SUPPORTING INFORMATION

Title: Ruthenium(II)-Catalyzed Cyclization of Oxabenzonorbornenes with Propargylic Alcohols: Formation of Isochromenes
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**General Information**

All reactions were carried out in an atmosphere of dry nitrogen at ambient temperature unless otherwise stated. Standard column chromatography was performed on 230-400 mesh silica gel (obtained from Silicycle) using flash column chromatography techniques. Analytical thin-layer chromatography (TLC) was performed on Silicycle precoated silica gel F254 plates. All glassware was flame dried under an inert atmosphere of dry nitrogen. Infrared spectra were taken on a Bomem MB-100 FTIR spectrophotometer. $^1$H and $^{13}$C NMR spectra were recorded on Bruker Avance-300 and 400 spectrometers. Chemical shifts for $^1$H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent resonance as the internal standard (chloroform: $\delta$ 7.26 ppm). Chemical shifts for $^{13}$C NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (deuterochloroform: $\delta$ 77.0 ppm). Chemical shifts for $^2$H NMR spectra are reported in parts per million (ppm) from tetramethylsilane with the solvent as the internal standard (deuterochloroform: $\delta$ 7.26 ppm). High resolution mass spectra were done by McMaster Regional Centre for Mass Spectrometry at McMaster University, Hamilton, Ontario. Elemental analyses were performed by Canadian Microanalytical Service Ltd., British Columbia or by Quantitative Technologies Inc., New Jersey.

**Reagents:** Unless stated otherwise, commercial reagents were used without purification. Solvents were purified by distillation under dry nitrogen: from magnesium/iodine (MeOH) and from potassium/benzophenone (THF). Alkene 2f was bought from Sigma-Aldrich Co. and used without further purification. [Cp*Ru(CH3CN)]PF6 was bought from Strem Chemicals. Alkynes 4a, 4a-d, bicyclic alkenes 2a, 2b, 2c, 2e, 2g and Cp*Ru(COD)Cl were prepared according to literature procedures.

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Part A: Synthesis of Alkynes

**General procedure (A) for the preparation of alkynes.** To a cold solution (-70 °C) of hexamethyldisilazane (HMDS, 1.2 equiv.) in THF (0.6 M versus ethyl propiolate) was added dropwise a solution of butyllithium in hexanes (BuLi, 2.5 M, 1.2 equiv.). The reaction was stirred for 15 min then ethyl propiolate (1.0 equiv.) was added dropwise. The resulting mixture was allowed to stir at –70 °C for 20 min prior to add the electrophile (1.4 equiv.). The reaction was monitored by TLC and upon completion, quenched with water and allowed to warm to room temperature. The reaction mixture was diluted with ethyl acetate the layers were separated. The aqueous layer was extracted three times with ethyl acetate, and the combined organic extracts were then washed with brine, dried over anhydrous magnesium sulfate, filtrated and concentrated to dryness. The crude product was the purified by column chromatography.

Propargylic alcohol 4b: Following the above general procedure (A) with HMDS (0.75 mL, 3.6 mmol), THF (5.0 mL), BuLi (1.40 mL, 3.54 mmol), ethyl propiolate (0.30 mL, 3.0 mmol) and cyclohexylcarboxaldehyde (0.60 mL, 4.0 mmol). The crude product was purified by column chromatography (gradient EtOAc/hexanes = 1: 9 to 3:7) to give 4b (269.7 mg, 1.283 mmol, 43 %) as a colorless oil. R_f 0.23 (EtOAc/hexanes = 1:9); IR (neat) 3417, 2930, 2855, 2234, 1714, 1630, 1451, 1241 cm^{-1}; \(^1\)H NMR (CDCl₃, 400 MHz) δ 4.26 (app t, \(J = 6.1\) Hz, 1 H), 4.22 (q, \(J = 7.1\) Hz, 2 H), 2.44 (d, \(J = 6.0\) Hz, 1 H), 1.84-1.87 (m, 2 H), 1.75-1.78 (m, 2 H), 1.58-1.68 (m, 2 H), 1.30 (t, \(J = 7.1\) Hz, 3 H), 1.00-1.26 (m, 5 H); \(^13\)C NMR (APT, CDCl₃, 100 MHz) δ 153.5, 87.2, 77.3, 66.8, 62.1, 43.6, 28.3, 28.1, 26.1, 25.7, 13.9; HRMS (CI) calcd. for C_{12}H_{18}O_{3} ((M+H)^+): 211.1336; found: 211.1334.

