Electronic Supplementary Material (ESI) for RSC Advances.

Supplementary Information

Synthesis of Dendrobatid Alkaloid (+)-167B and (+)-209D and the Investigation on Diastereoselectivity using DFT Calculations

Wen-Hua Chiou* and Hao-Yu Chen

wchiou@dragon.nchu.edu.tw

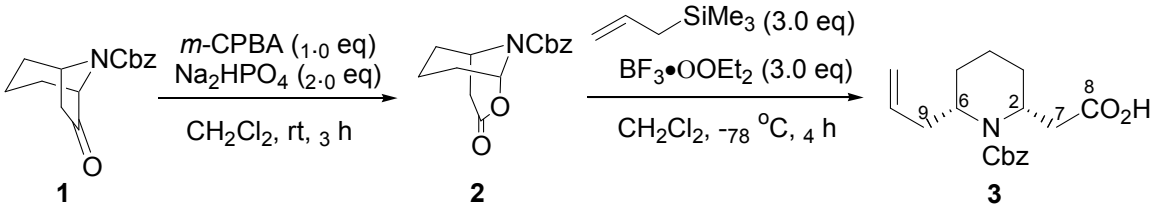
Department of Chemistry, National Chung Hsing University, Taichung 402 Taiwan, R.O.C.

Table of Contents

General Methods: All NMR spectra, i.e., ^{1}H, ^{13}C, DEPT, gCOSY, gHSQC, gHMBC, ROESY, were recorded on a Varian 600 or 400 MHz NMR spectrometer, which provided all necessary data for the full assignment of each compound. Melting points were measured on a Büchi 535 melting point apparatus and uncorrected. High-resolution mass spectrometry (HRMS) analyses were conducted at the Instrument Center of National Chung Hsing University. GC-MS analyses were performed on an HP 5890 Series GC system equipped with an Rtx-®-5MS capillary column (50 m X 0.25 mm, 0.5 □m). IR spectra were measured on a Bruker Equinox 55 or Bruker Tensor 27 spectrophotometer. TLC analyses were performed on Merck DC-alufolien with Kieselgel 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 (Merck, 230-400 mesh ASTM). Microwave reactions were performed in a *Discover* system of CEM.

Materials: Chemicals, reagents and solvents were purchased from Sigma Aldrich Company or Acros Organic Fischer Company. The reagents were used as received. Dichloromethane, pyridine, triethylamine, acetonitrile, DMSO and methanol were dried and distilled over calcium hydride under argon before use. Ether was dried and distilled over sodium-benzophenone ketyl under argon before use. THF was dried and distilled over potassium metal under argon before use. Toluene and benzene were dried and distilled over sodium metal under argon or argon before use. The reaction flasks were dried in a 110 °C oven and allowed to cool to room temperature in a desiccator over "*Drierite*" (calcium sulfate) and assembled under argon atmosphere.

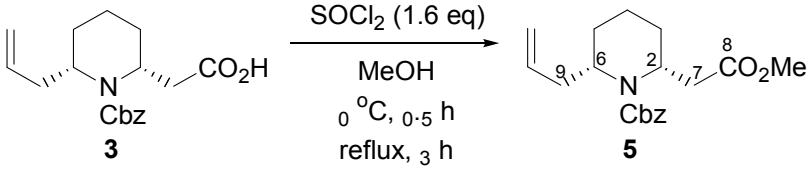
(−)-(2*R*,6*S*)-6-(2-propenyl)-1-benzyloxycarbonyl-2-piperidineacetic acid, (−)-(3):



To a mixture of ketone **1** (852 mg, 3.29 mmol, 1.0 equiv) and Na_2HPO_4 (933 mg, 6.57 mmol, 2.0 equiv) in CH_2Cl_2 (66 mL), was added *meta*-chloroperoxybenzoic acid (*m*-CPBA 70-75%, 810 mg, ~1.0 equiv). The solution was allowed to be stirred for 3 h at room temperature. Upon completion of the reaction monitored by TLC analysis, the reaction mixture was washed with saturated $NaHCO_3$ solution (68 mL). The aqueous layer was extracted with CH_2Cl_2 (30 mL × 5). The organic layer was dried over anhydrous Na_2SO_4. After removal of the solid dehydrating agent, and then concentrated under reduced pressure to give a colorless oil **2** (956 mg). The product was used directly without further purification. To a CH_2Cl_2 solution (32 mL) of crude lactone **2** (956 mg) at -78 °C, was added dropwise allyltrimethylsilane (1.6 mL, 9.86 mmol, 3.0 equiv), followed by BF_3•OEt_2 (1.3 mL, 9.86 mmol, 3.0 equiv). The reaction mixture was allowed to be stirred at -78 °C for 4 h. Upon completion of the reaction monitored by TLC analysis, a saturated $NaHCO_3$ solution (20 mL) was slowly added into the reaction mixture at 0 °C, and then warmed up to room temperature. After separation of the organic layer, the aqueous layer was extracted with CH_2Cl_2 (25 mL × 5). The combined organic dried over Na_2SO_4. After removal of the solid dehydrating agent,

the organic layer was concentrated under reduced pressure to give a crude product. Purification of the crude product by flash chromatography on silica gel, EtOAc/*n*-Hex as the eluant to give the titled product as a colorless oil (875 mg, 2.76 mmol, 84% over two steps): R_f = 0.41; EtOAc. $[\alpha]_D^{25}$ −25.6 (*c* 1.1, $CHCl_3$). ^1H NMR (400 MHz, 25 °C, $CDCl_3$, δ): 1.51−1.57 (m, 2H, H-4, H-5), 1.63−1.66 (m, 2H, H-3, H-4), 1.70−1.73 (m, 2H, H-3, H-5), 2.22−2.31 (m, 2H, H-9 × 2), 2.59 (dd, *J* = 3.2, 15.2 Hz, 1H, H-7), 2.69 (dd, *J* = 10.4, 15.2 Hz, 1H, H-7), 4.26 (brs, 1H, H-6), 4.71 (t, *J* = 4.4 Hz, 1H, H-2), 5.00−5.05 (m, 2H, H-11 × 2), 5.12 (d, *J* = 12.4 Hz, 1H, -OC<u>H</u>$_2$Ph), 5.17 (d, *J* = 12.4 Hz, 1H, -OC<u>H</u>$_2$Ph), 5.70−5.72 (m, 1H, H-10), 7.29−7.31 (m, 1H, H-4' in Ph), 7.32−7.36 (m, 4H, H-2' and H-3' in Ph), 9.70 (br, 1H, -COO<u>H</u>). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$, δ): 13.5 (t, C-4), 26.2 (t, C-5), 27.7 (t, C-3), 38.7 (t, C-9), 38.8 (t, C-7), 47.0 (d, C-2), 50.0 (d, C-6), 67.1 (t, -O<u>C</u>H$_2$Ph), 117.2 (t, C-11), 127.7 (d, C-2 in Ph), 127.8 (d, C-4 in Ph), 128.3 (d, C-3 in Ph), 135.5 (d, C-10), 136.4 (s, C-1 in Ph), 155.7 (s, N-<u>C</u>O-O), 176.4 (s, C-8).

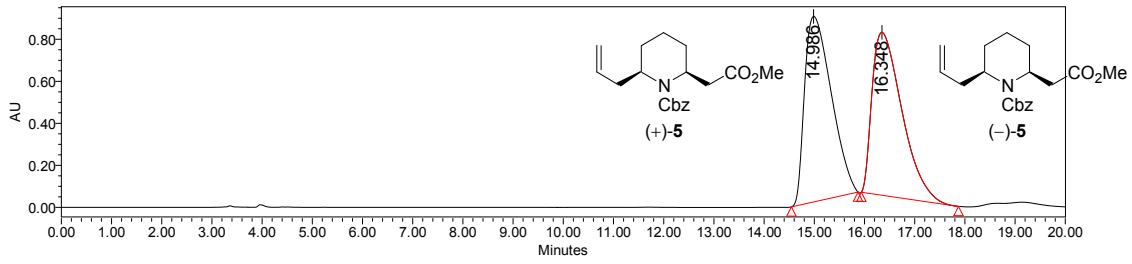
(−)-(2*R*,6*S*)-methyl -6-(2-propenyl)-1-benzyloxycarbonyl-2- piperidineacetate, (−)-(5):



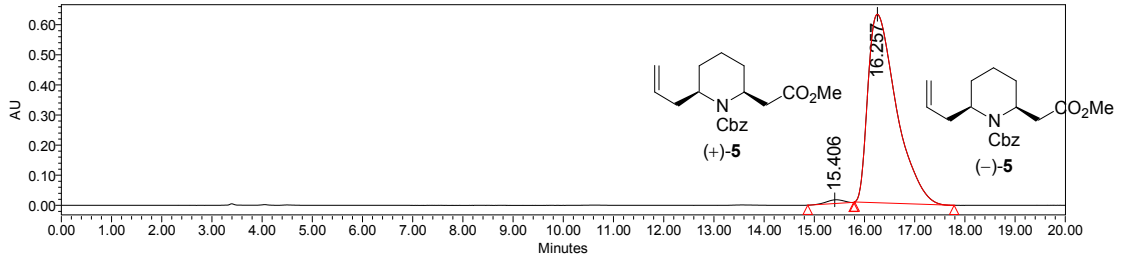
To a solution of the acid **3** (1.02 g, 3.21 mmol, 1.0 equiv) in MeOH (29 mL) at 0 °C, was slowly added Thionyl chloride (380 µL, 5.20 mmol, 1.6 equiv). The reaction mixture was allowed to be stirred at 0 °C for 0.5 h.

The reaction mixture was warmed to room temperature, followed by heated under reflux condition for 3 h. Upon completion of the reaction monitored by TLC analysis, the reaction mixture was concentrated under reduced pressure to a brown crude product. Purification of the crude product by flash chromatography on silica gel, EtOAc/*n*-Hex as the eluant to give the titled product as a colorless oil (980 mg, 2.96 mmol, 92%): R_f = 0.35; EtOAc/*n*-Hex = 1:5. $[\alpha]_D^{22}$ –26.0 (*c* 1.6, $CHCl_3$). ^1H NMR (400 MHz, 25 ^oC, $CDCl_3$, δ): 1.45−1.54 (m, 2H, H-4, H-5), 1.56−1.72 (m, 4H, H-3 × 2, H-4 and H-5), 2.21−2.35 (m, 2H, H-9 × 2), 2.54 (dd, *J* = 4.4, 14.8 Hz, 1H, H-7), 2.63 (dd, *J* = 10.0, 14.8 Hz, 1H, H-7), 3.64 (s, 3H, -$CO_2C\underline{H}_3$), 4.25 (d, *J* = 4.0 Hz, 1H, H-6), 4.69 (dt, *J* = 2.0, 4.8 Hz, 1H, H-2), 5.00 (d, *J* = 10.0 Hz, 1H, H-11), 5.01 (d, *J* = 16.0 Hz, 1H, H-11), 5.11 (d, *J* = 12.8 Hz, 1H, -O$C\underline{H}_2$Ph), 5.15 (d, *J* = 12.4 Hz, 1H, -O$C\underline{H}_2$Ph), 5.66−5.76 (m, 1H, H-10), 7.27−7.32 (m, 1H, H-4’ in Ph), 7.33−7.37 (m, 4H, H-2’ and H-3’ in Ph). ^{13}C NMR (100 MHz, 25 ^oC, $CDCl_3$, δ): 13.6 (t, C-4), 26.3 (t, C-5), 27.8 (t, C-3), 38.8 (t, C-7), 38.9 (t, C-9), 47.2 (d, C-2), 50.0 (d, C-6), 51.5 (q, -$CO_2\underline{C}H_3$), 66.9 (t, -O$\underline{C}H_2$Ph), 117.0 (t, C-11), 127.6 (d, C-2 in Ph), 127.8 (d, C-4 in Ph), 128.3 (d, C-3 in Ph), 135.7 (d, C-10), 136.6 (s, C-1 in Ph), 155.5 (s, N-$\underline{C}$O-O), 171.6 (s, C-8). ESI-HRMS (m/z): $[M+H]^+$ calcd for $C_{19}H_{26}NO_4^+$, 332.1862; found, 332.1845 (Δ = 5.1 ppm).

HPLC condition: CHIRACEL OD, 250 mm X 4.6 mm, 5 μm; Mobile phase A: IPA : n-Hex = 1 : 20 (v/v); Mobile phase B: pure n-Hex; isocratic, 20% A : 80% B; flow rate 1.0 mL per min; detection UV 215 nm, *t*R: 15.0 min for (+)-**5**, 16.3 min for (–)-**5.**

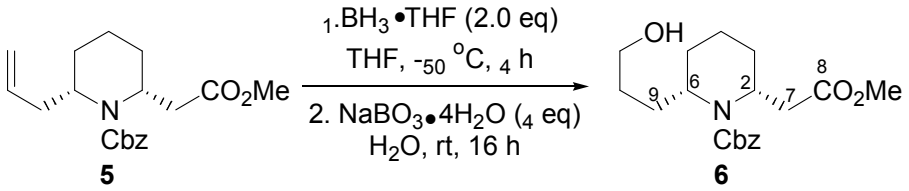


	Retention Time	Area	% Area	Height
1	14.986	32618292	50.31	883201
2	16.348	32210342	49.69	775355



	Retention Time	Area	% Area	Height
1	15.406	284824	1.14	12328
2	16.257	24708348	98.86	626057

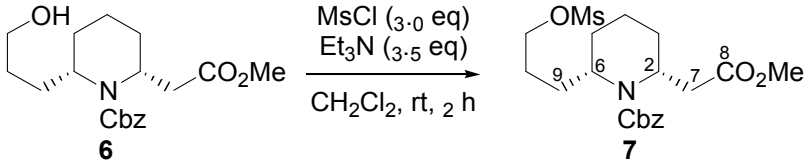
(–)-(2*R*,6*S*)-methyl-6-(3-hydroxypropyl)-1-benzyloxycarbonyl-2-piperidineacetate, (–)-(6):



To a solution of the olefin **5** (900 mg, 2.72 mmol, 1.0 equiv) in THF (10.8 mL) at −50 °C, was slowly added BH_3•THF solution (1 M, in THF, 5.5 mL, 2.7 mmol, 2.0 equiv). The reaction mixture was allowed to be stirred at −50 °C for 4 h. The reaction mixture was then warmed to 0 °C, water (8.4 mL) was slowly added, followed by $NaBO_3$•$4H_2O$ (1.67 g, 10.9

mmol, 4.0 equiv), and the reaction mixture was allowed to be stirred at room temperature for 16 h. Upon completion of the reaction monitored by TLC analysis, the aqueous solution was partitioned with EtOAc (10 mL) and water (10 mL). The resulting aqueous layer was extracted with EtOAc (10 mL × 5). The combined organic layers dried over anhydrous Na_2SO_4. After removal of the solid dehydrating agent, the organic layer was concentrated under reduced pressure to give a crude product. Purification of the crude product by flash chromatography on silica gel, EtOAc/*n*-Hex as the eluant to give the titled product as a colorless oil (760 mg, 2.18 mmol, 80%): R_f = 0.19; EtOAc/*n*-Hex = 1:1. $[\alpha]_D^{23}$ –31.9 (*c* 1.6, $CHCl_3$). ^{1}H NMR (400 MHz, 25 ^{o}C, $CDCl_3$, δ): 1.41 (brs, 2H, H-4, H-10), 1.53−1.59 (m, 8H, H-3 × 2, H-4, H-5 × 2, H-9 × 2 and H-10), 2.47−2.60 (m, 2H, H-7 × 2), 3.33 (br, 1H, -OH), 3.54 (s, 5H, H-11 × 2, -$CO_2C\underline{H}_3$), 4.14 (brs, 1H, H-6), 4.65 (brs, 1H, H-2), 5.04 (d, *J* = 12.4 Hz, 1H, -OC$\underline{H}_2$Ph), 5.09 (d, *J* = 12.8 Hz, 1H, -OC$\underline{H}_2$Ph), 7.22−7.24 (m, 1H, H-4’ in Ph), 7.28−7.29 (m, 4H, H-2’ and H-3’ in Ph). ^{13}C NMR (100 MHz, 25 ^{o}C, $CDCl_3$, δ): 13.4 (t, C-4), 26.8 (t, C-5), 27.7 (t, C-3), 29.6 (t, C-10), 30.3 (t, C-9), 38.5 (t, C-7), 47.1 (d, C-2), 49.9 (d, C-6), 51.3 (q, -$CO_2\underline{C}H_3$), 61.6 (t, C-11), 66.8 (t, -O$\underline{C}H_2$Ph), 127.4 (d, C-2 in Ph), 127.5 (d, C-4 in Ph), 128.1 (d, C-3 in Ph), 136.2 (s, C-1 in Ph), 155.5 (s, N-$\underline{C}$O-O), 171.5 (s, C-8). EI-HRMS (m/z): $[M]^+$ calcd for $C_{19}H_{27}NO_5^+$, 349.1889; found, 349.1891 (Δ = 0.6 ppm).

