Cationic Rh(I)/Modified-BINAP-Catalyzed Reactions of Carbonyl Compounds with 1,6-Diynes Leading to Dienones and *Ortho*-Functionalized Aryl Ketones

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I. General

Anhydrous CH_2Cl_2 (No. 27099-7) and anhydrous $(\text{CH}_2\text{Cl})_2$ (No. 28450-5) were obtained from Aldrich and used as received. H_8 -BINAP, Segphos, and DTBM-Segphos were obtained from Takasago International Corporation. All other reagents were obtained from commercial sources and used as received. All reactions were carried out under an atmosphere of argon or nitrogen in oven-dried glassware with magnetic stirring. Diynes **1a**,¹ **1b**,² **1c**,³ and **1d**⁴ were prepared according to the literatures. Carbonyl compounds **2b**,⁵ **2f**,⁶ and **2h**⁷ were prepared according to the literatures.

II. Rh-Catalyzed Reactions of 1,6-Diynes with Carbonyl Compounds (Table 1 and Scheme 1)

General Procedure-1 (Table 1, entry 1). H_8 -BINAP (9.5 mg, 0.015 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (6.1 mg, 0.015 mmol) were dissolved in CH_2Cl_2 (2.0 mL), and the mixture was stirred at rt for 5 min. H_2 was introduced to the resulting solution in a Schlenk tube. After stirring at rt for 0.5 h, the resulting solution was concentrated to dryness and dissolved in $(\text{CH}_2\text{Cl})_2$ (0.5 mL). To this solution was added dropwise a solution of **1a** (70.9 mg, 0.300 mmol) and **2a** (57.5 mg, 0.330 mmol) in $(\text{CH}_2\text{Cl})_2$ at rt and washed remaining substrates away by using $(\text{CH}_2\text{Cl})_2$ (1.0 mL). The mixture was stirred at 50 °C for 3 h. The resulting solution was concentrated and purified by preparative TLC (hexane:ethyl acetate = 5:1), which furnished **3aa** (116.5 mg, 0.284 mmol, 95% yield) as a pale yellow oil.

3-Acetyl-4-(2,2-bisethoxycarbonyl-1-methylvinyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3aa, Table 1, entry 1, 95% yield)

IR (neat) 2957, 1732, 1666, 1247, 735 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 4.27 (q, $J = 7.2$ Hz, 2H), 4.12 (q, $J = 7.2$ Hz, 2H), 3.75 (s, 6H), 3.38–3.32 (m, 4H), 2.21 (s, 3H), 2.18 (s, 3H), 1.30 (t, $J = 7.2$ Hz, 3H), 1.19 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 195.1, 171.1, 164.3, 163.8, 150.8, 149.6, 134.1, 125.9, 61.3, 61.2, 57.0, 53.0, 45.0, 41.0, 28.5, 19.7, 13.9, 13.8; HRMS (EI) calcd for $\text{C}_{20}\text{H}_{26}\text{O}_9$ $[\text{M}-\text{CO}_2\text{Et}]^+$ 337.1288, found 337.1198.

3-Acetyl-4-(2-ethoxycarbonyl-1-methyl-2-phenylvinyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethylester (3ab, Table 1, entry 2, 98% yield, $E:Z = 1:2$)

Pale yellow oil; IR (neat) 2954, 1738, 1660, 1268, 732 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.42–7.30 (m, 3H), 7.29–7.23 (m, 2H), 4.09 (q, $J = 7.2$ Hz, 2H), 3.78 (s, 6H), 3.47 (t, $J = 1.5$ Hz, 2H), 3.38 (t, $J = 1.5$ Hz, 2H), 2.33 (s, 3H), 1.87 (s, 3H), 1.14 (t, $J = 7.2$ Hz, 3H); E -isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 7.29–7.23 (m, 3H), 7.16–7.10 (m, 2H), 4.22 (q, $J = 7.2$ Hz, 2H), 3.65 (s, 6H), 3.16 (t, $J = 1.5$ Hz, 2H), 3.09 (t, $J = 1.5$ Hz, 2H), 2.23 (s, 3H), 2.19 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 195.6, 171.5, 171.2, 167.8, 166.8, 152.7, 150.6, 141.9, 140.5, 136.2, 135.8, 135.2, 133.4, 132.2, 132.1, 129.0, 128.29, 128.25, 128.0, 127.7, 127.6, 60.9, 57.0, 56.6, 53.0, 45.7, 45.1, 41.1, 28.7, 28.6, 20.2, 19.8, 14.1, 13.9; HRMS (EI) calcd for $\text{C}_{23}\text{H}_{26}\text{O}_7$ $[\text{M}]^+$ 414.1679, found 414.1733.

