Synthesis of (–)-Epibatidine

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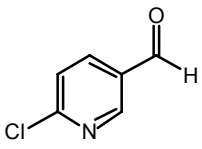
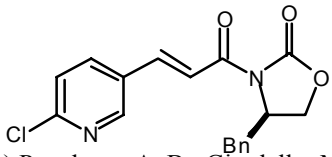
Supporting Information

General Information. All reactions were carried out under an atmosphere of argon or nitrogen in flame-dried glassware with magnetic stirring. THF, Et_2O, CH_2Cl_2 and toluene were purified by passage through a bed of activated alumina.[1] MeOH was distilled from $Mg(OMe)_2$. Reagents were purified prior to use unless otherwise stated following the guidelines of Perrin and Armarego.[2] Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and anisaldehyde, ceric ammonium nitrate stain, or ninhydrin followed by heating. Optical rotations were measured on a Jasco DIP-0181 digital polarimeter with a sodium lamp and are reported as follows: $[\alpha]_\lambda^{T\,^\circ C}$ (c = g/100 mL, solvent). Infrared spectra were recorded on a Perkin Elmer 1600 series FT-IR spectrometer. ^{1}H-NMR spectra were recorded on a Varian Inova-500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration. Proton-decoupled ^{13}C-NMR spectra were recorded on a Varian Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm). Low and high resolution mass spectra were obtained on Jeol AX-505 or SX-102 spectrometers in the Harvard University Mass Spectrometry Laboratory. Analytic high performance liquid chromatography (HPLC) was performed on a Hewlett-Packard 1100 Series HPLC with a diode array detector (UV monitoring at 240 nm and 280 nm) using a Zorbax SB-C8 column (4.6 x 250 mm).



6-Chloropyridine-3-carboxyaldehdye (5). To 0 °C solution of 6-chloronicotinic acid (12.8 g, 81.2 mmol) in THF (150 mL) was added a solution of $LiAlH_4$ in THF (100 mL, 1.0 M). CAUTION-gas evolution. The resulting orange reaction mixture was stirred for 3 h at 0 °C at which time the reaction was quenched by the sequential addition of 3.0 mL H_2O, 3.0 mL of 15% aqueous NaOH, and 9.0 mL H_2O. The reaction was thinned with THF, then filtered through Celite with the aid of EtOAc. The solution was concentrated *in vacuo* to yield 8.4 g of 6-chloro-3-pyridylcarbinol as a yellow oil that was used directly: ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (bs, 1H), 7.70 (d, J = 8.1 Hz, 1H), 7.30 (d, J = 8.1 Hz, 1H), 4.71 (s, 2H).

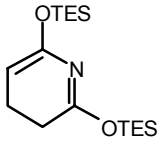
To a –78 °C solution of oxalyl chloride (8.0 mL, 92.0 mmol) in CH_2Cl_2 (250 mL) was added DMSO (10.50 mL, 148.0 mmol). After 10 min, a –78 °C solution of 6-chloro-3-pyridylcarbinol in CH_2Cl_2 (50 mL) was added via cannula. After 15 min at –78 °C, Et_3N (20.0 mL, 144.0 mmol) was added and the reaction was warmed to 0 °C. The reaction mixture was diluted with Et_2O (500 mL) then washed with saturated aqueous $NaHCO_3$ (500 mL), 1.0 M $KHSO_4$ (2 x 500 mL), saturated aqueous $NaHCO_3$ (500 mL), then saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield 7.0 g of 6-chloropyridine-3-carboxyaldehdye (**5**) as light yellow solid (86%) whose spectral characteristics matched those reported previously.[3]



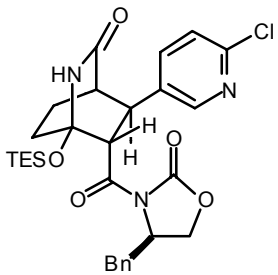
3-[(2*E*)-3-(6-Chloro(3-pyridyl))prop-2-enoyl](4*R*)-4-benzyl-1,3-oxazolidin-2-one (7). To a solution of (4*R*)-3-(dimethylphosphonoacetyl)-4-phenylmethyl-2-

(1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.
(2) Perrin, D. D. and Armarego, W. L. *Pruification of Laboratory Chemicals;* 3rd ed., Pergamon Press, Oxford. 1988.
(3) Pandey, G.; Bagul, T. D.; Sahoo, A. K. *J. Org. Chem.* **1998**, *63*, 760-768.

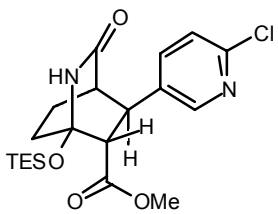
oxazolidinone (**6**)[4] (14.9 g, 45.5 mmol) in CH_3CN (115 mL) was added in one portion 6-chloropyridine-3-carboxyaldehdye (**5**) (5.40 g, 38.0 mmol). To this mixture was added *i*-Pr_2NEt (18.0 mL, 103.0 mmol) and anhydrous LiCl (16.0 g, 377.0 mmol). After 1 h, the thick reaction mixture was diluted with EtOAc and washed with saturated aqueous NH_4Cl (2 x 300 mL) and saturated aqueous NaCl (1 x 300 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated *in vacuo*. The resulting solid was recrystallized from EtOAc/hexanes to yield 10.62 g of a white solid (81 % yield). Analytical data for **7**: mp = 144 °C; $[\alpha]_D^{25}$ = –81.8 ° (*c* 1.22, CH_2Cl_2); IR (film) 3096, 3028, 2992, 1776, 1678, 1623, 1377, 1353 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.56 (m, 1H), 7.96 (d, J = 15.7 Hz, 1H), 7.92 (m, 1H), 7.83 (d, J = 15.7 Hz, 1H), 7.40-7.23 (m, 6H), 4.80 (m, 1H), 4.30-4.21 (m, 2H), 3.36 (dd, J = 13.5, 3.3 Hz, 1H), 2.85 (dd, J = 13.5, 9.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 153.5, 153.1, 150.3, 140.8, 136.7, 135.0, 129.4, 129.3, 129.0, 127.4, 124.6, 119.6, 66.3, 55.3, 37.8; LRMS (APCI): Mass calcd for $C_{18}H_{15}N_2O_3Cl$ $[M]^+$, 343. Found 343.



2,6-Bis-(triethylsilyloxy)-3,4-dihydropyridine (8). To suspension of glutarimide (3.01 g, 26.6 mmol) in diethyl ether (30 mL) was added Et_3N (8.10 mL, 58.2 mmol). The reaction was cooled to 5 °C and triethylsilyl trifluoromethanesulfonate (12.0 mL, 53.1 mmol) was added. After 10 min, the reaction became biphasic and the cooling bath was removed. After a total of 30 min, the top layer was decanted and the lower layer was extract with Et_2O (2 x 10 mL). The combined top layer and etheral layers were concentrated *in vacuo*. The resulting oil was distilled under reduced pressure (Kuglerohr, 100 mT, 120-130 °C) to afford 8.20 g (90%) of **8** as a clear oil whose spectral characteristics were analogous to the bis-trimethylsilyl and bis-*t*-butyldimethylsilyl analogs reported previously:[5] ^1H NMR (500 MHz, $CDCl_3$) δ 4.63 (m, 1H), 2.20 (m, 2H), 2.15 (m, 2H), 0.97 (ap t, J = 7.8 Hz, 18H), 0.82 (ap q, J = 8.3 Hz, 6H), 0.70 (ap q, J = 7.3 Hz).



