Synthesis of Functionalized Olefins via Cross and Ring-Closing Metatheses

Arnab K. Chatterjee, John P. Morgan, Matthias Scholl,
and Robert H. Grubbs*

Contribution from the Arnold and Mabel Beckman Laboratory of Chemical Synthesis,
Division of Chemistry and Chemical Engineering, California Institute of Technology,
Pasadena, CA 91125

Supporting Material

Experimental procedures and characterization (1H and 13C NMR, HRMS/elemental analysis, FTIR) employed in the preparation of cross and ring-closing metathesis products. 1H NMR spectra for 3, 15, 16, 17, 18, 22, 23, 24 (8 pages). 13C NMR spectra for 15, 16, 17, 18 (4 pages), 31P NMR spectra for 3 (1 page).

General Experimental Section. NMR spectra were recorded on either a JEOL GX-400 or GE-300 NMR. Chemical shifts are reported in parts per million
(ppm) downfield from tetramethylsilane (TMS) with reference to internal solvent. Multiplicities are abbreviated as follows: singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), and multiplet (m). The reported $^1$H NMR data refer to the major olefin isomer unless stated otherwise. The reported $^{13}$C NMR data include all peaks observed and no peak assignments were made. High-resolution mass spectra (EI and FAB) were provided by the UCLA Mass Spectrometry Facility (University of California, Los Angeles).

Analytical thin-layer chromatography (TLC) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness) with a fluorescent indicator. Flash column chromatography was performed using silica gel 60 (230-400 mesh) from EM Science. All other chemicals were purchased from the Aldrich, Strem, or Nova Biochem Chemical Companies, and used as delivered unless noted otherwise. CH$_2$Cl$_2$ was purified by passage through a solvent column prior to use.

NMR scale experiments were performed in J. Young valve NMR tubes under an N$_2$ atmosphere with 20 equivalents of functionalized olefin to 1 equivalent of catalyst 3 in CD$_2$Cl$_2$.

**Compound 3.** A 250-mL flame-dried round bottom flask equipped with a magnetic stirbar was charged with 1,3-dimesityl-4,5-dihydro-imidazolium tetrafluoroborate (3.08 g, 7.80 mmol, 1.6 equiv.) and dry THF (30 mL) under nitrogen atmosphere. A solution of potassium tert-butoxide (0.88 g, 7.80 mmol, 1.6 equiv.) in dry THF (30 mL) was slowly added at room temperature. The reaction mixture was allowed to stir for 1/2 hour and was then slowly transferred to a 500-mL flame-dried Schlenk flask containing a solution of RuCl$_2$(=CH=C(CH$_3$)$_2$)(PC$_5$)$_2$ (3.50 g, 4.88 mmol, 1.0 equiv.) in dry toluene (200 mL). This mixture was stirred at 80°C for 15 min, at which point
the reaction was complete as indicated by \(^1^H\) NMR. The reaction mixture was filtered through a glass frit under argon and all volatiles were removed under high vacuum. The residue was recrystallized three times from anhydrous methanol (40 mL) at \(-78^\circ\)C to give 3 as a pinkish-brown microcrystalline solid (2.95 g) in 77% yield: \(^1^H\) NMR (\(\text{C}_6\text{H}_6\), 400 MHz) \(\delta\) 19.16 (d, \(J = 11\) Hz, 1H), 7.71 (d, \(J = 11\) Hz, 1H), 6.89 (s, 2H), 6.62 (s, 2H), 3.36-3.24 (m, 4H), 2.80 (s, 6H), 2.54 (s, 6H), 2.41-1.26 (br m, 27H), 2.20 (s, 3H), 2.02 (s, 3H), 1.06 (s, 3H), 0.90 (s, 3H); \(^{31}\)P NMR (\(\text{C}_6\text{H}_6\), 161.9 MHz) \(\delta\) 28.05; HRMS (FAB) \(\text{C}_{41}\text{H}_{51}\text{Cl}_2\text{N}_2\text{PRu}[\text{M}^+]\) 784.2993, found 784.2963.

**Reaction of Compound 3 with ethyl vinyl ether.** After 8 hours at 45°C, catalyst 3 is only partially converted to a new Fischer carbene species. The new carbene species has the following characteristic resonances (CD\(_2\)Cl\(_2\)): \(^1^H\) NMR: 13.6 ppm; \(^{31}\)P NMR: 27.3 ppm. Some additional uncharacterized phosphine-containing products were observed by \(^{31}\)P NMR during the course of the reaction.

