Supporting Information

Radical Addition to "Cation Pool". Reverse Process of Radical Cation Fragmentations

Tomokazu Maruyama, Seiji Suga,* and Jun-ichi Yoshida*

Department of Synthetic Chemistry & Biological Chemistry, Graduate School of Engineering, Kyoto University, Kyoto 615-8510, Japan

General Remarks. ^{1}H and ^{13}C NMR spectra were recorded on Varian GEMINI-2000 (^{1}H 300 MHz, ^{13}C 75 MHz), Varian MERCURYplus-400 (^{1}H 400 MHz, ^{13}C 100MHz), JEOL A-500 (^{1}H 500 MHz, ^{13}C 125 MHz) and JEOL ECA-600 (^{1}H 600 MHz, ^{13}C 150 MHz) spectrometers in $CDCl_3$. EI and CI mass spectra were recorded on JMS-SX102A spectrometer. IR spectra were measured with a SHIMADZU FTIR 1600 spectrometer. GC analysis was performed on a gas chromatograph (SHIMADZU GC-14B) equipped with a flame ionization detector using a fused silica capillary. Gel permeation chromatography (GPC) was carried out on Japan Analytical Industry LC-908 equipped with JAIGEL-1H and 2H using $CHCl_3$ as eluent.

Materials. Dichloromethane was washed with water and distilled from P_2O_5, then removal of a trace amount of acid was carried out by distillation from dried K_2CO_3 and distillate was stored over molecular sieves 4A. Trifluoromethanesulfonic acid (TfOH) was purchased from Nacalai and was used without purification. Tetrabutylammonium tetrafluoroborate (Bu_4NBF_4) was purchased from TCI and dried with P_2O_5 under vacuum. All reactions were carried out under Ar atmosphere unless otherwise noted.

Generation of *N*-Acyliminium Ion Pool (2). The anodic oxidation was carried out in an H-type divided cell (4G glass filter) equipped with a carbon felt anode (Nippon Carbon JF-20-P7, ca. 320 mg, dried at 250 ^{o}C/1 mmHg for 1 h before use) and a platinum plate cathode (40 mm x 20 mm). In the anodic chamber was placed a solution of **1** (563.8 mg, 2.8 mmol) in 0.3 M Bu_4NBF_4/CH_2Cl_2 (56 mL). In the cathodic chamber were placed 0.3 M Bu_4NBF_4/CH_2Cl_2 (56 mL) and trifluoromethanesulfonic acid (0.62 mL, 7.0 mmol). The constant current electrolysis (20 mA) was carried out at –78 ^{o}C with magnetic stirring until 2.5 F/mol of electricity was consumed.

NMR Spectra. NMR spectra of carbamates were usually very broad and sometimes separated to two sets of signals due to the existence of rotamers because of the restricted rotation around the CO-N bond.

Methyl 2-Heptylpyrrolidinecarboxylate (3). Typical Procedure. The electrolysis of **1** was carried out as described above. To the cation pool **2** generated from **1** (56.4 mg, 0.28 mmol) was added 1-iodoheptane (0.20 mL, 1.25 mmol) and hexabutyldistannane (0.19 mL, 0.375 mmol) at –20 ^{o}C, and the reaction mixture was stirred for 1 h. Triethylamine was added to the solution at –20 ^{o}C, and the resulting mixture was warmed up to room temperature. Solvent was removed under reduced pressure. DBU (1.2 mL, 0.90 mmol) and diethyl ether (10 mL) were added to the residue, and the resulting solution was quickly filtered through a short column (10 cm) of silica gel. The silica gel was washed with ether (150 mL). The combined filtrate was concentrated by a rotary evaporator, and the crude product thus obtained was purified using flash chromatography (hexane/EtOAc 9:1) and GPC to obtain the title compound (49 mg, 77% yield by GC analysis): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.8 Hz, 3H), 1.20-1.36 (m, 11H), 1.63-1.71 (m, 2H), 1.76-1.97 (m, 3H), 3.30-3.49 (m, 2H), 3.67 (s, 3H) 3.73-3.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 22.8, 23.6, 26.3, 29.4, 29.7, 30.2, 31.9, 34.2, 46.4, 52.1, 57.7, 155.4; IR (neat) 2926.4, 1705.3 cm^{-1}; LRMS (CI) *m/z* 228 (M^+ + H), HRMS (CI) calcd for $C_{13}H_{26}NO_2$ (M^+ + H): 228.1964, found: 228.1965.

Methyl 2-Cyclohexylpyrrolidinecarboxylate. Typical Procedure for the Slow Addition of Hexabutyldistannane. The electrolysis of **1** was carried out as described above. To the cation pool of **2** generated from **1** (56.4 mg, 0.28 mmol) was added 1-iodocyclohexane (0.16 mL, 1.25 mmol) at –20 ^{o}C. Hexabutyldistannane (0.19 mL, 0.375 mmol) was added dropwise over a period of 30 min at the same temperature. The reaction mixture was stirred for 1 h at –20 ^{o}C. Triethylamine was added to the solution at –20 ^{o}C, and the resulting mixture was warmed to room temperature. The solvent was removed under reduced pressure. DBU (1.2 mL, 0.90 mmol) and diethyl ether (10 mL) was added to the residue, and the resulting solution was quickly filtered through a short column (10 cm) of silica gel. The silica gel was washed with diethyl ether (150 mL). The combined filtrate was concentrated by rotary evaporator, and the crude product thus obtained was purified by flash chromatography (hexane/EtOAc 9:1) and GPC to obtain the title compound. (33.6 mg, 0.159 mmol, 60% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87-1.09 (m, 2H), 1.09-1.30 (m, 3H), 1.54-1.70 (m, 4H), 1.70-1.90 (m, 6H), 3.21-3.31 (m, 1H) 3.40-3.83 (m, 2H) 3.69 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.6 and 24.4, 26.2, 26.4, 26.6, 27.3 and 27.7, 30.0, 40.6 and 41.3, 46.7, 52.1, 61.8 and 62.4, 156.0; IR (neat) 2926.4, 1703.4 cm^{-1}; LRMS (CI) *m/z* 212 (M^+ + H); HRMS (CI) calcd for $C_{12}H_{22}NO_2$ (M^+ + H): 212.1651, found: 212.1656.

Methyl 2-Isoropylpyrrolidinecarboxylate. Prepared from cation pool of **2** generated from **1** (56.4 mg, 0.28

mmol), hexabutyldistannane (0.19 mL, 0.375 mmol) and isopropyl iodide (0.12 mL, 1.25 mmol), and purified by flash chromatography (hexane/EtOAc 9:1) and GPC (20.6 mg, 0.120 mmol, 43% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.77-0.94 (m, 6H), 1.69-1.94 (m, 4H), 2.00-2.30 (m, 1H), 3.20-3.30 (m, 1H), 3.54-3.80 (m, 2H), 3.64 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.2, 19.9, 24.8, 26.0, 30.4, 47.4, 52.4, 63.3, 156.2; IR (neat) 2961.1, 1703.4 cm^{-1}; LRMS (CI) *m/z* 172 (M^+ + H); HRMS (CI) calcd for $C_9H_{18}NO_2$ (M^+ + H): 172.1338, found: 172.1337.

Methyl 2-Benzylpyrrolidinecarboxylate. Prepared from cation pool of **2** generated from **1** (56.4 mg, 0.28 mmol), hexabutyldistannane (0.19 mL, 0.375 mmol) and benzyl bromide (0.15 mL, 1.25 mmol), and purified by flash chromatography (hexane/EtOAc 9:1) and GPC (42.4 mg, 0.190 mmol, 69% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.69-1.89 (m, 4H), 2.58 (dd, *J* = 13.2, 9.6 Hz, 1H), 2.96-3.26 (m, 1H), 3.31-3.50 (m, 2H), 3.73 (s, 3H), 3.99-4.14 (m, 1H), 7.12-7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.8 and 23.6, 29.0 and 29.9, 39.6 and 40.6, 46.6, 52.2, 58.6 and 59.3, 126.0, 128.2, 129.3, 138.8, 155.4; IR (neat) 2953.4, 1699.5, 702.2 cm^{-1}; LRMS (CI) *m/z* 220 (M^+ + H); HRMS (CI) calcd for $C_{13}H_{18}NO_2$ (M^+ + H): 220.1338, found: 220.1337.

Methyl 2-Heptylpiperidinecarboxylate. Prepared from cation pool generated from methyl piperidinecarboxylate (60.3 mg, 0.28 mmol), 1-iodoheptane (0.20 mL, 1.25 mmol) and hexabutyldistannane (0.19 mL, 0.375 mmol) and purified by flash chromatography (hexane/EtOAc 9:1) and GPC (23.7 mg, 0.098 mmol, 35% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.14-1.33 (m, 10H), 1.33-1.71 (m, 8H), 2.74-2.87 (m, 1H), 3.67 (s, 3H), 3.90-4.06 (m, 1H), 4.14-4.27 (m, 1H); ^{13}C NMR (150 MHz $CDCl_3$) δ 14.1, 18.9, 22.6, 25.6, 26.2, 28.3, 29.3, 29.5, 29.5, 31.8, 40.0, 50.7, 52.3, 156.3; IR (neat) 2930.2, 2856.9, 1701.4 cm^{-1}; LRMS (CI) *m/z* 242 (M^+ + H); HRMS (CI) calcd for $C_{14}H_{28}NO_2$ (M^+ + H): 242.2115, found: 242.2120.

