$AlCl_3$-Catalyzed Ring-Expansion Cascades of Bicyclic Cyclobutenamides Involving Highly Strained *Cis*,*Trans*-Cycloheptadienone Intermediates

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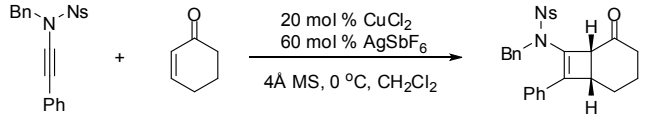
Supporting Information Part 1 – Experimental

GENERAL EXPERIMENTAL INFORMATION

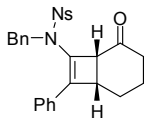
All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. Chromatographic separations were performed using 40-63μm SiO_2 from Silicycle. ^1H and ^{13}C NMR spectra were obtained on Varian VI-400 and VI-500 spectrometers using $CDCl_3$ as solvent with TMS or residual solvent as standard unless otherwise noted. Melting points were determined using a Laboratory Devices MEL-TEMP. Infrared spectra were obtained on Bruker EQUINOX 55 FTIR, and relative intensities are expressed qualitatively as s (strong), m (medium), and w (weak). TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and $KMnO_4$ stain. Low-resolution mass spectra were obtained using Waters LCT® (ESI) and Agilent 1100 series LS/MSD (APCI). High-resolution mass spectra (HRMS) was performed on Waters LCT™ (ESI-TOF-MS). All spectral data obtained for new compounds are reported here.

General Procedure for Synthesis of 4,6-Fused Cyclobutenamides 1.[1]



ynamide **S1d** **1d**

To a stirring suspension of $CuCl_2$ (23.8 mg, 0.18 mmol) and 4Å MS (347.9 mg) in CH_2Cl_2 (3.0 mL) was added $AgSbF_6$ (182.8 mg, 0.53 mmol) in the dark at rt. After stirring for 1 h at rt, a solution of ynamide **S1d** (347.9 mg, 0.89 mmol) and 2-cyclohexen-1-one (102.3 mg, 1.06 mmol) in CH_2Cl_2 (3.0 mL) was added to the catalyst mixture at 0 °C over 1 h via a syringe pump. After stirring for an additional 30 min at the same temperature post addition, the reaction mixture was filtered through a small silica gel column, concentrated *in vacuo*, and purified using silica gel flash column chromatography [gradient eluent: 10% to 20% EtOAc in Hexane] to afford product **1d** (97.8 mg, 0.20 mmol) in 23% yield.

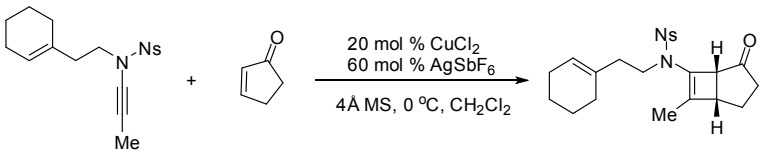


1d

1d: R_f = 0.29 [25% EtOAc in Hexane]; pale yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 1.54-1.73 (m, 3H), 2.01-2.12 (m, 2H), 2.26-2.30 (m, 1H), 3.32-3.35 (m, 2H), 4.54 (d, 1H, J = 14.5 Hz), 4.60 (d, 1H, J =

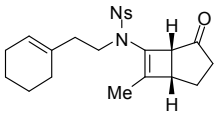
14.5 Hz), 7.01-7.03 (m, 2H), 7.16-7.22 (m, 3H), 7.31-7.35 (m, 5H), 8.11 (d, 2H, J = 9.0 Hz), 8.33 (d, 2H, J = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.6, 25.0, 37.4, 40.9, 52.0, 55.0, 124.5, 125.8, 127.3, 128.4, 128.6, 128.70, 128.74, 129.3, 129.4, 131.6, 134.6, 145.3, 146.4, 150.4, 210.3; IR (film) cm^{-1} 2935brm, 2872w, 1694m, 1529s, 1348s, 1166s; mass spectrum (ESI): m/e (% relative intensity) 506 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{27}H_{28}N_3O_5S$ $[M+NH_4]^+$: 506.1745; found 506.1763.

General Procedure for Synthesis of 4,5-Fused Cyclobutenamides 2.[1]



ynamide **S2d** **2d**

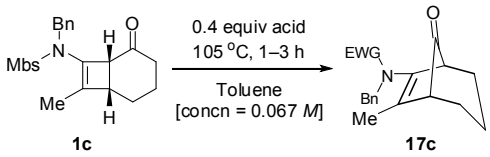
To a stirring suspension of $CuCl_2$ (77.2 mg, 0.57 mmol) and 4Å MS (1.0 g) in CH_2Cl_2 (9.6 mL) was added $AgSbF_6$ (0.6 mg, 1.72 mmol) in the dark at rt. After stirring for an additional 1 h at rt, a solution of ynamide **S2d** (1.0 g, 2.87 mmol) and 2-cyclopenten-1-one (282.8 mg, 3.44 mmol) in CH_2Cl_2 (9.6 mL) was added to the catalyst mixture dropwise at 0 °C over 1 h via a syringe pump. After stirring for an additional 30 min at the same temperature post addition, the reaction mixture was filtered through a small bed of silica gel column and concentrated *in vacuo*. The resulting crude residue was purified via silica gel flash column chromatography [gradient eluent: 10% to 15% EtOAc in Hexane] to afford product **2d** (118.3 mg, 0.27 mmol) in 10% yield.



