

SUPPORTING INFORMATION FOR:

Olefinic-Amide and Olefinic-Lactam Cyclizations

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General Information

NMR spectra were recorded on either Varian Inova-500 MHz or Varian VXR-500 MHz spectrometers. Chemical shifts were reported in δ , parts per million (ppm), relative to benzene (7.15) or chloroform (7.25) as internal standards. Coupling constants, J, were reported in Hertz (Hz) and refer to apparent peak multiplicities and not true coupling constants. Mass spectra were recorded at the Mass Spectrometry Facility at the Department of Chemistry of the University of Utah at Salt Lake City on a Finnigan MAT 95 mass spectrometer and at the Mass Spectrometry Facility at the Department of Chemistry of the University of California at Riverside on a Agilent LCTOF mass spectrometer. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer. Solvents were purified according to the guidelines in Purification of Common Laboratory Chemicals (Perrin, Armarego, and Perrin: Oxford, 1966). (*i*-Pr)₂NEt, 2,6-lutidine, TMEDA and pyridine were distilled from CaH₂. Spectroscopic grade DMF was stored over activated 4Å molecular sieves and used without purification. Zn dust (<10 μ m, Aldrich) was activated by sequentially washing with HCl, H₂O, ether, and acetone and then drying under vacuum overnight. All other reagents were used without purification. Unless otherwise stated, all reactions were run under an atmosphere of dried nitrogen in flame-dried glassware. Concentration refers to removal of solvent under reduced pressure (house vacuum at ca. 20 mmHg).

General Procedure for the Formation of N-tosyl protected amides

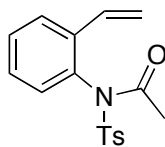
To a cold (0 °C) solution of NaH (26 mg, 60% dispersion in mineral oil, 0.65 mmol) in dry THF (2.0 mL) was added a solution of amide (0.5 mmol) in THF (1 mL). The reaction mixture was stirred at 0 °C for 1 h. To this mixture was added a solution of tosyl chloride (123.5 mg, 0.65 mmol) in dry THF (1.0 mL) via cannula. The reaction mixture was warmed to rt over 1 h and quenched with sat. NH₄Cl (aq., 5 mL) once the starting material had been completely consumed. The aqueous phase was extracted with CH₂Cl₂ (3 \times 30 mL), dried (MgSO₄) and concentrated. The resulting residue was purified by flash chromatography.

General Procedure for the Formation of N-tosyl protected lactams

To a solution of lactam in THF at 0 °C was added a solution of n-BuLi in THF. After the resulting reaction mixture had stirred for 1 h, a solution of tosyl chloride in THF was added via cannula. The ice bath was removed after 0.5 h, the reaction mixture was warmed to rt, and the reaction was quenched with water. The aqueous phase was extracted with CH₂Cl₂, the extracts were dried (MgSO₄) and concentrated. The resulting residue was purified by flash chromatography.

General procedure for olefinic amide/lactam cyclizations:

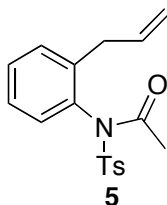
A flame-dried three-necked flask fitted with a condenser was cooled to 0 °C and charged with CH₂Cl₂ followed by TiCl₄. To the resulting solution was added THF dropwise at which time the solution turned yellow. The addition of THF was followed by the dropwise addition of TMEDA resulting in the formation of a brown solution. The ice bath was removed and the mixture was allowed to stir for 20 min. Activated Zn dust and PbCl₂ were then added. The resulting mixture went through a series of color changes from brown to green to purple and finally to blue-green over the course of 3-5 min. To the slurry was transferred a solution of N-tosyl protected lactam or amide and CH₃CHBr₂ in CH₂Cl₂ via cannula. The reaction mixture was then heated at reflux for 2-4 h. Following this time period the mixture was cooled to 0 °C and quenched with sat. K₂CO₃ (aq., 6.5 mL/mmol substrate). After stirring for 30 min at 0 °C, the resulting mixture was filtered and the filtrate was concentrated. The resulting residue was purified by flash chromatography.



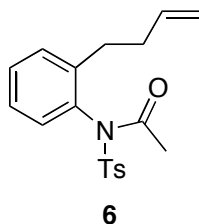
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N-tosyl-N-(2-vinylphenyl)acetamide (4). Prepared according the general procedure described above using N-(2-ethenylphenyl) acetamide¹ (80. mg, 0.50 mmol), NaH (26 mg of a 60% dispersion in mineral oil, 0.65 mmol) and tosyl chloride (124 mg, 0.650 mmol) to give 140 mg (89%) of N-tosyl protected amide **4** as a white waxy solid after flash chromatography (hexanes:ethyl acetate, 20:1 to 10:1). mp 73-74 °C; ¹H NMR (500 MHz, C₆D₆) δ 8.16 (d, *J* = 8.3 Hz, 2 H), 7.34 (d, *J* = 7.8 Hz, 1 H), 7.00-6.91 (m, 4 H), 6.77 (d, *J* = 8.8 Hz, 2 H), 5.50 (d, *J* = 17.0 Hz, 1 H), 5.02 (d, *J* = 10.7 Hz, 1 H), 1.85 (s, 3 H), 1.38 (s, 3 H); ¹³C NMR (125 MHz, C₆D₆) δ 169.4, 144.6, 138.2, 137.2, 135.5, 131.9, 130.6, 130.2, 129.9, 129.3, 129.0,

126.5, 117.9, 24.4, 21.2; IR (film) 3066, 2921, 1709, 1423, 1167 cm^{-1} ; LRMS m/z calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_3\text{SNa}$ 338.1 ($\text{M}+\text{Na}^+$), found 338.1.



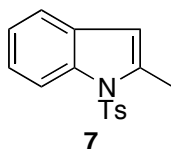
N-(2-allylphenyl)-N-tosylacetamide (5). Prepared according the general procedure described above using N-[2-(2-propen-1-yl)phenyl]-acetamide² (88 mg, 0.50 mmol), NaH (26 mg of a 60% dispersion in mineral oil, 0.65 mmol) and tosyl chloride (123.5 mg, 0.65 mmol) to give 140 mg (85%) of N-tosyl protected amide **5** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 10:1). ¹H NMR (500 MHz, C_6D_6) δ 8.14 (d, J = 8.3 Hz, 2 H), 7.10 (d, J = 7.8 Hz, 1 H), 7.01 (dd, J = 7.7, 7.6 Hz, 1 H), 6.88 (ddd, J = 7.8, 7.8, 1.5 Hz, 1 H), 6.77-6.75 (m, 3 H), 5.77 (dddd, J = 17.6, 10.3, 7.8 Hz, 1 H), 5.08 (ddt, J = 17.1, 1.8, 1.8 Hz, 1 H), 4.96 (dd, J = 9.8, 0.9 Hz, 1 H), 3.59-3.46 (m, 2 H), 1.84 (s, 3 H), 1.40 (s, 3 H); ¹³C NMR (125 MHz, C_6D_6) δ 169.4, 144.5, 141.2, 137.3, 136.8, 135.7, 131.0, 130.1, 129.9, 129.8, 129.3, 128.3, 127.5, 117.4, 36.1, 24.6, 21.1; IR (film) 2923, 1708, 1360, 1167 cm^{-1} ; LRMS m/z calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_3\text{SNa}$ 352.1 ($\text{M}+\text{Na}^+$), found 352.1.



