Supporting Information for

A Direct and Versatile Access to α,α-Disubstituted 2-Pyrrolidinyl-methanols by SmI_2-Mediated Reductive Coupling

Olga N. Burchak, Christian Philouze, Pierre Yves Chavant,* and Sandrine Py*

Département de Chimie Moléculaire (SERCO) UMR-5250, ICMG FR-2607, CNRS – Université Joseph Fourier, BP 53, 38041 Grenoble Cedex 09, France.
Sandrine.Py@ujf-grenoble.fr; Pierre-Yves.Chavant@ujf-grenoble.fr

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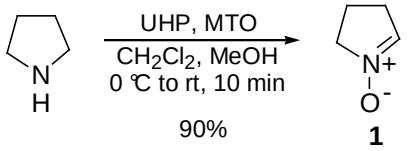
General

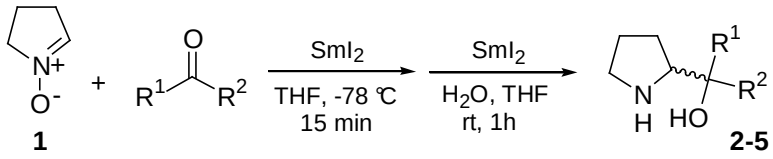
Reactions were performed under a positive pressure of dry argon in oven-dried glassware equipped with a magnetic stir bar. Standard inert atmosphere techniques were used in handling all air and moisture sensitive reagents. THF was freshly distilled from sodium and CH_2Cl_2 from CaH_2. Purchased reagents were used without purification. Reactions were monitored by thin layer chromatography (TLC) using commercial aluminum-backed silica gel plates. TLC spots were viewed under ultraviolet light and by heating the plate after treatment with either a 0.5% solution of ninhydrine in 3% ethanolic acetic acid or a 2% solution of potassium permanganate in 7% aqueous sodium carbonate; *N*,*N*-disubstituted hydroxylamines were detected with 1% triphenyl tetrazolium chloride (TTC) in ethanol (red color). Products were purified by gravity column chromatography on Silica Gel 60 (70-230 mesh). Melting points were determined in capillary tubes and are uncorrected. Infrared (IR) spectra were recorded on a Fourier transform infrared (FTIR) spectrometer equipped with an ATR (Attenuated Total Reflection) device and are reported in reciprocal centimeters (cm^{-1}). Chemical shifts for ^1H spectra are values downfield from tetramethylsilane in $CDCl_3$ (δ 0.00), CD_3OD or $(CD_3)_2SO$ and are reported as follows: chemical shift (ppm), multiplicity, integration, and coupling constants (Hz).

1-Pyrroline-*N*-oxide[1] **(1)**



To a stirred suspension of methyltrioxorhenium (MTO) (0.012 g, 0.05 mmol, 0.5% mol equiv) and urea hydrogen peroxide (UHP) (6.8 g, 70.0 mmol) in CH_2Cl_2 (200 mL) 5 mL of MeOH was added at room temperature. Within 15 min the yellow color appeared, the reaction mixture was cooled in an ice bath and pyrrolidine (0.71 g, 10.0 mmol) was added in one portion, the yellow color disappeared. The ice bath was removed and another portion of MTO (0.012 g, 0.05 mmol) was added at room temperature, the colour of reaction mixture turned pale yellow. The excess of UHP was filtered off, CH_2Cl_2 and MeOH were evaporated under reduced pressure. The residue was diluted with CH_2Cl_2 (100 mL), a solid substance was filtered off, and the filtrate was washed with 10% aqueous solution of $Na_2S_2O_3$ (2×10 mL), brine, dried over Na_2SO_4, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel (CH_2Cl_2-MeOH, 9:1) to afford 1 (0.77 g, 90%) as colourless oil. The product was found to be unstable, but it could be stored for several days as a 0.5 M solution in THF at 5 °C under Ar atmosphere. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.22-2.32 (m, 2H), 2.73-2.78 (m, 2H), 3.95-4.01 (m, 2H), 6.89-6.92 (m, 1H).

General procedure for the synthesis of α,α-disubstituted-2-pyrrolidinyl-methanols 2-5 (Method A)

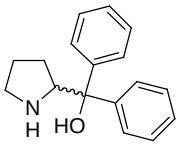


To a stirred and carefully deoxygenated solution of the nitrone **1** (60 mg, 0.7 mmol) and aromatic ketone (0.5 mmol) in 5 mL of dry THF, a 0.1 M solution of SmI_2 (11.0 mL, 1.1 mmol) was added at −78 °C under argon. After 15 min degassed water (36 μL, 2.0 mmol) and a second portion of SmI_2 solution (14.0 mL, 1.4 mmol) were added and the reaction mixture was allowed to reach room temperature. After 1 hour, a saturated solution of $Na_2S_2O_3$ (5 mL), a 1M NaOH solution (15 mL) and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine,

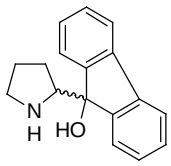
[1] Ballistreri, F. P.; Chiacchio, U.; Rescifina, A.; Tomaselli, G. A.; Toscano, R. M. *Tetrahedron* **1992**, *48*, 8677.

dried over Na_2SO_4, filtered, and concentrated. Column chromatography using CH_2Cl_2-MeOH-$EtNMe_2$ (89:10:1) yielded racemic products **2-5**.

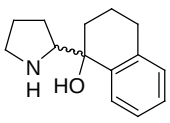
(±)-Diphenyl-pyrrolidin-2-yl-methanol[2] **(2)** (105 mg, 83%) was obtained from benzophenone (91 mg, 0.5 mmol) as a colourless oil, which solidified upon standing; mp 80-81 °C (lit.[2] 82-83 °C). IR (neat): 700, 750, 1445, 1490, 1595, 2870, 2955, 3055, 3340, 3360 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.52-1.76 (m, 4H), 2.90-3.06 (m, 2H), 4.25 (t, *J* = 7.7 Hz, 1H), 7.13-7.18 (m, 2H), 7.24-7.31 (m, 4H), 7.48-7.58 (m, 4H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 25.5, 26.3, 46.7, 64.5, 77.1, 125.5 (2 C), 125.9 (2 C), 126.3, 126.4, 127.9(2C), 128.2(2C), 145.4, 148.2.



(±)-9-Pyrrolidin-2-yl-9*H*-fluoren-9-ol (3) (60 mg, 48%) was obtained from fluorenone (90 mg, 0.5 mmol) as a white solid. Crystals were obtained via recrystallization from MeOH; mp 189-190 °C. IR (neat): 725, 765, 845, 1420, 1445, 1585, 1605, 2865, 3035, 2965, 3270, 3310 cm^{-1}. ^1H NMR (300 MHz, $(CD_3)_2SO$): δ = 0.72-0.86 (m, 1H), 1.19-1.44 (m, 3H), 2.67-2.81 (m, 2H), 3.61 (t, *J* = 7.6 Hz, 1H), 7.21-7.36 (m, 4H), 7.48-7.51 (m, 1H), 7.69-7.75 (m, 3H). ^{13}C NMR (300 MHz, $(CD_3)_2SO$): δ = 25.2, 26.3, 46.4, 65.5, 82.8, 119.2, 119.5, 123.8, 125.9, 126.9, 127.2, 128.0, 128.1, 139.3, 139.9, 147.8, 149.3. MS (ES^+): *m/z* (%) = 252 (100) $[M + H]^+$, 234 (27) $[M + H - H_2O]^+$. Anal. Calcd (%) for $C_{17}H_{17}NO$: C, 81.25; H, 6.82; N, 5.58. Found: C, 81.39; H, 6.84; N, 5.77.

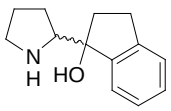


(±)-1-Pyrrolidin-2-yl-1,2,3,4-tetrahydro-naphthalen-1-ol[3] **(4)** (90 mg, 83%) was obtained from tetralone (73 mg, 0.5 mmol) as a colourless oil, which solidified upon standing; mp 71-72 °C (lit.[3] 66 °C, $CHCl_3$). IR (neat): 745, 815, 930, 1030, 1125, 1190, 1455, 1485, 2870, 2940, 3320 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.41-1.49 (m, 1H), 1.55-1.59 (m, 1H), 1.60-1.90 (m, 5H), 1.98-2.04 (m, 1H), 2.78-2.83 (m, 3H), 2.93-2.99 (m, 2H), 3.48 (t, *J* = 7.1 Hz, 1H), 7.03-7.06 (m, 1H), 7.11-7.18 (m, 2H), 7.64-7.67 (m, 1H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 19.2, 26.4, 26.5, 28.9, 35.3, 46.7, 64.8, 72.0, 125.5, 126.6, 126.8, 128.5, 137.0, 140.8. MS (ES^+): *m/z* (%) = 218 (100) $[M + H]^+$, 200 (48) $[M + H - H_2O]^+$. Anal. Calcd (%) for $C_{14}H_{19}NO$: C, 77.38; H, 8.82; N, 6.45. Found: C, 77.00; H, 8.95; N, 6.22.



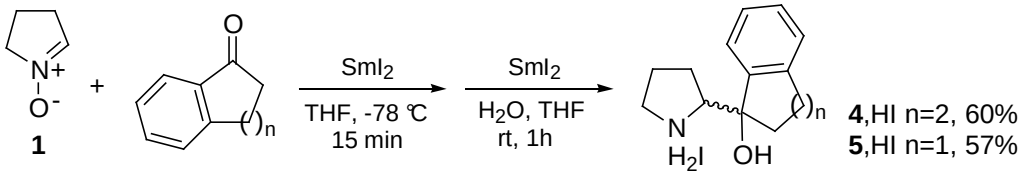
[2] Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C.-P.; Singh, V. K. *J. Am. Chem. Soc*. **1987**, *109*, 7925.
[3] Seebach, D.; Wykypiel, W. *Synthesis*, **1979**, *6*, 423.

(±)-1-Pyrrolidin-2-yl-indan-1-ol (5) (mixture of diastereomers, 89 mg, 88%) was obtained from



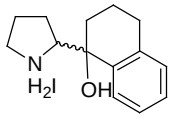
indanone (66 mg, 0.5 mmol) as a colourless oil. Pure major diastereomer *(unlike)* (54 mg, 53%) was obtained after additional chromatography CH_2Cl_2-MeOH-$EtNMe_2$ (94:5:1) as a colorless oil. IR (neat): 725, 760, 880, 1065, 1290, 1400, 1460, 1475, 2865, 2940, 3320 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.63-1.79 (m, 4H), 2.06-2.17 (m, 1H), 2.26-2.34 (m, 1H), 2.77-3.18 (m, 6H), 3.35-3.40 (m, 1H), 7.16-7.26 (m, 3H), 7.38-7.41 (m, 1H). ^{13}C NMR (300 MHz, ($CDCl_3$): δ = 26.3, 26.4, 29.3, 39.4, 46.9, 64.6, 83.5, 124.2, 124.7, 126.4, 128.0, 143.5, 145.5. MS (ES^+): *m/z* (%) = 204 (95) $[M + H]^+$, 186 (100) $[M + H - H_2O]^+$. HRMS: m/z [M + H] calcd for $C_{13}H_{18}NO$: 204.1388; found: 204.1381.

General procedure for the synthesis of the iodohydrates of 4, 5



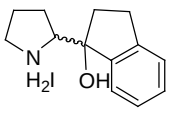
The same procedure as for products **2-5**, but after completion of the reaction (1 hour), 5 mL of water was added, and the mixture was stirred for 10 min at room temperature under argon. Products **4,**HI and **5**,HI were extracted with ether and purified by column chromatography (CH_2Cl_2-MeOH, 90:10). Carefully degassed water and freshly distilled solvents were used during the work up and purification procedures to avoid any degradation of iodohydrates.

(±)-1-Pyrrolidin-2-yl-1,2,3,4-tetrahydro-naphthalen-1-ol iodohydrate (4,HI**)** (104 mg, 60%)



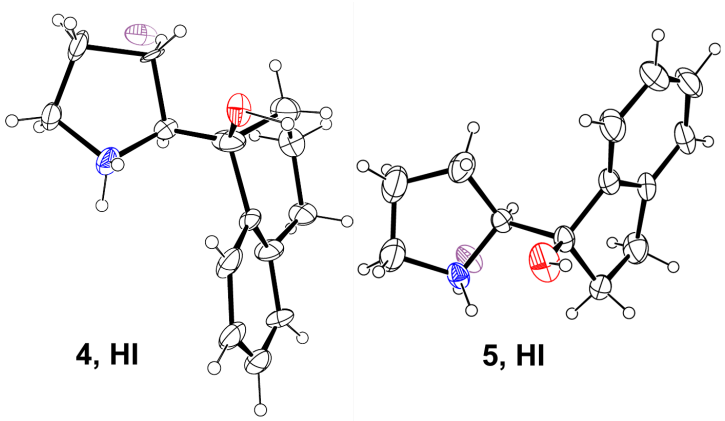
was obtained from tetralone (73 mg, 0.5 mmol) as a pale yellow oil. White crystals precipitated from concentrated chloroformic solution; mp 190-193 °C. IR (neat): 735, 760, 880, 1020, 1190, 1280, 1370, 1450, 1545, 2680, 2720, 2915, 2950, 3375 cm^{-1}. ^1H NMR (300 MHz, CD_3OD): δ = 1.62-1.72 (m, 1H), 1.83-2.13 (m, 6H), 2.19-2.33 (m, 1H), 2.86-2.91 (m, 2H), 3.28-3.42 (m, 3H), 3.92 (dd, J_1 = 10.7 Hz, J_2 = 6.6 Hz, 1H), 7.10-7.15 (m, 1H), 7.18-7.23 (m, 2H), 7.61-7.66 (m, 1H). ^{13}C NMR (300 MHz, CD_3OD): δ = 20.1, 25.1, 26.8, 29.1, 36.0, 47.1, 66.9, 71.2, 126.8, 127.6, 129.0, 130.1, 138.3, 140.7. MS (ES^+): *m/z* (%) = 218 (100) $[M + H]^+$, 200 (48) $[M + H - H_2O]^+$. Anal. Calcd (%) for $C_{14}H_{20}INO$: C, 48.71; H, 5.84; N, 4.06. Found: C, 49.01; H, 6.01; N, 4.07.

