Supporting Information

Pd-Catalyzed Hydroamination of Alkoxyallenes with Azole Heterocycles: Examples and Mechanistic Proposal

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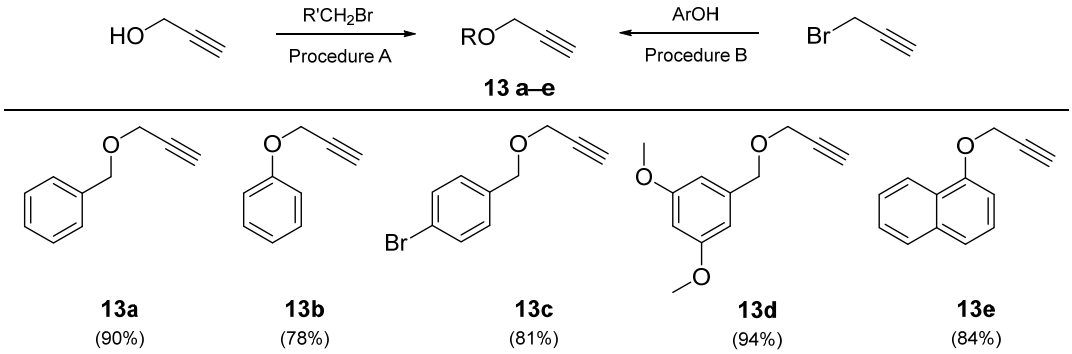
Contents

General methods

^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 400 MHz or Bruker 500 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) relative to tetramethylsilane (TMS), or residual solvents as the internal standard. NMR data is presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet and/or multiple resonances), coupling constant in hertz (Hz), integration. All NMR signals were assigned on the basis of ^{1}H NMR, ^{13}C NMR, COSY, HSQC, HMBS and NOESY experiments. Mass spectra were recorded on an JEOL AccuTOF CS JMST100CS (ESI) mass spectrometer. Optical rotations were measured at 589 nm using a Perkin Elmer Polarimeter Model 241 MC. CD and HV spectra were recorded on Jasco J-815 CD spectrometer. Automatic flash column chromatography was performed using Biotage Isolera Spektra One, using SNAP cartridges (Biotage, 30–100 μm, 60 Å), 10–50 g. TLC-analysis was conducted on Silicagel F_{254} (Merck KGaA) with detection by UV-absorption (254 nm) where applicable, and by dipping into a solution of $KMnO_4/Na_2CO_3$/NaOH in water followed by charring at ca. 150 °C. The chiral HPLC measurements were performed on a Shimadzu LC2010C Analytical HPLC system equipped with a Diacel Chiralpak OD-H or Phenomenex Lux 3u Cellulose-1 column using the stated eluents. Melting points were analyzed with a Büchi melting point B-545. IR spectra were recorded on an ATI Mattson Genesis Series FTIR spectrometer or a Bruker Tensor 27 FTIR spectrometer. DCM, THF and toluene were freshly distilled. Molecular sieves (4 Å) were flame activated under vacuum prior to use. All inert reactions were carried out under argon atmosphere using flame-dried flasks.

Synthesis of allenyl ethers from propargyl derivatives

Scheme 1. Synthesis of Propargyl Ethers



General procedure A:[1] Propargyl alcohol (1.0 g, 17.8 mmol, 1.0 equiv.) was added dropwise at 0 °C to a suspension of sodium hydride (780 mg, 60% dispersion in mineral oil, 19.6 mmol, 1.1 equiv.) in THF (40 mL) and the reaction mixture was allowed to warm up to room temperature in 1 h. Tetrabutylammonium iodide (330 mg, 0.9 mmol, 0.05 equiv.) and corresponding benzyl bromide (19.6 mmol, 1.1 equiv.) were added to the mixture successively. After completion of the reaction (TLC), the mixture was filtered over a diatomaceous-earth pad and concentrated. Obtained crude product was used directly in the next step without further purification.

General procedure B:[2] Mixture of the corresponding phenol (17.8 mmol, 1.0 equiv.) and anhydrous Cs_2CO_3 (6.9 g, 21.4 mmol, 1.2 equiv.) in DMF (40 mL) was heated to 60 °C for half an hour under inert atmosphere. The reaction mixture was then cooled to room temperature and propargyl bromide (3.4 g, 80 wt% solution in toluene, 23.1 mmol, 1.3 equiv.) was added slowly. After completion of the reaction (TLC), the mixture was diluted with ether and washed at least 3 times with brine. Obtained crude product after solvent evaporation was used directly in the next step without further purification.

{[(Prop-2-yn-1-yl)oxy]methyl}benzene 13a was prepared in 90% yield through the general procedure A. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.47 (t, *J* = 2.4 Hz, 1 H), 4.17 (d, *J* = 2.4 Hz, 2 H), 4.61 (s, 2 H), 7.27–7.39 (m, 5 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 57.1, 71.4, 74.5, 79.4, 127.5, 128.1, 128.3, 137.2. These data are identical to those reported previously.[3]

[(Prop-2-yn-1-yl)oxy]benzene 13b was prepared in 78% yield through the general procedure B. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.52 (t, *J* = 2.4 Hz, 1 H), 4.70 (d, *J* = 2.4 Hz, 2 H), 6.96–7.03 (m, 3 H), 7.28–7.31 (m, 2 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 55.6, 75.4, 78.6, 114.8, 117.8, 121.5, 129.4, 157.4. These data are identical to those reported previously.2

1-Bromo-4-{[(prop-2-yn-1-yl)oxy]methyl}benzene 13c was prepared through the general procedure A. The mixture residue was purified by column chromatography on silica gel (*n*-heptane/EtOAc 20:1 → 10:1) to afford the product as yellow oil in 81% yield. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.47 (t, *J* = 2.4 Hz, 1 H), 4.17 (d, *J* = 2.3 Hz, 2 H), 4.56 (s, 2 H), 7.21–7.25 (m, 2 H), 7.45–7.50 (m, 2 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 57.2, 70.7, 74.8, 79.3, 121.8, 129.6, 131.5, 136.3. **IR** ($CHCl_3$): ν = 482, 630, 801, 1011, 1070, 1488, 2852, 2922 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{10}H_9BrONa$ $(M + Na)^+$ 246.9729, found 246.9725.

1,3-Dimethoxy-5-{[(prop-2-yn-1-yl)oxy]methyl}benzene 13d was prepared in 94% yield through the general procedure A. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.47 (t, *J* = 2.4 Hz, 1 H), 3.79 (s, 6 H), 4.17 (d, *J* = 2.4 Hz, 2 H), 4.56 (s, 2 H), 6.40 (t, *J* = 2.3 Hz, 1 H), 6.52 (d, *J* = 2.3 Hz, 2 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 55.3, 57.0, 71.5, 74.6, 79.6, 100.0, 105.7, 139.6, 160.9. These data are identical to those reported previously.[4]

1-[(Prop-2-yn-1-yl)oxy]naphthalene 13e was prepared in 84% yield through the general procedure B. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.54 (t, *J* = 2.4 Hz, 1 H), 4.89 (d, *J* = 2.4 Hz, 2 H), 6.94 (d, *J* = 7.6 Hz, 1 H), 7.38 (t, *J* = 8.0 Hz, 1 H), 7.45–7.52 (m, 3 H), 7.78–7.82 (m, 1 H), 8.24–8.30 (m, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 56.1, 75.5, 78.6, 105.5, 121.2, 122.0, 125.4, 125.5, 125.6, 126.5, 127.4, 134.5, 153.3. These data are identical to those reported previously.2

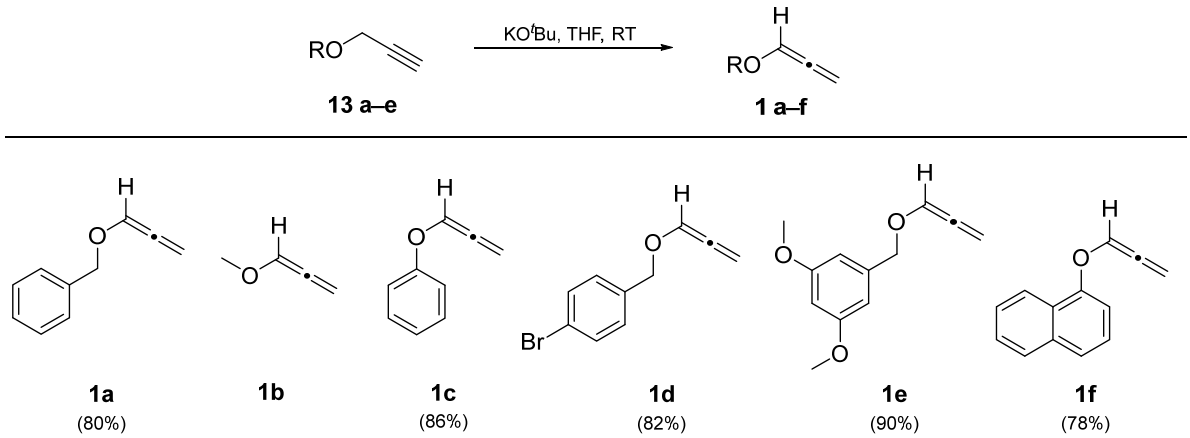
[1] Achard T.; Lepronier A.; Gimbert Y.; Clavier H.; Giordano L.; Tenaglia A.; Buono G. *Angew. Chem. Int. Ed*. **2011**, *15*, 3552.

[2] Efe C.; Lykakis I. N.; Stratakis M. *Chem. Commun*. **2011**, *47*, 803.

[3] Ishikawa T.; Mizuta T.; Hagiwara K.; Aikawa T.; Kudo T.; Saito S. *J. Org. Chem*. **2003**, *68*, 3702.

[4] Lee J. W.; Kim J. H.; Kim B.-K.; Shin W. S.; Jin S.-H. *Tetrahedron* **2006**, *62*, 894.

Scheme 2. Synthesis of Allenyl Ethers



Allene substrates **1a**, **1c**–**f** were prepared according to the literature.[5] Allene **1b** was directly purchased from Sigma Aldrich.

General procedure: Potassium *tert*-butoxide (3.0 mmol, 0.3 equiv.) was added at room temperature to a solution of propargyl ether **13a–e** (10 mmol, 1 equiv.) in THF (25 mL). The suspension was stirred at room temperature for the appropriate time (6–12 h, TLC), then filtered through a diatomaceous-earth pad and washed with *n*-heptane. The solvent mixture was removed *in vacuo* and the crude residue was purified by column chromatography as indicated.

{[(Propa-1,2-dien-1-yl)oxy]methyl}benzene 1a. Column chromatography (*n*-heptane/EtOAc 20:1 → 10:1; silica gel was washed with 1% NEt_3 before running column) afforded the product **4a** as a slightly yellow oil (80%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.61 (s, 2 H), 5.48 (d, *J* = 6.0 Hz, 2 H), 6.84 (t, *J* = 5.9 Hz, 1 H), 7.28–7.38 (m, 5 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.6, 91.1, 121.6, 127.7, 127.8, 128.3, 137.3, 201.3. These data are identical to those reported previously.[5]

[(Propa-1,2-dien-1-yl)oxy]benzene 1c. Column chromatography (*n*-heptane/EtOAc 40:1 → 20:1; silica gel was washed with 1% NEt_3 before running column) afforded the product **4c** as a slightly yellow oil (86%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.45 (d, *J* = 5.9 Hz, 2 H), 6.85 (t, *J* = 5.9 Hz, 1 H), 7.03–7.10 (m, 2 H), 7.28–7.35 (m, 3 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 89.5, 116.7, 122.7, 129.5, 202.8. These data are identical to those reported previously.[6]

1-Bromo-4-{[(propa-1,2-dien-1-yl)oxy]methyl}benzene 1d. Column chromatography (*n*-heptane/EtOAc 20:1; silica gel was washed with 1% NEt_3 before running column) afforded the product **4d** as a slightly yellow oil (82%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.56 (s, 2 H), 5.47 (d, *J* = 5.7 Hz, 2 H), 6.81 (t, *J* = 6.0 Hz, 1 H), 7.20–7.25 (m, 2 H), 7.44–7.51 (m, 2 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 69.6, 91.7, 121.5, 121.9, 129.3, 131.4, 136.6, 201.2. These data are identical to those reported previously.[7]

1,3-Dimethoxy-5-{[(propa-1,2-dien-1-yl)oxy]methyl}benzene 1e. Column chromatography (*n*-heptane/EtOAc 40:1 → 20:1; silica gel was washed with 1% NEt_3 before running column) afforded the product **4e** as a slightly yellow oil (90%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.79 (s, 6 H), 4.55 (s, 2 H), 5.48 (d, *J* = 6.0 Hz, 2 H), 6.40 (t, *J* = 2.3 Hz, 1 H), 6.51 (dt, *J* = 0.5, 2.3 Hz, 2 H), 6.83 (t, *J* = 5.9 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 55.3, 70.5, 91.2, 100.0, 105.4, 121.5, 139.6, 160.8, 201.2. **IR** ($CHCl_3$): ν = 832, 1153, 1205, 1461, 1598, 2838, 2936 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{12}H_{14}O_3Na$ $(M + Na)^+$ 229.0835, found 229.0833.

1-[(Propa-1,2-dien-1-yl)oxy]naphthalene 1f. Column chromatography (*n*-heptane/EtOAc 40:1 → 20:1; silica gel was washed with 1% NEt_3 before running column) afforded the product **4f** as a slightly yellow oil (78%). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.48 (d, *J* = 5.9 Hz, 2 H), 7.00 (t, *J* = 5.8 Hz, 1 H), 7.09 (d, *J* = 7.5 Hz, 1 H), 7.34–7.57 (m, 4 H), 7.76–7.85 (m, 1 H), 8.21–8.31 (m, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 89.6, 109.5, 118.1, 121.9, 122.5, 125.5, 125.7, 126.5, 127.5, 134.6, 153.1, 203.0. These data are identical to those reported previously.[8]

[5] Helms M.; Schade W.; Pulz R.; Watanabe T.; Al-Harrasi A.; Fisera L.; Hlobilova I.; Zahn G.; Reissig H.-U. *Eur. J. Org. Chem.* **2005**, *6*, 1003.

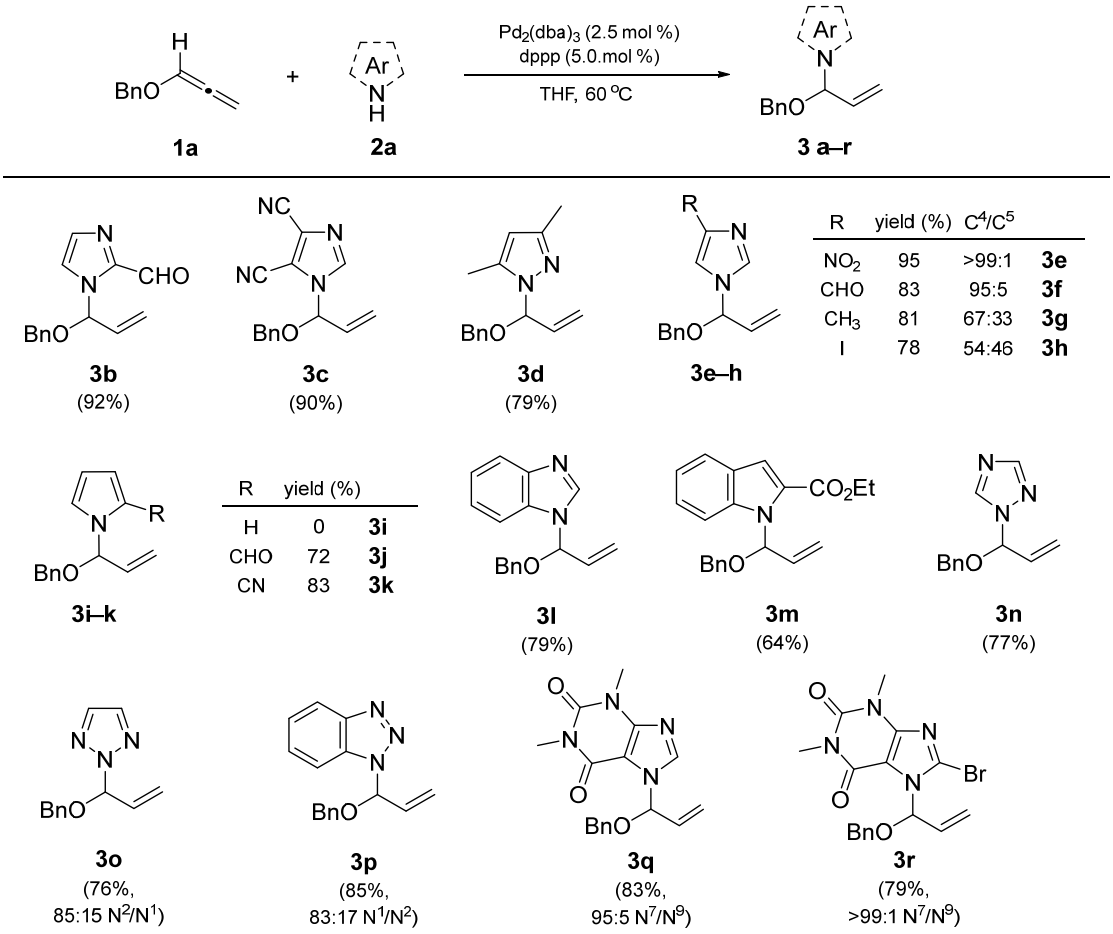
[6] Ocello R.; De Nisi A.; Jia M.; Yang Q.-Q.; Monari M.; Giacinto P.; Bottoni A.; Miscione G. P.; Bandini M. *Chem. Eur. J.* **2015**, *21*, 18445.

[7] Reddy M. N.; Swamy K. C. K. *Synthesis* **2014**, *46*, 1091.

[8] Moghaddam F.M.; Emami R. *Synth. Comm.* **1997**, *27*, 4073.

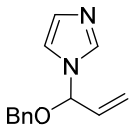
General procedures for the palladium-catalyzed addition of benzyloxyallene 1a to azole heterocycles

Scheme 3. Scope of the Azole Heterocycles



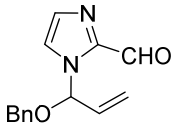
General procedure: The reaction was performed in a 5.0 mL Schlenk tube under Argon. $Pd_2(dba)_3$ (6.9 mg, 0.0075 mmol, 0.025 equiv.) and 1,3-bis(diphenylphosphino)propane (6.2 mg, 0.015 mmol, 0.05 equiv.) were solved in dry tetrahydrofuran (3.0 mL). Azole heterocycle (0.36 mmol, 1.2 equiv.) and benzyloxyallene **1a** (43.9 mg, 0.3 mmol, 1.0 equiv.) were added and the flask was sealed. The reaction mixture was stirred at 60 °C for the appropriate time (3–18 h). After cooling down to room temperature, the solvent was removed in vacuo and the crude residue was purified by column chromatography as indicated.

1-[1-(Benzyloxy)allyl]-1*H*-imidazole (**3a**). Imidazole (24.5 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 3 h. The solvent was removed in vacuo and the crude residue was filtrated over diatomaceous-earth pad with *n*-heptane to afford the product **3a** as slightly yellow oil (60 mg, 93%).


3a

R$_F$ (silica gel, *n*-heptane): 0.43 (UV, KMnO4-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.34 (d, *J* = 11.9 Hz, 1 H), 4.53 (d, *J* = 11.9 Hz, 1 H), 5.39 (ddd, *J* = 0.9, 1.5, 10.5 Hz, 1 H), 5.41 (ddd, *J* = 0.9, 1.6, 17.2 Hz, 1 H), 5.90 (dt, *J* = 1.5, 4.3 Hz, 1 H), 6.04 (ddd, *J* = 4.3, 10.5, 17.2 Hz, 1 H), 7.06 (t, *J* = 1.3 Hz, 1 H), 7.14 (t, *J* = 0.9 Hz, 1 H), 7.27–7.40 (m, 5 H), 7.63 (t, *J* = 1.0 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 69.7, 84.3, 116.9, 127.9, 128.2, 128.6, 130.0, 134.1, 136.3. **IR** ($CHCl_3$): ν = 700, 741, 811, 1062, 1218, 1496, 2873, 3031 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{13}H_{15}N_2O$ $(M + H)^+$ 215.1184, found 215.1179.

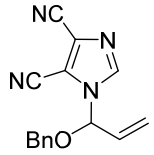
1-[1-(Benzyloxy)allyl]-1*H*-imidazole-2-carbaldehyde (**3b**). Reaction was conducted according to the general procedure using $Pd_2(dba)_3$ (23.0 mg, 0.025 mmol, 0.025 equiv.), 1,3-bis(diphenylphosphino)propane (20.5 mg, 0.05 mmol, 0.05 equiv.), imidazole-2-carbaldehyde (115.0 mg, 1.2 mmol), benzyloxyallene (146.0 mg, 1.0 mmol), in THF (10.0 mL) and heated for 4 h. Column chromatography (*n*-heptane/EtOAc 20:1 → 4:1) afforded product **3b** as a slightly yellow oil (223.0 mg, 92%).



3b

R$_F$ (silica gel, *n*-heptane/EtOAc = 1:1): 0.69 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.49 (d, *J* = 11.5 Hz, 1 H), 4.54 (d, *J* = 11.5 Hz, 1 H), 5.35 (ddd, *J* = 0.9, 1.4, 10.5 Hz, 1 H), 5.40 (ddd, *J* = 0.9, 1.5, 17.2 Hz, 1 H), 5.98 (ddd, *J* = 4.5, 10.5, 17.2 Hz, 1 H), 6.98 (dt, *J* = 1.4, 4.6 Hz, 1 H), 7.24–7.28 (m, 2 H), 7.30–7.36 (m, 4 H), 7.47 (t, *J* = 1.0 Hz, 1 H), 9.83 (d, *J* = 1.0 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 71.1, 84.8, 119.0, 122.7, 127.9, 128.2, 128.5, 132.4, 134.1, 136.2, 182.5. **IR** ($CHCl_3$): ν = 700, 754, 831, 1069, 1406, 1688, 2844, 3032 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{14}H_{15}N_2O_2$ $(M + H)^+$ 243.1134, found 243.1128.

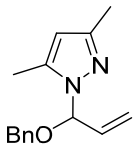
1-[1-(Benzyloxy)allyl]-1*H*-imidazole-4,5-dicarbonitrile (3c). Imidazole-4,5-dicarbonitrile (42.5 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 4 h. Column chromatography (*n*-heptane/EtOAc 20:1 → 4:1) afforded the product **3c** as slightly yellow oil (71.4 mg, 90%).



3c

R$_F$ (silica gel, *n*-heptane/EtOAc = 2:1): 0.44 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.60 (d, *J* = 11.9 Hz, 1 H), 4.68 (d, *J* = 11.9 Hz, 1 H), 5.59 (dd, *J* = 1.3, 10.3 Hz, 1 H), 5.60 (dd, *J* = 1.3, 17.2 Hz, 1 H), 5.88 (dt, *J* = 1.3, 4.9 Hz, 1 H), 6.02 (ddd, *J* = 4.9, 10.4, 17.1 Hz, 1 H), 7.24–7.28 (m, 2 H), 7.28–7.40 (m, 5 H), 7.80 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 72.0, 86.8, 107.6, 110.7, 111.3, 122.1, 123.8, 128.1, 128.9, 130.0, 131.6, 134.6, 139.7. **IR** ($CHCl_3$): ν = 699, 738, 803, 1023, 1343, 1454, 1655, 2241, 2922, 3032 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{15}H_{13}N_4O$ $(M + H)^+$ 265.1089, found 265.1082.

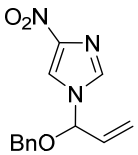
1-[1-(Benzyloxy)allyl]-3,5-dimethyl-1*H*-pyrazole (3d). 3,5-Dimethylpyrazole (34.6 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 4 h. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:1) afforded the product **3d** as slightly yellow oil (57.4 mg, 79%).



3d

R$_F$ (silica gel, *n*-heptane/EtOAc = 10:1): 0.22 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.22 (s, 3 H), 2.24 (s, 3 H), 4.42 (d, *J* = 11.9 Hz, 1 H), 4.46 (d, *J* = 12.0 Hz, 1 H), 5.34 (ddd, *J* = 1.2, 1.7, 10.5 Hz, 1 H), 5.36 (ddd, *J* = 1.2, 1.7, 17.3 Hz, 1 H), 5.86 (s, 1 H), 5.90 (dt, *J* = 1.7, 4.3 Hz, 1 H), 6.15 (ddd, *J* = 4.4, 10.6, 17.3 Hz, 1 H), 7.25–7.35 (m, 5 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 11.4, 13.5, 69.5, 88.2, 107.1, 118.2, 127.8, 127.9, 128.4, 134.3, 137.1, 139.6, 147.9. **IR** ($CHCl_3$): ν = 699, 737, 824, 1066, 1314, 1456, 1559, 2843, 3032 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{15}H_{19}N_2O$ $(M + H)^+$ 243.1497, found 243.1493.

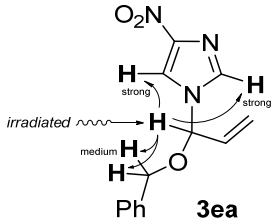
1-[1-(Benzyloxy)allyl]-4-nitro-1*H*-imidazole (3ea). 4(5)-Nitroimidazole (40.7 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 4 h. Ratio C-4/C-5 > 99:1 was determined by ^{1}H NMR spectroscopy. Crude product was filtered with CH_2Cl_2 through a diatomaceous-earth pad affording the product **3ea** as slightly yellow oil (73.9 mg, 95%).



3ea

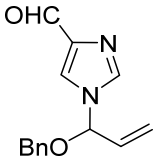
R$_F$ (silica gel, *n*-heptane/EtOAc = 1:1): 0.42 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.48 (d, *J* = 12.0 Hz, 1 H), 4.64 (d, *J* = 12.0 Hz, 1 H), 5.53 (ddd, *J* = 0.8, 1.5, 10.9 Hz, 1 H), 5.56 (ddd, J = 0.9, 1.5, 17.2 Hz, 1 H), 5.69 (dt, *J* = 1.4, 4.6 Hz, 1 H), 6.00 (ddd, *J* = 4.6, 10.5, 17.2 Hz, 1 H), 7.27–7.32 (m, 2 H), 7.35 – 7.42 (m, 3 H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.84 (d, *J* = 1.6 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.8, 85.8, 117.2, 120.8, 128.0, 128.8, 128.9, 132.7, 134.6. **IR** ($CHCl_3$): ν = 700, 752, 824, 1070, 1276, 1340, 1491, 2856, 3029 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{13}H_{14}N_3O_3$ $(M + H)^+$ 260.1035, found 260.1039.

sel. NOE:



3ea

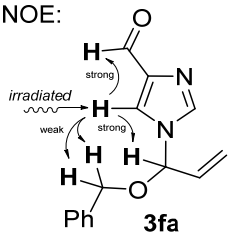
1-[1-(Benzyloxy)allyl]-1*H*-imidazole-4-carbaldehyde (3fa). Imidazole-4(5)-carbaldehyde (34.6 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 3 h. Ratio C-4/C-5 = 95:5 was determined by ^{1}H NMR spectroscopy. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:2) afforded the product **3fa** as slightly yellow oil (50.9 mg, 70%).



3fa

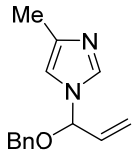
R$_F$ (silica gel, *n*-heptane/EtOAc = 1:1): 0.16 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.42 (d, *J* = 11.9 Hz, 1 H), 4.59 (d, *J* = 11.9 Hz, 1 H), 5.47 (ddd, *J* = 0.7, 1.5, 10.7 Hz, 1 H), 5.49 (ddd, *J* = 0.6, 1.5, 17.2 Hz, 1 H), 5.70 (dt, *J* = 1.5, 4.5 Hz, 1 H), 6.02 (ddd, J = 4.5, 10.4, 17.2 Hz, 1 H), 7.26–7.42 (m, 5 H), 7.70 (d, *J* = 1.2 Hz, 1 H), 7.74 (d, *J* = 1.2 Hz, 1 H), 9.91 (s, 1 H).**^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.4, 85.2, 120.1, 122.5, 127.9, 128.6, 128.8, 133.2, 137.5, 186.2. **IR** ($CHCl_3$): ν = 700, 774, 807, 1070, 1534, 1685, 2841, 3033 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{14}H_{15}N_2O_2$ $(M + H)^+$ 243.1134, found 243.1136.

sel. NOE:

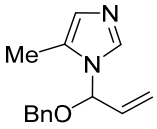


3fa

1-[1-(Benzyloxy)allyl]-4-methyl-1*H*-imidazole (**3ga**) and **1-[1-(benzyloxy)allyl]-5-methyl-1*H*-imidazole** (**3gb**). 4(5)-Methylimidazole (30.0 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 3 h. Ratio C-4/C-5 = 67:33 was determined by ^{1}H NMR spectroscopy. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:2) afforded the product as non-separable mixture of both regioisomers **3ga** and **3gb** (55.5 mg, 81%) as a slightly yellow oil.



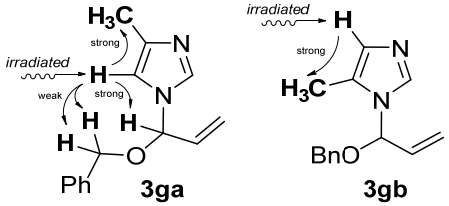
3ga



3gb

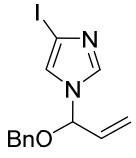
R$_F$ (silica gel, *n*-heptane/EtOAc = 1:2): 0.06–0.29 (UV, $KMnO_4$-solution). The signals of main isomer are indicated with an asterisk in superscript (*). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 2.18 (d, *J* = 1.0 Hz, 3 H)*, 2.25 (d, *J* = 1.0 Hz, 3 H), 4.34 (d, *J* = 11.9 Hz, 1 H)*, 4.35 (d, *J* = 11.8 Hz, 1 H), 4.52 (d, *J* = 11.9 Hz, 1 H), 4.55 (d, *J* = 11.8 Hz, 1 H), 5.29 (ddd, *J* = 0.9, 1.7, 17.2 Hz, 1 H), 5.37 (ddd, *J* = 0.9, 1.5, 10.5 Hz, 1 H)*¥, 5.37 (ddd, *J* = 0.6, 1.5, 10.6 Hz, 1 H)¥, 5.41 (ddd, *J* = 1.0, 1.6, 17.2 Hz, 1 H)*, 5.57 (dt, *J* = 1.5, 4.3 Hz, 1 H)*, 5.65 (dt, *J* = 1.7, 4.1 Hz, 1 H), 6.01 (ddd, *J* = 4.4, 10.5, 17.2 Hz, 1 H)*, 6.04 (ddd, *J* = 4.2, 10.3, 17.2 Hz, 1 H), 6.76 (dd, *J* = 1.1, 1.3 Hz, 1 H)*, 6.83 (dd, *J* = 1.1, 1.3 Hz, 1 H), 7.27–7.39 (m, 10 H)*, 7.55 (d, *J* = 1.3 Hz, 1 H)*, 7.57 (d, *J* = 1.3 Hz, 1 H)(¥Overlapping of the signals) ppm. **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 9.9, 13.7*, 69.5*, 69.6, 83.7, 84.3*, 113.2, 118.7, 118.8*, 127.7, 127.8*, 127.8, 128.1*, 128.2, 128.5*, 128.6, 134.2*, 134.3, 135.5*, 136.2, 136.3*, 139.0*. **IR** ($CHCl_3$): ν = 669, 739, 814, 1065, 1494, 2871, 3032 cm^{-1}. **HRMS** (ESI$^+$) calcd. for $C_{14}H_{17}N_2O$ $(M + H)^+$ 229.1341, found 229.1348.

sel. NOE: sel. NOE:



3ga 3gb

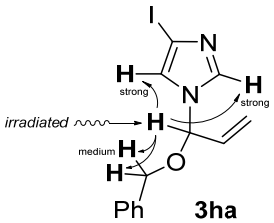
1-[1-(Benzyloxy)allyl]-4-iodo-1*H*-imidazole (**3ha**) and **1-[1-(benzyloxy)allyl]-5-iodo-1*H*-imidazole** (**3hb**). 4(5)-Iodoimidazole (100 mg, 0.52 mmol) was treated with benzyloxyallene (85 mg, 0.57 mmol) according to the general procedure and heated for 3 h. C-4/C-5 > 54:46 was determined by ^{1}H NMR spectroscopy. Column chromatography (*n*-heptane/EtOAc 10:1→1:2) afforded the product **3ha** (70 mg, 36%) and the product **3hb** (81 mg, 42%) as a slightly yellow oil.



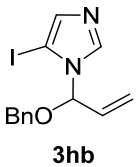
3ha

Compound 3ha: **R$_F$** (silica gel, *n*-heptane/EtOAc = 1:1): 0.69 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.37 (d, *J* = 12.0 Hz, 1 H), 4.56 (d, *J* = 12.0 Hz, 1 H), 5.41 (ddd, *J* = 0.8, 1.5, 10.5 Hz, 1 H), 5.44 (ddd, *J* = 0.8, 1.5, 17.2 Hz, 1 H), 5.61 (dt, *J* = 1.5, 4.3 Hz, 1 H), 5.98 (ddd, *J* = 4.3, 10.5, 17.2 Hz, 1 H), 7.14 (d, *J* = 1.4 Hz, 1 H), 7.27–7.41 (m, 5 H), 7.51 (d, *J* = 1.4 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): 70.0, 84.6, 119.6, 122.6, 127.9, 128.4, 128.7, 133.6, 135.8, 137.7. **IR** ($CHCl_3$): ν = 462, 698, 738, 803, 1072, 1209, 1454, 2873, 3027 cm^{-1}. **HRMS** (ESI$^+$) calcd. for $C_{13}H_{14}IN_2O$ $(M + H)^+$ 341.0151, found 341.0159.

sel. NOE:



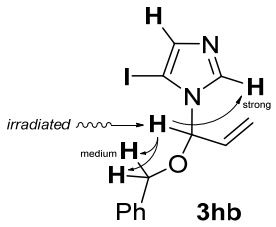
3ha



3hb

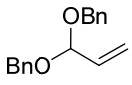
Compound 3hb: **R$_F$** (silica gel, *n*-heptane/EtOAc = 1:1): 0.59 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.45 (d, *J* = 11.7 Hz, 1 H), 4.59 (d, *J* = 11.7 Hz, 1 H), 5.39 (ddd, *J* = 0.7, 1.5, 17.1 Hz, 1 H), 5.42 (ddd, *J* = 0.7, 1.5, 10.6 Hz, 1 H), 5.76 (dt, *J* = 1.5, 4.5 Hz, 1 H), 5.98 (ddd, *J* = 4.4, 10.6, 17.1 Hz, 1 H), 7.28–7.40 (m, 6 H), 7.77 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.7, 87.8, 119.8, 128.1, 128.4, 128.7, 133.4, 135.7, 140.4. **IR** ($CHCl_3$): ν = 432, 682, 804, 1062, 1254, 2871, 3033 cm^{-1}. **HRMS** (ESI$^+$) calcd. for $C_{13}H_{14}IN_2O$ $(M + H)^+$ 341.0151, found 341.0160.

sel. NOE:



3hb

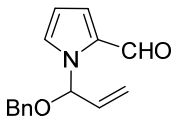
1-[1-(Benzyloxy)allyl]-1*H*-pyrrole (3i) and 3,3-bis(benzyloxy)prop-1-ene (14). Pyrrole (24.2 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 6 h. Column chromatography (*n*-heptane/CH_2Cl_2 40:1 → 10:1) afforded the product **3i** (<1 mg, trace) and the product **14** (28.2 mg, 37%) as a slightly yellow oils.



14

Compound 14: R_F (silica gel, *n*-heptane/CH_2Cl_2 = 2:1): 0.11 (UV, $KMnO_4$ solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.58 (d, *J* = 11.8 Hz, 2 H), 4.67 (d, *J* = 11.8 Hz, 2 H), 5.14 (dt, *J* = 1.2, 4.7 Hz, 1 H), 5.39 (ddd, *J* = 0.9, 1.3, 10.6 Hz, 1 H), 5.51 (ddd, *J* = 0.9, 1.3, 17.4 Hz, 1 H), 5.95 (ddd, *J* = 4.7, 10.6, 17.4 Hz, 1 H), 7.26–7.38 (m, 10 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 67.1, 100.3, 119.0, 127.6, 127.8, 128.4, 134.9, 138.0. These data are identical to those reported previously.[9]

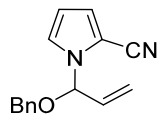
1-[1-(Benzyloxy)allyl]-1*H*-pyrrole-2-carbaldehyde (3j). 1*H*-Pyrrole-2-carbaldehyde (34.2 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 6 h. Column chromatography (*n*-heptane/EtOAc 20:1 → 4:1) afforded the product **3j** as slightly yellow oil (52.1 mg, 72%).