3-Acetyl-4-(2-ethoxycarbonyl-1-methylpropenyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3ac, Table 1, entry 3, 99% yield, $E:Z = 6:1$)

Pale yellow oil; IR (neat) 2955, 1737, 1660, 1250, 773 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 4.02 (q, $J = 7.2$ Hz, 2H), 3.69 (s, 6H), 3.25 (s, 4H), 2.07 (s, 3H), 1.91 (s, 3H), 1.88 (s, 3H), 1.13 (t, $J = 7.2$ Hz, 3H); Z -isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 4.19 (q, $J = 7.2$ Hz, 2H), 3.69 (s, 6H), 3.31–3.29 (m, 2H), 3.21–3.19 (m, 2H), 2.17 (s, 3H), 2.07 (s, 3H), 1.76–1.72 (m, 3H), 1.28 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 171.6, 171.6, 171.5, 167.4, 154.1, 141.0, 132.3, 126.0, 60.5, 56.8, 56.3, 53.0, 52.9, 45.5, 45.2, 41.1, 40.9, 28.3, 28.1, 19.3, 16.6, 15.1, 14.1, 14.0; HRMS (EI) calcd for $\text{C}_{18}\text{H}_{24}\text{O}_7$ $[\text{M}]^+$ 352.1522, found 352.1537.

3-Acetyl-4-(1-methyl-2-phenylvinyl)cyclopent-3-ene-1,1-dicarboxylic acid

dimethyl ester (**3ad**, Table 1, entry 4, 97% yield, *E:Z* = 9:1)

Pale yellow oil; IR (neat) 2954, 1737, 1686, 1267, 733 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.40–7.16 (m, 5H), 6.44 (s, 1H), 3.77 (s, 6H), 3.40 (s, 4H), 2.29 (s, 3H), 2.07 (s, 3H); *Z*-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 7.40–7.16 (m, 5H), 6.41 (s, 1H), 3.72 (s, 6H), 3.37 (t, J = 1.8 Hz, 2H), 3.30 (t, J = 1.8 Hz, 2H), 2.22 (s, 3H), 2.07 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 197.8, 196.0, 171.6, 171.5, 153.0, 151.6, 136.4, 136.2, 135.4, 134.7, 133.1, 133.0, 130.5, 128.8, 128.4, 128.2, 127.6, 127.1, 127.0, 56.3, 56.0, 52.9, 52.8, 45.5, 44.9, 41.6, 41.2, 29.1, 28.0, 24.5, 16.9; HRMS (EI) calcd for $\text{C}_{20}\text{H}_{22}\text{O}_5$ $[\text{M}]^+$ 342.1467, found 342.1513.

3-Acetyl-4-(1-methylbuta-1,3-dienyl)cyclopent-3-ene-1,1-dicarboxylic acid diethyl ester (3ae, Table 1, entry 5, 55% yield, *E:Z* = >20:1)

Yellow oil; IR (neat) 2954, 1735, 1660, 1266, 736 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.64–6.52 (m, 1H), 6.00–5.97 (m, 1H), 5.28–5.20 (m, 2H), 3.73 (s, 6H), 3.32 (t, J = 1.8 Hz, 2H), 3.28 (t, J = 1.8 Hz, 2H), 2.18 (s, 3H), 1.91 (d, J = 1.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 198.2, 171.7, 151.9, 134.7, 132.6, 132.0, 131.4, 119.6, 56.4, 53.0, 45.3, 41.7, 29.2, 29.1, 15.7; HRMS (EI) calcd for $\text{C}_{16}\text{H}_{20}\text{O}_5$ $[\text{M}]^+$ 292.1311, found 292.1280.

3-Acetyl-4-(1,2-dimethylpropenyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3af) and 1,3,3,4-tetramethyl-3,5-dihydro-7*H*-cyclopenta[*c*]pyran-6,6-dicarboxylic acid dimethyl ester (3af, Table 1, entry 6, 51% yield, dienone:ether = 3:1)

Pale yellow oil; IR (neat) 2954, 1732, 1659, 1619, 733 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 3.72 (s, 6H), 3.30 (s, 2H), 3.18 (s, 2H), 2.16 (d, J = 0.3 Hz, 3H), 1.77 (s, 3H), 1.70 (s, 3H), 1.57 (s, 3H); ether-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 3.71 (s, 6H), 2.94 (s, 2H), 2.90 (s, 2H), 1.73 (s, 3H), 1.59 (s, 3H), 1.24 (s, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 196.8,

171.9, 155.0, 141.7, 134.4, 129.3, 128.8, 124.4, 117.3, 78.9, 59.6, 56.0, 52.9, 52.7, 45.9, 40.8, 39.0, 36.9, 35.6, 34.04, 34.01, 27.6, 24.7, 21.4, 19.7, 17.3, 17.0, 14.2; HRMS (EI) calcd for C₁₆H₂₂O₅ [M]⁺ 294.1467, found 294.1415.

