Chemoenzymatic synthesis of optically active 2-(2- or 4-substituted-1H-imidazol-1-yl)cycloalcanols. Chiral additives for (L)-proline.

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Table S.I.1. Melting temperatures of different complex (S,S)-4a: (L)-proline.

| Entry | Ratio | Imidazole Molar fraction | T<sub>m</sub> (°C) imidazole<sup>a</sup> | T<sub>m</sub> (°C) L-proline<sup>a</sup> |
|-------|-------|--------------------------|--------------------------------|---------------------------------|
| 1     | 1:0   | 1                        | 88.28                          | -                               |
| 2     | 0:1   | 0                        | -                               | 222.13                          |
| 3     | 1:1   | 0.5                      | 67.76                          | 168.51                          |
| 4     | 1:2.5 | 0.3                      | 87.91                          | 175.91                          |
| 5     | 1:5   | 0.17                     | 91.56                          | 192.46                          |
| 6     | 2.5:1 | 0.71                     | 71.44                          | 177.74                          |
| 7     | 5:1   | 0.83                     | 75.02                          | 155.63                          |

<sup>a</sup> The melting temperature (T<sub>m</sub>) was determined as the onset of the transition.

Table S.I.2 Melting temperatures of different complexes formed by diverse imidazoles and (L)-proline with ratio 1:1.

| Entry | -OX | R<sub>1</sub> | R<sub>2</sub> | Imidazole | Imidazole: (L)-proline (1:1) |
|-------|-----|--------------|--------------|-----------|-------------------------------|
|       |     |              |              | T<sub>m</sub> (°C)<sup>a</sup> | T<sub>m</sub> (°C) imidazole<sup>a</sup> | T<sub>m</sub> (°C) (L)-proline<sup>a</sup> |
| 1     | R,R-OAc | H     | H            | -56       | < -50                         | 142                             |
| 2     | S,S-OH  | H     | H            | 88        | 86                            | 166                             |
| 3     | R,R-OAc | CH<sub>3</sub> | H          | -48       | -47                           | 150                             |
| 4     | S,S-OH  | CH<sub>3</sub> | H          | 64        | 81                            | 180                             |
| 5     | S,S-OH  | H     | Ph           | 173       | 179                           | 195                             |

<sup>a</sup> The melting temperature (T<sub>m</sub>) was determined as the onset of the transition.
Spectroscopical data of (1S,2S)-2-(1H-imidazol-1-yl)cyclopentanol (3a)

(1S,2S)-2-(1H-imidazol-1-yl)cyclopentanol (3a). \( R_t \) (10% MeOH/CHCl\(_3\)): 0.22; Mp: 72-74 °C; IR (KBr): \( \nu \) 3192, 3096, 2974, 2348, 1604, 1574, 1412, 1353, 1287, 1231, 1149, 1113, 1097, 1060 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300.13 MHz): \( \delta \) 1.62-1.89 (m, 4H), 2.01-2.13 (m, 1H), 2.15-2.29 (m, 1H), 4.08-4.18 (m, 2H), 6.32 (brs, 1H), 6.83 (s, 1H), 6.89 (s, 1H), 7.26 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz): \( \delta \) 20.3 (CH\(_2\)), 30.3 (CH\(_2\)), 32.2 (CH\(_2\)), 65.9 (CH), 77.9 (CH), 117.4 (CH), 128.7 (CH), 136.3 (CH); MS (ESI\(^+\), m/z): 175 [(M+Na\(^+\)], 100%), 153 [(M+H\(^+\)], 35%; \((S,S)-3a: [\alpha]_{D}^{20} = +41.9 \) (c 1, CHCl\(_3\)), 99% ee; Analytical separation (HPLC): Chiralcel OB-H \( n \)-hexane/EtOH (97:3), 0.5 mL/min, 20 °C, \( t_R \) \((R,R) = 39.6 \) min, \( t_R \) \((S,S) = 45.9 \) min.

Spectroscopical data of (1S,2S)-2-(4-methyl-1H-imidazol-1-yl)cyclopentanol (3b)

