Concise synthesis of bicyclic iminosugars *via* reductive functionalization of sugar-derived lactams and subsequent RCM reaction

Piotr Szcześniak and Bartłomiej Furman*

Institute of Organic Chemistry, Polish Academy of Sciences

Kasprzaka 44/52, 01-224 Warsaw, Poland

Corresponding authors: bfurman@icho.edu.pl

Table of Context:

1. General Information. *S2*

2. Experimental Section. *S2-S13*

2.1 *One-pot* lactam reduction/C-allylation. General procedure for the synthesis of **3a** and **3b**. *S4-S5*

2.2 *One-pot* -lactam reduction/C-vinylation. General procedure for the synthesis of **8a** and **8b**. *S5-S6*

2.3 *N*-allylation of **3a**, **3b**, **8a** and **8b**. General procedure for the synthesis of **5a**, **5b**, **10a** and **10b**. *S6-S8*

2.4 *N*-acylation of **3a**, **3b** and **8b**. General procedure for the synthesis of: **4a**, **4b** and **9b**. *S8-S9*

2.5 Ring Closing Metathesis of **4a**, **4b**, **5a** or **5b**. General procedure for the synthesis of **6a**, **6b**, **7a** or **7b**. *S10-S11*

2.6 The synthesis of **12a**. *S11-S12*

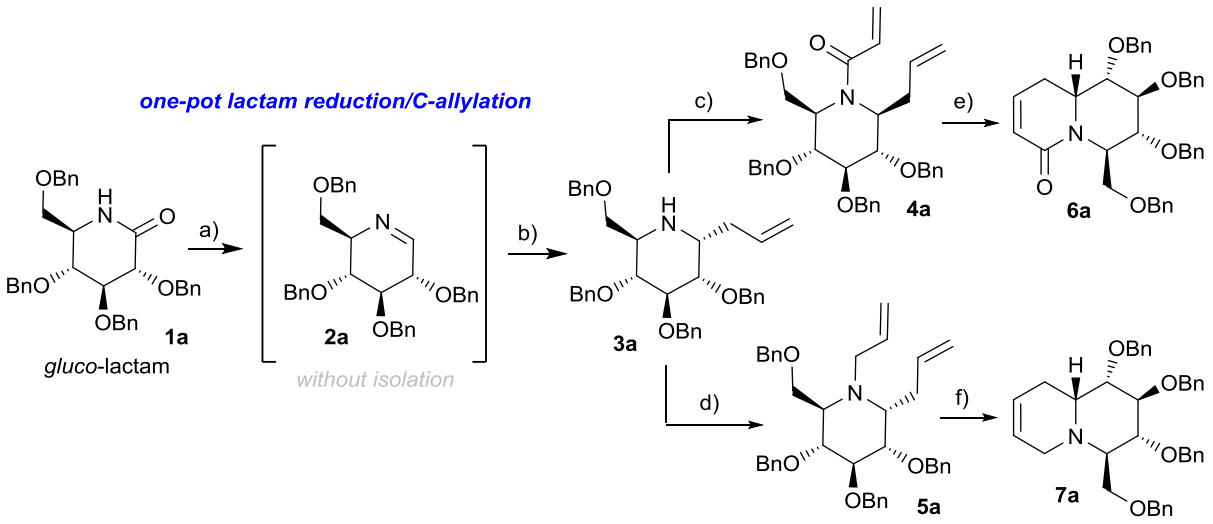
2.7 The synthesis of **11b**. *S12*

2.8 The synthesis of **12b**. *S12-S13*

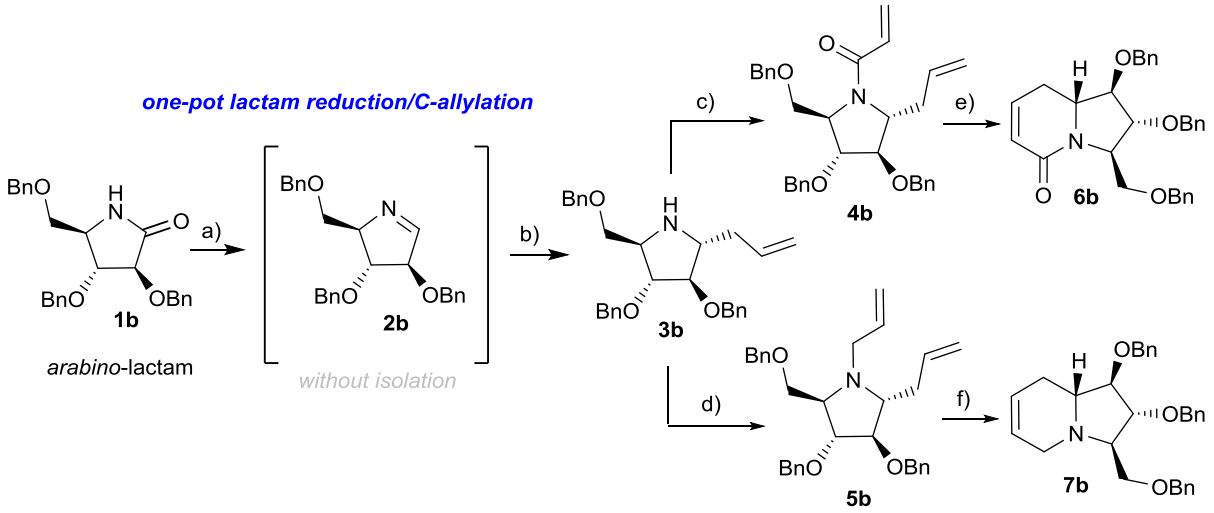
3. Copies of ^{1}H, ^{13}C NMR, HPLC spectra. *S14-S47*

General information:

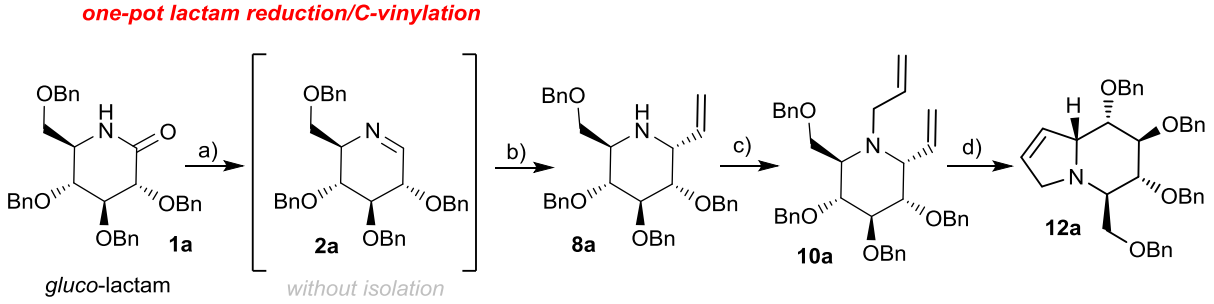
^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian VNMRS 500 and Varian VNMRS 600 spectrometers, in $CDCl_3$, unless otherwise stated, and with TMS used as an internal standard. Chemical shifts (δ) were given in ppm and coupling constants (*J*) were given in Hertz (Hz). Infrared spectra were recorded on a FT-IR Jasco 6200 and FT-IR Spectrum 2000 Perkin Elmer spectrophotometer. High-resolution mass spectra were recorded on ESI-TOF Mariner Spectrometer, SYNAPT G2-S HDMS or AMD 604 mass spectrometer. Optical rotations were measured with Jasco P-2000 polarimeter. Thin layer chromatography was performed on Merck aluminium sheet Silica Gel 60 F254. Column chromatography was carried out using Merck silica gel (230-400 mesh).



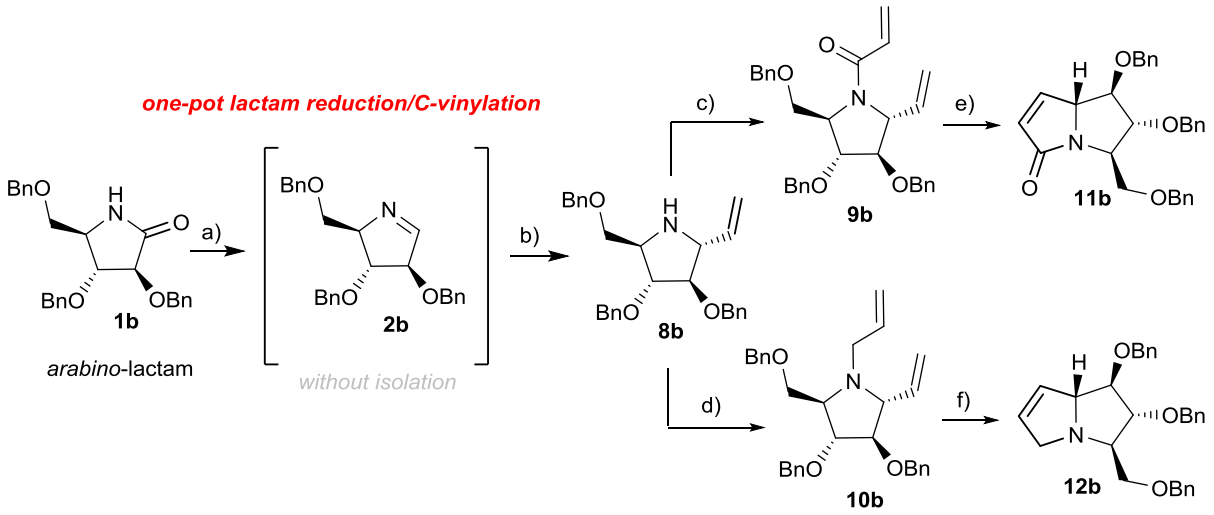
Scheme 1. *Reagent and conditions*: a) $Cp_2Zr(H)Cl$ (1.6 equiv.), THF, rt, 10 min.; b) $Yb(OTf)_3$ (1.0 equiv.), allyltributylstannane (3.0 equiv.),THF, –25 °C to rt., overall yield for two steps 84%, *d.r.* 90:10; c) acryloyl chloride, Et_3N, CH_2Cl_2, 68%; d) allyl bromide (10 equiv.), K_2CO_3 (1.6 equiv.), Bu_4NI (cat.), DMF, quant. yield; e) Grubbs catalyst 2nd generation **Ru2**, (5 mol%), toluene, 60 °C, 74%; f) Grubbs catalyst 2nd generation **Ru2**, (5 mol%), toluene, 60 °C, 81%.



Scheme 2. *Reagent and conditions*: a) 1) $Cp_2Zr(H)Cl$ (1.6 equiv.), THF, rt, 10 min.; b) $Yb(OTf)_3$ (1.0 equiv.), allyltributylstannane (3.0 equiv.),THF, -25 °C, rt. overall yield for two steps 70%, *d.r.*79:21; c) acryloyl chloride, Et_3N, CH_2Cl_2, 58% d) allyl bromide (10 equiv.), K_2CO_3 (1.6 equiv.), Bu_4NI (cat.), DMF, quant. yield; e) Grubbs catalyst 2nd generation **Ru2**, (5 mol%), toluene, 60 °C, 76%; f) Grubbs catalyst 2nd generation **Ru2**, (5 mol%), toluene, 60 °C, 83%.



Scheme 3. *Reagent and conditions*: a) $Cp_2Zr(H)Cl$ (1.6 equiv.), THF, rt, 10 min.; b) vinylmagnesiumbromide (7.0 equiv.), THF, –45 °C to rt., 56% overall yield for two steps, *d.r.*>95%; c) allyl bromide (10 equiv.), K_2CO_3 (1.6 equiv.), Bu_4NI (cat.), DMF, 98%; d) **Ru4**, (2 mol%), xylene, b.p., 89%.



Scheme 4. *Reagent and conditions*: a) $Cp_2Zr(H)Cl$ (1.6 equiv.), THF, rt. 10 min.; b) vinylmagnesium bromide (7.0 equiv.),THF, -45 °C, to r.t., overall yield for two steps 72%, *d.r.* >95:5; c) acryloyl chloride (2 equiv.), Et_3N (2 equiv.), CH_2Cl_2, 88%; d) allyl bromide (10 equiv.), K_2CO_3 (1.6 equiv.), Bu_4NI (cat.), DMF, quant. yield; e) nitro-Grela catalyst **Ru3**, (2% mol), DCE, b.p., 64%; f) Grubbs catalyst 2nd generation **Ru2**, (10% mol), DCE, b.p., 79%.

Experimental Section:

***One-pot* lactam reduction/C-allylation. General procedure:**

A solution of sugar lactam **1a** or **1b** (0.5 mmol) in THF (5 mL) was added dropwise to suspension of $Cp_2Zr(H)Cl$ (1.6 equiv, 0.8 mmol, 206 mg) in THF (5 mL) at rt under argon atmosphere. The mixture was stirred until white suspension disappeared (ca. 10 min.) and clear solution arisen. Then the solution was cooled to –25 °C and $Yb(OTf)_3$ was added (1.0 equiv., 0.5 mmol, 310 mg). After 10 min allyltributylstannane (3 equiv., 1.5 mmol, 460 ml) was added dropwise. The mixture was warmed gradually to ambient temperature and stirred overnight. Solvent was removed under diminished pressure and the residue was diluted with MeCN (5 mL), and washed with hexanes (3 x 5 mL). Acetonitrile solution was separated, and concentrated under reduced pressure. The residue was chromatographed on silica gel to afford the corresponding allylamines **3a** or **3b**. Diastereomeric ratio of products was determined by HPLC of crude reaction mixture. The spectral data for major isomer are given.

(*2R*,3*S*,*4R*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-(benzyloxymethyl) piperidine (3a) and **(2-*epi*-3a):** inseparable mixture of diastereoisomers; colorless oil; 84%; *d.r.* 90:10 (determined by HPLC); R*f* 0.25 (25% AcOEt/hexanes); column chromatography (20% AcOEt/hexanes); $[\alpha]_D^{22}$ +47.9 (*c* 0.5, CH_2Cl_2); major isomer **3a**: ^{1}H NMR (600 MHz, C_6D_6) δ: 7.40–7.10 (m, 20H), 5.78–5.67 (m, 1H), 5.10–5.02 (m, 2H), 4.98 (d, *J* 11.2 Hz, 1H), 4.91 (d, *J* 11.4 Hz, 1H), 4.78 (d, *J* 11.2 Hz, 1H), 4.46 (d, *J* 11.3 Hz, 1H), 4.40 (d, *J* 5.4 Hz, 1H), 4.25 (d, *J* 12.0 Hz, 1H), 4.17 (d, *J* 12.0 Hz, 1H), 3.78–3.72 (m, 1H), 3.65 (dd, *J* 8.7, 2.6 Hz, 1H), 3.61 (dd, *J* 9.5, 5.6 Hz, 1H), 3.47 (dd, *J* 8.8, 6.7 Hz, 1H), 3.38–3.34 (m, 1H), 3.10–3.02 (m, 2H), 2.53–2.43 (m, 1H), 2.31 (ddd, *J* 14.4, 11.6, 8.2 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 138.9, 138.5, 138.3, 138.2, 135.8, 128.38, 128.35, 128.34, 128.33, 128.30, 128.0, 127.9, 127.7, 127.68, 127.61, 127.5, 127.4, 117.5, 83.3, 82.0, 80.5, 75.5, 75.2, 73.0, 72.5, 70.6, 53.6, 52.6, 29.8; HRMS (ESI-TOF) *m/z* calc for $C_{37}H_{42}NO_4$ $[M+H^+]$ 564.3114. Found 564.3114; IR (film) *v*: 3030, 2920, 2858, 1496, 1453,

1100, 1068, 735, 697 cm^{-1}; HPLC: Chiralpak® AD-H, 1% *i*- PrOH/heksan, 0.5 ml/min., UV 218 nm, R_t 40.0 min (**3a**), 52.6 min (**2-*epi*-3a**).

(2*R*,3*R*,4*R*,5*R*)-2-Allyl-3,4-bis(benzyloxy)-5-(benzyloxymethyl) pyrrolidine (**3b**) and (**2-*epi*-3b**): inseparable mixture of diastereoisomers; colorless oil; 70%; *d.r.* 79:21 (determined by HPLC and ^{1}H-NMR); R*f* 0.38 (3:2 AcOEt/hexanes); column chromatography (1:1 AcOEt/hexanes); $[\alpha]_D^{25}$ +19.1 (c 0.24, CH2Cl2); major isomer (**3a**): ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.36–7.21 (m, 15H), 5.79 (ddt, *J* 17.2, 10.2, 7.1 Hz, 1H), 5.11–5.04 (m, 2H), 4.56–4.48 (m, 6H), 3.89–3.87 (m, 1H), 3.74–3.73 (m, 1H), 3.51 (dd, *J* 6.1, 3.2 Hz, 2H), 3.40 (dt, *J* 10.2, 5.2 Hz, 1H), 3.19 (dd, *J* 12.8, 5.5 Hz, 1H), 2.36 (dt, *J* 13.4, 6.5 Hz, 1H), 2.29–2.21 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 138.19, 138.17, 138.16, 135.2, 128.38, 128.34, 128.33, 128.30, 127.78, 127.74, 127.7, 127.65, 127.64, 127.63, 127.60, 127.59, 117.3, 88.6, 86.3, 73.2, 71.8, 71.7, 70.8, 61.7, 61.3, 38.0; minor isomer (**2-*epi*-3a**) selected signals: ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 3.82 (d, J 3.9 Hz, 1H), 3.77 (d, J 4.0 Hz, 1H), 3.56 (m, 2H), 3.27 (dd, J 9.5, 5.4 Hz, 1H), 2.42 (dt, J 13.8, 6.8 Hz, 1H); IR (film) v: 3422, 2923, 2856, 1453, 1362, 1094, 912, 735, 697 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{39}H_{34}NO_3$ [M+H^+] 444.2539. Found 444.2574; HPLC: Chiralpak® AD-H, 5% i-PrOH in hexanes, flow 0.5 ml/min, UV 218 nm, R_t 23.5 min (**2-*epi*-3a**), 26.0 min (**3a**).

***One-pot* -lactam reduction/C-vinylation. General procedure:**

A solution of sugar lactam **1a** or **1b** (0.5 mmol) in THF (5 mL) was added dropwise to suspension of $Cp_2Zr(H)Cl$ (1.6 equiv., 0.8 mmol, 206 mg) in THF (5 mL) at rt under argon atmosphere. The mixture was stirred until white suspension disappeared (ca. 10 min.) and clear solution arisen. Next, the imine solution was cannulated to solution of vinylmagnesiumbromide (7.0 equiv., 3.5 mmol) in Et_2O at –45 ˚C. The mixture was gradually warmed to ambient temperature and stirred until all imine was consumed. Then, the mixture was diluted with Et_2O, and quenched by dropwise addition of H_2O. The aqueous phase was separated and washed with Et_2O (2 x 5 mL). The combined organic layers were dried over anhyd. Na_2SO_4, filtered and solvents were removed under diminished pressure to give the residue. The residue was chromatographed on silica gel to afford the corresponding vinylamines **8a** or **8b**.

(2*R*,3*R*,4*R*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-2-((benzyloxy)methyl)-6-vinylpiperidine; (8a): colorless oil; 56%, *d.r.* >95:5 (determined by ^{1}H NMR); R*f* 0.56 (50% AcOEt/hexanes); column chromatography (20% AcOEt/hexanes); $[\alpha]_D^{23}$ +62.7 (*c* 1.06, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.35–7.24 (m, 15H), 7.18–7.15 (m, 2H), 6.22–6.15 (m, 1H), 5.36 (d, *J* 17.5 Hz, 1H), 5.32 (d, *J* 10.7 Hz, 1H), 4.93 (d, *J* 10.8 Hz, 1H), 4.84 (d, *J* 10.9 Hz, 1H), 4.76 (d, *J* 10.8 Hz, 1H), 4.68 (d, *J* 11.6 Hz, 1H), 4.65 (d, *J* 11.6 Hz, 1H), 4.49 (d, *J* 11.9 Hz, 1H), 4.46 (d, *J* 10.9 Hz, 1H), 4.42 (d, *J* 11.9 Hz, 1H), 3.87–3.82 (m, 1H), 3.73–3.64 (m, 3H), 3.50 (dd, *J* 9.0, 6.1 Hz, 1H), 3.39 (t, *J* 9.0 Hz, 1H), 3.13–3.09 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 141.5, 141.0, 140.7, 131.02, 131.00, 130.7, 130.6, 130.50, 130.46, 130.33, 130.29, 130.15, 120.6, 86.2, 84.3, 83.0, 78.3, 77.85, 75.93, 75.1, 72.9, 58.5, 56.1; HRMS (ESI-TOF) *m/z* calc. for $C_{36}H_{40}NO_4$ [M+H$^+$], 550,2957. Found 550,2964; IR (film) *v*: 3344, 3030, 2903, 2864, 1496, 1454,1362, 1093, 1069, 736, 697 cm^{-1}.

(2*R*,3*R*,4*R*,5*R*)-3,4-bis(benzyloxy)-2-(benzyloxymethyl)-5-vinylpyrrolidine; (8b): colorless oil; 72%, *d.r.* >95:5 (determined by ^{1}H-NMR); R_f 0.34 (40% AcOEt in hexanes); column chromatography (25% AcOEt in hexanes); $[\alpha]_D^{23}$ +7.35 (*c* 0.9, CH_2Cl_2); ^{1}H NMR (600 MHz, C_6D_6) *δ*: 7.26–7.23 (m, 3H), 7.19–7.16 (m, 2H), 7.14–7.08 (m, 8H), 7.06– 7.01 (m, 2H), 5.91–5.84 (m, 1H), 5.22–5.18 (m, 1H), 4.94 (ddd, *J* 10.2, 1.6, 1.2 Hz, 1H), 4.47–4.42 (m, 3H), 4.40 (d, *J* 11.9 Hz, 1H), 4.24 (d, *J* 12.1 Hz, 1H), 4.21 (d, *J* 12.1 Hz, 1H), 3.98 (t, *J* 4.2 Hz, 1H), 3.90 (dd, *J* 5.6, 4.0 Hz, 1H), 3.72 (dd, *J* 6.7, 5.8 Hz, 1H), 3.50 (dd, *J* 10.6, 6.0 Hz, 1H), 3.37 (dd, *J* 9.2, 5.7 Hz, 1H), 3.32 (dd, *J* 9.2, 6.5 Hz, 1H); ^{13}C NMR (151 MHz, C_6D_6) *δ*: 139.5, 138.7, 138.6, 138.5, 128.18, 128.11, 127.57, 127.52, 127.43, 127.32, 127.30, 127.27, 114.9, 89.7, 86.3, 72.8, 71.7, 71.5, 71.3, 64.4, 61.5; HRMS (ESI-TOF) *m/z* calcd for $C_{28}H_{32}NO_3$ [M+H$^+$], 430,3303, found 430,3382; IR (film) *v*: 3030, 2860, 1496, 1453, 1326, 1206, 1095, 737, 697cm^{-1}.

***N*-allylation of 3a, 3b, 8a and 8b. General procedure for the synthesis of 5a, 5b, 10 a and 10b:**

A solution of amine **3a**, **3b**, **8a** or **8b** (0.5 mmol) in dry. DMF (8 mL) was treated sequentially with potassium carbonate (0.8 mmol, 110 mg), allyl bromide (5.0 mmol, 605 mg, 433 µL) and tetrabutylammonium iodide (cat. 4 mg) at ambient temperature under argon atmosphere. The reaction mixture was stirred for additional 12 h, and then diluted with water (10 mL) and extracted with hexane (3 x 10 mL). The combined organic extracts were washed with

brine, dried over $MgSO_4$ and evaporated under reduced pressure to give pure adduct **5a**, **5b**, **10a** or **10b** that did not need further purification.

