Intramolecular Oxamidation of Unsaturated *O*-Alkyl Hydroxamates: A Remarkably Versatile Entry to Hydroxy Lactams

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1. General Comments

1.1 General Methods

All non-aqueous reactions were carried out in oven- or flame-dried glassware under an atmosphere of dry nitrogen, unless otherwise noted. Except as otherwise indicated, all reactions were magnetically stirred and monitored by analytical thin-layer chromatography using Merck pre-coated silica gel plates with F_{254} indicator. Visualization was accomplished by UV light and/or potassium permanganate solution. Flash column chromatography was performed according to the method of Still[1] using silica gel 60 (mesh 230-400) supplied by E. Merck. Yields refer to chromatographically and spectrographically pure compounds, unless otherwise noted.

1.2 Materials

Methanol (MeOH) was dried from magnesium methoxide, prepared from magnesium turnings and iodine. Acetonitrile (CH_3CN), dichloromethane (CH_2Cl_2), pyridine and triethylamine (Et_3N) were distilled from calcium hydride, under an atmosphere of dry nitrogen. Saturated solutions of ammonia in methanol (NH_3-MeOH) were prepared by bubbling anhydrous $NH_3(g)$ through cold (0 °C), anhydrous MeOH for 20 min. The molarity of this solution was titrated against a standardized aqueous solution of HCl using bromocresol blue as an indicator (average of three determinations). Brine refers to a saturated aqueous solution of NaCl. Phenyliodine(III) bis(trifluoroacetate) (PIFA) was prepared from phenyliodine(III) bis(acetate) using the method reported by Loudon.[2] All other reagents and starting materials, unless otherwise noted, were purchased from commercial vendors and used without further purification.

1.3 Instrumentation

All melting points were determined in unsealed Pyrex capillaries with a Thomas Hoover Unimelt melting point apparatus and are uncorrected. Infrared spectra were recorded as thin films on sodium chloride plates using an ATI Mattson Genesis series FTIR spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance 400 (400 MHz ^{1}H, 100 MHz ^{13}C) or a Bruker Avance 500 (500 MHz ^{1}H, 125 MHz ^{13}C) spectrometer. Chemical shift values (δ) are reported in ppm relative to residual

1. Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
2. G. M. Loudon, A. S. Radhakrishna, M. R. Almond, J. K. Blodgett, R. H. Boutin, *J. Org. Chem.,* 1984, **49**, 4272

chloroform (δ 7.27 ppm for ^{1}H; δ 77.23 ppm for ^{13}C), methanol (δ 3.31 ppm for ^{1}H; δ 49.15 ppm for ^{13}C), acetone (δ 2.05 ppm for ^{1}H; δ 29.92 ppm for ^{13}C) and dimethyl sulfoxide (δ 2.50 ppm for ^{1}H; δ 39.51 ppm for ^{13}C). Multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), p (pentet), h (heptet), m (multiplet) and br (broad) app (apparent). The identification of ^{1}H and ^{13}C signals was achieved using a combination of ^{1}H, ^{13}C, DEPT, COSY, HMBC, HMQC and NOESY experiments. High-resolution electrospray ionization (HRMS-ESI) mass spectra were obtained on a Micro Mass QTOF II instrument at the University of Illinois Research Resources Center.

1.4 Literature Preparations

(*E*)-Hex-4-enoic acid (**11c**), (*E*)-hept-4-enoic acid (**11d**), 4-methylpent-4-enoic acid (**11g**), (*E*)-4-methylhex-4-enoic acid (**11j**), (*E*)-5-phenylpent-4-enoic acid (**11v**), and (*E*)-5-(4-trifluoromethylphenyl)pent-4-enoic acid (**11w**) were prepared by the method of Johnson.[3] (*E*)-Pent-3-enoic acid (**11b**),[4] (*E*)-oct-6-enoic acid (**11f**),[5] 5-methylhex-5-enoic acid (**11h**) and 6-methylhept-6-enoic acid (**11i**),[6] *endo*-(±)-bicyclo[2.2.1]hep-5-ene-2-carboxylic acid (**11l**),[7] 1-methylcyclopent-3-enecarboxylic acid (**11m**),[8] (±)-4-methylcyclohex-3-enecarboxylic acid (**11p**),[9] (1*R**,5*S**)-5-azidocyclohex-3-enecarboxylic acid (**11q**),[10] (1*R**,5*S**)-5-ethylcyclohex-3-enecarboxylic acid (**11r**),[11] *cis*-5-hydroxycyclohex-3-enecarboxylic acid,[12] *cis*/*trans*-5-hydroxycyclohex-3-enecarboxylic acid,[13] and (*E*)-5-(4-methoxyphenyl)pent-4-enoic acid (**11x**),[14] and were prepared according to literature methods.

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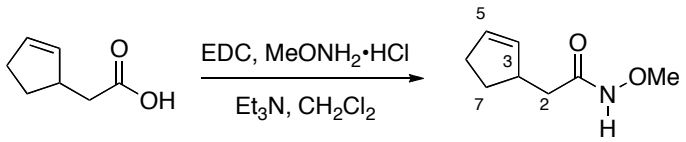
2 Experimental Details

2.1 Preparation of Cyclization Substrates

2.1.1 Representative Procedure 1. Preparation of *O*-Alkyl Hydroxamates

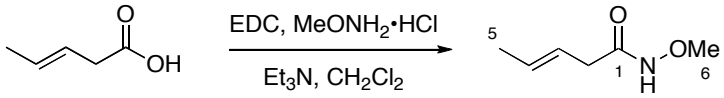
***O*-Methyl (±)-2-cyclopent-2-enyl-acetohydroxamate (1a).**



11a **1a**

To a solution of **11a** (750 mg, 5.94 mmol, 1.0 equiv) in CH_2Cl_2 (8.0 mL) was added Et_3N (1.33 mL, 9.50 mmol, 1.6 equiv) and the mixture stirred for 5 min. EDC (2.05 g, 10.69 mmol, 1.8 equiv) and $MeONH_2$•HCl (793 mg, 9.50 mmol, 1.6 equiv) were then added in one portion. After 10 h, aqueous HCl (1 M, 20 mL) was added and the aqueous phase extracted with EtOAc (4 x 15 mL). The combined organic extracts were dried (Na_2SO_4), filtered and concentrated under reduced pressure. The residue purified by flash chromatography on silica gel (EtOAc) to provide **1a** (921 mg, 99%): colorless oil; R_f 0.33 (EtOAc); IR (film) υ_{max} 3180, 2940, 1659, 1518, 1361, 1191, 982, 943, 697 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.82-5.74 (m, 1 H), 5.70-5.62 (m, 1 H), 3.68 (s, 3 H, H-8), 3.09-3.02 (m, 1 H, H-3), 2.44-2.34 (m, 1 H), 2.34-2.24 (m, 1 H), 2.14 (dd, *J* = 13.8, 6.9 Hz, 1 H), 2.11-2.04 (m, 1 H), 2.02 (dd, *J* = 13.8, 8.2 Hz, 1 H), 1.48 (ddt, *J* = 12.6, 9.0, 6.2 Hz, 1 H); ^{13}C NMR (125 MHz, CD_3OD) δ 170.3 (C-1), 133.2, 131.0, 62.9 (C-8), 42.3 (C-3), 38.4, 31.2, 28.9; HRMS-ESI calcd for $C_8H_{13}NO_2Na$ $[M+Na]^+$ 178.0844, found: 178.0840.

***O*-Methyl (*E*)-pent-3-enohydroxamate (1b).**

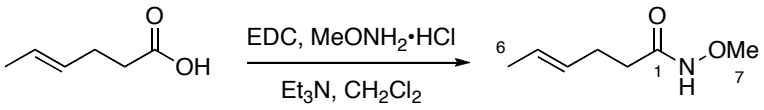


11b **1b**

Following Representative Procedure 1, a solution of **11b** (1.00 g, 9.98 mmol, 1.0 equiv) in CH_2Cl_2 (13.0 mL) was treated sequentially with Et_3N (2.20 mL, 15.9 mmol, 1.6 equiv), EDC (3.42 g, 17.9 mmol, 1.8 equiv) and $MeONH_2$•HCl (1.32 g, 15.9 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1b** (1.15 g, 89%):

colorless oil; R_f 0.36 (EtOAc); IR (film) υ_{max} 3176, 2973, 2942, 1651, 1513, 1441, 1063, 969 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.67-5.57 (m, 1 H), 5.53-5.44 (m, 1 H), 3.67 (s, 3 H, H-6), 2.78 (dd, *J* = 6.9, 1.0 Hz, 2 H, H-2), 1.72-1.65 (m, 3 H, H-5); ^{13}C NMR (125 MHz, CD_3OD) δ 169.6 (C-1), 129.3, 122.9, 62.9 (C-6), 36.4 (C-2), 16.7 (C-5); HRMS-ESI calcd for $C_6H_{12}NO_2$ $[M+H]^+$ 130.0868, found: 130.0872.

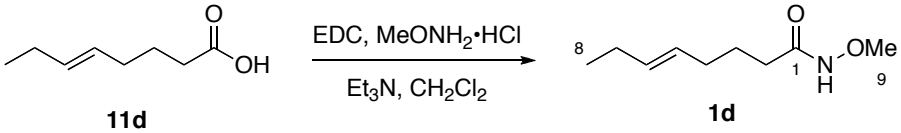
***O*-Methyl (*E*)-hex-4-enohydroxamate (1c).**



11c **1c**

Following Representative Procedure 1, a solution of **11c** (1.58 g, 13.8 mmol, 1.0 equiv) in CH_2Cl_2 (18.0 mL) was treated sequentially with Et_3N (3.10 mL, 22.1 mmol, 1.6 equiv), EDC (4.76 g, 24.9 mmol, 1.8 equiv) and $MeONH_2$•HCl (1.84 g, 22.1 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1c** (1.87 g, 94%): colorless oil; R_f 0.45 (EtOAc); IR (film) υ_{max} 3183, 2968, 2940, 1660, 1515, 1442, 1370, 1067, 969 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 10.07 (br s, 1 H, NH), 5.45-5.33 (m, 2 H, H-4, H-5), 3.68 (s, 3 H, H-7), 2.27-2.24 (m, 2 H), 2.14-2.11 (m, 2 H), 1.55 (d, *J* = 6.8 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0 (C-1), 129.5, 126.7, 64.4 (C-7), 33.4, 28.7, 18.2 (C-6); HRMS-ESI calcd for $C_7H_{13}NO_2Na$ $[M+Na]^+$ 166.0844, found: 166.0843.

***O*-Methyl (*E*)-oct-5-enehydroxamate (1d).**

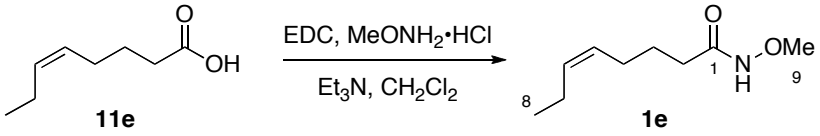


11d **1d**

Following Representative Procedure 1, a solution of **11d** (2.48 g, 17.4 mmol, 1.0 equiv) in CH_2Cl_2 (30.0 mL) was treated sequentially with Et_3N (3.90 mL, 27.9 mmol, 1.6 equiv), EDC (6.00 g, 31.3 mmol, 1.8 equiv) and $MeONH_2$•HCl (2.33 g, 27.9 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1d** (2.96 g, 99%): colorless oil; R_f 0.48 (EtOAc); FTIR (film) υ_{max} 3169, 2963, 2936, 1658, 1515, 1449, 1073, 967, 915, 743 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.48 (dt, *J* = 15.3, 5.9 Hz, 1 H), 5.37 (dt, *J* = 15.3, 6.2 Hz, 1 H)), 3.62 (s, 3 H, H-9), 2.14-1.98 (m, 6 H), 1.68-1.62 (m, 2 H), 0.93 (t, *J* = 7.5 Hz, 3 H, H-8); ^{13}C NMR (125 MHz, CD_3OD) δ 172.8 (C-1), 133.2,

128.2, 63.3 (C-9), 32.2, 32.0, 25.6, 25.5, 13.4 (C-8); HRMS-ESI calcd for $C_9H_{17}NO_2Na$ $[M+Na]^+$ 194.1157, found 194.1151.

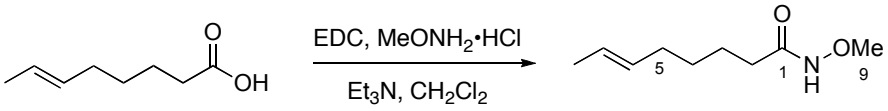
***O*-Methyl (*Z*)-oct-5-enehydroxamate (1e).**



11e **1e**

Following Representative Procedure 1, a solution of **11e** (1.05 g, 7.38 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL) was treated sequentially with Et_3N (1.60 mL, 11.8 mmol, 1.6 equiv), EDC (2.54 g, 13.3 mmol, 1.8 equiv) and $MeONH_2$•HCl (986 mg, 11.8 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1e** (1.25 g, 99%): colorless oil; R_f 0.50 (EtOAc); FTIR (film) υ_{max} 3189, 2965, 3872, 1662, 1517, 1459, 1372, 1076, 1035, 942, 711, 572 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.43-5.37 (m, 1 H), 5.30-5.28 (m, 1 H), 3.67 (s, 3 H, H-9), 2.08-1.99 (m, 6 H), 1.68-1.62 (m, 2 H), 0.94 (t, J = 7.6 Hz, 3 H, H-8); ^{13}C NMR (125 MHz, CD_3OD) δ 171.6 (C-1), 132.6, 127.9, 63.3 (C-9), 32.2 (C-2), 26.3, 25.6, 20.4, 13.7 (C-8); HRMS-ESI calcd for $C_9H_{18}NO_2$ $[M+H]^+$ 172.1338, found 172.1343.

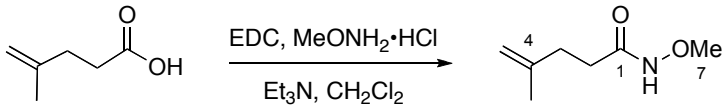
***O*-Methyl (*E*)-oct-6-enohydroxamate (1f).**



11f **1f**

Following Representative Procedure 1, a solution of **11f** (1.00 g, 7.04 mmol, 1.0 equiv) in CH_2Cl_2 (6.0 mL) was treated sequentially with Et_3N (1.56 mL, 11.3 mmol, 1.6 equiv), EDC (2.44 g, 12.7 mmol, 1.8 equiv) and $MeONH_2$•HCl (940 mg, 11.3 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1f** (0.91 g, 76%): white solid; R_f 0.55 (EtOAc); IR (film) υ_{max} 3181, 2997, 2934, 2856, 1657, 1515, 1439, 1376, 1059, 967 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.48-5.36 (m, 2 H, H-6, H-7), 3.67 (s, 3 H, H-9), 2.06 (t, J = 7.5 Hz, 2 H, H-2), 2.02-1.96 (m, 2 H, H-5), 1.63 (d, J = 4.8 Hz, 3 H, H-8), 1.60 (p, J = 7.5 Hz, 2 H), 1.36 (p, J = 7.5 Hz, 2 H); ^{13}C NMR (125 MHz, CD_3OD) δ 171.7 (C-1), 131.0, 125.2, 63.3 (C-9), 32.6, 32.2, 29.0, 25.1, 17.1 (C-8); HRMS-ESI calcd for $C_9H_{15}NO_2$ $[M+H]^+$ 172.1338, found: 172.1342.

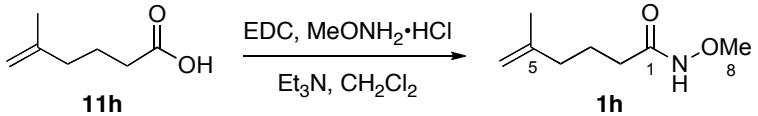
***O*-Methyl 4-methyl-pent-4-enohydroxamate (1g).**



11g **1g**

Following Representative Procedure 1, a solution of **11g** (500 mg, 4.38 mmol, 1.0 equiv) in CH_2Cl_2 (6.0 mL) was treated sequentially with Et_3N (984 μL, 7.00 mmol, 1.6 equiv), EDC (1.47 g, 7.70 mmol, 1.8 equiv) and $MeONH_2$•HCl (585 mg, 7.00 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1g** (589 mg, 94%): colorless oil; R_f 0.38 (EtOAc); IR (film) υ_{max} 3413, 2971, 2929, 1692, 1590, 1380, 1050, 750, 704 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 4.75 (s, 1 H, H-5), 4.71 (s, 1 H, H-5), 3.67 (s, 3 H, H-7), 2.31 (t, J = 7.6 Hz, 2 H), 2.21 (t, J = 7.7 Hz, 2 H), 1.74 (s, 3 H, H-6); ^{13}C NMR (125 MHz, CD_3OD) δ 170.7 (C-1), 143.8 (C-4), 109.9 (C-5), 62.9 (C-7), 32.8, 30.8, 21.1 (C-6); HRMS-ESI calcd for $C_7H_{13}NO_2Na$ $[M+Na]^+$ 166.0844, found: 166.0851.

