O^2-(*N*-Hydroxy(methoxy)-2-ethanesulfonamido) Protected Diazen-1-ium-1,2-diolates: Nitric Oxide Release via a Base-induced β-Elimination Cleavage

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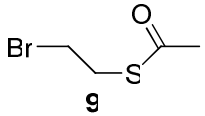
Supplementary Information

Content:

General Information

Melting points were determined on a Thomas-Hoover capillary apparatus and are uncorrected. Infrared (IR) spectra were recorded as films on NaCl plates using a Nicolet 550 Series II Magna FT-IR spectrometer. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were measured on a Bruker AM-300 spectrometer with TMS as the internal standard, where *J* (coupling constant) values are estimated in Hertz (Hz). Mass spectra (MS) were recorded on a Water's Micromass ZQ 4000 mass spectrometer using the ESI ionization mode. Microanalyses were performed for C, H, N by the Microanalytical Service Laboratory, Department of Chemistry, University of Alberta. Compounds **4**-**7**, **9**-**17** showed a single spot on Macherey-Nagel Polygram Sil G/UV$_{254}$ silica gel plates (0.2 mm) using a low, medium and highly polar solvent system, and no residue remained after combustion, indicating a purity >95%. Column chromatography was performed on a Combiflash@ Rf system using either a gold silica (**4**-**7**, **9**-**10**, **12**, and **15-16**), or a C18 (**13** and **17**), column. All other reagents, purchased from the Aldrich Chemical Company (Milwaukee, WI), were used without further purification.

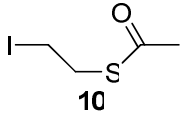
2-Bromoethyl thioacetate (**9**)



9

The title compound **9** was prepared using the previously reported method.[1] 1,2-Dibromoethane **8** (6 mL, 0.07 mol) and potassium thioacetate (4 g, 0.035 mol) were dissolved in THF (80 mL). The resulting solution was stirred at reflux for 8 h. After filtration, the filtrate was concentrated in vacuo to give a yellowish residue which was purified using ethyl acetate-hexane (1:10, v/v) as eluent to give the title compound **9** as a colorless oil (4.01 g, 63%); ^{1}H NMR ($CDCl_3$): δ 2.36 (s, 3H, CH_3), 3.31 (t, J = 4.2 Hz, 2H, $BrCH_2CH_2S$), 3.46 (t, J = 4.2 Hz, 2H, $BrCH_2CH_2S$).[2]

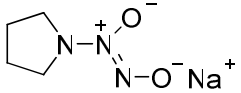
2-Iodoethyl thioacetate (**10**)



10

2-Bromoethyl thioacetate **9** (4.37 g, 24.4 mmol) was dissolved in dry acetone (50 mL) and sodium iodide (4.40 g, 29.3 mmol) was added. This mixture was allowed to stir at room temperature for 4 h during which time a precipitate (sodium bromide) formed. After filtration, the filtrate was condensed in vacuo, and then ethyl acetate (100 mL) was added. The organic solution was washed consecutively with water (80 mL), 2N sodium thiosulfate solution (80 mL), and then brine (80 mL). After the organic fraction was dried ($MgSO_4$), the organic fraction was condensed under vacuum to give the title compound **10** as a pink oil (4.59 g, 87%) which was used without further purification; ^{1}H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 3.22-3.28 (m, 2H, ICH_2CH_2S), 3.31-3.37 (m, 2H, ICH_2CH_2S). [3]

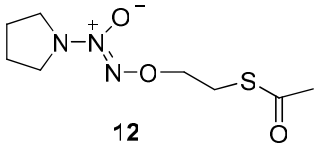
Sodium 1-(pyrrolidin-1-yl)diazen-1-ium-1,2-diolate (**11**)



11

A solution of pyrrolidine (32.8 mL, 0.397 mol) in acetonitrile (100 mL) and ether (100 mL) was mixed with 25% sodium methoxide in methanol (94 mL, 0.4 mol). The resulting solution was flushed with nitrogen, charged with 40-50 psi of NO, and stirred at room temperature. Two days later, the pressure was released and the product was collected by filtration, washed with ether, and dried under vacuum to give **11** (30.3 g, 51%) as a white powder; ^{1}H NMR (D_2O): δ 1.89 (m, 4H), 3.15 (m, 4H).[4]

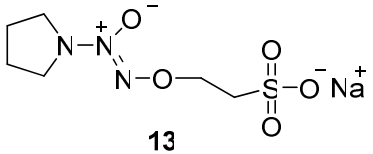
O^2-(2-Acetthioethyl) 1-(pyrrolidin-1-yl)diazen-1-ium-1,2-diolate (**12**)



12

The PYRRO/NO **11** (3.33 g, 21.8 mmol) was added to a mixture of sodium bicarbonate (500 mg, 6.0 mmol) and 15-crown-5 (5 drops) in dry DMF (20 mL) and dry THF (20 mL) at room temperature with stirring during 5 min. 2-Iodoethyl thioacetate **10** (4.55 g, 20.0 mmol) was added drop wise, and the reaction was allowed to proceed at room temperature for 15 h with stirring under argon. Ethyl acetate (200 mL) was added to dilute the reaction, the solids were filtered off, and the organic phase was washed with water (5 × 80 mL) and the organic fraction was dried ($MgSO_4$). The solvent was removed in vacuo to give a liquid residue which was purified by flash column chromatography using EtOAc-hexane (1:2, v/v) as eluent to furnish the title compound **12** (1.01 g, 20%) as a brown oil; IR (film): 2985, 2935, 2879, 1698, 1486 cm^{-1}; ESI-MS: 256 $[M+Na]^+$; ^{1}H NMR ($CDCl_3$): δ 1.92-1.97 (m, 4H, pyrrolidin-1-yl H-3 and H-4), 2.35 (s, 3H, CH_3), 3.22 (t, J = 6.8 Hz, 2H, OCH_2CH_2S), 3.53-3.57 (m, 4H, pyrrolidin-1-yl H-2 and H-5), 4.26 (t, J = 6.8 Hz, 2H, OCH_2CH_2S); ^{13}C NMR ($CDCl_3$): δ 22.8, 30.5, 50.9, 61.7, 71.3, 194.8.

O^2-(2-Oxysulfonylethyl sodium salt) 1-(pyrrolidin-1-yl)diazen-1-ium-1,2-diolate (**13**)

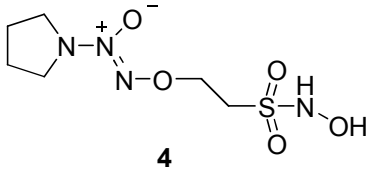


13

The thioacetate **12** (330 mg, 1.42 mmol) was dissolved in H_2O_2 (30% w/v, 0.72 mL) and AcOH (2.2 mL). Sodium acetate (140 mg, 1.70 mmol) was added, the reaction was allowed to proceed with stirring for 10 h at 55 °C, and then 10% Pd/C (about 1 g) was added to destroy the excess peroxide. After filtration, H_2O (5 mL) was added to the filtrate, and this aqueous solution was washed with ethyl acetate (2 × 5 mL). The aqueous solution was coevaporated with ethanol (2 × 5 mL) under reduced pressure to afford the crude sulfonate sodium salt **13** (244 mg, 66 %). Purification was performed on a C18 column (diameter 2 cm × length 7 cm) using H_2O-acetonitrile (95:5, v/v) as eluent to furnish the **13** as a colorless syrup; IR (film): 2960, 2879, 1658, 1201 cm^{-1}; ESI-MS: 238 $[M-Na]^-$;

^{1}H NMR (DMSO-d_6): δ 1.80-1.89 (m, 4H, pyrrolidin-1-yl H-3 and H-4), 2.83 (t, J = 7.9 Hz, 2H, OCH$_2$*CH$_2$*S), 3.48-3.65 (m, 4H, pyrrolidin-1-yl H-2 and H-5), 4.25 (t, J = 7.9 Hz, 2H, O*CH$_2$*CH$_2$S); ^{13}C NMR (DMSO-d_6): δ 22.2, 50.2, 50.5, 69.4.

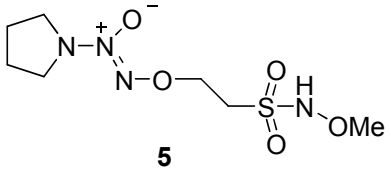
O^2-(2-Hydroxyaminosulfonylethyl) 1-(pyrrolidin-1-yl)diazen-1-ium-1,2-diolate (**4**)



4

The sulfonic acid sodium salt **13** (250 mg, 0.96 mmol) was dissolved in DMF (3 mL) and $SOCl_2$ (0.35 mL) was added drop wise. The reaction mixture was stirred at 25 °C for 1.5 h, poured into cold water (30 mL), and extracted with diethyl ether (3 x 30 mL). The combined organic fractions were washed with 2N HCl and brine, and the organic fraction was dried ($MgSO_4$). After concentration in vacuo at room temperature, the resulting brown syrup of the sulfonyl chloride product was used immediately for the next reaction without further purification. This ethanesulfonyl chloride residue was dissolved in dry THF (5 mL) and then hydroxylamine hydrochloric (200 mg, 2.88 mmol) and potassium carbonate (793 mg, 5.75 mmol) were added. The reaction mixture was vigorously stirred at room temperature until the sulfonyl chloride had completely disappeared (TLC; EtOAc-hexane, 1:2, v/v) in about 2 hours. The reaction mixture was filtered through a pad of Celite that provided a clear filtrate which was added to ethyl acetate (20 mL), this mixture was washed with water (20 mL) and brine (20 mL), and the organic fraction was dried ($MgSO_4$). Removal of the solvent from the organic fraction in vacuo gave a residue that was purified by flash silica gel column chromatography using n-hexane-EtOAc (2:1, v/v) as eluent to afford the title compound **4** (61 mg, 20%, two steps) as a white solid; mp 111-113 °C; IR (film): 3368, 3220, 2967, 2923, 1743, 1261 cm^{-1}; ESI-MS: 255 $[M+H]^+$, 253 $[M-H]^-$; ^{1}H NMR (DMSO-d_6): δ 1.85-1.89 (m, 4H, pyrrolidin-1-yl H-3 and H-4), 3.44-3.48 (m, 4H, pyrrolidin-1-yl H-2 and H-5), 3.56 (t, J = 6.1 Hz, 2H, OCH$_2$*CH$_2$*S), 4.43 (t, J = 6.1 Hz, 2H, O*CH$_2$*CH$_2$S), 9.19 and 9.71 (two d, J = 3.7 Hz, 1H each, *H*O-N*H*); ^{13}C NMR (DMSO-d_6): δ 22.3, 46.1, 50.5, 65.9. Anal. Calcd for $C_6H_{14}N_4O_5S$: C, 28.34; H, 5.55. Found: C, 28.10; H, 5.55.

O^2-(2-Methoxyaminosulfonylethyl) 1-(pyrrolidin-1-yl)diazen-1-ium-1,2-diolate (**5**)

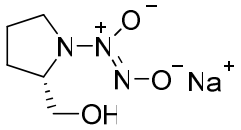


5

The sulfonic acid sodium salt **13** (250 mg, 0.96 mmol) was dissolved in DMF (3 mL) and $SOCl_2$ (0.35 mL) was added drop wise. The reaction mixture was allowed to stir at 25 °C for 1.5 h, poured into cold water (30 mL), and extracted with ethyl ether (3 x 30 mL). The combined organic fractions were washed with 2N HCl solution and brine, and the organic fraction was dried ($MgSO_4$). After concentration in vacuo at room temperature, the resulting brown syrup of the sulfonyl chloride product was dissolved in dry THF (5 mL), and then methoxylamine hydrochloride (160 mg, 1.92 mmol) and $NaHCO_3$ (320 mg, 3.84 mmol) were added. The reaction mixture was vigorously stirred at 25 °C until the sulfonyl chloride had completely disappeared (TLC; EtOAc-hexane, 1:2, v/v) in about 3 hours. The reaction mixture was filtered through a pad of Celite that provided a clear filtrate which was added to ethyl acetate (20 mL), this mixture was washed with water (20 mL) and brine (20 mL), and the organic fraction was dried ($MgSO_4$). Removal of the solvent from the organic fraction in vacuo

gave a residue that was purified by flash silica gel column chromatography using n-hexane-EtOAc (2:1, v/v) as eluent to afford the title compound **5** (72 mg, 28%, two steps) as a white solid; mp 85-86 °C; IR (film): 3228, 3220, 2968, 2941, 1742, 1338, 1172 cm^{-1}; ESI-MS: 269 $[M+H]^+$, 267 $[M-H]^-$; ^1H NMR (DMSO-d_6): δ 1.84-1.89 (m, 4H, pyrrolidin-1-yl H-3 and H-4), 3.43-3.47 (m, 4H, pyrrolidin-1-yl H-2 and H-5), 3.58 (t, J = 6.1 Hz, 2H, OCH_2CH_2S), 3.67 (s, 3H, OCH_3), 4.42 (t, J = 6.1 Hz, 2H, OCH_2CH_2S), 10.1 (s, 1H, N*H*); ^{13}C NMR (DMSO-d_6): δ 22.2, 47.3, 50.4, 64.4, 65.7. Anal. Calcd for $C_7H_{16}N_4O_5S$: C, 31.34; H, 6.01. Found: C, 31.68; H, 6.29.