(2*R*,3*S*,4*R*,5*R*,6*R*)-1,2-Diallyl-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)piperidine (5a): colorless oil; quatn. yield; R*f* 0.67 (1:6 AcOEt/hexane); $[\alpha]_D^{21}$ +34.5 (*c* 0.15, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.36–7.15 (m, 20H), 5.90–5.82 (m, 1H), 5.78 (ddt, *J* 16.6, 10.1, 6.3 Hz, 1H), 5.11 (dd, *J* 17.2, 1.6 Hz, 1H), 5.06 (dd, *J* 10.2, 1.5 Hz, 1H), 5.02 (dd, *J* 17.1, 1.6 Hz, 1H), 4.97 (dd, *J* 2.7, 1.8 Hz, 1H), 4.95 (dd, *J* 3.2, 2.3 Hz, 1H), 4.86 (d, *J* 10.7 Hz, 1H), 4.78 (d, *J* 10.9 Hz, 1H), 4.60 (dd, *J* 26.6, 11.6 Hz, 2H), 4.50 (d, *J* 10.7 Hz, 1H), 4.46 (q, *J* 12.0 Hz, 2H), 3.79 (dd, *J* 10.4, 4.4 Hz, 1H), 3.75–3.72 (m, 2H), 3.67–3.61 (m, 2H), 3.44 (dd, *J* 14.3, 6.5 Hz, 1H), 3.35 (dd, *J* 14.3, 6.1 Hz, 1H), 3.32–3.27 (m, 1H), 2.88 (ddd, *J* 10.1, 4.3, 2.1 Hz, 1H), 2.42 (ddd, *J* 11.8, 9.1, 5.4 Hz, 1H), 2.33–2.27 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 139.0, 138.6, 138.5, 138.0, 137.7, 137.3, 128.33, 128.32, 128.28, 128.27, 127.90, 127.85, 127.84, 127.76, 127.61, 127.53, 127.49, 127.38, 116.3, 115.2, 83.8, 79.7, 78.5, 75.3, 75.1, 72.9, 72.2, 67.6, 57.5, 57.2, 52.3, 28.5; HRMS (ESI-TOF) *m/z* calc for $C_{40}H_{46}NO_4$ [M+H$^+$], 604.3427. Found 604.3428; IR (film): 3030, 2919, 2860, 1453, 1097, 1070, 1028, 911, 734, 697 cm^{-1}.

(2*R*,3*R*,4*R*,5*R*)-1,2-Diallyl-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)pyrrolidine; (5b): colorless oil; quant. yield; R*f* 0.58 (1:6 AcOEt/hexanes); $[\alpha]_D^{21}$ –6.7 (*c* 0.14, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.36–7.21 (m, 15H), 5.96–5.87 (m, 1H), 5.78–5.69 (m, 1H), 5.21 (d, *J* 17.1 Hz, 1H), 5.15–4.98 (m, 3H), 4.59–4.37 (m, 6H), 3.89 (s, 1H), 3.78–3.74 (m, 1H), 3.64 (dd, *J* 9.4, 4.7 Hz, 1H), 3.54–3.47 (m, 2H), 3.28–3.02 (m, 3H), 2.49–2.39 (m, 1H), 2.22–2.10 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 138.3, 136.4, 135.4, 128.33, 128.29, 128.25, 128.23, 128.0, 127.9, 127.8, 127.69, 127.65, 127.61, 127.5, 117.1, 116.5, 85.7, 73.2, 73.0, 71.6, 71.3, 71.2, 70.6, 69.2, 65.6, 65.0, 55.9, 51.1, 31.9; HRMS (ESI-TOF) *m/z* calc. for $C_{32}H_{38}NO_3$ [M+H$^+$], 484.2852. Found 484.2849; IR (film) *v*: 3065, 3030, 2917, 2859, 1453, 1364, 1099, 1073, 915, 735, 697 cm^{-1}.

(2*R*,3*R*,4*R*,5*S*,6*R*)-1-Allyl-3,4,5-tris(benzyloxy)-2-(benzyloxymethyl)-6-vinylpiperidine (10a): colorless oil; 98%; R_f 0.75 (40% AcOEt in hexanes); $[\alpha]_D^{23}$ +30.8 (*c* 1.9, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.35–7.23 (m, 18H), 7.15–7.07 (m, 2H), 6.00–5.92 (m, 1H), 5.86–5.77 (m, 1H), 5.40 (dd, *J* 10.4, 2.0 Hz, 1H), 5.24 (dd, *J* 17.0, 1.9 Hz, 1H), 5.10–5.08 (m, *J* 4.2 Hz, 1H), 5.08–5.06 (m, 1H), 4.96 (d, *J* 11.0 Hz, 1H), 4.88 (d, *J* 10.7 Hz, 1H), 4.75 (d, *J* 11.0 Hz, 1H), 4.65 (d, *J*

11.6 Hz, 1H), 4.57 (d, *J* 11.6 Hz, 1H), 4.46 – 4.44 (m, 2H), 4.42 (d, *J* 10.7 Hz, 1H), 3.78–3.72 (m, 3H), 3.67 (dd, *J* 10.6, 3.0 Hz, 1H), 3.64–3.60 (m, 1H), 3.58 (dd, *J* 10.5, 2.1 Hz, 1H), 3.48–3.44 (m, 1H), 3.09 (dd, *J* 13.9, 8.4 Hz, 1H), 2.78 (dt, *J* 9.9, 2.5 Hz, 1H); 13C NMR (151 MHz, $CDCl_3$) δ: 139.1, 138.47, 138.37, 137.8, 136.5, 130.5, 128.34, 128.31, 128.25, 128.24, 128.20, 127.97, 127.95, 127.78, 127.76, 127.54, 127.32, 121.4, 116.89, 83.6, 80.3, 78.9, 75.2, 73.1, 71.9, 66.3, 61.2, 59.1, 52.3; IR (film) *v*: 3064, 3030, 2921, 2858, 1496, 1454, 1362, 1095, 1070, 735, 697 cm^{-1}; HRMS (ESI-TOF) *m/z* calc. for $C_{39}H_{44}NO_4$ $[M+H^+]$, 590,3270. Found 590,3270.

(2*R*,3*R*,4*R*,5*R*)-1-allyl-3,4-bis(benzyloxy)-2-(benzyloxymethyl)-5-vinylpyrrolidine (10b): colorless oil; quant. yield; R_f 0.93 (2:3 AcOEt/hexanes); ^1H NMR (500 MHz, $CDCl_3$) *δ*: 7.34–7.23 (m, 15H), 5.89–5.79 (m, 2H), 5.26–5.17 (m, 2H), 5.12 (d, *J* 17.3 Hz, 1H), 5.05 (d, *J* 9.8 Hz, 2H), 4.56–4.45 (m, 6H), 3.99–3.95 (m, 1H), 3.82–3.78 (m, 1H), 3.63–3.55 (m, 2H), 3.54–3.49 (m, 1H), 3.36 (d, *J* 14.0 Hz, 1H), 3.28 (s, 1H), 3.16–3.10 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 138.34, 138.28, 137.8, 136.4, 128.29, 128.25, 127.8, 127.7, 127.6, 127.5, 118.5, 116.4, 88.0, 85.7, 73.3, 71.6, 71.4, 70.3, 68.7, 64.7, 50.8; HRMS (ESI-TOF) *m/z* calc. for $C_{31}H_{35}NO_3Na$ $[M+Na^+]$, 492.2531. Found 492.2538; IR (film) *v*: 3051, 3035, 2920, 2867, 1493, 1458, 1364, 1078, 1071, 735, 697 cm^{-1}.

***N*-acylation of 3a, 3b and 8b. General procedure for the synthesis of: 4a, 4b and 9b:**

To the solution of amine **3a**, **3b** or **8b** (0.5 mmol) in CH_2Cl_2 (5 mL) Et_3N (1.0 mmol, 101 mg, 140 µL) was added under an argon atmosphere. The reaction was cooled to –20 ˚C, after being stirred for 20 min acryloyl chloride (1.0 mmol, 90 mg, 80 µL) was added at the same temperature, and the mixture was warmed gradually to ambient temperature and stirred for overnight. Then, the solvent was evaporated under diminished pressure to afforded the residue which was chromatographed on silica gel to afford the corresponding product **4a**, **4b** or **9b**.

1-((*2S*,3*S*,4*R*,5*R*,6*R*)-2-Allyl-3,4,5-tris(benzyloxy)-6-((benzyloxy)methyl)piperidin-1-yl)prop-2-en-1-one (4a): colorless oil; 68%; $[\alpha]_D^{22}$ +2.1 (*c* 0.1, $CHCl_3$); R*f* 0.48 (1:4 AcOEt/hexane); column chromatography (1:7 AcOEt/hexanes than 1:5 AcOEt/hexanes); ^1H NMR (600 MHz, $CDCl_3$) *δ*: 7.40–7.22 (m, 20H), 6.48 (dd, *J* 16.6, 10.4 Hz, 1H), 6.31 (dd, *J* 16.6, 1.3 Hz, 1H), 5.94–5.83 (m, 1H), 5.63 (dd, *J* 10.4, 1.9 Hz, 1H), 5.03 (d, *J* 17.8 Hz, 1H), 4.97 (d, *J* 9.9 Hz, 1H),

4.69–4.45 (m, 9H), 4.02 (dd, *J* 3.7, 2.0 Hz, 1H), 3.91 (d, *J* 8.1 Hz, 1H), 3.72 (dd, *J* 8.1, 5.5 Hz, 1H), 3.68–3.58 (m, 1H), 2.73–2.67 (m, 1H), 2.54–2.47 (m, 1H); HRMS (ESI-TOF) *m/z* calc. for $C_{40}H_{43}NO_5Na$ [M+Na^+], 640,3038. Found 640,3039; IR (film) *v*: 3028, 2922, 2871, 1651, 1613, 1424, 1363, 1087, 736, 697 cm^{-1}.

1-((2*R*,3*R*,4*R*,5*R*)-2-Allyl-3,4-bis(benzyloxy)-5-((benzyloxy)methyl)pyrrolidin-1-yl)prop-2-en-1-one (4b): colorless oil; 58%; R*f* 0.52 (1:3 AcOEt/hexanes); column chromatography (1:7 AcOEt/hexanes); $[\alpha]_D^{21}$ + 0.5 (*c* 1.2, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) mixture of rotamers *δ*: 7.41–7.12 (m, 25H), 6.43–6.38 (m, 2H), 6.38–6.33 (m, 2H), 5.83–5.74 (m, 1H), 5.71–5.64 (m, 2H), 5.60 (dd, *J* 9.4, 2.8 Hz, 1H), 5.08–5.01 (m, 3H), 4.66 (d, *J* 12.0 Hz, 1H), 4.62 (d, *J* 12.1 Hz, 1H), 4.56 (dt, *J* 22.5, 7.9 Hz, 3H), 4.50–4.38 (m, 5H), 4.33 (d, *J* 11.9 Hz, 1H), 4.30 (d, *J* 12.0 Hz, 1H), 4.26–4.16 (m, 3H), 4.10 (dd, *J* 8.9, 4.2 Hz, 1H), 3.98–3.92 (m, 2H), 3.67–3.62 (m, 1H), 3.52 (dd, *J* 9.4, 4.6 Hz, 1H), 3.41 (dd, *J* 10.4, 8.9 Hz, 1H), 3.00–2.94 (m, 1H), 2.62 (ddd, *J* 14.3, 12.0, 8.2 Hz, 1H), 2.39–2.32 (m, 1H), 2.19 (ddd, *J* 13.4, 11.2, 9.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) mixture of rotamers *δ*: 165.1, 164.8, 138.5, 137.8, 137.8, 137.6, 137.4, 135.1, 133.9, 129.0, 128.5, 128.42, 128.37, 128.34, 128.28, 127.83, 127.81, 127.77, 127.68, 127.62, 127.59, 127.55, 127.49, 118.3, 117.7, 84.1, 83.5, 81.8, 81.0, 73.1, 73.0, 71.3, 71.1, 71.0, 70.9, 70.0, 67.3, 64.1, 63.8, 63.5, 63.1, 37.9, 34.6; HRMS (ESI-TOF) *m/z* calc. for $C_{32}H_{35}NO_4Na$ [M+Na^+] 520,2464. Found 520.2480; IR (film): 3031, 2925, 2864, 1650, 1613, 1422, 1360, 1094, 737, 697 cm^{-1}.

1-((2R,3R,4R,5R)-3,4-Bis(benzyloxy)-2-(benzyloxymethyl)-5-vinylpyrrolidin-1-yl)prop-2-en-1-one (9b): yellow oil; 88%; R_f 0.75 (1:1 AcOEt/hexanes); column chromatography (20% AcOEt in hexanes); $[\alpha]_D^{22}$ +3.14 (*c* 0.98, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) mixture of rotamers *δ*: 7.39–7.19 (m, 15H), 6.34–6.33 (m, 1H), 6.33–6.32 (m, 1H), 5.89 (ddd, *J* 17.5, 10.2, 8.1 Hz, 1H), 5.59–5.56 (m, 1H), 5.14 (d, *J* 11.0 Hz, 1H), 5.11 (d, *J* 4.0 Hz, 1H), 4.65 (d, *J* 12.0 Hz, 1H), 4.60 (d, *J* 12.1 Hz, 1H), 4.47–4.39 (m, 6H), 4.23–4.21 (m, 1H), 4.08 (dd, *J* 8.9, 4.3 Hz, 1H), 3.94–3.92 (m, 1H), 3.48 (dd, *J* 10.3, 9.0 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 168.3, 141.2, 140.4, 140.0, 139.87, 132.1, 131.16, 131.11, 130.99, 130.94, 130.6, 130.33, 130.31, 130.26, 130.13, 129.89, 119.2, 90.3, 83.0, 75.6, 74.2, 73.5, 70.4, 70.0, 65.8; HRMS (ESI-TOF) *m/z* calc. for $C_{31}H_{33}NO_4Na$ [M+Na^+], 506,2307. Found 506,2309; IR (film) *v*: 3062, 3031, 2925, 2864, 1651, 1613, 1421, 1360, 1095, 737, 698 cm^{-1}.

Ring Closing Metathesis (RCM)

(RCM) of 4a, 4b, 5a or 5b. General procedure for the synthesis of 6a, 6b, 7a or 7b:

To a solution of **4a**, **4b**, **5a** or **5b** (0.5 mmol) in anhydrous toluene (10 mL) a solution of Grubbs catalyst 2nd generation **Ru2** (5% mol 21.2 mg, 0.025 mmol) in 10 ml toluene was added under argon atmosphere. The resulting mixture was stirred at 60 °C until all consumption of starting material (TLC monitoring). Then, the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography to give the corresponding adduct **6a**, **6b**, **7a**, or **7b**.

(6*R*,7*R*,8*R*,9*S*,9*aR*)-7,8,9-Tris(benzyloxy)-6-((benzyloxy)methyl)-1,6,7,8,9,9a-hexahydro-4H quinolizin-4-one (6a): colorless oil; 74%; R*f* 0.33 (1:2 AcOEt/hexanes); column chromatography (1:3 AcOEt/hexanes then 2:3 AcOEt/hexanes); $[\alpha]_D^{24}$ –18.1 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.34–7.21 (m, 20H), 6.44 (dt, *J* 9.8, 4.1 Hz, 1H), 5.88 (dt, *J* 9.9, 1.9 Hz, 1H), 4.89 (dd, *J* 10.0, 4.6 Hz, 1H), 4.72 (d, *J* 12.0 Hz, 1H), 4.69 (d, *J* 10.7 Hz, 1H), 4.67 (d, *J* 11.9 Hz, 1H), 4.64 (d, *J* 11.8 Hz, 1H), 4.55 (d, *J* 11.5 Hz, 1H), 4.48 (d, *J* 11.9 Hz, 1H), 4.44 (d, *J* 12.0 Hz, 1H), 4.41 (d, *J* 11.9 Hz, 1H), 4.02 (ddd, *J* 8.4, 6.0, 4.2 Hz, 1H), 2.52 (dddd, *J* 18.4, 8.3, 3.8, 2.2 Hz, 1H), 2.41–2.34 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 164.2, 138.24, 138.15, 138.06, 138.04, 128.42, 128.32, 128.30, 128.28, 127.94, 127.77, 127.74, 127.62, 127.60, 127.58, 123.8, 79.9, 79.5, 75.0, 73.5, 72.9, 72.6, 72.5, 68.74, 52.9, 51.1, 25.1; HRMS (ESI-TOF) *m/z* calc. for $C_{38}H_{39}NO_5$ [M+H$^+$], 612.2726. Found 612.2732; IR (film) *v*: 3030, 2922, 2864, 1670, 1611, 1453, 1095, 1072, 1028, 807, 736, 698 cm^{-1}.

(1*S*,2*R*,3*R*,4*R*,9a*R*)-1,2,3-Tris(benzyloxy)-4-((benzyloxy)methyl)-1,3,4,6,9,9a-hexahydro-2H-quinolizine (7a): colorless oil; 81%; R*f* 0.47 (1:3 AcOEt/hexanes); column chromatography (1:8 AcOEt/hexanes then 1:6 AcOEt/hexanes); $[\alpha]_D^{24}$ +27.9 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.42–7.22 (m, 18H), 7.13–7.09 (m, 2H), 5.81–5.76 (m, 1H), 5.62–5.58 (m, 1H), 4.95 (d, *J* 11.0 Hz, 1H), 4.87 (d, *J* 10.8 Hz, 1H), 4.79 (d, *J* 11.0 Hz, 1H), 4.66 (d, *J* 11.6 Hz, 1H), 4.63 (d, *J* 11.6 Hz, 1H), 4.52 (d, *J* 12.2 Hz, 1H), 4.46 (d, *J* 12.2 Hz, 1H), 4.38 (d, *J* 10.8 Hz, 1H), 3.84–3.80 (m, 1H), 3.78 (dd, *J* 16.9, 8.3 Hz, 1H), 3.72 (d, *J* 9.5 Hz, 1H), 3.65–3.60 (m, 1H), 3.59 (dd, *J* 17.1, 7.6 Hz, 1H), 3.52 (dd, *J* 10.7, 2.2 Hz, 1H), 3.45 (dd, *J* 36.4, 18.2 Hz, 1H), 2.80 (d, *J* 9.9 Hz, 1H), 2.31–2.22 (m, 1H), 2.03 (d, *J* 18.6 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 138.0, 137.4, 136.7, 127.4, 127.36, 127.31, 127.29, 127.26, 126.8, 126.7, 126.56, 126.50, 126.3, 124.2,

123.4, 82.5, 79.3, 78.1, 74.3, 74.2, 72.4, 71.2, 64.7, 55.1, 54.4, 46.2, 18.8; HRMS (ESI-TOF) *m/z* calc. for $C_{38}H_{42}NO_4$ [M+H$^+$], 576.3114. Found 576.3126; IR (film) *v*: 3029, 2919, 2853, 1453, 1090, 1027, 734, 696 cm^{-1}.

(1*R*,2*R*,3*R*,8a*R*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-2,3,8,8a-tetrahydroindolizin-5(1H)-one; (6b): colorless oil; 76%; R*f* 0.27 (1:2 AcOEt/hexanes); column chromatography (1:3 AcOEt/hexanes then 2:3 AcOEt/hexanes); $[\alpha]_D^{24}$ +48.9 (*c* 0.72, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.37–7.19 (m, 15H), 6.46 (ddd, *J* 9.7, 6.3, 2.1 Hz, 1H), 5.89 (dd, *J* 9.9, 2.9 Hz, 1H), 4.63–4.59 (m, 2H), 4.54–4.47 (m, 4H), 4.33 (dt, *J* 6.6, 3.2 Hz, 1H), 4.24–4.22 (m, 1H), 3.89–3.80 (m, 3H), 3.71 (dd, *J* 9.3, 3.5 Hz, 1H), 2.52 (dt, *J* 17.1, 5.9 Hz, 1H), 2.29–2.22 (m, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 162.7, 138.2, 137.9, 137.73, 137.66, 128.43, 128.39, 128.30, 127.94, 127.87, 127.79, 127.70, 127.63, 127.55, 125.5, 89.6, 83.4, 73.2, 72.1, 71.9, 67.9, 60.6, 59.9, 29.2; HRMS (ESI-TOF) *m/z* calc. for $C_{30}H_{31}NO_4Na$ [M+Na$^+$], 492.2151. Found 492.2162; IR (film) *v*: 3031, 2865, 1665, 1608, 1453, 1442, 1099, 1078, 737, 697 cm^{-1}.

(1*R*,2*R*,3*R*,8a*R*)-1,2-Bis(benzyloxy)-3-((benzyloxy)methyl)-1,2,3,5,8,8a-hexahydroindolizine (7b): colorless oil; 83%; R*f* 0.35 (1:3 AcOEt/hexanes); column chromatography (1:5 AcOEt/hexanes); $[\alpha]_D^{24}$ +34.5 (*c* 0.97, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 7.39–7.21 (m, 15H), 5.76–5.71 (m, 1H), 5.67 (ddd, *J* 10.1, 4.0, 1.9 Hz, 1H), 4.58–4.47 (m, 6H), 3.93 (t, *J* 2.8 Hz, 1H), 3.70 (dd, *J* 4.5, 2.5 Hz, 1H), 3.66 (dd, *J* 9.7, 5.0 Hz, 1H), 3.55 (dd, *J* 9.7, 5.7 Hz, 1H), 3.49–3.43 (m, 1H), 3.39 (td, *J* 5.3, 3.3 Hz, 1H), 3.33 (ddd, *J* 17.1, 3.7, 1.8 Hz, 1H), 3.11 (td, *J* 7.3, 4.8 Hz, 1H), 2.18–2.13 (m, 2H); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 137.33, 137.30, 137.23, 127.30, 127.29, 127.24, 126.80, 126.72, 126.60, 126.55, 126.52, 126.49, 124.1, 122.9, 87.8, 85.1, 72.2, 70.6, 70.4, 68.3, 63.9, 58.6, 44.7, 27.4; HRMS (ESI-TOF) *m/z* calc. for $C_{30}H_{34}NO_3$ [M+H$^+$], 459.2539. Found 576.3126; IR (film) *v*: 3030, 2911, 2863, 1662, 1453, 1364, 1098, 736, 696 cm^{-1}.

5*R*,6*R*,7*R*,8*S*,8a*R*)-6,7,8-Tris(benzyloxy)-5-((benzyloxy)methyl)-3,5,6,7,8,8a-hexahydroindolizine (12a): To a solution of **10a** (50 mg, 0.085 mmol) in anhydrous xylene (3 mL). The ruthenium catalyst **Ru4** (2 mol%, 0.0017 mmol, 1.3 mg) was added under argon atmosphere, and the resulting mixture was refluxed until all consumption of starting material **10a**, ~30 min (TLC monitoring). Then, the solvent was evaporated under reduced

pressure and the residue was purified by silica gel column chromatography to give the corresponding adduct **12a** in 89% yield as a colorless oil; $[\alpha]_D^{24}$ +25.6 (*c* 0.27, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.35–7.20 (m, 20H), 5.96–5.93 (m, 1H), 5.66 (ddd, *J* 6.2, 3.9, 2.1 Hz, 1H), 4.75 (d, *J* 10.3 Hz, 1H), 4.62 (d, *J* 11.2 Hz, 1H), 4.59–4.44 (m, 6H), 4.16 (d, *J* 4.8 Hz, 20H), 4.00 (d, *J* 13.4 Hz, 1H), 3.80 (dd, *J* 10.9, 6.2 Hz, 1H), 3.76 (dd, *J* 6.2, 0.9 Hz, 1H), 3.67–3.65 (m, *J* 2.2 Hz, 2H), 3.56 – 3.53 (m, 1H), 3.48 (dd, *J* 13.3, 5.5 Hz, 1H); HRMS (ESI-TOF) *m/z* calc. for $C_{37}H_{40}NO_4$ [M+H$^+$], 562.2957. Found 562.2953; IR (film) *v*: 3043, 2911, 2846, 1448, 1097, 1026, 733, 696 cm^{-1}.

