

## SUPPORTING INFORMATION FOR:

### Olefinic-Amide and Olefinic-Lactam Cyclizations

Jie Zhou and Jon D. Rainier\*

Department of Chemistry, University of Utah, 315 South 1400 East, Salt Lake City, UT, 84112

#### General Information

NMR spectra were recorded on either Varian Inova-500 MHz or Varian VXR-500 MHz spectrometers. Chemical shifts were reported in  $\delta$ , 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)<sub>2</sub>NEt, 2,6-lutidine, TMEDA and pyridine were distilled from CaH<sub>2</sub>. Spectroscopic grade DMF was stored over activated 4Å molecular sieves and used without purification. Zn dust (<10  $\mu$ m, Aldrich) was activated by sequentially washing with HCl, H<sub>2</sub>O, 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

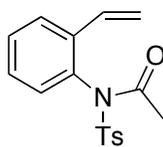
To a cold (0 °C) solution of NaH (26 mg, 60% dispersion in mineral oil, 0.65 mmol) in dry THF (2.0 mL) was added a solution of amide (0.5 mmol) in THF (1 mL). The reaction mixture was stirred at 0 °C for 1 h. To this mixture was added a solution of tosyl chloride (123.5 mg, 0.65 mmol) in dry THF (1.0 mL) via cannula. The reaction mixture was warmed to rt over 1 h and quenched with sat. NH<sub>4</sub>Cl (aq., 5 mL) once the starting material had been completely consumed. The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3  $\times$  30 mL), dried (MgSO<sub>4</sub>) 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 CH<sub>2</sub>Cl<sub>2</sub>, the extracts were dried (MgSO<sub>4</sub>) and concentrated. The resulting residue was purified by flash chromatography.

### General procedure for olefinic amide/lactam cyclizations:

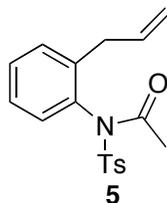
A flame-dried three-necked flask fitted with a condenser was cooled to 0 °C and charged with CH<sub>2</sub>Cl<sub>2</sub> followed by TiCl<sub>4</sub>. To the resulting solution was added THF dropwise at which time the solution turned yellow. The addition of THF was followed by the dropwise addition 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 PbCl<sub>2</sub> 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 CH<sub>3</sub>CHBr<sub>2</sub> in CH<sub>2</sub>Cl<sub>2</sub> 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. K<sub>2</sub>CO<sub>3</sub> (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.



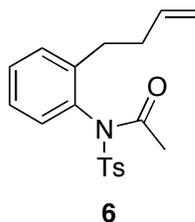
4

**N-tosyl-N-(2-vinylphenyl)acetamide (4).** Prepared according the general procedure described above using N-(2-ethenylphenyl) acetamide<sup>1</sup> (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; <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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  $\text{cm}^{-1}$ ; 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.



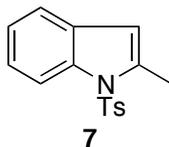
**N-(2-allylphenyl)-N-tosylacetamide (5).** Prepared according the general procedure described above using N-[2-(2-propen-1-yl)phenyl]-acetamide<sup>2</sup> (88 mg, 0.50 mmol), NaH (26 mg of a 60% dispersion in mineral oil, 0.65 mmol) and tosyl chloride (123.5 mg, 0.65 mmol) to give 140 mg (85%) of N-tosyl protected amide **5** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 10:1). <sup>1</sup>H NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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); <sup>13</sup>C NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.



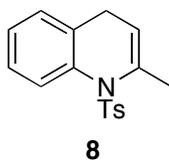
**N-(2-(but-3-enyl)phenyl)-N-tosylacetamide (6).** To a solution of 2-(3-butenyl)aniline<sup>3</sup> (106 mg, 0.720 mmol) in  $\text{CH}_2\text{Cl}_2$  (4.0 mL) at 0 °C was added pyridine (0.064 mL, 0.79 mmol) followed by a solution of acetyl chloride (0.065 mL, 0.79 mmol) in  $\text{CH}_2\text{Cl}_2$  (1.5 mL). After 12 h, the mixture was quenched with sat.  $\text{NH}_4\text{Cl}$  (aq., 5 mL). The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 20$  mL), dried ( $\text{MgSO}_4$ ) 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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.

