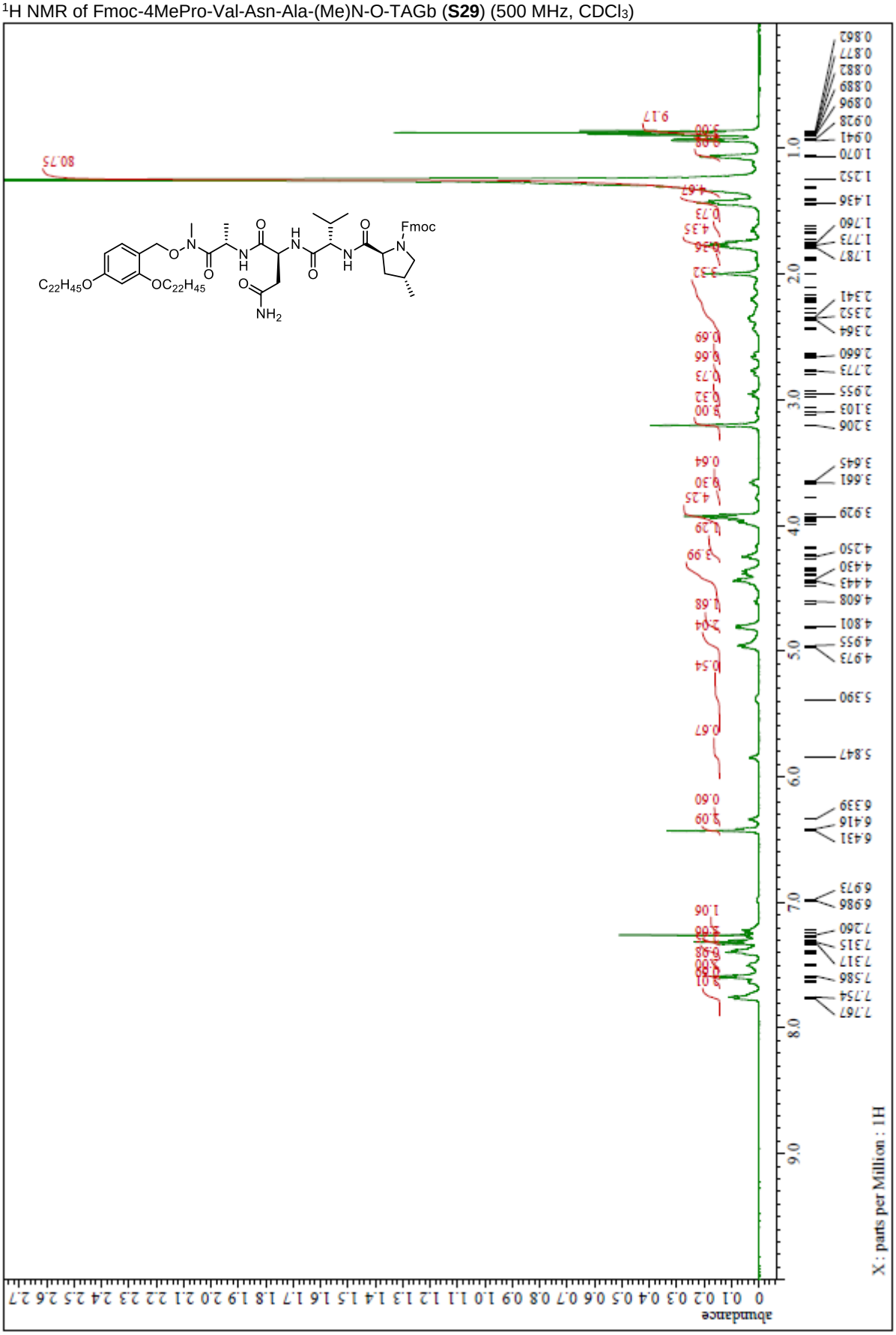
^{1}H NMR of Val-Asn-Ala-(Me)N-O-TAGb (**S28**) (500 MHz, $CDCl_3$)



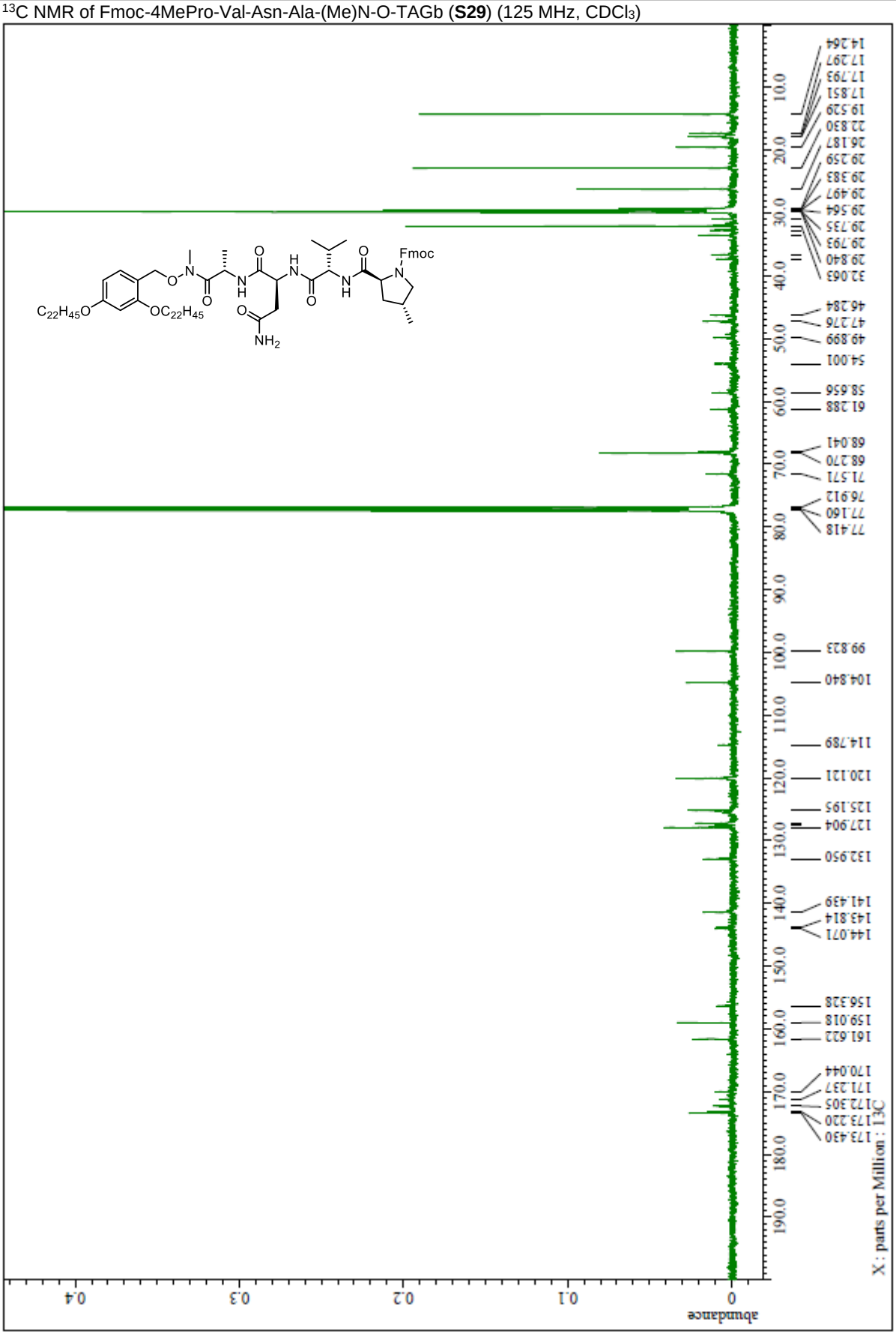
^{13}C NMR of Val-Asn-Ala-(Me)N-O-TAGb (**S28**) (125 MHz, $CDCl_3$)