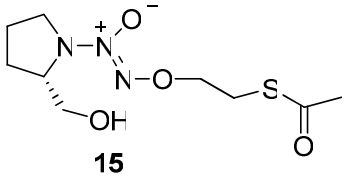
(S)-1-[2-(Hydroxymethyl)pyrrolidin-1-yl]diazen-1-ium-1,2-diolate sodium salt (**14**)



14

(*S*)-2-(Hydroxymethyl)pyrrolidine (5.0 g, 49 mmol) was dissolved in a 1:1 mixture of THF-diethyl ether (100 mL) and sodium methoxide (56 mmol, 11 mL of a 30% w/v solution in methanol) was added with stirring at room temperature during 5 min. This mixture was flushed with dry argon for 5 min, and the reaction was allowed to proceed under an atmosphere of nitric oxide (40-50 psi internal pressure) with stirring at room temperature for 24 h. The product, which precipitated as a fine white powder, was isolated by filtration and then washing with dry diethyl ether to give the title compound **14** (7.7 g, 85.0%); mp 123-127 °C;[5] ^1H NMR (D_2O): δ 1.64-2.09 (m, 4H, pyrrolidin-1-yl H-3 and H-4), 3.10-3.57 (m, 5H, pyrrolidin-1-yl H-2, H-5 and CH_2OH).[5]

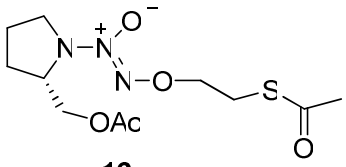
(S)-O^2-(2-Acetthioethyl) 1-[2-(hydroxymethyl)pyrrolidin-1-yl]diazen-1-ium-1,2-iolate (**15**)



15

The title compound **15** was synthesized, using a method similar to that used to prepare **12** starting from 2-iodoethyl thioacetate **10** and **14**, in 24% yield as a brownish oil; IR (film): 3431, 2953, 2874, 1710, 1452; ESI-MS: 286 $[M+Na]^+$; ^1H NMR ($CDCl_3$): δ 1.76-1.84 (m, 1H, pyrrolidin-1-yl H-3), 1.90-2.09 (m, 3H, pyrrolidin-1-yl H'-3, H-4 and H'-4), 2.35 (s, 3H, CH_3), 2.77 (brs, 1H, CH_2OH), 3.21 (t, J = 6.1 Hz, 2H, OCH_2CH_2S), 3.53-3.66 (m, 3H, pyrrolidin-1-yl H'-5, H-5 and CH*H*'OH), 3.76 (dd, J = 11.6, 3.6 Hz, 1H, C*H*H'OH), 4.03-4.10 (m, 1H, pyrrolidin-1-yl H-2), 4.28 (t, J = 6.1 Hz, 2H, OCH_2CH_2S); ^{13}C NMR ($CDCl_3$): δ 23.0, 26.8, 27.9, 30.5, 52.8, 64.1, 65.2, 17.6, 194.9.

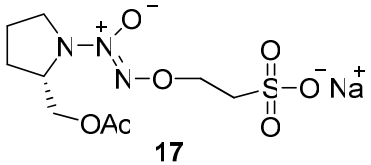
(S)-O^2-(2-Acetthioethyl) 1-[2-(acetoxymethyl)pyrrolidin-1-yl]diazen-1-ium-1,2-diolate (**16**)



16

Compound **15** (160 mg, 0.61 mmol) and 4-dimethylaminopyridine (DMAP) (148 mg, 1.21 mmol) were dissolved in dry CH_2Cl_2 (8 mL), acetyl bromide (150 mg, 1.22 mmol) was added with stirring at ice-water bath temperature, and the reaction was allowed to proceed at room temperature for 1 h. Additional CH_2Cl_2 (20 mL) was added to the reaction mixture, the combined organic phase was washed with 1N HCl solution (2 × 10 mL), brine (10 mL), and the organic fraction was dried (Mg_2SO_4). After filtration and removal of the solvent, the title compound **16** was obtained as a brownish oil (160 mg, 86%); IR (film): 2957, 2877, 1750, 1704, 1247; ESI-MS: 328 $[M+Na]^+$; ^{1}H NMR ($CDCl_3$): δ 1.74-1.82 (m, 1H, pyrrolidin-1-yl H-3), 1.92-1.99 (m, 3H, pyrrolidin-1-yl H'-3, H-4 and H'-4), 2.05 (s, 3H, OCO*CH*$_3$), 2.33 (s, 3H, SCO*CH*$_3$), 3.21 (t, J = 6.1 Hz, 2H, OCH_2CH_2S), 3.50-3.64 (m, 2H, pyrrolidin-1-yl H-5' and H-5), 4.18-4.56 (m, 3H, pyrrolidin-1-yl H-2 and CH_2OAc), 4.26 (t, J = 6.1 Hz, 2H, OCH_2CH_2S); ^{13}C NMR ($CDCl_3$): δ 20.9, 22.7, 26.8, 27.1, 30.5, 52.7, 61.0, 65.4, 71.5, 170.6, 194.8.

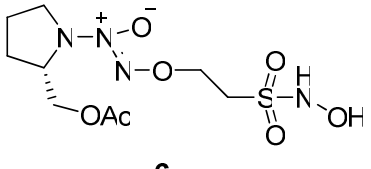
O^2-(2-Oxysulfonylethyl sodium salt) 1-[2-(acetoxymethyl)pyrrolidin-1-yl]diazen-1-ium-1,2-diolate (**17**)



17

The title compound **17** was synthesized, using a method similar to that used to prepare **13** starting from **16**, in 75% yield, as a brownish syrup; IR (film): 2960, 2874, 1755, 1697, 1200 cm^{-1}; ESI-MS: 310 $[M-Na]^-$; ^{1}H NMR (DMSO-d_6): δ 1.67-1.71 (m, 1H, pyrrolidin-1-yl H-3), 1.82-2.07 (m, 3H, pyrrolidin-1-yl H'-3, H-4 and H'-4), 2.00 (s, 3H, OCO*CH*$_3$), 2.83 (t, J = 7.9 Hz, 2H, OCH_2CH_2S), 3.36-3.51 (m, 2H, pyrrolidin-1-yl H'-5 and H-5), 4.08-4.12 (m, 3H, pyrrolidin-1-yl H-2 and CH_2OAc), 4.27 (t, J = 7.9 Hz, 2H, OCH_2CH_2S); ^{13}C NMR (DMSO-d_6): δ 20.5, 22.1, 26.2, 50.2, 52.2, 59.5, 64.9, 69.6, 170.0.

(S)-O^2-(2-Hydroxyaminosulfonylethyl) 1-[2-(acetoxymethyl)pyrrolidin-1-yl]diazen-1-ium-1,2-diolate (**6**)

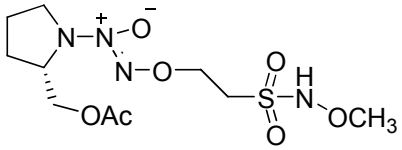


6

The title compound **6** was synthesized, using a method similar to that used to prepare **4** starting from **17**, in 23% yield (two steps), as a brownish oil; IR (film): 3371, 3225, 2969, 2929, 1748, 1261 cm^{-1}; $[\alpha]^{21.0}_D$ = – 66.10 (c 0.1800; EtOAc); ESI-MS: 349 $[M+Na]^+$, 325 $[M-H]^-$; ^{1}H NMR (DMSO-d_6): δ 1.55-1.58 (m, 1H, pyrrolidin-1-yl H-3), 1.84-2.03 (m, 3H, pyrrolidin-1-yl H'-3, H-4 and H'-4), 2.00 (s, 3H, OCO*CH*$_3$), 3.41-3.51 (m, 2H, pyrrolidin-1-yl H'-5 and H-5), 3.55 (t, J = 6.1 Hz, 2H, OCH_2CH_2S), 4.07-4.11 (m, 2H, CH_2OAc), 4.14-4.17 (m, 1H, pyrrolidin-1-yl H-2), 4.44 (t, J = 6.1 Hz, 2H, OCH_2CH_2S), 9.19 and 9.69 (two d, J = 3.1 Hz, 1H each, N*H*-O*H*); ^{13}C NMR (DMSO-d_6): δ 20.5, 22.2, 26.2, 46.2, 52.1, 59.6, 64.8, 66.1, 170.1. Anal. Calcd for $C_9H_{18}N_4O_7S$: C, 33.13; H, 5.56; N,

17.17. Found: C, 35.23; H, 5.95; N, 15.67 (Diazen-1-ium-1,2-diolates such as **6** often do not give microanalytical data within ± 0.4% of theoretical values even when the compound is pure).

(S)-O^2-(2-Methoxyaminosulfonylethyl) 1-[2-(acetoxymethyl)pyrrolidin-1-yl]diazen-1-ium-1,2-diolate (**7**)



7

The title compound **7** was synthesized, using a method similar to that used to prepare **5** starting from **17**, in 21% yield (two steps), as a brownish oil; IR (film): 3204, 2961, 2921, 2865, 1742, 1266, 1028 cm^{-1}; $[\alpha]^{21.0}_{D} = -35.69$ (c 0.1300; EtOAc); ESI-MS: 363 $[M+Na]^+$, 339 $[M-H]^-$; ^{1}H NMR (DMSO-d_6): δ 1.68-1.73 (m, 1H, pyrrolidin-1-yl H-3), 1.84-2.06 (m, 3H, pyrrolidin-1-yl H'-3, H-4 and H'-4), 2.01 (s, 3H, OCO*CH$_3$*), 3.41-3.54 (m, 2H, pyrrolidin-1-yl H'-5 and H-5), 3.58 (t, *J* = 6.1 Hz, 2H, OCH$_2$*CH$_2$*S), 3.66 (s, 3H, O*CH$_3$*), 4.08-4.11 (m, 2H, *CH$_2$*OAc), 4.13-4.19 (m, 1H, pyrrolidin-1-yl H-2), 4.43 (t, *J* = 6.1 Hz, 2H, O*CH$_2$*CH$_2$S), 10.2 (s, 1H, N*H*); ^{13}C NMR (DMSO-d_6): δ 20.5, 22.2, 26.2, 47.3, 52.1, 59.6, 64.4, 64.8, 65.8, 170.1. Anal. Calcd for $C_{10}H_{20}N_4O_7S$: C, 35.29; H, 5.92; N, 16.46. Found: C, 36.83; H, 6.08; N, 15.25 (Diazen-1-ium-1,2-diolates such as **7** often do not give microanalytical data within ± 0.4% of theoretical values even when the compound is pure).

The recovery of ibuprofen from *N*-methoxyethanesulfonylamide ester of ibuprofen **3**

N-methoxyethanesulfonylamide ester of ibuprofen **3** (30 mg, 0.087 mmol) [6] was dissolved in dry THF (2 mL), and then 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (60 mg, 0.39 mmol) was added. The reaction was proceeded at room temperature for 16 h during which time a white precipitate formed. The reaction mixture was acidified to pH 3-4 using 1N HCl solution, and then was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic fractions were collected and washed with brine (8 mL), dried (Mg_2SO_4). Removal of the solvent from the organic fraction in vacuo gave a residue that was purified by flash silica gel column chromatography using n-hexane-EtOAc (3:1, v/v) as eluent to afford ibuprofen (13 mg, 72%) as a white solid; ^{1}H NMR ($CDCl_3$): ^{1}H NMR (DMSO-d_6): δ 0.90 (d, *J* = 6.7 Hz, 6H, *(CH$_3$)$_2$*CHCH$_2$), 1.50 (d, *J* = 7.4 Hz, 3H, CH*CH$_3$*), 1.85 (heptet, *J* = 6.7 Hz, 1H, (CH$_3$)$_2$*CH*CH$_2$), 2.45 (d, *J* = 6.7 Hz, 2H, (CH$_3$)$_2$CH*CH$_2$*), 3.73 (q, *J* = 7.4 Hz, 1H, Ar*CH*), 7.10 (d, *J* = 8.0 Hz, 2H, phenyl H-3 and H-5), 7.19 (d, *J* = 8.0 Hz, phenyl H-2 and H-6).

