Supporting Information for synthesis of oxazoles.

General Methods: Melting point determinations are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX400, operating at 400 or 100 MHz respectively. 2D spectra were recorded on a Bruker DPX400 or Bruker DRX500. Electrospray ionization mass spectra were obtained on a Micromass Platform LCZ. All reactions were run under a N_2 atmosphere. Reactions were followed by TLC on pre-coated Uniplate silica gel plates purchased from Analtech. Compounds were isolated from the plates by removal of the silica gel and eluting with 0.3 mL acetonitrile through a 4 mm Millex-HV syringe filter unit. Flash chromatography was done on Redi Sep prepacked disposable columns using the Isco Combiflash. THF was distilled from Na/benzophenone immediately before use. Boc protected amino acids were purchased from Advanced ChemTech. Ethyl acetate, dichloromethane, and hexane solvents were purchased from EM Science. All other solvents and reagents were purchased from the Aldrich Chemical Company.

Typical Experimental Procedures

Preparation of the Weinreb amide:

N-Boc-L-alanine, **6a,** (15g, 79.3 mmol) was dissolved in dichloromethane (200 mL). Carbonyldiimidazole (14.2 g, 87.7 mmol) was added, and the resultant mixture was stirred for 1 hour. Subsequently, N,O-dimethylhydroxylamine hydrochloride (8.58 g, 88 mmol) was added and the reaction mixture was stirred for 16 hours, after which time it was diluted with ethyl acetate and washed successively with 1N HCl, saturated aqueous $NaHCO_3$, and brine, and dried with Na_2SO_4. Evaporation of solvents provided 18.3g (99%) **6b** as a white solid, mp 144-5.

Removal of the *t*-butoxycarbonyl protecting group:

6b prepared above (5 g, 21.5 mmol) was dissolved in 4M HCl in dioxane (50 mL, 200 mmol) and the resultant mixture was stirred at room temperature for 2 hours. Solvent was removed with vacuum leaving 3.5 g (93%) of the hydrochloride salt as a thick waxy substance.

Benzoylation of the amino Weinreb amide:

The hydrochloride salt prepared above (330 mg, 1.957 mmol) was dispersed in dichloromethane (25 mL). Triethylamine (1.25 mL, 9 mmol) was added followed by benzoyl chloride (0.325 mL, 2.8 mmol). The resultant mixture was stirred for 16 hours, after which time it was washed with brine, and dried with Na_2SO_4. Evaporation of solvents gave a solid, which was purified by flash chromatography yielding 450 mg (95%) **6c** as a white solid, mp 100-101.

Alternate method for acylation of an amino Weinreb amide:

5b was deprotected using the method described above for **6b**, and the resulting amine hydrochloride (1g, 4.3 mmol) was dispersed in dichloromethane (25 mL) to which pyridine (0.4 mL, 5 mmol) was added. The mixture was stirred at room temperature for 1 hour, during which time the acyl imidazole was prepared in a separate flask by addition of carbonyldiimidazole (475.6 mg, 4.7 mmol) to a solution of phenylacetic acid (612.7 mg, 4.5 mmol) in dichloromethane (25 mL). After 1 hour, the amino Weinreb amide reaction mixture was added to the phenylacetylimidazole reaction mixture, and the resulting combination was stirred at room temperature for 16 hours. The reaction mixture was diluted with water (100 mL), and the organic layer was separated and washed successively with 1N HCl, saturated aqueous $NaHCO_3$, and brine, and dried with Na_2SO_4. Evaporation of solvents provided 870 mg (64.2%) **5c** as a white solid, mp 124-5.

Reduction of the Weinreb amide:

Lithium aluminum hydride (201 mg, 5.3 mmol) was weighed into an oven-dried flask, which was subsequently flushed with N_2 and sealed with a septum. Tetrahydrofuran (10 mL) was added via syringe, and the resultant solution was cooled to –78 ^{o}C. **6c**, prepared above, (1.2g, 5.08 mmol) was dissolved in tetrahydrofuran (10 mL) and added dropwise via syringe. The cooling bath was removed and replaced with an ice bath at 0 ^{o}C. After 20 minutes the reaction was again cooled to –78 ^{o}C, and an aqueous solution of potassium bisulfate (3.5 g, 25 mmol) was added quickly. The mixture allowed to warm to room temperature and extracted several times with ethyl acetate. The combined extracts were washed with brine and dried with Na_2SO_4. The solvents were evacuated with vacuum providing 885 mg (98%) **6d** as a waxy solid.