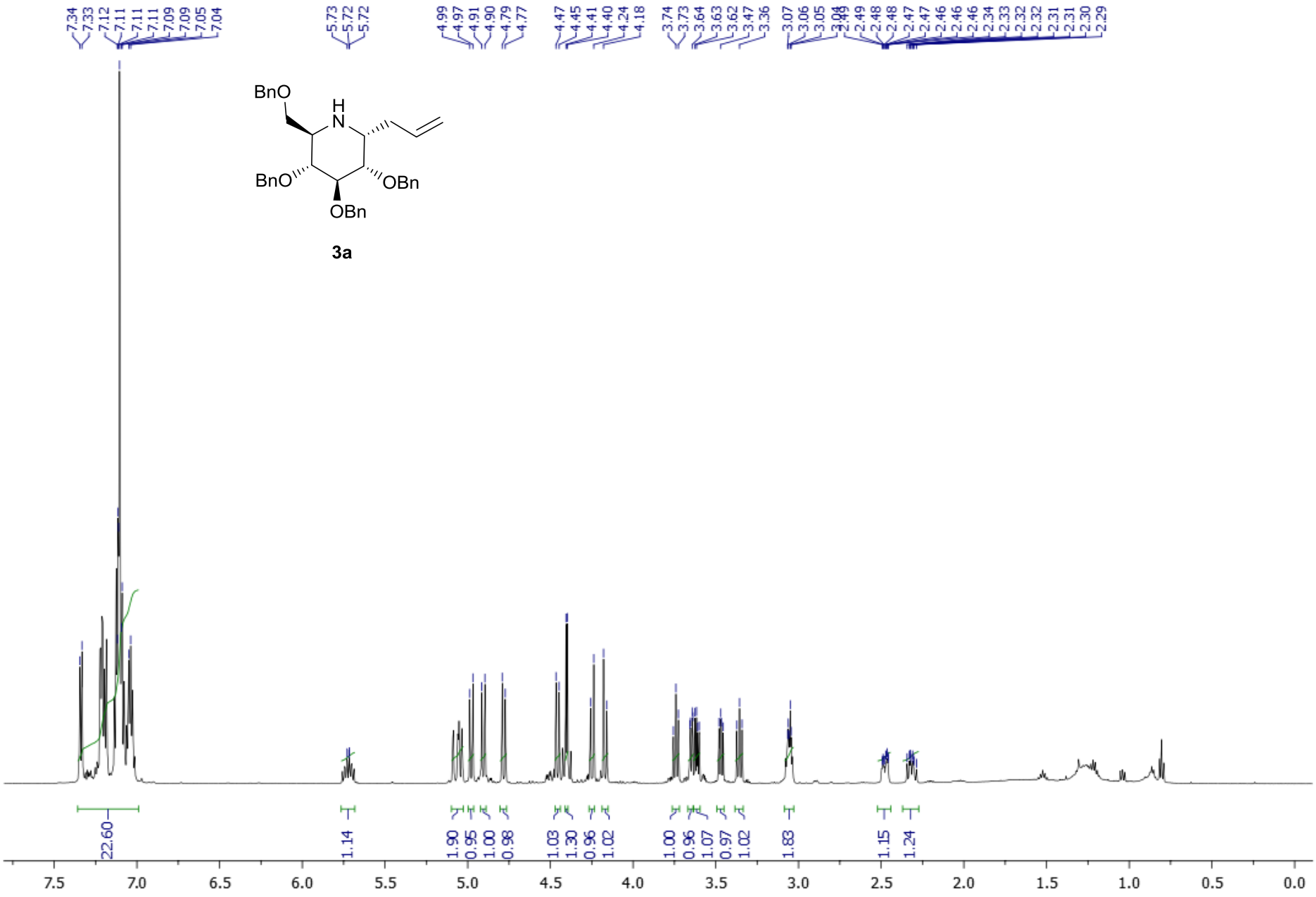
(1*R*,2*R*,3*R*,7a*R*)-1,2-Bis(benzyloxy)-3-(benzyloxymethyl)-2,3-dihydro-1H-pyrrolizin-5(7aH)-one; (11b): To a solution of **9b** (50 mg, 0.1 mmol) in anhydrous 1,2 dichloroethane (3 mL). The nitro-Grela catalyst **Ru3** was added (1% mol 0.7 mg, 0.001 mmol) under argon atmosphere, and the resulting mixture was refluxed for overnight. Then, another portion of the catalyst **Ru3** was added (1% mol 0.7 mg, 0.001 mmol) and the mixture was refluxed over two days. After complete conversion of substrate **9b** (TLC monitoring) the solvent was evaporated under reduced pressure and the residue was purified by silica gel column chromatography to give the corresponding product **11b** in 64% yield as a colorless oil; R*f* 0.43 (2:3 AcOEt/hexanes); column chromatography (30% AcOEt in hexanes); $[\alpha]_D^{23}$ +37.3 (*c* 2.2, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.38–7.22 (m, 15H), 6.94 (dd, *J* 5.7, 1.4 Hz, 1H), 6.04 (d, *J* 4.9 Hz, 1H), 4.67 (d, *J* 11.8 Hz, 1H), 4.62–4.60 (m, 2H), 4.58 (d, *J* 4.6 Hz, 1H), 4.56 (d, *J* 4.8 Hz, 1H), 4.52–4.48 (m, *J* 14.5, 8.9 Hz, 2H), 4.26 (d, *J* 8.2 Hz, 1H), 3.96 (dd, *J* 8.9, 4.7 Hz, 1H), 3.67 (dd, *J* 9.9, 5.0 Hz, 1H), 3.61 (dd, *J* 9.9, 3.7 Hz, 1H), 3.53 (dd, *J* 8.1, 6.6 Hz, 1H); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 174.2, 147.4, 138.0, 137.8, 137.4, 128.6, 128.39, 128.37, 128.36, 128.1, 127.82, 2x127.79, 127.65, 127.64, 89.0, 85.9, 73.3, 73.2, 72.7, 70.2, 68.9, 58.5; HRMS (ESI-TOF) *m/z* calc. for $C_{29}H_{29}NO_4Na$ [M+Na$^+$], 478.1994. Found 478.2001; IR (film) *v*: 3376, 3031, 2923, 2860, 1697, 1496, 1454, 1362, 1118, 1100, 812, 739, 698 cm^{-1}.

(1*R*,2*R*,3*R*,7a*R*)-1,2-Bis(benzyloxy)-3-(benzyloxymethyl)-2,3,5,7a-tetrahydro-1H-pyrrolizine; (12b): To a solution of **10b** (72 mg, 0.15 mmol) in anhydrous 1,2-dichloroethane (3 mL) Grubbs catalyst 2nd generation **Ru2** (10% mol 8.4 mg, 0.015 mmol) was added under argon atmosphere, and the resulting mixture refluxed for overnight. After complete conversion of substrate **10b** (TLC monitoring) the solvent was evaporated under reduced pressure and the

residue was purified by silica gel column chromatography to give the corresponding adduct **12b** in 79% yield as an colorless oil; agreement with literature data[1]; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.14–7.30 (m, 15H), 5.63–5.69 (m, 2H), 4.65 (d, *J* 11.6 Hz, 1H), 4.23–4.57 (m, 5H), 4.05–4.10 (m, 1H), 3.96 (dd, *J* 6.5, 8.1 Hz), 3.75–3.83 (m, 2H), 3.55 (dd, *J* 9.7, 3.9 Hz, 1H), 3.43–3.52 (m, 2H), 2.87 (ddd, *J* 8.1, 5.9, 3.9 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 62.2, 68.8, 71.9 72.2, 72.7, 73.4, 74.9, 83.7, 87.6 , 127.4, 127.6, 127.7, 127.7, 127.8, 127.9, 128.3, 128.3, 128.5, 129.2, 138.1, 138.5, 138.5; HRMS (ESI-TOF) *m/z* calc. for $C_{29}H_{31}NO_3Na$ [M+Na^+], 464.2002. Found 464.2008.

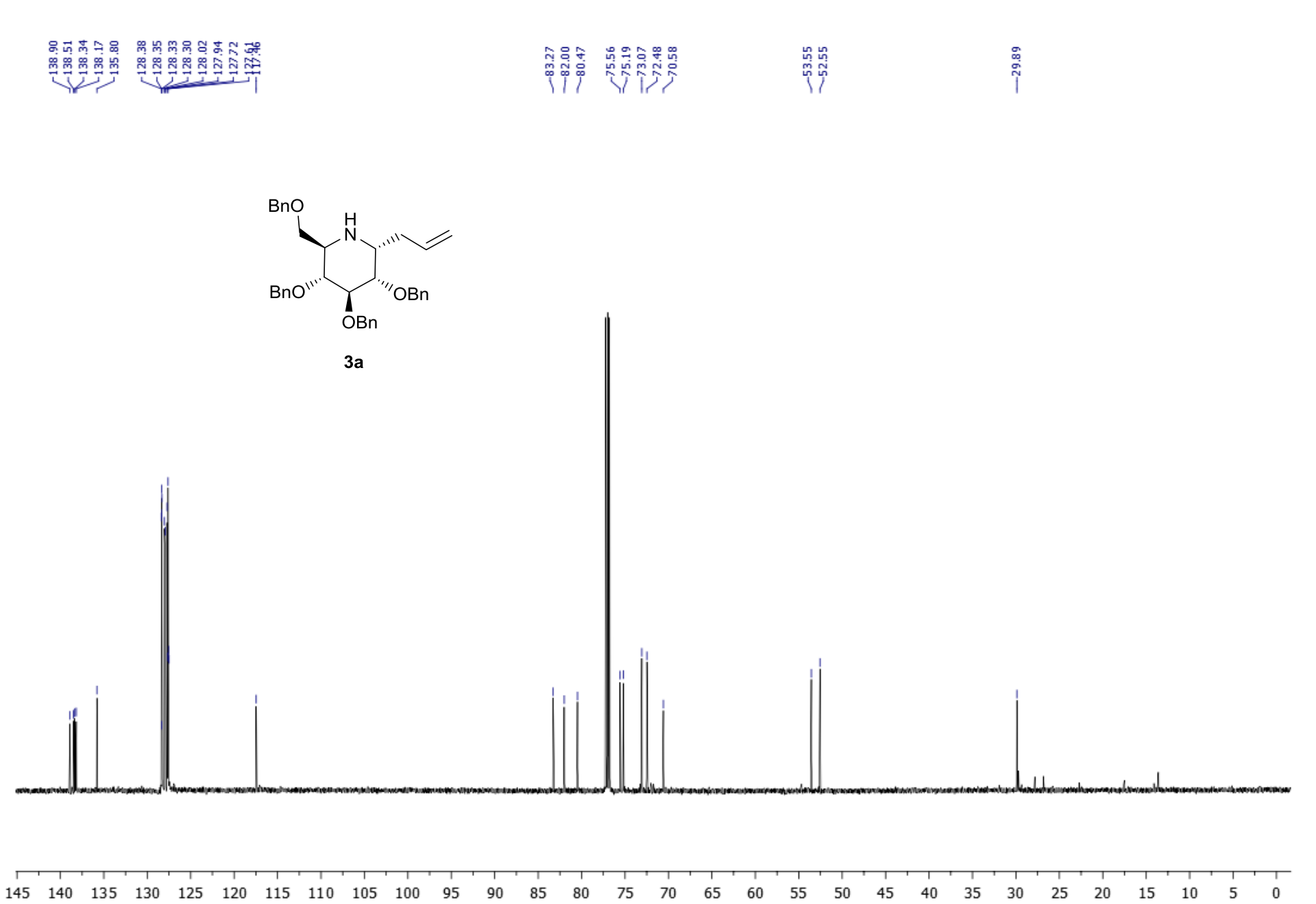
Literature

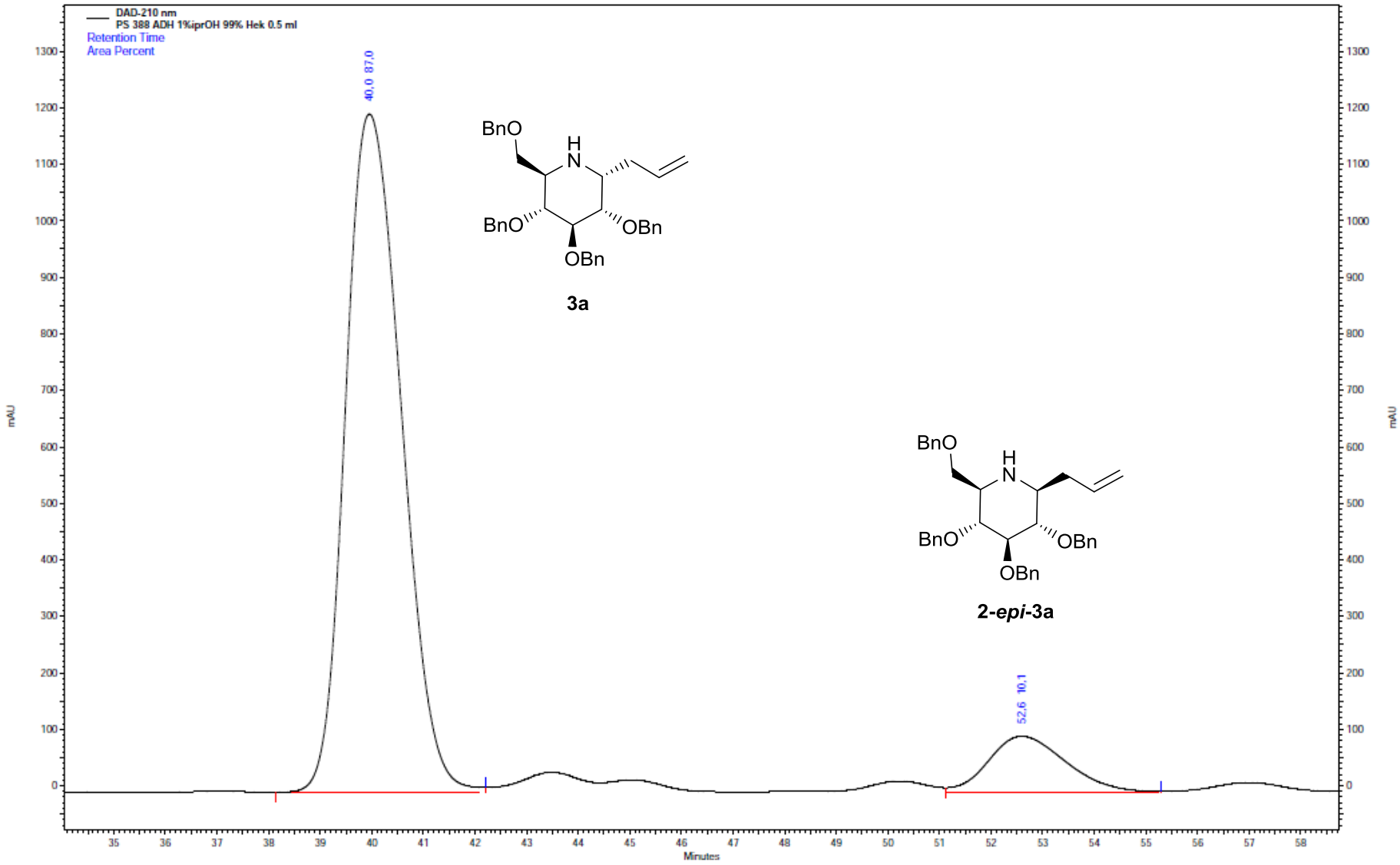
1. I. Delso, T. Tejero, A. Goti, P. Merino *Tetrahedron* **2010**, *66*, 1220.

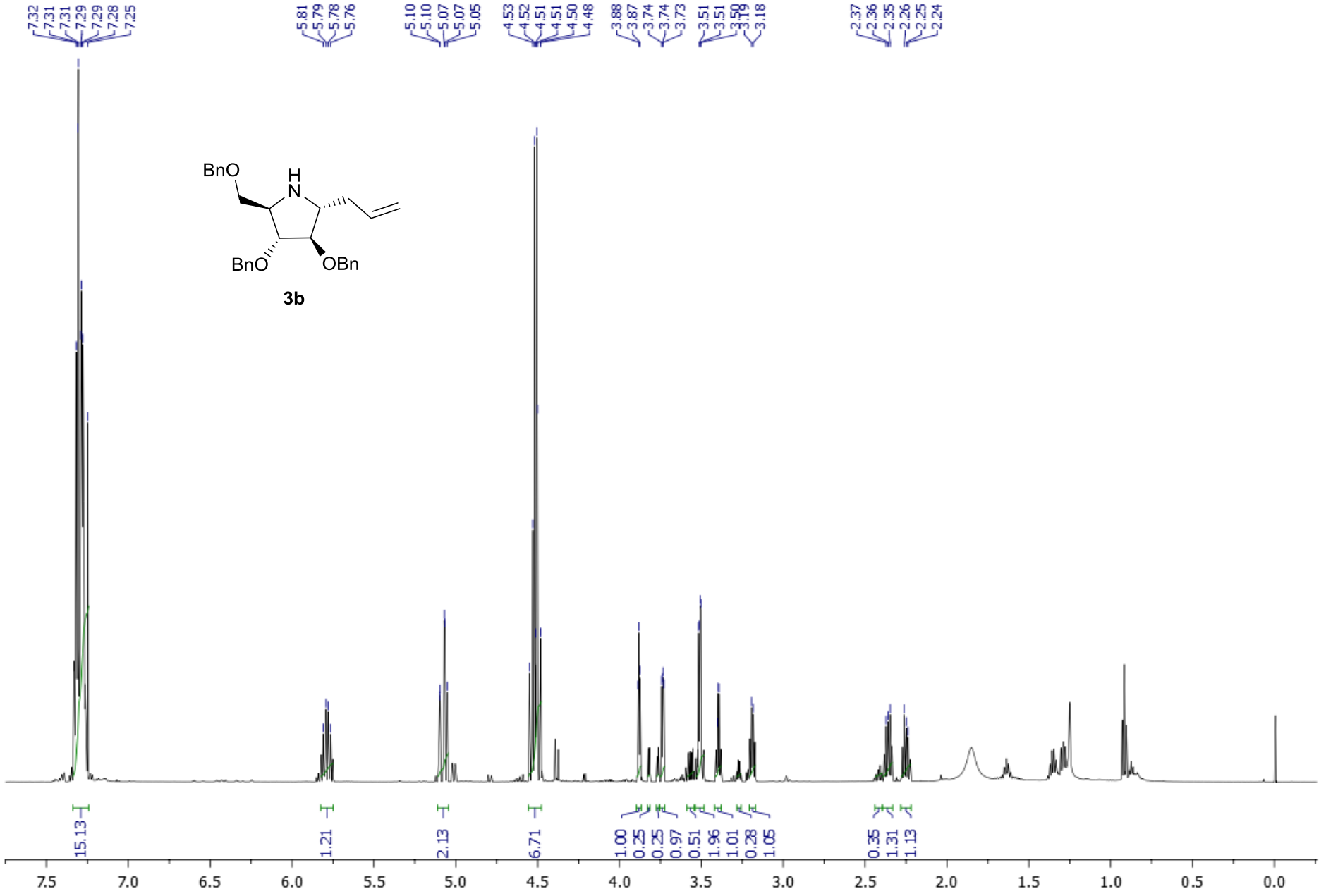


3a

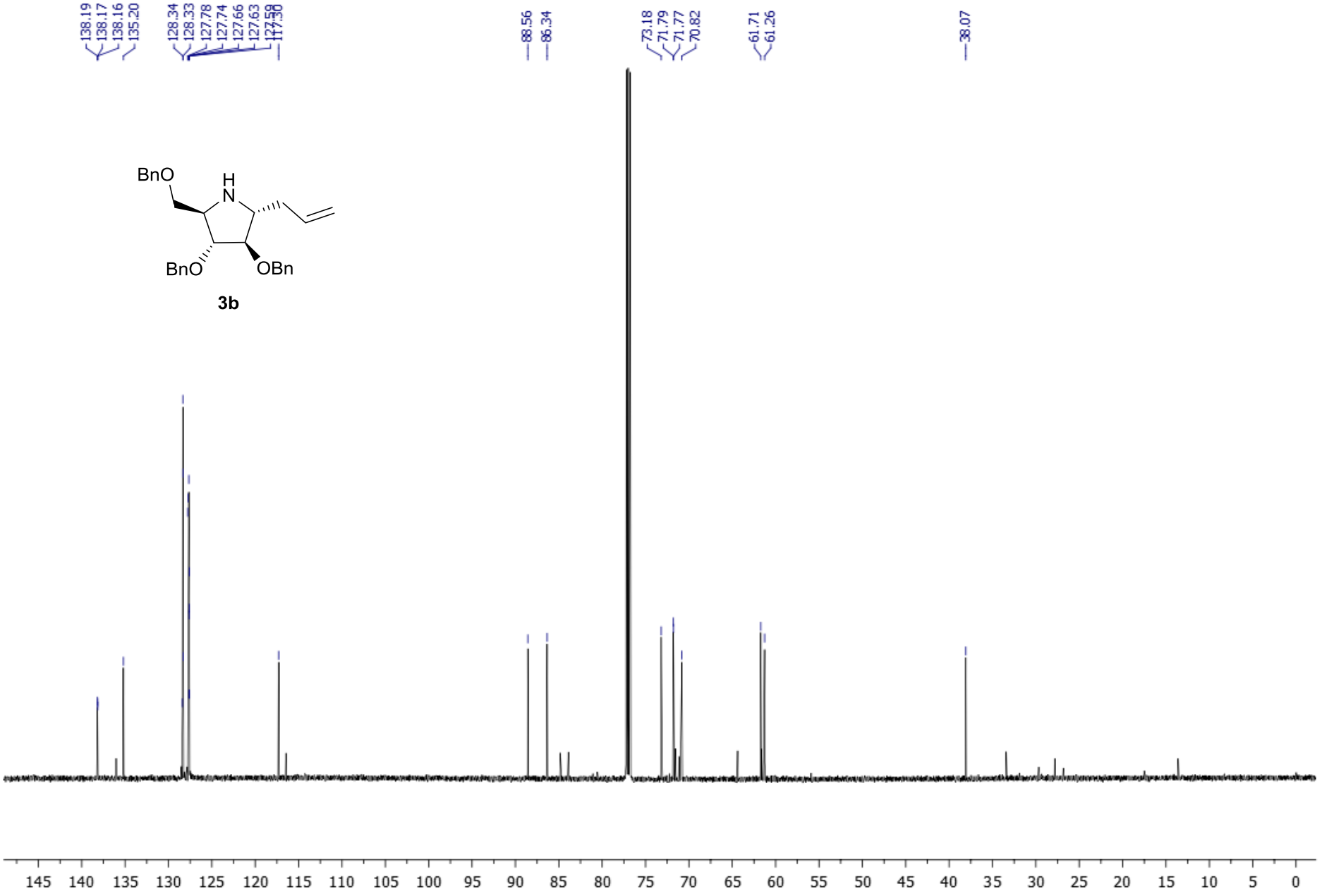
The impurities between 0.5 and 2.0 ppm comes from high-boiling hexanes fraction

