Intramolecular Oxyallyl–Carbonyl (3+2) Cycloadditions

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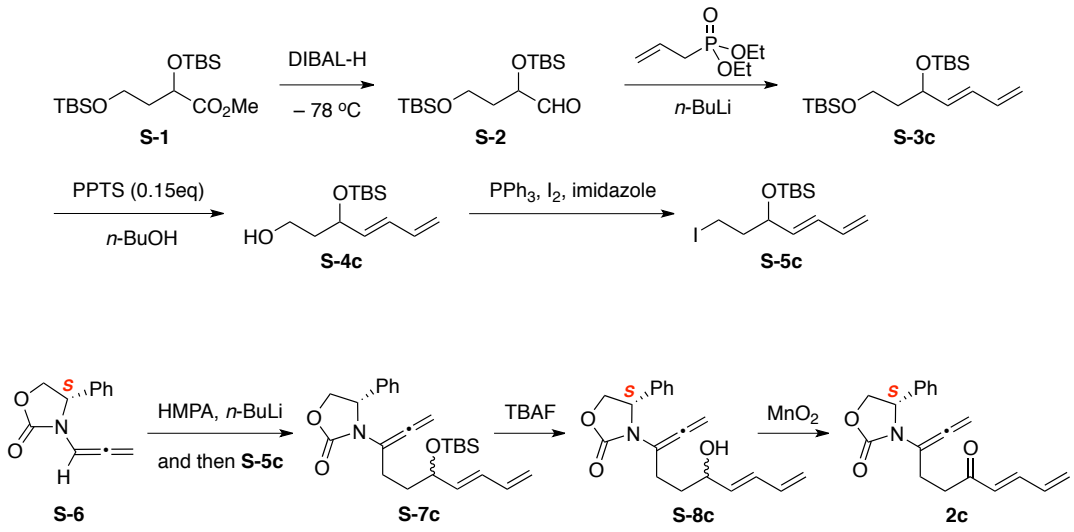
SUPPORTING INFORMATION

Part 1. Experimental Procedures and Compound Characterizations

GENERAL EXPERIMENTAL INFORMATION.

All reactions were performed in flame-dried glassware under nitrogen atmosphere. Solvents were distilled prior to use. Reagents were used as purchased from Aldrich, Acros, Alfa Aesar, or TCI unless otherwise noted. Chromatographic separations were performed using Silicycle 43-60 Å 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 and are uncorrected/calibrated. 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, *p*-anisoladehyde and phosphomolybdic acid stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LS/MSD and are APCI. All spectral data obtained for new compounds are reported here.

PROCEDURE FOR PREPARATION OF CYCLOADDITION PRECURSOR 2C.



Synthesis of Diene S-3c. To a solution of ester **S-1** (3.62 g, 10 mmol) in toluene (60 mL) at –78 °C was slowly added DIBAL-H (1.0 *M* in Hexane, 12.0 mL, 12 mmol). After all the starting material was consumed (monitored by TLC), the reaction was quenched by careful addition of sat. $NaHCO_3$ solution. The reaction mixture was allowed to warm to ambient temperature and diluted with methyl *t*-butyl ether. The aqueous phase was extracted with methyl t-butyl ether. The combined organic extracts were

washed with sat aq NaCl and dried over anhyd Na_2SO_4. After filtered and concentrated under reduced pressure, the crude **S-2** was obtained as colorless oil. This compound could be directly used in next step without further purification.

To a –78 ^oC solution of diethyl allylphosphonate (2.28 g, 12.0 mmol) in anhydrous THF (15 mL) was added HMPA (3.0 mL, 18 mmol) and *n*-butyllithium (5.00 mL, 12.5 mmol). After the solution was stirred for 40 min, a solution of the crude aldehyde **S-2** produced above in THF (5 mL) was added dropwise. The resulting solution was stirred for 2 h at –78 ^oC and then for an additional 10 h at rt before quenching with sat aq NH_4Cl solution. The mixture was extracted with ether 3 times. The combined organic phases were washed with sat aq NaCl, dried over anhyd Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography using EtOAc/hexanes as eluent to give the desired product in 65% yield over 2 steps.

