Supporting Information

Catalytic Asymmetric Total Synthesis of (+)-Caprazol

Purushothaman Gopinath, Lu Wang, Hikaru Abe, Gandamala Ravi, Takashi Masuda, Takumi Watanabe,* and Masakatsu Shibasaki*

Institute of Microbial Chemistry (BIKAKEN), Tokyo, Japan

twatanabe@bikaken.or.jp; mshibasa@bikaken.or.jp

1. General

The reactions were performed in an oven-dried test tube or round bottom flask with a Teflon-coated magnetic stirring bar unless otherwise noted. All work-up and purification procedures were carried out with reagent-grade solvents under ambient atmosphere.

2. Instrumentation

Infrared (IR) spectra were recorded on a JASCO FT/IR 4100 Fourier transform infrared spectrophotometer. NMR was recorded on JEOL ECS-400 (^{1}H NMR: 400 MHz, ^{13}C NMR: 100 MHz) or on JEOL ECA-600 (^{13}C NMR: 150 MHz) or on Bruker AVANCE 500 (^{13}C NMR: 125 MHz depicted with *) spectrometers. Chemical shifts for proton are reported in parts per million downfield from tetramethylsilane and are referenced to residual protium in the NMR solvent ($CDCl_3$: δ 7.26 ppm, CD_3OD: δ 3.30 ppm). For ^{13}C NMR, chemical shifts were reported in the scale relative to NMR solvent ($CDCl_3$: δ 77.0 ppm, CD_3OD: δ 49.0 ppm) as an internal reference, or calibrated based on independently recorded peak of 3-trimethylsilylpropanoic acid (TSP) at 0 ppm in D_2O. NMR data are reported as follows: chemical shifts, multiplicity (s: singlet, d: doublet, dd: doublet of doublets, t: triplet, q: quartet, m: multiplet, br: broad signal), coupling constant (Hz), and integration. Optical rotation was measured using a 2 mL cell with a 1.0 dm path length on a JASCO polarimeter P-1030. High-resolution mass spectra (ESI-Orbitrap) were measured on ThermoFisher Scientific LTQ Orbitrap XL. HPLC analysis was conducted on a JASCO HPLC system equipped with Daicel chiral-stationary-phase columns (ϕ 0.46 cm × 25 cm). Centrifugal liquid-liquid partition chromatography (CPC) was performed with a CPC240 system (Senshu Scientific Co., LTD).

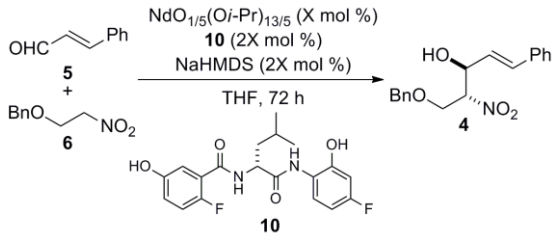
3. Materials

Unless otherwise noted, materials were purchased from commercial suppliers and were used without purification. For reaction, THF, DMF, CH_3CN, toluene, AcOEt, and CH_2Cl_2 were purified by passing through a solvent purification system (Glass Contour). Dry 1,4-dioxane, MeOH, DMSO, and pyridine were purchased from Wako Pure Chemical Co. Ltd. (Osaka, Japan) and used as received. Compound **5** was purified by washing with saturated $NaHCO_3$ followed by silica gel column chromatography just before use. Compound **6** was prepared according to the procedure reported by Hwu and Hakimelahi, [1] then distilled under reduced pressure. Compound **21** was prepared according to the procedure reported by Ichikawa and Matsuda. [2]

(1) Hwu, J. R.; Jain, M. L.; Tsai, F. –Y.; Tsai, S. –C.; Balakumar, A.; Hakimelahi, G. H. *J. Org. Chem.* **2000**, *65*, 5077.
(2) Hirano, S.; Ichikawa, S.; Matsuda, A. *Angew. Chem. Int. Ed.* **2005**, *44*, 1854.

4. Synthetic procedure for (+)-caprazol (1)

(3*S*,4*R*,*E*)-5-(Benzyloxy)-4-nitro-1-phenylpent-1-en-3-ol (**4**).



To a flame-dried test tube or round bottom flask (depending on scale), chiral amide ligand (**10**, 544 mg, 18 mol%), was added and kept under vacuum for 30 min, followed by the addition of 16 mL of THF. To this solution was added 3.6 mL of $NdO_{1/5}(O\textit{i}\text{-}Pr)_{13/5}$ (0.2 M, based on Nd, 9 mol%) and the mixture was stirred for 5 min. The reaction mixture was then cooled to 0 °C followed by the addition of NaHMDS (1 M in THF, 1.44 mL, 18 mol %) (white precipitates appeared). The reaction was then stirred at the same temperature for 5 min and then at room temperature for 5 min. Finally, nitroethane (4.8 mL) was added to the solution (solution become clear) and then the reaction mixture was kept at room temperature until white precipitates appeared (usually It appears within 30 min). The resulting suspension was then transferred to two test tubes and then centrifuged. The supernatants were then discarded; 10 mL of THF was added to each test tube, stirred for 1 min and again centrifuged. The supernatants were discarded (washing process) and this procedure was repeated at least three to four times. The resulting precipitates were then transferred to a flame-dried test tube containing **6** (1.27 mL, 1.46 g, 8.00 mmol) using 32 mL THF (0.25 M). The reaction mixture was then cooled to –60 °C followed by the addition of **5** (5.03 mL, 40.0 mmol). The reaction mixture was then stirred at that temperature for 5 days followed by the addition of 0.5 M HCl (15 mL). The reaction mixture freezes and it was kept at that temperature for 5 min and then removed from the cooling bath. AcOEt (40 mL) was immediately added and the reaction mixture was stirred until the frozen solution thawed. The resultant biphasic mixture was then transferred to a separating funnel. Ethyl acetate layer was then collected separately. The aqueous phase was again extracted with ethyl acetate. The organic layer was then washed with saturated $NaHCO_3$, brine and dried over Na_2SO_4. Solvents were then removed and the crude mixture was purified by CPC. Crude ^{1}H-NMR shows 72% yield with 12:1 dr (*vide infra*).

CPC conditions:

After making the two layers (*n*-hexane/AcOEt/CH_3CN = 5:1:4), compound was injected (2 g crude). Upper layer (1.5 L) was passed through first to remove all aldehyde in the ascending mode. The mode

was then changed to descending and then the lower layer was run in recycle mode (flow rate = 4 mL/min).

After separation of the desired compound **4**, the enantioselectivity of the reaction was determined to be 95% ee with HPLC method: Daicel CHIRALCEL AY-H, detection: 254 nm, eluent: *n*-hexane/2-propanol = 85/15, flow rate: 1.0 mL/min, retention time: t_R = 12.1 min (major), t_R = 19.2 min (minor).

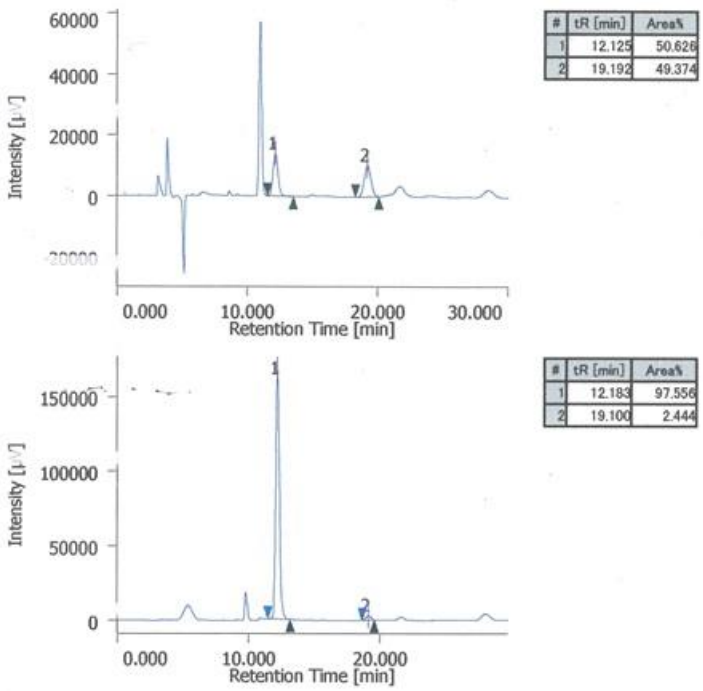


Figure S1. HPLC profiles of **4** (upper: racemic, lower: the product from entry 11 in Table 1). Stirring equimolar amount of **5**, **6**, and DBU in THF for 1 h at 0 ^{o}C gave racemic **4** accompanied with *syn*-isomer, and many byproducts (mainly Michael adducts and double nitroaldol adducts).

The sample was purified by CPC under the conditions described above upon use in the succeeding step.

The reactions demonstrated in Table 1 were performed according to the protocol described above with modifications in parameters as depicted except for entry 7 under carbon nanotube conditions: the catalyst confined in carbon nanotube was prepared as described in the literature (therein described as "Cat. C").[3]

(3) Sureshkumar, D.; Hashimoto, K.; Kumagai, N.; Shibasaki, M. *J. Org. Chem.* **2013**, *78*, 11494.

Chemical yield was determined by comparison of peak area for PhCH=C**H**- from the both isomers (6.16 – 6.05 ppm) and for the internal standard, 1,1,2,2-tetrachloroethane (**2H** at 5.95 ppm), doped upon work up.

Diastereomeric ratio was determined by ^{1}H NMR comparing the peak areas at 6.13 ppm (*anti*-isomer) and 6.08 ppm (*syn*-isomer) corresponding to PhCH=C**H**-.

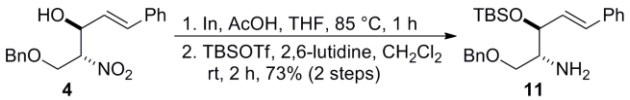
Enantiomeric excess for each reaction was determined according to the HPLC method described above.

4: pale yellow oil; $[\alpha]_D^{23}$ +4.68 (*c* 0.55, $CHCl_3$, 96% ee); IR (neat) ν 3419, 1554, 1452, 1362, 1123, 970, 749 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{18}H_{19}NNaO_4$ *m/z* 336.1212 $[M+Na]^+$, found 336.1206; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 10H), 6.71 (1H, dd, *J* = 15.9 Hz, 0.9 Hz), 6.13 (1H, dd, *J* = 15.9 Hz, 6.6 Hz), 4.84 (1H, m), 4.78 (1H, m), 4.56 (1H, d, *J* = 12.1 Hz), 4.54 (1H, d, *J* = 12.1 Hz), 4.12 (1H, dd, *J* = 11.0 Hz, 8.0 Hz), 3.98 (1H, dd, *J* = 11.0 Hz, 3.4 Hz), 2.70 (1H, d, *J* = 4.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.8, 135.5, 134.0, 128.7, 128.51, 128.47, 128.1, 127.8, 126.8, 125.0, 89.8, 73.6, 72.0, 66.9.

The partially purified racemic *syn*-isomer gave a readable ^{1}H NMR spectrum.
syn-**4**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37–7.25 (m, 10H), 6.70 (1H, dd, *J* = 15.8 Hz, 0.9 Hz), 6.08 (1H, dd, *J* =15.8 Hz, 6.6 Hz), 4.80 (1H, m), 4.75 (1H, m), 4.55 (1H, d, *J* = 11.9 Hz), 4.48 (1H, d, *J* = 11.9 Hz), 3.97 (1H, dd, *J* = 10.8 Hz, 7.6 Hz), 3.84 (1H, dd, *J* = 10.8 Hz, 3.4 Hz), 2.47 (1H, br).

.

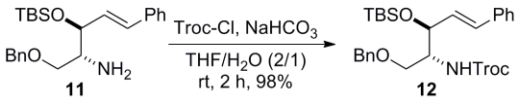
(2*R*,3*S*,*E*)-1-(Benzyloxy)-3-((tert-butyldimethylsilyl)oxy)-5-phenylpent-4-en-2-amine (**11**).



Compound **4** (313 mg, 1.00 mmol) was dissolved in THF (15 mL). Indium (920 mg, 8.01 mmol) was added followed by the addition of AcOH (286 μL, 5.00 mmol). The mixture was heated at 85 – 90 °C for 1.5 h. The mixture was then brought to room temperature. After the reaction was quenched with saturated $NaHCO_3$, the mixture was extracted with AcOEt and dried over Na_2SO_4. Solvents were then removed and connected to vacuo for 1 h. The reaction mixture was then cooled to 0 °C, and dissolved in CH_2Cl_2 (5 mL) followed by the addition of 2,6-lutidine (291 μL, 2.50 mmol) and TBSOTf (459 μL, 2.00 mmol). After 2 h, the reaction was quenched with MeOH. Solvent was then removed and the crude mixture was purified by silica gel column chromatography (40% AcOEt/*n*-hexane) to give **11** as

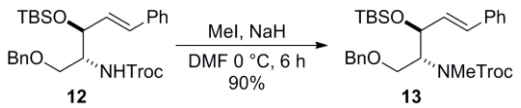
a colorless oil (73% yield for 2 steps); $[\alpha]_D^{23}$ 17.6 (*c* 1.84, $CHCl_3$, 96% ee); IR (neat) ν 2954, 2928, 2856, 1496, 1471, 1361, 1254, 1073, 814 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{24}H_{35}NO_2Si$ *m*/*z* 398.2515 $[M+H]^+$, found 398.2507; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.22 (m, 10H), 6.55 (1H, d, *J* = 16.0 Hz), 6.16 (1H, dd, *J* = 16.0 Hz, 7.1 Hz), 4.55 (1H, d, *J* = 10.9 Hz), 4.50 (1H, d, *J* = 10.9 Hz), 4.28 (1H, m), 3.61 (1H, dd, *J* = 9.2 Hz, 4.4 Hz), 3.50 (1H, dd, *J* =9.2 Hz, 6.6 Hz), 3.05 (1H, m), 0.90 (9H, s), 0.07 (6H, s), 0.03 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2, 136.6, 131.8, 129.7, 128.5, 128.4, 127.8, 127.6, 126.4, 75.4, 73.3, 71.8, 56.2, 25.8, 18.1, –4.1, –4.9.

2,2,2-Trichloroethyl((2*R*,3*S*,*E*)-1-(benzyloxy)-3-((tert-butyldimethylsilyl)oxy)-5-phenylpent-4-en-2-yl)carbamate (**12**).



Compound **11** (636 mg, 1.60 mmol), was dissolved in THF/H_2O (2:1, 15 mL) followed by the addition of $NaHCO_3$ (269 mg, 3.20 mmol). The reaction mixture was then cooled to 0 °C, Troc-Cl (429 µL, 3.12 mmol) was added dropwise. After 10 min, the reaction mixture was brought to room temperature and stirred for 2 h. After the completion of reaction, the crude mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4 and filtered. The crude mixture was purified by silica gel column chromatography (12.5% AcOEt/*n*-hexane) to give **12** as a colorless oil (900 mg, 98%); $[\alpha]_D^{23}$ –9.39 (*c* 1.05, $CHCl_3$, 96% ee); IR (neat) ν 2953, 2925, 2857, 1743, 1507, 1253, 1088, 836 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{27}H_{36}Cl_3NNaO_4Si$ *m*/*z* 594.1377 $[M+Na]^+$, found 594.1366; ^1H NMR (400 MHz, $CDCl_3$) δ 7.37–7.21 (10H, m), 6.53 (1H, d, *J* = 16.0 Hz), 6.15 (1H, dd, *J* = 16.0 Hz, 7.4 Hz), 5.29 (1H, d, *J* = 9.4 Hz), 4.71 (1H, d, *J* = 12.2 Hz), 4.55–4.44 (4H, m), 3.91 (1H, m), 3.84 (1H, dd, *J* = 4.3 Hz, 9.5 Hz), 3.60 (1H, dd, *J* = 4.0 Hz, 9.5 Hz), 0.89 (9H, s), 0.07 (6H, s), 0.03 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 137.8, 136.5, 132.0, 129.5, 128.5, 128.4, 127.9, 127.8, 127.7, 126.5, 95.5, 74.3, 73.5, 73.3, 68.2, 55.7, 25.8, 18.1, –4.1, –5.0.

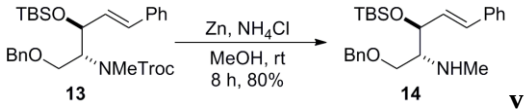
2,2,2-Trichloroethyl((2*R*,3*S*,*E*)-1-(benzyloxy)-3-((tert-butyldimethylsilyl)oxy)-5-phenylpent-4-en-2-yl)(methyl)carbamate (**13**).



To a solution of **12** (108 mg, 0.188 mmol) in DMF (8 mL) at 0 °C was added MeI (23.5 µL, 0.377 mmol) followed by the addition of NaH (9.0 mg of 60% dispersion, 0.225 mmol). The reaction

mixture was stirred at 0 °C for 6 h and then quenched with water (8 mL) followed by extraction with AcOEt. The organic layer was then washed with brine, dried over Na_2SO_4 and column chromatographed on silica gel (20% AcOEt/*n*-hexane) to give the corresponding *N*-methyl compound **13** (mixture of rotamers (6/4)) in 74% yield (82.0 mg) as a colorless oil; $[\alpha]_D^{23}$ +17.9 (*c* 0.50, $CHCl_3$, 96% ee); IR (neat) ν 3027, 2954, 2857, 1717, 1457, 1403, 1319, 1149, 1075 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{28}H_{38}Cl_3NNaO_4Si$ *m*/*z* 608.1533 $[M+Na]^+$, found 608.1521; ^1H NMR (400 MHz, $CDCl_3$) δ 7.35–7.21 (10H, m), 6.54 (0.4H, d, *J* = 16.0 Hz), 6.50 (0.4H, d, *J* = 16.0 Hz), 6.13 (0.6H, dd, *J* = 16.0 Hz, 7.8 Hz), 6.12 (0.4H, dd, *J* = 16.0 Hz, 7.3 Hz), 4.83–4.75 (1H, m), 4.65–4.47 (4H, m), 4.27 (1H, br), 3.90-3.85 (1H, m), 3.80–3.77 (1H, m), 2.99 (0.4H, s), 2.98 (0.6H, s), 0.88 (3.6H, s), 0.87 (5.4H, s), 0.039 (3.6H, s), 0.036 (2.4H, s), 0.005 (3.6H, s) , 0.001 (2.4H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1155.1, 138.1, 136.4, 131.8, 131.7, 130.4, 129.9, 128.58, 128.55, 128.4, 128.3, 127.82, 127.76, 127.7, 127.6, 126.5, 95.7, 77.2, 75.2, 74.9, 73.0, 67.2, 25.81, 25.78, 18.0, –3.87, –3.94, –4.9, –5.0.

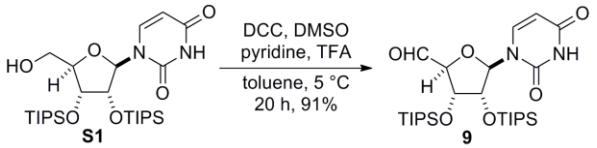
(2*R*,3*S*,*E*)-1-(benzyloxy)-3-((tert-butyldimethylsilyl)oxy)-*N*-methyl-5-phenylpent-4-en-2-amine (**14**).



v

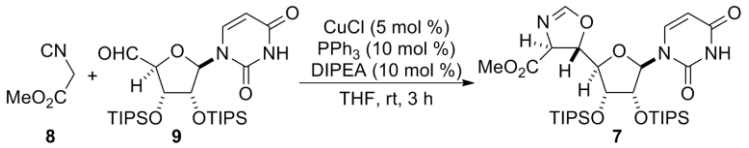
A mixture of **13** (341 mg, 0.58 mmol), NH_4Cl (931 mg, 17.4 mmol), and Zn powder (379 mg, 5.80 mmol) in MeOH (8 mL) was stirred at room temperature for 8 h. The reaction mixture was then quenched with solid $NaHCO_3$ (2.44 g, 29.0 mmol), stirred for at room temperature for 10 min. Insoluble materials were filtered off through a celite pad, and the filtrate was concentrated. The residue was purified by silica gel column chromatography (9% to 33% AcOEt/*n*-hexane) to give the corresponding *N*-methyl amine **14** in 80% yield (190 mg) as a colorless oil; $[\alpha]_D^{23}$ +1.09 (*c* 2.70, $CHCl_3$, 96% ee); IR (neat) ν 2953, 2928, 2856, 1472, 1455, 1362, 1253, 1101, 1072, 836 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{25}H_{38}NO_2Si$ *m*/*z* 412.2672 $[M+H]^+$, found 412.2664; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.20 (10H, m), 6.54 (1H, d, *J* = 15.8 Hz), 6.21 (1H, dd, *J* = 15.8 Hz, 7.1 Hz), 4.56 (1H, d, *J* = 11.9 Hz), 4.48 (1H, d, *J* = 11.7 Hz), 4.47 (1H, d, *J* = 11.9 Hz), 3.56 (12H, d, *J* = 5.9 Hz), 3.80 (1H, m), 2.48 (3H, s), 2.26 (1H, br), 0.90 (9H, s), 0.08 (6H, s), 0.04 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.3, 136.8, 131.4, 129.7, 128.5, 128.3, 127.7, 127.6, 127.5, 126.5, 73.7, 73.3, 69.2, 65.0, 35.3, 25.8, 18.1, –4.1, –4.9.

(2*S*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-carbaldehyde (**9**).



To a solution of **S1**[4] (4.20 g, 7.54 mmol) in toluene (20 mL), was added DMSO (16 mL), pyridine (0.95 mL), TFA (0.4 mL) and DCC (5.00 g) at 0 °C, and the solution was stirred for 20 h at 5 °C. The reaction mixture was filtered through sintered funnel, diluted with AcOEt, washed with bine and dried over Na_2SO_4. Evaporation of the solvent and purification of the resultant residue over silica gel column chromatography (33% to 50% AcOEt/*n*-hexane) gave **9** (3.79 g, 6.83 mmol) in 91% yield as a colorless foam; $[\alpha]_D^{23}$ –15.4 (*c* 0.33, $CHCl_3$); IR (neat) ν 2945, 2868, 1691, 1464, 1068 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{27}H_{51}N_2O_6Si_2$ *m*/*z* 555.3286 $[M+H]^+$, found 555.3279; ^1H NMR (400 MHz, $CDCl_3$) δ 9.82 (1H, s), 8.48 (1H, brs), 7.63 (1H, d, *J* = 8.1 Hz), 5.79–5.77 (2H, m), 4.58 (1H, dd, *J* = 8.4 Hz, 6.6 Hz), 4.54–4.52 (2H, m), 1.15–0.93 (42H, m); ^{13}C NMR (150 MHz, $CDCl_3$) δ 199.9, 162.7, 150.0, 14204, 102.7, 92.5, 88.3, 73.9, 73.7, 18.1, 18.0, 17.9, 17.8, 12.8, 12.5.

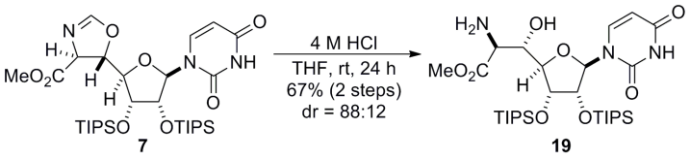
(4*S*,5*S*)-Methyl 5-((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)-4,5-dihydrooxazole-4-carboxylate (**7**).



To the aldehyde **9** (4.00 g, 7.21 mmol), CuCl (35.6 mg, 0.360 mmol, 5 mol %), PPh_3 (189 mg, 0.72 mmol, 10 mol %) and DIPEA (0.12 mL, 0.720 mmol, 10 mol %) in THF (80 mL) was added **8** (0.786 mL, 8.65 mmol) at room temperature, and the mixture was stirred for 3 h at the same temperature. After completion of the reaction, H_2O was added to the mixture and extracted with CH_2Cl_2 three times. The combined organic layers were dried over Na_2SO_4, and concentrated to dryness. The resulting residue containing **7** was used in the next reaction without further purification. From NMR spectra of the crude sample (the diagnostic peaks are at 6.96 ppm (major) and 6.91 ppm (minor), see page S31), diastereomeric ratio is estimated to be 88:12.

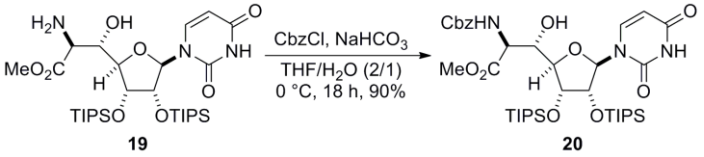
(2*S*,3*S*)-Methyl 2-amino-3-((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)-3-hydroxypropanoate (**19**).

(4) Hwu, J. R.; Jain, K.; Kumagai, M. L.; Tsai, F.-Y.; Tsay, S.-C.; Balakumar, A.; Gholam, H. *J. Org. Chem.* **2000**, *65*, 5077.



To the crude mixture containing **7** obtained from the previous reaction in THF (100 mL) was added 4 M HCl (50 mL) at room temperature, and the solution was stirred for 24 h. After completion of the reaction, ice-cold saturated $NaHCO_3$ was added until pH of the mixture became around 9. Then, the mixture was extracted with CH_2Cl_2, the combined organic layers were dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (4% MeOH/CH_2Cl_2) gave **19** (3.10 g, 4.81 mmol) in 67% yield as a colorless foam; $[\alpha]_D^{23}$ +13.7 (*c* 0.26, $CHCl_3$); IR (neat) ν 2949, 2867, 1685, 1459, 1385, 1171, 881 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{30}H_{58}N_3O_8Si_2$ *m*/*z* 644.3762 $[M+H]^+$, found 644.3757; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (1H, d, *J* = 8.0 Hz), 5.99 (1H, d, *J* = 6.2 Hz), 5.72 (1H, d, *J* = 8.0 Hz), (1H, m), 4.58 (1H, dd, *J* = 6.2 Hz, 4.2 Hz), 4.09 (1H, brd), 3.73 (3H, s), 3.63 (1H, d, *J* = 8.3 Hz), 3.58 (1H, d, *J* = 8.3 Hz), 1.05–0.98 (42H, m); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 163.1, 150.5, 141.4, 102.5, 88.8, 84.3, 75.0, 74.5, 70.9, 55.7, 52.6, 18.2, 18.15, 18.12, 13.0, 12.9, 12.8 .