2d

2d: R_f = 0.38 [25% EtOAc in Hexane]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.50-1.63 (m, 4H), 1.86 (s, 3H), 1.86-1.98 (m, 6H), 2.09-2.15 (m, 3H), 2.61-2.70 (m, 1H), 3.07-3.09 (m, 2H), 3.33 (dt, 1H, J = 13.6, 7.6 Hz), 3.44 (dt, 1H, J = 13.6, 7.6 Hz), 5.41 (s, 1H), 7.97 (d, 2H, J = 8.8 Hz), 8.35 (d, 2H, J = 8.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.2, 20.1, 22.4, 22.9, 25.4, 28.3, 34.7, 37.8, 40.6, 46.9, 54.2, 124.49, 124.52, 128.2, 128.7, 133.5, 145.2, 145.8, 150.4, 215.1; IR (film) cm^{-1} 2929brm, 2857w, 1730m, 1530s, 1350s, 1165s; mass spectrum (ESI): m/e (% relative intensity) 448 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{30}N_3O_5S$ $[M+NH_4]^+$: 448.1901, found 448.1903.

Screening of Acids for the Rearrangement of 4,6-Fused Cyclobutenamide 1c.

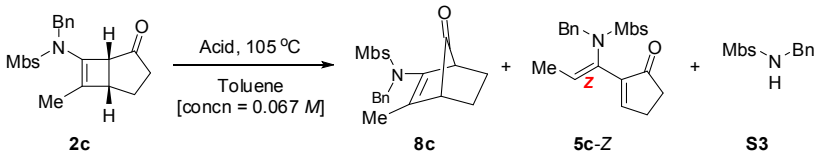


1c **17c**

entry	catalyst [equiv]	time [h]	yield [%][a]
1	PPTS [0.4]	7.5	0
2	$HNTF_2$ [0.4]	1.0	trace
3	$AgSbF_6$ [0.4]	1.0	50
4	$CuCl_2$ [0.4]	7.0	0
5	$Zn(OTf)_2$ [0.4]	24.5	60
6	$AlCl_3$ [0.4]	1.0	96[b]
7	$CuCl_2$ [0.2]/$AgSbF_6$ [0.6]	1.0	55
8	BF_3-Et_2O [0.4]	1.0	93[b]
9	$Ti(O^iPr)_2Cl_2$ [0.4]	1.0	20
10	TMSOTf [0.4]	1.0	10
11	$AlMe_2Cl$ (1M in hexanes) [0.4]	1.0	92[b]

[a] All are NMR yields except entries 6, 8 and 11. [b] Isolated yields.

Screening of Acids for the Rearrangement of 4,5-Fused Cyclobutenamide 2c.

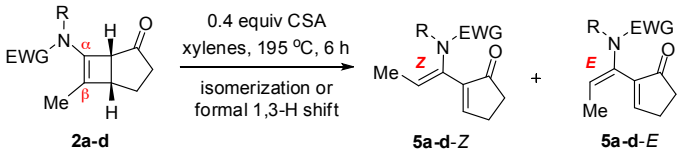


2c **8c** **5c**-*Z* **S3**

entry	catalyst [equiv]	time [h]	yield [%][a] **8c**	yield [%][a] **5c**-*Z*	yield [%][a] **S3**	**2c**[b]
1	$HNTF_2$ [0.4]	1.0	0	0	20	0
2	TFMSA [0.4]	1.0	0	0	15	0
3[c]	CSA [0.4]	36.0	0	trace	trace	70
4[c]	$AgSbF_6$ [0.4]	21.0	0	trace	76	0
5[c]	$CuCl_2$ [0.4]	22.5	0	0	trace	90
6[c]	$Zn(OTf)_2$ [0.4]	23.0	0	10	15	50
7	$AlCl_3$ [0.4]	3.0	29	33	0	12
8[c]	$CuCl_2$ [0.2]/$AgSbF_6$ [0.6]	2.5	0	trace	80	0
9	BF_3-Et_2O [0.4]	16.5	0	45	54	0
10	$Ti(O^iPr)_2Cl_2$ [0.4]	16.5	0	trace	trace	90
11[c]	$TiCl_4$ (1M in DCM) [0.4]	0.5	0	0	10	0
12	TMSOTf [0.4]	21.5	0	trace	93	0
13	$AlMe_3$ (2M toluene) [0.4]	16.0	0	0	0	87
14	$AlMe_2Cl$ (1M in hexanes) [0.4]	18.0	0	0	0	95
15	$AlEtCl_2$ (1M in hexanes) [0.4]	17.5	0	0	0	95

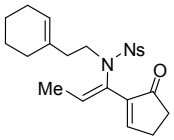
[a] All are isolated yields except entries 3, 4, 5, 6, 8 and 11. [b] Recovered starting **2c**. [c] NMR yields.