S-3c: R_f = 0.71 (Hexanes:EtOAc = 10:1); ^1H NMR (300 MHz, $CDCl_3$) δ 0.04-0.08 (m, 12H), 0.91 (s, 18H), 1.61-1.82 (m, 2H), 3.60-3.76 (m, 2H), 4.35 (ddd, *J* = 6.3, 6.3, 6.3 Hz, 1H), 5.07-5.24 (m, 2H), 5.69 (dd, *J* = 15.3, 6.6 Hz, 1H), 6.15 (dd, *J* = 15.3, 10.5 Hz, 1H), 6.33 (ddd, *J* = 16.8, 10.2, 10.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.3, -4.9, -4.3, 18.3, 25.9, 26.0, 41.4, 59.4, 70.0, 116.5, 130.0, 136.7, 137.4; IR (neat) cm^{-1} 2956s, 2928s, 2856s, 1472m, 1256m; mass spectrum (APCI): m/e (% relative intensity) 357 (24) $(M+H)^+$, 246 (10), 180 (82), 135 (100); HRMS (EI, m/z) Calcd for $C_{19}H_{40}O_2Si_2Na$ $(M + Na)^+$: 379.2459, found: 379.2468.

Synthesis of Iodo-Diene S-5c. To a solution of diene **S-3c** (1.00 g, 2.81 mmol) in *n*-BuOH (60 ml) at rt was added PPTS (100.0 mg, 0.42 mmol). After 50 h, the reaction was quenched by addition of sat. $NaHCO_3$ solution. Then 100 mL ether was added. The aqueous solution was extracted with ether. The combined organic phases were washed with sat aq NaCl, dried over anhyd Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography using EtOAc/hexanes as eluent to give **S-4c** in 81% yield.

To a solution of PPh_3 (0.65 g, 2.5 mmol) in CH_2Cl_2 (10 mL) was added iodine (0.64 g, 2.5 mmol) at room temperature. After 30 min, 1H-imidazole (0.17 g, 2.5 mmol) was added to the reaction mixture. After another 5 min, **S-4c** obtained above was added to the reaction. The mixture was stirred for 2 h at room temperature before concentrated under reduced pressure and filtered through a short silica gel

column with hexanes as the eluent. The filtrate was concentrated under reduced pressure to give the pure iodo-diene **S-5c** in 86% yield.

S-5c: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.07 (s, 3H), 0.13 (s, 3H), 0.93 (s, 9H), 1.98-2.06 (m, 2H), 3.20-3.26 (m, 2H), 4.28 (m, 1H), 5.12 (d, *J* = 9.9 Hz, 1H), 5.24 (d, *J* = 15.6 Hz, 1H), 5.67 (dd, *J* = 15.3, 6.6 Hz, 1H), 6.16-6.40 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -4.3, -4.8, 2.6, 18.1, 25.8, 41.7, 72.8, 117.4, 130.8, 135.7, 136.2.

Synthesis of Allenamide S-7c. To a –78°C solution of allenamide **S-6** (0.55 g, 2.73 mmol) and HMPA (0.477 mL, 2.73 mmol) in anhydrous THF (10 mL) was added, dropwise, *n*-BuLi (1.6 mL, 2.2 *M* in Hexanes). After stirring for one hour for complete deprotonation, a solution of iodide **S-5c** (0.75 g, 2.23 mmol) in THF was added. The resulting solution was stirred at –78°C for 2 h. The cooled reaction mixture was quenched with H_2O, and the aqueous layer was extracted with methyl *t*-butyl ether. The combined organic layers were washed with sat aq NaCl, dried over anhyd Na_2SO_4, and concentrated under reduced pressure. The residue was purified by flash column chromatography using EtOAc/hexanes as eluent to give **S-7c** in 80% yield.