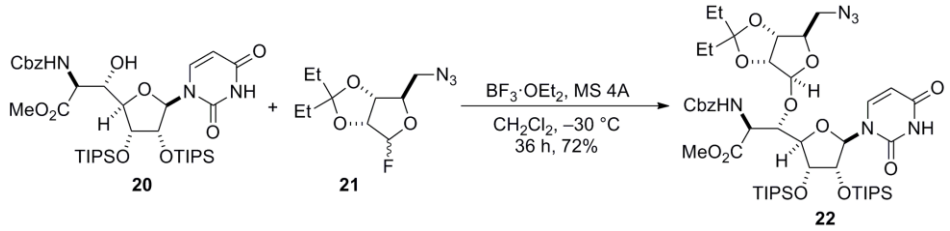
(2*S*,3*S*)-Methyl 2-(((benzyloxy)carbonyl)amino)-3-((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)-3-hydroxypropanoate (**20**).



To the aminoalcohol **19** (1.70 g, 2.64 mmol) in THF/H_2O (2:1, 15 mL) was added $NaHCO_3$ (443 mg, 5.27 mmol) and Cbz-Cl (0.56 mL, 3.96 mmol) at 0 °C and the solution was stirred for 20 h at the same temperature. The reaction mixture was diluted with H_2O and extracted with AcOEt. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (40% AcOEt/*n*-hexane) gave **20** (1.85 g, 2.38 mmol) in 90% yield as a white powder; mp 198 – 200 °C; $[\alpha]_D^{23}$ –8.36 (*c* 0.28, $CHCl_3$); IR (neat) ν 2945, 2868, 1734, 1696, 1666, 1537, 1468, 1132, 1068 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{38}H_{63}N_3NaO_{10}Si_2$ *m*/*z* 800.3950 $[M+Na]^+$, found 800.3944; ^1H NMR (400 MHz, CD_3OD) δ 8.10 (1H, d, *J* = 8.0 Hz), 7.35–7.25 (5H, m), 6.01 (1H, d, *J* = 7.3 Hz), 5.70 (1H, d, *J* = 8.0 Hz), 5.10 (1H, d, *J* = 12.5 Hz), 4.96 (1H, d, *J* = 12.5 Hz), 4.68 (1H, dd, *J* = 7.3 Hz, 4.3 Hz), 4.44 (1H, d, *J* = 6.5 Hz),

4.36 (1H, d, *J* = 4.3 Hz), 4.21 (1H, brd), 4.04 (1H, d, *J* = 6.5 Hz), 3.68 (3H, s), 3.58 (1H, d, *J* = 8.3 Hz), 1.10–0.97 (42H, m); ^{13}C NMR (100 MHz, CD_3OD) δ 170.9, 164.7, 157.2, 151.4, 141.9, 136.7, 128.1, 127.7, 127.5, 102.1, 87.2, 85.9, 75.9, 75.3, 70.1, 66.5, 56.8, 51.6, 17.4, 17.31, 17.27, 17.0, 12.8, 12.6.

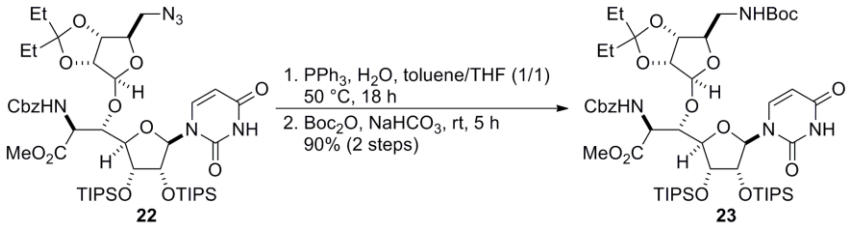
(2*S*,3*S*)-Methyl 3-(((3a*R*,4*S*,6*R*,6a*R*)-6-(azidomethyl)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)oxy)-2-(((benzyloxy)carbonyl)amino)-3-((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)propanoate (**22**).



The glycosyl acceptor **20** (430 mg, 0.552 mmol), the donor **21** (271 mg, 1.11 mmol), and finely powdered MS 4A (430 mg) in CH_2Cl_2 (5 mL) was stirred at –30 °C for 15 min. To the suspension was added $BF_3{\cdot}OEt_2$ (five injections every 1 h, 139 μL, 1.38 mmol altogether), and stirring was continued for additional 36 h. The reaction mixture was filtered through sintered funnel and diluted, and saturated $NaHCO_3$ was added. The mixture was extracted with AcOEt, and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (33% AcOEt/*n*-hexane) gave **22** (398 mg, 0.397 mmol) in 72% yield as a colorless foam (no noticeable amount of *α*-anomer was obtained); $[\alpha]_D^{23}$ +29.5 (*c* 0.29, $CHCl_3$); IR (neat) ν 2945, 2868, 2106, 1719, 1693, 1460, 1270, 1103, 1068 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{48}H_{78}N_6NaO_{13}Si_2$ *m*/*z* 1025.5063 $[M+Na]^+$, found 1025.5058; ^{1}H NMR (400 MHz, CD_3OD) δ 7.82 (1H, d, *J* = 8.3 Hz), 7.34–7.22 (5H, m), 5.77 (1H, d, *J* = 6.0 Hz), 5.65 (1H, d, *J* = 8.3 Hz), 5.47 (2H, s), 5.20 (1H, s), 5.17 (1H, d, *J* = 12.4 Hz), 4.96 (1H, d, *J* = 12.4 Hz), 4.73 (1H, d, *J* = 6.0 Hz), 4.60–4.53 (3H, m), 4.44 (1H, brt, *J* = 2.8 Hz), 4.30 (1H, brt, *J* = 2.8 Hz), 4.27 (1H, brt, *J* = 2.8 Hz), 4.21 (1H, brt, *J* = 2.8 Hz), 3.70 (3H, s), 3.67–3.56 (2H, m), 1.65 (2H, q, *J* = 7.3 Hz), 1.54 (2H, q, *J* = 7.3 Hz), 1.11-1.00 (42H, m), 0.88 (3H, t, *J* = 7.3 Hz), 0.83 (3H, t, *J* = 7.3 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 170.5, 164.6, 156.9, 150.8, 141.6, 136.6, 128.1, 127.9, 127.9, 117.2, 112.7, 101.5, 89.2, 86.3, 85.9, 85.6, 81.9, 78.7, 74.9, 74.0, 66.6, 56.0, 53.0, 51.9, 28.9, 28.5, 17.5, 17.4, 17.2, 12.9, 12.6, 7.5, 6.6.

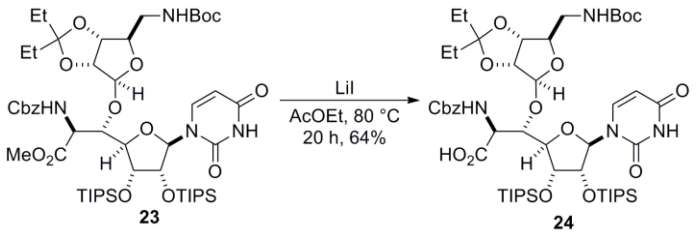
(2*S*,3*S*)-Methyl 2-(((benzyloxy)carbonyl)amino)-3-(((3a*R*,4*S*,6*R*,6a*R*)-6-(((*tert*-butoxycarbonyl)amino)methyl)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)oxy)-3-

((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)propanoate (**23**).



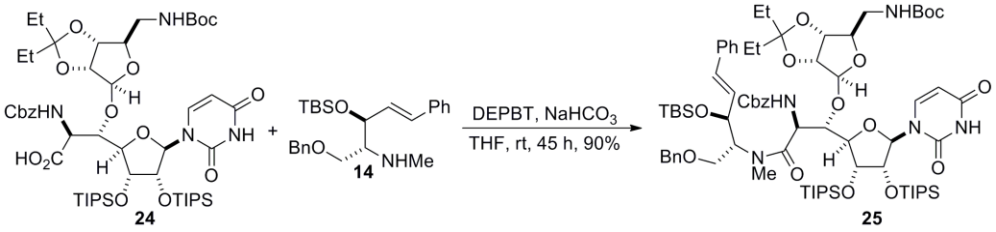
To the azide **22** (650 mg, 0.647 mmol) in H_2O (0.58 mL) and THF/toluene (1:1, 20 mL) was added PPh_3 (510 mg, 1.94 mmol), and the resulting solution was stirred at 50 °C for 18 h. After the mixture was cooled down to room temperature, $NaHCO_3$ (109 mg, 1.30 mmol) and Boc_2O (283 mg, 1.30 mmol) were added successively, and stirring was continued for another 5 h at the same temperature. The mixture was diluted with AcOEt, washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (30% AcOEt/*n*-hexane) gave **23** (560 mg, 0.520 mmol) in 80% yield as a colorless oil; $[\alpha]_D^{23}$ +6.59 (*c* 0.54, $CHCl_3$); IR (neat) ν 2944, 2867, 1696, 1462, 1172 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{53}H_{88}N_4NaO_{15}Si_2$ *m*/*z* 1099.5682 $[M+Na]^+$, found 1099.5677; ^1H NMR (400 MHz, CD_3OD) δ 7.75 (1H, d, *J* = 8.0 Hz), 7.37–7.26 (5H, m), 5.88 (1H, d, *J* = 7.3 Hz), 5.83 (1H, d, *J* = 8.0 Hz), 5.26 (1H, s), 5.08 (2H, s), 4.73 (1H, m), 4.62 (2H, s, overlap), 4.57 (1H, d, *J* = 3.9 Hz), 4.33–4.30 (2H, m), 4.22 (1H, d, *J* = 3.9 Hz), 4.12 (1H, brt, *J* = 7.4 Hz), 3.68 (3H, s), 3.14–3.08 (1H, m), 1.63 (2H, q, *J* = 7.3 Hz), 1.51 (2H, q, *J* = 7.3 Hz), 1.42 (9H, s), 1.13–1.02 (42H, m), 0.89–0.81 (6H, m); ^{13}C NMR (150 MHz, CD_3OD) δ 171.7, 165.9, 158.5, 152.4, 143.9, 137.8, 129.5, 129.2, 118.2, 114.4, 103.8, 90.8, 87.8, 87.6, 86.2, 83.4, 81.7, 80.5, 76.1, 75.6, 68.2, 57.2, 53.4, 44.3, 30.4, 30.0, 28.8, 18.9, 18.80, 18.76, 18.6, 14.3, 13.9, 8.8, 7.9.

(2*S*,3*S*)-2-(((Benzyloxy)carbonyl)amino)-3-(((3a*R*,4*S*,6*R*,6a*R*)-6-(((*tert*-butoxycarbonyl)amino)methyl)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)oxy)-3-((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)propanoic acid (**24**).



To the ester **23** (60.0 mg, 55.7 μmol) in AcOEt (2 mL) was added LiI (22.0 mg, 0.167 mmol), and the mixture kept from light was stirred for 20 h at 80 °C. The mixture was diluted with AcOEt, washed with 0.1 M HCl and brine, dried over Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by silica gel column chromatography (10% MeOH/CH_2Cl_2) gave **24** (38.0 mg, 35.7 μmol) in 64% yield as a colorless amorphous; $[\alpha]_D^{23}$ –0.62 (*c* 0.35, $CHCl_3$); IR (neat) ν 2945, 2868, 1693, 1464, 1216, 1172, 1057 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{52}H_{86}N_4NaO_{15}Si_2$ *m*/*z* 1085.5526 $[M+Na]^+$, found 1085.5520; ^1H NMR (400 MHz, CD_3OD) δ 7.90 (1H, d, *J* = 8.3 Hz), 7.36–7.24 (5H, m), 6.11 (1H, d, *J* = 7.8 Hz), 5.78 (1H, d, *J* = 8.3 Hz), 5.31 (1H, brs), 5.06 (2H, s), 4.59 (1H, m), 4.40 (1H, d, *J* = 3.7 Hz), 4.34–4.25 (3H, m), 4.22 (1H, d, *J* = 3.9 Hz), 4.14 (1H, brt, *J* = 6.5 Hz), 3.06 (1H, dd, *J* = 14.4, 8.0 Hz), 1.62 (2H, q, *J* = 7.3 Hz), 1.51 (2H, q, *J* = 7.3 Hz), 1.41 (9H, s), 1.11–0.98 (42H, m), 0.85 (3H, t, *J* = 7.3 Hz), 0.83 (2H, t, *J* = 7.3 Hz); ^{13}C NMR (150 MHz, CD_3OD) δ 166.0, 158.7, 158.5, 143.5, 138.0, 129.5, 129.2, 129.1, 118.1, 112.5, 103.7, 88.9, 88.1, 87.8, 87.7, 83.5, 80.9, 80.4, 76.4, 67.9, 44.7, 30.4, 30.1, 28.9, 19.0, 18.9, 18.8, 18.5, 14.4, 13.9, 8.8, 7.9.

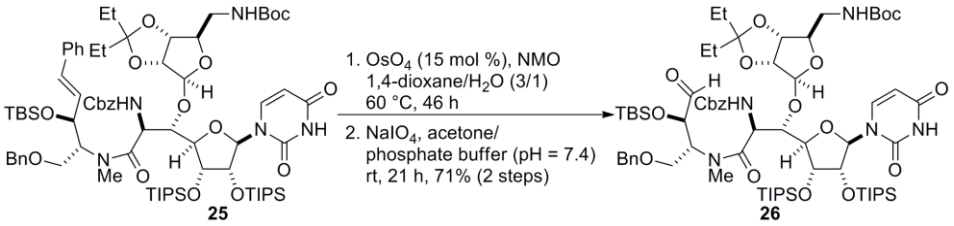
Benzyl ((1*S*,2*S*)-1-(((3a*R*,4*S*,6*R*,6a*R*)-6-(*tert*-butoxycarbonylaminomethyl)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)oxy)-3-(((2*R*,3*S*,*E*)-1-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-5-phenylpent-4-en-2-yl)(methyl)amino)-1-((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)-3-oxopropan-2-yl)carbamate (**25**).



Carboxylic acid **24** (355 mg, 0.334 mmol) and **14** (165 mg, 0.401 mmol) in THF (1 mL) was treated with $NaHCO_3$ (112 mg, 1.33 mmol) and DEPBT (3-(Diethoxyphosphoryloxy)-1,2,3-benzotriazin-4(3*H*)-one, 400 mg, 1.34 mmol) at room temperature for 45 h. The reaction was then quenched with 0.5 M HCl and extracted with AcOEt. The organic layer was then washed with saturated $NaHCO_3$, brine, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by silica gel column chromatography (25% AcOEt/*n*-hexane) to give the corresponding amide **25** in 90% yield (440 mg, ca. 1:1 mixture of rotamers) as a colorless oil; $[\alpha]_D^{23}$ –25.8 (*c* 0.46, $CHCl_3$); IR (neat) ν 2945, 1690, 1641, 1462, 1258, 1173, 1084 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{77}H_{121}N_5NaO_{16}Si_3$ *m*/*z* 1478.8014 $[M+Na]^+$, found 1478.7966; ^1H NMR (400 MHz, CD_3OD) δ 7.81 (0.5H, d, *J* = 8.0 Hz), 7.61 (0.5H, d, *J* = 8.0 Hz), 7.35–7.11 (15H, m), 6.53 (0.5H, d, *J* = 11.9 Hz), 6.49 (0.5H, d, *J* = 12.2 Hz), 6.35 (0.5H,

d, *J* = 7.8 Hz), 6.21 (0.5H, d, *J* = 7.6 Hz), 6.11–6.00 (1H, m), 5.92 (0.5H, d, *J* = 8.0 Hz), 5.82 (0.5H, d, *J* = 8.0 Hz), 5.26 (1H, m), 5.14–5.10 (1.5H, m), 5.00 (0.5H, d, *J* = 12.3 Hz), 4.57–4.16 (10H, m), 4.09 (0.5H, m), 4.01 (0.5H, dd, *J* = 9.5 Hz, 4.7 Hz), 3.91 (0.5H, m), 3.80–3.71 (1H, m), 3.63 (0.5H, m), 3.54 (0.5H, dd, *J* = 10.3 Hz, 3.1 Hz), 3.46 (0.5H, m), 3.33 (0.5H, m), 3.02 (1.5H, s), 2.89–2.78 (1H, m), 2.80 (1.5H, s), 1.71–1.63 (2H, m), 1.58–1.50 (2H, m), 1.40 (4.5H, s), 1.38 (4.5H, s), 1.12-0.94 (42H, m), 0.93-0.79 (6H, m), 0.85 (4.5H, s), 0.83 (4.5H, s), –0.00 (1.5H, s), –0.01 (1.5H, s), –0.05 (1.5H, s), –0.10 (1.5H, s); ^{13}C NMR (150 MHz, CD_3OD) δ 172.6, 171.7, 165.7, 165.4, 159.2, 158.7, 158.2, 158.1, 152.5, 152.4, 141.8, 141.6, 139.5, 139.4, 138.2, 138.1, 138.0, 137.6, 134.3, 133.6, 131.1, 130.3, 129.9, 129.70, 129.67, 129.5, 129.43, 129.36, 129.1, 129.0, 128.80, 128.78, 128.6, 127.8, 127.7, 118.8, 118.5, 114.9, 114.4, 104.8, 104.4, 87.9, 87.6, 87.5, 87.2, 87.0, 83.5, 83.1, 80.7, 80.5, 77.7, 76.9, 76.4, 75.9, 75.6, 74.2, 73.9, 68.3, 68.2, 68.0, 67.7, 62.4, 53.7, 52.7, 44.8, 44.6, 30.8, 30.6, 30.5, 29.4, 28.9, 28.8, 26.43, 26.39, 19.0, 18.92, 18.90, 18.84, 18.81, 18.76, 18.59, 18.58, 14.4, 14.3, 14.2, 14.0, 13.9, 8.8, 7.9, –3.4, –3.6, –4.5, –4.6.

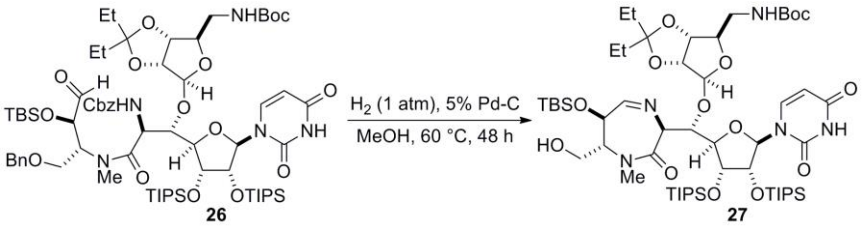
Benzyl ((1*S*,2*S*)-1-(((3a*R*,4*S*,6*R*,6a*R*)-6-(*tert*-butoxycarbonylaminomethyl)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)oxy)-3-(((2*R*,3*R*)-1-(benzyloxy)-3-((*tert*-butyldimethylsilyl)oxy)-4-oxobutan-2-yl)(methyl)amino)-1-((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)-3-oxopropan-2-yl)carbamate (**26**).



To a solution of **25** (412 mg, 0.283 mmol) in 1,4-dioxane/H_2O (3:1, 12.8 mL), were added OsO_4 (0.41 mL, 70 mM, 10 mol %), and NMO (99.5 mg, 0.849 mmol). The reaction mixture was then heated at 60 °C and stirred for 42 h. Then, 5 mol % of OsO_4 (0.20 mL, 70 mM) was added and stirring was continued for further 4 h. The mixture was cooled with ice bath, and the reaction was quenched with saturated $Na_2S_2O_3$. After stirring for 10 min at room temperature, the mixture was extracted with AcOEt four times. The combined organic layers were dried Na_2SO_4 and concentrated in vacuo. The resultant residue was partially purified with short pad of silica gel (50% AcOEt/*n*-hexane containing 3% of MeOH). Then, the residue was dissolved in acetone (3 mL)/phosphate buffer (0.2 M, pH = 7.4, 0.75 mL). After addition of $NaIO_4$ (160 mg, 0.750 mmol) the mixture was stirred for 14 h at room temperature. Then, acetone (1 mL), the buffer (0.2 mL), and another portion of $NaIO_4$ (80.2 mg, 0.375 mmol) was added, and stirring was continued for 4 h. Again, acetone (2 mL), the buffer (0.5 mL), and

$NaIO_4$ (321 mg, 1.50 mmol) was added, and stirring was continued for 3 h. The reaction was quenched with saturated $Na_2S_2O_3$ and extracted with AcOEt three times. The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Repeated silica gel column chromatography (2 to 3% acetone/$CHCl_3$) gave aldehyde **26** as a colorless oil (278 mg, 0.201 mmol, 71%); $[\alpha]_D^{22}$ –15.6 (*c* 0.79, $CHCl_3$); IR (neat) ν 2945, 1698, 1637, 1523, 1459, 1366, 1259, 1173, 1087 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{70}H_{116}N_5O_{17}Si_3$ *m*/*z* 1382.7674 $[M+H]^+$, found 1382.7633; ^1H NMR (400 MHz, $CDCl_3$, 7:3 mixture of conformers) δ 9.45 (0.7H, d, *J* = 1.6 Hz), 9.37 (0.3H, br), 8.10 (0.7H, br), 7.97 (0.3H, br), 7.54 (0.7H, d, *J* = 7.8 Hz), 7.36–7.22 (10H, m), 6.14 (0.3H, d, *J* = 7.1 Hz), 6.08–5.99 (1H, m), 5.93 (0.3H, brd, *J* = 7.8 Hz), 5.85 (0.7H, brd, *J* = 7.8 Hz), 5.81–5.70 (1H, m), 4.16–4.07 (2H, m), 4.04–4.01 (1H, m), 3.73–3.38 (3H, m), 3.07 (2.1H, s), 2.95–2.84 (1H, m), 2.86 (0.9H, s), 1.67–1.60 (2H, m), 1.51–1.44 (2H, m), 1.40 (9H, s), 1.07–0.99 (42H, m), 0.89–0.80 (6H, m), 0.87 (9H, s), 0.04 (4.2H, s), 0.09 (0.9H, s), 0.02 (0.9H, s), –0.01 (2.1H, s), –0.05 (2.1H, s); ^{13}C NMR* (125 MHz, $CDCl_3$, peaks for main conformer are shown) δ 200.4, 170.5, 162.3, 156.6, 155.5, 150.3, 140.7, 137.4, 136.1, 128.5, 128.40, 128.36, 127.8, 127.7, 127.6, 117.7, 113.0, 103.4, 86.4, 86.1, 85.6, 81.8, 79.6, 75.2, 74.3, 73.3, 67.3, 66.3, 58.6, 54.7, 51.7, 43.3, 32.8, 29.4, 28.9, 28.4, 25.6, 18.25, 18.15, 18.1, 17.9, 13.0, 12.6, 8.3, 7.4, –4.6, –5.3.

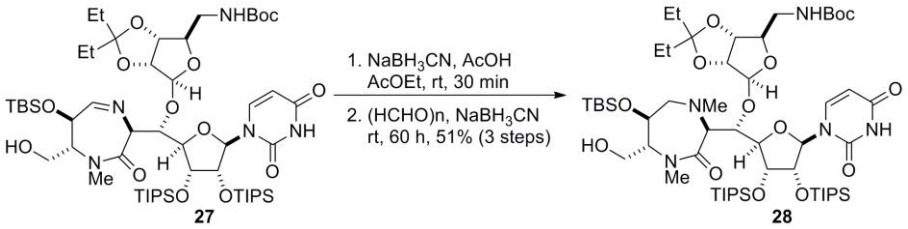
tert-Butyl (((3a*R*,4*R*,6*S*,6a*R*)-6-((*S*)-((3*S*,6*R*,7*R*)-6-((*tert*-butyldimethylsilyl)oxy)-7-(hydroxymethyl)-1-methyl-2-oxo-2,3,6,7-tetrahydro-1*H*-1,4-diazepin-3-yl)((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)methoxy)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methyl)carbamate (**27**).



To a solution of **26** (20.7 mg, 15.0 μmol) in 2 mL of MeOH were added 5% Pd-C (6.4 mg), and the mixture was stirred at 60 °C for 40 h under atmospheric pressure of H_2. Then, the catalyst was filtered of on pad of celite. The filtrate was concentrated in vacuo to give a crude material containing **27**, which was used without purification for the next step.

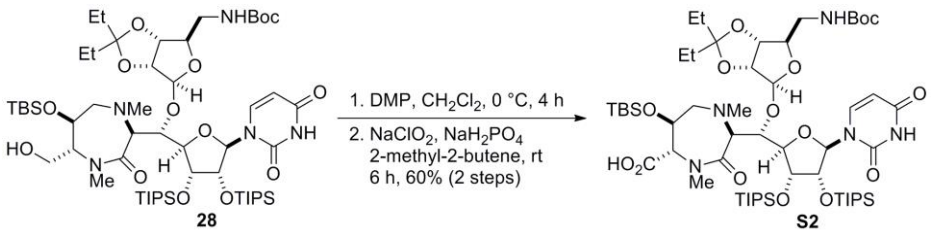
tert-Butyl (((3a*R*,4*R*,6*S*,6a*R*)-6-((*S*)-((2*S*,5*R*,6*S*)-6-((*tert*-butyldimethylsilyl)oxy)-5-(hydroxymethyl)-1,4-dimethyl-3-oxo-1,4-diazepan-2-yl)((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-

3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)methoxy)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)methyl)carbamate (**28**).



