Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information

A Benzotriazole-Mediated Route to Protected Marine-Derived Hetero-2,5-Diketopiperazines Containing Proline

Olivier Nsengiyumva,[a] Sadra Hamedzadeh,[a] James McDaniel,[a] Jocelyn Macho,[a] Grant Simpson,[a] Siva S. Panda,[a] Khanh Ha,[a] Iryna Lebedyeva,[a] Hassan M. Faidallah,[b] Manal Metgen Al-Mohammadi,[b] C. Dennis Hall,[a,]* and the late Alan R. Katritzky,[a,b]

[a]*Center for Heterocyclic Compounds, Department of Chemistry, University of Florida, Gainesville, FL 32611-7200, USA*

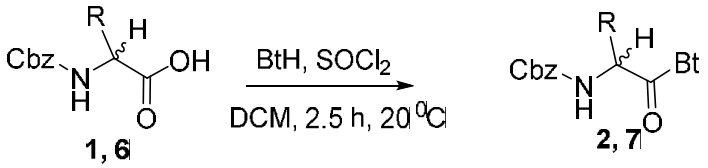
[b]*Chemistry Department, Faculty of Science, King Abdulaziz University, Jeddah 21589, Saudi Arabia*

E-mail: charlesdennishall@gmail.com

Experimental Section

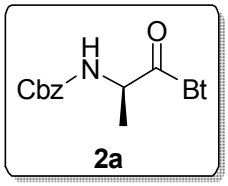
Melting points were determined on a capillary point apparatus equipped with a digital thermometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, DMSO-d_6, acetone-d_6, or CD_3OD using a 300 or 500 MHz spectrometer (with TMS as an internal standard). The following abbreviations are used to describe spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br s = broad singlet, dd = doublet of doublets, ddd = doublet of doublets of doublets, and dt = doublet of triplets. HPLC–MS analyses were performed on a reverse phase gradient using 0.2% acetic acid in H_2O/methanol as mobile phases; wavelength = 254 nm; mass spectrometry was done with electrospray ionization (ESI), matrix-assisted laser desorption/ionisation-time of flight (MALDI-TOF) or atmospheric-pressure chemical ionization (APCI). Ether refers to diethyl ether.

General procedure for the preparation of benzotriazolides 2a-d and 7a,b

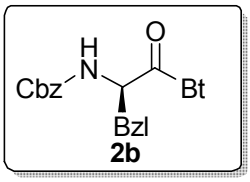


A stirred solution of 1*H*-benzotriazole (BtH) (4 equiv.) in dry tetrahydrofuran (THF) (10 mL/1 g of BtH) was treated at 20 °C with thionyl chloride ($SOCl_2$) (1.1 equiv.). After 20 minutes, a solution of Cbz-protected amino acid **1** (1 equiv.) or **6** (0.5 equiv) in dry THF (10 mL/1 g) was added slowly and the resulting solution was then stirred for 2.5 h at 20 °C. Upon completion, the mixture was filtered, and THF was removed under reduced pressure. The residue was dissolved by dichloromethane (CH_2Cl_2 50 mL/1 g of BtH) and washed successively with aq. Na_2CO_3 (10%, 3× 1 mL/1 mL CH_2Cl_2) HCl (4N, 1× 1 mL/1 mL CH_2Cl_2), and brine (1 mL/1 mL

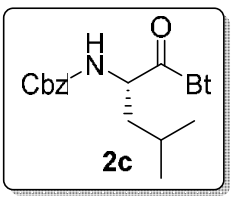
CH_2Cl_2). The organic layer was dried over magnesium sulfate ($MgSO_4$), filtered and evaporated to give the crude product. The solid was recrystallized from CH_2Cl_2/hexanes to yield benzotriazolides **2** or **7.**



Cbz-D-Ala-Bt (2a). White solid, 2.64 g, 8.15 mmol, 91% yield; mp 113.0–115.0 °C (114.0–115.0). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.25 (d, *J* = 8.2 Hz, 1H), 8.13 (dt, *J* = 8.3, 1.0 Hz, 1H), 7.67 (td, *J* = 8.3, 1.0 Hz, 1H), 7.52 (td, *J* = 8.3, 1.1 Hz, 1H), 7.22 – 7.43 (m, 5H), 5.81 (dq, *J* = 7.3, 5.1 Hz, 1H), 5.68 (d, *J* = 4.4 Hz, 1H), 5.19 - 5.02 (m, 2H), 1.69 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.5, 155.8, 146.2, 131.3, 130.9, 128.7, 128.4, 128.3, 126.7, 120.5, 114.5, 67.4, 50.8, 19.3. Anal. Calcd for $C_{17}H_{16}N_4O_3$: C 62.95, H 4.97, N 17.27. Found: C 62.94, H 4.92, N 17.30. HRMS (ESI): calcd for $C_{17}H_{16}N_4O_3Na$ $[M + Na]^+$ 347.1114, found 347.1116

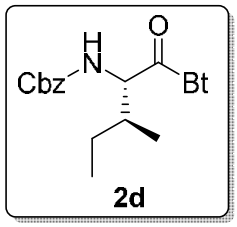


Cbz-D-Phe-Bt (2b). White solid, 2.60 g, 6.48 mmol, 97% yield; mp 145.0–147.0 °C (148.0–150.0). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.31 (d, *J* = 8.2 Hz, 1H), 8.23 (d, *J* = 8.2 Hz, 1H), 7.75 (td, *J* = 7.1, 1.1 Hz, 1H), 7.61 (td, *J* = 7.1, 1.1 Hz, 1H), 7.48 – 7.19 (m, 10H), 6.27-6.13 (m, 1H), 5.81 (m, *J* = 5.7 Hz, 1H), 5.18 (s, 2H), 3.57 (dd, *J* = 13.9, 5.1 Hz, 1H), 3.31 (dd, *J* = 14.0, 7.9 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.0, 155.9, 146.1, 136.2, 135.2, 131.1, 130.9, 129.4, 128.8, 128.6, 128.3, 128.2, 127.5, 126.7, 120.5, 114.4, 67.3, 55.8, 38.9. Anal. Calcd for $C_{23}H_{20}N_4O_3$: C 68.99, H 5.03, N 13.99. Found: C 68.96, H 4.90, N 13.99.

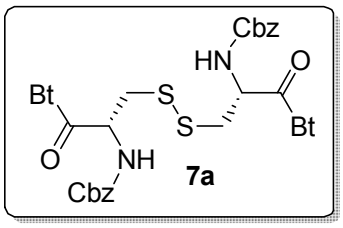


Cbz-L-Leu-Bt (2c). Sticky oil, 2.65 g, 7.24 mmol, 96% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.24 (d, *J* = 8.2 Hz, 1H), 8.12 (d, *J* = 8.1 Hz, 1H), 7.65 (t, *J* = 6.7 Hz, 1H), 7.51 (t, *J* = 6.7 Hz , 1H), 7.40 – 7.27 (m, 5H), 5.84

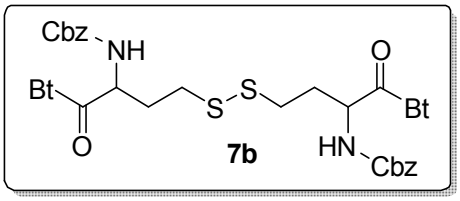
(dd, J = 10.1, 3.1 Hz, 1H), 5.61 (d, J = 8.0 Hz, 1H), 5.17 – 5.03 (m, 2H), 1.96 – 1.81 (m, 2H), 1.79 – 1.70 (m, 1H), 1.10 (d, J = 5.4 Hz, 3H), 0.96 (d, J = 5.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.6, 156.3, 146.1, 136.2, 131.3, 130.8, 128.7, 128.3, 126.6, 120.4, 114.5, 67.4, 53.6, 42.0, 25.3, 23.4, 21.4. HRMS (ESI): calcd for $C_{20}H_{22}N_4O_3Na$ $[M + Na]^+$ 389.1584, found 389.1583



Cbz-L-Ile-Bt (2d). Sticky oil, 2.65 g, 7.24 mmol, 96% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.26 (d, J = 8.2 Hz, 1H), 8.12 (d, J = 8.3 Hz, 1H), 7.65 (td, J = 8.2, 1.0 Hz, 1H), 7.52 (td, J = 7.2, 1.1 Hz, 1H), 7.43 – 7.25 (m, 5H), 5.85 – 5.65 (m, 2H), 5.17 – 5.08 (m, 2H), 2.29 – 2.19 (m, 1H), 1.66 – 1.46 (m, 1H), 1.30 – 1.13 (m, 1H), 1.08 (d, J = 6.8 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.8, 156.4, 146.1, 136.2, 131.1, 130.8, 128.6, 128.3, 126.6, 120.5, 114.5, 67.4, 59.3, 38.3, 24.3, 16.1, 11.4. HRMS (ESI): calcd for $C_{20}H_{22}N_4O_3Na$ $[M + Na]^+$ 389.1584, found 389.1587

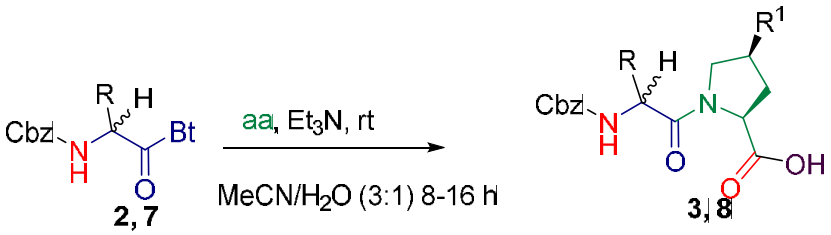


Bis-Cbz-L-Cys-Bt (7a). White solid, 2.54 g, 3.58 mmol, 91% yield; mp °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.21 (d, J = 8.3 Hz, 2H), 8.07 (d, J = 8.3 Hz, 2H), 7.67 (t, J = 7.7 Hz, 2H), 7.52 (t, J = 7.7 Hz, 2H), 7.41 – 7.25 (m, 10H), 6.11 – 6.00 (m, 2H), 5.92 (d, J = 8.6 Hz, 2H), 5.12 (br s, 4H), 3.45 (dd, J = 14.4, 3.0 Hz, 2H), 3.32 (dd, J = 15.0, 6.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.5, 155.9, 146.1, 136.1, 131.2, 128.7, 128.4, 126.9, 120.6, 114.5, 67.7, 54.3, 40.9. Anal. Calcd for $C_{34}H_{30}N_8O_6S_2$: HRMS (ESI): calcd for $C_{34}H_{30}N_8O_6S_2Na$ $[M + Na]^+$ 733.1621, found 733.1628

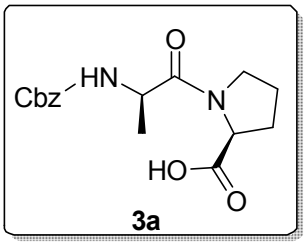


Bis-Cbz-Homo-D,L-Cys-Bt (7b). White solid, 2.42 g, 3.28 mmol, 88% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.30 – 8.20 (m, 2H), 8.18 – 8.05 (m, 2H), 7.67 (t, *J* = 7.5 Hz, 2H), 7.58 – 7.46 (m, 2H), 7.46 – 7.24 (m, 10H), 6.03 (d, *J* = 9.1 Hz, 2H), 5.98 – 5.81 (m, 2H), 5.12 (s, 4H), 2.98 – 2.78 (m, 4H), 2.66 – 2.44 (m, 2H), 2.24 (dddd, *J* = 14.2, 7.0, 7.0, 7.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.3, 171.2, 156.3, 146.2, 131.3, 131.1, 128.7, 128.4, 126.8, 120.7, 114.5, 67.70, 54.3, 35.0, 33.2. Anal. Calcd for $C_{36}H_{34}N_8O_6S_2$: HRMS (ESI): calcd for $C_{36}H_{34}N_8O_6S_2Na$ $[M + Na]^+$ 761.1934, found 761.1939

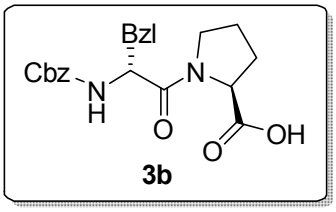
General procedure for the preparation of dipeptides 3a-g, 8a,b



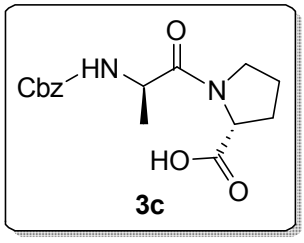
Benzotriazolides **2** or **7** (1 equiv.) were each suspended in acetonitrile/water (3:1) (25 mL/1 g) and a solution of amino acid (D- or L-Pro, or trans-4-hydroxy-L-Pro-benzyl ester), (1 equiv.) in water (5 mL/1 g of amino acid) containing triethylamine (1.0–1.1 equiv for **2** and 2.0–2.2 equiv for **7**.) was added slowly. The mixtures were stirred at 20 °C for 16-24 h until TLC revealed consumption of the starting materials. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate. The solution was washed with 4N HCl (3 × 1.5 mL/1 mL of ethyl acetate) and brine (1 mL/1 mL of ethyl acetate). Recrystallization from ethyl acetate/hexanes yielded dipeptides **3** or **8**



Cbz-D-Ala-L-Pro-OH (3a). Sticky oil, 0.96 g, 3.01 mmol, 65% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.79 (s, 1H), 7.37 – 7.15 (m, 5H), 6.25 (d, *J* = 8.0 Hz, 1H), 5.14 – 4.89 (m, 2H), 4.56 – 4.37 (m, 2H), 3.64 (dt, *J* = 9.6, 6.5 Hz, 1H), 3.51 (dt, *J* = 10.3, 6.5 Hz, 1H), 2.26 – 2.02 (m, 1H), 2.02 – 1.71 (m, 3H), 1.28 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.8, 174.6, 173.4, 172.2, 156.3, 155.9, 136.3, 128.5, 128.4, 128.1, 128.0, 127.9, 127.8, 66.8, 59.6, 59.4, 49.5, 48.4, 47.1, 31.1, 28.9, 24.6, 22.4, 20.7, 18.1. HRMS (ESI): calcd for $C_{16}H_{19}N_2O_5$ $[M - H]^-$ 319.1288, found 319.1293

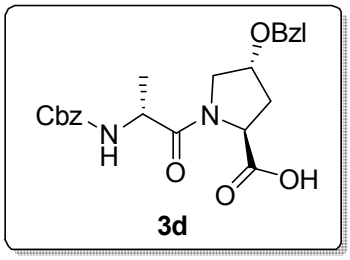


Cbz-D-Phe-L-Pro-OH (3b). Sticky oil, 1.40 g, 3.52 mmol, 92% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ ^{1}H NMR (300 MHz, Chloroform-*d*) δ 11.07 (s, 1H), 7.39 – 7.01 (m, 10H), 6.18 (d, *J* = 8.5 Hz, 1H), 5.14 – 4.83 (m, 3H), 4.72 (dd, *J* = 9.0, 6.1 Hz, 1H), 4.35 – 4.22 (m, 1H), 3.63 – 3.46 (m, 1H), 3.25 – 2.77 (m, 2H), 2.72 – 2.55 (m, 1H), 2.05 – 1.88 (m, 1H), 1.88 – 1.66 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 174.7, 174.3, 172.4, 171.4, 156.5, 155.9, 136.8, 136.3, 136.0, 129.5, 128.5, 128.4, 128.1, 128.0, 127.9, 127.6, 127.1, 127.0, 126.7, 125.9, 66.9, 66.8, 59.7, 59.3, 54.2, 53.6, 47.2, 47.1, 39.7, 37.8, 31.1, 28.6, 24.3, 22.5. HRMS (ESI): calcd for $C_{22}H_{23}N_2O_5$ $[M - H]^-$ 395.1601, found 395.1605



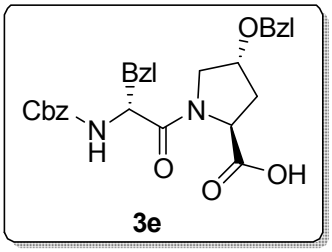
Cbz-D-Ala-D-Pro-OH (3c). Sticky oil, 1.11 g, 3.47 mmol, 75% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.82 (br s, 1H), 7.46 – 7.22 (m, 5H), 6.28 (d, *J* = 8.0 Hz, 1H), 5.12 – 4.96 (m, 2H), 4.58 – 4.44 (m, 2H), 3.70 – 3.62 (m, 1H), 3.61 – 3.45 (m, 1H), 2.27 – 2.05 (m, 1H),

2.06 – 1.76 (m, 3H), 1.32 (d, J = 7.1 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 175.9, 174.5, 172.5, 156.1, 155.9, 136.4, 128.5, 128.1, 128.0, 127.9, 66.8, 59.0, 49.5, 48.3, 47.0, 28.7, 24.7, 18.3, 17.5. HRMS (ESI): calcd for $C_{16}H_{19}N_2O_5$ $[M - H]^-$ 319.1288, found 319.1295



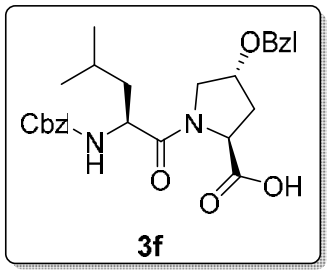
3d

Cbz-D-Ala-L-Hyp(OBzl)-OH (3d). Sticky oil, 1.26 g, 2.96 mmol, 64% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.81 (s, 1H), 7.47 – 7.18 (m, 10H), 6.19 (d, J = 8.3 Hz, 1H), 5.23 – 4.99 (m, 3H), 4.63 – 4.46 (m, 2H), 4.41 (t, J = 7.4 Hz, 1H), 4.33 – 4.22 (m, 1H), 3.83 (dd, J = 11.2, 4.6 Hz, 1H), 3.68 (d, J = 11.4 Hz, 1H), 2.42 (ddd, J = 12.6, 8.5, 3.6 Hz, 1H), 2.18 (ddd, J = 13.0, 7.3, 5.0 Hz, 1H), 1.42 (d, J = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.5, 171.6, 170.2, 156.0, 155.8, 146.1, 146.0, 137.5, 136.6, 131.2, 130.8, 130.7, 128.7, 128.6, 128.3, 128.2, 128.1, 127.7, 126.6, 126.5, 77.8, 71.4, 67.3, 66.9, 58.7, 52.9, 50.7, 48.5, 35.2, 18.8, 18.6. HRMS (ESI): calcd for $C_{23}H_{25}N_2O_6$ $[M - H]^-$ 425.1707, found 425.1712

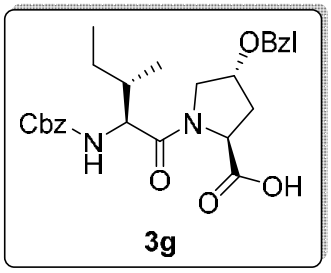


3e

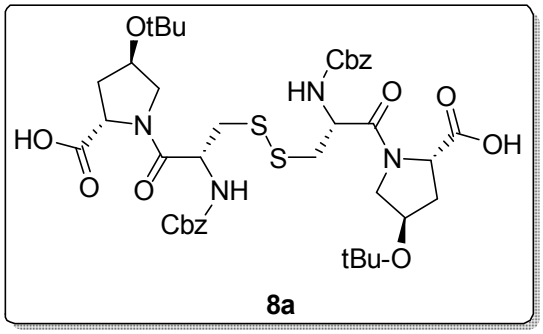
Cbz-D-Phe-L-Hyp(OBzl)-OH (3e). Sticky oil, 1.41 g, 2.81 mmol, 75% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 10.72 (s, 1H), 7.45 – 7.12 (m, 15H), 6.28 (d, J = 8.9 Hz, 1H), 5.21 – 4.89 (m, 4H), 4.87 – 4.77 (m, 1H), 4.77 – 4.66 (m, 1H), 4.60 – 4.42 (m, 1H), 4.29 – 4.12 (m, 1H), 3.85 (dd, J = 11.0, 5.1 Hz, 1H), 3.26 (dd, J = 14.3, 4.8 Hz, 1H), 3.21 (dd, J = 11.3, 3.6 Hz, 1H), 3.10 (dd, J = 19.7, 7.0 Hz, 1H), 3.04 – 2.79 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.2, 172.0, 167.7, 164.6, 152.1, 137.6, 135.9, 134.9, 134.8, 130.1, 129.5, 129.1, 128.9, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.7, 127.4, 76.2, 74.5, 71.6, 70.8, 69.5, 67.1, 62.7, 57.6, 54.2, 51.7, 39.1, 38.6, 35.5, 33.9, 29.9, 28.3. HRMS (ESI): calcd for $C_{29}H_{29}N_2O_6$ $[M - H]^-$ 501.2020, found 501.2017



Cbz-L-Leu-L-Hyp(OBzl)-OH (3f). Sticky oil, 1.30 g, 2.78 mmol, 68% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.62 (s, 1H), 7.37 – 7.16 (m, 10H), 6.03 (d, *J* = 9.0 Hz, 1H), 5.14 – 5.03 (m, 3H), 4.58 – 4.44 (m, 2H), 4.38 (ddd, *J* = 13.6, 7.4, 3.1 Hz, 1H), 4.28 – 4.10 (m, 1H), 3.85 (dd, *J* = 11.2, 4.6 Hz, 1H), 3.63 (dd, *J* = 11.1, 1.1 Hz, 1H), 2.35 (ddd, *J* = 12.8, 8.3, 3.9 Hz, 1H), 2.16 (dt, *J* = 13.0, 6.2 Hz, 1H), 1.76 – 1.57 (m, 2H), 1.57 – 1.34 (m, 1H), 0.98 – 0.71 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.8, 174.6, 172.8, 156.6, 156.4, 137.4, 136.4, 136.3, 128.6, 128.5, 128.2, 128.1, 127.9, 127.6, 126.1, 71.4, 67.1, 58.3, 52.5, 52.4, 51.1, 41.6, 41.5, 34.4, 24.8, 24.6, 23.4, 23.0, 21.9, 21.8. HRMS (ESI): calcd for $C_{26}H_{31}N_2O_6$ $[M - H]^-$ 467.2176, found 467.2177



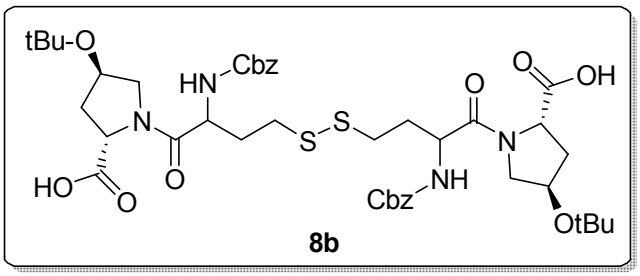
Cbz-L-Ile-L-Hyp(OBzl)-OH (3g). Sticky oil, 1.36 g, 2.91 mmol, 71% yield. ^{1}H NMR (500 MHz, Methanol-d_4) δ 7.39 – 7.22 (m, 10H), 5.14 – 5.02 (m, 4H), 4.68 – 4.54 (m, 1H), 4.52 – 4.45 (m, 1H), 4.34 – 4.25 (m, 1H), 4.13 (d, *J* = 5.6 Hz, 1H), 3.73 – 3.66 (m, 1H), 1.96 – 1.77 (m, 1H), 1.68 – 1.55 (m, 1H), 1.49 (dqd, *J* = 15.0, 7.5, 4.5 Hz, 1H), 1.30 – 1.13 (m, 2H), 1.02 – 0.91 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.5, 156.4, 139.7, 136.3, 128.7, 128.4, 128.3, 128.1, 127.9, 76.7, 71.2, 67.3, 67.1, 58.4, 58.3, 57.1, 52.5, 38.0, 37.6, 35.1, 25.0, 24.5, 15.6, 15.3, 11.8, 11.1. HRMS (ESI): calcd for $C_{26}H_{31}N_2O_6$ $[M - H]^-$ 467.2176, found 467.2179



Bis-Cbz-L-Cys-L-Hyp(O-*t*Bu)-OH (8a). Sticky oil, 1.47 , 1.73 mmol, 82% yield. ^{1}H NMR (CD_3OD, 300 MHz): δ 7.42 – 7.21 (m, 10H), 5.09

(br s, 4H), 5.15 – 5.03 (m, 4H), 4.80 (dd, 2H), 4.54 – 4.32 (m, 4H), 3.92 (dd, J = 10.7, 5.5 Hz, 2H), 3.66 (dd, 2H), 3.17 (dd, J = 14.1, 4.8 Hz, 2H), 2.89 (dd, J = 14.3, 9.2 Hz, 2H), 2.25 – 1.98 (m, 4H), 1.19 (br s, 18H). ^{13}C NMR (CD_3OD, 75 MHz): δ 171.5, 158.5, 138.1, 130.0, 129.6, 129.4, 129.1, 129.0, 128.9, 75.6, 71.1, 68.4, 68.0, 59.6, 55.5, 53.5, 41.0, 38.2, 29.1, 28.7.

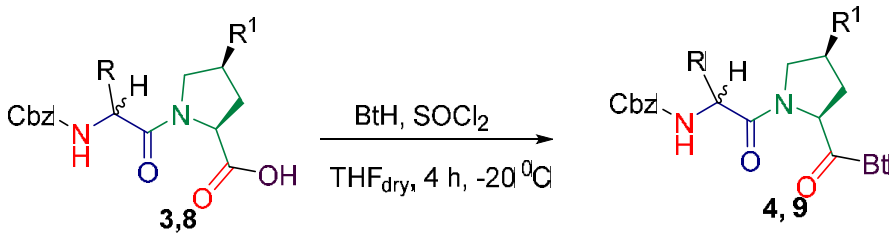
HRMS (ESI): calcd for $C_{40}H_{53}N_4O_{12}S_2$ $[M - H]^-$ 845.3095, found 845.3091



8b

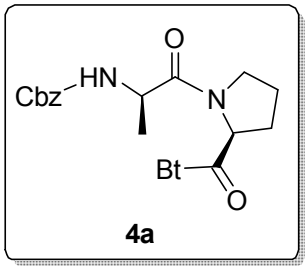
Bis-Cbz-Homo-D,L-Cys-L-Hyp(O-*t*Bu)-OH (8b). White solid, 0.24 g, 0.65 mmol, 77% yield; mp 79.0–83.0 °C. ^{1}H NMR (CD_3OD, 300 MHz): δ 7.38 – 7.26 (m, 10H), 5.18 – 5.04 (m, 4H), 4.66 – 4.58 (m, 2H), 4.49 (t, J = 6.7 Hz, 2H), 4.46 – 4.29 (m, 2H), 3.92 – 3.82 (m, 2H), 3.74 – 3.62 (m, 2H), 2.87 – 2.63 (m, 4H), 2.23 – 2.13 (m, 4H), 2.13 – 2.05 (m, 2H), 2.05 – 1.91 (m, 2H), 1.33 – 1.11 (m, 18H). ^{13}C NMR (CD_3OD, 75 MHz): δ 175.5, 172.6, 158.5, 138.3, 129.6, 129.2, 129.1, 129.0, 110.2, 75.7, 71.2, 69.3, 67.9, 67.8, 59.5, 59.3, 55.7, 54.2, 52.6, 38.4, 38.3, 35.6, 35.0, 32.5, 28.74, 28.71. HRMS (ESI): calcd for $C_{42}H_{57}N_4O_{12}S_2$ $[M - H]^-$ 873.3408, found 873.3401

General procedure for the preparation of dipeptidoyl bentrotriazolides 4a-g, 9a,b



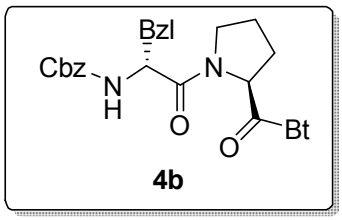
A stirred solution of BtH (4 equiv.) in dry tetrahydrofuran (THF) (15 mL/1 g) was treated at -20 °C with $SOCl_2$ (1 equiv.). After 20 minutes, the solution of BtH and $SOCl_2$ was cooled down

on ice and salt (NaCl) for 5mins and a solution of **3** (1 equiv.) or **8** (0.5 equiv.) in dry THF (20 mL/1 g of dipeptide) was added drop-wise and the resulting solutions were then stirred for 4 h at -20 °C. THF was removed under reduced pressure and the residue was dissolved ethyl acetate (85 mL/1 g BtH) and washed successively with Na_2CO_3 10 wt.-% in water (3× 1 mL/1 mL of ethyl acetate), HCl (4N, 1 × 1 mL/1 mL of CH_2Cl_2), and brine (1 × 30 mL/1 mL of CH_2Cl_2). The organic layer was dried over magnesium sulfate, filtered and evaporated. The crude product was then recrystallized from CH_2Cl_2/hexanes to yield dipeptidoyl bentrotriazolides **4** or **9**



4a

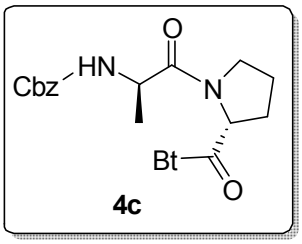
Cbz-D-Ala-L-Pro-Bt (4a). Sticky oil, 0.92 g, 2.19 mmol, 70% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.26 (d, *J* = 8.8 Hz, 1H), 8.12 (d, *J* = 8.2 Hz, 1H), 7.64 (t, *J* = 8.4 Hz, 1H), 7.51 (t, *J* = 8.0 Hz, 1H), 7.45 – 7.21 (m, 5H), 5.93 (d, *J* = 9.0 Hz, 1H), 5.75 (d, *J* = 7.9 Hz, 1H), 5.21 – 5.02 (m, 2H), 4.73 – 4.61 (m, 1H), 4.17 – 3.88 (m, 1H), 3.75 – 3.52 (m, 1H), 2.65 – 2.48 (m, 1H), 2.31 – 2.08 (m, 3H), 1.40 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.8, 171.4, 170.1, 167.4, 165.9, 155.6, 146.1, 136.5, 131.3, 130.8, 130.6, 130.5, 128.8, 128.5, 128.0, 126.6, 126.5, 126.2, 120.3, 114.6, 114.5, 69.3, 66.8, 60.5, 59.8, 48.6, 47.5, 45.6, 38.3, 29.7, 25.0, 23.3, 21.1, 19.0, 18.7 (Compound was partially hydrolyzed). HRMS (ESI): calcd for $C_{22}H_{23}N_5O_4Na$ $[M + Na]^+$ 444.1642, found 444.1649



4b

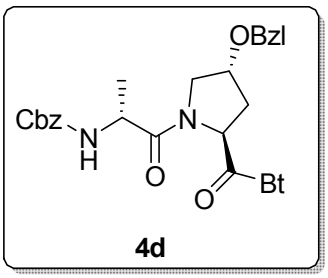
Cbz-D-Phe-L-Pro-Bt (4b). Sticky oil, 0.73 g, 1.46 mmol, 53% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.15 (ddd, *J* = 8.3, 1.1, 1.1 Hz, 1H), 8.02 (ddd, *J* = 8.3, 1.0, 1.0 Hz, 1H), 7.54 (ddd, *J* = 8.3, 7.1, 1.1 Hz, 1H), 7.41 (ddd, *J* = 8.2, 7.1, 1.1 Hz, 1H), 7.35 – 7.09 (m, 10H), 5.70 (dd, *J* = 8.9, 4.6 Hz, 1H), 5.65 (d, *J* = 8.8 Hz, 1H), 5.11 – 4.95 (m, 2H), 4.73 (ddd, *J* = 9.0, 8.9, 5.4 Hz, 1H), 3.62 (ddd, *J* = 9.5, 7.2, 5.3 Hz, 1H), 3.03 (dd, *J* = 13.0, 5.5 Hz,

1H), 2.90 (dd, *J* = 12.7, 9.4 Hz, 1H), 2.74 (ddd, *J* = 9.9, 6.9, 6.9 Hz, 1H), 2.30 – 2.10 (m, 1H), 2.06 – 1.69 (m, 2H), 1.66 – 1.46 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.2, 170.0, 155.7, 146.1, 136.5, 136.2, 131.3, 130.9, 130.6, 129.6, 129.4, 128.8, 128.7, 128.6, 128.2, 128.1, 127.3, 126.5, 120.5, 120.3, 114.6, 114.4, 67.3, 67.0, 59.5, 54.2, 47.4, 40.3, 29.7, 24.8. HRMS (ESI): calcd for $C_{28}H_{27}N_5O_4Na$ $[M + Na]^+$ 520.1955, found 520.1957



4c

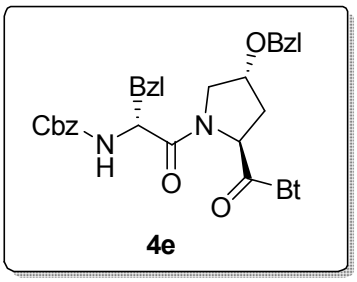
Cbz-D-Ala-D-Pro-Bt (4c). Sticky oil, 1.00 g, 2.37 mmol, 76% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.17 (d, *J* = 8.2 Hz, 1H), 8.04 (d, *J* = 8.3 Hz, 1H), 7.61 – 7.49 (m, 1H), 7.48 – 7.37 (m, 1H), 7.36 – 7.16 (m, 5H), 6.01 (d, *J* = 8.1 Hz, 1H), 5.91 (dd, *J* = 7.8, 3.9 Hz, 1H), 5.19 – 4.93 (m, 2H), 4.62 (dq, *J* = 7.0, 6.9 Hz, 1H), 3.95 – 3.78 (m, 1H), 3.78 – 3.63 (m, 1H), 2.64 – 2.40 (m, 1H), 2.21 – 2.01 (m, 3H), 1.41 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.8, 172.2, 171.5, 170.0, 155.7, 145.8, 136.3, 131.0, 130.5, 130.4, 130.2, 128.5, 128.3, 128.0, 127.9, 127.7, 126.3, 126.2, 126.0, 120.1, 120.0, 119.9, 114.7, 114.2, 66.9, 66.6, 59.6, 50.5, 48.3, 47.2, 29.5, 25.1, 23.0, 20.5, 18.4, 18.0. HRMS (ESI): calcd for $C_{22}H_{23}N_5O_4Na$ $[M + Na]^+$ 444.1642, found 444.1645



4d

Cbz-D-Ala-L-Hyp(OBzl)-Bt (4d). Sticky oil, 1.14 g, 2.16 mmol, 92% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.27 (d, *J* = 8.2 Hz, 1H), 8.14 (ddd, *J* = 7.7, 2.6 Hz, 1H), 7.66 (td, *J* = 9.5, 8.5, 5.8 Hz, 1H), 7.59 – 7.47 (m, 1H), 7.46 – 7.26 (m, 10H), 6.36 – 6.06 (m, 1H), 5.97 (d, *J* = 8.0 Hz, 1H), 5.92 – 5.72 (m, 1H), 5.31 – 5.04 (m, 2H), 4.79 – 4.51 (m, 2H), 4.50 – 4.38 (m, 1H), 4.28 – 4.00 (m, 1H), 3.92 (d, *J* = 10.6 Hz, 1H), 2.92 – 2.71 (m, 1H), 2.40 – 2.24 (m, 1H), 1.69 (d, *J* = 6.3 Hz, 2H), 1.44 (d, *J* = 6.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.2, 174.6, 172.6, 156.3, 156.2, 138.7, 137.4, 136.2, 128.7, 128.6, 128.3,

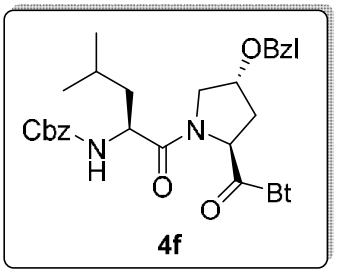
128.1, 128.0, 127.7, 126.2, 115.0, 71.4, 67.1, 58.6, 52.6, 49.8, 48.7, 34.5, 18.5, 18.1. HRMS (ESI): calcd for $C_{29}H_{29}N_5O_5Na$ $[M + Na]^+$ 550.2060, found 550.2062



4e

Cbz-D-Phe-L-Hyp(OBzl)-Bt (4e). Sticky oil, 1.08 g, 1.79 mmol, 90% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.37 – 8.22 (m, 1H), 8.21 – 8.08 (m, 1H), 7.77 – 7.64 (m, 1H), 7.63 – 7.47 (m, 1H), 7.46 – 7.08 (m, 15H), 6.24 – 6.08 (m, 1H), 6.08 – 5.93 (m, 1H), 5.92 – 5.74 (m, 1H), 5.24 – 4.96 (m, 2H), 4.66 – 4.26 (m, 2H), 4.25 – 3.91 (m, 1H), 3.48 (t, *J* = 17.3 Hz, 1H), 3.34 – 3.16 (m, 1H), 3.16 – 2.87 (m, 2H), 2.37 – 2.14 (m, 1H), 2.13 – 1.95 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.6, 171.0, 170.7, 169.9, 156.0, 146.1, 138.9, 137.5, 136.4, 135.8, 135.2, 131.2, 131.1, 130.9, 130.7, 129.5, 129.4, 128.8, 128.7, 128.6, 128.3, 128.2, 128.1, 128.0, 127.7, 127.5, 127.3, 126.7, 126.5, 125.9, 120.5, 120.3, 115.1, 114.4, 76.3, 71.5, 67.4, 67.0, 60.6, 58.6, 58.4, 55.9, 54.1, 52.7, 39.0, 38.9, 35.1, 28.2, 14.3.

HRMS (ESI): calcd for $C_{35}H_{33}N_5O_5Na$ $[M + Na]^+$ 626.2373, found 626.2368

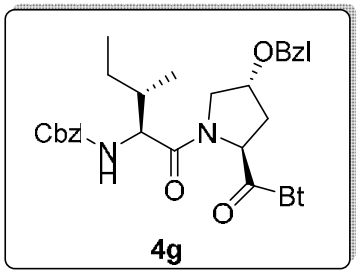


4f

Cbz-L-Leu-L-Hyp(OBzl)-Bt (4f). Sticky oil, 0.91 g, 1.60 mmol, 75% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.23 (dd, *J* = 7.7, 3.6 Hz, 1H), 8.16 – 8.02 (m, 1H), 7.62 (td, *J* = 10.6, 9.5, 5.3 Hz, 1H), 7.49 (t, *J* = 8.1 Hz, 1H), 7.41 – 7.24 (m, 10H), 6.09 – 5.98 (m, 1H), 5.97 – 5.55 (m, 2H), 5.19 – 5.00 (m, 2H), 4.74 – 4.44 (m, 2H), 4.44 – 4.32 (m, 1H), 4.08 (dd, *J* = 11.1, 4.4 Hz, 1H), 3.88 (d, *J* = 11.3 Hz, 1H), 2.77 (ddd, *J* = 12.5, 8.4, 3.3 Hz, 1H), 2.41 – 2.15 (m, 1H), 1.93 – 1.80 (m, 1H), 1.79 – 1.65 (m, 1H), 1.55 (dt, *J* = 8.8, 4.3 Hz, 1H), 1.05 – 0.80 (m, 6H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.6, 171.7, 170.0, 156.2, 146.1, 137.4, 136.5,

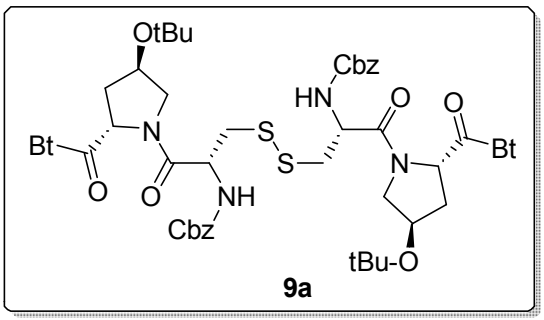
131.2, 130.7, 130.5, 128.6, 128.5, 128.2, 128.1, 127.9, 127.5, 126.5, 126.4, 120.3, 120.2, 114.5, 114.4, 71.4, 67.3, 66.9, 58.6, 53.5, 52.7, 51.0, 42.2, 41.8, 35.2, 25.2, 24.6, 23.4, 23.2, 22.0, 21.3.

