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Rhodium(III)/Amine Synergistically Catalyzed Enantioselective Alkylation of Aldehydes with α,β-Unsaturated 2-Acyl Imidazoles

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A synergistic catalysis combination of chiral-at-metal rhodium complex and amine catalyst was developed for enantioselective alkylation of aldehydes with α,β-unsaturated 2-acyl imidazoles. The corresponding adducts were obtained in good yields with excellent enantioselectivities (up to 99% *ee*).

Keywords alkylation of aldehyde, chiral-at-metal complex, synergistic catalysis

Introduction

The combination of transition metal catalysis and organocatalysis has attracted increasing attention as it can allow access to development of many unattainable chemical transformations by using single catalytic system.[1] In a synergistic catalysis system, the transition metal catalyst and the organocatalyst can simultaneously activate the nucleophile and the electrophile in two separate but directly coupled catalytic cycles, leading to the formation of a product.[2] In particular, the combination of enamine and transition metal catalysis[3] has been intensively investigated since Córdova's group firstly reported the direct α-allylic alkylation of aldehydes and cyclic ketones through the merger of enamine and palladium catalysis.[4] Generally, the aldehyde (or ketone) condenses with an amine catalyst to form a transient enamine intermediate that can trap an electrophilic intermediate generated by metal catalyst, creating an α-substituted iminium ion, which can be hydrolyzed to release the α-substituted product and regenerate the amine catalyst.[5]

Recently, Meggers and coworkers have developed a novel class of chiral-at-metal complexes in which the metal center (Ir(III)[6] or Rh(III)[7]) serves as the exclusive source of chirality.[8] Due to the presence of two substitutionally labile CH_3CN ligands, the metal center can coordinate and activate substrates. This activating model increases the electrophilicity of α,β-unsaturated carbonyl compounds and promotes 1,4-conjugate addition of nucleophiles (such as indole[6a] and CH-acidic carbonyl compounds[7a]) to the α,β-unsaturated carbonyl compounds. However, there is no report on the combination of chiral-at-metal complexes with organocatalysis. Therefore, developing a synergistic system of chiral-at-metal complex and organocatalysis for catalytic asymmetric synthesis is desirable. In this context, we wish to describe the enantioselective alkylation of aldehydes[9] with α,β-unsaturated 2-acyl imidazoles through the merger of enamine and chiral-at-metal catalysis (Scheme 1).[10]

Experimental

General method

All non-aqueous reactions were performed in oven-dried glassware and standard Schlenk tubes under an atmosphere of nitrogen. 1,2-Dichloroethane (DCE) and dichloromethane (DCM) were distilled from CaH_2 under inert atmosphere. Tetrahydrofuran (THF) and toluene (PhMe) were distilled from sodium and benzophenone under inert atmosphere. All other solvents and reagents were used as received unless otherwise noted. Thin layer chromatography was performed using silica gel 60 F-254 precoated plates (0.2—0.3 mm) and visualized by short-wave UV (254 nm) irradiation, potassium permanganate, or iodine stain. Column chromatography was performed with silica gel (200—300 mesh, Yantai Jiangyou Silica Gel Development Co., Ltd). The infrared spectra were recorded on a VERTEX 70 IR spectrometer as KBr pellets, with absorption reported in

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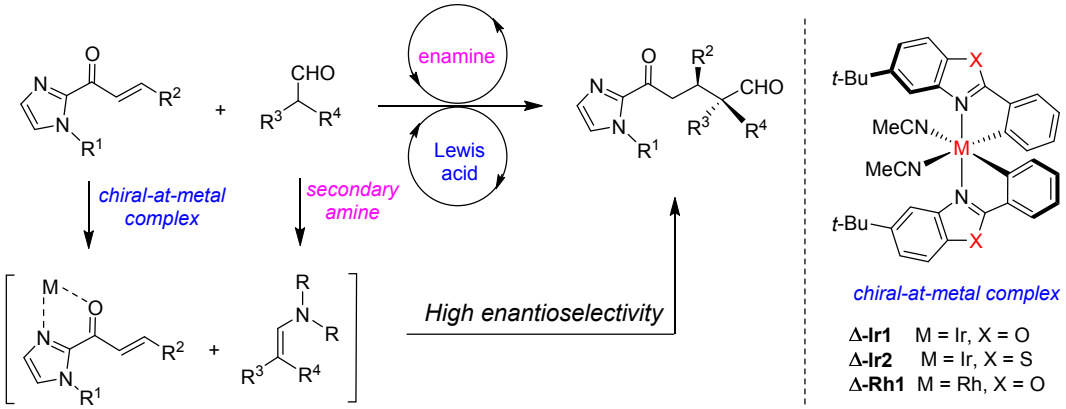
Scheme 1 Enantioselective alkylation of aldehyde via the combination of enamine catalysis and chiral-at-metal complex



cm^{-1}. HRMS data were obtained on a Thermo Fisher Scientific LTQ FT Ultrasystem. Optical rotation was recorded on an INESA SGW-1 polarimeter at concentrations of 1.0 g/100 mL or 0.5 g/100 mL. Enantiomeric excess was determined by HPLC analysis on a Chiralpak IA, IC column (Daicel Chemical Industries, LTD) on Shimadzu LC-20AD. The crystallographic measurement was made on an Agilent SuperNova (Dual, Cu at zero, Atlas) diffractometer. The structure was solved by direct method and refined to convergence by least squares method on F^2 using the SHELXTL-2014 software suit.

General procedures

General procedure A: To a solution of catalyst Δ-Rh1 or Λ-Rh1 (2.0—4.0 mol%) in anhydrous CH_2Cl_2 (0.2 mL) was added the *α*,*β*-unsaturated 2-acylimidazoles **1a**—**1n** (0.20 mmol) in a Schlenk tube. Then the Schlenk tube was sealed and allowed to stir at room temperature for 20 min. On the other hand, to a solution of secondary amine (0.04 mmol) in anhydrous CH_2Cl_2 (0.2 mL) was added the aldehyde **2a**, **2f** or **2g** (0.60 mmol) in a glass vial and the mixture was stirred at room temperature for 10 min. Next, the solution in the glass vial was transferred to the Schlenk tube containing *α*,*β*-unsaturated 2-acylimidazole. The reaction mixture was stirred at 25 ℃ for the indicated time (monitored by TLC) under argon atmosphere. Afterwards, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc＝10∶1 to 2∶1) to afford the products **3a**—**3n**, **3s** and **3t**. The *dr* values were determined by ^{1}H NMR analysis of the crude products, and the *ee* values were determined by chiral HPLC chromatography using a Daicel Chiralpak IA or IC column (250×4.6 mm).

General procedure B: To a solution of catalyst Δ-Rh1 (4.0 mol%) in anhydrous DCE (0.2 mL) was added the *α*,*β*-unsaturated 2-acylimidazoles **1a** (0.20 mmol) in a Schlenk tube. Then the Schlenk tube was sealed and allowed to stir at room temperature for 20 min. On the other hand, to a solution of Et_2NH (0.04 mmol) in anhydrous DCE (0.2 mL) was added the aldehydes **2b**—**2e** (0.60 mmol) in a glass vial and the mixture was stirred at room temperature for 10 min. Next, the solution in the glass vial was transferred to the Schlenk tube containing *α*,*β*-unsaturated 2-acylimidazole. The reaction mixture was stirred at 50 ℃ for the indicated time (conversion monitored by TLC) under argon atmosphere. Afterwards, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc＝10∶1 to 2∶1) to afford the products **3o**—**3r**. The *ee* values were determined by chiral HPLC chromatography using a Daicel Chiralpak IA or IC column (250×4.6 mm).

(*S*)-2,2-Dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-*oxo*-3-phenylpentanal (3a) Following general procedure A, the reaction of **1a** (42.5 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3a** as a light yellow oil (56.5 mg, 0.198 mmol, yield: 99%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IA column, *ee*＝97% (HPLC: IA, 254 nm, *n*-hexane/isopropanol＝95∶5, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)＝18.6 min, t_r(major)＝20.6 min). $[\alpha]_D^{25}$ −37.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.59 (s, 1H), 7.25—7.24 (m, 4H), 7.21—7.17 (m, 1H), 7.11 (s, 1H), 6.95 (s, 1H), 3.94 (dd, *J*＝10.6, 17.3 Hz, 1H), 3.83 (s, 3H), 3.73 (dd, *J*＝3.7, 10.6 Hz, 1H), 3.20 (dd, *J*＝3.7, 17.3 Hz, 1H), 1.13 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 205.7, 190.5, 143.0, 139.5, 129.5, 129.0, 128.1, 127.0, 126.9, 49.3, 45.0, 39.6, 36.0, 21.1, 18.3; IR (film) ν_{max}: 3108, 2969, 2955, 2819, 2723, 1727, 1685, 1677, 1465, 1452, 1419, 1290, 1235, 1004, 991, 915, 779, 736, 708, 693 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{17}H_{21}N_2O_2$ $[M+H]^+$: 285.1598, found 285.1595.

