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Supporting Information

Biomass Derived Furfural-Based Facile Synthesis of Protected (2*S*)-phenyl-3-piperidone, a Common Intermediate for Many Drugs

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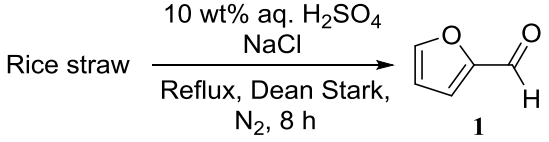
1. General Methods

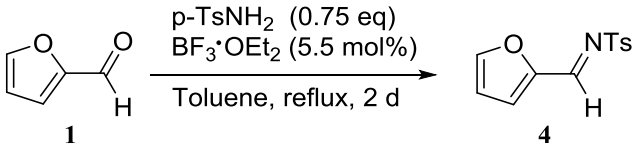
All reagents were commercially purchased and were used as received for the reactions. All reactions were carried out in oven-dried glassware while THF was freshly distilled from Na/Benzophenone ketyl and DCM was freshly distilled from Calcium Hydride. Rice straw used was collected from a rice straw farm in Jiangxi Province Fengcheng Area, China after being sun-dried. Upon receiving the rice straw, it was further dried in a vacuum oven at 80 ^{o}C for 6 h and stored in an air-tight container. The rice straw is cut into small pieces of about 2-3 cm in length before being used for reaction. Thin-layer chromatography (TLC) was conducted with Merck 60 F254 precoated silica gel plate (0.2 mm thickness) and visualized under UV, by potassium permanganate or ceric ammonium molybdate stain. Flash chromatography was performed using Merck silica gel 60 with distilled solvents. ^{1}H-NMR spectra were performed on a Bruker Avance 300, Bruker Avance 400 or Bruker Avance 500 NMR spectrometer and are reported in ppm downfield from $SiMe_4$ (δ 0.0), relative to the signal of chloroform-d (δ = 7.26, singlet) or methanol-d_4 (δ = 3.31, quintet). Data reported as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ^{13}C-NMR spectra were recorded on Bruker Avance 300 (75 MHz) or 400 (100MHz) or 500 (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.16 ppm, CD_3OD at 49.15 ppm). IR spectra were recorded using nujol mull technique on NaCl plates on a Shimadzu IRPrestige-21 FT-IR Spectrophotometer or under attenuated total reflection (ATR) conditions on a PerkinElmer Spectrum 100 FT-IR Spectrometer and were reported in frequency of absorption (cm^{-1}). High-resolution mass spectral analysis (HRMS) was performed on Q-Tof Premier mass spectrometer (Waters Corporation).

2. Synthesis and characterization of compounds



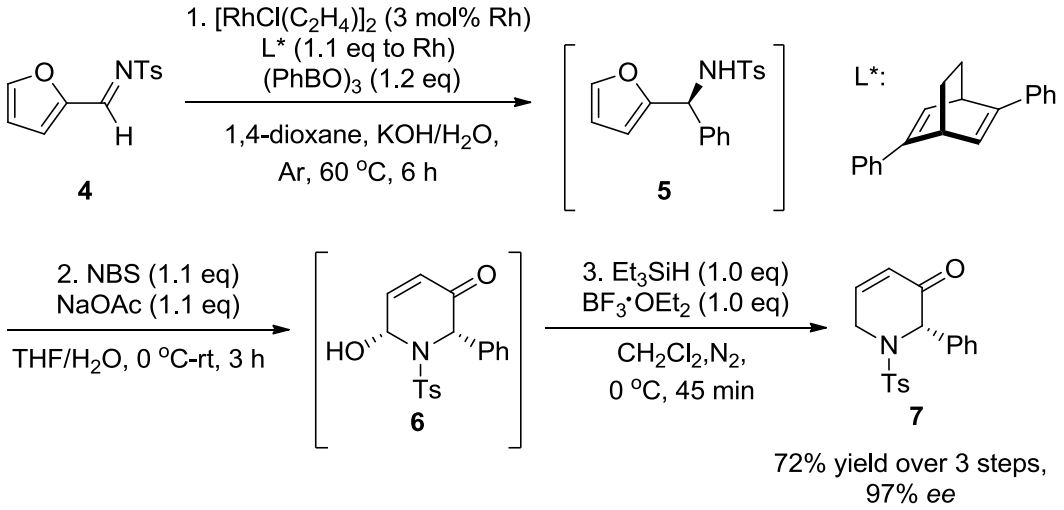
Furan-2-carbaldehyde (1)

To a 250 mL round-bottom flask equipped with a stir bar was added rice straw (10.5 g, 2-3 cm length), NaCl (14 g) and 10 wt% aqueous H_2SO_4 (70 mL). The round-bottom flask was then fitted with a Dean Stark trap with a stopcock at the bottom of the trap and then fitted with water condenser. DCM (10 mL) was added into the Dean Stark trap initially and the reaction mixture was heated to reflux at 150 ^oC. After 1 h, the DCM in the Dean Stark trap was collected *via* the stopcock and fresh DCM (10 mL) was added into the Dean Stark trap through the top of the water condenser. This process was repeated hourly for a total of 8 h and the combined organic layers were washed with saturated aqueous $NaHCO_3$ solution (40 mL) and brine (10 mL) before drying over anhydrous magnesium sulphate, filtered and concentrated under reduced pressure to give **1** as a pale yellow oil (851 mg, 8.86 mmol, 8.1 wt%) ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 9.68 (s, 1H), 7.70 (t, *J* = 0.8 Hz, 1H), 7.26 (dd, *J* = 3.6 Hz, 0.5 Hz 1H), 6.61 (dd, *J* = 3.6 Hz, 1.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 177.9, 152.9, 148.1, 121.2, 112.6; Other characterization data are similar to the authentic sample.



N-(furan-2-ylmethylene)-4-methylbenzenesulfonamide (4)

1 (14.0 g, 146 mmol, 1.0 eq), 4-methylbenzenesulfonamide (18.8 g, 110 mmol, 0.75 eq), boron trifluoride etherate (1.0 mL, 1.15 g, 8.1 mmol, 5.5 mol%) and toluene (150 mL) were added into a round-bottom flask fitted with a Dean Stark trap. The mixture was heated at reflux for 2 days and activated charcoal was added and stirred for 1 h. The mixture was filtered and the filtrate concentrated under reduced pressure to give a brown solid. Recrystallization from benzene gave *N*-(furan-2-ylmethylene)-4-methylbenzenesulfonamide **4** as brown crystals (20.5 g, 82.5 mmol, 75%). mp = 100-101 ^oC (lit[1] 100-101 ^oC); TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.32; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 8.81 (s, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.74 (d, *J* = 1.6 Hz, 1H), 7.34-7.31 (m, 3H), 6.65 (dd, *J* = 3.6 Hz, 1.7 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 155.7, 149.8, 149.1, 144.6, 135.2, 129.8, 128.1, 124.7, 113.7, 21.7; FTIR (Nujol, NaCl, cm^{-1}): 1607, 1315, 1155, 932; HRMS (ESI) *m/z* Calcd for $C_{12}H_{12}NO_3S$ $[M+H]^+$: 250.0538; found: 250.0541.



(*S*)-N-(furan-2-yl(phenyl)methyl)-4-methylbenzenesulfonamide (5)

To the solution of $[RhCl(C_2H_4)_2)]_2$ (5.8 mg, 0.015 mmol, 3 mol% Rh) and (*R*,*R*)-Ph-bod* (8.5 mg, 0.033 mmol, 1.1 eq to Rh) in anhydrous 1,4-dioxane (2.5 mL) was added aqueous KOH (65.0 µL, 3.1 M, 20 mol% KOH, H_2O: 1 eq to boron) at room temperature and stirred for 15 min. This solution containing the catalyst was added to the solution of imine **4** (249 mg, 1.0 mmol, 1.0 eq) and 2,4,6-triphenylboroxine (374 mg, 1.2 mmol, 1.2 eq) in anhydrous 1,4-dioxane (4.0 mL) at the same temperature. After 6 h stirring at 60 °C, the mixture was passed through a short silica gel column (pre-treated with methanol, eluent: ethyl acetate) to give **5** as the crude product and was immediately subjected to the next step without any further purification.

Data for **5** after purification using silica gel chromatography (Eluent: Hexane/Ethyl Acetate = 5:1) to give (*S*)-N-(furan-2-yl(phenyl)methyl)-4-methylbenzenesulfonamide **5** as a pale yellow solid in 97% yield, *ee* = 99%. The *ee* was determined on Chiralcel OD-H column with hexane/2-propanol = 90:10, flow = 0.5 mL/min, wavelength = 220 nm. Retention times: 20.5 min [(*S*)-enantiomer], 22.0 min [(*R*)-enantiomer]. mp = 129-130 °C; TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.53; $[\alpha]^{22}_D$ = -18.1 (c = 1.03, $CHCl_3$) for 99% *ee* (Lit[2]: $[\alpha]^{20}_D$ = -21.6 (c = 1.03, $CHCl_3$) for 99% ee.); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.58 (d, *J* = 8.3 Hz, 2H), 7.26-7.22 (m, 4H), 7.19-7.14 (m, 4H), 6.19 (dd, *J* = 3.2 Hz, 1.9 Hz, 1H), 5.99 (d, *J* = 3.2 Hz, 1H), 5.61 (d, *J* = 7.7 Hz, 1H), 5.23 (d, *J* = 7.6 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 152.3, 143.3, 142.7, 138.4, 137.5, 129.5, 128.7, 128.1, 127.3, 127.2, 110.3, 108.5, 55.6, 21.6; FTIR (Nujol, NaCl, cm^{-1}): 3265, 1597, 1319, 1159, 928; HRMS (ESI) *m/z* Calcd for $C_{18}H_{18}NO_3S$ $[M+H]^+$: 328.1007; found: 328.0992.

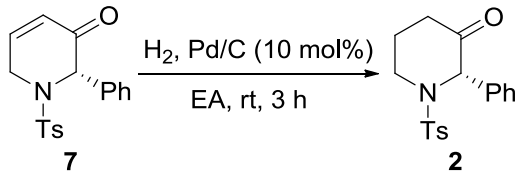
Crude **5** from the previous step was dissolved in a mixture of THF (10.0 mL) and H_2O (3.3 mL) at 0 °C. Sodium acetate (90 mg, 1.1 mmol, 1.1 eq) was added before *N*-bromosuccinimide (196 mg, 1.1 mmol, 1.1 eq) was slowly added in portions at 0 °C over 15 min. The mixture was stirred for 3 h at room temperature after the addition of *N*-bromosuccinimide before solid $Na_2S_2O_3$ and brine (7 mL) was added. The mixture was extracted with ethyl acetate (3 x 20 mL) and the combined organic layers were washed with

brine (25 mL), dried over anhydrous magnesium sulphate, filtered and concentrated under reduced pressure to give **6** as the crude product and **6** was immediately subjected to the next step without any further purification.

Data for ***rac*-6** (recrystallized in CH_2Cl_2 from crude product as pale yellow crystals): mp = 122-123 ^oC (Decomposed); TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.26; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.64 (d, *J* = 8.3 Hz, 2H), 7.56-7.53 (m, 2H), 7.33-7.24 (m, 5H), 6.86 (dd, *J* = 10.4 Hz, 4.1 Hz, 1H), 6.11 (dd, *J* = 10.4 Hz, 1.4 Hz, 1H), 5.99-5.96 (m, 1H), 5.47 (s, 1H), 3.48-3.46 (m, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 191.2, 144.6, 143.7, 136.8, 136.3, 130.3, 128.8, 128.4, 127.8, 127.6, 127.0, 73.6, 64.2, 21.7; FTIR (Nujol, NaCl, cm^{-1}): 3480, 1682, 1649, 1597, 1321, 1155; HRMS (ESI) *m/z* Calcd for $C_{18}H_{18}NO_4S$ $[M+H]^+$: 344.0957; found: 344.0970.

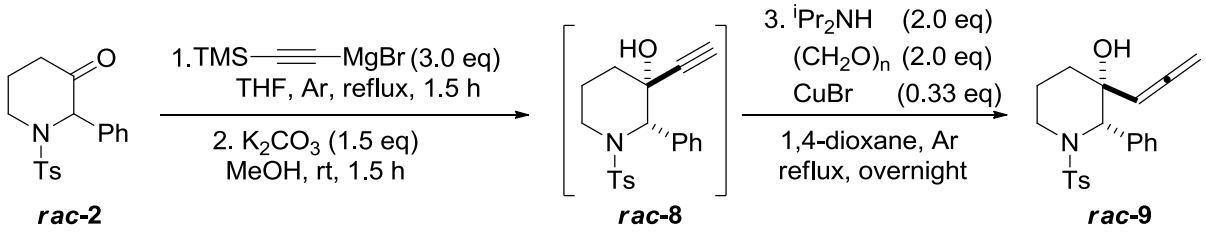
(S)-2-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one (7)

The crude rearrangement product **6** was dissolved in anhydrous CH_2Cl_2 (9.0 mL) and cooled down to 0 ^oC under N_2 protection. Triethylsilane (159 μL, 116 mg, 1.0 mmol, 1.0 eq) was added followed by boron trifluoride etherate (123 μL, 142 mg, 1.0 mmol, 1.0 eq) and the mixture was allowed to stirred at 0 ^oC for 45 min before H_2O (10 mL) was added to quench the reaction. The mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine (25 mL), dried over anhydrous magnesium sulphate and filtered. Concentration under reduced pressure and purification using silica gel chromatography (Eluent: Hexane/Ethyl acetate = 4:1) gave (*S*)-2-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one **7** as a brown solid (234 mg, 0.72 mmol, 72% over 3 steps), *ee* = 97%. The *ee* was determined on Chiralcel OD-H column with hexane/2-propanol = 90:10, flow = 0.5 mL/min, wavelength = 220 nm. Retention times: 29.7 min [(*R*)-enantiomer], 34.0 min [(*S*)-enantiomer]. mp = 131-132 ^oC (lit[3] = yellow oil); TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.42; $[\alpha]^{21}_D$ = +123 (c = 1.32, CH_2Cl_2) for 97% *ee*. (Lit[3]: $[\alpha]^{20}_D$ = -145 (c = 0.3, CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$) δ (ppm): 7.62 (d, *J* = 8.3 Hz, 2H), 7.35-7.29 (m, 5H), 7.25 (d, *J* = 8.0 Hz, 2H), 6.69 (ddd, *J* = 10.4 Hz, 4.9 Hz, 1.9 Hz, 1H), 5.94 (ddd, *J* = 10.4 Hz, 2.4 Hz, 1.6 Hz, 1H), 5.62 (s, 1H), 4.46 (ddd, *J* = 20.9 Hz, 4.8 Hz, 1.4 Hz, 1H), 3.84 (dt, *J* = 20.9 Hz, 2.4 Hz, 1.6 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 192.3, 144.6, 144.2, 136.5, 133.2, 130.1, 129.1, 128.7, 127.8, 127.2, 127.0, 64.1, 41.8, 21.7; FTIR (Nujol, NaCl, cm^{-1}): 1688, 1628, 1597, 1341, 1159; HRMS (ESI) *m/z* Calcd for $C_{18}H_{18}NO_3S$ $[M+H]^+$: 328.1007; found: 328.1020.



(*S*)-2-phenyl-1-tosylpiperidin-3-one (2)

(*S*)-2-phenyl-1-tosyl-1,6-dihydropyridin-3(2H)-one **7** (151 mg, 0.462 mmol, 1.0 eq) was dissolved in ethyl acetate (10 mL) and palladium on activated charcoal (10 wt%, 49 mg, 0.046 mmol, 10 mol%) was added. The round bottom flask was evacuated and refilled with H_2 thrice using a H_2 balloon. The reaction was stirred for 3 h at room temperature before being filtered through a pad of celite. Concentration under reduced pressure gave (*S*)-2-phenyl-1-tosylpiperidin-3-one **2** as a pale yellow solid (152 mg, 0.462 mmol, 100%), *ee* = 97%. The *ee* was determined on Chiralcel OD-H column with hexane/2-propanol = 90:10, flow = 0.5 mL/min, wavelength = 220 nm. Retention times: 19.7 min [(*R*)-enantiomer], 23.0 min [(*S*)-enantiomer]. mp = 152-153 ^{o}C (lit[3] = deliquescent solid, lit[4] = 152-154 ^{o}C); TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.50; $[\alpha]^{23}_{D}$ = -10.0 (c = 1.01, CH_2Cl_2) for 97% *ee* (Lit[4]: $[\alpha]^{20}_{D}$ = +5 (c = 0.2, CH_2Cl_2)); ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.71 (d, *J* = 8.3 Hz, 2H), 7.36-7.26 (m, 7H), 5.57 (s, 1H), 3.86 (dt, *J* = 14.0 Hz, 5.0 Hz, 1H), 3.44 (ddd, *J* = 14.0 Hz, 9.6 Hz, 4.3 Hz, 1H), 2.43 (s, 3H), 2.40-2.31 (m, 1H), 2.17 (dt, *J* = 16.0 Hz, 5.3 Hz, 1H), 1.79-1.61 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 204.6, 144.0, 137.3, 134.0, 130.1, 129.3, 128.3, 127.2, 125.9, 66.9, 41.3, 36.9, 23.6, 21.7; FTIR (Nujol, NaCl, cm^{-1}): 1721, 1595, 1342, 1157; HRMS (ESI) *m/z* Calcd for $C_{18}H_{20}NO_3S$ $[M+H]^+$: 330.1164; found: 330.1166.



***rac*-3-ethynyl-2-phenyl-1-tosylpiperidin-3-ol (*rac*-8)**

An oven-dried 50 mL two-neck round bottom flask equipped with a stir bar and a reflux condenser was cooled under vacuum and back-filled with Ar thrice before being charged with methylmagnesium bromide (2.0 mL of a 3.0 M solution in ether, 6.0 mmol, 3.0 eq), anhydrous THF (2.7 mL) and trimethylsilylacetylene (1.3 mL, 882 mg, 9.0 mmol, 4.5 eq). The mixture was heated at reflux for 1.5 h before **rac-2** (658 mg, 2.0 mmol, 1.0 eq) in anhydrous THF (16.0 mL) was added and the mixture was allowed to stir at reflux for 1.5 h before saturated aqueous NH_4Cl solution (10 mL) was added to quench the reaction. The layers were separated and the aqueous phase extracted with ethyl acetate (3 x 15 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution (30 mL),

brine (30 mL), dried over anhydrous magnesium sulphate and filtered. Concentration under reduced pressure gave the crude product which was used immediately in the next step without further purification.

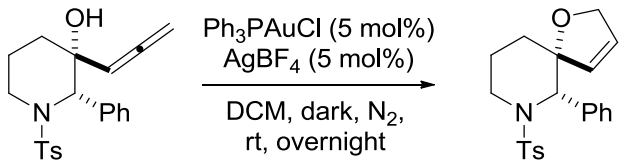
The crude product from the Grignard reaction was dissolved in MeOH (20 mL) and solid K_2CO_3 (414 mg, 3.0 mmol, 1.5 eq) was added and the mixture was allowed to stir at room temperature for 1.5 h. The solvent was removed under reduced pressure and saturated aqueous NH_4Cl solution (10 mL) and EA (20 mL) were added and the layers were separated. The aqueous phase was extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ solution (20 mL), brine (20 mL), dried over anhydrous magnesium sulphate and filtered. Concentration under reduced pressure gave ***rac*-8** as the crude product which was used immediately in the next step without further purification.

Data for ***rac*-8** after purification using silica gel chromatography (Eluent: Hexane/Ethyl Acetate = 2:1) to give *rac*-3-ethynyl-2-phenyl-1-tosylpiperidin-3-ol ***rac*-8** as a white solid. mp = 169-170 ^oC; TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.34; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.41 (d, *J* = 8.3 Hz, 2H), 7.34-7.32 (m, 2H), 7.26-7.22 (m, 3H), 7.06 (d, *J* = 8.1 Hz, 2H), 5.31 (s, 1H), 3.82 (dd, *J* = 13.8 Hz, 4.1 Hz, 1H), 3.39-3.29 (m, 1H), 2.53 (s, 1H), 2.34 (s, 3H), 2.02-1.98 (m, 2H), 1.94 (s, 1H), 1.87-1.83 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 143.0, 136.9, 136.2, 129.7, 129.2, 128.4, 128.3, 127.4, 86.1, 73.6, 69.0, 65.6, 41.2, 32.5, 22.0, 21.6; FTIR (ATR, cm^{-1}): 3469, 3297, 3067, 3032, 1597, 1324, 1161; HRMS (ESI) *m/z* Calcd for $C_{20}H_{22}NO_3S$ $[M+H]^+$: 356.1320; found: 356.1311.

***rac*-2-phenyl-3-(propa-1,2-dien-1-yl)-1-tosylpiperidin-3-ol (*rac*-9)**

Isopropylamine (560 μL, 404 mg, 4.0 mmol, 2.0 eq) was added to a suspension of crude ***rac*-8**, paraformaldehyde (120 mg, 4.0 mmol, 2.0 eq) and CuBr (95 mg, 0.67 mg, 33 mol%) in anhydrous 1,4-dioxane (16.0 mL). The reaction was refluxed overnight and then cooled to room temperature before being filtered through a pad of celite. Concentration under reduced pressure and purification using silica gel chromatography (Eluent: Hexane/Ethyl Acetate = 5:1) gave *rac*-2-phenyl-3-(propa-1,2-dien-1-yl)-1-tosylpiperidin-3-ol ***rac*-9** as a yellow solid (510 mg, 1.38 mmol, 69%) over 3 steps.

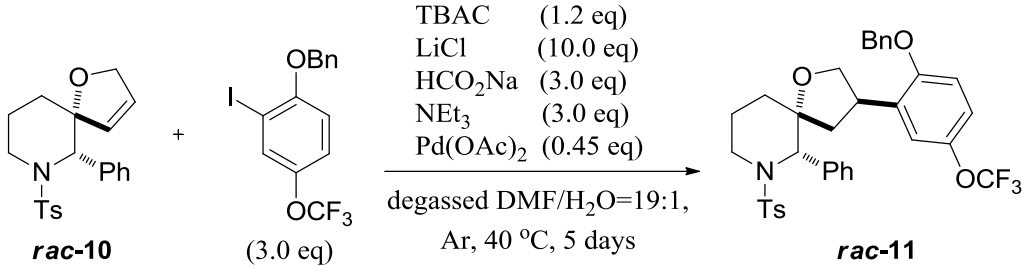
Melting point = 96-97 ^oC; TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.38; ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.30 (d, *J* = 8.2 Hz, 2H), 7.25-7.16 (m, 5H), 7.02 (d, *J* = 8.0 Hz, 2H), 5.52 (t, *J* = 6.7 Hz, 1H), 5.01 (s, 1H), 4.99-4.92 (m, 2H), 3.80 (dd, *J* = 13.1 Hz, 4.5 Hz, 1H), 3.38 (td, *J* = 12.1 Hz, 4.3 Hz, 1H), 2.32 (s, 3H), 1.97-1.91 (m, 2H), 1.82-1.79 (m, 1H), 1.73-1.67 (m, 1H), 1.63 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 206.7, 142.8, 136.8, 129.7, 129.2, 128.2 x 2, 128.0, 127.2, 98.1, 80.1, 71.3, 65.6, 41.2, 32.1, 21.5 x 2; FTIR (Nujol, NaCl, cm^{-1}): 3532, 1960, 1597, 1329, 1153; HRMS (ESI) *m/z* Calcd for $C_{21}H_{24}NO_3S$ $[M+H]^+$: 370.1477; found: 370.1461.