HRMS (ESI): calcd for $C_{32}H_{35}N_5O_5Na$ $[M + Na]^+$ 592.2530, found 592.2535



4g

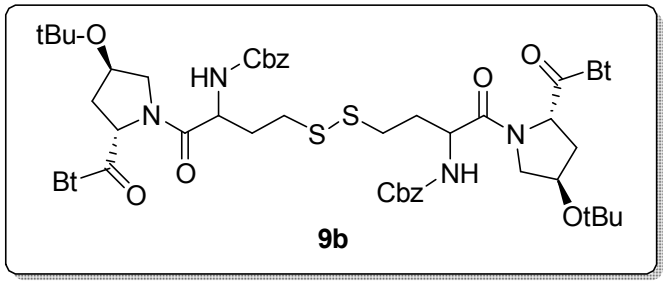
Cbz-L-Ile-L-Hyp(OBzl)-Bt (4g). Sticky oil, 0.97 g, 1.71 mmol, 80% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.27 – 8.14 (m, 1H), 8.05 (dd, *J* = 8.3, 3.5 Hz, 1H), 7.58 (t, *J* = 7.7 Hz, 1H), 7.45 (t, 1H), 7.38 – 7.16 (m, 10H), 5.98 (d, *J* = 9.2 Hz, 1H), 5.86 – 5.68 (m, 2H), 5.18 – 4.93 (m, 4H), 4.66 – 4.41 (m, 1H), 4.40 – 4.26 (m, 1H), 3.94 – 3.79 (m, 1H), 2.34 – 1.99 (m, 2H), 1.95 – 1.68 (m, 1H), 1.66 – 1.34 (m, 1H), 1.32 – 1.10 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.93 – 0.74 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.7, 170.3, 156.4, 145.9, 137.5, 136.3, 130.9, 130.6, 130.4, 128.4, 128.1, 128.0, 127.8, 127.7, 126.4, 120.2, 114.3, 76.9, 70.9, 67.2, 66.8, 59.1, 58.8, 56.8, 52.6, 38.1, 37.6, 35.7, 24.3, 24.1, 15.9, 15.3, 11.2, 11.0. HRMS (ESI): calcd for $C_{32}H_{35}N_5O_5Na$ $[M + Na]^+$ 592.2530, found 592.2531



9a

Bis-Cbz-L-Cys-L-Hyp(O-*t*Bu)-Bt (9a). White solid, 0.84 g, 0.80 mmol, 68% yield; mp 74.0–80.0 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.25 (d, *J* = 8.0 Hz, 2H), 8.12 (d, *J* = 8.4 Hz, 2H), 7.71 – 7.57 (m, 2H), 7.56 – 7.46 (m, 2H), 7.45 – 7.21 (m, 10H), 6.12 – 5.92 (m, 2H), 5.87 (d, *J* = 8.9 Hz, 2H), 5.20 – 5.03 (m, 4H), 5.03 – 4.82 (m, 2H), 4.73 – 4.19 (m, 2H), 4.18 – 3.86 (m, 2H), 3.75 (t, *J* = 12.9 Hz, 2H), 3.41 – 2.71 (m, 4H), 2.60 – 2.40 (m, 2H), 2.37 – 2.19 (m, 2H), 1.19 (s, 18H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.4, 169.4, 166.7,

156.1, 152.5, 146.2, 136.3, 131.3, 130.7, 128.8, 128.7, 128.3, 128.2, 128.1, 127.7, 126.6, 120.4, 114.7, 74.8, 74.6, 69.9, 69.4, 67.6, 67.3, 67.1, 58.9, 58.8, 55.0, 54.0, 52.2, 42.1, 41.4, 39.3, 38.5, 37.8, 29.9, 28.4. HRMS (ESI): calcd for $C_{52}H_{60}N_{10}O_{10}S_2Na$ $[M + Na]^+$ 1071.3827, found 1071.3825



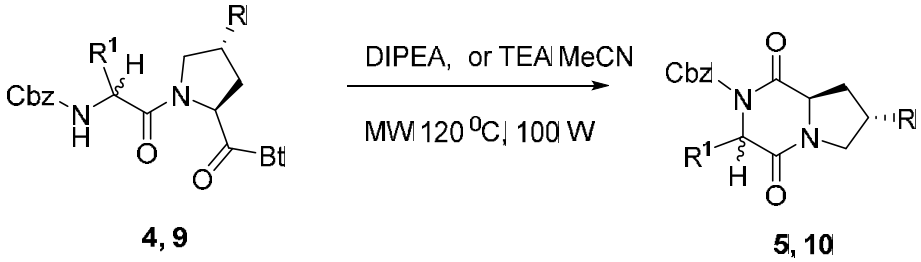
9b

Bis-Cbz-D,L-Homo-Cys-L-Hyp(O-*t*Bu)-Bt (9b). White solid, 0.94 g, 0.87 mmol, 76% yield; mp 77.0–82.0 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.31 – 8.19 (m, 2H), 8.18 – 8.05 (m, 2H), 7.74 – 7.57 (m, 2H), 7.57 – 7.44 (m, 2H), 7.40 – 7.27 (m, 10H), 6.13 – 5.95 (m, 2H), 5.93 – 5.58 (m, 2H), 5.19 – 5.00 (m, 4H), 4.86 – 4.71 (m, 2H), 4.55 – 4.40 (m, 2H), 4.15 – 3.89 (m, 2H), 3.79 – 3.56 (m, 2H), 2.88 – 2.65 (m, 4H), 2.62 – 2.43 (m, 2H), 2.34 – 2.21 (m, 6H), 1.25 – 1.12 (m, 18H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 170.5, 170.4, 156.3, 146.3, 136.4, 131.3, 130.8, 128.9, 128.7, 128.4, 128.3, 128.2, 126.6, 126.3, 120.5, 114.7, 74.9, 70.0, 69.7, 67.2, 58.6, 54.7, 51.5, 37.6, 32.5, 29.9, 28.4, 28.3. HRMS (ESI): calcd for $C_{54}H_{64}N_{10}O_{10}S_2Na$ $[M + Na]^+$ 1099.4140, found 1099.4135

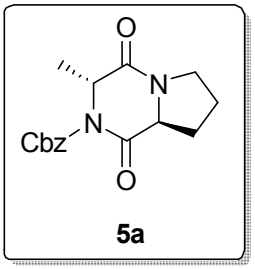
General procedure for the synthesis of DKPs 5a-g and bis-DKPs 10a,b

A solution of dipeptidoyl benzotriazolide **4** or **9** (1mmol) and triethylamine (1.5mmol for **4** and 3 mmol for **9**) or DIPEA (1.5mmol for **4** and 3 mmol for **9**) in dry acetonitrile, using a 10mL microwave tube (80% filled) was subjected to microwave activation (100^{o}C, 70 W) for 2-3h. The solvent was removed under reduced pressure and the residue was dissolved in ethyl acetate. The solution was washed with 4N HCl (3 × 1.5 mL/1 mL of ethyl acetate) and brine (1 mL/1 mL of ethyl acetate). Recrystallization from ethyl acetate/hexanes and direct purification

by column chromatography (hexanes/ethyl acetate gradient) gave the corresponding DKP product.

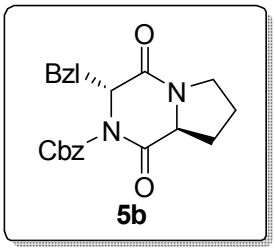


4, 9 **5, 10**



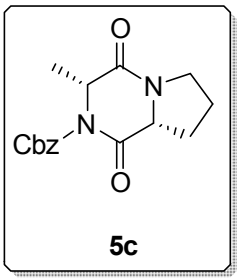
5a

***Cyclo*-[Cbz-D-Ala-L-Pro] (5a).** Sticky oil, 173 mg, 0.57 mmol, 69% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46 – 7.32 (m, 5H), 5.31 (s, 2H), 4.87 (q, *J* = 7.2 Hz, 1H), 4.21 (dd, *J* = 9.3, 7.1 Hz, 1H), 3.64 – 3.52 (m, 2H), 2.44 (dtd, *J* = 13.2, 6.9, 2.9 Hz, 1H), 2.19 (dddd, *J* = 12.8, 11.1, 9.3, 7.1 Hz, 1H), 2.11 – 1.85 (m, 2H), 1.54 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.5, 166.0, 152.0, 134.8, 128.8, 128.4, 69.4, 59.5, 57.7, 45.7, 29.3, 22.8, 17.4. HRMS (ESI): calcd for $C_{16}H_{18}N_2O_4Na$ $[M + Na]^+$ 325.1158, found 325.1163



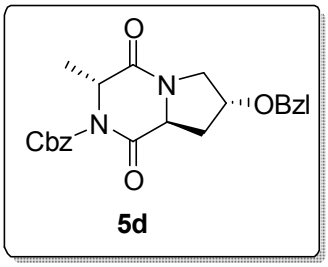
5b

***Cyclo*-[Cbz-D-Phe-L-Pro] (5b).** Sticky oil, 141 mg, 0.37 mmol, 53% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.39 – 6.97 (m, 10H), 5.25 – 5.09 (m, 2H), 5.00 (dd, *J* = 5.0, 5.0 Hz, 1H), 3.44 (ddd, *J* = 12.2, 8.9, 7.2 Hz, 1H), 3.30 (ddd, *J* = 12.0, 9.2, 2.8 Hz, 1H), 3.23 – 3.03 (m, 2H), 2.54 (dd, *J* = 9.6, 6.5 Hz, 1H), 2.12 – 1.86 (m, 1H), 1.86 – 1.64 (m, 2H), 1.63 – 1.42 (m, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.3, 164.2, 152.0, 135.0, 134.7, 130.1, 128.8, 128.7, 128.6, 128.4, 128.3, 128.1, 127.9, 127.7, 69.2, 67.7, 62.5, 58.8, 45.1, 38.4, 29.7, 29.3, 28.1, 25.6, 22.0 HRMS (ESI): calcd for $C_{22}H_{22}N_2O_4Na$ $[M + Na]^+$ 401.1471, found 401.1473



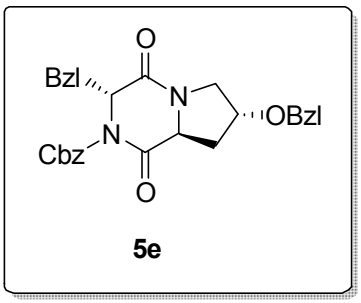
5c

***Cyclo*-[Cbz-D-Ala-D-Pro] (5c).** Sticky oil, 198 mg, 0.66 mmol, 79% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.47 – 7.27 (m, 5H), 5.29 (s, 2H), 4.86 (q, *J* = 7.2 Hz, 1H), 4.19 (dd, *J* = 9.3, 7.0 Hz, 1H), 3.66 – 3.44 (m, 2H), 2.42 (ddd, *J* = 13.4, 6.9, 2.9 Hz, 1H), 2.26 – 2.09 (m, 1H), 2.09 – 1.96 (m, 1H), 1.96 – 1.82 (m, 1H), 1.52 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.6, 163.9, 152.1, 134.7, 128.9, 128.7, 128.6, 128.5, 69.6, 67.3, 57.9, 53.6, 45.8, 33.5, 29.9, 22.8, 20.1, 19.9. HRMS (ESI): calcd for $C_{16}H_{18}N_2O_4Na$ $[M + Na]^+$ 325.1158, found 325.1159



5d

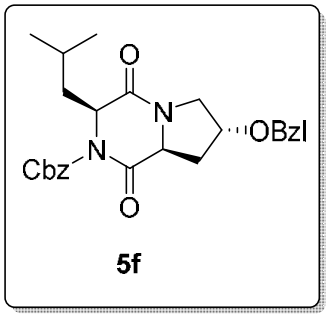
***Cyclo*-[Cbz-D-Ala-L-Hyp(OBzl)] (5d).** Sticky oil, 190 mg, 0.46 mmol, 70% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.47 – 7.22 (m, 10H), 5.30 (s, 2H), 5.21 – 5.03 (m, 1H), 4.89 (dd, *J* = 7.0, 6.6 Hz, 1H), 4.54 (s, 2H), 4.26 – 4.18 (m, 1H), 3.71 (dd, *J* = 14.5, 13.9 Hz, 1H), 2.66 (dd, *J* = 13.7, 6.3 Hz, 1H), 2.20 – 2.09 (m, 2H), 1.55 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 167.6, 166.1, 151.9, 137.3, 134.8, 128.8, 128.7, 128.6, 128.4, 128.2, 127.9, 75.0, 71.2, 69.4, 67.3, 58.1, 57.6, 51.7, 35.5, 18.7, 17.5 HRMS (ESI): calcd for $C_{23}H_{24}N_2O_5Na$ $[M + Na]^+$ 431.1577, found 431.1573



5e

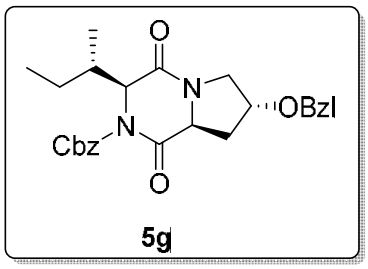
***Cyclo*-[Cbz-D-Phe-L-Hyp(OBzl)] (5e).** Sticky oil, 140 mg, 0.29 mmol, 50% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.45 – 7.06 (m, 15H), 5.35 – 5.20 (m, 1H), 5.18 – 4.95 (m, 2H), 4.53 – 4.29 (m, 2H), 3.81 – 3.53 (m, 1H), 3.34 – 3.16 (m, 1H), 3.09 (dd, *J* = 10.5, 4.5 Hz, 1H), 3.01 (dd, *J* = 11.2, 5.6 Hz, 1H), 2.35 (dd, *J* = 13.6, 6.0 Hz, 1H), 2.34 – 2.20 (m, 1H), 2.16 – 1.97 (m, 1H), 1.84 (ddd, *J* = 13.5, 11.3, 4.4 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.7, 164.6, 155.9, 152.2, 137.5, 135.8, 134.9, 130.1, 129.5, 129.1, 128.9, 128.8, 128.7, 128.6, 128.3, 128.2, 128.1, 127.9, 127.8, 127.4, 76.2, 74.5, 71.6, 70.8, 69.5,

67.2, 62.7, 58.5, 57.6, 51.7, 39.1, 38.6, 35.5, 28.3. HRMS (ESI): calcd for $C_{29}H_{28}N_2O_5Na$ [M + Na]$^+$ 507.1890, found 507.1885



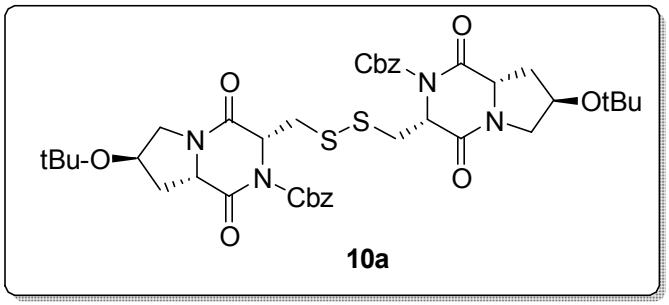
5f

***Cyclo*-[Cbz-L-Leu-L-Hyp(OBzl)] (5f).** Sticky oil, 210 mg, 0.47 mmol, 76% yield. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.46 – 7.12 (m, 10H), 5.34 – 5.21 (m, 2H), 5.22 – 5.02 (m, 1H), 4.88 (dd, *J* = 7.7, 7.7 Hz , 1H), 4.58 – 4.48 (m, 2H), 4.46 – 4.33 (m, 1H), 4.25 – 4.12 (m, 1H), 3.82 – 3.59 (m, 1H), 2.66 (dd, *J* = 13.6, 6.6 Hz, 1H), 2.18 – 2.00 (m, 1H), 1.79 – 1.67 (m, 1H), 1.67 – 1.56 (m, 1H), 1.30 – 1.17 (m, 1H), 0.97 (d, *J* = 5.6 Hz, 3H), 0.93 (d, , *J* = 5.7 Hz, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz): δ 168.2, 165.5, 152.1, 137.4, 134.8, 128.8, 128.6, 128.3, 127.9, 75.1, 71.2, 69.5, 61.5, 60.0, 58.3, 52.7, 51.7, 42.0, 41.9, 41.3, 35.8, 24.9, 23.5, 23.0, 22.0. HRMS (ESI): calcd for $C_{26}H_{30}N_2O_5Na$ [M + Na]$^+$ 473.2046, found 473.2047



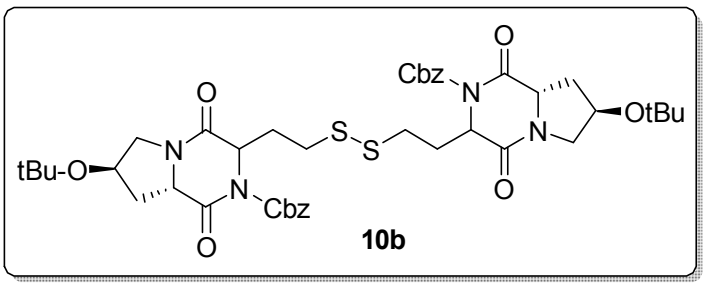
5g

***Cyclo*-[Cbz-L-Ile-L-Hyp(OBzl)] (5g).** Sticky oil, 227 mg, 0.50 mmol, 82% yield. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46 – 7.19 (m, 10H), 5.44 – 5.22 (m, 1H), 5.21 – 4.99 (m, 3H), 4.55 – 4.45 (m, 1H), 4.45 – 4.27 (m, 2H), 4.17 – 4.04 (m, 1H), 3.45 – 3.30 (m, 1H), 2.12 – 1.99 (m, 1H), 1.98 – 1.69 (m, 1H), 1.64 – 1.35 (m, 2H), 1.35 – 1.06 (m, 3H), 1.05 – 0.71 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 176.7, 176.2, 167.7, 166.3, 156.4, 152.6, 137.4, 136.3, 134.9, 128.7, 128.6, 128.3, 128.2, 128.0, 127.9, 74.3, 70.8, 69.4, 67.2, 65.4, 60.6, 58.2, 57.2, 51.5, 38.0, 37.6, 34.4, 29.8, 26.4, 25.7, 25.0, 20.9, 15.6, 14.5, 11.9, 11.3. HRMS (ESI): calcd for $C_{26}H_{30}N_2O_5Na$ [M + Na]$^+$ 473.2046, found 473.2049



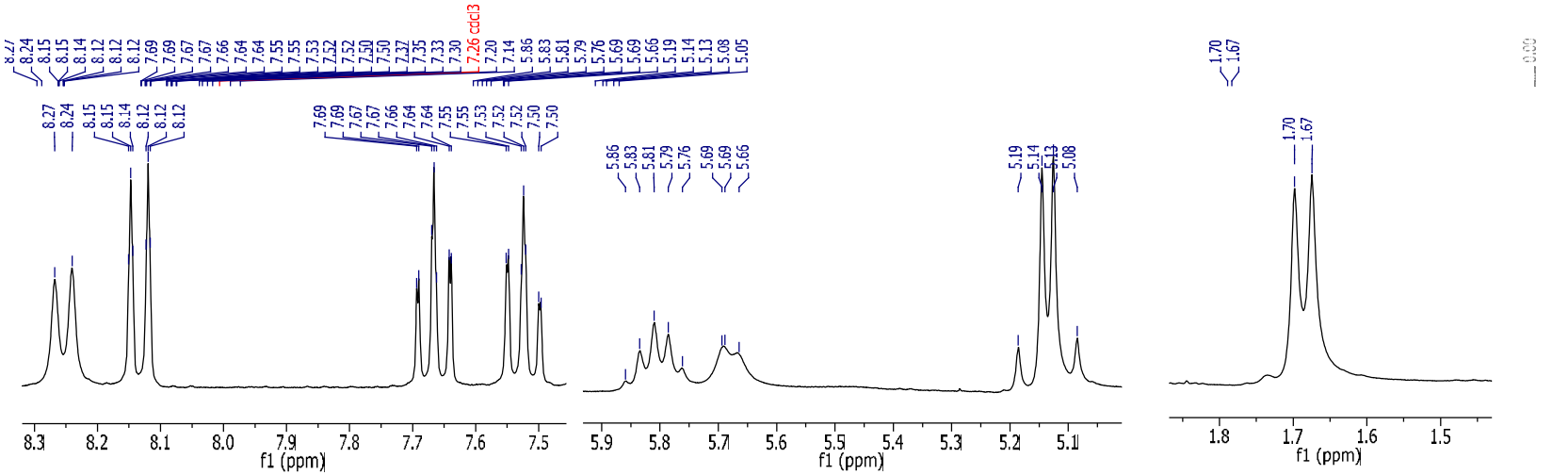
10a

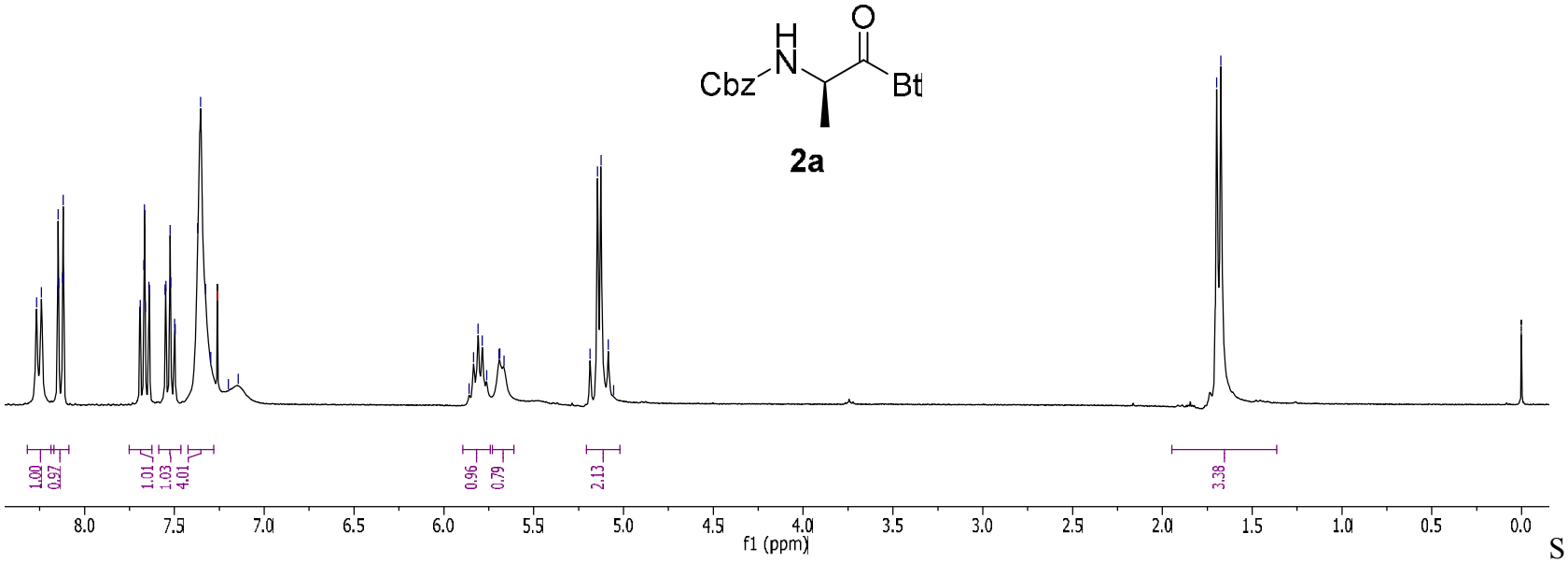
***Cyclo*-[Bis-Cbz-L-Cys-L-Hyp(O-*t*Bu)] (10a).** Sticky oil, 227 mg, 0.28 mmol, 84% yield. ^{1}H NMR (CD_3OD, 300 MHz): δ 7.51 – 7.22 (m, 10H), 5.48 (dd, *J* = 4.0, 2.0 Hz, 2H), 5.34 (s, 4H), 4.59 (dd, *J* = 5.5, 4.1 Hz, 2H), 3.78 (dd, *J* = 11.6, 5.6 Hz, 2H), 3.59 (dd, *J* = 11.8, 4.1 Hz, 2H), 3.47 (dd, *J* = 14.3, 4.5 Hz, 2H), 3.35 (dd, *J* = 4.2, 0.9 Hz, 2H), 2.88 (dd, *J* = 14.2, 5.2, 1.0 Hz, 2H), 2.33 (dd, *J* = 14.2, 5.8 Hz, 2H), 2.23 – 2.20 (m, 2H), 1.21 (s, 18H). ^{13}C NMR (CD_3OD, 75 MHz): δ 168.6, 167.3, 166.3, 164.7, 152.5, 136.7, 136.6, 131.6, 130.1, 130.0, 129.7, 129.6, 129.4, 127.2, 75.9, 71.6, 70.6, 69.2, 60.1, 59.2, 57.0, 55.5, 52.7, 39.8, 38.6, 34.0, 32.4, 28.7. HRMS (ESI): calcd for $C_{40}H_{50}N_4O_{10}S_2Na$ $[M + Na]^+$ 833.2860, found 833.2862

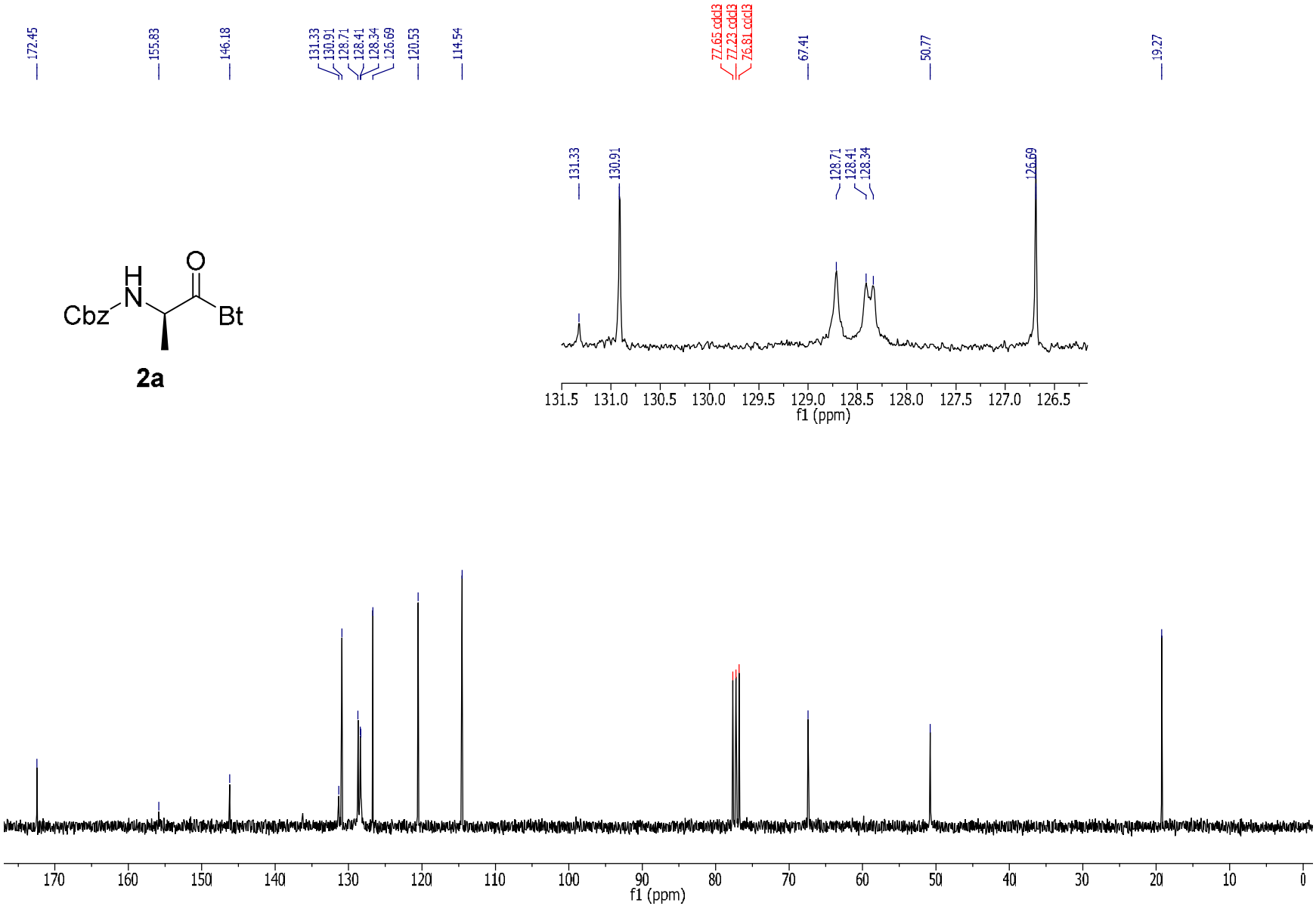


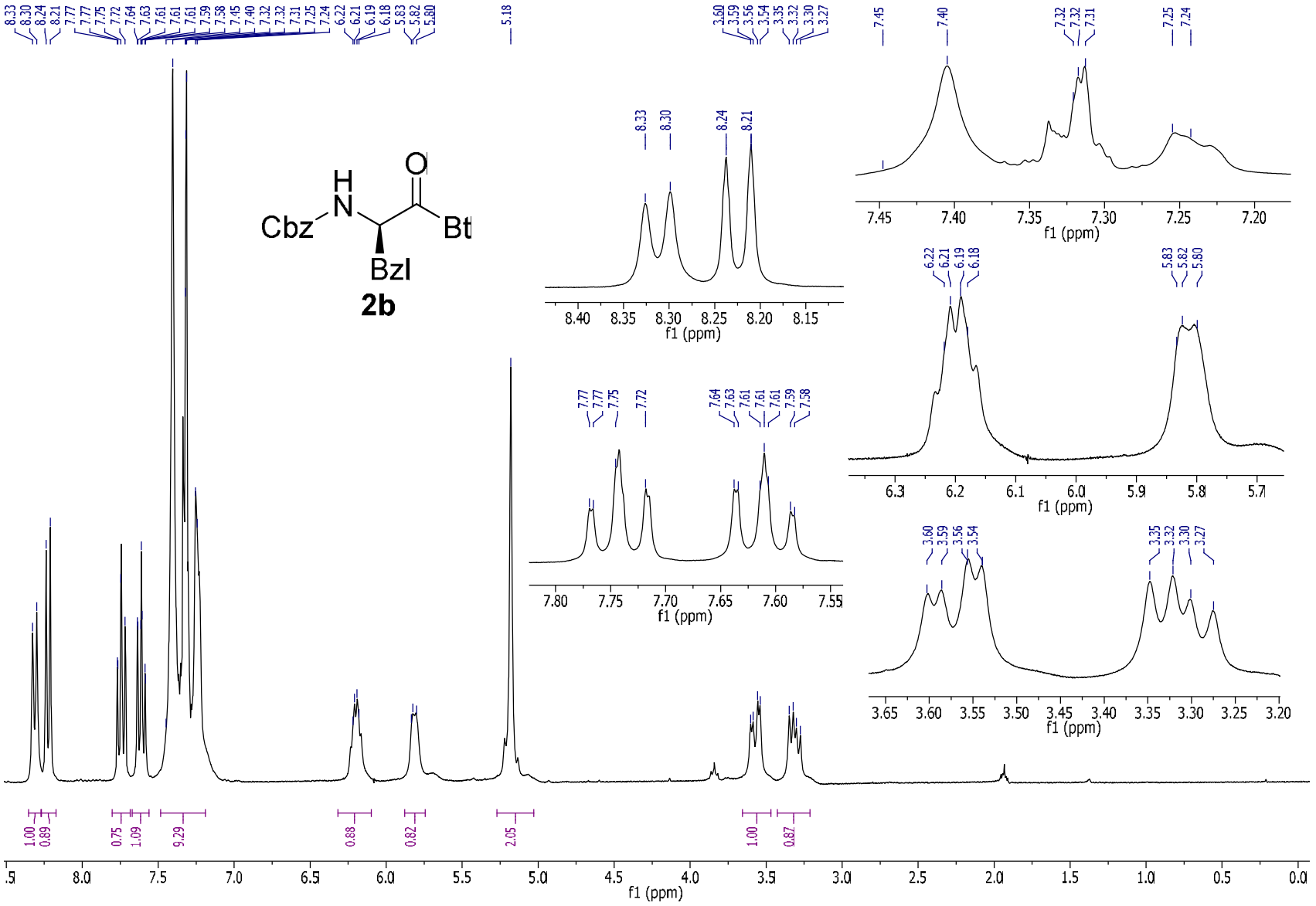
10b

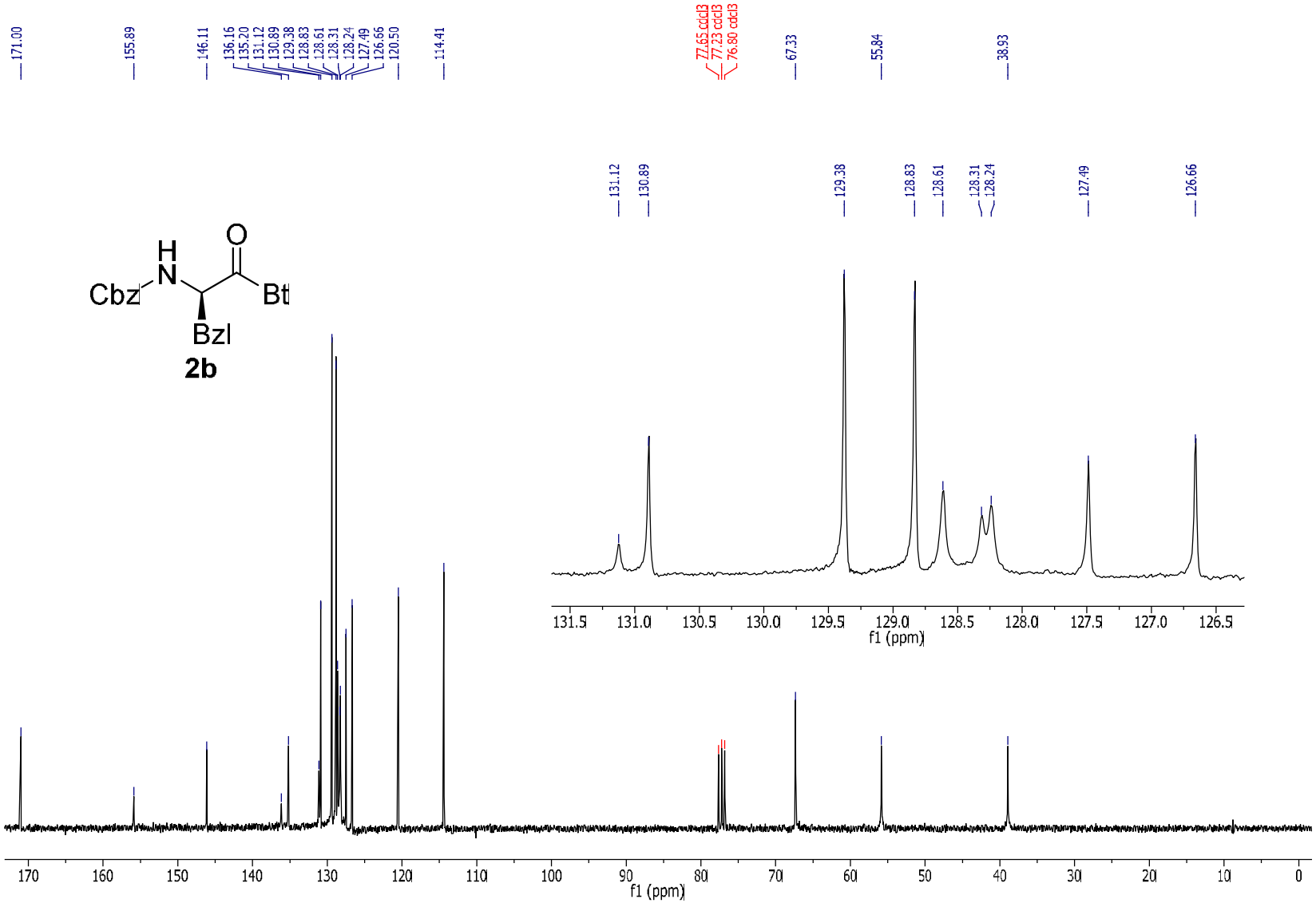
***Cyclo*-[Bis-Cbz-Homo-D,L-Cys-L-Hyp(O-*t*Bu)] (10b).** Sticky oil, 240 mg, 0.29 mmol, 88% yield. ^{1}H NMR (CD_3OD, 500 MHz): δ 7.49 – 7.25 (m, 10H), 5.35 – 5.24 (m, 4H), 4.98 – 4.87 (m, 2H), 4.72 – 4.50 (m, 2H), 4.48 – 4.33 (m, 2H), 3.80 – 3.69 (m, 2H), 3.60 – 3.38 (m, 2H), 2.83 – 2.65 (m, 4H), 2.53 – 2.43 (m, 2H), 2.34 – 2.18 (m, 4H), 2.17 – 1.95 (m, 2H), 1.25 – 1.16 (m, 18H). ^{13}C NMR (CD_3OD, 75 MHz): δ 172.1, 169.6, 169.0, 166.7, 153.5, 136.7, 136.6, 130.0, 129.8, 129.7, 129.6, 129.4, 129.2, 129.0, 121.2, 76.0, 75.6, 71.2, 70.4, 69.4, 68.9, 68.7, 67.7, 61.4, 60.2, 59.6, 59.0, 55.5, 53.9, 53.4, 44.8, 39.0, 37.8, 35.4, 35.3, 32.3, 30.9, 28.7, 28.6. HRMS (ESI): calcd for $C_{42}H_{54}N_4O_{10}S_2Na$ $[M + Na]^+$ 861.3173, found 861.3175

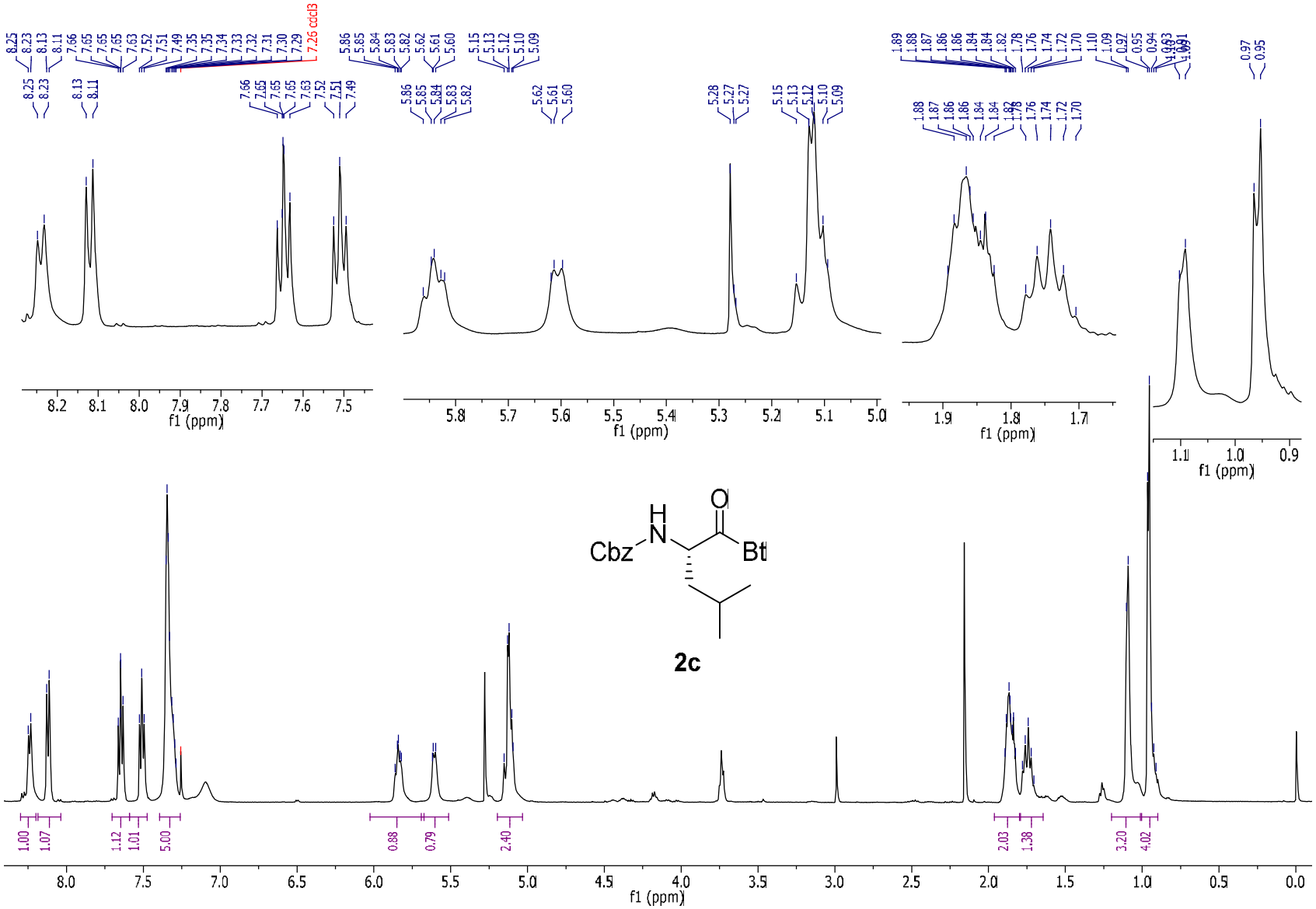

f1 (ppm)