2-[1-{4-Acetyl-1-(toluene-4-sulfonyl)-2,5-dihydro-1H-pyrrol-3-yl}ethylidene]malonic acid diethyl ester (3ba, Table 1, entry 8, 88% yield)

Pale yellow oil; IR (neat) 2983, 1726, 1668, 1350, 1166 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 8.4 Hz, 2H), 4.43–4.39 (m, 2H), 4.38–4.33 (m, 2H), 4.28 (q, *J* = 7.2 Hz, 2H), 3.48 (q, *J* = 7.2 Hz, 2H), 2.44 (s, 3H), 2.18 (s, 3H), 2.11 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 193.3, 163.9, 163.2, 146.6, 146.3, 143.8, 133.4, 132.1, 129.8, 127.7, 127.5, 61.6, 61.4, 58.2, 55.3, 28.4, 21.4, 19.9, 13.9, 13.6; HRMS (EI) calcd for C₂₂H₂₇NO₇S [M]⁺ 449.1508, found 449.1466.

2-[1-(4-Propionyl-2,5-dihydrofuran-3-yl)propylidene]malonic acid diethyl ester (3ca, Table 1, entry 9, 84% yield)⁸

Pale yellow oil; ¹H NMR (CDCl₃, 300 MHz) δ 4.93 (t, *J* = 4.5 Hz, 2H), 4.84 (t, *J* = 4.5 Hz, 2H), 4.28 (q, *J* = 7.2 Hz, 2H), 4.14 (q, *J* = 7.2 Hz, 2H), 2.56 (q, *J* = 7.2 Hz, 2H), 2.50 (q, *J* = 7.2 Hz, 2H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H), 1.03 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 196.7, 164.4, 163.7, 152.5, 146.6, 134.2, 126.7, 79.5, 76.7, 61.51, 61.46, 34.7, 27.9, 14.0, 13.9, 12.3, 7.4.

3-Acetyl-4-(1-methyl-4-phenylbut-1-en-3-ynyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3ah, Scheme 1, 90% yield, *E:Z* = >20:1)

Pale yellow oil; IR (neat) 2954, 1736, 1660, 1265, 759 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.48–7.42 (m, 2H), 7.36–7.30 (m, 3H), 5.73–5.71 (m, 1H), 3.76 (s, 6H), 3.37 (t, J = 1.8 Hz, 2H), 3.33 (t, J = 1.8 Hz, 2H), 2.28 (s, 3H), 2.14 (d, J = 1.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 198.1, 171.4, 148.6, 144.1, 135.7, 131.3, 128.3, 128.2, 123.0, 111.3, 96.5, 86.2, 56.4, 53.0, 45.0, 42.0, 29.3, 18.5; HRMS (EI) calcd for $\text{C}_{21}\text{H}_{19}\text{O}_4$ $[\text{M}-\text{OMe}]^+$ 335.1283, found 335.1332.

5-Acetyl-4,7-dimethyl-6-phenylindan-2,2-dicarboxylic acid dimethyl ester (4, Scheme 1, 99% yield)

Colorless solid; Mp 160.0–161.2 $^{\circ}\text{C}$; IR (neat) 2953, 1737, 1694, 1248, 733 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.40–7.30 (m, 3H), 7.19–7.14 (m, 2H), 3.79 (s, 6H), 3.61 (s, 4H), 2.15 (s, 3H), 2.00 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 207.7, 172.1, 142.1, 139.5, 138.9, 138.4, 136.6, 130.1, 129.1, 128.2, 127.3, 125.7, 59.1, 53.0, 40.3, 40.0, 32.1, 16.5, 16.0; HRMS (EI) calcd for $\text{C}_{21}\text{H}_{21}\text{O}_3$ $[\text{M}-\text{CO}_2\text{Me}]^+$ 321.1491, found 321.1527.