3j

R_F (silica gel, *n*-heptane/EtOAc = 1:1): 0.74 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.47 (d, *J* = 11.5 Hz, 1 H), 4.53 (d, *J* = 11.5 Hz, 1 H), 5.28 (ddd, *J* = 0.8, 1.3, 10.5 Hz, 1 H), 5.33 (ddd, *J* = 0.8, 1.3, 17.1 Hz, 1 H), 6.01 (ddd, *J* = 4.4, 10.5, 17.1 Hz, 1 H), 6.33 (dd, *J* = 2.7, 3.9 Hz, 1 H), 6.97–7.01 (m, 2 H), 7.26–7.35 (m, 6 H), 9.58 (d, *J* = 1.0 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.6, 85.1, 111.0, 118.1, 125.4, 127.8, 127.9, 128.1, 128.4, 135.2, 137.0, 179.8. **IR** ($CHCl_3$): ν = 700, 747, 803, 1064, 1242, 1468, 1681, 2853, 3032 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{15}H_{16}NO_2$ $(M + H)^+$ 242.1181, found 242.1163.

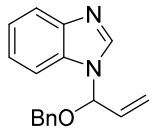
1-[1-(Benzyloxy)allyl]-1*H*-pyrrole-2-carbonitrile (3k). 1*H*-Pyrrole-2-carbonitrile (33.2 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 6 h. Column chromatography (*n*-heptane/EtOAc 20:1 → 4:1) afforded the product **3k** as slightly yellow oil (59.3 mg, 83%).



3k

R_F (silica gel, *n*-heptane/EtOAc = 10:1): 0.42 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.45 (d, *J* = 11.6 Hz, 1 H), 4.51 (d, *J* = 11.6 Hz, 1 H), 5.39 (ddd, *J* = 0.8, 1.4, 10.5 Hz, 1 H), 5.41 (ddd, *J* = 0.8, 1.5, 17.1 Hz, 1 H), 5.86 (dt, *J* = 1.5, 4.4 Hz, 1 H), 6.04 (ddd, *J* = 4.5, 10.5, 17.2 Hz, 1 H), 6.27 (dd, *J* = 2.9, 3.8 Hz, 1 H), 6.86 (dd, *J* = 1.6, 3.9 Hz, 1 H), 7.04 (dd, *J* = 1.6, 2.8 Hz, 1 H), 7.28–7.39 (m, 5 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.5, 86.2, 103.1, 110.6, 113.4, 119.3, 120.8, 124.2, 128.0, 128.2, 128.6, 133.9, 136.1. **IR** ($CHCl_3$): ν = 699, 740, 809, 1063, 1268, 1452, 2218, 2917, 3031 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{15}H_{15}N_2O$ $[M+H]^+$ 239.1184, found 239.1177.

1-[1-(Benzyloxy)allyl]-1*H*-benzimidazole (3l). Benzimidazole (42.5 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 4 h. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:1) afforded the product **3l** as slightly yellow oil (62.6 mg, 79%).

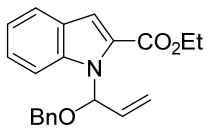


3l

R_F (silica gel, *n*-heptane/EtOAc = 1:1): 0.27 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.36 (d, *J* = 11.9 Hz, 1 H), 4.55 (d, *J* = 11.9 Hz, 1 H), 5.42 (d, *J* = 10.7 Hz, 1 H), 5.47 (d, *J* = 17.3 Hz, 1 H), 5.95–5.99 (m, 1 H), 6.15 (ddd, *J* = 4.1, 10.5, 17.0 Hz, 1 H), 7.24–7.27 (m, 2 H), 7.28–7.40 (m, 5 H), 7.48–7.53 (m, 1 H), 7.80–7.87 (m, 1 H), 8.00 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 69.9, 83.9, 111.5, 119.3, 120.5, 122.7, 123.3, 128.0, 128.3, 128.6, 133.6, 136.1, 141.9, 144.3. **IR** ($CHCl_3$): ν = 699, 723, 809, 1061, 1223, 2884, 3032 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{17}H_{17}N_2O$ $(M + H)^+$ 265.1341, found 265.1328.

Ethyl 1-[1-(benzyloxy)allyl]-1*H*-indole-2-carboxylate (3m). Ethyl indole-2-carboxylate (68.1 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 18 h. Column chromatography (*n*-heptane/EtOAc 20:1 → 1:1) afforded the product **3m** as slightly yellow oil (64.4 mg, 64%).

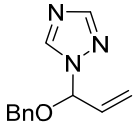
[9] Cui D.-M.; Zheng Z.-L.; Zhang C. *J. Org. Chem.* **2009**, *74*, 1426.



3m

R_F (silica gel, *n*-heptane/EtOAc = 10:1): 0.39 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 1.37 (t, *J* = 7.1 Hz, 3 H), 4.33 (dq, *J* = 1.6, 7.1 Hz, 2 H), 4.39 (d, *J* = 11.7 Hz, 1 H), 4.42 (d, *J* = 11.7 Hz, 1 H), 5.26 (dd, *J* = 1.4, 10.6 Hz, 1 H), 5.34 (dd, *J* = 1.4, 17.3 Hz, 1 H), 6.21 (ddd, *J* = 4.1, 10.6, 17.2 Hz, 1 H), 7.15 (ddd, *J* = 0.9, 7.0, 8.0 Hz, 1 H), 7.19–7.30 (m, 7 H), 7.36 (d, *J* = 0.8 Hz, 1 H), 7.66 (dt, *J* = 0.8, 8.0 Hz, 1 H), 7.84 (ddd, *J* = 0.7, 1.6, 8.3 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 14.4, 60.8, 70.0, 85.0, 112.3, 115.1, 117.9, 121.2, 122.5, 125.0, 126.9, 127.8, 128.0, 128.1, 128.3, 134.9, 137.3, 138.0, 162.2. **IR** ($CHCl_3$): ν = 698, 750, 813, 1065, 1198, 1703, 2869, 3031 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{21}H_{22}NO_3$ $(M + H)^+$ 336.1600, found 336.1617.

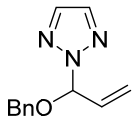
1-[1-(Benzyloxy)allyl]-1*H*-1,2,4-triazole (**3n**)**.** 1,2,4-Triazole (24.9 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 4 h. Column chromatography (*n*-heptane/EtOAc 20:1 → 4:1) afforded the product **3n** as slightly yellow oil (71.4 mg, 90%).



3n

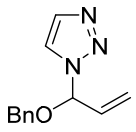
R_F (silica gel, *n*-heptane/EtOAc = 2:1): 0.44 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.60 (d, *J* = 11.9 Hz, 1 H), 4.68 (d, *J* = 11.9 Hz, 1 H), 5.59 (dd, *J* = 1.3, 10.3 Hz, 1 H), 5.60 (dd, *J* = 1.3, 17.2 Hz, 1 H), 5.88 (dt, *J* = 1.3, 4.9 Hz, 1 H), 6.02 (ddd, *J* = 4.9, 10.4, 17.1 Hz, 1 H), 7.24–7.28 (m, 2 H), 7.28–7.40 (m, 5 H), 7.80 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 72.0, 86.8, 107.6, 110.7, 111.3, 122.1, 123.8, 128.1, 128.9, 130.0, 131.6, 134.6, 139.7. **IR** ($CHCl_3$): ν = 678, 699, 740, 808, 1073, 1273, 1500, 2874, 3032 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{12}H_{14}N_3O$ $(M + H)^+$ 216.1137, found 216.1129.

2-[1-(Benzyloxy)allyl]-2*H*-1,2,3-triazole (**3oa**) and **1-[1-(benzyloxy)allyl]-1*H*-1,2,3-triazole** (**3ob**). 1H-1,2,3-Triazole (24.9 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 6 h. Ratio N-2/N-1 = 85:15 was determined by ^{1}H NMR spectroscopy. Column chromatography (*n*-heptane/EtOAc 10:1 → 2:1) afforded the product **3oa** (50 mg, 76%) and the product **3ob** (8 mg, 12%) as a slightly yellow oil.



3oa

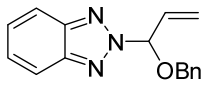
Compound 3oa: **R_F** (silica gel, *n*-heptane/EtOAc = 1:1): 0.69 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.47 (d, *J* = 12.1 Hz, 1 H), 4.53 (d, *J* = 12.1 Hz, 1 H), 5.44 (dt, *J* = 1.1, 10.5 Hz, 1 H), 5.56 (dt, *J* = 1.1, 17.2 Hz, 1 H), 6.16 (dt, *J* = 1.2, 5.4 Hz, 1 H), 6.27 (ddd, *J* = 5.3, 10.5, 17.1 Hz, 1 H), 7.26–7.38 (m, 5 H), 7.71 (s, 2 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.4, 90.7, 119.6, 127.0, 128.4, 132.7, 135.0, 136.5. **IR** ($CHCl_3$): ν = 699, 738, 820, 1064, 1314, 2874, 3032 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{12}H_{14}N_3O$ $(M + H)^+$ 216.1137, found 216.1133.



3ob

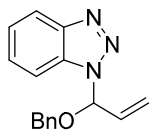
Compound 3ob: **R_f** (silica gel, *n*-heptane/EtOAc = 1:1): 0.46 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.50 (s, 2 H), 5.45 (ddd, *J* = 0.9, 1.6, 10.6 Hz, 1 H), 5.57 (ddd, *J* = 0.9, 1.6, 17.2 Hz, 1 H), 6.06 (ddd, *J* = 4.2, 10.6, 17.2 Hz, 1 H), 6.35 (dt, *J* = 1.6, 4.2 Hz, 1 H), 7.27–7.39 (m, 5 H), 7.72 (d, *J* = 1.1 Hz, 1 H), 7.78 (dd, *J* = 0.6, 1.2 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 69.6, 86.1, 118.9, 120.1, 127.0, 127.2, 127.6, 131.7, 133.6, 135.0. **IR** ($CHCl_3$): ν = 672, 816, 1064, 1086, 1250, 2902, 3030 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{12}H_{14}N_3O$ $(M + H)^+$ 216.1137, found 216.1130.

2-[1-(Benzyloxy)allyl]-2*H*-benzotriazole (**3pa**) and **1-[1-(benzyloxy)-allyl]-2*H*-benzotriazole** (**3pb**). Benztriazole (42.9 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 6 h. Ratio N-1/N-2 = 87:13 was determined by ^{1}H NMR spectroscopy. Column chromatography (*n*-heptane/EtOAc 20:1 → 10:1) afforded the product **3pa** (5 mg, 6%) and the product **3pb** (68 mg, 85%) as a slightly yellow oil.



3pa

Compound 3pa: **R_F** (silica gel, *n*-heptane/EtOAc = 10:1): 0.35 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.53 (d, *J* = 12.0 Hz, 1 H), 4.06 (d, *J* = 12.0 Hz, 1 H), 5.47–5.51 (m, 1 H), 5.61–5.68 (m, 1 H), 6.38 (ddd, *J* = 5.4, 10.5, 17.4 Hz, 1 H), 6.40–6.44 (m, 1 H), 7.26–7.37 (m, 5 H), 7.40–7.45 (m, 2 H), 7.90–7.95 (m, 2 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.9, 92.7, 118.6, 120.1, 126.9, 128.1, 128.4, 132.7, 136.1. **IR** ($CHCl_3$): ν = 698, 747, 816, 849, 1082, 1251, 2918, 3030 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{16}H_{16}N_3O$ $(M + H)^+$ 266.1293, found 266.1282.



3pb

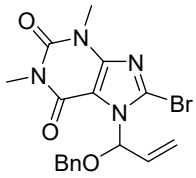
Compound 3pb: **R_F** (silica gel, *n*-heptane/EtOAc = 10:1): 0.23 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.43 (d, *J* = 11.9 Hz, 1 H), 4.47 (d, *J* = 11.9 Hz, 1 H), 5.48 (ddd, *J* = 0.9, 1.8, 10.6 Hz, 1 H), 5.60 (ddd, *J* = 0.9, 1.7, 17.2 Hz, 1 H), 6.20 (ddd, *J* = 3.9, 10.6, 17.2 Hz, 1 H), 6.67 (dt, *J* = 1.8, 3.7 Hz, 1 H), 7.24–7.35 (m, 5 H), 7.39 (ddd, *J* = 1.1, 7.0, 8.1 Hz, 1 H), 7.46 (ddd, *J* = 1.1, 7.0, 8.2 Hz, 1 H), 7.71 (dt, *J* = 1.0, 8.3 Hz, 1 H), 8.09 (dt, *J* = 1.0, 8.2 Hz, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 70.4, 87.7, 111.7, 119.8,120.0, 124.3, 127.5, 128.1, 128.2, 128.5, 132.5, 136.1. **IR** ($CHCl_3$): ν = 699, 747, 815, 927, 1077, 1237, 1450, 2916, 3030 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{16}H_{16}N_3O$ $(M + H)^+$ 266.1293, found 266.1285.

7-[1-(Benzyloxy)allyl]-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (**3q**). Theophylline (64.9 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 6 h. Ratio N-7/N-9 > 95:5 was determined by ^{1}H NMR spectroscopy. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:1) afforded the product **3q** as a white powder. (81.3 mg, 83%).

3q

R_F (silica gel, *n*-heptane/EtOAc = 1:1): 0.38 (UV, $KMnO_4$-solution). M_p: 84–88 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.43 (s, 3 H), 3.60 (s, 3 H), 4.62 (d, *J* = 11.5 Hz, 1 H), 4.71 (d, *J* = 11.6 Hz, 1 H), 5.43 (ddd, *J* = 0.9, 1.3, 10.7 Hz, 1 H), 5.55 (ddd, *J* = 4.1, 10.4, 17.3 Hz, 1 H), 6.07 (ddd, *J* = 4.8, 10.5, 17.1 Hz, 1 H), 6.70 (dt, *J* = 1.4, 4.7 Hz, 1 H), 7.25–7.35 (m, 5 H), 7.82 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 28.1, 29.8, 71.6, 85.2, 106.7, 119.7, 127.8, 128.2, 128.5, 133.6, 136.4, 139.4, 148.6, 151.5, 155.2. **IR** ($CHCl_3$): ν = 699, 747, 1064, 1540, 1659, 1702, 2918, 3112 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{17}H_{19}N_4O_3$ $(M + H)^+$ 327.1457, found 327.1450.

7-[1-(Benzyloxy)allyl]-8-bromo-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione (**3r**). 2-Bromotheophylline (93.2 mg, 0.36 mmol) was treated with benzyloxyallene according to the general procedure and heated for 6 h. Ratio N-7/N-9 > 99:1 was determined by ^{1}H NMR spectroscopy. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:1) afforded the product **3r** as yellow solid (96.0 mg, 79%).

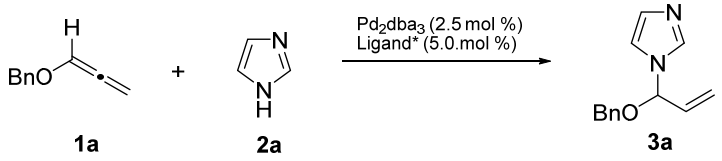


3r

R_F (silica gel, *n*-heptane/EtOAc = 1:1): 0.23 (UV, $KMnO_4$-solution). M_p: 92–94 °C. **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.41 (s, 3 H), 3.54 (s, 3 H), 4.56 (d, *J* = 11.9 Hz, 1 H), 4.67 (d, *J* = 11.9 Hz, 1 H), 5.38–5.50 (m, 2 H), 6.36 (ddd, *J* = 5.2, 10.2, 16.1 Hz, 1 H), 6.85 (s, 1 H), 7.27–7.30 (m, 6 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 28.2, 29.8, 71.8, 87.5, 108.8, 120.2, 127.9, 128.1, 128.3, 132.9, 136.1, 148.2, 151.0, 154.0. **IR** ($CHCl_3$): ν = 513, 700, 747, 977, 1087, 1361, 1532, 1658, 1702, 2923 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{17}H_{18}BrN_4O_3$ $(M + H)^+$ 405.0562, found 405.0553.

Screenings of reaction conditions for enantioselective hydroamination reactions

Table 1. Screening of the Catalysts[a]

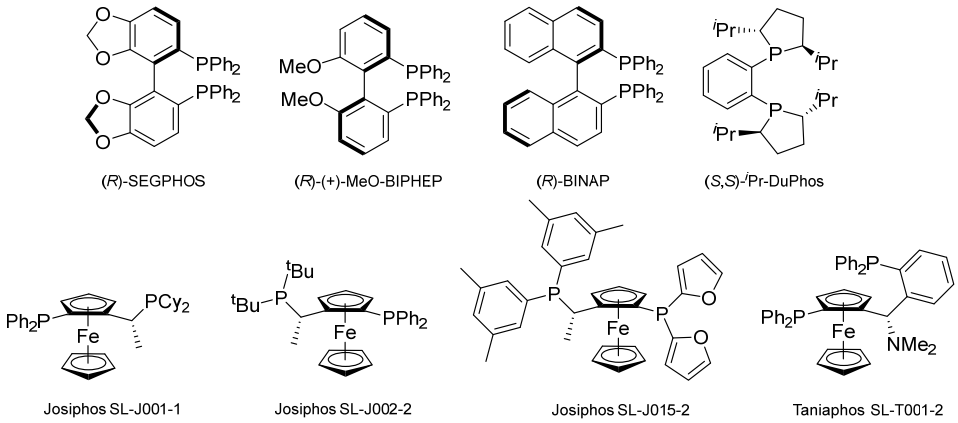


1a **2a** **3a**

entry	ligands	yield (%)[b]	ee (%)[c]
1	(*R*)-(+)-MeO-BIPHEP	n.r.	–
2	(*R*)-SEGPHOS	56	–
3	(*R*)-BINAP	72	11
4	(*S*,*S*)-iPr-DuPhos	32	33
5	(*R*,*R*)-DACH-phenyl Trost ligand	74	77
6	(*R*,*R*)-DACH-naphthyl Trost ligand	61	83
7	Josiphos SL-J001-1	82	–
8	Josiphos SL-J002-2	85	–
9	Josiphos SL-J015-2	42	–
10	Taniaphos SL-T001-2	14	–

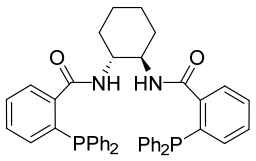
[a]Conditions: 2.5 mol % Pd_2dba_3, 5 mol % of ligand, 0.3 mmol of **1a** and 0.36 mmol of **2a**, 3.0 mL THF, 60 °C for 18 h. [b]Isolated yield. [c]Enantiomeric excess was determined by HPLC.

Chiral ligands widely used in palladium asymmetric catalysis:

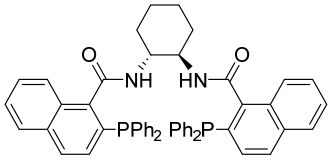


Chiral palladium ligands successfully applied by different groups in the synthesis of chiral *O*,*O*- and *N*,*O*-acetals:[10]

[10] (a) Trost, B. M.; Jäkel, C.; Plietker, B. *J. Am. Chem. Soc.* **2003**, *125*, 4438; (b) Kim H.; Rhee Y. H. *J. Am. Chem. Soc.* **2012**, *134*, 4011; (c) Jiang L.; Jia T.; Wang M.; Liao J.; Cao P. *Org. Lett.* **2015**, *17*, 1070 and references therein.



(*R*,*R*)-DACH-phenyl Trost ligand



(*R*,*R*)-DACH-naphthyl Trost ligand

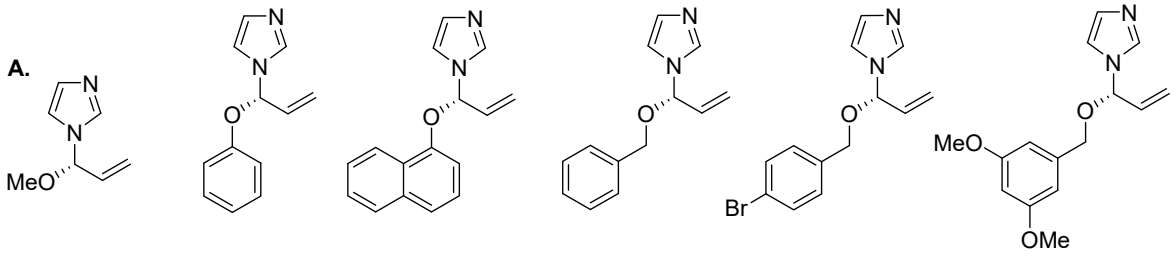
Table 2. Screening of the Reaction Conditions[a]:

entry	solvent	T (°C)	time (h)	yield (%)[b]	ee (%)[c]
1	MeCN	60	18	55	87
2	1,4-Dioxane	60	18	63	82
3	DCE	60	18	59	92
4	DCE	23	18	21	87
5	DCE	40	18	44	82
6	DCE	60	30	70	78
7[d]	DCE	60	18	74	82

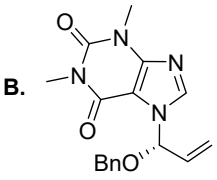
[a]Conditions: 2.5 mol % Pd_2dba_3, 5 mol % of (*R*,*R*)-DACH-naphthyl Trost Ligand, 0.3 mmol of **1a** and 0.36 mmol of **2a**, 3.0 mL of solvent. [b]Isolated yield. [c]Enantiomeric excess was determined by HPLC. [d]150 mol % DBU.

General procedures for enantioselective palladium-catalyzed hydroamination reactions

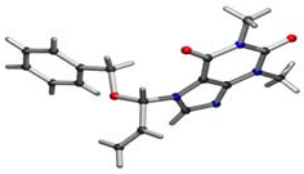
Scheme 4. (A) Scope of Alkoxyallenes. (B) Determination of the Absolute Configuration on Example of (*S*)-**3q**



(*S*)-**3s** (54%, 83% ee) (*S*)-**3t** (72%, 90% ee) (*S*)-**3u** (67%, 94% ee) (*S*)-**3a** (89%, 92% ee) (*S*)-**3v** (89%, 93% ee) (*S*)-**3w** (90%, 94% ee)



(*S*)-**3q** (74%, 92% ee)

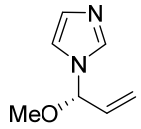


crystal structure of (*S*)-**3q**

General procedure: The reaction was performed in a 5.0 mL Schlenk tube under argon. $Pd_2(dba)_3$ (6.9 mg, 0.0075 mmol, 0.025 equiv.) and (*R*,*R*)-DACH-naphthyl Trost Ligand (6.2 mg, 0.015 mmol, 0.05 equiv.) were dissolved in dry DCE (3.0 mL). The re-

sulting catalyst solution was stirred for 30 minutes. Imidazole (24.5 mg, 0.36 mmol, 1.2 equiv.) and alkoxyallene (0.3 mmol, 1.0 equiv.) were added and the flask was sealed. The reaction mixture was stirred at 60 °C for 18 h. After cooling down to room temperature, the solvent was removed *in vacuo* and the crude residue was purified by column chromatography as indicated.

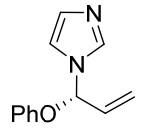
(*S*)-1-(1-Methoxyallyl)-1*H*-imidazole ((*S*)-**3s**). Imidazole was treated with allene **1b** (21.0 mg, 0.3 mmol) according to the general procedure. Column chromatography (*n*-heptane/EtOAc 40:1 → 20:1) afforded the product **3s** as slightly yellow oil (22.4 mg, 54%, 83% ee).



(*S*)-**3s**

R$_F$ (silica gel, *n*-heptane/EtOAc = 20:1): 0.58 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.28 (s, 3 H), 4.34 (d, *J* = 11.9 Hz, 1 H), 4.53 (d, *J* = 11.9 Hz, 1 H), 5.39 (ddd, *J* = 0.9, 1.5, 10.6 Hz, 1 H), 5.40 (ddd, *J* = 0.9, 1.5, 17.2 Hz, 1 H), 5.52 (dt, *J* = 1.3, 4.2 Hz, 1 H), 6.01 (ddd, *J* = 4.4, 10.5, 17.2 Hz, 1 H), 7.03 (s, 1 H), 7.12 (s, 1 H), 7.66 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 55.7, 87.3, 116.8, 119.0, 129.7, 133.9, 136.2. **IR** ($CHCl_3$): ν = 1067, 1218, 1411, 1491, 2939, 3112 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_7H_{11}N_2O$ $(M + H)^+$ 139.0871, found 139.0862. **HPLC**: ee: 83%, Chiralpak OD-H (250 × 4.6 mm), flow: 1.0 mL/min, *n*-heptane/ethanol 98/2, retention times: (*R*)-**3s**: 24.201 min, (*S*)-**3s**: 26.823 min. $[\alpha]_D^{22}$= +0.9 (c 0.3, $CHCl_3$).

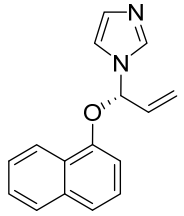
(*S*)-1-(1-Phenoxyallyl)-1*H*-imidazole ((*S*)-**3t**)**.** Imidazole was treated with allene **1c** (39.7 mg, 0.3 mmol) according to the general procedure. Column chromatography (*n*-heptane/EtOAc 40:1 → 20:1) afforded the product **6s** as slightly yellow oil (43.2 mg, 72%, 90% ee).



(*S*)-**3t**

R$_F$ (silica gel, *n*-heptane/EtOAc = 10:1): 0.28 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.52 (ddd, *J* = 0.6, 1.4, 10.5 Hz, 1 H), 5.57 (ddd, *J* = 0.6, 1.5, 17.1 Hz, 1 H), 6.18 (ddd, *J* = 4.3, 10.5, 17.1 Hz, 1 H), 6.30 (dt, *J* = 1.5, 4.3 Hz, 1 H), 6.84–6.89 (m, 2 H), 7.03–7.11 (m, 3 H), 7.23–7.31 (m, 2 H), 7.61 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 85.2, 116.9, 117.7, 119.9, 123.6, 129.8, 129.9, 133.3, 136.0, 155.9. **IR** ($CHCl_3$): ν = 692, 755, 796, 1071, 1210, 1489, 1589, 2916, 3109 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{12}H_{13}N_2O$ $(M + H)^+$ 201.1028, found 201.1018. **HPLC**: ee: 90%, Chiralpak OD-H (250 × 4.6 mm), flow: 1.0 mL/min, *n*-heptane/ethanol 97/3, retention times: (*R*)-**3t**: 20.989 min, (*S*)-**3t**: 27.478 min. $[\alpha]_D^{22}$= +0.7 (c 0.25, $CHCl_3$).

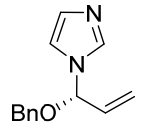
(*S*)-1-[1-(Naphthalen-1-yloxy)allyl]-1*H*-imidazole ((*S*)-**3u**). Imidazole was treated with allene **1f** (54.7 mg, 0.3 mmol) according to the general procedure. Column chromatography (*n*-heptane/EtOAc 20:1 → 4:1) afforded the product **3u** as slightly yellow oil (50.3 mg, 67%, 94% ee).



(*S*)-**3u**

R$_F$ (silica gel, *n*-heptane/EtOAc = 1:2): 0.36 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 5.60 (dd, *J* = 0.9, 10.5 Hz, 1 H), 5.71 (dd, *J* = 1.0, 17.1 Hz, 1 H), 6.30 (ddd, *J* = 4.3, 10.5, 17.1 Hz, 1 H), 6.45 (dt, *J* = 1.4, 4.3 Hz, 1 H), 6.74 (d, *J* = 7.5 Hz, 1 H), 7.12 (d, *J* = 13.6 Hz, 2 H), 7.30 (t, *J* = 8.0 Hz, 1 H), 7.46–7.53 (m, 2 H), 7.55 (d, *J* = 8.3 Hz, 1 H), 7.64 (s, 1 H), 7.78–7.85 (m, 1 H), 8.09–8.15 (m, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 85.3, 110.5, 120.1, 121.5, 123.4, 125.5, 126.0, 126.3, 126.7, 127.8, 130.0, 133.2, 134.7, 151.7. **IR** ($CHCl_3$): ν = 662, 773, 794, 1069, 1262, 1393, 1579, 2919, 3054 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{16}H_{15}N_2O$ $(M + H)^+$ 251.1184, found 251.1172. **HPLC**: ee: 94%, Chiralpak OD-H (250 × 4.6 mm), flow: 1.0 mL/min, *n*-heptane/ethanol 97/3, retention times: (*R*)-**3u**: 23.367 min, (*S*)-**3u**: 28.622 min. $[\alpha]_D^{22}$= +1.3 (c 0.3, $CHCl_3$).

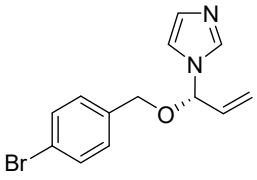
(*S*)-1-[1-(Benzyloxy)allyl]-1*H*-imidazole ((*S*)-**3a**). Imidazole was treated with allene **1a** (43.9 mg, 0.3 mmol) according to the general procedure. The solvent was removed in vacuo and the crude residue was filtrated over diatomaceous-earth pad with *n*-heptane to afford the product **3a** as slightly yellow oil (57 mg, 89%, 92% ee).



(*S*)-**3a**

All analytical data are identical to those reported previously. **HPLC**: ee: 92%, Chiralpak OD-H (250 × 4.6 mm), flow: 1.0 mL/min, *n*-heptane/ethanol 97/3, retention times: (*R*)-**3a**: 19.953 min, (*S*)-**3a**: 22.876 min. $[\alpha]_D^{22}$= +0.5 (c 0.2, $CHCl_3$).

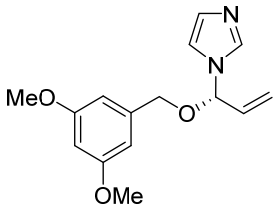
(*S*)-1-{1-[(4-Bromobenzyl)oxy]allyl}-1*H*-imidazole ((*S*)-**3v**). Imidazole was treated with allene **1d** (67.5 mg, 0.3 mmol) according to the general procedure. Column chromatography (*n*-heptane/EtOAc 20:1 → 10:1) afforded the product **3v** as slightly yellow oil (78 mg, 89%, 93% ee).



(*S*)-**3v**

R$_F$ (silica gel, *n*-heptane/EtOAc = 10:1): 0.17 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 4.31 (d, *J* = 12.0 Hz, 1 H), 4.43 (d, *J* = 12.0 Hz, 1 H), 5.40 (ddd, *J* = 0.9, 1.5, 10.5 Hz, 1 H), 5.41 (ddd, *J* = 0.9, 1.5, 17.2 Hz, 1 H), 5.65 (dt, *J* = 1.5, 4.3 Hz, 1 H), 6.04 (ddd, *J* = 4.3, 10.5, 17.2 Hz, 1 H), 7.05 (s, 1 H), 7.11–7.18 (m, 2 H), 7.45–7.51 (m, 2 H), 7.64 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 68.9, 84.6, 119.2, 122.1, 129.4, 130.1, 131.7, 133.9, 135.3, 136.3. **IR** ($CHCl_3$): ν = 479, 663, 805, 1011, 1068, 1216, 1488, 2873, 3109 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{13}H_{13}BrN_2ONa$ $(M + Na)^+$ 315.0103, found 315.0111. **HPLC**: ee: 93%, Chiralpak OD-H (250 × 4.6 mm), flow: 1.0 mL/min, *n*-heptane/ethanol 97/3, retention times: (*R*)-**3v**: 22.208 min, (*S*)-**3v**: 27.493 min. $[\alpha]_D^{22}$= +0.8 (c 0.3, $CHCl_3$).

(*S*)-1-{1-[(3,5-Dimethoxybenzyl)oxy]allyl}-1*H*-imidazole ((*S*)-**3w**). Imidazole was treated with allene **1e** (61.9 mg, 0.3 mmol) according to the general procedure. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:1) afforded the product **3w** as slightly yellow oil (74.0 mg, 90%, 94% ee).



(*S*)-**3w**

R$_F$ (silica gel, *n*-heptane/EtOAc = 1:1): 0.43 (UV, $KMnO_4$-solution). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 3.78 (s, 6 H), 4.27 (d, *J* = 12.2 Hz, 1 H), 4.48 (d, *J* = 12.2 Hz, 1 H), 5.39 (ddd, *J* = 0.8, 1.4, 10.5 Hz, 1 H), 5.42 (ddd, *J* = 0.8, 1.5, 17.2 Hz, 1 H), 5.67 (dt, *J* = 1.3, 4.3 Hz, 1 H), 6.04 (ddd, *J* = 4.3, 10.5, 17.2 Hz, 1 H), 6.41 (t, *J* = 2.1 Hz, 1 H), 6.43 (d, *J* = 2.0 Hz, 2 H), 7.06 (s, 1 H), 7.14 (s, 1 H), 7.64 (s, 1 H). **^{13}C NMR** (400 MHz, $CDCl_3$): δ = 55.3, 69.6, 84.3, 100.1, 105.6, 116.9, 119.0, 130.0, 134.1, 136.3, 138.5, 161.0. **IR** ($CHCl_3$): ν = 664, 833, 1060, 1064, 1153, 1205, 1462, 1597, 2931, 3110 cm^{-1}. **HRMS** (ESI^+) calcd. for $C_{15}H_{19}N_2O_3$ $(M + H)^+$ 275.1396, found 275.1384. **HPLC**: ee: 94%, Chiralpak OD-H (250 × 4.6 mm), flow: 1.0 mL/min, *n*-heptane/ethanol 97/3, retention times: (*R*)-**3w**: 30.201 min, (*S*)-**3w**: 35.069 min. $[\alpha]_D^{22}$= +1.0 (c 0.3, $CHCl_3$).

(*S*)-7-[1-(Benzyloxy)allyl]-1,3-dimethyl-1*H*-purine-2,6(3*H*,7*H*)-dione ((*S*)-**3q**). Theophylline (64.9 mg, 0.36 mmol) was treated with allene **1a** (43.9 mg, 0.3 mmol) according to the general procedure. Column chromatography (*n*-heptane/EtOAc 10:1 → 1:1) afforded the product **3q** as a white powder (72.0 mg, 74%, 92% ee).

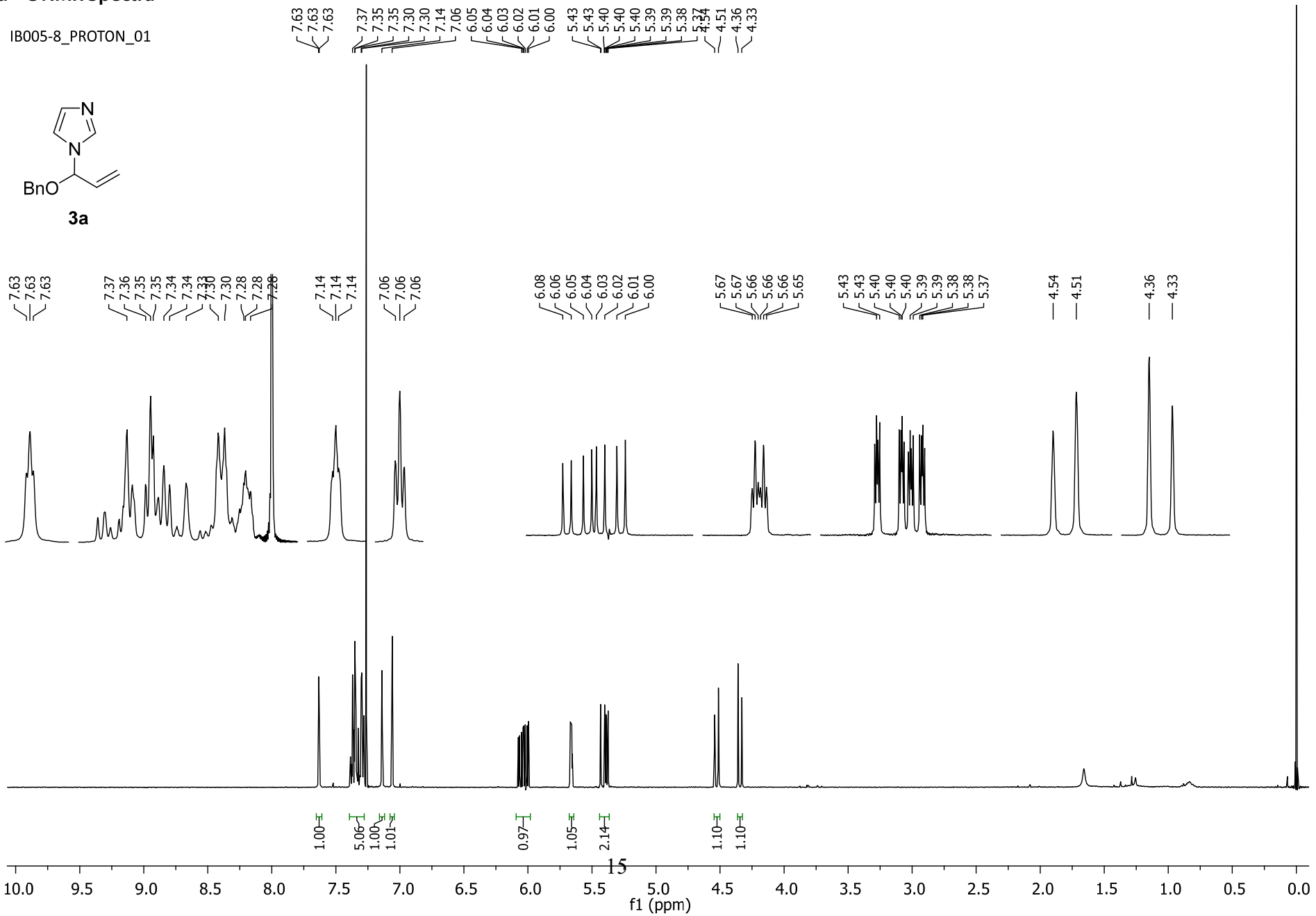
(*S*)-**3q**

All analytical data are identical to those reported previously. **HPLC**: ee: 92%, Phenomenex Lux 3u Cellulose-1, flow: 0.5 mL/min, *n*-heptane/2-propanol 70/30, retention times: (*R*)-**3q**: 15.832 min, (*S*)-**3q**: 16.518 min. $[\alpha]_D^{22}$= +0.4 (c 0.2, $CHCl_3$).