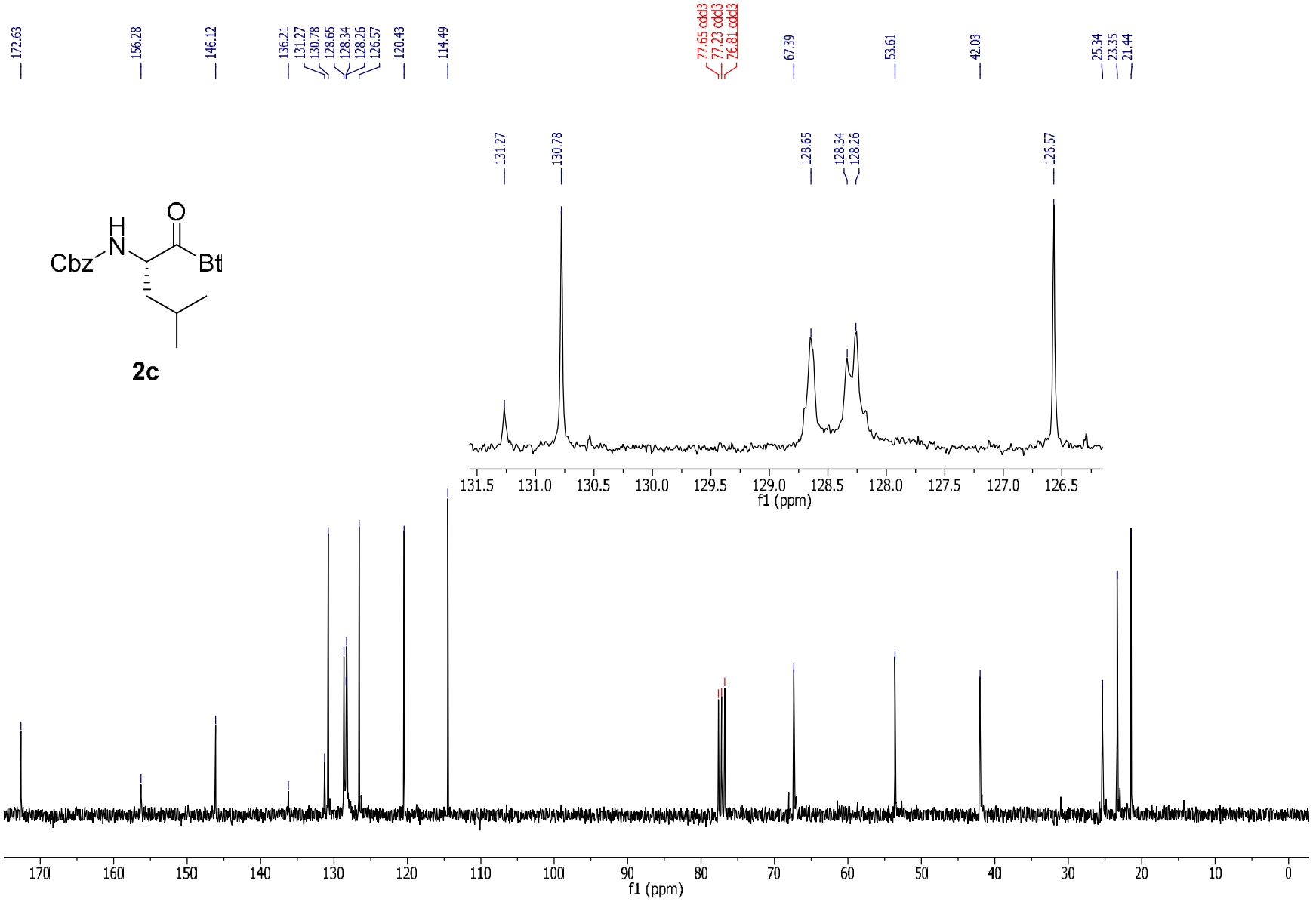

H
N
O
Cbz
Bt
2a
f1 (ppm)

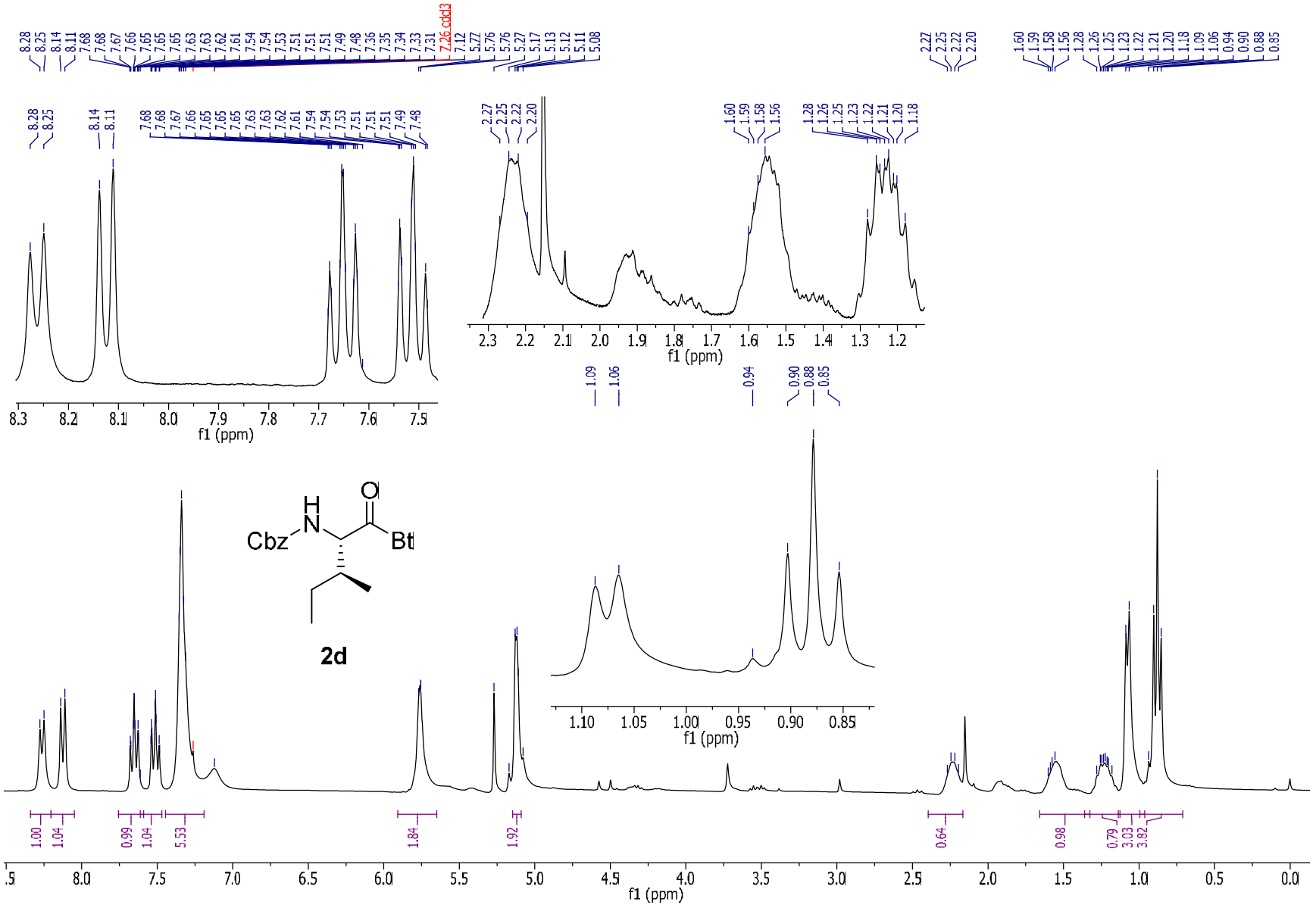

172.45
155.83
146.18
131.33
130.91
128.71
128.41
128.34
126.69
120.53
114.54
77.65 cdcl3
77.23 cdcl3
76.81 cdcl3
67.41
50.77
19.27
Cbz
H
N
O
Bt
2a
131.33
130.91
128.71
128.41
128.34
126.69
131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5
f1 (ppm)
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

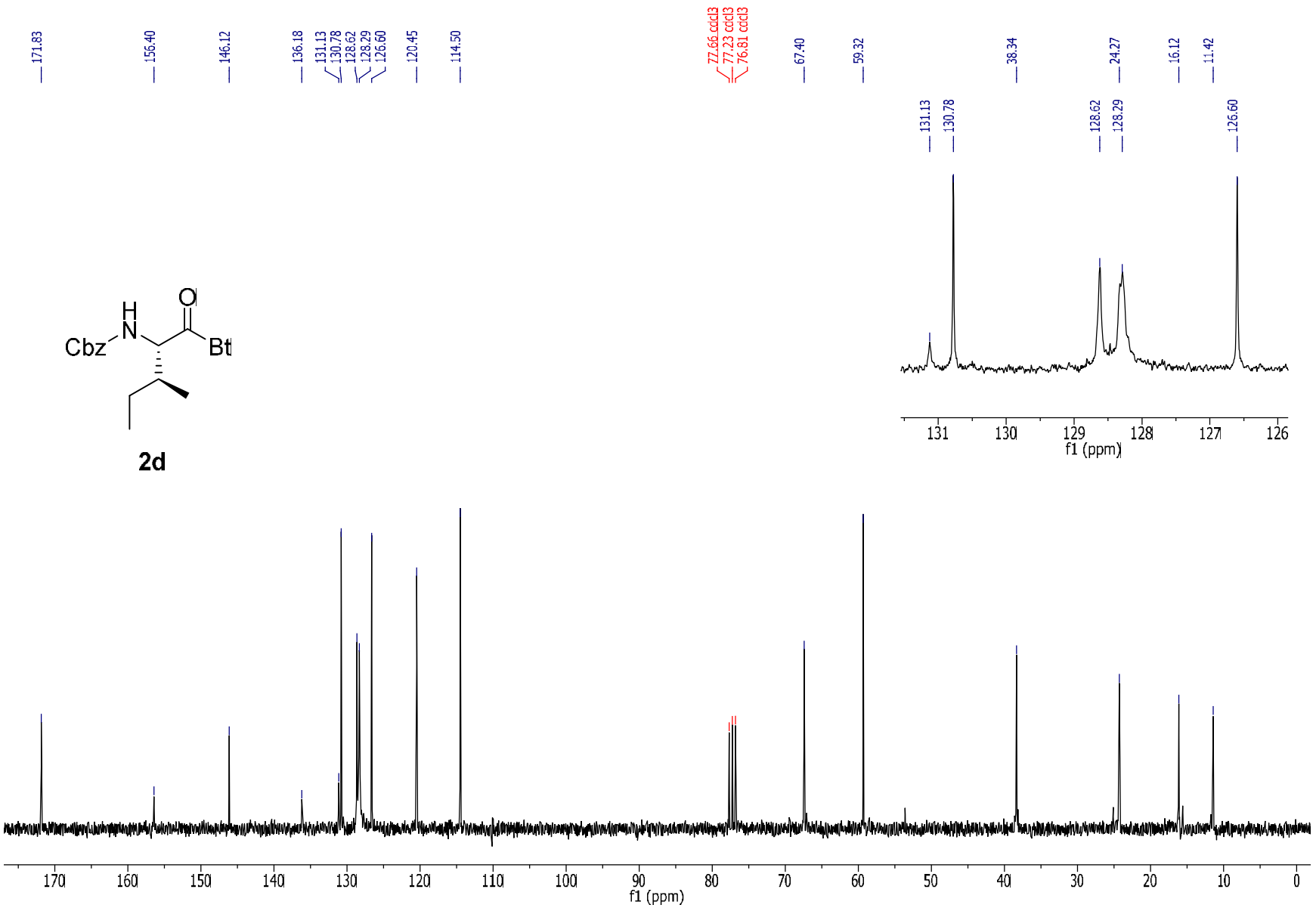

8.33
8.30
8.24
8.21
7.77
7.77
7.75
7.72
7.64
7.63
7.61
7.61
7.61
7.59
7.58
7.45
7.40
7.32
7.32
7.31
7.25
7.24
6.22
6.21
6.19
6.18
5.83
5.82
5.80
5.18
3.60
3.59
3.56
3.54
3.35
3.32
3.30
3.27
H
N
O
Cbz
Bt
Bzl
2b
f1 (ppm)
1.00
0.89
0.75
1.09
9.29
0.88
0.82
2.05
1.00
0.87

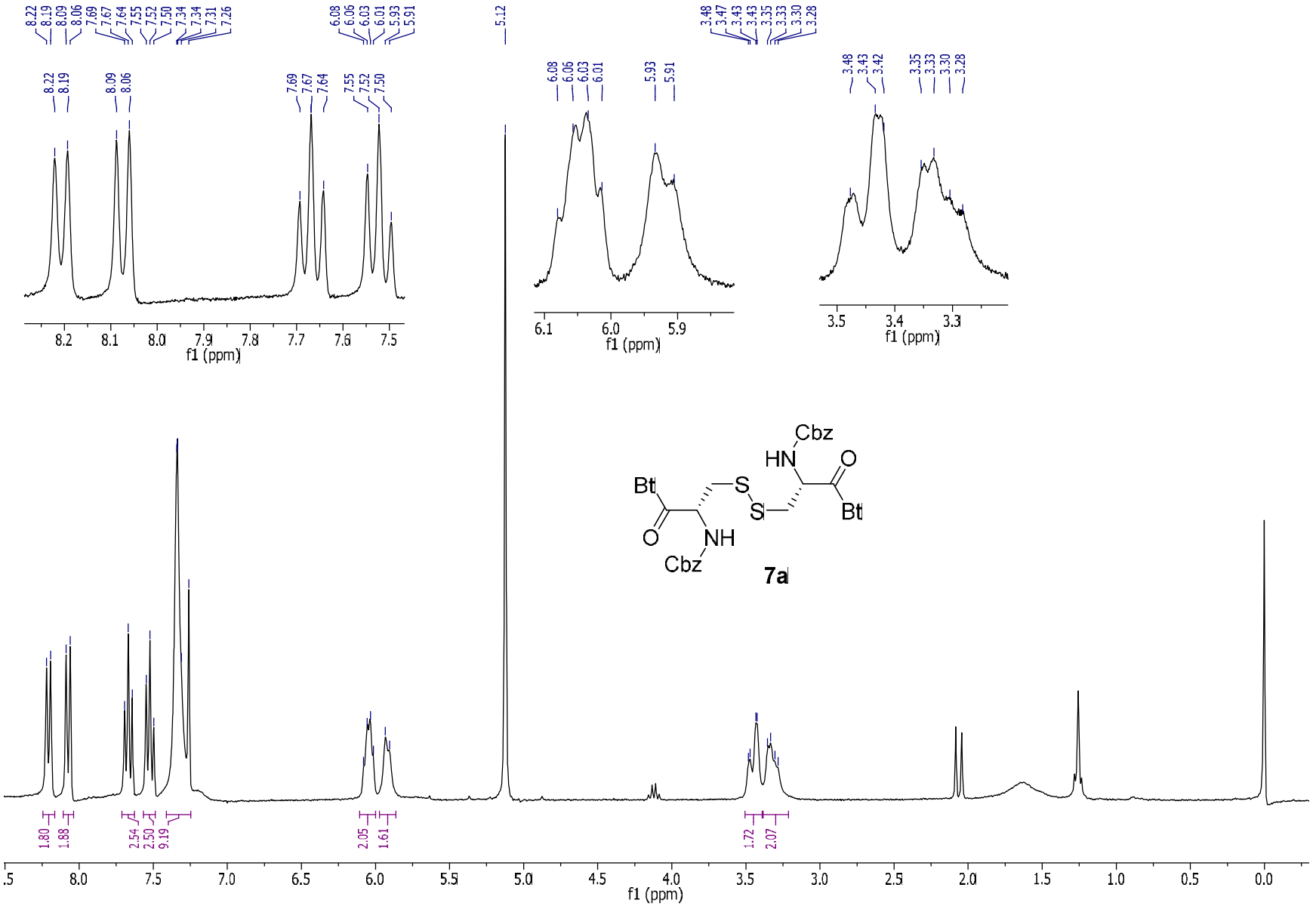

171.00
155.89
146.11
136.16
135.20
131.12
130.89
129.38
128.83
128.61
128.31
128.24
127.49
126.66
120.50
114.41
77.65 cdcl3
77.23 cdcl3
76.80 cdcl3
67.33
55.84
38.93
H
N
O
Cbz
Bt
Bzl
2b
f1 (ppm)

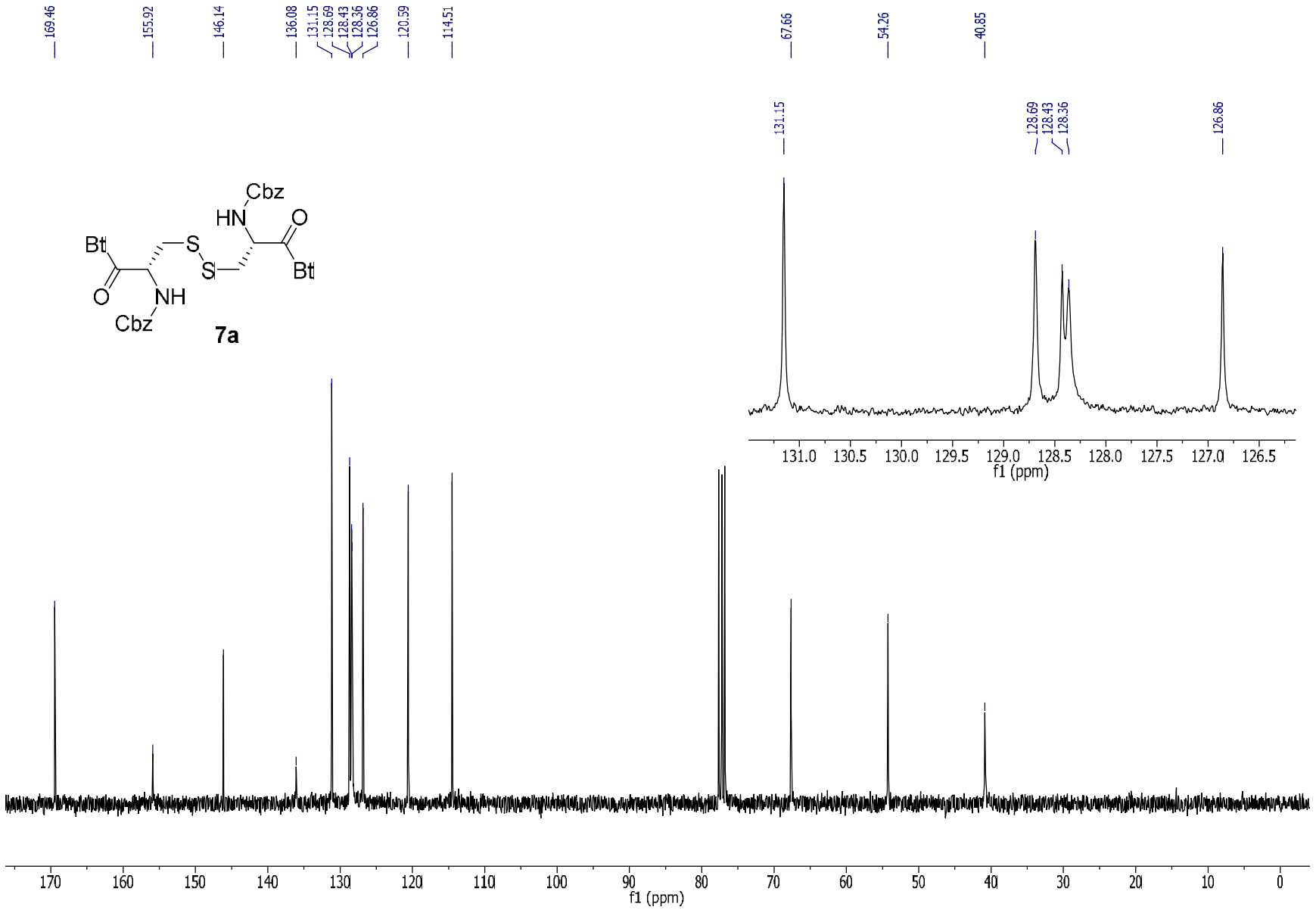

Cbz
H
N
O
Bt
2c
f1 (ppm)

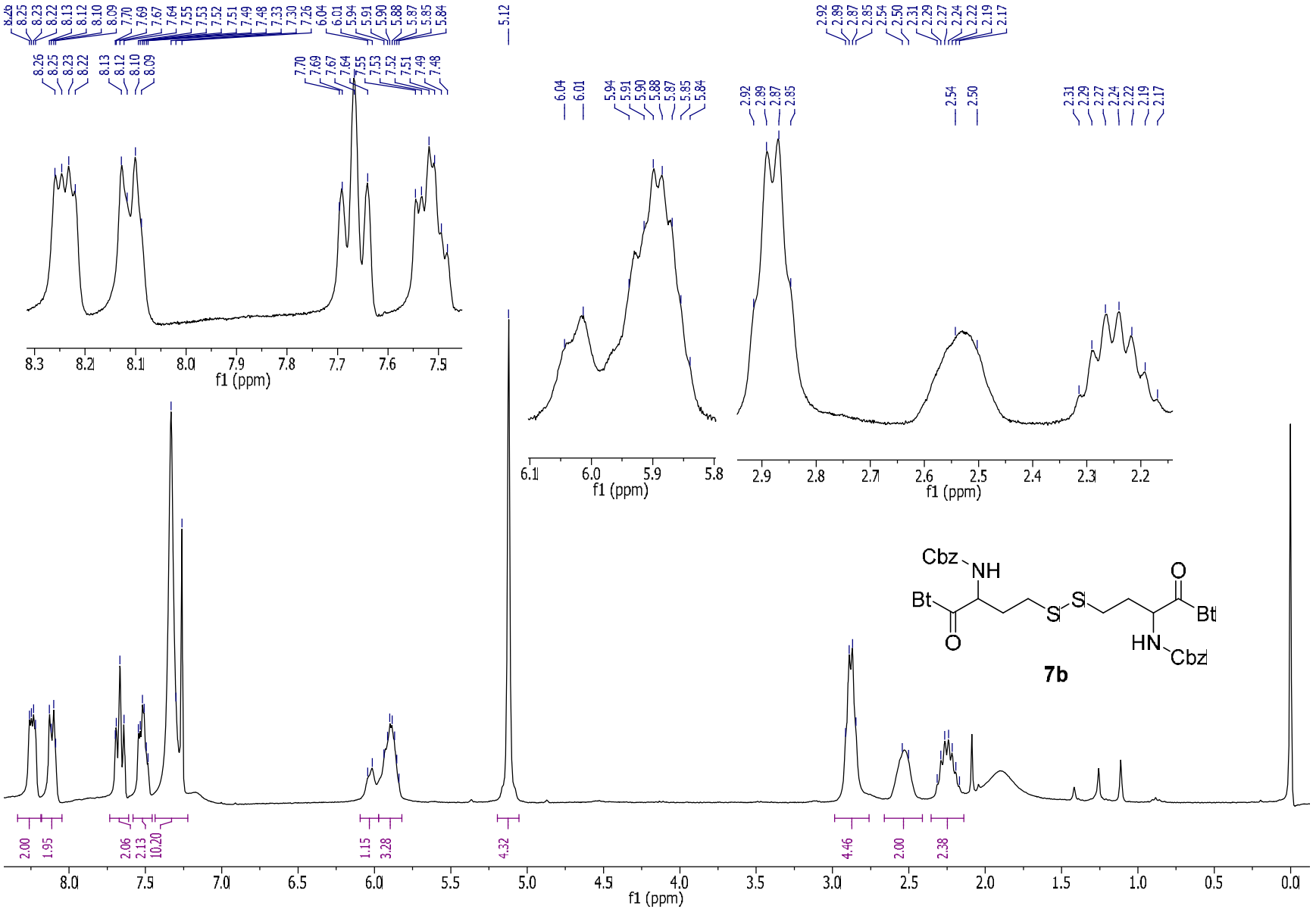

172.63
156.28
146.12
136.21
131.27
130.78
128.65
128.34
128.26
126.57
120.43
114.49
77.65 cdcl3
77.23 cdcl3
76.81 cdcl3
67.39
53.61
42.03
25.34
23.35
21.44
Cbz
H
N
O
Bt
2c
f1 (ppm)

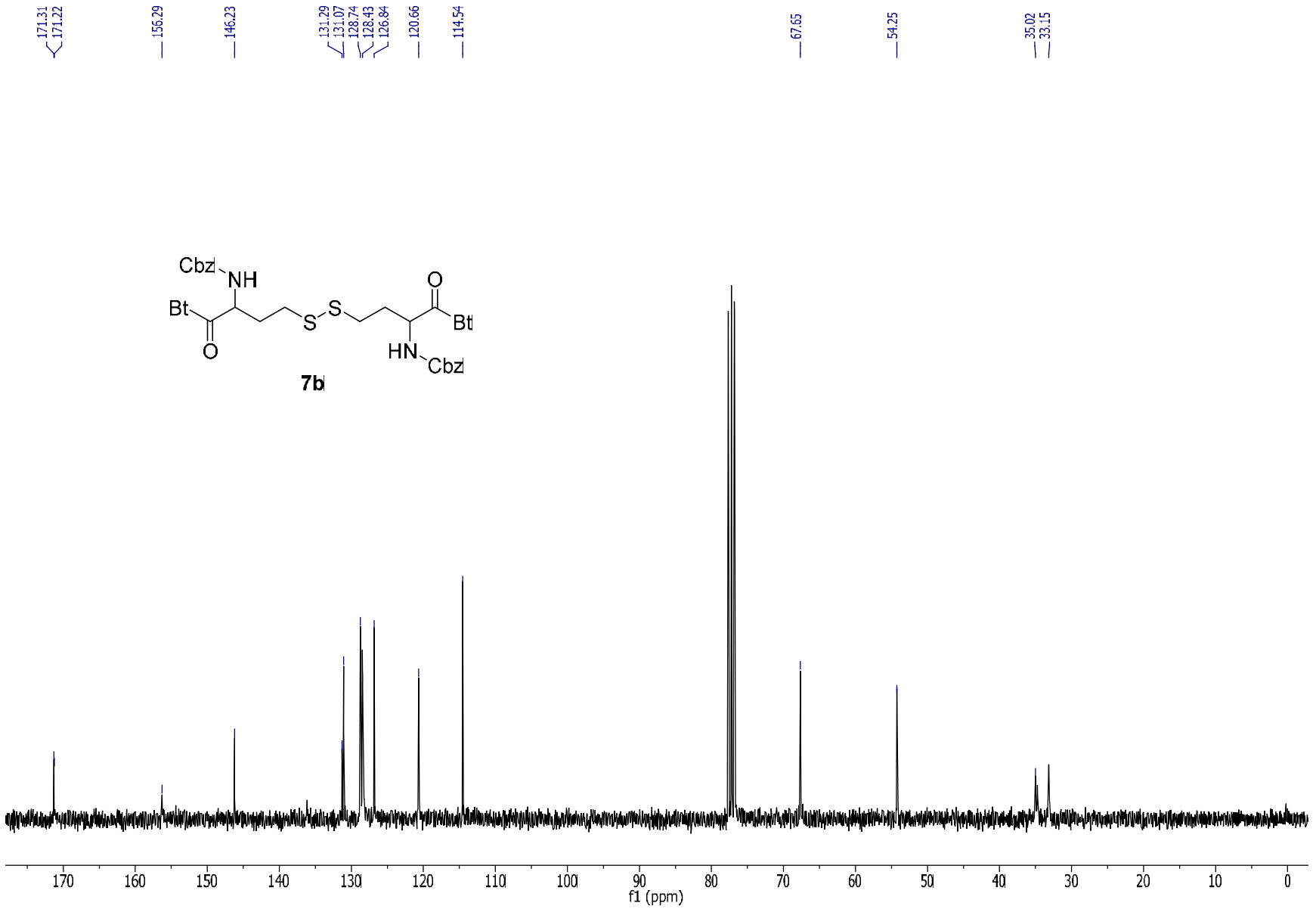

8.28 8.25 8.14 8.11 7.68 7.68 7.67 7.66 7.65 7.65 7.65 7.63 7.63 7.62 7.61 7.54 7.54 7.53 7.51 7.51 7.51 7.49 7.48 7.36 7.35 7.34 7.33 7.31 7.26 cdcl3 7.12 5.77 5.76 5.76 5.27 5.17 5.13 5.12 5.11 5.08
2.27 2.25 2.22 2.20 1.60 1.59 1.58 1.56 1.28 1.26 1.25 1.23 1.22 1.21 1.20 1.18 1.09 1.06 0.94 0.90 0.88 0.85
f1 (ppm)
Cbz
N
H
O
Bt
2d
1.00 1.04 0.99 1.04 5.53 1.84 1.92 0.64 0.98 0.79 3.03 3.82

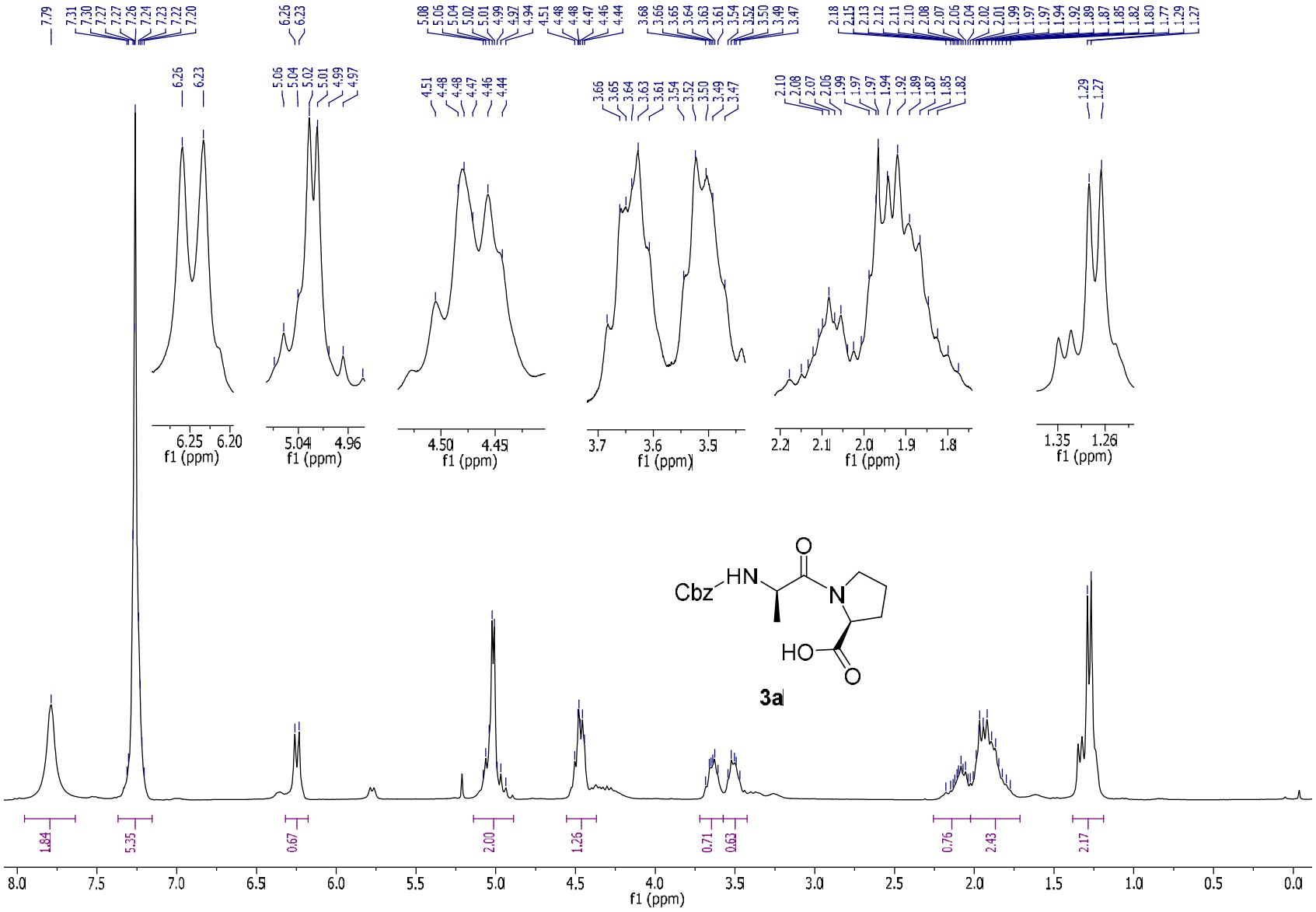

171.83
156.40
146.12
136.18
131.13
130.78
128.62
128.29
126.60
120.45
114.50
77.66 cdcl3
77.23 cdcl3
76.81 cdcl3
67.40
59.32
38.34
24.27
16.12
11.42
131.13
130.78
128.62
128.29
126.60
131
130
129
128
127
126
f1 (ppm)
H
N
O
Cbz
Bt
2d
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

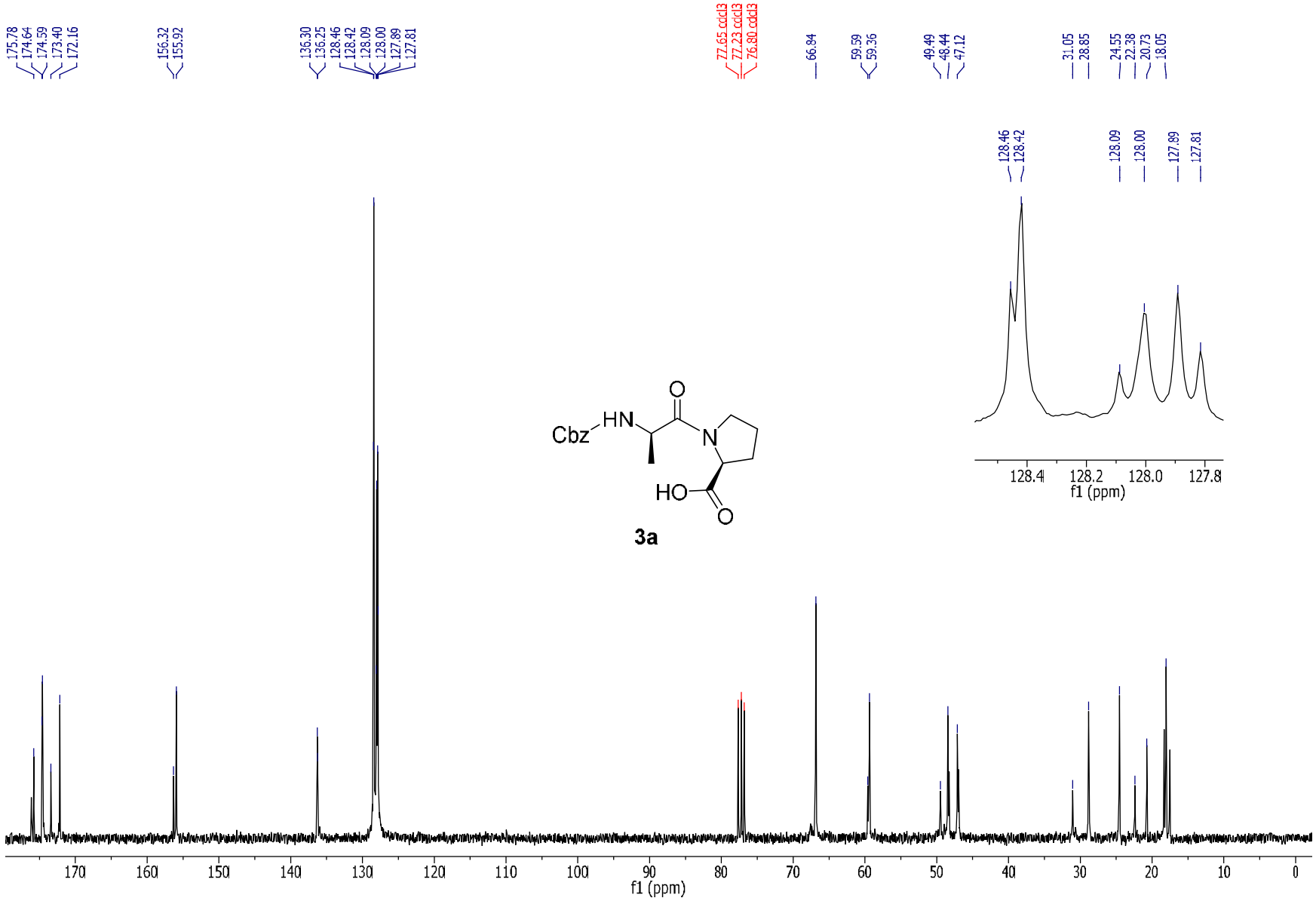

8.22
8.19
8.09
8.06
7.69
7.67
7.64
7.55
7.52
7.50
7.34
7.31
7.26
6.08
6.06
6.03
6.01
5.93
5.91
5.12
3.48
3.47
3.43
3.42
3.35
3.33
3.30
3.28
f1 (ppm)
Cbz
HN
O
Bt
S
S
Bt
O
NH
Cbz
7a
1.80
1.88
2.54
2.50
9.19
2.05
1.61
1.72
2.07

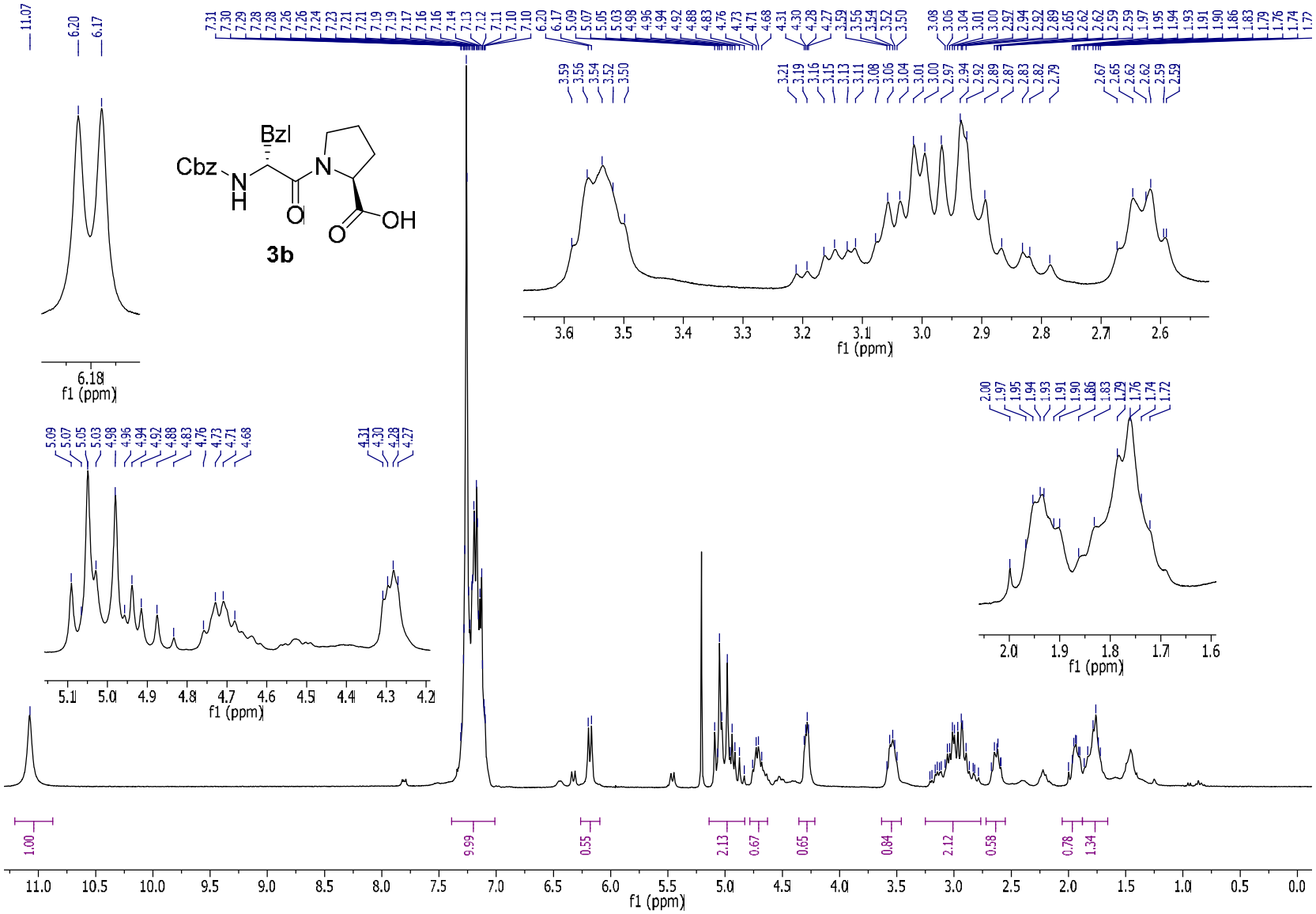

169.46
155.92
146.14
136.08
131.15
128.69
128.43
128.36
126.86
120.59
114.51
67.66
54.26
40.85
Cbz
HN
O
Bt
S
S
Bt
O
NH
Cbz
7a
f1 (ppm)
f1 (ppm)