***rac*-9** **rac-10**

rac-6-phenyl-7-tosyl-1-oxa-7-azaspiro[4.5]dec-3-ene (_rac_-10)

α-allenic alcohol ***rac*-9** (200 mg, 0.54 mmol, 1.0 eq), chloro(triphenylphosphine)gold (I) (13 mg, 0.027 mmol, 5 mol%) and silver tetrafluoroborate (5 mg, 0.027 mmol, 5 mol%) were dissolved in anhydrous CH_2Cl_2 (2.0 mL) under N_2 and in the dark. The mixture was allowed to stir at room temperature in the dark overnight. The mixture was then filtered through a pad of celite and concentrated under reduced pressure. Purification using silica gel chromatography (Eluent: Hexane/Ethyl Acetate = 7:1) gave *rac*-6-phenyl-7-tosyl-1-oxa-7-azaspiro[4.5]dec-3-ene ***rac*-10** as a pale yellow solid (170 mg, 0.46 mmol, 85%). mp = 105-106 ^oC; TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.60; ^1H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.39 (d, *J* = 8.3 Hz, 2H), 7.26-7.24 (m, 2H), 7.17-7.13 (m, 3H), 7.07 (d, *J* = 8.1 Hz, 2H), 6.07 (dt, *J* = 6.7 Hz, 2.5 Hz, 1H), 5.87 (d, *J* = 6.2 Hz, 1H), 4.96 (s, 1H), 4.55 (dt, *J* = 13.2 Hz, 2.0 Hz, 1H), 4.29 (dd, *J* = 13.1 Hz, 2.0 Hz, 1H), 3.87-3.81 (m, 1H), 3.35 (ddd, *J* = 13.2 Hz, 11.1 Hz, 5.1 Hz, 1H), 2.35 (s, 3H), 1.95-1.82 (m, 3H), 1.70-1.65 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 142.8, 137.8, 137.5, 132.1, 129.3, 129.3, 127.7, 127.6, 127.2 x 2, 90.4, 75.4, 64.7, 41.3, 30.9, 22.5, 21.6; FTIR (Nujol, NaCl, cm^{-1}): 1651, 1599, 1331, 1171; HRMS (ESI) *m/z* Calcd for $C_{21}H_{24}NO_3S$ $[M+H]^+$: 370.1477; found: 370.1480.

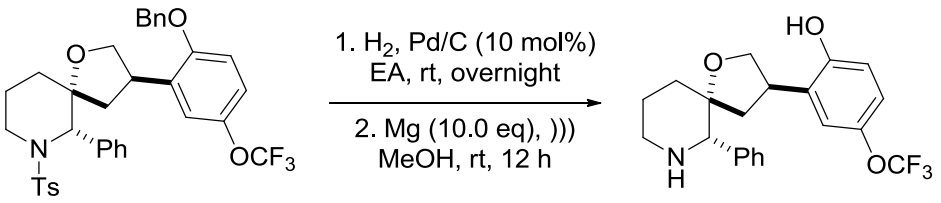


***rac*-10** (3.0 eq) ***rac*-11**

rac-3-(2-(benzyloxy)-5-(trifluoromethoxy)phenyl)-6-phenyl-7-tosyl-1-oxa-7-azaspiro[4.5]decane (_rac_-11)

An oven-dried 10 mL Schlenk tube equipped with a stir bar was charged with spirocycle ***rac*-10** (243 mg, 0.66 mmol, 1.0 eq), 1-(benzyloxy)-2-iodo-4-(trifluoromethoxy)benzene (779 mg, 1.98 mmol, 1.98 mmol, 3.0 eq), tetrabutylammonium chloride (220 mg, 0.79 mmol, 1.2 eq), lithium chloride (279 mg, 6.6 mmol, 10.0 eq), sodium formate (134 mg, 1.98 mmol, 3.0 eq), triethylamine (275 µL, 200 mg, 1.98 mmol, 3.0 eq) and a solution of DMF/H_2O = 19:1 (2.5 mL) under Ar. The mixture was degassed in liquid N_2, allowed to warm to room temperature and backfilled with Ar. The degassing procedure was repeated thrice before palladium (II) acetate (66 mg, 0.30 mmol, 0.45 eq) was added and the mixture was degassed

again before being heated to 40 ^{o}C and stirred for 5 days under Ar. The mixture was filtered through a pad of celite, concentrated under reduced pressure and purified using silica gel chromatography (Eluent: Hexane/Ethyl Acetate = 10:1 to 6:1) to give *rac*-3-(2-(benzyloxy)-5-(trifluoromethoxy)phenyl)-6-phenyl-7-tosyl-1-oxa-7-azaspiro[4.5]decane ***rac*-11** as a pale brown oil (235 mg, 0.37 mmol, 56%). TLC (Hexane/Ethyl Acetate = 2:1): R_f = 0.68; ^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 7.45-7.35 (m, 5H), 7.28-7.21 (m, 4H), 7.18-7.12 (m, 4H), 7.05 (d, *J* = 9.2 Hz, 1H), 6.97 (d, *J* = 8.1 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 1H), 5.13 (d, *J* = 11.8 Hz, 1H), 5.08 (d, *J* = 11.9 Hz, 1H), 5.02 (s, 1H), 4.20 (t, *J* = 7.7 Hz, 1H), 3.98-3.87 (m, 1H), 3.81-3.76 (m, 2H), 3.18 (dt, *J* = 12.2 Hz, 4.5 Hz, 1H), 2.74 (dd, *J* = 12.6 Hz, 7.7 Hz, 1H), 2.29 (s, 3H), 2.07-2.00 (m, 2H), 1.84-1.81 (m, 2H), 1.60-1.55 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ (ppm): 155.2, 142.9, 142.7, 137.7, 136.7, 136.6, 131.9, 129.5, 129.1, 128.9, 128.3, 128.0, 127.5, 127.4, 127.1, 121.0, 120.7 (q, *J* = 254.6 Hz), 120.2, 112.6, 83.6, 72.4, 70.8, 64.2, 43.0, 41.5, 39.1, 31.6, 23.4, 21.5; FTIR (ATR, cm^{-1}): 3064, 3033, 1599, 1334, 1152; HRMS (ESI) *m/z* Calcd for $C_{35}H_{35}F_3NO_5S$ $[M+H]^+$: 638.2188; found: 638.2167.



***rac*-11** ***rac*-3**

***rac*-2-(6-phenyl-1-oxa-7-azaspiro[4.5]decan-3-yl)-4-(trifluoromethoxy)phenol (*rac*-3)**

The reductive Heck reaction product ***rac*-11** (126 mg, 0.20 mmol, 1.0 eq) was dissolved in ethyl acetate (2.0 mL) before palladium on activated charcoal (10 wt%, 21 mg, 0.02 mmol, 10 mol%) was added. The round bottom flask was evacuated and refilled with H_2 thrice using a H_2 balloon. The reaction was stirred overnight at room temperature before being filtered through a pad of celite. Concentration under reduced pressure gave the crude product which was used in the next step without further purification.

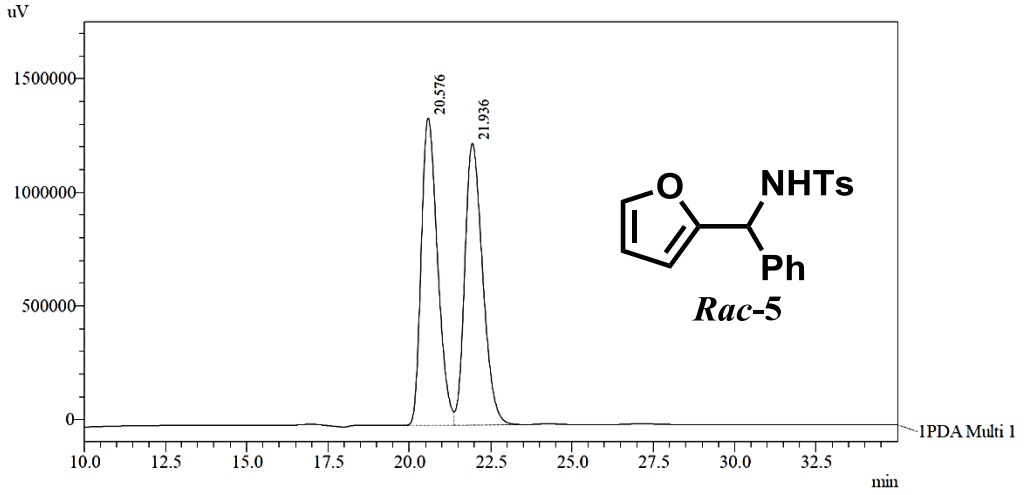
The crude hydrogenation product was dissolved in anhydrous MeOH (3 mL) and magnesium powder (48 mg, 2.0 mmol, 10.0 eq) was added. The suspension was sonicated overnight and 15% aqueous HCl solution (1 mL) was added and the mixture allowed to stir for an additional 15 min before saturated aqueous $NaHCO_3$ solution was added to neutralise the mixture. Ethyl acetate (30 mL) was added and the layers separated. The aqueous phase was extracted with ethyl acetate (3 x 30 mL) and the combined organic extracts were washed with brine (50 mL), dried over anhydrous magnesium sulphate and filtered. Concentration under reduced pressure and purification using silica gel chromatography (Eluent: Hexane/Ethyl Acetate = 2:1 to Ethyl Acetate/Methanol = 2:1) to give *rac*-2-(6-phenyl-1-oxa-7-azaspiro[4.5]decan-3-yl)-4-(trifluoromethoxy)phenol ***rac*-3** (40 mg, 0.102 mmol, 51%) as a pale yellow solid. mp = 203-204 ^{o}C (decomposed) (lit[5] = yellow oil); TLC (Ethyl Acetate/ Methanol = 2:1): R_f = 0.32; ^{1}H NMR (300 MHz, CD_3OD) δ (ppm): 7.48 (dd, *J* = 7.8 Hz, 1.6 Hz, 2H), 7.38-7.31 (m,

3H), 6.84 (dd, *J* = 8.7 Hz, 2.0 Hz, 1H), 6.75 (d, *J* = 2.6 Hz, 1H), 6.64 (d, *J* = 8.7 Hz, 1H), 3.96 (t, *J* = 7.5 Hz, 1H), 3.65 (dd, *J* = 9.9 Hz, 8.0 Hz, 1H), 3.58 (s, 1H), 3.14-3.09 (m, 1H), 2.73 (dd, *J* = 12.7 Hz, 2.9 Hz, 1H), 2.28-2.14 (m, 2H), 2.05-1.97 (m, 2H), 1.80-1.70 (m, 2H), 1.60 (d, *J* = 11.9 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ (ppm): 156.0, 142.9, 141.8, 130.4, 129.8, 129.2, 128.8, 122.2 (q, *J* = 252.7 Hz), 121.7, 121.1, 116.6, 83.6, 72.9, 70.1, 47.7, 42.8, 40.4, 38.7, 24.6; FTIR (ATR, cm^{-1}): 3290, 3062, 3032, 1607, 1510, 1494; HRMS (ESI) *m/z* Calcd for $C_{21}H_{23}F_3NO_3$ $[M+H]^+$: 394.1630; found: 394.1611.

References:

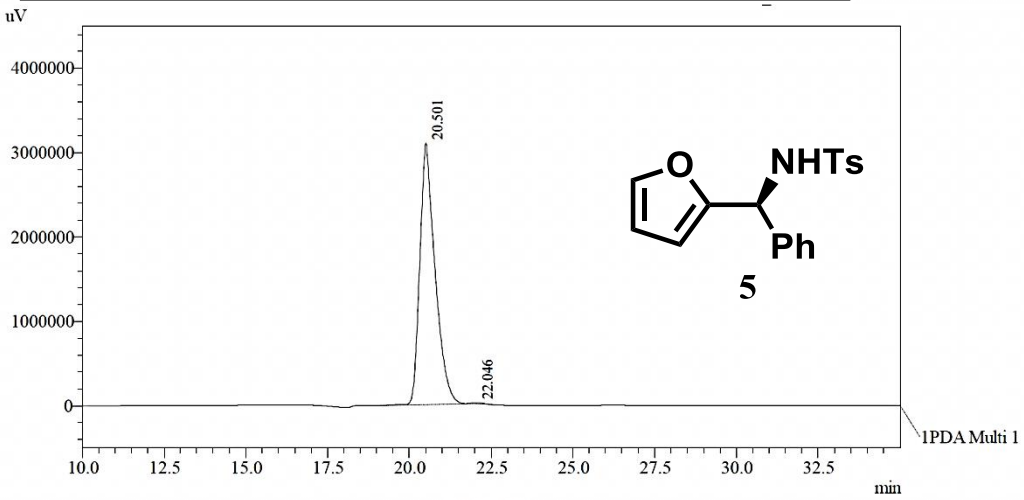
1. J. M. Harris and A. Padwa, *Org. Lett.*, 2002, **4**, 2029-2031.
2. N. Tokunaga, Y. Otomaru, K. Okamoto, K. Ueyama, R. Shintani and T. Hayashi, *J. Am. Chem. Soc.*, 2004, **126**, 13584-13585.
3. X. Gaucher, M. Jida and J. Ollivier, *Synlett*, 2009, 3320-3322.
4. C. G. Kokotos and V. K. Aggarwal, *Chem. Commun.*, 2006, 2156-2158.
5. D. J. Wallace, J. M. Goodman, D. J. Kennedy, A. J. Davies, C. J. Cowden, M. S. Ashwood, I. F. Cottrell, U.-H. Dolling and P. J. Reider, *Org. Lett.*, 2001, **3**, 671-674.

3.1 Determination of enantiomeric excess by HPLC for 5:



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.576	47118803	1351718	49.814	52.162
2	21.936	47470292	1239669	50.186	47.838
Total		94589095	2591387	100.000	100.000



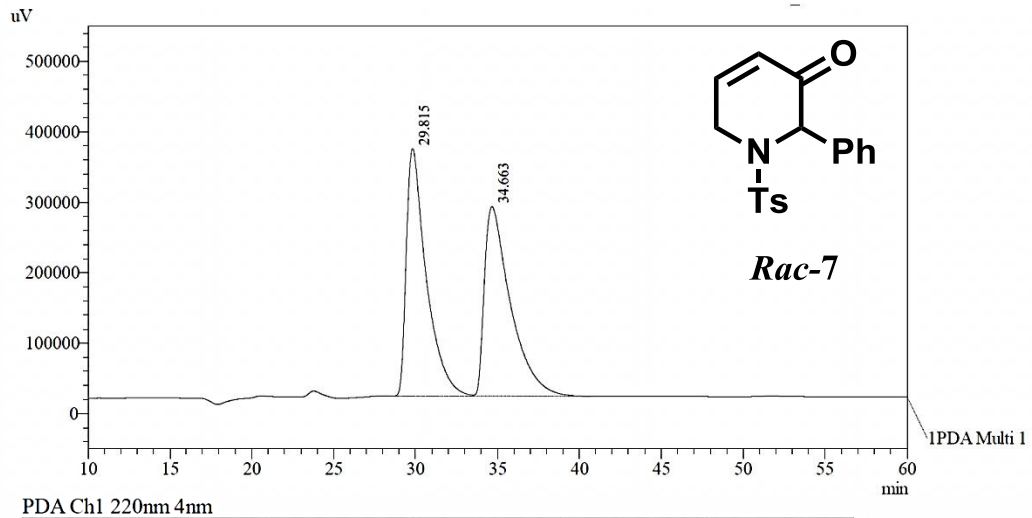
PeakTable

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	20.501	99918858	3095665	99.650	99.526
2	22.046	351238	14730	0.350	0.474
Total		100270096	3110395	100.000	100.000

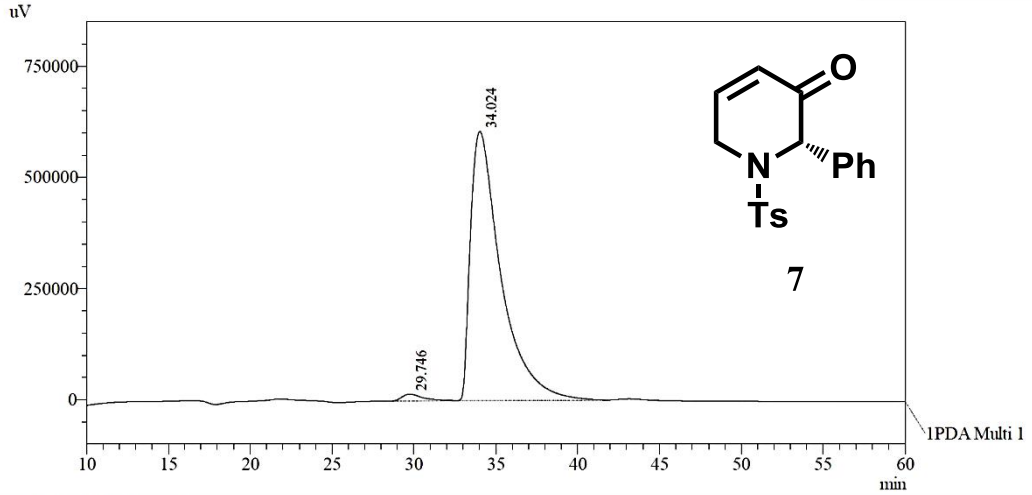
HPLC trace of **5** (Chiralpak OD-H, Hexanes:i-PrOH = 90:10, 0.5 mL/min, 220 nm)

3.2 Determination of enantiomeric excess by HPLC for 7:



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.815	29804785	351211	49.930	56.633
2	34.663	29888398	268941	50.070	43.367
Total		59693183	620152	100.000	100.000

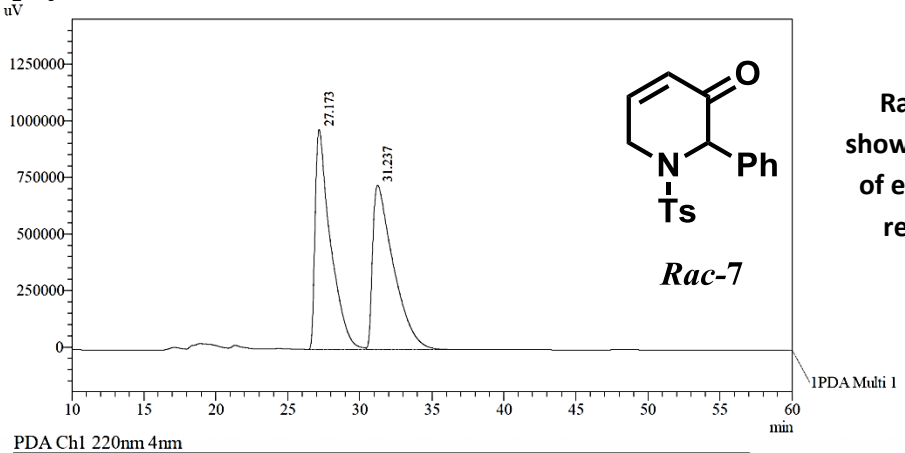


PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	29.746	1324658	15138	1.665	2.442
2	34.024	78252880	604692	98.335	97.558
Total		79577538	619830	100.000	100.000

HPLC trace of **7** (Chiralpak OD-H, Hexanes:i-PrOH = 90:10, 0.5 mL/min, 220 nm)

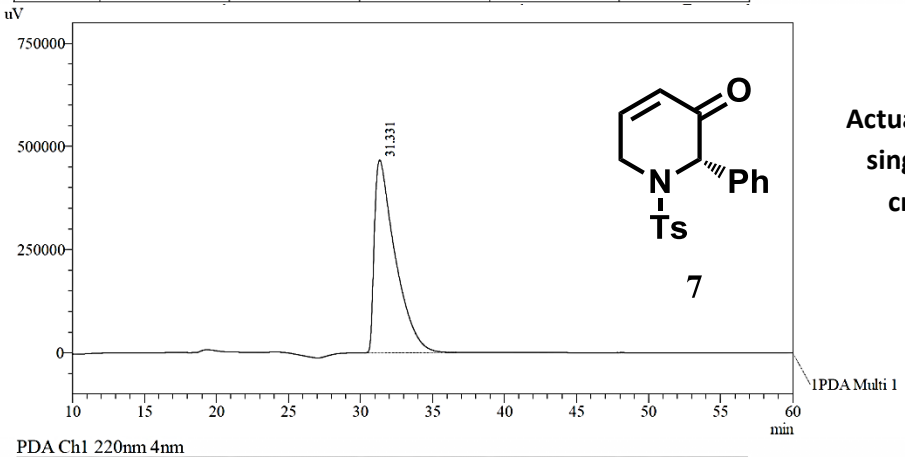
3.2.1 Determination of enantiomeric excess by HPLC for 7 after single-crystal X-ray crystallography:



Racemic mixture shown for comparison of elution order and retention times.