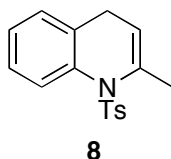
N-(2-(but-3-enyl)phenyl)-N-tosylacetamide (6). To a solution of 2-(3-butenyl)aniline³ (106 mg, 0.720 mmol) in CH_2Cl_2 (4.0 mL) at 0 °C was added pyridine (0.064 mL, 0.79 mmol) followed by a solution of acetyl chloride (0.065 mL, 0.79 mmol) in CH_2Cl_2 (1.5 mL). After 12 h, the mixture was quenched with sat. NH_4Cl (aq., 5 mL). The aqueous phase was extracted with CH_2Cl_2 (3×20 mL), dried (MgSO_4) and concentrated. The resulting residue containing the acetamide corresponding to 2-(3-butenyl)aniline was taken on to the next step without additional purification.

The tosyl amide **6** was prepared according the general procedure using the acetamide from above, NaH (26 mg of a 60% dispersion in mineral oil, 0.65 mmol) and tosyl chloride (124 mg, 0.650 mol) to give 136 mg (55% over 2 steps) of N-

tosyl protected amide **6** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 10:1). ^1H NMR (500 MHz, C_6D_6) δ 8.14 (d, $J = 8.3$ Hz, 2 H), 7.06-7.01(m, 2 H), 6.90-6.86 (m, 1 H), 6.79 (d, $J = 7.8$ Hz, 1 H), 6.77 (d, $J = 7.9$ Hz, 2 H), 5.74 (ddt, $J = 17.1, 10.3, 6.3$ Hz, 1 H), 5.04 (ddd, $J = 17.1, 1.8, 1.8$ Hz, 1 H), 4.94 (dd, $J = 9.8, 1.0$ Hz, 1 H), 2.96-2.90 (m, 1 H), 2.78-2.72 (m, 1 H), 2.44-2.41 (m, 1 H), 2.33-2.25 (m, 1 H), 1.85 (s, 3 H), 1.40 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 169.4, 144.5, 142.6, 137.8, 137.4, 136.8, 130.4, 130.1, 129.8, 129.8, 129.3, 127.2, 115.6, 33.7, 30.6, 24.4, 21.1; IR (film) 3072, 2925, 1708, 1362, 1167 cm^{-1} ; LRMS m/z calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_3\text{SNa}$ 366.1 ($\text{M}+\text{Na}^+$), found 366.1.

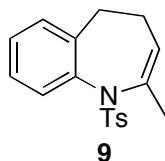


2-methyl-1-tosyl-1H-indole (7). The general cyclization protocol was carried out on amide **4** (17 mg, 0.054 mmol) using TiCl_4 (0.19 mL, 1.7 mmol) in CH_2Cl_2 (15.5 mL), THF (0.91 mL, 10. mmol), TMEDA (1.55 mL, 10.4 mmol), activated Zn dust (252 mg, 3.88 mmol), PbCl_2 (57 mg, 0.20 mmol), and CH_3CHBr_2 (0.157 mL, 1.72 mmol) in CH_2Cl_2 (1.0 mL + 1.0 mL rinse) to give 10.8 mg (70 %) of **7** as a waxy solid after flash chromatography (hexanes: ethyl acetate, 20:1 to 10:1 to 5:1). mp 65-67 $^\circ\text{C}$ ^1H NMR (500 MHz, C_6D_6) δ 8.50 (d, $J = 8.3$ Hz, 1 H), 7.50 (d, $J = 8.3$ Hz, 2 H), 7.19 (d, $J = 7.8$ Hz, 1 H), 7.11-7.10 (partially obscured m, 1 H), 7.02 (t, $J = 7.6$ Hz, 1 H), 6.38 (d, $J = 7.8$ Hz, 2 H), 5.91 (d, $J = 0.98$ Hz, 1 H), 2.40 (s, 3 H), 1.58 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 144.1, 137.2, 130.2, 129.7, 128.2, 127.8, 126.4, 124.1, 123.8, 120.3, 115.2, 109.9, 20.9, 15.7; IR (film) 2921, 1596, 1449, 1367, 1172, 1091 cm^{-1} ; LRMS m/z calcd for $\text{C}_{16}\text{H}_{15}\text{NO}_2\text{SNa}$ 308.1 ($\text{M}+\text{Na}^+$), found 308.1.



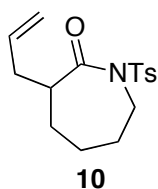
2-methyl-1-tosyl-1,4-dihydroquinoline (8). The general cyclization protocol was carried out on amide **5** (20. mg, 0.061 mmol) using TiCl_4 (0.21 mL, 1.9 mmol) in CH_2Cl_2 (17.5 mL), THF (1.03 mL, 11.8 mmol), TMEDA (1.75 mL, 11.8 mmol), activated Zn dust (285 mg, 4.38 mmol), PbCl_2 (64 mg, 0.23 mmol), and CH_3CHBr_2 (0.18 mL, 1.97 mmol) in CH_2Cl_2 (1.2 mL + 1.2 mL rinse) to give 14 mg (78 %) of **8** as a colorless oil following flash chromatography (hexanes: ethyl acetate, 20:1 to 10:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 8.02 (d, $J = 8.3$ Hz, 1 H), 7.39 (d, $J =$

7.8 Hz, 2 H), 7.05 (t, $J = 7.8$ Hz, 1 H), 6.89 (dt, $J = 7.4, 1.0$ Hz, 1 H), 6.54 (d, $J = 7.3$ Hz, 1 H), 6.50 (d, $J = 7.8$ Hz, 2 H), 5.12-5.10 (m, 1 H), 2.32-2.31 (m, 3 H), 1.86 (brs, 2 H), 1.74 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.3, 138.7, 138.7, 135.5, 134.9, 129.1, 128.3, 127.8, 127.2, 126.7, 126.6, 120.7, 27.4, 22.6, 21.0; IR (film) 3032, 2921, 2850, 1487, 1455, 1356, 1169, 1089 cm^{-1} ; LRMS m/z calcd for $\text{C}_{17}\text{H}_{17}\text{NO}_2\text{SNa}$ 322.1 ($\text{M}+\text{Na}^+$), found 322.1.

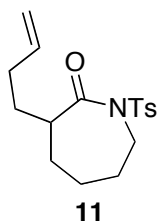


(Z)-2-methyl-1-tosyl-4,5-dihydro-1H-benzo[b]azepine (9). The general cyclization protocol was carried out on amide **6** (35 mg, 0.10 mmol) using TiCl_4 (0.37 mL, 3.4 mmol) in CH_2Cl_2 (31 mL), THF (1.82 mL, 20.8 mmol), TMEDA (3.10 mL, 20.8 mmol), activated Zn dust (504 mg, 7.75 mmol), PbCl_2 (110 mg, 0.41 mmol), and CH_3CHBr_2 (0.31 mL, 3.4 mmol) in CH_2Cl_2 (2.0 mL + 2.0 mL rinse) to give 18 mg (58 %) of **9** and 6.8 mg (18%) of the acyclic enamine as colorless oils following flash chromatography (hexanes: ethyl acetate, 20:1 to 10:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 7.7 (d, $J = 8.3$ Hz, 2 H), 7.29 (dd, $J = 7.8, 1.5$ Hz, 1 H), 6.94 (dt, $J = 7.2, 1.4$ Hz, 1 H), 6.91 (t, $J = 7.6, 2.0$ Hz, 1 H), 6.79 (dd, $J = 7.32, 1.5$ Hz, 1 H), 6.65 (d, $J = 7.8$ Hz, 2 H), 4.79 (t, $J = 3.5$ Hz, 1 H), 2.88 (dt, $J = 14.7, 5.4$ Hz, 1 H), 2.30-2.29 (m, 3 H), 1.97-1.90 (m, 2 H), 1.81 (s, 3 H), 1.66-1.58 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.9, 142.4, 141.2, 138.8, 135.8, 129.5, 129.4, 129.2, 128.6, 127.8, 126.8, 121.8, 29.2, 28.0, 25.5, 21.1; IR (film) 2922, 1487, 1453, 1346, 1162, 1091 cm^{-1} ; LRMS m/z calcd for $\text{C}_{18}\text{H}_{19}\text{NO}_2\text{SNa}$ 336.1 ($\text{M}+\text{Na}^+$), found 336.1.