Propargylic alcohol 4c: Following the above general procedure (A) with HMDS (0.75 mL, 3.6 mmol), THF (5.0 mL), BuLi (1.40 mL, 3.54 mmol), ethyl propiolate (0.30 mL, 3.0 mmol) and trimethylacetaldehyde (0.45 mL, 4.1 mmol). The crude product was purified by column chromatography.
chromatography (gradient EtOAc/hexanes = 1:9 to 1:4) to give 4c (298.5 mg, 1.620 mmol, 55 %) as a colorless oil. Rf 0.21 (EtOAc/hexanes = 1:9); IR (neat) 3457, 2967, 2872, 2234, 1716, 1254 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 4.22 (q, J = 7.1 Hz, 2 H), 4.12 (s, 1 H), 2.36 (br s, 1 H), 1.30 (t, J = 7.1 Hz, 3 H), 1.01 (s, 9 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 153.4, 86.9, 77.5, 71.0, 62.1, 36.0, 26.2, 25.2, 14.0; HRMS (CI) calcd. for C₁₀H₁₆O₃ ((M+H)⁺): 185.1178; found: 185.1184.

Propargylic alcohol 4d: Following the above general procedure (A) with HMDS (0.75 mL, 3.6 mmol), THF (5.0 mL), BuLi (1.40 mL, 3.54 mmol), ethyl propiolate (0.30 mL, 3.0 mmol) and 3,3-dimethylbutaldehyde (0.50 mL, 4.0 mmol). The crude product was purified by column chromatography (gradient EtOAc/hexanes = 1:19 to 1:4) to give 4d (276.8 mg, 1.396 mmol, 47 %) as a colorless oil. Rf 0.26 (EtOAc/hexanes = 1:9); IR (neat) 3432, 2956, 2907, 2871, 2235, 1714, 1245 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 4.55-4.60 (m, 1H), 4.22 (q, J = 7.1 Hz, 2 H), 2.05 (m, 1 H), 2.01-2.08 (m, 2 H), 1.30 (t, J = 7.1 Hz, 3 H), 0.98 (s, 9 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 153.5, 88.8, 76.4, 62.1, 59.9, 50.5, 30.2, 29.8, 14.0; HRMS (EI) calcd. for C₁₁H₁₈O₃ (M⁺): 198.1256; found: 198.1262.
Part B: Synthesis of Alkenes

Alkene 2e: To a stirring solution of isoamyl nitrite (14.5 mL, 109 mmol) and 2-acetylfuran (7.3 mL, 73 mmol) in dry THF (100 mL) under N₂, a solution of anthranilic acid (5.0 g, 37 mmol) in dry THF (25 mL) was added slowly by drop funnel. The solution was warmed up to 65-70 °C during the addition of anthranilic acid and refluxed for 2 h following the addition. The resulting mixture was concentrated and purified by column chromatography (EtOAc/hexanes = 1.5:8.5) to afford alkene 2e as a pale yellow oil (4.57 g, 24.5 mmol, 65%).

Rf 0.53 (EtOAc/hexanes = 3:7); IR (neat) 3070, 3016, 1715, 1454, 1441, 1417, 1365, 1320, 1274, 1234 cm⁻¹; ¹H NMR (CDCl₃, 400MHz) δ 7.26 (m, 2 H), 7.04 (m, 4 H), 5.82 (br. s, 1 H), 2.42 (br s, 3 H); ¹³C NMR (APT, CDCl₃, 100MHz) δ 205.2, 148.0, 147.4, 143.4, 142.3, 125.6, 125.2, 120.6, 119.5, 114.5, 95.7, 82.3, 26.8. HRMS (EI) calcd. for C₁₂H₁₀O₂ (M⁺): 186.0681; found: 186.0688.

Alkene 18: In a round-bottomed flask equipped with a condenser were successively loaded 2d (0.5012 g, 2.479 mmol), THF (7.5 mL), H₂O (2.5 mL) and LiOH (1.24 g, 29.6 mmol). The biphasic reaction mixture was allowed to gently refluxed for 30 min, prior to be cooled to 0 °C. The mixture was acidified with conc. H₂SO₄ to ca. pH = 3. The solid was filtrated and washed with cold water, then dissolved in EtOAc, dried over magnesium sulfate and concentrated to dryness to give 18 as a beige solid (463.2 mg, 2.461 mmol, quantitative yield). ¹H NMR (CDCl₃, 400 MHz) δ 7.43-7.47 (m, 1 H), 7.28-7.31 (m, 1 H), 7.01-7.14 (m, 4 H), 5.87 (d, J = 1.5 Hz, 1 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 172.7, 147.4, 146.6, 143.7, 142.1, 125.9, 125.4, 120.7, 120.0, 90.1, 82.6. HRMS (CI) calcd. for C₁₁H₈O₃ ((M+H)+): 189.0552; found: 189.0560. Acid 18 was used for the next step without further purification.