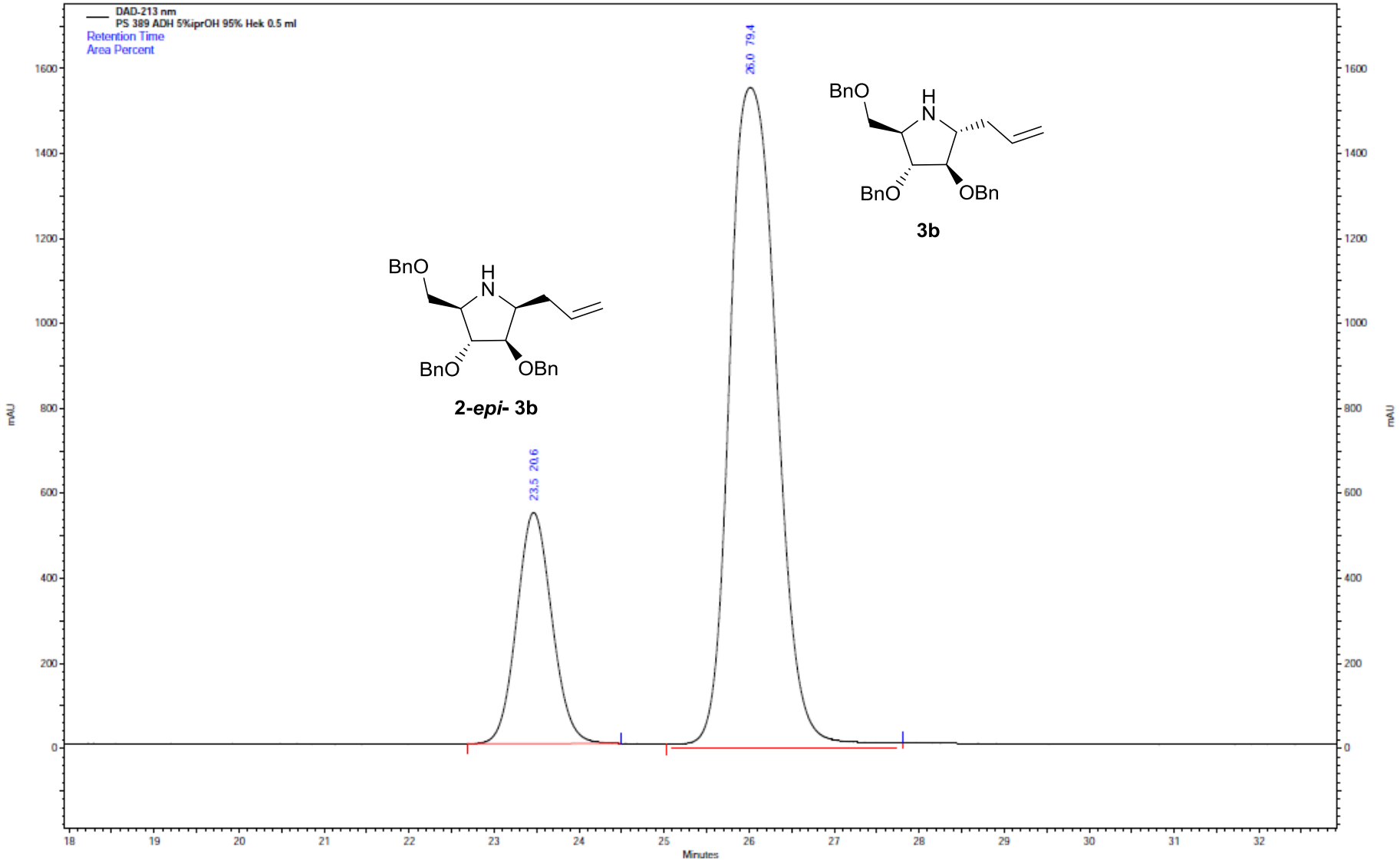

138.90
138.51
138.34
138.17
135.80
128.38
128.35
128.33
128.30
128.02
127.94
127.72
83.27
82.00
80.47
75.56
75.19
73.07
72.48
70.58
53.55
52.55
29.89
BnO
H
N
BnO
OBn
OBn
3a
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0

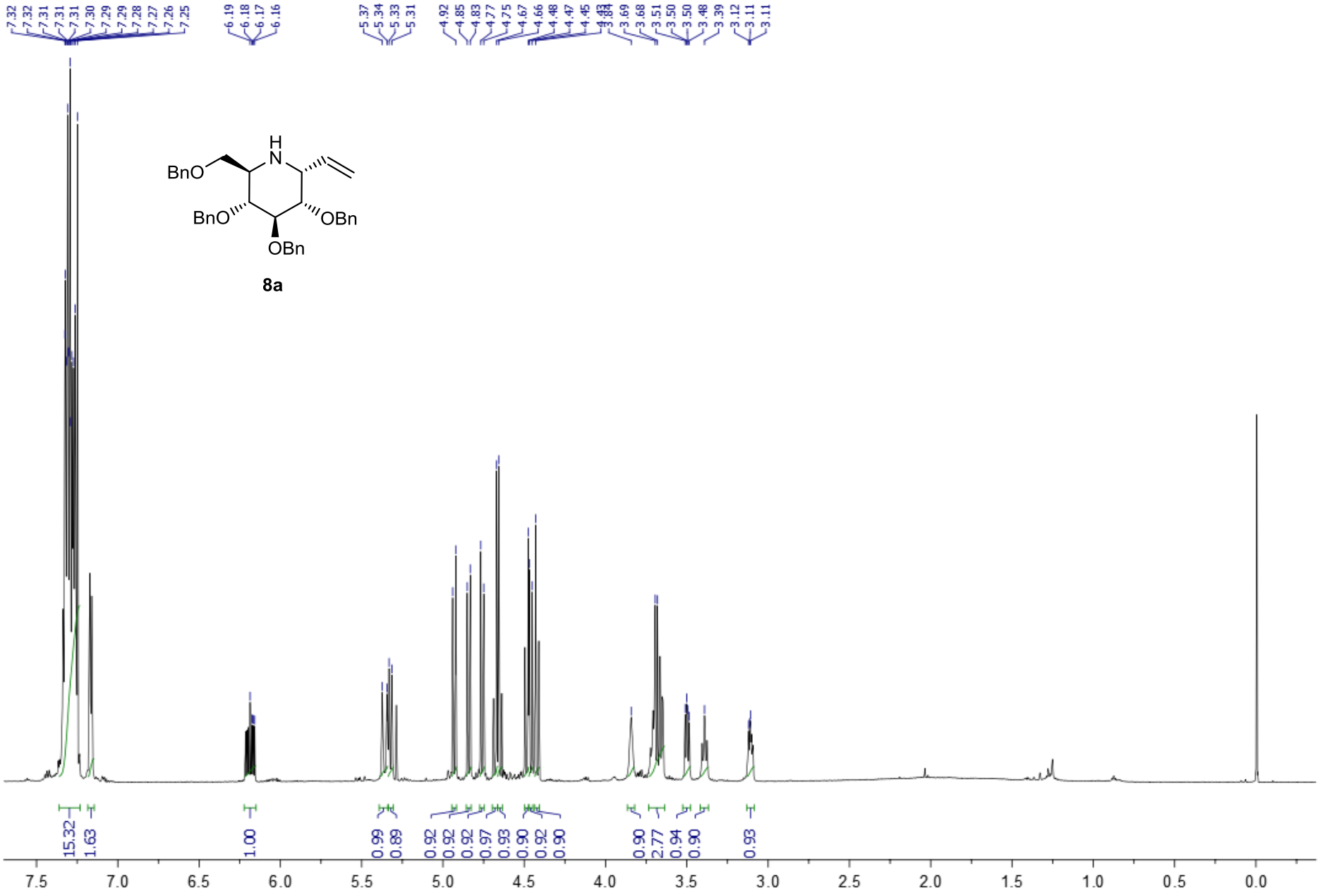

DAD-210 nm
PS 388 ADH 1%iprOH 99% Hek 0.5 ml
Retention Time
Area Percent
40.0 87.0
52.6 10.1
mAU
Minutes
BnO
H
N
BnO
OBn
OBn
3a
BnO
H
N
BnO
OBn
OBn
2-epi-3a



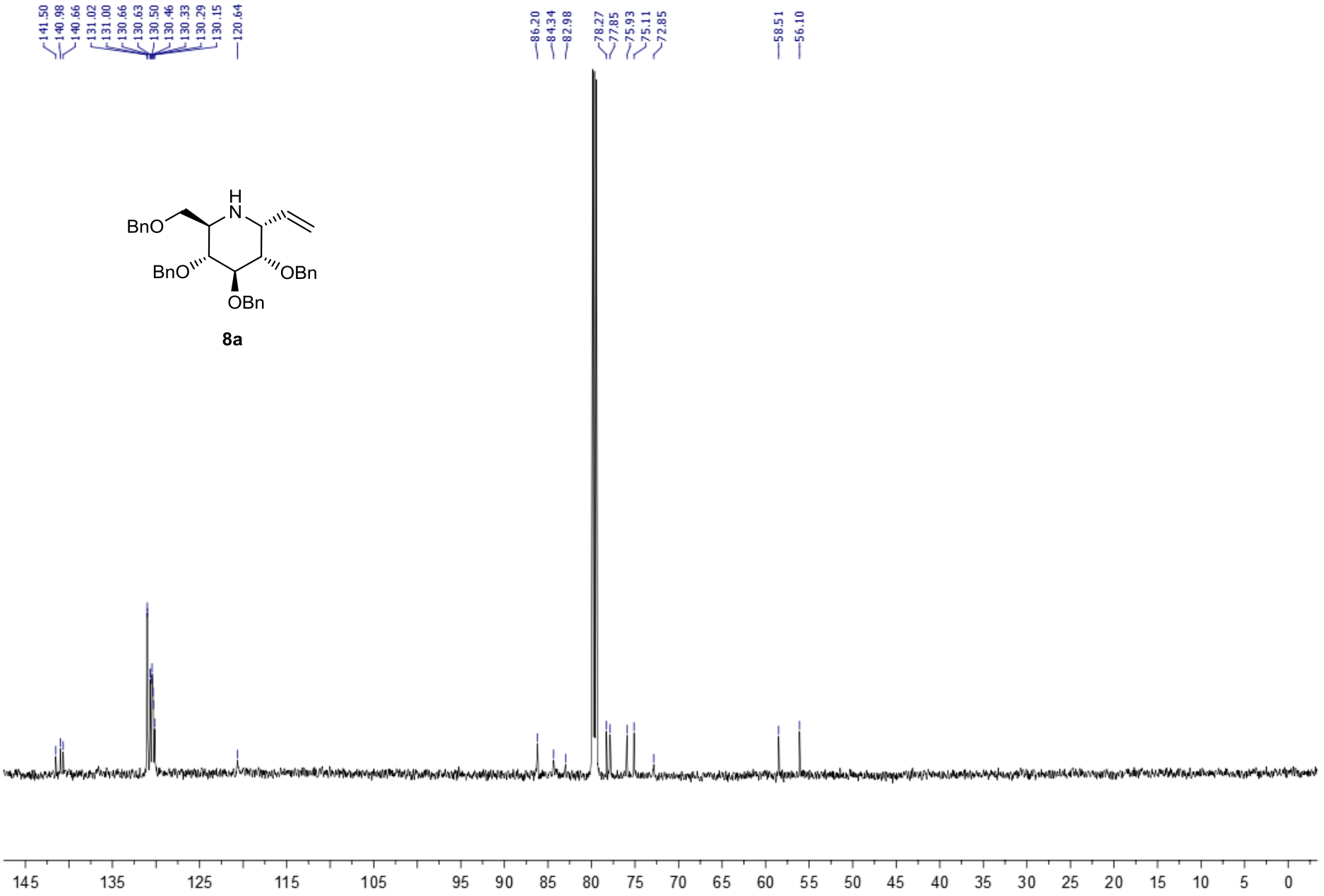
The impurities between 0.5 and 2.0 ppm comes from high-boiling hexanes fraction


138.19
138.17
138.16
135.20
128.34
128.33
127.78
127.74
127.66
127.63
88.56
86.34
73.18
71.79
71.77
70.82
61.71
61.26
38.07
BnO
H
N
BnO
OBn
3b
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0

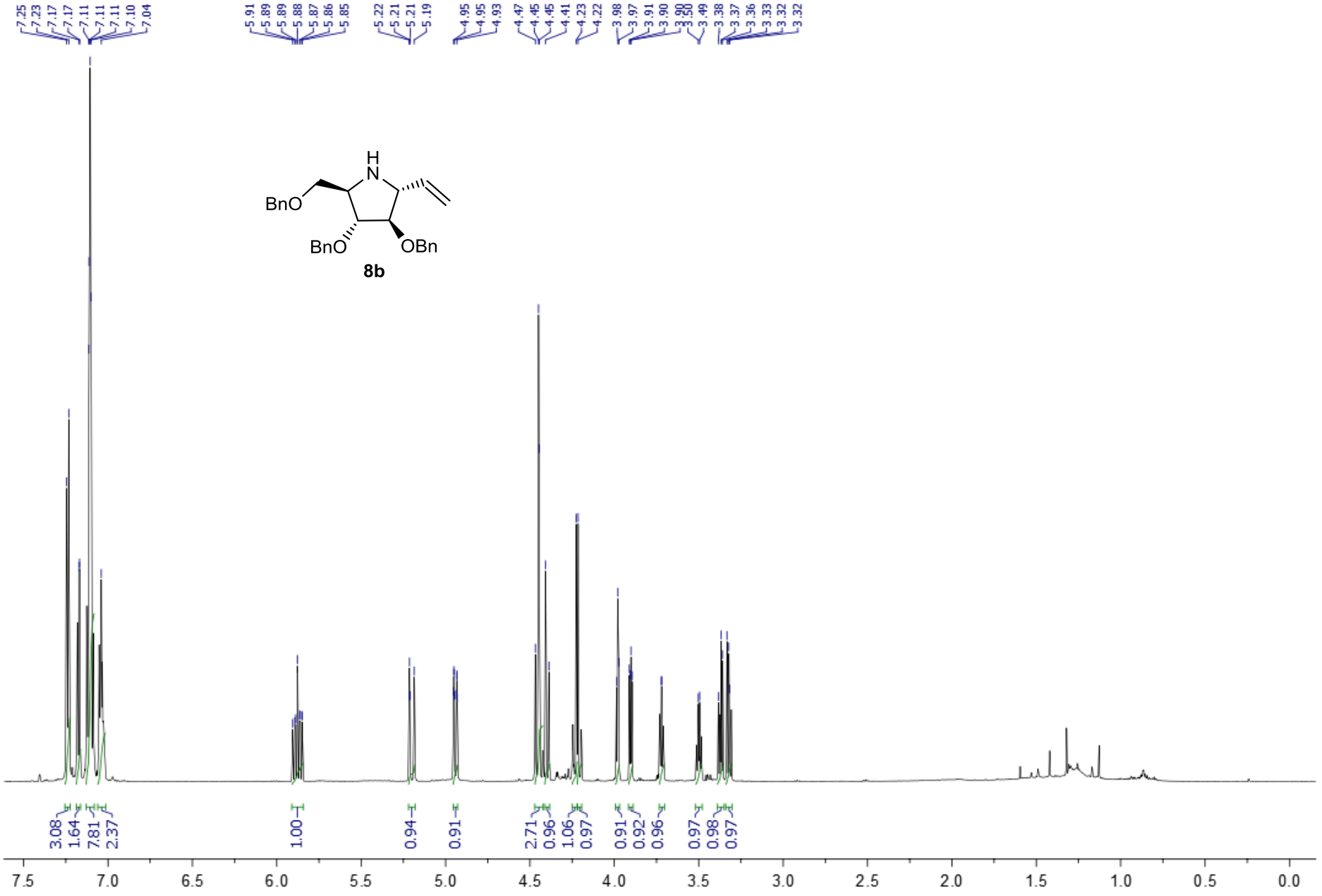

DAD-213 nm
PS 389 ADH 5%iprOH 95% Hek 0.5 ml
Retention Time
Area Percent
23.5 20.6
26.0 79.4
BnO
H
N
BnO
OBn
3b
2-epi- 3b
mAU
Minutes

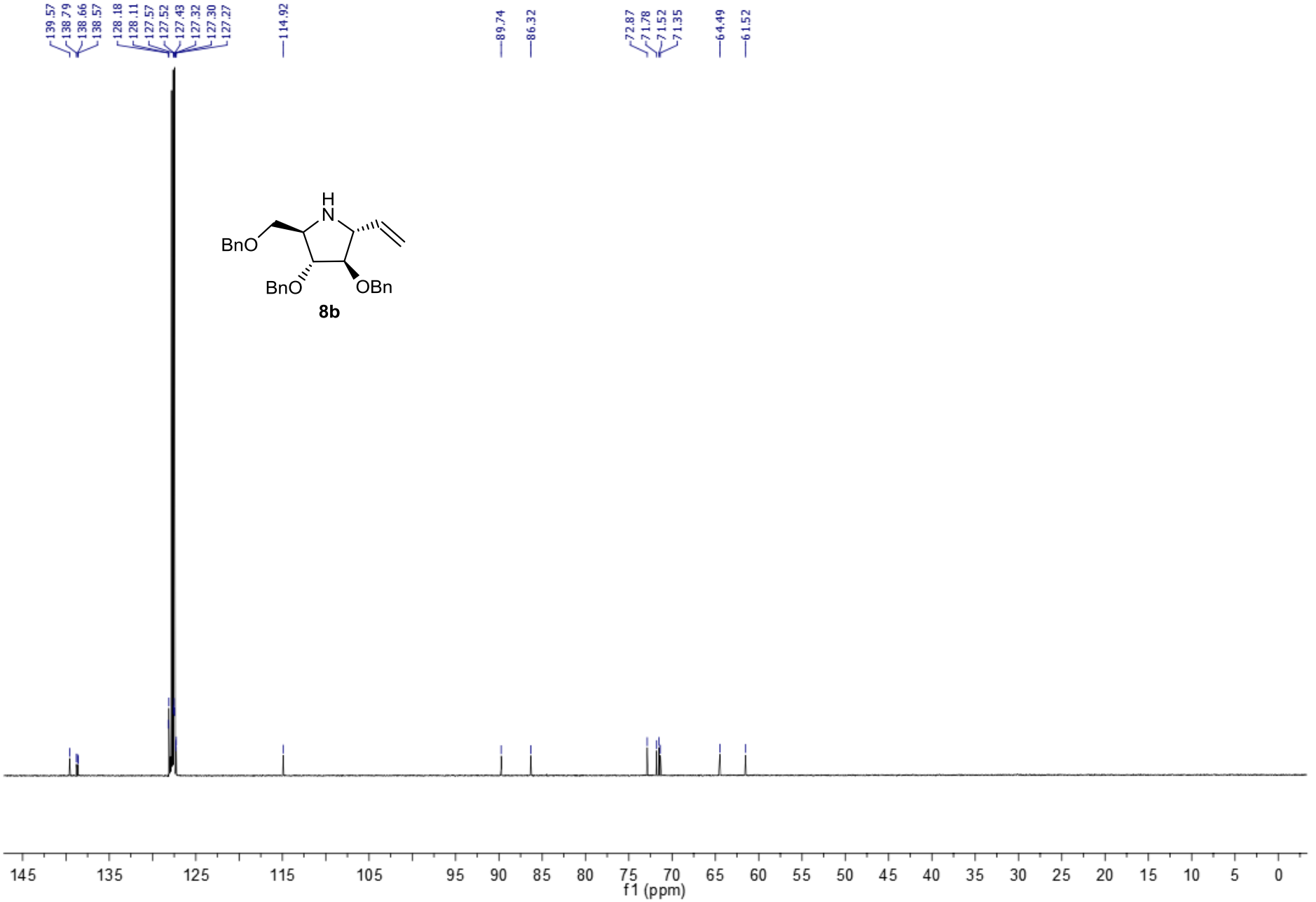

7.32
7.32
7.31
7.31
7.31
7.30
7.29
7.29
7.28
7.27
7.26
7.25
6.19
6.18
6.17
6.16
5.37
5.34
5.33
5.31
4.92
4.85
4.83
4.77
4.75
4.67
4.66
4.48
4.47
4.45
3.69
3.68
3.51
3.50
3.50
3.48
3.39
3.12
3.11
3.11
H
N
BnO
BnO
OBn
OBn
15.32
1.63
1.00
0.99
0.89
0.92
0.92
0.92
0.97
0.93
0.90
0.92
0.90
0.90
2.77
0.94
0.90
0.93
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