Conversion of the Weinreb amide to the *n*-butyl ketone:

13k (170 mg, 0.7 mmol) was dissolved in anhydrous tetrahydrofuran (25 mL) in an oven-dried flask, and the resultant solution was cooled to –78 ^oC. *n*-Butyllithium (1.5M in hexane, 1 mL, 1.5 mmol) was added dropwise, and the reaction mixture was stirred at –78 ^oC for 3 hours and 0 ^oC for 30 minutes. The reaction was quenched by addition to a 10% aqueous solution of NH_4Cl (100 mL). Extraction with ethyl acetate, washing the extracts with brine, drying with Na_2SO_4 and evaporation of solvents yielded the product, which was purified by flash chromatography providing 105 mg (62%) **13m** as an oil which crystallized on standing, mp 95-6.

Method A: Triphenylphosphine (335 mg, 1.28 mmol) was dissolved in anhydrous acetonitrile (20 mL) and I_2 (320 mg, 1.28 mmol) was added. The mixture was stirred for several minutes, during which time the aldehyde **2d** (166 mg, 0.64 mmol) was dissolved in anhydrous acetonitrile (2 mL) and was added to a solution of triethylamine (0.4 mL, 2.9 mmol) in the same solvent (2 mL). This second solution was added to the first, and the resultant mixture was stirred for 1.5 hours. The reaction mixture was added to a saturated aqueous solution of $NaHCO_3$ (100 mL). Following extraction with ethyl acetate, washing with brine, drying with $Na_2SO_{4,}$ evaporation of solvents, and flash chromatography, 55 mg (37%) **2** was isolated as an oil.

Method B: Hexachloroethane (3.55 g, 15 mmol) was dissolved in anhydrous acetonitrile (40 mL). The aldehyde **1d** (1.09 g, 5 mmol) was dissolved in the same solvent (15 mL) and added. The reaction mixture was cooled to 0 ^oC, and triethylamine (4.1 mL, 30 mmol) was added via syringe. Triphenylphosphine (3.93 g, 15 mmol) was added as a solid in portions. The ice bath was removed and the reaction mixture was stirred for 2 hours, after which time it was added to brine (200 mL) and extracted with ethyl acetate. The combined extracts were washed with brine and dried with Na_2SO_4. The solvents were evaporated and the residue was purified by flash chromatography yielding 766 mg (76%) of **1** as an oil.

Method C: Hexachloroethane (142 mg, 0.6 mmol) and triphenylphosphine (157 mg, 0.6 mmol) were weighed into a reaction vessel, and anhydrous acetonitrile (3 mL) was added. After complete solution was attained (2-3 minutes) the aldehyde **7d** (55 mg, 0.3 mmol) was dissolved in the same solvent (1 mL) and added. The resulting solution was stirred for 10 minutes, and pyridine (0.1 mL, 1.2 mmol) was added. The reaction mixture was stirred for 2 hours at room temperature, heated to 60^{o}C, and stirred for an additional 2.5 hours at 60^{o}C, after which time it was added to brine (10 mL) and extracted with ethyl acetate. The combined extracts were washed with brine and dried with Na_2SO_4. The solvents were evaporated and the residue was purified by flash chromatography yielding 30 mg (61%) of **7** as an oil.

1: Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.69 (d, *J* = 5 Hz, 1H); 8.06 (d, *J* = 8 Hz, 1H); 7.76 (dd, *J* = 8, 8 Hz, 1H); 7.49 (s, 1H); 7.31 (dd, *J* = 5, 8 Hz, 1H); 2.45 (d, *J* = 8 Hz, 2H); 2.03 (m, 1H); 0.93 (d, *J* = 8 Hz, 6H); ^{13}C NMR (100MHz, $CDCl_3$) ppm 160.0, 150.0, 146.2, 141.9, 136.6, 135.7, 124.4, 121.8, 35.4, 27.6, 22.3; ESMS *m/z* 203 (M+1).

2: Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.69 (ddd, *J* = 1, 1.7, 5 Hz, 1H); 8.06 (ddd, *J* = 1, 1, 8 Hz, 1H); 7.76 (ddd, *J* = 1.7, 8, 8 Hz, 1H); 7.47 (s, 1H); 7.30 (ddd, *J* = 1, 5, 8 Hz, 1H); 2.44 (d, *J* = 6.4 Hz, 2H); 1.60-1.74 (m, 3 H); 1.10-1.23 (m, 4H); 0.78-1.10 (m, 4H); ^{13}C NMR (100MHz, $CDCl_3$) ppm 160.0, 150.0, 146.2, 141.5, 136.8, 135.8, 124.3, 121.8, 36.9, 34.1, 33.1, 26.4, 26.1, ESMS *m/z* 243 (M+1).