3-Acetyl-4-(2-ethoxycarbonyl-1-methyl-4-phenylbut-1-en-3-ynyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3aj, Scheme 1, 96% yield, $E:Z$ = 1:>20)

Pale yellow oil; IR (neat) 2954, 1737, 1661, 1255, 759 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.50–7.42 (m, 2H), 7.34–7.28 (m, 3H), 4.14 (q, J = 7.2 Hz, 2H), 3.73 (s, 6H), 3.37–3.32 (m, 4H), 2.28 (s, 3H), 2.16 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 195.1, 171.2, 163.5, 153.9, 151.5, 132.8, 131.4, 128.5, 128.2, 122.6, 114.6, 96.4, 84.1, 61.2, 57.2, 52.9, 45.1, 40.9, 28.6, 22.3, 13.9; HRMS (EI) calcd for $\text{C}_{25}\text{H}_{26}\text{O}_7$ $[\text{M}]^+$ 438.1679, found 438.1714.

III. Rh-Catalyzed Reactions of 1,6-Diynes with Arylketones (Table 2 and Schemes 2,3)

General Procedure (Table 2, entry 1). Segphos (9.2 mg, 0.015 mmol) and $[\text{Rh}(\text{cod})_2]\text{BF}_4$ (6.1 mg, 0.015 mmol) were dissolved in CH_2Cl_2 (2.0 mL), and the mixture was stirred at rt for 5 min. H_2 was introduced to the resulting solution in a Schlenk tube.

After stirring at rt for 0.5 h, the resulting solution was concentrated to dryness and dissolved in CH₂Cl₂ (0.5 mL). To this solution was added dropwise a solution of **1a** (70.9 mg, 0.300 mmol) and **2k** (360.5 mg, 3.00 mmol) in CH₂Cl₂ at rt and washed remaining substrates away by using CH₂Cl₂ (1.0 mL). The mixture was stirred at rt for 3 h. The resulting solution was concentrated and purified by silica gel column chromatography (CH₂Cl₂:hexane = 1:1) followed by preparative TLC (hexane:ethyl acetate = 5:1), which furnished **5ak** (93.6 mg, 0.263 mmol, 88% yield) as a pale yellow oil.

3-[1-(2-Acetylphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid dimethyl ester (5ak**, Table 2, entry 1, 88% yield, *E:Z* = 1:>20)**

IR (neat) 2954, 1736, 1690, 1253, 733 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.63–7.61 (m, 1H), 7.47–7.42 (m, 1H), 7.34–7.29 (m, 1H), 7.12–7.09 (m, 1H), 4.55–4.45 (m, 1H), 3.78–2.74 (m, 6H), 3.12 (s, 2H), 2.94 (s, 2H), 2.42 (s, 3H), 2.02 (s, 3H), 1.40 (d, *J* = 7.2 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 201.4, 172.0, 171.8, 143.4, 138.1, 136.3, 132.5, 131.8, 129.4, 129.3, 128.5, 126.7, 121.1, 56.8, 52.72, 52.68, 39.8, 38.0, 28.7, 24.0, 15.2; HRMS (EI) calcd for C₂₀H₂₁O₄ [M–OMe]⁺ 325.1440, found 325.1512.

3-[1-(2-Acetyl-5-methoxyphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid dimethyl ester (5al**, Table 2, entry 2, 89% yied, *E:Z* = 1:5)**

Although crude NMR showed only *E*-isomer, *E/Z* isomerization occurred during isolation by silica gel chromatography. Pale yellow oil; IR (neat) 2954, 1736, 1681, 1257, 733 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.73 (d, *J* = 9.0 Hz, 1H), 6.82 (dd, *J* = 9.0, 2.7 Hz, 1H), 6.58 (d, 2.7 Hz, 1H), 4.62–4.54 (m, 1H), 3.83 (s, 3H), 3.76 (s, 6H), 3.11 (s, 2H), 2.94 (s, 2H), 2.40 (s, 3H), 2.01 (s, 3H), 1.42 (d, *J* = 6.9 Hz, 3H); *Z*-isomer: ¹H NMR (CDCl₃, 300 MHz) δ 7.73 (d, *J* = 9.0 Hz, 1H), 6.82 (dd, *J* = 9.0, 2.7 Hz, 1H), 6.61 (d, *J* = 2.7 Hz, 1H), 5.93–5.86 (m, 1H), 3.85 (s, 3H), 3.68 (s, 3H), 3.66 (s, 3H), 3.06 (s, 2H), 3.02 (s, 2H), 2.44 (s, 3H), 2.16 (s, 3H), 1.80 (d, *J* = 6.9 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 198.9, 172.0, 171.8, 162.2, 146.5, 137.7, 136.2, 131.9, 131.7, 131.6, 130.1, 130.0, 122.4, 120.9, 114.3, 111.9, 111.8, 56.9, 56.8, 55.2, 52.70, 52.66, 52.6, 40.7, 39.8, 38.1, 38.0, 28.6, 28.4, 23.9, 22.7, 15.4, 15.3; HRMS (EI) calcd for C₂₂H₂₆O₆ [M]⁺ 386.1729, found 386.1675.

