Double axial chirality promoted asymmetric [2,3] Stevens rearrangement of \(N\)-cinnamyl L-alanine amide-derived ammonium ylides

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Effects of the base and solvent in the rearrangement of 1d

To investigate the effects of base and solvent on the asymmetric [2,3] Stevens rearrangement, we examined the reactions of 1d under various conditions. When the reaction was performed with solid potassium tert-butoxide under the same conditions, nearly the same yield and selectivity were obtained (Entry 1). We tested analogous bases, such as sodium tert-butoxide in THF or potassium bis(trimethylsilyl)amide (KHMDS) in toluene, and did not observe remarkable improvements (Entries 2 and 3). The use of other solvents such as dichloromethane, tert-butyl methyl ether, acetonitrile, and DMF, resulted in lower yields or enantioselectivities (Entries 4–8). The rearrangement in DMSO at room temperature yielded a messy mixture (Entry 9). Alcoholic solvents, such as tert-butanol, resulted in a lower yield and selectivity (Entry 10).

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Base</th>
<th>Temp (°C)</th>
<th>Yield of 2d (%)&lt;sup&gt;a,b&lt;/sup&gt;</th>
<th>Ee of 2d (%)&lt;sup&gt;c&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>1</td>
<td>THF</td>
<td>'BuOK solid</td>
<td>0</td>
<td>72</td>
<td>71</td>
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<tr>
<td>2</td>
<td>THF</td>
<td>'BuONa in THF</td>
<td>0</td>
<td>48</td>
<td>71</td>
</tr>
<tr>
<td>3</td>
<td>THF</td>
<td>KHMDS in toluene</td>
<td>0</td>
<td>78</td>
<td>64</td>
</tr>
<tr>
<td>4</td>
<td>CH₂Cl₂</td>
<td>'BuOK in THF</td>
<td>0</td>
<td>39</td>
<td>51</td>
</tr>
<tr>
<td>5</td>
<td>CH₂Cl₂</td>
<td>'BuOK solid</td>
<td>0</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>6</td>
<td>'BuOMe</td>
<td>'BuOK solid</td>
<td>0</td>
<td>67</td>
<td>56</td>
</tr>
<tr>
<td>7</td>
<td>MeCN</td>
<td>'BuOK in THF</td>
<td>0</td>
<td>27</td>
<td>50</td>
</tr>
<tr>
<td>8</td>
<td>DMF</td>
<td>'BuOK in THF</td>
<td>0</td>
<td>34</td>
<td>53</td>
</tr>
<tr>
<td>9</td>
<td>DMSO</td>
<td>'BuOK in THF</td>
<td>rt</td>
<td>messy</td>
<td>–</td>
</tr>
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<td>10</td>
<td>'BuOH</td>
<td>'BuOK in THF</td>
<td>rt</td>
<td>45</td>
<td>65</td>
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</table>

<sup>a</sup> Isolated yield.

<sup>b</sup> Obtained as a single diastereomer.

<sup>c</sup> Determined by HPLC analysis using a chiral column.
Experimental details and products characterizations

**General**: Infrared spectra were recorded on a Perkin Elmer Spectrum GX FT-IR spectrometer. $^1$H and $^{13}$C NMR spectra were measured on a Varian 400 MHz spectrometer ($^1$H: 400 MHz, $^{13}$C: 100 MHz) and a 700 MHz spectrometer ($^1$H: 700 MHz, $^{13}$C: 175 MHz). The splitting patterns are denoted as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; and br, broad peak. Specific rotations (over 10% ee compounds) were recorded on a JASCO Polarimeter P–1010. High-resolution mass spectra were measured on a Thermo Fisher Scientific LC/FT-MS spectrometer. Elemental analyses were recorded on a J-Science Lab Micro Corder JM10. HPLC analyses were performed using a JASCO HPLC pump PU-2080 and a UV/VIS detector UV-2075. Reactions involving air- or moisture-sensitive compounds were conducted in appropriate round-bottomed flasks with a magnetic stirring bars under an argon atmosphere. Reactions under lower temperature were carried out using a Constant Temp. Bath with Magnetic Stirrer (PSL-1400 and PSL-1800, EYELA, Japan) and a Ultra-Cooling Reactor (UCR-150, Techno Sigma Co., Ltd., Japan). Tetrahydrofuran (THF) was purchased from KANTO Chemical Co., Inc., Japan as an anhydrous solvent. Aminomethylated polystyrene EHL (200–400 mesh), 2% DVB was purchased from Merck Millipore (Novabiochem). For thin layer chromatography (TLC) analysis throughout this work, Merck TLC plates (silica gel 60 F254) were used. The products were purified by preparative column chromatography on silica gel (silica gel 60N, spherical neutral, KANTO Chemical Co., Inc., Japan).

