Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Lewis Acid-Promoted [2 + 2] Cycloadditions of Alkenes with Arylketenes

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SUPPORTING INFORMATION

General. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at room temperature using a Varian I400 (^{1}H-NMR at 400MHz and ^{13}C-NMR at 100 MHz), Varian VXR400 (^{1}H-NMR at 400 MHz and ^{13}C-NMR at 100 MHz), and Varian I500 (^{1}HNMR at 500 MHz and ^{13}C-NMR at 125 MHz). Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (^{1}H NMR $CDCl_3$: δ 7.26 ppm ^{13}C NMR $CDCl_3$: δ 77.2 ppm). Data are reported as follows: chemical shift, integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), and coupling constants (Hz). Infrared spectra (IR) were obtained on an Avatar 360-FT IR E.S.P. on a NaCl salt plate and recorded in wavenumbers (cm^{-1}). Melting points were obtained on a Thomas Hoover capillary melting point apparatus without correction. High Resolution Mass (HRMS) analysis was obtained using Electron Impact Ionization (EI) or Chemical Ionization (CI) and reported as m/z (relative intensity) for the $[M]^+$ or $[M+H]^+$ molecular ion. GC-MS data was acquired using an Agilent 6890N Gas Chromatograph and 5973 Inert Mass Selective Detector.

Unless otherwise noted, all reactions have been carried out with distilled and degassed solvents under an atmosphere of dry N_2 in oven- (135 °C) and flame-dried glassware with standard vacuum-line techniques. Dichloromethane and tetrahydrofuran were purified under a positive pressure of dry argon by passage through two columns of activated alumina columns. Toluene was purified under a positive pressure of dry argon by passage through columns of activated alumina and Q5 (Grubbs apparatus). All work-up and purification procedures were carried out with reagent grade solvents (purchased from Sigma-Aldrich) in air. Standard column chromatography techniques using ZEOprep 60/40-63 μm silica gel were used for purification.

■ Reagents:

Allyltrimethylsilane was purchased from Alfa Aesar and was used as received.
Bis(dimethylphenylsilyl)zinc was prepared according to the literature.[1]
But-3-en-2-yldimethyl(phenyl)silane was prepared according to the literature.[2]
2-Bromophenylacetic acid was purchased from Oakwood Chemical and was used as received.
2-Butanol(anhydrous) was purchased from Alfa Aesar and was used as received.
Chlorodimethyl(phenyl)silane was purchased from Alfa Aesar and was used as received.
Cyclohexene was purchased from Sigma-Aldrich and was used as received.
Cyclohexa-1,3-diene was purchased from Sigma-Aldrich and was used as received.
Cyclooctene was purchased from Sigma-Aldrich and was used as received.
Cyclopentene was purchased from Alfa Aesar and was distilled for purification before use.
(Dimethyl(phenyl)silyl)lithium was prepared according to the literature.[3]
Ethylaluminum dichloride (1 M in hexanes) was purchased from Sigma-Aldrich and was used as received.
Hydrogen peroxide was purchased from Macron Fine Chemicals and was used as received.
Hex-1-ene was purchased from TCI and was used as received.
Iodomethane was purchased from Sigma-Aldrich and was used as received.
Lithium rod (packed in mineral oil) was purchased from Strem Chemicals and was used as received.
4-Methoxyphenylacetic acid was purchased from Alfa Aesar and was used as received.
2-Methylbut-2-ene was purchased from Alfa Aesar and was used as received.
***N,N*-Diisopropylethylamine** was purchased from Sigma-Aldrich and distilled over CaH_2 prior to use.
***N,N*-Dimethylformamide (anhydrous)** was purchased from Sigma-Aldrich and was used as received.
Oxalyl chloride was purchased from Alfa Aesar and was used as received.
Phenylacetyl chloride was purchased from Sigma-Aldrich and was distilled for purification before use.
Potassium bis(trimethylsilyl)amide was purchased from Strem Chemicals and was used as received.
1,10-Phenanthroline was purchased from Sigma-Aldrich and was used as received.
Sodium hydroxide was purchased from Macron Fine Chemicals and was used as received.
Triethylamine was purchased from EMD and distilled over CaH_2 before use.
Trimethylaluminum (2 M in toluene) was purchased from Sigma-Aldrich and was used as received.
1,3,5-Trimethoxybenzene was purchased from Sigma-Aldrich and was used as received.

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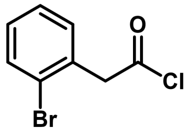
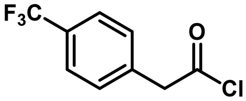
[1] Oestreich, M.; Auer, G. *Adv. Synth. Catal.* **2005**, *347*, 637.
[2] Vyas, D. J.; Oestreich, M. *Chem. Commun.* **2010**, *46*, 568.
[3] Naito, S.; Escobar M.; Kym P. R.; Liras S.; Martin S. F. *J. Org. Chem.* **2002**, *67*, 4200.

4-(Trifluoromethyl)phenylacetic acid was purchased from Matrix Scientific and was used as received.
***tert*-Butyllithium** was purchased from Sigma-Aldrich and was used as received.

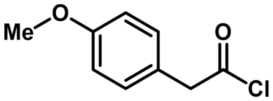
■ Synthesis of acid chlorides



2-bromophenylacetyl chloride (19): 2-bromophenylacetic acid (4.3 g, 1.0 equiv, 20 mmol) and thionyl chloride (2.2 mL, 1.5 equiv, 30 mmol) were added to a 25 mL flame-dried round bottom flask. The solution was heated to reflux at 80 °C for 1.5 h and the thionyl chloride was then removed under reduced pressure. The crude product was purified via Kugelrohr distillation (180 °C, 0.1 torr) to provide the pure acid chloride as a clear yellow liquid (yields typically ranged from 75-90%).