General Procedure for Brønsted Acid-Catalyzed Rearrangements of Cyclobutenamides 2.



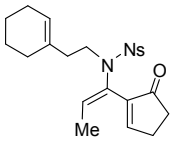
2a-d **5a-d-*Z*** **5a-d-*E***

To a flamed-dried sealed tube were added cyclobutenamide **2d** (15.0 mg, 0.035 mmol), CSA (3.2 mg, 0.014 mmol) and xylenes (1.4 mL, cyclobutenamide *concn* = 0.025 *M*) at rt. The reaction vessel was then capped and directly heated to 195 °C. After stirring at 195 °C for 6 h, the reaction mixture was allowed to cool to rt slowly. The crude mixture was purified using silica gel flash column chromatography [first using hexane to wash xylenes away, and then gradient eluent: 15% to 25% EtOAc in Hexane] to afford amido-dienes **5d**-*Z* (10.3 mg, 0.024 mmol) in 69% yield and **5d**-*E* (3.7 mg, 0.0086 mmol) in 24% yield, respectively.



5d-*Z*

5d-*Z*: R_f = 0.38 [25% EtOAc in Hexane]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ1.36 (d, 3H, *J* = 7.0 Hz), 1.50-1.54 (m, 2H), 1.59-1.61 (m, 2H), 1.82-1.89 (m, 2H), 1.92-1.98 (m, 2H), 2.15-2.19 (m, 2H), 2.54-2.57 (m, 4H), 3.39-3.48 (m, 2H), 5.40 (s, 1H), 7.17 (q, 1H, *J* = 7.2 Hz), 7.41 (s, 1H), 8.03 (d, 2H, *J* = 8.5 Hz), 8.36 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 22.4, 22.9, 25.4, 25.5, 28.6, 36.7, 37.8, 49.6, 124.0, 124.5, 128.8, 130.0, 132.9, 133.9, 140.1, 146.3, 150.2, 159.9, 206.8; IR (film) cm^{-1} 2923brm, 2851m, 1702s, 1531s, 1351s, 1165s; mass spectrum (ESI): m/e (% relative intensity) 448 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{30}N_3O_5S$ $[M+NH_4]^+$: 448.1901, found 448.1905.

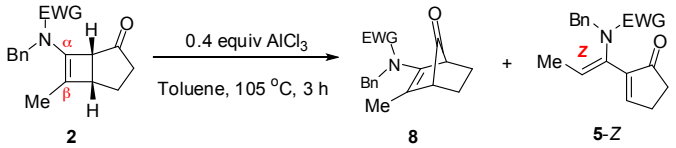


5d-*E*

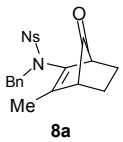
5d-*E*: R_f = 0.31 [25% EtOAc in Hexane]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.52-1.63 (m, 4H), 1.58 (d, 3H, *J* = 7.0 Hz), 1.88-1.91 (m, 2H), 1.95-1.97 (m, 2H), 2.19 (t, 2H, *J* = 7.2 Hz), 2.45-2.47 (m, 2H), 2.70-2.72 (m, 2H), 3.41 (t, 2H, *J* = 7.5 Hz), 5.35 (q, 1H, *J* = 7.2 Hz), 5.41 (s, 1H), 7.73 (t, 1H, *J* = 2.7 Hz), 8.01 (d, 2H, *J* = 9.0 Hz), 8.35 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 22.4, 23.0, 25.4, 27.2, 28.4, 34.9, 36.8, 49.0, 123.9, 124.1, 128.8, 129.3, 131.1, 134.1, 143.3, 144.4, 150.1,

164.1, 205.8; IR (film) cm^{-1} 2923brm, 2855m, 1708s, 1530s, 1350s, 1166s; mass spectrum (ESI): m/e (% relative intensity) 448 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{30}N_3O_5S$ $[M+NH_4]^+$: 448.1901, found 448.1906.

General Procedure for $AlCl_3$-Catalyzed Rearrangements of 4,5-Fused Cyclobutenamides 2.

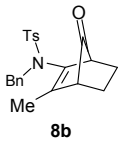


To a flamed-dried sealed tube were added cyclobutenamide **2a** (82.5 mg, 0.20 mmol), toluene (3.0 mL, cyclobutenamide *concn* = 0.067 *M*) and $AlCl_3$ (1.0 *M* in nitrobenzene: 80.0 μL, 0.080 mmol) at rt. The reaction vessel was then capped and directly heated to 105 °C. After stirring at 105 °C for 3.0 h, the reaction mixture was allowed to cool to rt slowly. The crude mixture was purified using silica gel flash column chromatography [first using hexane to wash toluene away, and then gradient eluent: 15% to 33% EtOAc in Hexane] to afford bicyclic ketone **8a** (56.1 mg, 0.14 mmol) in 68% yield and 2-amidodiene **5a**-*Z*[2] (8.6 mg, 0.021 mmol) in 10% yield.



