Palladium Catalyzed Arylation of Trimethylsilyl Enolates of Esters and Imides. High Functional Group Tolerance and Stereoselective Synthesis of α-Aryl Carboxylic Acid Derivatives

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Supporting Information

Full Experimental Section

General Methods. Reactions were conducted using standard drybox techniques. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a 400 MHz spectrometer with tetramethylsilane or residual protiated solvent used as a reference and coupling constants reported in Hertz (Hz). Chromatographic purifications were performed by flash chromatography using silica gel (200-400 mesh) or using an automated chromatography system. Yields for final products in all tables refer to isolated yields and are the average of two runs. Products that had been reported previously were isolated in greater than 95% purity, as determined by ^{1}H NMR and capillary gas chromatography (GC). All ^{13}C NMR spectra were proton decoupled. GC analyses were obtained with a DB-1301 narrow bore column for high temperature ramp applications (max. 120 ˚C/min). Methyl trimethylsilyl ketene acetal, ZnF_2 and $Zn(O^tBu)_2$ were purchased from commercial supplies. The silyl ketene acetal of *t*-butyl propionate[1] and the trimethylsilyl ether derivative of the Evans auxiliary[2] were prepared according to literature procedures. The racemic version$Ley, 2001 #75& of the available non-racemic Ley auxiliary$Diez, 2001 #49& was used to determine diastereoselectivities and was prepared by literature procedures.

Representive Procedure for the Arylation of Silyl Ketene Acetals.

Methyl phenylisobutyrate, (Table 2, entry 1).[3] To a screw-capped vial containing P^tBu_3 (40 μL of a 0.500 M solution in toluene, 0.020 mmol), $Pd(dba)_2$ (5.8 mg, 0.010

mmol), ZnF_2 (52.0 mg, 0.500 mmol) and phenyl bromide (157.0 mg, 1.000 mmol) was added *tert*-butyl trimethylsilyl methyl ketene acetal (301.0 mg, 1.49 mmol), followed by DMF (4.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the dry box. The heterogeneous reaction mixture was stirred at 80 ˚C for 12 h. The crude reaction was then allowed to cool to room temperature and was diluted with Et_2O (50 mL). The resulting solution was washed with H_2O (5 X 20 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated at reduced pressure. The residue was then purified by chromatography on silica gel eluting with a 1-2% gradient of EtOAc in hexane to provide the title compound (162 mg) in 91% yield. ^{1}H NMR ($CDCl_3$): δ 7.27-7.38 (5H, m), 3.69 (3H, s), 1.62 (6H, s). ^{13}C NMR ($CDCl_3$): δ 177.72, 145.08, 128.85, 127.15, 126.02, 52.64, 46.94, 26.98.

Methyl (4-nitrophenyl)isobutyrate, (Table 2, entries 2 and 12).[4]

^{1}H NMR ($CDCl_3$): δ 8.20 (2H, d, J =9.0 Hz), 7.52 (2H, d, J =9.0 Hz), 3.70 (3H, s), 1.64 (6H, s). ^{13}C NMR ($CDCl_3$): δ 176.44, 152.35, 147.08, 127.25, 124.01, 52.97, 47.34, 26.79.

***tert*-Butyl (4-nitrophenyl)propionate, (Table 2, entry 3).**

^{1}H NMR ($CDCl_3$): δ 8.19 (2H, d, J = 8.7 Hz), 7.47 (2H, d, J = 8.7 Hz), 3.74 (1H, q, J = 7.2 Hz), 1.50 (3H, d, J = 7.2 Hz), 1.40 (9H, s). ^{13}C NMR ($CDCl_3$): δ 172.81, 148.90, 147.39, 128.84, 124.13, 81.75, 46.83, 28.26, 18.71. Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 62.32; H, 6.98; N, 5.74.

Methyl (4-methoxycarbonylphenyl)isobutyrate, (Table 2, entry 4, 13).[5]

^{1}H NMR ($CDCl_3$): δ 8.01 (2H, d, J= 8.4 Hz), 7.42 (2H, d, J = 8.4 Hz), 3.93 (3H, s), 3.68 (3H, s), 1.62 (6H, s). ^{13}C NMR ($CDCl_3$): δ 177.02, 167.18, 150.16, 130.12, 128.99, 126.16, 52.74, 52.47, 47.19, 26.79.

