Supporting Information

Asymmetric and Stereodivergent Syntheses of 3-Hydroxypiperidine Derivatives and 3-Hydroxypipecolic Acids

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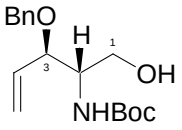
General Methods: All NMR spectra, i.e., ^{1}H, gCOSY, gHSQC, gHMBC, ROESY , were recorded on a 600 MHz NMR spectrometer, ^{13}C and DEPT, were recorded on a 400 MHz or a 600 MHz NMR spectrometer, which provided all necessary data for the full assignment of each compound. GC-MS analyses were performed with an Rtx-®-5MS capillary column (50 m X 0.25 mm, 0.5 μm). TLC analyses were performed on 60F-254, and were visualized with UV light, iodine chamber, 10% sulfuric acid or 10% PMA solution. Purifications were performed by flash chromatography on silica gel 60.

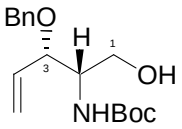
Materials: Chemicals, reagents and solvents were used after purification. Dichloromethane, pyridine, triethylamine, acetonitrile, DMSO and methanol were dried and distilled over calcium hydride under nitrogen before use. Ether was dried and distilled over sodium-benzophenone ketyl under nitrogen before use. THF was dried and distilled over potassium metal under nitrogen before use. Toluene and benzene were dried and distilled over sodium metal under nitrogen or argon before use. The reaction flasks were dried in a 110 °C oven and allowed to cool to room temperature in a desiccator containing calcium sulfate and assembled under nitrogen or argon atmosphere.

(2*S*,3*R*)-2-*tert*-butyloxycarbonylamino-3-benzyloxypent-4-en-1-ol, (4a): white solid; mp 58-59 °C; $[\alpha]_D^{23}$ –66.6° (*c*: 2.06, $CHCl_3$), lit. $[\alpha]_D^{25}$ –51.8° (*c*: 0.953, $CHCl_3$);[1] ^{1}H-NMR (600 MHz, 25 °C, $CDCl_3$, δ): 1.40 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 2.62 (brs, -OH), 3.58-3.66 (m, 2H, H-1 and H-2), 3.90-3.93 (m, 1H, H-1), 4.03-4.08 (m, 1H, H-3); 4.30 (d, *J* = 12.0 Hz, 1H, -OC<u>H</u>$_2$Ph), 4.61 (d, *J* = 12.0 Hz, 1H, -OC<u>H</u>$_2$Ph), 5.27 (d, *J* = 7.2 Hz, 1H, -N<u>H</u>Boc), 5.33-5.38 (m, 2H, H-5), 5.65 (ddd, *J* = 7.8, 10.8, 18.0 Hz, 1H, H-4), 7.25-7.33 (m, 5H, -Ph); ^{13}C-NMR (100 MHz, 25 °C, $CDCl_3$, δ): 28.3 (q, -C(<u>C</u>H$_3$)$_3$), 54.4 (d, C-2), 61.9 (t, C-1), 71.0 (t, -O<u>C</u>H$_2$Ph), 79.4 (s, -O<u>C</u>(CH$_3$)$_3$), 81.9 (d, C-3), 119.2 (t, C-5), 127.7 (d, *ortho*-Ph), 127.8 (d, *para*-Ph), 128.4 (d, *meta*-Ph), 135.0 (d, C-4), 137.6 (s, *ipso*-Ph), 155.9 (s, O-<u>C</u>O-N). HRMS-FAB (m/z): $[M + H]^+$ calcd for $C_{17}H_{25}NO_4 \bullet H^+$, 308.1862; found, 308.1852 (Δ = 3.3 ppm).



4a

(2*S*,3*S*)-2-*tert*-butyloxycarbonylamino-3-benzyloxypent-4-en-1-ol, (4b): colorless oil, $[\alpha]_D^{23}$ +10.5° (*c*: 1.14, $CHCl_3$), lit. $[\alpha]_D^{20}$ –49.3° (*c*: 0.25, $CHCl_3$);[1] ^{1}H-NMR (600 MHz, 25 °C, $CDCl_3$, δ): 1.42 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 1.81 (brs, -OH), 3.67-3.72 (m, 3H, H-2 and H-1 X 2), 4.01 (d, *J* = 6.6 Hz, 1H, H-3); 4.31 (d, *J* = 12.0 Hz, 1H, -OC<u>H</u>$_2$Ph), 4.60 (d, *J* = 12.0 Hz, 1H, -OC<u>H</u>$_2$Ph), 5.05 (brs, 1H, -N<u>H</u>Boc), 5.32-5.35 (m, 2H, H-5), 5.82 (ddd, *J* = 7.8, 10.2, 17.4 Hz, 1H, H-4), 7.27-7.35 (m, 5H, -Ph); ^{13}C-NMR (100 MHz, 25 °C, $CDCl_3$, δ): 28.3 (q, -C(<u>C</u>H$_3$)$_3$), 55.3 (d, C-2), 63.6 (t, C-1), 70.5 (t, -O<u>C</u>H$_2$Ph), 79.5 (C-3 and -O<u>C</u>(CH$_3$)$_3$), 119.1 (t, C-5), 127.8 (d, *para*-Ph), 127.9 (d, *ortho*-Ph), 128.4 (d, *meta*-Ph), 134.9 (d, C-4), 137.7 (s, *ipso*-Ph), 156.4 (s, O-<u>C</u>O-N). HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_{17}H_{25}NO_4 \bullet H^+$, 308.1862; found, 308.1871, (Δ: 2.9 ppm).

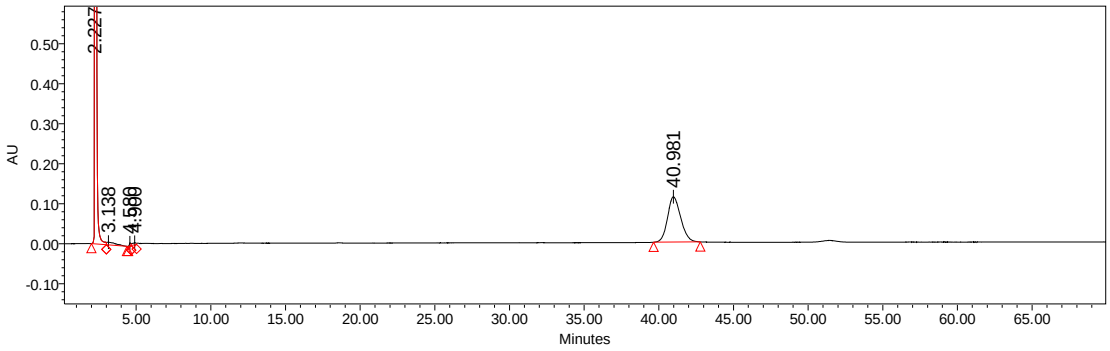


4b

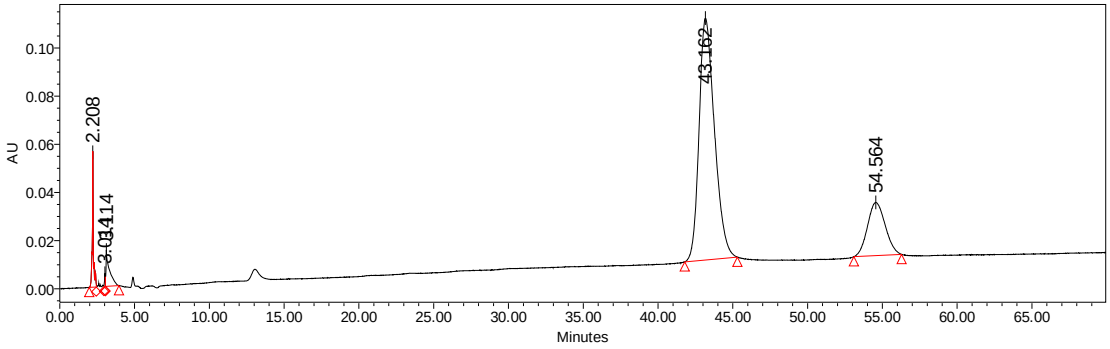
[1] Srivastava, A. K.; Panda, G. *Chem. Eur. J.* **2008**, *14*, 4675-4688.

HPLC condition for **4a** and **4b**: Supelcosil LC-SI, 250 mm X 4.6 mm, 5 μm; 1 vol% IPA in hexane/hexane = 1/1; flow rate 1.5 mL per min; detection UV 210 nm; t_R: 41 min for **4a**; t_R: 54 min for **4b** (**4a**:**4b** = 4.0:1).

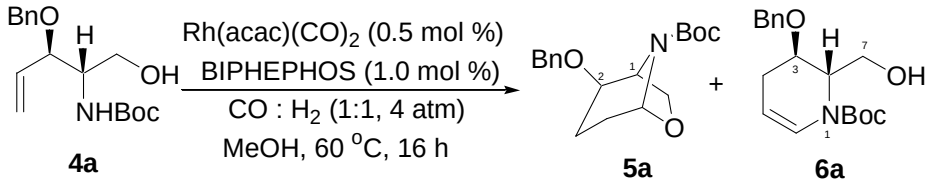
***Pure* 4a:**



Crude product of **4a** and **4b:**



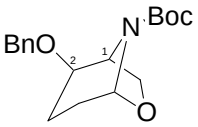
(1*S*,2*R*,6*R*)-2-benzyloxy-8-*tert*-butyloxycarbonyl-6-oxa-8-azabicyclo[3.2.1]octane, (5a) and (2*S*,3*R*)-1-*tert*-butyloxycarbonyl-2-hydroxymethyl-3-benzyloxy-5,6-dide-hydropiperidine (6a):



4a **5a** **6a**

$Rh(acac)(CO)_2$ (1.3 mg, 5.0 μmol, 0.5 mol %) and BIPHEPHOS (7.9 mg, 10 μmol, 1.0 mol %) were dissolved in toluene (1 mL) under nitrogen. The resulting catalyst solution was degassed by a frozen-thawed procedure at least three times. Olefin **4a** (307 mg, 1.0 mmol, 1.00 equiv) was placed in a 50 mL flask. The catalyst solution was transferred to the reaction flask containing the substrate by a pipette, and then the total volume was adjusted to 20 mL. The reaction flask was placed in a 300 mL stainless steel autoclave and then was pressurized with CO (2 atm) followed by H_2 (2 atm). The reaction mixture was stirred at 60 ^oC for 16-20 h. Upon completion of the reaction, the gas was carefully released in a good ventilated hood and the reaction mixture was concentrated under reduced pressure to give a crude product. The residue was purified by flash chromatography on silica gel, using ethyl acetate / n-hexane as the eluant to give amidal **5a** (57 mg, 0.18 mmol, 18%) and encarbamate **6a** (241 mg, 0.76 mmol, 76%).

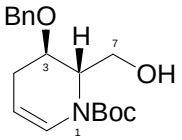
5a: white solid; mp 73-75 °C, $[\alpha]_D^{23}$ +84.5° (*c*: 1.00, $CHCl_3$), ^1H NMR (600 MHz, 25 ^oC, $CDCl_3$, δ): 1.47 (s, 9H, -C($C\underline{H}_3$)$_3$), 1.66-1.72 (m, 1H, H-4), 1.70-1.76 (m, 1H, H-3), 1.88-1.96 (m, 2H, H-3 and H-4), 3.51 (brs, 1H, H-2), 3.72 (s, 1H, H-7), 3.73 (s, 1H, H-7), 4.51 (d, *J* = 12.6 Hz, 1H, -O$C\underline{H}_2$Ph), 4.73 (brs, 1H, H-1), 4.77 (d, *J* = 12.0 Hz, 1H, -O$C\underline{H}_2$Ph), 5.70 (brs, 1H, H-5),



5a

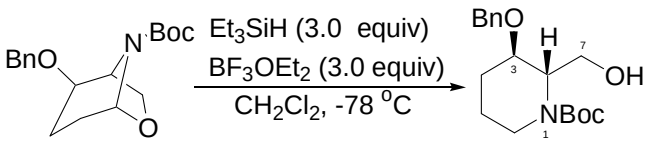
7.26-7.38 (m, 5H, -Ph); ^{13}C-NMR (150 MHz, 25 ^{o}C, $CDCl_3$, δ): 22.7 (t, C-4), 28.3 (-C($\underline{C}H_3)_3$ and C-3), 54.3 (d, br, C-1), 66.9 (t, C-7), 70.0 (t, -O$\underline{C}H_2$Ph), 73.4 (d, C-2), 80.4 (s, -O$\underline{C}(CH_3)_3$), 85.5 (d, br, C-5), 127.5 (d, -Ph), 127.6 (d, br, -Ph), 128.3 (d, -Ph), 138.4 (s, *ipso*-Ph), 153.3 (s, O-$\underline{C}$O-N), EI-HRMS (m/z): $[M]^+$ calcd for $C_{18}H_{25}NO_4^+$, 319.1784; found, 319.1788 (Δ = 1.3 ppm).

6a: colorless oil; $[\alpha]_D^{23}$ +3.3° (*c*: 1.05, C_6H_6); ^{1}H-NMR (600 MHz, 40 ^{o}C, C_6D_6, δ): 1.34 (s, 9H, -C(C$\underline{H}_3)_3$), 1.88 (dddd, *J* = 18.0, 4.8, 2.4, 2.4 Hz, 1H, H-4β), 2.01 (dd, *J* = 18.0, 4.2 Hz, 1H, H-4α), 2.37 (brs, 1H, -OH), 3.32 (brs, 1H, H-7), 3.60 (brs, 1H, H-7), 3.75 (brs, 1H, H-3), 4.32 (d, *J* = 12.0 Hz, 1H, -OC$\underline{H}_2$Ph), 4.42 (d, *J* = 12.0 Hz, 1H, -OC$\underline{H}_2$Ph), 4.56 (brs, 1H, H-5), 4.83 (brs, 1H, H-2), 6.86 (brs, 1H, H-6), 7.05 (t, *J* = 7.2 Hz, 1H, *para*-Ph), 7.12 (t, *J* = 7.2 Hz, 2H, *meta*-Ph), 7.25 (d, *J* = 7.2 Hz, 2H, *ortho*-Ph); ^{13}C-NMR (150 MHz, 40 ^{o}C, C_6D_6, δ): 24.7 (t, C-4), 28.7 (q, -C($\underline{C}H_3)_3$), 55.6 (d, C-2), 62.8 (t, C-7), 70.5 (d, C-3), 70.8 (d, -O$\underline{C}H_2$Ph), 81.4 (s, -O$\underline{C}(CH_3)_3$), 102.1 (d, C-5), 125.2 (d, C-6), 128.0 (d, *para*-Ph), 128.3 (d, *ortho*-Ph), 129.0 (d, *meta*-Ph), 139.8 (s, *ipso*-Ph), 154.4 (s, O-$\underline{C}$O-N), EI-HRMS (m/z): $[M]^+$ calcd for $C_{18}H_{25}NO_4^+$, 319.1784; found, 319.1780 (Δ = 1.3 ppm).



6a

(2*S*,3*R*)-1-*tert*-butyloxycarbonyl-2-hydroxymethyl-3-benzyloxypiperidine, (7a).



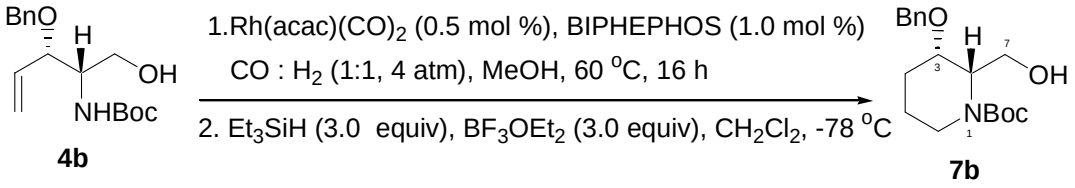
5a **7a**

To a CH_2Cl_2 solution (8 mL) of amidal **5** (57 mg, 0.18 mmol, 1.00 equiv) at -78 °C under nitrogen, was added dropwise triethylsilane (Et_3SiH, 80 μL, 0.54 mmol, 3.0 equiv), followed by boron trifluoride etherate ($BF_3{\cdot}OEt_2$, 63 μL, 0.54 mmol, 3.0 equiv). The reaction mixture was allowed to be stirred at -78 °C overnight (~ 16 h). The reaction was monitored by TLC analysis. Upon completion of the reaction, a saturated $NaHCO_3$ solution (5 mL) was slowly added into the reaction mixture so that the temperature was kept below -60 °C, and then warmed up to room temperature. After separation of the organic layer, the aqueous layer was extracted with ethyl acetate (10 mL X 4). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and then concentrated under reduced pressure to give a crude residue. The crude product was purified by flash chromatography on silica gel using ethyl acetate / n-hexane (R_f = 0.40, ethyl acetate / n-hexane = 1/3 X 3) as the eluant to give product **7** as a colorless oil (54 mg, 94%): $[\alpha]_D^{23}$ +39.5° (*c*: 1.73, $CHCl_3$), lit. $[\alpha]_D^{20}$ –40.1° (*c*: 0.9, $CHCl_3$);[2] ^{1}H-NMR (600 MHz, 25 °C, $CDCl_3$, δ): 1.36-1.40 (m, 1H, H-5α), 1.44 (s, 9H, -C(C$\underline{H}_3$)$_3$), 1.54-1.60 (m, 1H, H-4α), 1.83-1.93 (m, 2H, H-4β and H-5β), 2.33 (brs, 1H, -OH), 2.86 (t, *J* = 12.6 Hz, 1H, H-6α), 3.56 (d, *J* = 2.4 Hz, 1H, H-3), 3.61 (dd, *J* = 6.0, 10.8 Hz, 1H, H-7), 3.74 (dd, *J* = 8.4, 10.8 Hz, 1H, H-7), 3.96 (brs, 1H, H-6β), 4.48 (d, *J* = 12.0 Hz, 1H, -

[2] Martín, R.; Murruzzu, C.; Pericàs, M. A.; Riera, A. *J. Org. Chem.* **2005**, *70*, 2325-2328.