8a

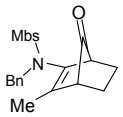
8a: R_f = 0.39 [25% EtOAc in Hexane]; white solid; mp = 150–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.97-1.05 (m, 2H), 1.57 (s, 3H), 1.67-1.74 (m, 1H), 1.83-1.90 (m, 1H), 2.34 (d, 1H, *J* = 2.5 Hz), 2.66 (d, 1H, *J* = 3.0 Hz), 4.27 (d, 1H, *J* = 14.0 Hz), 4.75 (d, 1H, *J* = 14.0 Hz), 7.24-7.33 (m, 5H), 7.99 (d, 2H, *J* = 9.0 Hz), 8.39 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.3, 21.7, 21.9, 48.6, 52.2, 53.9, 124.7, 128.5, 128.6, 128.7, 128.9, 132.1, 135.2, 145.2, 145.4, 150.4, 200.0; IR (film) cm^{-1} 2926brw, 2875w, 1785s, 1531s, 1352s, 1169s; mass spectrum (ESI): m/e (% relative intensity) 430 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{21}H_{24}N_3O_5S$ $[M+NH_4]^+$: 430.1432, found 430.1432.



8b

Bicyclic ketone **8b** (45.6 mg, 0.12 mmol) and 2-amidodiene **5b**-*Z*[2] (26.6 mg, 0.070 mmol) were prepared from cyclobutenamide **2b** (90.0 mg, 0.24 mmol) in 51% yield and 30% yield, respectively, after stirring at 105 °C for 3 h.

8b: R_f = 0.43 [25% EtOAc in Hexane]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95-1.09 (m, 2H), 1.56 (m, 3H), 1.64-1.72 (m, 1H), 1.78-1.85 (m, 1H), 2.36 (dd, 1H, *J* = 3.6, 1.2Hz), 2.45 (s, 3H), 2.60 (dd, 1H, *J* = 4.0, 1.2 Hz), 4.21 (d, 1H, *J* = 14.0 Hz), 4.68 (d, 1H, *J* = 14.4 Hz), 7.22-7.36 (m, 7H), 7.69 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 21.8, 21.9, 48.3, 52.0, 53.4, 127.6, 128.1, 128.5, 128.7, 130.1, 132.8, 136.0, 136.6, 144.0, 144.3, 200.7, one carbon missing due to overlap; IR (film) cm^{-1} 2943brm, 2873m, 1783s, 1348s, 1161s; mass spectrum (ESI): m/e (% relative intensity) 399 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{24}NO_3S$ $[M+H]^+$: 382.1472, found 382.1475.

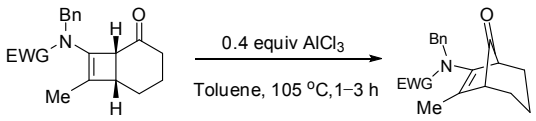


8c

Bicyclic ketone **8c** (23.0 mg, 0.058 mmol) and 2-amidodiene **5c**-*Z*[2] (26.5 mg, 0.067 mmol) were prepared from cyclobutenamide **2c** (79.5 mg, 0.20 mmol) in 29% yield and 33% yield, respectively, after stirring at 105 °C for 3.0 h with some recovery of **2c** (9.8 mg, 0.025 mmol, 12%).

8c: R_f = 0.33 [25% EtOAc in Hexane]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95-1.08 (m, 2H), 1.58 (s, 3H), 1.64-1.72 (m, 1H), 1.78-1.84 (m, 1H), 2.39 (d, 1H, *J* = 3.6 Hz), 2.61 (d, 1H, *J* = 4.0 Hz), 3.89 (s, 3H), 4.21 (d, 1H, *J* = 14.4 Hz), 4.68 (d, 1H, *J* = 14.0 Hz), 7.01 (d, 2H, *J* = 7.6 Hz), 7.23-7.31 (m, 5H), 7.74 (d, 2H, *J* = 7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.2, 21.7, 21.9, 48.2, 52.0, 53.3, 55.8, 114.6, 128.1, 128.5, 128.6, 129.7, 131.0, 132.9, 136.0, 144.2, 163.3, 200.7; IR (film) cm^{-1} 2944brm, 2874w, 1783s, 1596m, 1497m, 1348s, 1260s, 1159s; mass spectrum (ESI): m/e (% relative intensity) 415 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{27}N_2O_4S$ $[M+NH_4]^+$: 415.1687, found 415.1680.

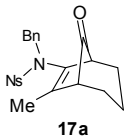
General Procedure for $AlCl_3$-Catalyzed Rearrangements of 4,6-Fused Cyclobutenamides 1.