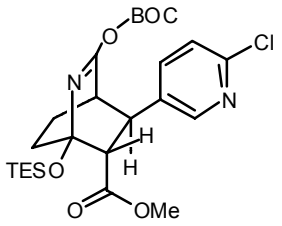
(4*R*)-3-{[(2*S*,1*R*,3*R*,4*R*)-6-Aza-1-(triethysilyloxy)-3-(6-chloro(3-pyridyl))-5-oxobicyclo[2.2.2]oct-2-yl]carbonyl}-4-benzyl-1,3-oxazolidin-2-one (9). To a –78 °C solution of imide **7** (2.00 g, 5.8 mmol) in CH_2Cl_2 (30 mL) was added Me_2AlCl (1.8 M in toluene, 8.00 mL). To the resulting orange solution was added via cannula a –78 °C solution of 2,6-bis-(triethylsilyloxy)-3,4-dihydropyridine (**8**) (4.00 mL, 10.5 mmol) in CH_2Cl_2 (10 mL). After 15 min, the reaction was quenched *carefully* by the addition of saturated aqueous NH_4Cl. The reaction was diluted with EtOAc and the organic layer was separated, then washed with saturated aqueous $NaHCO_3$ (2 x 100 mL) followed by saturated aqueous NaCl. The organic layer was dried over Na_2SO_4, filtered, then concentrated *in vacuo.* The residue was purified by flash column chromatography (SiO_2, 5% MTBE/CH_2Cl_2) to afford **9** (2.60 g, 79%) as a white solid (dr 20:1). Analytical data for **9**: mp = 178 °C; $[\alpha]_D^{25}$ = –25.5 (*c* 0.89, CH_2Cl_2); IR (film) 3410, 2960, 2880, 1782, 1694, 1462, 1390, 1160 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.15 (bs, 1H), 7.65 (d, J = 8.3 Hz, 1H), 7.36-7.24 (m, 6H), 6.08 (bs, 1H), 4.96 (d, J = 7.8 Hz, 1H), 4.63 (m, 1H), 4.08 (m, 2H), 3.54 (d, J = 8.8 Hz, 1H), 3.46 (dd, J = 13.2, 2.9 Hz, 1H), 2.60 (s, 1H), 2.58 (ddd, J = 11.7, 11.7, 4.9 Hz, 1H), 2.51 (dd, J = 11.2, 11.2, 1H), 2.05 (ap t, J = 10.7 Hz, 1H), 1.98 (ap t, J = 8.8 Hz, 1H), 1.79 (ap t, J = 12.2 Hz, 1H), 1.01 (m, 9H), 0.73 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 171.7, 152.6, 150.6, 148.8, 136.9, 136.4, 135.2, 129.1, 127.5, 124.8, 86.8, 65.7, 55.9, 55.7, 44.8, 42.6, 38.3, 29.4, 26.9, 23.8, 6.8, 6.3; LRMS (APCI): Mass calcd for $C_{29}H_{36}N_3O_5SiCl$ $[M]^+$, 570. Found 570.



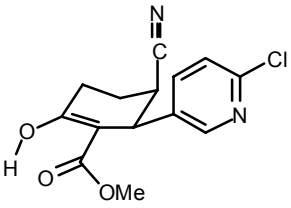
Methyl (2*S*,1*R*,3*R*,4*R*)-6-aza-1-(triethylsilyloxy)-3-(6-chloro(3-pyridyl))-5-oxobicyclo[2.2.2] octane-2-carboxylate (10). To a suspension of **9** (2.30 g, 4.00 mmol) in anhydrous MeOH (20 mL) was added $Sm(OTf)_3$ (2.40 g, 4.00 mmol). The reaction was heated at 60 °C. After 12 h, the reaction was diluted with EtOAc (150 mL), the washed with saturated aqueous NaCl followed by saturated aqueous $NaHCO_3$

(4) Johnson, J. S. Ph.D. Thesis, Harvard University, Cambridge, MA, 1999.
(5) Ghosez, L.; Bayard, P.; Nshimyumukiza, P.; Gouverneur, V.; Sainte, F.; Beaudegnies, R.; Rivera, M.; Frisque-Hesbain, A. M.; Wynants, C. *Tetrahedron* **1995**, *51*, 11021-11042.

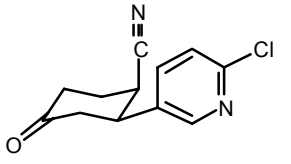
(2 x 100) and saturated aqueous NaCl again. The organic layer was then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified using flash column chromatagrahy (SiO_2, 45-50% EtOAc/hexanes) to yield 1.43 g (84%) of **10** as a clear oil that solidified upon standing in a freezer. Analytical data for **10**: mp =86-89 °C; $[\alpha]_D^{25}$ = –27.3 ° (*c* 1.69, CH_2Cl_2); IR (film) 3169 (b), 3059, 2958, 2878, 1731, 1682, 1462, 1105 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.56 (m, 1H), 7.56 (m, 1H), 6.40 (bs, 1H), 3.70 (s, 3H), 3.44 (d, J = 7.3 Hz, 1H), 2.88 (dd, J = 6.8, 2.4, 1H), 2.63 (s, 1H), 2.49 (ddd, J = 11.2, 11.2, 4.4 Hz, 1H), 2.09 (m, 1H), 1.97 (m, 1H), 1.75 (m, 1H), 0.94 (m, 9H), 0.63 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 172.2, 150.4, 148.7, 136.9, 136.6, 124.6, 85.7, 60.6, 52.3, 43.5, 42.6, 29.0, 23.7, 6.7, 6.1; LRMS (APCI): Mas calcd for $C_{20}H_{29}N_2O_4SiCl$ $[M]^+$, 425. Found 425.



(5*S*,1*R*,4*R*,6*R*)-3-Aza-4-(triethylsilyloxy)-6-(6-chloro(3-pyridyl))-5-(methoxycarbonyl)bicyclo [2.2.2]oct-2-en-2-yl (tert-butoxy)formate (11). To a solution of **10** (400 mg, 0.94 mmol) in CH_2Cl_2 (5.0 mL) was added DMAP (38 mg, 0.31 mmol), Et_3N (1.00 mL, 7.20 mmol) and BOC_2O (1.10 g, 5.0 mmol) in succession. The reaction was stirred for 3 h, at which time it was diluted with EtOAc. The mixture was then washed with saturated aqueous NH_4Cl (3 x 75 mL) and saturated aqueous NaCl (1 x 50 mL), then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 20% EtOAc/hexanes) to afford 520 mg of **11** (98%) as clear oil. Analytical data for **11**: $[\alpha]_D^{25}$ = –53.3° (*c* 0.3, CH_2Cl_2); IR (film) 2953, 2912, 2876, 1783, 1759, 1738, 1659, 1462, 1371, 1130 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 2.4 Hz, 1H), 7.44 (dd, J = 8.3, 2.9 Hz, 1H), 7.28 (d, J = 8.3 Hz, 1H), 3.68 (s, 3H), 3.34 (d, J = 6.8 Hz, 1H), 2.73 (dd, J = 6.8, 2.0 Hz, 1H), 2.58 (dd, J = 6.8, 2.0 Hz, 1H), 2.29 (ddd, J = 13.7, 9.8, 3.9 Hz, 1H), 1.94 (m, 1H), 1.80 (m, 1H), 1.51 (s, 9H), 1.38 (m, 1H), 0.95 (m, 9H), 0.69, m 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 163.1, 150.4, 148.8, 137.4, 136.8, 124.6, 89.8, 85.0, 57.4, 52.1, 43.9, 39.2, 27.4, 27.1, 24.5, 6.9, 6.1; HRMS (Electrospray): Exact mass calcd for $C_{25}H_{38}N_2O_6SiCl$ $[M+H]^+$, 525.2187. Found 525.2189.

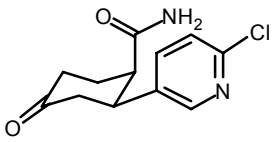


Methyl (6*S*,5*R*)-6-(6-chloro(3-pyridyl))-5-cyano-2-hydroxycyclohex-1-enecarboxylate (12). To a solution of **11** (220 mg, 0.42 mmol) in THF (2.00 mL) and H_2O (0.40 mL) was added a solution of *n*-Bu_4F in THF (1.0 M, 2.00 mL). After 14 h, the reaction was diluted with EtOAc, the washed with saturated aqueous NH_4Cl. The aqueous layer was separated the extracted with an addition portion of EtOAc. The combined organic extracts were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 40% EtOAc/hexanes) to afford 100 mg of **12** (81%) as an amorphous white solid. Analytical data for **12**: $[\alpha]_D^{25}$ = +124.9° (*c* 0.49, CH_2Cl_2); IR (film) 3450-3200 (b), 2954, 1659, 1619, 1566, 1461, 1230, 1107 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 12.53 (bs, 1H), 8.27 (d, J = 2.4 Hz, 1H), 7.58 (d, J = 8.3, 2.4 Hz, 1H), 7.33 (d, J = 8.3 Hz, 1H), 4.14 (d, J = 4.9 Hz, 1H), 3.58 (s, 3H), 3.10 (m, 1H), 2.64-2.50 (m, 2H), 2.08 (m, 1H), 1.91 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 171.0, 151.0, 149.9, 139.3, 133.6, 123.9, 119.3, 97.4, 52.1, 37.2, 31.4, 27.6, 20.3; HRMS (Electrospray): Exact mass calcd for $C_{14}H_{14}N_2O_3SiCl$ $[M+H]^+$, 293.0693. Found 293.0699.

