

Supporting Information for:

An Efficient Method for the Synthesis of Cyclopropanes via Pd(II/IV) Catalysis

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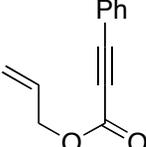
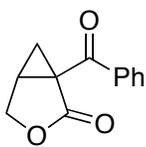
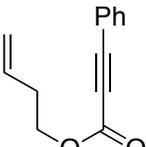
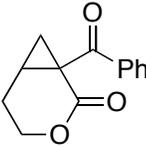
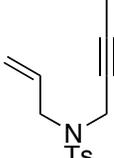
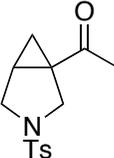
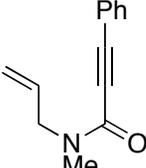
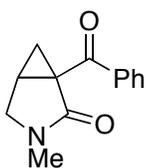
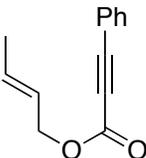
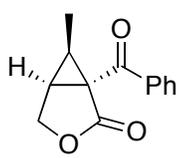
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General Procedures: NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for ^1H ; 125.70 MHz for ^{13}C) or a Varian Inova 400 (399.96 MHz for ^1H ; 100.57 MHz for ^{13}C ; 376.34 MHz for ^{19}F) spectrometer. ^1H NMR chemical shifts are reported in parts per million (ppm) relative to TMS, with the residual solvent peak used as an internal reference. Multiplicities are reported as follows: singlet (s), doublet (d), doublet of doublets (dd), doublet of doublets of doublets (ddd), doublet of triplets (dt), doublet of quartets (dq), doublet of triplets of doublets (dtd), triplet (t), triplet of triplets (tt) quartet (q), quintet (quin), multiplet (m), and broad resonance (br). IR spectra were obtained on a Perkin-Elmer "Spectrum BX" FT-IR spectrometer. Melting points were obtained on a MEL-TEMP 3.0 from Laboratory Devices Inc., USA.

Materials and Methods:

Enyne substrates were prepared according to literature procedure unless otherwise noted.¹ $\text{PhI}(\text{OAc})_2$ was obtained from Merck Research Laboratories and used as received. 2,2'-Bipyridine were obtained from Aldrich or Acros and used as received. $\text{Pd}(\text{OAc})_2$ was obtained from Pressure Chemical and used as received. Acetic acid was dried by distillation from acetic anhydride/potassium permanganate. Flash chromatography was performed on EM Science silica gel 60 (0.040-0.063 mm particle size, 230-400 mesh) and thin layer chromatography was performed on Merck TLC plates pre-coated with silica gel 60 F254. HPLC separations were performed on a Varian ProStar 210 HPLC using Waters $\mu\text{Porasil}^\circledast$ 10 μm silica (19 x 300 mm) columns. Gas chromatography was performed on a Shimadzu GC-17A equipped with a Restek Rtx^\circledast -5 column (15m, 0.25 mm ID, 0.25 μm df) and an FID detector. GC analysis of all of the products reported herein was carried out using the following method: 100 $^\circ\text{C}$ start temperature, ramp 15 $^\circ\text{C}/\text{min}$ to 240 $^\circ\text{C}$, and hold for 10 min. GCMS analysis was performed on a Shimadzu GCMS QP-5000 equipped with a Restek Rtx^\circledast -5 column (30 m, 0.25 mm ID, 0.25 μm df). Control reactions (without added Pd catalyst) were run for each substrate and showed no reaction. All GC yields reported are corrected GC yields based on calibration curves against an internal standard (biphenyl).

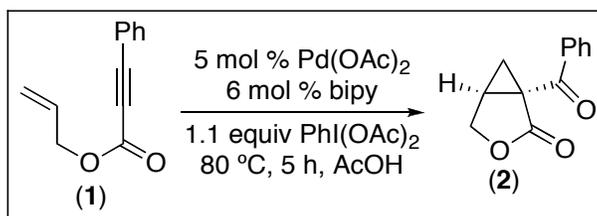
Table S1. Effect of Added Bipyridine on the Yield of Cyclopropane Products

Starting Material	Product	Yield with 6 mol% bipy	Yield without 6 mol% bipy
		94%	96%
		9%	59%
		61%	71%
		54%	9%
		29%	59%

Conditions: Optimized conditions for each substrates. Yields determined by GC relative to an internal standard (biphenyl). Each experiment is the average of at least two runs.

Conclusions: The addition/absence of bipyridine can dramatically alter the yield of cyclopropane products in many of these transformations. As summarized in Table S1, this effect is highly variable depending on the structure of the substrate. Further mechanistic studies will be required to fully determine the origin of this effect.

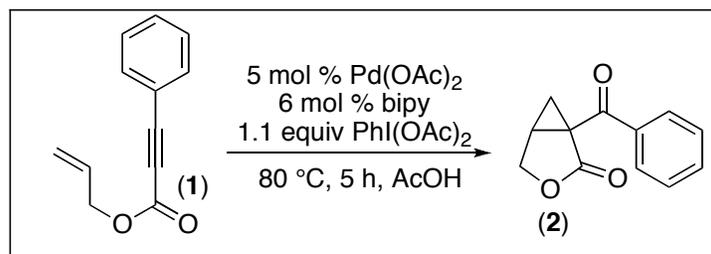
Table S2. Oxidant Study for Pd(OAc)₂-Catalyzed Transformation of **1** to **2**



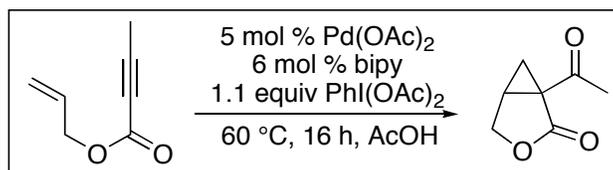
Oxidant	Yield Cyclopropane 2 ^a
PhI(OAc) ₂	94 %
Oxone	50 %
K ₂ S ₂ O ₈	27 %
CuCl ₂	0 %
Cu(OAc) ₂	0 %
Benzoquinone	0 %
Air	0 %

^a Yields based on calibrated GC yield relative to an internal standard (biphenyl).

Experimental Procedures

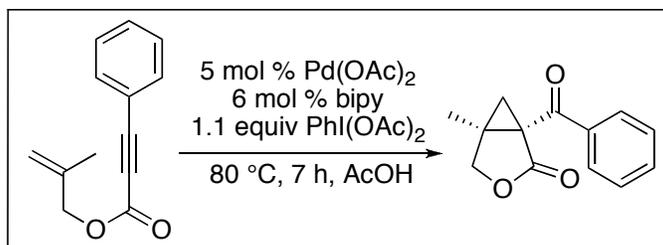


Enyne **1** (0.301 g, 1.6 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (0.571 g, 1.8 mmol, 1.1 equiv), 2,2'-bipyridine (0.016 g, 0.10 mmol, 6 mol %), and $\text{Pd}(\text{OAc})_2$ (0.018 g, 0.082 mmol, 5 mol %) were combined in acetic acid (10.1 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 5 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by gradient column chromatography on silica gel (25% ethyl acetate/75% hexanes to 75% ethyl acetate/25% hexanes, $R_f = 0.49$ in 50% ethyl acetate/50% hexanes). Product **2** was obtained as a pale orange solid (0.259 g, 79% yield). mp = 101.0-103.5 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.89 (dt, 2H, $J = 8.5, 1.6$ Hz), 7.60 (tt, 1H, $J = 7.2, 1.4$ Hz), 7.48 (tt, 2H, $J = 7.7, 1.5$ Hz), 4.58 (dd, 1H, $J = 9.5, 4.5$ Hz), 4.36 (d, 1H, $J = 10.0$ Hz), 2.84 (dtd, 1H, $J = 8.0, 5.0, 0.7$ Hz), 2.13 (dd, 1H, $J = 8.0, 4.5$ Hz), 1.45 (t, 1H, $J = 5.0$ Hz). ^{13}C { ^1H } NMR (125.7 MHz, CDCl_3): δ 192.0, 172.7, 135.5, 133.7, 129.2, 128.5, 67.9, 35.8, 27.1, 19.2. IR (Thin film): 1771, 1674 cm^{-1} . Anal. Calcd for $\text{C}_{12}\text{H}_{10}\text{O}_3$: C, 71.28, H, 4.98; Found: C, 70.99, H, 4.89.