Alkene 2f: To a mixture of 18 (152.8 mg, 0.8077 mmol) and K₂CO₃ (181.2 mg, 1.311 mmol) in DMF (3.0 mL) was added potassium iodide (ca. 10 mg). The flask was then equipped with a condenser and purged with nitrogen prior to slowly add 4-bromo-1-butene (0.40 mL, 3.9 mmol). The reaction was heated at 60 °C for 24 h then allowed to cool to room temperature.
The mixture was partitioned between 1N aqueous HCl and diethyl ether. Layers were separated; aqueous phase was extracted three times with diethyl ether. The combined organic layers were washed with brine, dried over MgSO₄ and concentrated under reduced pressure. The crude product was purified by column chromatography (gradient EtOAc/hexanes = 1:19 to 1:9) to provide 2f (112.3 mg, 0.4635 mmol, 58%) as a pale yellow oil. $R_f$ 0.29 (EtOAc/hexanes = 1:4); IR (CH₂Cl₂) 3134, 3076, 3052, 3015, 2980, 2961, 2902, 1737 cm⁻¹; $^1$H NMR (CDCl₃, 400 MHz) $\delta$ 7.40-7.43 (m, 1 H), 7.30-7.32 (m, 1 H), 7.03-7.13 (m, 4 H), 5.84-5.95 (m, 1 H), 5.85 (s, 1 H), 5.22 (dm, $J = 17.2$ Hz, 1 H), 5.17 (dm, $J = 10.2$ Hz, 1 H), 4.51 (t, $J = 7.8$ Hz, 1 H), 2.59 (app qt, $J = 6.8$, 1.3 Hz, 2 H); $^{13}$C NMR (APT, CDCl₃, 100 MHz) $\delta$ 167.6, 147.7, 147.2, 143.5, 142.5, 133.3, 125.6, 125.1, 120.5, 119.9, 117.8, 90.3, 82.4, 64.7, 33.0. HRMS (EI) calcd. for C₁₅H₁₄O₃ (M⁺): 242.0943; found: 242.0942.
Part C: Ruthenium-Catalyzed Reactions

General procedure (B) for ruthenium-catalyzed formation of cyclobutene, cyclopropane and/or isochromene products. A mixture of alkene 2 (1.1-1.4 equiv.), acetylene 4 (1.0 equiv.) and MeOH (0.5 M versus acetylene) in an oven-dried vial was added via a cannula to an oven-dried screw-cap vial containing Cp*Ru(COD)Cl (weighed out from a dry box, 5-6 mol%) under nitrogen. The reaction mixture was stirred at 60 °C for 1 h. The solvent was evaporated and the crude product was purified by column chromatography.

General procedure (C) for ruthenium-catalyzed formation of isochromene or cyclopropane products from ethyl diazoacetate. A solution of alkene 2 (1 equiv.) in THF (0.5 M) in an oven-dried vial was added via cannula to an oven-dried vial containing [Cp*Ru(NCCH3)3]PF6 (weighed out from a dry box, 5-6 mol%) under nitrogen. The reaction mixture was stirred at 60 °C, then a solution of ethyl diazoacetate (2-3 equiv.) in THF (1.1 M) was added over 30-45 min using a syringe. The reaction was monitored by ¹H NMR and upon completion, the solvent was evaporated and the crude product was purified by column chromatography.

Isochromene 7a: Following the above general procedure (B) with alkene 2a (204.9 mg, 1.421 mmol), alkyn 4a (180.0 mg, 1.266 mmol), MeOH (1.6 mL), and Cp*Ru(COD)Cl (17.2 mg, 0.0453 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient EtOAc/hexanes= 1:19 to 1:4) to provide 7a (181.2 mg, 0.6330 mmol, 50%) as a white solid (mp = 60-62 °C, Et2O/hexanes). Rf 0.33 (EtOAc/hexanes = 1:4); IR (neat) 3070, 2985, 2955, 2936, 1720, 1713, 1622 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.22-7.26 (m, 2 H), 7.17 (app t, J = 7.5 Hz, 1 H), 6.99 (app t, J = 7.5 Hz, 2 H), 6.53 (d, J = 5.7 Hz, 1 H), 5.84 (d, J = 5.7 Hz, 1 H), 5.73 (d, J = 8.8 Hz, 1 H), 4.17-4.23 (m, 2 H), 3.63 (d, J = 17.1 Hz, 1 H), 3.53 (d, J = 17.1 Hz, 1 H), 2.23 (s, 3 H), 1.29 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 204.5, 166.5, 144.5, 139.5, 129.5, 129.4, 128.7, 128.0, 127.2, 124.4, 123.5, 105.5, 73.7, 61.4, 41.8, 29.9,14.1. HRMS (EI) calcd. for C₁₇H₁₈O₄(M⁺): 286.1205; found: 286.1207.
Isochromene 7a-d: Following the above general procedure (B) with alkene 2a (60.5 mg, 0.420 mmol), alkyne 4a-d (49.9 mg, 0.349 mmol), MeOH (0.6 mL), and Cp*Ru(COD)Cl (6.3 mg, 0.017 mmol). The reaction mixture was stirred at 60 °C for 2.5 h. The crude product was purified by column chromatography (gradient EtOAc/hexanes = 1:9 to 1:4) to provide 7a-d (19.5 mg, 0.0678 mmol, 19%). 7a-d (major diastereomer) Rf 0.33 (EtOAc/hexanes = 1:4); IR (CH2Cl2) 3066, 2981, 2906, 1713, 1252 cm⁻¹; 1H NMR (CDCl3, 300 MHz) δ 7.13-7.25 (m, 3 H), 6.97-7.01 (m, 2 H), 6.53 (d, J = 5.7 Hz, 1 H), 5.84 (d, J = 5.7 Hz, 1 H), 5.73 (d, J = 8.8 Hz, 1 H), 4.17-4.23 (m, 2 H), 3.61 (br s, 1 H), 2.23 (s, 3 H), 1.29 (t, J = 7.1 Hz, 3 H); 13C NMR (CDCl3, 75 MHz) δ 204.5, 166.5, 144.5, 139.5, 129.7, 129.4, 128.7, 128.1, 127.2, 124.4, 123.5, 105.5, 73.7, 61.4, 41.6 (t, J = 20 Hz), 29.9, 14.1. 2H NMR (CHCl3, 61 MHz) δ 3.57. HRMS (EI) calcd. for C17H17O4 (M⁺): 287.1267; found: 287.1281.