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2. Bauer, L.; Suresh, K. S.; Ghosh, B. K. *J. Org. Chem.* **1965**, *30*, 949-951.
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4. Saavedra, J. E.; Billiar, T. R.; Williams, D. L.; Kim, Y.; Watkins, S. C.; Keefer, L. K. *J. Med. Chem.* **1997,** *40,* 1947-1954.
5. Velázquez, C. A.; Chen, Q. H.; Citro, M. L. Keefer, L. K.; Knaus, E. E. *J. Med. Chem.* **2008**, *51,* 1954–1961.
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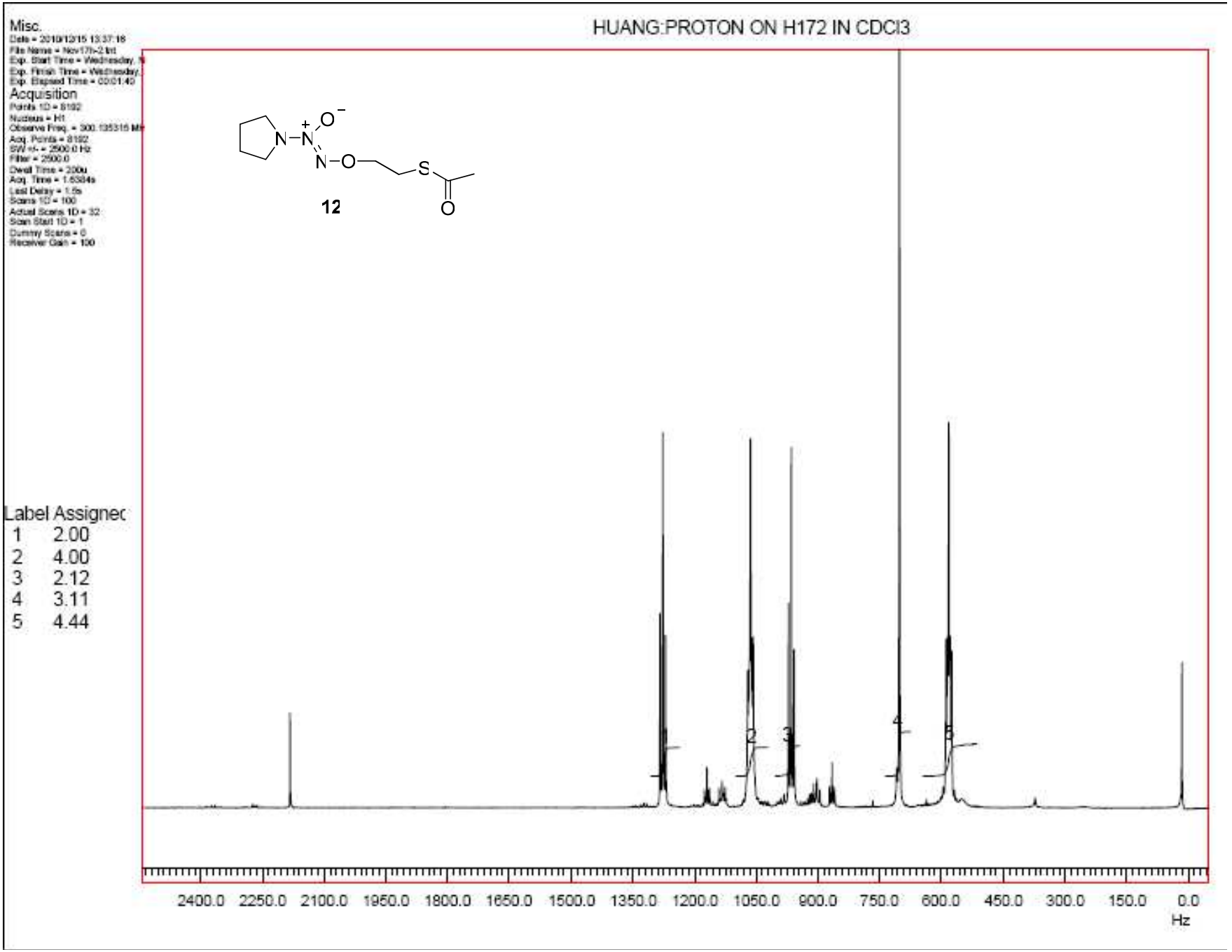
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SW +/- = 2500.0 Hz
Filter = 2500.0
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Acq. Time = 1.6384s
Last Delay = 1.5s
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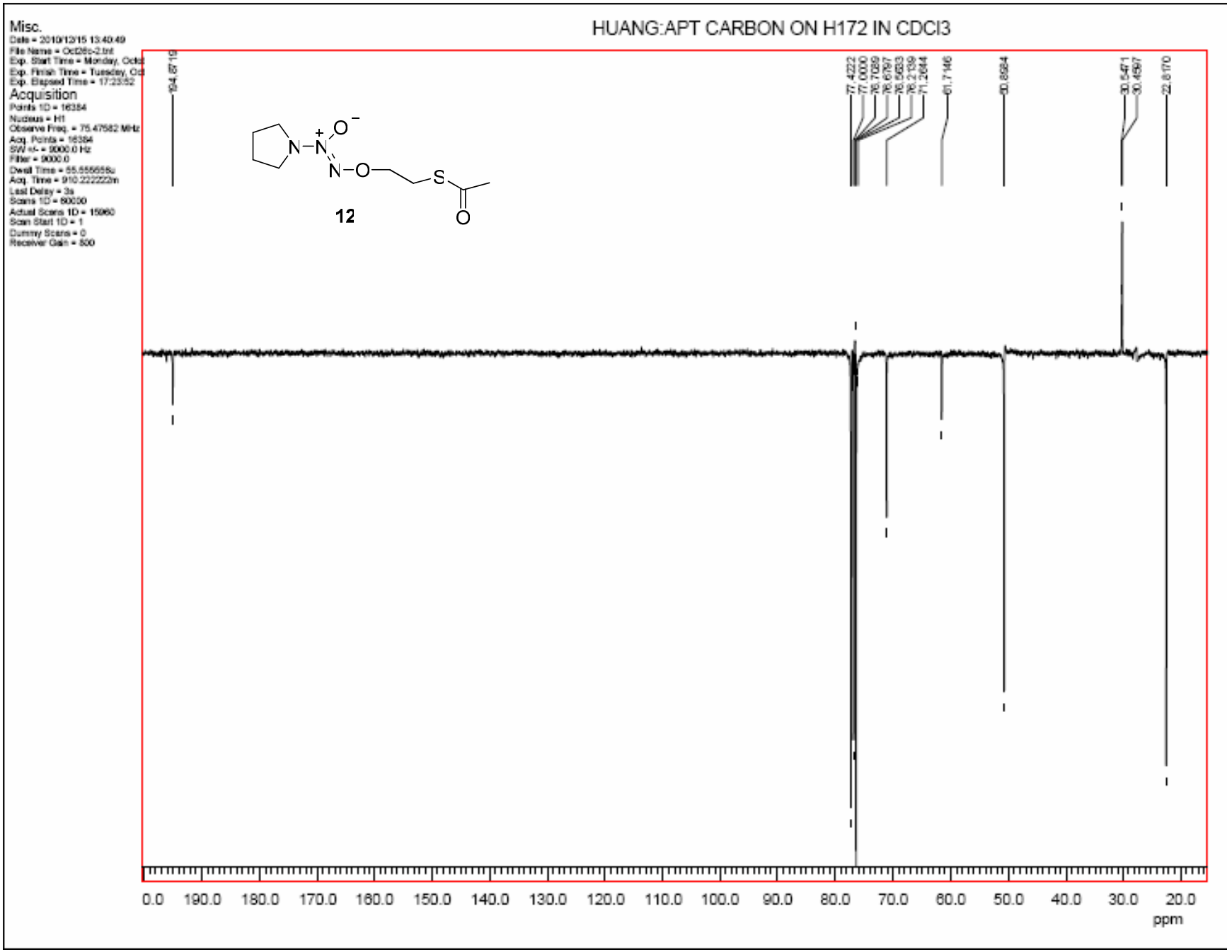
Dummy Scans = 0
Receiver Gain = 100
HUANG:PROTON ON H172 IN CDCl3
12
Label Assigned
1 2.00
2 4.00
3 2.12
4 3.11
5 4.44
2400.0 2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0 150.0 0.0