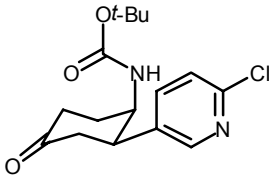


(2*S*,1*R*)-2-(6-Chloro(3-pyridyl))-4-oxocyclohexanecarbonitrile (13). A solution of **12** (340 mg, 1.16 mmol) in wet DMSO (4.0 mL) was heated at 130 °C. After 24 h, the reaction was partitioned between EtOAc and saturated aqueous NaCl. The organic layer was separated and washed with saturated aqueous NaCl (3 x 25 mL). The combined aqueous layers were extracted with EtOAc (20 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, EtOAc) to afford 270 mg of **13** (99%) as a crystalline white solid. Analytical data for **13**: mp = 156 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.33 (d, J = 2.9 Hz, 1H), 7.71 (dd, J = 8.3, 2.4 Hz, 1H), 7.40 (d, J = 8.3 Hz, 1H), 3.33 (ddd, J =

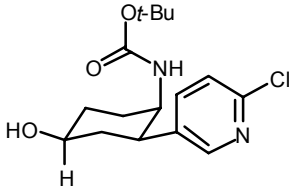
13.7, 3.9, 3.9 Hz, 1H), 3.23 (m, 1H), 3.03 (dd, J = 14.6, 14.6 Hz, 1H), 2.78 (ddd, J = 14.9, 5.9, 5.9 Hz, 1H), 2.60 (m, 2H), 2.46 (m 1H), 2.13 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 205.5, 151.6, 148.0, 136.9, 133.6, 124.8, 118.2, 42.8, 41.9, 37.1, 34.5, 28.2; LRMS (APCI): Mass calcd for $C_{12}H_{15}N_3OSiCl$ $[M+NH_4]^+$, 253. Found 253.



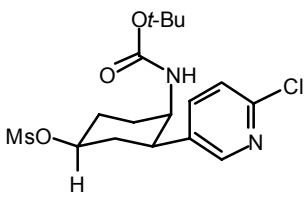
(2*S*,1*R*)-2-(6-Chloro(3-pyridyl))-4-oxocyclohexanecarboxamide (14). To a 70 °C solution of **13** (270 mg, 1.15 mmol) in toluene (8.0 mL) was added in one portion potassium trimethylsilanolate (711 mg, 5.54 mmol). After 2 h, the reaction was cooled and partitioned between EtOAc and saturated aqueous NH_4Cl. The aqueous layer was extracted with EtOAc and the combined organic layers were dried over K_2CO_3, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 5% MeOH/CH_2Cl_2) to afford 208 mg of **14** (72%) as a clear oil. Analytical data for **14**: $[\alpha]_D^{25}$ = –68.7 ° (*c* 0.36, CH_2Cl_2); IR (film) 3342, 3200, 2926, 1711, 1668, 1461, 1106 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 (d, J = 2.9 Hz, 1H), 7.59 (dd, J = 8.3, 2.4 Hz, 1H), 7.29 (d, J= 8.3 Hz, 1H), 5.43, (bs, 2H), 3.56 (dd, J = 13.2, 13.2 Hz, 1H), 3.40 (ddd, J = 12.2, 4.4, 4.4 Hz, 1H), 2.80 (dd, J = 8.3, 4.4 Hz, 1H), 2.47 (dd, J = 14.2, 4.4 Hz, 1H), 2.40 (m, 1H), 2.28 (m, 1H), 2.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.6, 174.3, 150.5, 149.2, 137.8, 135.6, 124.3, 45.1, 42.6, 42.3, 37.5, 28.0; LRMS (APCI): Mass calcd for $C_{12}H_{13}N_2O_2Cl$ $[M]^+$, 253. Found 253.



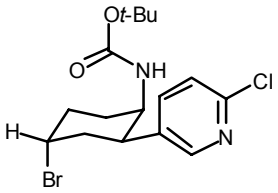
***N*-[(1*R*,2*R*)-2-(6-Chloro(3-pyridyl))-4-oxocyclohexyl](tert-butoxy)carboxamide (15).** To a 50 °C solution of **14** (116 mg, 0.46 mmol) in *t*-butanol (5.0 mL) was added lead(IV) acetate (1.0 g, 2.31 mmol). The resulting brown solution was stirred for 3 h, at which time the reaction was cooled and diluted with EtOAc (50 mL). This mixture was passed through SiO_2 with the aid of EtOAc. This filtrate was washed with saturated aqueous $NaHCO_3$ (2 x 40 mL) and saturated aqueous NaCl, then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 50% EtOAc/hexanes) to afford 105 mg of **15** (70%) as a clear oil. Analytical data for **15**: $[\alpha]_D^{25}$ = +19.5° (*c* 0.32, CH_2Cl_2); IR (film) 3353, 3265, 2975, 2930, 1711, 1693, 1461, 1392, 1366, 1166 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 333K) δ 8.19 (d, J = 2.4 Hz, 1H), 7.43 (dd, J = 8.3, 2.4 Hz, 1H), 7.28 (d, J = 8.3, 1H), 4.39 (bs, 1H), 4.29 (m, 1H), 3.61 (m, 1H), 2.75-2.67 (m, 2H), 2.55 (ap t, J = 6.8 Hz, 2H), 2.05 (m, 1H), 1.89 (m, 1H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, 333K) δ 208.9, 155.2, 150.5, 149.7, 138.5, 134.3, 124.1, 80.4, 60.5, 49.8, 42.6, 38.6, 28.3, 14.3; HRMS (Electrospray): Exact mass calcd for $C_{16}H_{21}N_2O_3Cl$ $[M]^+$, 325.1319. Found 325.1329.



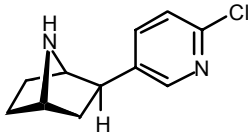
***N*-[(4*S*,1*R*,2*R*)-2-(6-Chloro(3-pyridyl))-4-hydroxycyclohexyl](tert-butoxy)carboxamide (16).** To a –40 °C solution of **15** (65 mg, 0.20 mmol) in MeOH (3.00 mL) was added $NaBH_4$ (80 mg, 2.10 mmol). After 1 h, the reaction was quenched by the addition of saturated aqueous NH_4Cl (5.0 mL). The reaction was diluted with EtOAc and the organic layer was separated, then washed with saturated aqueousNaCl. The organic layer was then dried over Na2SO4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 75% EtOAc/hexanes) to afford 58 mg of **16/17** (89%) as a 92:8 mixture of diastereomers as determined by ^{1}H NMR. Analytical data for **16**: $[\alpha]_D^{25}$ = –48.3 ° (*c* 0.39, CH_2Cl_2); IR (film) 3356, 2934, 2977, 2869, 1694, 1520, 1458, 1366, 1168, 1059 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$, 333K) δ 8.24 (d J = 2.0 Hz, 1H), 7.51 (dd, J = 7.8, 2.4 Hz, 1H), 7.23 (d, J = 8.3 Hz, 1H), 4.66 (bd, J = 9.3 Hz, 1H), 3.78 (m, 1H), 2.89 (d, J = 13.7 Hz, 1H), 2.08-1.65 (m, 3H), 1.78-1.65 (m, 2H), 1.39, (m, 1H), 1.26 (bs, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 149.9, 148.8, 138.6, 1363, 124.0, 79.9, 69.9, 48.6, 42.3, 34.5, 29.9, 29.7, 28.4; LRMS (APCI): Mass calcd for $C_{16}H_{23}N_2O_3Cl$ $[M]^+$, 327. Found 327.