Methyl Ethyl(1-methyloctyl)aminecarboxylate. The electrolysis of diethylaminecarboxylate (52.5 mg, 0.40 mmol) was carried out as described above. To the cation pool thus obtained was added 1-iodoheptane (0.33 mL, 2.0 mmol) and hexabutyldistannane (0.30 mL, 0.60 mmol) at –20 °C and the reaction mixture was stirred for 1 h. Triethylamine was added at –20 °C and the mixture was warmed to room temperature. The solvent was removed under reduced pressure and the residue was quickly filtered through a short column (10 cm) of silica gel to remove Bu_4NBF_4. The silica gel was washed with diethyl ether (150 mL). The crude product thus obtained was purified using flash chromatography (hexane/EtOAc 9:1) and GPC to obtain the title compound (28.6 mg, 0.125 mmol, 31% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.87 (t, *J* = 6.8 Hz, 3H), 1.00-1.57 (m, 18H), 3.00-3.29 (m, 2H), 3.69 (s, 3H), 3.91-4.21 (m, 1H); ^{13}C NMR (100 MHz $CDCl_3$) δ 14.5, 15.4 and 16.1, 19.6 and 20.0, 23.1, 27.1, 29.6, 30.0, 32.2, 35.3, 37.4 and 38.2, 52.3, 52.5, 156.9; IR (neat) 2928.3, 1703.4 cm^{-1}; LRMS (CI) *m/z* 230 (M^+ + H); HRMS (CI) calcd for $C_{13}H_{28}NO_2$ (M^+ + H): 230.2120, found: 230.2119.

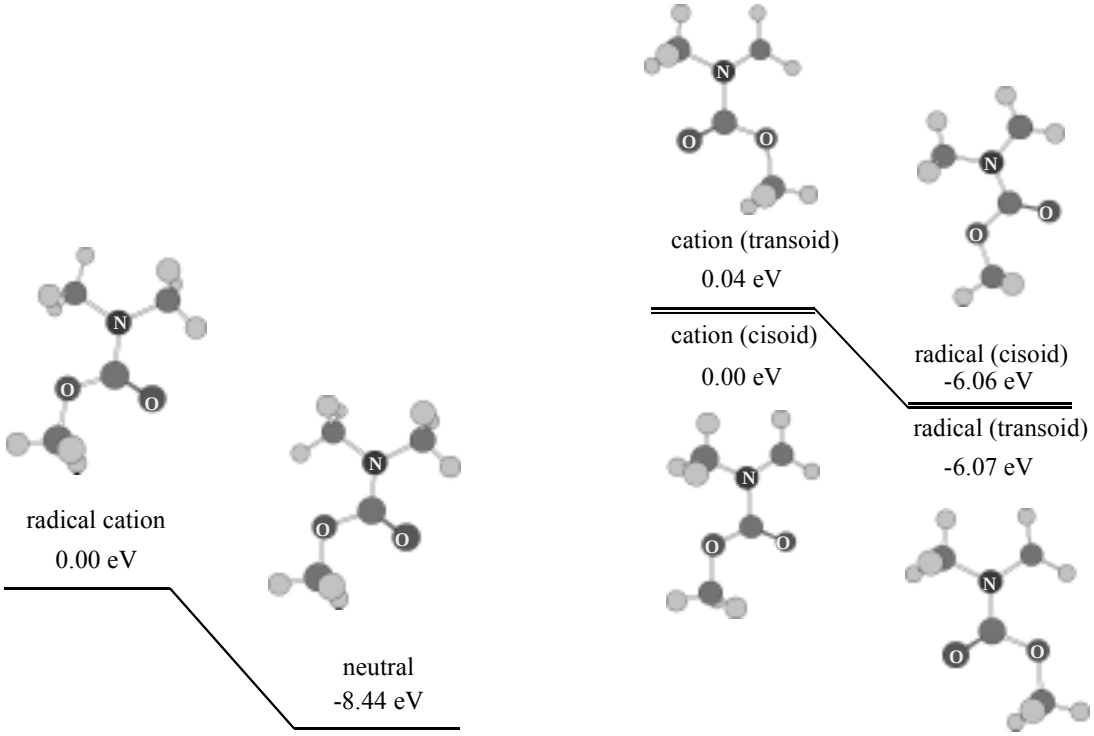
The Reaction of 2 with Cyclopropylmethyl Iodide. Cation pool of **2** generated from **1** (56.4 mg, 0.28 mmol) was allowed to react with hexabutyldistannane (0.19 mL, 0.375 mmol) and cyclopropylmethyl iodide (227.5 mg, 1.25 mmol) to obtain methyl 2-(3-butenyl)pyrrolidinecarboxylate and methyl 2-(cyclopropylmethylpyrrolidinecarboxylate as a mixture.

Methyl 2-(3-Butenyl)pyrrolidinecarboxylate. Purified by flash chromatography (hexane/EtOAc 9:1) and GPC (5.5 mg, 0.030 mmol, 11% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.30-2.11 (m, 8H), 3.28-3.47 (m, 2H), 3.74-3.88 (m, 1H) 4.88-5.11 (m, 2H), 5.72-5.88 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.9 and 23.8, 29.8 and 30.4, 33.0 and 33.5, 46.2, 52.0, 56.8 and 57.4, 114.5, 138.2, 155.6; IR (neat) 2953.9, 1701.4, 733.0 cm^{-1}; LRMS (EI) *m/z* 183 (M^+); HRMS (EI) calcd for $C_{10}H_{17}NO_2$ (M^+): 183.1259, found: 183.1256.

Methyl 2-(Cyclopropylmethylpyl)pyrrolidinecarboxylate Purified by flash chromatography (hexane/EtOAc 9:1) and GPC (22.0 mg, 0.12 mmol, 42% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.01-0.16 (m, 2H), 0.37-0.50 (m, 2H), 0.54-0.67 (m, 1H), 1.33-1.46 and 1.49-1.59 (m, 2H), 1.77-2.03 (m, 4H), 3.29-3.51 (m, 2H), 3.67 (s, 3H), 3.80-3.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 4.3, 5.2, 8.3, 23.5 and 24.3, 30.2 and 30.9, 38.7 and 39.6, 46.6, 52.4, 58.0 and 58.5, 155.8; IR (neat) 2955.3, 1703.4 cm^{-1}; LRMS (CI) *m/z* 184 (M^+ + H); HRMS (CI) calcd for $C_{10}H_{18}NO_2$ (M^+ + H): 184.1338, found: 184.1339.

The Reaction in the Absence of an Alkyl Halide. The electrolysis of **1** was carried out as described above. To the cation pool of **2** (0.056 M, 5.0 ml, 0.28 mmol) thus obtained, was added hexabutyldistannane (0.19 mL, 0.375 mmol) at –20 °C and the reaction mixture was stirred for 5 h at the same temperature. Triethylamine (0.25 mL) was added at –20 °C and the mixture was warmed to room temperature. Solvent was removed under reduced pressure and the residue was quickly filtered through a short column (10 cm) of silica gel to remove Bu_4NBF_4. The silica gel was washed with diethyl ether (150 mL). The crude product thus obtained was purified using flash chromatography (hexane/EtOAc 9:1) and GPC to obtain *N*,*N*'-dimethoxycarbonyl-2,2'-bipyrrolidine (**8**) (29.3 mg, 0.114 mmol, 82% yield) as a mixture of two diastereomers (36:64), which was identified by comparison of its ^{1}H NMR spectrum with that of an authentic sample reported previously.[1]

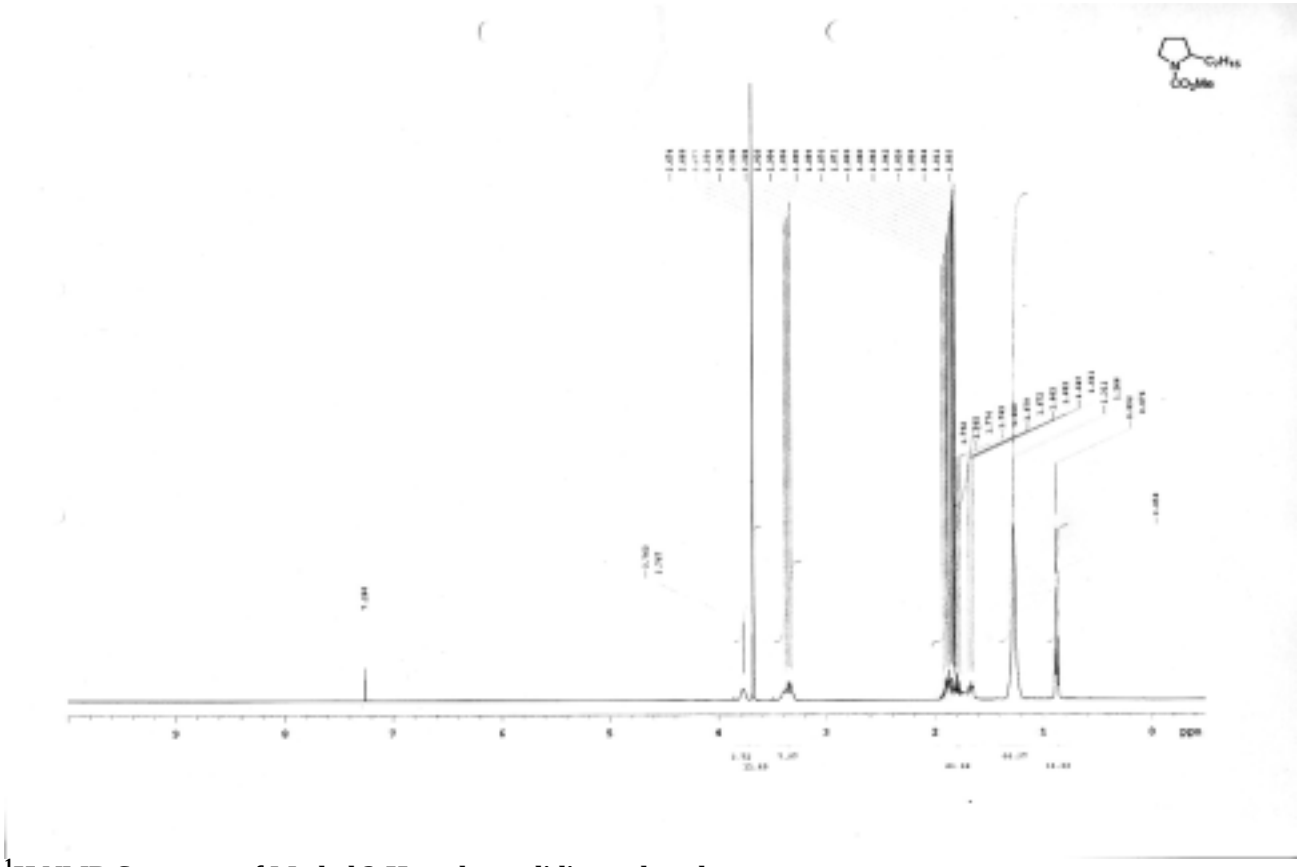
DFT Calculations. The DFT calculations were carried out with model compounds (methyl dimethylaminecarboxylate, its radical cation, radical, and cation) at B3LYP/6-31G(d) level using the Gaussian 98W and 2003W.[2] Geometries were fully optimized. All the optimized structures were local minima according to the vibration analysis. The results are summarized as follows:



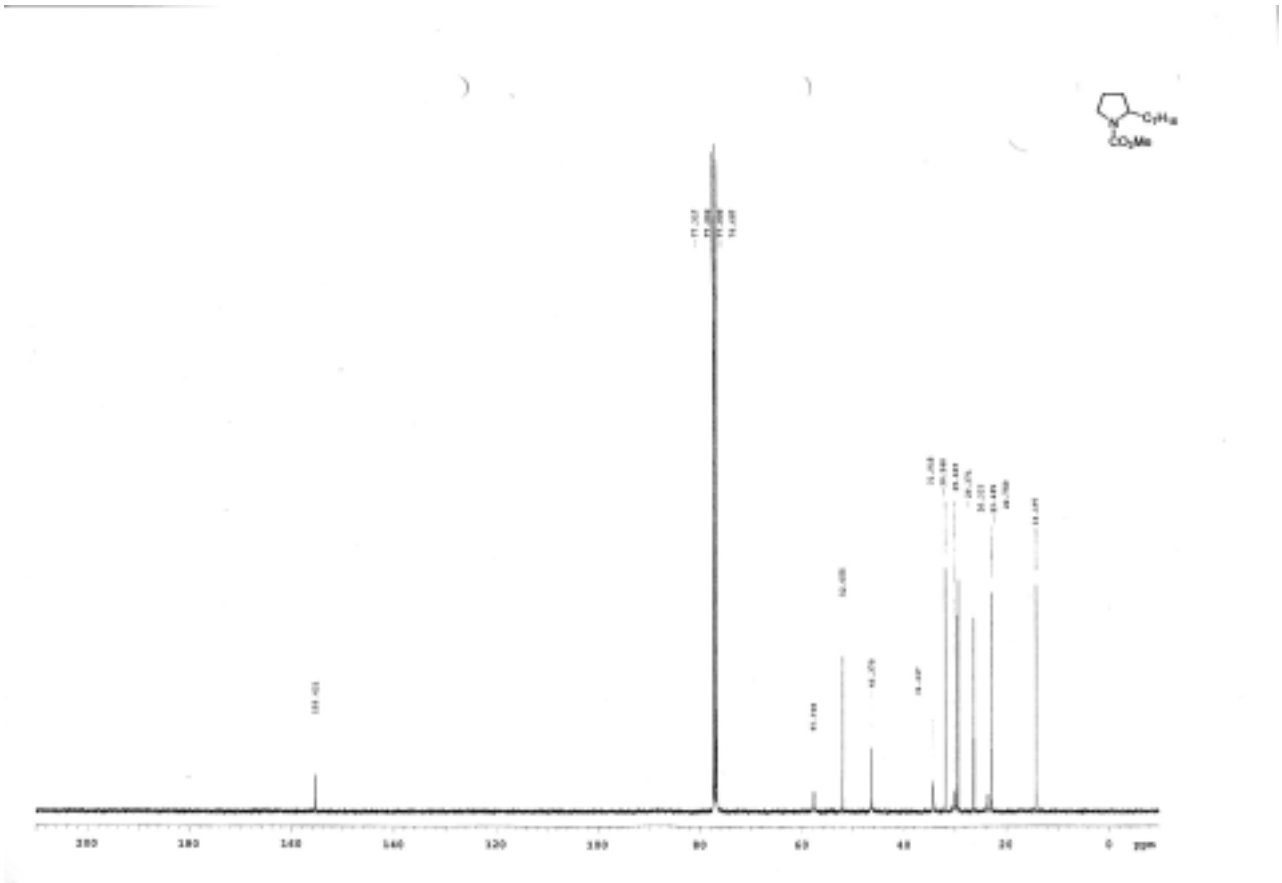
(1) (a) Suga, S.; Suzuki, S.; Yoshida, J. *J. Am. Chem. Soc.* **2002**, *124*, 30. (b) Suga, S.; Suzuki, S.; Maruyama, T.; Yoshida, J. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 1545.

(2) Gaussian 03, Revision B.05, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, Jr., J. A.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.;Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A.; Gaussian, Inc., Pittsburgh PA, 2003.

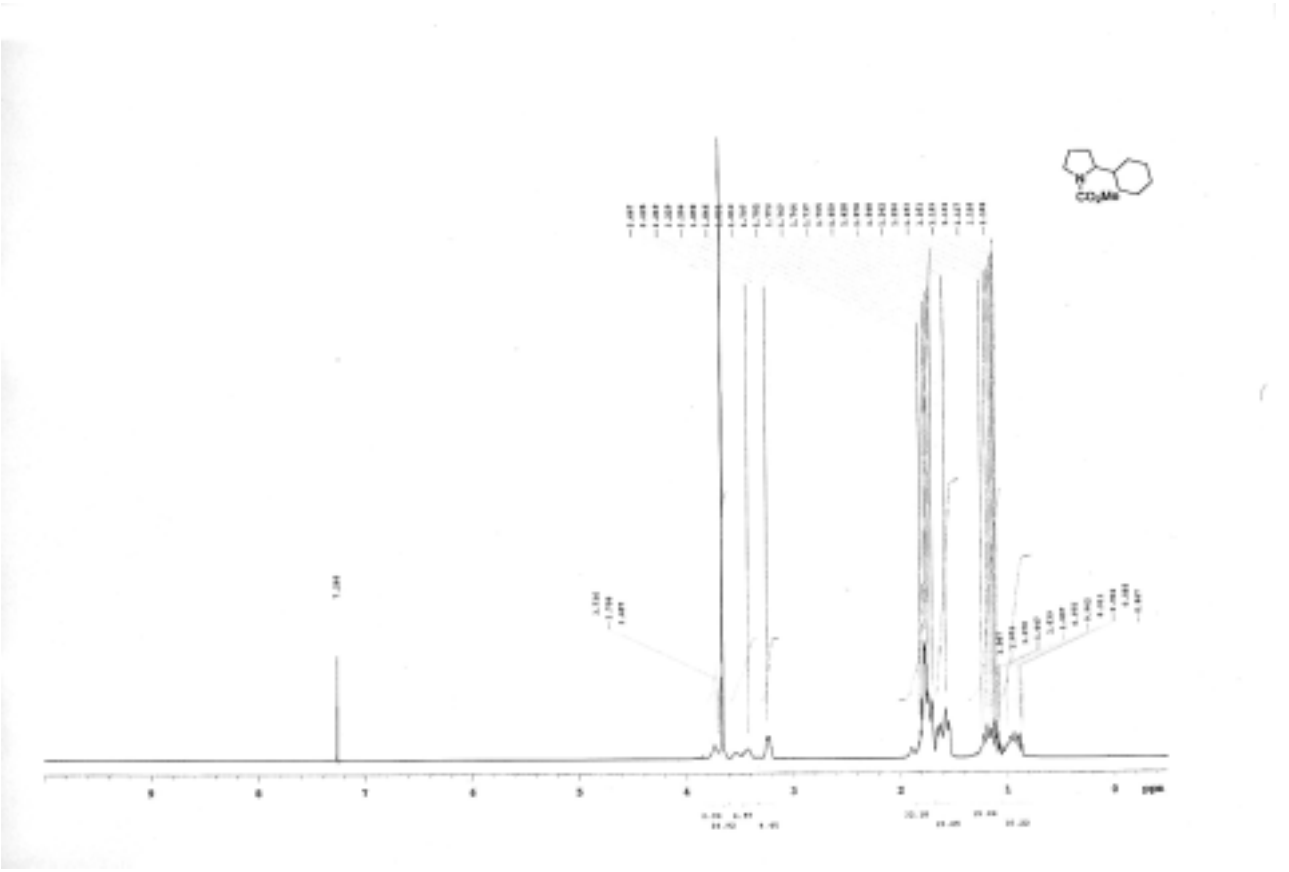
^{1}H and ^{13}C NMR spectra of unknown compounds are as follows:



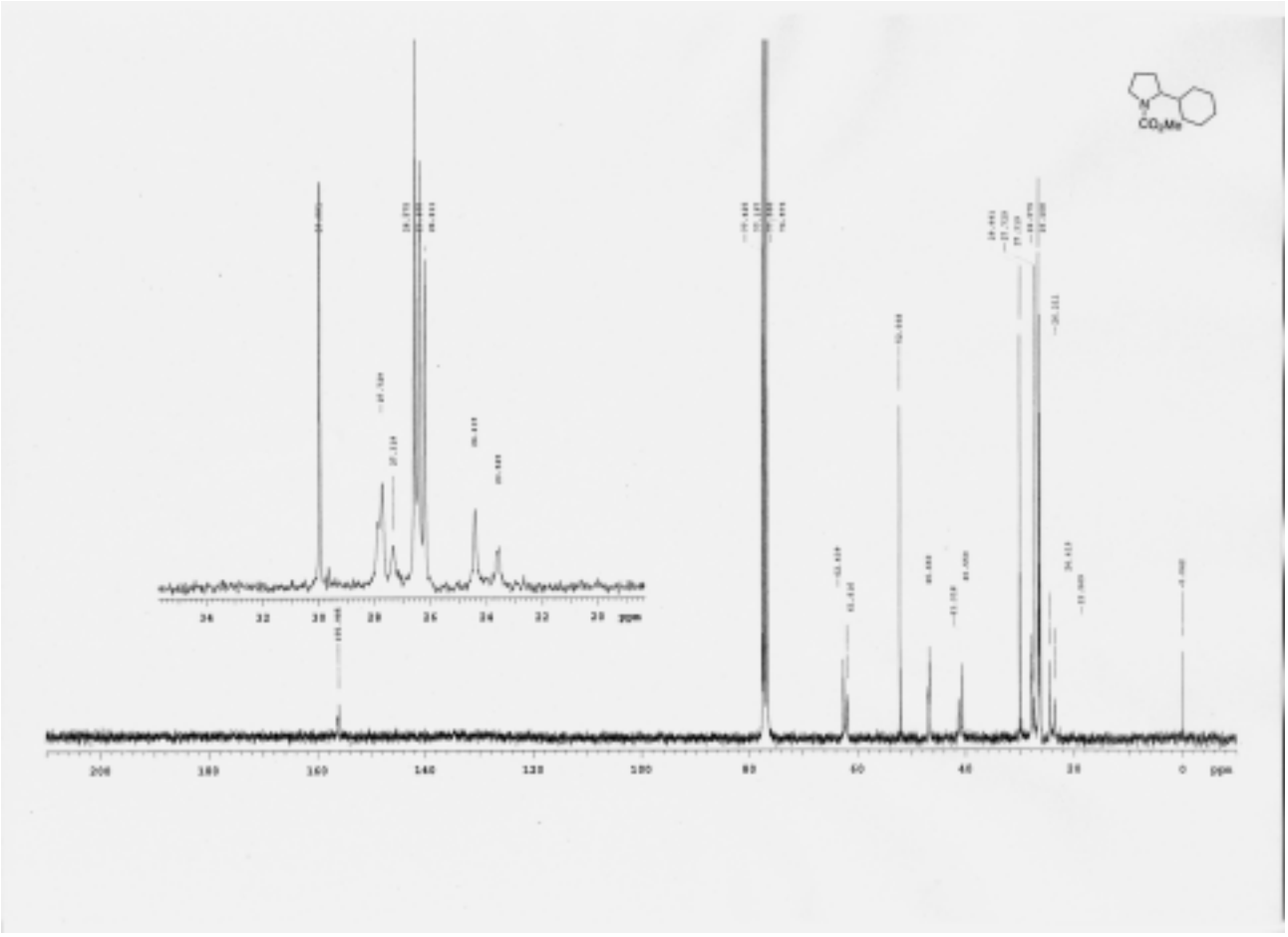
^{1}H NMR Spectrum of Methyl 2-Heptylpyrrolidinecarboxylate



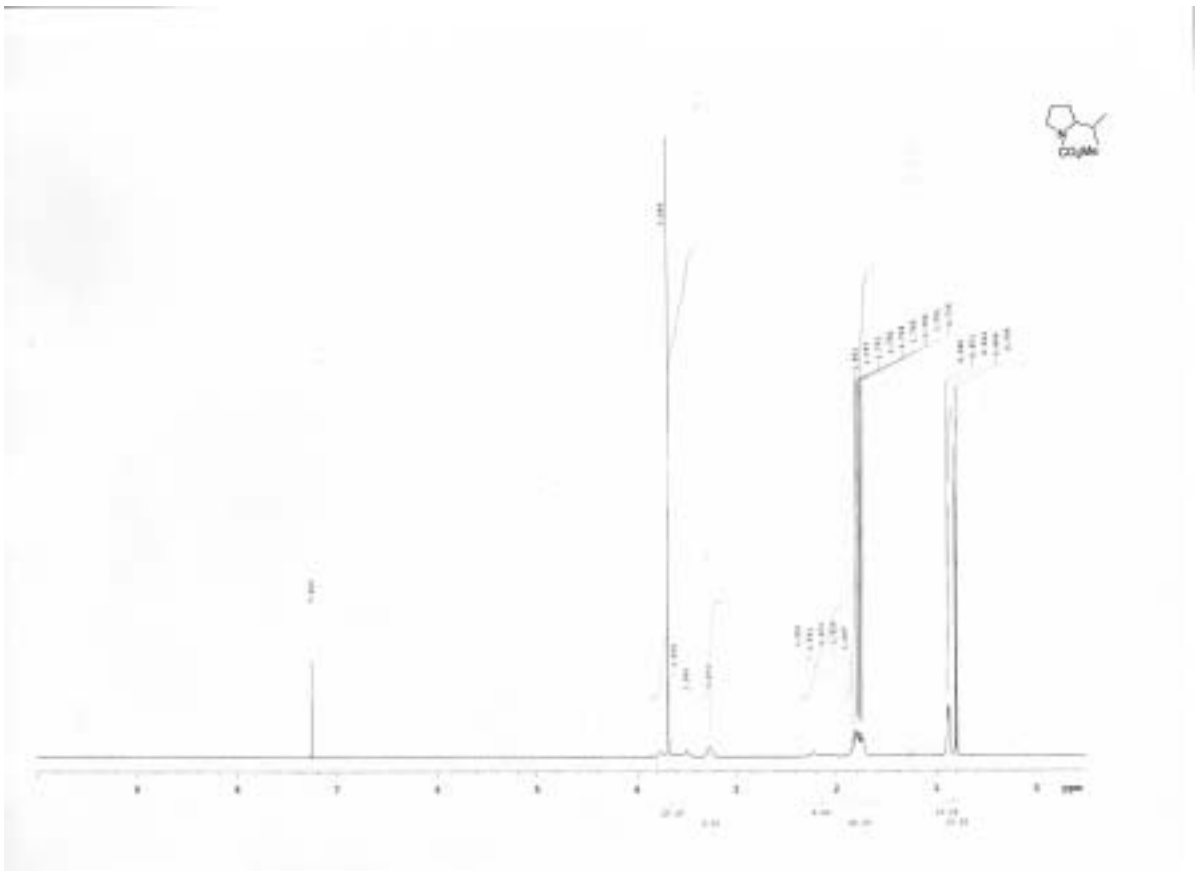
^{13}C NMR Spectrum of Methyl 2-Heptylpyrrolidinecarboxylate



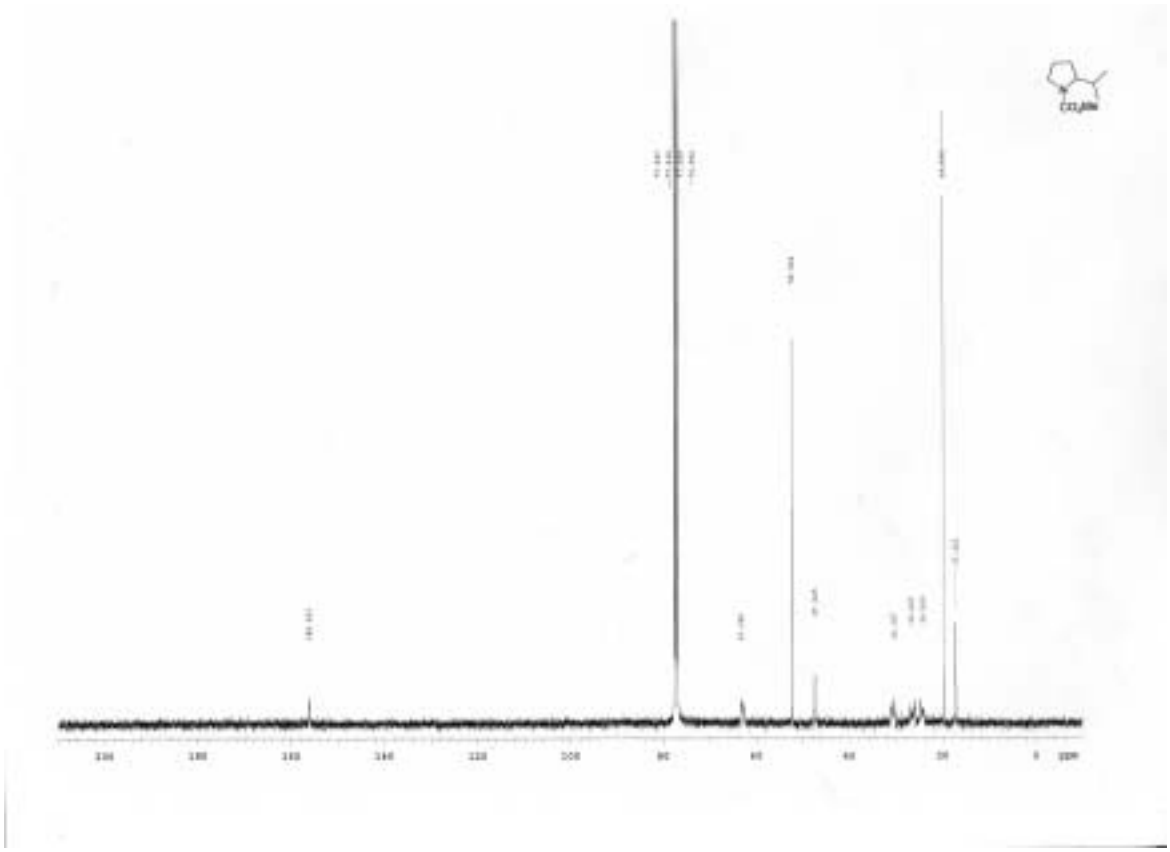
^{1}H NMR Spectrum of Methyl 2-Cyclohexylpyrrolidinecarboxylate.



