Experimental Section

General Methods

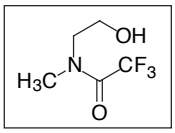
Proton (^1H) and carbon (^{13}C) nuclear magnetic resonance spectra were acquired on a Bruker AC-250 or a Varian VXR-400S spectrometer as indicated. Chemical shifts are reported in parts per million (δ scale) from residual proton resonance of the solvent. Data is reported as follows: chemical shift (multiplicity: s=singlet, bs=broad singlet, d=doublet, q=quartet, m=muliplet). Infrared spectra were acquired on a Perkin-Elmer 1600 Series FTIR. Mass spectra were acquired on a Hewlett Packard 5890 Series II GC, 5971A Mass Selective Detector utilizing electron impact ionization (70 eV). Combustion analyses were either performed by Galbraith Laboratories or Oneida Research Services. X-ray crystal structures were determined at Jackson State University.

Flash column chromatography was performed utilizing the method of Still with Merck silica gel 60, 200-400 mesh with the indicated solvent system. Thin-layer chromatography was conducted with E. Merck precoated silica gel plates F-254 (thickness 0.25 mm).

Melting points are uncorrected and were determined on a Buchi melting point apparatus. THF was distilled from potassium-benzophenone ketyl and diethyl ether from sodium-benzophenone ketyl. Benzene and dichloromethane were distilled from CaH_2 under argon. Methanol was distilled from magnesium. Anhydrous acetonitrile and dimethylformamide were purchased from Aldrich Chemical and used without further purification.

All compounds were obtained from Aldrich Chemical unless otherwise noted. All compounds were used as received unless otherwise noted. Organolithiums were titrated prior to use using the diphenylacetic acid method. All reaction vessels were either flame dried or oven dried (120°C for 12 h) to rigorously exclude moisture. All reactions were conducted under an argon atmosphere unless otherwise noted.

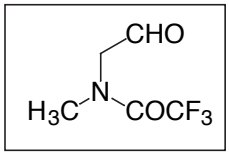
N-methyl-N-trifluoroacetyl ethanolamine



To a 200 mL round bottom flask containing a stirred solution of N-methyl ethanolamine (20.0 g, 266.7 mmol, Aldrich Chemical) in 50 mL of reagent grade chloroform at 25°C was added a solution of ethyl trifluoroacetate (38 mL, 320 mmol, Aldrich Chemical) in 50 mL of chloroform dropwise over a 5 h period during which time the solution takes on a yellow-orange color. After addition was complete, the solution was allowed to stir for an additional 5h at room temperature. The solution was concentrated under reduced pressure to give the crude amide as an orange oil. The oily residue was purified by flash column chromatography with hexane/ ethyl acetate (1:1) as eluent to give 42.8 g (94%) of the amide as a colorless oil which becomes pale yellow upon standing. TLC R_f=0.19 (hexane/ethyl acetate= 1:1); ^1H NMR (250 MHz, $CDCl_3$) δ3.76 (t, J=5.4 Hz, 2H, -C**H$_2$**-OH), 3.54 (t, J=5.4 Hz, 2H, -N-C**H$_2$**-), 3.47 (bs, 1H, -O**H)**, 3.17 (2 lines (mixture of rotational isomers) , 3H, -N-C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 157.4, 116.3 (q, J_{CF}=288 Hz), 59.8, 51.8, 35.9; IR (cm^{-1}, neat) 3447, 2652, 2891,

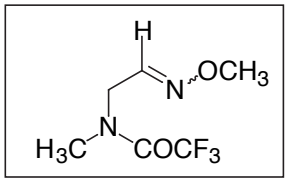
1688, 1424, 1244, 1149; MS (m/z): (M^+)171, 153, 140,128, 69. Anal. Calcd for $C_5H_8NO_2F_3$: C, 35.09; H; 4.71. Found: C, 35.06; H, 4.52.

N-trifluoroacetyl-N-methyl-2-aminoacetaldehyde.



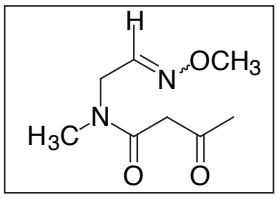
A 500 mL flask was fitted with a 50 mL pressure equalizing dropping funnel and an argon inlet. The flask was then charged with a suspension of PCC (9.43 g, 43.8 mmol), sodium acetate (3.54 g, 43.8 mmol) and 4A molecular sieves in 200 mL of dry dichloromethane. The dropping funnel was then charged with a solution of the protected aminoalcohol (5.0 g, 29.2 mmol) in 20 mL of dichloromethane and the solution added at such a rate so that the internal temperature did not rise above 30°C. The orange solution turned to a thick black suspension and was allowed to stir for 6 h (reaction was monitored by TLC) at ambient temperature. Celite (7 g) was added and the solution passed through a filter containing a 2 inch pad of silica and a 1 inch pad of celite and then the pad was washed with an additional 250 mL of dichloromethane. The solution was concentrated under reduced pressure in cold water to give a thick brown oil (caution! the aldehyde is somewhat volatile). The crude residue 3.71 g (75%) was used immediately without benefit of further purification. TLC R_f=0.24 (hexane/ethyl acetate=1:1); ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.75 (bs, 1H, -C**H**O), 4.28-4.25 (m, 2H, -N-C**H$_2$**-), 3.16 (s, 3H, -N-C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ196.4, 155.7, 115.9, 65.9, 24.5; IR(cm^{-1}, neat) 2957, 2847, 2726, 1736, 1699, 1424, 1258, 1200, 1148, 1103; MS (m/z): 169(M^+), 140, 69.

N-trifluoroacetyl-N-methyl-2-aminoacetaldehyde-O-methyloxime (2).



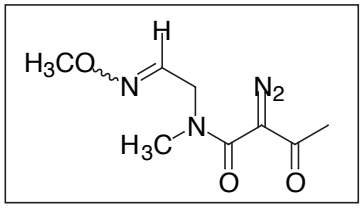
The protected amino aldehyde (3.0 g, 17.8 mmol) was dissolved in 10 mL of absolute methanol and sequentially treated with methoxyl-amine hydrochloride (2.37 g, 28.4 mmol) and pyridine (3.15 mL, 39.0 mmol). The solution was allowed to stir at room temperature for 6 h and the solvent was removed under reduced pressure to give a gummy residue. The residue was purified by flash column chromatography with hexane/ ethyl acetate (1:5 for a mixture of isomers or 1:1 to separate isomers) to give 3.05 g (87%) of the oximes as a 1.6-2.5:1 mixture of oxime isomers, both as pale yellow oils. **Z-isomer (major)**. TLC R_f=0.79 (hexane/ethyl acetate=1:5); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.19 (t, J=5.5 Hz, 1H, -C**H**=N); 4.13 (d, J=5.5 Hz, 2H, -N-C**H$_2$**-), 3.75 (s, 3H, -O-C**H$_3$**), 3.03 (s, 3H, -N-C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 145.1, 142.8, 118.4, 61.6, 48.3, 47.4; IR(cm-1, neat) 2946, 2825, 1757, 1699, 1420, 1251, 1193, 1099; MS (m/z): 198(M^+), 140, 84, 69; Anal. Calcd for $C_6H_9N_2O_2F_3$: C, 36.37; H, 4.58. Found: C, 36.53; H, 4.63. **E-isomer (minor)**. TLC R_f=0.88 (hexane/ ethyl acetate=1:5); ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.52 (t, J=4.6 Hz, 1H, -C**H**=N-), 4.18 (d, J=4.6 Hz, 2H, -N-C**H$_2$**-), 3.81 (s, 3H, -O-C**H$_3$**), 2.93 (s, 3H, -N-C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 145.3, 143.1, 113.8, 61.8, 50.3, 44.6; IR(cm^{-1}, neat) 2946, 2825, 1757, 1699, 1420, 1251, 1193, 1099; MS(m/z): 198(M^+), 140, 84, 69; Anal. Calcd for $C_6H_9N_2O_2F_3$: C, 36.37; H, 4.58. Found: C, 36.53; H, 4.63.