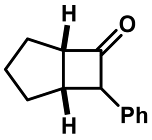


2-(4-(trifluoromethyl)phenyl)acetyl chloride: 2-(4-(trifluoromethyl)phenyl)acetic acid (2.0 g, 1.0 equiv, 10 mmol), dichloromethane (10 mL) and *N,N*-dimethylformamide (2-3 drops, cat.) were added to a 25 mL flame-dried round bottom flask. Oxalyl chloride (1.3 mL, 1.7 equiv, 17 mmol) was then added portion wise over 10 minutes (~0.1 mL/min). The reaction was allowed to stir at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure and the crude product was purified by Kugelrohor distillation (115 °C, 0.1 torr) to provide the pure acid chloride as a clear yellow liquid (yields typically ranged from 70-80%).

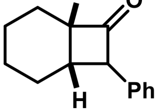


2-(4-methoxyphenyl)acetyl chloride: 2-(4-methoxyphenyl)acetic acid (1.7 g, 1.0 equiv, 10 mmol), dichloromethane (10 mL) and *N,N*-dimethylformamide (2-3 drops, cat.) were added to a 25 mL flame-dried round bottom flask. Oxalyl chloride (1.3 mL, 1.7 equiv, 17 mmol) was then added portionwise over 10 minutes (~0.1 mL/min). The reaction was allowed to stir at room temperature for 1 hour. The reaction mixture was concentrated under reduced pressure and the crude product was purified by Kugelrohor distillation (120 °C, 0.1 torr) to provide the pure acid chloride as a clear yellow liquid (yields typically ranged from 70-80%).

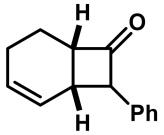
■ Lewis acid-promoted ketene-alkene [2+2] cycloadditions (reactions were performed on 2.0 mmol scale):



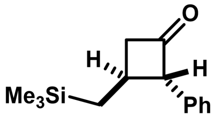
7-phenylbicyclo[3.2.0]heptan-6-one (8): To a flame-dried 25 mL round-bottom flask was added cyclopentene (3.5 mL, 20 equiv, 40 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed into a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (0.26 mL, 1.0 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added dropwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and stirred for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified via Kugelrohr distillation (140 °C, 0.1 torr) to provide the pure cyclobutanone as a clear liquid (0.32 g, 1.7 mmol, 87% yield, 2:1 dr, dr determined by analysis of the pure ^{1}H NMR, major diastereomer not confirmed). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3060, 3026, 2952, 2857, 1770, 1695, 1601, 1496, 1448, 1385, 1069, 699 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.34 - 7.17 (m, 5H major diastereomer; 5H minor diatereomer), 4.67 (dd, *J* = 10.5, 2.9 Hz, 1H major diastereomer), 3.84 (dd, *J* = 5.2, 3.4 Hz, 1H minor diastereomer), 3.69 - 3.60 (m, 1H major diastereomer; 1H minor diastereomer), 3.28 (qd, *J* = 7.3, 3.5 Hz, 1H major diastereomer), 3.04 (q, *J* = 6.5 Hz, 1H minor diastereomer), 2.18 - 1.50 (m, 5H major diastereomer; 6H minor diastereomer), 1.31 (dddd, *J* = 17.3, 10.3, 7.6, 4.6 Hz, 1H major diastereomer); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 214.5, 213.0, 136.9, 134.4, 128.7, 128.4, 127.6, 126.9, 126.8, 126.8, 68.6, 64.4, 62.9, 62.8, 37.7, 36.4, 33.2, 29.6, 29.5, 27.3, 26.1, 25.3; **HRMS (EI):** Calcd for $C_{13}H_{14}O$ (M^+): 186.1039, Found: 186.1041.



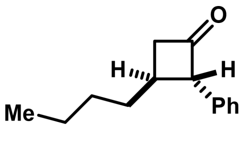
8-phenylbicyclo[4.2.0]octan-7-one (9): To a flame-dried 25 mL round-bottom flask was added cyclohexene (4.0 mL, 20 equiv, 40 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (0.26 mL, 1 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (5% Et_2O/hexanes) to provide the pure cyclobutanone as a clear liquid (0.32 g, 1.6 mmol, 79% yield and 1:1 dr, dr determined by analysis of the pure ^{1}H NMR). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3059, 3026, 2930, 2854, 1772, 1601, 1496, 1448, 698 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.39 - 7.18 (m, 10H), 4.60 (dd, *J* = 9.3, 1.9 Hz, 1H), 4.32 (dd, *J* = 7.4, 2.2 Hz, 1H), 3.35 (t, *J* = 8.6 Hz, 1H), 3.26 (tdd, *J* = 9.1, 7.5, 2.3 Hz, 1H), 2.82 (dtd, *J* = 10.9, 9.4, 7.4 Hz, 1H), 2.68 (dtd, *J* = 9.2, 7.1, 4.8 Hz, 1H), 2.10 (ddd, *J* = 14.7, 4.4, 2.2 Hz, 1H), 1.99 (m, 1H), 1.88 – 1.64 (m, 4H), 1.63 - 1.48 (m, 5H), 1.48 - 1.30 (m, 2H), 1.09 (m, 2H), 0.81 (dddd, *J* = 16.2, 13.9, 11.1, 3.4 Hz, 1H); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 209.0, 207.8, 136.6, 135.1, 128.6, 128.2, 128.1, 126.9, 126.8, 126.7, 66.3, 64.1, 53.9, 53.8, 30.3, 28.1, 26.3, 26.0, 22.6, 22.5, 22.4, 22.0, 21.4, 20.9.; **HRMS (EI):** Calcd for $C_{14}H_{16}O$ (M^+): 200.1196, Found: 200.1201