***tert*-Butyl (4-methoxycarbonylphenyl)propionate, (Table 2, entry 5).**

^{1}H NMR ($CDCl_3$): δ 8.00 (2H, d, J= 8.3 Hz), 7.37 (2H, d, J = 8.3 Hz), 3.92 (3H, s), 3.68 (1H, q, J = 7.1 Hz), 1.47 (3H, d, J = 7.1 Hz), 1.39 (9H, s). ^{13}C NMR ($CDCl_3$): δ 173.48,

167.35, 146.76, 130.21, 129.20, 127.91, 81.25, 52.44, 46.94, 28.28, 18.67. Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.07; H, 7.88.

***tert*-Butyl (2-cyanophenyl)propionate, (Table 2, entry 6).**

^{1}H NMR ($CDCl_3$): δ 7.66 (1H, dd, *J* = 7.8 and 1.0 Hz), 7.58 (1H, dt, *J* = 7.6 and 1.2 Hz), 7.47 (1H, d, *J* =7.9 Hz), 7.36 (1H, dt, *J* = 7.6 and 1.0 Hz), 4.11 (1H, q, *J* =7.2 Hz), 1.52 (3H, d, *J* =7.2 Hz), 1.42 (9H, s). ^{13}C NMR ($CDCl_3$): δ 172.52, 145.33, 133.99, 133.32, 127.78, 127.74, 118.16, 113.09, 81.86, 44.84, 28.27, 18.45. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.43; H, 7.21; N, 6.24.

***tert*-Butyl (3-cyanophenyl)propionate, (Table 2, entry 7).**

^{1}H NMR ($CDCl_3$): δ 7.60 (1H, s), 7.55-7.57 (2H, m), 7.44 (1H, t, *J* = 7.8 Hz), 3.66 (1H, q, *J* = 7.2 Hz), 1.48 (3H, d, *J*= 7.2 Hz), 1.41 (9H, s). ^{13}C NMR ($CDCl_3$): δ 173.09, 142.88, 132.49, 131.65, 131.08, 129.69, 119.19, 112.98, 81.65, 46.49, 28.03, 18.71. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.59; H, 7.46; N, 6.21.

Methyl (4-benzoylphenyl)isobutyrate, (Table 2, entry 8).[3]

^{1}H NMR ($CDCl_3$): δ 7.79-7.84 (4H, m), 7.61 (1H, t, *J* = 7.4 Hz), 7.45-7.52 (4H, m), 3.70 (3H, s), 1.65 (6H, s). ^{13}C NMR ($CDCl_3$): δ 196.67, 177.10, 149.74, 137.98, 136.38, 132.84, 130.73, 130.44, 128.70, 126.12, 52.84, 47.25, 26.86.

Methyl (4-acetylphenyl)isobutyrate, (Table 2, entry 9).

^{1}H NMR ($CDCl_3$): δ 7.93 (2H, d, *J* =8.5 Hz), 7.43 (2H, d, *J* =8.5 Hz), 3.67 (3H, s), 2.60 (3H, s), 1.61 (6H, s). ^{13}C NMR ($CDCl_3$): δ 198.01, 176.98, 150.39, 136.04, 128.92, 126.37, 52.77, 47.24, 26.98, 26.79. Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.66; H, 7.60.

***tert*-Butyl (4-acetylphenyl)propionate, (Table 2, entry 10).**

^{1}H NMR ($CDCl_3$): δ 7.93 (2H, d, *J* =8.3 Hz), 7.40 (2H, d, *J* =8.3 Hz), 3.68 (1H, q, *J* = 7.1Hz), 2.60 (3H, s), 1.48 (3H, d, *J* = 7.2 Hz), 1.40 (9H, s). ^{13}C NMR ($CDCl_3$): δ 198.16,

173.42, 146.98, 136.27, 129.01, 128.10, 81.32, 46.93, 28.30, 26.99, 18.70. Anal. Calcd for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.31; H, 8.15.

