Torquoselective Ring-Opening of Fused Cyclobutenamides: Evidence for a *Cis,Trans*-Cyclooctadienone Intermediate

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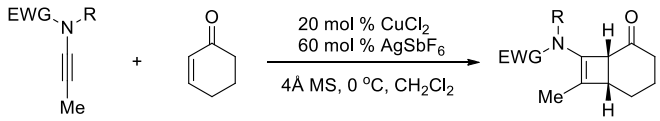
Supporting Information Part 1

General Experimental Information

GENERAL EXPERIMENTAL INFORMATION

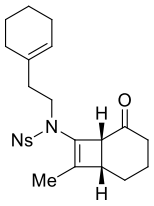
All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. Chromatographic separations were performed using Silicycle 40-63μm SiO_2. ^1H and ^{13}C NMR spectra were obtained on Varian VI-400 and VI-500 spectrometers using $CDCl_3$ with TMS or 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. TLC analysis was performed using Aldrich 254 nm polyester-backed plates (60 Å, 250 μm) and visualized using UV and $KMnO_4$ stain. All spectral data obtained for new compounds are reported here.

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



S1 **S2** **1**

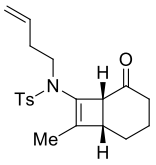
To a stirring suspension of $CuCl_2$ (26.9 mg, 0.20 mmol) and 4Å MS (348.3 mg) in CH_2Cl_2 (3.3 mL) was added $AgSbF_6$ (20.6 mg, 0.60 mmol) in the dark at room temperature. After stirring for 1 h at RT, a solution of ynamide **S1f** (348.3 mg, 1.00 mmol) and 2-cyclohexen-1-one (115.4 mg, 1.20 mmol) in CH_2Cl_2 (3.3 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 filtrated through a small silica gel column, concentrated *in vacuo*, and then purified by flash silica gel column chromatography [gradient eluent: 8:1 ~4:1 Hexane/EtOAc] to afford product **1f** (42.2 mg, 0.095 mmol) in 9% yield.



1f

1f: R_f = 0.39 [3:1 Hexane/EtOAc]; yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 1.52-1.71 (m, 8H), 1.77 (s, 3H), 1.88-1.98 (m, 6H), 2.15 (t, 2H, *J* = 7.2 Hz), 2.95 (s, 1H), 3.31 (s, 1H), 3.46 (dt, 1H, *J* = 13.5, 7.0 Hz), 3.58 (dt, 1H, *J* = 13.5, 7.5 Hz), 5.43 (s, 1H), 7.96 (d, 2H, *J* = 8.5 Hz), 8.33 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.7, 17.6, 22.4, 23.0, 24.1, 25.5, 28.3, 37.9, 38.8, 41.0, 46.9, 53.1, 124.3, 124.5, 126.0, 128.8, 133.7, 145.3, 146.0, 150.3, 209.6; IR (film) cm^{-1} 2922brm, 2852w, 1693m, 1531s,

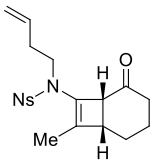
1350s, 1167m; mass spectrum (ESI): m/e (% relative intensity) 462 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{32}N_3O_5S$ $[M+NH_4]^+$: 462.2058; found 462.2050.



1g

Cyclobutenamide **1g** (102.1 mg, 0.28 mmol) was prepared from the corresponding ynamide **S1g** (1.2 g, 4.56 mmol) in 6% yield.

1g: R_f = 0.35 [3:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.52-1.70 (m, 3H), 1.72 (q, 3H, *J* = 1.2 Hz), 1.89-1.98 (m, 2H), 2.08-2.14 (m, 1H), 2.27 (q, 2H, *J* = 7.2 Hz), 2.89 (s, 1H), 3.30-3.32 (m, 1H), 3.44 (dt, 1H, *J* = 13.6, 7.2 Hz), 3.54 (dt, 1H, *J* = 13.6, 7.2 Hz), 5.09 (q, 1H, *J* = 1.5 Hz), 5.75 (ddt, 1H, *J* = 17.2, 10.4, 6.8 Hz), 7.27 (d, 2H, *J* = 8.0 Hz), 7.65 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.5, 17.4, 21.6, 23.9, 33.9, 38.6, 40.4, 47.2, 53.7, 117.2, 126.8, 127.5, 129.6, 134.4, 137.0, 143.6, 143.7, 210.1; IR (film) cm^{-1} 2926brm, 2873w, 1694s, 1346s, 1160s; mass spectrum (ESI): m/e (% relative intensity) 377 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{20}H_{26}NO_3S$ $[M+H]^+$: 360.1628; found 360.1636.