(1S,2S)-2-(4-methyl-1H-imidazol-1-yl)cyclopentanol (3b). \( R_t \) (10% MeOH/CHCl\(_3\)): 0.16; Mp: 95-97 °C; IR (KBr): \( \nu \) 3112, 2964, 2859, 2763, 2362, 1602, 1561, 1497, 1356, 1322, 1227, 1171, 1114, 1070 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300.13 MHz): \( \delta \) 1.65-1.90 (m, 5H), 2.05 (s, 3H), 2.21-2.33 (m, 1H), 4.01-4.10 (m, 1H), 4.17 (q, \(^3\)J\(_{HH} = 7.5 \) Hz, 1H), 4.70 (brs, 1H), 6.61 (s, 1H), 7.18 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz): \( \delta \) 13.2 (CH\(_3\)), 19.8 (CH\(_2\)), 29.8 (CH\(_2\)), 31.5 (CH\(_2\)), 65.6 (CH), 77.5 (CH), 122.9 (CH), 128.0 (C), 135.1 (CH); MS (ESI\(^+\), m/z): 189 [(M+Na\(^+\)], 20%), 167 [(M+H\(^+\)], 100%]; \((S,S)-3b: [\alpha]_{D}^{20} = +50.2 \) (c 1, CHCl\(_3\)), 99% ee; Analytical separation (HPLC) Chiralpak AS \( n \)-hexane/EtOH (96:4), 0.8 mL/min, 40 °C, \( t_R \) \((S,S) = 17.4 \) min, \( t_R \) \((R,R) = 20.8 \) min.
Spectroscopical data of \((1S,2S)-2-(4\text{-phenyl}-1H\text{-imidazol}-1-y\text{l})\text{cyclopentanol} (3c)\)

\((1S,2S)-2-(4\text{-phenyl}-1H\text{-imidazol}-1-y\text{l})\text{cyclopentanol} (3c)\). \(R_f\) (10\% MeOH/CHCl\(_3\)): 0.23; Mp: 168-170 °C; IR (KBr): \(\nu\) 3129, 2964, 2868, 2345, 2344, 1602, 1484, 1449, 1366, 1310, 1202, 1067 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300.13 MHz): \(\delta\) 1.66-1.88 (m, 4H), 2.07-2.23 (m, 2H), 4.04-4.18 (m, 2H), 4.50 (bres, 1H), 6.99 (s, 1H), 7.31-7.42 (m, 4H), 7.56 (d, \(^3\)J\(_{HH}\) = 7.8 Hz, 2H); \(^13\)C NMR (CDCl\(_3\), 75.5 MHz): \(\delta\) 19.4 (CH\(_2\)), 29.7 (CH\(_2\)), 31.2 (CH\(_2\)), 65.8 (CH), 77.4 (CH), 112.5 (CH), 124.5 (2CH), 126.7 (CH), 128.4 (2CH), 133.4 (C), 136.2 (CH), 141.3 (C); MS (ESI\(^+\), m/z): 251 [(M+Na)\(^+\), 20\%], 209 [(M+H)\(^+\), 100\%]; \((S,S)-3c\): \([\alpha]^{20}_D\): +71.5 (c 1, CHCl\(_3\)), >99% ee; Analytical separation (HPLC) Chiralpak AS nr-hexane/EtOH (96:4), 0.8 mL/min, 40 °C, \(t_R (R,R)\) = 19.9 min, \(t_R (S,S)\) = 24.6 min.

Spectroscopical data of \((1S,2S)-2-(2\text{-methyl}-1H\text{-imidazol}-1-y\text{l})\text{cyclopentanol} (3d)\)

\((1S,2S)-2-(2\text{-methyl}-1H\text{-imidazol}-1-y\text{l})\text{cyclopentanol} (3d)\). \(R_f\) (10\% MeOH/CHCl\(_3\)): 0.21; Mp: 72-74 °C; IR (KBr): \(\nu\) 3111, 2963, 2876, 2360, 2359, 1666, 1529, 1449, 1423, 1349, 1282, 1153, 1133, 1087, 1057, 990, 934, 907, 852, 729 cm\(^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300.13 MHz): \(\delta\) 1.63-1.90 (m, 4H), 1.98-2.18 (m, 2H), 2.20 (s, 3H), 4.09-4.19 (m, 2H), 6.63 (s, 1H), 6.73 (s, 1H); \(^13\)C NMR (CDCl\(_3\), 75.5 MHz): \(\delta\) 13.1 (CH\(_3\)), 20.1 (CH\(_3\)), 29.9 (CH\(_2\)), 31.8 (CH\(_2\)), 63.9 (CH), 77.8 (CH), 114.9 (CH), 126.6 (CH), 145.1 (C); MS (ESI\(^+\), m/z): 189 [(M+Na)\(^+\), 20\%], 167 [(M+H)\(^+\), 100\%]; \((S,S)-3d\): \([\alpha]^{20}_D\): +14.7 (c 1, CHCl\(_3\)), >99% ee; Analytical separation (HPLC) Chiralcel OD nr-hexane/EtOH (90:10), 0.8 mL/min, 20 °C, \(t_R (S,S)\) = 13.0 min, \(t_R (R,R)\) = 17.2 min.
Spectroscopical data of (1S,2S)-2-(2-phenyl-1H-imidazol-1-yl)cyclopentanol (3e)