Methyl (4-methoxyphenyl)isobutyrate, (Table 2, entry 11).[3]

^{1}H NMR ($CDCl_3$): δ 7.29 (2H, d, *J* =8.8 Hz), 6.88 (2H, d, *J* =8.9 Hz), 3.82 (3H, s), 3.67 (3H, s), 1.59 (6H, s). ^{13}C NMR ($CDCl_3$): δ 177.90, 158.63, 137.16, 127.15, 114.11, 55.65, 52.63, 46.16, 27.05.

Benzyloxy-phenyl-acetic acid tert-butyl ester (table 4, entry 1): ^{1}H NMR ($CDCl_3$): δ 7.17-7.38 (10H, m), 4.73 (1H, s), 4.54 (1H, d, J = 9.5 Hz), 4.49 (1H, d, J = 9.5 Hz), 1.31 (9H, s); ^{13}C NMR ($CDCl_3$): δ 170.36, 137.95, 137.32, 128.84, 128.79, 128.76, 128.39, 128.17, 127.68, 82.15, 80.61, 71.49, 28.34. Anal. Calc. for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43; Found: C, 76.67; H, 7.62.

Benzyloxy-(4-nitro-phenyl)-acetic acid tert-butyl ester (table 4, entry 2) : ^{1}H NMR ($CDCl_3$): δ8.13 (2H, d, J = 7.0 Hz), 7.57 (2H, d, J = 7.0 Hz), 7.23-7.28 (5H, m), 4.83 (1H, s), 4.62 (1H, d, J = 9.4 Hz), 4.51 (1H, d, J = 9.4 Hz), 1.32 (9H, s); ^{13}C NMR ($CDCl_3$): δ 169.14, 148.31, 144.52, 137.23, 128.96, 128.55, 128.43, 128.26, 124.03, 83.17, 79.76, 72.18, 28.30. Anal. Calc. for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08; Found: C, 66.54; H, 6.43; N, 4.01.

Benzyloxy-(4-methoxy-phenyl)-acetic acid tert-butyl ester (table 4, entry 3): ^{1}H NMR ($CDCl_3$): δ7.30-7.40 (7H, m), 6.90 (2H, d, J = 8.6 Hz), 4.77 (1H, s), 4.61 (1H, d, J = 12.0 Hz), 4.58 (1H, d, J = 12.0 Hz), 3.83 (3H, s), 1.42 (9H, s); ^{13}C NMR ($CDCl_3$): δ 170.62, 160.07, 138.00, 129.42, 129.06, 128.79, 128.41, 128.16, 114.26, 82.04, 80.04, 71.24, 55.67, 28.36. Anal. Calc. for $C_{20}H_{24}O_4$: C, 73.15; H, 7.37; Found: C, 73.33; H, 7.28.

2-Benzyloxy-2-phenyl-propionic acid methyl ester (table 4, entry 4): ^{1}H NMR ($CDCl_3$): δ7.56-7.59 (2H, m), 7.30-7.46 (8H, m), 4.59 (1H, d, J = 11.2 Hz), 4.45 (1H, d, J = 11.2 Hz), 3.77 (3H, s), 1.91 (3H, s); ^{13}C NMR ($CDCl_3$): δ 174.07, 141.53, 138.89, 128.82, 128.75, 128.42, 127.90, 126.27, 82.41, 67.22, 52.94, 23.94. Anal. Calc. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71; Found: C, 75.67; H, 6.79.

(4-tert-Butyl-phenyl)-methoxy-acetic acid ethyl ester (table 4, entry 5): ^{1}H NMR ($CDCl_3$): □7.37-7.42 (4H, m), 4.75 (1H, s), 4.15-4.28 (2H, m), 3.42 (3H, s), 1.33 (9H, s), 1.24 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$): □ 171.30, 152.07, 133.63, 127.32, 125.97, 82.86, 61.61, 52.72, 35.01, 31.70, 14.55. Anal. Calc. for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86; Found: C, 72.41; H, 8.85.

