Supporting Information

Reactions of Nitroso Hetero Diels-Alder Cycloadducts with Azides: Stereoselective Formation of Triazolines and Aziridines

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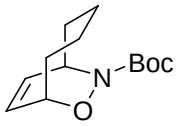
Experimental Section

General Methods. All chemicals purchased were reagent grade and used without purification unless noted otherwise. Benzyl azide, *n*-octyl azide, and cyclopropyl azide were prepared according to the procedure described by Alvarez et al.[1] 1-Azidoadamantane was purchased from Aldrich and used without purification. Tosyl azide was prepared according to the procedure described by Pollex et al.[2] Phenyl azide was prepared according to the procedure published in *Organic Synthesis*.[3] Reactions were carried out under an inert atmosphere of argon only when specified in the experimental details, and were monitored by TLC as described in the experimental procedure using aluminum-backed 0.2 mm silica gel 60 F-254 plates. Visualization of TLC plates was performed under a UV lamp irradiating at 254 nmr or by

staining with CAM stain (Ceric Ammonium Molybdate stain, Hanessian's stain). Column chromatography was conducted using silica gel 60 (230-400 mesh). All melting points are uncorrected. All NMR spectra were recorded under ambient temperatures unless otherwise noted. Chemical shift values for NMR spectra are reported as δ in ppm relative to the $CDCl_3$ solvent residual peak (7.26 ppm). Infrared spectra were recorded using an FT-IR spectrometer and are reported in cm^{-1}. Mass spectra were obtained as specified.

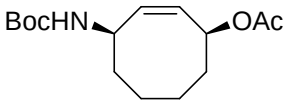
CAUTION!!! Even though it has been reported that azides are potentially explosive, THE AUTHORS DID NOT OBSERVE EXPLOSIVE PROPERTIES OF ANY OF THE MOLECULES AND/OR REAGENTS DESCRIBED IN THIS REPORT. As a precautionary measure, **All reactions involving azides were carried out behind a blast shield in a safety hood with the sash closed all the way down to minimize the risk of injury or harm**.



1c

(±)-*tert*-butyl 8-oxa-7-aza-bicyclo[4.2.2]dec-9-ene-7-carboxylate (1c).[4] *tert*-butyl hydroxycarbamate (12.1 g, 90.6 mmol) was dissolved in 470 mL of MeOH in a 1-L 3-necked round-bottomed flask equipped with a mechanical stirrer and an addition funnel. The solution was cooled in a crushed ice/H_2O bath to 3 °C (internal temperature). *cis*,*cis*-1,3-cyclooctadiene (15.0 mL, 120 mmol) was suspended in the reaction while stirring vigorously and a solution of sodium periodate (20.6 g, 95.3 mmol) in 230 mL of H_2O was added to the reaction dropwise through the addition funned. After a few minutes, the reaction turned yellow and a lot of white solid formed. After 1.5 h, the addition of the $NaIO_4$ solution was complete and the reaction was

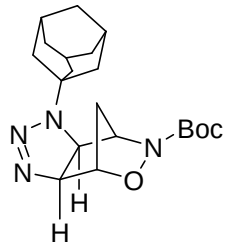
stirred at 25 °C for an additional 5.5 h. The solid material was removed by filtration and washed with EtOAc (150 mL) until all of the yellow color was removed from the solid. The volume of the orange filtrate was reduced by rotary evaporation to about 300 mL (35-40 °C, 21 mm Hg). 250 mL of brine and 200 mL of Et_2O were added and the layers were separated. The aqueous layer was extracted with Et_2O (3 x 200 mL) and the combined Et_2O layers were washed with brine (2 x 200 mL), dried over $MgSO_4$, filtered, and concentrated (35-40 °C, 21 mm Hg) to yield an orange solid. The crude material was loaded onto silica and purified in two portions through a Biotage 40M column using a solvent gradient from 90% CH_2Cl_2/hexanes to 100% CH_2Cl_2 to afford **1c** as a light yellow solid (10.2 g, 47% yield). mp = 88-89 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.37 (dd, *J* = 9.7, 6.9 Hz, 1H), 5.76 (dd, *J* = 10.1, 4.4 Hz, 1H), 4.90 (br-m, 1H), 4.56 (br-m, 1H), 2.15-1.96 (m, 2H), 1.80-1.53 (m, 6H), 1.46 (s, 9H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.9, 131.9, 126.2, 81.1, 75.2, 54.0, 34.1, 31.4, 28.0, 25.7, 22.1 ppm; HRMS (FAB) *m/z* $(M+H)^+$: calcd for $C_{13}H_{22}NO_2^+$, 240.1600; obsd, 240.1606.



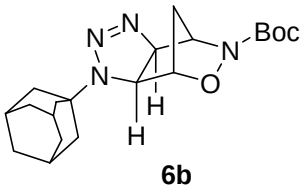
4c

(±)-*cis*-*Z*-4-(tert-butoxycarbonylamino)cyclooct-2-enyl acetate (4c). Cycloadduct **1c** (3.79 g, 15.8 mmol) was dissolved in 160 mL of 15:1 CH_3CN/H_2 in a 500-mL single-necked round-bottomed flask and heated in an oil bath maintained at 55 °C. Molybdenum hexacarbonyl (4.19 g, 15.9 mmol) was added to the reaction in one portion. The flask was fitted with a condensor and the yellow solution was heated to reflux (oil bath temperature = 95-100 °C). The progress of the reaction was monitored by TLC (1:1 hexanes/EtOAc – Hanessian's stain) for the disappearance of **1c**. After 15 h, the mixture was cooled to ambient temperature,

then in a crushed ice/H_2O bath for 15 minutes. The solid material was removed by filtration through celite and the yellow filtrate was concentrated by rotary evaporation (40 °C, 21 mm Hg). The crude material was purified through silica using a solvent gradient from 100% CH_2Cl_2 to 60% CH_2Cl_2/EtOAc to afford the intermediate alcohol as a white solid (3.20 g, 84% yield). The intermediate alcohol (101 mg, 0.420 mmol) was dissolved in 5 mL of anhydrous pyridine in a 25-mL single-necked round-bottomed flask under Ar. Acetic anhydride (0.11 mL, 1.2 mmol) was added and the solution was stirred at ambient temperature. The progress of the reaction was monitored by TLC (1:1 hexanes/EtOAc) for the disappearance of the alcohol. After 15 h, the solution was concentrated by rotary evaporation (40-45 °C, 21 mm Hg) and the yellow residue was partitioned between 1M HCl (20 mL) and EtOAc (20 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined EtOAc layers were washed with 1M HCl (2 x 20 mL), H_2O (20 mL), saturated $NaHCO_3$ (2 x 20 mL), and brine (2 x 20 mL), dried over Na_2SO_4, filtered, and concentrated by rotary evaporation (40 °C, 21 mm Hg) to yield a white solid. The solid was purified through 10 g of silica using a solvent gradient from 100% CH_2Cl_2 to 80% CH_2Cl_2/EtOAc to afford **4c** as a white solid (107 mg, 76% yield from **1c**). mp = 117-119 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.60 (m, 1H), 5.54 (dd, *J* = 10.2, 7.6 Hz, 1H), 5.33 (t, *J* = 9.3 Hz, 1H), 4.57 (br-m, 1H), 4.37 (br-m, 1H), 2.00 (s, 3H), 1.92 (m, 2H), 1.62-1.44 (m, 4H), 1.41 (s, 9H), 1.36-1.29 (m, 2H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.0, 154.9, 131.2, 129.7, 79.2, 72.1, 49.0, 36.2, 35.1, 28.3, 23.8, 23.0, 21.2 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{15}H_{26}NO_4^+$, 284.1862; obsd, 284.1847.

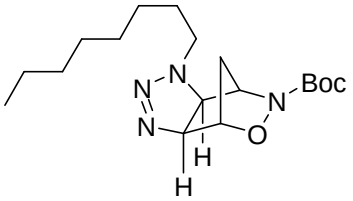


5b

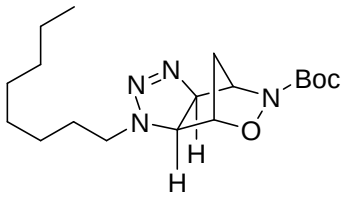


6b

***tert*-butyl (3aα,4β,7β,7aα)-1-(1-adamantyl)-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(1*H*)-carboxylate (5b) and *tert*-butyl (3aα,4β,7β,7aα)-3-(1-adamantyl)-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(3*H*)-carboxylate (6b).** Prepared following the general procedure for the synthesis of triazolines using Method B. Cycloadduct **1a** (104 mg, 0.527 mmol) and 1-azidoadamantane (140 mg, 0.79 mmol) were reacted for 4 weeks. The crude material was purified through 20 g of silica using a solvent gradient from 100% CH_2Cl_2 to 97% CH_2Cl_2/EtOAc to afford **6b** (86 mg, 43% yield) as a white solid, then 85% CH_2Cl_2/EtOAc to afford **5b** (102 mg, 52% yield) as a white solid (95% total combined yield). **5b:** mp > 144 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.93 (s, 1H), 4.77 (dt, *J* = 9.5, 1.5 Hz, 1H), 4.42 (s, 1H), 3.85 (d, *J* = 9.5 Hz, 1H), 2.14-2.07 (m, 6H), 1.84-1.81 (m, 4H), 1.72-1.65 (m, 6H), 1.47 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 83.2, 82.7, 80.4, 63.1, 57.2, 41.7, 36.0, 32.4, 29.2, 28.1 ppm.; HRMS (FAB) *m/z* (M+H): calcd for $C_{20}H_{31}N_4O_3^+$, 375.2396; obsd, 375.2375. **6b:** mp > 166 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.85 (m, 1H), 4.76 (dt, *J* = 10.0, 1.4 Hz, 1H), 4.49 (t, *J* = 1.4 Hz, 1H), 3.80 (dt, *J* = 10.0, 1.2 Hz, 1H), 2.12 (m, 2H), 2.03 (ddd, *J* = 11.6, 4.7, 3.0 Hz, 4H), 1.77 (m, 4H), 1.70-1.62 (m, 6H), 1.47 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 82.782.3, 81.5, 61., 57.0, 56.7, 41.7, 36.0, 32.3, 29.2, 28.0 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{20}H_{31}N_4O_3^+$, 375.2396; obsd, 375.2372.

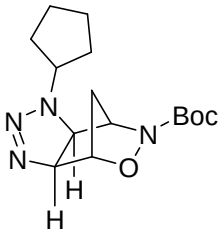


5c

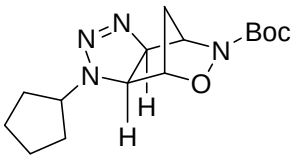


6c

***tert*-butyl (3aα,4β,7β,7aα)-1-(*n*-octyl)-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(1*H*)-carboxylate (5c) and *tert*-butyl (3aα,4β,7β,7aα)-3-(*n*-octyl)-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(3*H*)-carboxylate (6c).** Prepared following the general procedure for the synthesis of triazolines using Method C. Cycloadduct **1a** (199 mg, 1.01 mmol) and *n*-octyl azide (237 mg, 1.53 mmol) were reacted for 2 days. The crude material was purified through 40 g of silica using 80% hexanes/EtOAc to afford **6c** (124 mg, 35% yield), mixed **5c**/**6c** (192 mg, 54%), and **5c** (38 mg, 11% yield) as off-white semi-solids (99% total combined yield). **5c:** mp = 58-59 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.97 (s, 1H), 4.87 (d, *J* = 9.5 Hz, 1H), 4.55 (s, 1H), 3.71-3.66 (m, 2H), 3.58-3.52 (m, 1H), 1.80 (dt, *J* = 11.5, 1.5 Hz, 1H), 1.70-1.64 (m, 2H), 1.50 (m, 10H), 1.33-1.24 (m, 12H), 0.88 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.9, 84.0, 83.0, 80.2, 61.6, 60.1, 49.3, 32.4, 31.7, 29.7, 29.1, 28.8, 28.1, 26.7, 22.6, 14.1 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{18}H_{33}N_4O_3^+$, 353.2553; obsd, 353.2525. **6c:** mp = 49-50 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.87 (m, 1H), 4.58 (s, 1H), 3.66-3.61 (m, 2H), 3.52-3.47 (m, 1H), 1.80 (dt, *J* = 11.5, 1.5 Hz, 1H), 1.61-1.58 (m, 2H), 1.48 (m, 10H), 1.30-1.24 (m, 12H), 0.86 (t, *J* = 7.0 Hz, 3H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 83.0, 82.9, 80.0, 61.7, 60.1, 49.3, 32.4, 31.7, 29.0, 28.8, 28.1, 26.6, 22.6, 14.0 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{18}H_{33}N_4O_3^+$, 353.2553; obsd, 353.2525.

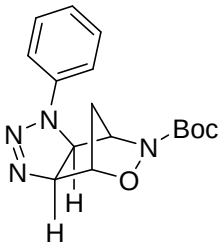


5d

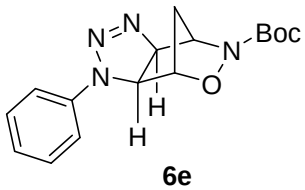


6d

***tert*-butyl (3aα,4β,7β,7aα)-1-cyclopentyl-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(1*H*)-carboxylate (5d) and *tert*-butyl (3aα,4β,7β,7aα)-3-cyclopentyl-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(3*H*)-carboxylate (6d).** Prepared following the general procedure for the synthesis of triazolines using Method C. Cycloadduct **1a** (201 mg, 1.02 mmol) and 1-azidocyclopentane (155 mg, 1.39 mmol) were reacted for 2 days. The crude material was purified through 30 g of silica using 80% hexanes/EtOAc to afford **6d** (88 mg, 28% yield) as a white solid, mixed **5d/6d** (194 mg, 62%) as an off-white solid, and **5d** (25 mg, 8% yield) as a colorless oil (97% total combined yield). **5d:** mp >70 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.96 (s, 1H), 4.85 (d, *J* = 9.5 Hz, 1H), 4.52 (s, 1H), 4.05 (p, *J* = 7.0 Hz, 1H), 3.70 (d, *J* = 9.5 Hz, 1H), 2.08-1.92 (m, 2H), 1.83-1.62 (m, 8H), 1.49 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.7, 83.7, 82.9, 80.3, 62.1, 60.9, 59.4, 32.5, 31.6, 31.1, 28.1, 23.6, 23.4 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{15}H_{25}N_4O_3^+$, 309.1927; obsd, 309.1913. **6d:** mp > 120 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.84 (s, 1H), 4.81 (d, *J* = 9.5 Hz, 1H), 4.55 (s, 1H), 3.97 (p, *J* = 7.0 Hz, 1H), 3.61 (d, *J* = 9.5 Hz, 1H), 2.02-1.95 (m, 1H), 1.87-1.83 (m, 1H), 1.78-1.57 (m, 7H), 1.45-1.42 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 82.8, 82.7, 80.4, 61.6, 60.8, 59.8, 32.3, 31.5, 31.1, 28.0, 23.5, 23.3 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{15}H_{25}N_4O_3^+$, 309.1927; obsd, 309.1913.

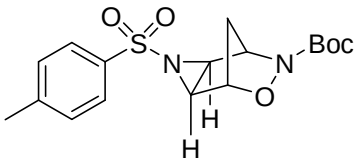


5e



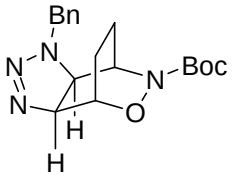
6e

***tert*-butyl (3aα,4β,7β,7aα)-1-phenyl-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(1*H*)-carboxylate (5e) and *tert*-butyl (3aα,4β,7β,7aα)-3-phenyl-3a,4,7,7a-tetrahydro-4,7-methano[1,2,3]triazole[4,5-d][1,2]oxazine-6(3*H*)-carboxylate (6e).** Prepared following the general procedure for the synthesis of triazolines using Method D. Cycloadduct **1a** (202 mg, 1.02 mmol) and phenyl azide[3] (165 mg, 1.39 mmol) were reacted for 3 h. The crude material was purified through 35 g of silica using 100% CH_2Cl_2 to afford **6e** (175 mg, 54% yield) as a light yellow solid, then 80% CH_2Cl_2/EtOAc to afford **5e** (144 mg, 45% yield) as a light yellow oil that solidified upon standing (99% total combined yield). **5e:** mp = 117-120 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41-7.35 (m, 4H), 7.10 (t, *J* = 7.0 Hz, 1H), 5.09 (d, *J* = 10.0 Hz, 1H), 5.085 (s, 1H), 4.86 (s, 1H), 4.46 (d, *J* = 10.0 Hz, 1H), 1.91 (dt, *J* = 12.0, 2.0 Hz, 1H), 1.54 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.4, 139.3, 129.6, 123.0, 113.8, 83.9, 83.2, 79.7, 60.2, 57.1, 32.2, 28.0 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{16}H_{21}N_4O_3^+$, 317.1614; obsd, 317.1622. **6e:** mp > 158 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37 (t, *J* = 8.0 Hz, 3H), 7.30 (d, *J* = 8.5 Hz, 2H), 7.08 (t, *J* = 7.5 Hz, 1H), 5.10 (d, *J* = 9.5 Hz, 1H), 5.02 (s, 1H), 4.92 (s, 1H), 4.24 (d, *J* = 9.5 Hz, 1H), 1.86 (dt, *J* = 12.0, 2.0 Hz, 1H), 1.54 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 139.4, 129.7, 123.1, 113.9, 83.2, 78.7, 61.4, 58.0, 32.3, 28.1 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{16}H_{21}N_4O_3^+$, 317.1614; obsd, 317.1605.



8

***tert*-butyl (1α,2β,4β,5α)-3-[(4-methylphenyl)sulfonyl]-6-oxa-3,7-diazatricyclo[3.2.1.0^{2,4}]octane-7-carboxylate (8).** Cycloadduct **1a** (205 mg, 1.04 mmol) and tosyl azide (268 mg, 1.36 mmol) were dissolved in 10 mL of $PhCH_3$ in a 25-mL single-necked round-bottomed flask fitted with a condenser and heated to reflux in an oil bath (oil temperature = 125 °C). The reaction was monitored by TLC (1:1 hexanes/EtOAc; UV lamp) for the disappearance of **1a**. After 9h, the reaction was complete and the solution was concentrated to yield a brown oil. The oil was purified through 35 g of silica using a solvent gradient from 100% CH_2Cl_2 to 90% CH_2Cl_2/EtOAc to yield **8** as a tan solid (263 mg, 69% yield). mp = 111-115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 4.78 (s, 1H), 4.62 (s, 1H), 3.26 (d, *J* = 6.0 Hz, 1H), 3.22 (d, *J* = 6.0 Hz, 1H), 2.40 (s, 3H), 2.01 (d, *J* = 11.0 Hz. 1H), 1.44 (s, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.6, 145.0, 133.9, 129.7, 127.8, 82.9, 78.1, 59.4, 36.5, 36.2, 29.0, 27.9, 21.5 ppm; MS (FAB) *m/z* 367 (M+H), 311, 267 (100%); HRMS (FAB) *m/z* (M+H): calcd for $C_{17}H_{23}N_2O_5S^+$, 367.1328; obsd, 367.1314



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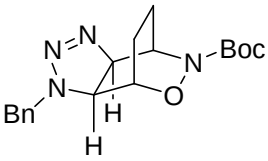

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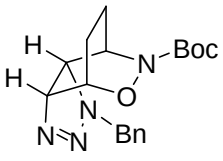

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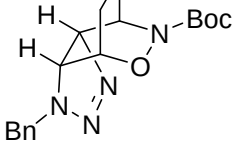
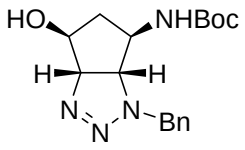


12

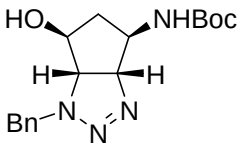
Reaction of 1b With Benzyl Azide: Formation of triazolines 9, 10, 11, and 12. 1b (421 mg, 1.99 mmol) and benzyl azide (1.33 g, 9.97 mmol) were dissolved in 10 mL of toluene

in a 25-mL single-necked round-bottomed flask fitted with a condensor and heated to reflux in an oil bath (oil temp. = 125 °C). The reaction was monitored by TLC (1:1 hexanes/EtOAc; UV lamp) for the disappearance of **1b**. After 28h, the deep brown solution was concentrated to yield a brown oil. The oil was chromatographed through silica using a solvent gradient from 100% hexanes to 50% hexanes/EtOAc to afford **10** (136 mg, 20% yield), **9** (128 mg, 19% yield), and an inseparable mixture of **11** and **12** (163 mg, 24% yield), all as brown solids (62% total combined yield). **9:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.38-7.30 (m, 5H), 4.99 (ddd, *J* = 13.0, 4.5, 1.5 Hz, 1H), 4.85 (d, *J* = 14.5 Hz, 1H), 4.77 (d, *J* = 14.5 Hz, 1H), 4.54 (t, *J* = 4.0 Hz, 3.83 (br-s, 1H), 3.63 (dd, *J* = 13.0, 4.0 Hz, 1H), 1.98-1.90 (m, 1H), 1.76-1.70 (m, 1H), 1.63 (tdd, *J* = 13.8, 4.2, 2.5 Hz, 1H), 1.52-1.46 (m, 1H), 1.43 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 132.9, 128.8, 128.5, 128.2, 81.9, 78.1, 69.5, 53.5, 47.2, 28.1, 19.6, 18.5 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{18}H_{25}N_4O_3^+$, 345.1927; obsd, 345.1931. **10:** ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.21 (m, 5H), 4.90 (ddd, *J* = 12.5, 4.0, 1.0 Hz, 1H), 4.75 (d, *J* = 14.5 Hz, 1H), 4.66 (d, *J* = 14.5 Hz, 1H), 4.45 (m, 1H), 3.71 (m, 1H), 3.60 (dd, *J* = 12.5, 4.5 Hz, 1H), 1.86-1.80 (m, 1H), 1.77-1.70 (m, 1H), 1.55-1.49 (m, 1H), 1.47-1.43 (m, 1H), 1.42 (m, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.7, 134.9, 128.9, 128.7, 128.4, 82.1, 78.4, 70.3, 54.2, 54.1, 47.6, 47.6, 28.2, 20.2, 17.9 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{18}H_{25}N_4O_3^+$, 345.1927; obsd, 345.1931. **11** and **12** were obtained as ~1:1 mixture as evidenced by ^{1}H NMR. HRMS (FAB) *m/z* (M+H): calcd for $C_{18}H_{25}N_4O_3^+$, 345.1927; obsd, 345.1931.



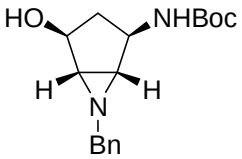
14

General Procedure for N-O Bond Reduction Using the $Mo(CO)_6/NaBH_4$ System. *tert*-butyl (3aα,4α,6α,6aα)-3-benzyl-6-hydroxy-3,3a,4,5,6,6a-hexahydrocyclopenta[d][1,2,3]triazol-4-ylcarbamate (14). Triazoline **5a** (207 mg, 0.628 mmol) was dissolved in 5 mL of 4:1 CH_3CN/H_2O in a 25-mL single-necked round-bottomed flask and heated in a 50 °C oil bath. Molybdenum hexacarbonyl (72 mg, 0.27 mmol) was added to the solution in one portion, followed by sodium borohydride (80 mg, 2.1 mmol) added in portions. Bubbling was observed and the color of the reaction changed from light yellow to a deep, murky brown. After the bubbling subsided, the reaction was heated to reflux (oil temperature = 70 °C) and monitored by TLC (1:1 hexanes/EtOAc; UV lamp) for the disappearance of **5a**. After 18 h, the reaction was cooled in a crushed ice/H_2O bath and the solid material was removed by filtration through a pad of celite. The celite was washed with EtOAc (20 mL) and the filtrate was concentrated to yield an off-white solid, which was purified through 20 g of silica using 50% hexanes/EtOAc to afford **14** as a white solid (123 mg, 59% yield). mp = 153-155 °C (dec.); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.28 (m, 5H), 5.60 (d, *J* = 9.0 Hz, 1H), 5.15 (d, *J* = 15.0 Hz, 1H), 4.78 (d, *J* = 10.8 Hz, 1H), 4.63 (d, *J* = 15.0 Hz, 1H), 4.51 (d, *J* = 4.2 Hz, 1H), 4.11 (m, 1H), 3.66 (d, *J* = 10.8 Hz, 1H), 1.76 (d, *J* = 14.4 Hz, 1H), 1.55-1.49 (m, 1H), 1.43 (s, 9H) ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{17}H_{25}N_4O_3^+$, 333.1927; obsd, 333.1906.



15

***tert*-butyl (3aα,4α,6α,6aα)-1-benzyl-6-hydroxy-1,3a,4,5,6,6a-hexahydrocyclopenta[d][1,2,3]triazol-4-ylcarbamate (15).** Compound **15** was prepared according to the general procedure for N-O bond reduction using the $Mo(CO)_6/NaBH_4$ system using **6ab** (506 mg, 1.53 mmol), molybdenum hexacarbonyl (181 mg, 0.686 mmol) and $NaBH_4$ (220 mg, 5.8 mmol) to afford an amber foam (540 mg). The foam was purified through 10 g of silica using 83% CH_2Cl_2/EtOAc to yield **15** as a light yellow solid (295 mg, 58% yield). mp > 110 °C (dec.); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30-7.20 (m, 5H), 5.63 (br-m, 1H), 4.91-4.85 (m, 2H), 4.63 (d, *J* = 15.0 Hz, 1H), 4.21 (t, *J* = 8.0 Hz, 1H), 4.07 (d, *J* = 4.0 Hz, 1H), 3.64 (d, *J* = 10.5 Hz, 1H), 1.69 (d, *J* = 14.0 Hz, 1H), 1.53 (br-s, 1H), 1.39 (s, 10H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.1, 136.0, 128.7, 128.2, 127.9, 89.4, 79.6, 76.0, 66.9, 56.7, 52.9, 37.8, 28.4 ppm; HRMS (FAB) *m/z* (M+H): calcd for $C_{17}H_{25}N_4O_3^+$, 333.1927; obsd, 333.1930.



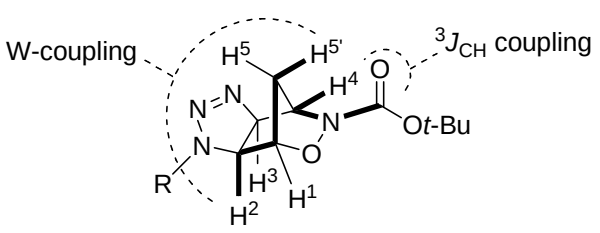
16

***tert*-butyl (1α,2α,4α,5α)-6-benzyl-4-hydroxy-6-aza-bicyclo[3.1.0]hexan-2-ylcarbamate (16).** Triazoline **14** (108 mg, 0.323 mmol) was dissolved in 300 mL of degassed CH_3CN in a 450-mL photochemical reaction reaction vessel. The solution was irradiated in an immersion-well reactor under a stream of Ar with a Hanovia 450W mercury lamp fitted with a Vycor filter sleeve. The progress of the reaction was monitored by ^{1}H NMR. After 5 h, the

solution was concentrated (40 °C, 21 torr) to yield an amber oil (110 mg). The oil was purified through a pad of silica using a solvent gradient from 100% CH_2Cl_2 to 40% CH_2Cl_2/EtOAc to afford **16** as a yellow oil (89.9 mg, 91% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32-7.23 (m, 5H), 5.16 (m, 1H), 4.26 (d, *J* = 5.0 Hz, 1H), 4.08 (t, *J* = 7.5 Hz, 1H), 3.52 (d, *J* = 14 Hz, 1H), 3.32 (d, *J* = 14 Hz, 1H), 2.30 (m, 2H), 2.05 (m, 1H), 1.47 (d, *J* = 15 Hz, 1H), 1.43 (s, 9H), 1.25 (m, 1H) ppm; ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.4, 138.7, 128.3, 127.3, 126.9, 71.8, 60.7, 51.0, 48.4, 47.6, 39.8, 29.6, 28.3 ppm; HRMS (FAB) *m/z* ($M^{\bullet+}$): calcd for $C_{17}H_{24}N_2O_3^+$, 304.1787; obsd, 304.1785.

Structural Determination Techniques for Triazolines 5, 6, 9, and 10

The determination of *endo/exo* stereochemistry for triazolines **5b**, **5d**, **5e**, **6b**, **6d**, **6e**, **9**, and **10** was accomplished by the analysis of the COSY and ROESY spectra. COSY spectra confirmed the *exo* geometry of the triazoline group from the observed coupling of H^2 to $H^{5'}$ and H^3 to $H^{5'}$, but not from H^2 to H^5 or H^3 to H^5. This ^4J-coupling ("W-coupling") was observed in all triazolines. Coupling of H^2 or H^3 to *either* H^5 or $H^{5'}$ would not be observed in the COSY experiment if the triazoline moiety were in the *endo* geometry due to the rigid conformation of the bicyclo[2.2.1] system. In the case of triazolines **9** and **10**, the process is the same, except W-coupling is observed between H^2 and $H^{5'}$, and H^3 and $H^{6'}$ (the diagram below illustrates this method for structural determination of triazolines **6** and **10**). Again, this coupling would not be observed for triazolines **11** or **12**.



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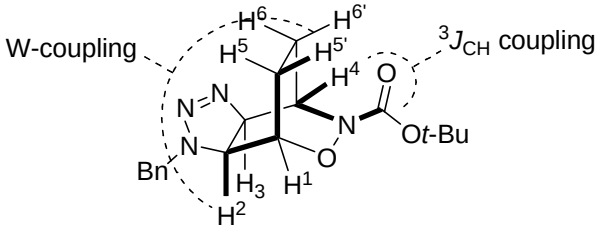


10

The relationship of R and the Boc group was determined from gHMBC experiments. The HETCOR experiments established the assignment of all the ^{13}C NMR signals. Using gHMBC and HETCOR correlations, protons H^1-H^4 could be assigned unambiguously. The $^3J_{CH}$-coupling between H^1 and the carbonyl signal or H^4 and the carbonyl signal confirmed the structural assignment of the molecule as triazoline **5** or triazoline **6** respectively. Triazoline **6d** did not exhibit this $^3J_{CH}$-coupling; however, the structure was assigned as **6d** based on the confirmed structure of **5d**. Likewise, the structure of triazoline **6b** was assigned based on the confirmed structure of **5b**.