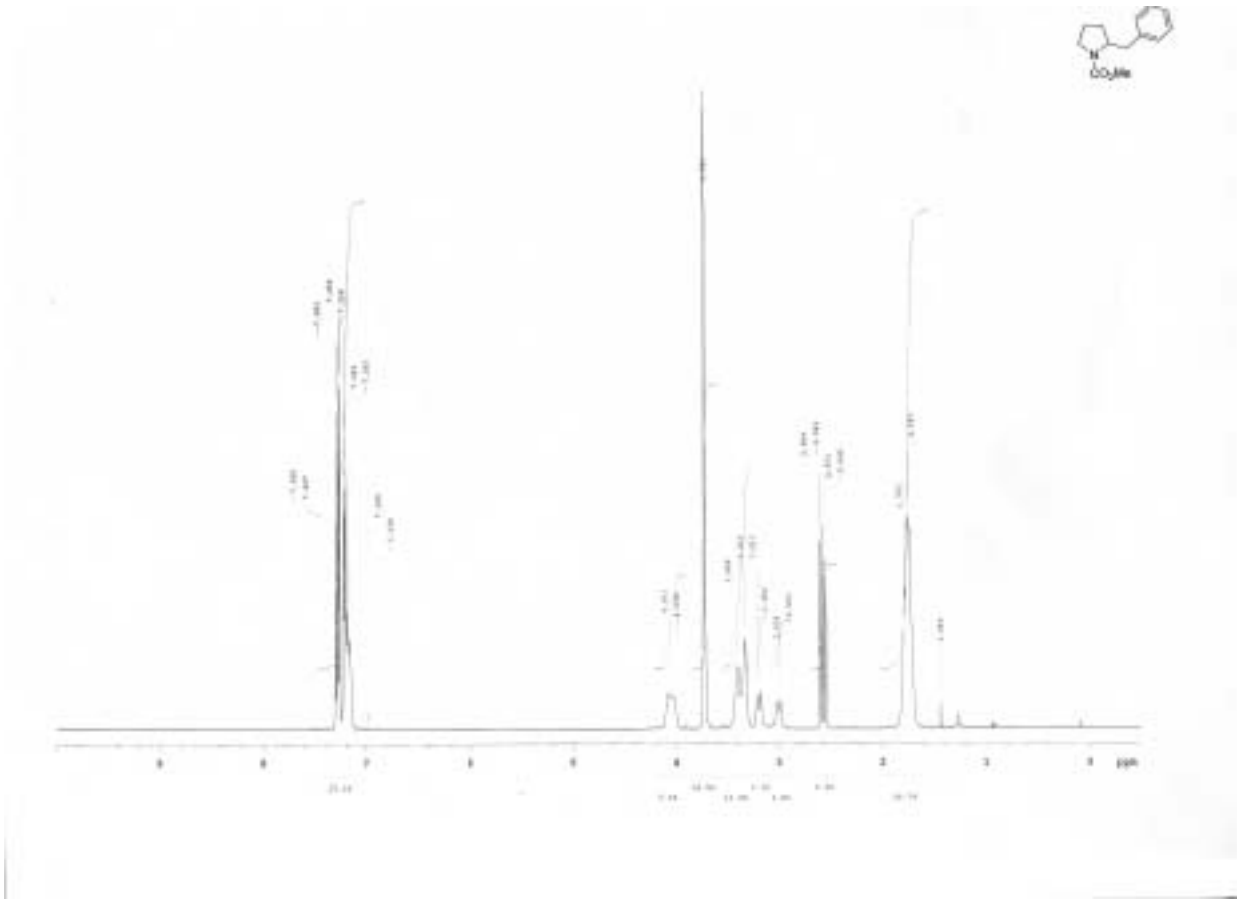
^{13}C NMR Spectrum of Methyl 2-Cyclohexylpyrrolidinecarboxylate.



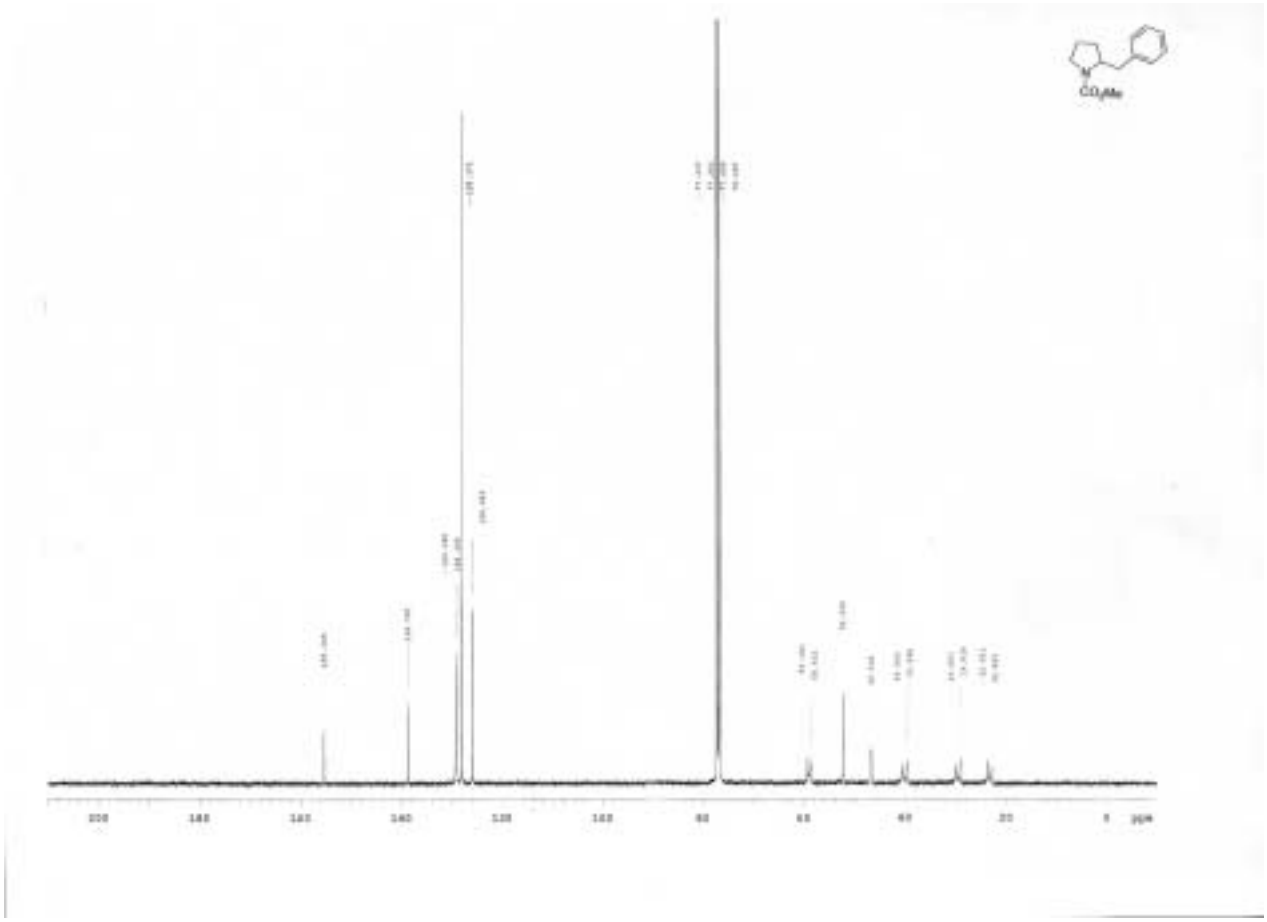
^{1}H NMR Spectrum of Methyl 2-Isoropylpyrrolidinecarboxylate.