3-Ethylidene-4-[1-(2-propionylphenyl)ethylidene]cyclopentane-1,1-dicarboxylic acid dimethyl ester (5an, Table 2, entry 4, 94% yield, *E:Z* = 1:2)

Although crude NMR showed only *E*-isomer, *E/Z* isomerization occurred during isolation by silica gel chromatography. Yellow oil; IR (neat) 2954, 1737, 1692, 1436, 1255, 648 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.59–7.54 (m, 1H), 7.47–7.39 (m, 1H), 7.34–7.27 (m, 1H), 7.14–7.08 (m, 1H), 4.55–4.45 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.10 (s, 2H), 2.92 (s, 2H), 2.87–2.69 (m, 2H), 2.01 (s, 3H), 1.40 (d, J = 6.9 Hz, 3H), 1.10 (t, J = 7.2 Hz, 3H); vinyl, Me, and Et protons of *E*-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 5.92–5.83 (m, 1H), 2.87–2.69 (m, 2H), 2.16 (s, 3H), 1.79 (d, J = 7.2 Hz, 3H), 1.12 (t, J = 7.2 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 205.2, 204.6, 172.1, 171.8, 144.3, 143.2, 138.5, 138.4, 137.7, 136.4, 133.6, 132.2, 131.5, 131.1, 130.9, 129.6, 129.5, 129.0, 128.1, 126.73, 126.66, 122.6, 121.0, 57.0, 56.8, 52.8, 52.7, 52.6, 40.9, 39.8, 38.1, 38.0, 34.5, 34.1, 24.2, 23.1, 15.5, 15.3, 8.5, 8.4; HRMS (EI) calcd for $\text{C}_{22}\text{H}_{26}\text{O}_5$ $[\text{M}]^+$ 370.1780, found 370.1761.

3-Ethylidene-4-[1-(2-isobutyrylphenyl)ethylidene]cyclopentane-1,1-dicarboxylic acid dimethyl ester (5ao, Table 2, entry 5, 82% yield, *E:Z* = 1:>20)

Pale yellow oil; IR (neat) 2972, 1737, 1690, 1253, 734 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.56–7.50 (m, 1H), 7.46–7.38 (m, 1H), 7.34–7.27 (m, 1H), 7.14–7.09 (m, 1H), 4.58–4.47 (m, 1H), 3.77–3.75 (m, 6H), 3.28 (sept, J = 6.9 Hz, 1H), 3.17–3.04 (m, 2H), 2.98–2.84 (m, 2H), 2.00 (s, 3H), 1.40 (d, J = 7.2 Hz, 3H), 1.07 (dd, J = 13.2, 7.2 Hz, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 208.3, 172.1, 143.4, 137.9, 136.3, 132.0, 131.3, 129.7, 129.5, 128.4, 126.6, 121.1, 56.8, 52.7, 39.8, 38.13, 38.11, 24.1, 19.1, 18.7, 15.2; HRMS (EI) calcd for $\text{C}_{23}\text{H}_{28}\text{O}_5$ $[\text{M}]^+$ 384.1937, found 384.1959.

3-[1-(2-Benzoylphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid dimethyl ester (5ap, Table 2, entry 6, 97% yield, *E:Z* = 1:9)

Although crude NMR showed only *E*-isomer, *E/Z* isomerization occurred during isolation by silica gel chromatography. Pale yellow oil; IR (neat) 2954, 1736, 1665, 1263, 733 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.66–7.63 (m, 2H), 7.55–7.19 (m, 7H), 4.73–4.62 (m, 1H), 3.68 (s, 3H), 3.66 (s, 3H), 3.02–2.86 (m, 2H), 2.68–2.52 (m, 2H), 1.88 (s, 3H), 1.42 (d, $J = 6.9$ Hz, 3H); vinyl and Me protons of *E*-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 5.40–5.32 (m, 1H), 1.92 (s, 3H), 1.65 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 197.2, 172.0, 171.6, 143.9, 137.8, 137.7, 134.0, 132.3, 130.1, 129.6, 129.4, 129.3, 129.2, 128.3, 127.9, 127.8, 126.0, 121.4, 56.6, 52.59, 52.56, 39.3, 37.5, 23.9, 15.2; HRMS (EI) calcd for $\text{C}_{25}\text{H}_{23}\text{O}_4$ [$\text{M}-\text{OMe}$] $^+$ 387.1596, found 387.1581.