1 **17**

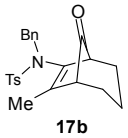
To a flamed-dried sealed tube were added cyclobutenamide **1a** (58.7 mg, 0.14 mmol), toluene (2.1 mL, cyclobutenamide *concn* = 0.067 *M*) and $AlCl_3$ (1 *M* in nitrobenzene) (55.1 μL, 0.055 mmol) at rt. The reaction vessel was then capped it and directly heated to 105 °C. After stirring at 105 °C for 1 h, the reaction mixture was cooled to rt slowly. The crude mixture was purified using silica gel flash column

chromatography [first using hexane to wash toluene away, and then isocratic eluent: 15% EtOAc in Hexane] to afford bicyclic ketone **17a** (57.0 mg, 0.13 mmol) in 97% yield.



17a

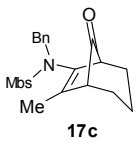
17a: R_f = 0.38 [25% EtOAc in Hexane]; white solid; mp = 150–151 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.08-1.17 (m, 1H), 1.23-1.27 (m, 1H), 1.41-1.51 (m, 2H), 1.54-1.61 (m, 1H), 1.63 (s, 3H), 1.71-1.75 (m, 1H), 2.29 (s, 1H), 2.61 (s, 1H), 4.37 (d, 1H, *J* = 14.5 Hz), 4.71 (d, 1H, *J* = 14.5 Hz), 7.28-7.35 (m, 5H), 8.01 (d, 2H, *J* = 8.5 Hz), 8.39 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6, 17.2, 27.4, 29.0, 51.3, 53.5, 55.3, 124.7, 128.1, 128.4, 128.5, 128.6, 128.8, 135.4, 140.9, 145.8, 150.4, 212.4; IR (film) cm^{-1} 2940brm, 2861m, 1764s, 1530s, 1350s, 1166s; mass spectrum (ESI): m/e (% relative intensity) 444 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{26}N_3O_5S$ $[M+NH_4]^+$: 444.1588, found 444.1589.



17b

Bicyclic ketone **17b** (35.9 mg, 0.091 mmol) was prepared from cyclobutenamide **1b** (39.6 mg, 0.10 mmol) in 91% yield after stirring at 105 °C for 1.5 h.

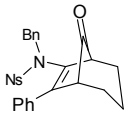
17b: R_f = 0.42 [25% EtOAc in Hexane]; white solid; mp = 99–100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.09-1.22 (m, 2H), 1.36-1.44 (m, 1H), 1.48-1.58 (m, 2H), 1.67 (s, 3H), 1.67-1.73 (m, 1H), 2.28 (t, 1H, *J* = 1.8 Hz), 2.45 (s, 3H), 2.56 (t, 1H, *J* = 2.0 Hz), 4.28 (d, 1H, *J* = 14.4 Hz), 4.67 (d, 1H, *J* = 14.4 Hz), 7.27-7.31 (m, 5H), 7.34 (d, 2H, *J* = 8.0 Hz), 7.71 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.5, 17.2, 21.8, 27.6, 29.2, 50.9, 52.9, 55.3, 127.4, 128.1, 128.3, 128.6, 128.7, 130.1, 136.2, 137.1, 140.0, 144.1, 213.3; IR (film) cm^{-1} 2940brm, 2860m, 1764s, 1454m, 1348s, 1163s; mass spectrum (ESI): m/e (% relative intensity) 413 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{26}NO_3S$ $[M+H]^+$ 396.1628, found 396.1622.



17c

Bicyclic ketone **17c** (39.3 mg, 0.096 mmol) was prepared from cyclobutenamide **1c** (41.1 mg, 0.10 mmol) in 96% yield after stirring at 105 °C for 2.0 h.

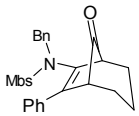
17c: R_f = 0.27 [25% EtOAc in Hexane]; white solid; mp = 113–114 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.09-1.22 (m, 2H), 1.38-1.45 (m, 1H), 1.51-1.58 (m, 2H), 1.67 (s, 3H), 1.67-1.72 (m, 1H), 2.30 (s, 1H), 2.56 (s, 1H), 3.89 (s, 3H), 4.27 (d, 1H, *J* = 14.5 Hz), 4.67 (d, 1H, *J* = 14.5 Hz), 7.00 (d, 2H, *J* = 9.0 Hz), 7.26-7.30 (m, 5H), 7.75 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5, 17.2, 27.6, 29.2, 50.9, 52.9, 55.3, 55.8, 114.6, 128.1, 128.3, 128.6, 128.7, 129.5, 131.6, 136.2, 139.9, 163.3, 213.3; IR (film) cm^{-1} 2941brm, 2860m, 1761s, 1596s, 1497s, 1345s, 1260s, 1156s; mass spectrum (ESI): m/e (% relative intensity) 429 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{29}N_2O_4S$ $[M+NH_4]^+$: 429.1843, found 429.1847.



17d

Bicyclic ketone **17d** (30.6 mg, 0.063 mmol) was prepared from cyclobutenamide **1d** (33.5 mg, 0.069 mmol) in 91% yield after stirring at 105 °C for 1.5 h.

