Supporting Information

for

Palladium-Catalyzed Oxidative Amination on Alkenes: Improved Catalyst Reoxidation Enables the Use of Alkene as the Limiting Reagent

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General Considerations

All commercially available compounds were used as received, and all were purchased from Aldrich, TCI America, Lancaster Synthesis except Palladium that was donated by Eli Lilly.

\(^1\)H, and \(^{13}\)C spectra were recorded on a Bruker AC-300 MHz, Varian Mercury-300 MHz, Varian Unity-500 MHz or Varian Inova-500 MHz spectrometers, and CDCl\(_3\) was purchased from Aldrich. The chemical shifts (\(\delta\)) are given in parts per million relative to internal TMS (0 ppm for \(^1\)H), CDCl\(_3\) (77.24 ppm for \(^{13}\)C).

Flash column chromatography was performed on silica gel 60 (particle size 0.040-0.063mm, 230-400 mesh ASTM, purchased from Silicycle) with hexanes/ether or hexanes/ethyl acetate.

General Procedure for Catalyst Screening.

In a disposable culture tube, Palladium complexes (0.018 mmol), Copper complexes (0.018 mmol), additive (0.0375 – 0.375 mmol) and Phthalimide (0.45 mmol) were combined. Reaction tubes were placed in a 48-well parallel reactor mounted on a Large Capacity Mixer (Glas-Col) and the headspace was purged with molecular oxygen for ca. 20 min. A benzonitrile solution containing octadecane (0.40 mL) was added and the reactor was warmed to 60 °C. After warming 1-tetradecene (0.375 mmol, 0.095 mL) was added to each tube to initiate the reaction. The reactions were vortexed for 24 hours under 1 atm of molecular oxygen. After the reactions were stopped, 1,3,5-trimethoxybenzene (1mL of a known concentration solution in 1D-chloroform) was added to the reaction mixture. Samples were evaluated by GC and NMR for the products and remaining starting materials.

Preparation of Alkenes with Protected Alcohols.

The alkenes employed in Table 2, entries 10 and15-19 were prepared according to literature precedent.\(^1,2\) Characterization data for these compounds agreed with the literature reportes.\(^1,3,4,5,6,7,8\)

General Procedure for Palladium-Catalyzed Intermolecular Oxidative Amination.

Into an Ace Glass heavy walled pressure tube (rated to 120 psig) was weighed Pd(OAc)\(_2\) (22.4 mg, 0.1 mmol) and the nucleophile (1.2 mmol). The reaction tube was connected to a custom swagelock reactor system. Benzonitrile (1.33 mL, 0.75M) was added. The reactor was pressurized to 20 psig and heated to 60 °C. Once the reactor had reached temperature, the alkene (1.0 mmol) was added via syringe and the reactor was then pressurized to 60 psig. The reaction was stirred to 36-40 hours. The benzonitrile solvent was removed \textit{in vacuo}, and the product was purified by column chromatography.
Product Characterization Data.

2-(1-Tridecyl-vinyl)-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 72% (227 mg). Major Isomer: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.89-7.84 (m, 2H), 7.75-7.72 (m, 2H), 5.38 (t, $J = 1.2$ Hz, 1H), 5.13 (s, 1H), 2.45 (t, $J = 2.9$ Hz, 2H), 1.43-1.23 (m, 20H), 0.87 (t, $J = 6.9$ Hz, 3H); Minor Isomer (integrations relative to the major isomer): $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.52 (tq, $J = 7.5$, 1.2 Hz, 0.15H), 2.21 (q, $J = 7.2$ Hz, 0.41H), 1.96 (d, $J = 1.2$ Hz, 0.62H); Major Isomer: $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$) $\delta$ 167.4, 139.4, 134.3, 132.1, 123.7, 114.9, 34.1, 32.1, 29.8, 29.7, 29.4, 29.3, 29.1, 27.9, 27.3, 22.8, 14.3; HRMS m/z (ESI) calculated[M]$^+$ = 341.2356, measured 341.2355.

2-(1-Methylene-heptyl)-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 67% (174 mg). Characterization data agrees with literature report.

2-Cyclopent-2-enyl-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 83% (177 mg). Characterization data agrees with literature report.