(4-Methoxycarbonylphenyl)-methoxy-acetic acid ethyl ester (table 4, entry 6): ^{1}H NMR ($CDCl_3$): □8.06 (2H, d, J = 8.4 Hz), 7.55 (2H, d, J = 8.2 hz), 4.83 (1H, s), 4.16-4.25 (2H, m), 3.94 (3H, s), 3.46 (3H, s), 1.24 (3H, t, J = 7.1 Hz); ^{13}C NMR ($CDCl_3$): □ 170.50, 167.10, 141.61, 130.81, 130.28, 127.45, 82.58, 61.93, 57.98, 52.60, 14.47. Anal. Calc. for $C_{13}H_{16}O_5$: C, 61.90; H, 6.39; Found: C, 61.85; H, 6.40.

Arylation of the Trimethylsilyl ketenimines of the Evans Auxiliary. (4S, 2'S)-4-isopropyl-3-(2'-phenyl-propanoyl)oxazolidin-2-one (table 3, entries 1, 2):[6] To a screw-capped vial containing P^{t}Bu$_3$ (0.500 M solution in toluene, 200 □L, 0.010 mmol), $Pd(dba)_2$ (29 mg, 0.050 mmol), ZnF_2 (52 mg, 0.50 mmol) and phenyl bromide (157 mg, 1.00 mmol) was added the trimethylsilyl enolate **2** of the Evans imide (370.0 mg, 1.44 mmol), followed by DMF (10 mL). The vial was sealed with a cap containing a PTFE septum and removed from the dry box. The heterogeneous reaction mixture was stirred at 80 ˚C for 12 h. The crude reaction was then allowed to cool to room temperature and was diluted with Et_2O. The resulting solution was washed with H_2O. The organic phase was dried over Na_2SO_4, filtered, and concentrated at reduced pressure. Purification of the crude material by flash chromatography, eluting with 2% EtOAc in hexanes, gave 67% yield of the □-aryl imide. ^{1}H NMR ($CDCl_3$): □7.27 (2H, d, *J* =7.4 Hz), 7.22 (2H, t, *J* = 7.3 Hz), 7.15 (1H, t, *J* = 7.3 Hz), 5.06 (1H, q, *J* = 7.0 Hz), 4.25-4.28 (1H, m), 4.00-4.07 (2H, m), 2.33-2.37 (1H, m), 1.43 (3H, d, *J* = 7.0 Hz), 0.84 (3H, d, *J* = 6.6 Hz), 0.82 (3H, d, *J* = 6.1 Hz). ^{13}C NMR ($CDCl_3$): □ 175.04, 153.99, 140.72, 128.98, 128.56, 127.59, 63.50, 59.43, 43.45, 28.94, 20.09, 18.42, 15.11.

4-tert-Butyl-3-(2-phenyl-propionyl)-oxazolidin-2-one (table 3, entries 3 and 4):[7] ^{1}H NMR ($CDCl_3$): □7.27-7.38 (5H, m), 5.18 (1H, q, *J* = 7.0 Hz), 4.41 (1H, dd, J = 7.5 and 1.3 Hz), 4.24 (1H, dd, J = 9.3 and 1.4 Hz), 4.09 (1H, dd, J = 9.2 and 7.6 Hz), 1.58 (3H, d, *J* = 7.0 Hz), 0.98 (9H, s). ^{13}C NMR ($CDCl_3$): □ 175.16, 154.65, 140.53, 128.96, 128.60, 127.60, 65.41, 61.78, 43.38, 36.22, 26.15, 20.71.