(1S,2S)-2-(2-phenyl-1H-imidazol-1-yl)cyclopentanol (3e). \( R_t \) (5% MeOH/CHCl\textsubscript{3}): 0.17; Mp: 162-164 °C; IR (KBr): ν 3404, 3144, 3109, 2957, 2873, 2771, 2360, 2341, 1602, 1468, 1444, 1422, 1352, 1331, 1300, 1280, 1202, 1157, 1131, 1105, 1069, 1022, 775, 753, 719 cm\textsuperscript{-1}; \(^1\)H NMR (CDCl\textsubscript{3}, 300.13 MHz): \( \delta \) 1.57-1.80 (m, 4H), 1.99-2.12 (m, 2H), 4.24 (q, \(^3\)J\textsubscript{HH} = 7.6 Hz, 1H, H\textsubscript{2}), 4.43 (q, \(^3\)J\textsubscript{HH} = 7.6 Hz, 1H), 6.88 (s, 2H), 7.31-7.34 (m, 3H), 7.54-7.56 (m, 2H); \(^{13}\)C NMR (CDCl\textsubscript{3}, 75.5 MHz): \( \delta \) 19.8 (CH\textsubscript{2}), 31.2 (CH\textsubscript{2}), 31.9 (CH\textsubscript{2}), 63.4 (CH), 78.2 (CH), 116.0 (CH), 128.2 (2CH), 128.5 (CH), 128.5 (2CH), 129.5 (2CH), 130.1 (C), 148.4 (C); MS (ESI\textsuperscript{+}, m/z): 251 [(M+Na)\textsuperscript{+}, 32%], 229 [(M+H)\textsuperscript{+}, 100%]; (S,S)-3e: [\( \alpha \)]\textsubscript{20}D: -45.0 (c 1, CHCl\textsubscript{3}), >99% ee; Analytical separation (HPLC): Chiralcel OD n-hexane/EtOH (90:10), 0.8 mL/min, 20 °C, \( t_R \) (S,S)= 16.6 min, \( t_R \) (R,R)= 20.6 min.

Spectroscopical data of (1S,2S)-2-(1H-imidazol-1-yl)cyclohexanol (4a)

(1S,2S)-2-(1H-imidazol-1-yl)cyclohexanol (4a). \( R_t \) (10% MeOH/CHCl\textsubscript{3}): 0.34; Mp: 132-133 °C; IR (KBr): ν 3725, 2975, 1492, 1230, 1054, 1031 cm\textsuperscript{-1}; \(^1\)H NMR (CDCl\textsubscript{3}, 300.13 MHz): \( \delta \) 1.32-1.47 (m, 3H), 1.59-1.88 (m, 3H), 2.01-2.16 (m, 2H), 3.53-3.69 (m, 2H), 4.77 (s, 1H), 6.82 (s, 1H), 6.89 (s, 1H), 7.31 (s, 1H); \(^{13}\)C NMR (CDCl\textsubscript{3}, 75.5 MHz): \( \delta \) 24.3 (CH\textsubscript{2}), 29.0 (CH\textsubscript{2}), 34.2 (CH\textsubscript{2}), 63.8 (CH), 72.8 (CH), 117.0 (CH), 128.0 (CH), 136.0 (CH); MS (ESI\textsuperscript{+}, m/z): 167 [(M+H)\textsuperscript{+}, 100%]; (S,S)-4a: [\( \alpha \)]\textsubscript{20}D: +12.1 (c 1, CHCl\textsubscript{3}), >99% ee; Analytical separation (HPLC) Chiralpak AS n-hexane/2-propanol (90:10), 0.8 mL/min, 20 °C, \( t_R \) (S,S)= 21.9 min, \( t_R \) (R,R)= 30.3 min.
Spectroscopical data of (1S,2S)-2-(4-methyl-1H-imidazol-1-yl)cyclohexanol (4b)

(1S,2S)-2-(4-methyl-1H-imidazol-1-yl)cyclohexanol (4b). R<sub>f</sub> (10% MeOH/CHCl<sub>3</sub>): 0.36; Mp: 89-91 °C; IR (KBr): ν 3456, 2984, 1503, 1125, 1039 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300.13 MHz): δ 1.32-1.42 (m, 3H), 1.59-1.84 (m, 3H), 1.99-2.17 (m, 2H), 2.04 (s, 3H), 3.53-3.69 (m, 2H), 5.00 (s, 1H), 6.60 (s, 1H), 7.27 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz): δ 13.2 (CH<sub>3</sub>), 24.3 (CH<sub>2</sub>), 25.1 (CH<sub>2</sub>), 32.0 (CH<sub>2</sub>), 34.0 (CH<sub>2</sub>), 64.0 (CH), 72.8 (CH), 113.3 (CH), 135.0 (CH), 136.8 (C); MS (ESI<sup>+</sup>, m/z): 181 [(M+H)<sup>+</sup>, 100%]; (S,S)-4b: [α]<sup>20</sup> <sub>D</sub>: +20.5 (c 1, CHCl<sub>3</sub>), 95% ee; Analytical separation (HPLC): Chiralcel OD n-hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, t<sub>R</sub> (S,S)= 19.1 min, t<sub>R</sub> (R,R)= 24.2 min.