Cyclopent-2-enyl-sulfamic acid 2,2,2-trichloro-ethyl ester. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 54% (243 mg). Major Isomer: $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 6.05-6.01 (m, 1H), 5.82-5.79 (m, 1H), 4.68-4.57 (m, 2H), 4.64 (s, 2H), 2.54-2.26 (m, 3H), 1.88-1.75 (m, 1H); (75 MHz, CDCl$_3$) $\delta$ 136.5, 130.0, 93.7, 78.4, 61.5, 31.5, 31.2; Minor Isomer (integrations relative to the major isomer): $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 5.72 (s, 0.2), 4.68-4.57 (m, 0.2H), 4.63 (s, 0.2H), 4.30-4.19 (m, 0.12 H), 2.79 (dd, $J = 15.3$, 7.2 Hz, 0.2H), 2.54-2.26 (m, 0.2H); Major Isomer: $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$) $\delta$ 136.5, 129.9, 93.9, 78.3, 61.4, 31.4, 31.1; Minor Isomer: $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$) $\delta$ 128.7, 93.7, 78.3, 54.7, 40.2; Melting Point 59-60 °C; HRMS m/z (ESI) calculated[M+Na]$^+$ = 315.9345, measured 315.9332.

2-Cyclooct-2-enyl-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 44% (113 mg). Characterization data agrees with literature report.
Cyclooct-2-enyl-sulfamic acid 2,2,2-trichloro-ethyl ester. Column chromatography (ether/hexane, 1:4) afforded a white solid, 63% (211 mg). Allyl Isomer (integrations relative to the homoallyl isomer): 1H NMR (500 MHz, CDCl3) δ 5.79-5.64 (m, 6H), 5.40 (ddd, J = 6.3, 5.1, 0.9 Hz, 29H), 4.82 (d, J = 4.5 Hz, 30H), 4.60 (s, 63H), 4.48-4.42 (m, 30H), 2.35-2.27 (m, 0.6H), 2.06-1.98 (m, 6H), 1.72-1.24 (m, 4.8H); Homoallyl Isomer: 1H NMR (500 MHz, CDCl3) δ 6.10 (dt, J = 6.6, 4.8 Hz, 1H), 4.76 (d, J = 5.1 Hz, 1H), 4.61 (d, J = 0.9 Hz, 1H), 3.75-3.86 (m, 1H), 2.51 (ddd, J = 7.8, 5.1, 2.4 Hz, 1H), 2.42 (dt, J = 8.1, 4.5 Hz, 1H), 2.17-2.12 (m, 4H), 1.92-1.86 (m, 2H), 1.72-1.24 (m, 4H); Allyl Isomer: 13C{1H} NMR (125 MHz, CDCl3) δ 131.0, 129.8, 93.8, 78.4, 55.7, 36.1, 26.2, 25.9, 24.5, 23.3; Homoallyl Isomer: 13C{1H} NMR (125 MHz, CDCl3) δ 134.5, 125.1, 93.9, 78.4, 56.2, 32.6, 31.4, 28.8, 26.3, 22.5; Melting Point 72-75 ºC; HRMS m/z (ESI) calculated [M+Na]+ = 357.9814, measured 357.9819.

2-(1-Phenyl-vinyl)-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 24% (58.5 mg). Characterization data agrees with literature report.10

2-(1-Benzzyloxyethyl-vinyl)-isoindole-1,3-dione. Column chromatography (ether/hexanes, 1:4) afforded a white solid, 68% (296.2 mg). 1H NMR (300 MHz, CDCl3) δ 7.87 (dd, J = 5.4, 3.0 Hz, 2H), 7.74 (dd, J = 5.7, 3.0 Hz, 2H), 7.29-7.23 (m, 5H), 5.66 (t, J = 1.2 Hz, 1H), 5.44 (s, 1H), 4.53 (s, 2H), 4.35 (d, J = 1.2 Hz, 2H); 13C{1H} NMR (75 MHz, CDCl3) δ 167.2, 137.9, 135.6, 134.4, 132.0, 128.5, 128.0, 127.8, 123.8, 117.0, 72.1, 69.1; Melting Point 60-61 ºC; HRMS m/z (ESI) calculated [M+Na]+ = 316.0950, measured 316.0956.

2-[1-(2-Benzxyo-ethyl)-vinyl]-isoindole-1,3-dione. Column chromatography (ether/hexanes, 1:3) afforded a white solid, 63% (194.3 mg). 1H NMR (300 MHz, CDCl3) δ 7.90-7.86 (m, 2H), 7.78-7.43 (m, 2H), 5.42 (s, 1H), 5.19 (s, 1H), 4.10 (t, J = 6.6 Hz, 2H), 2.56 (t, J = 8.1 Hz, 2H), 2.02 (s, 3H), 1.84-1.75 (m, 2H). Minor Isomer (integrations relative to the major isomer): 1H NMR (300 MHz, CDCl3) δ 5.57-5.51 (m, 0.12H), 4.19 (t, J = 6.9 Hz, 0.3H), 2.08 (s, 0.4H); Major Isomer: 13C{1H} NMR (75 MHz, CDCl3) δ 171.2, 167.4, 134.55, 134.51, 123.8, 115.8, 63.6, 30.6, 26.1, 21.1. Minor Isomer: 13C{1H} NMR (75 MHz, CDCl3) δ 168.0, 167.5, 138.0, 134.3, 131.9, 127.3, 63.1, 29.9, 27.6, 16.1; Melting Point 64-68 ºC; HRMS m/z (ESI) calculated [M+Na]+ = 296.0899, measured 296.0909.