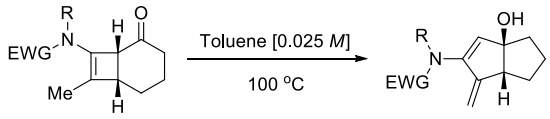


1h

Cyclobutenamide **1h** (36.0 mg, 0.092 mmol) was prepared from the corresponding ynamide **S1h** (325.2 mg, 1.11 mmol) in 8% yield.

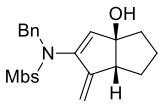
1h: R_f = 0.32 [3:1 Hexane/EtOAc]; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.60-1.73 (m, 3H), 1.77-1.78 (m, 3H), 1.94-2.03 (m, 2H), 2.12-2.18 (m, 1H), 2.27-2.32 (m, 2H), 2.95 (s, 1H), 3.31 (s, 1H), 3.48 (dt, 1H, *J* = 13.6, 6.8 Hz), 3.58 (dt, 1H, *J* = 13.6, 7.6 Hz), 5.07 (s, 1H), 5.09-5.11 (m, 1H), 5.70-5.80 (m, 1H), 7.95-7.97 (m, 2H), 8.33-8.35 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.6, 17.6, 24.0, 33.7, 38.8, 41.0, 47.6, 53.1, 117.8, 124.3, 125.8, 128.7, 134.0, 145.7, 145.8, 150.3, 209.6; IR (film) cm^{-1} 2923brm, 2870w, 1693m, 1529s, 1349s, 1166s; mass spectrum (ESI): m/e (% relative intensity) 408 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{26}N_3O_5S$ $[M+NH_4]^+$: 408.1588; found 408.1599.

General Procedure for Thermal Rearrangements of 4,6-Fused Cyclobutenamides 1.



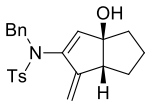
1 3

To a flamed-dried sealed tube were added cyclobutenamide **1a** (88.8 mg, 0.22 mmol) and toluene (8.8 mL, cyclobutenamide *concn* = 0.025 *M*), then capped it and directly heated the mixture to 100 °C. After stirred at 100 °C for 32.0 h, the reaction mixture was then allowed to cool to room temperature slowly. The mixture was purified using silica gel flash column chromatography [first using hexane to wash toluene away, and then gradient eluent: 5:1~2:1 Hexane/EtOAc] to afford hydroxypentalane **3a** (49.6 mg, 0.12 mmol) in 56% yield with **1a** (19.6 mg, 0.048 mmol, 22%) recovered.



3a

3a: R_f = 0.41 [1:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93-1.00 (m, 1H), 1.33-1.35 (m, 1H), 1.51-1.54 (m, 2H), 1.60-1.67 (m, 1H), 1.92-2.00 (m, 1H), 2.31 (brs, 1H), 2.68 (d, 1H, *J* = 8.5 Hz), 3.87 (s, 3H), 4.43 (d, 1H, *J* = 14.0 Hz), 4.57 (d, 1H, *J* = 14.0 Hz), 4.73 (s, 1H), 4.93 (s, 1H), 5.54 (s, 1H), 6.96 (d, 2H, *J* = 9.0 Hz), 7.218-7.224 (m, 5H), 7.77 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.9, 33.9, 39.0, 53.82, 53.84, 55.8, 89.1, 106.4, 114.2, 128.0, 128.4, 129.2, 130.2, 130.4, 135.8, 139.9, 142.4, 152.3, 163.2; IR (film) cm^{-1} 2922m, 2850w, 1596m, 1498m, 1347m, 1261s, 1157s; mass spectrum (ESI): m/e (% relative intensity) 429 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{26}NO_4S$ $[M+H]^+$: 412.1578; found 412.1576.

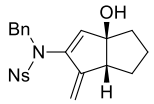


3b

Hydroxypentalane **3b** (37.3 mg, 0.094 mmol) was prepared from the corresponding cyclobutenamide **1b** (60.5 mg, 0.15 mmol) in 62% yield.