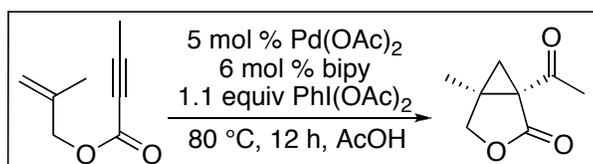


The enyne (0.300 g, 2.4 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (0.857 g, 2.7 mmol, 1.1 equiv), 2,2'-bipyridine (0.023 g, 0.14 mmol, 6 mol %), and $\text{Pd}(\text{OAc})_2$ (0.028 g, 0.12 mmol, 5 mol %) were combined in acetic acid (15 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 60 °C for 16 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by gradient column chromatography on silica gel (5% ethyl acetate/95% hexanes to 40% ethyl acetate/60% hexanes,

$R_f = 0.37$ in 50% ethyl acetate /50% hexanes). The product was obtained as an orange oil along with a trace amount of an unidentified minor product [0.188 g, 55% isolated yield (99% pure by GC, 76% GC yield)]. ^1H NMR (500 MHz, CDCl_3): δ 4.32 (dd, 1H, $J = 9.5, 5.0$ Hz), 4.18 (d, 1H, $J = 9.5$ Hz), 2.78 (dtd, 1H, $J = 8.0, 5.0, 0.8$ Hz), 2.55 (s, 3H), 2.04 (dd, 1H, $J = 8.0, 4.2$ Hz), 1.40 (dd, 1H, $J = 5.5, 4.2$ Hz). ^{13}C $\{^1\text{H}\}$ NMR (125.7 MHz, CDCl_3): δ 200.5, 172.8, 67.2, 36.5, 29.9, 29.3, 24.2. IR (Thin film): 1771, 1698 cm^{-1} . HRMS (EI $^+$) (m/z): $[\text{M}^+]$ calculated for $\text{C}_7\text{H}_8\text{O}_3$, 140.0473, found, 140.0476.

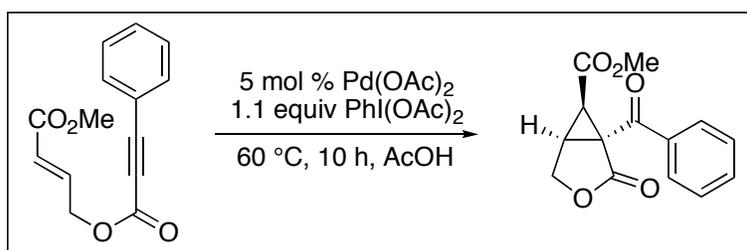


The enyne (0.300 g, 1.5 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (0.533 g, 1.6 mmol, 1.1 equiv), 2,2'-bipyridine (0.014 g, 0.091 mmol, 6 mol %), and $\text{Pd}(\text{OAc})_2$ (0.017 g, 0.075 mmol, 5 mol %) were combined in acetic acid (9.4 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 7 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by column chromatography on silica gel ($R_f = 0.22$ in 25% ethyl acetate/75% hexanes). The product was obtained as a cream-colored solid (0.252 g, 78% yield). mp = 108-110 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.72 (d, 2H, $J = 0.7$ Hz), 7.59 (tt, 1H, $J = 7.5, 1.2$ Hz), 7.48 (t, 2H, $J = 7.6$ Hz), 4.43 (d, 1H, $J = 10.0$ Hz), 4.40 (d, 1H, $J = 9.5$ Hz), 2.22 (d, 1H, $J = 5.0$ Hz), 1.44 (d, 1H, $J = 5.0$ Hz), 1.33 (s, 3H). ^{13}C $\{^1\text{H}\}$ NMR (125.7 MHz, CDCl_3): δ 191.8, 173.9, 136.5, 133.5, 128.7, 128.5, 72.6, 40.2, 37.0, 22.8, 14.3. IR (Thin film): 1766, 1672 cm^{-1} . Anal. Calcd for $\text{C}_{13}\text{H}_{12}\text{O}_3$ C, 72.21, H, 5.59; Found, C, 72.56, H, 5.67.



The enyne (0.114 g, 0.83 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (0.293 g, 0.90 mmol, 1.1 equiv), 2,2'-bipyridine (0.0078 g, 0.050 mmol, 6 mol %), and $\text{Pd}(\text{OAc})_2$ (0.0093 g, 0.041 mmol, 5 mol %) were

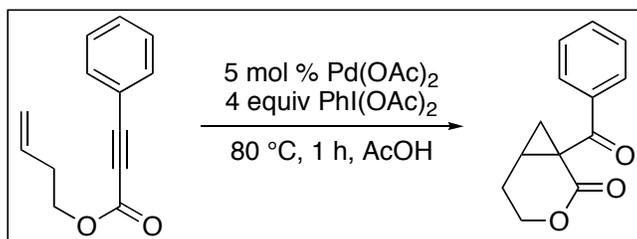
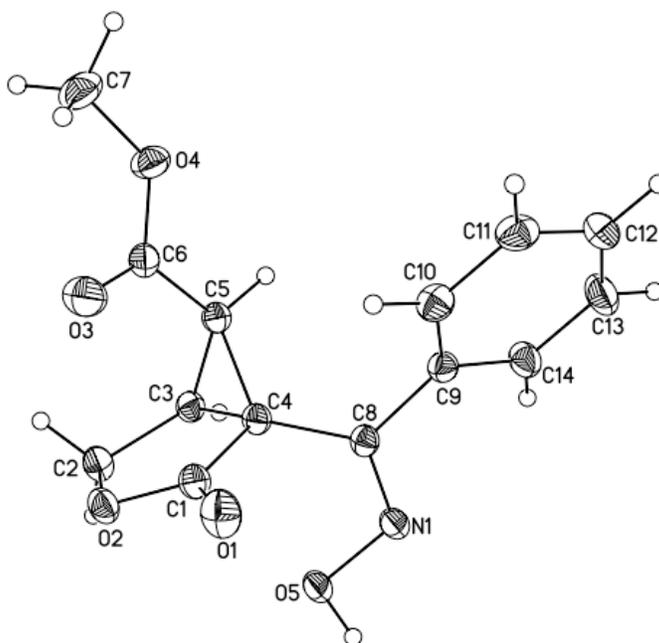
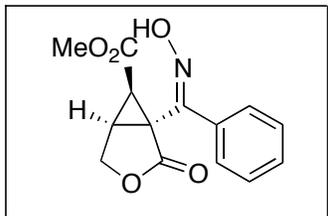
combined in acetic acid (5.2 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 12 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO₄. The solvent was removed under vacuum, and the resulting oily residue was purified by column chromatography on silica gel (*R_f* = 0.22 in 25% ethyl acetate/75% hexanes). The product was obtained as a yellow oil (0.0836 g, 66% yield). ¹H NMR (500 MHz, CDCl₃): δ 4.19 (d, 1H, *J* = 9.5 Hz), 4.05 (d, 1H, *J* = 9.5 Hz), 2.43 (s, 3H), 2.04 (d, 1H, *J* = 4.0 Hz), 1.35 (d, 1H, *J* = 4.0 Hz), 1.30 (s, 3H). ¹³C {¹H} NMR (125.7 MHz, CDCl₃): δ 199.2, 173.8, 72.1, 40.4, 39.2, 30.1, 26.9, 13.1. IR (Thin film): 1770, 1694 cm⁻¹. HRMS (EI⁺) (*m/z*): [*M*⁺] calculated for C₈H₁₀O₃: 154.0630, found, 154.0630.