In the gram-scale reaction, to a solution of catalyst Δ-Rh1 (41.5 mg, 0.05 mmol) in anhydrous CH_2Cl_2 (4.0 mL) was added the *α*,*β*-unsaturated 2-acylimidazoles **1a** (1.06 g, 5.0 mmol) in a Schlenk tube. Then the Schlenk tube was sealed and allowed to stir at room temperature for 20 min. On the other hand, to a solution of Et_2NH (103.0 μL, 1.0 mmol) in anhydrous CH_2Cl_2 (4.0 mL)

was added the aldehyde **2a** (1.37 mL, 15.0 mmol) in a glass vial and the mixture was stirred at room temperature for 10 min. Next, the solution in the glass vial was transferred to the Schlenk tube containing α,β-unsaturated 2-acylimidazole. The reaction mixture was stirred at 25 ℃ for 48 h under argon atmosphere. Afterwards, the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (petroleum ether/EtOAc＝10∶1 to 2∶1) to afford **3a** as a light yellow oil (1.38 g, 4.85 mmol, yield: 97%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IA column, *ee*＝95% (HPLC: IA, 254 nm, *n*-hexane/isopropanol＝95∶5, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)＝18.4 min, t_r(major)＝20.1 min).

(*S*)-2,2-Dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-oxo-3-(*p*-tolyl)pentanal (3b) Following general procedure A, the reaction of **1b** (45.3 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3b** as a light yellow oil (58.8 mg, 0.197 mmol, yield: 98%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*＝96% (HPLC: IC, 254 nm, *n*-hexane/isopropanol＝85∶15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)＝17.1 min, t_r(major)＝28.5 min). $[\alpha]_D^{25}$ −35.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.58 (s, 1H), 7.12 (d, *J*＝8.0 Hz, 2H), 7.11 (s, 1H), 7.05 (d, *J*＝8.0 Hz, 2H), 6.95 (s, 1H), 3.91 (dd, *J*＝10.6, 17.3 Hz, 1H), 3.83 (s, 3H), 3.69 (dd, *J*＝3.7, 10.6 Hz, 1H), 3.18 (dd, *J*＝3.7, 17.3 Hz, 1H), 2.27 (s, 3H), 1.12 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.9, 189.5, 141.9, 135.4, 135.3, 128.2, 127.9, 127.8, 125.9, 48.3, 43.5, 38.6, 35.0, 20.0, 19.9, 17.3. IR (film) ν_{max}: 3111, 2968, 2926, 2871, 2816, 2715, 1724, 1683, 1472, 1409, 1288, 1155, 1021, 915, 824 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{18}H_{23}N_2O_2$ $[M+H]^+$: 299.1754, found 299.1751.

(*S*)-2,2-Dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-*oxo*-3-(*o*-tolyl)pentanal (3c) Following general procedure A, the reaction of **1c** (45.3 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3c** as a colorless oil (58.4 mg, 0.196 mmol, yield: 98%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*＝94% (HPLC: IC, 254 nm, *n*-hexane/isopropanol＝85∶15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)＝17.6 min, t_r(major)＝20.0 min). $[\alpha]_D^{25}$ −28.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.57 (s, 1H), 7.24 (d, *J*＝8.0 Hz, 1H), 7.13－7.05 (m, 4 H), 6.93 (s, 1 H), 4.07 (dd, *J*＝3.5, 10.8 Hz, 1H), 3.92 (dd, *J*＝10.8, 17.2 Hz, 1H), 3.81 (s, 3H), 3.20 (dd, *J*＝3.5, 17.2 Hz, 1H), 2.46 (s, 3H), 1.18 (s, 3H), 0.99 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.8, 189.5, 141.9, 137.3, 136.5, 129.4, 127.9, 126.8, 125.8, 125.5, 124.7, 48.9, 40.0, 37.8, 34.9, 19.7, 19.4, 17.6. IR (film) ν_{max}: 3108, 2964, 2931, 2874, 2816, 2714, 1724, 1678, 1467, 1410, 1288, 1017, 915, 797, 763, 738 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{18}H_{23}N_2O_2$ $[M+H]^+$: 299.1754, found 299.1753.

(*S*)-3-(4-Bromophenyl)-2,2-dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-oxopentanal (3d) Following general procedure A, the reaction of **1d** (58.2 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3d** as a pale yellow solid (61.2 mg, 0.168 mmol, yield: 84%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*＝93% (HPLC: IC, 254 nm, *n*-hexane/isopropanol＝85∶15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)＝13.2 min, t_r(major)＝19.7 min). $[\alpha]_D^{25}$ −25.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.57 (s, 1H), 7.38 (d, *J*＝8.4 Hz, 2H), 7.13 (d, *J*＝8.4 Hz, 2H), 7.11 (s, 1H), 6.98 (s, 1H), 3.93 (dd, *J*＝11.0, 17.3 Hz, 1H), 3.85 (s, 3H), 3.70 (dd, *J*＝3.4, 11.0 Hz, 1H), 3.15 (dd, *J*＝3.5, 17.3 Hz, 1H), 1.12 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.2, 189.1, 141.8, 137.6, 130.2, 130.1, 128.1, 126.1, 119.8, 48.0, 43.4, 38.3, 35.0, 20.0, 17.2. IR (film) ν_{max}: 3135, 2965, 2931, 2870, 2827, 2738, 1717, 1664, 1491, 1420, 1261, 1159, 1075, 1009, 984, 917, 830, 803, 745, 698 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{17}H_{20}N_2O_2Br$ $[M+H]^+$: 363.0703, found 363.0701.

(*R*)-3-(2-Bromophenyl)-2,2-dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-oxopentanal (3e) Following general procedure A, the reaction of **1e** (58.2 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3e** as a pale yellow oil (62.3 mg, 0.171 mmol, yield: 85%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*＝86% (HPLC: IC, 254 nm, *n*-hexane/isopropanol＝85∶15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)＝13.4 min, t_r(major)＝23.6 min). $[\alpha]_D^{25}$ −36.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.66 (s, 1H), 7.56 (dd, *J*＝0.9, 8.0 Hz, 1H), 7.31 (dd, *J*＝1.3, 7.8 Hz, 1H), 7.23 (t, *J*＝7.1 Hz, 1H), 7.10 (s, 1H), 7.05 (ddd, *J*＝1.5, 7.9, 7.3 Hz, 1H), 6.96 (s, 1H), 4.45 (dd, *J*＝3.6, 10.7 Hz, 1H), 3.88－3.81 (m, 4H), 3.29 (dd, *J*＝3.7, 17.3 Hz, 1H), 1.18 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.0, 188.9, 141.8, 138.3, 132.2, 128.3, 128.0, 127.3, 126.3, 126.0, 125.9, 49.2, 41.1, 39.5, 35.0, 19.2, 17.3. IR (film) ν_{max}: 3109, 2970, 2933, 2874, 2817, 2716, 1725, 1679, 1471, 1436, 1410, 1288, 1155, 1022, 915, 761, 743 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{17}H_{20}N_2O_2Br$ $[M+H]^+$: 363.0703, found 363.0703.

(*S*)-3-(4-Chlorophenyl)-2,2-dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-oxopentanal (3f) Following general procedure A, the reaction of **1f** (49.3 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3f** as a pale yellow oil (59.5 mg, 0.186 mmol, yield: 93%). Enantiomeric excess was determined by HPLC analysis

using a Chiralpak IC column, *ee*=95% (HPLC: IC, 254 nm, *n*-hexane/isopropanol = 85 ∶ 15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=10.7 min, t_r(major)=16.8 min). $[\alpha]_D^{25}$ −25.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.57 (s, 1H), 7.23 (d, *J*=8.4 Hz, 2H), 7.19 (d, *J*=8.6 Hz, 2H), 7.11 (s, 1H), 6.98 (s, 1H), 3.93 (dd, *J*=10.9, 17.3 Hz, 1H), 3.84 (s, 3H), 3.71 (dd, *J*=3.4, 10.9 Hz, 1H), 3.15 (dd, *J*=3.5, 17.3 Hz, 1H), 1.12 (s, 3H), 0.95 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 205.3, 190.1, 142.8, 138.1, 132.7, 130.7, 129.1, 128.3, 127.1, 49.1, 44.4, 39.4, 36.1, 21.1, 18.3. IR (film) ν_{max}: 3127, 3112, 2981, 2967, 2932, 2825, 2737, 1718, 1674, 1491, 1472, 1419, 1296, 1092, 1013, 981, 916, 828, 797, 748, 698 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{17}H_{20}N_2O_2Cl$ $[M+H]^+$: 319.1208, found 319.1210.