OC$\underline{H}_2$Ph), 4.50 (t, J = 6.0 Hz, 1H, H-2), 4.61 (d, J = 11.4 Hz, 1H, -OC$\underline{H}_2$Ph), 7.23-7.33 (m, 5H, -Ph); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$, δ): 19.5 (t, C-5), 25.1 (t, C-4), 28.3 (q, -C($\underline{C}H_3)_3$), 39.6 (t, C-6), 55.5 (d, C-2), 60.5 (t, C-7), 70.0 (t, -O$\underline{C}H_2$Ph), 71.5 (d, C-3), 79.8 (s, -O$\underline{C}(CH_3)_3$), 127.3 (d, *para*-Ph), 127.4 (d, *ortho*-Ph), 128.2 (d, *meta*-Ph), 138.6 (s, *ipso*-Ph), 156.3 (s, O-$\underline{C}$O-N); HRMS-FAB (m/z): $[M + H]^+$ calcd for $C_{18}H_{27}NO_4 \bullet H^+$, 322.2018; found, 322.2007 (Δ = 3.4 ppm).

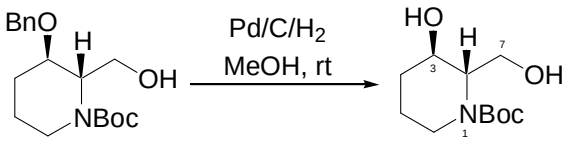
(2*S*,3*S*)-1-*tert*-butyloxycarbonyl-2-hydroxymethyl-3-benzyloxypiperidine, (7b).



$Rh(acac)(CO)_2$ (1.1 mg, 4.3 μmol, 0.5 mol %) and BIPHEPHOS (6.7 mg, 8.5 μmol, 1.0 mol %) were dissolved in methanol (2 mL) under nitrogen. The resulting catalyst solution was degassed by a frozen-thawed procedure at least three times. Olefin **4b** (261 mg, 0.85 mmol, 1.00 equiv) was placed in a 50 mL flask. The catalyst solution was transferred to the reaction flask containing the substrate by a pipette, and then the total volume was adjusted to 17 mL with methanol. The reaction flask was placed in a 300 mL stainless steel autoclave and then was pressurized with CO (2 atm) followed by H_2 (2 atm). The reaction mixture was stirred at 60 ^{o}C for 16-20 h. Upon completion of the reaction, the gas was carefully released in a good ventilated hood. The reaction mixture was concentrated under reduced pressure to give a crude product, and then diluted with CH_2Cl_2 (15 mL).

To the CH_2Cl_2 solution, was added dropwise triethylsilane (Et_3SiH, 407 μL, 2.55 mmol, 3.0 equiv), followed by boron trifluoride etherate ($BF_3{\cdot}OEt_2$, 323 μL, 2.55 mmol, 3.0 equiv). The reaction mixture was allowed to be stirred at -78 ^oC overnight (~ 16 h). The reaction was monitored by TLC analysis. Upon completion of the reaction, a saturated $NaHCO_3$ solution (5 mL) was slowly added into the reaction mixture so that the temperature was kept below -60 ^oC, and then warmed up to room temperature. After separation of the organic layer, the aqueous layer was extracted with ethyl acetate (10 mL X 4). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and then concentrated under reduced pressure to give a crude residue. The crude product was purified by flash chromatography on silica gel using ethyl acetate / n-hexane (R_f = 0.49, ethyl acetate / n-hexane = 1/3 X 3) as the eluant to give product **7b** as a colorless oil (213 mg, 78%): $[\alpha]_D^{25}$ +16.7° (*c*: 1.31, $CHCl_3$), ^{1}H-NMR (600 MHz, 25 ^oC, $CDCl_3$, δ): 1.37-1.44 (m, 1H, H-5β), 1.43 (s, 9H, -C(C$\underline{H}_3$)$_3$), 1.54 (dddd, *J* = 4.2, 12.0, 12.0, 12.0 Hz, 1H, H-4α), 1.63-1.70 (m, 1H, H-5α), 1.87-1.95 (m, 1H, H-4β), 2.68 (brs, 2H, H-6α and 6β), 3.59 (ddd, *J* = 6.0, 6.0, 12.0 Hz, 1H, H-3), 3.74 (brs, 1H, H-7), 3.87 (brs, 1H, H-2), 3.98 (dd, *J* = 6.0, 12.0, Hz, 1H, H-7), 4.59 (brs, 2H, -OC$\underline{H}_2$Ph), 4.72 (brs, 1H, -OH), 7.25-7.35 (m, 5H, -Ph); ^{13}C-NMR (100 MHz, 25 ^oC, $CDCl_3$, δ): 23.7. (t, C-5), 25.6 (t, C-4), 28.2 (q, -C($\underline{C}H_3$)$_3$), 39.0 (t, C-6), 53.8 (d, C-2), 58.7 (t, C-7), 70.7 (t, -O$\underline{C}H_2$Ph), 75.8 (d, C-3), 79.9 (s, -O$\underline{C}$(CH$_3$)$_3$), 127.4 (d, *ortho*-Ph), 127.6 (d, *para*-Ph), 128.3 (d, *meta*-Ph), 137.9 (s, *ipso*-Ph), 155.6 (s, O-$\underline{C}$O-N). EI-HRMS (m/z): $[M]^+$ calcd for $C_{18}H_{27}NO_4^+$, 321.1940; found, 321.1949 (Δ = 2.8 ppm).

(2*S*,3*R*)-1-*tert*-butyloxycarbonyl-2-hydroxymethyl-3-hydroxypiperidine, (8a).

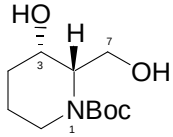


7a **8a**

Pd/C (10%, 18 mg, 0.017 mmol, 5 mol %) was added to a methanol solution (5 mL) of alcohol **7a** (108 mg, 0.34 mmol, 1.00 equiv). The reaction flask was placed in a 300 mL stainless steel autoclave and then was pressurized with H_2 (2 atm). The reaction mixture was stirred at room temperature overnight (~ 18 h). Filtration with a short celite pad followed by concentration gave a crude residue. The residue was purified by flash chromatography on silica gel, using ethyl acetate / n-hexane as the eluant to give product **8a**. Recrystallization with chloroform-heptane afforded white needle crystals (58 mg, 75%, R_f = 0.33, pure ethyl acetate)**:** mp 124-126 °C; $[\alpha]_D^{25}$ +29.8° (*c*: 0.99, MeOH), lit. $[\alpha]_D^{20}$ –5.2° (*c*: 0.25, MeOH);[3] ^{1}H-NMR (600 MHz, 25 ^{o}C, $CDCl_3$, δ): 1.37-1.44 (m, 1H, H-5α), 1.44 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 1.63-1.70 (m, 1H, H-4α), 1.70-1.76 (m, 1H, H-4β), 1.83 (ddddd, *J* = 4.8, 4.8, 12.6, 12.6, 12.6 Hz, 1H, H-5β), 2.91 (t, *J* = 12.0 Hz, 1H, H-6α), 3.05 (brs, 2H, -OH), 3.67 (dd, *J* = 7.2, 11.4 Hz, 1H, H-7), 3.71 (dd, *J* = 7.2, 11.4 Hz, 1H, H-7), 3.83 (brs, 1H, H-6β), 3.97 (d, *J* = 3.0 Hz, 1H, H-3), 4.15 (ddd, *J* = 6.0, 6.0, 1.8 Hz, 1H, H-2); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$, δ): 19.5 (t, C-5), 27.2 (t, C-4), 28.4 (q, -C(<u>C</u>H$_3$)$_3$), 40.6 (t, C-6), 60.0 (d, C-2), 60.5 (t, C-7), 64.7 (d, C-3), 80.2 (s, -O<u>C</u>(CH$_3$)$_3$), 156.7 (s, O-<u>C</u>O-N). EI-HRMS (m/z): $[M]^+$ calcd for $C_{11}H_{21}NO_4^+$, 231.1471; found, 231.1465 (Δ = 2.6 ppm).

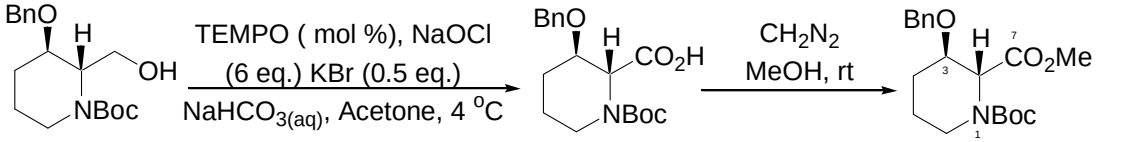
[3] Kumar, P.; Bodas, M. S. **2005**, *70*, 360-363.

(2*S*,3*S*)-1-*tert*-butyloxycarbonyl-2-hydroxymethyl-3-hydroxypiperidine, (8b): 90% yield; R_f = 0.33, pure ethyl acetate; white needle crystal; mp 114-116 °C, $[\alpha]_D^{25}$ +23.1° (*c*: 1.03, MeOH), lit. $[\alpha]_D^{22}$ +19.5° (*c*: 1.6, CH_2Cl_2);[4] ^{1}H-NMR (600 MHz, 25 ^{o}C, $CDCl_3$, δ): 1.43-1.50 (m, 1H, H-5β), 1.45 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 1.63 (dddd, *J* = 3.6, 12.0, 12.0, 12.0 Hz, 1H, H-4α), 1.71 (ddddd, *J* = 3.6, 3.6, 3.6, 3.6, 12.6 Hz, 1H, H-5α), 1.85 (dddd, *J* = 4.2, 4.2, 4.2, 12.0 Hz, 1H, H-4β), 2.82 (brs, 1H, -OH), 2.92 (brs, 2H, H-6α and β), 3.74 (dd, *J* = 6.6, 11.4 Hz, 1H, H-7), 3.79 (brs, 1H, -OH), 3.92 (ddd, *J* = 4.8, 4.8, 10.8 Hz, 1H, H-3), 4.11 (dd, *J* = 6.6, 11.4 Hz, 1H, H-7), 4.41 (ddd, *J* = 6.6, 6.6, 6.6 Hz, 1H, H-2); ^{13}C-NMR (100 MHz, 25 ^{o}C, $CDCl_3$, δ): 23.7. (t, C-5), 28.2 (t, C-4), 28.3 (q, -C(<u>C</u>H$_3$)$_3$), 39.3 (t, C-6), 55.8 (d, C-2), 59.0 (t, C-7), 69.2 (d, C-3), 80.2 (s, -O<u>C</u>(CH$_3$)$_3$), 155.6 (s, O-<u>C</u>O-N). EI-HRMS (m/z): $[M]^+$ calcd for $C_{11}H_{21}NO_4^+$, 231.1471; found, 231.1465 (Δ = 2.6 ppm).



8b

(2*R*,3*R*)-1-*tert*-butyloxycarbonyl-2-methoxycarbonyl-3-benzyloxypiperidine, (10a).



7a 82% **9a** **10a** 90% from **7a**

To a solution of alcohol **7a** (337 mg, 1.05 mmol, 1.00 equiv) in acetone (8 mL) in an ice bath, an aqueous $NaHCO_3$ solution (5%, 8 mL), KBr (60 mg, 0.5 mmol, 0.5 equiv), and tetramethylpiperidine nitroxyl free radical (TEMPO, 30 mg, 0.20 mmol, 0.20 equiv) were added. Then, a bleach solution (4.5 mL, 1.0 M by titration, 4.5 mmol, 3.2 equiv)

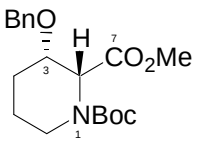
[4] Knight, D. W.; Lewis, N.; Share, A. C.; Haigh, D. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3673-3684.

was added dropwise via a syringe over 5 min. The solution became white cloudy. After stirring for 1 h in an ice bath, additional $NaHCO_3$ (5%, 8 mL) and additional bleach (4.5 mL, 1.0 M, 4.5 mmol, 3.2 equiv) were added. The reaction mixture was stirred in an ice bath for another 1 h. Concentration of the reaction mixture under reduced pressure to remove volatile substances gave a clean aqueous solution. The aqueous solution was washed with ether (10 mL), and covered with ethyl acetate (20 mL). The solution with two phases was acidified with an aqueous $KHSO_4$ solution (2 M) in an ice bath until pH became 2~3. A white precipitate was observed during acidification. The resulting aqueous layer was extracted with ethyl acetate (30 mL X 4). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 and then concentrated to give a crude acid **9a**. The residue was purified by flash chromatography on silica gel, using ethyl acetate / n-hexane as the eluant to give white solid **9a** (290 mg, 82%, R_f = 0.33, pure ethyl acetate)**:** mp 58-60 °C; $[\alpha]_D^{25}$ +17.4° (*c*: 1.15, $CHCl_3$); ^{1}H-NMR (600 MHz, 50 ^{o}C, $CDCl_3$, δ): 1.32-1.48 (m, 2H, H-4 and H-5), 1.47 (s, 9H, -C(C$\underline{H}_3$)$_3$), 1.88-1.99 (m, 2H, H-4 and H-5), 3.04 (brs, 1H, H-6), 4.00 (brs, 1H, H-6), 4.10 (brs, 1H, H-3), 4.52 (d, *J* = 11.6 Hz, 1H, -OC$\underline{H}_2$Ph), 4.65 (brs, 1H, -OC$\underline{H}_2$Ph), 4.96-5.16 (brs, 1H, H-2), 7.25-7.36 (m, 5H, -Ph), 9.43 (brs, 1H, -COO$\underline{H}$); ^{13}C-NMR (150 MHz, 50 ^{o}C, $CDCl_3$, δ): 18.7 (t, C-5), 26.2 (t, C-4), 28.4 (q, -C($\underline{C}H_3$)$_3$), 41.1 (t, C-6), 56.9 (d, C-2), 70.6 (t, -O$\underline{C}H_2$Ph), 72.8 (d, C-3), 80.5 (s, -O$\underline{C}$(CH$_3$)$_3$), 127.5 (d, *ortho*-Ph and *para*-Ph), 128.3 (d, *meta*-Ph), 138.2 (s, *ipso*-Ph), 156.0 (s, O-$\underline{C}$O-N), 174.5 (s, C-7). HRMS-FAB (m/z): $[M + H]^+$ calcd for $C_{18}H_{25}NO_5 \bullet H^+$, 336.1811; found, 336.1829 (Δ = 5.4 ppm).

Methylation: To a solution of crude acid **9a** in MeOH (~ 0.1 M), was added an ether solution of diazomethane slowly until yellow color persisted. Concentration under

reduced pressure gave a yellowish crude syrup. The crude product was purified by flash chromatography on silica gel using ethyl acetate / n-hexane (R_f = 0.38, ethyl acetate / n-hexane = 1/3) as the eluant to give product **10a** as a colorless oil (90% yield over 2 steps): $[\alpha]_D^{25}$ +2.1° (*c*: 0.92, $CHCl_3$); ^{1}H-NMR (600 MHz, 50 °C, $CDCl_3$, δ): 1.34-1.52 (m, 2H, H-4 and H-5), 1.45 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 1.87-1.96 (m, 2H, H-4 and H-5), 3.00 (brs, 1H, H-6), 3.73 (s, 3H, -CO_2C<u>H</u>$_3$), 4.02 (brs, 1H, H-6), 4.05 (brs, 1H, H-3), 4.51 (d, *J* = 12.0 Hz, 1H, -OC<u>H</u>$_2$Ph), 4.64 (d, *J* = 12.0 Hz, 1H, -OC<u>H</u>$_2$Ph), 5.15 (brs, 1H, H-2), 7.24-7.36 (m, 5H, -Ph); ^{13}C-NMR (150 MHz, 50 °C, $CDCl_3$, δ): 18.7 (t, C-5), 26.1 (t, C-4), 28.3 (q, -C(<u>C</u>H$_3$)$_3$), 41.5 (t, C-6), 52.0 (q, -CO_2<u>C</u>H$_3$), 57.0 (d, C-2), 70.6 (t, -O<u>C</u>H$_2$Ph), 72.4 (d, C-3), 80.1 (s, -O<u>C</u>(CH$_3$)$_3$), 127.4 (d, *ortho*-Ph and *para*-Ph), 128.3 (d, *meta*-Ph), 138.3 (s, *ipso*-Ph), 155.9 (s, O-<u>C</u>O-N), 170.8 (s, C-7). EI-HRMS (m/z): $[M]^+$ calcd for $C_{19}H_{27}NO_5^+$, 349.1889; found, 349.1892 (Δ = 0.9 ppm).