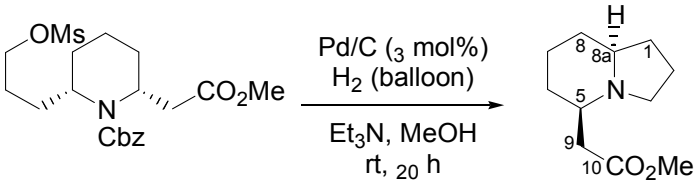
(−)-(2*R*,6*S*)-methyl-6-(3-methylsulfonyloxypropyl)-1-benzyloxycarbonyl-2- piperidineacetate, (−)-(7):



To a solution of the alcohol **6** (545 mg, 1.56 mmol, 1.0 equiv) in CH_2Cl_2 (6.6 mL), was added Et_3N (761 μL, 5.46 mmol, 3.5 equiv). After the solution was stirred in an ice bath for 5 min, Methanesulfonyl chloride (362 μL, 4.68 mmol, 3.0 equiv) was added by a syringe. The reaction mixture was allowed to warm to room temperature and then stirred for 2 h. Upon completion of the reaction monitored by TLC analysis, the aqueous solution was partitioned with CH_2Cl_2 (10 mL) and water (10 mL). The resulting organic layer was extracted with water (5 mL × 3), and dried over anhydrous Na_2SO_4. After removal of the solid dehydrating agent, the organic layer was concentrated under reduced pressure to give a crude product. Purification of the crude product by flash chromatography on silica gel, EtOAc/*n*-Hex as the eluant to give the titled product as a light yellow oil (635 mg, 1.49 mmol, 95%): R_f = 0.29; EtOAc/*n*-Hex = 1:1. $[\alpha]_D^{22}$ −28.3 (*c* 1.7, $CHCl_3$). ^{1}H NMR (400 MHz, 25 ^{o}C, $CDCl_3$, δ): 1.48 (brs, 1H, H-4), 1.60−1.71 (m, 9H, H-3 × 2, H-4, H-5 × 2, H-9 × 2 and H-10 × 2), 2.48−2.57 (m, 2H, H-7 × 2), 2.60 (s, 3H, -$SO_2C\underline{H}_3$), 3.59 (s, 3H, -$CO_2C\underline{H}_3$), 4.18 (brs, 3H, H-6, H-11 × 2), 4.71 (brs, 1H, H-2), 5.07 (d, *J* = 12.4 Hz, 1H, -OC$\underline{H}_2$Ph), 5.13 (d, *J* = 12.4 Hz, 1H, -OC$\underline{H}_2$Ph), 7.29 (brs, 1H, H-4’ in Ph), 7.32 (s, 4H, H-2’ and H-3’ in Ph). ^{13}C NMR (100 MHz, 25 ^{o}C, $CDCl_3$, δ): 13.8 (t, C-4), 26.6 (t, C-10), 27.4

(t, C-5), 27.9 (t, C-3), 30.3 (t, C-9), 37.1 (q, -$SO_2\underline{C}H_3$), 38.8 (t, C-7), 47.2 (d, C-2), 49.6 (d, C-6), 51.5 (q, -$CO_2\underline{C}H_3$), 67.0 (t, -$O\underline{C}H_2Ph$), 69.6 (t, C-11), 127.7 (d, C-2 in Ph), 127.8 (d, C-4 in Ph), 128.3 (d, C-3 in Ph), 136.4 (s, C-1 in Ph), 155.6 (s, N-$\underline{C}O$-O), 171.4 (s, C-8). EI-HRMS (m/z): $[M]^+$ calcd for $C_{20}H_{29}NO_7S^+$, 427.1665; found, 427.1655 (Δ = 0 ppm).

(+)-(5*R*,8a*S*)-5-(2-ethyloxycarbonylmethyl)indolizidine (8):

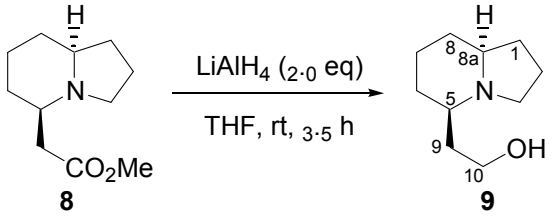


7 **8**

To a MeOH solution (1.8 mL) of mesylate **7** (345 mg, 0.807 mmol, 1.0 equiv), was added Et_3N (76 μL, 0.55 mmol, 0.7 equiv) and Pd on carbon (10%, 26 mg, 0.024 mmol, 3 mol%). The reaction suspension was allowed to stir for 20 h under hydrogen balloon. Upon completion of the reaction monitored by TLC analysis, the suspension was filtered by celite to remove the catalyst. The filtrate solution was concentrated under reduced pressure to give a crude oil. Purification of the crude product by flash chromatography on silica gel, MeOH/CH_2Cl_2/Et_3N as the eluant to give the titled product as a light yellow oil (140 mg, 0.710 mmol, 88%): R_f = 0.25; EtOAc/*n*-Hex/Et_3N = 1:1:0.01. $[\alpha]_D^{25}$ +68.4 (*c* 1.3, $CHCl_3$). ^1H NMR (400 MHz, 25 °C, $CDCl_3$, δ): 1.12−1.40 (m, 4H, H-1, H-6, H-7 and H-8), 1.56−1.82 (m, 6H, H-1, H-2 × 2, H-6, H-7 and H-8), 1.83−1.93 (m, 1H, H-8a), 2.01 (dd, *J* = 8.4, 18 Hz, 1H, H-3), 2.26 (dd, *J* = 8.8, 15.2 Hz, 1H, H-9), 2.40−2.46 (m, 1H, H-5), 2.68 (dd, *J* = 5.2, 15.2 Hz, 1H, H-9),

3.10 (dt, J = 2.0, 8.4 Hz, 1H, H-3), 3.62 (s, 3H, -$CO_2C\underline{H}_3$). ^{13}C NMR (100 MHz, 25 ^{o}C, $CDCl_3$, δ): 20.2 (t, C-2), 24.2 (t, C-7), 30.4 (t, C-1), 30.7 (t, C-8), 31.9 (t, C-6), 40.3 (t, C-9), 51.4 (t, C-3), 51.5 (q, - $CO_2\underline{C}H_3$), 60.0 (d, C-5), 64.7 (d, C-8a), 172.7 (s, C-10). EI-HRMS (m/z): $[M]^+$ calcd for $C_{11}H_{19}NO_2^+$, 197.1416; found, 197.1419 (Δ = 1.5 ppm).

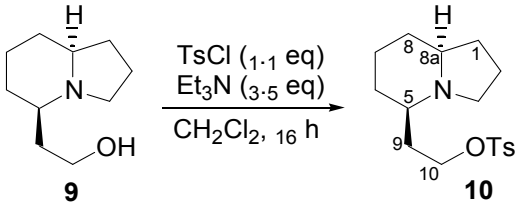
(+)-(5*R*,8a*S*)-5-(2-hydroxyethyl)indolizidine (9):



To a solution of ester **8** (305 mg, 1.55 mmol, 1.0 equiv) in THF (12.5 mL), was added $LiAlH_4$ (117 mg, 3.09 mmol, 2.0 equiv) in an ice bath. After completion of addition, the ice bath was removed, and the reaction mixture was allowed to be stirred at room temperature for 3.5 h. Upon completion of the reaction monitored by TLC analysis, Slow addition of cold water (1.6 mL) in order would result in the formation of a white bulk gel after stirring for a while. The clear solution was separated from the gel, which reduced pressure to give a crude product. Purification of the crude product by flash chromatography on silica gel, MeOH/CH_2Cl_2 as the eluant to give the titled product as a colorless oil (234 mg, 1.38 mmol, 89%): R_f = 0.14; MeOH/CH_2Cl_2 = 1:4. $[\alpha]_D^{29}$ +51.0 (*c* 1.1, $CHCl_3$). ^{1}H NMR (400 MHz, 25 ^{o}C, $CDCl_3$, δ): 1.04−1.14 (m, 1H, H-6), 1.16−1.45 (m, 3H, H-1, H-7 and H-8), 1.52−1.63 (m, 4H, H-1, H-2 × 2 and H-9), 1.65−1.78 (m, 4H, H-6, H-7, H-8 and H-8a), 1.79−1.87 (m, 1H, H-9),

1.91 (q, J = 8.2 Hz, 1H, H-3), 2.14−2.19 (m, 1H, H-5), 3.29 (dt, J = 2.4, 8.8 Hz, 1H, H-3), 3.54−3.60 (m, 1H, H-10), 3.77−3.84 (m, 1H, H-10), 4.21 (br, 1H, -OH). ^{13}C NMR (100 MHz, 25 ^{o}C, $CDCl_3$, δ): 20.0 (t, C-2), 24.3 (t, C-7), 29.4 (t, C-1), 30.2 (t, C-8), 30.3 (t, C-6), 34.6 (t, C-9), 51.6 (t, C-3), 59.7 (t, C-10), 61.4 (d, C-5), 65.1 (d, C-8a). EI-HRMS (m/z): $[M]^+$ calcd for $C_{10}H_{19}NO^+$, 169.1467; found, 169.1468 (Δ = 1.2 ppm).

(+)-(5*R*,8a*S*)-5-(2-*p*-toluenesulfonyloxyethyl)indolizidine (10):

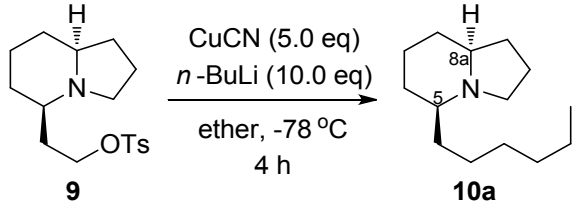


9 **10**

To a solution of the alcohol **9** (88 mg, 0.52 mmol, 1.0 equiv) in CH_2Cl_2 (6.6 mL), was added Et_3N (250 μL, 1.82 mmol, 3.5 equiv). After the solution was stirred in an ice bath for 5 min, *p*-Toluenesulfonyl chloride (109 mg, 0.572 mmol, 1.1 equiv) was added by a syringe. The reaction mixture was allowed to warm to room temperature and then stirred for 16 h. Upon completion of the reaction monitored by TLC analysis, the aqueous solution was partitioned with CH_2Cl_2 (5 mL) and water (5 mL). The resulting aqueous layer was extracted with CH_2Cl_2 (5 mL × 3). The combined organic layers dried over anhydrous Na_2SO_4. After removal of the solid dehydrating agent, the organic layer was concentrated under reduced pressure to give a crude product. Purification of the crude product by flash chromatography on *Chromatorex* N-H typed silica gel, EtOAc/*n*-Hex as the eluant to give the titled product as a light yellow oil

(155 mg, 0.479 mmol, 92%): R_f = 0.38; EtOAc/*n*-Hex = 1:3. $[\alpha]_D^{28}$ +50.0 (*c* 1.3, $CHCl_3$). ^1H NMR (400 MHz, 25 °C, $CDCl_3$, δ): 0.99−1.11 (m, 2H, H-6, H-8), 1.14−1.21 (m, 1H, H-7), 1.30 (ddd, *J* = 4.8, 4.8, 10.4 Hz, 1H, H-1), 1.48 (d, *J* = 12.4 Hz, 1H, H-6), 1.54−1.75 (m, 7H, H-1, H-2 × 2, H-7, H-8, H-8a and H-9), 1.86 (q, *J* = 8.8 Hz, 1H, H-3), 1.96−2.04 (m, 2H, H-5, H-9), 2.39 (s, 3H, $-CH_3$), 3.03 (t, *J* = 8.4 Hz, 1H, H-3), 3.99−4.09 (m, 2H, H-10 × 2), 7.29 (d, *J* = 7.6 Hz, 2H, H-3' in Ph), 7.73 (d, *J* = 8.4 Hz, 2H, H-2' in Ph). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$, δ): 20.1 (t, C-2), 21.5 (q, $-CH_3$), 24.2 (t, C-7), 30.2 (t, C-1), 30.4 (t, C-8), 30.5 (t, C-6), 33.4 (t, C-9), 51.2 (t, C-3), 59.7 (d, C-5), 64.7 (d, C-8a), 67.9 (t, C-10), 127.7 (d, C-2 in Ph), 129.7 (d, C-3 in Ph), 132.8 (s, C-1 in Ph), 144.6 (s, C-4 in Ph). EI-HRMS (m/z): $[M]^+$ calcd for $C_{17}H_{25}NO_3S^+$, 323.1555; found, 323.1558 (Δ = –0.6 ppm).

(+)-(5*S*,8a*S*)-Indolizidine 209D (11a):

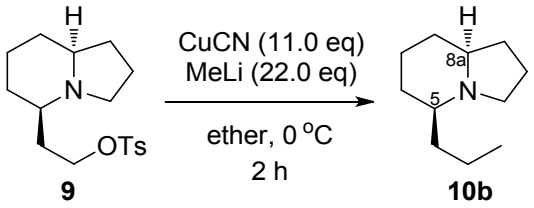


9 **10a**

To a solution of Cuprous cyanide (138 mg, 1.40 mmol, 5.0 equiv) in ether (5.8 mL) at –78 °C, was slowly added *n*-BuLi (0.67 M in hexane, 4.2 mL, 2.81 mmol, 10.0 equiv). The heterogeneous mixture was allowed to warm to –10 °C to give a homogeneous solution and then recooled to -78 °C. The reaction mixture was slowly added a tosylate **10** (90 mg, 0.28 mmol, 1.0 equiv) solution in ether (2.0 mL). The reaction mixture was allowed to be stirred at –78 °C for 4 h. Upon completion of the reaction monitored

by TLC analysis, ammonia solution (2 mL) was added to quench the reaction in an ice bath, the aqueous solution was partitioned with EtOAc (2 mL). The resulting organic layer was extracted with water (2 mL × 3), and dried over anhydrous Na_2SO_4. After removal of the solid dehydrating agent, the organic layer was concentrated under reduced pressure to give a crude product. Purification of the crude product by flash chromatography on *Chromatorex* N-H typed silica gel, EtOAc/*n*-Hex as the eluant to give the titled product as a colorless oil (37 mg, 0.18 mmol, 64%): R_f = 0.36; EtOAc/*n*-Hex = 1:10. $[\alpha]_D^{27}$ +92.6 (*c* 1.0, CH_2Cl_2), [lit[1] $[\alpha]_D^{25}$ +81.8 (*c* 0.5, CH_2Cl_2)]. ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$, δ): 0.85 (t, *J* = 6.4 Hz, 3H), 1.06−1.45 (m, 13H), 1.57−1.88 (m, 9H), 1.93 (dd, *J* = 9.2, 18.0 Hz, 1H), 3.23 (dt, *J* = 2.0, 8.8 Hz, 1H). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$, δ): [1] 14.1 (s), 20.4 (t), 22.6 (t), 24.7 (t), 25.8 (t), 29.7 (t), 30.5 (t), 30.8 (t), 31.0 (t), 31.8 (t), 34.6 (t), 51.5 (t), 63.9 (d), 65.0 (d). EI-HRMS (m/z): $[M]^+$ calcd for $C_{14}H_{27}N^+$, 209.2143; found, 209.2136 (Δ = 3.3 ppm).

(+)-(5*S*,8a*S*)-Indolizidine 167B (11b):



9 **10b**

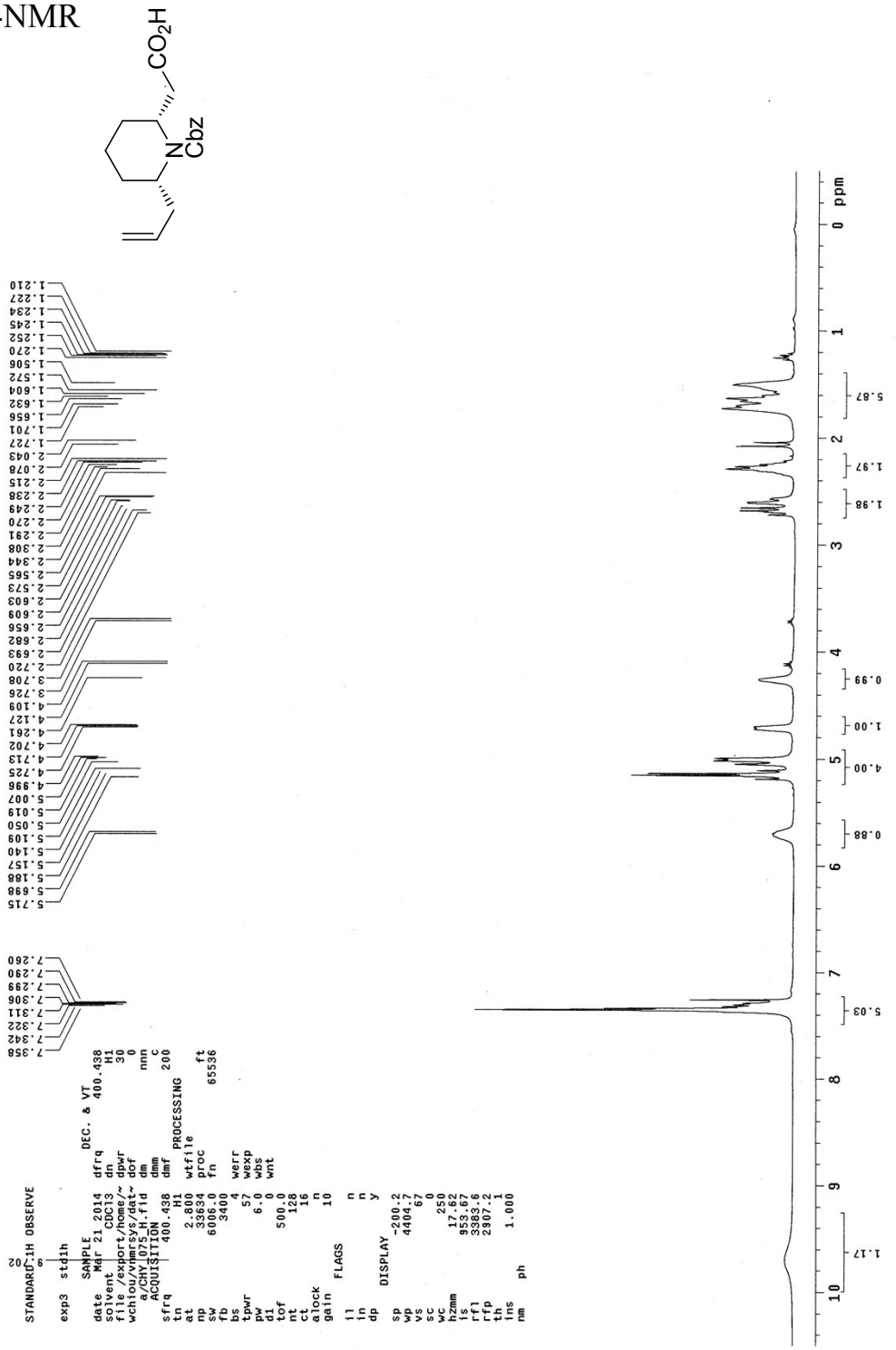
To a solution of Cuprous cyanide (339 mg, 4.46 mmol, 11.0 equiv) in ether (2.2 mL) at –78 °C, was added MeLi (2.21 M in ether, 4.0 mL, 8.92 mmol, 22.0 equiv). The heterogeneous mixture was allowed to warm to

[1] The ^{13}C NMR data of *cis*-209D see, see Yu, R. T.; Lee, E. E.; Malik, G.; Rovis, T. *Angew. Chem. Int. Ed.* **2009**, *48*, 2379.