(*S*)-2,2-Dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-3-(naphthalen-1-yl)-5-oxopentanal (3g) Following general procedure A, the reaction of **1g** (52.5 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3g** as a pale yellow soild (57.6 mg, 0.172 mmol, yield: 86%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=94% (HPLC: IC, 254 nm, *n*-hexane/isopropanol = 85 ∶ 15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=18.6 min, t_r(major)=22.9 min). $[\alpha]_D^{25}$ −118.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.66 (s, 1H), 8.37 (d, *J*=8.6 Hz, 1H), 7.82 (d, *J*=8.0 Hz, 1H), 7.70 (d, *J*=8.1 Hz, 1H), 7.56 (t, *J*=7.1 Hz, 1H), 7.50−7.45 (m, 2 H), 7.39 (t, *J*=7.8 Hz, 1H), 7.10 (s, 1H), 6.89 (s, 1H), 4.84 (dd, *J*=3.8, 10.5 Hz, 1H), 4.09 (dd, *J*=10.5, 17.2 Hz, 1H), 3.70 (s, 3H), 3.36 (dd, *J*=3.8, 17.2 Hz, 1H), 1.22 (s, 3H), 0.92 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 205.7, 190.4, 142.9, 136.4, 133.8, 133.1, 129.0, 128.9, 127.5, 126.9, 126.1, 125.8, 125.4, 125.0, 123.9, 50.1, 41.1, 37.2, 35.9, 21.2, 18.5. IR (film) ν_{max}: 3128, 3112, 2982, 2933, 2817, 2725, 1716, 1674, 1415, 1280, 1164, 1088, 979, 915, 805, 783, 689 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{21}H_{23}N_2O_2$ $[M+H]^+$: 335.1754, found 335.1753.

(*R*)-2,2-Dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-*oxo*-3-(thiophen-2-yl)pentanal (3h) Following general procedure A, the reaction of **1h** (43.7 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3h** as a pale yellow oil (52.7 mg, 0.181 mmol, yield: 90%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=96% (HPLC: IC, 254 nm, *n*-hexane/isopropanol = 85 ∶ 15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=21.7 min, t_r(major)=27.3 min). $[\alpha]_D^{25}$ −49.813 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.60 (s, 1H), 7.12 (s, 2H), 6.98 (s, 1H), 6.90 (s, 1H), 6.89 (s, 1H), 4.08 (dd, *J*=3.2, 10.7 Hz, 1H), 3.88 (s, 3H), 3.85 (dd, *J*=10.8, 17.2 Hz, 1H), 3.18 (dd, *J*=3.3, 17.2 Hz, 1H), 1.20 (s, 3H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 205.2, 189.8, 142.9, 142.8, 129.1, 127.0, 126.5, 126.4, 123.9, 49.3, 41.5, 40.3, 36.1, 20.9, 18.5. IR (film) ν_{max}: 3109, 2970, 2930, 2815, 2713, 1724, 1676, 1466, 1410, 1287, 1156, 915, 699 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{15}H_{19}N_2O_2S$ $[M+H]^+$: 291.1162, found 291.1161.

(*R*)-3-(Furan-2-yl)-2,2-dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-oxopentanal (3i) Following general procedure A, the reaction of **1i** (40.5 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3i** as a pale yellow oil (22.3 mg, 0.081 mmol, yield: 40%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=96% (HPLC: IC, 254 nm, *n*-hexane/isopropanol=85 ∶ 15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor) = 33.6 min, t_r(major) = 43.6 min). $[\alpha]_D^{25}$ −56.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.60 (s, 1H), 7.29 (dd, *J*=0.7, 1.8 Hz, 1H), 7.13 (d, *J*=0.8 Hz, 1H), 7.00 (s, 1H), 6.24 (dd, *J*=1.8, 3.2 Hz, 1H), 6.11 (d, *J*=3.2 Hz, 1H), 3.92 (s, 3H), 3.82 (dd, *J*=10.7, 24.4 Hz, 2H), 3.14 (dd, *J*=10.7, 24.4 Hz, 1H), 1.15 (s, 3H), 1.02 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 205.1, 190.1, 154.2, 142.8, 141.5, 129.1, 127.1, 110.0, 107.6, 49.2, 38.8, 38.2, 36.1, 20.4, 18.9. IR (film) ν_{max}: 3114, 2972, 2933, 2819, 2717, 1726, 1680, 1472, 1411, 1288, 1155, 1014, 915, 739 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{15}H_{18}N_2O_3Na$ $[M+H]^+$: 297.1210, found 297.1209.

(*R*)-2,2,3-Trimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-oxopentanal (3j) Following general procedure A, the reaction of **1j** (60.1 mg, 0.40 mmol) and isobutyraldehyde **2a** (86.6 mg, 109.6 μL, 1.20 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and pyrolidine (3.3 μL, 0.04 mmol) afforded the product **3j** as a pale yellow oil (45.7 mg, 0.206 mmol, yield: 51%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=98% (HPLC: IC, 254 nm, *n*-hexane/isopropanol=90 ∶ 10, flow rate: 1.0 mL/min, 25 ℃, t_r(minor) = 15.4 min, t_r(major) = 23.5 min). $[\alpha]_D^{25}$ +19.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.49 (s, 1H), 7.11 (s, 1H), 7.02 (s, 1H), 3.98 (s, 3H), 3.05 (dd, *J*=9.7, 16.6 Hz, 1H), 2.97 (dd, *J*=3.4, 16.6 Hz, 1H), 2.58−2.48 (m, 1H), 1.03 (s, 6H), 0.89 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 206.2, 191.9, 143.1, 129.1, 127.1, 48.8, 41.1, 36.2, 33.1, 18.6, 18.4, 15.1. IR (film) ν_{max}: 3112, 2927, 2938, 2880, 2817, 2707, 1724, 1676, 1473, 1407, 1288, 1157, 1012, 991, 915, 800, 782 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{12}H_{19}N_2O_2$ $[M+H]^+$: 223.1441, found 223.1442.

(*R*)-3-((Benzyloxy)methyl)-2,2-dimethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-oxopentanal (3k) Following general procedure A, the reaction of **1k** (51.3 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and pyrolidine (3.3 μL, 0.04 mmol) afforded the product **3k** as a colorless oil (46.2 mg, 0.141 mmol, yield: 70%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=94% (HPLC: IC, 254 nm, *n*-hexane/isopropanol=85 ∶ 15, flow rate: 1.0 mL/

min, 25 ℃, t_r(minor)=18.4 min, t_r(major)=21.5 min). $[\alpha]_D^{25}$ +9.7 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.55 (s, 1H), 7.28−7.26 (m, 1H), 7.24−7.22 (m, 2H), 7.16 (d, *J*=1.7 Hz, 1H), 7.14 (s, 1H), 7.12 (s, 1H), 6.98 (s, 1H), 4.34 (dd, *J*=11.8, 20.1 Hz, 2H), 3.85 (s, 3H), 3.47−3.39 (dd, *J*=6.4, 9.4 Hz, 2H), 3.26 (dd, *J*=9.4, 16.6 Hz, 1H), 3.01 (dd, *J*=3.5, 16.6 Hz, 1H), 2.90−2.84 (m, 1H), 1.08 (s, 3H), 1.07 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.9, 191.3, 143.1, 137.9, 128.9, 128.2, 127.6, 127.4, 127.0, 73.1, 70.5, 47.5, 39.8, 36.7, 36.0, 20.7, 17.7. IR (film) ν_{max}: 3110, 3030, 2965, 2926, 2870, 2714, 1724, 1676, 1467, 1455, 1410, 1366, 1288, 1155, 1100, 1010, 914, 740, 699 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{19}H_{24}N_2O_3Na$ $[M+H]^+$: 351.1679, found 351.1677.

(*R*)-Ethyl 3,3-dimethyl-2-(2-(1-methyl-1*H*-imidazol-2-yl)-2-oxoethyl)-4-oxobutanoate (3l) Following general procedure A, the reaction of **1l** (41.6 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3l** as a pale yellow oil (55.4 mg, 0.197 mmol, yield: 98%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IA column, *ee*=97% (HPLC: IA, 254 nm, *n*-hexane/isopropanol = 90 ∶ 10, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=15.5 min, t_r(major)=18.3 min). $[\alpha]_D^{25}$ −27.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.55 (s, 1H), 7.12 (s, 1H), 7.02 (s, 1H), 4.18−4.06 (m, 2H), 3.95 (s, 3H), 3.69 (dd, *J*=11.0, 18.1 Hz, 1H), 3.33 (dd, *J*=3.0, 11.0 Hz, 1H), 3.18 (dd, *J*=3.0, 18.0 Hz, 1H), 1.20 (t, *J*=7.1, 3H), 1.12 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 203.2, 190.2, 172.7, 142.5, 129.2, 127.1, 61.0, 47.2, 45.0, 36.2, 36.1, 19.9, 18.9, 14.1. IR (film) ν_{max}: 3112, 2979, 2933, 2854, 2718, 1729, 1679, 1468, 1414, 1371, 1223, 1175, 1095, 1031, 995, 915, 768 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{14}H_{20}N_2O_4Na$ $[M+H]^+$: 303.1315, found 303.1319.