**Representative procedure for base-induced asymmetric [2,3] Stevens rearrangement of 1d via memory of chirality**

\[ \text{1d} \xrightarrow{^t\text{BuOK, THF solution}} \text{2d} \]

A 1.0 M THF solution of potassium tert-butoxide (0.29 mL, 0.29 mmol) was added to a suspension of 1d (112 mg, 0.239 mmol) in THF (2.4 mL) at –92 °C under an argon atmosphere. After stirring for 3 h at the same temperature, the resulting mixture was poured into saturated aqueous ammonium chloride. The mixture was diluted with water and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and brine. The solution was dried over sodium sulfate and concentrated. Purification of the residue by chromatography on silica gel (hexane/ethyl acetate = 10/1 as the eluent) gave 1-(3,4-dihydroquinolin-1(2H)-yl)-2-methyl-3-phenyl-2-(piperidin-1-yl)pent-4-en-1-one (2d) (57.9 mg, 62% yield) as colorless crystals; [α]$_{24}^{25}$ +159.0 (c 1.00, EtOH); 91% ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 98.7/1.3 as the eluent (pre-eluted with n-hexane/2-propanol = 90/10), flow rate = 0.50 mL/min, $t_R = 22.3$ min for minor-2d and 60.4 min for major-2d]; IR (KBr) 3084, 3058, 3030, 2925, 1770, 1674, 1596, 1438, 1398, 1360, 1264, 1168, 1083, 975, 775 cm$^{-1}$; NMR (CDCl$_3$), etc.
3014, 2985, 2937, 2850, 2808, 2814, 2985, 2937, 2850, 2808, 1631, 1598, 1489, 1455, 1440, 1389, 1368, 1276, 1256, 1235, 1206, 1158, 1104, 1064, 1035, 1001, 950, 915, 889, 861, 799, 758, 702 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.31 (2H, d, J = 7.4 Hz, ArH), 7.25-7.19 (2H, m, ArH), 7.13 (1H, tt, J = 7.4, 1.6 Hz, ArH), 7.00-6.96 (1H, m, ArH), 6.90 (1H, ddd, J = 7.4, 1.6 Hz, ArH), 6.86 (1H, ddd, J = 7.4, 1.6 Hz, ArH), 6.56 (1H, d, J = 7.4 Hz, ArH), 6.33 (1H, ddd, J = 17.0, 10.2, 9.0 Hz, CHCH=CH₂), 5.54 (1H, br, CH₂), 5.08-4.97 (2H, m, CHCH=C₂H₅), 4.08 (1H, d, J = 9.0 Hz, C₂H₅CH=CH₂), 3.20-2.70 (3H, br, CH₂), 2.70-2.56 (2H, br, CH₂), 2.46 (2H, br, CH₂), 2.10-1.96 (1H, m, CH₂), 1.94-1.82 (1H, m, CH₂), 1.65-1.39 (6H, m, CH₂), 1.53 (3H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ (mixture of rotamers) 172.6, 172.1, 142.1, 141.6, 140.7, 140.13, 140.06, 139.2, 130.8, 130.2, 130.0, 129.1, 128.6, 128.3, 128.2, 128.1, 126.7, 126.4, 125.2, 125.1, 124.9, 124.8, 124.2, 124.1, 116.3, 115.8, 74.4, 73.4, 57.0, 56.9, 49.3, 48.6, 45.1, 44.1, 26.9, 26.8, 26.3, 25.9, 24.84, 24.79, 24.71, 15.3; HRMS–ESI (m/z): [M+H]⁺ calef for C₂₆H₃₃N₂O: 389.2587. Found: 389.2581. Anal. Calef for C₂₆H₃₃N₂O: C, 78.55; H, 8.37; N, 7.05. Found: C, 78.48; H, 8.25; N, 6.75.