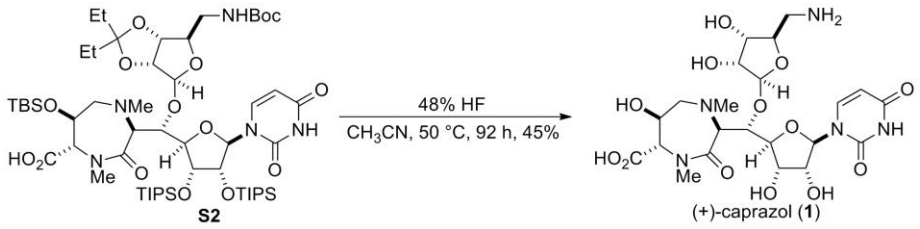
To a crude material containing **27** obtained from the preceding experiment, AcOEt (1 mL) was added followed by the addition of $NaBH_3CN$ (3.8 mg, 60.5 μmol), and AcOH (13.0 μL, 0.227 mmol). The reaction mixture was stirred for 30 min at room temperature. Then, $(HCHO)_n$ (4.5 mg, 0.150 mmol) was added followed by the addition of $NaBH_3CN$ (7.5 mg, 0.119 mmol). The reaction mixture was stirred for 60 h at room temperature, quenched with saturated $NaHCO_3$, stirred for 30 min, extracted with AcOEt. The combined organic extracts were dried over Na_2SO_4 and concentrated. The crude mixture was then purified by silica gel column chromatography (33% AcOEt/*n*-hexane) to give **28** (8.8 mg, 7.61 μmol, 51% yield over 3 steps) as a colorless amorphous; $[\alpha]_D^{27}$ –46.7 (*c* 0.25, $CHCl_3$); IR (neat) ν 2942, 1699, 1644, 1464, 1257, 1174, 1095, 1077 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{56}H_{106}N_5O_{14}Si_3$ *m*/*z* 1156.7039 $[M+H]^+$, found 1156.7023; ^1H NMR (400 MHz, $CDCl_3$, 2:1 mixture of conformers) δ 8.07 (0.33H, br), 8.02 (0.67H, br), 7.75 (0.67H, d, *J* = 8.0 Hz), 7.69 (0.33H, d, *J* = 8.5 Hz), 7.44 (0.67H, br), 7.14 (0.33H, br), 6.27 (0.67H, dd, *J* = 8.2, 1.8 Hz), 6.21 (0.67H, d, *J* = 8.0 Hz), 6.09 (0.33H, br), 5.77 (0.33H, br), 5.20 (1H, br), 4.79 (0.67H, d, *J* = 6.0 Hz), 4.64 (0.33H, d, *J* = 5.5 Hz), 4.50–4.44 (4.33H, m), 4.38–4.30 (2.33H, m), 4.03 (0.67H, br), 3.94 (0.33H, br), 3.87–3.67 (3.33H, m), 3.69–3.53 (1H, m), 3.48–3.35 (1.33H, m), 3.26–3.15 (1.33H, m), 3.06 (3H, br), 2.94 (0.67H, m), 2.82–2.65 (0.67H, m), 2.43 (3H, br), 2.04 (0.67H, br), 1.94 (0.33H, br), 1.77–1.67 (2H, m), 1.58–1.50 (2H, m), 1.47 (9H, s), 1.19–0.97 (42H, m), 0.94–0.81 (6H, m), 0.86 (9H, s), 0.08–0.04 (6H, m); ^{13}C NMR* (125 MHz, $CDCl_3$, peaks for main conformer are shown) δ 162.9, 154.8, 150.7, 140.9, 116.8, 113.7, 104.5, 88.6, 87.5, 86.7, 86.3, 83.6, 79.2, 75.4, 74.0, 69.0, 68.6, 62.3, 61.2, 59.8, 43.8, 38.4, 30.0, 29.7, 29.5, 28.5, 25.7, 18.3, 18.2, 18.1, 18.0, 13.0, 12.0, 8.2, 7.4, –4.9.

(2*S*,5*S*,6*S*)-2-((*S*)-(((3a*R*,4*S*,6*R*,6a*R*)-6-(((tert-butoxycarbonyl)amino)methyl)-2,2-diethyltetrahydrofuro[3,4-*d*][1,3]dioxol-4-yl)oxy)((2*R*,3*R*,4*R*,5*R*)-5-(2,4-dioxo-3,4-dihydropyrimidin-1(2*H*)-yl)-3,4-bis((triisopropylsilyl)oxy)tetrahydrofuran-2-yl)methyl)-6-((*tert*-butyldimethylsilyl)oxy)-1,4-dimethyl-3-oxo-1,4-diazepane-5-carboxylic acid (**S2**).



To a solution of the alcohol **28** (15.0 mg, 13.0 μmol) in CH_2Cl_2 (1 mL) was added DMP (16.5 mg, 38.9 μmol) at 0 °C and stirred for 4 h. The reaction was quenched with saturated $NaHCO_3$/saturated $Na_2S_2O_3$ (2:1, 1 mL) and stirred for 15 min followed by extraction with AcOEt, dried over Na_2SO_4, concentrated and connected to vacuo. The crude mixture was then dissolved in THF/*t*-BuOH/H_2O (1:3:5, 1 mL) followed by the addition NaH_2PO_4 (4.7 mg, 39.2 μmol), 2-methyl-2-butene (11.0 μL, 0.104 mmol), and $NaClO_2$ (3.5 mg, 38.7 μmol) at 0 °C. After 5 min, the reaction was brought to room temperature and stirring continued for 6 h. Quenched with phosphate buffer (pH = 6.8, 1 mL), extracted with AcOEt, dried over Na_2SO_4 and concentrated in vacuo. The crude mixture was then purified by preparative TLC (10% MeOH/CH_2Cl_2) to give **S2** (9.1 mg, 7.77 μmol, 60% yield over 2 steps) as a colorless amorphous; $[\alpha]_D^{26}$ –22.0 (*c* 0.37, $CHCl_3$); IR (neat) ν 2944, 1711, 1659, 1467, 1258, 1175, 1099 cm^{-1}; HRMS (ESI) Anal. calcd. for $C_{56}H_{104}N_5O_{15}Si_3$ *m*/*z* 1170.6837 $[M+H]^+$, found 1170.6798; ^1H NMR (400 MHz, acetone-d_6, 2:1 mixture of conformers) δ 10.12 (0.67H, br), 9.97 (0.33H, br), 7.93 (0.67H, d, *J* = 8.2 Hz), 7.81 (0.3H, d, *J* = 7.8 Hz), 7.17 (0.33H, brd, *J* = 8.2 Hz), 6.97 (0.67H, br), 6.22–6.20 (1H, m), 6.13 (0.33H, brd,), 5.76 (0.67H, d, *J* = 7.6 Hz), 5.29 (1H, s), 4.87 (0.33H, brd, *J* = 4.8 Hz), 4.78 (0.67H, d, *J* = 6.0 Hz), 4.65–4.57 (2H, m), 4.51–4.30 (6H, m), 3.90 (0.33H, d, *J* = 10.0 Hz), 3.78 (0.67H, d, *J* = 9.6 Hz), 3.69–3.48 (2H, m), 3.21 (3H, s), 3.16–3.00 (2H, m), 2.56 (1H, s), 2.54 (2H, s), 1.80–1.57 (4H, m), 1.54 (3H, s), 1.49 (6H, s), 1.36–0.87 (48H, m), 0.98 (9H, s), 0.22 (6H, m); ^{13}C NMR* (125 MHz, acetone-d_6, peaks for main conformer are shown) δ 171.6, 170.8, 163.3, 157.1, 151.6, 140.4, 117.5, 113.7, 103.7, 88.7, 87.7, 87.2, 86.9, 84.0, 79.2, 78.1, 77.4, 75.6, 70.6, 67.8, 64.1, 61.5, 43.9, 38.6, 28.8, 26.2, 18.8, 18.7, 18.6, 18.4, 13.8, 12.9, 8.6, 7.6, –4.8, –5.2.

(+)-caprazol (**1**).

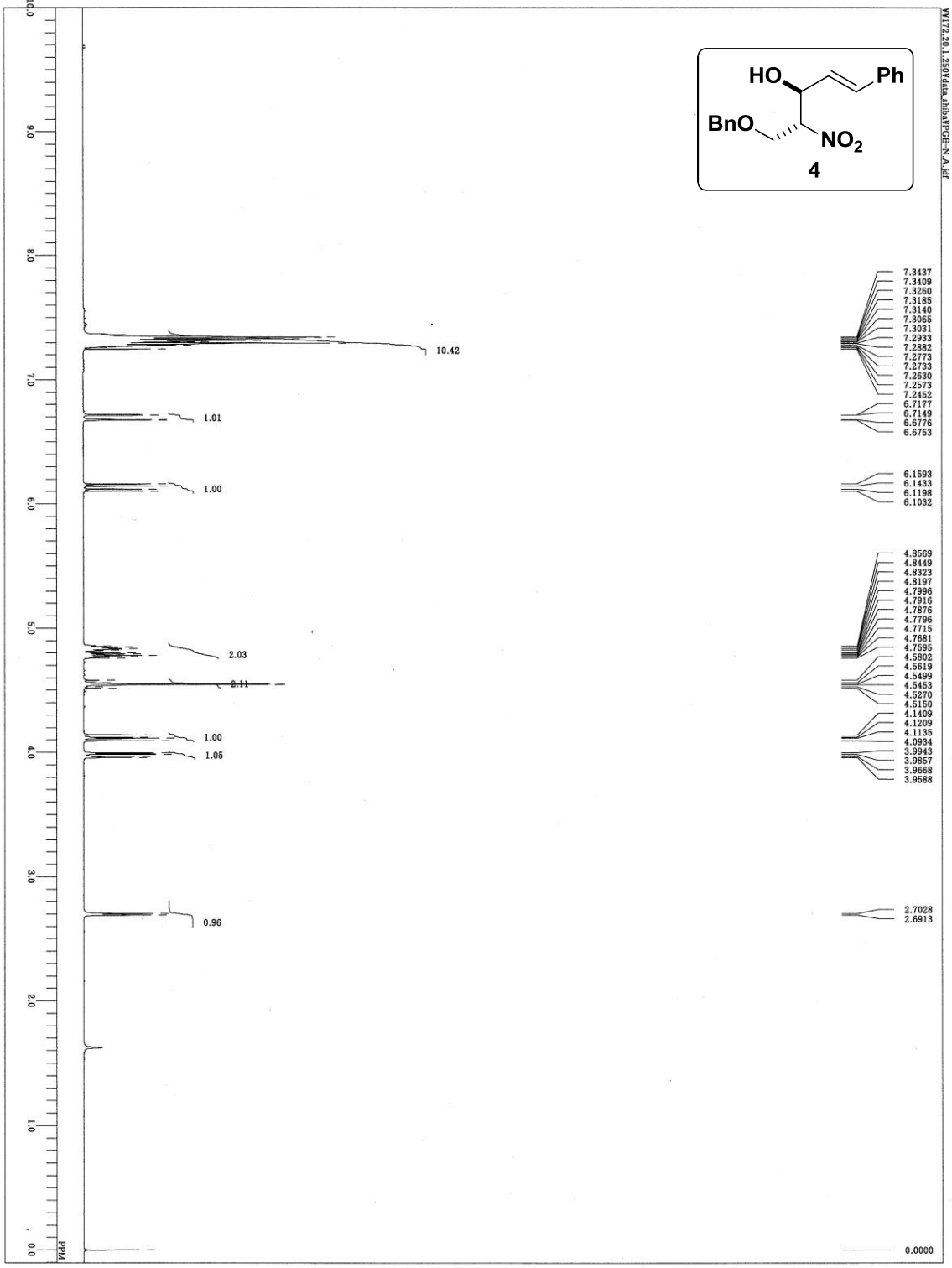


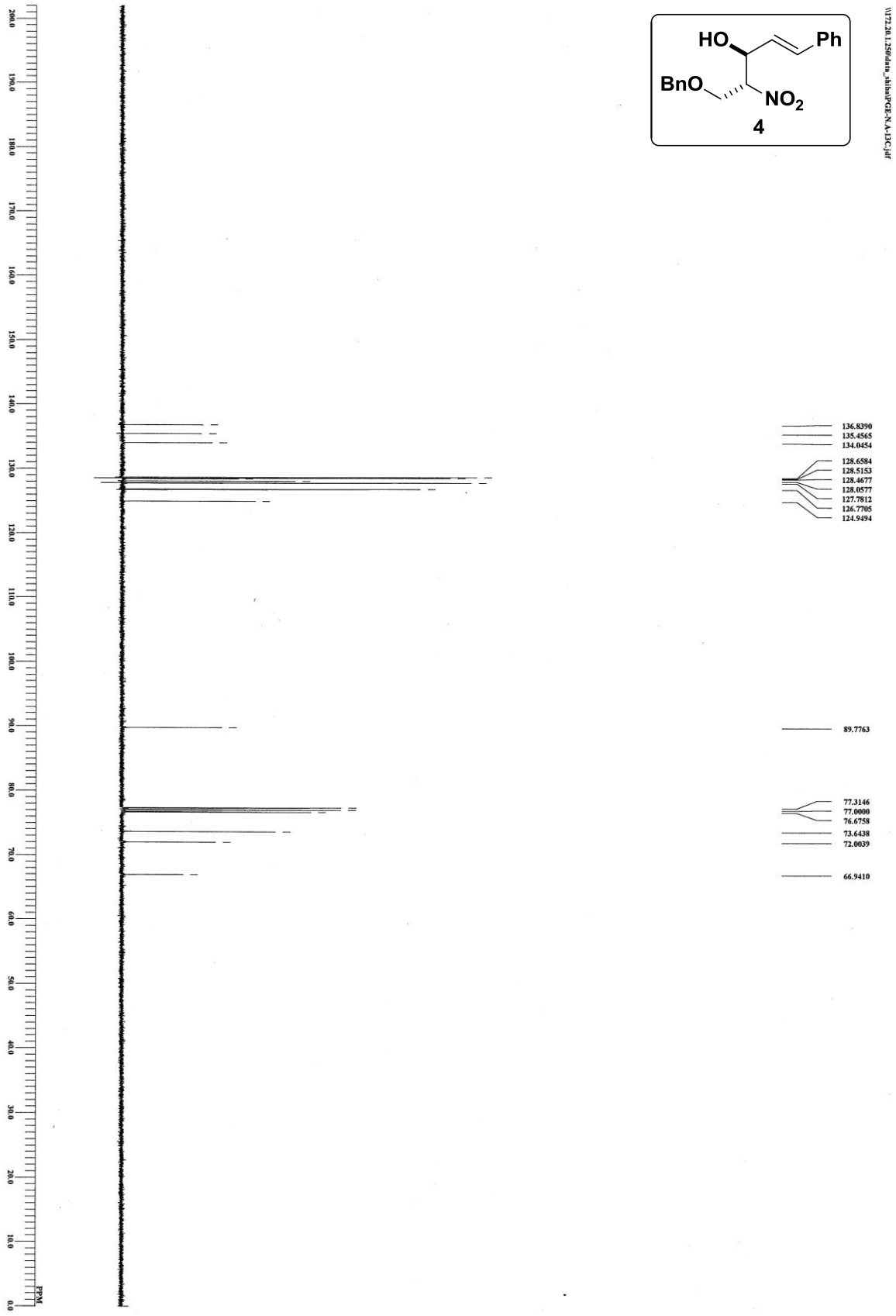
To a solution of **S2** (11.7 mg, 9.94 μmol) in 1.58 mL of CH_3CN was added 0.158 mL of 48% HF and stirred for 92 h at 50 °C. The reaction mixture was quenched with saturated $NaHCO_3$ (added at 0 °C to adjust pH to ca. 6), and concentrated to dryness. The resultant residue was dissolved in 50% MeOH, and purified by repeated gel filtration chromatography (Sephadex® LH-20) using 50% MeOH as eluent to give 2.6 mg (4.52 μmol. 45%) of (+)-caprazol (**1**) a white solid; mp 201–203 °C; $[\alpha]_D^{27}$ +23.2 (*c* 0.10, H_2O); HRMS (ESI) Anal. calcd. for $C_{22}H_{34}N_5O_{13}$ *m*/*z* 576.2153 $[M+H]^+$, found 576.2148; ^1H NMR (600 MHz, D_2O) δ 7.73 (1H, d, *J* = 8.3 Hz), 5.78 (1H, d, *J* = 8.3 Hz), 5.56 (1H, d, *J* = 2.1 Hz), 5.13 (1H, s), 4.40 (1H, m), 4.35 (1H, dd, *J* = 9.4 Hz, 2.1 Hz), 4.27 (1H, d, *J* = 5.3 Hz, 2.1 Hz), 4.21 (1H, 6.8 Hz, 4.4 Hz), 4.19–4.15 (2H, m), 4.10–4.08 (2H, m), 4.04 (1H, dd, *J* = 8.4 Hz, 5.3 Hz), 3.81 (1H, d, *J* = 9.4 Hz), 3.28 (1H, dd, *J* = 13.8 Hz, 3.9 Hz), 3.16 (1H, dd, *J* = 13.8 Hz, 4.4 Hz), 3.09 (1H, dd, *J* = 15.1 Hz, 2.1 Hz), 3.03 (3H, s), 2.97 (1H, d, *J* = 15.1 Hz, 2.5 Hz), 2.39 (3H, s); ^{13}C NMR* (125 MHz, D_2O) δ 176.6, 175.2, 169.7, 154.4, 145.3, 113.7, 104.1, 94.2, 84.9, 81.5, 80.0, 77.9, 76.5, 73.0, 72.5, 71.8, 65.9, 61.6, 42.6, 41.7, 39.4. The dada was identical to that of caprazol from natural caprazamycin.

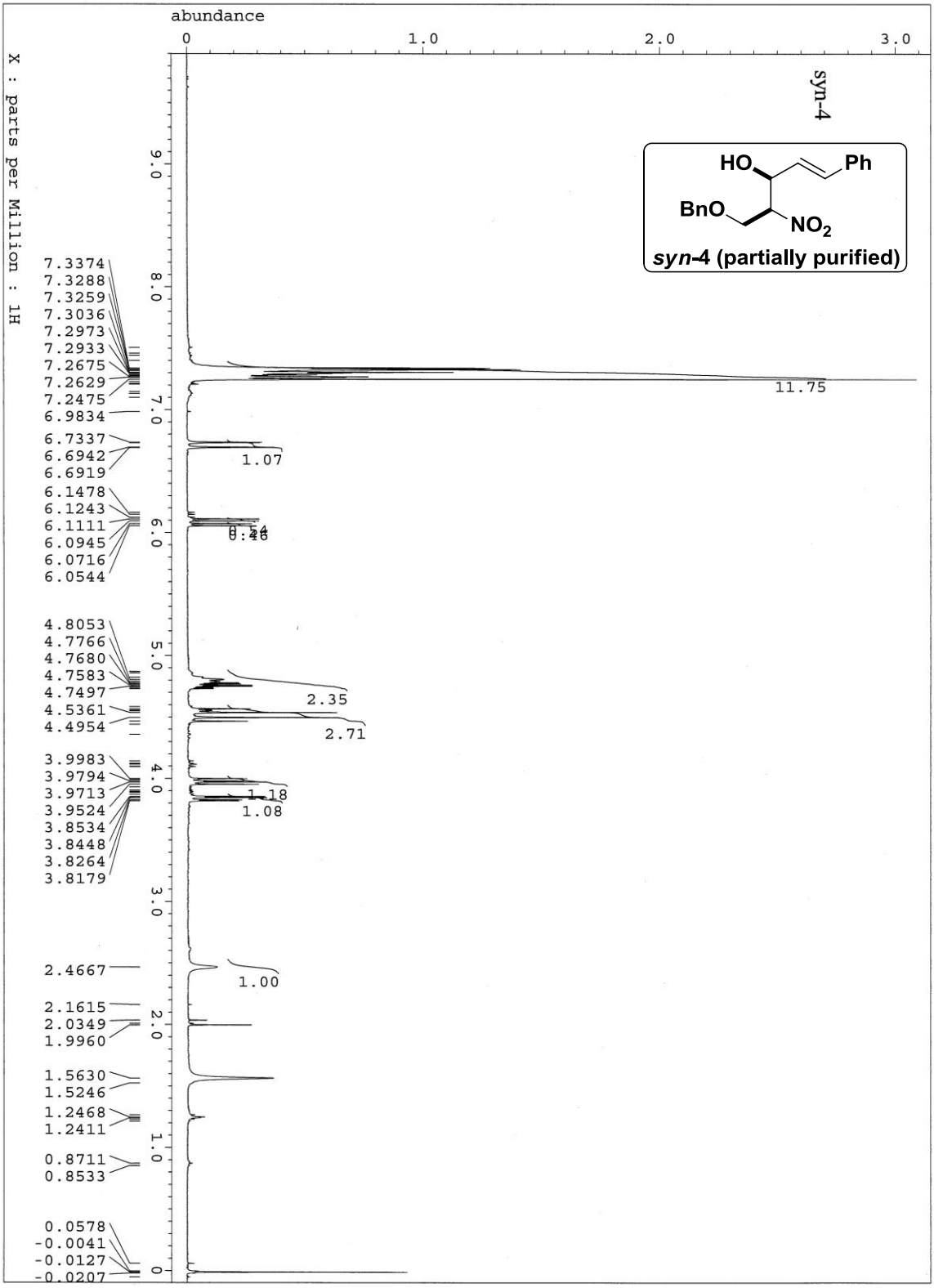
Another sample of (+)-caprazol (**1**) was independently prepared from natural caprazamycin B given by Dr. M. Igarashi (BIKAKEN) according to the reported procedure.[5] Optical rotation was measured; $[\alpha]_D^{27}$ +16.9 (*c* 0.10, H_2O, lit. $[\alpha]_D^{19}$ +28 (*c* 0.5, DMSO)).

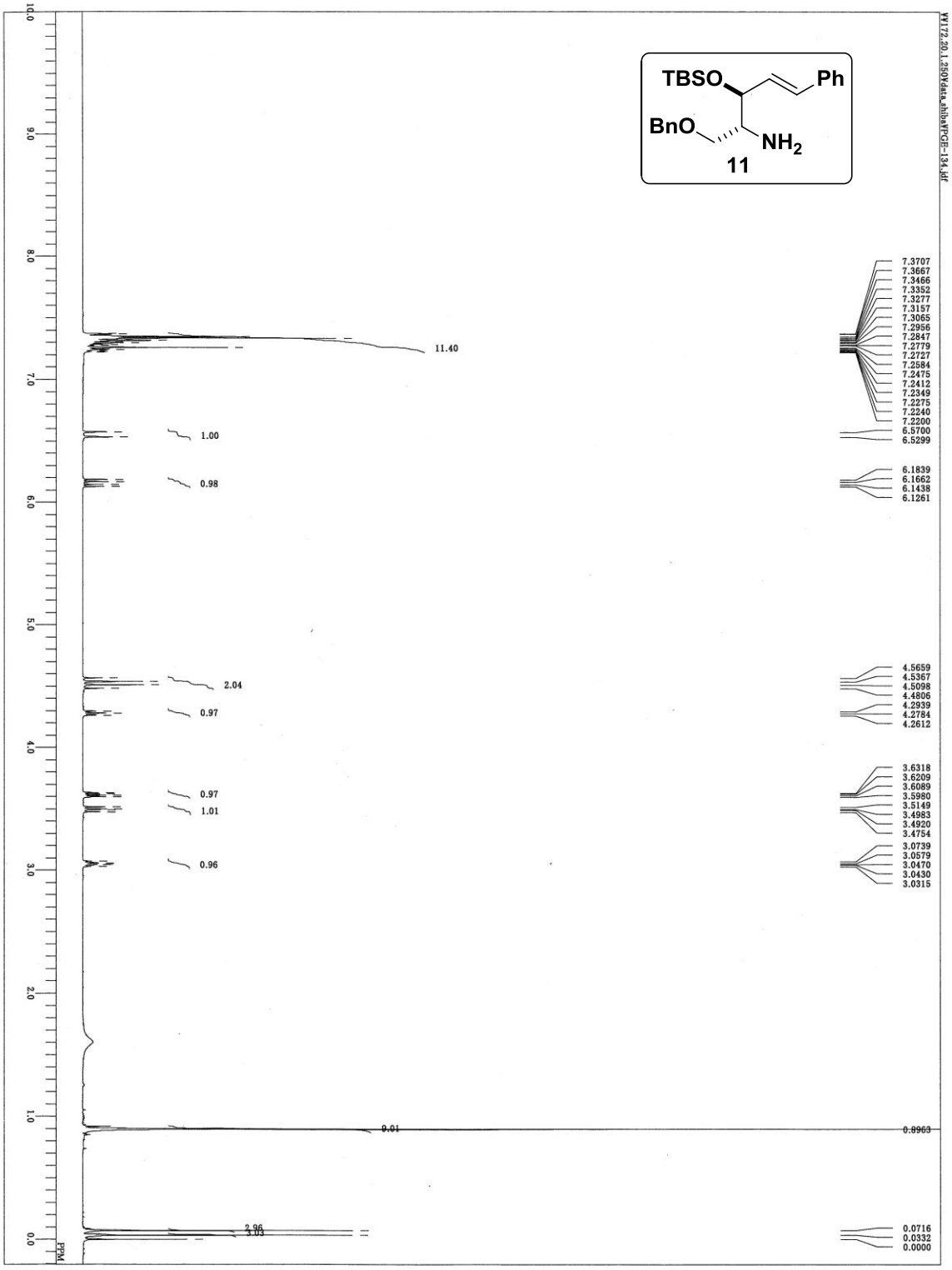
(5) Igarashi, M.; Takahashi, Y.; Shitara, T.; Nakamura, H.; Naganawa, H.; Miyake, T.; Akamatsu, Y. *J. Antibiot.* **2005**, *58*, 327.