(*S*)-5-(1-Isopropyl-1*H*-imidazol-2-yl)-2,2-dimethyl-5-*oxo*-3-phenylpentanal (3m) Following general procedure A, the reaction of **1m** (48.1 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3m** as a pale yellow oil (49.8 mg, 0.159 mmol, yield: 79%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=95% (HPLC: IC, 254 nm, *n*-hexane/isopropanol=90 ∶ 10, flow rate: 1.0 mL/min, 25 ℃, t_r(minor) = 16.2 min, t_r(major) = 19.0 min). $[\alpha]_D^{25}$ −15.6 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.60 (s, 1H), 7.24−7.22 (m, 4H), 7.19−7.17 (m, 2H), 7.14 (s, 1H), 5.36−5.25 (m, 1H), 3.92 (dd, *J*=10.6, 16.9 Hz, 1H), 3.72 (dd, *J*=4.0, 10.6 Hz, 1H), 3.24 (dd, *J*=4.0, 16.9 Hz, 1H), 1.30 (d, *J*=6.7 Hz, 3H), 1.24 (d, *J*=6.7 Hz, 3H), 1.13 (s, 3H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.8, 190.7, 142.3, 139.5, 129.5, 129.4, 128.0, 126.8, 121.1, 49.3, 49.0, 45.4, 40.2, 23.5, 23.3, 21.0, 18.4. IR (film) ν_{max}: 3030, 2974, 2933, 2875, 2816, 2713, 1725, 1676, 1465, 1456, 1395, 1256, 1087, 917, 704 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{19}H_{24}N_2O_2Na$ $[M+Na]^+$: 335.1730, found 335.1732.

(*S*)-2,2-Dimethyl-5-*oxo*-3-phenyl-5-(1-phenyl-1*H*-imidazol-2-yl)pentanal (3n) Following general procedure A, the reaction of **1n** (54.9 mg, 0.20 mmol) and isobutyraldehyde **2a** (43.3 mg, 54.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3n** as a pale yellow oil (55.8 mg, 0.161 mmol, yield: 80%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=97% (HPLC: IC, 254 nm, *n*-hexane/isopropanol=70 ∶ 30, flow rate: 1.0 mL/min, 25 ℃, t_r(minor) = 17.7 min, t_r(major) = 45.5 min). $[\alpha]_D^{25}$ +23.7 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.57 (s, 1H), 7.39−7.30 (m, 3H), 7.24−7.19 (m, 6H), 7.09 (d, *J*=0.8 Hz, 1H), 6.91 (s, 1H), 6.89 (d, *J*=1.5 Hz, 1H), 3.89 (dd, *J*=10.5, 16.5 Hz, 1H), 3.69 (dd, *J*=4.3, 10.5 Hz, 1H), 3.22 (dd, *J*=4.3, 16.5 Hz, 1H), 1.12 (s, 3H), 0.96 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.6, 188.2, 142.0, 138.1, 137.0, 128.7, 128.5, 127.8, 127.5, 127.0, 125.9, 124.5, 48.3, 44.4, 38.7, 19.9, 17.3. IR (film) ν_{max}: 3061, 3030, 2965, 2928, 2872, 2814, 2712, 1725, 1685, 1597, 1493, 1447, 1405, 1306, 1261, 1087, 1062, 1022, 965, 914, 801, 759, 704, 692 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{22}H_{23}N_2O_2$ $[M+H]^+$: 347.1754, found 347.1754.

(*S*)-1-(3-(1-Methyl-1*H*-imidazol-2-yl)-3-*oxo*-1-phenylpropyl)cyclopropanecarbaldehyde (3o) Following general procedure B, the reaction of **1a** (42.5 mg, 0.20 mmol) and cyclopropanecarboxaldehyde **2b** (42.0 mg, 44.8 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3o** as a pale yellow oil (25.2 mg, 0.089 mmol, yield: 44%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IA column, *ee*=99% (HPLC: IA, 254 nm, *n*-hexane/isopropanol=95 ∶ 5, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=30.3 min, t_r(major)=32.0 min). $[\alpha]_D^{25}$ −60.2 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.84 (s, 1H), 7.29−7.23 (m, 4H), 7.20−7.15 (m, 1H), 7.13 (s, 1H), 6.98 (s, 1H), 4.04 (dd, *J*=9.7, 17.1 Hz, 1H), 3.88 (s, 3H), 3.87 (dd, *J*=9.8, 4.9 Hz, 1H), 3.53 (dd, *J*=4.9, 17.2 Hz, 1H), 1.20−1.02 (m, 3H), 0.78−0.73 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.0, 190.7, 143.0, 140.9, 129.0, 128.4, 128.3, 126.9, 126.8, 41.6, 39.5, 36.2, 36.1, 13.4, 11.6. IR (film) ν_{max}: 3029, 2925, 2854, 2727, 1706, 1676, 1457, 1410, 1289, 1155, 915, 899, 764, 702 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{17}H_{19}N_2O_2$ $[M+H]^+$: 283.1441, found 283.1444.

(*S*)-1-(3-(1-Methyl-1*H*-imidazol-2-yl)-3-*oxo*-1-phenylpropyl)cyclopentanecarbaldehyde (3p) Following general procedure B, the reaction of **1a** (42.5 mg, 0.20 mmol) and cyclopentanecarboxaldehyde **2c** (58.9 mg, 64.1 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3p** as a pale yellow oil (61.8 mg, 0.199 mmol, yield: 99%). Enantiomeric excess was deter-

mined by HPLC analysis using a Chiralpak IA column, *ee*=93% (HPLC: IA, 254 nm, *n*-hexane/isopropanol=95∶5, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=21.2 min, t_r(major)=22.5 min). $[\alpha]_D^{25}$ −9.9 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.60 (s, 1H), 7.24 (s, 2H), 7.23 (s, 2H), 7.19−7.14 (m, 1H), 7.11 (s, 1H), 6.95 (s, 1H), 3.97 (dd, *J*=10.8, 17.2 Hz, 1H), 3.82 (s, 3H), 3.75 (dd, *J*=3.5, 10.8 Hz, 1H), 3.29 (dd, *J*=3.5, 17.2 Hz, 1H), 2.04−1.92 (m, 2H), 1.68−1.38 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 204.7, 190.5, 143.0, 140.4, 129.1, 129.0, 128.2, 126.9, 126.8, 61.8, 45.1, 40.7, 36.0, 31.1, 30.2, 24.8, 24.7. IR (film) ν_{max}: 3108, 2955, 2930, 2858, 2801, 2692, 1718, 1676, 1418, 1291, 987, 914, 777, 706 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{19}H_{22}N_2O_2Na$ $[M+H]^+$: 333.1573, found 333.1574.

(*S*)-1-(3-(1-Methyl-1*H*-imidazol-2-yl)-3-*oxo*-1-phenylpropyl)cyclohexanecarbaldehyde (3q) Following general procedure B, the reaction of **1a** (42.5 mg, 0.20 mmol) and cyclohexanecarboxaldehyde **2d** (67.3 mg, 72.7 μL, 0.60 mmol) catalyzed by Δ-Rh1 (6.6 mg, 0.008 mmol) and Et_2NH (4.1 μL, 0.04 mmol) afforded the product **3q** as a pale yellow oil (31.8 mg, 0.098 mmol, yield: 49%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IA column, *ee*=93% (HPLC: IA, 254 nm, *n*-hexane/isopropanol=90∶10, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=13.9 min, t_r(major)=15.4 min). $[\alpha]_D^{25}$ −20.4 (*c* 0.5, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.55 (s, 1H), 7.25−7.22 (m, 2H), 7.19−7.17 (m, 3H), 7.10 (d, *J*=0.68 Hz, 1H), 6.94 (s, 1H), 3.85 (dd, *J*=10.5, 17.3 Hz, 1H), 3.80 (s, 3H), 3.52 (dd, *J*=4.0, 10.5 Hz, 1H), 3.34 (dd, *J*=4.0, 17.3 Hz, 1H), 2.07 (d, *J*=12.3 Hz, 1H), 2.00 (d, *J*=14.2 Hz, 1H), 1.63−1.54 (m, 3H), 1.36 (ddd, *J*=3.1, 12.8, 13.0 Hz, 1H), 1.28−1.13 (m, 3H), 1.10−0.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 207.6, 190.7, 143.0, 139.3, 129.6, 129.0, 128.0, 126.9, 126.8, 52.4, 46.8, 38.9, 36.0, 30.5, 28.8, 25.4, 23.1, 22.8. IR (film) ν_{max}: 3110, 2913, 2849, 2800, 2691, 1717, 1677, 1449, 1417, 1292, 1158, 977, 915, 776, 707 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{20}H_{24}N_2O_2Na$ $[M+H]^+$: 347.1730, found 347.1731.