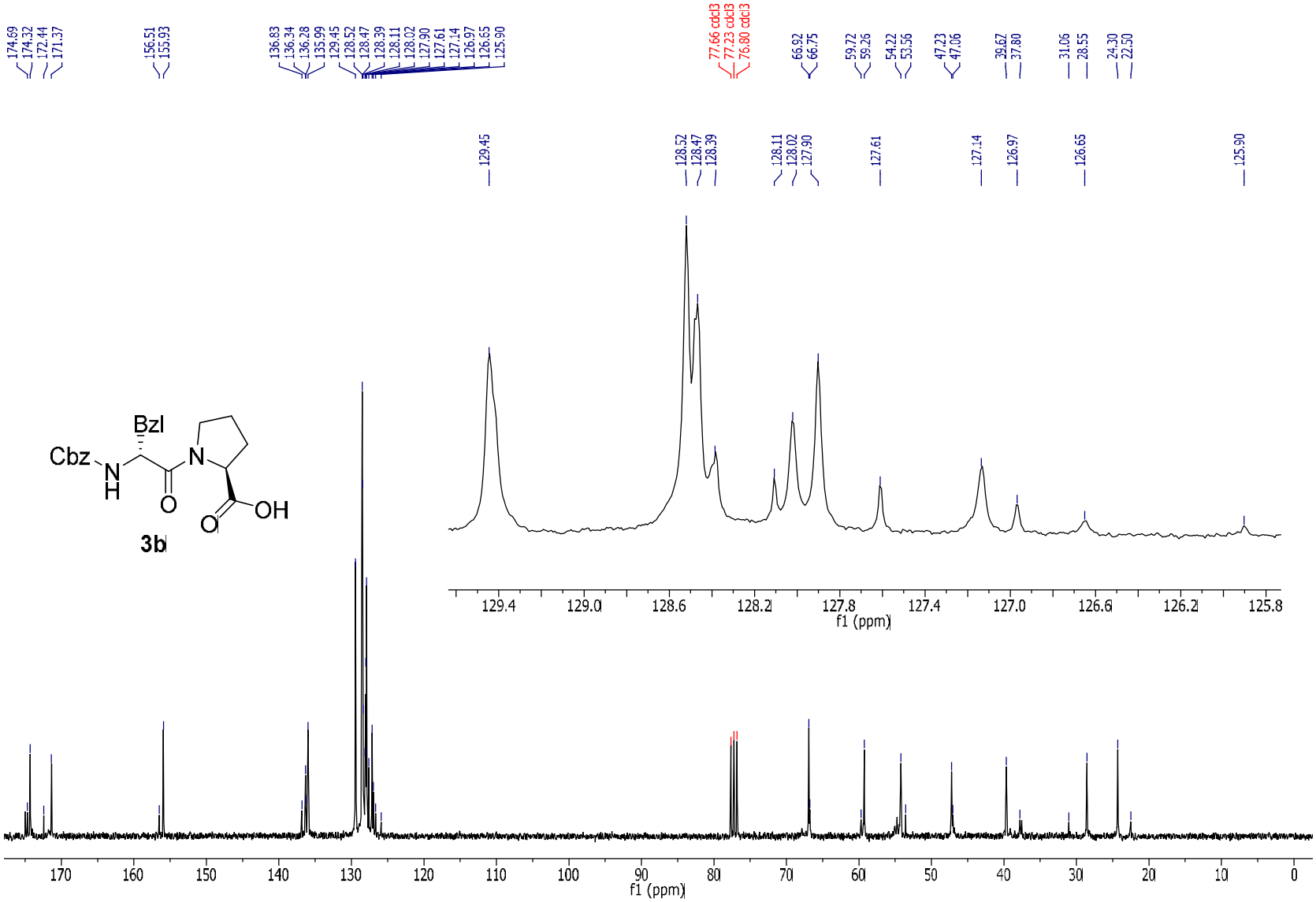

8.26
8.25
8.23
8.22
8.13
8.12
8.10
8.09
7.70
7.69
7.67
7.64
7.55
7.53
7.52
7.51
7.49
7.48
7.33
7.30
7.26
6.04
6.01
5.94
5.91
5.90
5.88
5.87
5.85
5.84
5.12
2.92
2.89
2.87
2.85
2.54
2.50
2.31
2.29
2.27
2.24
2.22
2.19
2.17
f1 (ppm)
Cbz
NH
Bt
O
S
S
O
Bt
HN
Cbz
7b
2.00
1.95
2.06
2.13
10.20
1.15
3.28
4.32
4.46
2.00
2.38

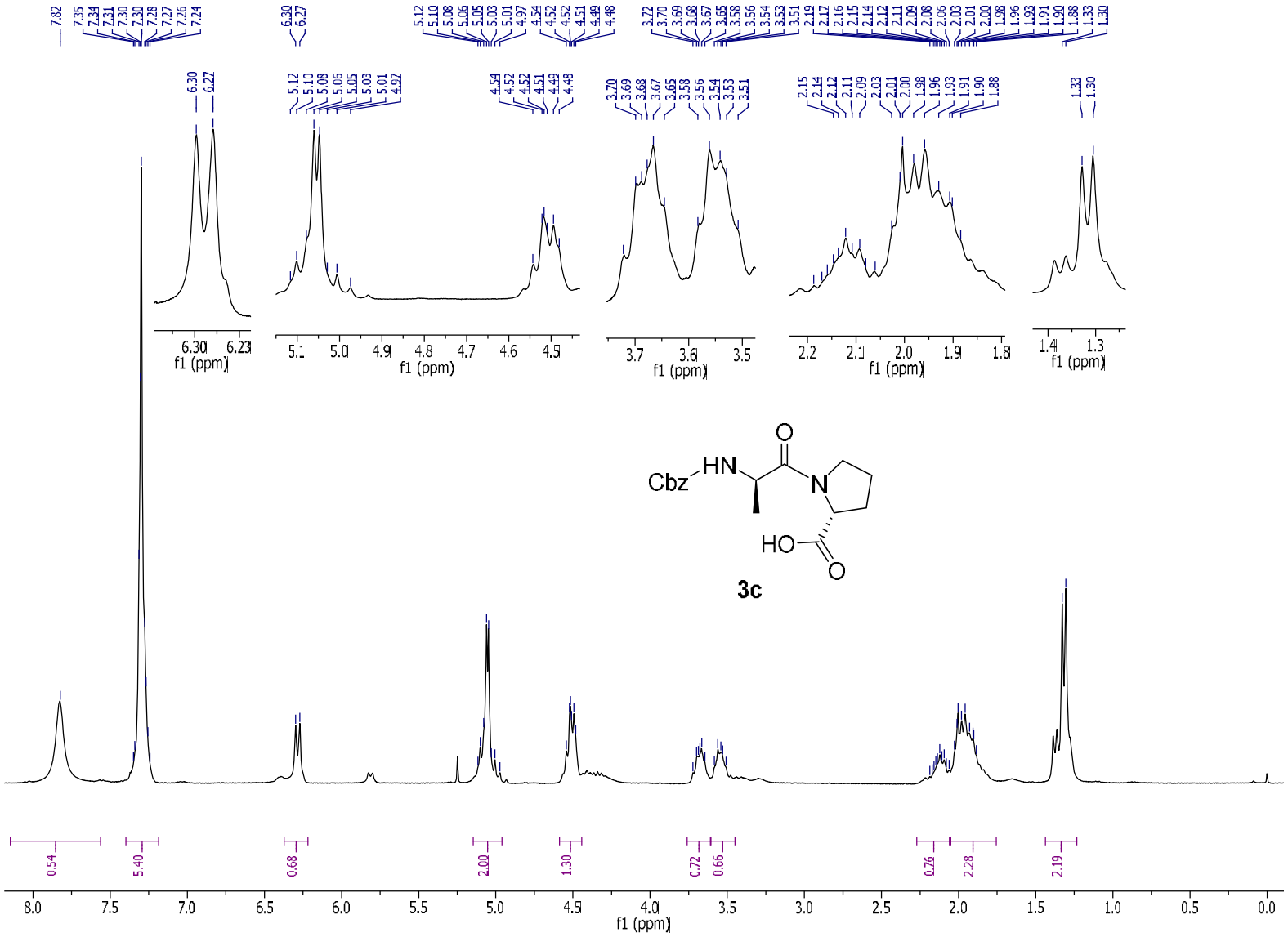

171.31
171.22
156.29
146.23
131.29
131.07
128.74
128.43
126.84
120.66
114.54
67.65
54.25
35.02
33.15
Cbz
NH
Bt
O
S
S
O
Bt
HN
Cbz
7b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

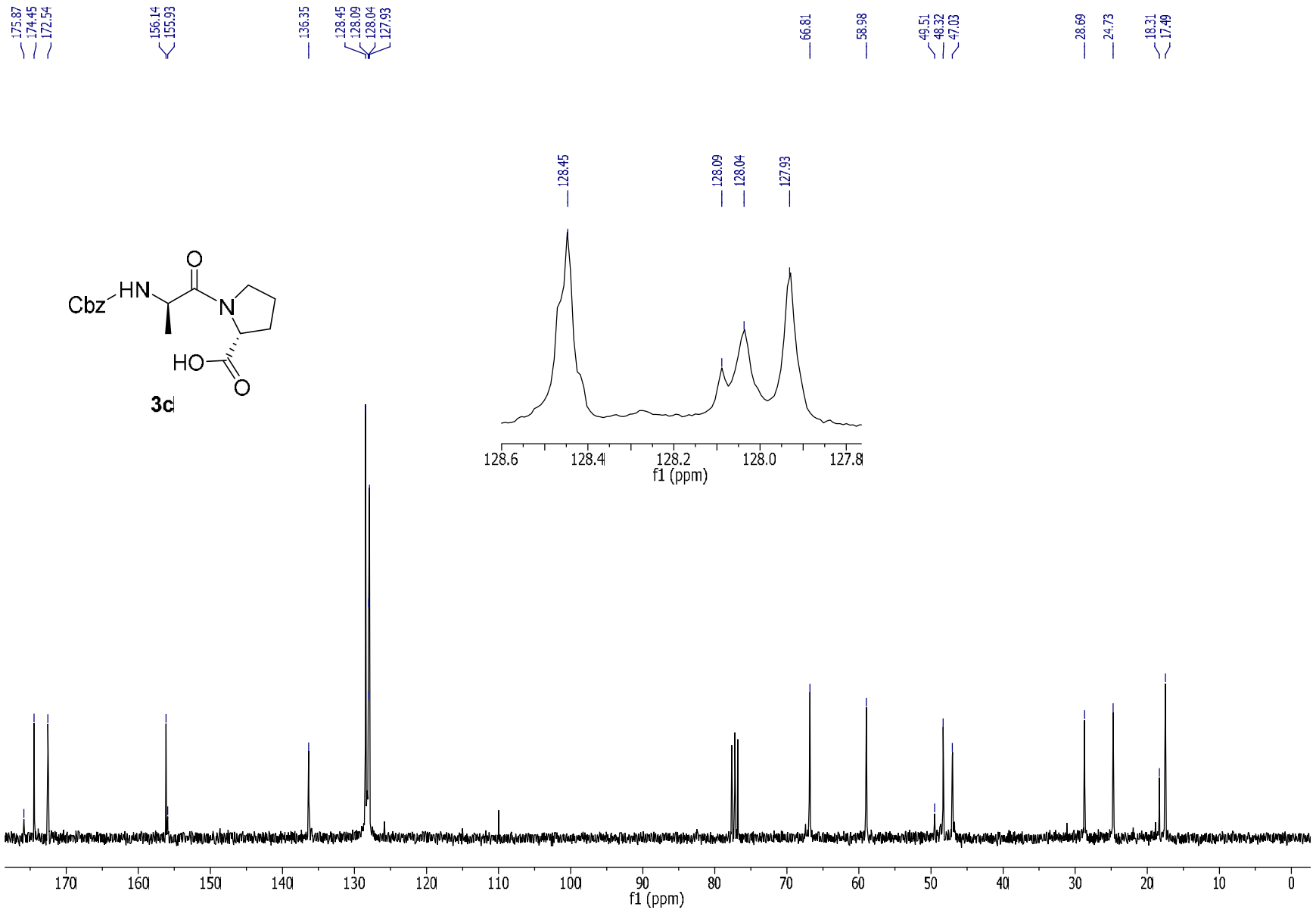

Cbz
HN
O
N
HO
O
O
3a
f1 (ppm)

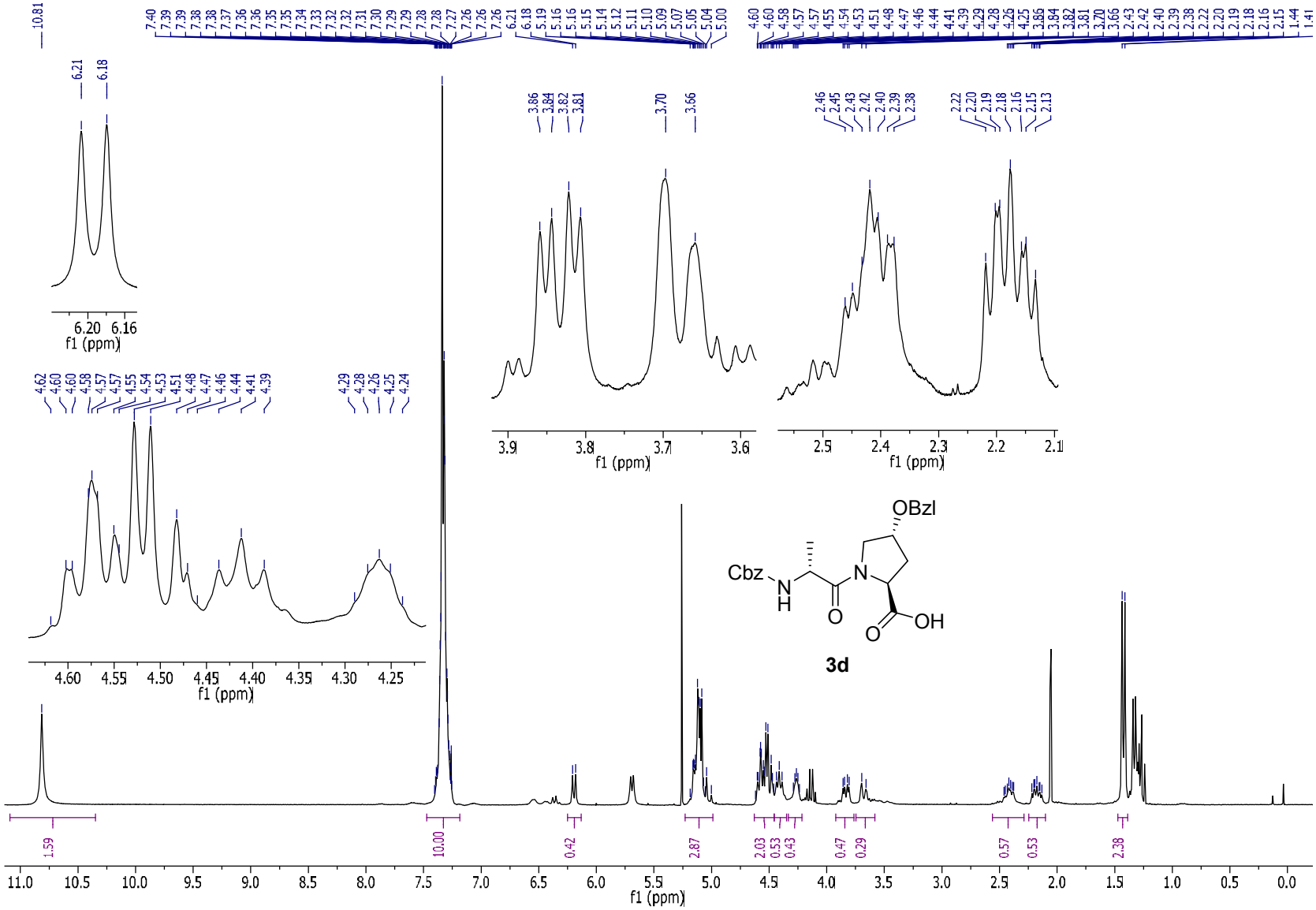

175.78
174.64
174.59
173.40
172.16
156.32
155.92
136.30
136.25
128.46
128.42
128.09
128.00
127.89
127.81
77.65 cdcl3
77.23 cdcl3
76.80 cdcl3
66.84
59.59
59.36
49.49
48.44
47.12
31.05
28.85
24.55
22.38
20.73
18.05
Cbz
HN
O
N
HO
O
3a
f1 (ppm)

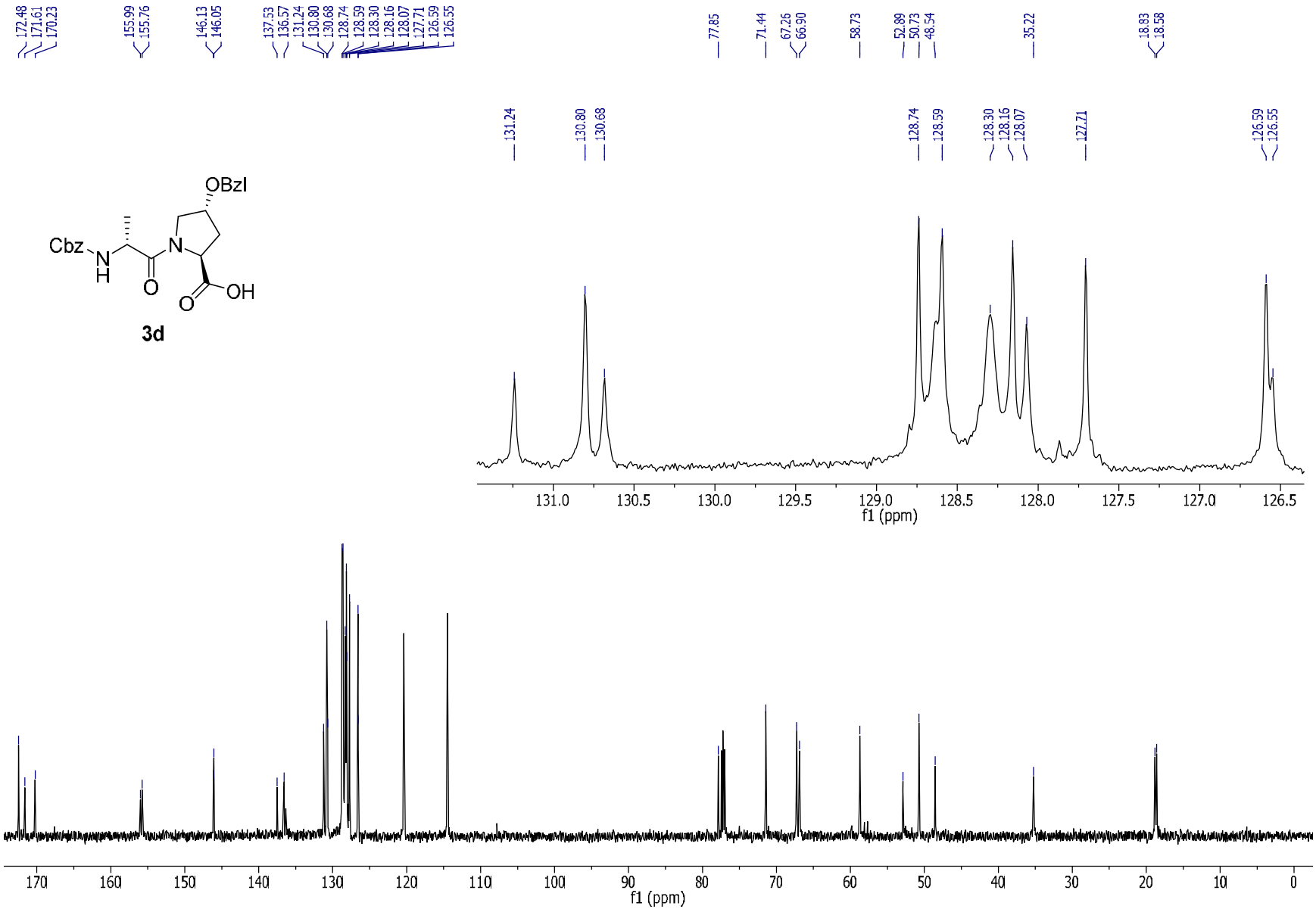

Bzl
Cbz
N
H
N
O
O
OH
3b
f1 (ppm)

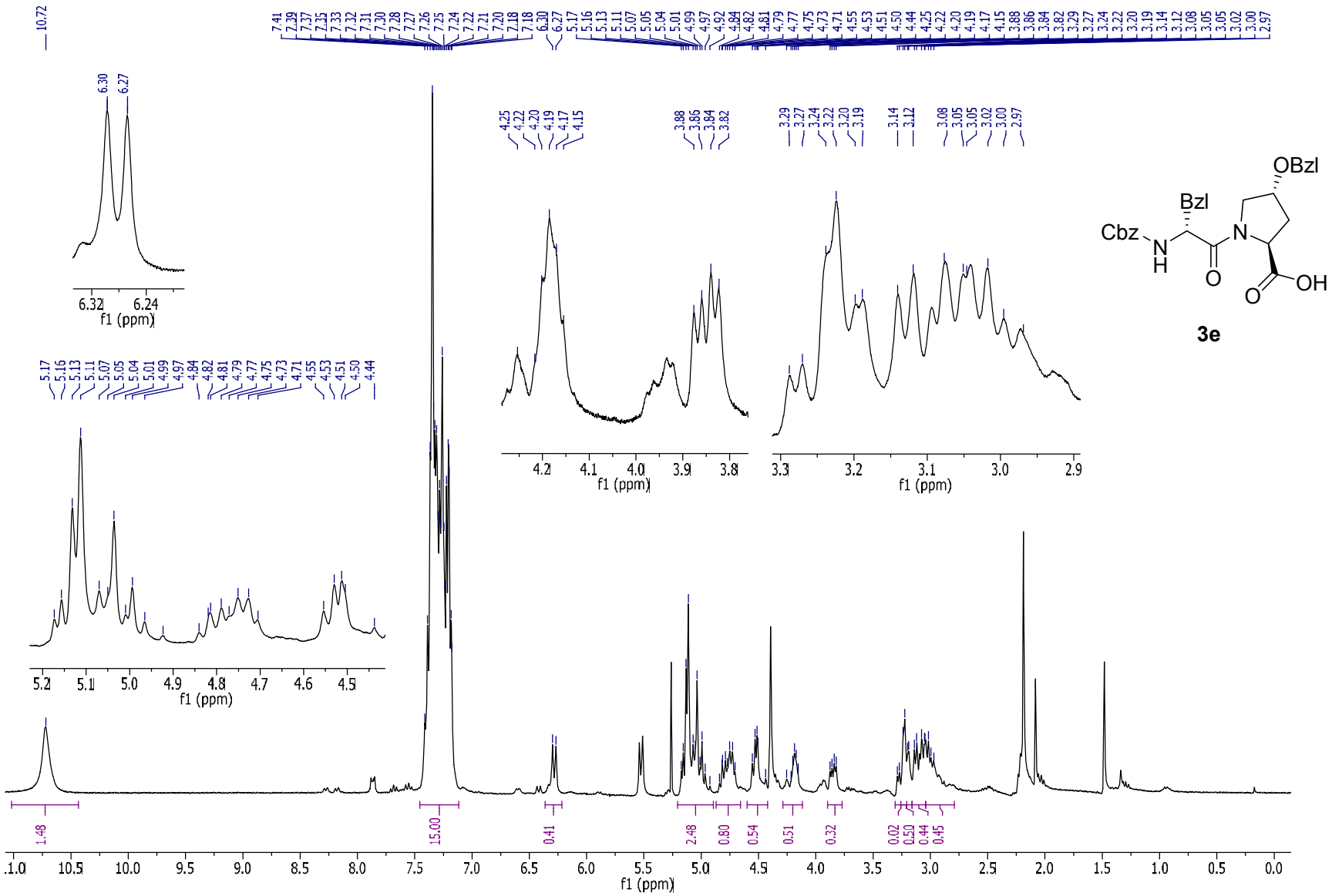

174.69
174.32
172.44
171.37
156.51
155.93
136.83
136.34
136.28
135.99
129.45
128.52
128.47
128.39
128.11
128.02
127.90
127.61
127.14
126.97
126.65
125.90
77.66 cdcl3
77.23 cdcl3
76.80 cdcl3
66.92
66.75
59.72
59.26
54.22
53.56
47.23
47.06
39.67
37.80
31.06
28.55
24.30
22.50
Bzl
Cbz
N
H
O
N
O
OH
3b
f1 (ppm)
f1 (ppm)

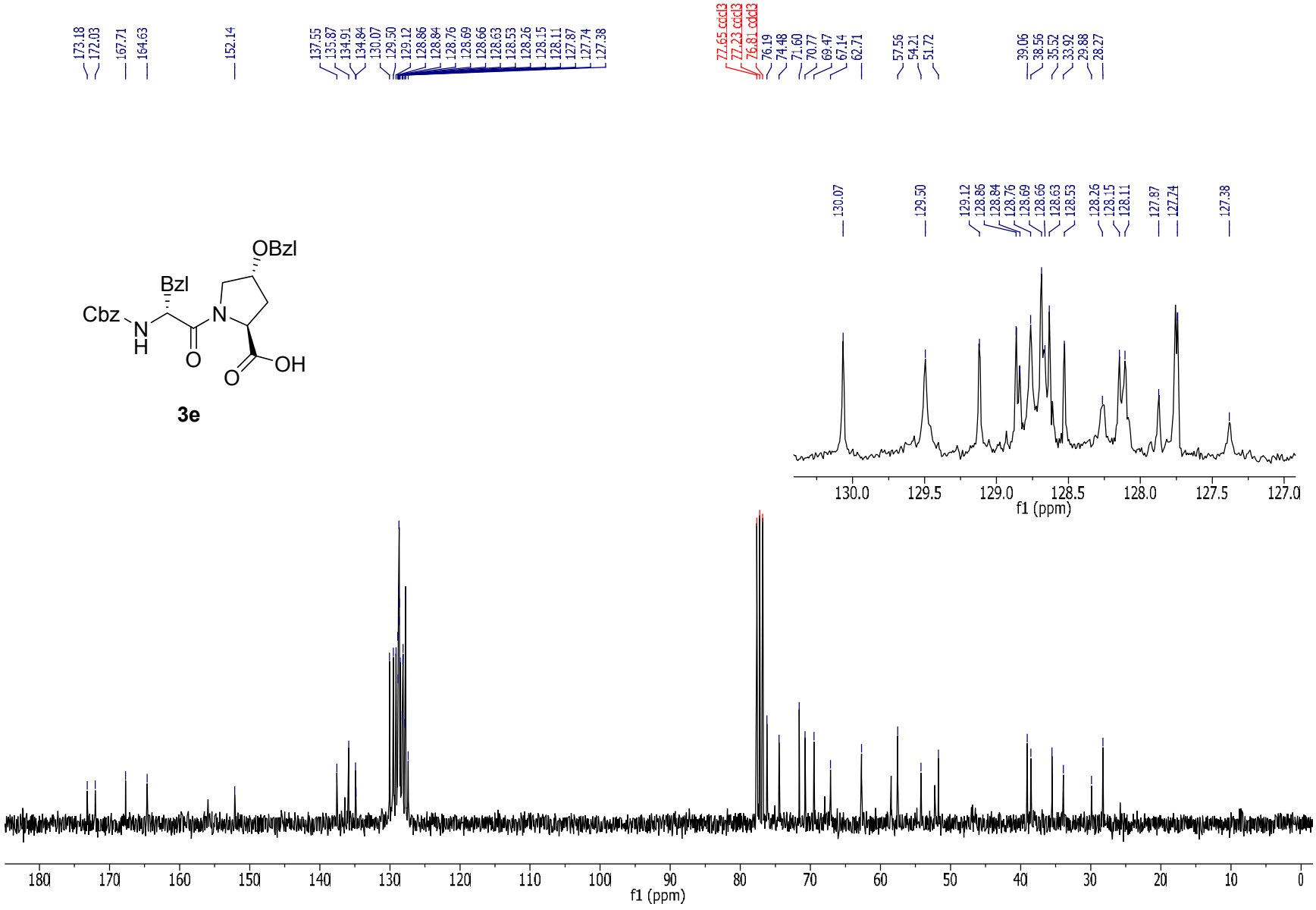

Cbz
HN
O
N
HO
O
3c
f1 (ppm)

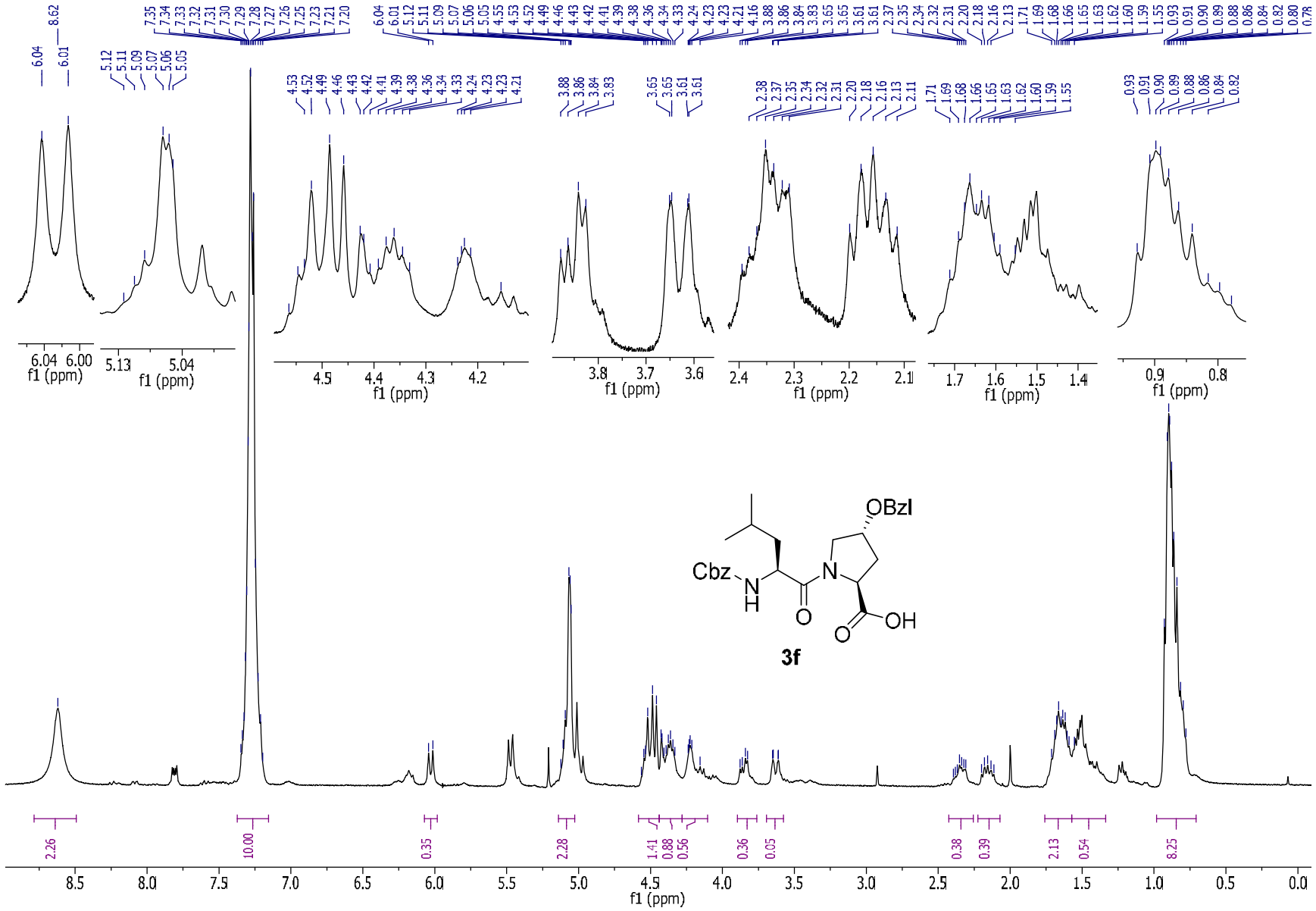

175.87
174.45
172.54
156.14
155.93
136.35
128.45
128.09
128.04
127.93
66.81
58.98
49.51
48.32
47.03
28.69
24.73
18.31
17.49
Cbz
HN
N
HO
O
O
3c
128.45
128.09
128.04
127.93
128.6
128.4
128.2
128.0
127.8
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

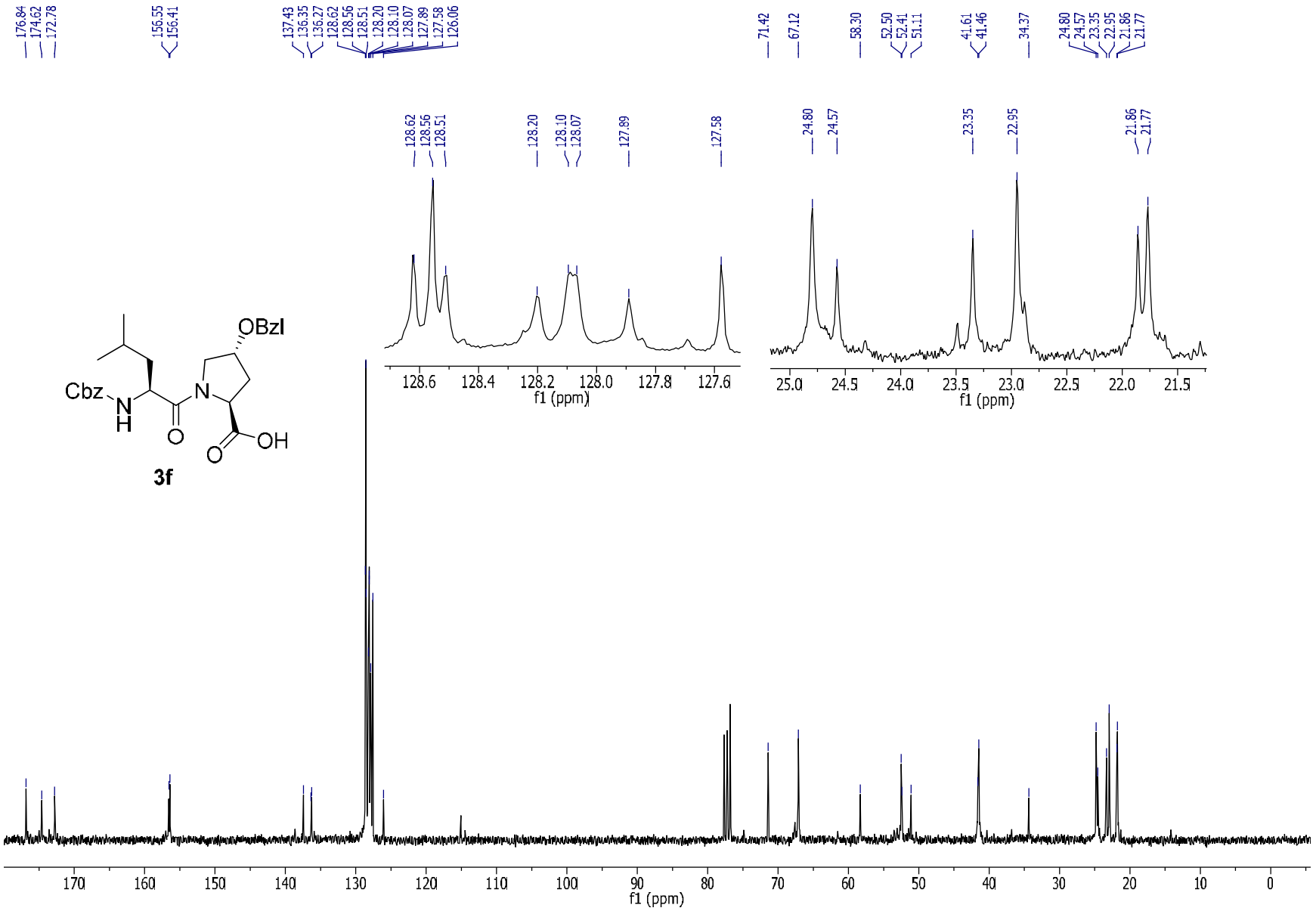

OBzl
Cbz
N
H
O
N
O
OH
3d
f1 (ppm)

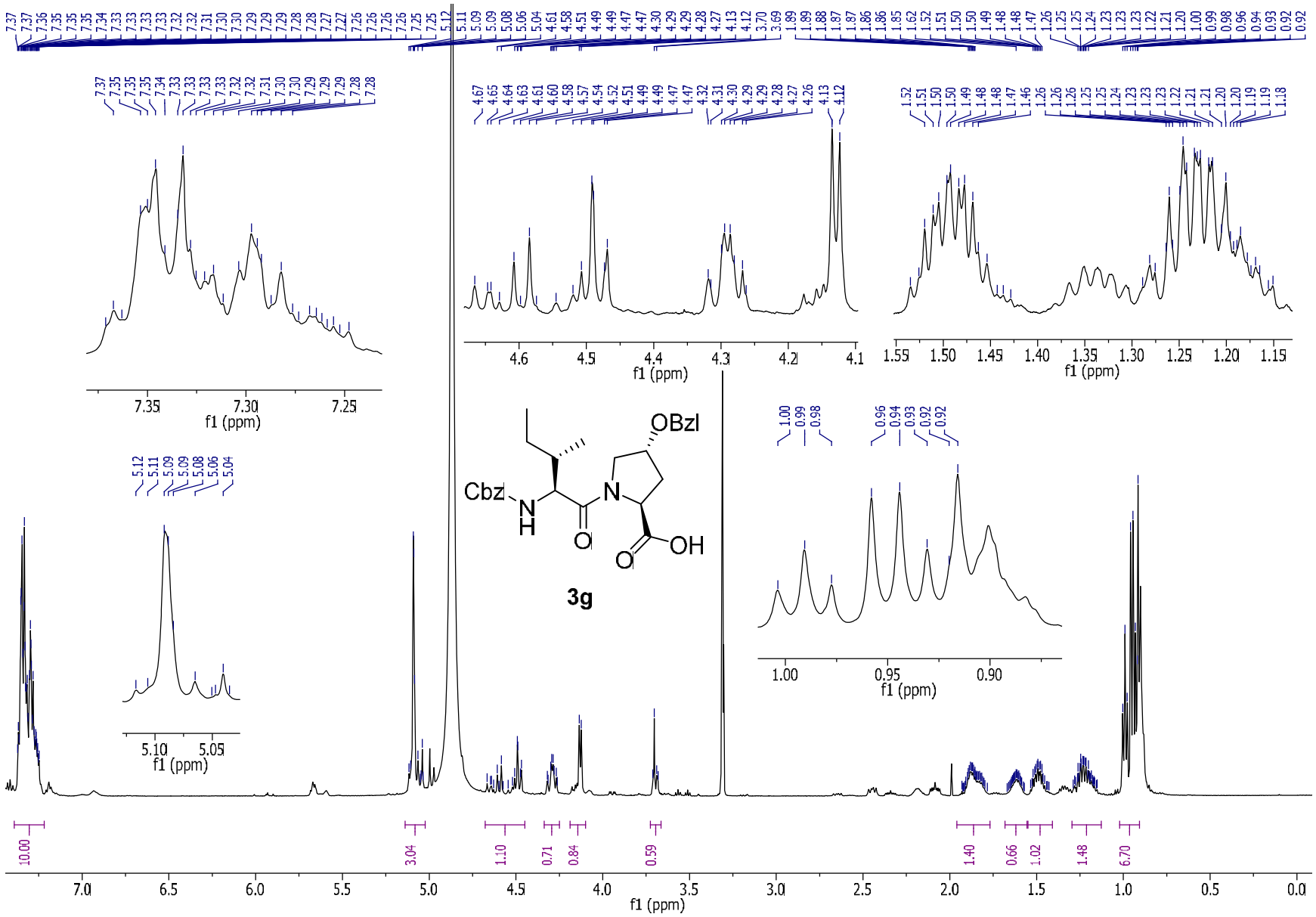

172.48
171.61
170.23
155.99
155.76
146.13
146.05
137.53
136.57
131.24
130.80
130.68
128.74
128.59
128.30
128.16
128.07
127.71
126.59
126.55
77.85
71.44
67.26
66.90
58.73
52.89
50.73
48.54
35.22
18.83
18.58
OBzl
Cbz
N
H
O
N
O
OH
3d
f1 (ppm)
f1 (ppm)

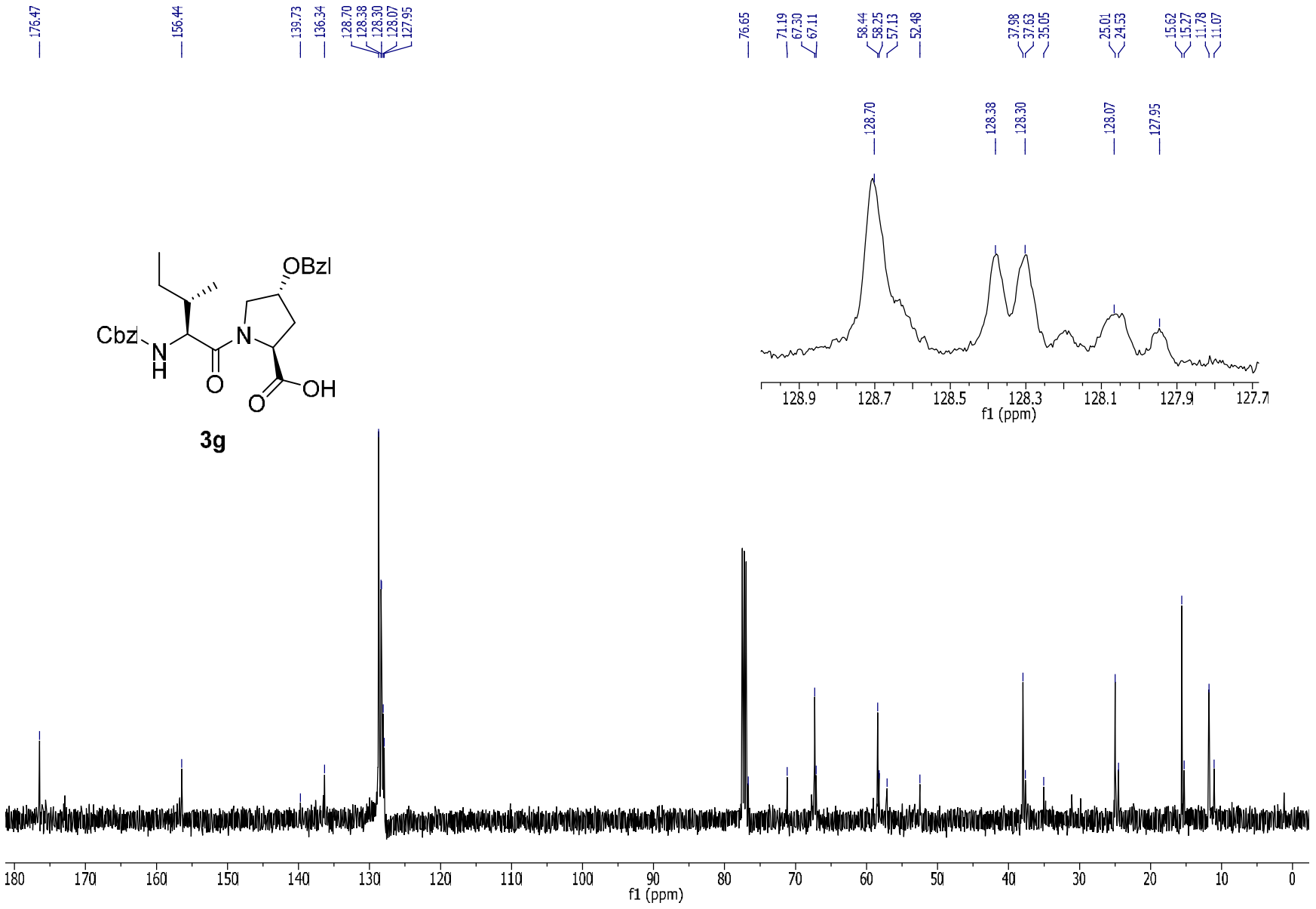

OBzl
Bzl
Cbz
N
H
N
O
O
OH
3e
f1 (ppm)