Isochromene 7b: Following the above general procedure (B) with alkene 2a (50.8 mg, 0.352 mmol), alkyne 4b (52.7 mg, 0.252 mmol), MeOH (0.7 mL), and Cp*Ru(COD)Cl (6.4 mg, 0.017 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient Et2O/hexanes = 1:9 to 1:4) to provide 7b (44.2 mg, 0.125 mmol, 50%) as a white solid (mp = 60-62 °C, uncrist.). Rf 0.49 (EtOAc/hexanes = 3:7); IR (CH2Cl2) 2981, 2929, 2853, 1709 cm⁻¹; 1H NMR (CDCl3, 400 MHz) δ 7.21-7.25 (m, 2 H), 7.17 (app td, J = 7.6, 1.3 Hz, 1 H), 6.99 (d, J = 7.5 Hz, 2 H), 6.53 (d, J = 5.7 Hz, 1 H), 5.84 (d, J = 5.7 Hz, 1 H), 5.70 (d, J = 8.8 Hz, 1 H), 4.24-4.15 (m, 2 H), 3.67 (d, J = 17.2 Hz, 1 H), 3.54 (d, J = 17.2 Hz, 1 H), 2.46 (tt, J = 11.2, 3.4 Hz, 1 H), 1.88-1.91 (m, 2 H), 1.77-1.80 (m, 2 H), 1.65-1.68 (m, 1 H), 1.27 (t, J = 7.1 Hz, 3 H), 1.17-1.40 (m, 5 H); 13C NMR (APT, CDCl3, 100 MHz) δ 209.5, 166.6, 144.6, 139.3, 129.8, 129.7, 128.6, 128.1, 127.2, 124.5, 123.4, 105.4, 73.8, 61.2, 50.8, 39.0, 28.5, 28.4, 25.8, 25.61, 25.55, 14.1. HRMS (Cl) calcd. for C22H26O4 ((M+H⁺): 355.1909; found: 355.1915.
Cyclobutene 5c and isochromene 7c: Following the above general procedure (B) with alkene 2a (42.1 mg, 0.292 mmol), alkyne 4c (42.0 mg, 0.228 mmol), MeOH (0.6 mL), and Cp*Ru(COD)Cl (6.2 mg, 0.016 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient Et₂O/hexanes = 1:9 to 2:3) to provide cycloadduct 5c (40.7 mg, 0.124 mmol, 54%) and 7c (19.5 mg, 0.0593 mmol, 26%).

5c (major diastereomer): white solid (mp = 88-89 °C, uncr); R₇ 0.25 (EtOAc/hexanes = 2:3); IR (CH₂Cl₂) 3408, 3058, 2963, 2906, 2869, 1712, 1682 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.28-7.35 (m, 2 H), 7.17-7.19 (m, 2 H), 5.17 (d, J = 8.9 Hz, 1 H), 5.09 (s, 1 H), 5.08 (s, 1 H), 4.27-4.31 (m, 2 H), 4.01 (br d, J = 8.9 Hz, 1 H), 2.86 (br d, J = 3.2 Hz, 1 H), 2.70 (br d, J = 3.4 Hz, 1 H), 1.37 (t, J = 7.1 Hz, 3 H), 1.00 (s, 9 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 166.3, 163.5, 144.3, 143.9, 132.1, 126.9, 126.8, 120.0, 119.7, 78.4, 75.5, 75.2, 61.2, 49.0, 44.8, 37.4, 26.1, 14.2. HRMS (EI) calcd. for C₂₀H₂₄O₄ (M⁺): 328.1675; found: 328.1670. 7c: colorless oil; R₇ 0.49 (EtOAc/hexanes = 3:7); IR (CH₂Cl₂) 3066, 2981, 2930, 2872, 1711 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.21-7.25 (m, 2 H), 7.18 (app td, J = 7.6, 1.3 Hz, 1 H), 6.99 (d, J = 7.6 Hz, 2 H), 6.54 (d, J = 5.7 Hz, 1 H), 5.85 (d, J = 5.7 Hz, 1 H), 5.67 (d, J = 8.8 Hz, 1 H), 4.24-4.16 (m, 2 H), 3.75 (d, J = 17.6 Hz, 1 H), 3.59 (d, J = 17.6 Hz, 1 H), 1.27 (t, J = 7.1 Hz, 3 H), 1.20 (s, 9 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 211.5, 166.6, 144.7, 139.2, 130.3, 129.7, 128.6, 128.2, 127.2, 124.5, 123.4, 105.4, 73.8, 61.2, 44.4, 35.4, 26.6, 14.1. HRMS (CI) calcd. for C₂₀H₂₄O₄ ((M+H)⁺): 329.1753; found: 329.1744.