(*S*)-*tert*-Butyl 4-formyl-4-(3-(1-methyl-1*H*-imidazol-2-yl)-3-*oxo*-1-phenylpropyl)piperidine-1-carboxylate (3r) Following general procedure B, the reaction of **1a** (42.5 mg, 0.20 mmol) and 1-*tert*-butoxycarbonyl-4-piperidinecarboxaldehyde **2e** (85.3 mg, 0.40 mmol) catalyzed by Δ-Rh1 (9.9 mg, 0.012 mmol) and Et_2NH (6.2 μL, 0.06 mmol) afforded the product **3r** as a colorless oil (39.9 mg, 0.094 mmol, yield: 46%). Enantiomeric excess was determined by HPLC analysis using a Chiralpak IA column, *ee*=95% (HPLC: IA, 254 nm, *n*-hexane/isopropanol=92∶8, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=29.0 min, t_r(major)=31.7 min). $[\alpha]_D^{25}$ −29.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.63 (s, 1H), 7.24 (d, *J*=7.5 Hz, 2H), 7.20 (dd, *J*=1.4, 7.0 Hz, 1H), 7.18 (d, *J*=1.5 Hz, 1H), 7.16 (s, 1H), 7.11 (d, *J*=0.6 Hz, 1H), 6.96 (s, 1H), 3.95 (br, 2H), 3.84 (dd, *J*=10.4, 17.2 Hz, 1H), 3.81 (s, 3H), 3.57 (dd, *J*=4.1, 10.4 Hz, 1H), 3.35 (dd, *J*=4.1, 17.2 Hz, 1H), 2.65 (br, 2H), 2.07 (dd, *J*=2.2, 13.6 Hz, 1H), 1.94 (dd, *J*=2.2, 13.6 Hz, 1H), 1.65 (br, 2 H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 206.1, 190.2, 154.7, 142.8, 138.5, 129.5, 129.1, 128.2, 127.2, 127.0, 79.6, 51.2, 46.7, 38.8, 36.0, 29.8, 28.6, 28.4. IR (film) ν_{max}: 3001, 2969, 2927, 2854, 2720, 1724, 1684, 1457, 1418, 1364, 1288, 1248, 1176, 1141, 984, 914, 766, 707 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{24}H_{32}N_3O_4$ $[M+H]^+$: 426.2387, found 426.2387.

2-Ethyl-5-(1-methyl-1*H*-imidazol-2-yl)-5-*oxo*-3-phenylpentanal (3s) Following general procedure A, the reaction of **1a** (42.5 mg, 0.20 mmol) and butyraldehyde **2f** (43.3 mg, 53.0 μL, 0.60 mmol) catalyzed by Δ-Rh1 (3.3 mg, 0.004 mmol) and morpholine (3.5 μL, 0.04 mmol) afforded the product **3s** as a pale yellow oil (56.6 mg, 0.199 mmol, yield: 99%). The diastereomeric ratio was determined as 1∶3.6 by ^{1}H NMR. Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=92%/88% (HPLC: IC, 254 nm, *n*-hexane/isopropanol=85∶15, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=20.1 min, t_r(major)=26.0 min, t_r(major)=38.7 min, t_r(minor)=46.3 min). $[\alpha]_D^{25}$ −6.3 (*c* 1.0, $CHCl_3$). For major diastereomer: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.53 (d, *J*=3.5 Hz, 1H), 7.25−7.23 (m, 4H), 7.19−7.16 (m, 1H), 7.12 (d, *J*=0.8 Hz, 1H), 6.98 (s, 1H), 3.87 (s, 3H), 3.73 (dd, *J*=10.8, 24.3 Hz, 2H), 3.51 (dd, *J*=4.5, 16.2 Hz, 1H), 2.56−2.48 (m, 1H), 1.78−1.60 (m, 2H), 0.91 (t, *J*=7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 204.6, 190.5, 142.9, 141.2, 129.1, 128.5, 128.3, 127.0, 126.9, 58.3, 41.9, 40.8, 36.1, 20.3, 11.8. IR (film) ν_{max}: 3029, 2965, 2934, 2877, 2927, 1718, 1676, 1456, 1411, 1290, 1156, 915, 775, 702 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{17}H_{21}N_2O_2$ $[M+H]^+$: 285.1598, found 285.1600.

2-(3-*oxo*-1-Phenyl-3-(1-phenyl-1*H*-imidazol-2-yl)-propyl)octanal (3t) Following general procedure A, the reaction of **1n** (54.9 mg, 0.20 mmol) and octanal **2g** (76.9 mg, 93.5 μL, 0.60 mmol) catalyzed by Δ-Rh1 or Λ-Rh1 (6.6 mg, 0.008 mmol) and (*S*)-**4** (13.0 mg, 0.04 mmol) afforded the product **3t** as colorless oil. For Δ-Rh1 catalyzed reaction, **3t** was afforded in 98% yield (79.0 mg, 0.196 mmol). The diastereomeric ratio was determined as 1∶4.0 by ^{1}H NMR. Enantiomeric excess was determined by HPLC analysis using a Chiralpak IC column, *ee*=98%/62% (HPLC: IC, 254 nm, *n*-hexane/isopropanol=70∶30, flow rate: 1.0 mL/min, 25 ℃, t_r(minor)=11.5 min, t_r(major)=15.1 min, t_r(major)=25.3 min, t_r(minor)=56.4 min). $[\alpha]_D^{25}$ +12.8 (*c* 1.0, $CHCl_3$). For diastereomer A: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 9.48 (d, *J*=3.7 Hz, 1H), 7.40−7.34 (m, 3H), 7.25 (d, *J*=0.7 Hz, 2H), 7.23 (s, 1H), 7.19 (s, 2H), 7.17 (s, 1H), 7.12 (d, *J*=0.8 Hz, 1H), 7.00 (d, *J*=1.3 Hz, 1H), 6.98 (d, *J*=1.8 Hz, 1H), 3.74−3.67 (m, 2H), 3.50 (dd, *J*=9.2, 20.1 Hz, 1H), 2.58−2.52 (m, 1H), 1.69−1.63 (m, 2H), 1.58−1.51 (m, 1H), 1.26−1.22 (br, 7H), 0.85 (t, *J*=7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 204.6, 189.2, 143.0, 141.0, 138.1, 129.6, 128.9, 128.7,

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128.5, 128.4, 127.0, 126.9, 125.6, 56.8, 42.2, 41.4, 31.5, 29.3, 27.3, 27.2, 22.5, 14.0. IR (film) ν_{max}: 3030, 2955, 2928, 2856, 2720, 1718, 1685, 1506, 1494, 1457, 1407, 1307, 962, 760, 701 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{26}H_{31}N_2O_2$ $[M+H]^+$: 403.2380, found 403.2380.

For diastereomer B: ^1H NMR (400 MHz, $CDCl_3$) δ: 9.59 (d, J=4.1 Hz, 1H), 7.40−7.34 (m, 3H), 7.26 (s, 1H), 7.25 (s, 1H), 7.22 (d, J=0.8 Hz, 1H), 7.19 (d, J=1.6 Hz, 2H), 7.17 (d, J=1.6 Hz, 1H), 7.10 (d, J=0.9 Hz, 1H), 7.02 (d, J=1.4 Hz, 1H), 7.00 (d, J=2.0 Hz, 1H), 3.66 (s, 1H), 3.64 (dd, J=5.0, 11.2 Hz, 1H), 3.45−3.38 (m, 1H), 2.54−2.49 (m, 1H), 1.50−1.40 (m, 1H), 1.22−1.10 (m, 9H), 0.81 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.0, 189.1, 142.9, 141.3, 138.1, 129.6, 128.9, 128.6, 128.5, 128.4, 127.0, 126.8, 125.6, 57.7, 43.7, 40.6, 31.5, 29.1, 27.4, 27.0, 22.5, 14.0. IR (film) ν_{max}: 3030, 2955, 2927, 2856, 2715, 1719, 1685, 1506, 1494, 1457, 1407, 1307, 962, 761, 701 cm^{-1}. HRMS (ESI, *m/z*) calcd for $C_{26}H_{31}N_2O_2$ $[M+H]^+$: 403.2380, found 403.2381.

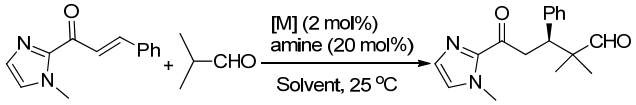
Results and Discussion

We started our studies on this topic by choosing α,β-unsaturated 2-acyl imidazole **1a** and isobutyraldehyde **2a** as model substrates for optimization of reaction conditions. Using iridium catalysts, Δ-Ir1 (2.0 mol%) or Δ-Ir2 (2.0 mol%) and secondary amine catalyst, Et_2NH (20 mol%) at 25 ℃, the desired adduct **3a** was afforded with good enantioselectivity (Table 1, Entries 1 and 2). However, the conversion was incomplete after 48 h, which prompted us to investigate the effect of Rh catalyst. To our delight, when the rhodium catalyst, Δ-Rh1 (2.0 mol%) in combination with Et_2NH (20 mol%) was employed in this reaction, **3a** was obtained in 99% yield with 97% *ee* after 24 h (Entry 3). This advantage of rhodium over iridium congeners is ascribed to a much faster ligand exchange kinetics involved in the catalytic cycle.[7a,7d] When pyrolidine was used instead of Et_2NH, the reaction proceeded in 99% yield, albeit with a slightly reduced enantioselectivity (94% *ee*, Entry 4). However, when Δ-Rh1 in combination with other secondary amine such as piperidine, morpholine or $^iPr_2NH$ was applied to this system, the conversion was incomplete after 28 h (Entries 5−7). Replacing the solvent DCE with CH_2Cl_2 did not affect the yield and *ee* (Entry 8), and other solvents did not provide satisfactory yield (Entries 9−11). Reducing the loading of Et_2NH to 10 mol% can afford the adduct **3a** in 77% yield but still with high enantioselectivity (Entry 12). Importantly, control experiments in the absence of either rhodium catalyst (Entry 13) or amine catalyst (Entry 14) failed to provide any product, thereby demonstrating that this reaction crucially depends on the combination of rhodium and amine catalysts.