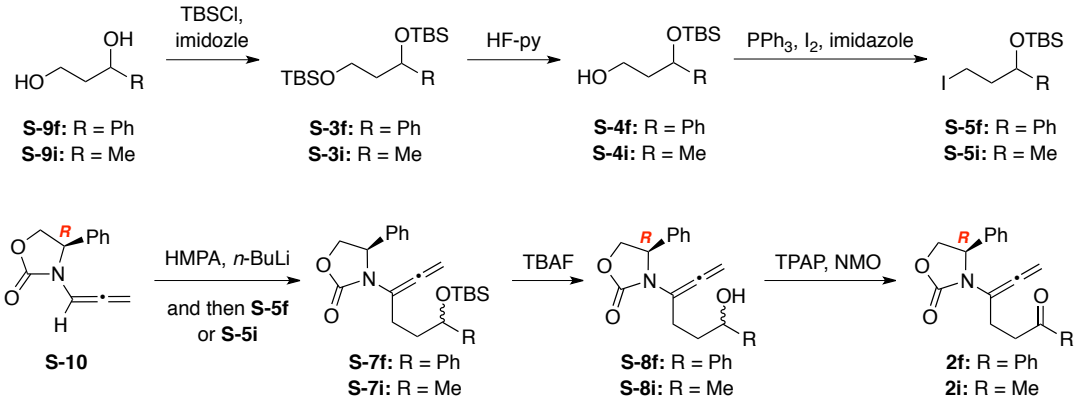
S-7c: *[a pair of diastereomers.]* R_f = 0.52 (Hexanes:EtOAc = 3:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ -0.03-0.03 (m, 6H), 0.87 (s, 9H), 1.46-1.60 (m, 2H), 2.30-2.52 (m, 2H), 4.09-4.17 (m, 2H), 4.60-4.65 (m, 1H), 4.89-4.98 (m, 2H), 4.99-5.07 (m, 2H), 5.16 (d, *J* = 16.5, 1H), 5.58 (ddd, *J* = 15.5, 6.0, 6.0 Hz, 1H), 6.03-6.13 (m, 1H), 6.29 (ddd, *J* = 17.0, 10.0, 10.0 Hz, 1H), 7.26-7.31 (m, 2H), 7.33-7.41 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ -5.04, -5.00, -4.54, -4.49, 18.0, 25.3, 25.7, 34.9, 35.1, 61.0, 69.7, 71.9, 72.2, 84.5, 108.7, 108.8, 116.6, 126.8, 126.9, 128.6, 128.7, 128.9, 130.0, 130.1, 136.5, 136.8, 136.9, 138.3, 155.9, 204.38, 204.42; IR (neat) cm^{-1} 2953s, 2929s, 2856s, 1761s; mass spectrum (APCI): m/e (% relative intensity) 426(16) $(M+H)^+$, 294 (100), 250 (22); HRMS (EI, m/z) Calcd for $C_{25}H_{35}NO_3SiNa$ $(M + Na)^+$: 448.2278, found: 448.2277.

Synthesis of Allenamide 2c. To a solution of allenamide **S-7c** in THF (0.1 *M*) at 0 ºC was added TBAF (1.0 *M* in THF, 2 equiv) dropwise. The reaction mixture was stirred at this temperature until completion (monitored by TLC). The reaction was quenched with sat aq $NaHCO_3$, extracted with Et_2O. The combined organic extracts were washed with sat aq NaCl and dried over anhyd Na_2SO_4. After filtered and concentrated under reduced pressure, the crude **S-8c** was used for next step without further purification.

To a solution of crude allenamide **S-8c** produced above in CH_2Cl_2 (0.1 *M*) at rt was added activated MnO_2 (5-8 equiv). The reaction mixture was stirred at this temperature until completion (monitored by TLC). The reaction mixture was filtered through Celite™, and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography using EtOAc/hexanes as eluent to give the desired allenamide **2c** in 76% yield over 2 steps.

2c: R_f = 0.44 (Hexanes:EtOAc = 1:1); $[\alpha]^{23}_D$ = 33.85 (c = 0.13, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.58-2.82 (m, 4H), 4.14 (dd, *J* = 8.5, 8.5 Hz, 1H), 4.64 (dd, *J* = 8.5, 8.5 Hz, 1H), 4.91-4.98 (m, 2H), 4.99-5.05 (m, 1H), 5.52 (d, *J* = 10.0 Hz, 1H), 5.64 (d, J = 16.0 Hz, 1H), 6.12 (d, *J* = 16.0, 1H), 6.42 (ddd, *J* = 10.0, 10.0, 17.0 Hz, 1H), 6.08 (dd, *J* = 11.0, 15.5 Hz, 1H), 7.26-7.31 (m, 2H), 7.33-7.41 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.0, 37.6, 61.0, 69.8, 85.1, 108.1, 126.3, 126.9, 128.7, 128.9, 129.9, 135.1, 138.2, 142.5, 156.0, 198.9, 204.2; IR (neat) cm^{-1} 2972m, 2911m, 1759s, 1398s; mass spectrum (APCI): m/e (% relative intensity) 310(100) $(M+H)^+$, 164 (80), 147 (97); HRMS (EI, m/z) Calcd for $C_{19}H_{19}NO_3Na$ $(M + Na)^+$: 332.1257, found: 332.1242.

PROCEDURE FOR PREPARATIONS OF CYCLOADDITION PRECURSORS 2F AND 2I.