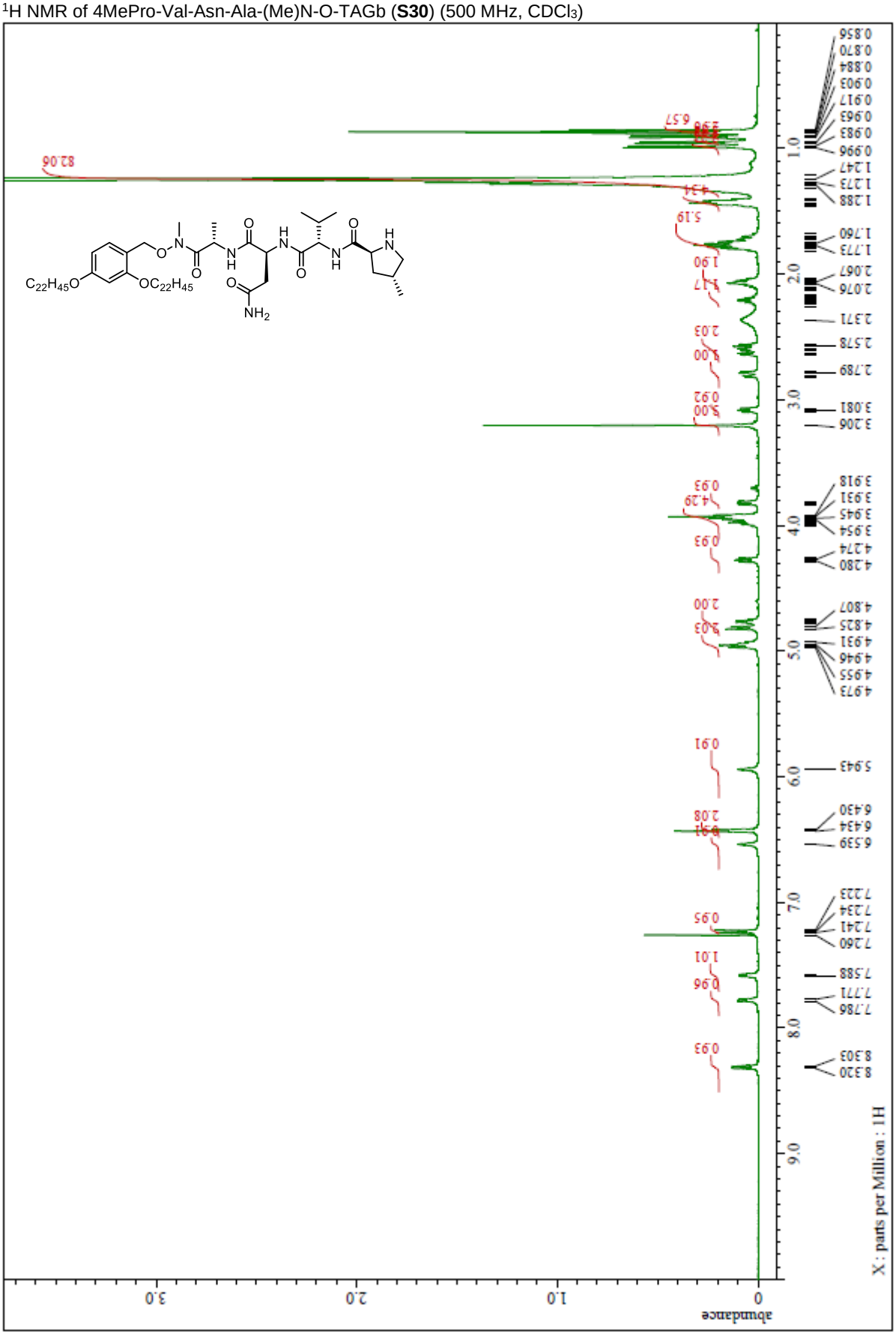
^{1}H NMR of Fmoc-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S29**) (500 MHz, $CDCl_3$)



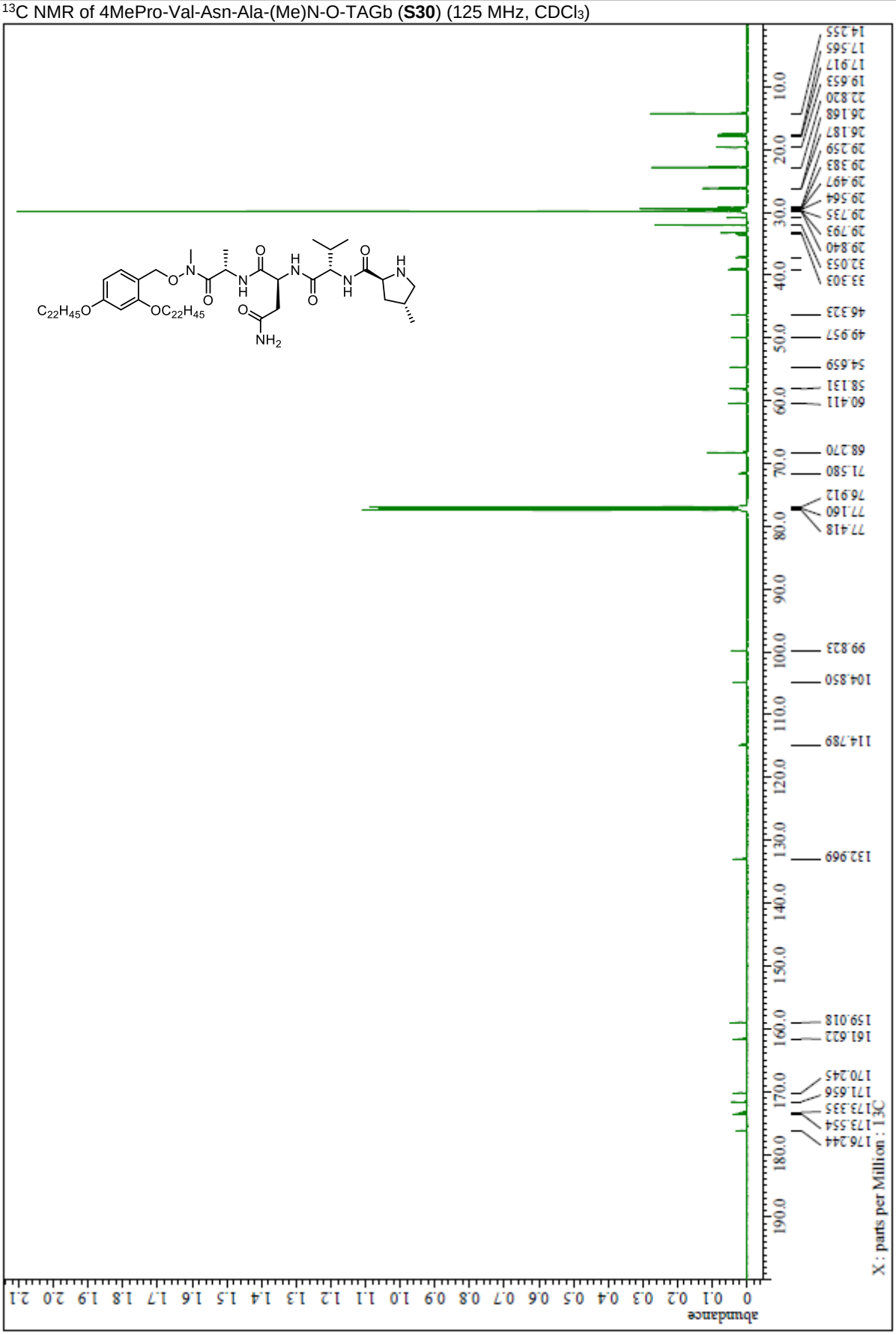
^{13}C NMR of Fmoc-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S29**) (125 MHz, $CDCl_3$)