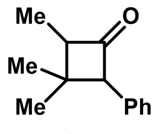
8-phenylbicyclo[4.2.0]oct-2-en-7-one (10): To a flame-dried 25 mL round-bottom flask was added cyclohexa-1,3-diene (0.19 mL, 2.0 equiv, 2.0 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (0.26 mL, 1.0 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (5% Et_2O/hexanes) to provide the cyclobutanone as a clear liquid (0.26 g, 1.3 mmol, 66% yield and 1:1 dr, dr determined by analysis of the pure ^{1}H NMR). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3024, 2918, 1770, 1495, 1448, 1274, 1039, 696 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.32 - 7.05 (m, 10H), 6.05 (ddt, *J* = 10.1, 4.0, 1.9 Hz, 1H), 5.91 (dtd, *J* = 10.0, 4.3, 1.2 Hz, 1H), 5.86 - 5.76 (m, 1H), 5.36 (ddd, *J* = 10.6, 4.1, 2.3 Hz, 1H), 4.60 (dd, *J* = 10.0, 2.0 Hz, 1H), 4.08 (dd, *J* = 6.1, 2.8 Hz, 1H), 3.63 (ddd, *J* = 9.2, 4.4, 2.1 Hz, 1H), 3.58 - 3.45 (m, 1H), 3.35 - 3.17 (m, 1H), 3.00 (dddt, *J* = 9.2, 4.3, 2.9, 1.5 Hz, 1H), 2.15 - 1.82 (m, 6H), 1.72 (dddd, *J* = 13.4, 8.2, 6.9, 5.0 Hz, 1H), 1.61 - 1.45 (m, 1H); **^{13}C NMR (100 MHz, CDCl$_3$):** δ 210.7, 209.7, 136.5, 134.3, 130.2, 128.8, 128.8, 128.7, 128.1, 128.1, 127.0, 127.0, 126.8, 126.1, 70.5, 65.0, 55.4, 54.9, 31.3, 30.1, 21.5, 21.4, 20.3, 18.4; **HRMS (EI):** Calcd for $C_{14}H_{14}O$ (M^+): 198.1039, Found: 198.1045.



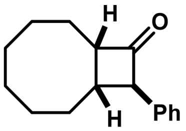
***(2S,3S)*-2-phenyl-3-((trimethylsilyl)methyl)cyclobutan-1-one (11):** To a flame-dried 25 mL round-bottom flask was added allyltrimethylsilane (0.64 mL, 2.0 equiv, 2.0 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (0.26 mL, 1.0 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified via Kugelrohr distillation (120 °C, 0.1 torr) to provide the pure cyclobutanone as a clear liquid (0.30 g, 1.3 mmol, 65% yield, 9:1 dr, major diastereomer shown above, dr determined by analysis of the pure ^{1}H NMR). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3061, 3029, 2952, 2894, 1779, 1601, 1496, 1451, 1404, 1248, 1112, 1073, 861, 839, 745, 697 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.40 - 7.20 (m, 5H major diastereomer, 5H minor diastereomer), 4.73 (dt, *J* = 10.0, 2.5 Hz, 1H minor diastereomer), 4.05 (dd, *J* = 8.0, 2.4 Hz, 1H major diastereomer), 3.41 (ddd, *J* = 17.3, 9.2, 2.9 Hz, 1H minor diastereomer), 3.17 (ddd, *J* = 17.0, 8.5, 2.2 Hz, 1H major diastereomer), 2.83 (ddd, *J* = 17.1, 8.3, 2.4 Hz, 1H major diastereomer), 2.62 (dqd, *J* = 10.5, 8.3, 4.7 Hz, 1H major diastereomer), 1.34 (dd, *J* = 14.5, 4.7 Hz, 1H major diastereomer), 1.04 (dd, *J* = 14.6, 10.3 Hz, 1H major diastereomer), 0.05 (s, 9H major diastereomer); **^{13}C NMR (100 MHz, CDCl$_3$):** δ 208.0, 137.3, 129.9, 128.4, 128.3, 74.7, 53.5, 31.0, 26.5, 0.0; **HRMS (EI):** Calcd for $C_{14}H_{20}OSi$ (M^+): 232.1278, Found: 232.1276.



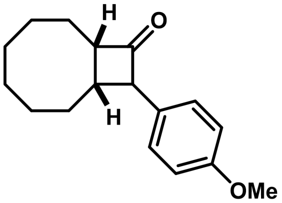
***(2S,3S)*-3-butyl-2-phenylcyclobutan-1-one (12):** To a flame-dried 25 mL round-bottom flask was added hex-1-ene (5.0 mL, 20 equiv, 40 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\ (S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (0.26 mL, 1.0 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\ (S)}$ / MeCN) bath and allowed to stir for 3 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified via Kugelrohr distillation (120 °C, 0.1 torr) to provide the pure cyclobutanone as a clear liquid (0.34 g, 1.7 mmol, 85% yield, 8:1 dr, major diastereomer shown above, ~10% of regioisomer detected by GC/MS, dr determined by analysis of the pure ^1H NMR). Due to isomerization during purification, the dr varied from 14:1 to 8:1 from crude reaction mixture to purified product. The dr also varied from 17:1 to 8:1 between experiments. Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3061, 3028, 2957, 2926, 2854, 1779, 1602, 1496, 1451, 1079, 743, 697 cm^{-1}; **^1H NMR (400 MHz, $CDCl_3$):** δ 7.36 – 7.14 (m, 5H major diastereomer; 5H minor diastereomer), 5.00 (d, J = 7.6 Hz, 1H regioisomer), 4.65 (dt, J = 10.1, 2.4 Hz, 1H minor diastereomer), 4.26 (t, J = 2.2 Hz, 1H regioisomer), 4.02 (dt, J = 8.0, 2.5 Hz, 1H major diastereomer), 3.28 (ddd, J = 17.3, 9.0, 2.7 Hz, 1H minor diastereomer), 3.10 (ddd, J = 17.3, 8.6, 2.4 Hz, 1H major diastereomer), 2.79 (ddd, J = 17.3, 8.0, 2.5 Hz, 1H major diastereomer), 2.53 (pd, J = 8.1, 6.5 Hz, 1H major diastereomer), 1.86 (dq, J = 14.0, 7.5, 7.0 Hz, 1H major diastereomer), 1.71 (tt, J = 13.8, 6.9 Hz, 1H major diastereomer), 1.44 – 1.28 (m, 4H major diastereomer), 1.01 (t, J = 7.4 Hz, 1H minor diastereomer), 0.97 – 0.82 (m, 3H major diastereomer), 0.78 (t, J = 7.0 Hz, 1H minor diastereomer), 0.66 (t, J = 7.4 Hz, 1H minor diastereomer); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 206.7, 136.3, 128.6, 127.1, 127.0, 70.1, 50.1, 36.4, 32.7, 30.4, 22.6, 14.0; **HRMS (EI):** Calcd for $C_{14}H_{18}O$ (M^+): 202.1352, Found: 202.1349.