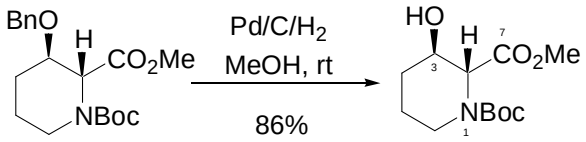
(2*R*,3*S*)-1-*tert*-butyloxycarbonyl-2-methoxycarbonyl-3-benzyloxypiperidine, (10b): 57% yield; colorless oil; R_f = 0.38, ethyl acetate / n-hexane = 1/3; $[\alpha]_D^{25}$ –35.3° (*c*: 1.90, $CHCl_3$), ^{1}H-NMR (600 MHz, 50 °C, $CDCl_3$, δ): 1.46 (s, 9H, -C(C<u>H</u>$_3$)$_3$), 1.45-1.52 (m, 1H, H-5), 1.72-1.83 (m, 2H, H-4 and H-5), 1.87 (dddd, *J* = 4.2, 4.2, 4.2, 12.6 Hz, 1H, H-4), 3.34 (brs, 1H, H-6), 3.64 (ddd, *J* = 4.2, 6.0, 10.2 Hz, 1H, H-3), 3.71 (s, 3H, -CO_2C<u>H</u>$_3$), 3.89 (brs, 1H, H-6), 4.56 (d, *J* = 12.0 Hz, 1H, -OC<u>H</u>$_2$Ph), 4.77 (brs, 1H, -OC<u>H</u>$_2$Ph), 5.13 (brs, 1H, H-2), 7.26-7.35 (m, 5H, -Ph); ^{13}C-NMR (150 MHz, 50 °C, $CDCl_3$, δ): 22.8 (t, C-5), 26.1 (t, C-4), 28.4 (q, -C(<u>C</u>H$_3$)$_3$), 40.6 (t, C-6), 51.5 (q, -CO_2<u>C</u>H$_3$), 56.1 (d, C-2), 70.9 (t, -O<u>C</u>H$_2$Ph), 74.8 (d, C-3), 80.4 (s, -O<u>C</u>(CH$_3$)$_3$), 127.5 (d, *ortho*-Ph), 127.6 (d, *para*-Ph), 128.4 (d,



10b

meta-Ph), 138.3 (s, *ipso*-Ph), 155.4 (s, O-CO-N), 171.0 (s, C-7). HRMS-FAB (m/z): [M + H]$^+$ calcd for $C_{19}H_{27}NO_5 \bullet H^+$,, 350.1967; found, 350.1976 (Δ = 2.6 ppm).

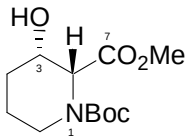
(2*R*,3*R*)-1-*tert*-butyloxycarbonyl-2-methoxycarbonyl-3-hydroxypiperidine, (11a).



10a **11a**

Pd/C (5%, 23 mg, 0.01 mmol, 5 mol %) was added to a methanol solution (3 mL) of ester **10a** (77 mg, 0.22 mmol, 1.00 equiv). The reaction flask was placed in a 300 mL stainless steel autoclave and then was pressurized with H_2 (2 atm). The reaction mixture was stirred at room temperature for 4 h. Filtration with a short celite pad followed by concentration gave a crude residue. The residue was purified by flash chromatography on silica gel, using ethyl acetate / n-hexane (R_f = 0.55, pure ethyl acetate) as the eluant to give product **11a**. The crude product was purified by flash chromatography on silica gel using ethyl acetate / n-hexane as the eluant to give product **11a** as a colorless oil (48 mg, 0.19 mmol, 86% yield): $[\alpha]_D^{25}$ +36.8° (*c*: 0.95, $CHCl_3$), ^{1}H-NMR (600 MHz, 50 ^{o}C, $CDCl_3$, δ): 1.37-1.45 (m, 1H, H-5α), 1.43 (s, 9H, -C(C$\underline{H}_3$)$_3$), 1.47 (dddd, *J* = 3.6, 3.6, 13.2, 13.2 Hz, 1H, H-4α), 1.74-1.79 (m, 1H, H-4β), 1.83 (ddddd, *J* = 4.8, 4.8, 13.2, 13.2, 13.2 Hz, 1H, H-5β), 2.48 (brs, 1H, -OH), 2.91 (brs, 1H, H-6α), 3.71 (s, 3H, -OC$\underline{H}_3$), 3.92 (brs, 1H, H-6β), 4.35 (brs, 1H, H-3), 4.75 (brs, 1H, H-2); ^{13}C-NMR (150 MHz, 50 ^{o}C, $CDCl_3$, δ): 18.3 (t, C-5), 27.7 (t, C-4), 28.3 (q, -C($\underline{C}H_3$)$_3$), 41.6 (t, C-6), 51.9 (q, -O$\underline{C}H_3$), 61.1 (d, C-2), 65.4 (d, C-3), 80.3 (s, -O$\underline{C}$(CH$_3$)$_3$), 156.3 (s, O-$\underline{C}$O-N), 170.3 (s, C-7). EI-HRMS (m/z): [M]$^+$ calcd for $C_{12}H_{21}NO_5^+$, 259.1420; found, 259.1429 (Δ = 3.5 ppm).

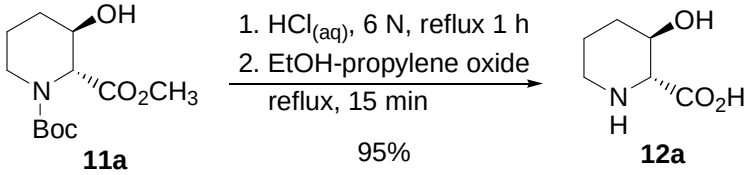
(2*R*,3*S*)-1-*tert*-butyloxycarbonyl-2-methoxycarbonyl-3-hydroxy-piperidine, (11b):



11b

84% yield; colorless oil; R_f = 0.59, pure ethyl acetate; $[\alpha]_D^{25}$ +60.0° (*c*: 1.10, $CHCl_3$), lit. $[\alpha]_D^{23}$ +47.9° (*c*: 3.8, CH_2Cl_2);[4] ^{1}H-NMR (600 MHz, 50 ^{o}C, $CDCl_3$, δ): 1.44-1.56 (m, 2H, H-4 and H-5), 1.47 (s, 9H, -C($C\underline{H}_3$)$_3$), 1.68-1.74 (m, 1H, H-5), 1.96-2.01 (m, 1H, H-4), 2.70 (brs, 1H, H-6), 3.31 (brs, 1H, -OH), 3.75 (ddd, *J* = 4.2, 4.2, 10.8 Hz, 1H, H-3), 3.77 (s, 3H, -$CO_2C\underline{H}_3$), 3.93 (brs, 1H, H-6), 4.98 (brs, 1H, H-2); ^{13}C-NMR (150 MHz, 50 ^{o}C, $CDCl_3$, δ): 23.6 (t, C-5), 30.3 (t, C-4), 28.3 (q, -C($\underline{C}H_3$)$_3$), 41.1 (t, C-6), 52.1 (q, -$CO_2\underline{C}H_3$), 58.7 (d, C-2), 69.0 (d, C-3), 80.6 (s, -O$\underline{C}$(CH$_3$)$_3$), 155.0 (s, O-$\underline{C}$O-N), 172.3 (s, C-7). HRMS-FAB (m/z): $[M + H]^+$ calcd for $C_{12}H_{21}NO_5 \bullet H^+$, 260.1498; found, 260.1503 (Δ = 1.9 ppm).

(2*R*,3*R*)-3-Hydroxypipecolinic acid (12a):



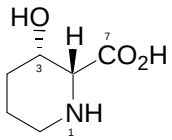
11a **12a**

A solution of methyl ester **11a** (48 mg, 0.19 mmol, 1.00 equiv) in a hydrochloric acid solution (6 N, 4 mL) was stirred under reflux for 1 h, and then concentrated under reduced pressure to give a residue. Reflux of the crude product in EtOH (3 mL) and propylene oxide (0.35 mL) gave a brown precipitate. Filtration followed by washing with cold ether afforded the titled product as a light brown solid (27 mg, 0.18 mmol, 95%): mp 241 °C dec, lit. mp 234-239 °C dec; [5] $[\alpha]_D^{25}$ –15.9° (*c*: 2.70, H_2O), lit. $[\alpha]_D^{28}$ –12.9° (*c*:

[5] Battistini, L.; Zanardi, F.; Rassu, G.; Spanu, P.; Pelosi, G.; Fava, G. G.; Ferrari, M. B.; Casiraghi, G. *Tetrahedron Asymm.* **1997**, *8*, 2975-2987.

1.0, H_2O);[6] ^{1}H-NMR (600 MHz, 25 ^oC, D_2O, δ): 1.64-1.76 (m, 2H, H-4 and H-5), 1.90-1.96 (m, 1H, H-4), 1.97-2.04 (m, 1H, H-5), 3.09 (ddd, *J* = 3.6, 8.4, 12.0 Hz, 1H, H-6), 3.35 (ddd, *J* = 4.2, 7.2, 12.0 Hz, 1H, H-6), 3.61 (d, *J* = 7.2 Hz, 1H, H-2), 4.14 (ddd, *J* = 3.0, 7.2, 7.2 Hz, 1H, H-3); ^{13}C-NMR (150 MHz, 25 ^oC, D_2O, δ): 18.4 (t, C-5), 28.3 (t, C-4), 42.5 (t, C-6), 62.0 (d, C-2), 66.0 (d, C-3), 172.1 (s, C-7). HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_6H_{11}NO_3 \bullet H^+$, 146.0817; found, 146.0810, (Δ: 4.8 ppm).

(2*R*,3*S*)-3-Hydroxypipecolinic acid (12b): 99% yield; light brown solid; mp 242 °C dec; $[\alpha]_D^{25}$ +49.1° (*c*: 0.55, H_2O), lit. $[\alpha]_D^{27}$ +51.0° (*c*: 0.75, H_2O); [6] ^{1}H-NMR (600 MHz, 25 ^oC, D_2O, δ): 1.70-1.81 (m, 2H, H-4 and H-5), 1.93-2.02 (m, 2H, H-4 and H-5), 3.00 (ddd, *J* = 3.2, 13.2, 13.2 Hz, 1H, H-6), 3.40 (ddd, *J* = 2.4, 4.2, 13.2 Hz, 1H, H-6), 3.69 (s, 1H, H-2), 4.51 (s, 1H, H-3); ^{13}C-NMR (150 MHz, 25 ^oC, D_2O, δ): 16.0 (t, C-5), 28.9 (t, C-4), 43.7 (t, C-6), 62.3 (d, C-2), 64.3 (d, C-3), 172.4 (s, C-7). HRMS-FAB (*m/z*): $[M + H]^+$ calcd for $C_6H_{11}NO_3 \bullet H^+$, 146.0817; found, 146.0826, (Δ: 6.2 ppm).



12b

[6] Yoshimura, Y.; Ohara, C.; Imahori, T.; Saito, Y.; Kato, A.; Miyauchi, S.; Adachi, I.; Takahata, H. *Bioorg. Med. Chem.* **2008**, *16*, 8273-8286.

Table 1. Crystal data and structure refinement for **8a**.

Identification code	**8a**	
Empirical formula	C11 H21 N O4	
Formula weight	231.29	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 5.7989(5) Å	α= 90°.
	b = 12.0265(10) Å	β= 107.068(9)°.
	c = 9.0540(8) Å	γ = 90°.
Volume	603.62(9) $Å^3$	
Z	2	
Density (calculated)	1.273 Mg/m^3	
Absorption coefficient	0.096 mm^{-1}	
F(000)	252	
Crystal size	0.33 x 0.15 x 0.08 mm^3	
Theta range for data collection	2.90 to 29.15°.	
Index ranges	-7<=h<=7, -15<=k<=16, -11<=l<=12	
Reflections collected	7989	
Independent reflections	2834 [R(int) = 0.0568]	
Completeness to theta = 26.00°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.00000 and 0.89313	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2834 / 1 / 153	
Goodness-of-fit on F^2	0.933	
Final R indices [I>2sigma(I)]	R1 = 0.0464, wR2 = 0.0593	
R indices (all data)	R1 = 0.0762, wR2 = 0.0630	
Absolute structure parameter	-0.4(9)	
Largest diff. peak and hole	0.259 and -0.238 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **8a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	4795(2)	8693(1)	1417(2)	18(1)
O(2)	4116(2)	7653(1)	3344(1)	17(1)
O(3)	-1611(3)	5661(1)	2608(2)	30(1)
O(4)	4015(2)	4703(1)	995(2)	20(1)
C(1)	1537(3)	6136(2)	1513(2)	13(1)
C(2)	1570(3)	5095(2)	578(2)	16(1)
C(3)	587(3)	5274(2)	-1157(2)	17(1)
C(4)	1929(4)	6221(2)	-1658(2)	20(1)
C(5)	1795(3)	7278(2)	-763(2)	18(1)
C(6)	3917(3)	7874(2)	1856(2)	14(1)
C(7)	5563(3)	8354(2)	4632(2)	16(1)
C(8)	5204(3)	7757(2)	6024(2)	22(1)
C(9)	4550(4)	9515(2)	4501(2)	23(1)
C(10)	8185(3)	8338(2)	4674(2)	25(1)
C(11)	-996(4)	6430(2)	1592(2)	22(1)
N(1)	2637(3)	7074(1)	914(2)	13(1)

Table 3. Bond lengths [Å] and angles [°] for **8a**.

O(1)-C(6)	1.227(2)
O(2)-C(6)	1.344(2)
O(2)-C(7)	1.483(2)
O(3)-C(11)	1.421(2)
O(3)-H(3A)	0.80(2)
O(4)-C(2)	1.436(2)
O(4)-H(4A)	0.795(19)
C(1)-N(1)	1.475(2)
C(1)-C(2)	1.514(2)
C(1)-C(11)	1.533(2)
C(1)-H(1A)	1.0000
C(2)-C(3)	1.521(2)
C(2)-H(2A)	1.0000
C(3)-C(4)	1.522(3)
C(3)-H(3B)	0.9900
C(3)-H(3C)	0.9900
C(4)-C(5)	1.522(3)
C(4)-H(4B)	0.9900
C(4)-H(4C)	0.9900
C(5)-N(1)	1.472(2)
C(5)-H(5A)	0.9900
C(5)-H(5B)	0.9900
C(6)-N(1)	1.354(2)
C(7)-C(9)	1.506(3)
C(7)-C(10)	1.510(3)
C(7)-C(8)	1.516(2)
C(8)-H(8A)	0.9800
C(8)-H(8B)	0.9800
C(8)-H(8C)	0.9800
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-H(10A)	0.9800
C(10)-H(10B)	0.9800

C(10)-H(10C)	0.9800
C(11)-H(11A)	0.9900
C(11)-H(11B)	0.9900

C(6)-O(2)-C(7)	122.54(14)
C(11)-O(3)-H(3A)	108.8(18)
C(2)-O(4)-H(4A)	109.7(14)
N(1)-C(1)-C(2)	110.40(14)
N(1)-C(1)-C(11)	111.44(15)
C(2)-C(1)-C(11)	112.72(15)
N(1)-C(1)-H(1A)	107.3
C(2)-C(1)-H(1A)	107.3
C(11)-C(1)-H(1A)	107.3
O(4)-C(2)-C(1)	107.38(15)
O(4)-C(2)-C(3)	111.09(14)
C(1)-C(2)-C(3)	113.44(16)
O(4)-C(2)-H(2A)	108.3
C(1)-C(2)-H(2A)	108.3
C(3)-C(2)-H(2A)	108.3
C(2)-C(3)-C(4)	110.14(15)
C(2)-C(3)-H(3B)	109.6
C(4)-C(3)-H(3B)	109.6
C(2)-C(3)-H(3C)	109.6
C(4)-C(3)-H(3C)	109.6
H(3B)-C(3)-H(3C)	108.1
C(3)-C(4)-C(5)	110.81(15)
C(3)-C(4)-H(4B)	109.5
C(5)-C(4)-H(4B)	109.5
C(3)-C(4)-H(4C)	109.5
C(5)-C(4)-H(4C)	109.5
H(4B)-C(4)-H(4C)	108.1
N(1)-C(5)-C(4)	110.89(15)
N(1)-C(5)-H(5A)	109.5
C(4)-C(5)-H(5A)	109.5
N(1)-C(5)-H(5B)	109.5
C(4)-C(5)-H(5B)	109.5

H(5A)-C(5)-H(5B)	108.0
O(1)-C(6)-O(2)	124.18(17)
O(1)-C(6)-N(1)	124.72(17)
O(2)-C(6)-N(1)	111.10(16)
O(2)-C(7)-C(9)	110.33(15)
O(2)-C(7)-C(10)	110.24(14)
C(9)-C(7)-C(10)	112.30(17)
O(2)-C(7)-C(8)	101.61(15)
C(9)-C(7)-C(8)	111.00(16)
C(10)-C(7)-C(8)	110.86(16)
C(7)-C(8)-H(8A)	109.5
C(7)-C(8)-H(8B)	109.5
H(8A)-C(8)-H(8B)	109.5
C(7)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
C(7)-C(9)-H(9A)	109.5
C(7)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(7)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(7)-C(10)-H(10A)	109.5
C(7)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(7)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
O(3)-C(11)-C(1)	107.86(16)
O(3)-C(11)-H(11A)	110.1
C(1)-C(11)-H(11A)	110.1
O(3)-C(11)-H(11B)	110.1
C(1)-C(11)-H(11B)	110.1
H(11A)-C(11)-H(11B)	108.4
C(6)-N(1)-C(5)	119.02(14)
C(6)-N(1)-C(1)	121.90(15)