Spectroscopical data of (1S,2S)-2-(4-phenyl-1H-imidazol-1-yl)cyclohexanol (4c)

(1S,2S)-2-(4-phenyl-1H-imidazol-1-yl)cyclohexanol (4c). R<sub>f</sub> (10% MeOH/CHCl<sub>3</sub>): 0.35; Mp: 184-186 ºC; IR (KBr): ν 3200, 3123, 1575, 1503, 1324, 1021 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300.13 MHz): δ 1.25-1.40 (m, 3H), 1.54-1.79 (m, 3H), 1.93-2.18 (m, 2H), 3.53-3.63 (m, 1H), 5.90 (s, 1H), 6.97 (s, 1H), 7.18-7.28 (m, 4H), 7.48 (d, 3<sup>3</sup>J<sub>HH</sub> = 8.1 Hz, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75.5 MHz): δ 24.2 (CH<sub>2</sub>), 24.9 (CH<sub>2</sub>), 32.0 (CH<sub>2</sub>), 34.0 (CH<sub>2</sub>), 64.2 (CH), 72.6 (CH), 113.0 (CH), 124.4 (2CH), 126.3 (CH), 128.2 (2CH), 133.6 (C), 136.1 (CH), 140.6 (C); MS (ESI<sup>+</sup>, m/z): 243 [(M+H)<sup>+</sup>, 100%]; (S,S)-4c: [α]<sup>20</sup> <sub>D</sub>: +31.5 (c 1, CHCl<sub>3</sub>), 99% ee; Analytical separation (HPLC) Chiralcel OD n-hexane/2-propanol (80:20), 0.8 mL/min, 20 ºC, t<sub>R</sub> (R,R)= 17.2 min, t<sub>R</sub> (S,S)= 22.2 min.
Spectroscopical data of \((1S,2S)\)-2-(2-methyl-1\(H\)-imidazol-1-yl)cyclohexanol (4d)

\(1S,2S\)-2-(2-methyl-1\(H\)-imidazol-1-yl)cyclohexanol (4d). \(R_f\) (10% MeOH/CHCl\(_3\)): 0.36; Mp: 137-139 \(^\circ\)C; IR (KBr): \(\nu\) 3319, 2925, 1525, 1221, 1123 \(\text{cm}^{-1}\); \(^1\)H NMR (CDCl\(_3\), 300.13 MHz): \(\delta\) 1.30-2.10 (m, 8H), 2.24 (s, 3H), 3.53-3.63 (m, 2H), 5.90 (s, 1H), 6.54 (s, 1H), 6.69 (s, 1H); \(^{13}\)C NMR (CDCl\(_3\), 75.5 MHz): \(\delta\) 13.2 (CH\(_3\)), 24.2 (CH\(_2\)), 25.0 (CH\(_2\)), 32.0 (CH\(_2\)), 34.2 (CH\(_2\)), 61.8 (CH), 72.9 (CH), 114.4 (CH), 126.7 (CH), 145.0 (C); MS (ESI\(^+\), \(m/z\)): 181 [(M+H\(^+\)), 100%]; \((S,S)\)-4d: \([\alpha]_{D}^{20\circ}\) = +11.3 (c 1, CHCl\(_3\)), 95% ee; Analytical separation (HPLC) Chiralcel OD \(n\)-hexane/2-propanol (90:10), 0.8 mL/min, 20 \(^\circ\)C, \(t_R\) (S,S) = 15.8 min, \(t_R\) (R,R) = 25.1 min.

Spectroscopical data of \((1S,2S)\)-2-(2-phenyl-1\(H\)-imidazol-1-yl)cyclohexanol (4e)

\(1S,2S\)-2-(2-phenyl-1\(H\)-imidazol-1-yl)cyclohexanol (4e). \(R_f\) (3% MeOH/CHCl\(_3\)): 0.30; Mp: 201-203 \(^\circ\)C; IR (KBr): \(\nu\) 2953, 2924, 2854, 1465, 1377, 1265, 1090, 961 \(\text{cm}^{-1}\); \(^1\)H NMR (CD\(_3\)OD, 300.13 MHz): \(\delta\) 1.40-2.29 (m, 8H), 3.98-4.20 (m, 2H), 7.27 (s, 1H), 7.55 (s, 1H), 7.66-7.85 (m, 5H); \(^{13}\)C NMR (CD\(_3\)OD, 75.5 MHz): \(\delta\) 26.6 (CH\(_3\)), 27.4 (CH\(_2\)), 35.7 (CH\(_2\)), 37.2 (CH\(_2\)), 64.7 (CH), 75.1 (CH), 119.6 (CH), 129.8 (CH), 130.9 (2CH), 131.5 (CH), 132.1 (2CH), 133.2 (C), 150.5 (C); MS (ESI\(^+\), \(m/z\)): 243 [(M+H\(^+\)), 100%]; Analytical separation (HPLC) Chiralpak IA \(n\)-hexane/2-propanol (90:10), 0.8 mL/min, 40 \(^\circ\)C, \(t_R\) (S,S) = 15.8 min, \(t_R\) (R,R) = 25.1 min.
Spectroscopical data of (1S,2S)-2-(1H-imidazol-1-yl)cyclopentyl acetate (5a)