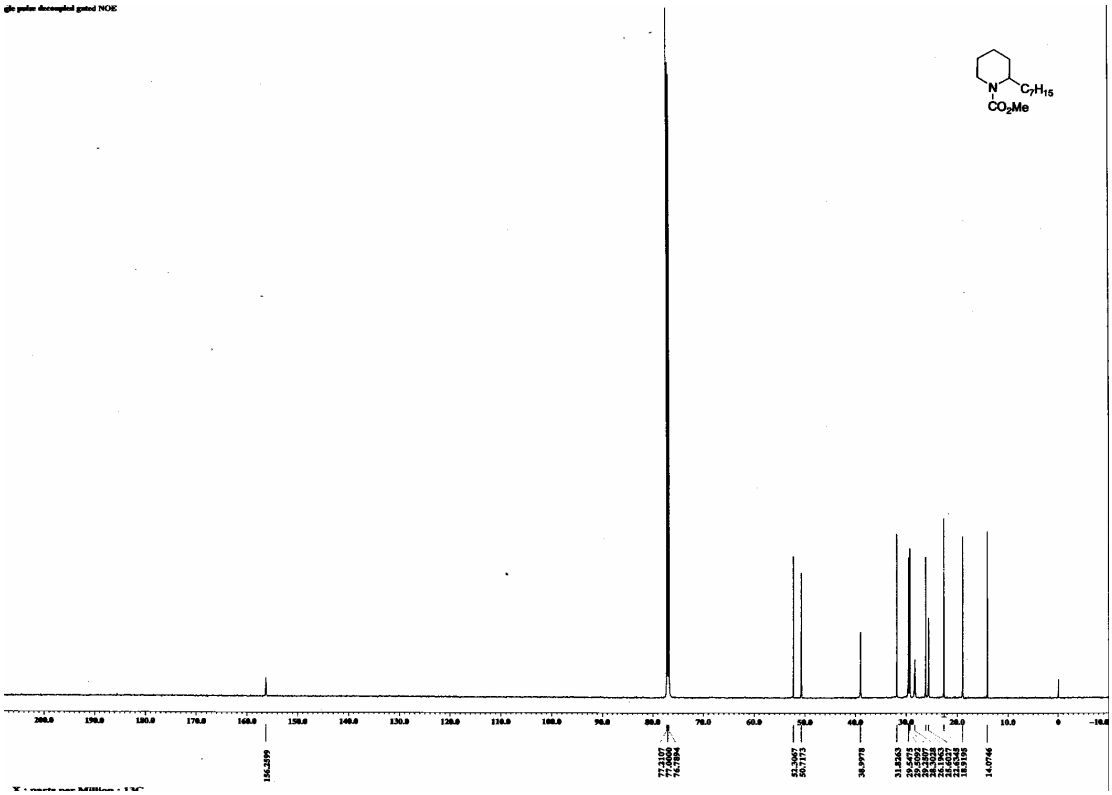
^{13}C NMR Spectrum of Methyl 2-Isoropylpyrrolidinecarboxylate.



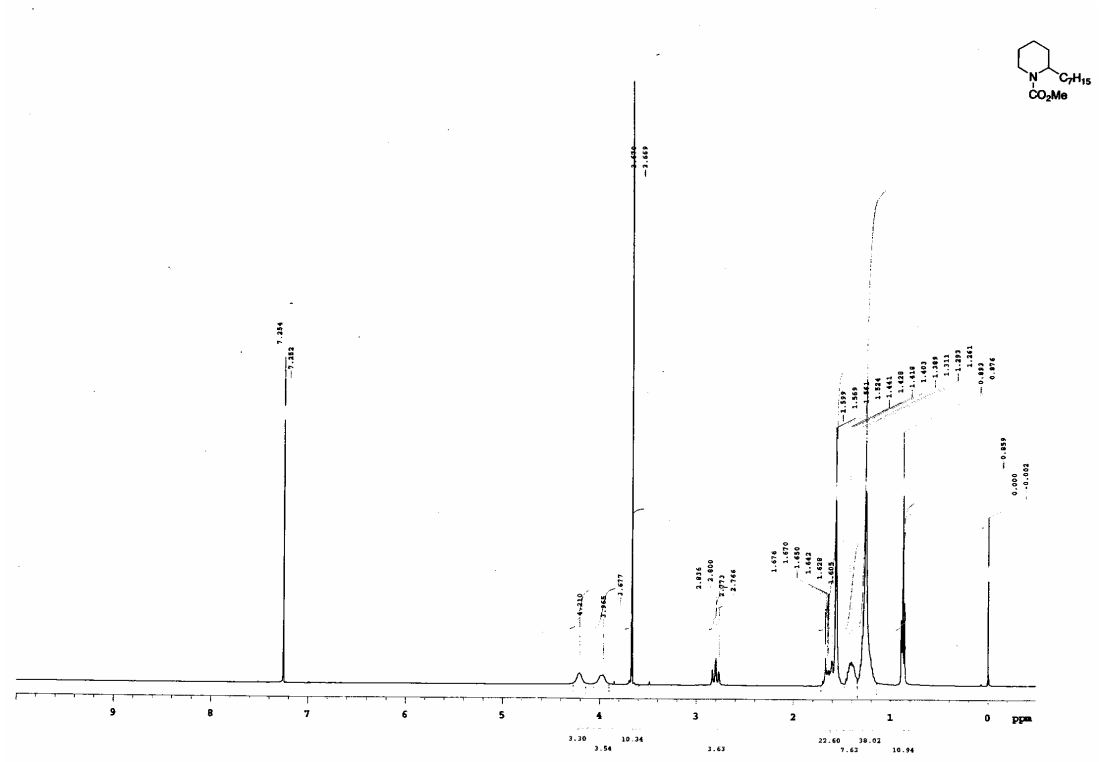
^{1}H NMR Spectrum of Methyl 2-Benzylpyrrolidinecarboxylate.



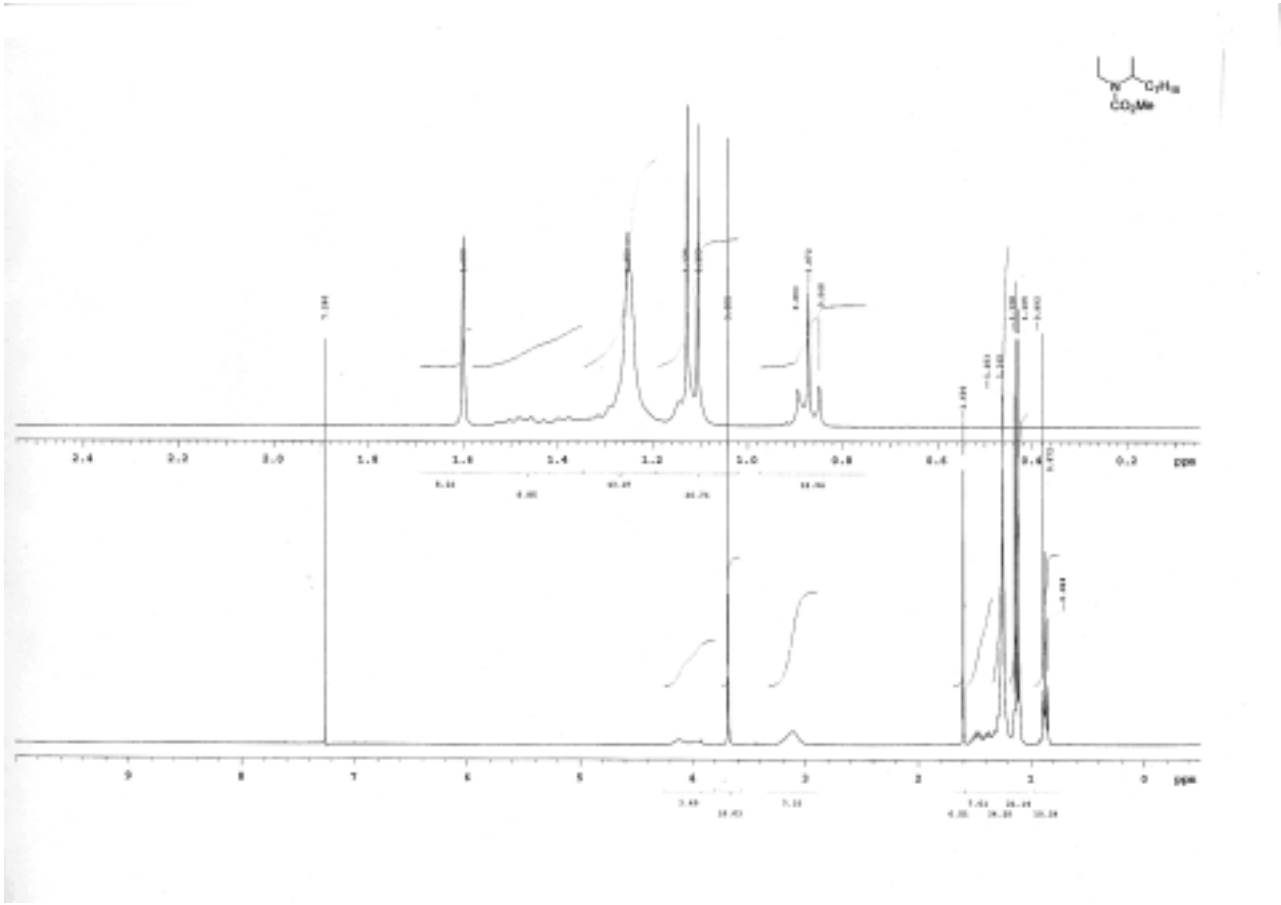
^{13}C NMR Spectrum of Methyl 2-Benzylpyrrolidinecarboxylate.