To a solution of **S-9f** (or **S-9i**) in CH_2Cl_2 was added imidazole (2.5 equiv) and TBSCl (2.2 equiv). After stirred overnight, the reaction was quenched with water, extracted with ether. The organic layer was washed with sat aq NaCl, dried over anhyd $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography using Hexane:EA = 10:1 as the eluent to give **S-3f** (or **S-3i**) as colorless oil.

To a solution of **S-3f** (or **S-3i**) in THF was added a stock solution of HF•py (6.5 mL/mmol **S-3f/i**, prepared by addition of 1 mL HF•py in 4 mL pyridine, then diluted with 10 mL THF). The reaction was stirred at ambient temperature until completion (usually 12 h, monitored by TLC). Then the reaction was quenched with $NaHCO_3$ solution, and extracted with ether. The combined organic layers were washed with 1 *M* HCl, sat aq $NaHCO_3$, H_2O, and sat aq NaCl. After dried over anhyd $MgSO_4$ and concentrated under reduced pressure. The crude residue was purified by flash column chromatography using Hexane:EA = 5:1 as the eluent to give **S-4f** (or **S-4i**) as colorless oil.

To a solution of PPh_3 (1.1 equiv) in CH_2Cl_2 was added iodine (1.1 equiv) at rt. After 30 min, 1H-imidazole (1.1 equiv) was added to the reaction mixture. After another 5 min, **S-4f** (or **S-4i**) obtained above was added to the reaction. The mixture was stirred for 2 h at rt before concentrated under reduced pressure and filtered through a short silica gel column with hexanes as the eluent. The filtrate was concentrated under reduced pressure to give the pure iodo-diene **S-5f** (or **S-5i**) as colorless oil.

Allenamide Synthesis. To a –78°C solution of allenamide **S-10** (1 equiv) and HMPA (1 equiv) in anhyd THF was added, dropwise, *n*-BuLi (1.2 equiv). After stirring for one hour for complete deprotonation, a solution of iodide **S-5f** or **S-5i** (1.4 equiv) in THF was added. The resulting solution was stirred at –78°C for 2 h. The cooled reaction mixture was quenched with water, and extracted with ether. The combined organic layers were washed with sat aq NaCl, dried over anhyd Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography using EtOAc/hexanes as eluent to give pure **S-7f** (or **S-7i**).

S-7f: *[a pair of diastereomers]* R_f = 0.50 (Hexanes:EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ -0.20 (d, *J* = 5.6 Hz, 3H), 0.01 (d, *J* = 4.0 Hz, 3H), 0.86 (s, 9H), 1.65-1.75 (m, 2H), 2.30-2.41 (m, 1H), 2.42-2.52 (m, 1H), 4.07-4.15 (m, 2H), 4.57- 4.63 (m, 1H), 4.82-4.88 (m, 1H), 4.92-5.02 (m, 2H), 7.21-7.29 (m, 6H), 7.30-7.38 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.7, -4.3, 14.4, 14.5, 18.5, 26.2, 26.3, 38.1, 38.2, 61.3, 61.4, 70.2, 74.4, 74.7, 84.8, 109.0, 109.2, 126.2, 126.8, 127.2, 128.3, 129.0, 129.3, 138.8, 145.6, 156.3, 204.8, 204.9.

S-7i: *[a pair of diastereomers]* R_f = 0.52 (Hexanes:EtOAc = 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ -.03 (m, 6H), 0.87 (s, 9H), 1.09 (dd, *J* = 9.6, 6.0 Hz, 3H), 1.41-1.51 (m, 2H), 2.32-2.57 (m, 2H), 3.66-3.70

(m, 0.5H), 3.76-3.83 (m, 0.5H), 4.15 (m, 1H), 4.64 (td, *J* = 8.8, 2.0 Hz), 4.92-4.99 (m, 2H), 5.01-5.07 (m, 1H), 7.29-7.32 (m, 2H), 7.35-7.41 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -4.5, -4.1, 14.4, 14.5, 18.3, 23.9, 24.1, 26.2, 26.3, 36.8, 36.9, 61.4, 48.0, 68.2, 70.1, 84.8, 109.3, 109.5, 127.2, 127.3, 129.0, 129.1， 129.2, 138.8, 156.3, 204.7, 204.8.