N-methyl-N-(2-acetaldehyde-O-methyloxime)-3-oxo-butanamide.



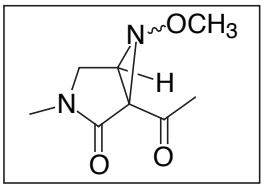
The protected oxime (mixture of isomers) (900 mg, 4.55 mmol) was treated with a solution of methanol (30 mL) saturated (0°C) with ammonia and allowed to stir overnight at ambient temperature. The clear solution gradually turned to a dark orange color. Volatiles were removed in vacuo at room temperature (caution ammonia odor) and the resulting dark yellow oil was taken up in dry dichloromethane (8 mL). A single drop of triethylamine was added followed by the addition of diketene (800 μL, 10 mmol). The solution was allowed to stir for 4 h and then poured into water. The layers were separated and the aqueous layer was extracted (3x 3 mL) with dichloromethane. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was subjected to silica gel chromatography with hexane/ ethyl acetate (1:5) as eluent to give the keto-amide as a yellow oil (769 mg, 91% for two steps). The two isomers are indistinguishable by TLC. Several additional resonances appear in the ^1H and ^{13}C NMR spectra due to the presence of amide rotamers and keto-enol tautomers. Only the principal signals are reported. TLC R_f=0.12 (hexane:ethylacetate/1:5) **Z-oxime (major)** ^1H NMR (250 MHz, $CDCl_3$) δ7.16 (t, J=5.7 Hz, 1H. -C**H**=N-), 3.98 (d, J=5.7 Hz, -N-C**H$_2$**-), 3.70 (s, 3H, -O-C**H$_3$**), 3.47 (bs, 2H, -CO-C**H$_2$**-CO-), 2.85 (s, 3H, -N-C**H$_3$**), 2.14 (s, 3H, -CO-C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 201.9, 166.9, 144.8, 61.7, 50.0, 46.1, 35.6, 30.1; **E-oxime (minor)** ^1H NMR (250 MHz, $CDCl_3$) δ 6.50 (t, J=4.5 Hz, 1H, -C**H**=N-). 4.11 (d, J=4.5 Hz, 2H, -N-C**H$_2$**-), 3.76 (s, 3H, -O-C**H$_3$**), 3.45 (bs, 2H, -CO-C**H$_2$**-CO-), 2.89 (s, 3H, N-C**H$_3$**), 1.83 (s, 3H, -CO-C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 201.7, 167, 147.3, 61.9, 29.8, 43.6, 36.7, 30.2; IR(cm^{-1}, neat) 3504, 2939, 1721, 1644, 1492, 1037; MS (m/z): 186(M^+), 155, 140, 113, 85, 71, 43. Anal. Calcd for $C_8H_{14}N_2O_3$: C, 51.60; H, 7.58. Found: C, 50.91; H, 7.52.

N-methyl-N-(2-acetaldehyde-O-methyloxime)-2-diazo-3-oxo-butanamide (3).



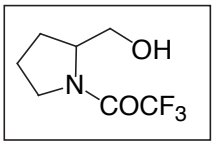
To a solution of 200 mg (1.08 mmol) of the keto-amide in 5 mL of anhydrous acetonitrile was added p-acetamidobenzenesulfonyl azide (308 mg, 1.24 mmol) in one portion. The solution was cooled to 0°C and DBU (192 μL, 1.29 mmol) was added dropwise over a 5 minute period. The bright yellow solution was allowed to stir for an additional 1h at 0°C at which time the solution was concentrated under reduced pressure to give a viscous black oil. The residue was taken up in a minimum amount of dichloromethane and placed on a silica gel column. The compound was eluted with hexane/ethyl acetate (1:5) to give the diazo oxime ethers (193 mg, 85%) as a bright yellow oil. TLC R_f=0.38 (hexane:ethylacetate /1:5) **Z-oxime (major)** ^1H NMR (250 MHz, $CDCl_3$) δ 7.26 (t, J=5.6 Hz, 1H, -C**H**=N-), 3.65 (s, 3H, -O-C**H$_3$**), 3.60 (d, J=5.6 Hz, 2H, -N-C**H$_2$**-), 2.39 (s, 3H, -N-C**H$_3$**), 1.88 (s, 3H, -CO-C**H$_3$**); ^{13}C NMR(62.5 MHz, $CDCl_3$) δ 172.9, 161.6, 147.4, 73.4, 61.9, 47.9, 35.8, 26.8; **E-oxime (minor)** ^1H NMR δ 6.53 (t, J=3.8 Hz, 1H, -C**H**=N-), 3.94 (d, J=3.8 Hz, 2H, -N-C**H$_2$**-), 3.69 (s, 3H, -O-C**H$_3$**), 2.33 (s, 3H, -N-C**H$_3$**), 1.84 (s, 3H, -CO-C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 168, 161.5, 145.1, 69.5, 61.6, 45.3, 35.1, 26.7; IR (cm^{-1}, neat) 2938, 2115, 1703, 1646, 1590, 1531, 1488, 1367, 1165.

cis-2-methyl-3-keto-4-acetyl-6-methoxy-2,6-diazabicyclo[3.1.0]hexane (4).



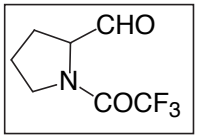
To a stirred solution of the diazoamide (180 mg, 0.85 mmol) in 3 mL of dichloromethane was added dirhodium tetraacetate (1.1 mg, 0.025 mmol) in one portion. The solution was allowed to stir at 25°C until complete consumption of the starting material was observed by TLC (3.5h). The solution was filtered through a small plug of alumina and then concentrated under reduced pressure. The residue was purified by silica gel chromatography with hexane/ ethyl acetate (1:1) as eluent to give 156 mg (86%) of the aziridines (colorless oil) as a separable 2.5 :1 mixture of oxime invertomers. **Major** TLC R_f=0.11; ^{1}H NMR (250 MHz, C_6D_6) δ 3.41 (s, 3H, -OC**H$_3$**), 2.92 (d, J=4.75 Hz, 1H, -N-C**H**H-), 2.76 (d, J=11.7Hz, 1H, -N-C**H**H-), 2.48 (s, 3H, -N-C**H$_3$**), 2.38 (dd, J=4.75 Hz 11.7Hz, 1H, -CH_2-C**H**-N-), 2.34 (s, 3H, -COC**H$_3$**); ^{13}C NMR (62.5 MHz, C_6D_6) δ 198.5, 164.5, 60.5, 48.7, 44.0, 30.2, 28.7, 28.3; IR (cm^{-1}, neat) 2928, 1718, 1687, 1493, 1369, 1316, 1281; MS (m/z): 184(M^+), 153, 142, 125, 111, 97, 83. Anal. Calcd for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.57. Found: C, 51.98; H, 6.23. **Minor** TLC R_f=0.16; ^{1}H NMR (250 MHz, C_6D_6) δ 3.47 (s, 3H, -OC**H$_3$**), 2.84 (d, J=4.2 Hz, 1H, -N-C**H**H-), 2.62 (d, J=10.8Hz, 1H, -N-C**H**H-), 2.53 (s, 3H, -N-C**H$_3$**), 2.15 (dd, J=4.2 Hz 10.8Hz, 1H, -CH_2-C**H**-N-), 2.31 (s, 3H, -COC**H$_3$**); ^{13}C NMR (62.5 MHz, C_6D_6) δ 194.4, 164.8, 60.6, 48.2, 43.1, 30.3, 28.8, 28.3; IR (cm^{-1}, neat) 2928, 1718, 1687, 1493, 1369, 1316, 1281; MS (m/z): 184(M^+), 153, 142, 125, 111, 97, 83. Anal. Calcd for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.57. Found: C, 51.74; H, 6.53.

