Synthetic Studies on Didymeline using Spirocyclization of Phenols with Diazo Functionality

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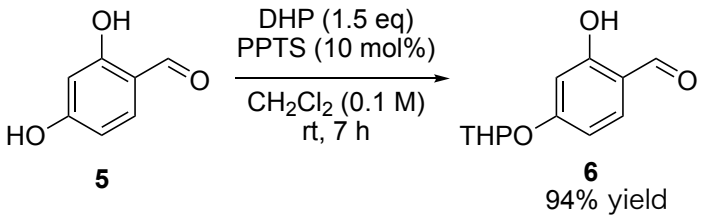
1. Experimental Section

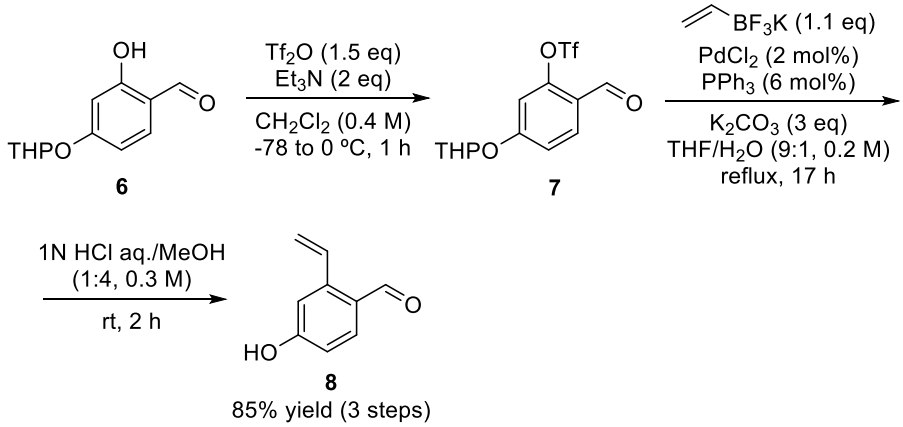
NMR spectra were recorded on a JEOL ecs 400, eca 600 spectrometer. Chemical shifts in $CDCl_3$, were reported downfield from TMS (= 0 ppm) for ^1H NMR. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, and br = broad), integration and coupling constants in Hz. For ^{13}C NMR, chemical shifts were reported in the scale relative to the solvent signal [$CHCl_3$ (77.0 ppm)] as an internal reference. ESI mass spectra were measured on JEOL AccuTOF LC-plus JMS-T100LP. Optical rotations were measured on a JASCO P-1020 polarimeter. The enantiomeric excess (ee) was determined by HPLC analysis. HPLC was performed on JASCO HPLC systems consisting of the following: pump, PU-980; detector, UV-970; column DAICEL CHIRALCEL OJ-H; mobile phase, n-hexane/i-PrOH. Melting points were measured with a SIBATA NEL-270 melting point apparatus. Analytical thin layer chromatography was performed on Kieselgel 60F254, 0.25 mm thickness plates. Column chromatography was performed with silica gel 60 N (spherical, neutral 63-210 mesh). Reactions were conducted in dry solvent. Other reagents were purified by the usual methods.



5 **6**
94% yield

2-hydroxy-4-((tetrahydro-2H-pyran-2-yl)oxy)benzaldehyde (6)

This compound was prepared using the previously reported procedure.
(ref: T. Ueno, Y. Urano, H. Kojima, and T. Nagano, *J. Am. Chem. Soc.*, 2006, **128**, 10640.)



6 **7** **8**
85% yield (3 steps)

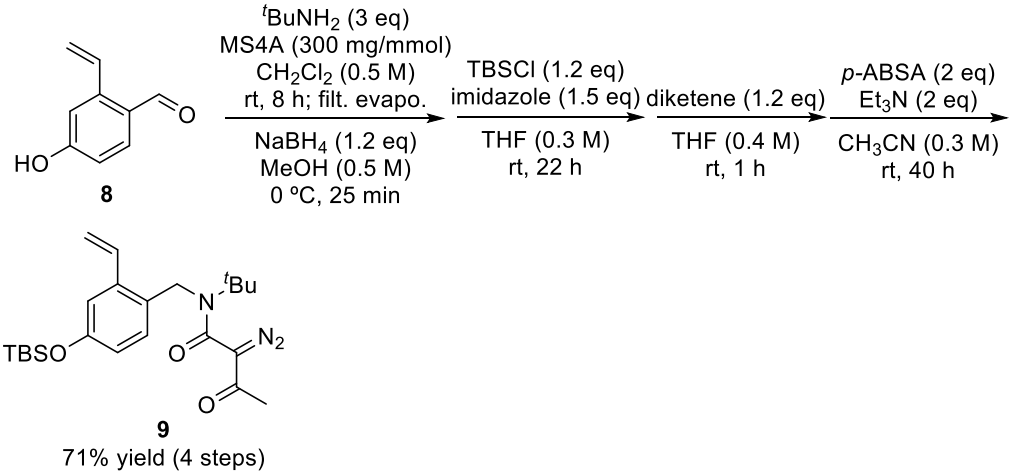
4-hydroxy-2-vinylbenzaldehyde (8)

To a stirred solution of **6** (2095.6 mg, 9.43 mmol) and Et_3N (2,63 mL, 2 eq, 18.9 mmol) in CH_2Cl_2 (24 mL, 0.4 M) was added triflic anhydride (2.32 mL, 1.5 eq, 14.1 mmol) at –78 °C. The reaction mixture was stirred at 0 ° C for 1 h. After completion of reaction, saturated aqueous $NaHCO_3$ was added, and the product was extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, and the solvent was removed in vacuo. The obtained crude mixture was passed through a short pad of silica gel to remove polar compounds (n-hexane/EtOAc = 3/1) and was used for the next reaction without further

purification.

A solution of potassium vinyltrifluoroborate (1393.1 mg, 1.1 eq, 10.4 mmol), $PdCl_2$ (33.5 mg, 2 mol%, 0.189 mmol), PPh_3 (148.7 mg, 6 mol%, 0.566 mmol), K_2CO_3 (3911.3 mg, 3 eq, 28.3 mmol), and crude mixture in THF/H_2O (9:1) (47 mL, 0.2 M) was refluxed at 85 °C under a N_2 atmosphere for 17 h, then cooled to room temperature and diluted with H_2O followed by extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure. The obtained crude mixture was passed through a short pad of silica gel to remove polar compounds (*n*-hexane/EtOAc = 1/1) and was used for the next reaction without further purification.

The obtained crude mixture was dissolved in MeOH (25 mL, 0.3 M). After addition of 1 N HCl aq. (6.3 mL), the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with water, concentrated under reduced pressure to remove most of the MeOH, and extracted with EtOAc, washed with saturated aqueous $NaHCO_3$ solution and brine, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (*n*-hexane/EtOAc, 7/1) to afford **8** (1187.5 mg, 85% yield in 3 steps) as pale orange powder: mp = 72—73°C; R_f = 0.31 (*n*-hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.50 (d, *J* = 11.2 Hz, 1H), 5.69 (d, *J* = 17.2 Hz, 1H), 6.92 (dd, *J* = 1.6, 8.8 Hz, 1H) 7.03 (d, *J* = 1.6 Hz, 1H), 7.51 (dd, *J* = 11.2, 17.2 Hz, 1H), 7.78 (d, *J* = 8.8 Hz, 1H), 10.11 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 114.0, 115.5, 119.7, 125.3, 132.8, 134.6, 144.1, 162.4, 192.5; IR (ATR) ν 3200, 2861, 1661, 1582, 1556, 1447, 1305, 1249, 1226, 1201 cm^{-1}; HRMS (ESI-TOF) [M + Na]$^+$ calcd for $C_9H_8NaO_2^+$ *m*/*z* 172.0450, found 172.0453.



_N_-(*tert*-butyl)-_N_-(4-((*tert*-butyldimethylsilyl)oxy)-2-vinylbenzyl)-2-diazo-3-oxobutanamide (9)

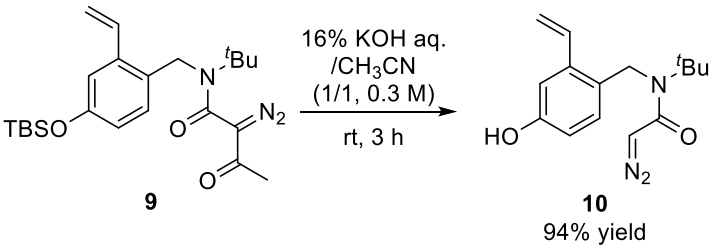
To a stirred solution of **8** (1033.7 mg, 6.98 mmol) and activated MS4A (300 mg/mmol) in CH_2Cl_2 (14 mL, 0.5 M) was added *tert*-butylamine (2.2 mL, 3 eq, 20.9 mmol), and the reaction mixture was stirred for 8 h at room temperature. The obtained suspension was filtered through a short pad of celite and concentrated under reduced pressure to give crude residue. The obtained crude residue was dissolved in MeOH (14 mL, 0.5 M). Then $NaBH_4$ (316.9 mg, 1.2 eq, 8.38 mmol) was added to the mixture at 0 °C, and stirring was continued for 25 min at 0 °C. The reaction was quenched with water, concentrated under reduced pressure to remove most of the MeOH, and extracted with EtOAc. The organic layer was acidified with 1 N aqueous HCl, and the water layer was washed with EtOAc. The aqueous solution was basified with 1 N aqueous NaOH, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to affored crude secondary amine, which was used for the next step without further purification.

To a stirred solution of the crude secondary amine and imidazole (712.8 mg, 1.5 eq, 10.5

mmol) in THF (23 mL, 0.3 M) was added TBSCl (1262.4 mg, 1.2 eq, 8.38 mmol) at 0 °C, and the reaction mixture was stirred for 22 h at room temperature. The reaction mixture was quenched with water, extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give crude silylated product.

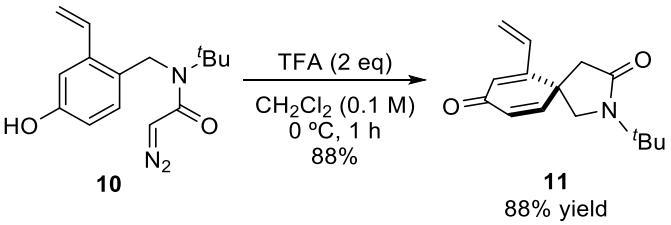
To a stirred solution of the crude silylated product in THF (17.5 mL, 0.4 M) was added diketene (0.65 mL, 1.2 eq, 8.4 mmol) at 0 °C. After being stirred for 1 h at room temperature, the reaction was extracted with EtOAc, washed with 1 N aqueous $KHSO_4$, dried over Na_2SO_4, and concentrated under reduced pressure to afford crude acetoacetylated product.

The crude residue obtained above was dissolved in CH_3CN (23 mL, 0.3 M), and 4-acetamidobenzenesulfonyl azide (3353.8 mg, 2 eq, 14.0 mmol) and Et_3N (1.9 mL, 2 eq, 14.0 mmol) were added at 0 °C. After being stirred for 40 h at room temperature, the reaction mixture was filtered through a short pad of celite and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel (*n*-hexane/EtOAc, 10/1 → 3/1) to afford **9** (2140.5 mg, 71% yield in 4 steps) as yellow powder: mp = 73—74°C; R_f = 0.41 (*n*-hexane/EtOAc, 3/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.21 (s, 6H), 0.99 (s, 9H), 1.43 (s, 9H), 2.30 (s, 3H), 4.60 (s, 2H), 5.35 (d, *J* = 10.8 Hz, 1H), 5.57 (d, *J* = 16.8 Hz, 1H), 6.77 (dd, *J* = 2.4, 8.4 Hz, 1H), 6.83 (dd, *J* = 10.8, 16.8 Hz, 1H), 6.92 (d, 2.4 Hz, 1H), 7.09 (d, 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ -4.6, 14.1, 18.1, 25.5, 27.2, 28.2, 48.1, 58.8, 117.46, 117.47, 118.1, 119.4, 127.3, 128.3, 133.1, 136.8, 154.8, 163.1; IR (ATR) ν 2956, 2930, 2858, 2099, 1642, 1487, 1383, 1361, 1252, 1190 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{23}H_{35}N_3NaO_3Si^+$ *m*/*z* 452.2340, found 452.2337.



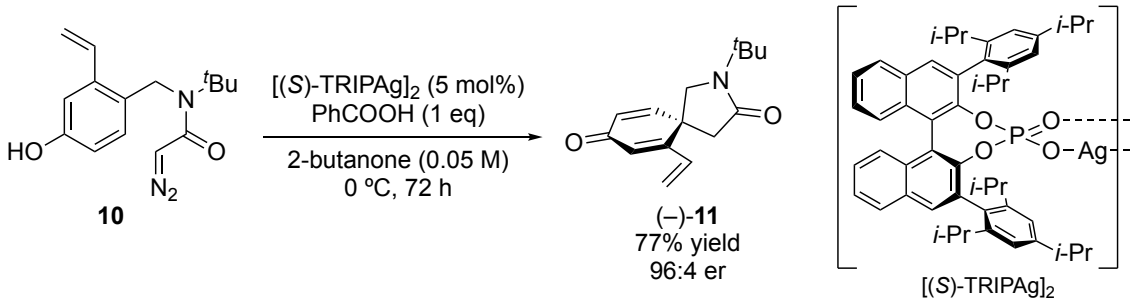
N-(*tert*-butyl)-2-diazo-N-(4-hydroxy-2-vinylbenzyl)acetamide (10)

A solution of **9** (2140.5 mg, 4.98 mmol) in 16% aqueous KOH/CH_3CN (1/1, 16 mL, 0.3 M) was stirred for 3 h at room temperature. The reaction was extracted with EtOAc, washed with saturated aqueous NH_4Cl and brine, dried over Na_2SO_4, concentrated under reduced pressure. The crude mixture was prified by recrystallized from EtOAc/MeOH to afford **10** (1273.5 mg, 94% yield) as yellow crystal: mp = 153—154°C; R_f = 0.33 (*n*-hexane/EtOAc, 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.47 (s, 9H), 4.37 (s, 2H), 4.67 (s, 1H), 4.91 (br s, 1H), 5.38 (dd, *J* = 1.2, 10.8 Hz, 1H), 5.66 (dd, *J* = 1.2, 17.6 Hz, 1H), 6.789 (dd, *J* = 2.8, 8.4 Hz, 1H), 6.793 (dd, *J* = 10.8, 17.6 Hz, 1H), 6.96 (d, *J* = 2.8 Hz, 1H), 7.15 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (150 MHz, acetone-d_6) δ 28.7, 46.8, 48.8, 58.4, 113.4, 115.8, 116.7, 127.8, 127.9, 134.3, 137.0, 157.2, 168.2; IR (ATR) ν 3260, 3100, 2963, 2921, 2101, 1580, 1448, 1415, 1348, 1249, 1225, 1184 cm^{-1}; HRMS (ESI-TOF) [M + Na]$^+$ calcd for $C_{15}H_{19}N_3NaO_2^+$ *m*/*z* 296.1370, found 296.1359.



