Supporting Information for:

**Oxone® as an Inexpensive, Safe, and Environmentally Benign
Oxidant for C-H Bond Oxygenation**

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Experimental Procedures for the synthesis of **2a-19b**

General Procedures: NMR spectra were obtained on a Varian Inova 500 (499.90 MHz for ^1H ; 125.70 MHz for ^{13}C) unless otherwise noted. ^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), triplet (t), quartet (q), quintet (quin), multiplet (m), and broad resonance (br). IR spectra were obtained on a Perkin-Elmer Spectrum BX FT-IR spectrometer.

Materials and Methods:

Oxime substrates **2** – **11**, **12**, **13** and **19** were prepared following the procedure described previously.¹ The isoxazoline **13** was prepared following a procedure by Mapp et al.² The amide substrates **12**, **17** and **18** were prepared by palladium-catalyzed arylation of the corresponding lactone.³ $\text{Pd}(\text{OAc})_2$ was obtained from Pressure Chemical and used as received, and $\text{PhI}(\text{OAc})_2$ was obtained from Merck Research Laboratories and used as received. Oxone® was obtained from Acros and used as received, and $\text{K}_2\text{S}_2\text{O}_8$ was obtained from Fisher Chemical and used as received. Solvents were obtained from Fisher Chemical and used without further purification. 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. Control reactions (in the absence of Pd catalyst) were run for each substrate, and generally showed no reaction. The regioselectivity of acetoxylation and etherification was determined based on coupling constant analysis and assignment of each aromatic proton of the products as detailed below.

General Procedure for Table 1:

Peroxide (1.75 mmol, 2.0 equiv) and Pd(OAc)₂ (9.81 mg, 0.044 mmol, 0.05 equiv) were combined in AcOH (3.7 mL) and Ac₂O (3.7 mL) in a 20 mL vial. Substrate **2** (200 mg, 0.88 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100 °C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether. A 10% aqueous solution of Na₂SO₃ (450 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.25 in 88% hexanes/12% ethyl acetate; minor oxime isomer: R_f = 0.23 in 88% hexanes/12% ethyl acetate). The two oxime isomers were isolated as yellow oils in a ratio of 5:1. The ratio of regioisomers was >20:1.

Procedure for large scale reaction:

Oxone® (80.79 g, 131.41 mmol, 2.0 equiv) and Pd(OAc)₂ (441 mg, 1.97 mmol, 0.03 equiv) were combined in AcOH (493 mL) and Ac₂O (55 mL) in a 1000 mL round bottom flask. Substrate **2** (15 g, 65.7 mmol, 1.0 equiv) was then added to the mixture. The reaction was refluxed for 18 h. The reaction mixture was diluted with ethyl acetate (500 mL) and filtered through a pad of celite and washed with ethyl acetate (1 L). The ethyl acetate, AcOH and Ac₂O were removed under reduced pressure. The product was obtained as a yellow oil through Kugelrohr distillation (10.15 g, 54% yield).

Procedure for reaction using PhI(OAc)₂

PhI(OAc)₂ (311 mg, 0.97 mmol, 1.1 equiv) and Pd(OAc)₂ (9.8 mg, 0.04 mmol, 0.05 equiv) were combined in AcOH (3.7 mL) and Ac₂O (3.7 mL) in a 20 mL vial. Substrate **2** (200 mg, 0.88 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100 °C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.25, 88% in hexanes/12% ethyl acetate; minor oxime isomer: R_f = 0.23, 88% in hexanes/12% ethyl acetate). The two oxime isomers were isolated as yellow oils (202.5 mg total, 81% yield, ratio of oxime isomers = 5:1). The ratio of regioisomers was >20:1.

Major Oxime Isomer: ¹H NMR (CDCl₃): δ 7.56 (d, J = 2.4 Hz, 1H_a), 7.47 (dd, J = 8.6, 2.4 Hz, 1H_b), 6.98 (d, J = 8.6 Hz, 1H_c), 3.97 (s, 3H), 2.27 (s, 3H), 2.13 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 168.82, 152.23, 147.02, 132.49, 132.23, 132.09, 124.87, 119.07, 62.07, 20.96, 14.89. Minor Oxime Isomer: ¹H NMR (CDCl₃): δ 7.48 (dd, J = 8.7,

2.4 Hz, 1H_b), 7.32 (d, *J* = 2.4 Hz, 1H_a), 7.03 (d, *J* = 8.7 Hz, 1H_c), 3.79 (s, 3H), 2.25 (s, 3H), 2.12 (s, 3H). IR (thin film): 2937, 1768 cm⁻¹. HRMS electrospray (*m/z*): [M⁺] calcd for C₁₁H₁₂BrNO₃, 285.0000; found, 285.0005. GC analysis (RESTEK Rtx[®]-5, FID detector): 99% integration. Anal. Calcd. for C₁₁H₁₂BrNO₂ (mixture of oxime isomers): C, 46.18, H, 4.23, N, 4.90; Found: C, 46.20, H, 4.19, N, 4.90.

Oxone[®] (808 mg, 1.31 mmol, 2.0 equiv) and Pd(OAc)₂ (15 mg, 0.07 mmol, 0.1 equiv) were combined in MeOH (5.48 mL) in a 20 mL vial. Substrate **2** (150 mg, 0.66 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was stirred at rt for 12 h and then stirred at 80 °C for another 12 h. The reaction mixture was diluted with ethyl acetate, and extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: 0.28 R_f = 90% in hexanes/10% ethyl acetate; minor oxime isomer: R_f = 0.26 in 90% hexanes/10% ethyl acetate). The two isomers were isolated as yellow oils. Under the reaction conditions oxime **2b** underwent partial hydrolysis to the corresponding ketone. Isolated product (119 mg total, 70% yield, ratio of oxime isomers = 5:1, ratio of oxime to ketone = 4:1). The ratio of regioisomers was >20:1.