**Compound 13.** 9-Decen-1(tert-butyldimethylsilane)-yl (330 \(\mu\)L, 1.0 mmol) and Methyl methacrylate (55 \(\mu\)L, 0.51 mmol) were added simultaneously via syringe to a stirring solution of 3 (21 mg, 0.026 mmol, 5.2 mol %) in CH\(_2\)Cl\(_2\) (2.5 ml). The flask was fitted with a condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm), eluting with 9:1 hexane:ethyl acetate. A viscous oil was obtained (110 mg, 62% yield, \textit{trans/cis} as determined by relative heights at 143.2 and 143.1 ppm of \(^{13}\)C NMR spectra). \(^1^H\) NMR (300 MHz, CDCl\(_3\), ppm): \(\delta\) 6.75 (1H, m), 3.71 (3H, s), 3.57 (2H, t, \(J = 6.3\) Hz), 2.14 (2H, m), 1.81 (3H, app s), 1.50 – 1.05 (12H, broad m), 0.87 (9H, s), 0.02 (6H, s). \(^{13}\)C NMR (75 MHz, CDCl\(_3\), ppm): \(\delta\) 169.2,
143.2, 143.1, 128.0, 63.8, 52.1, 33.4, 30.0, 29.8, 29.2, 29.1, 26.5, 26.3, 18.9, 12.9. $R_f$
= 0.81 (9:1 hexane:ethyl acetate); HRMS (EI) calcd for C$_{19}$H$_{38}$O$_5$Si [M+ H]$^+$
343.2668, found 343.2677. Elemental analysis Calcd: C: 66.61, H: 11.18; Found: C:
66.47, H: 11.03.

**Compound 14.** 9-Decen-1-yl benzoate (145 µl, 0.52 mmol) and Methyl acrylate (90
µl, 1.0 mmol) were added simultaneously via syringe to a stirring solution of 3 (17
mg, 0.022 mmol, 4.2 mol %) in CH$_2$Cl$_2$ (2.5 ml). The flask was fitted with a
condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then
reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm),
eluting with 9:1 hexane:ethyl acetate. A white crystalline solid was obtained (151.4
mg, 91% yield, 4.5:1 trans/cis as determined by relative integrations of $^1$H peaks at
3.75 and 3.68 ppm). $^1$H NMR (300 MHz, CDCl$_3$, ppm): δ 8.01 (2H, app d, $J$ = 7.2
Hz), 7.50 (1H, m), 7.45 (2H, m), 6.93 (1H, dt, $J$ = 15.9 Hz, 6.9 Hz), 5.78 (1H, app d, $J$
= 15.9 Hz), 4.28 (2H, t, $J$ = 6.6 Hz), 3.68 (3H, s), 2.15 (2H, m), 1.74 (2H, p, $J$ = 6.6
Hz), 1.49 – 1.05 (10H, broad m). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): δ 167.5, 167.1,
150.0, 133.3, 131.1, 130.0, 128.8, 121.5, 65.5, 51.8, 32.7, 29.8, 29.5, 29.2, 28.5, 26.5.
$R_f$ = 0.40 (9:1 hexane:ethyl acetate); HRMS (EI) calcd for C$_{19}$H$_{26}$O$_4$ [M+ H]$^+$
319.1909, found 319.1914. Elemental analysis Calcd: C: 71.67, H: 8.23; Found: C:
71.31, H: 8.24.

**Compound 15.** A flame-dried round-bottomed flask equipped with reflux condenser
was charged with 5-acetoxy-1-hexene (184 mg, 1.3 mmol, 2.5 eq.), methacrolein (35
mg, 0.5 mmol, 1.0 eq.), and dichloromethane (2.5 mL). Catalyst 3 (20 mg, 25 µmol,
0.05 eq.) was subsequently added as a solid, producing a light brown solution which
was refluxed for 12 hours. The mixture was then concentrated in vacuo to a dark brown oil. Purification of this residue by silica gel chromatography (8:2 hexanes:ethyl acetate) allows isolation of 85 mg (0.46 mmol, 92%) of a clear oil (Rf = 0.44). This compound darkens rapidly (under one hour) in air at room temperature and/or in the presence of light, resulting in isomerization and production of uncharacterized polar side products. 1H NMR (400 MHz, CDCl3, ppm): δ 9.34 (1H, s), 6.43 (1H, t, J = 5.5 Hz), 4.02 (2H, t, J = 5.0 Hz), 2.34 (2H, t, J = 5.5 Hz), 1.99 (3H, s), 1.68 (3H, s), 1.65-1.50 (4 H, m). HRMS (EI) calcd. for C10H16O3 [M]+ 184.1099, found 184.1094.