3b: R_f = 0.17 [3:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92-1.04 (m, 1H), 1.32-1.37 (m, 1H), 1.49-1.56 (m, 2H), 1.60-1.67 (m, 1H), 1.92-2.01 (m, 1H), 2.13 (brs, 1H), 2.44 (s, 3H), 2.68 (d, 1H, *J* = 7.2 Hz), 4.45 (d, 1H, *J* = 14.0 Hz), 4.57 (d, 1H, *J* = 14.0 Hz), 4.73 (t, 1H, *J* = 1.6 Hz), 4.92 (d, 1H, *J* = 1.6 Hz), 5.52 (s, 1H), 7.20-7.25 (m, 5H), 7.30 (d, 2H, *J* = 8.0 Hz), 7.72 (d, 2H, *J* = 8.0

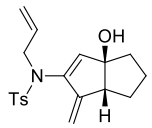
Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 24.9, 33.9, 39.0, 53.86, 53.88, 89.2, 106.4, 128.0, 128.1, 128.4, 129.2, 129.7, 135.8, 140.0, 142.3, 143.9, 152.2, one carbon missing due to overlap; IR (film) cm^{-1} 2952brm, 2866w, 1598m, 1348s, 1162s; mass spectrum (ESI): m/e (% relative intensity) 413 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{29}N_2O_3S$ $[M+NH_4]^+$: 413.1894; found 413.1904.



3c

Hydroxypentalane **3c** (43.3 mg, 0.10 mmol) was prepared from the corresponding cyclobutenamide **1c** (77.0 mg, 0.18 mmol) in 56% yield with **1c** (14.9 mg, 0.035 mmol, 19%) recovered.

3c: R_f = 0.23 [3:1 Hexane/EtOAc]; pale yellow solid; mp = 65–66 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99-1.09 (m, 1H), 1.34-1.38 (m, 1H), 1.55-1.76 (m, 3H), 1.96-2.06 (m, 1H), 2.28 (brs, 1H), 2.72 (d, 1H, *J* = 8.4 Hz), 4.56 (d, 1H, *J* = 13.6 Hz), 4.63 (d, 1H, *J* = 13.6 Hz), 4.739 (s, 1H), 4.743 (s, 1H), 5.62 (s, 1H), 7.21-7.28 (m, 5H), 8.00 (d, 2H, *J* = 8.4 Hz), 8.33 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.0, 33.9, 39.1, 53.88, 53.91, 89.1, 106.4, 124.3, 128.5, 128.7, 129.1, 129.2, 135.2, 141.1, 141.5, 145.0, 150.3, 151.7; IR (film) cm^{-1} 2954brm, 2866w, 1530s, 1349s, 1313m, 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 444.1593.

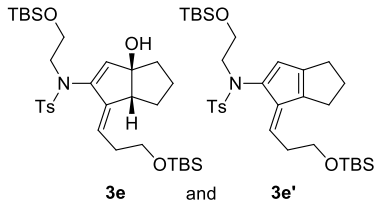


3d

Hydroxypentalane **3d** (41.0 mg, 0.12 mmol) was prepared from the corresponding cyclobutenamide **1d** (71.9 mg, 0.21 mmol) in 57% yield with **1d** (13.6 mg, 0.039 mmol, 19%) recovered.

3d: R_f = 0.15 [3:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.28-1.37 (m, 1H), 1.50-1.55 (m, 1H), 1.65-1.78 (m, 3H), 2.03-2.11 (m, 1H), 2.43 (s, 3H), 2.48 (s, 3H), 2.81 (d, 1H, *J* = 7.5 Hz), 3.97 (ddd, 2H, *J* = 32.0, 14.5, 6.5 Hz), 4.82 (t, 1H, *J* = 1.5 Hz), 5.00 (d, 1H, *J* = 2.0 Hz), 5.07 (s, 1H), 5.10 (dd, 1H, *J* = 8.5, 1.5 Hz), 5.65 (s, 1H), 5.72 (ddt, 1H, *J* = 16.7, 10.0, 6.7 Hz), 7.29 (d, 2H, *J* = 8.0 Hz), 7.70 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.7, 25.2, 34.0, 39.2, 52.9, 53.8, 89.3, 106.1, 119.1, 128.0, 129.6, 132.8, 135.9, 139.3, 142.4, 143.9, 152.7; IR (film) cm^{-1} 2954brm, 2866w,

1599m, 1345s, 1161s; mass spectrum (ESI): m/e (% relative intensity) 363 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{27}N_2O_3S$ $[M+NH_4]^+$: 363.1737; found 363.1748.

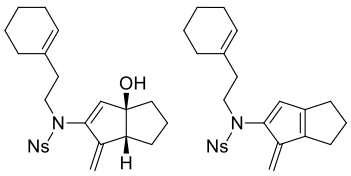


3e and **3e'**

Hydroxypentalane **3e** (24.8 mg, 0.040 mmol) and fulvene **3e'** (16.1 mg, 0.027 mmol) was prepared from the corresponding cyclobutenamide **1e** (72.8 mg, 0.12 mmol) in 34% yield and 22% yield, respectively, with **1e** (30.1 mg, 0.048 mmol, 41%) recovered.