(1*S*,3*R*,4*R*)-4-[(*tert*-Butoxy)carbonylamino]-3-(6-chloro(3-pyridyl))cyclohexyl methylsulfonate (18). To 0 °C solution of **16** (33 mg, 0.10 mmol) in CH_2Cl_2 (2.0 mL) was added MsCl (0.100 mL, 1.29 mmol) and Et_3N (0.200 mL, 1.44 mmol). After 20 min, the reaction was diluted with EtOAc (50 mL). This solution was washed with saturated aqueous $NaHCO_3$ (2 x 30 mL), saturated aqueous NH_4Cl (2 x 30 mL) and saturated aqueous NaCl, then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 60% EtOAc/hexanes) to afford 38 mg of **18** (94%) as a clear oil. Analytical data for **18**: $[\alpha]_D^{25}$ = –59.1° (*c* 0.665, CH_2Cl_2); IR (film) 3393, 3268, 2976, 2939, 1695, 1461, 1353, 1174 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$, 368K) δ 8.23 (bs, 1H), 7.47 (dd, J = 8.3, 2.4 Hz, 1H), 7.24 (m, 1H), 4.76 (dddd, J = 11.2, 11.2, 6.4, 6.4 Hz, 1H), 4.12 (bs, J = 6.8 Hz, 1H), 4.07 (bs, 1H), 3.03 (s, 3H), 2.98 (bd, J = 13.7 Hz, 1H), 2.31 (bd, J = 13.2 Hz, 1H), 2.20 (bd, J = 12.2 Hz, 1H), 2.08 (m, 1H), 1.97 (m, 1H), 1.82 (m, 1H), 1.67 (m, 1H), 1.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 150.0, 148.4, 138.1, 135.0, 123.9, 78.9, 60.4, 41.0, 38.9, 31.5, 28.0, 22.6, 21.0, 14.2; LRMS (APCI): Mass calcd for $C_{17}H_{25}N_2O_3Cl$ $[M]^+$, 405. Found 405.



***N*-[(1*R*,2*R*,4*R*)-4-Bromo-2-(6-chloro(3-pyridyl))cyclohexyl](tert-butoxy)carboxamide (19).** To a solution of **18** (20.0 mg, 0.05 mmol) in THF (3.0 mL) was added anhydrous LiBr (100 mg, 1.15 mmol). The reaction was heated at reflux for 36 h, at which time it was diluted with EtOAc (30 mL). The organic layer was washed with saturated aqueous NaCl (2 x 30 mL), then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 25% EtOAc/hexanes) to afford 16.0 mg of **19** (84%) as an amorphous white solid. Analytical data for **19** Analytical data for **19**: $[\alpha]_D^{25}$ = –30.5° (*c* 0.15, CH_2Cl_2); IR (film) 3265, 2975, 2929, 2858, 1694, 1456, 199, 1366, 1247, 1168 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (bs, 1H), 7.52 (d, J = 8.3, 2.4 Hz, 1H), 7.27 (d, J = 2.4 Hz, 1H), 4.80 (m, 1H), 4.63 (bs, 1H), 4.12 (m, 1H), 3.54 (m, 1H), 2.35-2.18 (m, 3H), 2.08 (m, 1H), 1.96 (m, 1H), 1.85 (m, 1H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$, rotamers) δ 171.2, 149.7, 148.5, 138.6, 128.3, 123.8, 79.8, 60.4, 38.6, 36.6, 34.6, 31.5, 28.0, 22.6, 21.0; HRMS (Electrospray): Exact mass calcd for $C_{16}H_{23}N_2O_2SiBrCl$ $[M]^+$, 389.0651. Found 389.0615.



(–)-Epibatidine (1). To a solution of **19** (15.0 mg, 0.04 mmol) in CH_2Cl_2 (2.50 mL) was added trifluoroacetic acid (0.30 mL). After 1 h at 25 °C, the reaction was diluted with $CHCl_3$ (20 mL) and 10% aqueous K_2CO_3 (20 mL) was added. The aqueous layer was extracted with $CHCl_3$ (10 mL) and the combined organic extracts were dried over anhydrous K_2CO_3, filtered and concentrated *in vacuo* to afford (1*R*,2*R*,4*R*)-4-bromo-2-(6-chloro(3-pyridyl))cyclohexylamine (**20**) (10.2 mg, 91%) as a clear oil whose spectral characteristics mactched those reported previously.[6] Partial data for **20**: ^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (d, J = 2.4 Hz, 1H), 7.53 (dd, J = 8.3, 2.4 Hz, 1H), 7.29 (d, J = 7.8 Hz, 1H), 4.87 (dd, J = 2.9, 2.9 Hz, 1H), 3.46 (d, J = 12.7 Hz, 1H), 3.36 (s, 1H), 2.67 (ddd, J = 14.2, 14.2, 2.9 Hz, 1H), 2.35 (dd, 13.7, 13.7 Hz, 1H), 2.28 (m, 1H), 1.98 (dd, J = 14.2, 2.9 Hz, 1H), 1.92 (dd, J = 11.7, 2.4 Hz, 1H), 1.68 (d, J = 10.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) 149.8, 149.3, 138.3, 137.2, 124.0, 54.1, 50.0, 39.1, 31.8, 28.3, 27.7.

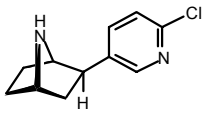
A solution of **20** (10.0 mg, 0.034 mmol) in $CHCl_3$ (3.0 mL) was heated at reflux. After 72 h, the reaction was diluted with additional $CHCl_3$, then 10% aqueous K_2CO_3 was added (25 mL). The layers were separated in the aqueous layer was extracted with $CHCl_3$ (1 x 10 mL). The combined organic layers were dried over anhydrous K_2CO_3, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 95/5/0.5 CH_2Cl_2/MeOH/concentrated NH_4OH) to afford 6.8 mg of (–)-epibatdine (95%) as a white solid. Analytical data for **1**: $[\alpha]_D^{25}$ = –6.7° (*c* 0.21, CH_2Cl_2)[7]; IR (film) 3265, 2961, 2872, 1562, 1458, 1396, 1103, 1025, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, J = 2.4 Hz, 1H), 7.77 (dd, J = 8.3, 2.4 Hz, 1H), 7.23 (d, J = 8.3 Hz, 1H), 3.80 (dd, J = 4.0, 4.0 Hz, 1H), 3.56 (d, J = 2.4 Hz, 1H), 2.76 (dd, J = 9.3, 4.9

(6) Aoyagi, S.; Tanaka, R.; Naruse, M.; Kibayashi, C. *J. Org. Chem.* **1998**, *63*, 8397-8406.

(7) Reported literature optical rotation value for (–)-epibatidine: $[\alpha]_D^{25}$ = –6.2° (*c* 0.42, CH_2Cl_2), Trost, B. M.; Cook, G. R. *Tetrahedron Lett.* **1996**, *37*, 7485-7488.

Hz, 1H), 1.91 (dd, J = 12.2, 9.3 Hz, 1H), 1.65-1.50 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.9, 148.8, 141.1, 137.7, 123.9, 62.8, 56.4, 44.5, 40.4, 31.4, 30.2; HRMS (CI): Exact mass calcd for $C_{13}H_{17}N_3Cl$ $[M+H+CH_3CN]^+$, 250.1111. Found 250.1115.

^{1}H and ^{13}C NMR Spectral Comparison of Synthetic Epibatidine



(–)-epibatidine

	Evans, Scheidt, Downey (–)-epibatidine	Trudell, Zhang *J. Org. Chem.* **1996**, *61*, 7189-7191 (±)-epibatidine	Kibayashi et al. *J. Org. Chem.* **1998**, *63*, 8397-8406 (–)-epibatidine
^{1}H NMR			
	8.27 (d, *J* = 2.4 Hz, 1H) 7.77 (dd, *J* = 8.3, 2.4 Hz, 1H) 7.23 (d, *J* = 8.3 Hz, 1H) 3.80 (dd, *J* = 4.4, 4.4 Hz,1H) 3.57 (d, *J* = 2.4 Hz,1H) 2.76 (dd, *J* = 9.3, 4.9 Hz, 1H) 1.91 (dd, *J* = 12.2, 9.3 Hz, 1H) 1.65-1.50 (m, 5H)	8.26 (d, *J* = 2.5 Hz, 1H) 7.75 (dd, *J* = 8.3, 2.5 Hz, 1H) 7.23 (d, *J* = 8.3 Hz, 1H) 3.80 (br s, 1H) 3.57 (br s, 1H) 2.77 (dd, *J* = 8.8, 4.9 Hz, 1H) 1.91 (dd, *J* = 12.2, 9.0 Hz, 1H) 1.63-1.51 (m, 5H)	8.27 (d, *J* = 2.5 Hz, 1H) 7.76 (dd, *J* = 8.3, 2.5 Hz, 1H) 7.23 (d, *J* = 8.3 Hz, 1H) 3.80 (t, *J* = 4.0 Hz,1H) 3.60 (d, *J* = 2.0 Hz1H) 2.77 (dd, *J* = 9.0, 4.9 Hz, 1H) 1.91 not reported (?) 1.65-1.48 (m, 5H)
^{13}C NMR			
	148.9 148.8 141.1 137.7 123.9 62.8 56.4 44.5 40.4 31.4 30.2	148.8 148.6 140.7 137.5 123.8 62.8 56.5 44.5 40.3 31.3 30.2	149.0 148.9 141.1 137.7 124.0 62.8 56.5 44.6 40.4 31.4 30.2