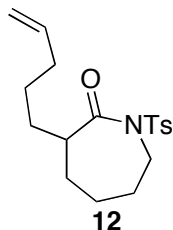
acyclic enamine from the cyclization of **6**: ^1H NMR (500 MHz, C_6D_6) δ 7.80 (d, $J = 8.3$ Hz, 2 H), 7.11-6.86 (m, 8 H), 6.72 (d, $J = 8.3$ Hz, 2 H), 5.78-5.74 (m, 1 H), 5.52-5.45 (m, 2 H), 3.0-2.77 (m, 3 H), 2.38 (m, 2 H), 2.0 (m, 3 H), 1.87-1.84 (m, 6 H), 1.69 (m, 6 H), 1.61-1.56 (m, 6 H), 1.37-1.32 (m, 16 H), 0.99-0.90 (m, 5 H); IR (film) 3057, 2920, 2851, 1712, 1350, 1265, 1160, 1092 cm^{-1} ; LRMS m/z calcd for $\text{C}_{22}\text{H}_{27}\text{NO}_2\text{SNa}$ 392.2 ($\text{M}+\text{Na}^+$), found 392.3.



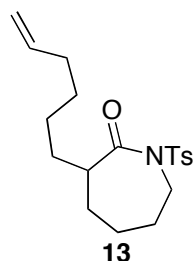
3-allyl-1-tosylazepan-2-one (10). Prepared according to the general procedure described above using hexahydro-3-(2-propen-1-yl)-2H-azepin-2-one⁶ (77 mg, 0.50 mmol), n-BuLi (0.34 mL of a 1.6 M solution in THF, 0.55 mmol), tosyl chloride (124 mg, 0.650 mmol) to give 131 mg (85%) of N-tosyl protected lactam **10** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 8.08 (d, *J* = 8.3 Hz, 2 H), 6.79 (d, *J* = 8.3 Hz, 2 H), 5.60 (dddd, *J* = 17.1, 10.3, 8.3, 5.8 Hz, 1 H), 4.90-4.84 (m, 2 H), 4.48 (ddd, *J* = 15.5, 5.0, 3.0 Hz, 1 H), 2.84 (ddd, *J* = 15.7, 9.8, 2.5 Hz, 1H), 2.39 (dt, *J* = 14.1, 9.3, 1.5 Hz, 1 H), 2.01-1.97 (m, 1 H), 1.89-1.83 (partially obscured m, 1 H), 1.83 (s, 3 H), 1.37-1.26 (m, 4 H), 0.92-0.86 (m, 2 H); ¹³C NMR (125 MHz, C₆D₆) δ 175.1, 143.9, 138.0, 136.4, 129.2, 127.8, 116.9, 45.3, 45.1, 36.4, 28.9, 28.3, 21.1; IR (film) 3071, 2933, 2859, 1700, 1348, 1107, 1037 cm⁻¹; LRMS *m/z* calcd for C₁₆H₂₁NO₃Na 330.1 (M+Na⁺), found 330.1.



3-(but-3-enyl)-1-tosylazepan-2-one (11). Prepared according to the general procedure described above using hexahydro-3-(3-buten-1-yl)-2H-azepin-2-one⁷ (84 mg, 0.50 mmol), n-BuLi (0.34 mL of a 1.6 M solution in THF, 0.55 mmol), tosyl chloride (124 mg, 0.650 mmol) to give 135 mg (84%) of N-tosyl protected lactam **11** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 8.07 (d, *J* = 8.3 Hz, 2 H), 6.79 (d, *J* = 8.3 Hz, 2 H), 5.64-5.56 (m, 1 H), 4.92-4.88 (m, 2 H), 4.50 (ddd, *J* = 16.1, 3.9, 2.9 Hz, 1 H), 2.96 (ddd, *J* = 15.6, 9.8, 2.4 Hz, 1H), 2.07-2.02 (m, 1 H), 1.89-1.78 (m, 3 H), 1.83 (s 3 H), 1.37-1.28 (m, 3H), 1.14-1.07 (m, 2 H), 0.94 (m, 2 H); ¹³C NMR (125 MHz, C₆D₆) δ 175.3, 143.9, 138.5, 138.1, 129.2, 127.8, 115.0, 45.1, 44.7, 31.5, 31.4, 29.8, 28.7, 28.0, 21.1; IR (film) 3060, 2935, 2860, 1699, 1348, 1167, 1088 cm⁻¹; LRMS *m/z* calcd for C₁₇H₂₃NO₃Na 344.1 (M+Na⁺), found 344.1.

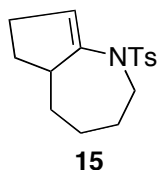


3-(pent-4-enyl)-1-tosylazepan-2-one (12). Prepared according the general procedure described above using hexahydro-3-(4-penten-1-yl)-2H-azepin-2-one⁸ (91 mg, 0.50 mmol), n-BuLi (0.34 mL of a 1.6 M solution in THF, 0.55 mmol), tosyl chloride (124 mg, 0.650 mmol) to give 144 mg (86%) of N-tosyl protected lactam **12** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 8.08 (d, *J* = 8.3 Hz, 2 H), 6.76 (d, *J* = 8.3 Hz, 2 H), 5.68 (dddd, *J* = 17.1, 10.3, 6.8, 6.8 Hz, 1 H), 4.98-4.92 (m, 2 H), 4.50 (ddd, *J* = 16.2, 3.9, 3.9 Hz, 1 H), 2.95-2.90 (m, 1 H), 1.97-1.84 (m, 3 H), 1.82 (s, 3 H), 1.73-1.66 (m, 1 H), 1.38-0.92 (m, 9H); ¹³C NMR (125 MHz, C₆D₆) δ 175.3, 143.8, 138.8, 138.3, 129.2, 129.1, 114.7, 45.7, 45.1, 34.2, 32.0, 30.0, 28.7, 28.1, 26.8, 21.1; IR (film) 3062, 2934, 2860, 1700, 1350, 1168, 1107, 1089 cm⁻¹; LRMS *m/z* calcd for C₁₈H₂₅NO₃Na 358.1 (M+Na⁺), found 358.1.