1-[2-{1-(4-Ethylidene-1-(toluene-4-sulfonyl)pyrrolidin-3-ylidene)ethyl}phenyl]ethanone (5bk, Table 2, entry 7, 84% yield, *E:Z* = 1:>10)

Although crude NMR showed only *E*-isomer, *E/Z* isomerization occurred during isolation by silica gel chromatography. Pale yellow solid; Mp 73.8–74.5 $^{\circ}\text{C}$; IR (neat) 2983, 1686, 1346, 1164, 670 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.79–7.67 (m, 3H), 7.46 (dt, $J = 7.5, 1.5$ Hz, 1H), 7.38–7.32 (m, 3H), 7.01 (dd, $J = 7.8, 1.2$ Hz, 1H), 4.43–4.34 (m, 1H), 4.19–4.13 (m, 1H), 4.01–3.92 (m, 2H), 3.84–3.77 (m, 1H), 2.46 (s, 3H), 2.40 (s, 3H), 1.92 (s, 3H), 1.33 (d, $J = 7.2$ Hz, 3H); vinyl and Me protons of *E*-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 5.90–5.82 (m, 1H), 2.43 (s, 3H), 2.42 (s, 3H), 2.11 (s, 3H), 1.73 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 200.1, 143.7, 142.7, 137.1, 133.4, 133.0, 132.6, 130.8, 129.7, 129.6, 129.3, 129.2, 128.2, 127.8, 127.3, 122.4, 120.5, 52.7, 51.5, 28.6, 23.7, 21.5, 15.3; HRMS (EI) calcd for $\text{C}_{23}\text{H}_{25}\text{NO}_3\text{S}$ [M] $^+$ 395.1555, found 395.1541.

1-{2-[1-(4-Ethylidenedihydrofuran-3-ylidene)ethyl]-4-methoxyphenyl}ethanone (5dl, Table 2, entry 8, 69% yield, *E:Z* = 1:>10)

Although crude NMR showed only *E*-isomer, *E/Z* isomerization occurred during isolation by silica gel chromatography. Colorless oil; IR (neat) 2940, 1682, 1596, 1131, 731 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.81 (d, J = 8.7 Hz, 1H), 6.86 (dd, J = 8.7, 2.7 Hz, 1H), 6.65 (d, J = 2.7 Hz, 1H), 4.64–4.55 (m, 2H), 4.54–4.39 (m, 3H), 3.85 (s, 3H), 2.46 (s, 3H), 1.94 (s, 3H), 1.38 (d, J = 6.9 Hz, 3H); phenyl, vinyl, and Me protons of *E*-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 7.74 (d, J = 8.7 Hz, 1H), 6.83 (dd, J = 2.7 Hz, 1H), 6.62 (d, J = 2.7 Hz, 1H), 5.96–5.89 (m, 1H), 3.84 (s, 3H), 2.20 (s, 3H), 1.76 (d, J = 6.9 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 198.4, 162.9, 145.8, 136.3, 132.1, 132.0, 130.1, 129.6, 128.2, 119.7, 117.6, 114.3, 112.4, 105.6, 72.8, 71.8, 55.4, 28.5, 23.4, 22.1, 15.4; HRMS (EI) calcd for $\text{C}_{17}\text{H}_{20}\text{O}_3$ $[\text{M}]^+$ 272.1421, found 272.1356.

1-[2-{1-(4-Ethylfuran-3-yl)ethyl}-4-methoxyphenyl]ethanone (6, Scheme 2, 71% yield)

Colorless oil; IR (neat) 2966, 1674, 1604, 1046, 742 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.75–7.67 (m, 1H), 7.30–7.27 (m, 1H), 7.15–7.11 (m, 1H), 6.70–6.60 (m, 2H), 4.94 (dq, J = 7.2, 1.2 Hz, 1H), 3.75 (s, 3H), 2.58 (s, 3H), 2.12–1.98 (m, 1H), 1.94–1.81 (m, 1H), 1.48 (d, J = 6.9 Hz, 3H), 0.96 (t, J = 7.5 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 200.3, 162.1, 149.5, 139.6, 139.1, 132.0, 129.64, 129.61, 126.6, 114.6, 110.2, 55.1, 31.0, 29.6, 22.0, 16.7, 13.0; HRMS (EI) calcd for $\text{C}_{17}\text{H}_{20}\text{O}_3$ $[\text{M}]^+$ 272.1421, found 272.1356.

