Catalytic Conjugate Additions of Carbonyl Anions Under Neutral Aqueous Conditions

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General Methods: Tetrahydrofuran (THF) was purified by passage through a bed of activated alumina.¹ EtOH (200 proof), MeOH (HPLC grade), and Ethylene glycol (Fisher, certified grade) were used without further purification. Deionized water was used to make the buffered solutions. Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on

¹ Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometal.* **1996**, *15*, 1518-1520.

EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light and potassium permanganate, or phosphomolybic acid stains followed by heating. Melting points (**mp**) were obtained on a Thomas Hoover Capillary Melting Point Apparatus and are uncorrected. Infrared spectra (**IR**) were obtained on a Bio-Rad FTS-40 FTIR spectrophotometer. Infrared spectra for liquid products were obtained as a thin film on a KBr disk, and spectra for solid products were collected by preparing a KBr pellet containing the title compound. Proton nuclear magnetic resonances (^1H NMR) were recorded in deuterated solvents on a Varian Inova 500 (500 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm, δ) relative to tetramethylsilane (δ 0.00). If tetramethylsilane was not present in the deuterated solvent, the residual protio solvent is referenced (CDCl_3 , δ 7.27; D_2O , δ 4.80; DMSO, δ 2.50) ^1H NMR splitting patterns are designated as singlet (s), doublet (d), triplet (t), quartet (q), or septet (sep). Splitting patterns that could not be interpreted or easily visualized are designated as multiplet (m) or broad (br). Coupling constants are reported in Hertz (Hz). Proton-decoupled (^{13}C -NMR) spectra were recorded on a Varian Inova 500 (125 MHz) spectrometer and are reported in ppm using the solvent as an internal standard (CDCl_3 , δ 77.0; DMSO, δ 39.5). Electrospray mass spectra (**ESI-MS**) were obtained using a Micromass Quattro II Triple Quadrupole HPLC/MS/MS Mass Spectrometer. Gas Chromatography (**GC**) analysis data were obtained on Hewlett Packard 6890 Series GC System with a 7683 Series Injector. An HP-5 capillary 30 m column was employed (19091J-413). Methyl trifluoromethanesulfonate was distilled prior to use. Unless otherwise noted, all other commercially available reagents and solvents were purchased from Aldrich and used without further purification.

Abbreviations: (DABCO), 1,4-diazabicyclo[2.2.2]octane; (DBU), 1,8-diazabicyclo[5.4.0.]undec-7-ene; (DMAP), 4-(dimethylamino)pyridine; (RBF), round bottom flask.

2-acetyl-1-methylimidazole (I): 4-acetylmorpholine (11.6 mL, 100 mmol, 1.0 equiv) and THF (100 mL) were added to a 500 mL RBF and cooled to -78°C . 1-methylimidazole (8.8 mL, 110 mmol, 1.1 equiv) and THF (75 mL) were added to a 250 mL RBF and cooled to 0°C . A solution of BuLi in hexanes (1.4 M, 78.6 mL, 110 mmol, 1.1 equiv) was added to the 250 mL RBF over 5 min. The solution was allowed to stir at 0°C for 10 min. The lithiated imidazole solution was then cannula transferred to the 500 mL RBF over 15 min and stirred for 1 h at -78°C . After stirring 1 h the solution was taken out of the -78°C bath and stirred for 15 min. The solution was quenched with HCl (1.0 M, 10 mL), stirred for

5 min, and saturated NaCl (30 mL) and saturated NaHCO₃ (30 mL) were added. The resulting mixture was transferred to a separatory funnel, and extracted with EtOAc (3 x 100 mL). The organic extracts were combined and dried over sodium sulfate. The solution was concentrated on a rotatory evaporator and dried under vacuum to give a pale orange oil. The unpurified oil was enriched in the product (~90%, ¹H NMR) and used without further purification. A portion was purified by flash column chromatography (90% Et₂O/hexane, colorless oil) to obtain an analytically pure sample for the characterization data. R_f = 0.30 (90% ether/hexanes); ¹H NMR (500 MHz, CDCl₃) δ 7.12 (s, 1H), 7.01 (s, 1H), 3.98 (s, 3H), 2.64 (s, 3H); LRMS (electrospray): Mass calculated for C₆H₈N₂O [M]⁺, 124.14. Found 124. Spectroscopic data were consistent with the literature data for this compound.^{2,3}

General Procedure (A) to Form α,β-Unsaturated Substrates⁴

2-acetyl-1-methylimidazole (**I**) (1.24 g, 10.0 mmol, 1.0 equiv) and EtOH (20 mL) were added to a 100 mL RBF followed by the desired aromatic aldehyde (10.0 mmol, 1.0 equiv) and a catalytic amount of KOH (2 pellets, ~100 mg). The solution was stirred for 1-12 h depending upon how quickly the product precipitated from the solution. The solution was filtered and the product was washed with water (20 mL) and EtOH (25 mL).

General Procedure (B) to Form α,β-Unsaturated Substrates⁴

2-acetyl-1-methylimidazole (**I**) (1.24 g, 10.0 mmol, 1.0 equiv) and EtOH (20 mL) were added to a 100 mL RBF followed by the desired aromatic aldehyde (10.0 mmol, 1.0 equiv) and a catalytic amount of KOH (2 pellets, 100 mg). The solution was stirred for 12 h then transferred to a separatory funnel. Saturated NaCl (30 mL) and H₂O (10 mL) were added and the mixture was extracted with EtOAc (4 x 75 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated on a rotatory evaporator. The resulting residue was purified by flash column chromatography on silica gel.

² Davies, D. H.; Hall, J.; Smith, E. H. *J. Chem. Soc. Perkin Trans. I* **1991**, 2691-2698.

³ Abarca, B. G.; Jones, A. R.; Medio, M. S.; Quilez, P. J.; Sepulveda, J. A.; Zaballos, G. E. *Synth. Commun.* **1990**, 321-331.

⁴ Hayakawa, S.; Michiue, T.; Okamoto, M.; Hatakeyama, S.; Ohta, S. *Heterocycles* **1980**, 647-650.