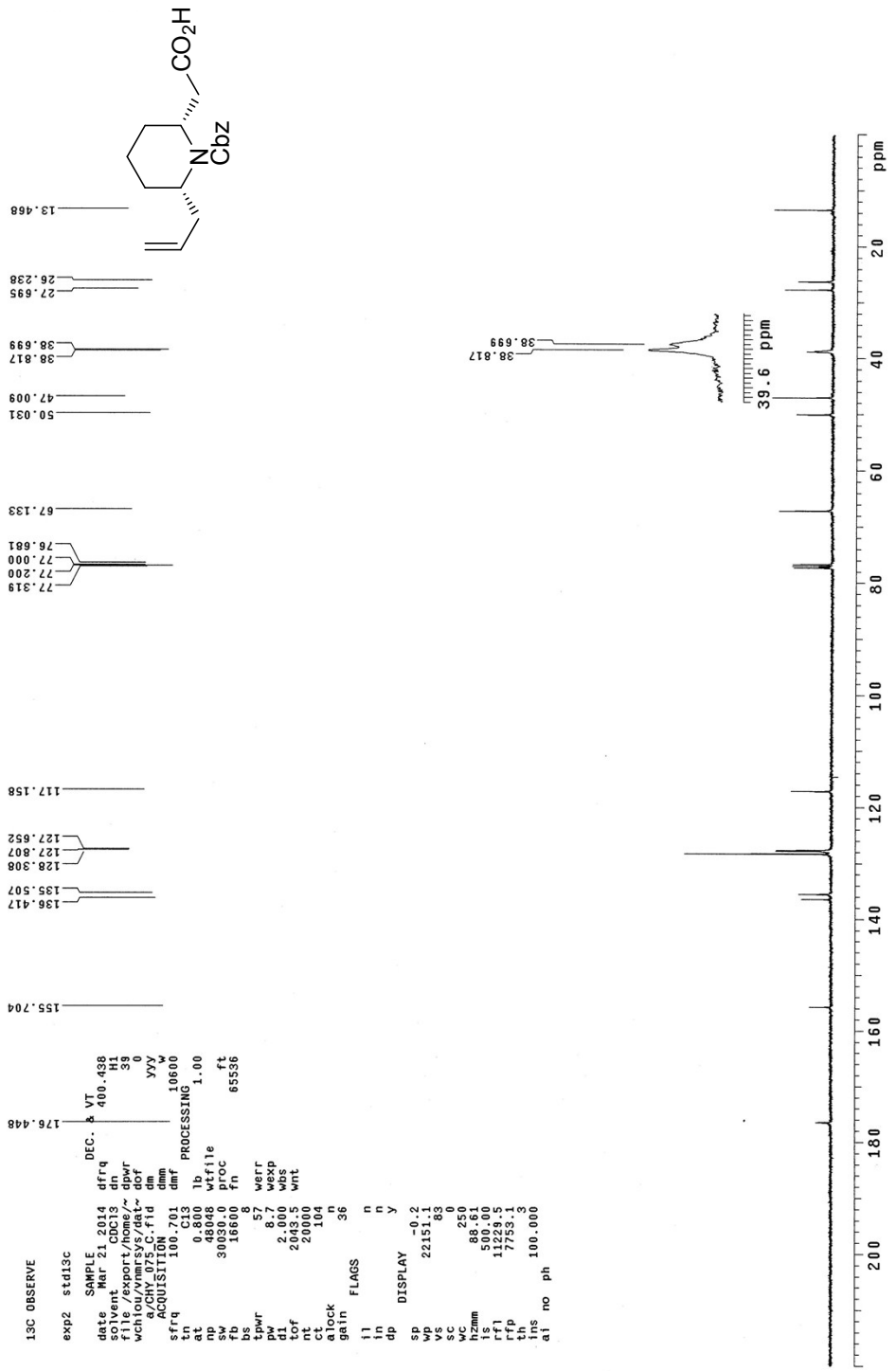
−10 °C to give a homogeneous solution and then recooled to -78 °C. The reaction mixture was slowly added a tosylate **10** (130 mg, 0.40 mmol, 1.0 equiv) solution in ether (2.2 mL). The reaction mixture was allowed to be stirred at 0 °C for 2 h. Upon completion of the reaction monitored by TLC analysis, a mixture of a saturated solution of NH4Cl/NH_3 (9:1, 10 mL) was added to quench the reaction in an ice bath, the aqueous solution was partitioned with ether (10 mL). The resulting aqueous layer was extracted with ether (5 mL × 5). The combined organic layers dried over anhydrous $MgSO_4$. After removal of the solid dehydrating agent, the organic layer was concentrated under reduced pressure to give a crude product. Purification of the crude product by flash chromatography on *Chromatorex* N-H typed silica gel, ether/*n*-Hex as the eluant to give the titled product as a light yellow oil (41 mg, 0.25 mmol, 61%): R_f = 0.34; EtOAc/*n*-Hex = 1:10. $[\alpha]_D^{28}$ +115.0 (*c* 1.3, CH_2Cl_2), [lit[2] $[\alpha]_D^{26}$ +86.6 (*c* 1.3, CH_2Cl_2)]. ^{1}H NMR (400 MHz, 25 °C, $CDCl_3$, δ): 0.87 (t, *J* = 7.2 Hz, 3H), 1.05−1.32 (m, 5H), 1.34−1.45 (m, 2H), 1.55−1.66 (m, 2H), 1.68−1.89 (m, 7H), 1.93 (dd, *J* = 8.8, 17.6 Hz, 1H), 3.23 (dt, *J* = 2.0, 8.8 Hz, 1H). ^{13}C NMR (100 MHz, 25 °C, $CDCl_3$, δ):[2] 14.5 (s), 19.1 (t), 20.3 (t), 24.6 (t), 30.5 (t), 30.8 (t), 30.9 (t), 36.8 (t), 51.5 (t), 63.6 (d), 64.9 (d). EI-HRMS (m/z): $[M]^+$ calcd for $C_{11}H_{21}N^+$, 167.1674; found, 167.1669 (Δ = 3.0 ppm).

[2] The ^{13}C NMR data of *cis*-167B see, see Kapat, A.; Nyfeler, E.; Giuffredi, G. T.; Renaud, P. *J. Am. Chem. Soc.* **2009**, *131*, 17746.

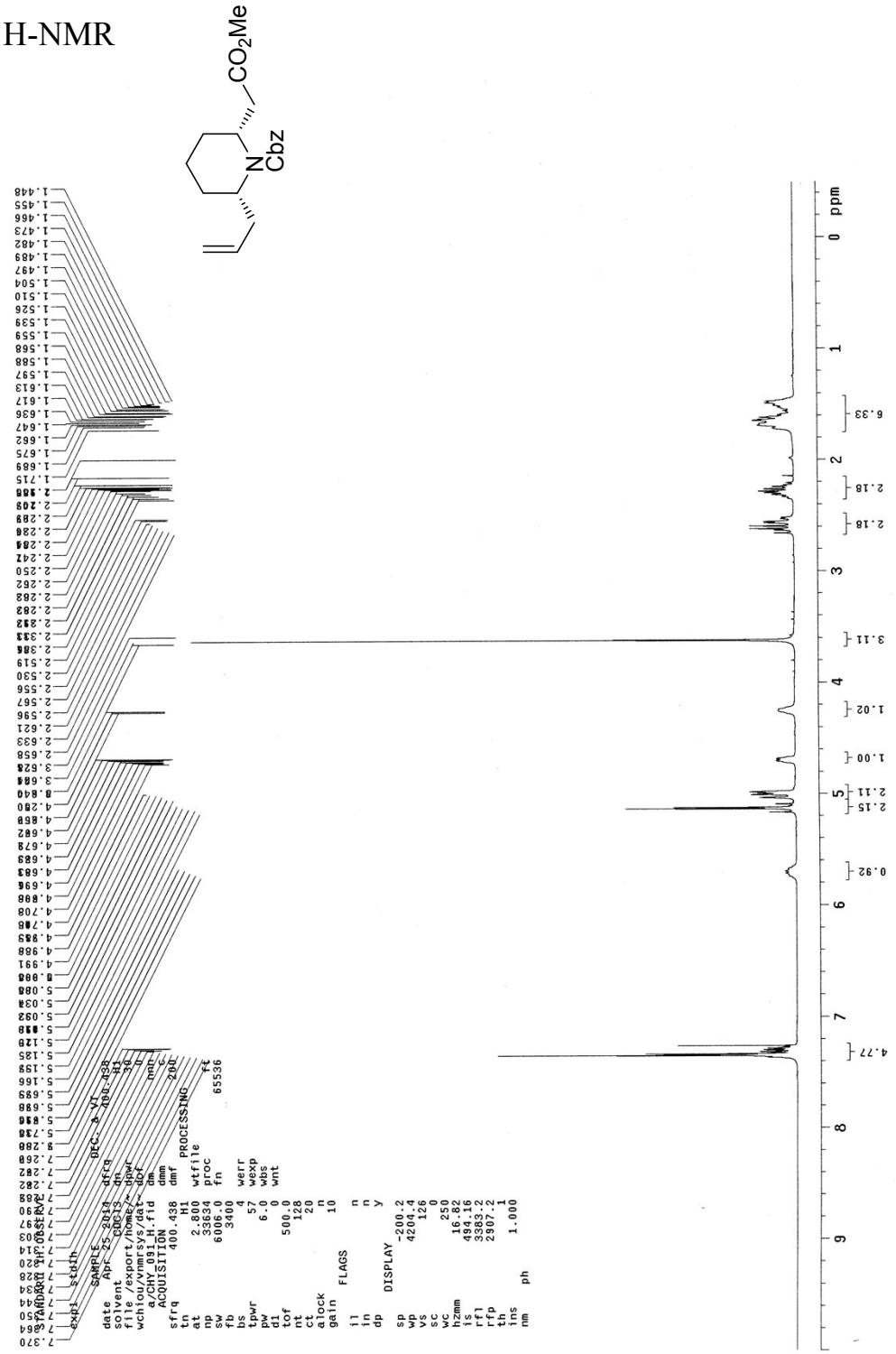
3 ^{1}H-NMR



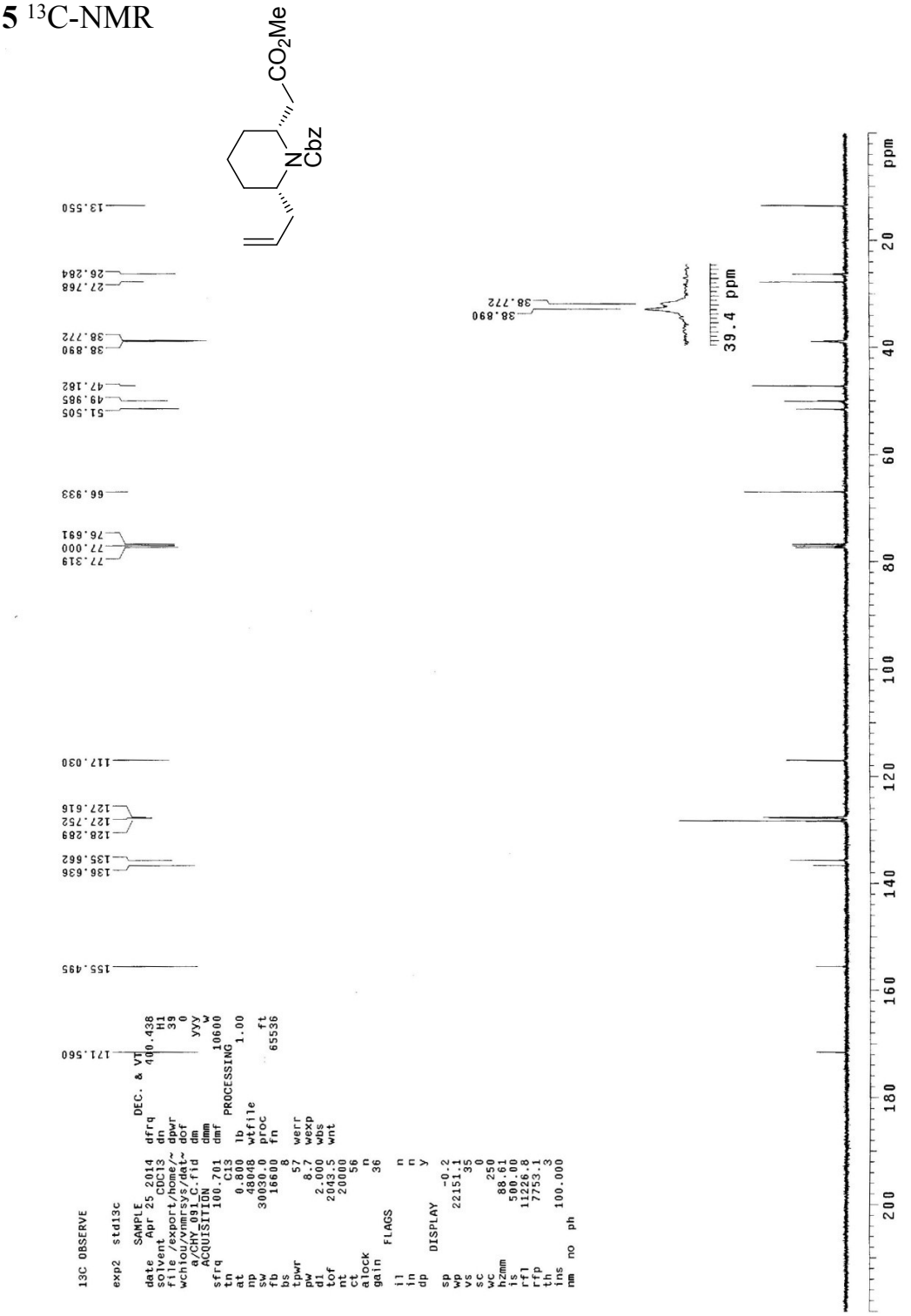
3 ^{13}C-NMR


CO2H
N
Cbz
13.468
26.238
27.695
38.699
38.817
47.009
50.031
67.133
76.681
77.000
77.200
77.319
117.158
127.652
127.807
128.308
135.507
136.417
155.704
176.448
38.699
38.817
39.6 ppm
ppm