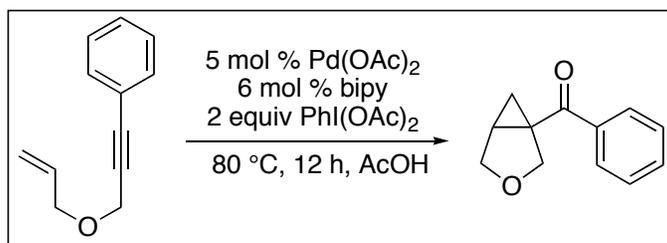
The enyne (42:1 *E:Z* ratio, 0.301 g, 1.2 mmol, 1 equiv), PhI(OAc)₂ (0.436 g, 1.3 mmol, 1.1 equiv), and Pd(OAc)₂ (0.014 g, 0.061 mmol, 5 mol %) were combined in acetic acid (7.68 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 60 °C for 10 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO₄. The solvent was removed under vacuum, and the resulting oily residue was purified by gradient column chromatography on silica gel (10% ethyl acetate/90% hexanes to 70% ethyl acetate/30% hexanes, *R_f* = 0.38 in 50% ethyl acetate/50% hexanes). The product was obtained as an orange oil (0.253 g, 79% yield, 99% pure by GC). ¹H NMR (400 MHz, CDCl₃): δ 7.91 (d, 2 H, *J* = 7.8 Hz), 7.58 (tt, 1H, *J* = 7.4, 1.2 Hz), 7.46 (t, 2H, *J* = 7.6 Hz), 4.64 (dd, 1H, *J* = 10.4, 5.2 Hz), 4.49 (d, 1H, *J* = 10.4 Hz), 3.77 (s, 3H), 3.12 (ddd, 1H, *J* = 8.4, 5.0, 0.8 Hz), 2.92 (d, 1H, *J* = 8.4 Hz). ¹³C {¹H} NMR (100.57 MHz, CDCl₃): δ 190.0, 169.6, 166.7, 134.6, 134.0, 129.3, 128.5, 65.1, 52.7, 42.3, 32.1, 30.0. IR (Thin film): 1769, 1738, 1679 cm⁻¹. Anal. Calcd for C₁₄H₁₃NO₅ (as the N-OH oxime): C, 61.09, H, 4.76, N, 5.09; Found: C, 61.04, H, 4.89, N, 4.89. The product was converted to an oxime in order to obtain a crystalline material. Needles were grown by the vapor diffusion of hexanes into an acetone solution of the cyclopropyl oxime at 22 °C. The structure is shown below in Figure 1, and it definitively establishes the inversion of

starting olefin geometry in the product. More information about this structure can be found on p. S17.

Figure S1. Crystal Structure of Oxime

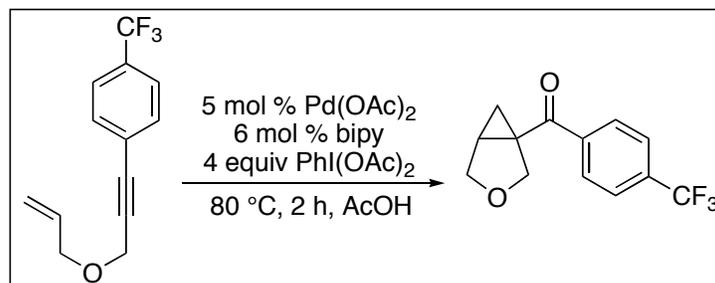


The enyne (0.303 g, 1.5 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (1.949 g, 6.0 mmol, 4 equiv), and $\text{Pd}(\text{OAc})_2$ (0.017 g, 0.075 mmol, 5 mol %) were combined in acetic acid (9.4 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 1 hour. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by gradient column chromatography on silica gel (25% ethyl acetate/75% hexanes to 75% ethyl acetate/25% hexanes, $R_f = 0.28$ in 50% ethyl acetate/50% hexanes). The product was obtained as a pale yellow solid (0.182 g, 55% yield). mp = 77.3-80.4 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.83 (dd, 2 H, $J = 8.5, 1.5$ Hz), 7.55 (tt, 1H, $J = 7.5, 1.5$ Hz), 7.45 (tt, 2H, $J = 7.0, 1.5$ Hz), 4.45 (ddt, 1H, $J = 12.0, 6.0, 1.5$ Hz), 4.26 (td, 1H, $J = 12.5, 3.5$ Hz), 2.51 (m, 1H), 2.13 (quin, 1H, $J = 2.0$ Hz), 2.13 (m, 1H), 2.09 (m, 1H), 1.85 (t, 1H, $J = 5.5$ Hz). ^{13}C $\{^1\text{H}\}$ NMR (125.7 MHz, CDCl_3): δ 193.3, 168.8, 135.9, 133.1, 128.6, 128.5, 64.8, 33.7, 23.9, 20.3, 13.3. (Note: the ^{13}C NMR spectrum shown in the other Supporting Information file is a ^1H coupled ^{13}C NMR spectrum.) IR (Thin film): 1722, 1681 cm^{-1} . HRMS (Electrospray) (m/z): $[\text{M}+\text{Na}^+]$ calculated for $\text{C}_{13}\text{H}_{12}\text{O}_3$ 239.0684, found, 239.0682.

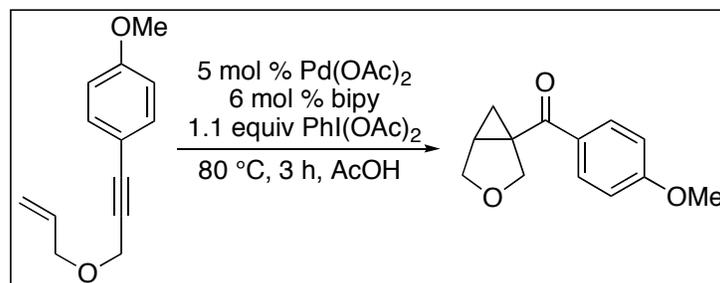


The enyne (0.300 g, 1.7 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (1.13 g, 3.5 mmol, 2 equiv), 2,2'-bipyridine (0.016 g, 0.10 mmol, 6 mol %), and $\text{Pd}(\text{OAc})_2$ (0.019 g, 0.087 mmol, 5 mol %) were combined in acetic acid (10.9 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 12 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by gradient column chromatography on silica gel (2% ethyl acetate/98% hexanes to 10% ethyl acetate/90% hexanes, $R_f = 0.44$ in 25% ethyl acetate/75% hexanes). The product was obtained as a yellow oil (0.158 g, 48% yield). ^1H NMR (500 MHz, CDCl_3): δ 7.70 (d, 2H, $J = 8.0$ Hz), 7.51 (t, 1H, $J = 7.5$ Hz), 7.42 (t, 2H, $J = 6.7$ Hz), 4.19 (dd, 1H, $J = 8.5, 2.0$ Hz), 3.94 (d, 1H, 8.5 Hz), 3.87 (dd, 1H, $J = 8.5, 2.5$ Hz), 3.82 (d, 1H, $J = 8.5$ Hz), 2.38 (m, 1H), 1.53 (dd, 1H, $J = 4.1, 0.7$ Hz), 1.20 (t, 1H, $J = 4.8$ Hz). ^{13}C $\{^1\text{H}\}$ NMR (125.7 MHz,

CDCl_3): δ 200.4, 138.2, 132.4, 128.5, 127.8, 70.2, 68.7, 38.8, 29.4, 18.9. IR (Thin film): 1665 cm^{-1} . HRMS (EI^+) (m/z): [M^+] calculated for $\text{C}_{12}\text{H}_{12}\text{O}_2$ 187.0759, found, 187.0760.

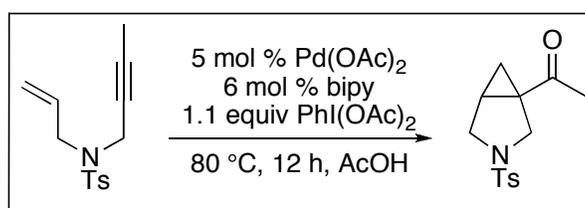


The enyne (0.298 g, 1.2 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (1.598 g, 5.0 mmol, 4 equiv), and $\text{Pd}(\text{OAc})_2$ (0.014 g, 0.063 mmol, 5 mol %) were combined in acetic acid (7.8 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 2 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by column chromatography on silica gel ($R_f = 0.42$ in 25% ethyl acetate/75% hexanes). The product was obtained as a pale yellow oil (0.141 g, 44% yield). ^1H NMR (500 MHz, CDCl_3): δ = 7.79 (d, 2H, $J = 8.0$ Hz), 7.72 (d, 2H, $J = 8.0$ Hz), 4.19 (d, 1H, $J = 9.0$ Hz), 3.95 (d, 1H, $J = 8.5$ Hz), 3.91 (d, 1H, $J = 8.5$ Hz), 3.85 (dd, 1H, $J = 8.5, 3.0$ Hz), 2.43 (m, 1H), 1.60 (dd, 1H, $J = 8.5, 4.2$ Hz), 1.29 (t, 1H, $J = 4.7$ Hz). ^{13}C [^1H] NMR (125.7 MHz, CDCl_3): δ 199.7, 141.2, 133.7 (q, $^2J_{\text{C-F}} = 33$ Hz), 128.0, 125.6 (q, $^3J_{\text{C-F}} = 3.6$ Hz), 123.5 (q, $^1J_{\text{C-F}} = 273$ Hz), 69.9, 68.7, 39.0, 30.2, 19.2. ^{19}F NMR (376.3 MHz, CDCl_3) δ -63.1. IR (Thin film): 1672 cm^{-1} . HRMS (EI^+) (m/z): [M^+] calculated for $\text{C}_{13}\text{H}_{11}\text{F}_3\text{O}_2$ 255.0633, found, 255.0634.