2-cinnamoyl-1-methyl-1H-imidazole (6): Prepared following general procedure (A) to give 1.40 g (66%) of **6** as an off-white solid. R_f = 0.41 (90% ether/hexanes); mp = 119-121 °C; IR (film) 3105, 1653, 1595 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.08 (d, J = 16.0, 1H), 7.83 (d, J = 15.5 Hz, 1H), 7.70 (m, 2H), 7.39 (m, 3H), 7.22 (s, 1H), 7.07 (s, 1H), 4.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.4, 144.0, 143.3, 134.8, 130.4, 129.3, 128.8, 128.7, 127.2, 122.7, 36.3; LRMS (electrospray): Mass calculated for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}$ $[\text{M}]^+$, 212.25. Found 213.

(E)-1-(1-methyl-1H-imidazol-2-yl)-3-p-tolylprop-2-en-1-one (8a): Prepared following general procedure (B), purified with 40% EtOAc/hexanes, to give 1.20 g (55%) of **8a** as an off-white solid. R_f = 0.33 (40% ether/hexanes); mp = 84-86 °C; IR (film) 3103, 3028, 1654, 1598 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.04 (d, J = 16.0, 1H), 7.80 (d, J = 16.5 Hz, 1H), 7.59 (d, J = 7.5 Hz, 2H), 7.20 (m, 2H), 7.19 (s, 1H), 7.05 (s, 1H), 4.07 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.4, 144.0, 143.3, 140.8, 132.1, 129.5, 129.1, 128.6, 127.1, 121.6, 36.2, 21.4; LRMS (electrospray): Mass calculated for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}$ $[\text{M}]^+$, 226.27. Found 227.

(E)-3-(4-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (9a): Prepared following general procedure (A) to give 1.24 g (51%) of **9a** as an off-white solid. R_f = 0.39 (90% ether/hexanes); mp = 115-116 °C; IR (film) 3111, 1652, 1590 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.95 (d, J = 15.5 Hz, 1H), 7.80 (d, J = 16.0 Hz, 1H), 7.65 (d, J = 8.5 Hz, 2H), 7.21 (s, 1H), 7.06 (s, 1H), 6.92 (d, J = 8.5 Hz, 2H), 4.09 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.5, 161.6, 144.1, 143.2, 130.5, 129.1, 127.6, 127.0, 120.4, 114.2, 55.3, 36.3; LRMS (electrospray): Mass calculated for $\text{C}_{13}\text{H}_{12}\text{N}_2\text{O}_2$ $[\text{M}]^+$, 242.47. Found 243.

(E)-3-(4-chlorophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (10a): Prepared following general procedure (A) to give 1.73 g (70%) of **10a** as an off-white solid. R_f = 0.38 (90% ether/hexanes); mp = 125-127 °C; IR (film) 3106, 1656, 1597 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.04 (d, J = 15.5 Hz, 1H), 7.75 (d, J = 15.5 Hz, 1H), 7.61 (d, J = 8.5 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.22 (s, 1H), 7.09 (s, 1H), 4.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.1, 143.8, 141.7, 136.2, 133.3, 129.8, 129.3, 129.0, 127.3, 123.2, 36.3; LRMS (electrospray): Mass calculated for $\text{C}_{13}\text{H}_{11}\text{ClN}_2\text{O}$ $[\text{M}]^+$, 246.69. Found 247.

(E)-3-(4-bromophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (11a): Prepared following general procedure (A) to give 1.75 g (60%) of **11a** as an off-white solid. R_f = 0.45 (90% ether/hexanes); mp = 139-141 °C; IR (film) 3108, 1655, 1597 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.05 (d, J = 16.0, 1H), 7.58 (d, J = 15.5 Hz, 1H), 7.53 (m, 4H), 7.21 (s, 1H), 7.08 (s, 1H), 4.08 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.0, 143.8, 141.7, 133.7, 132.0, 130.0, 129.3, 127.3, 124.6, 123.3, 36.3; LRMS (electrospray): Mass

calculated for $C_{13}H_{11}BrN_2O$ $[M]^+$, 291.14. Found 292.

(E)-3-(2-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (12a): Prepared following general procedure (B), purified with 40% EtOAc/hexanes, to give 1.57 g (65%) of **12a** as an off-white solid. R_f = 0.45 (90% EtOAc/hexanes); mp = 90-93 °C; IR (film) 3106, 2957, 1657, 1595 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, J = 15.5 Hz, 1H), 7.79 (d, J = 15.5 Hz, 1H), 7.32-7.27 (m, 2H), 7.21 (m, 2H), 7.07 (s, 1H), 6.94 (d, J = 7.5 Hz, 1H), 4.08 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 180.3, 159.8, 143.9, 143.2, 136.1, 129.7, 129.2, 127.2, 122.8, 121.6, 116.6, 112.8, 55.2, 36.3; LRMS (electrospray): Mass calculated for $C_{14}H_{14}N_2O_2$ $[M]^+$, 242.27. Found 243.

(E)-3-(2-chlorophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (13a): Prepared following general procedure (A) to give 1.98 g (80%) of **13a** as a white solid. R_f = 0.38 (90% ether/hexanes); mp = 147-148 °C; IR (film) 3130, 1656, 1603 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 8.26 (d, J = 16.0 Hz, 1H), 8.07 (d, J = 16.0 Hz, 1H), 7.87 (d, J = 7.0 Hz, 1H), 7.42 (d, J = 7.0 Hz, 1H), 7.30 (m, 2H), 7.22 (s, 1H), 7.09 (s, 1H), 4.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.9, 143.8, 138.8, 135.6, 133.0, 131.1, 130.1, 129.4, 127.9, 127.4, 126.9, 124.9, 36.3; LRMS (electrospray): Mass calculated for $C_{13}H_{11}ClN_2O$ $[M]^+$, 246.69. Found 247.

(E)-3-(2-bromophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (14a): Prepared following general procedure (A) to give 2.78 g (95%) of **14a** as white solid. R_f = 0.38 (90% ether/hexanes); mp = 142-143 °C; IR (film) 3116, 1659, 1595 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 16.0 Hz, 1H), 8.03 (d, J = 16.0 Hz, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.33 (t, J = 7.5 Hz, 1H), 7.24-7.21 (m, 2H), 7.09 (s, 1H), 4.09 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.8, 143.8, 141.3, 134.7, 133.3, 131.2, 129.3, 128.0, 127.5, 127.4, 126.0, 125.1, 36.3; LRMS (electrospray): Mass calculated for $C_{13}H_{11}BrN_2O$ $[M]^+$, 291.14. Found 292.