Cyclohexyl 2-methyl-3-phenyl-2-(pyrrolidin-1-yl)pent-4-enoate (2a): colorless oil; 0% ee (determined by HPLC analysis: Daicel Chiralcel OD–H column, n-hexane as the eluent, flow rate = 0.50 mL/min, tᵣ = 19.2 min and 21.1 min); IR (film) 3062, 2936, 2858, 1713, 1636, 1601, 1495, 1453, 1413, 1380, 1358, 1332, 1287, 1230, 1194, 1143, 1106, 1079, 1036, 1013, 988, 968, 946, 912, 866, 842, 827, 789, 742, 704 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.27-7.12 (5H, m, Ph), 6.42 (1H, ddd, J = 17.2, 10.4, 8.2 Hz, CHCH₂), 5.19 (1H, ddd, J = 10.4, 1.4, 1.4 Hz, CHCH=CH₂), 5.10 (1H, ddd, J = 17.2, 1.4, 1.4 Hz, CHCH=CH₂), 4.70 (1H, tt, J = 8.6, 3.6 Hz, OCH), 4.16 (1H, d, J = 8.2 Hz, CHCH₂), 3.12-3.00 (2H, m, CH₂), 2.80-2.68 (2H, m, CH₂), 1.83-1.62 (6H, m, CH₂), 1.62-1.14 (8H, m, CH₂), 1.35 (3H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 171.7, 140.6, 137.7, 130.3, 127.7, 126.5, 116.9, 72.4, 68.2, 53.7, 46.8, 31.9, 31.7, 25.3, 24.0, 23.6, 23.5, 18.3; HRMS–ESI (m/z): [M+H]⁺ calef for C₂₂H₃₂NO₂: 342.2428. Found: 342.2414. Anal. Calef for C₂₂H₃₁NO₂: C, 77.38; H, 9.15; N, 4.10. Found: C, 77.23; H, 9.07; N, 4.08.