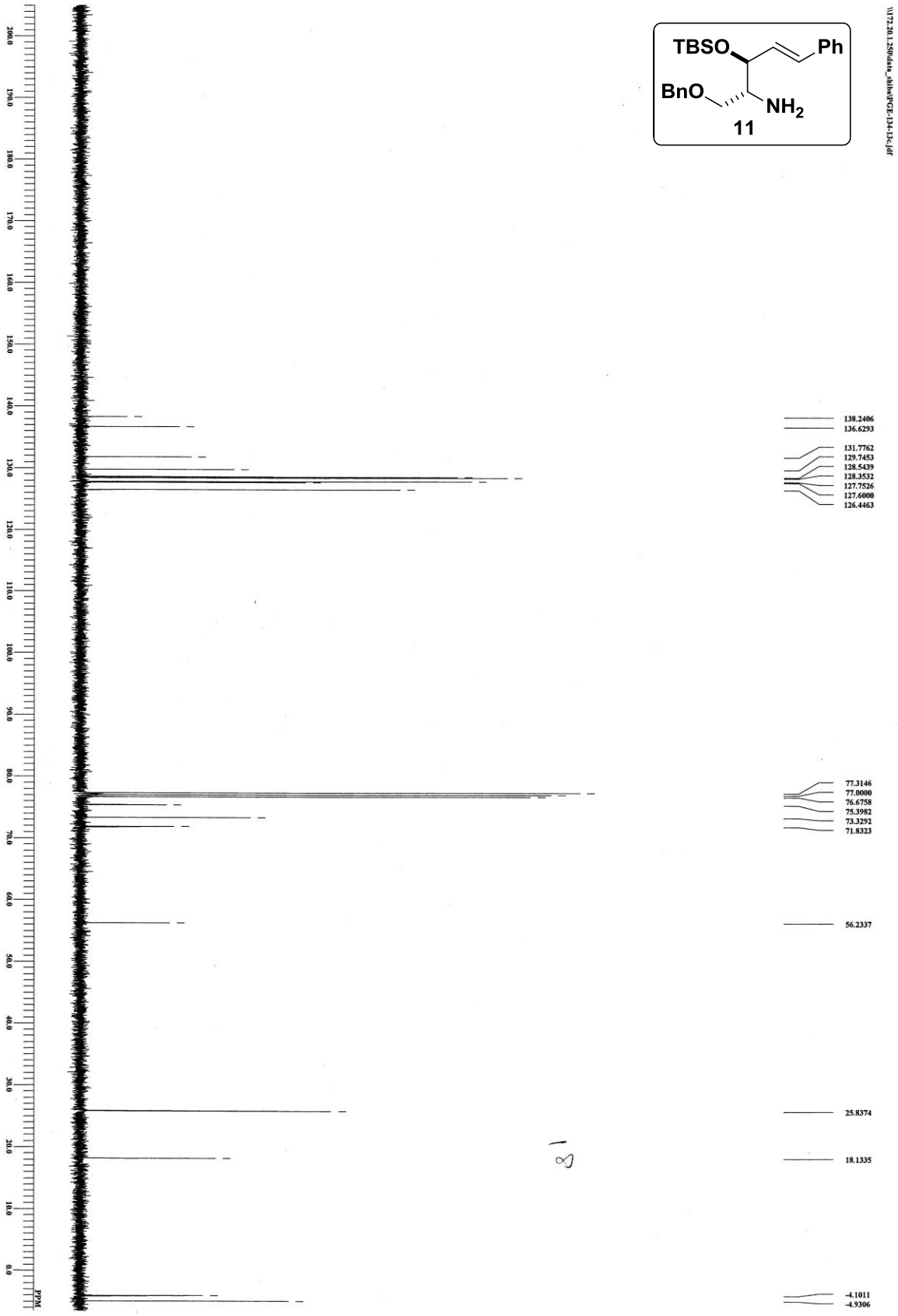
5. NMR spectra

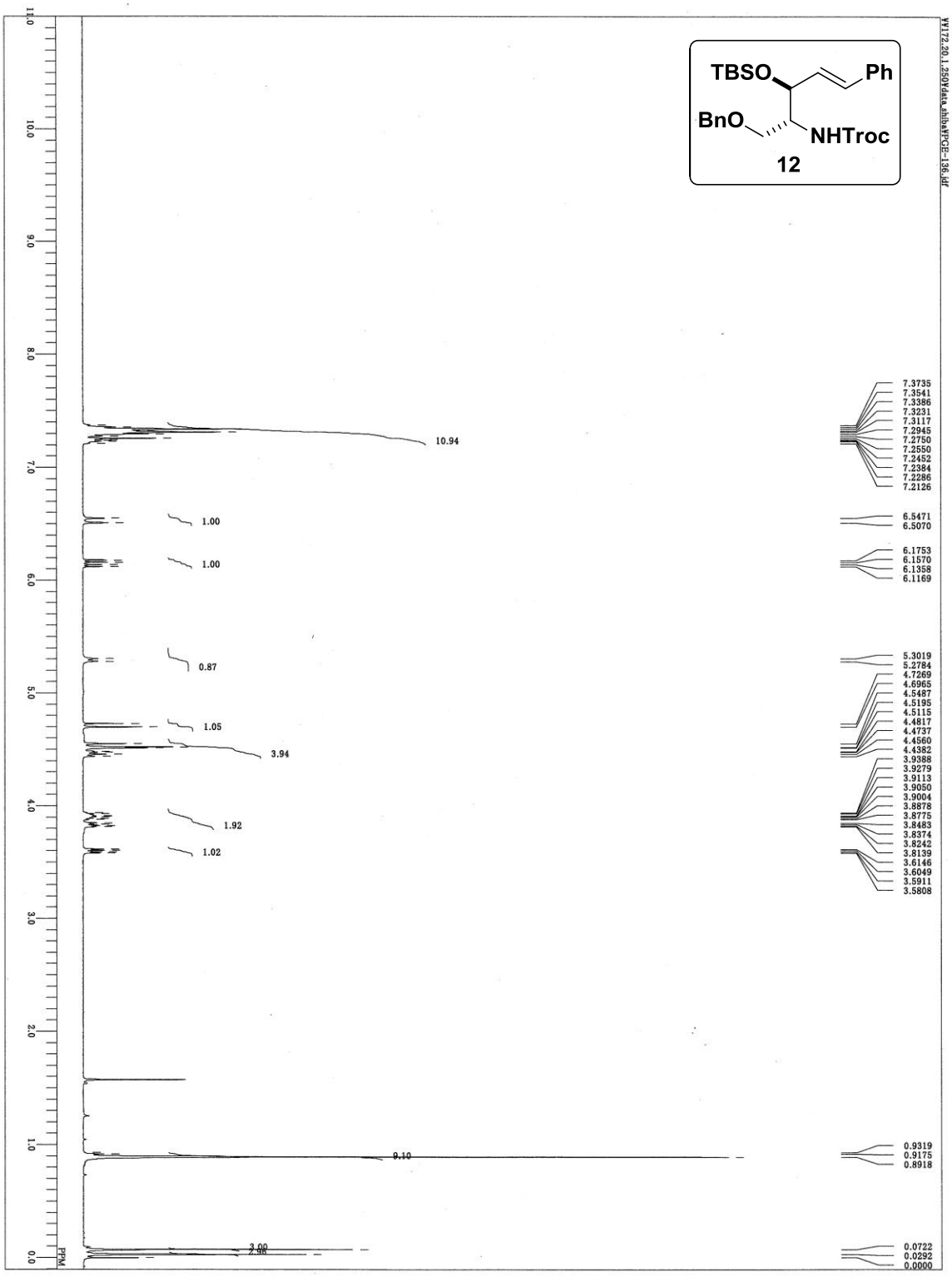


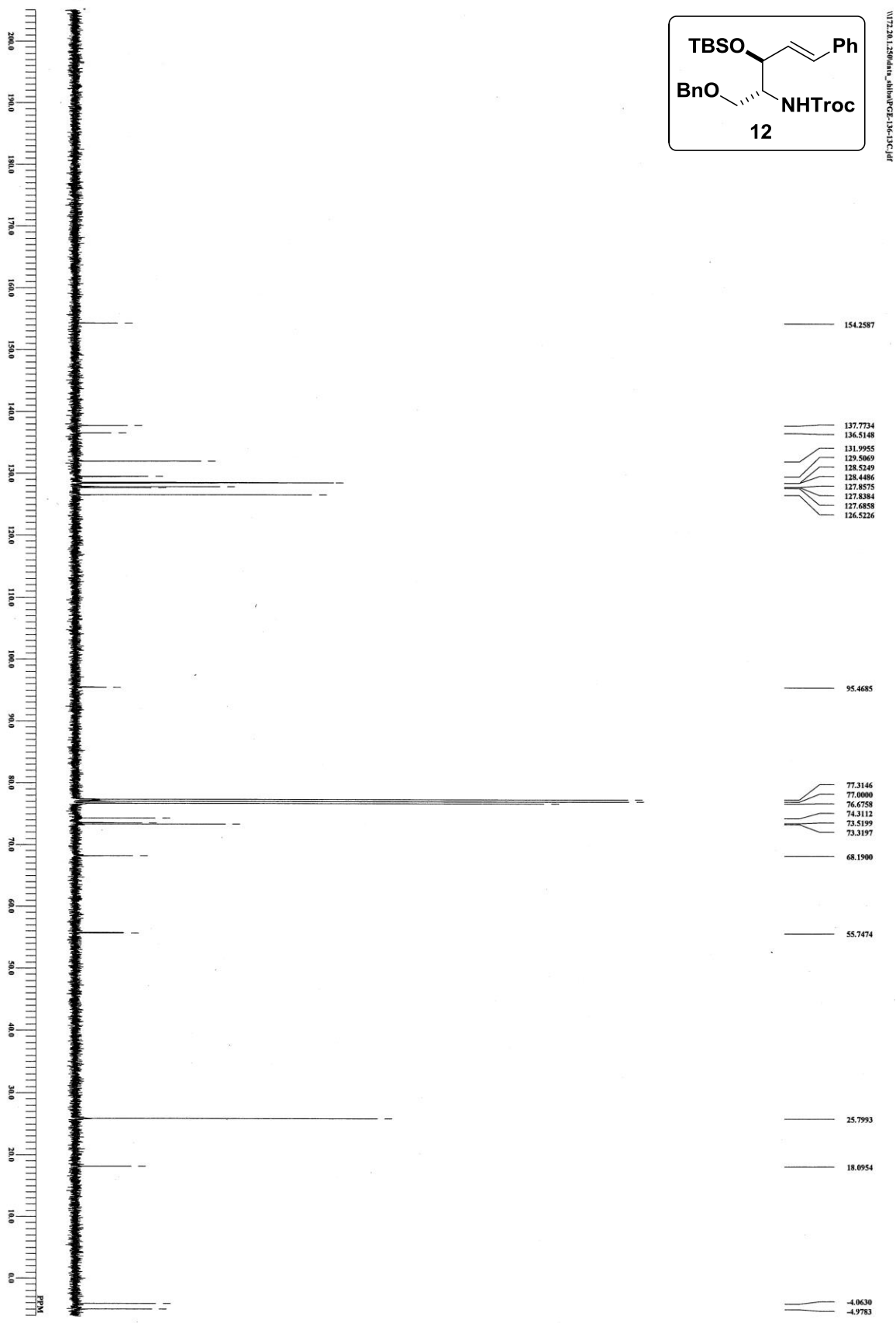

HO
Ph
BnO
NO2
4
136.8390
135.4565
134.0454
128.6584
128.5153
128.4677
128.0577
127.7812
126.7705
124.9494
89.7763
77.3146
77.0000
76.6758
73.6438
72.0039
66.9410
PPM

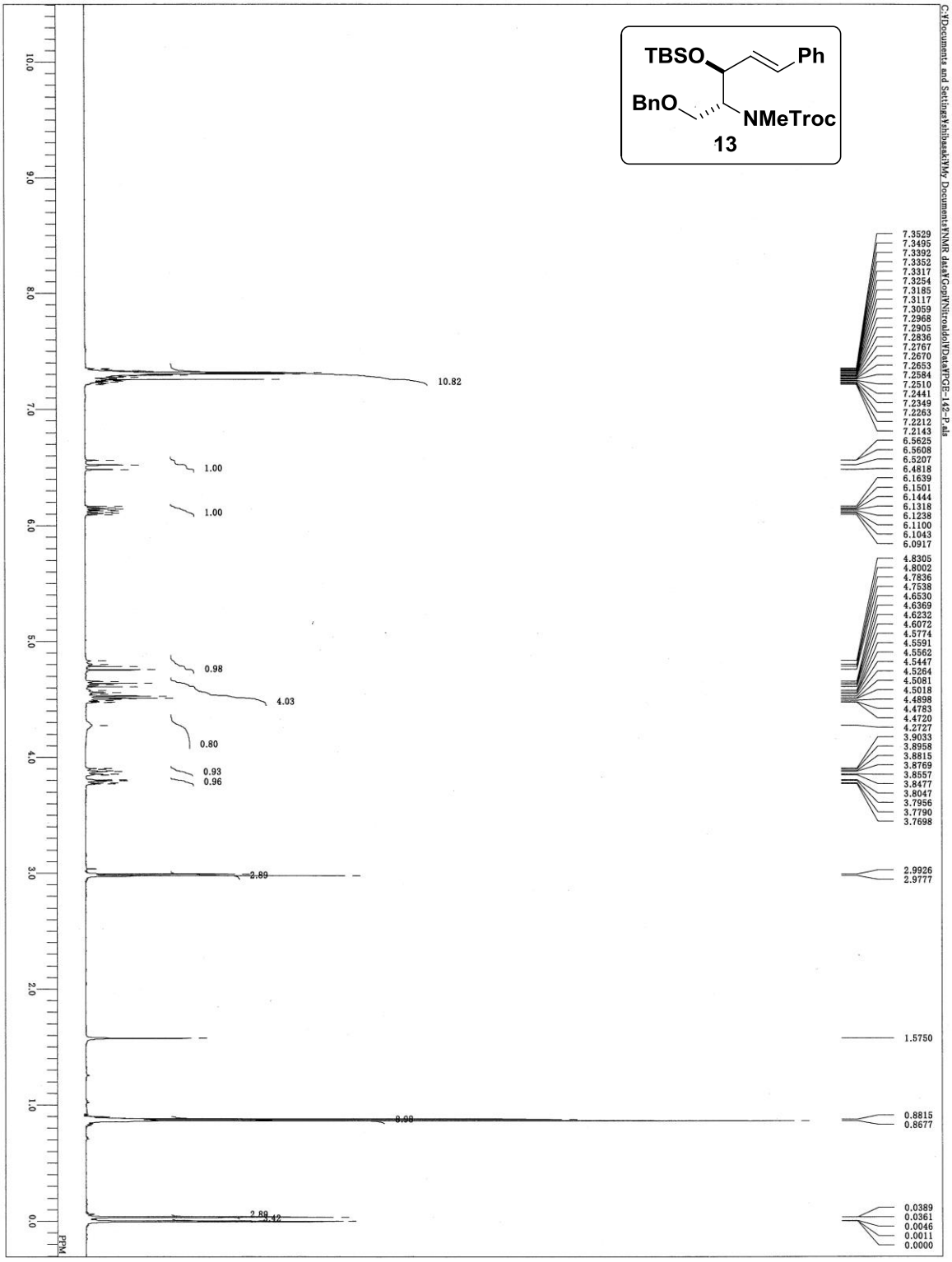

abundance
0
1.0
2.0
3.0
X : parts per Million : 1H
syn-4
HO
Ph
BnO
NO2
syn-4 (partially purified)
7.3374
7.3288
7.3259
7.3036
7.2973
7.2933
7.2675
7.2629
7.2475
6.9834
6.7337
6.6942
6.6919
6.1478
6.1243
6.1111
6.0945
6.0716
6.0544
4.8053
4.7766
4.7680
4.7583
4.7497
4.5361
4.4954
3.9983
3.9794
3.9713
3.9524
3.8534
3.8448
3.8264
3.8179
2.4667
2.1615
2.0349
1.9960
1.5630
1.5246
1.2468
1.2411
0.8711
0.8533
0.0578
-0.0041
-0.0127
-0.0207
11.75
1.07
2.35
2.71
1.18
1.08
1.00

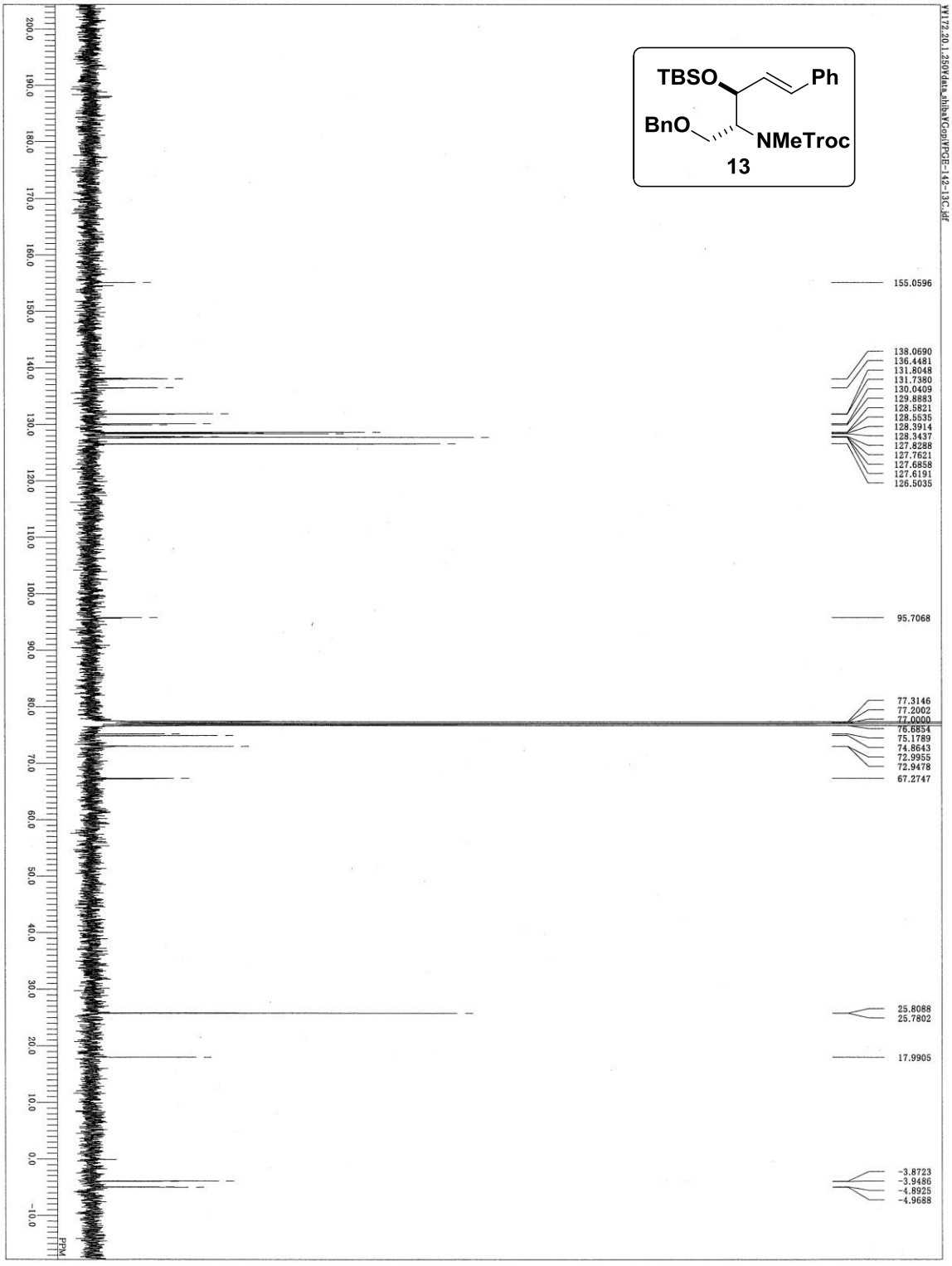

TBSO
Ph
BnO
NH2
11
11.40
1.00
0.98
2.04
0.97
0.97
1.01
0.96
9.01
2.96
3.03
0.8963
7.3707
7.3667
7.3466
7.3352
7.3277
7.3157
7.3065
7.2956
7.2847
7.2779
7.2727
7.2584
7.2475
7.2412
7.2349
7.2275
7.2240
7.2200
6.5700
6.5299
6.1839
6.1662
6.1438
6.1261
4.5659
4.5367
4.5098
4.4806
4.2939
4.2784
4.2612
3.6318
3.6209
3.6089
3.5980
3.5149
3.4983
3.4920
3.4754
3.0739
3.0579
3.0470
3.0430
3.0315
0.0716
0.0332
0.0000
PPM

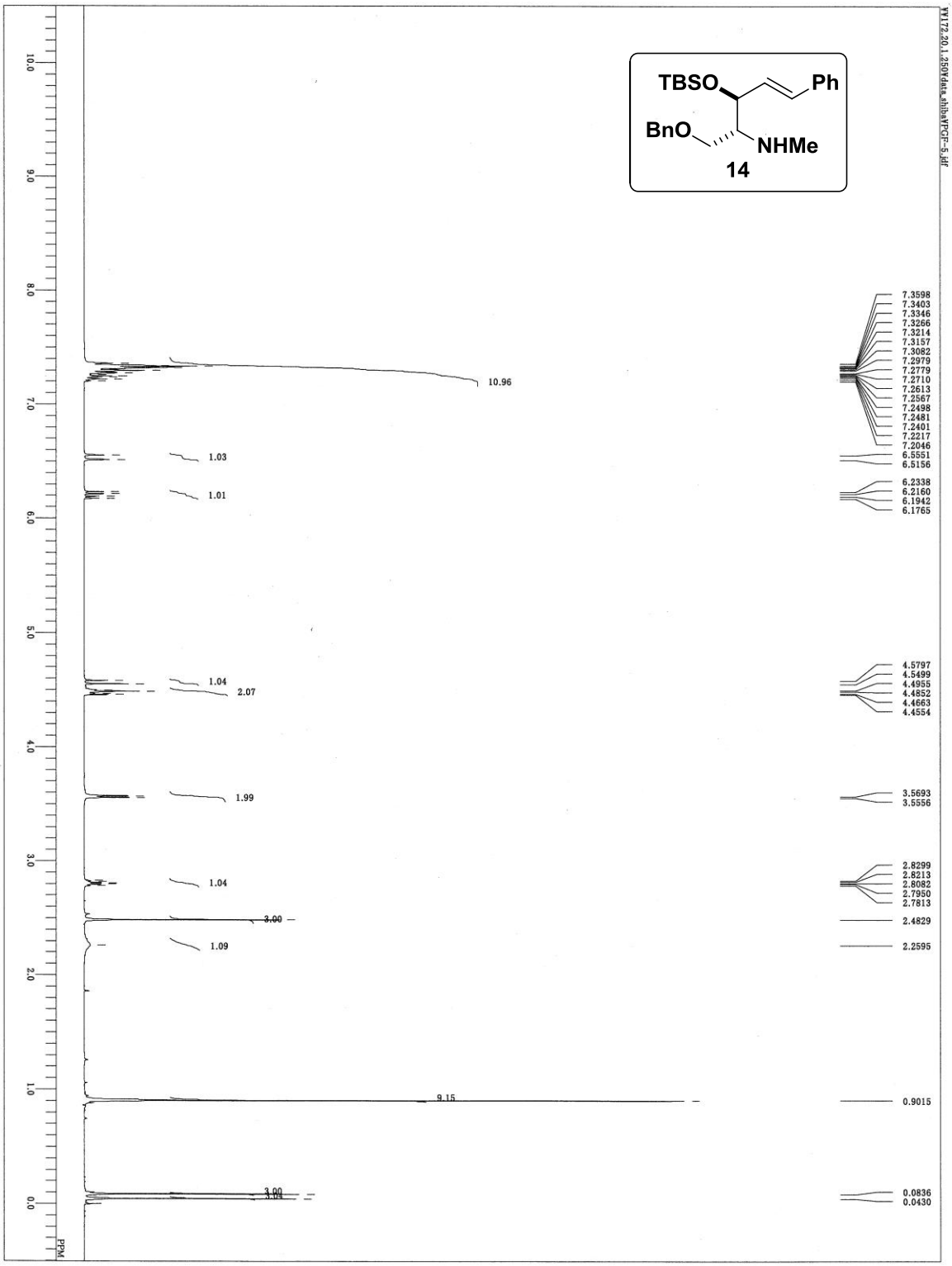

TBSO
Ph
BnO
NH2
11
\\172.20.1.250\data_shiba\PGE-134-13C.jdf
138.2406
136.6293
131.7762
129.7453
128.5439
128.3532
127.7526
127.6000
126.4463
77.3146
77.0000
76.6758
75.3982
73.3292
71.8323
56.2337
25.8374
18.1335
-4.1011
-4.9306
PPM

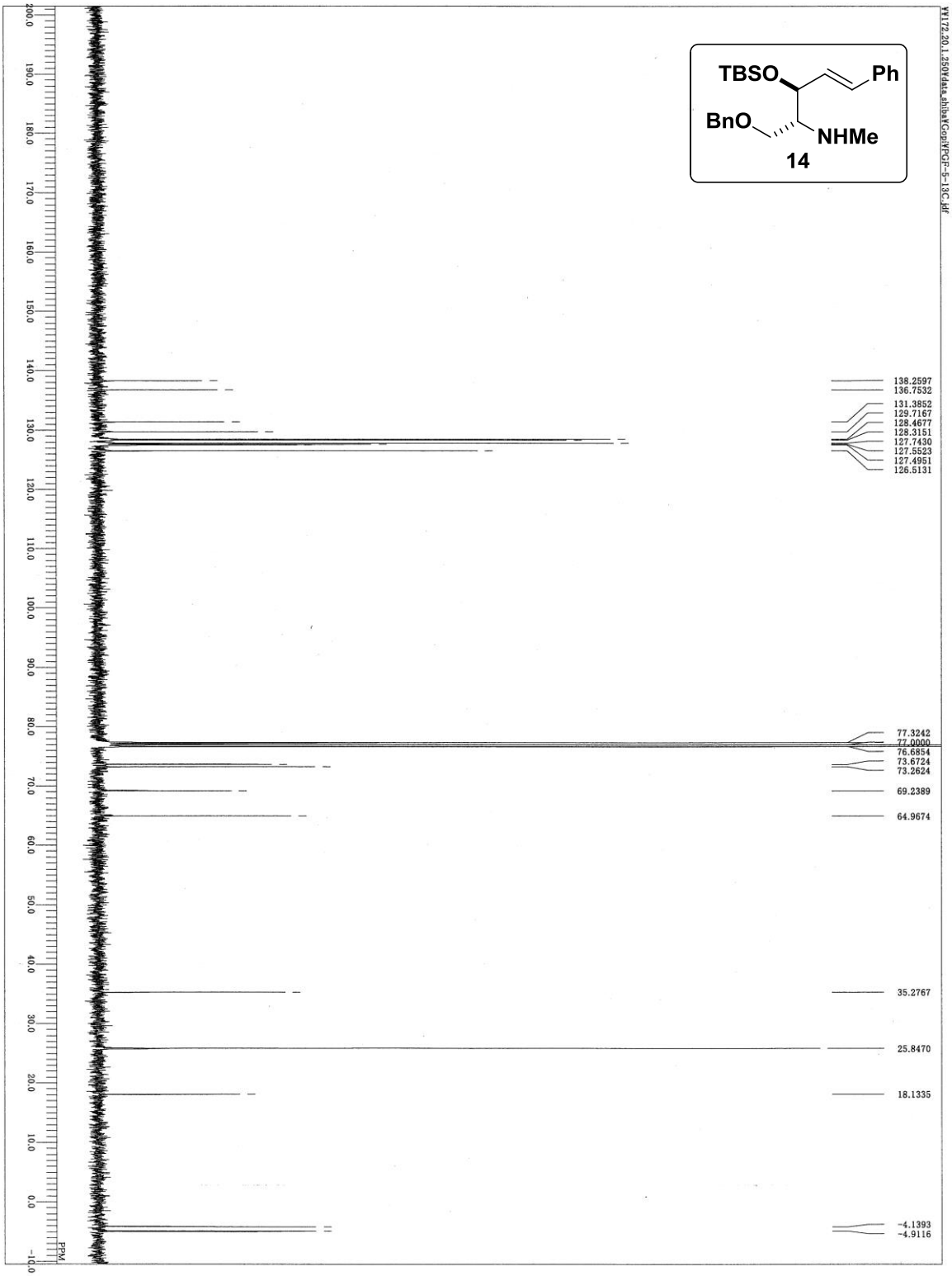

TBSO
Ph
BnO
NHTroc
12
10.94
1.00
1.00
0.87
1.05
3.94
1.92
1.02
9.10
3.00
2.98
7.3735
7.3541
7.3386
7.3231
7.3117
7.2945
7.2750
7.2550
7.2452
7.2384
7.2286
7.2126
6.5471
6.5070
6.1753
6.1570
6.1358
6.1169
5.3019
5.2784
4.7269
4.6965
4.5487
4.5195
4.5115
4.4817
4.4737
4.4560
4.4382
3.9388
3.9279
3.9113
3.9050
3.9004
3.8878
3.8775
3.8483
3.8374
3.8242
3.8139
3.6146
3.6049
3.5911
3.5808
0.9319
0.9175
0.8918
0.0722
0.0292
0.0000
PPM