C(5)-N(1)-C(1)	117.26(14)

Symmetry transformations used to generate equivalent atoms:

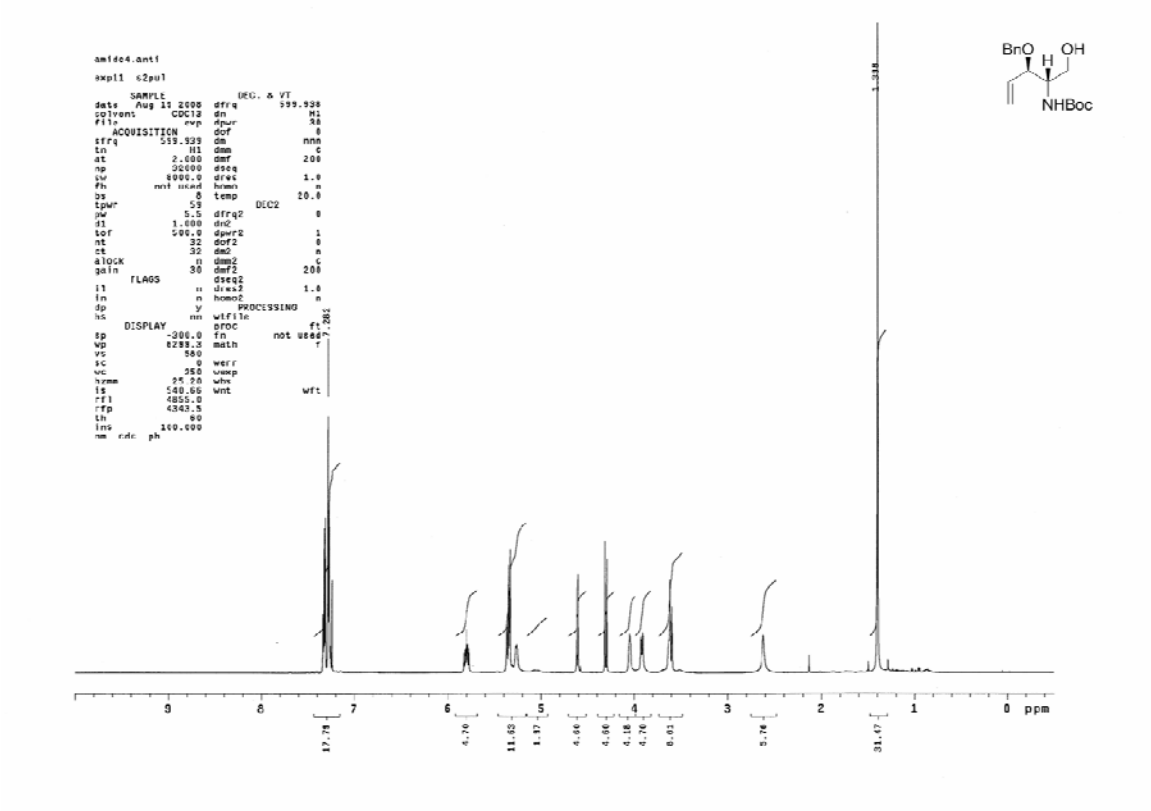
Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **8a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	24(1)	14(1)	18(1)	1(1)	6(1)	-7(1)
O(2)	19(1)	20(1)	11(1)	-4(1)	4(1)	-7(1)
O(3)	20(1)	44(1)	28(1)	6(1)	12(1)	-8(1)
O(4)	21(1)	23(1)	16(1)	-2(1)	4(1)	7(1)
C(1)	10(1)	11(1)	16(1)	2(1)	3(1)	0(1)
C(2)	16(1)	14(1)	18(1)	1(1)	6(1)	-3(1)
C(3)	14(1)	19(1)	16(1)	-5(1)	1(1)	2(1)
C(4)	21(1)	29(1)	8(1)	-1(1)	1(1)	-2(1)
C(5)	22(1)	19(1)	14(1)	2(1)	4(1)	0(1)
C(6)	11(1)	15(1)	18(1)	0(1)	6(1)	2(1)
C(7)	17(1)	17(1)	12(1)	-4(1)	1(1)	-5(1)
C(8)	25(1)	26(1)	14(1)	-3(1)	4(1)	-3(1)
C(9)	28(1)	18(1)	20(1)	-6(1)	4(1)	-3(1)
C(10)	19(1)	36(1)	17(1)	-1(1)	4(1)	-1(1)
C(11)	19(1)	25(2)	24(1)	-3(1)	11(1)	0(1)
N(1)	17(1)	13(1)	9(1)	-3(1)	4(1)	-3(1)

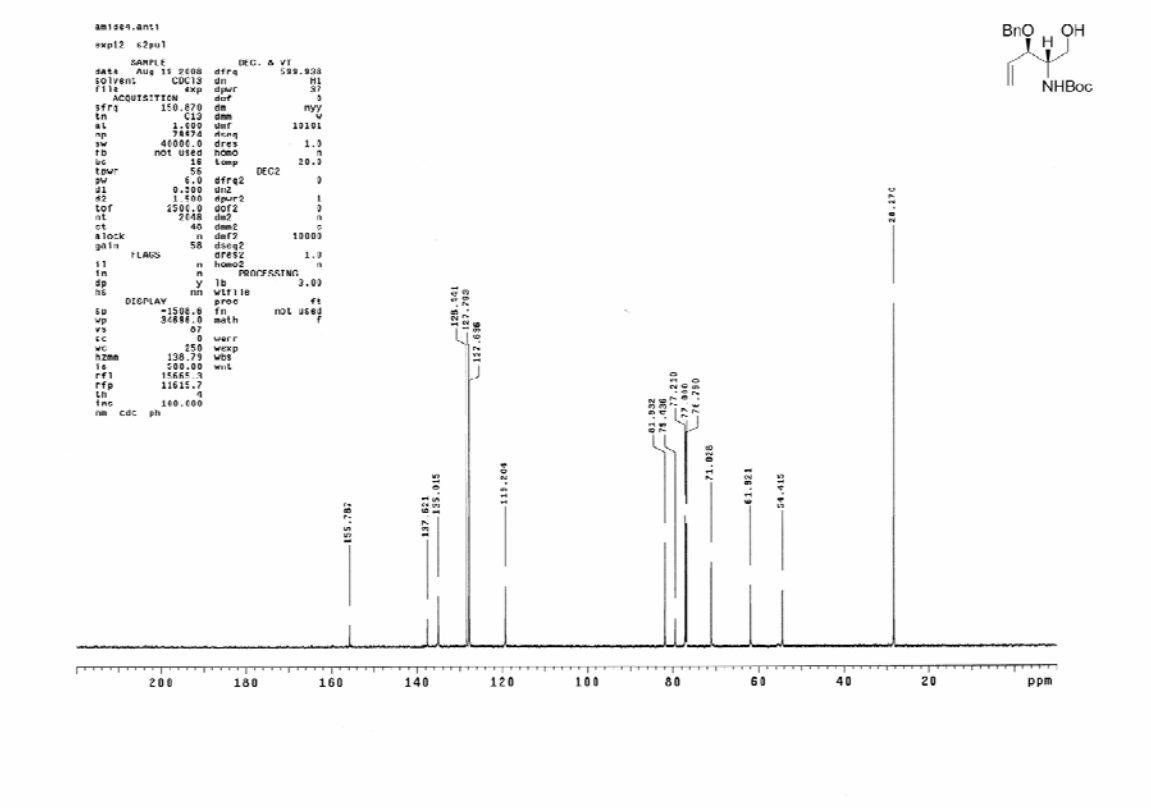
Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **8a**.

	x	y	z	U(eq)
H(3A)	-2920(40)	5420(20)	2200(30)	45(9)
H(4A)	4240(30)	4367(17)	290(20)	21(6)
H(1A)	2562	5989	2592	15
H(2A)	558	4518	886	19
H(3B)	-1155	5453	-1432	20
H(3C)	777	4584	-1705	20
H(4B)	1213	6360	-2778	24
H(4C)	3639	6009	-1479	24
H(5A)	2804	7862	-1034	22
H(5B)	109	7549	-1055	22
H(8A)	3492	7776	5972	33
H(8B)	6155	8128	6971	33
H(8C)	5733	6983	6028	33
H(9A)	4806	9883	3596	34
H(9B)	5368	9936	5434	34
H(9C)	2819	9481	4389	34
H(10A)	8375	8727	3766	37
H(10B)	8728	7567	4670	37
H(10C)	9155	8711	5614	37
H(11A)	-1018	7198	1982	26
H(11B)	-2173	6382	551	26

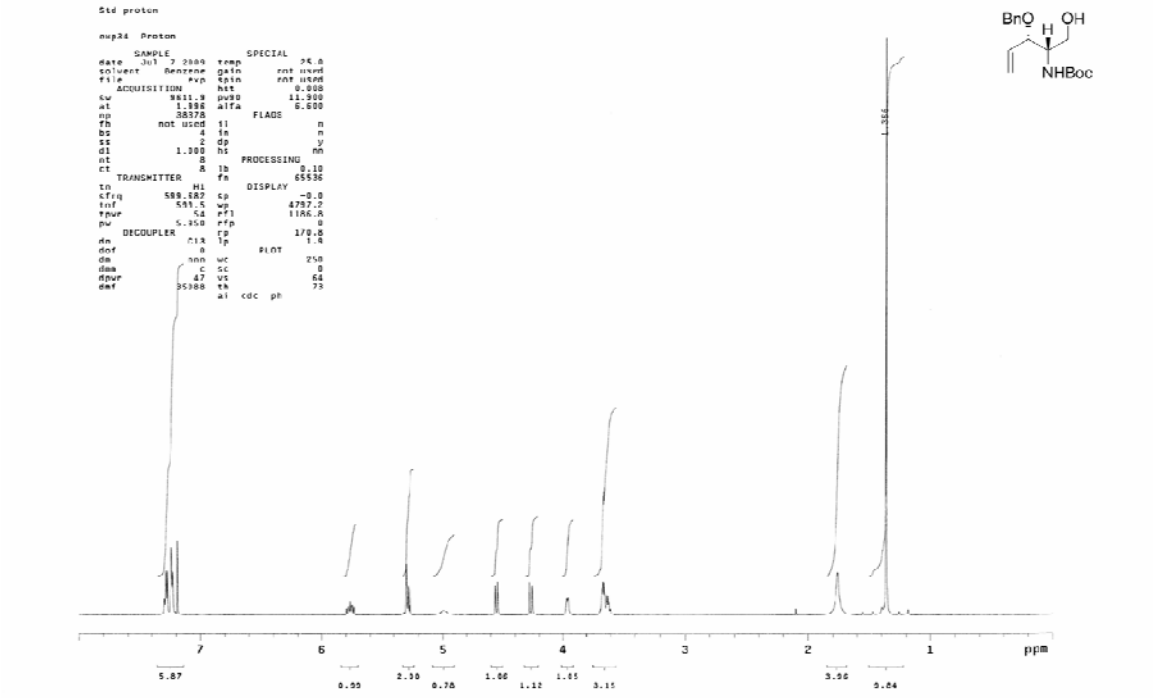
^{1}H-NMR of **4a**.



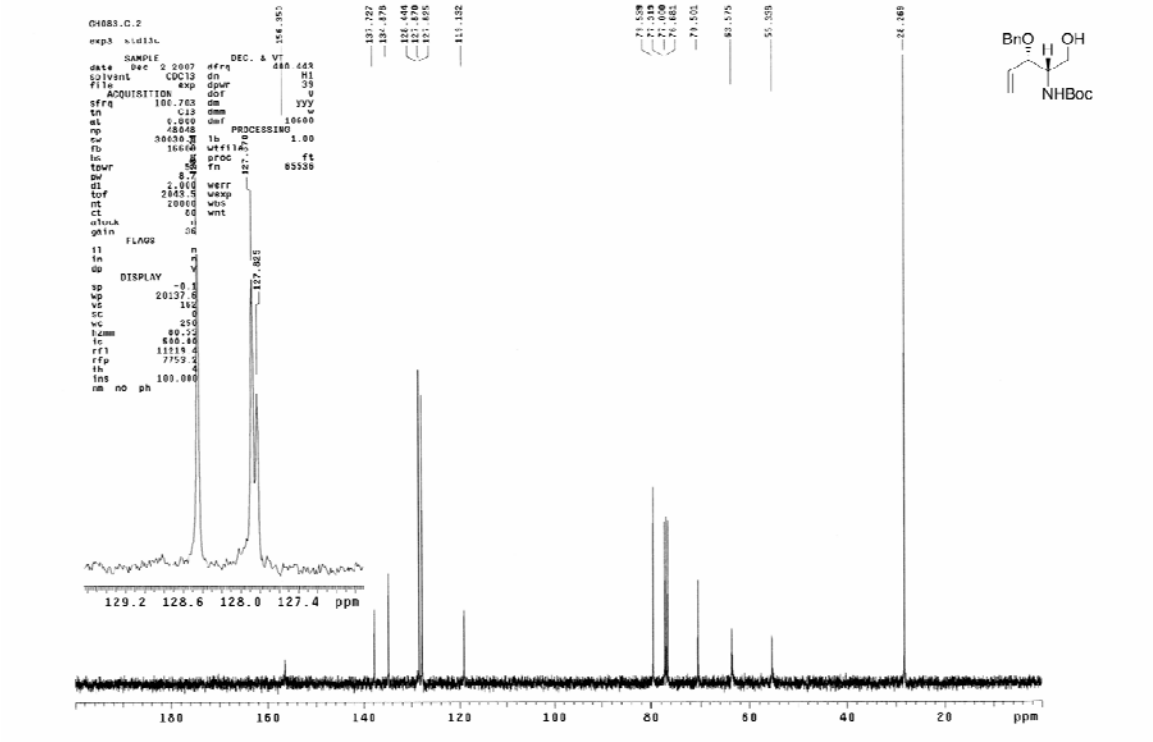
^{13}C-NMR of **4a**.



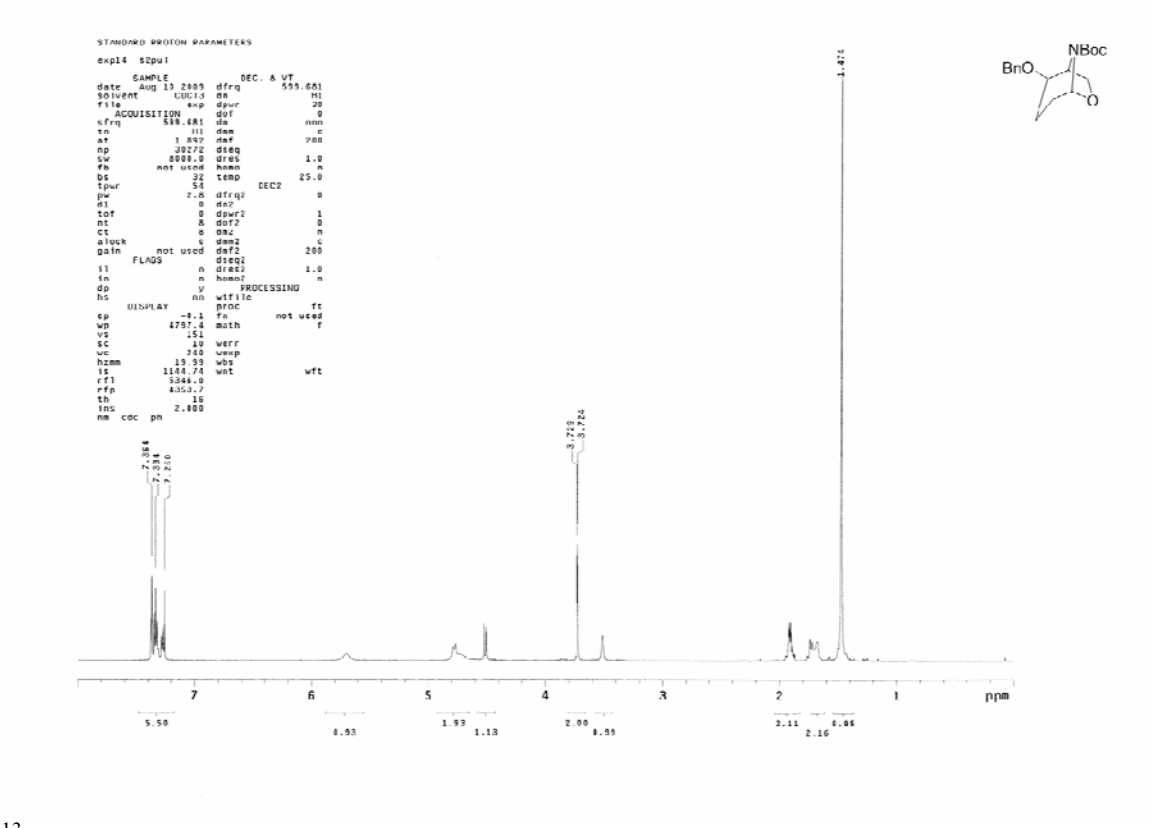
^{1}H-NMR of **4b**.