2-(tert-butyl)-6-vinyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (11)

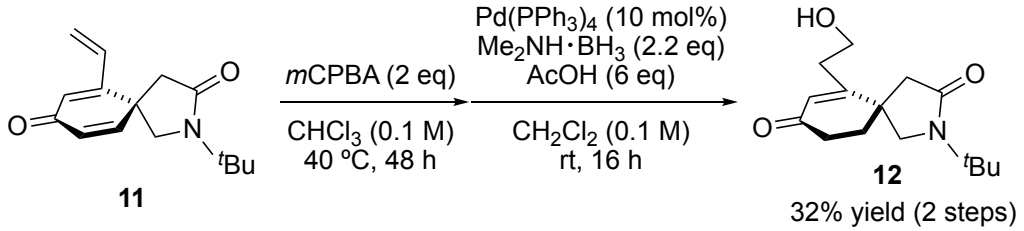
To a stirred solution of diazocarbonyl compound **10** (109.4 mg, 0.4 mmol) in CH_2Cl_2 (0.1 M, 4 mL) was added trifluoroacetic acid (0.8 mL, 2 eq, 0.8 mmol) at 0 °C, and resulting mixture was stirred at 0 °C for 1 h. The reaction mixture was washed with saturated aqueous $NaHCO_3$, and the product was extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, and purified by flash chromatography on silica gel (column condition; gradient elution: n-hexane/EtOAc, 1/1 → 1/2) to afford **11** (86.4 mg, 88% yield) as pale orange gum: R_f = 0.35 (*n*-hexane/EtOAc, 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (s, 9H), 2.53 (d, *J* = 17.6 Hz, 1H), 2.78 (d, *J* = 17.6 Hz, 1H), 3.47 (d, *J* = 10.8 Hz, 1H), 3.65 (d, *J* = 10.8 Hz, 1H), 5.56 (d, *J* = 10.8 Hz, 1H), 5.75 (d, *J* = 17.2 Hz, 1H), 6.30 (dd, *J* = 2.0, 10.0 Hz, 1H), 6.43 (d, *J* = 2.0 Hz, 1H), 6.44 (dd, *J* = 10.8, 17.2 Hz, 1H), 6.92 (d, *J* = 10.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.2, 39.9, 41.8, 52.8, 54.5, 121.6, 125.5, 126.8, 132.5, 151.4, 157.3, 171.2, 185.4; IR (ATR) ν 2974, 2936, 1682, 1657, 1624, 1411, 1364, 1281, 1243, 1219 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{15}H_{19}NNaO_2^+$ *m*/*z* 268.1308, found 268.1319.



(R)-2-(*tert*-butyl)-6-vinyl-2-azaspiro[4.5]deca-6,9-diene-3,8-dione (11)

To a stirred solution of diazocarbonyl compound **10** (54.7mg, 0.2 mmol) in 2-butanone (0.05 M, 4 mL) in a test tube, wrapped with aluminum foil to avoid light, were added

benzoic acid (0.2 mmol, 1 eq, 24.4 mg) and [(*S*)-TRIPAg]$_2$ (17.2 mg, 5 mol%, 0.01 mmol) at 0 °C, and the reaction mixture was stirred at 0 °C for 72 h. The reaction mixture was concentrated to about 0.5 mL under reduced pressure, from which benzoic acid and Ag catalyst were removed by filtration through short pad of NH silica gel, and the solid was washed with *n*-hexane/EtOAc (1/2). The filtrate was concentrated under reduced pressure and purified by flash chromatography on silica gel (column condition; gradient elution: n-hexane/EtOAc, 1/1 → 1/2) to afford **11** (37.9 mg, 77% yield) as pale orange gum: $[\alpha]^{20}_{D}$ – 1.06° (*c* 1, $CHCl_3$). The enantiomeric ratio was determined to be 96 : 4 by analytical chiral HPLC. Retention time: 14 min, 17 min (OJ-H column, 80/20 n-hexane/i-PrOH, 1 mL/min, 254 nm).

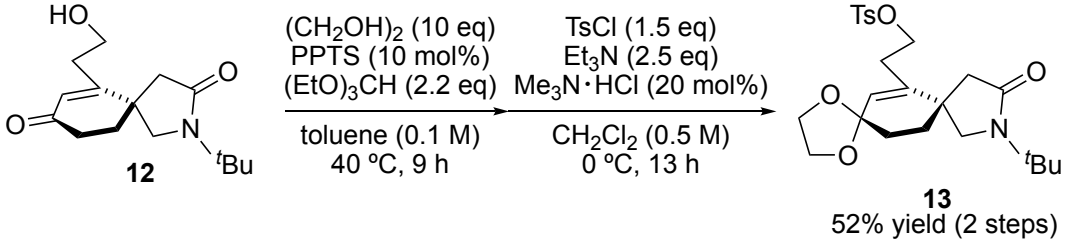


2-(*tert*-butyl)-6-(2-hydroxyethyl)-2-azaspiro[4.5]dec-6-ene-3,8-dione (12)

To a stirred solution of **11** (245.3 mg, 1.0 mmol) in $CHCl_3$ (10 mL, 0.1 M) was added MCPBA (345.1 mg, 2 eq, 2.0 mmol) at room temperature, and resulting mixture was stirred at 40 °C for 48 h. The reaction mixture was washed with saturated aqueous $NaHCO_3$, and the product was extracted with $CHCl_3$. The combined organic layer was dried over Na_2SO_4, and the solvent was removed in vacuo to give crude epoxide.

To a mixture of tetrakis[triphenylphosphine]palladium (115.6 mg, 10 mol%, 0.1 mmol), $Me_2NH \cdot BH_3$ (129.6 mg, 2.2 eq, 2.2 mmol) in CH_2Cl_2 (5 ml) was added a solution of crude epoxide and AcOH (0.34 mL, 6 eq, 6.0 mmol) in CH_2Cl_2 (5 ml) at room temperature

under argon atmosphere. After being stirred for 16 h, the reaction mixture was washed with saturated aqueous $NaHCO_3$, and the product was extracted with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, and the residue was purified by flash chromatography on silica gel (column condition; gradient elution: $CHCl_3$/MeOH, 40/1) to afford **12** (83.6 mg, 32% yield in 2 steps) as pale yellow oil: R_f = 0.29 ($CHCl_3$/MeOH, 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (s, 9H), 2.10 (m, 2H), 2.36 (d, *J* = 17.2 Hz, 1H), 2.46 (m, 2H), 2.52 (t, *J* = 6.4 Hz, 2H), 2.72 (d, *J* = 17.2 Hz, 1H), 2.93 (br, 1H), 3.40 (d, *J* = 10.8 Hz, 1H), 3.61 (d, *J* = 10.8 Hz, 1H), 3.85 (t, *J* = 6.4 Hz, 2H), 5.96 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.6, 33.9, 34.8, 35.0, 38.9, 43.0, 53.6, 54.5, 60.2, 127.2, 163.6, 172.8, 197.9; IR (ATR) ν 3384, 2964, 2932, 2878, 1656, 1414, 1364, 1302, 1247, 1222, 1049 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{15}H_{23}NNaO_3^+$ *m*/*z* 288.1570, found 288.1569.

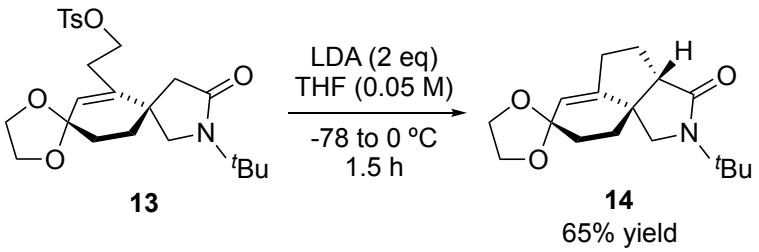


2'-(2-(*tert*-butyl)-9,12-Dioxa-2-azadispiro[4.2.4.2]tetradec-6-en-3-one-6-yl)ethyl 4-methylbenzenesulfonate (13)

To a mixture of **12** (64.8 mg, 0.244 mmol) and pyridinium *p*-toluenesulfonate (6.1 mg, 10 mol%, 0.0244 mmol) in toluene (2.4 mL, 0.1 M) was added ethylene glycol (0.14 mL, 10 eq, 2.44 mmol) and triethyl orthoformate (97 μL, 2.4 eq, 0.586 mmol) at room temperature. The resulting solution was stirred at 40 °C for 9 h. The mixture was cooled

to room temperature, quenched with Et_3N, and concentrated under reduced pressure. The residue was dissolved in CH_2Cl_2 and washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, concentrated under reduced pressure to give crude dioxolane.

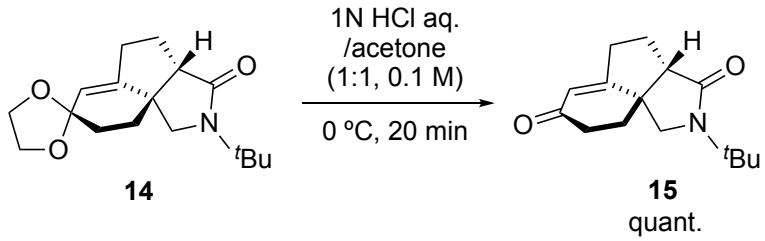
To a stirred solution of crude dioxolane, Et_3N (85 μL, 2.5 eq, 0.610 mmol) and Me_3N・HCl (4.7 mg, 20 mol%, 0.0488 mmol) in CH_2Cl_2 (0.2 mL) was added TsCl (69.8 mg, 1.5 eq, 0.366 mmol) in CH_2Cl_2 (0.3 mL) at 0 °C. The reaction mixture was stirred at 0 ° C for 13 h. After completion of reaction, saturated aqueous $NaHCO_3$ was added, and the product was extracted with CH_2Cl_2, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (CH_2Cl_2/EtOAc, 3/1) to afford **13** (58.7 mg, 52% yield in 2 steps) as white powder: mp = 85 °C (decomp.); R_f = 0.23 (*n*-hexane/EtOAc, 1/5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.37 (s, 9H), 1.72—1.90 (m, 4H), 2.13 (d, *J* = 17.2 Hz, 1H), 2.39 (d, *J* = 17.2 Hz, 1H), 2.38 (m, 2H), 2.46 (s, 3H), 3.19 (d, *J* = 10.4 Hz, 1H), 3.34 (d, *J* = 10.4 Hz, 1H), 3.96 (m, 4H), 4.15 (m, 2H), 5.31 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.79 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 21.6, 27.6, 29.7, 30.3, 34.3, 38.0, 43.7, 54.2, 54.3, 64.5, 64.6, 68.1, 104.8, 126.3, 127.9, 130.0, 132.7, 141.0, 145.0, 172.9; IR (ATR) ν 2959, 2928, 2880, 2360, 1677, 1411, 1359, 1224, 1173, 1095 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{24}H_{33}NNaO_6S^+$ *m*/*z* 486.1921, found 486.1919.



13 **14**
65% yield

2'-(*tert*-butyl)-1',2',4',5',8',9'-hexahydrospiro[[1,3]dioxolane-2,7'-indeno[1,7a-c]pyrrol]-3'(3a'H)-one (14)

To a stirred solution of **13** (25.4 mg, 0.0548 mmol) in THF (1 mL) was added LDA (2 eq, 0.110 mmol) in THF (0.1 mL) at −78 °C. The reaction mixture was warmed to 0 °C gradually. After completion of reaction, saturated aqueous NH_4Cl was added, and the product was extracted with EtOAc, wash with brine, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (*n*-hexane/EtOAc, 1/2 → 1/5) to afford **14** (10.3 mg, 65% yield) as white powder: mp = 114—115°C; R_f = 0.28 (*n*-hexane/EtOAc, 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 9H), 1.76 (m, 2H), 1.88—1.95 (m, 3H), 2.05 (m, 1H), 2.24 (m, 2H), 2.52 (m, 1H), 3.25 (d, *J* = 10.4 Hz, 1H), 3.46 (d, *J* = 10.4 Hz, 1H), 3.88—4.00 (m, 2H), 4.01—4.07(m, 2H), 5.34 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 27.5, 28.7, 31.1, 31.4, 33.9, 42.4, 53.8, 54.1, 55.5, 64.4, 64.8, 106.1, 117.9, 153.6, 176.3; IR (ATR) ν 2955, 2875, 1672, 1412, 1362, 1309, 1221, 1155, 1108, 1073 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{17}H_{25}NNaO_3^+$ *m/z* 314.1727, found 314.1724.

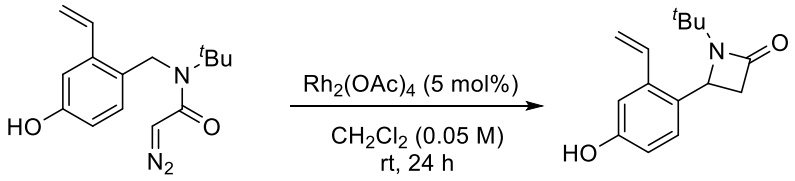


14 **15** quant.

2-(tert-butyl)-4,5,8,9-tetrahydro-1H-indeno[1,7a-c]pyrrole-3,7(2H,3aH)-dione (15)

To a stirred solution of **14** (10.3 mg, 0.0353 mmol) in acetone (0.18 mL) was added 1N aqueous HCl (0.18 mL) at 0 °C. The resultant mixture was stirred at 0 °C for 20 min.

After completion of reaction, saturated aqueous $NaHCO_3$ was added, and the product was extracted with EtOAc, wash with brine, dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by flash chromatography on silica gel (n-hexane/EtOAc, 1/2 → 1/5) to afford **15** (8.7 mg, quant.) as white powder: mp = 98—99°C; Rf = 0.19 (n-hexane/EtOAc, 1/2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.41 (s, 9H), 1.93—2.06 (m, 2H), 2.19 (dt, J = 3.6, 12.0 Hz, 1H), 2.26 (ddt, J = 2.4, 8.4, 13.2 Hz, 1H), 2.44—2.51 (m, 4H), 2.67 (dd, J = 1.2, 9.6 Hz, 1H), 3.37 (d, J = 6.8 Hz, 1H), 3.67 (d, J = 6.8 Hz, 1H), 5.86 (d, J = 1.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 27.5, 28.1, 32.5, 33.9, 34.7, 43.3, 53.6, 54.4, 54.6, 121.0, 174.3, 175.2, 198.4; IR (ATR) ν 2961, 2930, 2871, 1661, 1455, 1411, 1363, 1312, 1278, 1220, 1207 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{15}H_{21}NNaO_2^+$ m/z 270.1465, found 270.1477.