17d: R_f = 0.43 [25% EtOAc in Hexane]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.50-1.52 (m, 1H), 1.66-1.79 (m, 3H), 1.89-1.92 (m, 1H), 2.04-2.06 (m, 1H), 2.80 (d, 1H, *J* = 4.5 Hz), 3.09 (t, 1H, *J* = 2.2 Hz), 4.35 (d, 1H, *J* = 14.5 Hz), 4.57 (d, 1H, *J* = 14.5 Hz), 6.95 (d, 2H, *J* = 7.0 Hz), 7.02 (d, 2H, *J* = 7.0 Hz), 7.18-7.29 (m, 6H), 7.91 (d, 2H, *J* = 9.0 Hz), 8.28 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 29.0, 29.8, 53.7, 54.3, 55.6, 124.5, 127.3, 128.7, 128.8, 128.9, 130.0, 133.3, 135.0, 138.3, 145.6, 150.3, 212.2, three carbons missing due to overlap; IR (film) cm^{-1} 2922brm, 2851m, 1530s, 1350s, 1312m, 1166s; mass spectrum (ESI): m/e (% relative intensity) 506 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{27}H_{28}N_3O_5S$ $[M+NH_4]^+$: 506.1745; found 506.1741.

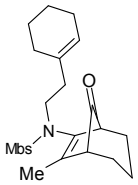


17e

Bicyclic ketone **17e** (35.1 mg, 0.074 mmol) was prepared from cyclobutenamide **1e** (38.5 mg, 0.081 mmol) in 91% yield after stirring at 105 °C for 2.0 h.

17e: R_f = 0.28 [25% EtOAc in Hexane]; white solid; mp = 123–124 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.40-1.45 (m, 1H), 1.55-1.73 (m, 3H), 1.85-1.87 (m, 1H), 2.14-2.15 (m, 1H), 2.87 (d, 1H, *J* = 3.0 Hz), 3.05 (s, 1H), 3.90 (s, 3H), 4.19 (d, 1H, *J* = 14.5 Hz), 4.44 (d, 1H, *J* = 14.5 Hz), 6.90 (d, 2H, *J* = 8.0 Hz), 7.01 (d, 4H, *J* = 8.5 Hz), 7.15-7.29 (m, 6H), 7.78 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ

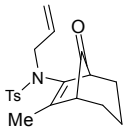
17.5, 29.1, 30.0, 52.6, 54.4, 55.4, 55.9, 114.6, 127.6, 128.2, 128.51, 128.54, 128.58, 128.59, 129.9, 130.5, 131.3, 133.8, 135.7, 136.4, 163.5, 213.1; IR (film) cm^{-1} 2926brm, 2856m, 1761s, 1595m, 1496m, 1352m, 1261s, 1155s; mass spectrum (ESI): m/e (% relative intensity) 491 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{28}H_{31}N_2O_4S$ $[M+NH_4]^+$: 491.2000; found 491.2003.



17f

Bicyclic ketone **17f** (18.3 mg, 0.043 mmol) was prepared from cyclobutenamide **1f** (20.0 mg, 0.047 mmol) in 92% yield after stirring at 105 ^oC for 3.0 h.

17f: R_f = 0.41 [25% EtOAc in Hexane]; colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 1.52-1.63 (m, 6H), 1.69-1.77 (m, 3H), 1.80 (s, 3H), 1.82-1.96 (m, 5H), 2.14 (t, 2H, *J* = 7.6 Hz), 2.39 (s, 1H), 2.71 (s, 1H), 3.16-3.23 (m, 1H), 3.42-3.49 (m, 1H), 3.87 (s, 3H), 5.39 (s, 1H), 6.97 (d, 2H, *J* = 8.8 Hz), 7.71 (d, 2H, *J* = 8.4 Hz),; ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 18.0, 22.4, 23.0, 25.4, 28.0, 28.3, 29.3, 37.9, 47.7, 50.9, 55.5, 55.8, 114.5, 124.0, 129.0, 129.5, 131.8, 134.1, 139.4, 163.2, 213.7; IR (film) cm^{-1} 2932brm, 2857m, 1764s, 1596m, 1497m, 1348m, 1260m, 1158s; mass spectrum (ESI): m/e (% relative intensity) 447 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{24}H_{32}NO_4S$ $[M+H]^+$: 430.2047; found 430.2057.

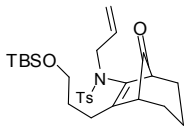


17g

Bicyclic ketone **17g** (28.9 mg, 0.084 mmol) was prepared from cyclobutenamide **1g** (32.1 mg, 0.093 mmol) in 90% yield after stirring at 105 ^oC for 2.0 h.