Major Oxime Isomer of **2b**: ¹H NMR (acetone-*d*₆): δ 7.51 (dd, *J* = 8.8, 2.6 Hz, 1H_b), 7.38 (d, *J* = 2.6 Hz, 1H_a), 7.03 (d, *J* = 8.8 Hz, 1H_c), 3.90 (s, 3H), 3.87 (s, 3H), 2.10 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 156.64, 155.28, 132.64, 132.16, 128.78, 112.84, 112.69, 61.86, 55.72, 15.77. IR (thin film): 2932, 1606, 1486 cm⁻¹. HRMS electrospray (*m/z*): [M⁺] calcd for C₁₀H₁₂BrNO₂, 257.0051; found, 257.0045. GC analysis (RESTEK Rtx[®]-5, FID detector): 100% integration. Ketone: ¹H NMR (CDCl₃): δ 7.49 (d, *J* = 2.4 Hz, 1H), 7.32 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 1H), 4.01 (s, 3H), 2.28 (s, 3H).

Procedure using Oxone[®] as the oxidant

Oxone® (783 mg, 1.27 mmol, 0.95 equiv) and Pd(OAc)₂ (15 mg, 0.07 mmol, 0.05 equiv) were combined in AcOH (11.2 mL) in a 20 mL vial. Substrate **3** (200 mg, 1.34 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (25 mL), and the vial was washed with copious diethyl ether. A 10% aqueous solution of Na₂SO₃ (450 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated, and the organic layer was extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime E/Z isomers (major oxime isomer: R_f = 0.26 in 89% hexanes/11% ethyl acetate; minor oxime isomer: R_f = 0.25 in 89% hexanes/11% ethyl acetate). The two isomers were isolated as yellow oils (147 mg total, 53% yield, ratio of oxime isomers = 5:1).

Procedure using PhI(OAc)₂ as the oxidant

PhI(OAc)₂ (475 mg, 1.48 mmol, 1.10 equiv), and Pd(OAc)₂ (15.0 mg, 0.07 mmol, 0.05 equiv) were combined in AcOH (5.6 mL) and Ac₂O (5.6 mL) in a 20 mL vial. Substrate **3** (200 mg, 1.34 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.26, 89% in hexanes/11% ethyl acetate; minor oxime isomer: R_f = 0.25, 89% in hexanes/11% ethyl acetate). The two isomers were isolated as yellow oils (203.2 mg total, 73% yield, ratio of oxime isomers = 5:1).

Major Oxime Isomer: ¹H NMR (CDCl₃): δ 7.43 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.37 (td, *J* = 7.8, 1.7 Hz, 1H), 7.25 (td, *J* = 7.5, 1.2 Hz, 1H), 7.10 (dd, *J* = 8.1, 1.2 Hz, 1H), 3.97 (s, 3H), 2.29 (s, 3H), 2.16 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 169.25, 153.44, 147.95, 130.30, 129.72, 129.45, 126.10, 123.21, 61.94, 21.08, 15.09. Minor Oxime Isomer: ¹H NMR (CDCl₃): δ 7.37 (dd, *J* = 7.4, 1.8 Hz, 1H), 7.29 (m, 1H), 7.21 (dd, *J* = 7.6, 1.8 Hz, 1H), 7.14 (dd, *J* = 8.1, 1.5 Hz, 1H), 3.79 (s, 3H), 2.26 (s, 3H), 2.14 (s, 3H). IR (thin film): 2938, 1764 cm⁻¹. Anal. Calcd. for C₁₁H₁₃NO₃ (mixture of oxime isomers): C, 63.76, H, 6.32, N, 6.76; Found: C, 63.88, H, 6.08, N, 6.81.

Procedure using Oxone® as the oxidant

Oxone® (755 mg, 1.23 mmol, 1.1 equiv) and Pd(OAc)₂ (12.5 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (9.3 mL) in a 20 mL vial. Substrate **4** (200 mg, 1.12 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. Under the

reaction conditions the OAc of **4a** partially hydrolyzed to the corresponding alcohol. The reaction mixture was concentrated under vacuum and Ac₂O (2.2 mL) and pyridine (0.43 mL) was added and the reaction stirred for 18 h. The reaction was stirred in water (5 mL) for 30 minutes and then extracted with ether. The ethereal layer was washed with water (2 x 50 mL), and NaHCO₃ (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford the product as a 3:1 mixture of oxime isomers (major oxime isomer: R_f = 0.23 in 85% hexanes/15% ethyl acetate; minor oxime isomer: R_f = 0.18 in 85% hexanes/15% ethyl acetate). The two oxime isomers were isolated as yellow oils (180 mg total, 69% yield, ratio of oxime isomers = 9:1). The ratio of regioisomers was 18:1.

Procedure using PhI(OAc)₂ as the oxidant

PhI(OAc)₂ (375 mg, 1.17 mmol, 1.10 equiv) and Pd(OAc)₂ (12 mg, 0.05 mmol, 0.05 equiv) were combined in AcOH (8.8 mL) in a 20 mL vial. Substrate **4** (190 mg, 1.06 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford the product as a 6:1 mixture of oxime isomers (major oxime isomer: R_f = 0.23 in 85% hexanes/15% ethyl acetate; minor oxime isomer: R_f = 0.18 in 85% hexanes/15% ethyl acetate). The two oxime isomers were isolated as yellow oils (201.6 mg total, 78% yield, ratio of oxime isomers = 9:1). The ratio of regioisomers was 18:1.

Major Oxime Isomer: ¹H NMR (acetone-*d*₆) (399.97 Hz): δ 7.05 (d, *J* = 8.7 Hz, 1H_c), 6.99 (d, *J* = 3.0 Hz, 1H_a), 6.95 (dd, *J* = 8.7, 3.0 Hz, 1H_b), 3.90 (s, 3H), 3.81 (s, 3H), 2.22 (s, 3H), 2.11 (s, 3H). ¹³C{¹H} NMR (acetone-*d*₆) (100.57 Hz): δ 169.87, 158.12, 153.83, 142.69, 132.13, 125.17, 115.58, 115.06, 62.14, 56.03, 20.99, 15.12. Minor Oxime Isomer: ¹H NMR (CDCl₃): δ 7.05 (d, *J* = 8.9 Hz, 1H_c), 6.88 (dd, *J* = 8.9, 3.0 Hz, 1H_b), 6.70 (d, *J* = 3.0 Hz, 1H_a), 3.80 (s, 3H), 3.80 (s, 3H), 2.24 (s, 3H), 2.12 (s, 3H). IR (thin film): 2939, 1764 cm⁻¹. Anal. Calcd. for C₁₂H₁₅NO₄ (mixture of oxime isomers): C, 60.75, H, 6.37, N, 5.90; Found: C, 60.97, H, 6.23, N, 6.09.