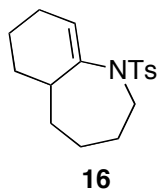


3-(hex-5-enyl)-1-tosylazepan-2-one (13). To a solution of ε-caprolactam (95 mg, 0.80 mmol) in THF (5 mL) at 0 °C was added n-BuLi (0.65 mL of a 2.5 M solution in hexane, 1.6 mmol) dropwise. The resulting reaction mixture was stirred for 1 h, after which 6-bromo-1-hexene (0.11 mL, 0.80 mmol) was added. The reaction was quenched after 1 h by pouring the mixture into sat. NaCl (aq., 10 mL). The organic phase was separated and the aqueous phase was extracted with CH₂Cl₂ (3 x 20 mL). The combined organic extracts were dried (Na₂SO₄) and concentrated to give a pale brown oil which was taken to the next step without further purification. The oil from above was subjected to the general tosylation procedure using n-BuLi (0.344 mL of a 1.6 M solution in THF, 0.55 mmol), tosyl chloride (124 mg, 0.650 mmol) to give 142 mg (51% for 2 steps) of N-tosyl protected lactam **13** as a colorless oil following flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 8.09 (d, *J* = 8.3 Hz, 2 H), 6.75 (d, *J* = 8.3 Hz, 2 H),

5.72 (dddd, $J = 17.1, 10.3, 6.8, 6.8$ Hz, 1 H), 5.01-4.95 (m, 2 H), 4.50 (ddd, $J = 16.1, 3.4, 3.4$ Hz, 1 H), 2.89 (ddd, $J = 15.6, 6.4, 6.4$ Hz, 1 H), 1.95-1.87 (m, 3 H), 1.80 (s, 3 H), 1.74-1.67 (m, 1 H), 1.37-0.88 (m, 11 H); ^{13}C NMR (125 MHz, C_6D_6) δ 175.4, 143.8, 139.0, 138.2, 129.2, 129.1, 114.5, 45.8, 45.1, 33.9, 32.3, 30.0, 29.3, 28.8, 28.1, 27.0, 21.1; IR (film) 2929, 2857, 1700, 1348, 1166 cm^{-1} ; LRMS m/z calcd for $\text{C}_{19}\text{H}_{27}\text{NO}_3\text{SNa}$ 372.2 ($\text{M}+\text{Na}^+$), found 372.2.

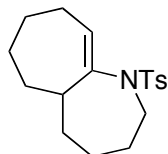


1-tosyl-1,2,3,4,5,5a,6,7-octahydrocyclopenta[b]azepine (15). The general cyclization protocol was carried out on lactam **11** (15 mg, 0.047 mmol) using TiCl_4 (0.165 mL, 1.51 mmol) in CH_2Cl_2 (13.5 mL), THF (0.79 mL, 9.0 mmol), TMEDA (1.35 mL, 9.07 mmol), activated Zn dust (219 mg, 3.37 mmol), PbCl_2 (50. mg, 0.18 mmol), and CH_3CHBr_2 (0.137 mL, 1.50 mmol) in CH_2Cl_2 (1.0 mL + 1.0 mL rinse) to give 10.9 mg (80 %) of **15** as a colorless oil following flash chromatography (hexane: ethyl acetate, 20:1 to 10:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 7.78 (d, $J = 8.3$ Hz, 2 H), 6.75 (d, $J = 7.9$ Hz, 2 H), 5.85 (dd, $J = 4.4, 2.5$ Hz, 1 H), 4.24-4.19 (m, 1 H), 2.73-2.67 (m, 1 H), 2.23-2.07 (m, 2 H), 1.85 (s, 3 H), 1.82-1.75 (m, 1 H), 1.54-1.09 (m, 6 H), 1.02-0.94 (m, 1 H), 0.87-0.76 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 144.2, 142.7, 138.4, 129.3, 127.7, 115.8, 49.3, 46.5, 34.8, 32.5, 29.7, 29.6, 28.7, 21.0; IR (film) 2922, 2850, 1450, 1343, 1160, 1090 cm^{-1} ; LRMS m/z calcd for $\text{C}_{16}\text{H}_{21}\text{NO}_2\text{SNa}$ 314.1 ($\text{M}+\text{Na}^+$), found 314.1.



1-tosyl-2,3,4,5,5a,6,7,8-octahydro-1H-benzo[b]azepine (16). The general cyclization protocol was carried out on lactam **12** (25 mg, 0.075 mmol) using TiCl_4 (0.26 mL, 2.4 mmol) in CH_2Cl_2 (21.5 mL), THF (1.26 mL, 14.4 mmol), TMEDA (2.15 mL, 14.4 mmol), activated Zn dust (350 mg, 5.4 mmol), PbCl_2 (79 mg, 0.28 mmol), and CH_3CHBr_2 (0.22 mL, 2.4 mmol) in CH_2Cl_2 (1.4 mL + 1.4 mL rinse) to give 19 mg (82 %) of **16** as a colorless oil after flash chromatography (hexane: ethyl acetate, 20:1 to 10:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 7.80 (d, $J = 7.8$ Hz,

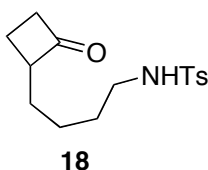
2 H), 6.80 (d, $J = 7.8$ Hz, 2 H), 5.56-5.55 (m, 1 H), 3.59 (ddd, $J = 12.7, 7.8, 4.4$ Hz, 1 H), 3.14 (ddd, $J = 12.2, 7.3, 3.4$ Hz, 1 H), 2.24-2.20 (m, 1 H), 1.89 (s, 3 H), 1.88-1.82 (m, 1 H), 1.77-1.70 (m, 1 H), 1.64-1.56 (m, 1 H), 1.52-1.46 (m, 2 H), 1.41-1.09 (m, 7 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.3, 140.9, 139.4, 129.3, 127.6, 127.6, 50.6, 38.8, 33.8, 30.3, 28.8, 25.44, 25.41, 21.1, 19.6; IR (film) 2929, 2858, 1450, 1340, 1158, 1112, 1090 cm^{-1} ; LRMS m/z calcd for $\text{C}_{17}\text{H}_{23}\text{NO}_2\text{S}$ 306.2 (MH^+), found 306.1.



17

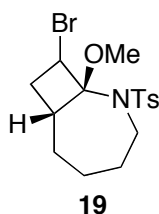
(E)-1-tosyl-1,2,3,4,5,5a,6,7,8,9-decahydrocyclohepta[b]azepine (17). The general cyclization protocol was carried out on lactam **13** (31 mg, 0.089 mmol) using TiCl_4 (0.31 mL, 2.9 mmol) in CH_2Cl_2 (26 mL), THF (1.5 mL, 17 mmol), TMEDA (2.50 mL, 16.8 mmol), activated Zn dust (417 mg, 6.41 mmol), PbCl_2 (94 mg, 0.33 mmol), and CH_3CHBr_2 (0.26 mL, 2.8 mmol) in CH_2Cl_2 (1.7 mL + 1.7 mL rinse) to give 17 mg (60 %) of **17** and 2.7 mg (10%) of the corresponding acyclic enamide as colorless oils after flash chromatography (hexane: ethyl acetate, 20:1 to 10:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 7.82 (d, $J = 7.8$ Hz, 2 H), 6.79 (d, $J = 7.8$ Hz, 2 H), 5.72 (dd, $J = 6.8, 6.8$ Hz, 1 H), 3.76 (ddd, $J = 13.2, 4.4$ Hz, 1 H), 2.95 (ddd, $J = 13.2, 10.3, 3.0$ Hz, 1 H), 2.33 (dd, $J = 9.8, 9.8$ Hz, 1 H), 1.89 (s, 3 H), 1.85-1.55 (m, 7 H), 1.51-1.23 (m, 6 H), 1.11-1.04 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.1, 140.2, 132.6, 129.3, 128.3, 128.2, 52.4, 45.1, 33.5, 32.4, 30.5, 29.3, 27.3, 26.9, 25.9, 21.1; IR (film) 3282, 2928, 1599, 1328, 1160, 1093 cm^{-1} ; LRMS m/z calcd for $\text{C}_{18}\text{H}_{25}\text{NO}_3\text{SNa}$ 342.1 ($\text{M}+\text{Na}^+$), found 342.1.