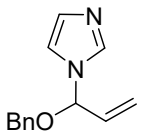
Determination of the absolute configuration

High quality single crystal of (*S*)-**3q** was obtained through slow solvent evaporation: a saturated solution of **3q** in toluene was prepared and filtered over an Acrodisc HPLC syringe filter to ensure the absence of crystallites. The resulting filtrate was transferred to a scintillation flask that was sealed and equipped with a hollow needle to allow slow evaporation of the solvent. The acquired single crystal was subjected to single X-ray diffraction and was subsequently analyzed with chiral HPLC to unambiguously link the absolute configuration with the retention time of one of the enantiomers of **3q**.

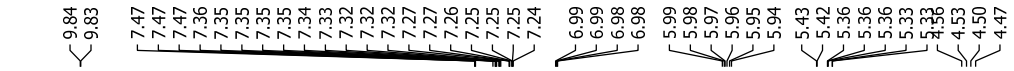
^{1}H and ^{13}C NMR Spectra



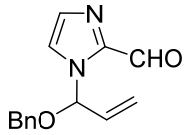
IB005-8_C13__CARBON_01



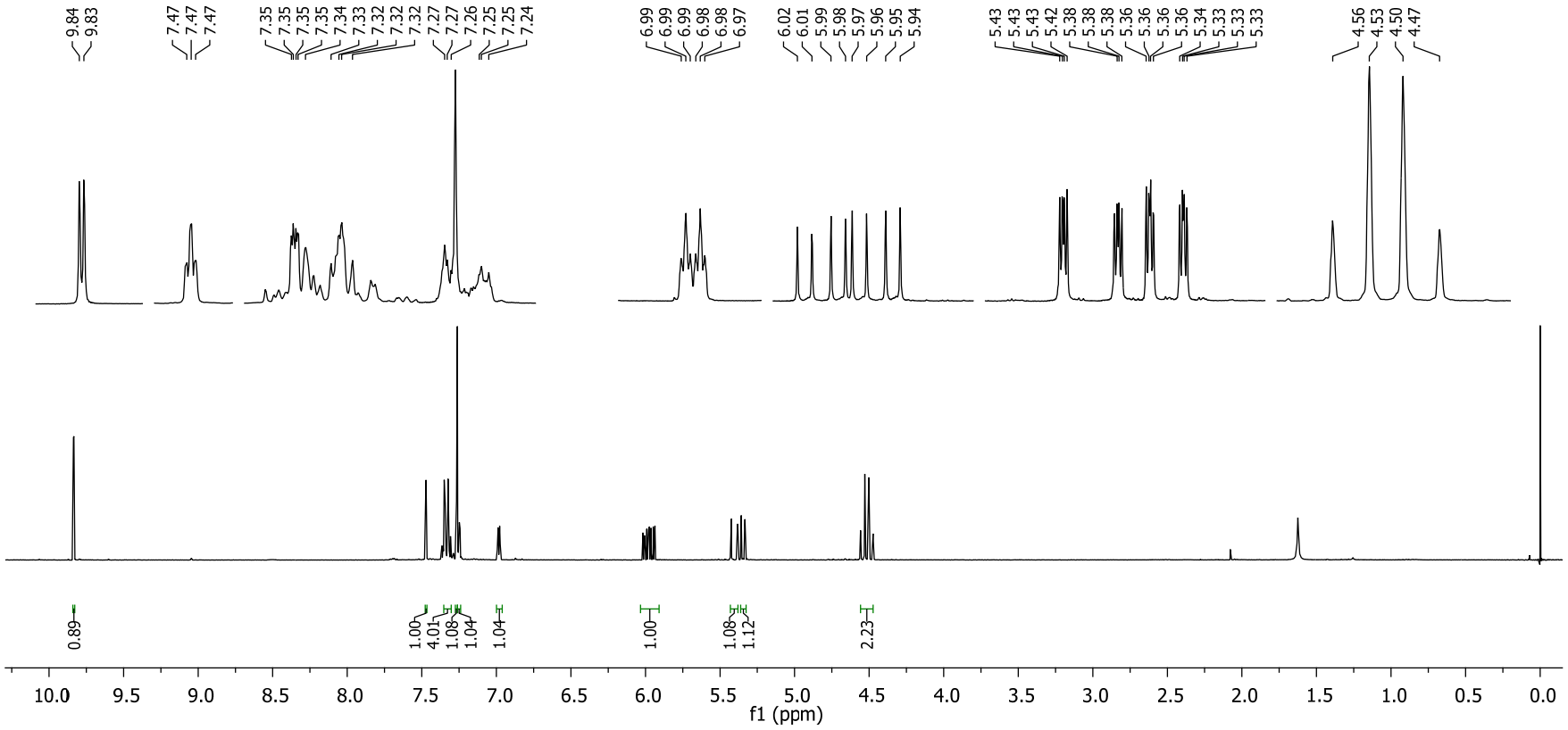
3a

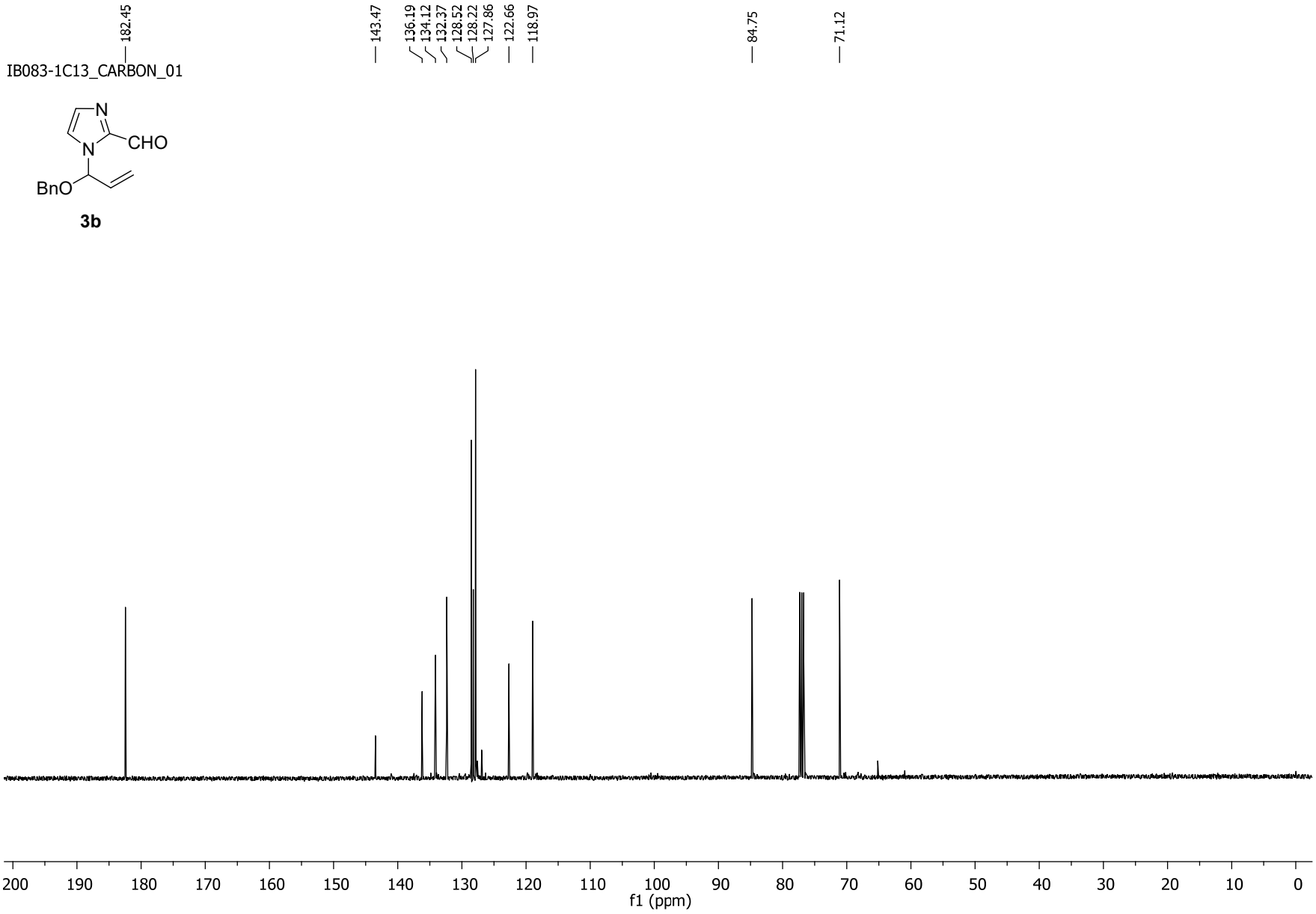


IB083-1_PROTON_01

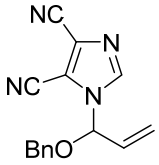


3b



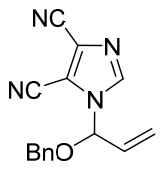

182.45
IB083-1C13_CARBON_01
143.47
136.19
134.12
132.37
128.52
128.22
127.86
122.66
118.97
84.75
71.12
N
CHO
N
BnO
3b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

IB262-2F1Full_PROTON_01



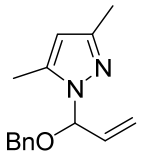
3c

IB262-2F1Full_CARBON_01

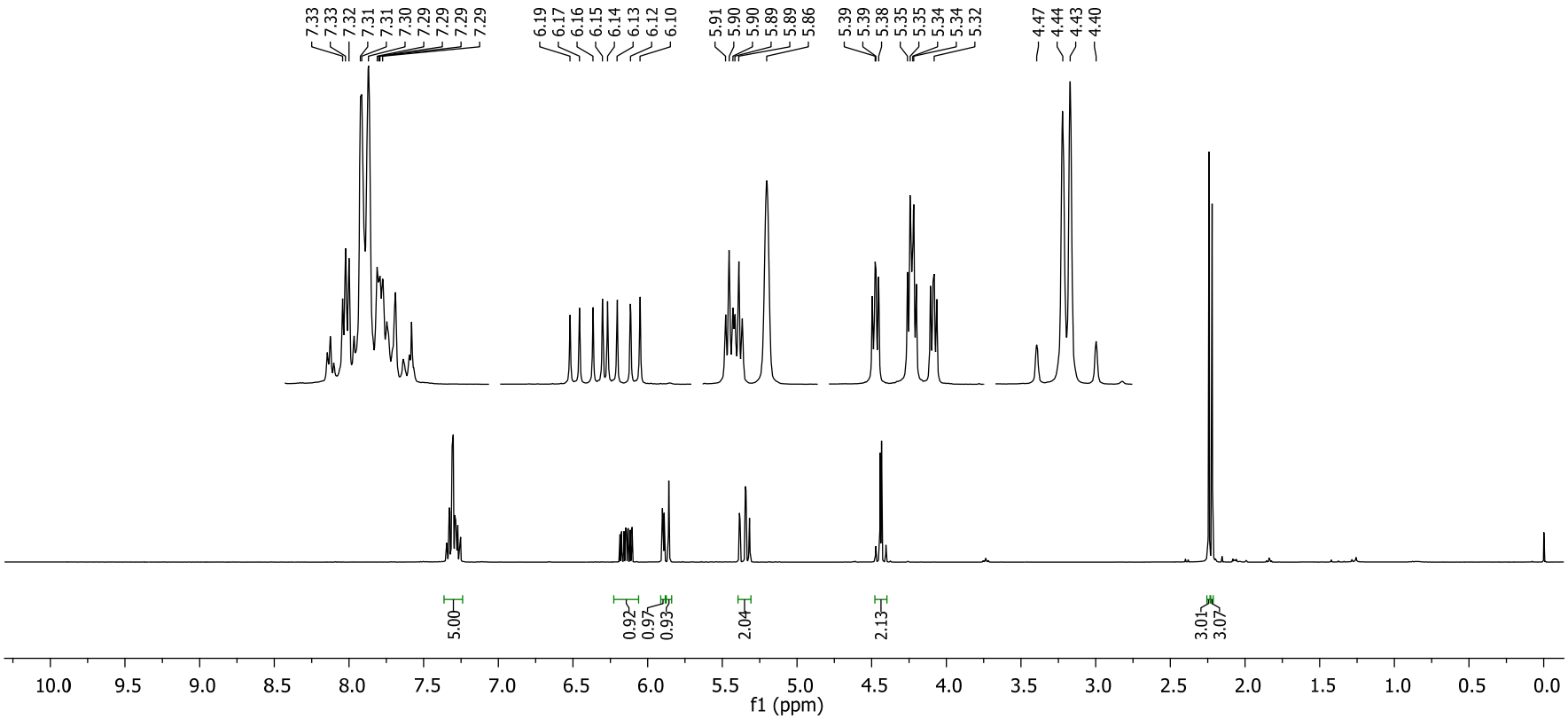


3c

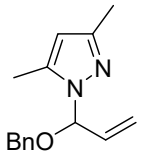
IB016_PROTON_01



3d

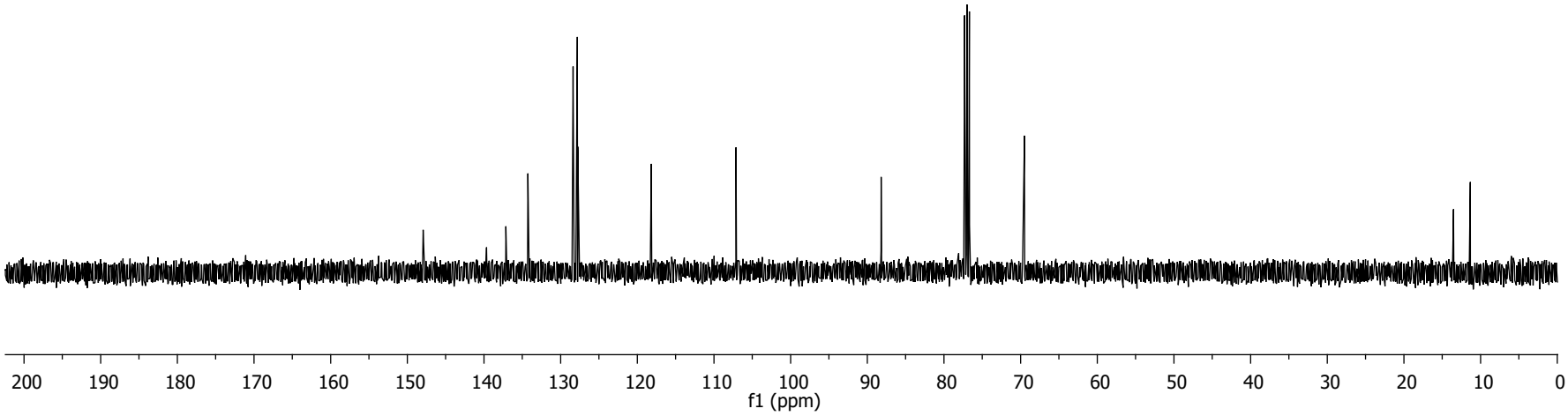


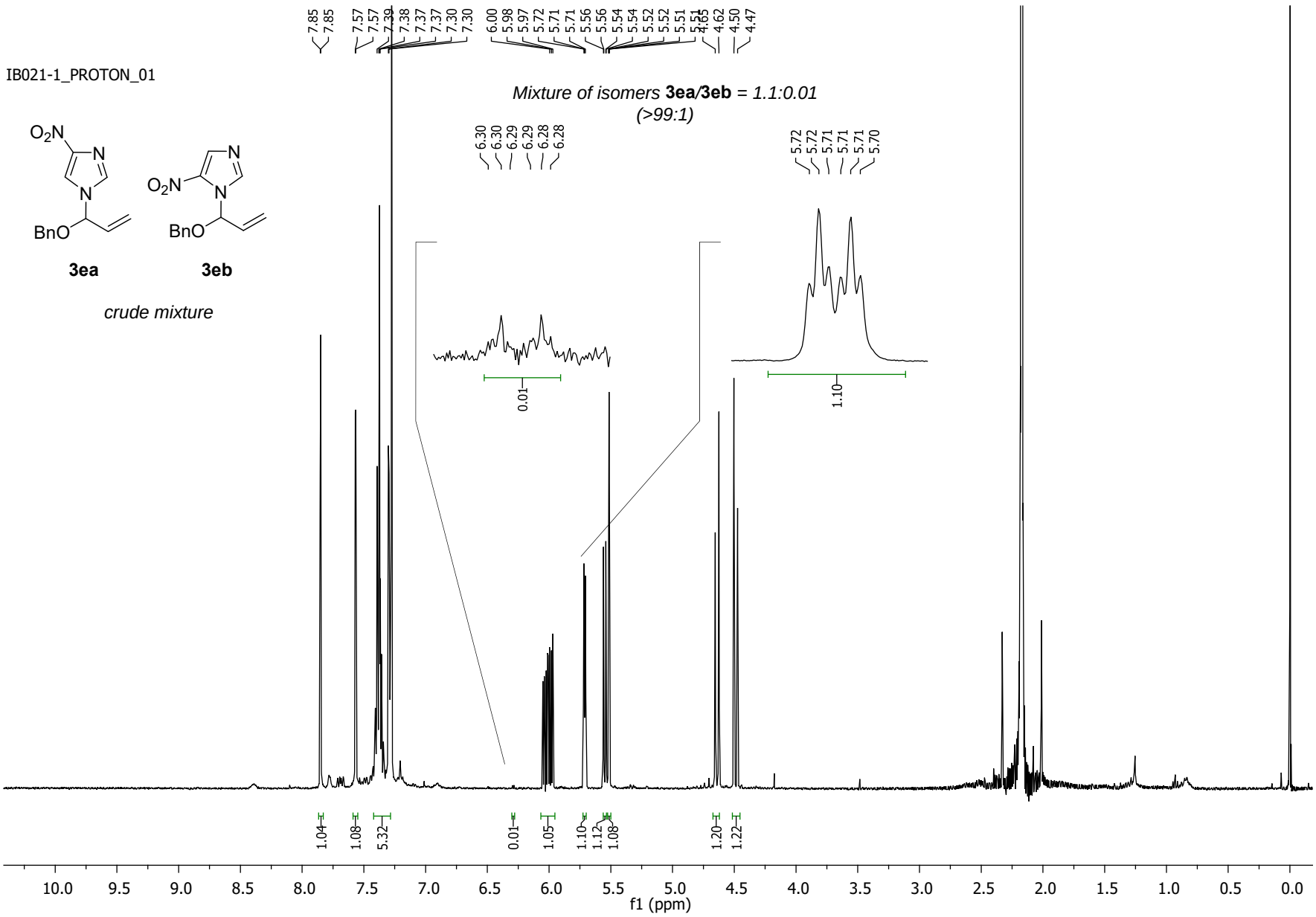
IB016_CARBON_01



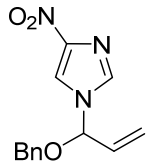
3d

147.93
139.63
137.08
134.26
128.38
127.82
127.76
118.17
107.13
88.20
69.51
13.53
11.35




IB021-1_PROTON_01
Mixture of isomers 3ea/3eb = 1.1:0.01
(>99:1)
3ea
3eb
crude mixture
f1 (ppm)

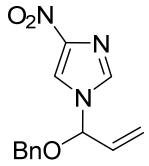
IB021_PROTON_01



3ea

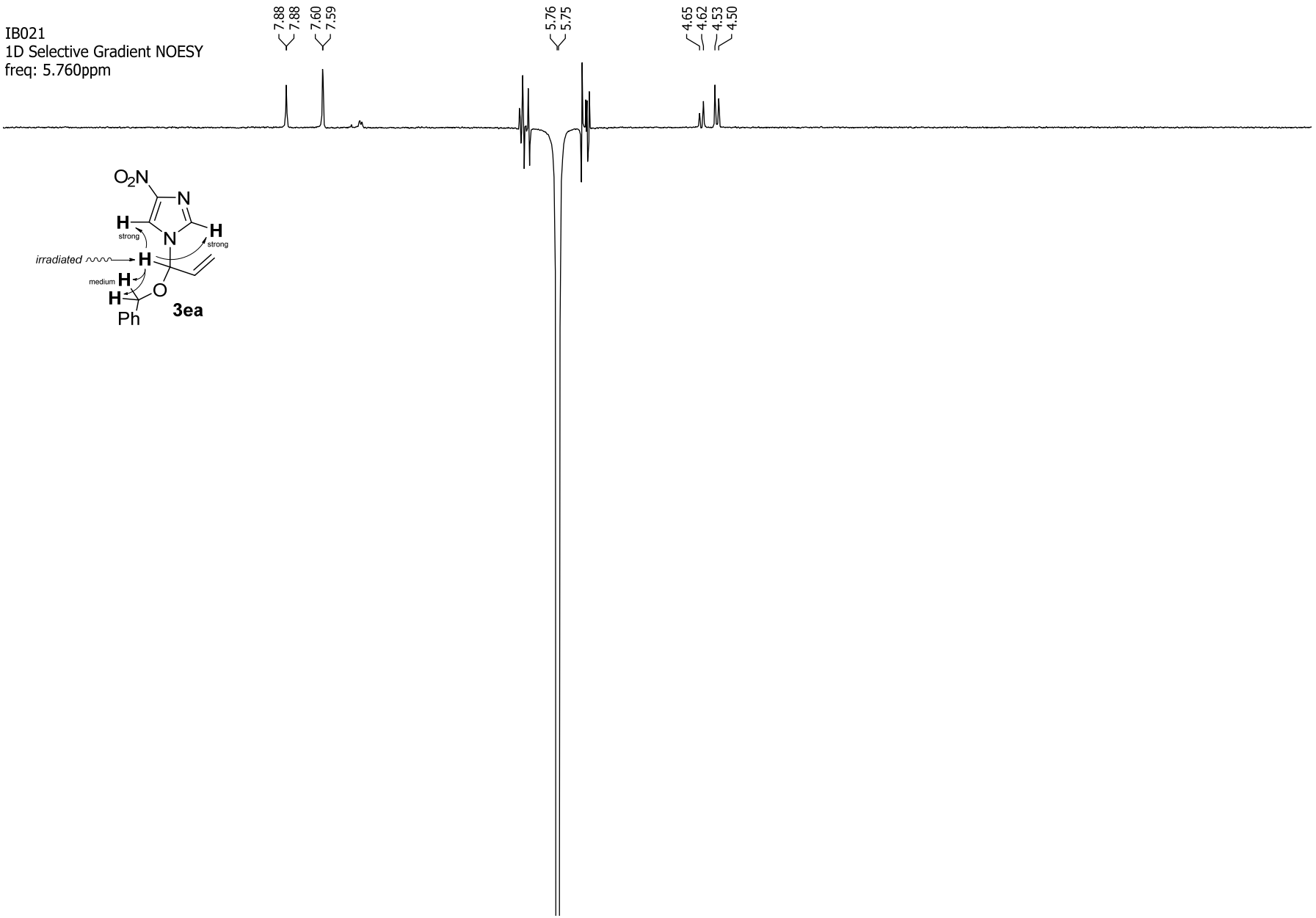
after purification

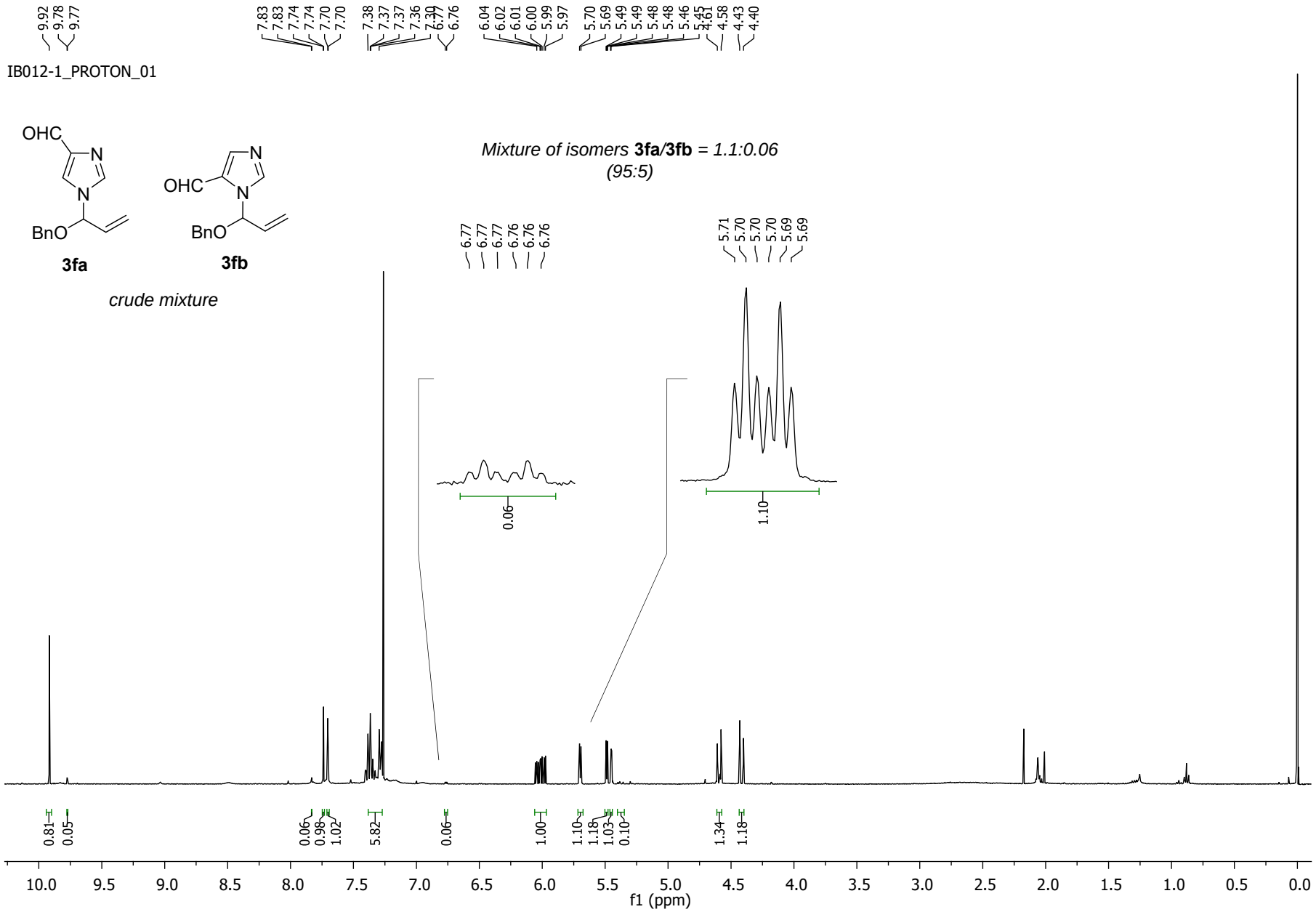
IB021_CARBON_01



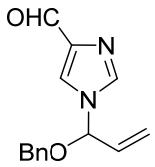
3ea

after purification


IB021
1D Selective Gradient NOESY
freq: 5.760ppm
7.88
7.88
7.60
7.59
5.76
5.75
4.65
4.62
4.53
4.50
O2N
N
H
strong
N
H
strong
irradiated
H
medium
H
H
O
Ph
3ea

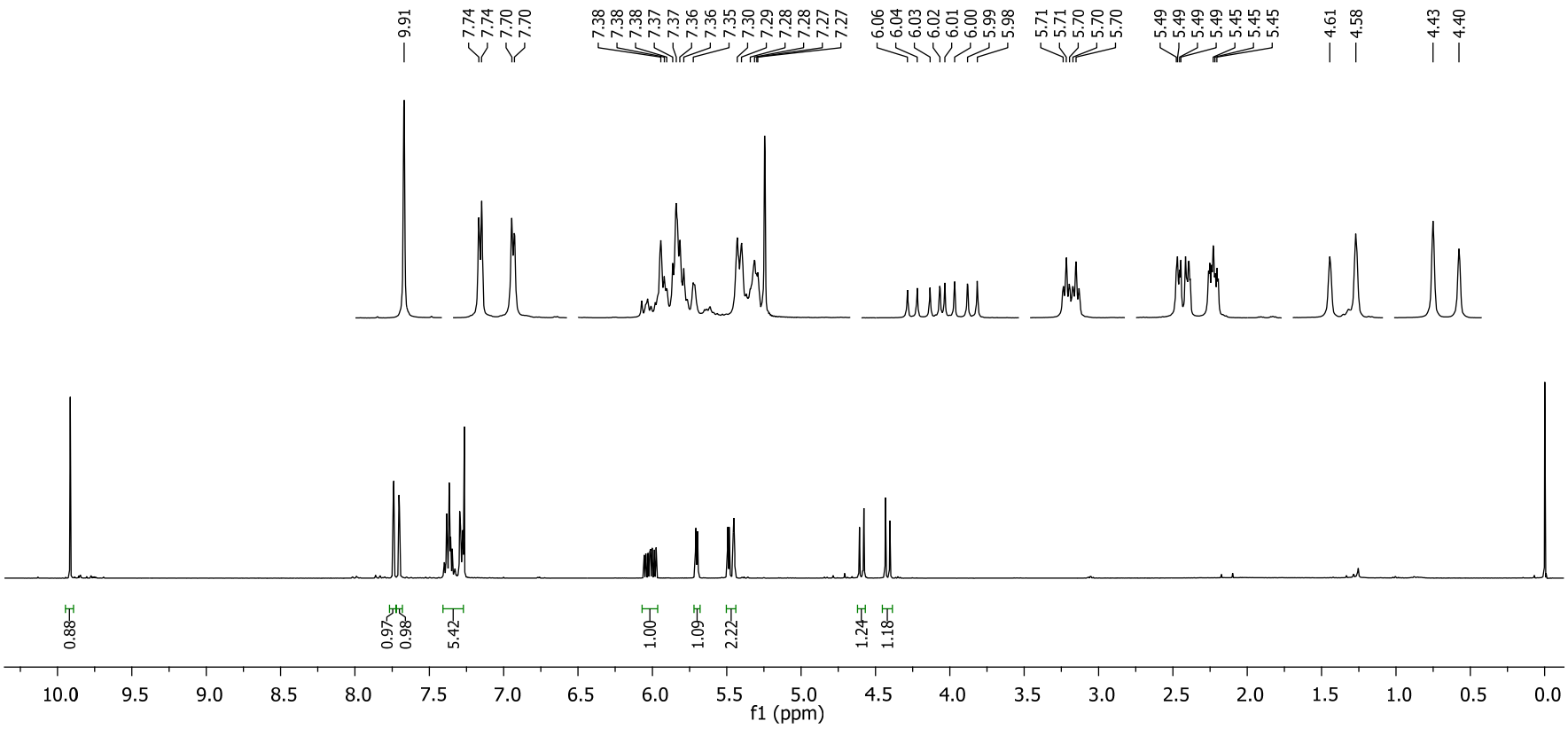

IB012-1_PROTON_01
OHC
N
N
BnO
3fa
OHC
N
N
BnO
3fb
crude mixture
Mixture of isomers 3fa/3fb = 1.1:0.06
(95:5)
0.06
1.10
f1 (ppm)

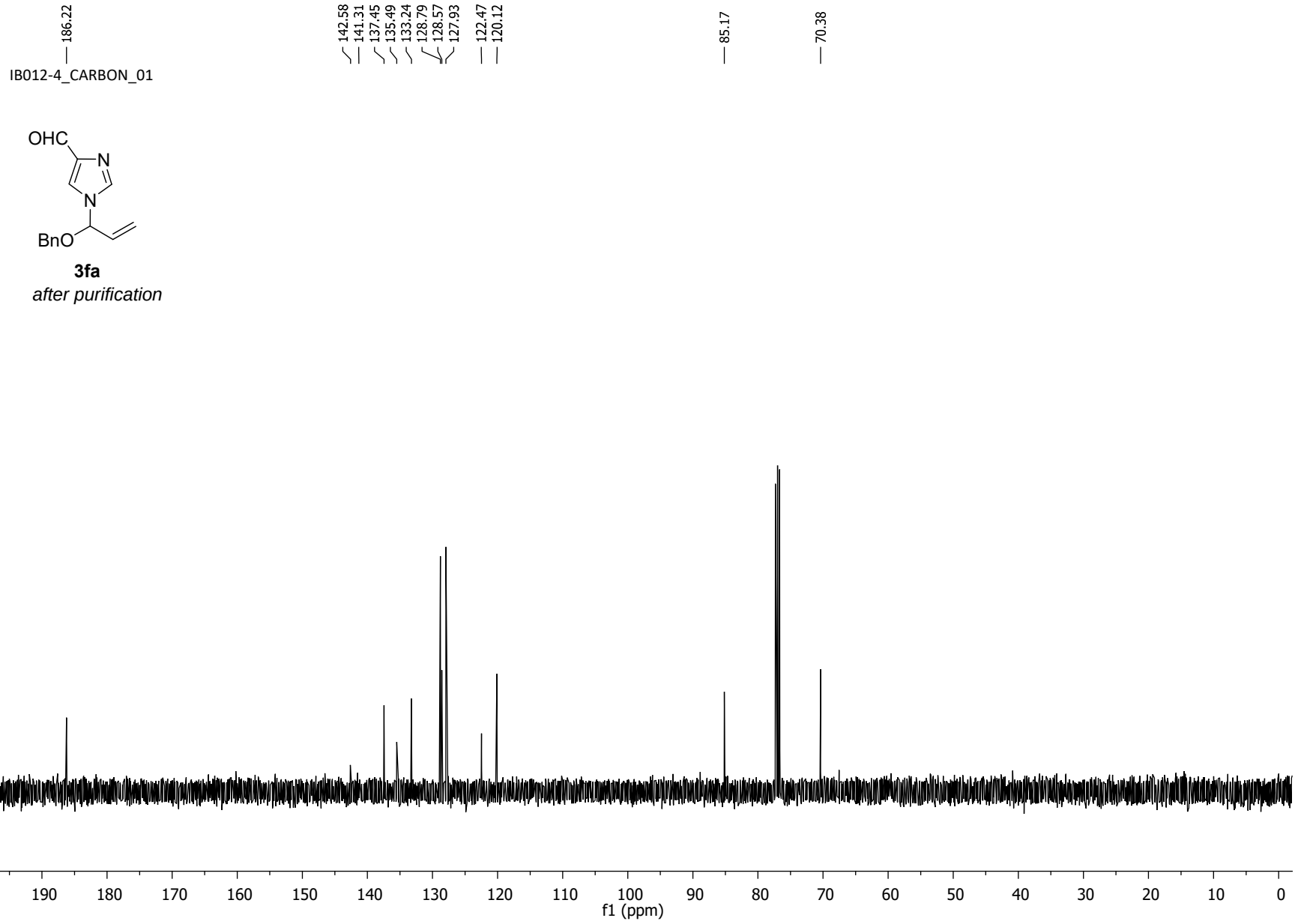
IB012-4_PROTON_01



3fa

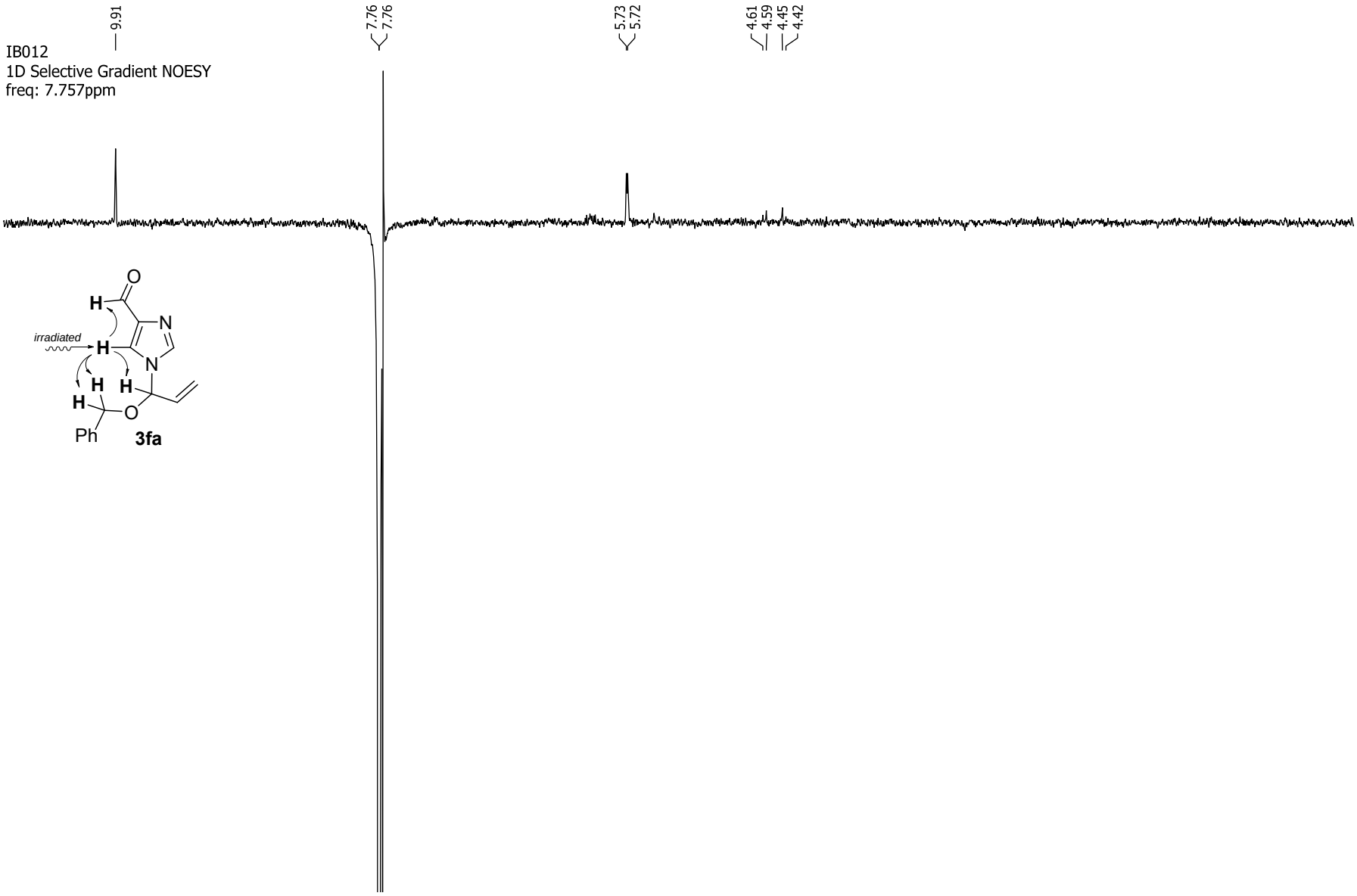
after purification



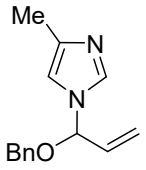


3fa

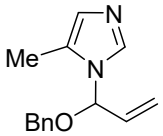
after purification


9.91
7.76
7.76
5.73
5.72
4.61
4.59
4.45
4.42
IB012
1D Selective Gradient NOESY
freq: 7.757ppm
irradiated
O
H
N
H
N
H
H
H
O
Ph
3fa