3-[1-(2-Acetyl-4-methoxyphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid diethyl ester (5aq, Scheme 3, 95% yield, *E:Z* = 1:6)

Although crude NMR showed only *E*-isomer, *E/Z* isomerization occurred during isolation by silica gel chromatography. Pale yellow oil; IR (neat) 2954, 1736, 1691, 1283,

734 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.15–7.11 (m, 1H), 6.99–6.96 (m, 2H), 4.62–4.53 (m, 1H), 3.82 (s, 3H), 3.74 (s, 6H), 3.06 (s, 2H), 2.92 (s, 2H), 2.38 (s, 3H), 1.97 (s, 3H), 1.41 (d, $J = 6.9$ Hz, 3H); vinyl, Me, and OMe protons of *E*-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 5.88–5.79 (m, 1H), 3.64 (s, 3H), 2.40 (s, 3H), 2.14 (s, 3H), 1.77 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 201.5, 172.1, 171.9, 158.1, 139.2, 136.4, 135.8, 133.0, 130.6, 129.0, 121.2, 118.1, 117.7, 113.2, 56.8, 55.3, 52.79, 52.77, 40.0, 38.2, 28.8, 24.4, 23.3, 15.4; HRMS (EI) calcd for $\text{C}_{22}\text{H}_{26}\text{O}_6$ $[\text{M}]^+$ 386.1729, found 386.1735.

3-[1-(2-Acetyl-4,6-dimethoxyphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid diethyl ester (5ar, Scheme 3, 44% yield, *E:Z* = 1:>20, 39% ee)

Pale yellow oil; $[\alpha]_D^{25} +5.47$ (c 1.18, CHCl_3 , 39% ee) IR (neat) 2954, 1736, 1695, 1206, 733 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.59 (d, $J = 2.4$ Hz, 1H), 6.57 (d, $J = 2.4$ Hz, 1H), 4.68–4.57 (m, 1H), 3.83 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 3.74 (s, 3H), 3.15 (d, $J = 16.2$ Hz, 1H), 3.04 (d, $J = 16.2$ Hz, 1H), 2.91 (s, 2H), 2.33 (s, 3H), 1.97 (s, 3H), 1.44 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 202.5, 172.1, 172.0, 159.3, 157.6, 141.2, 136.6, 134.3, 125.3, 123.8, 120.1, 103.3, 101.6, 56.8, 56.0, 55.4, 52.9, 52.8, 40.0, 38.2, 29.3, 23.1, 15.4; HRMS (EI) calcd for $\text{C}_{22}\text{H}_{25}\text{O}_6$ $[\text{M}-\text{OMe}]^+$ 385.1651, found 385.1643. CHIRALPAK AD-H, hexane:2-PrOH = 95:5, 1.0 mL/min, retention times: 12.7 min (major isomer) and 14.6 min (minor isomer).

3-Acetyl-4-[2-(3,5-dimethoxyphenyl)-1-methylpropenyl]cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3ar, Scheme 3, 30% yield, *E:Z* = 2:1)

Pale yellow oil; IR (neat) 2954, 1735, 1659, 1591, 704 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 6.73 (t, $J = 2.4$ Hz, 1H), 6.28 (d, $J = 2.4$ Hz, 2H), 3.79 (s, 6H), 3.76 (s, 6H), 3.40–3.36 (m, 2H), 3.35–3.31 (m, 2H), 2.33 (s, 3H), 1.90–1.85 (m, 3H), 1.78–1.72 (m, 3H); *Z*-isomer: ^1H NMR (CDCl_3 , 300 MHz) δ 6.28 (t, $J = 2.1$ Hz, 1H), 6.20 (d, $J = 2.1$ Hz, 2H), 3.71 (s, 6H), 3.63 (s, 6H), 3.18–3.14 (m, 2H), 3.05–3.00 (m, 2H), 2.26 (s, 3H), 2.06–2.02

(m, 3H), 1.90–1.83 (m, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 196.4, 196.3, 171.9, 171.5, 160.7, 160.2, 154.3, 153.8, 145.3, 144.6, 134.9, 134.7, 134.0, 127.7, 127.6, 105.9, 105.2, 99.2, 98.3, 56.3, 56.1, 55.3, 55.1, 53.0, 52.8, 46.0, 41.0, 28.4, 28.0, 21.7, 20.6, 19.1, 19.0; HRMS (EI) calcd for $\text{C}_{22}\text{H}_{25}\text{O}_6$ $[\text{M}-\text{OMe}]^+$ 385.1651, found 385.1643.