(E)-3-(2-(trifluoromethyl)phenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (15a): Prepared following general procedure (B), purified with 40% EtOAc/hexanes, to give 1.1 g (40%) of **15a** as an off-white solid. R_f = 0.35 (90% EtOAc/hexanes); mp = 109-110 °C; IR (film) 3110, 1654, 1599 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 8.20 (d, J = 16.0 Hz, 1H), 8.08 (d, J = 15.5 Hz, 1H), 7.96 (d, J = 8.5 Hz, 1H), 7.71 (d, J = 7.5 Hz, 1H), 7.58 (t, J = 7.5 Hz, 1H), 7.48 (t, J = 7.5 Hz, 1H), 7.22 (s, 1H), 7.11 (s, 1H), 4.10 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.6, 143.7, 138.2, 133.7, 131.9, 129.6, 129.4, 128.1, 127.5, 126.0, 126.0, 126.0, 125.0, 122.9, 36.3; LRMS (electrospray): Mass calculated for $C_{14}H_{11}F_3N_2O$ $[M]^+$, 280.25. Found 281.

(E)-3-(furan-2-yl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (16a): Prepared following general procedure (B), purified with 40% EtOAc/hexanes, to give 1.31 g (65%) of **16a** as a yellow solid. R_f = 0.20 (40% EtOAc/hexanes); mp = 79-80 °C; IR (film) 3130, 1657, 1602 cm^{-1} ;

^1H NMR (500 MHz, CDCl_3) δ 7.92 (d, J = 16.0 Hz, 1H), 7.59 (d, J = 16.0 Hz, 1H), 7.51 (s, 1H), 7.20 (s, 1H), 7.07 (s, 1H), 6.73 (d, J = 3.0 Hz, 1H), 6.49 (br s, 1H), 4.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.2, 151.8, 144.9, 143.9, 129.3, 129.2, 127.1, 120.7, 115.6, 112.4, 36.18; LRMS (electrospray): Mass calculated for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_2$ $[\text{M}]^+$, 202.21. Found 203.

(E)-1-(1-methyl-1H-imidazol-2-yl)-3-(thiophen-2-yl)prop-2-en-1-one

(17a): Prepared following general procedure (B), purified with 40% EtOAc/hexanes, to give 1.38 g (63%) of **17a** as a yellow solid. R_f = 0.20 (40% EtOAc/hexanes); mp = 103-105 °C; IR (film) 3128, 3014, 1655,

1596 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.95 (d, J = 15.5 Hz, 1H), 7.84 (d, J = 15.5 Hz, 1H), 7.41 (d, J = 5.0 Hz, 1H), 7.37 (d, J = 3.0 Hz, 1H), 7.21 (s, 1H), 7.20 (s, 1H), 7.07-7.06 (m, 2H), 4.07 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 180.0, 143.8, 140.4, 135.7, 131.8, 129.2, 129.0, 128.1, 127.1, 121.6, 36.2; LRMS (electrospray): Mass calculated for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{OS}$ $[\text{M}]^+$, 218.27. Found 219.

General Procedure C for Converting α -Keto Acids to the Sodium Carboxylate Salts

R	Time (min)	Yield (%)
propyl	60	83
phenyl	45	78
furyl	15	72
thiophene	60	54
1-Me-imidazole	45	81
4-butene	15	47
CF_3	30	76

The carboxylate salts sodium pyruvate and sodium 4-methyl-2-oxopentanoate are commercially available. Commercially available α -keto acids (2-oxopentanoic acid; oxo(phenyl)acetic acid; 2-furyl(oxo)acetic acid; oxo(2-thienyl)acetic acid) were converted to the corresponding sodium carboxylate salts.

The α -keto acid (10.0 mmol, 1.0 equiv) was added to a 100 mL RBF followed by EtOH (20 mL). The solution was stirred at 23 °C, and finely ground NaOH (600 mg, 15.0 mmol, 1.5 equiv) was added in one portion to the reaction flask. The solution was stirred for the allotted time and the sodium carboxylate precipitated from the reaction solution. The resulting solid was filtered, washed with EtOH (50 mL) and Et_2O (50 mL), and dried under vacuum. The sodium

carboxylate salts were used without further purification.

Sodium-2-(1-methyl-1H-imidazol-2-yl)-2-oxoacetate was prepared in four steps starting from the procedure of Mosher and co-workers.⁵ ¹H NMR (500 MHz, D₂O) δ 7.43 (s, 1H), 7.24 (s, 1H), 4.03 (s, 3H); LRMS (electrospray):

Mass calculated for C₆H₅N₂O₃ [M]⁻, 153.03. Found 153.

Sodium-2-oxohex-5-enoate was prepared in three steps starting from diethyl oxalate.^{6,7} ¹H NMR (500 MHz, D₂O) δ 5.96-5.88 (m, 1H), 5.13-5.05 (m, 2H), 2.90 (t, *J* = 7.0 Hz, 2H) 2.41-2.36 (m, 2H); ¹³C NMR (125

MHz, D₂O), (Note: The ketone peak was set as the reference peak at δ 207.0) δ 207.0, 170.8, 137.4, 115.6, 38.4, 27.0; LRMS (electrospray): Mass calculated for C₆H₇O₃ [M]⁻, 127.04. Found 127.

Sodium 3,3,3-trifluoro-2-oxopropanoate was prepared in two steps starting from methyl 3,3,3-trifluoropyruvate. ¹³C NMR (125 MHz, D₂O), (Note: residual EtOH served as an internal standard for the ¹³C NMR peaks) δ 175.7, 172.0,

126.3, 124.0, 121.7, 119.4; LRMS (electrospray): Mass calculated for C₃F₃O₃ [M]⁻, 140.98. Found 141; Mass calculated for C₃F₃O₃-H₂O [M]⁻ (hydrated compound), 158.99. Found 159.

General Procedure D for Thiazolium Catalyzed α-keto acid Additions

A screw-capped tube was charged with 3-benzyl-5-(2-hydroxyethyl)-4-methyl-thiazolium chloride (**5**) (thiazole carbene precursor) (22 mg, 0.08 mmol, 20 mol%), α-keto carboxylate sodium salt (0.72 mmol, 1.8 equiv), and α,β-unsaturated-keto-*N*-methylimidazole substrate (0.40 mmol, 1.0 equiv) on the benchtop. Next, MeOH (450 μL) and pH 7.2 phosphate buffer (350 μL, 100 mM,) were added via syringe to the screw-capped tube. The resulting mixture was heated to 70 °C and allowed to stir for the allotted time (8 h to 24 h). Upon completion of the reaction (as judged by TLC, 90% ether/hexanes), the reaction was cooled to room temperature, diluted with

⁵ Nimitz, J. S.; Mosher, H. S. *J. Org. Chem.* **1981**, *46*, 211-213.