N-trifluoroacetyl prolinemethanol (5a).



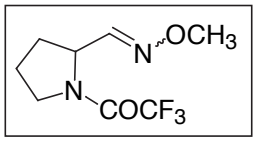
To a 100 mL round bottom flask containing a stirred solution of pyrrolidine-2-methanol (2.0 g, 19.8 mmol) in 25 mL of reagent grade chloroform at 25°C was added a solution of ethyl trifluoracetate (2.81 g , 19.8 mmol, Aldrich Chemical) in 25 mL of chloroform dropwise over a 3 h period and the solution takes on an orange color. After addition was complete, the solution was allowed to stir overnight for an additional 10 h at room temperature. The solution was concentrated under reduced pressure to give the crude amide as an orange oil. The oily residue was purified by flash column chromatography with hexane/ethyl acetate (1:10) as eluent to give 4.0 g (95%) of the amide as a colorless oil . TLC R_f=0.53 (hexane/ethyl acetate=1:10); ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.69 (dd, J=2.5, 11.2 Hz, 1H, -C**H**HOH), 3.57 (bs, 1H, -CH_2O**H**), 3.49 (dd, J=11.2, 18.5 Hz, 1H, -CH**H**OH), 3.47 (bs, 1H, NC**H**CH_2OH), 2.18 (broad, 2H, -C**H$_2$**N), 2.0-1.4 (m, 4H, -C**H$_2$**C**H$_2$**-); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 161.8, 116.2 (q, J_{CF}=293 Hz), 61.3, 60.4, 45.1, 25.7, 23.6; IR (cm^{-1}, neat) 3377, 2992, 1672, 1429, 1201, 1135; MS(m/z): 197(M^+), 166, 128, 96, 69; Anal. Calcd for $C_7H_{10}NO_2F_3$-H_2O: C, 39.07; H, 5.62. Found: C, 39.01; H, 5.63.

N-trifluoroacetyl pyrrolidine-2-carboxaldehyde.



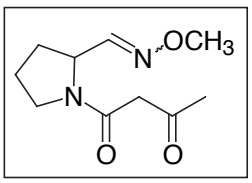
A 100 mL round bottom flask was fitted with a septum and an argon inlet. The flask was then charged with a suspension of PCC (0.82 g, 3.87 mmol), sodium acetate (0.31 g, 3.87 mmol) and 4A molecular sieves (1.6 g) in 200 mL of dry dichloromethane and then cooled to 0°C. A solution of the protected amino-alcohol (0.50 g, 2.53 mmol) in 5 mL of dichloromethane was added via cannula over a 5 min period. The orange solution turned to a thick black suspension and was allowed to stir for 8 h (reaction was monitored by TLC) at ambient temperature. Celite (7 g) was added and the solution passed through a filter containing a 1 inch pad of celite and was then followed by an additional 200 mL of diethyl ether. The solution was concentrated under reduced pressure to one-half volume and then an equal volume of toluene was added and the solution allowed to stir for ten min. Filtration of this solution through a 1 inch pad of silica gel followed by extensive washing (5X 25 mL) of the filter cake with a 1:1 ether/toluene solution gives a dark orange solution which was concentrated under reduced pressure to give a dark oil. The unstable aldehyde was used immediately without the benefit of further purification. IR(cm^{-1}, neat) 2958, 2900, 2828, 1734, 1685, 1456, 1234, 1146; MS (m/z): 195(M^+), 166, 96, 69.

N-trifluoroacetyl pyrrolidine-2-carboxaldehyde-O-methyloxime (6a).



The protected amino aldehyde (0.45 g, 2.3 mmol) was dissolved in 3 mL of absolute methanol and sequentially treated with methoxyl-amine hydrochloride (0.31 g, 3.69 mmol) and pyridine (0.26 mL, 5.07 mmol). The solution was allowed to stir at room temperature for 10 h and the solvent was removed under reduced pressure to give a gummy residue. The residue was purified by flash column chromatography with hexane/ethyl acetate (1:1) to give a mixture of isomers (455mg, 88%) as a colorless oil. **Z-isomer (major)**. TLC R_f=0.21 (hexane/ ethyl acetate=1:5); ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.37 (d, J=4.5 Hz, 1H, -C**H**=N); 5.0 (m, 1H, -N-C**H**=N-), 3.81 (s, 3H, -O-C**H_3**), 3.76-3.58 (m, 2H, -N-C**H_2**), 2.37-1.71 (m, 4H, -C**H_2**C**H_2**-); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 150.1, 146.5, 115.8 (q, J_{CF}=287 Hz), 61.2, 57.2, 46.5, 27.4, 24.1. **E-isomer (minor)**. TLC R_f=0.23 (hexane/ ethyl acetate=1:5); ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.59 (d, J=5.0 Hz, 1H, -C**H**=N); 4.75 (m, 1H, -N-C**H**=N-), 3.89 (s, 3H, -O-C**H_3**), 3.76-3.58 (m, 2H, -N-C**H_2**), 2.32-1.71 (m, 4H, -C**H_2**C**H_2**-); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 155.5, 147.1, 106.5 (q, J_{CF}=317 Hz), 61.7, 54.8, 47.6, 28.3, 25.0; IR(cm^{-1}, neat) 2955, 2896, 1684, 1448, 1237, 1197, 1046; MS (m/z): 224(M^+), 166, 69. Anal. Calcd For: $C_8H_{11}N_2O_2F_3$: C, 42.86; H, 4.95. Found: C, 43.07; H, 4.96.

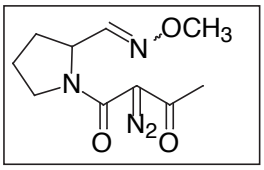
N-(1,3-dioxobutyl)-pyrrolidine-2-carboxaldehyde-O-methyloxime.