**Compound 16.** A flame-dried round-bottomed flask equipped with reflux condenser was charged with 5-acetoxy-1-hexene (71 mg, 0.5 mmol, 1.0 eq.), acrolein (73 mt, 1.3 mmol, 2.6 eq.), and dichloromethane (2.5 mL). Catalyst 3 (20 mg, 25 μmol, 0.05 eq.) was subsequently added as a solid, producing a light brown solution which was refluxed for 12 hours. The mixture was then concentrated in vacuo to a dark brown oil. Purification of this residue by silica gel chromatography (9:1 hexanes:ethyl acetate) allows isolation of 52 mg (0.3 mmol, 62%) of a clear, colorless oil (Rf = 0.23). The title compound is produced as a mixture of isomers, trans:cis = 1:1 determined by integration of peaks at 9.50, 9.47, 7.03 and 6.83 ppm 1H NMR (300 MHz, CDCl3, ppm): δ 9.50 (1H, s), 9.47 (1H, s), 7.03 (1H, dt, J = 7.1, 18 Hz), 6.83 (1H, dt, J = 6.8, 15.6 Hz), 6.1 (1H, qt, J = 1.5, 8.1 Hz), 5.82 (1H, dt, J = 1.5, 15.6 Hz), 4.05 (2H, dt, J = 4.5, 6.3 Hz), 2.38 (2H, q, J = 6.9 Hz), 2.24 (2H, q, J = 6.9 Hz), 2.03 (3H, s), 1.69-1.52 (4H, m). 13C NMR (75 MHz, CDCl3, ppm): δ 194.0, 171.2, 157.9, 151.1, 133.2, 121.0, 63.9, 32.1, 31.7, 28.0, 24.2, 22.6, 20.9, 14.0. HRMS (EI) calcd. for C9H14O3 [M]+ 170.0943, found 170.0878.
**Compound 17.** A flame-dried round-bottomed flask equipped with reflux condenser was charged with 5-acetoxy-1-hexene (32 mg, 0.2 mmol, 1.0 eq.), phenyl vinyl ketone (60 mg, 0.5 mmol, 2.5 eq.), and dichloromethane (1 mL). Catalyst 3 (7 mg, 8 µmol, 0.04 eq.) was subsequently added as a solid, producing a light brown solution which was refluxed for 12 hours. The mixture was then concentrated *in vacuo* to a dark brown oil. Purification of this residue by silica gel chromatography (7:3 hexanes:ethyl acetate) allows isolation of 49 mg (0.2 mmol, 99%) of a thin, clear yellow oil (R<sub>f</sub> = 0.54). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 7.85 (1H, dd, J = 1.2, 6.9 Hz), 7.48 (2H, tt, J = 1.2, 7.2 Hz), 7.39 (2H, t, J = 7.5 Hz), 7.00 (1H, dt, J = 7.6, 15 Hz, *trans* isomer), 6.83 (1H, dt, J = 1.1, 15.6 Hz), 4.01 (2H, t, J = 6.3 Hz), 2.28 (2H, q, J = 6.9 Hz), 1.97 (3H, s), 1.64-1.49 (4H, m). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>, ppm): δ 190.4, 170.8, 148.6, 137.7, 132.4, 128.3, 126.1, 108.5, 63.8, 32.0, 27.9, 24.4, 20.6. HRMS (EI) calcd. For C<sub>15</sub>H<sub>18</sub>O<sub>3</sub> [M]<sup>+</sup> 246.1256, found 246.1255.

**Compound 18.** A flame-dried round-bottomed flask equipped with reflux condenser was charged with 5-acetoxy-1-hexene (71 mg, 0.5 mmol, 1.0 eq.), methyl vinyl ketone (91 mg, 1.3 mmol, 2.2 eq.), and dichloromethane (2.5 mL). Catalyst 3 (20 mg, 25 µmol, 0.05 eq.) was subsequently added as a solid, producing a light brown solution which was refluxed for 12 hours. The mixture was then concentrated *in vacuo* to a dark brown oil. Purification of this residue by silica gel chromatography (7:3 hexanes:ethyl acetate) allows isolation of 87 mg (0.47 mmol, 95%) of a clear, colorless oil (R<sub>f</sub> = 0.33). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>, ppm): δ 6.68 (1H, dt, J = 6.9, 15.9 Hz), 5.97 (1H, dt, J = 1.5, 6 Hz), 3.96 (2H, t, J = 6.6 Hz), 2.17 (2H, pentet, J = 1.5 Hz), 2.13 (3H, s), 1.93 (3H, s), 1.55-1.44 (4H, broad multiplet). <sup>13</sup>C NMR (75
MHz, CDCl₃, ppm): δ 198.2, 170.8, 147.3, 131.3, 63.7, 31.7, 27.9, 26.6, 24.2, 22.4, 20.7. HRMS (EI) calcd. For C₁₀H₁₆O₃ [M⁺] 184.1099, found 184.1099.