⁶ Weinstock, L. M.; Currie, R. B.; Lovell, A. V. *Synth. Commun.* **1981**, *11*, 943-946.

⁷ Imoto, H.; Imamiya, E.; Momose, Y.; Sugiyama, Y.; Kimura, H.; Sohda, T. *Chem. Pharm. Bull.* **2002**, *50*, 1349-1357.

EtOAc (10 mL) and transferred to a separatory funnel. Saturated NaCl (10 mL), saturated NaHCO₃ (10 mL), and H₂O (10 mL) were added and the aqueous layer was extracted with EtOAc (3 x 40 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated on a rotary evaporator. The resulting residue was purified by flash column chromatography on silica gel. *Note: Reactions that were conducted under non-aqueous conditions (MeOH only) using DBU employed N-methyl-4,5-dimethylthiazolium iodide as the catalyst.*

1-(1-methyl-1H-imidazol-2-yl)-3-phenylpentane-1,4-dione (7):

Purified with 40% EtOAc/hexanes, to give 94 mg (92%) of **7** as an off-white solid. *R*_f = 0.35 (90% ether/hexanes); mp = 72–74 °C; IR (film) 3107, 3028, 2959, 1715, 1677 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.25–7.21 (m, 5H), 7.19 (s, 1H), 7.05 (s, 1H), 4.26 (dd, *J* = 10.3, 3.5 Hz, 1H), 4.09 (dd, *J* = 18.3, 10.0 Hz, 1H), 3.89 (s, 3H), 3.26 (dd, *J* = 18.5, 3.5 Hz, 1H), 2.11 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 207.3, 190.8, 142.8, 138.0, 129.4, 129.2, 128.6, 127.8, 127.1, 54.1, 42.5, 36.3, 29.2; LRMS (electrospray): Mass calculated for C₁₅H₁₆N₂O₂ [M]⁺, 256.30. Found 257.

1-(1-methyl-1H-imidazol-2-yl)-3-p-tolylpentane-1,4-dione (8):

Purified with 45% EtOAc/hexanes, to give 94 mg (87%) of **8** as a white solid. *R*_f = 0.34 (90% ether/hexanes); mp = 125–127 °C; IR (film) 3002, 1713, 1674 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.14–7.09 (m, 5H), 7.08 (s, 1H), 6.97 (s, 1H), 4.27 (dd, *J* = 10.0, 3.5 Hz, 1H), 4.11 (dd, *J* = 18.3, 10.0 Hz, 1H), 3.92 (s, 3H), 3.27 (dd, *J* = 18.0, 4.0 Hz, 1H), 2.29 (s, 3H), 2.13 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 207.2, 190.7, 142.6, 137.2, 134.7, 129.7, 129.1, 128.3, 126.8, 53.5, 42.2, 36.0, 28.8, 21.0; LRMS (electrospray): Mass calculated for C₁₆H₁₈N₂O₂ [M]⁺, 270.33. Found 271.

3-(4-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-dione (9):

Purified with 35% EtOAc/hexanes, to give 93 mg (81%) of **9** as a white solid. *R*_f = 0.30 (90% ether/hexanes); mp = 107–109 °C; IR (film) 2957, 2932, 1712, 1675 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.15 (d, *J* = 8.5 Hz, 2H), 7.08 (s, 1H), 6.97 (s, 1H), 6.82 (d, *J* = 8.5 Hz, 2H), 4.24 (dd, *J* = 10.0, 3.5 Hz, 1H), 4.08 (dd, *J* = 18.3, 10.0 Hz, 1H), 3.91 (s, 3H), 3.75 (s, 3H), 3.27 (dd, *J* = 18.0, 4.0 Hz, 1H), 2.13 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 207.3, 190.7, 158.9, 142.6, 129.7, 129.4, 129.1, 126.8, 114.3, 55.2, 53.0, 42.3, 36.0, 28.8; LRMS (electrospray): Mass calculated for C₁₆H₁₈N₂O₃ [M]⁺, 286.33. Found 287.

3-(4-chlorophenyl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-

dione (10): Purified with 40% EtOAc/hexanes, to give 102 mg (87%) of **10** as a white solid. R_f = 0.30 (90% ether/hexanes); mp = 108-110 °C; IR (film) 3119, 2957, 1715, 1676 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.22 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H) 7.03 (s, 1H), 6.94 (s, 1H), 4.23 (dd, J = 10.0, 4.0 Hz, 1H), 4.02 (dd, J = 18.5, 10.5 Hz, 1H), 3.87 (s, 3H), 3.26 (dd, J = 18.5, 4.0 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.4, 190.1, 142.4, 136.2, 133.4, 129.6, 129.1, 129.1, 126.9, 53.1, 42.1, 35.9, 28.9; LRMS (electrospray): Mass calculated for $\text{C}_{15}\text{H}_{15}\text{ClN}_2\text{O}_2$ $[\text{M}]^+$, 290.74. Found 291.

3-(4-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-

dione (11): Purified with 40% EtOAc/hexanes, to give 95 mg (71%) of **11** as a white solid. R_f = 0.25 (90% ether/hexanes); mp = 119-120 °C; IR (film) 3110, 2958, 1714, 1675 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.42 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.0 Hz, 2H) 7.09 (s, 1H), 6.99 (s, 1H), 4.27 (dd, J = 10.0, 3.5 Hz, 1H), 4.07 (dd, J = 18.0, 10.0 Hz, 1H), 3.92 (s, 3H), 3.31 (dd, J = 18.0, 4.0 Hz, 1H), 2.14 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.4, 190.1, 142.4, 136.7, 132.0, 130.0, 129.2, 126.9, 121.5, 53.2, 42.0, 35.9, 28.9; LRMS (electrospray): Mass calculated for $\text{C}_{15}\text{H}_{15}\text{BrN}_2\text{O}_2$ $[\text{M}]^+$, 335.20. Found 336.