PDA Ch1 220nm 4nm

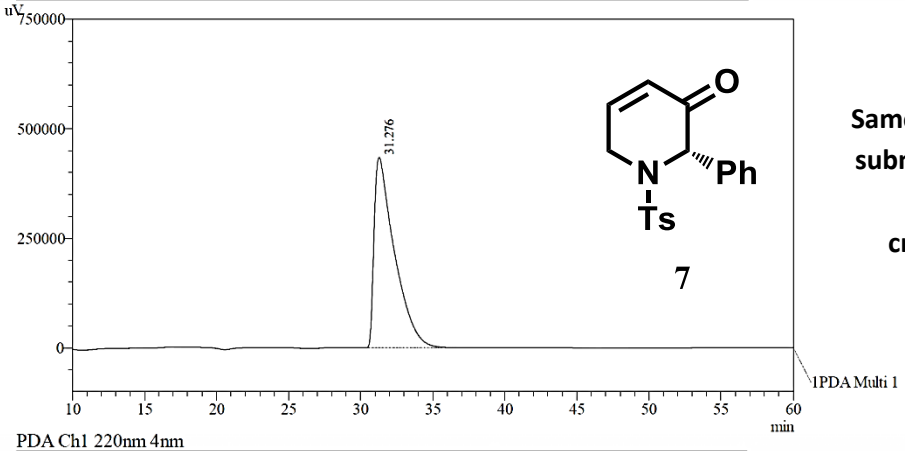
Peak#	Ret. Time	Area	Height	Area %	Height %
1	27.173	72385288	974821	49.624	57.266
2	31.237	73481504	727457	50.376	42.734
Total		145866793	1702278	100.000	100.000



Actual crystal used for single-crystal X-ray crystallography

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.331	46998573	466616	100.000	100.000
Total		46998573	466616	100.000	100.000



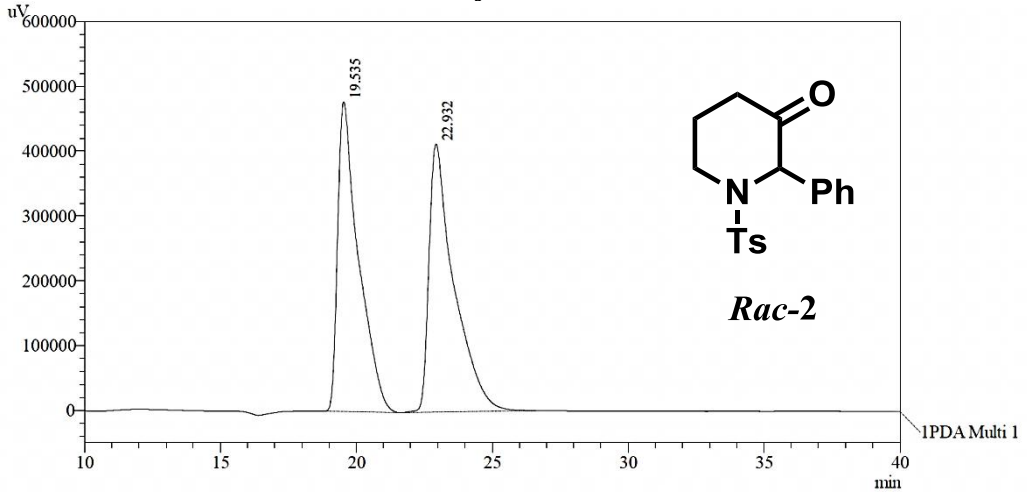
Same batch of crystal submitted for single-crystal X-ray crystallography

PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	31.276	42637428	433836	100.000	100.000
Total		42637428	433836	100.000	100.000

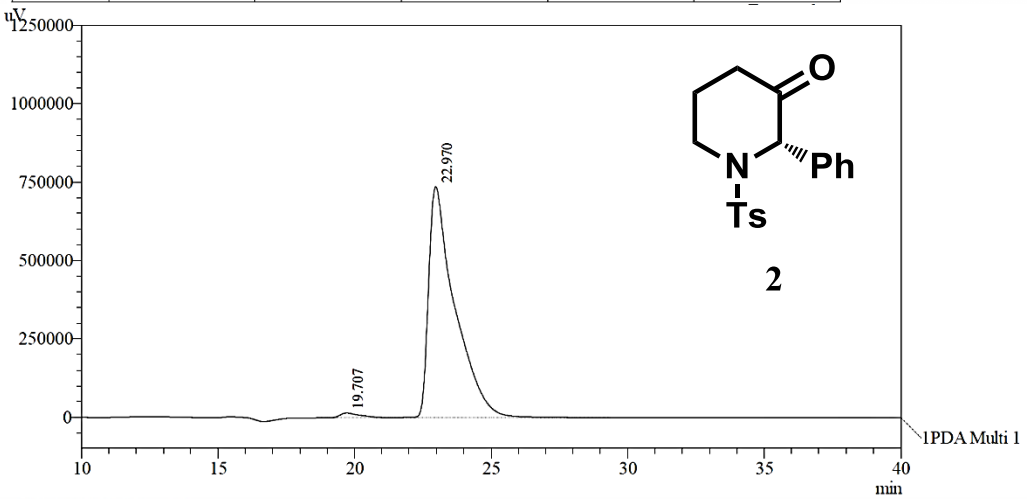
HPLC trace of **7** after X-ray (Chiralpak OD-H, Hexanes:i-PrOH = 90:10, 0.5 mL/min, 220 nm)

3.3 Determination of enantiomeric excess by HPLC for 2:



PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.535	25536746	478258	49.108	53.620
2	22.932	26464316	413679	50.892	46.380
Total		52001062	891937	100.000	100.000

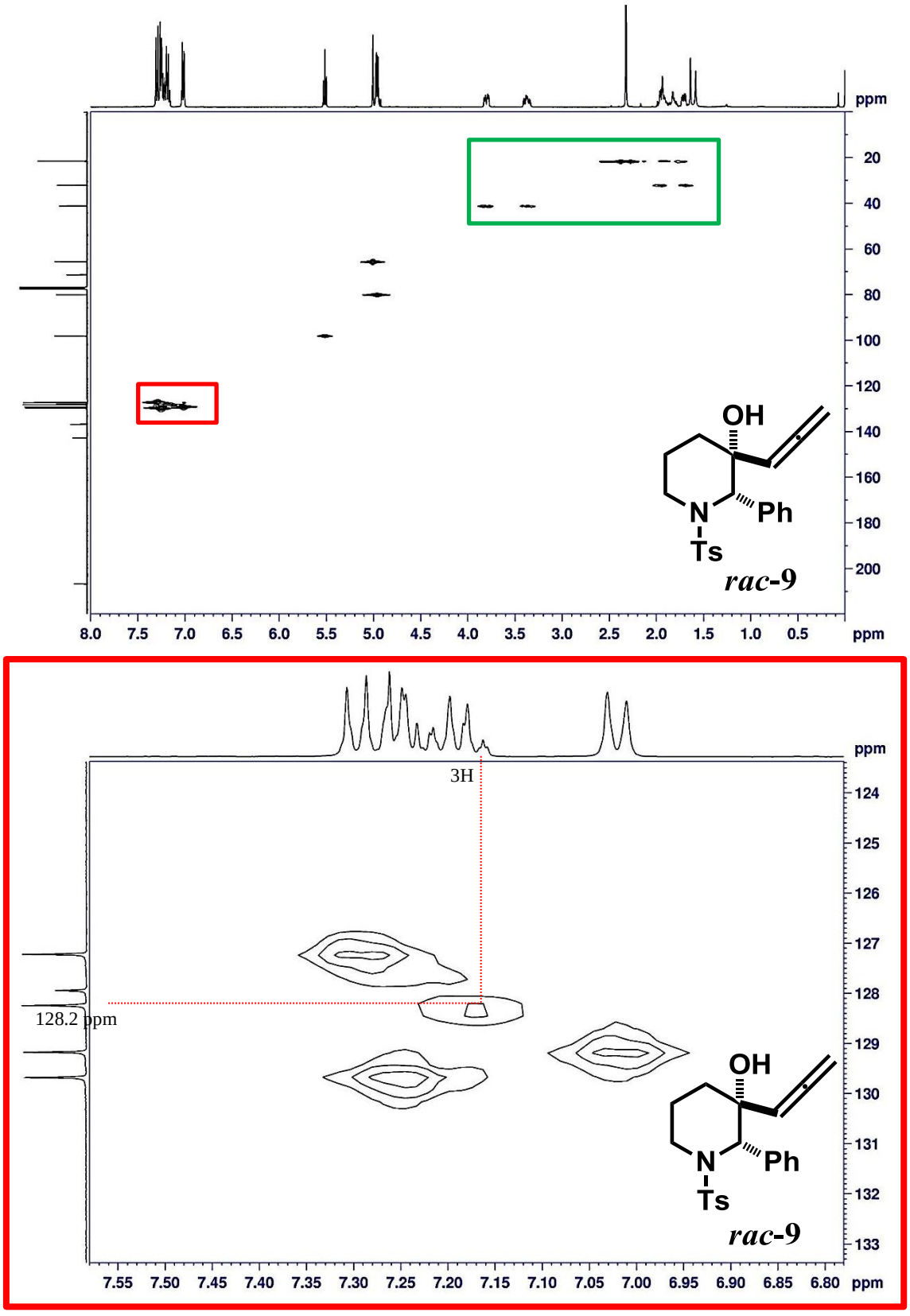


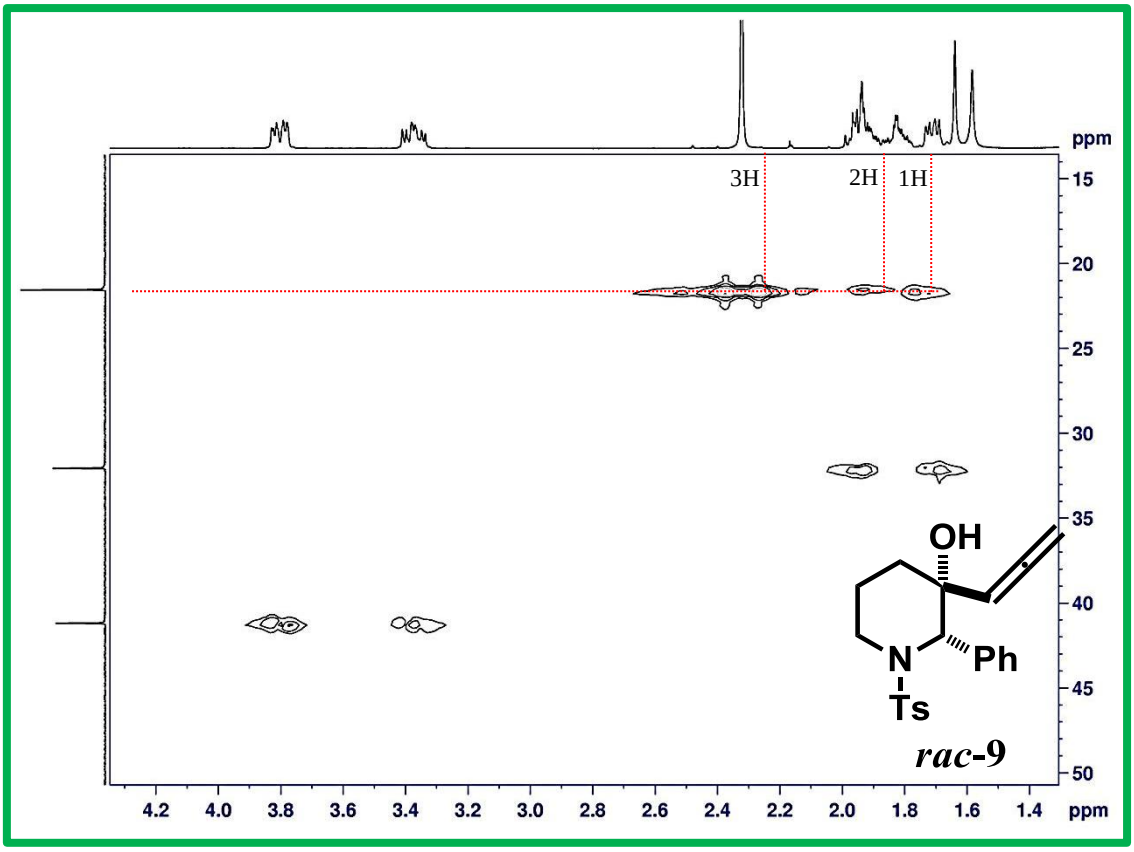
PDA Ch1 220nm 4nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	19.707	854017	15977	1.697	2.121
2	22.970	49485143	737184	98.303	97.879
Total		50339160	753161	100.000	100.000

HPLC trace of **2** (Chiralpak OD-H, Hexanes:i-PrOH = 90:10, 0.5 mL/min, 220 nm)

4.1 Determination of overlapping ^{13}C NMR Signals in *rac*-9 using HMQC

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2H
1H
15
20
25
30
35
40
45
50
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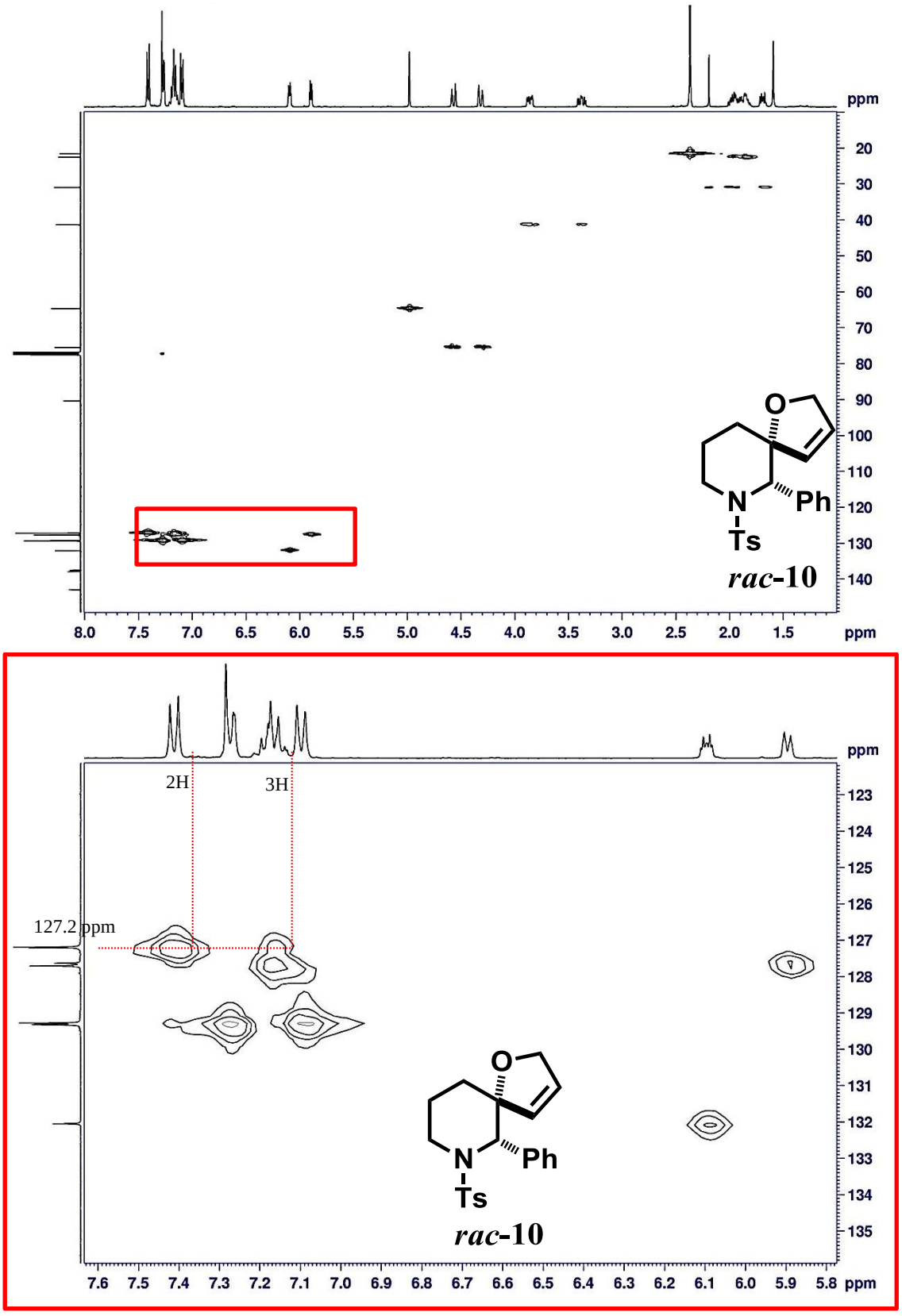
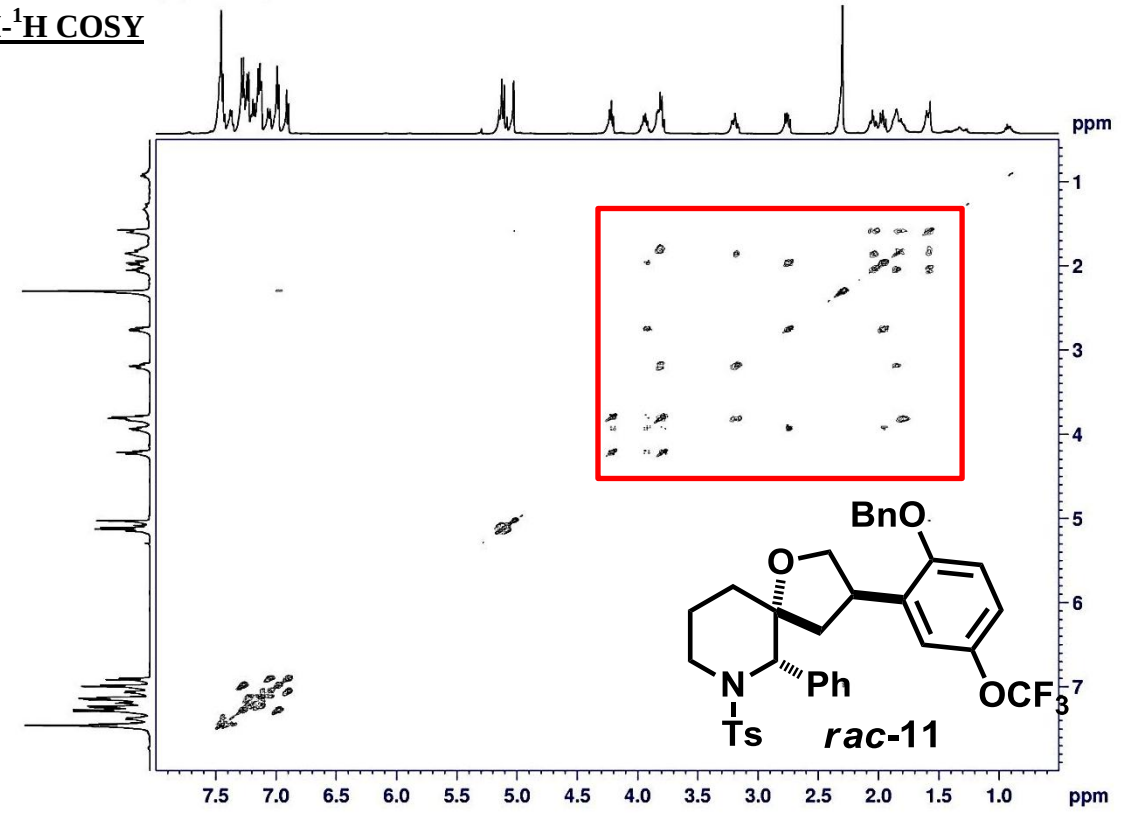
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
ppm
OH
N
Ph
Ts
rac-9

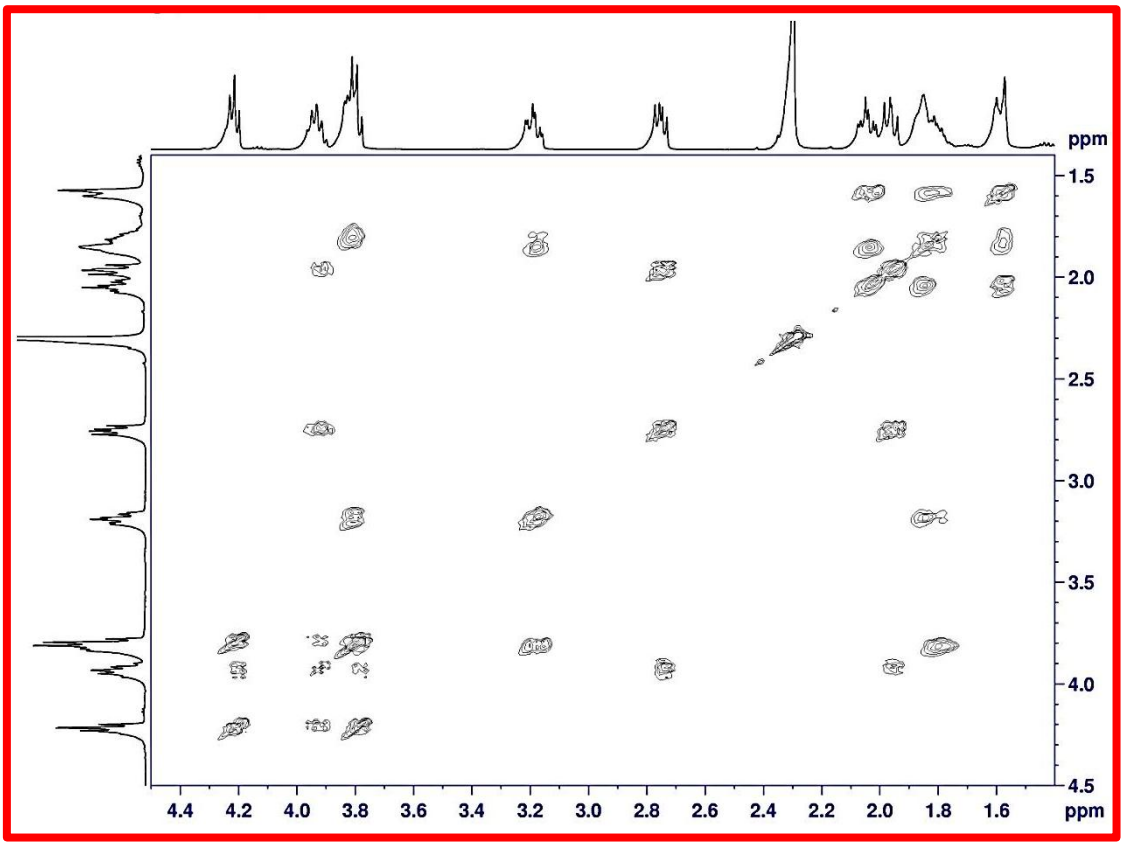
4.2 Determination of overlapping ^{13}C NMR Signals in *rac*-10 using HMQC



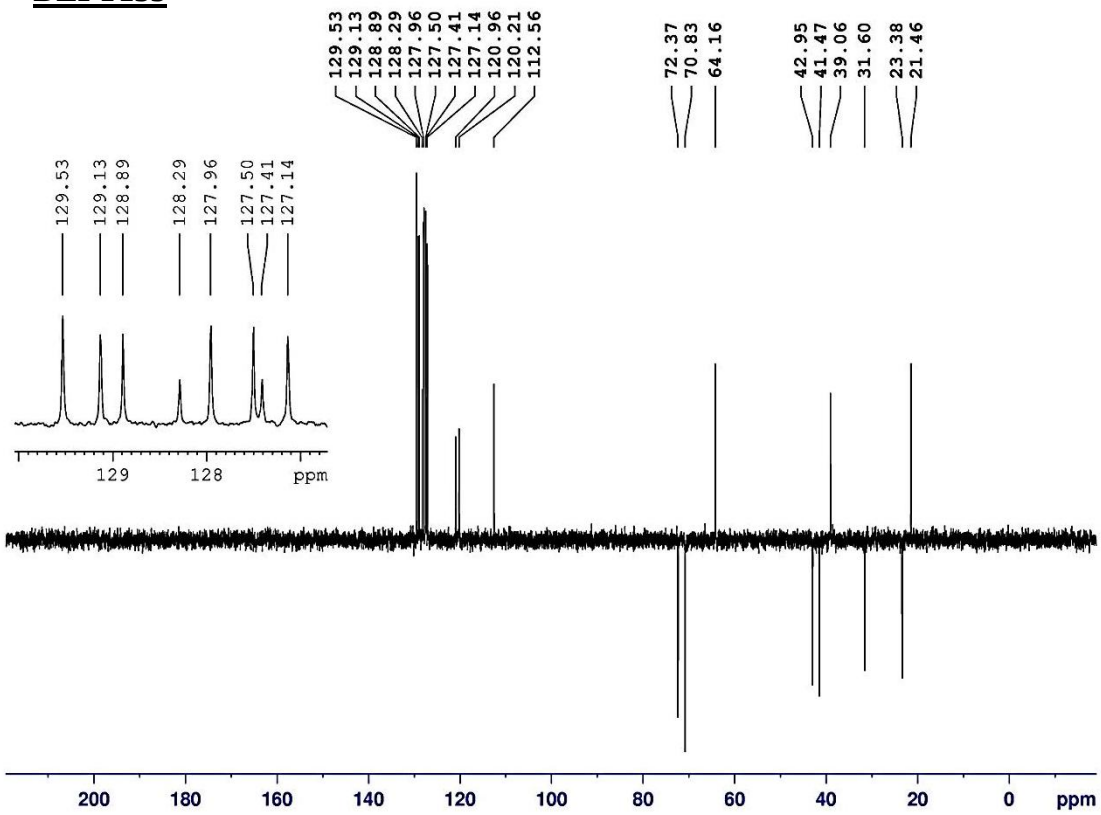
5. Determination of relative stereochemistry in *rac*-11 using NMR analysis