The trifluoroacetamide protected oxime (mixture of isomers) (220 mg, 0.089 mmol) was treated with a solution of methanol (10 mL) saturated (0°C for 15 min.) with ammonia and allowed to stir overnight at ambient temperature. The clear solution gradually turned to a black color. Volatiles were removed in vacuo at room temperature (caution ammonia odor) and the resulting dark oil was taken up in dry dichloromethane (3 mL), TLC R_f=0.05 (free amine). A single drop of triethylamine was added followed by the addition of diketene (151 μL, 1.96 mmol). The solution was allowed to stir for 6 h and then poured into water. The

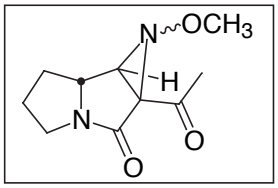
layers were separated and the aqueous layer was extracted (3x 3 mL) with dichloromethane. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The residue was subjected to silica gel chromatography with hexane/ ethyl acetate (1:5) as eluent to give the keto-amide as a yellow oil (196 mg, 94% for two steps). TLC R_f=0.27, The two isomers are indistinguishable by TLC. Several additional resonances appear in the ^1H and ^{13}C NMR spectra due to the presence of amide rotamers and keto-enol tautomers. Only the principal signals are reported. **Z-isomer (major)** ^1H NMR (250 MHz, $CDCl_3$) δ 7.39 (d, J=4.3 Hz, 1H, -C**H**=N); 4.75 (bs, 1H, -N-C**H**=N-), 3.82 (s, 3H, -O-C**H$_3$**), 3.34 (s, 2H, C(O)C**H$_2$**C(O)), 2.1-1.9 (m, 2H, -N-C**H$_2$**), 2.24 (s, 3H, C(O)C**H$_3$**), 1.4-1.2 (m, 4H, -C**H$_2$**C**H$_2$**-); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 201.9, 167.9, 130.8, 68.1, 50.1, 38.7,32.2, 30.3, 22.9, 10.9; **E-isomer (minor)**.^1H NMR (250 MHz, $CDCl_3$) δ 6.58 (d, J=5.4 Hz, 1H, -C**H**=N); 5.0 (bs, 1H, -N-C**H**=N-), 3.89 (s, 3H, -O-C**H$_3$**), 3.42 (s, 2H, C(O)C**H$_2$**C(O)), 2.1-1.9 (m, 2H, -N-C**H$_2$**), 1.89 (s, 3H, C(O)C**H$_3$**), 1.4-1.2 (m, 4H, -C**H$_2$**C**H$_2$**-); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 201.7, 167.8, 128.8, 61.8, 49.8, 39.8,30.9, 30.1, 23.7, 14.0; IR(cm^{-1}, neat) 3475, 2938, 2876, 1714, 1634, 1435; MS(m/z): 212(M^+), 181, 154, 43.

N-(1,3-dioxo-2-diazo-butyl)-pyrrolidine-2-carboxaldehyde-O-methyloxime (7a).



To a solution of 120 mg (0.57 mmol) of the keto-amide in 3 mL of anhydrous acetonitrile was added p-acetamidobenzenesulfonyl azide (163 mg, 0.68 mmol) in one portion. The solution was cooled to 0°C and DBU (101 μL, 0.68 mmol) was added dropwise over a 5 min period. The bright yellow solution was allowed to stir for an additional 1h at 0°C and then at room temperature for one 1h at which time the solution was concentrated under reduced pressure to give a viscous black oil. The residue was taken up in a minimum amount of dichloromethane and placed on a silica gel column. The compound was eluted with hexane/ ethyl acetate (1:5) to give the diazo-oxime ethers (124 mg, 92%) as a bright yellow oil. The isomers are indistinguishable by TLC. TLC R_f=0.41 (hexane :ethyl acetate/ 1:5), **Z-isomer (major)** ^1H NMR (250 MHz, C_6D_6) δ 7.28 (d, J=4.4 Hz, 1H, -C**H**=N); 4.41 (m, 1H, -N-C**H**=N-), 3.64 (s, 3H, -O-C**H$_3$**), 3.0-2.8 (m, 2H, -N-C**H$_2$**), 2.30 (s, 3H, C(O)C**H$_3$**), 1.6-1.0 (m, 4H, -C**H$_2$**C**H$_2$**-); ^{13}C NMR (62.5 MHz, C_6D_6) δ ; **E-isomer (minor)**.^1H NMR (250 MHz, C_6D_6) δ6.22 (d, J=5.4 Hz, 1H, -C**H**=N); 5.0 (m, 1H, -N-C**H**=N-), 3.70 (s, 3H, -O-C**H$_3$**), 3.0-2.8 (m, 2H, -N-C**H$_2$**), 2.35 (s, 3H, C(O)C**H$_3$**), 1.6-1.0 (m, 4H, -C**H$_2$**C**H$_2$**-); IR(cm^{-1}, neat) 2950, 2109, 1702, 1658; Anal. Calcd for $C_{10}H_{14}N_4O_3$: C, 50.41; H, 5.92. Found: C, 50.93; H, 6.14.

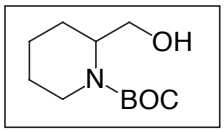
5a-Acetyl-1-methoxy-hexahydro-1,4a-diaza-cyclopropa[a]pentalen-5-one (8).



A solution of 95 mg (0.39 mmol) of the diazoamide in 2 mL of anhydrous chloroform was heated to reflux temperature under an argon atmosphere. The reaction was monitered by TLC and was shown to be complete after 12 h. The pale yellow solution was concentrated under reduced pressure and the resulting residue was taken up in a minimum amount of dichloromethane and placed on a silica gel column.

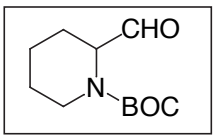
The compound was eluted with hexane / ethyl acetate (1:5) to give the aziridines (63 mg, 75%) as a separable 3:1 mixture of oxime invertomers. **Major** TLC R_f=0.20 (hexane/ethyl acetate : 1/1); ^{1}H NMR (250 MHz, C_6D_6) δ 3.87 (dd, J=3.2Hz, 11.1Hz, 1H, -CH_2-C**H**-CH-), 3.41 (s, 3H, -OC**H$_3$**), 3.0 (s (apparent), 1H, -CH-C**H**-$NOCH_3$), 2.74 (s, 3H, -COC**H$_3$**), 2.3 (m, 2H, -CH_2-C**H$_2$**-N-), 2.1-0.8 (m, 4H, -C**H$_2$**-C**H$_2$**-CH-) ;^{13}C NMR (62.5 MHz, C_6D_6) δ 195.5, 162.4, 60.6, 56.4, 56.1, 47.8, 39.3, 27.5, 24.1, 23.3; IR (cm^{-1}, neat) 2945, 2859, 1712, 1690, 1436, 1364, 1285, 1037; MS (m/z): 210(M^+), 179, 167, 151; Anal. Calcd for $C_{10}H_{14}N_2O_3$: C, 57.13; H, 6.71. Found: C, 57.32; H,6.53. **Minor** TLC R_f=0.14 (hexane/ethyl acetate : 1/1); ^{1}H NMR (250 MHz, C_6D_6) δ 3.85 (dd, J=3.3Hz, 11.2Hz, 1H, -CH_2-C**H**-CH-), 3.51 (s, 3H, -OC**H$_3$**), 2.8 (s (apparent), 1H, -CH-C**H**-$NOCH_3$), 2.75 (s, 3H, -COC**H$_3$**), 2.4 (m, 2H, -CH_2-C**H$_2$**-N-), 2.1-0.8 (m, 4H, -C**H$_2$**-C**H$_2$**-CH-) ;^{13}C NMR (62.5 MHz, C_6D6) δ 195.7, 161.7, 60.5, 56.4, 56.1, 47.7, 39.2, 27.5, 24.1, 23.4; IR (cm^{-1}, neat) 2945, 2859, 1712, 1690, 1436, 1364, 1285, 1037; MS (m/z): 210(M^+), 179, 167, 151; Anal. Calcd for $C_{10}H_{14}N_2O_3$: C, 57.13; H, 6.71. Found: C, 57.21; H, 6.63.

N-tert-butyloxycarbonyl-piperidine-2-methanol (5b).