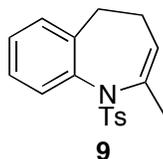


**2-methyl-1-tosyl-1H-indole (7).** The general cyclization protocol was carried out on amide **4** (17 mg, 0.054 mmol) using  $\text{TiCl}_4$  (0.19 mL, 1.7 mmol) in  $\text{CH}_2\text{Cl}_2$  (15.5 mL), THF (0.91 mL, 10. mmol), TMEDA (1.55 mL, 10.4 mmol), activated Zn dust (252 mg, 3.88 mmol),  $\text{PbCl}_2$  (57 mg, 0.20 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.157 mL, 1.72 mmol) in  $\text{CH}_2\text{Cl}_2$  (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  $^\circ\text{C}$   $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.



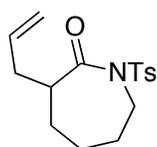
**2-methyl-1-tosyl-1,4-dihydroquinoline (8).** The general cyclization protocol was carried out on amide **5** (20. mg, 0.061 mmol) using  $\text{TiCl}_4$  (0.21 mL, 1.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (17.5 mL), THF (1.03 mL, 11.8 mmol), TMEDA (1.75 mL, 11.8 mmol), activated Zn dust (285 mg, 4.38 mmol),  $\text{PbCl}_2$  (64 mg, 0.23 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.18 mL, 1.97 mmol) in  $\text{CH}_2\text{Cl}_2$  (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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.



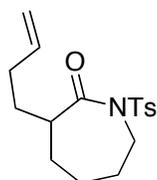
**(Z)-2-methyl-1-tosyl-4,5-dihydro-1H-benzo[b]azepine (9).** The general cyclization protocol was carried out on amide **6** (35 mg, 0.10 mmol) using  $\text{TiCl}_4$  (0.37 mL, 3.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (31 mL), THF (1.82 mL, 20.8 mmol), TMEDA (3.10 mL, 20.8 mmol), activated Zn dust (504 mg, 7.75 mmol),  $\text{PbCl}_2$  (110 mg, 0.41 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.31 mL, 3.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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**:  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.



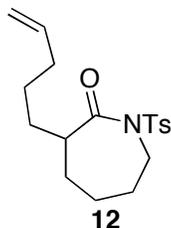
10

**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-one<sup>6</sup> (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). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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 (dtt, *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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>3</sub>SNa 330.1 (M+Na<sup>+</sup>), found 330.1.

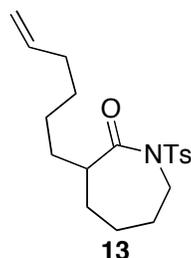


11

**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-one<sup>7</sup> (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). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub>SNa 344.1 (M+Na<sup>+</sup>), found 344.1.

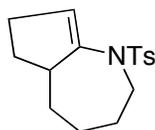


**3-(pent-4-enyl)-1-tosylazepan-2-one (12).** Prepared according the general procedure described above using hexahydro-3-(4-penten-1-yl)-2H-azepin-2-one<sup>8</sup> (91 mg, 0.50 mmol), n-BuLi (0.34 mL of a 1.6 M solution in THF, 0.55 mmol), tosyl chloride (124 mg, 0.650 mmol) to give 144 mg (86%) of N-tosyl protected lactam **12** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>18</sub>H<sub>25</sub>NO<sub>3</sub>SNa 358.1 (M+Na<sup>+</sup>), found 358.1.



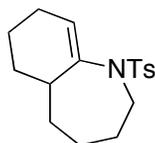
**3-(hex-5-enyl)-1-tosylazepan-2-one (13).** To a solution of ε-caprolactam (95 mg, 0.80 mmol) in THF (5 mL) at 0 °C was added n-BuLi (0.65 mL of a 2.5 M solution in hexane, 1.6 mmol) dropwise. The resulting reaction mixture was stirred for 1 h, after which 6-bromo-1-hexene (0.11 mL, 0.80 mmol) was added. 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 CH<sub>2</sub>Cl<sub>2</sub> (3 x 20 mL). The combined organic extracts were dried (Na<sub>2</sub>SO<sub>4</sub>) 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). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.