^{1}H-^{1}H COSY

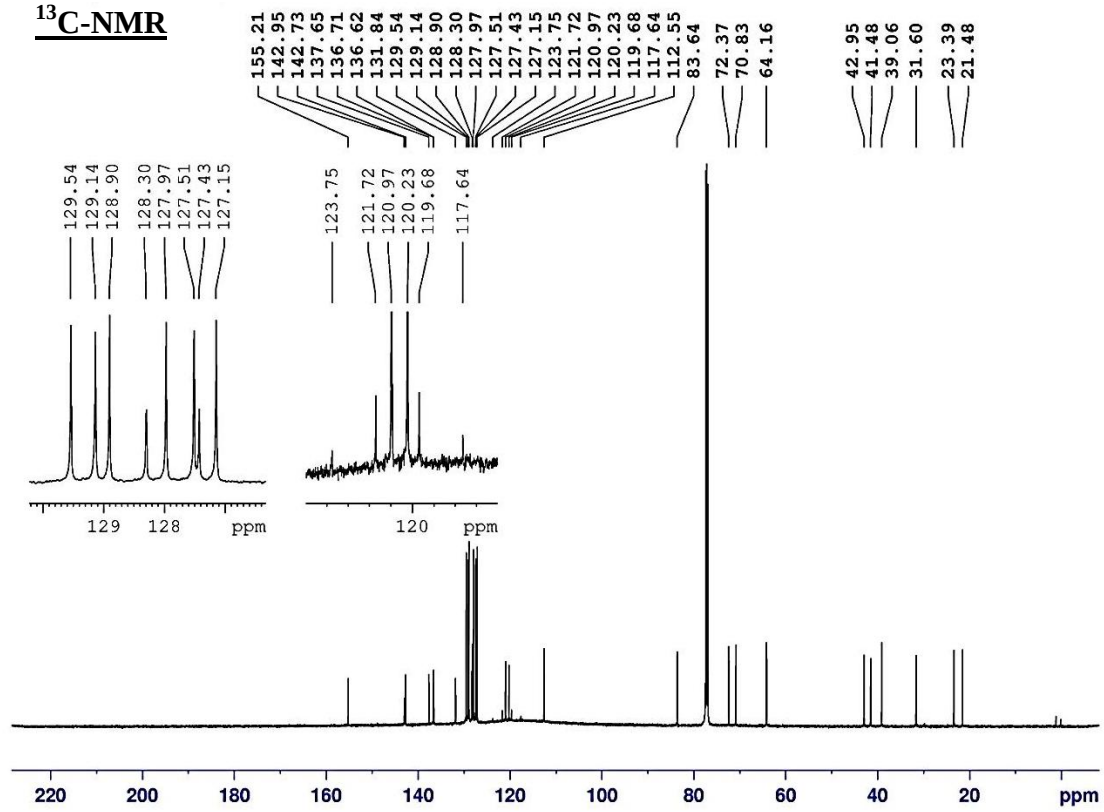




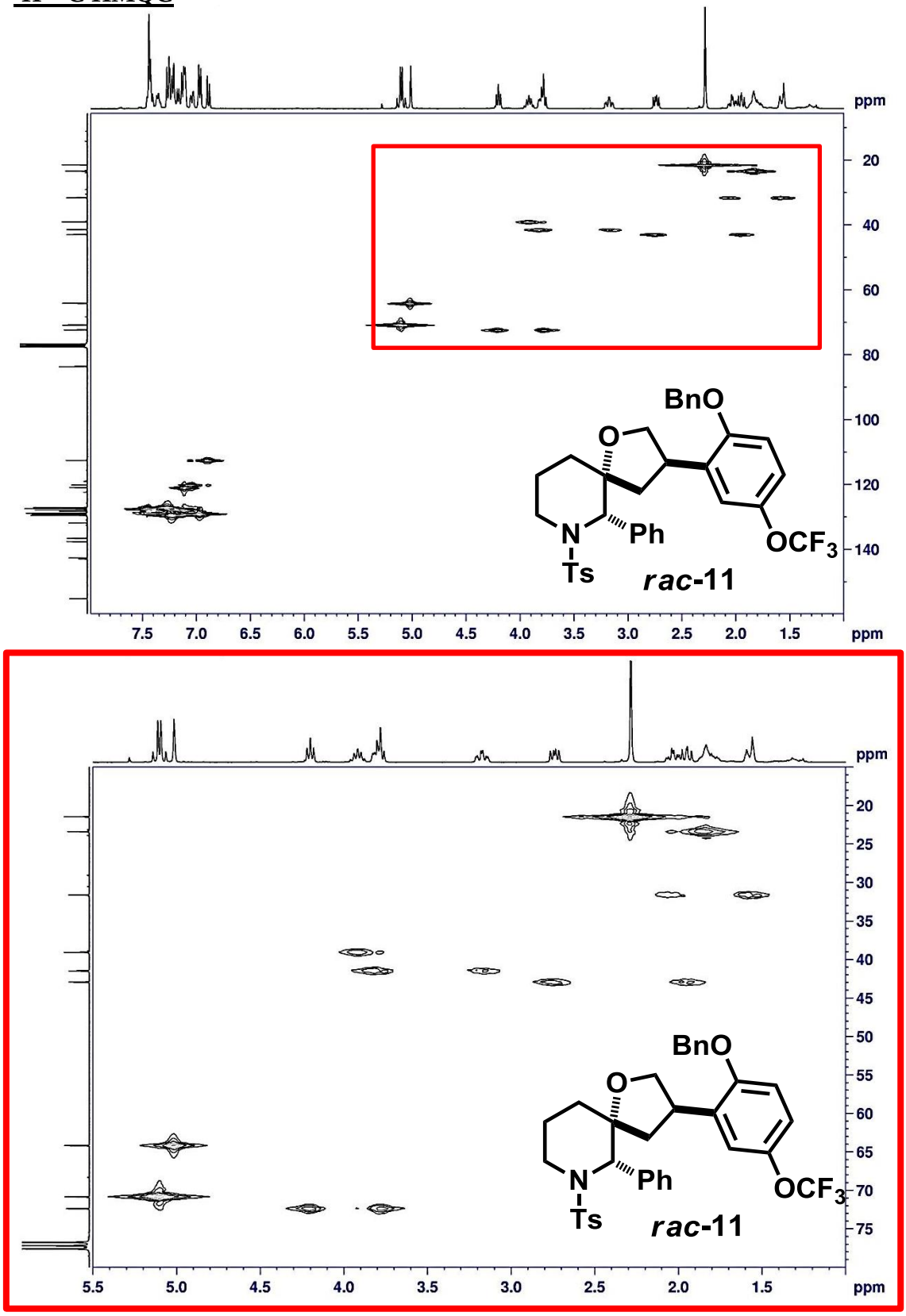
DEPT135



^{13}C-NMR



^{1}H-^{13}C HMQC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80
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120
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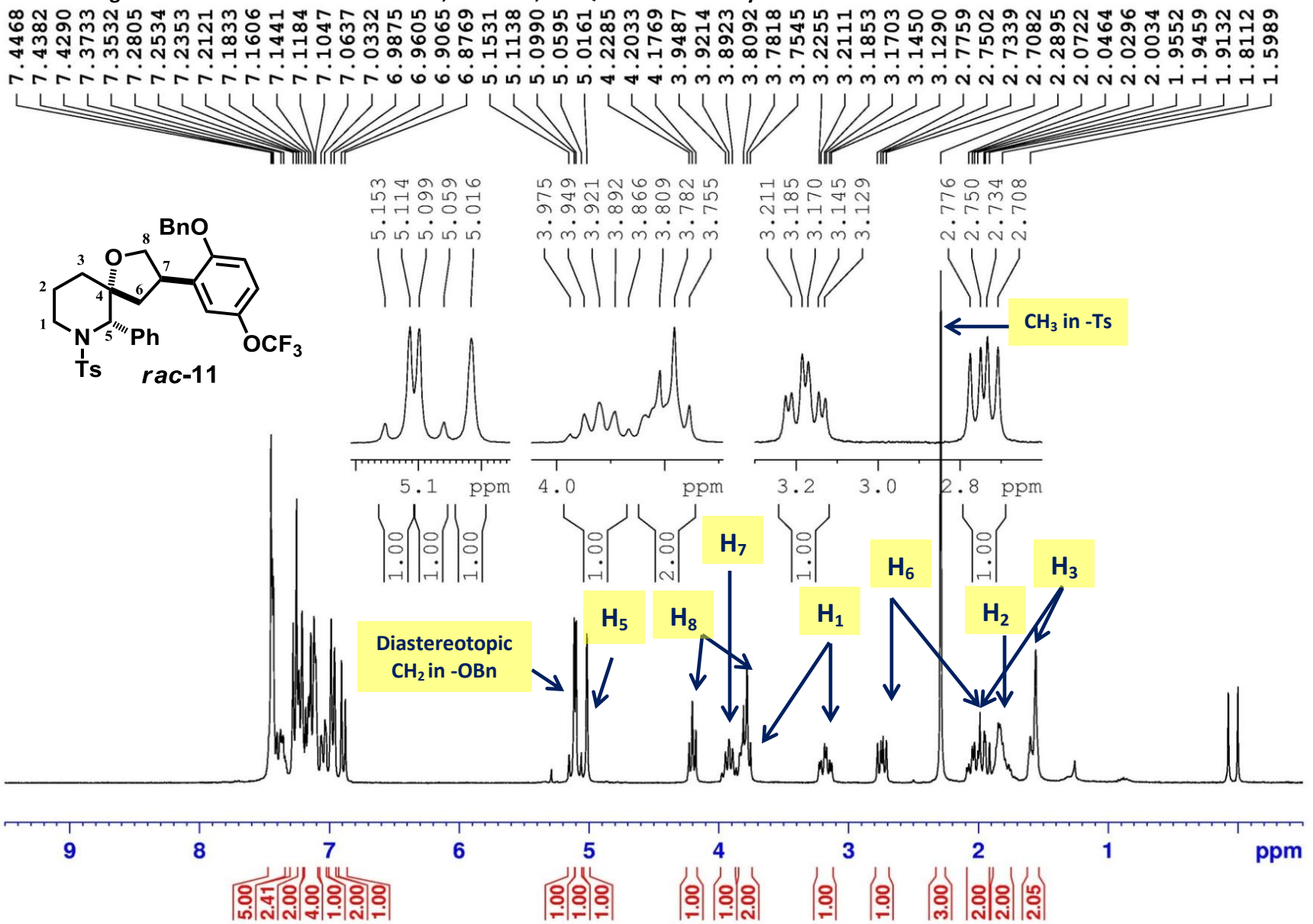
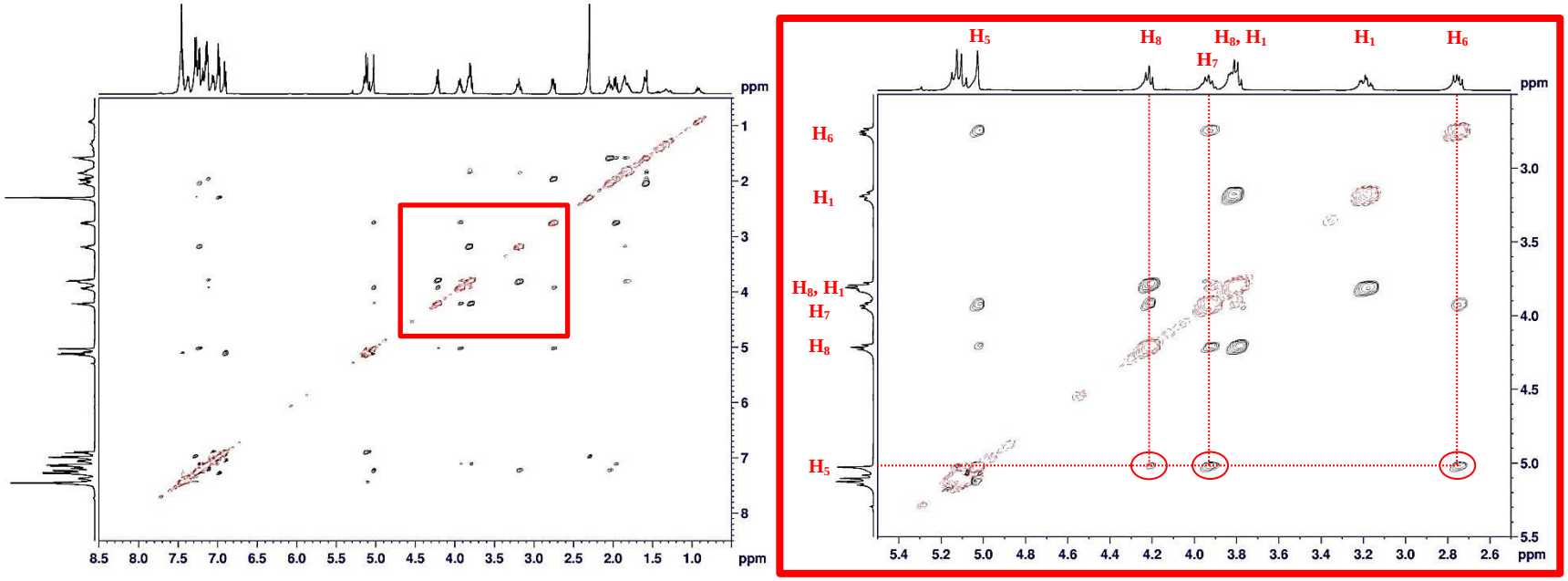
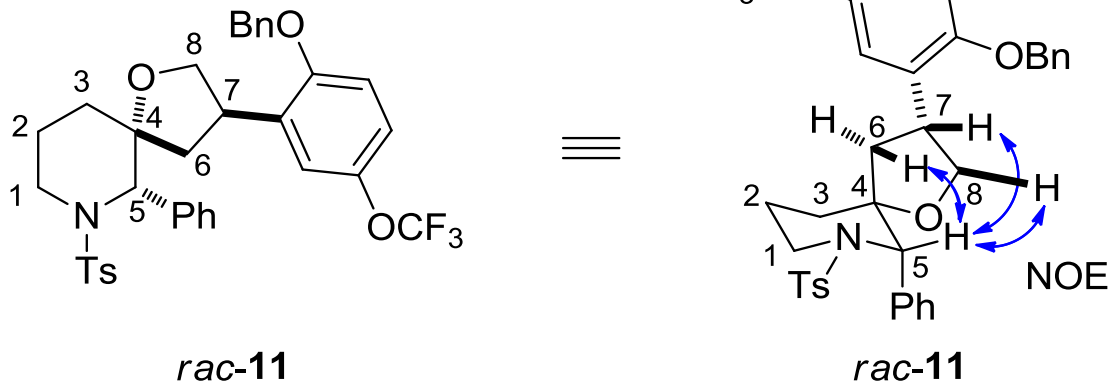
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
BnO
O
N
Ts
Ph
OCF3
rac-11
ppm
20
25
30
35
40
45
50
55
60
65
70
75
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
ppm
BnO
O
N
Ts
Ph
OCF3
rac-11

^{1}H NMR assignment of *rac*-11 based on ^{13}C NMR, DEPT135, HMQC and COSY analysis



^{1}H-^{1}H NOESY

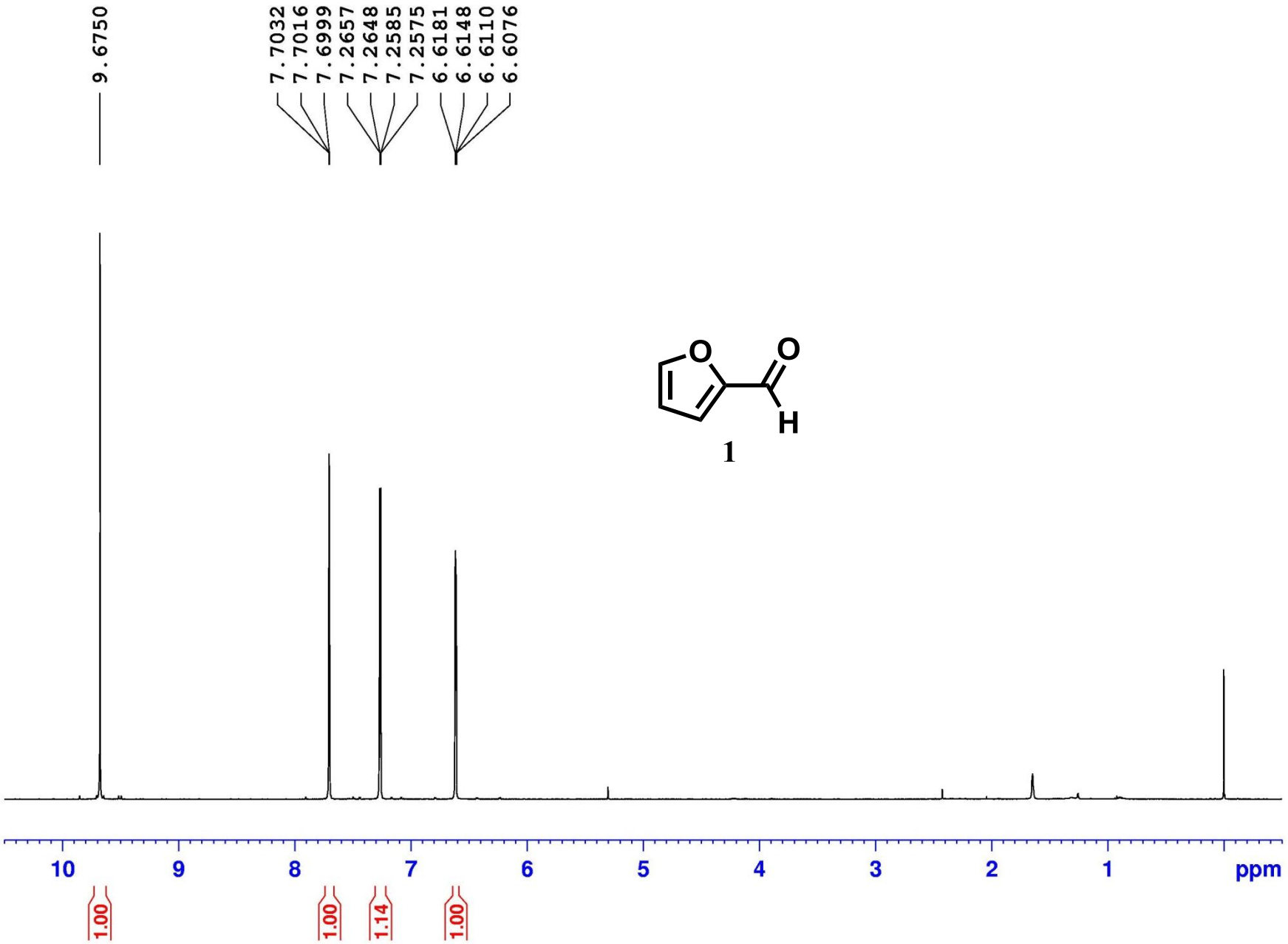




rac-**11** ≡ *rac*-**11**

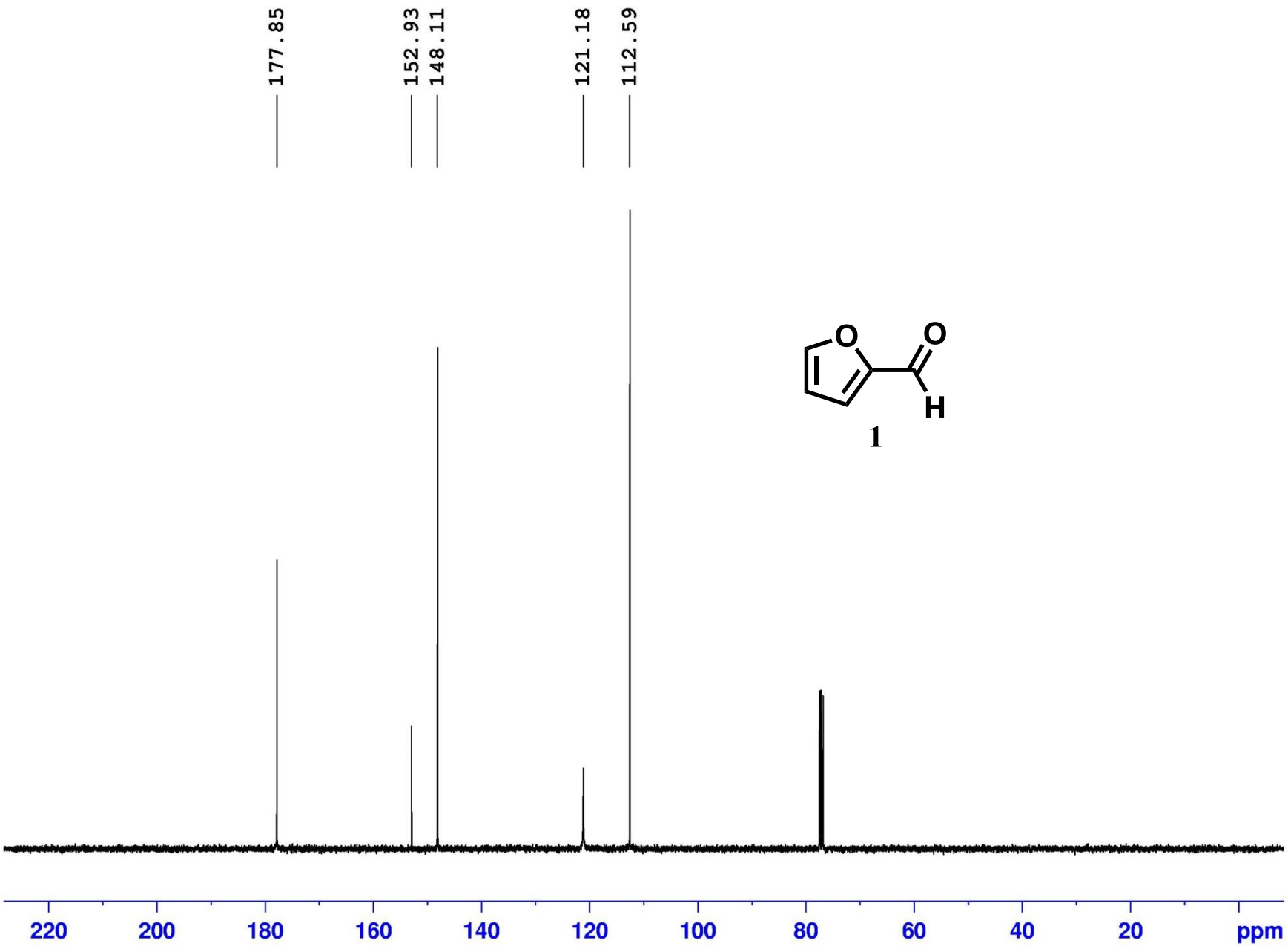
6. ^{1}H NMR and ^{13}C NMR Spectra

500 MHz

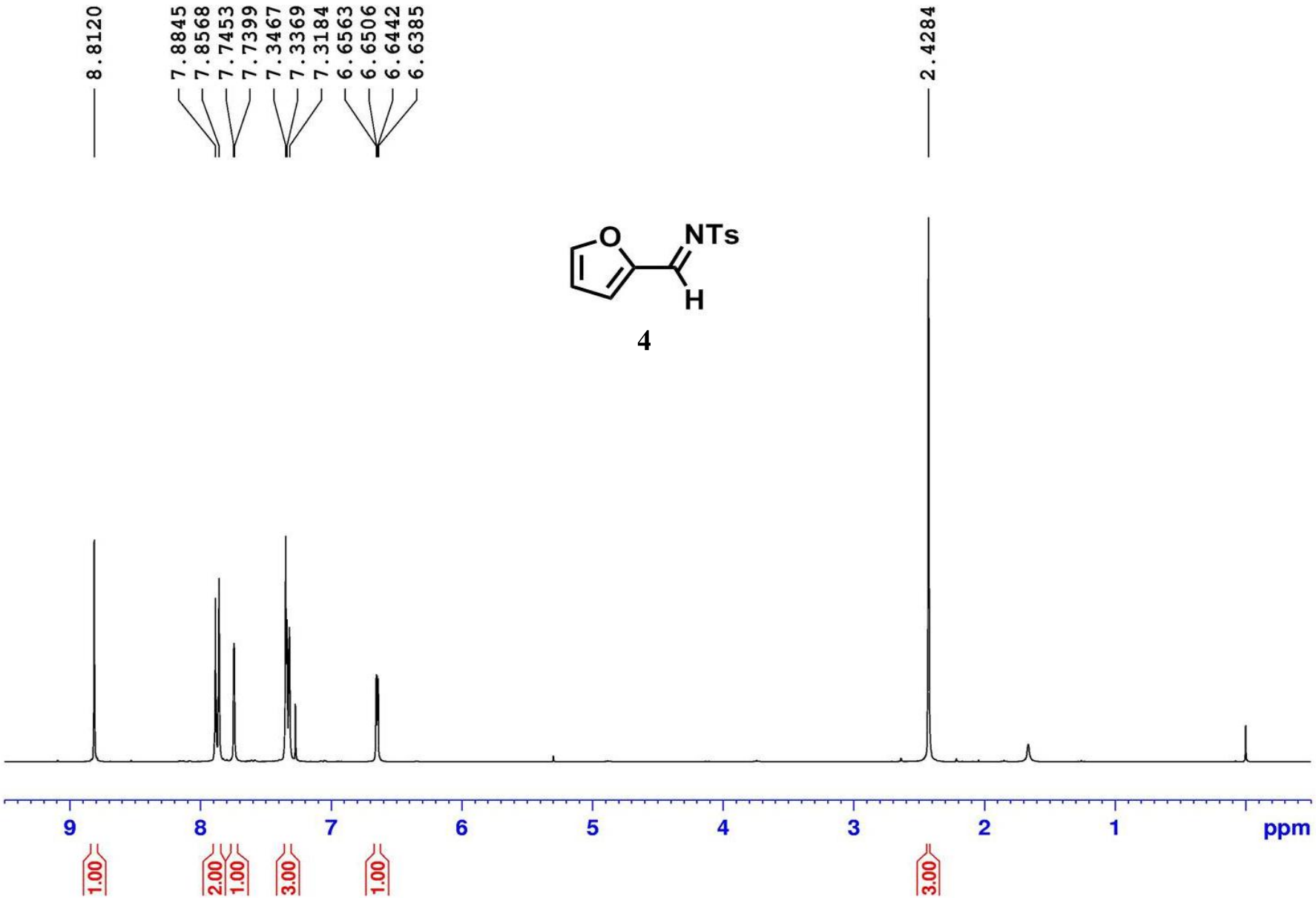


1

100 MHz


177.85
152.93
148.11
121.18
112.59
O
O
H
1
220
200
180
160
140
120
100
80
60
40
20
ppm