10 **16** 30% yield

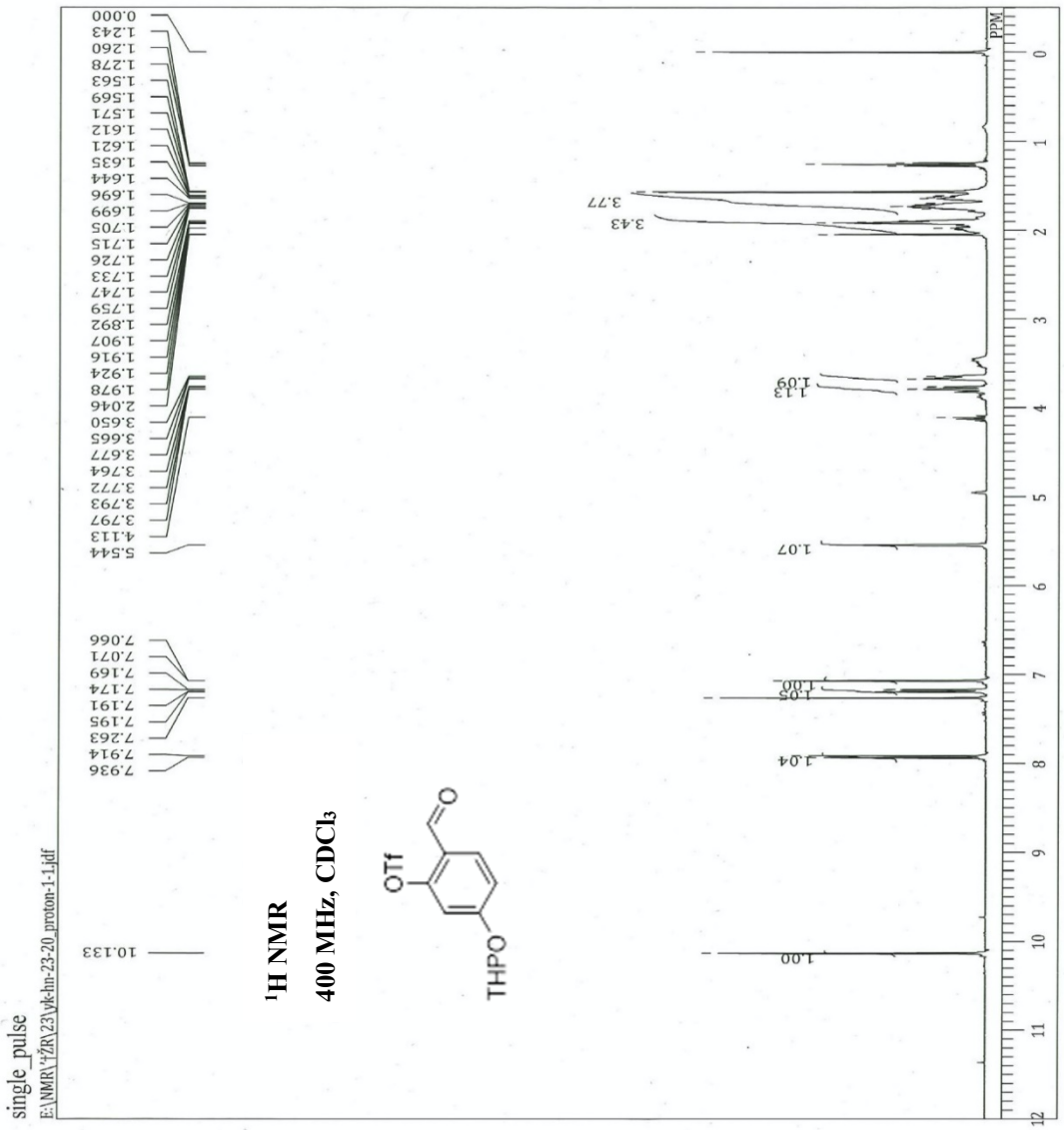
1-(*tert*-butyl)-4-(4-hydroxy-2-vinylphenyl)azetidin-2-one (16)

To a stirred solution of $Rh_2(OAc)_4$ (4.4 mg, 0.01 mmol) in CH_2Cl_2 (4 mL) was added **10** (54.7 mg, 0.2 mmol) at room temperature. The resulting mixture was stirred at room temperature for 24 h. After completion of reaction, the solvent was removed in vacuo. The crude mixture was purified by flash chromatography on silica gel (n-hexane/EtOAc, 3/1 → 2/1) to afford **16** (14.5 mg, 30% yield) as brown gum: Rf = 0.63 (n-hexane/EtOAc, 1/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 9H), 2.62 (d, J = 14 Hz, 1H), 3.20 (dd, J = 5.0, 14.4 Hz, 1H), 4.86 (br, 1H), 5.20 (br, 1H), 5.39 (d, J = 10.8 Hz, 1H), 5.58 (d, J = 17.2 Hz, 1H), 6.81 (dd, J = 2.6, 8.4 Hz, 1H), 6.89 (d, J = 2.0 Hz, 1H), 7.01 (dd, J = 11, 17.6 Hz, 1H), 7.36 (d, J = 8.4 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 28.0, 45.6, 48.6, 54.6,

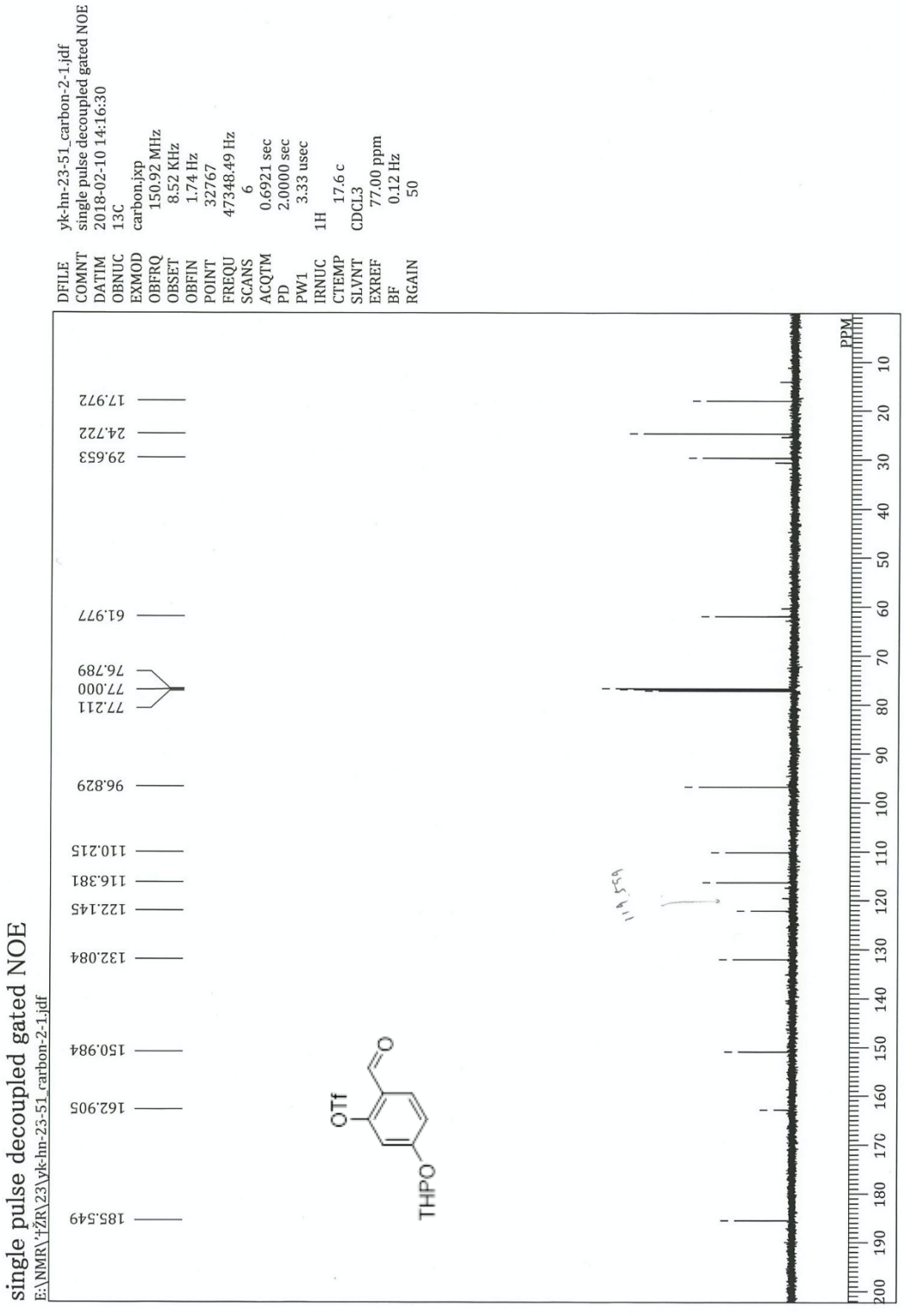
113.3, 115.7, 117.9, 127.1, 129.3, 133.4, 138.0, 155.8, 168.4; IR (ATR) ν 3273, 2974, 1710, 1604, 1573, 1496, 1450, 1365, 1294, 1256, 1168, 1049 cm^{-1}; HRMS (ESI-TOF) $[M + Na]^+$ calcd for $C_{15}H_{19}NNaO_2^+$ m/z 268.1308, found 268.1290.

2. Charts of ^{1}H- and ^{13}C-NMR Spectra

7



7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OBFIN 1.74 Hz
POINT 32767
FREQU 47348.49 Hz
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ACQTM 0.6921 sec
PD 2.0000 sec
PW1 3.33 usec
IRNUC 1H
CTEMP 17.6 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 50
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162.905
150.984
132.084
122.145
116.381
110.215
96.829
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76.789
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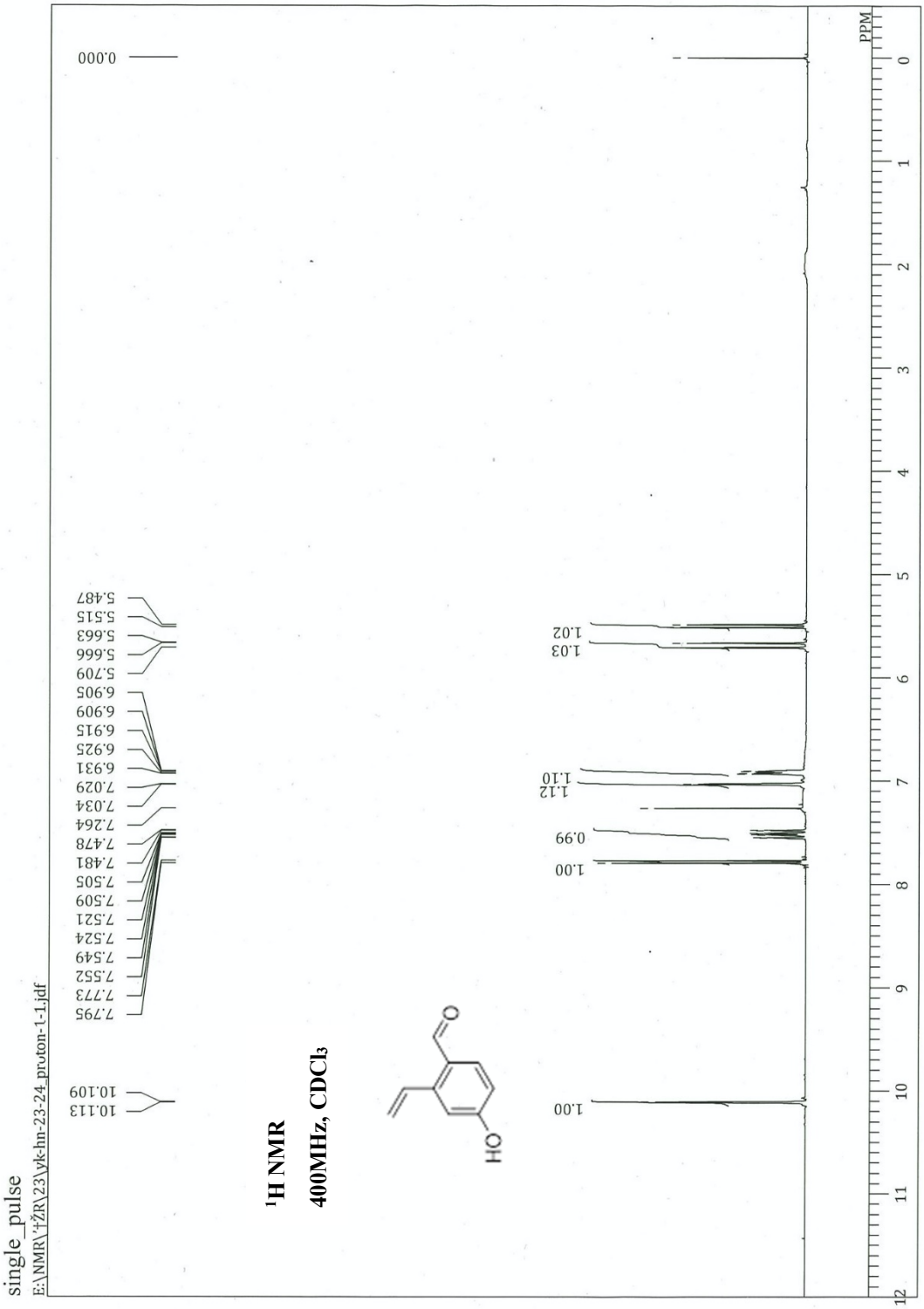
29.653
24.722
17.972
OTf
O
THPO
PPM