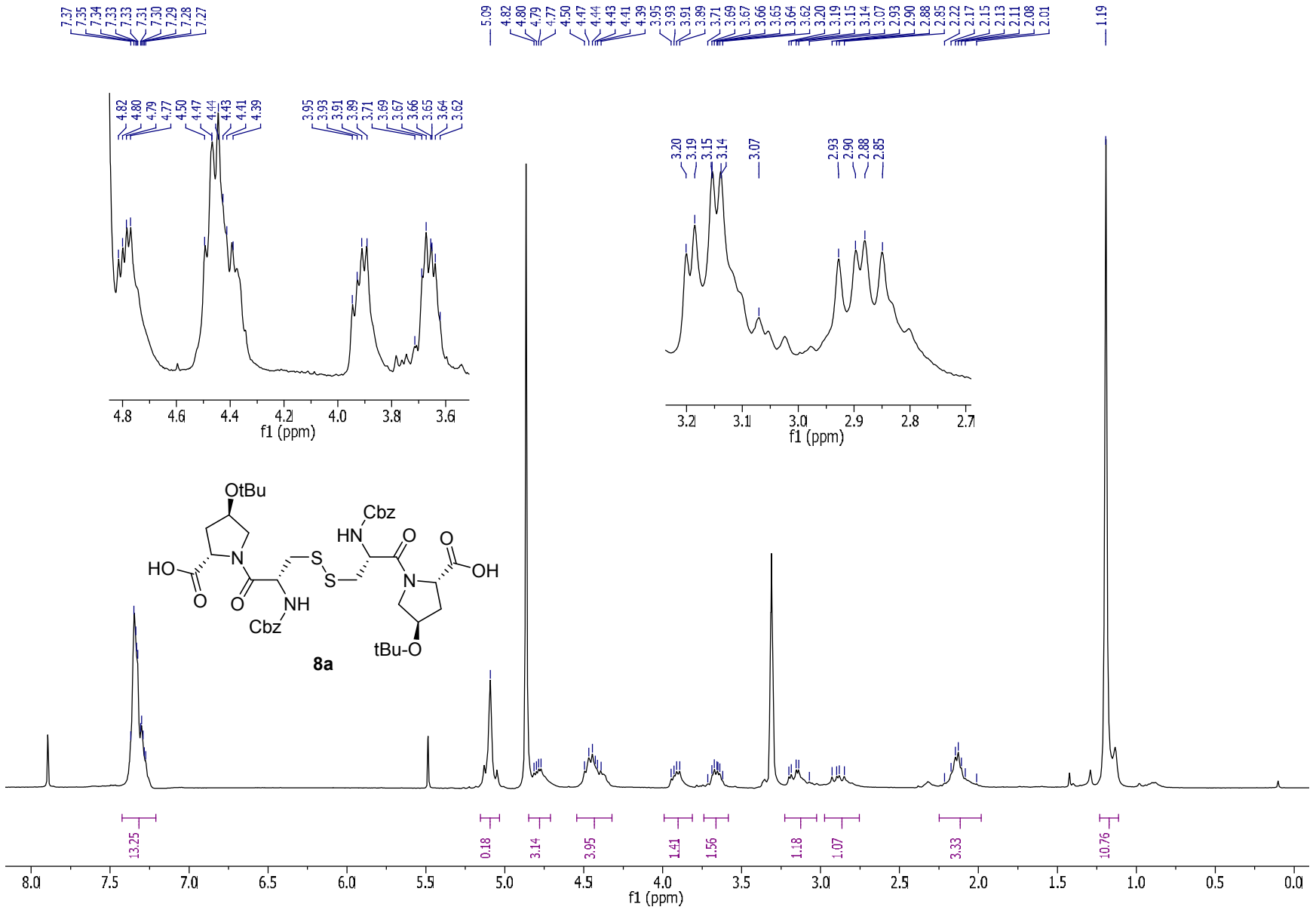

173.18
172.03
167.71
164.63
152.14
137.55
135.87
134.91
134.84
130.07
129.50
129.12
128.86
128.84
128.76
128.69
128.66
128.63
128.53
128.26
128.15
128.11
127.87
127.74
127.38
77.65 cdcl3
77.23 cdcl3
76.81 cdcl3
76.19
74.48
71.60
70.77
69.47
67.14
62.71
57.56
54.21
51.72
39.06
38.56
35.52
33.92
29.88
28.27
OBzl
Bzl
Cbz
N
H
O
N
O
OH
3e
f1 (ppm)
f1 (ppm)

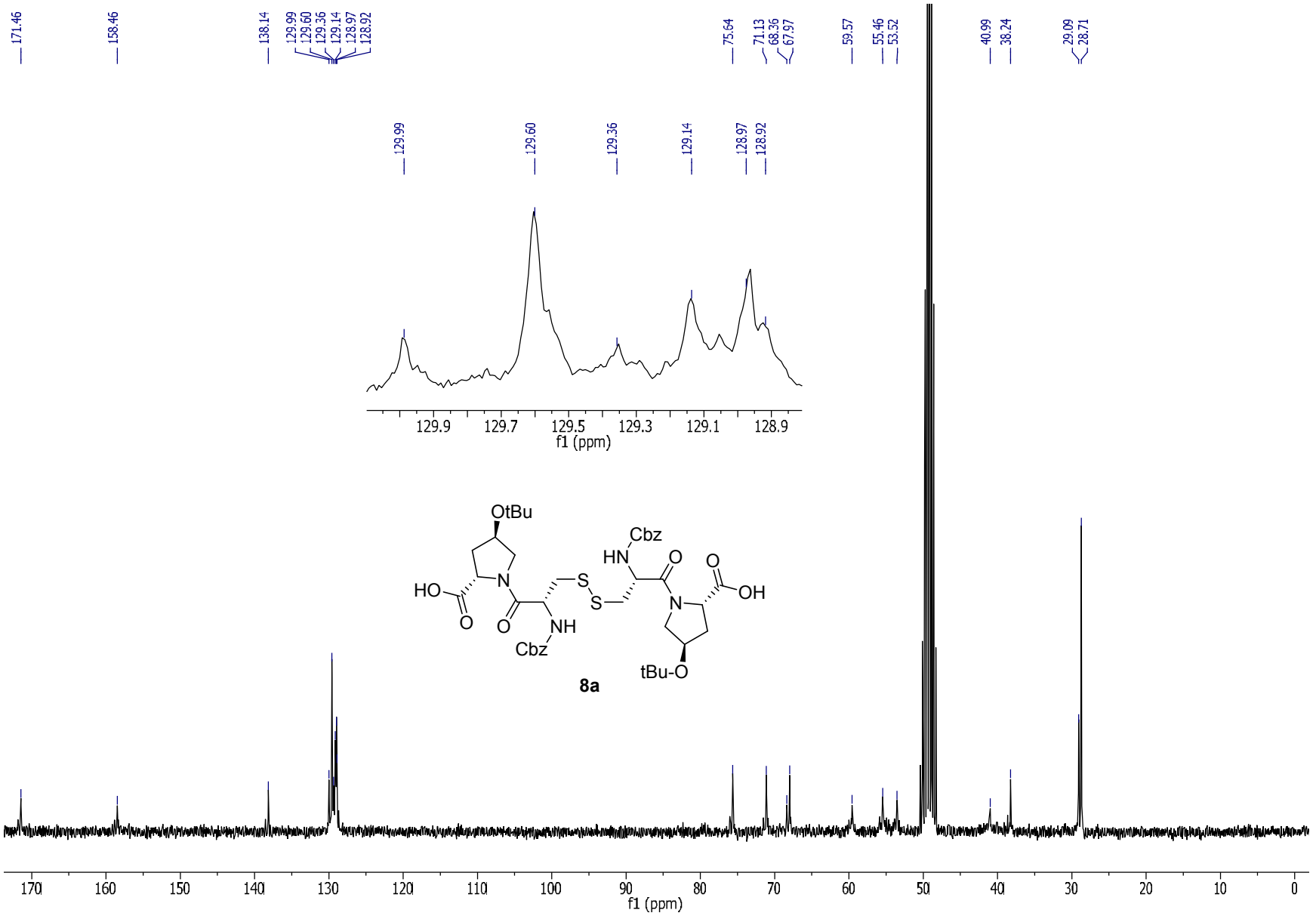

OBzl
Cbz
N
H
O
N
O
OH
3f
f1 (ppm)

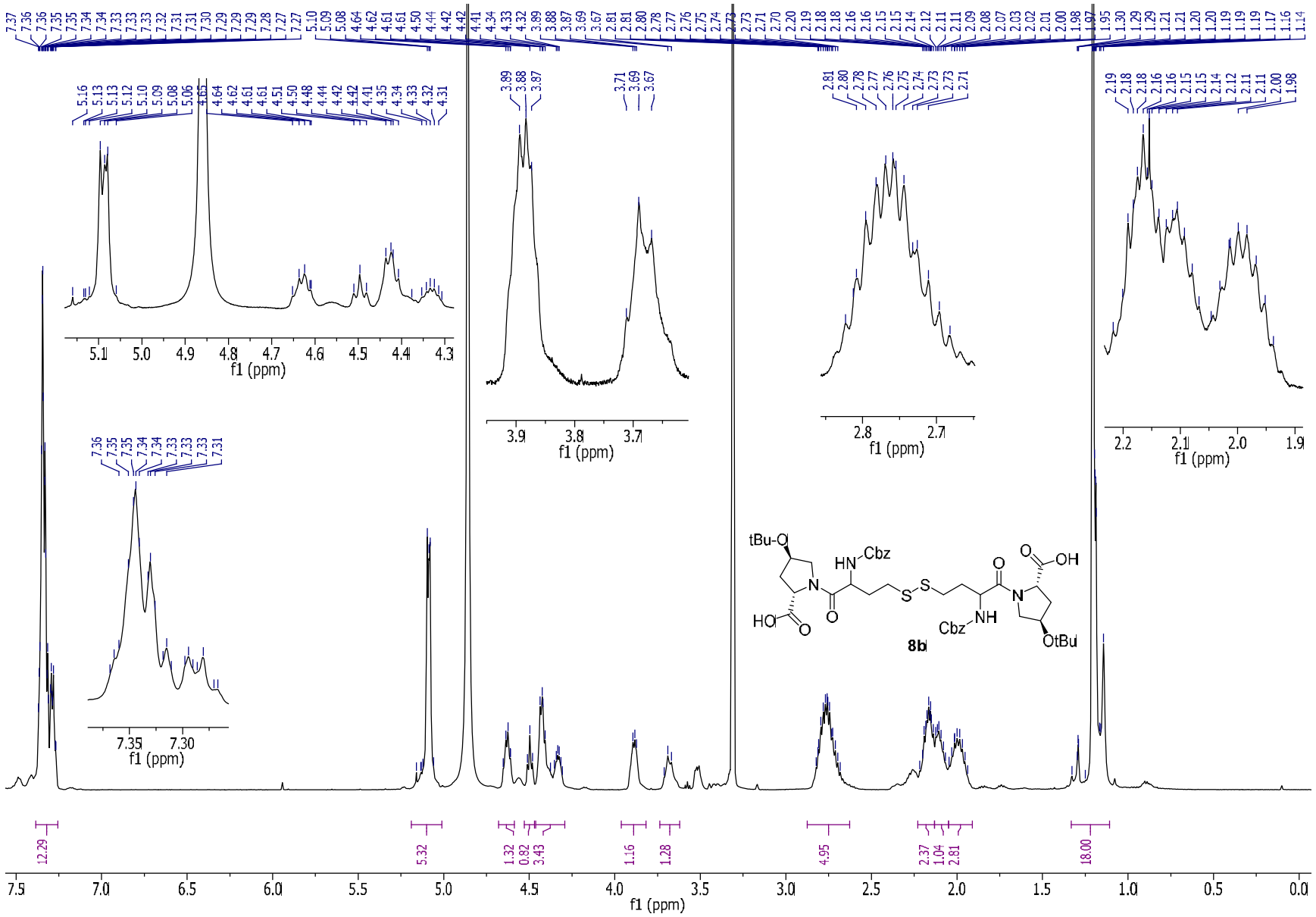

176.84
174.62
172.78
156.55
156.41
137.43
136.35
136.27
128.62
128.56
128.51
128.20
128.10
128.07
127.89
127.58
126.06
71.42
67.12
58.30
52.50
52.41
51.11
41.61
41.46
34.37
24.80
24.57
23.35
22.95
21.86
21.77
OBzl
Cbz
N
H
N
O
O
OH
3f
f1 (ppm)
f1 (ppm)
f1 (ppm)

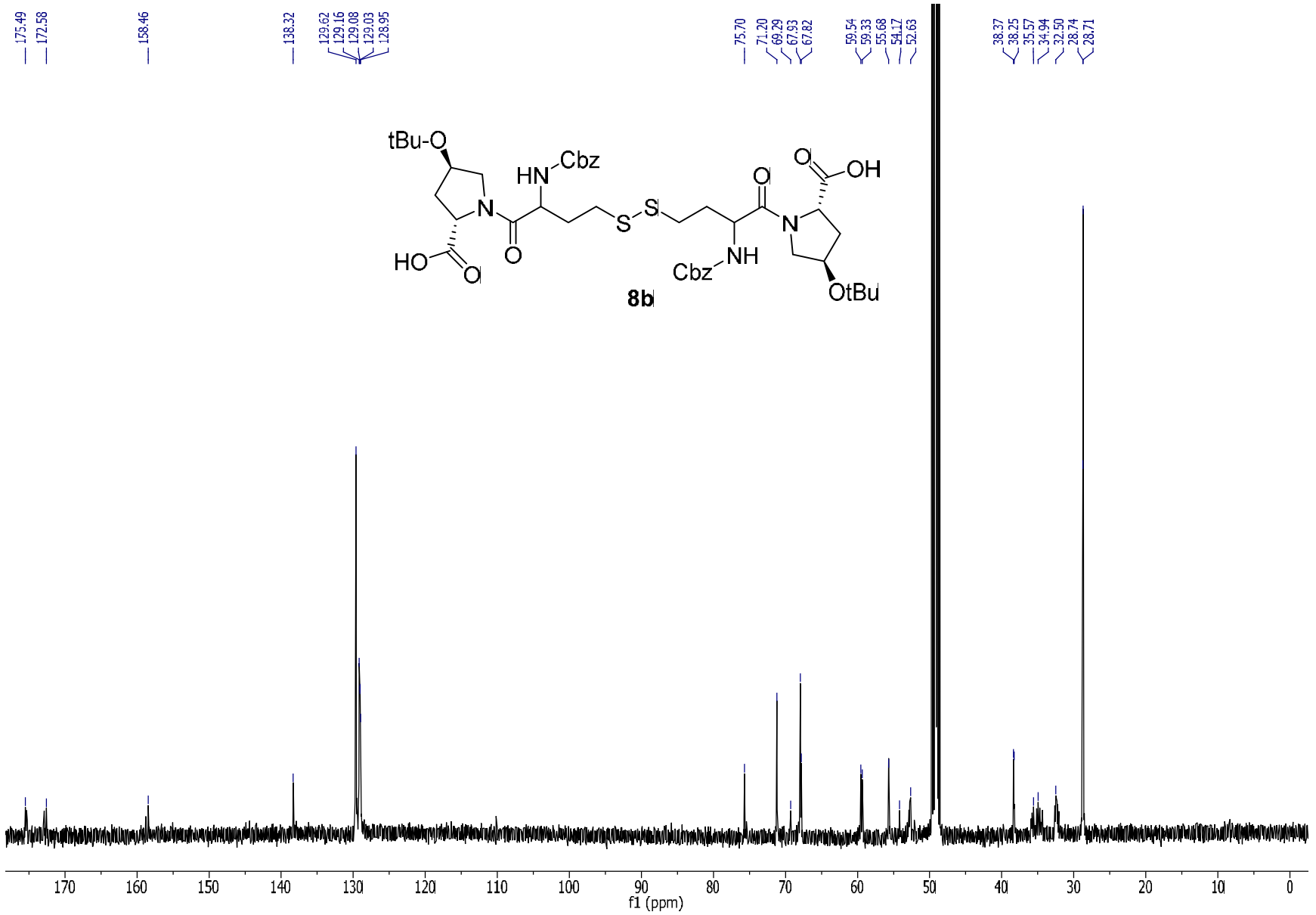

Cbz
N
H
O
N
OBzl
O
OH
3g
f1 (ppm)

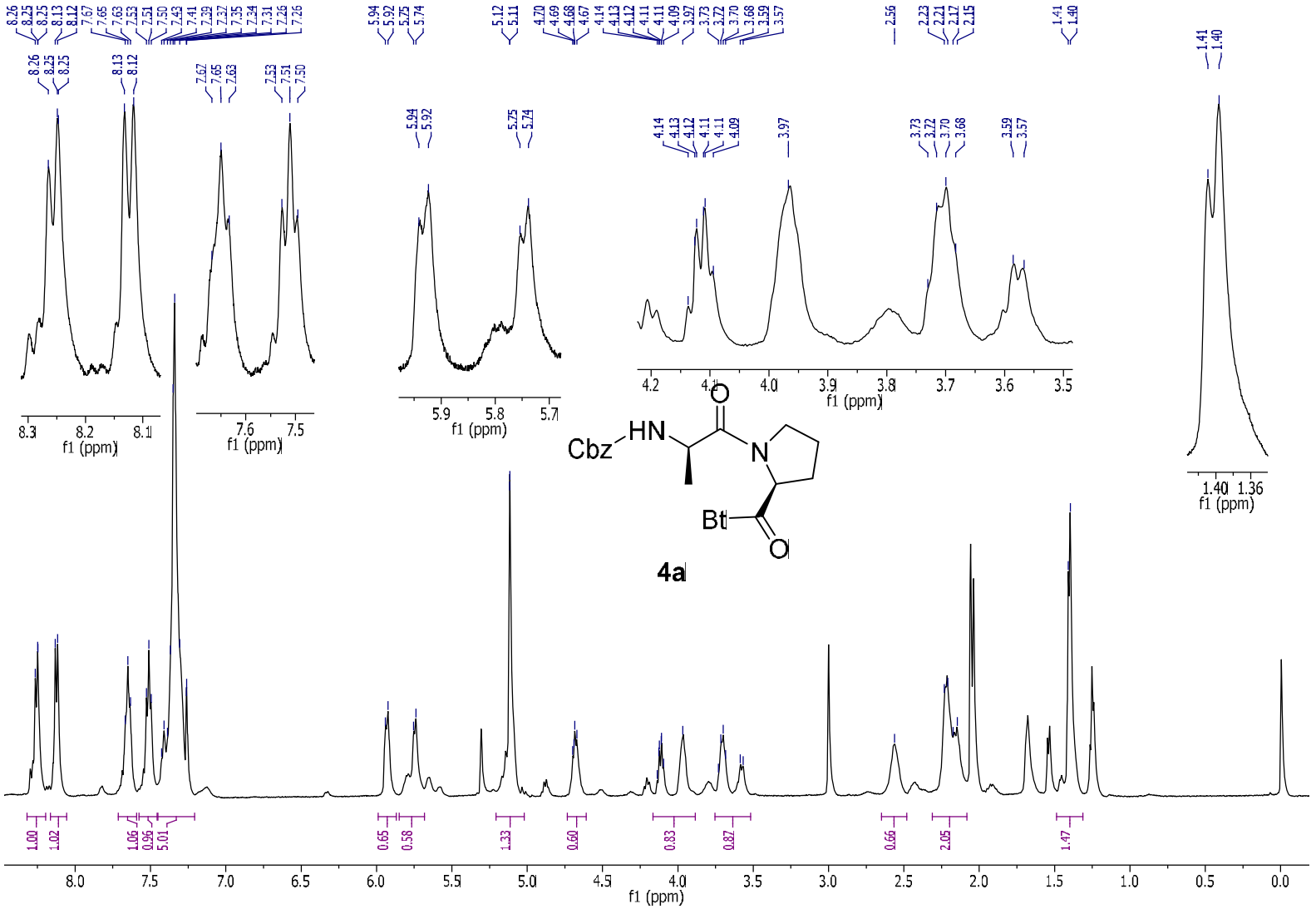

176.47
156.44
139.73
136.34
128.70
128.38
128.30
128.07
127.95
76.65
71.19
67.30
67.11
58.44
58.25
57.13
52.48
37.98
37.63
35.05
25.01
24.53
15.62
15.27
11.78
11.07
OBzl
Cbz
N
H
O
N
O
OH
3g
128.9
128.7
128.5
128.3
128.1
127.9
127.7
f1 (ppm)
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

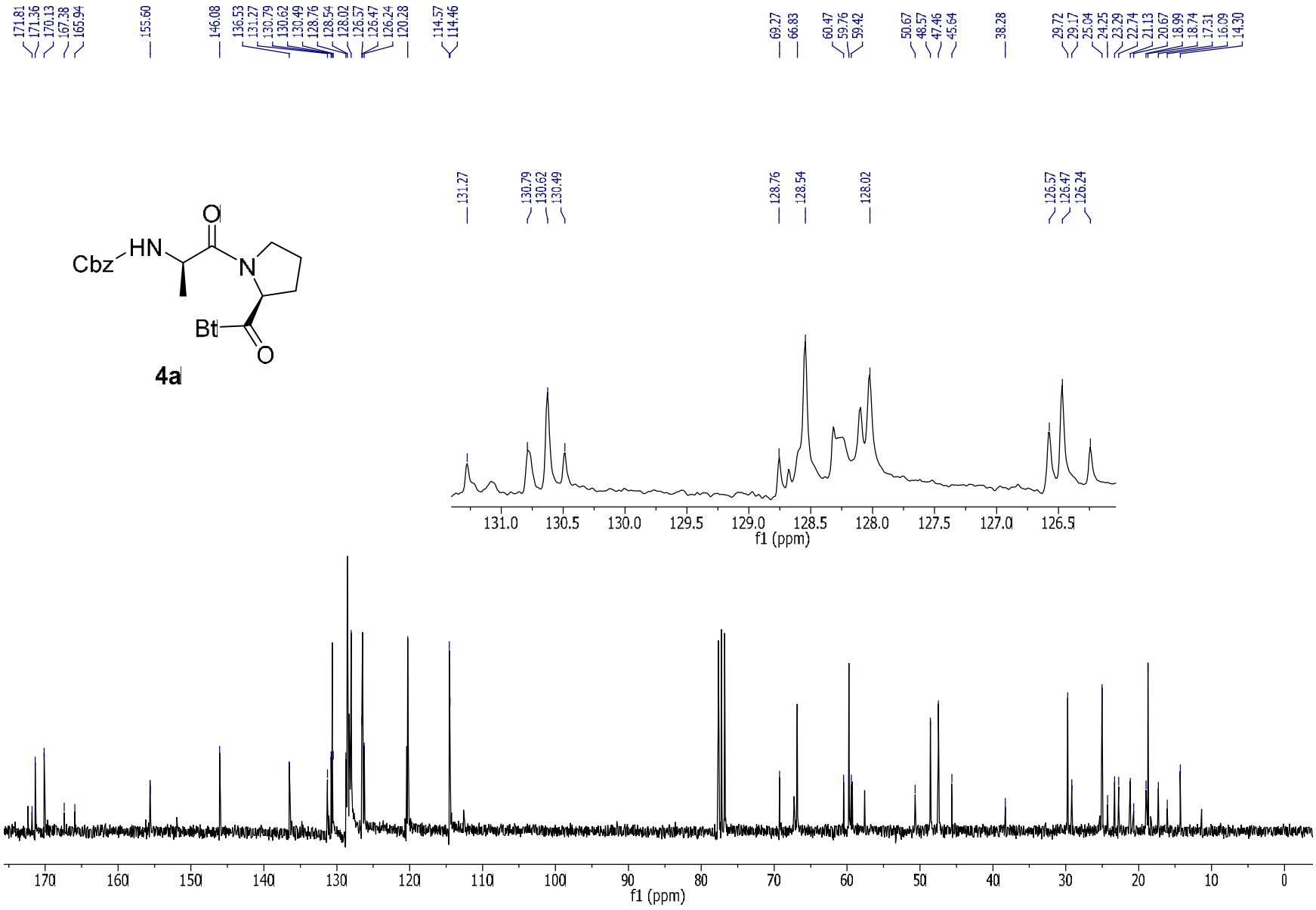

7.37
7.35
7.34
7.33
7.33
7.31
7.30
7.29
7.28
7.27
5.09
4.82
4.80
4.79
4.77
4.50
4.47
4.44
4.43
4.41
4.39
3.95
3.93
3.91
3.89
3.71
3.69
3.67
3.66
3.65
3.64
3.62
3.20
3.19
3.15
3.14
3.07
2.93
2.90
2.88
2.85
2.22
2.17
2.15
2.13
2.11
2.08
2.01
1.19
f1 (ppm)
OtBu
HO
O
N
O
NH
Cbz
S
S
HN
Cbz
O
O
OH
N
tBu-O
8a
13.25
0.18
3.14
3.95
1.41
1.56
1.18
1.07
3.33
10.76
f1 (ppm)

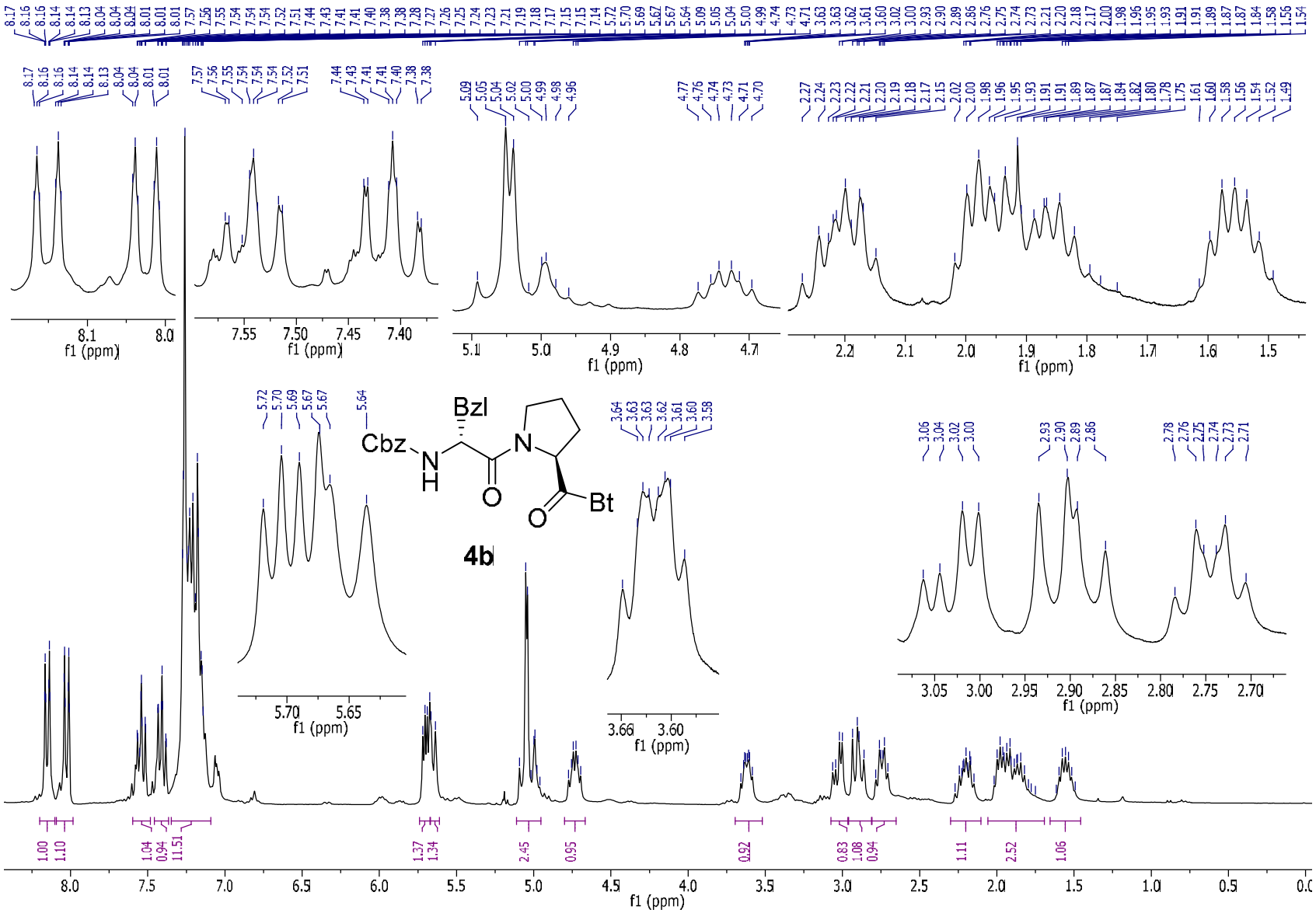

171.46
158.46
138.14
129.99
129.60
129.36
129.14
128.97
128.92
75.64
71.13
68.36
67.97
59.57
55.46
53.52
40.99
38.24
29.09
28.71
129.9
129.7
129.5
129.3
129.1
128.9
f1 (ppm)
OtBu
HO
O
N
O
NH
Cbz
S
S
HN
Cbz
O
O
OH
N
tBu-O
8a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

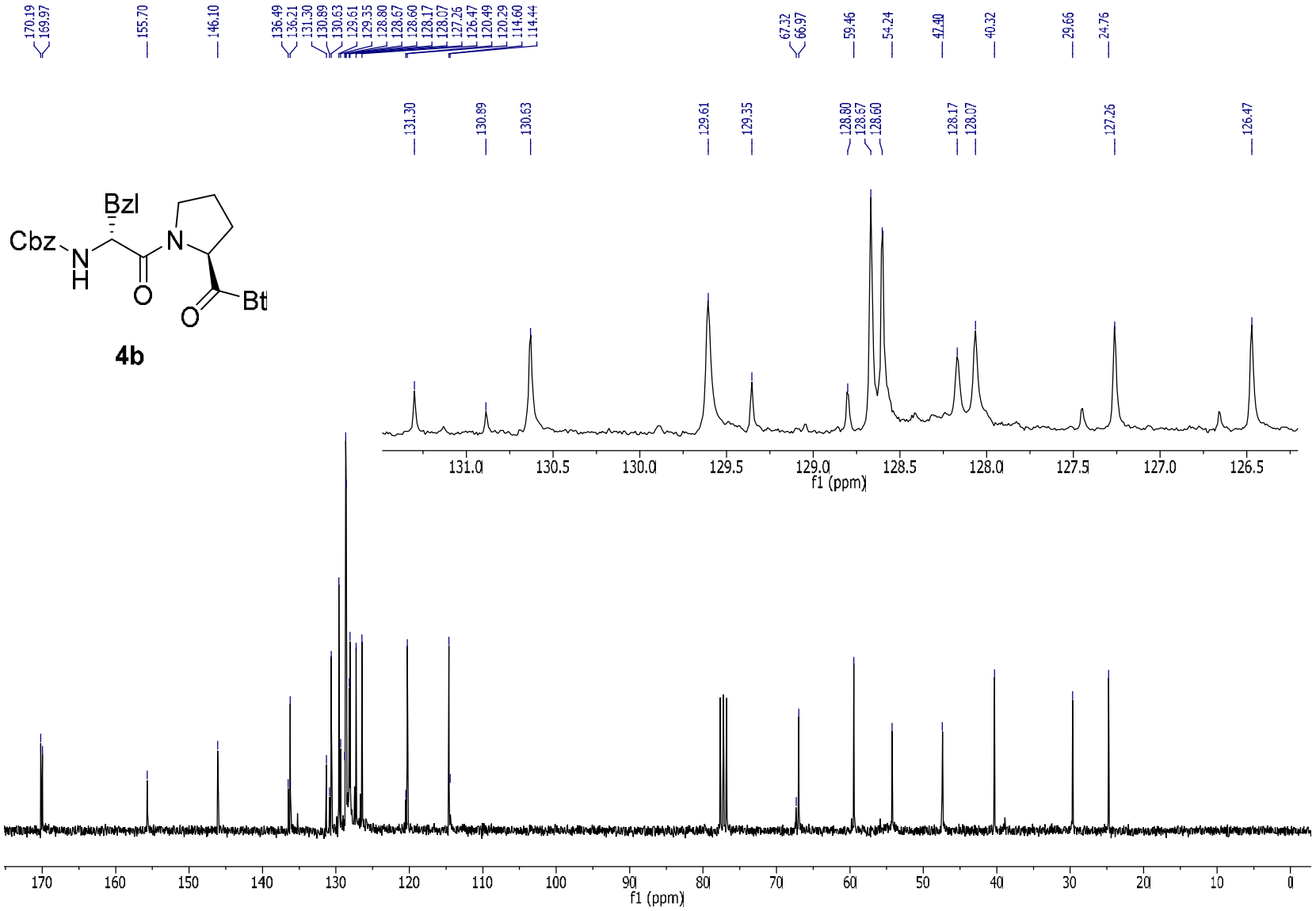

tBu-O
HN
Cbz
HO
O
N
S
S
O
NH
Cbz
OH
OtBu
8bi
f1 (ppm)

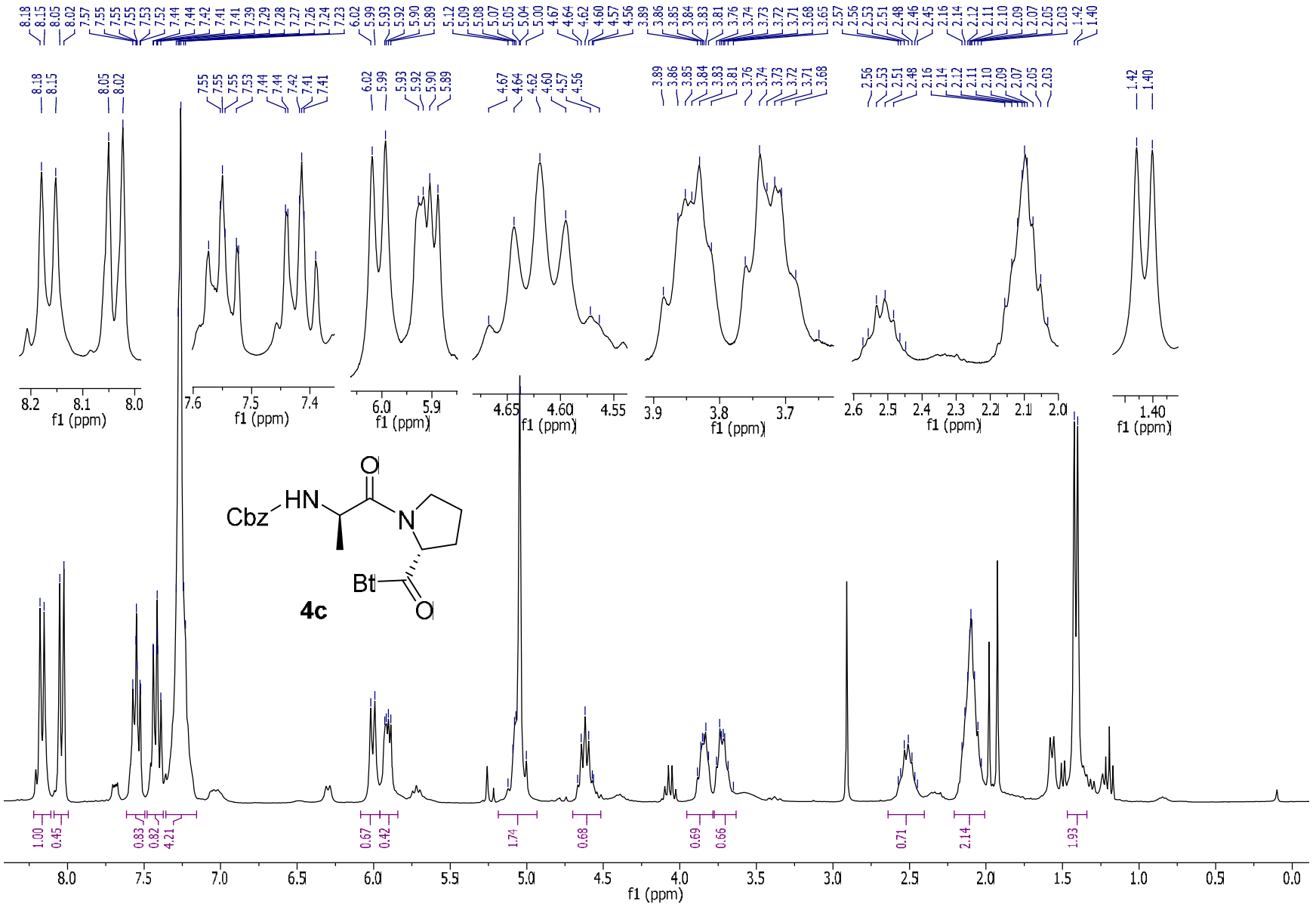

175.49
172.58
158.46
138.32
129.62
129.16
129.08
129.03
128.95
75.70
71.20
69.29
67.93
67.82
59.54
59.33
55.68
54.17
52.63
38.37
38.25
35.57
34.94
32.50
28.74
28.71
tBu-O
HN
Cbz
N
O
S
S
O
O
OH
N
HO
O
Cbz
NH
OtBu
8b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

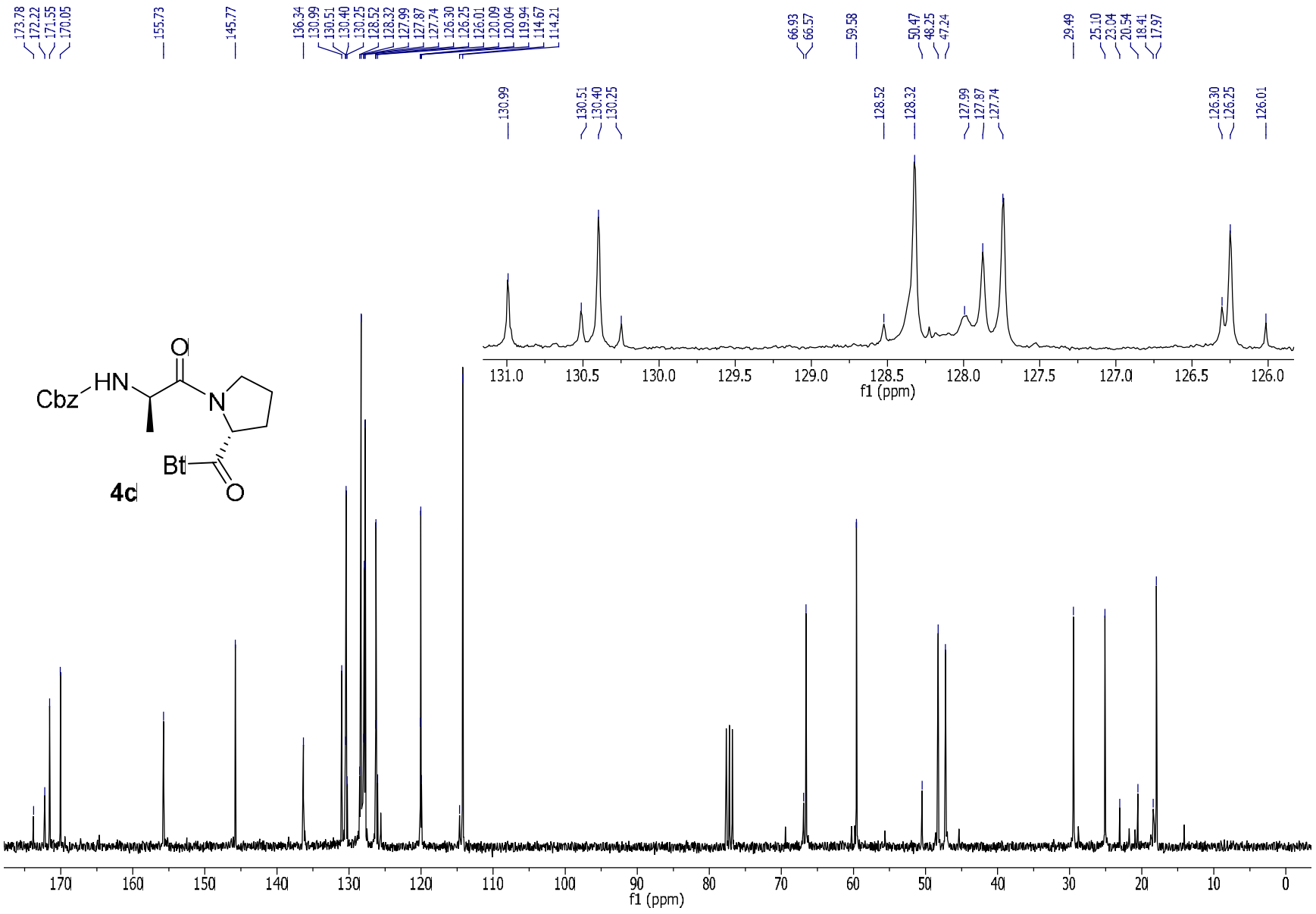

Cbz
HN
O
N
Bt
O
4a
f1 (ppm)