acyclic byproduct: ^1H NMR (500 MHz, C_6D_6) δ 8.09 (d, $J = 7.82$ Hz, 2 H), 6.75 (d, $J = 7.81$ Hz, 2 H), 5.46-5.34 (m, 2 H), 4.51-4.47 (m, 1 H), 2.9 (m, 1 H), 1.95-1.89 (m, 2 H), 1.81 (s, 3 H), 1.74 (m, 1 H), 1.59 (m, 2 H), 1.52-1.48 (m, 1 H), 1.35-1.30 (m, 3 H), 1.26-1.22 (m, 1 H), 1.18-1.16 (m, 2 H), 1.13-1.02 (m, 3 H), 1.0-0.93 (m, 2 H), 0.83 (m, 1 H); IR (film) 2928, 2856, 1700, 1597, 1348, 1166, 1087 cm^{-1} ; LRMS m/z calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_3\text{SNa}$ 386.2 ($\text{M}+\text{Na}^+$), found 386.2.



4-methyl-N-(4-(2-oxocyclobutyl)butyl)benzenesulfonamide (18). The general cyclization protocol was carried out on lactam **10** (10.0 mg, 0.0325 mmol) using TiCl_4 (0.116 mL, 1.06 mmol) in CH_2Cl_2 (9.5 mL), THF (0.56 mL, 6.4 mmol), TMEDA (0.95 mL, 6.4 mmol), activated Zn dust (154 mg, 2.37 mmol), PbCl_2 (35.0 mg, 0.126 mmol), and CH_3CHBr_2 (0.096 mL, 1.05 mmol) in CH_2Cl_2 (0.6 mL + 0.6 mL rinse) to give **14**. Because of its instability, **14** was characterized as the hydrolyzed product **20** as described below.

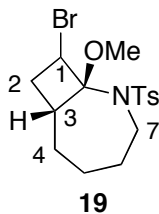
To a solution of the residue from the cyclization of **10** in ethyl acetate (3 mL) at 0 °C was added 1M HCl (2 mL). After the reaction mixture was allowed to warm to rt over 1 h the reaction was quenched with sat. NaHCO_3 (aq., 10 mL). The aqueous phase was extracted with CH_2Cl_2 (3×30 mL), dried (MgSO_4) and concentrated. The resulting residue was purified by flash chromatography (hexanes:ethyl acetate, 5:1 to 2:1) to give ketone **20** (6.0 mg, 63% for 2 steps) as a colorless oil. ^1H NMR (500 MHz, CDCl_3) δ 7.72 (d, $J = 8.2$ Hz, 2 H), 7.29 (d, $J = 7.9$ Hz, 2 H), 4.32 (broad s, 1 H), 3.20 (broad s, 1 H), 3.04-2.96 (m, 1 H), 2.93-2.84 (m, 3 H), 2.41 (s, 3 H), 2.14 (ddd, $J = 21.0, 10.3, 4.9$ Hz, 1 H), 1.63-1.55 (m, 2 H), 1.47-1.23 (m, 5 H); ^{13}C NMR (125 MHz, CDCl_3) δ 211.8, 143.4, 137.0, 129.7, 127.1, 60.1, 44.5, 42.9, 29.4, 29.0, 24.0, 21.5, 16.8; IR (film) 3425 (broad), 1769, 1643, 1324, 1157, 1091 cm^{-1} ; LRMS m/z calcd for $\text{C}_{15}\text{H}_{21}\text{NO}_3\text{SNa}$ 318.1, ($\text{M}+\text{Na}^+$), found 318.1.



(1S,7R,9S)-9-bromo-1-methoxy-2-tosyl-2-aza-bicyclo[5.2.0]nonane (19).

To a solution containing crude **14** (0.072 mmol) in methanol (5 mL) at 0 °C was added NBS (20 mg, 0.11 mmol). The reaction mixture was stirred at 0 °C for 2 h. Then the reaction was quenched with sat. NaHCO_3 (aq., 2 mL), extracted with CH_2Cl_2 (3×20 mL), dried (MgSO_4) and concentrated. The resulting residue was purified by flash chromatography (hexanes: ethyl acetate, 10:1 to 5:1) to give diastereomers **19a** (10.9 mg, 39% for 2 steps) and **19b** (5.3 mg, 19% for 2 steps) as colorless oils. Isomer **19a**: ^1H NMR (500 MHz, C_6D_6) δ 7.92 (d, $J = 8.3$ Hz, 2 H),

6.76 (d, $J = 7.8$ Hz, 2 H), 5.34 (dd, $J = 9.6, 9.6$ Hz, 1 H), 3.66-3.62 (m, 1 H), 3.17 (s, 3 H), 2.60 (ddd, $J = 15.0, 12.5, 1.0$ Hz, 1 H), 2.42-2.36 (m, 1 H), 2.12-2.07 (m, 1 H), 1.85 (s, 3 H), 1.64-1.59 (m, 1 H), 1.47-1.11 (m, 4 H), 1.02-0.99 (m, 1 H), 0.77-0.68 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.9, 139.5, 129.4, 128.3, 128.2, 127.8, 94.7, 52.1, 48.4, 47.4, 47.2, 35.1, 32.0, 29.5, 29.0, 21.1; IR (film) 2918, 2852, 1441, 1160, 1087, 1041 cm^{-1} ; LRMS m/z calcd for $\text{C}_{18}\text{H}_{22}\text{BrNO}_3\text{SNa}$ 410.0 ($\text{M}+\text{Na}^+$); found 410.0, 412.0 ($\text{M}+\text{Na}^++2$).



Summary of COSY spectrum for **19a** (500 MHz, C_6D_6):

Proton at 5.34 ppm (C-1) shows crosspeaks at 2.39 ppm (C-2) and 1.61 ppm (C-2)
 Proton at 2.09 ppm (C-3) shows crosspeaks at 2.39 ppm (C-2), 1.61 ppm (C-2) and 1.24 (C-4)

Proton at 3.64 ppm (C-7) shows crosspeaks at 2.60 ppm (C-7) and 1.14 ppm (C-6)

Proton at 2.60 ppm (C-7) shows crosspeaks at 3.64 ppm (C-7) and 1.42 ppm (C-6)

19b. ^1H NMR (500 MHz, C_6D_6) δ 8.18 (d, $J = 7.8$ Hz, 2 H), 6.77 (d, $J = 8.3$ Hz, 2 H), 4.82 (dd, $J = 5.4, 5.4$ Hz, 1 H), 3.61 (d, $J = 16.1$ Hz, 1 H), 3.23 (s, 3 H), 2.82-2.75 (m, 1 H), 2.68 (ddd, $J = 12.7, 8.8$ Hz, 1 H), 2.55 (ddd, $J = 13.3$ Hz, 1 H), 2.17-2.10 (m, 1 H), 1.86 (s, 3 H), 1.69 (d, $J = 12.7$ Hz, 1 H), 1.46-1.35 (m, 2 H), 1.12-1.09 (m, 2 H), 0.76-0.68 (m, 1 H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.0, 138.7, 129.3, 128.3, 128.2, 127.8, 95.6, 52.0, 49.9, 48.1, 47.4, 36.4, 34.1, 29.98, 29.96, 21.1; IR (film) 3056, 2927, 2854, 1443, 1342, 1264, 1162, 1088, 1045 cm^{-1} ; LRMS m/z calcd for $\text{C}_{18}\text{H}_{22}\text{BrNO}_3\text{SNa}$ 410.0 ($\text{M}+\text{Na}^+$), found 410.0, 412.0 ($\text{M}+\text{Na}^++2$).