8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7.549
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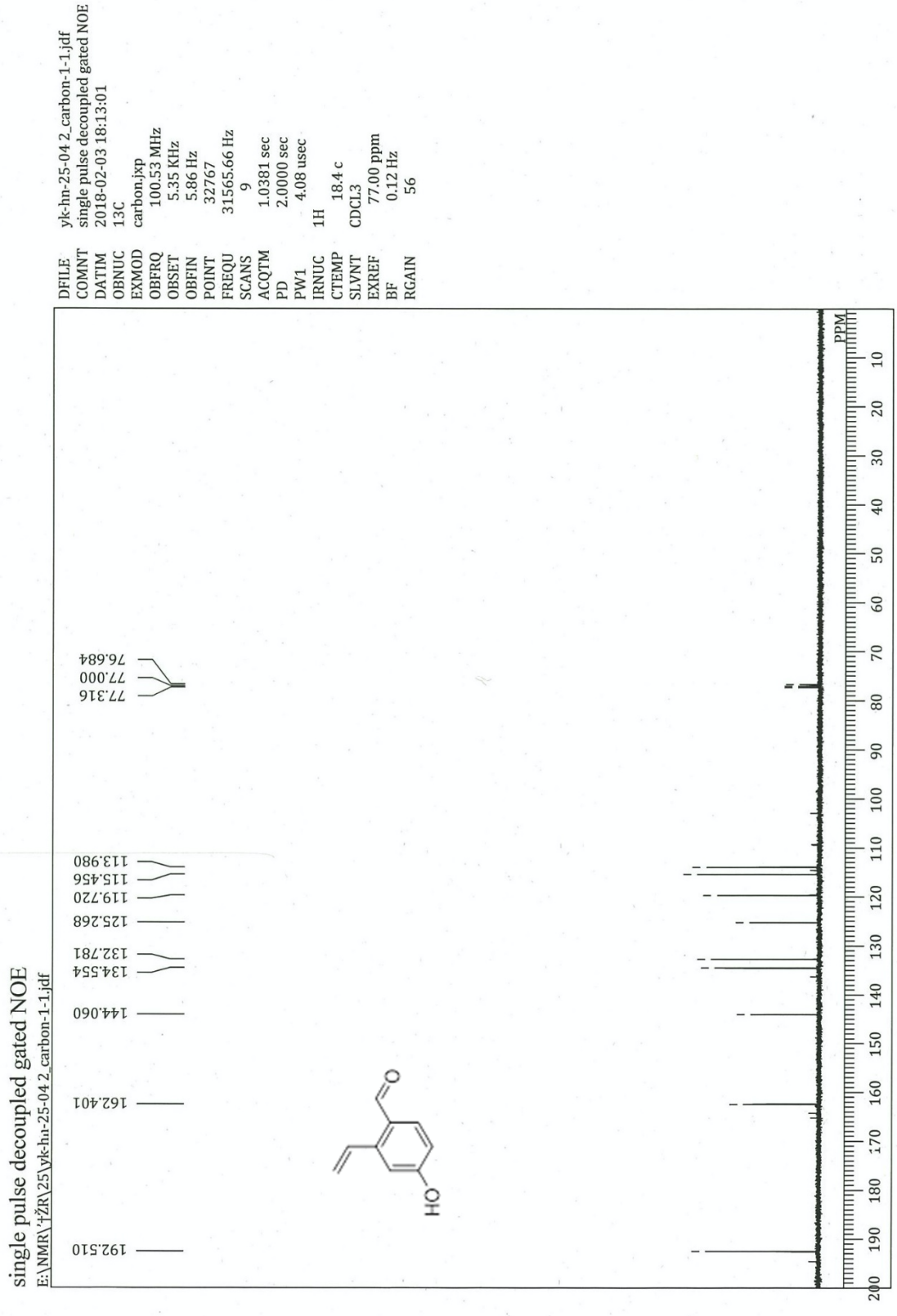
7.521
7.509
7.505
7.481
7.478
7.264
7.034
7.029
6.931
6.925
6.915
6.909
6.905
5.709
5.666
5.663
5.515
5.487
1.03
1.02
1.12
1.10
0.99
1.00
1.00
PPM
0
1
2
3
4
5
6
7
8
9
10
11
12
^{1}H NMR
400MHz, CDCl$_3$
OH

8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144.060
134.554
132.781
125.268
119.720
115.456
113.980
77.316
77.000
76.684
HO
O
PPM
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EXMOD carbon.jxp
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OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 32767
FREQU 31565.66 Hz
SCANS 9
ACQTM 1.0381 sec
PD 2.0000 sec
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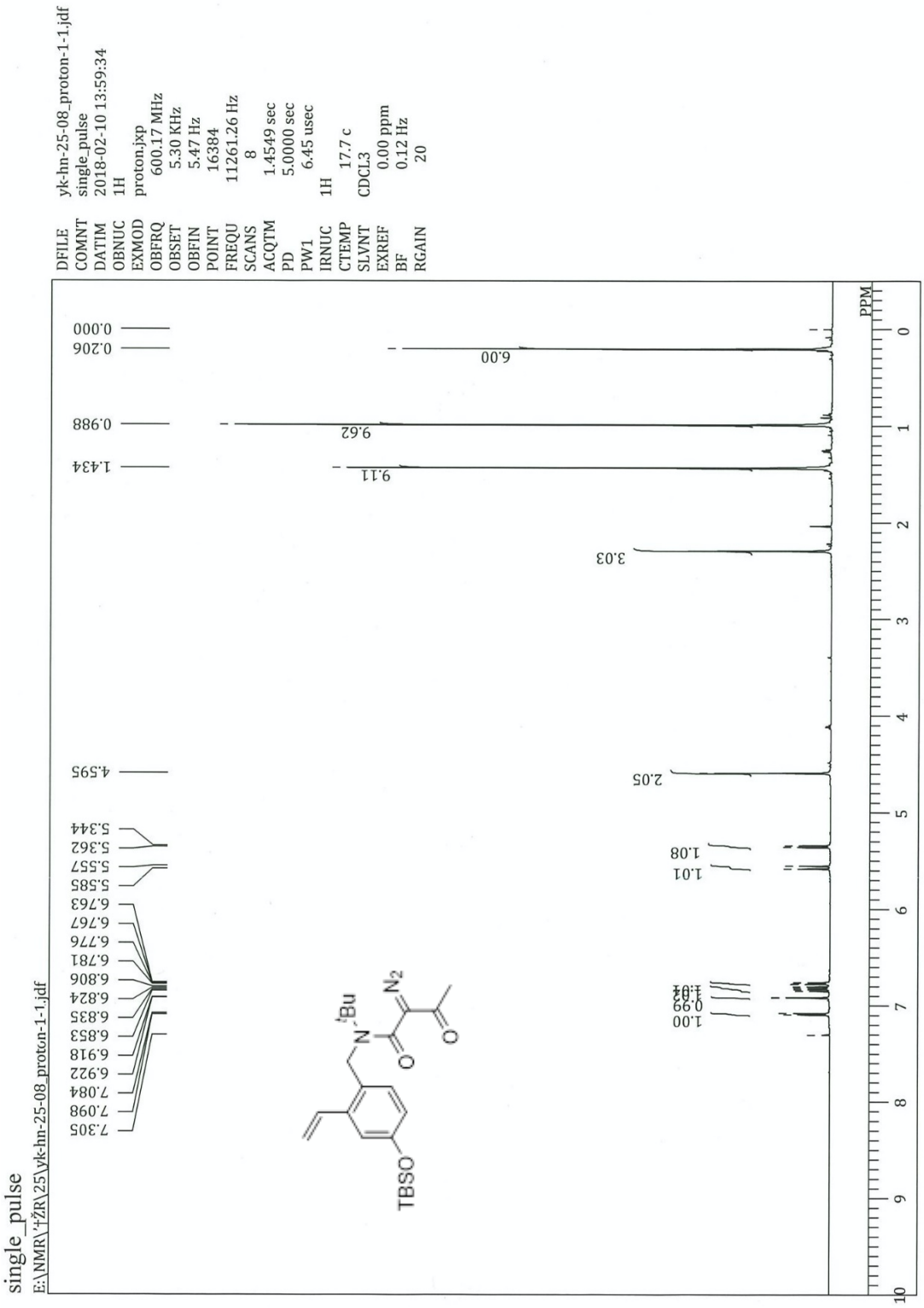
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 56

9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EXMOD proton.jxp
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OBSET 5.30 KHz
OBFIN 5.47 Hz
POINT 16384
FREQU 11261.26 Hz
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ACQTM 1.4549 sec
PD 5.0000 sec
PW1 6.45 usec
IRNUC 1H
CTEMP 17.7 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
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0.206
0.988
1.434
4.595
5.344
5.362
5.557
5.585
6.763
6.767
6.776
6.781
6.806
6.824
6.835
6.853
6.918
6.922
7.084
7.098
7.305
6.00
9.62
9.11
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1.08
1.01
1.00
0.99
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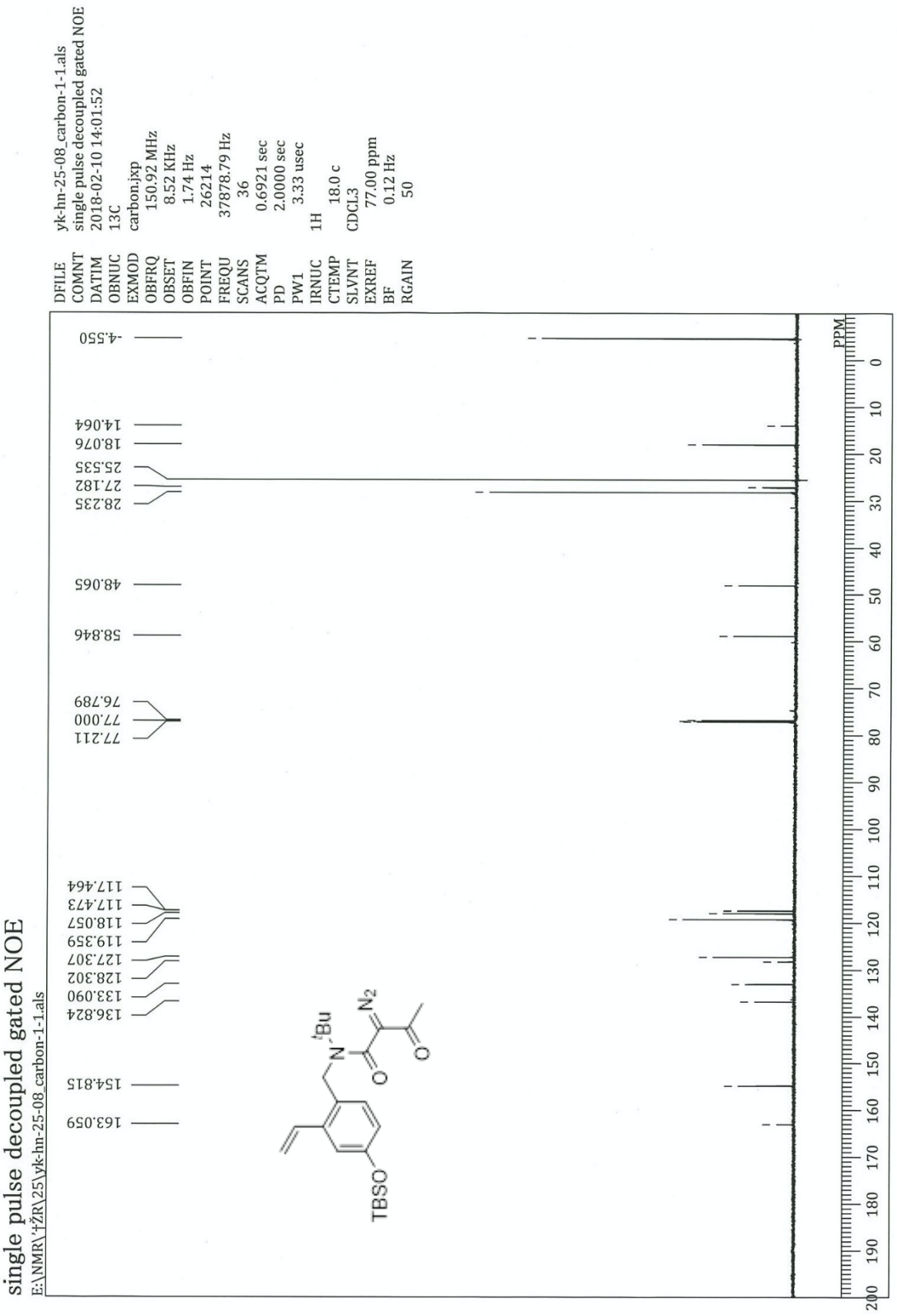
O
O
N2
TBSO
PPM

9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OBFIN 1.74 Hz
POINT 26214
FREQU 37878.79 Hz
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ACQTM 0.6921 sec
PD 2.0000 sec
PW1 3.33 usec
IRNUC 1H
CTEMP 18.0 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
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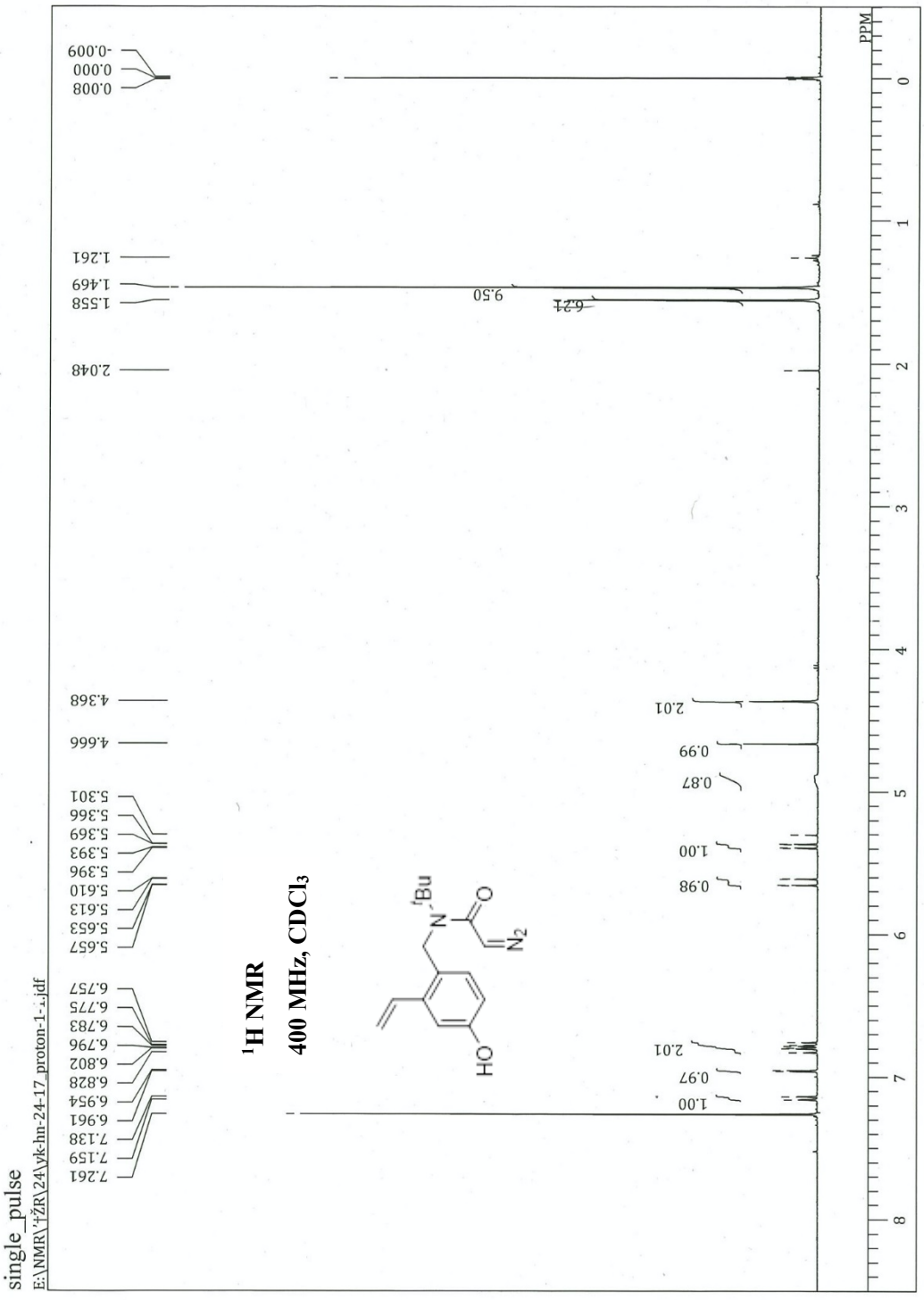
18.076
25.535
27.182
28.235
48.065
58.846
76.789
77.000
77.211
117.464
117.473
118.057
119.359
127.307
128.302
133.090
136.824
154.815
163.059
TBSO
O
N
tBu
O
N2
PPM