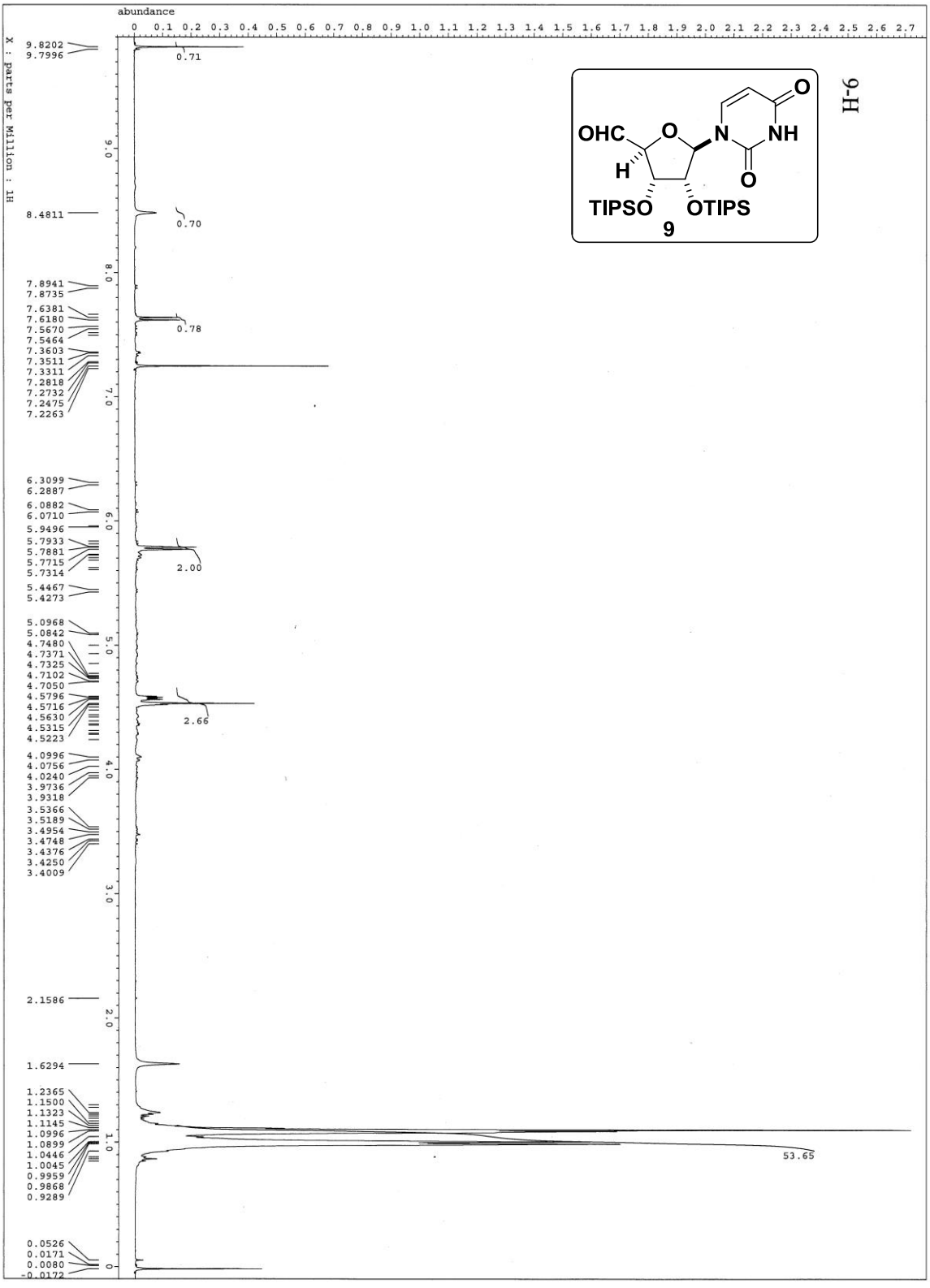

TBSO
Ph
BnO
NHTroc
12
154.2587
137.7734
136.5148
131.9955
129.5069
128.5249
128.4486
127.8575
127.8384
127.6858
126.5226
95.4685
77.3146
77.0000
76.6758
74.3112
73.5199
73.3197
68.1900
55.7474
25.7993
18.0954
-4.0630
-4.9783

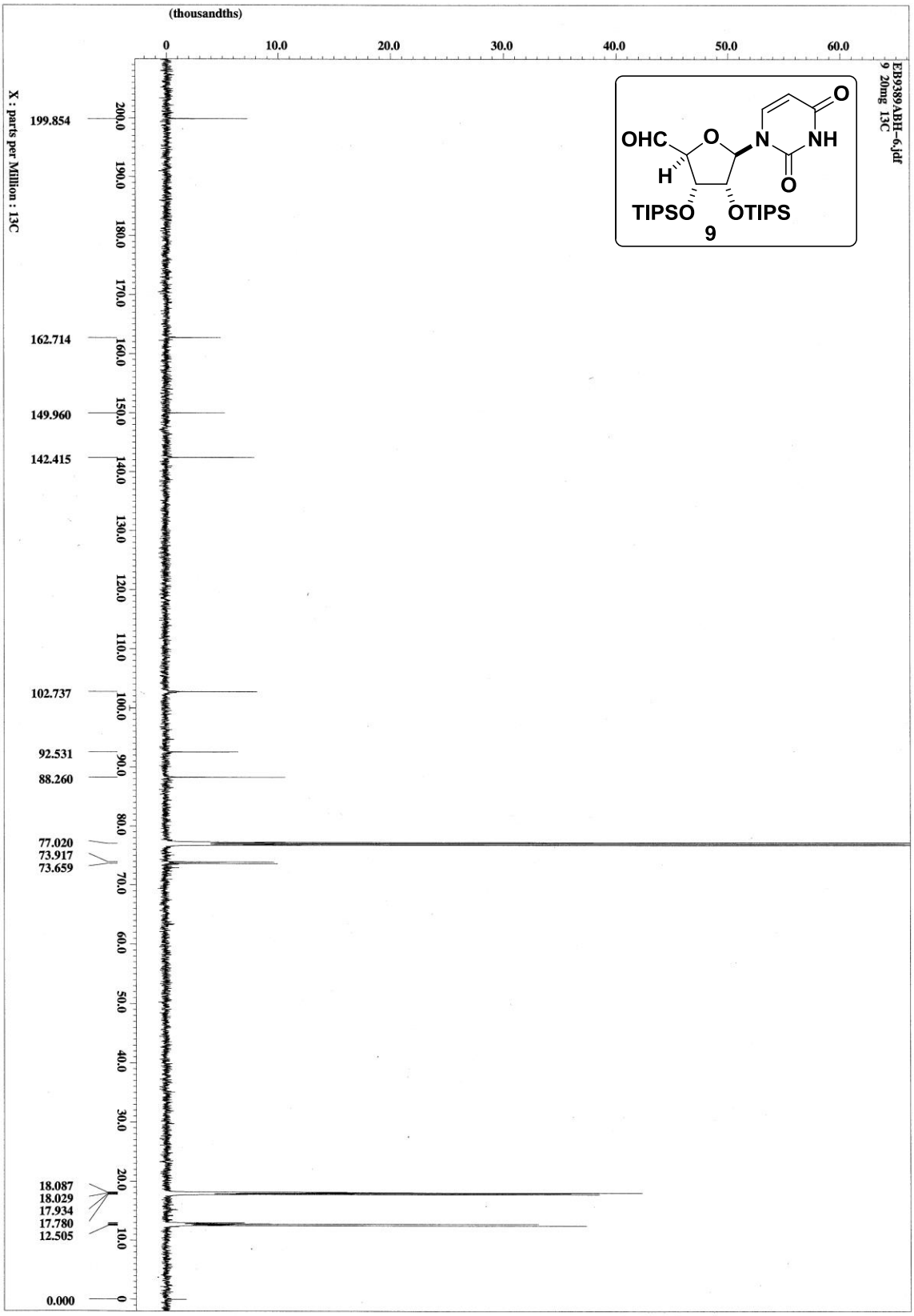

TBSO
Ph
BnO
NMeTroc
13
10.82
1.00
1.00
0.98
4.03
0.80
0.93
0.96
2.89
8.08
2.88
2.12
7.3529
7.3495
7.3392
7.3352
7.3317
7.3254
7.3185
7.3117
7.3059
7.2968
7.2905
7.2836
7.2767
7.2670
7.2653
7.2584
7.2510
7.2441
7.2349
7.2263
7.2212
7.2143
6.5625
6.5608
6.5207
6.4818
6.1639
6.1501
6.1444
6.1318
6.1238
6.1100
6.1043
6.0917
4.8305
4.8002
4.7836
4.7538
4.6530
4.6369
4.6232
4.6072
4.5774
4.5591
4.5562
4.5447
4.5264
4.5081
4.5018
4.4898
4.4783
4.4720
4.2727
3.9033
3.8958
3.8815
3.8769
3.8557
3.8477
3.8047
3.7956
3.7790
3.7698
2.9926
2.9777
1.5750
0.8815
0.8677
0.0389
0.0361
0.0046
0.0011
0.0000
PPM

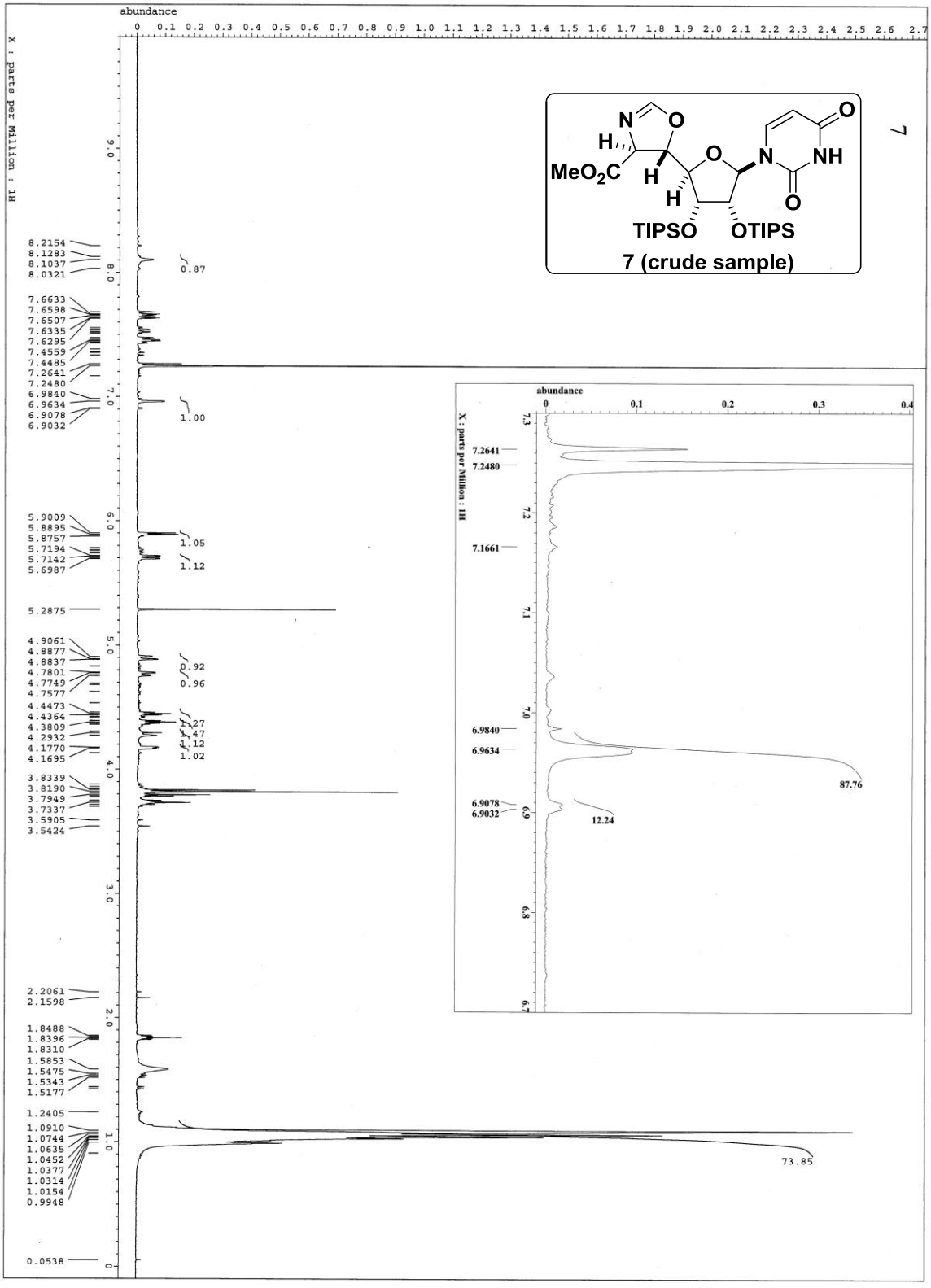

TBSO
Ph
BnO
NMeTroc
13
155.0596
138.0690
136.4481
131.8048
131.7380
130.0409
129.8883
128.5821
128.5535
128.3914
128.3437
127.8288
127.7621
127.6858
127.6191
126.5035
95.7068
77.3146
77.2002
77.0000
76.6854
75.1789
74.8643
72.9955
72.9478
67.2747
25.8088
25.7802
17.9905
-3.8723
-3.9486
-4.8925
-4.9688
PPM

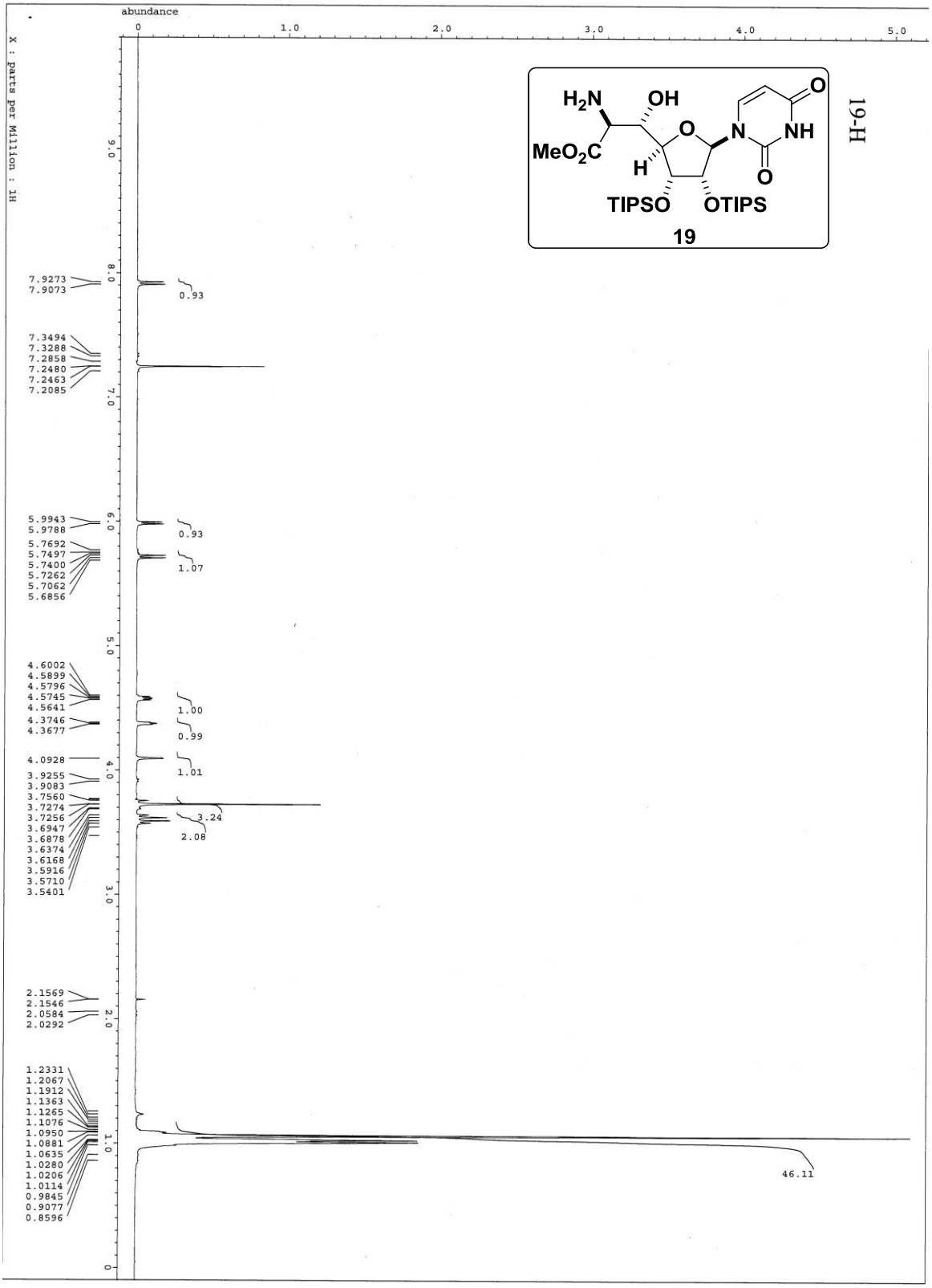

TBSO
Ph
BnO
NHMe
14
10.96
1.03
1.01
1.04
2.07
1.99
1.04
3.00
1.09
9.15
3.00
7.3598
7.3403
7.3346
7.3266
7.3214
7.3157
7.3082
7.2979
7.2779
7.2710
7.2613
7.2567
7.2498
7.2481
7.2401
7.2217
7.2046
6.5551
6.5156
6.2338
6.2160
6.1942
6.1765
4.5797
4.5499
4.4955
4.4852
4.4663
4.4554
3.5693
3.5556
2.8299
2.8213
2.8082
2.7950
2.7813
2.4829
2.2595
0.9015
0.0836
0.0430
PPM

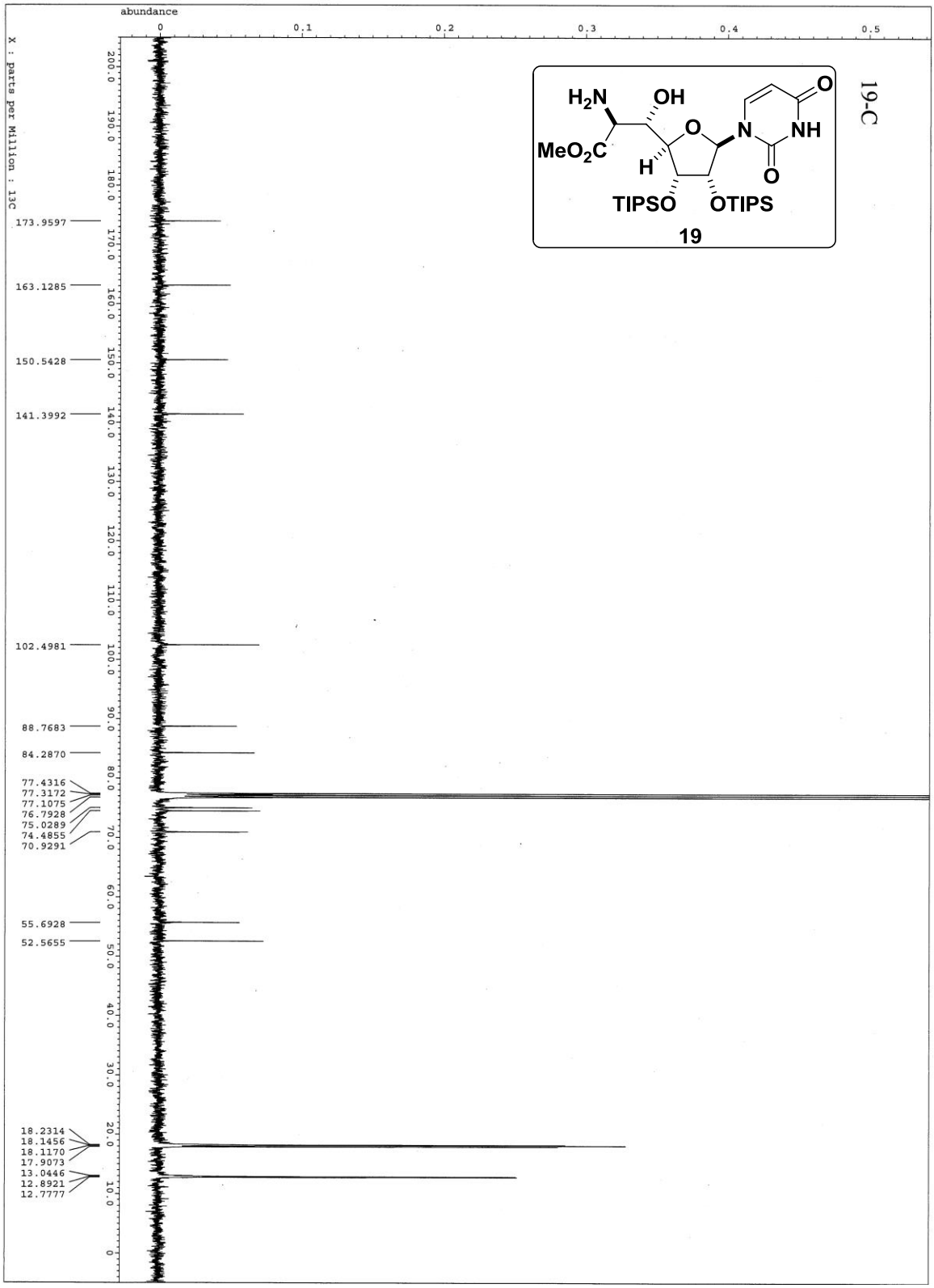

TBSO
Ph
BnO
NHMe
14
138.2597
136.7532
131.3852
129.7167
128.4677
128.3151
127.7430
127.5523
127.4951
126.5131
77.3242
77.0000
76.6854
73.6724
73.2624
69.2389
64.9674
35.2767
25.8470
18.1335
-4.1393
-4.9116
PPM

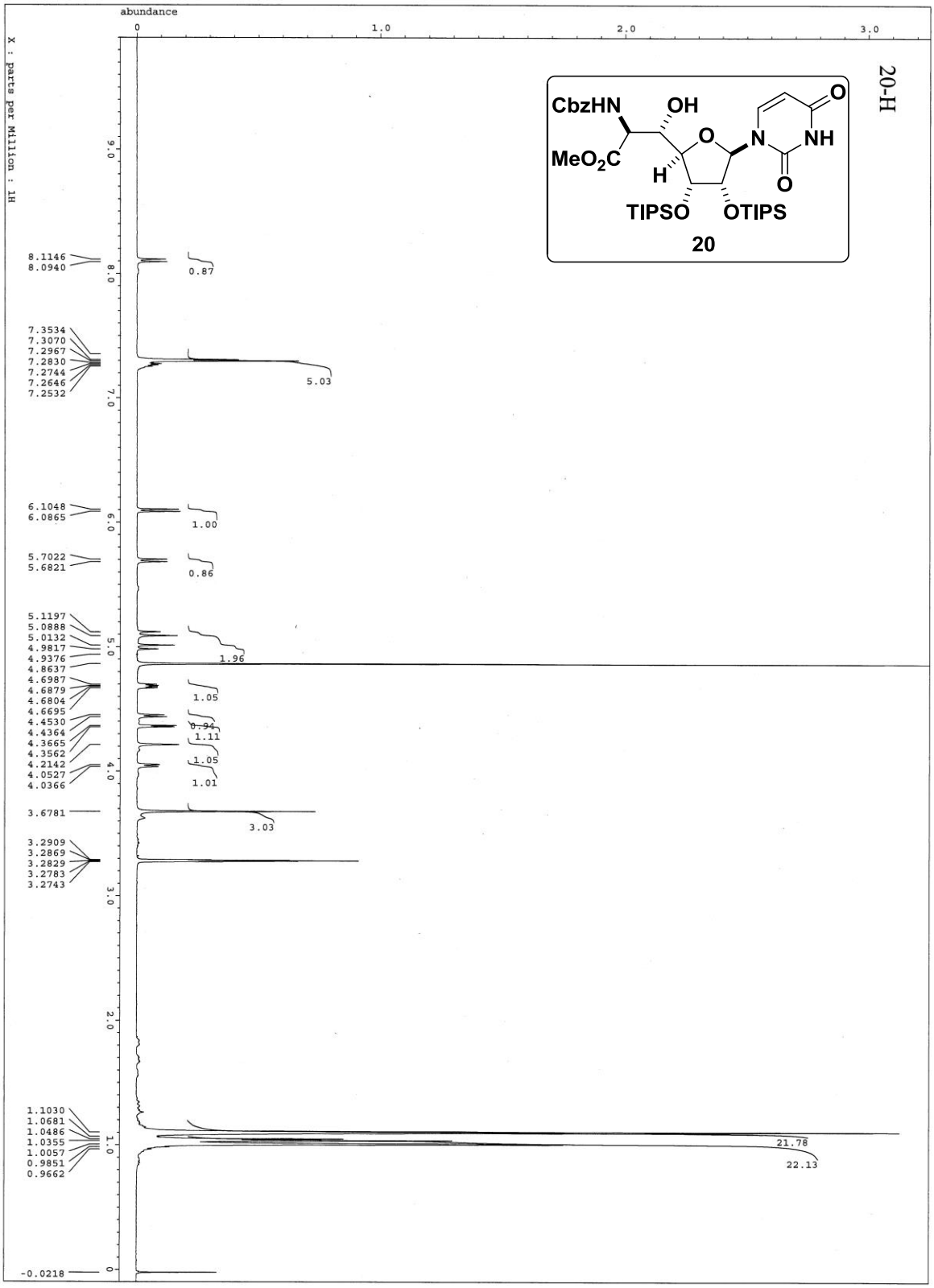

abundance
X : parts per Million : 1H
9.8202
9.7996
8.4811
7.8941
7.8735
7.6381
7.6180
7.5670
7.5464
7.3603
7.3511
7.3311
7.2818
7.2732
7.2475
7.2263
6.3099
6.2887
6.0882
6.0710
5.9496
5.7933
5.7881
5.7715
5.7314
5.4467
5.4273
5.0968
5.0842
4.7480
4.7371
4.7325
4.7102
4.7050
4.5796
4.5716
4.5630
4.5315
4.5223
4.0996
4.0756
4.0240
3.9736
3.9318
3.5366
3.5189
3.4954
3.4748
3.4376
3.4250
3.4009
2.1586
1.6294
1.2365
1.1500
1.1323
1.1145
1.0996
1.0899
1.0446
1.0045
0.9959
0.9868
0.9289
0.0526
0.0171
0.0080
-0.0172
0.71
0.70
0.78
2.00
2.66
53.65
OHC
O
N
NH
O
H
O
TIPSO
OTIPS
9
9-H