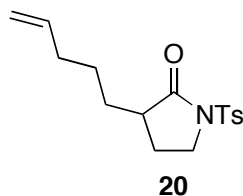
Summary of COSY spectrum for **19b** (500 MHz, C_6D_6):

Proton at 4.82 ppm (C-1) shows crosspeaks at 2.68 ppm (C-2)

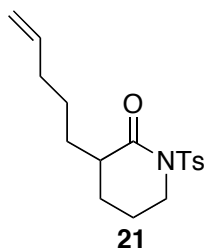
Proton at 2.55 ppm (C-3) shows crosspeaks at 2.68 ppm (C-2), 2.13 ppm (C-4), and 1.46 (C-4)

Proton at 3.61 ppm (C-7) shows crosspeaks at 2.79 ppm (C-7) and 1.11 ppm (C-6)

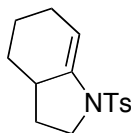
Proton at 2.79 ppm (C-7) shows crosspeaks at 3.61 ppm (C-7) and 1.11 ppm (C-6)



3-(pent-4-enyl)-1-tosylpyrrolidin-2-one (20). Prepared according the general tosylate forming procedure described above using 3-(4-penten-1-yl)-2-pyrrolidinone⁷ (77 mg, 0.50 mmol), n-BuLi (0.34 mL of a 1.6 M solution in THF, 0.55 mmol), and tosyl chloride (124 mg, 0.650 mmol) to give 130 mg (85%) of N-tosyl protected lactam **20** as a colorless oil following flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 8.10 (d, *J* = 8.3 Hz, 2 H), 6.74 (d, *J* = 8.3 Hz, 2 H), 5.59 (dddd, *J* = 16.2, 11.2, 6.8, 6.8 Hz, 1 H), 4.92-4.88 (m, 2 H), 3.54 (ddd, *J* = 9.8, 8.8, 2.5 Hz, 1 H), 3.16 (ddd, *J* = 9.3, 9.3, 7.3 Hz 1H), 1.79 (s, 3 H), 1.74-1.69 (m, 2 H), 1.60-1.45 (m, 2H), 1.17-1.11 (m, 1H), 1.04-0.71 (m, 4H); ¹³C NMR (125 MHz, C₆D₆) δ 172.4, 144.5, 138.3, 136.6, 129.5, 128.6, 114.8, 45.2, 42.7, 33.6, 29.7, 26.2, 24.6, 21.1; IR (film) 2930, 2857, 1699, 1347, 1166, 1088 cm⁻¹; LRMS *m/z* calcd for C₁₆H₂₁NO₃S 308.1 (M+H⁺), found 308.1.



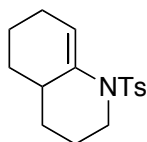
3-(pent-4-enyl)-1-tosylpiperidin-2-one (21). Prepared according to the general tosylate forming procedure using 3-(4-penten-1-yl)- 2-piperidinone⁸ (91 mg, 0.50 mmol), n-BuLi (0.34 mL of a 1.6 M solution in THF, 0.55 mmol), and tosyl chloride (124 mg, 0.650 mmol) to give 141 mg (88%) of N-tosyl protected lactam **21** as a colorless oil following flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 8.08 (d, *J* = 8.3 Hz, 2 H), 6.80 (d, *J* = 8.3 Hz, 2 H), 5.64 (dddd, *J* = 16.6, 10.3, 6.4, 6.4 Hz, 1 H), 4.95-4.91 (m, 2 H), 3.66-3.56 (m, 2H), 1.84 (s, 3 H), 1.81-1.71 (m, 3 H), 1.66-1.60 (m, 1H), 1.29-1.22 (m, 1H), 1.19-1.02 (m, 5H), 0.79-0.71 (m, 1H); ¹³C NMR (125 MHz, C₆D₆) δ 172.5, 144.0, 138.6, 137.6, 129.2, 114.7, 46.5, 43.3, 33.9, 30.6, 26.3, 25.6, 22.2, 21.1; IR (film) 3072, 2932, 2867, 1694, 1352, 1168, 1120, 1090 cm⁻¹; LRMS *m/z* calcd for C₁₇H₂₃NO₃SNa 344.1 (M+Na⁺), found 344.1.



22

1-tosyl-2,3,3a,4,5,6-hexahydro-1H-indole (22). The general cyclization protocol was carried out on lactam **20**⁸ (19 mg, 0.062 mmol) using TiCl₄ (0.22 mL, 2.0 mmol) in CH₂Cl₂ (18 mL), THF (1.04 mL, 11.9 mmol), TMEDA (1.77 mL, 11.9 mmol), activated Zn dust (289 mg, 4.45 mmol), PbCl₂ (65 mg, 0.23 mmol), and CH₃CHBr₂ (0.18 mL, 2.0 mmol) in CH₂Cl₂ (1.2 mL + 1.2 mL rinse) to give 11 mg (65 %) of **22** and 2 mg (10%) of the corresponding acyclic enamide as colorless oils after flash chromatography (hexane: ethyl acetate, 20:1 to 10:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 7.80 (d, *J* = 7.8 Hz, 2 H), 6.76 (d, *J* = 7.8 Hz, 2 H), 6.07 (dd, *J* = 6.4, 3.5 Hz, 1 H), 3.61 (dd, *J* = 8.8, 8.8 Hz, 1 H), 2.96 (ddd, *J* = 10.7, 9.7, 5.8, 1 H), 2.03-1.88 (m, 2 H), 1.84 (s, 3 H), 1.49-1.40 (m, 3 H), 1.19 (ddd, *J* = 11.7, 6.3, 6.3 Hz, 1 H), 1.08-0.98 (m, 1 H), 0.85-0.69 (m, 2 H); ¹³C NMR (125 MHz, C₆D₆) δ 143.0, 139.9, 136.1, 129.4, 127.7, 105.0, 49.2, 39.5, 29.4, 28.3, 24.1, 22.0, 21.0; IR (film) 3055, 2987, 2926, 2850, 1420, 1362, 1266, 1222, 1164, 1091 cm⁻¹; LRMS *m/z* calcd for C₁₅H₁₉NO₂SNa 300.1 (M+Na⁺), found 300.1.

acyclic enamide: ¹H NMR (500 MHz, C₆D₆) δ 7.80 (d, *J* = 8.3 Hz, 2 H), 7.76 (d, *J* = 7.82 Hz, 2 H), 6.75 (m, 4 H), 5.33-5.22 (m, 3 H), 3.52-3.46 (m, 1 H), 3.33-3.23 (m, 2 H), 2.2 (m, 2 H), 1.89-1.80 (m, 10 H), 1.73-1.68 (m, 4 H), 1.58-1.57 (m, 6 H), 1.50-1.46 (m, 4 H), 1.35-1.18 (m, 7 H), 1.14-1.06 (m, 3 H), 1.01-0.70 (m, 16 H), 0.57 (t, 1 H); IR (film) 2930, 1349, 1165, 1092 cm⁻¹; LRMS *m/z* calcd for C₁₉H₂₇NO₂SNa 356.2 (M+Na⁺), found 356.2.