3: [1] Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.07-8.05 (m, 2H); 7.72 (s, 1H); 7.48-7.45(m, 3H); 7.25 (m, 1H); ESMS *m/z* 146 (M + 1).

4: Solid, mp: 80-81; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.90 (s, 1H); 7.80-7.82 (m, 2H); 7.74 (dd, *J* = 1.2, 3.7 Hz, 1H); 7.41-7.46 (m, 3H); 7.32-7.38 (m, 1H); 7.14 (dd, *J* = 3.7, 5.0 Hz, 1H); ^{13}C NMR (100MHz,

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[1] Eissenstat, M. A.; Weaver, J. D. *J. Org. Chem*. **1993**, *58*, 3387.

CDCl3) ppm 158.5, 142.0, 132.8, 130.8, 130.0, 128.7, 128.6, 128.4, 128.2, 128.0, 125.7; ESMS *m/z* 228 (M+1).

Anal. Calcd for $C_{13}H_9NOS$: C, 68.70; H, 3.99; N, 6.16; found: C, 68.39; H, 4.24; N, 5.93.

4j: ESMS *m/z* 264 (M+1).

5: Solid, mp 40-41; ^{1}H NMR (400MHz, CDCl$_3$) δ 7.83 (s, 1H); 7.72-7.74 (m, 2H); 7.38-7.40 (m, 2H); 7.31-7.75 (m, 6H); 4.19 (s, 2H); ^{13}C NMR (100MHz, CDCl3) ppm 165.2, 142.7, 137.3, 135.6, 135.5, 133.0, 130.7, 130.6, 129.9, 129.0, 127.4, 36.7; ESMS *m/z* 236 (M+1).

Anal. Calcd for $C_{16}H_{13}NO$: C, 81.68; H, 5.57; N, 5.95; found: C, 81.34; H, 5.65; N, 5.74.

6: Colorless oil; ^{1}H NMR (400MHz, CDCl$_3$) δ 8.00-8.03 (m, 2H); 7.42-7.44 (m, 4H); 2.25 (d, *J* = 1 Hz, 3H); ^{13}C NMR (100MHz, CDCl$_3$) ppm 160.8, 137.0, 133.7, 129.5, 128.1, 127.0, 125.6, 11.1; ESMS *m/z* 160 (M+1).

6i: ESMS *m/z* 196 (M+1).

6j: ESMS *m/z* 196 (M+1).

7: Colorless oil; ^{1}H NMR (400MHz, CDCl$_3$) δ 7.66 (dd, *J* = 2, 5 Hz, 1H); 7.43 (dd, *J* = 2, 7 Hz, 1H); 7.38 (q, *J* = 1 Hz, 1H); 7.12 (dd, *J* = 5, 7 Hz, 1H); 2.25 (d, *J* =1 Hz, 3H); ^{13}C NMR (100MHz, CDCl$_3$) ppm 157.6, 137.7, 133.7, 130.1, 128.0, 127.9, 127.4, 11.6; ESMS *m/z* 166 (M+1).

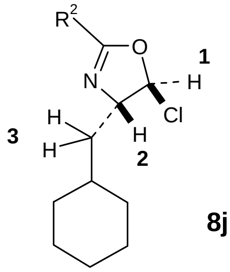
7i: ESMS *m/z* 202 (M+1).

7j: ESMS *m/z* 202 (M+1).

8: Colorless oil; ^{1}H NMR (400MHz, CDCl$_3$) δ 8.67 (d, *J* = 5.5 Hz, 2H); 7.82 (d, *J* = 5.5 Hz, 2H); 7.44 (s, 1H); 2.42 (d, *J* = 7 Hz, 2H); 1.59-1.69 (m, 6H); 1.13-1.23 (m, 3H); .91-.97 (m, 2H); ^{13}C NMR (100MHz, CDCl$_3$) ppm 158.9, 150.3, 141.9, 135.9, 134.6, 119.9, 36.9, 34.0, 33.0, 26.4, 26.1 ESMS *m/z* 243 (M+1).

8i: ESMS *m/z* 279 (M+1).