2-Methyl-3-phenyl-1,2-di(pyrrolidin-1-yl)pent-4-en-1-one (2b): colorless crystals; < 7% ee [determined by HPLC analysis: Daicel Chiralpak AS–H column, n-hexane/ethanol = 98.5/1.5 as the eluent, flow rate = 0.50 mL/min, tᵣ = 11.3 min and 12.7 min (not baseline separation)]; IR (KBr) 3026, 2968, 2944, 2871, 2814, 1614, 1490, 1453, 1424, 1371, 1336, 1294, 1248, 1216, 1192, 1160, 1147, 1109, 1073, 1031, 1003, 963, 940, 911, 891, 876, 855, 821, 760, 704 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.26-7.11 (5H, m, Ph), 6.36 (1H, ddd, J = 17.2, 10.0, 9.2 Hz, CHCH₂), 5.19 (1H, d, J = 10.0 Hz, CHCH₂), 5.00 (1H, d, J = 17.2 Hz, CHCH₂), 4.70 (1H, d, J = 9.2 Hz, CHCH₂), 3.47-3.18 (3H, m, CH₃), 3.11-2.96 (1H, m, CH₂), 2.95-2.83 (2H, m, CH₂), 2.62-2.50 (2H, m, CH₂), 1.77-1.63 (4H, m, CH₂), 1.63-1.47 (4H, m, CH₂), 1.41 (3H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.3, 142.0, 139.9, 128.8, 127.9, 126.4, 116.0, 69.1, 56.8, 47.7, 47.1, 46.9, 27.0, 24.0, 22.8, 14.1; HRMS–ESI (m/z): [M+H]⁺ calef for C₂₀H₂₉NO⁺: 313.2274. Found: 313.2268. Anal. Calef for C₂₀H₂₉NO: C, 76.88; H, 9.03; N, 8.97. Found: C, 76.54; H, 9.10; N, 8.69.
1-(3,4-Dihydroquinolin-1(2H)-yl)-2-methyl-3-phenyl-2-(pyrrolidin-1-yl)pent-4-en-1-one (2c): colorless crystals; [α]D 330 +70.4 (c 1.00, EtOH); 42% ee (determined by HPLC analysis: Daicel Chiralcel OD–H column, n-hexane/isopropanol = 98/2 as the eluent, flow rate = 0.50 mL/min, tR = 12.8 min for minor-2c and 16.9 min for major-2c); IR (KBr) 3058, 3018, 2945, 2871, 2809, 1636, 1599, 1490, 1454, 1436, 1387, 1340, 1300, 1281, 1256, 1228, 1200, 1172, 1142, 1129, 1121, 1085, 1065, 1032, 1000, 964, 947, 927, 907, 895, 840, 809, 757, 699 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.33-7.28 (2H, m, ArH), 7.28-7.21 (2H, m, ArH), 7.17 (1H, tt, J = 7.2, 1.4 Hz, ArH), 7.00 (1H, dd, J = 7.6, 1.2 Hz, ArH), 6.92 (1H, ddd, J = 7.6, 7.6, 1.2 Hz, ArH), 6.86 (1H, ddd, J = 7.6, 7.6, 1.2 Hz, ArH), 6.45 (1H, dd, J = 7.6, 1.2 Hz, ArH), 6.36 (1H, ddd, J = 17.0, 10.2, 8.4 Hz, CHCH=CH₂), 5.15-5.02 (3H, m, CHCH=CH₂ and CH₂), 4.21 (1H, d, J = 8.4 Hz, CHCH=CH₂), 3.18 (1H, ddd, J = 12.0, 9.2, 5.6 Hz, CH₂), 2.99-2.88 (2H, m, CH₂), 2.74-2.53 (4H, m, CH₂), 2.02-1.78 (2H, m, CH₂), 1.78-1.66 (4H, m, CH₂), 1.45 (3H, s, CH₃), 13C NMR (100 MHz, CDCl₃) δ 172.7, 142.0, 139.7, 131.3, 132.0, 128.2, 128.1, 126.5, 125.0, 124.8, 124.3, 116.5, 70.3, 56.8, 46.9, 44.3, 25.7, 24.0, 23.7, 14.7; HRMS–ESI (m/z): [M+H]+ calcd for C₂₅H₃₁N₂O: 375.2431. Found: 375.2425. Anal. Calcd for C₂₅H₃₀N₂O: C, 80.17; H, 8.07; N, 7.48. Found: C, 80.03; H, 8.09; N, 7.46.

1-(3,4-Dihydroquinolin-1(2H)-yl)-2-(dimethylamino)-2-methyl-3-phenylpent-4-en-1-one (2e): colorless viscous oil; [α]D 2433 +54.0 (c 1.00, EtOH); 30% ee (determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/2-propanol = 90/10 as the eluent, flow rate = 0.50 mL/min, tR = 10.9 min for minor-2e and 12.8 min for major-2e); IR (KBr) 3082, 3058, 3003, 2947, 2868, 2830, 2788, 1634, 1598, 1490, 1452, 1391, 1368, 1340, 1299, 1282, 1259, 1228, 1202, 1159, 1122, 1095, 1046, 1002, 962, 950, 897, 811, 760, 701 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.32 (2H, d, J = 7.6, 1.2 Hz, ArH), 7.24 (2H, dd, J = 7.6, 7.6 Hz, ArH), 7.16 (1H, tt, J = 7.6, 1.2 Hz, ArH), 6.99 (1H, dd, J = 7.6, 1.2 Hz, ArH), 6.92 (1H, ddd, J = 7.6, 7.6, 1.2 Hz, ArH), 6.85 (1H, ddd, J = 7.6, 7.6, 1.2 Hz, ArH), 6.39 (1H, d, J = 7.6 Hz, ArH), 6.33 (1H, ddd, J = 17.1, 10.1, 9.0 Hz, CHCH=CH₂), 5.21 (1H, br, CH₂), 5.14-5.02 (2H, m, CHCH=CH₂), 4.11 (1H, d, J = 9.0 Hz, CHCH=CH₂), 3.06 (1H, ddd, J = 12.0, 9.6, 5.2 Hz, CH₂), 2.71-2.54 (2H, m, CH₂), 2.38 (6H, s, N(CH₃)₂), 2.11-1.98 (1H, m, CH₂), 1.90-1.79 (1H, m, CH₂), 1.44 (3H, s, 2-CH₃); 13C NMR (100 MHz, CDCl₃) δ 172.2, 142.0, 140.4, 139.9, 131.3, 128.8, 128.3, 128.2, 126.6, 125.0, 124.8, 124.4, 116.4, 72.4, 56.7, 44.6, 40.2, 25.7, 23.8, 14.1; HRMS–ESI (m/z): [M+H]+ calcd for C₂₃H₂₉N₂O: 349.2274. Found: 349.2271. Anal. Calcd for C₂₃H₂₉N₂O: 349.2274. Found: 349.2271. Anal. Calcd for C₂₃H₂₉N₂O·(as 0.5H₂O): C, 77.27; H, 8.18; N, 7.84. Found: C, 77.23; H, 8.17; N, 7.94.