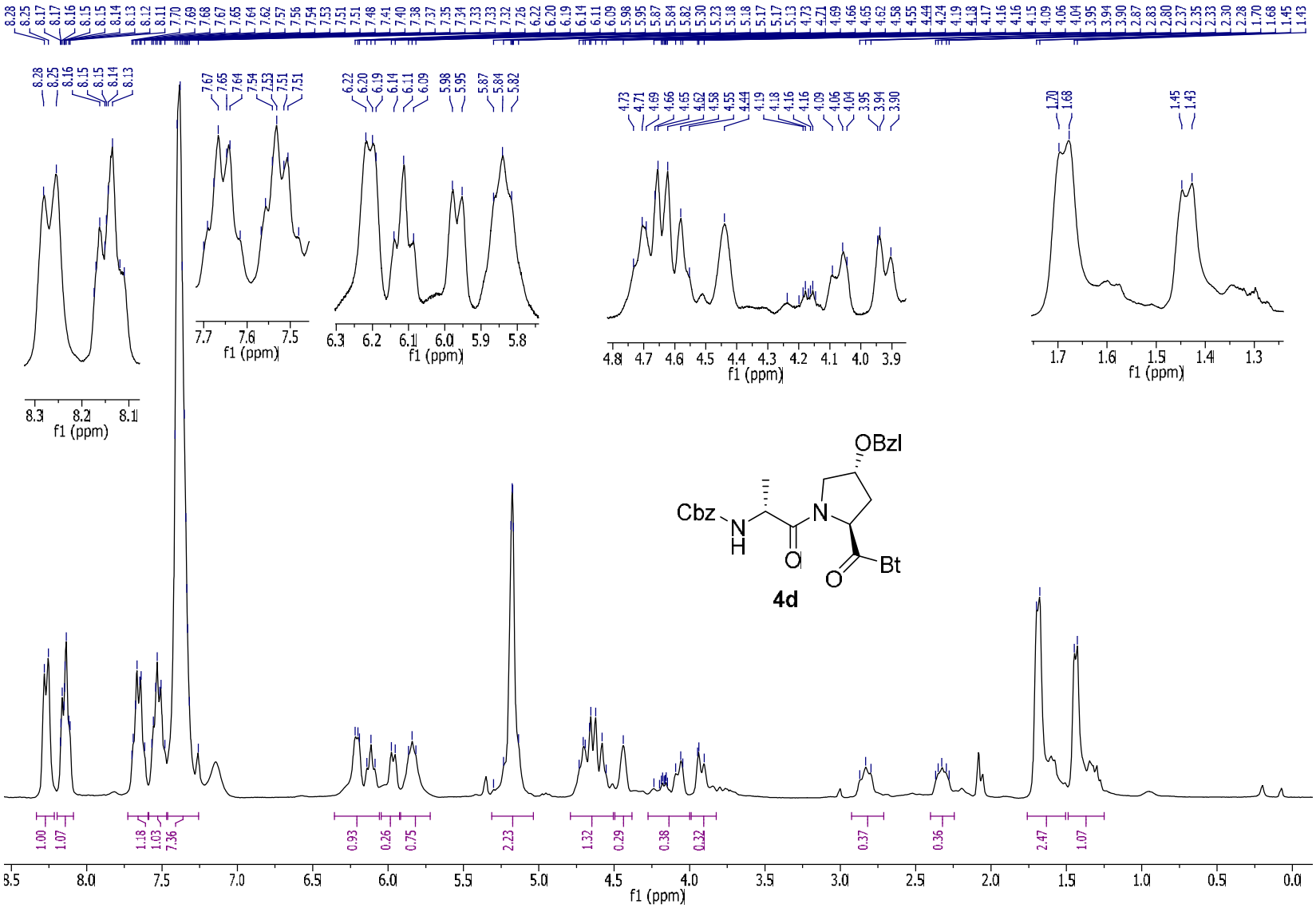

171.81
171.36
170.13
167.38
165.94
155.60
146.08
136.53
131.27
130.79
130.62
130.49
128.76
128.54
128.02
126.57
126.47
126.24
120.28
114.57
114.46
69.27
66.83
60.47
59.76
59.42
50.67
48.57
47.46
45.64
38.28
29.72
29.17
25.04
24.25
23.29
22.74
21.13
20.67
18.99
18.74
17.31
16.09
14.30
Cbz
HN
O
N
Bt
O
4a
f1 (ppm)
f1 (ppm)

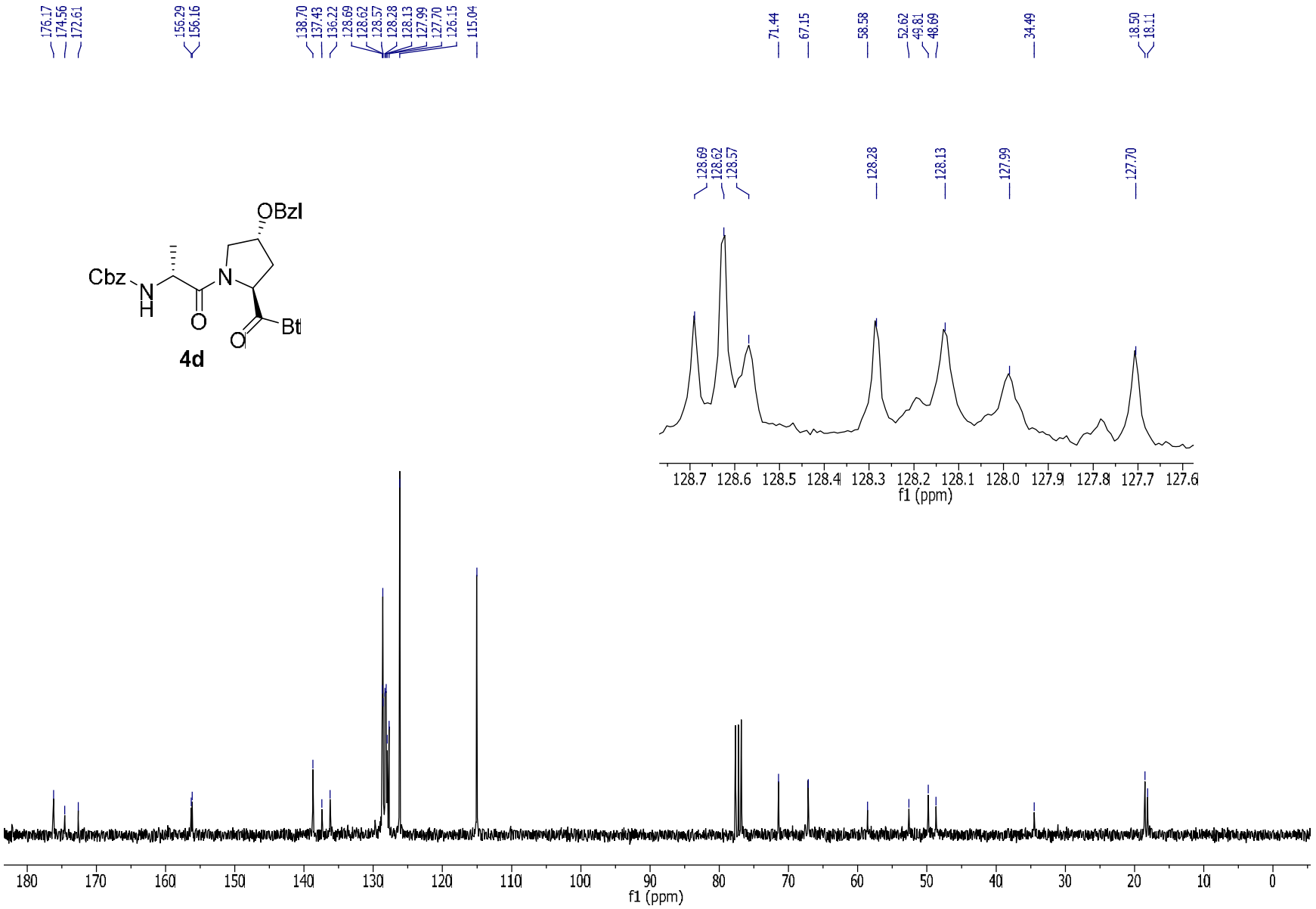

Cbz
N
H
Bzl
N
O
O
Bt
4b
f1 (ppm)

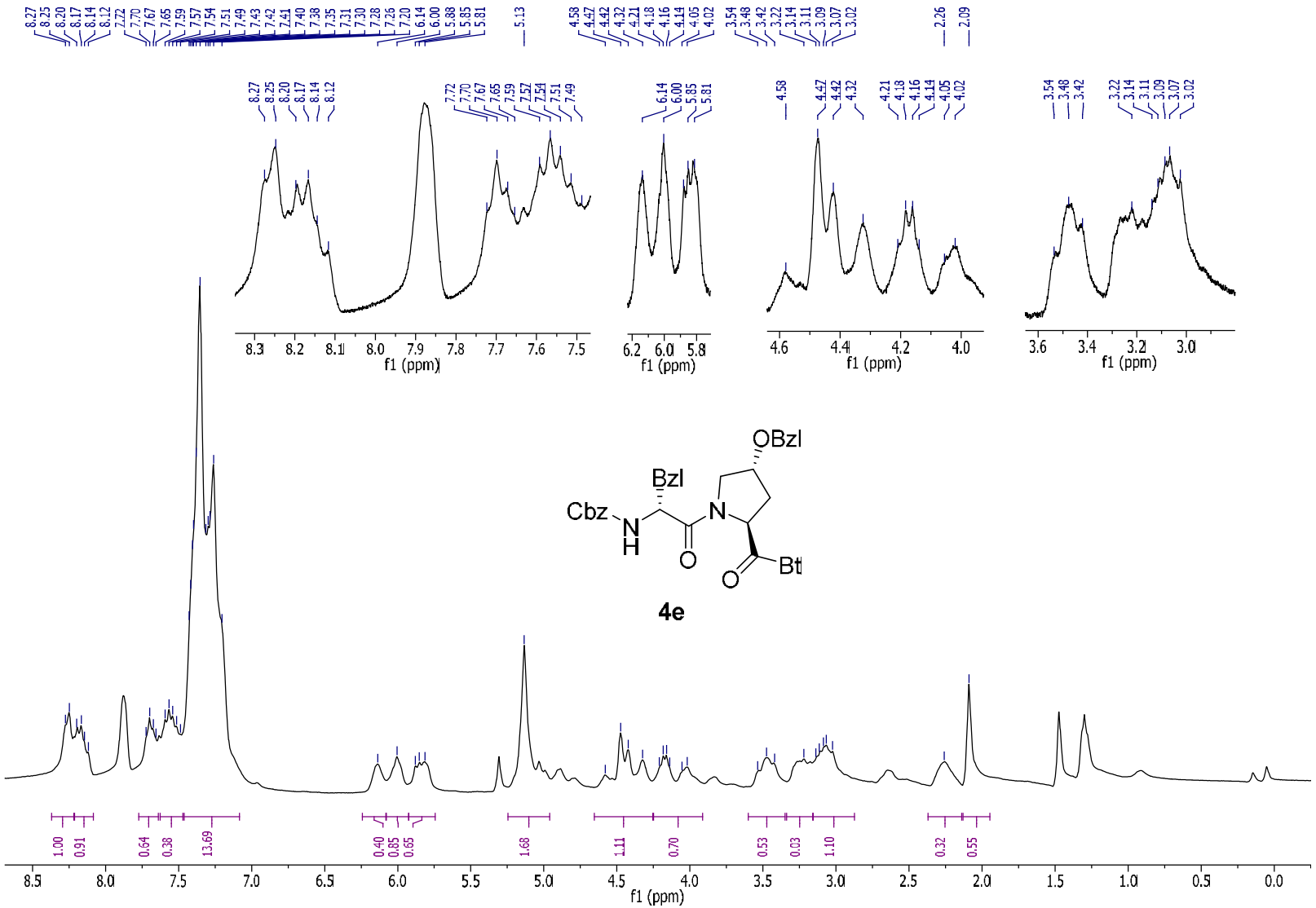

170.19
169.97
155.70
146.10
136.49
136.21
131.30
130.89
130.63
129.61
129.35
128.80
128.67
128.60
128.17
128.07
127.26
126.47
120.49
120.29
114.60
114.44
67.32
66.97
59.46
54.24
47.40
40.32
29.66
24.76
Bzl
Cbz
N
H
O
N
O
Bt
4b
f1 (ppm)
f1 (ppm)

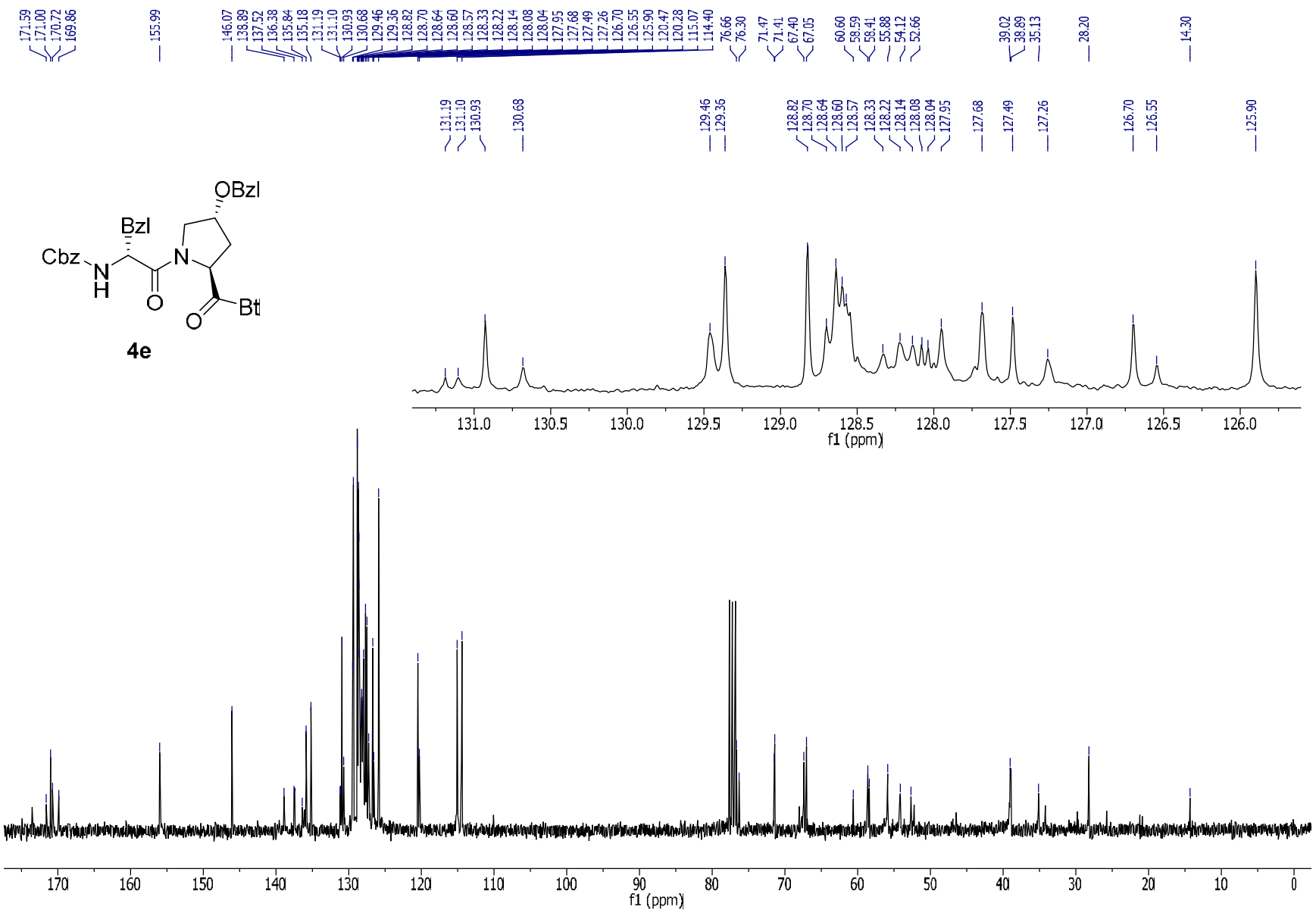

Cbz
HN
O
N
Bt
O
4c
f1 (ppm)

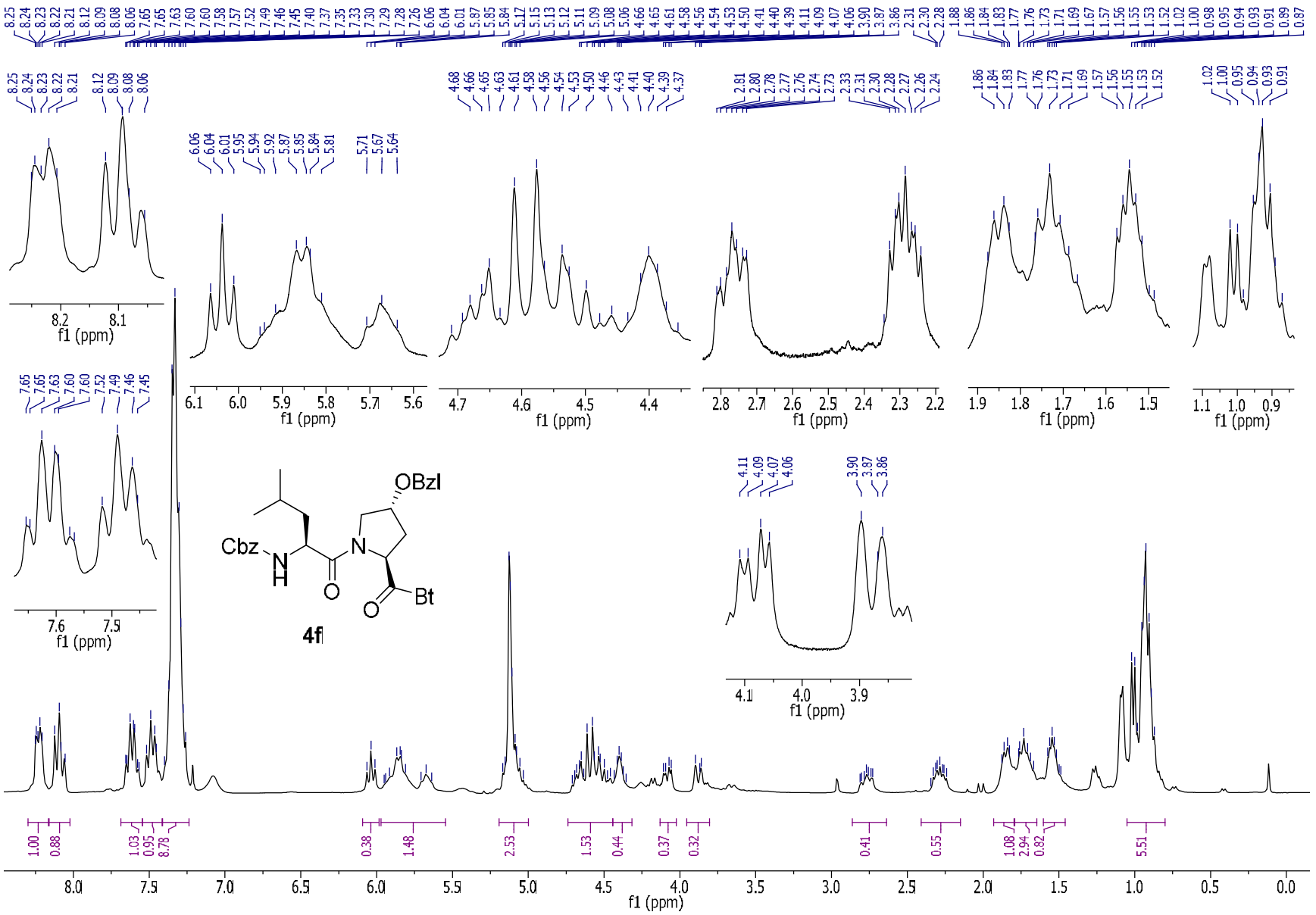

173.78
172.22
171.55
170.05
155.73
145.77
136.34
130.99
130.51
130.40
130.25
128.52
128.32
127.99
127.87
127.74
126.30
126.25
126.01
120.09
120.04
119.94
114.67
114.21
66.93
66.57
59.58
50.47
48.25
47.24
29.49
25.10
23.04
20.54
18.41
17.97
Cbz
HN
O
N
Bt
O
4c
f1 (ppm)
f1 (ppm)

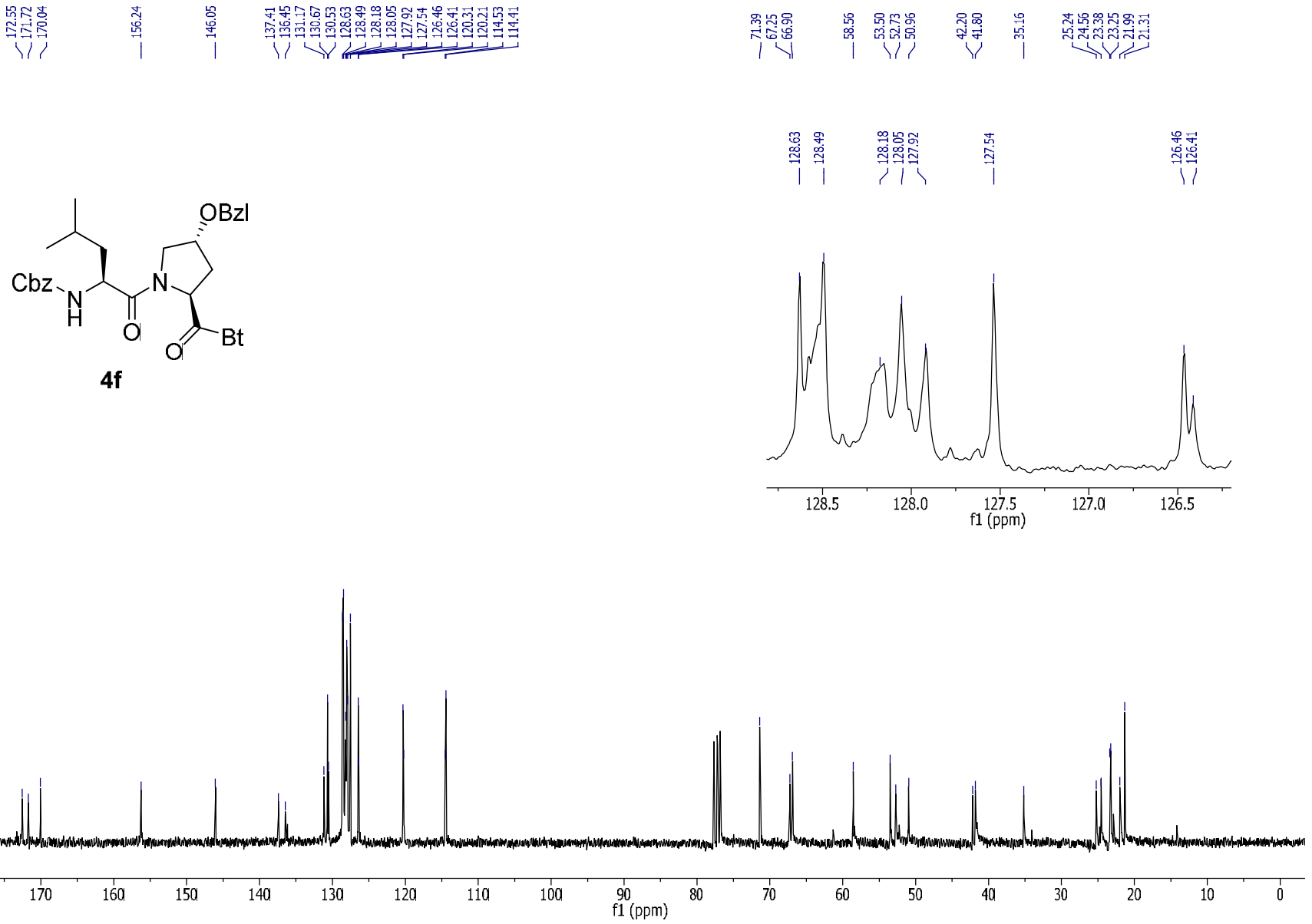

OBzl
Cbz
N
H
O
N
O
Bt
4d
f1 (ppm)

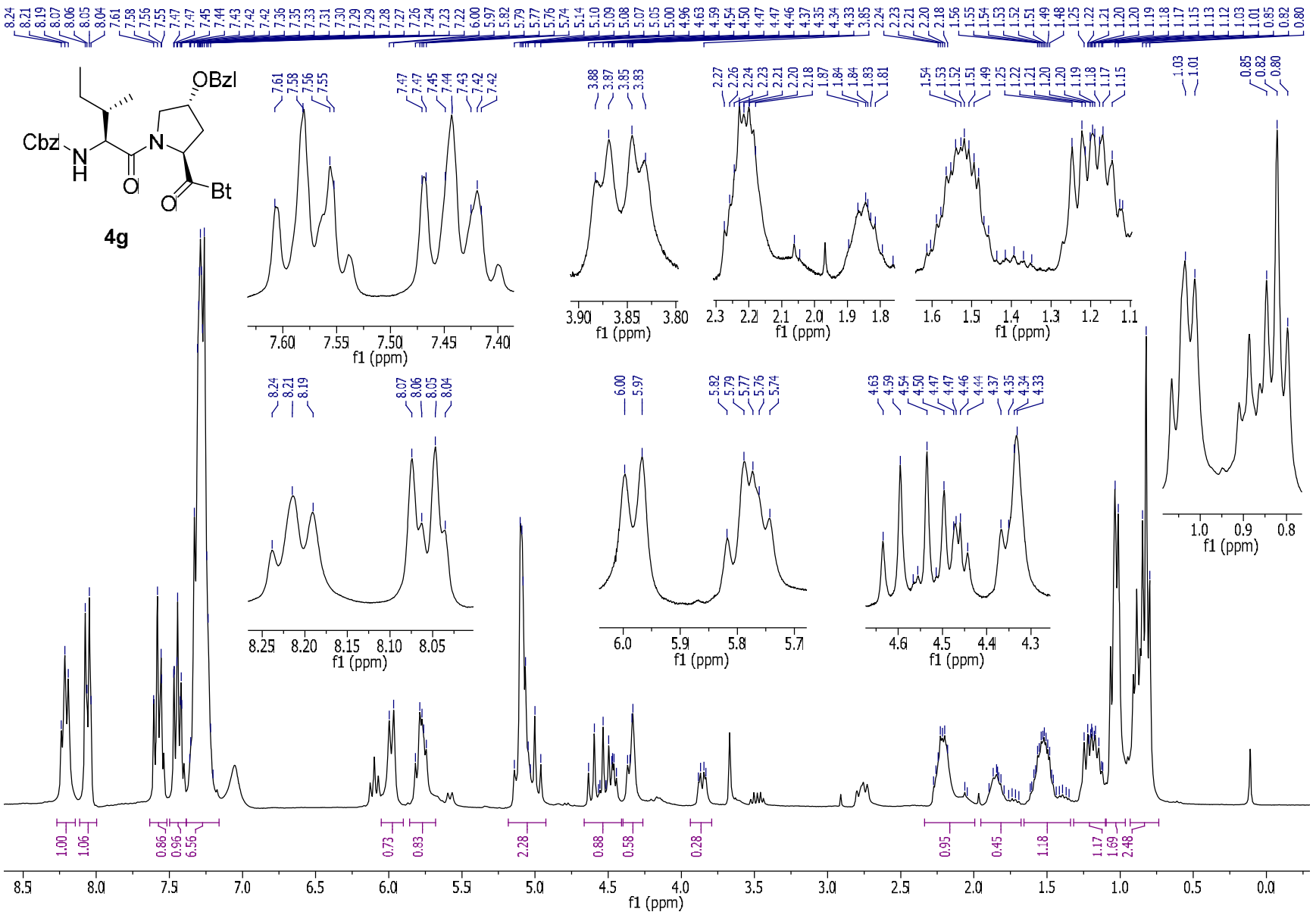

176.17
174.56
172.61
156.29
156.16
138.70
137.43
136.22
128.69
128.62
128.57
128.28
128.13
127.99
127.70
126.15
115.04
71.44
67.15
58.58
52.62
49.81
48.69
34.49
18.50
18.11
OBzl
Cbz
N
H
O
N
O
Bt
4d
f1 (ppm)
f1 (ppm)

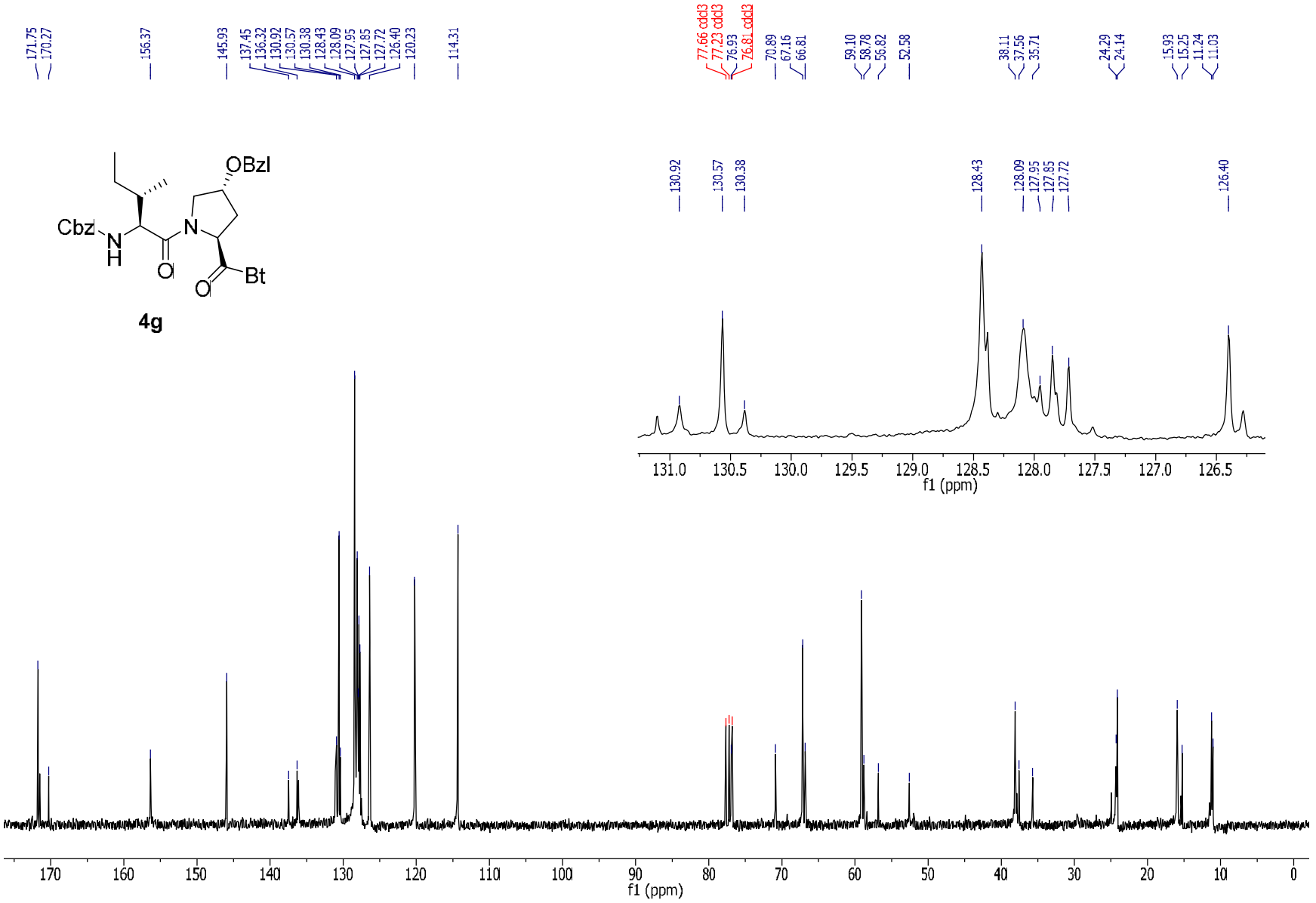

OBzl
Bzl
Cbz
N
H
N
O
O
Bt
4e
f1 (ppm)

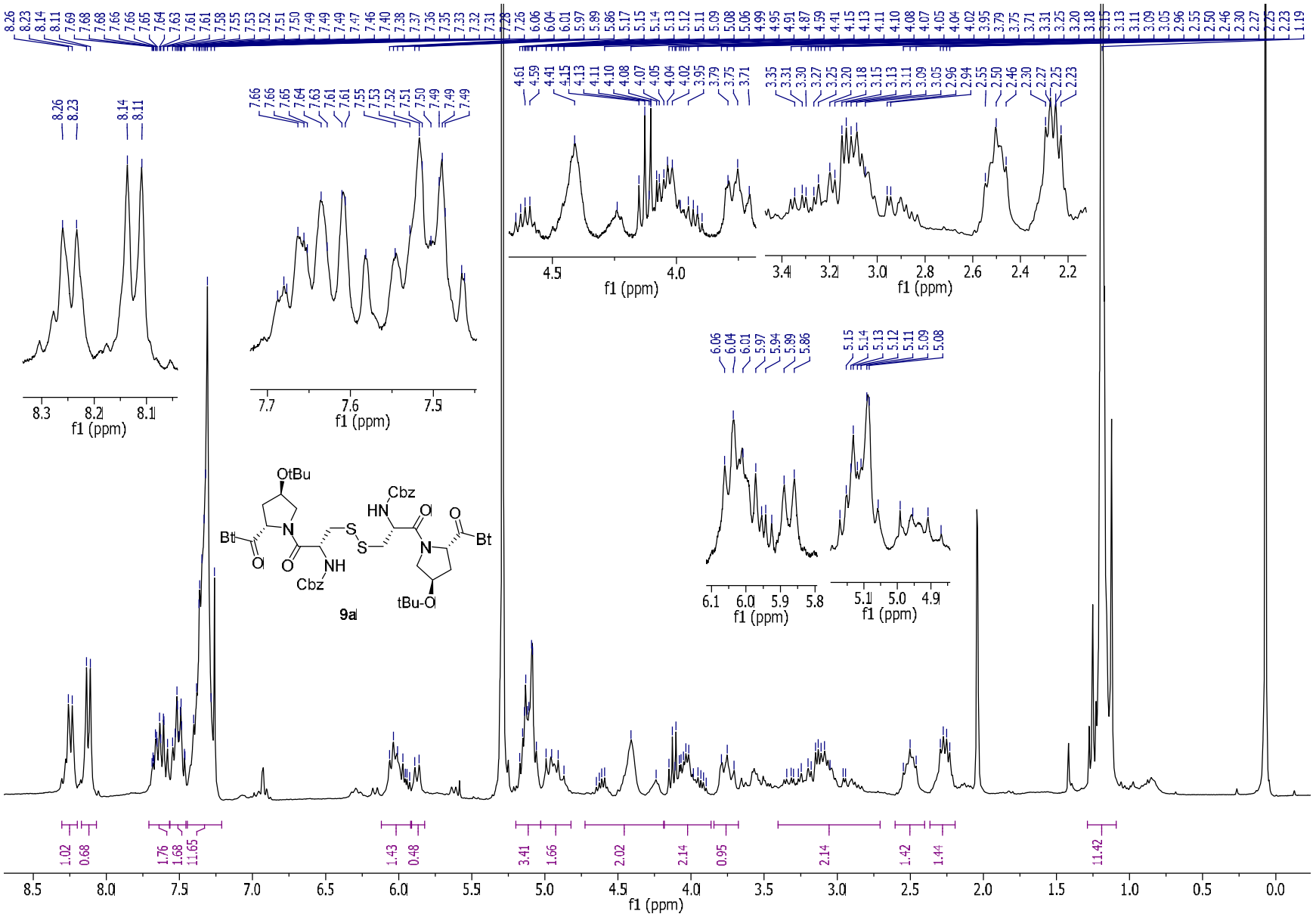

171.59
171.00
170.72
169.86
155.99
146.07
138.89
137.52
136.38
135.84
135.18
131.19
131.10
130.93
130.68
129.46
129.36
128.82
128.70
128.64
128.60
128.57
128.33
128.22
128.14
128.08
128.04
127.95
127.68
127.49
127.26
126.70
126.55
125.90
120.47
120.28
115.07
114.40
76.66
76.30
71.47
71.41
67.40
67.05
60.60
58.59
58.41
55.88
54.12
52.66
39.02
38.89
35.13
28.20
14.30
OBzl
Bzl
Cbz
N
H
O
N
O
Bt
4e
f1 (ppm)
f1 (ppm)

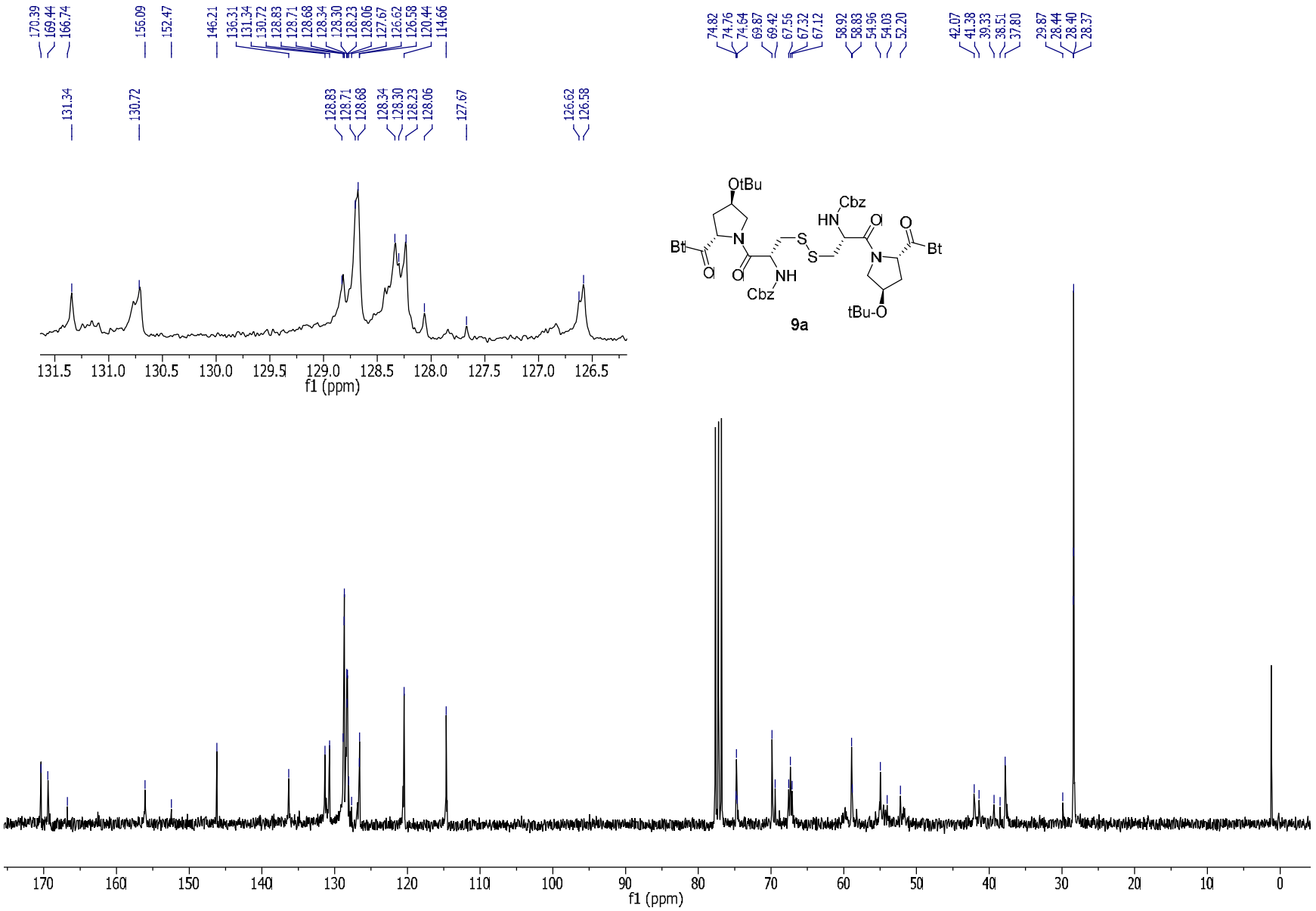

OBzl
Cbz
N
H
N
O
O
Bt
4f
f1 (ppm)