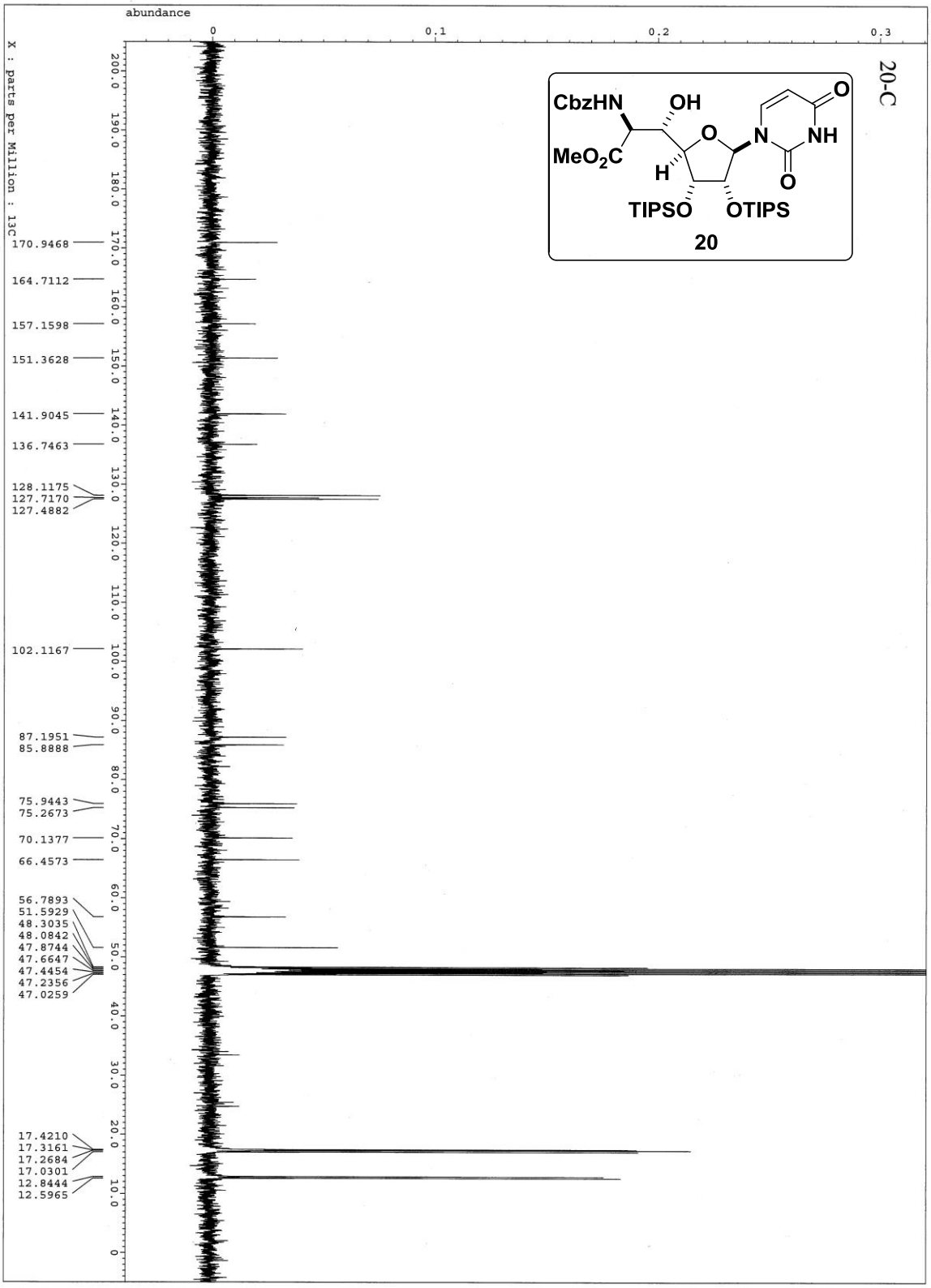

(thousandths)
0
10.0
20.0
30.0
40.0
50.0
60.0
EB9389ABH-6.jdf
9 20mg 13C
X : parts per Million : 13C
199.854
162.714
149.960
142.415
102.737
92.531
88.260
77.020
73.917
73.659
18.087
18.029
17.934
17.780
12.505
0.000
OHC
O
N
NH
H
O
TIPSO
OTIPS
9

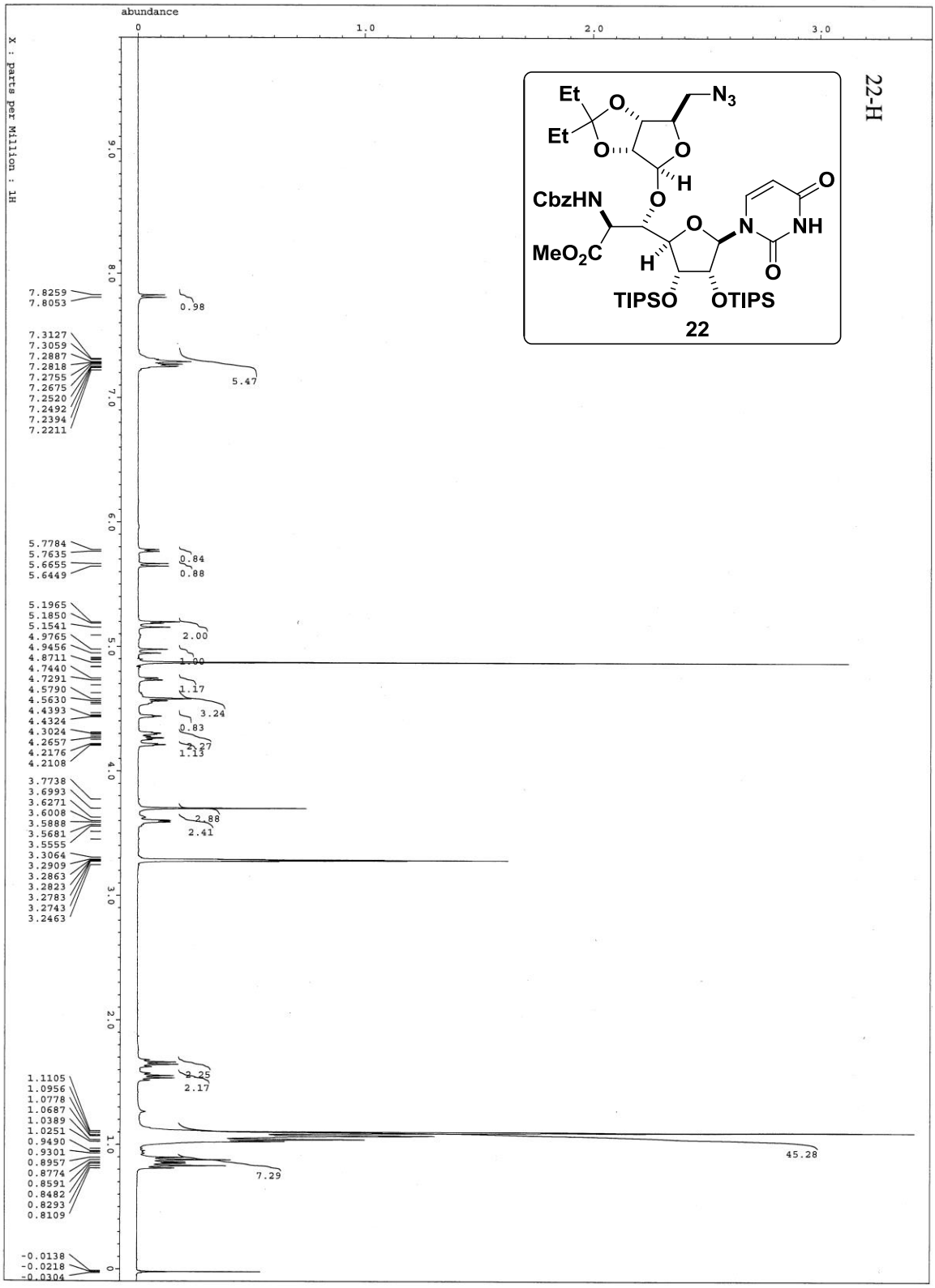

abundance
X : parts per Million : 1H
7
TIPSO OTIPS
7 (crude sample)
8.2154
8.1283
8.1037
8.0321
7.6633
7.6598
7.6507
7.6335
7.6295
7.4559
7.4485
7.2641
7.2480
6.9840
6.9634
6.9078
6.9032
5.9009
5.8895
5.8757
5.7194
5.7142
5.6987
5.2875
4.9061
4.8877
4.8837
4.7801
4.7749
4.7577
4.4473
4.4364
4.3809
4.2932
4.1770
4.1695
3.8339
3.8190
3.7949
3.7337
3.5905
3.5424
2.2061
2.1598
1.8488
1.8396
1.8310
1.5853
1.5475
1.5343
1.5177
1.2405
1.0910
1.0744
1.0635
1.0452
1.0377
1.0314
1.0154
0.9948
0.0538
0.87
1.00
1.05
1.12
0.92
0.96
1.27
1.47
1.12
1.02
73.85
abundance
X : parts per Million : 1H
7.2641
7.2480
7.1661
6.9840
6.9634
6.9078
6.9032
87.76
12.24

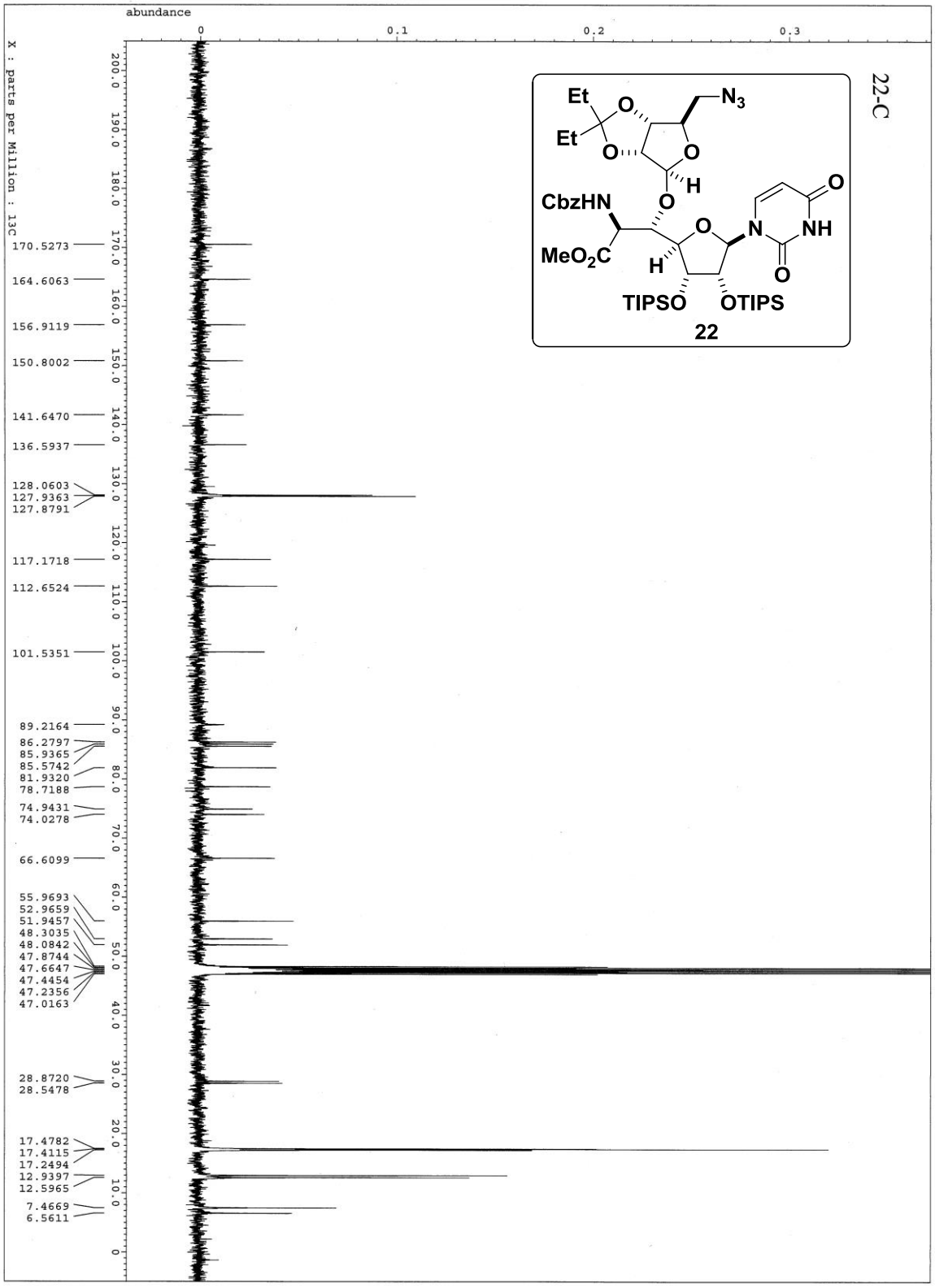

abundance
X : parts per Million : 1H
19
19-H
7.9273
7.9073
0.93
7.3494
7.3288
7.2858
7.2480
7.2463
7.2085
5.9943
5.9788
0.93
5.7692
5.7497
5.7400
5.7262
5.7062
5.6856
1.07
4.6002
4.5899
4.5796
4.5745
4.5641
1.00
4.3746
4.3677
0.99
4.0928
1.01
3.9255
3.9083
3.7560
3.7274
3.7256
3.6947
3.6878
3.6374
3.6168
3.5916
3.5710
3.5401
3.24
2.08
2.1569
2.1546
2.0584
2.0292
1.2331
1.2067
1.1912
1.1363
1.1265
1.1076
1.0950
1.0881
1.0635
1.0280
1.0206
1.0114
0.9845
0.9077
0.8596
46.11

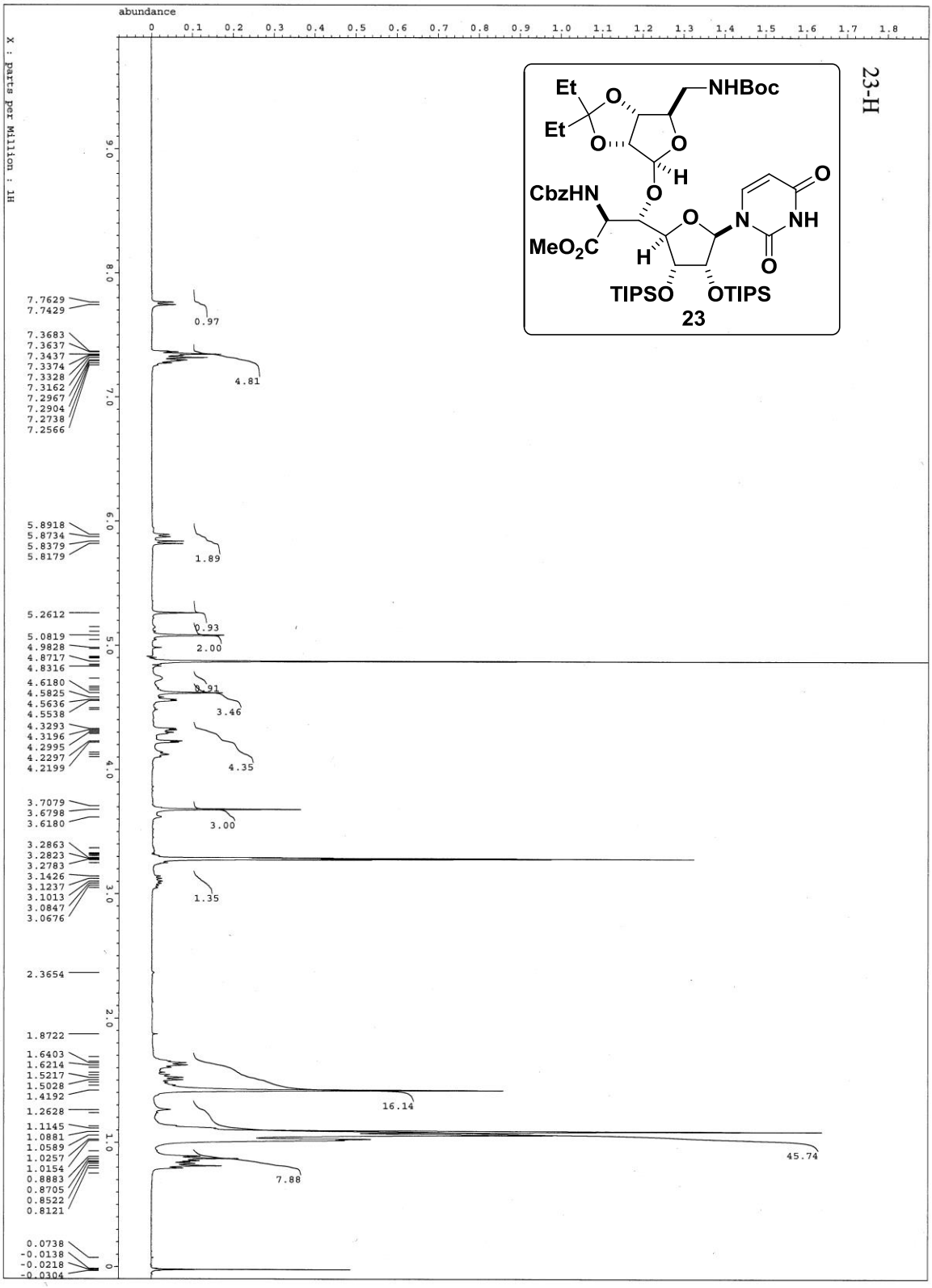

abundance
X : parts per Million : 13C
173.9597
163.1285
150.5428
141.3992
102.4981
88.7683
84.2870
77.4316
77.3172
77.1075
76.7928
75.0289
74.4855
70.9291
55.6928
52.5655
18.2314
18.1456
18.1170
17.9073
13.0446
12.8921
12.7777
19
19-C

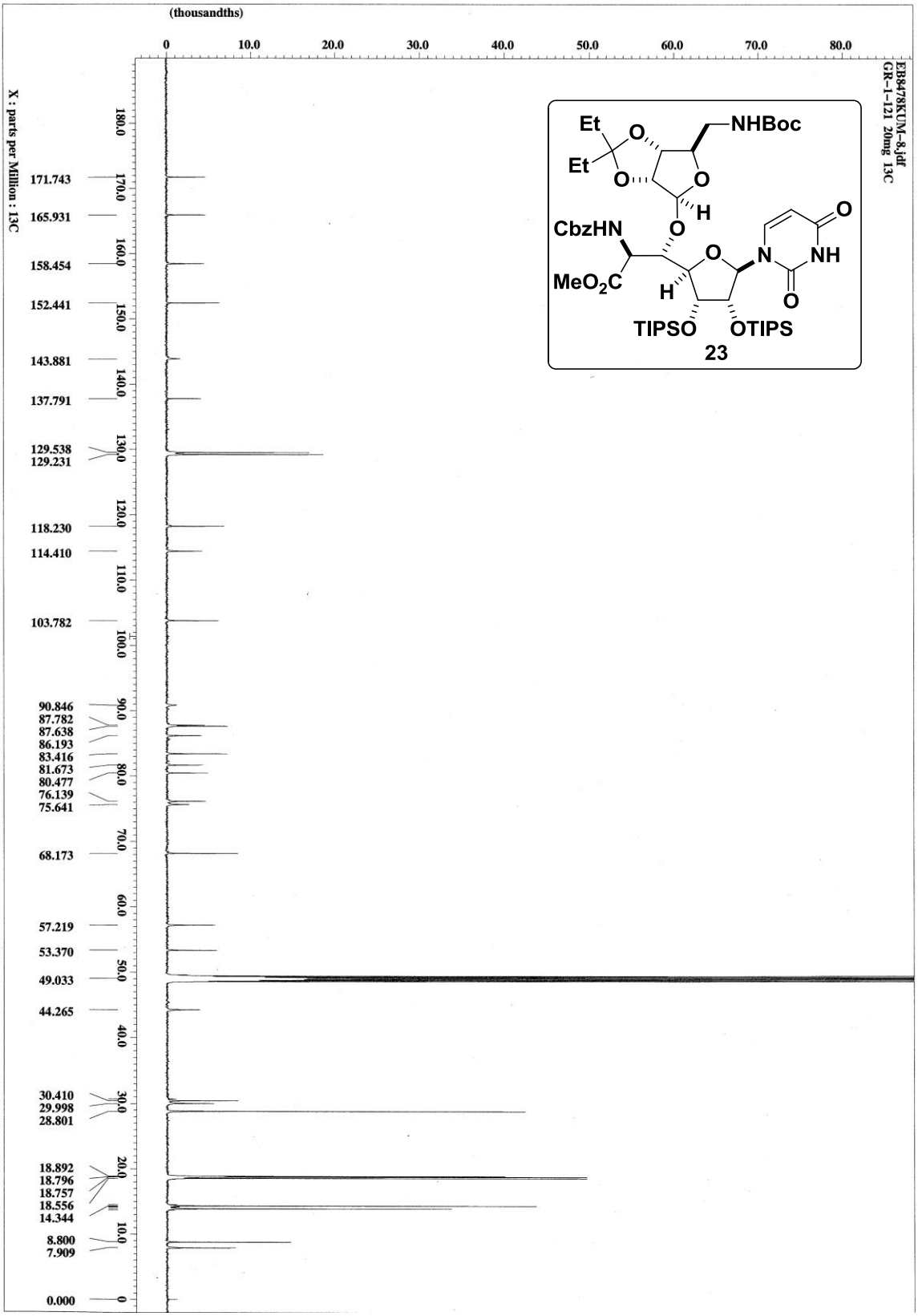

20-H
CbzHN
OH
MeO2C
H
TIPSO
OTIPS
20
abundance
8.1146
8.0940
7.3534
7.3070
7.2967
7.2830
7.2744
7.2646
7.2532
6.1048
6.0865
5.7022
5.6821
5.1197
5.0888
5.0132
4.9817
4.9376
4.8637
4.6987
4.6879
4.6804
4.6695
4.4530
4.4364
4.3665
4.3562
4.2142
4.0527
4.0366
3.6781
3.2909
3.2869
3.2829
3.2783
3.2743
1.1030
1.0681
1.0486
1.0355
1.0057
0.9851
0.9662
-0.0218
0.87
5.03
1.00
0.86
1.96
1.05
0.94
1.11
1.05
1.01
3.03
21.78
22.13

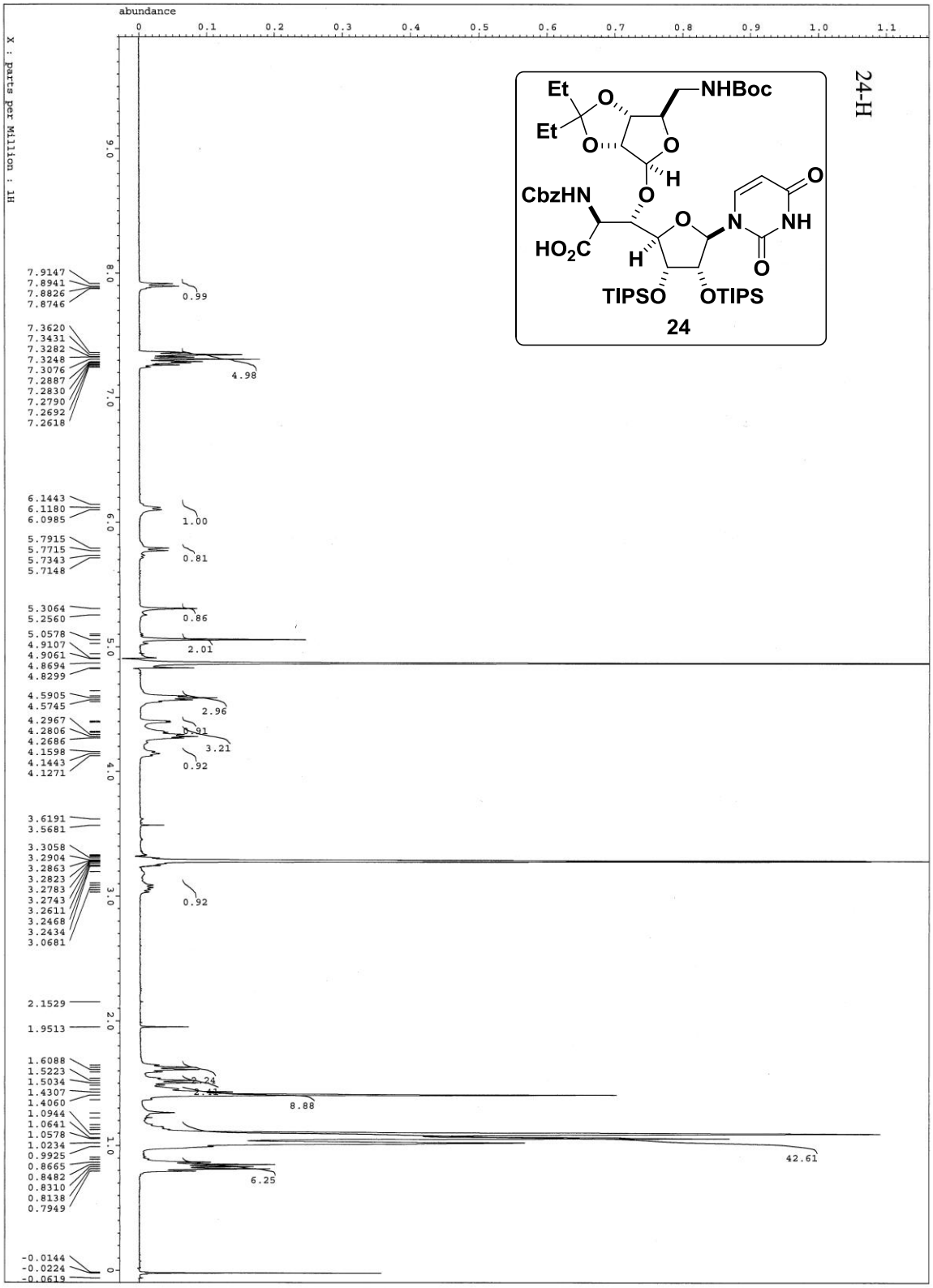

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.9468
164.7112
157.1598
151.3628
141.9045
136.7463
128.1175
127.7170
127.4882
102.1167
87.1951
85.8888
75.9443
75.2673
70.1377
66.4573
56.7893
51.5929
48.3035
48.0842
47.8744
47.6647
47.4454
47.2356
47.0259
17.4210
17.3161
17.2684
17.0301
12.8444
12.5965
CbzHN
OH
MeO2C
O
N
NH
H
O
TIPSO
OTIPS
20
20-C