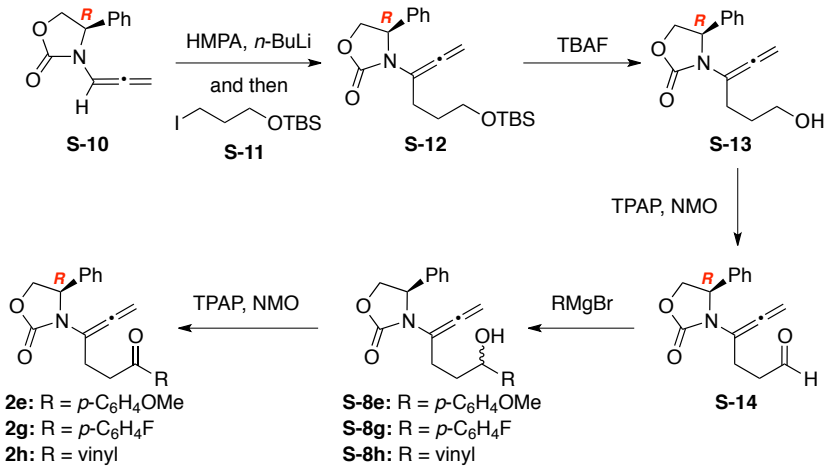
To a solution of allenamide **S-7f** (or **S-7i**) in THF at 0 ºC was added TBAF (2 equiv) dropwise. The reaction mixture was allowed to warm to rt and stirred until completion (12~24 h, monitored by TLC). The reaction was quenched with sat aq $NaHCO_3$, extracted with ether. The combined organic layers were washed with sat aq NaCl and dried over anhyd $MgSO_4$. After filtered and concentrated under reduced pressure, the crude product was purified by flash column chromatography using EtOAc/hexanes as eluent to give pure **S-8f** (or **S-8i**).

To a solution of **S-8f** (or **S-8i**) in CH_2Cl_2 with dried 4Å MS was added TPAP (0.1 equiv) and NMO (1.5 equiv). The reaction was stirred at room temperature for 2 h and then filtered through a pad of Celite™. After concentrated under reduced pressure, the crude product was purified by flash column chromatography using EtOAc/hexanes as eluent to give pure allenamide **2f** (or **2i**).

2f: R_f = 0.22 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -37.0 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80-2.92 (m, 2H), 3.03-3.08 (m, 2H), 4.15 (dd, *J* = 8.8, 7.2 Hz, 1H), 4.65 (t, *J* = 8.8 Hz, 1H), 4.92-5.04 (m, 3H), 7.28-7.38 (m, 5H), 7.41-7.45 (m, 2H), 7.54 (tt, *J* = 7.6, 1.6 Hz, 1H), 7.89 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.5, 36.2, 61.4, 70.2, 85.5, 108.6, 127.1, 128.2, 128.8, 129.1, 129.2, 133.2, 137.1, 138.6, 156.3, 198.8, 204.5; IR (neat) cm^{-1}, 1777s, 1721s, 1648s, 1557s, 1540s, 1520s; mass spectrum (APCI): m/e (% relative intensity) 334.2 (100) $(M+H)^+$.

2i: R_f = 0.45 (Hexanes:EtOAc = 1:1); $[\alpha]^{23}_D$ = -62.0 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.47-2.52 (m, 2H), 2.59-2.67 (m, 1H), 2.72-2.80 (m, 1H), 4.14 (dd, *J* = 8.8, 7.2 Hz, 1H), 4.65 (t, *J* = 8.8 Hz, 1H), 4.86-4.89 (m, 2H), 5.08-5.30 (m, 1H), 7.28-7.32 (m, 2H), 7.35-7.41 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.0, 30.0, 40.9, 61.4, 70.2, 85.5, 108.5, 127.1, 129.1, 129.2, 138.5, 156.3, 204.4, 207.4; IR (neat) cm^{-1},1771s, 1684s, 1648s, 1557s, 1540s, 1521s, 1396s, 727s; mass spectrum (APCI): m/e (% relative intensity) 272.2 (100) $(M+H)^+$.

PROCEDURE FOR PREPARATIONS OF CYCLOADDITION PRECURSORS 2E, 2G AND 2H.



To a –78°C solution of allenamide **S-10** (1 equiv) and HMPA (1 equiv) in anhyd THF was added *n*-BuLi (1.2 equiv) dropwise. After stirring for 1 h, a solution of iodide **S-11** (1.4 equiv) in THF was added. The resulting solution was stirred at –78°C for 2 h. The cooled reaction mixture was quenched with water, and extracted with ether. The combined organic layers were washed with sat aq NaCl, dried over anhyd Na_2SO_4, and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography using EtOAc/hexanes as eluent to give pure **S-12** in 80% yield.