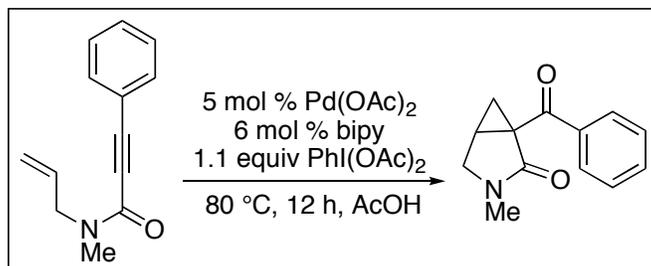


The enyne (0.301 g, 1.5 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (0.526 g, 1.6 mmol, 1.1 equiv), 2,2'-bipyridine (0.014 g, 0.09 mmol, 6 mol %), and $\text{Pd}(\text{OAc})_2$ (0.017 g, 0.075 mmol, 5 mol %) were combined in acetic acid (9.4 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 3 h. The reaction was diluted with water (40 mL) and

extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO₄. The solvent was removed under vacuum, and the resulting oily residue was purified by column chromatography on silica gel ($R_f = 0.31$ in 25% ethyl acetate/75% hexanes). The product was obtained as a yellow oil (0.143 g, 44% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.75 (dt, 2H, $J = 9.0, 1.7$ Hz), 6.91 (dt, 2H, $J = 9.0, 2.0$ Hz), 4.20 (d, 1H, $J = 8.5$ Hz), 3.95 (d, 1H, $J = 8.5$ Hz), 3.91-3.85 (multiple peaks, 5H), 2.35 (m, 1H), 1.45 (dd, 1H, $J = 8.0, 4.0$ Hz), 1.16 (t, 1H, $J = 4.7$ Hz). ¹³C {¹H} NMR (125.7 MHz, CDCl₃): δ 198.1, 163.1, 130.7, 130.4, 113.7, 70.5, 68.8, 55.4, 38.5, 28.4, 18.5. IR (Thin film): 1661 cm⁻¹. HRMS (EI⁺) (m/z): [M^+] calculated for C₁₃H₁₄O₃ 217.0864, found, 217.0861.

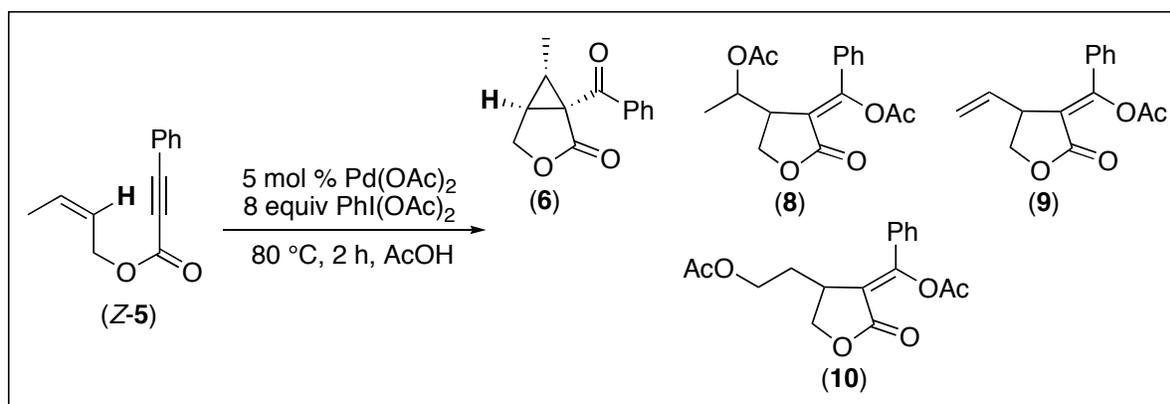


The enyne substrate was prepared according to known literature procedure.² The enyne (0.300 g, 1.1 mmol, 1 equiv), PhI(OAc)₂ (0.408 g, 1.3 mmol, 1.1 equiv), 2,2'-bipyridine (0.011 g, 0.068 mmol, 6 mol %), and Pd(OAc)₂ (0.012 g, 0.055 mmol, 5 mol %) were combined in acetic acid (6.9 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 12 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO₄. The solvent was removed under vacuum, and the resulting oily residue was purified by column chromatography on silica gel ($R_f = 0.40$ in 50% ethyl acetate/50% hexanes). The product was obtained as an orange oil (0.226 g, 71% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.67 (d, 2H, $J = 8.5$ Hz), 7.32 (d, 2H, $J = 8.5$ Hz), 3.60 (t, 2H, $J = 10.0$ Hz), 3.37 (d, 1H, $J = 9.5$ Hz), 3.04 (dd, 1H, 9.5, 3.7 Hz), 2.42 (s, 3H), 2.03 (m, 1H), 1.92 (s, 3H), 1.48 (dd, 1H, $J = 8.0, 5.5$ Hz) 1.24 (t, 1H, $J = 5.2$ Hz). ¹³C {¹H} NMR (125.7 MHz, CDCl₃): δ 204.4, 143.8, 132.6, 129.7, 127.6, 49.0, 48.8, 38.8, 27.2, 25.5, 21.5, 17.5. IR (Thin film): 1684, 1346, 1165 cm⁻¹. HRMS (Electrospray) (m/z): [$M+Na^+$] calculated for C₁₄H₁₇NO₃S 302.0827, found, 302.0820.



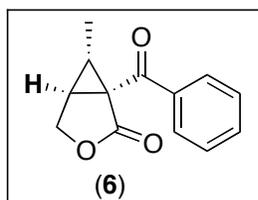
The enyne substrate was synthesized according to literature procedure.³ The enyne (0.100 g, 0.50 mmol, 1 equiv), PhI(OAc)₂ (0.178 g, 0.55 mmol, 1.1 equiv), 2,2'-bipyridine (0.0047 g, 0.030 mmol, 6 mol %), and Pd(OAc)₂ (0.0056 g, 0.025 mmol, 5 mol %) were combined in dry acetic acid (3.14 mL) in a 20 mL vial. The vial was sealed with a Teflon-lined cap, and the reaction was heated at 80 °C for 12 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 × 50 mL). The combined organic layers were washed with water (3 × 100 mL) and brine (1 × 100 mL) and then dried over anhydrous MgSO₄. The solvent was removed under vacuum, and the resulting oily residue was purified by column chromatography on silica gel (*R_f* = 0.19 in 70% ethyl acetate/30% hexanes). The product was obtained as a yellow oil (0.051 g, 47% yield). ¹H NMR (500 MHz, CDCl₃): δ 7.84 (dd, 2H, *J* = 7, 1.0 Hz), 7.51 (t, 1H, *J* = 7.5 Hz), 7.41 (t, 2H, *J* = 7.5 Hz), 3.74 (dd, 1H, *J* = 10.5, 6.0 Hz), 3.35 (d, 1H, *J* = 10.5 Hz), 2.80 (s, 3H), 2.38 (dt, 1H, *J* = 8.0, 2.5 Hz), 1.96 (dd, 1H, *J* = 8.0, 4.5 Hz), 1.10 (t, 1H, *J* = 4.5 Hz). ¹³C {¹H} NMR (125.7 MHz, CDCl₃): δ 194.7, 171.4, 136.5, 133.1, 129.0, 128.3, 49.9, 38.5, 29.7, 22.2, 19.2. IR (Thin Film): 1684, 1598 cm⁻¹. HRMS (EI⁺) (*m/z*): [*M*⁺] calculated for C₁₃H₁₃NO₂, 214.0868, found: 214.0863.