Under the optimized reaction conditions, the substrate scope of the enantioselective alkylation of isobutyraldehyde **2a** with α,β-unsaturated 2-acyl imidazoles **1a**−**1n** was investigated and the results were summarized in Scheme 2. Electron-donating methyl group on the phenyl ring had no significant impact on the outcome, leading to the products **3b** and **3c** with 96% *ee* and 94% *ee*, respectively (**3b**−**3c**). Substrates with electron-withdrawing Br or Cl groups on the phenyl ring were also tolerable, affording the products with good to excellent enantioselectivity (86%−95% *ee*, **3d**−**3f**). Furthermore, other substrates either containing a bulky naphthyl moiety (**3g**) or heterocyclic ring (**3h**−**3i**) were all well converted with excellent enantioselectivity (94%−96% *ee*). To be noted, the reaction is tolerant of a methyl group (**3j**), an ether moiety (**3k**) and an ester group (**3l**) in β-position to the carbonyl group, leading to corresponding products in moderate to good yield and with excellent enantioselectivity. Replacement of the *N*-methyl (**1a**) with an isopropyl (**1m**) or a phenyl (**1n**) substituent did not encumber the reactions, and good results were still perceived (**3m**−**3n**).

It is noteworthy that a gram-scale reaction was conducted to demonstrate the synthetic potential of current methodology. In the presence of 1.0 mol% of Δ-Rh1 as catalyst, the enantioselective alkylation of **1a** (5 mmol, 1.06 g) with **2a** (15 mmol, 1.08 g) occurred smoothly, delivering **3a** in 97% yield with 95% *ee*. The absolute configuration of product **3g** was assigned as *S* by an X-ray crystallographic analysis (Figure 1, for details,

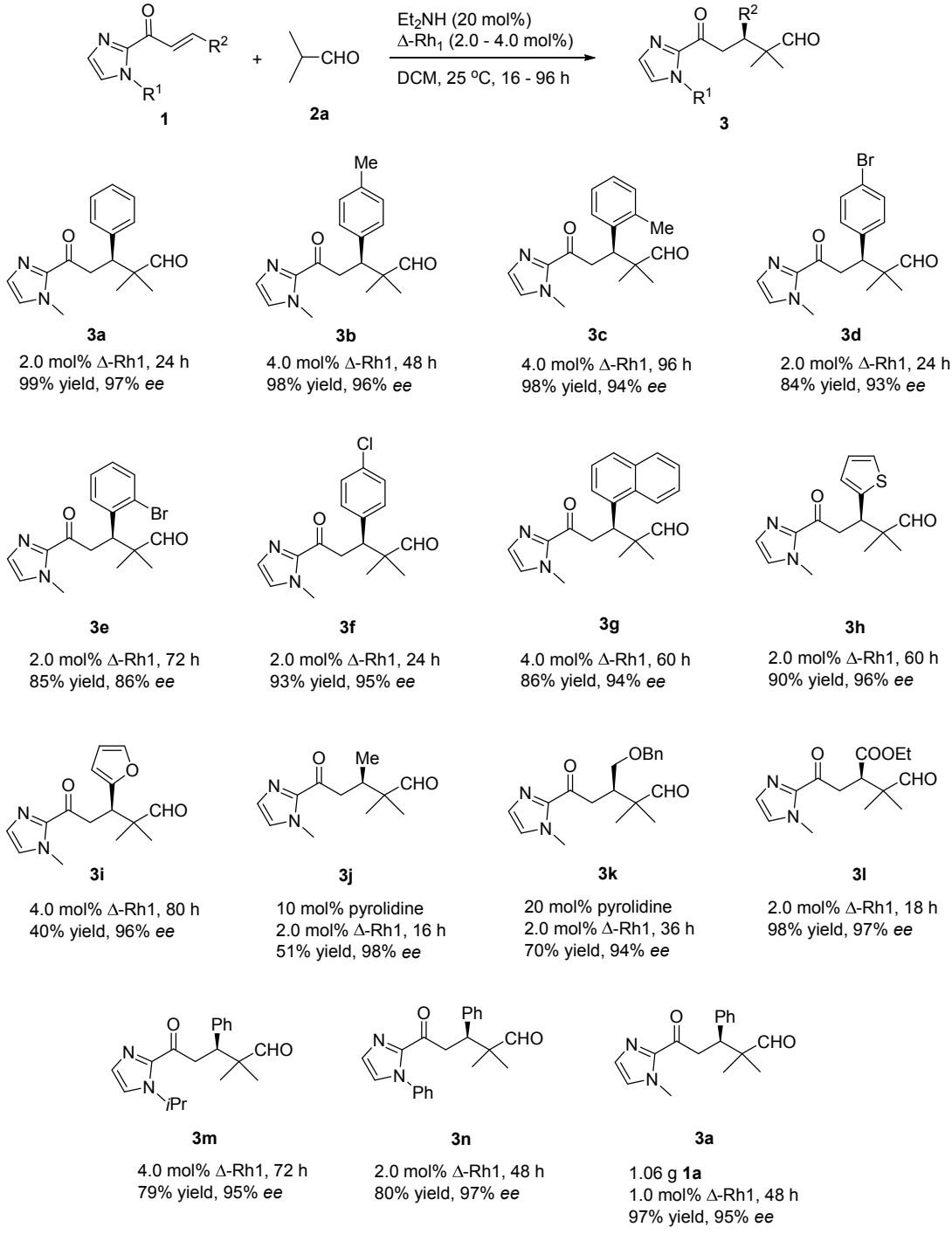
Table 1 Optimization of reaction conditions[a]



Entry	[M]	Amine	Solvent	*t*/h	Yield[b]/%	*ee*[c]/%
1	Δ-Ir1	Et_2NH	DCE	48	23	96
2	Δ-Ir2	Et_2NH	DCE	48	17	94
3	Δ-Rh1	Et_2NH	DCE	24	99	97
4	Δ-Rh1	pyrolidine	DCE	24	99	94
5	Δ-Rh1	piperidine	DCE	28	47	95
6	Δ-Rh1	morpholine	DCE	28	46	97
7	Δ-Rh1	$^iPr_2NH$	DCE	28	20	97
8	Δ-Rh1	Et_2NH	CH_2Cl_2	24	99	97
9	Δ-Rh1	Et_2NH	THF	24	58	97
10	Δ-Rh1	Et_2NH	$CHCl_3$	24	54	96
11	Δ-Rh1	Et_2NH	toluene	24	79	96
12	Δ-Rh1	Et_2NH (10 mol%)	DCE	24	77	96
13	none	Et_2NH	DCE	48	0	n.d.
14	Δ-Rh1	none	DCE	48	0	n.d.

[a] Reaction conditions: **1a** (0.20 mmol), **2a** (0.60 mmol), amine (20 mol%), and metal catalyst (2.0 mol%) in solvent (0.4 mL) at 25 ℃ under argon. [b] Isolated yield. [c] Chiral HPLC analysis, n.d. =not determined.

Scheme 2 Substrate scope of α,β-unsaturated 2-acyl imidazoles



see the Supporting Information).[11]

Next, we chose the α,β-unsaturated 2-acyl imidazoles **1a** for the evaluation of various of symmetric aldehydes. When cyclopropanecarboxaldehyde (**2b**) was employed, the adduct was afforded with excellent enantioselectivity (99% *ee*, Scheme 3, **3o**), albeit in a moderate yield after 96 h. We assumed that this could be traced back to the ring strain, which encumbered **2b** to condense with the amine catalyst to form an enamine intermediate. This hypothesis was further supported by the result that cyclopentanecarboxaldehyde (**2c**) afforded the product in 99% yield (Scheme 3, **3p**). However, when cycloheanecarboxaldehyde (**2d**) and *N*-Boc-4-piperidinecarboxaldehyde (**2e**) were used, the conversion was incomplete even after 72 h, which can be ascribed to unfavored steric hindrance (Scheme 3, **3q** and **3r**).

The linear aldehydes with an aliphatic chain were also investigated in this reaction. Under the optimal reaction conditions, **1a** could react with butyraldehyde **2f** smoothly, providing the adduct **3s** in 99% yield, albeit with a low diastereoselectivity (1.0 ∶ 1.4 *dr*) (Table 2,

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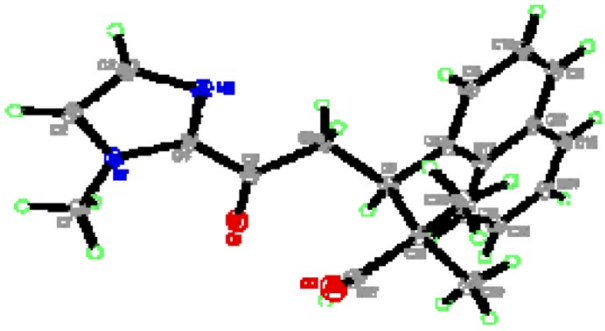


Figure 1 X-ray derived ORTEP of **3g** with thermal ellipsoids shown at the 35% probability level.