3-(2-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-

dione (12): Purified with 45% EtOAc/hexanes, to give 99 mg (87%) of **12** as a colorless oil. R_f = 0.25 (90% ether/hexanes); IR (film) 3109, 3003, 2957, 2837, 1716, 1680 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.15 (t, J = 9.0 Hz, 1H), 7.03 (s, 1H), 6.93 (s, 1H) 6.78 (d, J = 7.5 Hz, 1H), 6.72 (m, 2H), 4.22 (dd, J = 10.0, 2.5 Hz, 1H), 4.07 (dd, J = 18.2, 10.5 Hz, 1H), 3.87 (s, 3H), 3.70 (s, 3H), 3.24 (dd, J = 18.0, 3.0 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.8, 190.4, 159.9, 142.4, 139.1, 129.9, 129.0, 126.8, 120.7, 113.6, 113.00, 55.1, 53.8, 42.0, 35.9, 28.8; LRMS (electrospray): Mass calculated for $\text{C}_{16}\text{H}_{18}\text{N}_2\text{O}_3$ $[\text{M}]^+$, 286.33. Found 287.

3-(2-chlorophenyl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-

dione (13): Purified with 45% EtOAc/hexanes, to give 111 mg (95%) of **13** as a colorless oil. R_f = 0.25 (90% ether/hexanes); IR (film) 3110, 2957, 2922, 1723, 1680 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.3 (m, 1H), 7.13 (m, 3H), 7.02 (s, 1H) 6.94 (s, 1H), 4.83 (dd, J = 10.0, 3.0 Hz, 1H), 4.04 (dd, J = 18.5, 10.0 Hz, 1H), 3.87 (s, 3H), 3.19 (dd, J = 18.5, 3.5 Hz, 1H), 2.10 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.1, 189.8, 142.3, 135.4, 133.8, 129.9, 129.1, 129.0, 128.6, 127.3, 126.8, 49.5, 41.1, 35.8, 29.0; LRMS (electrospray): Mass calculated for $\text{C}_{15}\text{H}_{15}\text{ClN}_2\text{O}_2$ $[\text{M}]^+$, 290.74. Found 291.

3-(2-bromophenyl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-dione

(14): Purified with 45% EtOAc/hexanes, to give 120 mg (89%) of **14** as a colorless oil. $R_f = 0.25$ (90% ether/hexanes); IR (film) 3110, 2957, 2921, 1739, 1676 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.52 (d, $J = 8.5$ Hz, 1H), 7.18 (t, $J = 7.0$ Hz, 1H), 7.10 (d, $J = 7.5$ Hz, 1H), 7.05 (m, 2H), 7.02 (s, 1H), 6.94 (s, 1H), 4.84 (dd, $J = 10.0, 2.5$ Hz, 1H), 4.03 (dd, $J = 18.5, 10.5$ Hz, 1H), 3.88 (s, 3H), 3.18 (dd, $J = 18.5, 3.0$ Hz, 1H), 2.11 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.1, 189.8, 142.3, 137.1, 133.3, 129.1, 129.0, 128.9, 127.9, 126.8, 124.8, 52.1, 41.3, 35.9, 29.1; LRMS (electrospray): Mass calculated for $\text{C}_{15}\text{H}_{15}\text{BrN}_2\text{O}_2$ $[\text{M}]^+$, 335.2. Found 336.

3-(2-(trifluoromethyl)phenyl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-dione

(15): Purified with 45% EtOAc/hexanes, to give 99 mg (76%) as a tan oil. $R_f = 0.33$ (90% ether/hexanes); IR (film) 3112, 2961, 2925, 1718, 1676 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.71 (d, $J = 7.5$ Hz, 1H), 7.50 (t, $J = 7.5$ Hz, 1H), 7.38 (t, $J = 7.5$ Hz, 1H), 7.33 (d, $J = 8.0$ Hz, 2H), 7.10 (s, 1H), 7.02 (s, 1H), 4.77 (dd, $J = 10.5, 2.5$ Hz, 1H), 4.03 (dd, $J = 18.5, 10.5$ Hz, 1H), 3.97 (s, 3H), 3.20 (dd, $J = 18.5, 2.5$ Hz, 1H), 2.17 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 206.1, 189.6, 142.1, 136.2, 132.3, 129.6, 129.4, 129.1, 128.8, 127.5, 126.9, 126.4, 48.5, 43.0, 36.0, 29.1; LRMS (electrospray): Mass calculated for $\text{C}_{16}\text{H}_{15}\text{F}_3\text{N}_2\text{O}_2$ $[\text{M}]^+$, 324.30. Found 325.

3-(furan-2-yl)-1-(1-methyl-1H-imidazol-2-yl)pentane-1,4-dione

(16): Purified with 50% EtOAc/hexanes, to give 79 mg (80%) of **16** as a tan oil. $R_f = 0.25$ (90% ether/hexanes); IR (film) 3114, 1719, 1675 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.36 (br s, 1H), 7.13 (s, 1H), 7.04 (s, 1H), 6.33 (br s, 1H), 6.22 (br d, $J = 2.0$ Hz, 1H), 4.45 (dd, $J = 10.0, 4.0$ Hz, 1H), 4.09 (dd, $J = 18.5, 10.0$ Hz, 1H), 3.95 (s, 3H), 3.44 (dd, $J = 18.0, 4.0$ Hz, 1H), 2.25 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 204.5, 189.7, 151.1, 142.3, 142.2, 129.1, 126.9, 110.6, 107.2, 47.1, 39.3, 35.9, 28.7; LRMS (electrospray): Mass calculated for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_3$ $[\text{M}]^+$, 246.26. Found 247.

1-(1-methyl-1H-imidazol-2-yl)-3-(thiophen-2-yl)pentane-1,4-dione

(17): Purified with 50% EtOAc/hexanes, to give 95 mg (90%) of **17** as a tan oil. $R_f = 0.30$ (90% ether/hexanes); IR (film) 3107, 2920, 1717, 1674 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.22 (m, 1H), 7.21 (s, 1H), 7.12 (s, 1H), 7.02 (m, 2H), 4.60 (dd, $J = 10.0, 4.0$ Hz, 1H), 4.15 (dd, $J = 18.5, 10.0$ Hz, 1H), 3.95 (s, 3H), 3.46 (dd, $J = 18.0, 3.5$ Hz, 1H), 2.26 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 204.5, 189.7, 151.1, 142.3, 142.2, 129.1, 126.9, 110.6, 107.2, 47.1, 39.3, 35.9, 28.7; LRMS (electrospray): Mass calculated for $\text{C}_{13}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$ $[\text{M}]^+$, 262.33. Found 263.