Isochromene 7d: Following the above general procedure (B) with alkene 2a (58.6 mg, 0.406 mmol), alkyne 4d (55.8 mg, 0.281 mmol), MeOH (0.6 mL), and Cp*Ru(COD)Cl (6.1 mg, 0.016 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient Et₂O/hexanes = 1:9 to 2:3) to provide 7d (67.0
mg, 0.196 mmol, 70%) as a white solid (mp = 52-55 °C, uncrist.); Rf 0.45 (EtOAc/hexanes = 1:9); IR (CH₂Cl₂) 3065, 2954, 2869, 1713, 1626 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.15-7.25 (m, 3 H), 6.98-7.00 (m, 2 H), 6.53 (d, J = 5.7 Hz, 1 H), 5.84 (d, J = 5.7 Hz, 1 H), 5.71 (d, J = 8.8 Hz, 1 H), 4.26-4.16 (m, 2 H), 3.61 (d, J = 17.3 Hz, 1 H), 3.50 (d, J = 17.0 Hz, 1 H), 2.40 (s, 2 H), 1.28 (t, J = 7.1 Hz, 3 H), 1.03 (s, 9 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 206.0, 166.6, 144.6, 139.2, 129.7, 129.6, 128.6, 128.1, 127.2, 124.5, 123.4, 105.4, 73.7, 61.2, 54.8, 43.2, 31.0, 29.6, 14.1. HRMS (CI) calcd. for C₂₁H₂₆O₄ ((M+H)+): 343.1909; found: 343.1912.

Isochromene 7e: Following the above general procedure (B) with alkene 2b (112.4 mg, 0.550 mmol), alkyne 4a (70.5 mg, 0.496 mmol), MeOH (0.9 mL), and Cp*Ru(COD)Cl (13.3 mg, 0.035 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient Et₂O/hexanes = 1:9 to 1:1) to provide 7e (103.1 mg, 0.2976 mmol, 60%) as a colorless oil. Rf 0.23 (EtOAc/hexanes = 3:7); IR (CH₂Cl₂) 3098, 3060, 2979, 2959, 2939, 2907, 2836, 1712, 1438, 1261 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.23 (d, J = 9.4 Hz, 1 H), 6.71 (d, J = 8.9 Hz, 1 H), 6.62 (d, J = 8.9 Hz, 1 H), 6.45 (d, J = 5.9 Hz, 1 H), 6.09 (d, J = 9.4 Hz, 1 H), 6.08 (d, J = 5.8 Hz, 1 H), 4.12-4.18 (m, 2 H), 3.78 (s, 3 H), 3.70 (s, 3 H), 3.63-3.74 (m, 2 H), 2.21 (s, 3 H), 1.24 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 204.9, 167.1, 148.7, 147.5, 143.2, 138.2, 127.0, 119.3, 116.7, 110.8, 109.1, 99.0, 68.1, 61.2, 56.0, 55.5, 41.8, 29.4, 14.1. HRMS (CI) calcd. for C₁₉H₂₂O₆ ((M+H)+): 347.1495; found: 347.1495.