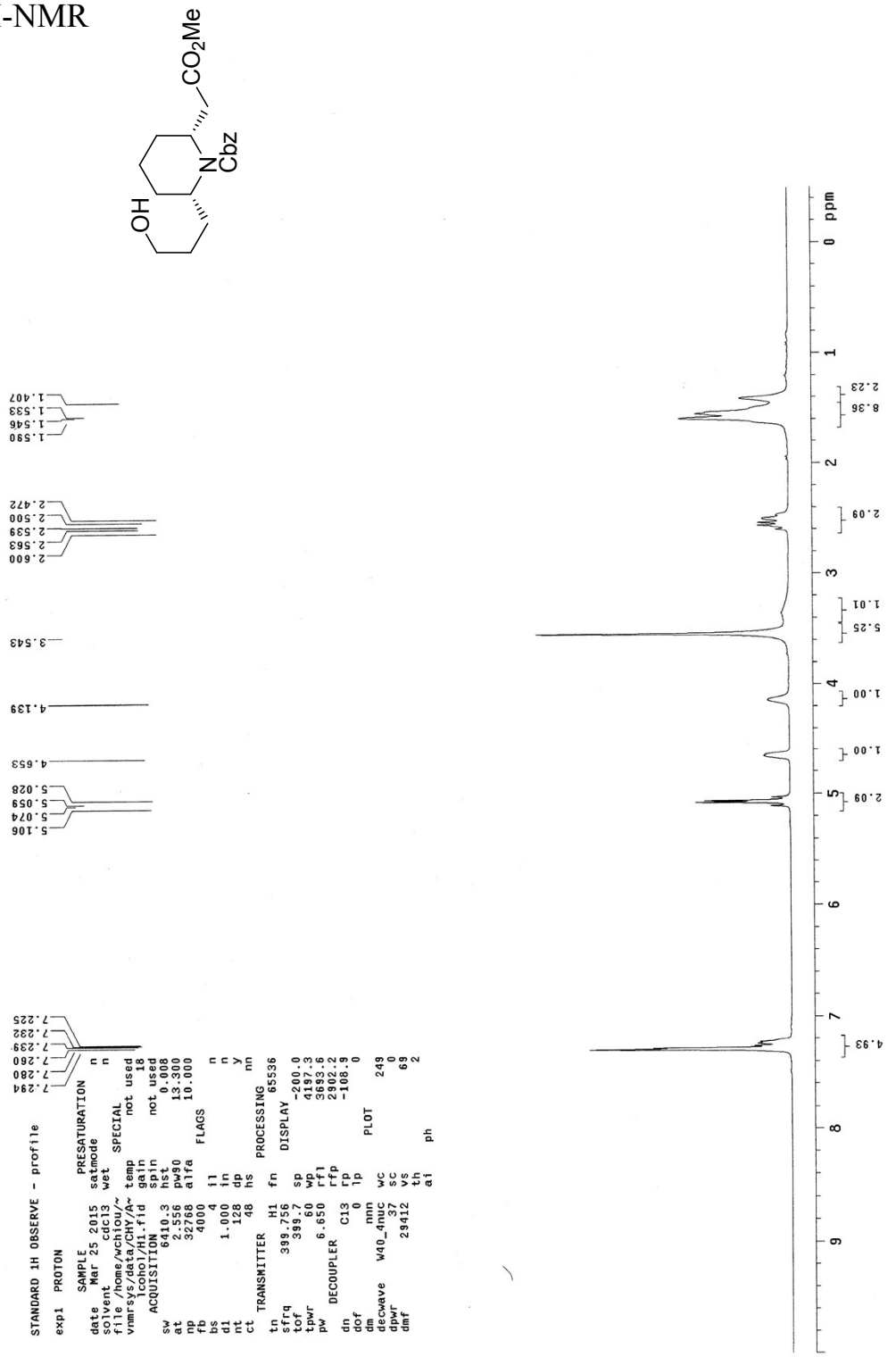
5 ^{1}H-NMR



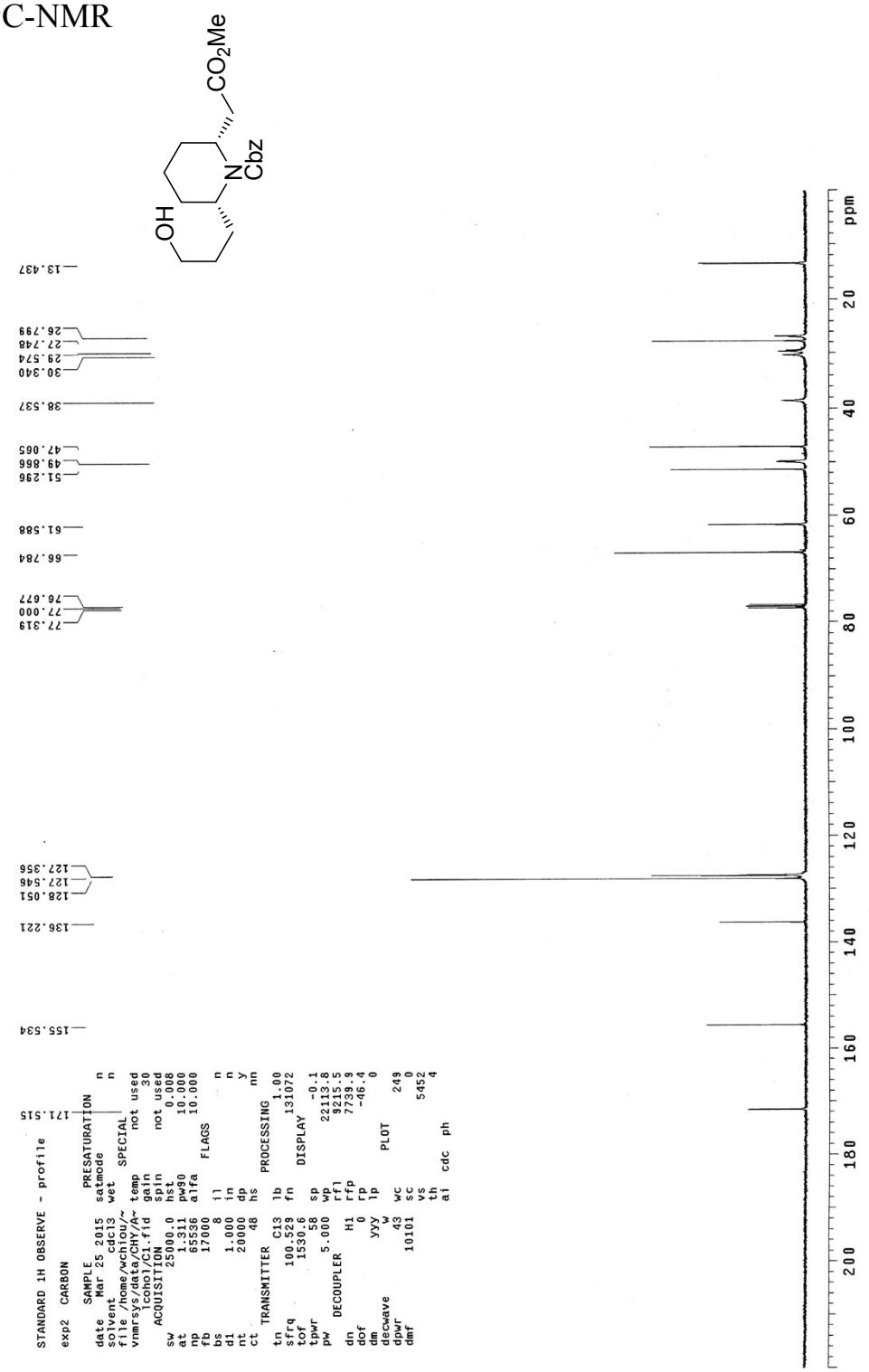
5 ^{13}C-NMR


CO2Me
N
Cbz
13.550
26.264
27.768
38.772
38.890
47.182
49.985
51.505
66.933
76.691
77.000
77.319
117.030
127.616
127.752
128.289
135.662
136.636
155.495
171.560
38.772
38.890
39.4 ppm
ppm

6 ^{1}H-NMR

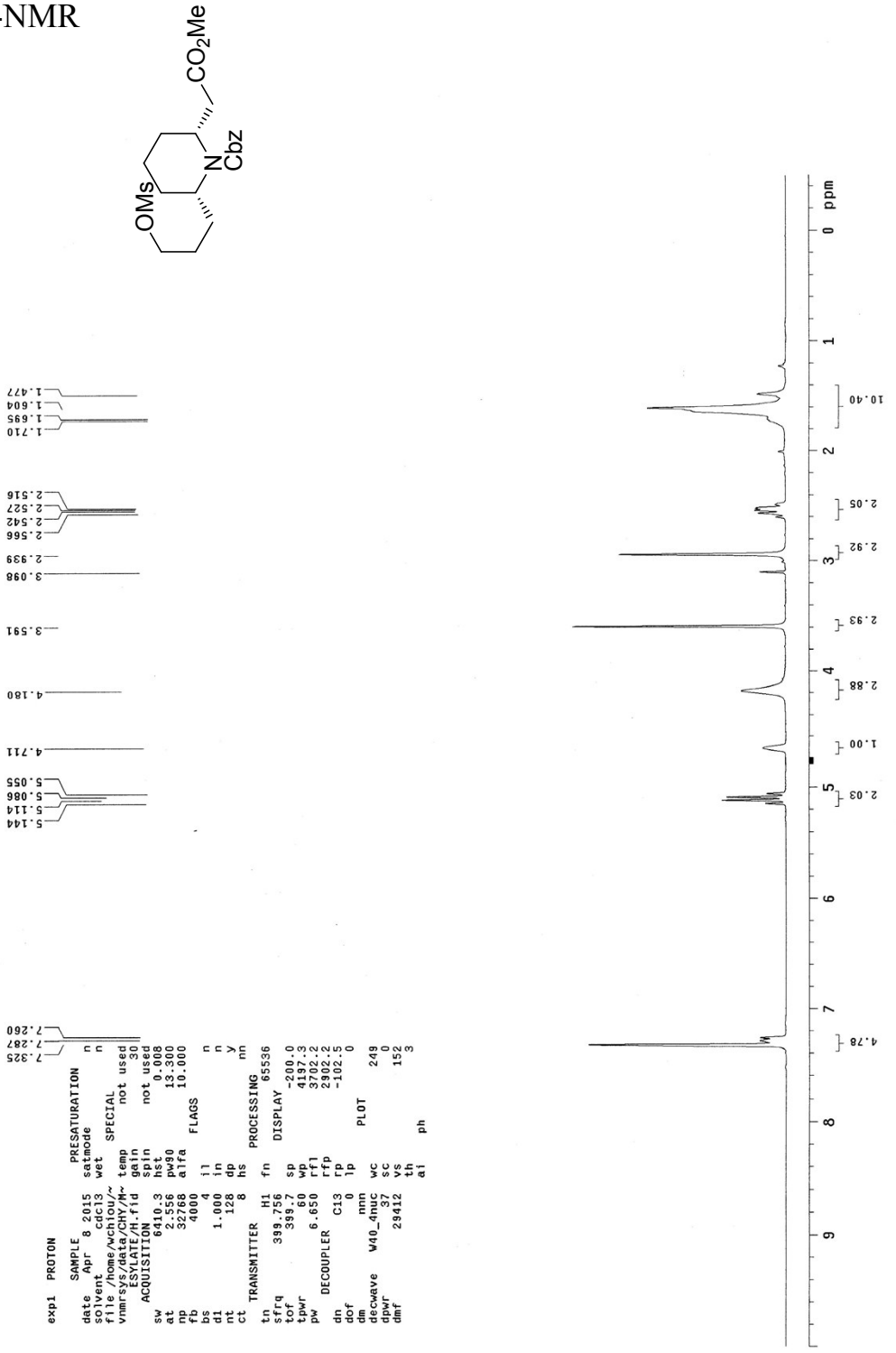

CO2Me
Cbz
N
OH
STANDARD 1H OBSERVE - profile
exp1 PROTON
SAMPLE
date Mar 25 2015
solvent cdcl3
file /home/wchiou/vnmrsys/data/CHY/A-1cohol/H1.fid
ACQUISITION
sw 6410.3
at 2.556
np 32768
fb 4000
bs 4
d1 1.000
nt 128
ct 48
TRANSMITTER
tn H1
sfrq 399.756
tof 399.7
tpwr 60
pw 6.650
DECOUPLER
dn C13
dof 0
dm nnn
decwave W40_4nuc
dpwr 37
dmf 29412
PRESATURATION n
satmode n
wet SPECIAL not used
temp not used
gain not used
spin 0.008
pw90 13.300
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 4197.3
rf1 3693.6
rfp 2902.2
rp -108.9
lp 0
PLOT
wc 249
sc 0
vs 69
th 2
ph
ai
7.294
7.280
7.260
7.239
7.232
7.225
5.106
5.074
5.059
5.028
4.653
4.139
3.543
2.600
2.563
2.539
2.500
2.472
1.590
1.546
1.533
1.407
4.93
2.09
1.00
1.00
5.25
1.01
2.09
8.36
2.23
ppm

6 ^{13}C-NMR

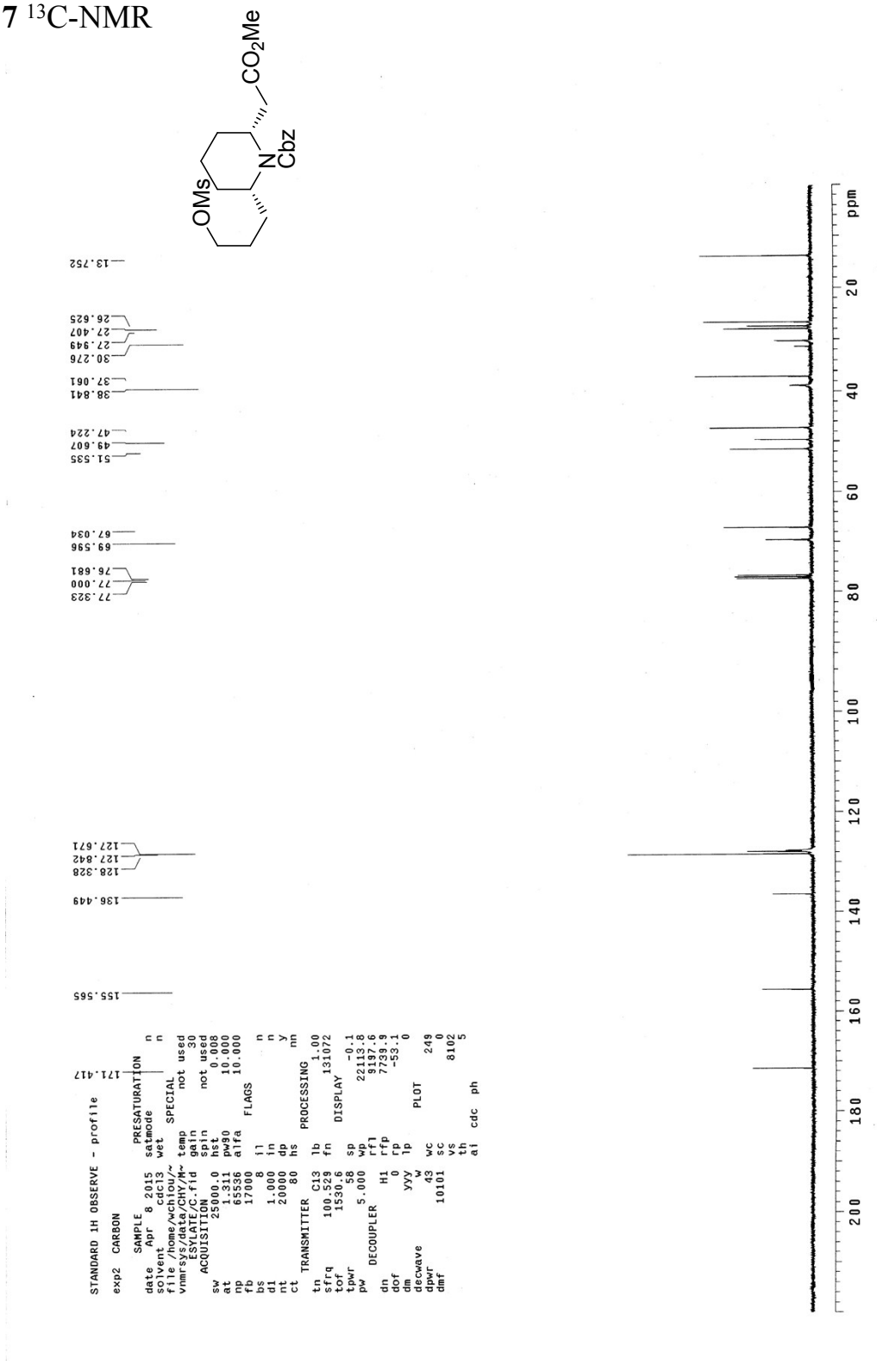



```
STANDARD 1H OBSERVE - profile

exp2  CARBON

     SAMPLE          PRESATURATION
date   Mar 25 2015   satmode          n
solvent    cdcl3     wet      SPECIAL  n
file /home/wchiou/~
vnmrsys/data/CHY/A~  temp          not used
      1cohol/C1.fid  gain          30
   ACQUISITION       spin          not used
sw          25000.0   hst           0.008
at              1.311 pw90         10.000
np             65536  alfa        10.000
fb             17000
bs                 8  FLAGS          n
ss                 1  il             n
d1             1.000  in             n
nt             20000  dp             y
ct                48  hs             nn
   TRANSMITTER       PROCESSING
tn                C13  lb          1.00
sfrq         100.529  fn        131072
tof           1530.6  DISPLAY
tpwr              58   sp          -0.1
pw             5.000   wp       22113.8
   DECOUPLER          rfl        9215.5
dn                H1   rfp        7739.9
dof                0   rp          -46.4
dm               yyy   lp               0
decwave            w       PLOT
dpwr              43   wc         249
dmf            10101   sc           0
                       vs        5452
                       th           4
                       al  cdc  ph
```