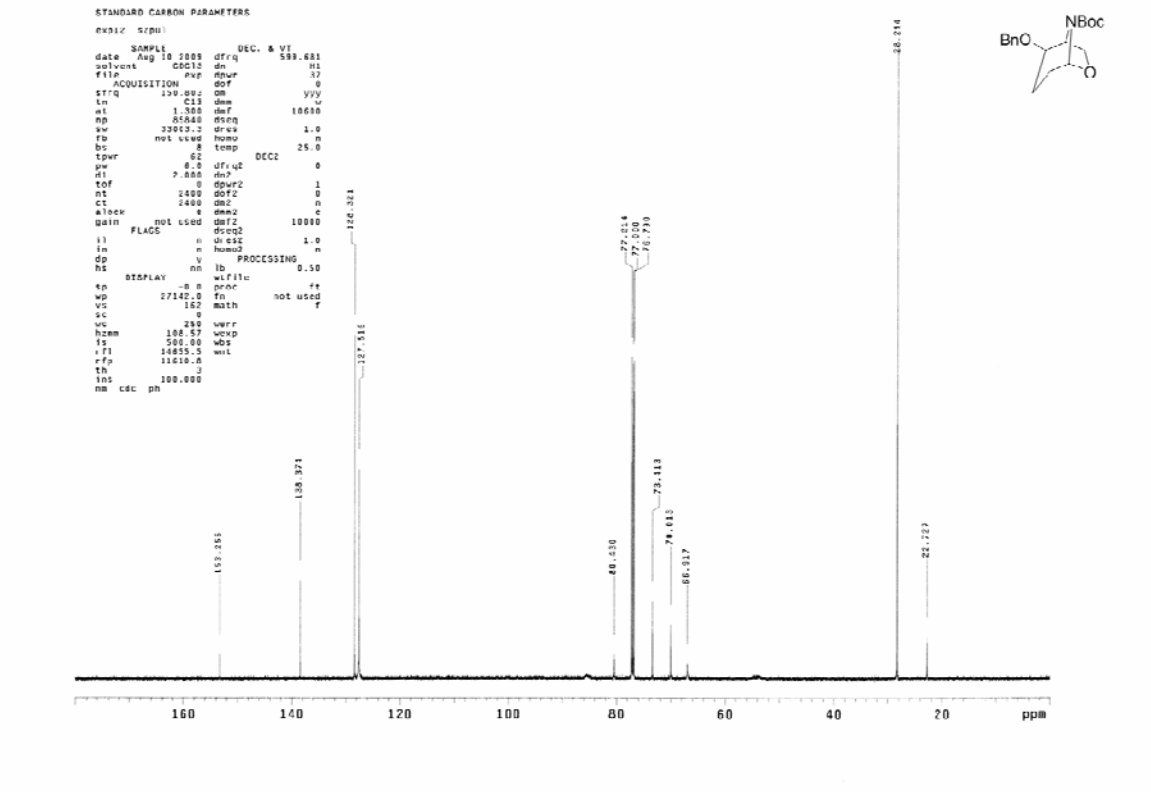
^{13}C-NMR of **4b**.



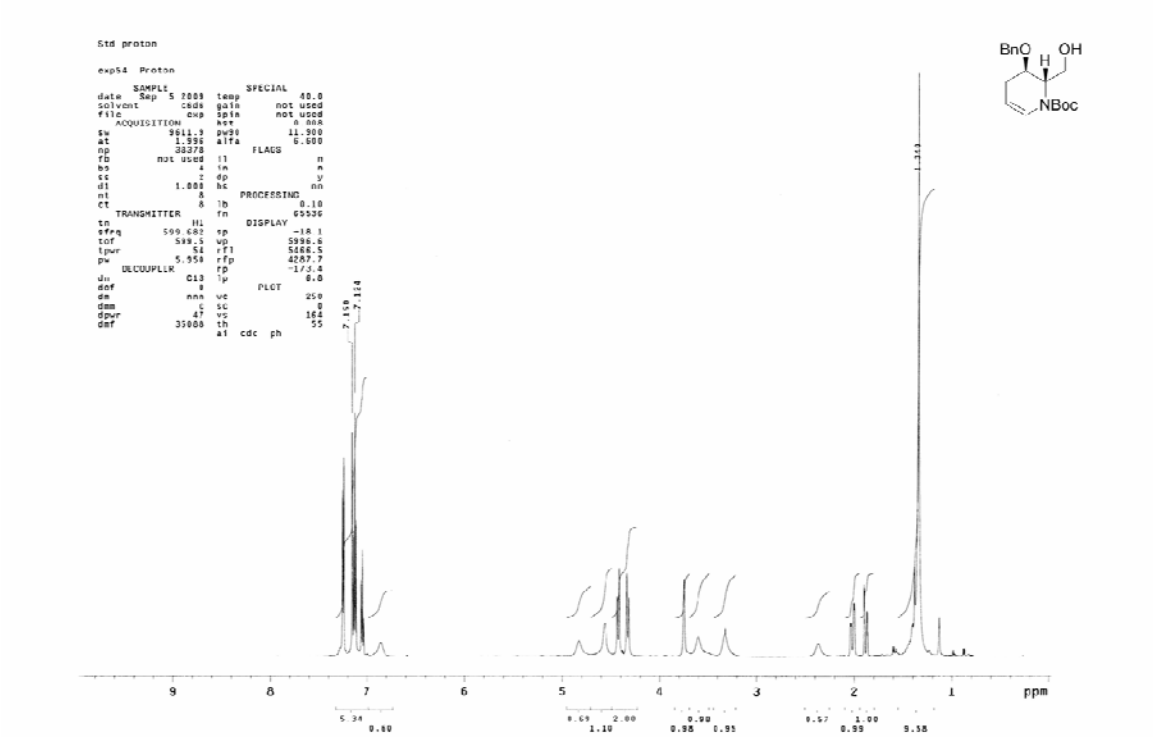
^{1}H-NMR of **5a**.



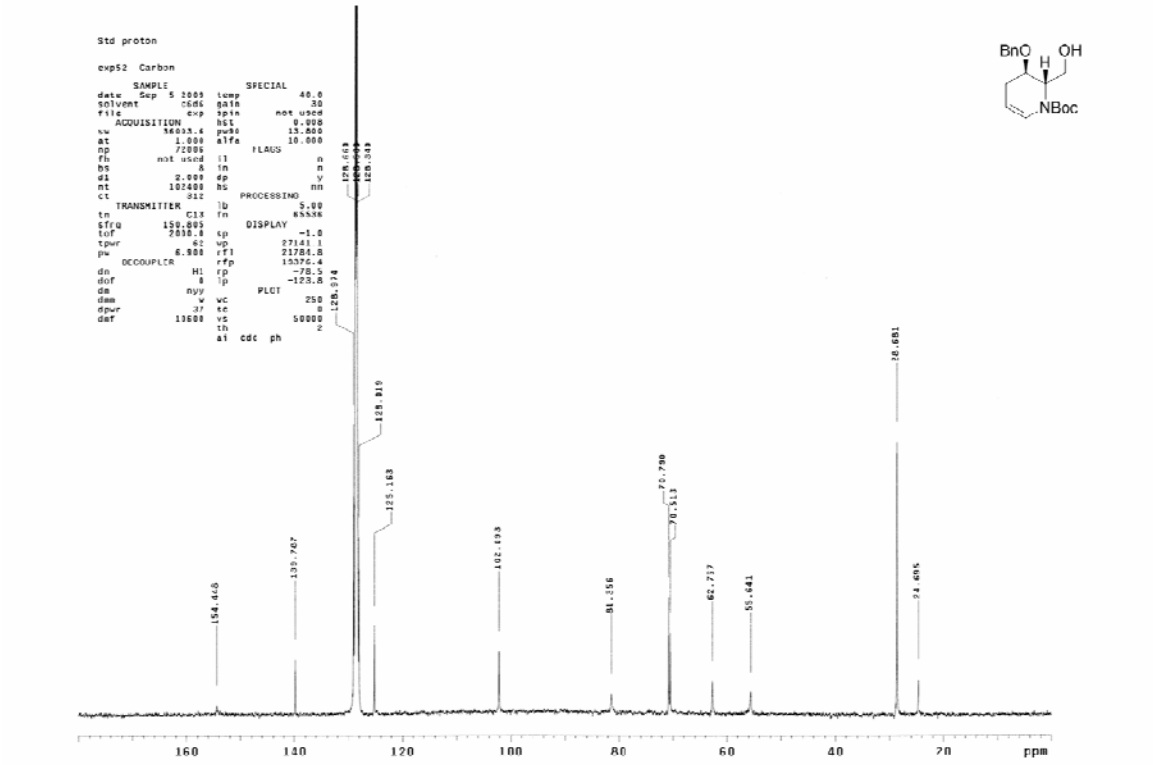
^{13}C-NMR of **5a**.



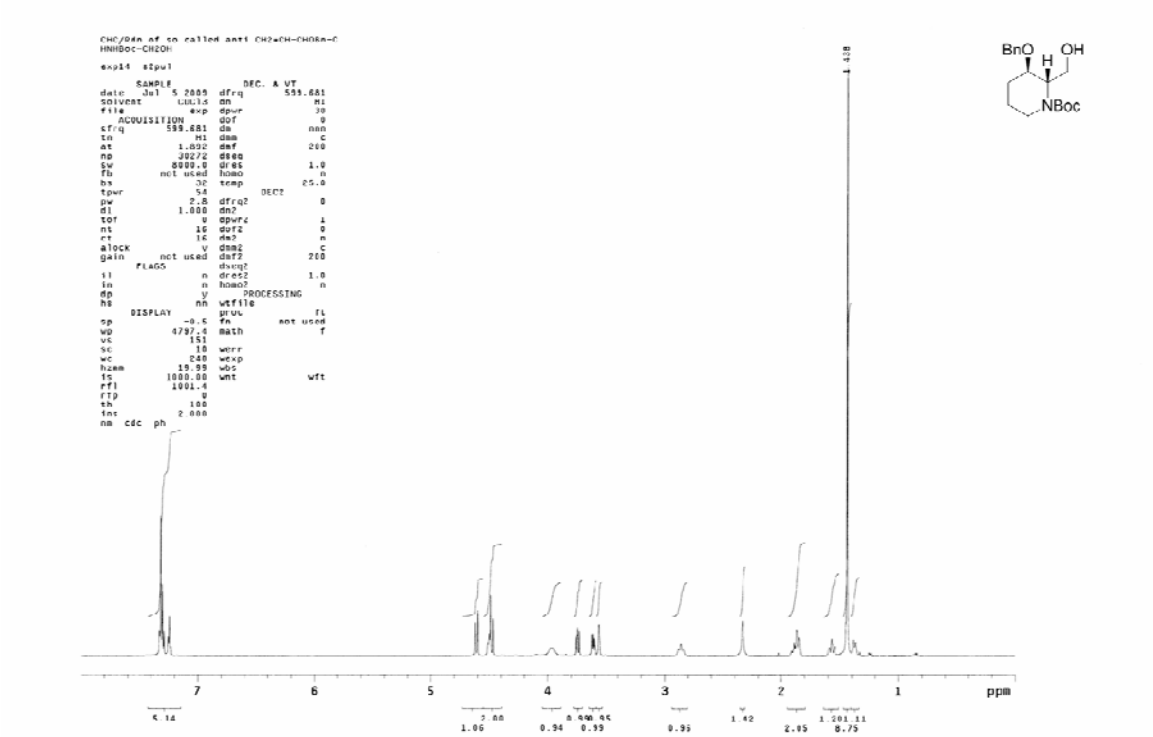
^{1}H-NMR of **6a**.



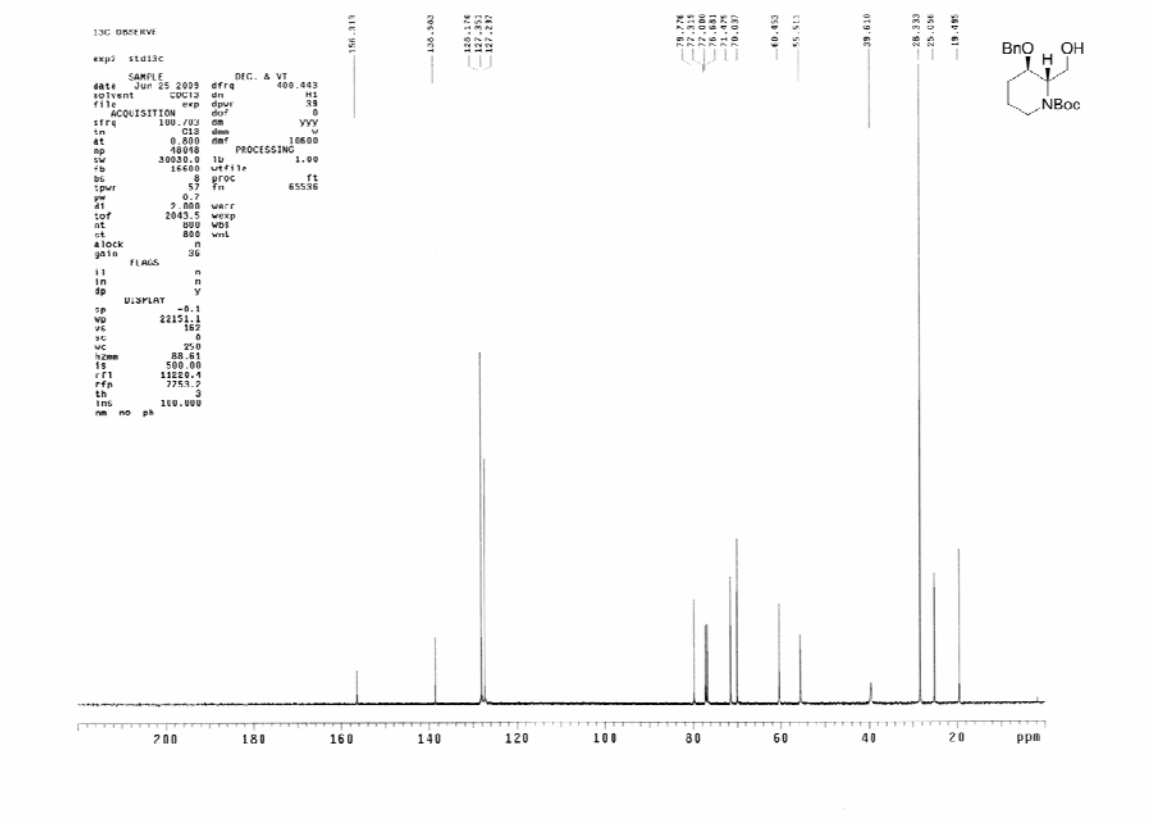
^{13}C-NMR of **6a**.



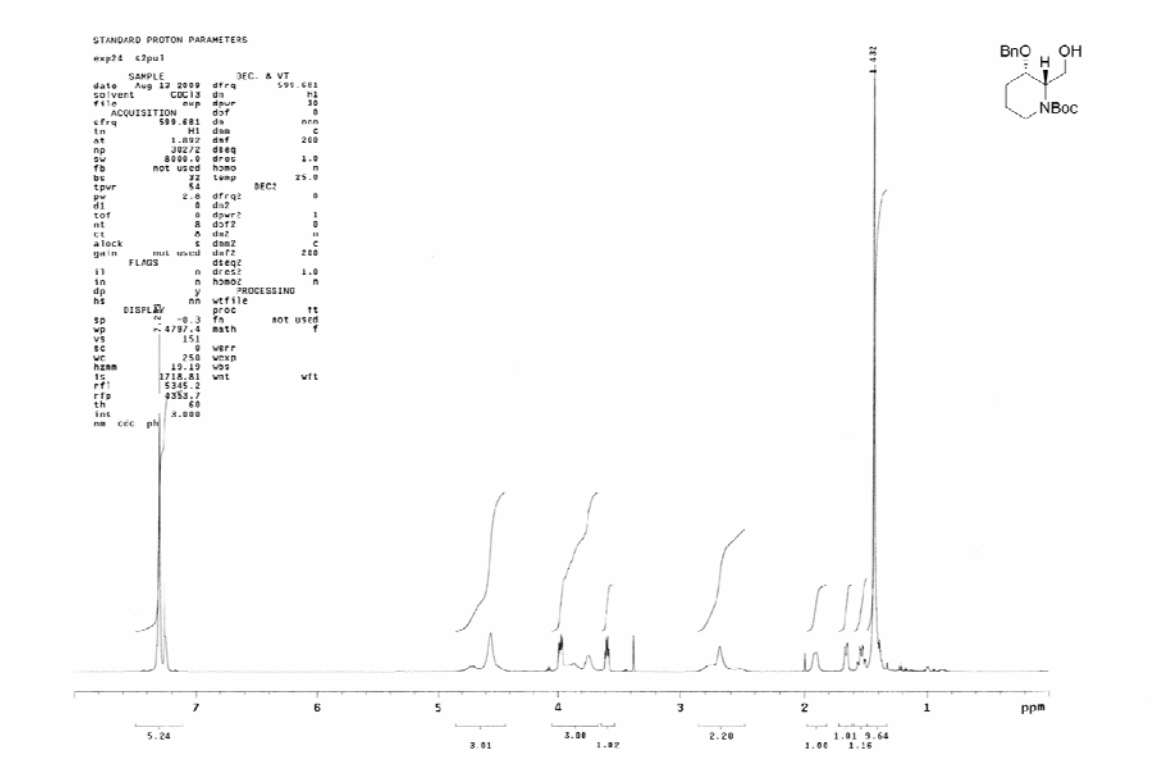
^{1}H-NMR of **7a**.