3e: R_f = 0.39 [3:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.02 (s, 6H), 0.05 (s, 6H), 0.86 (s, 9H), 0.89 (s, 9H), 1.44-1.46 (m, 2H), 1.73-1.75 (m, 2H), 1.80-1.86 (m, 1H), 1.93 (s, 1H), 2.12-2.19 (m, 1H), 2.25 (q, 2H, *J* = 7.3 Hz), 2.42 (s, 3H), 2.83 (d, 1H, *J* = 9.0 Hz), 3.38-3.44 (m, 1H), 3.48-3.54 (m, 3H), 3.67 (t, 2H, *J* = 7.0 Hz), 5.24 (t, 1H, *J* = 7.5 Hz), 5.64 (s, 1H), 7.26 (d, 2H, *J* = 8.0 Hz), 7.69 (d, 2H, *J* = 8.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.2, -5.1, 18.4, 18.5, 21.7, 25.5, 26.0, 26.1, 33.1, 33.7, 39.2, 51.6, 51.9, 61.5, 62.7, 89.5, 119.4, 128.0, 129.5, 136.5, 137.3, 143.3, 143.7, 145.0; IR (film) cm^{-1} 2953m, 2928m, 2857m, 1471m, 1349m, 1255m, 1165s, 1090s; mass spectrum (ESI): m/e (% relative intensity) 639 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{32}H_{59}N_2O_5SSi$ $[M+NH_4]^+$: 639.3678; found 639.3694.

3e': R_f = 0.47 [8:1 Hexane/EtOAc]; yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.002 (s, 6H), 0.06 (s, 6H), 0.84 (s, 9H), 0.89 (s, 9H), 2.21-2.28 (m, 2H), 2.42 (s, 3H), 2.42-2.44 (m, 2H), 2.64-2.72 (m, 4H), 3.48 (t, 2H, *J* = 7.0 Hz), 3.66 (q, 4H, *J* = 6.5 Hz), 5.85 (s, 1H), 6.21 (t, 1H, *J* = 7.8 Hz), 7.26 (d, 2H, *J* = 8.0 Hz), 7.67 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.2, -5.1, 18.4, 18.5, 21.7, 26.0, 26.1, 27.7, 28.5, 29.7, 34.0, 54.4, 61.3, 62.4, 125.3, 128.1, 129.4, 135.77, 135.79, 136.17, 136.21, 139.3, 143.2, 148.4; IR (film) cm^{-1} 2954m, 2928m, 2856m, 1353m, 1255m, 1166s, 1095s; mass spectrum (ESI): m/e (% relative intensity) 621 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{32}H_{54}NO_4SSi_2$ $[M+H]^+$: 604.3307; found 604.3326.

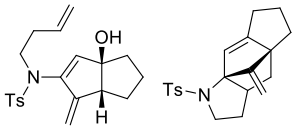


3f and **3f'**

Hydroxypentalane **3f** (8.0 mg, 0.018 mmol) and fulvene **3f'** (4.4 mg, 0.010 mmol) was prepared from the corresponding cyclobutenamide **1f** (16.0 mg, 0.036 mmol) in 50% yield and 29% yield, respectively.

3f: R_f = 0.29 [3:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34-1.52 (m, 1H), 1.53-1.60 (m, 5H), 1.75-1.84 (m, 3H), 1.89 (s, 2H), 1.96 (s, 3H), 2.09-2.17 (m, 3H), 2.85 (d, 1H, *J* = 8.5 Hz), 3.43-3.55 (m, 2H), 4.79 (d, 2H, *J* = 10.5 Hz), 5.41 (s, 1H), 5.81 (s, 1H), 8.00 (d, 2H, *J* = 8.5 Hz), 8.34 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.4, 22.9, 25.4, 25.5, 28.4, 34.1, 37.5, 39.7, 49.0, 54.1, 89.3, 106.6, 124.27, 124.29, 129.0, 133.6, 140.5, 141.8, 145.1, 150.3, 151.9; IR (film) cm^{-1} 2930brm, 2964w, 1532s, 1313s, 1167s; 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 462.2047.