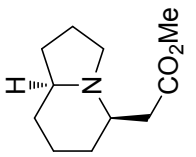
7 ^{1}H-NMR

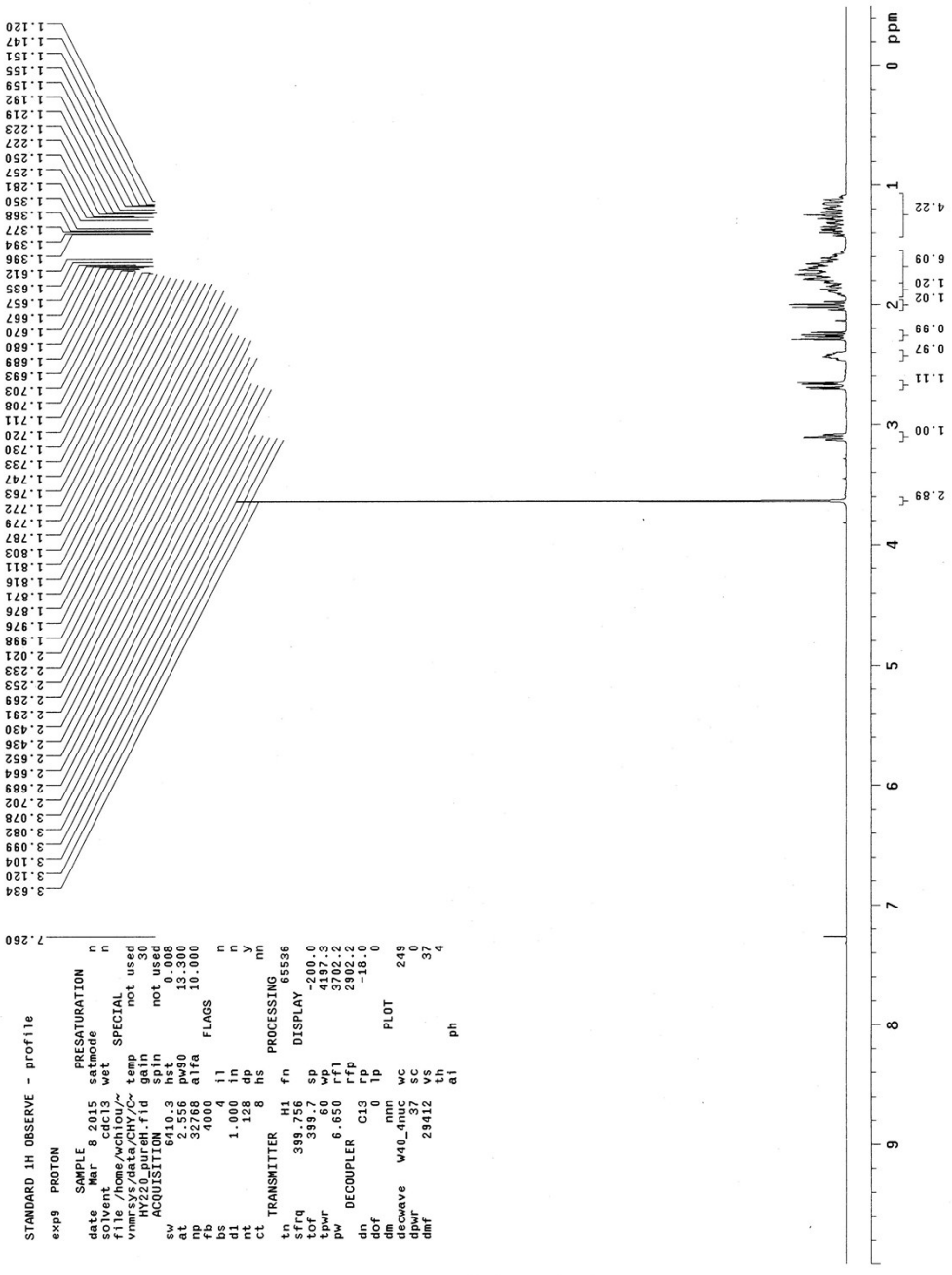


7 ^{13}C-NMR

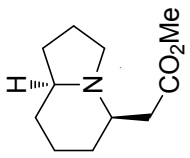


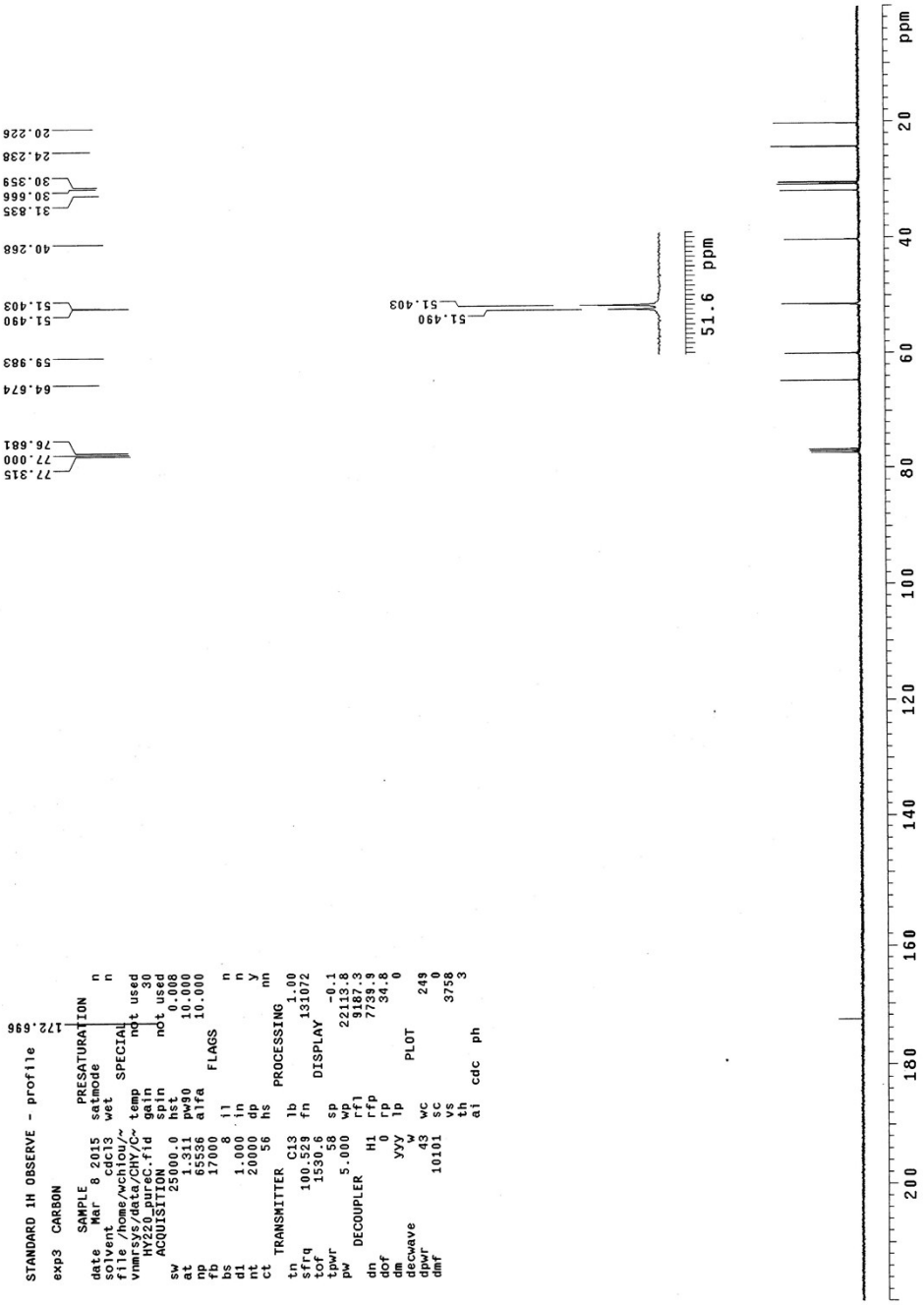
8 ^{1}H-NMR


H
N
CO2Me

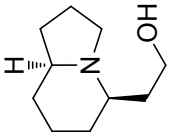

STANDARD 1H OBSERVE - profile
exp9 PROTON
SAMPLE
date Mar 8 2015
solvent cdcl3
file /home/wchiou/~
vnmrsys/data/CHY/C~
HY220_pureH.fid
ACQUISITION
sw 6410.3
at 2.556
np 32768
fb 4000
bs 4
d1 1.000
nt 128
ct 8
TRANSMITTER
tn H1
sfrq 399.756
tof 399.7
tpwr 60
pw 6.650
DECOUPLER
dn C13
dof 0
dm nnn
decwave W40_4mqc
dpwr 37
dmf 29412
PRESATURATION
satmode
wet
SPECIAL
temp
gain
spin
hst
pwd
alfa
FLAGS
i1
in
dp
hs
PROCESSING
fn
DISPLAY
sp
wp
rf1
rfp
rp
lp
PLOT
wc
sc
vs
th
al
ph
not used
not used
0.000
13.300
10.000
n
n
y
nn
65536
-200.0
4197.3
3702.2
2902.2
-18.0
0
249
0
37
4
7.260
3.634
3.120
3.104
3.099
3.082
3.078
2.702
2.689
2.664
2.652
2.436
2.430
2.291
2.269
2.253
2.233
2.021
1.998
1.976
1.876
1.871
1.816
1.811
1.803
1.787
1.779
1.772
1.763
1.747
1.733
1.730
1.720
1.711
1.708
1.703
1.693
1.689
1.680
1.670
1.667
1.657
1.635
1.612
1.396
1.394
1.377
1.368
1.350
1.281
1.257
1.250
1.227
1.223
1.219
1.192
1.159
1.155
1.151
1.147
1.120
9
8
7
6
5
4
3
2
1
0 ppm
2.89
1.00
1.11
0.97
0.99
1.02
1.20
6.09
4.22

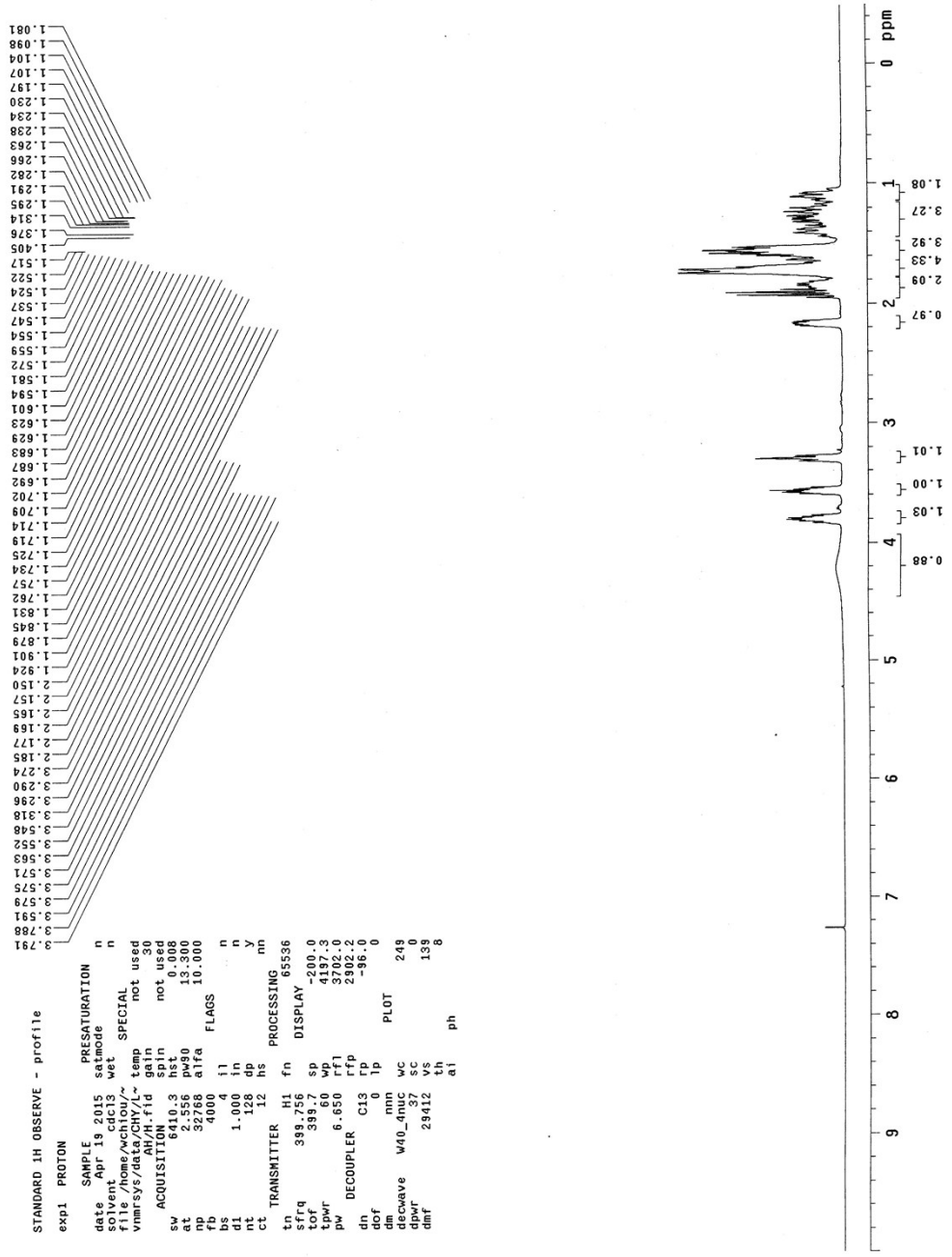
8 ^{13}C-NMR


H
N
CO2Me

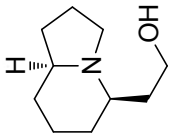

172.696
77.315
77.000
76.681
64.674
59.983
51.490
51.403
40.268
31.835
30.666
30.359
24.238
20.226
51.490
51.403
51.6 ppm
ppm
200
180
160
140
120
100
80
60
40
20
STANDARD 1H OBSERVE - profile
exp3 CARBON
SAMPLE
date Mar 8 2015
solvent cdcl3
file /home/wchiou/~
vnmrsys/data/CHY/C~
HY220_pureC.fid
ACQUISITION
sw 25000.0
at 1.311
np 65536
fb 17000
bs 8
d1 1.000
nt 20000
ct 56
PRESATURATION n
satmode n
wet SPECIAL not used
temp not used
gain 30
spin not used
hst 0.008
pw90 10.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
TRANSMITTER
tn C13
sfrq 100.528
tof 15300.6
tpwr 58
pw 5.000
DECOUPLER
dn H1
dof 0
dm yyy
decwave w
dpwr 43
dmf 10101
PROCESSING
lb 1.00
fn 131072
DISPLAY
sp -0.1
wp 22113.8
rfl 9187.3
rfp 7739.9
rp 34.8
lp 0
PLOT
wc 249
sc 0
vs 3758
th 3
ai cdc ph

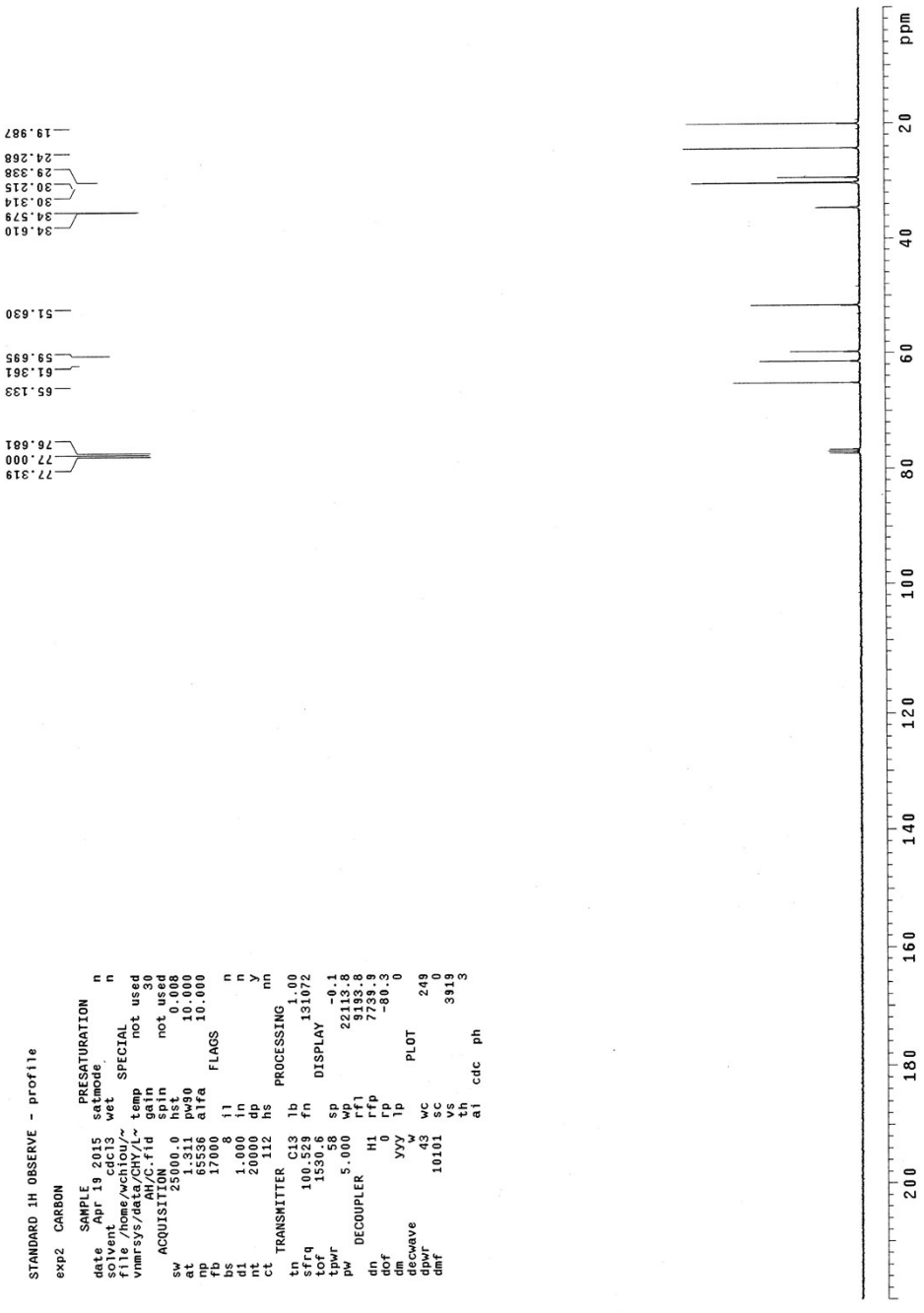
9 ^{1}H-NMR




STANDARD 1H OBSERVE - profile
exp1 PROTON
SAMPLE
date Apr 19 2015
solvent cdcl3
file /home/wchiou/~
vnmrsys/data/CHY/L~
AH/H.fid
ACQUISITION
sw 6410.3
at 2.556
np 32768
fb 4000
bs 4
d1 1.000
nt 128
ct 12
TRANSMITTER
tn H1
sfrq 399.756
tof 399.7
tpwr 60
pw 6.650
DECOUPLER
dn C13
dof 0
dm nnn
decwave W40_4nuc
dmf 29412
PRESATURATION n
satmode n
wet
SPECIAL
temp not used
gain 30
spin not used
hst 0.008
pw90 13.000
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 4197.3
rf1 3702.0
rfp 2902.2
rp -96.0
lp 0
PLOT
wc 249
sc 0
vs 139
th 8
ai ph
ppm
0.97
2.09
4.33
3.92
3.27
1.08
1.01
1.00
1.03
0.88