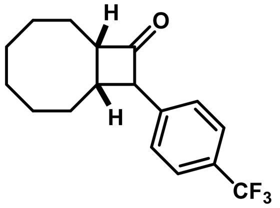
2,3,3-trimethyl-4-phenylcyclobutan-1-one (13): To a flame-dried 25 mL round-bottom flask was added 2-methylbut-2-ene (4.2 mL, 20 equiv, 40 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\ (S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (0.26 mL, 1.0 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified via Kugelrohr distillation (120 °C, 0.1 torr) to provide the pure cyclobutanone as a clear liquid (0.25 g, 1.3 mmol, 66% yield, 2:1 dr, dr determined by analysis of the pure ^{1}H NMR, major diastereomer not confirmed). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3061, 3027, 2960, 2868, 1773, 1602, 1496, 1451, 1372, 704, 699 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 7.35 - 7.05 (m, 5H major diastereomer; 5H minor diastereomer), 4.23 (d, J = 2.4 Hz, 1H major diastereomer), 4.18 (d, J = 2.2 Hz, 1H minor diastereomer), 3.14 - 3.05 (m, 1H major diastereomer), 2.93 – 2.84 (m, 1H minor diastereomer), 1.52 (d, J = 1.4 Hz, 3H major diastereomer), 1.33 (d, J = 1.5 Hz, 3H minor diastereomer), 1.19 (dd, J = 7.5, 1.4 Hz, 3H minor diastereomer), 1.04 (dd, J = 7.1, 1.4 Hz, 3H major diastereomer), 0.90 (d, J = 1.4 Hz, 3H minor diastereomer), 0.68 (d, J = 1.5 Hz, 3H major diastereomer); **^{13}C NMR (100 MHz, $CDCl_3$):** δ 212.6, 208.4, 135.3, 135.3, 134.2, 128.4, 128.3, 127.9, 127.0, 126.9, 71.3, 70.4, 61.88, 60.6, 35.3, 34.9, 29.7, 25.4, 23.9, 19.0, 10.2, 7.2; **HRMS (EI):** Calcd for $C_{13}H_{16}O$ (M^+): 188.1196, Found: 188.1198.



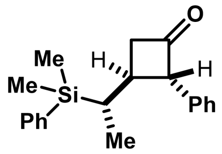
(1R,8S,10R)-10-phenylbicyclo[6.2.0]decan-9-one (14): To a flame-dried 25 mL round-bottom flask was added *cis*-cyclooctene (5.2 mL, 20 equiv, 40 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (0.26 mL, 1.0 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified via Kugelrohr distillation (179 °C, 0.1 torr) to provide the pure cyclobutanone as a clear liquid (0.43 g, 1.9 mmol, 94% yield and 5:1 dr, dr determined by analysis of the pure ^{1}H NMR, major diastereomer shown above). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3060, 3027, 2921, 2851, 1773, 1602, 1496, 1446, 1120, 697 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.36 – 7.10 (m, 5H major diastereomer; 5H minor diastereomer), 4.72 (dd, *J* = 10.9, 2.5 Hz, 1H minor diastereomer), 3.97 (dd, *J* = 7.9, 2.6 Hz, 1H major diastereomer), 3.28 (ddt, *J* = 12.4, 9.8, 2.6 Hz, 1H minor diastereomer), 3.17 (ddt, *J* = 11.9, 9.5, 2.4 Hz, 1H major diastereomer), 2.80 (qd, *J* = 10.6, 2.5 Hz, 1H minor diastereomer), 2.55 (dddd, *J* = 11.9, 9.9, 7.9, 2.4 Hz, 1H major diastereomer), 2.05 – 1.11 (m, 12H major diastereomer; 12H minor diastereomer); **^{13}C NMR (100 MHz, CDCl$_3$):** δ 212.1, 210.8, 136.6, 134.0, 129.4, 129.0, 128.7, 128.4, 127.0, 126.9, 691, 66.1, 61.4, 60.2, 37.8, 36.6, 30.5, 29.8, 29.4, 28.2, 27.7, 26.1, 25.9, 25.8, 25.6, 25.2, 24.0, 20.6; **HRMS (EI):** Calcd for C$_{16}$H$_{20}$O (M^{+}): 228.1509, Found: 228.1511.