(±)-1-Pyrrolidin-2-yl-indan-1-ol iodohydrate (5,HI**)** (mixture of diastereomers, 95 mg, 57%)

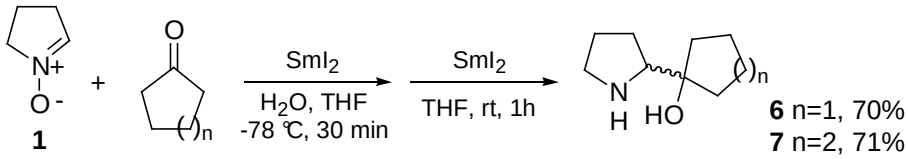


was obtained from indanone (66 mg, 0.5 mmol) as a pale yellow oil. Pure major diastereomer *(unlike)* (60 mg, 36%) precipitated from concentrated chloroformic solution of diastereomer mixture as white crystals; mp 178-180 °C. IR (neat): 720, 755, 835, 955, 1110, 1210, 1275, 1370, 1450, 1470, 1545, 2735, 2950, 2980, 3380 cm^{-1}. ^1H NMR (300 MHz, CD_3OD): δ = 1.89-2.01 (m, 2H), 2.04-2.14 (m, 1H), 2.15-2.31 (m, 2H), 2.37-2.45 (m, 1H), 2.94-2.99 (m, 2H), 3.26-3.42 (m, 3H), 3.73 (dd, J_1 = 10.1 Hz, J_2 = 6.9 Hz, 1H), 7.23-7.33 (m, 3H), 7.41-7.45 (m, 1H). ^{13}C NMR (300 MHz, CD_3OD): δ = 25.4, 26.4, 29.6, 40.7, 47.3, 66.8, 82.1, 125.2, 126.2, 127.9, 130.1, 144.4, 145.1. MS (ES^+): *m/z* (%) = 204 (95) $[M + H]^+$, 186 (100) $[M + H – H_2O]^+$. Anal. Calcd (%) for $C_{13}H_{18}INO$: C, 47.14; H, 5.48; N, 4.23. Found: C, 47.36; H, 5.75; N, 4.22.

The relative configurations of **4**,HI and **5**,HI were determined by X-ray crystallography:



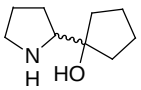
General procedure for the synthesis of α,α-disubstituted-2-pyrrolidinyl-methanols 6,7 (method B)



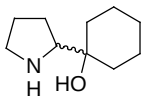
To a stirred and carefully deoxygenated solution of the nitrone **1** (60 mg, 0.7 mmol), aliphatic ketone (0.5 mmol) and degassed water (90 μL, 5.0 mmol) in 5 mL of dry THF, a 0.1 M solution of SmI_2 (11.0 mL, 1.1 mmol) was added at −78 °C under argon. After 30 min a second portion of SmI_2 solution (14.0 mL, 1.4 mmol) was added and the reaction mixture was allowed to reach room temperature. After 1 hour, a saturated solution of $Na_2S_2O_3$ (5 mL), a 1M NaOH solution (15

mL) and EtOAc (20 mL) were added. After extraction the organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated. Column chromatography using CH_2Cl_2-MeOH-$EtNMe_2$ (78:20:2) yielded racemic products **6** or **7**.

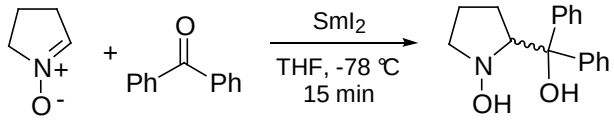
(±)-1-Pyrrolidin-2-yl-cyclopentanol (6)[4] (54 mg, 70%) was obtained from cyclopentanone (42 mg, 0.5 mmol) as a colourless oil, which solidified upon standing; mp 45-47 °C (for (*S*)-enantiomer lit.[4] 34 °C). IR (neat): 910, 990, 1065, 1090, 1380, 1425, 2830, 2865, 2935, 2955, 3280 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.44-1.85 (m, 12H), 2.75 (br. s., 2H, NH, OH), 2.94-3.01 (m, 2H), 3.07-3.12 (m, 1H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 24.1 (2 C), 25.9, 26.3, 36.2, 40.0, 46.9, 66.2, 81.8.



(±)-1-Pyrrolidin-2-yl-cyclohexanol (7)[4] (60 mg, 71%) was obtained from cyclohexanone (49 mg, 0.5 mmol) as a colourless oil, which solidified upon standing; mp 51-53 °C (for (*S*)-enantiomer lit.[4] 54 °C). IR (neat): 960, 980, 1040, 1260, 1400, 1445, 2850, 2920, 3295, 3425 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.18-1.32 (m, 3H), 1.51-1.70 (m, 11H), 2.60 (br. s., 2H, NH, OH), 2.90-3.04 (m, 3H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 21.9, 22.0, 25.0, 25.9, 26.0, 33.9, 37.2, 46.7, 65.9, 70.6.



(±)-2-(Hydroxy-diphenyl-methyl)-pyrrolidin-1-ol (8)



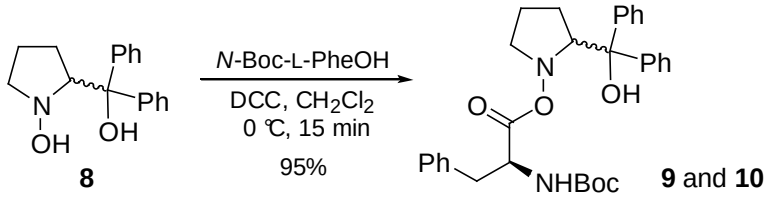
1 **8**

To a stirred and carefully deoxygenated solution of the nitrone **1** (60 mg, 0.7 mmol) and benzophenone (91 mg, 0.5 mmol) in dry THF, a 0.1 M solution of SmI_2 (11.0 mL, 1.1 mmol) was added at −78 °C under argon. After 15 min, saturated solutions of $Na_2S_2O_3$ (5 mL), $NaHCO_3$ (5 mL) and EtOAc (20 mL) were added at −78 °C. After extraction the organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. Column chromatography using pentane-EtOAc (4:1) yielded racemic **8** (85 mg, 63%) as a white solid, crystals were obtained via recrystallization from EtOH, mp 126-128 °C. IR (neat): 700, 740, 1000, 1035, 1170, 1385, 1450, 1490, 1595, 2950, 2970, 3065, 3415 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ = 1.59-1.76 (m, 3H), 1.79-1.91 (m, 1H), 2.89-2.97 (m, 1H), 3.15-3.20 (m, 1H), 4.15 (dd, J_1 = 9.2 Hz, J_2 = 6.5 Hz, 1H),

[4] Reiners, I.; Wilken, J., Martens. J. *Tetrahedron: Asymmetry*, **1995**, *6*, 3063.

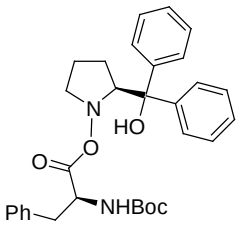
7.12-7.18 (m, 2H), 7.24-7.31 (m, 4H), 7.47-7.49 (m, 2H), 7.62-7.65 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 21.4 (2 C), 59.0, 74.0, 77.9, 125.5 (2 C), 126.0 (2 C), 126.5, 126.6, 128.1 (4 C), 145.3, 147.2. MS (ES^+): *m/z* (%) = 292 (100) $[M + Na]^+$, 270 (73) $[M + H]^+$, 252 (45) $[M + H - H_2O]^+$. Anal. Calcd (%) for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 76.05; H, 7.31; N, 5.09.

Acylation of *N*-hydroxy-pyrrolidine 8: preparation of diastereoisomeric 9 and 10.



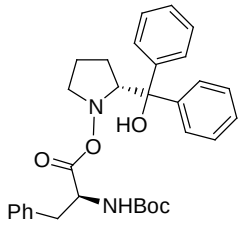
A solution of **8** (269 mg, 1.0 mmol) in CH_2Cl_2 (5 mL) was added to a solution of *N*-Boc-L-PheOH (318 mg, 1.2 mmol) and DCC (247 mg, 1.2 mmol) in CH_2Cl_2 (5 mL) at 0 °C. After 30 min, the urea was filtered off and the filtrate was concentrated. Column chromatography using pentane-EtOAc (4:1) yielded a mixture (1:1) of diastereomers **9** and **10** (490 mg, 95%) as a colourless oil. The diastereomers **9** (217 mg, 84%, first eluted) and **10** (194 mg, 75%) were separated by column chromatography (pentane-EtOAc, 9:1). Separation by recrystallization was also possible: 980 mg of a 1:1 mixture of **9** and **10** were dissolved in 10 mL of a refluxing mixture of pentane and EtOAc (4:1). On cooling, 150 mg (31 % yield) of pure **9** fell out. The mother liquor was concentrated, then recrystallized in 5 mL of the same solvent. 100 mg (20 % yield) of pure **10** cristallized.

(*S*)-2-*tert*-Butoxycarbonylamino-3-phenyl-propionic acid (*S*)-2-(hydroxy-diphenyl- methyl)-pyrrolidin-1-yl ester (9) white solid, crystals were obtained via recrystallization from pentane-EtOAc, mp 127-128 °C. IR (neat): 705, 745, 1060, 1155, 1345, 1490, 1705, 1755, 2925, 2980, 3445 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.45 (s, 9H), 1.68-1.84 (m, 4H), 2.63-2.86 (m, 3H), 3.30-3.34 (m, 1H), 3.65-3.70 (m, 1H), 4.31-4.35 (m, 1H), 4.49 (d, *J* = 7.1 Hz, 1H), 7.02-7.05 (m, 2H), 7.06-7.15 (m, 2H), 7.19-7.27 (m, 7H), 7.47-7.50 (m, 2H), 7.54-7.58 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 19.8, 24.6, 28.4 (3 C), 38.5, 52.9, 56.6, 71.4, 77.2, 79.6, 125.1 (2 C), 125.8 (2 C), 126.5, 126.7, 126.8, 127.8 (2 C), 128.1 (2 C), 128.3 (2 C), 129.4 (2 C), 136.1, 145.4, 146.4, 154.3, 170.6. MS (ES^+): *m/z* (%) = 539 (28) $[M + Na]^+$, 517 (77) $[M + H]^+$, 499 (34) [M +

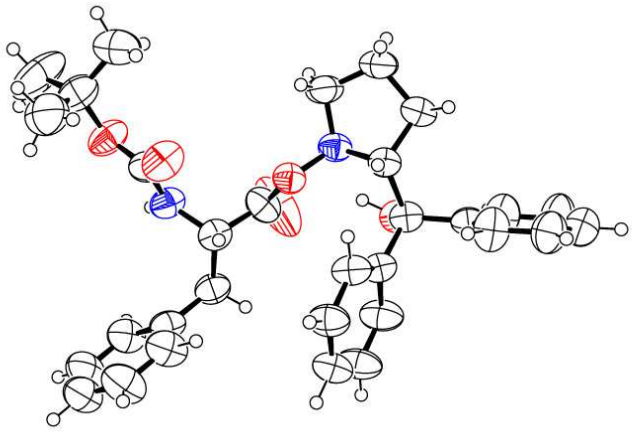


H – H_2O]$^+$, 234 (100). HRMS: m/z [M + Na] calcd for $C_{31}H_{36}N_2O_5Na$: 539.2522; found: 539.2516.

(*S*)-2-*tert*-Butoxycarbonylamino-3-phenyl-propionic acid (*R*)-2-(hydroxy-diphenyl-methyl)-pyrrolidin-1-yl ester (10) white solid, crystals were obtained via recrystallization from pentane-EtOAc, mp 133-134 °C. IR (neat): 695, 750, 1140, 1495, 1700, 1745, 2895, 2935, 2975, 3060, 3400 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.38 (s, 9H), 1.75-1.87 (m, 4H), 2.27-2.43 (m, 2H), 2.93-3.01 (m, 1H), 3.38-3.43 (m, 1H), 3.83-3.90 (m, 1H), 4.39-4.50 (m, 2H), 6.98-7.01 (m, 2H), 7.06-7.15 (m, 2H), 7.20-7.27 (m, 7H), 7.47-7.50 (m, 2H), 7.61-7.64 (m, 2H). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 20.5, 25.3, 28.2 (3 C), 37.0, 53.2, 57.2, 71.6, 76.8, 79.9, 125.3 (2 C), 126.0 (2 C), 126.5, 126.6, 126.7, 127.9 (2 C), 128.0 (2 C), 128.3 (2 C), 129.3 (2 C), 136.2, 145.5, 146.7, 154.7, 170.4. MS (ES$^+$): *m/z* (%) = 539 (61) [M + Na]$^+$, 517 (100) [M + H]$^+$, 499 (21) [M + H – H_2O]$^+$. HRMS: m/z [M + Na] calcd for $C_{31}H_{36}N_2O_5Na$: 539.2522; found: 539.2517.