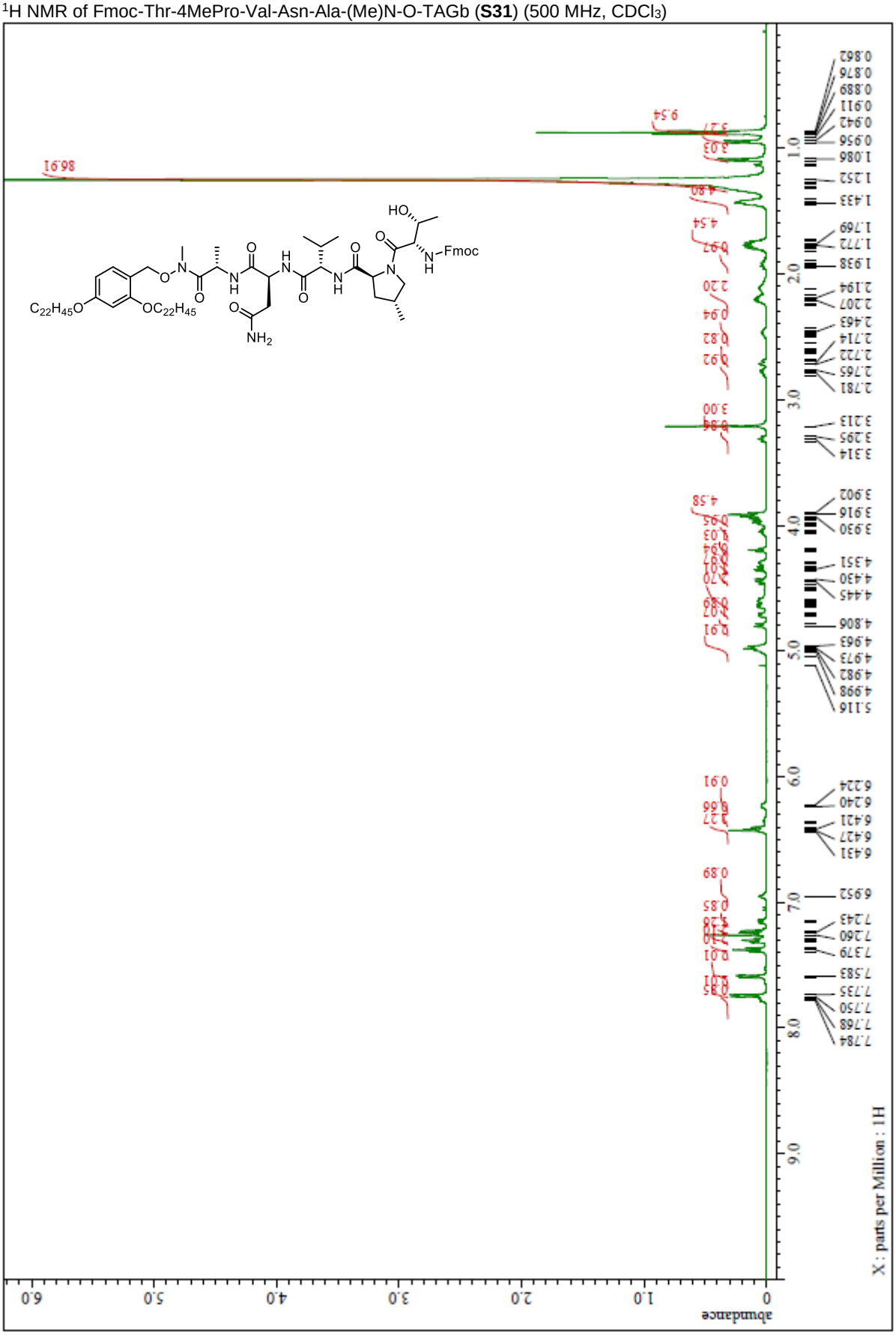
^{1}H NMR of 4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S30**) (500 MHz, $CDCl_3$)



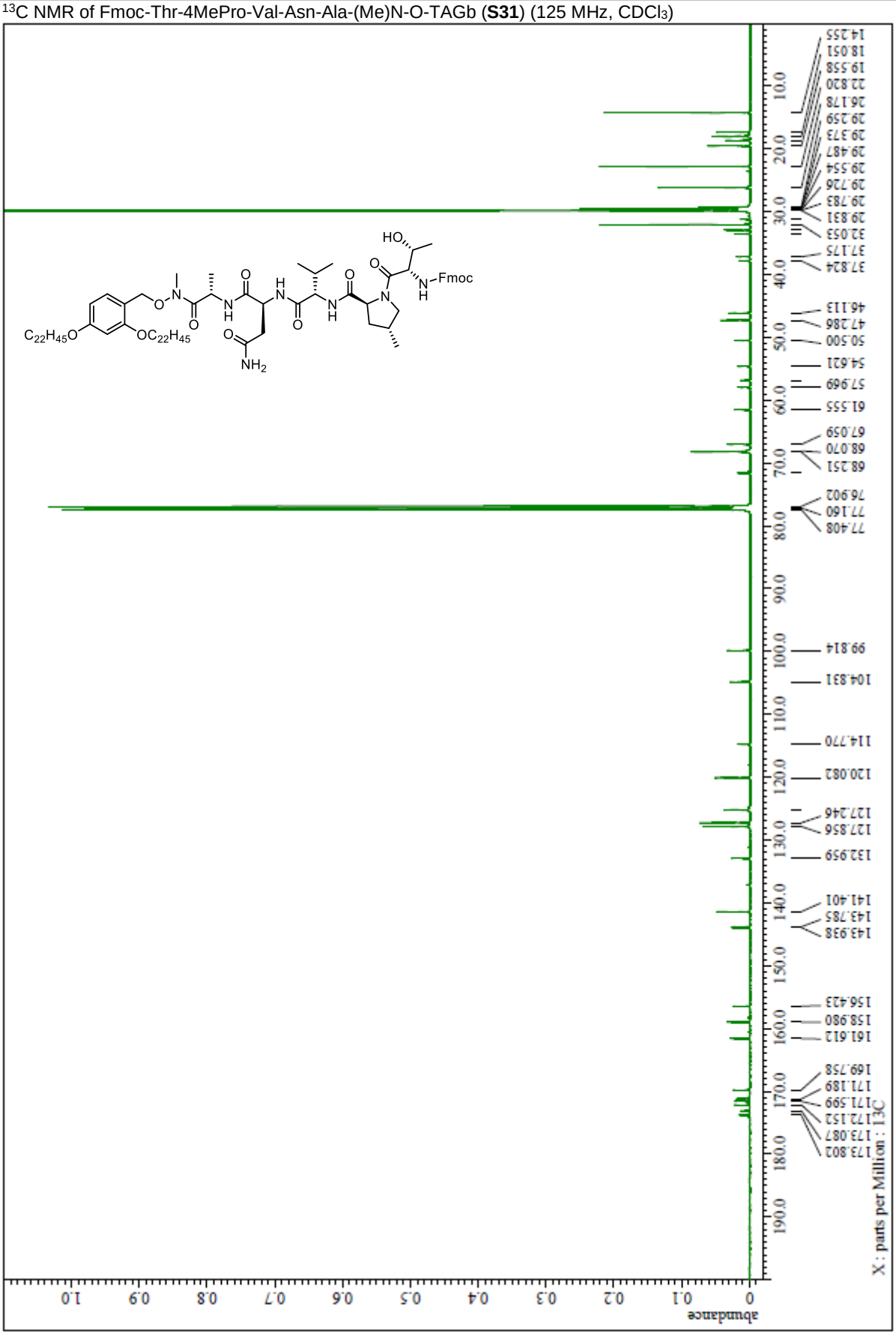
^{13}C NMR of 4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S30**) (125 MHz, $CDCl_3$)