3-[2-(3-Acetyl-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (table 3, entry 5): ^{1}H NMR ($CDCl_3$, mixture of two isomers) □7.94-7.95 (1H, m), 7.85-7.87 (1H, m), 7.57-7.60 (1H, m), 7.43 (1H, t, J = 7.7 Hz), 5.15-5.24 (1H, m), 4.51 (0.13H, dt, J = 8.6 and 3.5 Hz), 4.40 (0.87H, dt, J = 7.9 and 4.0 Hz), 4.12-4.30 (2H, m), 2.62 (2.6H, s), 2.61 (0.4H, s), 2.40-2.56 (0.87H, m), 2.21-2.26 (0.13H, m), 1.56 (2.6H, d, J = 7.0 Hz), 1.51 (0.4H, d, J = 7.0 Hz), 0.94 (2.6H, d, J = 7.0 Hz), 0.93 (2.6H, d, J = 6.9 Hz), 0.83 (0.4H, d, J = 7.1 Hz), 0.49 (0.4H, d, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$, mixture of two isomers, major isomer reported): □ 198.48, 174.57, 153.99, 141.19, 137.86, 133.54, 129.25, 128.49, 127.64, 63.59, 59.34, 43.48, 28.86, 27.16, 20.10, 18.41, 15.09. Anal. Calc. for $C_{17}H_{21}NO_4$: C, 67.31; H, 6.98; N, 4.62;; Found: C, 67.29; H, 7.24; N, 4.51.

4-Isopropyl-3-(2-o-tolyl-propionyl)-oxazolidin-2-one (table 3, entry 6): ^{1}H NMR ($CDCl_3$): □7.13-7.18 (4H, m), 5.19 (1H, q, *J* = 6.9 Hz), 4.42-4.45 (1H, m), 4.12-4.19 (2H, m), 2.46-2.51 (1H, m), 2.43 (3H, s), 1.46 (3H, d, *J* = 7.0 Hz), 0.96 (3H, d, *J* = 7.1 Hz), 0.93 (3H, d, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$): □ 175.27, 153.89, 139.48, 136.88, 131.10, 127.38, 126.66, 125.90, 63.56, 59.57, 41.03, 28.97, 19.71, 18.71, 18.48, 15.11. Anal. Calc. for $C_{16}H_{21}NO_3$: C, 69.79; H, 7.69; N, 5.09; Found: C, 69.73; H, 7.72; N, 5.05.

Experimental Procedure for the evaluation of epimerization during the □-arylation: To a screw-capped vial containing P^{t}Bu$_3$ (0.500 M solution in toluene, 20 □L, 0.010 mmol), $Pd(dba)_2$ (2.9 mg, 0.0050 mmol), ZnF_2 (5.2 mg, 0.050 mmol) and phenyl bromide (15.7 mg, 0.100 mmol) was added the trimethylsilyl enolate **2** of the Evans imide (37.0 mg, 0.144 mmol) and compound **1** (> 90% de),[6] followed by DMF (1.0 mL). The vial was sealed with a cap containing a PTFE septum and removed from the dry box. The heterogeneous reaction mixture was stirred at 80 ˚C for 12 h. The crude reaction was

then allowed to cool to room temperature and was diluted with Et_2O (5.0 mL). The resulting solution was washed with H_2O (5 x 2.0 mL). The organic phase was dried over Na_2SO_4, filtered, and concentrated at reduced pressure. The residue was then analyzed by ^1H NMR spectroscopy. Only one set of signals was observed for compound **1** and its (2')epimer.[6] From integration of the ^1H NMR signals, the diastereomeric ratio of the isopropyl derivative formed from the α-arylation was 88:12. The same reaction on a 1.00 mmol scale in the absence of the added α-aryl imide provided the major diastereomer in 67% yield after purification by flash chromatography eluting with 2% EtOAc in hexanes.

3-[2-(4-tert-Butyl-phenyl)-propionyl]-4-isopropyl-oxazolidin-2-one (table 3, entry 7): ^1H NMR ($CDCl_3$): δ 7.28-7.35 (4H, m), 5.15 (1H, q, *J* = 7.0 Hz), 4.36-4.40 (1H, m), 4.13-4.18 (2H, m), 2.45 (1H, m), 1.53 (3H, d, *J* = 7.0 Hz), 1.32 (9H, s), 0.94 (3H, d, *J* = 7.0 Hz), 0.93 (3H, d, *J* = 7.0 Hz). ^{13}C NMR ($CDCl_3$): δ 175.29, 154.04, 150.37, 137.54, 128.16, 125.89, 63.46, 59.40, 42.84, 34.85, 31.76, 28.91, 20.09, 18.45, 15.11. Anal. Calc. for $C_{19}H_{27}NO_3$: C, 71.89; H, 8.57; N, 4.41; Found: C, 72.28; H, 8.62; N, 4.39.