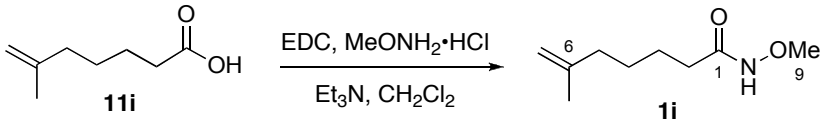
***O*-Methyl 5-methyl-hex-5-enohydroxamate (1h).**



11h **1h**

Following Representative Procedure 1, a solution of **11h** (1.00 g, 7.8 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL) was treated sequentially with Et_3N (1.27 mL, 9.0 mmol, 1.15 equiv), EDC (1.57 g, 8.20 mmol, 1.05 equiv) and $MeONH_2$•HCl (715 mg, 8.6 mmol, 1.1 equiv) to provide, after purification by flash chromatography (EtOAc), **1h** (1.04 g, 85%): colorless oil; R_f 0.49 (EtOAc); IR (film) υ_{max} 3179, 2967, 2936, 1653, 1519, 1456, 1084, 1049, 888 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 4.73 (s, 1 H, H-6), 4.69 (s, 1 H, H-6), 3.68 (s, 3 H, H-8), 2.10-1.99 (m, 4 H), 1.75 (p, J = 7.7 Hz, 2 H, H-3), 1.71 (s, 3 H, H-7); ^{13}C NMR (125 MHz, CD_3OD) δ 171.5 (C-1), 145.0 (C-5), 110.3 (C-6), 63.3 (C-8), 37.0, 32.1, 23.4, 21.4 (C-7); HRMS-ESI calcd for $C_8H_{15}NO_2Na$ $[M+Na]^+$ 180.1000, found: 180.1006.

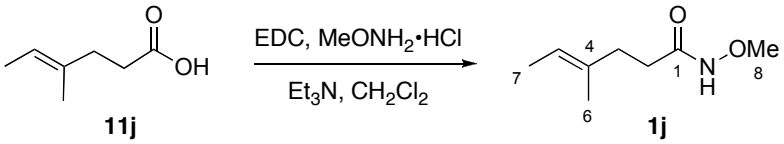
***O*-Methyl 6-methyl-hept-6-enohydroxamate (1i).**



11i **1i**

Following Representative Procedure 1, a solution of **11i** (1.03 g, 7.26 mmol, 1.0 equiv) in CH_2Cl_2 (15.0 mL) was treated sequentially with Et_3N (1.16 mL, 8.4 mmol, 1.15 equiv), EDC (1.46 g, 7.62 mmol, 1.05 equiv) and $MeONH_2$•HCl (660 mg, 8.0 mmol, 1.1 equiv) to provide, after purification by flash chromatography (EtOAc), **1i** (0.85 g, 69%): colorless oil; R_f 0.51 (EtOAc); IR (film) υ_{max} 3182, 2967, 2935, 1653, 1520, 1507, 1456, 1438, 1089, 1053, 886 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 4.69 (s, 1 H, H-7), 4.67 (s, 1 H, H-7), 3.68 (s, 3 H, H-9), 2.08 (t, J = 7.4, 7.4 Hz, 2 H), 2.04 (t, J = 7.5, 7.5 Hz, 2 H), 1.70 (s, 3 H, H-8), 1.64-1.54 (m, 2 H), 1.51-1.40 (m, 2 H); ^{13}C NMR (100 MHz, CD_3OD) δ 171.2 (C-1), 145.1 (C-6), 109.4 (C-7), 62.9 (C-9), 37.0, 32.2, 26.6, 24.7, 21.0 (C-8); HRMS-ESI calcd for $C_9H_{18}NO_2$ $[M+H]^+$ 172.1338, found: 172.1342.

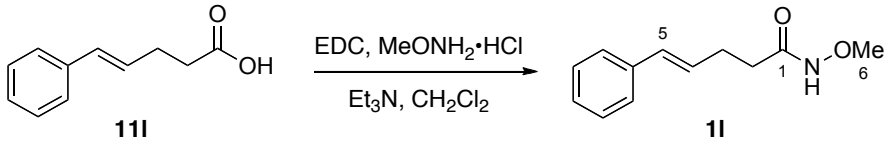
***O*-Methyl (*E*)-4-methyl-hex-4-enohydroxamate (1j).**



11j **1j**

Following Representative Procedure 1, a solution of **11j** (200 mg, 1.55 mmol, 1.0 equiv) in CH_2Cl_2 (3.0 mL) was treated sequentially with Et_3N (348 μL, 2.48 mmol, 1.6 equiv), EDC (533 mg, 2.79 mmol, 1.8 equiv) and $MeONH_2$•HCl (207 mg, 2.48 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1j** (229 mg, 93%): colorless oil; R_f 0.48 (EtOAc); IR (film) υ_{max} 3216, 2977, 2937, 2859, 1654, 1436, 1383, 1201, 1076, 976 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 9.23 (br s, 1 H, NH), 5.24 (q, J = 6.8 Hz, 1 H, H-6), 3.67 (s, 3 H, H-8), 2.31-2.18 (m, 2 H), 2.13-2.05 (m, 2 H), 1.59 (s, 3 H, H-7), 1.54 (d, J = 6.8 Hz, 3 H, H-6); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3 (C-1), 134.3 (C-5), 120.2 (C-4), 64.6 (C-8), 35.4, 32.4, 15.9, 13.8; HRMS-ESI calcd for $C_8H_{15}NO_2Na$ $[M+Na]^+$ 181.1000, found: 181.1007.

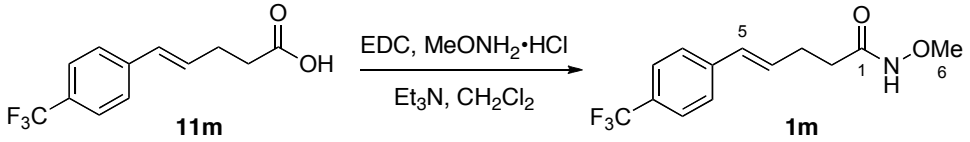
***O*-Methyl (*E*)-5-phenyl-pent-4-enohydroxamate (1l).**



11l **1l**

Following Representative Procedure 1, a solution of **11l** (501 mg, 2.84 mmol, 1.0 equiv) in CH_2Cl_2 (4.0 mL) was treated sequentially with Et_3N (638 μL, 4.54 mmol, 1.6 equiv), EDC (980 mg, 5.11 mmol, 1.8 equiv) and $MeONH_2$•HCl (379 mg, 4.54 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1l** (579 mg, 99%): white solid: mp 55-56 °C; R_f 0.48 (EtOAc); IR (film) υ_{max} 3181, 2996, 2936, 1656, 1516, 1494, 1440, 1071, 965, 745 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 7.34 (d, J = 7.5 Hz, 2 H, Ph), 7.26 (t, J = 7.6 Hz, 2 H, Ph), 7.17 (t, J = 7.3 Hz, 1 H, Ph), 6.44 (d, J = 15.8 Hz, 1 H, H-5), 6.21 (dt, J = 15.7, 7.0 Hz, 1 H, H-4), 3.64 (s, 3 H, H-6), 2.53-2.48 (m, 2 H, H-3), 2.23 (t, J = 7.3 Hz, 2 H, H-2); ^{13}C NMR (125 MHz, CD_3OD) δ 170.5 (C-1), 137.3, 131.1, 128.1, 127.6, 126.8, 125.6, 63.0 (C-6), 32.2, 28.4; HRMS-ESI calcd for $C_{12}H_{15}NO_2Na$ $[M+Na]^+$ 228.1000, found: 228.0992.

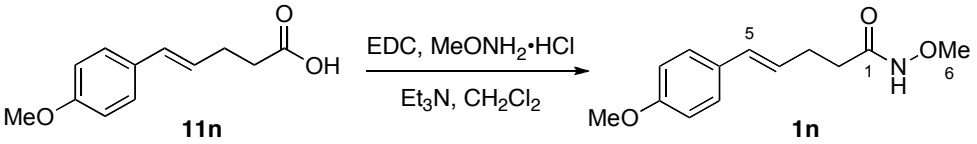
***O*-Methyl (*E*)-5-(4-trifluoromethylphenyl)-pent-4-enohydroxamate (1m).**



11m **1m**

Following Representative Procedure 1, a solution of **11m** (1.01 g, 4.14 mmol, 1.0 equiv) in CH_2Cl_2 (6.0 mL) was treated sequentially with Et_3N (620 μL, 4.35 mmol, 1.05 equiv), EDC (0.87 g, 4.6 mmol, 1.1 equiv) and $MeONH_2$•HCl (360 mg, 4.35 mmol, 1.05 equiv) to provide, after purification by flash chromatography (EtOAc), **1m** (0.97 g, 86%): white solid; mp 79-81 °C (CH_2Cl_2/hexanes); R_f 0.38 (EtOAc); IR (film) υ_{max} 3217, 3004, 2819, 1652, 1591, 1330, 1110, 1068 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 7.57 (d, J = 8.4 Hz, 2 H, Ar), 7.52 (d, J = 8.4 Hz, 2 H, Ar), 6.52 (d, J = 15.9 Hz, 1 H, H-5), 6.44-6.35 (m, 1 H, H-4), 3.65 (s, 3 H, H-6), 2.58-2.51 (m, 2 H, H-3), 2.26 (t, J = 7.3 Hz, 2 H, H-2); ^{13}C NMR (125 MHz, CD_3OD) δ 171.9 (C-2), 142.8, 132.6, 131.2, 130.0 (q, J_{C-F} = 32.0 Hz), 127.6, 126.6, 125.9 (q, J_{C-F} = 269 Hz), 64.5 (C-6), 33.4, 30.0; HRMS-ESI calcd for $C_{13}H_{15}NO_2F_3$ $[M+H]^+$ 274.1055, found: 274.1061.

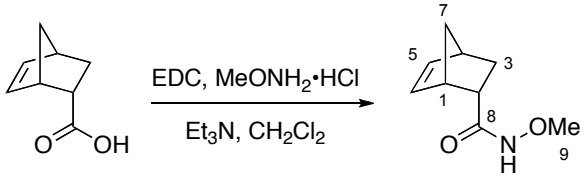
***O*-Methyl (*E*)-5-(4-methylphenyl)-pent-4-enohydroxamate (1n).**



11n **1n**

Following Representative Procedure 1, a solution of **11n** (0.95 g, 4.28 mmol, 1.0 equiv) in CH_2Cl_2 (6.0 mL) was treated sequentially with Et_3N (620 μL, 4.49 mmol, 1.05 equiv), EDC (0.90 g, 4.71 mmol, 1.1 equiv) and $MeONH_2$•HCl (370 mg, 4.49 mmol, 1.05 equiv) to provide, after purification by flash chromatography (EtOAc), **1n** (0.81 g, 76%): white solid; mp 106-108 °C (CH_2Cl_2/hexanes); R_f 0.41 (EtOAc); IR (film) υ_{max} 3219, 3012, 2956, 2937, 1653, 1558, 1540, 1506, 1253, 966 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 7.30-7.22 (m, 2 H, Ar), 6.85-6.79 (m, 2 H, Ar), 6.38 (d, *J* = 15.8 Hz, 1 H, H-5), 6.05 (dt, *J* = 15.8, 7.3 Hz, 1 H, H-4), 3.76 (s, 3 H, OMe), 3.64 (s, 3 H, OMe), 2.47 (m, 2 H, H-3), 2.21 (t, *J* = 7.3 Hz, 2 H, H-2); ^{13}C NMR (125 MHz, CD_3OD) δ 171.0 (C-1), 159.5, 131.0, 130.5, 127.2, 125.6, 113.9, 63.4, 54.6, 32.8, 28.9; HRMS-ESI calcd for $C_{13}H_{18}NO_3$ $[M+H]^+$ 236.1287, found: 236.1288.

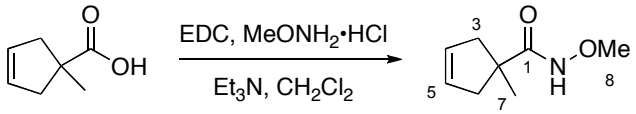
***O*-Methyl (±)-bicyclo[2.2.1]hept-5-ene-2-carbohydroxamate (1o).**



11o **1o**

Following Representative Procedure 1, a solution of **11o** (250 mg, 1.80 mmol, 1.0 equiv) in CH_2Cl_2 (3.0 mL) was treated sequentially with Et_3N (404 μL, 2.88 mmol, 1.6 equiv), EDC (621 mg, 3.24 mmol, 1.8 equiv) and $MeONH_2$•HCl (240 mg, 2.88 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1o** (290 mg, 96%): colorless oil; R_f 0.32 (EtOAc); IR (film) υ_{max} 3197, 2972, 2871, 1660, 1506, 1446, 1337, 1223, 1081, 923, 846, 776, 709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.35 (br s, 1 H, NH), 6.17 (dd, *J* = 5.6, 3.1 Hz, 1 H), 5.93 (dd, *J* = 5.6, 2.7 Hz, 1 H), 3.67 (s, 3 H, H-9), 3.11 (s, 1 H, H-2), 2.87 (br s, 1 H), 2.77 (br s, 1 H), 2.01 (d, *J* = 5.8 Hz, 1 H), 1.87-1.81 (m, 1 H), 1.39-1.34 (m, 1 H), 1.24-1.20 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5 (C-8), 137.7, 131.9, 63.9 (C-9), 49.9, 46.3, 42.6, 41.7, 29.2; HRMS-ESI calcd for $C_9H_{13}NO_2Na$ $[M+Na]^+$ 178.0844, found: 178.0836.

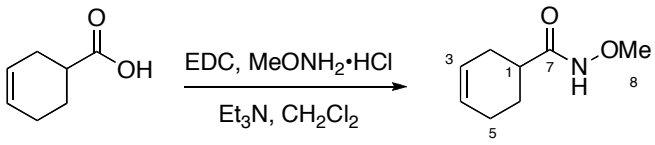
***O*-Methyl 1-methyl-cyclopent-3-enecarbohydroxamate (1p).**



11p **1p**

Following Representative Procedure 1, a solution of **11p** (530mg, 4.2 mmol, 1.0 equiv) in CH_2Cl_2 (6.0 mL) was treated sequentially with Et_3N (914 μL, 6.5 mmol, 1.6 equiv), EDC (1.33 g, 6.9 mmol, 1.7 equiv) and $MeONH_2$•HCl (684 mg, 8.2 mmol, 2.0 equiv) to provide, after purification by flash chromatography (EtOAc/hexanes, 3:1), **3p** (575 mg, 88%): colorless oil; R_f 0.41 (EtOAc/hexanes, 3:1); FTIR (film) υ_{max} 3165, 2984, 2898, 1650, 1533, 1069, 937, 688, 652 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.62 (s, 2 H, H-4/5), 3.67 (s, 3 H, H-8), 2.79 (d, J = 14.7 Hz, 2 H), 2.19 (d, J = 14.8 Hz, 2 H), 1.24 (s, 3 H, H-7); ^{13}C NMR (125 MHz, CD_3OD) δ 177.9 (C-1), 129.3, 64.2 (C-8), 48.3 (C-2), 45.3 (C-3/6), 26.7 (C-7); HRMS-ESI calcd for $C_8H_{13}NO_2Na$ $[M+Na]^+$ 178.0844, found: 178.0838.

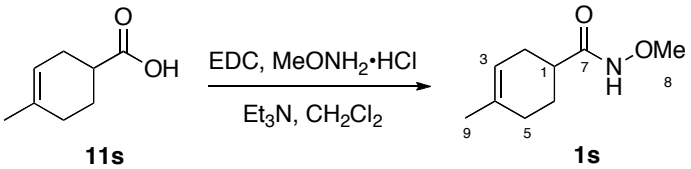
***O*-Methyl (±)-cyclohex-3-enecarbohydroxamate (1q).**



11q **1q**

Following Representative Procedure 1, a solution of **11q** (1.00 g, 7.93 mmol, 1.0 equiv) in CH_2Cl_2 (11.0 mL) was treated sequentially with Et_3N (1.78 mL, 12.7 mmol, 1.6 equiv), EDC (2.73 g, 14.2 mmol, 1.8 equiv) and $MeONH_2$•HCl (1.06 g, 12.7 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1q** (1.15 g, 93%): white solid: mp 68-69 °C; R_f 0.43 (EtOAc); FTIR (film) υ_{max} 3164, 2930, 1655, 1516, 1444, 1087, 1944, 918, 744, 650 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.71-5.56 (m, 2 H, H-3, H-4), 3.68 (s, 3 H, H-8), 2.33-2.12 (m, 2 H), 2.12-1.93 (m, 3 H), 1.83-1.69 (m, 1 H), 1.69-1.54 (m, 1 H); ^{13}C NMR (100 MHz, CD_3OD) δ 175.7 (C-7), 127.6, 126.3, 64.4 (C-8), 39.4 (C-8), 28.8, 26.8, 25.8; HRMS-ESI calcd for $C_8H_{13}NO_2Na$ $[M+Na]^+$ 178.0844, found: 178.0836.

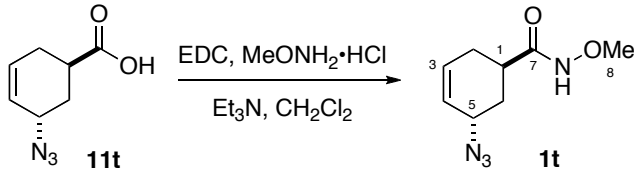
***O*-Methyl (±)-4-methylcyclohex-3-enohydroxamate (1s).**



11s **1s**

Following Representative Procedure 1, a solution of **11s** (500 mg, 3.57 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL) was treated sequentially with Et_3N (0.70 mL, 5.71 mmol, 1.6 equiv), EDC (1.23 g, 6.42 mmol, 1.8 equiv), and $MeONH_2$•HCl (476 mg, 5.71 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1s** (0.49 g, 81%): white solid; m.p. 102-103 ºC; R_f 0.51 (EtOAc); FTIR (film) υ_{max} 3164, 2966, 2928, 2907, 1650, 1525, 1441, 1381, 1254, 1235, 1201, 1144, 1082, 1054, 1000, 938, 918, 833, 796 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.70 (s, 1H, NH), 5.34 (s, 1H, H-3), 3.71 (s, 3H, H-8), 2.24-2.17 (m, 2H, H-1, H-2), 2.12-1.89 (m, 3H, H-2, H-6), 1.87-1.80 (m, 1H, H-5), 1.77-1.66 (m, 1H, H-5), 1.62 (s, 3H, H-9); ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.3 (C-7), 133.8 (C-4), 119.4 (C-3), 64.2 (C-8), 38.2 (C-1), 29.5, 28.0, 25.9, 23.6 (C-9); HRMS-ESI calcd for $C_9H_{16}NO_2$ $[M+H]^+$ 170.1181, found: 170.1177.