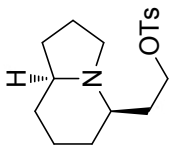
9 ^{13}C-NMR

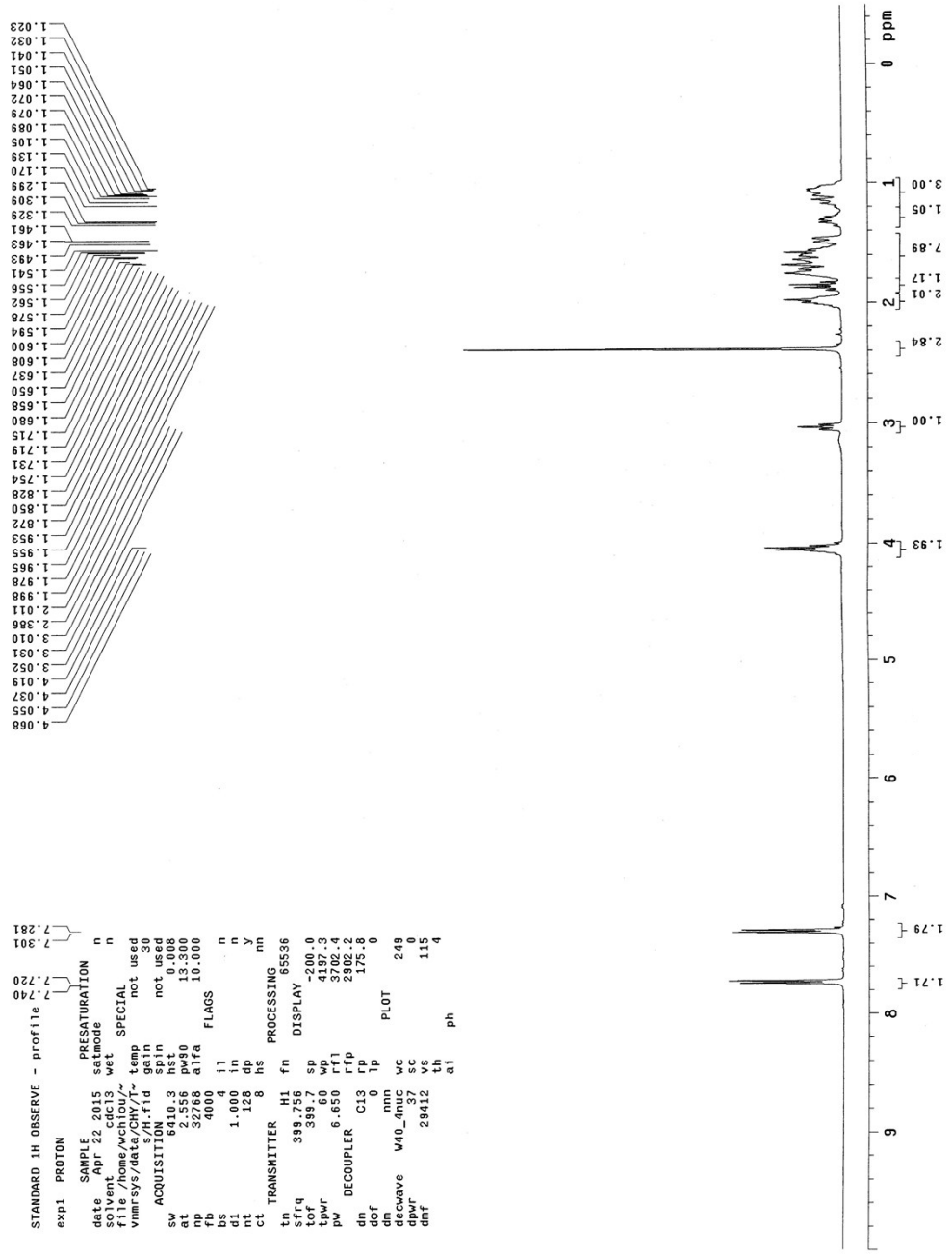




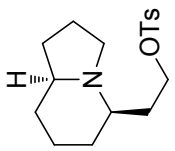

```
STANDARD 1H OBSERVE - profile

exp2  CARBON

      SAMPLE          PRESATURATION     n
date   Apr 19 2015    satmode           n
solvent    cdcl3      wet               n
file /home/wchiou/~     SPECIAL
vnmrsys/data/CHY/L~     temp          not used
        AH/C.fid        gain              30
  ACQUISITION           spin          not used
sw          25000.0     hst               0.008
at              1.311   pw90             10.000
np              65536   alfa             10.000
fb              17000   FLAGS
bs                  8   fl                   n
d1              1.000   in                   n
nt              20000   dp                   y
ct                112   hs                  nn
  TRANSMITTER           PROCESSING
tn          C13         lb                1.00
sfrq      100.529       fn              131072
tof        1530.6       DISPLAY
tpwr            58      sp                -0.1
pw           5.000      wp             22113.8
  DECOUPLER             rfl             9193.8
dn              H1      rfp             7739.9
dof              0      rp                -80.3
dm             yyy      lp                   0
decwave          w      PLOT
dpwr            43      wc                 249
dmf          10101      sc                   0
                        vs                3919
                        th                   3
                        ai  cdc  ph
```

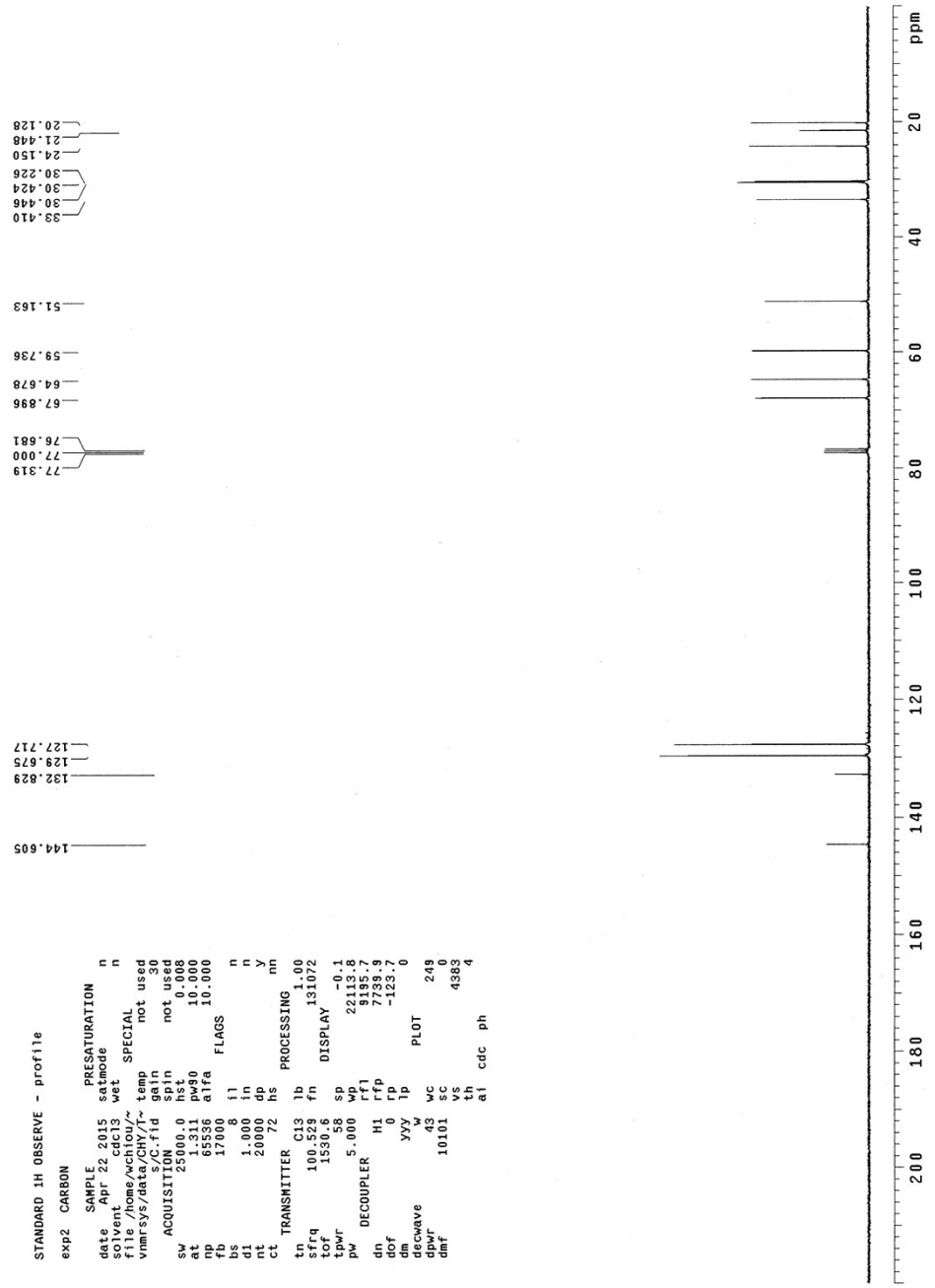
10 ^{1}H-NMR


H
N
OTs


STANDARD 1H OBSERVE - profile
exp1 PROTON
SAMPLE
date Apr 22 2015
solvent cdcl3
file /home/wchiou/~
vnmrsys/data/CHY/T~
s/H.fid
ACQUISITION
sw 6410.3
at 2.556
np 32768
fb 4000
bs 4
d1 1.000
nt 128
ct 8
TRANSMITTER
tn H1
sfrq 399.756
tof 399.7
tpwr 60
pw 6.650
DECOUPLER
dn C13
dof 0
dm nnn
decwave W40_4nuc
dpwr 37
dmf 29412
PRESATURATION
satmode n
wet n
SPECIAL
temp not used
gain 30
spin not used
hst 0.008
pw90 13.300
alfa 10.000
FLAGS
il n
in n
dp y
hs nn
PROCESSING
fn 65536
DISPLAY
sp -200.0
wp 4197.3
rfl 3702.4
rfp 2902.2
rp 175.8
lp 0
PLOT
wc 249
sc 0
vs 115
th 4
ph
ppm
3.00
1.05
7.89
1.17
2.01
2.84
1.00
1.93
1.79
1.71

10 ^{13}C-NMR



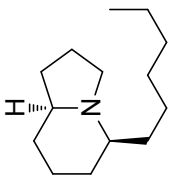


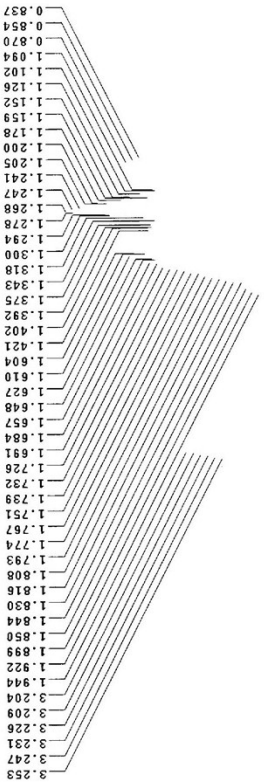
STANDARD 1H OBSERVE - profile

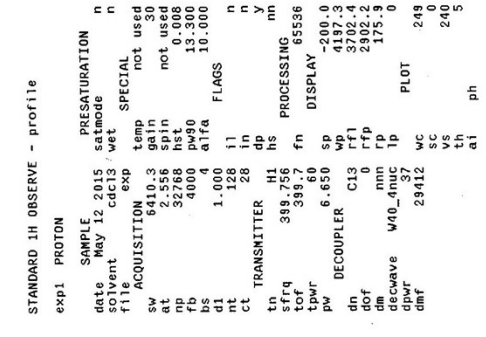
exp2 CARBON

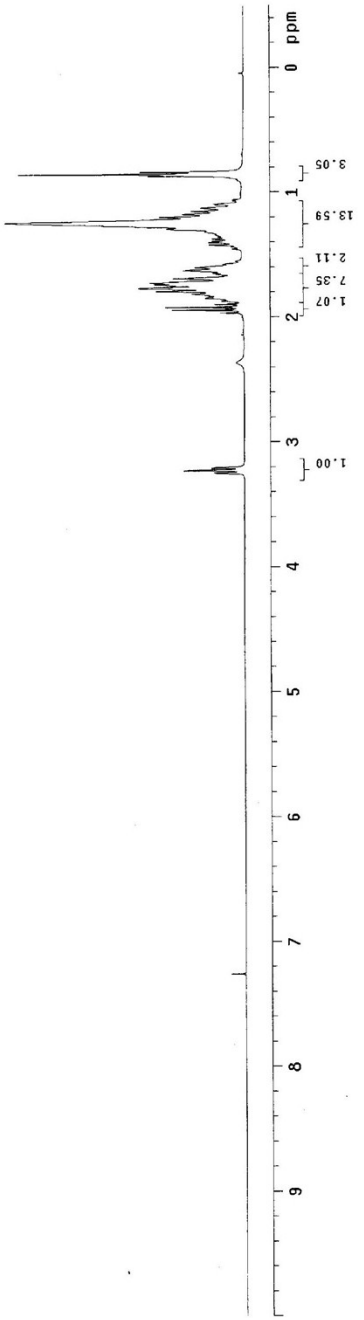
	SAMPLE	PRESATURATION	
date	Apr 22 2015	satmode	n
solvent	cdcl3	wet	n
file	/home/wchiou/~	SPECIAL	
vnmrsys	/data/CHY/T~	temp	not used
	s/C.fid	gain	30
	ACQUISITION	spin	not used
sw	25000.0	hst	0.008
at	1.311	pw90	10.000
np	65536	alfa	10.000
fb	17000	FLAGS	
bs	8	il	n
d1	1.000	in	n
nt	20000	dp	y
ct	72	hs	nn
	TRANSMITTER	PROCESSING	
tn	C13	lb	1.00
sfrq	100.529	fn	131072
tof	1530.6	DISPLAY	
tpwr	58	sp	-0.1
pw	5.000	wp	22113.8
	DECOUPLER	rf1	9195.7
dn	H1	rfp	7739.9
dof	0	rp	-123.7
dm	yyy	lp	0
decwave	w	PLOT	
dpwr	43	wc	249
dmf	10101	sc	0
		vs	4383
		th	4
		ai	cdc ph

11a ^{1}H-NMR

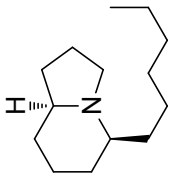


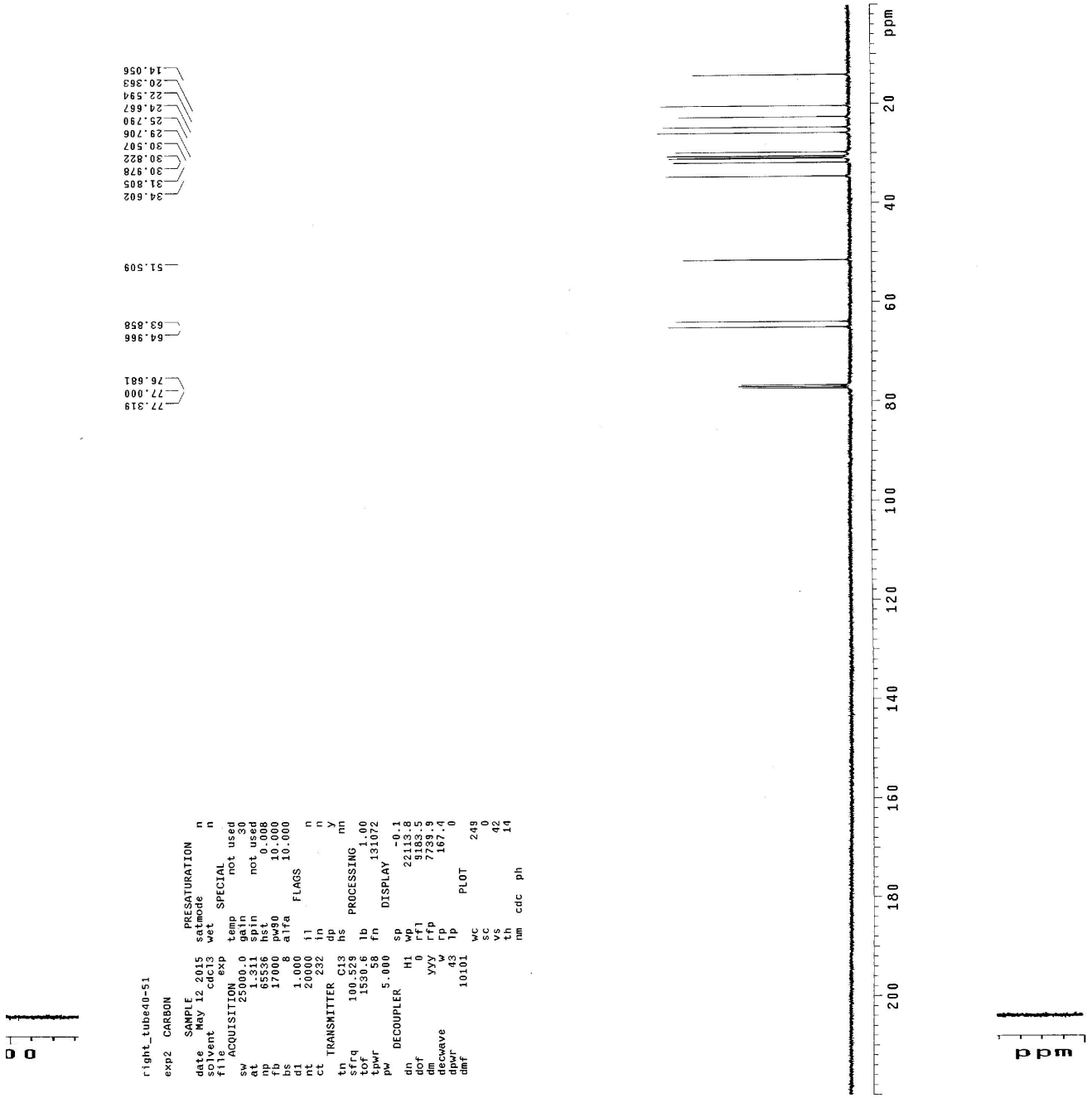



STANDARD 1H OBSERVE - profile
exp1 PROTON
SAMPLE PRESATURATION n
date May 12 2015 satmode n
solvent cdcl3 wet n
file exp SPECIAL
ACQUISITION not used
sw 6410.3 temp 30
at 2.556 gain not used
np 32768 hst 0.008
fb 4000 pw90 13.300
bs 4 alfa 10.000
d1 1.000 FLAGS
nt 128 ii n
ct 28 in n
TRANSMITTER dp y
tn H1 hs nn
sfrq 399.756 PROCESSING
tof 399.7 fn 65536
tpwr 60 DISPLAY
pw 6.650 sp -200.0
wp 4197.3
DECOUPLER rf1 3702.4
dn C13 rfp 2902.2
dof 0 rp 175.9
dm nnn lp 0
decwave W40_4nuc PLOT
dpwr 37 wc 249
dmf 29412 sc 0
vs 240
th 5
ai ph