IB010-1



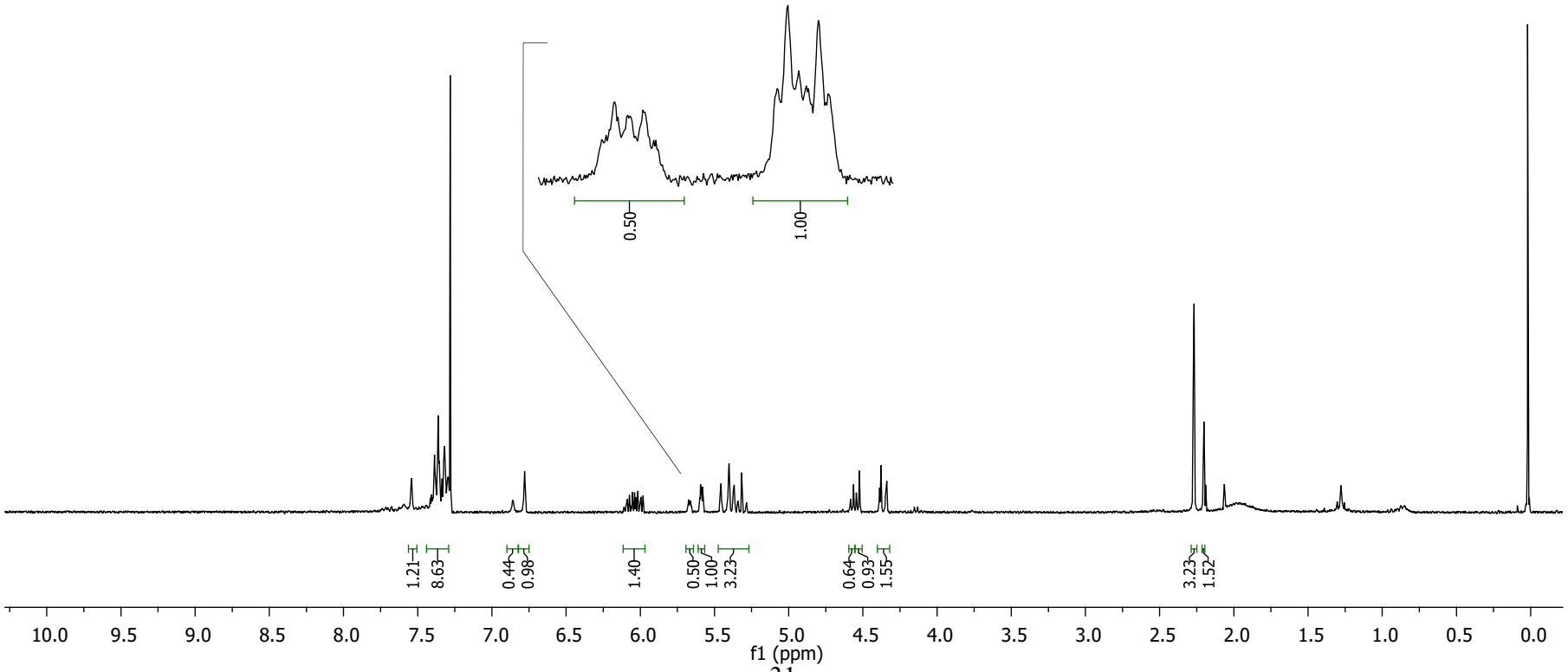
3ga

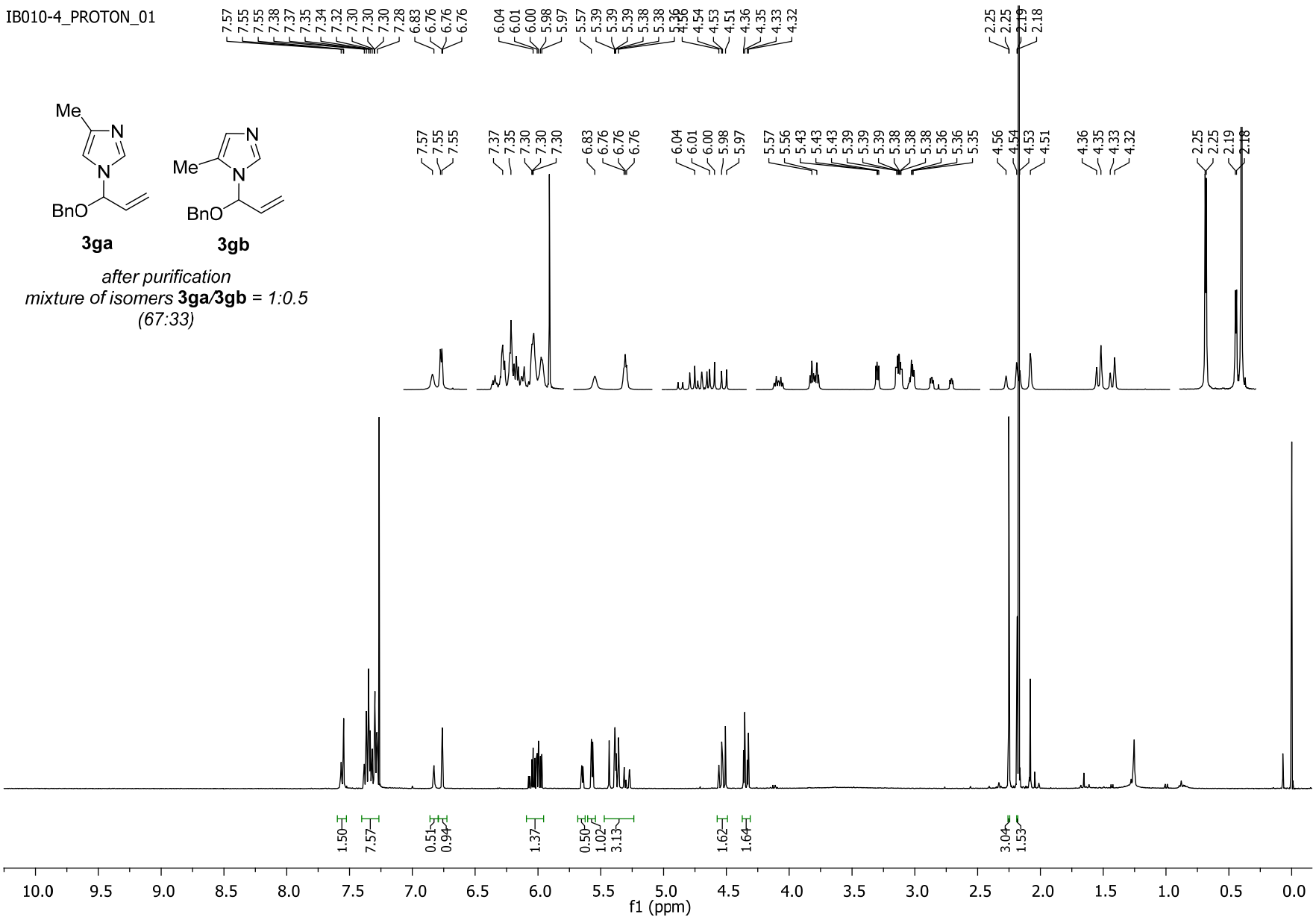


3gb

crude mixture

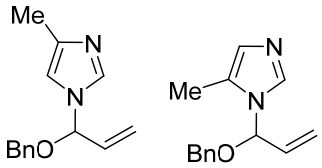
Mixture of isomers **3ga**/**3gb** = *1:0.5 (67:33)*




IB010-4_PROTON_01
Me
N
N
BnO
3ga
Me
N
N
BnO
3gb
after purification
mixture of isomers 3ga/3gb = 1:0.5
(67:33)
f1 (ppm)

IB010-F1_CARBON_01

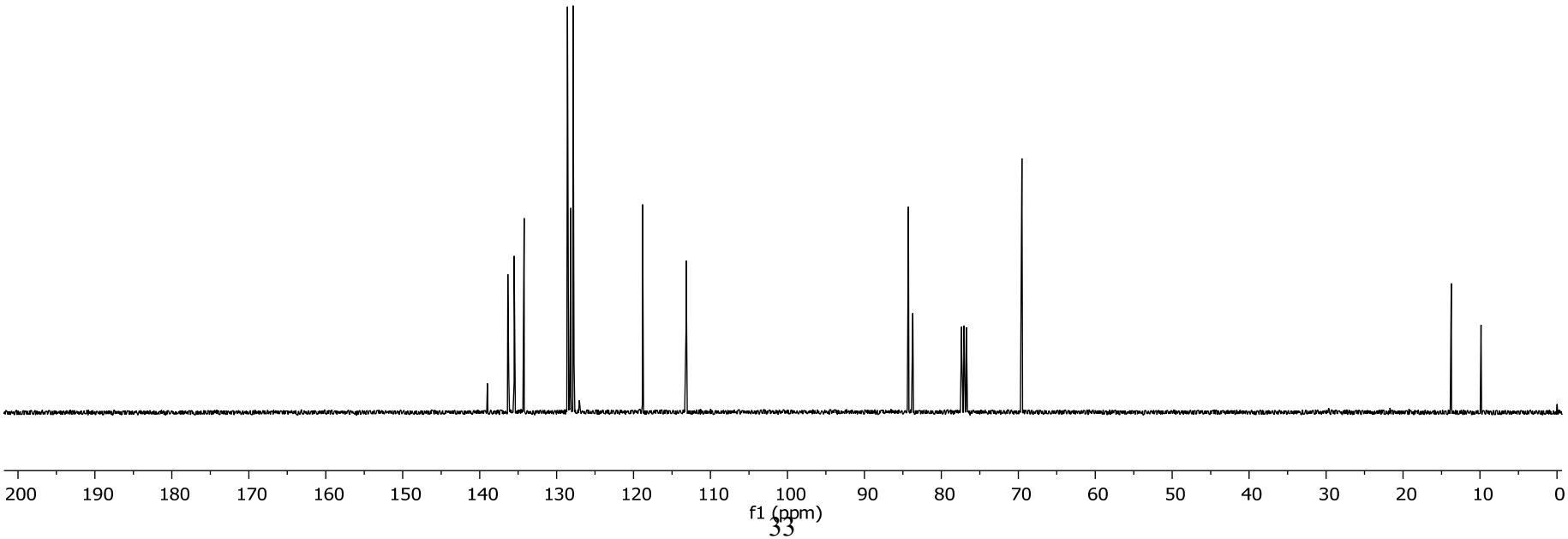
138.99
136.34
136.22
135.51
134.32
134.23
128.61
128.58
128.21
128.15
127.92
127.86
127.73
118.82
118.78
113.17
84.28
83.71
69.63
69.53
13.72
9.86

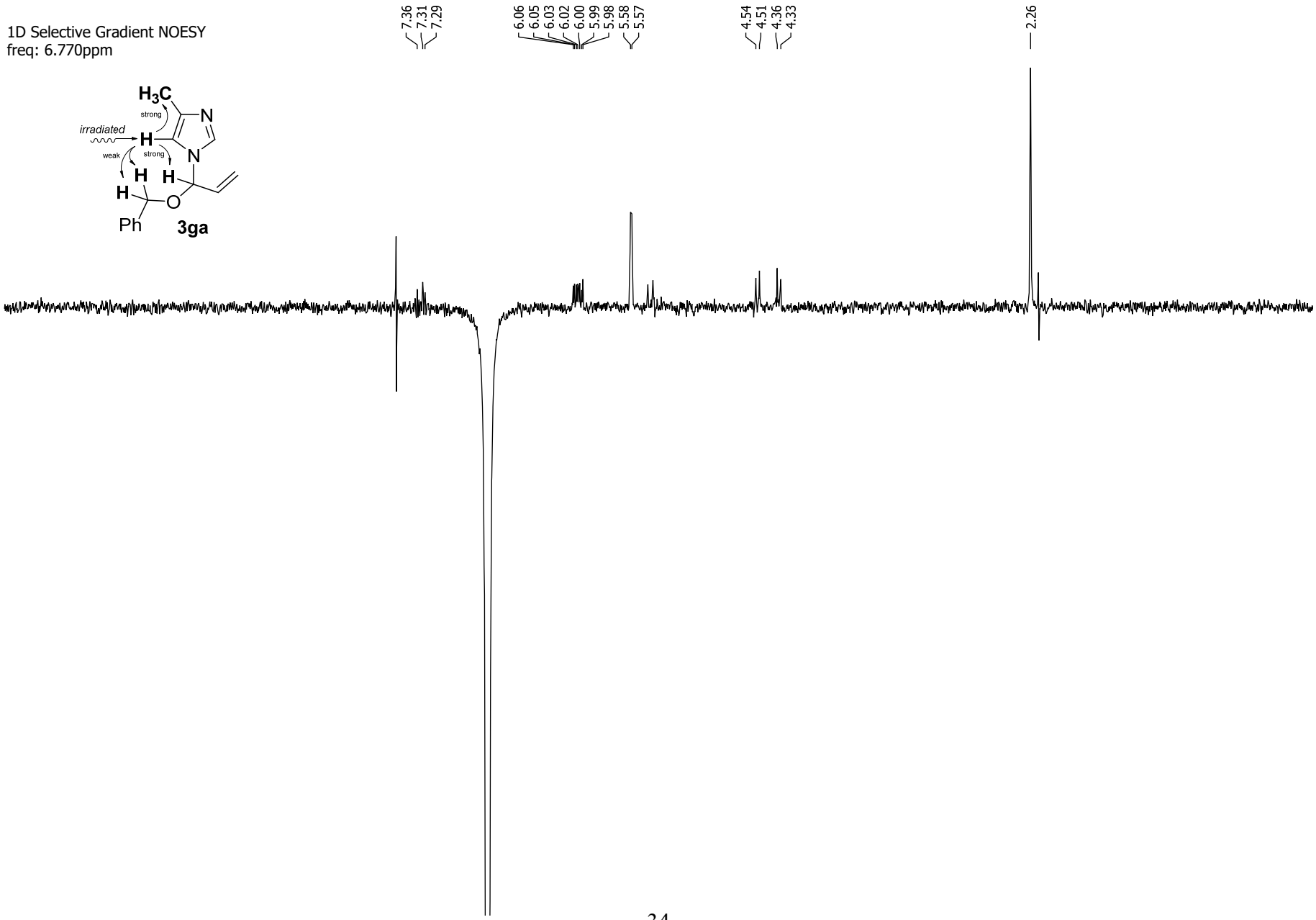


3ga

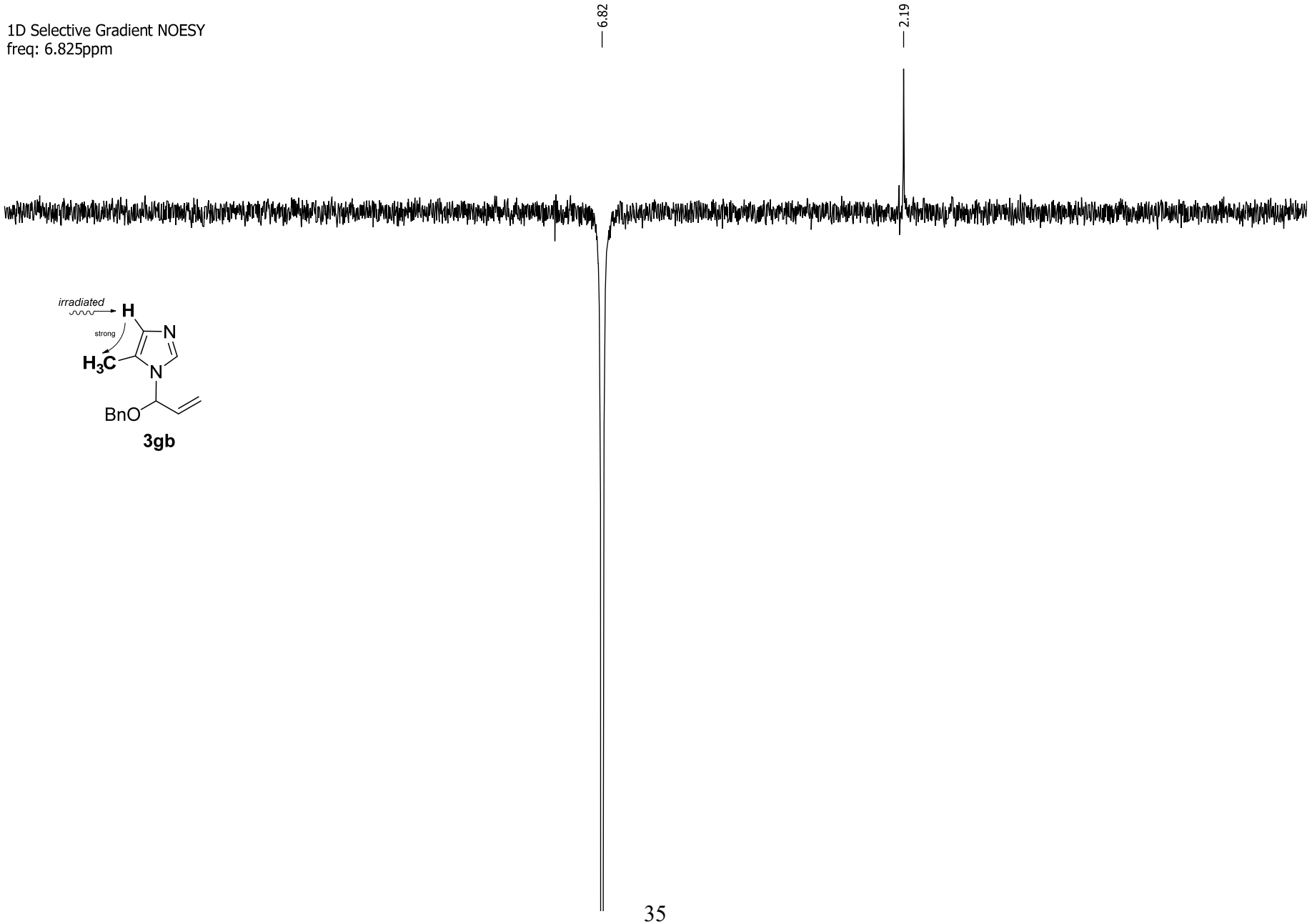
3gb

after purification
mixture of isomers **3ga**/**3gb** = *1:0.5*
(67:33)

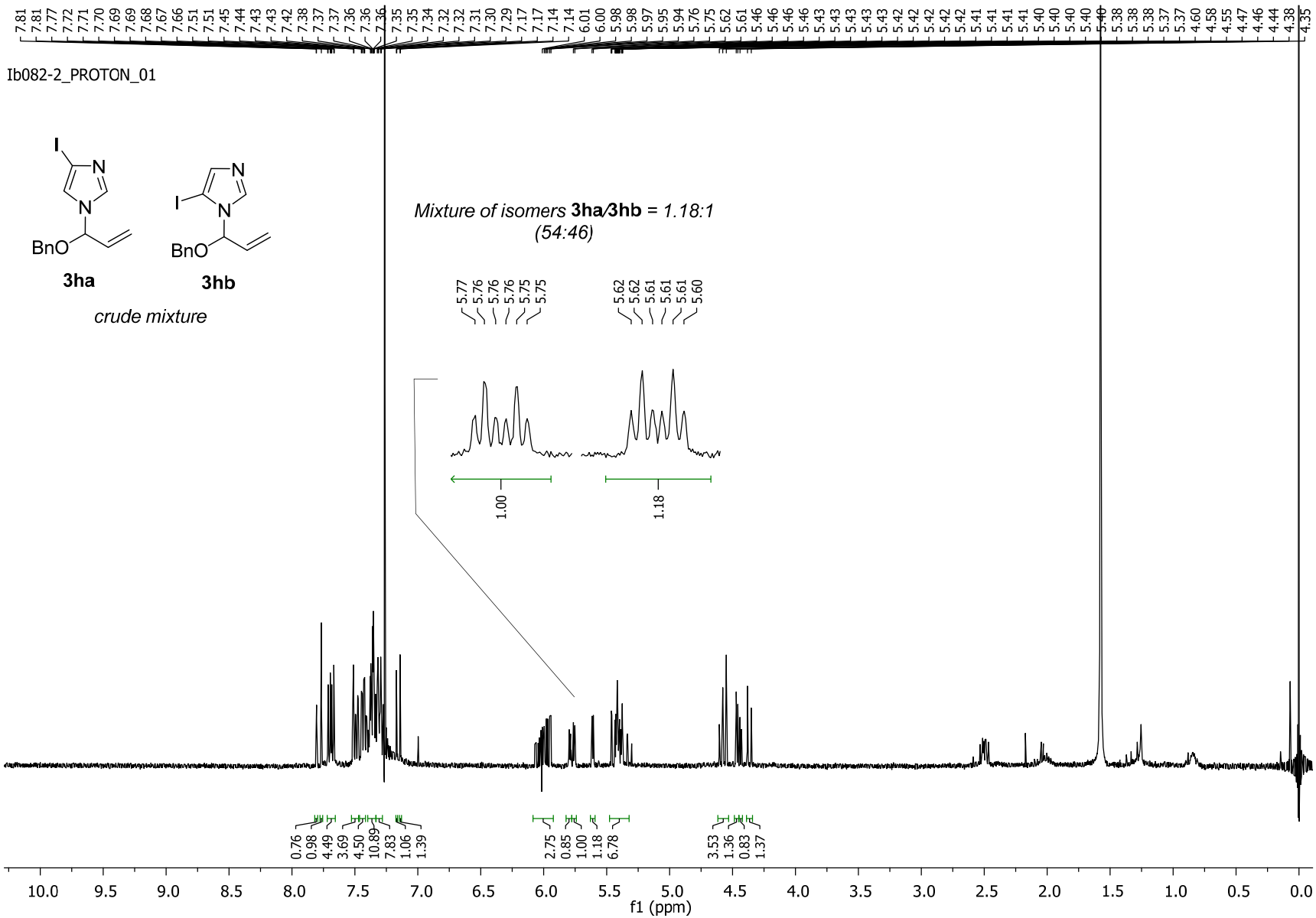



1D Selective Gradient NOESY
freq: 6.770ppm
7.36
7.31
7.29
6.06
6.05
6.03
6.02
6.00
5.99
5.98
5.58
5.57
4.54
4.51
4.36
4.33
2.26
H3C
strong
N
irradiated
H
weak
strong
N
H
H
H
O
Ph
3ga

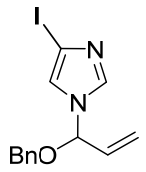
1D Selective Gradient NOESY
freq: 6.825ppm



3gb

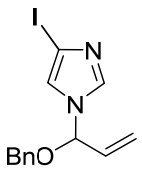

Ib082-2_PROTON_01
3ha
3hb
crude mixture
Mixture of isomers 3ha/3hb = 1.18:1
(54:46)
1.00
1.18
f1 (ppm)

IB080-2-F3_PROTON_01



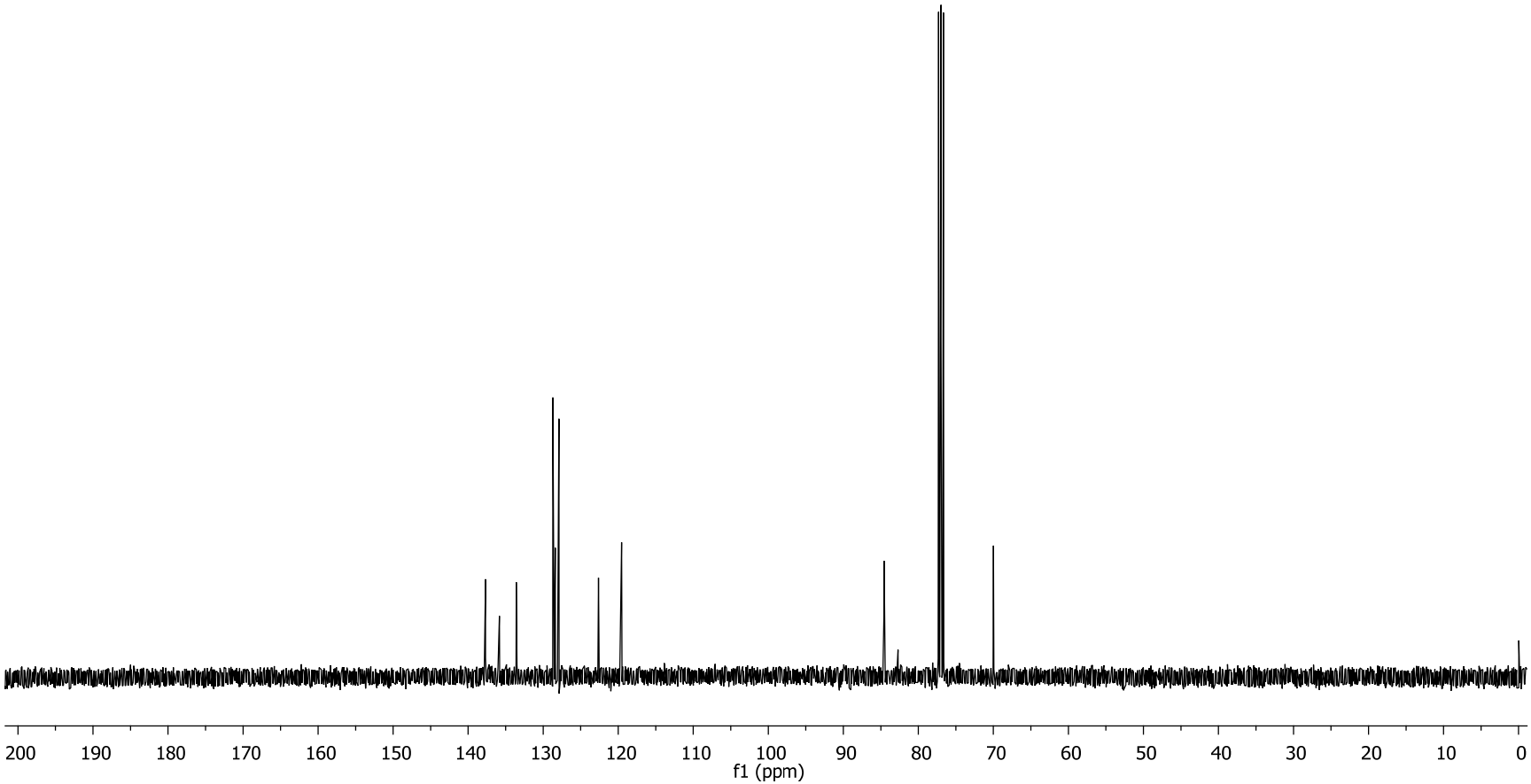
3ha

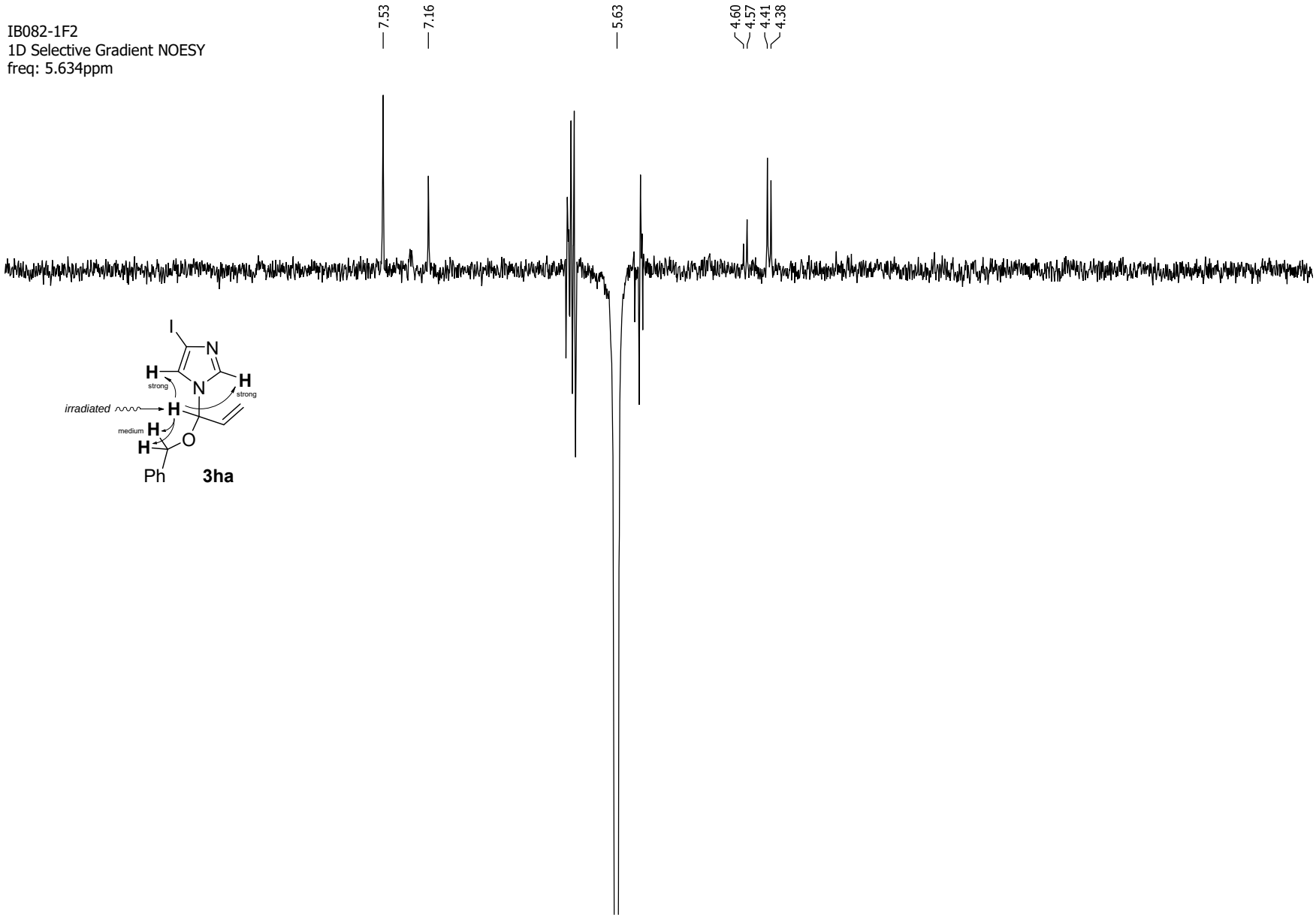
IB080-2-F3_CARBON_01



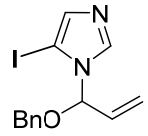
3ha

137.69
135.83
133.59
128.70
128.39
127.90
122.63
119.55
84.56
82.59
69.98

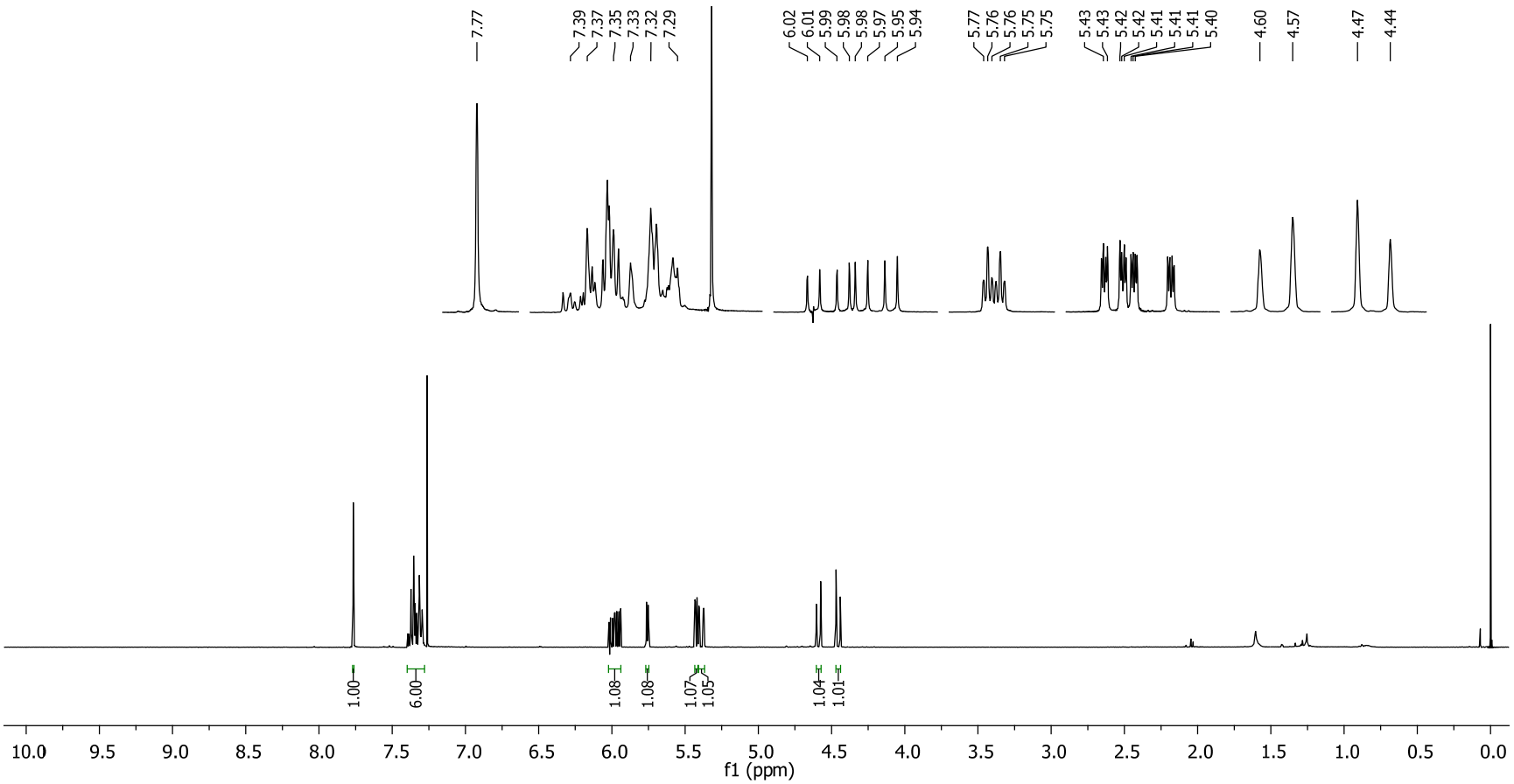



IB082-1F2
1D Selective Gradient NOESY
freq: 5.634ppm
7.53
7.16
5.63
4.60
4.57
4.41
4.38
I
N
H
strong
N
H
strong
irradiated
H
medium
H
H
O
Ph
3ha