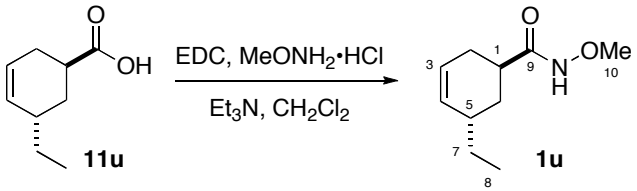
***O*-Methyl (±)-*trans*-5-azidocyclohex-3-enohydroxamate (1t).**



11t **1t**

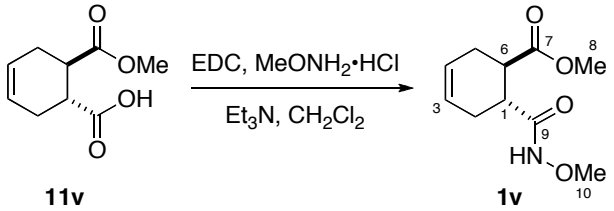
Following Representative Procedure 1, a solution of **11t** (753 mg, 4.50 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL) was treated sequentially with Et_3N (0.89 mL, 7.21 mmol, 1.6 equiv), EDC (1.56 g, 8.11 mmol, 1.8 equiv), and $MeONH_2$•HCl (602 mg, 7.21 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1t** (0.51 g, 58%): white solid; m.p. 72-73 °C; R_f 0.51 (EtOAc); IR (film) υ_{max} 3185, 3033, 2975, 2932, 2099, 1660, 1514, 1442, 1315, 1231, 1067, 1034, 938, 889, 821, 755 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 6.07 (ddd, J = 9.8, 4.6, 2.3 Hz, 1H, H-3), 5.84-5.79 (m, 1H, H-4), 4.06 (br s, 1H, H-5), 3.68 (s, 3H, H-8), 2.48-2.40 (m, 1H, H-1), 2.29-2.13 (m, 2H, H-2, H-6), 1.9-1.85 (m, 2H, H-2, H-6); ^{13}C NMR (500 MHz, CD_3OD) δ 174.4 (C-1), 132.6, 124.3, 64.5 (C-8), 55.5 (C-5), 34.7, 32.7, 28.9; Elemental analysis calcd for C 48.96%, H 6.18%, N 28.56%, found C 49.26%, H 6.07%, N 28.35%.

***O*-Methyl (±)-*trans*-5-ethylcyclohex-3-enohydroxamate (1u).**



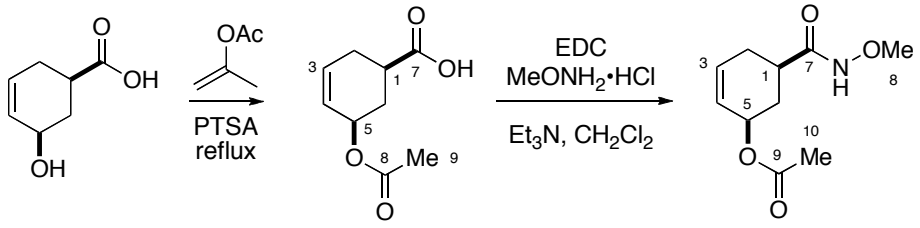
Following Representative Procedure 1, a solution of **11u** (500 mg, 3.24 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL) was treated sequentially with Et_3N (0.64 mL, 5.18 mmol, 1.6 equiv), EDC (1.12 g, 5.83 mmol, 1.8 equiv), and $MeONH_2$•HCl (433 mg, 5.18 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1u** (0.43 g, 72%): white solid; m.p. 52-54 °C; R_f 0.58 (EtOAc); IR (film) υ_{max} 3171, 3020, 2962, 2932, 2871, 1659, 1514, 1461, 1067 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 5.70-5.62 (m, 2H, H-3, H-4), 3.66 (s, 3H, H-10), 2.35-2.29 (m, 1H, H-1), 2.22-2.16 (m, 1H, H-2), 2.06-2.02 (m, 2H, H-2, H-5), 1.80 (dt, J = 13.1, 5.9 Hz, 1H, H-6), 1.63 (d, J = 13.1 Hz, 1H, H-6), 1.46-1.37 (m, 1H, H-7), 1.35-1.26 (m, 1H, H-7), 0.93 (t, J = 7.4 Hz, 3H, H-8); ^{13}C NMR (500 MHz, CD_3OD) δ 175.7 (C-9), 132.0, 125.7, 64.4 (C-10), 36.8, 35.5, 31.2, 29.6, 28.9, 12.5 (C-8); HRMS-ESI calcd for $C_{10}H_{18}NO_2$ $[M]^+$ 184.1338, found: 184.1334.

***O*-Methyl (±)-*trans*-6-(methoxycarbamoyl)cyclohex-3-enohydroxamate (1v).**



Following Representative Procedure 1, a solution of **11v** (0.58 g, 3.15 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL) was treated sequentially with Et_3N (0.621 mL, 5.05 mmol, 1.6 equiv), EDC (1.09 g, 5.67 mmol, 1.8 equiv), and $MeONH_2$•HCl (422 mg, 5.05 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1v** (0.40 g, 60%): white solid; m.p. 74-75 ºC; R_f 0.52 (EtOAc); FTIR (film) υ_{max} 3186, 2992, 2951, 2933, 1736, 1656, 1437, 1210, 1196, 1173, 1060, 658 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.72-5.66 (m, 2H, H-3, H-4), 3.65 (s, 6H, H-8, H-10), 2.83 (dt, J = 11.5, 5.5 Hz, 1H, H-6), 2.47 (dt, J = 11.5, 8.3 Hz, 1H, H-1), 2.43-2.37 (m, 1H, H-5), 2.22-2.17 (m, 2H, H-2, H-5), 2.16-2.06 (m, 1H, H-2); ^{13}C NMR (400 MHz, CD_3OD) δ 176.7, 174.3, 126.3, 126.0, 64.3, 52.5, 42.6, 41.1, 30.0, 29.5; HRMS-ESI calcd for $C_{10}H_{16}NO_4$ $[M+H]^+$ 214.1079, found: 214.1075.

***O*-Methyl (±)-*cis*-cyclohex-3-enohydroxam-5-yl ethanoate (1t).**



Part 1.

***cis*-(±)-5-(Ethanoyloxy)cyclohex-3-enecarboxylic acid (11w).**

A solution of (±)-*cis*-5-hydroxycyclohex-3-enecarboxylic acid (0.25 g, 1.60 mmol, 1.0 equiv) and PTSA (30 mg, 0.16 mmol, 0.1 equiv) in isopropenyl acetate (4.0 mL) was heated at reflux for 1 h. After cooling to room temperature, the reaction mixture was concentrated, partitioned between aqueous K_2CO_3 (0.5 M) and EtOAc. The aqueous phase was separated, acidified aq. HCl (1 M), and then extracted with EtOAc. These organic extracts were dried over Na_2SO_4, and concentrated under reduced pressure to provide **11w** (66.6 mg, 23%): yellow oil; R_f 0.63 (EtOAc); FTIR (film) υ_{max} 3039, 2935, 2852, 2749, 1738, 1708, 1657, 1457, 1436, 1373, 1241, 1152, 1031, 955, 924, 749, 700, 626 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.89 (ddt, J = 10.1, 3.6, 1.8 Hz, 1H, H-3), 5.66 (dd, J = 10.6, 1.8 Hz, 1H, H-4), 5.40 (ddd, J = 10.6, 5.6, 2.3 Hz, 1H, H-5), 2.76 (ddt, J = 11.2, 7.6, 3.1 Hz, 1H, H-1), 2.42-2.30 (m, 3H, H-2, H-6), 2.10 (s, 3H, H-9), 1.80 (dt, J = 12.1, 8.9 Hz, 1H, H-6); ^{13}C NMR (400 MHz, $CDCl_3$) δ 180.6 (C-7), 171.0 (C-8), 129.3, 126.8, 69.1 (C-5), 37.7, 30.3, 27.0, 21.4. HRMS-ESI calcd for $C_9H_{12}0_4Na$ $[M+Na]^+$ 207.0633, found: 207.0631.

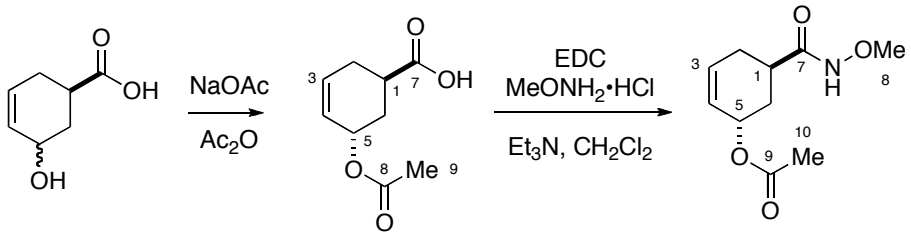
Part 2.

***O*-Methyl (±)-*cis*-cyclohex-3-enohydroxam-5-yl ethanoate (1w).**

Following Representative Procedure 1, a solution of **11w** (260 mg, 1.41 mmol, 1.0 equiv) in CH_2Cl_2 (10.0 mL) was treated sequentially with Et_3N (0.28 mL, 2.26 mmol, 1.6 equiv), EDC (490 mg, 2.54 mmol, 1.8 equiv), and $MeONH_2$•HCl (188 mg, 2.26 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1w** (0.43 g, 72%): colorless oil; R_f 0.51 (EtOAc); υ_{max} 3194, 3166, 3037, 2990, 2976, 2938, 1728, 1662, 1513, 1440, 1372, 1242, 1086, 1070, 1032, 974, 958, 921, 889, 790, 720, 629 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.85 (ddd, J = 9.9, 4.9, 2.5 Hz, 1H, H-3), 5.60 (d, J = 9.9

Hz, 1H, H-4), 5.38-5.32 (m, 1H, H-5), 3.69 (s, 3H, H-8), 2.52-2.43 (m, 1H, H-1), 2.32-2.18 (m, 1H, H-2), 2.17-2.07 (m, 2H, H-2, H-6), 2.02 (s, 3H, H-10), 1.70 (dt, J = 12.6, 10.2 Hz, 1H, H-6); ^{13}C NMR (400 MHz, CD_3OD) δ 173.7, 172.6, 130.1, 128.1, 71.2, 64.5, 38.2, 32.1, 28.7, 21.2; HRMS-ESI calcd for $C_{10}H_{16}NO_4$ $[M+H]^+$ 214.1079, found: 214.1081.

***O*-Methyl (±)-*trans*-cyclohex-3-enohydroxam-5-yl ethanoate (1x).**



Part 1.

***trans*-(±)-5-(Ethanoyloxy)cyclohex-3-enecarboxylic acid (11x).**

A mixture of *cis*- and *trans*-5-hydroxycyclohex-3-enecarboxylic acid (1.64 g, 11.53 mmol, 1.0 equiv), sodium acetate (1.56 g, 19.0 mmol, 1.65 equiv) and acetic anhydride (44.6 mL) were heated at 40 °C for 45 min. The reaction was then filtered and the filtrate concentrated at reduced pressure. After removing remaining traces of acetic anhydride by flash chromatography, the eluent was concentrated and **11x** separated from the non-polar lactone by back extraction with aqueous K_2CO_3 (0.5 M, 25.0 mL). The aqueous extracts were then acidified with aqueous HCl (1 M) and extracted with EtOAc. The combined organic extracts were dried over sodium sulfate and concentrated at reduced pressure to provide **11x** (240 mg, 11%): yellow oil; R_f 0.65 (EtOAc); FTIR (film) υ_{max} 3243, 3203, 3103, 3038, 2941, 2718, 2697, 2666, 1735, 1717, 1654, 1446, 1429, 1395, 1373, 1241, 1162, 1095, 1048, 1021, 959, 911, 830, 733, 667, 636, 612, 574 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 (ddd, J = 9.9, 5.2, 2.3 Hz, 1H, H-3), 5.84 (ddd, J = 9.9, 2.9, 1.8 Hz, 1H, H-4), 5.30 (br s, 1H, H-5), 2.86-2.78 (m, 1H, H-1), 2.44 (dt, J = 18.2, 5.2 Hz, 1H, H-2), 2.25 (dd, J = 9.5, 2.3 Hz, 1H, H-2), 2.20 (d, J = 14.2 Hz, 1H, H-6), 2.05 (s, 3H, H-9), 1.86 (ddd, J = 14.2, 12.6, 4.2 Hz, 1H, H-6); ^{13}C NMR (400 MHz, $CDCl_3$) δ 181.4, 170.8, 131.5, 124.6, 66.0, 35.2, 30.6, 27.5, 21.5; HRMS-ESI calcd for $C_9H_{12}O_4Na$ $[M+Na]^+$ 207.0634, found: 207.0627.

Part 2.

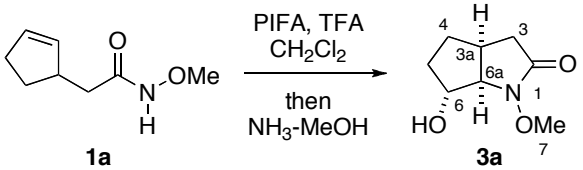
_O_-Methyl (±)-_trans_-cyclohex-3-enohydroxam-5-yl ethanoate (1x).

Following Representative Procedure 1, a solution of **11x** (568 mg, 3.08 mmol, 1.0 equiv) in CH_2Cl_2 (9.0 mL) was treated sequentially with Et_3N (0.61 mL, 4.94 mmol, 1.6 equiv), EDC (1.06 g, 5.55 mmol, 1.8 equiv), and $MeONH_2$•HCl (412 mg, 4.94 mmol, 1.6 equiv) to provide, after purification by flash chromatography (EtOAc), **1x** (499 mg, 86%): white solid; m.p. 104-105 °C; R_f 0.42 (EtOAc); FTIR (film) υ_{max} 3205, 2964, 2936, 2846, 2816, 1728, 1659, 1527, 1514, 1502, 1442, 1371, 1325, 1240, 1161, 1069, 1037, 1022, 958, 913, 886, 812, 733 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 6.01 (ddd, J = 9.9, 4.3, 3.1 Hz, 1H, H-3), 5.82-5.76 (m, 1H, H-4), 5.20 (br s, 1H, H-5), 3.66 (s, 3H, H-8), 2.52-2.44 (m, 1H, H-1), 2.27-2.15 (m, 2H, H-6), 2.00 (s, 3H, H-10), 1.94-1.83 (m, 2H, H-2); ^{13}C NMR (400 MHz, CD_3OD) δ 174.6, 172.3, 132.8, 125.1, 67.3, 64.5, 34.8, 32.3, 28.9, 21.2; HRMS-ESI calcd for $C_{10}H_{15}NO_4Na$ $[M+Na]^+$ 236.0899, found: 236.0907.

2.2 Cyclization of Unsaturated *O*-Alkyl Hydroxamates

2.2.1 Representative Procedure 2. Hydroxamate Cyclization using PIFA-TFA/*In-Situ* Ester Ammonolysis

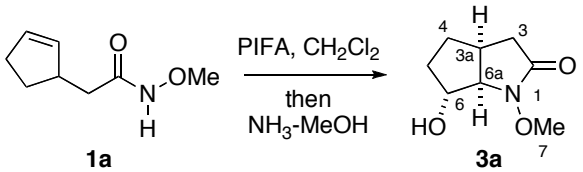
(3a*S,6*R**,6a*R**)-6-Hydroxy-1-methoxyhexahydrocyclopenta[*b*]pyrrol-2-one (3a).**



To a stirred solution of **1a** (49 mg, 0.31 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 0 °C was added trifluoroacetic acid (23 μL, 0.31 mmol, 1.0 equiv). After 30 seconds, a solution of PIFA (162 mg, 0.38 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) was rapidly added (~1 sec). After stirring for 2 h, NH_3 in MeOH (0.8 M, 2.0 mL) was added and the reaction then stirred for an additional 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (EtOAc) to provide **3a** (49 mg, 92%): colorless oil; R_f 0.41 (acetone); IR (film) υ_{max} 3387, 2940, 1687, 1456, 1411, 1272, 1191, 1062, 1016, 962 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.39-4.37 (m, 1 H, H-6), 4.01 (d, J = 7.8 Hz, 1 H, H-6a), 3.84 (s, 3 H, H-7), 2.88-2.83 (m, 1 H, H-3a), 2.61 (dd, J = 17.6, 10.6 Hz, 1 H, H_α-3), 2.24-2.17 (m, 1 H, H_α-4), 2.01 (dd, J = 17.6, 3.6 Hz, 1 H, H_β-3), 1.91-1.73 (m, 3 H, H-5, OH), 1.52-1.43 (m, 1 H, H_α-4); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4 (C-2), 74.3 (C-6), 68.3 (C-6a), 62.2 (C-7), 34.6 (C-3), 32.7 (C-4), 31.4 (C-3), 31.2 (C-3a); HRMS-ESI calcd for $C_8H_{13}NO_3Na$ $[M+Na]^+$ 194.0793, found: 194.0794. Structural assignment of **3a** confirmed by conversion to **15** (Section 2.3).