10-(4-methoxyphenyl)bicyclo[6.2.0]decan-9-one (15): To a flame-dried 25 mL round-bottom flask was added with *cis*-cyclooctene (5.2 mL, 20 equiv, 40 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C (CO$_{2\,(S)}$ / acetone) bath. A solution of Me$_3$Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of 2-(4-methoxyphenyl)acetyl chloride (0.31 mL, 1.0 equiv, 2.0 mmol) in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C (CO$_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et$_3$N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL) and washed with saturated NaHCO$_3$ (1 x 10 mL). The combined organic layers were dried over MgSO$_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (5% Et$_2$O/hexanes) to provide the pure cyclobutanone as a clear yellow liquid (0.34 g, 1.3 mmol, 66% yield and 4:1 dr, dr determined by analysis of the pure ^{1}H NMR, major diastereomer not confirmed). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 2922, 2850, 2359, 1770, 1610, 1513, 1463, 1248, 1177, 1033, 830 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.15 – 6.80 (m, 4H major diastereomer; 4H minor diastereomer), 4.67 (dd, *J* = 10.8, 2.6 Hz, 1H minor diastereomer), 3.90 (dd, *J* = 8.0, 2.6 Hz, 1H major diastereomer), 3.76 (s, 3H major diastereomer; 3H minor diastereomer), 3.25 (ddt, *J* = 12.4, 9.8, 2.6 Hz, 1H minor diastereomer), 3.14 (ddt, *J* = 12.0, 9.5, 2.4 Hz, 1H major diastereomer), 2.75 (q, *J* = 10.6 Hz, 1H minor diastereomer), 2.47 (tdd, *J* = 9.4, 7.9, 2.4 Hz, 1H major diastereomer), 2.06 - 1.06 (m, 12H major diastereomer; 12H minor diastereomer); **^{13}C NMR (100 MHz, CDCl$_3$):** δ 212.8, 211.3, 158.5, 131.2, 130.1, 128.7, 128.0, 126.0, 114.1, 113.7, 68.4, 65.6, 61.3, 60.1, 55.3, 55.2, 38.1, 36.6, 30.5, 29.8, 29.4, 28.1, 27.7, 26.0, 25.9, 25.8, 25.6, 25.2, 24.0, 20.5; **HRMS (EI):** Calcd for $C_{17}H_{22}O_2$ (M$^+$): 258.1614, Found: 258.1611.

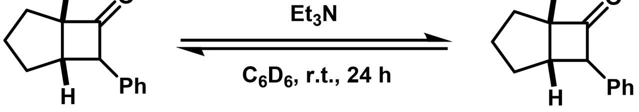


10-(4-(trifluoromethyl)phenyl)bicyclo[6.2.0]decan-9-one (16): To a flame-dried 25 mL round-bottom flask was added with *cis*-cyclooctene (5.2 mL, 20 equiv, 40 mmol) and dry dichloromethane (3.0 mL). *N,N*-diisopropylethylamine (0.38 mL, 1.1 equiv, 2.2 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 2.5 mL, 2.5 equiv, 5.0 mmol) was added in one portion down the walls of the flask. A solution of 2-(4-(trifluoromethyl)phenyl)acetyl (0.45 g, 1.0 equiv, 2.0 mmol) chloride in dichloromethane (1.0 mL) was then added portionwise to the flask over a period of 15 minutes (~0.2 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The reaction mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~20 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified via Kugelrohr distillation (140 °C, 0.1 torr) to provide the pure cyclobutanone as a white solid (0.30 g, 1.0 mmol, 51% yield and 4:1 dr, dr determined by analysis of the pure ^{1}H NMR, major diastereomer not confirmed). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 2922, 2853, 1773, 1618, 1463, 1445, 1412, 1322, 1162, 1119, 1064, 1017, 776 cm^{-1}; **^{1}H NMR (400 MHz, CDCl$_3$):** δ 7.60 – 7.20 (m, 4H major diastereomer; 4H minor diastereomer), 4.74 (dd, *J* = 10.9, 2.3 Hz, 1H minor diastereomer), 4.01 (dd, *J* = 8.0, 2.6 Hz, 1H major diastereomer), 3.30 (ddd, *J* = 12.2, 7.4, 4.9 Hz, 1H minor diastereomer), 3.17 (td, *J* = 10.6, 9.5, 2.5 Hz, 1H major diastereomer), 2.83 (qd, *J* = 10.3, 3.1 Hz, 1H minor diastereomer), 2.64 - 2.47 (m, 1H major diastereomer), 2.05 – 1.08 (m, 12H major diastereomer; 12H minor diastereomer); **^{13}C NMR (100 MHz, CDCl$_3$):** δ 210.8, 209.6, 140.3, 129.3, 129.0, 127.2, 125.6, 125.4, 125.3, 122.7, 68.4, 65.4, 61.7, 60.5, 37.6, 36.5, 30.4, 29.7, 29.3, 28.2, 27.5, 26.0, 25.8, 25.8, 25.8, 25.8, 25.5, 25.1, 24.0, 20.5; **HRMS (EI):** Calcd for $C_{17}H_{19}F_3O$ (M$^+$): 296.1383, Found: 296.1369.