X-ray Crystallographic Data for Diels-Alder adduct **9**:

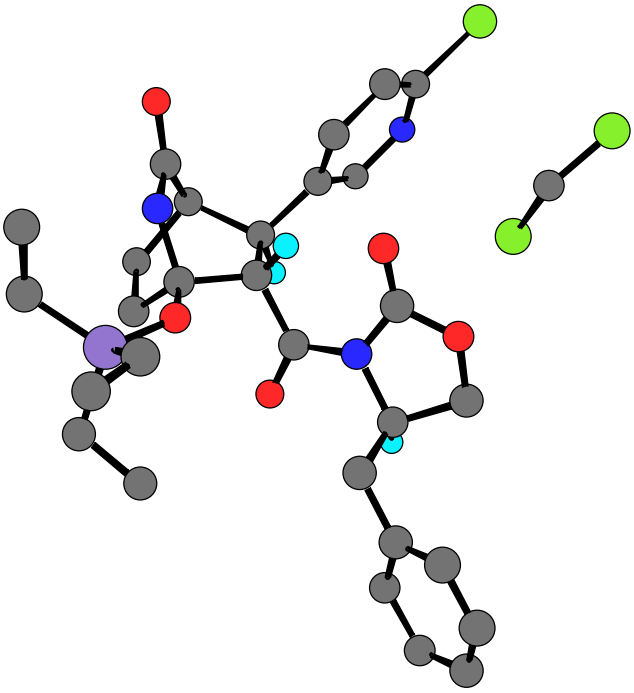


Table 1. Crystal data and structure refinement for **9**.

Identification code	cwd78t	
Empirical formula	C29 H36 Cl N3 O5 Si	
Formula weight	570.15	
Temperature	213(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 14.4435(16) Å	α= 90°.
	b = 7.4513(8) Å	β= 103.141(2)°.
	c = 15.3056(18) Å	γ = 90°.
Volume	1604.1(3) $Å^3$	
Z	2	
Density (calculated)	1.180 Mg/m^3	
Absorption coefficient	0.195 mm^{-1}	
F(000)	604	
Crystal size	1.6 x 1.8 x 5.2 mm^3	
Theta range for data collection	1.37 to 28.35°.	
Index ranges	-19<=h<=14, -9<=k<=9, -15<=l<=20	
Reflections collected	12104	
Independent reflections	7745 [R(int) = 0.0296]	
Completeness to theta = 28.35°	99.7 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7745 / 1 / 379	
Goodness-of-fit on F^2	1.055	
Final R indices [I>2sigma(I)]	R1 = 0.0757, wR2 = 0.2145	
R indices (all data)	R1 = 0.0876, wR2 = 0.2254	
Absolute structure parameter	0.02(11)	
Largest diff. peak and hole	1.438 and -0.868 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **9**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Si(1)	6867(1)	8193(2)	4172(1)	39(1)
Cl(1)	13079(1)	6276(2)	9343(1)	60(1)
Cl(1S)	10463(2)	8863(3)	9639(2)	103(1)
C(1S)	11220(7)	10720(13)	9515(6)	104(3)
O(2)	7636(2)	8005(4)	5166(2)	31(1)
N(3)	8969(2)	6283(4)	5112(2)	29(1)
C(5)	8168(2)	6534(5)	5546(2)	26(1)
O(1)	10376(2)	4826(4)	5240(2)	41(1)
O(5)	8798(2)	11472(4)	8353(2)	43(1)
O(4)	9550(2)	10281(4)	7372(2)	39(1)
C(2)	9318(3)	3999(5)	6201(3)	32(1)
C(28)	11954(3)	6109(6)	8625(3)	38(1)
O(3)	7257(2)	6628(5)	7138(2)	45(1)
C(4)	7619(3)	4764(5)	5460(3)	33(1)
C(1)	9626(2)	5040(5)	5467(2)	28(1)
N(2)	8120(2)	9103(5)	7597(2)	32(1)
C(14)	8896(3)	10262(5)	7730(3)	33(1)
C(24)	9237(3)	5339(5)	6962(2)	29(1)
C(26)	10836(3)	6970(6)	7312(3)	35(1)
C(13)	7961(3)	7520(5)	7097(2)	30(1)
N(1)	11368(3)	4951(6)	8873(2)	48(1)
C(12)	8648(2)	6987(5)	6540(2)	25(1)
C(16)	7434(3)	9702(6)	8121(3)	35(1)
C(25)	10207(3)	5765(5)	7530(2)	30(1)
C(15)	8055(3)	10954(7)	8786(3)	43(1)
C(18)	5881(3)	11201(7)	8051(3)	41(1)
C(3)	8312(3)	3229(6)	5823(3)	37(1)
C(27)	11745(3)	7144(6)	7870(3)	40(1)
C(29)	10511(3)	4827(6)	8335(3)	41(1)
C(17)	6579(3)	10632(8)	7509(3)	45(1)
C(10)	6841(3)	10649(7)	3988(3)	46(1)
C(23)	5318(3)	9955(8)	8358(3)	51(1)
C(19)	5786(4)	12964(7)	8276(3)	50(1)
C(8)	5669(4)	7355(7)	4243(4)	62(2)
C(22)	4694(4)	10487(10)	8883(4)	61(1)
C(20)	5154(4)	13491(9)	8793(4)	59(1)
C(21)	4629(4)	12245(10)	9106(4)	62(2)
C(6)	7152(5)	6788(10)	3250(4)	71(2)
C(7)	7945(6)	7340(13)	2877(5)	92(2)
C(11)	6110(4)	11292(9)	3168(4)	72(2)
C(9)	5356(5)	8010(9)	5071(7)	84(2)
Cl(3S)	12244(5)	10748(5)	10275(5)	336(5)

Table 3. Bond lengths [Å] and angles [°] for **9**.

Si(1)-O(2)	1.674(3)
Si(1)-C(10)	1.851(5)
Si(1)-C(8)	1.866(6)
Si(1)-C(6)	1.876(7)
Cl(1)-C(28)	1.747(4)
Cl(1S)-C(1S)	1.800(11)
C(1S)-Cl(3S)	1.662(10)
O(2)-C(5)	1.388(4)
N(3)-C(1)	1.349(5)
N(3)-C(5)	1.471(4)
C(5)-C(4)	1.529(5)
C(5)-C(12)	1.559(5)
O(1)-C(1)	1.220(4)
O(5)-C(14)	1.343(5)