4-[2-(4-Isopropyl-2-oxo-oxazolidin-3-yl)-1-methyl-2-oxo-ethyl]-benzonitrile (table 3, entry 8, major isomer): ^1H NMR ($CDCl_3$): δ 7.61 (2H, d, J = 8.3 Hz), 7.47 (2H, d, J = 8.4 Hz), 5.20 (1H, q, *J* = 7.0 Hz), 4.38-4.41 (1H, m), 4.16-4.21 (2H, m), 2.39-2.47 (1H, m), 1.53 (3H, d, *J* = 7.0 Hz), 0.94 (3H, d, *J* = 7.0 Hz), 0.92 (3H, d, *J* = 7.0 Hz). ^{13}C NMR ($CDCl_3$): δ 173.83, 153.95, 145.88, 132.79, 129.52, 119.17, 111.54, 63.64, 59.32, 43.72, 28.80, 19.98, 18.38, 15.06. Anal. Calc. for $C_{16}H_{18}N_2O_3$: C, 67.12; H, 6.34; N, 9.78; Found: C, 66.86; H, 6.69; N, 9.61.

4-[2-(4-Isopropyl-2-oxo-oxazolidin-3-yl)-1-methyl-2-oxo-ethyl]-benzonitrile (table 3, entry 8, minor isomer): ^1H NMR ($CDCl_3$): δ 7.62 (2H, d, J = 8.3 Hz), 7.50 (2H, d, J = 8.3 Hz), 5.18 (1H, q, *J* = 6.9 Hz), 4.50 (1H, dt, J = 8.5 and 3.5 Hz), 4.29 (1H, t, J = 9.0 Hz), 4.16 (1H, dd, J = 9.2 and 3.2 Hz), 2.18-2.24 (1H, m), 1.49 (3H, d, *J* = 6.9 Hz), 0.84 (3H, d, *J* = 7.0 Hz), 0.52 (3H, d, *J* = 6.9 Hz). ^{13}C NMR ($CDCl_3$): δ 173.58, 153.88, 146.20, 132.82, 129.37, 119.12, 111.55, 63.57, 58.65, 43.89, 28.42, 19.08, 18.19, 14.61.

Anal. Calc. for $C_{16}H_{18}N_2O_3$: C, 67.12; H, 6.34; N, 9.78; Found: C, 66.80; H, 5.98; N, 9.48.

Representative procedures for the arylation of the Ley auxiliary:

5,6-Dimethoxy-5,6-dimethyl-3-phenyl-[1,4]dioxan-2-one (table 5, entry 1, 2):[8] 5,6-Dimethoxy-5,6-dimethyl-[1,4]dioxan-2-one **8**[8,9](1.00 g, 5.26 mmol) was dissolved in anhydrous THF (20 mL), and the mixture was cooled to -78 °C under N_2. LDA (3.2 mL of a 2.0 M solution in THF/heptane, 6.4 mmol) was then added dropwise. After addition, the mixture was stirred for another 5 min before addition of TMSCl (0.83 mL, 6.6 mmol). The resulting solution was then allowed to warm to room temperature overnight. The THF was then removed under reduced pressure, and hexanes (20 mL) was added to the residue. The resulting suspension was filtered through Celite, and the hexanes were removed in vacuo to afford 1.40 g of the desired trimethylsilyl ketene acetal (judged to be 90-95% pure from NMR). ^{1}H NMR ($CDCl_3$): □5.55 (1H, s), 3.41(3H, s), 3.26 (3H, s), 1.49 (3H, s), 1.42 (3H, s), 0.25 (9H, s). This material was directly employed in the arylation step. In a dry box, to a screw cap vial was added PhBr (78.5 mg, 0.500 mmol), ZnF_2 (26.0 mg, 0.0250 mmol), $Pd(dba)_2$ (15.0 mg, 0.00250 mmol) and P(^{t}Bu)$_3$ (100 □L, 0.5 M solution in toluene, 0.005 mmol). The trimethylsilyl ketene acetal prepared above (170 mg calculated amount according to the purity, 0.650 mmol) was added to the mixture followed by 4.0 mL DMF. The vial was then sealed and heated at 80 °C for 12 h. The solution was then allowed to cool to room temperature and partitioned in ethyl ether (50 mL) and water (10 mL). The ether layer was washed with water and brine and dried over Na_2SO_4. After removing the ether, the residue was subjected to automated flash chromatography using 8% EtOAc/hexanes to provide the desired product (88.4 mg) in 66% yield. ^{1}H NMR ($CDCl_3$): □7.59 (2H, d, J = 6.8 Hz), 7.32-7.41 (3H, m), 5.21 (1H, s), 3.47 (3H, s), 3.45 (3H, s), 1.58 (3H, s), 1.52 (3H, s); ^{13}C NMR ($CDCl_3$): □168.85, 136.44, 129.01, 128.91, 128.22, 105.65, 98.98, 74.07, 50.46, 49.78, 18.40, 17.47.