2.2.2 Representative Procedure 3. Hydroxamate Cyclization using PIFA/*In-Situ* Ester Ammonolysis

(3a*S,6*R**,6a*R**)-6-Hydroxy-1-methoxyhexahydrocyclopenta[*b*]pyrrol-2-one (3a).**

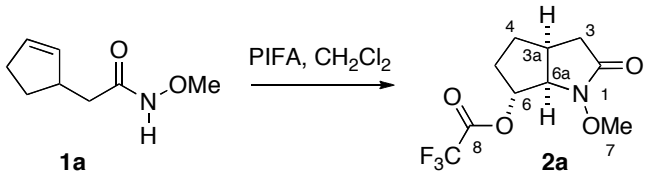


To a stirred solution of **1a** (50 mg, 0.32 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 0 °C was rapidly added a solution of PIFA (167 mg, 0.39 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL).

After stirring for 2 h, NH_3 in MeOH (0.8 M, 2.0 mL) was added and the reaction then stirred for an additional 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (EtOAc) to provide **3a** (38 mg, 70%).

2.2.3 Representative Procedure 4. Hydroxamate Cyclization using PIFA/No *In-Situ* Ester Hydrolysis.

(3a*S,6*R**,6a*R**)-Trifluoroacetic acid 1-methoxy-2-oxo-octahydrocyclopenta[*b*]pyrrol-6-yl ester (2a).**

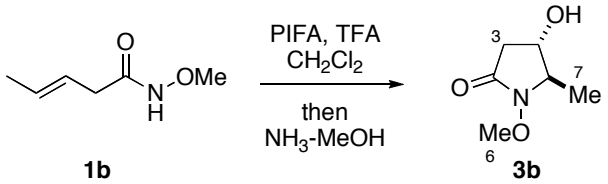


1a **2a**

To a solution of **1a** (52 mg, 0.34 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 0 °C was rapidly added a solution of PIFA (146 mg, 0.34 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 10 min, the reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (EtOAc) to provide **2a** (85 mg, 93%): colorless oil; R_f 0.37 (EtOAc); IR (film) υ_{max} 2970, 2942, 1785, 1706, 1382, 1060, 960, 885, 727 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.42-5.40 (m, 1 H, H-6), 4.19 (d, J = 7.7 Hz, 1 H, H-6a), 3.84 (s, 3 H, H-7), 2.95-2.93 (m, 1 H, H-3a), 2.66 (dd, J = 15.2, 10.6 Hz, 1 H, H_α-3), 2.18-2.12 (m, 1 H, H_β-4), 2.08-1.99 (m, 3 H), 1.67-1.63 (m, 1 H, H_α-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.2 (C-2), 156.8 (q, $J_{C\text{-}F}$ = 42.4 Hz, C-8), 113.4 (q, $J_{C\text{-}F}$ = 284.0 Hz, C-9), 80.3 (C-6), 65.5 (C-6a), 62.4 (C-7), 34.1 (C-3), 31.8 (C-3a), 31.2 (C-5), 29.2 (C-4); HRMS-ESI calcd for $C_{10}H_{12}F_3NO_4Na$ $[M+Na]^+$ 290.0617, found: 290.0625.

2.2.4 Representative Procedure 5. Hydroxamate Cyclization using PIFA-TFA/*In-Situ* Ester Hydrazinolysis

(4*R,5*S**)-4-Hydroxy-1-methoxy-5-methylpyrrolidin-2-one (3b).**

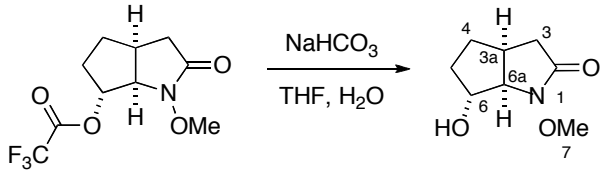


1b **3b**

To a stirred solution of **1b** (58 mg, 0.45 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 0 °C was added trifluoroacetic acid (33 μL, 0.45 mmol, 1.0 equiv). After 30 seconds, a solution of PIFA (232 mg, 0.54 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) was added over 1 second. After stirring for 2 h, N_2H_4 in MeOH (0.8 M, 2.0 mL) was added and the reaction then stirred for an additional 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (EtOAc) to provide **3b** (49 mg, 75%): colorless oil; R_f 0.29 (acetone); IR (film) υ_{max} 3268, 2969, 2878, 1683, 1430, 1264, 1264, 1047, 658 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.29 (br s, 1 H, OH), 4.06-4.02 (m, 1 H, H-4), 3.79 (s, 3 H, H-6), 3.72 (dq, J = 6.5, 3.3 Hz, 1 H, H-5), 2.72 (dd, J = 17.3, 7.1 Hz, 1 H, H_β-3), 2.32 (dd, J = 17.3, 3.8 Hz, 1 H, H_α-3), 1.30 (d, J = 6.5 Hz, 3 H, H-7); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4 (C-2), 69.0, 62.8, 61.6, 37.3 (C-3), 16.3 (C-7); HRMS-ESI calcd for $C_6H_{11}NNaO_3$ $[M+Na]^+$ 168.0637, found: 168.0634. Workup with methanol-ammonia triggered partial dehydration of **2b** and/or **3b**. The relative stereochemistry of **3b** was confirmed by conversion to the known N-H lactam **16** (Section 2.3).

2.2.5 Representative Procedure 6. Aqueous Saponification of Trifluoroacetate Adducts

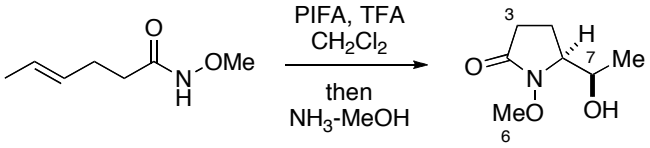
(3a*S,6*R**,6a*R**)-6-Hydroxy-1-methoxyhexahydrocyclopenta[*b*]pyrrol-2-one (3a).**



2a **3a**

A mixture of **4** (580 mg, 2.17 mmol), THF (5.0 mL) and saturated aqueous sodium bicarbonate (5.0 mL) was stirred for 10 h at rt. Brine (10 mL) and CH_2Cl_2 (10 mL) were then added, the organic phase separated and the aqueous phase extracted with CH_2Cl_2 (4 x 10 mL). The combined extracts were dried (Na_2SO_4), filtered, concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (EtOAc) to provide **3a** (359 mg, 97%).

(5*S,7*R**)-5-(1-Hydroxyethyl)-1-methoxypyrrolidin-2-one (3c).**



1c **3c**

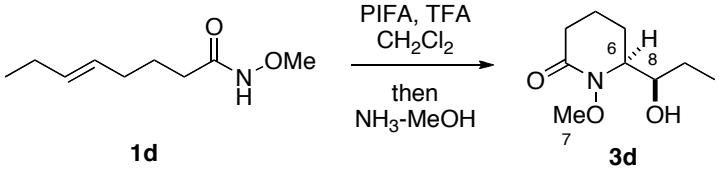
Following Representative Procedure 2, a solution of **1c** (64.3 mg, 0.45 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (33 μL, 0.45 mmol, 1.0 equiv), PIFA (232 mg, 0.54 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3c** (68 mg, 93%).

Following Representative Procedure 3, a solution of **1c** (58 mg, 0.40 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (206 mg, 0.48 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3c** (58 mg, 91%).

Analytical Data for **3c**: colorless oil; R_f 0.28 (acetone); IR (film) υ_{max} 3405, 2973, 2886, 1697, 1438, 1279, 1142, 1059, 963, 824 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.20 (dq, *J* = 6.6, 1.6 Hz, 1 H, H-7), 3.79 (s, 3 H, H-6), 3.66 (ddd, *J* = 7.6, 4.8, 1.6 Hz, 1 H, H-5), 2.57 (br s, 1 H, OH), 2.37 (ddd, *J* = 16.8, 10.3, 6.0 Hz, 1 H, H-3), 2.24 (ddd, *J* = 16.8, 10.3, 5.5 Hz, 1 H, H-3), 2.06-2.02 (m, 1 H, H-4), 2.01-1.92 (m, 1 H, H-4), 1.16 (d, *J* = 6.6

Hz, 3 H, H-8); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6 (C-2), 64.5 (C-7), 62.3 (C-6), 61.4 (C-5), 27.1, 18.1 (C-8), 14.9; HRMS-ESI calcd for $C_7H_{13}NNaO_3$ $[M+Na]^+$ 182.0793, found: 182.0787. The relative stereochemistry of **3c** was confirmed by conversion to the known N-H lactam **17** (Section 2.3).

(6*S,8*R**)-6-(1-Hydroxypropyl)-1-methoxypiperidin-2-one (3d).**



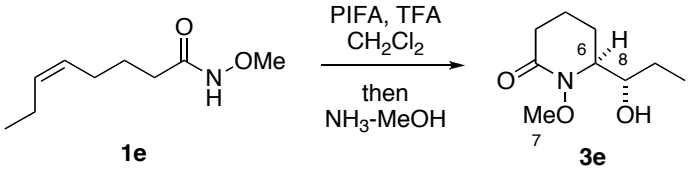
1d **3d**

Following Representative Procedure 2, a solution of **1d** (59.1 mg, 0.346 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (26 μL, 0.346 mmol, 1.0 equiv), PIFA (178 mg, 0.413 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3d** (54.3 mg, 84%).

Following Representative Procedure 3, a solution of **1d** (51.0 mg, 0.298 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (154 mg, 0.358 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 4.0 mL) to provide, after purification by flash chromatography (EtOAc), **3d** (42.2 mg, 74%).

Analytical Data for **3d**: colorless oil; R_f 0.46 (acetone); FTIR (film) υ_{max} 3400, 2933, 2879, 1650, 1453, 1411, 1325, 1137, 978 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.99 (br s, 1 H, OH), 3.97-3.91 (m, 1 H, H-8), 3.69 (s, 3 H, H-7), 2.52 (ddd, J = 8.0, 5.9, 2.6 Hz, 1 H, H-6), 2.52 (dd, J = 10.4, 4.4 Hz, 2 H), 2.04-1.84 (m, 3 H), 1.59-1.53 (m, 1 H), 1.44-1.36 (m, 2 H), 0.97 (t, J = 7.5 Hz, 3 H, H-10); ^{13}C (100 MHz, $CDCl_3$) δ 167.4 (C-2), 69.9, 63.0, 62.2, 33.2, 26.1, 22.3, 19.1, 10.4 (C-10); HRMS-ESI calcd for $C_9H_{17}NO_3Na$ $[M+Na]^+$ 210.1106, found 210.1105. The relative stereochemistry of **3d** was confirmed by conversion to the alkaloid β-conhydrine (**18**) (Section 2.3).

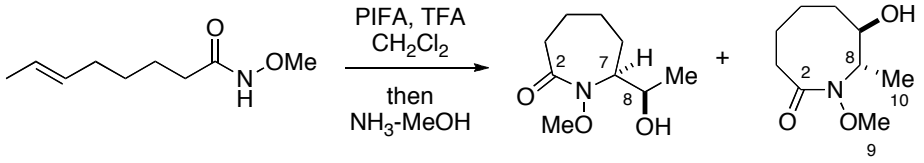
(6*S,8*S**)-6-(1-Hydroxypropyl)-1-methoxypiperidin-2-one (3e).**



1e **3e**

Following Representative Procedure, a solution of **1e** (50 mg, 0.29 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (124 mg, 0.29 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) and NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (EtOAc), **3e** (53 mg, 98%): colorless oil; R_f 0.31 (acetone); FTIR (film) υ_{max} 3250, 2964, 1648, 1549, 1389, 1198, 1066, 969, 671 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.24 (br s, 1 H, OH), 3.85-3.78 (m, 1 H, H-8), 3.77-3.78 (m, 4 H), 2.47-2.44 (m, 2 H), 2.02-1.98 (m, 1 H), 1.87-1.81 (m, 2 H), 1.64-1.58 (m, 2 H), 1.54-1.49 (m, 1 H), 0.99 (t, J = 7.4 Hz, 3 H, H-10); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0 (C-2), 75.5 (C-8), 62.7, 61.3, 33.4, 27.0, 26.8, 18.9, 10.6 (C-10); HRMS-ESI calcd for $C_9H_{18}NO_3$ $[M+H]^+$ 188.1287, found 188.1293. The relative stereochemistry of **3e** was confirmed by conversion to the alkaloid α-conhydrine (**19**) (Section 2.3).

(7*S,9*R**)-7-(1-Hydroxyethyl)-1-methoxy-azepan-2-one (3f) and (7*S**,8*R**)-7-Hydroxy-1-methoxy-8-methyl-azocan-2-one (12).**



1f **3f** **12**

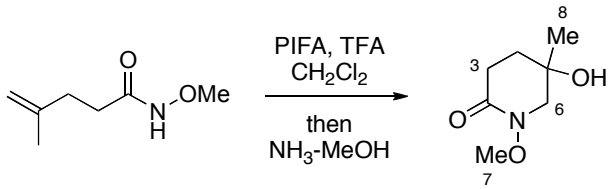
Following Representative Procedure 2, a solution of **1f** (59 mg, 0.35 mmol, 1.0 equiv) in CH_2Cl_2 (1.5 mL) was sequentially treated with trifluoroacetic acid (26 μL, 0.35 mmol, 1.0 equiv), PIFA (178 mg, 0.41 mmol, 1.2 equiv) in CH_2Cl_2 (3.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3f** (31 mg, 49%) and **12** (12 mg, 18%). Compound **12** is not shown in Table 1.

Following Representative Procedure 3, a solution of **1f** (59 mg, 0.35 mmol, 1.0 equiv) in CH_2Cl_2 (1.5 mL) was sequentially treated with PIFA (178 mg, 0.41 mmol, 1.2 equiv) in CH_2Cl_2 (3.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3f** (14 mg, 21%) and **12** (6.3 mg, 10%).

Analytical Data for **3f**: colorless oil; R_f 0.15 (EtOAc); IR (film) υ_{max} 3419, 2933, 2867, 1639, 1449, 1304, 1044, 973 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.27 (dq, *J* = 6.5, 4.5 Hz, 1 H, H-9), 3.82 (s, 3 H, H-8), 3.62-3.60 (m, 1 H, H-7), 2.54 (ddd, *J* = 14.0, 9.8, 3.6 Hz, 1 H, H-3), 2.44 (ddd, *J* = 14.0, 8.3, 3.2 Hz, 1 H, H-3), 1.94-1.82 (m, 3 H), 1.79-1.54 (m, 3 H), 1.26 (d, *J* = 6.5 Hz, 3 H, H-10); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1 (C-2), 67.8, 67.4, 63.1, 35.1, 25.9, 25.7, 23.3, 20.7 (C-10); HRMS-ESI calcd for $C_9H_{17}NNaO_3$ $[M+Na]^+$ 210.1106, found: 210.1110. The HMBC spectrum of **3f** displayed a cross peak between C2 and H-7, which is diagnostic of a 7-membered ring.

Analytical Data for **12**: crystalline solid; mp 166-168 °C (MeOH/hexanes); R_f 0.25 (EtOAc); IR (film) υ_{max} 3390, 2935, 2878, 1642, 1450, 1391, 1072, 1013, 1001, 715 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.98-3.96 (m, 2 H, H-7/8), 3.80 (s, 3 H, H-9), 2.43 (m, 2 H, H-3), 2.00-1.95 (m, 1 H), 1.91-1.84 (m, 1 H), 1.80-1.60 (m, 3 H), 1.49 (d, *J* = 5.8 Hz, 3 H, H-10), 1.50-1.45 (m, 1 H), 1.35-1.24 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.6 (C-2), 73.6 (C-7), 64.4 (C-9), 57.9 (C-8), 35.3, 32.6, 29.5, 20.6, 12.8 (C-10); HRMS-ESI calcd for $C_9H_{17}NNaO_3$ $[M+Na]^+$ 210.1106, found: 210.1103. The HMBC spectrum of **12** displayed a cross peak between C2 and H-8, which is diagnostic of an 8-membered ring.

(±)-5-Hydroxy-1-methoxy-5-methylpiperidin-2-one (3g).



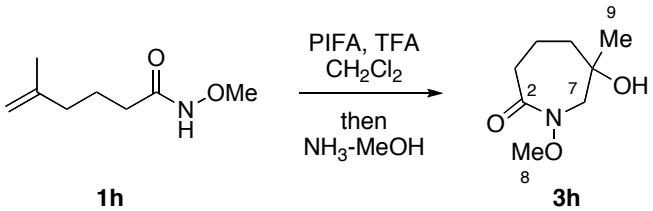
1g **3g**

Following Representative Procedure 2, a solution of **1g** (67 mg, 0.43 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (32 μL, 0.43 mmol, 1.0 equiv), PIFA (222 mg, 0.52 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3g** (70 mg, 95%).

Following Representative Procedure 3, a solution of **1g** (67 mg, 0.43 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (222 mg, 0.52 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3g** (43.8 mg, 60%).

Analytical Data for **3g**: colorless oil; R_f 0.38 (acetone); IR (film) υ_{max} 3377, 2972, 2937, 1640, 1451, 1309, 1273, 1203, 1133, 1062, 995, 851, 719 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 3.72 (s, 3 H, H-7), 3.57-3.47 (m, 2 H), 3.34 (br s, 1 H), 2.69 (ddd, *J* = 17.8, 11.4, 6.7 Hz, 1 H), 2.38 (ddd, *J* = 17.5, 5.9, 3.3 Hz, 1 H), 1.87-1.80 (m, 1 H), 1.77 (ddd, *J* = 13.7, 11.5, 6.0 Hz, 1 H), 1.38 (s, 3 H, H-8); ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.2 (C-2), 68.4 (C-5), 60.6 (C-7), 59.7 (C-6), 33.4, 28.6, 27.4 (C-8); HRMS-ESI calcd for $C_7H_{13}NO_3Na$ $[M+Na]^+$ 182.0793, found: 182.0789.

(±)-6-Hydroxy-1-methoxy-6-methyl-azopan-2-one (3h).