1-(1-methyl-1H-imidazol-2-yl)-3-phenylheptane-1,4-dione

(18): Purified with 35% EtOAc/hexanes, to give 104 mg (92%) of **18** as a colorless oil. $R_f = 0.45$ (90% ether/hexanes); IR (film) 2955, 2933, 2875, 1721, 1676 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.24-7.17 (m, 5H), 7.01 (s, 1H), 6.91 (s, 1H), 4.24 (dd, $J = 10.8, 3.5$ Hz, 1H), 4.10 (dd, $J = 18.0, 10.5$ Hz, 1H), 3.85 (s, 3H), 3.22 (dd, $J = 18.3, 3.5$ Hz, 1H), 2.49-2.42 (m, 1H), 2.36-2.30 (m, 1H), 1.52-1.48 (m, 1H), 1.45-1.41 (m, 1H), 0.71 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 209.0, 190.5, 142.5, 137.8, 129.0, 129.0, 128.8, 128.6, 128.3, 127.3, 126.7, 53.2, 43.3,

42.2, 35.9, 16.9, 13.4; LRMS (electrospray): Mass calculated for $C_{17}H_{20}N_2O_2$ $[M]^+$, 284.35. Found 285.

4-(1-methyl-1H-imidazol-2-yl)-1,2-diphenylbutane-1,4-dione (19):

The synthesis of **19** employed a thiazolium catalyst (20 mol%), DBU (7 μ L, 0.056 mmol, 14%), and MeOH (750 μ L) under non-aqueous conditions, 18 h at 70 °C. Purified with 40% EtOAc/hexanes, to give 115 mg (90%) of **19** as an off-white solid. R_f = 0.40 (90% ether/hexanes); mp = 127-130 °C; IR (film) 3060, 3028, 1674, 1411 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 8.03 (d, J = 7.5 Hz, 2H), 7.46 (t, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 2H), 7.33 (d, J = 7.5 Hz, 2H), 7.27 (t, J = 7.5 Hz, 2H), 7.19 (t, J = 7.0 Hz, 1H), 7.13 (s, 1H), 6.99 (s, 1H), 5.23 (dd, J = 10.7, 3.5 Hz, 1H), 4.37 (dd, J = 18.7, 10.5 Hz, 1H), 3.92 (s, 3H), 3.49 (dd, J = 18.7, 3.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 198.7, 190.5, 142.5, 138.3, 136.4, 132.8, 129.2, 129.0, 128.9, 128.5, 128.2, 127.2, 126.8, 48.5, 44.0, 36.0; LRMS (electrospray): Mass calculated for $C_{20}H_{18}N_2O_2$ $[M]^+$, 318.37. Found 319.

6-methyl-1-(1-methyl-1H-imidazole-2-yl)-3-phenylheptane-1,4-dione (20):

Purified with 40% EtOAc/hexanes, to give 86 mg (72%) of **20** as an off-white solid. R_f = 0.41 (90% ether/hexanes); mp = 78-79 °C; IR (film) 2956, 2930, 2871, 1720, 1680, cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.33-7.25 (m, 5H), 7.11 (s, 1H), 7.00 (s, 1H), 4.30 (dd, J = 10.5, 3.5 Hz, 1H), 4.19 (dd, J = 18.0, 10.5 Hz, 1H), 3.94 (s, 3H), 3.29 (dd, J = 18.0, 3.5 Hz, 1H), 2.46 (dd, J = 16.5, 6.0 Hz, 1H), 2.28 (dd, J = 16.5, 7.5 Hz, 1H), 2.13 (sep, J = 7.0 Hz, 1H), 0.88 (d, J = 6.5 Hz, 3H), 0.72 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 208.5, 190.5, 142.5, 137.7, 129.0, 128.8, 128.4, 127.3, 126.7, 53.6, 50.3, 42.1, 35.9, 24.0, 22.5, 22.1; LRMS (electrospray): Mass calculated for $C_{18}H_{22}N_2O_2$ $[M]^+$, 298.38. Found 299.

1-(furan-2-yl)-4-(1-methyl-1H-imidazol-2-yl)-2-phenylbutane-1,4-dione (21):

Purified with 40% EtOAc/hexanes, to give 118 mg (96%) of **21** as an off-white solid. R_f = 0.25 (90% ether/hexanes); mp = 146-148 °C; IR (film) 3130, 1670, 1412 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.46 (s, 1H), 7.30 (d, J = 7.0 Hz, 2H), 7.21 (t, J = 7.0 Hz, 2H), 7.13 (m, 2H), 7.04 (s, 1H), 6.92 (s, 1H), 6.39 (m, 1H), 4.93 (dd, J = 10.2, 3.5 Hz, 1H), 4.24 (dd, J = 18.8, 10.5 Hz, 1H), 3.84 (s, 3H), 3.46 (dd, J = 18.3, 3.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.2, 187.5, 152.0, 146.3, 142.4, 137.8, 129.1, 128.7, 128.3, 127.2, 126.8, 117.9, 112.1, 48.4, 42.8, 35.9; LRMS (electrospray): Mass calculated for $C_{18}H_{16}N_2O_3$ $[M]^+$, 308.33. Found 309.

4-(1-methyl-1H-imidazol-2-yl)-2-phenyl-1-(thiophen-2-yl)butane-1,4-dione (22):

(Note: MeOH (400 μ L) and pH 7.2 phosphate buffer (200 μ L) were used in the reaction). Purified with 40% EtOAc/hexanes, to give 99 mg (76%) of **22** as a white solid. R_f = 0.30 (90% ether/hexanes); mp = 177-181 °C; IR (film) 3105, 1662, 1411 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 4.0 Hz, 1H), 7.49 (d, J = 4.5 Hz, 1H), 7.30 (d, J =

7.5 Hz, 2H), 7.22 (t, J = 8.0 Hz, 2H), 7.14 (t, J = 7.5 Hz, 1H), 7.06 (s, 1H), 6.98 (t, J = 4.5 Hz, 1H), 6.93 (s, 1H), 4.97 (dd, J = 10.5, 3.5 Hz, 1H), 4.27 (dd, J = 18.2, 10.5 Hz, 1H), 3.86 (s, 3H), 3.42 (dd, J = 18.8, 3.5 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 191.5, 190.2, 143.4, 142.5, 138.4, 133.5, 132.7, 129.2, 128.9, 128.2, 128.0, 127.4, 126.9, 49.9, 43.6, 36.0; LRMS (electrospray): Mass calculated for $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}_3\text{S}$ $[\text{M}]^+$, 324.40. Found 325.