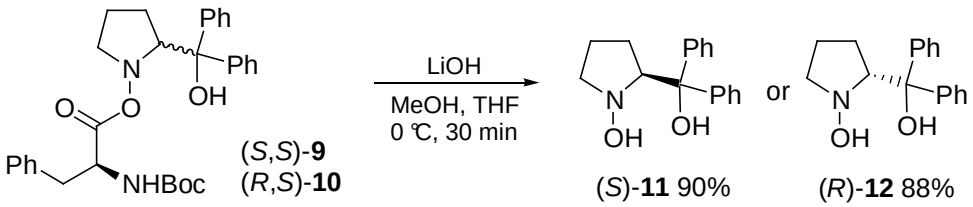


The absolute configuration of **10** was determined by X-ray crystallography:



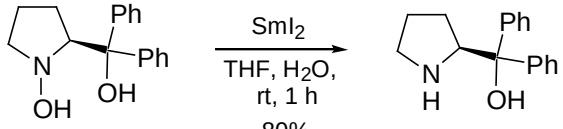
10

Hydrolysis of 9 and 10



A 1M methanolic solution of LiOH (0.4 mL, 0.4 mmol) was added to a solution of **9** (103 mg, 0.2 mmol) in THF (5 mL) at 0 °C. After 30 min, the reaction mixture was diluted with H_2O (10 mL) and EtOAc (15 mL). After extraction, the organic phase was washed with brine, dried over $MgSO_4$, filtered, and concentrated. Column chromatography using pentane-EtOAc (4:1) yielded (*S*)-2-(hydroxy-diphenyl-methyl)-pyrrolidin-1-ol **11**[5] (48 mg, 90%, $[\alpha]_D^{20}$ +23.7, (*c* 2.2, $CHCl_3$), 97% ee) as a colourless oil, which solidified upon standing. The same procedure for diastereomer **10** yielded (*R*)-2-(hydroxy-diphenyl-methyl)-pyrrolidin-1-ol **12** (47 mg, 88%, $[\alpha]_D^{20}$ –24.8, (*c* 2.2, $CHCl_3$), 96% ee) as a colorless oil, which solidified upon standing. The enantiomeric purity of **11** and **12** was determined by chiral HPLC on a Daicel Chiralpak AD-RH column, 4.6 x 100 mm, eluent acetonitrile/water 70/30, 0.9 mL/min, retention time for (*S*)-**11** 6.83 min and for (*R*)-**12** 4.23 min.

Reduction of (+)-(*S*)-2-(hydroxy-diphenyl-methyl)-pyrrolidin-1-ol 11 to (-)-(*S*)-DPP.

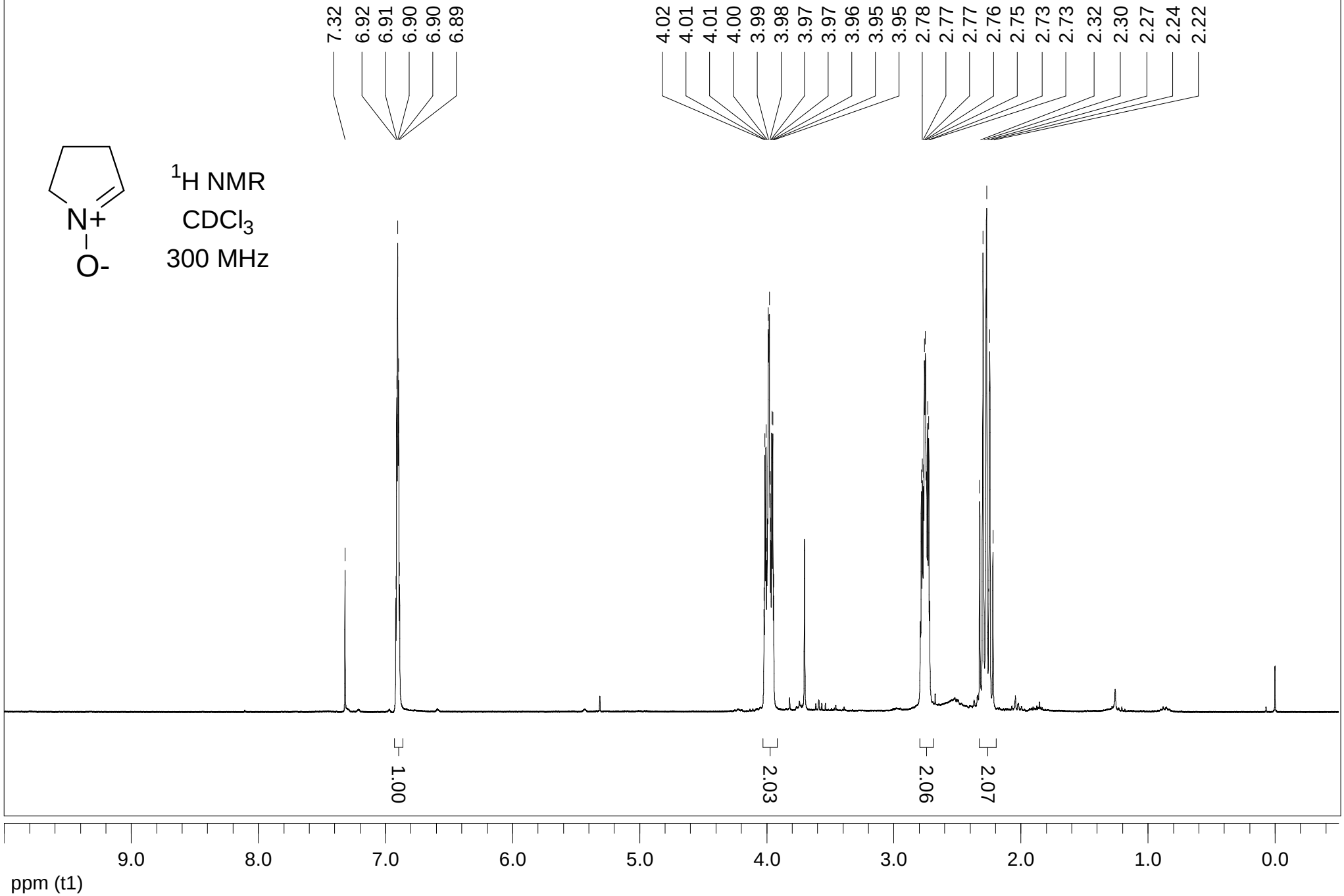


11 (*S*)-**DPP**

To a stirred and carefully deoxygenated solution of the product **11** (27 mg, 0.1 mmol) and degassed water (9 μL, 0.5 mmol) in 1 mL of dry THF, a 0.1 M solution of SmI_2 (2.5 mL, 0.25 mmol) was added at r.t. under argon. After 1 hour, a saturated solution of $Na_2S_2O_3$ (1 mL), a 1M NaOH solution (5 mL) and EtOAc (10 mL) were added. After extraction the organic phase was washed with brine, dried over Na_2SO_4, filtered, and concentrated affording 20 mg (80%) of crude (*S*)-**DPP** as a colourless oil. The sample was identical to commercial (*S*)-DPP. $[\alpha]_D^{20}$ of the crude material was –44.2, (*c* 1.3, MeOH) (lit.[6] $[\alpha]_D^{20}$ –54.3 (*c* 0.261, MeOH) and lit.[7] $[\alpha]_D^{20}$ –58.8, (*c* 3.0, MeOH)).

[5] O'Neil, I. A.; Cleator, E.; Tapolczay, D. J. *Tetrahedron Lett.* **2001**, *42*, 8247.
[6] Mathre, D. J.; Jones, T. K.; Xavier, L. C.; Blacklock, T. J.; Reamer, R. A.; Mohan, J. J.; Jones, E. T. T.; Hoogsteen, K.; Baum, M. W.; Grabowski, E. J. J. *J. Org. Chem.* **1991**, *56*, 751.
[7] Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551.

product 1

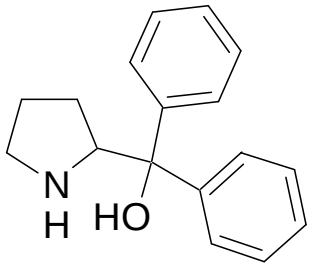

7.32
6.92
6.91
6.90
6.90
6.89
4.02
4.01
4.01
4.00
3.99
3.98
3.97
3.97
3.96
3.95
3.95
2.78
2.77
2.77
2.76
2.75
2.73
2.73
2.32
2.30
2.27
2.24
2.22
N+
O-
1H NMR
CDCl3
300 MHz
1.00
2.03
2.06
2.07
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

product 2

7.58 7.58 7.55 7.55 7.51 7.50 7.48 7.48 7.31 7.28 7.26 7.26 7.25 7.24 7.18 7.18 7.17 7.16 7.15 7.13 7.13

4.27 4.25 4.22 3.06 3.03 3.01 2.99 2.97 2.95 2.93 2.92 2.89

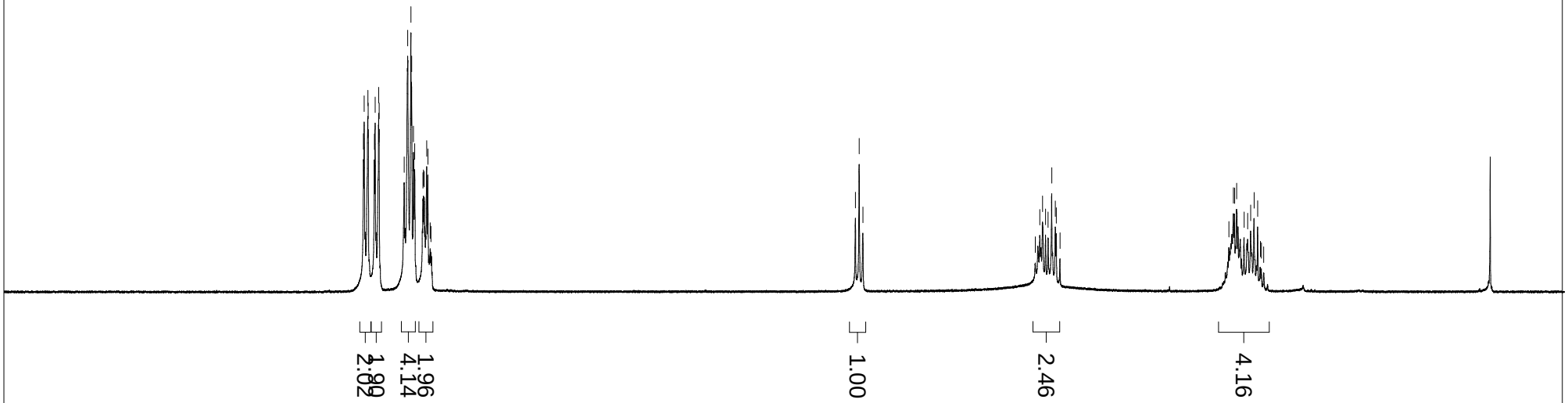
1.76 1.73 1.72 1.71 1.66 1.63 1.61 1.59 1.56 1.55 1.54 1.52