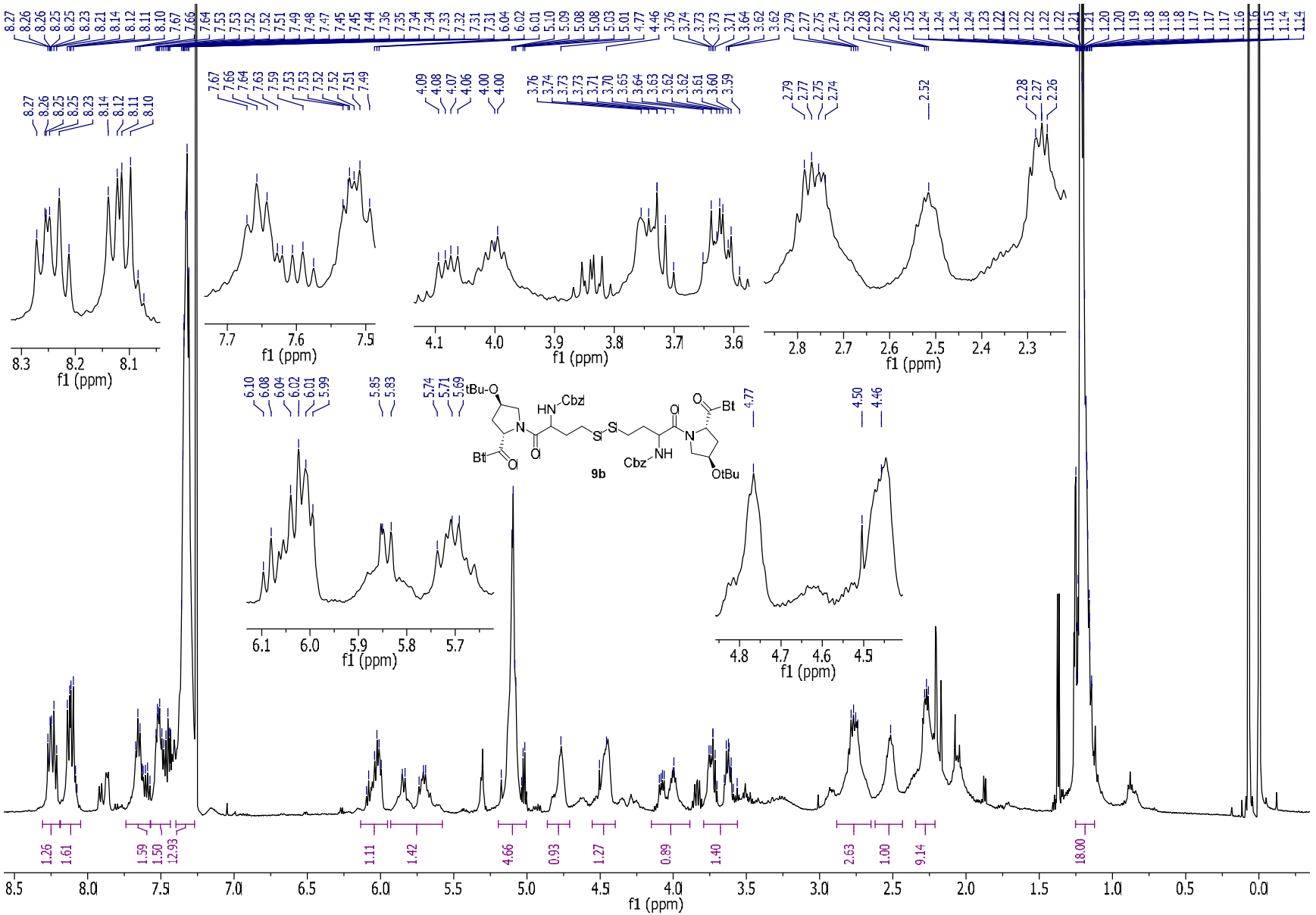

172.55
171.72
170.04
156.24
146.05
137.41
136.45
131.17
130.67
130.53
128.63
128.49
128.18
128.05
127.92
127.54
126.46
126.41
120.31
120.21
114.53
114.41
71.39
67.25
66.90
58.56
53.50
52.73
50.96
42.20
41.80
35.16
25.24
24.56
23.38
23.25
21.99
21.31
OBzl
Cbz
N
H
N
O
O
Bt
4f
f1 (ppm)
f1 (ppm)

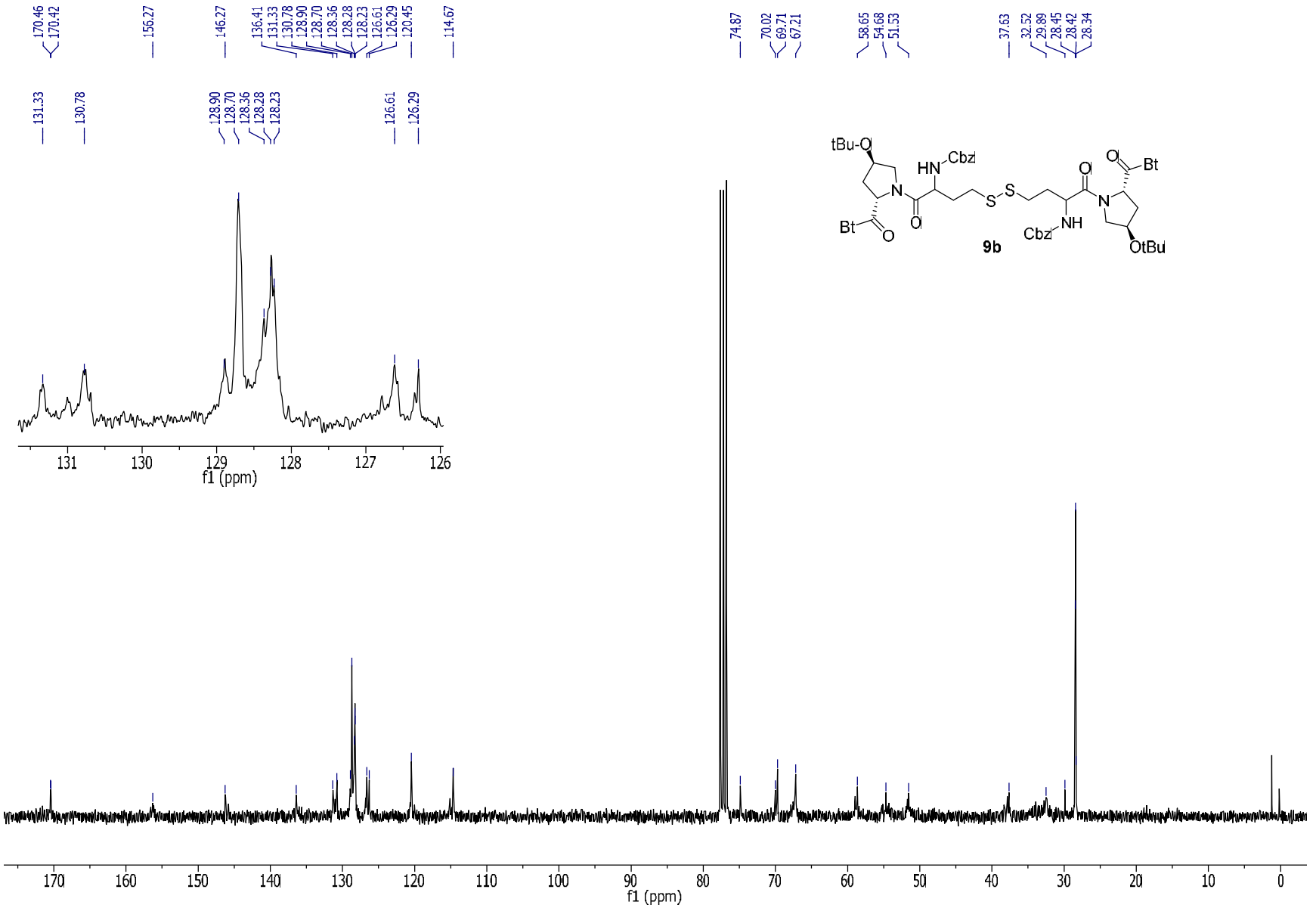

OBzl
Cbz
N
H
O
N
O
Bt
4g
f1 (ppm)

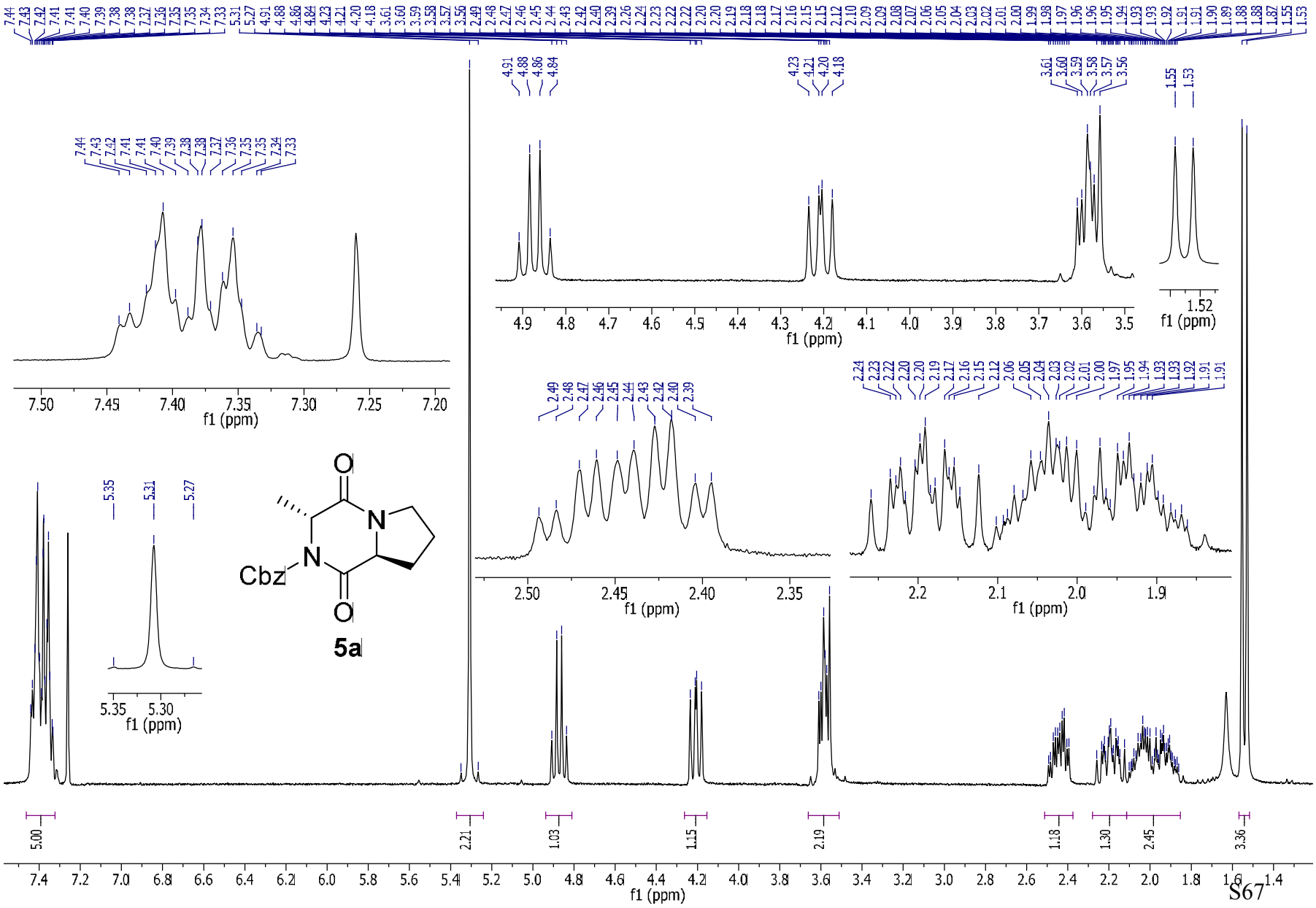

171.75
170.27
156.37
145.93
137.45
136.32
130.92
130.57
130.38
128.43
128.09
127.95
127.85
127.72
126.40
120.23
114.31
77.66 cdcl3
77.23 cdcl3
76.93
76.81 cdcl3
70.89
67.16
66.81
59.10
58.78
56.82
52.58
38.11
37.56
35.71
24.29
24.14
15.93
15.25
11.24
11.03
OBzl
Cbz
N
H
O
N
O
Bt
4g
130.92
130.57
130.38
128.43
128.09
127.95
127.85
127.72
126.40
131.0
130.5
130.0
129.5
129.0
128.5
128.0
127.5
127.0
126.5
f1 (ppm)
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

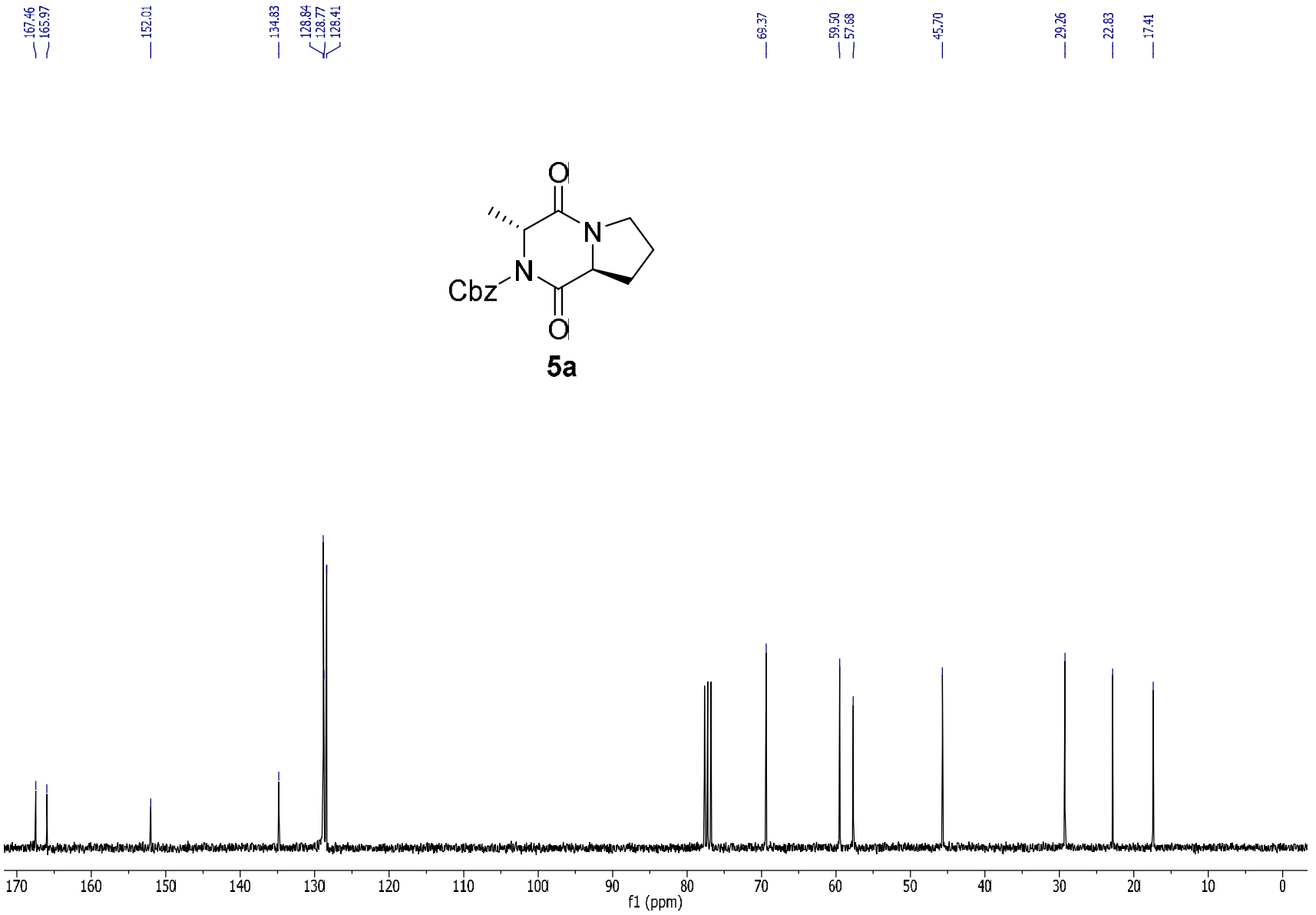

OtBu
Cbz
HN
O
O
N
S
S
Bt
O
O
NH
Cbz
tBu-O
9a
f1 (ppm)

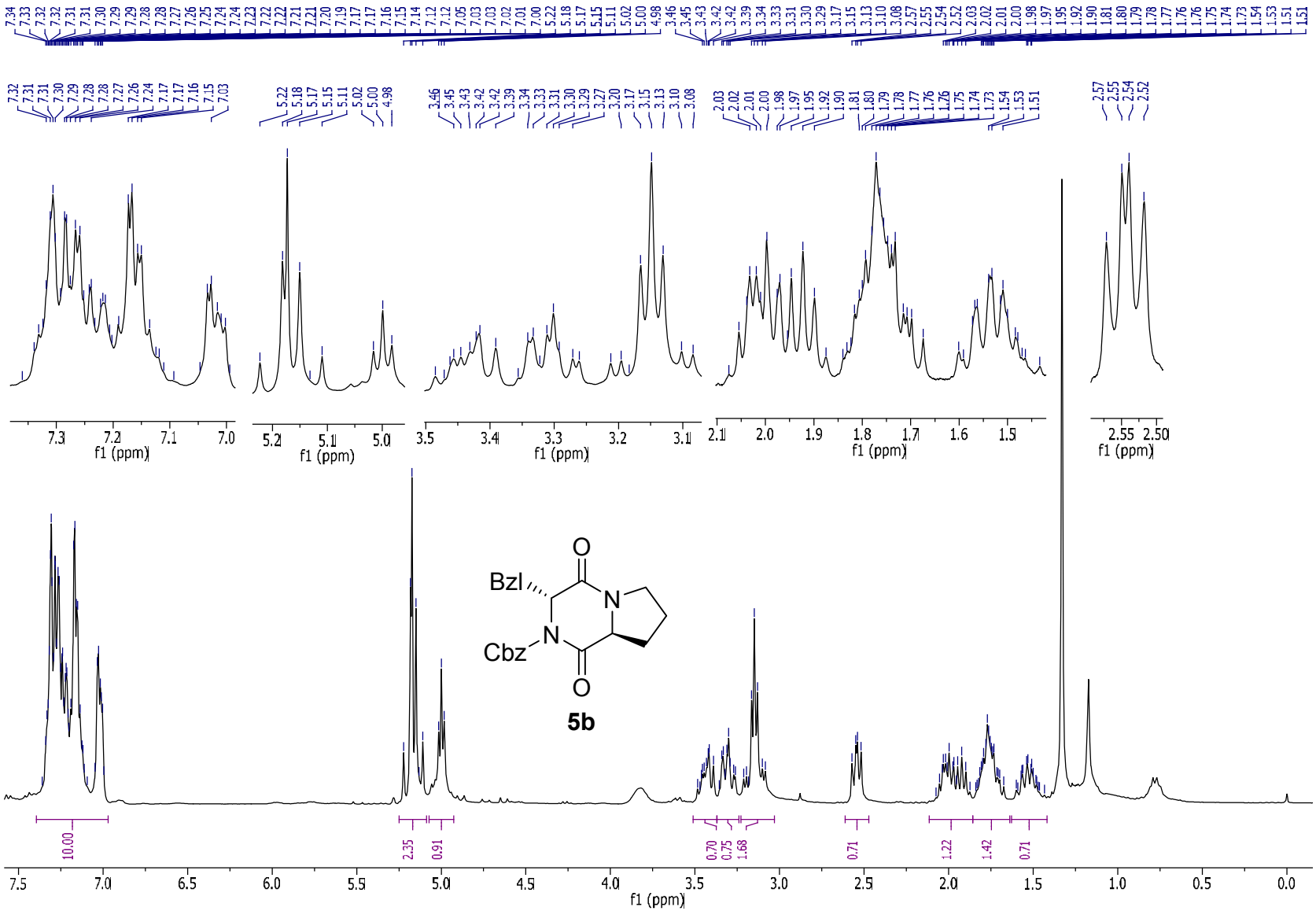

170.39
169.44
166.74
156.09
152.47
146.21
136.31
131.34
130.72
128.83
128.71
128.68
128.34
128.30
128.23
128.06
127.67
126.62
126.58
120.44
114.66
74.82
74.76
74.64
69.87
69.42
67.56
67.32
67.12
58.92
58.83
54.96
54.03
52.20
42.07
41.38
39.33
38.51
37.80
29.87
28.44
28.40
28.37
131.34
130.72
128.83
128.71
128.68
128.34
128.30
128.23
128.06
127.67
126.62
126.58
131.5 131.0 130.5 130.0 129.5 129.0 128.5 128.0 127.5 127.0 126.5
f1 (ppm)
OtBu
Cbz
HN
O
O
Bt
N
S
S
N
Bt
O
O
NH
Cbz
tBu-O
9a
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

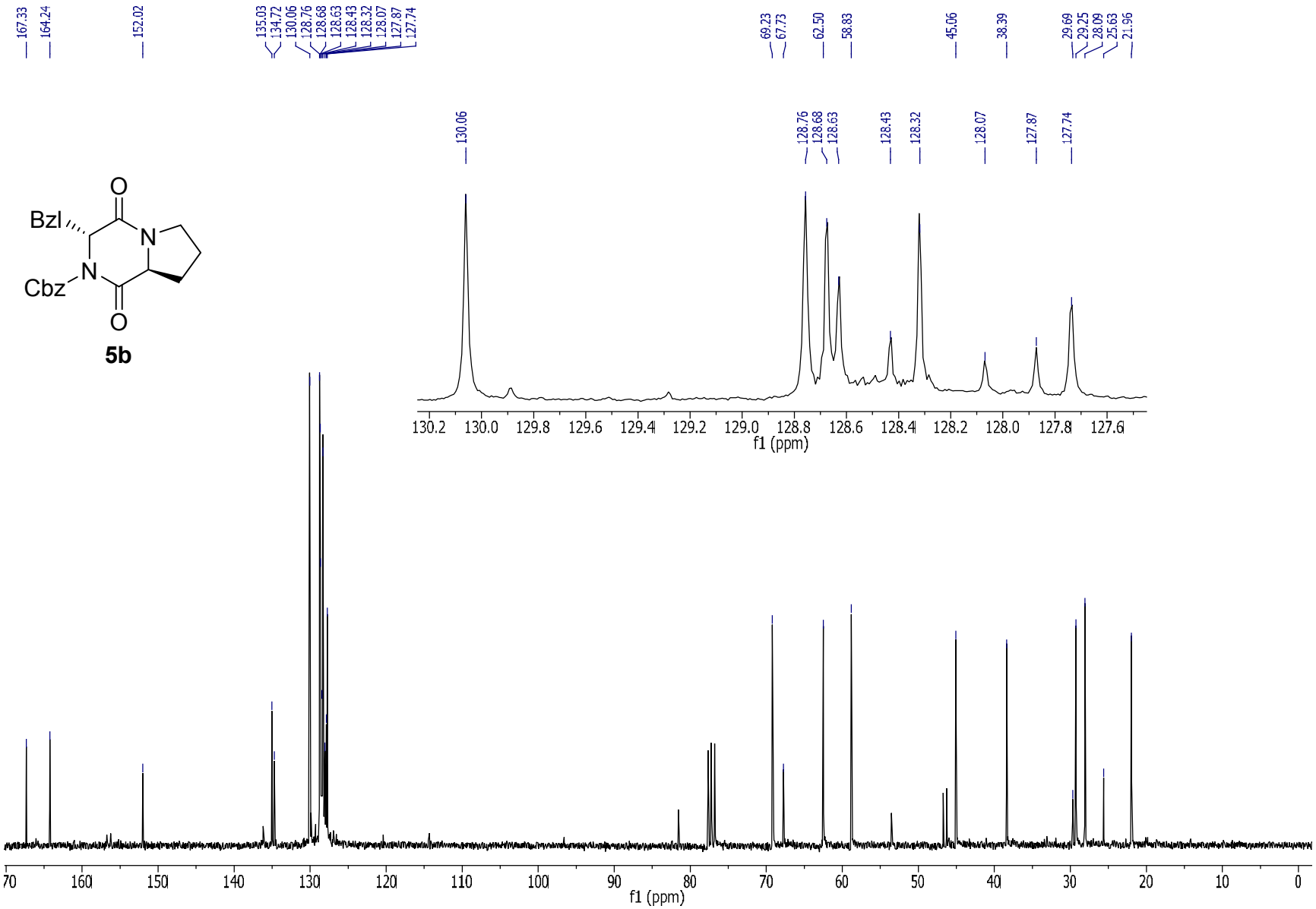

f1 (ppm)
9b

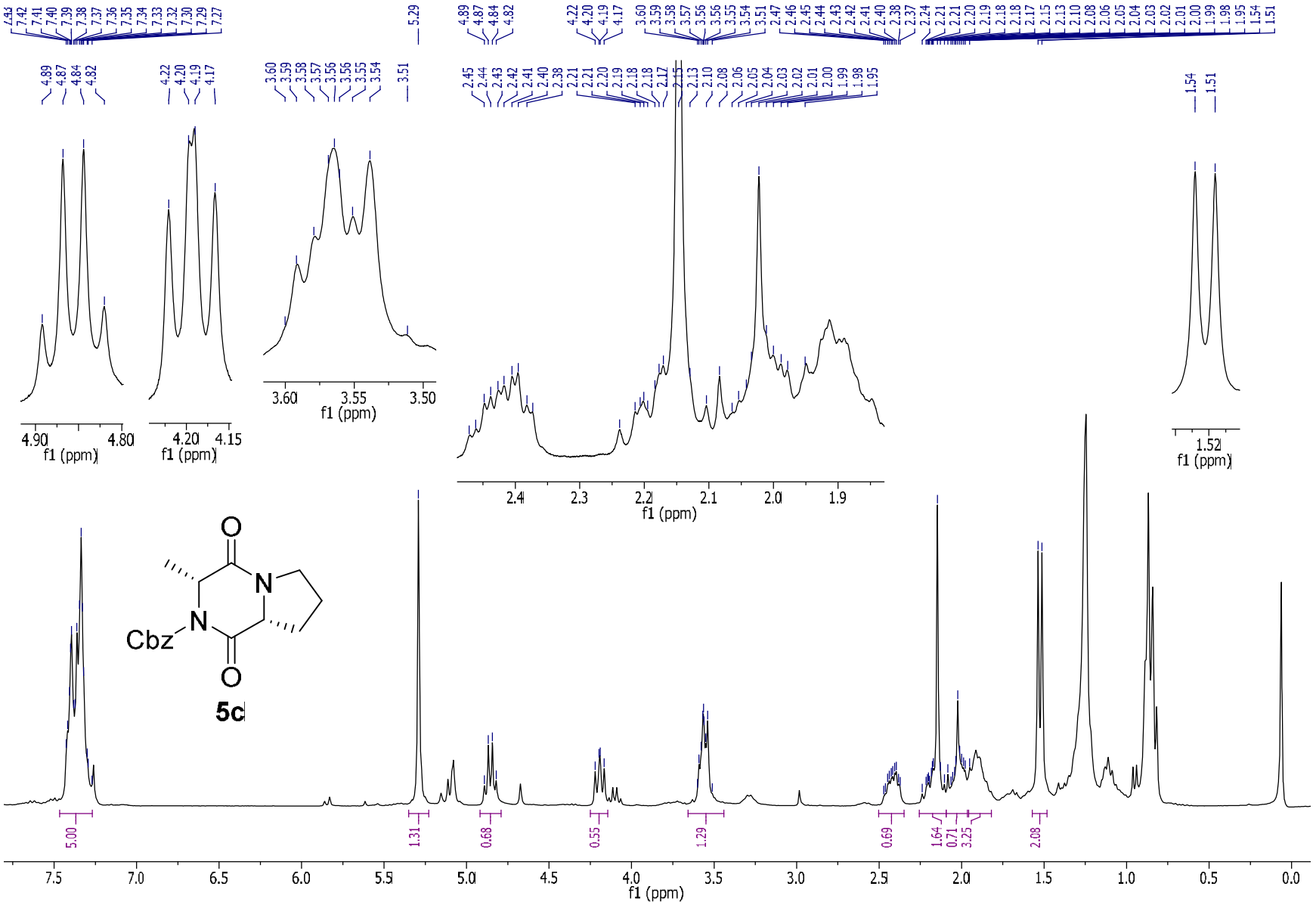

170.46
170.42
156.27
146.27
136.41
131.33
130.78
128.90
128.70
128.36
128.28
128.23
126.61
126.29
120.45
114.67
74.87
70.02
69.71
67.21
58.65
54.68
51.53
37.63
32.52
29.89
28.45
28.42
28.34
tBu-O
HN
Cbz
N
O
S
S
O
O
Bt
N
Bt
O
Cbz
NH
OtBu
9b
f1 (ppm)
f1 (ppm)

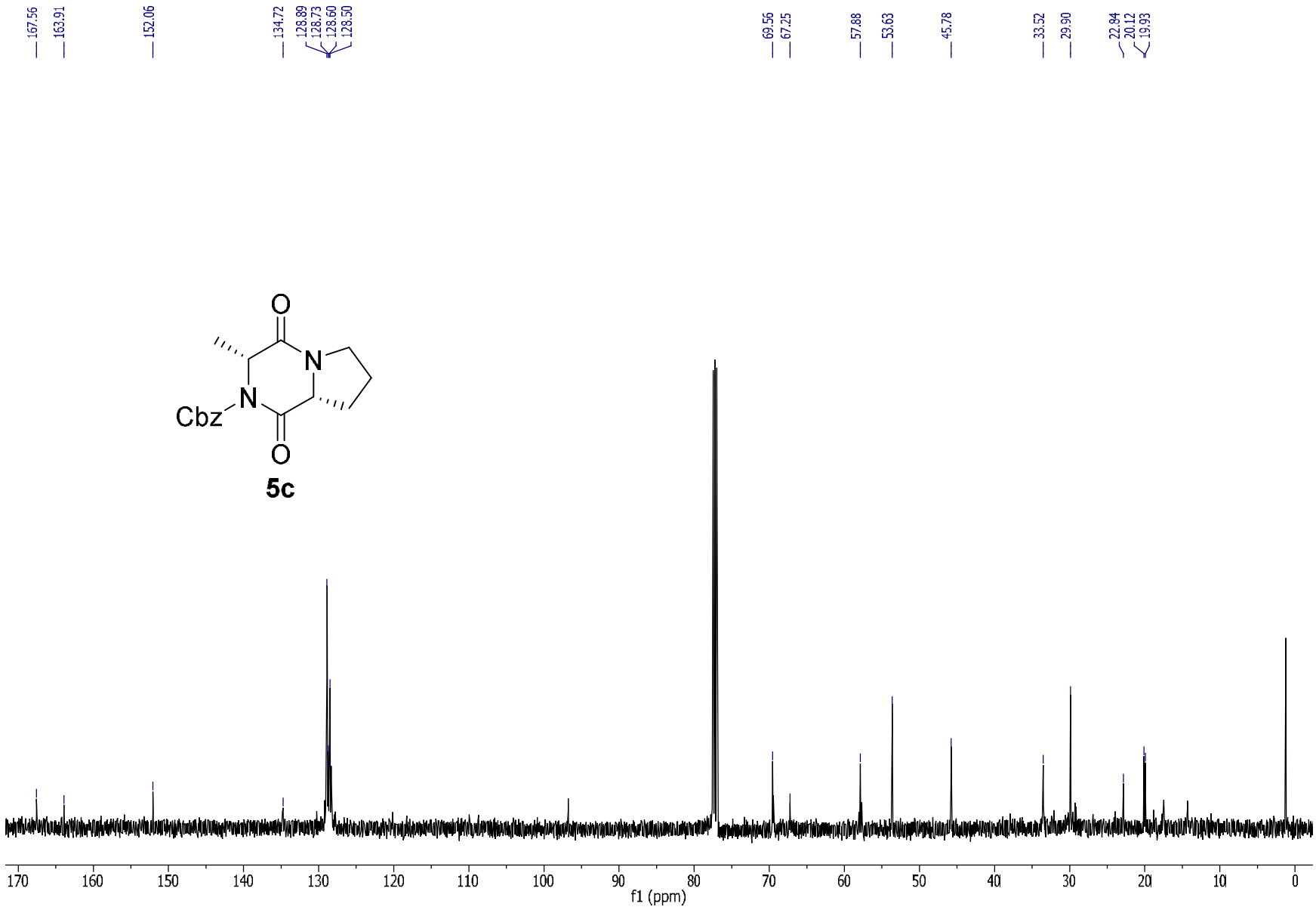

Cbz
5a
f1 (ppm)

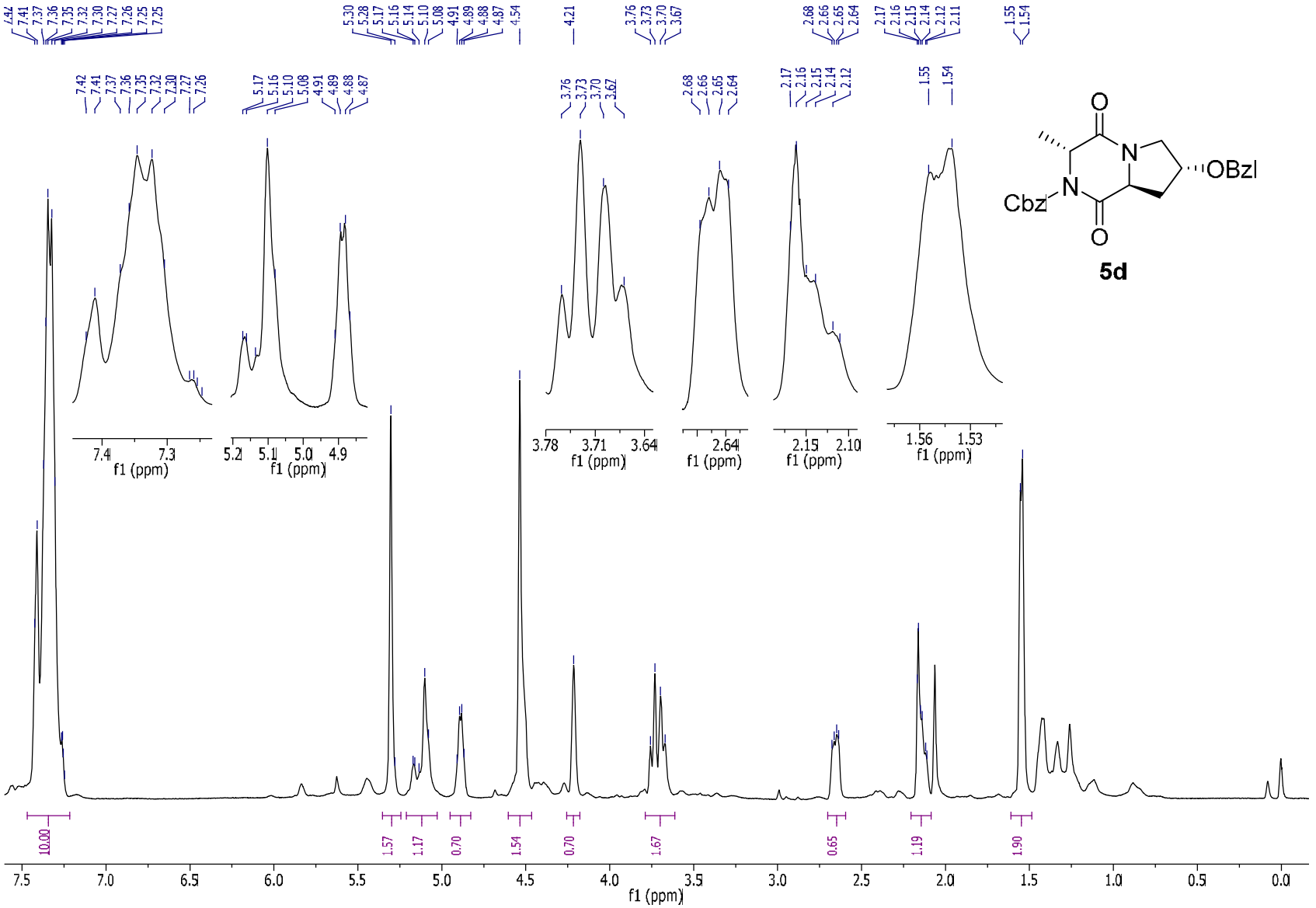

167.46
165.97
152.01
134.83
128.84
128.77
128.41
69.37
59.50
57.68
45.70
29.26
22.63
17.41
O
N
N
Cbz
O
5a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Bzl
Cbz
N
N
O
O
5b
f1 (ppm)


167.33
164.24
152.02
135.03
134.72
130.06
128.76
128.68
128.63
128.43
128.32
128.07
127.87
127.74
69.23
67.73
62.50
58.83
45.06
38.39
29.69
29.25
28.09
25.63
21.96
Bzl
Cbz
N
N
O
O
O
5b
f1 (ppm)
f1 (ppm)

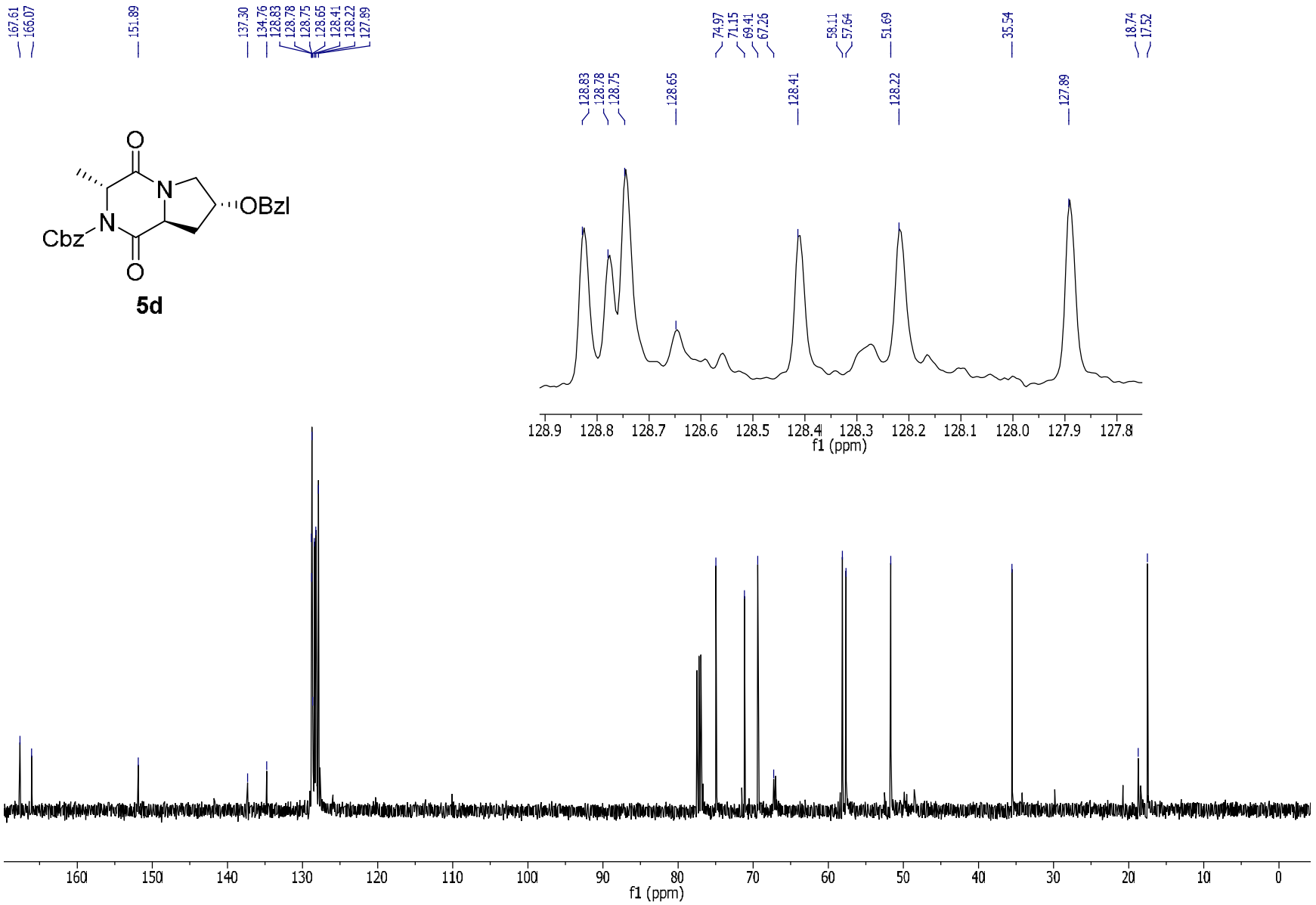

Cbz
5c
f1 (ppm)

