Electronic supplementary information (ESI)

DNA–Based Asymmetric Catalysis: Role of Ionic Solvents and Glymes

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Synthesis of (E)-(1-methyl-1H-imidazole-2-yl)-3-phenylprop-2-en-1-one (1a) via direct ketolization of trans-cinnamic acid

This preparation is based on a literature method (in its supporting information).\(^1\) \(N\)-Methylimidazole (2.2 equiv, 18 g) was dissolved in 180 mL anhydrous THF in a dried 500 mL round-bottom flask. The mixture was cooled to -78 °C for 30 min using dry ice-ethanol bath.\(^2\) Then 89 mL 2.5 M \(n\)-butyllithium in hexanes (2.2 equiv) was added dropwise at -78 °C under agitation. After 5 min, the dry ice-ethanol bath was removed and the mixture was allowed to warm to r.t. over 30 min. The mixture was cooled back to -78 °C for 20 min. 15 g (1 equiv) trans-cinnamic acid in 100 mL THF was added dropwise to the reaction mixture. The mixture was further stirred at -78 °C for 10 min before the removal of dry ice-ethanol bath. The reaction was warmed to r.t. over 30 min. The reaction was slowly quenched with 100 mL saturated NaHCO\(_3\) solution. The aqueous layer was separated and evaporated under vacuum to remove THF. The product was taken into 200 mL ethyl acetate and washed with distilled water three times (100 mL

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each). The organic layer was dried by Na$_2$SO$_4$ and decolored by activated carbon. After filtering the salt and activated carbon, the solvent was removed under vacuum evaporation. The crude product (7.56 g, 35% yield) was recrystallized from hot ethyl acetate three times. The purified product weighed 1.27 g (6% yield). m.p. 105-108 °C; IR (think solid film) 3132, 3111, 1651, 1595 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ/ppm = 4.10 (s, 3H), 7.08 (s, 1H), 7.22 (s, 1H), 7.37-7.44 (m, 3H), 7.68-7.71 (m, 2H), 7.82 (d, $J$ = 16.1 Hz, 1H), 8.08 (d, $J$ = 16.1 Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ/ppm = 36.5, 122.8, 127.4, 128.85, 128.93, 129.4, 130.6, 135.0, 143.5, 144.1, 180.5.

**Synthesis of α,β-unsaturated 2-acyl imidazoles via Aldol condensation**

\[
\text{N} \quad \text{O} \\
\text{R} \quad \text{N} \quad \text{O} \\
\text{H} \quad \text{O} \\
\text{R} \quad \text{Et} \quad \text{O} \\
\text{H} \quad \text{OH} \\
\text{w} \quad \text{a} \\
\text{e} \quad \text{c} \\
\text{d} \\
\text{f} \\
\text{a}: R = \text{Ph} \\
\text{b}: R = 4-\text{ClPh} \\
\text{c}: R = 4-\text{BrPh} \\
\text{d}: R = 4-\text{MePh} \\
\text{e}: R = 4-\text{MeOPh} \\
\text{f}: R = 2-\text{furanyl}
\]

At first, 2-acetyl-1-methylimidazole was prepared following the literature method (see *Supporting Information* in Ref 3). Preparation of α,β-unsaturated 2-acyl imidazoles was a modification of a literature method.\textsuperscript{3,4} 2-acetyl-1-methylimidazole (1.24 g, 10.0 mmol, 1.0 equiv) was added to 20 mL ethanol, followed by the addition of aromatic aldehyde (10.0 mmol, 1.0 equiv) and 0.7 g KOH (12.5 mmol) in 20 mL distilled water. The solution was stirred at r.t. for 24 h. 100 mL distilled water was added into the mixture and stirred for 1 h to precipitate the product, followed by filtration and washing with distilled water. The crude product was recrystallized from ethyl acetate.
**2-acetyl-1-methylimidazole**: light yellow liquid. $^1$H NMR (300 MHz, CDCl$_3$) δ/ppm = 2.67 (s, 3H), 4.01 (s, 3H), 7.04 (s, 1H), 7.14 (m, 1H).

*(E)-(1-methyl-1H-imidazole-2-yl)-3-phenylprop-2-en-1-one (1a)*: off-white solid. m.p. 95-100 °C; IR (think solid film) 3132, 3111, 1650, 1598 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ/ppm = 4.06 (s, 3H), 7.05 (s, 1H), 7.19 (s, 1H), 7.37 (m, 3H), 7.67 (m, 2H), 7.80 (d, $J = 16.1$ Hz, 1H), 8.06 (d, $J = 15.8$ Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ/ppm = 36.4, 122.9, 127.3, 128.8, 128.9, 129.4, 130.5, 135.0, 143.5, 144.1, 180.6.

*(E)-3-(4-chlorophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (1b)*: off-white solid. m.p. 124-126 °C; IR (think solid film) 3108, 1655, 1586 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ/ppm = 4.09 (s, 3H), 7.09 (s, 1H), 7.22 (s, 1H), 7.37 (d, $J = 8.6$ Hz, 2H), 7.62 (d, $J = 8.6$ Hz, 2H), 7.76 (d, $J = 15.8$ Hz, 1H), 8.05 (d, $J = 16.1$ Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ/ppm = 36.5, 123.4, 127.5, 129.2, 129.4, 130.0, 133.6, 136.5, 142.0, 144.0, 180.3.