O(5)-C(15)	1.437(5)
O(4)-C(14)	1.194(5)
C(2)-C(1)	1.512(5)
C(2)-C(3)	1.547(5)
C(2)-C(24)	1.559(5)
C(28)-N(1)	1.323(6)
C(28)-C(27)	1.364(7)
O(3)-C(13)	1.229(5)
C(4)-C(3)	1.538(6)
N(2)-C(14)	1.392(5)
N(2)-C(13)	1.396(5)
N(2)-C(16)	1.479(5)
C(24)-C(25)	1.505(5)
C(24)-C(12)	1.549(5)
C(26)-C(25)	1.371(6)
C(26)-C(27)	1.400(6)
C(13)-C(12)	1.501(5)
N(1)-C(29)	1.324(5)
C(16)-C(15)	1.514(6)
C(16)-C(17)	1.535(6)
C(25)-C(29)	1.398(5)
C(18)-C(19)	1.373(7)
C(18)-C(23)	1.385(8)
C(18)-C(17)	1.505(6)
C(10)-C(11)	1.522(6)
C(23)-C(22)	1.393(7)
C(19)-C(20)	1.394(7)
C(8)-C(9)	1.521(11)
C(22)-C(21)	1.363(10)
C(20)-C(21)	1.353(9)
C(6)-C(7)	1.452(10)
O(2)-Si(1)-C(10)	101.97(18)
O(2)-Si(1)-C(8)	110.6(2)
C(10)-Si(1)-C(8)	110.7(2)
O(2)-Si(1)-C(6)	115.0(2)
C(10)-Si(1)-C(6)	115.9(3)
C(8)-Si(1)-C(6)	102.8(3)
Cl(3S)-C(1S)-Cl(1S)	113.6(6)
C(5)-O(2)-Si(1)	129.5(2)
C(1)-N(3)-C(5)	117.3(3)
O(2)-C(5)-N(3)	109.2(3)
O(2)-C(5)-C(4)	114.7(3)
N(3)-C(5)-C(4)	107.3(3)
O(2)-C(5)-C(12)	108.6(3)
N(3)-C(5)-C(12)	104.3(3)
C(4)-C(5)-C(12)	112.2(3)
C(14)-O(5)-C(15)	110.9(3)
C(1)-C(2)-C(3)	108.8(3)
C(1)-C(2)-C(24)	108.1(3)
C(3)-C(2)-C(24)	107.0(3)
N(1)-C(28)-C(27)	125.4(4)
N(1)-C(28)-Cl(1)	115.4(3)
C(27)-C(28)-Cl(1)	119.2(3)
C(5)-C(4)-C(3)	109.1(3)
O(1)-C(1)-N(3)	124.2(4)
O(1)-C(1)-C(2)	125.1(3)
N(3)-C(1)-C(2)	110.7(3)
C(14)-N(2)-C(13)	129.1(3)
C(14)-N(2)-C(16)	110.5(3)
C(13)-N(2)-C(16)	120.3(3)
O(4)-C(14)-O(5)	122.6(4)
O(4)-C(14)-N(2)	129.4(4)

O(5)-C(14)-N(2)	108.0(3)
C(25)-C(24)-C(12)	115.1(3)
C(25)-C(24)-C(2)	110.4(3)
C(12)-C(24)-C(2)	108.9(3)
C(25)-C(26)-C(27)	119.6(4)
O(3)-C(13)-N(2)	117.7(3)
O(3)-C(13)-C(12)	123.2(3)
N(2)-C(13)-C(12)	119.2(3)
C(29)-N(1)-C(28)	115.8(4)
C(13)-C(12)-C(24)	110.1(3)
C(13)-C(12)-C(5)	114.0(3)
C(24)-C(12)-C(5)	108.4(3)
N(2)-C(16)-C(15)	100.5(3)
N(2)-C(16)-C(17)	110.5(3)
C(15)-C(16)-C(17)	113.8(4)
C(26)-C(25)-C(29)	116.6(3)
C(26)-C(25)-C(24)	125.4(3)
C(29)-C(25)-C(24)	118.0(3)
O(5)-C(15)-C(16)	104.2(3)
C(19)-C(18)-C(23)	117.2(4)
C(19)-C(18)-C(17)	121.7(5)
C(23)-C(18)-C(17)	121.1(5)
C(4)-C(3)-C(2)	109.8(3)
C(28)-C(27)-C(26)	117.4(4)
N(1)-C(29)-C(25)	125.1(4)
C(18)-C(17)-C(16)	109.7(3)
C(11)-C(10)-Si(1)	115.0(4)
C(18)-C(23)-C(22)	120.8(5)
C(18)-C(19)-C(20)	121.9(5)
C(9)-C(8)-Si(1)	113.4(4)
C(21)-C(22)-C(23)	120.5(6)
C(21)-C(20)-C(19)	120.0(6)
C(20)-C(21)-C(22)	119.7(5)
C(7)-C(6)-Si(1)	117.8(5)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **9**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Si(1)	36(1)	45(1)	30(1)	-1(1)	-2(1)	8(1)
Cl(1)	34(1)	83(1)	54(1)	-16(1)	-10(1)	2(1)
Cl(1S)	99(1)	119(2)	98(1)	47(1)	38(1)	41(1)
C(1S)	140(8)	83(5)	80(5)	-7(4)	7(5)	19(5)
O(2)	29(1)	35(1)	28(1)	1(1)	2(1)	7(1)
N(3)	32(1)	31(1)	24(1)	2(1)	10(1)	-2(1)
C(5)	26(2)	29(2)	24(2)	0(1)	4(1)	2(1)
O(1)	39(2)	39(2)	50(2)	-2(1)	18(1)	7(1)
O(5)	46(2)	39(2)	44(2)	-8(1)	12(1)	-4(1)
O(4)	42(2)	34(1)	44(2)	-2(1)	16(1)	-8(1)
C(2)	34(2)	24(2)	34(2)	4(1)	1(1)	2(1)
C(28)	24(2)	45(2)	41(2)	-13(2)	-3(1)	3(2)
O(3)	42(2)	53(2)	46(2)	-15(2)	21(1)	-14(1)
C(4)	31(2)	29(2)	36(2)	0(2)	3(1)	-5(1)
C(1)	29(2)	26(2)	29(2)	-8(1)	5(1)	0(1)
N(2)	31(2)	36(2)	29(2)	-3(1)	10(1)	1(1)
C(14)	37(2)	28(2)	31(2)	3(1)	1(2)	-3(2)
C(24)	34(2)	29(2)	24(2)	3(1)	5(1)	0(1)
C(26)	32(2)	40(2)	31(2)	1(2)	5(1)	4(2)
C(13)	26(2)	37(2)	27(2)	-1(1)	6(1)	-1(1)

N(1)	47(2)	57(2)	33(2)	3(2)	-7(2)	6(2)
C(12)	24(2)	29(2)	22(2)	0(1)	5(1)	-3(1)
C(16)	35(2)	42(2)	29(2)	-1(2)	8(1)	5(2)
C(25)	31(2)	34(2)	24(2)	-2(1)	4(1)	2(1)
C(15)	44(2)	51(2)	33(2)	-8(2)	9(2)	-1(2)
C(18)	31(2)	59(3)	28(2)	-4(2)	-3(1)	7(2)
C(3)	36(2)	27(2)	42(2)	2(2)	0(2)	-9(2)
C(27)	28(2)	45(2)	45(2)	-4(2)	7(2)	-7(2)
C(29)	38(2)	44(2)	35(2)	9(2)	-2(2)	-7(2)
C(17)	39(2)	62(3)	31(2)	-5(2)	5(2)	15(2)
C(10)	35(2)	51(2)	44(2)	19(2)	-7(2)	-7(2)
C(23)	40(2)	67(3)	41(2)	-9(2)	2(2)	7(2)
C(19)	53(3)	52(3)	40(2)	9(2)	1(2)	11(2)
C(8)	44(3)	46(3)	81(4)	2(3)	-17(3)	-8(2)
C(22)	39(2)	83(4)	60(3)	4(3)	9(2)	3(3)
C(20)	49(3)	72(4)	50(3)	-13(3)	2(2)	23(3)
C(21)	39(2)	101(5)	47(3)	-6(3)	10(2)	20(3)
C(6)	78(4)	77(4)	54(3)	-12(3)	8(3)	-15(3)
C(7)	110(6)	96(5)	69(4)	1(4)	19(4)	-21(5)
C(11)	67(3)	57(3)	72(4)	27(3)	-28(3)	-11(3)
C(9)	61(4)	51(3)	150(7)	-13(4)	48(4)	-10(3)
Cl(3S)	346(7)	70(2)	428(9)	26(3)	-250(7)	-22(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **9**.

	x	y	z	U(eq)
H(1SA)	11353	10670	8915	124
H(1SB)	10879	11842	9558	124
H(3A)	9018	6912	4646	34
H(2A)	9776	3028	6434	38
H(4A)	7314	4540	4829	39
H(4B)	7122	4829	5801	39
H(24A)	8874	4732	7353	35
H(26A)	10658	7675	6792	42
H(12A)	9092	7999	6540	30
H(16A)	7222	8675	8436	42
H(15A)	7693	12004	8904	51
H(15B)	8316	10337	9353	51
H(3B)	8332	2376	5340	44
H(3C)	8094	2588	6298	44
H(27A)	12194	7942	7730	48
H(29A)	10074	4047	8508	49
H(17A)	6795	11685	7227	54
H(17B)	6270	9806	7033	54
H(10A)	6714	11239	4520	55
H(10B)	7473	11034	3928	55
H(23A)	5357	8737	8211	61
H(19A)	6157	13840	8075	60
H(8A)	5201	7745	3707	74
H(8B)	5677	6040	4245	74
H(22A)	4316	9625	9085	73
H(20A)	5094	14711	8926	70
H(21A)	4221	12591	9474	74
H(6A)	6793	5760	3038	85
H(7A)	8019	6502	2413	138
H(7B)	8522	7358	3347	138
H(7C)	7824	8532	2620	138
H(11A)	6142	12589	3126	108

H(11B)	5479	10943	3224	108
H(11C)	6242	10755	2632	108
H(9A)	4732	7527	5072	125
H(9B)	5327	9311	5066	125
H(9C)	5808	7611	5606	125

Table 6. Torsion angles [°] for **9**.