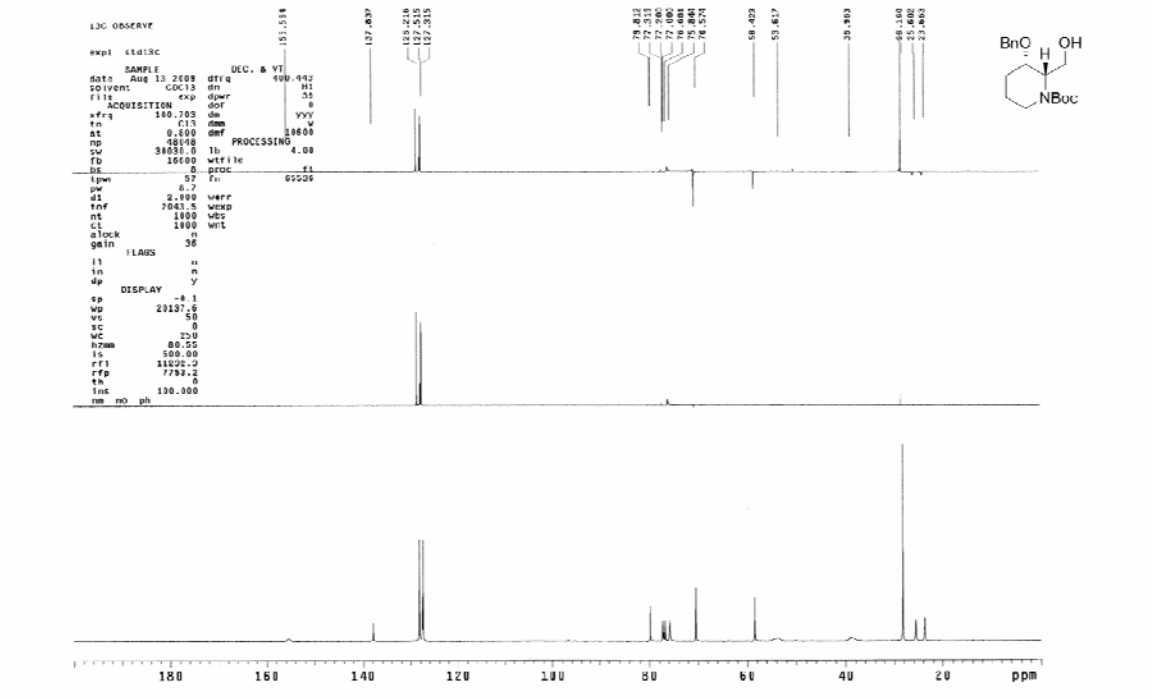
^{13}C-NMR of **7a**.



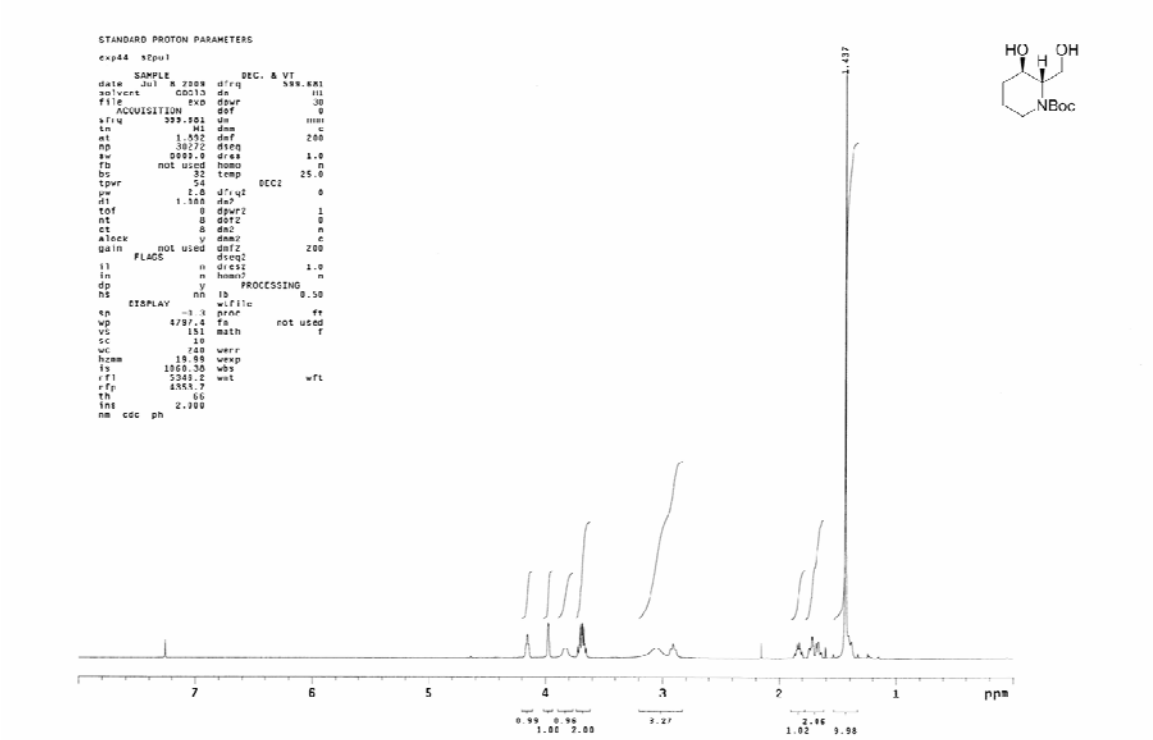
^{1}H-NMR of **7b**.



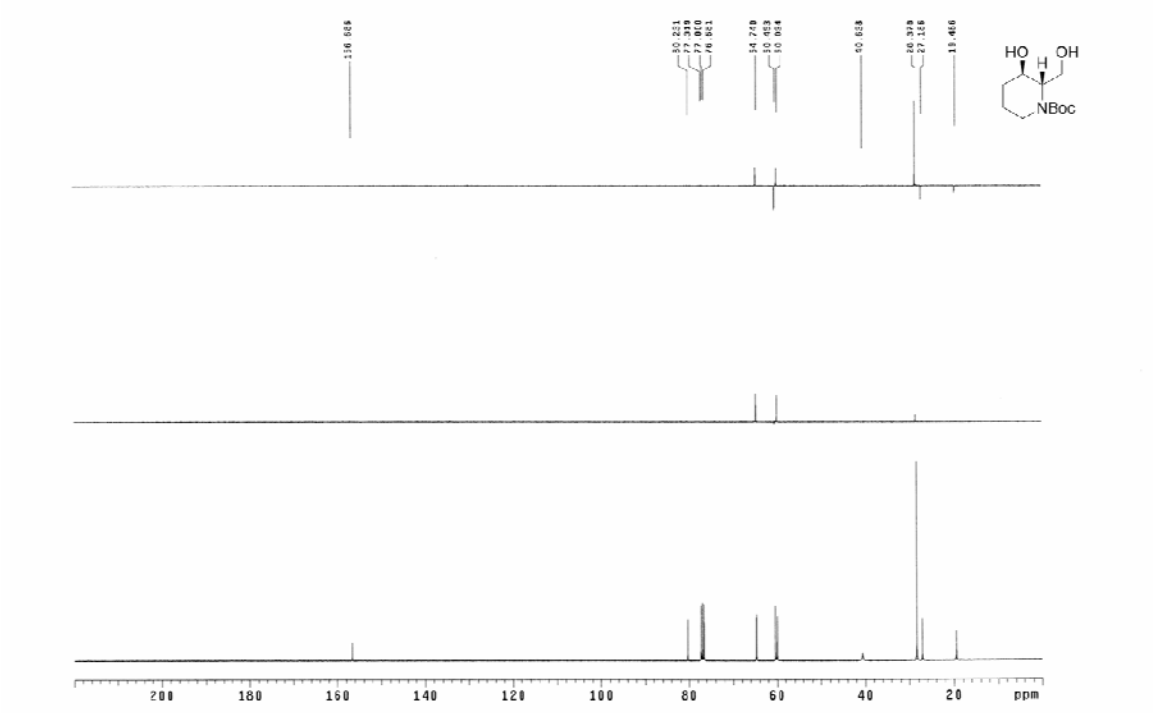
^{13}C-NMR of **7b**.



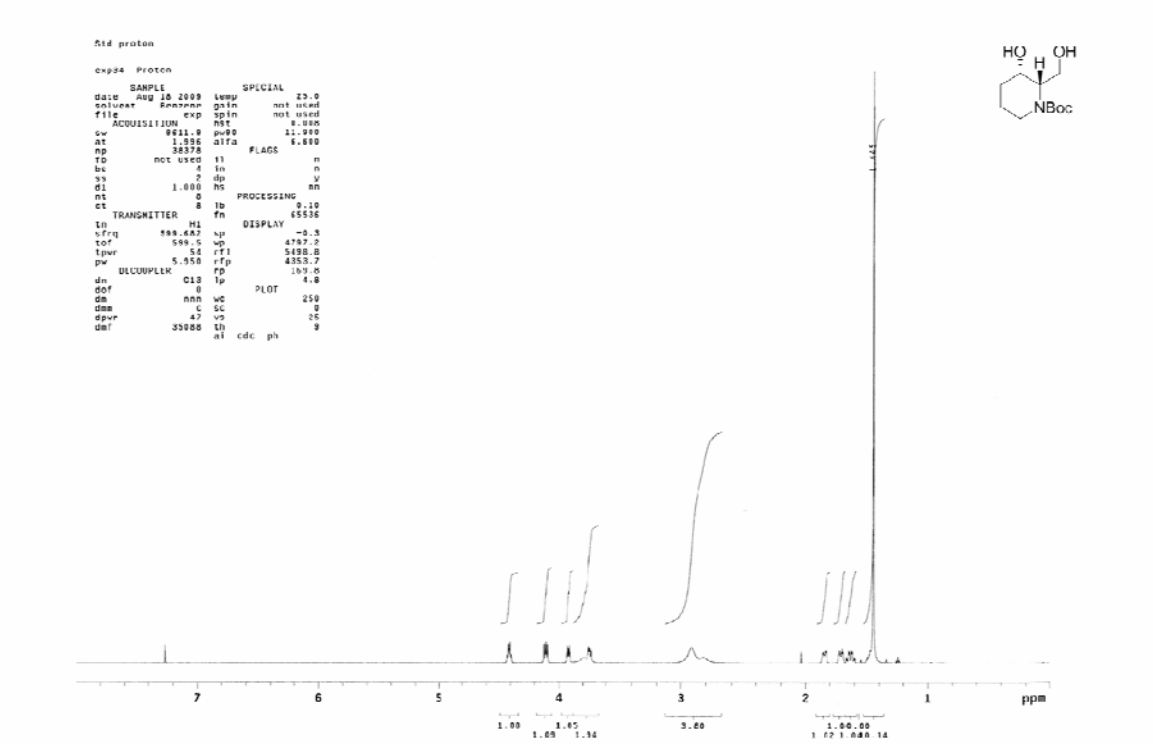
^{1}H-NMR of **8a**.



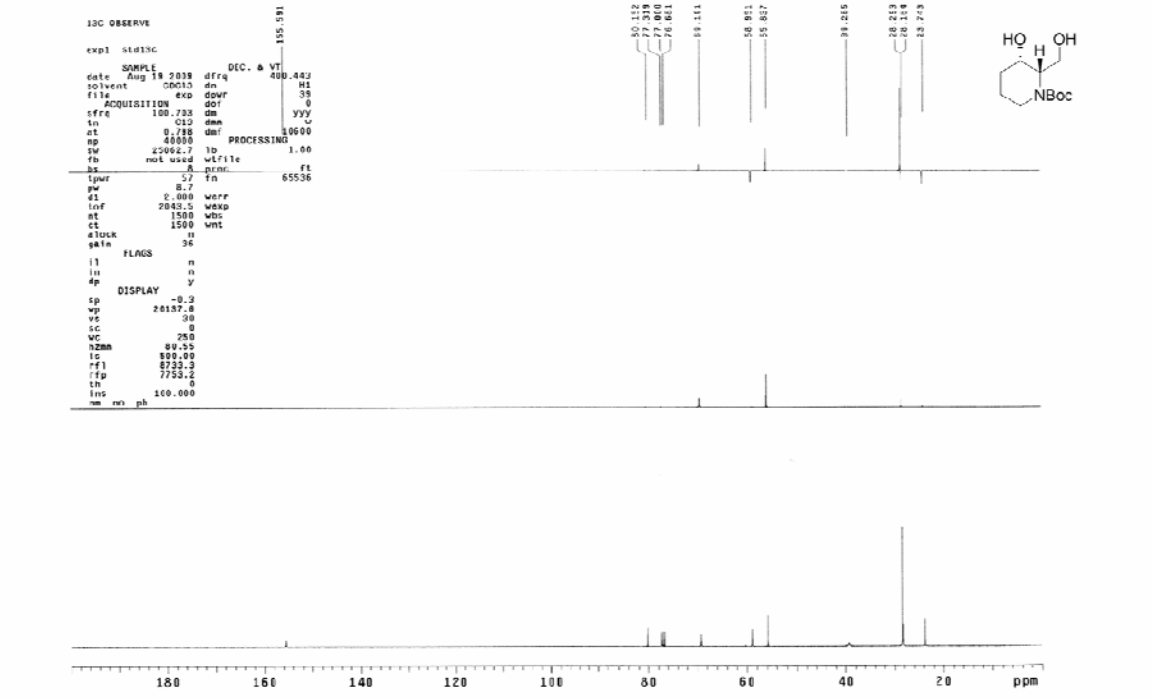
^{13}C-NMR of **8a**.



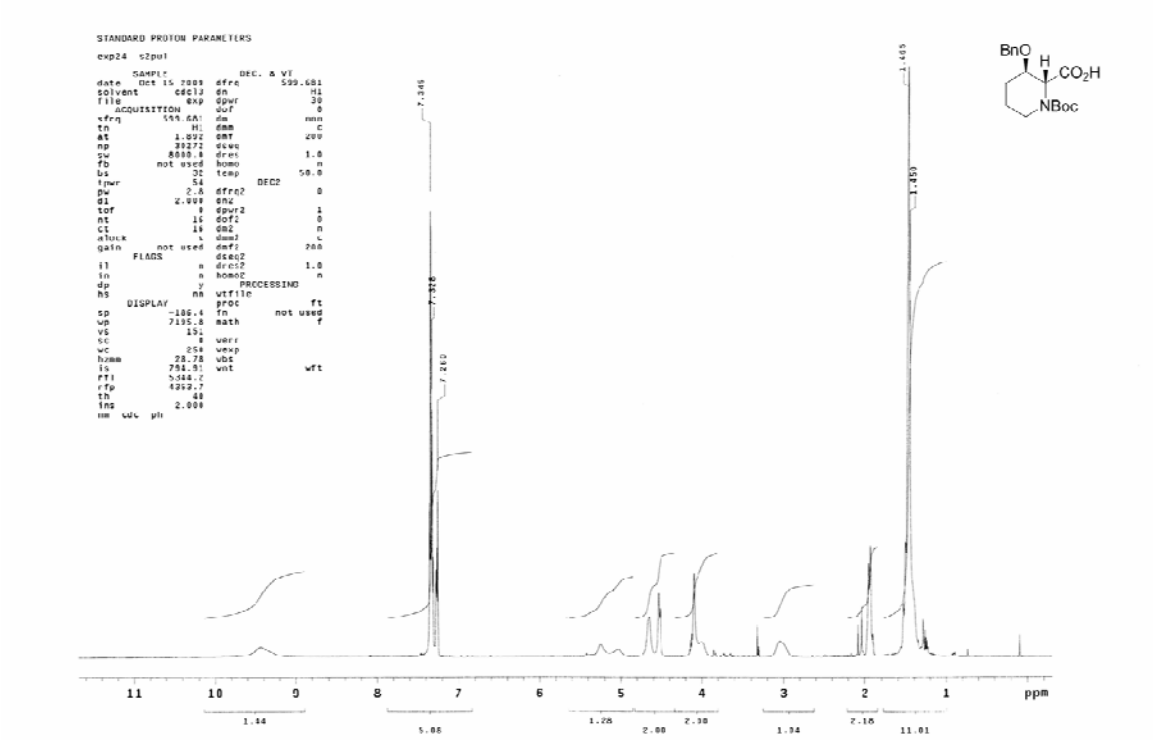
^{1}H-NMR of **8b**.