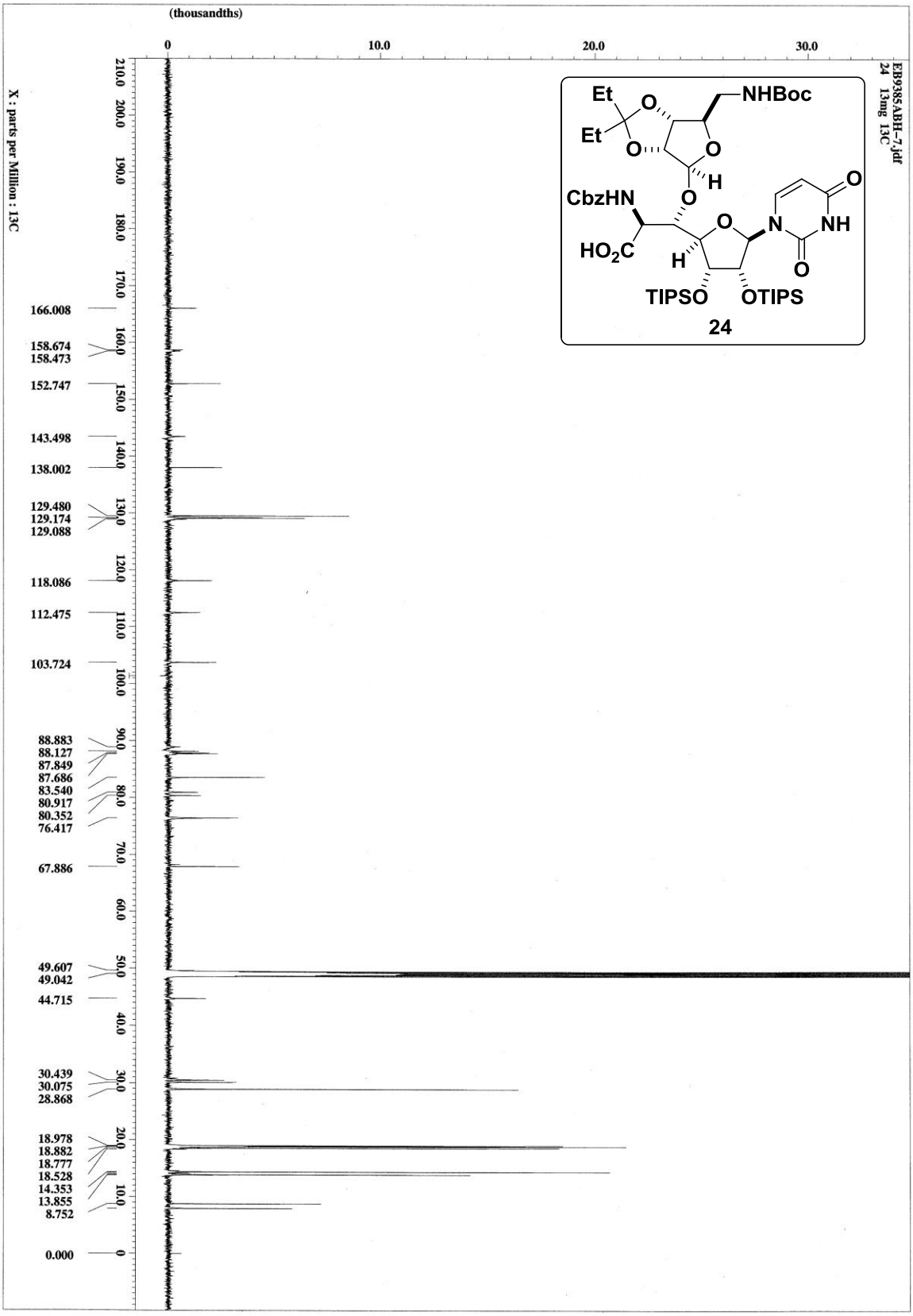

22-H
abundance
X : parts per Million : 1H
22

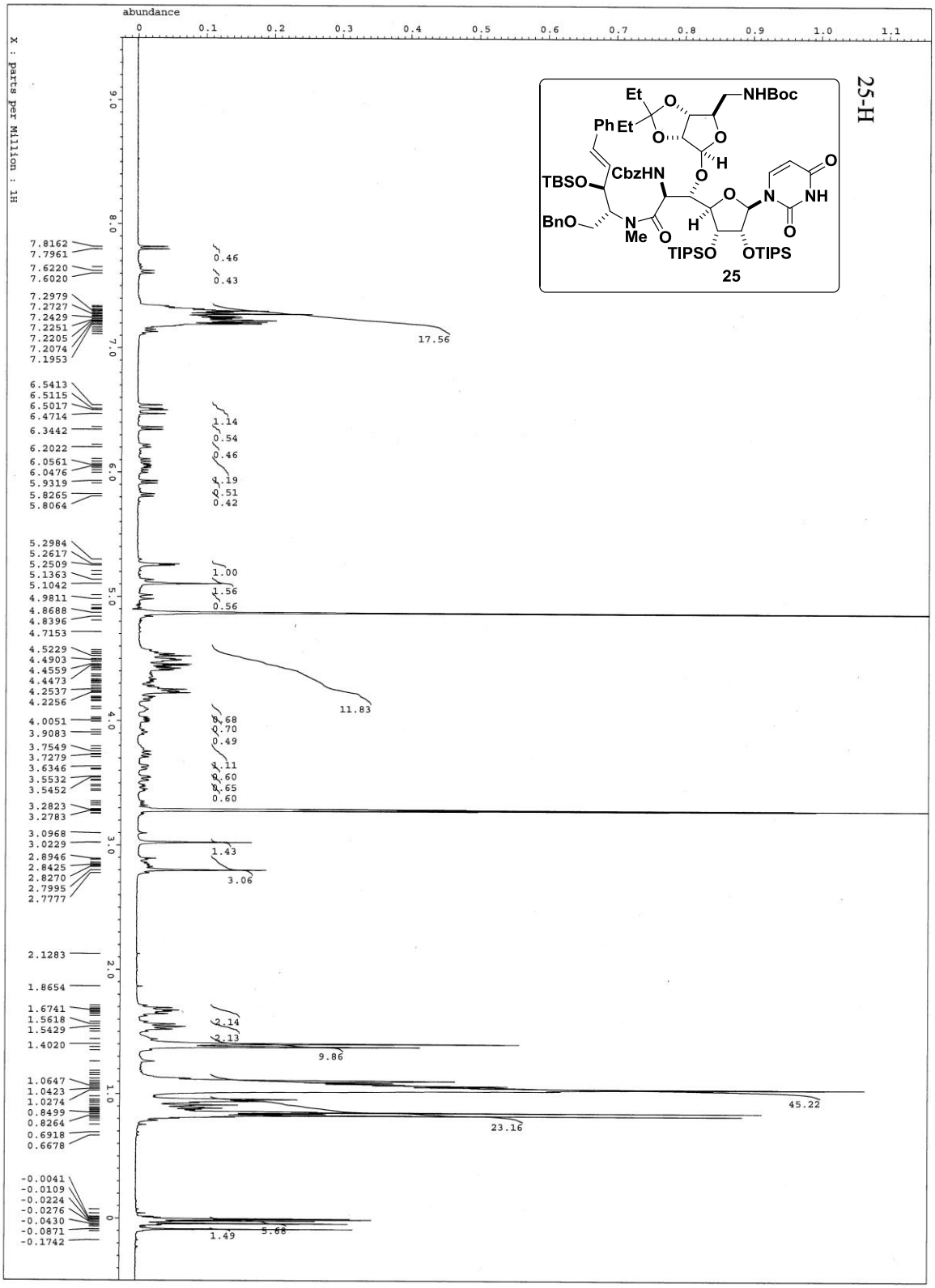

abundance
0
0.1
0.2
0.3
X : parts per Million : 13C
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
170.5273
164.6063
156.9119
150.8002
141.6470
136.5937
128.0603
127.9363
127.8791
117.1718
112.6524
101.5351
89.2164
86.2797
85.9365
85.5742
81.9320
78.7188
74.9431
74.0278
66.6099
55.9693
52.9659
51.9457
48.3035
48.0842
47.8744
47.6647
47.4454
47.2356
47.0163
28.8720
28.5478
17.4782
17.4115
17.2494
12.9397
12.5965
7.4669
6.5611
Et
Et
O
O
O
N3
H
O
CbzHN
MeO2C
O
H
O
N
NH
O
O
TIPSO
OTIPS
22
22-C

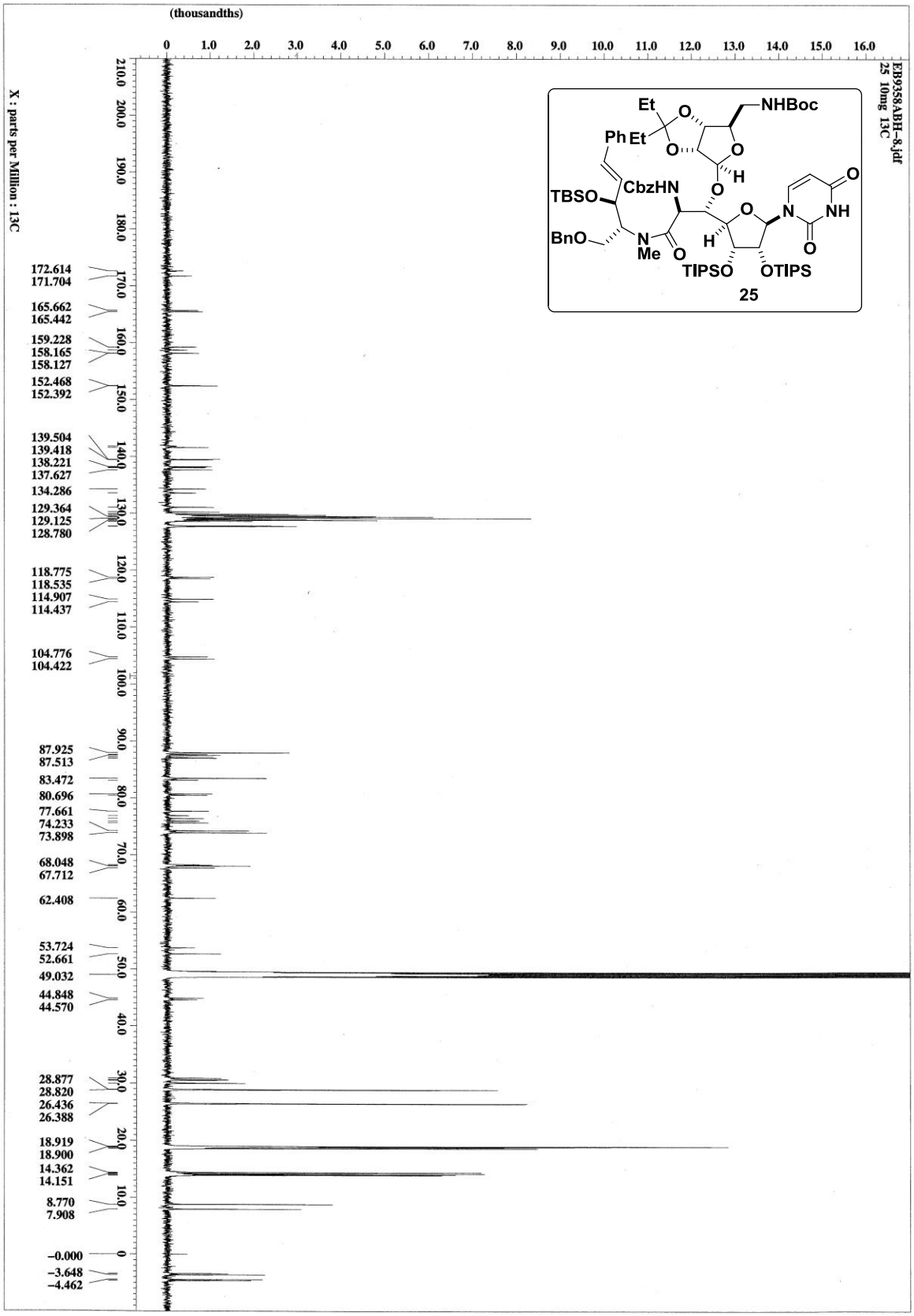

23-H
abundance
X : parts per Million : 1H
Et
Et
O
O
O
O
NHBoc
H
O
CbzHN
MeO2C
O
N
NH
O
H
O
TIPSO
OTIPS
23
7.7629
7.7429
7.3683
7.3637
7.3437
7.3374
7.3328
7.3162
7.2967
7.2904
7.2738
7.2566
5.8918
5.8734
5.8379
5.8179
5.2612
5.0819
4.9828
4.8717
4.8316
4.6180
4.5825
4.5636
4.5538
4.3293
4.3196
4.2995
4.2297
4.2199
3.7079
3.6798
3.6180
3.2863
3.2823
3.2783
3.1426
3.1237
3.1013
3.0847
3.0676
2.3654
1.8722
1.6403
1.6214
1.5217
1.5028
1.4192
1.2628
1.1145
1.0881
1.0589
1.0257
1.0154
0.8883
0.8705
0.8522
0.8121
0.0738
-0.0138
-0.0218
-0.0304
0.97
4.81
1.89
0.93
2.00
0.91
3.46
4.35
3.00
1.35
16.14
45.74
7.88

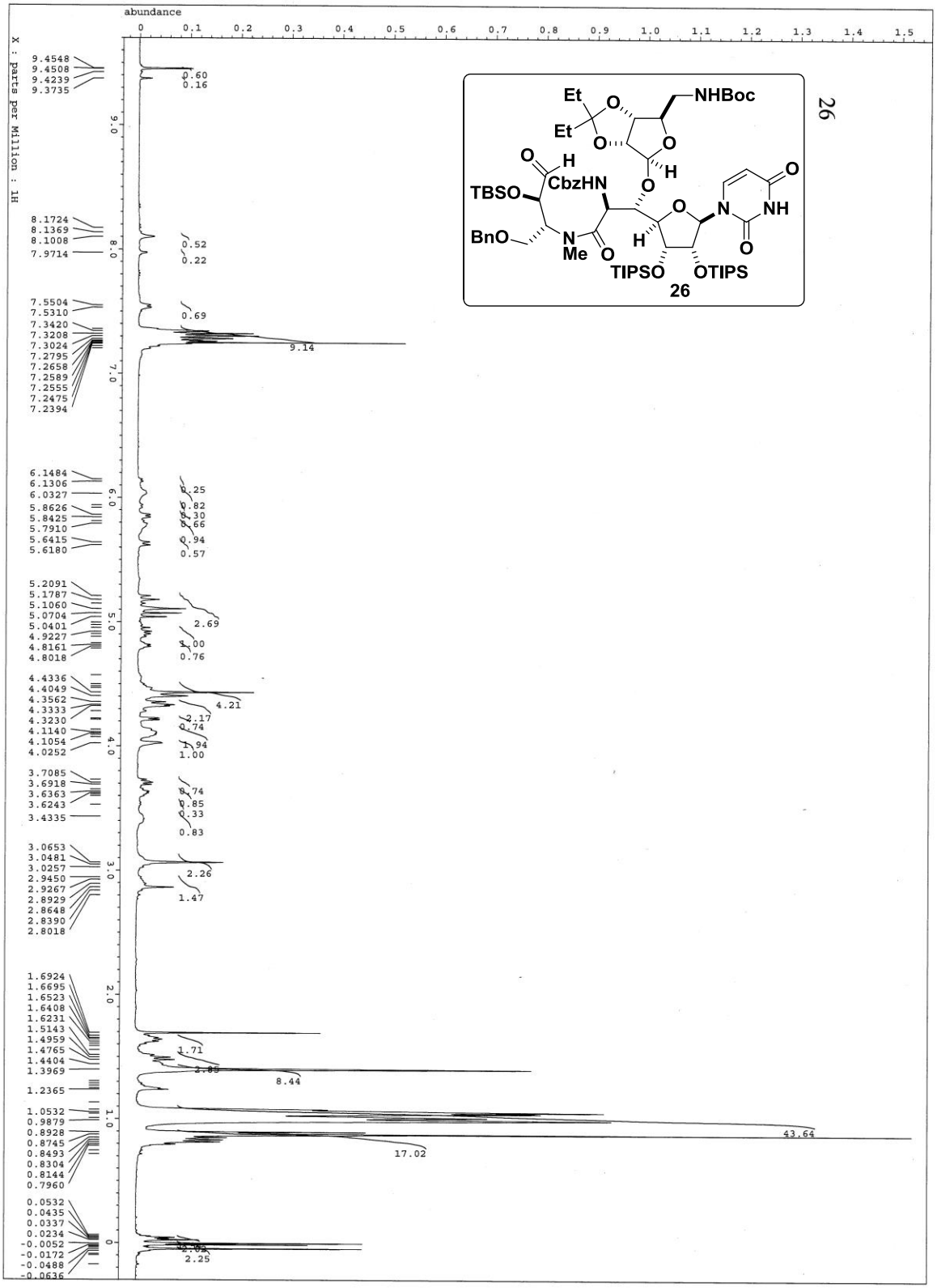

(thousandths)
0
10.0
20.0
30.0
40.0
50.0
60.0
70.0
80.0
EB8478KUM-8.jdf
GR-1-121 20mg 13C
X : parts per Million : 13C
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
171.743
165.931
158.454
152.441
143.881
137.791
129.538
129.231
118.230
114.410
103.782
90.846
87.782
87.638
86.193
83.416
81.673
80.477
76.139
75.641
68.173
57.219
53.370
49.033
44.265
30.410
29.998
28.801
18.892
18.796
18.757
18.556
14.344
8.800
7.909
0.000
Et
Et
O
O
O
NHBoc
H
O
CbzHN
MeO2C
O
O
N
NH
H
O
O
TIPSO
OTIPS
23

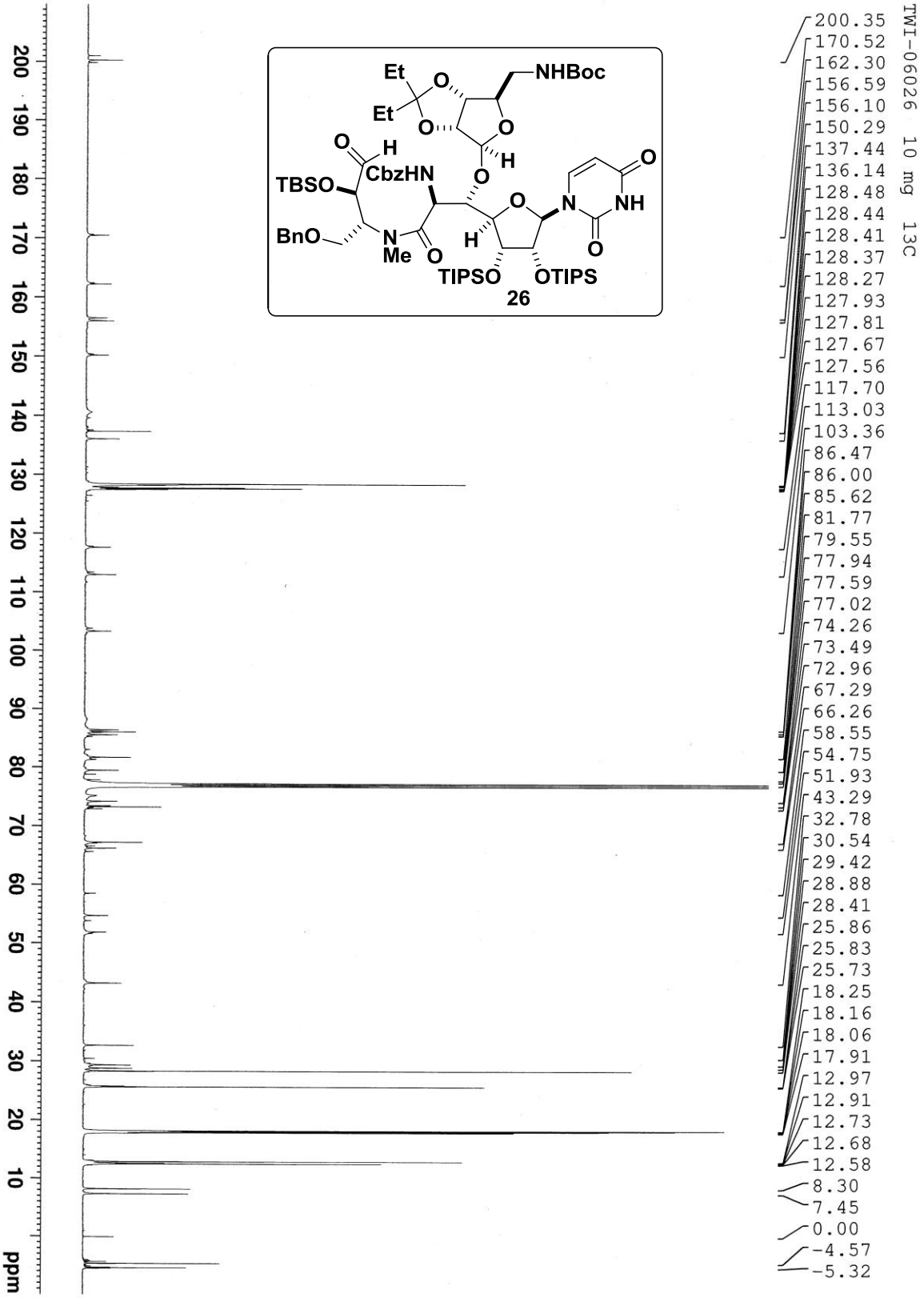

24-H
24
X : parts per Million : 1H
abundance

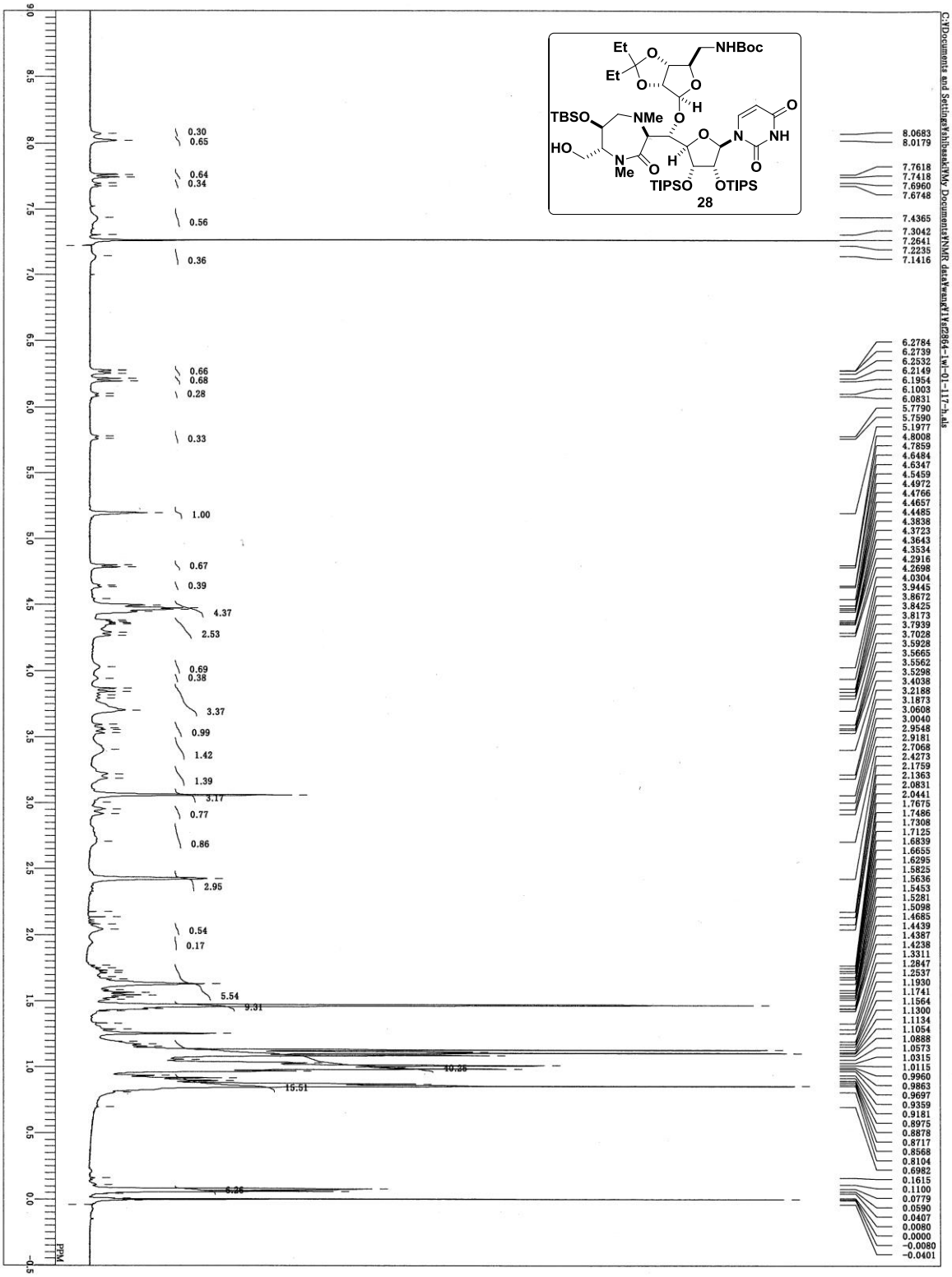

(thousandths)
0
10.0
20.0
30.0
EB9385ABH-7.jdf
24 13mg 13C
X : parts per Million : 13C
166.008
158.674
158.473
152.747
143.498
138.002
129.480
129.174
129.088
118.086
112.475
103.724
88.883
88.127
87.849
87.686
83.540
80.917
80.352
76.417
67.886
49.607
49.042
44.715
30.439
30.075
28.868
18.978
18.882
18.777
18.528
14.353
13.855
8.752
0.000
Et
Et
O
O
O
NHBoc
H
O
CbzHN
O
N
NH
O
HO2C
H
O
TIPSO
OTIPS
24