2-piperidine-methanol (2.0 g, 17.4 mmol, Aldrich Chemical) was dissolved in anhydrous acetonitrile (20 mL). The light yellow solution was then treated with BOC-pyrocarbonate (4.17 g, 19.1 mmol) and allowed to stir for 24 h at room temperature. Upon completion, the yellow solution in concentrated under reduced pressure to give a thick orange residue. Purification by column chromatography (1:5 / hexane/ethyl acetate) gave the BOC alcohol (3.7 g, 99%) an a colorless oil that crystallizes upon standing to give colorless cubes. TLC R_f=0.34 (hexane: ethyl acetate /1:5); ^{1}H NMR (250MHz, $CDCl_3$) δ 4.16 (m, 1H, -C**H**-CH_2OH), 3.83 (app. d, J=14.2Hz, 1H, -CH_2O**H**), 3.66 (dd, J=8.5, 11 Hz, 1H, -CH**H**OH), 3.50 (dd, J=11, 6.5 Hz, 1H, -C**H**HOH), 2.81-2.65 (m, 2H, -C**H$_2$**N-), 1.67-1.39 (m, 6H, -(C**H$_2$**)**$_3$**-), 1.44(s, 9H, CO_2C(C**H$_3$**)**$_3$**); ^{13}C NMR (62.5MHz, $CDCl_3$) δ 155.3, 78.9, 59.9, 53.0, 51.6, 39.4, 27.9, 24.8, 24.3, 18.8; IR (cm^{-1}, thin film) 3450, 2924, 1741, 1681, 1412, 1373, 1285; MS (m/z): 315(M^+), 184, 128, 84, 57. Anal. Calcd for $C_{11}H_{21}NO_3$: C, 61.37; H, 9.83. Found: C, 61.27; H, 9.20.

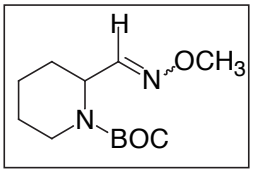
N-tert-butyloxycarbonyl-piperidine-2-carboxaldehyde.



Oxalyl chloride (1.82 mL, 20.9 mmol) was added to a 100 mL round bottom flask containing 15mL of dry dichloromethane. The solution was cooled to -78° C (dry ice/acetone) and dimethyl sulfoxide (4.94 mL, 69.7 mmol) was added dropwise with a syringe, (Caution! evolution of gas). The cold solution was allowed to stir for 5 min at -78°C at which time a solution of BOC-piperidine-methanol (3.0 g, 13.9 mmol) in 5 mL of dichloromethane was cautiously added via cannula (5 min. addition time). The solution was maintained at -78°C for an additional 25 min and then triethylamine (19.4 mL, 139 mmol) was added via syringe to produce a bright yellow solution. The solution was stirred for an additional 5 min and then warmed to 0°C for 20 min. At that time, the reaction mixture was poured into saturated ammonium chloride (20 mL) and stirred for 30 min. The layers were separated and the aqueous phase extracted (3X 10 mL) with dichloromethane. The combined organic phases were

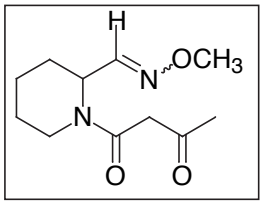
washed ($NaHCO_{3(sat)}$ and brine), dried (Na_2SO_4), and concentrated to give a yellow residue. Purification by column chromatography using (Hex : Ea/ 1 :5) gave the aldehyde (2.82g, 95%) as a colorless oil. TLC R_f=0.37 (hexane: ethyl acetate /1:5); ^{13}C NMR (62.5MHz, $CDCl_3$) δ 200.9, 155.5, 80.1, 60.9, 60.5, 28.1, 24.5, 23.4, 20.7; IR (cm^{-1}, thin film) 2936, 2862, 1734, 1696, 1405, 1251, 1164; MS (m/z): 213(M^+), 184, 128, 84, 57; Anal. Calcd for $C_{11}H_{19}NO_3$: C, 61.95; H,8.98. Found: C, 61.55; H, 8.66.

N-tert-butyloxycarbonyl-piperidine-2-carboxaldehyde-O-methyloxime 6b.



The BOC-protected amino aldehyde (220 mg, 1.03 mmol) was dissolved in 3 mL of absolute methanol and sequentially treated with methoxyl-amine hydrochloride (138 mg, 1.65 mmol) and pyridine (119μL, 2.27 mmol). The solution was allowed to stir at room temperature for 12 h and the solvent was removed under reduced pressure to give a gummy residue. The residue was purified by flash column chromatography with hexane/ ethyl acetate (1:5) to give 219 mg (88%) of the oximes as a 3-5:1 mixture of oxime isomers, both as colorless oils. TLC R_f=0.74 (hexane: ethyl acetate /1:10); **Major** ^1H NMR (250 MHz, $CDCl_3$) δ 7.22 (d, J=3.6Hz, 1H, -C**H**=N-), 4.79 (m, 1H, -NC**H**CH=N-), 3.77 (s, 3H, -OC**H_3**), 3.91 (bd, J=13.1 Hz, 1H, -CH**H**N-), 2.7 (dt, J=2.2, 13.1 Hz, 1H, -C**H**HN-), 1.9-1.3 (m, 6H, -(C**H_2**)**$_3$**-), 1.39 (s, 9H, -O(C**H_3**)**$_3$**) ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 155.1, 150.1, 79.7, 61.9, 50.3, 48.1, 28.3, 27.4, 25.1, 19.7; **Minor** ; ^1H NMR (250 MHz, $CDCl_3$) δ 6.68 (d, J=5.6 Hz, 1H, -C**H**=N-), 5.2 (m, 1H, -NC**H**CH=N-), 3.81 (s, 3H, -OC**H_3**), 3.91 -2.7 (obscured, 2H, -C**HH**N-), 1.9-1.3 (m, 6H, -(C**H_2**)**$_3$**-), 1.38 (s, 9H, -O(C**H_3**)**$_3$**) ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 155.4 148.7, 79.8, 61.6, 49.7, 47.8, 28.1, 26.8, 20.8, 19.1; IR (cm^{-1}, neat) 2936, 2855, 1689, 1463, 1398, 1162; MS (m/z): 242(M^+), 186, 169, 128, 111, 94, 86, 57. Anal. Calcd For $C_{12}H_{22}N_2O_3$: C, 59.48; H, 9.15. Found: C, 58.99; H, 8.69.

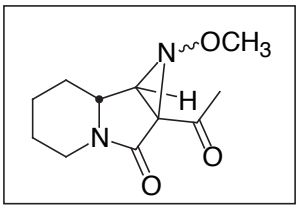
N-(1,3-dioxobutyl)-piperidine-2-carboxaldehyde-O-methyloxime.