Hz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Nucleus = H1
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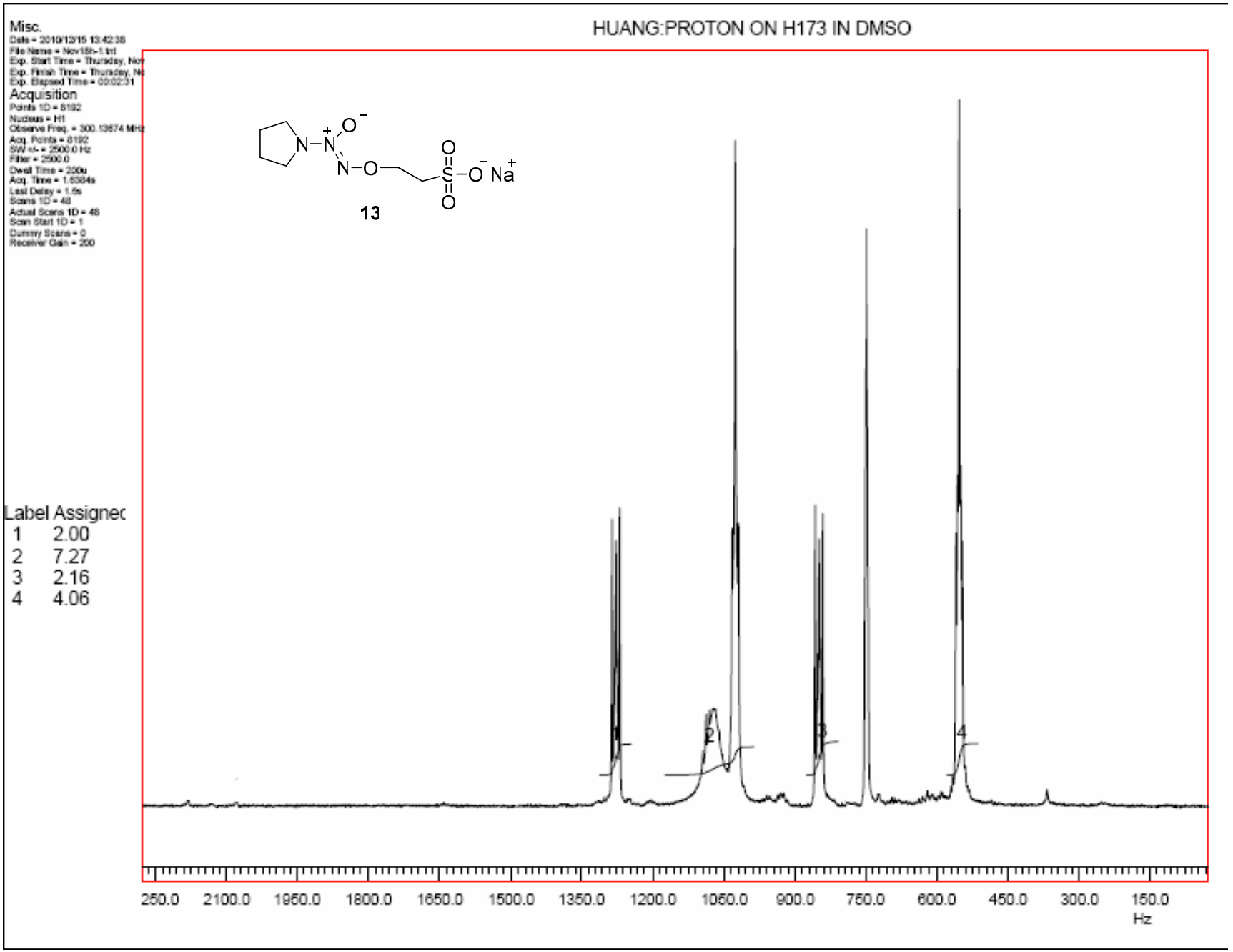
Acq. Points = 16384
SW +/- = 9000.0 Hz
Filter = 9000.0
Dwell Time = 55.555555u
Acq. Time = 910.222222m
Last Delay = 3s
Scans 1D = 50000
Actual Scans 1D = 15960
Scan Start 1D = 1
Dummy Scans = 0
Receiver Gain = 500
HUANG:APT CARBON ON H172 IN CDCl3
194.6719
77.4222
77.0000
76.7089
76.6797
76.5633
76.2139
71.2644
61.7146
30.8624
30.5471
30.4597
22.8170
12
0.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
ppm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Exp. Finish Time = Thursday, No
Exp. Elapsed Time = 00:02:31
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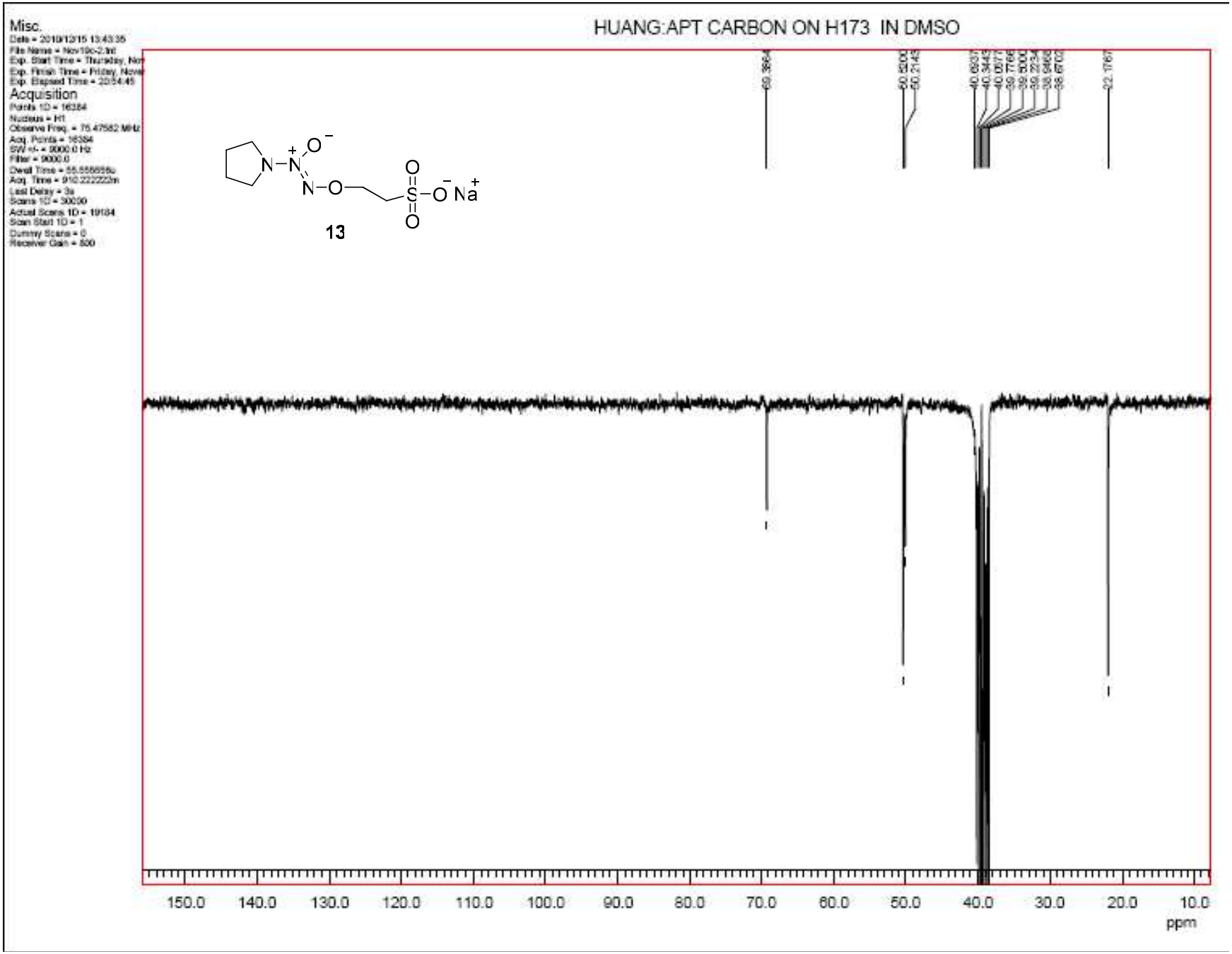
Nucleus = H1
Observe Freq. = 300.13674 MHz
Acq. Points = 8192
SW +/- = 2500.0 Hz
Filter = 2500.0
Dwell Time = 200u
Acq. Time = 1.6384s
Last Delay = 1.5s
Scans 1D = 48
Actual Scans 1D = 48
Scan Start 1D = 1
Dummy Scans = 0
Receiver Gain = 200
HUANG:PROTON ON H173 IN DMSO
13