10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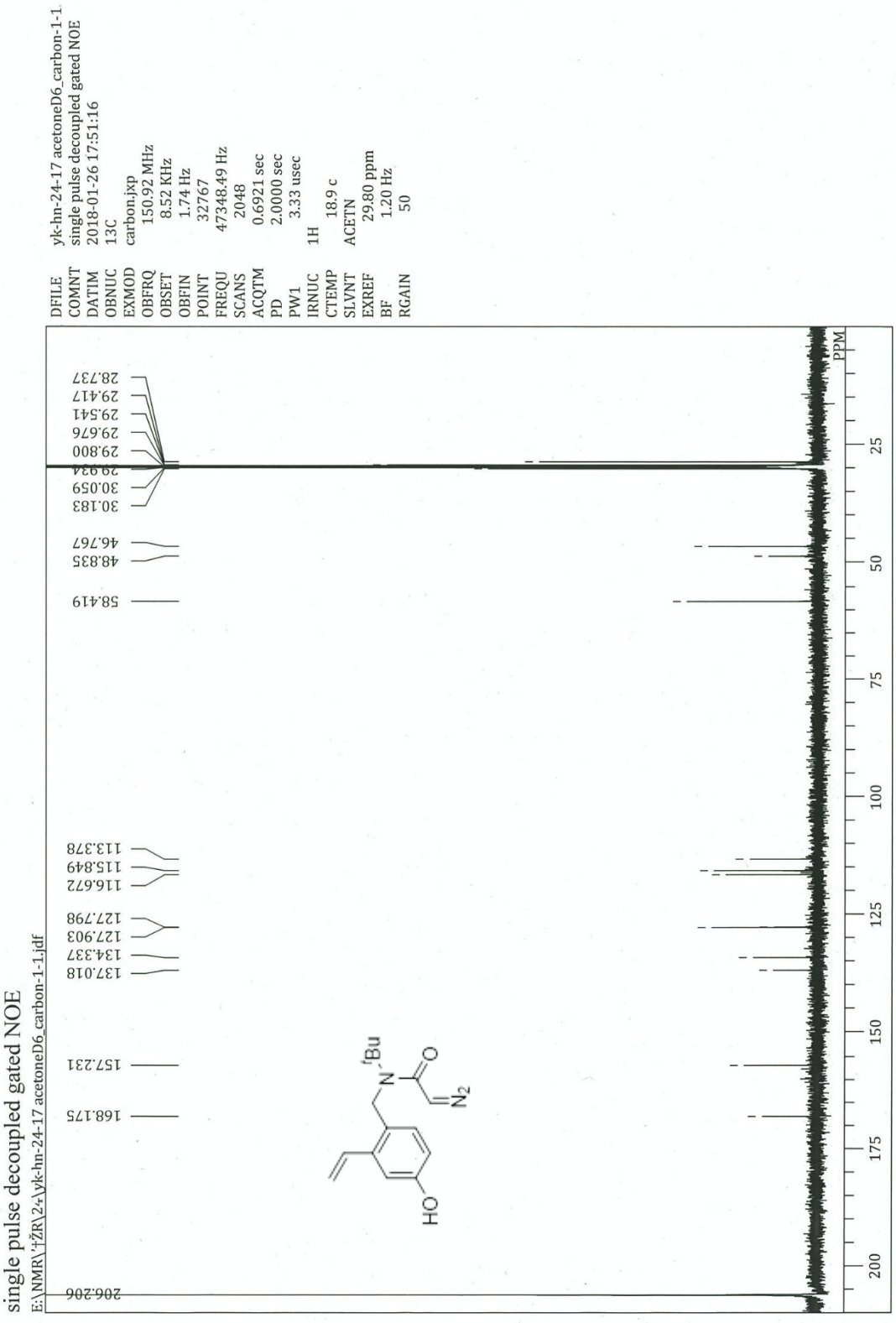
1.469
1.558
2.048
4.368
4.666
5.301
5.366
5.369
5.393
5.396
5.610
5.613
5.653
5.657
6.757
6.775
6.783
6.796
6.802
6.828
6.954
6.961
7.138
7.159
7.261
9.50
6.21
2.01
0.99
0.87
1.00
0.98
2.01
0.97
1.00
PPM
0
1
2
3
4
5
6
7
8
^{1}H NMR
400 MHz, CDCl$_3$
^{t}Bu
N
O
N$_2$
HO

10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OBFIN 1.74 Hz
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FREQU 47348.49 Hz
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PD 2.0000 sec
PW1 3.33 usec
IRNUC 1H
CTEMP 18.9 c
SLVNT ACETN
EXREF 29.80 ppm
BF 1.20 Hz
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168.175
157.231
137.018
134.337
127.903
127.798
116.672
115.849
113.378
58.419
48.835
46.767
30.183
30.059
29.934
29.800
29.676
29.541
29.417
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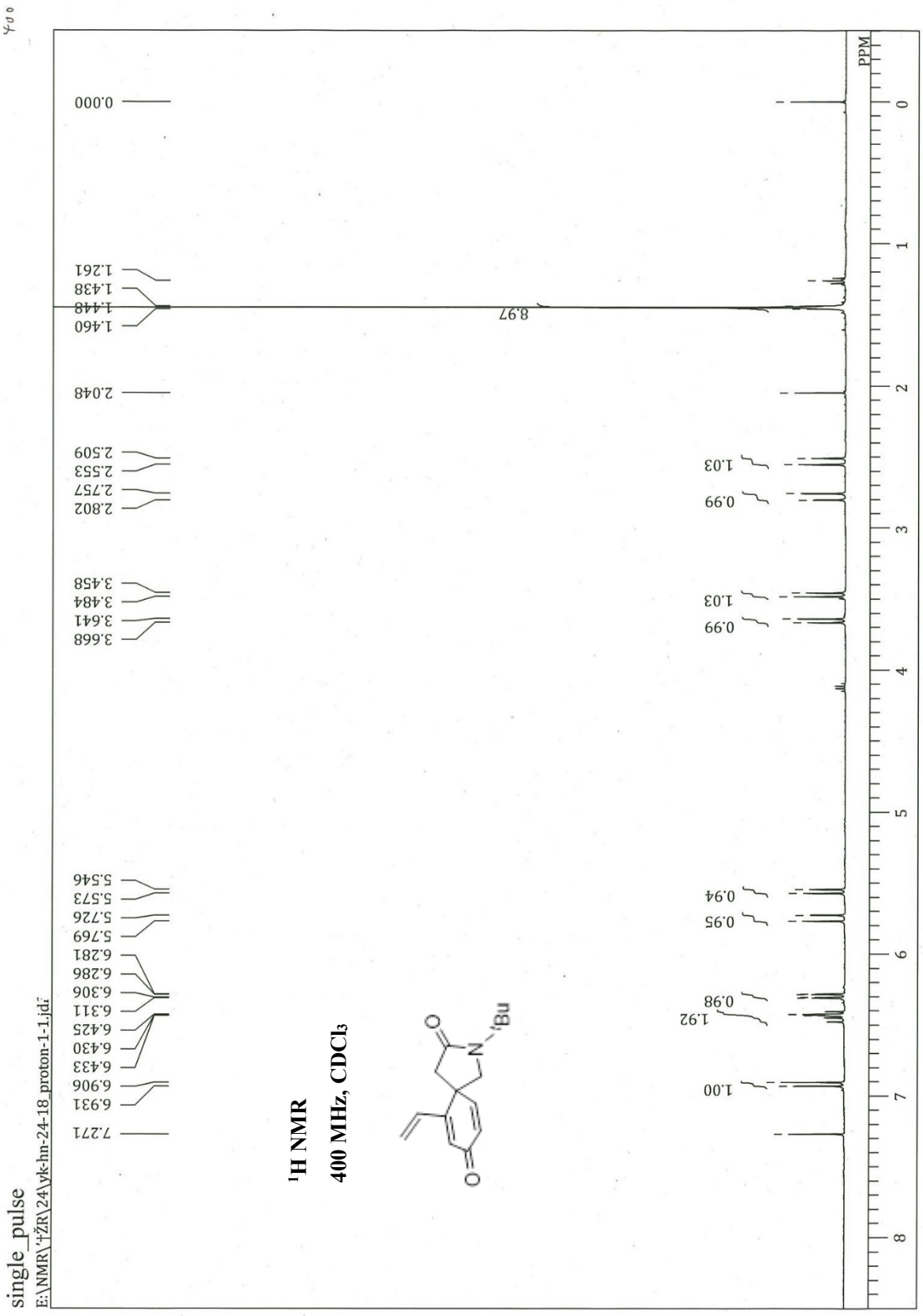
PPM
25
50
75
100
125
150
175
200
HO
N
tBu
O
N2

11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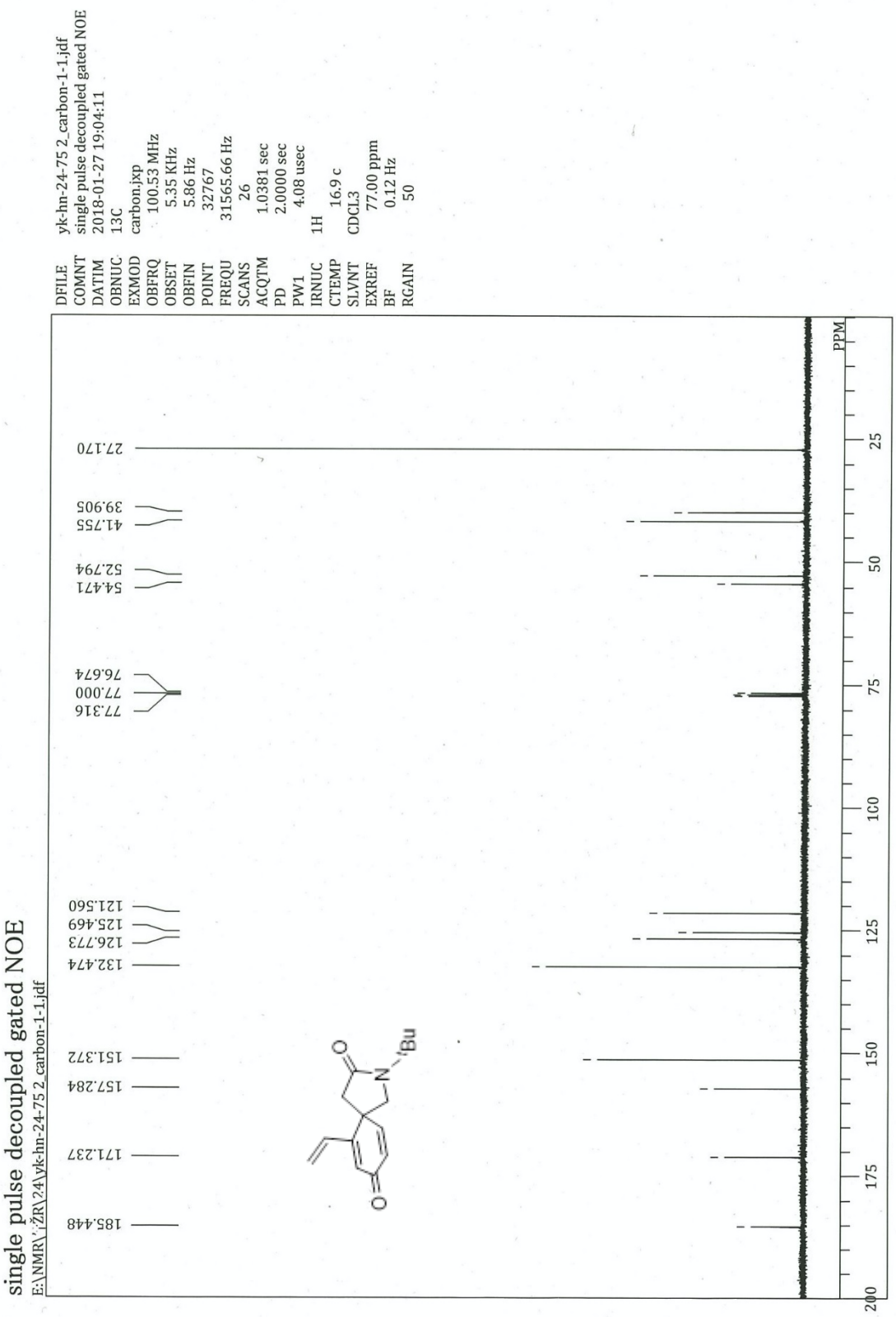
6.425
6.311
6.306
6.286
6.281
5.769
5.726
5.573
5.546
3.668
3.641
3.484
3.458
2.802
2.757
2.553
2.509
2.048
1.460
1.448
1.438
1.261
0.000
8.97
1.00
1.92
0.98
0.95
0.94
0.99
1.03
0.99
1.03
0.99
1.03
PPM
0
1
2
3
4
5
6
7
8
^{1}H NMR
400 MHz, CDCl$_3$
O
N
^{t}Bu
O