300 MHz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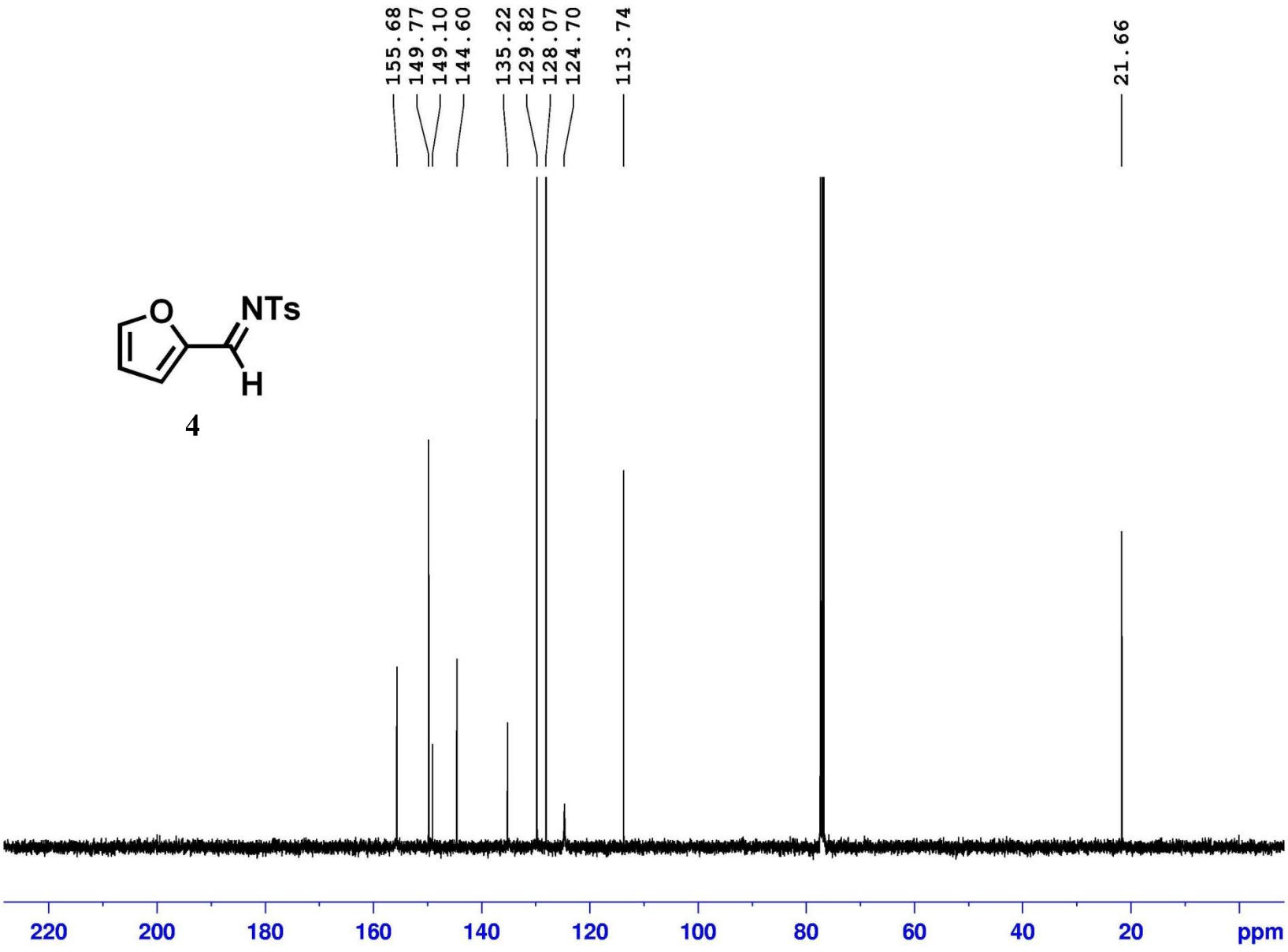
7.8568
7.7453
7.7399
7.3467
7.3369
7.3184
6.6563
6.6506
6.6442
6.6385
2.4284
O
NTs
H
9
8
7
6
5
4
3
2
1
ppm
1.00
2.00
1.00
3.00
1.00
3.00

4

100 MHz


155.68
149.77
149.10
144.60
135.22
129.82
128.07
124.70
113.74
21.66
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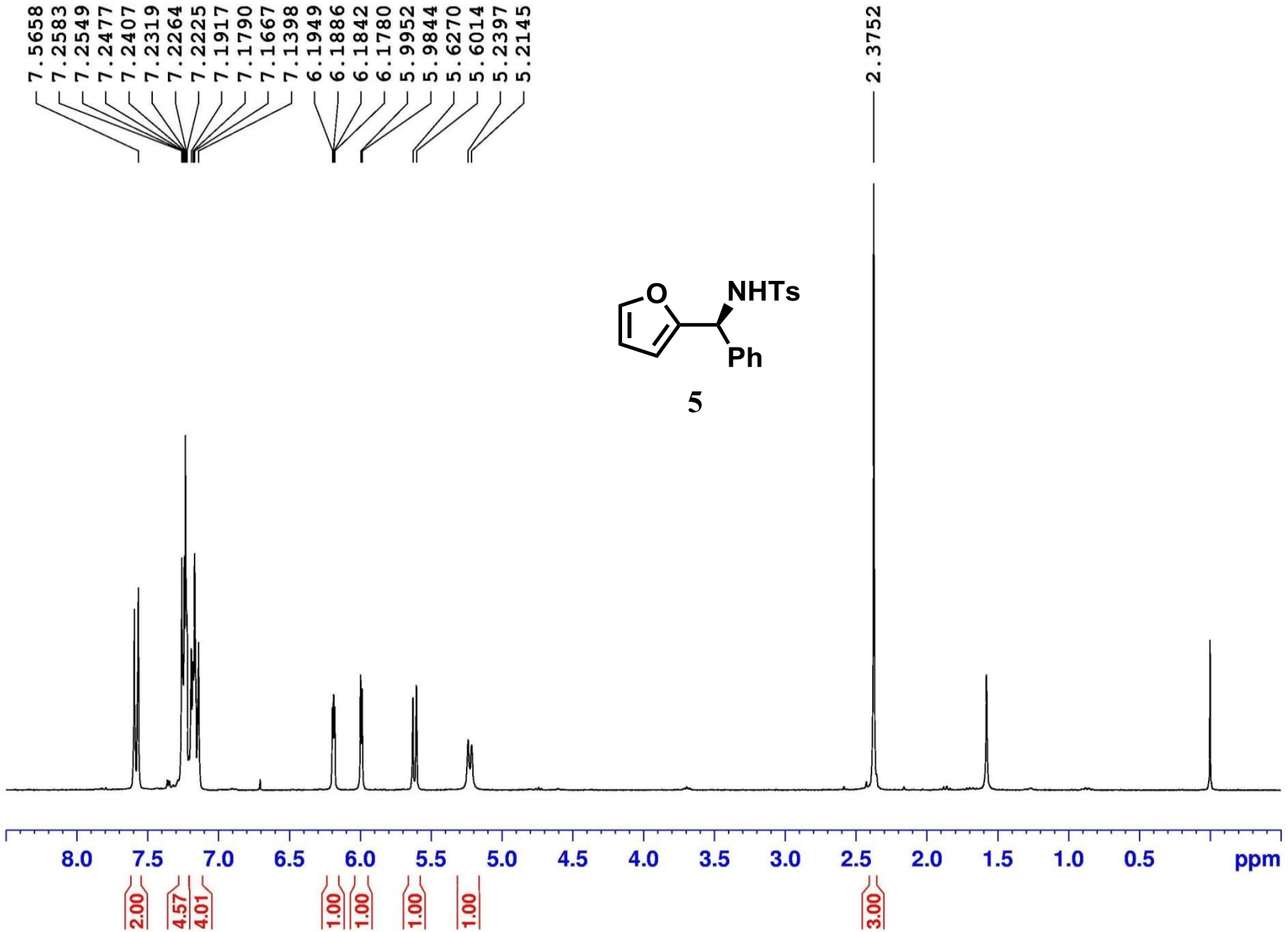
NTs
H
220
200
180
160
140
120
100
80
60
40
20
ppm

4

300 MHz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7.2477
7.2407
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7.2264
7.2225
7.1917
7.1790
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7.1398
6.1949
6.1886
6.1842
6.1780
5.9952
5.9844
5.6270
5.6014
5.2397
5.2145
2.3752
O
NHTs
Ph
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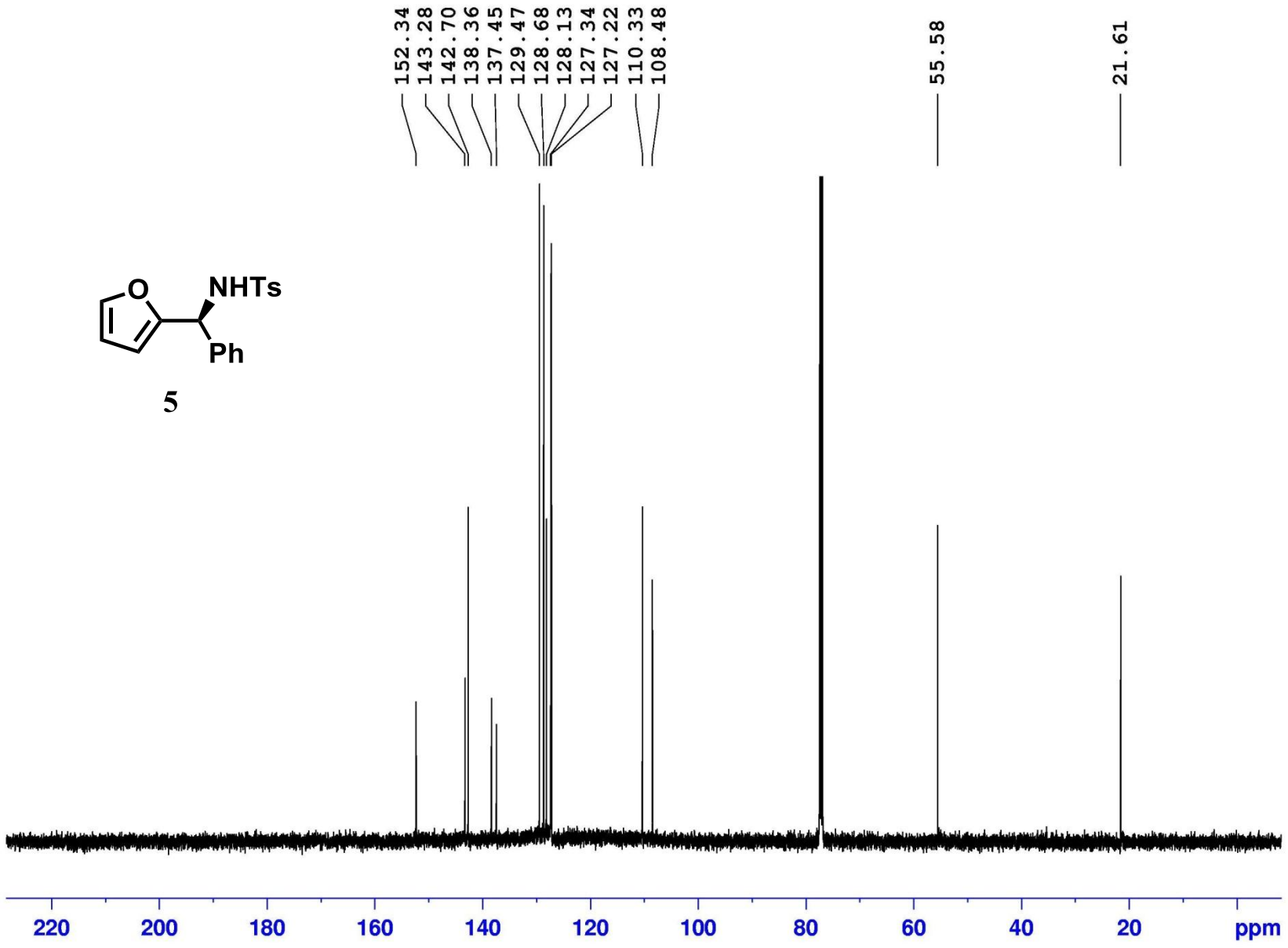
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
4.57
4.01
1.00
1.00
1.00
1.00
3.00

5

125 MHz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142.70
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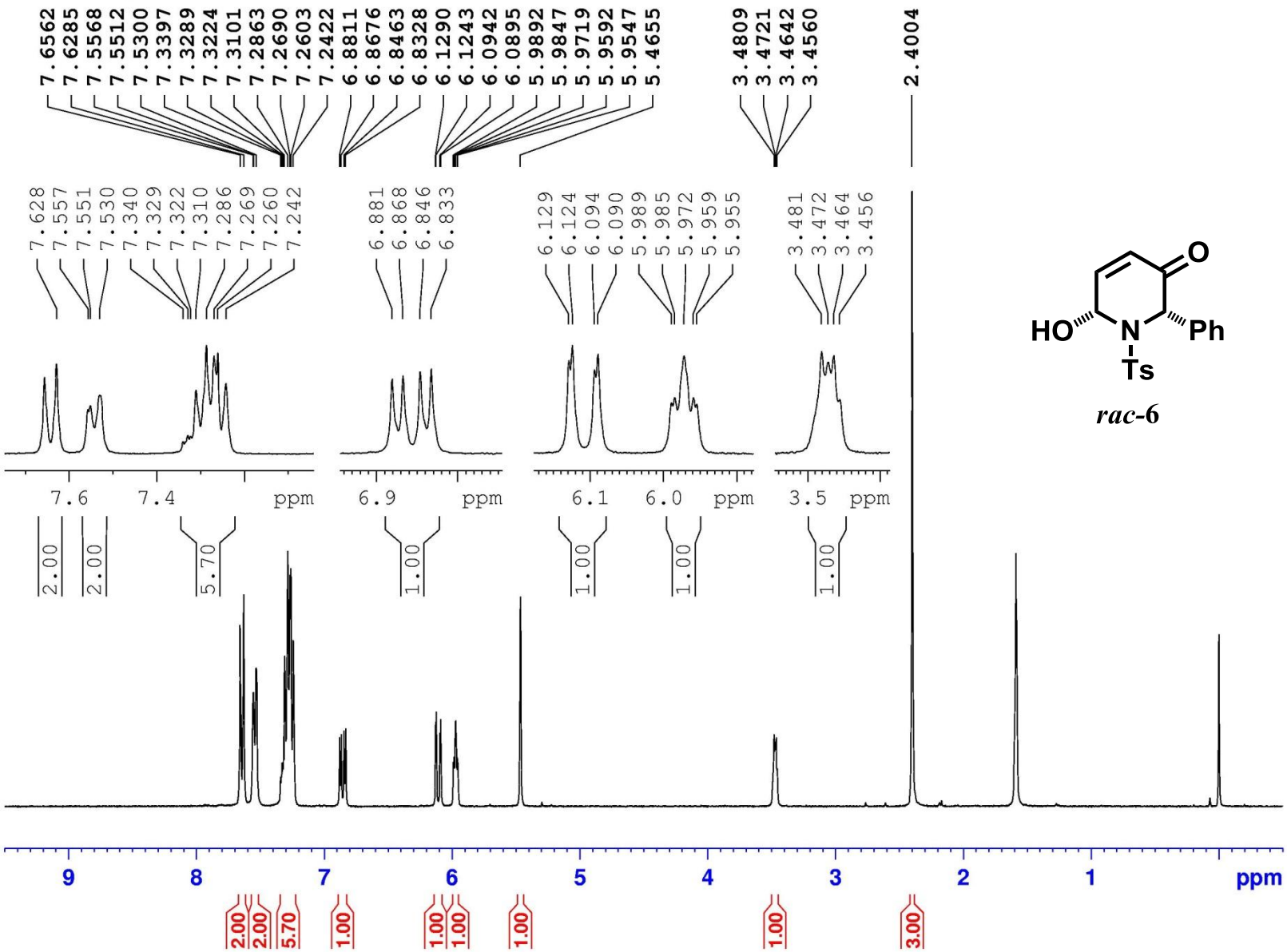
137.45
129.47
128.68
128.13
127.34
127.22
110.33
108.48
55.58
21.61
O
NHTs
Ph
220
200
180
160
140
120
100
80
60
40
20
ppm

5

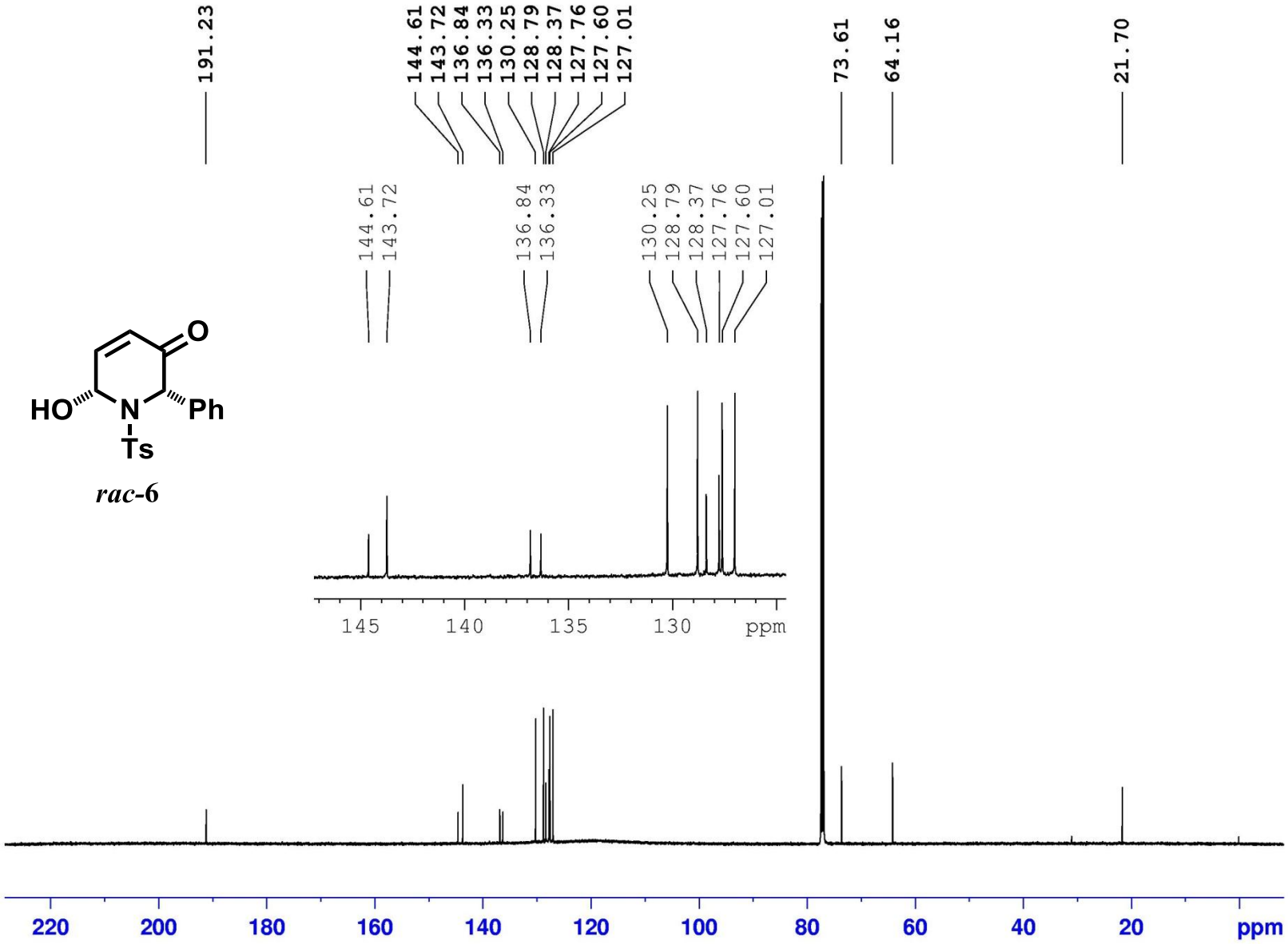
300 MHz


7.6562
7.6285
7.5568
7.5512
7.5300
7.3397
7.3289
7.3224
7.3101
7.2863
7.2690
7.2603
7.2422
6.8811
6.8676
6.8463
6.8328
6.1290
6.1243
6.0942
6.0895
5.9892
5.9847
5.9719
5.9592
5.9547
5.4655
3.4809
3.4721
3.4642
3.4560
2.4004
7.628
7.557
7.551
7.530
7.340
7.329
7.322
7.310
7.286
7.269
7.260
7.242
6.881
6.868
6.846
6.833
6.129
6.124
6.094
6.090
5.989
5.985
5.972
5.959
5.955
3.481
3.472
3.464
3.456
7.6
7.4
ppm
6.9
ppm
6.1
6.0
ppm
3.5
ppm
2.00
2.00
5.70
1.00
1.00
1.00
1.00
1.00
9
8
7
6
5
4
3
2
1
ppm
2.00
2.00
5.70
1.00
1.00
1.00
1.00
3.00