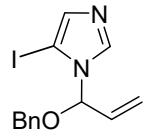
IB082-F1_PROTON_01



3hb

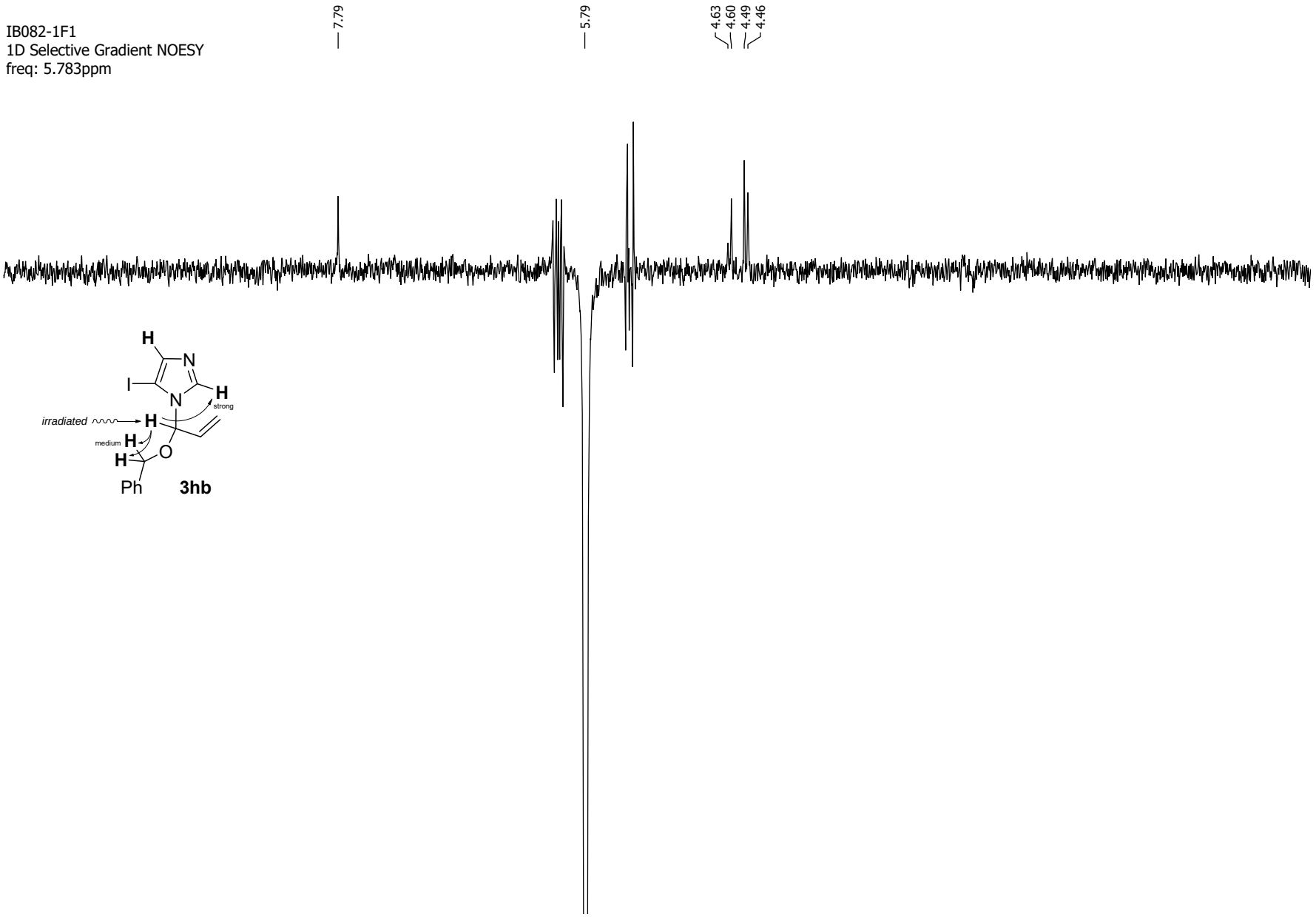


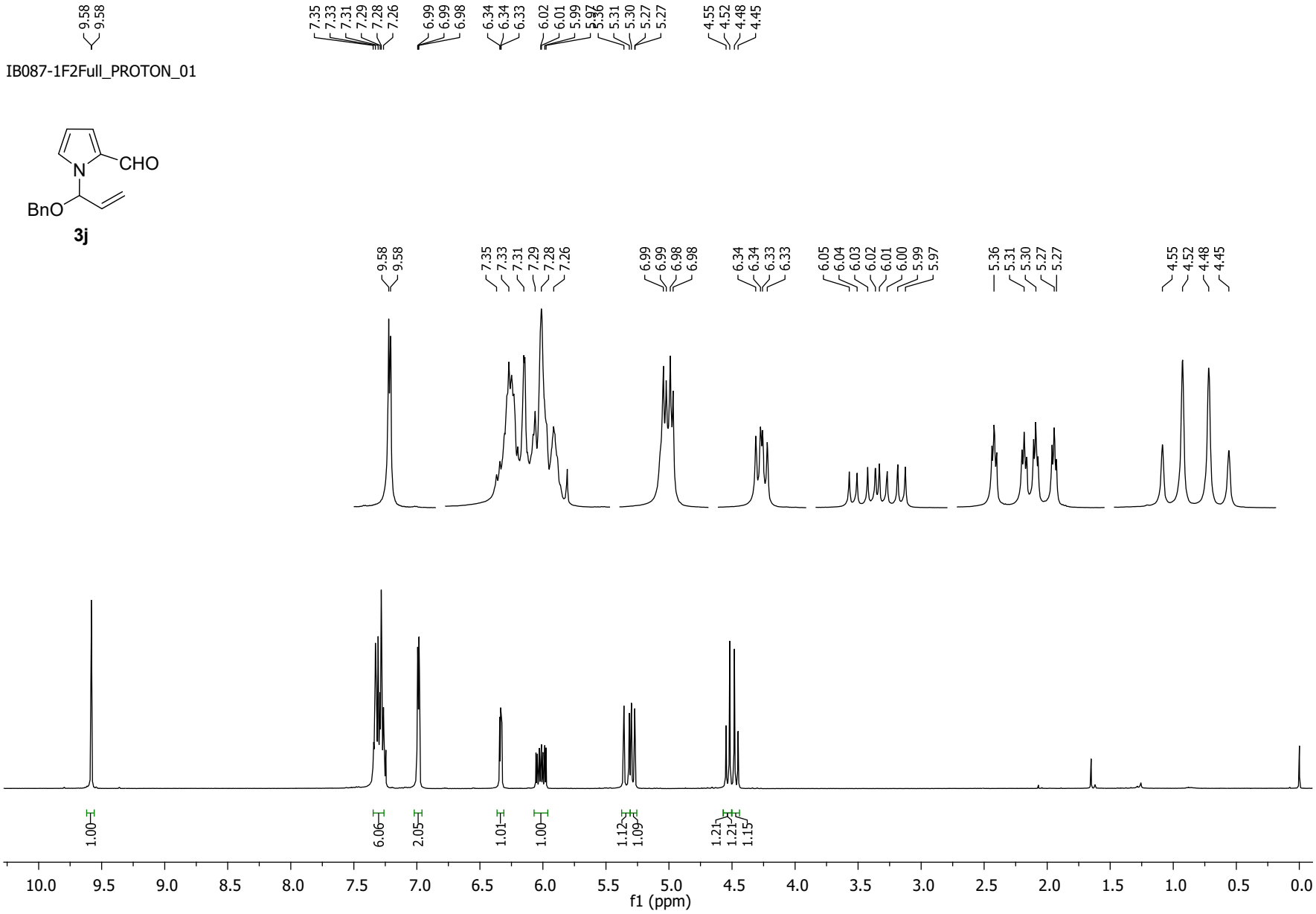
IB082-F1_CARBON_01

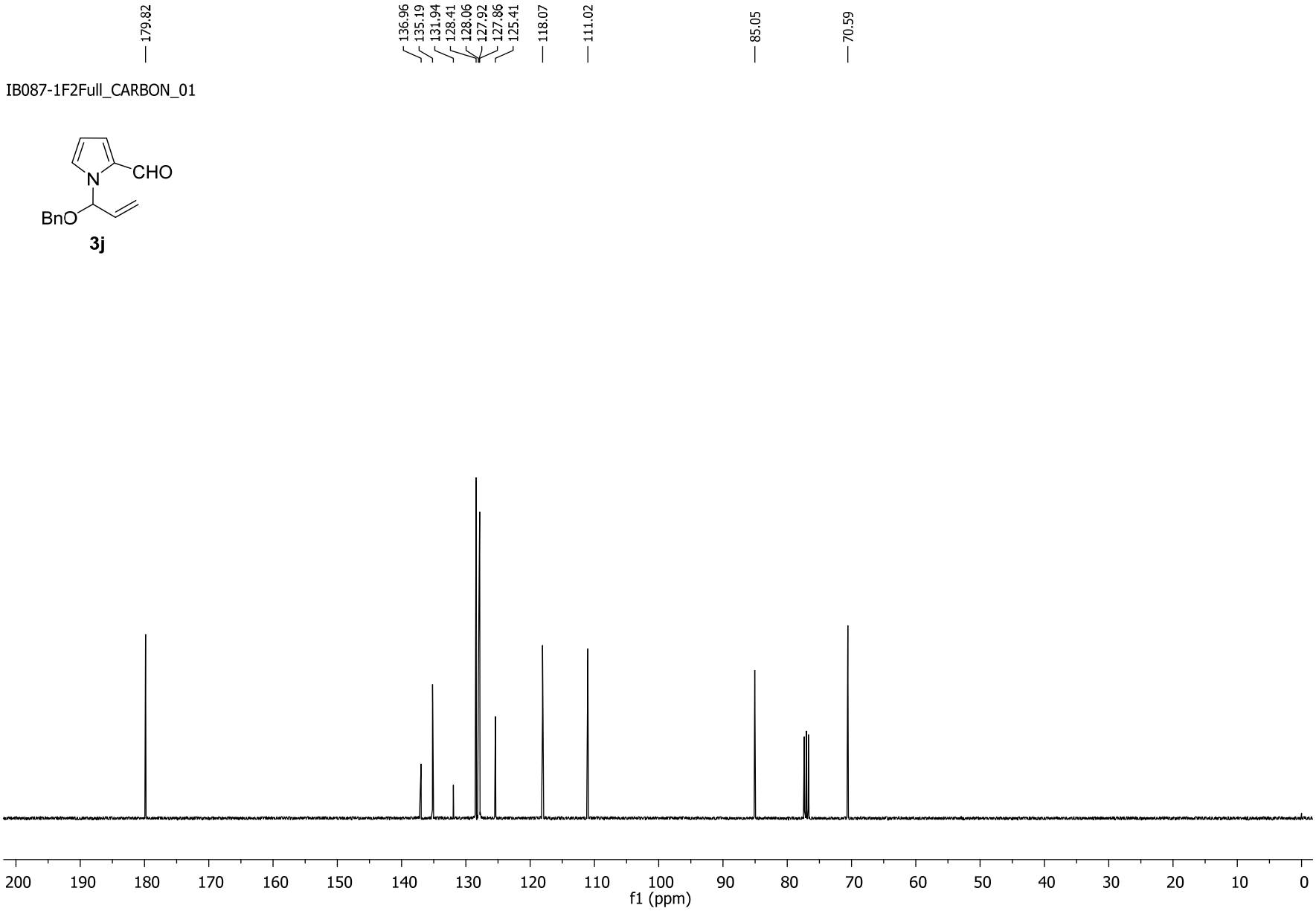


3hb

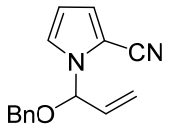
IB082-1F1
1D Selective Gradient NOESY
freq: 5.783ppm




9.58
9.58
7.35
7.33
7.31
7.29
7.28
7.26
6.99
6.99
6.98
6.34
6.34
6.33
6.02
6.01
5.99
5.97
5.36
5.31
5.30
5.27
5.27
4.55
4.52
4.48
4.45
IB087-1F2Full_PROTON_01
CHO
N
BnO
3j
6.05
6.04
6.03
6.02
6.01
6.00
5.99
5.97
1.00
6.06
2.05
1.01
1.00
1.12
1.09
1.21
1.21
1.15
10.0
9.5
9.0
8.5
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
f1 (ppm)

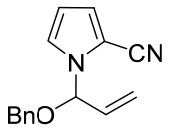

179.82
136.96
135.19
131.94
128.41
128.06
127.92
127.86
125.41
118.07
111.02
85.05
70.59
IB087-1F2Full_CARBON_01
CHO
N
BnO
3j
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

IB023_PROTON_01



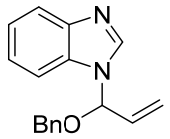
3k

IB023_CARBON_01



3k

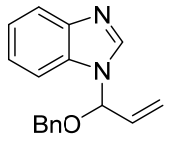
IB019-3_PROTON_01



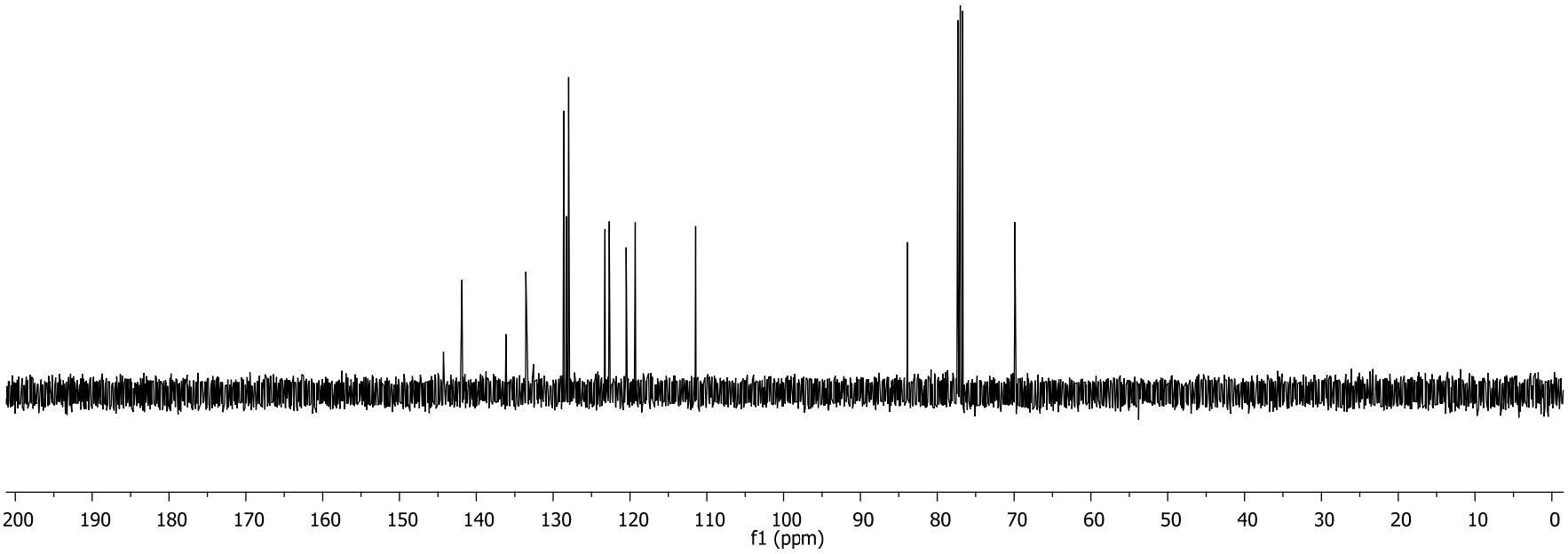
3l

IB019-3_CARBON_01

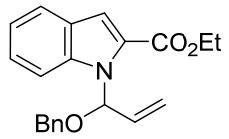
144.28
141.86
136.13
133.55
128.62
128.27
127.99
123.26
122.69
120.50
119.31
111.45
83.89
69.91



3l

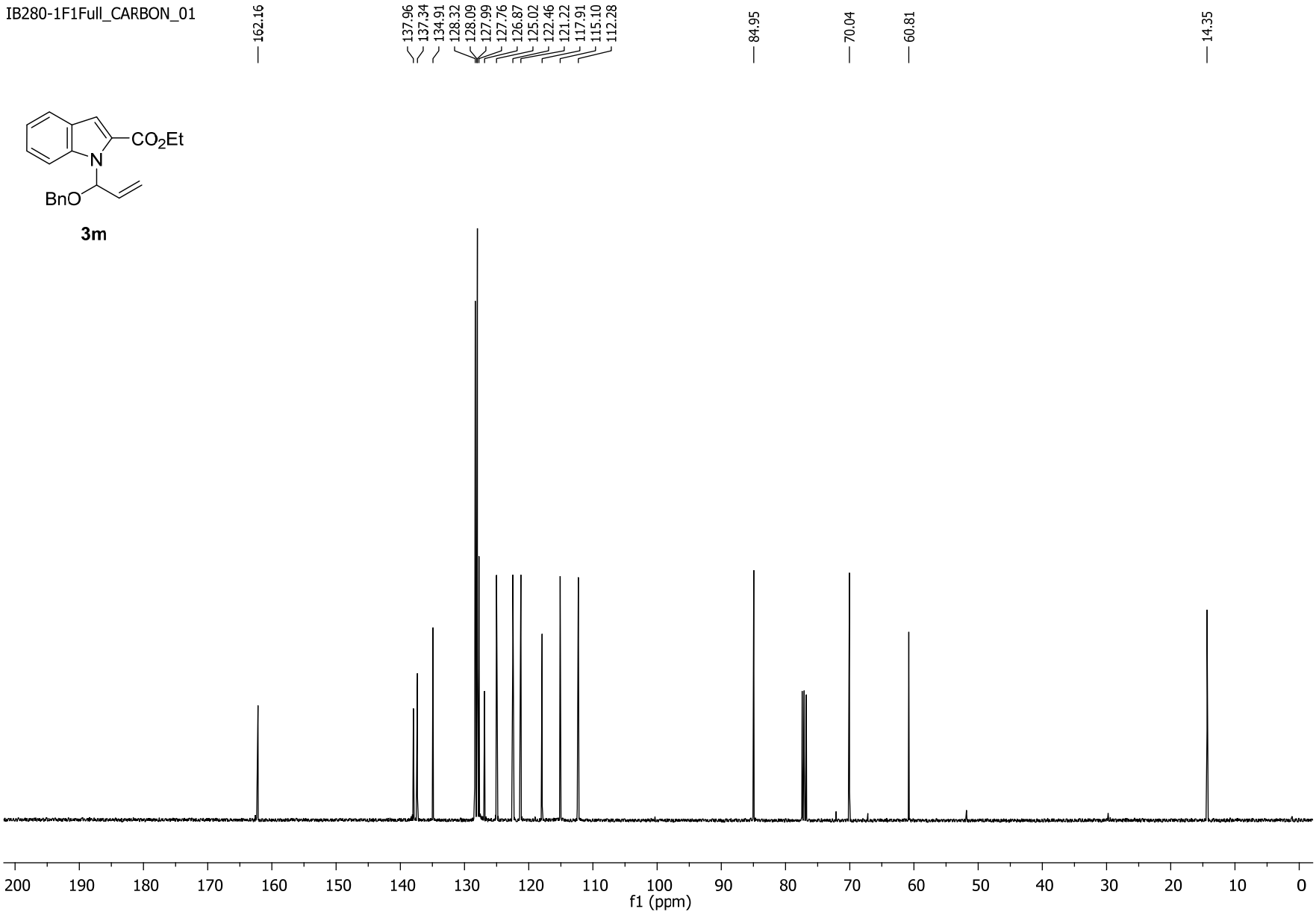


IB280-1F1Full_PROTON_01



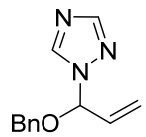
3m

IB280-1F1Full_CARBON_01



3m

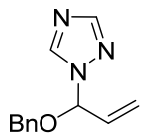
IB018-2_PROTON_01



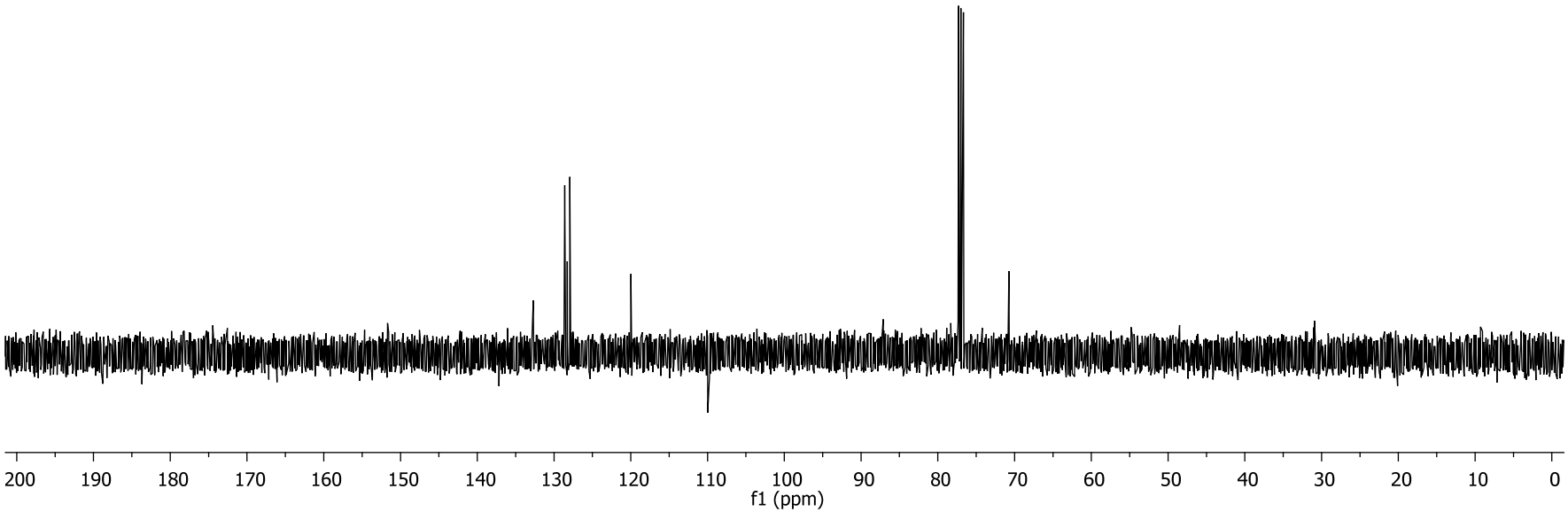
3n

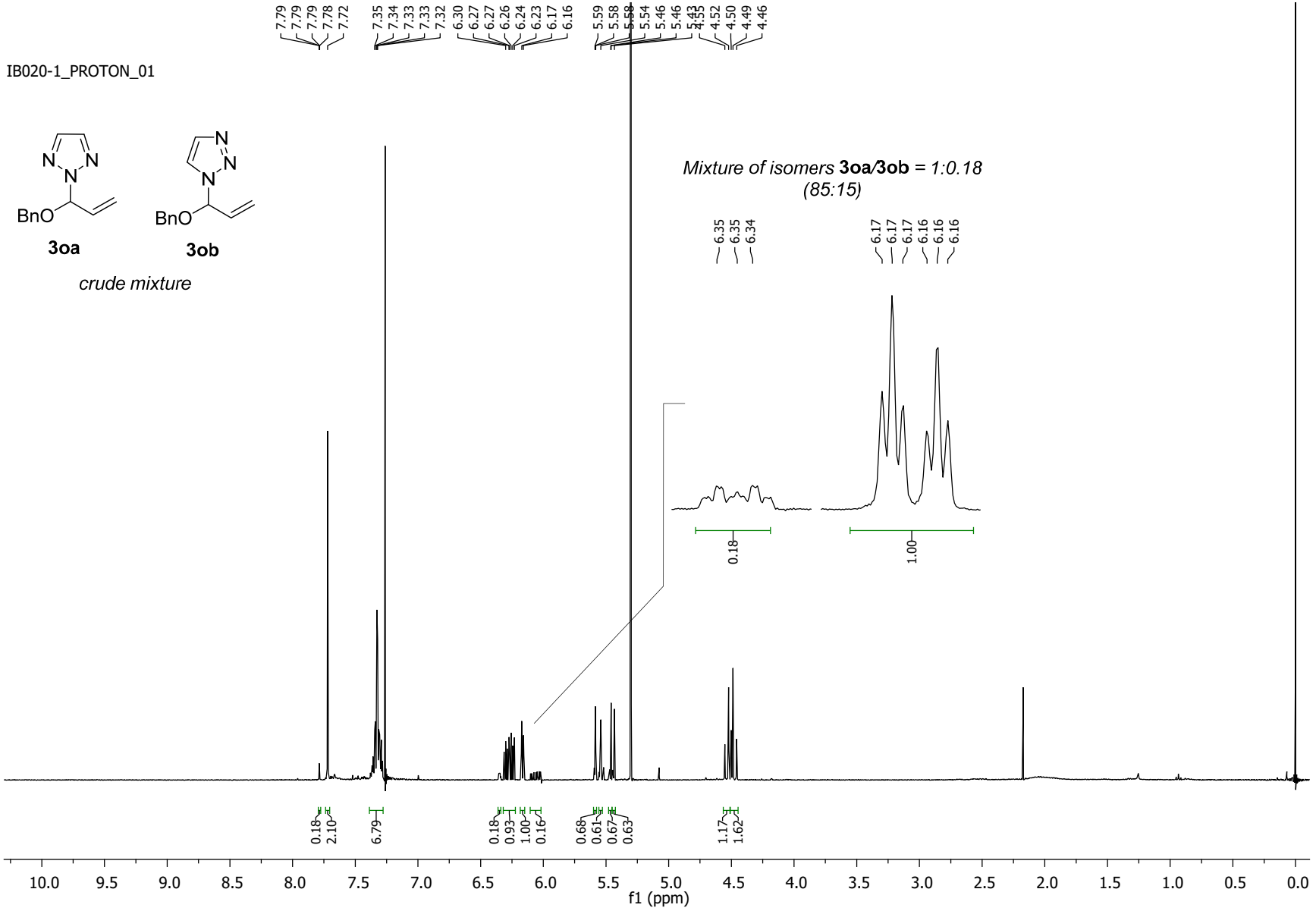
IB018-2_CARBON_01

132.71
128.60
128.27
127.94
119.99
109.96
87.11
70.74

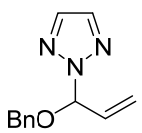


3n



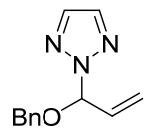

IB020-1_PROTON_01
3oa
3ob
crude mixture
Mixture of isomers 3oa/3ob = 1:0.18
(85:15)
f1 (ppm)