11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OBFIN 5.86 Hz
POINT 32767
FREQU 31565.66 Hz
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ACQTM 1.0381 sec
PD 2.0000 sec
PW1 4.08 usec
IRNUC 1H
CTEMP 16.9 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
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39.905
41.755
52.794
54.471
76.674
77.000
77.316
121.560
125.469
126.773
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tBu
PPM
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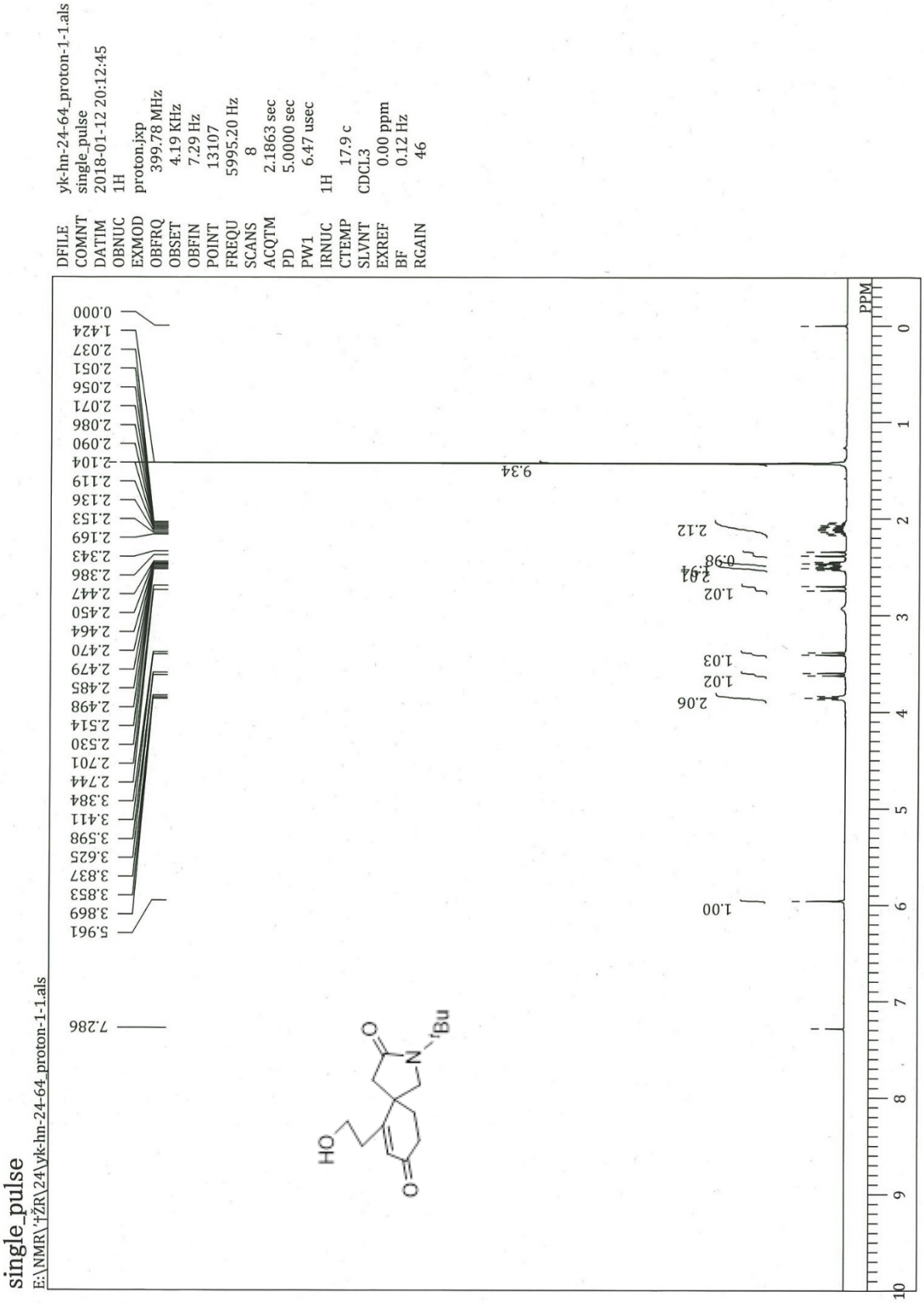
175
150
125
100
75
50
25

12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POINT 13107
FREQU 5995.20 Hz
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PD 5.0000 sec
PW1 6.47 usec
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CTEMP 17.9 c
SLVNT CDCl3
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BF 0.12 Hz
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2.056
2.071
2.086
2.090
2.104
2.119
2.136
2.153
2.169
2.343
2.386
2.447
2.450
2.464
2.470
2.479
2.485
2.498
2.514
2.530
2.701
2.744
3.384
3.411
3.598
3.625
3.837
3.853
3.869
5.961
7.286
9.34
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1.03
1.02
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1.00
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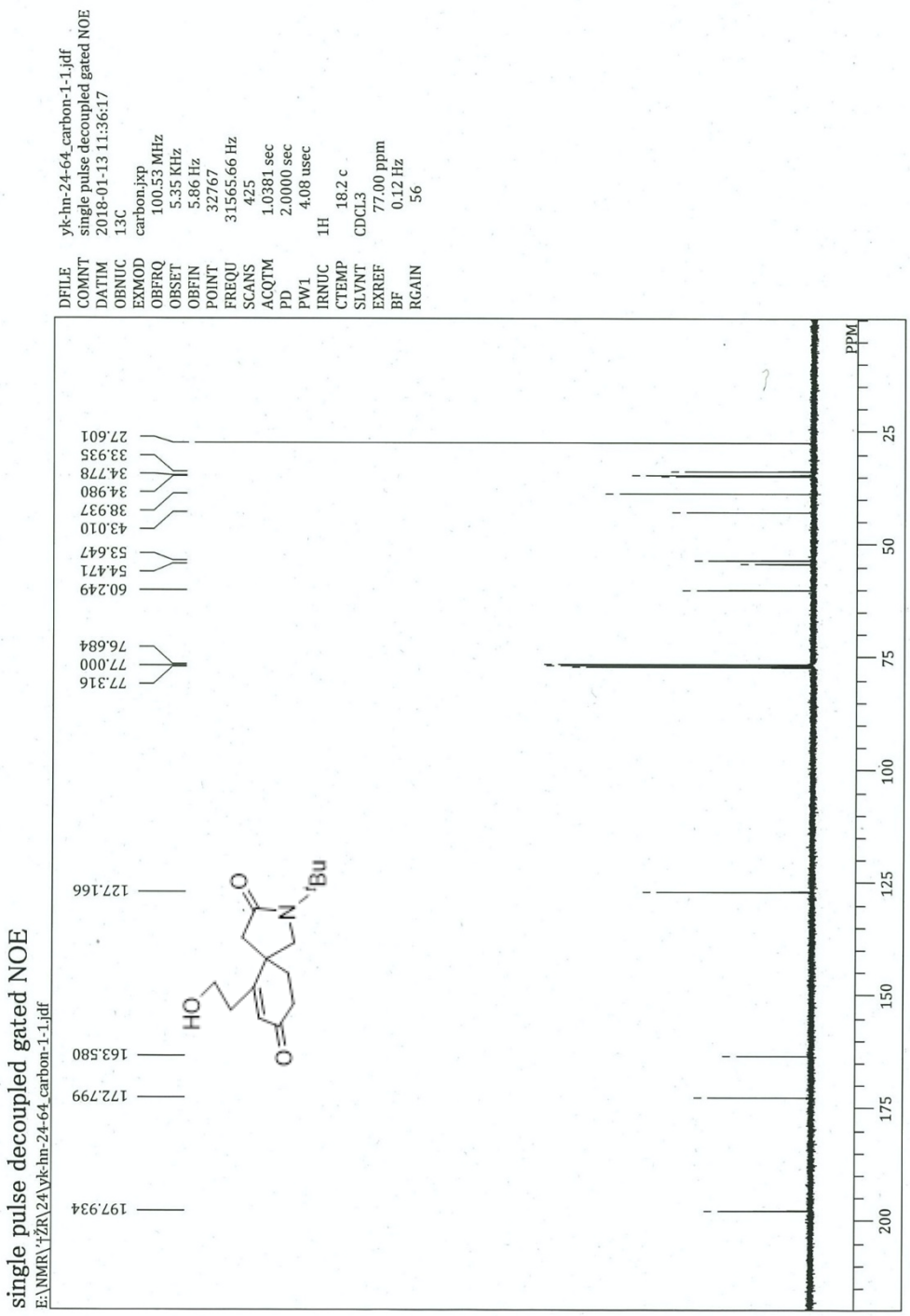
N
tBu
O
PPM

12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OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 32767
FREQU 31565.66 Hz
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ACQTM 1.0381 sec
PD 2.0000 sec
PW1 4.08 usec
IRNUC 1H
CTEMP 18.2 c
SLVNT CDCl3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 56
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172.799
163.580
127.166
77.316
77.000
76.684
60.249
54.471
53.647
43.010
38.937
34.980
34.778
33.935
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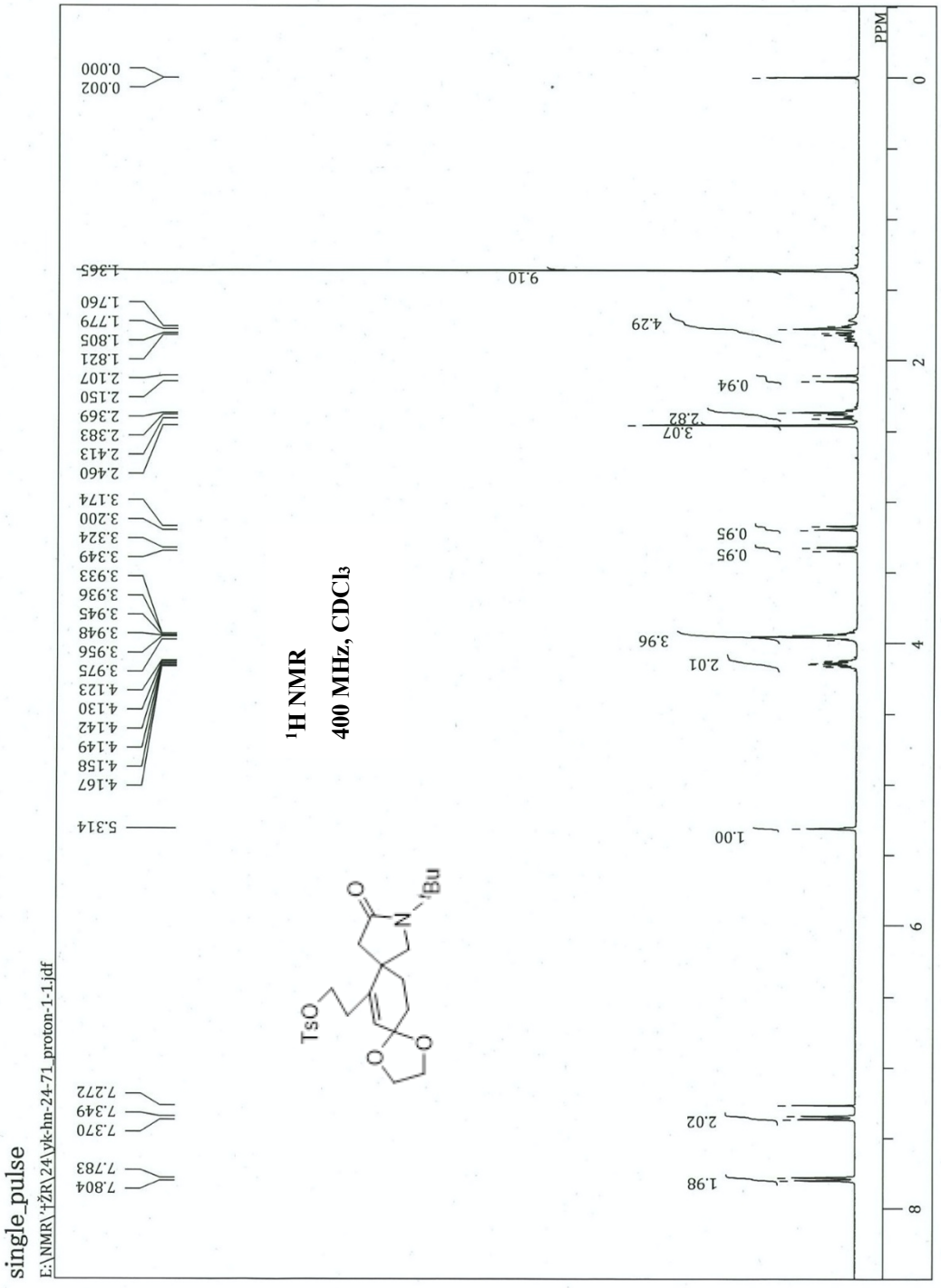
HO
O
N
tBu
O
PPM
200
175
150
125
100
75
50
25

13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^{1}H NMR
400 MHz, CDCl$_3$
TsO
^{t}Bu
PPM
0.000
0.002
1.365
9.10
1.760
1.779
1.805
1.821
2.107
2.150
2.369
2.383
2.413
2.460
3.174
3.200
3.324
3.349
3.933
3.936
3.945
3.948
3.956
3.975
4.123
4.130
4.142
4.149
4.158
4.167
5.314
7.272
7.349
7.370
7.783
7.804
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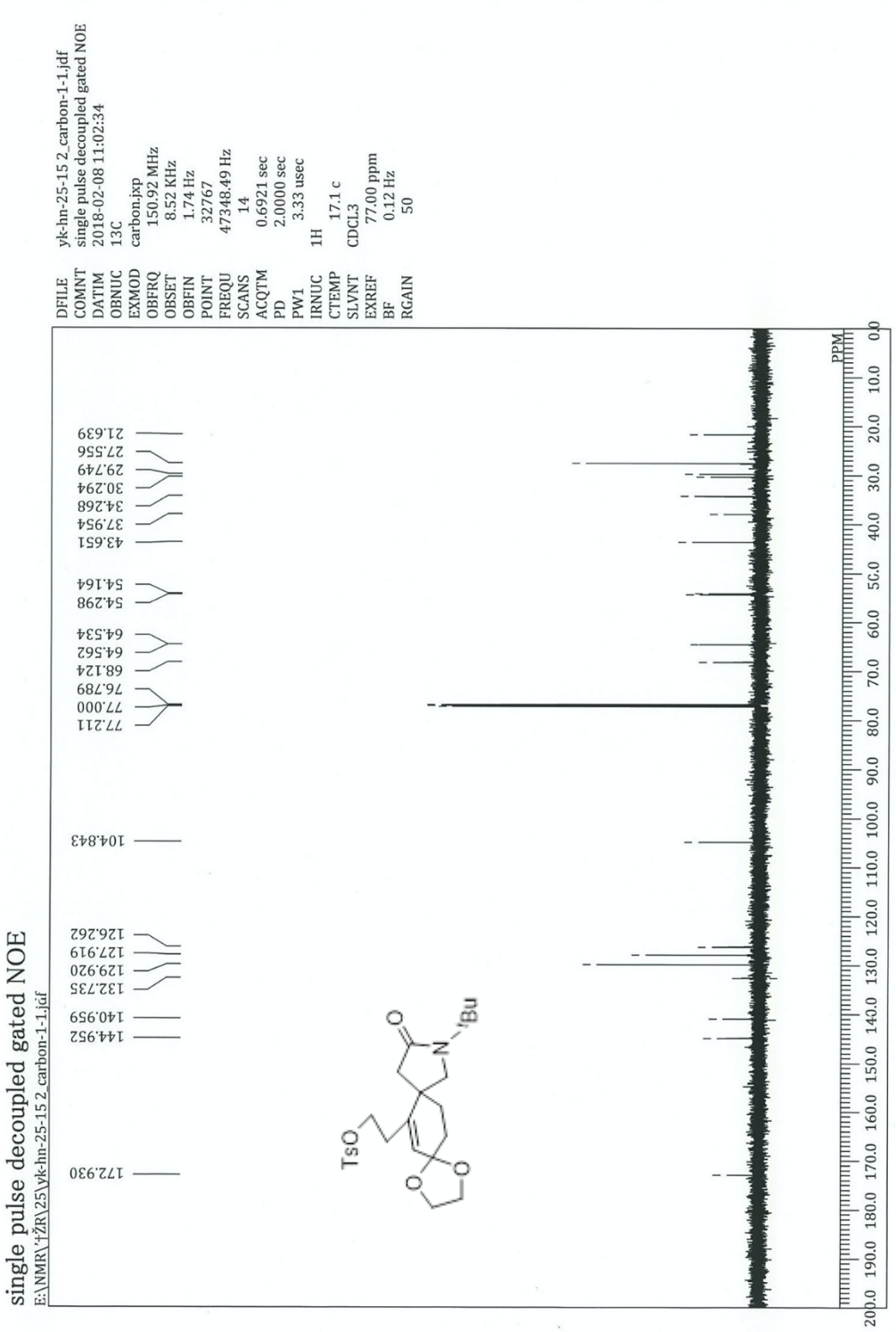
3.07
2.82
0.95
0.95
3.96
2.01
1.00
2.02
1.98