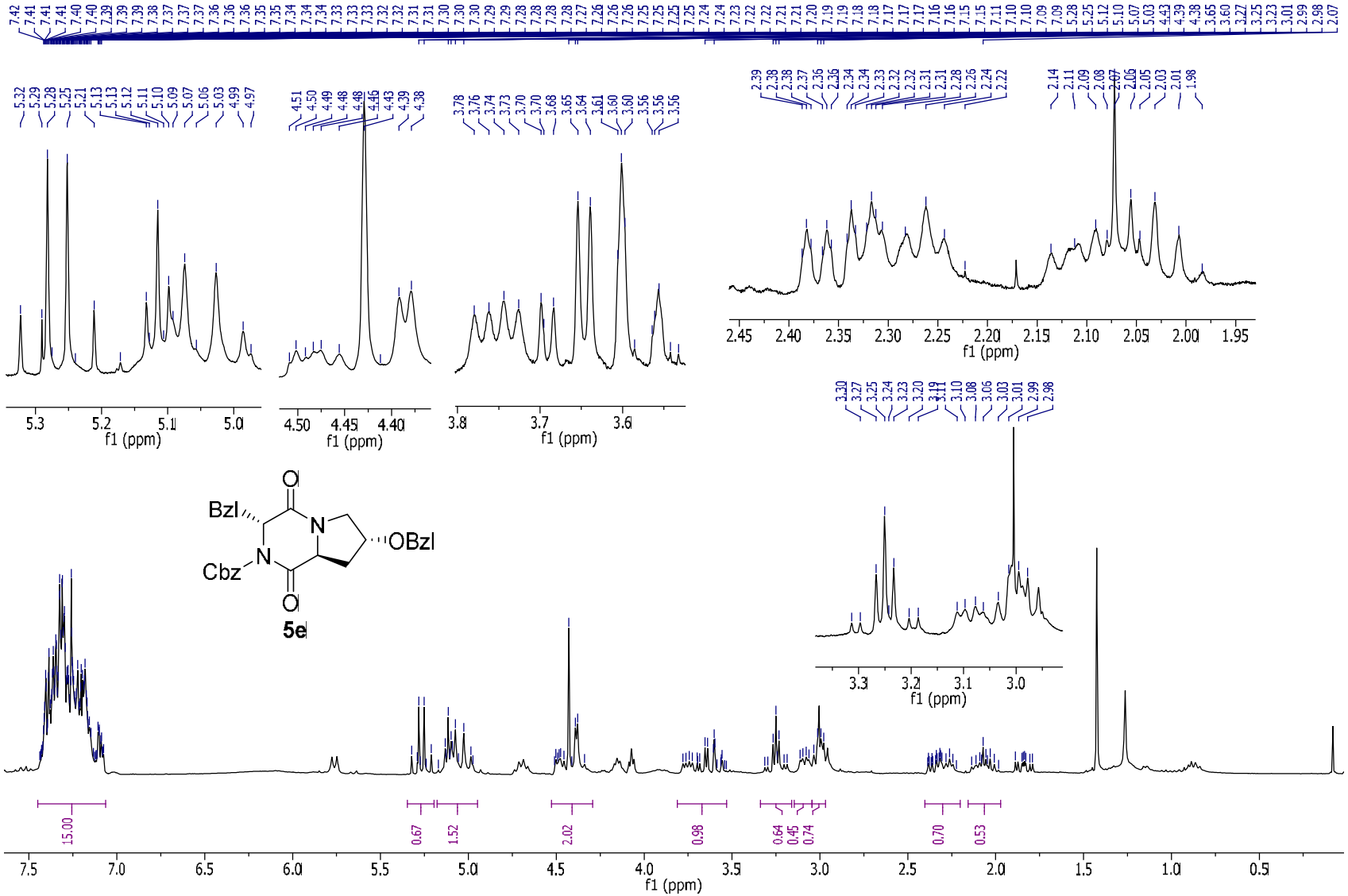

167.56
163.91
152.06
134.72
128.89
128.73
128.60
128.50
69.56
67.25
57.88
53.63
45.78
33.52
29.90
22.84
20.12
19.93
O
N
N
Cbz
O
5c
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

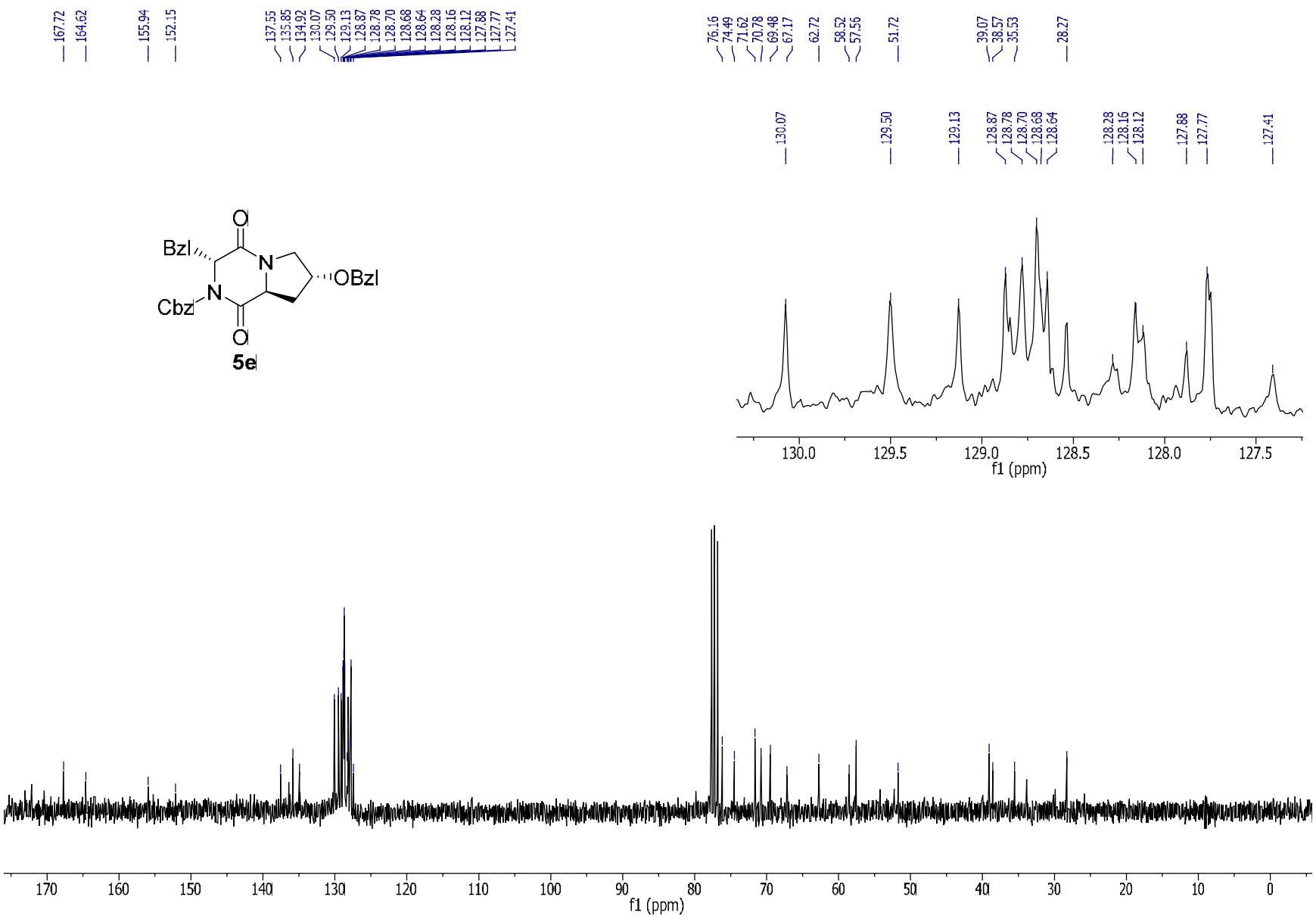

7.42
7.41
7.37
7.36
7.35
7.32
7.30
7.27
7.26
7.25
5.30
5.28
5.17
5.16
5.14
5.10
5.08
4.91
4.89
4.88
4.87
4.54
4.21
3.76
3.73
3.70
3.67
2.68
2.66
2.65
2.64
2.17
2.16
2.15
2.14
2.12
2.11
1.55
1.54
f1 (ppm)
10.00
1.57
1.17
0.70
1.54
0.70
1.67
0.65
1.19
1.90
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

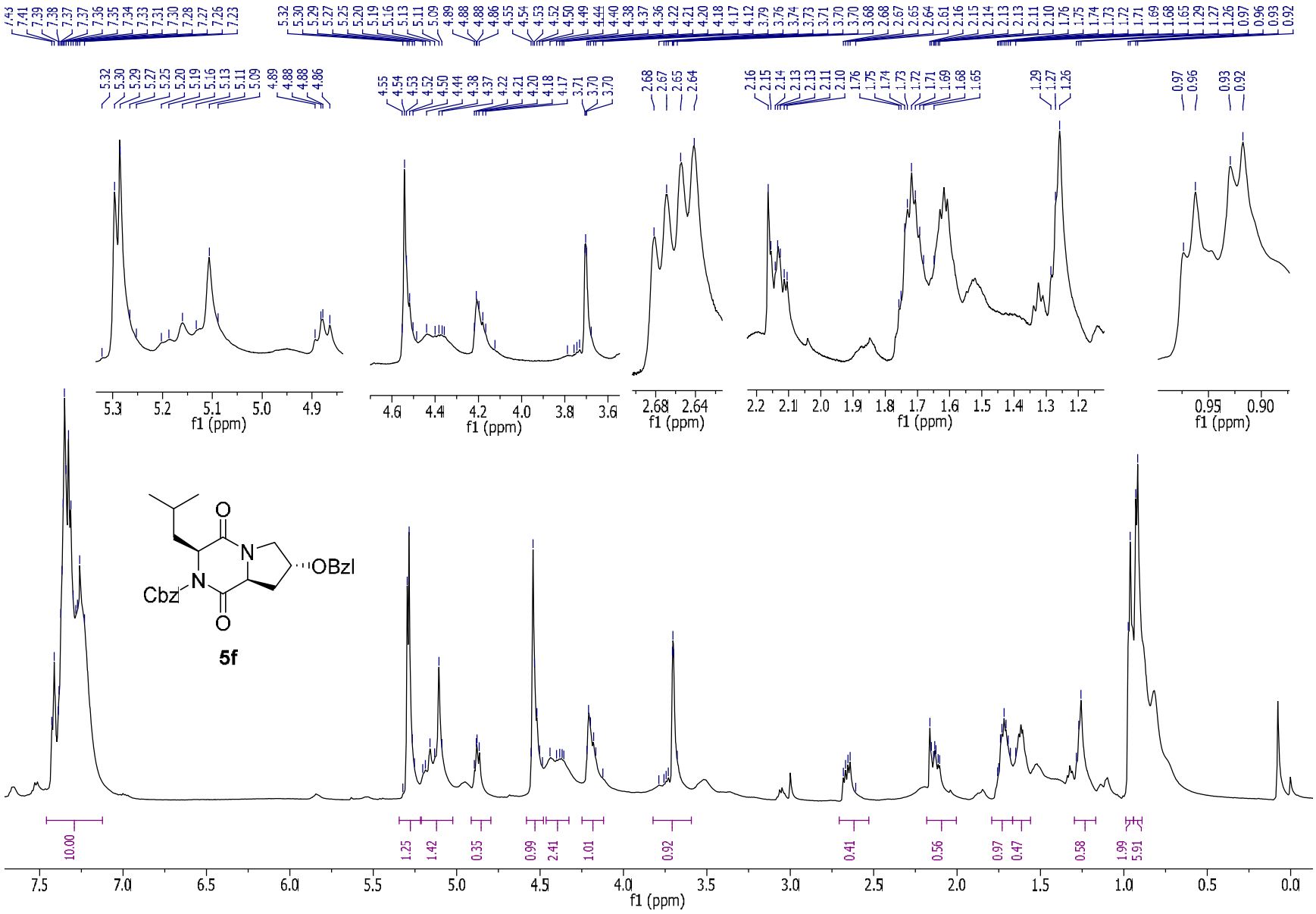
O
N
N
OBzl
Cbz
O

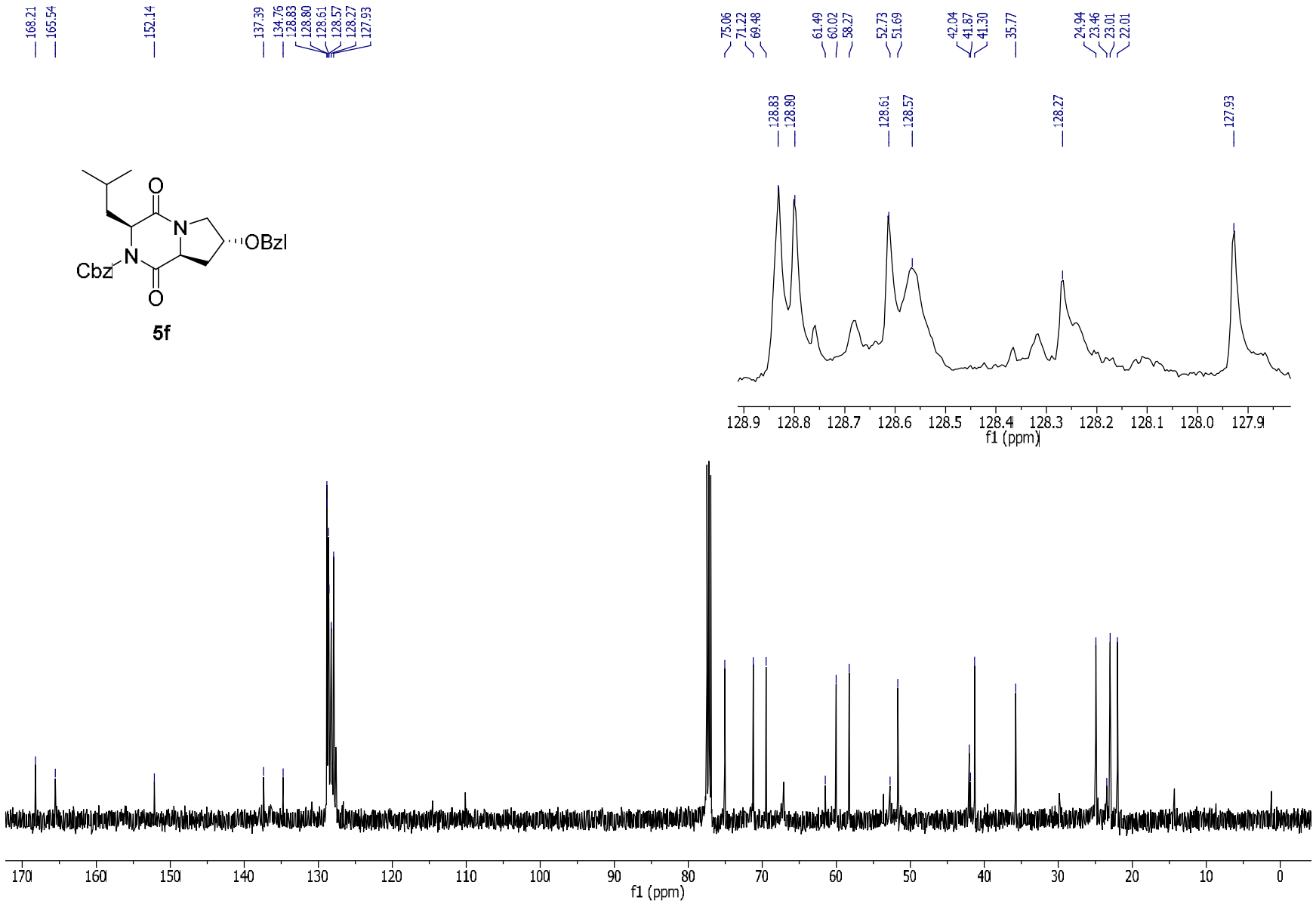
5d

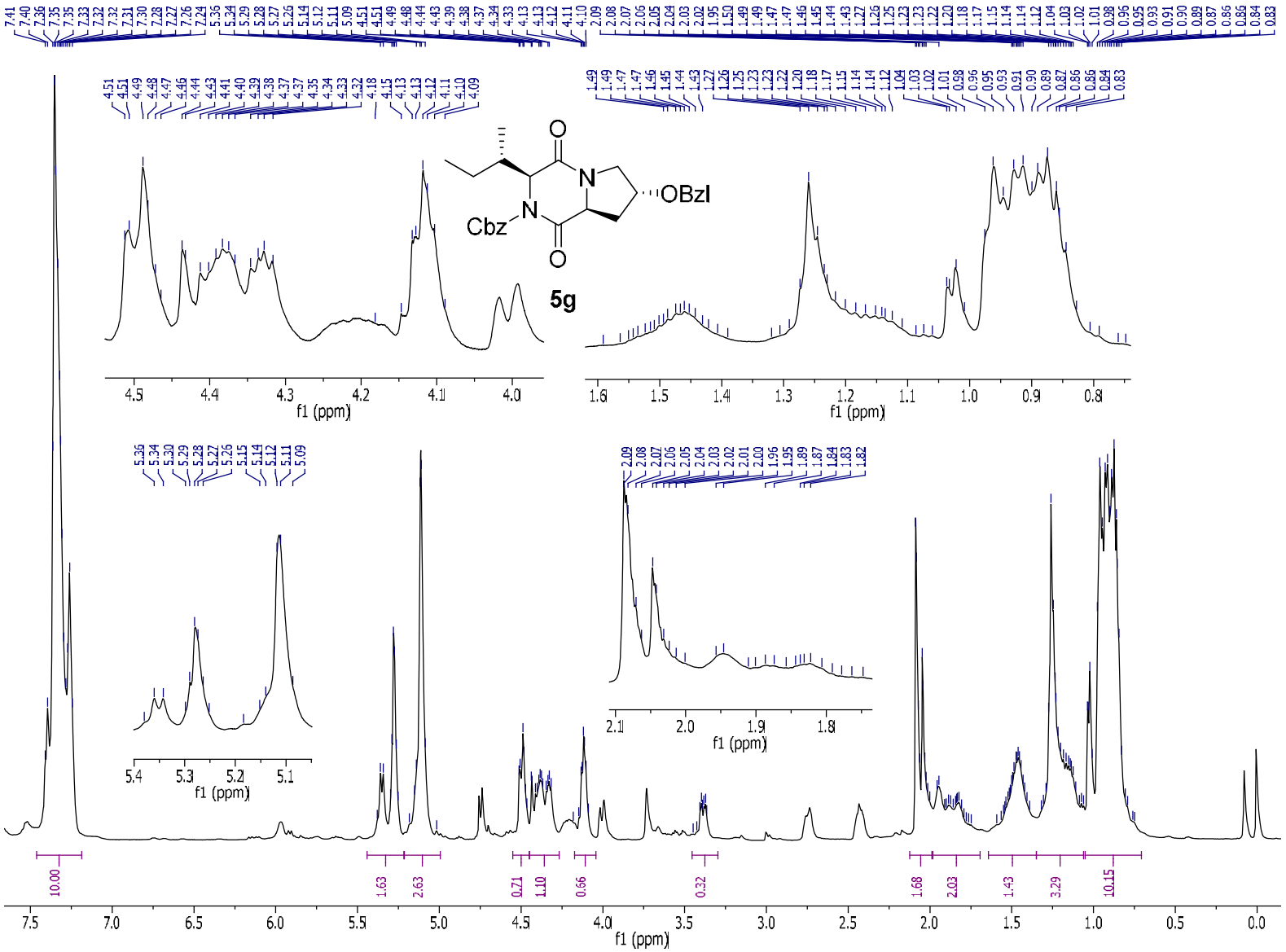

167.61
166.07
151.89
137.30
134.76
128.83
128.78
128.75
128.65
128.41
128.22
127.89
74.97
71.15
69.41
67.26
58.11
57.64
51.69
35.54
18.74
17.52
OBzl
Cbz
5d
f1 (ppm)
f1 (ppm)

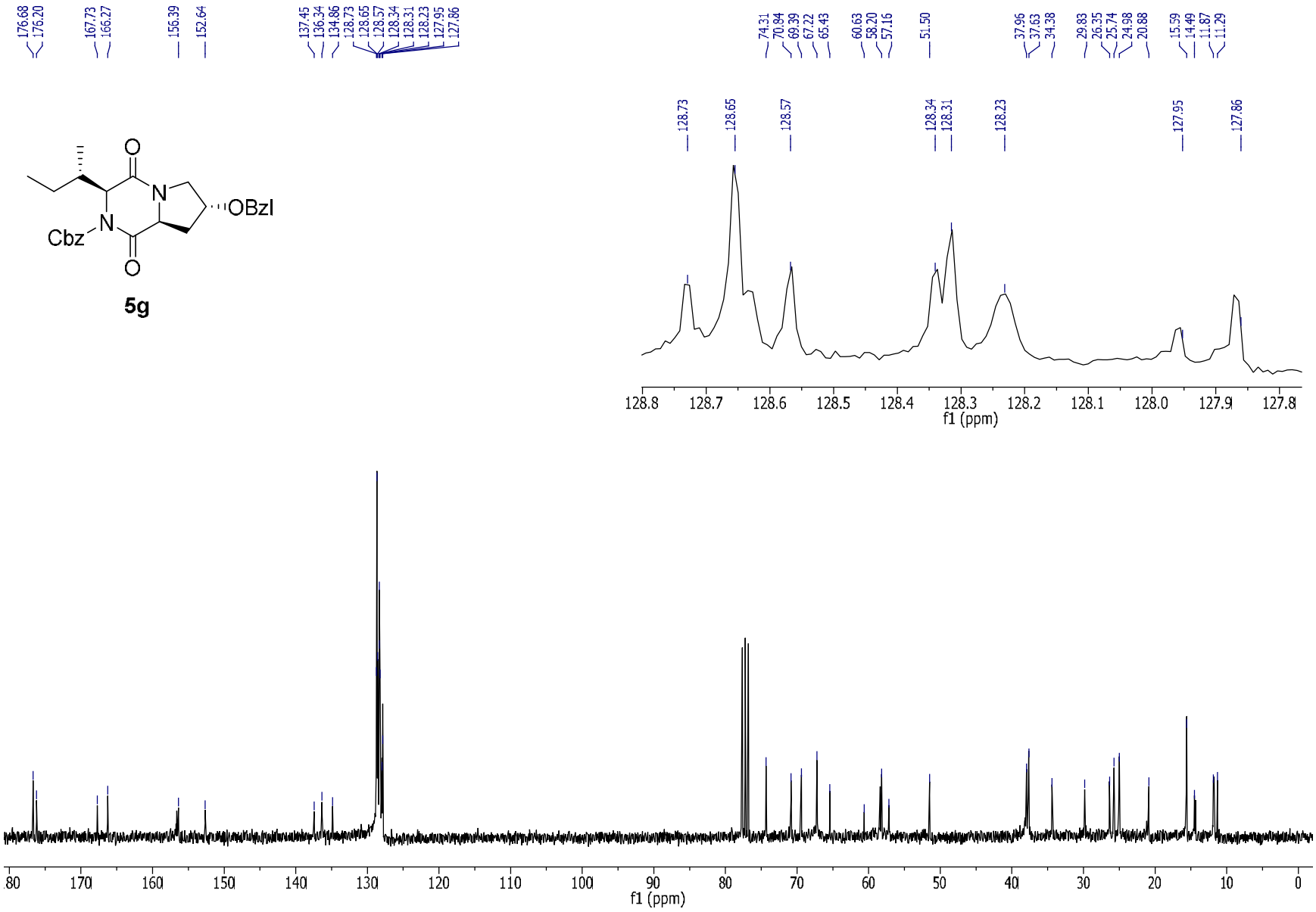

BzI
N
OBzI
Cbz
N
O
O
O
5e
f1 (ppm)

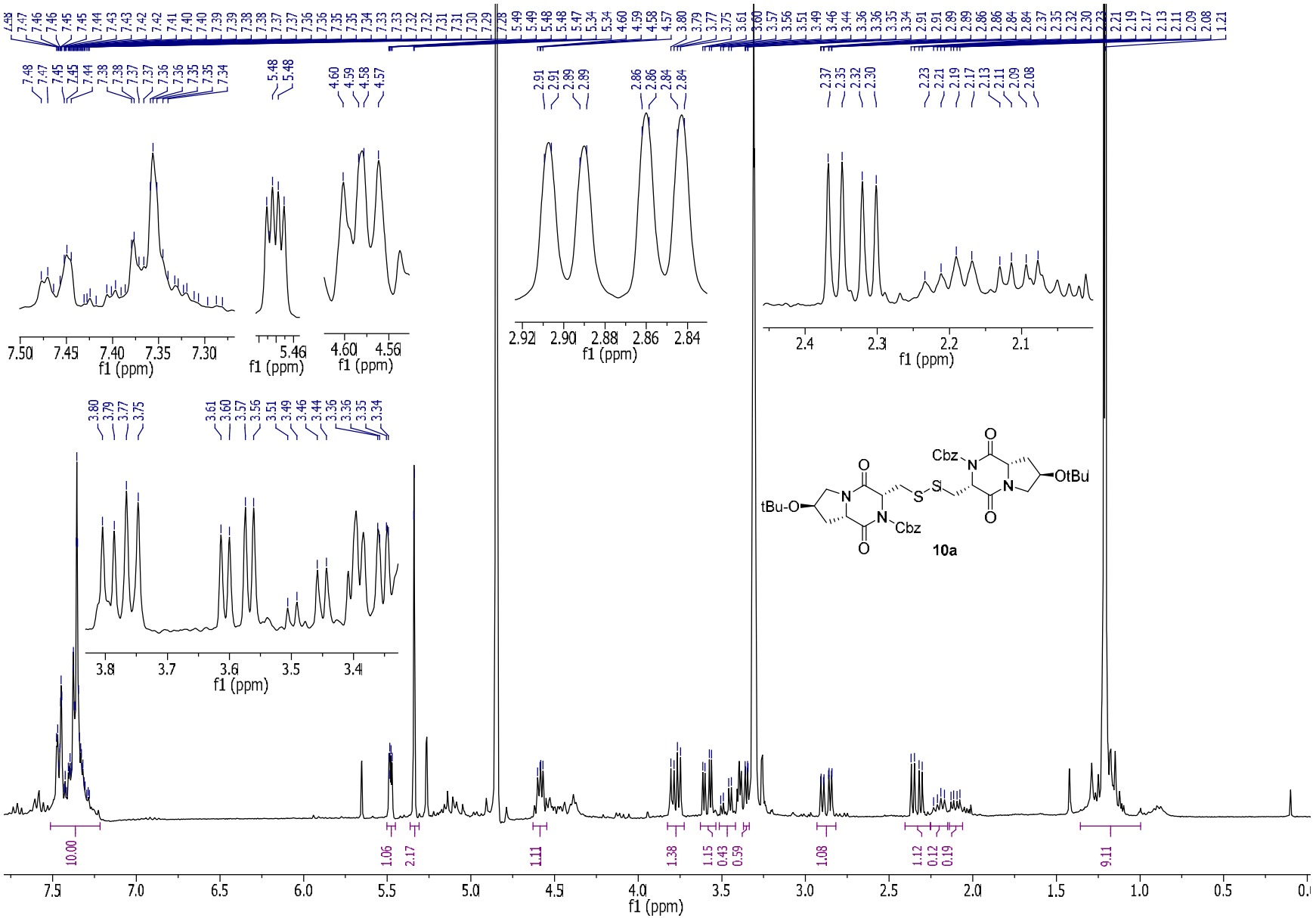

167.72
164.62
155.94
152.15
137.55
135.85
134.92
130.07
129.50
129.13
128.87
128.78
128.70
128.68
128.64
128.28
128.16
128.12
127.88
127.77
127.41
76.16
74.49
71.62
70.78
69.48
67.17
62.72
58.52
57.56
51.72
39.07
38.57
35.53
28.27
Bzl
N
OBzl
N
Cbz
O
O
5e
f1 (ppm)
f1 (ppm)

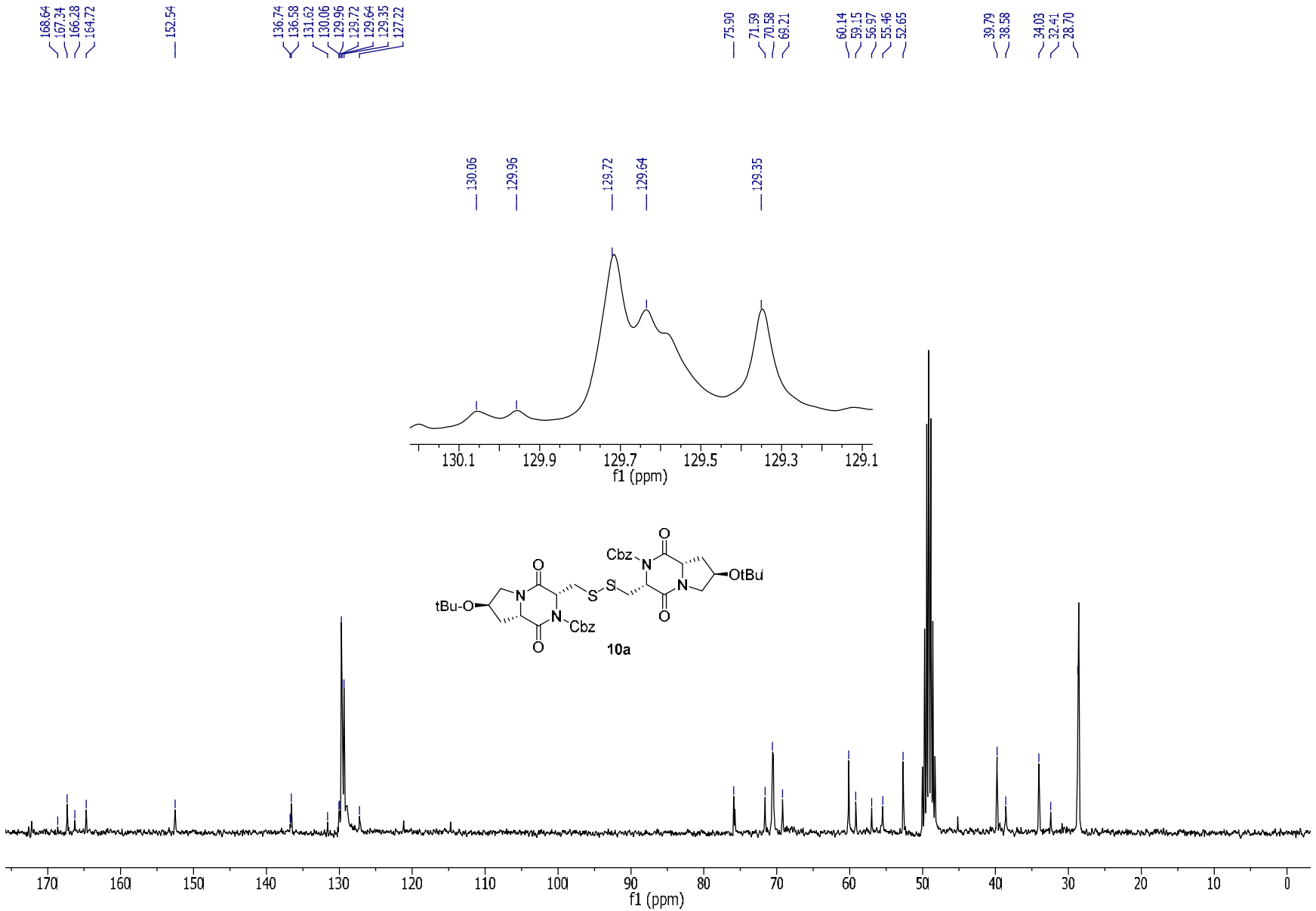

f1 (ppm)
Cbz
OBzl
5f

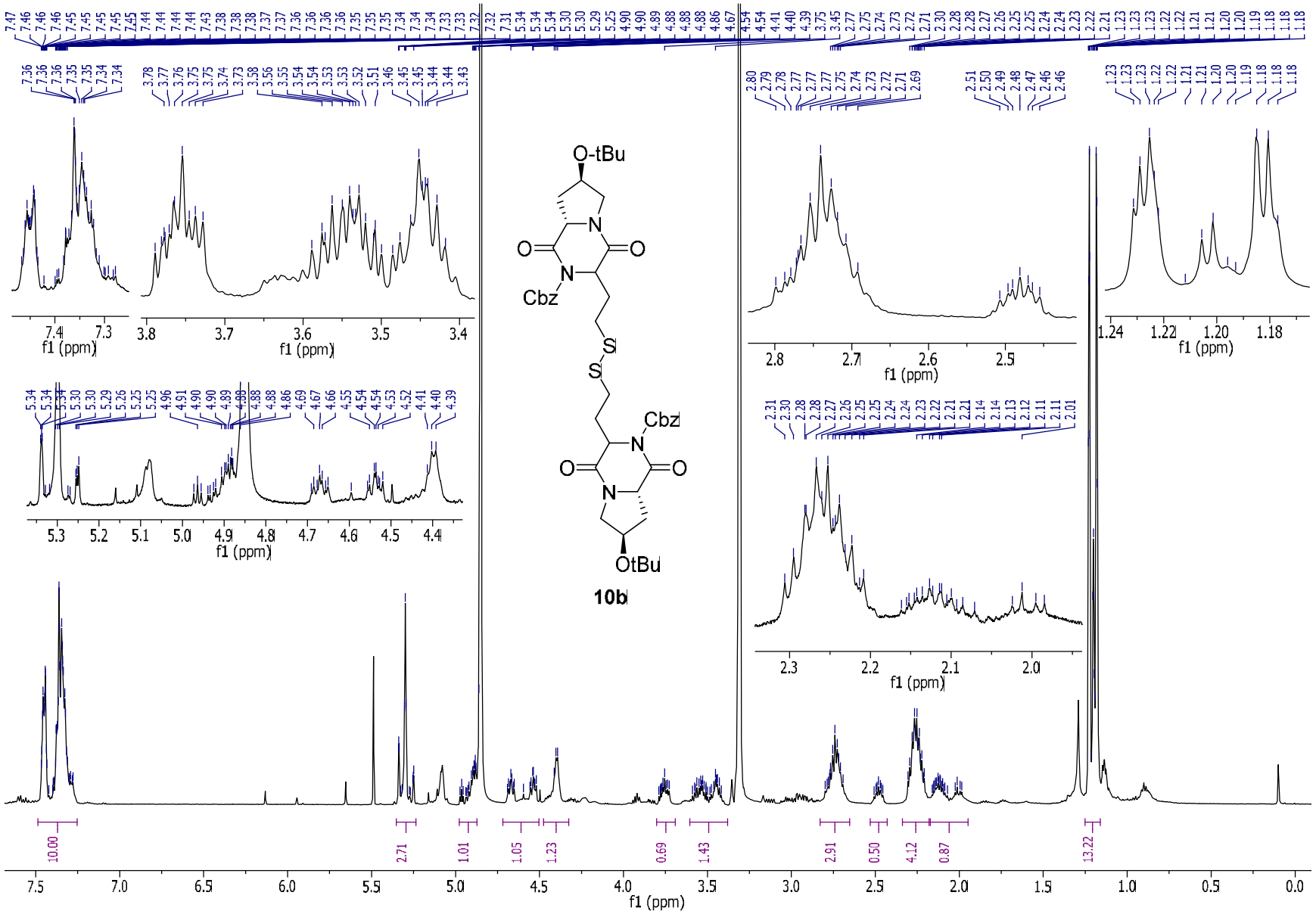

168.21
165.54
152.14
137.39
134.76
128.83
128.80
128.61
128.57
128.27
127.93
75.06
71.22
69.48
61.49
60.02
58.27
52.73
51.69
42.04
41.87
41.30
35.77
24.94
23.46
23.01
22.01
O
N
OBzl
N
Cbz
O
5f
f1 (ppm)
f1 (ppm)

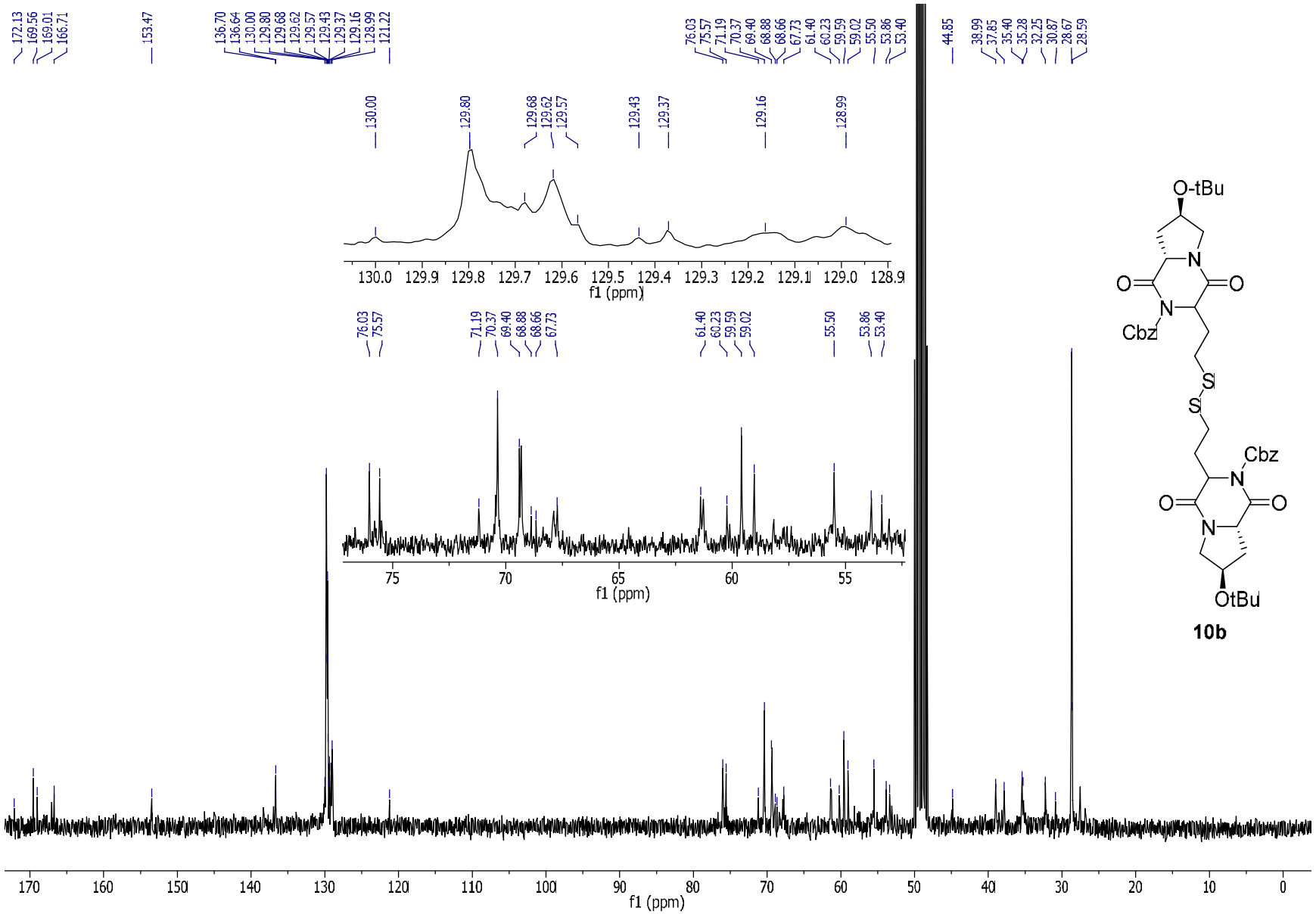

OBzl
Cbz
5g
f1 (ppm)


176.68
176.20
167.73
166.27
156.39
152.64
137.45
136.34
134.86
128.73
128.65
128.57
128.34
128.31
128.23
127.95
127.86
74.31
70.84
69.39
67.22
65.43
60.63
58.20
57.16
51.50
37.96
37.63
34.38
29.83
26.35
25.74
24.98
20.88
15.59
14.49
11.87
11.29
O
N
N
Cbz
OBzl
O
5g
128.8
128.7
128.6
128.5
128.4
128.3
128.2
128.1
128.0
127.9
127.8
f1 (ppm)
f1 (ppm)


Cbz
N
O
OtBu
tBu-O
S
Si
N
N
Cbz
O
O
O
10a
f1 (ppm)


168.64
167.34
166.28
164.72
152.54
136.74
136.58
131.62
130.06
129.96
129.72
129.64
129.35
127.22
75.90
71.59
70.58
69.21
60.14
59.15
56.97
55.46
52.65
39.79
38.58
34.03
32.41
28.70
130.06
129.96
129.72
129.64
129.35
130.1
129.9
129.7
129.5
129.3
129.1
f1 (ppm)
Cbz
N
O
OtBu
tBu-O
S
Si
Cbz
10a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O-tBu
Cbz
S
S
Cbz
OtBu
10b
f1 (ppm)


172.13
169.56
169.01
166.71
153.47
136.70
136.64
130.00
129.80
129.68
129.62
129.57
129.43
129.37
129.16
128.99
121.22
76.03
75.57
71.19
70.37
69.40
68.88
68.66
67.73
61.40
60.23
59.59
59.02
55.50
53.86
53.40
44.85
38.99
37.85
35.40
35.28
32.25
30.87
28.67
28.59
f1 (ppm)
O-tBu
Cbz
OtBu
10b