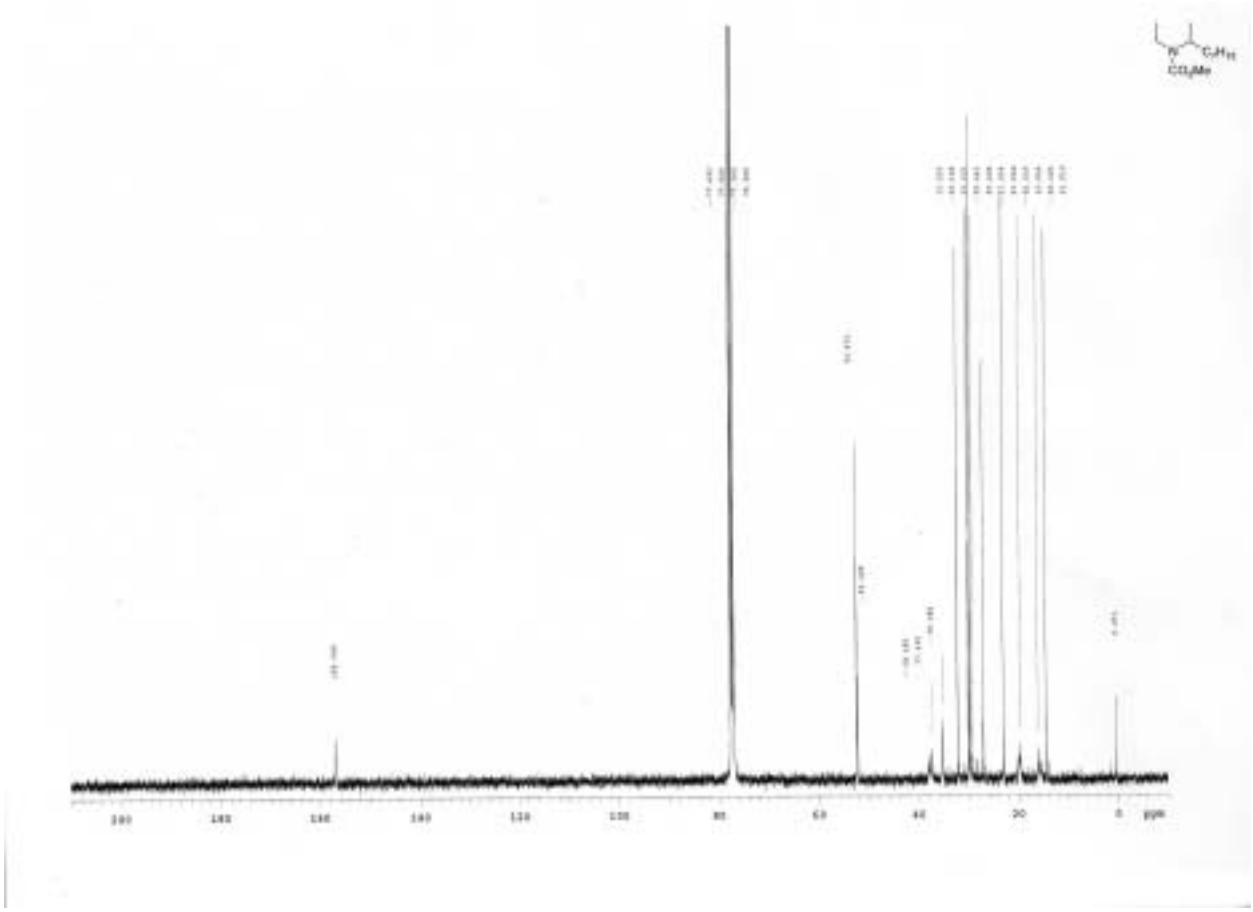
^{1}H NMR Spectrum of Methyl 2-Heptylpiperidinecarboxylate.



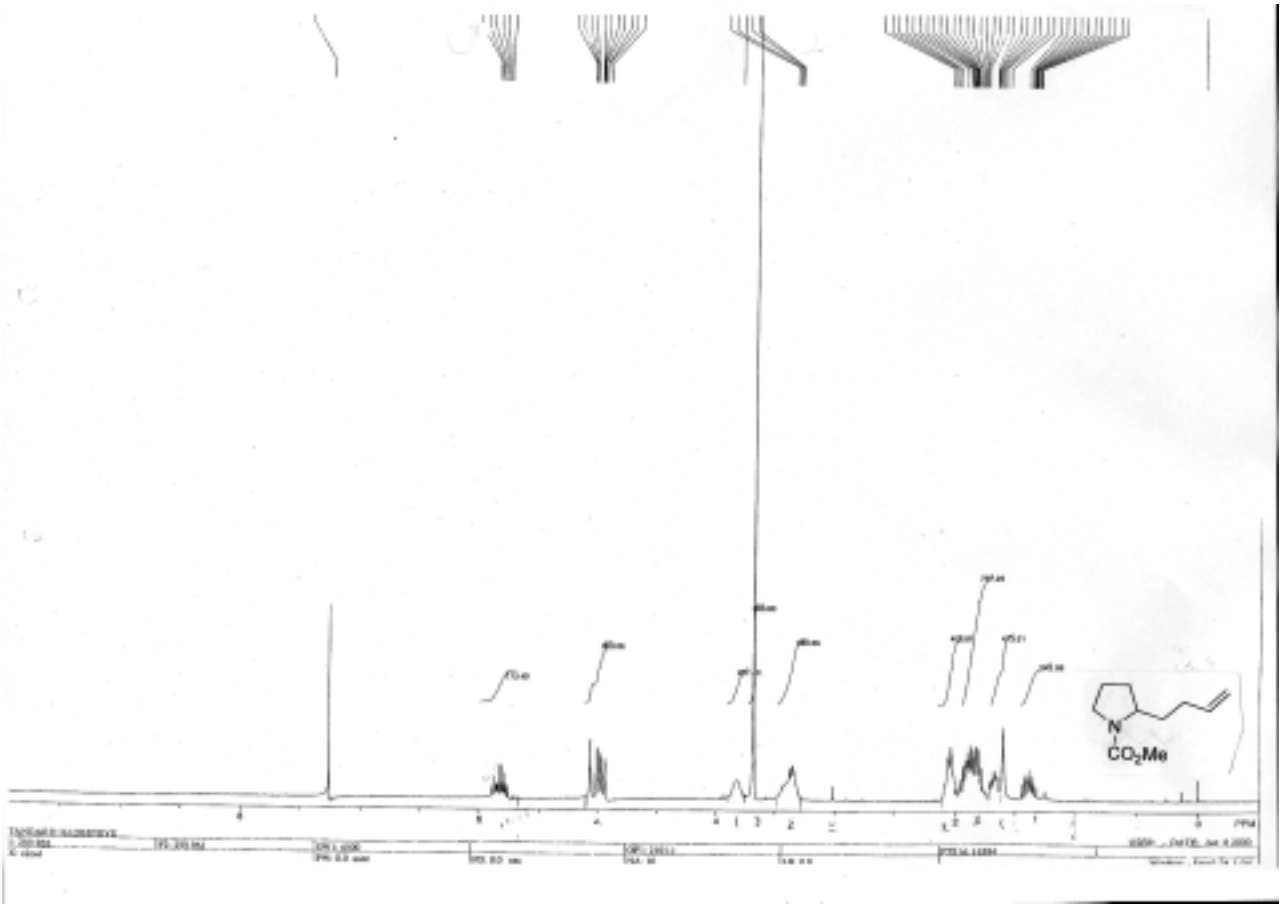
^{13}C NMR Spectrum of Methyl 2-Heptylpiperidinecarboxylate.



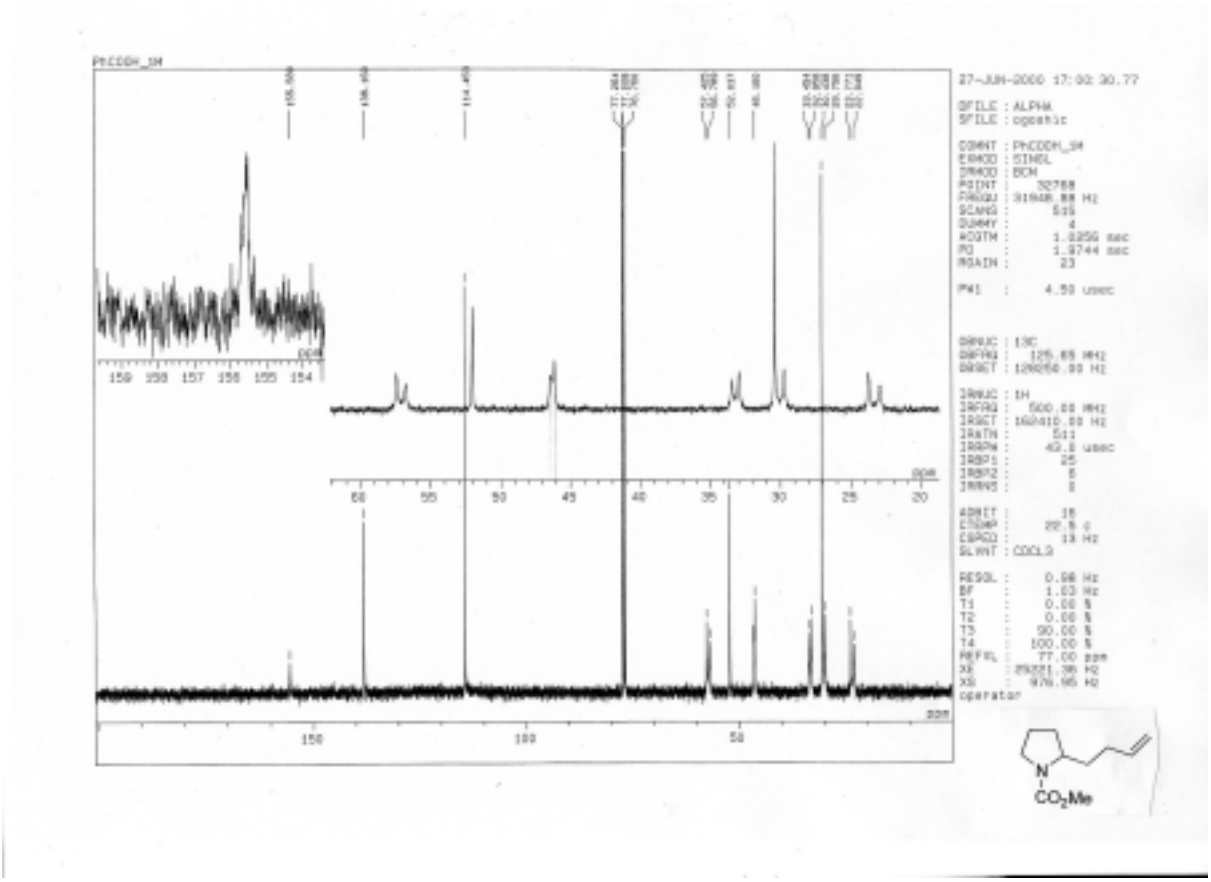
^{1}H NMR Spectrum of Methyl Ethyl(1-methyloctyl)aminecarboxylate.