**Compound 22.** 9-Decen-1-yl benzoate (145 µl, 0.52 mmol) and butadiene monoxide (160 µl, 1.98 mmol) and was added simultaneously via syringe to a stirring solution of 3 (21 mg, 0.027 mmol, 5.0 mol %) in CH₂Cl₂ (2.5 ml). The flask was fitted with a condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm), eluting with 20:1 hexane:ethyl acetate. A clear oil was obtained (95 mg, 55% yield, 5:1 trans/cis as determined by relative integrations of ¹H peaks at 5.94 and 5.75 ppm).

¹H NMR (300 MHz, CDCl₃, ppm): δ 8.03 (2H, app d, J = 7.2 Hz), 7.55 (1H, m), 7.44 (2H, m), 5.94 (1H, dt, J = 15.3 Hz, 6.9 Hz), 5.12 (1H, dd, J = 8.7 Hz, 6.3 Hz), 4.31 (2H, t, J = 6.6 Hz), 3.30 (1H, m), 2.63 (1H, m), 2.03 (1H, m) 1.76 (2H, m), 1.51-1.22 (10H, broad m). ¹³C NMR (75 MHz, CDCl₃, ppm): δ 167.2, 137.8, 137.6, 133.3, 130.1, 128.9, 128.1, 65.6, 53.0, 49.3, 32.9, 29.9, 29.7, 29.6, 29.4, 29.3, 26.6. Rᶠ = 0.38 (9:1 hexane:ethyl acetate); HRMS (EI) calcd for C₁₉H₂₆O₃ [M+ H]+ 303.1960, found 303.1960.

**Compound 23.** 2,2,3,3,4,4,5,5,6,6,6-Nonafluoro-1-hexene (175 µl, 1.0 mmol) and 5-Hexenyl-1-acetate (85 µl, 0.51 mmol) were added simultaneously via syringe to a stirring solution of 3 (17 mg, 0.022 mmol, 4.2 mol %) in CH₂Cl₂ (2.5 ml). The flask was fitted with a condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm), eluting with 9:1 hexane:ethyl acetate. An amber oil was obtained (62 mg, 34% yield, 2.3:1 trans/cis as determined by relative intensities of ¹³C peaks at
143.0 and 143.2 ppm). $^1$H NMR (300 MHz, CDCl$_3$, ppm): 6.40 (1H, m), 5.65 (1H, m), 4.07 (2H, t, $J = 6.3$ Hz), 2.10 (2H, m), 2.05 (3H, app s), 1.72 (2H, m), 1.53 (2H, m) $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): 171.6, 143.2, 143.0, 118.2, 117.8, 117.5, 64.5, 32.1, 32.0, 28.5, 25.0, 23.2, 21.4, 14.6. $R_t = 0.72$ (9:1 hexane:ethyl acetate).

**Compound 24.** Vinyltrithoxysilane (190 µl, 1.0 mmol) and 5-Hexenyl-1-acetate (85 µl, 0.51 mmol) were added simultaneously via syringe to a stirring solution of 3 (21 mg, 0.027 mmol, 5.2 mol %) in CH$_2$Cl$_2$ (2.5 ml). The flask was fitted with a condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm), eluting with 10:1 hexane:ethyl acetate. A clear oil was obtained (126 mg, 81% yield, 11:1 trans/cis as determined by integration of $^1$H NMR peaks at 5.40 and 5.28 ppm). $^1$H NMR (300 MHz, CDCl$_3$, ppm): δ 6.38 (1H, dt, $J = 18.9$ Hz, 6.3 Hz), 5.41 (1H, app d, $J = 18.9$ Hz), 4.03 (2H, t, $J = 6.3$ Hz), 3.79 (6H, q, 6.9 Hz), 2.16 (2H, m), 2.02 (3H, s), 1.59 (2H, m), 1.47 (m, 2H), 1.20 (9H, t, $J = 7.1$ Hz). $^{13}$C NMR (75 MHz, CDCl$_3$, ppm): δ 171.6, 153.4, 120.3, 64.8, 64.4, 58.9, 58.8, 36.5, 36.3, 28.8, 28.6, 25.2, 24.4, 18.7. $R_t = 0.31$ (10:1 hexane:ethyl acetate). HRMS (FAB) calcd for C$_{14}$H$_{26}$O$_3$Si [M+H]$^+$ 305.1784, found 305.1770.