A 50 mL round bottom flask was charged with a solution of the protected oxime (300 mg, 1.24 mmol) in 15 mL of dry dichloromethane and fitted with a vented septum. Trifluoroacetic acid (2.4 mL, 31.0 mmol) was added in one portion to the solution. The solution takes on a deep red orange color after 5 min of stirring. At that time the reaction was monitored every 2-3 min by TLC until the reaction was judged to be complete. When the reaction was judged complete, solid sodium bicarbonate (5.2 g, 62 mmol) was cautiously added in portions to the mixture over a 5 min period. Upon completion of the addition , the light yellow mixture was allowed to stir for 20 min at room temperature. The flask was then flushed with argon and diketene was added (96 μL, 2.72 mmol) and the solution was allowed to stir overnight. The reaction mixture was then cast into saturated ammonium chloride and allowed to stir for 10 min. The layers were separated and the aqueous layer extracted (3X 10mL) with dichloromethane. The combined organic layers were washed (water, brine), dried (Na_2SO_4), and concentrated to give an orange oil. Purification by column chromatography (hexane/ethyl acetate=1:1) gave the ketoamide (258mg, 92% for two steps) as a pale yellow oil. TLC R_f=0.31 (ethyl acetate:hexane / 1:5); **Major** ^1H NMR (250 MHz, $CDCl_3$) δ 7.22 (d,

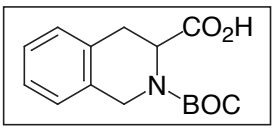
J=4.0Hz, 1H, -C**H**=N-), 5.32 (bs, 1H, -NC**H**CH=N-), 3.72 (s, 3H, -OC**H$_3$**), 3.44 (s, 2H, C(O)C**H$_2$**C(O)Me), 2.16 (s, 3H, -C(O)C**H$_3$**), 1.8-1.2 (m, 8H, -(C**H$_2$**)$_4$-); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 202.1, 165.7, 147.8, 86.4, 61.6, 50.3, 47.9, 43.5, 26.2, 25.5, 19.5; **Minor** ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.65 (d, J=5.8Hz, 1H, -C**H**=N-), 4.4 (bs, 1H, -NC**H**CH=N-), 3.79 (s, 3H, -OC**H$_3$**), 3.43 (s, 2H, C(O)C**H$_2$**C(O)Me), 2.14 (s, 3H, -C(O)C**H$_3$**), 1.8-1.2 (m, 8H, -(C**H$_2$**)$_4$-); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 204.4, 165.8, 147.2, 86.5, 61.8, 52.9, 49.5, 38.4, 27.9, 26.2, 19.6; IR(cm^{-1}, neat) 3477, 2940, 2866, 1714, 1629, 1436, 1351; MS (m/z): 226(M^+), 195, 136, 111, 89.

6a-Acetyl-1-methoxy-octahydro-1,5a-diaza-cyclopropa[a]inden-6-one (10).



To a solution of 340 mg (1.50 mmol) of the keto-amide in 10 mL of anhydrous acetonitrile was added p-acetamidobenzenesulfonyl azide (433 mg, 1.80 mmol) in one portion. The solution was cooled to 0°C and DBU (269 mL, 1.80 mmol) was added dropwise over a 5 min period. The bright yellow solution was allowed to stir for an additional h at 0°C at which time the solution was concentrated under reduced pressure to give a viscous black oil. The residue was taken up in a minimum amount of dichloromethane and placed on a silica gel column. The compound was eluted with hexane/ ethyl acetate (1:5) to give the aziridines (296 mg, 88%) as a separable 3.2:1 mixture of oxime invertomers. **Major** TLC R_f=0.22 (hexane/ethyl acetate : 1/1); ^{1}H NMR (250 MHz, C_6D_6) δ 3.94 (dd, J=4.3Hz, 11.3Hz, 1H, -CH_2-C**H**-CH-), 3.33 (s, 3H, -OC**H$_3$**), 3.19 (s (apparent), 1H, -CH-C**H**-$NOCH_3$) , 2.78 (s, 3H, -COC**H$_3$**), 2.0 (dt, J=3.5Hz, 10.3Hz, 2H, -CH_2-C**H$_2$**-N-), 1.9-0.6 (m, 6H, -C**H$_2$**-C**H$_2$**-C**H$_2$**-CH-) ;^{13}C NMR (62.5 MHz, C_6D_6) δ 194.4, 163.5, 60.3, 57.9, 56.7, 48.9, 39.2, 30.0, 28.8, 24.7, 23.1; IR (cm^{-1}, neat) 2940, 2859, 1709, 1690, 1431, 1364, 1284, 1043; MS (m/z): 224(M^+), 193, 181, 165, 151, 123; Anal. Calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19. Found: C, 58.73; H, 7.45. **Minor** TLC R_f=0.16 (hexane/ethyl acetate : 1/1); ^{1}H NMR (250 MHz, C_6D_6) δ 3.99 (dd, J=2.5Hz, 10Hz, 1H, -CH_2-C**H**-CH-), 3.42 (s, 3H, -OC**H$_3$**), 2.89 (s (apparent), 1H, -CH-C**H**-$NOCH_3$) , 2.5 (s, 3H, -COC**H$_3$**), 2.21 (dt, J=3.4Hz, 11.1Hz, 2H, -CH_2-C**H$_2$**-N-), 1.4-0.6 (m, 6H, -C**H$_2$**-C**H$_2$**-C**H$_2$**-CH-) ;^{13}C NMR (62.5 MHz, C_6D_6) δ 198.7, 161.3, 54.9, 53.4, 51.9, 49.9, 39.1, 29.5, 28.6, 25.1, 23.7; IR (cm^{-1}, neat) 2940, 2859, 1709, 1690, 1431, 1364, 1284, 1043; MS (m/z): 224(M^+), 193, 181, 165, 151, 123. ; Anal. Calcd for $C_{11}H_{16}N_2O_3$: C, 58.91; H, 7.19. Found: C, 58.58; H, 7.40

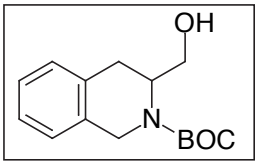
N-tert-butyloxycarbonyl-1,2,3,4-tetrahydroisoquinoline-2-carboxylicacid.



A 250 mL round bottom flask was charged with sodium hydroxide (1.0 g, 25.7 mmol) and 50 mL of distilled water. The flask was fitted with a septum and an exit line leading to a mineral oil bubbler. 1,2,3,4-tetrahydroisoquinoline-2-carboxylic acid hydrochloride (2.5 g, 12.15 mmol, Aldrich Chemical) was added in one portion and partially dissolves to give a cloudy solution. At that time, tert-butanol (35 mL) was added to give a homogenous solution. Once the solution became clear, BOC-anhydride (2.55g, 12.15 mmol) was added dropwise via syringe. The solution slightly warmed and was allowed to stir at room temperature for an additional twelve h. The

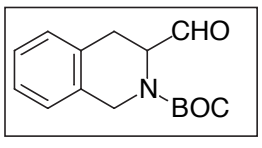
reaction mixture was then taken up in a separatory funnel and extracted (3x10 mL) with petroleum ether. The petroleum ether extracts were then washed (3x10 mL) with a saturated solution of sodium bicarbonate and the washings combined with the previous aqueous layer. Solid potassium bisulfate was added (caution! evolution of gas) until the solution had reached pH 1. The aqueous layers were extracted (5x 20 mL with diethyl ether) and the ether extractions were washed with brine (50 mL) and dried ($MgSO_4$). Evaporation of the solvent gives the crude acid which can be recrystallised form ethyl acetate/ hexane to give the acid (3.2 g, 99%) as a white solid. TLC R_f=0.08 (1 : 10 /Hexane : Ethyl Acetate). The presence of two distinct rotational isomers results in double ^1H and ^{13}C NMR spectra. Where possible both rotamers are reported. ^1H NMR (250 MHz, $CDCl_3$) δ 10.78 (bs, 1H, -CO_2**H**), 7.2-7.1 (m, 4H, -C=C**H**), 5.15-4.72 (m, 1H, -C**H**-CO_2H), 4.71-4.38 (complicated, 2H, Ar-C**H$_2$**-N-), 1.44 (2 lines, 9H, -OC(C**H$_3$**)**$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (177.1,176.5), (155.8,155), (133.8, 132.6), (132,131.6), (128.5,128.4), (127.8,126.9), (126.8,126.7), (126.4,126.2), (81.1,81), (54.2,52.4), (44.5, 43.9), (31.4,31), (28.4, 28.2); MS (m/z): 277(M^+), 232, 176, 132, 57; Anal. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.90. Found C, 64.82; H, 6.91.