HO
N
Ph
Ts
O

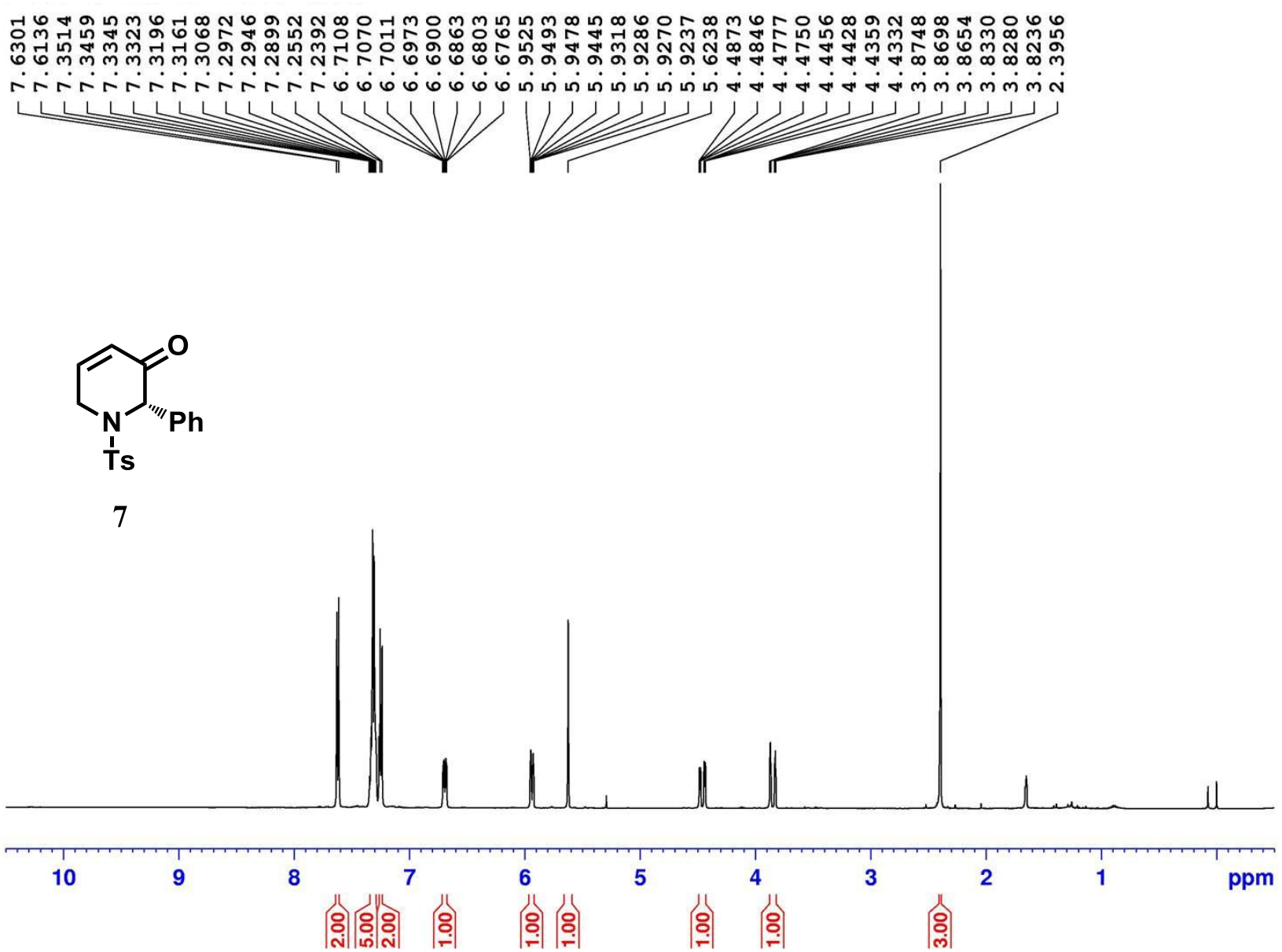
rac-6

125 MHz


191.23
144.61
143.72
136.84
136.33
130.25
128.79
128.37
127.76
127.60
127.01
73.61
64.16
21.70
HO
N
Ts
Ph
O
145
140
135
130
ppm
220
200
180
160
140
120
100
80
60
40
20
ppm

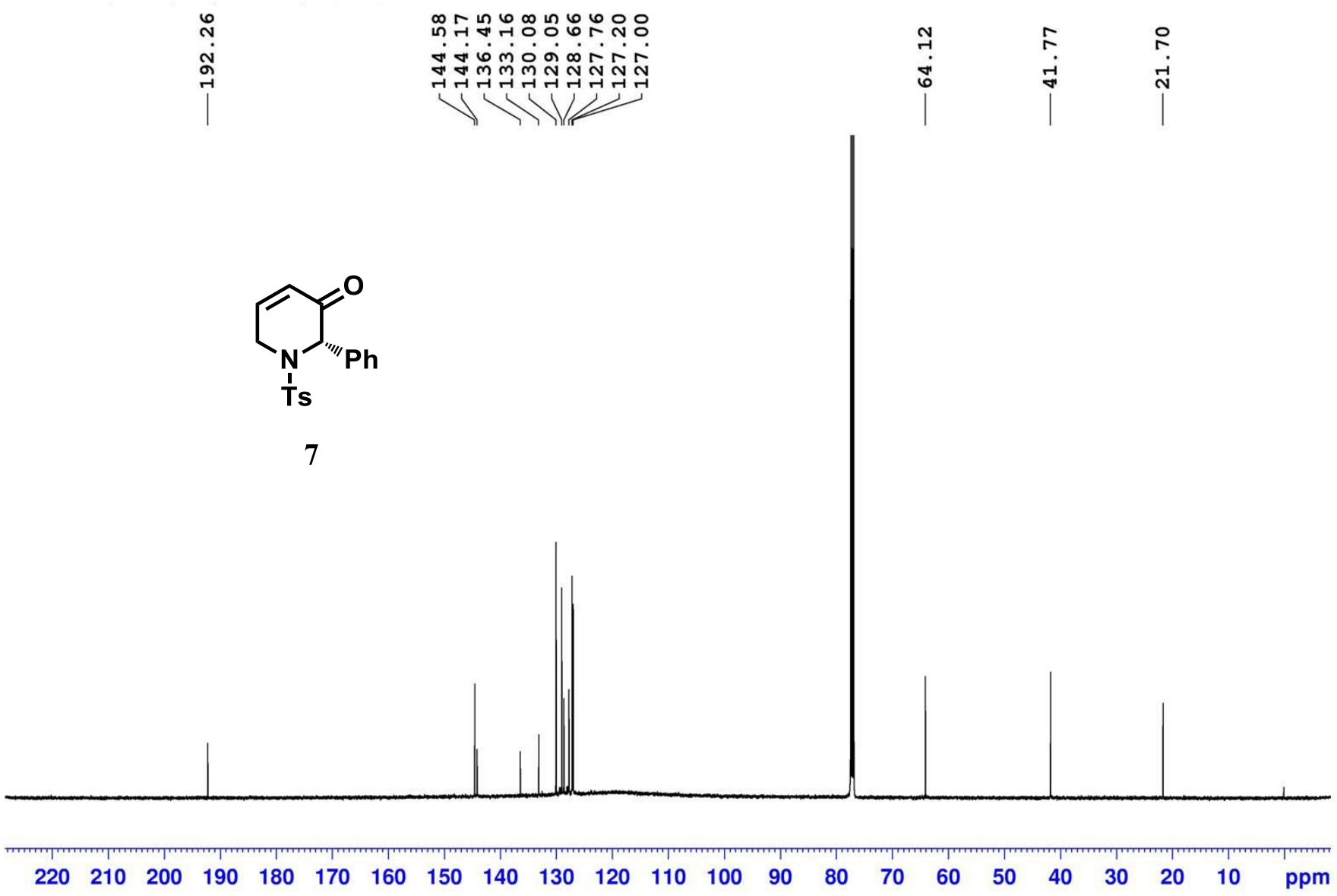
rac-6

500 MHz


7.6301
7.6136
7.3514
7.3459
7.3345
7.3323
7.3196
7.3161
7.3068
7.2972
7.2946
7.2899
7.2552
7.2392
6.7108
6.7070
6.7011
6.6973
6.6900
6.6863
6.6803
6.6765
5.9525
5.9493
5.9478
5.9445
5.9318
5.9286
5.9270
5.9237
5.6238
4.4873
4.4846
4.4777
4.4750
4.4456
4.4428
4.4359
4.4332
3.8748
3.8698
3.8654
3.8330
3.8280
3.8236
2.3956
O
N
Ts
Ph
10
9
8
7
6
5
4
3
2
1
ppm
2.00
5.00
2.00
1.00
1.00
1.00
1.00
1.00
3.00

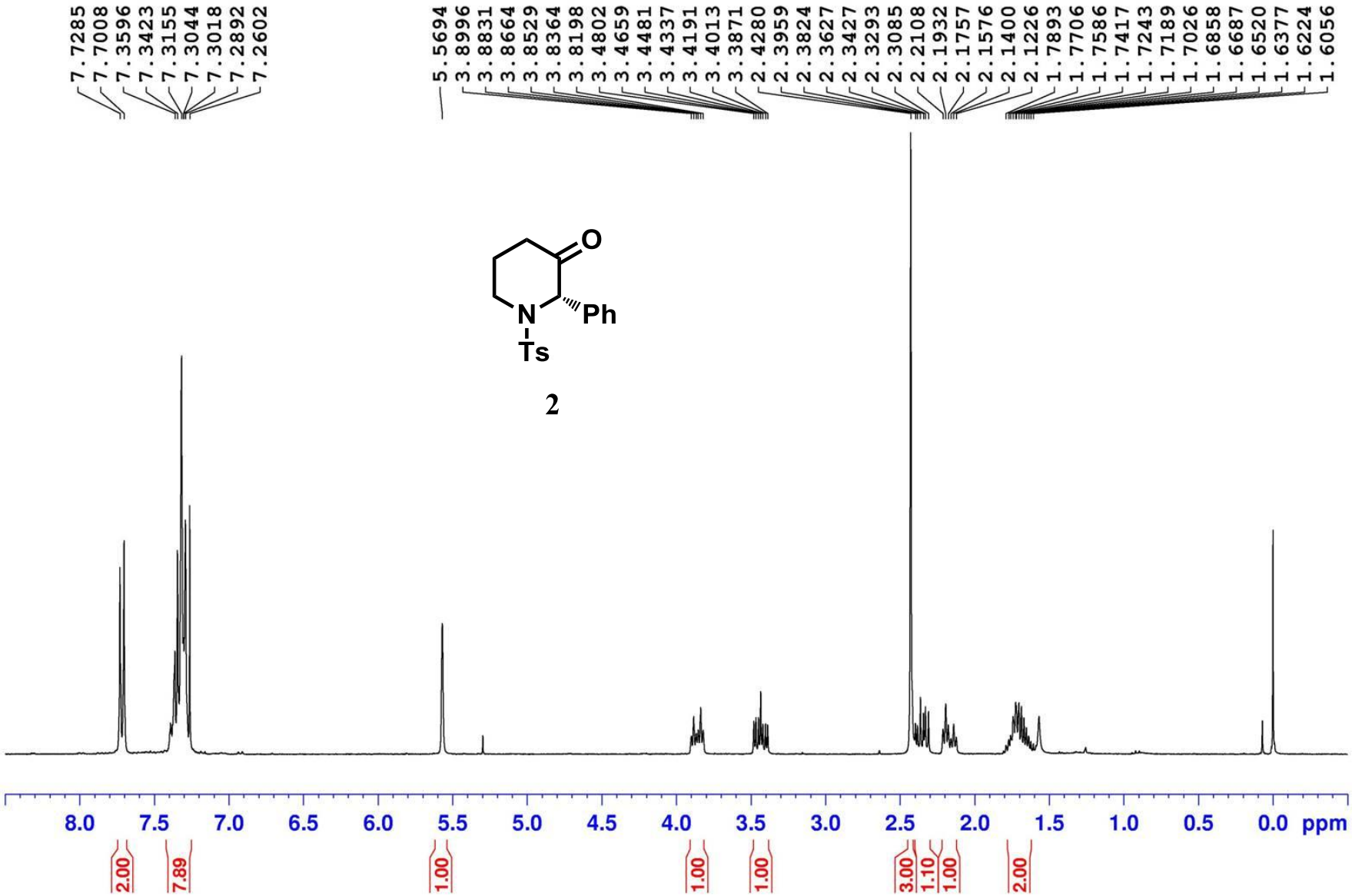
7

125 MHz


192.26
144.58
144.17
136.45
133.16
130.08
129.05
128.66
127.76
127.20
127.00
64.12
41.77
21.70
O
N
Ts
Ph
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

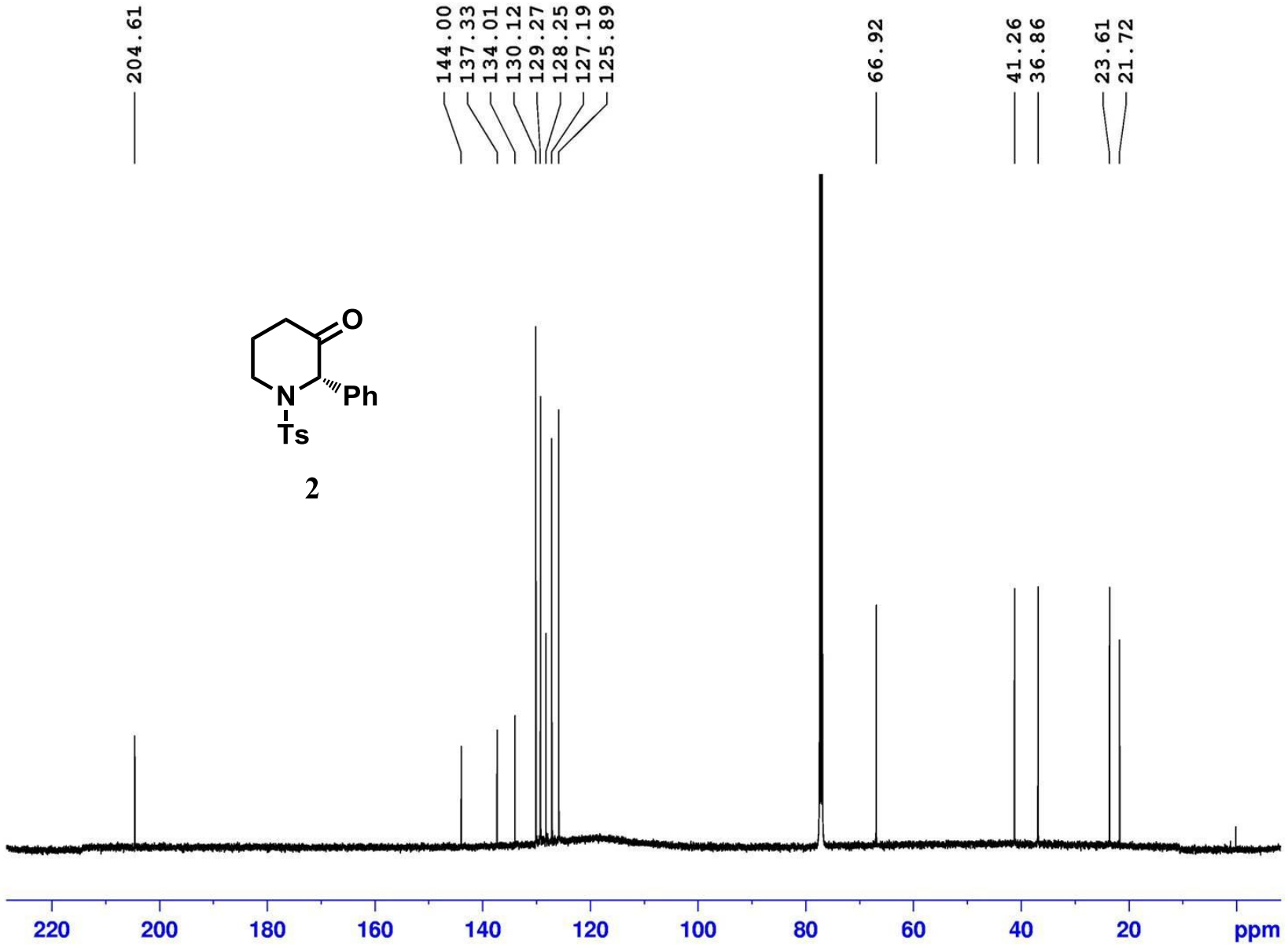
7

300 MHz


7.7285
7.7008
7.3596
7.3423
7.3155
7.3044
7.3018
7.2892
7.2602
5.5694
3.8996
3.8831
3.8664
3.8529
3.8364
3.8198
3.4802
3.4659
3.4481
3.4337
3.4191
3.4013
3.3871
2.4280
2.3959
2.3824
2.3627
2.3427
2.3293
2.3085
2.2108
2.1932
2.1757
2.1576
2.1400
2.1226
1.7893
1.7706
1.7586
1.7417
1.7243
1.7189
1.7026
1.6858
1.6687
1.6520
1.6377
1.6224
1.6056
O
N
Ts
Ph
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
7.89
1.00
1.00
1.00
3.00
1.10
1.00
2.00

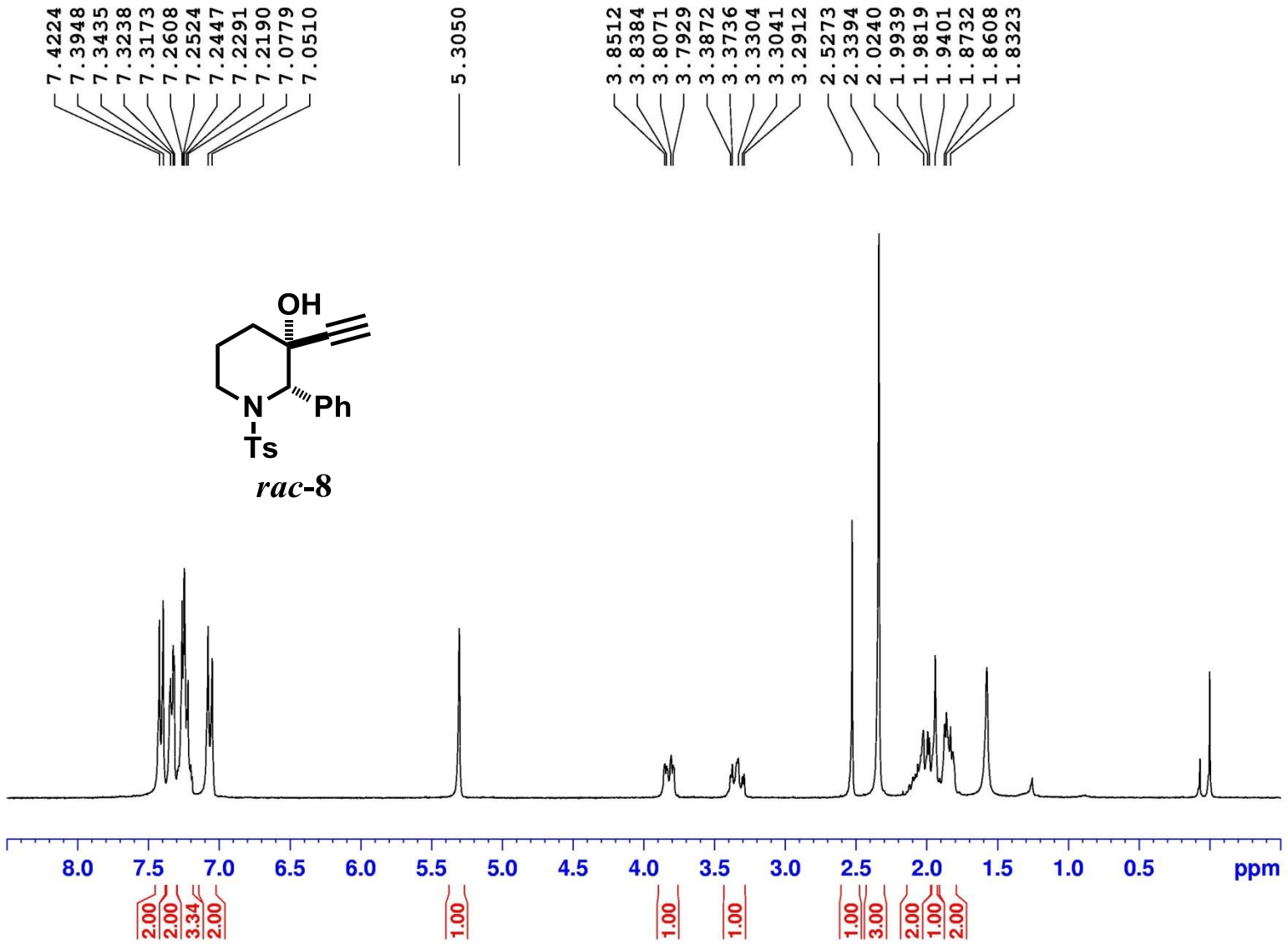
2

125 MHz


204.61
144.00
137.33
134.01
130.12
129.27
128.25
127.19
125.89
66.92
41.26
36.86
23.61
21.72
O
N
Ts
Ph
220
200
180
160
140
120
100
80
60
40
20
ppm