To a solution of allenamide **S-12** in THF at 0°C was added TBAF (1.5 equiv) dropwise. The reaction mixture was allowed to warm to rt and stirred until completion (4~8 h, monitored by TLC). The reaction was quenched with sat aq $NaHCO_3$, extracted with EtOAc. The combined organic layers were washed with sat aq NaCl and dried over anhyd $MgSO_4$. After filtered and concentrated under reduced pressure, the crude product was purified by flash column chromatography using EtOAc/hexanes as eluent to give pure **S-13** in 63% yield.

To a 0°C solution of **S-13** (1 equiv) and NMO (1.5 equiv) in CH_2Cl_2 with dried 4Å MS was added TPAP (0.05 equiv). The reaction mixture was stirred at room temperature for 2 h and then filtered through a pad of Celite™. After concentrated under reduced pressure, the crude product was purified by flash column chromatography using EtOAc/hexanes as eluent to give pure allenamide **S-14** in 30% yield.

To a solution of **S-14** in THF was added 4-methoxyphenylmagnesium bromide (or 4-fluorophenylmagnesium bromide, or vinylmagnesium bromide) (1.5 equiv) at –78°C. The reaction mixture was stirred at –78°C for 1h and then at rt for 1h. The reaction was cooled to 0°C and quenched with sat aq $NaHCO_3$, extracted with EtOAc. The combined organic layers were washed with sat aq NaCl and dried over anhyd $MgSO_4$. After filtered and concentrated under reduced pressure, the crude product was purified by flash column chromatography using EtOAc/hexanes as eluent to give pure **S-8e** (or **S-8g, S-8h**).

To a 0°C solution of NMO (1.5 equiv) in CH_2Cl_2 with dried 4Å MS was added TPAP (0.1 equiv). Then a solution of **S-8e** (or **S-8g, S-8h**) (1 equiv) in CH_2Cl_2 was added dropwise into the mixture at 0°C. The reaction mixture was stirred at room temperature for 1 h and then filtered through a pad of Celite™. After concentrated under reduced pressure, the crude product was purified by flash column chromatography using EtOAc/hexanes as eluent to give pure allenamide **2e** (or **2g**, **2h**).

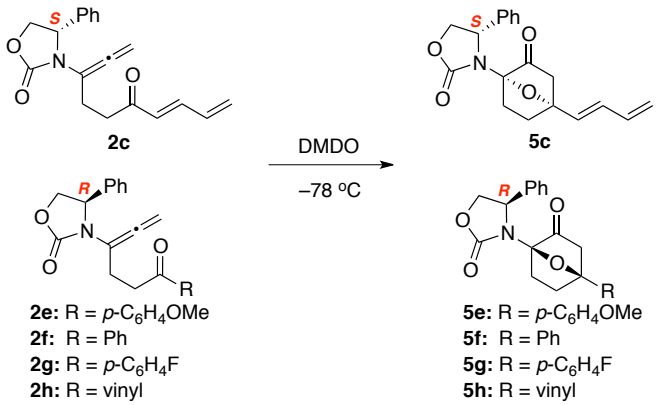
2e: R_f = 0.20 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -42.5 (c = 2.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80-2.88 (m, 2H), 2.96-3.06 (m, 2H), 3.86 (s, 3H), 4.15 (dd, *J* = 8.8, 7.2 Hz, 1H), 4.65 (t, *J* = 8.8 Hz, 1H), 4.92-5.02 (m, 3H), 6.90 (d, *J* = 7.2 Hz, 2H), 7.28-7.40 (m, 5H), 7.89 (d, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.7, 35.9, 55.7, 61.4, 70.2, 85.3, 108.6, 113.9, 127.1, 129.1, 129.2, 130.1, 130.5, 138.6, 156.3, 163.6, 197.4, 204.6; IR (neat) cm^{-1}, 3481w, 2929w, 2356s, 1750s, 1599s, 1359s, 1256s, 1210s, 1170s, 1028s, 700s; mass spectrum (APCI): m/e (% relative intensity) 364.2 (100) $(M+H)^+$.

2g: R_f = 0.25 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -41.3 (c = 1.0, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.80-2.95 (m, 2H), 2.98-3.08 (m, 2H), 4.15 (dd, *J* = 8.8, 7.6 Hz, 1H), 4.66 (t, *J* = 8.8 Hz, 1H), 4.94-5.02 (m, 3H), 7.20 (t, *J* = 8.8 Hz, 2H), 7.29-7.37 (m, 5H), 7.93 (dd, *J* = 9.2, 5.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.6, 36.2, 61.4, 70.2, 85.5, 108.6, 115.7, 116.0, 127.1, 129.1, 129.3, 130.8, 133.5, 138.5, 156.3, 164.6, 167.2, 197.2, 204.5; IR (neat) cm^{-1}, 3492w, 2922w, 1752s, 1709s, 1360s, 1221s, 1042s, 701s; mass spectrum (APCI): m/e (% relative intensity) 350.2 (100) $(M-H)^-$.