1-(Indolin-1-yl)-2-methyl-3-phenyl-2-(piperidin-1-yl)pent-4-en-1-one (2f): colorless crystals; 4% ee (determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 90/10 as the eluent, flow rate = 0.50 mL/min, tR = 9.5 min for major-2f and 12.0 min for minor-2f); IR (KBr) 3076, 3027, 2997, 2933, 2841, 1629, 1595, 1476, 1461, 1377, 1332, 1308, 1253, 1224, 1206, 1168, 1128, 1110, 1075, 1040, 998, 961, 946, 917, 877, 858, 829, 798, 759, 703 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.97 (1H, d, J = 7.6 Hz, ArH), 7.24 (2H, d, J = 7.6 Hz, ArH), 7.14 (2H, t, J = 7.6 Hz, ArH), 7.11-7.03 (3H, m, ArH), 6.93 (1H, ddd, J = 7.6, 7.6, 0.8 Hz, ArH), 6.32 (1H, ddd, J = 16.8, 9.6, 9.6 Hz, CHCH=CH₂), 5.04 (1H, dd, J = 9.6, 1.2 Hz, CHCH=CH₂), 4.99 (1H, d, J = 16.8 Hz, CHCH=CH₂), 4.79-4.63 (1H, m, CH₂), 4.01 (1H, br, CH₂), S5
3.97 (1H, d, J = 9.6 Hz, CHCH=CH2), 3.05-2.67 (2H, m, CH2), 2.90 (2H, br, CH2), 2.49-2.35 (2H, m, CH2), 1.66-1.40 (6H, m, CH2) 1.51 (3H, s, CH3); 13C NMR (100 MHz, CDCl3) δ 171.9, 144.4, 141.8, 140.4, 131.7, 128.6, 128.1, 126.8, 126.5, 123.9, 123.4, 118.3, 115.9, 73.2, 56.1, 49.5, 48.7, 29.2, 26.8, 24.9, 14.8; HRMS–ESI (m/z): [M+H]+ calcd for C25H31N2O: 375.2431. Found: 375.2427.

2-Methyl-1-(phenanthridin-5(6H)-yl)-3-phenyl-2-(piperidin-1-yl)pent-4-en-1-one (2g): colorless crystals; [α]22589 +209.6 (c 1.00, CHCl3); 81% ee (determined by HPLC analysis: Daicel Chiralcel OD–H column, n-hexane/ethanol = 99/1 as the eluent, flow rate = 0.50 mL/min, τR = 18.6 min for minor-2g and 24.8 min for major-2g); IR (KBr) 3068, 3023, 3002, 2940, 2855, 2806, 2764, 1642, 1599, 1486, 1441, 1385, 1315, 1313, 1282, 1263, 1225, 1162, 1103, 1029, 990, 947, 906, 764, 759, 735, 698 cm−1; 1H NMR (400 MHz, CDCl3) δ 7.70 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.61 (1H, dd, J = 8.0, 1.2 Hz, ArH), 7.09 (1H, ddd, J = 17.0, 10.0, 8.6 Hz, CHCH=CH2), 5.07 (1H, d, J = 10.0 Hz, CHCH=C2H), 5.05 (1H, d, J = 17.0 Hz, CHCH=C2H), 4.24 (1H, d, J = 12.0 Hz, CH3), 3.90 (1H, d, J = 8.8 Hz, CHC=CH2), 2.86 (2H, br, CH2), 2.27 (2H, br, CH2), 1.58 (3H, s, CH3), 1.42 (6H, br, CH2); 13C NMR (100 MHz, CDCl3) δ 171.7, 142.0, 141.0, 137.9, 135.1, 132.2, 129.0, 128.5, 128.1, 127.9, 127.1, 126.79, 126.76, 126.1, 125.3, 125.1, 123.4, 123.1, 115.9, 73.3, 57.6, 48.4, 48.1, 26.41, 26.39, 24.5; HRMS–ESI (m/z): [M+H]+ calcd for C30H33N2O: 437.2587. Found: 437.2585.