3f': R_f = 0.76 [3:1 Hexane/EtOAc]; yellow solid; mp = 132–133 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.51-1.59 (m, 4H), 1.88 (s, 2H), 1.94 (s, 2H), 2.15 (t, 2H, *J* = 7.5 Hz), 2.26 (t, 2H, *J* = 7.0 Hz), 2.46 (s, 2H), 2.55 (s, 2H), 3.50 (t, 2H, *J* = 7.5 Hz), 5.37 (s, 1H), 5.69 (s, 1H), 5.73 (s, 1H), 5.88 (s, 1H), 7.96 (d, 2H, *J* = 7.5 Hz), 8.33 (d, 2H, *J* = 7.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.4, 23.0, 25.4, 26.8, 27.4, 28.4, 29.1, 37.3, 51.4, 119.9, 124.0, 124.1, 127.9, 129.2, 133.9, 134.8, 138.9, 144.5, 144.9, 148.3, 150.1; IR (film) cm^{-1} 2923brm, 2851w, 1531s, 1351s, 1167s; HRMS (ESI): *m/z* calcd for $C_{23}H_{29}N_2O_4S$ $[M+NH_4]^+$: 429.1843; found 429.1847. mass spectrum (ESI): m/e (% relative intensity) 427 (100) $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{27}N_2O_4S$ $[M+H]^+$: 427.1687; found 427.1698.

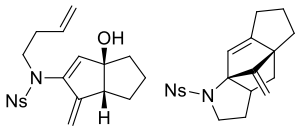


3g and **3g''**

Hydroxypentalane **3g** (7.7 mg, 0.021 mmol) and fulvene **3g''** (16.7 mg, 0.049 mmol) was prepared from the corresponding cyclobutenamide **1f** (30.0 mg, 0.083 mmol) in 26% yield and 59% yield, respectively, after stirred at 100 °C for 30.0 h.

3g: R_f = 0.17 [3:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.32-1.41 (m, 1H), 1.56-1.60 (m, 1H), 1.70-1.79 (m, 3H), 1.96 (s, 1H), 2.06-2.15 (m, 1H), 2.23-2.29 (m, 2H), 2.43 (s, 3H), 2.84 (d, 1H, *J* = 6.8 Hz), 3.41-3.45 (m, 2H), 4.83 (t, 1H, *J* = 1.6 Hz), 4.99 (d, 1H, *J* = 2.0 Hz), 5.01-5.04 (m, 1H), 5.07 (q, 1H, *J* = 1.6 Hz), 5.68 (s, 1H), 5.67-5.77 (m, 1H), 7.28 (d, 2H, *J* = 8.0 Hz), 7.68 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 25.4, 33.3, 34.1, 39.4, 49.7, 54.0, 89.4, 106.6, 117.3, 128.0, 129.6, 134.7, 135.9, 139.1, 143.0, 143.8, 152.5; IR (film) cm^{-1} 2953m, 2925m, 2867w, 1598w, 1348s, 1162s; mass spectrum (ESI): m/e (% relative intensity) 377 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{20}H_{29}N_2O_3S$ $[M+NH_4]^+$: 377.1894; found 377.1901.

3g'': R_f = 0.34 [8:1 Hexane/EtOAc]; white solid; mp = 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (dd, 1H, *J* = 11.2, 4.4 Hz), 1.40 (dd, 1H, *J* = 11.2, 8.8 Hz), 1.53-1.69 (m, 2H), 1.90-2.15 (m, 4H), 2.19-2.27 (m, 1H), 2.30-2.37 (m, 1H), 2.42 (s, 3H), 3.52 (ddd, 1H, *J* = 11.0, 11.0, 6.4 Hz), 3.78 (t, 1H, *J* = 8.8 Hz), 4.29 (s, 1H), 4.35 (s, 1H), 6.11 (s, 1H), 7.30 (d, 2H, *J* = 8.0 Hz), 7.80 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 25.87, 25.92, 28.1, 29.9, 34.7, 48.4, 52.0, 60.1, 81.3, 88.7, 122.4, 127.3, 129.7, 138.5, 143.0, 156.4, 164.9; IR (film) cm^{-1} 2947brm, 2869m, 1691w, 1598w, 1450w, 1340s, 1163s, 1110s; mass spectrum (ESI): m/e (% relative intensity) 359 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{20}H_{24}NO_2S$ $[M+H]^+$: 342.1523; found 342.1534.



3h and **3h''**

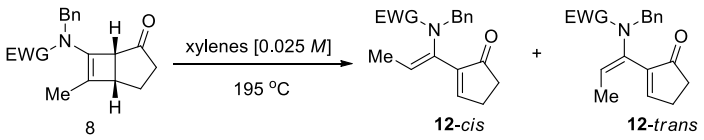
Hydroxypentalane **3h** (7.5 mg, 0.019 mmol) and fulvene **3h''** (6.2 mg, 0.017 mmol) was prepared from the corresponding cyclobutenamide **1f** (24.0 mg, 0.061 mmol) in 31% yield and 27% yield, respectively, after stirred at 100 ^{o}C for 36.0 h.