1,4-bis(1-methyl-1H-imidazol-2-yl)-2-phenylbutane-1,4-dione (23):

The synthesis of **23** employed a thiazolium catalyst (20 mol%), DBU (7 μL , 0.056 mmol, 14%), and MeOH (750 μL) under non-aqueous conditions, 20 h at 70 $^\circ\text{C}$. Purified with 100% EtOAc, to give 117 mg (91%) of **23** as a white solid. R_f = 0.40 (100% EtOAc); mp = 154-155 $^\circ\text{C}$; IR (film) 3107, 2957, 2918, 1670, 1406 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.49 (d, J = 7.5 Hz, 2H), 7.26 (t, J = 7.5 Hz, 2H), 7.18 (t, J = 7.5 Hz, 1H), 7.15 (s, 1H), 7.11 (s, 1H), 6.97 (s, 1H), 6.94 (s, 1H), 5.70 (dd, J = 11.0, 2.5 Hz, 1H), 4.30 (dd, J = 18.5, 11.0 Hz, 1H), 3.90 (br s, 6H), 3.64 (dd, J = 18.5, 3.0 Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 191.0, 190.3, 142.4, 142.4, 138.0, 129.3, 129.0, 128.6, 128.5, 127.0, 126.7, 47.5, 42.8, 35.9, 35.9; LRMS (electrospray): Mass calculated for $\text{C}_{18}\text{H}_{18}\text{N}_4\text{O}_2$ $[\text{M}]^+$, 322.14. Found 323.

1-(1-methyl-1H-imidazol-2-yl)-3-phenyloct-7-ene-1,4-dione (24):

Purified with 50% EtOAc/hexanes, to give 113 mg (95%) of **24** as a colorless oil. R_f = 0.33 (90% ether/hexanes); IR (film) 3079, 3063, 3028, 2921, 1715, 1675, 1412 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.33-7.25 (m, 5H), 7.11 (s, 1H), 7.00 (s, 1H), 4.30 (dd, J = 10.5, 3.5 Hz, 1H), 4.19 (dd, J = 18.0, 10.5 Hz, 1H), 3.94 (s, 3H), 3.29 (dd, J = 18.0, 3.5 Hz, 1H), 2.46 (dd, J = 16.5, 6.0 Hz, 1H), 2.28 (dd, J = 16.5, 7.5 Hz, 1H), 2.13 (sep, J = 7.0 Hz, 1H), 0.88 (d, J = 6.5 Hz, 3H), 0.72 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 208.5, 190.5, 142.5, 137.7, 129.0, 128.8, 128.4, 127.3, 126.7, 53.6, 50.3, 42.1, 35.9, 24.0, 22.5, 22.1; LRMS (electrospray): Mass calculated for $\text{C}_{18}\text{H}_{20}\text{N}_2\text{O}_2$ $[\text{M}]^+$, 296.15. Found 297.

Larger Scale (5 mmol) Preparation of 7

The procedure to prepare 7 was scaled by 12.5 times from the original scale (0.4 mmol) to determine the applicability of larger scale thiazolium catalyzed acyl anion additions in an aqueous system.

A 50 mL RBF was charged with 3-benzyl-5-(2-hydroxyethyl)-4-methyl-thiazolium chloride (**5**) (thiazole carbene precursor) (269 mg, 1.0 mmol, 20 mol%), sodium pyruvate (**1b**) (990 mg, 9.0 mmol, 1.8 equiv), and 2-cinnamoyl-1-methyl-1H-imidazole (**6**) (1.06 g, 5.0 mmol, 1.0 equiv) on the benchtop. Next, MeOH (9.0 mL) and pH 7.2 phosphate buffer (6.0 mL, 100 mM,) were added via syringe to the reaction flask. The resulting mixture was heated to 70 $^\circ\text{C}$ and allowed

to stir for 16 h. The reaction was cooled to room temperature, diluted with EtOAc (50 mL) and transferred to a separatory funnel. Saturated NaCl (25 mL), saturated NaHCO₃ (25 mL), and H₂O (15 mL) were added and the aqueous layer was extracted with EtOAc (3 x 100 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated on a rotary evaporator. The residue was purified by flash column chromatography 40% EtOAc/hexanes, to give 1.14 g (89%) of **7** as a white solid.

General procedure E for the preparation of **8** and **10** in ethylene glycol at 23 °C

A 25 mL RBF was charged with 3-benzyl-5-(2-hydroxyethyl)-4-methyl-thiazolium chloride (**5**) (thiazole carbene precursor) (161 mg, 0.6 mmol, 30 mol%), sodium pyruvate (**1b**) (400 mg, 3.6 mmol, 1.8 equiv), and α,β -unsaturated-keto-*N*-methylimidazole substrate (2.0 mmol, 1.0 equiv) on the benchtop. Next, ethylene glycol (5.0 mL) and DBU (90 μ L, 0.6 mmol, 30 mol%) were added via syringe to the reaction flask. The resulting mixture was stirred at 23 °C for 6 to 8 h. The reaction was diluted with H₂O (15 mL), filtered, and washed with additional H₂O (2 x 20 mL). The resulting products **8** and **10** were dried by filtering for 10 min and placed under high vacuum overnight. The 1,4-diketone products **8** and **10** prepared using this procedure were as pure as the same products prepared in the aqueous system with subsequent column chromatography.

Experimental details of the product inhibition study

Product inhibition studies utilized α,β -unsaturated-keto-*N*-methylimidazole **8a** as the conjugate acceptor due to its higher solubility in MeOH at 23 °C over compound **6**.

Reaction Procedure *Without* Product **8** as an Additive

A screw-capped tube was charged with 3-benzyl-5-(2-hydroxyethyl)-4-methyl-thiazolium chloride (**5**) (thiazole carbene precursor) (14 mg, 0.05 mmol, 26 mol%), sodium pyruvate (**1b**) (40 mg, 0.36 mmol, 1.8 equiv), and α,β -unsaturated-keto-*N*-methylimidazole substrate **8a** (0.2 mmol, 1.0 equiv) on the benchtop. Next, MeOH (750 μ L) and DBU (12 μ L, 0.08 mmol, 40 mol%) were added via syringe to the screw-capped tube. The resulting mixture was stirred at 23 °C for an allotted time. After stirring for the appropriate time period (2.25 h to 21.25 h) the reactions were diluted with EtOAc (4 mL) and a portion was run through a silica gel plug

(pipette size) before GC analysis. Experiments were monitored by GC and starting material **8a** : product **8** ratios were determined by peak integrations. Starting material and products peak integrations were linear over numerous mole fraction ratios (1:2, 2:2, 2:1).