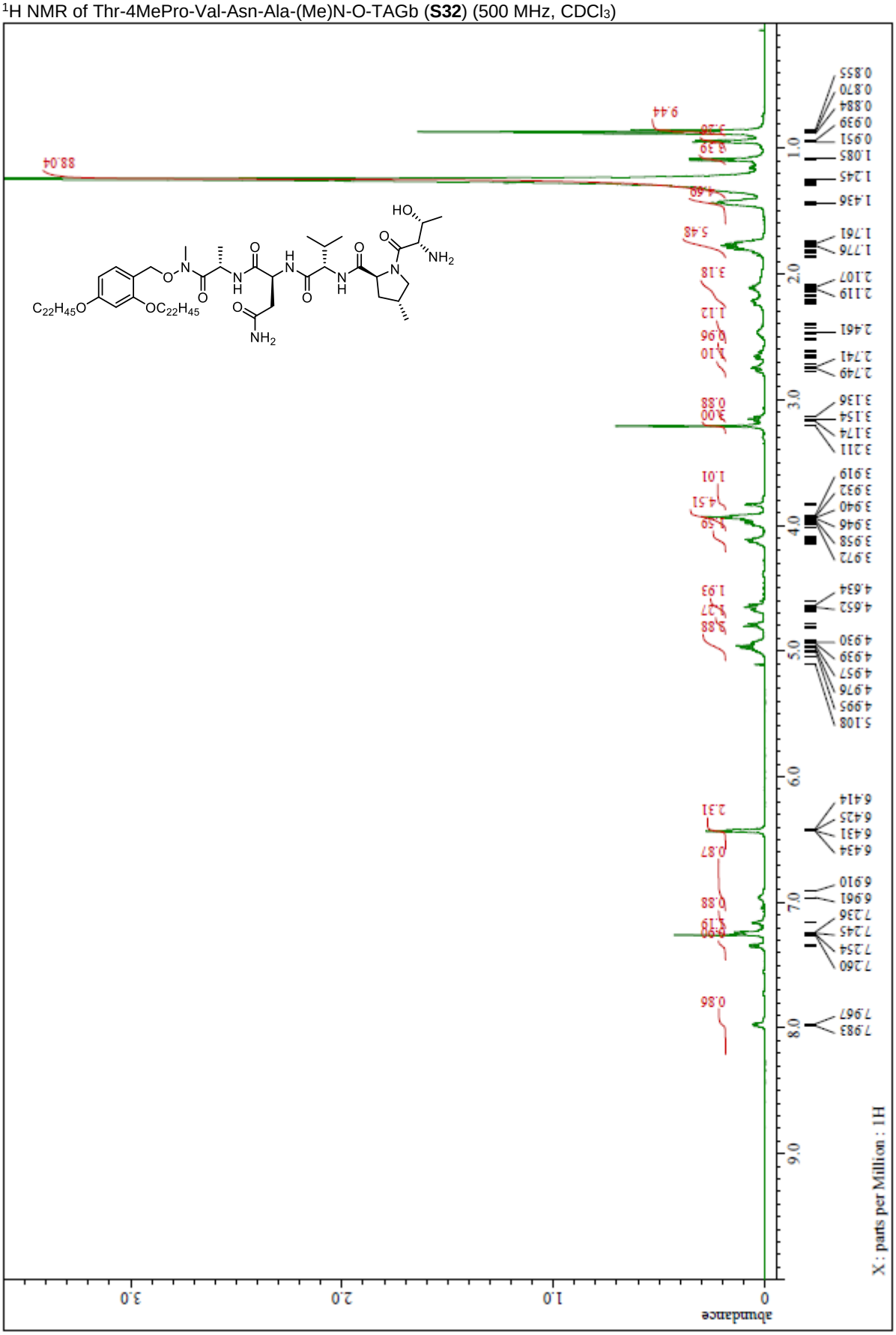
^{1}H NMR of Fmoc-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S31**) (500 MHz, $CDCl_3$)



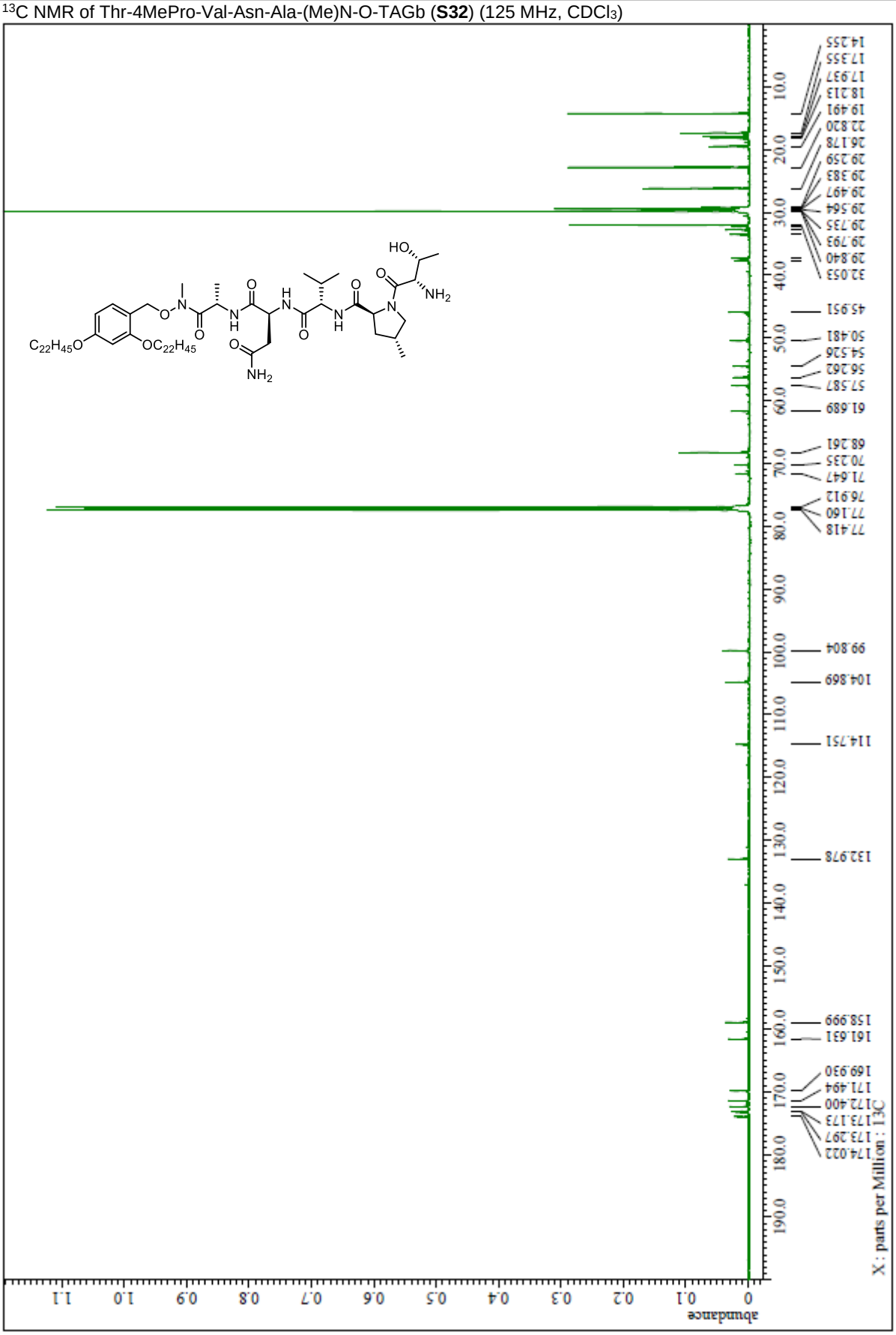
^{13}C NMR of Fmoc-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S31**) (125 MHz, $CDCl_3$)