ORTEP diagrams for 5a and 6a

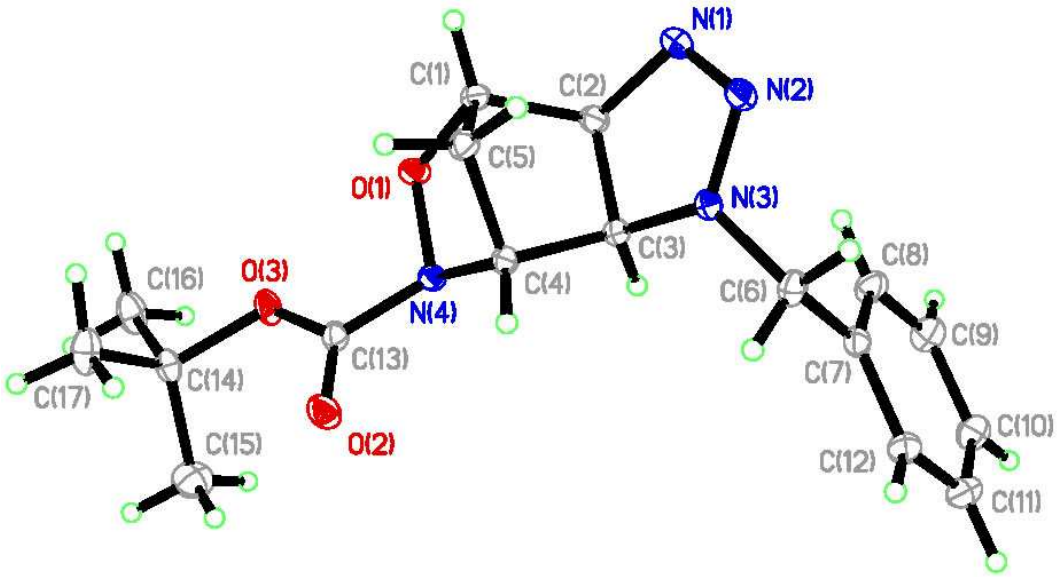


Figure 1. Ortep diagram of 5a

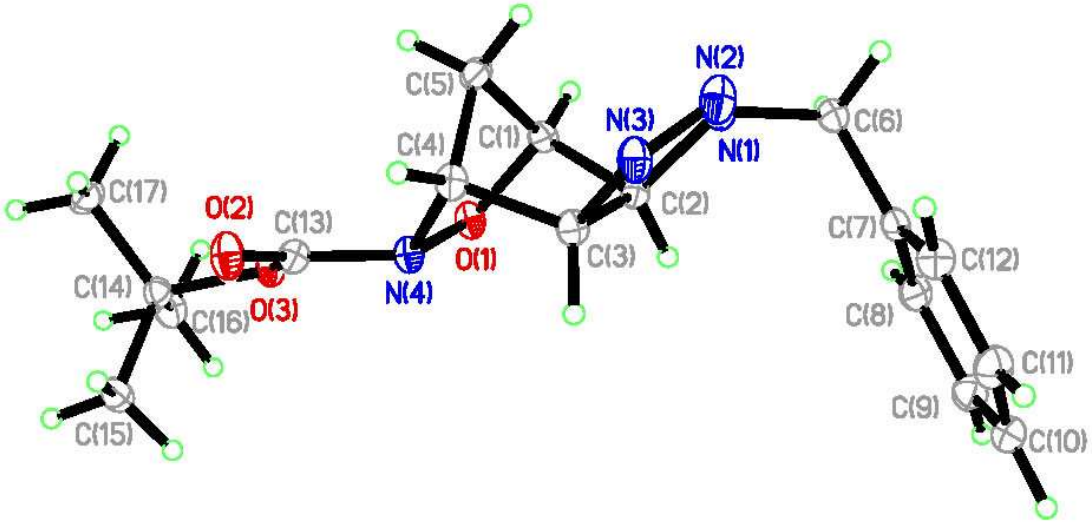
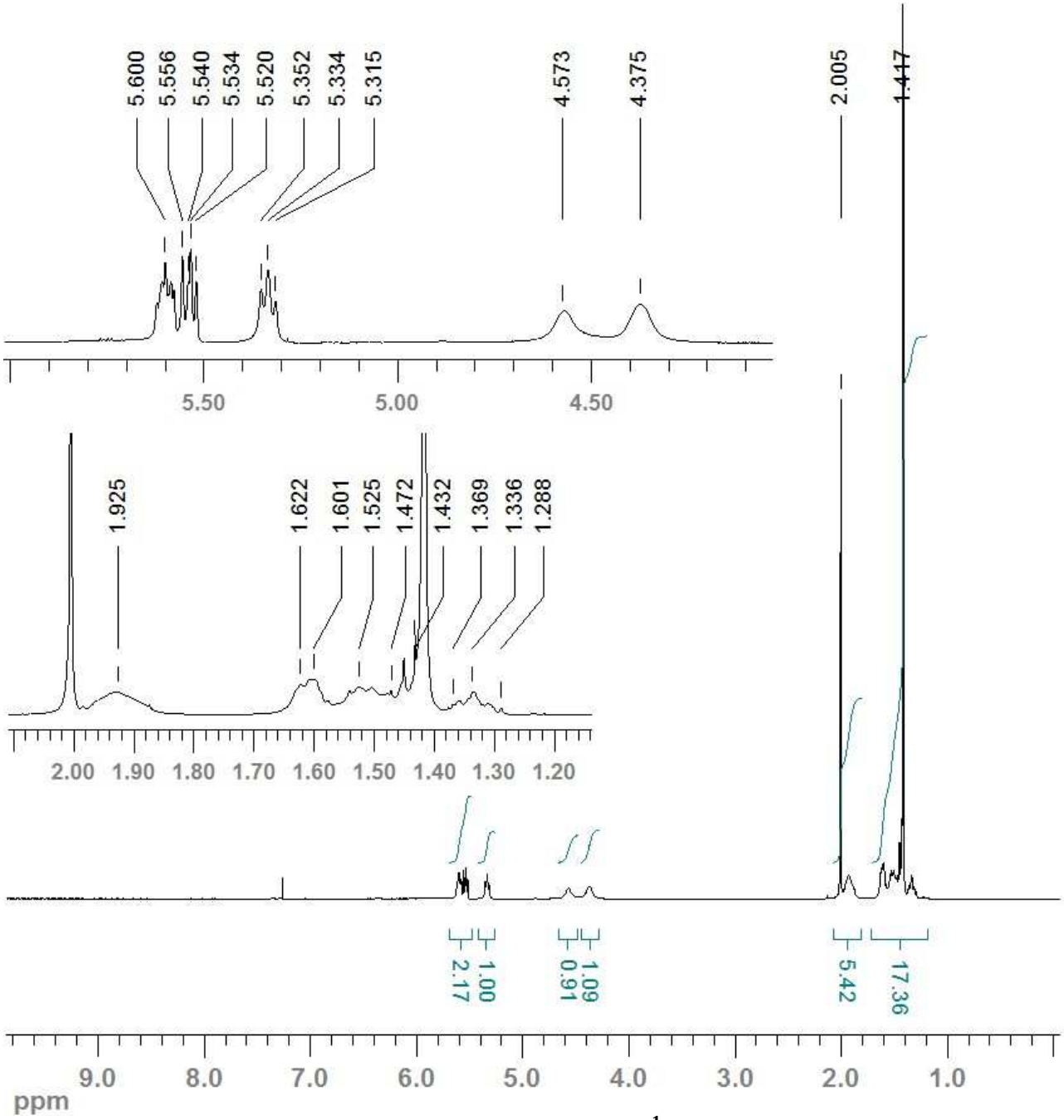


Figure 2. Ortep diagram of 6a



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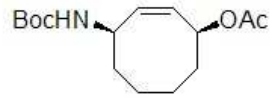
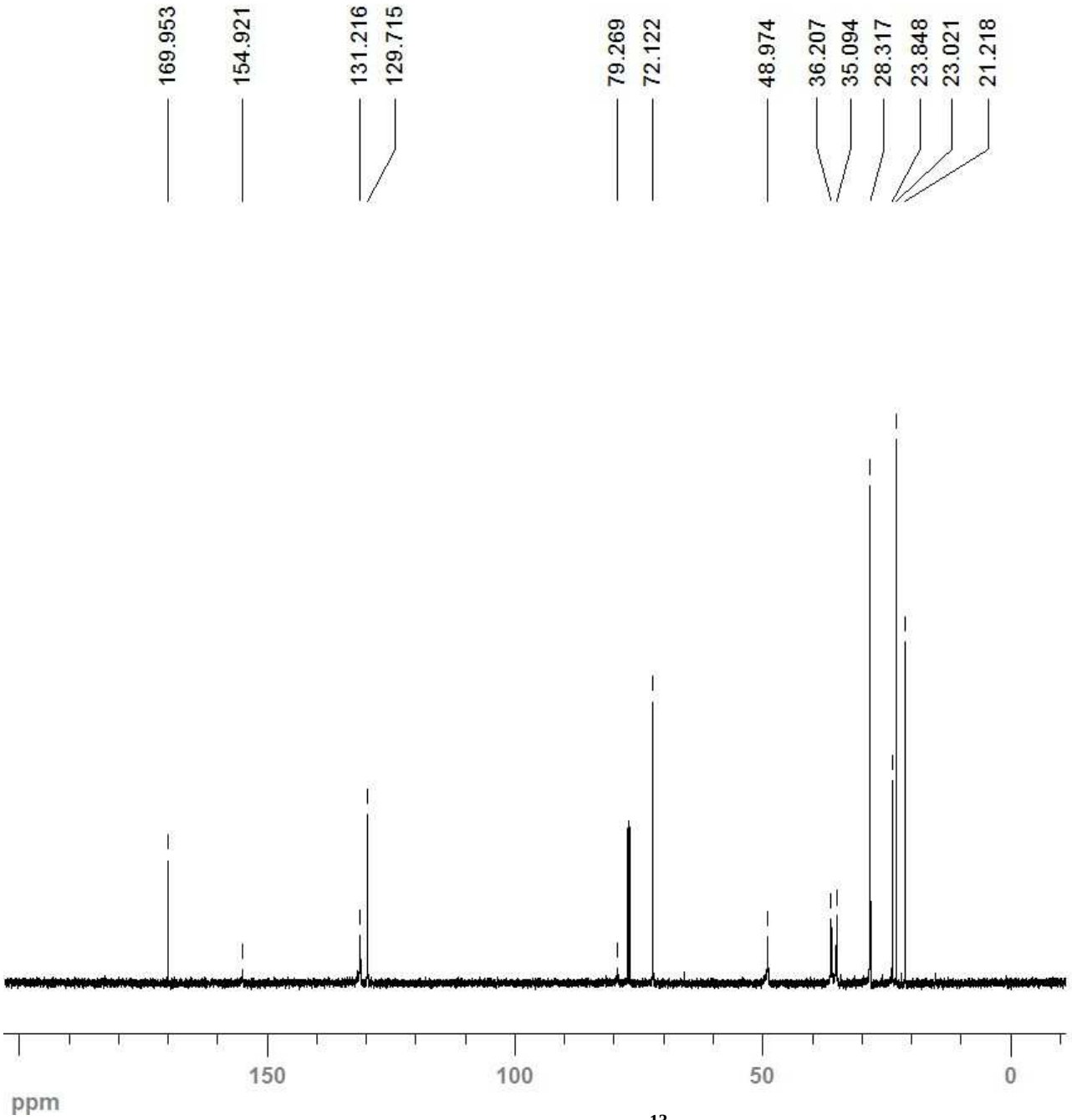


4c

Figure 3. ^{1}H NMR spectrum of 4c



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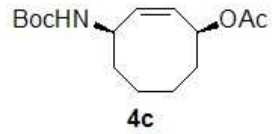


4c

Figure 4. ^{13}C NMR spectrum of 4c

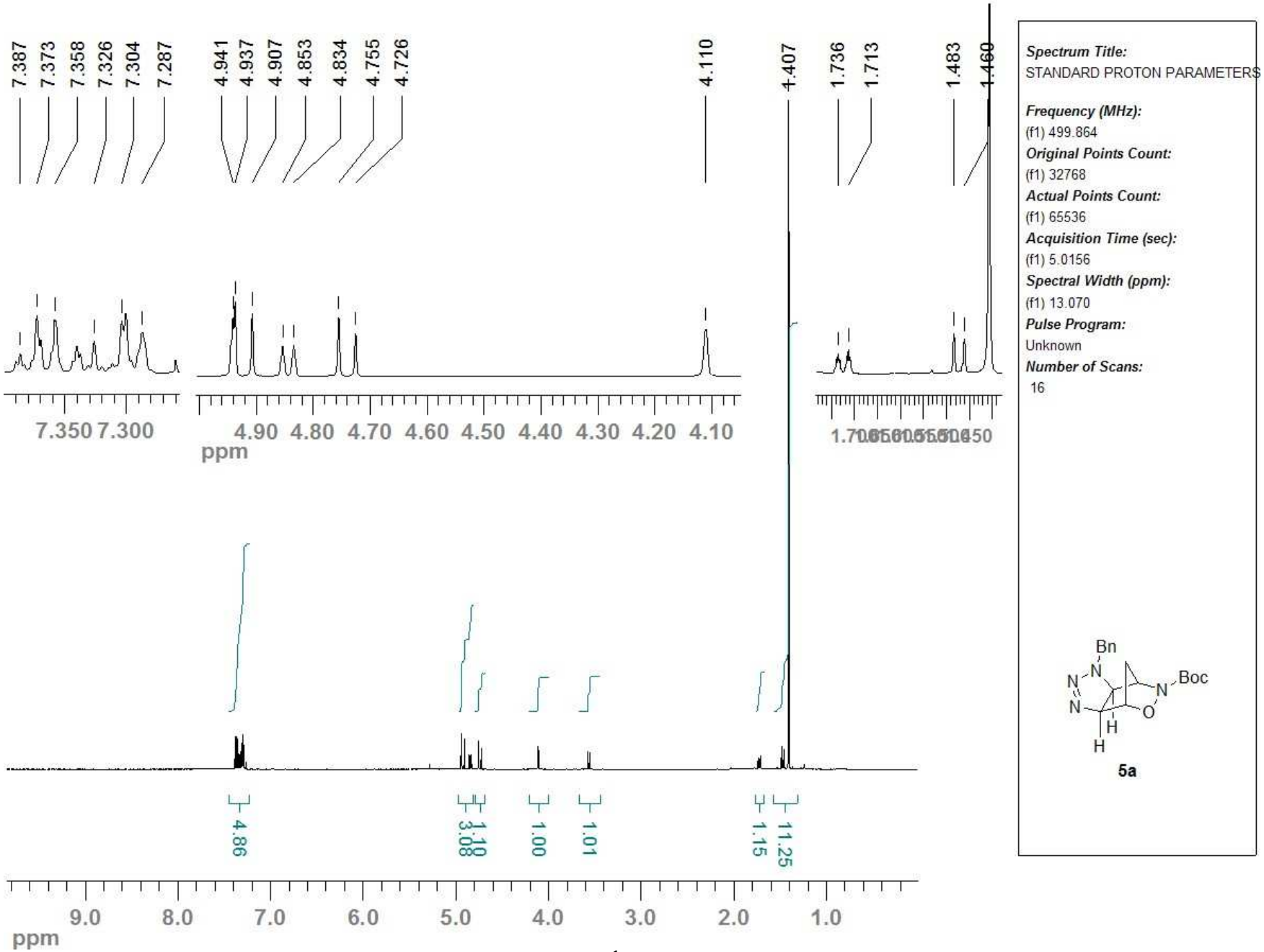
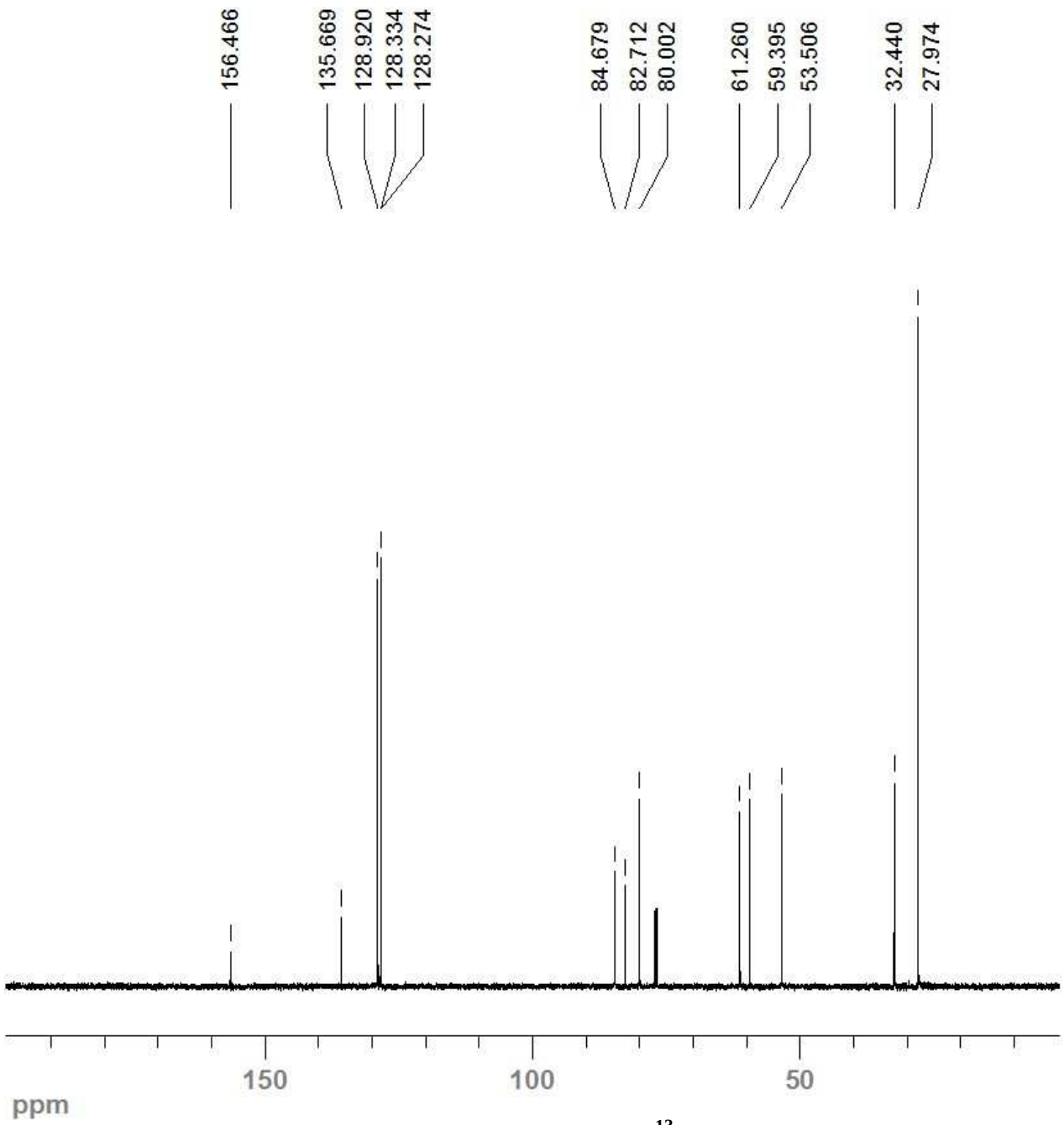


Figure 5. ^{1}H NMR of 5a



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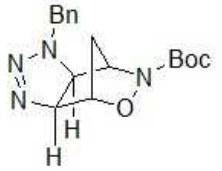


5a

Figure 6. ^{13}C NMR spectrum of 5a

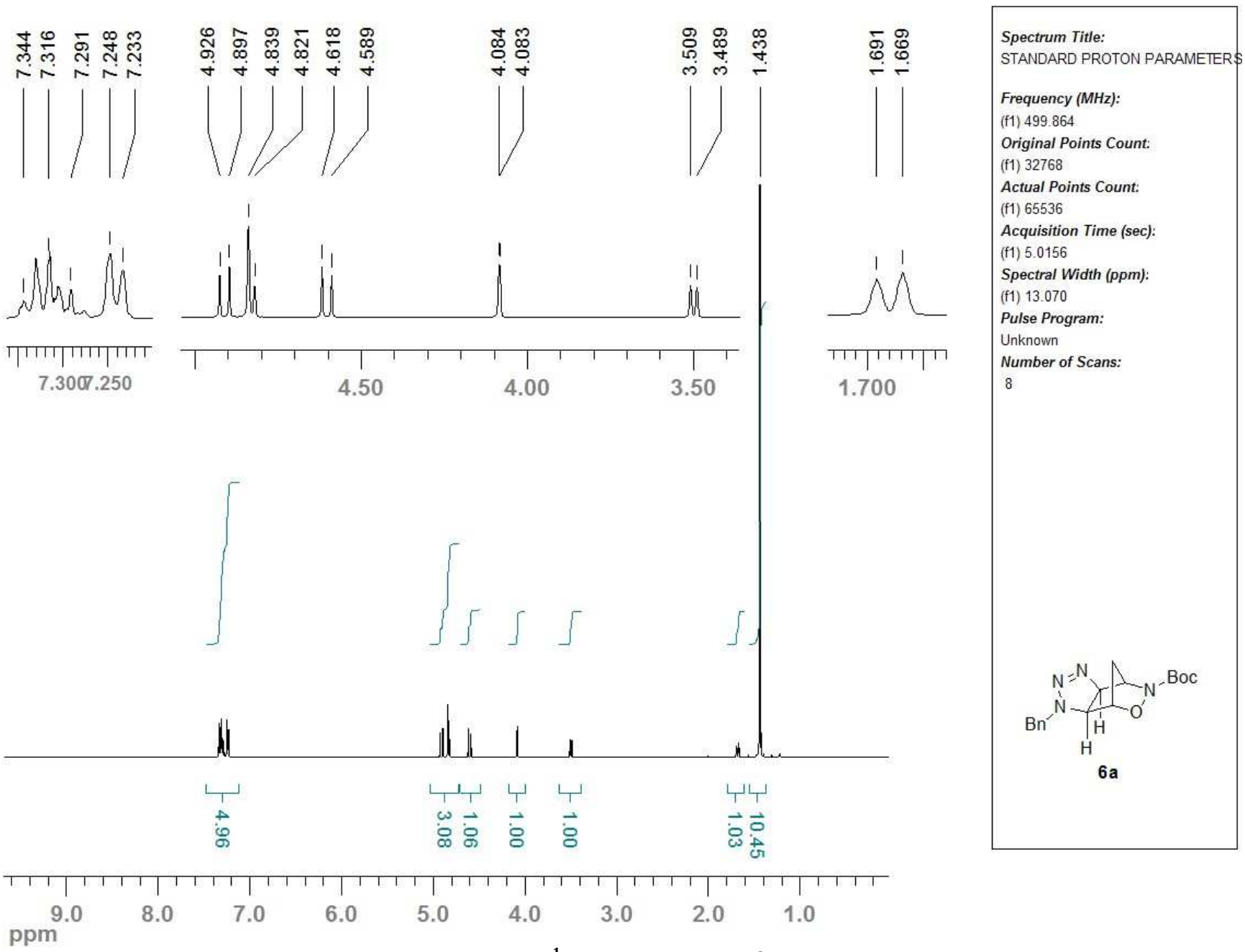
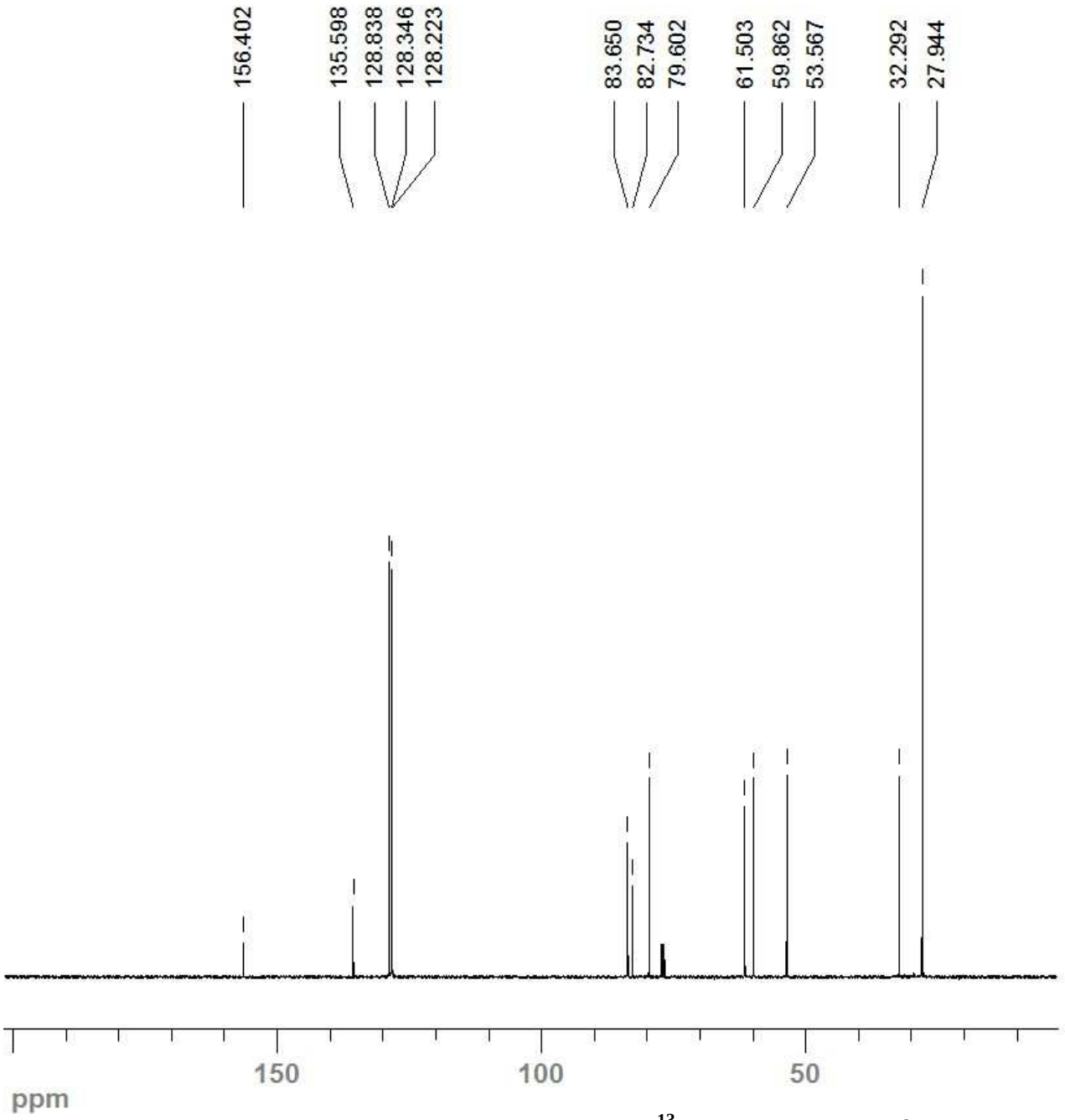


Figure 7. ^{1}H NMR spectrum of 6a



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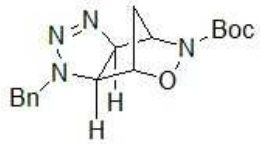
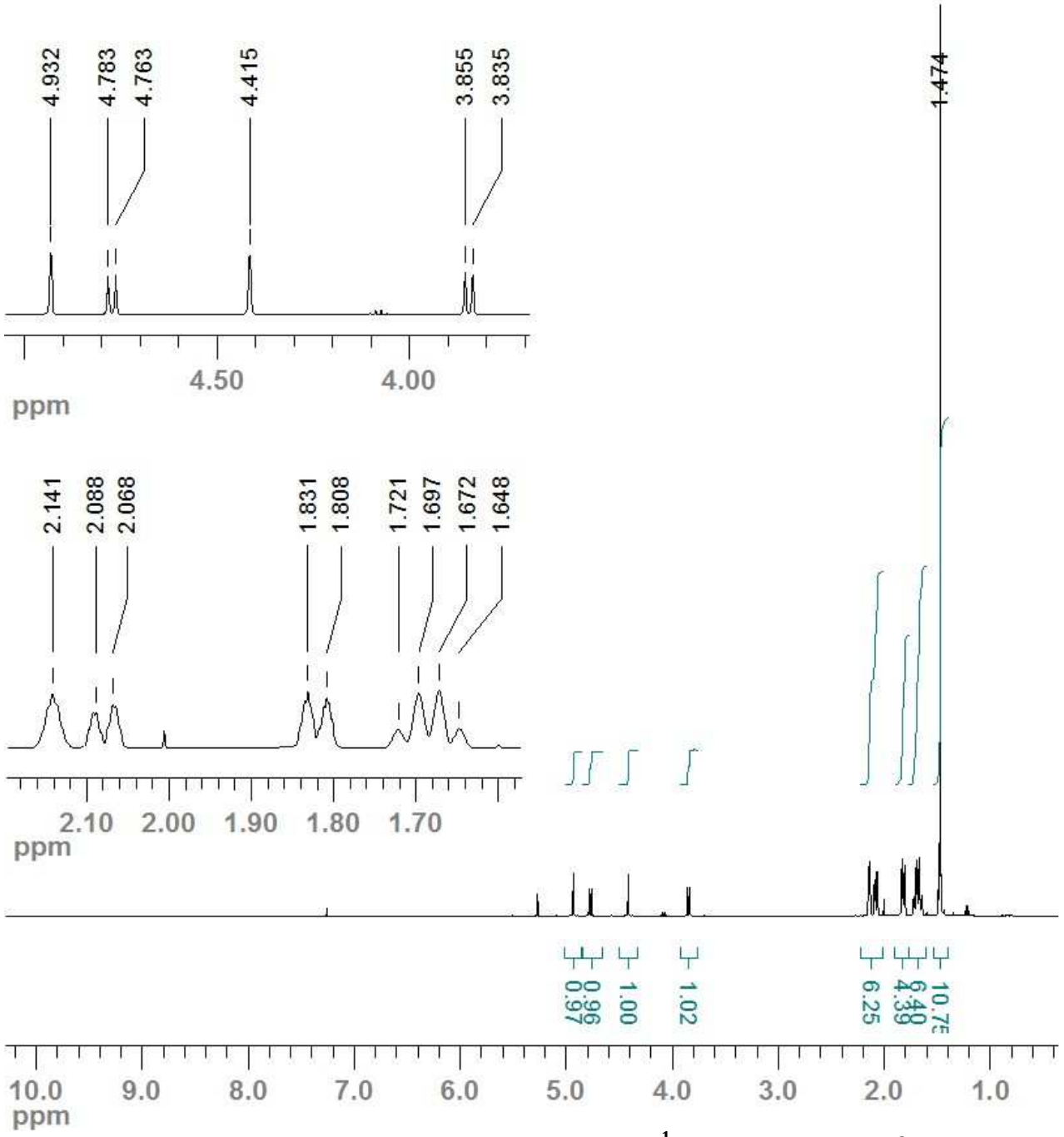


6a

Figure 8. ^{13}C NMR spectrum of 6a



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Actual Points Count:
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Acquisition Time (sec):
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Spectral Width (ppm):
(f1) 13.070
Pulse Program:
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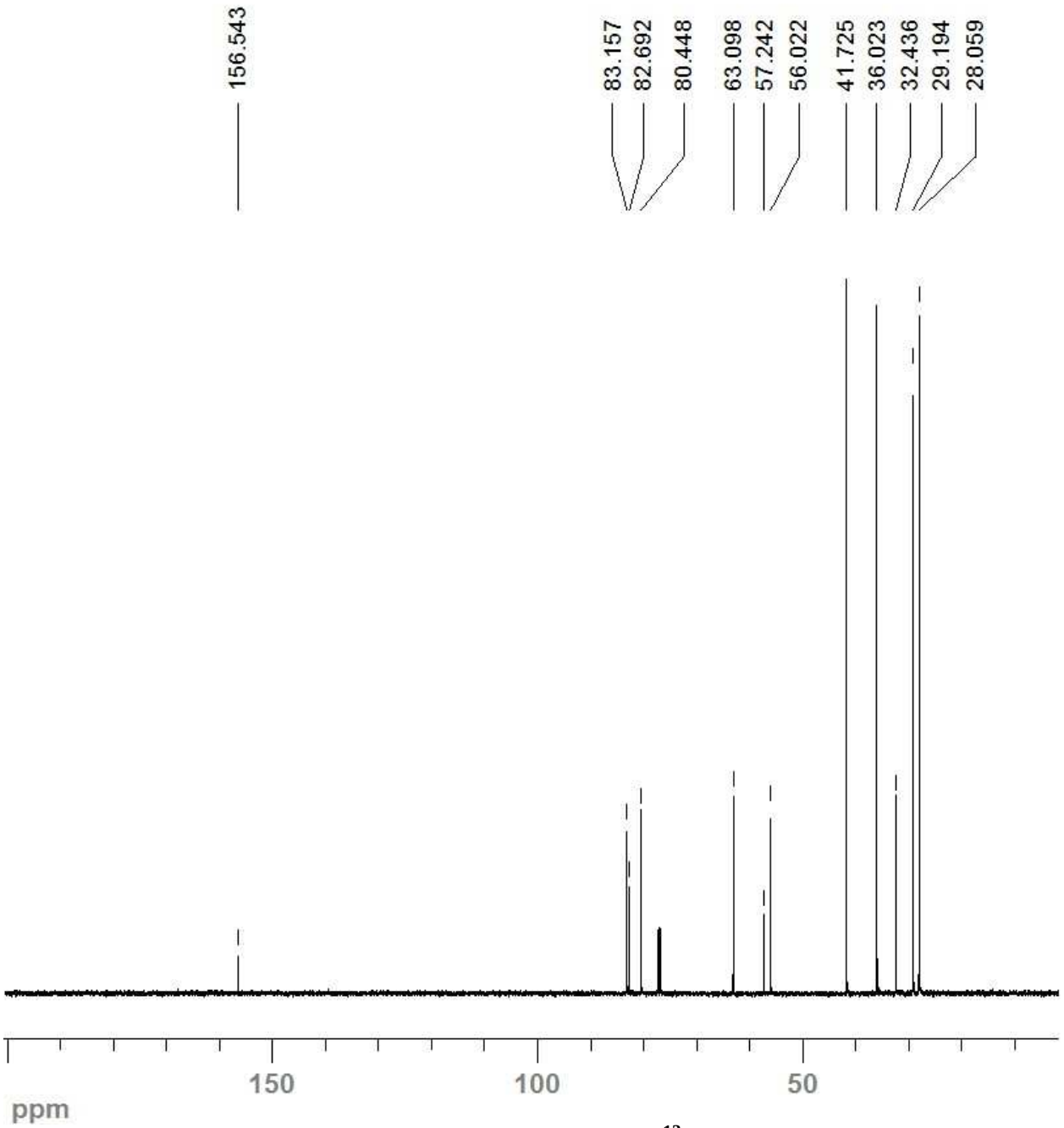
Number of Scans:
16

5b

Figure 9. ^{1}H NMR spectrum of 5b



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Number of Scans:
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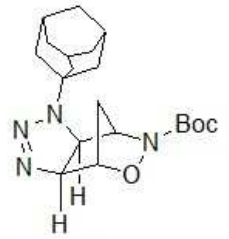


