Electronic supplementary information (ESI)

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

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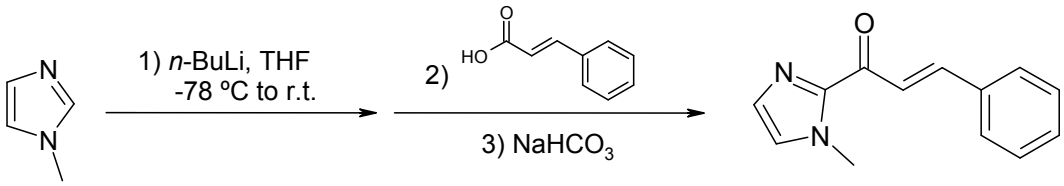
Synthesis of (*E*)-(1-methyl-1*H*-imidazole-2-yl)-3-phenylprop-2-en-1-one (1a) via direct ketolization of *trans*-cinnamic acid



1a

This preparation is based on a literature method (in its supporting information).[1] *N*-Methylimiazole (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 ºC 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 ºC 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 ºC 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 ºC 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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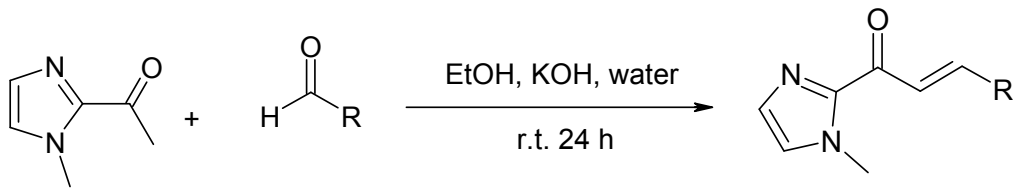
each). The organic layer was dried by Na_2SO_4 and decolored by activated carbon. After filtering the salt and activated carbon, the solvent was removed under vacuum evaporation. The crude product (7.56 g, 35% yield) was recrystallized from hot ethyl acetate three times. The purified product weighed 1.27 g (6% yield). m.p. 105-108 °C; IR (think solid film) 3132, 3111, 1651, 1595 cm^{-1}; ^1H 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



a: R = Ph
b: R = 4-ClPh
c: R = 4-BrPh
d: R = 4-MePh
e: R = 4-MeOPh
f: R = 2-furanyl

1a-f

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.[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-1*H*-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-1*H*-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-1*H*-imidazol-2-yl)-3-*p*-tolylprop-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-1*H*-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}; ^{1}H NMR (300 MHz, $CDCl_3$) 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). ^{13}C NMR ($CDCl_3$) 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-1*H*-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}; ^{1}H NMR (300 MHz, $CDCl_3$) 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). ^{13}C NMR ($CDCl_3$) 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)(NO_3)$_2$

This preparation is based on a literature method (in its Supporting Information).[5] A solution of $Cu(NO_3)_2 \cdot 3H_2O$ (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.

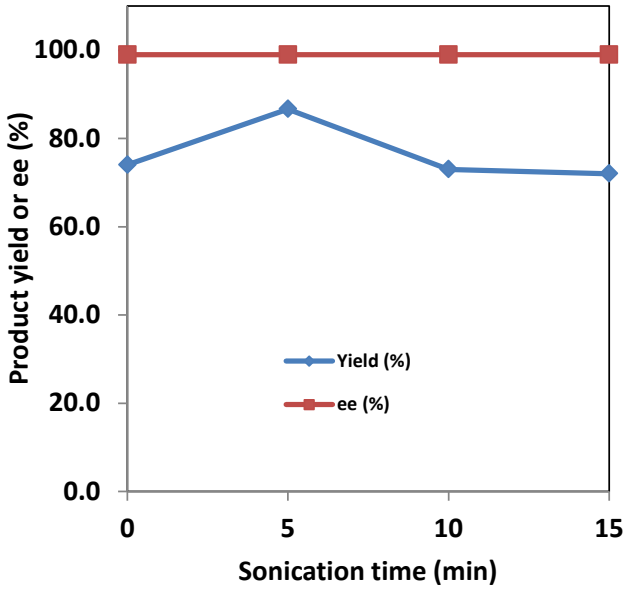
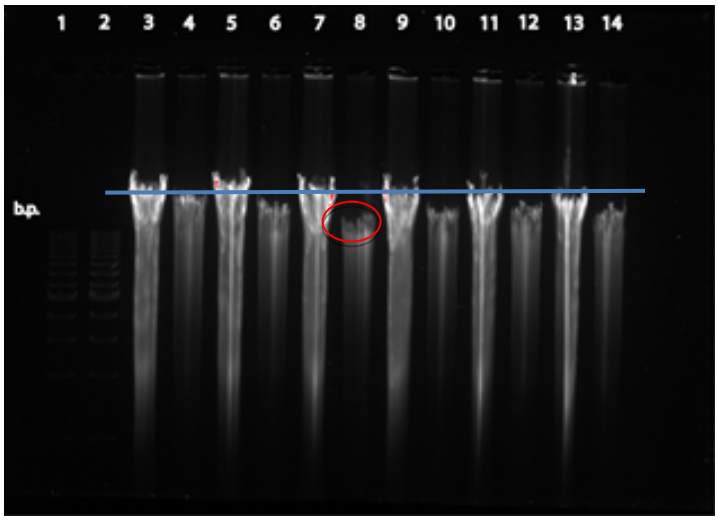