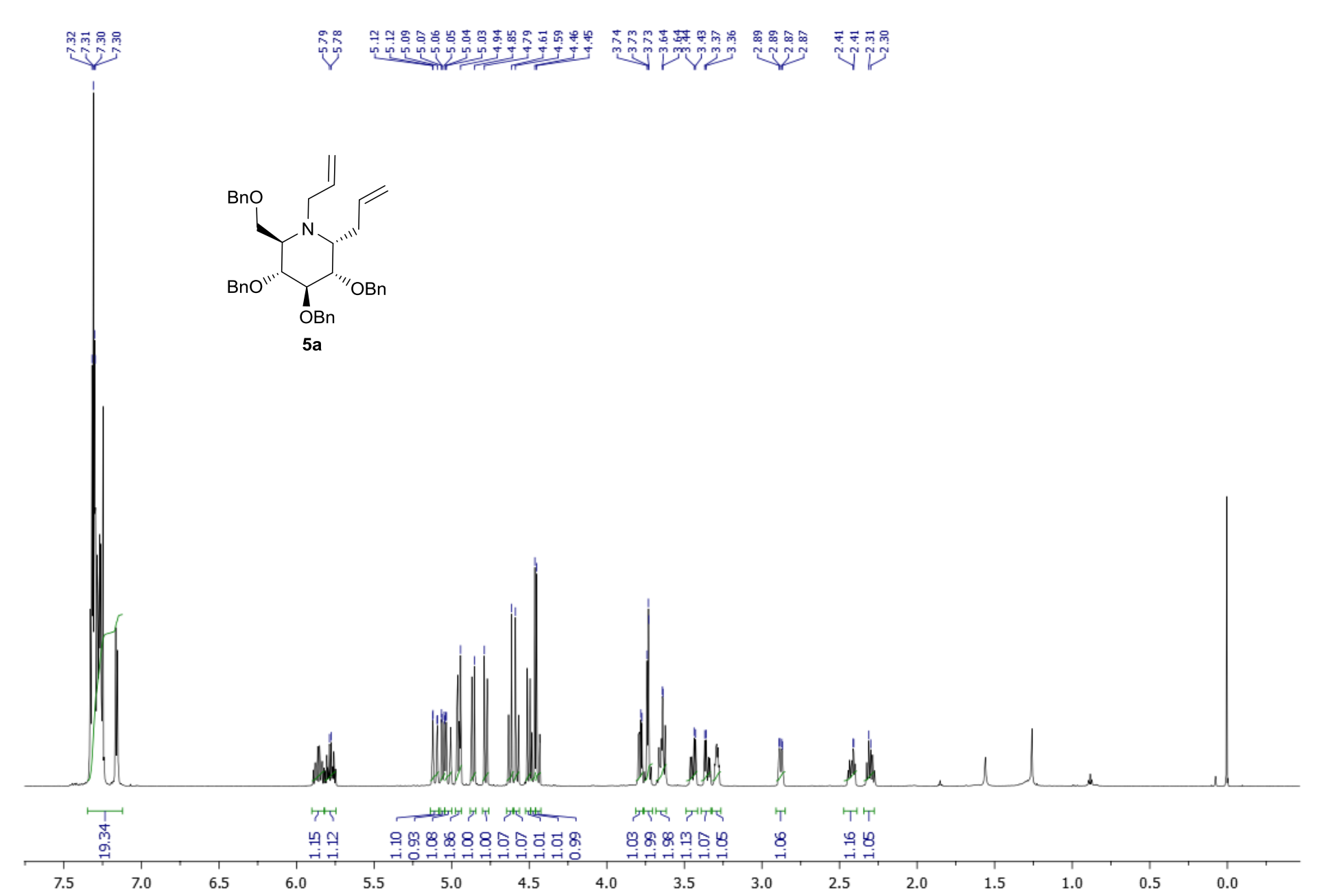
8a

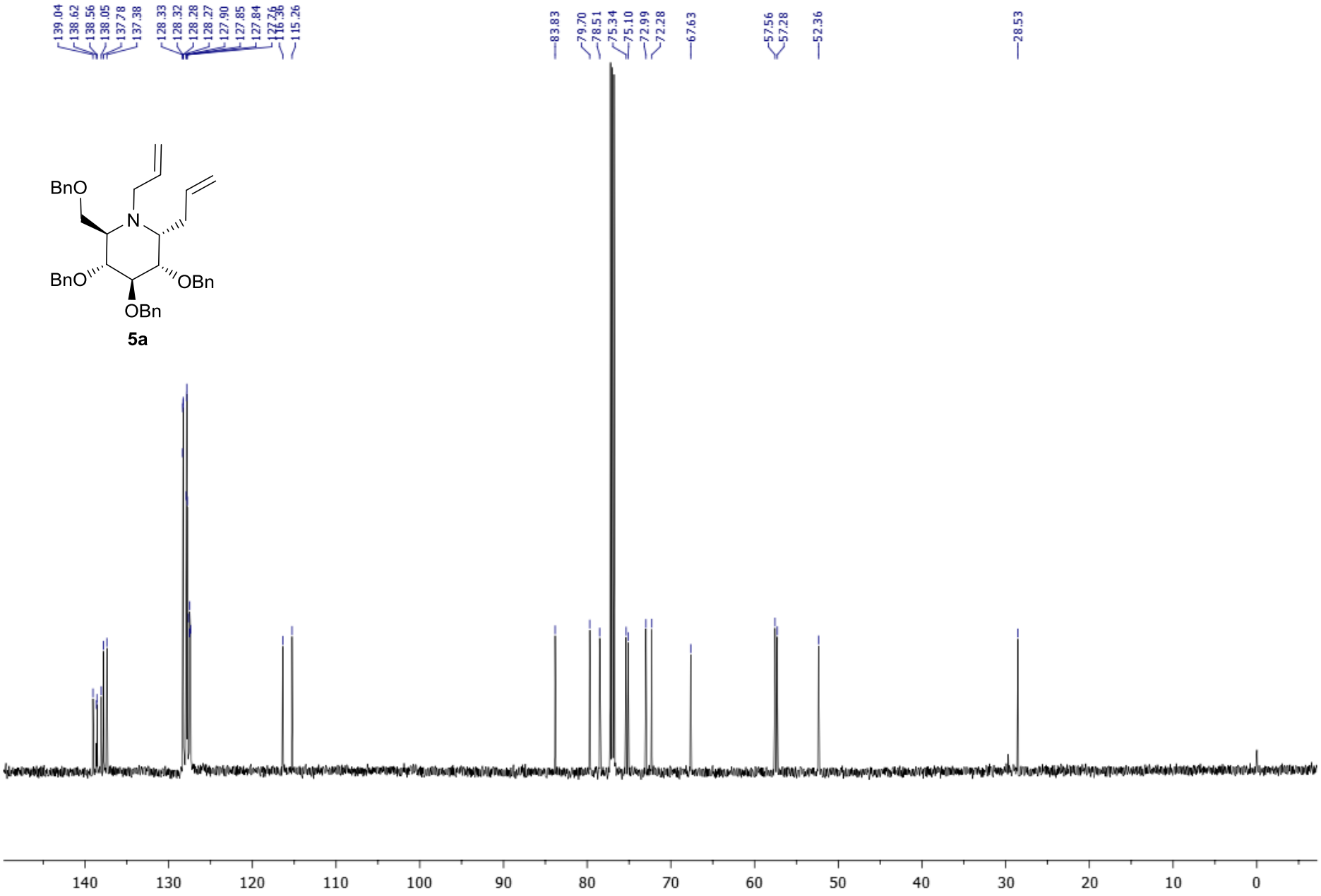

141.50
140.98
140.66
131.02
131.00
130.66
130.63
130.50
130.46
130.33
130.29
130.15
120.64
86.20
84.34
82.98
78.27
77.85
75.93
75.11
72.85
58.51
56.10
BnO
H
N
BnO
OBn
OBn
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0

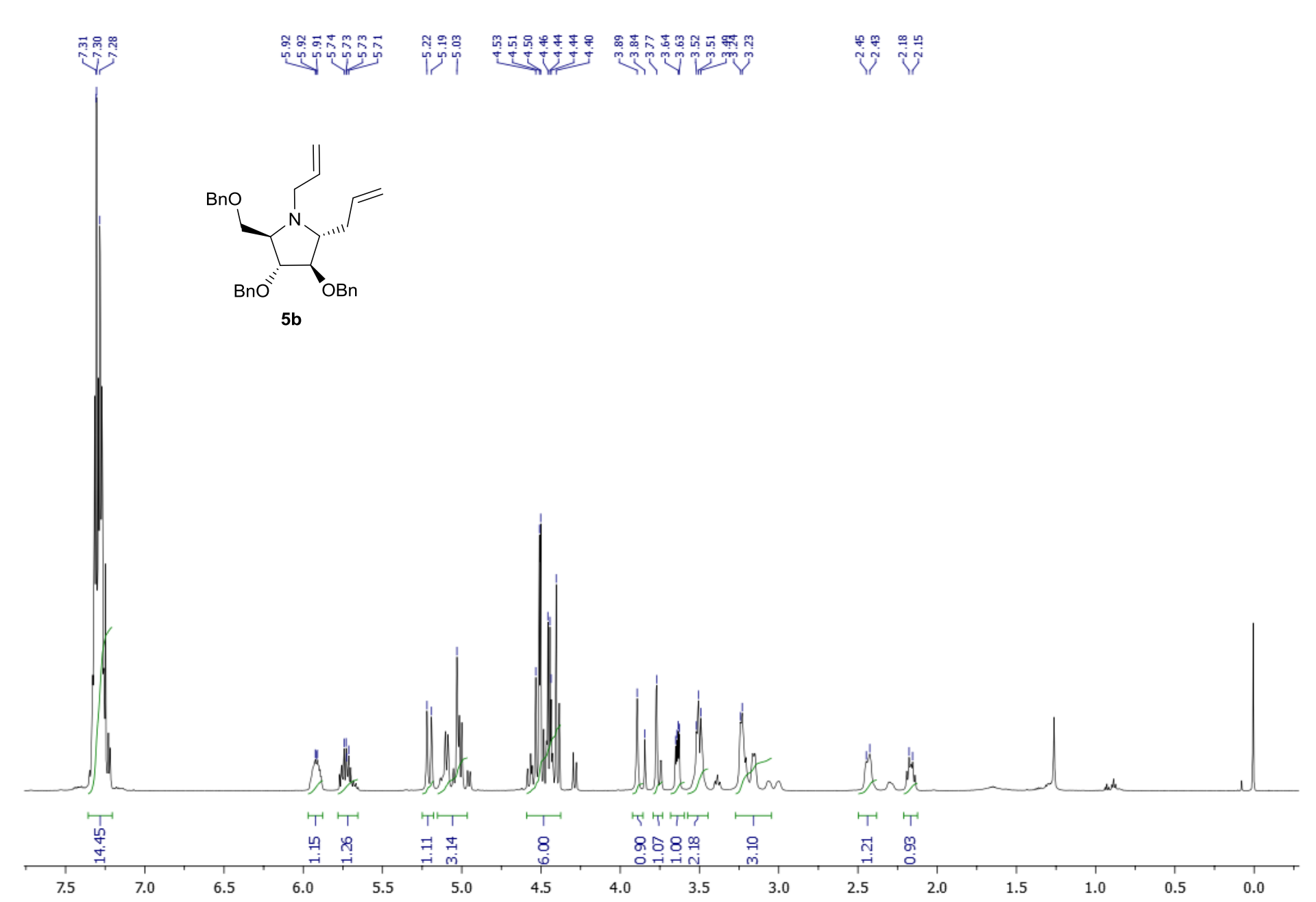
8a

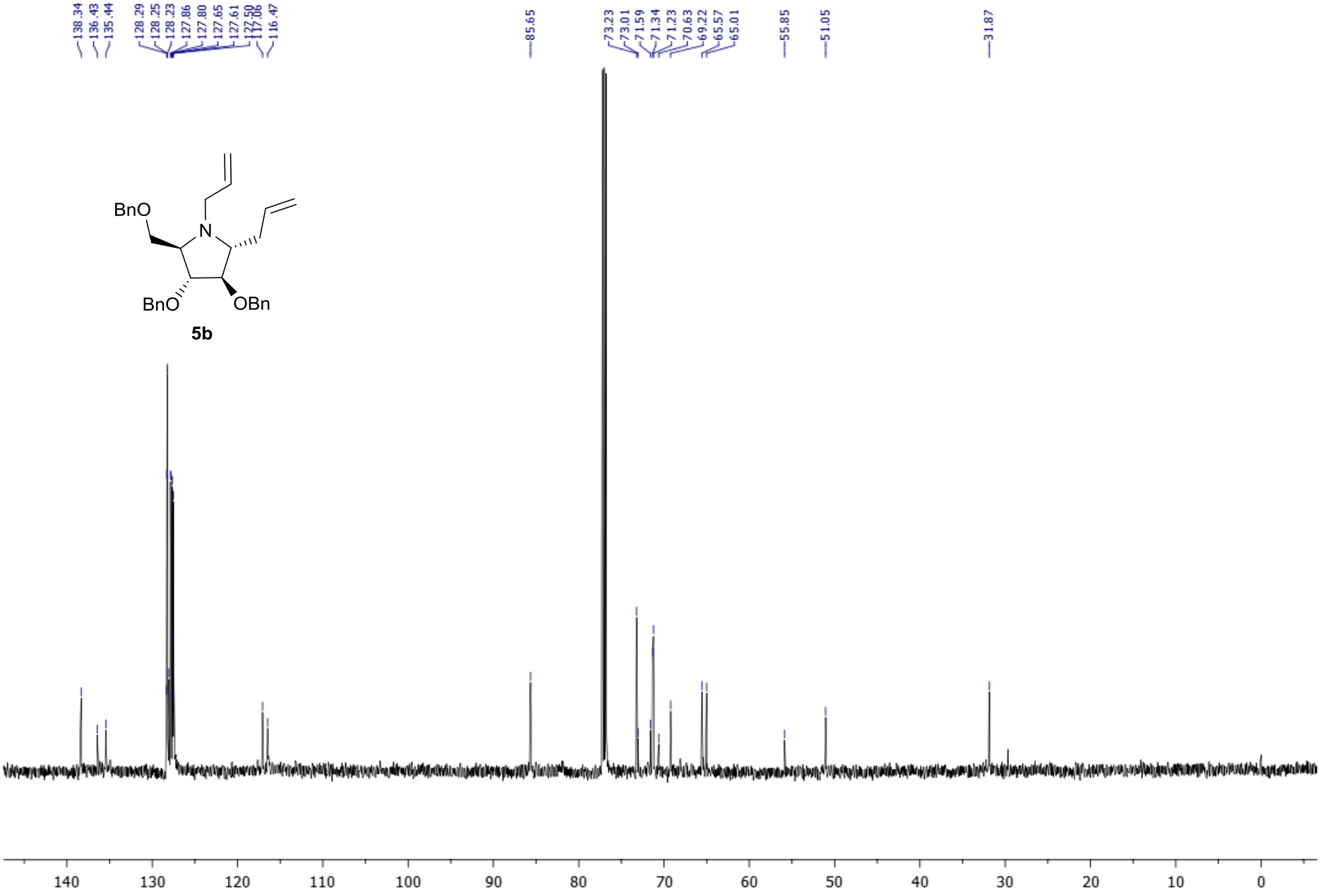

7.25
7.23
7.17
7.17
7.11
7.11
7.11
7.10
7.04
5.91
5.89
5.89
5.88
5.87
5.86
5.85
5.22
5.21
5.21
5.19
4.95
4.95
4.93
4.47
4.45
4.45
4.41
4.23
4.22
3.98
3.97
3.91
3.90
3.50
3.49
3.38
3.37
3.36
3.33
3.32
3.32
H
N
BnO
BnO
OBn
8b
3.08
1.64
7.81
2.37
1.00
0.94
0.91
2.71
0.96
1.06
0.97
0.91
0.92
0.96
0.97
0.98
0.97
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

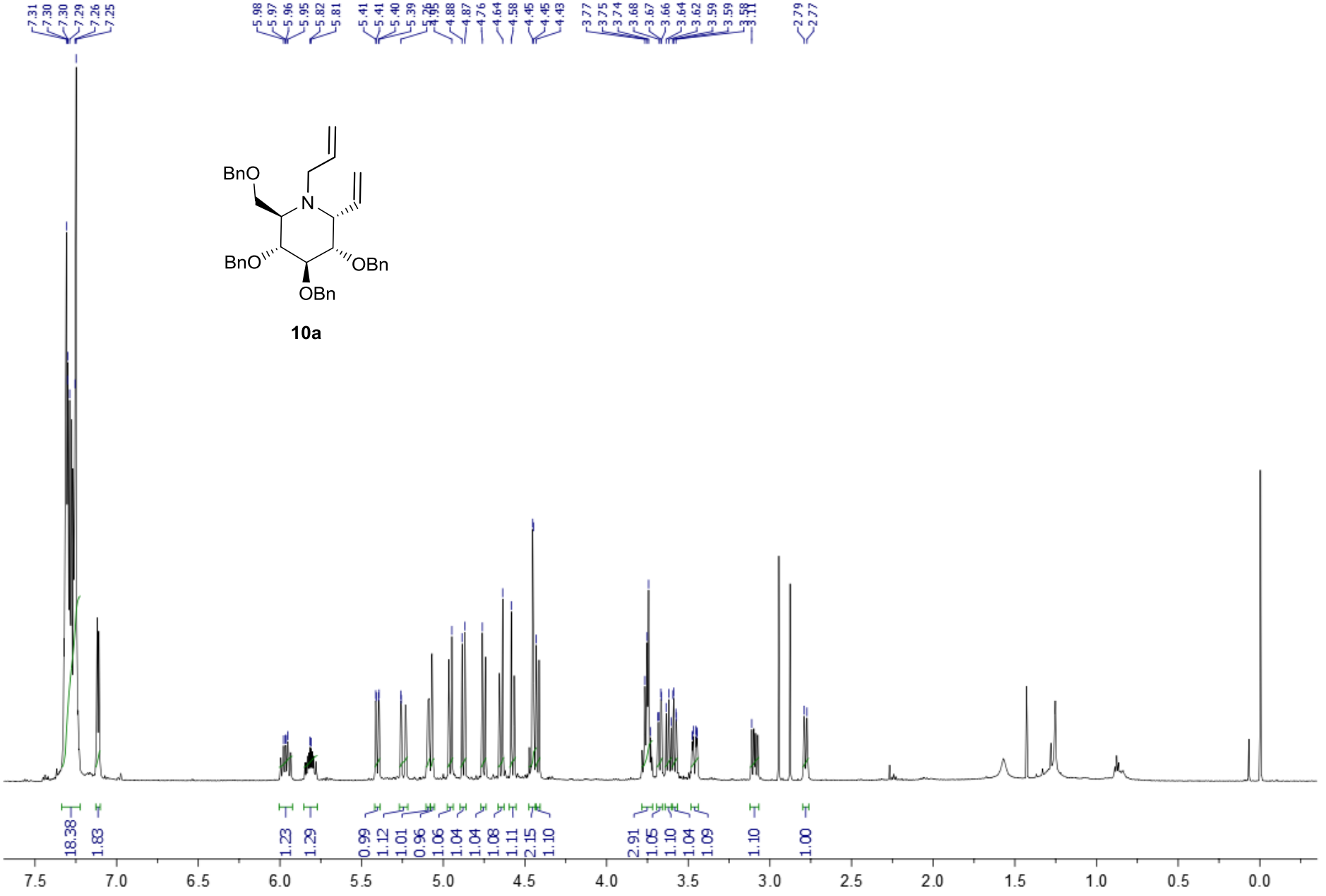

139.57
138.79
138.66
138.57
128.18
128.11
127.57
127.52
127.43
127.32
127.30
127.27
114.92
89.74
86.32
72.87
71.78
71.52
71.35
64.49
61.52
H
N
BnO
BnO
OBn
8b
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)


7.32
7.31
7.30
7.30
5.79
5.78
5.12
5.12
5.09
5.07
5.06
5.05
5.04
5.03
4.94
4.85
4.79
4.61
4.59
4.46
4.45
3.74
3.73
3.73
3.64
3.44
3.43
3.37
3.36
2.89
2.89
2.87
2.87
2.41
2.41
2.31
2.30
BnO
N
BnO
OBn
OBn
5a
19.34
1.15
1.12
1.10
0.93
1.08
1.86
1.00
1.00
1.07
1.07
1.01
1.01
0.99
1.03
1.99
1.98
1.13
1.07
1.05
1.06
1.16
1.05
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


139.04
138.62
138.56
138.05
137.78
137.38
128.33
128.32
128.28
128.27
127.90
127.85
127.84
127.76
116.36
115.26
83.83
79.70
78.51
75.34
75.10
72.99
72.28
67.63
57.56
57.28
52.36
28.53
BnO
N
BnO
OBn
OBn
5a
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

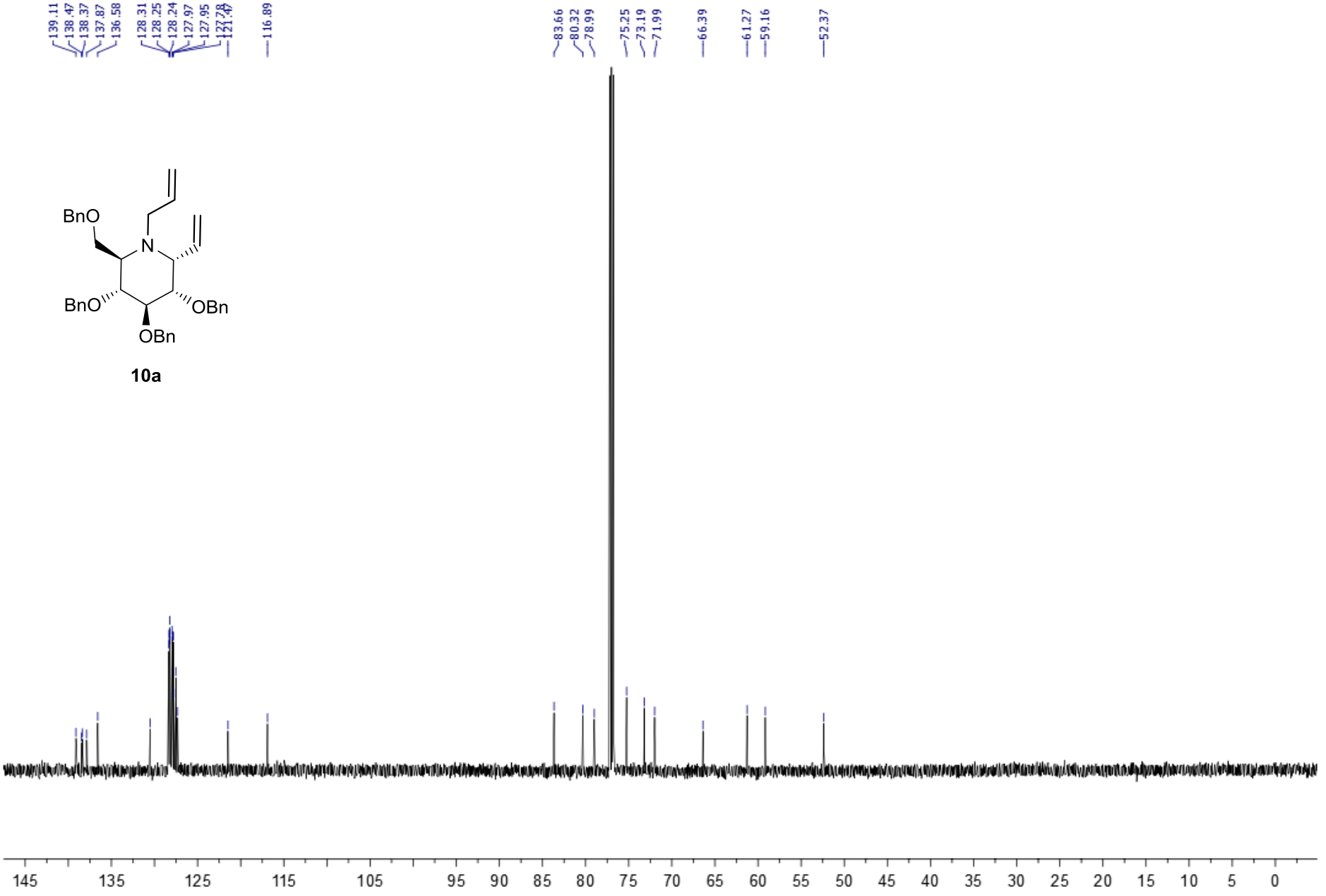

7.31
7.30
7.28
5.92
5.92
5.91
5.74
5.73
5.73
5.71
5.22
5.19
5.03
4.53
4.51
4.50
4.46
4.44
4.44
4.40
3.89
3.84
3.77
3.64
3.63
3.52
3.51
3.23
2.45
2.43
2.18
2.15
BnO
N
BnO
OBn
5b
14.45
1.15
1.26
1.11
3.14
6.00
0.90
1.07
1.00
2.18
3.10
1.21
0.93
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0


138.34
136.43
135.44
128.29
128.25
128.23
127.86
127.80
127.65
127.61
116.47
85.65
73.23
73.01
71.59
71.34
71.23
70.63
69.22
65.57
65.01
55.85
51.05
31.87
BnO
N
BnO
OBn
5b
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