*(E)-3-(4-bromophenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (1c)*: off-white solid. m.p. 141-144 °C; IR (think solid film) 3114, 1659, 1605 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ/ppm = 4.10 (s, 3H), 7.09 (s, 1H), 7.22 (s, 1H), 7.54 (m, 4H), 7.74 (d, $J = 16.1$ Hz, 1H), 8.07 (d, $J = 16.1$ Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ/ppm = 36.5, 123.5, 124.8, 127.5, 129.5, 130.2, 132.2, 134.0, 142.0, 144.0, 180.3.

*(E)-1-(1-methyl-1H-imidazol-2-yl)-3-p-toly1prop-2-en-1-one (1d)*: yellowish solid. m.p. 65-68 °C; IR (think solid film) 3102, 3028, 1655, 1597 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$) δ/ppm = 2.38 (s, 3H), 4.10 (s, 3H), 7.07 (s, 1H), 7.19 (s, 1H), 7.22 (s, 2H), 7.60 (d, $J = 7.9$ Hz, 2H), 7.81 (d, $J = 15.8$ Hz, 1H), 8.04 (d, $J = 15.8$ Hz, 1H). $^{13}$C NMR (CDCl$_3$) δ/ppm = 21.6, 36.5, 121.8, 127.2, 128.9, 129.3, 129.7, 132.3, 141.1, 143.6, 144.2, 180.7.
(E)-3-(4-methoxyphenyl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (1e): yellowish solid. m.p. 100-105 °C; IR (think solid film) 3105, 1650, 1594 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ/ppm = 3.85 (s, 3H), 4.09 (s, 3H), 6.92 (d, J = 8.6 Hz, 2H), 7.06 (s, 1H), 7.22 (m, 1H), 7.65 (d, J = 8.9 Hz, 2H), 7.79 (d, J = 15.8 Hz, 1H), 7.95 (d, J = 16.1 Hz, 1H). ¹³C NMR (CDCl₃) δ/ppm = 36.4, 55.5, 114.4, 120.6, 127.2, 127.8, 129.2, 130.6, 143.3, 144.2, 161.7, 180.7.

(E)-3-(furan-2-yl)-1-(1-methyl-1H-imidazol-2-yl)prop-2-en-1-one (1f): brown solid. m.p. 62-65 °C; IR (think solid film) 3130, 3106, 1659, 1605 cm⁻¹; ¹H NMR (300 MHz, CDCl₃) δ/ppm = 4.08 (s, 3H), 6.49 (m, 1H), 6.74 (d, J = 3.4 Hz, 1H), 7.06 (s, 1H), 7.21 (m, 1H), 7.51 (m, 1H), 7.59 (d, J = 15.8 Hz, 1H), 7.92 (d, J = 15.8 Hz, 1H). ¹³C NMR (CDCl₃) δ/ppm = 36.4, 112.6, 115.7, 121.0, 127.2, 129.4, 129.6, 144.1, 145.1, 152.0, 180.5.

Preparation of Cu(dmbipy)(NO₃)₂

This preparation is based on a literature method (in its Supporting Information).⁵ A solution of Cu(NO₃)₂·3H₂O (1.0 g or 4.14 mmol in 50 mL dissolved in ethanol) was mixed with a solution of 0.3825 g (2.08 mmol) 4,4'-dimethyl-2,2'-dipyridyl in 50 mL ethanol at room temperature. The mixture was incubated in an ethyl acetate bath for 2 days. The blue solid was collected by filtration and washed with ethanol. After drying in air, the product weighted 0.2920 g, 38% yield.

Gel electrophoresis of DNA

The compositions of DNA samples were characterized using agarose gel electrophoresis. Briefly, 10 µL Sybr safe DNA stain (10,000 X) was added into 100 mL 0.5% agarose gel during gel casting. For each well, 6 µL of DNA sample or DNA standard (GeneRuler 1
kb DNA ladder, Thermo Scientific) was loaded. Gel electrophoresis was conducted at 110 V for 1.5–2.5 hours. Gel images were acquired on a Bio-Rad Gel Doc EZ system. The concentration of DNA samples were quantitated by measuring their UV absorption at 260 nm on a Thermo Scientific Nanodrop 2000 system.
**Fig. S1** Effect of sonication time on the DNA-based Michael reaction (sonication was performed by dissolving DNA in MOPS buffer and incubating the mixture in ice bath during sonication. Reaction conditions: 15 µmol acyl donor (1a), 100 eq. dimethylmalonate, 0.15 mM [Cu(dmbipy)(NO3)2], 10 mg DNA, 30 mM pH 6.5 MOPS, reaction volume 15 mL, 5 °C for 3 days).

**Lane legend**
1. 0.1 mg/ml Fermentas GeneRuler 1 kb DNA ladder
2. 0.05 mg/ml Fermentas GeneRuler 1 kb DNA ladder
3. Not sonicated, 2 mg/mL
4. Not sonicated, diluted x5
5. Sonicated 2 min, 2 mg/mL
6. Sonicated 2 min, diluted x5
7. Sonicated 5 min, 2 mg/mL
8. **Sonicated 5 min, diluted x5**
9. Sonicated 10 min, 2 mg/mL
10. Sonicated 10 min, diluted x5
11. Sonicated 15 min, 2 mg/mL
12. Sonicated 15 min, diluted x5
13. Sonicated 20 min, 2 mg/mL
14. Sonicated 20 min, diluted x5

**Fig. S2** Gel electrophoresis of salmon testes DNA (Sigma D1626) (0.5% Agarose gel containing 10 µL Sybr® safe DNA gel stain, TAE buffer, 6 µL sample for each lane, 110 V, 1.5 h).
**Fig. S3** CD spectra of salmon testes DNA in aqueous solutions of ionic additives.

**Fig. S4** CD spectra of salmon testes DNA in aqueous solutions of inorganic salts.
References