8j: Colorless oil; ^{1}H NMR (400MHz, CDCl$_3$) δ 8.71 (d, *J* = 5 Hz, 2H); 7.77 (d,, *J* = 5 Hz, 2H); 6.13 (d, *J* = 2 Hz, 1H); 4.52 (dt, *J* = 2, 5 Hz, 1H); 1.71-1.85 (m, 5H); 1.52-1.56 (m, 2H);); 1.35-1.41 (m, 1H); 1.19-1.35 (m, 3H); .98-1.02 (m, 2H); ^{13}C NMR (100MHz, CDCl$_3$) ppm 159.0, 150.4, 134.0, 121.9, 95.0, 76.8, 41.4, 34.6, 33.2, 26.3, 26.0; ESMS *m/z* 279 (M+1).



8j

The molecule was mapped by ^{1}H, ^{13}C, DEPT 135, HMQC, HMBC. Distance between H1 and H2 (measured by Cerius^2; version 4.5; Molecular Simulations, Inc.): for **8j**, 2.97 Å (**8i**, 2.30 Å); Distance between H1 and H3: for **8j**, 2.59, 2.65 Å (**8i**, 3.44, 3.82 Å); NOESY spectrum shows a strong nOe between H1 and H3 and a weak nOe between H1 and H2, indicative of **8j**. Dihedral angle between H1 and

C3: for **8j**, -1.3^o (**8i,** -123^o). Strong polarization transfer between H1 and C3 (HMBC) indicates **8j.** Dihedral angle between H1 and H2: for **8j**, -126^o (**8i**, 2.5^o). Coupling constant between H1 and H2 of 2 Hz indicates **8j**.

9: Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.76 (ddd, *J* = 1, 2, 5 Hz, 1H); 8.12 (ddd *J* = 1, 1, 8 Hz, 1H); 7.84 (ddd, *J* = 2, 7, 8 Hz, 1H); 7.46 (t, *J* = 1 Hz, 1H); 7.38 (ddd, *J* = 1, 5, 7 Hz, 1H); 7.28-7.34 (m, 2H); 7.20-7.25 (m, 3H); 3.01-3.03 (m, 2H); 2.94-3.00 (m, 2H); ^{13}C NMR (100MHz, $CDCl_3$) ppm 158.5, 154.0, 148.4, 144.5, 140.4, 139.5, 135.2, 133.8, 126.7, 124.4, 123.3, 120.1, 32.9, 26.2; ESMS *m/z* 251 (M+1).

10: Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.02-8.14 (m, 2H); 7.69 (t, *J* = 1 Hz, 1H); 7.31-7.53 (m, 8H); 4.70 (s, 2H);); 4.58 (d, *J* = 1 Hz, 2H); ^{13}C NMR (100MHz, $CDCl_3$) ppm 161.4, 138.8, 137.3, 135.7, 129.9, 128.2, 127.9, 127.4, 127.3, 126.9, 125.9, 72.2, 63.6; ESMS *m/z* 266 (M+1).

11: Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ 8.72 (ddd, *J* = 1, 1, 8 Hz, 1H), 8.10 (ddd, *J* = 1, 1, 7 Hz, 1H), 7.80 (ddd, *J* = 1, 5, 7 Hz, 1H), 7.40 (t, *J* = 1 Hz, 1H), 7.35 (ddd, *J* = 1, 5, 7 Hz, 1H), 7.32-7.33 (m, 4H), 7.25-7.28 (m, 1H), 3.98 (d, *J* = 1 Hz, 2H); ESMS *m/z* 237 (M + 1).

12: Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ : 8.00 (dd, *J* = 1.5, 8 Hz, 2H), 7.47-7.41 (m, 3H), 6.84 (s, 1H), 2.72 (t, *J* = 7.5, 2H), 1.69 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.43 (qt, *J* = 7.5, 7.5 Hz, 2H), 0.96 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100MHz, CDCl3) ppm 160.6, 153.2, 129.9, 128.7, 127.8, 126.0, 123.5, 29.7, 25.3, 22.2, 13.8; ESMS *m/z* 202 (M + 1);

13: Colorless oil; ^{1}H NMR (400MHz, $CDCl_3$) δ 7.57 (dd, *J* = 1.2, 3.7 Hz, 1H); 7.35 (dd, *J* = 1.2, 5.0 Hz, 1H); 7.07 (dd, *J* = 3.7, 5.0 Hz, 1H); 2.63 (t, *J* = 7.4 Hz, 2H); 2.14 (s, 3H); 1.59-1.67 (m, 2H); 1.34-1.42 (m, 2H); 0.94 (t, *J*= 7.4, 3H); ^{13}C NMR (100MHz, $CDCl_3$) ppm 155.8, 147.4, 132.0, 131.1, 128.2, 127.6, 127.0, 30.9, 24.7, 14.2, 11.7; ESMS *m/z* 222 (M+1)