E and *Z* Olefin Studies



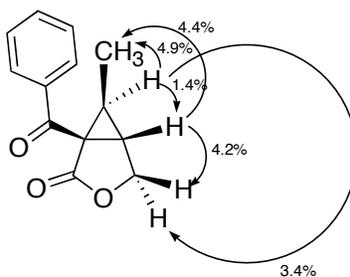
The *E*-alcohol required for the synthesis of *Z*-5 was prepared in three steps by (i) protection of 2-butyne-1-ol with TIPSCl,⁴ (ii) hydrozirconation of the resulting alkyne followed

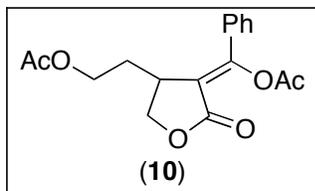
by an aqueous quench,⁵ and (iii) deprotection with TBAF.⁴ Z-5 (91:9 Z:E ratio, 0.304 g, 1.5 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (3.865 g, 12 mmol, 8 equiv, dried under vacuum for 24 h), and $\text{Pd}(\text{OAc})_2$ (0.0164 g, 0.073 mmol, 5 mol %) were combined in dry acetic acid (9.4 mL) in a schlenk flask. The reaction was heated at 80 °C for 2 h, then it was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by gradient column chromatography on silica gel (10% ethyl acetate/90% hexanes to 75% ethyl acetate/25% hexanes) and further purified with HPLC. Products **6** (25% GC yield), **10** (19% GC yield), **8** (11% GC yield), **9** (8% GC yield) were isolated from the reaction. [Note: GC yields are calibrated versus an internal standard (biphenyl).]



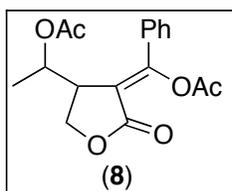
Product **6** was obtained as a white solid in an 13:1 mixture of diastereomers (**6** : **7**) along with a trace amount of an unidentified side product (0.091 g, 28% isolated yield, 96% pure by GC, $R_f = 0.19$ in 25% ethyl acetate/75% hexanes). mp = 109.9-113.0 °C. ^1H NMR (500 MHz, CDCl_3): δ 8.04 (dt, 2 H, $J = 8.0, 1.5$ Hz), 7.62 (tt, 1H, $J = 7.2, 1.4$ Hz), 7.51 (t, 2H, $J = 7.7$ Hz), 4.40 (dd, 1H, $J = 9.0, 5.0$ Hz), 4.29 (d, 1H, $J = 9.5$ Hz), 2.68 (t, 1H, $J = 4.7$ Hz), 1.92 (dq, 1H, $J = 5.9, 5.7$ Hz), 1.10 (d, 3H, $J = 6.0$ Hz). ^{13}C $\{^1\text{H}\}$ NMR (125.7MHz, CDCl_3): δ 191.5, 171.9, 136.0, 133.9, 130.1, 128.4, 67.8, 41.2, 29.1, 28.2, 12.5. IR (Thin film): 1761, 1734 cm^{-1} . HRMS (Electrospray): $[\text{M}+\text{Na}^+]$ calculated for $\text{C}_{13}\text{H}_{12}\text{O}_3$ 239.0684, found, 239.0685.

NOE Studies for **6**:

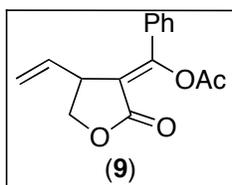




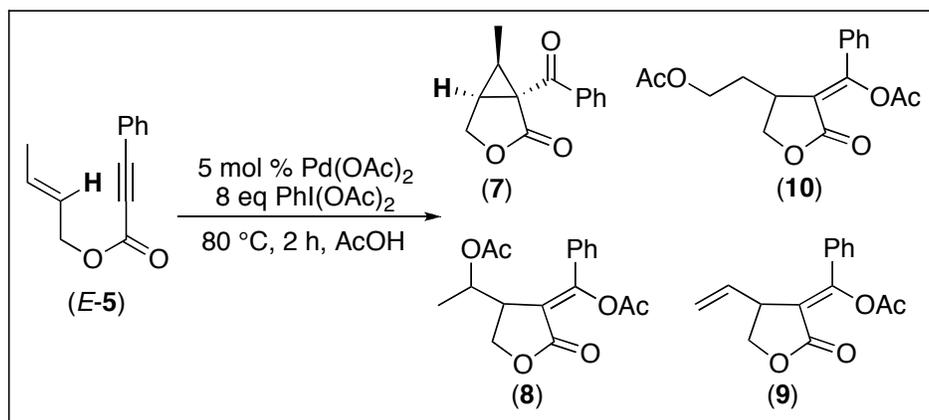
Product **10** was obtained as a pale yellow oil ($R_f = 0.08$ in 30% ethyl acetate/70% hexanes). ^1H NMR (500 MHz, CDCl_3): δ 7.51-7.53 (m, 2H), 7.42-7.44 (multiple peaks, 3H), 4.39 (dd, 1H, $J = 9.0, 7.5$ Hz), 4.14 (dd, 1H, $J = 9.5, 2.5$ Hz), 3.99-4.03 (m, 1H), 3.92-3.96 (m, 1H), 3.59 (m, 1H), 2.30 (s, 3H), 1.93 (s, 3H), 1.78 (m, 2H). ^{13}C $\{^1\text{H}\}$ NMR (125.7 MHz, CDCl_3): δ 170.5, 168.3, 167.8, 153.6, 133.7, 130.5, 128.7, 127.7, 117.6, 69.6, 61.2, 35.5, 32.0, 20.7, 20.6. IR (Thin Film): 1758, 1738, 1669 cm^{-1} . HRMS (Electrospray) calculated for $\text{C}_{17}\text{H}_{18}\text{O}_6$ $[\text{M}+\text{Na}^+]$: 341.1001, found: 341.0994.



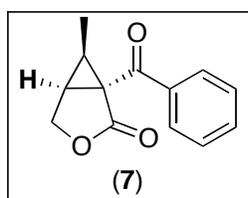
Product **8** was obtained as a yellow oil as predominantly (>6.5:1) one diastereomer ($R_f = 0.08$ in 30% ethyl acetate/70% hexanes). The stereochemistry of **8** could not be determined definitively by coupling constant analysis. Furthermore, this compound is an oil; therefore, an x-ray structure could not be obtained. Efforts to prepare a crystalline derivative of **8** are ongoing and will be reported in a full paper. ^1H NMR (500 MHz, CDCl_3): δ 7.55 (dd, 2H, $J = 8.0, 1.5$ Hz), 7.38-7.42 (multiple peaks, 3H), 5.26-5.28 (m, 1H), 4.41 (dd, 1H, $J = 12.5, 2.5$ Hz), 4.27 (dd, 1H, 12, 9 Hz), 3.62-3.65 (m, 1H), 2.29 (s, 3H), 2.05 (s, 3H), 1.24 (d, 3H, $J = 7$ Hz). ^{13}C $\{^1\text{H}\}$ NMR (125.7 MHz CDCl_3): δ 170.3, 168.1, 168.0, 158.3, 131.6, 130.8, 129.0, 128.0, 115.1, 69.5, 65.2, 42.7, 21.2, 20.9, 14.5. IR (Thin Film): 1767, 1739, 1662 cm^{-1} . HRMS (Electrospray) calculated for $\text{C}_{17}\text{H}_{18}\text{O}_6$ $[\text{M}+\text{Na}^+]$: 341.1001, found: 341.0998.