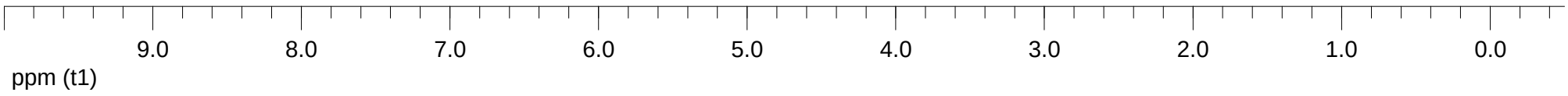


^{1}H NMR

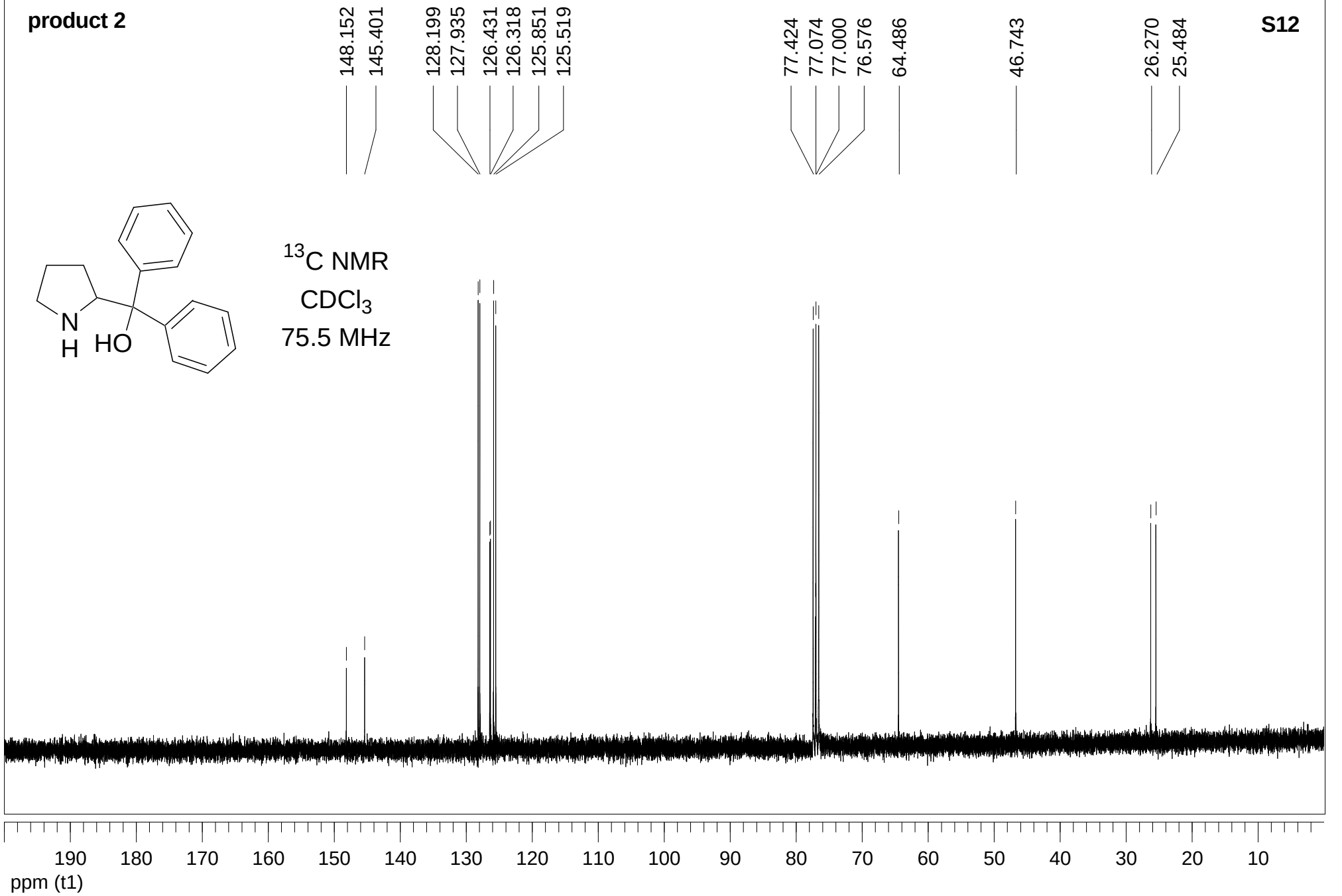
$CDCl_3$

300 MHz

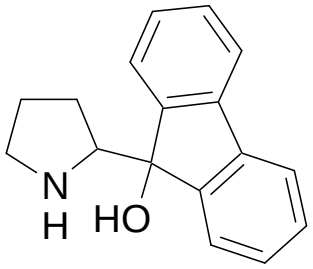




product 2


148.152
145.401
128.199
127.935
126.431
126.318
125.851
125.519
77.424
77.074
77.000
76.576
64.486
46.743
26.270
25.484
N
H
HO
13C NMR
CDCl3
75.5 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

product 3



^{1}H NMR

D_6-DMSO

300 MHz

7.747 7.720 7.693 7.506 7.481 7.361 7.357 7.336 7.332 7.311 7.308 7.286 7.282 7.258 7.235 7.232 7.211 7.207

3.634 3.609 3.584 2.806 2.774 2.752 2.748 2.727 2.705 2.694 2.673 2.506 2.500

1.440 1.435 1.398 1.378 1.298 1.283 1.260 1.230 1.213 1.204 1.188 0.855 0.824 0.799

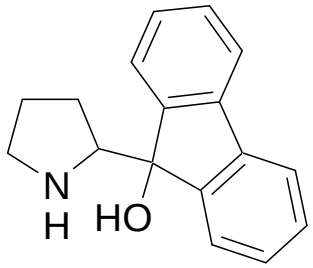
2.86 0.95 3.99 0.93 1.00 2.12 3.07 0.98

9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0

ppm (t1)

product 3

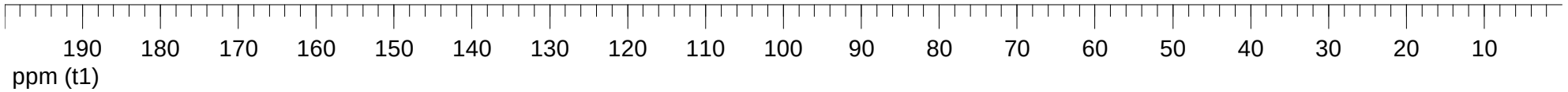
149.253
147.760
139.875
139.259
128.069
128.052
127.238
126.861
125.941
123.842
119.471
119.161
82.755
65.515
46.447
39.988
39.708
39.430
39.152
38.875
26.313
25.200



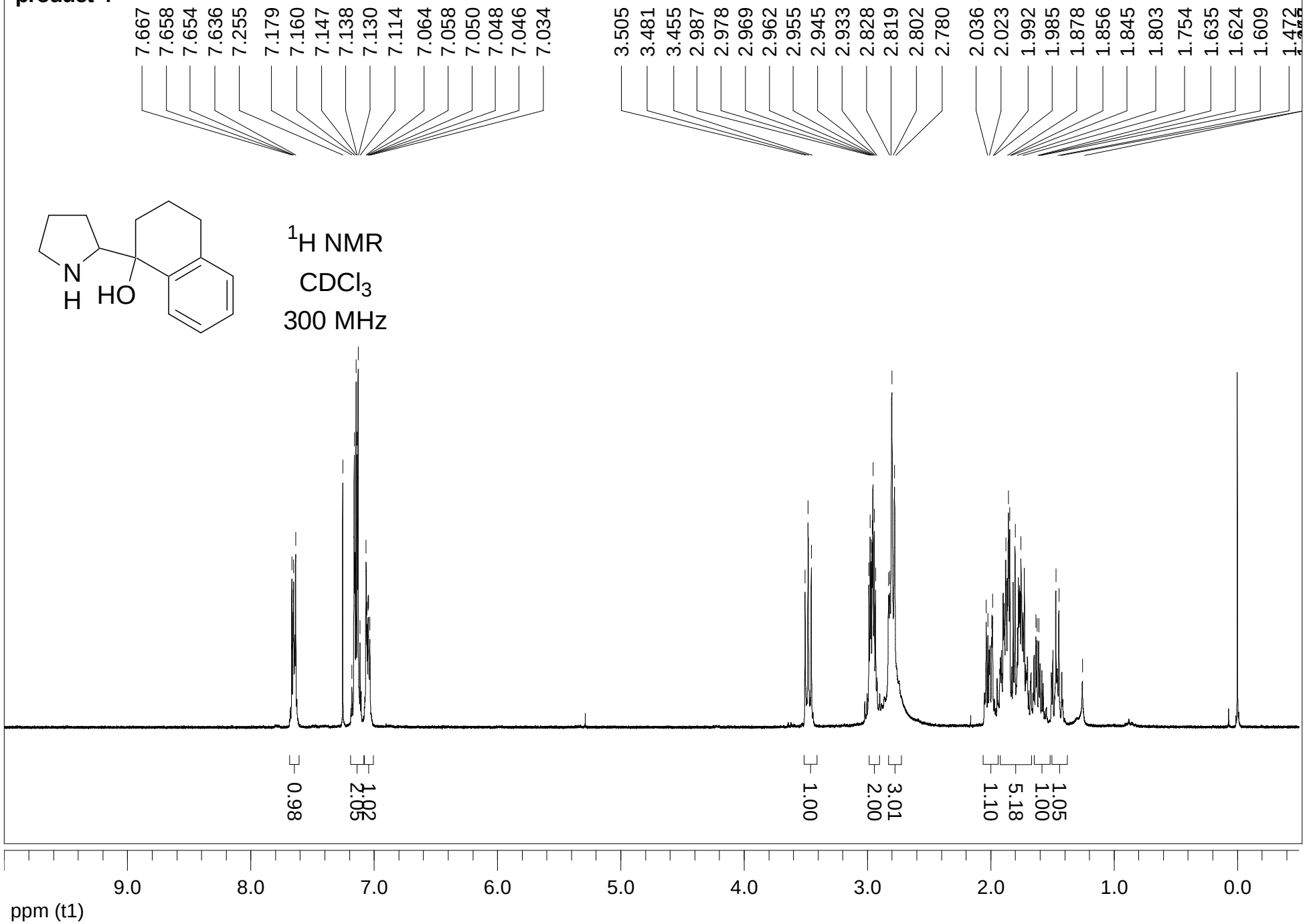
^{13}C NMR

D_6-DMSO

75.5 MHz



product 4


7.667
7.658
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7.636
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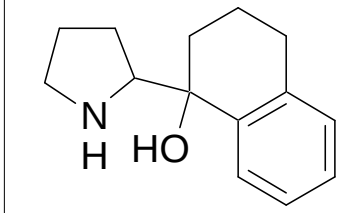
7.179
7.160
7.147
7.138
7.130
7.114
7.064
7.058
7.050
7.048
7.046
7.034
3.505
3.481
3.455
2.987
2.978
2.969
2.962
2.955
2.945
2.933
2.828
2.819
2.802
2.780
2.036
2.023
1.992
1.985
1.878
1.856
1.845
1.803
1.754
1.635
1.624
1.609
N
H
HO
1H NMR
CDCl3
300 MHz
0.98
2.05
1.02
1.00
2.00
3.01
1.10
5.18
1.00
1.05
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

product 4



^{13}C NMR

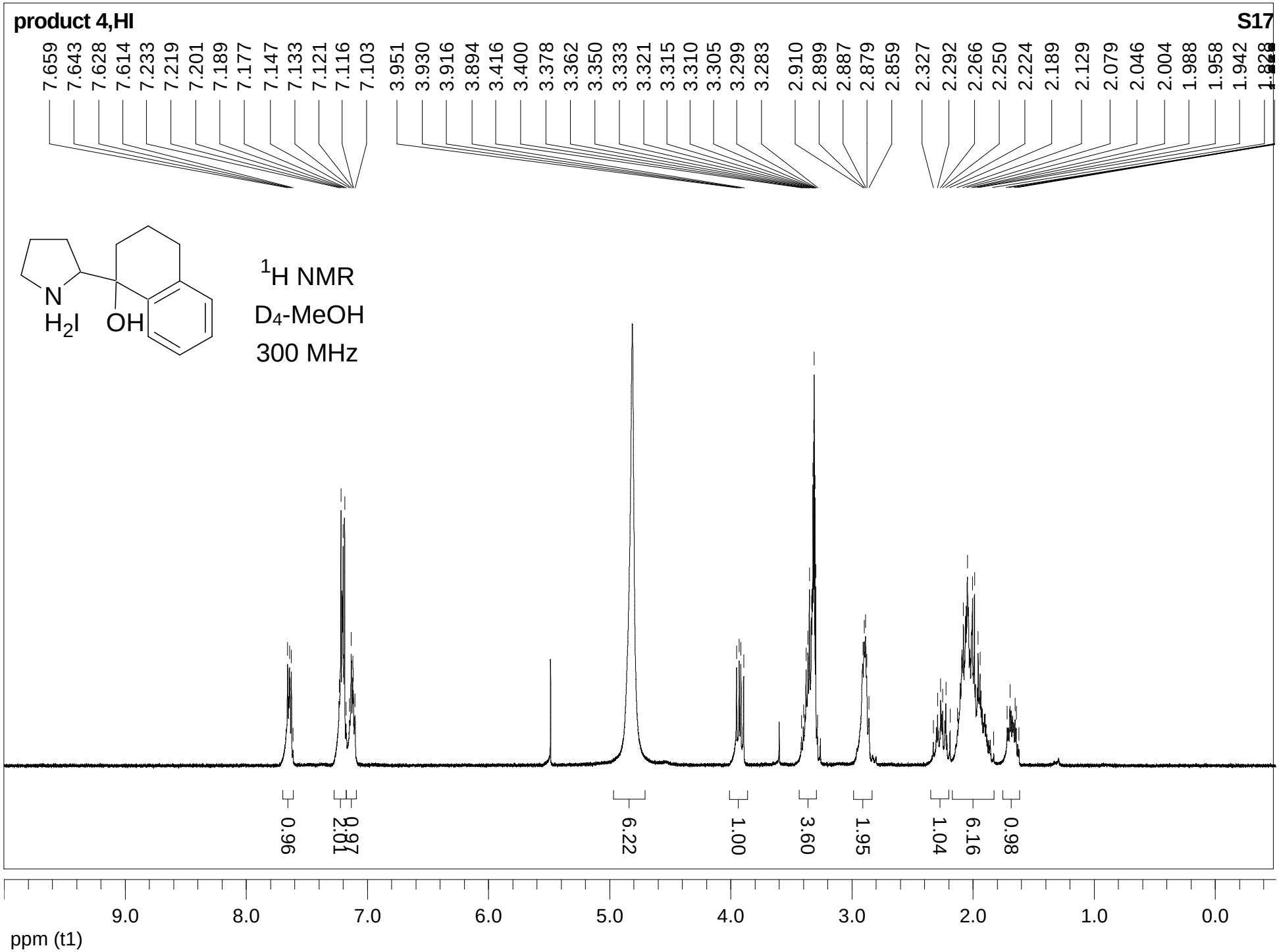
$CDCl_3$

75.5 MHz

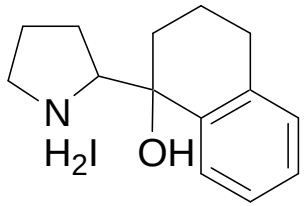
140.799
137.033
128.471
126.773
126.622
125.463
77.423
77.000
76.576
71.957
64.768
46.677
35.298
28.864
26.493
26.392
19.219