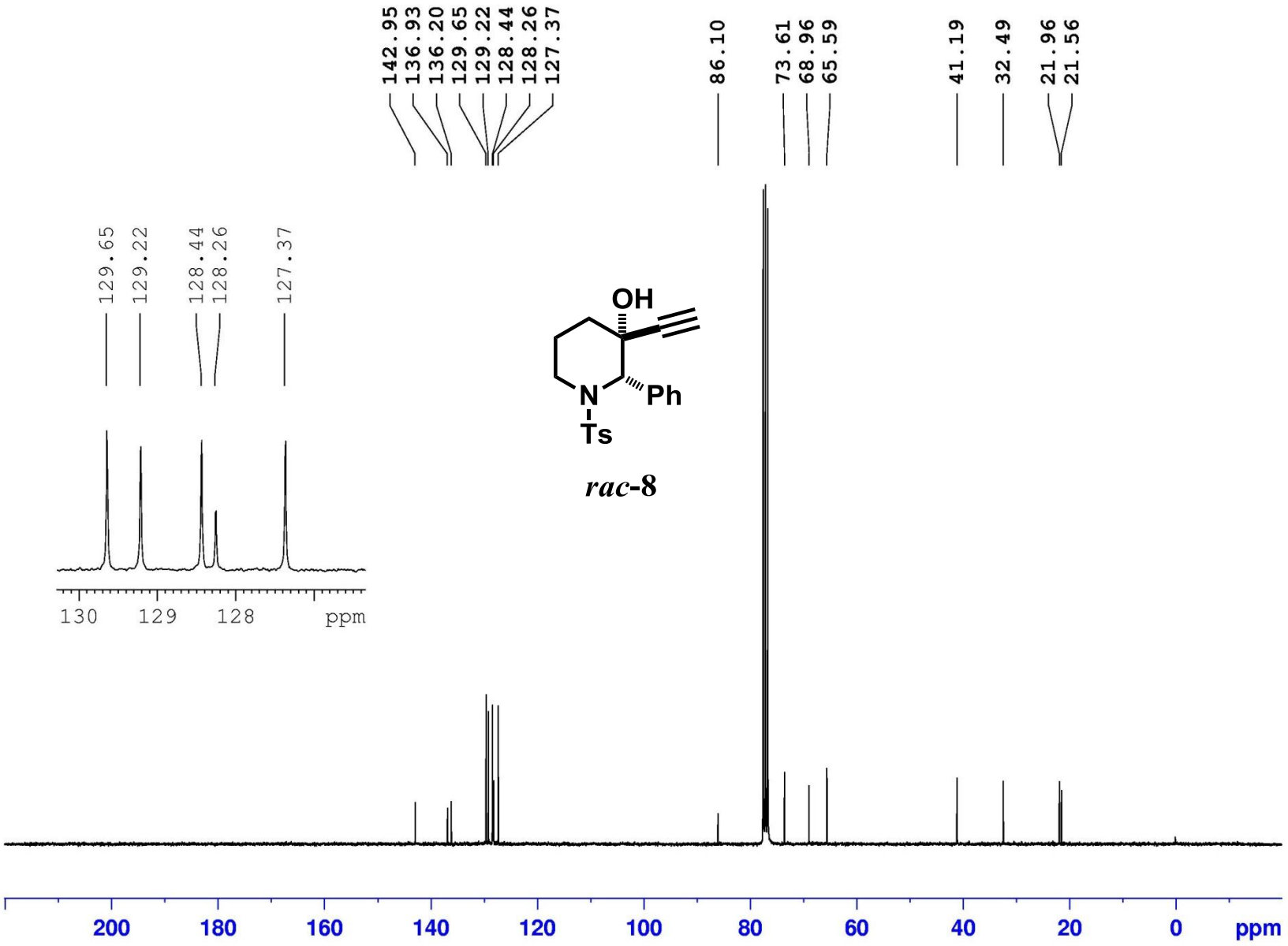
2

300 MHz

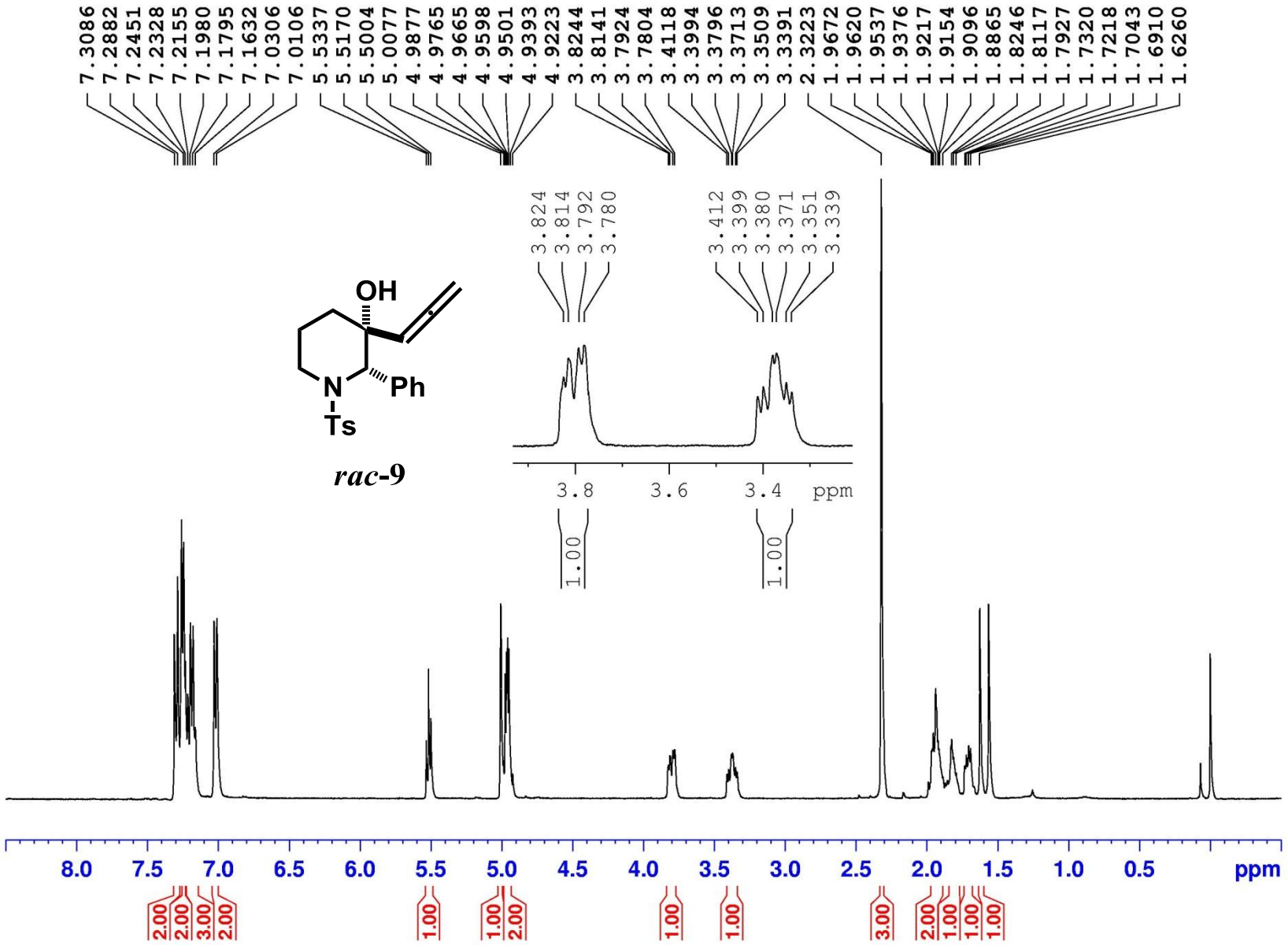

7.4224
7.3948
7.3435
7.3238
7.3173
7.2608
7.2524
7.2447
7.2291
7.2190
7.0779
7.0510
5.3050
3.8512
3.8384
3.8071
3.7929
3.3872
3.3736
3.3304
3.3041
3.2912
2.5273
2.3394
2.0240
1.9939
1.9819
1.9401
1.8732
1.8608
1.8323
OH
N
Ph
Ts
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
2.00
3.34
2.00
1.00
1.00
1.00
1.00
3.00
2.00
1.00
2.00

rac-8

100 MHz

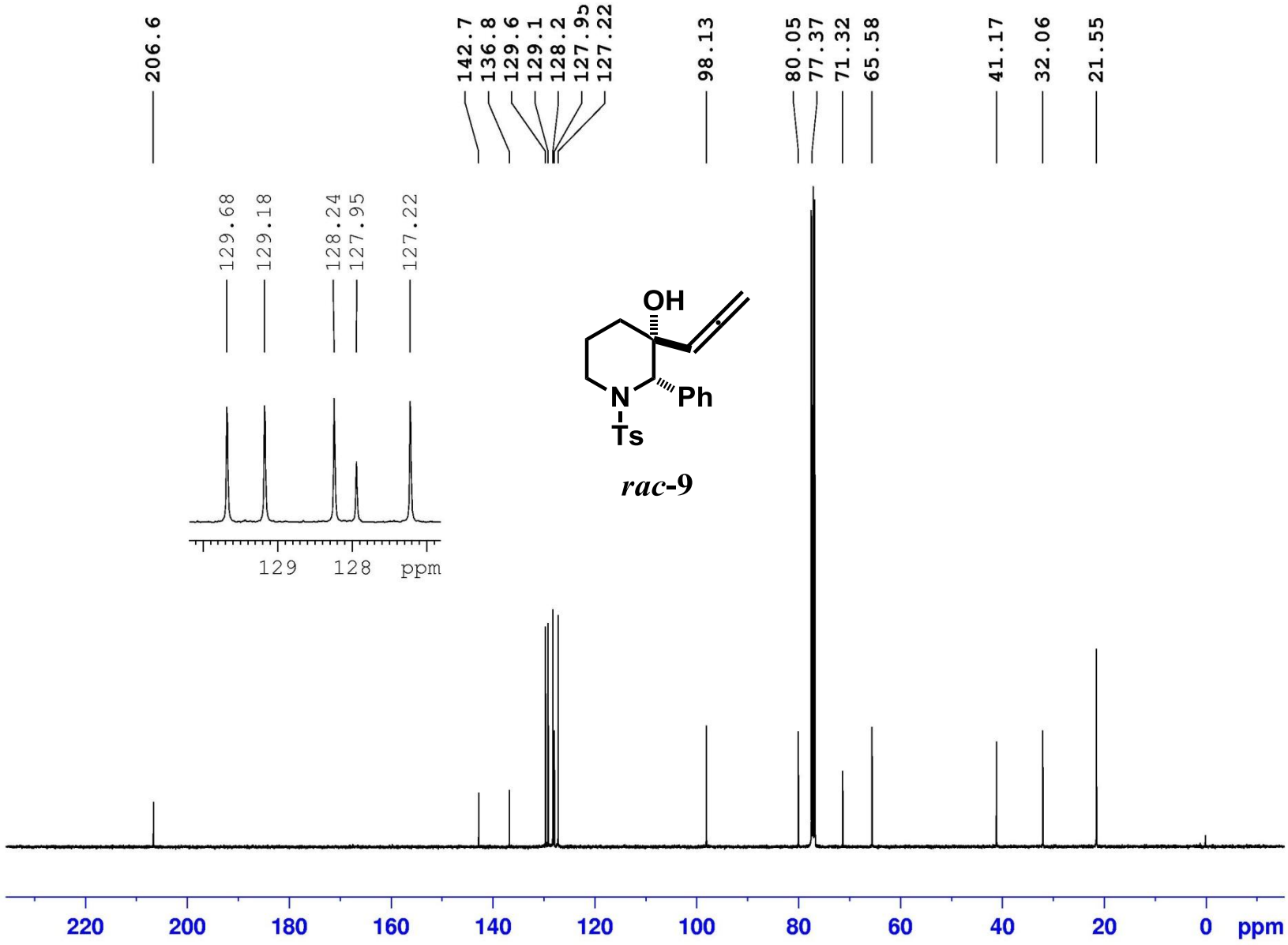

142.95
136.93
136.20
129.65
129.22
128.44
128.26
127.37
86.10
73.61
68.96
65.59
41.19
32.49
21.96
21.56
129.65
129.22
128.44
128.26
127.37
130
129
128
ppm
OH
Ph
N
Ts
rac-8
200
180
160
140
120
100
80
60
40
20
0
ppm

400 MHz


7.3086
7.2882
7.2451
7.2328
7.2155
7.1980
7.1795
7.1632
7.0306
7.0106
5.5337
5.5170
5.5004
5.0077
4.9877
4.9765
4.9665
4.9598
4.9501
4.9393
4.9223
3.8244
3.8141
3.7924
3.7804
3.4118
3.3994
3.3796
3.3713
3.3509
3.3391
2.3223
1.9672
1.9620
1.9537
1.9376
1.9217
1.9154
1.9096
1.8865
1.8246
1.8117
1.7927
1.7320
1.7218
1.7043
1.6910
1.6260
OH
N
Ph
Ts
3.824
3.814
3.792
3.780
3.412
3.399
3.380
3.371
3.351
3.339
3.8
3.6
3.4
ppm
1.00
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
2.00
2.00
3.00
2.00
1.00
1.00
2.00
1.00
1.00
3.00
2.00
1.00
1.00
1.00

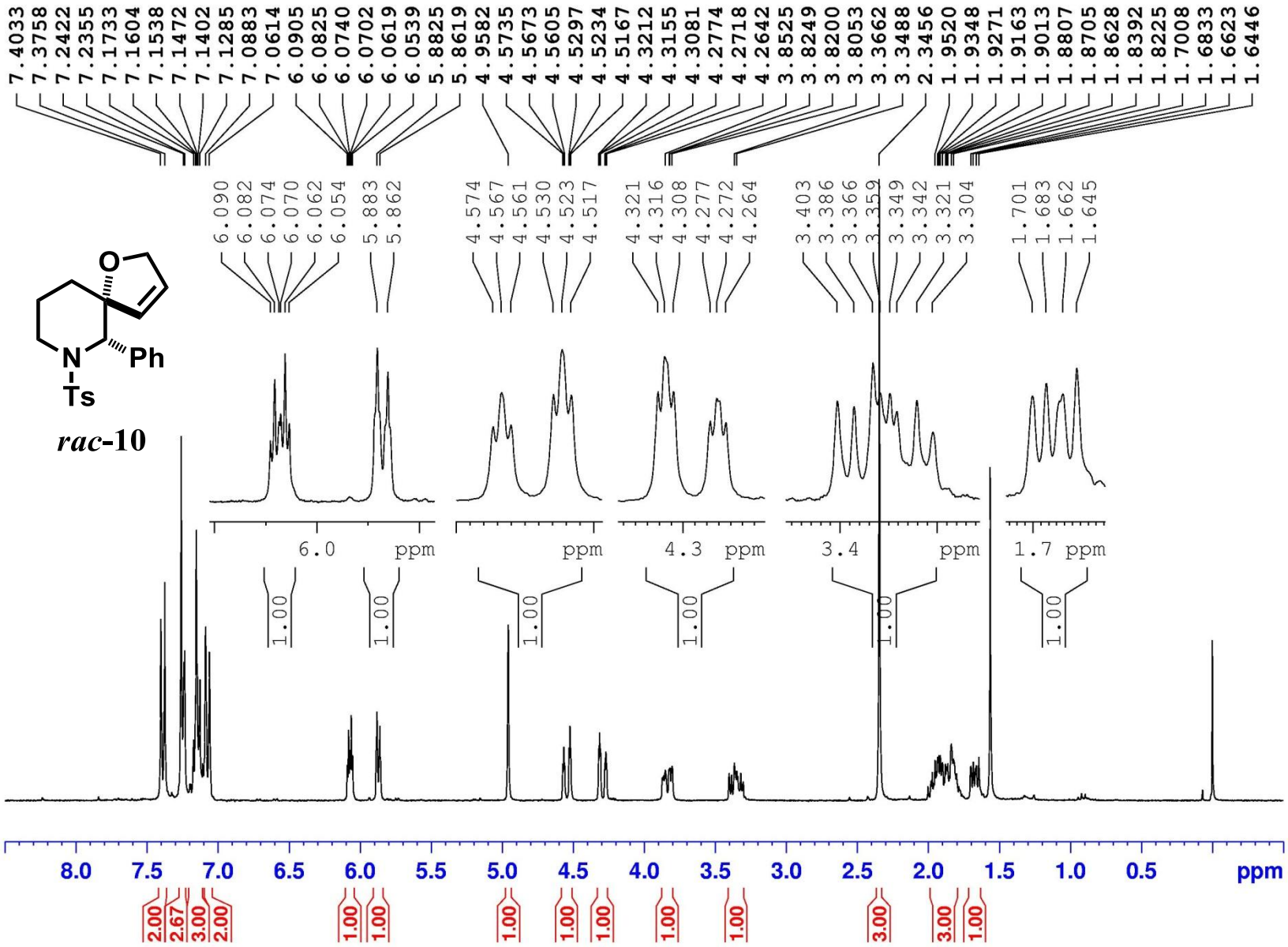
***rac*-9**

100 MHz

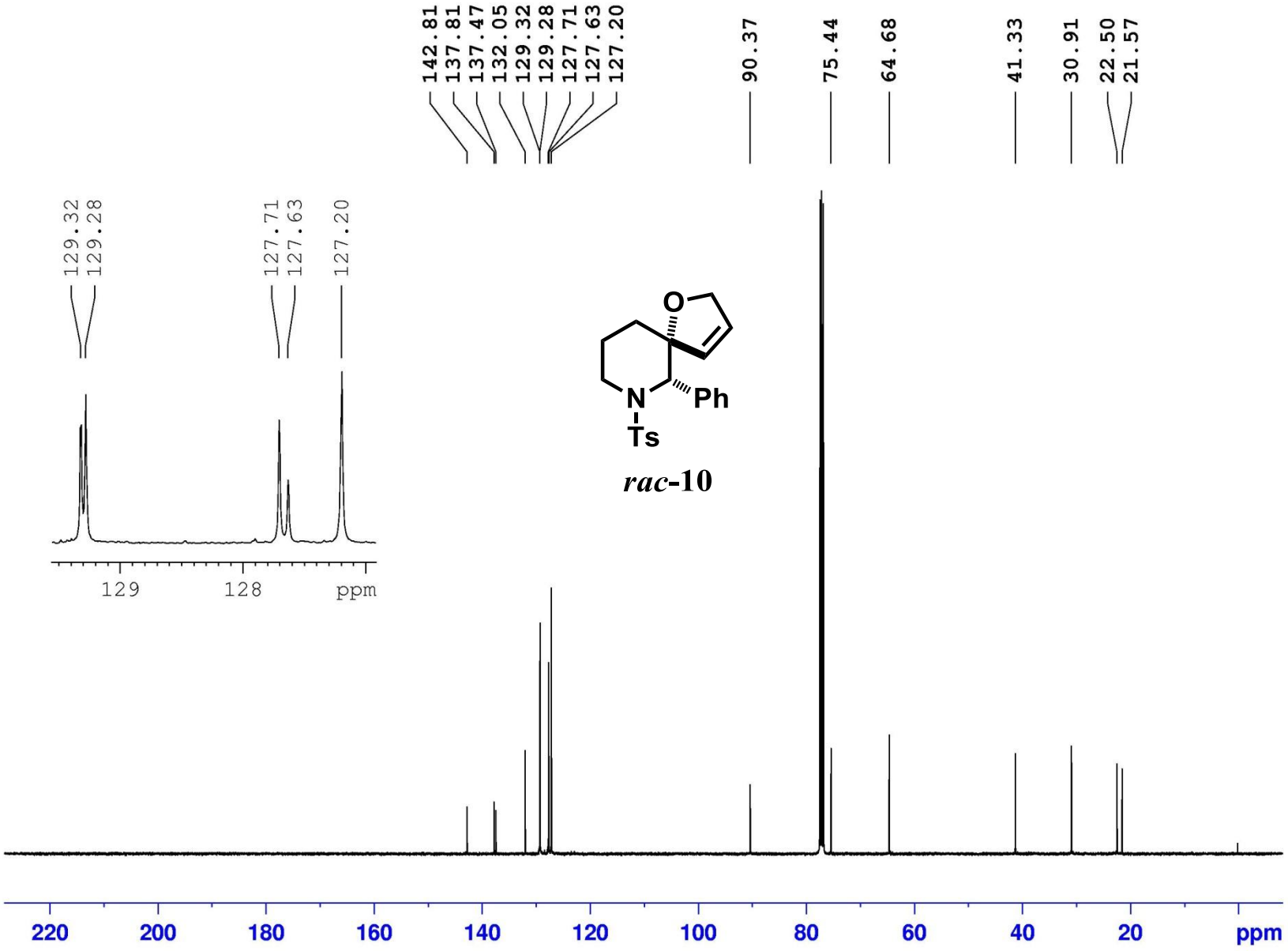

206.6
142.7
136.8
129.6
129.1
128.2
127.95
127.22
98.13
80.05
77.37
71.32
65.58
41.17
32.06
21.55
129.68
129.18
128.24
127.95
127.22
129
128
ppm
OH
N
Ts
Ph
220
200
180
160
140
120
100
80
60
40
20
0
ppm

rac-9

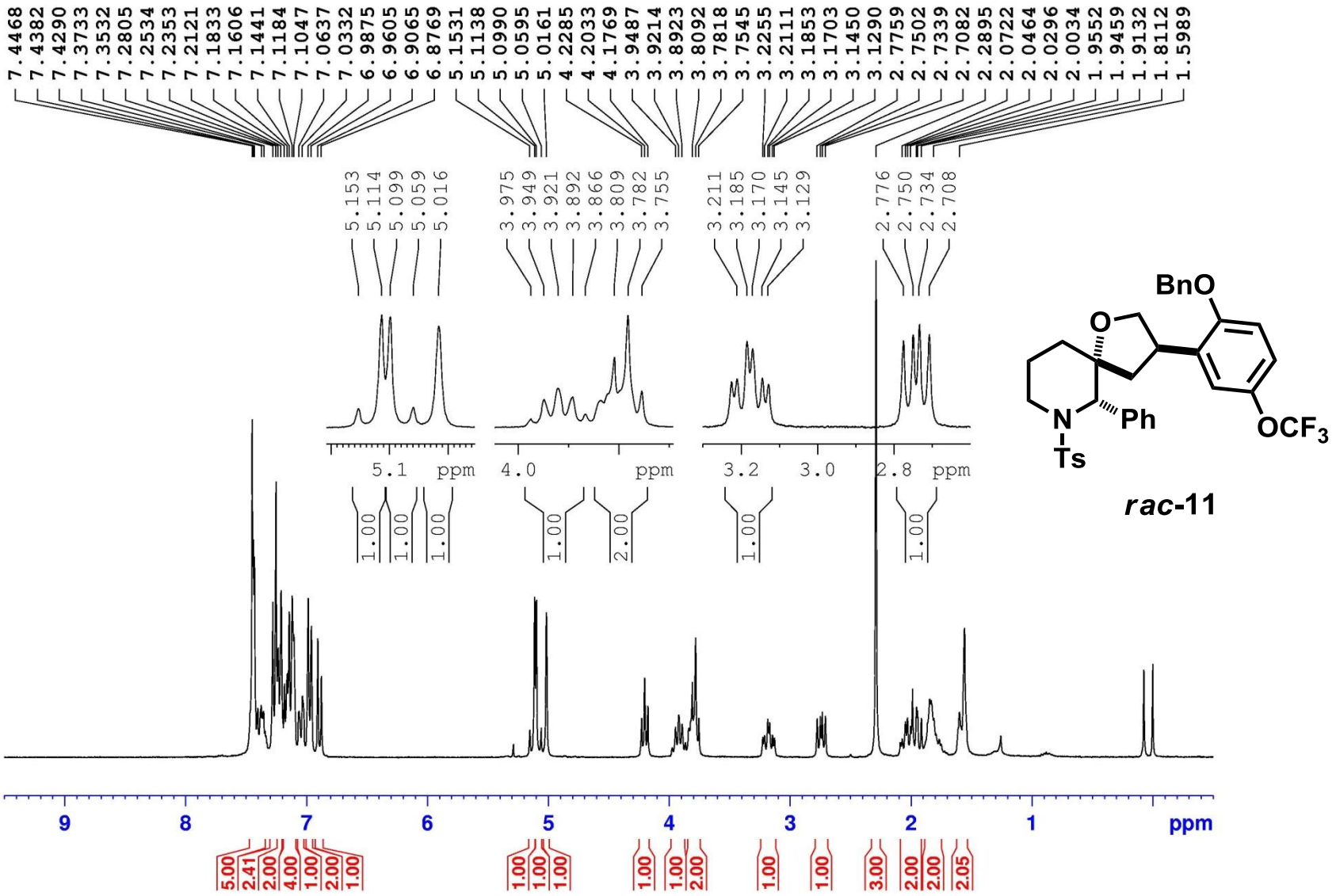
300 MHz


7.4033 7.3758 7.2422 7.2355 7.1733 7.1604 7.1538 7.1472 7.1402 7.1285 7.0883 7.0614 6.0905 6.0825 6.0740 6.0702 6.0619 6.0539 5.8825 5.8619 4.9582 4.5735 4.5673 4.5605 4.5297 4.5234 4.5167 4.3212 4.3155 4.3081 4.2774 4.2718 4.2642 3.8525 3.8249 3.8200 3.8053 3.3662 3.3488 2.3456 1.9520 1.9348 1.9271 1.9163 1.9013 1.8807 1.8705 1.8628 1.8392 1.8225 1.7008 1.6833 1.6623 1.6446
6.090 6.082 6.074 6.070 6.062 6.054 5.883 5.862
4.574 4.567 4.561 4.530 4.523 4.517
4.321 4.316 4.308 4.277 4.272 4.264
3.403 3.386 3.366 3.359 3.349 3.342 3.321 3.304
1.701 1.683 1.662 1.645
O
Ph
N
Ts
rac-10
6.0 ppm
ppm
4.3 ppm
3.4 ppm
1.7 ppm
1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00 2.67 3.00 2.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 3.00 3.00 1.00