IB020a_PROTON_01



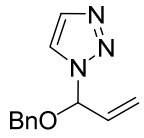
3oa

IB020a_CARBON_01



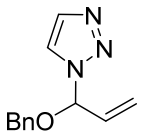
3oa

IB020-F1_PROTON_01



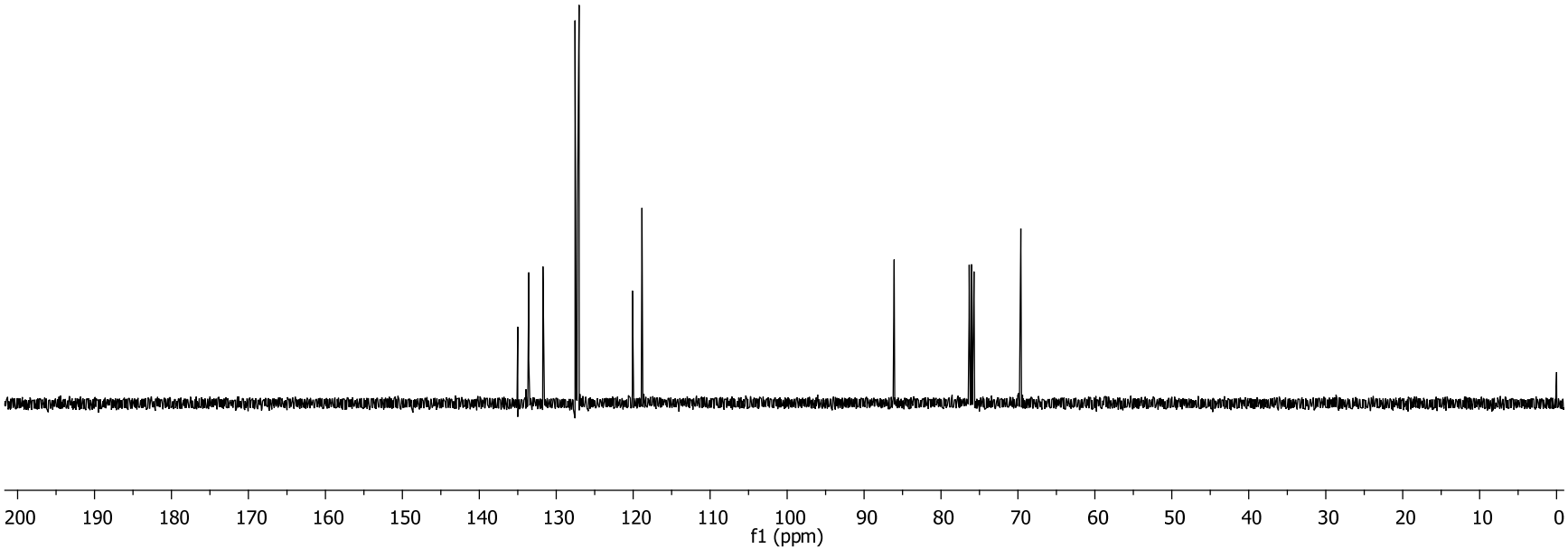
3ob

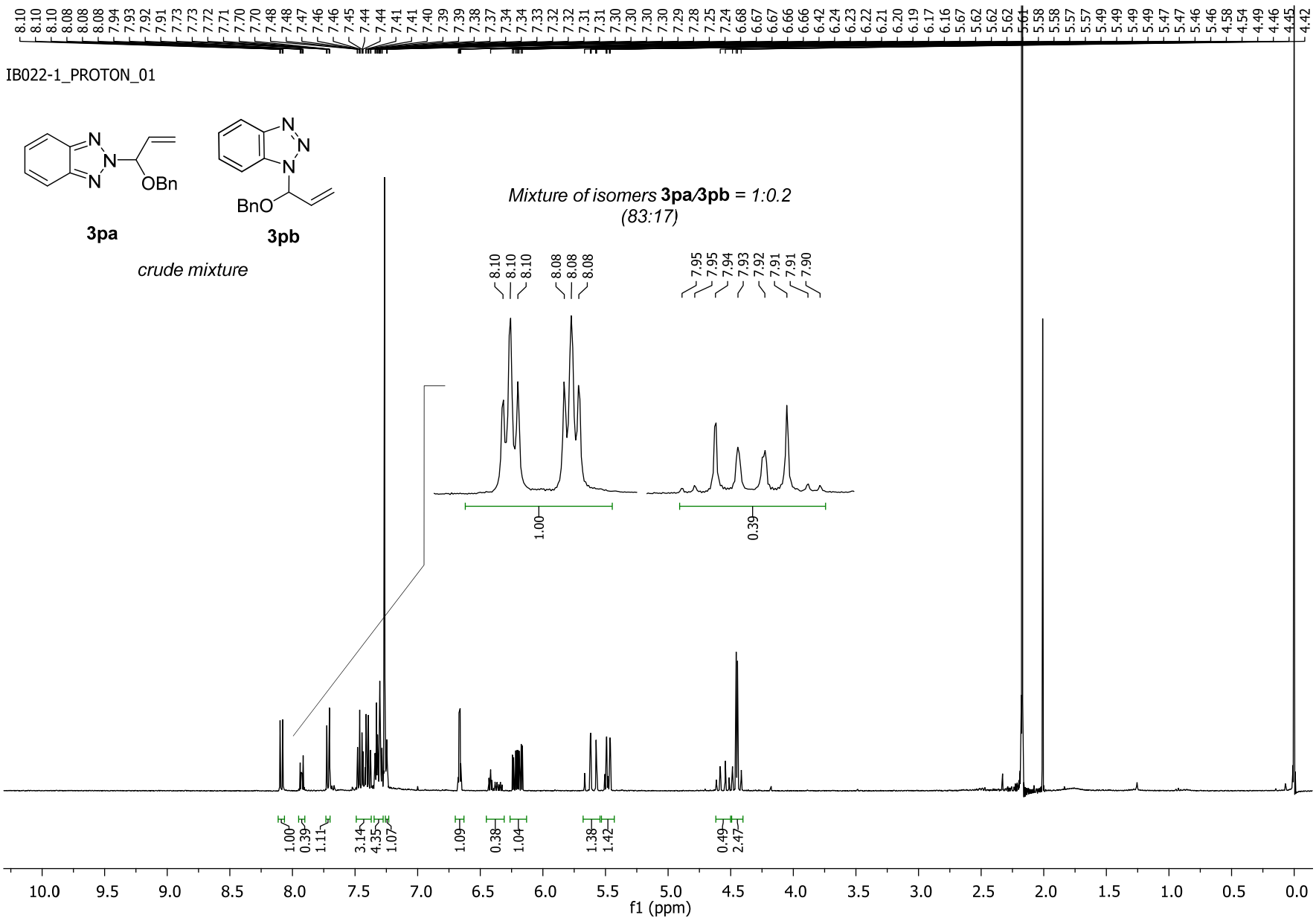
IB020b_CARBON_01

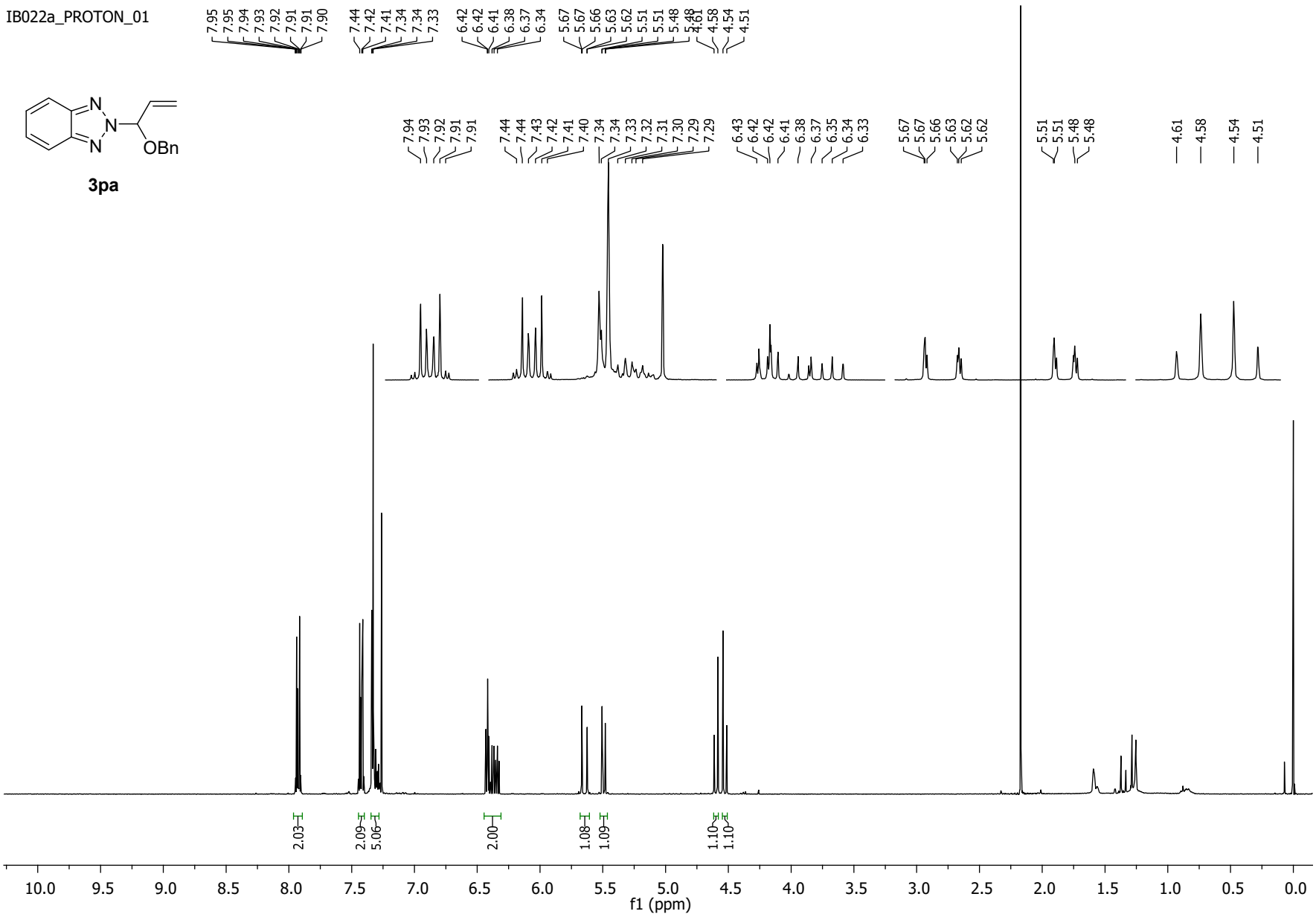


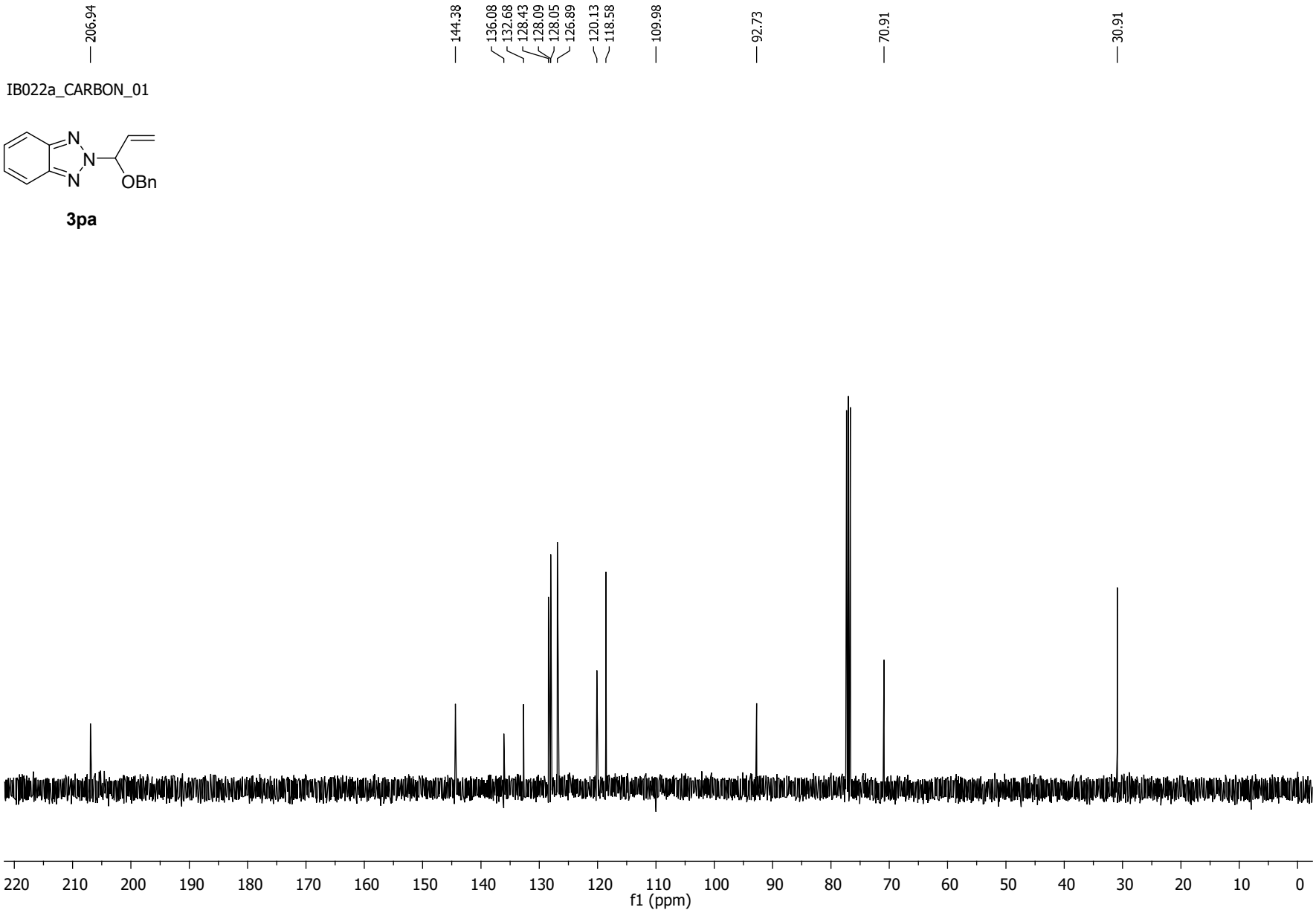
3ob

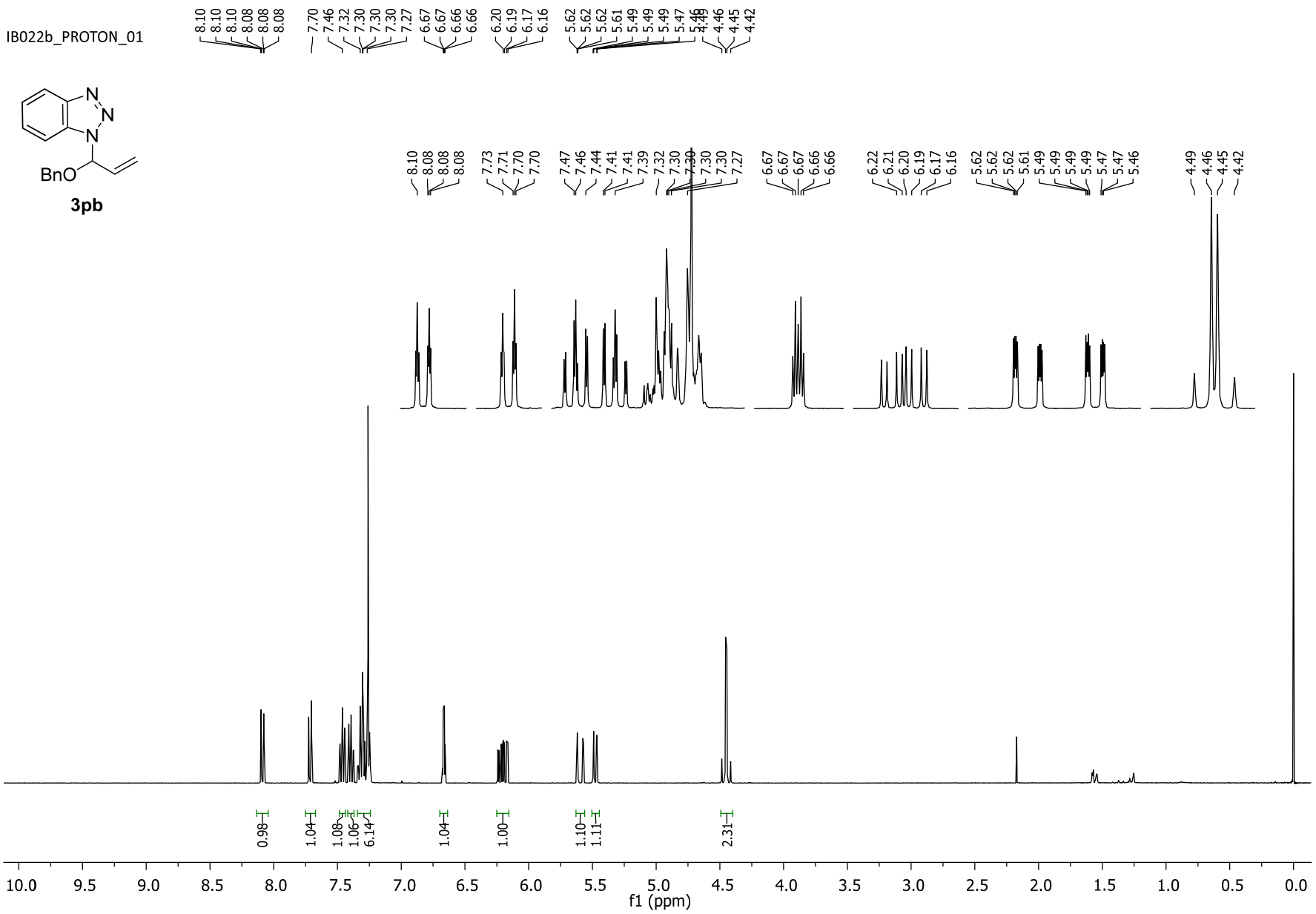
135.00
133.57
131.73
127.55
127.24
127.04
120.10
118.86
86.09
69.62



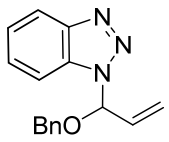

IB022-1_PROTON_01
3pa
3pb
crude mixture
Mixture of isomers 3pa/3pb = 1:0.2
(83:17)
f1 (ppm)


IB022a_PROTON_01
7.95 7.95 7.94 7.93 7.92 7.91 7.91 7.90
7.44 7.42 7.41 7.34 7.34 7.33
6.42 6.42 6.41 6.38 6.37 6.34
5.67 5.67 5.66 5.63 5.62 5.51 5.51 5.48 5.48 4.61 4.58 4.54 4.51
N
N
N
OBn
3pa
7.94 7.93 7.92 7.91 7.91
7.44 7.44 7.43 7.42 7.41 7.40 7.34 7.34 7.33 7.32 7.31 7.30 7.29 7.29
6.43 6.42 6.42 6.41 6.38 6.37 6.35 6.34 6.33
5.67 5.67 5.66 5.63 5.62 5.62
5.51 5.51 5.48 5.48
4.61 4.58 4.54 4.51
2.03 2.09 5.06 2.00 1.08 1.09 1.10 1.10
10.0 9.5 9.0 8.5 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
f1 (ppm)


206.94
144.38
136.08
132.68
128.43
128.09
128.05
126.89
120.13
118.58
109.98
92.73
70.91
30.91
IB022a_CARBON_01
N
N
N
OBn
3pa
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

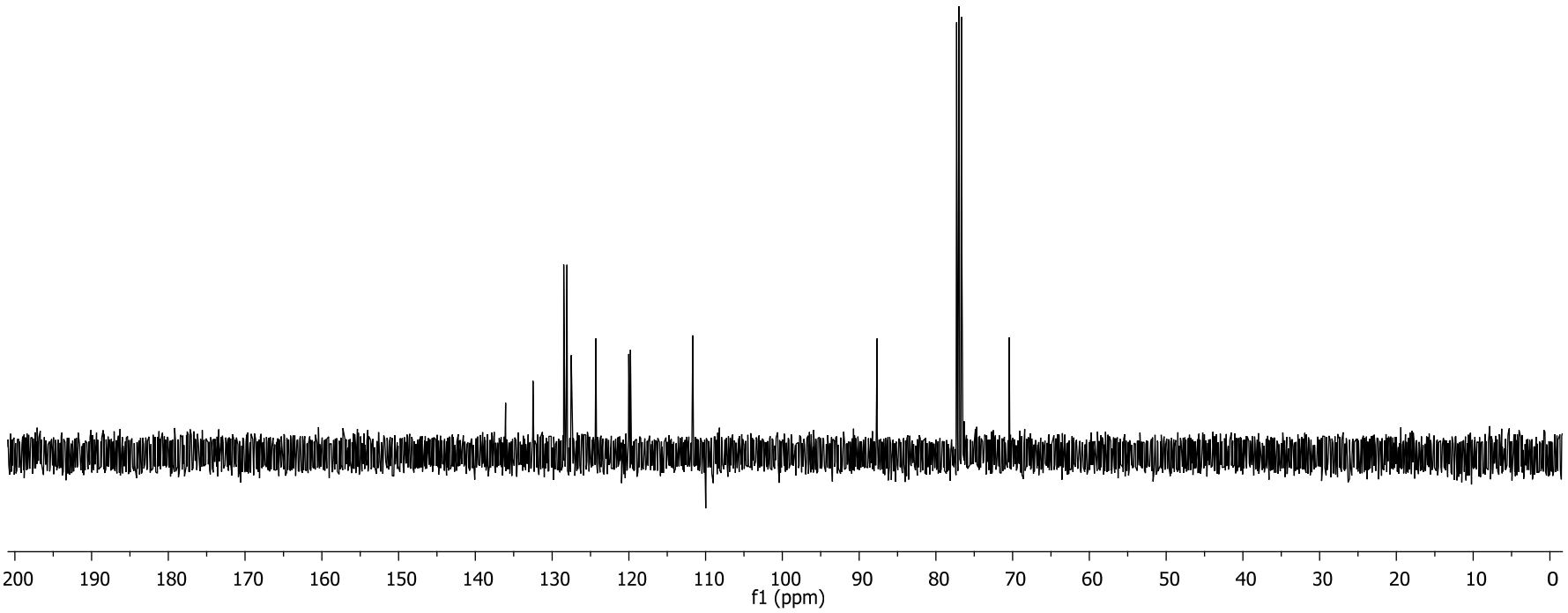

IB022b_PROTON_01
3pb
f1 (ppm)

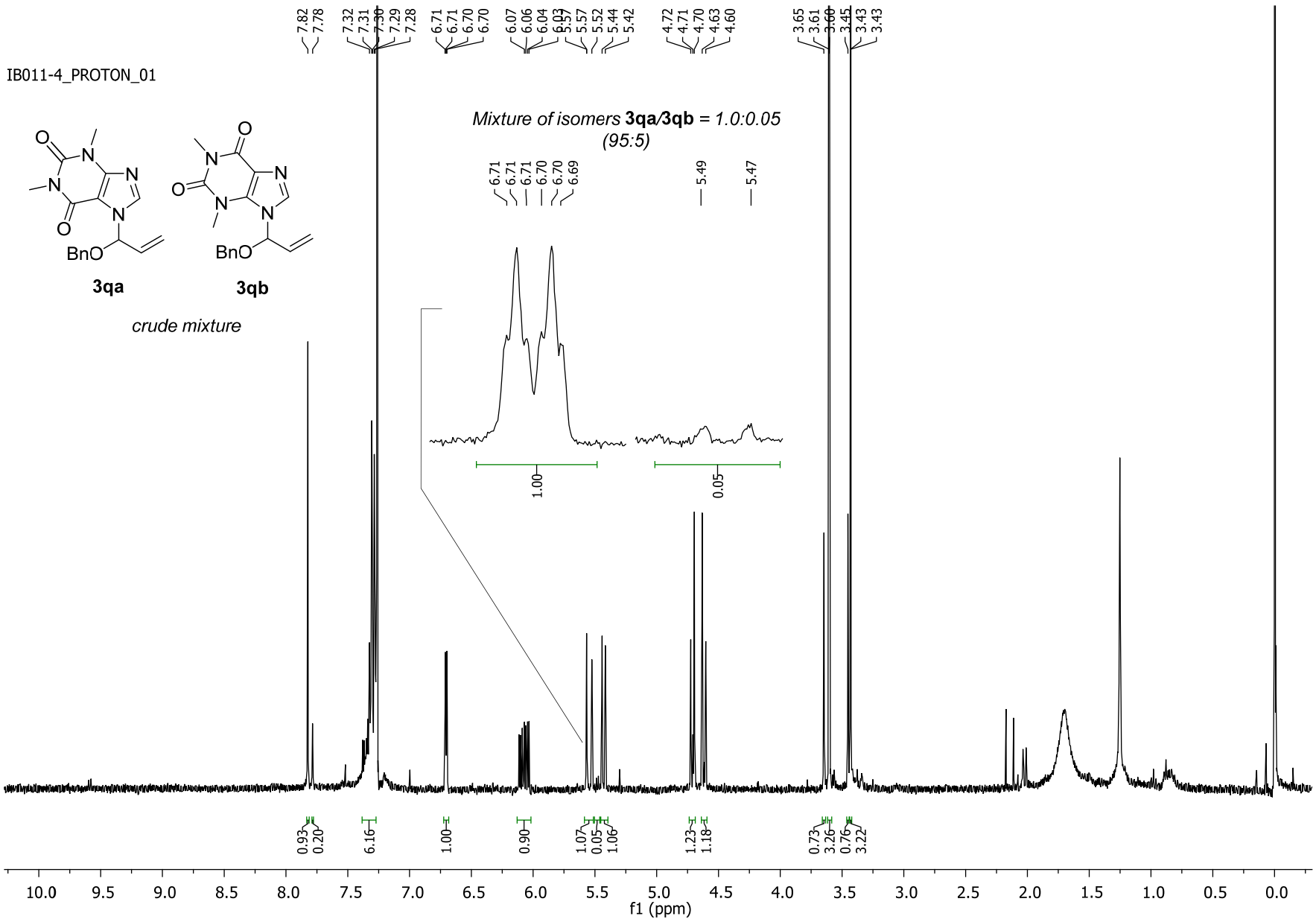
IB022b_CARBON_01

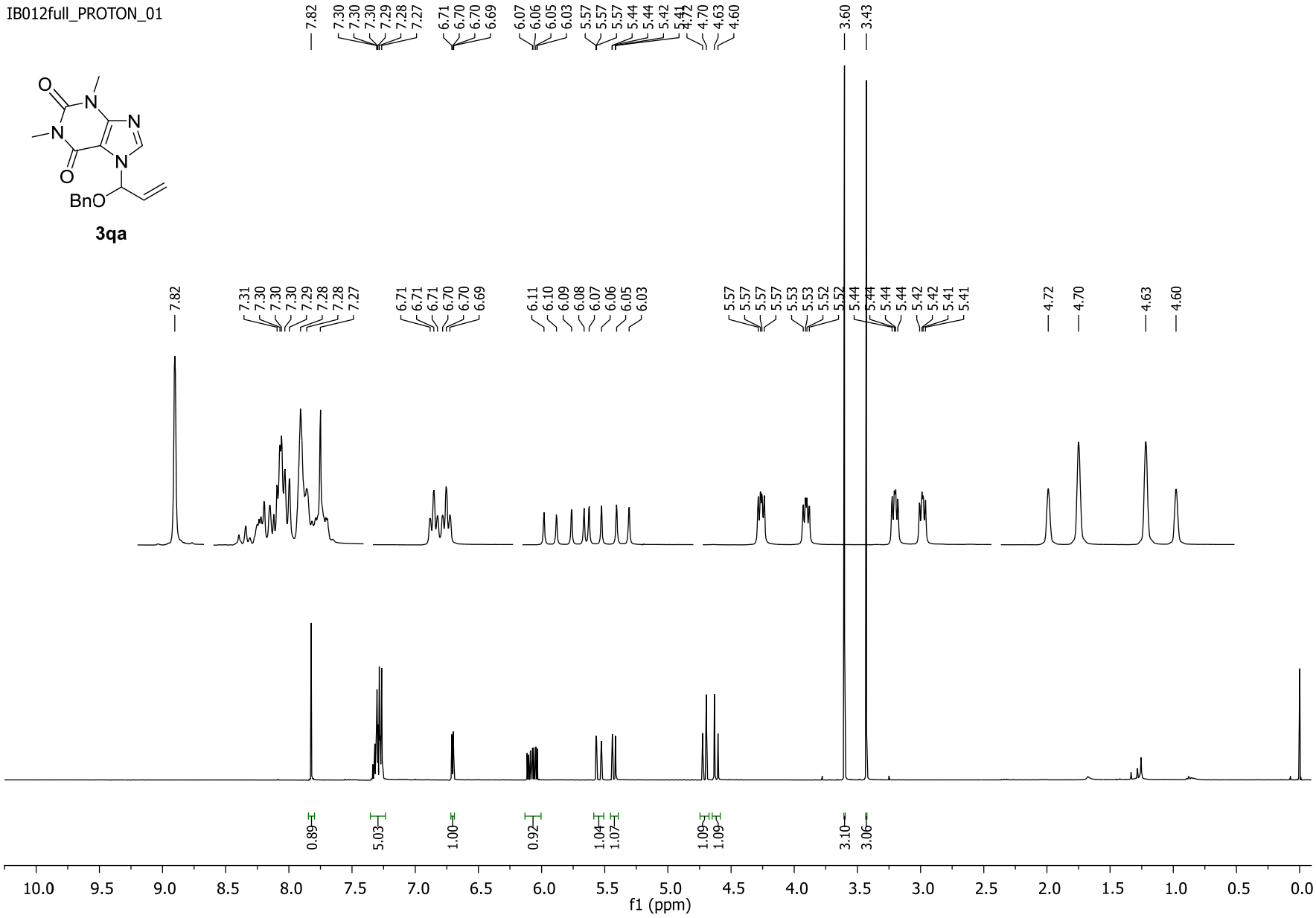


3pb

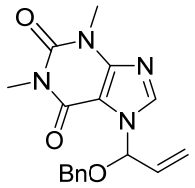
136.05
132.50
128.48
128.15
128.06
127.51
124.30
120.02
119.80
111.68
109.84
87.65
70.44




IB011-4_PROTON_01
Mixture of isomers 3qa/3qb = 1.0:0.05
(95:5)
3qa
3qb
crude mixture
f1 (ppm)

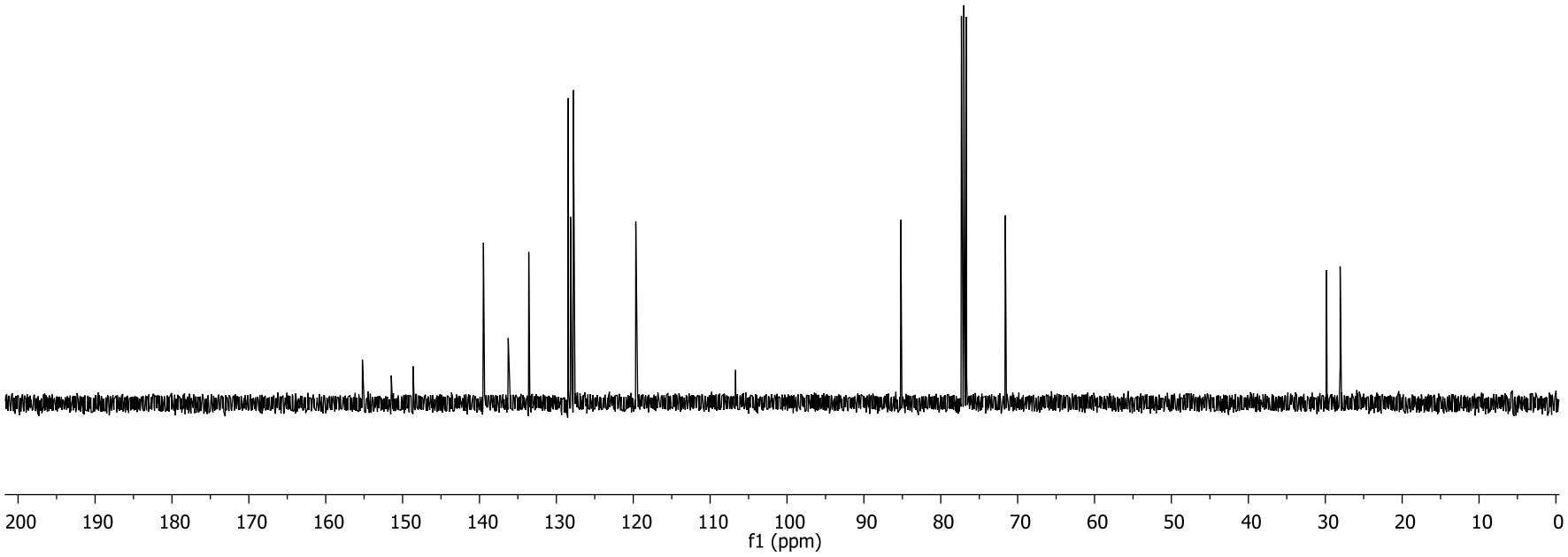

IB012full_PROTON_01
3qa
f1 (ppm)

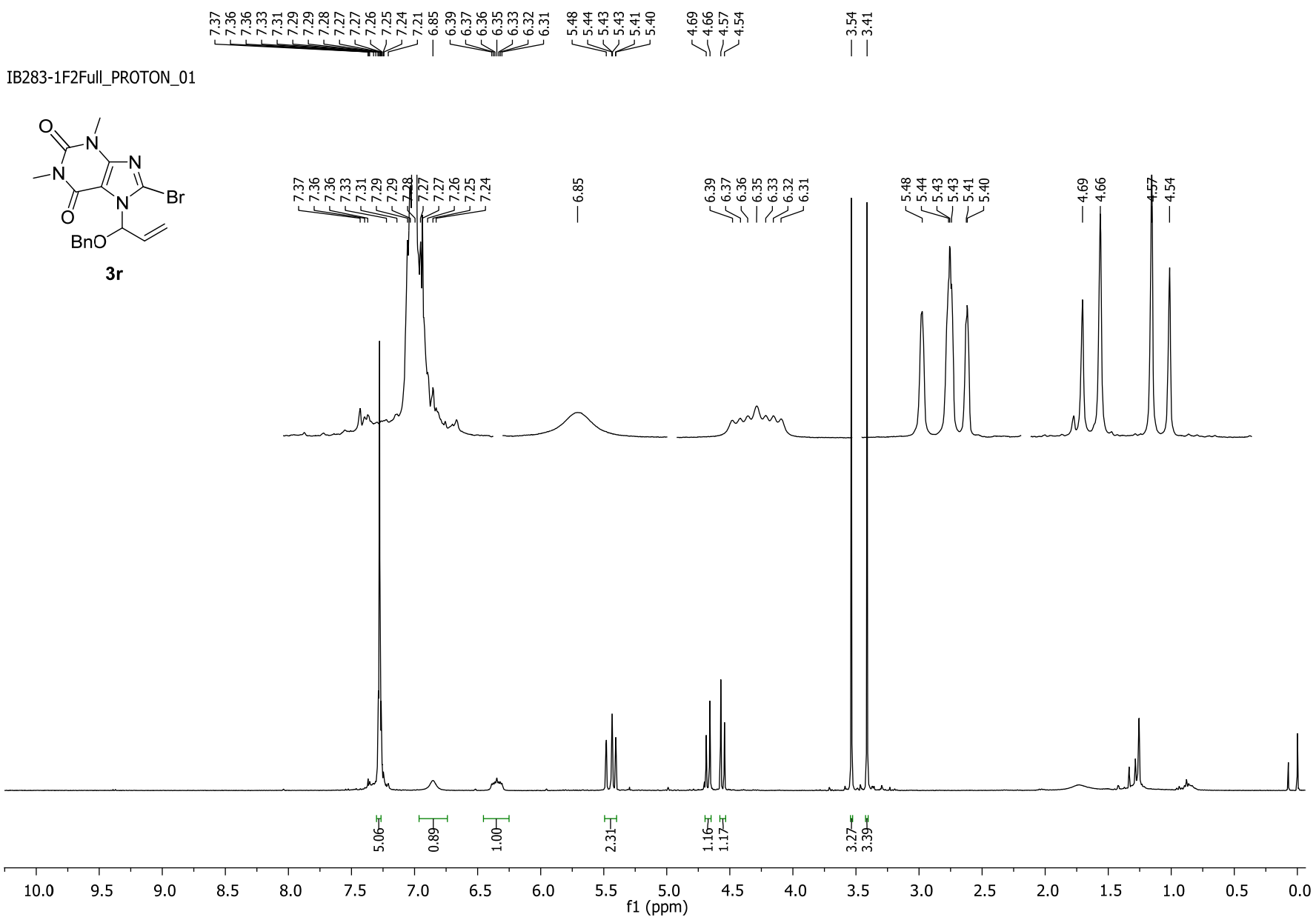
IB012full_CARBON_01

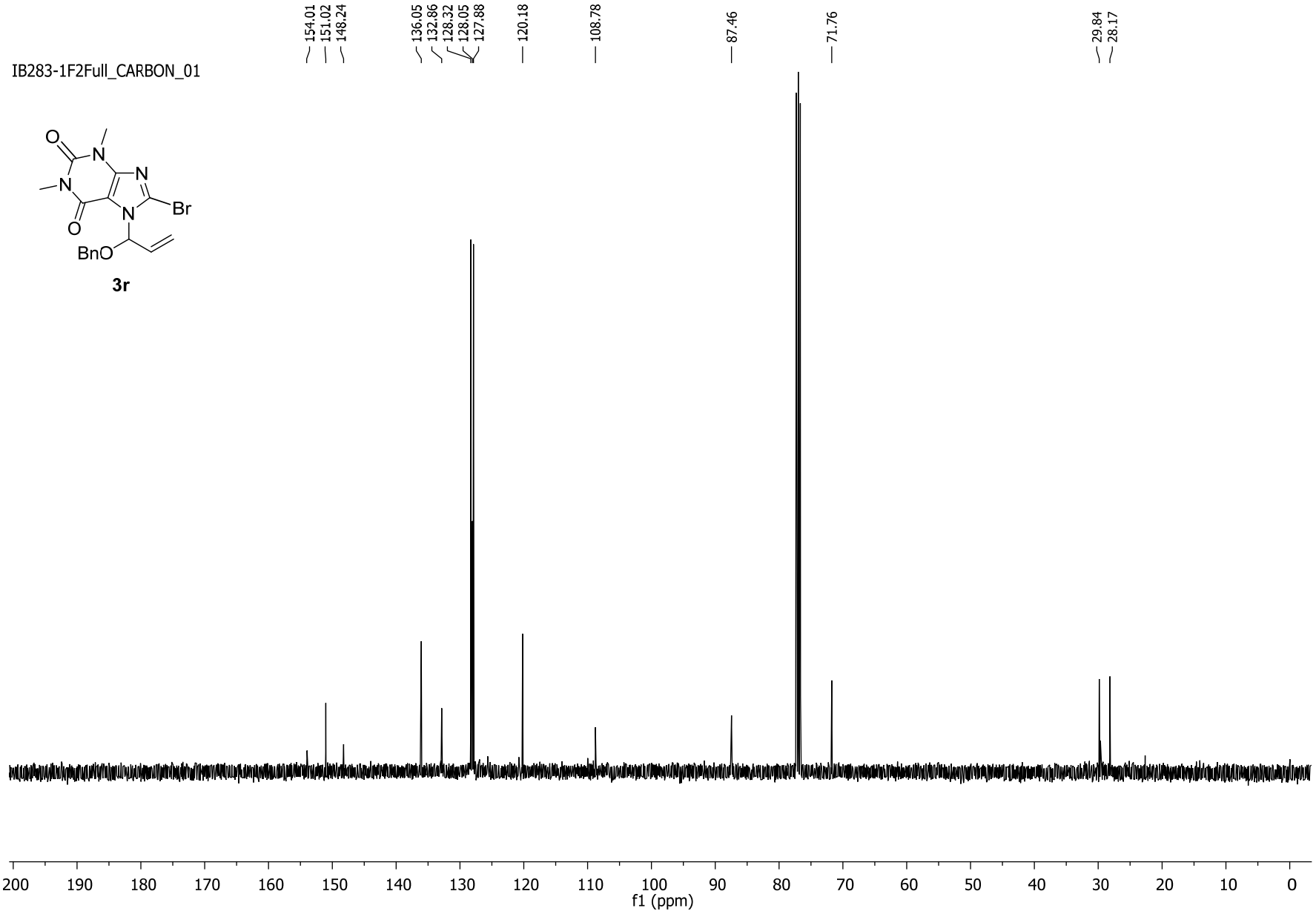


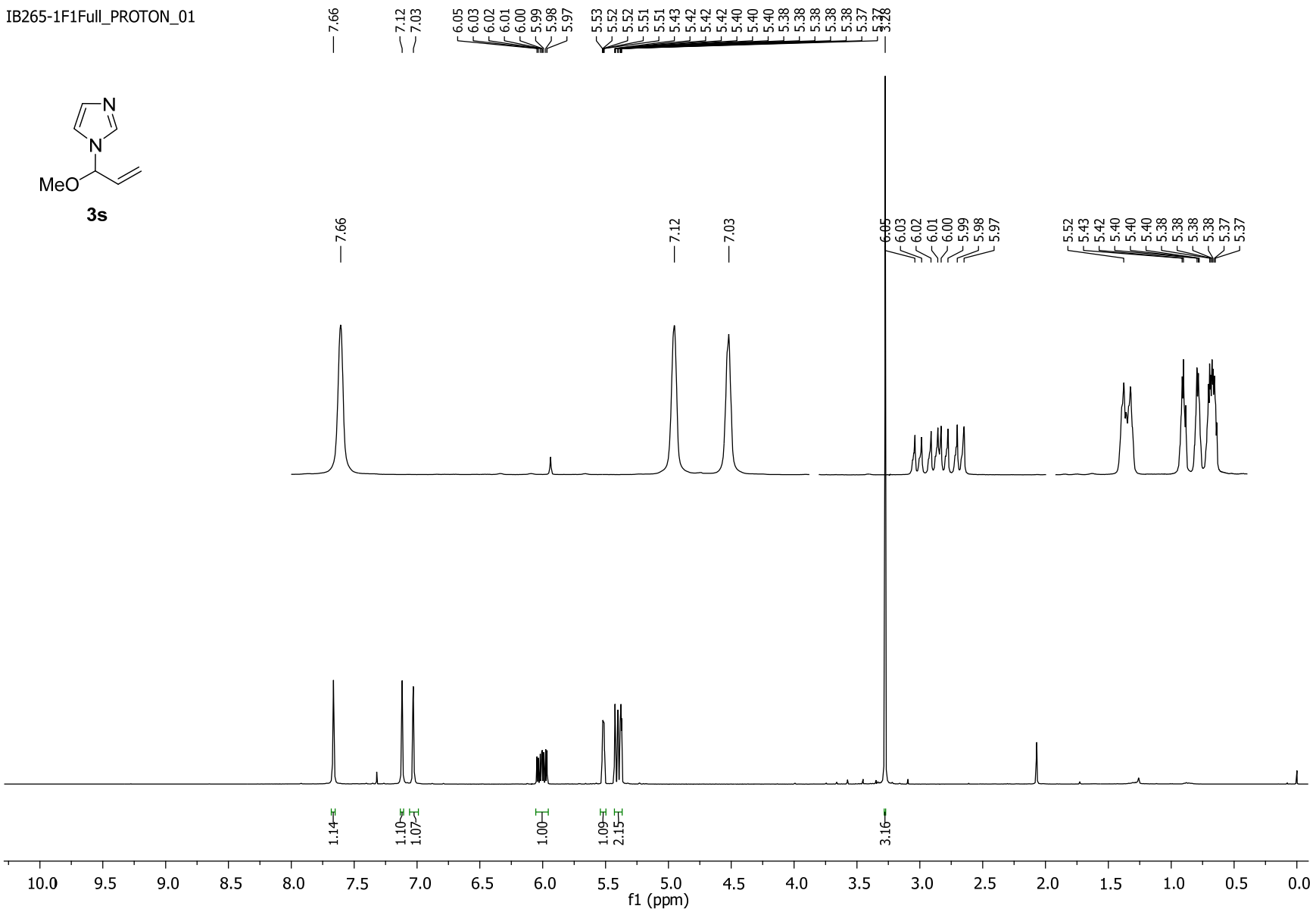
3qa

155.22
151.46
148.63
139.48
136.26
133.59
128.45
128.15
127.80
119.66
106.68
85.20
71.61
29.83
28.06

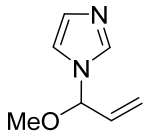



IB283-1F2Full_PROTON_01
3r
f1 (ppm)


154.01
151.02
148.24
136.05
132.86
128.32
128.05
127.88
120.18
108.78
87.46
71.76
29.84
28.17
IB283-1F2Full_CARBON_01
O
N
N
N
N
Br
O
BnO
3r
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

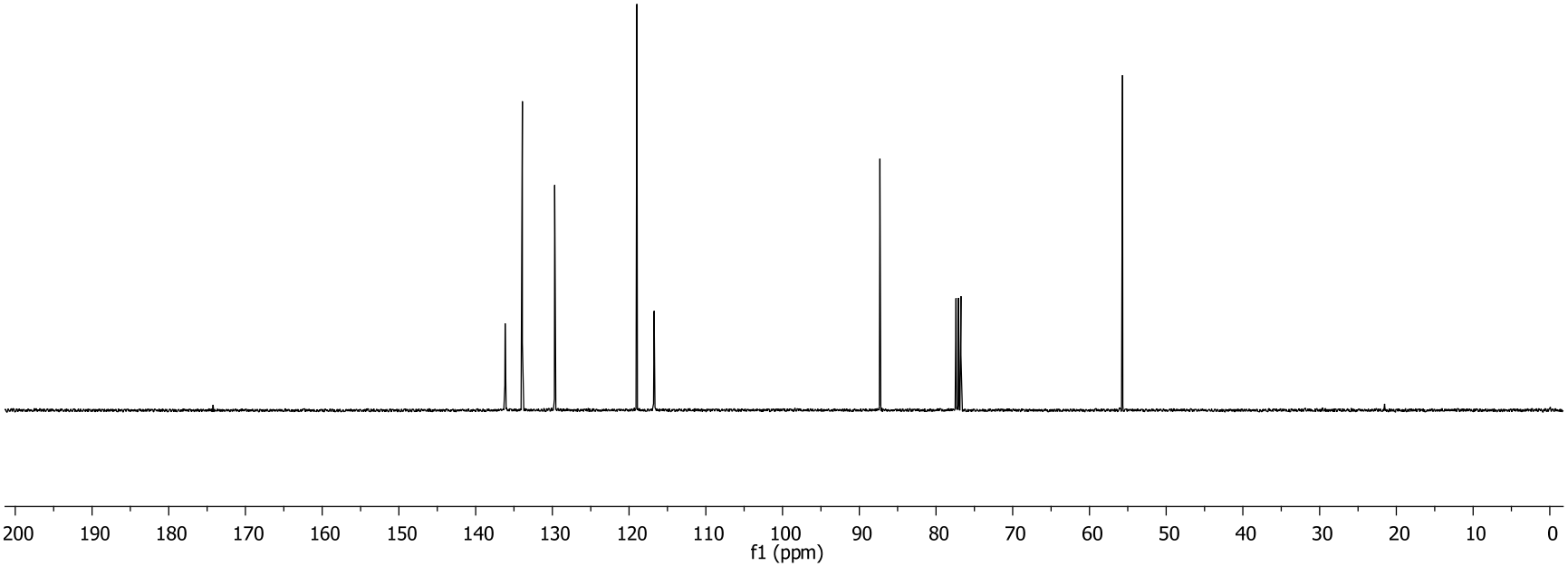

IB265-1F1Full_PROTON_01
N
N
MeO
3s
7.66
7.12
7.03
6.05
6.03
6.02
6.01
6.00
5.99
5.98
5.97
5.53
5.52
5.52
5.51
5.51
5.43
5.42
5.42
5.42
5.40
5.40
5.40
5.38
5.38
5.38
5.38
5.37
3.28
1.14
1.10
1.07
1.00
1.09
2.15
3.16
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