C(10)-Si(1)-O(2)-C(5)	-158.6(3)
C(8)-Si(1)-O(2)-C(5)	83.6(4)
C(6)-Si(1)-O(2)-C(5)	-32.3(4)
Si(1)-O(2)-C(5)-N(3)	75.6(4)
Si(1)-O(2)-C(5)-C(4)	-44.9(4)
Si(1)-O(2)-C(5)-C(12)	-171.3(2)
C(1)-N(3)-C(5)-O(2)	172.5(3)
C(1)-N(3)-C(5)-C(4)	-62.5(4)
C(1)-N(3)-C(5)-C(12)	56.6(4)
O(2)-C(5)-C(4)-C(3)	174.5(3)
N(3)-C(5)-C(4)-C(3)	52.9(4)
C(12)-C(5)-C(4)-C(3)	-61.0(4)
C(5)-N(3)-C(1)-O(1)	-171.7(3)
C(5)-N(3)-C(1)-C(2)	6.5(4)
C(3)-C(2)-C(1)-O(1)	-128.1(4)
C(24)-C(2)-C(1)-O(1)	116.0(4)
C(3)-C(2)-C(1)-N(3)	53.7(4)
C(24)-C(2)-C(1)-N(3)	-62.2(4)
C(15)-O(5)-C(14)-O(4)	-169.5(4)
C(15)-O(5)-C(14)-N(2)	11.4(4)
C(13)-N(2)-C(14)-O(4)	9.2(7)
C(16)-N(2)-C(14)-O(4)	-174.0(4)
C(13)-N(2)-C(14)-O(5)	-171.9(4)
C(16)-N(2)-C(14)-O(5)	4.9(4)
C(1)-C(2)-C(24)-C(25)	-78.3(4)
C(3)-C(2)-C(24)-C(25)	164.6(3)
C(1)-C(2)-C(24)-C(12)	48.9(4)
C(3)-C(2)-C(24)-C(12)	-68.1(4)
C(14)-N(2)-C(13)-O(3)	173.9(4)
C(16)-N(2)-C(13)-O(3)	-2.6(5)
C(14)-N(2)-C(13)-C(12)	-6.2(6)
C(16)-N(2)-C(13)-C(12)	177.3(3)
C(27)-C(28)-N(1)-C(29)	-0.6(7)
Cl(1)-C(28)-N(1)-C(29)	179.5(3)
O(3)-C(13)-C(12)-C(24)	-71.0(5)
N(2)-C(13)-C(12)-C(24)	109.0(4)
O(3)-C(13)-C(12)-C(5)	51.1(5)
N(2)-C(13)-C(12)-C(5)	-128.9(3)
C(25)-C(24)-C(12)-C(13)	-98.0(4)
C(2)-C(24)-C(12)-C(13)	137.5(3)
C(25)-C(24)-C(12)-C(5)	136.6(3)
C(2)-C(24)-C(12)-C(5)	12.1(4)
O(2)-C(5)-C(12)-C(13)	56.7(4)
N(3)-C(5)-C(12)-C(13)	173.0(3)
C(4)-C(5)-C(12)-C(13)	-71.2(4)
O(2)-C(5)-C(12)-C(24)	179.7(3)
N(3)-C(5)-C(12)-C(24)	-63.9(3)
C(4)-C(5)-C(12)-C(24)	51.9(4)
C(14)-N(2)-C(16)-C(15)	-17.6(4)
C(13)-N(2)-C(16)-C(15)	159.5(3)
C(14)-N(2)-C(16)-C(17)	102.9(4)
C(13)-N(2)-C(16)-C(17)	-80.0(5)

C(27)-C(26)-C(25)-C(29)	2.8(6)
C(27)-C(26)-C(25)-C(24)	-175.3(4)
C(12)-C(24)-C(25)-C(26)	-43.5(5)
C(2)-C(24)-C(25)-C(26)	80.2(5)
C(12)-C(24)-C(25)-C(29)	138.4(4)
C(2)-C(24)-C(25)-C(29)	-97.9(4)
C(14)-O(5)-C(15)-C(16)	-22.5(4)
N(2)-C(16)-C(15)-O(5)	23.0(4)
C(17)-C(16)-C(15)-O(5)	-95.2(4)
C(5)-C(4)-C(3)-C(2)	3.2(5)
C(1)-C(2)-C(3)-C(4)	-57.3(4)
C(24)-C(2)-C(3)-C(4)	59.3(4)
N(1)-C(28)-C(27)-C(26)	0.1(7)
Cl(1)-C(28)-C(27)-C(26)	180.0(3)
C(25)-C(26)-C(27)-C(28)	-1.3(6)
C(28)-N(1)-C(29)-C(25)	2.3(7)
C(26)-C(25)-C(29)-N(1)	-3.5(7)
C(24)-C(25)-C(29)-N(1)	174.7(4)
C(19)-C(18)-C(17)-C(16)	105.5(5)
C(23)-C(18)-C(17)-C(16)	-73.3(5)
N(2)-C(16)-C(17)-C(18)	179.0(4)
C(15)-C(16)-C(17)-C(18)	-68.8(5)
O(2)-Si(1)-C(10)-C(11)	-173.5(4)
C(8)-Si(1)-C(10)-C(11)	-55.9(5)
C(6)-Si(1)-C(10)-C(11)	60.7(5)
C(19)-C(18)-C(23)-C(22)	-0.9(6)
C(17)-C(18)-C(23)-C(22)	178.0(4)
C(23)-C(18)-C(19)-C(20)	0.2(7)
C(17)-C(18)-C(19)-C(20)	-178.6(4)
O(2)-Si(1)-C(8)-C(9)	44.8(5)
C(10)-Si(1)-C(8)-C(9)	-67.4(5)
C(6)-Si(1)-C(8)-C(9)	168.1(5)
C(18)-C(23)-C(22)-C(21)	-0.1(8)
C(18)-C(19)-C(20)-C(21)	1.4(7)
C(19)-C(20)-C(21)-C(22)	-2.5(8)
C(23)-C(22)-C(21)-C(20)	1.9(8)
O(2)-Si(1)-C(6)-C(7)	-72.9(6)
C(10)-Si(1)-C(6)-C(7)	45.8(7)
C(8)-Si(1)-C(6)-C(7)	166.8(6)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for **9** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)

X-ray Crystallographic Data for nitrile **13**:

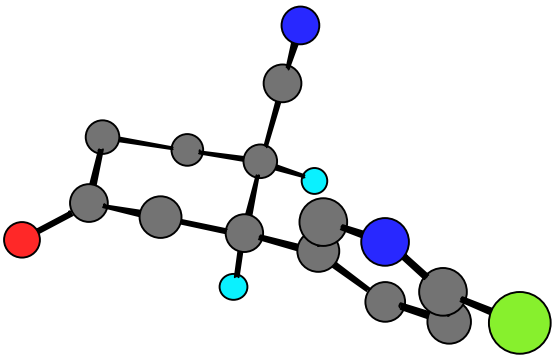


Table 1. Crystal data and structure refinement for **13**.