N-Benzhydryl-N2-dimethyl-3-phenyl-2-(piperidin-1-yl)pent-4-enamide (2i): colorless crystals; < 7% ee [determined by HPLC analysis: Daicel Chiralcel OD–H column, n-hexane/2-propanol = 99/1 as the eluent, flow rate = 0.50 mL/min, τR = 16.3 min and 17.4 min (not baseline separation)]; IR (KBr) 3054, 3026, 3005, 2985, 2930, 2851, 2806, 1619, 1493, 1475, 1452, 1418, 1382, 1306, 1276, 1237, 1213, 1160, 1105, 1074, 1032, 998, 954, 924, 891, 867, 832, 798, 751, 735, 702 cm−1; 1H NMR (400 MHz, CDCl3) δ 7.32-7.19 (8H, m, ArH), 7.15-7.09 (3H, m, ArH), 7.04 (2H, t, J = 7.4 Hz, ArH), 6.70 (1H, s, CHPh2), 6.30-6.06 (2H, m, ArH), 6.13 (1H, ddd, J = 17.0, 9.6, 8.8 Hz, CHCH=CH2), 4.94 (1H, d, J = 9.6 Hz, CHCH=CH2), 4.84 (1H, d, J = 17.0 Hz, CHCH=CH2), 3.90 (1H, d, J = 8.8 Hz, CHCH=CH2), 3.10 (3H, s, NCH3), 2.81 (2H, br, CH2), 2.33 (2H, br, CH2), 1.65-1.35 (6H, m, CH2), 1.54 (3H, s, 2-CH3); 13C NMR (100 MHz, CDCl3) δ 173.8, 141.8, 141.6, 139.9, 139.1, 129.1, 128.7, 128.6, 128.4, 128.1, 127.9, 127.0, 126.6, 126.5, 115.3, 71.9, 62.2, 57.2, 48.5, 33.3, 26.7, 24.9, 15.7; HRMS–ESI (m/z): [M+H]+ calcd for C31H37N2O: 453.2900. Found: 453.2901.

Found: C, 81.99; H, 8.02; N, 6.22.
N-Methoxy-N,2-dimethyl-3-phenyl-2-(piperidin-1-yl)pent-4-enamide (2j): pale brown viscous oil; < 2% ee [determined by HPLC analysis: Daicel Chiralcel OD–H column, n-hexane/2-propanol = 99/1 as the eluent, flow rate = 0.50 mL/min, \( t_R = 14.4 \) min and 15.3 min (not baseline separation)]; IR (film) 3060, 2931, 2852, 2813, 1651, 1492, 1452, 1408, 1370, 1306, 1277, 1259, 1233, 1158, 1106, 1073, 1029, 1000, 950, 915, 885, 860, 829, 796, 781, 761, 737, 702 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.28-7.12 (5H, m, Ph), 6.27 (1H, ddd, \( J = 17.1, 10.2, 8.8 \) Hz, CHCH=CH\(_2\)), 5.06 (1H, ddd, \( J = 10.2, 1.0, 1.0 \) Hz, CHCH=CH\(_2\)), 4.97 (1H, ddd, \( J = 17.1, 1.0, 1.0 \) Hz, CHCH=CH\(_2\)), 4.03 (1H, br, CHCH=CH\(_2\)), 3.33 (3H, br, OCH\(_3\)), 3.03 (3H, br, NCH\(_3\)), 2.82 (2H, br, CH\(_2\)), 2.47-2.32 (2H, m, CH\(_2\)), 1.62-1.50 (4H, m, CH\(_2\)), 1.49-1.39 (2H, m, CH\(_2\)), 1.44 (3H, s, 2-CH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 171.8, 141.9, 139.8, 129.1, 127.9, 126.4, 116.2, 71.3, 59.4, 55.3, 48.6, 35.4, 26.6, 24.9, 14.7; HRMS–ESI (m/z): [M+H]\(^+\) calcd for C\(_{26}\)H\(_{32}\)ClN\(_2\)O: 423.2198. Found: 423.2197. Anal. Calcd for C\(_{26}\)H\(_{31}\)ClN\(_2\)O: C, 73.83; H, 6.62. Found: C, 73.49; H, 7.43; N, 6.68.