15

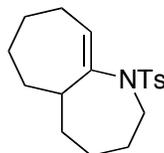
**1-tosyl-1,2,3,4,5,5a,6,7-octahydrocyclopenta[b]azepine (15).** **1-tosyl-1,2,3,4,5,5a,6,7-octahydrocyclopenta[b]azepine (15).** The general cyclization protocol was carried out on lactam **11** (15 mg, 0.047 mmol) using  $\text{TiCl}_4$  (0.165 mL, 1.51 mmol) in  $\text{CH}_2\text{Cl}_2$  (13.5 mL), THF (0.79 mL, 9.0 mmol), TMEDA (1.35 mL, 9.07 mmol), activated Zn dust (219 mg, 3.37 mmol),  $\text{PbCl}_2$  (50. mg, 0.18 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.137 mL, 1.50 mmol) in  $\text{CH}_2\text{Cl}_2$  (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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.



16

**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  $\text{TiCl}_4$  (0.26 mL, 2.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (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),  $\text{PbCl}_2$  (79 mg, 0.28 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.22 mL, 2.4 mmol) in  $\text{CH}_2\text{Cl}_2$  (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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.80 (d,  $J = 7.8$  Hz,

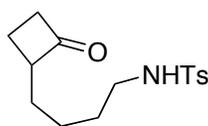
2 H), 6.80 (d,  $J = 7.8$  Hz, 2 H), 5.56-5.55 (m, 1 H), 3.59 (ddd,  $J = 12.7, 7.8, 4.4$  Hz, 1 H), 3.14 (ddd,  $J = 12.2, 7.3, 3.4$  Hz, 1 H), 2.24-2.20 (m, 1 H), 1.89 (s, 3 H), 1.88-1.82 (m, 1 H), 1.77-1.70 (m, 1 H), 1.64-1.56 (m, 1 H), 1.52-1.46 (m, 2 H), 1.41-1.09 (m, 7 H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; LRMS  $m/z$  calcd for  $\text{C}_{17}\text{H}_{23}\text{NO}_2\text{S}$  306.2 ( $\text{MH}^+$ ), 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  $\text{TiCl}_4$  (0.31 mL, 2.9 mmol) in  $\text{CH}_2\text{Cl}_2$  (26 mL), THF (1.5 mL, 17 mmol), TMEDA (2.50 mL, 16.8 mmol), activated Zn dust (417 mg, 6.41 mmol),  $\text{PbCl}_2$  (94 mg, 0.33 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.26 mL, 2.8 mmol) in  $\text{CH}_2\text{Cl}_2$  (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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.

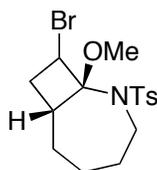
acyclic byproduct:  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  8.09 (d,  $J = 7.82$  Hz, 2 H), 6.75 (d,  $J = 7.81$  Hz, 2 H), 5.46-5.34 (m, 2 H), 4.51-4.47 (m, 1 H), 2.9 (m, 1 H), 1.95-1.89 (m, 2 H), 1.81 (s, 3 H), 1.74 (m, 1 H), 1.59 (m, 2 H), 1.52-1.48 (m, 1 H), 1.35-1.30 (m, 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  $\text{cm}^{-1}$ ; 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.



18

**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  $\text{TiCl}_4$  (0.116 mL, 1.06 mmol) in  $\text{CH}_2\text{Cl}_2$  (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),  $\text{PbCl}_2$  (35.0 mg, 0.126 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.096 mL, 1.05 mmol) in  $\text{CH}_2\text{Cl}_2$  (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.  $\text{NaHCO}_3$  (aq., 10 mL). The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  (3 × 30 mL), dried ( $\text{MgSO}_4$ ) 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.  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.