Product **9** was isolated as a pale yellow oil ($R_f = 0.29$ in 30% ethyl acetate/70% hexanes). The spectroscopic data for this product was identical to that previously reported in the literature.⁶



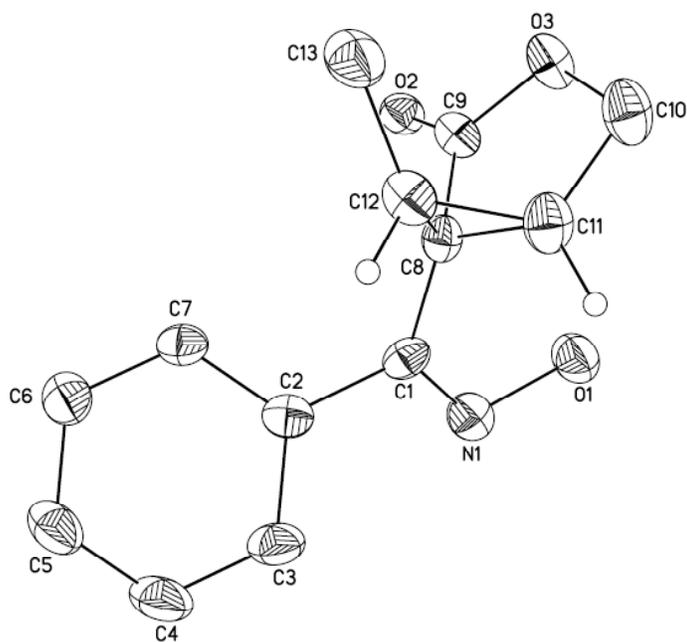
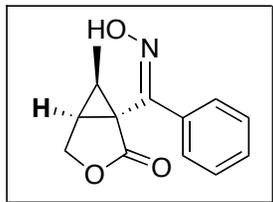
E-5 (86:14 *E:Z* ratio, 0.600 g, 2.9 mmol, 1 equiv), $\text{PhI}(\text{OAc})_2$ (7.727 g, 24.0 mmol, 8 equiv, dried under vacuum for 24 h), and $\text{Pd}(\text{OAc})_2$ (0.034 g, 0.15 mmol, 5 mol %) were combined in dry acetic acid (18.7 mL) in a dry schlenk flask, and the reaction was heated at 80 °C for 2 h. The reaction was diluted with water (40 mL) and extracted with ethyl acetate (2 x 50 mL). The combined organic layers were washed with water (3 x 100 mL) and brine (1 x 100 mL) and then dried over anhydrous MgSO_4 . The solvent was removed under vacuum, and the resulting oily residue was purified by gradient column chromatography on silica gel (10% ethyl acetate/90% hexanes to 75% ethyl acetate/25% hexanes). Products **7** (59% GC yield), **10** (8% GC yield), **8** (4% GC yield, stereochemistry not definitively determined), and **9** (8% GC yield) were isolated from the reaction. [Note: GC yields are calibrated versus an internal standard (biphenyl).]



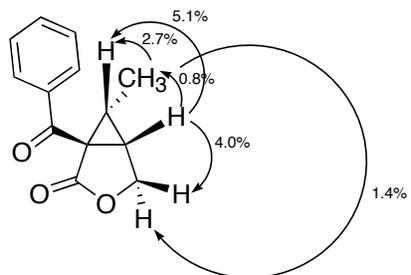
Product **7** was obtained as a white solid as an 11:1 mixture of diastereomers (**7** : **6**) (0.27 g, 42% isolated yield, $R_f = 0.23$ in 25% ethyl acetate/75% hexanes). mp = 107.6-112.1 °C. ^1H NMR (500 MHz, CDCl_3): δ 7.87 (dt, 2H, $J = 7.0, 1.5$ Hz), 7.58 (tt, 1H, $J = 7.5, 1.4$ Hz), 7.47 (t, 2H, $J = 7.7$ Hz), 4.57 (dd, 1H, $J = 10.2, 5.2$ Hz), 4.25 (d, 1H, $J = 10.0$ Hz), 2.89 (ddd, 1H, $J = 8.2, 5.2, 1.0$ Hz), 2.20 (dq, 1H, $J = 7.5, 6.6$ Hz), 1.32 (d, 3H, $J = 6.5$ Hz). ^{13}C $\{^1\text{H}\}$ NMR (126.7 MHz, CDCl_3): $\delta = 192.8, 171.2, 135.7, 133.6, 129.3, 128.5, 64.5, 41.8, 30.9, 25.1, 7.08$. IR (CH_2Cl_2): 1763, 1673 cm^{-1} . HRMS (Electrospray) calculated for $\text{C}_{13}\text{H}_{12}\text{O}_3$ [$\text{M}+\text{Na}^+$]: 239.0684, found: 239.0678. The product was converted to an oxime in order to obtain a crystalline material. Block-like crystals were grown by the vapor diffusion of pentanes into a chlorobenzene solution of the cyclopropyl oxime at 22 °C. The structure is shown below in Figure S2, and it definitively establishes the

inversion of starting olefin geometry in the product. More information about this structure can be found on p. S22.

Figure S2. Oxime of 7



NOE Studies of 7:



References:

1. Zhang, Q.; Lu, X.; Han, X. *J. Org. Chem.* **2001**, *66*, 7676-7684
2. Zhang, Q.; Xu, W.; Lu, X. *J. Org. Chem.* **2005**, *70*, 1505-1507
3. Xie, X.; Lu, X.; Liu, Y. *J. Org. Chem.* **2001**, *66*, 6545-6550
4. Gommermann, N.; Knochel, P. *Tetrahedron* **2005**, *61*, 11418-11426
5. Bray, K. L.; Lloyd-Jones, G. C. *Eur. J. Org. Chem.* **2001**, 1635-1642
6. Zhang, Q., Lu, X. *J. Am. Chem. Soc.* **2000**, *122*, 7604-7605

Structure Determination of Entry 5 (Oxime)

Colorless needles of **lw264** were grown by diffusion of acetone into a hexane solution at 22 deg. C. A crystal of dimensions 0.60 x 0.42 x 0.07 mm was mounted on a standard Bruker SMART CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube ($\lambda = 0.71073$ Å) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 123(2) K; the detector was placed at a distance 4.969 cm from the crystal. A total of 2393 frames were collected with a scan width of 0.5° in ω and ϕ with an exposure time of 20 s/frame. The integration of the data yielded a total of 25414 reflections to a maximum 2θ value of 56.66° of which 3235 were independent and 2578 were greater than $2\sigma(I)$. The final cell constants (Table 1) were based on the xyz centroids of 9364 reflections above $10\sigma(I)$. Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P2(1)/c with $Z = 4$ for the formula $C_{14}H_{13}NO_5$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions with the exception of the oxime hydrogen that was located on a difference Fourier map and was allowed to refine isotropically. Full matrix least-squares refinement based on F^2 converged at $R1 = 0.0358$ and $wR2 = 0.0942$ [based on $I > 2\sigma(I)$], $R1 = 0.0501$ and $wR2 = 0.1044$ for all data.

Sheldrick, G.M. SHELXTL, v. 6.12; Bruker Analytical X-ray, Madison, WI, 2001.

Sheldrick, G.M. SADABS, v. 2.10. Program for Empirical Absorption Correction of Area Detector Data, University of Gottingen: Gottingen, Germany, 2003.

Saint Plus, v. 7.01, Bruker Analytical X-ray, Madison, WI, 2003.

Table S2. Crystal data and structure refinement for lw264.

Identification code	lw264
Empirical formula	C ₁₄ H ₁₃ N O ₅
Formula weight	275.25
Temperature	123(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 5.8325(13) Å alpha = 90 deg. b = 11.574(3) Å beta = 97.913(3) deg. c = 19.466(4) Å gamma = 90 deg.
Volume	1301.5(5) Å ³
Z, Calculated density	4, 1.405 Mg/m ³
Absorption coefficient	0.108 mm ⁻¹
F(000)	576
Crystal size	0.60 x 0.42 x 0.07 mm
Theta range for data collection	2.05 to 28.33 deg.
Limiting indices	-7<=h<=7, -15<=k<=15, -25<=l<=25
Reflections collected / unique	24785 / 3235 [R(int) = 0.0337]
Completeness to theta = 28.33	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9925 and 0.9381
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	3235 / 0 / 186
Goodness-of-fit on F ²	1.045
Final R indices [I>2sigma(I)]	R1 = 0.0358, wR2 = 0.0942
R indices (all data)	R1 = 0.0501, wR2 = 0.1044
Largest diff. peak and hole	0.350 and -0.261 e.Å ⁻³

Table S3. Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å² x 10³) for lw264.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
N(1)	9419(2)	5752(1)	4399(1)	20(1)
O(1)	3969(2)	6112(1)	3433(1)	29(1)
O(2)	4989(2)	4720(1)	2742(1)	22(1)
O(3)	4993(2)	6651(1)	1835(1)	38(1)
O(4)	8065(2)	7594(1)	1539(1)	26(1)
O(5)	8578(2)	4630(1)	4246(1)	25(1)
C(1)	5425(2)	5668(1)	3142(1)	20(1)
C(2)	7054(2)	4328(1)	2472(1)	22(1)
C(3)	8957(2)	5176(1)	2725(1)	18(1)
C(4)	7931(2)	6019(1)	3187(1)	17(1)

C(5)	8716(2)	6436(1)	2517(1)	19(1)
C(6)	7021(2)	6881(1)	1935(1)	21(1)
C(7)	6597(3)	8101(1)	953(1)	32(1)
C(8)	9098(2)	6425(1)	3872(1)	17(1)
C(9)	9874(2)	7634(1)	3987(1)	18(1)
C(10)	8526(2)	8542(1)	3683(1)	23(1)
C(11)	9173(3)	9682(1)	3828(1)	27(1)
C(12)	11192(3)	9916(1)	4267(1)	32(1)
C(13)	12576(3)	9018(1)	4557(1)	33(1)
C(14)	11933(2)	7880(1)	4418(1)	25(1)

Table S4. Bond lengths [Å] and angles [deg] for lw264.