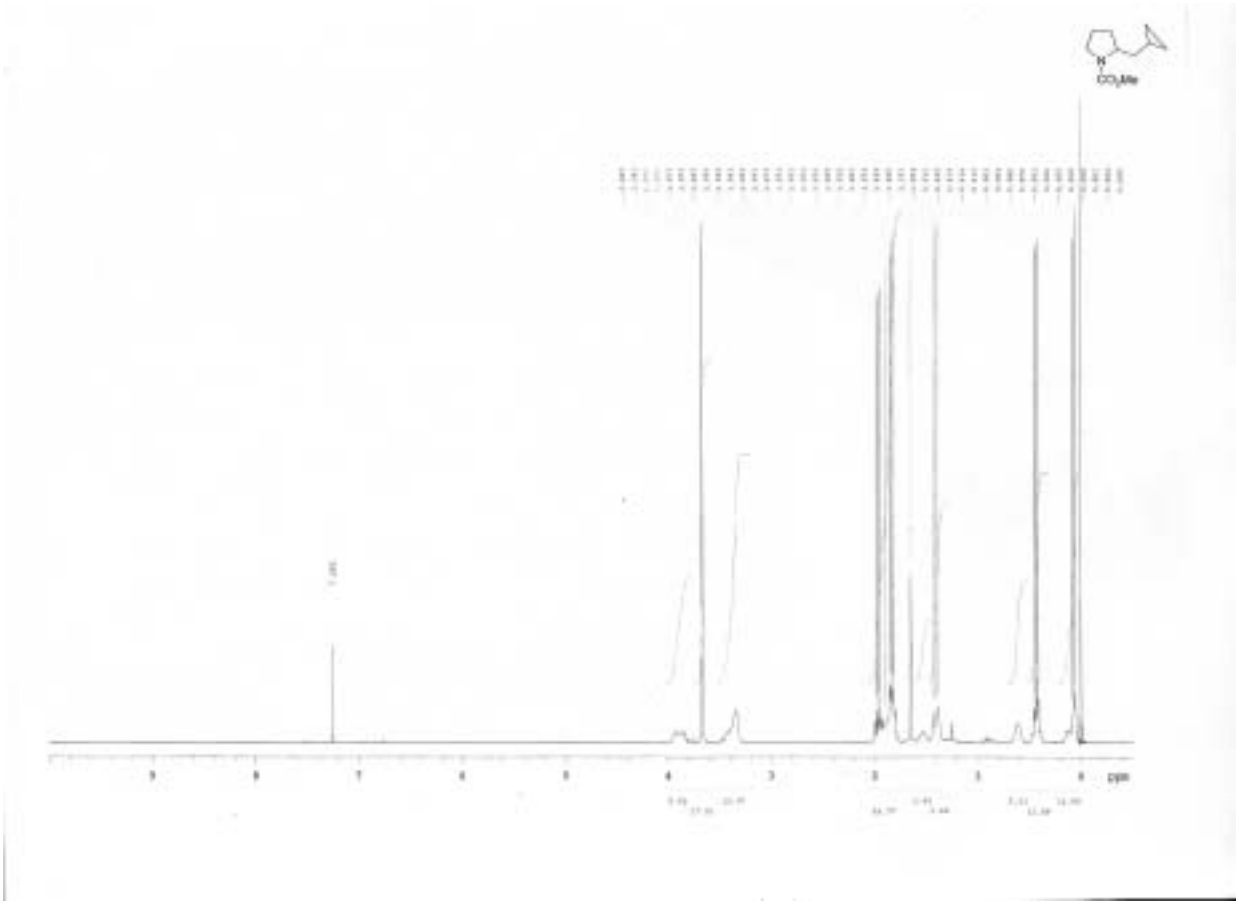
^{13}C NMR Spectrum of Methyl Ethyl(1-methyloctyl)aminecarboxylate.



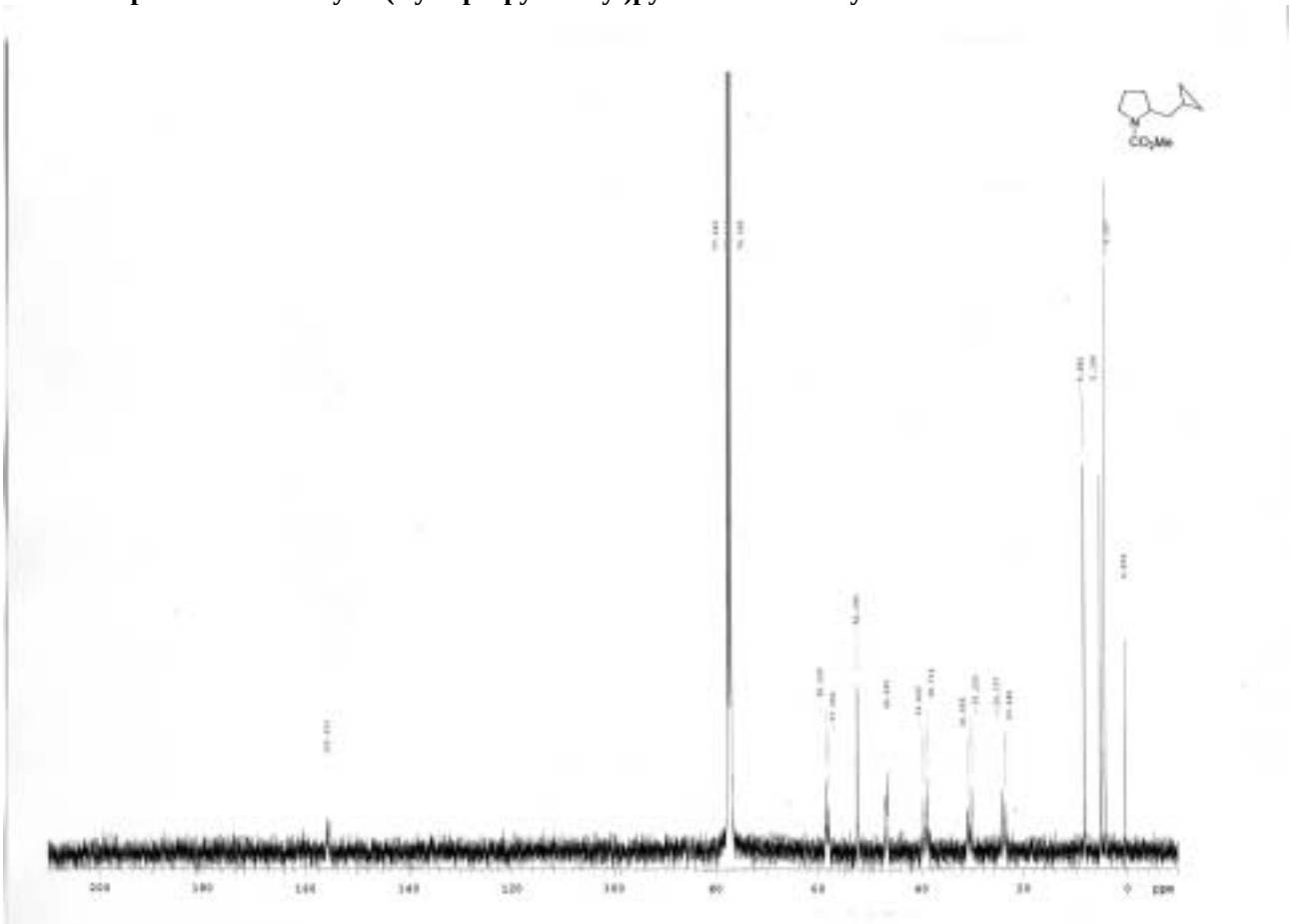
^{1}H NMR Spectrum of Methyl 2-(3-Butenyl)pyrrolidinecarboxylate



^{13}C NMR Spectrum of Methyl 2-(3-Butenyl)pyrrolidinecarboxylate.



^{1}H NMR Spectrum of Methyl 2-(Cyclopropylmethyl)pyrrolidinecarboxylate.



^{13}C NMR Spectrum of Methyl 2-(Cyclopropylmethyl)pyrrolidinecarboxylate