(1R,2R)-2-(1H-imidazol-1-yl)cyclopentyl acetate (5a). Rf (5% MeOH/CHCl3): 0.30; IR (NaCl): v 3433, 3116, 2970, 2880, 1738, 1502, 1375, 1241, 1084, 1050 cm⁻¹; ¹H NMR (CDCl₃, 300.13 MHz): δ 1.65-1.76 (m, 1H), 1.86-1.98 (m, 3H), 2.00 (s, 3H), 2.17-2.38 (m, 2H), 4.44 (dt, ²JHH = 7.9, 5.6 Hz, 1H), 5.06 (dt, ²JHH = 7.4, 5.6 Hz, 1H), 6.97 (s, 1H), 7.06 (s, 1H), 7.64 (s, 1H); ¹³C NMR (CDCl₃, 75.5 MHz): δ 20.9 (CH₂), 21.1 (CH₃), 29.9 (CH₂), 30.1 (CH₂), 62.5 (CH), 79.9 (CH), 117.3 (CH), 128.8 (CH), 136.0 (CH), 170.4 (C); MS (ESI⁺, m/z): 217 [(M+Na)⁺, 95%], 195 [(M+H)⁺, 100%]; (R,R)-5a: [α]²₀D: -61.8 (c 1, CHCl₃), >99% ee; Analytical separation (HPLC) Chiralcel OB-H n-hexane/EtOH (95:5), 0.8 mL/min, 20 ºC, tᵣ (S,S)= 20.8 min, tᵣ (R,R)= 24.0 min.

Spectroscopical data of (1R,2R)-2-(4-methyl-1H-imidazol-1-yl)cyclopentyl acetate (5b)

(1R,2R)-2-(4-methyl-1H-imidazol-1-yl)cyclopentyl acetate (5b). Rf (5% MeOH/CHCl3): 0.31; IR (NaCl): v 3129, 2969, 2879, 1737, 1498, 1475, 1374, 1240, 1046 cm⁻¹; ¹H NMR (CDCl₃, 300.13 MHz): δ 1.60-1.75 (m, 1H), 1.87-2.01 (m, 3H), 2.01 (s, 3H), 2.03-2.35 (m, 2H), 4.38 (q, ³JHH = 6.07 Hz, 1H), 4.98-5.14 (m, 1H), 6.69 (s, 1H), 7.62 (s, 1H); ¹³C NMR (CDCl₃, 75.5 MHz): δ 13.0 (CH₃), 20.1 (CH₂), 20.8 (CH₃), 29.9 (CH₂), 30.0 (CH₂), 62.5 (CH), 79.8 (CH), 113.6 (CH), 134.9 (CH), 137.6 (C), 170.4 (C); MS (ESI⁺, m/z): 231 [(M+Na)⁺, 100%], 209 [(M+H)⁺, 45%]; (R,R)-5b: [α]²₀D: -46.3 (c 1, CHCl₃), >99% ee; Analytical separation (HPLC) Chiralcel OB-H n-hexane/EtOH (98:2), 0.8 mL/min, 20 ºC, tᵣ (R,R)= 39.9 min, tᵣ (S,S)= 46.8 min.
Spectroscopical data of (1R,2R)-2-(4-phenyl-1H-imidazol-1-yl)cyclopentyl acetate (5c)