Entry 1). Replacing Et_2NH with pyrolidine did not improve the diastereoselectivity (Table 2, Entry 2). Gratifyingly, when morpholine in combination with Δ-Rh1 was applied to this system, the reaction afforded the adduct **3s** with an improved *dr* of 1.0∶3.6 and 92% *ee* for the major diastereomer (Table 2, Entry 3). But under the same condition, due to the background reaction, the reaction of substrate **1n** and octanal **2g** provided a disappointing result (1∶1 *dr*, 15% and 70% *ee*) (Table 2, Entry 4), which prompted us to use a chiral amine catalyst[12] to improve *ee* and *dr* value. Fortunately, when chiral amine (*S*)-**4**[13] was used with Δ-Rh1 in this reaction, the adduct **3t** was afforded with an improved *dr* of 1.0∶4.0 and 98% *ee* for the major diastereomer (Table

Scheme 3 Substrate scope of symmetric aldehydes

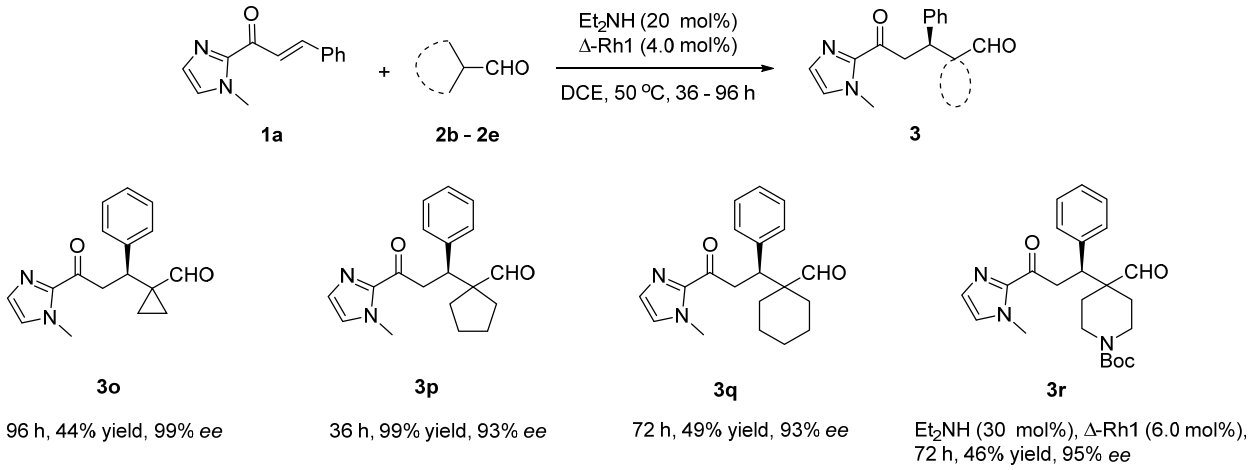
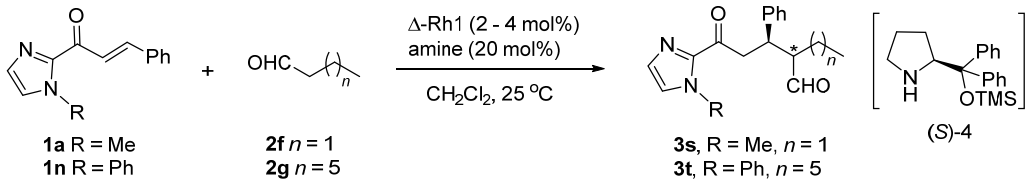


Table 2 Substrate scope of linear aldehydes[a]



Entry	1	2	Δ-Rh1 (mol %)	Amine (mol%)	*t*/h, Yield[b]/%	*dr*[c]	*ee*[d]/%
1	**1a**	**2f**	Δ-Rh1 (2.0)	Et_2NH (20)	24, 99	1.4∶1.0	n.d.
2	**1a**	**2f**	Δ-Rh1 (2.0)	pyrolidine (20)	24, 94	1.4∶1.0	n.d.
3	**1a**	**2f**	Δ-Rh1 (2.0)	Morpholine (20)	24, 99	3.6∶1.0	92, 88
4	**1n**	**2g**	Δ-Rh1 (2.0)	Morpholine (20)	32, 93	1.0∶1.0	70, 14
5	**1n**	**2g**	Δ-Rh1 (4.0)	(*S*)-**4** (20)	36, 98	1.0∶4.0	62, 98
6	**1n**	**2g**	Λ-Rh1 (4.0)	(*S*)-**4** (20)	67, 60	1.2∶1.0	95, 42

[a] Reaction conditions: **1** (0.20 mmol), **2** (0.60 mmol), amine (20 mol%), and metal catalyst (2.0—4.0 mol%) in CH_2Cl_2 (0.4 mL) at 25 ℃ under argon. [b] Isolated yield. [c] *dr* ratio determined by crude ^1H NMR spectroscopy. [d] The *ee* of two diastereomers were determined by chiral HPLC analysis, n.d.＝not determined.

2, Entry 5). Intriguingly, when (*S*)-**4** was combined with Λ-Rh1, this reaction provided a reversed diastereoselectivity and stereoselectivity (1.2∶1.0 *dr*, 98% *ee* for the major diastereomers) (Table 2, Entry 6). These results demonstrated that the stereochemistry of the reaction is mainly controlled by the metal centrochirality of rhodium catalyst.

The proposed mechanism for this synergistic system is shown in Figure 2. The 2-acyl imidazole substrate **1a** is activated by the rhodium catalyst through bidentate *N*,*O*-coordination (intermediate **A**). Meanwhile, amine activates the aldehyde **2a** by forming an enamine intermediate, which can attack intermediate **A** to provide intermediate **B** in a fashion stereochemically controlled by the chiral rhodium complex. Then the iminium ion is hydrolyzed to regenerate the amine and afford the coordinated product **C**. The desired product **3a** is released by replacement of the coordinated product **C** by **1a**, and a new catalytic cycle is initiated.

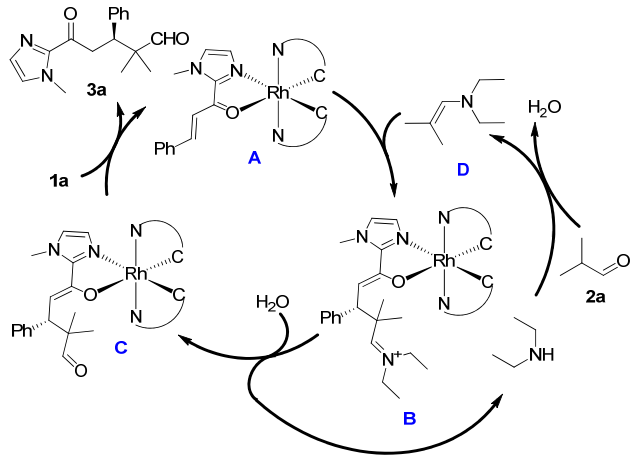


Figure 2 Proposed mechanism for the enantioselective Michael addition.

Conclusions

In conclusion, we have reported a synergistic catalysis combination of chiral-at-metal complex and amine catalyst which can be applied to the enantioselective alkylation of aldehydes with *α*,*β*-unsaturated 2-acyl imidazoles. In these transformations, chiral-at-metal complex exhibits a high catalytic activity that takes place with excellent enantioselectivity and tunable diastereoselectivity. Also, this work indicates that the amine catalyst is compatible with the chiral-at-metal complex. Further studies into the scope of this new transformation are ongoing in our laboratory.

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References

[1] (a) Shao, Z.; Zhang, H. *Chem. Soc. Rev.* **2009**, *38*, 2745; (b) Zhong, C.; Shi, X. *Eur. J. Org. Chem.* **2010**, 2999; (c) Du, Z.; Shao, Z. *Chem. Soc. Rev.* **2013**, *42*, 1337; (d) Chen, D.-F.; Han, Z.-Y.; Zhou, X.-L.; Gong, L.-Z. *Acc. Chem. Res.* **2014**, *47*, 2365; (e) Fernández-Ibañez, M. Á.; Maciá, B.; Alonso, D. A.; Pastor, I. M. *Molecules* **2013**, *18*, 10108.

[2] (a) Allen, A. E.; MacMillan, D. W. C. *Chem. Sci.* **2012**, *3*, 633; (b) Inamdar, S. M.; Shinde, V. S.; Patil, N. T. *Org. Biomol. Chem.* **2015**, *13*, 8116.

[3] (a) Deng, Y.; Kumar, S.; Wang, H. *Chem. Commun.* **2014**, *50*, 4272; (b) Gualandi, A.; Mengozzi, L.; Wilson, C. M.; Cozzi, P. G. *Chem. Asian J.* **2014**, *9*, 984; (c) Meazza, M.; Rios, R. *Synthesis* **2016**, *48*, 960.