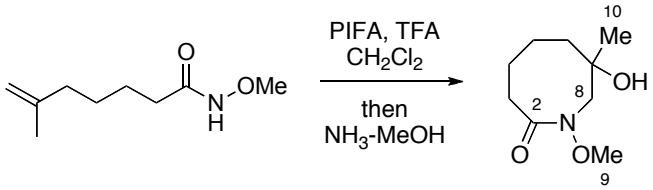
1h **3h**

Following Representative Procedure 2, a solution of **1h** (54 mg, 0.34 mmol, 1.0 equiv) in CH_2Cl_2 (1.5 mL) was sequentially treated with trifluoroacetic acid (26 μL, 0.34 mmol, 1.0 equiv), PIFA (177 mg, 0.41 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and then NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (EtOAc), provided **3h** (49 mg, 83%).

Following Representative Procedure 3, a solution of **1h** (71 mg, 0.45 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (235 mg, 0.55 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and NH_3 in MeOH (0.8 M, 2.5 mL) to provide, after purification by flash chromatography (EtOAc), **3h** (53 mg, 67%).

Analytical Data for **3h**: colorless oil; R_f 0.10 (EtOAc); IR (film) υ_{max} 3408, 2933, 2862, 1645, 1450, 1133, 1114, 710 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 3.74 (d, *J* = 15.5 Hz, 1 H, H-7), 3.70 (s, 3 H, H-9), 3.63 (d, *J* = 15.5 Hz, 1 H, H-7), 2.50-2.37 (m, 2 H, H-3), 1.92-1.77 (m, 1 H), 1.77-1.56 (m, 3 H), 1.22 (s, 3 H, H-8); ^{13}C NMR (125 MHz, CD_3OD) δ 172.4 (C-2), 67.6 (C-6), 60.3 (C-7), 60.2 (C-9), 42.2, 34.7, 25.5 (C-8), 18.9; HRMS-ESI calcd for $C_8H_{15}NO_3Na$ $[M+Na]^+$ calc. 196.0950 found 196.0953. The HMBC spectrum of **3h** displayed a cross peak between C2 and H-7, which is diagnostic of a 7-membered ring.

(±)-7-Hydroxy-1-methoxy-7-methyl-azocin-2-one (3i).



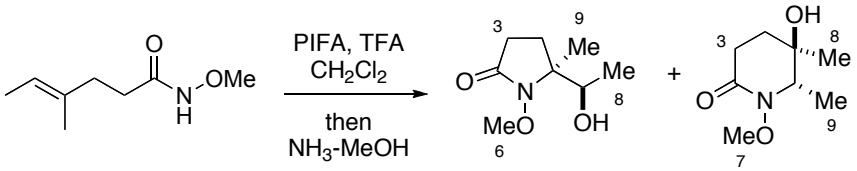
1i **3i**

Following Representative Procedure 2, a solution of **1i** (39 mg, 0.23 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (17 μL, 0.23 mmol, 1.0 equiv), PIFA (120 mg, 0.28 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and then NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (EtOAc), provided **3i** (36 mg, 83%).

Following Representative Procedure 3, a solution of **1i** (41 mg, 0.24 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (122 mg, 0.29 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and NH_3 in MeOH (0.8 M, 2.5 mL) to provide, after purification by flash chromatography (EtOAc), **3i** (29 mg, 66%).

Analytical Data for **3i**: colorless oil; R_f 0.10 (EtOAc); IR (film) υ_{max} 3408, 2933, 2862, 1645, 1450, 1133, 1114, 710 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 3.84-3.72 (m, 1 H, H-8), 3.71-3.67 (m, 1 H, H-8), 3.66 (s, 3 H, H-10), 2.43-2.28 (m, 2 H, H-3), 1.83-1.56 (m, 4 H), 1.53-1.40 (m, 2 H), 1.21 (s, 3 H, H-9); ^{13}C NMR (125 MHz, CD_3OD) δ 170.3 (C-2), 73.3 (C-7), 60.1 (C-10), 56.7 (C-8), 38.7, 34.4, 28.4, 27.5 (br, C-7), 21.7; HRMS-ESI calcd for $C_9H_{18}NO_3$ $[M+H]^+$ 188.1287, found: 188.1283. The HMBC spectrum of **3i** displayed a cross peak between C2 and H-8, which is diagnostic of an 8-membered ring.

(5*S,7*R**)-5-(1-Hydroxyethyl)-5-methyl-1-methoxypyrrolidin-2-one (3j) and (5*R**,6*S**)-5-Hydroxy-1-methoxy-5,6-dimethylpiperidin-2-one (3k).**



1j **3j** **3k**

Following Representative Procedure 2, a solution of **1j** (56 mg, 0.36 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (27 μL, 0.36 mmol, 1.0 equiv), PIFA (184 mg, 0.43 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH

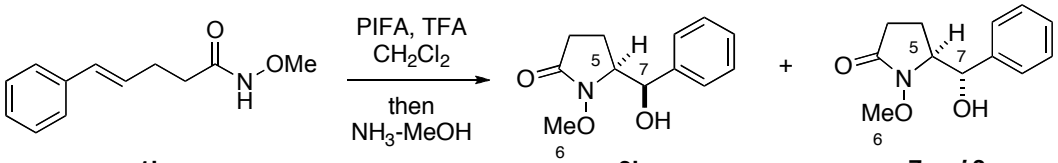
(0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3j** (35 mg, 58%) and **3k** (17 mg, 28%).

Following Representative Procedure 3, a solution of **1j** (58 mg, 0.37 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (193 mg, 0.45 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3j** (35 mg, 56%) and **3k** (12 mg, 19%).

Analytical Data for **3j**: colorless oil; R_f 0.52 (acetone); IR (film) υ_{max} 3369, 2865, 2830, 1679, 1590, 1484, 1442, 1378, 1288, 1255, 1129, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.00-3.95 (m, 1 H, H-7), 3.94 (s, 3 H, H-6), 2.49-2.16 (m, 3 H), 1.79 (br s, 1 H, OH), 1.64-1.56 (m, 1 H), 1.28 (s, 3 H, H-9), 1.16 (d, J = 6.5 Hz, 3 H, H-8); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5 (C-2), 69.3, 67.2, 64.4, 26.8, 23.0, 22.3 (C-8), 17.3 (C-9); HRMS-ESI calcd for $C_8H_{15}NO_3Na$ $[M+Na]^+$ 196.0950, found: 196.0947.

Analytical Data for **3k**: colorless oil; R_f 0.39 (acetone); IR (film) υ_{max} 3355, 2981, 2881, 1637, 1462, 1442, 1411, 1380, 1201, 1180, 1135 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 3.69 (s, 3 H), 3.64 (dq, J = 6.6, 1.7 Hz, 1 H, H-6), 2.58 (ddd, J = 17.7, 11.6, 7.4 Hz, 1 H, H-4), 2.30 (ddd, J = 17.7, 6.7, 1.7 Hz, 1 H, H-3), 1.94 (ddd, J =14.1, 11.6, 6.7 Hz, 1 H, H-2), 1.65 (dddd, J = 14.1, 7.4, 1.7, 1.7 Hz, 1 H, H-2), 1.27 (s, 3 H, H-8), 1.25 (d, J = 6.6 Hz, 3 H, H-9); ^{13}C NMR (125 MHz, CD_3OD) δ 167.3 (C-2), 70.5 (C-5), 65.0, 59.9, 28.7, 28.2, 25.4, 15.4; HRMS-ESI calcd for $C_8H_{15}NO_3Na$ $[M+Na]^+$ 196.0950, found: 196.0958.

(5*S,7*R**)-5-(Hydroxyphenylmethyl)-1-methoxypyrrolidin-2-one (3l) and (5*S**,7*S**)-5-(Hydroxyphenylmethyl)-1-methoxypyrrolidin-2-one (7-*epi*-3l).**



1l **3l** **7-*epi*-3v**

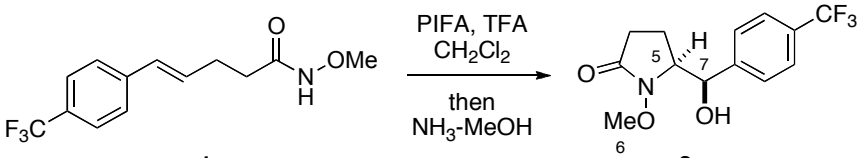
Following Representative Procedure 2, a solution of **1l** (52 mg, 0.25 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (19 μL, 0.25 mmol, 1.0 equiv), PIFA (130.3 mg, 0.30 mmol, 1.2 equiv) in CH_2Cl_2 (1.5 mL) and NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (EtOAc), **3l** (26 mg, 47%) and **7-*epi*-3l** (10 mg, 18%).

Following Representative Procedure 3, a solution of **1l** (56 mg, 0.27 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (142 mg, 0.33 mmol, 1.2 equiv) in CH_2Cl_2 (1.5 mL) and NH_3 in MeOH (0.8 M, 2.5 mL) to provide, after purification by flash chromatography (EtOAc), **3l** (25 mg, 40%) and **7-*epi*-3l** (9 mg, 15%).

Analytical Data for **3l**: colorless oil; R_f 0.15 (EtOAc); IR (film) υ_{max} 3392, 2936, 2818, 1697, 1449, 1282, 1062, 965, 744, 703 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38-7.26 (m, 5 H, Ph), 5.21 (d, J = 2.3 Hz, 1 H, H-7), 3.95 (ddd, J = 10.5, 4.1, 2.3 Hz, 1 H, H-5), 3.91 (s, 3 H, H-6), 2.63 (br s, 1 H, OH), 2.46-2.33 (m, 1 H, H-3), 2.27-2.13 (m, 1 H, H-3), 2.07-1.99 (m, 1 H, H-2), 1.73-1.65 (m, 1 H, H-2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2 (C-2), 139.6, 128.5, 127.7, 125.8, 70.2 (C-7), 62.7, 62.1, 27.1, 15.0; HRMS-ESI calcd for $C_{12}H_{15}NNaO_3$ $[M+Na]^+$ 244.0950, found: 244.0948. The relative stereochemistry of **3l**, and, through inference, **7-*epi*-3l** was confirmed by conversion of **3l** to known NH lactam **21** (Section 2.3).

Analytical Data for **7-*epi*-3l**: colorless oil; R_f 0.12 (EtOAc); IR (film) υ_{max} 3364, 2933, 1687, 1454, 1403, 1194, 1056, 747, 705 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43-7.29 (m, 5 H), 4.93 (d, J = 5.8 Hz, 1 H, H-7), 4.08 (app q, J = 5.8 Hz, 1 H, H-5), 3.88 (s, 3 H, H-6), 2.70 (br s, 1 H, OH), 2.03-1.94 (m, 1 H), 1.82 - 1.76 (m, 2 H), 1.64-1.55 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4 (C-2), 139.3, 129.0, 128.9, 127.0, 75.2 (C-7), 62.8, 60.9, 26.7, 18.0; HRMS-ESI calcd for $C_{12}H_{15}NNaO_3$ $[M+Na]^+$ 244.0950, found: 244.0956.

(5*S,7*R**)-5-[Hydroxy-(4-trifluoromethylphenyl)-methyl]-1-methoxy-pyrrolidin-2-one (3m).**



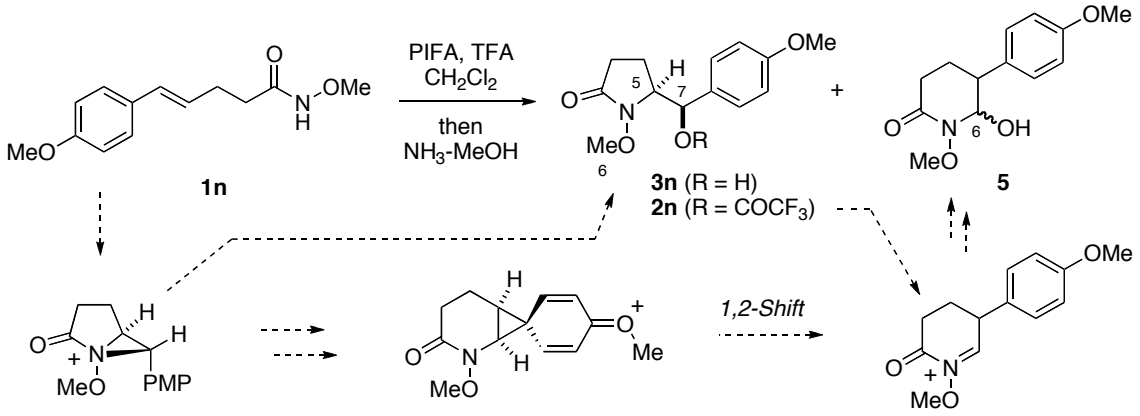
1m **3m**

Following Representative Procedure 2, a solution of **1m** (56 mg, 0.20 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (15 μL, 0.20 mmol, 1.0 equiv), PIFA (105 mg, 0.24 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and then NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (EtOAc), provided **3m** (50 mg, 85%).

Following Representative Procedure 3, a solution of **1m** (80 mg, 0.28 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (147 mg, 0.34 mmol, 1.2 equiv) in CH_2Cl_2 (1.5 mL) and NH_3 in MeOH (0.8 M, 2.5 mL) to provide, after purification by flash chromatography (EtOAc), **3m** (48 mg, 58%).

Analytical Data for **3m**: colorless oil; R_f 0.26 (EtOAc); IR (film) υ_{max} 3363, 2940, 2821, 1699, 1617, 1326, 1162, 1122 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, J = 8.2 Hz, 2 H, Ph), 7.53 (d, J = 8.3 Hz, 2 H, Ph), 5.33-5.26 (m, 1 H, H-7), 3.95 (ddd, J = 8.5, 3.4, 2.2 Hz, 1 H, H-5), 3.90 (s, 3 H, H-6), 2.45 (ddd, J = 17.1, 10.4, 6.8 Hz, 1 H, H-3), 2.20 (ddd, J = 17.0, 10.5, 4.4 Hz, 1 H, H-3), 1.97 (dddd, J = 14.2, 10.5, 4.1, 4.1 Hz, 1 H, H-2), 1.67 (dddd, J = 13.2, 10.4, 8.5, 6.9 Hz, 1 H, H-2); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.2 (C-2), 144.0, 129.8 (q, $J_{C\text{-}F}$ = 33.1 Hz, C-4'), 126.1, 125.4, 124.1 (q, $J_{C\text{-}F}$ = 271.9 Hz, CF_3), 69.8, 62.6, 61.9, 27.1, 14.8; HRMS-ESI calcd for $C_{13}H_{14}NO_2F_3$ $[M+Na]^+$ 312.0823, found: 312.0821. The relative stereochemistry of **3m** was confirmed by analysis of observed 5-H/7-H vicinal coupling constants, as outlined in Section 2.3.

(5*S,7*R**)-5-[Hydroxy-(4-methylphenyl)-methyl]-1-methoxy-pyrrolidin-2-one (3n) and (5*S**,6*RS**)-6-Hydroxy-1-methoxy-5-(4-methoxyphenyl)-piperidin-2-one (5).**



Following Representative Procedure 2, a solution of **1n** (53 mg, 0.22 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (17 μL, 0.22 mmol, 1.0 equiv), PIFA (116 mg, 0.27 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and then NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (EtOAc), provided **3n** (12 mg, 21%) and an inseparable mixture of **5** and **6-*epi*-5** (13 mg, 24%) [**5**/**6-*epi*-5**, 1:0.95, ratio determined by integration of the peaks at δ_H (major) and δ_H (minor) in the ^1H NMR spectrum].

Following Representative Procedure 3, a solution of **1n** (70 mg, 0.30 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (153 mg, 0.36 mmol, 1.2 equiv) in CH_2Cl_2 (1.5 mL) and NH_3 in MeOH (0.8 M, 2.5 mL) to provide, after purification by flash chromatography (EtOAc), **3n** (40 mg, 53%).

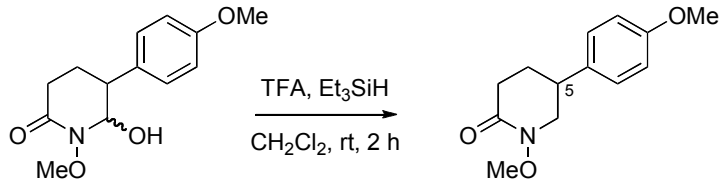
Analytical Data for **3n**: colorless oil; R_f 0.24 (EtOAc); IR (film) υ_{max} 3376, 2937, 2834, 1695, 1612, 1511, 1245, 1174, 1031 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29 (d, J = 8.7 Hz, 2 H, Ar), 6.94-6.88 (m, 2 H, Ar), 5.14 (s, 1 H, H-7), 3.95-3.87 (m, 1 H, H-5), 3.89 (s, 3 H), 3.81 (s, 3 H, H-6), 2.48 (bs, 1 H, OH), 2.32 (ddd, J = 16.9, 10.3, 6.5 Hz, 1 H, H-3), 2.17 (ddd, J = 16.9, 10.3, 4.8 Hz, 1 H, H-3), 2.03 (dddd, J = 13.2, 10.3, 4.8, 4.8 Hz, 1 H, H-4), 1.71 (dddd, J = 13.2, 10.3, 8.4, 6.5 Hz, 1 H, H-4); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5 (C-2), 159.6, 132.0, 127.4, 114.4, 71.1 (C-7), 63.0, 62.4, 55.7, 27.5, 15.6; HRMS-ESI calcd for $C_{13}H_{17}NO_4Na$ $[M+Na]^+$ 274.1055, found: 274.1063. The relative stereochemistry of **3n** was confirmed by analysis of observed 5-H/7-H vicinal coupling constants, as outlined in Section 2.3.