Procedure using Oxone® as the oxidant

Oxone® (753 mg, 1.22 mmol, 1.0 equiv), and Pd(OAc)₂ (13.7 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (10.21 mL) in a 20 mL vial. Substrate **5** (200 mg, 1.22 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. Under the reaction conditions the OAc of **5a** partially hydrolyzed to the corresponding alcohol. The reaction mixture was concentrated under vacuum and Ac₂O (2.4 mL) and pyridine (0.46 mL) was added and the

reaction stirred for 18 h. The reaction was stirred in water (5 mL) for 30 minutes and then extracted with ether. The ethereal layer was washed with water (2 x 50 mL), and NaHCO₃ (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford the product as a 2:1 mixture of oxime isomers (major oxime isomer: R_f = 0.25 in 89% hexanes/11% ethyl acetate; minor oxime isomer: R_f = 0.20 in 89% hexanes/11% ethyl acetate). The two oxime isomers were isolated as yellow oils (192 mg total, 71% yield, ratio of oxime isomers = 2:1). The ratio of regioisomers was 11:1.

Procedure using PhI(OAc)₂ as the oxidant

PhI(OAc)₂ (434 mg, 1.35 mmol, 1.10 equiv), and Pd(OAc)₂ (13.7 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (10.2 mL) in a 20 mL vial. Substrate 5 (200 mg, 1.22 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford the product as a 2:1 mixture of oxime isomers (major oxime isomer: R_f = 0.25 in 89% hexanes/11% ethyl acetate; minor oxime isomer: R_f = 0.20 in 89% hexanes/11% ethyl acetate). The two oxime isomers were isolated as yellow oils (194 mg total, 72% yield, ratio of oxime isomers of the major regioisomer 2:1). The ratio of regioisomers was 11:1.

Major Oxime Isomer/Major Regioisomer: ¹H NMR (CDCl₃): δ 7.23 (d, J = 2.2 Hz, 1H_a), 7.16 (dd, J = 8.2, 2.2 Hz, 1H_b), 6.98 (d, J = 8.2 Hz, 1H_c), 3.97 (s, 3H), 2.34 (s, 3H), 2.26 (s, 3H), 2.15 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 169.32, 153.53, 145.66, 135.68, 131.33, 130.22, 129.75, 122.79, 61.80, 20.95, 20.65, 15.04. Minor Oxime Isomer/Major Regioisomer: ¹H NMR (CDCl₃): δ 7.17 (d, J = 8.3, 2.2 Hz, 1H_b), 7.02 (dd, J = 8.3 Hz, 1H_c), 6.99 (d, J = 2.2 Hz, 1H_a), 3.79 (s, 3H), 2.35 (s, 3H), 2.24 (s, 3H), 2.12 (s, 3H). Major Oxime Isomer/Minor Regioisomer: ¹H NMR (CDCl₃): δ 7.23 (m, 2H), 7.17 (d, J = 7.6 Hz, 1H), 3.96 (s, 3H), 2.30 (s, 3H), 2.19 (s, 3H), 2.15 (s, 3H). IR (thin film): 2937, 1765 cm⁻¹. HRMS electrospray (m/z): [M⁺] calcd for C₁₂H₁₅NO₃, 221.1047; found, 221.1052. GC analysis (RESTEK Rtx[®]-5, FID detector): 100% integration.

Procedure using Oxone[®] as the oxidant

Oxone[®] (735 mg, 1.2 mmol, 1.0 equiv) and Pd(OAc)₂ (13 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (5 mL) and Ac₂O (5 mL) in a 20 mL vial. Substrate 6 (200 mg, 1.2 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether.

A 10% aqueous solution of Na₂SO₃ (50 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel in 90% hexanes/10% ethyl acetate to afford an inseparable mixture of four products (R_f = 0.27-0.24) – 2 regioisomers and 2 oxime isomers of each regioisomer – as a clear oil (170 mg total, 63% yield). The identity of the major regioisomer and its oxime isomers was confirmed by independent synthesis, and the NMR spectra reported below are for this independently synthesized product. Gas chromatographic analysis showed that the reaction afforded an 1.6:1 mixture of regioisomers and that each of the regioisomers was a 6:1 mixture of oxime isomers.

Procedure using PhI(OAc)₂ as the oxidant

PhI(OAc)₂ (501 mg, 1.56 mmol, 1.30 equiv), and Pd(OAc)₂ (13.4, 0.06 mmol, 0.05 equiv) were combined in AcOH (5 mL) and Ac₂O (5 mL) in a 20 mL vial. Substrate **6** (200 mg, 1.20 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered and concentrated. The resulting oil was purified by chromatography on silica gel in 90% hexanes/10% ethyl acetate to afford an inseparable mixture of four compounds (R_f = 0.27-0.24) – 2 regioisomeric products and 2 oxime isomers of each regioisomer – as a clear oil (154 mg total, 57% yield). The identity of the major regioisomer and its oxime isomers was confirmed by independent synthesis, and the NMR spectra reported below are for this independently synthesized product. Gas chromatographic analysis showed that the reaction afforded an 1.6:1 mixture of regioisomers and that each of the regioisomers was a 6:1 mixture of oxime isomers.

Major Oxime Isomer/Major Regioisomer: ¹H NMR (C₆D₆): δ 7.02 (dd, 9.0, 3.0 Hz, 1H), 6.71 (dd, 8.9, 5.0 Hz, 1H), 6.60 (m, 1H), 3.76 (s, 3H), 1.95 (s, 3H), 1.74 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 169.09, 159.87 (¹J_{CF} = 245 Hz), 152.29 (⁴J_{CF} = 1.7 Hz), 143.74 (⁴J_{CF} = 2.9 Hz), 131.66 (³J_{CF} = 8.0 Hz), 124.56 (³J_{CF} = 8.7 Hz), 116.16 (²J_{CF} = 23 Hz), 115.93 (²J_{CF} = 24 Hz), 61.93, 20.80, 14.67. ¹⁹F NMR (CDCl₃): δ -116.3 - -116.36 (m). Minor Oxime Isomer/Major Regioisomer: ¹H NMR (C₆D₆): δ 6.77 (dd, J = 8.9, 5.0 Hz, 1H), 6.62 (dd, J = 9.0, 3.0 Hz, 1H), 6.61-6.56 (overlapping peaks), 3.64 (s, 3H), 1.90 (s, 3H), 1.50 (s, 3H). IR (thin film): 2939, 1770 cm⁻¹. HRMS electrospray (m/z): [M⁺] calcd for C₁₁H₁₂FNO₃, 225.0801; found, 225.0797. GC analysis (RESTEK Rtx[®]-5, FID detector): 99% integration.