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

ppm (t1)


product 4,HI
S17
7.659
7.643
7.628
7.614
7.233
7.219
7.201
7.189
7.177
7.147
7.133
7.121
7.116
7.103
3.951
3.930
3.916
3.894
3.416
3.400
3.378
3.362
3.350
3.333
3.321
3.315
3.310
3.305
3.299
3.283
2.910
2.899
2.887
2.879
2.859
2.327
2.292
2.266
2.250
2.224
2.189
2.129
2.079
2.046
2.004
1.988
1.958
1.942
N
H2I
OH
1H NMR
D4-MeOH
300 MHz
0.96
2.01
0.97
6.22
1.00
3.60
1.95
1.04
6.16
0.98
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

product 4,HI



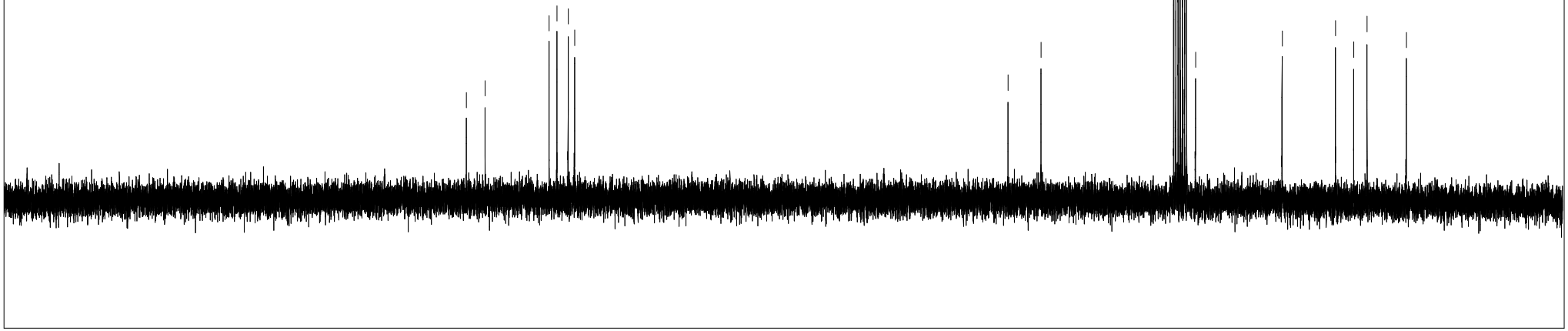
^{13}C NMR

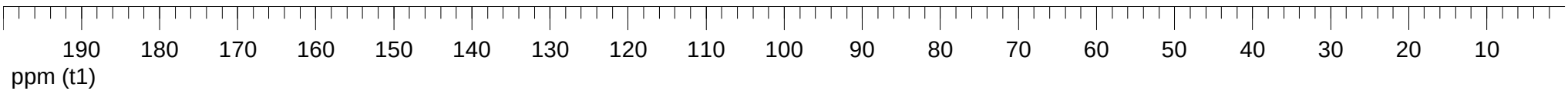
D_4-MeOH

75.5 MHz

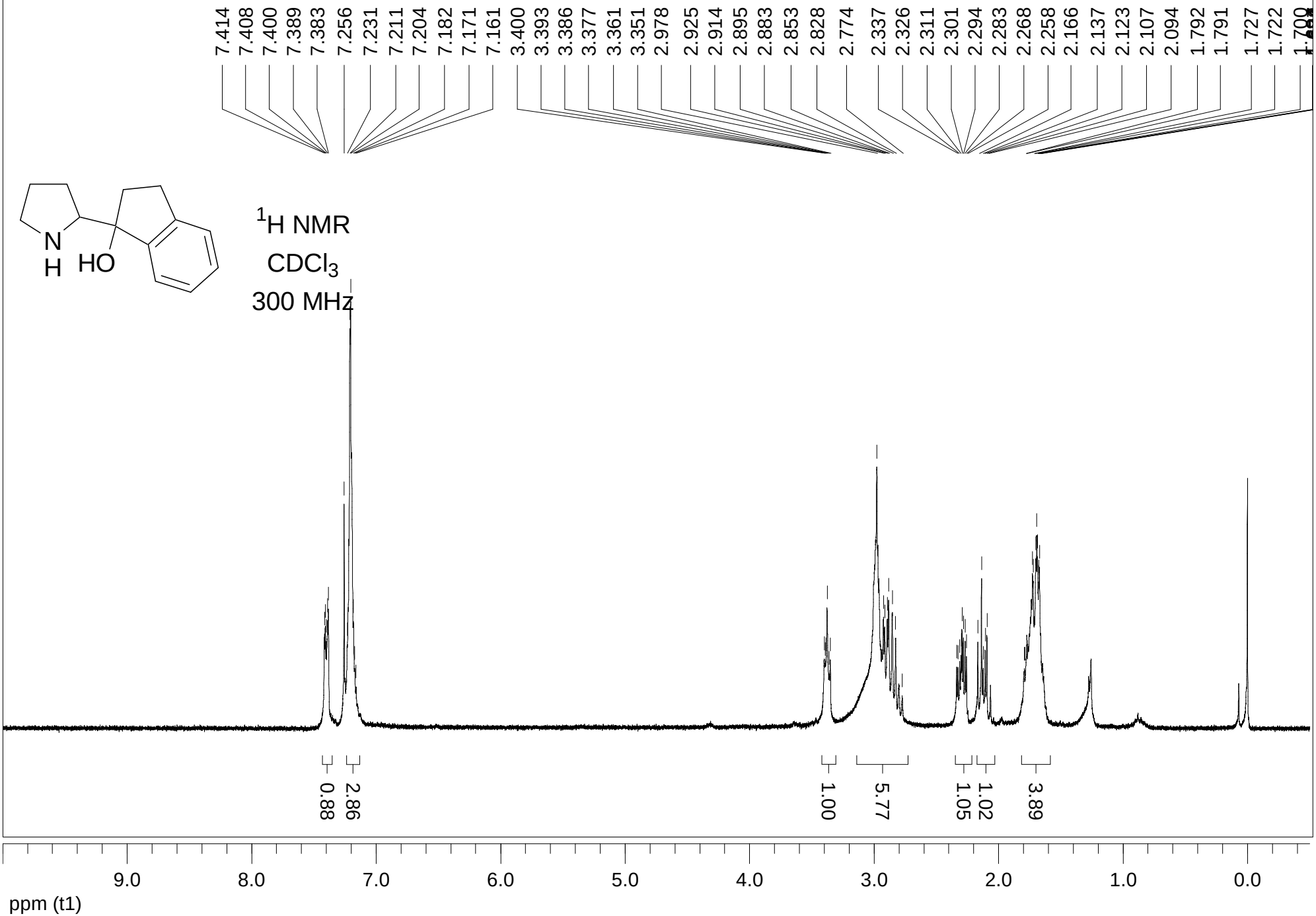
140.699 138.250 130.050 129.044 127.620 126.797

71.185 66.925 49.902 49.618 49.334 49.315 49.050 48.766 48.748 48.482 48.198 47.112 35.992 29.137 26.782 25.072 20.053

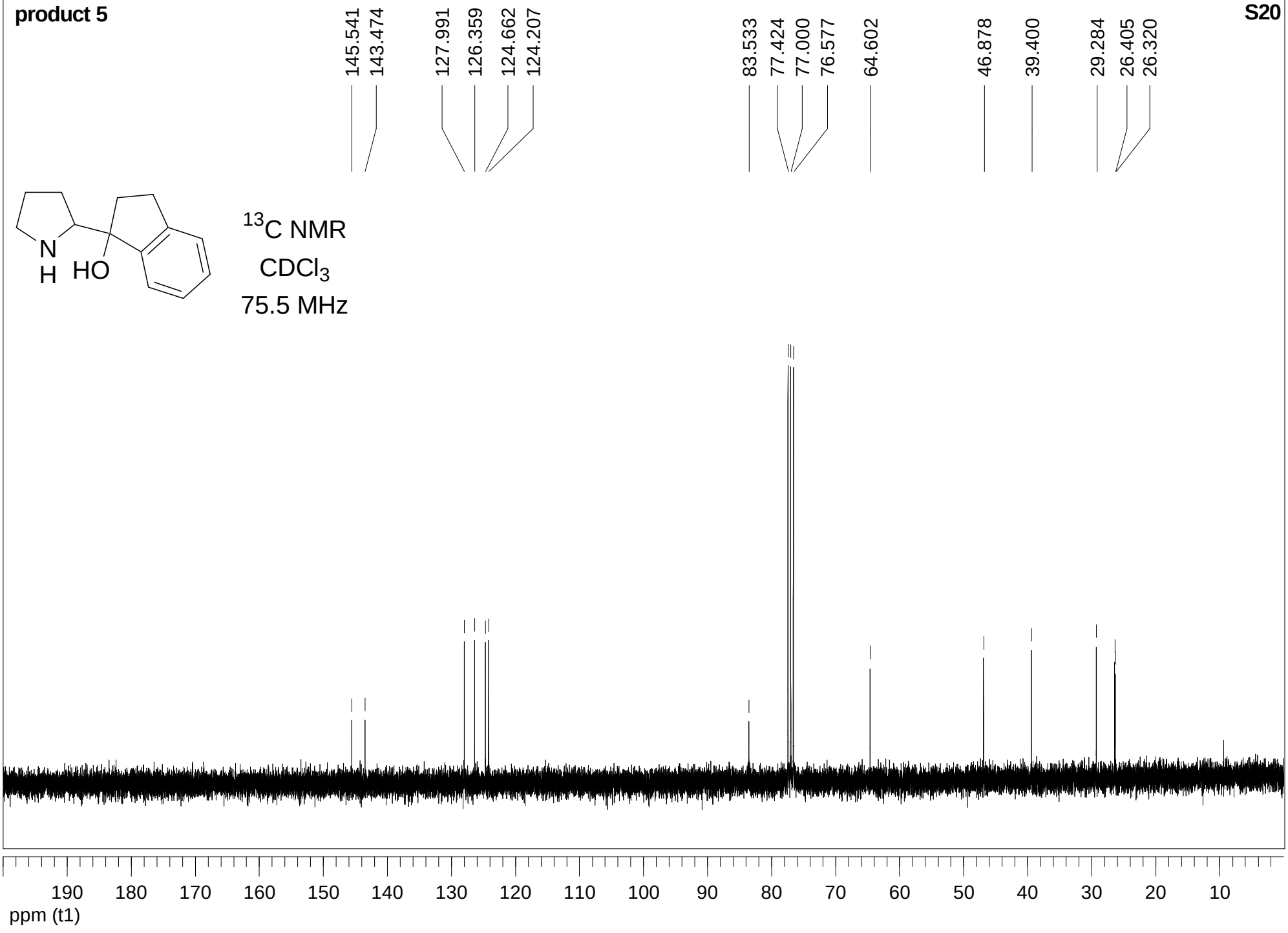




product 5


7.414
7.408
7.400
7.389
7.383
7.256
7.231
7.211
7.204
7.182
7.171
7.161
3.400
3.393
3.386
3.377
3.361
3.351
2.978
2.925
2.914
2.895
2.883
2.853
2.828
2.774
2.337
2.326
2.311
2.301
2.294
2.283
2.268
2.258
2.166
2.137
2.123
2.107
2.094
1.792
1.791
1.727
1.722
N
H
HO
1H NMR
CDCl3
300 MHz
0.88
2.86
1.00
5.77
1.05
1.02
3.89
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

product 5


145.541
143.474
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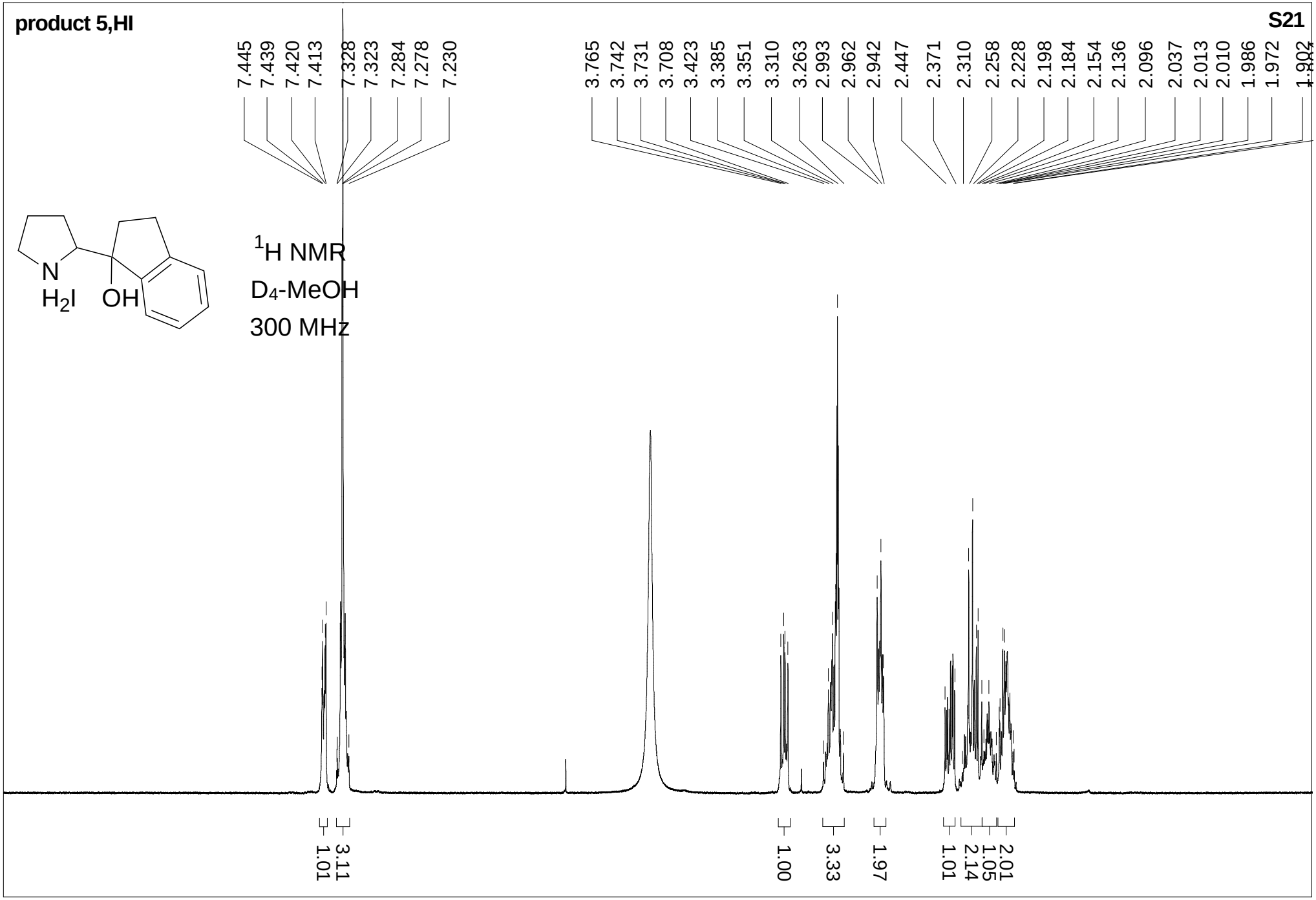
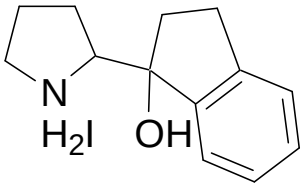
126.359
124.662
124.207
83.533
77.424
77.000
76.577
64.602
46.878
39.400
29.284
26.405
26.320
N
H
HO
13C NMR
CDCl3
75.5 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