Label Assignec
1 2.00
2 7.27
3 2.16
4 4.06
250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0 150.0
Hz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Nucleus = H1
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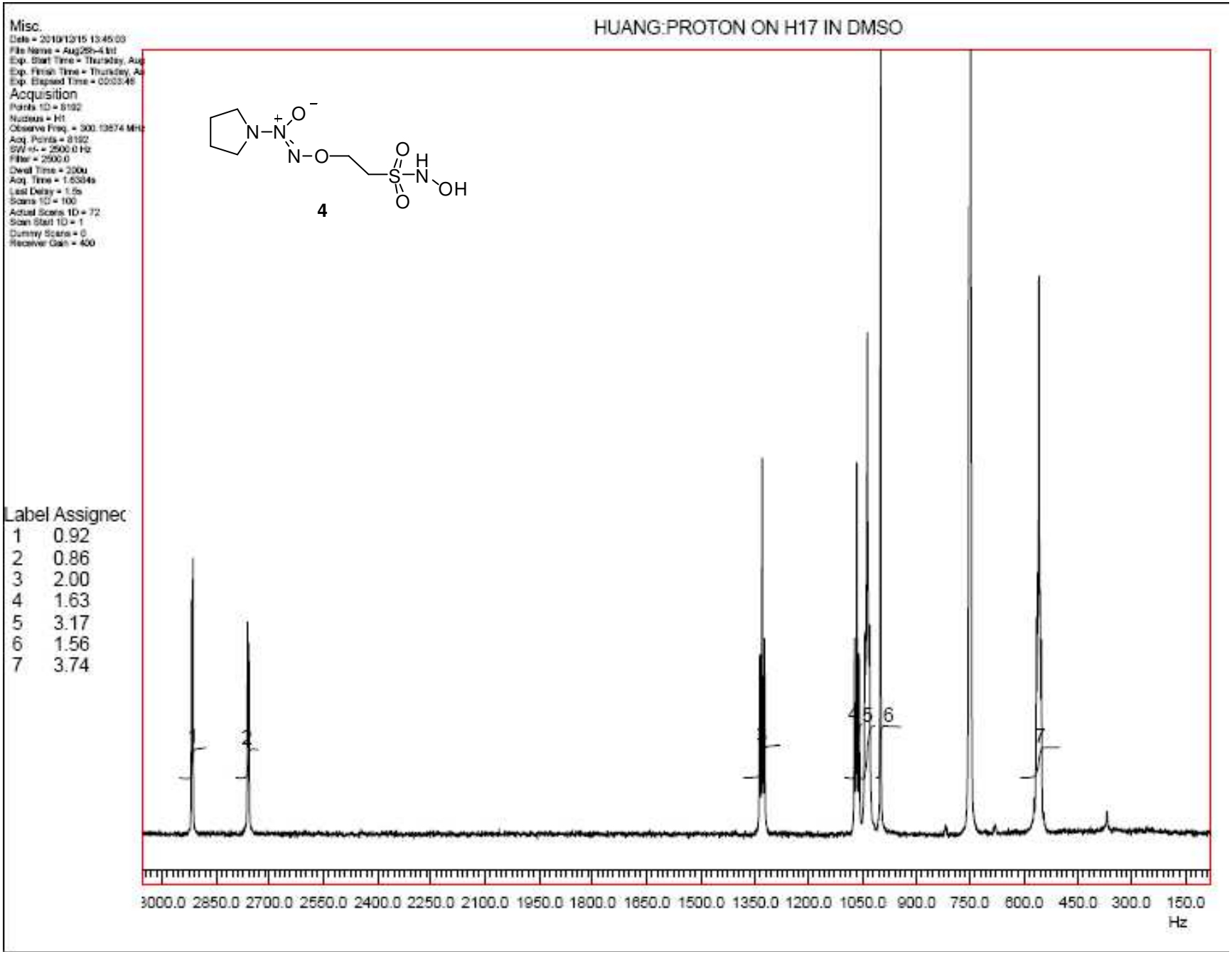
Acq. Points = 16384
SW +/- = 9000.0 Hz
Filter = 9000.0
Dwell Time = 55.555555u
Acq. Time = 910.222222m
Last Delay = 3s
Scans 1D = 30000
Actual Scans 1D = 19184
Scan Start 1D = 1
Dummy Scans = 0
Receiver Gain = 500
HUANG:APT CARBON ON H173 IN DMSO
13
69.364
50.5200
50.2143
40.6937
40.3443
40.0577
39.7766
39.5000
39.2234
38.9468
38.6702
22.1767
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
ppm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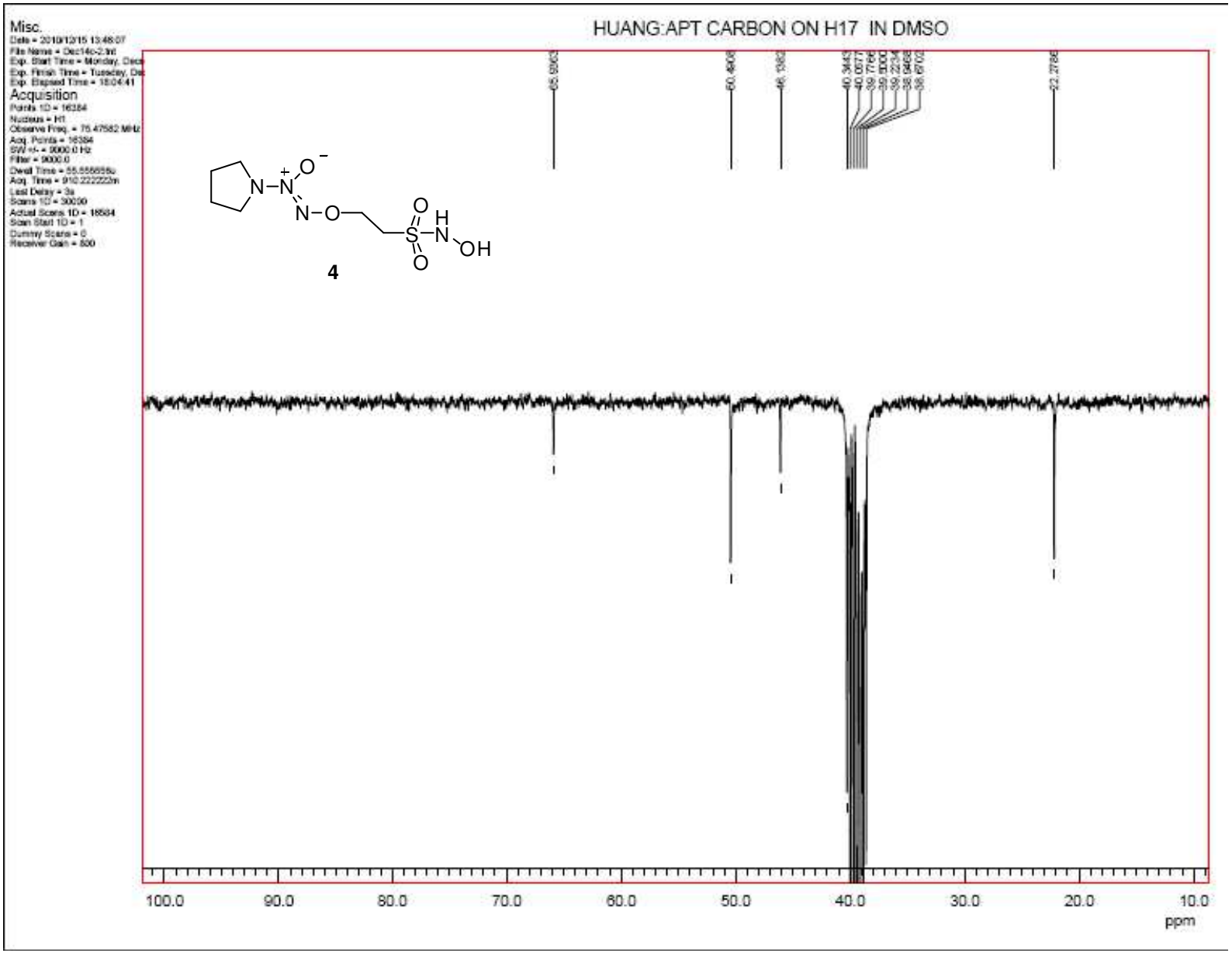
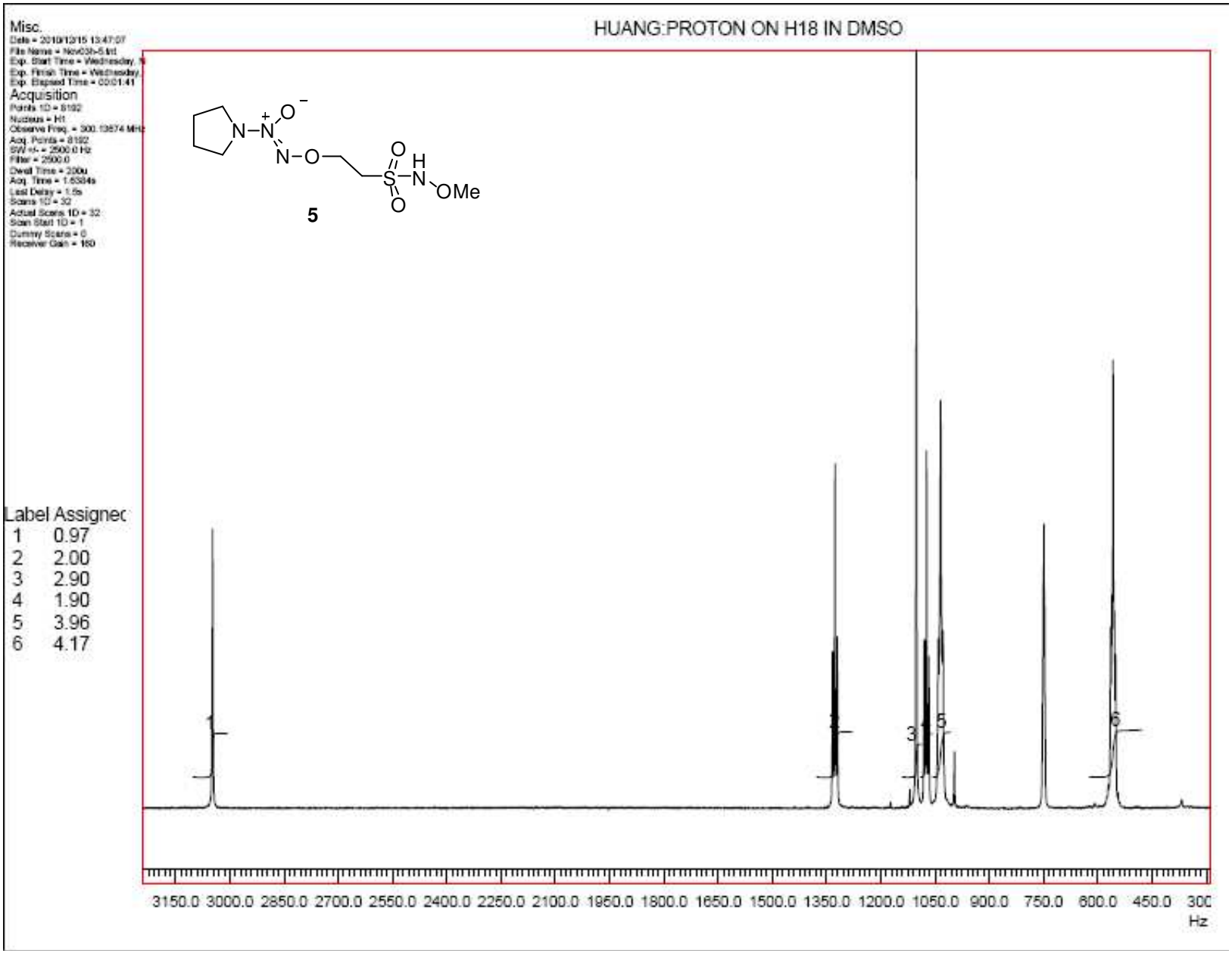
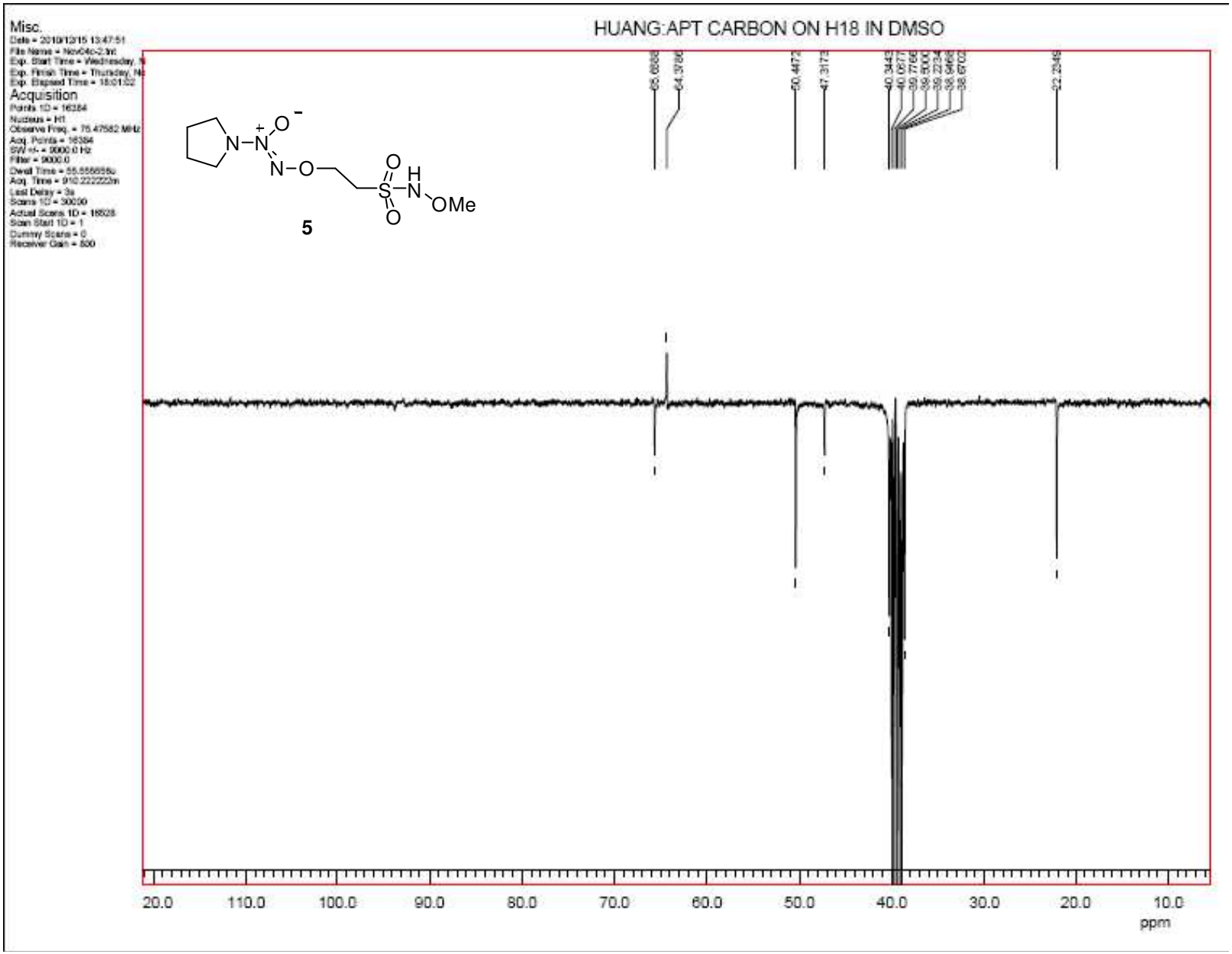
Misc.
Acquisition
Label Assigned
1 0.92
2 0.86
3 2.00
4 1.63
5 3.17
6 1.56
7 3.74
4
3000.0 2850.0 2700.0 2550.0 2400.0 2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0 150.0
Hz