5b

Figure 10. ^{13}**C NMR spectrum of 5b**

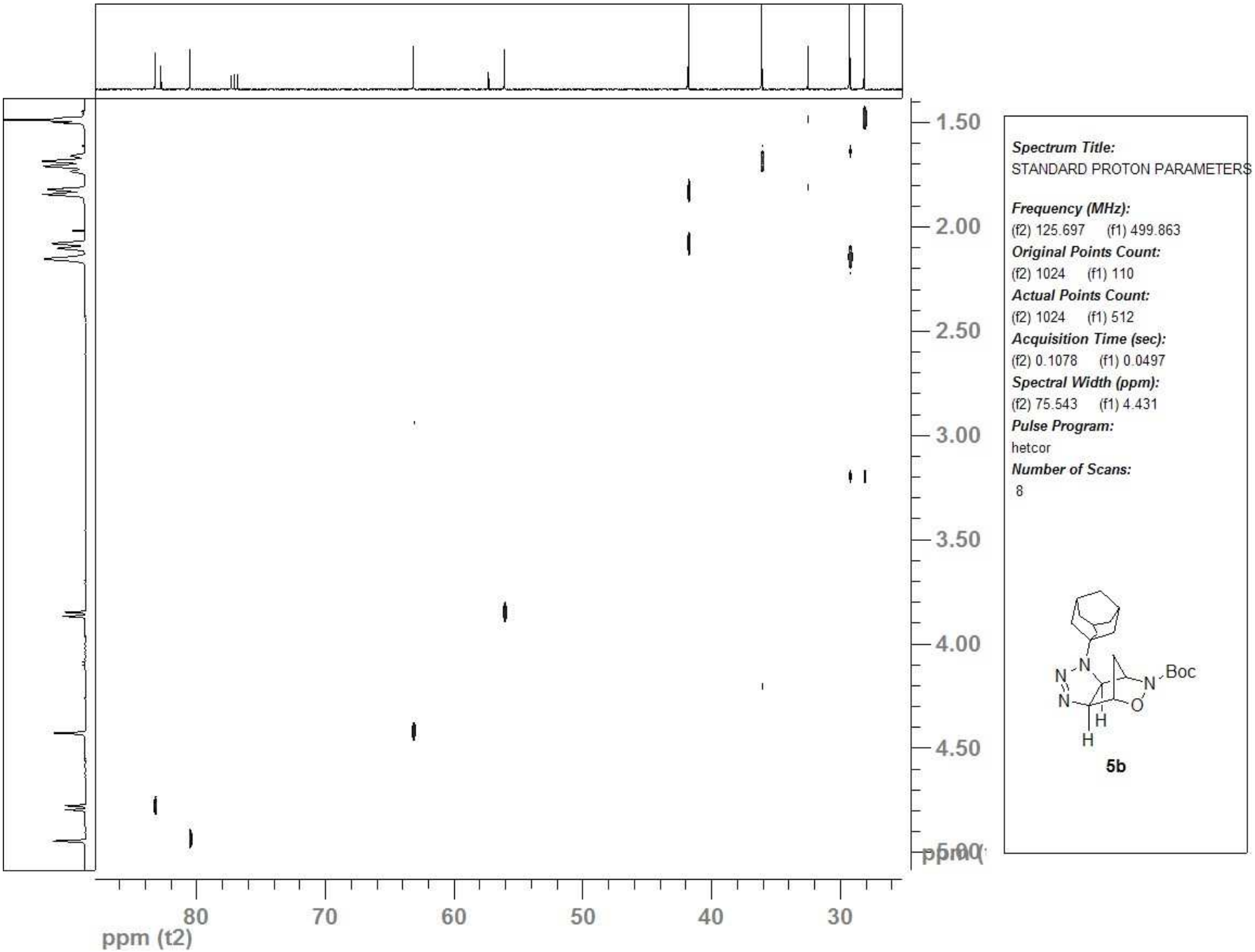


Figure 11. HETCOR spectrum of 5b

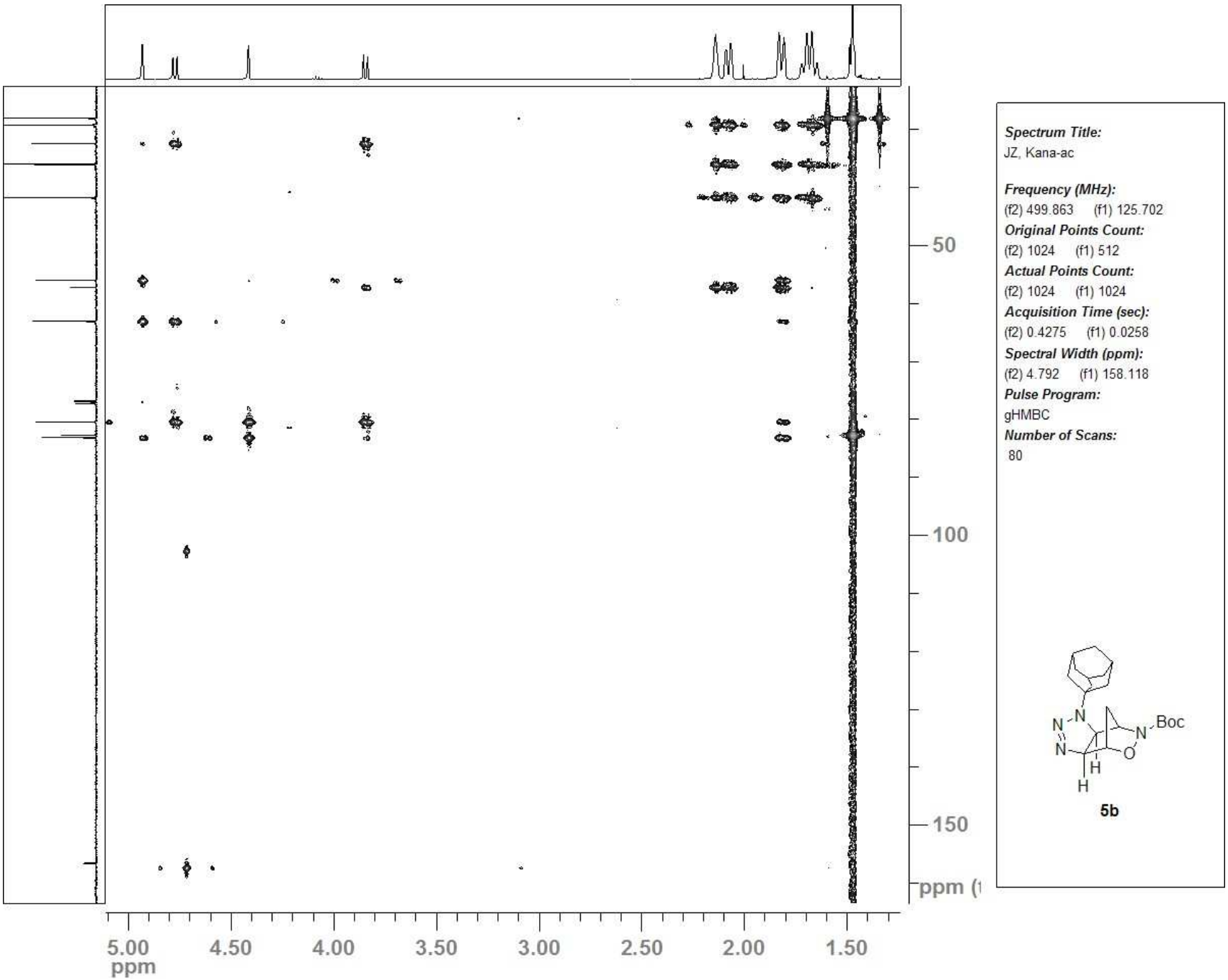
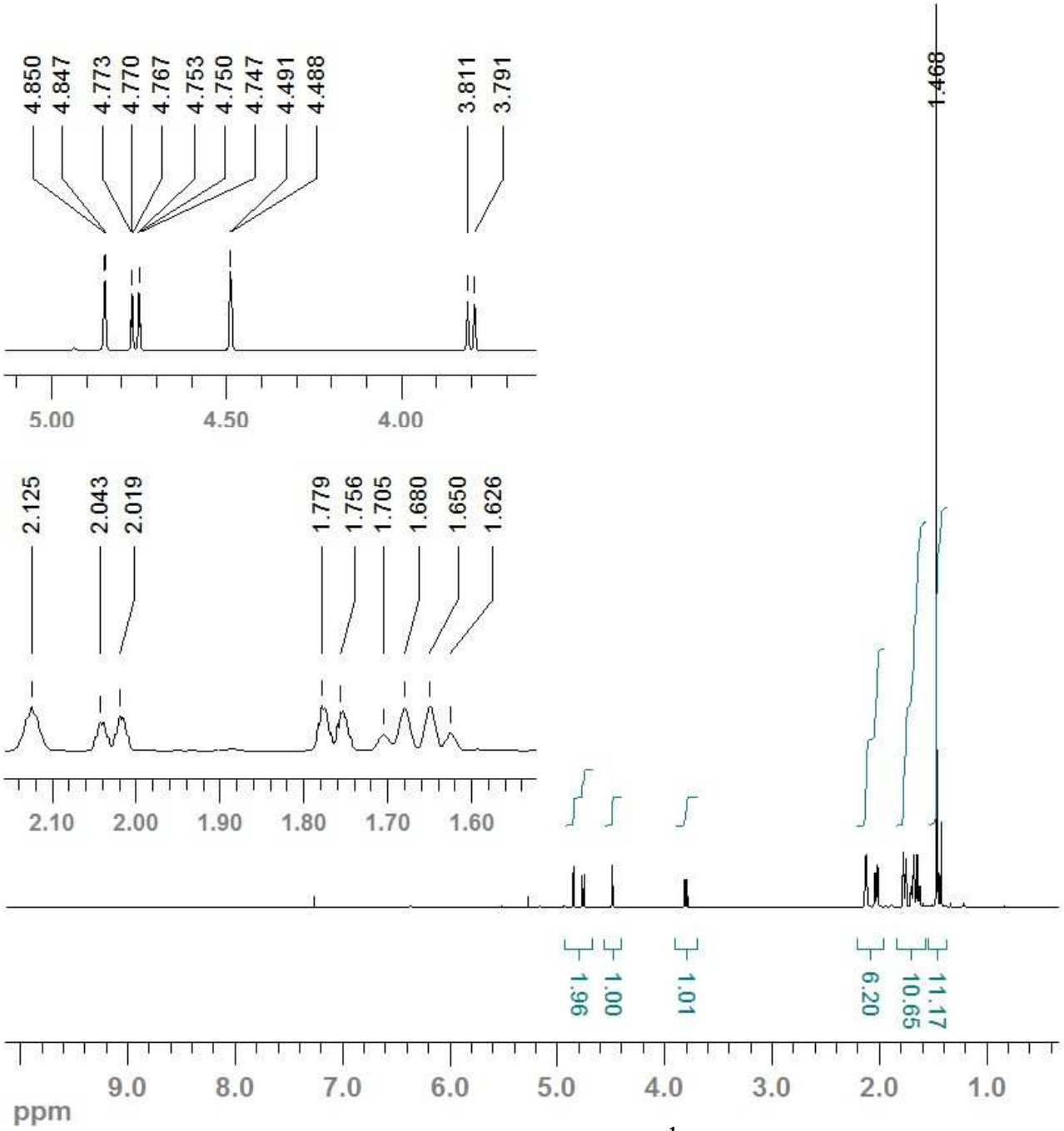


Figure 12. gHMBC spectrum of 5b



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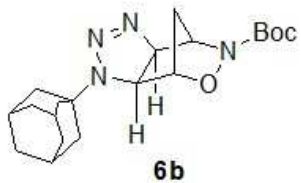
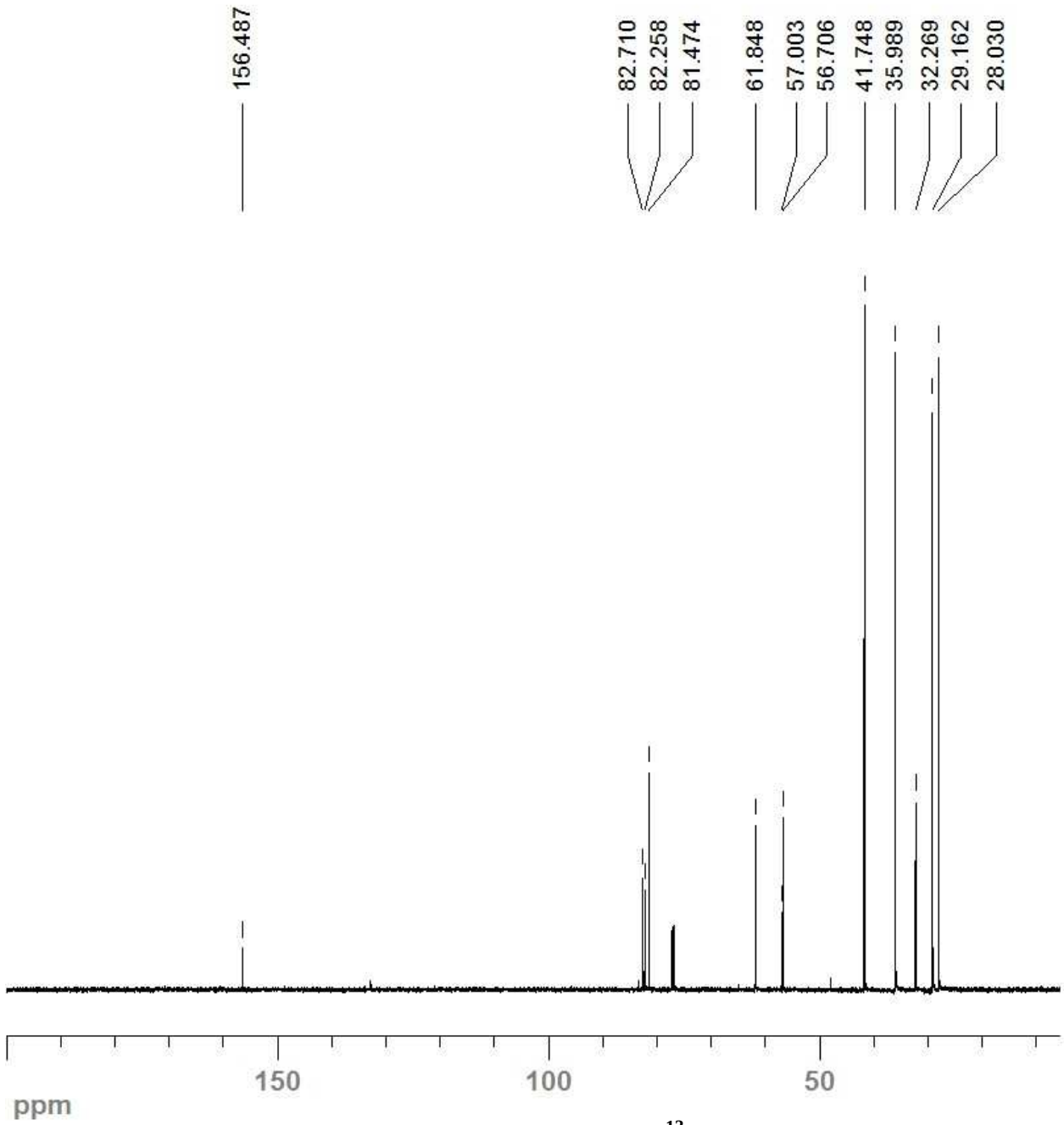


6b

Figure 13. ^{1}H NMR spectrum of 6b



Spectrum Title:
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Pulse Program:
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Number of Scans:
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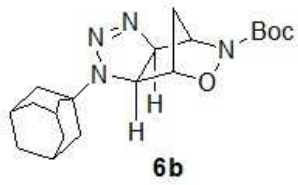


6b

Figure 14. ^{13}C NMR spectrum of 6b

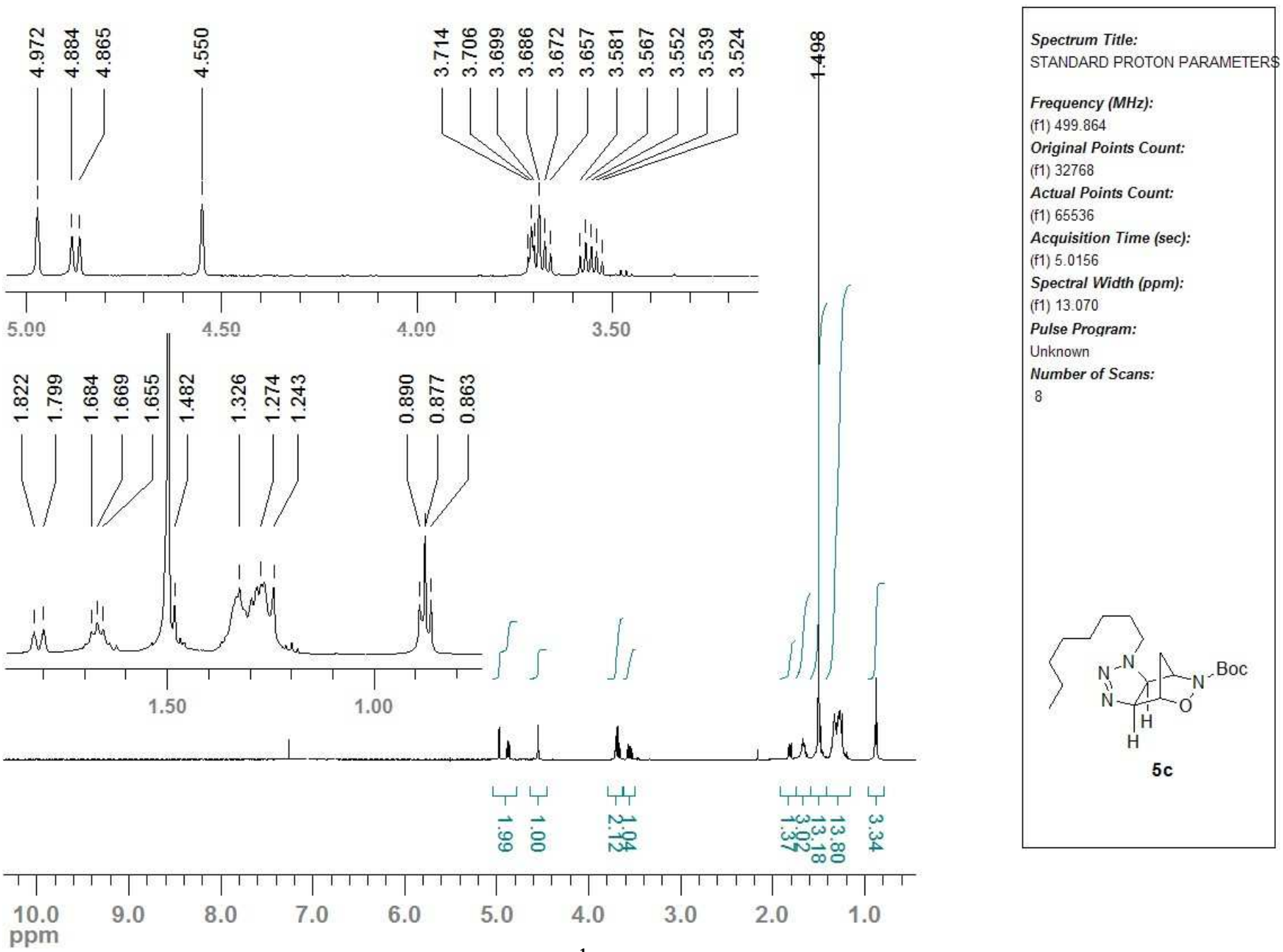
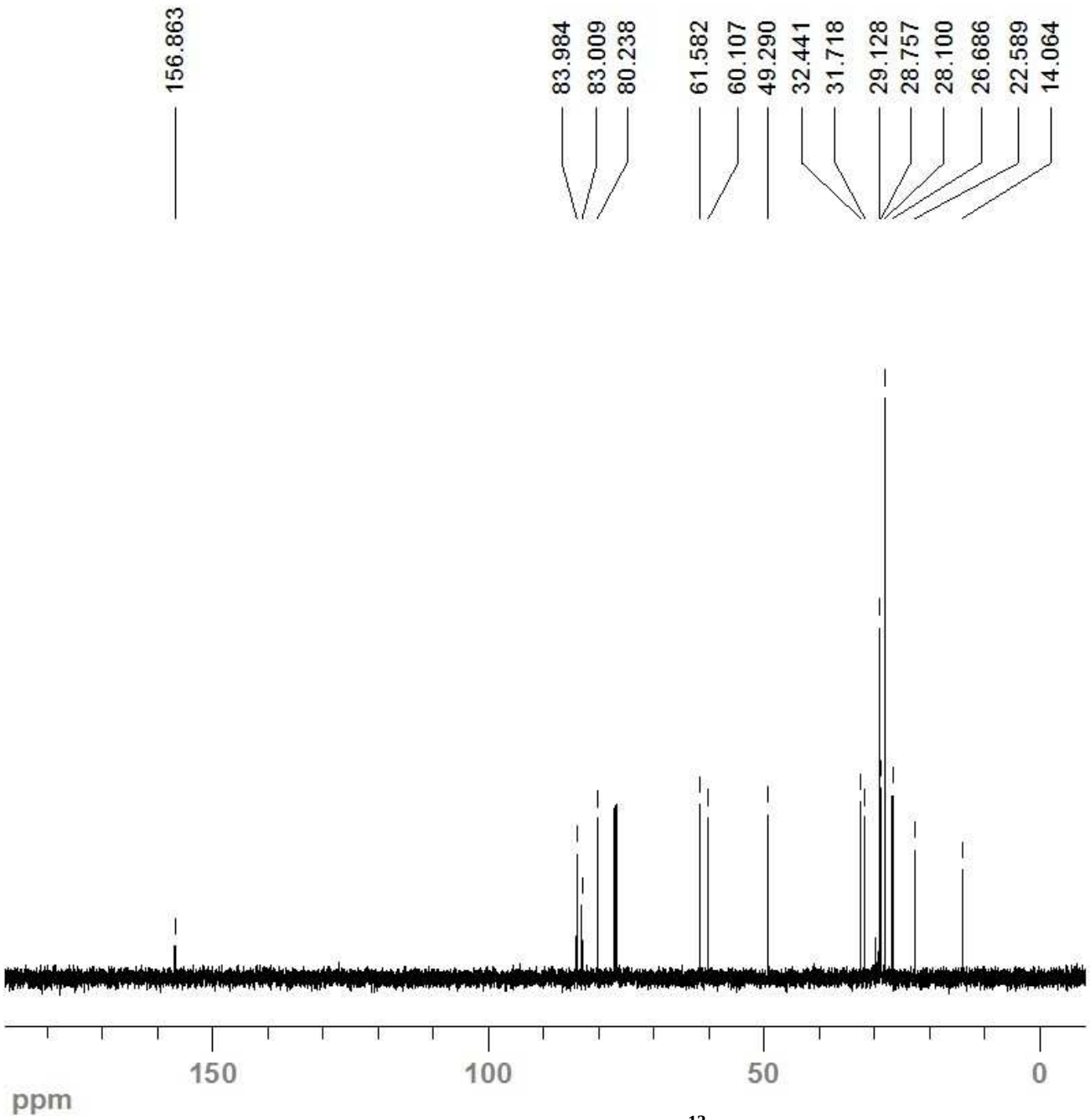
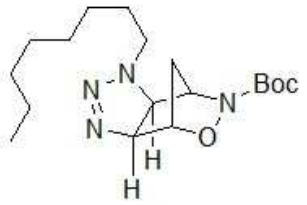


Figure 15. ^{1}H NMR spectrum of 5c



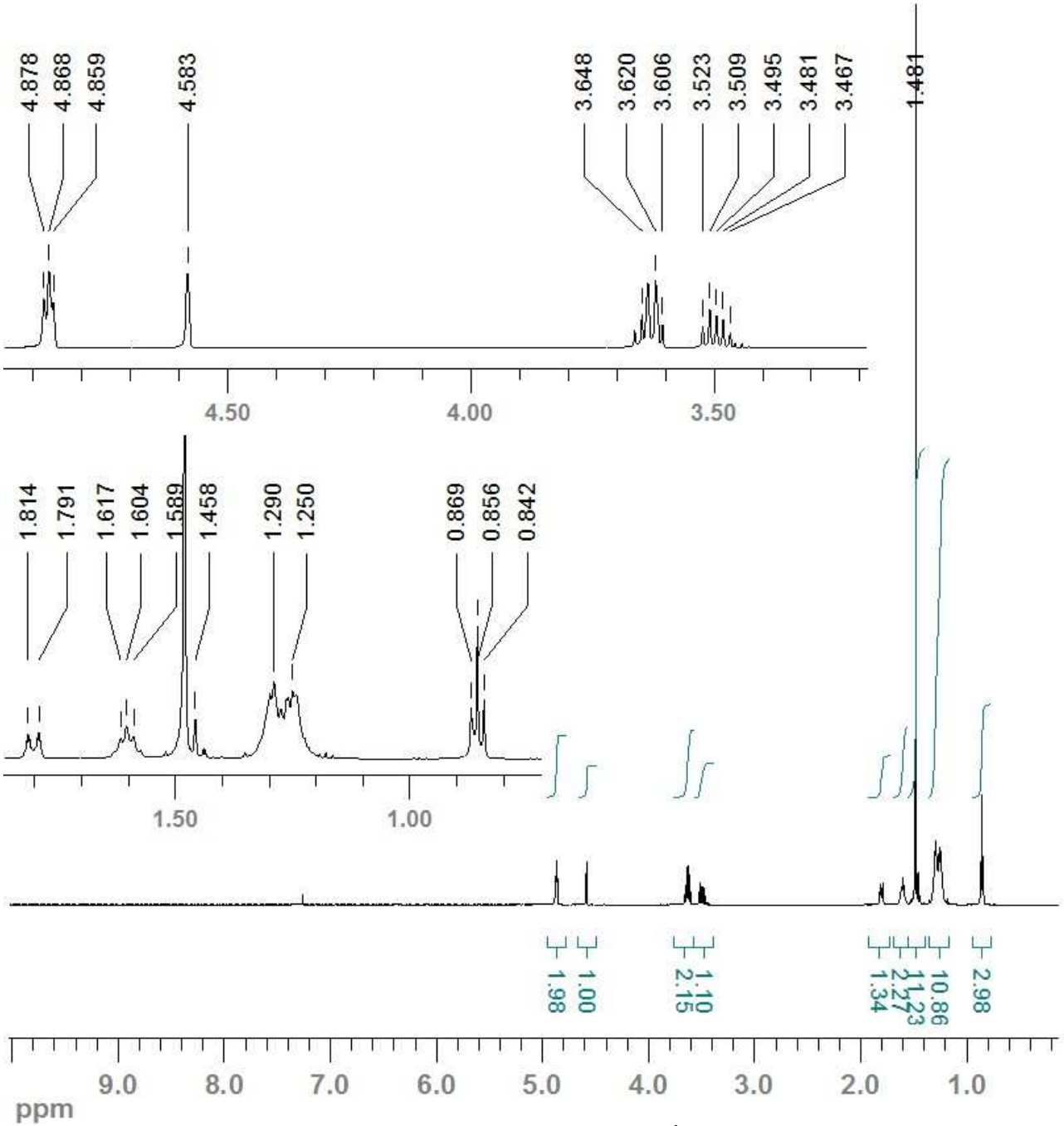
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



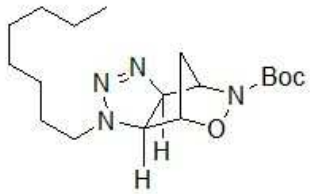
5c

Figure 16. ^{13}C NMR spectrum of 5c



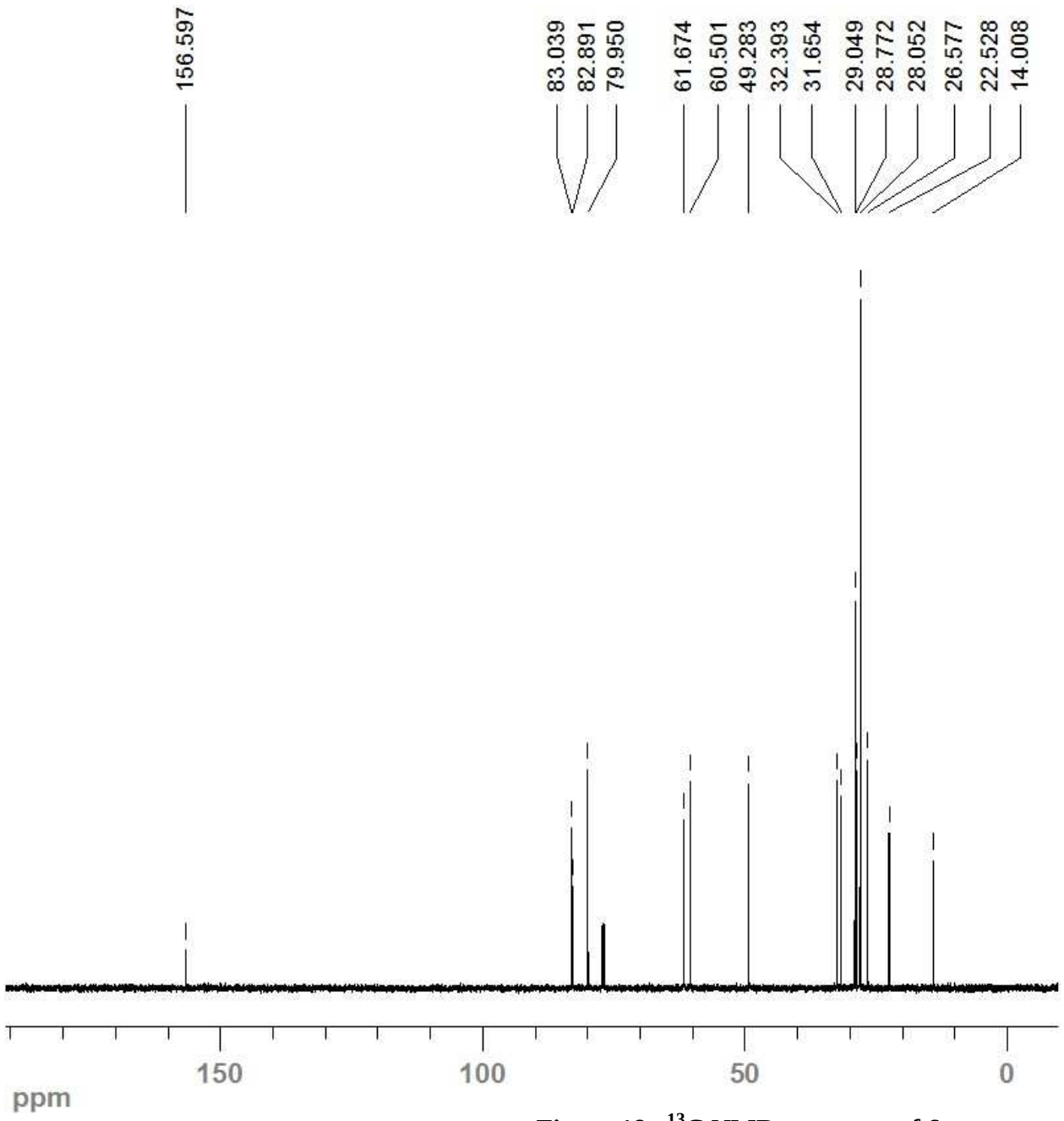
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 499.864
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 5.0156
Spectral Width (ppm):
(f1) 13.070
Pulse Program:
Unknown
Number of Scans:
8



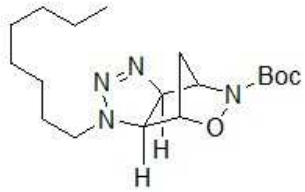
6c

Figure 17. ^{1}H NMR spectrum of 6c



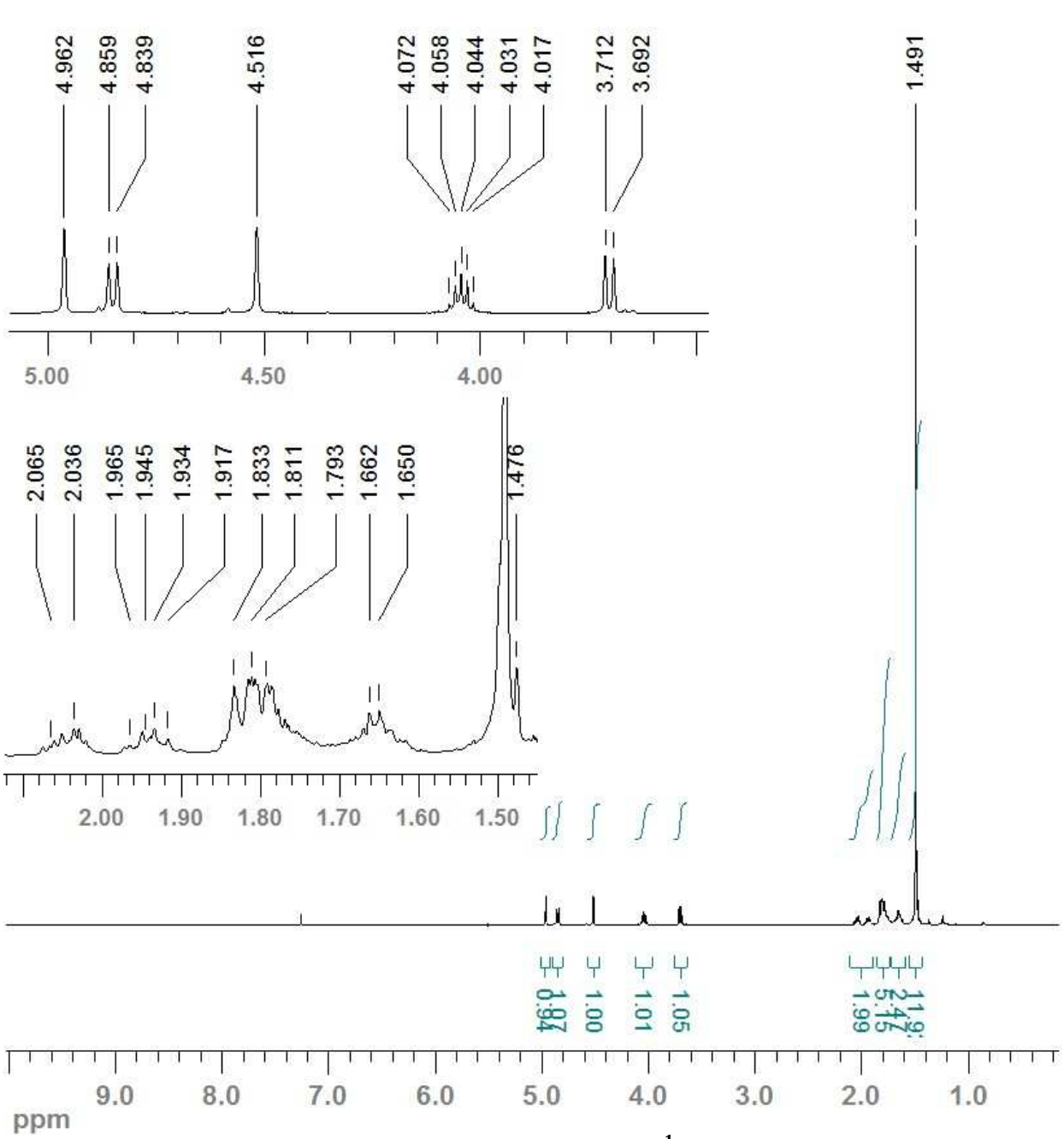
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



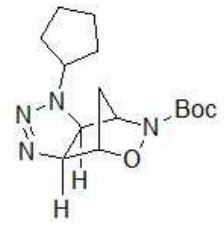
6c

Figure 18. ^{13}C NMR spectrum of 6c



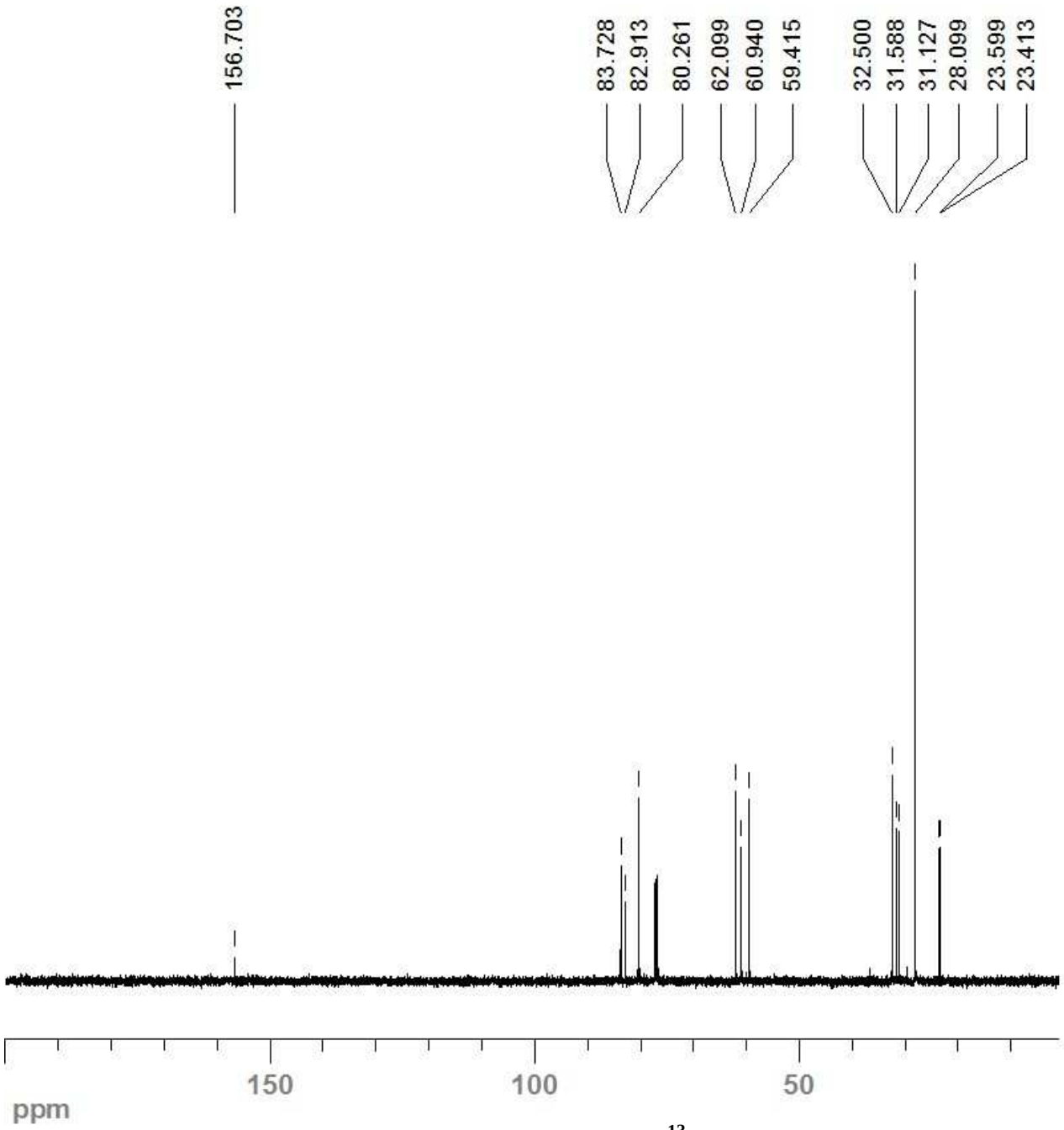
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 499.864
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 5.0156
Spectral Width (ppm):
(f1) 13.070
Pulse Program:
Unknown
Number of Scans:
8