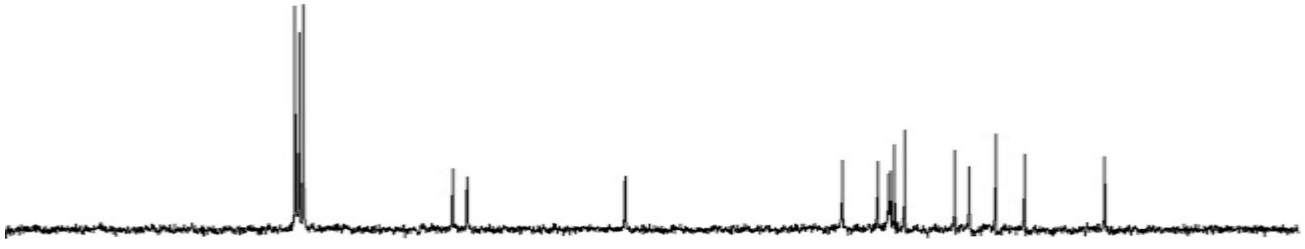

ppm
3.05
13.59
2.11
7.35
1.07
1.00

11a ^{13}C-NMR

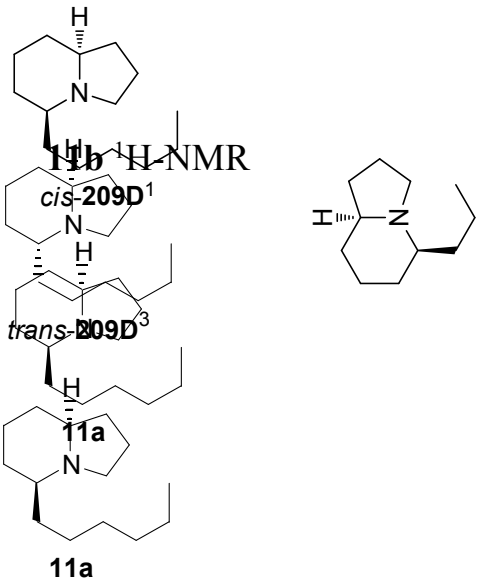




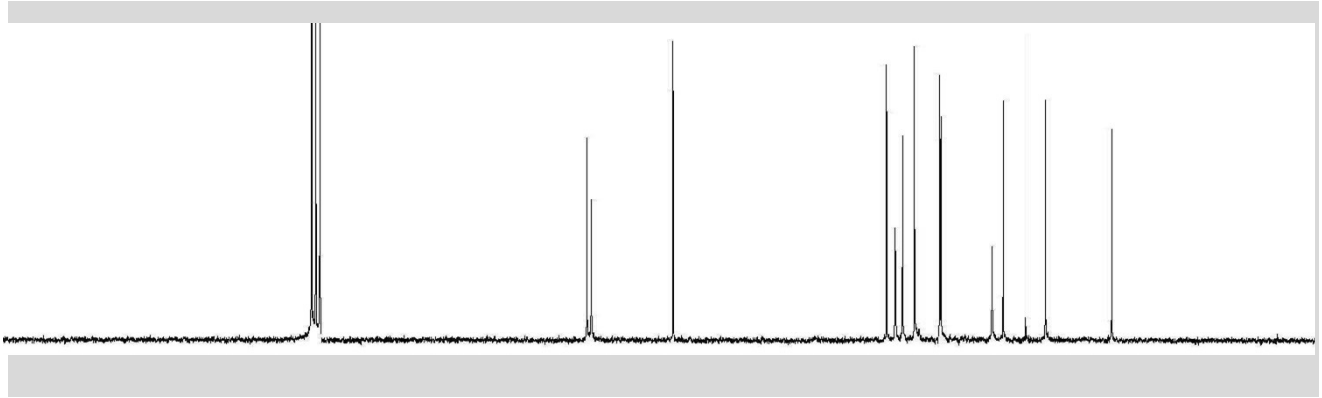
The standard spectraum of ***cis*-209D**



The standard spectraum of ***trans*-209D** [3]



^{1}H-NMR

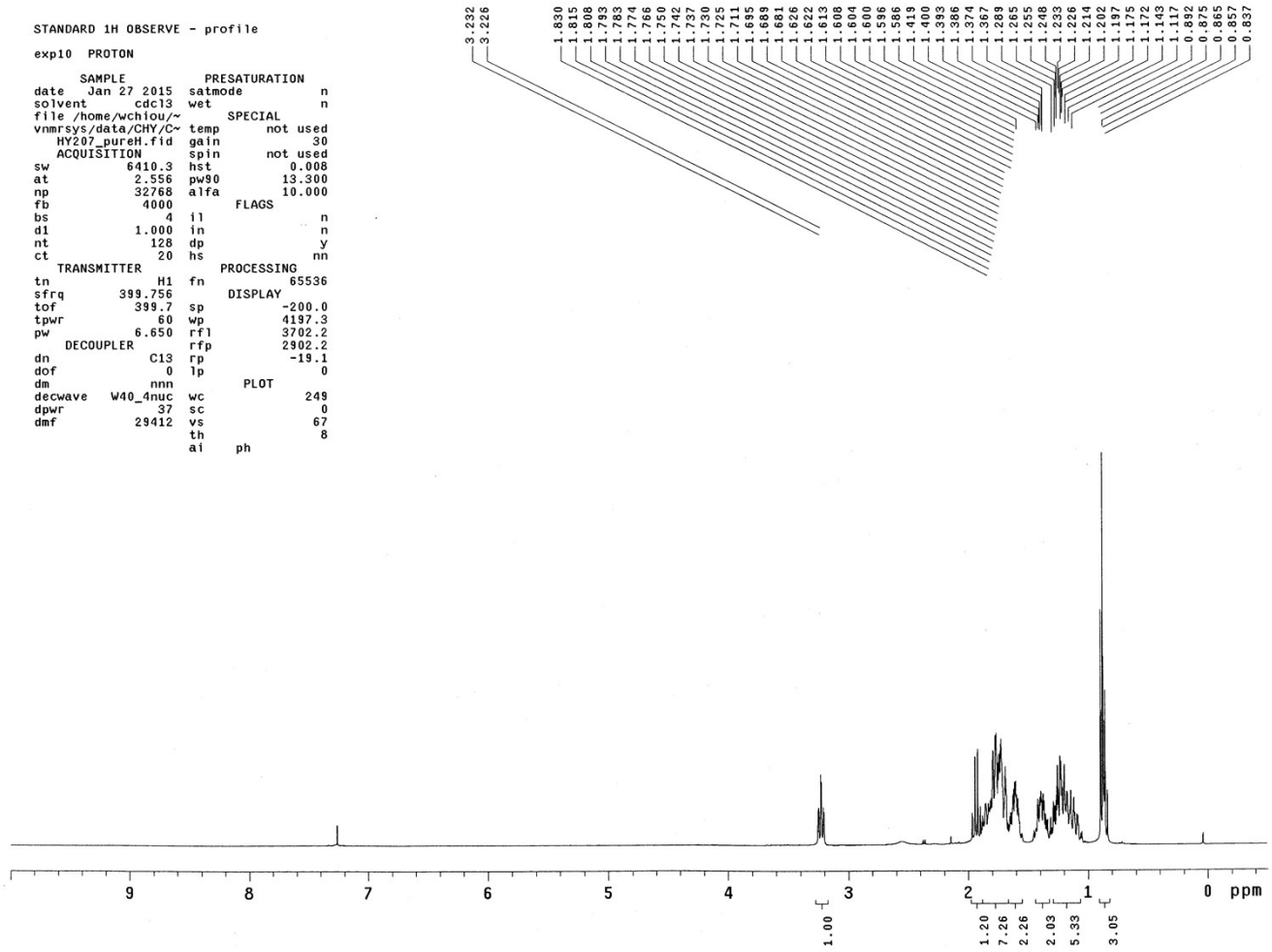


[3] The ^{13}C NMR data of *trans*-209D see Alegret, C.; Riera, A. *J. Org. Chem.* **2008**, *73*, 8661.

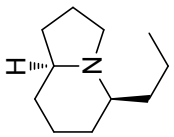
STANDARD 1H OBSERVE - profile

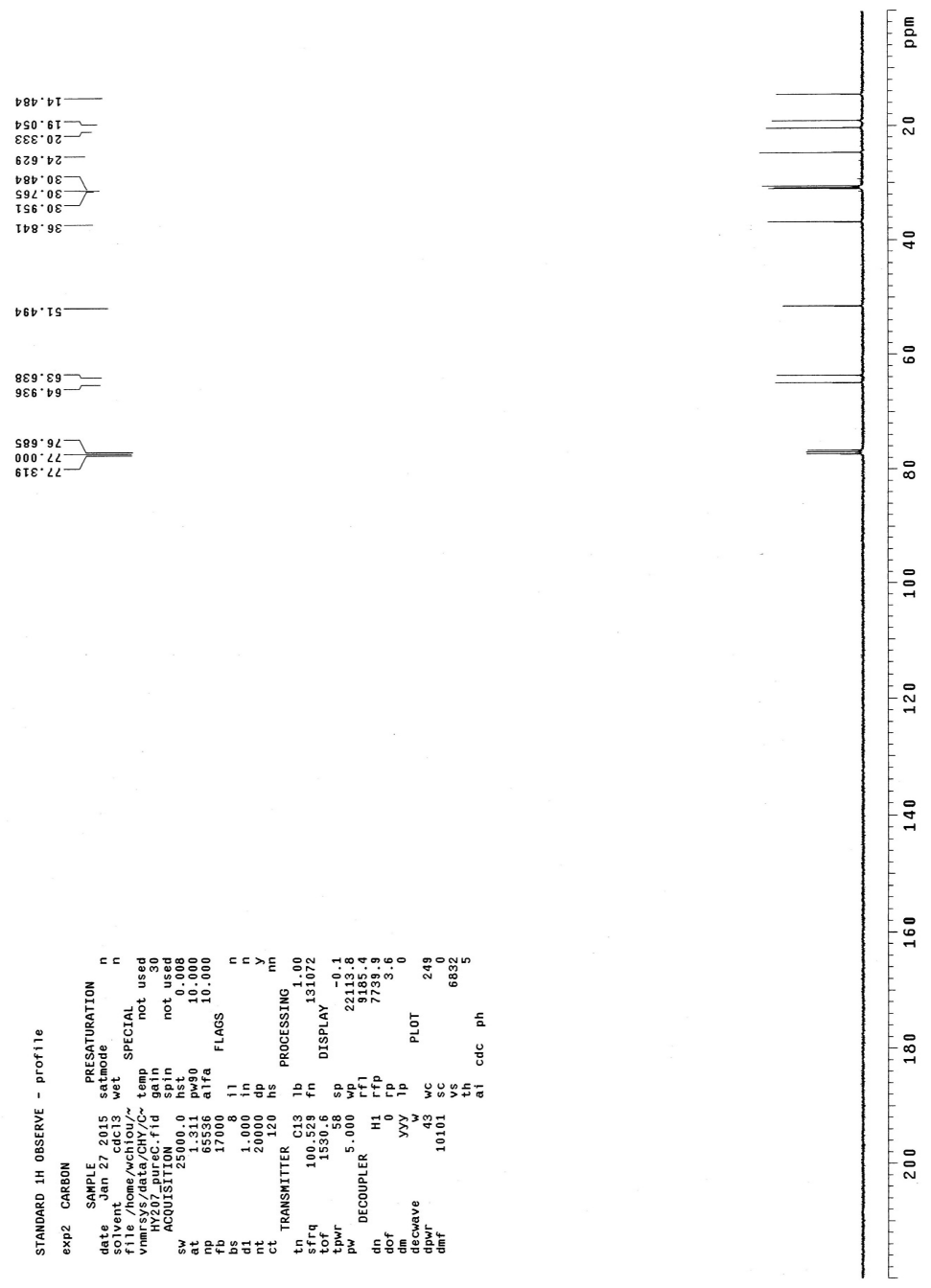
exp10 PROTON

SAMPLE		PRESATURATION	
date	Jan 27 2015	satmode	n
solvent	cdcl3	wet	n
file	/home/wchiou/~	SPECIAL	
vnmrsys/data/CHY/C~		temp	not used
HY207_pureH.fid		gain	30
ACQUISITION		spin	not used
sw	6410.3	hst	0.008
at	2.556	pw90	13.300
np	32768	alfa	10.000
fb	4000	FLAGS	
bs	4	il	n
d1	1.000	in	n
nt	128	dp	y
ct	20	hs	nn
TRANSMITTER		PROCESSING	
tn	H1	fn	65536
sfrq	399.756	DISPLAY	
tof	399.7	sp	-200.0
tpwr	60	wp	4197.3
pw	6.650	rfl	3702.2
DECOUPLER		rfp	2902.2
dn	C13	rp	-19.1
dof	0	lp	0
dm	nnn	PLOT	
decwave	W40_4nuc	wc	249
dpwr	37	sc	0
dmf	29412	vs	67
		th	8
		ai ph	

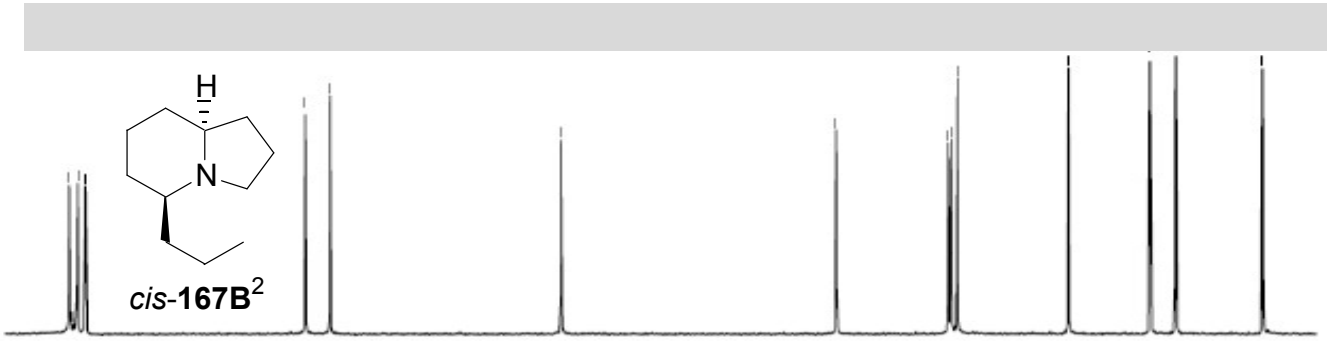


11b ^{13}C-NMR

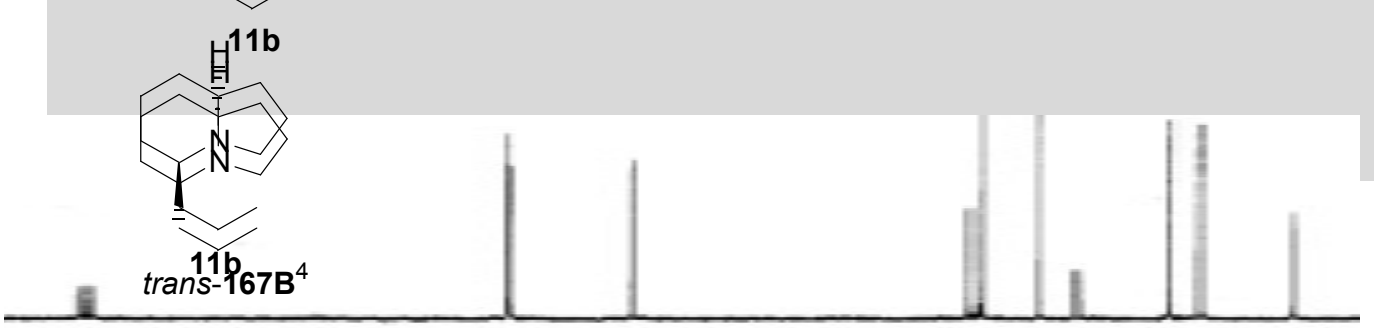



14.484
19.054
20.333
24.629
30.484
30.765
30.951
36.841
51.494
63.638
64.936
76.685
77.000
77.319
STANDARD 1H OBSERVE - profile
exp2 CARBON
SAMPLE PRESATURATION
date Jan 27 2015 satmode n
solvent cdcl3 wet n
file /home/wchiou/~ SPECIAL
vnmrsys/data/CHY/C~ temp not used
HY207_pureC.fid gain 30
ACQUISITION spin not used
sw 25000.0 hst 0.008
at 1.311 pw90 10.000
np 65536 alfa 10.000
fb 17000 FLAGS
bs 8 il n
d1 1.000 in n
nt 20000 dp y
ct 120 hs nn
TRANSMITTER PROCESSING
tn C13 lb 1.00
sfrq 100.529 fn 131072
tof 1530.6 DISPLAY
tpwr 58 sp -0.1
pw 5.000 wp 22113.8
DECOUPLER rfl 9185.4
dn H1 rfp 7739.9
dof 0 rp 3.6
dm yyy lp 0
decwave w
dmm c PLOT
dpwr 43 wc 249
dmf 10101 sc 0
vs 6832
th 5
ai cdc ph
200
180
160
140
120
100
80
60
40
20
ppm

The standard spectraum of *cis*-167B [2]



The standard spectraum of *trans*-167B[4]



[4] The [13]C NMR data of *trans*-167B see Saikia, A. K.; Indukuri, K.; Das, J. *Org. Biomol. Chem.* **2014**, *12*, 7026.

Computational Details: All calculations were performed at the level of B3LYP[5]/6-31++G**, using *Gausian* 09.[6] Stationary points for each reaction, i.e. reactant and product, were achieved by IRC calculation of the corresponding transition state, followed by geometry optimization. All geometries have been confirmed as either stationary points or saddle points by vibrational analyses at the same level. Thermal corrections were calculated at 1 atm 298.15 K in the gas phase. The coordinates of all 6 transition state geometries have been summarized as the text file "**TS geometries.xyz**", which can be opened directly by free software "*Mercury*".

[5] (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648; (b) Lee C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

[6] *Gaussian 09*, *Gaussian, Inc*.; 340 Quinnipiac St Bldg 40 Wallingford, CT 06492 USA.