5,6-Dimethoxy-5,6-dimethyl-3-naphthalen-2-yl-[1,4]dioxan-2-one (table 5, entry 3): ^{1}H NMR ($CDCl_3$): □8.07 (1H, s), 7.86-7.89 (3H, m), 7.72 (1H, dd, J = 8.6 and 1.7 Hz), 7.49-7.51 (2H, m), 5.39 (1H, s), 3.50 (3H, s), 3.49 (3H, s), 1.61 (3H, s), 1.57 (3H, s); ^{13}C

NMR ($CDCl_3$): 168.83, 133.81, 133.78, 133.55, 128.76, 128.65, 128.07, 127.80, 126.74, 126.56, 125.52, 105.74, 99.10, 74.22, 50.50, 49.84, 18.44, 17.51. Anal. Calc. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37; Found: C, 68.08; H, 6.02.

4-(5,6-Dimethoxy-5,6-dimethyl-3-oxo-[1,4]dioxan-2-yl)-benzoic acid methyl ester (table 5, entries 4, 5): ^{1}H NMR ($CDCl_3$): 8.06 (2H, d, J = 8.4 Hz), 7.70 (2H, d, J = 8.3 Hz), 5.28 (1H, s), 3.93 (3H, s), 3.45 (3H, s), 3.43 (3H, s), 1.58 (3H, s), 1.54 (3H, s); ^{13}C NMR ($CDCl_3$): 168.22, 167.22, 141.21, 130.63, 130.09, 128.09, 105.74, 99.08, 73.58, 52.60, 50.50, 49.88, 18.36, 17.44. Anal. Calc. for $C_{16}H_{20}O_7$: C, 59.25; H, 6.22; Found: C, 59.35; H, 6.18.

5,6-Dimethoxy-5,6-dimethyl-3-(3-nitro-phenyl)-[1,4]dioxan-2-one (table 5, entries 6, 7, 8): ^{1}H NMR ($CDCl_3$): 8.59 (1H, t, J = 1.9 Hz), 8.21 (1H, ddd, J = 8.2 and 2.2 and 1.0 Hz), 7.92-7.94 (1H, m), 7.56 (1H, t, J = 8.0 Hz), 5.31 (1H, s), 3.47 (3H, s), 3.46 (3H, s), 1.60 (3H, s), 1.56 (3H, s); ^{13}C NMR ($CDCl_3$): 167.92, 148.77, 138.58, 134.37, 129.72, 123.90, 123.28, 105.91, 99.26, 73.06, 50.60, 49.96, 18.28, 17.41. Anal. Calc. for $C_{14}H_{17}NO_7$: C, 54.02; H, 5.50; N, 4.50; Found: C, 53.71; H, 5.31; N, 4.19.

3-(3-Acetyl-phenyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxan-2-one (table 5, entry 9): ^{1}H NMR ($CDCl_3$): 8.23 (1H, t, J = 1.7 Hz), 7.95 (1H, dt, J = 7.8 and 1.3 Hz), 7.79 (1H, d, J = 7.7 Hz), 7.49 (1H, t, J = 7.7 Hz), 5.27 (1H, s), 3.49 (3H, s), 3.46 (3H, s), 2.63 (3H, s), 1.59 (3H, s), 1.54 (3H, s); ^{13}C NMR ($CDCl_3$): 198.14, 168.53, 137.74, 137.16, 132.92, 129.23, 128.89, 128.36, 105.80, 99.10, 73.70, 50.59, 49.89, 27.11, 18.36, 17.46. Anal. Calc. for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54; Found: C, 62.52; H, 6.70.