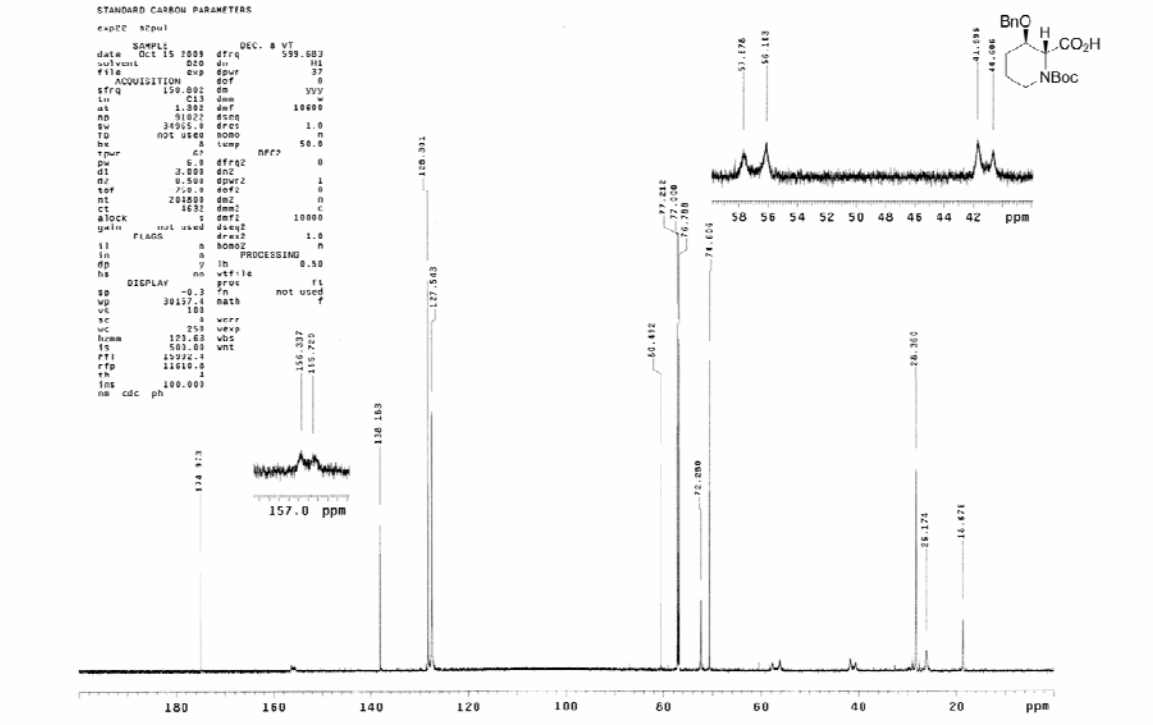
^{13}C-NMR of **8b**.



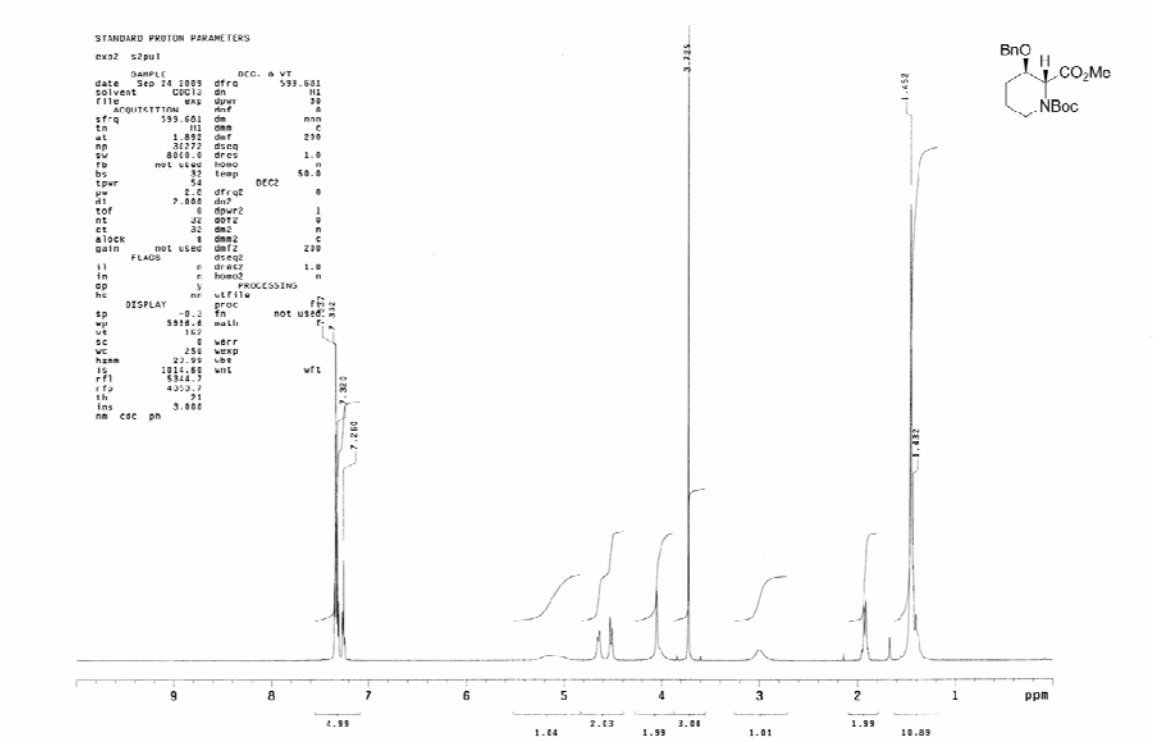
^{1}H-NMR of **9a**.



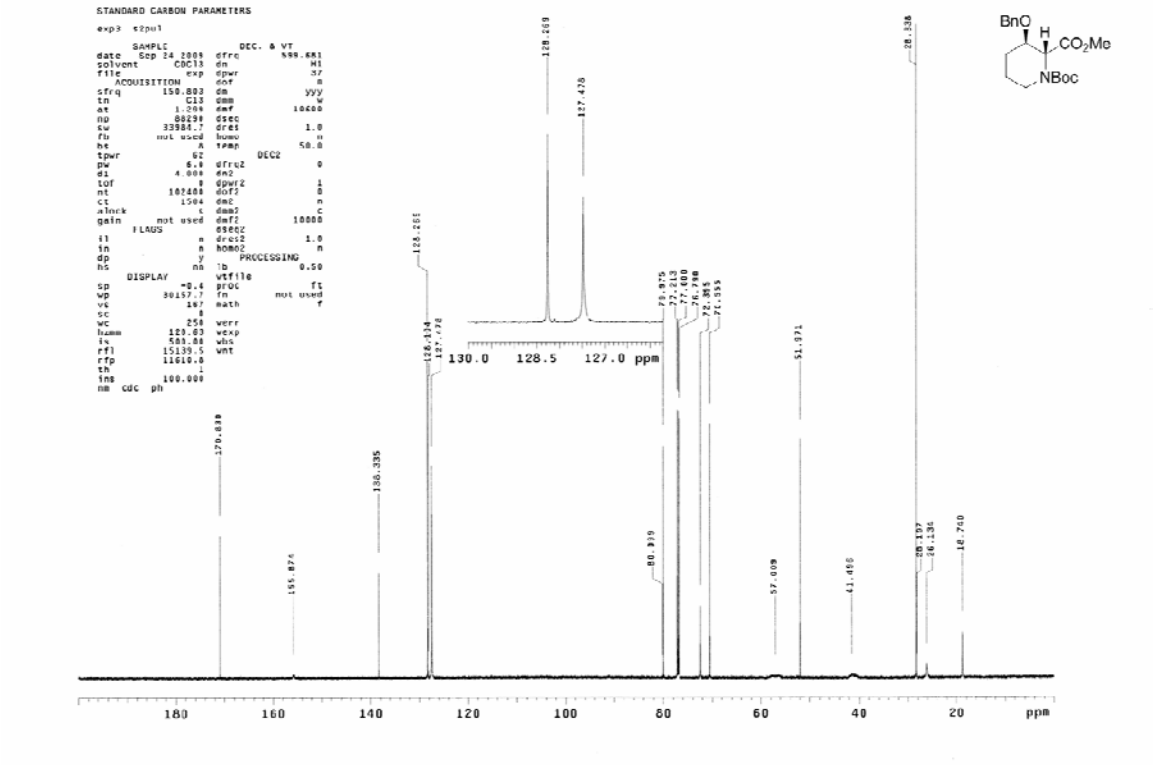
^{13}C-NMR of **9a**.



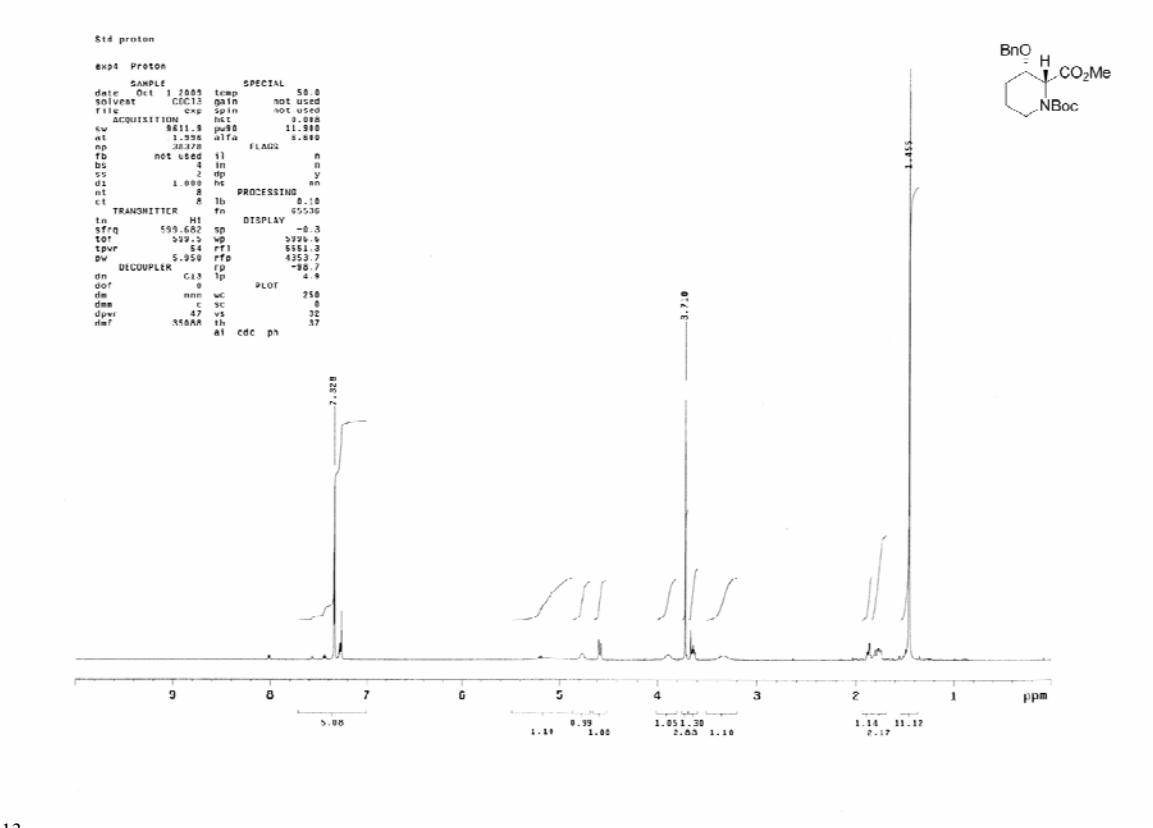
^{1}H-NMR of **10a**.



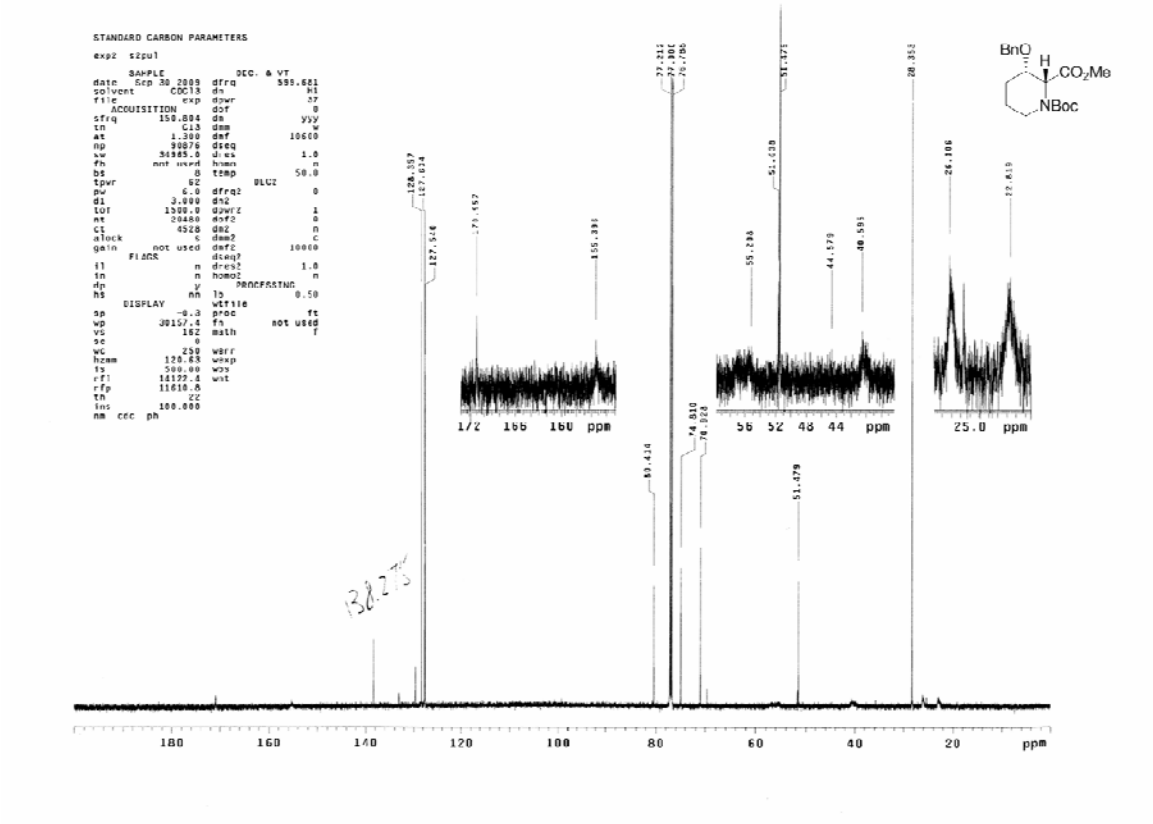
^{13}C-NMR of **10a**.



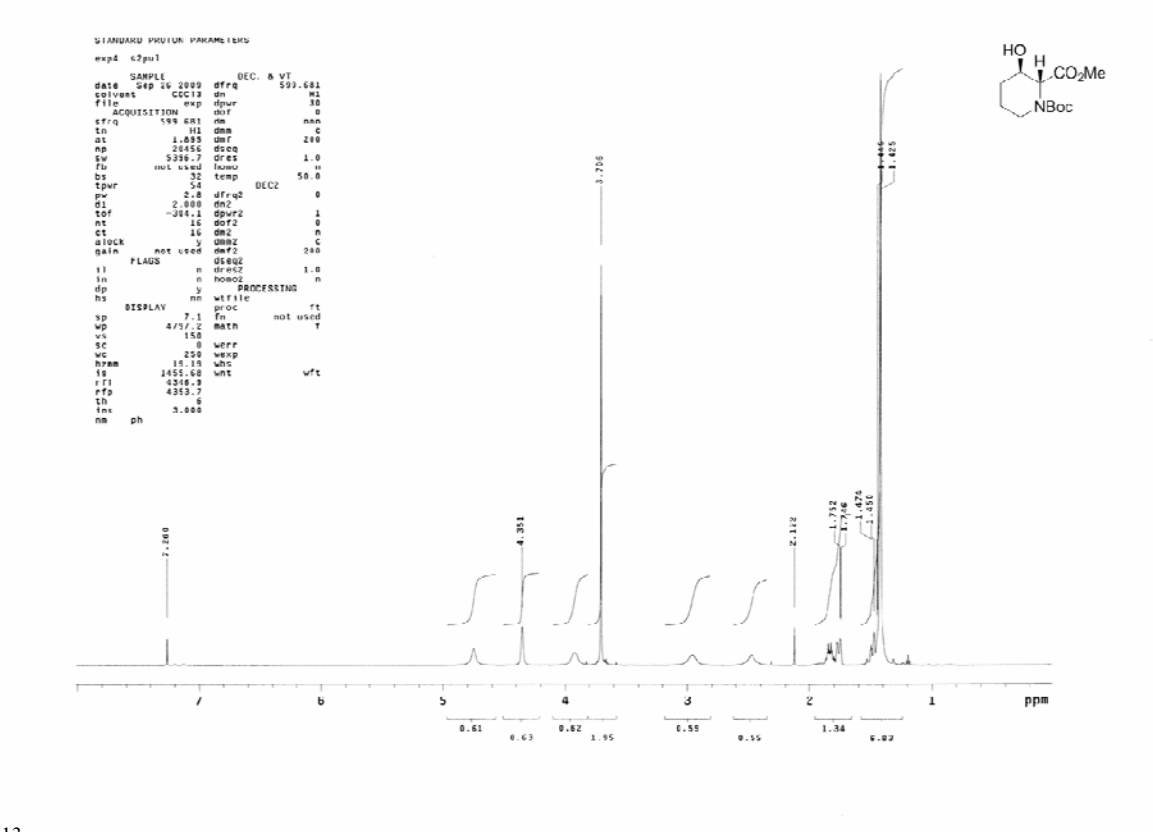
^{1}H-NMR of **10b**.