Procedure using $K_2S_2O_8$ as the oxidant

$K_2S_2O_8$ (373 mg, 1.38 mmol, 2.0 equiv) and $Pd(OAc)_2$ (7.7 mg, 0.03 mmol, 0.05 equiv) were combined in AcOH (2.88 mL) and Ac_2O (2.88 mL) in a 20 mL vial. Substrate **7** (150 mg, 0.69 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether. A 10% aqueous solution of Na_2SO_3 (50 mL) was added to the filtrate, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), $NaHCO_3$ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.27 in 87% hexanes/13% ethyl acetate; minor oxime isomer: R_f = 0.25 in 87% hexanes/13% ethyl acetate). The two oxime isomers were isolated as yellow oils (142 mg total, 75% yield, ratio of oxime isomers = 5:1). The ratio of regioisomers was >20:1.

Procedure using $PhI(OAc)_2$ as the oxidant

$PhI(OAc)_2$ (326 mg, 1.01 mmol, 1.10 equiv) and $Pd(OAc)_2$ (10.3 mg, 0.05 mmol, 0.05 equiv) were combined in AcOH (3.8 mL) and Ac_2O (3.8 mL) in a 20 mL vial. Substrate **7** (200 mg, 0.92 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), $NaHCO_3$ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.27 in 87% hexanes/13% ethyl acetate; minor oxime isomer: R_f = 0.25 in 87% hexanes/13% ethyl acetate). The two isomers were isolated as yellow oils (280.9 mg total, 95% yield, ratio of oxime isomers = 5:1). The ratio of regioisomers was >20:1.

Major Oxime Isomer: 1H NMR ($CDCl_3$): δ 7.71 (d, J = 2.3 Hz, $1H_a$), 7.63 (dd, J = 8.5, 2.3 Hz, $1H_b$), 7.24 (d, J = 8.5 Hz, $1H_c$), 3.99 (s, 3H), 2.31 (s, 3H), 2.17 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 168.62, 152.30, 150.49, 131.07, 128.38 ($^2J_{CF}$ = 33 Hz), 126.85 ($^3J_{CF}$ = 3.8 Hz), 126.62 ($^3J_{CF}$ = 3.6 Hz), 123.60 ($^1J_{CF}$ = 272 Hz), 123.91, 62.14, 20.96, 14.93. ^{19}F NMR ($CDCl_3$): δ -62.37 (s). **Minor Oxime Isomer:** 1H NMR ($CDCl_3$): δ 7.60 (m, $1H_b$), 7.43 (d, J = 2.7 Hz, $1H_a$), 7.20 (d, J = 8.5 Hz, $1H_c$), 3.76 (s, 3H), 2.25 (s, 3H), 2.12 (s, 3H). IR (thin film): 2942, 1770 cm^{-1} . HRMS electrospray (m/z): $[M^+]$ calcd for $C_{12}H_{12}F_3NO_3$, 275.0769; found, 275.0775. GC analysis (RESTEK Rtx[®]-5, FID detector): 100% integration.

Procedure using $K_2S_2O_8$ as the oxidant

Substrate **8** (150 mg, 0.86 mmol, 1.0 equiv), $K_2S_2O_8$ (466 mg, 1.72 mmol, 2.0 equiv), and $Pd(OAc)_2$ (10 mg, 0.04 mmol, 5 mol%) were combined in AcOH (3.59 mL) and Ac_2O (3.59 mL) in a 20 mL vial. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was concentrated under vacuum and Ac_2O (1.8 mL) and pyridine (0.33 mL) was added and the reaction stirred for 18 h. The reaction was stirred in water (5 mL) for 30 minutes and then extracted with ether. The ethereal layer was washed with water (2 x 50 mL), and $NaHCO_3$ (1 x 50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime E/Z isomers (major oxime isomer: R_f = 0.27 in 78% hexanes/22% ethyl acetate; minor oxime isomer: R_f = 0.25 in 78% hexanes/22% ethyl acetate). The two oxime isomers were isolated as a pale yellow solid (115 mg total, 57% yield, ratio of oxime isomers = 6:1). The ratio of regioisomers was 6:1.

Procedure using $PhI(OAc)_2$ as the oxidant

$PhI(OAc)_2$ (555 mg, 1.72 mmol, 1.10 equiv) and $Pd(OAc)_2$ (12.9 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (4.8 mL) and Ac_2O (4.8 mL) in a 20 mL vial. Substrate **8** (200 mg, 1.15 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), $NaHCO_3$ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.23, in 90% hexanes/10% ethyl acetate; minor oxime isomer: R_f = 0.20, in 90% hexanes/10% ethyl acetate). The two oxime isomers were isolated as pale yellow solid (176.2 mg total, 66% yield, ratio of oxime isomers = 6:1). The ratio of regioisomers was 6:1.

Major Oxime Isomer/Major Regioisomer: 1H NMR ($CDCl_3$): δ 7.78 (d, J = 2.1 Hz, $1H_a$), 7.68 (dd, J = 8.4, 2.1 Hz, $1H_b$), 7.27 (d, J = 8.4 Hz, $1H_c$), 4.01 (s, 3H), 2.33 (s, 3H), 2.17 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 168.26, 151.68, 151.31, 133.65, 133.18, 131.78, 124.51, 117.80, 110.19, 62.24, 20.98, 14.87. Minor Oxime Isomer/Major Regioisomer: 1H NMR ($CDCl_3$): δ 7.66 (dd, J = 8.4, 2.0 Hz, $1H_b$), 7.52 (d, J = 2.0 Hz, $1H_a$), 7.29 (d, J = 8.5 Hz, $1H_c$), 3.79 (s, 3H), 2.89 (s, 3H), 2.14 (s, 3H). Major Oxime Isomer/Minor Regioisomer: 1H NMR ($CDCl_3$): δ 7.67 (t, J = 8.8, 7.8 Hz, 2H), 7.37 (t, J = 7.8 Hz, 1H), 3.98 (s, 3H), 2.38 (s, 3H), 2.16 (s, 3H). IR (thin film): 2230, 1770 cm^{-1} . HRMS electrospray (m/z): $[M^+]$ calcd for $C_{12}H_{12}N_2O_3$, 232.0848; found, 232.0848. GC analysis (RESTEK Rtx[®]-5, FID detector): 100% integration.