IB265-1F1Full_CARBON_01

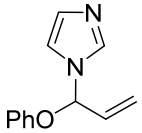


3s

136.16
133.92
129.70
118.99
116.75
87.31
55.69

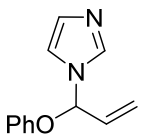


IB268-1F1Full_PROTON_01



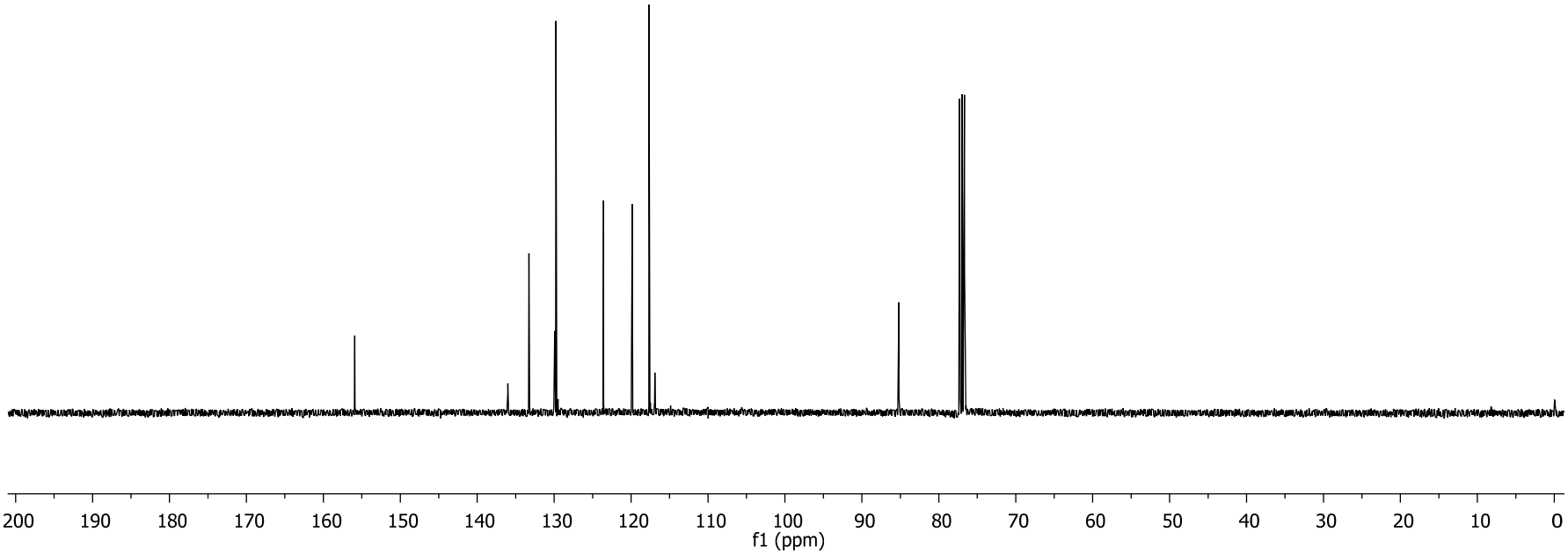
3t

IB268-1F1Full_CARBON_01

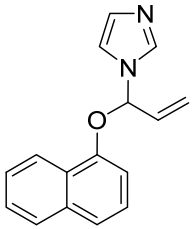


3t

155.92
136.03
133.28
129.94
129.77
123.58
119.86
117.67
116.90
85.19

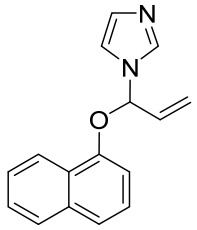


IB272-1Full_PROTON_01

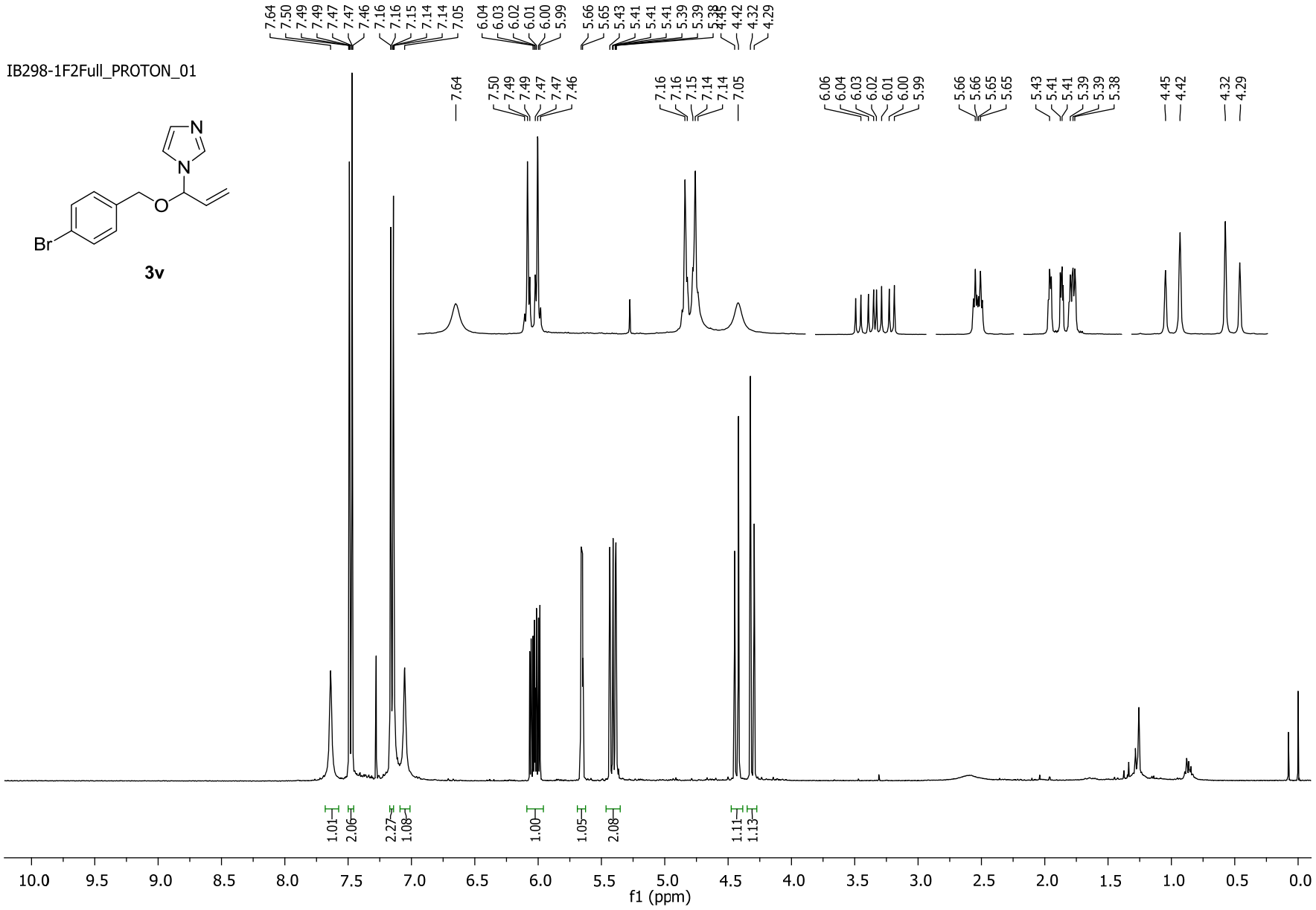


3u

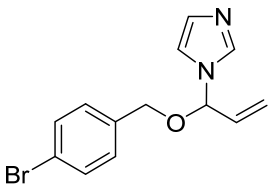
IB272-1Full_CARBON_01



3u

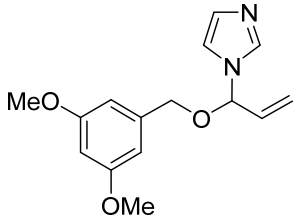

IB298-1F2Full_PROTON_01
Br
3v
f1 (ppm)

IB298-1F2Full_CARBON_01



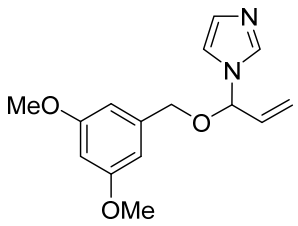
3v

IB282-1F1Full_PROTON_01



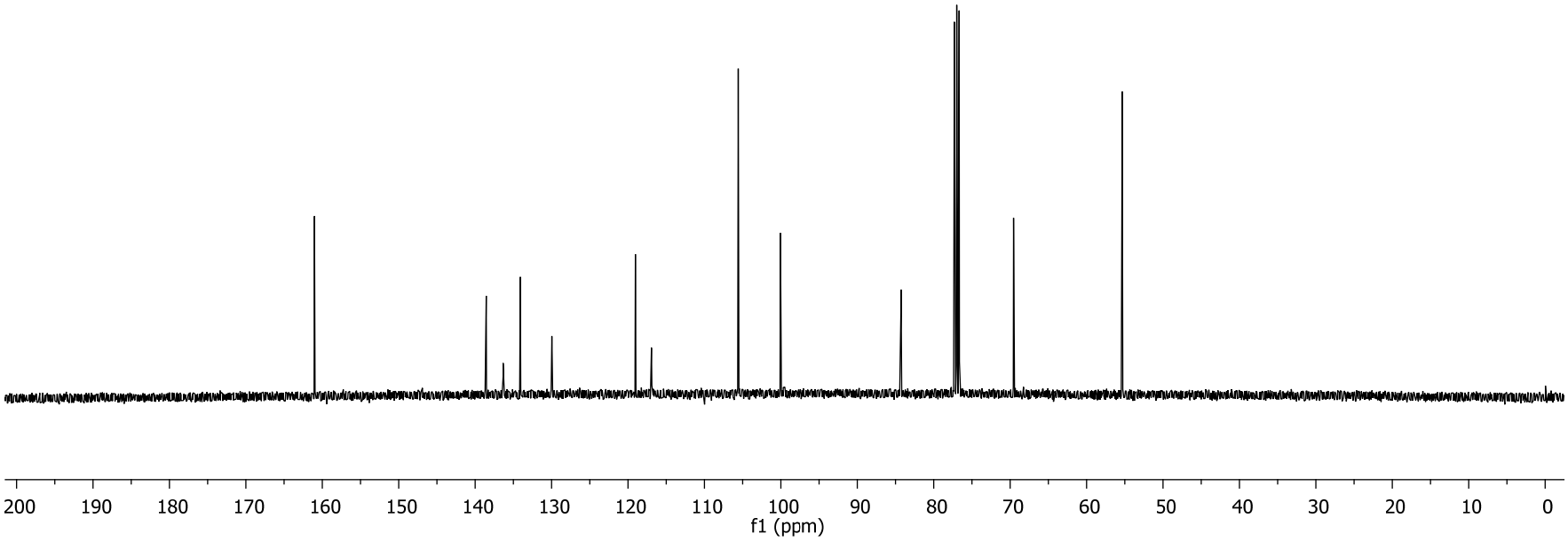
3w

IB282-1F1Full_CARBON_01



3w

161.02
138.54
136.33
134.10
129.97
119.03
116.93
105.59
100.05
84.27
69.55
55.33



Chiral HPLC chromatograms

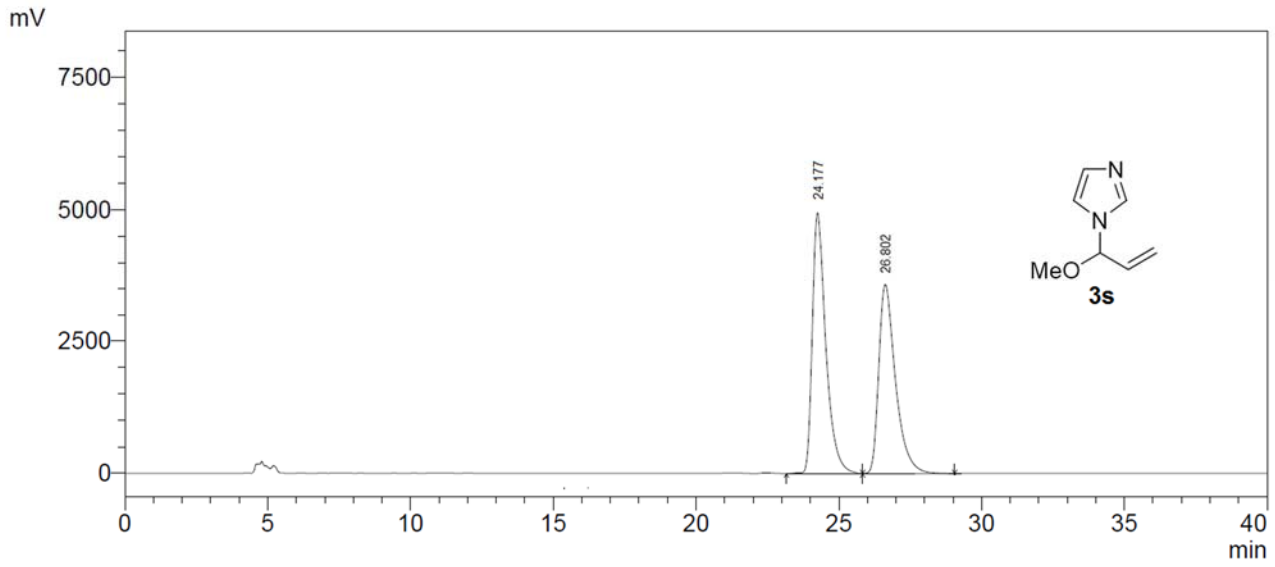
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 98:2 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	24.177	52059802	3816742	51.744	59.718
2	26.802	48550515	2574533	48.256	40.282
Total		100610317	6391275	100.000	100.000



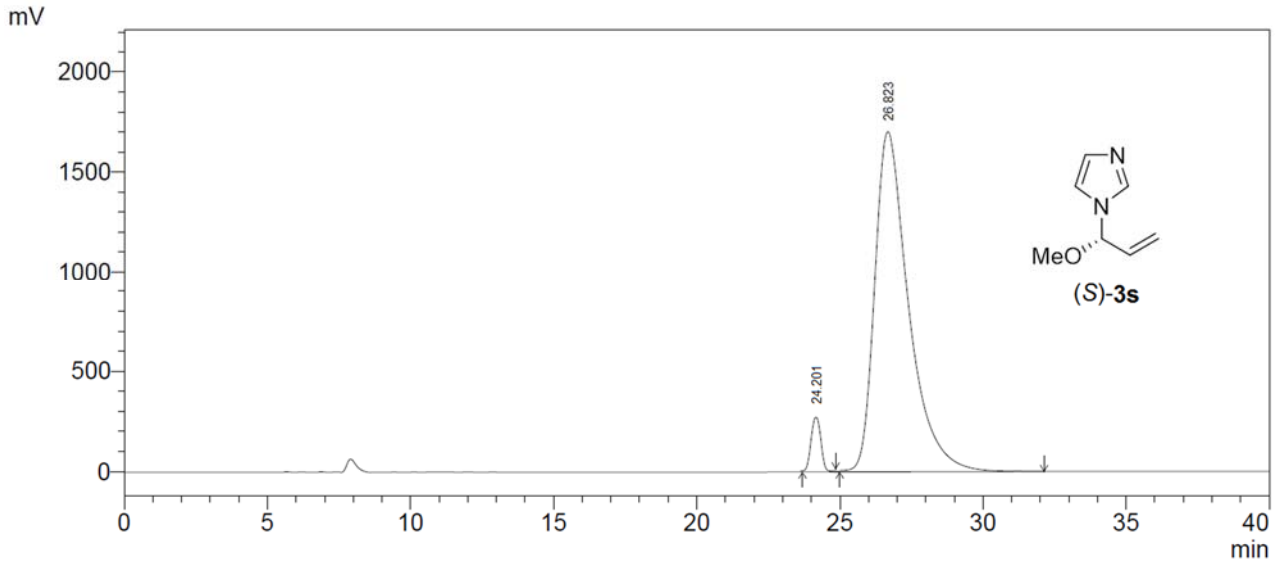
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 98:2 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	24.201	4812427	40504	9.033	8.368
2	26.823	48463640	443533	90.967	91.632
Total		53276067	484037	100.000	100.000



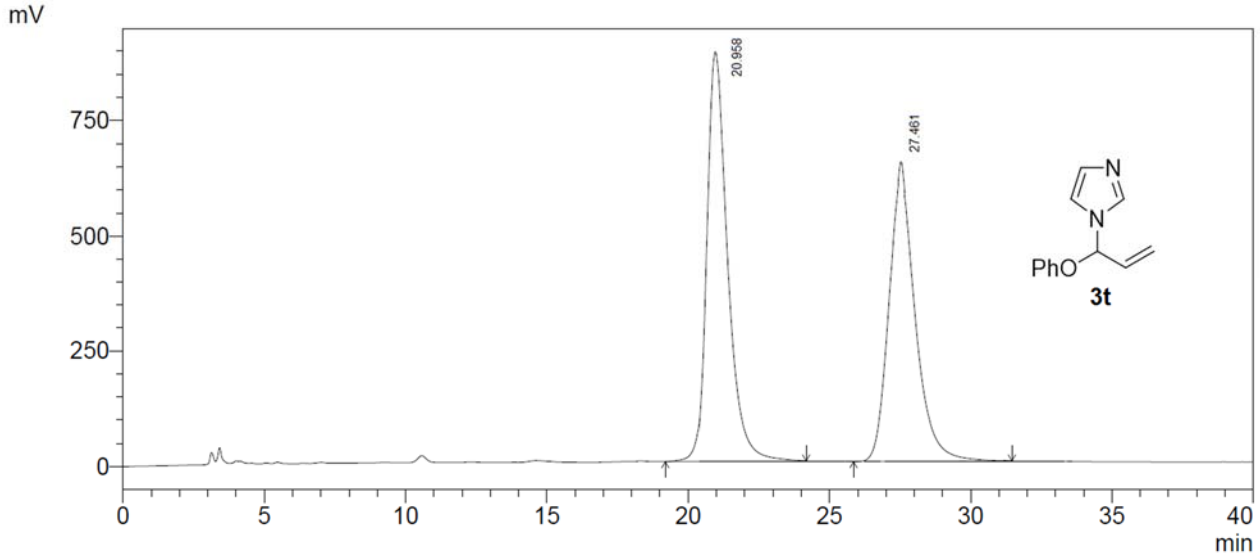
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	20.958	610857	282484	47.789	58.360
2	27.461	667381	201553	52.211	41.640
Total		1278238	484037	100.000	100.000



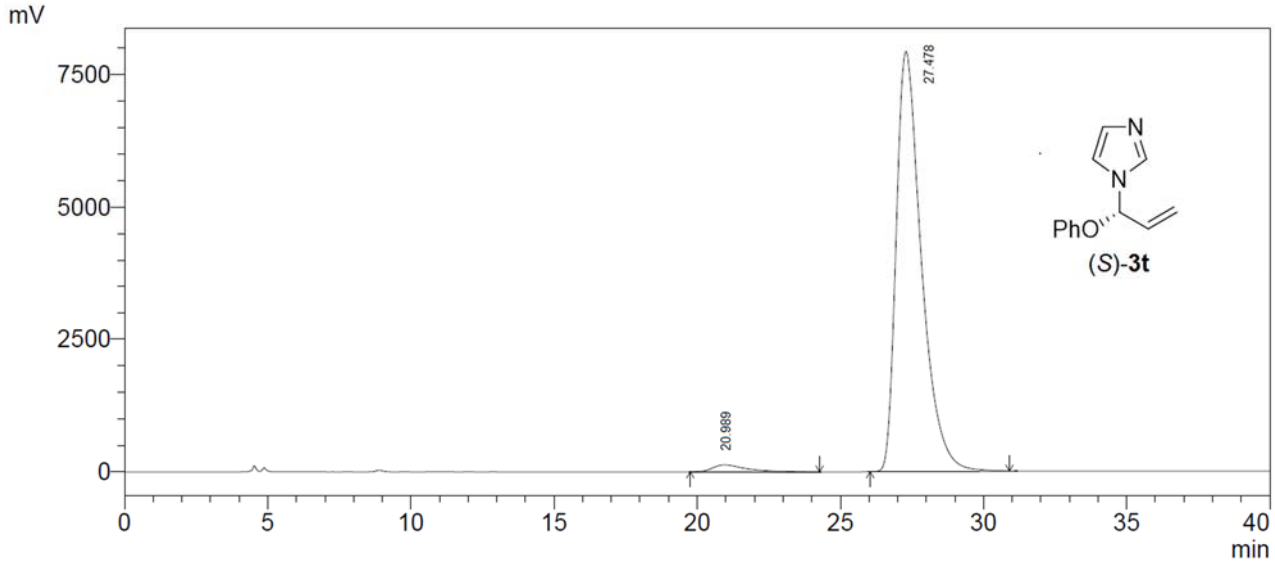
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	20.989	6123274	397268	5.218	5.009
2	27.478	111225781	7533818	94.782	94.991
Total		117349055	7931086	100.000	100.000



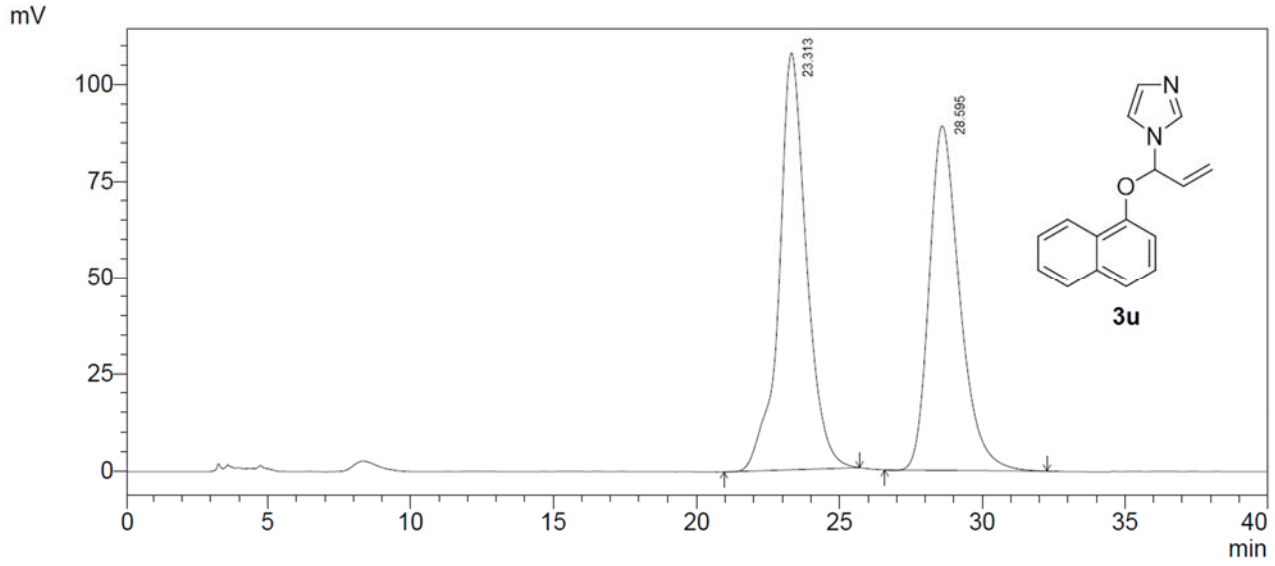
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	23.313	7214426	107874	52.048	54.764
2	28.595	6646667	89106	47.952	45.236
Total		13861093	196980	100.000	100.000



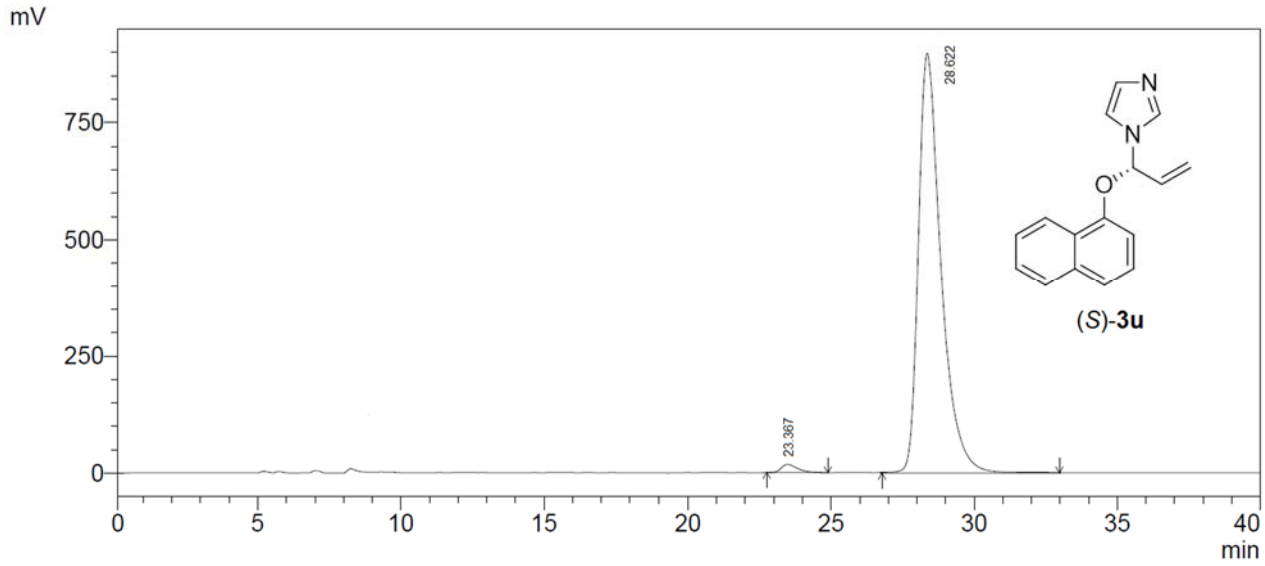
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	23.367	1492808	8104	3.788	2.987
2	28.622	37916075	263217	96.212	97.013
Total		39408883	271321	100.000	100.000



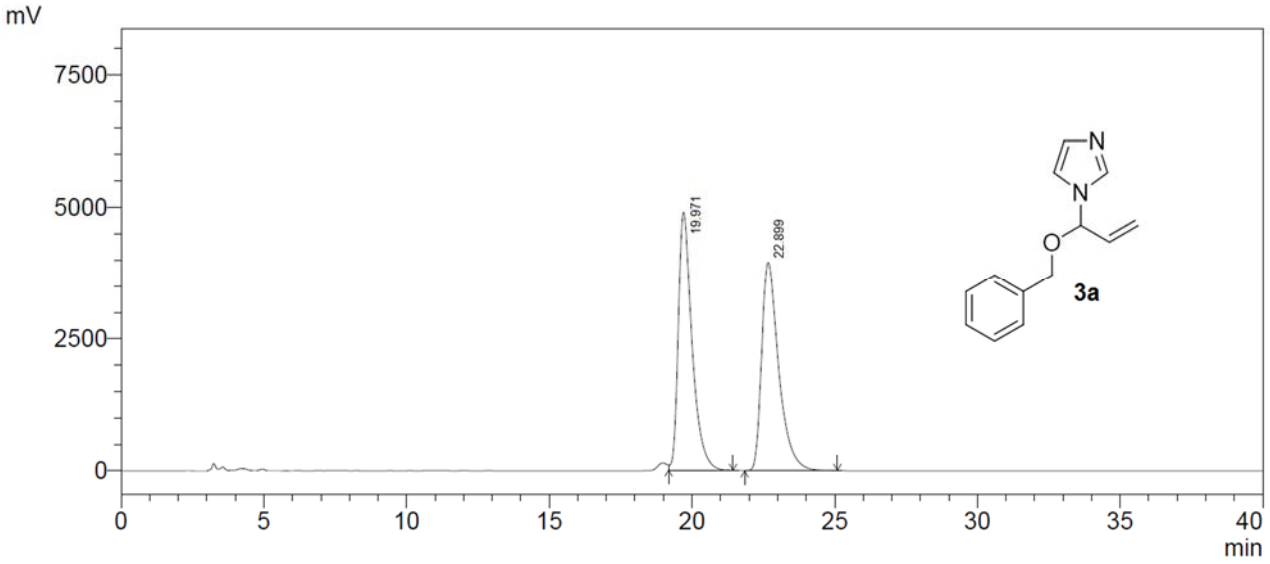
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	19.971	56134369	4320908	49.985	57.988
2	22.899	56168059	3130475	50.015	42.012
Total		112302428	7451383	100.000	100.000



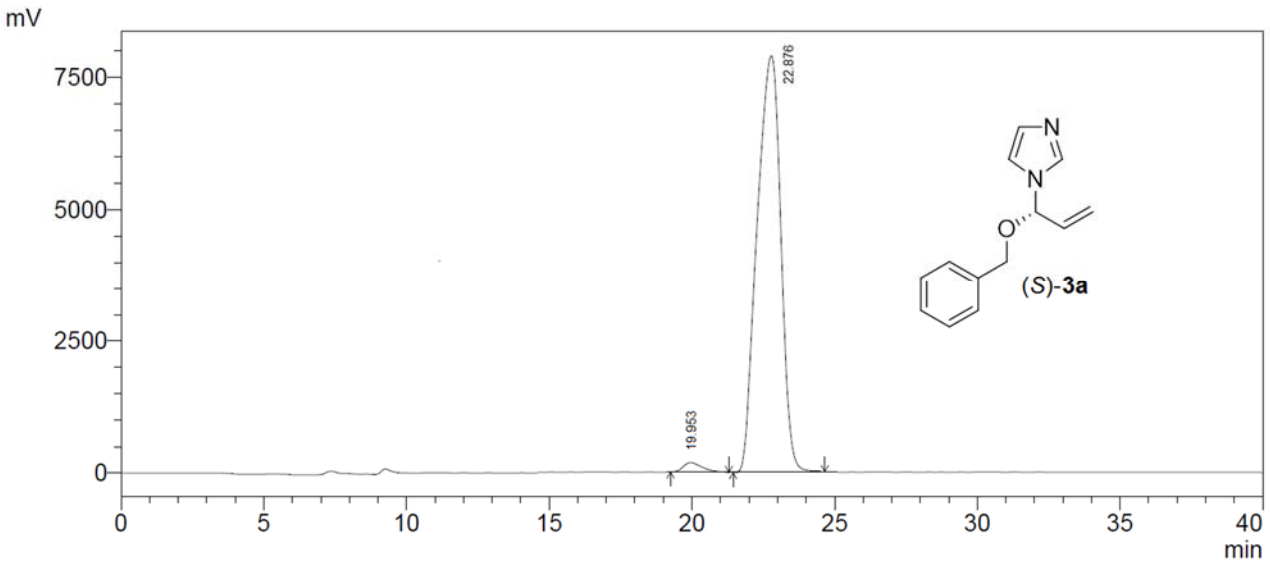
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	19.953	5941785	347969	4.124	3.999
2	22.876	138136426	8353426	95.876	96.001
Total		144078211	8701395	100.000	100.000



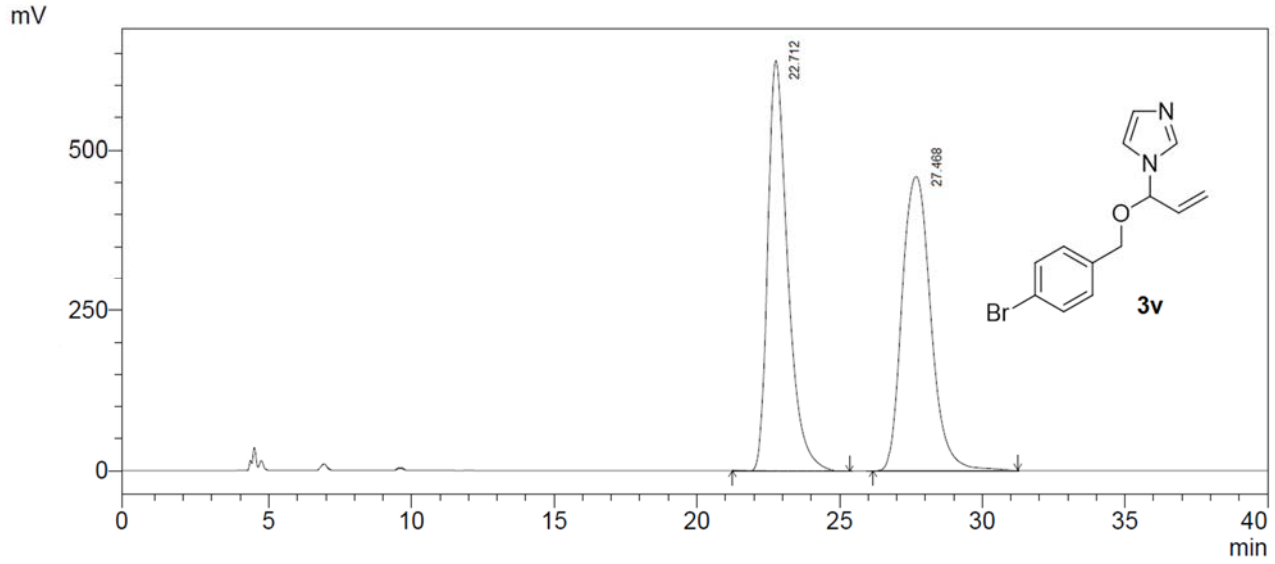
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	22.172	34384281	638868	49.605	58.355
2	27.468	34931559	455927	50.395	41.645
Total		69315840	1094795	100.000	100.000



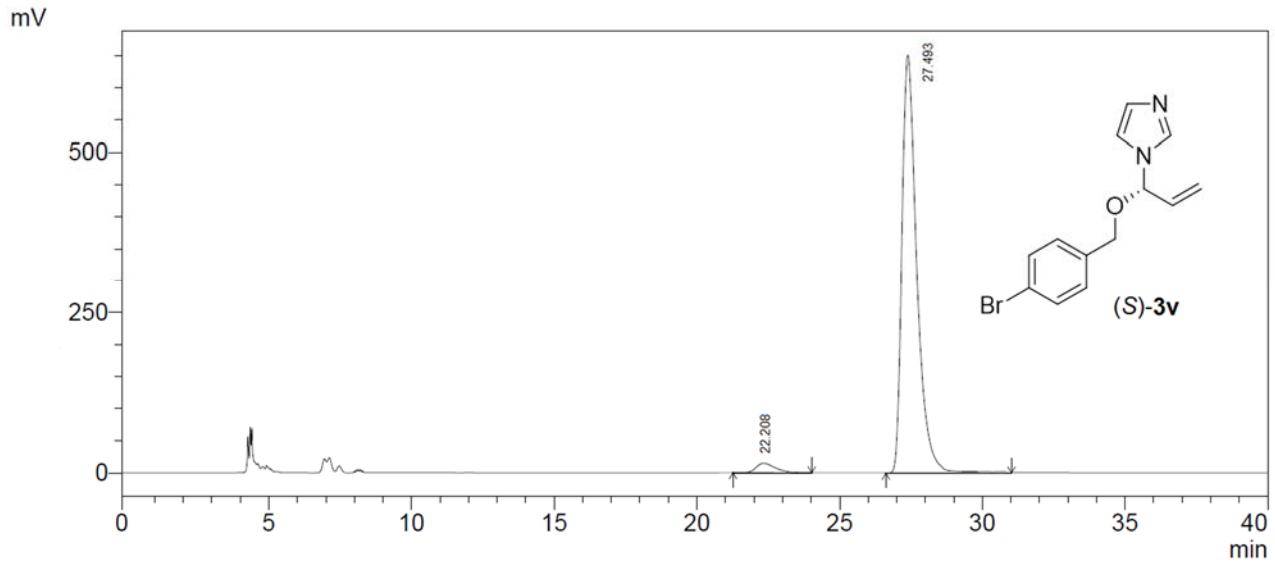
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	22.208	2089828	28307	3.988	3.567
2	27.493	50313085	765294	96.012	96.433
Total		52402913	793602	100.000	100.000