13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OBSET 8.52 KHz
OBFIN 1.74 Hz
POINT 32767
FREQU 47348.49 Hz
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ACQTM 0.6921 sec
PD 2.0000 sec
PW1 3.33 usec
IRNUC 1H
CTEMP 17.1 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 50
172.930
144.952
140.959
132.735
129.920
127.919
126.262
104.843
77.211
77.000
76.789
68.124
64.562
64.534
54.298
54.164
43.651
37.954
34.268
30.294
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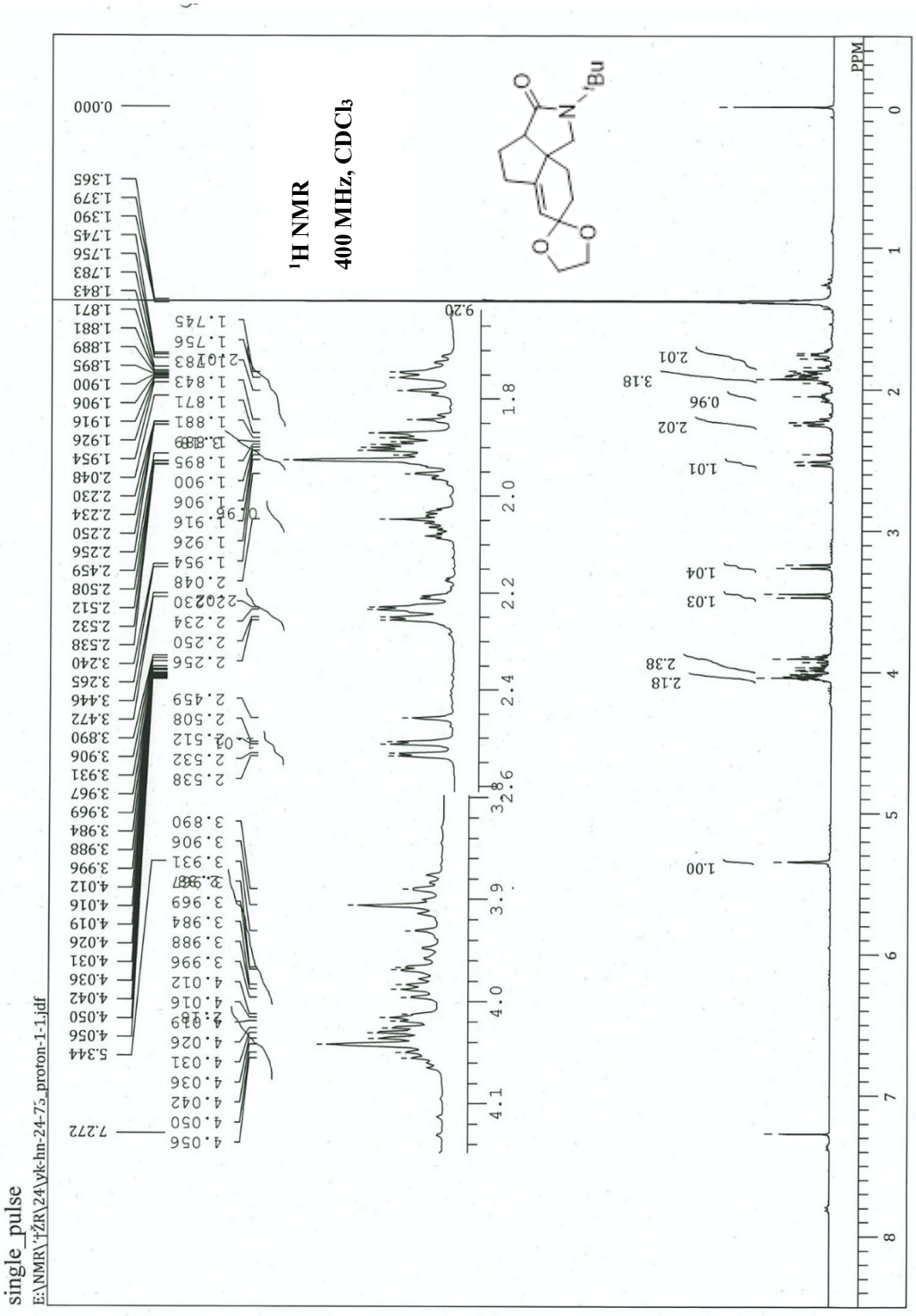
27.556
21.639
TsO
O
N
tBu
O
O
PPM
200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0.0

14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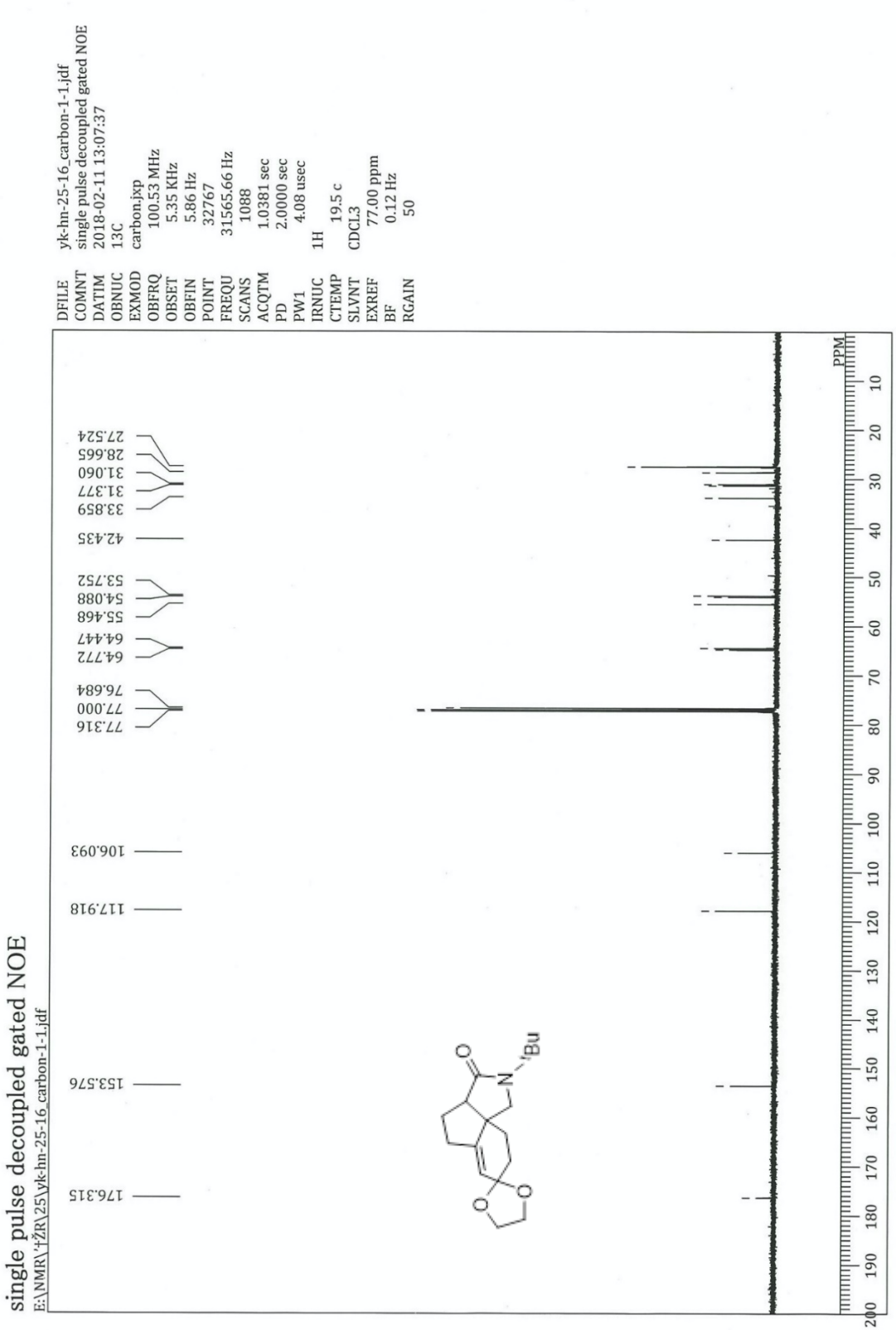
^{1}H NMR
400 MHz, CDCl$_3$
tBu
N
O
PPM

14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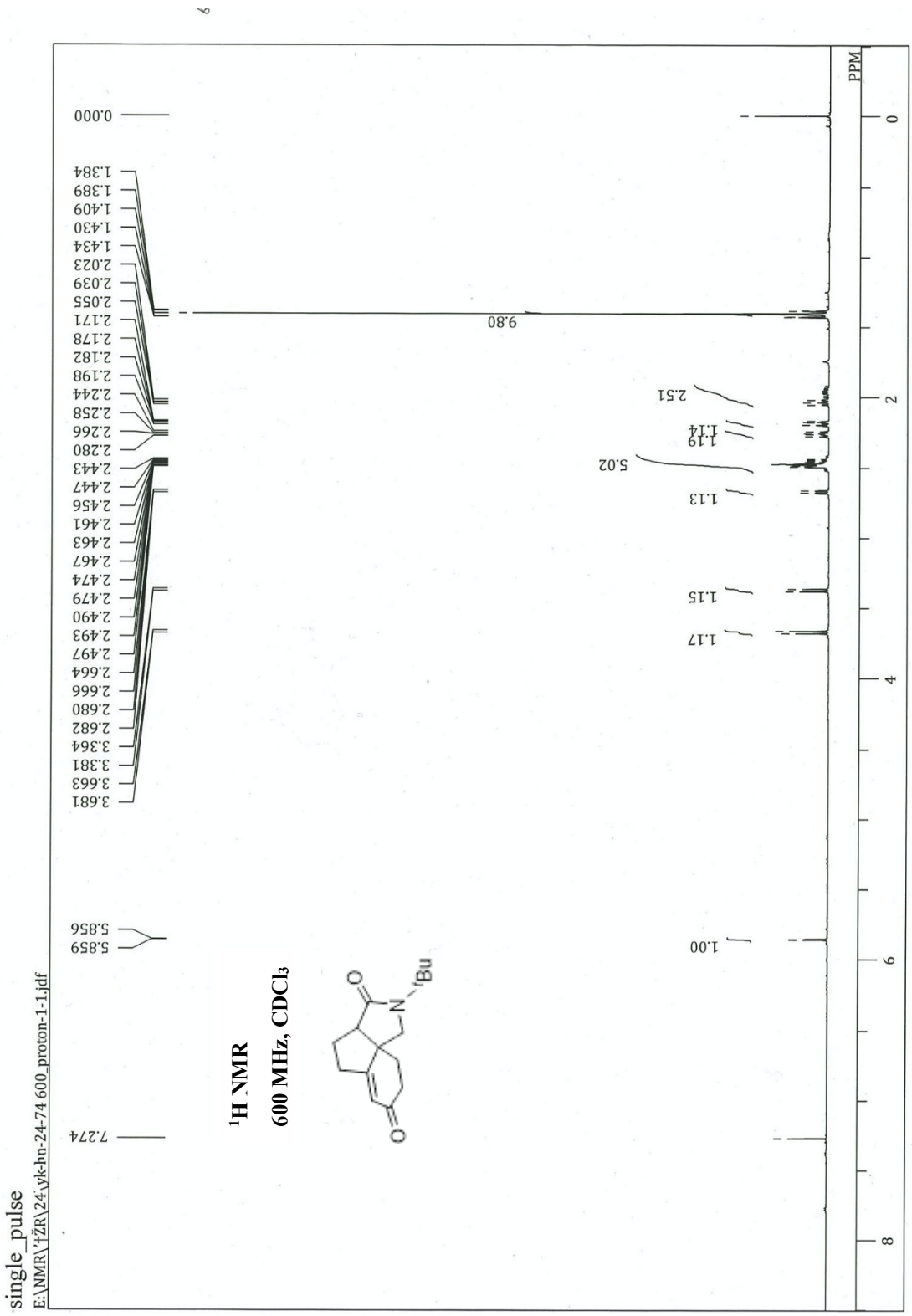
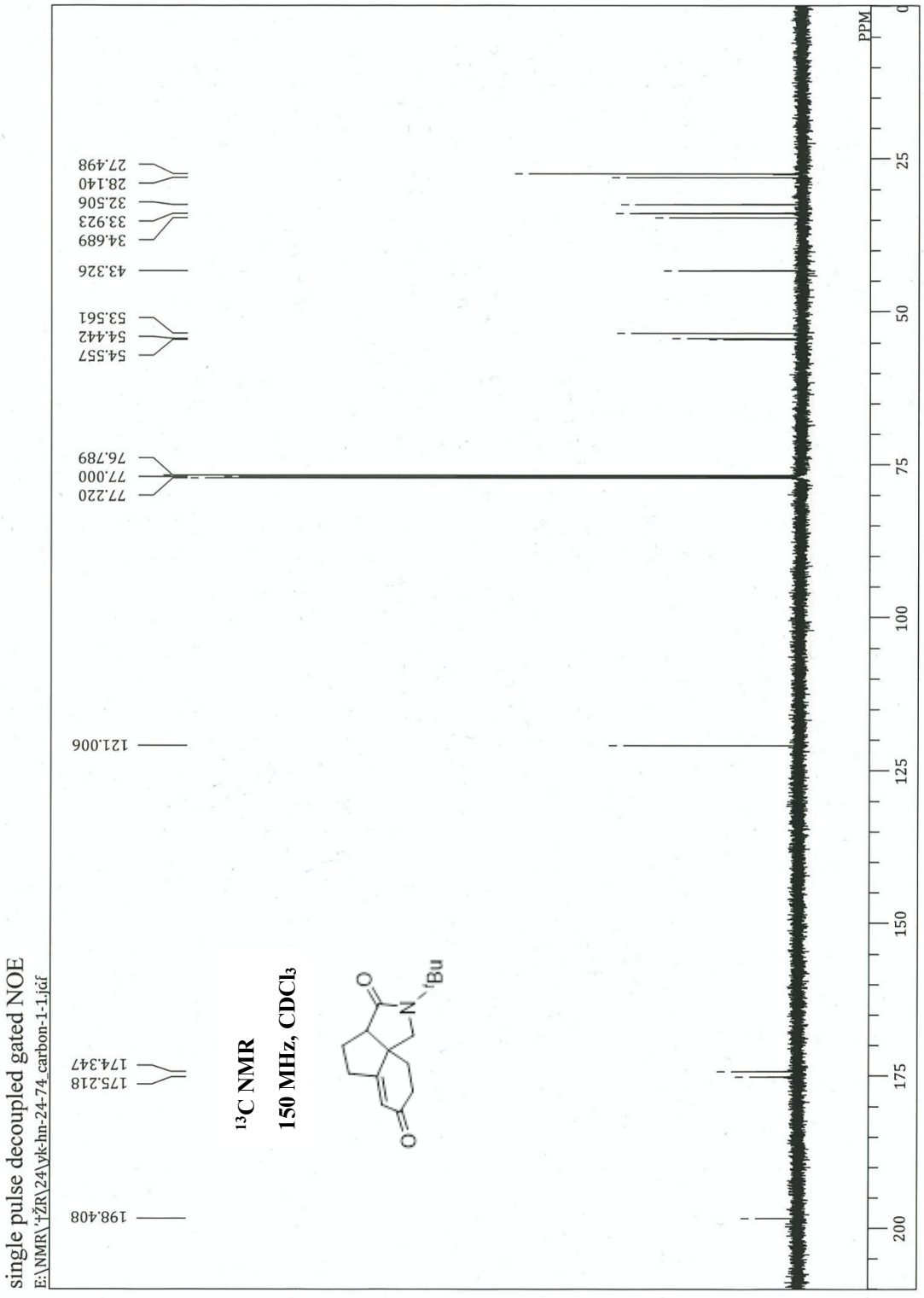
EXMOD carbon.jxp
OBFRQ 100.53 MHz
OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 32767
FREQU 31565.66 Hz
SCANS 1088
ACQTM 1.0381 sec
PD 2.0000 sec
PW1 4.08 usec
IRNUC 1H
CTEMP 19.5 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 50
176.315
153.576
117.918
106.093
77.316
77.000
76.684
64.772
64.447
55.468
54.088
53.752
42.435
33.859
31.377
31.060
28.665
27.524
tBu
PPM