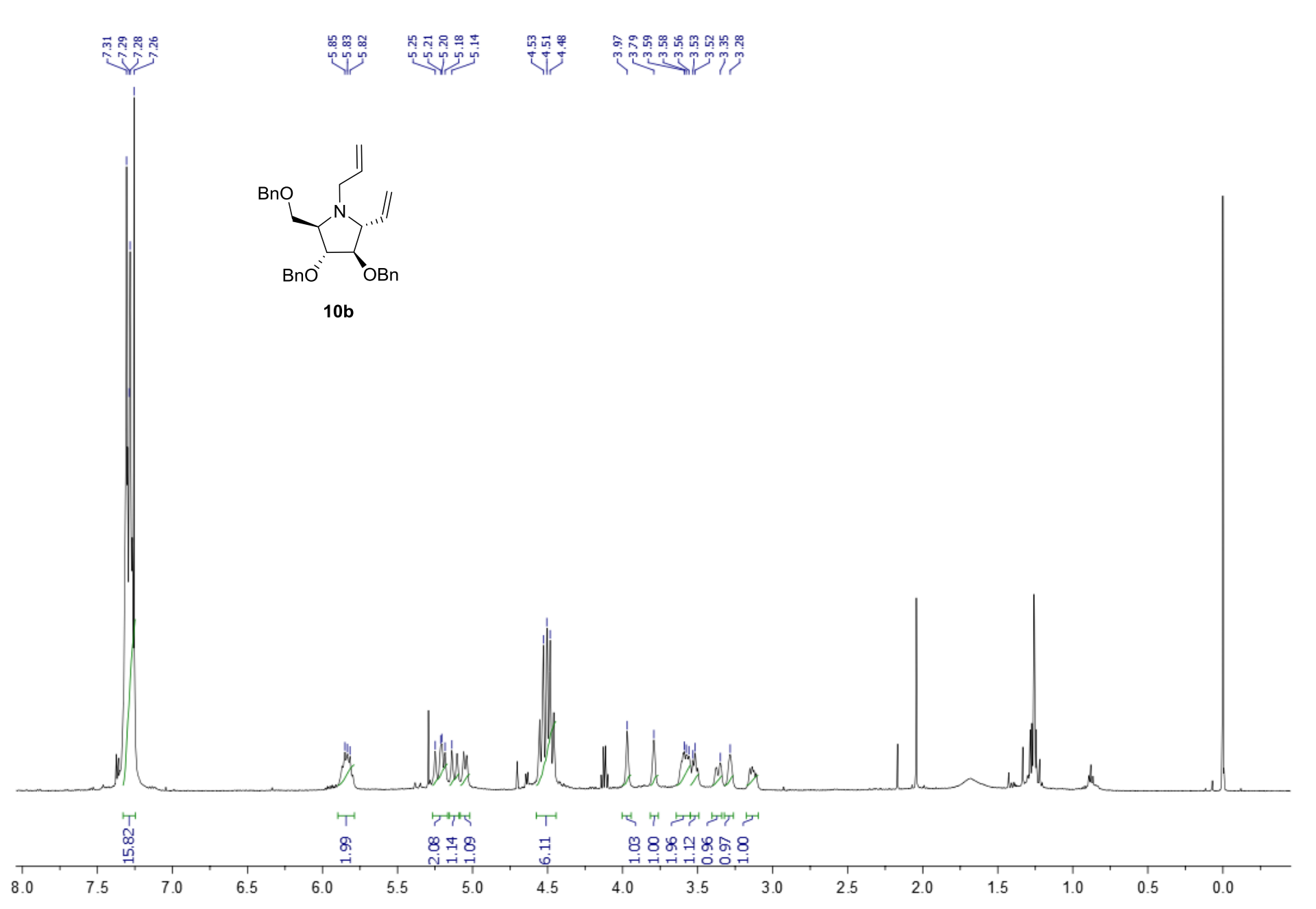


10a

The impurities between 0.5 and 2.0 ppm comes from high-boiling hexanes fraction

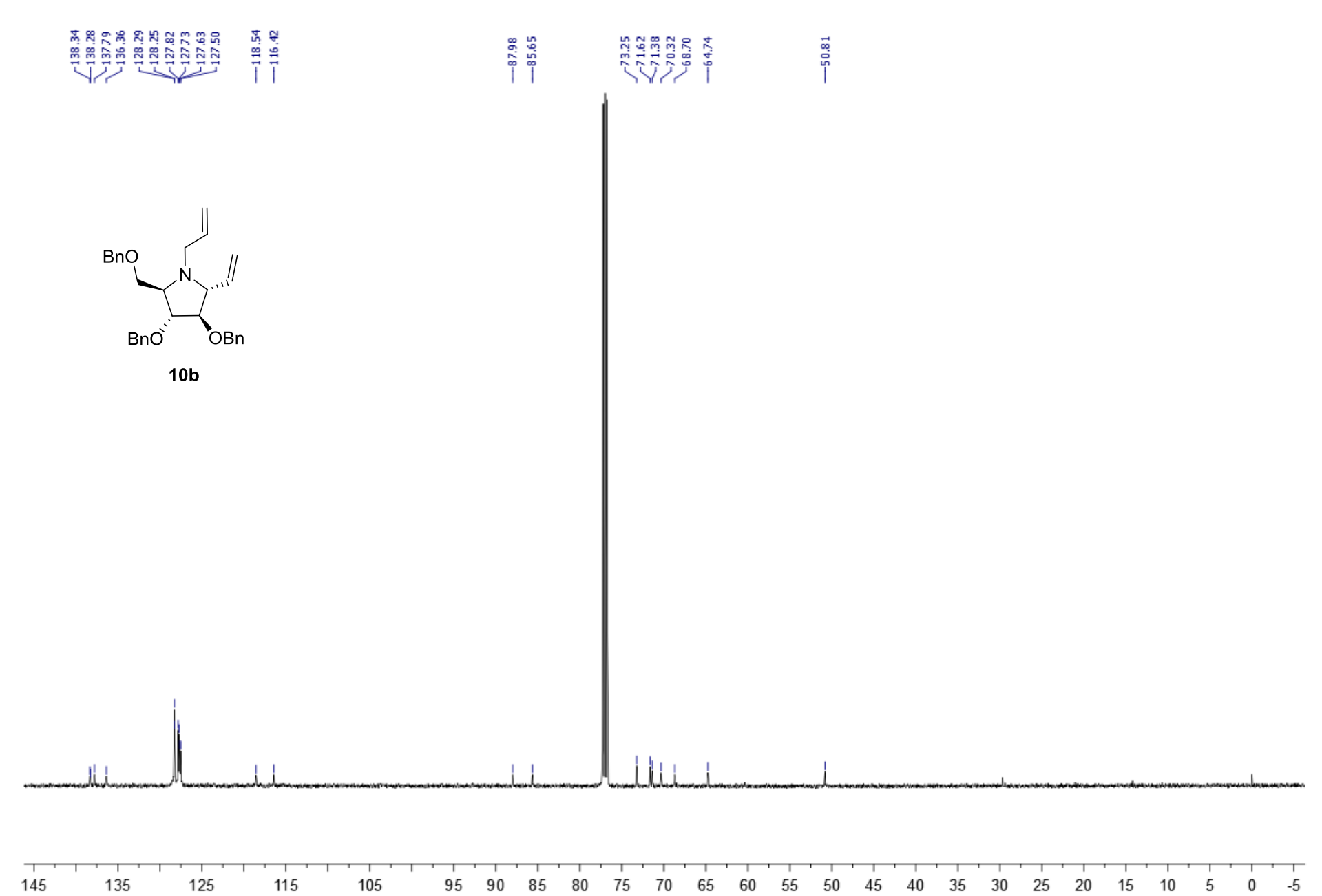

139.11
138.47
138.37
137.87
136.58
128.31
128.25
128.24
127.97
127.95
116.89
83.66
80.32
78.99
75.25
73.19
71.99
66.39
61.27
59.16
52.37
BnO
N
BnO
OBn
OBn
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0

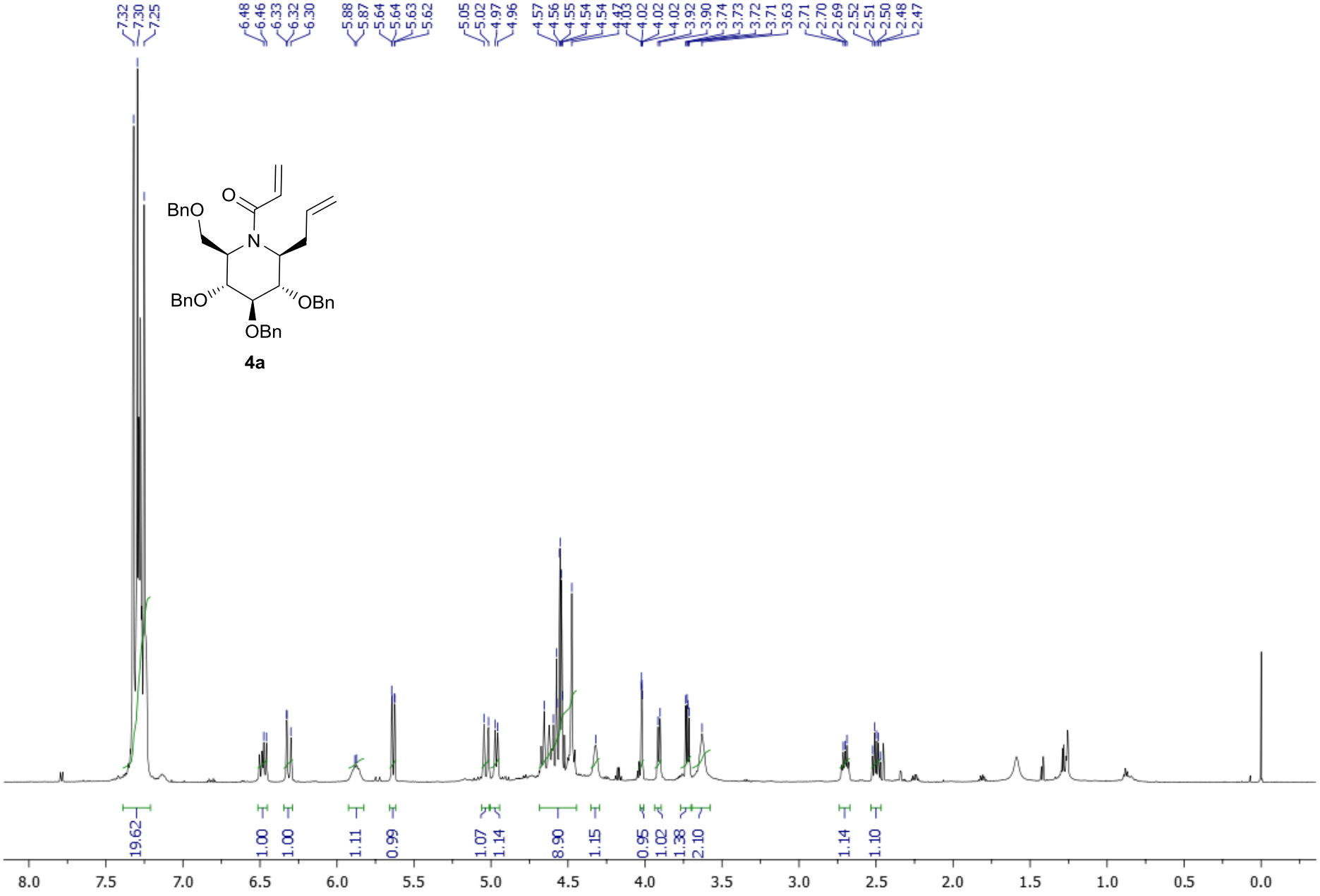
10a



10b

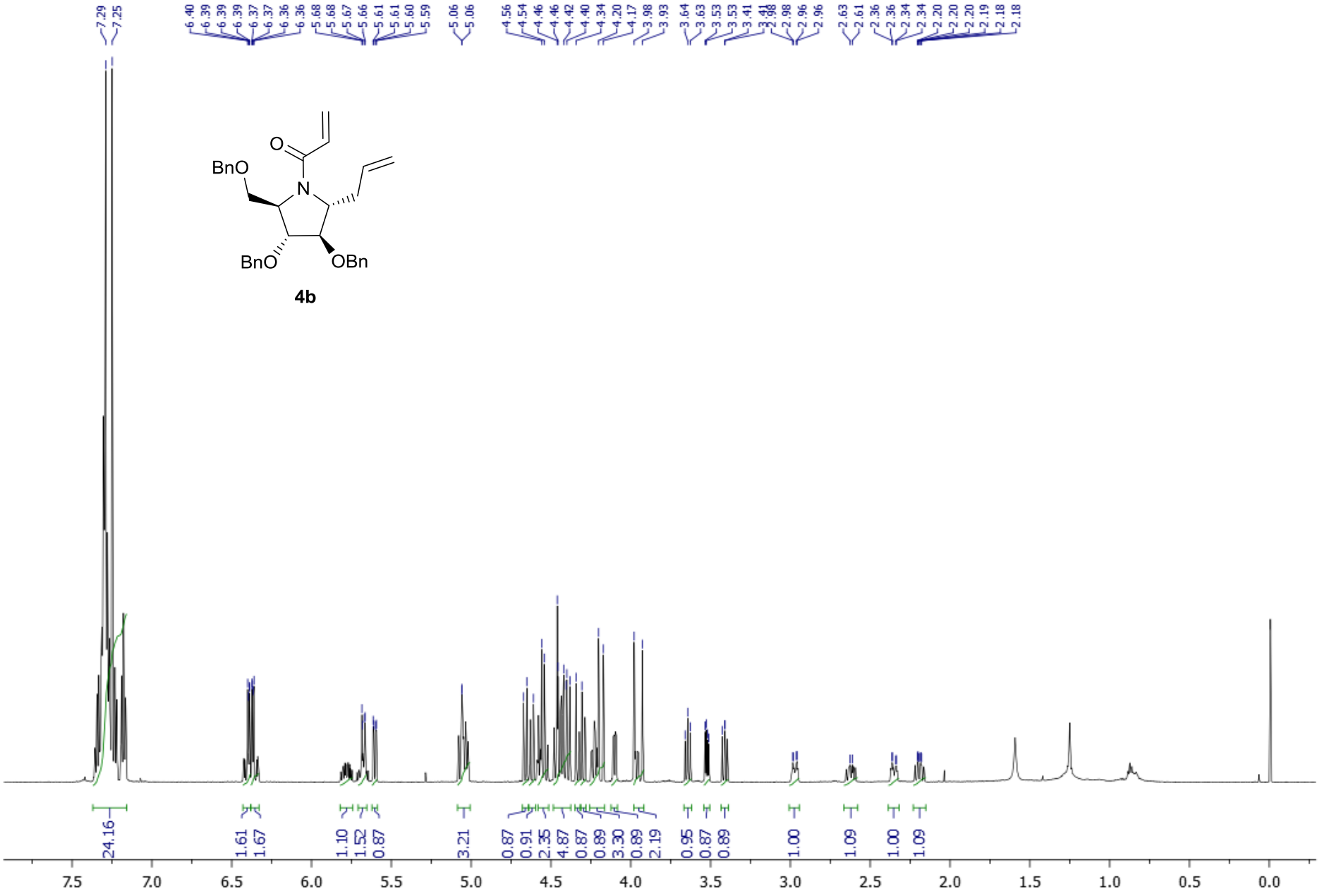
The impurities between 0.5 and 2.0 ppm comes from high-boiling hexanes fraction

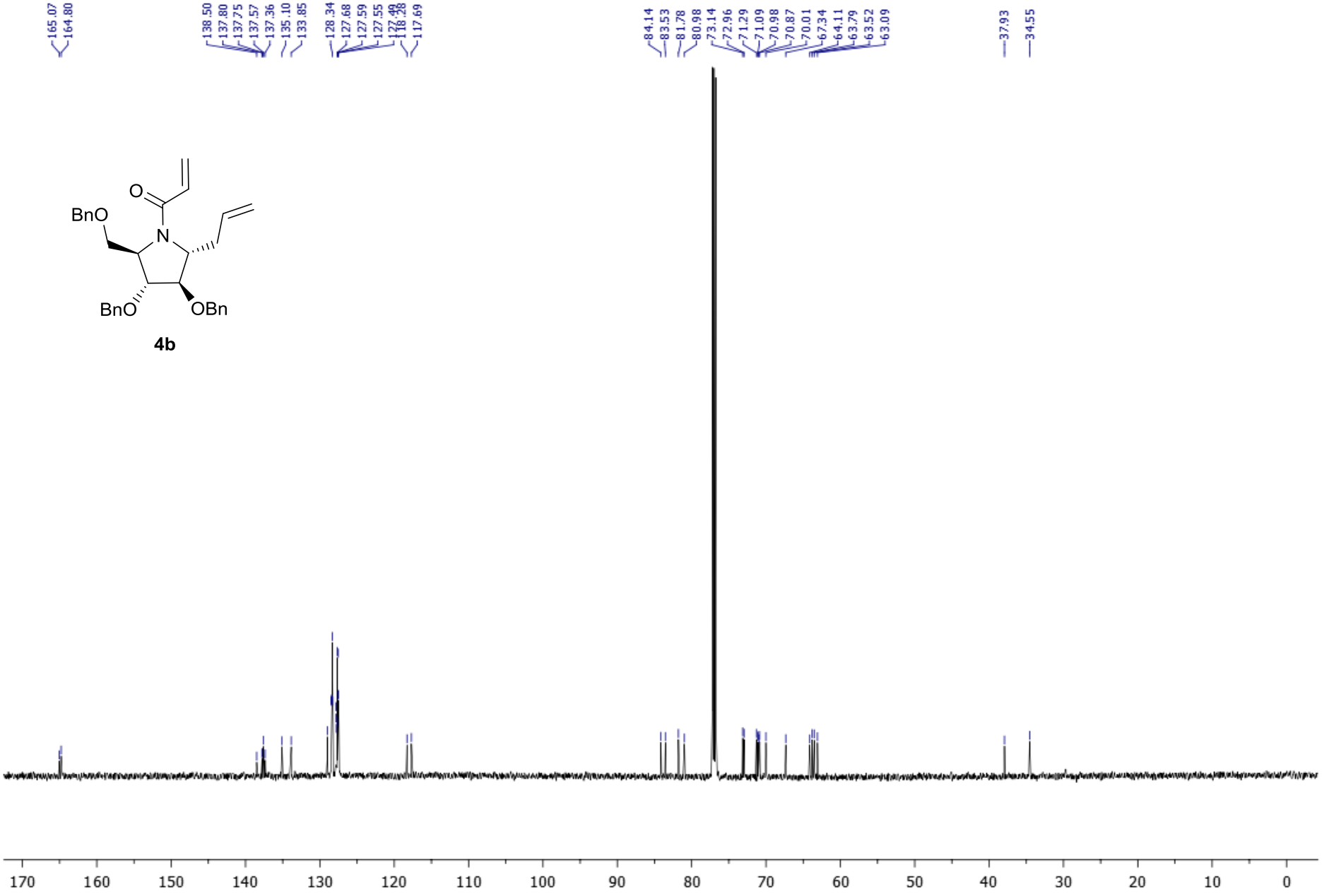

138.34
138.28
137.79
136.36
128.29
128.25
127.82
127.73
127.63
127.50
118.54
116.42
87.98
85.65
73.25
71.62
71.38
70.32
68.70
64.74
50.81
BnO
N
BnO
OBn
10b
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5

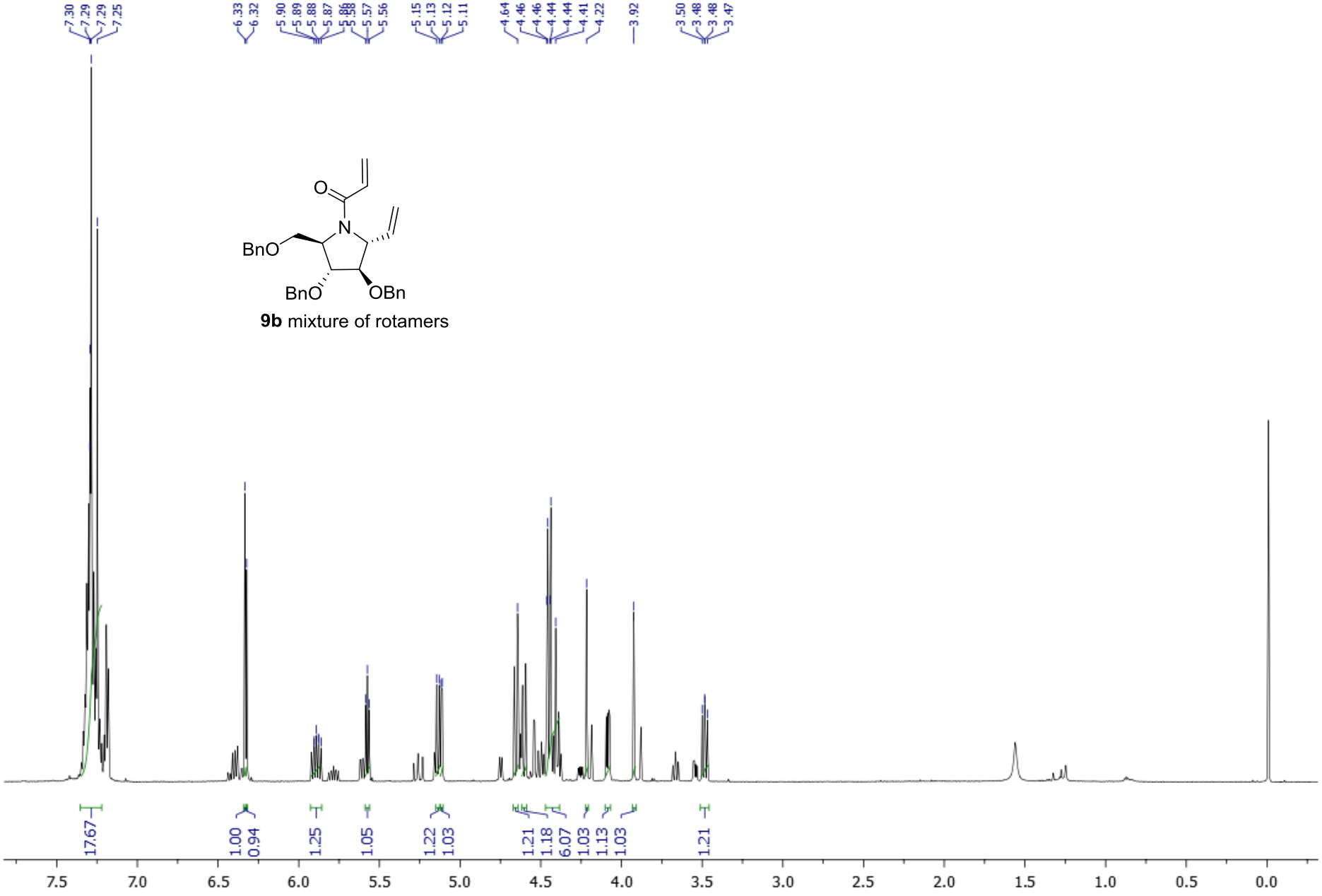


4a

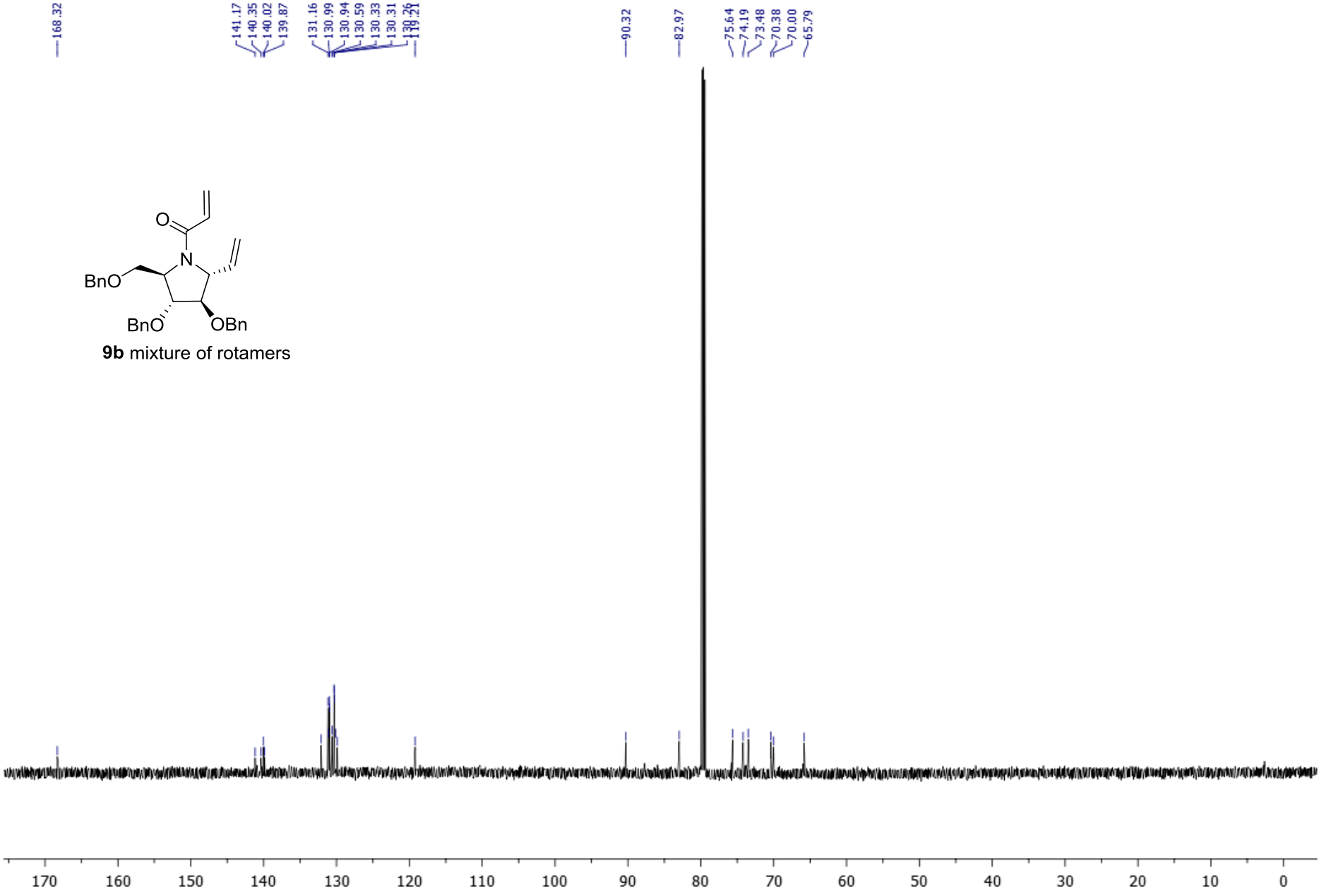
The impurities between 0.5 and 2.0 ppm comes from high-boiling hexanes fraction