Procedure using Oxone[®] as the oxidant

Oxone® (1498 mg, 2.44 mmol, 2.0 equiv) and Pd(OAc)₂ (13.6 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (10.15 mL) in a 20 mL vial. Substrate **9** (200 mg, 1.22 mmol, 1.0 equiv), was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, filtered through a pad of Celite, and washed with copious diethyl ether. A 10% aqueous solution of Na₂SO₃ (450 mL) was added to the filtrate, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.25 in 90% hexanes/10% ethyl acetate). Under the chromatography conditions the OAc underwent partial hydrolysis to the corresponding alcohol. The product was isolated as a pale yellow solid (100 mg total, 37% yield, ratio of OAc to free OH, 2:1); mp = 67 – 72 °C. The ratio of oxime isomers and regioisomers was >20:1.

¹H NMR of **9a** (CDCl₃): δ 11.65 (s, 1H), 7.31 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.06 (dd, *J* = 7.9, 1.5 Hz, 1H), 6.88 (t, *J* = 8.0 Hz, 1H), 3.99 (s, 3H), 2.35 (s, 3H), 2.30 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 169.08, 158.17, 149.79, 139.25, 125.09, 123.98, 119.81, 118.49, 62.54, 20.65, 11.61. IR (KBr): 2943, 1760 cm⁻¹. HRMS electrospray (*m/z*): [M⁺] calcd for C₁₁H₁₃NO₄, 223.0844; found, 223.0843. GC analysis (RESTEK Rtx®-5, FID detector): 100% integration. Hydrolyzed (OH) product: ¹H NMR (CDCl₃): δ 6.96 (t, *J* = 7.5 Hz, 2H), 6.81 (t, *J* = 7.9 Hz, 1H), 5.71 (s, 1H), 4.02 (s, 3H), 2.30 (s, 3H).

Procedure using K₂S₂O₈ as the oxidant

K₂S₂O₈ (655 mg, 2.42 mmol, 2.0 equiv) and Pd(OAc)₂ (13.0 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (10 mL) in a 20 mL vial. Substrate **10** (200 mg, 1.21 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, filtered, and the vial was washed with copious diethyl ether. A solution of 10% aqueous Na₂SO₃ (50 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.28 in 90% hexanes/10% ethyl acetate). The product was isolated as a yellow oil (143 mg, 53% yield). The ratio of oxime isomers 17:1 and regioisomers was >20:1.

Procedure using PhI(OAc)₂ as the oxidant

PhI(OAc)₂ (322 mg, 1.00 mmol, 1.10 equiv), and Pd(OAc)₂ (10.2 mg, 0.05 mmol, 0.05 equiv) were combined in AcOH (7.6 mL) in a 20 mL vial. Substrate **10** (150 mg, 0.91 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.28 in 90% hexanes/10% ethyl acetate). The product was isolated as a yellow oil (81.2 mg, 40% yield). The ratio of oxime isomers 17:1 and regioisomers was >20:1.

¹H NMR (CDCl₃): δ 8.07 (s, 1H), 7.28 (d, *J* = 3.0 Hz, 1H_a), 7.01 (d, *J* = 8.9 Hz, 1H_c), 6.93 (dd, *J* = 8.9, 3.0 Hz, 1H_b), 3.99 (s, 3H), 3.82 (s, 3H), 2.31 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 169.69, 157.46, 143.95, 142.54, 125.21, 123.95, 117.37, 110.97, 62.30, 55.79, 20.98. IR (thin film): 2938, 1763 cm⁻¹. HRMS electrospray (*m/z*): [M +] calcd for C₁₁H₁₃NO₄, 223.0845; found, 223.0842. GC analysis (RESTEK Rtx[®]-5, FID detector): 100% integration.

Procedure using K₂S₂O₈ as the oxidant

K₂S₂O₈ (544 mg, 2.011 mmol, 2.0 equiv) and Pd(OAc)₂ (11.3 mg, 0.05 mmol, 0.05 equiv) were combined in AcOH (8.38 mL) in a 20 mL vial. Substrate **11** (150 mg, 1.01 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether. A solution of 10% aqueous Na₂SO₃ (450 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.24 in 92% hexanes/8% ethyl acetate; minor oxime isomer: R_f = 0.24 in 92% hexanes/8% ethyl acetate). The product was isolated as a yellow oil (106 mg total, 53% yield, ratio of oxime isomers = 5:1).

Procedure using PhI(OAc)₂ as the oxidant

PhI(OAc)₂ (356 mg, 1.11 mmol, 1.10 equiv) and Pd(OAc)₂ (11.3 mg, 0.05 mmol, 0.05 equiv) were combined in AcOH (8.4 mL) in a 20 mL vial. Substrate **11** (200 mg, 1.34 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered,

and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: $R_f = 0.24$ in 92% hexanes/8% ethyl acetate; minor oxime isomer: $R_f = 0.24$ in 92% in hexanes/8% ethyl acetate). The two oxime isomers were isolated as yellow oils (153.1 mg total, 69% yield, ratio of oxime isomers = 5:1).

Major Oxime Isomer: ^1H NMR (CDCl_3): δ 8.25 (s, 1H), 7.27 (t, $J = 8.0, 7.5$ Hz, 1H), 7.12 (d, $J = 7.5$ Hz, 1H), 6.95 (d, $J = 8.0$ Hz, 1H), 3.99 (s, 3H), 2.47 (s, 3H), 2.33 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 169.69, 149.12, 144.60, 139.47, 129.93, 128.84, 123.32, 120.97, 62.19, 21.26, 21.13. Minor Oxime Isomer: ^1H NMR (CDCl_3): δ 7.39 (s, 1H), 7.29 (t, $J = 7.9$ Hz, 1H), 7.10 (d, $J = 7.7$ Hz, 1H), 6.96 (d, $J = 8.1$ Hz, 1H), 3.90 (s, 3H), 2.29 (s, 3H), 2.27 (s, 3H). IR (thin film): 2969, 1769 cm^{-1} . HRMS electrospray (m/z): $[\text{M}^+]$ calcd for $\text{C}_{11}\text{H}_{13}\text{NO}_3$, 207.0895; found, 207.0892. GC analysis (RESTEK Rtx[®]-5, FID detector): 99% integration.