Acetic acid 4-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-pent-4-enyl ester. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 67% (181.0 mg). Major Isomer: 1H NMR (300 MHz, CDCl3) δ 7.90-7.86 (m, 2H), 7.78-7.43 (m, 2H), 5.42 (s, 1H), 5.19 (s, 1H), 4.10 (t, J = 6.6 Hz, 2H), 2.56 (t, J = 8.1 Hz, 2H), 2.02 (s, 3H), 1.84-1.75 (m, 2H). Minor Isomer (integrations relative to the major isomer): 1H NMR (300 MHz, CDCl3) δ 5.57-5.51 (m, 0.12H), 4.19 (t, J = 6.9 Hz, 0.3H), 2.08 (s, 0.4H); Major Isomer: 13C{1H} NMR (75 MHz, CDCl3) δ 171.2, 167.4, 134.55, 134.51, 123.8, 115.8, 63.6, 30.6, 26.1, 21.1. Minor Isomer: 13C{1H} NMR (75 MHz, CDCl3) δ 168.0, 167.5, 138.0, 134.3, 131.9, 127.3, 63.1, 29.9, 27.6, 16.1; Melting Point 64-68 ºC; HRMS m/z (ESI) calculated [M+Na]+ = 296.0899, measured 296.0909.
2-(1-Oxiranylmethoxymethyl-vinyl)-isoindole-1,3-dione. Column chromatography (ethyl acetate/hexanes, 1:2) afforded a yellow oil, 63% (235.4 mg). \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.89\) (dd, \(J = 5.7, 3\) Hz, 2H), 7.74 (dd, \(J = 5.4, 3\) Hz, 2H), 5.66 (s, 1H), 5.42 (s, 1H), 4.38 (q, \(J = 12.9\) Hz, 2H), 3.77 (dd, \(J = 11.4, 3\) Hz, 1H), 3.42 (dd, \(J = 11.4, 6\) Hz, 1H), 3.12-3.06 (m, 1H), 2.73 (dd, \(J = 5.1, 4.5\) Hz, 1H), 2.56 (dd, \(J = 5.1, 4.5\) Hz, 1H); \(^1^3\)C{\(^1\)H} NMR (75 MHz, CDCl\(_3\)) \(\delta 167.3, 135.3, 134.5, 132.8, 117.4, 70.8, 70.3, 50.8, 44.3; HRMS m/z (ESI) calculated [M+Na]\(^+\) = 282.0742, measured 282.0743.

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2-[1-(2-Oxiranyl-ethyl)-vinyl]-isoindole-1,3-dione. Column chromatography (hexanes/EtOAc, 3:1) afforded a colorless oil, 76% (179.8 mg). Major Isomer: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.89\) (dd, \(J = 5.4, 3.0\) Hz, 2H), 7.76 (dd, \(J = 5.4, 3.0\) Hz, 2H), 5.54 (t, \(J = 1.0\) Hz, 1H), 5.21 (s, 1H), 3.01-2.95 (m, 1H), 2.75 (dd, \(J = 4.5, 3.9\) Hz, 1H), 2.66 (qd, \(J = 6.0, 0.6\) Hz, 2H), 2.94 (dd, \(J = 4.8, 2.7\) Hz, 1H), 1.80-1.60 (m, 2H); Major Isomer: \(^1^3\)C{\(^1\)H} NMR (75 MHz, CDCl\(_3\)) \(\delta 167.3, 138.0, 134.4, 131.9, 123.8, 115.8, 51.5, 47.3, 30.5, 30.0; HRMS m/z (ESI) calculated [M+Na]\(^+\) = 266.0793, measured 266.0786.

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2-[1-(2-Hydroxy-ethyl)-vinyl]-isoindole-1,3-dione. Column chromatography (hexanes/EtOAc, 1:1) afforded a white solid, 17% (36.8 mg). Major Isomer: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.92-7.85\) (m, 2H), (7.80-7.73 (m, 2H), 5.58 (s, 1H), 5.30 (s, 1H), 3.67 (q, \(J = 4.5\) Hz, 2H), 2.68 (td, \(J = 6.0, 0.2\) Hz, 2H), 2.34 (broad s, 1H); Minor Isomer (integrations to relative to the major isomer): \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 5.78\) (tq, \(J = 6.9, 1.2\) Hz, 0.18H) 4.37 (d, \(J = 6.3\) Hz, 0.38H), 2.07 (broad s, 0.18H), 2.05 (s, 0.57H); Major Isomer: \(^1^3\)C{\(^1\)H} NMR (75 MHz, CDCl\(_3\)) \(\delta 167.8, 135.8, 134.6, 131.9, 123.9, 119.8, 59.4, 38.1; HRMS m/z (ESI) calculated [M]\(^+\) = 217.0739, measured 217.0737.