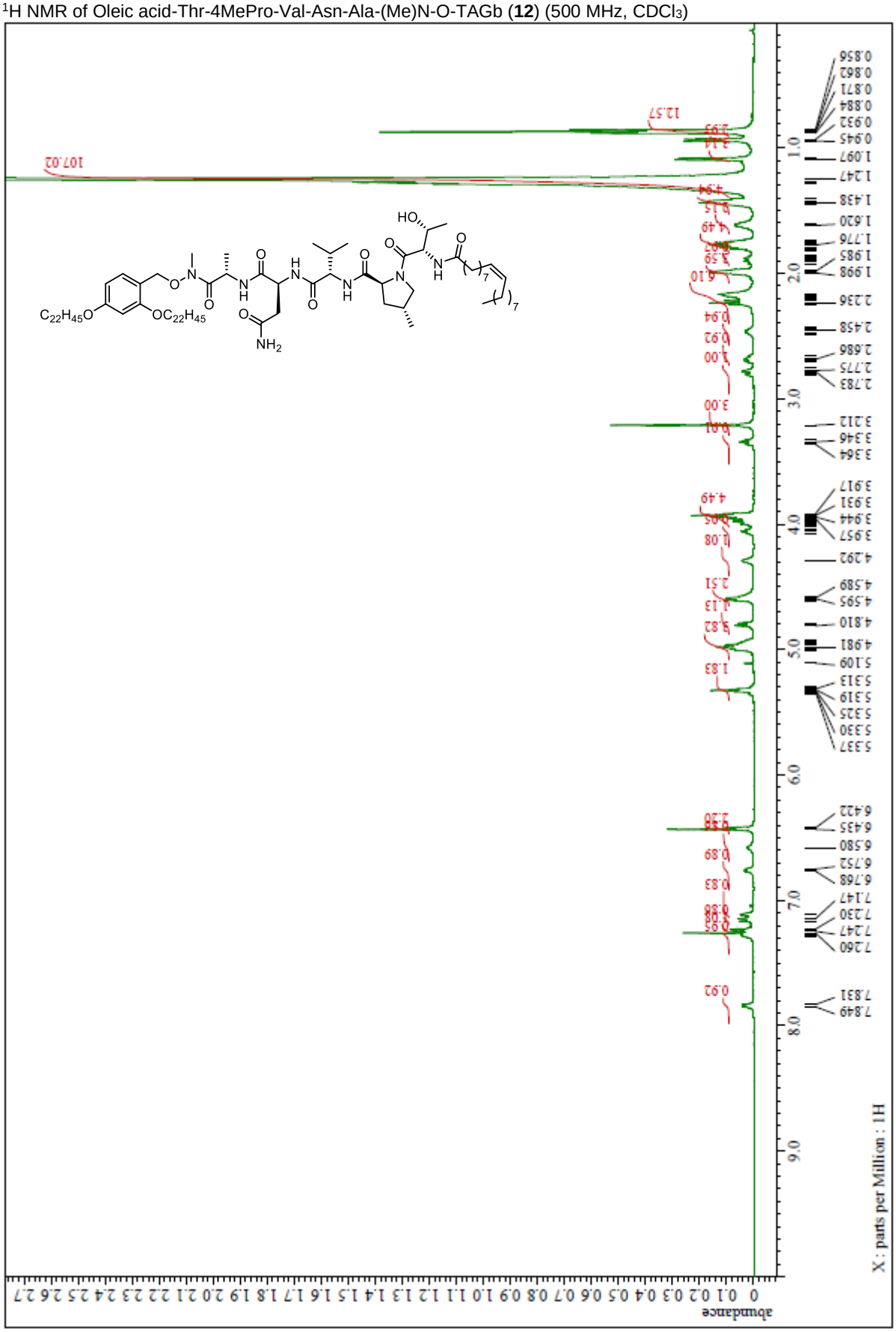
^{1}H NMR of Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S32**) (500 MHz, $CDCl_3$)