Oxone (1237 mg, 2.014 mmol, 2.0 equiv) and $\text{Pd}(\text{OAc})_2$ (22.5 mg, 0.1 mmol, 0.1 equiv) were combined in MeOH (6 mL) in a 20 mL vial. Substrate **11** (150 mg, 1.01 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction and the reaction was stirred at rt for 12 h and then the temperature was slowly ramped to 80 °C over 20 minutes for another 12 h. The reaction mixture was diluted with ethyl acetate and extracted with water (2 x 50 mL), NaHCO_3 (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO_4 , filtered and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: $R_f = 0.25$ in 95% hexanes/5% ethyl acetate; minor oxime isomer: $R_f = 0.24$ in 95% hexanes/5% ethyl acetate). The two oxime isomers were isolated as yellow oils (106 mg total, 59% yield, ratio of oxime isomers = 3:1). Major Oxime Isomer: ^1H NMR (CDCl_3): δ 8.51 (s, 1H), 7.21 (t, $J = 8$ Hz, 1H), 6.83 (d, $J = 8$ Hz, 1H), 6.74 (d, $J = 8.5$ Hz, 1H), 3.99 (s, 3H), 3.83 (s, 3H), 2.52 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 158.48, 146.23, 139.09, 129.73, 123.55, 119.42, 108.13, 61.89, 55.65, 22.123. Minor Oxime Isomer: ^1H NMR (CDCl_3): δ 7.52 (s, 1H), 7.23 (t, $J = 7.8$ Hz, 1H), 6.84 (d, $J = 7.8$ Hz, 1H), 6.74 (d, $J = 8.3$ Hz, 1H), 3.93 (s, 3H), 3.80 (s, 3H), 2.25 (s, 3H). IR (thin film): 2935, 1595 cm^{-1} . HRMS electrospray (m/z): $[\text{M}^+]$ calcd for $\text{C}_{10}\text{H}_{13}\text{NO}_2$, 179.0946; found, 179.0940. GC analysis (RESTEK Rtx[®]-5, FID detector): 99% integration.

Procedure using $K_2S_2O_8$ as the oxidant

Substrate **12** (200 mg, 1.24 mmol, 1.0 equiv), $K_2S_2O_8$ (503 mg, 1.86 mmol, 1.5 equiv), and $Pd(OAc)_2$ (0.014 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (10 mL) in a 20 mL vial. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether. A solution of 10% aqueous Na_2SO_3 (50 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), $NaHCO_3$ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.26 in 15% hexanes/85% ethyl acetate). The product was obtained as a yellow oil (272 mg, 75% yield).

Procedure using $PhI(OAc)_2$ as the oxidant

$PhI(OAc)_2$ (493 mg, 1.53 mmol, 1.2 equiv), and $Pd(OAc)_2$ (14.3 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (10 mL) in a 20 mL vial. Substrate **12** (206 mg, 1.28 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The solvent was removed under vacuum to afford an orange oil, which was purified by chromatography on silica gel (R_f = 0.26 in 15% hexanes/85% ethyl acetate). The product was obtained as a yellow oil (213 mg, 77% yield).

1H NMR ($CDCl_3$): δ 7.29-7.21 (multiple peaks, 3H), 7.15 (d, J = 7.6 Hz, 1H), 3.70 (t, J = 6.9 Hz, 2H), 2.49 (t, J = 8.0 Hz, 2H), 2.24 (s, 3H), 2.13 (quin, J = 7.2 Hz, 2H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 173.88, 168.53, 145.64, 130.80, 127.86, 126.89, 126.25, 123.41, 49.82, 30.94, 20.71, 19.02. IR (thin film): 1766, 1702 cm^{-1} . HRMS electrospray (m/z): $[M^+]$ calcd for $C_{12}H_{13}NO_3$, 219.0895; found, 219.0894. GC analysis (RESTEK Rtx[®]-5, FID detector): 100% integration.

Substrate **12** (100 mg, 0.62 mmol, 1.0 equiv), $K_2S_2O_8$ (335 mg, 0.93 mmol, 2.0 equiv), and $Pd(OAc)_2$ (7 mg, 0.03 mmol, 0.05 equiv) were combined in MeOH (5 mL) in a 20 mL vial. The vial was sealed with a Teflon lined cap, and the reaction was stirred at rt for 12 h and then at 40 °C for 12 h. The reaction mixture was

diluted with ethyl acetate and extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.26 in 25% hexanes/75% ethyl acetate). The product was obtained as a yellow oil (85 mg, 72% yield).

¹H NMR (CDCl₃): δ 7.29-7.25 (multiple peaks, 2H), 7.01-6.96 (multiple peaks, 2H), 3.84 (s, 3H), 3.76 (t, J = 7.0 Hz, 2H), 2.56 (t, J = 7.9 Hz, 2H), 2.19 (quin, J = 7.2 Hz, 2H). ¹³C{¹H} NMR (CDCl₃): δ 175.12, 154.80, 128.60, 128.59, 127.20, 120.85, 111.99, 55.57, 49.90, 31.18, 18.92. IR (thin film): 2945, 1696 cm⁻¹. HRMS electrospray (m/z): [M⁺] calcd for C₁₁H₁₃NO₂, 191.0946; found, 191.0943. GC analysis (RESTEK Rt^x-5, FID detector): 100% integration.

Procedure using K₂S₂O₈ as the oxidant

K₂S₂O₈ (400 mg, 1.29 mmol, 3.0 equiv) and Pd(OAc)₂ (10 mg, 0.05 mmol, 0.1 equiv) were combined in AcOH (3.6 mL) in a 20 mL vial. Substrate **13** (100 mg, 0.43 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether. A solution of 10% aqueous Na₂SO₃ (50 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.26 in 55% hexanes/45% ethyl acetate). The product was obtained as a pale yellow viscous oil (79.0 mg, 53% yield).