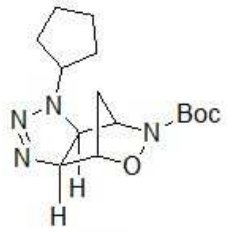
5d

Figure 19. ^{1}H NMR spectrum of 5d



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
128



5d

Figure 20. ^{13}C NMR spectrum of 5d

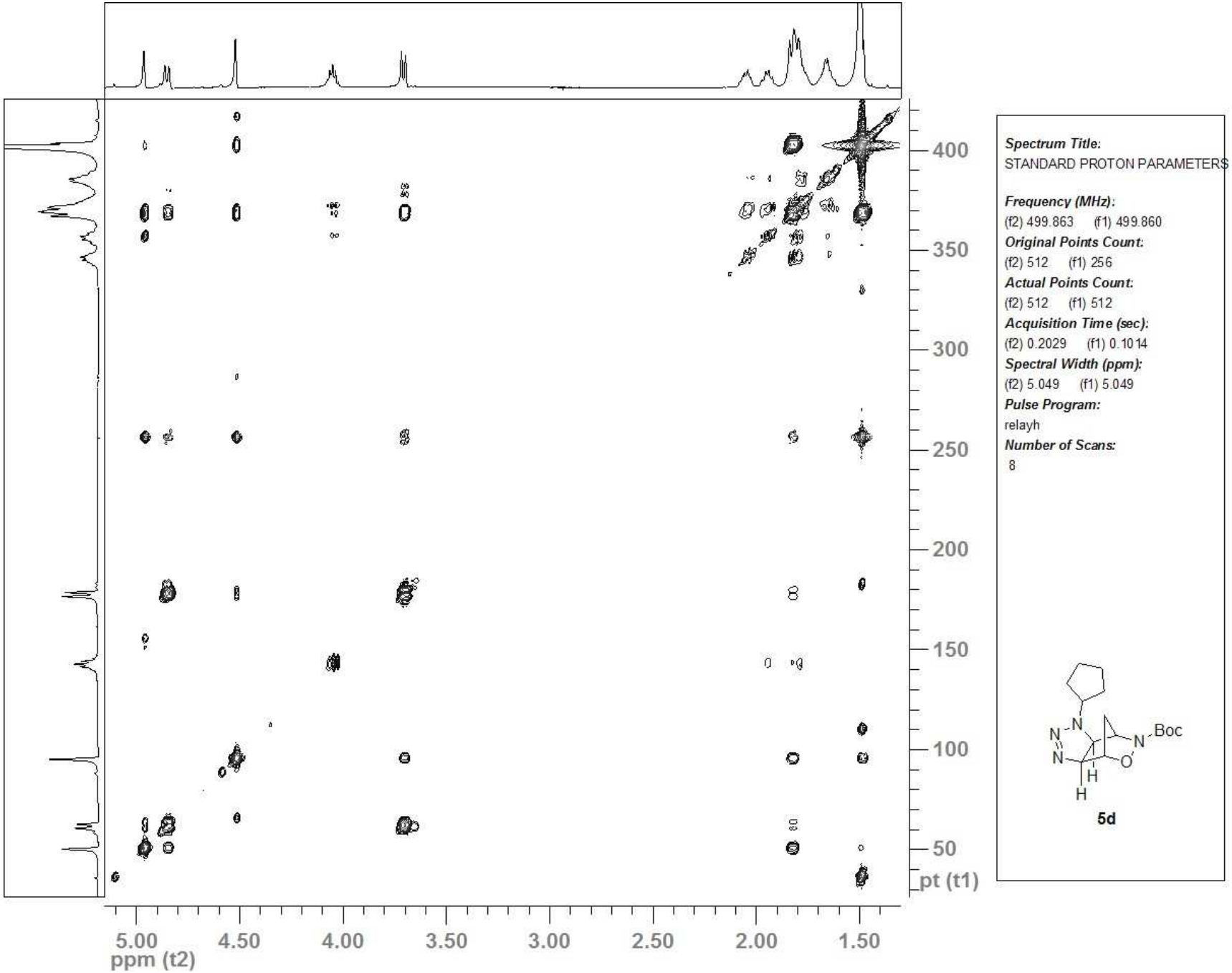


Figure 21. COSY spectrum of 5d

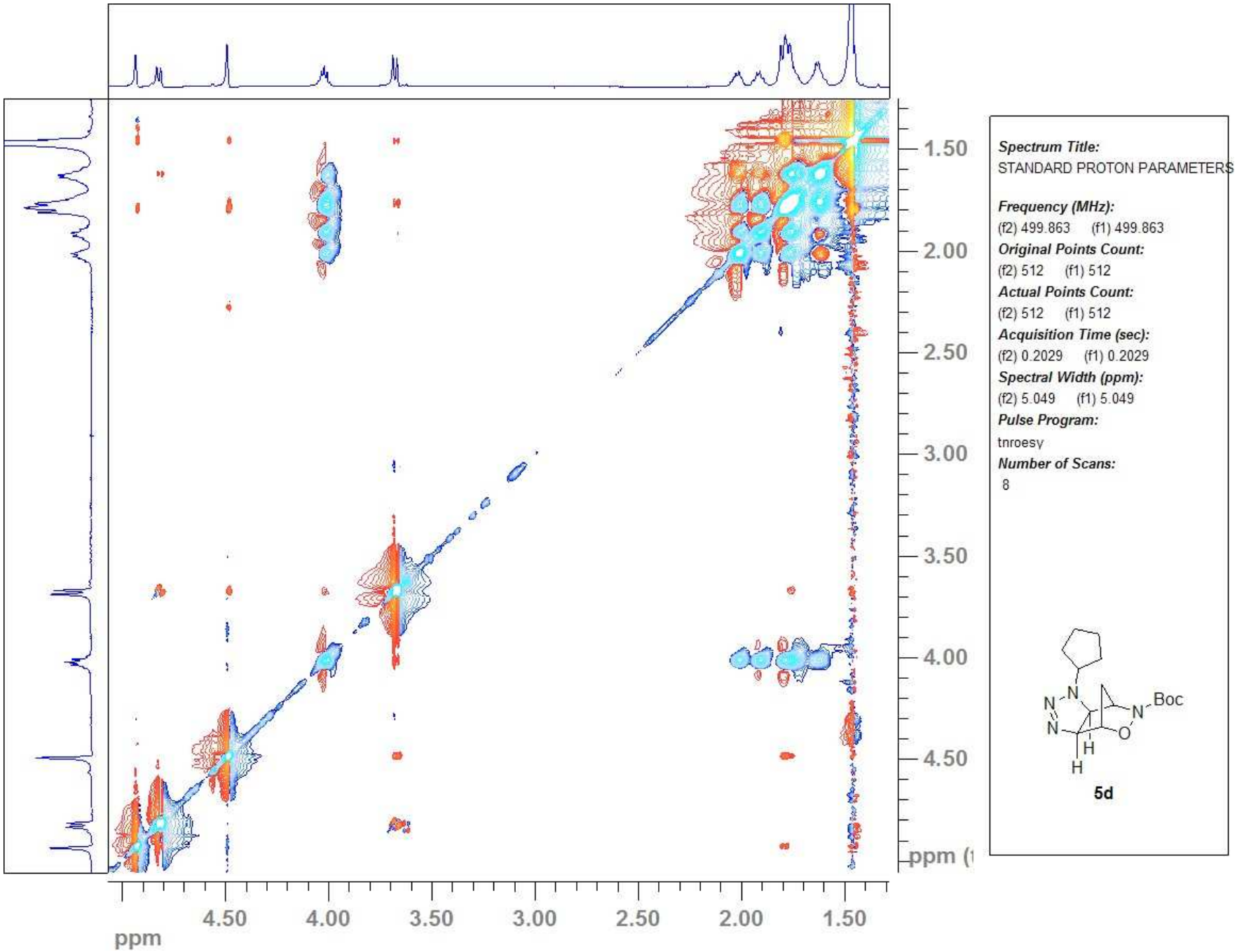


Figure 22. ROESY spectrum of 5d

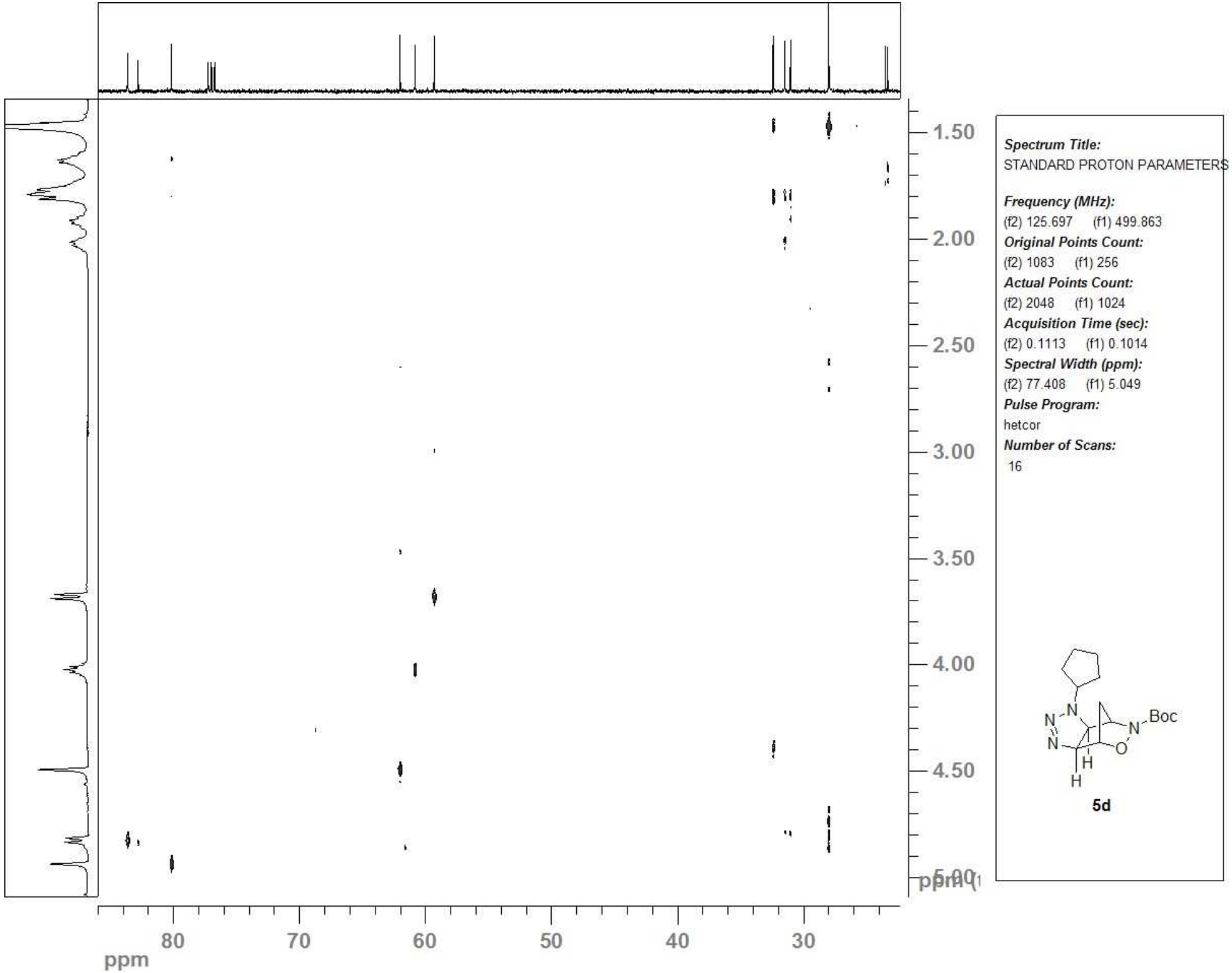


Figure 23. HETCOR spectrum of 5d

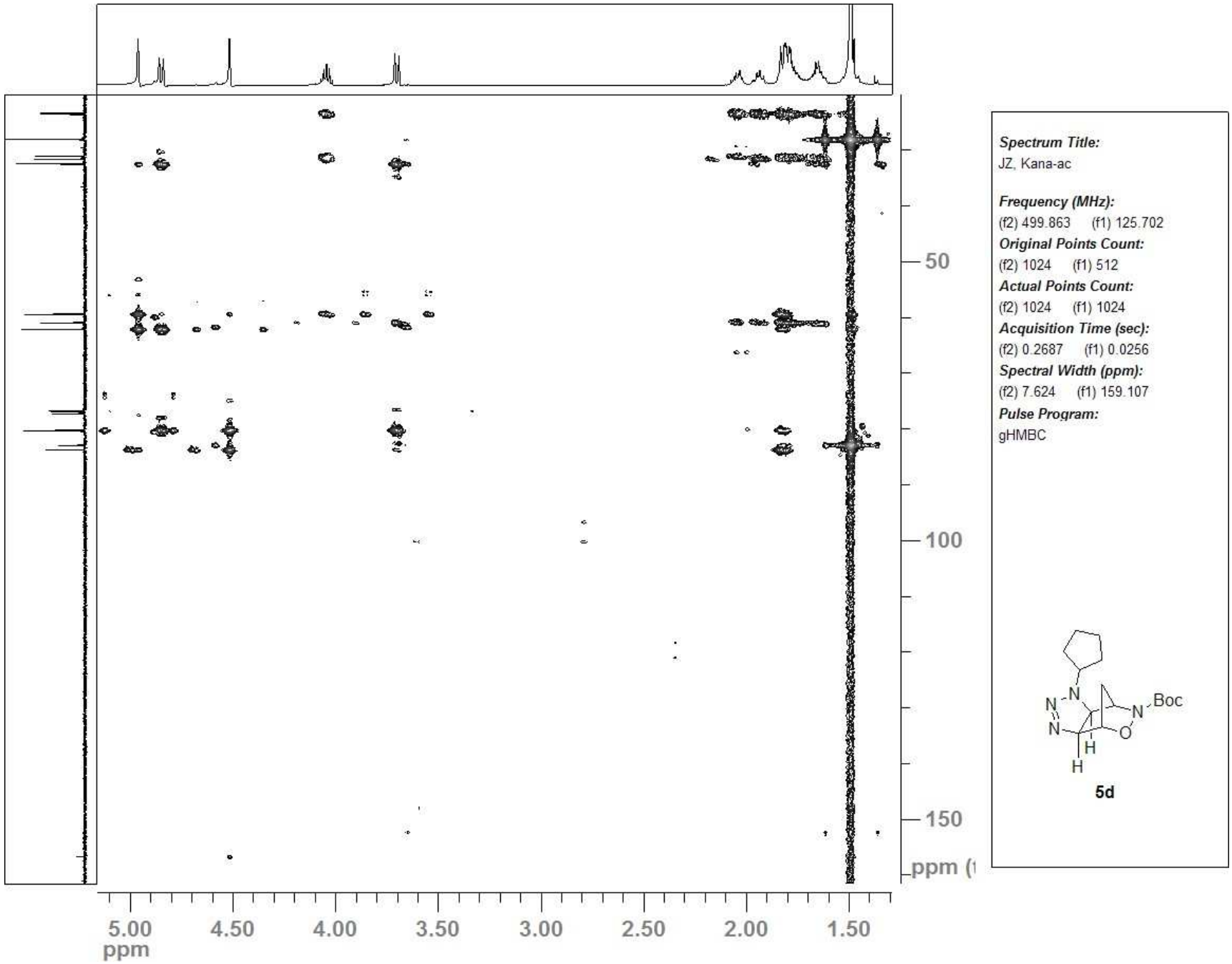
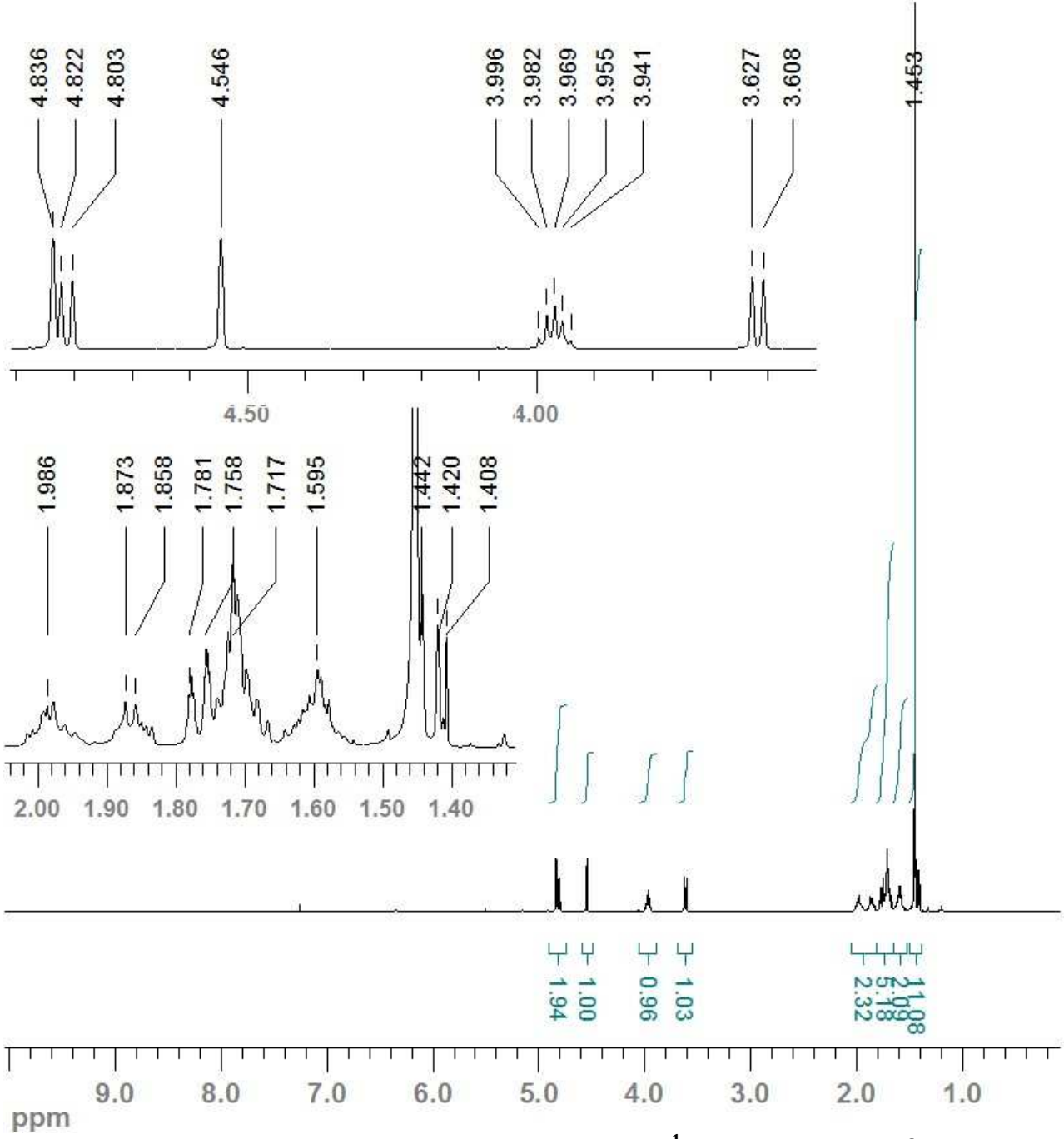
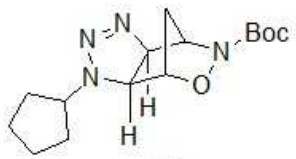


Figure 24. gHMBC spectrum of 5d



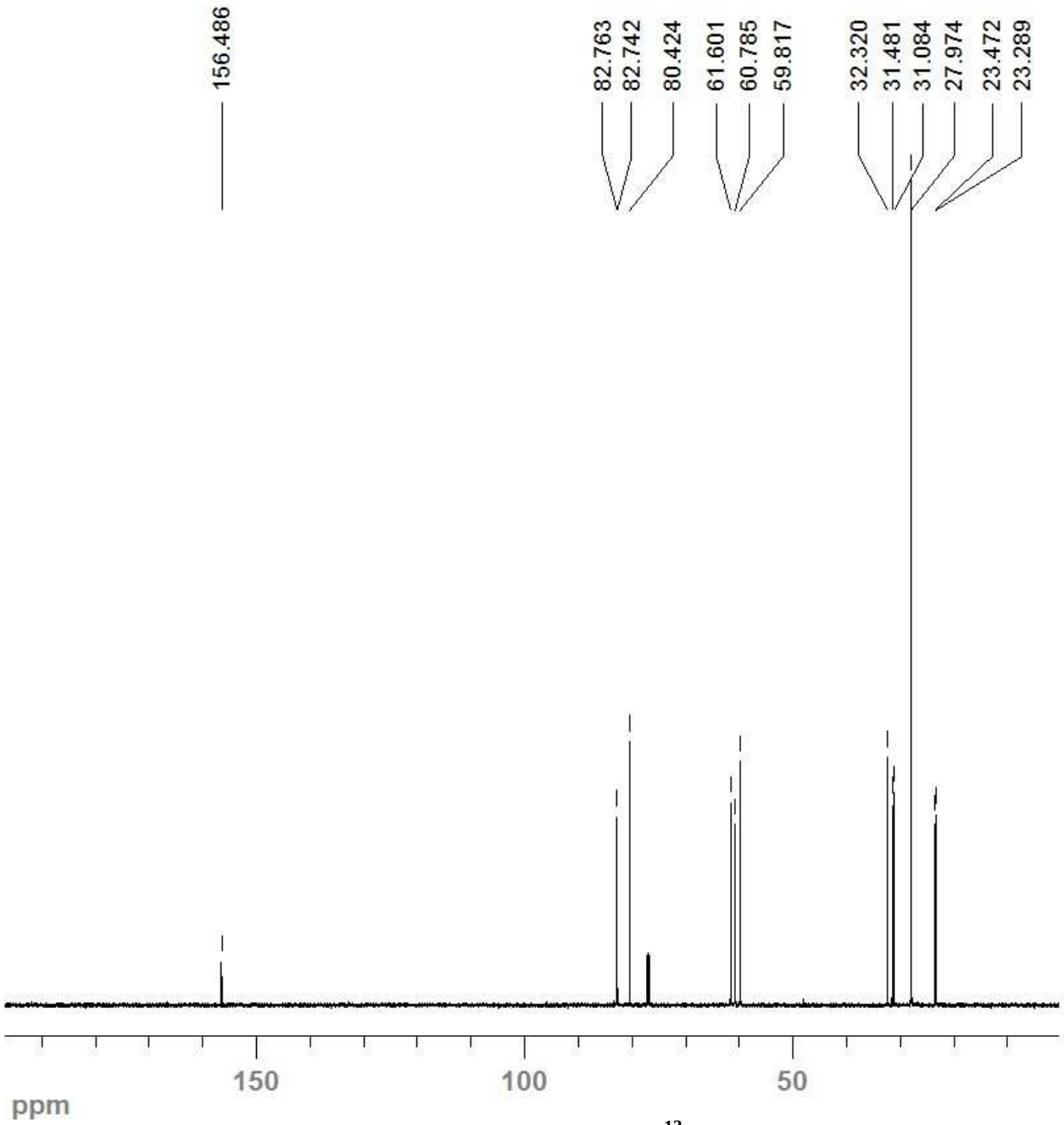
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 499.864
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 5.0156
Spectral Width (ppm):
(f1) 13.070
Pulse Program:
Unknown
Number of Scans:
8