Fig. S1 Effect of sonication time on the DNA-based Michael reaction (sonication was performed by dissolving DNA in MOPS buffer and incubating the mixture in ice bath during sonication. Reaction conditions: 15 µmol acyl donor (**1a**), 100 eq. dimethylmalonate, 0.15 mM [Cu(dmbipy)$(NO_3)_2$], 10 mg DNA, 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. Soinicated 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).

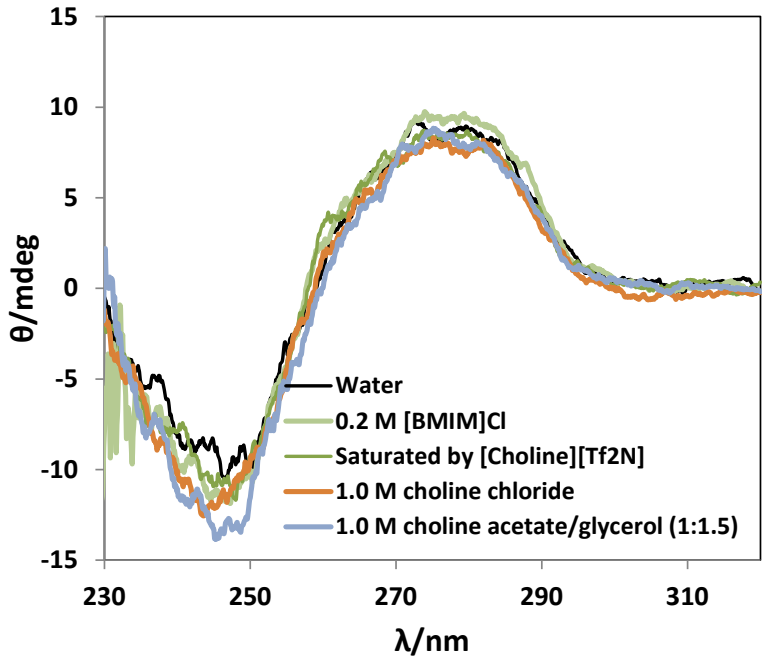


Fig. S3 CD spectra of salmon testes DNA in aqueous solutions of ionic additives.

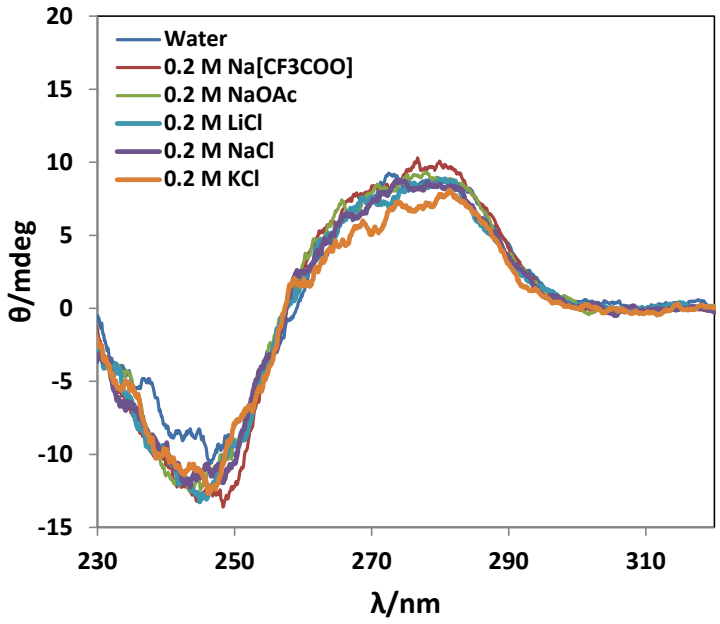


Fig. S4 CD spectra of salmon testes DNA in aqueous solutions of inorganic salts.

References

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