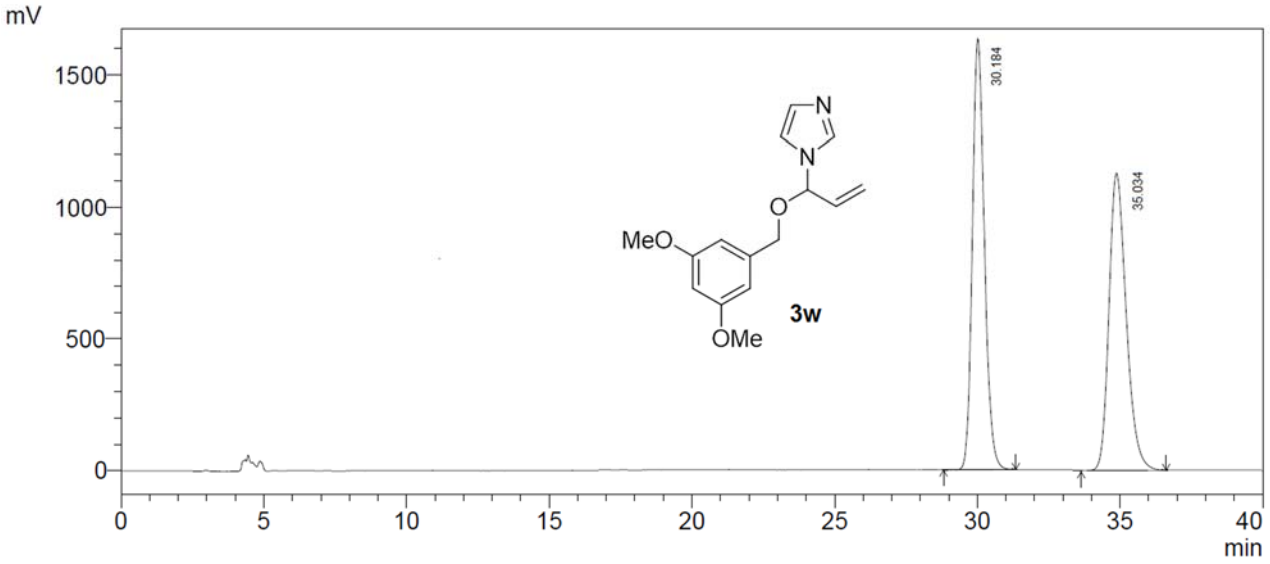
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	30.184	25135092	261437	50.233	59.122
2	35.034	24901920	180762	49.767	40.878
Total		50037012	442199	100.000	100.000



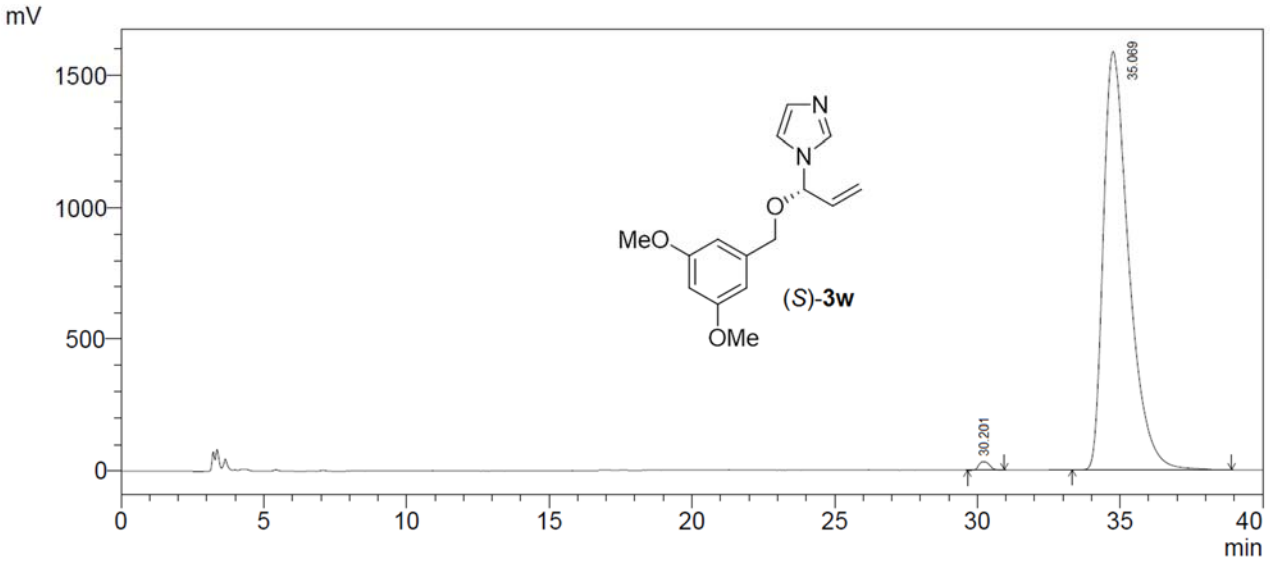
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: OD-H

Method: 97:3 *n*-heptane/ethanol

Peak	Ret. Time	Area	Height	Area %	Height %
1	30.201	2003561	14718	3.270	3.039
2	35.069	59267423	469588	96.730	96.961
Total		61270984	484306	100.000	100.000



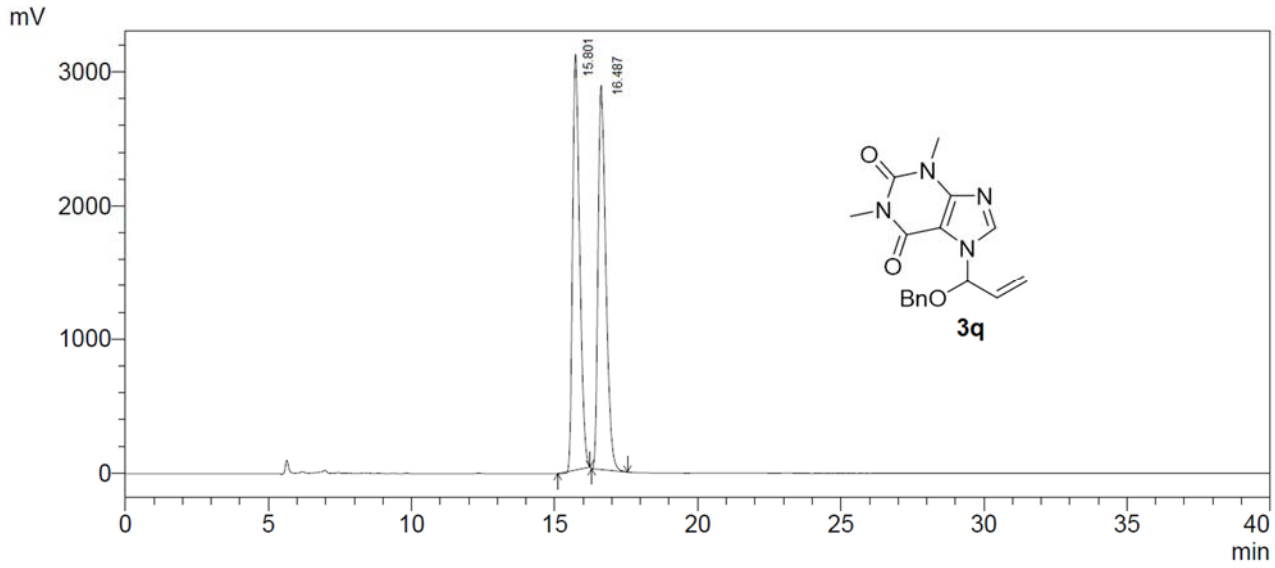
Detector A Ch1 254nm

Injection Volume : 10 uL

Column: Cellulose-1

Method: 70:30 *n*-heptane/IpA

Peak	Ret. Time	Area	Height	Area %	Height %
1	15.801	22800666	1945268	49.435	51.048
2	16.487	23321851	1865397	50.565	48.952
Total		46122517	3810665	100.000	100.000



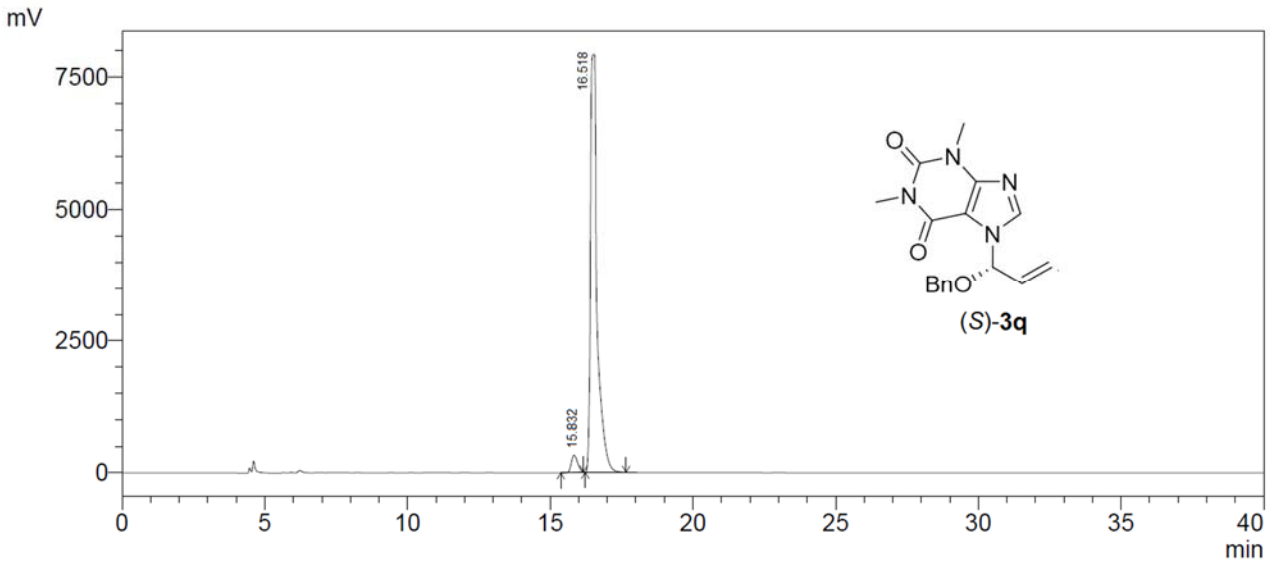
Detector A Ch1 254nm

Injection Volume : 10 uL

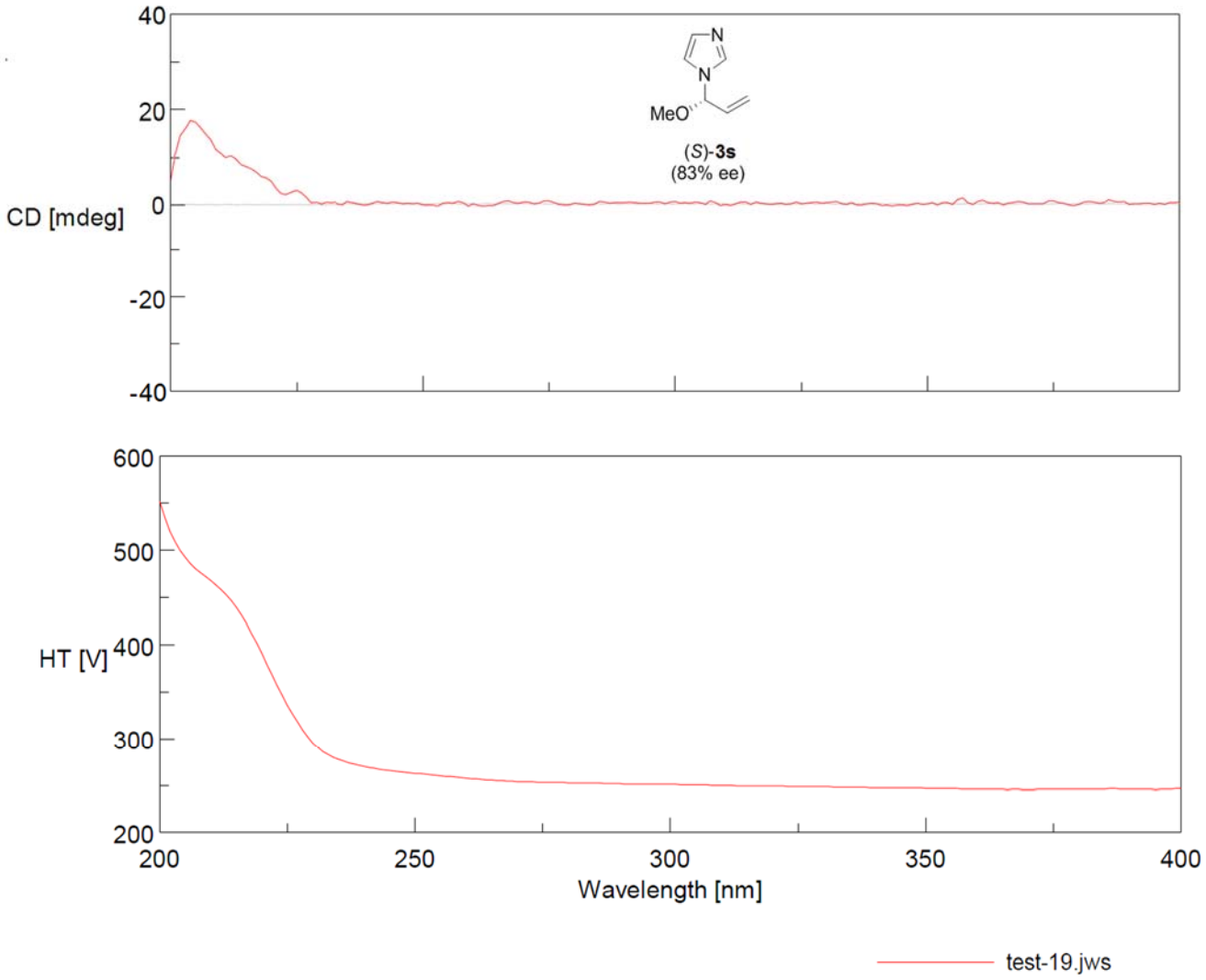
Column: Cellulose-1

Method: 70:30 *n*-heptane/IpA

Peak	Ret. Time	Area	Height	Area %	Height %
1	15.832	4912705	326088	3.640	3.957
2	16.518	130040912	7914178	96.360	96.043
Total		134953617	8240266	100.000	100.000



CD and HT chromatograms



Photometric Mode: CD, HT

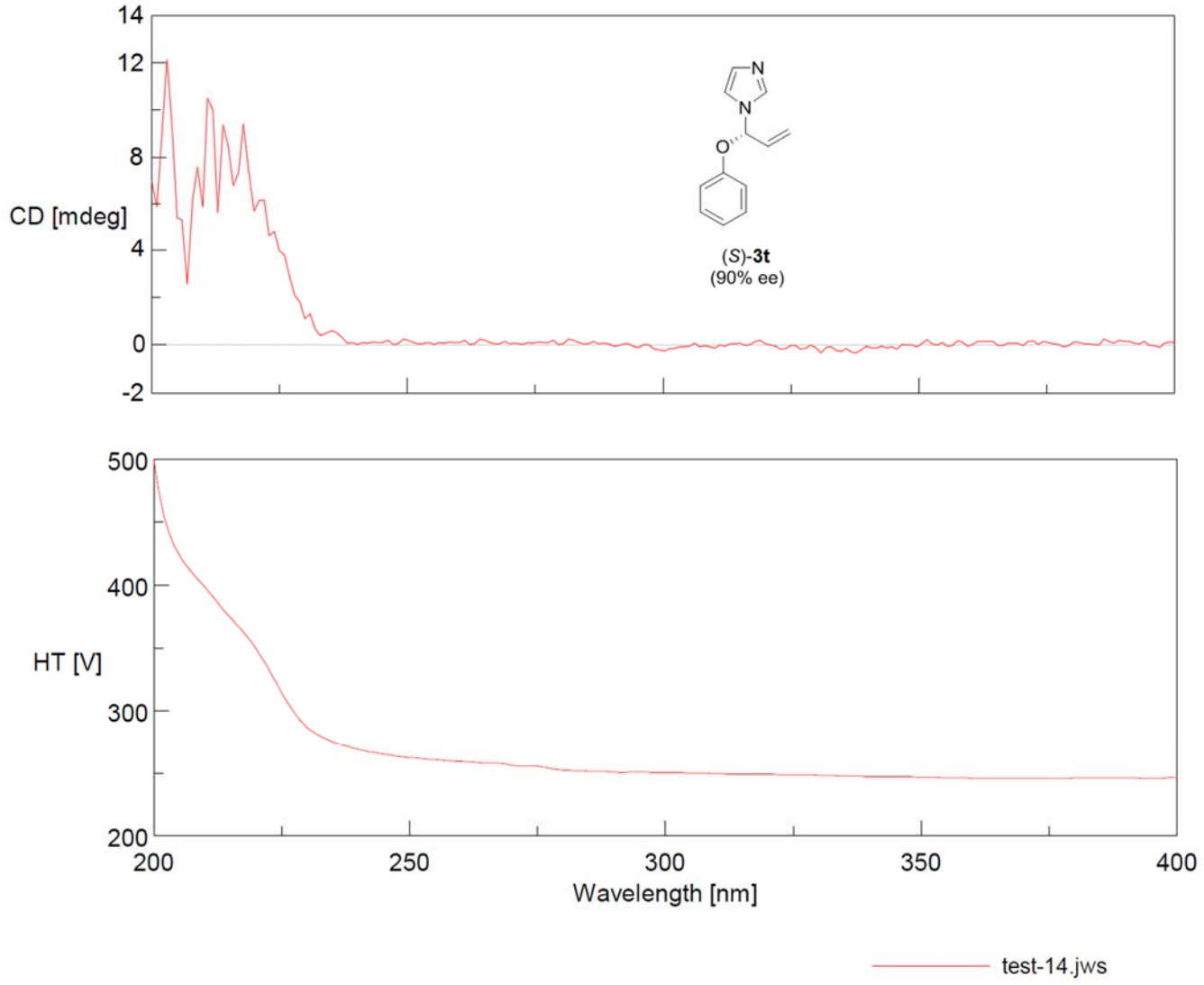
Measure Range: 400 - 200 nm

Concentration: 0.15 mg/ml

D.I.T.: 1 sec

Bandwidth: 1.00 nm

Solvent: Methanol



Photometric Mode: CD, HT

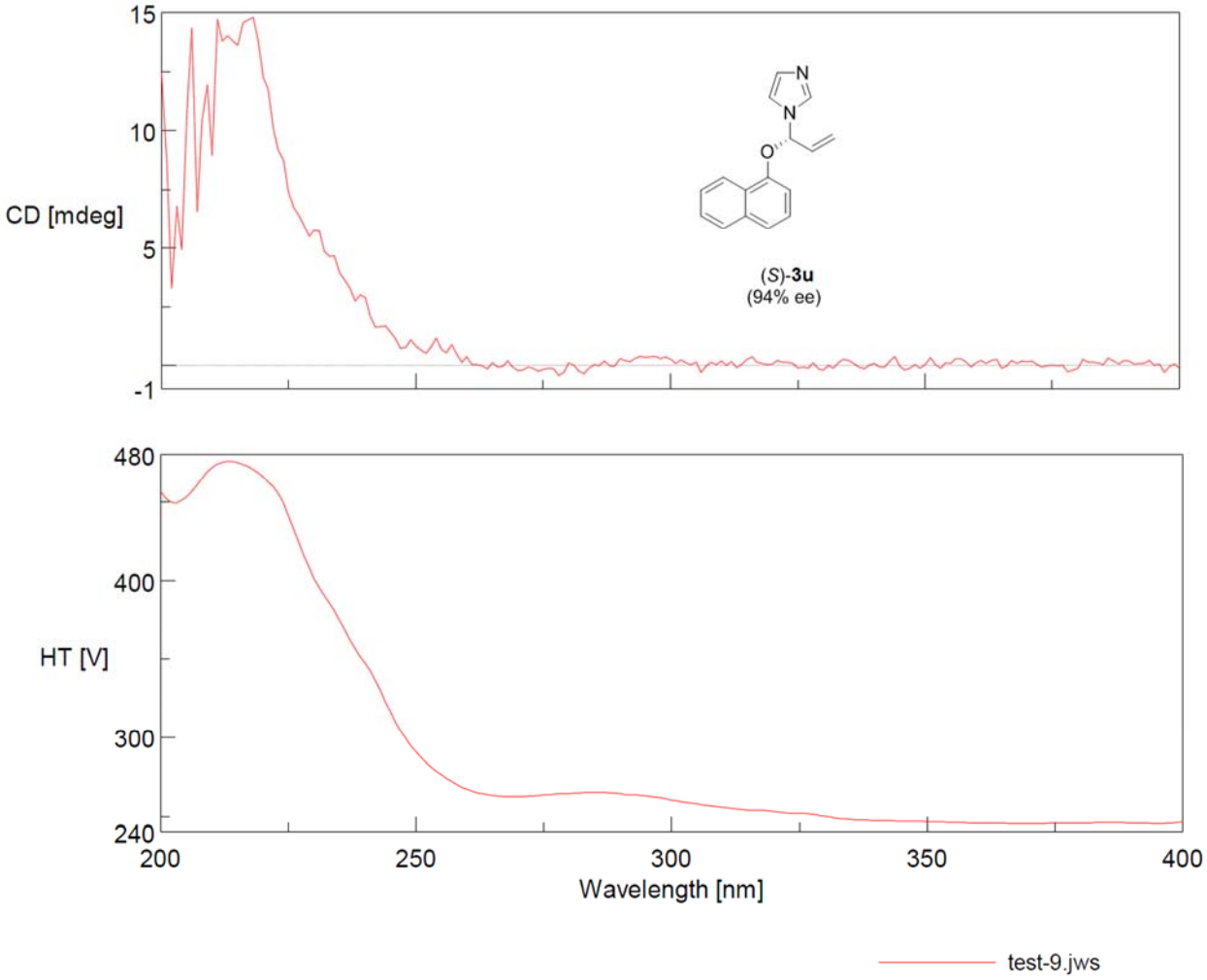
Measure Range: 400 - 200 nm

Concentration: 0.05 mg/ml

D.I.T.: 1 sec

Bandwidth: 1.00 nm

Solvent: Methanol



Photometric Mode: CD, HT

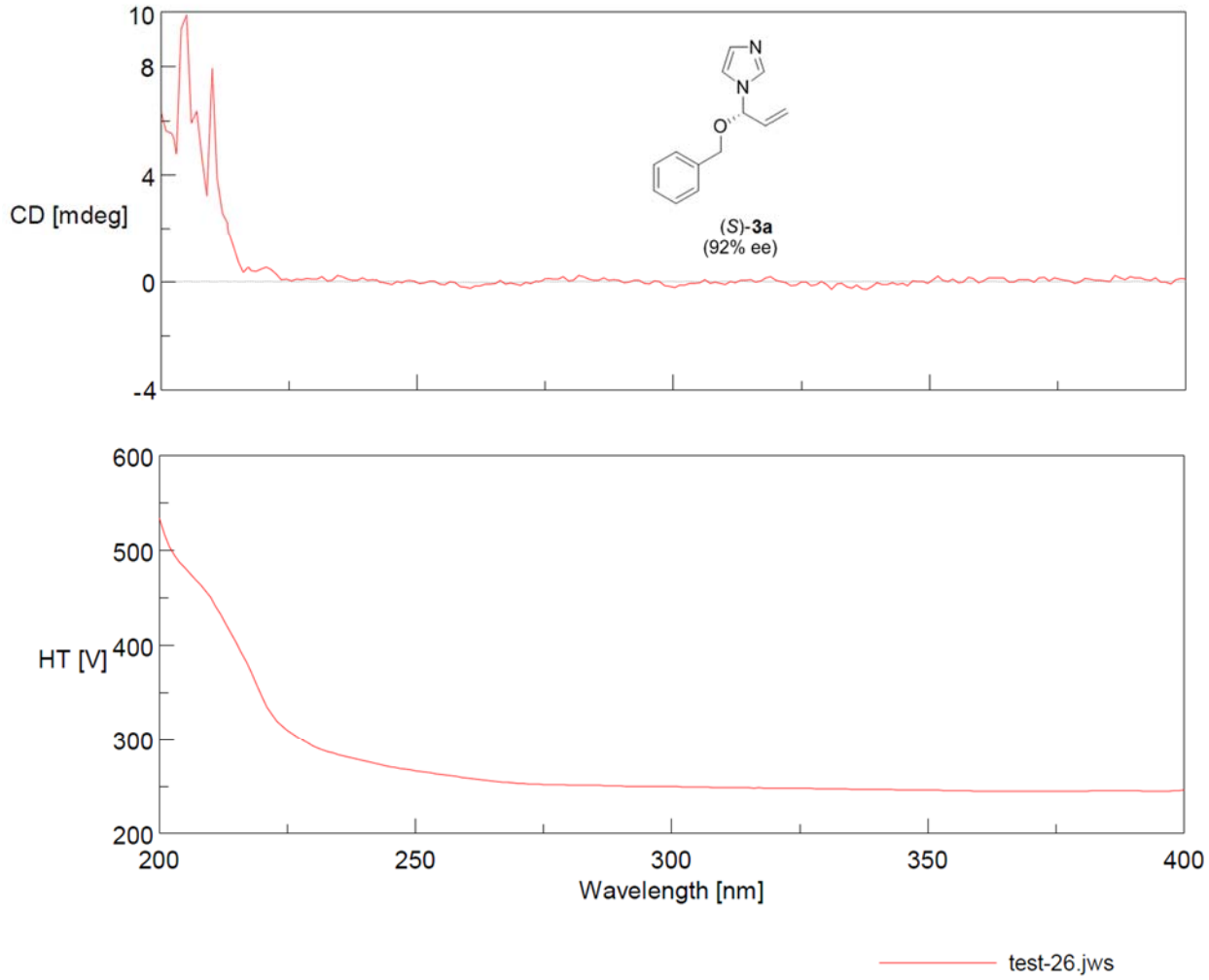
Measure Range: 400 - 200 nm

Concentration: 0.05 mg/ml

D.I.T.: 1 sec

Bandwidth: 1.00 nm

Solvent: Methanol



Photometric Mode: CD, HT

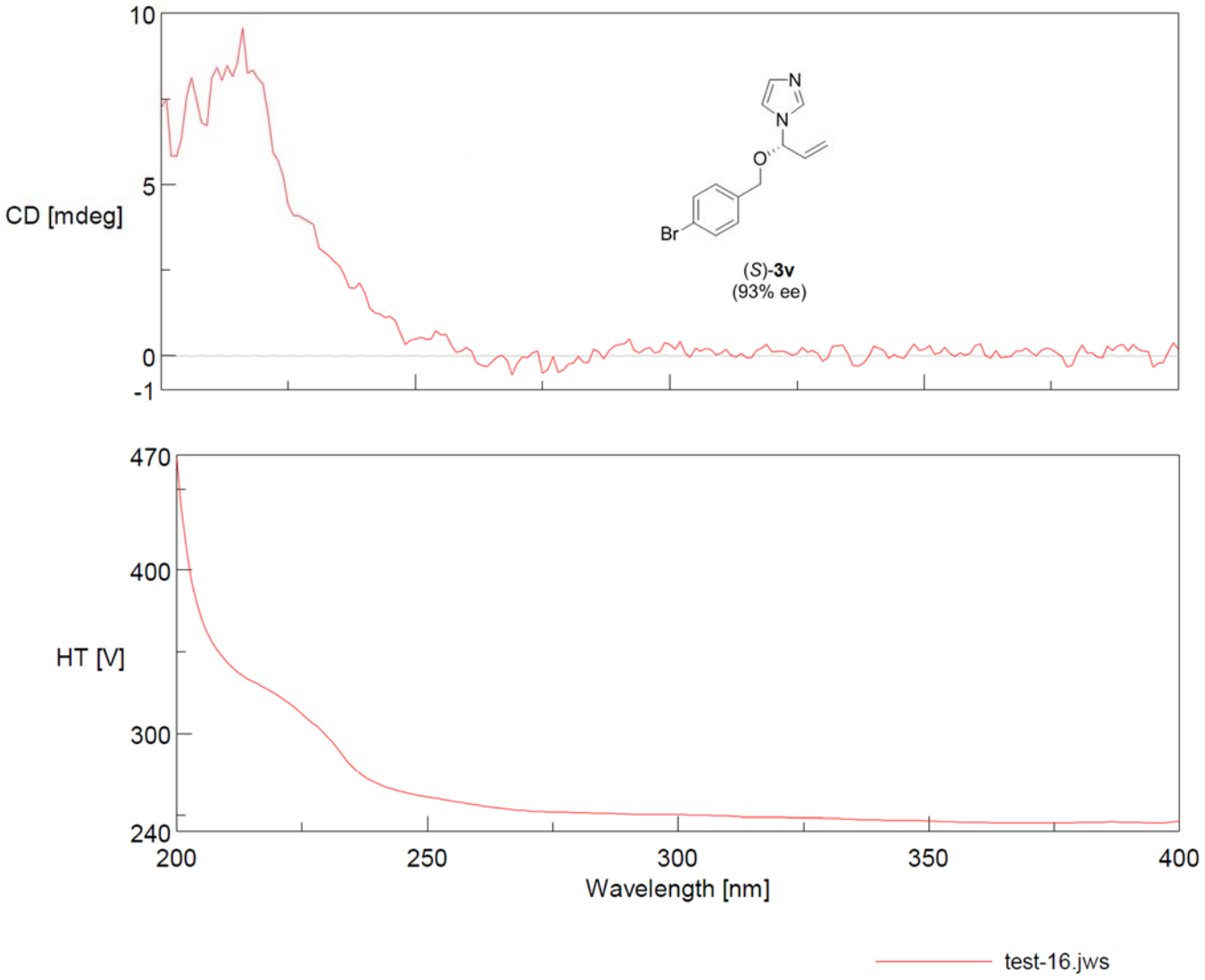
Measure Range: 400 - 200 nm

Concentration: 0.05 mg/ml

D.I.T.: 1 sec

Bandwidth: 1.00 nm

Solvent: Methanol



Photometric Mode: CD, HT

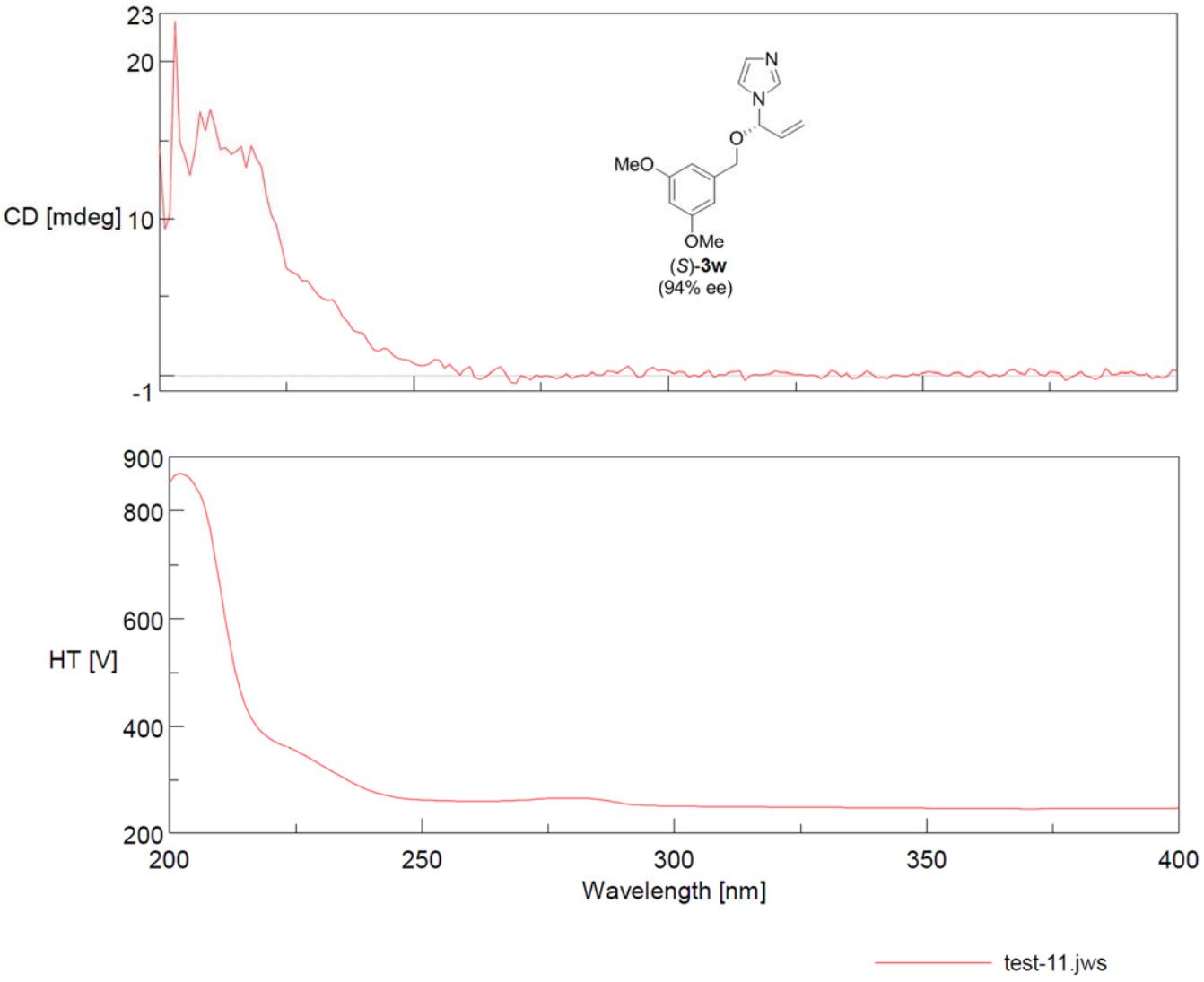
Measure Range: 400 - 200 nm

Concentration: 0.05 mg/ml

D.I.T.: 1 sec

Bandwidth: 1.00 nm

Solvent: Methanol



Photometric Mode: CD, HT

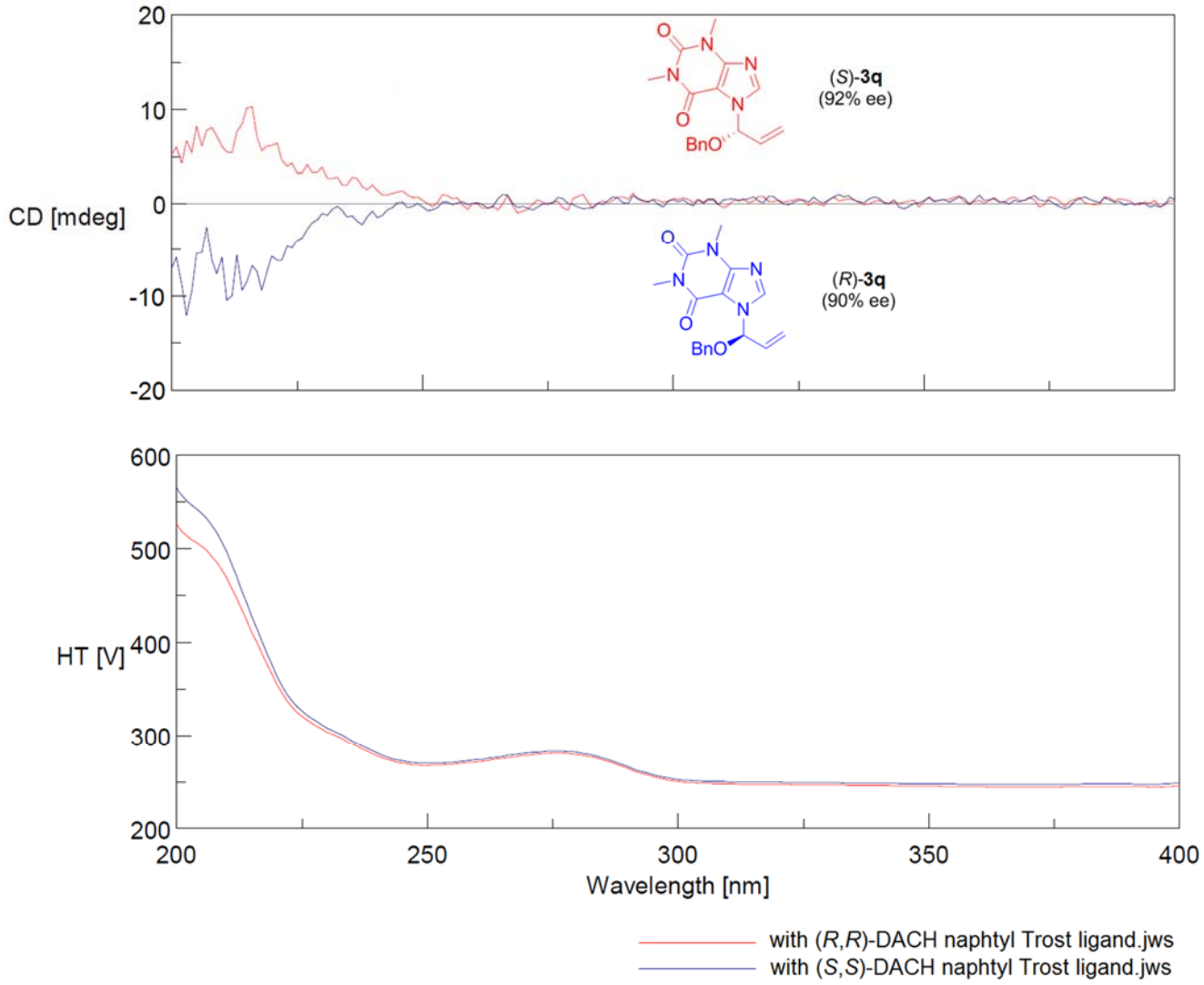
Measure Range: 400 - 200 nm

Concentration: 0.12 mg/ml

D.I.T.: 1 sec

Bandwidth: 1.00 nm

Solvent: Methanol



Photometric Mode: CD, HT

Measure Range: 400 - 200 nm

Concentration: 0.07 mg/ml

D.I.T.: 1 sec

Bandwidth: 1.00 nm

Solvent: Methanol

Crystal structure of (*S*)-3q