Reaction Procedure With Product **8** as an Additive

A screw-capped tube was charged with 3-benzyl-5-(2-hydroxyethyl)-4-methyl-thiazolium chloride (**5**) (thiazole carbene precursor) (14 mg, 0.05 mmol, 26 mol%), sodium pyruvate (**1b**) (40 mg, 0.36 mmol, 1.8 equiv), α,β -unsaturated-keto-*N*-methylimidazole substrate **8a** (45 mg, 0.2 mmol, 1.0 equiv), and product **8** (54 mg, 0.2 mmol, 1.0 equiv) on the benchtop. Next, MeOH (750 μ L) and DBU (12 μ L, 0.08 mmol, 40 mol%) were added via syringe to the screw-capped tube. The resulting mixture was stirred at 23 °C for an allotted time. After stirring for the appropriate time period (2.25 h to 21.25 h) the reactions were diluted with EtOAc (4 mL) and a portion was run through a silica gel plug (pipette size) before GC analysis. Experiments were monitored by GC and starting material **8a** : product **8** ratios were determined by peak integrations. Starting material and products peak integrations were linear over numerous mole fraction ratios (1:2, 2:2, 2:1).

Results from the product inhibition study show depressed conversion when **8** (1.0 equiv.) is used as an additive. This strongly indicates product inhibition at 23 °C, however, when these reactions are conducted at 70 °C the reactions go to 100% conversion. Below is a summary of the results in tabular and graphical format.

GC Analysis Conditions: 70 °C hold 1 min. 20 °C / min ramp up to 285 °C and holding for 3.25 min. Total run time 15 min. t_R (**8a**) = 12.62 min, t_R (**8**) = 12.73 min with baseline separation.

Preparation of methyl ester^{1,8} 26 and morpholine amide 27 from 7

Methyl-4-oxo-3-phenylpentanoate (26): 1-(1-methyl-1*H*-imidazol-2-yl)-3-phenylpentane-1,4-dione (**7**) (128 mg, 0.5 mmol, 1.0 equiv) was added to a screw-cap tube followed by CH₂Cl₂ (1.5 mL). The solution was stirred and MeOTf (280 μ L, 2.5 mmol, 5.0 equiv) was added dropwise. The solution was stirred at 23 °C for 5 h. A solution of MeOH (1.0 mL, 25.0 mmol, 50 equiv) and DABCO (1.1 mL, 10.0 mmol, 20 equiv) was prepared and added slowly to the reaction tube. An addition portion of CH₂Cl₂ (1.5 mL) was added to the reaction tube. The mixture stirred at 23 °C for an additional 4 h. The mixture was diluted with EtOAc (10 mL) and transferred to a separatory funnel. Saturated NaCl (20 mL), and H₂O (20 mL) were added and the aqueous layer was extracted with EtOAc (4 x 40 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated on a rotary evaporator. The residue was purified by flash column chromatography 30% EtOAc/hexanes, to give 79 mg (78%) of **26** as a colorless oil. *R*_f = 0.55 (30% EtOAc/hexanes); IR (film) 3028, 2953, 1737, 1717 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.33 (t, *J* = 7.5 Hz, 2H), 7.28 (t, *J* = 7.0 Hz, 1H), 7.21 (t, *J* = 7.0 Hz, 2H), 4.19 (dd, *J* = 10.0, 5.0 Hz, 1H), 3.64 (s, 3H), 3.21 (dd, *J* = 16.5, 10.0 Hz, 1H), 2.52 (dd, *J* = 17.0, 5.0 Hz, 1H), 2.10 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 206.6, 172.4, 137.3, 129.1, 128.1, 127.6, 54.7, 51.7, 36.6, 28.7; LRMS (electrospray): Mass calculated for C₁₂H₁₄NaO₃ [M+Na]⁺, 229.23. Found 229. Spectroscopic data were consistent with the literature data for this compound.⁹

1-morpholine-3-phenylpentane-1,4-dione (27): 1-(1-methyl-1*H*-imidazol-2-yl)-3-phenylpentane-1,4-dione (**7**) (128 mg, 0.5 mmol, 1.0 equiv) was added to a screw-cap tube followed by CH₂Cl₂ (1.5 mL). The solution was stirred and MeOTf (280 μ L, 2.5 mmol, 5.0 equiv) was added dropwise. The solution was stirred at 23 °C for 5 h. Next, morpholine (1.1 mL, 12.5 mmol, 25 equiv) was added slowly to the reaction tube. An addition portion of CH₂Cl₂ (1.5 mL) and DMAP (6.0 mg, 0.05 mmol, 10 mol%) were added to the reaction tube. The mixture stirred at 23 °C for an additional 4 h. The mixture was diluted with EtOAc (10 mL) and transferred to a separatory funnel. Saturated NaCl (20 mL), and H₂O (20 mL) were added and the aqueous layer was

⁸ Bakhtiar, C.; Smith, E. H. *J. Chem. Soc. Perkin Trans. 1* **1994**, 239-243.

⁹ Nozaki, K.; Komaki, H.; Kawashima, Y.; Hiyama, T.; Matsubara, T. *J. Am. Chem. Soc.* **2001**, 123, 534-544.

extracted with EtOAc (4 x 40 mL). The combined organic extracts were dried over sodium sulfate, filtered, and concentrated on a rotary evaporator. The residue was purified by flash column chromatography 95% EtOAc/hexanes, to give 122 mg (94%) of **27** as a colorless oil. R_f = 0.40 (95% EtOAc/hexanes); IR (film) 2965, 2920, 2858, 1728, 1660 cm^{-1} ; ^1H NMR (500 MHz, DMSO) δ 7.36-7.26 (m, 5H), 4.26 (dd, J = 10.5, 3.5 Hz, 1H), 3.58-3.36 (m, 8H), 3.22 (dd, J = 16.5, 11.0 Hz, 1H), 2.55 (dd, J = 16.5, 3.5 Hz, 1H), 2.09 (s, 3H); ^{13}C NMR (125 MHz, DMSO) δ 207.1, 169.2, 138.0, 128.8, 128.3, 127.3, 66.1, 53.7, 45.2, 41.5, 36.0, 29.0; LRMS (electrospray): Mass calculated for $\text{C}_{15}\text{H}_{19}\text{NNaO}_3$ $[\text{M}+\text{Na}]^+$, 284.31. Found 284.

Selected NMR spectra