**Compound 31.** A 250 mL oven-dried round bottom flask equipped with a stir bar was charged with CH$_2$Cl$_2$ (156 mL), 25 (1.00 g, 7.80 mmol, 1 equiv.) and 3 (331 mg, 0.42 mmol, 0.05 equiv.). The reaction mixture was refluxed overnight, at which time the $^1$H NMR indicated complete disappearance of the starting material. CH$_2$Cl$_2$ was distilled off at ambient pressure and the product was purified by bulb-to-bulb distillation to yield 30 as a colorless oil (382 mg, 3.78 mmol, 49% yield).

**Compound 33.** Compound 27 (35 μl, 0.25 mmol) was added via syringe to a stirring solution of 3 (11 mg, 0.022 mmol, 5.6 mol %) in CH₂Cl₂ (12.5 ml, 0.02 M). The flask was fitted with a condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm), eluting with 9:1 hexane:ethyl acetate (Rᵣ = 0.25). A clear oil of 32 was obtained (27 mg, 97% yield). Characterization by: Moriarty, R. M.; Vaid, R. K.; Hopkins, T. E.; Vaid, B. K.; Prakash, O. Tetrahedron Lett. 1990, 31, 197-200.

**Compound 34.** Compound 28 (40 μl, 0.26 mmol) was added via syringe to a stirring solution of 3 (9.8 mg, 0.013 mmol, 4.8 mol %) in CH₂Cl₂ (12.5 ml, 0.02 M). The flask was fitted with a condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm), eluting with 9:1 hexane:ethyl acetate (Rᵣ = 0.25). A clear oil of 33 was obtained (30 mg, 92% yield). Characterization by: Moriarty, R. M.; Vaid, R. K.; Hopkins, T. E.; Vaid, B. K.; Prakash, O. Tetrahedron Lett. 1990, 31, 197-200.

**Compound 35.** Compound 29 (70 μl, 0.51 mmol) was added via syringe to a stirring solution of 3 (18 mg, 0.023 mmol, 4.5 mol %) in CH₂Cl₂ (10 ml, 0.05 M). The flask was fitted with a condenser and refluxed under nitrogen for 12 hours. The reaction mixture was then reduced in volume to 0.5 ml and purified directly on a silica gel column (2x10 cm), eluting with 9:1 hexane:ethyl acetate (Rᵣ = 0.45). A clear oil of 34
was obtained (30 mg, 92% yield). Characterization by: Dupont, J.; Donato, A. J.


**Compound 36.** Compound 30 (0.11 g, 0.18 mL, 1.0 mmol) was added via syringe to a homogenous, stirred solution of 3 (41 mg, 0.052 mmol, 5.2 mol. %) in CH$_2$Cl$_2$ (50 mL, 0.02 M). The resultant dark brown solution was refluxed under a nitrogen stream for 12 hours. The reaction mixture was then concentrated *in vacuo* and purified by silica gel column chromatography (6:4 ethyl acetate:hexanes, R$_f$ = 0.55). The product, Cyclopent-2-en-1-one, was isolated as a clear oil in 93% yield (81 mg, 0.98 mmol) which is identical in all respects to an authentic sample obtained from Aldrich Chemicals.

Compound 15

\[ \text{H}_2\text{C} = \text{O} - \text{O}-\text{H} \]

$^1$H NMR, CDCl$_3$, 400 MHz

X: parts per Million: 1H
Compound 16

$^1$H NMR, CDCl$_3$, 300 MHz
Compound 16

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{O} \\
\text{O} & \quad \text{C} \\
\text{O} & \quad \text{H}
\end{align*}
\]

$^{13}$C NMR, CDCl$_3$, 75 MHz
Compound 17

$^1$H NMR, CDCl$_3$, 300 MHz
Compound 17

$^{13}$C NMR, CDCl$_3$, 75 MHz
Compound 18

$\text{CH}_3$ $\text{O}$ $\text{O}$ $\text{H}_3\text{C}$

$\text{C}^1$\text{NMR, CDCl}_3, 75 MHz
Compound 24

$\text{H NMR, CDCl}_3, 300 \text{ MHz}$

$1.21$

$1.61, 0.22, 2.73$

$1.90$

$4.59$

$2.00$

$0.00$

$0.84, 0.85, 0.90$

$0.40, 0.85, 0.90$

$0, 0, 0$