17g: R_f = 0.39 [25% EtOAc in Hexane]; colorless oil; ^1H NMR (500 MHz, $CDCl_3$) δ 1.44-1.49 (m, 1H), 1.51-1.58 (m, 1H), 1.64-1.76 (m, 3H), 1.76 (s, 3H), 1.87-1.91 (m, 1H), 2.38 (s, 1H), 2.43 (s, 3H), 2.68 (s, 1H), 3.81 (dd, 1H, *J* = 15.0, 6.0 Hz), 4.05 (dd, 1H, *J* = 15.0, 6.0 Hz), 5.15 (d, 1H, *J* = 10.5 Hz), 5.19 (d, 1H, *J* = 17.5 Hz), 5.79 (ddt, 1H, *J* = 17.0, 10.5, 6.2 Hz), 7.31 (d, 2H, *J* = 8.5 Hz), 7.67 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.5, 17.7, 21.7, 27.9, 29.1, 51.3, 52.1, 55.4, 118.6, 127.4, 129.2, 130.0, 133.5, 137.1, 139.5, 144.0, 213.6; IR (film) cm^{-1} 2933brm, 2860m, 1763s, 1349s, 1162s; mass

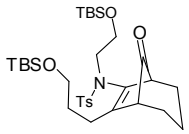
spectrum (ESI): m/e (% relative intensity) 363 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{24}NO_3S$ $[M+H]^+$: 346.1472; found 346.1480.



17h

Bicyclic ketone **17h** (38.1 mg, 0.076 mmol) was prepared from cyclobutenamide **1h** (44.0 mg, 0.087 mmol) in 87% yield after stirring at 105 °C for 1.0 h.

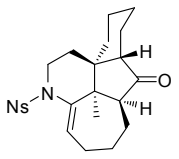
17h: R_f = 0.19 [11% EtOAc in Hexane]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.05 (s, 6H), 0.90 (s, 9H), 1.45-1.63 (m, 4H), 1.68-1.90 (m, 4H), 2.17-2.25 (m, 1H), 2.28-2.36 (m, 1H), 2.41 (s, 1H), 2.43 (s, 3H), 2.80 (s, 1H), 3.56 (t, 2H, *J* = 6.4 Hz), 3.83 (dd, 1H, *J* = 15.2, 6.4 Hz), 4.05 (dd, 1H, *J* = 15.2, 6.4 Hz), 5.14 (d, 1H, *J* = 8.8 Hz), 5.17 (d, 1H, *J* = 16.0 Hz), 5.78 (ddt, 1H, *J* = 17.0, 10.0, 6.2 Hz), 7.30 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.1, 17.8, 18.5, 21.7, 24.7, 26.1, 28.9, 29.0, 30.5, 51.4, 52.3, 53.4, 63.1, 118.8, 127.5, 129.0, 130.0, 133.5, 137.2, 143.3, 143.9, 213.4; IR (film) cm^{-1} 2952m, 2930m, 2858m, 1765s, 1353m, 1164s, 1093s; mass spectrum (ESI): m/e (% relative intensity) 521 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{27}H_{42}NO_4SSi$ $[M+H]^+$: 504.2599; found 504.2607.



17i

Bicyclic ketone **17i** (37.5 mg, 0.060 mmol) was prepared from cyclobutenamide **1i** (42.8 mg, 0.069 mmol) in 88% yield after stirring at 105 °C for 1.0 h.

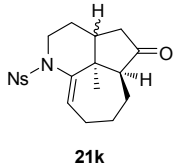
17i: R_f = 0.31 [11% EtOAc in Hexane]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.039 (s, 6H), 0.042 (s, 6H), 0.87 (s, 9H), 0.89 (s, 9H), 1.52-1.65 (m, 4H), 1.69-1.82 (m, 3H), 1.89-1.91 (m, 1H), 2.13-2.20 (m, 1H), 2.24-2.30 (m, 1H), 2.42 (s, 3H), 2.49 (s, 1H), 2.81 (s, 1H), 3.25-3.31 (m, 1H), 3.46-3.51 (m, 1H), 3.54 (t, 2H, *J* = 6.2 Hz), 3.70 (t, 2H, *J* = 6.7 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.2, -5.13, -5.12, 18.0, 18.5, 21.7, 24.8, 26.05, 26.12, 29.1, 29.2, 30.4, 51.7, 51.8, 53.5, 61.9, 63.1, 127.5, 129.7, 129.9, 137.1, 142.7, 143.9, 213.4; IR (film) cm^{-1} 2951m, 2929m, 2857m, 1765s, 1357m, 1254m, 1163m, 1093s; mass spectrum (ESI): m/e (% relative intensity) 639 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{32}H_{56}NO_5SSi_2$ $[M+H]^+$: 622.3413; found 622.3431.



21j

21j (24.8 mg, 0.056 mmol) was prepared from cyclobutenamide **1j** (28.6 mg, 0.064 mmol) in 87% yield after stirring at 105 ^{o}C for 1.5 h.