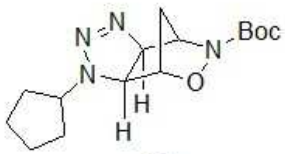
6d

Figure 25. ^{1}H NMR spectrum of 6d



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



6d

Figure 26. ^{13}C NMR spectrum of 6d

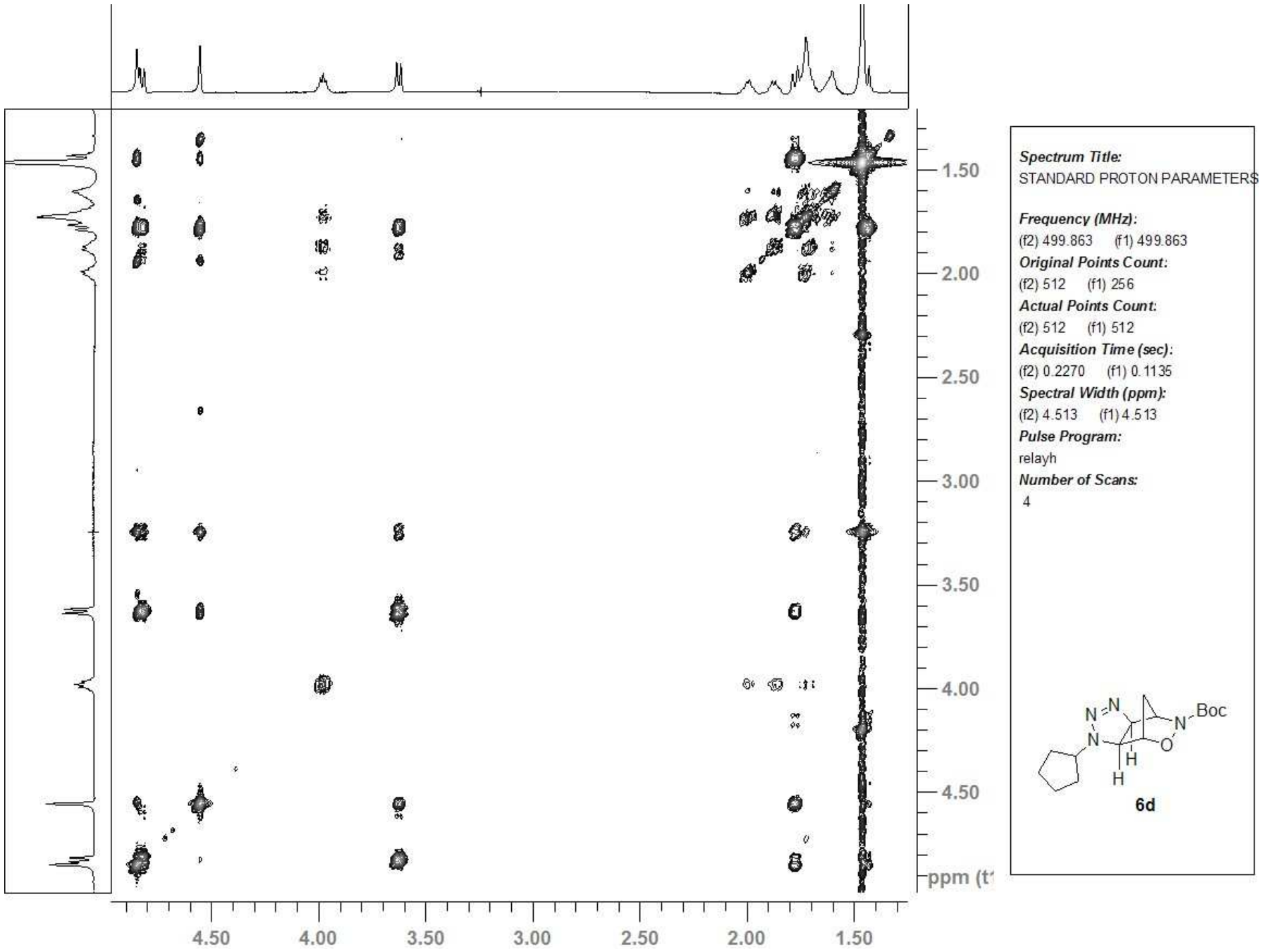


Figure 27. COSY spectrum of 6d

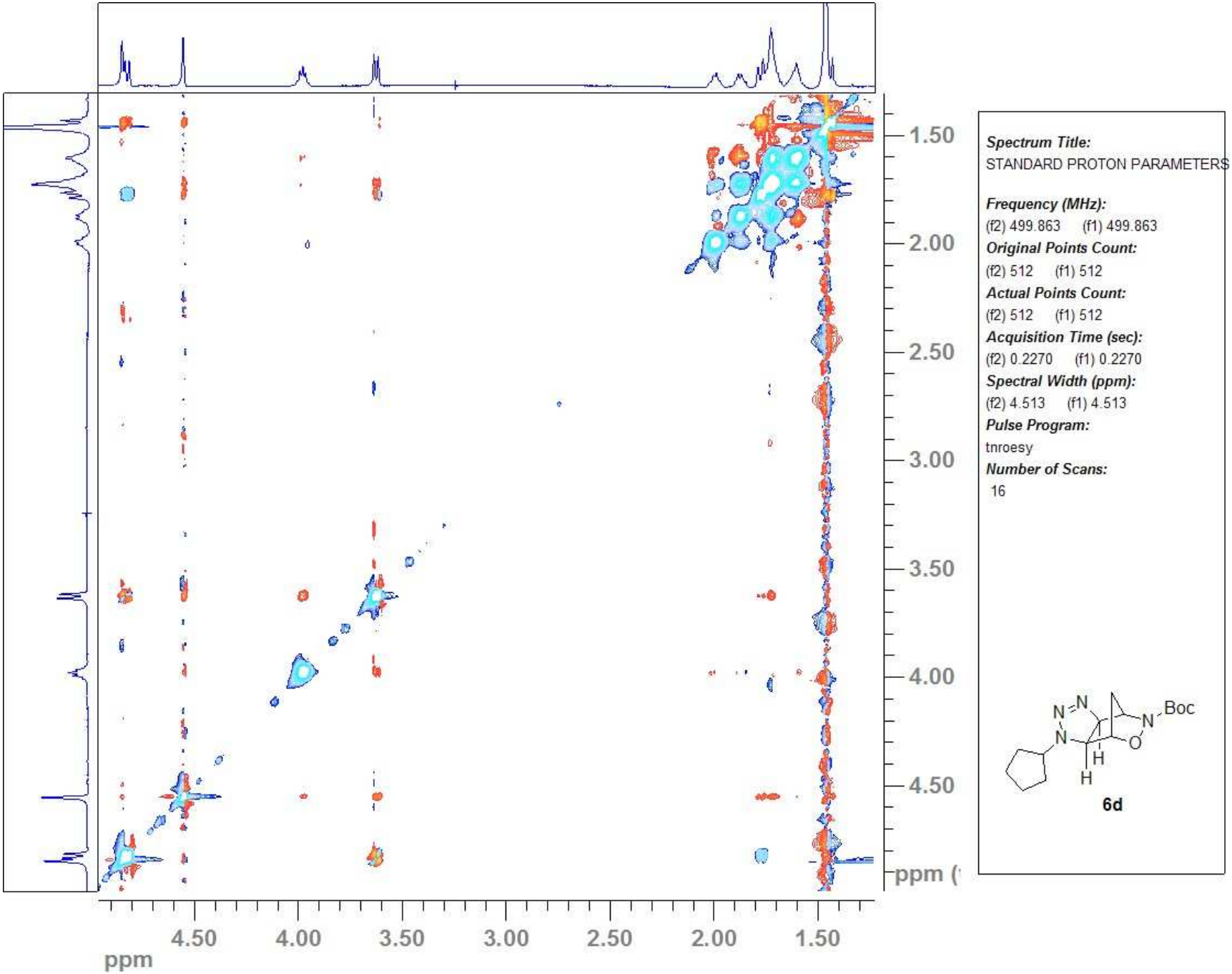


Figure 28. ROESY spectrum of 6d

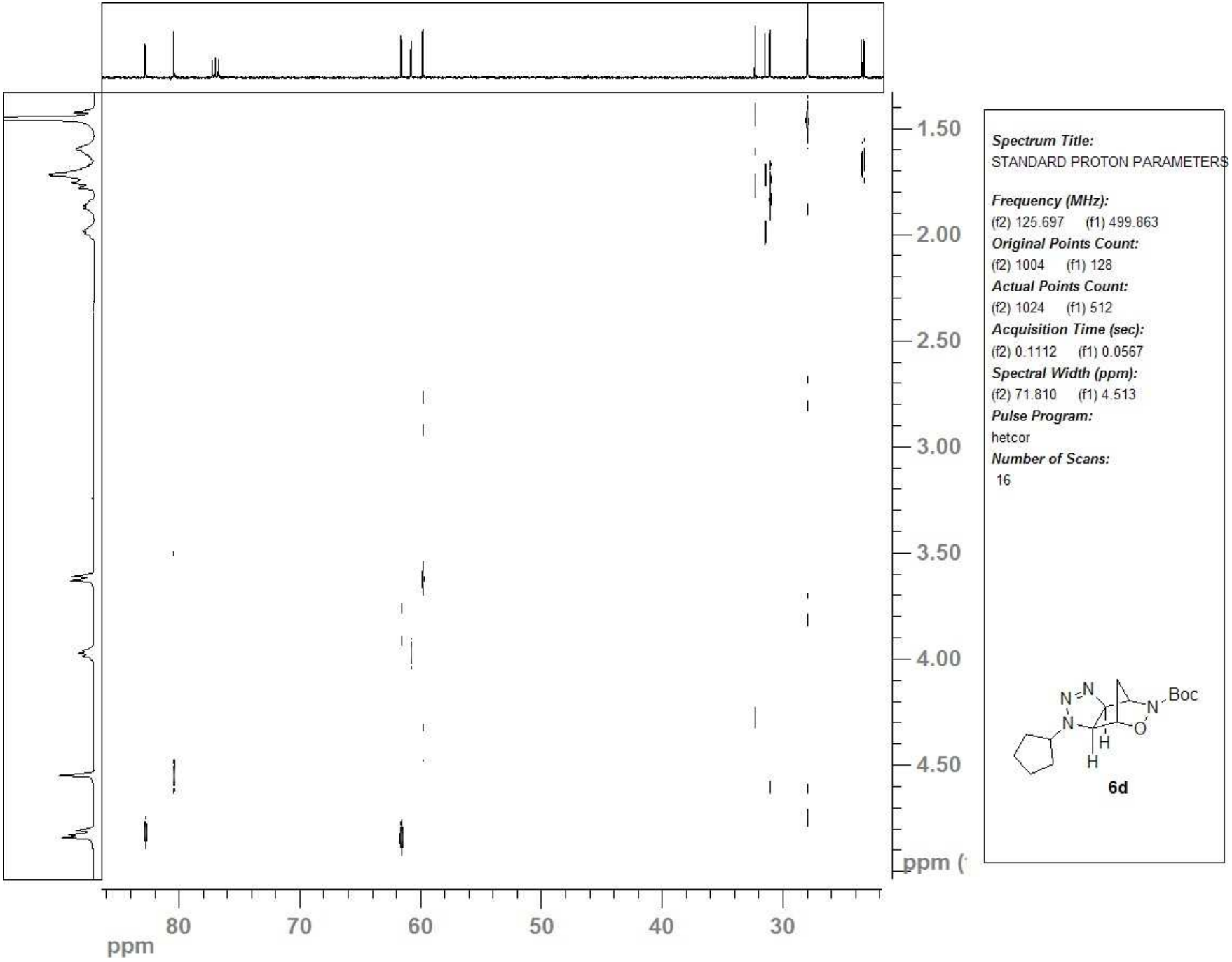


Figure 29. HETCOR spectrum of 6d

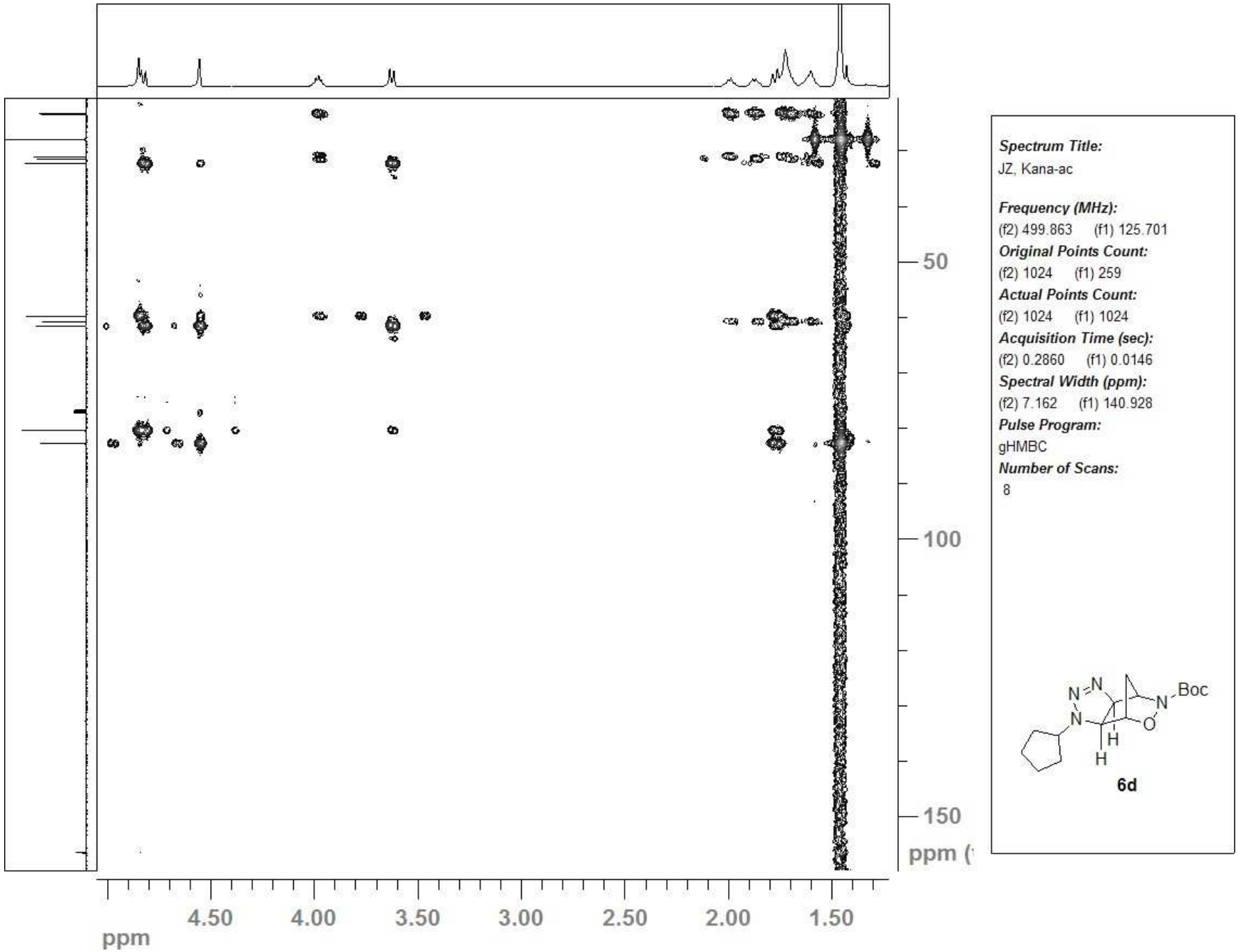


Figure 30. gHMBC spectrum of 6d

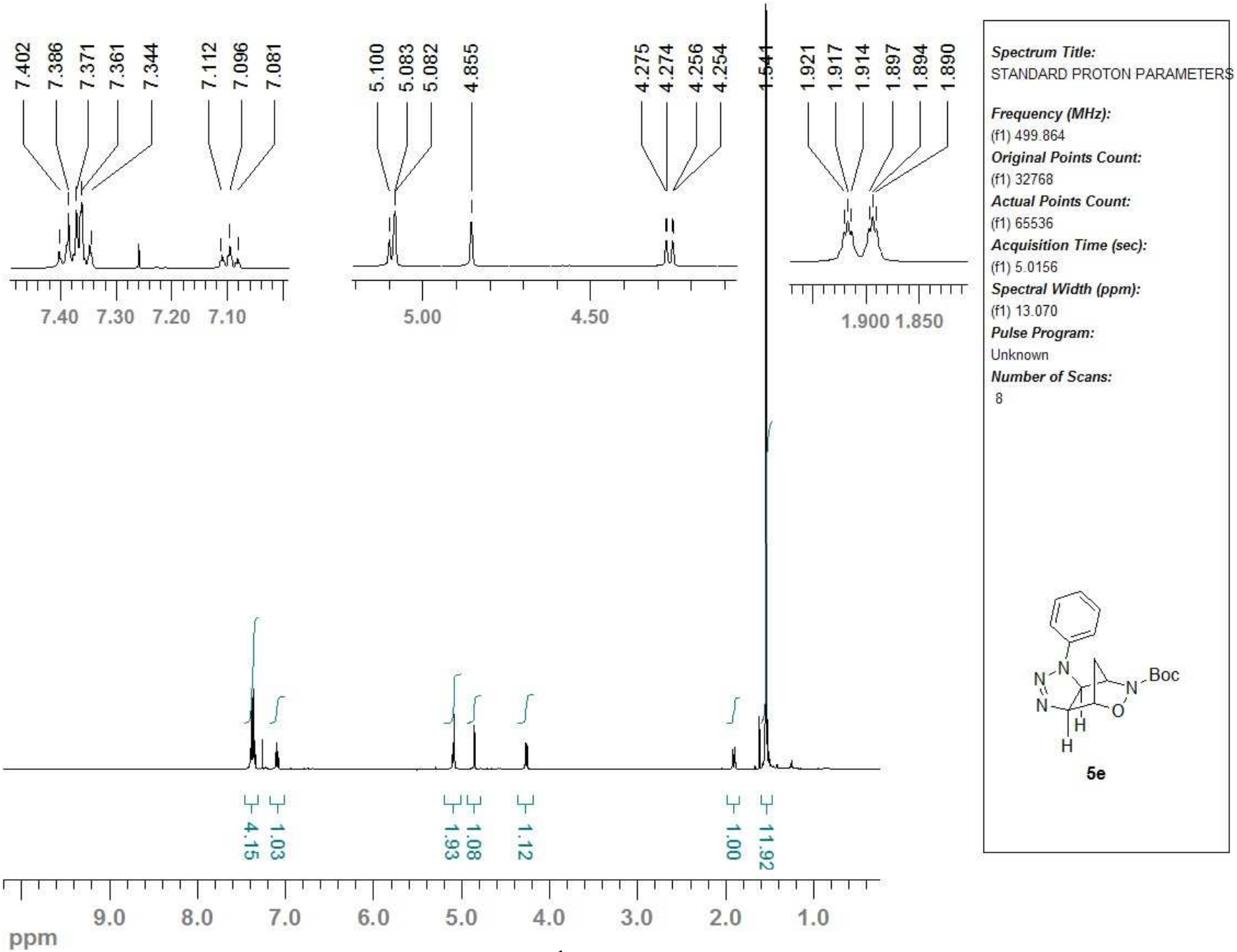
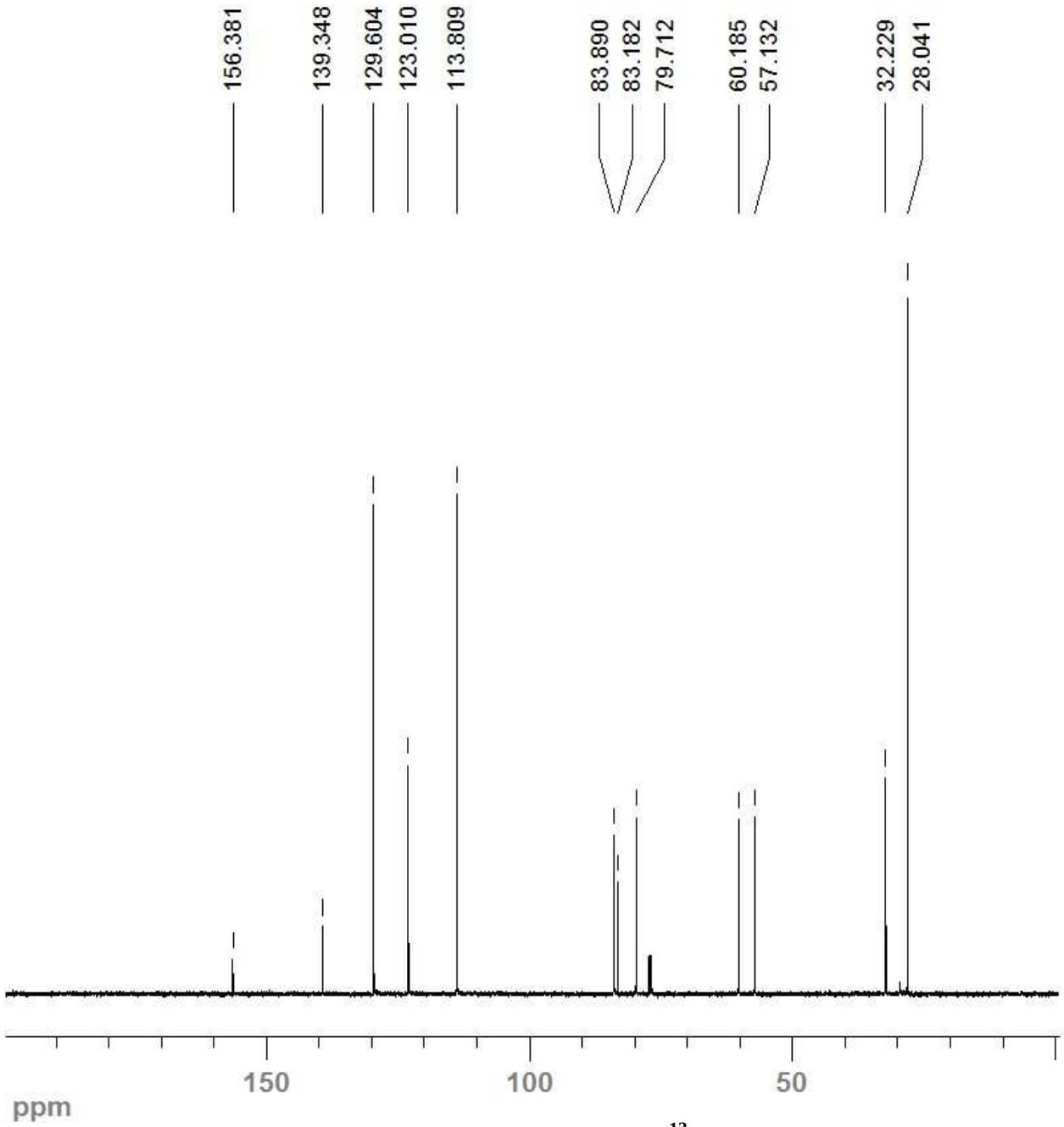
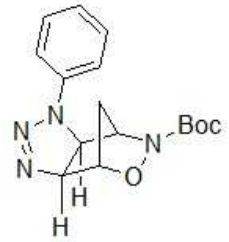


Figure 31. ^{1}H NMR spectrum of 5e



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



5e

Figure 32. ^{13}C NMR spectrum of 5e

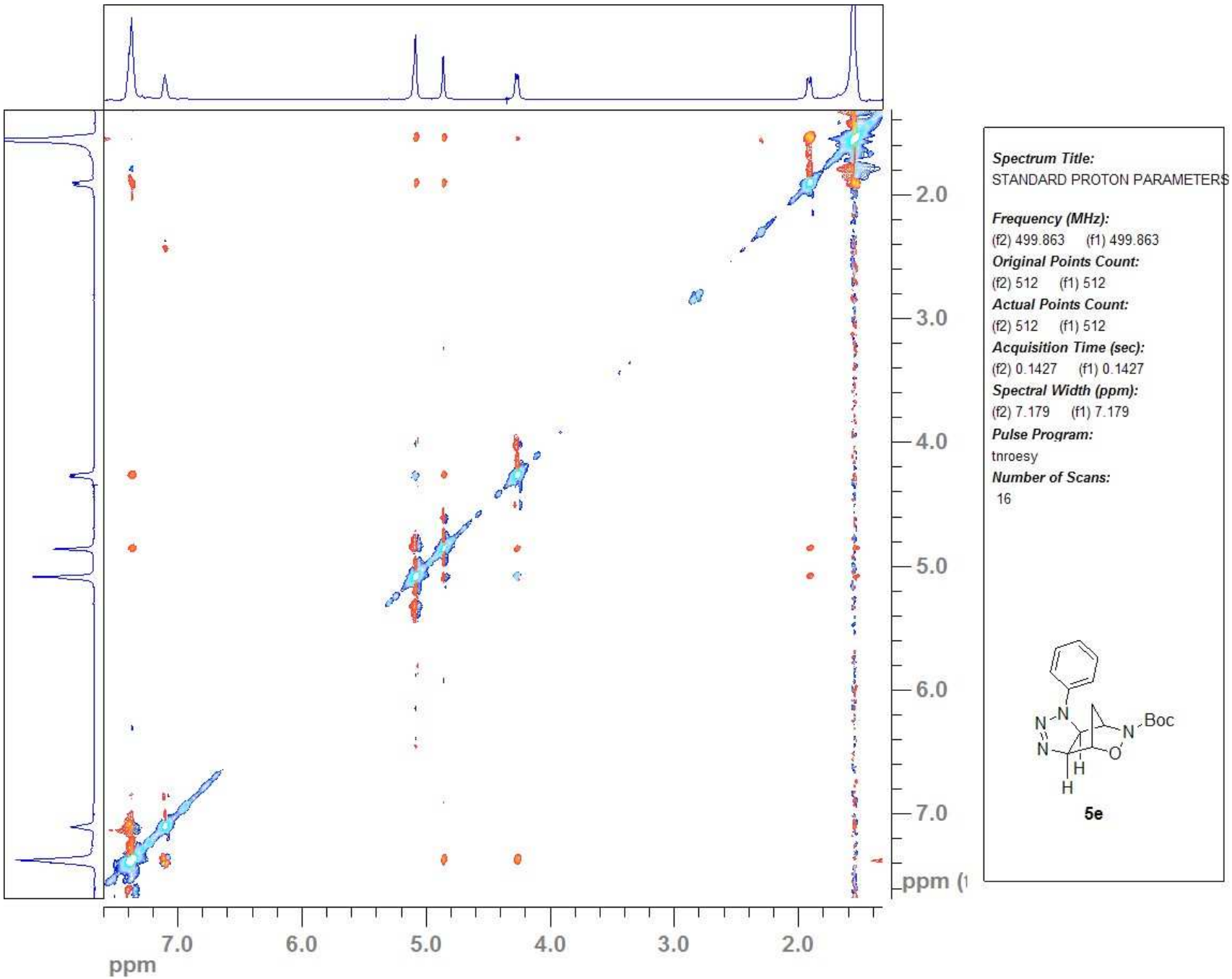


Figure 33. ROESY spectrum of 5e

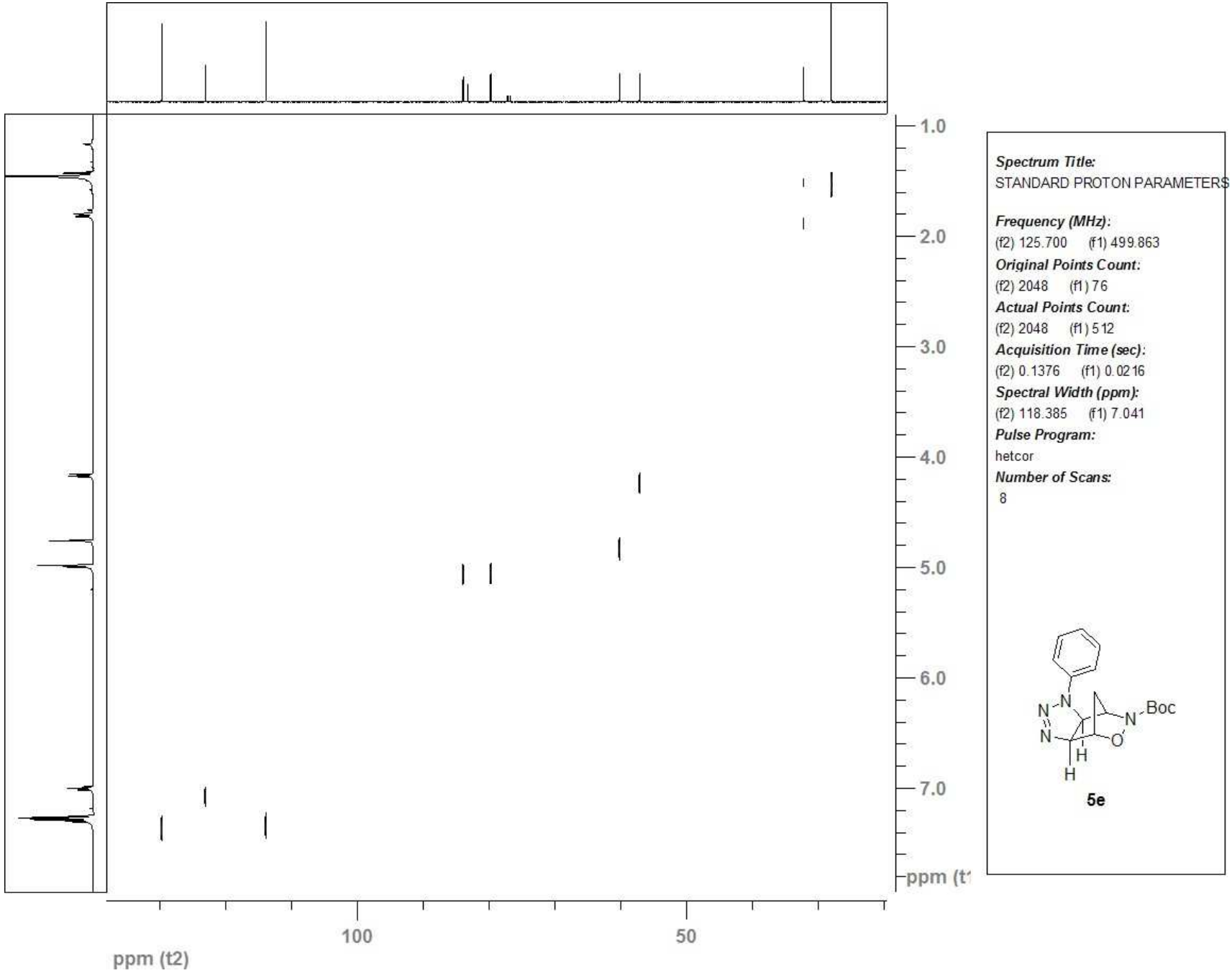


Figure 34. HETCOR spectrum of 5e

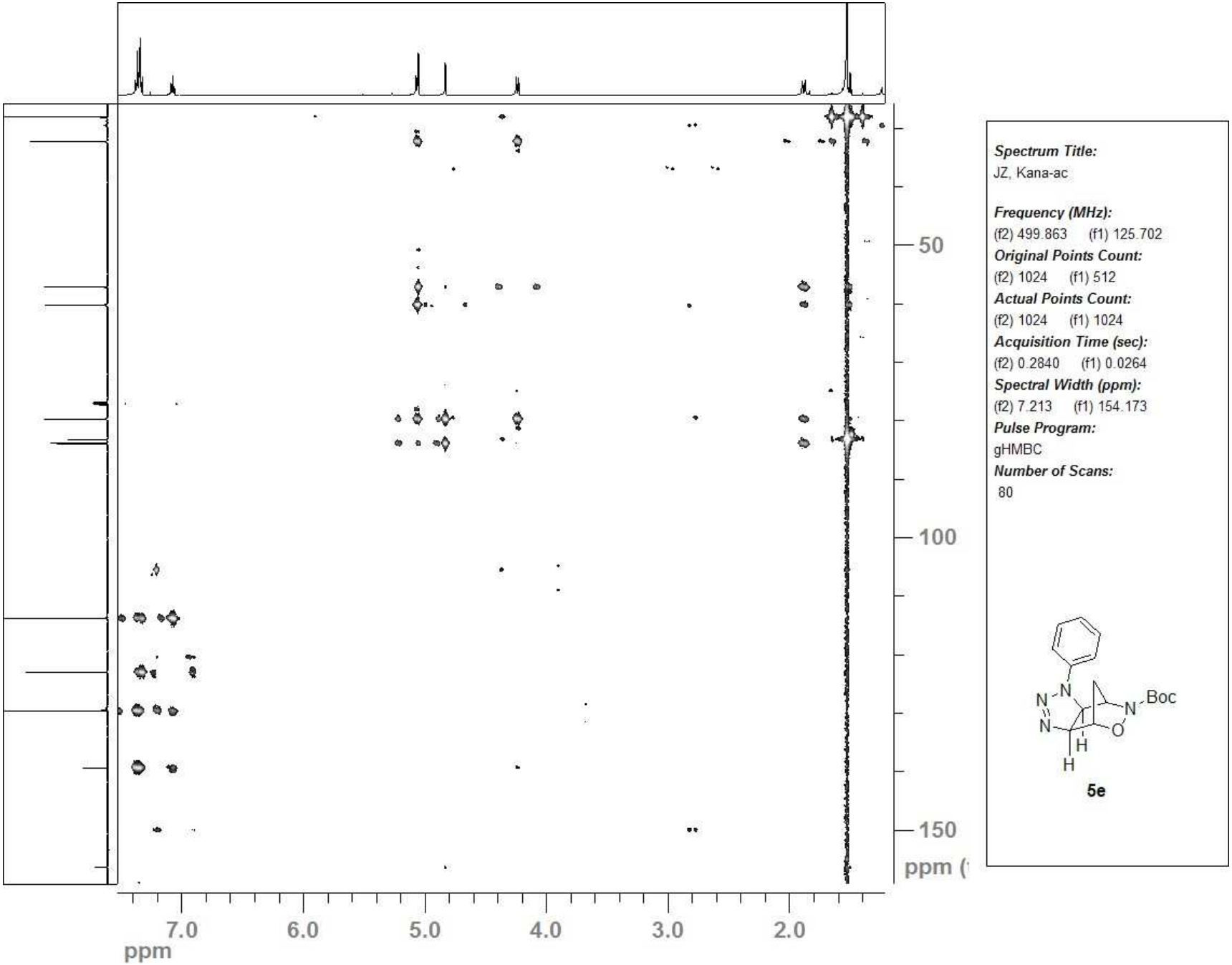


Figure 35. gHMBC spectrum of 5e

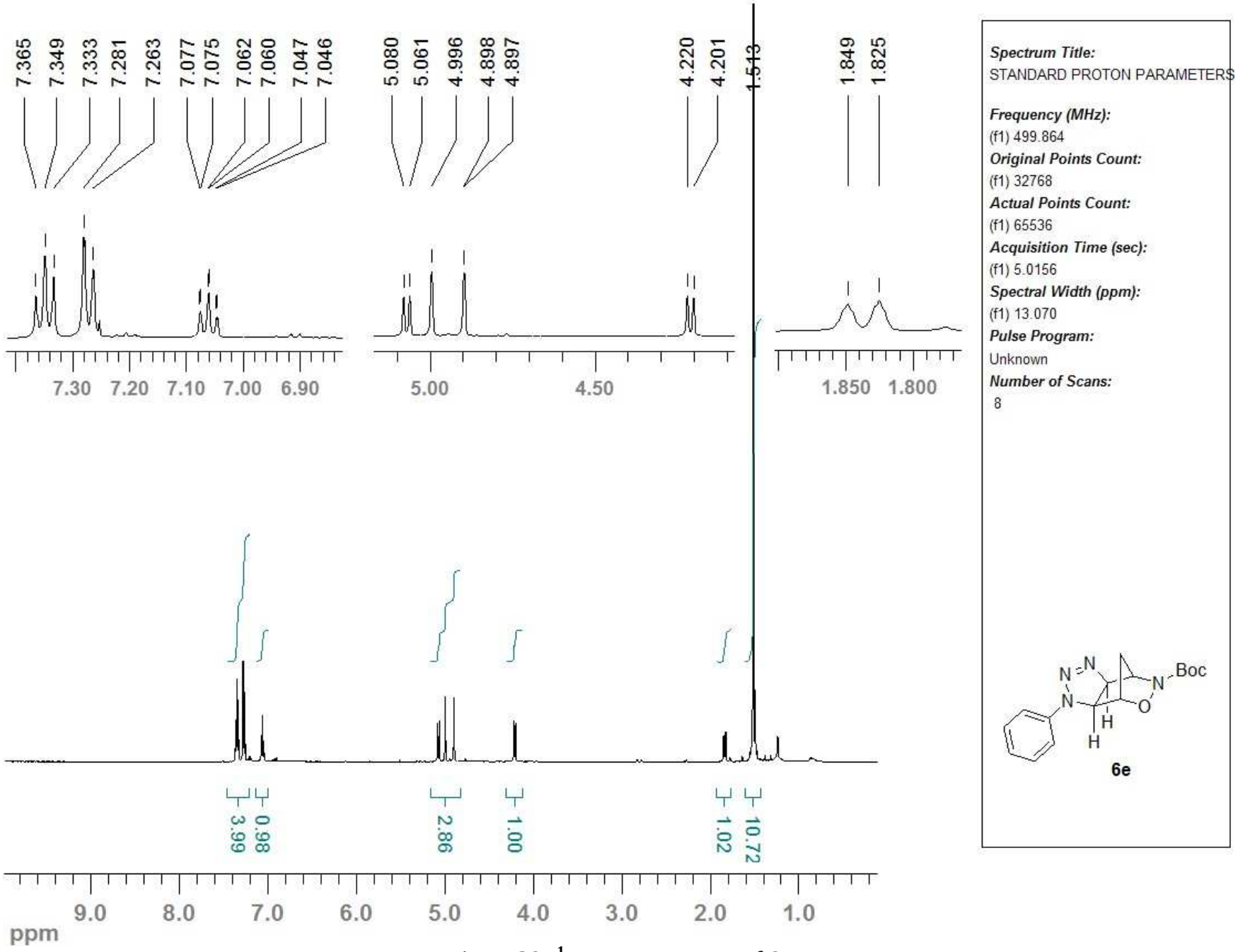
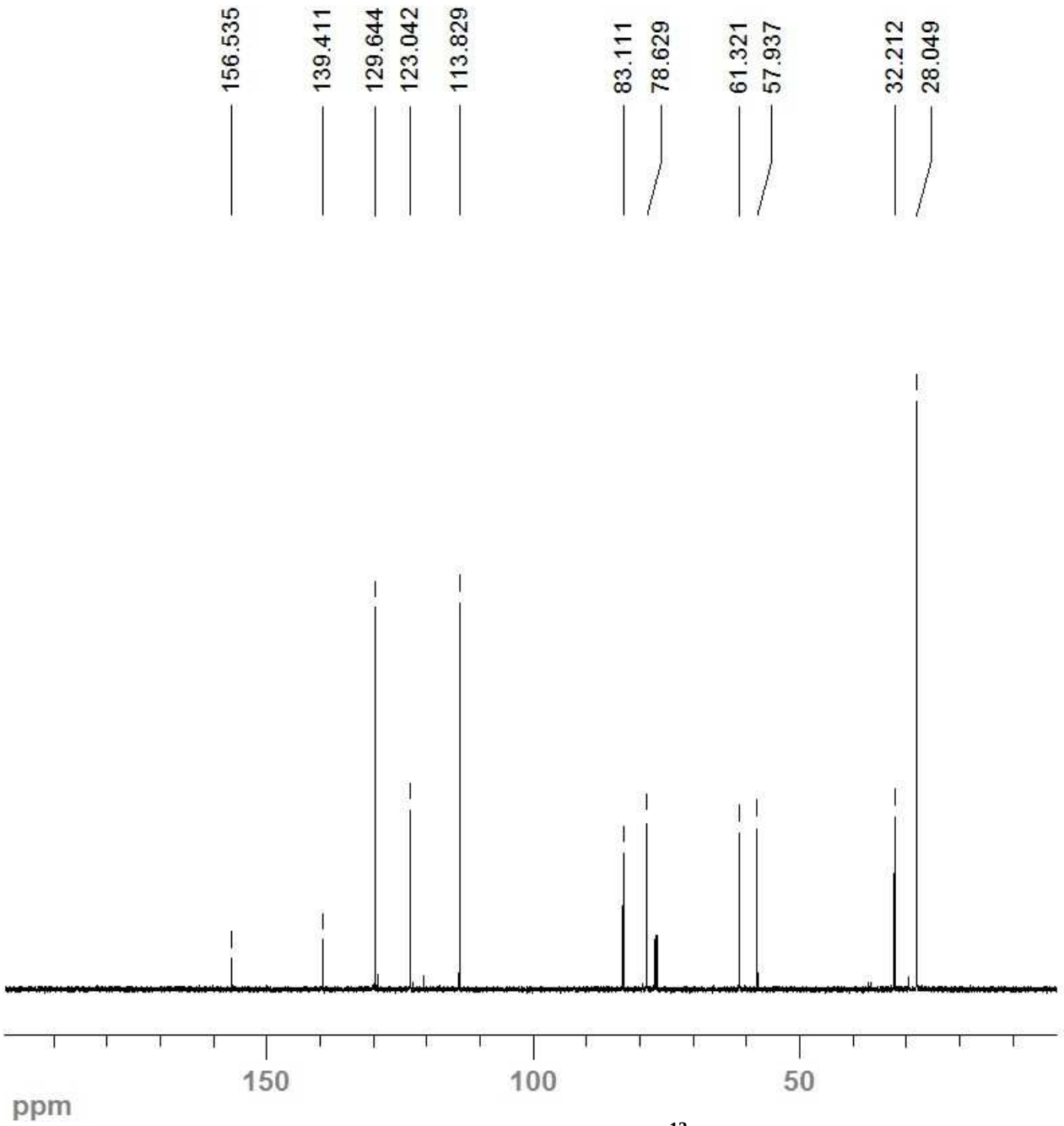
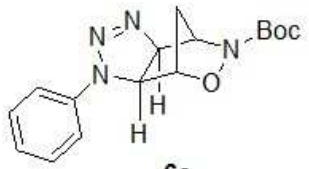