Misc.
Acquisition
HUANG:APT CARBON ON H17 IN DMSO
4
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
ppm


Misc.
Acquisition
HUANG:PROTON ON H18 IN DMSO
5
Label Assigned
1 0.97
2 2.00
3 2.90
4 1.90
5 3.96
6 4.17
3150.0 3000.0 2850.0 2700.0 2550.0 2400.0 2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300
Hz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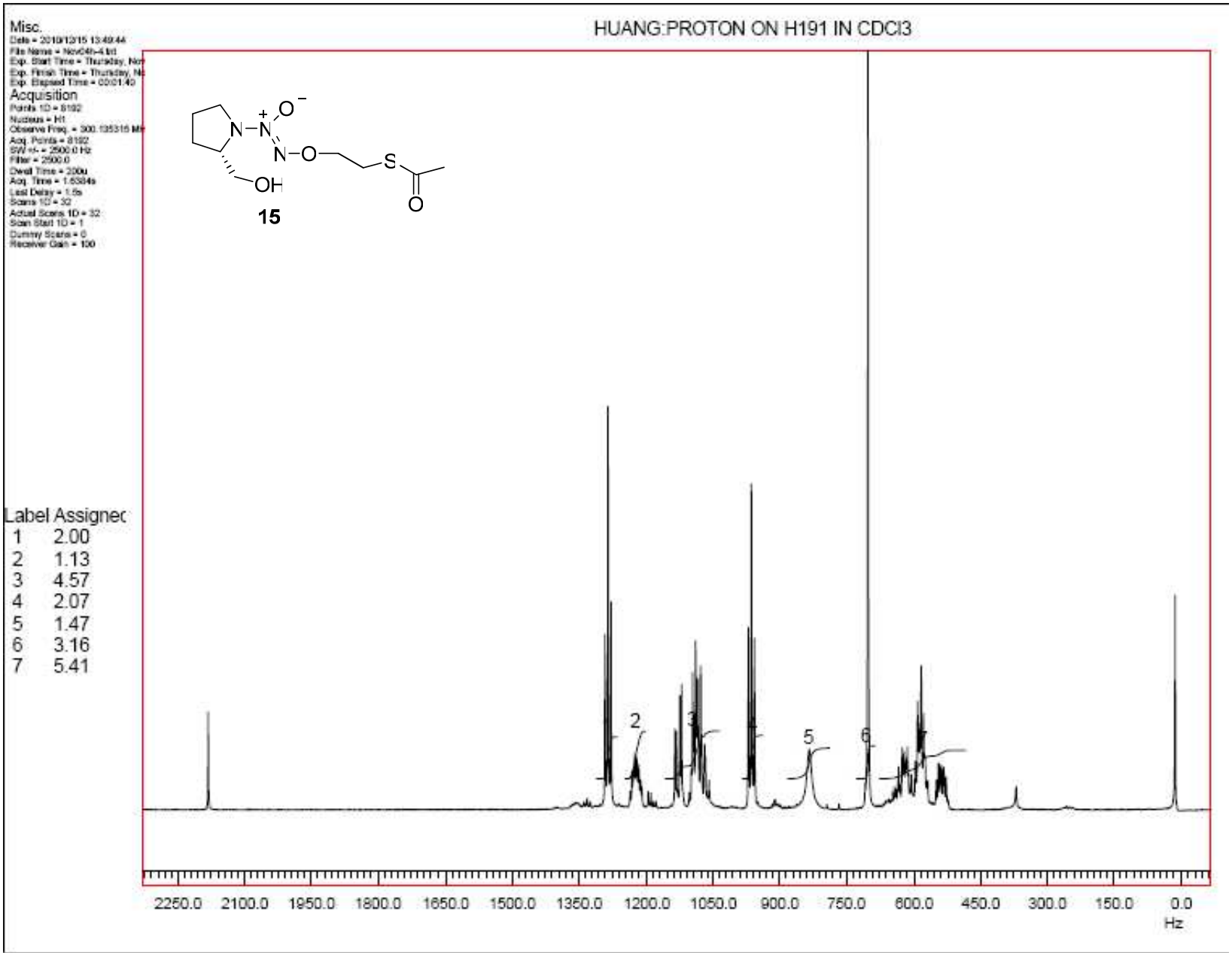
Acquisition
HUANG:APT CARBON ON H18 IN DMSO
5
65.6886
64.3786
50.4472
47.3173
40.3443
40.0677
39.7766
39.5000
39.2234
38.9468
38.6702
22.2548
20.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
ppm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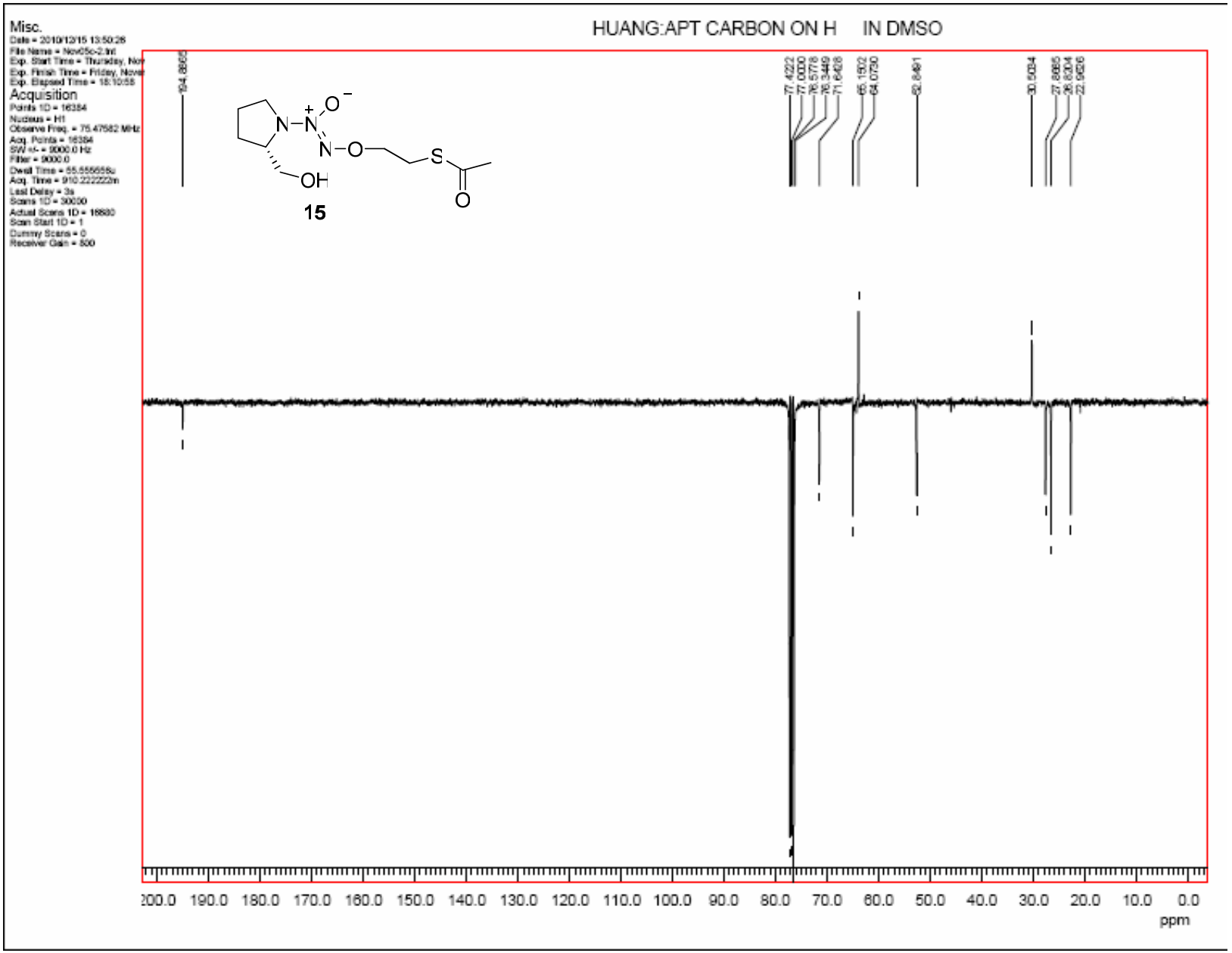
Nucleus = H1
Observe Freq. = 300.135315 MH
Acq. Points = 8192
SW =/- = 2500.0 Hz
Filter = 2500.0
Dwell Time = 200u
Acq. Time = 1.6384s
Last Delay = 1.5s
Scans 1D = 32
Actual Scans 1D = 32
Scan Start 1D = 1
Dummy Scans = 0
Receiver Gain = 100
HUANG:PROTON ON H191 IN CDCl3
15
Label Assigned
1 2.00
2 1.13
3 4.57
4 2.07
5 1.47
6 3.16
7 5.41
2
3
5
6
2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0 150.0 0.0
Hz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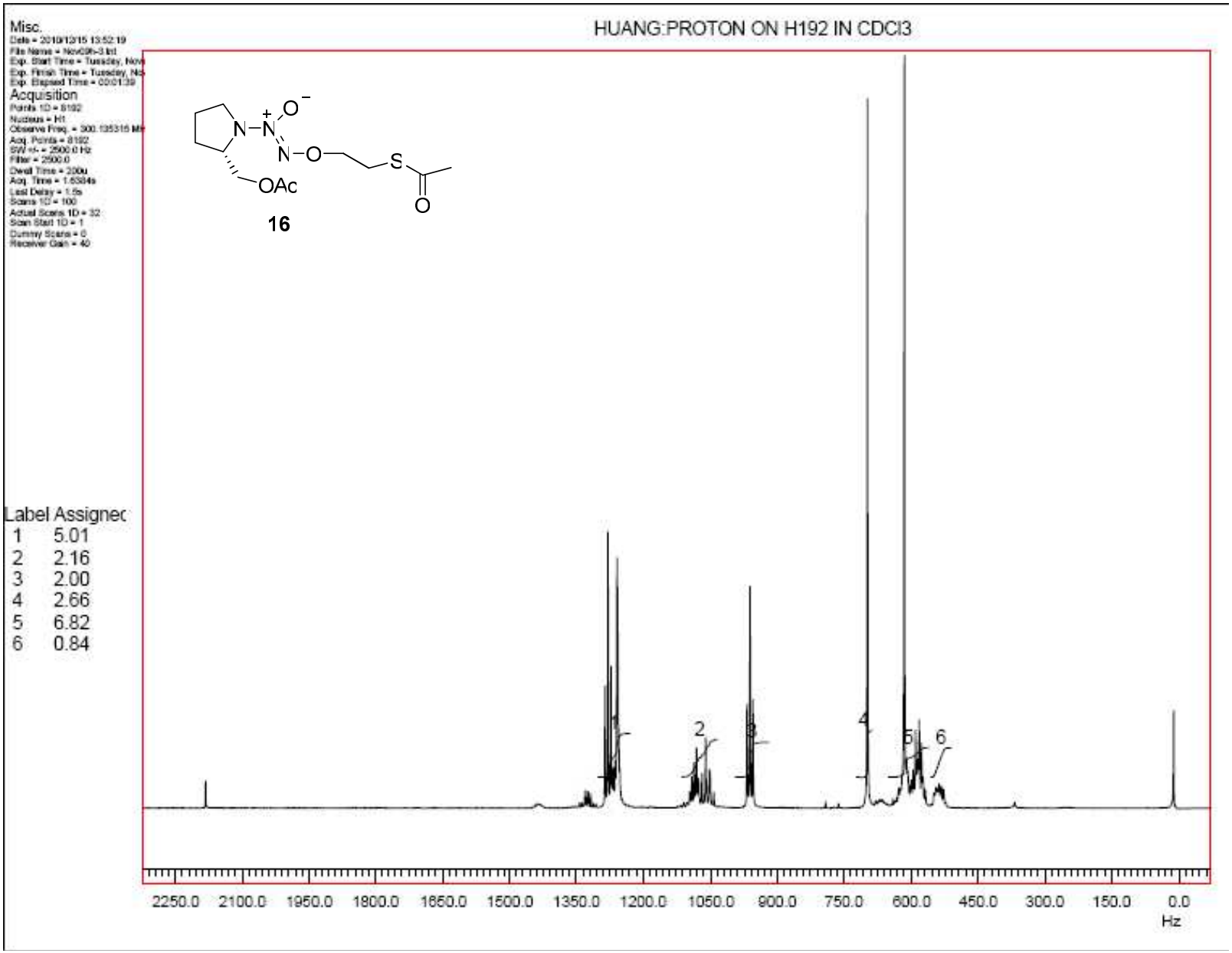
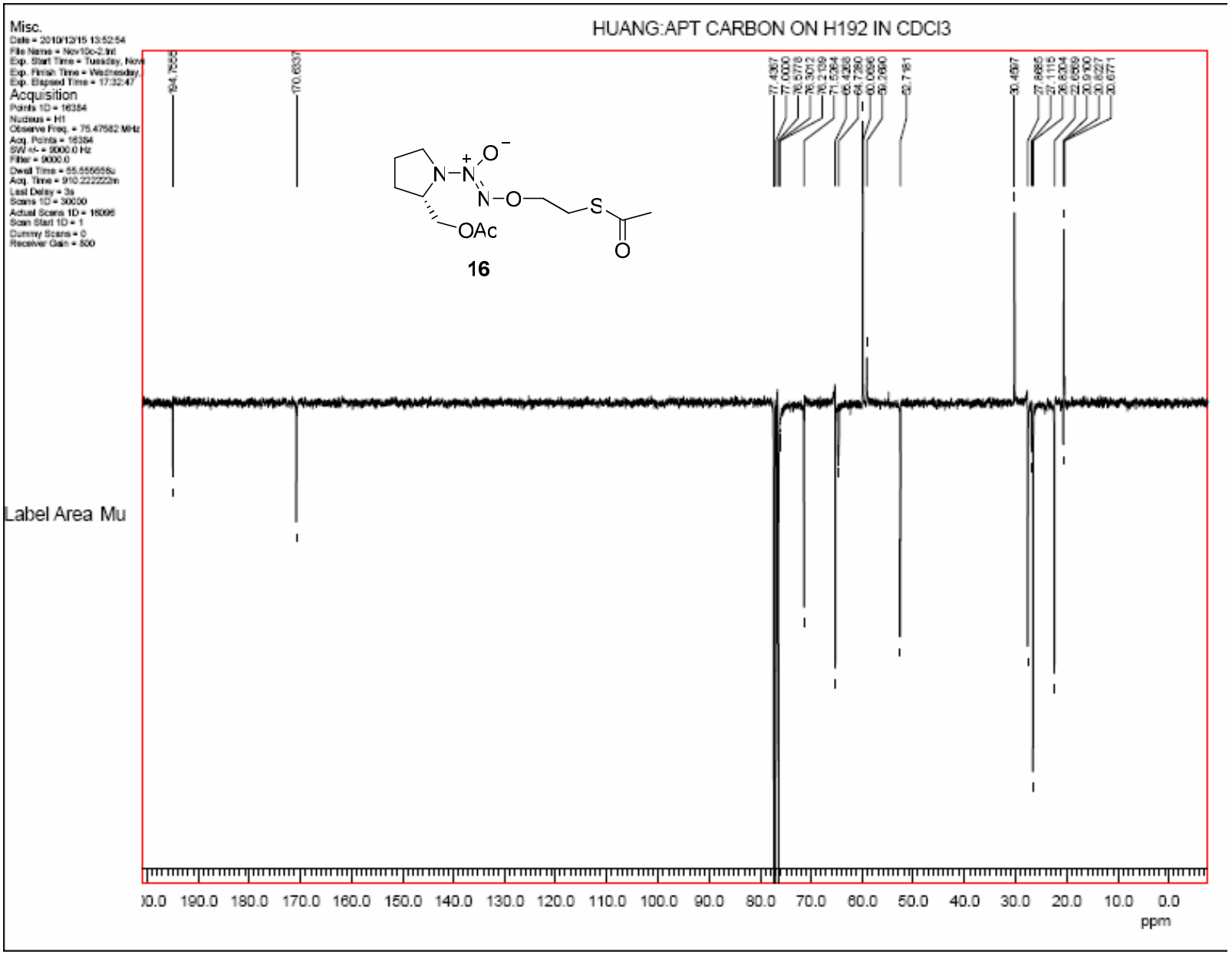
Nucleus = H1
Observe Freq. = 75.47582 MHz
Acq. Points = 16384
SW =/- = 9000.0 Hz
Filter = 9000.0
Dwell Time = 55.555555u
Acq. Time = 910.222222m
Last Delay = 3s
Scans 1D = 30030
Actual Scans 1D = 18880
Scan Start 1D = 1
Dummy Scans = 0
Receiver Gain = 500
HUANG:APT CARBON ON H IN DMSO
194.8955
77.4222
77.0000
76.5778
76.3449
71.6408
65.1902
64.0750
52.8491
30.5034
27.8885
26.8304
22.9826
15
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0
ppm