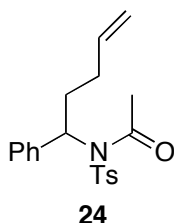


23

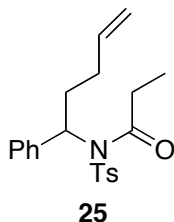
1-tosyl-1,2,3,4,4a,5,6,7-octahydroquinoline (23). The general cyclization protocol was carried out on lactam **21** (26 mg, 0.081 mmol) using TiCl₄ (0.28 mL, 2.56 mmol) in CH₂Cl₂ (23 mL), THF (1.37 mL, 15.6 mmol), TMEDA (2.32 mL, 15.6 mmol), activated Zn dust (378 mg, 5.82 mmol), PbCl₂ (85.5 mg, 0.31 mmol), and CH₃CHBr₂ (0.24 mL, 2.63 mmol) in CH₂Cl₂ (1.5 mL + 1.5 mL rinse) to give 16.5 mg (70 %) of **23** and 2.2 mg (8%) of the corresponding acyclic enamide as colorless oils after flash chromatography (hexane: ethyl acetate, 20:1 to 10:1 to 5:1). ¹H NMR (500 MHz, C₆D₆) δ 7.80 (d, *J* = 8.3 Hz, 2 H), 6.76 (d, *J* = 8.3 Hz, 2

H), 6.11 (dd, $J = 5.3, 2.9$ Hz, 1 H), 4.36-4.31 (m, 1 H), 2.79-2.73 (m, 1 H), 1.99-1.92 (m, 1 H), 1.86 (s, 3 H), 1.85-1.79 (m, 1 H), 1.58-1.51 (m, 1 H), 1.40-1.35 (m, 2 H), 1.28-1.18 (m, 3 H), 1.04-1.00 (m, 1 H), 0.92-0.71 (m, 2 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.4, 140.1, 137.4, 129.4, 128.3, 124.7, 48.1, 35.3, 32.7, 31.3, 25.6, 24.9, 21.6, 21.1; IR (film) 3056, 2931, 2857, 1452, 1337, 1265, 1158, 1087 cm^{-1} ; LRMS m/z calcd for $\text{C}_{16}\text{H}_{21}\text{NO}_2\text{SNa}$ 314.1 ($\text{M}+\text{Na}^+$), found 314.1.

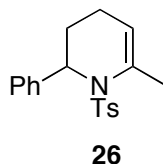
Acyclic enamide: ^1H NMR (500 MHz, C_6D_6) δ 7.84-7.78 (m, 3 H), 6.78-6.74 (m, 2 H), 5.75-5.71 (m, 1 H), 5.51-5.32 (m, 3 H), 4.14-4.11 (m, 1 H), 2.76-2.74 (m, 1 H), 2.40 (m, 1 H), 1.89-1.83 (m, 11 H), 1.74-1.60 (m, 8 H), 1.47-1.32 (m, 27 H); IR (film) 2925, 2856, 1711, 1452, 1339, 1267, 1160, 1092, 706 cm^{-1} ; LRMS m/z calcd for $\text{C}_{20}\text{H}_{29}\text{NO}_2\text{SNa}$ 370.2 ($\text{M}+\text{Na}^+$), found 370.2.



N-(1-phenylpent-4-enyl)-N-tosylacetamide (24). To a mixture of NaH (32 mg of a 60% dispersion in mineral oil, 0.79 mmol) in THF (2 ml) at 0°C was added **S1** (50. mg, 0.16 mmol). After stirring for 1 h, acetyl chloride (0.034 mL, 0.47 mmol) was added directly to the reaction mixture. The ice bath was removed and the reaction mixture was warmed to rt at which time the reaction was quenched with sat. NH_4Cl (aq., 5 mL). The aqueous phase was extracted with CH_2Cl_2 (3×30 mL), dried (MgSO_4) and concentrated. The resulting residue was purified by flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1) to give amide **24** (51 mg, 90%) as a colorless oil. ^1H NMR (500 MHz, C_6D_6) δ 7.56 (d, $J = 7.33$ Hz, 2 H), 7.38 (d, $J = 8.3$ Hz, 2 H), 7.15-7.05 (m, 3 H), 6.598 (d, $J = 8.3$ Hz, 2 H), 5.85 (t, $J = 7.81$ Hz, 1 H), 5.71 (dddd, $J = 17.1, 10.3, 6.8$ Hz, 1 H), 4.99-4.94 (m, 2 H), 2.56-2.49 (m, 1 H), 2.46-2.39 (m, 1 H), 2.13-2.08 (m, 2 H), 2.07 (s, 3 H), 1.79 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 170.2, 144.1, 139.3, 137.9, 137.7, 129.5, 129.5, 128.4, 128.2, 127.8, 115.6, 61.2, 31.9, 31.7, 26.0, 21.0; IR (film) 3066, 2930, 1770, 1698, 1356, 1237, 1166, 1089 cm^{-1} ; LRMS m/z calcd for $\text{C}_{20}\text{H}_{23}\text{NO}_3\text{SNa}$ 380.1 ($\text{M}+\text{Na}^+$), found 380.1.

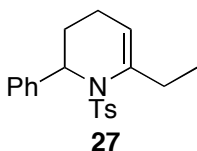


N-(1-phenylpent-4-enyl)-N-tosylpropionamide (25). Prepared according the procedure described above for the preparation of **24** using **S1** (50. mg, 0.16 mmol), NaH (32 mg of a 60% dispersion in mineral oil, 0.79 mmol) and propionyl chloride (0.041 mL, 0.47 mmol) to give 51.6 mg (88%) of N-tosyl protected amide **25** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 7.56 (d, J = 7.3 Hz, 2 H), 7.42 (d, J = 8.3 Hz, 2 H), 7.11-7.08 (m, 2 H), 7.05-7.03 (m, 1 H), 6.55 (d, J = 8.3 Hz, 2 H), 5.84 (dd, J = 7.8, 7.8 Hz, 1 H), 5.69 (dddd, J = 17.1, 10.2, 6.8, 6.8 Hz, 1 H), 4.97-4.91 (m, 2 H), 2.55-2.37 (m, 4 H), 2.15-2.04 (m, 2 H), 1.73 (s, 3 H), 0.83 (t, J = 7.08 Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 174.1, 144.1, 139.5, 138.2, 137.7, 129.5, 129.4, 129.2, 128.5, 128.5, 128.3, 128.2, 115.6, 61.2, 32.1, 31.8, 31.2, 21.0, 9.2; IR (film) 3066, 2981, 2940, 1761, 1700, 1353, 1162, 1086 cm^{-1} ; LRMS m/z calcd for $\text{C}_{21}\text{H}_{25}\text{NO}_3\text{SNa}$ 394.2 ($\text{M}+\text{Na}^+$), found 394.2.