***(2S,3S)*-3-(1-(dimethyl(phenyl)silyl)ethyl)-2-phenylcyclobutan-1-one (18):** To a flame-dried 10 mL round-bottom flask was added but-3-en-2-yldimethyl(phenyl)silane (39 mg, 1.0 equiv, 0.20 mmol) and dry dichloromethane (0.35 mL). *N,N*-diisopropylethylamine (40 µL, 1.1 equiv, 0.22 mmol) was then added and the solution was placed in a -78 ºC ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 0.26 mL, 2.5 equiv, 0.50 mmol) was added in one portion down the walls of the flask. A solution of phenylacetyl chloride (82 µL, 3.0 equiv, 0.60 mmol) in dichloromethane (0.15 mL) was then added dropwise into the flask over a period of 15 minutes (0.10 mL every 5 minutes). The reaction was transferred to a -45°C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (1 mL) and MeOH (1 mL). The mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1 M, ~5 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with diethyl ether (3 x 5 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (10% Et_2O/hexanes) to provide the pure cyclobutanone as a white solid (0.42 g, 1.7 mmol, 53% yield, > 20:1 dr, major diastereomer shown above, dr determined by analysis of the pure ^1H NMR). Analytically pure samples could be obtained by recrystallization from dichloromethane and heptane. **IR (neat):** 3065, 3021, 2947, 2865, 1774, 1600, 1496, 1421, 1248, 1117 cm^{-1}; **^1H NMR (600 MHz, Chloroform-d)** δ 7.52 – 7.49 (m, 2H), 7.41 – 7.33 (m, 3H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.22 (t, *J* = 7.4 Hz, 1H), 7.13 (d, *J* = 7.5 Hz, 2H), 4.07 (d, *J* = 7.7 Hz, 1H), 2.82 (dd, *J* = 17.5, 8.5 Hz, 1H), 2.59 (dd, *J* = 17.5, 8.2 Hz, 1H), 2.50 (p, *J* = 10.9, 8.2 Hz, 1H), 1.26 (dq, *J* = 11.0, 7.5 Hz, 1H), 1.04 (d, *J* = 7.4 Hz, 3H), 0.33 (d, *J* = 1.4 Hz, 6H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 207.0, 137.8, 136.8, 133.7, 129.2, 128.6, 127.9, 127.5, 126.9, 72.1, 50.6, 35.5, 28.9, 14.31, -4.1, -4.7. **HRMS (EI):** Calcd for $C_{20}H_{24}OSi$ (M^+): 308.1591, Found: 308.1591.

■ Procedure of epimerization (according to literature procedure[4])



2:1 dr

1:2 dr

7-phenylbicyclo[3.2.0]heptan-6-one (8) (2:1 dr): A solution of cyclobutanone **8** (0.19 g, 1.0 mmol) in benzene-d6 (1 mL) and triethylamine (20 µL) was allowed to stand for 24 hours at

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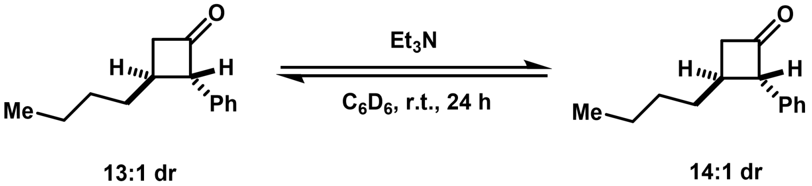
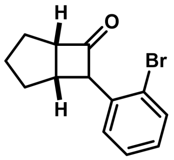
[4] Rey, M.; Roberts, S. M.; Dreiding, A. S.; Roussel, A.; Vanlierde, H.; Toppet, S.; Ghosez, L. *Helv. Chim. Acta.* **1982**, *65*, 703.

room temperature in a NMR tube. The dr was observed to change from 2:1 to 1:2 (dr was determined by analysis of the ^{1}H NMR).

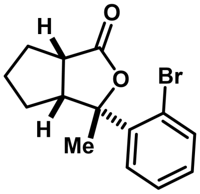


(2S,3S)-3-butyl-2-phenylcyclobutan-1-one (12) (13:1 dr): A solution of cyclobutanone **12** (0.20 g, 1.0 mmol) in benzene-d6 (1 mL) and triethylamine (20 µL) was allowed to stand for 24 hours at room temperature in a NMR tube. The dr was observed to change from 13:1 to 14:1 (dr was determined by analysis of the ^{1}H NMR).

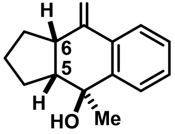
■ Total synthesis of the common scaffold



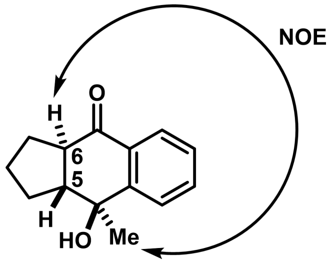
7-(2-bromophenyl)bicyclo[3.2.0]heptan-6-one (20): To a flame-dried 100 mL round-bottom flask was added cyclopentene (2.2 mL, 5.0 equiv, 25 mmol) and dry dichloromethane (40 mL). *N,N*-diisopropylethylamine (0.96 mL, 1.1 equiv, 5.5 mmol) was then added and the solution was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of Me_3Al (2 M in toluene, 6.2 mL, 2.5 equiv, 12.5 mmol) was added in one portion down the walls of the flask. A solution of 2-bromophenylacetyl chloride (0.74 mL, 1.0 equiv, 5.0 mmol) in dichloromethane (10 mL) was then added dropwise into the flask over a period of 30 minutes (~0.3 mL/min). The reaction was transferred to a -45 °C ($CO_{2\,(S)}$ / MeCN) bath and allowed to stir for 2 hours. After 2 hours, the reaction was quenched by the addition of Et_3N (3 mL) and MeOH (3 mL). The mixture was allowed to warm to room temperature and stirred for 2-3 minutes until a solid formed. Aqueous HCl (1M, ~10 mL) was then added until the solid dissolved completely. The reaction mixture was extracted with dichloromethane (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified via Kugelrohr distillation (180 °C, 0.1 torr) to provide the pure cyclobutanone as a clear liquid (1.1 g, 4.0 mmol, 80% yield, 1:1 dr, dr determined by analysis of the pure ^{1}H NMR). Due to the isolation of a mixture of diastereomers, integrations listed below may not be accurate. **IR (neat):** 3060, 2947, 2860, 1773, 1586, 1560, 1473 cm^{-1}; **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.53 (dd, *J* = 7.9, 1.4 Hz, 2H), 7.46 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.27 – 7.12 (m, 3H), 7.12 – 7.03 (m, 2H), 4.72 (dd, *J* = 10.2, 3.1 Hz, 1H), 4.15 (dd, *J* = 5.4, 3.3 Hz, 1H), 3.67 – 3.56 (m, 2H), 3.49 (dt, *J* = 10.6, 7.6 Hz, 1H), 2.84 (q, *J* = 6.8 Hz, 1H), 2.33 – 2.19 (m, 1H), 2.18 – 2.07 (m, 2H), 1.96 – 1.88 (m, 1H), 1.88 – 1.50 (m, 6H), 1.37 – 1.11 (m, 2H); **^{13}C NMR (101 MHz, $CDCl_3$)** 214.3, 213.1, 137.5, 134.0, 133.1, 132.8, 129.0, 128.6, 128.5, 128.3, 127.6, 127.2, 124.0, 123.7, 68.4, 65.1, 62.9, 62.5, 39.3, 36.6, 33.2, 30.2, 29.3, 27.6, 26.1, 25.2. **HRMS (EI):** Calcd for $C_{13}H_{14}OBr$ ($M+H^+$): 265.0223, Found: 265.0219.