Isochromene 7f: Following the above general procedure (B) with alkene 2c (69.2 mg, 0.339 mmol), alkyne 4a (41.6 mg, 0.293 mmol), MeOH (1.2 mL), and Cp*Ru(COD)Cl (6.1 mg, 0.016 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was
purified by column chromatography (gradient EtOAc/hexanes = 1:9 to 2:3) to provide 7f (52.8 mg, 0.155 mmol, 52%) as a colorless oil. $R_f$ 0.50 (EtOAc/hexanes = 1:1); IR (CH$_2$Cl$_2$) 2984, 2937, 2836, 1713, 1513, 1269 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 7.20 (d, $J = 8.8$ Hz, 1 H), 6.60 (s, 1 H), 6.55 (s, 1 H), 6.47 (d, $J = 5.7$ Hz, 1 H), 5.76 (d, $J = 5.7$ Hz, 1 H), 5.69 (d, $J = 8.8$ Hz, 1 H), 4.18-4.24 (m, 2 H), 3.861 (s, 3 H), 3.858 (s, 3 H), 3.70 (d, $J = 17.0$ Hz, 1 H), 3.45 (d, $J = 17.0$ Hz, 1 H), 2.23 (s, 3 H), 1.28 (t, $J = 7.1$ Hz, 3 H); $^{13}$C NMR (APT, CDCl$_3$, 100 MHz) $\delta$ 204.7, 166.5, 149.0, 148.2, 142.5, 138.4, 130.1, 129.7, 129.4, 128.9, 122.6, 120.0, 108.4, 107.2, 105.1, 73.5, 61.3, 56.2, 56.0, 41.8, 30.1, 14.1. HRMS (CI) calcd. for C$_{19}$H$_{22}$O$_6$ ((M+H)$^+$): 347.1495; found: 347.1485.

Isochromene 7g: Following the above general procedure (B) with alkene 2d (55.9 mg, 0.276 mmol), alkyne 4a (38.6 mg, 0.272 mmol), MeOH (0.6 mL), and Cp*Ru(COD)Cl (5.8 mg, 0.015 mmol). The reaction mixture was stirred at 60 ºC for 1 h. The crude product was purified by column chromatography (gradient Et$_2$O/hexanes= 1:4 to 1:1) to provide 7g (72.1 mg, 0.209 mmol, 77%) as a white solid (mp = 100-101 ºC, Et$_2$O/hexanes). $R_f$ 0.24 (EtOAc/hexanes = 1:4); IR (CH$_2$Cl$_2$) 3064, 2982, 2952, 1721, 1717, 1210 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 400 MHz) $\delta$ 7.26-7.32 (m, 2 H), 7.15-7.18 (m, 2 H), 7.08-7.10 (m, 1 H), 6.97 (s, 1 H), 5.87 (d, $J = 8.6$ Hz, 1 H), 4.23-4.14 (m, 2 H), 3.83 (s, 3 H), 3.71 (d, $J = 17.1$ Hz, 1 H), 3.52 (d, $J = 17.1$ Hz, 1 H), 2.23 (s, 3 H), 1.26 (t, $J = 7.1$ Hz, 3 H); $^{13}$C NMR (APT, CDCl$_3$, 100 MHz) $\delta$ 204.5, 166.2, 162.9, 142.5, 138.4, 130.1, 129.7, 129.4, 128.9, 128.7, 125.8, 124.7, 113.0, 74.8, 61.3, 52.3, 41.8, 30.0, 14.0. HRMS (CI) calcd. for C$_{19}$H$_{20}$O$_6$ ((M+H)$^+$): 345.1338; found: 345.1326. Anal. calcd. for C$_{19}$H$_{20}$O$_6$: C, 66.27%, H, 5.85%; found: C, 66.40%; H, 5.72%.
Isochromene 7h: Following the above general procedure (B) with alkene 2e (73.4 mg, 0.394 mmol), alkyne 4a (42.3 mg, 0.298 mmol), MeOH (0.8 mL), and Cp*Ru(COD)Cl (6.7 mg, 0.018 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient EtOAc/hexanes = 1:9 to 2:3) to provide 7h (61.6 mg, 0.188 mmol, 63%) as a white solid (m.p. = 99-102 °C, Et2O/hexanes). Rf 0.30 (EtOAc/hexanes = 3:7); IR (CH2Cl2) 3079, 2981, 2933, 1714, 1681, 1256 cm⁻¹; ¹H NMR (CDCl3, 400 MHz) δ 7.27-7.31 (m, 2 H), 7.19-7.21 (m, 1 H), 7.16 (d, J = 8.8 Hz, 1 H), 7.07-7.09 (m, 1 H), 6.85 (s, 1 H), 5.84 (d, J = 8.8 Hz, 1 H), 4.24-4.15 (m, 2 H), 3.68 (d, J = 17.1 Hz, 1 H), 3.53 (d, J = 17.1 Hz, 1 H), 2.34 (s, 3 H), 2.24 (s, 3 H), 1.27 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl3, 100 MHz) δ 204.4, 193.9, 166.3, 149.0, 138.6, 130.0, 129.9, 129.6, 129.0, 128.8, 126.4, 124.6, 111.0, 74.5, 61.4, 30.0, 25.7, 14.0. Anal. calcd. for C₁₉H₂₀O₅: C, 69.50%; H, 6.14%; found: C, 69.67%; H, 6.01%.