IV. References

- (1) Duong, H. A.; Cross, M. J.; Louie, J. *J. Am. Chem. Soc.* **2004**, *126*, 11438.
- (2) Tanaka, K.; Suzuki, N.; Nishida, G. *Eur. J. Org. Chem.* **2006**, 3917.
- (3) Tanaka, K.; Takeishi, K.; Noguchi, K. *J. Am. Chem. Soc.* **2006**, *128*, 4586.
- (4) Tekevac, T. N.; Zuo, G.; Simon, K.; Louie, J. *J. Org. Chem.* **2006**, *71*, 5834.
- (5) Creary, X. *J. Org. Chem.* **1987**, *52*, 5026.
- (6) Journet, M.; Cai, D.; DiMichele, L. M.; Larsen, R. D. *Tetrahedron Lett.* **1998**, *39*, 6427.
- (7) Guo, M.; Li, D.; Zhang, Z. *J. Org. Chem.* **2003**, *68*, 10172.
- (8) Takahashi, T.; Li, Y.; Ito, T.; Xu, F.; Nakajima, K.; Liu, Y. *J. Am. Chem. Soc.* **2002**, *124*, 1144.

3-Acetyl-4-(2,2-bisethoxycarbonyl-1-methylvinyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3aa)

3-Acetyl-4-(2-ethoxycarbonyl-1-methyl-2-phenylvinyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethylester (3ab, *E:Z* = 1:2)

3-Acetyl-4-(2-ethoxycarbonyl-1-methylpropenyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3ac, *E:Z* = 6:1)

3-Acetyl-4-(1-methyl-2-phenylvinyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3ad, *E:Z* = 9:1)

3-Acetyl-4-(1-methylbuta-1,3-dienyl)cyclopent-3-ene-1,1-dicarboxylic acid diethyl ester (3ae, *E:Z* = >20:1)

3-Acetyl-4-(1,2-dimethylpropenyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3af) and 1,3,3,4-tetramethyl-3,5-dihydro-7H-cyclopenta[c]pyran-6,6-dicarboxylic acid dimethyl ester (3af, dienone:ether = 3:1)

2-[1-{4-Acetyl-1-(toluene-4-sulfonyl)-2,5-dihydro-1*H*-pyrrol-3-yl}ethylidene]malonic acid diethyl ester (3ba)

2-[1-(4-Propionyl-2,5-dihydrofuran-3-yl)propylidene]malonic acid diethyl ester (3ca)

3-Acetyl-4-(1-methyl-4-phenylbut-1-en-3-ynyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3ah, *E:Z* = >20:1)

5-Acetyl-4,7-dimethyl-6-phenylindan-2,2-dicarboxylic acid dimethyl ester (4)

3-Acetyl-4-(2-ethoxycarbonyl-1-methyl-4-phenylbut-1-en-3-ynyl)cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3aj, *E:Z* = 1:>20)

3-[1-(2-Acetylphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic dimethyl ester (5ak, *E:Z* = >20:1) acid

3-[1-(2-Acetyl-5-methoxyphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid dimethyl ester (5al, *E:Z* = 5:1)

3-Ethylidene-4-[1-(2-propionylphenyl)ethylidene]cyclopentane-1,1-dicarboxylic acid dimethyl ester (5an, *E:Z* = 2:1)

3-Ethylidene-4-[1-(2-isobutyrylphenyl)ethylidene]cyclopentane-1,1-dicarboxylic acid dimethyl ester (5ao, *E:Z* = >20:1)

3-[1-(2-Benzoylphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic dimethyl ester (5ap, *E:Z* = 4:1) acid

1-[2-{1-(4-Ethylidene-1-(toluene-4-sulfonyl)pyrrolidin-3-ylidene)ethyl}phenyl]ethanone (5bk, *E:Z* = >20:1)

**1-{2-[1-(4-Ethylidenedihydrofuran-3-ylidene)ethyl]-4-methoxyphenyl}ethanone (5dl,
E:Z = 18:82)**

1-[2-{1-(4-Ethylfuran-3-yl)ethyl}-4-methoxyphenyl]ethanone (6)

3-[1-(2-Acetyl-4-methoxyphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid diethyl ester (5aq, *E:Z* = 6:1)

3-[1-(2-Acetyl-4,6-dimethoxyphenyl)ethylidene]-4-ethylidenecyclopentane-1,1-dicarboxylic acid diethyl ester (5ar, *E:Z* = >20:1)

3-Acetyl-4-[2-(3,5-dimethoxyphenyl)-1-methylpropenyl]cyclopent-3-ene-1,1-dicarboxylic acid dimethyl ester (3ar, *E:Z* = 2:1)