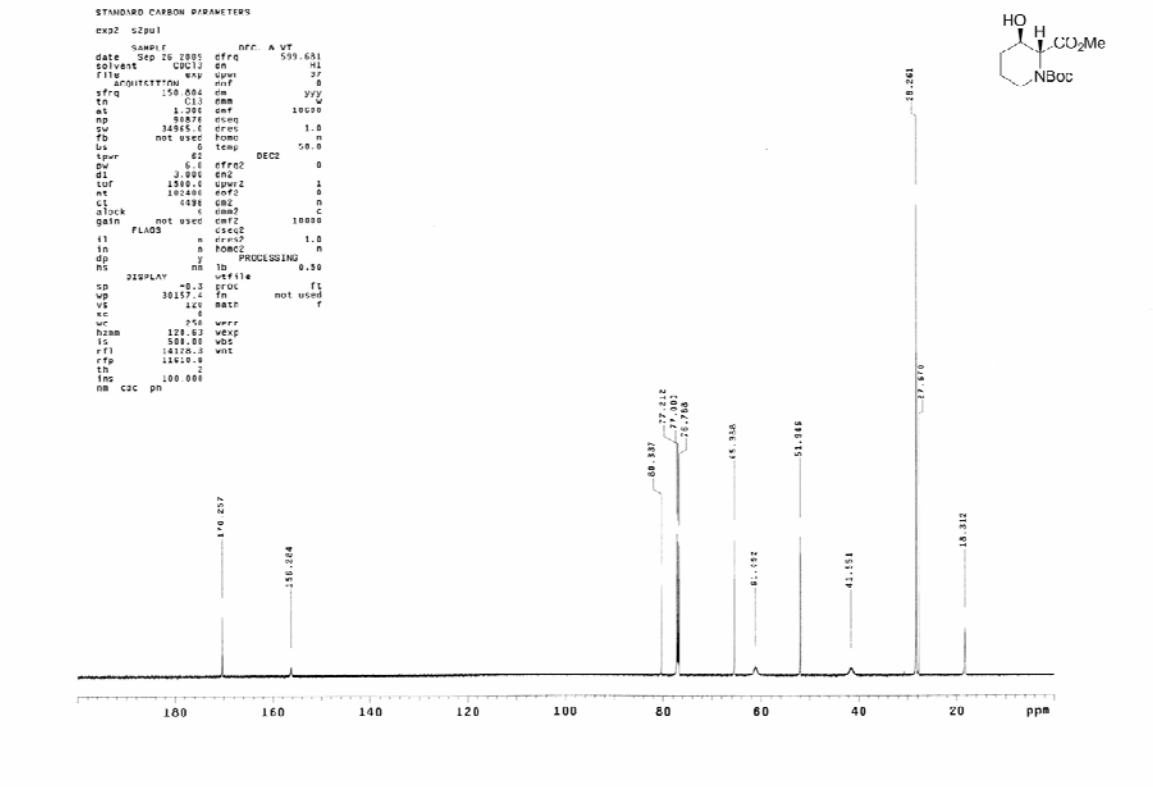
^{13}C-NMR of **10b**.



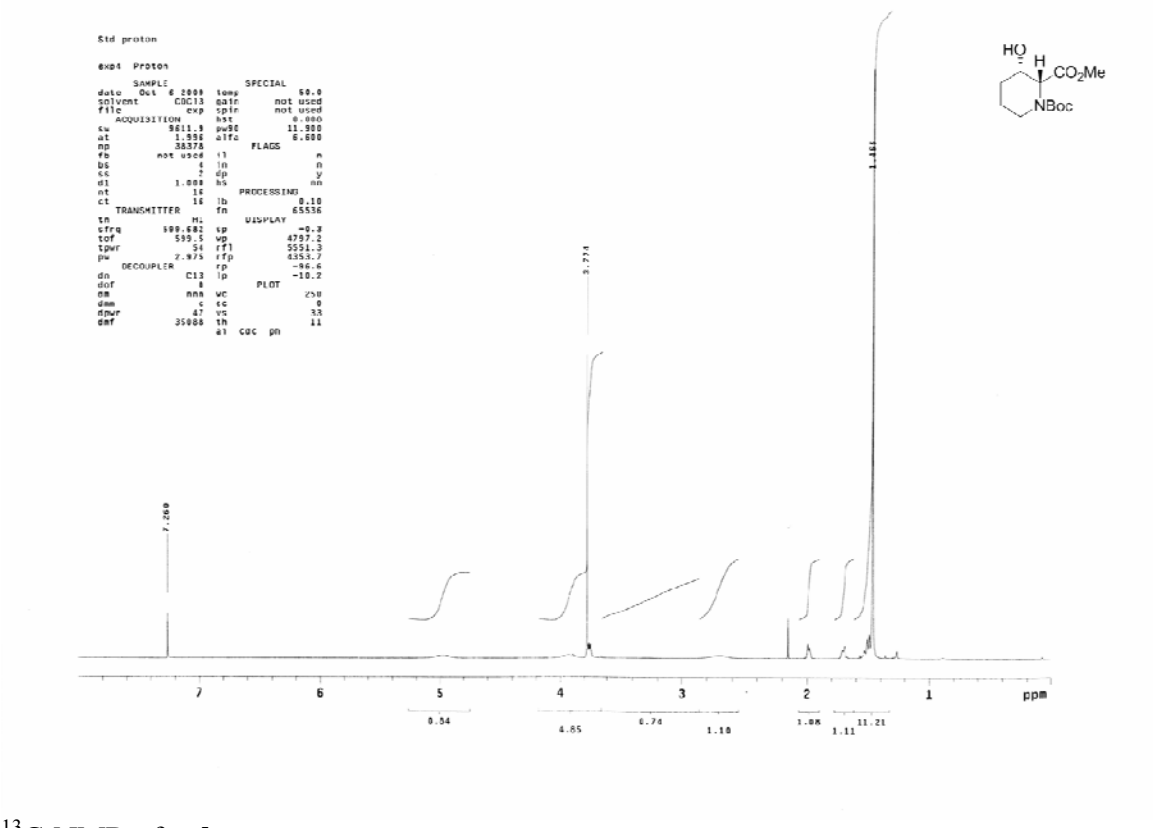
^{1}H-NMR of **11a**.



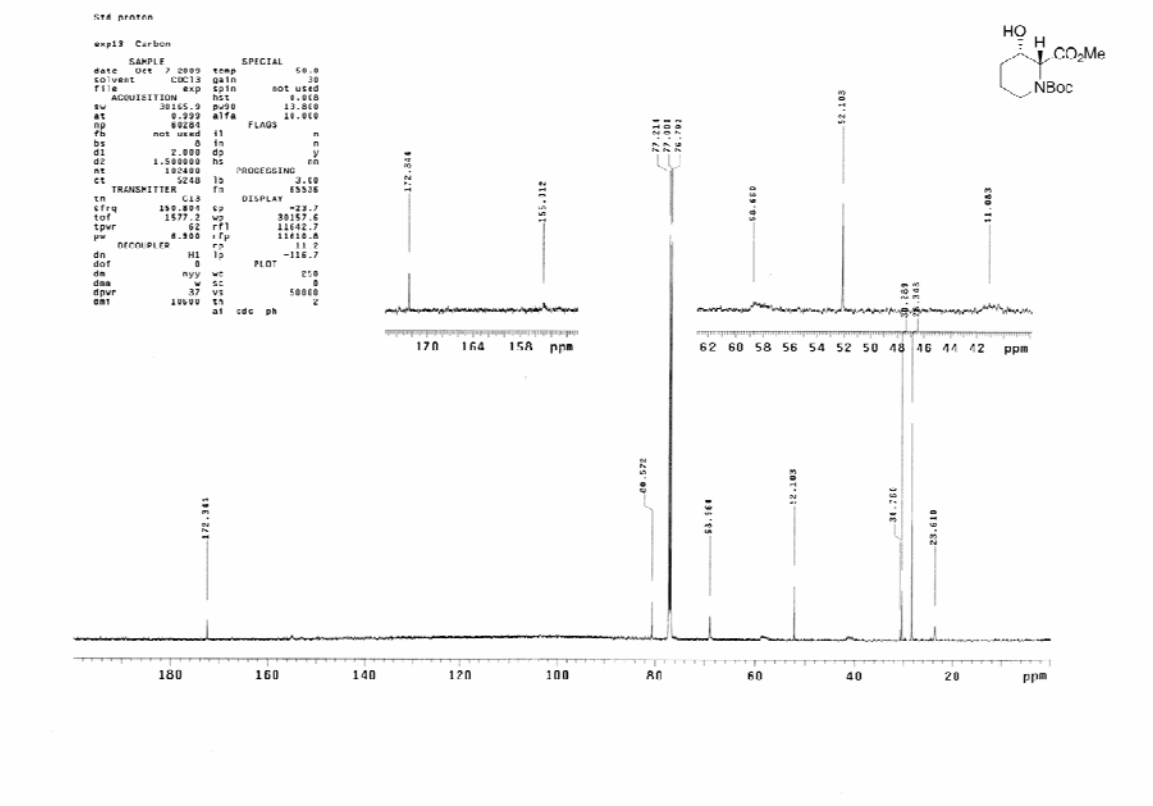
^{13}C-NMR of **11a**.



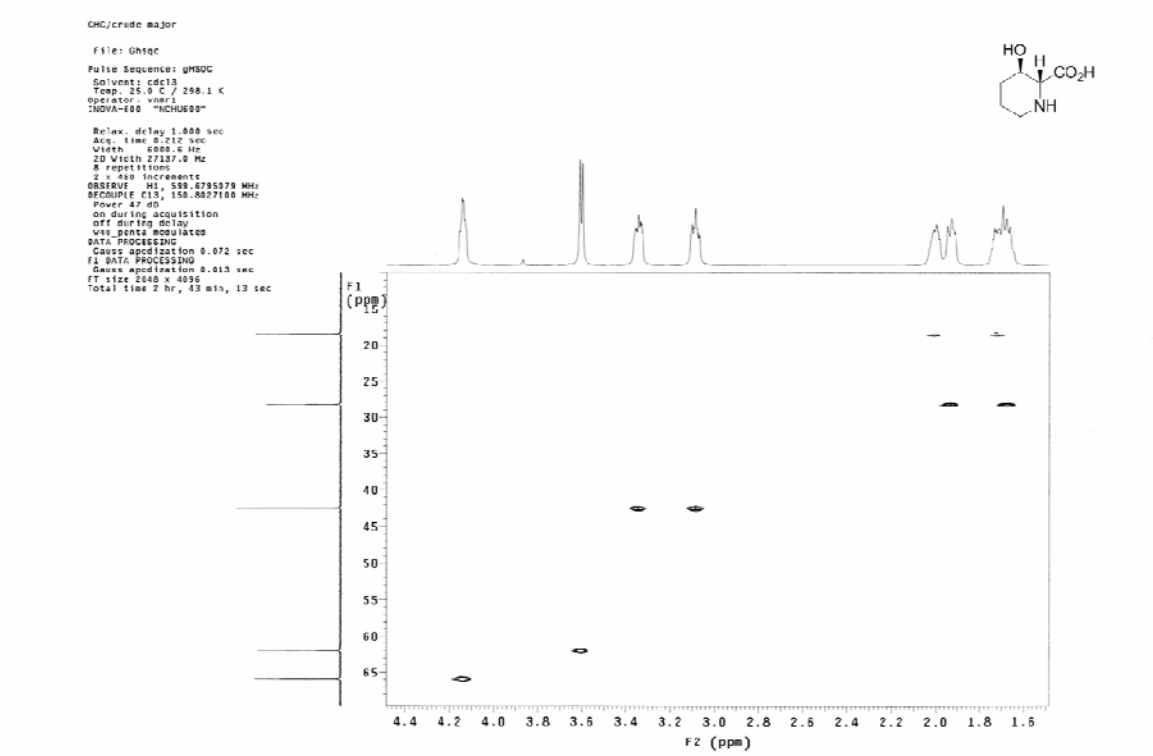
^{1}H-NMR of **11b**.



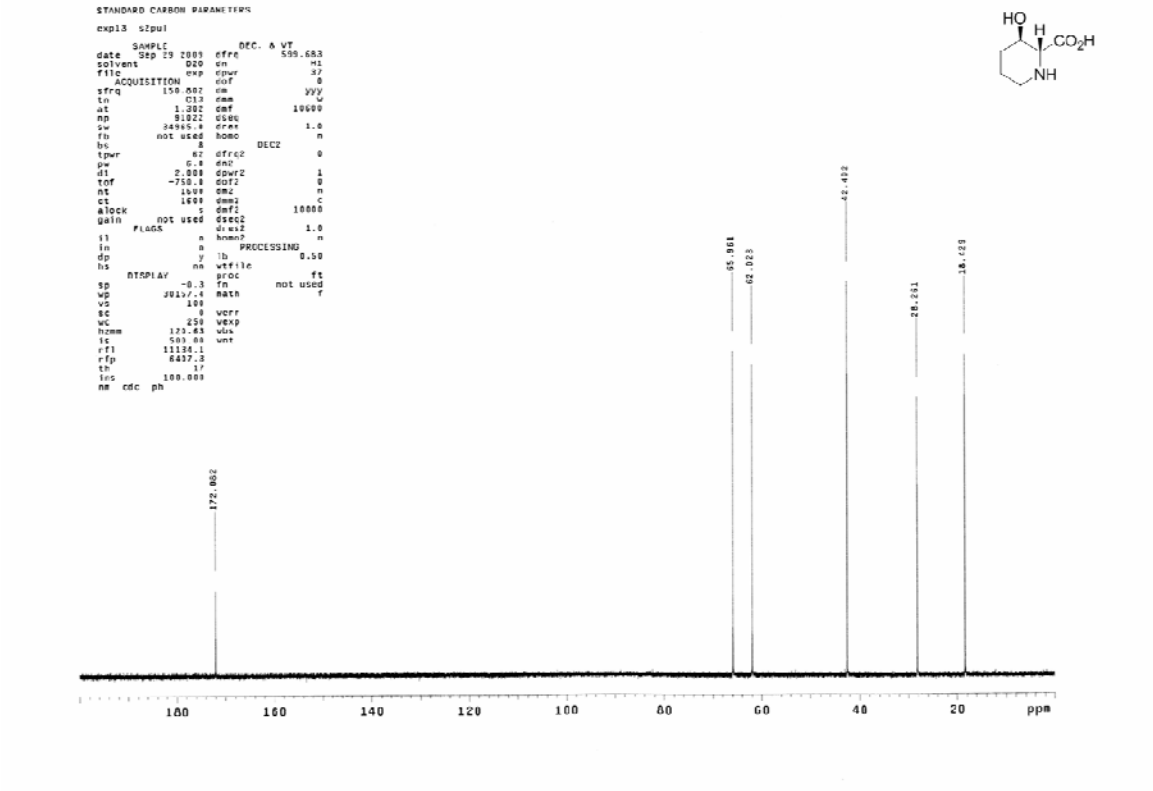
^{13}C-NMR of **11b**.



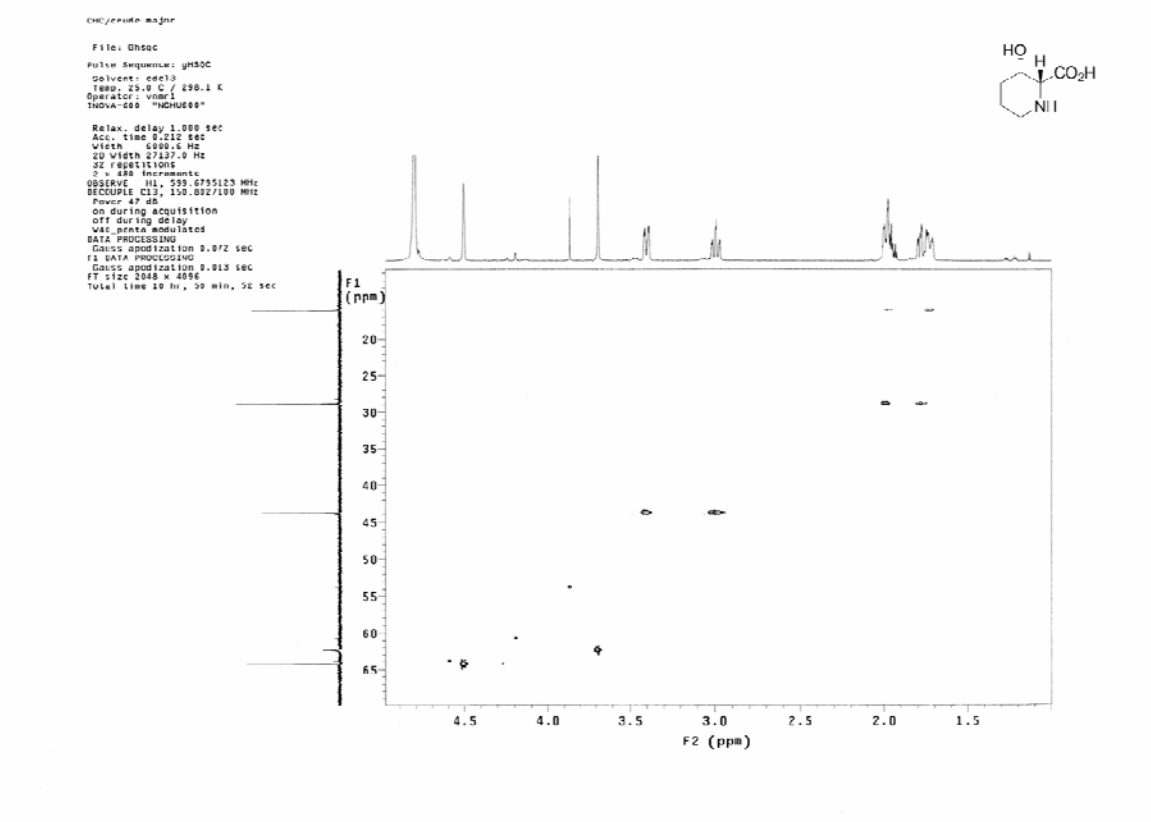
HSQC of **12a**.



^{13}C-NMR of **12a**.



HSQC of **12b**.



^{13}C-NMR of **12b**.