product 5,HI

S21



product 5,HI



^{13}C NMR

D_4-MeOH

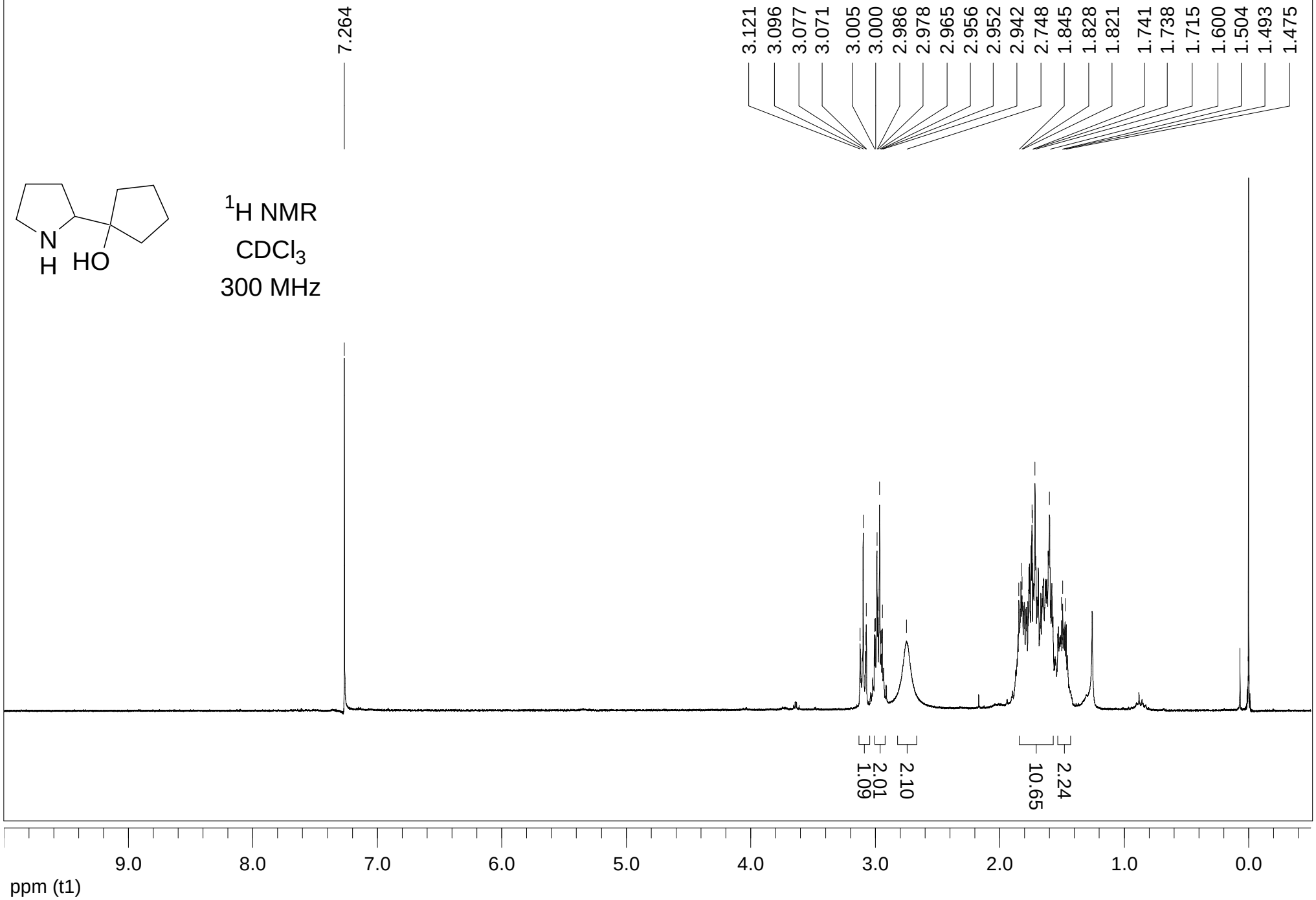
75.5 MHz

145.142
144.397
130.093
127.868
126.243
125.210
82.128
66.765
49.901
49.618
49.334
49.050
48.766
48.482
48.198
47.324
40.725
29.643
26.415
25.400

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10

ppm (t1)

product 6


7.264
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3.077
3.071
3.005
3.000
2.986
2.978
2.965
2.956
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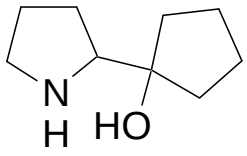
2.942
2.748
1.845
1.828
1.821
1.741
1.738
1.715
1.600
1.504
1.493
1.475
N
H
HO
^{1}H NMR
$CDCl_3$
300 MHz
1.09
2.01
2.10
10.65
2.24
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