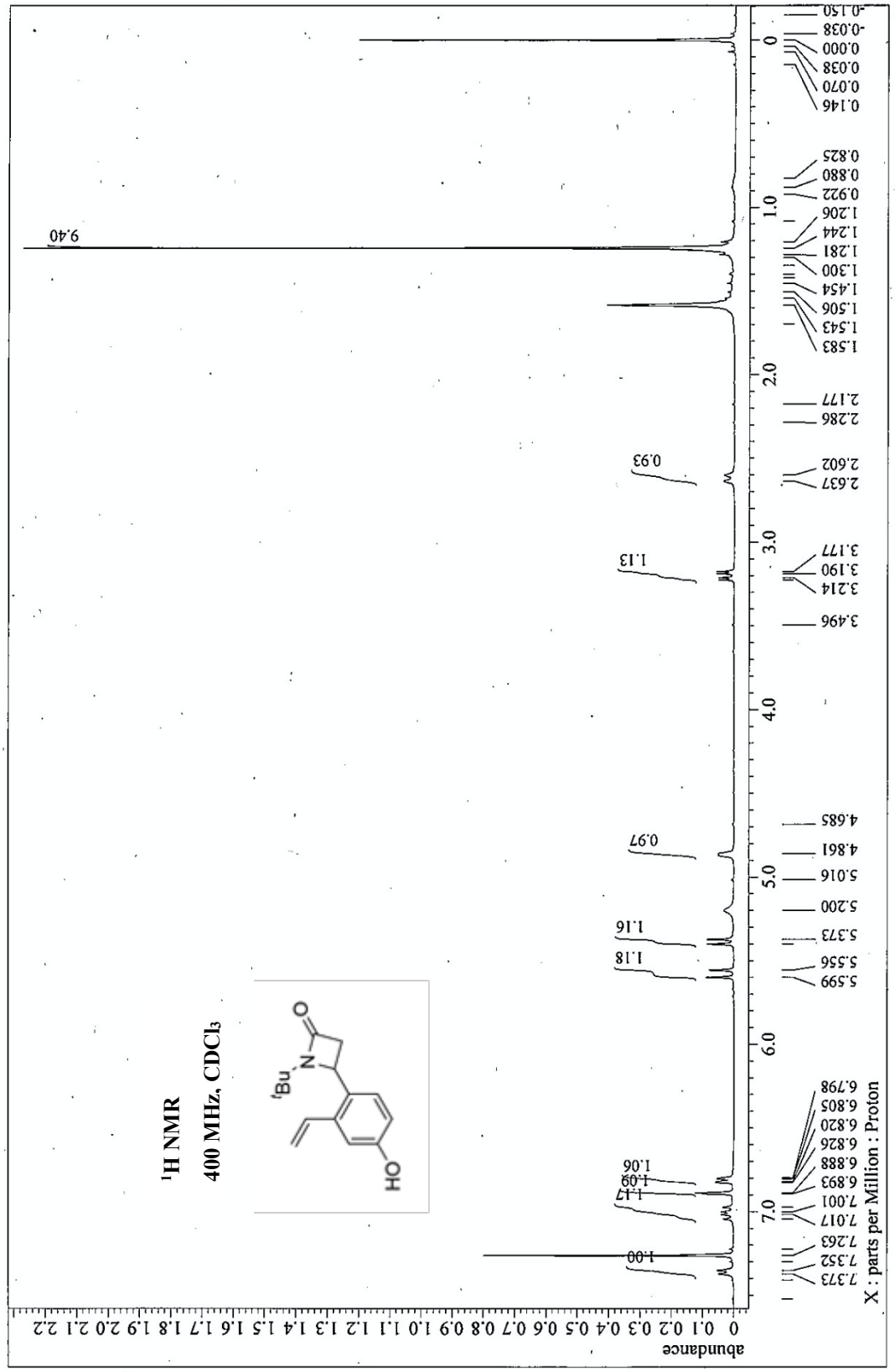
15


single_pulse
E:\NMR\ŽR\24\yk-hn-24-74 600_proton-1-1.jdf
^{1}H NMR
600 MHz, CDCl$_3$
^{t}Bu
PPM
0
2
4
6
8
0.000
1.384
1.389
1.409
1.430
1.434
2.023
2.039
2.055
2.171
2.178
2.182
2.198
2.244
2.258
2.266
2.280
2.443
2.447
2.456
2.461
2.463
2.467
2.474
2.479
2.490
2.493
2.497
2.664
2.666
2.680
2.682
3.364
3.381
3.663
3.681
5.856
5.859
7.274
9.80
1.00
1.15
1.17
1.13
5.02
1.19
1.14
2.51

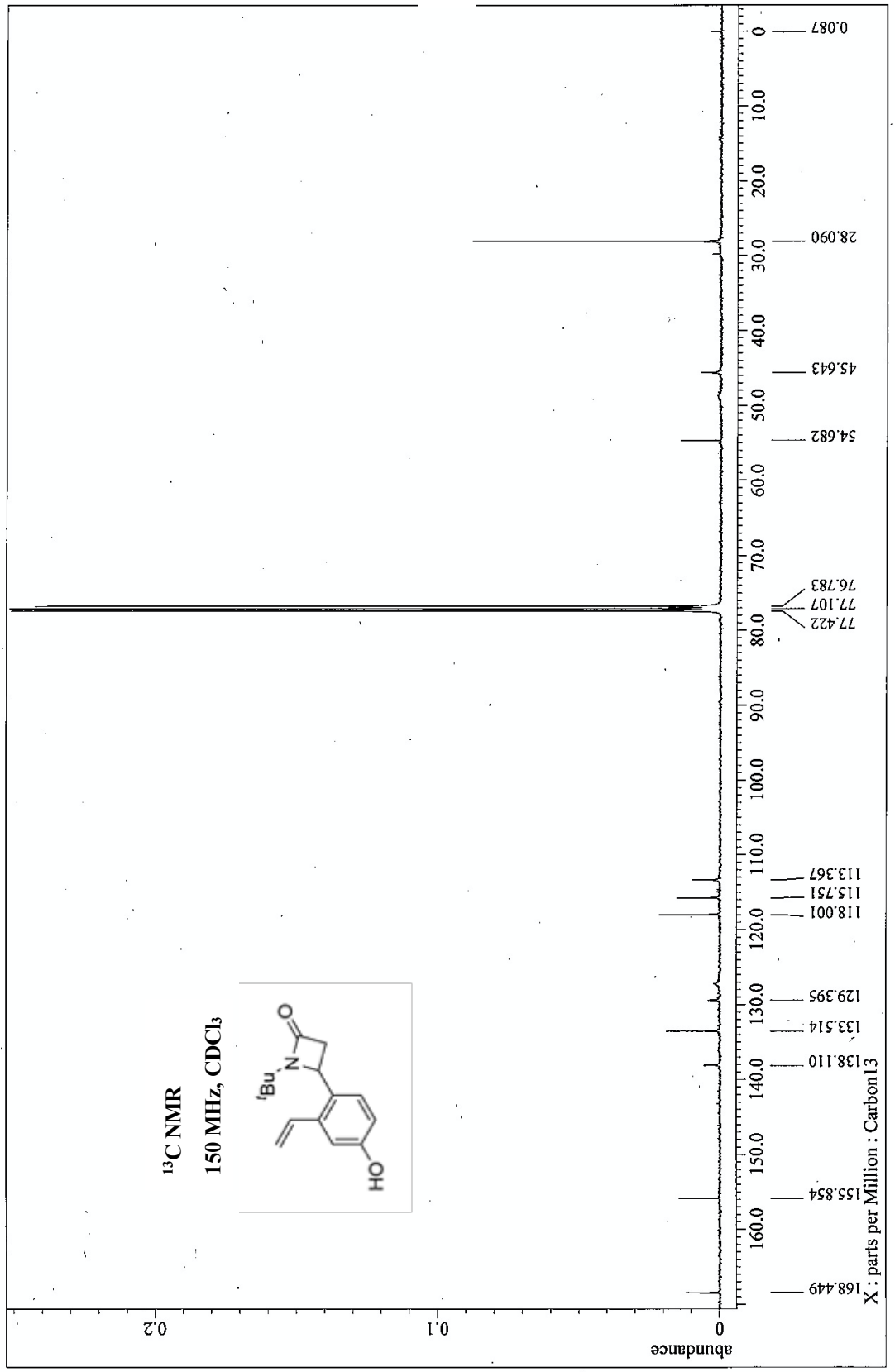
15


single pulse decoupled gated NOE
E:\NMR\ŤŽR\24\vk-hn-24-74_carbon-1-1.jdf
198.408
175.218
174.347
121.006
77.220
77.000
76.789
54.557
54.442
53.561
43.326
34.689
33.923
32.506
28.140
27.498
PPM
0
25
50
75
100
125
150
175
200
^{13}C NMR
150 MHz, CDCl$_3$
O
N
tBu
O

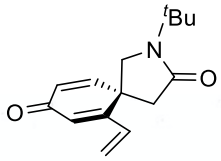
16



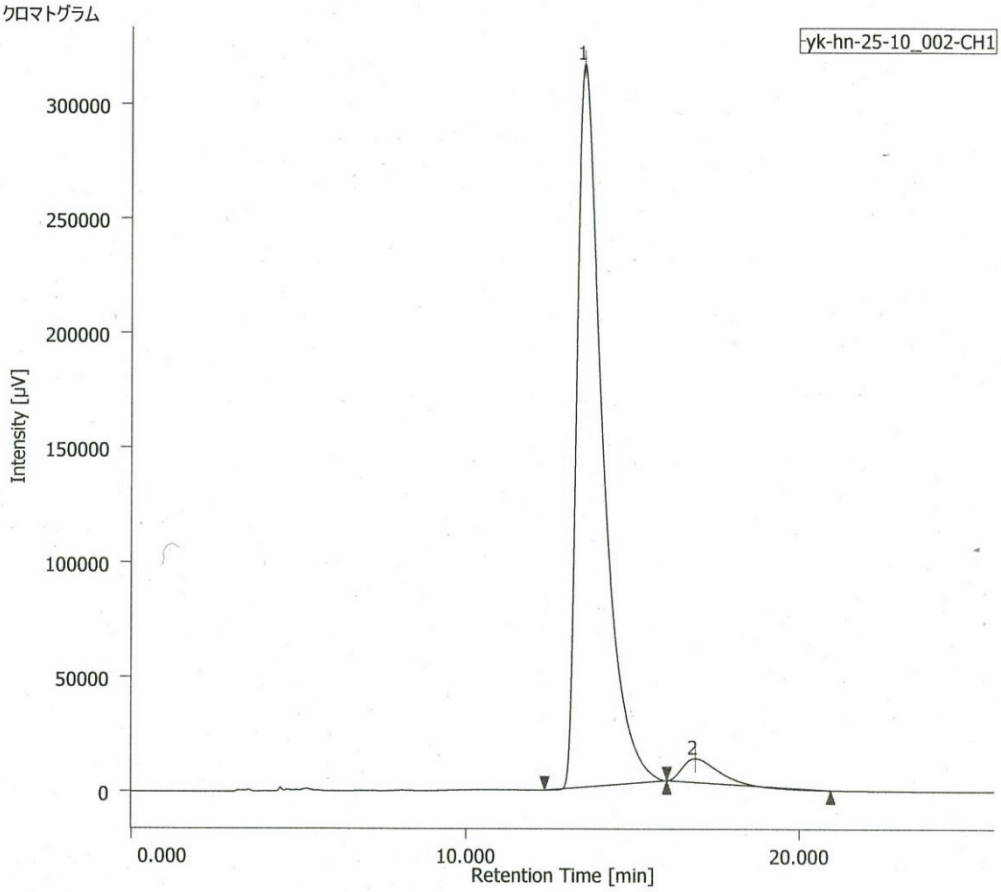
16


0.087
28.090
45.643
54.682
76.783
77.107
77.422
113.367
115.751
118.001
129.395
133.514
138.110
155.854
168.449
X : parts per Million : Carbon13
abundance
0
0.1
0.2
^{13}C NMR
150 MHz, CDCl$_3$
^{t}Bu
N
O
HO

3. Chiral HPLC Trace



yk-hn_0212 yk-hn-25-10_002 2018/02/12 22:11:43



クロマトグラムラベル	
測定済みシーケンス	yk-hn_0212 2018/02/12 20:57:38
クロマトグラム名	yk-hn-25-10_002
サンプル名	
クロマトグラム情報	
ユーザー名	yk
更新日時	2018/02/12 22:09:46
コメント	OJ-H, 80:20, 1mL/min
HPLC システム名	HPLC-1
測定日	2018/02/12 21:43:52
注入量	3.00 [μL]
サンプル#	1
プロジェクト名	test
取込時間	60.0 [min]
測定シーケンス	
コントロールメソッド	test
ピーク ID テーブル	
検量線テーブル	
追加情報	

ピーク情報

#	ピーク名	CH	tR [min]	面積 [μV*sec]	高さ [μV]	面積%	高さ%	定量値	NTP	分離度	シンメトリー係数	警告
1	Unknown	1	13.542	16925104	315746	95.706	96.821	N/A	1640	2.038	2.200	
2	Unknown	1	16.892	759350	10368	4.294	3.179	N/A	1189	N/A	1.604	