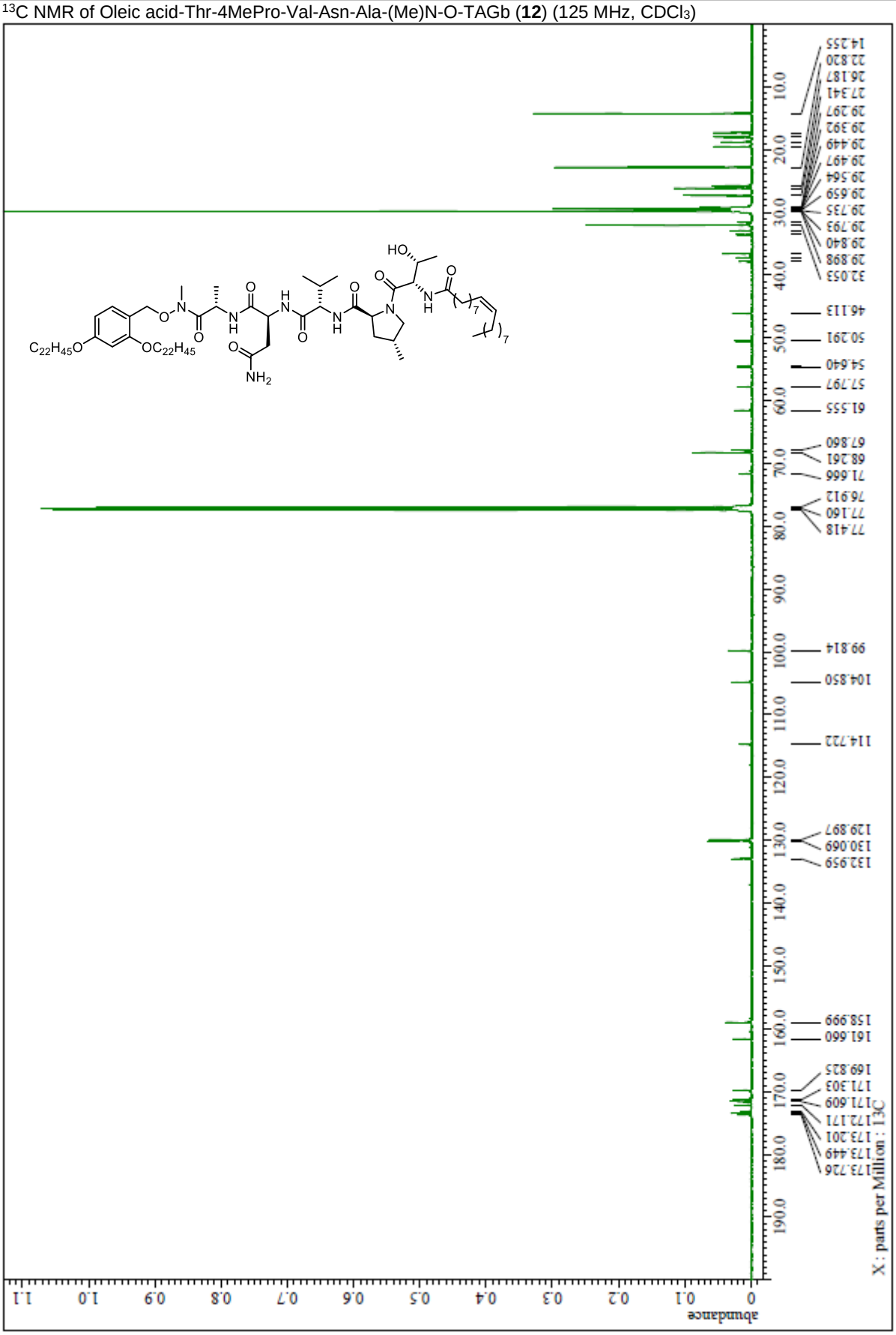
^{13}C NMR of Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**S32**) (125 MHz, $CDCl_3$)



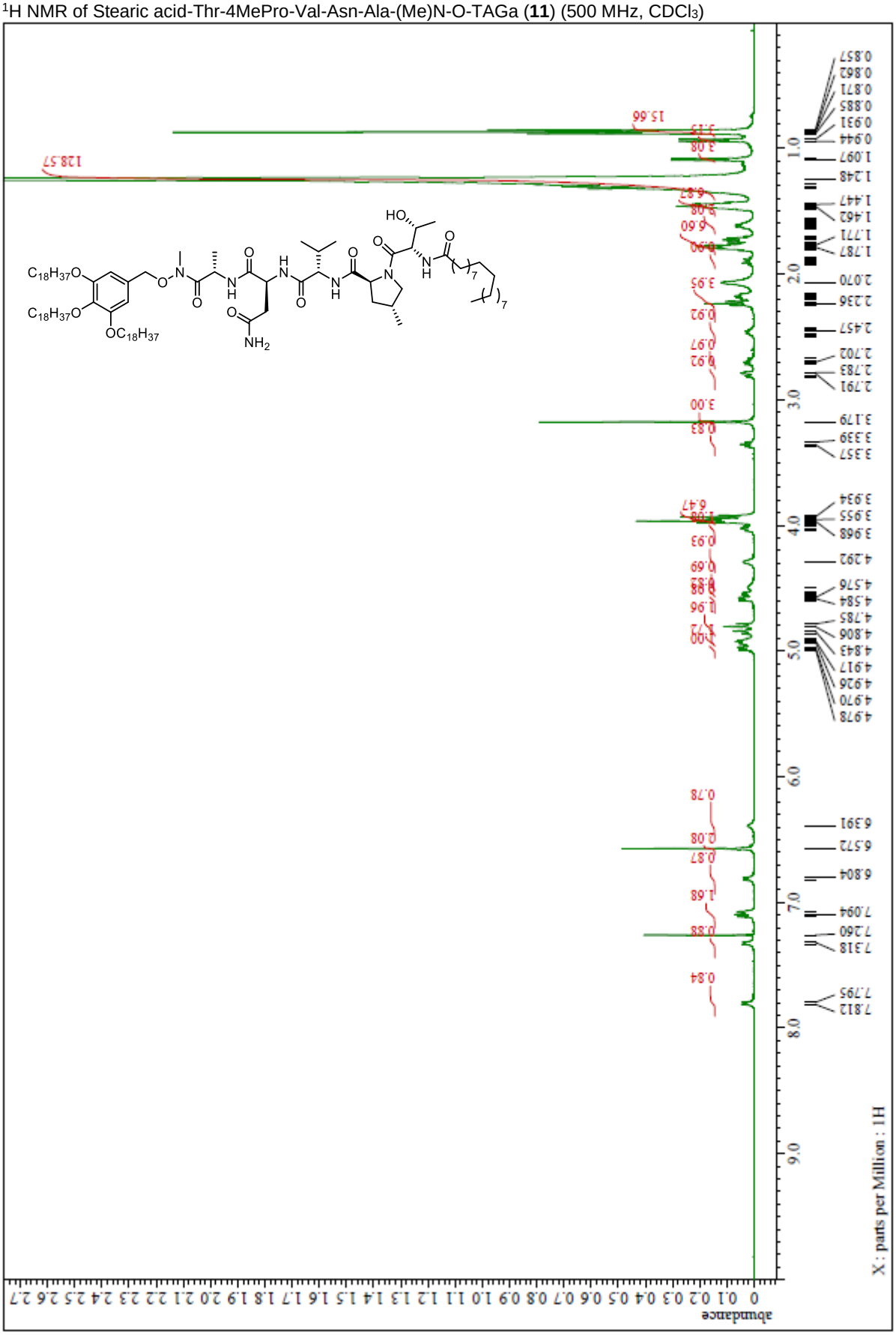
^{1}H NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**12**) (500 MHz, $CDCl_3$)