Figure 36. ^{1}H NMR spectrum of 6e



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
128



6e

Figure 37. ^{13}C NMR spectrum of 6e

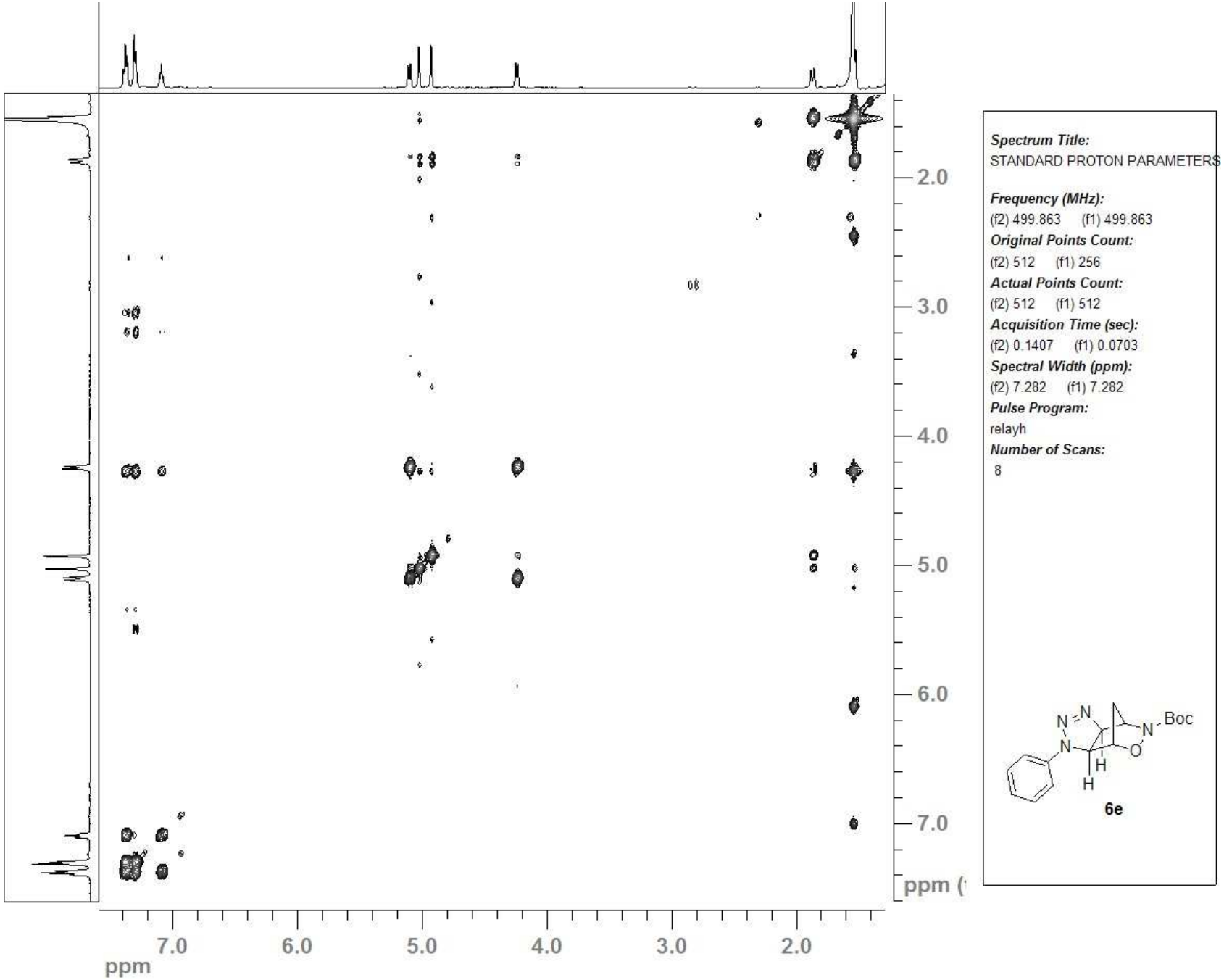


Figure 38. COSY spectrum of 6e

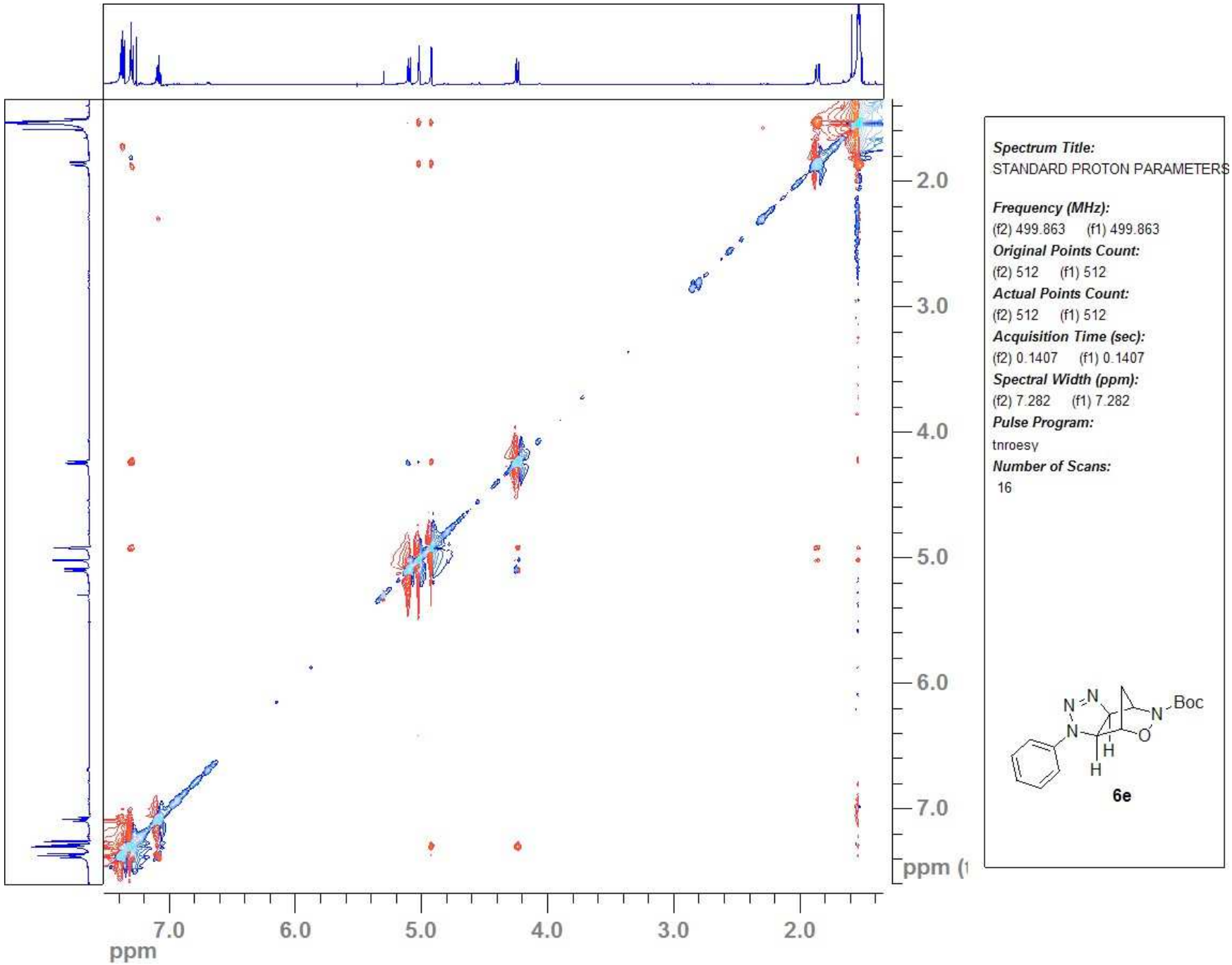


Figure 39. ROESY spectrum of 6e

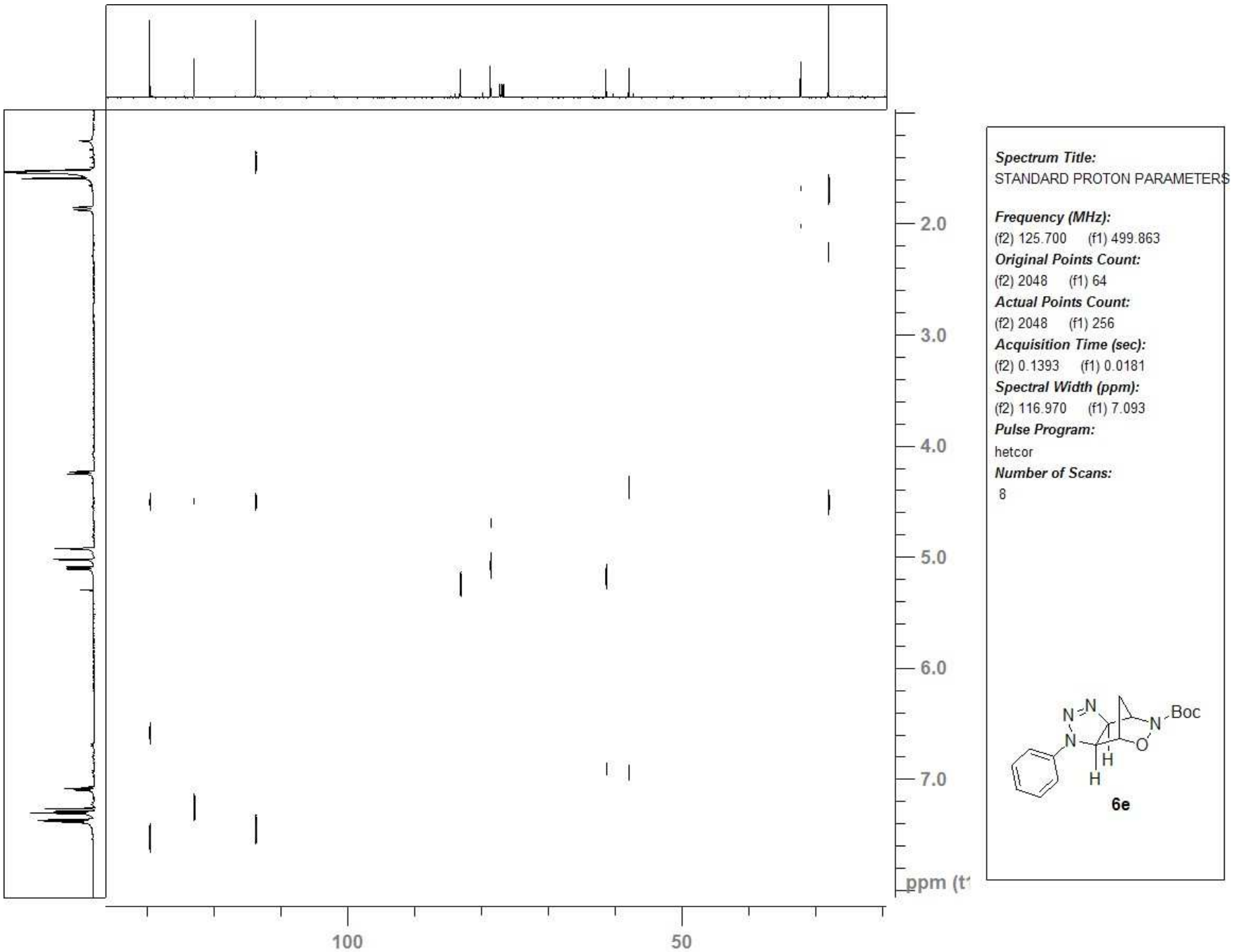


Figure 40. HETCOR spectrum of 6e

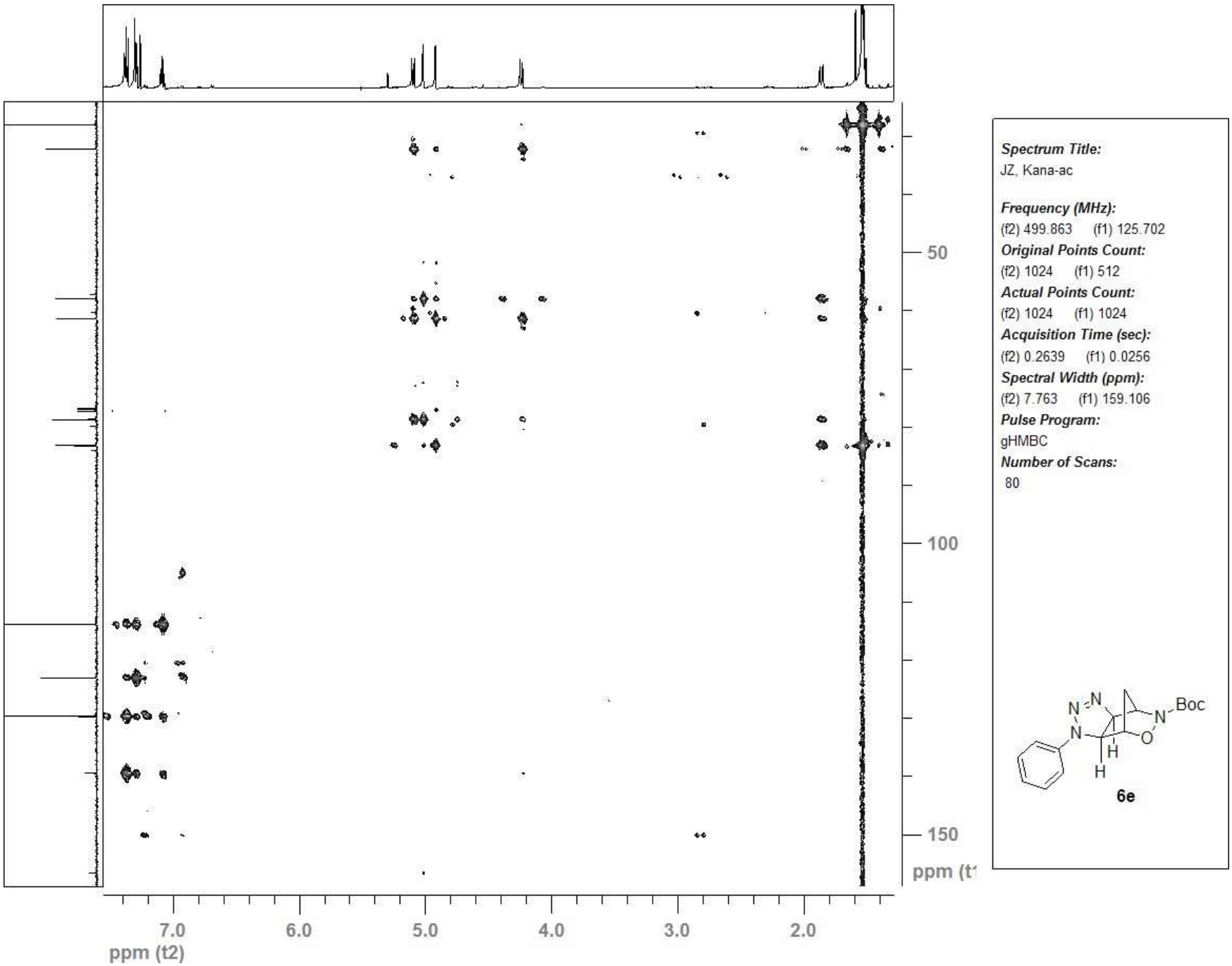


Figure 41. gHMBC spectrum of 6e

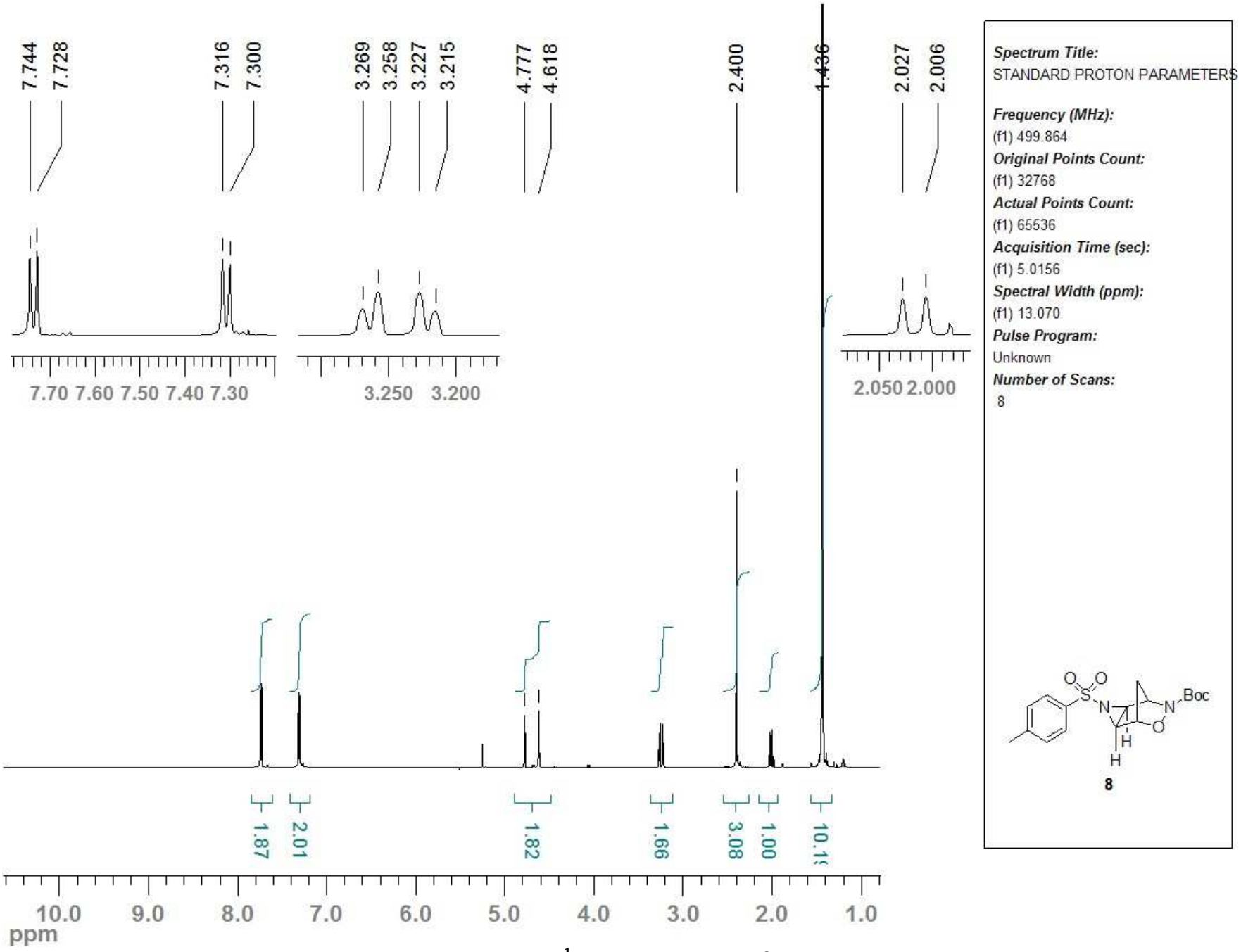
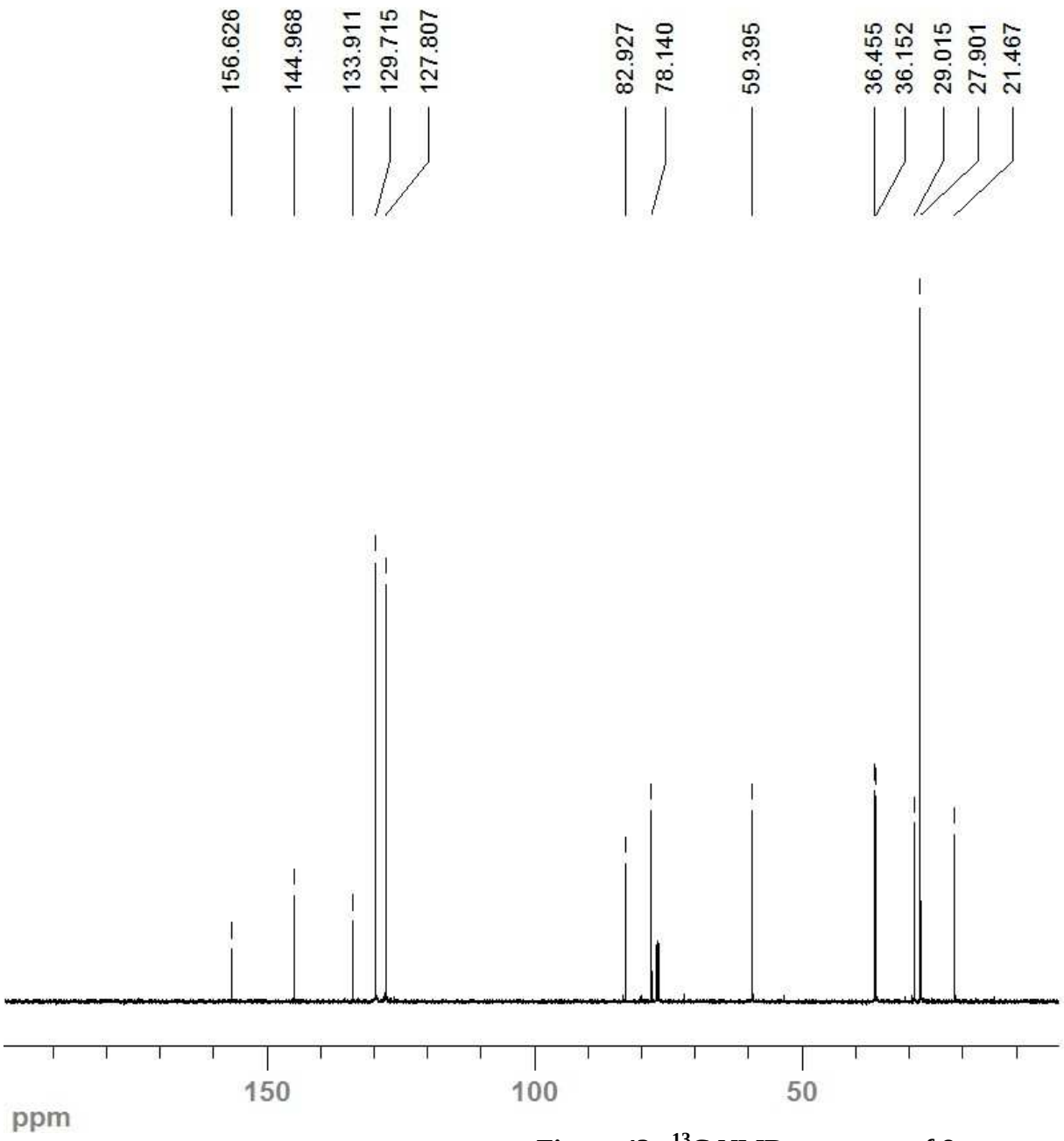
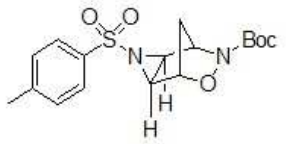


Figure 42. ^{1}H NMR spectrum of 8



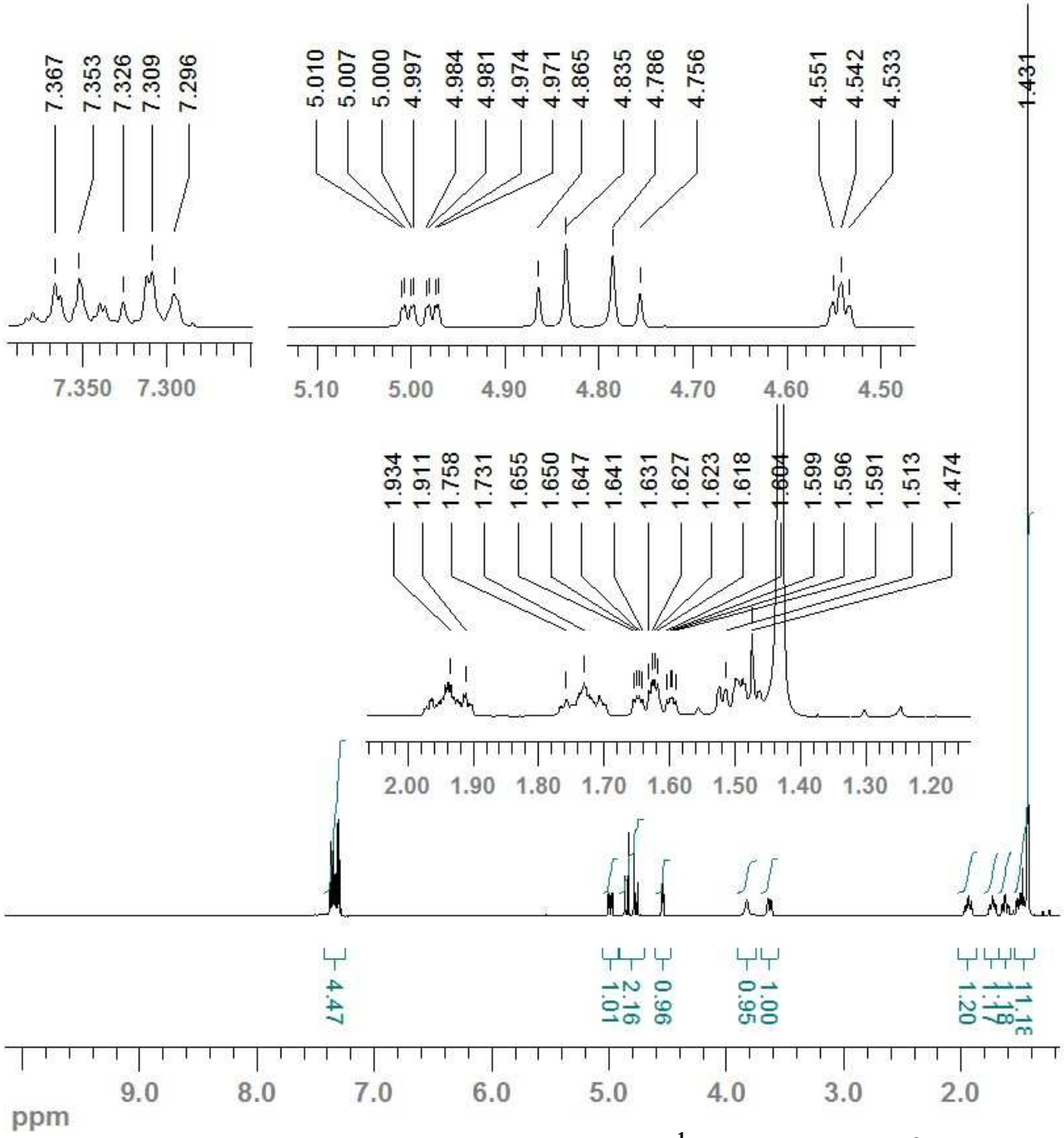
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



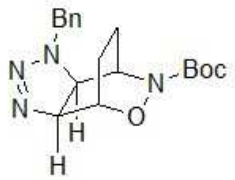
8

Figure 43. ^{13}C NMR spectrum of 8



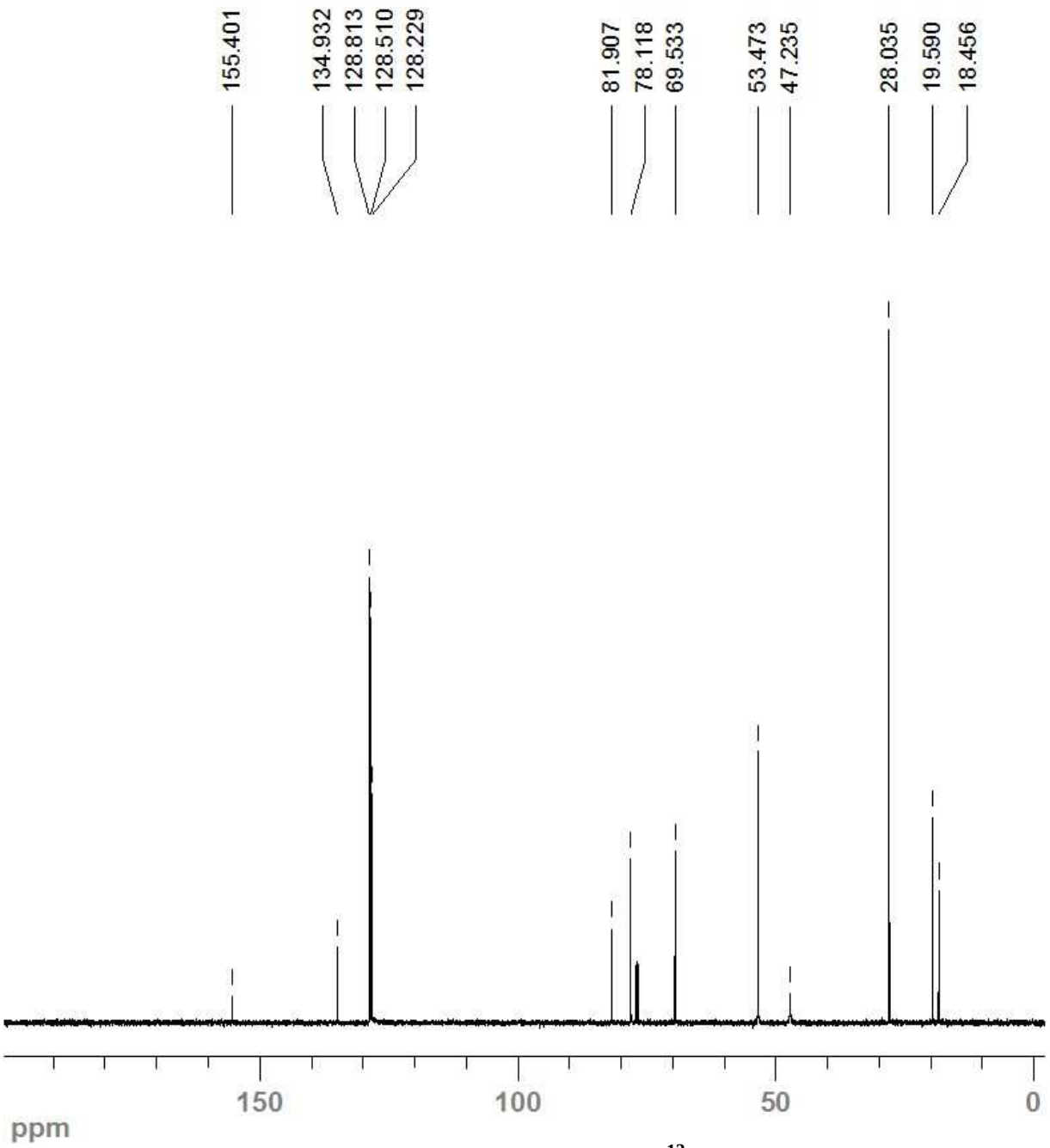
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 499.864
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 5.0156
Spectral Width (ppm):
(f1) 13.070
Pulse Program:
Unknown
Number of Scans:
8