TS01: $TS_{ax\text{-}cis}$ axial approach on single cis carbamate, substitutent free

C	2.12258100	-0.09859700	-0.79715200
H	1.68709800	0.90010100	-0.90675700
H	2.42170900	-0.49893400	-1.77351200
C	1.26876100	-1.01451600	-0.06594800
H	1.49898300	-2.07701200	-0.16237000
C	0.18581500	-0.66818600	0.71543900
H	0.03172300	0.38125100	0.94970400
C	-1.42964000	-0.76311500	-0.73291700
H	-0.86234800	-0.21118800	-1.47296500
N	-2.40839700	-0.02197700	-0.15915000
Si	3.86792100	0.18073000	0.10242200
C	-3.39182600	-0.62399000	0.78673300
H	-4.26046300	0.03016400	0.80873800
C	4.71228100	-1.49382800	0.27138900
H	5.72321600	-1.36402800	0.67466700
H	4.17706100	-2.16462500	0.95242600
H	4.81251800	-1.99836400	-0.69619900
C	4.80981000	1.32688700	-1.05421500
H	5.80003400	1.54615400	-0.63803200
H	4.96036000	0.87573100	-2.04088300
H	4.29206300	2.28212400	-1.19242900
C	3.54364600	0.98010100	1.77500200
H	4.49475100	1.19070000	2.27769400
H	3.01223100	1.93290000	1.67361100
H	2.96069600	0.33246000	2.43851300
H	-0.22215200	-1.39291800	1.41402600
C	-3.77568700	-2.04383100	0.37274100
H	-4.38560000	-2.47658500	1.17157600
H	-4.40608600	-2.00433400	-0.52398400
C	-1.67543200	-2.22949500	-0.97270500
H	-0.72632900	-2.74482100	-1.13116700
H	-2.20597100	-2.26548700	-1.93844700
C	-2.53605900	-2.90113300	0.10164300
H	-1.95821500	-3.03294900	1.02512100
H	-2.82301400	-3.90167900	-0.23377100
C	-2.30177900	1.39687100	-0.30443300
O	-1.38328800	1.91839900	-0.89959200

O	-3.31471300	2.01583000	0.28702400
C	-3.32664000	3.46781400	0.17756400
H	-4.21557800	3.77975400	0.72138900
H	-2.42313500	3.87831700	0.63018800
H	-3.38598500	3.75589700	-0.87276200
H	-2.94066100	-0.61273300	1.78746100

TS02: $TS_{ax\text{-}trans}$ axial approach on single trans carbamate, substitutent free

C	2.08118200	-0.09153800	-0.83331400
H	1.73191300	0.94299600	-0.91617000
H	2.37635000	-0.48371700	-1.81362700
C	1.15160900	-0.96059900	-0.14367900
H	1.30751100	-2.03315900	-0.26979700
C	0.08572000	-0.56319200	0.64200500
H	0.01039200	0.48480700	0.91955700
C	-1.54912500	-0.50975100	-0.71338300
H	-1.05790500	0.18234000	-1.38564500
N	-2.54271800	0.05384500	0.02119900
Si	3.82189800	0.02565500	0.12440100
C	-3.39980900	-0.77113500	0.91724700
H	-4.28493800	-0.17720900	1.13796000
C	4.50196900	-1.71848600	0.31706500
H	5.50698200	-1.67930400	0.75292200
H	3.88673600	-2.33603500	0.98066300
H	4.58828900	-2.23297000	-0.64654700
C	4.89515500	1.08287600	-1.00163200
H	5.88552800	1.21898300	-0.55160700
H	5.04088100	0.61670600	-1.98195900
H	4.46643400	2.07862100	-1.15785900
C	3.50946700	0.85284000	1.78497800
H	4.45789200	0.98579700	2.31829800
H	3.06187400	1.84610900	1.66807600
H	2.85480600	0.25641000	2.42928200
H	-0.35105500	-1.27841000	1.33327900
C	-3.75211200	-2.11303300	0.27982600
H	-4.27354500	-2.71961500	1.02646600
H	-4.45451200	-1.95111700	-0.54678700
C	-1.75300000	-1.92024100	-1.21343500

H	-0.79977900	-2.34300700	-1.53615100
H	-2.35968400	-1.79973300	-2.12560800
C	-2.49871400	-2.83038000	-0.23306700
H	-1.84615700	-3.10094300	0.60702900
H	-2.76499700	-3.76486400	-0.73513700
C	-2.67277700	1.46831700	0.15734000
O	-3.50645300	1.97196200	0.87136200
O	-1.78284900	2.12048600	-0.59728800
C	-1.89628000	3.57263800	-0.57713600
H	-1.10577700	3.92429800	-1.23699100
H	-2.87759700	3.86908200	-0.94958700
H	-1.75649800	3.94091200	0.43995900
H	-2.85599700	-0.91253400	1.86049900

TS03 $TS_{eq\text{-}cis}$: equatorial approach on single trans carbamate, substitutent free

C	2.12485500	-0.14068900	-0.79787800
H	1.69243000	0.85621300	-0.93156500
H	2.43267300	-0.56990600	-1.75865800
C	1.28351500	-1.03225800	-0.03391600
H	1.50717200	-2.09808500	-0.10605200
C	0.19739000	-0.65609000	0.74107000
H	0.07298400	0.40104700	0.95881800
C	-1.37565600	-0.78507700	-0.63102600
H	-0.82904300	-0.23425800	-1.38670200
N	-2.37065500	-0.02725000	-0.08887500
Si	3.87759100	0.17125400	0.09399500
C	-3.45999100	-0.57437100	0.76989600
H	-4.40317900	-0.25265900	0.32108200
C	4.72734500	-1.49561600	0.29919500
H	5.74160700	-1.35148300	0.68916200
H	4.20074900	-2.14867900	1.00371000
H	4.82028500	-2.02608600	-0.65505800
C	4.80110400	1.29215600	-1.10053400
H	5.79323500	1.52753300	-0.69775400
H	4.94651200	0.81649200	-2.07632500
H	4.27629300	2.24037500	-1.25833300
C	3.55409500	1.01044400	1.74599400

H	4.50728200	1.24764800	2.23285600
H	3.00844000	1.95277300	1.62526600
H	2.98795300	0.37225300	2.43268900
H	-0.19380200	-1.35357100	1.47622800
C	-1.63463900	-2.26500500	-0.88712100
H	-1.43937200	-2.44146700	-1.95175800
C	-2.27070100	1.37995500	-0.27830000
O	-1.32089300	1.90095900	-0.82624100
O	-3.33282500	1.99932300	0.22348400
C	-3.35895200	3.44613200	0.07130500
H	-4.29163100	3.75782700	0.53647100
H	-2.49959500	3.88617000	0.57912700
H	-3.34223700	3.70500600	-0.98821400
H	-3.39102900	-0.10425100	1.75499500
H	-0.91223300	-2.87623600	-0.34083100
C	-3.40315800	-2.09864500	0.86316300
H	-4.37540900	-2.44950300	1.22113300
H	-2.66277000	-2.41399100	1.60903800
C	-3.05568300	-2.69808600	-0.50044500
H	-3.10838900	-3.78985800	-0.47658000
H	-3.77800800	-2.35947400	-1.25289600

TS04, $TS_{equ\text{-}trans}$: equatorial approach on single trans carbamate, substitutent free

C	2.06711000	-0.08903600	-0.84592100
H	1.72486200	0.95058700	-0.86234700
H	2.37281600	-0.42393000	-1.84346300
C	1.14600100	-0.99462100	-0.20583100
H	1.29123800	-2.05656900	-0.41033800
C	0.08142400	-0.64202200	0.61497200
H	0.03489200	0.38487800	0.96832300
C	-1.52561600	-0.55175200	-0.65123800
H	-1.04333200	0.11738600	-1.35169700
N	-2.49901500	0.07881500	0.07053000
Si	3.80996800	-0.02706700	0.13059000
C	-3.47206900	-0.63858100	0.94288500
H	-4.45992600	-0.25161200	0.68200100
C	4.47246000	-1.78244600	0.26243900

H	5.47609000	-1.76599900	0.70308700
H	3.85011500	-2.41777800	0.90203200
H	4.55923200	-2.26381300	-0.71803000
C	4.89335800	1.06114900	-0.95447000
H	5.88015800	1.18003100	-0.49173600
H	5.04612200	0.62398100	-1.94693500
H	4.46892700	2.06246800	-1.08385500
C	3.48757800	0.74390500	1.81530600
H	4.43272900	0.85173900	2.36011400
H	3.04815600	1.74379800	1.72845300
H	2.82411100	0.13054000	2.43410100
H	-0.32630500	-1.39433900	1.28440300
C	-1.80699000	-1.96980400	-1.15022800
H	-1.71008700	-1.94449100	-2.24245700
C	-2.57970800	1.49490900	0.14657300
O	-3.42673300	2.05094800	0.80557800
O	-1.63140400	2.09475200	-0.58507400
C	-1.70261900	3.54841200	-0.61675300
H	-0.87317400	3.85642700	-1.25033100
H	-2.65656000	3.86140100	-1.04312100
H	-1.59821300	3.94705400	0.39321800
H	-3.28089600	-0.34681500	1.98010700
H	-1.04027400	-2.66065900	-0.79203900
C	-3.41078100	-2.15333900	0.74891100
H	-4.34741900	-2.57835200	1.12075700
H	-2.60801600	-2.59330800	1.35410800
C	-3.18865900	-2.48687400	-0.72700100
H	-3.24128500	-3.56499700	-0.90119600
H	-3.97424900	-2.02540000	-1.33703100

TS*syn*: Syn addn with axial approach on single cis carbamate, C-6 acetate

C	3.09298800	-0.01237500	-0.88081700
H	2.77018900	1.03502100	-0.90820400
H	3.62867300	-0.26742000	-1.80401500
C	1.99039800	-0.92509800	-0.61172200
H	2.13442000	-1.96835100	-0.89482600
C	0.76526600	-0.55990300	-0.06096900
H	0.72639600	0.40643000	0.43756300

C	-0.43909400	-0.07657700	-1.51780600
H	0.21897600	0.65456700	-1.97563700
N	-1.52900500	0.52572300	-0.92869700
Si	4.47940700	-0.09608800	0.50827000
C	-2.70615200	-0.25475200	-0.40540900
H	-3.55998400	0.41990100	-0.41305100
C	5.10539400	-1.87171100	0.62688500
H	5.93311300	-1.93511500	1.34280300
H	4.32407600	-2.55834900	0.97103200
H	5.47772300	-2.23713600	-0.33699800
C	5.84280100	1.06850500	-0.07816900
H	6.66134900	1.09276000	0.65075300
H	6.26404000	0.74958200	-1.03801400
H	5.47385700	2.09345200	-0.19487200
C	3.73908400	0.48273200	2.13964100
H	4.50991800	0.49715100	2.91913400
H	3.33198600	1.49692100	2.06159100
H	2.93586700	-0.17707100	2.48426200
H	0.16107600	-1.34110500	0.39256600
C	-3.01130100	-1.42631100	-1.34729100
H	-3.77454700	-2.03554200	-0.85822000
H	-3.45990400	-1.03626500	-2.27048300
C	-0.71908500	-1.32028200	-2.33709600
H	0.22214200	-1.83599900	-2.54802300
H	-1.10263400	-0.95808900	-3.30322100
C	-1.76566600	-2.24366400	-1.70424200
H	-1.35617300	-2.73419100	-0.81292000
H	-2.01971800	-3.04316500	-2.40798200
C	-1.36467600	1.88304500	-0.57707100
O	-0.31637900	2.48968800	-0.73009500
O	-2.48561700	2.40171000	-0.08180200
C	-2.42348800	3.78385800	0.33048400
H	-3.41765400	4.00429000	0.71512000
H	-1.66892500	3.90935900	1.10965800
H	-2.18271500	4.42100000	-0.52299800
C	-2.48626900	-0.66707400	1.05565100
H	-1.79161900	-1.50436400	1.16743300
H	-2.08961700	0.17165000	1.64021500

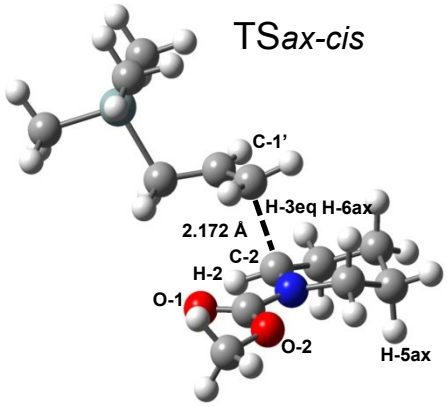
C	-3.85336400	-1.08482100	1.76085800
O	-4.89274400	-0.71638200	1.16572800
O	-3.67526100	-1.71353800	2.82427700

TS_{anti}: Anti addn with axial approach on single cis carbamate, C-6 acetate

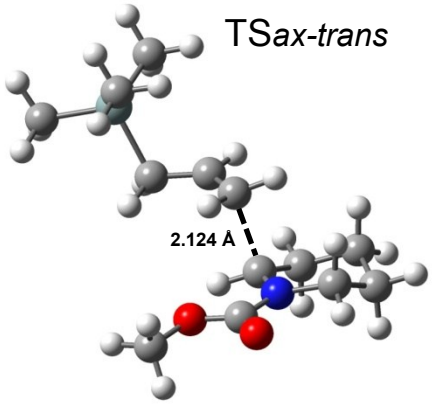
C	3.21818300	-0.61274000	-0.78550200
H	2.89002700	0.23490900	-1.39891300
H	3.62066800	-1.40969100	-1.42330800
C	2.18210200	-1.08648800	0.11680100
H	2.28245100	-2.10319500	0.49663600
C	1.03863200	-0.35422000	0.47635500
H	1.12688300	0.72701700	0.37772200
C	-0.25448100	-0.59417200	-0.85288400
H	0.27951300	-0.09443800	-1.65836100
N	-1.37222100	0.13760400	-0.45020600
Si	4.79806200	0.05254600	0.18207500
C	-2.60892900	-0.45406500	0.19056800
C	5.47938200	-1.34214400	1.25285700
H	6.40578700	-1.02480400	1.74555000
H	4.77458400	-1.63388600	2.03919200
H	5.71340900	-2.23332400	0.65953300
C	6.02482200	0.54536000	-1.16335900
H	6.94693700	0.93378100	-0.71519100
H	6.29746400	-0.30765500	-1.79451400
H	5.61675000	1.32885500	-1.81122100
C	4.28631100	1.53510900	1.22403700
H	5.16319500	1.96889800	1.71873900
H	3.83016900	2.32143500	0.61250600
H	3.57104700	1.25787800	2.00573200
H	-2.64785500	-0.08796100	1.21998600
H	0.51399200	-0.68824200	1.36893100
C	-2.61376900	-2.00098000	0.19238300
H	-3.18104500	-2.30225100	1.07547100
H	-3.19306700	-2.34117400	-0.67439600
C	-0.47833200	-2.07680900	-1.05163900
H	0.48602300	-2.56281400	-1.22779600
H	-1.07249900	-2.20000600	-1.96831900
C	-1.24730500	-2.67923600	0.12478600

H	-0.68310400	-2.55148400	1.05775800
H	-1.37589900	-3.75741200	-0.01649100
C	-1.17507300	1.53231100	-0.45042000
O	-0.23345200	2.07069700	-1.01511200
O	-2.08175900	2.17656000	0.28327700
C	-1.98520100	3.61632400	0.30128100
H	-2.81172900	3.94281500	0.93017800
H	-1.02672000	3.92643800	0.72275800
H	-2.08703100	4.01245200	-0.71119200
C	-3.87545200	0.03701900	-0.52602800
H	-3.88848200	1.11967100	-0.65438000
H	-3.96984000	-0.42498400	-1.51360000
C	-5.17449300	-0.30221100	0.33615900
O	-4.97427900	-0.47298500	1.56111100
O	-6.21642500	-0.31527700	-0.35089900

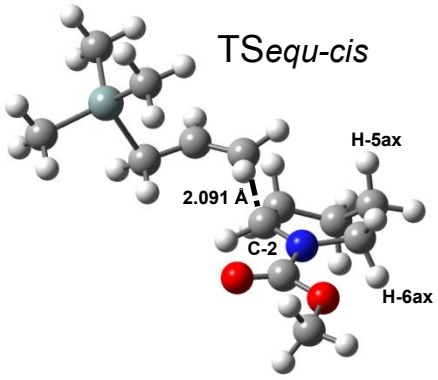
1.


TS*ax-cis*
C-1'
H-3eq H-6ax
2.172 Å
C-2
H-2
O-1
O-2
H-5ax

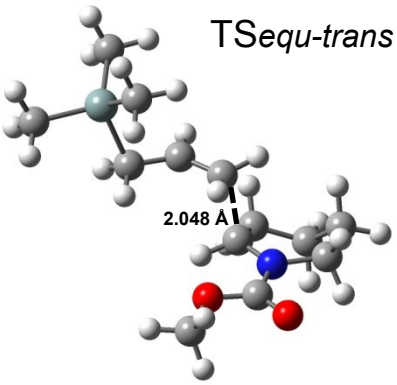
2.


TS*ax-trans*
2.124 Å

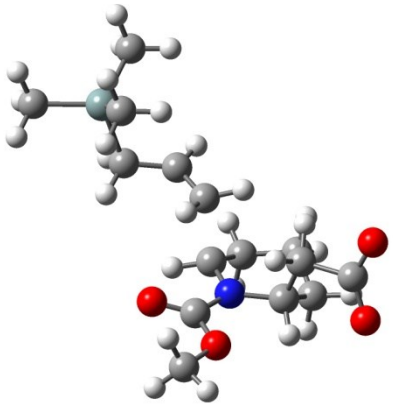
3.


TS*equ-cis*
H-5ax
2.091 Å
C-2
H-6ax

4.



5. cis- addition



6. *trans* addition