(1R,2R)-2-(4-phenyl-1H-imidazol-1-yl)cyclopentyl acetate (5c). \( R_f \) (5% MeOH/CHCl₃): 0.48; IR (NaCl): \( \nu = 2968, 1736, 1606, 1484, 1373, 1240, 1047, 749 \text{ cm}^{-1} \); \(^1\)H NMR (CDCl₃, 300.13 MHz): \( \delta = 1.74-1.85 \) (m, 1H), 1.93-2.05 (m, 3H), 2.07 (s, 3H), 2.24-2.34 (m, 1H), 4.56 (td, \( \frac{3}{2} J_{HH} = 7.9, 5.9 \text{ Hz}, 1H \)), 5.15 (dt, \( \frac{3}{2} J_{HH} = 7.4, 5.7 \text{ Hz}, 1H \)), 7.30-7.43 (m, 4H), 7.79 (d, \( \frac{3}{2} J_{HH} = 7.8 \text{ Hz}, 2H \)), 8.11 (s, 1H); \(^13\)C NMR (CDCl₃, 75.5 MHz): \( \delta = 20.9 \) (CH₂), 21.1 (CH₃), 30.0 (CH₂), 30.1 (CH₂), 63.5 (CH), 79.7 (CH), 113.1 (CH), 125.1 (2CH), 127.8 (CH), 128.7 (2CH), 135.7 (CH), 140.1 (C), 145.3 (C), 170.4 (C); MS (ESI\(^+\), \( m/z \)): 293 \([\text{M+Na}]^+, 65\%\), 271 \([\text{M+H}]^+, 100\%\); \( (R,R)-5c: [\alpha]_{20}^D = -54.5 \) (c 1, CHCl₃), >99% ee; Analytical separation (HPLC): Chiralpak AS n-hexane/EtOH (96:4), 0.8 mL/min, 40 °C, \( t_R (R,R) = 16.5 \text{ min}, t_R (R,R) = 19.9 \text{ min} \).

Spectroscopical data of (1R,2R)-2-(2-methyl-1H-imidazol-1-yl)cyclopentyl acetate (5d)

(1R,2R)-2-(2-methyl-1H-imidazol-1-yl)cyclopentyl acetate (5d). \( R_f \) (5% MeOH/CHCl₃): 0.29; IR (NaCl): \( \nu = 2972, 2881, 2487, 2361, 1959, 1793, 1528, 1498, 1422, 1374, 1240, 1152, 1048, 913, 754 \text{ cm}^{-1} \); \(^1\)H NMR (CDCl₃, 300.13 MHz): \( \delta = 1.66-1.70 \) (m, 1H), 1.72-1.98 (m, 3H), 2.02 (s, 3H), 2.18-2.37 (m, 2H), 2.45 (s, 3H), 4.45 (q, \( \frac{3}{2} J_{HH} = 7.1 \text{ Hz}, 1H \)), 5.04 (q, \( \frac{3}{2} J_{HH} = 7.1 \text{ Hz}, 1H \)), 6.84 (s, 1H), 6.95 (s, 1H); \(^13\)C NMR (CDCl₃, 75.5 MHz): \( \delta = 12.4 \) (CH₃), 20.5 (CH₂), 20.7 (CH₃), 29.6 (CH₂), 29.9 (CH₂), 60.5 (CH), 79.6 (CH), 114.9 (CH), 126.3 (CH), 144.6 (C), 169.8 (C); MS (ESI\(^+\), \( m/z \)): 231 \([\text{M+Na}]^+, 30\%\), 209 \([\text{M+H}]^+, 100\%\); \( (R,R)-5d: [\alpha]_{20}^D = +3.3 \) (c 1, CHCl₃), 95% ee; Analytical separation (HPLC) Chiralcel OD n-hexane/2-propanol (90:10), 0.8 mL/min, 20 °C, \( t_R (R,R) = 13.0 \text{ min}, t_R (S,S) = 18.1 \text{ min} \).
Spectroscopical data of (1S,2R)-2-(2-phenyl-1H-imidazol-1-yl)cyclopentyl acetate (5e)

(1R,2R)-2-(2-phenyl-1H-imidazol-1-yl)cyclopentyl acetate (5e). Rf (5% MeOH/CHCl₃): 0.46; IR (NaCl): ν 3101, 2970, 2883, 2350, 1727, 1530, 1468, 1416, 1355, 1246, 1130, 1039, 918, 770, 754 cm⁻¹; ¹H NMR (CDCl₃, 300.13 MHz): δ 1.59-1.70 (m, 1H), 1.73-1.94 (m, 3H), 1.95 (s, 3H), 2.16-2.35 (m, 2H), 4.57 (q, 3J_HH = 6.9 Hz, 1H), 5.16 (q, 3J_HH = 6.9 Hz, 1H), 7.06 (d, 3J_HH = 1.3 Hz, 1H), 7.18 (d, 3J_HH = 1.3 Hz, 1H), 7.45-7.71 (m, 3H), 7.65-7.71 (m, 2H); ¹³C NMR (CDCl₃, 75.5 MHz): δ 20.9 (CH₂), 21.1 (CH₂), 30.0 (CH₂), 31.1 (CH₂), 62.8 (CH), 79.8 (CH), 116.2 (CH), 128.4 (2CH), 128.7 (CH), 129.2 (CH), 129.3 (2CH), 130.6 (C), 148.5 (C), 170.1 (C); MS (ESI⁺, m/z): 293 [(M+Na)⁺, 47%], 271 [(M+H)⁺, 100%]; (R,R)-5e: [α]²⁰_D: +44.6 (c 1, CHCl₃), 96% ee; Analytical separation (HPLC): Chiralcel OD hexane/2-propanol (90:10), 0.8 mL/min, 40 ºC, tᵣ (S,S)= 17.7 min, tᵣ (R,R)= 21.7 min.