Analytical Data for **5**/**6-*epi*-5**: white solid; R_f 0.30 (EtOAc); IR (film) υ_{max} 3330, 2937, 2907, 2873, 1658, 1648, 1612, 1514, 1247, 1180, 1051, 1034, 834, 769 cm^{-1}; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.6, 168.2, 158.9, 131.9, 131.1, 129.2, 128.5, 128.2, 86.3, 84.1, 63.2, 62.7, 55.3, 55.3, 46.5, 45.2, 32.8, 31.6, 25.0, 21.2; HRMS-ESI calcd for $C_{13}H_{17}NO_4Na$ $[M+Na]^+$ 274.1055, found: 274.1047.

Partial ^1H NMR Data for **5**: ^1H NMR (500 MHz, $CDCl_3$) δ 5.23 (m, 1 H), 3.84 (s, 3 H), 3.08 (s, 3 H), 3.23-3.17 (m, 1 H), 2.89 (d, J = 3.1 Hz, 1 H, OH), 2.66-2.50 (m, 3 H), 1.95-1.82 (m, 1 H);

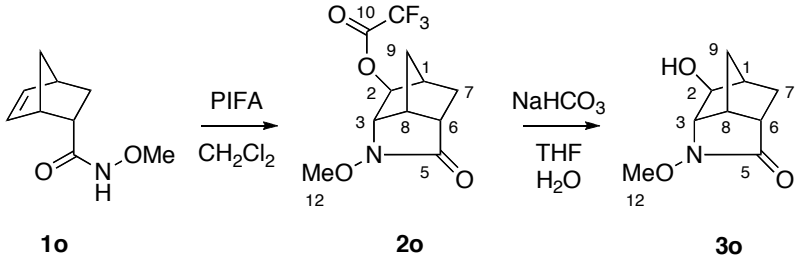
Partial ^1H NMR Data for **6-*epi*-5**: ^1H NMR (500 MHz, $CDCl_3$) δ 5.20 (dd, J = 8.0, 4.5 Hz, 1 H), 3.38 (d, J = 4.5, 1 H, OH), 3.10 (ddd, J = 12.5, 8.0, 5.0 Hz, 1 H), 2.57-2.46 (m, 2 H), 2.12-2.08 (m, 1 H), 2.04-1.97 (m, 1 H).

(±)-1-Methoxy-5-(4-methoxyphenyl)-piperidin-2-one (13).



To a stirred solution of **5** (13.4 mg, 0.053 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at room temperature was added triethylsilane (17 μL, 0.107 mmol, 2.0 equiv) and trifluoroacetic acid (0.5 mL). After 1 h, triethylsilane (17 μL, 0.107 mmol, 2.0 equiv) was again added and after 1 h, the mixture was concentrated under reduced pressure. The residue purified by flash chromatography on silica gel (EtOAc) to provide **13** (8 mg, 63%): colorless oil; R_f 0.17 (EtOAc); IR (film) υ_{max} 3068, 2999, 2932, 2836, 1669, 1514, 1458, 1246, 1180, 1032, 832 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.21-7.15 (m, 2 H), 6.92-6.85 (m, 2 H), 3.81 (s, 3 H), 3.79 (s, 3 H), 3.74 (ddd, J = 11.2, 5.5, 1.5 Hz, 1 H, H-6), 3.59 (t, J = 11.0 Hz, 1 H, H-6), 3.16 (dddd, J = 11.1, 11.1, 5.3, 3.7 Hz, 1 H, H-5), 2.63-2.57 (m, 1 H), 2.57-2.49 (m, 1 H), 2.05-1.92 (m, 2 H, H-3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (C-2), 158.8 (C-4'), 132.8 (C-1'), 127.9, 114.2, 61.0 (C-7), 55.3 (C-5'), 54.8 (C-6), 40.2 (C-5), 32.2, 28.0; HRMS-ESI calcd for $C_{13}H_{17}NO_3Na$ $[M+Na]^+$ 258.1106, found: 258.1112.

(2*R,3*R**,6*R**)-2-Hydroxy-4-methoxy-4-azatricyclo[4.2.1.$0^{0,0}$]nonan-5-one (3o).**



Step 1.

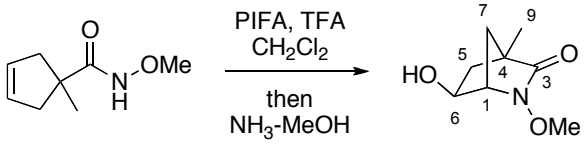
Following Representative Procedure 4, a solution of **1o** (250 mg, 1.49 mmol, 1.0 equiv) in CH_2Cl_2 (3.0 mL) was treated with a solution of PIFA (642 mg, 1.49 mmol, 1.0 equiv) in CH_2Cl_2 (6.0 mL) to provide, after purification by flash chromatography (EtOAc), **2o** (337 mg, 98%): colorless oil; R_f 0.29 (EtOAc); IR (film) υ_{max} 2973, 2885, 2821, 1785, 1730, 1456, 1354, 1223, 1161, 1070, 971, 653 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.79 (s, 1 H, H-2), 3.82 (d, J = 4.5 Hz, 1 H, H-3), 3.78 (s, 3 H, H-12), 2.99 (m, 1 H, H-6), 2.63 (br s, 1 H, H-1), 2.45 (dd, J = 10.4, 3.8 Hz, 1 H, H-8), 2.04 (ddd, J = 13.9, 10.4, 4.5 Hz, 1

H, H-9), 1.92 (d, J = 11.4 Hz, 1 H, H-7), 1.70 (d, J = 13.9 Hz, 1 H, H-9), 1.59 (d, J = 11.4 Hz, 1 H, H-7); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2 (C-5), 156.6 (q, $J_{C\text{-}F}$ = 42.8 Hz, C-10), 114.8 (q, $J_{C\text{-}F}$ = 283.5 Hz, C-11), 79.5 (C-2), 64.7 (C-3), 63.5 (C-12), 42.7 (C-6), 41.7 (C-1), 40.5 (C-8), 33.7 (C-9), 32.9 (C-7); HRMS-ESI calcd for $C_{11}H_{12}F_3NO_4Na$ $[M+Na]^+$ 302.0616, found: 302.0616.

Step 2.

Following Representative Procedure 7, a mixture of **2o** (325 mg, 2.17 mmol), THF (5.0 mL) and saturated aqueous sodium bicarbonate (5.0 mL) was stirred for 10 h to provide, after purification by flash chromatography (EtOAc), **3o** (189 mg, 89%): colorless oil; R_f 0.12 (EtOAc); IR (film) υ_{max} 3409, 2965, 2871, 1712, 1449, 1233, 1048, 1004, 734, 655 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3 H, H-12), 3.75 (s, 1 H, H-2), 3.59 (d, J = 4.3 Hz, 1 H, H-3), 2.85 (m, H-6), 2.37 (br s, 1 H, H-1), 2.33 (d, J = 4.3 Hz, 1 H, H-8), 2.01 (d, J = 10.6 Hz, 1 H, H_{endo}-7), 1.93 (ddd, J = 13.5, 10.6, 4.3 Hz, 1 H, H_{endo}-9), 1.54 (d, J = 13.5 Hz, 1 H, H_{exo}-9), 1.43 (d, J = 10.6 Hz, 1 H, H_{exo}-7); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3 (C-5), 73.8 (C-2), 66.7 (C-3), 62.9 (C-12), 44.9 (C-6), 39.9 (C-8), 38.9 (C-1), 33.1 (C-9), 32.9 (C-7); HRMS-ESI calcd for $C_9H_{13}NO_3Na$ $[M+Na]^+$ 206.0793, found: 206.0800.

(1*S,4*R**,6*S**)-6-Hydroxy-2-methoxy-4-methyl-2-azabicyclo[2.2.1]heptan-3-one (3p).**



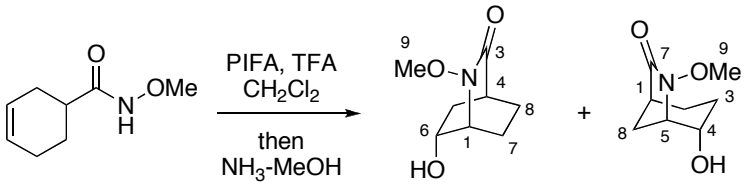
1m **3m**

Following Representative Procedure 2, a solution of **1p** (59 mg, 0.38 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with trifluoroacetic acid (28 μL, 0.38 mmol, 1.0 equiv), PIFA (197 mg, 0.46 mmol, 1.2 equiv) in CH_2Cl_2 (1.2 mL) and then NH_3 in MeOH (0.8 M, 4.0 mL) to provide, after purification by flash chromatography (EtOAc/hexanes, 3:1), **3p** (55 mg, 84%).

Following Representative Procedure 3, a solution of **1p** (48 mg, 0.31 mmol, 1.0 equiv) in CH_2Cl_2 (2.0 mL) was sequentially treated with PIFA (157 mg, 0.37 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (acetone/hexanes, 3:1), **3p** (43 mg, 82%).

Analytical data for **3p**: white needles; mp 79-81°C; R_f 0.39 (EtOAc); FTIR (film) υ_{max} 3433, 2966, 1715, 1025, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.36-4.35 (m, 1 H, H-6), 3.82 (s, 1 H, H-1), 3.77 (s, 3 H, H-9), 2.26 (br d, J = 2.8 Hz, 1 H, OH), 2.00 (ddd, J = 13.0, 7.0, 2.9 Hz, 1 H, H-5), 1.90 (dd, J = 10.0, 1.4 Hz, 1 H, H-7), 1.62 (br d, J = 10.0, 1.4 Hz, 1 H, H-7), 1.45 (dd J = 13.0, 2.9 Hz, 1 H, H-5); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.8 (C-3), 70.3, 64.3, 63.8, 49.0 (C-4), 43.9, 37.0, 14.4 (C-8); HRMS-ESI calcd for $C_8H_{13}O_3N$ $[M+Na]^+$ 194.0793, found: 194.0798.

(1*R,4*S**,6*R**)-6-Hydroxy-2-methoxy-2-azabicyclo[2.2.2]octan-3-one (3q) and (1*R**, 4*R**,5*S**)-4-Hydroxy-6-methoxy-6-azabicyclo[3.2.1]octan-7-one (3r).**



1q **3q** **3r**

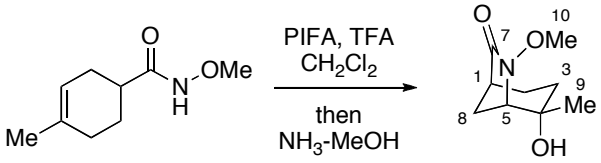
Following Representative Procedure 2, a solution of **1q** (50 mg, 0.32 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), at 40 ºC, was sequentially treated with trifluoroacetic acid (24 μL, 0.32 mmol, 1.0 equiv) and a solution of PIFA (166 mg, 0.39 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 3 h, the reaction was allowed to cool to room temperature, NH_3 in MeOH (0.8 M, 2.0 mL) added and the mixture stirred for 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography (EtOAc), to provide **3q** (35.4 mg, 64%) and **3r** (18.4 mg, 33%).

Following Representative Procedure 3, a solution of **1q** (66 mg, 0.42 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (219 mg, 0.51 mmol, 1.2 equiv) in CH_2Cl_2 (2.0 mL) and NH_3 in MeOH (0.8 M, 3.0 mL) to provide, after purification by flash chromatography (EtOAc), **3q** (44 mg, 61%) and **3r** (16 mg, 22%).

Analytical Data for **3q**: colorless oil; R_f 0.12 (EtOAc); IR (film) υ_{max} 3369, 2945, 2881, 1668, 1579, 1494, 1405, 1200, 1134, 1058, 981, 836, 758, 720 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.36 (br s, 1 H, OH), 4.23 (apt t, J = 2.9 Hz, 1 H, H-6), 3.88 (apt t, J = 4.5 Hz, 1 H, H-1), 3.79 (s, 3 H, H-9), 2.41 (apt t, J = 4.8 Hz, 1 H, H-4), 2.20 (d, J = 11.4 Hz, 1 H), 1.91-1.86 (m, 1 H), 1.82-1.65 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) 175.8 (C-3), 63.8, 63.2, 58.8 (C-1), 38.1, 26.9, 26.3, 23.0; HRMS-ESI calcd for $C_8H_{14}NO_3$ $[M+H]^+$ 172.0974, found: 172.0972.

Analytical Data for **3r**: white solid; mp 91-93 °C; R_f 0.08 (EtOAc); IR (film) υ_{max} 3398, 2943, 2824, 1684, 1452, 1370, 1272, 1040, 976, 763, 656 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.28-4.23 (m, 1 H, H-4), 3.83-3.77 (m, 1 H, H-5), 3.76 (m, 3 H, H-9), 3.19 (br s, 1 H, OH), 2.55-2.53 (m, 1 H, H-1), 2.53-2.22 (m, 2 H), 1.81-1.75 (m, 2 H), 1.48-1.38 (m, 2 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7 (C-7), 68.1 (C-4), 63.4, 61.2, 39.4, 33.9, 23.9, 20.1; HRMS-ESI calcd for $C_8H_{13}NO_3Na$ $[M+Na]^+$ 194.0793, found: 194.0793.

(±)-4-*endo*-Hydroxy-6-methoxy-4-methyl-6-azabicyclo[3.2.1]octan-7-one (3s).



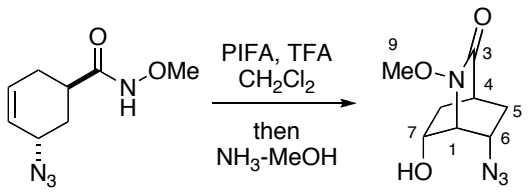
1s **3s**

Following Representative Procedure 2, a solution of **1s** (50 mg, 0.30 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), at 40 ºC, was sequentially treated with trifluoroacetic acid (22 µL, 0.30 mmol, 1.0 equiv) and a solution of PIFA (152 mg, 0.35 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 1 h, the reaction was allowed to cool to room temperature, NH_3 in MeOH (0.8 M, 2.0 mL) added and the mixture stirred for 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography (EtOAc) to provide **3s** (42 mg, 76%).

Following Representative Procedure 3, a solution of **1s** (51 mg, 0.30 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (156 mg, 0.36 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (EtOAc), **3s** (47 mg, 85%).

Analytical Data for **3s**: white solid; m.p. 89-90 °C; R_f 0.14 (EtOAc); FTIR (film) υ_{max} 3407, 2940, 2873, 1705, 1460, 1374, 1278, 1233, 1207, 1118, 1101, 1044, 1024, 1000, 985, 927, 899, 780, 759, 692 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.76 (s, 3H, H-10), 3.61 (d, J = 5.3 Hz, 1H, H-5), 2.44 (br s, 1H, OH), 2.39 (dd, J = 8.2, 3.5 Hz, 1H, H-1), 2.32 (d, J = 11.1 Hz, 1H, H-8), 1.92 (ddt, J = 11.1, 5.3 Hz, 1H, H-8), 1.80-1.74 (m, 2H, H-2, H-3), 1.65-1.60 (m, 2H, H-2, H-3), 1.35 (s, 3H, H-9); ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.0, 69.7, 63.4, 63.0, 38.0, 33.2, 29.5, 29.3, 23.1; HRMS-ESI calcd for $C_9H_{16}NO_3$ $[M+H]^+$ 186.1130, found: 186.1136.

(±)-6-*endo*-Azido-7-*endo*-hydroxy-2-methoxy-2-azabicyclo[2.2.2]octan-3-one (3t).



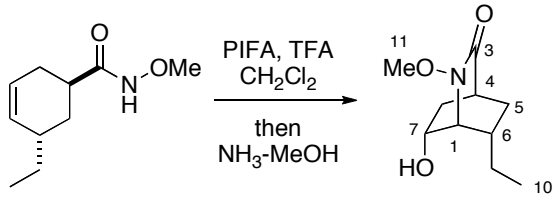
1t **3t**

Following Representative Procedure 3, a solution of **1t** (53 mg, 0.27 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), at 40 ºC, was sequentially treated with trifluoroacetic acid (20 µL, 0.27 mmol, 1.0 equiv) and a solution of PIFA (139 mg, 0.32 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 15 min, the reaction was allowed to cool to room temperature, NH_3 in MeOH (0.8 M, 2.0 mL) added and the mixture stirred for 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography (1:1, EtOAc:hexanes) to provide **3t** (42 mg, 73%).

Following Representative Procedure 3, a solution of **1t** (51 mg, 0.26 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (157 mg, 0.37 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (1:1, EtOAc:hexanes), **3t** (36 mg, 65%).

Analytical Data for **3t**: yellow oil; R_f 0.23 (EtOAc); IR (film) υ_{max} 3392, 2937, 2873, 2111, 1689, 1458, 1431, 1265, 1120, 1055, 991, 953 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 4.34-4.28 (m, 1H, H-7), 4.15-4.09 (m, 1H, H-6), 4.03-4.00 (m, 1H, H-1), 3.74 (s, 3H, H-9), 2.57-2.53 (m, 1H, H-4), 2.37-2.26 (m, 2H, H-5, H-8), 1.74 (ddd, J = 13.6, 5.3, 2.1 Hz, 1H, H-5), 1.59 (ddd, J = 13.6, 4.1, 2.1 Hz, 1H, H-8); ^{13}C NMR (400 MHz, CD_3OD) δ 174.7, 69.6, 64.1, 63.5, 58.2, 39.4, 34.4, 30.9; HRMS-EI calcd for $C_8H_{12}N_4O_3$ $[M]^+$ 212.0909, found: 212.0901.