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2-[1-[3-(Triethyl-silanyloxy)-propyl]-vinyl]-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a colorless oil, 70% (240.2 mg). Major Isomer: \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.89-7.85\) (m, 2H), 7.77-7.72 (m, 2H), 5.41 (t, \(J = 1.2\) Hz, 1H), 5.16 (s, 1H), 3.63 (t, \(J = 6.6\) Hz, 2H), 2.55 (t, \(J = 7.8\) Hz, 2H), 1.72-1.62 (m, 2H), 0.929 (t, \(J = 8.1\) Hz, 9H), 0.55 (q, \(J = 8.1\) Hz, 6H); Major Isomer: \(^1^3\)C{\(^1\)H} NMR (75 MHz, CDCl\(_3\)) \(\delta 167.3, 138.8, 134.3, 132.0, 123.6, 115.2, 61.8, 30.4, 30.1, 6.9, 4.5; HRMS m/z (ESI) calculated [M+Na]\(^+\) = 368.1658, measured 368.1653.

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2-[1-[3-(tert-Butyl-dimethyl-silanyloxy)-propyl]-vinyl]-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a colorless oil, 83% (303.6 mg). Major Isomer: $^1$H NMR (300 MHz, CDCl$_3$) δ 7.88-7.82 (m, 2H), 7.75-7.68 (m, 2H), 5.36 (t, J = 1.2 Hz, 1H), 5.13 (s, 1H), 3.60 (t, J = 6.3 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 1.67-1.58 (m, 2H), 0.84 (s, 9H), 0.00 (s, 6H); Minor Isomer (integrations relative to the major isomer): $^1$H NMR (300 MHz, CDCl$_3$) δ 7.88-7.82 (m, 2H), 7.75-7.68 (m, 2H), 5.36 (t, J = 1.2 Hz, 1H), 5.13 (s, 1H), 3.60 (t, J = 6.3 Hz, 2H), 2.52 (t, J = 7.5 Hz, 2H), 1.67-1.58 (m, 2H), 0.84 (s, 9H), 0.00 (s, 6H); Minor Isomer: $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$) δ 167.5, 138.8, 134.3, 132.0, 123.7, 115.3, 62.1, 30.4, 30.1, 26.1, 18.4, -5.1; HRMS m/z (ESI) calculated [M+Na]$^+$ = 368.1658, measured 368.1647.

![TBDSO](image1)

2-[1-2-(tert-Butyl-dimethyl-silanyloxy)-ethyl]-vinyl]-isoindole-1,3-dione. Column chromatography (ether/hexanes, 6:1) afforded a white solid, 77% (255.3 mg). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.94 (dd, J = 5.4, 3 Hz, 2H), 7.81 (dd, J = 5.7, 3 Hz, 2H), 5.49 (s, 1H), 5.28 (s, 1H), 3.83 (t, J = 6.3 Hz, 2H), 2.78 (t, J = 6.3 Hz, 2H), 0.84 (s, 9H), 0.01 (s, 6H); $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$) δ 167.3, 136.9, 134.2, 132.2, 123.6, 116.4, 61.7, 37.2, 25.9, 18.3, -5.4; HRMS m/z (ESI) calculated [M+Na]$^+$ = 354.1501, measured 354.1490.

![TBDSO](image2)

2-[1-(tert-Butyl-dimethyl-silanyloxy)-vinyl]-isoindole-1,3-dione. Column chromatography (hexanes/ether, 4:1) afforded a white solid, 76% (245.0 mg). $^1$H NMR (300 MHz, CDCl$_3$) δ 7.83 (dd, J = 5.4, 3.3 Hz, 2H), 7.69 (dd, J = 5.4, 3.3 Hz, 2H), 5.62 (t, J = 1.5 Hz, 1H), 5.25 (t, J = 1.5 Hz, 1H), 4.34 (t, J = 1.5 Hz, 2H), 0.78 (s, 9H), 0.00 (s, 6H); $^{13}$C($^1$H) NMR (75 MHz, CDCl$_3$) δ 167.3, 138.3, 134.4, 132.1, 132.2, 123.2, 114.3, 62.3, 25.9, 18.3, -5.2; Melting Point 80-82 ºC; HRMS m/z (ESI) calculated [M+Na]$^+$ = 340.1345, measured 340.1350.

![TBDSO](image3)

References:
Michelle Mommens Rogers
VK1075
in CDCl3
ref TMS
Hermes
Michelle Mompens Rogers
MMR6190.001
in CDC13
ref TMS
Homer
Michelle Monmew Rogers
MMR6907.001
in CDCl3
ref TMS
Athena