Misc.
Acquisition
HUANG:PROTON ON H192 IN CDCl3
OAc
16
Label Assigned
1 5.01
2 2.16
3 2.00
4 2.66
5 6.82
6 0.84
2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0 150.0 0.0
Hz


HUANG:APT CARBON ON H192 IN CDCl3
Misc.
Acquisition
Label Area Mu
194.7555
170.6537
77.4367
77.0000
76.5778
76.3012
76.2139
71.5364
66.4268
64.7280
60.0696
59.2660
52.7161
30.4997
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26.8304
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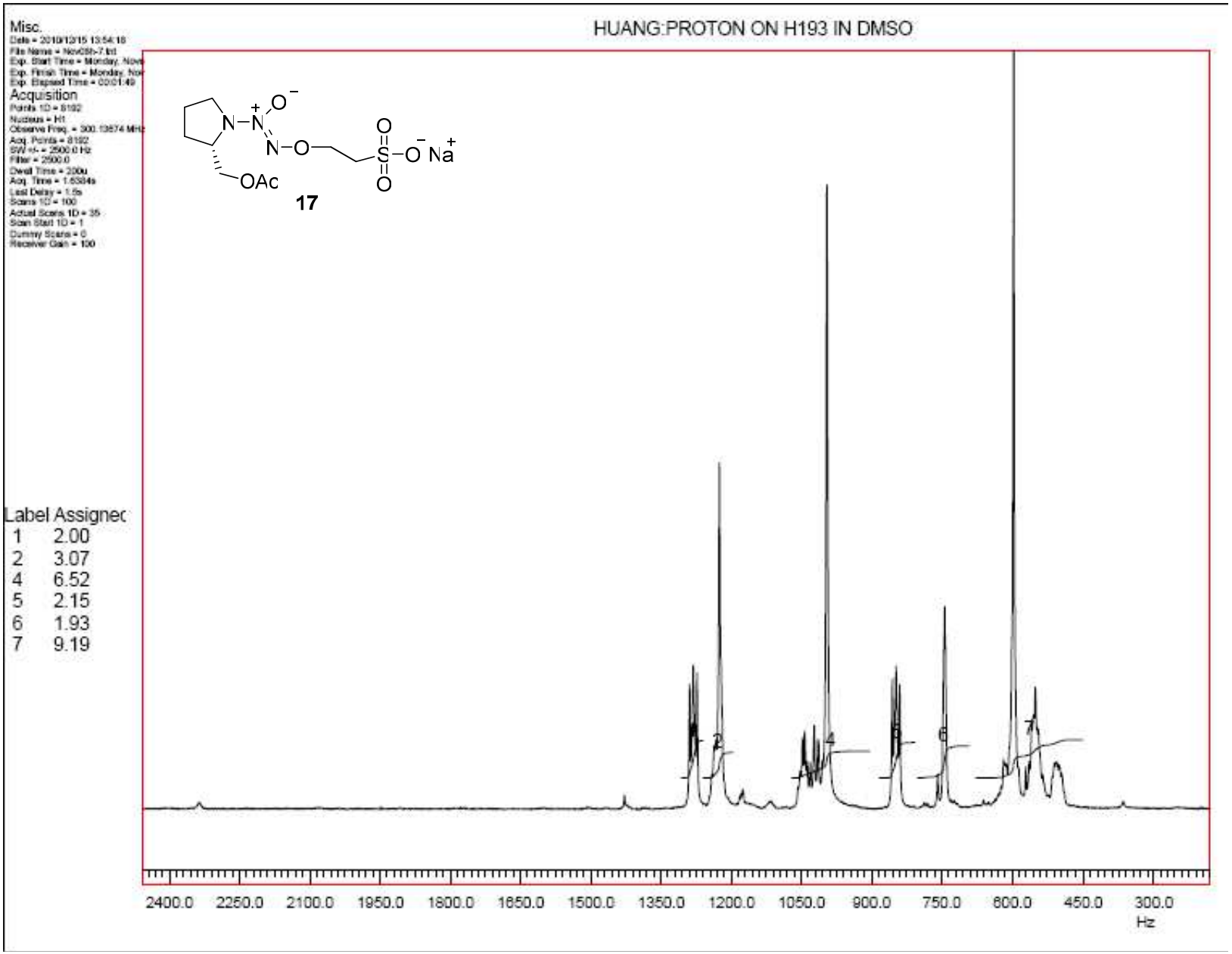
16
OAc
S
O
ppm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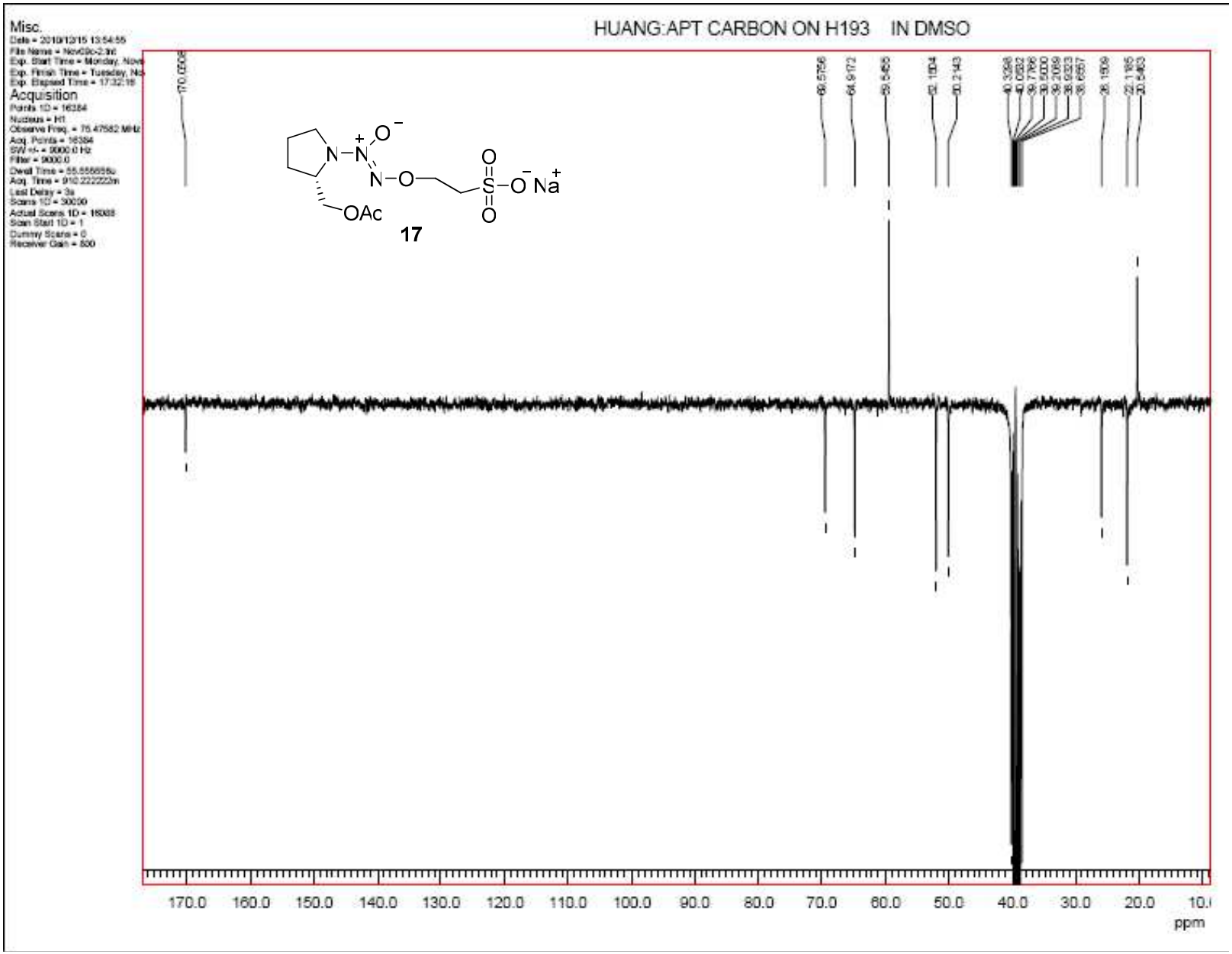
Points 1D = 8192
Nucleus = H1
Observe Freq. = 300.13674 MHz
Acq. Points = 8192
SW =/= = 2500.0 Hz
Filter = 2500.0
Dwell Time = 200u
Acq. Time = 1.6384s
Last Delay = 1.5s
Scans 1D = 100
Actual Scans 1D = 35
Scan Start 1D = 1
Dummy Scans = 0
Receiver Gain = 100
HUANG:PROTON ON H193 IN DMSO
OAc
17
Label Assigned
1 2.00
2 3.07
4 6.52
5 2.15
6 1.93
7 9.19
2400.0 2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0
Hz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Nucleus = H1
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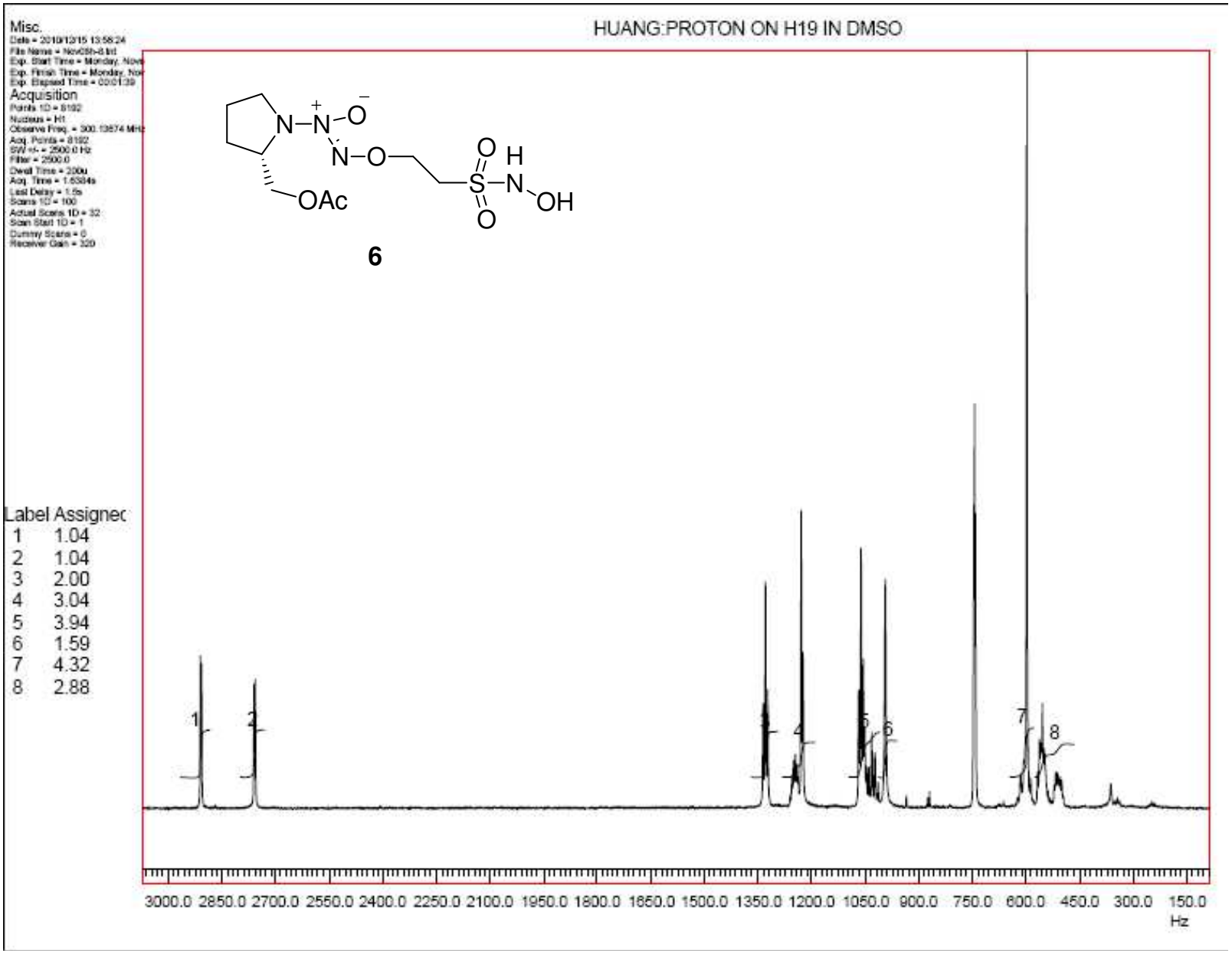
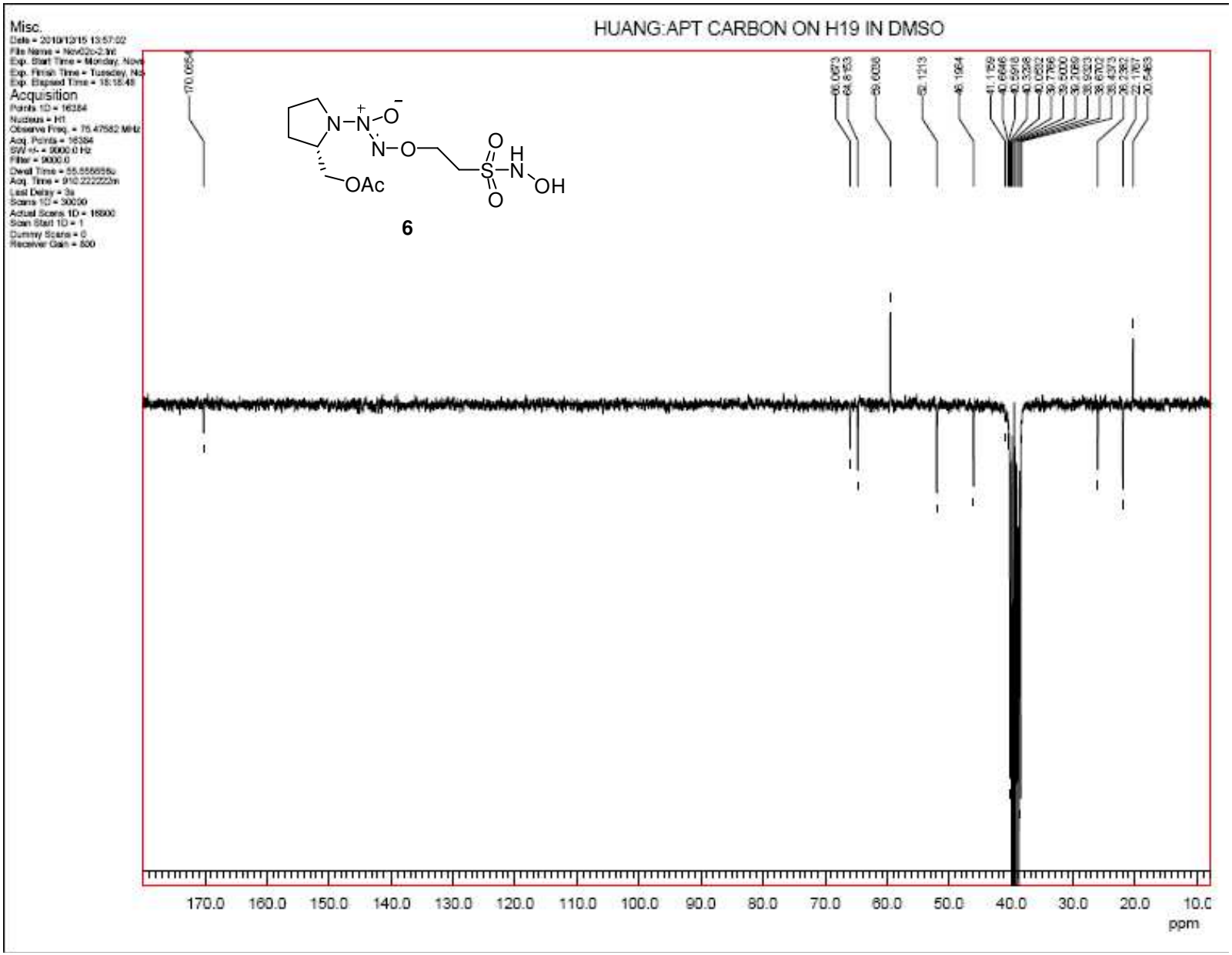
Acq. Points = 16384
SW +/- = 9000.0 Hz
Filter = 9000.0
Dwell Time = 55.555555u
Acq. Time = 910.222222m
Last Delay = 3s
Scans 1D = 30000
Actual Scans 1D = 18000
Scan Start 1D = 1
Dummy Scans = 0
Receiver Gain = 800
HUANG:APT CARBON ON H193 IN DMSO
170.0508
66.5756
64.9172
59.5455
52.1804
50.2143
40.3398
40.0532
39.7796
39.5060
39.2059
38.9323
38.6587
26.1509
22.1185
20.5463
17
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
ppm