Procedure using PhI(OAc)₂ as the oxidant

PhI(OAc)₂ (345 mg, 1.07 mmol, 2.5 equiv) and Pd(OAc)₂ (4.8 mg, 0.02 mmol, 0.05 equiv) were combined in AcOH (3.6 mL) in a 20 mL vial. Substrate **13** (100 mg, 0.43 mmol, 1.00 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate (30 mL). The organic layer was extracted with water (3 x 30 mL), NaHCO₃ (1 x 30 mL), and brine (1 x 30 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.26 in 55% hexanes/45% ethyl acetate). The product was obtained as a pale yellow viscous oil (108 mg, 72% yield). ¹H NMR (CDCl₃): δ 7.33 (t, J = 8.1 Hz, 1H), 6.99 (d, J = 8.2 Hz, 2H), 4.70-4.66 (m, 1H), 4.06-4.05 (multiple peaks, 2H), 3.59 (d, J = 3.3 Hz, 2H), 2.78 (dd, J = 17.4, 10.8 Hz, 1H), 2.44 (dd, J = 17.4, 7.8 Hz, 1H), 2.32 (s, 6H), 2.04 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 170.72, 169.22, 155.92, 150.10, 128.48, 120.89, 120.64, 77.76, 64.92,

38.22, 23.23, 20.78, 20.69. IR (thin film): 2939, 1769, 1742 cm^{-1} . HRMS electrospray (m/z): $[M^+]$ calcd for $\text{C}_{17}\text{H}_{19}\text{NO}_7$, 349.1162; found, 349.1160. GC analysis (RESTEK Rtx[®]-5, FID detector): 99% integration.

$\text{K}_2\text{S}_2\text{O}_8$ (837 mg, 3.1 mmol, 2.0 equiv) and $\text{Pd}(\text{OAc})_2$ (17.3 mg, 0.08 mmol, 0.05 equiv) were combined in AcOH (12.9 mL) in a 20 mL vial. Substrate **14** (200 mg, 1.54 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether. A solution of 10% aqueous Na_2SO_3 (50 mL) was added to the reaction, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO_3 (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO_4 , filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.3 in 90% hexanes/10% ethyl acetate; minor oxime isomer: R_f = 0.21 in 90% hexanes/10% ethyl acetate). The two oxime isomers were isolated as yellow oils (130 mg total, 45% yield, ratio of oxime isomers = 5:1). The NMR data was identical to that reported previously for this compound.¹

$\text{K}_2\text{S}_2\text{O}_8$ (895 mg, 3.31 mmol, 3.0 equiv) and $\text{Pd}(\text{OAc})_2$ (12 mg, 0.06 mmol, 0.05 equiv) were combined in AcOH (9.2 mL) in a 20 mL vial. Substrate **15** (200 mg, 1.1 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with ethyl acetate, and the vial was washed with copious diethyl ether. A solution of 10% aqueous Na_2SO_3 (50 mL) was added to the filtrate, and the resulting mixture was stirred at 25 °C for 15 min. The organic and the aqueous layers were separated and the organic layer was extracted with water (2 x 50 mL), NaHCO_3 (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO_4 , filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.28 in

90% hexanes/10% ethyl acetate). The product was isolated as a clear oil (166 mg total, 63% yield). The NMR data was identical to that reported previously for this compound.¹

Oxone® (853 mg, 1.39 mmol, 1.0 equiv) and Pd(OAc)₂ (16 mg, 0.07 mmol, 0.05 equiv) were combined in AcOH (11.6 mL) in a 20 mL vial. Substrate **16** (200 mg, 1.39 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was heated at 100°C for 12 h. The reaction mixture was diluted with chloroform and extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (*R_f* = 0.18 in 80% hexanes/20% ethyl acetate). The product was obtained as a yellow solid (28 mg, 10% yield). mp = 86-88 °C.

¹H NMR (399.96 Hz) (CDCl₃): δ 8.87 (s, 2H), 8.09 (d, *J* = 8.3 Hz, 1H), 7.84-7.75 (multiple peaks, 2H), 5.80 (s, 2H), 2.10 (s, 3H). ¹³C{¹H} NMR (100.57 Hz) (CDCl₃): δ 170.85, 145.03, 144.32, 142.83, 141.12, 134.71, 129.71, 129.70, 129.40, 61.85, 21.03. IR (KBr): 2927, 1739 cm⁻¹. HRMS electrospray (*m/z*): [M + Na] calcd for C₁₁H₁₀N₂O₂, 202.0742; found, 202.0738. GC analysis (RESTEK Rtx®-5, FID detector): 99% integration.

Along with the product **16a**, the *N*-oxide of the starting material (101 mg, 46% yield), (*R_f* = 0.15 in 70% hexanes/30% ethyl acetate) and the *N*-oxide of **16a** (27.0 mg, 9% yield), (*R_f* = 0.1 in 70% hexanes/30% ethyl acetate) were obtained, whose spectroscopic data are described below.

¹H NMR (CDCl₃): δ 8.70 (d, *J* = 3.5 Hz, 1H_a), 8.57 (d, *J* = 8.7 Hz, 1H_c), 8.38 (d, *J* = 3.5 Hz, 1H_b), 7.88 (d, *J* = 7.2 Hz, 1H_e), 7.75 (t, *J* = 7.3 Hz, 1H_d), 5.78 (s, 2H), 2.17 (s, 3H). ¹³C NMR (CDCl₃): 170.71, 145.31, 144.05, 137.59, 135.73, 130.83, 129.80, 129.35, 118.94, 61.78, 20.98. IR (KBr): 1735, 1242 cm⁻¹. mp = 112-113 °C. HRMS electrospray (*m/z*): [M + Na] calcd for C₁₁H₁₀N₂O₃, 218.0691; found, 218.0689. GC analysis (RESTEK Rtx®-5, FID detector): 99% integration. The assignment of the regioselectivity of *N*-oxidation was made based on comparison of the NMR of **16a-Ox** to **16a** as detailed in reference 4.

^1H NMR (CDCl_3): δ 8.62 (d, J = 3.45 Hz, 1H_a), 8.37 (d, J = 8.2 Hz, 1H_c), 8.31 (d, J = 3.46 Hz, 1H_b), 7.61-7.55 (multiple peaks, $2\text{H}_{d,e}$), 2.73 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 145.04, 144.38, 138.65, 137.59, 131.72, 129.77, 128.87, 116.56, 17.66. mp = 132-133 °C. IR (KBr): 1501, 1309 cm^{-1} . HRMS electrospray (m/z): $[\text{M} + \text{Na}]$ calcd for $\text{C}_9\text{H}_8\text{N}_2\text{O}$, 160.0637; found, 160.0634. GC analysis (RESTEK Rtx[®]-5, FID detector): 99% integration. The assignment of the regioselectivity of *N*-oxidation was made based on comparison of the NMR of **16-Ox** to **16** as detailed in reference 4.