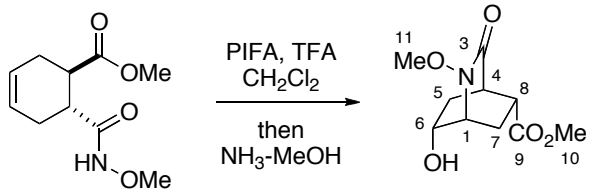
(±)-6-*endo*-Ethyl-7-*endo*-hydroxy-2-methoxy-2-azabicyclo[2.2.2]octan-3-one (3u).



1u **3u**

Following Representative Procedure 2, a solution of **1u** (53 mg, 0.29 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), at 40 ºC, was sequentially treated with trifluoroacetic acid (21 µL, 0.29 mmol, 1.0 equiv) and a solution of PIFA (149 mg, 0.35 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 15 min, the reaction was allowed to cool to room temperature, NH_3 in MeOH (0.8 M, 2.0 mL) added and the mixture stirred for 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography (1:1, EtOAc:hexanes) to provide **3u** (57 mg, 99%): white solid; m.p. 96-97 °C; R_f 0.10 (EtOAc); IR (film) υ_{max} 3396, 2961, 2936, 2873, 1684, 1459, 1379, 1172, 1087, 1048, 1023, 978 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.37-4.34 (m, 1 H, H-7), 3.77 (t, *J* = 3.1 Hz, 1 H, H-1), 3.75 (s, 3 H, H-11), 3.30 (br s, 1 H, OH), 2.54 (br s, 1 H, H-4), 2.32 (ddt, *J* = 13.6, 10.2, 3.2 Hz, 1 H, H-8), 2.17-2.04 (m, 2 H, H-5, H-6), 1.83-1.65 (m, 2 H, H-9), 1.47 (ddd, *J* = 13.6, 4.3, 2.2 Hz, 1 H, H-8), 1.39 (ddd, *J* = 12.4, 6.0, 1.9 Hz, 1 H, H-5), 0.93 (t, *J* = 7.4 Hz, 3 H, H-10); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.8 (C-3), 70.3, 64.0, 63.4, 41.5, 39.4, 34.7, 31.8, 27.4, 13.1 (C-10); HRMS-ESI calcd for $C_{10}H_{18}NO_3$ $[M+H]^+$ 200.1287, found: 200.1286.

Methyl (±)-6-*endo*-hydroxy-2-methoxy-3-oxo-2-azabicyclo[2.2.2]octane-8-*endo*-carboxylate (3v).

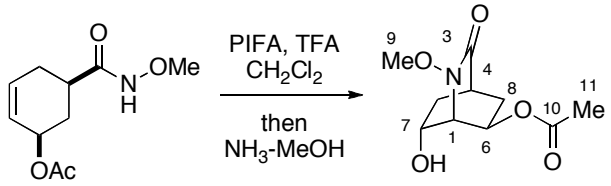


1v **3v**

Following Representative Procedure 2, a solution of **1v** (43 mg, 0.2 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), at 40 ºC, was sequentially treated with trifluoroacetic acid (15 µL, 0.2 mmol, 1.0 equiv) and a solution of PIFA (104 mg, 0.24 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 3 h, the reaction was allowed to cool to room temperature, NH_3 in MeOH (0.8 M, 2.0 mL) added and the mixture stirred for 20 min. The reaction mixture

was concentrated under reduced pressure and the residue purified by flash chromatography (1:1, EtOAc:hexanes), to provide **3v** (26 mg, 59%): colorless oil; R_f 0.19 (EtOAc); FTIR (film) υ_{max} 3405, 2951, 1733, 1681, 1437, 1221, 1199, 1064, 1040, 974, 887, 831, 761 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.11 (ddt, *J* = 9.8, 4.7 Hz, 1H, H-6), 4.01 (br s, 1H, OH), 3.77 (dt, *J* = 3.7, 1.2 Hz, 1H, H-1), 3.66 (s, 3H, H-10), 3.61 (s, 3H, H-11), 2.84 (ddt, *J* = 11.4, 4.9, 2.3 Hz, 1H, H-8), 2.75 (dd, *J* = 5.5, 2.8 Hz, 1H, H-4), 2.52 (ddd, *J* = 14.5, 5.1, 1.5 Hz, 1H, H-7), 2.06 (dddd, *J* = 14.5, 9.9, 2.8, 2.1 Hz, 1H, H-5), 1.97 (dddd, *J* = 15.1, 3.6, 1.0 Hz, 1H, H-7), 1.43 (ddd, *J* = 14.5, 3.7, 2.5 Hz, 1H, H-5); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.4, 170.9, 67.1, 63.3, 60.8, 52.5, 41.7, 39.4, 29.2, 23.0; HRMS-ESI calcd for $C_{10}H_{16}NO_5$ $[M+H]^+$ 230.1028, found: 230.1039.

***trans*-(±)-7-*endo*-Hydroxy-2-methoxy-3-oxo-2-azabicyclo[2.2.2]octan-*exo*-6-yl ethanoate (3w).**



1w **3w**

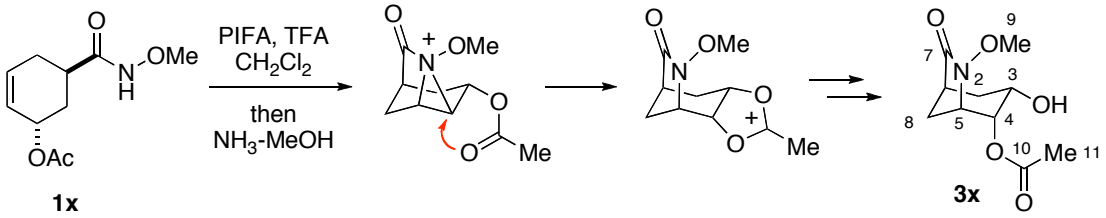
Following Representative Procedure 2, a solution of **1w** (50 mg, 0.23 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), at 40 ºC, was sequentially treated with trifluoroacetic acid (17.4 µL, 0.23 mmol, 1.0 equiv) and a solution of PIFA (136 mg, 0.32 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 15 min, the reaction was allowed to cool to room temperature, NH_3 in MeOH (0.8 M, 2.0 mL) added and the mixture stirred for 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography (1:1, EtOAc:hexanes) to provide **3w** (49 mg, 91%).

Following Representative Procedure 3, a solution of **1w** (150 mg, 0.70 mmol, 1.0 equiv) in CH_2Cl_2 (3.0 mL) was sequentially treated with PIFA (360 mg, 0.84 mmol, 1.2 equiv) in CH_2Cl_2 (3.0 mL) and NH_3 in MeOH (0.8 M, 6.0 mL) to provide, after purification by flash chromatography (1:1, EtOAc:hexanes), **3w** (78 mg, 49%).

Analytical Data for **3w**: white solid; m.p. 88-89 °C; R_f 0.14 (EtOAc); FTIR (film) υ_{max} 3402, 2939, 1739, 1678, 1456, 1441, 1375, 1243, 1204, 1152, 1127. 1050, 1020, 977, 861, 760, 664, 619, 575 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.44 (dt, *J* = 8.7, 2.5 Hz, 1H, H-6), 4.36 (dt, *J* = 9.7, 4.2 Hz, 1H, H-7), 4.07 (dd, *J* = 4.2, 2.5 Hz, 1H, H-1), 3.76 (s,

3H, H-9), 2.65-2.60 (t, *J* = 2.5 Hz, 1H, H-4), 2.37 (ddd, *J* = 14.5, 8.8, 2.6 Hz, 1H, H-5), 2.25 (ddt, *J* = 13.9, 9.8, 3.0 Hz, 1H, H-8), 2.06 (s, 3H, H-11), 1.73 (dq, *J* =14.5, 3.0 Hz, 1H, H-5), 1.40 (dt, *J* = 14.0, 2.7 Hz, 1H, H-8); ^{13}C NMR (400 MHz, $CDCl_3$) δ 170.9, 170.8, 67.8 (C-6), 67.3 (C-7), 64.8 (C-1), 63.3 (C-9), 39.5 (C-4), 33.1 (C-5), 32.8 (C-8), 29.8 (C-11); HRMS-EI calcd for $C_{10}H_{15}NO_5$ $[M]^+$ 229.0950, found: 229.0944.

_O_-Methyl (±)-*trans*-3-Hydroxy-6-methoxy-7-oxo-6-azabicyclo[3.2.1]octan-4-yl ethanoate (3x)



1x **3x**

Following Representative Procedure 2, a solution of **1x** (50 mg, 0.23 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL), at 40 ºC, was sequentially treated with trifluoroacetic acid (17 μL, 0.23 mmol, 1.0 equiv) and a solution of PIFA (119 mg, 0.28 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 2.5 h, the reaction was allowed to cool to room temperature, NH_3 in MeOH (0.8 M, 2.0 mL) added and the mixture stirred for 20 min. The reaction mixture was concentrated under reduced pressure and the residue purified by flash chromatography (1:1, EtOAc:hexanes), to provide **3x** (34 mg, 57%).

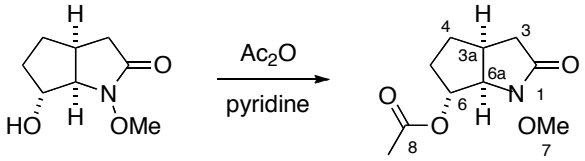
Following Representative Procedure 3, a solution of **1x** (50 mg, 0.23 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was sequentially treated with PIFA (121 mg, 0.28 mmol, 1.2 equiv) in CH_2Cl_2 (1.0 mL) and NH_3 in MeOH (0.8 M, 2.0 mL) to provide, after purification by flash chromatography (1:1, EtOAc:hexanes), **3x** (38 mg, 53%).

Analytical Data for **3x**: yellow oil; R_f 0.11 (EtOAc); IR (film) υ_{max} 3395, 2940, 2895, 2813, 1725, 1692, 1571, 1461, 1440, 1276, 1246, 1198, 1177, 1053, 1002, 972, 761 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD) δ 5.02 (s, 1H, H-4), 4.07 (s, 1H, H-3), 3.93 (d, *J* = 4.8 Hz, 1H, H-5), 3.81 (s, 3H, H-9), 2.38 (appt m, 1H, H-1), 2.10 (s, 3H, H-11), 2.07 (br s, 3H, H-2, H-8), 1.3 (d, *J* = 13.7 Hz, 1H, H-8); ^{13}C NMR (500 MHz, CD_3OD) δ 176.7, 171.6, 70.2, 68.7, 63.7, 56.7, 37.5, 32.8, 28.8, 21.0; HRMS-ESI calcd for $C_{10}H_{15}N_1O_5$ $[M+Na]^+$ 252.0848, found: 252.0854.

The presence of the *O*-acyl group at the C-4 position of **3u** was confirmed by a COSY experiment, which revealed a cross-peak between downfield H-4 and bridgehead H-5.

2.3 Structural Correlation Studies

(3aS*,6*R,6a*R**)-Acetic acid 1-methoxy-2-oxooctahydrocyclopenta[*b*]pyrrol-6-yl ester (14).**

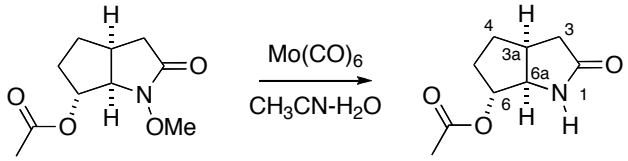


3a **14**

To a solution of **3a** (125 mg, 0.73 mmol, 1.0 equiv) in pyridine (5.0 mL) was added acetic anhydride (2.5 mL) which was stirred for 4 h at rt then concentrated under reduced pressure and the resulting residue purified by flash chromatography on silica gel (EtOAc) to provide **14** (143 mg, 92%): colorless oil; R_f 0.38 (EtOAc); IR (film) υ_{max} 2967, 2942, 1731, 1712, 1440, 1374, 1240, 1145, 1058, 1026, 965, 816, 661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.18-5.17 (m, 1 H, H-6), 4.02 (d, J = 7.6 Hz, 1 H, H-6a), 3.76 (s, 3 H, H-7), 2.82-2.79 (m, 1 H, H-3a), 2.56 (dd, J = 17.6, 10.5 Hz, 1 H, H_α-4), 2.05-1.97 (m, 1 H, H_α-3), 1.93 (s, 3 H, H-9), 1.94-1.86 (m, 1 H, H_β-3), 1.85-1.52 (m, 2 H, H-5), 1.51-1.49 (m, 1 H, H_β-4); ^{13}C NMR (125 MHz, $CDCl_3$) 170.5, 169.8, 76.7 (C-6), 66.4 (C-6a), 62.6 (C-7), 34.8, 32.0, 31.7, 29.8, 21.5 (C-9); HRMS-ESI calcd for $C_{10}H_{15}NO_4Na$ $[M+Na]^+$ 236.0899, found: 236.0908.

2.3.1 Representative Procedure 7. Reductive Cleavage of *N*-Methoxylactams

(3a*S,6*R**,6a*R**)-Acetic acid 2-oxooctahydrocyclopenta[*b*]pyrrol-6-yl ester (15).**



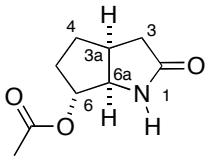
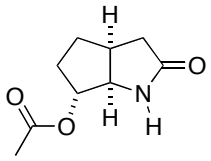
14 **15**

To a solution of **14** (25 mg, 0.11 mmol, 1.0 equiv) in CH_3CN-H_2O (15/1, 3.5 mL) was added $Mo(CO)_6$ (37 mg, 0.14 mmol, 1.2 equiv) and the reaction heated to reflux for 13 h. After cooling to room temperature, the black reaction mixture was then concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (hexanes→acetone) to provide **15** (19 mg, 88%): white solid; mp 64-65 °C [lit.[15] 63-64 °C]; R_f 0.29 (acetone); IR (film) υ_{max} 3242, 2955, 1733, 1680, 1368, 1248, 1039, 913, 745

15. Knapp, S.; Levorse, A.T. *J. Org. Chem.* **1988**, *53*, 4006.

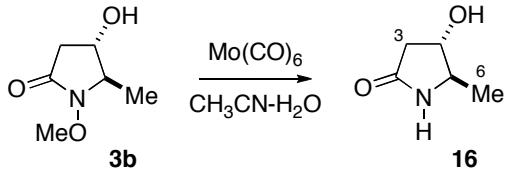
cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.09 (br s, 1 H, NH), 4.75-4-71 (m, 1 H, H-6), 3.82 (d, J = 7.9 Hz, 1 H, H-3a), 2.95-2.87 (m, 1 H, H-6a), 2.60 (dd, J = 17.7, 10.2 Hz, 1 H, H_α-4), 2.11-2.06 (m, 1 H, H_α-3), 2.05 (s, 3 H, H-8), 2.03-2.01 (m, 2 H, H-5), 1.81-1.79 (m, 1 H, H_β-3), 1.55-1.50 (m, 1 H, H_β-4); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 171.2, 81.2 (C-6), 64.6 (C-6a), 36.7, 36.5, 31.0, 29.9, 21.0 (C-8); HRMS-ESI calcd for $C_9H_{13}NO_3Na$ $[M+Na]^+$ 206.0793, found: 206.0789.

2.3.2 Tabular Comparison of Spectral Data for Compound 15.

Compound **15**		Knapp[15]
		
δ^1H (ppm)[a]	$\Delta\ \delta_H$	δ^1H (ppm)[a]
1.55-1.50 (m, 1 H)	0.06	1.61-1.48 (m, 1 H)
1.81-1.79 (m, 1 H)	0.00	1.81-1.73 (m, 1 H)
2.03-2.01 (m, 2 H)	0.00	2.03-1.98 (m, 2 H)
2.05 (s, 3 H)	0.00	2.05 (s, 3 H)
2.11-2.06 (m, 1 H)	0.03	2.14-2.07 (m, 1 H)
2.60 (dd, J = 17.7, 10.2, 1 H)	0.02	2.58 (dd, J = 18, 10, 1 H)
2.95-2.87 (m, 1 H)	0.01	2.94-2.90- (m, 1 H)
3.82 (d, J = 7.9, 1 H)	0.02	3.80 (d, J = 8, 1 H)
4.75-4-71 (m, 1 H)	0.03	4.72-4.69 (m, 1 H)
6.09 (br s, 1 H, NH)	0.14	5.95-5.89 (m, 1 H)

[a]400 MHz ($CDCl_3$).

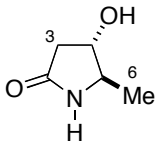
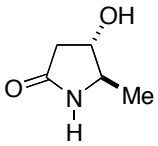
(4*S,5*R**)-4-Hydroxy-5-methylpyrrolidin-2-one (16).**



3b **16**

Following Representative Procedure 7, a solution of **3b** (35 mg, 0.24 mmol, 1.0 equiv) in CH_3CN-H_2O (15:1, 5.0 mL) was treated with $Mo(CO)_6$ (76 mg, 0.28 mmol, 1.2 equiv) to provide, after purification by flash chromatography (hexanes→acetone), known **16** (24 mg, 89%): colorless oil; R_f 0.47 (CH_2Cl_2-MeOH, 85:15); FTIR (film) υ_{max} 3326, 3239, 2964, 2932, 1675, 1433, 1268, 1048, 701 cm^{-1}; ^1H NMR (400 MHz, $(CD_3)_2SO$) δ 7.60 (br s, 1 H, NH), 5.17 (br s, 1 H, OH), 3.90-3.76 (m, 1 H,C-4), 3.29-3.23 (m, 1 H, H-5), 2.45 (dd, J = 16.7, 6.6 Hz, 1 H, H_α-3), 1.91 (dd, J = 16.7, 4.4 Hz, 1 H, H_β-3), 1.04 (d, J = 6.6 Hz, 3 H, H-6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3 (C-2), 73.9 (C-4), 58.7 (C-5), 39.4 (C-3), 19.7 (C-6); HRMS-ESI calcd for $C_5H_9NO_2Na$ $[M+Na]^+$ 138.0531, found 138.0534.