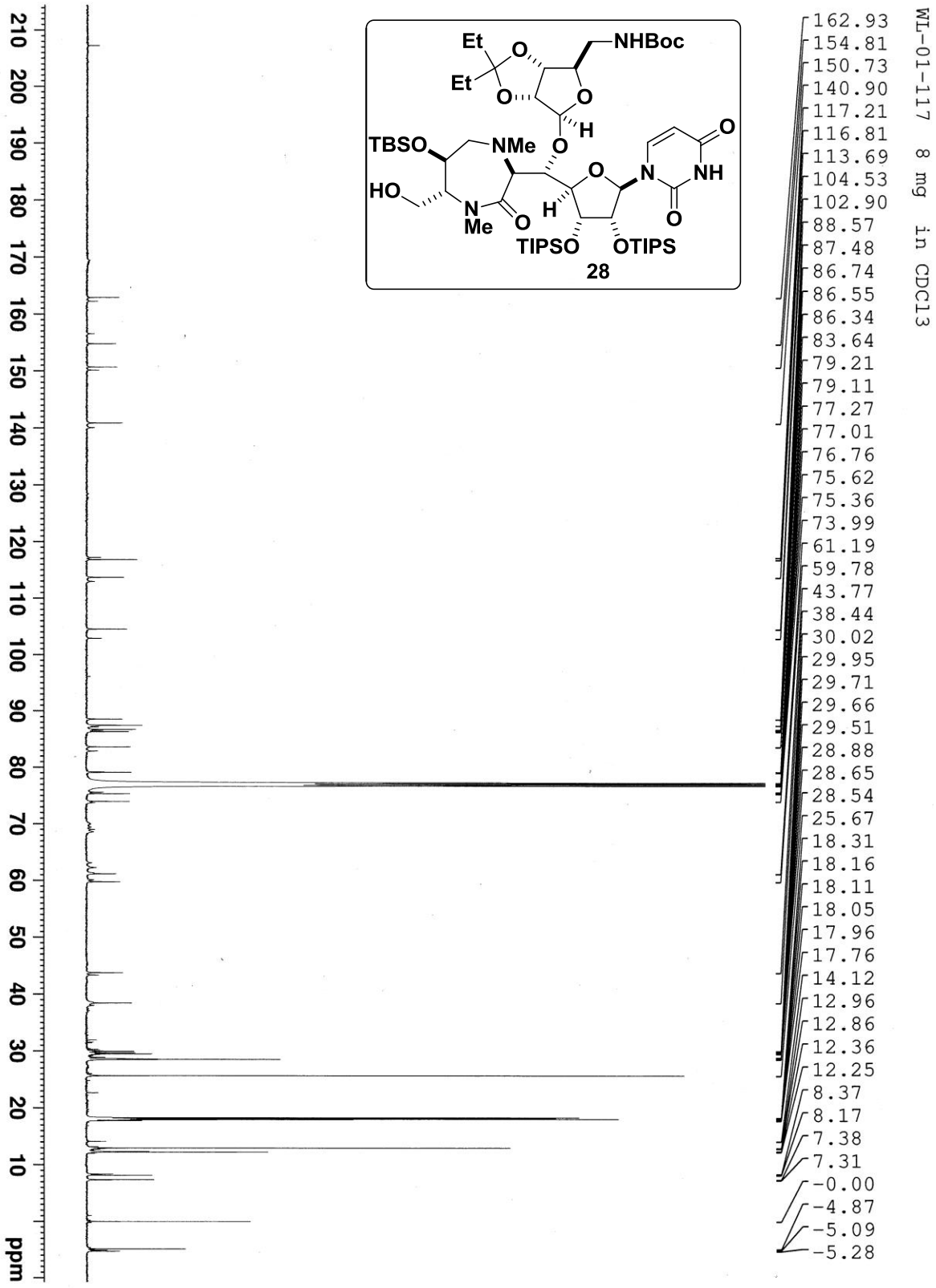

25-H
abundance
X : parts per Million : 1H
Et
NHBoc
Ph Et
O
H
CbzHN
TBSO
BnO
N
Me
NH
TIPSO
OTIPS
25
7.8162
7.7961
7.6220
7.6020
7.2979
7.2727
7.2429
7.2251
7.2205
7.2074
7.1953
6.5413
6.5115
6.5017
6.4714
6.3442
6.2022
6.0561
6.0476
5.9319
5.8265
5.8064
5.2984
5.2617
5.2509
5.1363
5.1042
4.9811
4.8688
4.8396
4.7153
4.5229
4.4903
4.4559
4.4473
4.2537
4.2256
4.0051
3.9083
3.7549
3.7279
3.6346
3.5532
3.5452
3.2823
3.2783
3.0968
3.0229
2.8946
2.8425
2.8270
2.7995
2.7777
2.1283
1.8654
1.6741
1.5618
1.5429
1.4020
1.0647
1.0423
1.0274
0.8499
0.8264
0.6918
0.6678
-0.0041
-0.0109
-0.0224
-0.0276
-0.0430
-0.0871
-0.1742
0.46
0.43
17.56
1.14
0.54
0.46
0.19
0.51
0.42
1.00
1.56
0.56
11.83
0.68
0.70
0.49
1.11
0.60
0.65
0.60
1.43
3.06
2.14
2.13
9.86
45.22
23.16
1.49
5.68

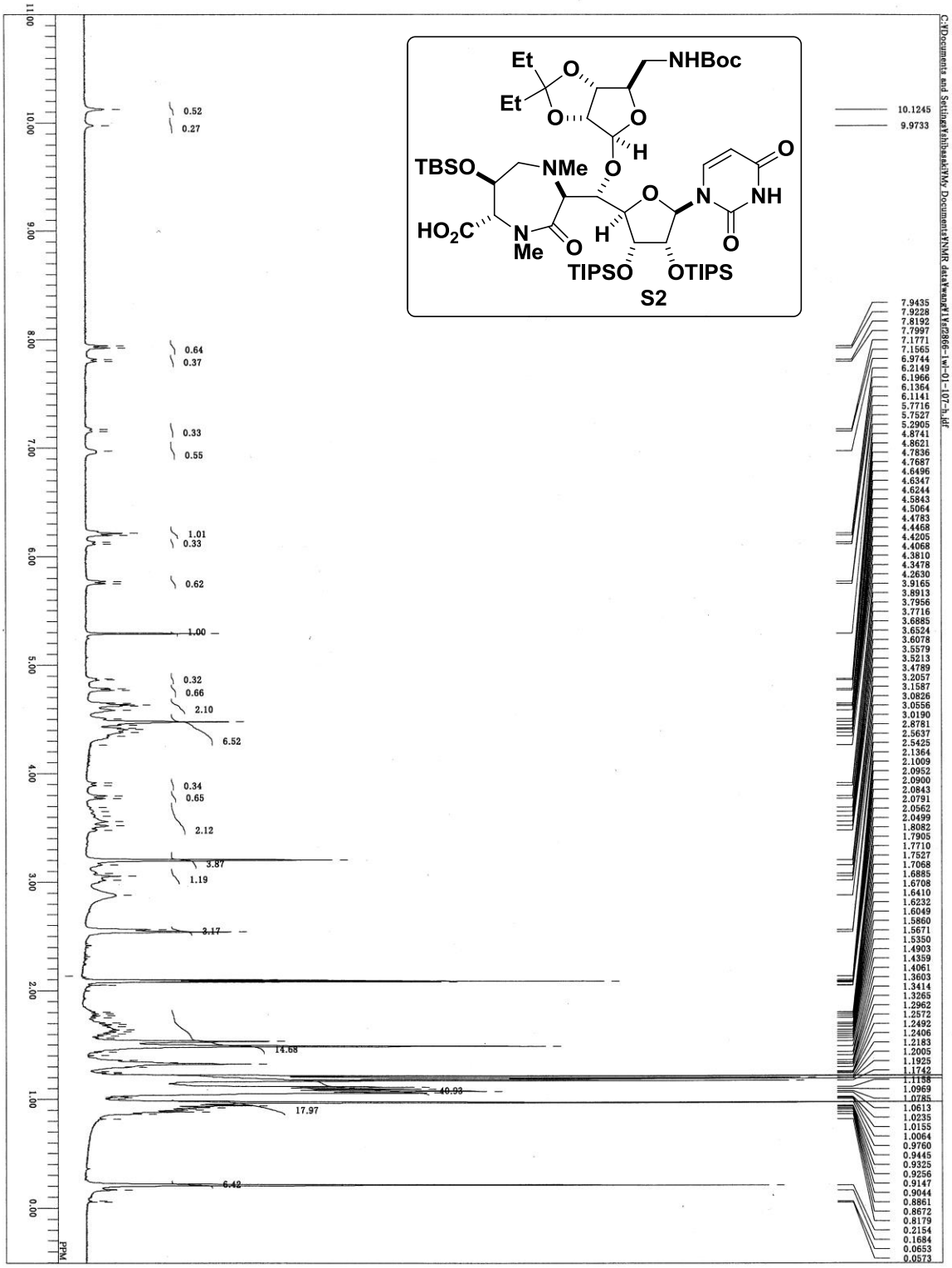

(thousandths)
X : parts per Million : 13C
EB9358ABH-8.jdf
25 10mg 13C
NHBoc
Et
Ph Et
CbzHN
TBSO
BnO
N
Me
TIPSO
OTIPS
NH
25

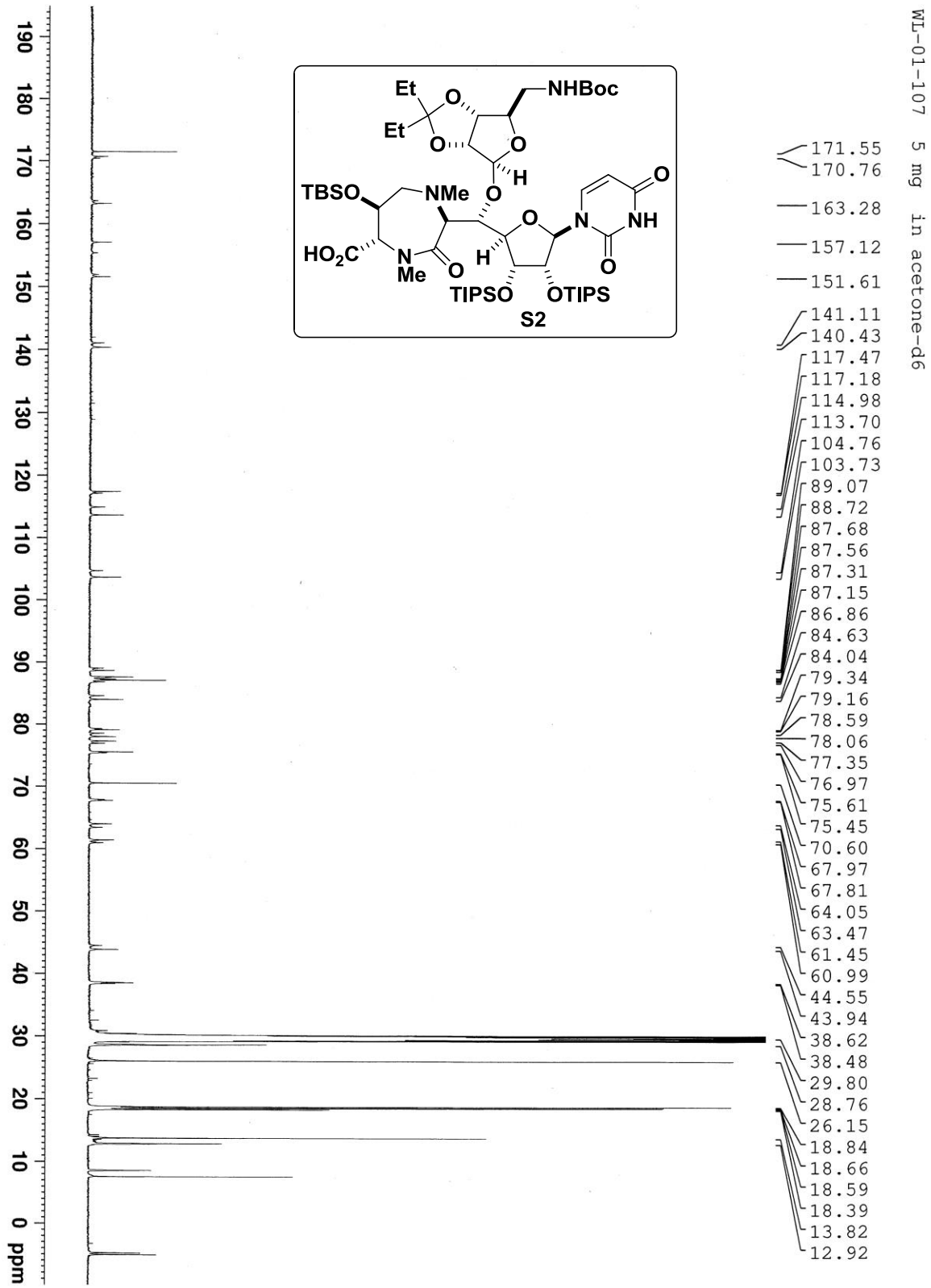

abundance
X : parts per Million : 1H
26
Et
Et
O
O
O
O
NHBoc
H
CbzHN
TBSO
BnO
N
Me
O
H
O
N
NH
O
O
TIPSO
OTIPS
26

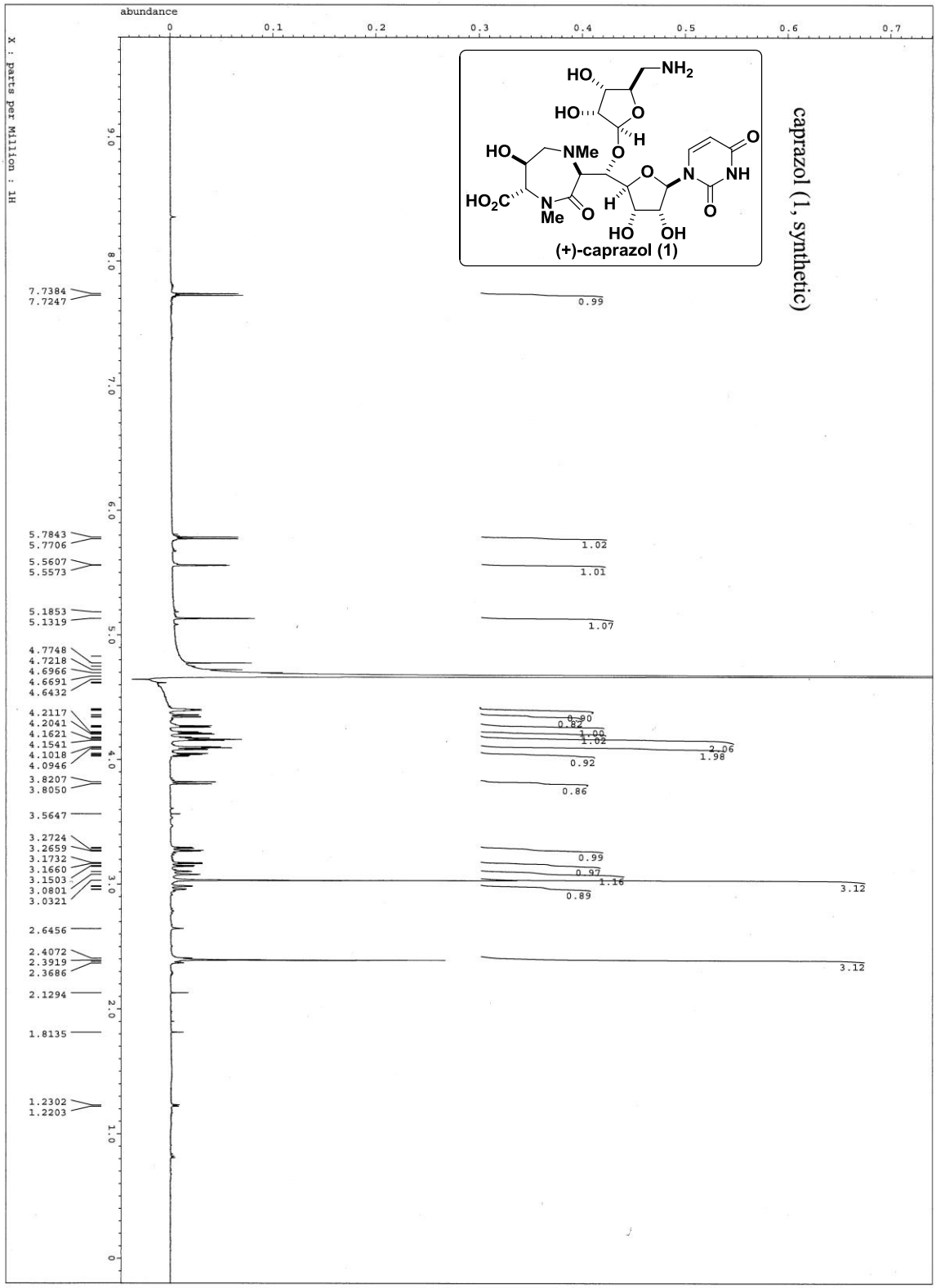

TWI-06026 10 mg 13C
200.35
170.52
162.30
156.59
156.10
150.29
137.44
136.14
128.48
128.44
128.41
128.37
128.27
127.93
127.81
127.67
127.56
117.70
113.03
103.36
86.47
86.00
85.62
81.77
79.55
77.94
77.59
77.02
74.26
73.49
72.96
67.29
66.26
58.55
54.75
51.93
43.29
32.78
30.54
29.42
28.88
28.41
25.86
25.83
25.73
18.25
18.16
18.06
17.91
12.97
12.91
12.73
12.68
12.58
8.30
7.45
0.00
-4.57
-5.32
ppm
Et
Et
NHBoc
TBSO
CbzHN
BnO
Me
TIPSO
OTIPS
NH
26

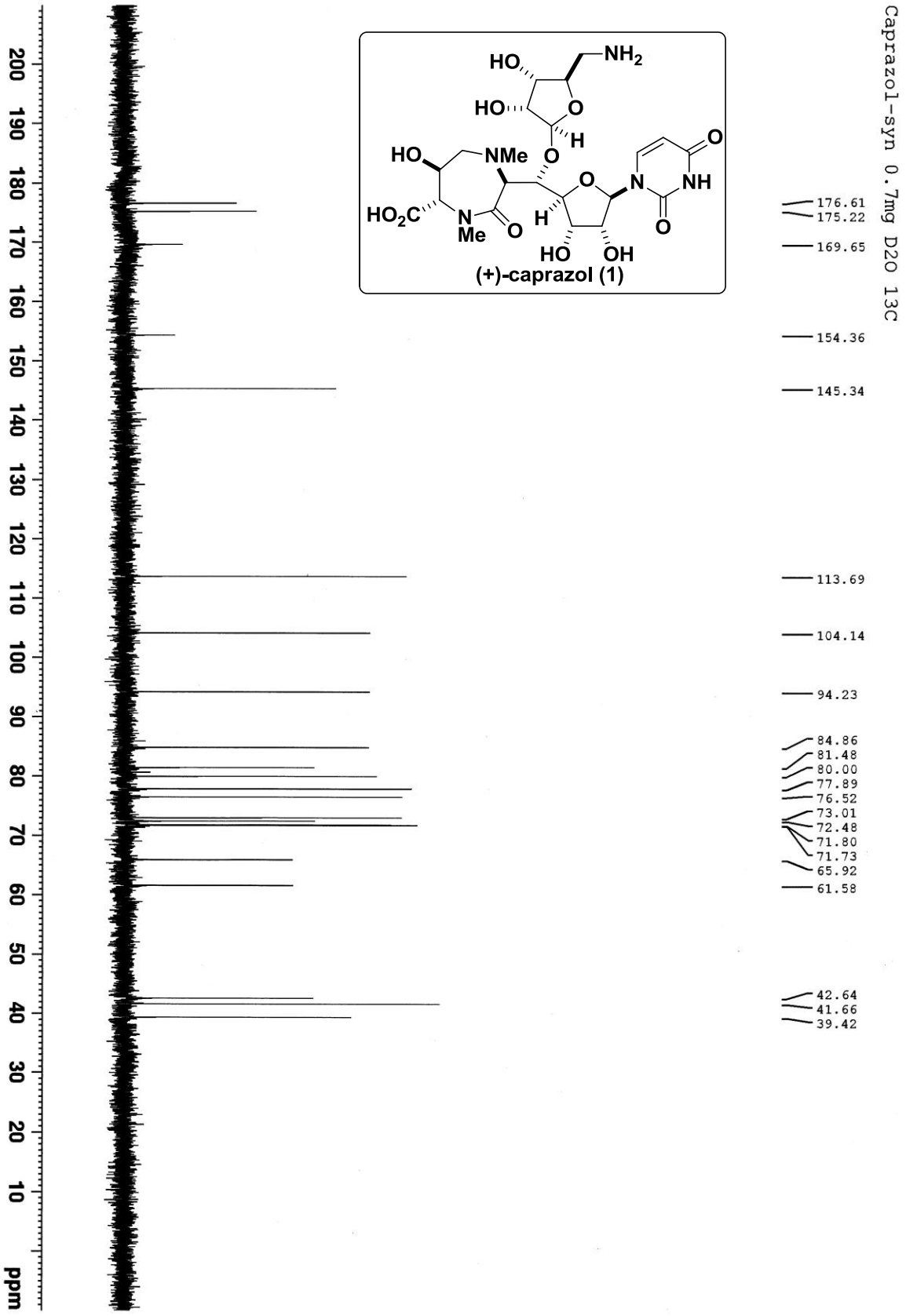

Et
Et
NHBoc
TBSO
NMe
HO
N
Me
TIPSO
OTIPS
NH
28

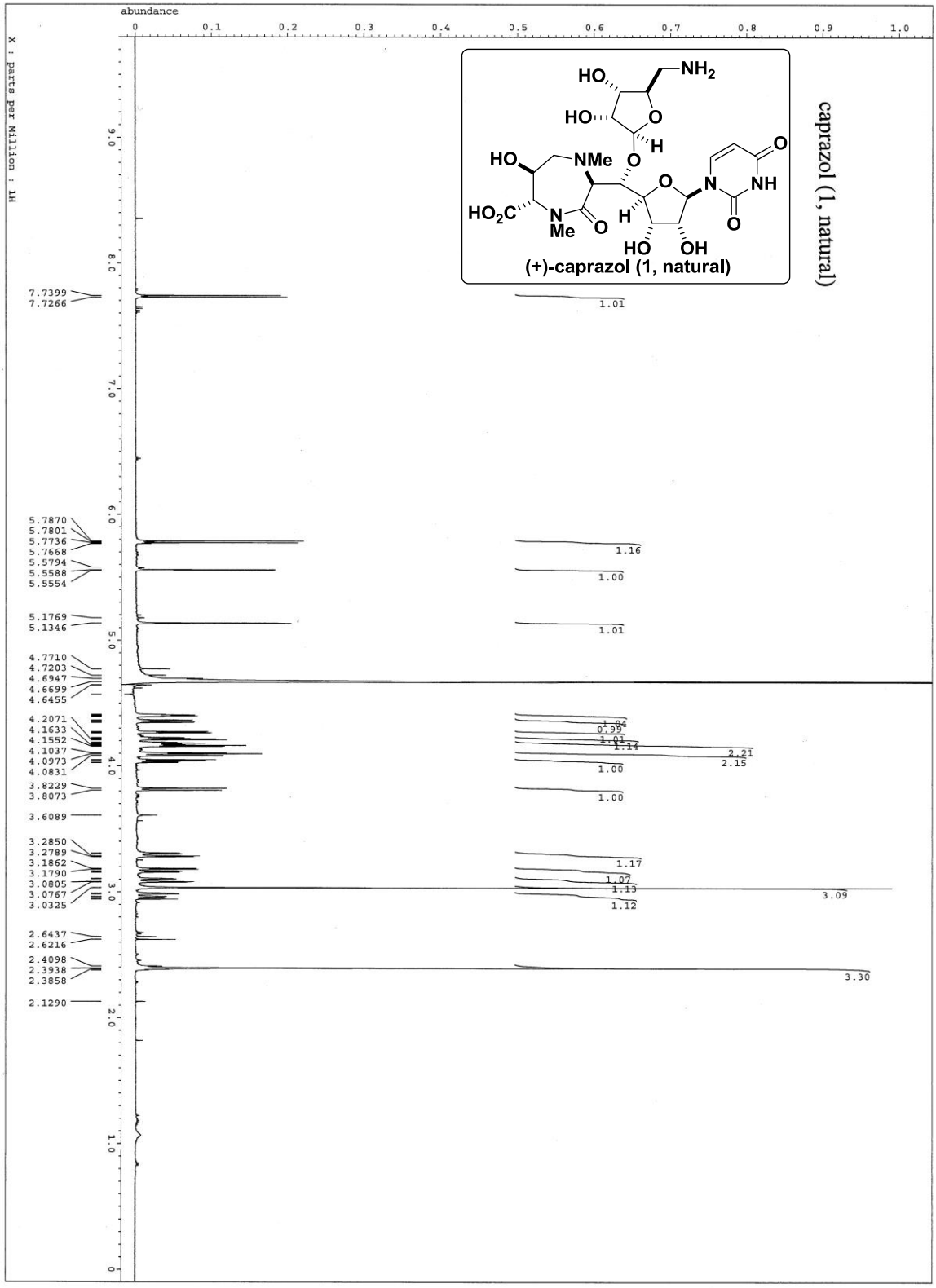

WL-01-117 8 mg in CDCl3
162.93
154.81
150.73
140.90
117.21
116.81
113.69
104.53
102.90
88.57
87.48
86.74
86.55
86.34
83.64
79.21
79.11
77.27
77.01
76.76
75.62
75.36
73.99
61.19
59.78
43.77
38.44
30.02
29.95
29.71
29.66
29.51
28.88
28.65
28.54
25.67
18.31
18.16
18.11
18.05
17.96
17.76
14.12
12.96
12.86
12.36
12.25
8.37
8.17
7.38
7.31
-0.00
-4.87
-5.09
-5.28
ppm
Et
Et
O
O
O
NHBoc
H
TBSO
NMe
O
O
N
NH
O
HO
N
Me
O
H
O
TIPSO
OTIPS
28


Et
O
NHBoc
Et
O
O
H
TBSO
NMe
O
O
N
NH
HO2C
N
Me
O
H
O
TIPSO
OTIPS
S2
10.1245
9.9733
0.52
0.27
0.64
0.37
0.33
0.55
1.01
0.33
0.62
1.00
0.32
0.66
2.10
6.52
0.34
0.65
2.12
3.87
1.19
3.17
14.68
40.93
17.97
6.42
PPM


WL-01-107 5 mg in acetone-d6
171.55
170.76
163.28
157.12
151.61
141.11
140.43
117.47
117.18
114.98
113.70
104.76
103.73
89.07
88.72
87.68
87.56
87.31
87.15
86.86
84.63
84.04
79.34
79.16
78.59
78.06
77.35
76.97
75.61
75.45
70.60
67.97
67.81
64.05
63.47
61.45
60.99
44.55
43.94
38.62
38.48
29.80
28.76
26.15
18.84
18.66
18.59
18.39
13.82
12.92
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm
Et
Et
O
O
O
H
NHBoc
TBSO
NMe
O
O
N
NH
O
O
HO2C
N
Me
O
H
TIPSO
OTIPS
S2


caprazol (1, synthetic)
(+)-caprazol (1)
abundance
X : parts per Million : 1H


Caprazol-syn 0.7mg D2O 13C
(+)-caprazol (1)
176.61
175.22
169.65
154.36
145.34
113.69
104.14
94.23
84.86
81.48
80.00
77.89
76.52
73.01
72.48
71.80
71.73
65.92
61.58
42.64
41.66
39.42
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


caprazol (1, natural)
(+)-caprazol (1, natural)
abundance
X : parts per Million : 1H