N(1)-C(8)	1.2803(16)
N(1)-O(5)	1.4047(13)
O(1)-C(1)	1.1985(16)
O(2)-C(1)	1.3500(15)
O(2)-C(2)	1.4515(15)
O(3)-C(6)	1.2021(16)
O(4)-C(6)	1.3319(16)
O(4)-C(7)	1.4526(16)
C(1)-C(4)	1.5076(16)
C(2)-C(3)	1.5123(17)
C(3)-C(4)	1.5061(17)
C(3)-C(5)	1.5159(17)
C(4)-C(8)	1.4877(16)
C(4)-C(5)	1.5203(16)
C(5)-C(6)	1.4896(17)
C(8)-C(9)	1.4787(17)
C(9)-C(10)	1.3941(17)
C(9)-C(14)	1.3969(18)
C(10)-C(11)	1.3911(19)
C(11)-C(12)	1.383(2)
C(12)-C(13)	1.387(2)
C(13)-C(14)	1.3855(19)
C(8)-N(1)-O(5)	112.63(10)
C(1)-O(2)-C(2)	111.31(9)
C(6)-O(4)-C(7)	115.96(11)
O(1)-C(1)-O(2)	122.09(11)
O(1)-C(1)-C(4)	126.96(12)
O(2)-C(1)-C(4)	110.89(10)
O(2)-C(2)-C(3)	106.71(10)
C(4)-C(3)-C(2)	106.32(10)
C(4)-C(3)-C(5)	60.41(8)
C(2)-C(3)-C(5)	119.99(11)
C(8)-C(4)-C(3)	124.71(10)

C(8)-C(4)-C(1)	117.23(10)
C(3)-C(4)-C(1)	104.64(10)
C(8)-C(4)-C(5)	120.96(10)
C(3)-C(4)-C(5)	60.12(8)
C(1)-C(4)-C(5)	116.10(10)
C(6)-C(5)-C(3)	124.33(10)
C(6)-C(5)-C(4)	121.08(11)
C(3)-C(5)-C(4)	59.48(8)
O(3)-C(6)-O(4)	124.17(12)
O(3)-C(6)-C(5)	125.56(12)
O(4)-C(6)-C(5)	110.26(11)
N(1)-C(8)-C(9)	116.59(11)
N(1)-C(8)-C(4)	121.58(11)
C(9)-C(8)-C(4)	121.80(10)
C(10)-C(9)-C(14)	119.33(12)
C(10)-C(9)-C(8)	120.40(11)
C(14)-C(9)-C(8)	120.24(11)
C(11)-C(10)-C(9)	120.47(12)
C(12)-C(11)-C(10)	119.67(12)
C(11)-C(12)-C(13)	120.22(13)
C(14)-C(13)-C(12)	120.40(13)
C(13)-C(14)-C(9)	119.85(12)

Symmetry transformations used to generate equivalent atoms:

Table S5. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for lw264.

The anisotropic displacement factor exponent takes the form:

$$-2 \pi^2 [h^2 a^*^2 U_{11} + \dots + 2 h k a^* b^* U_{12}]$$

	U11	U22	U33	U23	U13	U12
N(1)	22(1)	17(1)	21(1)	0(1)	0(1)	-4(1)
O(1)	18(1)	37(1)	33(1)	-8(1)	4(1)	0(1)
O(2)	17(1)	23(1)	24(1)	-2(1)	1(1)	-5(1)
O(3)	25(1)	43(1)	40(1)	17(1)	-12(1)	-10(1)
O(4)	26(1)	28(1)	23(1)	8(1)	1(1)	0(1)
O(5)	33(1)	18(1)	22(1)	2(1)	-4(1)	-9(1)
C(1)	16(1)	23(1)	20(1)	1(1)	0(1)	-2(1)
C(2)	20(1)	22(1)	23(1)	-4(1)	3(1)	-2(1)
C(3)	16(1)	20(1)	18(1)	0(1)	1(1)	-1(1)
C(4)	14(1)	18(1)	18(1)	0(1)	0(1)	-1(1)
C(5)	16(1)	21(1)	18(1)	1(1)	0(1)	-3(1)

C(6)	24(1)	19(1)	19(1)	0(1)	-1(1)	-2(1)
C(7)	35(1)	34(1)	24(1)	10(1)	-2(1)	4(1)
C(8)	14(1)	20(1)	17(1)	-1(1)	1(1)	0(1)
C(9)	20(1)	17(1)	17(1)	0(1)	3(1)	0(1)
C(10)	23(1)	23(1)	22(1)	2(1)	1(1)	4(1)
C(11)	37(1)	20(1)	26(1)	4(1)	9(1)	7(1)
C(12)	50(1)	18(1)	28(1)	-2(1)	6(1)	-5(1)
C(13)	39(1)	24(1)	33(1)	-2(1)	-8(1)	-9(1)
C(14)	26(1)	20(1)	25(1)	1(1)	-5(1)	-2(1)

Table S6. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for lw264.

	x	y	z	U(eq)
H(5A)	9040(30)	4275(17)	4674(11)	48(5)
H(2A)	6787	4312	1958	26
H(2B)	7480	3541	2642	26
H(3A)	10543	4866	2884	22
H(5B)	10210	6873	2587	23
H(7A)	6611	7608	544	47
H(7B)	7179	8870	857	47
H(7C)	5010	8166	1061	47
H(10A)	7155	8380	3374	28
H(11A)	8232	10297	3626	33
H(12A)	11631	10694	4370	38
H(13A)	13973	9185	4852	40
H(14A)	12891	7269	4617	29

Table S7. Hydrogen bonds for lw264 [\AA and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	$\angle(\text{DHA})$
O(5)-H(5A)...N(1)#1	0.93(2)	1.90(2)	2.7688(15)	153.2(18)

Symmetry transformations used to generate equivalent atoms:

#1 -x+2,-y+1,-z+1

Oxime of 7 Structure Determination

Colorless, block-like crystals of **tl129a** were grown by diffusion of pentane into a chlorobenzene solution at 22 deg. C. A crystal of dimensions 0.42 x 0.20 x 0.12 mm was mounted on a standard Bruker SMART 1K CCD-based X-ray diffractometer equipped with a LT-2 low temperature device and normal focus Mo-target X-ray tube ($\lambda = 0.71073$ Å) operated at 2000 W power (50 kV, 40 mA). The X-ray intensities were measured at 108(2) K; the detector was placed at a distance 4.912 cm from the crystal. A total of 3000 frames were collected with a scan width of 0.5° in ω and 0.45° in ϕ with an exposure time of 20 s/frame. The integration of the data yielded a total of 21476 reflections to a maximum 2θ value of 54.68° of which 2644 were independent and 2043 were greater than $2s(I)$. The final cell constants (Table 1) were based on the xyz centroids of 6349 reflections above $10s(I)$. Analysis of the data showed negligible decay during data collection; the data were processed with SADABS and corrected for absorption. The structure was solved and refined with the Bruker SHELXTL (version 6.12) software package, using the space group P2(1)/c with $Z = 4$ for the formula $C_{13}H_{13}NO_3$. All non-hydrogen atoms were refined anisotropically with the hydrogen atoms placed in idealized positions with the exception of H1 which participates in an inter-molecular hydrogen bond and was allowed to refine isotropically. Full matrix least-squares refinement based on F^2 converged at $R1 = 0.0557$ and $wR2 = 0.1618$ [based on $I > 2\sigma(I)$], $R1 = 0.0734$ and $wR2 = 0.1749$ for all data.