product 6

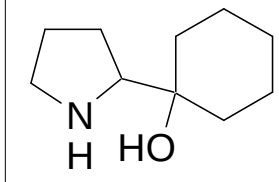


^{13}C NMR

$CDCl_3$

75.5 MHz

product 7

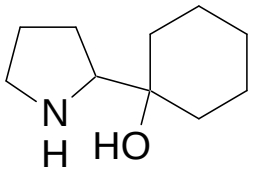


^{1}H NMR

$CDCl_3$

300 MHz

product 7

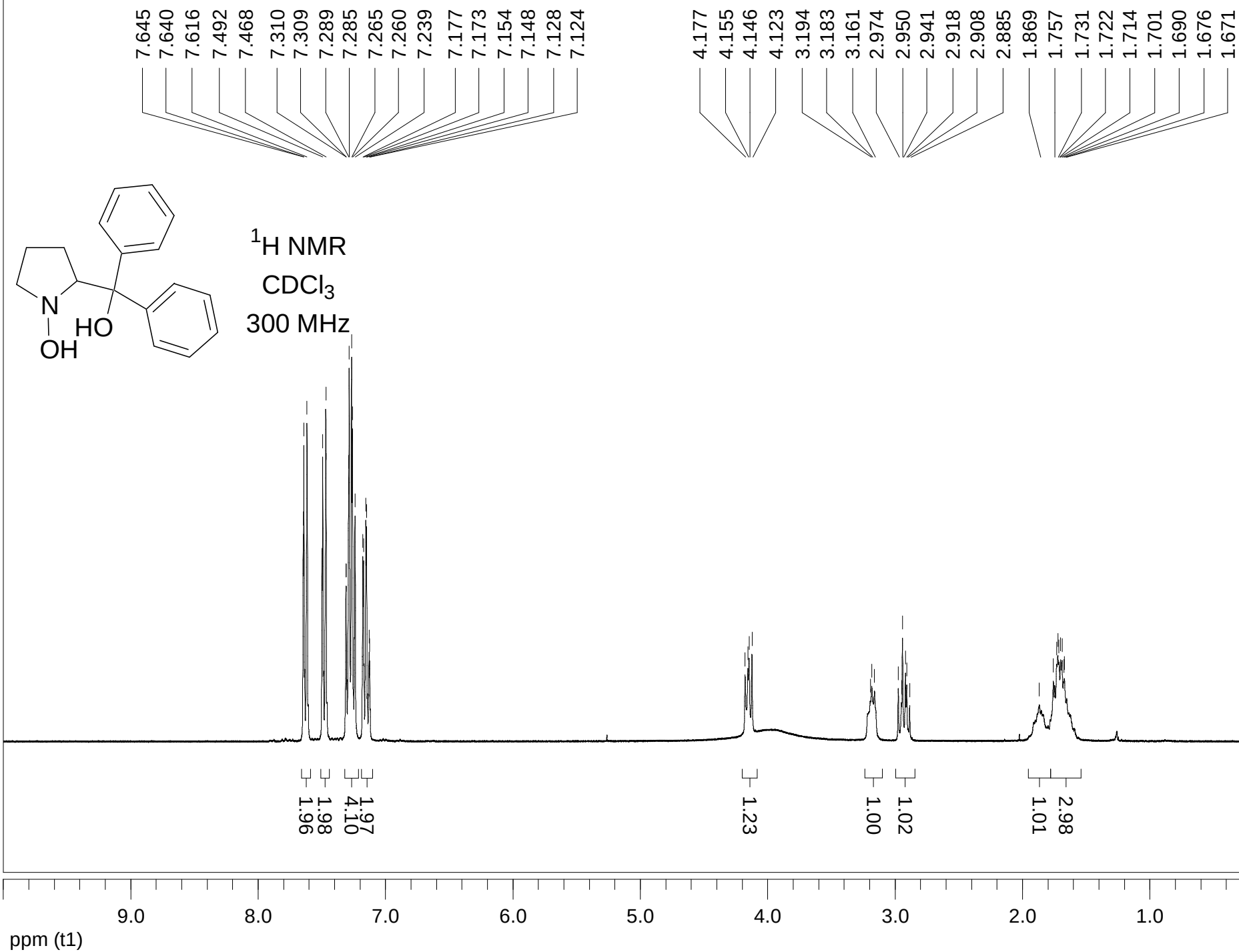


^{13}C NMR

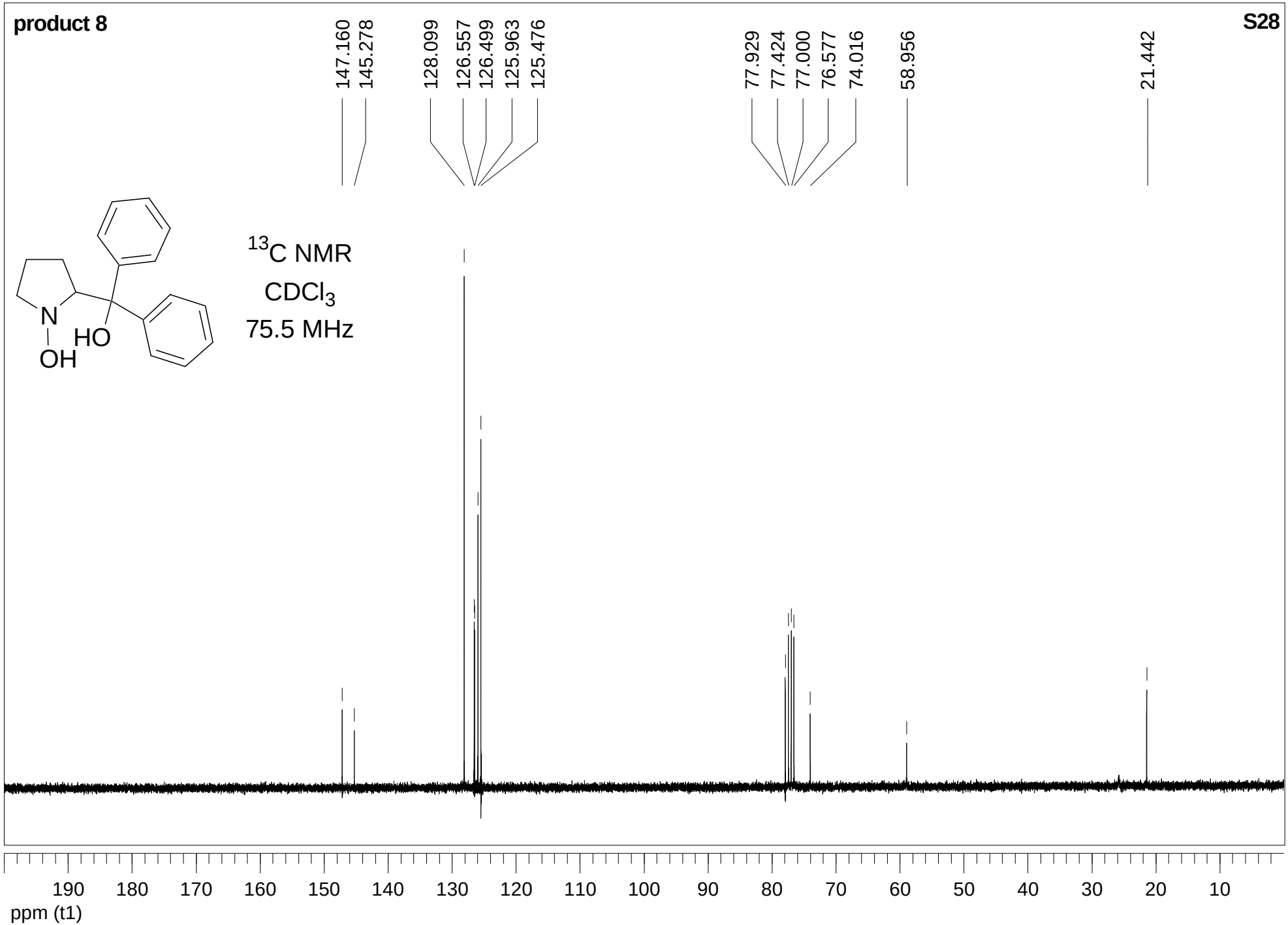
$CDCl_3$

75.5 MHz

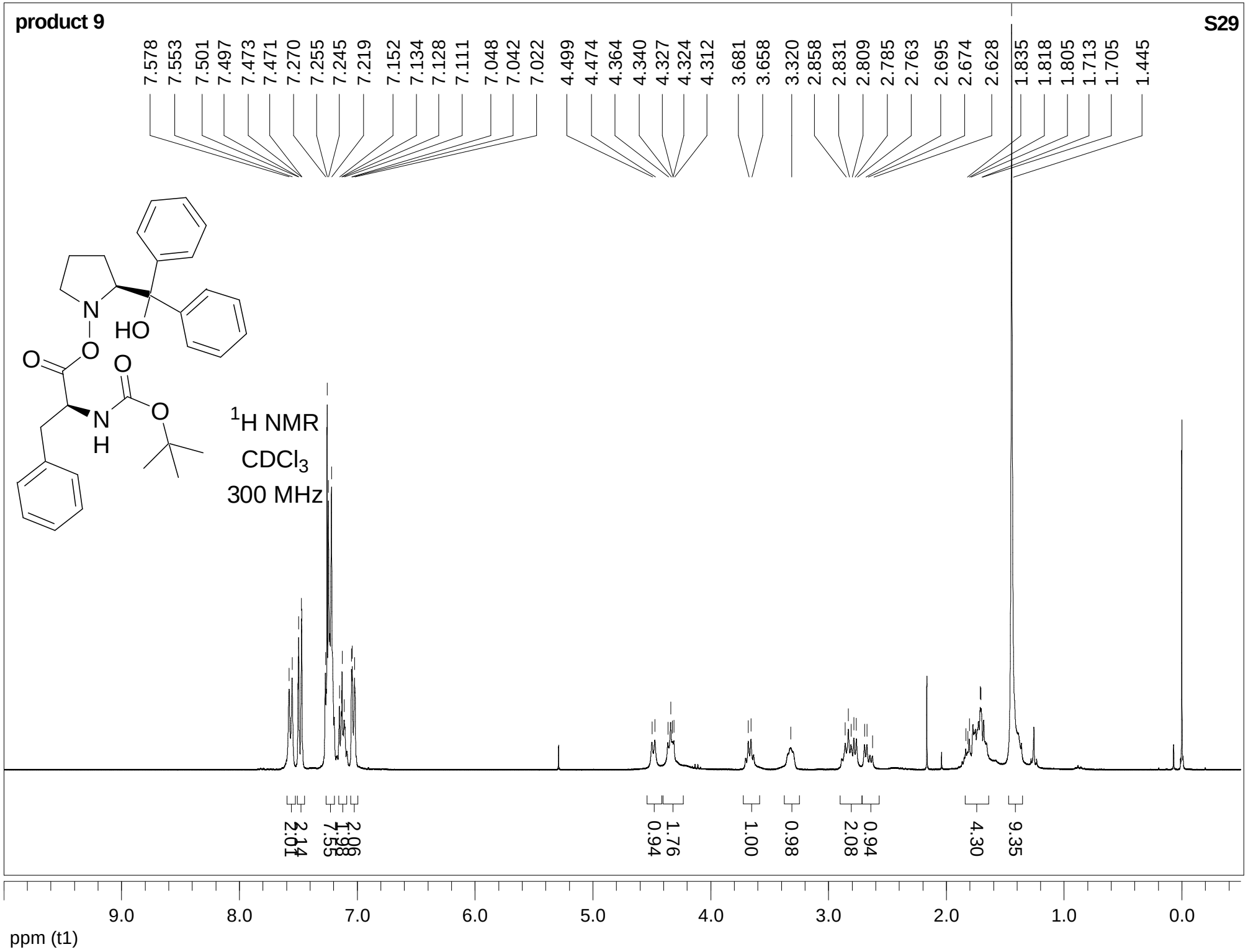
product 8

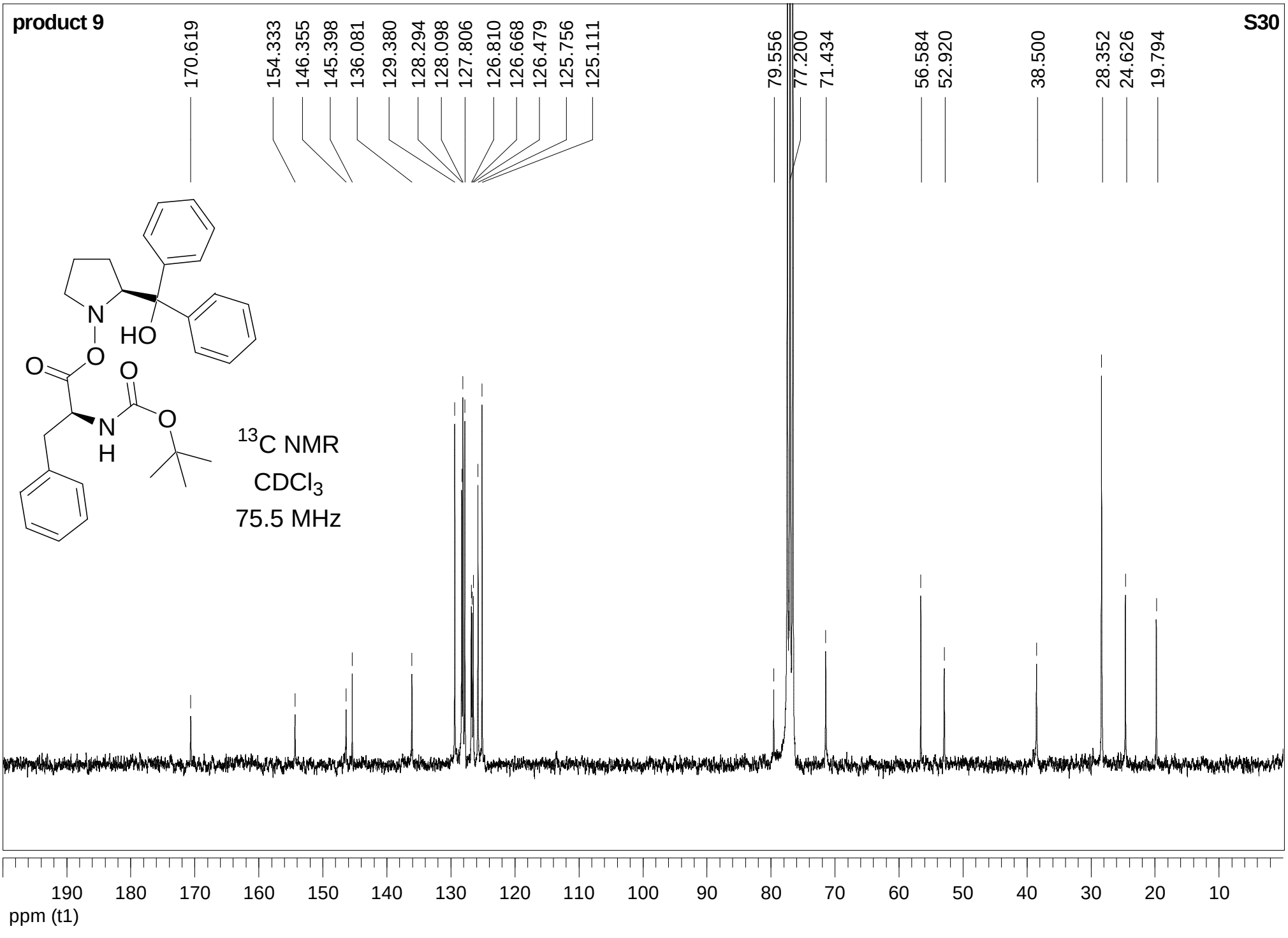

7.645
7.640
7.616
7.492
7.468
7.310
7.309
7.289
7.285
7.265
7.260
7.239
7.177
7.173
7.154
7.148
7.128
7.124
4.177
4.155
4.146
4.123
3.194
3.183
3.161
2.974
2.950
2.941
2.918
2.908
2.885
1.869
1.757
1.731
1.722
1.714
1.701
1.690
1.676
1.671
N
HO
OH
1H NMR
CDCl3
300 MHz
1.96
1.98
4.10
1.97
1.23
1.00
1.02
1.01
2.98
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

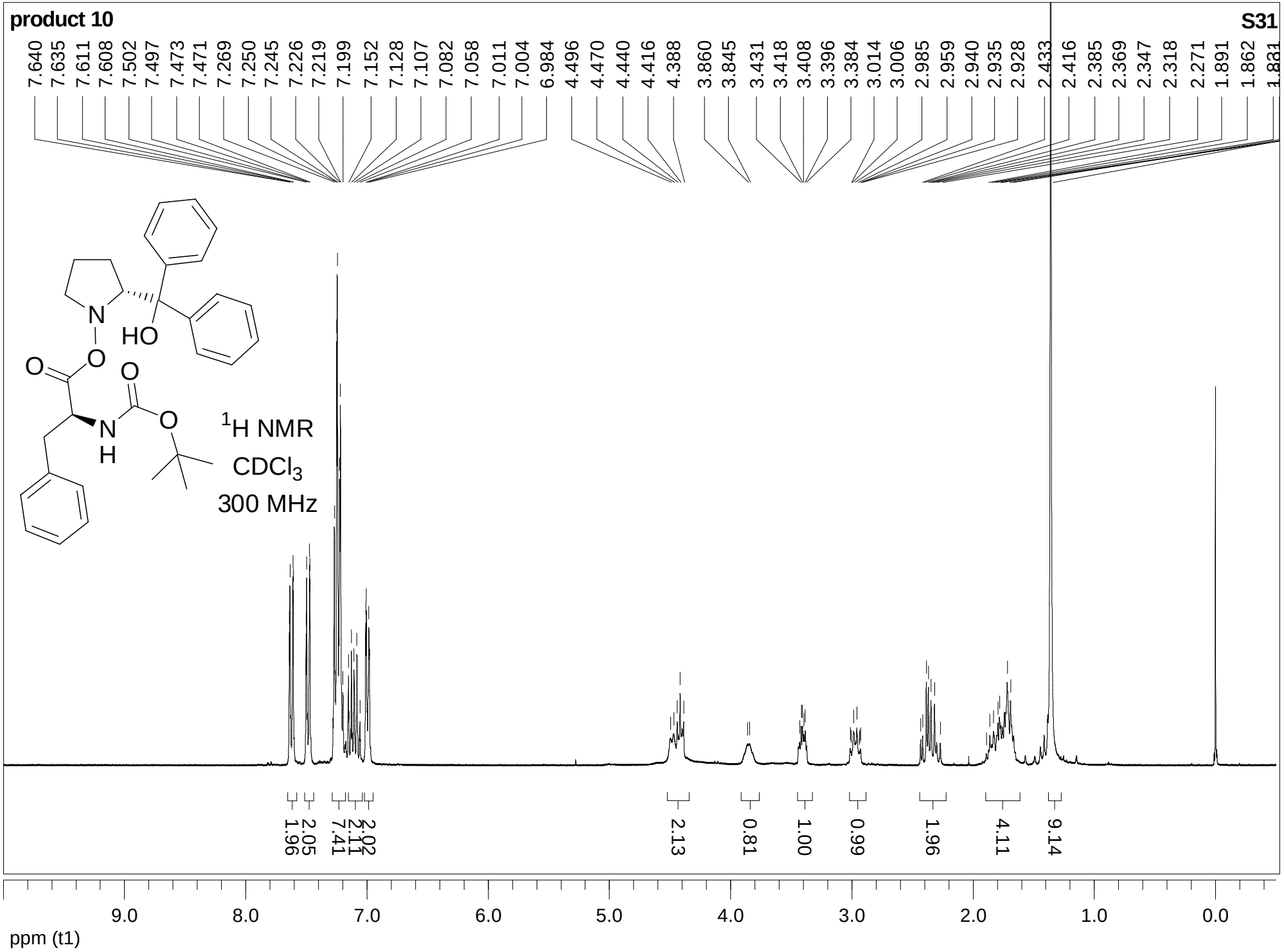
product 8


147.160
145.278
128.099
126.557
126.499
125.963
125.476
77.929
77.424
77.000
76.577
74.016
58.956
21.442
N
HO
OH
^{13}C NMR
$CDCl_3$
75.5 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