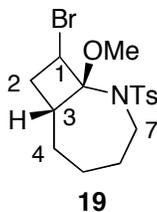


19

**(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.  $\text{NaHCO}_3$  (aq., 2 mL), extracted with  $\text{CH}_2\text{Cl}_2$  (3 × 20 mL), dried ( $\text{MgSO}_4$ ) 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**:  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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,  $\text{C}_6\text{D}_6$ ):

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.**  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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 ( $\text{M}+\text{Na}^++2$ ).

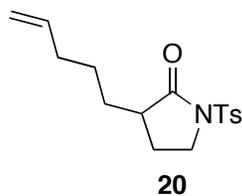
Summary of COSY spectrum for **19b** (500 MHz,  $\text{C}_6\text{D}_6$ ):

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

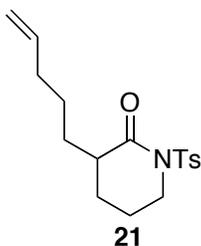
Proton at 2.55 ppm (C-3) shows crosspeaks at 2.68 ppm (C-2), 2.13 ppm (C-4), and 1.46 (C-4)

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

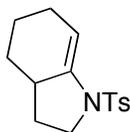
Proton at 2.79 ppm (C-7) shows crosspeaks at 3.61 ppm (C-7) and 1.11 ppm (C-6)



**3-(pent-4-enyl)-1-tosylpyrrolidin-2-one (20).** Prepared according to the general tosylate forming procedure described above using 3-(4-penten-1-yl)-2-pyrrolidinone<sup>7</sup> (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). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>16</sub>H<sub>21</sub>NO<sub>3</sub>S 308.1 (M+H<sup>+</sup>), found 308.1.



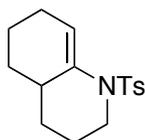
**3-(pent-4-enyl)-1-tosylpiperidin-2-one (21).** Prepared according to the general tosylate forming procedure using 3-(4-penten-1-yl)-2-piperidinone<sup>8</sup> (91 mg, 0.50 mmol), n-BuLi (0.34 mL of a 1.6 M solution in THF, 0.55 mmol), and tosyl chloride (124 mg, 0.650 mmol) to give 141 mg (88%) of N-tosyl protected lactam **21** as a colorless oil following flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>17</sub>H<sub>23</sub>NO<sub>3</sub>SNa 344.1 (M+Na<sup>+</sup>), 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**<sup>8</sup> (19 mg, 0.062 mmol) using TiCl<sub>4</sub> (0.22 mL, 2.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (18 mL), THF (1.04 mL, 11.9 mmol), TMEDA (1.77 mL, 11.9 mmol), activated Zn dust (289 mg, 4.45 mmol), PbCl<sub>2</sub> (65 mg, 0.23 mmol), and CH<sub>3</sub>CHBr<sub>2</sub> (0.18 mL, 2.0 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (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). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>15</sub>H<sub>19</sub>NO<sub>2</sub>SNa 300.1 (M+Na<sup>+</sup>), found 300.1.

acyclic enamide: <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>19</sub>H<sub>27</sub>NO<sub>2</sub>SNa 356.2 (M+Na<sup>+</sup>), found 356.2.

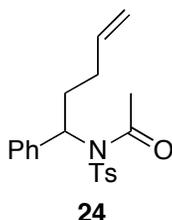


**23**

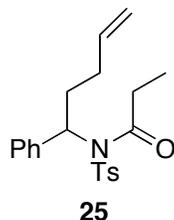
**1-tosyl-1,2,3,4,4a,5,6,7-octahydroquinoline (23).** The general cyclization protocol was carried out on lactam **21** (26 mg, 0.081 mmol) using TiCl<sub>4</sub> (0.28 mL, 2.56 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (23 mL), THF (1.37 mL, 15.6 mmol), TMEDA (2.32 mL, 15.6 mmol), activated Zn dust (378 mg, 5.82 mmol), PbCl<sub>2</sub> (85.5 mg, 0.31 mmol), and CH<sub>3</sub>CHBr<sub>2</sub> (0.24 mL, 2.63 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (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). <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.