Sheldrick, G.M. SHELXTL, v. 6.12; Bruker Analytical X-ray, Madison, WI, 2001.

Sheldrick, G.M. SADABS, v. 2.10. Program for Empirical Absorption Correction of Area Detector Data, University of Gottingen: Gottingen, Germany, 2003.

Saint Plus, v. 7.34, Bruker Analytical X-ray, Madison, WI, 2006.

Table S8. Crystal data and structure refinement for tl129a.

Identification code	tl129a
Empirical formula	$C_{13}H_{13}NO_3$
Formula weight	231.24
Temperature	108(2) K
Wavelength	0.71073 Å

Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 9.1687(15) Å alpha = 90 deg. b = 11.3315(19) Å beta = 102.627(2) deg. c = 11.5459(19) Å gamma = 90 deg.
Volume	1170.5(3) Å ³
Z, Calculated density	4, 1.312 Mg/m ³
Absorption coefficient	0.094 mm ⁻¹
F(000)	488
Crystal size	0.42 x 0.20 x 0.12 mm
Theta range for data collection	2.28 to 27.34 deg.
Limiting indices	-11<=h<=11, -14<=k<=14, -14<=l<=14
Reflections collected / unique	24176 / 2644 [R(int) = 0.0447]
Completeness to theta = 27.34	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9888 and 0.9616
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	2644 / 0 / 159
Goodness-of-fit on F ²	1.066
Final R indices [I>2sigma(I)]	R1 = 0.0557, wR2 = 0.1618
R indices (all data)	R1 = 0.0734, wR2 = 0.1749
Largest diff. peak and hole	0.352 and -0.445 e.Å ⁻³

Table S9. Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å² x 10³) for tl129a.

U(eq) is defined as one third of the trace of the orthogonalized Uij tensor.

	x	y	z	U(eq)
N(1)	7211(2)	4308(2)	3223(2)	33(1)
O(1)	5768(2)	4285(2)	3454(2)	37(1)
O(2)	5697(2)	1390(1)	2384(1)	27(1)
O(3)	5033(2)	1328(1)	4120(1)	33(1)
C(1)	7894(2)	3332(2)	3559(2)	24(1)
C(2)	9430(2)	3279(2)	3361(2)	25(1)
C(3)	10349(3)	4280(2)	3511(2)	34(1)
C(4)	11759(3)	4227(2)	3271(3)	43(1)
C(5)	12286(3)	3190(2)	2879(2)	40(1)
C(6)	11393(2)	2184(2)	2747(2)	33(1)
C(7)	9988(2)	2229(2)	2997(2)	27(1)
C(8)	7247(2)	2323(2)	4116(2)	24(1)
C(9)	5959(2)	1657(2)	3422(2)	27(1)
C(10)	5457(3)	1862(2)	5301(2)	37(1)
C(11)	6967(2)	2381(2)	5359(2)	32(1)
C(12)	8173(2)	1596(2)	5127(2)	29(1)
C(13)	8102(3)	265(2)	5158(2)	38(1)

Table S10. Bond lengths [Å] and angles [deg] for tl129a.

N(1)-C(1)	1.288(3)
N(1)-O(1)	1.407(3)
O(2)-C(9)	1.207(2)
O(3)-C(9)	1.345(2)
O(3)-C(10)	1.464(3)
C(1)-C(2)	1.476(3)
C(1)-C(8)	1.496(3)
C(2)-C(7)	1.396(3)
C(2)-C(3)	1.400(3)
C(3)-C(4)	1.381(3)
C(4)-C(5)	1.384(4)
C(5)-C(6)	1.392(3)
C(6)-C(7)	1.381(3)
C(8)-C(9)	1.481(3)
C(8)-C(11)	1.514(3)
C(8)-C(12)	1.527(3)
C(10)-C(11)	1.492(3)
C(11)-C(12)	1.488(3)
C(12)-C(13)	1.511(3)
C(1)-N(1)-O(1)	110.0(2)
C(9)-O(3)-C(10)	111.69(17)
N(1)-C(1)-C(2)	113.90(18)
N(1)-C(1)-C(8)	124.98(19)
C(2)-C(1)-C(8)	121.12(16)
C(7)-C(2)-C(3)	118.5(2)
C(7)-C(2)-C(1)	120.39(17)
C(3)-C(2)-C(1)	121.13(18)
C(4)-C(3)-C(2)	120.3(2)
C(3)-C(4)-C(5)	120.8(2)
C(4)-C(5)-C(6)	119.5(2)
C(7)-C(6)-C(5)	119.9(2)
C(6)-C(7)-C(2)	120.98(19)
C(9)-C(8)-C(1)	120.09(16)
C(9)-C(8)-C(11)	104.76(16)
C(1)-C(8)-C(11)	122.64(17)
C(9)-C(8)-C(12)	112.53(17)
C(1)-C(8)-C(12)	122.31(17)
C(11)-C(8)-C(12)	58.60(13)
O(2)-C(9)-O(3)	120.68(18)
O(2)-C(9)-C(8)	128.82(18)
O(3)-C(9)-C(8)	110.49(17)
O(3)-C(10)-C(11)	105.07(16)
C(12)-C(11)-C(10)	118.3(2)
C(12)-C(11)-C(8)	61.11(13)

C(10)-C(11)-C(8)	106.74(17)
C(11)-C(12)-C(13)	123.71(19)
C(11)-C(12)-C(8)	60.28(13)
C(13)-C(12)-C(8)	122.49(19)

Symmetry transformations used to generate equivalent atoms:

Table S11. Anisotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for tl129a.

The anisotropic displacement factor exponent takes the form:

$$-2 \pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$$

	U11	U22	U33	U23	U13	U12
N(1)	29(1)	32(1)	38(1)	0(1)	9(1)	-1(1)
O(1)	29(1)	35(1)	49(1)	4(1)	13(1)	2(1)
O(2)	28(1)	29(1)	24(1)	-3(1)	6(1)	-6(1)
O(3)	25(1)	45(1)	30(1)	1(1)	9(1)	-3(1)
C(1)	27(1)	20(1)	23(1)	-2(1)	-1(1)	1(1)
C(2)	28(1)	24(1)	22(1)	5(1)	1(1)	-2(1)
C(3)	36(1)	21(1)	45(1)	3(1)	5(1)	-3(1)
C(4)	34(1)	29(1)	66(2)	10(1)	8(1)	-8(1)
C(5)	28(1)	37(1)	55(2)	16(1)	12(1)	-1(1)
C(6)	32(1)	30(1)	36(1)	9(1)	9(1)	4(1)
C(7)	29(1)	22(1)	28(1)	3(1)	3(1)	-2(1)
C(8)	21(1)	26(1)	23(1)	-2(1)	4(1)	3(1)
C(9)	24(1)	31(1)	26(1)	4(1)	6(1)	-2(1)
C(10)	32(1)	54(1)	24(1)	-3(1)	7(1)	2(1)
C(11)	33(1)	41(1)	22(1)	-3(1)	6(1)	2(1)
C(12)	24(1)	35(1)	26(1)	5(1)	2(1)	0(1)
C(13)	36(1)	36(1)	45(1)	16(1)	14(1)	4(1)

Table S12. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($\text{\AA}^2 \times 10^3$) for tl129a.

x	y	z	U(eq)
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H(1)	5270(40)	5130(30)	3150(30)	69(10)
H(3A)	10002	4998	3779	41
H(4A)	12374	4910	3377	52
H(5A)	13249	3165	2702	48
H(6A)	11749	1467	2484	39
H(7A)	9393	1535	2921	32
H(10A)	5497	1258	5927	44
H(10B)	4733	2481	5402	44
H(11A)	7252	3115	5837	38
H(12A)	9200	1918	5434	35
H(13A)	8595	-16	5949	58
H(13B)	8609	-63	4567	58
H(13C)	7055	11	4978	58

Table S13. Hydrogen bonds for tl129a [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1)...O(2)#1	1.08(4)	1.73(4)	2.804(2)	174(3)

Symmetry transformations used to generate equivalent atoms:

#1 $-x+1, y+1/2, -z+1/2$