Spectroscopical data of (1R,2R)-2-(1H-imidazol-1-yl)cyclohexyl acetate (6a)

(1R,2R)-2-(1H-imidazol-1-yl)cyclohexyl acetate (6a). Rf (5% MeOH/CHCl₃): 0.25; IR (NaCl): ν 3390, 2942, 2864, 1734, 1499, 1376, 1329, 1083, 1053, 1031 cm⁻¹; ¹H NMR (CDCl₃, 300.13 MHz): δ 1.33-1.52 (m, 3H), 1.70-1.96 (m, 6H), 2.07-2.23 (m, 2H), 3.87-4.10 (m, 1H), 4.79-4.94 (m, 1H), 6.96 (s, 1H), 7.05 (s, 1H), 7.74 (s, 1H); ¹³C NMR (CDCl₃, 75.5 MHz): δ 20.6 (CH₃), 23.6 (CH₂), 24.5 (CH₂), 31.1 (CH₂), 32.1 (CH₂), 60.1 (CH), 74.3 (CH), 116.8 (CH), 127.9 (CH), 136.2 (CH), 169.7 (C); MS (ESI⁺, m/z): 209 [(M+H)⁺, 100%]; (R,R)-6a: [α]²⁰_D: -6.5 (c 1, CHCl₃), >99% ee; Analytical separation (HPLC) Chiralpak AS hexane/2-propanol (90:10), 0.8 mL/min, 20 ºC, tᵣ (S,S)= 20.7 min, tᵣ (R,R)= 30.9 min.
Spectroscopical data of (1R,2R)-2-(4-methyl-1H-imidazol-1-yl)cyclohexyl acetate (6b)

(1R,2R)-2-(4-methyl-1H-imidazol-1-yl)cyclohexyl acetate (6b). Rf (5% MeOH/CHCl₃): 0.27; IR (NaCl): ν 2965, 2910, 1737, 1525, 1501, 1365, 1331, 1089 cm⁻¹; ¹H NMR (CDCl₃, 300.13 MHz): δ 1.31-1.46 (m, 3H), 1.75-1.90 (m, 6H), 2.11-2.19 (m, 5H), 3.80-3.89 (m, 1H), 4.80-4.89 (m, 1H), 6.62 (s, 1H), 7.36 (s, 1H); ¹³C NMR (CDCl₃, 75.5 MHz): δ 13.6 (CH₃), 20.7 (CH₃), 23.8 (CH₂), 24.6 (CH₂), 31.2 (CH₂), 32.3 (CH₂), 59.6 (CH), 74.4 (CH), 112.8 (CH), 135.6 (CH), 138.1 (C), 169.8 (C); MS (ESI⁺, m/z): 223 [(M+H)⁺, 100%]; (R,R)-6b: [α]²⁰D: -9.4 (c 1, CHCl₃), >99% ee; Analytical separation (HPLC): Chiralcel OD n-hexane/2-propanol (90:10), 0.8 mL/min, 20 °C, tᵣ (S,S)= 12.0 min, tᵣ (R,R)= 14.0 min.

Spectroscopical data of (1R,2R)-2-(4-phenyl-1H-imidazol-1-yl)cyclohexyl acetate (6c)

(1R,2R)-2-(4-phenyl-1H-imidazol-1-yl)cyclohexyl acetate (6c). Rf (5% MeOH/CHCl₃): 0.24; IR (NaCl): ν 2950, 2899, 1735, 1503, 1379, 1329, 1083, cm⁻¹; ¹H NMR (CDCl₃, 300.13 MHz): δ 1.42-1.51 (m, 3H), 1.80-1.95 (m, 6H), 2.20-2.25 (m, 2H), 3.93-4.00 (m, 1H), 4.92-4.98 (m, 1H), 7.23-7.38 (m, 4H), 7.55 (s, 1H), 7.76 (d, 3JHH = 8.1 Hz, 2H); ¹³C NMR (CDCl₃, 75.5 MHz): δ 20.7 (CH₂), 23.8 (CH₂), 24.7 (CH₂), 31.3 (CH₂), 32.4 (CH₂), 60.0 (CH), 74.4 (CH), 112.4 (CH), 124.6 (2CH), 126.6 (CH), 128.5 (2CH), 134.0 (C), 136.7 (CH), 142.0 (C), 170.1 (C); MS (ESI⁺, m/z): 285 [(M+H)⁺, 100%]; (R,R)-6c: [α]²⁰D: -10.1 (c 1, CHCl₃), >99% ee; Analytical separation (HPLC): Chiralcel OD n-hexane/2-propanol (80:20), 0.8 mL/min, 20 °C, tᵣ (R,R)= 37.4 min, tᵣ (S,S)= 42.4 min.
Spectroscopical data of \((1R,2R)-2\text{-}(2\text{-methyl-1H-imidazol-1-yl})\text{cyclohexyl acetate (6d)}\)