7.29
7.25
6.40
6.39
6.39
6.39
6.37
6.37
6.36
6.36
5.68
5.68
5.67
5.66
5.61
5.61
5.60
5.59
5.06
5.06
4.56
4.54
4.46
4.46
4.42
4.40
4.34
4.20
4.17
3.98
3.93
3.64
3.63
3.53
3.53
3.41
2.98
2.98
2.96
2.96
2.63
2.61
2.36
2.36
2.34
2.34
2.20
2.20
2.20
2.19
2.18
2.18
O
BnO
N
BnO
OBn
4b
24.16
1.61
1.67
1.10
1.52
0.87
3.21
0.87
0.91
2.35
4.87
0.87
0.89
3.30
0.89
2.19
0.95
0.87
0.89
1.00
1.09
1.00
1.09
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

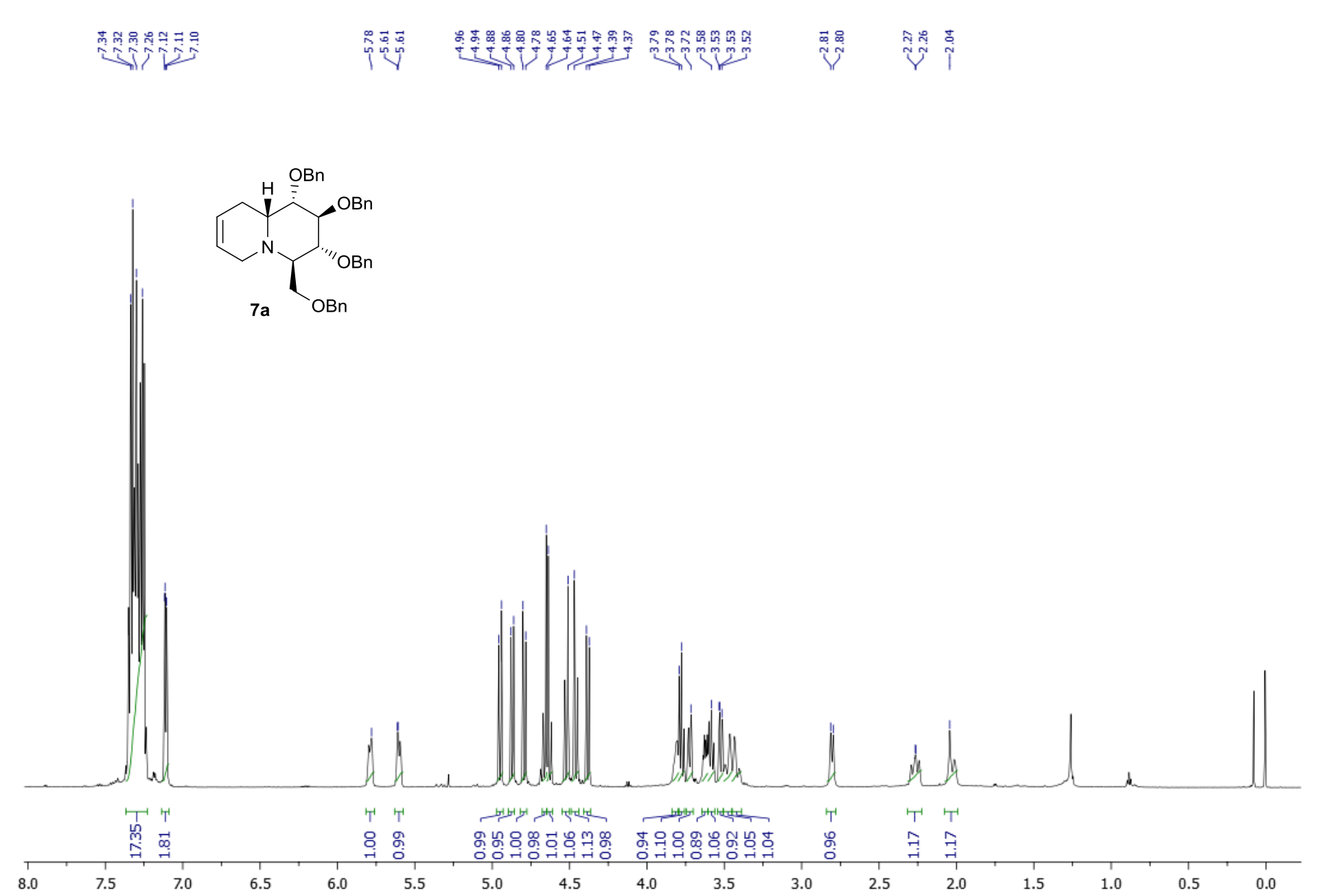

165.07
164.80
138.50
137.80
137.75
137.57
137.36
135.10
133.85
128.34
127.68
127.59
127.55
127.49
118.28
117.69
84.14
83.53
81.78
80.98
73.14
72.96
71.29
71.09
70.98
70.87
70.01
67.34
64.11
63.79
63.52
63.09
37.93
34.55
O
BnO
N
BnO
OBn
4b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

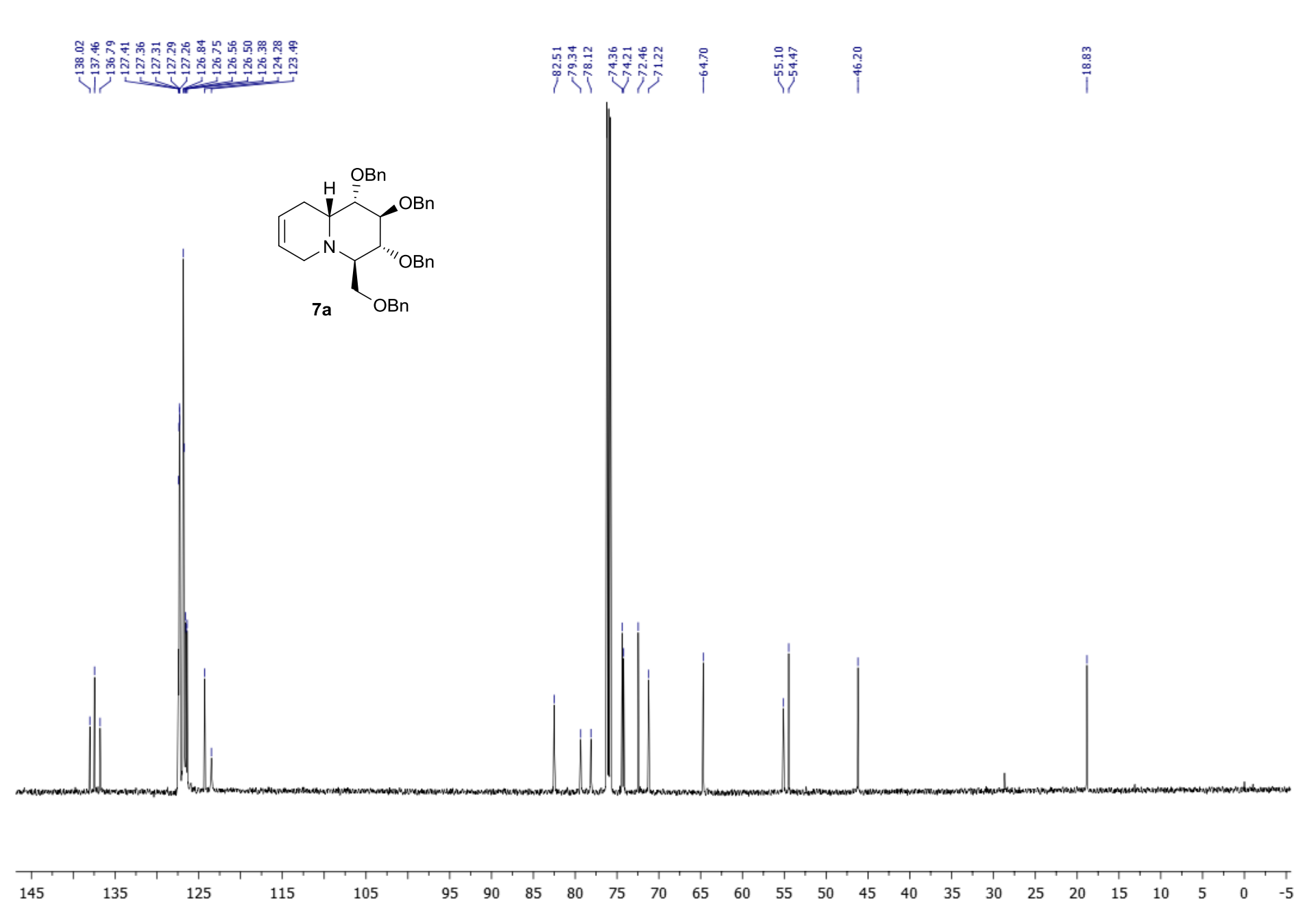


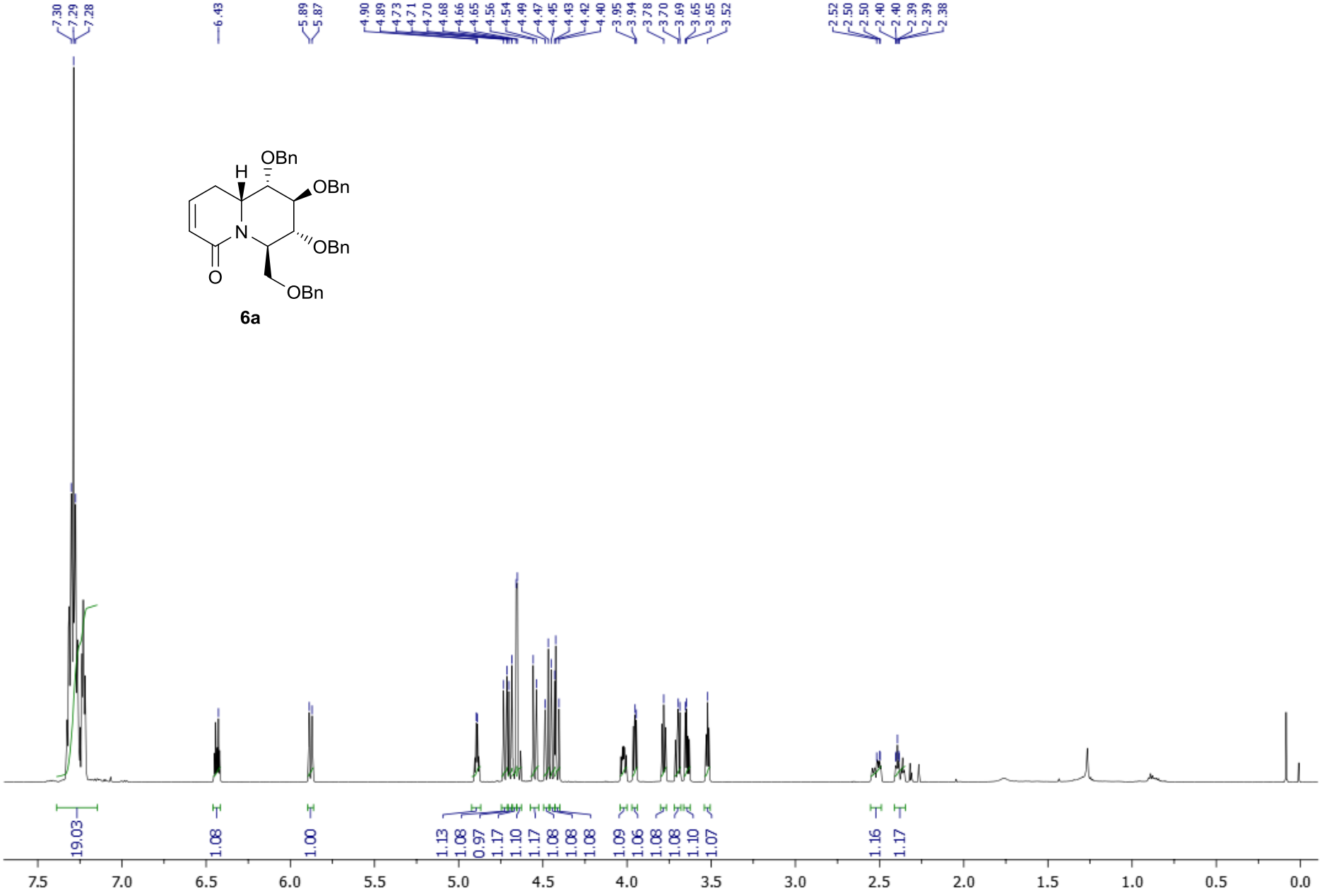
9b mixture of rotamers

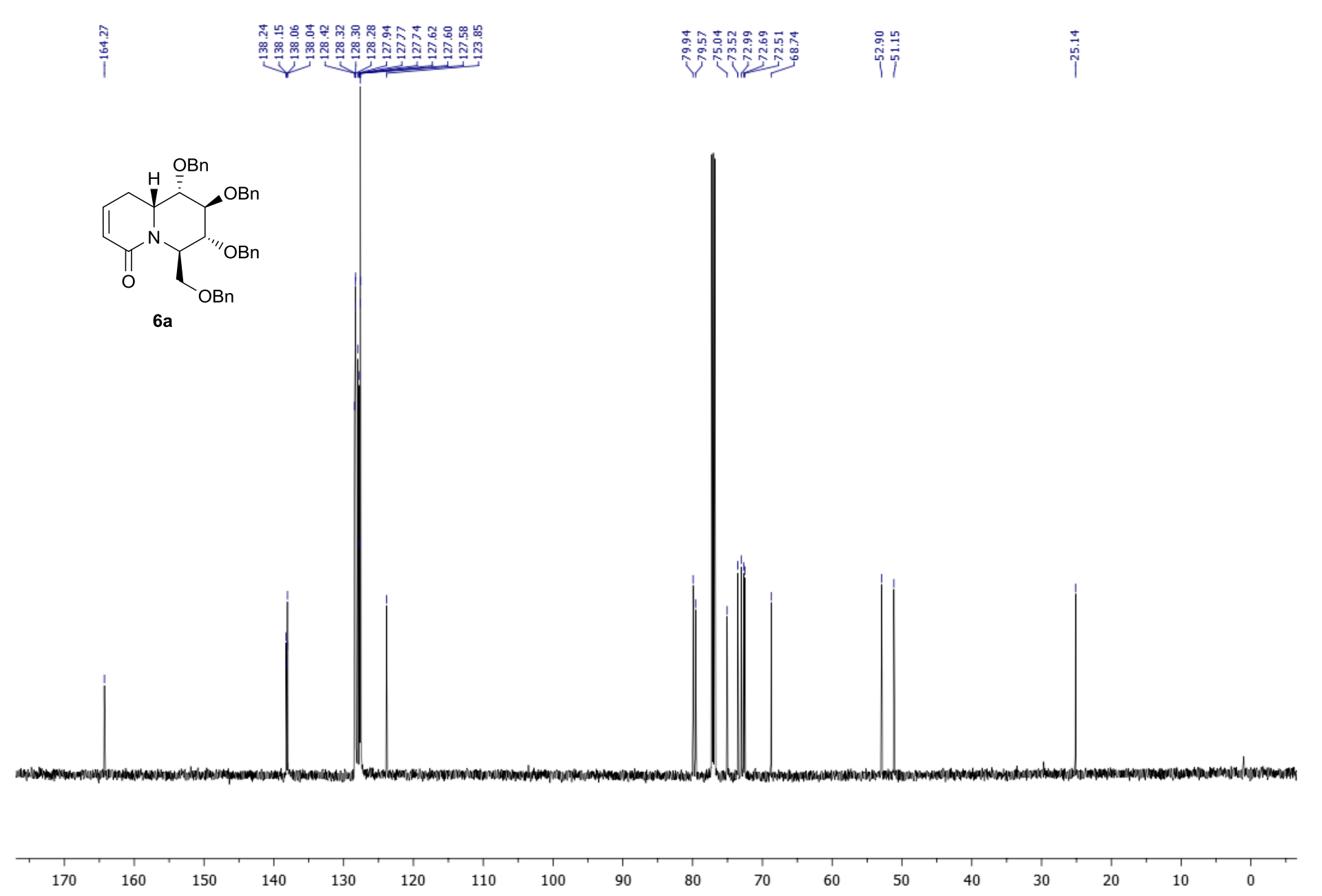


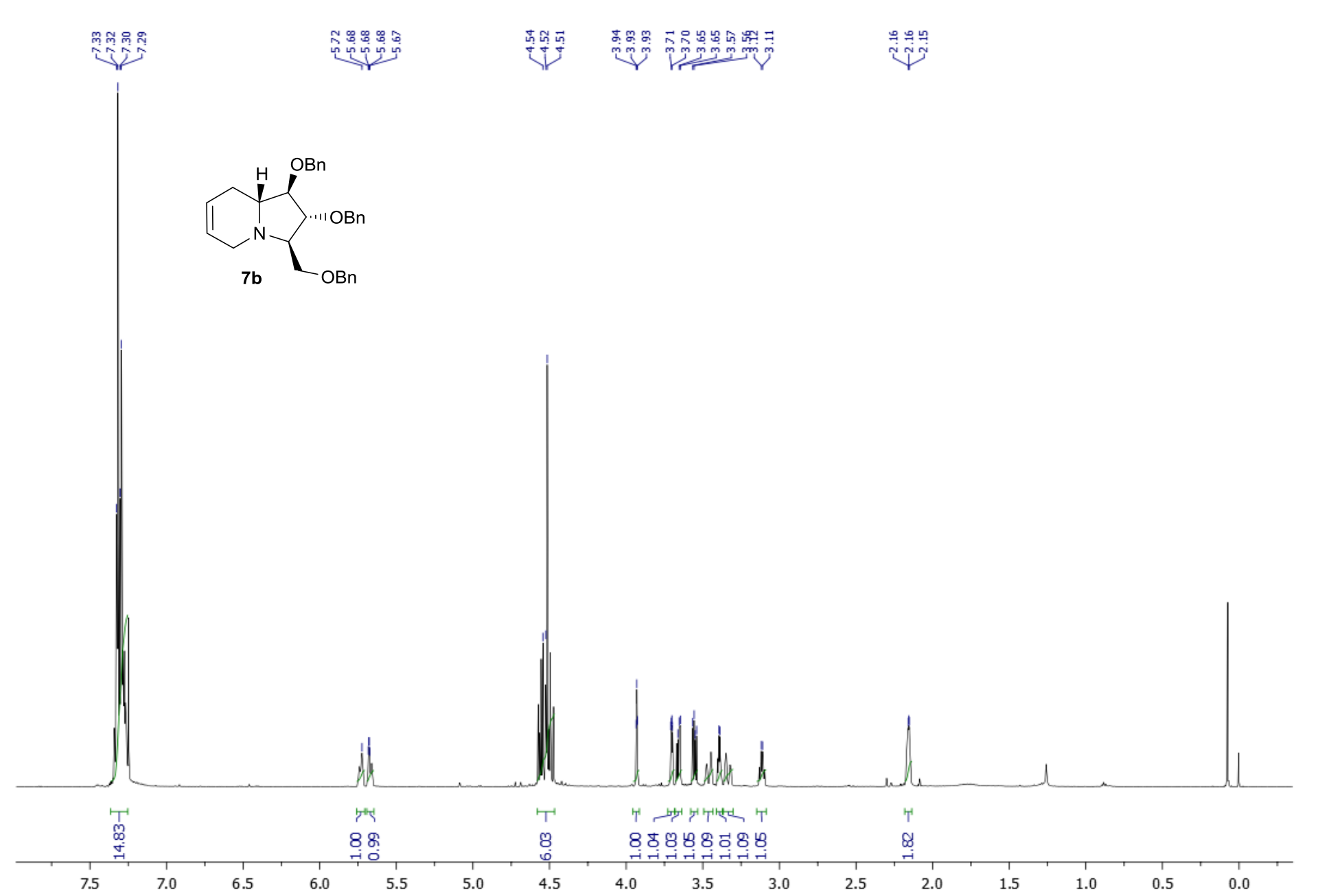
9b mixture of rotamers

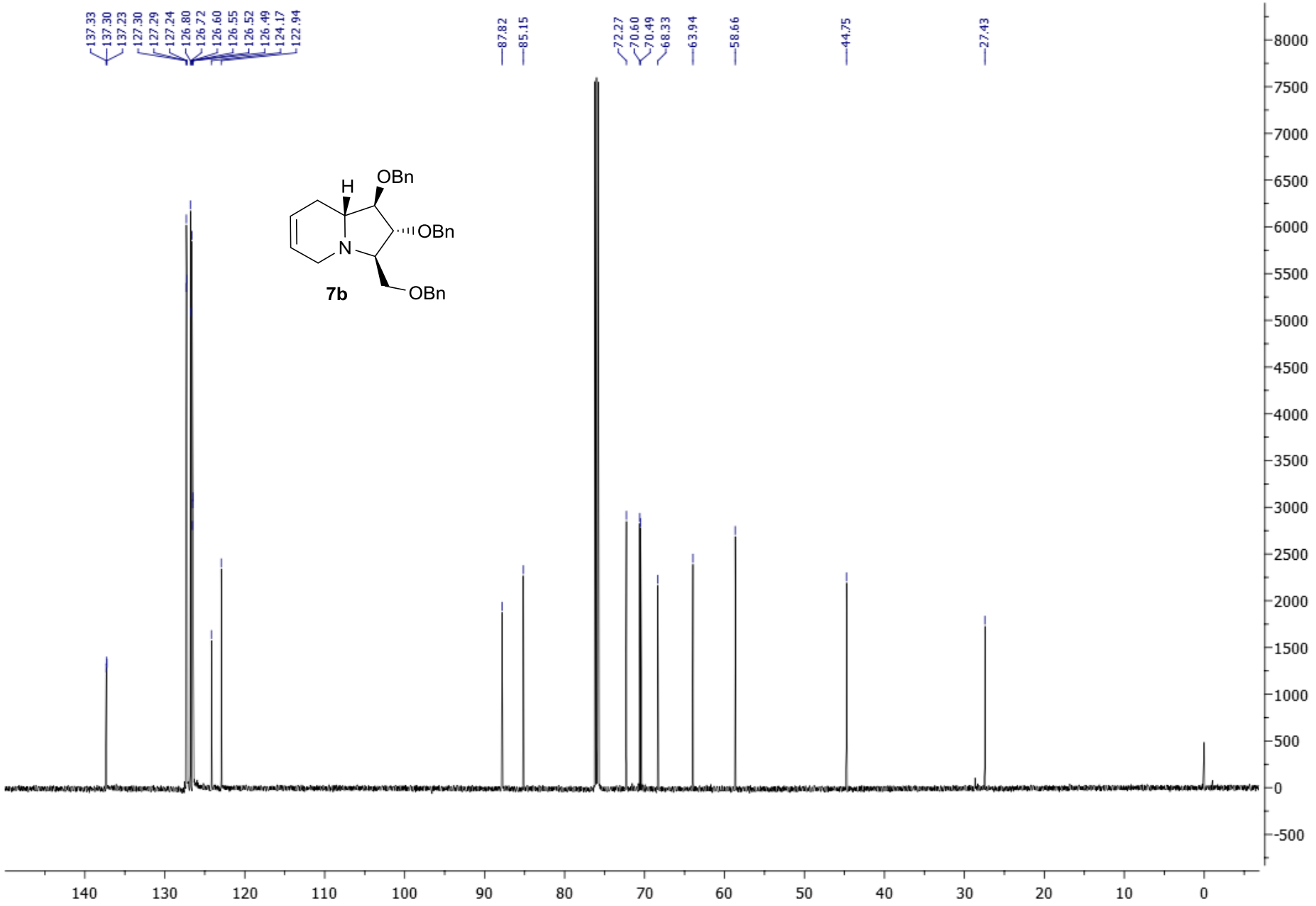

7.34
7.32
7.30
7.26
7.12
7.11
7.10
5.78
5.61
5.61
4.96
4.94
4.88
4.86
4.80
4.78
4.65
4.64
4.51
4.47
4.39
4.37
3.79
3.78
3.72
3.58
3.53
3.53
3.52
2.81
2.80
2.27
2.26
2.04
OBn
H
OBn
N
OBn
OBn
7a
17.35
1.81
1.00
0.99
0.99
0.95
1.00
0.98
1.01
1.06
1.13
0.98
0.94
1.10
1.00
0.89
1.06
0.92
1.05
1.04
0.96
1.17
1.17
8.0
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