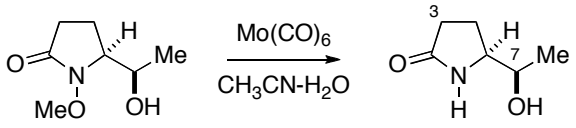
2.3.3 Tabular Comparison of Spectral Data for Compound 16.

Compound **16**		Poncet[16]
		
δ ^1H (ppm)[a]	$\Delta\delta_H$	δ ^1H (ppm)[b]
1.04 (d, J = 6.5, 1 H)	0.03	1.07 (d, J = 6.5, 3H)
1.91 (dd, J = 16.7, 4.4, 1H)	0.03	1.94 (dd, J = 16.8, 4.7, 1H)
2.45 (dd, J = 16.7, 6.8, 1H)	0.06	2.39 (dd, J = 16.8, 6.6, 1H)
3.29-3.23 (m, 1 H)	-	3.37-3.25 (m, 1H)
3.90-3.76 (m, 1 H))	-	3.95-3.77 (m, 1H)
5.17 (br s, 1H)	0.02	5.15 (br s, 1H)
7.60 (br s, 1H)	0.03	7.57 (br s, 1H)

[a] ^1H NMR 400 MHz ($(CD_3)_2CO$). [b] ^1H NMR 360 MHz ($(CD_3)_2CO$).

16. Galeotti, N.; Poncet, J.; Chiche, L.; Jouin, P. *J. Org. Chem.* **1993**, *58*, 5370.

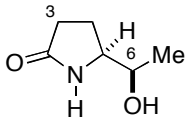
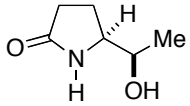
(5*S,6*R**)-5-(1-Hydroxyethyl)-pyrrolidin-2-one (17).**



3c **17**

Following Representative Procedure 7, a solution of **3c** (20 mg, 0.12 mmol, 1.0 equiv) in CH_3CN-H_2O (15:1, 3 mL) was treated with $Mo(CO)_6$ (40 mg, 0.15 mmol, 1.2 equiv) to provide, after purification by flash chromatography (hexanes→acetone), known **17** (15 mg, 94%): white solid; mp 84-85 °C [lit.[17] 85-86 °C]; R_f 0.13 (acetone); FTIR (film) υ_{max} 3361, 3279, 2971, 2887, 1683, 1456, 1270, 1079 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.62 (br, s, 1 H, NH), 3.87-3.84 (m, 1 H), 3.67-3.63 (m, 1 H), 2.38-2.30 (m, 2 H), 2.13-2.00 (m, 2 H), 1.15 (d, J = 6.4 Hz, 3 H, H-7); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4 (C-2), 68.7 (C-6), 59.2 (C-5), 30.1, 20.6, 18.0 (C-7); HRMS-ESI calcd for $C_6H_{11}NO_2Na$ $[M+Na]^+$ 152.0687, found 152.0686.

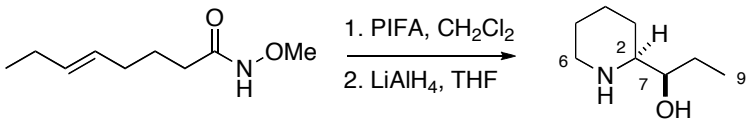
2.3.4 Tabular Comparison of Spectral Data for Compound 17.

Compound **17**		Georgiadis[17]
		
δ^1H (ppm)[a]	$\Delta\delta_H$	δH (ppm)[b]
1.15 (d, J = 6.4, 3 H)	0.03	1.18 (d, J = 6.3, 3 H)
2.13-2.00 (m, 2 H)	-	1.78 (m, 2 H)
2.38-2.30 (m, 2 H)	-	2.24 (m, 2 H)
3.67-3.63 (m, 1 H)	-	3.78 (m, 2 H)
3.87-3.84 (m, 1 H)	-	4.25 (br s, 1 H)
6.62 (br, s, 1 H, NH)	0.02	6.60 (br s, 1 H)
mp 84-85 °C		mp 85-86 °C

[a] ^1H NMR 400 MHz ($CDCl_3$). [b] ^1H NMR 300 MHz ($CDCl_3$).

17. Georgiadis, M. P.; Haroutounian, S. A.; Apostolopoulos, C. P. *Synthesis* **1991**, 379.

(±)-α-Conhydrine [(2*S,7*R**)-1-piperidin-2-yl-propan-1-ol] (18).**



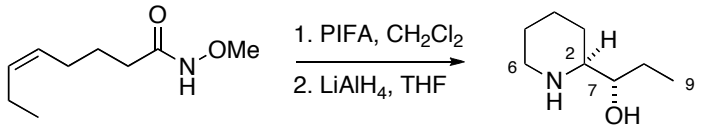
1d α-Conhydrine (**18**)

To a solution of **1d** (49 mg, 0.28 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 0 °C was added a solution of PIFA (123 mg, 0.28 mmol, 1.0 equiv) in CH_2Cl_2 (2.0 mL). After stirring for 10 min, the reaction mixture was concentrated under reduced pressure. The crude trifluoroacetate residue was then dissolved in THF (2.0 mL) and added to a stirred suspension of $LiAlH_4$ (106 mg, 2.8 mmol, 10 equiv) in THF (4.0 mL). The reaction mixture was then heated at reflux for 14 h, cooled to 0 °C, quenched with a sufficient amount of saturated aqueous Na_2SO_4 to cause a white precipitate to form. Solid anhydrous Na_2SO_4 was then added and the mixture stirred for 20 min before being filtered through a pad of Celite 521. The filtrate was concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (NH_3-MeOH/CH_2Cl_2, 1:1) to provide **18** (38 mg, 93%): colorless solid; mp 98-100 °C [lit.[18] 99-100 °C]; R_f 0.34 (NH_3-MeOH/EtOAc 1:1); FTIR (film) υ_{max} 3298, 3261, 2950, 1544, 1455, 1391, 1320, 1205, 1064, 977, 902 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.55-3.51 (m, 1 H, H-7), 3.48 (br s, 1 H), 3.21-3.18 (m, 1 H, H-2), 2.71 (ddd, *J* = 15.0, 12.1, 2.7 Hz, 1 H, H-6), 2.63 (dt, *J* = 11.0, 2.7 Hz, 1 H, H-6), 1.87-1.84 (m, 1 H), 1.65-1.60 (m, 2 H), 1.49-1.33 (m, 5 H), 0.97 (t, *J* = 7.5 Hz, 3 H, H-9); ^{13}C NMR (100 MHz, $CDCl_3$) δ 74.9 (C-7), 60.3 (C-2), 46.6 (C-6), 25.6 (C-5), 25.5 (C-8), 24.3 (C-4), 23.9 (C-3), 10.6 (C-9); HRMS-ESI calcd for $C_8H_{18}NO$ $[M+H]^+$ 144.1388, found 144.1382.

Analytical Data for Synthetic (-)-α-Conhydrine (**18**):[19] ^1H NMR (500 MHz, $CDCl_3$) δ 3.42 (m, 1 H, H-7), 3.12 (m, 1 H), 2.72 (dt, *J* = 12.0, 2.7 Hz, 1 H, H-6), 3.05 (br s, 2 H, OH, NH), 2.56 (dt, *J* = 10.7, 2.7 Hz, 1 H, H-6), 1.86 (m, 1 H), 1.60 (m, 2 H), 1.53-1.22 (m, 5 H), 0.98 (t, *J* = 7.5 Hz, 3 H, H-9); ^{13}C NMR (125 MHz, $CDCl_3$) δ 75.71 (C-7), 60.29 (C-2), 46.99 (C-6), 26.47 (C-5), 25.52 (C-8), 25.13 (C-4), 24.40 (C-3), 10.61 (C-9).

18. Hill, R. K. *J. Am. Chem. Soc.* **1958**, *80*, 1609.
19. Enders, D.; Nolte, B.; Raabe, G.; Runsink, J. *Tetrahedron-Asymmetry* **2002**, *13*, 285.

(±)-β-Conhydrine [(2*S,7*S**)-1-piperidin-2-yl-propan-1-ol] (19).**



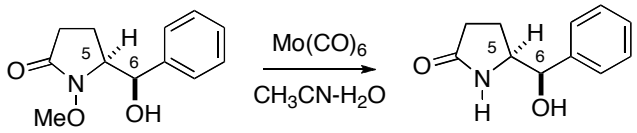
1e β-Conhydrine (**19**)

To a solution of **1e** (30 mg, 0.17 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) at 0 °C was added a solution of PIFA (73 mg, 0.17 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL). After stirring for 10 min, the reaction mixture was concentrated under reduced pressure. The crude trifluoroacetate residue was dissolved in THF (3.0 mL) and added to a stirred suspension of $LiAlH_4$ (64 mg, 1.7 mmol, 10 equiv) in THF (7.0 mL). The reaction mixture was then heated at reflux for 14 h, cooled to 0 °C, quenched with a sufficient amount of saturated aqueous Na_2SO_4 to cause a white precipitate to form. Solid anhydrous Na_2SO_4 was then added and the mixture stirred for 20 min before being filtered through a pad of Celite 521. The filtrate was concentrated under reduced pressure and the residue purified by flash chromatography on silica gel (NH_3-MeOH/CH_2Cl_2, 1:1) to provide **19** (23 mg, 92%): colorless solid; mp 67-68 °C [lit.[20] 68 °C]; R_f 0.24 (acetone); FTIR (film) υ_{max} 3369, 2950, 1590, 1484, 1442, 1378, 1288, 1255, 1063 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 3.27 (ddd, *J* = 11.3, 8.0, 3.4 Hz, 1 H, H-7), 3.14-3.10 (m, 1 H, H-2), 2.61 (ddd, *J* = 14.9, 11.8, 2.9 Hz, 1 H, H-6), 2.41(ddd, *J* = 10.6, 7.5, 2.9 Hz, 1 H, H-6), 2.24 (br, 2, 1 H), 1.80-1.69 (m, 1 H), 1.69-1.51 (m, 2 H), 1.49-1.30 (m, 3 H), 1.29-1.11 (m, 2 H), 0.98 (t, *J* = 7.4 Hz, 3 H, H-9); ^{13}C NMR (100 MHz, $CDCl_3$) δ 75.4 (C-7), 60.8 (C-2), 46.3 (C-6), 28.8 (C-5), 26.4 (C-8), 26.3 (C-4), 24.2 (C-3), 9.9 (C-9); HRMS-ESI calcd for $C_8H_{18}NO$ $[M+H]^+$ 144.1388, found 144.1391.

Analytical Data for Synthetic (-)-β-Conhydrine (**19**):[21] ^1H NMR (300 MHz, $CDCl_3$) δ 3.15 (td, *J* = 7.7, 3.4 Hz, 1 H), 3.05-2.98 (m, 1 H) 2.52 (td, *J* = 11.7, 2.7 Hz, 1 H), 2.29 (ddd, *J* = 10.0, 7.5, 2.5 Hz, 1 H), 1.50-1.02 (m, 8 H), 0.92 (t, *J* = 7.5 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 75.9 (C-7), 61.3 (C-2), 46.9 (C-6), 29.5 (C-5), 26.9 (C-8), 26.8 (C-4), 24.8 (C-3), 10.5 (C-9).

20. Beak, P.; Lee, W. K. *J. Org. Chem.* **1993**, *58*, 1109.
21. (a) Agami, C.; Couty, F.; Rabasso, N. *Tetrahedron Lett.* **2000**, *41*, 4113. (b) Agami, C.; Couty, F.; Rabasso, N. *Tetrahedron* **2001**, *57*, 5393.

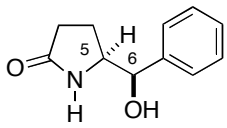
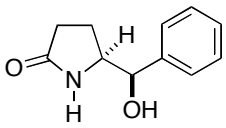
(5*S,6*R**)-5-(Hydroxyphenylmethyl)-pyrrolidin-2-one (20).**



3l **20**

Following Representative Procedure 7, a solution of **3l** (10.0 mg, 0.045 mmol, 1.0 equiv) in CH_3CN-H_2O (15:1, 2.0 mL) was treated with $Mo(CO)_6$ (14.3 mg, 0.054 mmol, 1.2 equiv) to provide, after purification by flash chromatography (hexanes→acetone), known **20** (8 mg, 93%): colorless oil; R_f 0.43 (acetone); FTIR (film) υ_{max} 3357, 3269, 2923, 1661, 1532, 1448, 1262, 1155, 1015, 847, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.41-7.25 (m, 5 H, Ph), 6.54 (br s, 1 H), 4.74 (br s, 1 H), 4.65 (d, J = 4.0 Hz, 1 H, H-6), 3.83-3.79 (m, 1 H, H-5), 2.05-1.43 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9 (C-2), 142.0, 127.9, 127.1, 126.5, 74.9 (C-6), 59.5 (C-5), 29.5, 21.1; HRMS-ESI calcd for $C_{11}H_{13}NO_2Na$ $[M+Na]^+$ 214.0844, found 214.0839.

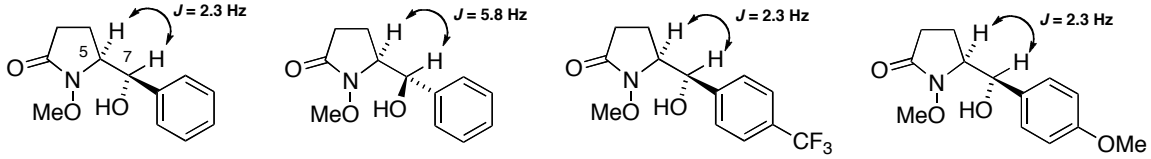
2.3.5 Tabular Comparison of Spectral Data for Compound 20.

Compound **20**		Langlois[22]
		
δ^1H (ppm)[a]	$\Delta\delta_H$	δ^1H (ppm)[b]
2.05-1.43 (m, 4 H)	-	1.50-2.35 (m, 4 H)
3.83-3.79 (m, 1 H)	-	3.60-1.05 (m, 2 H)
4.65 (d, J = 4.0, 1 H)	0.00	4.65 (d, J = 3.8, 1 H)
4.74 (br s, 1 H)	-	--
6.54 (br s, 1 H)	-	6.86 (s, 1 H)
7.41-7.25 (m, 5 H)	-	7.27 (m, 5 H)

[a] ^1H NMR 400 MHz ($CDCl_3$). [b] ^1H NMR 60 MHz ($CDCl_3$).

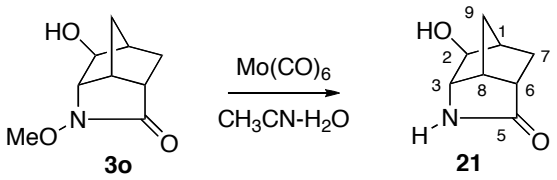
22. Calvez, O.; Chiaroni, A.; Langlois, N. *Tetrahedron Lett.* **1998**, *39*, 9447.

Having thus established the relative stereochemistry of **3l**, the stereochemical assignments made for **7-*epi*-3l**, **3m** and **3n** were confirmed by comparison of the observed 5-H/7-H vicinal coupling constants, as outlined below.



3l **7-*epi*-3l** **3m** **3n**

(2*S,3*S**,6*S**)-2-Hydroxy-4-azatricyclo[4.2.1.$0^{0,0}$]nonan-5-one (21).**

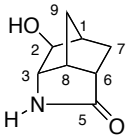
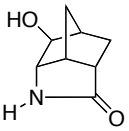


3o **21**

Following Representative Procedure 7, a solution of **3o** (21 mg, 0.11 mmol, 1.0 equiv) in CH_3CN-H_2O (15:1, 2.0 mL) was treated with $Mo(CO)_6$ (37 mg, 1.4 mmol, 1.2 equiv) to provide, after purification by flash chromatography (hexanes→acetone), known **21** (14 mg, 82%): white solid: mp 179-180 °C [lit.[23] 181-182 °C]; R_f 0.19 (acetone); FTIR (film) υ_{max} 3351, 2960, 2872, 1683, 1474, 1243, 1067 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 3.78 (s, 1 H), 3.66 (d, J = 4.4 Hz, 1 H), 3.39-3.38 (m, 1 H), 2.64-2.62 (m, 1 H), 2.49 (dd, J = 10.6, 4.4 Hz, 1 H), 2.20-2.13 (m, 2 H), 1.78-1.68 (m, 3 H); ^{13}C NMR (100 MHz, D_2O) δ 187.3 (C-5), 78.9 (C-2), 64.5 (C-3), 47.6 (C-6), 46.1 (C-8), 42.0 (C-1), 34.2 (C-9), 32.8 (C-7); HRMS-ESI calcd for $C_8H_{11}NO_2Na$ $[M+Na]^+$ 176.0698, found 176.0693.

23. Brown, I.; Edwards, O. E.; McIntosh, J. M.; Vocelle, D. *Can. J. Chem.* **1969**, *47*, 2751.

2.3.6 Tabular Comparison of Spectral Data for Compound 21.

Compound **21**	Edwards[23]
	
δ^1H (ppm)[a]	δ^1H (ppm)[b]
1.78-1.68 (m, 3 H)	1.40-2.78 (m, 6 H)
2.20-2.13 (m, 2 H)	
2.49 (dd, *J* = 10.6, 4.4 Hz, 1 H)	
2.64-2.62 (m, 1 H)	
3.39-3.38 (m, 1 H)	3.51-3.28 (m, 1 H)
3.66 (d, *J* = 4.4 Hz, 1 H)	3.74-3.55 (d, 1 H)
3.78 (s, 1 H)	3.80 (s, 1 H)
mp 179-180 °C	mp 181-182 °C

[a] ^{1}H NMR 400 MHz (D_2O). [b] ^{1}H NMR 60 MHz (D_2O).