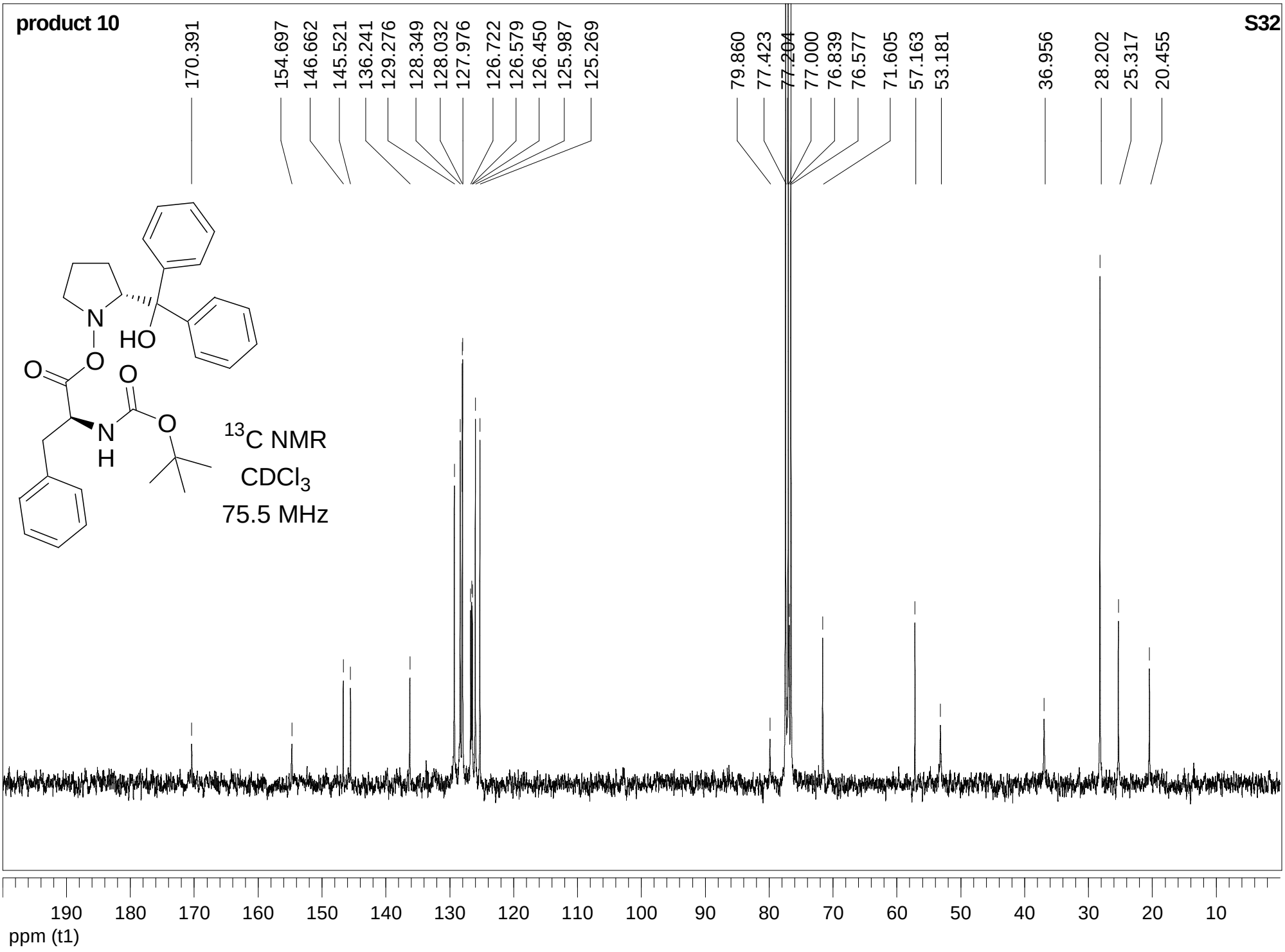
product 9


7.578
7.553
7.501
7.497
7.473
7.471
7.270
7.255
7.245
7.219
7.152
7.134
7.128
7.111
7.048
7.042
7.022
4.499
4.474
4.364
4.340
4.327
4.324
4.312
3.681
3.658
3.320
2.858
2.831
2.809
2.785
2.763
2.695
2.674
2.628
1.835
1.818
1.805
1.713
1.705
1.445
N
HO
O
O
O
O
N
H
O
^{1}H NMR
$CDCl_3$
300 MHz
2.01
2.14
7.55
4.00
2.06
0.94
1.79
1.00
0.98
2.08
0.94
4.30
9.35
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

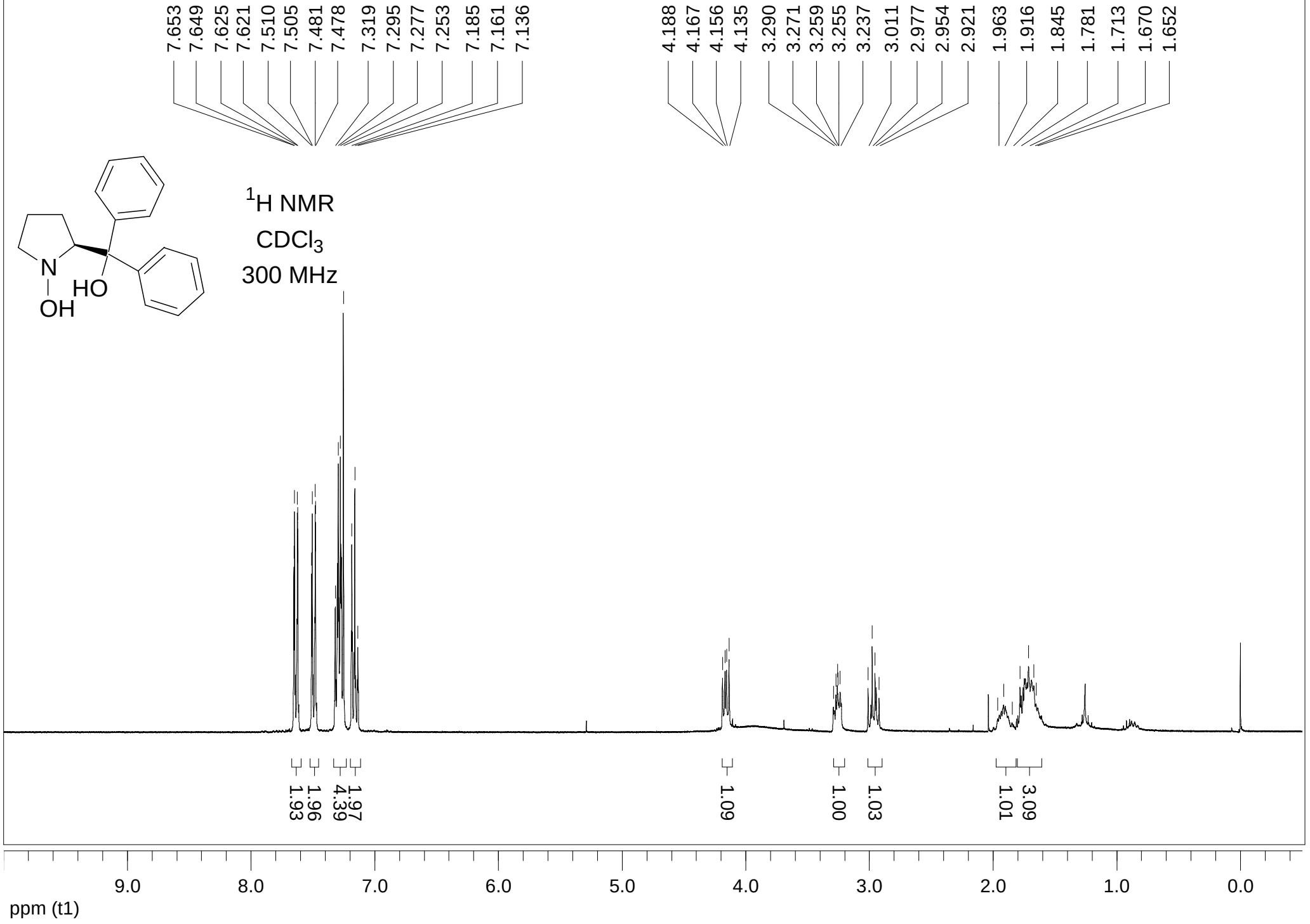

product 9
S30
170.619
154.333
146.355
145.398
136.081
129.380
128.294
128.098
127.806
126.810
126.668
126.479
125.756
125.111
79.556
77.200
71.434
56.584
52.920
38.500
28.352
24.626
19.794
HO
^{13}C NMR
$CDCl_3$
75.5 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

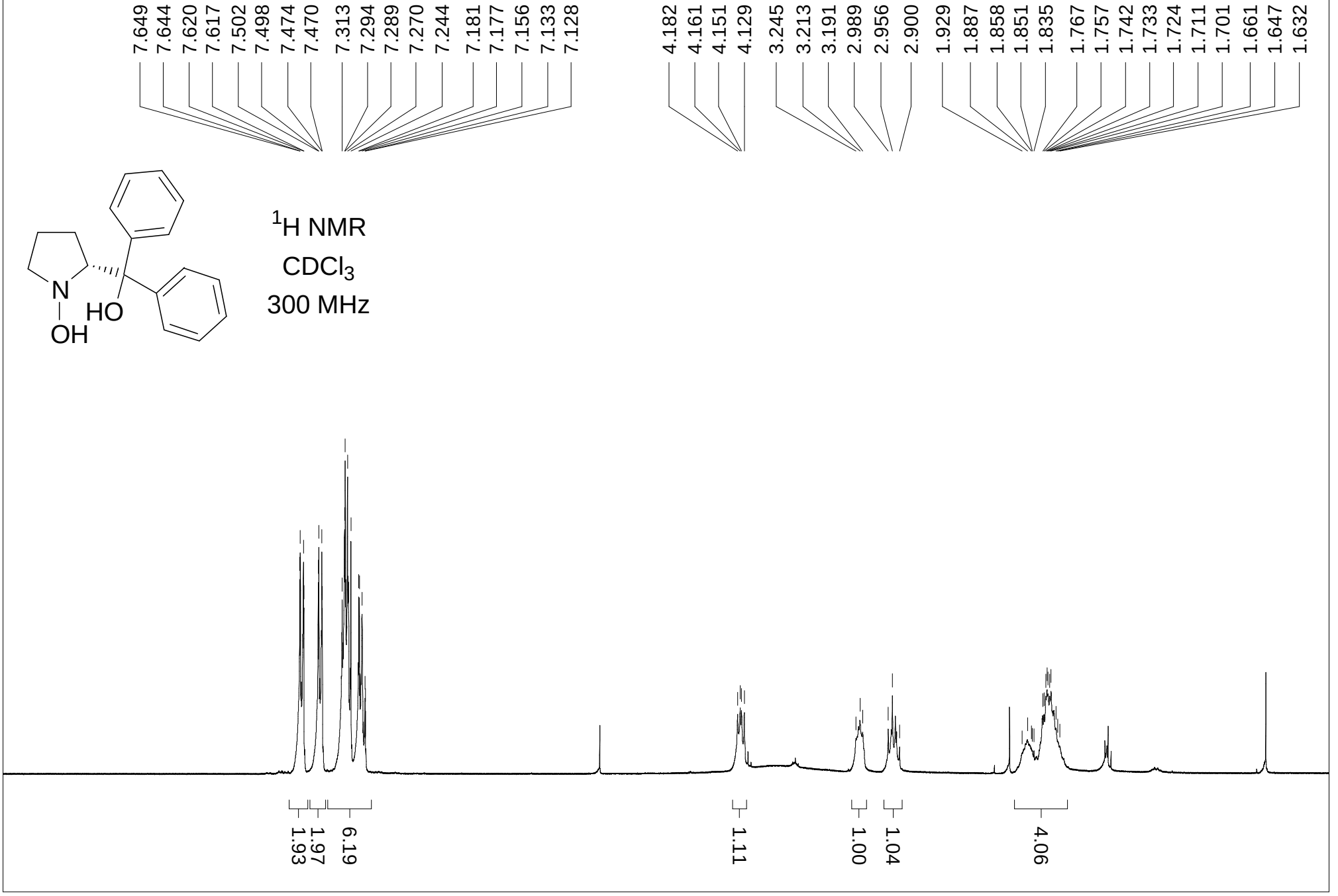

product 10
S31
7.640
7.635
7.611
7.608
7.502
7.497
7.473
7.471
7.269
7.250
7.245
7.226
7.219
7.199
7.152
7.128
7.107
7.082
7.058
7.011
7.004
6.984
4.496
4.470
4.440
4.416
4.388
3.860
3.845
3.431
3.418
3.408
3.396
3.384
3.014
3.006
2.985
2.959
2.940
2.935
2.928
2.433
2.416
2.385
2.369
2.347
2.318
2.271
1.891
1.862
1.821
HO
O
O
O
O
N
H
^{1}H NMR
$CDCl_3$
300 MHz
1.96
2.05
7.41
2.11
2.02
2.13
0.81
1.00
0.99
1.96
4.11
9.14
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)

product 10


170.391
154.697
146.662
145.521
136.241
129.276
128.349
128.032
127.976
126.722
126.579
126.450
125.987
125.269
79.860
77.423
77.204
77.000
76.839
76.577
71.605
57.163
53.181
36.956
28.202
25.317
20.455
N
HO
O
O
O
O
N
H
O
13C NMR
CDCl3
75.5 MHz
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm (t1)

product (S)-11


7.653
7.649
7.625
7.621
7.510
7.505
7.481
7.478
7.319
7.295
7.277
7.253
7.185
7.161
7.136
4.188
4.167
4.156
4.135
3.290
3.271
3.259
3.255
3.237
3.011
2.977
2.954
2.921
1.963
1.916
1.845
1.781
1.713
1.670
1.652
N
HO
OH
1H NMR
CDCl3
300 MHz
1.93
1.96
4.39
1.97
1.09
1.00
1.03
1.01
3.09
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)


7.649
7.644
7.620
7.617
7.502
7.498
7.474
7.470
7.313
7.294
7.289
7.270
7.244
7.181
7.177
7.156
7.133
7.128
4.182
4.161
4.151
4.129
3.245
3.213
3.191
2.989
2.956
2.900
1.929
1.887
1.858
1.851
1.835
1.767
1.757
1.742
1.733
1.724
1.711
1.701
1.661
1.647
1.632
N
HO
OH
^{1}H NMR
$CDCl_3$
300 MHz
1.93
1.97
6.19
1.11
1.00
1.04
4.06
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t1)