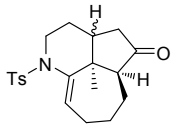
21j: R_f = 0.39 [25% EtOAc in Hexane]; pale yellow solid; mp = 223–224 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26-1.37 (m, 2H), 1.35 (s, 3H), 1.43-1.73 (m, 8H), 1.90 (td, 1H, *J* = 13.6, 5.6 Hz), 2.00 (q, 2H, *J* = 6.0 Hz), 2.05-2.16 (m, 2H), 2.34 (d, 1H, *J* = 4.8 Hz), 2.40-2.48 (m, 1H), 2.71 (t, 1H, *J* = 4.4 Hz), 3.10 (td, 1H, *J* = 13.2, 2.8 Hz), 3.98-4.03 (m, 1H), 5.58 (t, 1H, *J* = 5.6 Hz), 8.02 (d, 2H, *J* = 8.4 Hz), 8.36 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.2, 21.25, 21.33, 22.9, 23.66, 23.74, 27.2, 29.1, 31.8, 42.8, 44.1, 48.0, 50.8, 54.8, 124.6, 128.1, 131.5, 139.3, 148.3, 149.9, 217.8; IR (film) cm^{-1} 2933m, 2864w, 1733s, 1529s, 1348s, 1160s; mass spectrum (ESI): m/e (% relative intensity) 462 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{32}N_3O_5S$ $[M+NH_4]^+$: 462.2058; found 462.2056.



21k

21k (10.9 mg, 0.028 mmol) was prepared from cyclobutenamide **1k** (11.0 mg, 0.028 mmol) in 99% yield after stirring at 105 ^{o}C for 1.5 h.

21k: R_f = 0.14 [11% EtOAc in Hexane]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (s, 6H), 1.42-1.51 (m, 7H), 1.63-1.92 (m, 13H), 1.97-2.01 (m, 3H), 2.09-2.34 (m, 12H), 2.40-2.50 (m, 4H), 3.20 (td, 1H, *J* = 12.0, 3.0 Hz), 3.53 (dd, 2H, *J* = 10.5, 6.5 Hz), 3.94 (td, 2H, *J* = 11.0, 7.0 Hz), 4.01 (ddd, 1H, *J* = 12.6, 5.5, 3.0 Hz), 5.62 (t, 1H, *J* = 6.0 Hz), 5.81 (t, 1H, *J* = 6.2 Hz), 8.02 (d, 2H, *J* = 8.5 Hz), 8.06 (d, 4H, *J* = 8.5 Hz), 8.36 (d, 2H, *J* = 8.0 Hz), 8.38 (d, 4H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.3, 23.0, 23.2, 23.6, 24.1, 24.2, 25.3, 25.8, 26.38, 26.45, 38.4, 39.6, 40.2, 42.6, 43.7, 47.4, 48.5, 49.0, 54.0, 60.2, 124.5, 124.6, 128.2, 128.7, 129.2, 131.2, 138.1, 141.9, 146.9, 148.1, 150.0, 150.1, 215.9, 216.2; IR (film) cm^{-1} 2927brm, 2855w, 1738s, 1530s, 1350s, 1164s; mass spectrum (ESI): m/e (% relative intensity) 391 (100) $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{26}N_3O_5S$ $[M+NH_4]^+$: 408.1588; found 408.1595.



21l

21l (20.1 mg, 0.056 mmol) was prepared from cyclobutenamide **1l** (24.0 mg, 0.067 mmol) in 84% yield after stirring at 105 ^{o}C for 1.5 h.

21l: R_f = 0.19 [25% EtOAc in Hexane]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (s, 6H), 1.36-1.49 (m, 7H), 1.56-1.90 (m, 13H), 1.96-2.00 (m, 3H), 2.07-2.33 (m, 12H), 2.38-2.47 (m, 13H), 3.13 (td, 1H, *J* = 12.0, 3.6 Hz), 3.48-3.52 (m, 2H), 3.87 (td, 2H, *J* = 10.8, 8.0 Hz), 3.95 (ddd, 1H, *J* = 13.0, 5.8, 3.6 Hz), 5.72 (t, 1H, *J* = 6.2 Hz), 5.91 (dd, 2H, *J* = 6.8, 5.6 Hz), 7.29 (d, 2H, *J* = 7.6 Hz), 7.31 (d, 4H, *J* = 8.0 Hz), 7.71 (d, 2H, *J* = 8.4 Hz), 7.75 (d, 4H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 21.67, 21.72, 23.2, 23.5, 23.6, 24.2, 24.3, 25.6, 25.7, 26.3, 26.6, 38.6, 39.5, 40.3, 42.7, 43.2, 47.0, 48.5, 49.0, 54.2, 60.1, 127.1, 127.7, 127.9, 129.7, 129.8, 130.0, 138.0, 138.2, 139.3, 142.0, 143.2, 143.5, 216.6, 216.9; IR (film) cm^{-1} 2927brm, 2865w, 1739s, 1342m, 1159s; mass spectrum (ESI): m/e (% relative intensity) 360 (100) $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{20}H_{26}NO_3S$ $[M+H]^+$: 360.1628; found 360.1631.

References

1. Li, H.; Hsung, R. P.; DeKorver, K. A.; Wei, Y. *Org. Lett.* **2010**, *12*, 3780.

2. Wang, X.-N.; Krenske, E. H.; Johnston, R. C.; Houk, K. N.; Hsung, R. P. *J. Am. Chem. Soc.* **2014**, *136*, 9802.