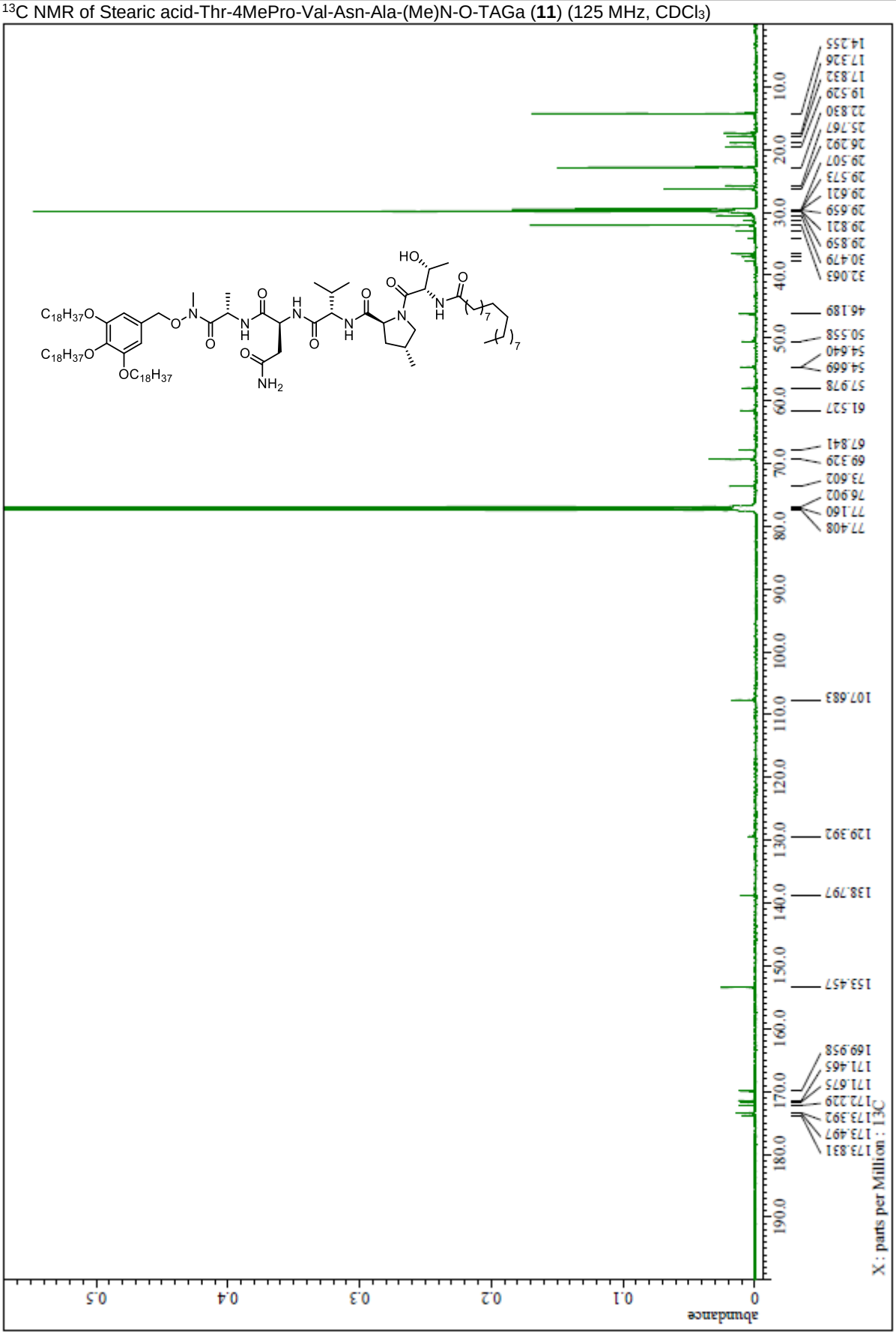
^{13}C NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGb (**12**) (125 MHz, $CDCl_3$)



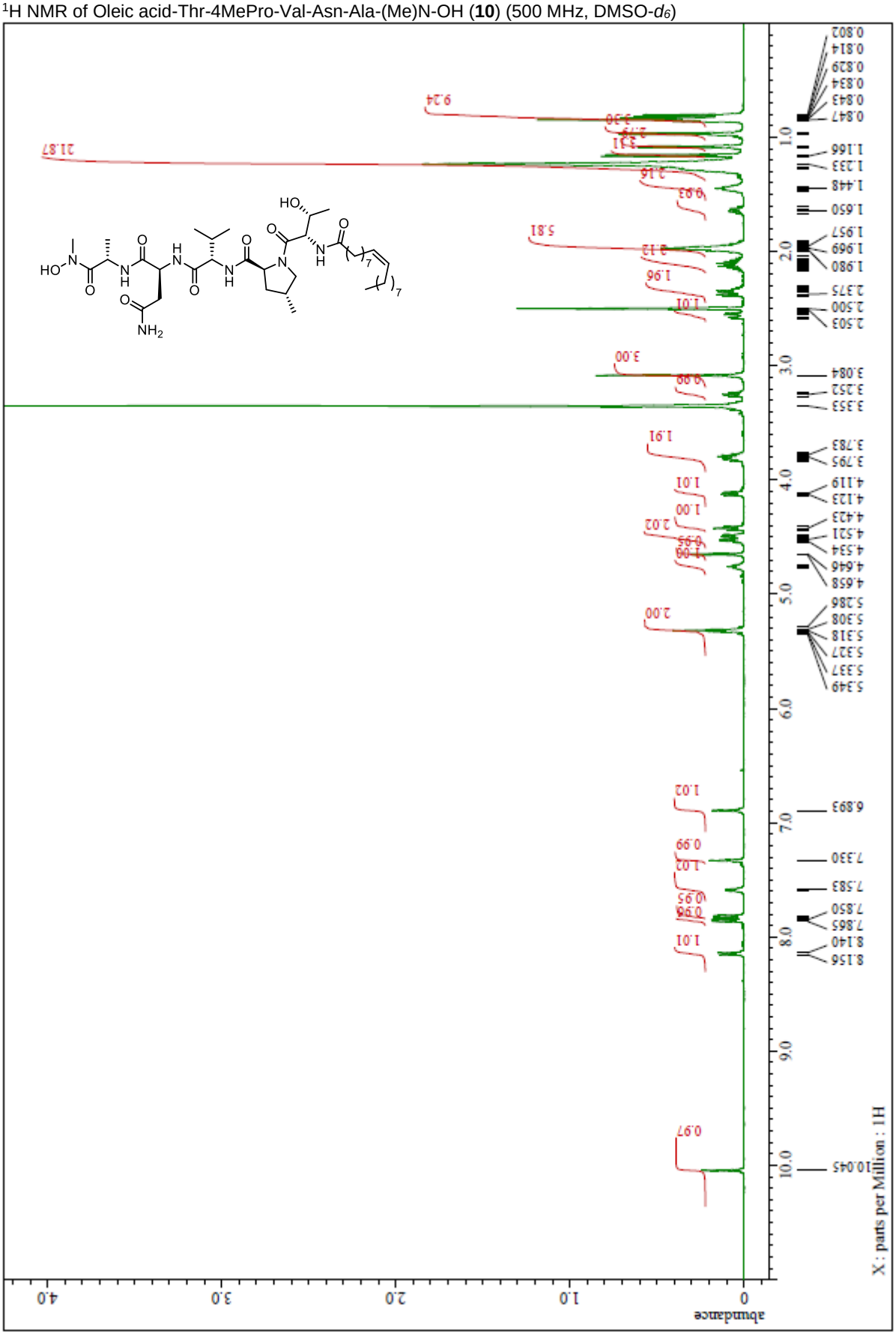
^{1}H NMR of Stearic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**11**) (500 MHz, $CDCl_3$)