$\text{K}_2\text{S}_2\text{O}_8$ (338 mg, 1.25 mmol, 3.0 equiv), and $\text{Pd}(\text{OAc})_2$ (10 mg, 0.04 mmol, 0.1 equiv) were combined in MeOH (3.5 mL) in a 20 mL vial. Substrate **17** (100 mg, 0.42 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was stirred at rt for 12 h and then stirred at 40 °C for another 12 h. The reaction mixture was diluted with ethyl acetate, and extracted with water (2 x 50 mL), NaHCO_3 (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO_4 , filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.25 in 25% hexanes/75% ethyl acetate). The product was obtained as a brown solid as a single regioisomer (67 mg, 61% yield); mp = 95-110 °C. ^1H NMR (CDCl_3): δ 7.40 (d, J = 2.5 Hz, 1H_a), 7.37 (dd, J = 9.0, 2.5 Hz, 1H_b), 6.84 (d, J = 8.5 Hz, 1H_c), 3.83 (s, 3H), 3.74 (t, J = 7.0 Hz, 2H), 2.55 (t, J = 7.9 Hz, 2H), 2.19 (q, J = 7.7 Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (CDCl_3): δ 175.07, 154.08, 131.460, 131.27, 128.55, 113.47, 112.35, 55.86, 49.79, 31.04, 18.96. IR (KBr): 2924, 1674 cm^{-1} . HRMS electrospray (m/z): $[\text{M}^+]$ calcd for $\text{C}_{11}\text{H}_{12}\text{BrNO}_2$, 269.0051; found, 269.0046. GC analysis (RESTEK Rtx[®]-5, FID detector): 100% integration.

K₂S₂O₈ (309 mg, 1.14 mmol, 2.0 equiv) and Pd(OAc)₂ (12.8 mg, 0.11 mmol, 0.1 equiv) were combined in MeOH (4.76 mL) in a 20 mL vial. Substrate **18** (100 mg, 0.57 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was stirred at rt for 12 h and then stirred at 40 °C for another 12 h. The reaction mixture was diluted with ethyl acetate, and extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel (R_f = 0.22 in 25% hexanes/75% ethyl acetate). The product was obtained as a single regioisomer as a viscous pale yellow oil (67.0 mg, 57% yield).

¹H NMR (C₆D₆): δ 7.18 (s, 1H_a), 6.85 (d, *J* = 8.3 Hz, 1H_b), 6.50 (d, *J* = 8.3 Hz, 1H_c), 3.39-3.35 (multiple peaks, 2H), 3.28 (s, 3H), 2.17 (t, *J* = 7.7 Hz, 2H), 2.10 (s, 3H), 1.47 (quin, *J* = 7.8 Hz, 2H). ¹³C{¹H} NMR (CDCl₃): δ 175.19, 152.69, 130.34, 129.14, 129.06, 126.86, 112.02, 55.75, 50.00, 31.25, 20.39, 18.96. IR (KBr): 2932, 1694 cm⁻¹. HRMS electrospray (*m/z*): [M⁺] calcd for C₁₂H₁₅NO₂, 205.1103; found, 205.1094. GC analysis (RESTEK Rtx®-5, FID detector): 99% integration.

Oxone® (100.4 mg, 1.63 mmol, 2.0 equiv) and Pd(OAc)₂ (0.9 mg, 0.04 mmol, 0.05 equiv) were combined in MeOH (6.81 mL) in a 20 mL vial. Substrate **19** (150 mg, 0.82 mmol, 1.0 equiv) was then added to the mixture. The vial was sealed with a Teflon lined cap, and the reaction was stirred at rt for 12 h and then stirred at 80 °C for another 12 h. The reaction mixture was diluted with ethyl acetate, and extracted with water (2 x 50 mL), NaHCO₃ (1 x 50 mL), and brine (1 x 50 mL). The organic layer was dried over MgSO₄, filtered, and concentrated. The resulting oil was purified by chromatography on silica gel to afford two oxime (E/Z) isomers (major oxime isomer: R_f = 0.26 in 97% hexanes/3% ethyl acetate; minor oxime isomer: R_f = 0.26 in 97% hexanes/3% ethyl acetate). The two oxime isomers were isolated as clear oils. Under the reaction conditions, oxime **19b** underwent partial hydrolysis to the corresponding ketone (102 mg total, 60% yield, ratio of oxime isomers = 3:1, Ratio of oxime : ketone = 7:1).

Major Oxime Isomer: ¹H NMR (CDCl₃): δ 7.22 (t, *J* = 8.2 Hz, 1H), 7.02 (dd, *J* = 8.1, 0.9 Hz, 1H), 6.82 (dd, *J* = 8.4, 0.9 Hz, 1H), 4.00 (s, 3H), 3.82 (s, 3H), 2.12 (s, 3H). ¹³C{¹H} NMR (CDCl₃): δ 158.39, 152.81, 133.83,

129.89, 125.97, 121.64, 109.28, 61.80, 55.98, 15.75. Minor Oxime Isomer: ^1H NMR (CDCl_3): δ 7.22 (t, J = 8.2 Hz, 1H), 7.01 (dd, J = 8.1, 0.9 Hz, 1H), 6.82 (dd, J = 8.1 Hz, 0.9 Hz, 1H), 4.02 (s, 3H), 3.82 (s, 3H), 2.32 (s, 3H). IR of **19b** (KBr): 2936, 1590, 1573 cm^{-1} . HRMS electrospray (m/z): $[\text{M}^+]$ calcd for $\text{C}_{10}\text{H}_{12}\text{ClNO}_2$, 213.0557; found, 213.0554. GC analysis (RESTEK Rtx[®]-5, FID detector): 99% integration. Ketone: ^1H NMR (CDCl_3): δ 7.13 (t, J = 8.1 Hz, 1H), 6.95 (dd, J = 8.0, 1.1 Hz, 1H), 6.89 (dd, J = 8.3, 1.1 Hz, 1H), 3.82 (s, 3H), 2.13 (s, 3H).

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