5,6-Dimethoxy-3-(4-methoxy-phenyl)-5,6-dimethyl-[1,4]dioxan-2-one (table 5, entry 10): ^{1}H NMR ($CDCl_3$): 7.50 (2H, d, J = 8.7 Hz), 6.92 (2H, d, J = 8.8 Hz), 5.15 (1H, s), 3.83 (3H, s), 3.48 (3H, s), 3.44 (3H, s), 1.57 (3H, s), 1.50 (3H, s); ^{13}C NMR ($CDCl_3$): 169.15, 160.25, 129.49, 128.66, 114.38, 105.59, 98.96, 73.69, 55.71, 50.44, 49.75, 18.39, 17.48. Anal. Calc. for $C_{15}H_{20}O_6$: C, 60.80; H, 6.80; Found: C, 60.82; H, 6.71.

3-(2-Chloro-phenyl)-5,6-dimethoxy-5,6-dimethyl-[1,4]dioxan-2-one (table 5, entry 11): ^{1}H NMR ($CDCl_3$): δ 7.58-7.60 (1H, m), 7.41-7.44 (1H, m), 7.28-7.32 (2H, m), 5.76 (1H, s), 3.55 (3H, s), 3.48 (3H, s), 1.59 (3H, s), 1.48 (3H, s); ^{13}C NMR ($CDCl_3$): δ 168.10, 134.82, 134.68, 130.49, 130.23, 130.14, 127.74, 106.05, 99.04, 70.37, 50.59, 49.83, 18.25, 17.48. Anal. Calc. for $C_{14}H_{17}ClO_5$: C, 55.91; H, 5.70; Found: C, 55.90; H, 5.64.

5,6-Dimethoxy-5,6-dimethyl-2-naphthalen-2-yl-[1,4]dioxan-2-one (table 1, entry 12): ^{1}H NMR ($CDCl_3$): δ 8.31 (1H, d, J = 8.5 Hz), 7.88 (2H, d, J = 8.2 Hz), 7.75 (1H, dd, J = 7.1 and 0.7 Hz), 7.48-7.60 (3H, m), 5.90 (1H, s), 3.60 (3H, s), 3.54 (3H, s), 1.64 (3H, s), 1.54 (3H, s); ^{13}C NMR ($CDCl_3$): δ 168.70, 134.46, 132.34, 131.77, 130.14, 129.13, 127.54, 126.96, 126.21, 125.65, 124.56, 106.22, 99.34, 71.42, 50.50, 49.90, 18.44, 17.58. Anal. Calc. for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37; Found: C, 68.63; H, 6.56.

Procedure for conducting the reactions without a glovebox: Procedure for conducting the reactions without a glovebox: To a round-bottom flask was added $Pd(dba)_2$ (2.9 mg, 0.0050 mmol), $Zn(O^tBu)_2$ (21.0 mg of commercial material, which is about 50% H_2O by weight), the trimethylsilyl enolate of the Ley auxiliary (34.0 mg calculated according to the purity, 0.130 mmol) and 3-bromonitrobenzene (20.2 mg, 0.100 mmol). The flask was purged with N_2 for 5 min before addition of $P(^tBu)_3$ (20 mL of 0.5 M solution in toluene, 0.010 mmol). DMF (1.0 mL) was then added, and the resulting mixture was stirred for 12 h. Trimethoxybenzene (12 mg, 0.071 mmol) as internal standard was then added to the solution, and the mixture was partitioned with Et_2O (5.0 mL) and H_2O (2.0 mL). The ether layer was washed with water, and the ether was evaporated in vacuo. The yield by NMR spectroscopy was determined with an internal standard to be within experimental error of quantitative, which is similar to that observed when the reactions are assembled in a drybox.

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