3h: R_f = 0.21 [3:1 Hexane/EtOAc]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.34-1.43 (m, 1H), 1.54-1.58 (m, 1H), 1.75-1.85 (m, 3H), 2.01 (s, 1H), 2.09-2.17 (m, 1H), 2.30 (q, 2H, *J* = 7.2 Hz), 2.85 (d, 1H, *J* = 8.0 Hz), 3.50 (ddd, 2H, *J* = 21.0, 13.0, 7.0 Hz), 4.77 (d, 1H, *J* = 2.0 Hz), 4.80 (s, 1H), 5.05 (s, 1H), 5.08 (d, 1H, *J* = 9.5 Hz), 5.71 (ddt, 1H, *J* = 17.0, 10.0, 6.7 Hz), 5.83 (s, 1H), 7.99 (d, 2H, *J* = 9.0 Hz), 8.34 (d, 2H, *J* = 9.0 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.5, 33.5, 34.1, 39.7, 49.7, 54.1, 89.3, 106.6, 117.9, 124.3, 129.0, 134.1, 140.7, 141.6, 145.0, 150.3, 151.8; IR (film) cm^{-1} 2930brm, 2867w, 1531s,

1351s, 1168s; mass spectrum (ESI): m/e (% relative intensity) 408 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{26}N_3O_5S$ $[M+NH_4]^+$: 408.1588; found 408.1598.

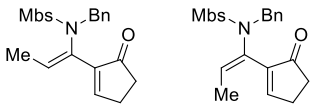
3h'': R_f = 0.22 [8:1 Hexane/EtOAc]; white solid; mp = 163–164 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.30 (dd, 1H, *J* = 11.5, 4.0 Hz), 1.42 (dd, 1H, *J* = 11.2, 9.0 Hz), 1.55-1.61 (m, 1H), 1.63-1.72 (m, 1H), 1.90-2.03 (m, 3H), 2.06-2.18 (m, 2H), 2.22-2.29 (m, 1H), 2.32-2.38 (m, 1H), 3.58 (ddd, 1H, *J* = 10.5, 10.5, 6.5 Hz), 3.86 (t, 1H, *J* = 9.2 Hz), 4.21 (s, 1H), 4.29 (s, 1H), 6.04 (s, 1H), 8.10 (d, 2H, *J* = 8.5 Hz), 8.36 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.8, 26.0, 28.2, 29.8, 34.6, 48.5, 52.4, 60.2, 81.5, 88.9, 121.5, 124.5, 128.4, 147.1, 150.0, 157.2, 164.5; IR (film) cm^{-1} 2921brm, 2850w, 1530s, 1350s, 1169m; mass spectrum (ESI): m/e (% relative intensity) 390 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{24}N_3O_4S$ $[M+NH_4]^+$: 390.1483; found 390.1488.

General Procedure for Thermal Rearrangements of 4,5-Fused Cyclobutenamides 8.



8 **12**-*cis* **12**-*trans*

To a flamed-dried sealed tube were added cyclobutenamide **8a** (104.3 mg, 0.26 mmol) and xylenes (10.5 mL, cyclobutenamide *concn* = 0.025 *M*), then capped it and directly heated the mixture to 195 °C. After stirred at 195 °C for 36.0 h, the reaction mixture was then allowed to cool to room temperature slowly. The mixture was purified using silica gel flash column chromatography [first using hexane to wash xylenes away, and then gradient eluent: 7:1~3:1 Hexane/EtOAc] to afford amido-dienes **12a**-*cis* (56.2 mg, 0.14 mmol) in 54% yield and **12a**-*trans* (16.5 mg, 0.042 mmol) in 16% yield.

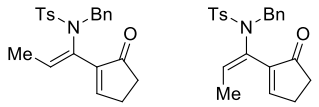


12a-*cis* and **12a**-*trans*

12a-*cis*: R_f = 0.16 [3:1 Hexane/EtOAc]; colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.19 (d, 3H, *J* = 7.0 Hz), 2.35-2.39 (m, 4H), 3.88 (s, 3H), 4.44-4.49 (m, 2H), 6.98 (d, 2H, *J* = 8.5 Hz), 7.02 (q, 1H, *J* = 7.2 Hz), 7.15-7.24 (m, 6H), 7.81 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.1, 25.4, 36.5, 53.4, 55.8, 114.3, 128.1, 128.4, 129.7, 129.8, 129.9, 132.9, 133.5, 136.1, 139.8, 160.2, 163.1, 207.1; IR (film) cm^{-1} 2920brw, 2845w, 1699s, 1596m, 1497m, 1344s, 1260s, 1154s; 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 415.1689.