Identification code	cwd70t	
Empirical formula	C12 H12 Cl N O3	
Formula weight	253.68	
Temperature	213(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 6.8015(4) Å	α= 90°.
	b = 10.4147(6) Å	β= 90°.
	c = 15.7193(8) Å	γ = 90°.
Volume	1113.49(11) $Å^3$	
Z	4	
Density (calculated)	1.513 Mg/m^3	
Absorption coefficient	0.338 mm^{-1}	
F(000)	528	
Crystal size	2.2 x 2.5 x 5.0 mm^3	
Theta range for data collection	2.35 to 27.79°.	
Index ranges	-8<=h<=5, -11<=k<=12, -19<=l<=15	
Reflections collected	7135	
Independent reflections	2368 [R(int) = 0.0305]	
Completeness to theta = 27.79°	92.2 %	
Absorption correction	None	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2368 / 0 / 145	
Goodness-of-fit on F^2	1.037	
Final R indices [I>2sigma(I)]	R1 = 0.0283, wR2 = 0.0744	
R indices (all data)	R1 = 0.0313, wR2 = 0.0765	
Absolute structure parameter	-0.02(5)	
Largest diff. peak and hole	0.201 and -0.136 e.$Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **13**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	-243(1)	-4398(1)	-4582(1)	41(1)
C(7)	-7432(2)	-4206(2)	-2424(1)	27(1)
N(2)	-2207(2)	-4804(1)	-3189(1)	32(1)
C(5)	-9497(2)	-5442(2)	-1373(1)	33(1)
O(1)	-10547(2)	-6384(1)	-1376(1)	42(1)
C(8)	-5570(2)	-4157(1)	-2947(1)	26(1)

C(10)	-3890(2)	-3526(2)	-4225(1)	32(1)
C(6)	-7577(2)	-5412(2)	-1862(1)	32(1)
C(11)	-2303(2)	-4222(2)	-3930(1)	29(1)
C(12)	-3844(2)	-4756(2)	-2709(1)	31(1)
C(1)	-6081(3)	-2777(2)	-1302(1)	35(1)
N(1)	-4760(3)	-2631(2)	-866(1)	53(1)
C(3)	-9719(3)	-3032(2)	-1411(1)	36(1)
C(9)	-5538(2)	-3493(2)	-3722(1)	31(1)
C(4)	-9953(3)	-4250(2)	-875(1)	39(1)
C(2)	-7756(2)	-2976(2)	-1884(1)	29(1)

Table 3. Bond lengths [Å] and angles [°] for **13**.

Cl(1)-C(11)	1.7452(15)
C(7)-C(8)	1.5107(19)
C(7)-C(6)	1.539(2)
C(7)-C(2)	1.553(2)
N(2)-C(11)	1.315(2)
N(2)-C(12)	1.346(2)
C(5)-O(1)	1.213(2)
C(5)-C(4)	1.500(2)
C(5)-C(6)	1.515(2)
C(8)-C(12)	1.382(2)
C(8)-C(9)	1.400(2)
C(10)-C(9)	1.373(2)
C(10)-C(11)	1.381(2)
C(1)-N(1)	1.139(2)
C(1)-C(2)	1.476(2)
C(3)-C(2)	1.530(2)
C(3)-C(4)	1.530(2)
C(8)-C(7)-C(6)	113.21(12)
C(8)-C(7)-C(2)	112.84(13)
C(6)-C(7)-C(2)	110.49(12)
C(11)-N(2)-C(12)	116.06(13)
O(1)-C(5)-C(4)	123.38(15)
O(1)-C(5)-C(6)	121.45(15)
C(4)-C(5)-C(6)	115.16(14)
C(12)-C(8)-C(9)	116.45(14)
C(12)-C(8)-C(7)	123.35(13)
C(9)-C(8)-C(7)	120.20(13)
C(9)-C(10)-C(11)	117.26(13)
C(5)-C(6)-C(7)	111.31(13)
N(2)-C(11)-C(10)	125.31(14)
N(2)-C(11)-Cl(1)	115.61(12)
C(10)-C(11)-Cl(1)	119.06(11)
N(2)-C(12)-C(8)	124.58(14)
N(1)-C(1)-C(2)	178.49(17)
C(2)-C(3)-C(4)	112.92(14)
C(10)-C(9)-C(8)	120.13(14)
C(5)-C(4)-C(3)	112.24(13)
C(1)-C(2)-C(3)	112.17(13)
C(1)-C(2)-C(7)	110.20(13)
C(3)-C(2)-C(7)	111.02(13)

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **13**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}

Cl(1)	36(1)	46(1)	39(1)	-3(1)	11(1)	-2(1)
C(7)	26(1)	28(1)	28(1)	-3(1)	-2(1)	0(1)
N(2)	29(1)	34(1)	35(1)	2(1)	0(1)	3(1)
C(5)	36(1)	34(1)	28(1)	5(1)	-2(1)	-4(1)
O(1)	45(1)	41(1)	39(1)	4(1)	2(1)	-15(1)
C(8)	29(1)	25(1)	24(1)	-3(1)	-2(1)	-2(1)
C(10)	37(1)	34(1)	26(1)	5(1)	-4(1)	-3(1)
C(6)	35(1)	25(1)	37(1)	-1(1)	4(1)	-1(1)
C(11)	29(1)	28(1)	29(1)	-5(1)	3(1)	-5(1)
C(12)	30(1)	35(1)	29(1)	4(1)	1(1)	3(1)
C(1)	40(1)	31(1)	34(1)	-5(1)	2(1)	-2(1)
N(1)	48(1)	60(1)	52(1)	-18(1)	-9(1)	-3(1)
C(3)	34(1)	33(1)	42(1)	-5(1)	5(1)	4(1)
C(9)	30(1)	34(1)	30(1)	4(1)	-4(1)	3(1)
C(4)	40(1)	41(1)	36(1)	-2(1)	10(1)	-4(1)
C(2)	31(1)	24(1)	32(1)	0(1)	0(1)	1(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{3}) for **13**.

	x	y	z	U(eq)
H(7A)	-8538	-4251	-2833	33
H(10A)	-3844	-3092	-4749	39
H(6A)	-7481	-6180	-2220	39
H(6B)	-6476	-5424	-1460	39
H(12A)	-3810	-5160	-2174	37
H(3A)	-10794	-2989	-1825	44
H(3B)	-9827	-2281	-1038	44
H(9A)	-6648	-3025	-3897	38
H(4A)	-9072	-4201	-383	47
H(4B)	-11305	-4299	-663	47
H(2B)	-7805	-2236	-2278	35

Table 6. Torsion angles [°] for **13**.

C(6)-C(7)-C(8)-C(12)	-26.6(2)
C(2)-C(7)-C(8)-C(12)	99.89(18)
C(6)-C(7)-C(8)-C(9)	152.56(14)
C(2)-C(7)-C(8)-C(9)	-81.01(16)
O(1)-C(5)-C(6)-C(7)	129.45(16)
C(4)-C(5)-C(6)-C(7)	-52.12(17)
C(8)-C(7)-C(6)-C(5)	-178.07(12)
C(2)-C(7)-C(6)-C(5)	54.26(16)
C(12)-N(2)-C(11)-C(10)	3.5(2)
C(12)-N(2)-C(11)-Cl(1)	-175.08(12)
C(9)-C(10)-C(11)-N(2)	-3.5(2)
C(9)-C(10)-C(11)-Cl(1)	175.04(11)
C(11)-N(2)-C(12)-C(8)	0.5(2)
C(9)-C(8)-C(12)-N(2)	-4.0(2)
C(7)-C(8)-C(12)-N(2)	175.14(14)
C(11)-C(10)-C(9)-C(8)	-0.5(2)
C(12)-C(8)-C(9)-C(10)	3.9(2)
C(7)-C(8)-C(9)-C(10)	-175.31(14)
O(1)-C(5)-C(4)-C(3)	-132.31(17)
C(6)-C(5)-C(4)-C(3)	49.30(19)
C(2)-C(3)-C(4)-C(5)	-49.83(19)
N(1)-C(1)-C(2)-C(3)	167(7)

N(1)-C(1)-C(2)-C(7)	42(7)
C(4)-C(3)-C(2)-C(1)	-70.01(18)
C(4)-C(3)-C(2)-C(7)	53.76(17)
C(8)-C(7)-C(2)-C(1)	-58.75(16)
C(6)-C(7)-C(2)-C(1)	69.12(16)
C(8)-C(7)-C(2)-C(3)	176.35(12)
C(6)-C(7)-C(2)-C(3)	-55.77(16)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for **13** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)