Misc.
Acquisition
HUANG:PROTON ON H19 IN DMSO
OAc
6
Label Assignec
1 1.04
2 1.04
3 2.00
4 3.04
5 3.94
6 1.59
7 4.32
8 2.88
3000.0 2850.0 2700.0 2550.0 2400.0 2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0 150.0
Hz


Misc.
Acquisition
HUANG:APT CARBON ON H19 IN DMSO
OAc
OH
6
170.0
160.0
150.0
140.0
130.0
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100.0
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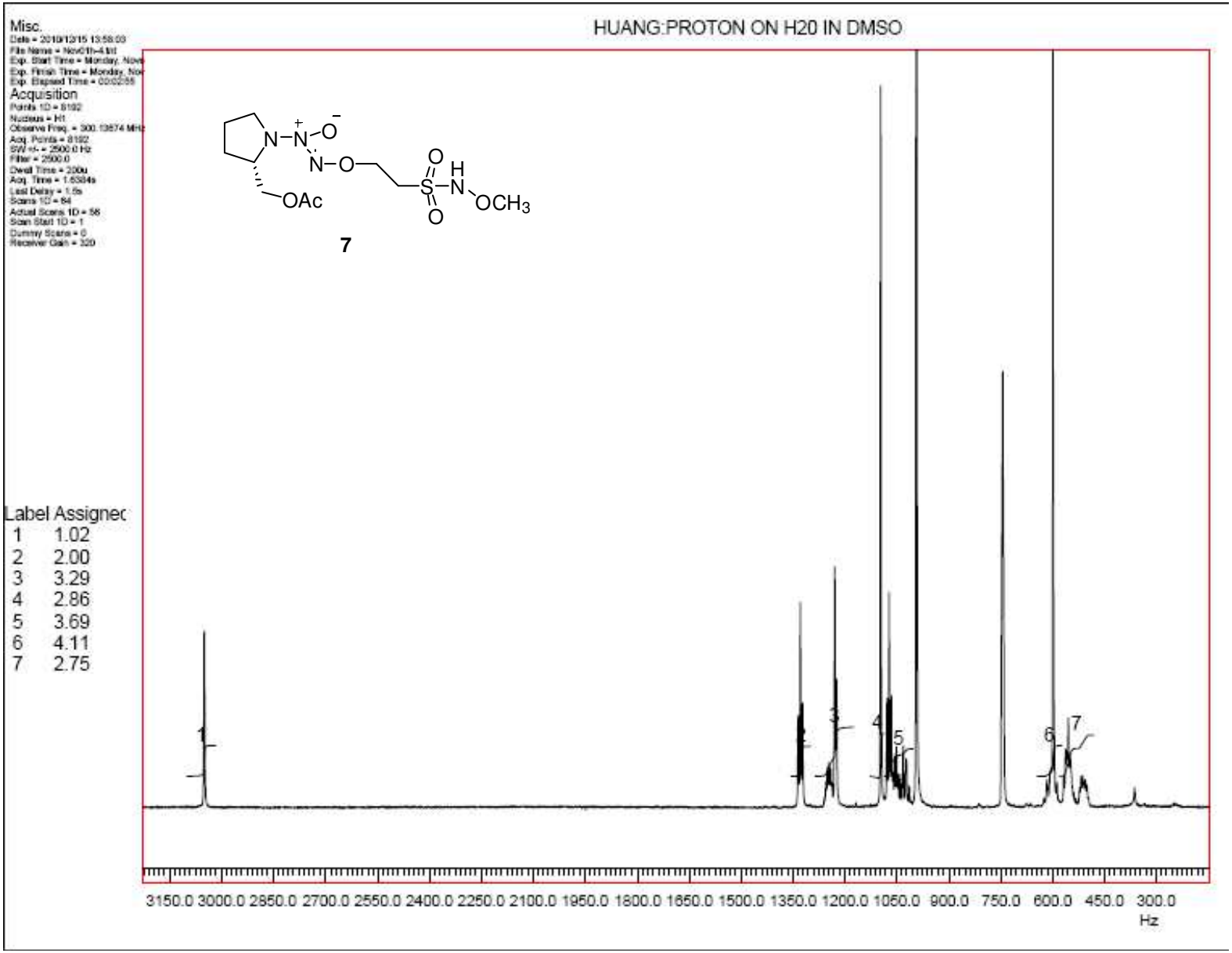
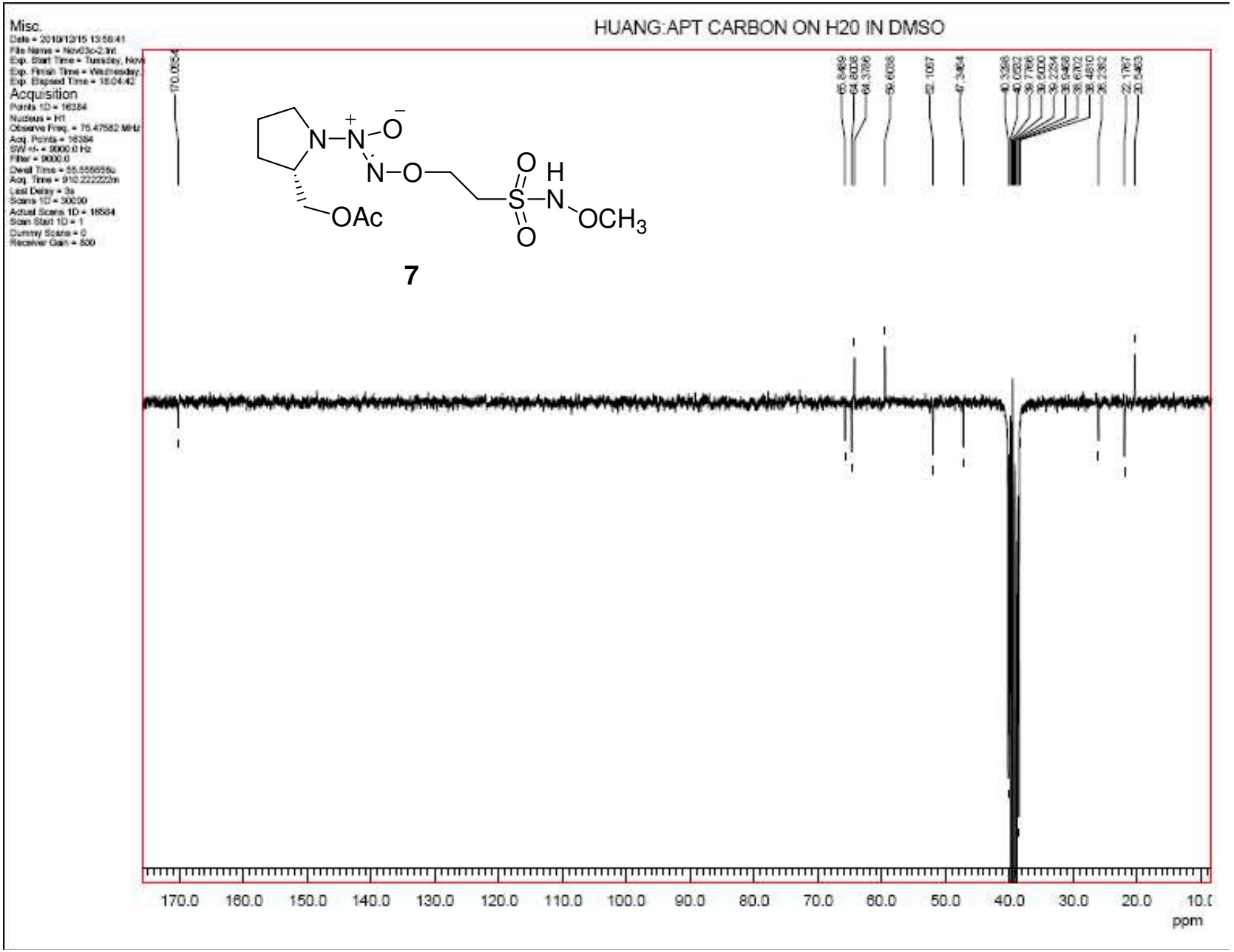
60.0
50.0
40.0
30.0
20.0
ppm


Misc.
HUANG:PROTON ON H20 IN DMSO
Acquisition
OAc
OCH3
7
Label Assignec
1 1.02
2 2.00
3 3.29
4 2.86
5 3.69
6 4.11
7 2.75
3150.0 3000.0 2850.0 2700.0 2550.0 2400.0 2250.0 2100.0 1950.0 1800.0 1650.0 1500.0 1350.0 1200.0 1050.0 900.0 750.0 600.0 450.0 300.0
Hz


Misc.
Acquisition
HUANG:APT CARBON ON H20 IN DMSO
OAc
OCH3
7
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
ppm