(3R,3aS,6aR)-3-(2-bromophenyl)-3-methylhexahydro-1H-cyclopenta[c]furan-1-one (21): To a flame-dried 50 mL round-bottom flask was added cyclobutanone **20** (0.64 g, 1.0 equiv, 2.4 mmol) and dry tetrahydrofuran (18 mL) and the flask was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of potassium bis(trimethylsilyl)amide (0.5 M, 5.8 ml, 1.2 equiv, 2.9 mmol, toluene) was added slowly down the walls of the flask of the flask over a period of 2 minutes. The reaction mixture turned yellow and was stirred for 10 minutes. Iodomethane (0.30 mL, 2.0 equiv, 4.8 mmol) was then added in one portion and the cold bath was removed. After stirring for 30 minutes, the reaction was placed into a -78 °C ($CO_{2\,(S)}$ / acetone) bath and was quenched with saturated ammonium chloride (~10 mL). The reaction mixture was warmed to room temperature and extracted with diethyl ether (3 x 10 mL), and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. Without further purification, the crude product was directly charged to a 50 mL round-bottom flask with methanol (16 mL), sodium hydroxide aqueous solution (4 M, 4 mL) and hydrogen peroxide aqueous solution (30%, 4 mL). The reaction was stirred at room temperature for 12 hours and the reaction mixture was extracted with diethyl ether (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (10% Et_2O/hexanes) to provide the pure lactone as a clear liquid (0.37 g, 1.2 mmol, 52% yield over two steps, > 20:1 dr, major diastereomer shown above, dr determined by analysis of the pure ^{1}H NMR). **IR (neat):** 3085, 3059, 2960, 2922, 1778, 1601, 1496, 1444, 1029 cm^{-1}; **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.69 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.53 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.27 (td, *J* = 7.7, 1.3 Hz, 1H), 7.10 (td, *J* = 7.7, 1.7 Hz, 1H), 3.45 (q, *J* = 8.3 Hz, 1H), 3.28 (td, *J* = 8.3, 3.4 Hz, 1H), 2.10 – 1.89 (m, 2H), 1.80 (s, 3H), 1.76 – 1.61 (m, 1H), 1.56 – 1.36 (m, 2H), 1.05 – 0.88 (m, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** 178.9, 141.4, 134.3, 129.0, 127.6, 127.4, 119.2, 88.7, 49.9, 45.7, 29.6, 29.3, 27.6, 25.7. **HRMS (EI):** Calcd for $C_{14}H_{16}O_2Br$ ($M+H^+$): 295.0328, Found: 295.0349.

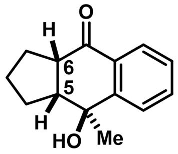
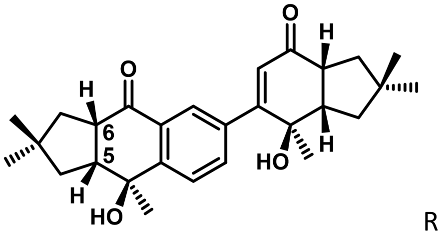
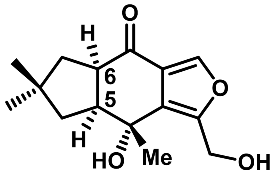
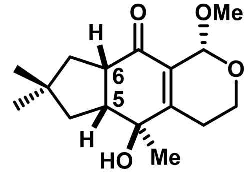
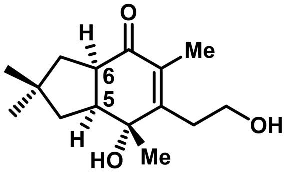
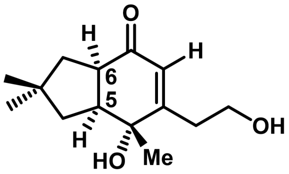