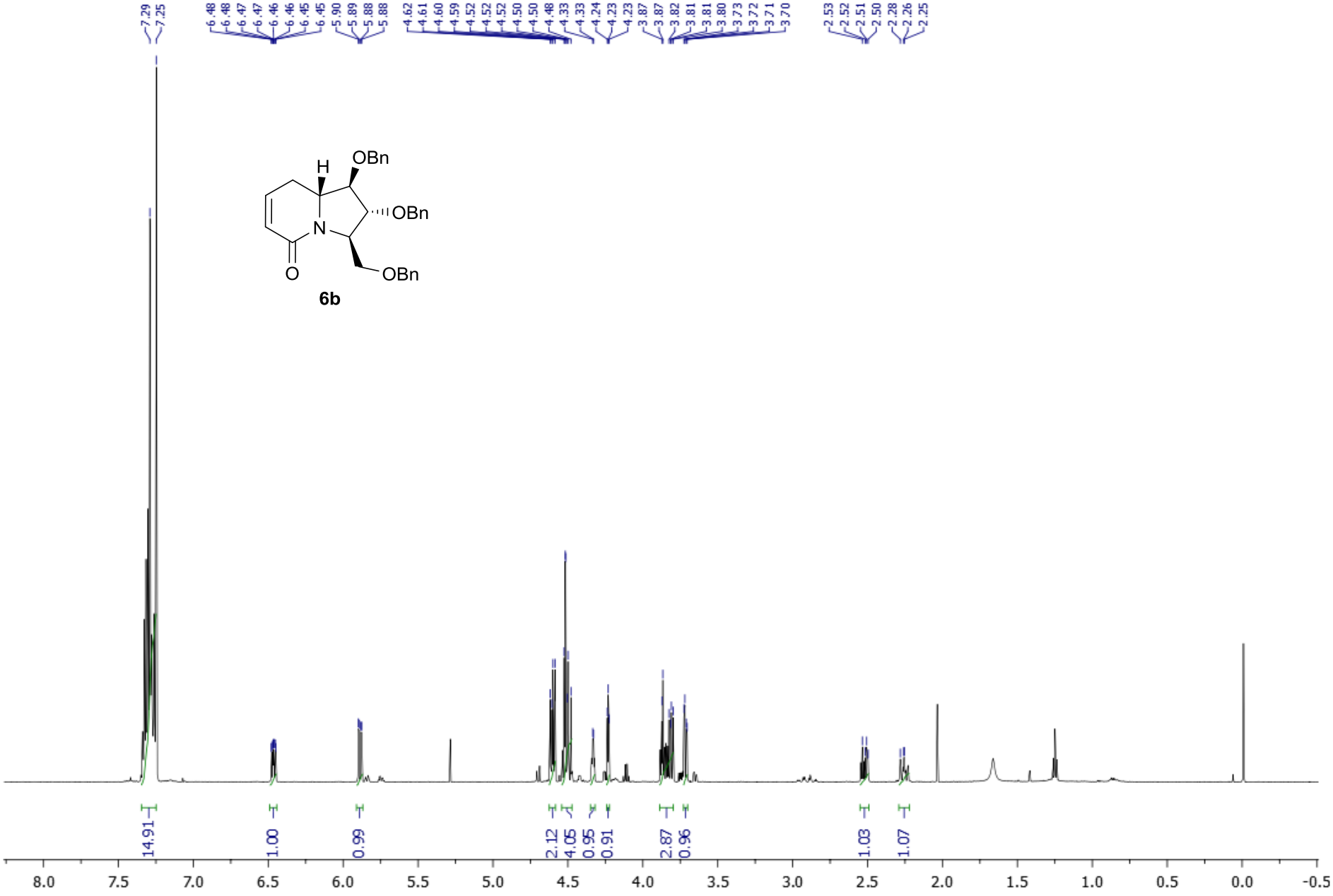

138.02
137.46
136.79
127.41
127.36
127.31
127.29
127.26
126.84
126.75
126.56
126.50
126.38
124.28
123.49
82.51
79.34
78.12
74.36
74.21
72.46
71.22
64.70
55.10
54.47
46.20
18.83
H
OBn
OBn
OBn
OBn
N
7a
145
135
125
115
105
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5

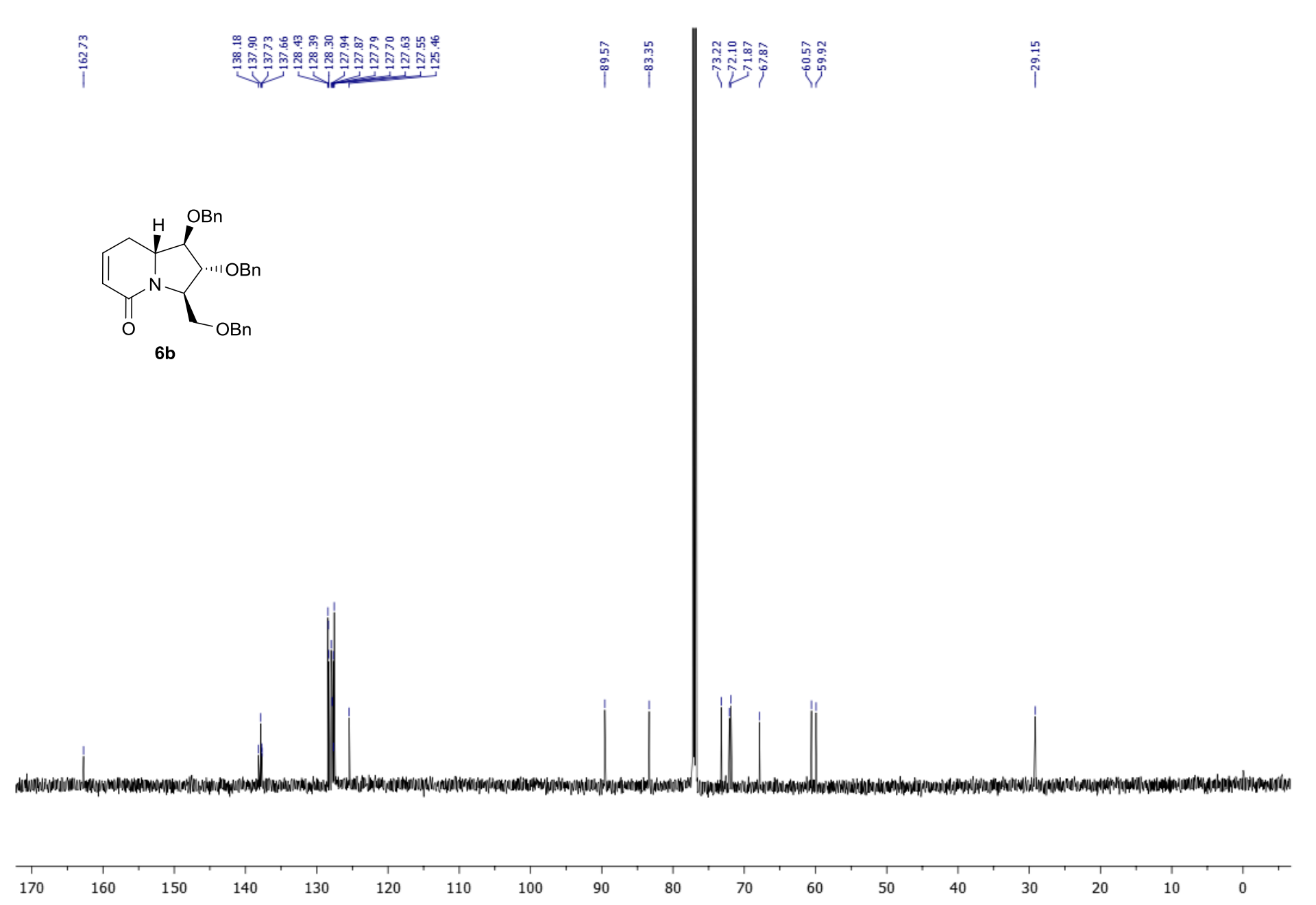

7.30
7.29
7.28
6.43
5.89
5.87
4.90
4.89
4.73
4.71
4.70
4.68
4.66
4.65
4.56
4.54
4.49
4.47
4.45
4.43
4.42
4.40
3.95
3.94
3.78
3.70
3.69
3.65
3.65
3.52
2.52
2.50
2.50
2.40
2.40
2.39
2.39
2.38
OBn
H
OBn
N
OBn
O
OBn
6a
19.03
1.08
1.00
1.13
1.08
0.97
1.17
1.10
1.17
1.08
1.08
1.08
1.09
1.06
1.08
1.08
1.10
1.07
1.16
1.17
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

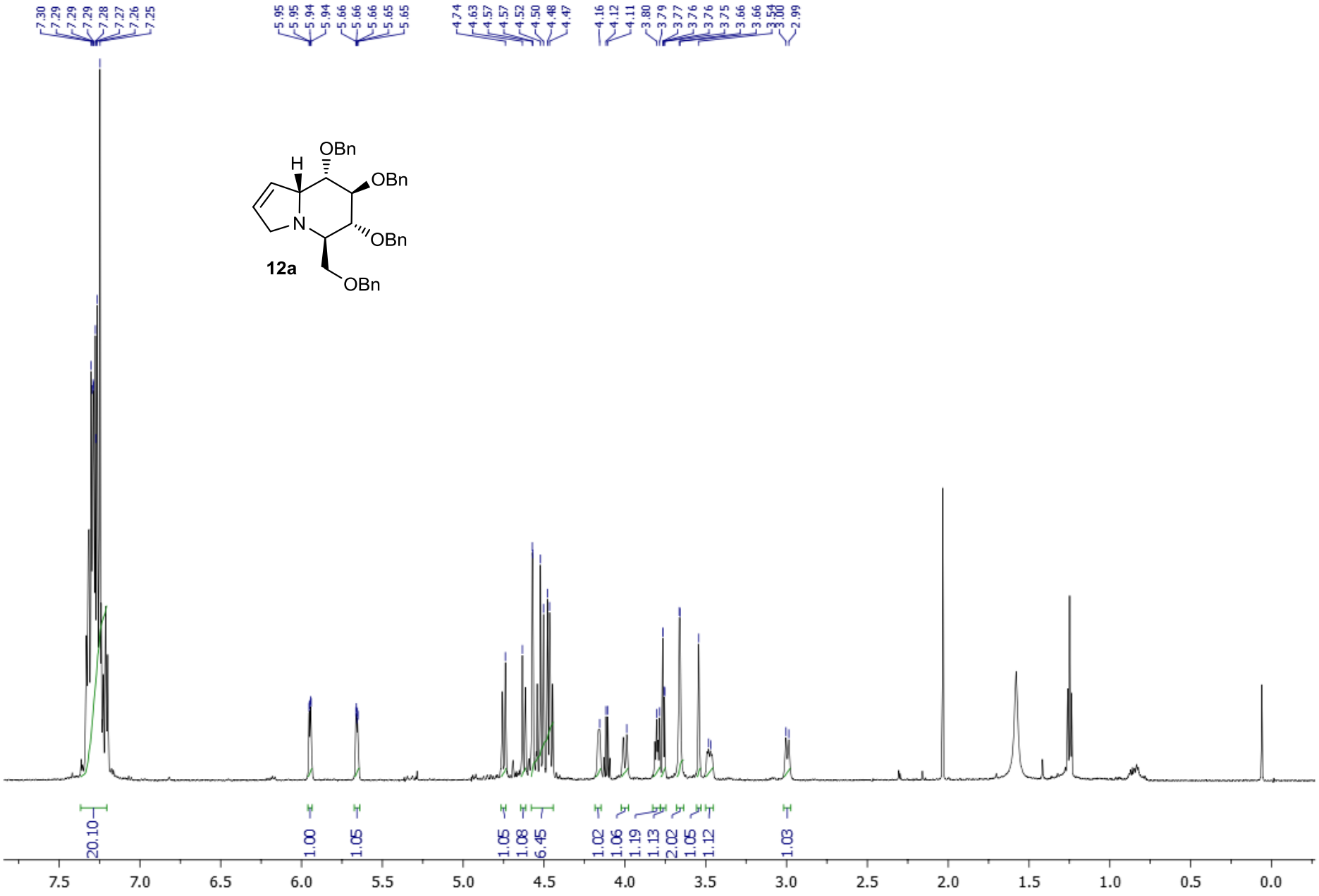

164.27
138.24
138.15
138.06
138.04
128.42
128.32
128.30
128.28
127.94
127.77
127.74
127.62
127.60
127.58
123.85
79.94
79.57
75.04
73.52
72.99
72.69
72.51
68.74
52.90
51.15
25.14
H
OBn
OBn
N
OBn
O
OBn
6a
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.33
7.32
7.30
7.29
5.72
5.68
5.68
5.68
5.67
4.54
4.52
4.51
3.94
3.93
3.93
3.71
3.70
3.65
3.65
3.57
3.56
3.12
3.11
2.16
2.16
2.15
H
OBn
OBn
N
OBn
7b
14.83
1.00
0.99
6.03
1.00
1.04
1.03
1.05
1.09
1.01
1.09
1.05
1.82
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

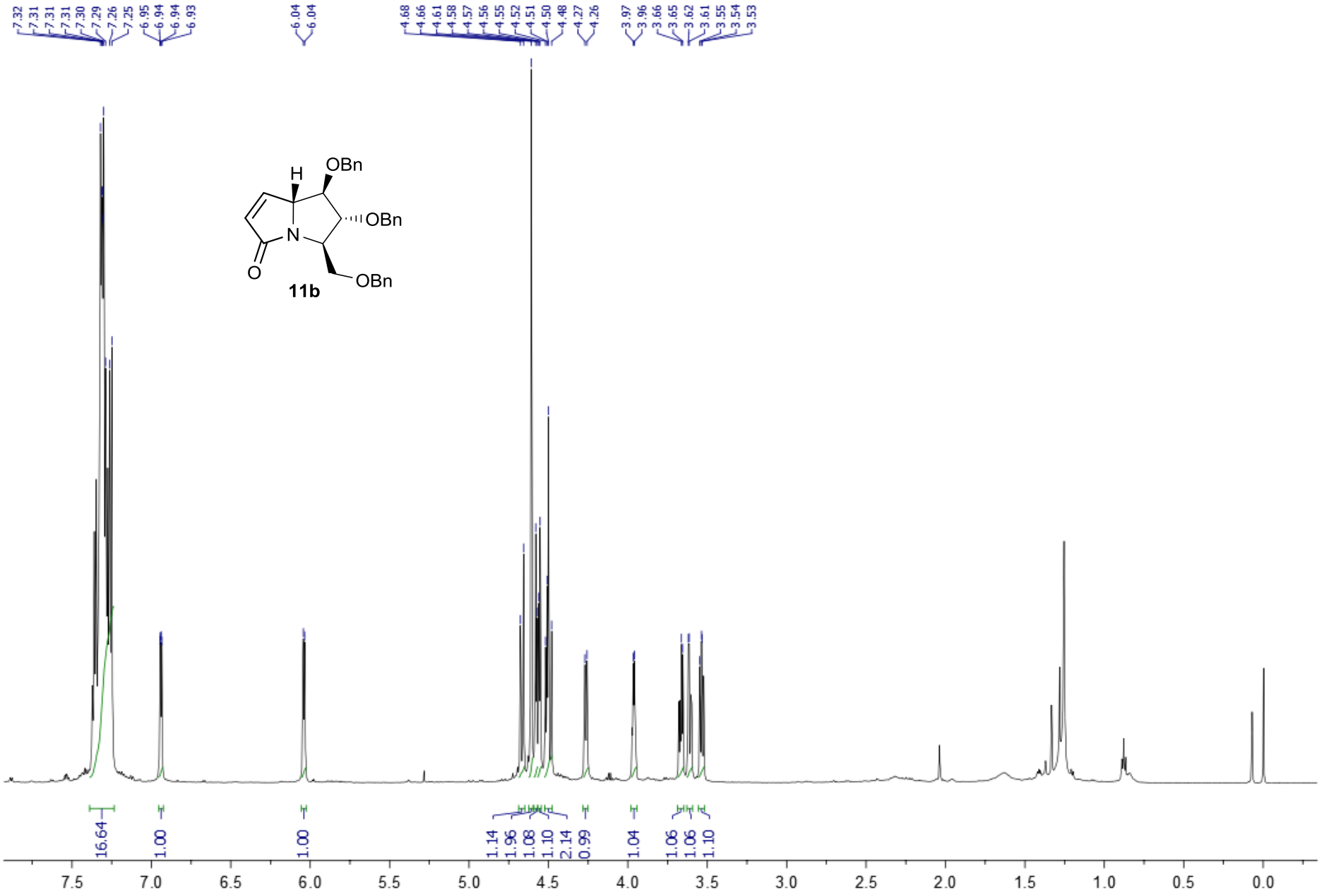

137.33
137.30
137.23
127.30
127.29
127.24
126.80
126.72
126.60
126.55
126.52
126.49
124.17
122.94
87.82
85.15
72.27
70.60
70.49
68.33
63.94
58.66
44.75
27.43
H
OBn
OBn
N
OBn
7b
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0


7.29
7.25
6.48
6.48
6.47
6.47
6.46
6.46
6.45
6.45
5.90
5.89
5.88
5.88
4.62
4.61
4.60
4.59
4.52
4.52
4.52
4.50
4.50
4.48
4.33
4.33
4.24
4.23
4.23
3.87
3.87
3.82
3.81
3.81
3.80
3.73
3.72
3.71
3.70
2.53
2.52
2.51
2.50
2.28
2.26
2.25
H
OBn
OBn
N
O
OBn
6b
14.91
1.00
0.99
2.12
4.05
0.95
0.91
2.87
0.96
1.03
1.07
8.0
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
-0.5

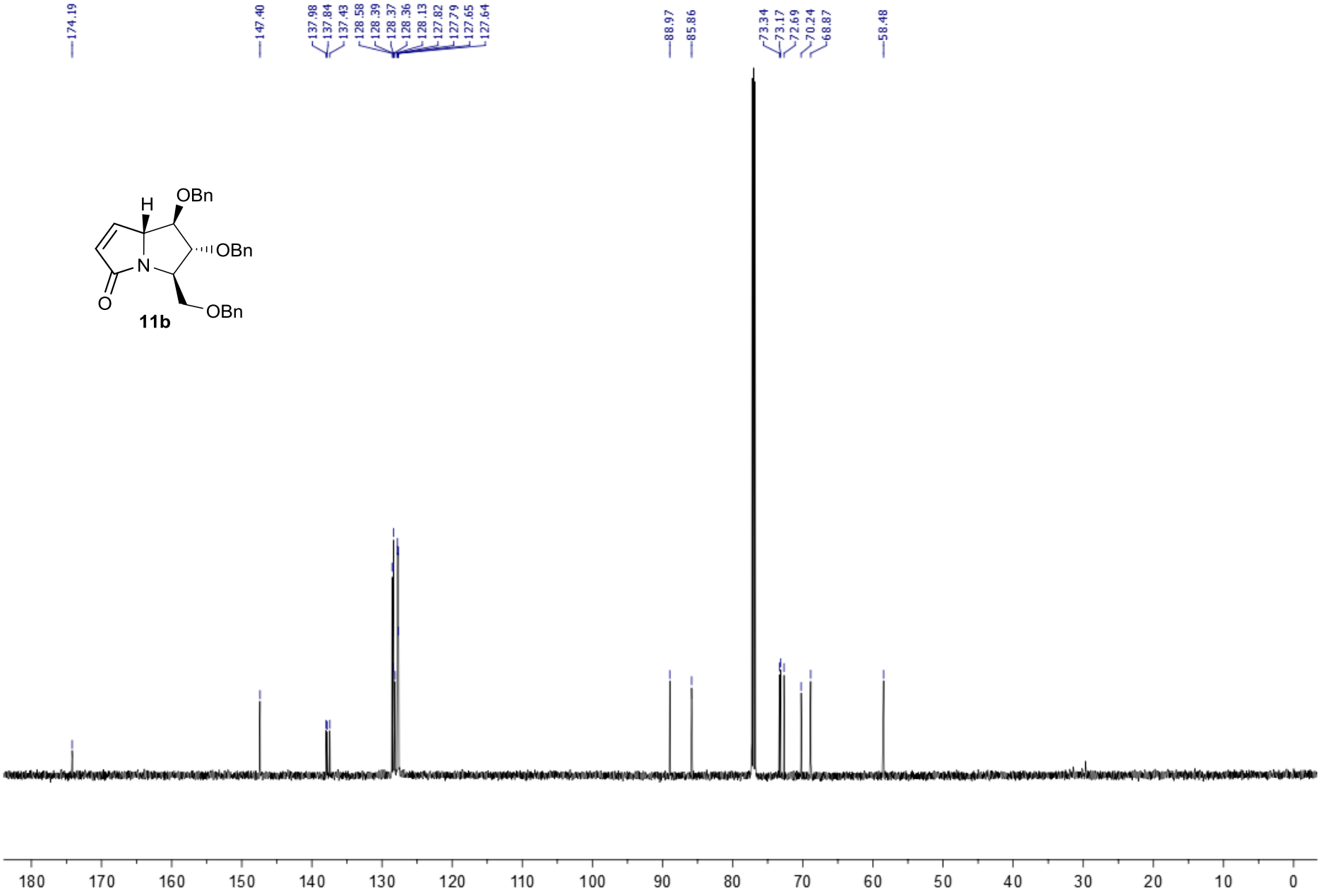

162.73
138.18
137.90
137.73
137.66
128.43
128.39
128.30
127.94
127.87
127.79
127.70
127.63
127.55
125.46
89.57
83.35
73.22
72.10
71.87
67.87
60.57
59.92
29.15
H
OBn
OBn
N
O
OBn
6b
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



The impurities between 0.5 and 2.0 ppm comes from high-boiling hexanes fraction



The impurities between 0.5 and 2.0 ppm comes from high-boiling hexanes fraction


174.19
147.40
137.98
137.84
137.43
128.58
128.39
128.37
128.36
128.13
127.82
127.79
127.65
127.64
88.97
85.86
73.34
73.17
72.69
70.24
68.87
58.48
H
OBn
OBn
N
O
OBn
11b
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0