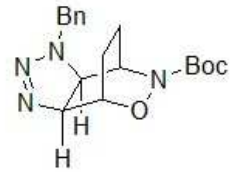
9

Figure 44. ^{1}H NMR spectrum of 9



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



9

Figure 45. ^{13}C NMR spectrum of 9

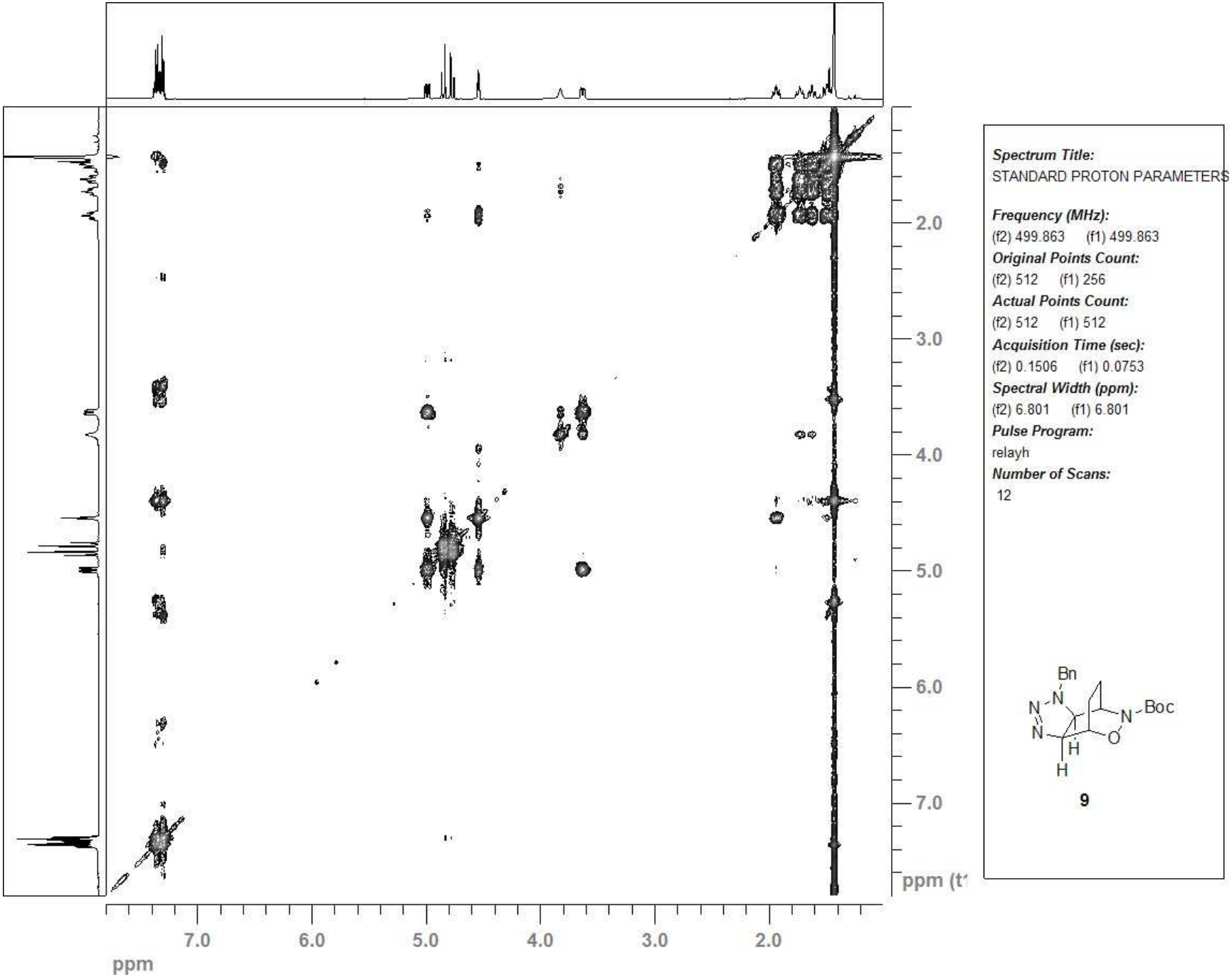


Figure 46. COSY spectrum of 9

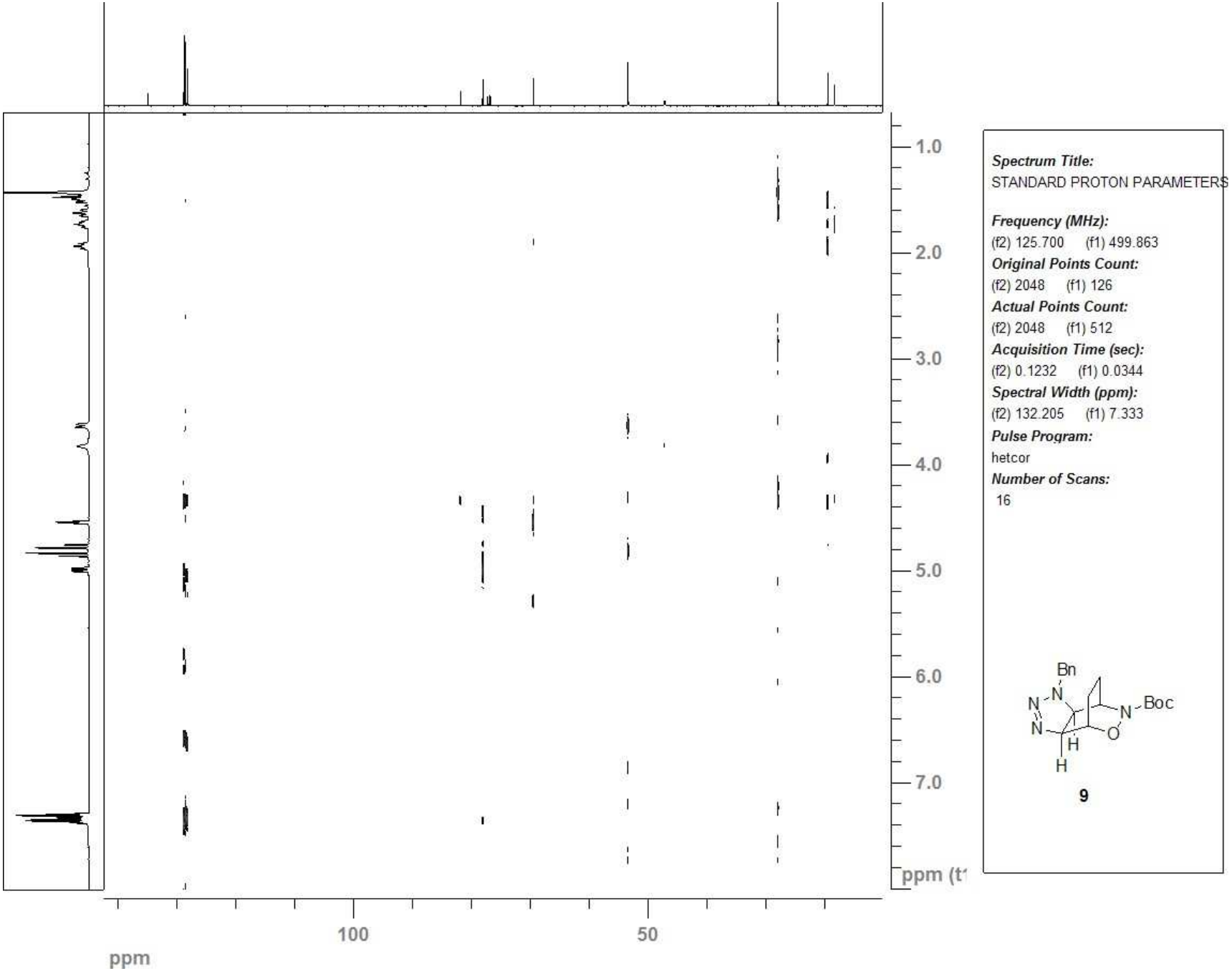


Figure 47. HETCOR spectrum of 9

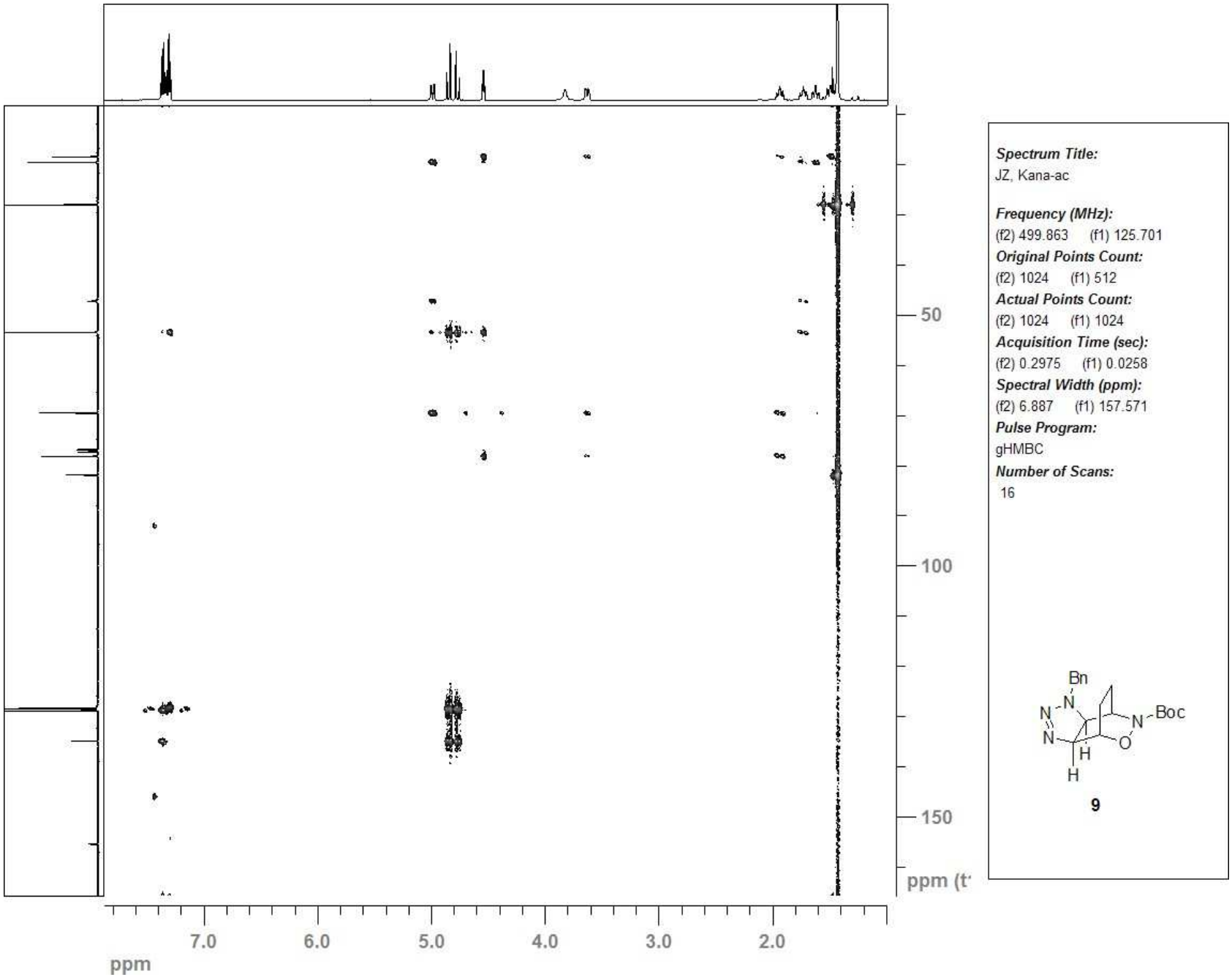
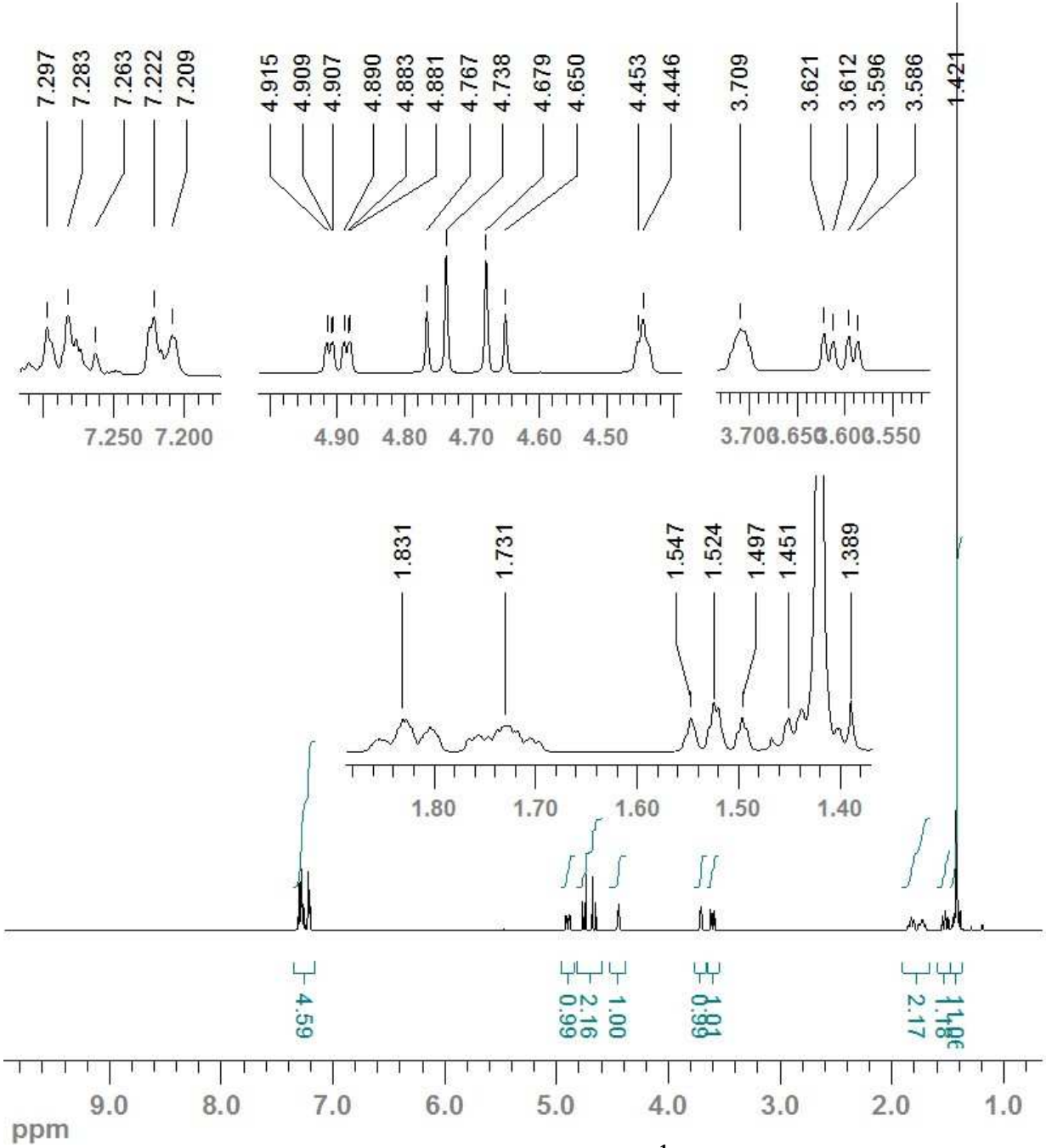


Figure 48. gHMBC spectrum of 9



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 499.864

Original Points Count:
(f1) 32768

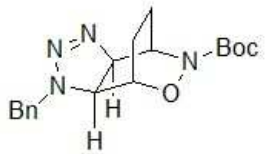
Actual Points Count:
(f1) 65536

Acquisition Time (sec):
(f1) 5.0156

Spectral Width (ppm):
(f1) 13.070

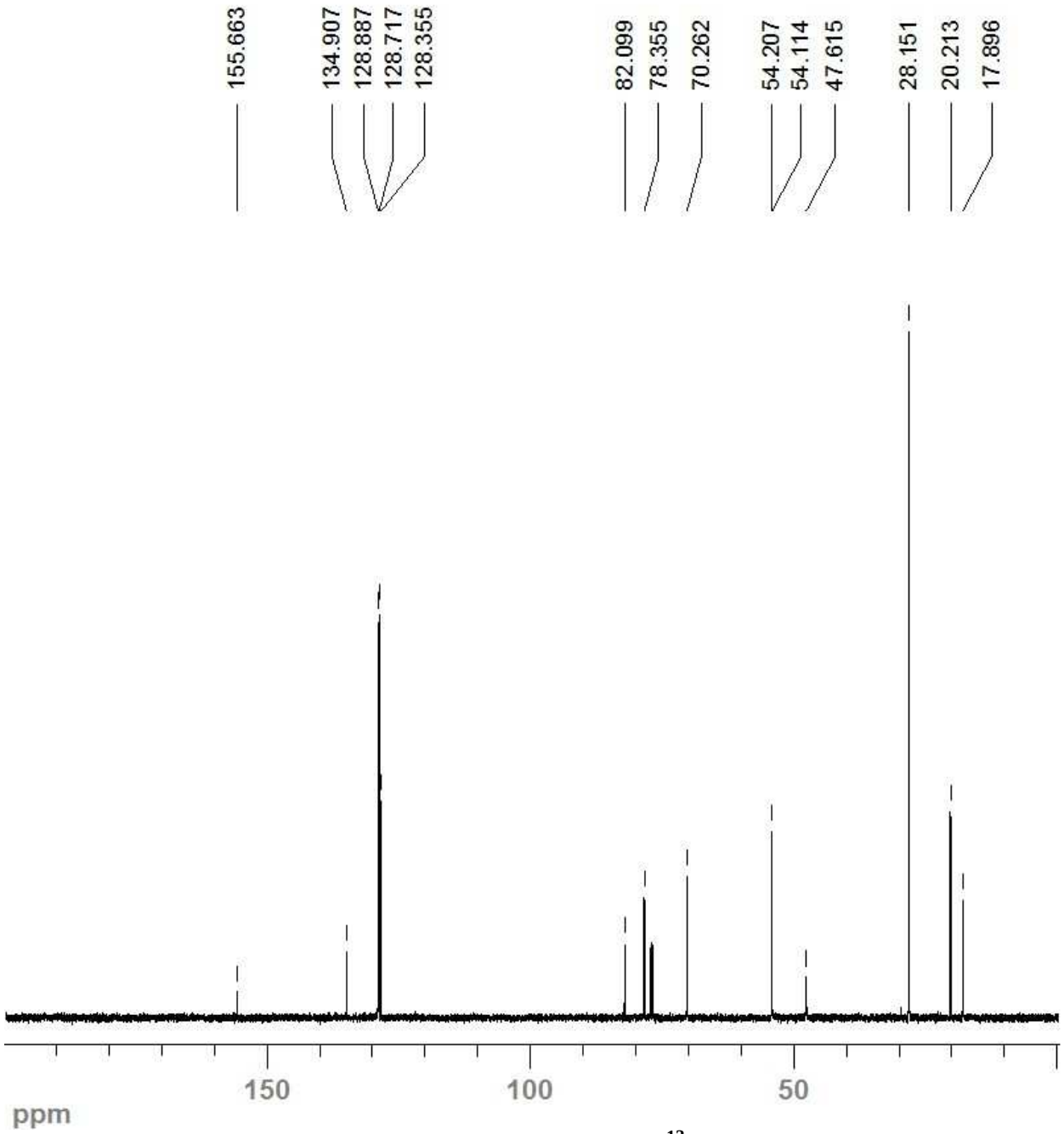
Pulse Program:
Unknown

Number of Scans:
8



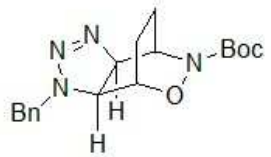
10

Figure 49. ^{1}H NMR spectrum of 10



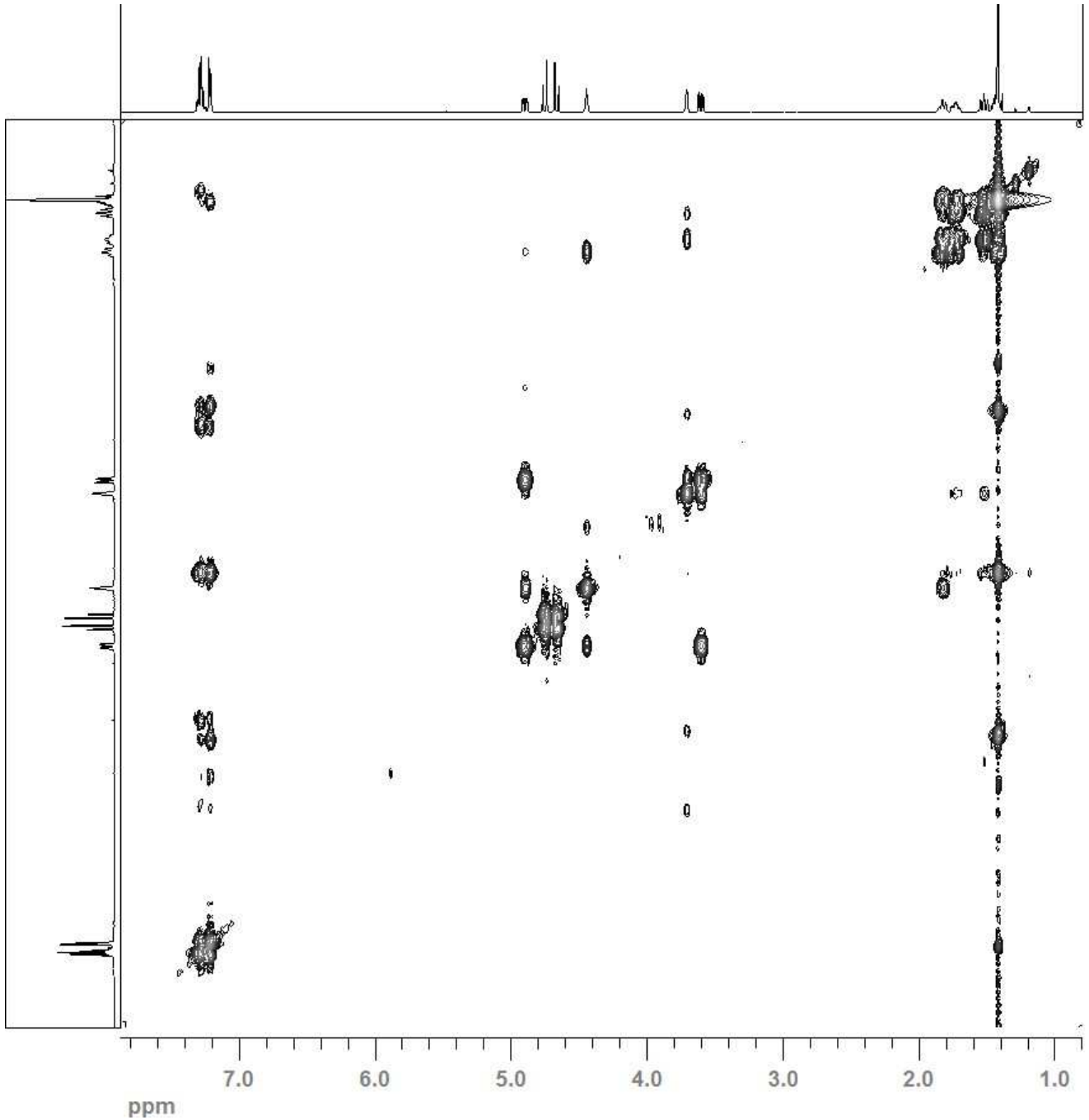
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



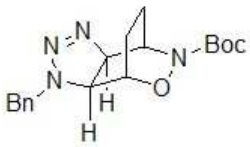
10

Figure 50. ^{13}C NMR spectrum of 10



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f2) 499.863 (f1) 499.863
Original Points Count:
(f2) 512 (f1) 132
Actual Points Count:
(f2) 512 (f1) 512
Acquisition Time (sec):
(f2) 0.1448 (f1) 0.0373
Spectral Width (ppm):
(f2) 7.076 (f1) 7.076
Pulse Program:
relayh
Number of Scans:
8



10

Figure 51. COSY spectrum of 10

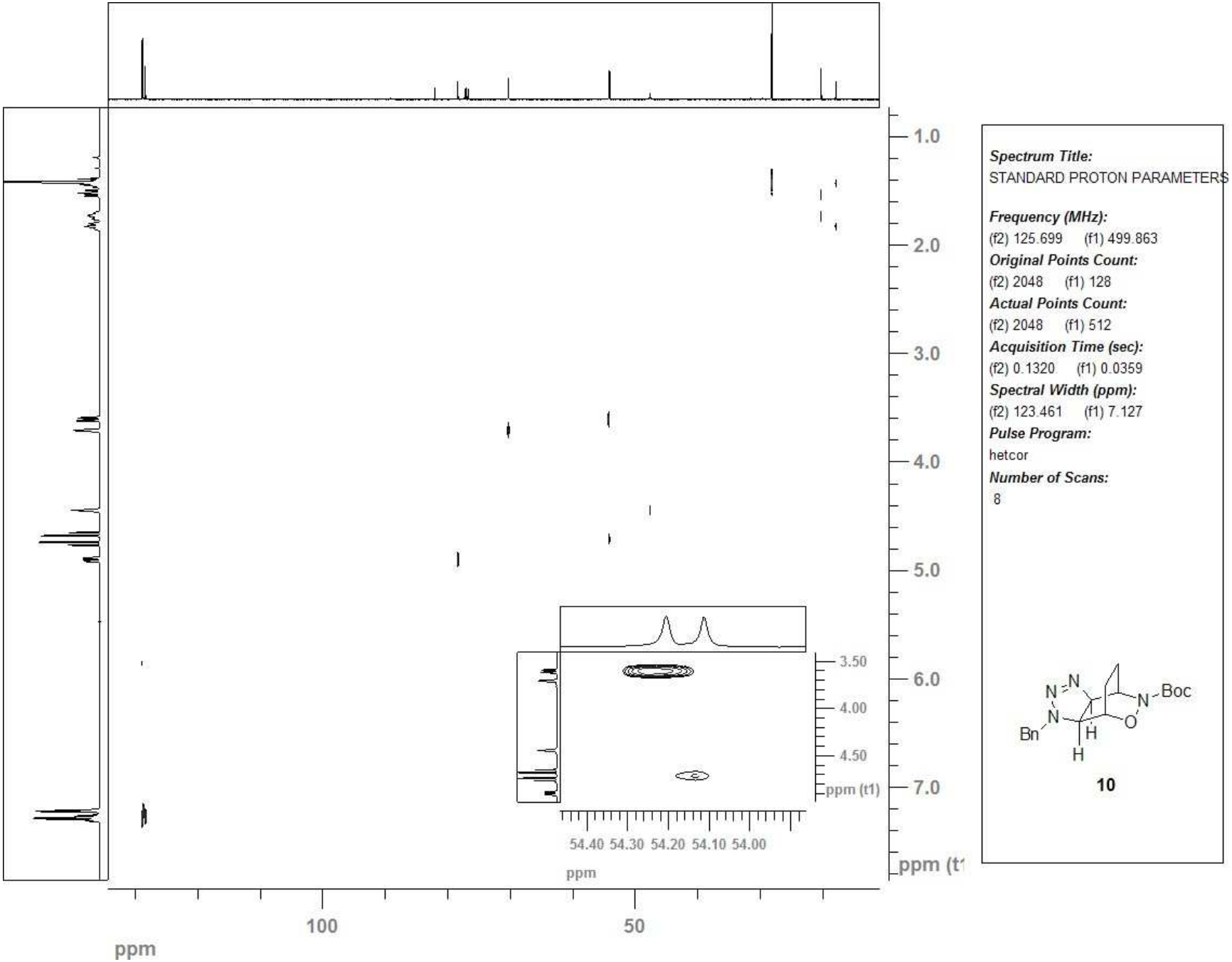


Figure 52. HETCOR spectrum of 10

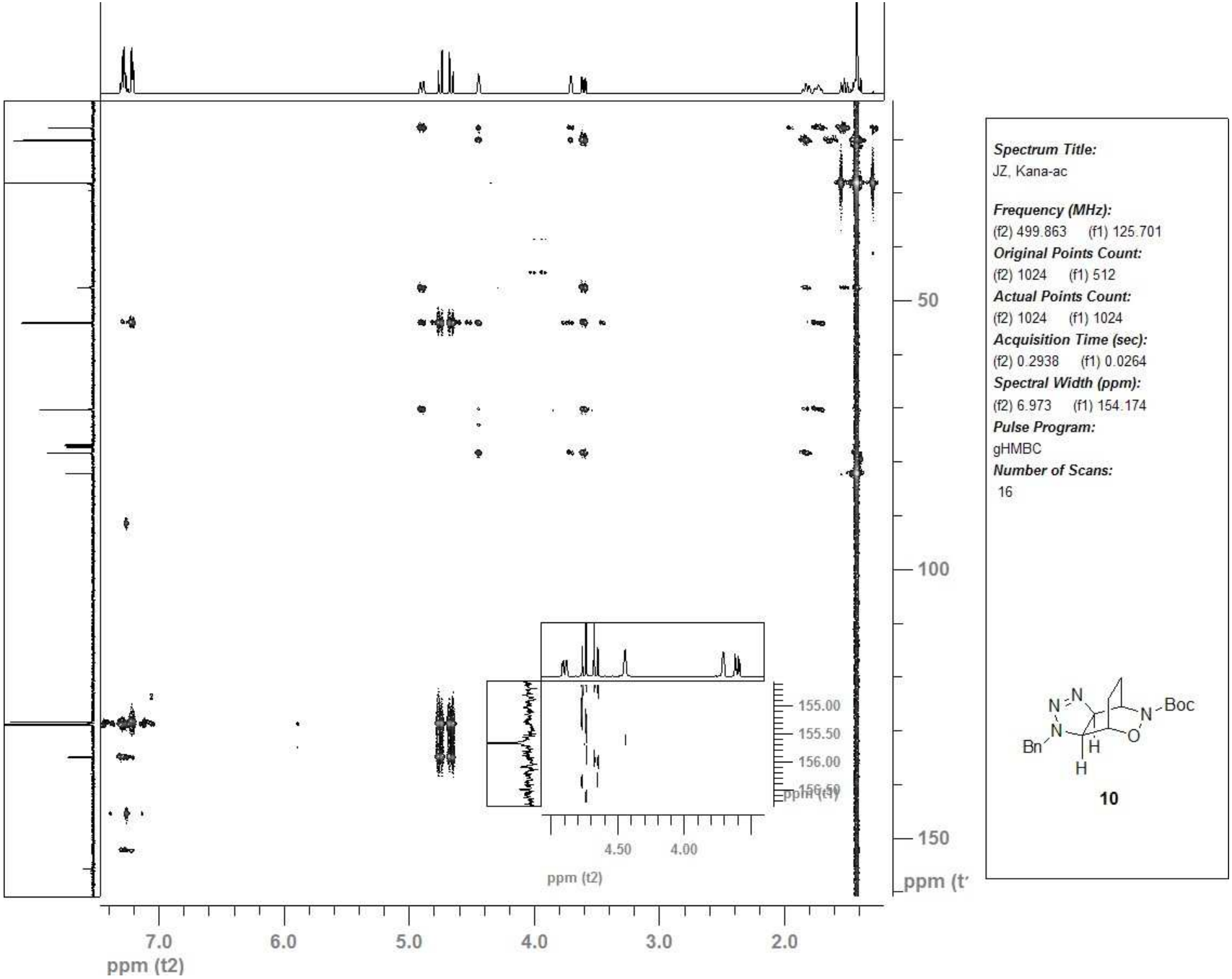


Figure 53. gHMBC spectrum of 10

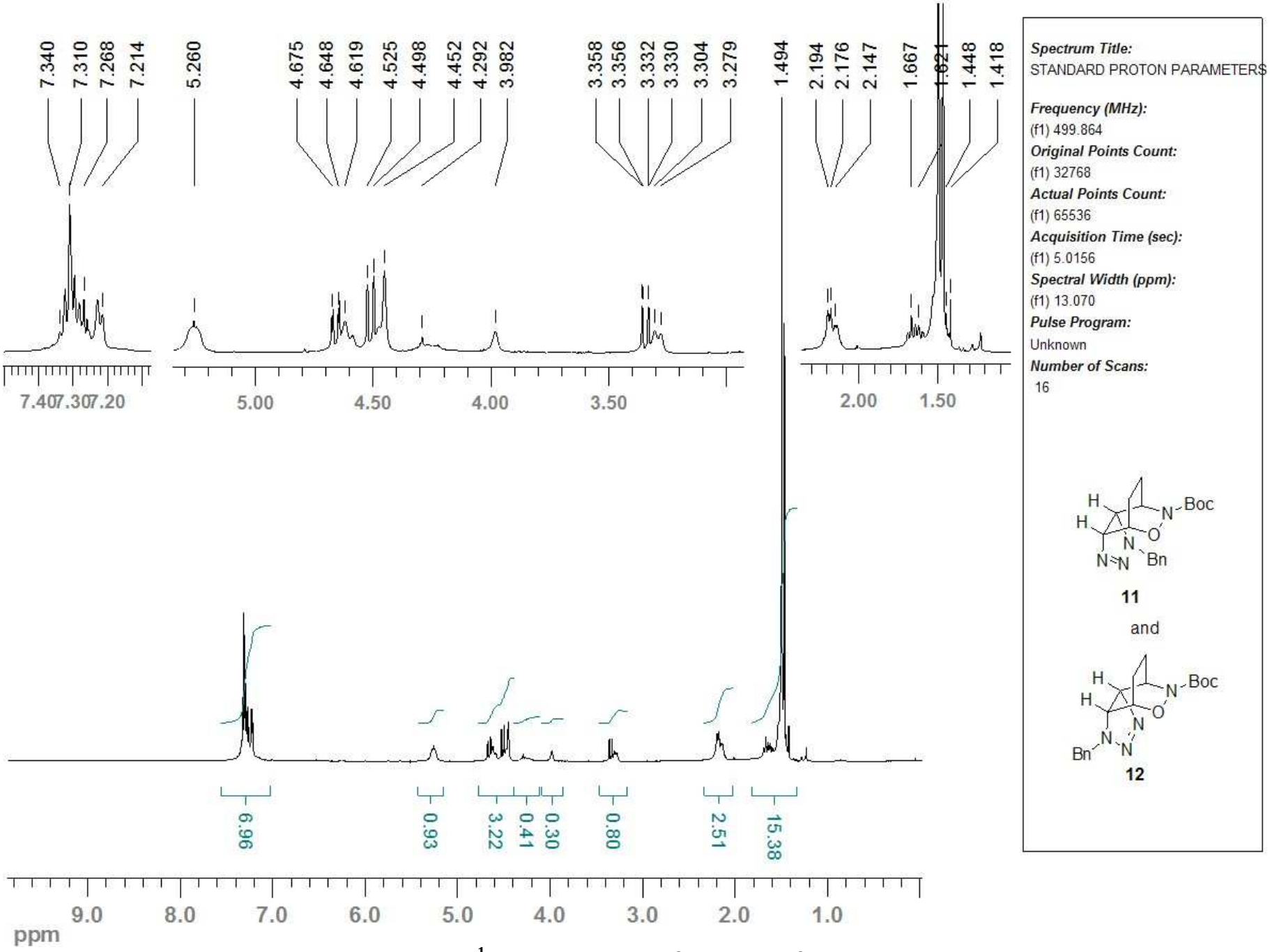
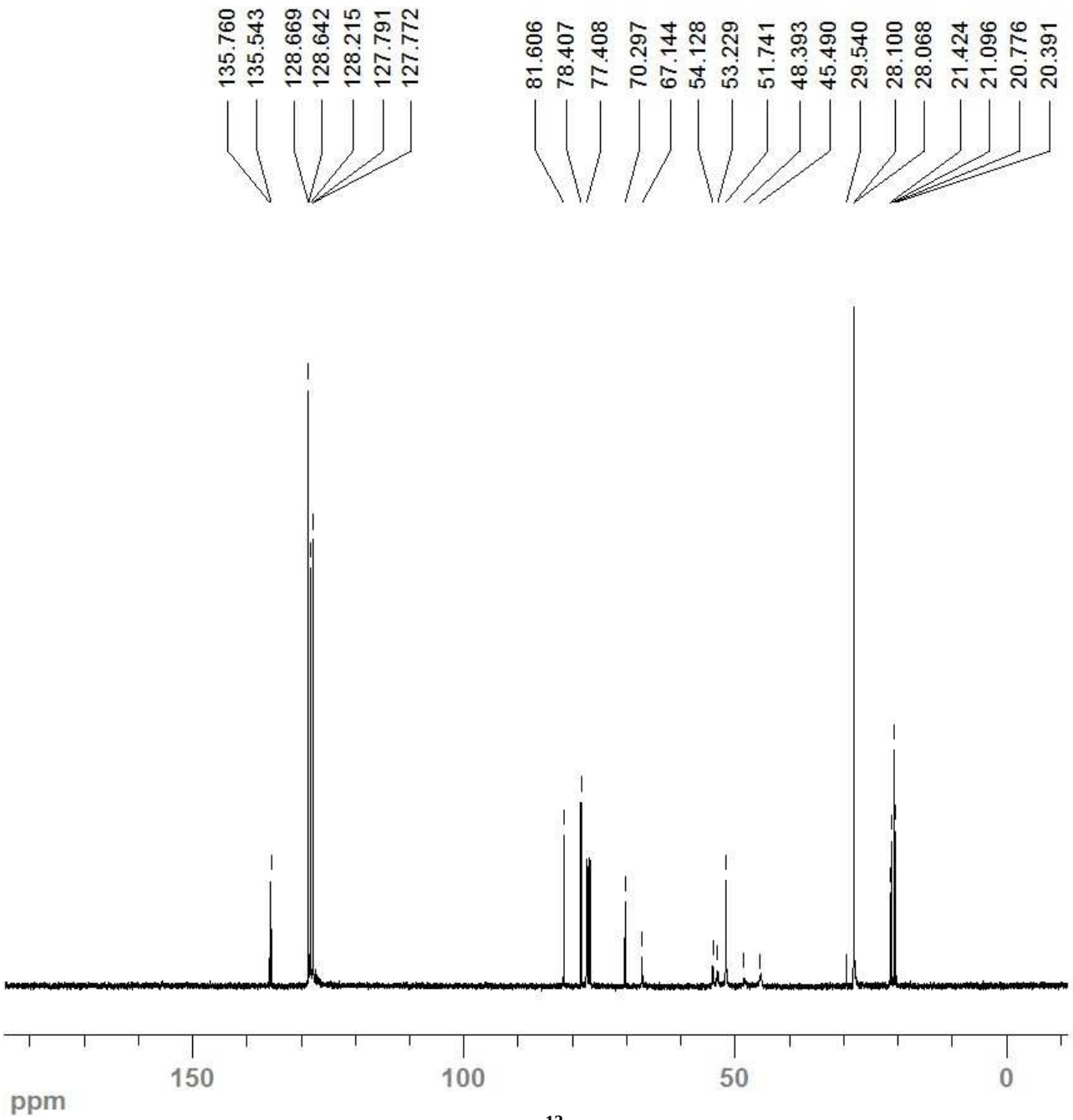