\((1R,2R)-2\text{-}(2\text{-methyl-1H-imidazol-1-yl})\text{cyclohexyl acetate (6d)).} \text{ Rf} (5\% \text{ MeOH/CHCl}_3): 0.27; IR (NaCl): \nu 2975, 2915, 1736, 1537, 1525, 1509, 1360, 1325 \text{ cm}^{-1}; ^1H \text{ NMR (CDCl}_3, 300.13 \text{ MHz): } \delta 1.34-1.50 \text{ (m, 3H), 1.70-1.90 (m, 6H), 2.05-2.18 (m, 2H), 2.41 (s, 3H), 3.86-3.95 (m, 1H), 6.85 (s, 1H), 6.90 (s, 1H); ^13C \text{ NMR (CDCl}_3, 75.5 \text{ MHz): } \delta 13.2 \text{ (CH}_3\text{), 20.7 \text{ (CH}_3\text{), 23.8 \text{ (CH}_2\text{), 24.8 \text{ (CH}_2\text{), 31.4 \text{ (CH}_2\text{), 32.4 \text{ (CH}_2\text{), 58.1 \text{ (CH), 74.8 \text{ (CH), 115.1 \text{ (CH), 127.3 \text{ (CH), 144.7 \text{ (C), 169.9 \text{ (C); MS (ESI}^+, m/z): 223 [(M+H)}^+, 100\%; (R,R)-6d: [\alpha]^{20\circ}_{D}: -2.4 \text{ (c 1, CHCl}_3), >99\% ee; Analytical separation (HPLC): Chiralcel OD n-hexane/2-propanol (90:10), 0.8 mL/min, 20 \text{ °C, t}_R (S,S) = 10.3 \text{ min, t}_R (R,R) = 11.4 \text{ min.}}\)

Spectroscopical data of \((1R,2R)-2\text{-}(2\text{-phenyl-1H-imidazol-1-yl})\text{cyclohexyl acetate (6e)}\)

\((1R,2R)-2\text{-}(2\text{-phenyl-1H-imidazol-1-yl})\text{cyclohexyl acetate (6e)).} \text{ Rf} (5\% \text{ MeOH/CHCl}_3): 0.27; \text{ Mp: 114-116 °C; IR (KBr): } \nu 2865, 1737, 1646, 1467, 1417, 1375, 1237, 1038 \text{ cm}^{-1}; ^1H \text{ NMR (CDCl}_3, 300.13 \text{ MHz): } \delta 1.26-1.46 \text{ (m, 3H), 1.73-1.85 (m, 6H), 2.00-2.14 (m, 2H), 4.17-4.27 (m, 1H), 4.98-5.07 \text{ (m, 1H), 7.07 \text{ (s, 1H), 7.13 \text{ (s, 1H), 7.44-7.49 (m, 5H); ^13C \text{ NMR (CDCl}_3, 75.5 \text{ MHz): } \delta 20.6 \text{ (CH}_3\text{), 23.7 \text{ (CH}_2\text{), 24.5 \text{ (CH}_2\text{), 31.3 \text{ (CH}_2\text{), 33.2 \text{ (CH}_2\text{), 58.5 \text{ (CH), 74.6 \text{ (CH), 116.4 \text{ (CH), 128.5 \text{ (2CH), 128.6 \text{ (CH), 128.7 \text{ (CH), 129.1 \text{ (2CH), 130.6 \text{ (C), 148.1 \text{ (C), 169.6 \text{ (C); MS (ESI}^+, m/z): 285 [(M+H)}^+, 100%; (R,R)-6e: [\alpha]^{20\circ}_{D}: +91.0 \text{ (c 1, CHCl}_3), >99\% ee; Analytical separation (HPLC): Chiralcel OJ-H n-hexane/2-propanol (90:10), 0.8 mL/min, 40 \text{ °C, t}_R (R,R) = 8.0 \text{ min, t}_R (S,S) = 8.8 \text{ min.}}\)
Chemoenzymatic Synthesis of Optically Active 2-(2- or 4-substituted-1H-imidazol-1-yl)cyloalcanols. Chiral additives for (L)-Proline

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(S,S)-3b
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(S,S)-3d
(S,S)-3d
(S,S)-3e
\[(S,S)-4a\]
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OH
N
N
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OH
N
N
(S,S)-4c

(S,S)-4c
$\text{(R,R)-5b}$
(R,R)-5e
\((R,R)-6a\)
(R,R)-6b

(R,R)-(_)-37b