2h: R_f = 0.20 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -40.5 (c = 0.5, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.64-2.82 (m, 4H), 4.15 (dd, *J* = 8.8, 7.6 Hz, 1H), 4.65 (t, *J* = 8.8 Hz, 1H), 4.94-4.96 (m, 2H), 5.00-5.02 (m, 1H), 5.79 (dd, *J* = 10.4, 1.2 Hz, 1H), 6.17 (dd, *J* = 17.6, 1.2 Hz, 1H), 6.29 (dd, *J* = 17.6, 10.4 Hz,

1H), 7.28-7.31 (m, 2H), 7.34-7.40 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.1, 37.1, 61.4, 70.2, 85.5, 108.5, 127.1, 128.4, 129.1, 129.3, 136.5, 156.3, 199.3, 204.5; IR (neat) cm^{-1}, 3487w, 2362s, 1752s, 1707s, 1399, 1361s, 1222s, 1092s, 1042s, 702s; mass spectrum (APCI): m/e (% relative intensity) 284.2 (100) $(M+H)^+$.

PROCEDURES FOR INTRAMOLECULAR (3+2) CYCLOADDITIONS



Cycloaddition of 2c. To a –78 °C solution of allenamide **2c** in CH_2Cl_2 with dried 4Å MS, was added 3.0 equiv of DMDO in acetone as a chilled solution (–78 °C) via syringe pump over 2 h. The syringe pump is cooled by dry ice at all time during the addition. After the addition, the reaction mixture was stirred for 10 min before being filtered and concentrated under *in vacuo*. The crude residue was purified via silica gel column chromatography using EtOAc/hexanes as eluent to give the desired hetero-(3+2) cycloadduct **5c**.

Cycloadditions of 2e~h. To a –78 °C solution of allenamide **2e** (or **2f**, **2g**, **2h**) in 2.0 mL of CH_2Cl_2 with dried 4Å MS, was added 3.0 equiv of DMDO in acetone as a chilled solution (–78 °C) via cannula over 30 min. After the addition, the reaction mixture was stirred for 10 min ~ 3 h before being filtered and concentrated under reduced pressure. The crude residue was purified via silica gel column chromatography using EtOAc/hexanes as eluent to give the desired hetero-(3+2) cycloadduct **5e** (or **5f**, **5g**, **5h**).

5c: 85% yield; R_f = 0.50 (Hexanes:EtOAc = 1:1); $[\alpha]^{23}_D$ = 138.18 (c = 0.11, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.35-1.43 (m,1H), 1.70-1.77 (m, 1H), 1.86-1.94 (m, 1H), 2.02-2.10 (m, 1H), 2.32 (d, *J* = 17.0 Hz, 1H), 2.61-2.67 (m, 1H), 4.11-4.17 (m, 1H), 4.72 (dd, *J* = 7.5, 7.5 Hz, 1H), 5.16-5.21 (m, 2H), 5.26-5.31 (m, 1H), 4.91 (d, J = 15.5 Hz, 1H), 6.24-6.38 (m, 2H), 7.28-7.48 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.0, 33.6, 48.5, 59.0, 71.3, 80.6, 94.8, 119.6, 126.7, 129.2, 129.5, 130.5, 132.8, 136.0, 139.6, 156.9, 206.0; IR (neat) cm^{-1} 2975m, 1780s, 1763s, 1406s; mass spectrum (EI, m/z) (% relative intensity) 348.1(100) $(M+Na)^+$; HRMS (EI, m/z) Calcd for $C_{19}H_{19}NO_4Na$ $(M + Na)^+$: 348.1206, found: 348.1208.