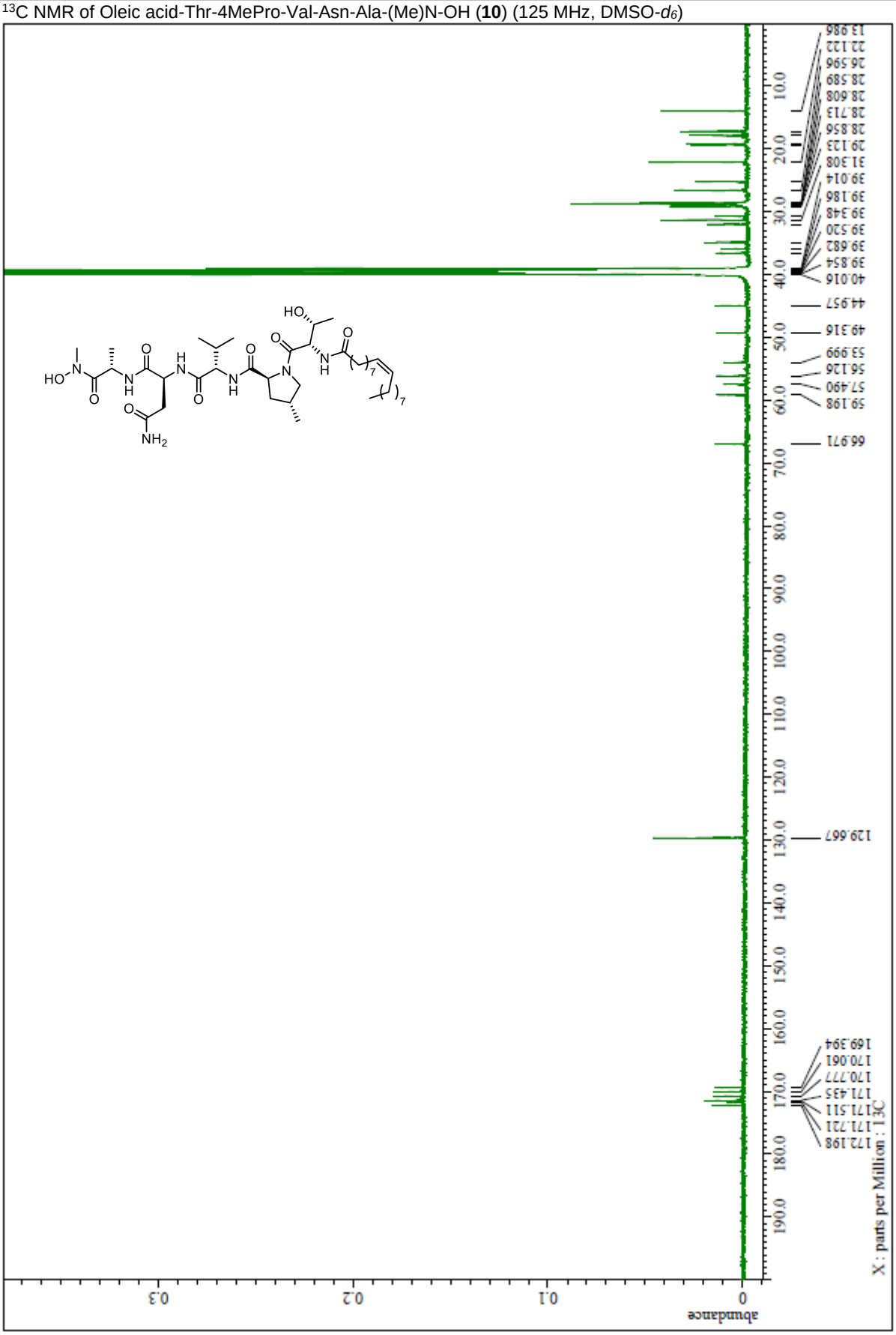
^{13}C NMR of Stearic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-O-TAGa (**11**) (125 MHz, $CDCl_3$)



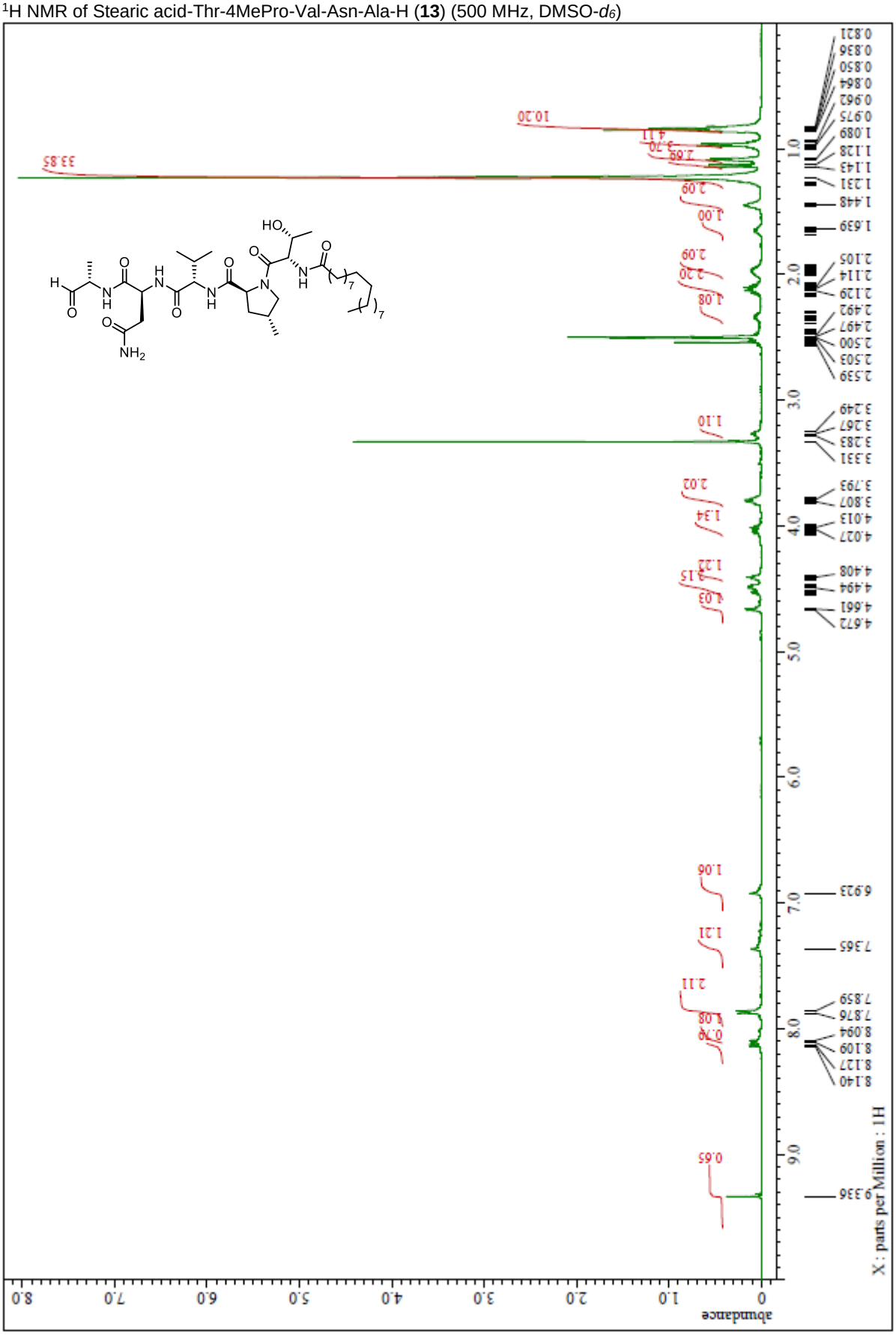
^{1}H NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-OH (**10**) (500 MHz, DMSO-d_6)



^{13}C NMR of Oleic acid-Thr-4MePro-Val-Asn-Ala-(Me)N-OH (**10**) (125 MHz, DMSO-d_6)



^{1}H NMR of Stearic acid-Thr-4MePro-Val-Asn-Ala-H (**13**) (500 MHz, DMSO-d_6)



^{13}C NMR of Stearic acid-Thr-4MePro-Val-Asn-Ala-H (**13**) (125 MHz, DMSO-d_6)