Figure 54. ^{1}H NMR spectrum of a mixture of 11 and 12

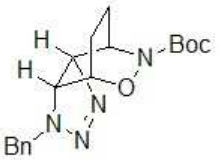


Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
256

11

and



12

Figure 55. ^{13}C NMR spectrum of a mixture of 11 and 12

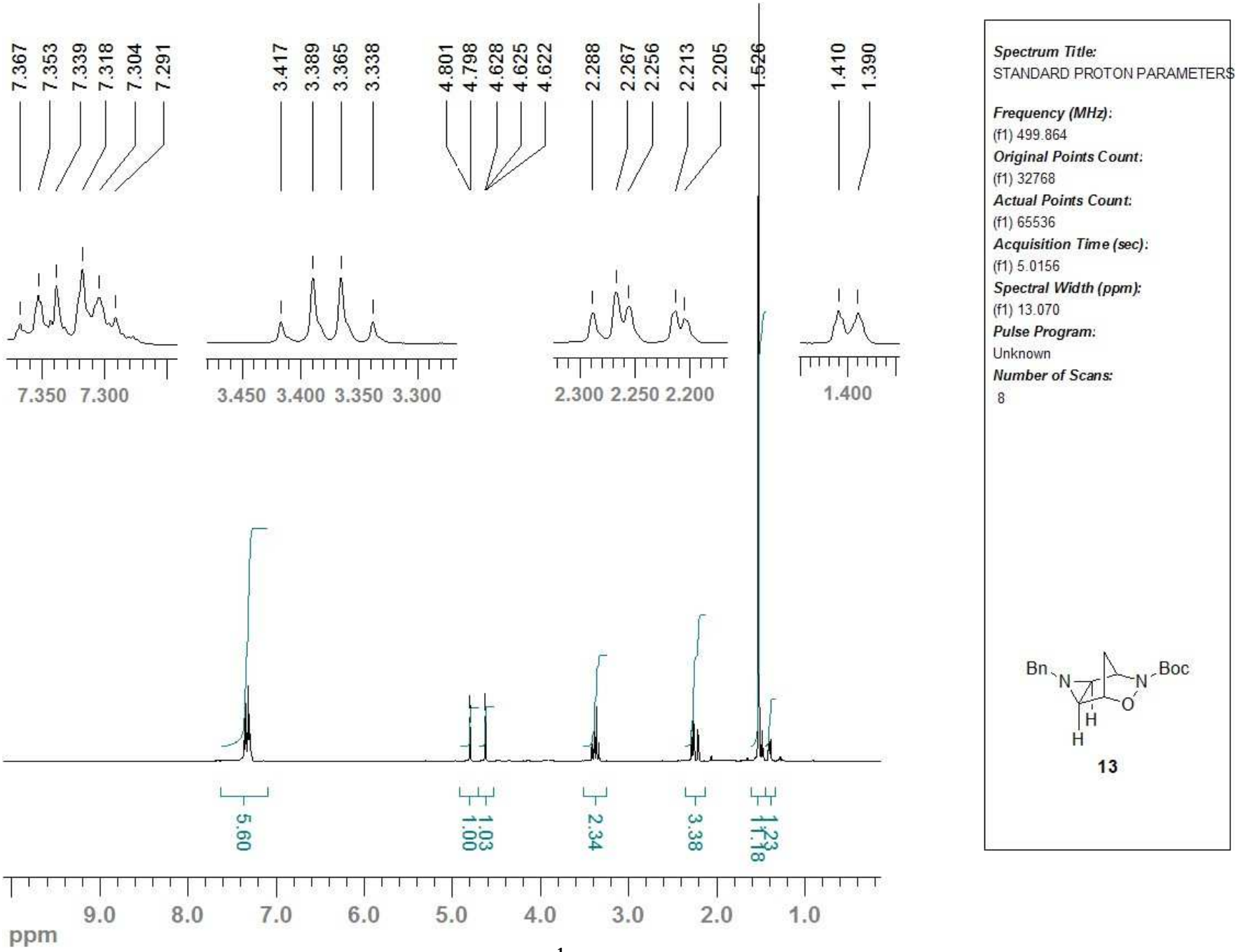
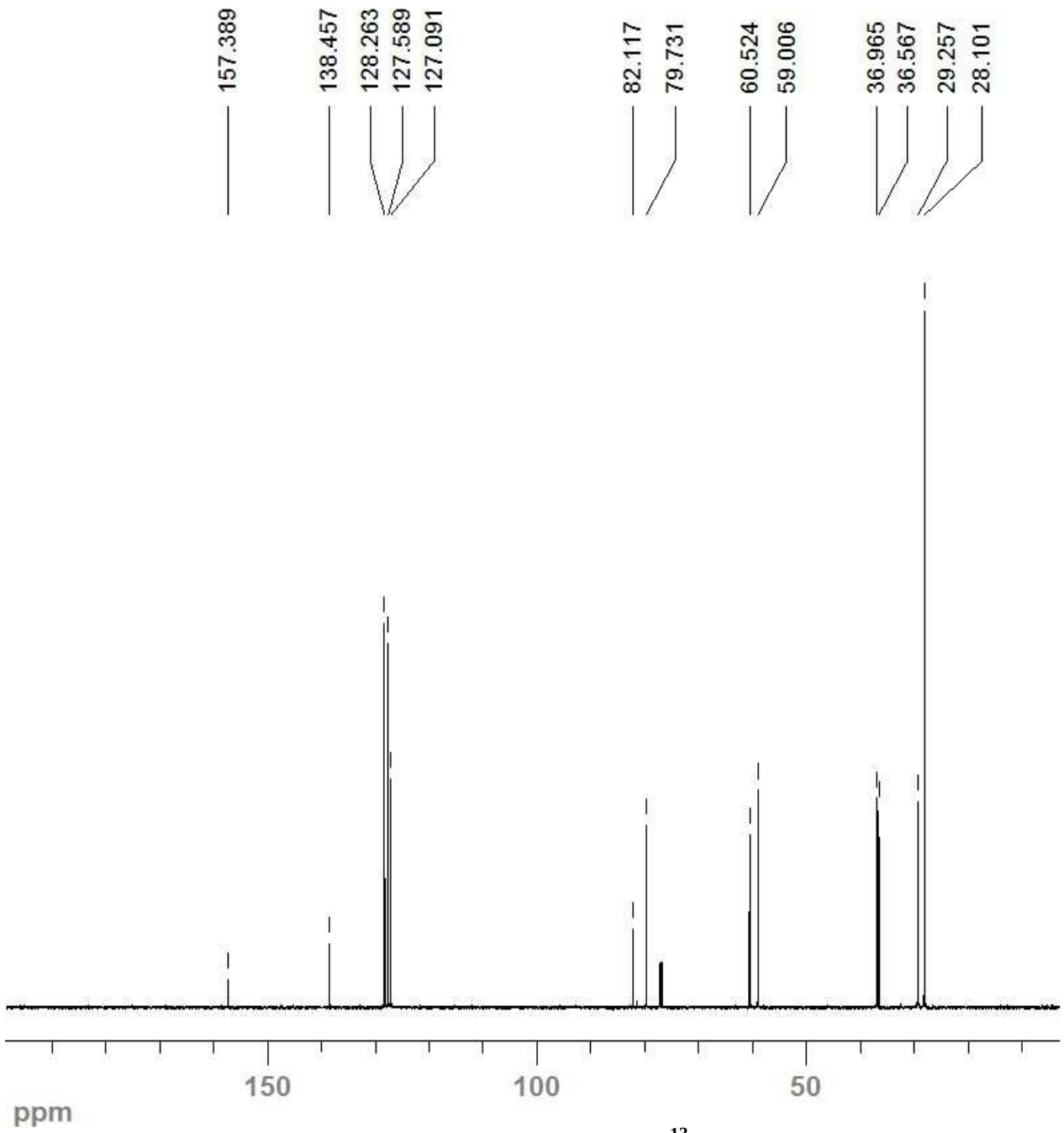


Figure 56. ^{1}H NMR spectrum of 13



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702

Original Points Count:
(f1) 32768

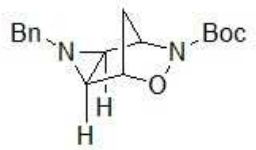
Actual Points Count:
(f1) 65536

Acquisition Time (sec):
(f1) 1.2153

Spectral Width (ppm):
(f1) 214.501

Pulse Program:
Unknown

Number of Scans:
128



13

Figure 57. ^{13}C NMR spectrum of 13

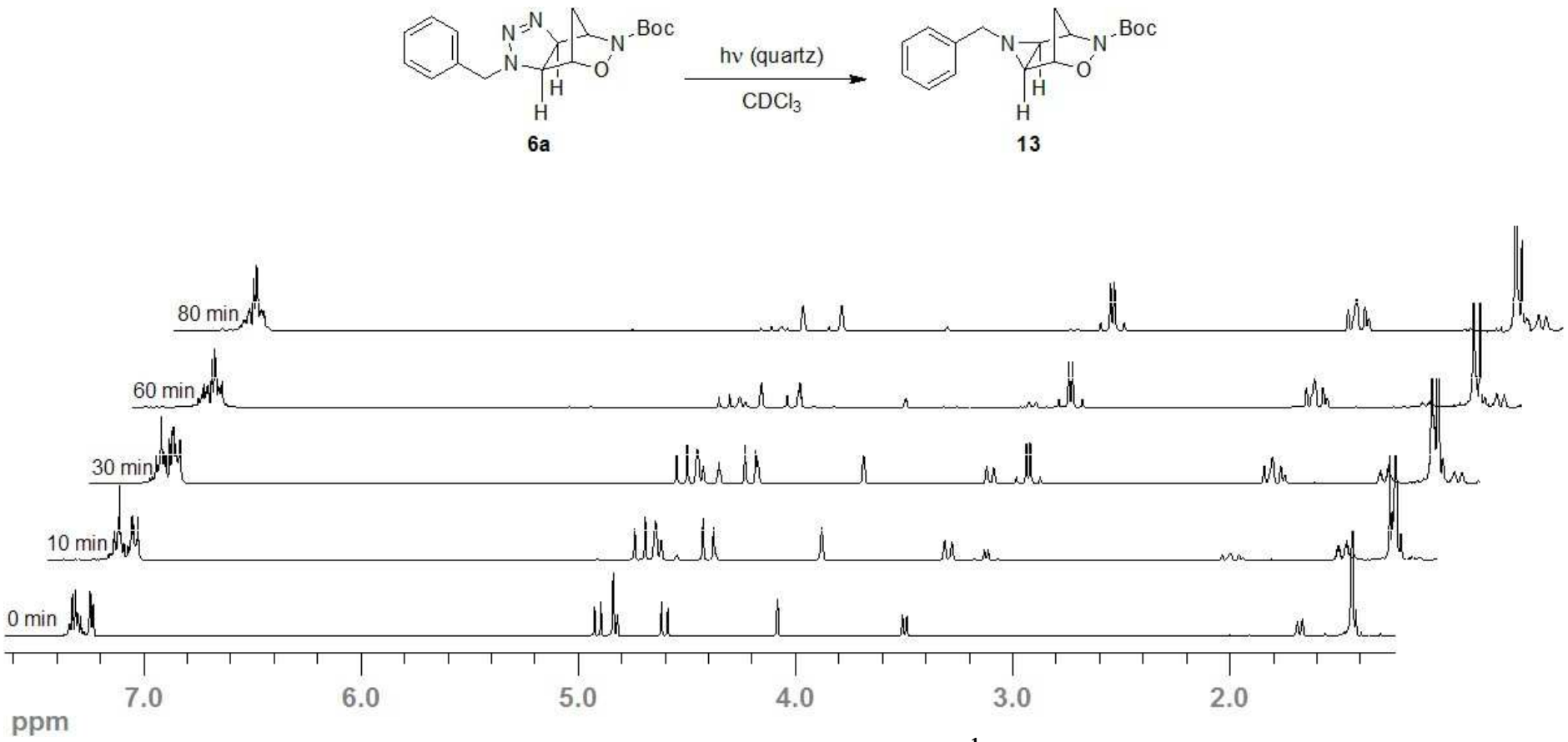


Figure 58. Photolysis of 6a monitored by ^{1}H NMR

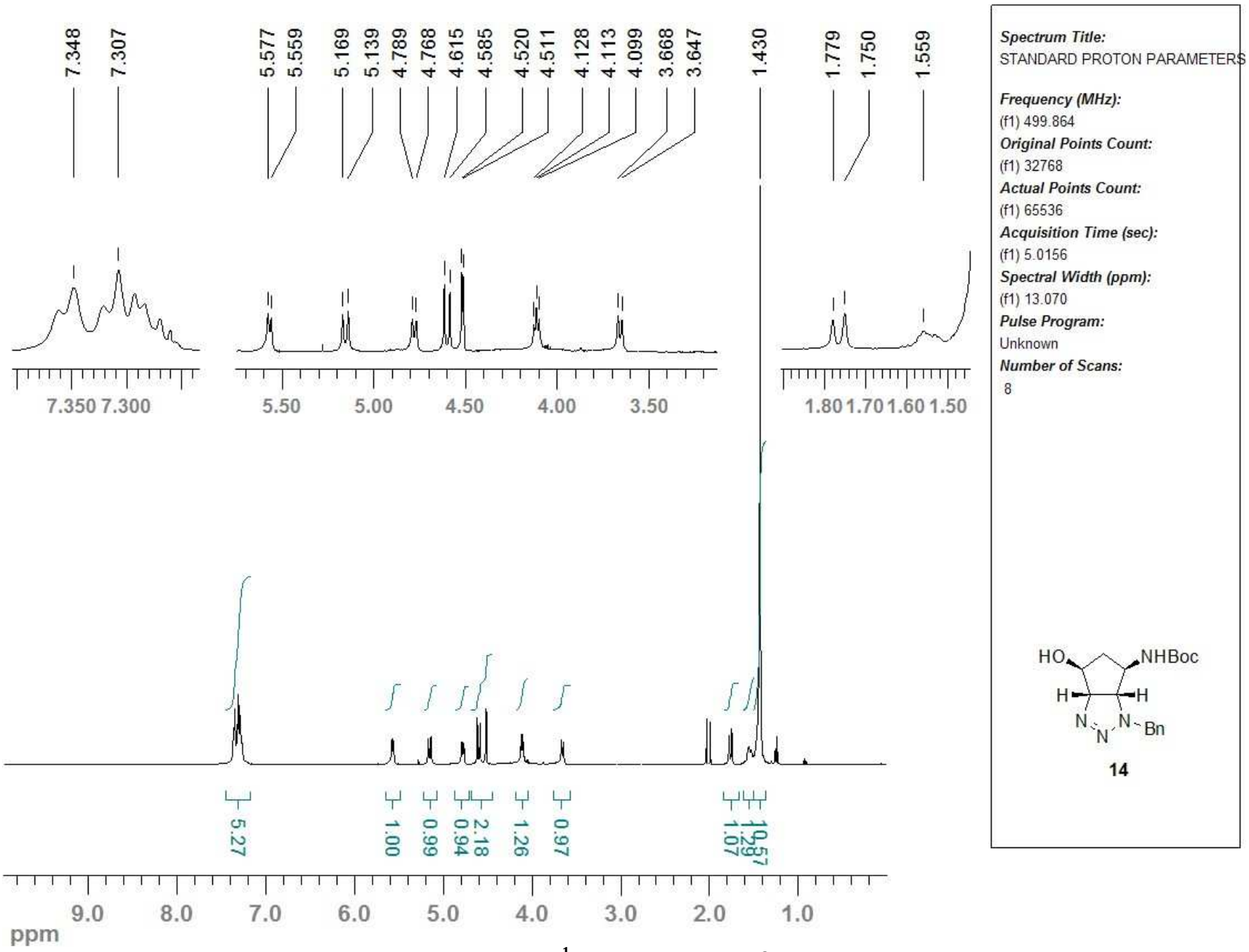
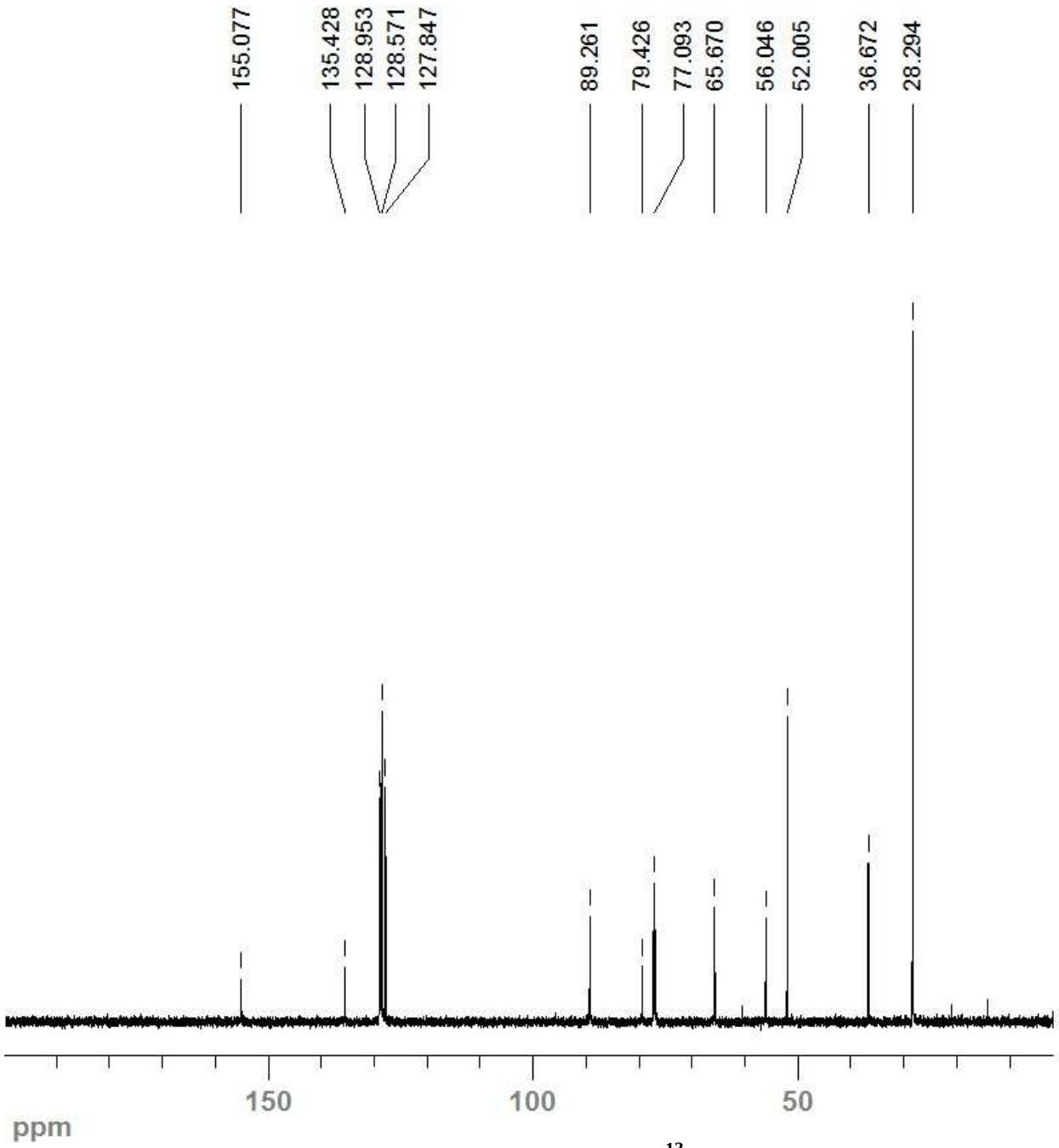
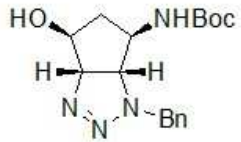


Figure 59. ^{1}H NMR spectrum of 14



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
128



14

Figure 60. ^{13}C NMR spectrum of 14

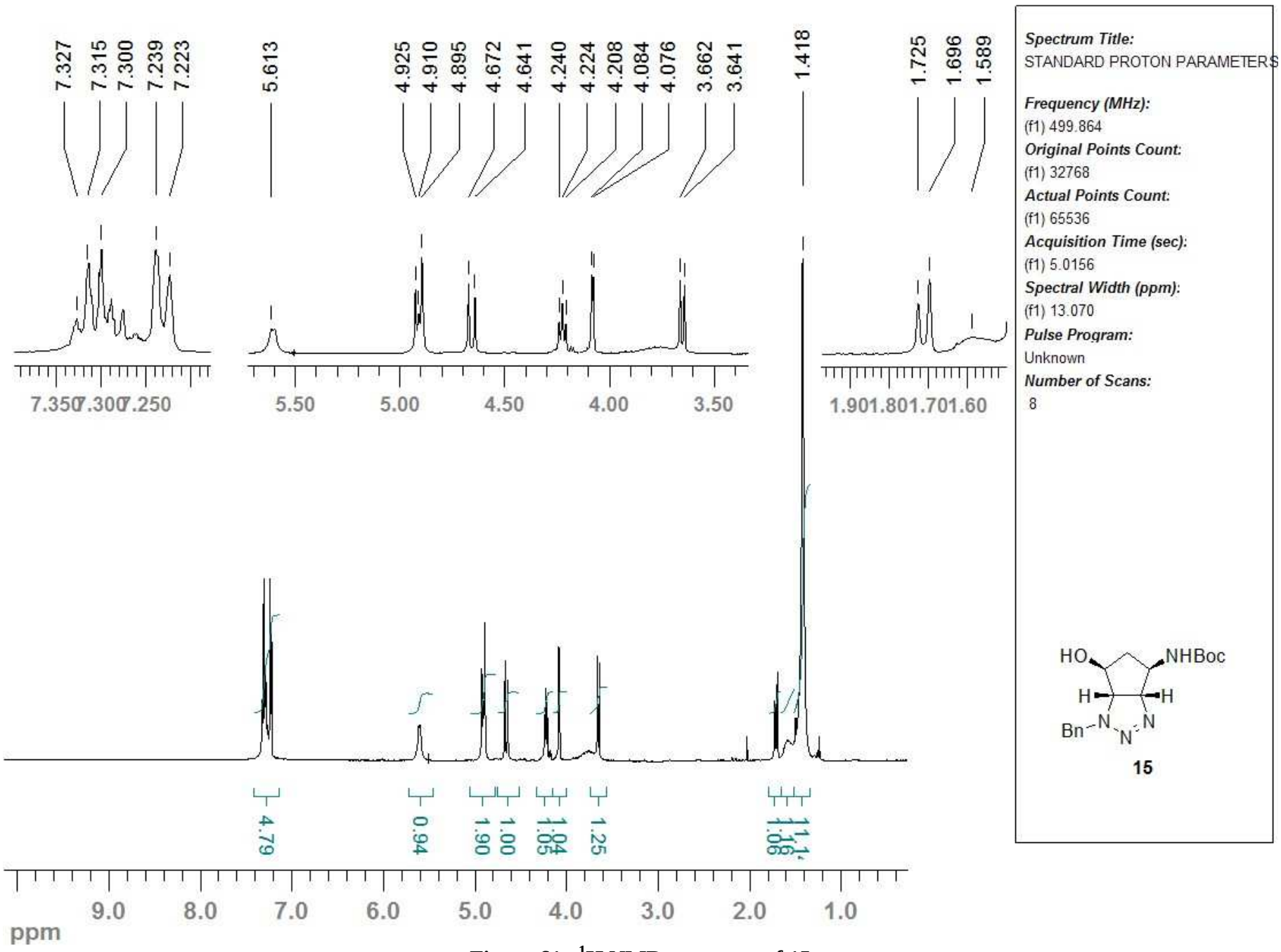
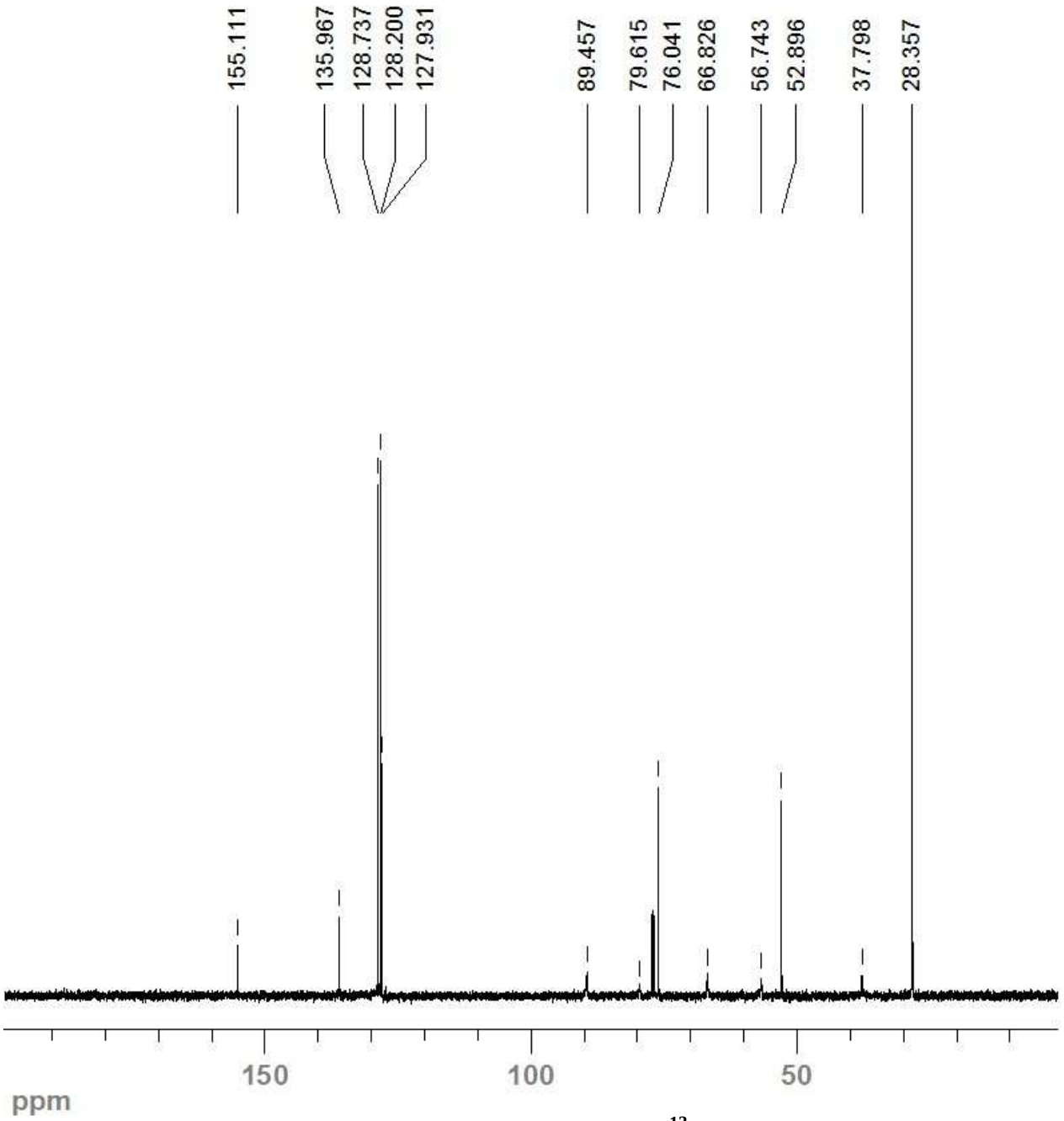
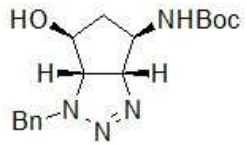


Figure 61. ^{1}H NMR spectrum of 15



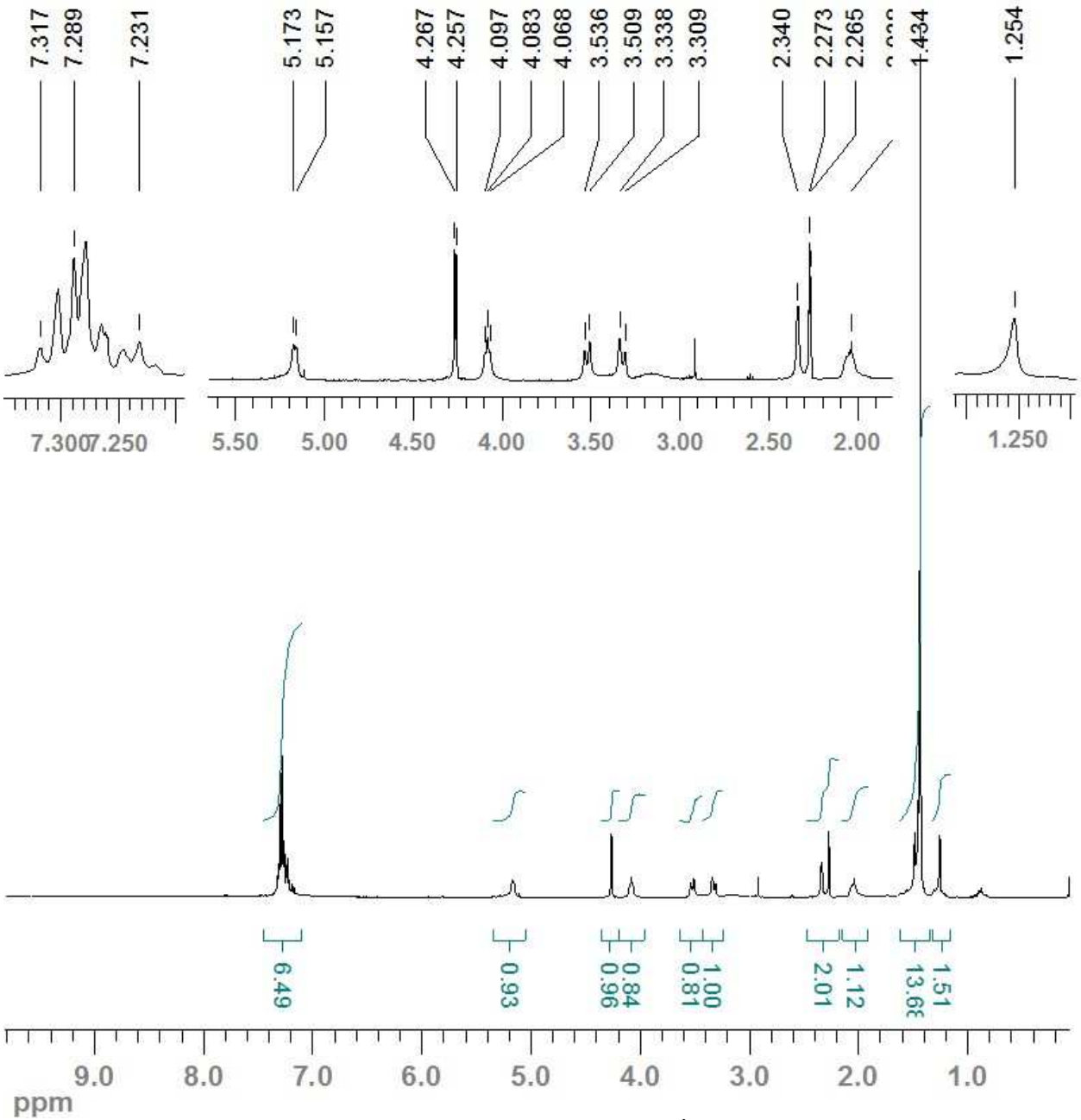
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
128



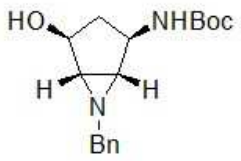
15

Figure 62. ^{13}C NMR spectrum of 15



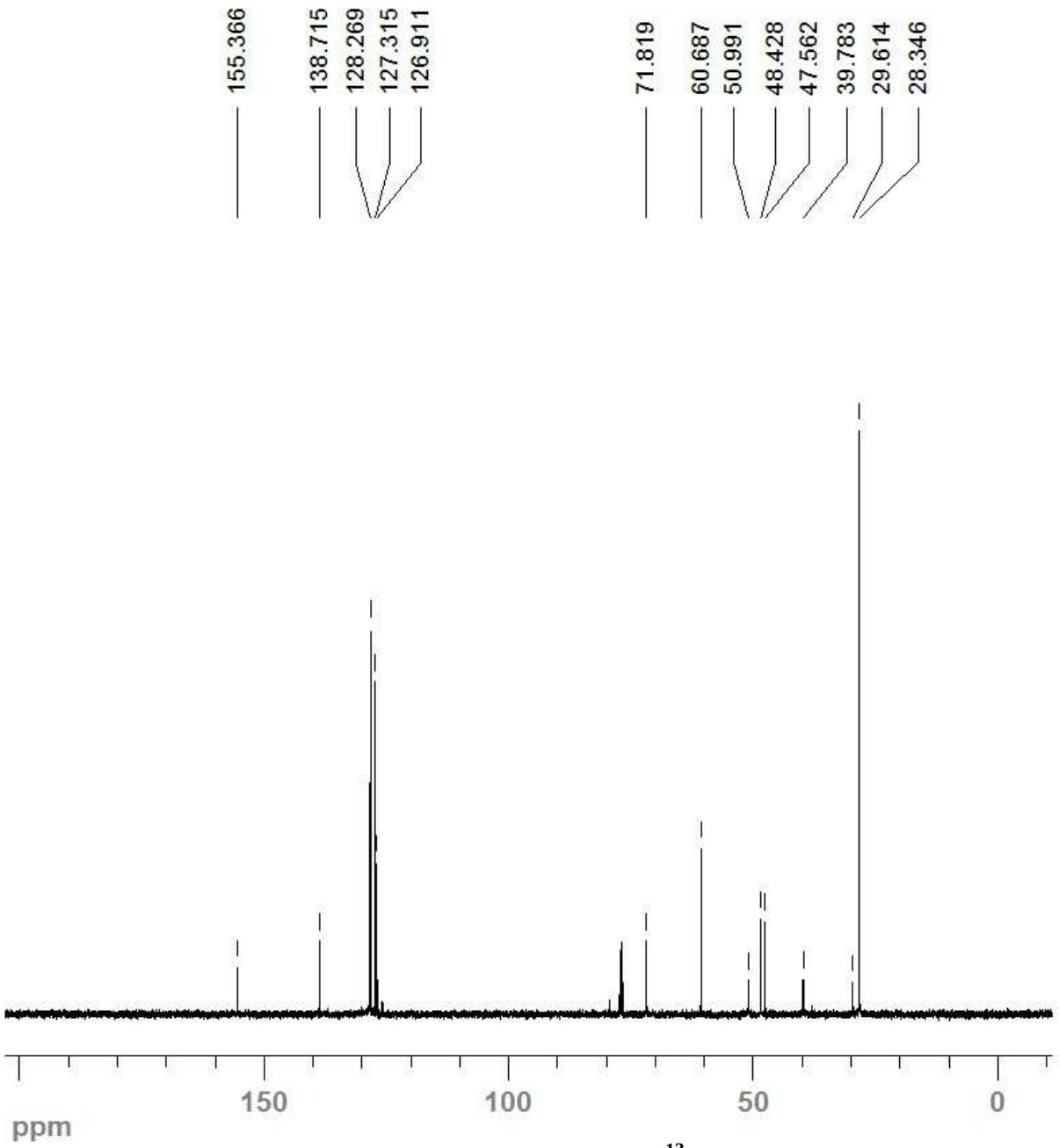
Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 499.864
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 5.0156
Spectral Width (ppm):
(f1) 13.070
Pulse Program:
Unknown
Number of Scans:
8



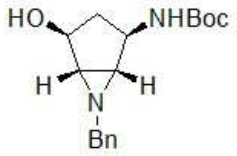
16

Figure 63. ^{1}H NMR spectrum of 16



Spectrum Title:
STANDARD PROTON PARAMETERS

Frequency (MHz):
(f1) 125.702
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 65536
Acquisition Time (sec):
(f1) 1.2153
Spectral Width (ppm):
(f1) 214.501
Pulse Program:
Unknown
Number of Scans:
64



16

Figure 64. ^{13}C NMR spectrum of 16

References

(1) Alvarez, S. G.; Alvarez, M. T. *Synthesis* **1997,** (4), 413-414.
(2) Pollex, A.; Hiersemann, M. *Org. Lett.* **2005,** *7*(25), 5705-5708.
(3) Lindsay, R. O.; Allen, C. F. H. *Org. Synth.* **1955,** *3*, 710.
(4) Lautens, M.; Mancuso, J. *J. Org. Chem.* **2004,** *69*(10), 3478-3487.