(3aS,9S,9aR)-9-hydroxy-9-methyl-1,2,3,3a,9,9a-hexahydro-4H-cyclopenta[b]naphthalen-4-one (22): To a flame-dried 10 mL round-bottom flask was added lactone (0.045 g, 1.0 equiv, 0.15 mmol), dry tetrahydrofuran (3.0 mL) and the flask was placed in a -78 °C ($CO_{2\,(S)}$ / acetone) bath. A solution of ^{t}BuLi (1.45 M, 190 µL, 1.8 equiv, 0.27 mmol, pentane) was added slowly down the walls of the flask over 15 minutes. The reaction was allowed to stir for 30 minutes at -78 °C ($CO_{2\ (S)}$ / acetone bath). After 30 minutes, the reaction was quenched with saturated ammonium chloride (1 mL). The reaction mixture was warmed to room temperature and extracted with diethyl ether (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (5% Et_2O/hexanes) to provide the pure ketone as a clear liquid (0.028 g, 0.13 mmol, 84% yield. Epimer at C-6 position was also isolated as a white solid, 0.0027 g, 0.012 mmol, 8% yield). The relative configuration of the major diastereomer was determined by comparison of the H-5 and H-6 coupling constant and chemical shift to related molecules of known with *cis*-fused ring structure (Table 1). **IR (neat):** 3060, 2947, 2860, 1773, 1586, 1560, 1473 cm^{-1}; **^{1}H NMR (400 MHz, Chloroform-d)** δ 7.85 (dd, *J* = 7.7, 1.4 Hz, 1H), 7.55 – 7.43 (m, 2H), 7.35 (td, *J* = 7.3, 1.7 Hz, 1H), 3.14 (td, *J* = 8.0, 5.0 Hz, 1H), 2.58 (dt, *J* = 10.8, 8.0 Hz, 1H), 2.06 – 1.84 (m, 2H), 1.84 – 1.73 (m, 1H), 1.64 (s, 3H), 1.56 – 1.49 (m, 1H), 1.26 – 1.14 (m, 1H), 1.00 (ddt, *J* = 12.8, 11.0, 8.9 Hz, 1H), 0.86 – 0.75 (m, 1H); **^{13}C NMR (101 MHz, $CDCl_3$)** 178.9, 141.4, 134.3, 129.0, 127.6, 127.4, 119.2, 88.7, 49.9, 45.7, 29.6, 29.3, 27.6, 25.7. **HRMS (EI):** Calcd for $C_{14}H_{17}O_2$ (M+H$^+$): 217.1223, Found: 217.1219.



Epimer at C6 position: The relative configuration of the minor diastereomer was determined by the NOE between H-6 and methyl group. **IR (neat):** 3480, 3065, 2961, 2870, 1678, 1591, 1448, 1226 cm^{-1}; **^{1}H NMR (400 MHz, Chloroform-*d*)** δ 7.96 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.76 (dd, *J* = 7.9, 1.3 Hz, 1H), 7.62 – 7.53 (m, 1H), 7.40 – 7.30 (m, 1H), 2.58 (dt, *J* = 13.8, 9.0 Hz, 1H), 2.21 (td, *J* = 13.8, 11.2, 6.6 Hz, 1H), 2.12 – 1.93 (m, 2H), 1.94 (s, 1H), 1.88 – 1.79 (m, 1H), 1.76 – 1.59 (m, 3H), 1.50 (s, 3H); **^{13}C NMR (100 MHz, $CDCl_3$)** δ 198.96, 152.23, 133.83, 131.61, 127.60, 126.65, 126.06, 73.98, 55.41, 52.11, 26.02, 23.99, 23.02, 22.11. **HRMS (EI):** Calcd for $C_{14}H_{17}O_2$ (M+H$^+$): 217.1223, Found: 217.1223.

Table 1. Structurally Related Natural Products-*cis* fused

Entry	H	δ_H (ppm)	*J* (Hz) Coupling between C-5 and C-6 in bold
	H-6	3.14	td (**8.0**, 5.0)
	H-5	2.58	dt (10.8, **8.0**)
 Ref 5	H-6	3.35	q (**8.6**)
	H-5	2.94	m
 Ref 5	H-6	3.03	m
	H-5	2.61	m
 Ref 6	H-6	2.93	m
	H-5	2.59	m
 Ref 7	H-6	2.97	dt (4.7, **8.1**)
	H-5	2.64	m
 Ref 7	H-6	2.92	m
	H-5	2.64	dt (12.7, **6.6**)

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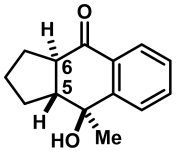
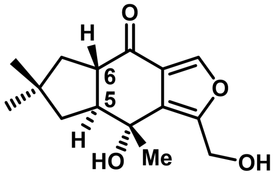
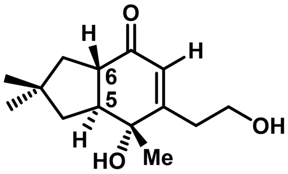
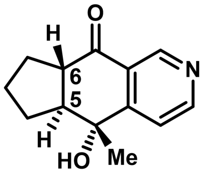
[5] Isaka, M.; Srisanoh, U.; Choowong, W.; Boonpratuang, T. *Org. Lett.* **2011**, *13*, 4886.

[6] Liu L-Y; Zhang L.; Feng T. et al. *Nat. Prod. and Bioprospect*. **2011,** *1*, 87.

[7] Isaka, M.; Srisanoh, U.; Sappan, M.; Supothina, S.; Boonpratuang, T. *Phytochemistry*. **2012,** *79*, 116.

Table 2. Structurally Related Natural Products-*trans* fused

Entry	H	δ_H (ppm)	*J* (Hz) Coupling between C-5 and C-6 in bold
	H-6	2.58	dt (**13.8**, 9.0)
	H-5	2.21	ddd (**13.8**, 11.2, 6.6)
 Ref [5]	H-6	2.69	ddd (**13.4**, 10.2, 8.1)
	H-5	2.54	ddd (**13.4**, 12.0, 6.7)
 Ref [7]	H-6	2.52	ddd (**13.7**, 10.7, 7.9)
	H-5	2.32	ddd (**13.7**, 12.2, 6.6)
 Ref [7]	H-6	2.77	m
	H-5	2.50	m