[4] For selected examples of the combination of enamine catalysis and transition metal catalysis, see: (a) Ibrahem, I.; Córdova, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 1952; (b) Bihelovic, F.; Matovic, R.; Vulovic, B.; Saicic, R. N. *Org. Lett.* **2007**, *9*, 5063; (c) Binder, J. T.; Crone, B.; Haug, T. T.; Menz, H.; Kirsch, S. F. *Org. Lett.* **2008**, *10*, 1025; (d) Nagib, D. A.; Scott, M. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2009**, *131*, 10875; (e) Capdevila, M. G.; Benfatti, F.; Zoli, L.; Stenta, M.; Cozzi, P. G. *Chem. Eur. J.* **2010**, *16*, 11237; (f) Allen, A. E.; Mac Millan, D. W. C. *J. Am. Chem. Soc.* **2010**, *132*, 4986; (g) Ikeda, M.; Miyake, Y.; Nishibayashi, Y. *Angew. Chem., Int. Ed.* **2010**, *49*, 7289; (h) Jiang, G.; List, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 9471; (i) Zhao, X.; Liu, D.; Xie, F.; Liu, Y.; Zhang, W. *Org. Biomol. Chem.* **2011**, *9*, 1871; (j) Allen, A. E.; MacMillan, D. W. C. *J. Am. Chem. Soc.* **2011**, *133*, 4260; (k) Xu, Z.; Liu, L.; Wheeler, K.; Wang, H. *Angew. Chem., Int. Ed.* **2011**, *50*, 3484; (l) Xiao, J. *Org. Lett.* **2012**, *14*, 1716; (m) Afewerki, S.; Ibrahem, I.; Rydfjord, J.; Breistein, P.; Córdova, A. *Chem. Eur. J.* **2012**, *18*, 2972; (n) Li, M.; Datta, S.; Barber, D. M.; Dixon, D. J. *Org. Lett.* **2012**, *14*, 6350; (o) Montaignac, B.; Praveen, C.; Vitale, M. R.; Michelet, V.; Ratovelomanana-Vidal, V. *Chem. Commun.* **2012**, *48*, 6559; (p) Chiarucci, M.; di Lillo, M.; Romaniello, A.; Cozzi, P. G.; Cera, G.; Bandini, M. *Chem. Sci.* **2012**, *3*, 2859; (q) Krautwald, S.; Sarlah, D.; Schafroth, M. A.; Carreira, E. M. *Science* **2013**, *340*, 1065; (r) Ma, G.; Afewerki, S.; Deiana, L.; Palo-Nieto, C.; Liu, L.; Sun, J.; Ibrahem, I.; Córdova, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 6050; (s) Deng, Y.; Liu, L.; Sarkisian, R. G.; Wheeler, K.; Wang, H.; Xu, Z. *Angew. Chem., Int. Ed.* **2013**, *52*, 3663; (t) Krautwald, S.; Schafroth, M. A.; Sarlah, D.; Carreira, E. M. *J. Am. Chem. Soc.* **2014**, *136*, 3020; (u) Schafroth, M. A.; Zuccarello, G.; Krautwald, S.; Sarlah, D.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2014**, *53*, 13898; (v) Wang, P.-S.; Lin, H.-C.; Zhai, Y.-J.; Han, Z.-Y.; Gong, L.-Z. *Angew. Chem., Int. Ed.* **2014**, *53*, 12218; (w) Nœsborg, L.; Halskov, K. S.; Tur, F.; Mønsted, S. M. N.; Jørgensen, K. A. *Angew. Chem., Int. Ed.* **2015**, *54*, 10193.

[5] Mukherjee, S.; Yang, J. W.; Hoffmann, S.; List, B. *Chem. Rev.* **2007**, *107*, 5471.

[6] (a) Huo, H.; Fu, C.; Harms, K.; Meggers, E. *J. Am. Chem. Soc.* **2014**, *136*, 2990; (b) Huo, H.; Shen, X.; Wang, C.; Zhang, L.; Röse, P.; Chen, L.-A.; Harms, K.; Marsch, M.; Hilt, G.; Meggers, E. *Nature* **2014**, *515*, 100; (c) Wang, C.; Zheng, Y.; Huo, H.; Röse, P.; Zhang, L.; Harms, K.; Hilt, G.; Meggers, E. *Chem. Eur. J.* **2015**, *21*, 7355; (d) Shen, X.; Huo, H.; Wang, C.; Zhang, B.; Harms, K.; Meggers, E. *Chem. Eur. J.* **2015**, *21*, 9720; (e) Huo, H.; Wang, C.; Harms, K.; Meggers, E. *J. Am. Chem. Soc.* **2015**, *137*, 9551; (f) Wang, C.; Shen, X.; Riedel, R.; Harms, K.; Meggers, E. *Angew. Chem., Int. Ed.* **2016**, *55*, 685.

[7] (a) Wang, C.; Chen, L.-A.; Huo, H.; Shen, X.; Harms, K.; Gong, L.; Meggers, E. *Chem. Sci.* **2015**, *6*, 1094; (b) Huang, Y.; Song, L.; Gong, L.; Meggers, E. *Chem. Asian J.* **2015**, *10*, 2738; (c) Tan, Y.;

Yuan, W.; Gong, L.; Meggers, E. *Angew*. *Chem*., *Int*. *Ed*. **2015**, *54*, 13045; (d) Shen, X.; Harms, K.; Marsch, M.; Meggers, E. *Chem*. *Eur*. *J*. **2016**, *22*, 9102; (e) Ma, J.; Shen, X.; Harms, K.; Meggers, E. *Dalton Trans*. **2016**, *45*, 8320; (f) Huo, H.; Harms, K.; Meggers, E. *J*. *Am*. *Chem*. *Soc*. **2016**, *138*, 6936.

[8] (a) Bauer, E. B. *Chem*. *Soc*. *Rev*. **2012**, *41*, 3153; (b) Gong, L.; Chen, L.-A.; Megger, E. *Angew*. *Chem*., *Int*. *Ed*. **2014**, *53*, 10868; (c) Cao, Z.-Y.; Brittain, W. D. G.; Fossey, J. S.; Zhou, F. *Catal*. *Sci*. *Technol*. **2015**, *5*, 3441.

[9] For selected examples of asymmetric Michael addition of aldehyde, see: (a) Wang, W.; Wang, J.; Li, H. *Angew*. *Chem*., *Int*. *Ed*. **2005**, *44*, 1369; (b) Lalonde, M. P.; Chen, Y.; Jacobsen, E. N. *Angew*. *Chem*., *Int*. *Ed*. **2006**, *45*, 6366; (c) Zhu, S.; Yu, S.; Ma, D. *Angew*. *Chem*., *Int*. *Ed*. **2008**, *47*, 545; (d) Zhu, Q.; Lu, Y. *Chem*. *Commun*. **2010**, *46*, 2235; (e) Kano, T.; Shirozu, F.; Tatsumi, K.; Kubota, Y.; Maruoka, K. *Chem*. *Sci*. **2011**, *2*, 2311; (f) Ma, Z.; Liu, Y.; Li, P.; Ren, H.; Zhu, Y.; Tao, J. *Tetrahedron*: *Asymmetry* **2011**, *22*, 1740; (g) Kano, T.; Shirozu, F.; Akakura, M.; Maruoka, K. *J*. *Am*. *Chem*. *Soc*. **2012**, *134*, 16068; (h) Kokotos, C. G. *Org*. *Lett*. **2013**, *15*, 2406; (i) Qiao, Y.; Headley, A. D. *Green Chem*. **2013**, *15*, 2690; (j) He, J.; Chen, Q.; Ni, B. *Tetrahedron Lett*. **2014**, *55*, 3030; (k) Wang, Y.; Li, D.; Lin, J.; Wei, K. *RSC Adv*. **2015**, *5*, 5863; (l) Vízcaíno-Milla, P.; Sansano, J. M.; Nájera, C.; Fiser, B.; Gómez-Bengoa, E. *Synthesis* **2015**, *47*, 2199; (m) Xia, A.-B.; Zhang, C.; Zhang, Y.-P.; Guo, Y.-J.; Zhang, X.-L.; Li, Z.-B.; Xu, D.-Q. *Org*. *Biomol*. *Chem*. **2015**, *13*, 9593; (n) Hu, X.; Wei, Y.-F.; Wu, N.; Jiang, Z.; Liu, C.; Luo, R.-S. *Tetrahedron*: *Asymmetry* **2016**, *27*, 420.

[10] During the preparation of our manuscript, Meggers and Gong reported a single rhodium precatalyst catalysed Michael addition of α,α-disubstituted aldehydes to α,β-unsaturated 2-acyl imidazoles, Song, L.; Gong, L.; Meggers, E. *Chem*. *Commun*. **2016**, 7699.

[11] CCDC 1485412 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[12] Sarah, S. M.; Alexandre, A. *Chem*. *Commun*. **2007**, 3123.

[13] (a) Marigo, M.; Wabnitz, T. C.; Fielenbach, D.; Jørgensen, K. A. *Angew*. *Chem*., *Int*. *Ed*. **2005**, *44*, 794; (b) Hayashi, Y.; Gotoh, H.; Hayashi, T.; Shoji, M. *Angew*. *Chem*., *Int*. *Ed*. **2005**, *44*, 4212; (c) Mielgo, A.; Palomo, C. *Chem*. *Asian J*. **2008**, *3*, 922; (d) Jensen, K. L.; Dickmeiss, G.; Jiang, H.; Albrecht, Ł.; Jørgensen, K. A. *Acc*. *Chem*. *Res*. **2012**, *45*, 248.

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