N-tert-butyloxycarbonyl-1,2,3,4-tetrahydroisoquinoline-2-methanol (5c).



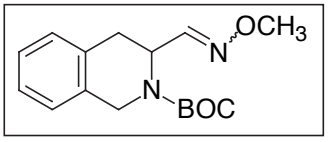
The BOC protected amino acid (1.0 g, 3.61 mmol) was dissolved in 20 mL of freshly distilled THF and transferred to a flame dried 50 mL flask under argon and cooled (0°C). The flask was fitted with a pressure equalizing dropping funnel and then charged with borane-THF complex (1.0 M in THF, 5.42 mmol). The borane was added at a rate to maintain a steady flow of gas from the reaction vessel. After completion of the addition, the mixture was allowed to stir for 30 min at 0°C and then warmed to ambient temperature and stirred overnight. The mixture was then cast into a 250 mL beaker containing 20 mL of ice-cold saturated ammonium chloride. The mixture was allowed to stir for 10 min and then extracted (4X 10 mL) with ether. The organic extracts were washed (water then brine) and dried ($MgSO_4$). Concentration under reduced pressure gave a colorless oil which was purified by column chromatography (hexane:ethyl acetate/ 1:1) to give the alcohol (930 mg, 98%) as a colorless oil. TLC R_f=0.38 (hexane:ethyl acetate /1:1); ^1H NMR (250 MHz, $CDCl_3$) δ 7.1 (m, 4H, Ar**H**), 4.64 (d, J=16.0 Hz, 1H, Ar-CH**H**-N-), 4.42 (bs, 1H, -NC**H**CH_2OH), 4.24 (d, J=16.0 Hz, 1H, Ar-C**H**H-N-), 3.42 (m, 5 lines, 2H, -C**H$_2$**OH), 2.95 (dd, J=6.0, 16.1 Hz, 1H, ArC**H**HN-), 2.75 (dd, J=2.7, 16.1 Hz, ArCH**H**N-), 2.66 (bs, 1H, O**H**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 150.5, 133.1, 132.9, 128.6, 126.8, 126.3, 126.0, 80.3, 63.7, 51.8, 43.8, 29.9, 28.4; IR(cm^{-1}, neat) 3379, 2956, 2658, 1672, 1409, 1171; MS (m/z): 263(M^+), 232, 176, 132, 57, Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.42; H, 8.04 . Found: C, 68.36; H, 8.11.

N-tert-butyloxycarbonyl-1,2,3,4-tetrahydroisoquinoline-2-carboxaldehyde .



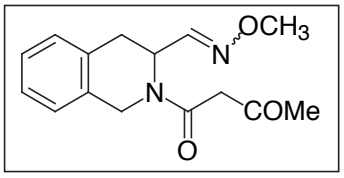
Oxallyl chloride (249 μL, 2.85 mmol) was added to a 25 mL round bottom flask containing 5 mL of dry dichloromethane. The solution was cooled to -78°C (dry ice/acetone) and dimethyl sulfoxide (4.94 mL, 69.7 mmol) was added dropwise with a syringe. (Caution! evolution of gas). The cold solution was allowed to stir for 5 min at -78°C at which time a solution of BOC-isoquinoline-methanol (0.5g, 1.90 mmol) in 2 mL of dichloromethane was cautiously added via cannula (2 min addition time). The solution was maintained at -78°C for an additional 25 min and then triethylamine (2.64 mL, 19 mmol) was added via syringe to produce a pale -yellow solution. The solution was stirred for an additional 5 min and then warmed to 0°C for 20 min. At that time, the reaction mixture was poured into saturated ammonium chloride (10mL) and stirred for 30 min. The layers were separated and the aqueous phase extracted (3x 10 mL) with dichloromethane. The combined organic phases were washed ($NaHCO_{3(sat)}$ and brine), dried (Na_2SO_4), and concentrated to give a yellow residue. Purification by column chromatography using (hexane: ethyl acetate/ 1 :1) gave the aldehyde (446 mg, 90%) as a pale-yellow oil. TLC R_f=0.48 (hexane:ethyl acetate/1:1); ^{1}H NMR (250 MHz, $CDCl_3$) δ 9.22 (bs, 1H, C**H**O), 6.92 (m, 4H, Ar**H**), 4.50 (ab quartet, J=16.0 Hz, 2H, Ar-C**HH**-N-), 4.51 (bs, 1H, -NC**H**CH_2OH), 2.78 (dd, J=4.5, 15.7 Hz, 1H, ArC**H**HN-), 2.64 (dd, J=6.4, 15.7 Hz, ArCH**H**N-), 1.44 (s, 9H, CC**H$_3$)$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 199.4 ,154.1, 137.7, 132.6, 129.4, 127.1, 126.9, 126.4, 86.7, 80.5, 69.2, 52.8, 28.4; IR(cm^{-1}, neat) 2984, 2713, 1732, 1701, 1452, 1391; MS (m/z) 261(M^+), 232, 176, 132, 57; Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33. Found: C, 68.76; H, 7.21.

N-t-butyloxycarbonyl-1,2,3,4-tetrahydroisoquinoline-2-carboxaldehyde-O-methyloxime (6c).



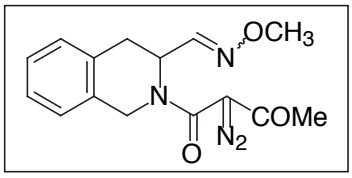
The BOC-protected amino aldehyde (270 mg, 1.03 mmol) was dissolved in 5 mL of absolute methanol and sequentially treated with methoxyl-amine hydrochloride (138 mg, 1.65 mmol) and pyridine (183μL, 2.27 mmol). The solution was allowed to stir at room temperature for 12 h and the solvent was removed under reduced pressure to give a gummy residue. The residue was purified by flash column chromatography with hexane/ ethyl acetate (1:1) to give 261 mg (88%) of the oximes as a 3-5:1 mixture of oxime isomers, both as colorless oils. TLC R_f=0.58 (hexane:ethyl acetate/1:10); **Major** ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.1-6.9 (obscured, 1H, C**H=**NOMe), 7.14 (m, 4H, Ar**H**), 4.91 (bs, 1H, -NC**H**CH=N). 4.67 (d, J=16.5 Hz, 1H, Ar-C**H**H-N-), 4.32 (d, J=16.5 Hz, 1H, Ar-CH**H**-N-), 3.68 (s, 3H, -OC**H$_3$**), 3.05 (6 lines,1H, ArC**H**HN-), 2.91 (dd, J=2.8, 17.7 Hz, ArCH**H**N-), 1.44 (s, 9H, CC**H$_3$)$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 154.1, 133.4, 128.4, 126.9, 126.6, 126.3, 126.9, 125.9, 99.1, 65.7, 61.9, 43.6, 31.6 , 28.3. **Minor** ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.14 (m, 4H, Ar**H**), 6.38 (d, J=5.6 Hz, 1H, C**H=**NOMe), 4.91 (bs, 1H, -NC**H**CH=N). 4.60 (d, J=15.2 Hz, 1H, Ar-C**H**H-N-), 4.39 (d, J=15.2 Hz, 1H, Ar-CH**H**-N-), 3.83 (s, 3H, -OC**H$_3$**), 3.1- 2.8 (obscured ,2H, ArC**H**HN-), 1.42 (s, 9H, CC**H$_3$)$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 148.4, 132.2, 128.4, 126.9, 126.6, 126.3, 126.9, 125.9, 99.2, 65.5, 61.8, 43.6, 31.6 , 28.2; IR(cm^{-1}, neat) 2984, 2713, 1689, 1454, 1397; MS (m/z): 290(M^+), 232, 176, 132, 57; Anal. Calcd for $C_{16}H_{22}N_2O_3$: C, 66.18; H, 7.64 . Found: C,65.87; H, 7.53.