12a-*trans*: R_f = 0.15 [3:1 Hexane/EtOAc]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.46 (d, 3H, *J* = 7.2 Hz), 2.27-2.29 (m, 2H), 2.49-2.52 (m, 2H), 3.88 (s, 3H), 4.49 (s, 2H), 5.30 (q, 1H, *J* = 7.2 Hz), 6.97 (d, 2H, *J* = 9.2 Hz), 7.21-7.31 (m, 5H), 7.34 (t, 1H, *J* = 2.8 Hz), 7.76 (d, 2H, *J* = 9.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 27.0, 34.8, 54.4, 55.8, 114.0, 127.9, 128.5, 129.2, 129.6, 130.1, 131.1, 131.2, 136.7, 143.6, 163.0, 163.9, 205.8; IR (film) cm^{-1} 2921brw, 2845w, 1705s, 1596m, 1498m, 1343m, 1260s, 1157s; mass spectrum (ESI): m/e (% relative intensity) 415 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{24}NO_4S$ $[M+H]^+$: 398.1421; found 398.1429.

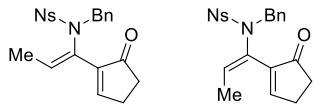


12b-*cis* and **12b**-*trans*

Amido-dienes **12b**-*cis* (30.2 mg, 0.079 mmol) and **12a**-*trans* (10.7 mg, 0.028 mmol) was prepared from the corresponding cyclobutenamide **8b** (66.4 mg, 0.17 mmol) in 46% yield and 16% yield, respectively.

12b-*cis*: R_f = 0.26 [3:1 Hexane/EtOAc]; colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.16 (d, 3H, *J* = 7.2 Hz), 2.33-2.44 (m, 4H), 2.44 (s, 3H), 4.37-4.51 (m, 2H), 7.03 (q, 1H, *J* = 7.2 Hz), 7.11-7.28 (m, 6H), 7.31 (d, 2H, *J* = 7.6 Hz), 7.77 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 21.7, 25.3, 36.5, 53.5, 127.6, 128.2, 128.4, 129.7, 129.8, 130.0, 133.6, 136.0, 138.2, 139.8, 143.6, 160.2, 207.0; IR (film) cm^{-1} 2923brm, 2853w, 1700s, 1347s, 1159s; 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 382.1464.

12b-*trans*: R_f = 0.20 [3:1 Hexane/EtOAc]; pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.45 (d, 3H, *J* = 7.2 Hz), 2.24-2.27 (m, 2H), 2.44 (s, 3H), 2.48-2.51 (m, 2H), 4.51 (s, 2H), 5.29 (q, 1H, *J* = 7.2 Hz), 7.25-7.30 (m, 7H), 7.35 (t, 1H, *J* = 2.8 Hz), 7.70 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.9, 21.7, 27.0, 34.8, 54.6, 127.9, 128.0, 128.5, 129.1, 129.5, 129.7, 131.5, 136.6, 136.7, 143.4, 143.5, 164.1, 205.8; IR (film) cm^{-1} 2922brm, 2851w, 1738s, 1365s, 1229s, 1216s, 1161m; 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 382.1465.



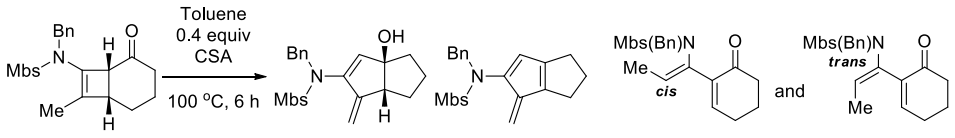
12c-*cis* and **12c**-*trans*

Amido-dienes **12c**-*cis* (38.7 mg, 0.094 mmol) and **12a**-*trans* (17.0 mg, 0.041 mmol) was prepared from the corresponding cyclobutenamide **8c** (76.6 mg, 0.18 mmol) in 51% yield and 22% yield, respectively, with **8c** (12.0 mg, 0.029 mmol, 16%) recovered.