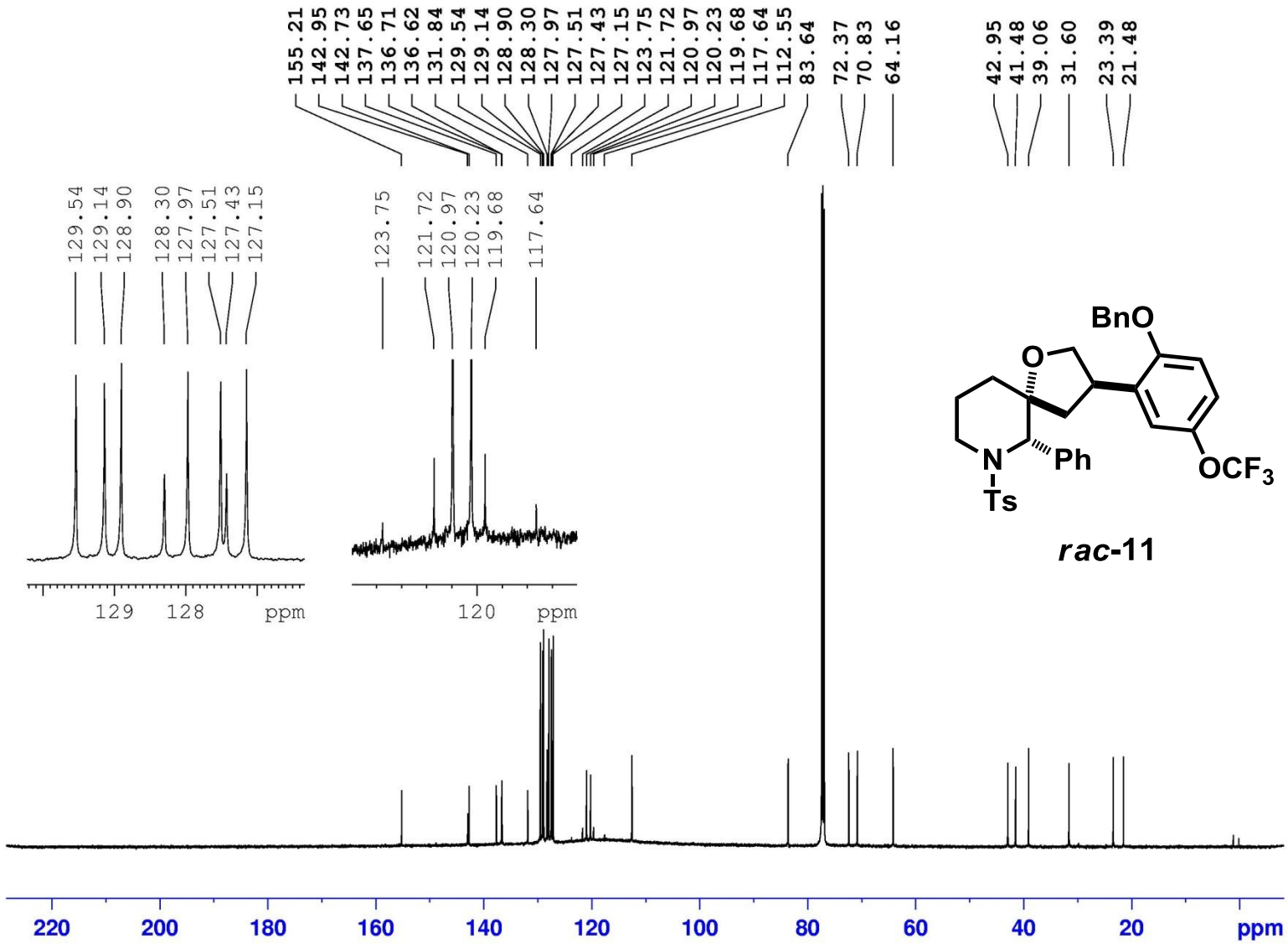
100 MHz


142.81
137.81
137.47
132.05
129.32
129.28
127.71
127.63
127.20
90.37
75.44
64.68
41.33
30.91
22.50
21.57
129.32
129.28
127.71
127.63
127.20
129
128
ppm
O
N
Ph
Ts
rac-10
220
200
180
160
140
120
100
80
60
40
20
ppm

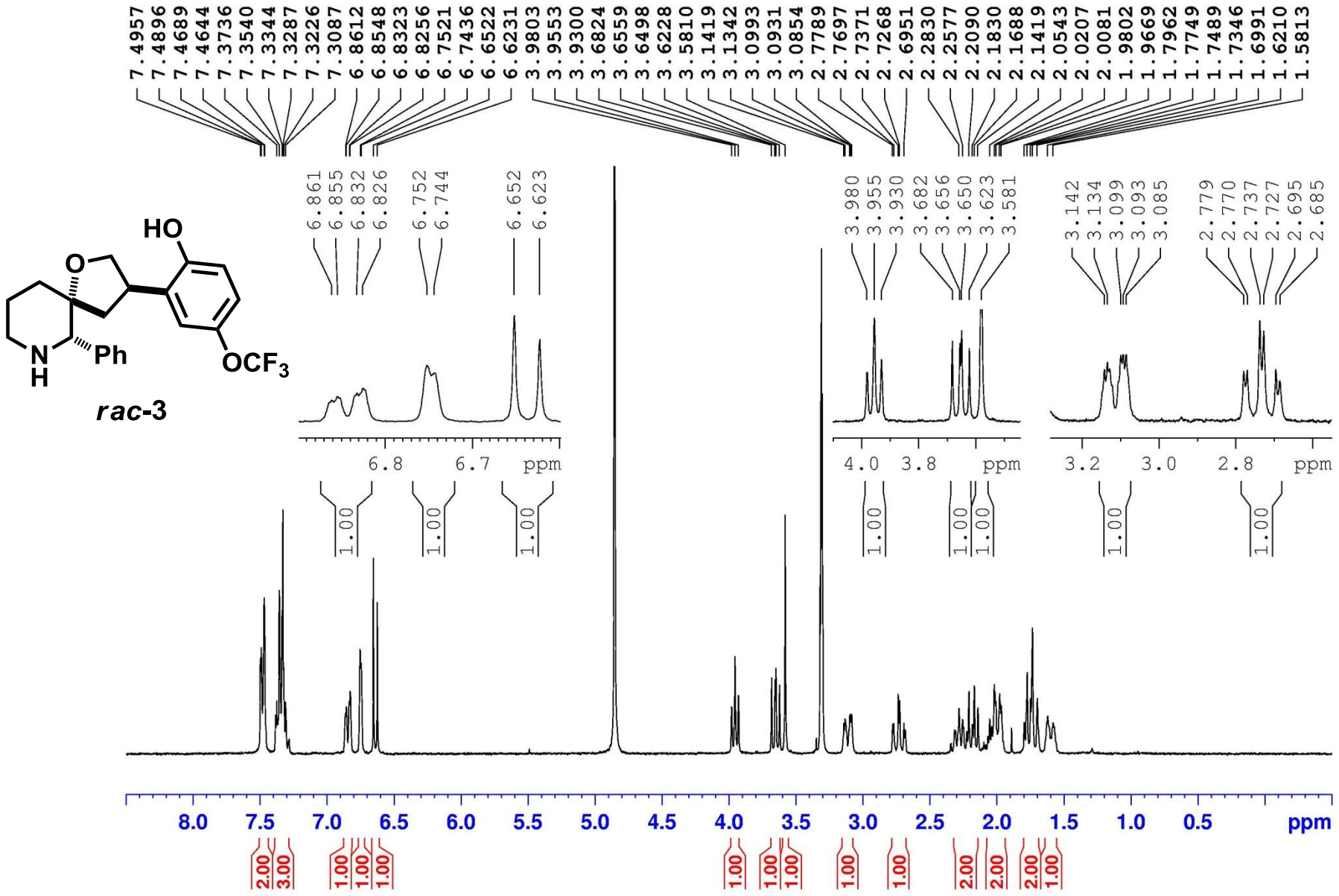
300 MHz


7.4468 7.4382 7.4290 7.3733 7.3532 7.2805 7.2534 7.2353 7.2121 7.1833 7.1606 7.1441 7.1184 7.1047 7.0637 7.0332 6.9875 6.9605 6.9065 6.8769
5.1531 5.1138 5.0990 5.0595 5.0161
4.2285 4.2033 4.1769 3.9487 3.9214 3.8923 3.8092 3.7818 3.7545
3.2255 3.2111 3.1853 3.1703 3.1450 3.1290
2.7759 2.7502 2.7339 2.7082 2.2895 2.0722 2.0464 2.0296 2.0034 1.9552 1.9459 1.9132 1.8112 1.5989
5.153 5.114 5.099 5.059 5.016
3.975 3.949 3.921 3.892 3.866 3.809 3.782 3.755
3.211 3.185 3.170 3.145 3.129
2.776 2.750 2.734 2.708
5.1 ppm
4.0 ppm
3.2 3.0 2.8 ppm
1.00 1.00 1.00
1.00 2.00
1.00
1.00
9 8 7 6 5 4 3 2 1 ppm
5.00 2.41 2.00 4.00 1.00 2.00 1.00
1.00 1.00 1.00
1.00 1.00 2.00
1.00
1.00
3.00
2.00 2.00 2.05
BnO
O
N
Ts
Ph
OCF3
rac-11

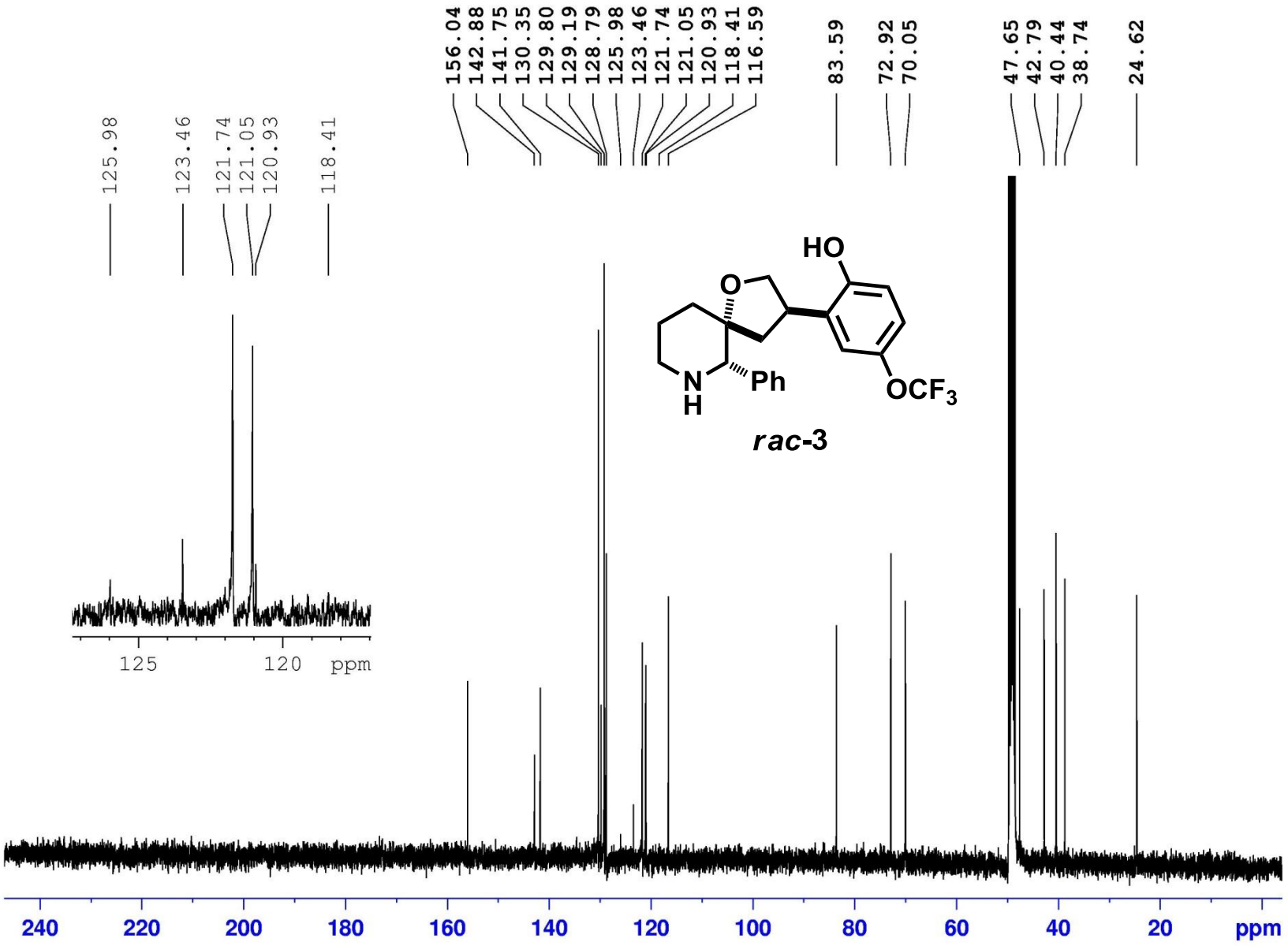
125 MHz


155.21
142.95
142.73
137.65
136.71
136.62
131.84
129.54
129.14
128.90
128.30
127.97
127.51
127.43
127.15
123.75
121.72
120.97
120.23
119.68
117.64
112.55
83.64
72.37
70.83
64.16
42.95
41.48
39.06
31.60
23.39
21.48
129 128 ppm
120 ppm
BnO
O
N
Ts
Ph
OCF3
rac-11
220 200 180 160 140 120 100 80 60 40 20 ppm

300 MHz, MeOD

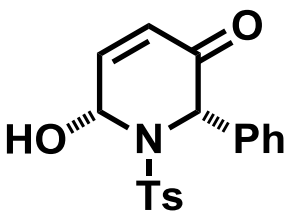

7.4957 7.4896 7.4689 7.4644 7.3736 7.3540 7.3344 7.3287 7.3226 7.3087 6.8612 6.8548 6.8323 6.8256 6.7521 6.7436 6.6522 6.6231 3.9803 3.9553 3.9300 3.6824 3.6559 3.6498 3.6228 3.5810 3.1419 3.1342 3.0993 3.0931 3.0854 2.7789 2.7697 2.7371 2.7268 2.6951 2.2830 2.2577 2.2090 2.1830 2.1688 2.1419 2.0543 2.0207 2.0081 1.9802 1.9669 1.7962 1.7749 1.7489 1.7346 1.6991 1.6210 1.5813
6.861 6.855 6.832 6.826 6.752 6.744 6.652 6.623
3.980 3.955 3.930 3.682 3.656 3.650 3.623 3.581
3.142 3.134 3.099 3.093 3.085 2.779 2.770 2.737 2.727 2.695 2.685
HO
O
N
H
Ph
OCF3
rac-3
6.8 6.7 ppm
4.0 3.8 ppm
3.2 3.0 2.8 ppm
1.00
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
2.00 3.00 1.00 1.00 1.00 1.00 1.00 1.00 1.00 2.00 2.00 2.00 1.00

100 MHz, MeOD

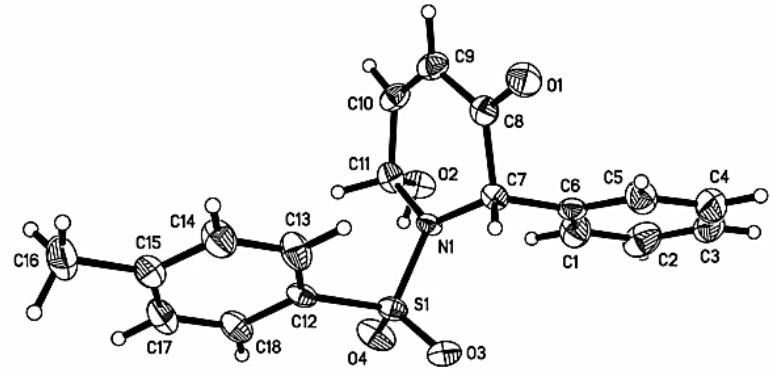

156.04
142.88
141.75
130.35
129.80
129.19
128.79
125.98
123.46
121.74
121.05
120.93
118.41
116.59
83.59
72.92
70.05
47.65
42.79
40.44
38.74
24.62
125.98
123.46
121.74
121.05
120.93
118.41
125
120
ppm
HO
O
N
H
Ph
OCF3
rac-3
240
220
200
180
160
140
120
100
80
60
40
20
ppm

7.1 X-Ray Structure for *Rac*-6

Cambridge Crystallographic Data Centre Deposition Number: 917487

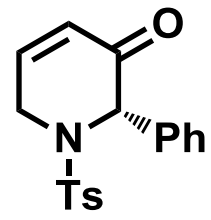


rac-6

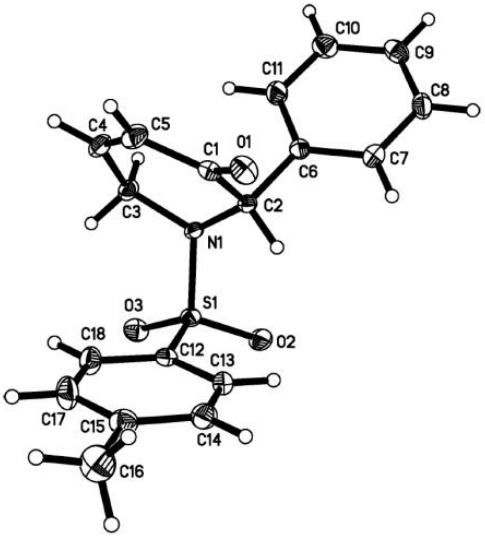


7.2 X-Ray Structure for 7

Cambridge Crystallographic Data Centre Deposition Number: 917485

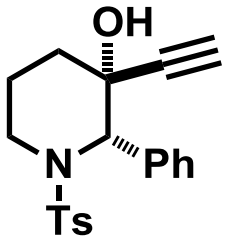


7

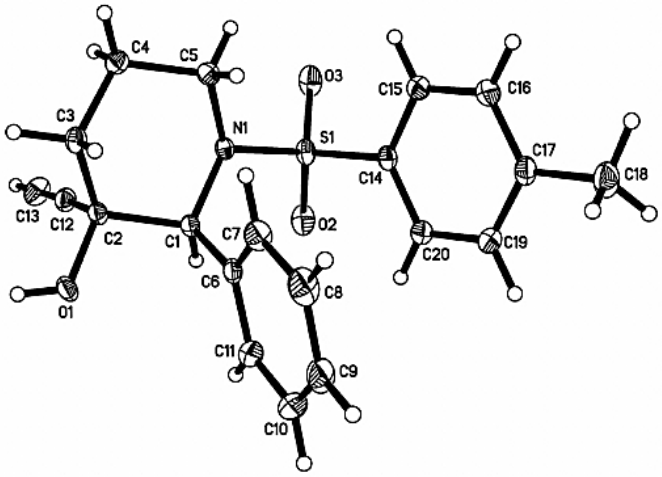


7.3 X-Ray Structure for *Rac*-8

Cambridge Crystallographic Data Centre Deposition Number: 917488

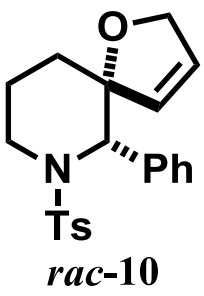


rac-8

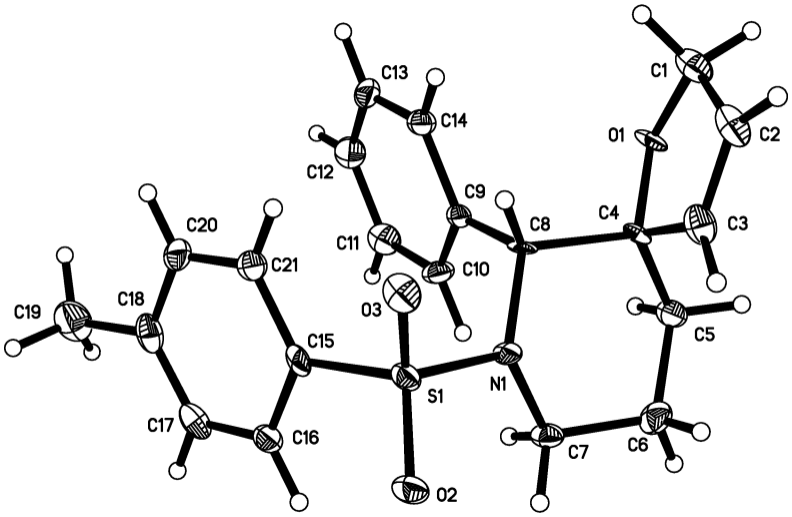


7.4 X-Ray Structure for *Rac*-10

Cambridge Crystallographic Data Centre Deposition Number: 917489

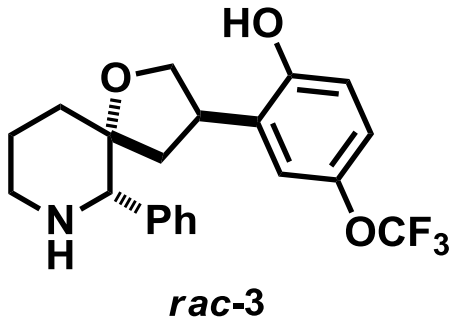


***rac*-10**

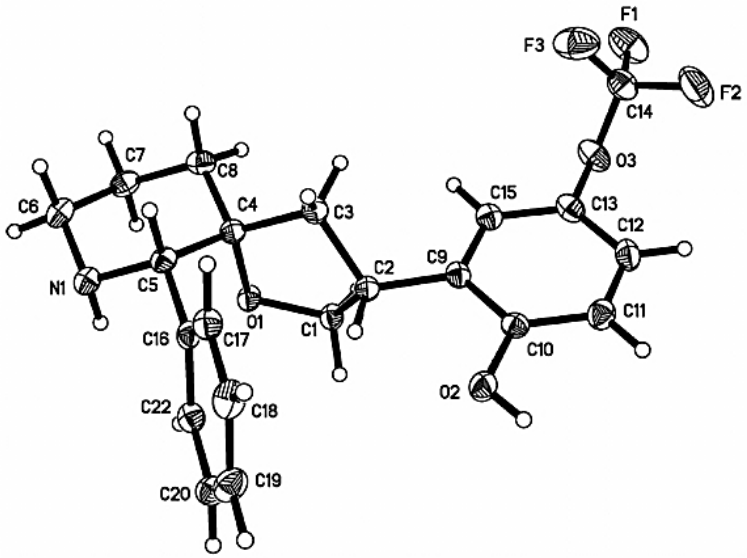


7.5 X-Ray Structure for *Rac*-3

Cambridge Crystallographic Data Centre Deposition Number: 917486



***rac*-3**



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9. Generally accepted mechanism for the aza-Achmatowicz Rearrangement