N-(1,3-dioxobutyl)-1,2,3,4-tetrahydroisoquinoline-2-carboxaldehyde-O-methyloxime.



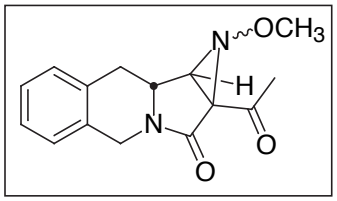
A 50 mL round bottom flask was charged with a solution of the protected oxime (600 mg, 2.07 mmol) in 20 mL of dry dichloromethane and fitted with a vented septum. Trifluoroacetic acid (3.98 mL, 51.7 mmol) was added in one portion to the solution. The reaction was monitored every 2-3 min by TLC until the reaction was judged to be complete. When the reaction was judged complete, solid sodium bicarbonate (8.7 g, 103 mmol) was cautiously added in portions to the mixture over a 5 min period. Upon completion of the addition, the light yellow mixture was allowed to stir for 20 min at room temperature. The flask was then flushed with argon and diketene was added (366 μL, 4.55 mmol) and the solution was allowed to stir overnight. The reaction mixture was then cast into saturated ammonium chloride and allowed to stir for 10 min. The layers were separated and the aqueous layer extracted (3x 10mL) with dichloromethane. The combined organic layers were washed (water, brine), dried (Na_2SO_4), and concentrated to give an orange oil. Purification by column chromatography with hexane : ethyl acetate (1:5) gave the ketoamide (527mg, 93% for two steps) as a colorless oil. TLC R_f=0.22 (hexane:ethyl acetate/1:1) **Major** ^{1}H NMR (250 MHz, $CDCl_3$) δ 7.1 (d,J=5.9 Hz, 1H, C**H=**NOMe), 7.14 (m, 4H, Ar**H**), 5.53 (bs, 1H, -NC**H**CH=N). 4.85 (ab quartet, J=16.2 Hz, 2H, Ar-C**HH**-N-), 3.66 (s, 3H, -OC**H$_3$**), 3.58 (bs, 2H, -C(O)C**H$_2$**C(O)-), 3.28-3.20 (m,2H, ArC**HH**N-), 2.21 (s,3H, -C(O)C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 202.2, 166.2, 147.3, 132.2, 130.9, 128.3, 127.2, 126.9, 125.7, 62.2, 61.9, 50.3, 47.3, 32.9, 30; **Minor** ^{1}H NMR (250 MHz, $CDCl_3$) δ , 7.14 (m, 4H, Ar**H**), 6.36 (d,J=6.3 Hz, 1H, C**H=**NOMe), 5.67 (bs, 1H, -NC**H**CH=N). 4.8 (m, 2H, Ar-C**HH**-N-), 3.84 (s, 3H, -OC**H$_3$**), 3.55 (bs, 2H, -C(O)C**H$_2$**C(O)-), 3.28-3.20 (m,2H, ArC**HH**N-), 1.91 (s,3H, -C(O)C**H$_3$**); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ 201.9, 166.5, 147.1, 132.1, 131.3, 128.8, 127.0, 127.1, 126.4, 62.1, 61.6, 51.8, 50.6, 43.1, 30.8; IR(cm^{-1}, neat) 3508, 3094, 2936, 1718, 1642, 1429, 1397; MS (m/z) (M^+)274, 227, 184, 167, 149.

N-(1,3-dioxo-2-diazobutyl)-1,2,3,4-tetrahydroisoquinoline-2-carboxaldehyde-O-methyl oxime (7c).



To a solution of 100 mg (0.36 mmol) of the keto-amide in 3 mL of anhydrous acetonitrile was added p-acetamidobenzenesulfonyl azide (105 mg, 0.44 mmol) in one portion. The solution was cooled to 0°C and DBU (65 _L, 0.44 mmol) was added dropwise over a 3 min period. The bright yellow-orange solution was allowed to stir for an additional h at 0°C with an aluminum foil covering at which time the solution was concentrated under reduced pressure to give a viscous black oil. The residue was taken up in a minimum amount of dichloromethane and placed on a silica gel column. The compound was quickly eluted with hexane/ethyl acetate (1:5) to give the diazoamide (296 mg, 88%) as a yellow oil. The compound was used immediately without further purification. TLC R_f=0.41(hexane :ethyl acetate/ 1:1),

8a-Acetyl-1-methoxy-1,1a,1b,2,7,8a-hexahydro-1,7a-diaza-cyclopropa[3,4] cyclopenta[1,2-b]naphthalen-8-one (11).



To a stirred solution of the Z-oxime diazoamide (90 mg, 0.33 mmol) in 2 mL of dichloromethane was added dirhodium tetraacetate (4.3 mg, 0.010mmol) in one portion. The solution was allowed to stir at 25^{o} C until complete consumption of the starting material was observed by TLC (0.5h). The solution was filtered through a small plug of alumina and then concentrated under reduced pressure. The residue was purified by silica gel chromatography with hexane/ ethyl acetate (1:1) as eluent to give 78mg (87%) of the aziridine as a yellow solid. The aziridine was recrystallised form 1% ethyl acetate in hexane to give pale-yellow crystals suitable for X-ray analysis (mp 148°C). TLC R_f=0.50 (Hex:EA/ 1:1); ^{1}H NMR (250 MHz, C_6D_6) δ 6.87 (m, 5 lines, 2H, -CH=C**H**=C**H**=CH-), 6.61-6,48 (m, 2H, -C**H**=CH=CH=C**H**), 4.83 (d, 1H, J=17.2Hz =C-C**H**H-N-), 4.27 (s, 3H, -OC**H$_3$**), 3.53 (d, 1H, J=17.2 Hz, =C-CH**H**-N-), 3.31 (d, 1H, J=2.38Hz, -CH-C**H**-NOCH$_3$), 3.08 (dt, 1H, J=2.4Hz 7.3 Hz, -CH$_2$-C**H**-N-), 2.75 (s, 3H, -COC**H$_3$**) 1.88-1.85 (m, 2H, =C-C**H$_2$**-CH-); ^{13}C NMR (62.5 MHz, C_6D_6) δ 194.2, 164.4, 132.2, 131.6, 129.4, 127.8, 126.8, 126.5, 60.7, 58.1, 52.9, 49.8, 41.4, 31.9, 30.4; IR (cm^{-1}, neat) 3040, 2937, 1759. 1688, 1268, 1134, 1043; MS (m/z): 272(M^+), 241, 220, 176; Anal. Calcd for $C_{15}H_{16}N_2O_3$: C, 66.16; H, 5.92. Found: C, 66.17; H, 5.88.