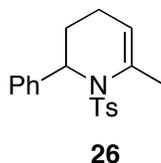
Acyclic enamide:  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  7.84-7.78 (m, 3 H), 6.78-6.74 (m, 2 H), 5.75-5.71 (m, 1 H), 5.51-5.32 (m, 3 H), 4.14-4.11 (m, 1 H), 2.76-2.74 (m, 1 H), 2.40 (m, 1 H), 1.89-1.83 (m, 11 H), 1.74-1.60 (m, 8 H), 1.47-1.32 (m, 27 H); IR (film) 2925, 2856, 1711, 1452, 1339, 1267, 1160, 1092, 706  $\text{cm}^{-1}$ ; 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  $0^\circ\text{C}$  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.  $\text{NH}_4\text{Cl}$  (aq., 5 mL). The aqueous phase was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 30$  mL), dried ( $\text{MgSO}_4$ ) 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.  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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.

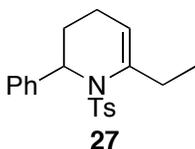


**N-(1-phenylpent-4-enyl)-N-tosylpropionamide (25).** Prepared according the procedure described above for the preparation of **24** using **S1** (50. mg, 0.16 mmol), NaH (32 mg of a 60% dispersion in mineral oil, 0.79 mmol) and propionyl chloride (0.041 mL, 0.47 mmol) to give 51.6 mg (88%) of N-tosyl protected amide **25** as a colorless oil after flash chromatography (hexanes:ethyl acetate, 20:1 to 5:1).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; LRMS  $m/z$  calcd for  $\text{C}_{21}\text{H}_{25}\text{NO}_3\text{SNa}$  394.2 (M+Na<sup>+</sup>), found 394.2.

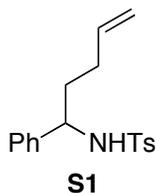


**6-methyl-2-phenyl-1-tosyl-1,2,3,4-tetrahydropyridine (26).** The general cyclization protocol was carried out on amide **24** (30. mg, 0.084 mmol) using  $\text{TiCl}_4$  (0.29 mL, 2.65 mmol) in  $\text{CH}_2\text{Cl}_2$  (24.0 mL), THF (1.42 mL, 16.2 mmol), TMEDA (2.41 mL, 16.2 mmol), activated Zn dust (392 mg, 6.03 mmol),  $\text{PbCl}_2$  (88 mg, 0.32 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.24 mL, 2.63 mmol) in  $\text{CH}_2\text{Cl}_2$  (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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; LRMS  $m/z$  calcd for  $\text{C}_{19}\text{H}_{21}\text{NO}_2\text{SNa}$  350.1 (M+Na<sup>+</sup>), found 350.1.

acyclic enamide:  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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  $\text{TiCl}_4$  (0.23 mL, 2.1 mmol) in  $\text{CH}_2\text{Cl}_2$  (19 mL), THF (1.13 mL, 12.8 mmol), TMEDA (1.92 mL, 12.8 mmol), activated Zn dust (310 mg, 4.8 mmol),  $\text{PbCl}_2$  (70.8 mg, 0.255 mmol), and  $\text{CH}_3\text{CHBr}_2$  (0.195 mL, 2.14 mmol) in  $\text{CH}_2\text{Cl}_2$  (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).  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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);  $^{13}\text{C}$  NMR (125 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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:  $^1\text{H}$  NMR (500 MHz,  $\text{C}_6\text{D}_6$ )  $\delta$  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  $\text{cm}^{-1}$ ; 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 bromide<sup>4</sup> (3.8 mL, 0.80 M) was added dropwise to a solution of N-benzylidenebenzenesulfonamide<sup>5</sup> (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. NH<sub>4</sub>Cl (aq., 5 mL). The aqueous phase was extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 × 30 mL), dried (MgSO<sub>4</sub>) 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 ; <sup>1</sup>H NMR (500 MHz, C<sub>6</sub>D<sub>6</sub>) 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); <sup>13</sup>C NMR (125 MHz, C<sub>6</sub>D<sub>6</sub>) 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<sup>-1</sup>; LRMS *m/z* calcd for C<sub>18</sub>H<sub>21</sub>NO<sub>2</sub>SNa 338.1 (M+Na<sup>+</sup>), found 338.1.

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