5e: 82% yield; R_f = 0.20 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -92.8 (c = 0.5, CH_2Cl_2); mp 163℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48-1.53 (m, 1H), 2.00-2.05 (m, 2H), 2.22-2.30 (m, 1H), 2.52 (d, J_{ab} = 17.2 Hz, 1H), 2.65 (d, J_{ab} = 17.2 Hz, 1H), 3.80 (s, 3H), 4.18 (dd, *J* = 8.8, 6.4 Hz, 1H), 4.74 (t, *J* = 8.8 Hz, 1H), 5.24 (dd, *J* = 9.2, 6.4 Hz, 1H), 6.86-6.92 (d, *J* = 8.8 Hz, 2H), 7.20-7.24 (m, 2H), 7.34-7.48 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.0, 35.1, 50.6, 55.5, 59.0, 71.2, 82.0, 95.1, 114.1, 126.4, 126.9, 129.1, 129.4, 130.3, 132.2, 139.7, 159.6, 206.4; IR (neat) cm^{-1} 3510w, 2928w, 1757s, 1518s, 1402s, 1250s, 1038s, 833s, 702s; mass spectrum (APCI): m/e (% relative intensity) 378.2 (100) $(M-H)^-$.

5f: 84% yield; R_f = 0.20 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -110.8 (c = 1.0, CH_2Cl_2); mp 165-166 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48-1.55 (m, 1H), 1.98-2.12 (m, 2H), 2.28 (td, *J* = 12.8, 5.6 Hz, 1H), 2.55 (d, J_{ab} = 17.2 Hz, 1H), 2.66 (dd, J_{ab} = 17.2 Hz, *J* = 2.8 Hz, 1H), 4.18 (dd, *J* = 8.8, 6.4 Hz, 1H), 4.75 (t, *J* = 8.8 Hz, 1H), 5.24 (dd, *J* = 8.8, 6.4 Hz, 1H), 7.28-7.48 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 35.1, 50.5, 59.0, 71.2, 82.1, 95.1, 125.0, 126.9, 128.3, 128.8, 129.2, 129.5, 139.7, 140.2, 157.0, 206.2; IR (neat) cm^{-1} 2570w, 1723s, 1648s, 1557s, 1507s; mass spectrum (APCI): m/e (% relative intensity) 348.1 (100) $(M-H)^-$.

5g: 70% yield; R_f = 0.30 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -100.9 (c = 1.0, CH_2Cl_2); mp 182℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.48-1.55 (m, 1H), 1.97-2.08 (m, 2H), 2.30 (td, *J* = 12.8, 4.8 Hz, 1H), 2.54 (d, J_{ab} = 17.2 Hz, 1H), 2.62 (dd, J_{ab} = 17.2 Hz, *J* = 2.4 Hz, 1H), 4.19 (dd, *J* = 8.8, 6.4 Hz, 1H), 4.75 (t, *J* = 8.8 Hz, 1H), 5.24 (dd, *J* = 8.8, 6.4 Hz, 1H), 7.03 (t, *J* = 8.8 Hz, 2H), 7.25-7.28 (m, 2H), 7.34-7.48 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 35.2, 50.6, 59.0, 71.2, 81.7, 95.2, 115.6, 115.8, 126.8, 126.9, 129.2,

129.5, 136.1, 139.5, 156.9, 161.4, 163.8, 205.9; IR (neat) cm^{-1} 3418w, 2923w, 1750s, 1707s, 1362s, 1223s, 1023s, 833s, 700s; mass spectrum (APCI): m/e (% relative intensity) 366.2 (100) $(M-H)^-$.

5h: 64% yield; R_f = 0.20 (Hexanes:EtOAc = 2:1); $[\alpha]^{23}_D$ = -88.8 (c = 0.5, CH_2Cl_2); mp 156℃; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34-1.40 (m, 1H), 1.68-1.75 (m, 1H), 1.84-1.93 (m, 1H), 2.02-2.10 (m, 1H), 2.29 (d, J_{ab} = 17.2 Hz, 1H), 2.62 (d, J_{ab} = 17.2 Hz, J = 2.8 Hz, 1H), 4.14 (dd, J = 8.8, 6.4 Hz, 1H), 4.71 (t, J = 8.8 Hz, 1H), 5.18 (dd, J = 8.8, 6.4 Hz, 1H), 5.28 (dd, J = 5.6, 0.8 Hz, 1H), 5.31 (dd, J = 12.8, 0.8 Hz, 1H), 6.10 (dd, J = 17.2, 10.8 Hz, 1H), 7.33-7.46 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 28.9, 33.3, 48.1, 58.9, 71.3, 81.0, 94.8, 117.3, 126.6, 129.1, 129.5, 135.8, 139.6, 156.6, 206.1; IR (neat) cm^{-1} 3426w, 1703s, 1412s, 1364s, 1228s; mass spectrum (APCI): m/e (% relative intensity) 298.2 (100) $(M-H)^-$.