Isochromene 7i: Following the above general procedure (B) with alkene 2f (50.9 mg, 0.210 mmol), alkyne 4a (27.1 mg, 0.191 mmol), MeOH (0.5 mL), and Cp*Ru(COD)Cl (5.2 mg, 0.0137 mmol). The reaction mixture was stirred at 60 °C for 1 h. The crude product was purified by column chromatography (gradient Et₂O/hexanes = 1:9 to 2:3) to provide 7i (51.9 mg, 0.141 mmol, 74%) as a white solid (mp = 55-57 °C, Et₂O/hexanes). Rf 0.39 (EtOAc/hexanes = 1:4); IR (CH₂Cl₂) 3076, 2981, 2904, 1722, 1714 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.30-7.32 (m, 2 H), 7.16-7.19 (m, 2 H), 7.09-7.11 (m, 1 H), 6.95 (s, 1 H), 5.88 (d, J = 8.6 Hz, 1 H), 5.79-5.87 (m, 1 H), 5.16 (dd, J = 17.1, 1.6 Hz, 1 H), 5.11 (dd, J = 10.3, 1.5 Hz, 1 H), 4.81 (t, J = 6.8 Hz, 2 H), 4.17-4.24 (m, 2 H), 3.73 (d, J = 17.1 Hz, 1 H), 3.54 (d, J = 17.1 Hz, 1 H), 2.49 (app qt, J = 6.8, 1.2 Hz, 2 H), 2.25 (s, 3 H), 1.28 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 204.6, 166.3, 162.4, 142.6, 138.6, 130.0, 129.6, 129.0, 128.8, 126.4, 124.6, 111.0, 74.5, 61.4, 41.8, 30.0, 25.7, 14.0. Anal. calcd. for C₁₉H₂₀O₅: C, 69.50%, H, 6.14%; found: C, 69.67%; H, 6.01%.
Cyclobutene 19 and cyclopropane 8: Following the above general procedure (B) with alkene 2g (58.3 mg, 0.316 mmol), alkyne 4a (45.0 mg, 0.317 mmol), MeOH (0.8 mL), and Cp*Ru(COD)Cl (6.1 mg, 0.016 mmol). The reaction mixture was stirred at 60 ºC for 1 h. The crude product was purified by column chromatography (gradient Et₂O/hexanes = 1:9 to 1:1) to provide cycloadduct 19 (16.1 mg, 0.0493 mmol, 16%) and 8 (31.0 mg, 0.0950 mmol, 30%).

19 (major diastereomer): pale yellow oil; R_f 0.13 (EtOAc/hexanes = 3:2); IR (CH₂Cl₂) 3435, 2978, 2930, 2893, 2879, 2813, 1712, 1205, 1102 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 4.86 (br d, J = 3.7 Hz, 1 H), 4.54-4.56 (m, 1 H), 4.15-4.25 (m, 2 H), 4.17 (s, 1 H), 4.11 (s, 1 H), 3.13-3.38 (m, 4 H), 3.31 (s, 6 H), 2.83-2.84 (m, 1 H), 2.73 (br d, J = 3.3 Hz, 1 H), 1.93-2.14 (m, 2 H), 1.30 (d, J = 6.8 Hz, 3 H), 1.28 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 166.5, 163.4, 128.4, 75.9, 75.3, 70.8, 70.5, 65.2, 60.9, 58.8, 47.3, 46.8, 45.6, 44.9, 44.5, 21.2, 14.2. HRMS (EI) calcd. for C₁₇H₂₆O₆ (M⁺): 326.1729; found: 326.1732.

8: pale yellow oil; R_f 0.35 (EtOAc/hexanes = 2:3); IR (CH₂Cl₂) 2981, 2928, 2892, 2812, 1723, 1714, 1203 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 4.37 (s, 2 H), 4.04 (q, J = 7.1 Hz, 2 H), 3.28-3.32 (m, 2 H), 3.29 (s, 6 H), 3.18 (s, 2 H), 3.16-3.21 (m, 2 H), 2.25-2.27 (m, 2 H), 2.11 (s, 3 H), 1.81 (s, 2 H), 1.17 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 207.1, 173.1, 78.4, 70.4, 61.1, 58.7, 46.1, 38.9, 29.8, 29.7, 25.4, 14.0. HRMS (EI) calcd. for C₁₇H₂₆O₆ (M⁺): 326.1729; found: 326.1735.