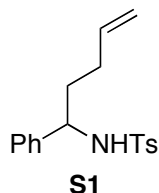


6-methyl-2-phenyl-1-tosyl-1,2,3,4-tetrahydropyridine (26). The general cyclization protocol was carried out on amide **24** (30. mg, 0.084 mmol) using TiCl_4 (0.29 mL, 2.65 mmol) in CH_2Cl_2 (24.0 mL), THF (1.42 mL, 16.2 mmol), TMEDA (2.41 mL, 16.2 mmol), activated Zn dust (392 mg, 6.03 mmol), PbCl_2 (88 mg, 0.32 mmol), and CH_3CHBr_2 (0.24 mL, 2.63 mmol) in CH_2Cl_2 (1.5 mL + 1.5 mL rinse) to give 16.5 mg (60 %) of **26** and 6.4 mg (20%) of the corresponding acyclic enamine as colorless oils after flash chromatography (hexane:ethyl acetate, 20:1 to 10:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 7.71 (d, J = 8.3 Hz, 2 H), 7.24 (dd, J = 6.8, 1.0 Hz, 2 H), 7.12 (partially obscured t, J = 7.8 Hz, 1 H), 7.04 (t, J = 7.4 Hz, 1 H), 6.71 (d, J = 8.3 Hz, 2 H), 5.68 (broad s, 1 H), 4.60 (broad s, 1 H), 2.31 (d, J = 1.0 Hz, 3 H), 1.83 (s, 3 H), 1.71-1.69 (m, 1 H), 1.43-1.35 (m, 4 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.9, 140.3, 138.7, 133.1, 129.6, 128.6, 128.3, 127.8, 127.5, 127.0, 126.3, 113.7, 57.6, 24.6, 23.9, 21.1, 19.2; IR (film) 2921, 1450, 1344, 1164, 1092 cm^{-1} ; LRMS m/z calcd for $\text{C}_{19}\text{H}_{21}\text{NO}_2\text{SNa}$ 350.1 ($\text{M}+\text{Na}^+$), found 350.1.

acyclic enamide: ^1H NMR (500 MHz, C_6D_6) δ 7.85-7.82 (m, 2 H), 7.26-7.25 (m, 2 H), 7.0-7.0 (m, 4 H), 6.75 (m, 2 H), 5.48-5.28 (m, 2 H), 4.94-4.88 (m, 1 H), 1.93 (m, 2 H), 1.86 (s, 3 H), 1.83-1.78 (m, 2 H), 1.64-1.56 (m, 2 H), 1.53 (s, 3 H), 1.35-1.32 (m, 2 H), 1.26-1.17 (m, 5 H), 0.91 (m, 1 H), 0.81 (m, 3 H); IR (film) 2928, 1338, 1160, 1092 cm^{-1} ; LRMS m/z calcd for $\text{C}_{22}\text{H}_{29}\text{NO}_2\text{SNa}$ 406.2 ($\text{M}+\text{Na}^+$), found 406.2.



6-ethyl-2-phenyl-1-tosyl-1,2,3,4-tetrahydropyridine (27). The general cyclization protocol was carried out on amide **25** (25 mg, 0.067 mmol) using TiCl_4 (0.23 mL, 2.1 mmol) in CH_2Cl_2 (19 mL), THF (1.13 mL, 12.8 mmol), TMEDA (1.92 mL, 12.8 mmol), activated Zn dust (310 mg, 4.8 mmol), PbCl_2 (70.8 mg, 0.255 mmol), and CH_3CHBr_2 (0.195 mL, 2.14 mmol) in CH_2Cl_2 (1.2 mL + 1.2 mL rinse) to give 13.8 mg (60 %) of **27** and 5.3 mg (20%) of the corresponding acyclic enamide as colorless oils after flash chromatography (hexane: ethyl acetate, 20:1 to 10:1 to 5:1). ^1H NMR (500 MHz, C_6D_6) δ 7.74 (d, $J = 8.3$ Hz, 2 H), 7.33 (d, $J = 8.3$ Hz, 2 H), 7.14 (partially obscured t, $J = 7.8$ Hz, 2 H), 7.05 (t, $J = 7.3$ Hz, 1 H), 6.73 (d, $J = 8.3$ Hz, 2 H), 5.58 (broad d, $J = 3.4$ Hz, 1 H), 4.77 (broad s, 1 H), 3.03 (dq, $J = 14.6, 7.3$ Hz, 1 H), 2.57 (dq, $J = 14.6, 7.3$ Hz, 1 H), 1.83 (s, 3 H), 1.71-1.67 (m, 1 H), 1.57-1.50 (m, 1 H), 1.40-1.33 (m, 2 H), 1.14 (t, $J = 7.3$ Hz, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 142.9, 140.2, 139.0, 138.3, 129.6, 128.5, 128.3, 127.6, 127.1, 126.7, 113.4, 57.2, 30.0, 23.7, 21.1, 19.2, 13.3; IR (film) 2924, 1451, 1345, 1166, 1092, 1022 cm^{-1} ; LRMS m/z calcd for $\text{C}_{20}\text{H}_{23}\text{NO}_2\text{SNa}$ 364.1 ($\text{M}+\text{Na}^+$), found 364.1. Acyclic enamide: ^1H NMR (500 MHz, C_6D_6) δ 7.87-7.83 (m, 2 H), 7.31-7.18 (m, 3 H), 7.06-7.0 (m, 5 H), 6.78 (m, 2 H), 5.40-5.25 (m, 3 H), 5.01-4.92 (m, 1 H), 2.28-2.15 (m, 1H), 2.09-1.96 (m, 3 H), 1.88 (m, 7 H), 1.81 (s, 2 H), 1.65 (m, 1 H), 1.56 (d, $J = 5.86$ Hz, 3 H), 1.36-1.30 (m, 5 H), 1.09 (m, 1 H), 1.02-0.98 (m, 3 H), 0.80 (t, $J = 7.33$ Hz, 1 H); IR (film) 2934, 1454, 1339, 1160, 1092, 1005, 703, 667 cm^{-1} ; LRMS m/z calcd for $\text{C}_{24}\text{H}_{31}\text{NO}_2\text{SNa}$ 420.2 ($\text{M}+\text{Na}^+$), found 420.2.



4-methyl-N-(1-phenylpent-4-enyl)benzenesulfonamide (S1). 3-Butenylmagnesium bromide⁴ (3.8 mL, 0.80 M) was added dropwise to a solution of N-benzylidenebenzenesulfonamide⁵ (259 mg, 1.00 mmol) in THF (1.0 mL) at -78 °C. The resulting reaction mixture was warmed to rt over 1 h after which time the reaction was quenched with sat. NH₄Cl (aq., 5 mL). The aqueous phase was extracted with CH₂Cl₂ (3 × 30 mL), dried (MgSO₄) and concentrated. The resulting residue was purified by flash chromatography (hexanes:ethyl acetate, 10:1 to 3:1) to give **S1** (246 mg, 78%) as a colorless solid. mp 66-68 °C ; ¹H NMR (500 MHz, C₆D₆) δ 7.74 (d, *J* = 8.3, 2 H), 7.00-6.98 (m, 2 H), 6.94-6.88 (m, 3 H), 6.67 (d, *J* = 8.3, 2 H), 6.43 (d, *J* = 8.3 Hz, 1 H), 5.63-5.55 (m, 1 H), 4.91-4.87 (m, 2 H), 4.45 (ddd, *J* = 7.3, 7.3, 7.3 Hz, 1 H), 1.95-1.82 (m, 3 H), 1.85 (s, 3 H), 1.70-1.61 (m, 1 H); ¹³C NMR (125 MHz, C₆D₆) δ 142.5, 141.6, 139.0, 137.6, 129.4, 128.5, 127.4, 127.2, 127.0, 115.4, 58.1, 37.2, 30.4, 21.0; IR (film) 3276 (broad), 3064, 2924, 1641, 1599, 1453, 1323, 1158, 1092 cm⁻¹; LRMS *m/z* calcd for C₁₈H₂₁NO₂SNa 338.1 (M+Na⁺), found 338.1.

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