12c-*cis*: R_f = 0.27 [3:1 Hexane/EtOAc]; pale yellow solid; mp = 174–175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.12 (d, 3H, *J* = 7.2 Hz), 2.31-2.42 (m, 4H), 4.47-4.59 (m, 2H), 7.05-7.10 (m, 2H), 7.22-7.31 (m, 5H), 8.04 (d, 2H, *J* = 9.2 Hz), 8.35 (d, 2H, *J* = 8.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 25.4, 36.5, 54.3, 124.5, 128.6, 128.7, 128.8, 129.5, 130.1, 133.5, 135.3, 139.7, 146.7, 150.2, 160.2, 206.7; IR (film) cm^{-1} 2924brw, 2855w, 1699m, 1530s, 1350s, 1164s; 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 430.1435.

12c-*trans*: R_f = 0.21 [3:1 Hexane/EtOAc]; white solid; mp = 190–191 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.48 (d, 3H, *J* = 7.0 Hz), 2.31-2.33 (m, 2H), 2.54-2.56 (m, 2H), 4.56 (s, 2H), 5.29 (q, 1H, *J* = 7.2 Hz), 7.29-7.31 (m, 6H), 7.99 (d, 2H, *J* = 9.0 Hz), 8.33 (d, 2H, *J* = 8.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.9, 27.1, 34.7, 54.9, 124.1, 128.3, 128.7, 128.9, 129.2, 129.7, 132.1, 135.9, 143.1, 144.9, 150.1, 164.1, 205.8; IR (film) cm^{-1} 2921brm, 2852w, 1705s, 1529s, 1349s, 1164s; mass spectrum (ESI): m/e (% relative intensity) 430 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{21}H_{21}N_2O_5S$ $[M+H]^+$: 413.1166; found 413.1167.

Procedure for Rearrangements of 4,6-Fused Cyclobutenamide 1a Catalyzed by CSA.



1a **3a:** 7% **3a':** 8% **i**-*cis* 26%; *dr* 2:1 **i**-*trans*

To a flamed-dried sealed tube were added cyclobutenamide **1a** (80.0 mg, 0.19 mmol), CSA (18.1 mg, 0.078 mmol) and toluene (7.8 mL, cyclobutenamide *concn* = 0.025 *M*), then capped it and directly heated the mixture to 100 °C. After stirred at 100 °C for 6.0 h, the reaction mixture was then allowed to cool to room temperature slowly. The mixture was purified using silica gel flash column chromatography [first using hexane to wash toluene away, and then gradient eluent: 7:1~3:1

Hexane/EtOAc] to afford amido-dienes **3a** (5.4 mg, 0.013 mmol, 7%), **3a'** (6.0 mg, 0.015 mmol, 8%), **i**-*cis* and **i**-*trans* (20.8 mg, 0.051 mmol, 26%).

3a': R_f = 0.46 [3:1 Hexane/EtOAc]; yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.15-2.21 (m, 2H), 2.37-2.40 (m, 2H), 2.43-2.46 (m, 2H), 3.88 (s, 3H), 4.55 (s, 2H), 5.51 (s, 1H), 5.58 (s, 1H), 5.85 (s, 1H), 6.96 (d, 2H, J = 9.0 Hz), 7.21-2.26 (m, 5H), 7.74 (d, 2H, J = 9.0 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.7, 27.3, 29.0, 55.8, 56.5, 114.0, 119.5, 127.7, 127.8, 128.4, 129.0, 130.2, 130.6, 136.0, 136.8, 138.3, 144.8, 148.2, 163.0; IR (film) cm^{-1} 2920m, 2849m, 1693w, 1596m, 1497m, 1346s, 1259s, 1157s; mass spectrum (ESI): m/e (% relative intensity) 394 (100) $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{24}NO_3S$ $[M+H]^+$: 394.1472; found 394.1476.

i-*cis* and **i**-*trans*: R_f = 0.20 [3:1 Hexane/EtOAc]; cocorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) [special peaks of **i**-*cis* and **i**-*trans* mixture with 2.3:1 dr ratio] δ (*cis*) 1.12 (d, 7H, J = 7.0 Hz), 2.20-2.31 (m, 14H), 6.29 (q, 2.3H, J = 7.2 Hz), δ (*trans*) 1.36 (d, 3H, J = 7.0 Hz), 1.79-1.89 (m, 6H), 5.21 (q, 1H, J = 7.2 Hz); IR (film) cm^{-1} 2935brw, 1675m, 1596m, 1498m, 1338m, 1259s, 1154s; mass spectrum (ESI): m/e (% relative intensity) 429 (100) $(M+NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{23}H_{26}NO_4S$ $[M+H]^+$: 412.1578; found 412.1579.

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References

1. Li, H.; Hsung, R. P.; DeKorver, K. A.; Wei, Y. *Org. Lett.* **2010**, *12*, 3780–3783.