Isochromene 15: Following the above general procedure (C) with alkene 2a (151.3 mg, 1.049 mmol), THF (1.0 mL), [Cp*Ru(NCCH₃)₃]PF₆ (30.2 mg, 0.0599 mmol), ethyl diazoacetate (250 µL, 2.41 mmol) and THF (2.1 mL). The addition was done over 45 min and the reaction
mixture was stirred at 60 ºC for 1.5 h. The crude product was purified by column chromatography (gradient Et₂O/hexanes = 1:19 to 1:9) to provide 15 (76.7 mg, 0.333 mmol, 32%) as a colorless oil. If diethyl fumarate and/or diethyl maleate were still present at this stage, they were distilled off under reduced pressure (kugelrohr distillation). Rf 0.45 (EtOAc/hexanes = 1:9); IR (neat) 3070, 2981, 2937, 2903, 1720, 1628, 1274 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 7.16-7.27 (m, 2 H), 7.06 (dd, J = 1.5, 5.2 Hz, 1 H), 6.97-7.01 (m, 2 H), 6.54 (d, J = 5.7 Hz, 1 H), 5.96 (d, J = 15.7 Hz, 1 H), 5.78 (d, J = 5.7 Hz, 1 H), 5.72 (d, J = 5.0 Hz, 1 H), 4.19 (q, J = 7.1 Hz, 2 H), 1.28 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 166.0, 144.2, 144.0, 129.3, 128.7, 127.9, 127.1, 124.7, 123.7, 122.3, 104.9, 75.9, 60.6, 14.2. HRMS (CI) calcd. for C₁₄H₁₄O₃ ((M+H)+): 231.1021; found: 231.1025.

Cyclopropanes 16 and 17: Following the above general procedure (C) with alkene 2g (115.9 mg, 0.629 mmol), THF (0.5 mL), [Cp*Ru(NCCH₃)₃]PF₆ (34.1 mg, 0.0676 mmol), ethyl diazoacetate (170 µL, 1.64 mmol) and THF (1.1 mL). The addition was done over 30 min and the reaction mixture was stirred at 60 ºC for 1.5 h. The crude product was purified by column chromatography (gradient Et₂O/hexanes = 1:19 to 1:1) to provide 16 (139.5 mg, 0.5161 mmol, 82%) and 17 (23.8 mg, 0.0866 mmol, 14%) as colorless oils. Assignment of structures to these 2 epimers was based on the close analogies between these systems and that described by Sauers and co-workers,[⁹] and Takahashi et al.[¹⁰]

16: Rf 0.35 (EtOAc/hexanes = 2:3); IR (neat) 2974, 2926, 2893, 2813, 1729, 1407, 1267 cm⁻¹; ¹H NMR (CDCl₃, 400 MHz) δ 4.26 (s, 2 H), 4.04 (q, J = 7.1 Hz, 2 H), 3.24-3.28 (m, 2 H), 3.26 (s, 6 H), 3.14-3.18 (m, 2 H), 2.17-2.20 (m, 2 H), 1.62-1.65 (m, 3 H), 1.18 (t, J = 7.1 Hz, 3 H); ¹H NMR (C₆D₆, 400 MHz) δ 4.28 (s, 2 H), 3.93 (q, J = 7.1 Hz, 2 H), 3.08 (dd, J = 8.8, 5.4 Hz, 2 H), 3.00-3.05 (m, 2 H), 3.00 (s, 6 H), 2.01-2.05 (m, 2 H), 1.98 (t, J = 2.6 Hz, 1 H), 1.57 (d, J = 2.6 Hz, 2 H), 0.93 (t, J = 7.1 Hz, 3 H); ¹³C NMR (APT, CDCl₃, 100 MHz) δ 172.9, 78.2, 70.5, 60.5, 58.8, 45.8, 25.2, 16.4, 14.2. HRMS (EI) calcd. for C₁₄H₂₂O₅ (M⁺): 270.1467; found: 270.1464.

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17: \( R_f 0.17 \) (EtOAc/hexanes = 2:3); IR (CH\(_2\)Cl\(_2\)) 2980, 2930, 2811, 1729, 1219, 1126 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 400 MHz) \( \delta \) 4.42 (s, 2 H), 4.09 (q, \( J = 7.1 \) Hz, 2 H), 3.30-3.34 (m, 2 H), 3.30 (s, 6 H), 3.20-3.24 (m, 2 H), 2.23-2.26 (m, 2 H), 1.42-1.45 (m, 3 H), 1.24 (t, \( J = 7.1 \) Hz, 3 H); \(^1\)H NMR (C\(_6\)D\(_6\), 400 MHz) \( \delta \) 4.60 (s, 2 H), 4.08 (q, \( J = 7.1 \) Hz, 2 H), 3.14 (dd, \( J = 8.8, 5.4 \) Hz, 2 H), 3.03-3.09 (m, 2 H), 3.00 (s, 6 H), 2.05-2.09 (m, 2 H), 1.06 (t, \( J = 7.2 \) Hz, 1 H), 1.02 (t, \( J = 7.1 \) Hz, 3 H), 0.87 (d, \( J = 7.2 \) Hz, 2 H); \(^13\)C NMR (APT, CDCl\(_3\), 100 MHz) \( \delta \) 170.6, 78.5, 70.6, 60.3, 58.8, 46.3, 21.0, 19.5, 14.2. HRMS (EI) calcd. for C\(_{14}\)H\(_{22}\)O\(_5\)(M\(^+\)): 270.1467; found: 270.1470.