N-(tert-Butoxy)-N,2-dimethyl-3-phenyl-2-(piperidin-1-yl)pent-4-enamide (2k): pale brown oil; [\( \alpha \)^2\(^{389}\) - 37.1 (c 1.00, EtOH); 64% ee (determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 98/2 as the eluent, flow rate = 0.50 mL/min, \( t_R = 8.5 \) min for major-2k and 9.4 min for minor-2k); IR (film) 3059, 3026, 2976, 2931, 2851, 2814, 1678, 1473, 1452, 1413, 1386, 1364, 1315, 1302, 1264, 1235, 1189, 1167, 1112, 1065, 1035, 999, 949, 914, 888, 858, 824, 797, 736, 703 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.34 (2H, dd, \( J = 7.6, 1.2 \) Hz, Ph), 7.23 (2H, t, \( J = 7.6 \) Hz, Ph), 7.14 (1H, tt, \( J = 7.6, 1.2 \) Hz, Ph), 6.39 (1H, ddd, \( J = 16.8, 9.6, 9.6 \) Hz, CHCH=CH\(_2\)), 5.07-4.98 (2H, m, CHCH=CH\(_2\)), 4.04 (1H, br, CHCH=CH\(_2\)), 3.23 (3H, s, NCH\(_3\)), 2.84 (2H, br, CH\(_2\)), 2.53 (2H, br, CH\(_2\)), 1.57-1.38 (6H, m, CH\(_2\)), 1.44 (3H, s, 2-CH\(_3\)), 1.08 (9H, s, t-Bu); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 174.2, 142.2, 139.9, 129.8, 128.0, 126.3, 116.1, 81.9, 71.8, 55.8, 48.4, 42.8, 27.6, 26.7, 25.0, 18.1; HRMS–ESI (m/z): [M+H]\(^+\) calcd for C\(_{22}\)H\(_{29}\)N\(_2\)O\(_2\): 359.2693. Found: 359.2683. Anal. Calcd for C\(_{22}\)H\(_{29}\)N\(_2\)O\(_2\): C, 73.70; H, 9.56; N, 7.81. Found: C, 73.32; H, 9.85; N, 7.64.

3-(4-Chlorophenyl)-1-(3,4-dihydroquinolin-1(2H)-yl)-2-methyl-2-(piperidin-1-yl)pent-4-en-1-one (2l): colorless crystals; [\( \alpha \)^2\(^{389}\) +96.9 (c 1.00, EtOH); 71% ee (determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 95/5 as the eluent, flow rate = 0.50 mL/min, \( t_R = 11.1 \) min for minor-2l and 17.8 min for major-2l); IR (KBr) 3003, 2935, 2850, 2811, 1638, 1600, 1490, 1453, 1442, 1385, 1368, 1342, 1282, 1261, 1231, 1206, 1160, 1092, 1068, 1040, 1013, 1000, 944, 913, 889, 828, 756, 709 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.28 (2H, d, \( J = 8.6 \) Hz, ArH), 7.19 (2H, d, \( J = 8.6 \) Hz, ArH), 7.04-6.98 (1H, m, ArH), 6.98-6.90 (2H, m, ArH), 6.70 (1H, br, ArH), 6.31 (1H, ddd, \( J = 16.8, 10.0, 8.8 \) Hz, CHCH=CH\(_2\)), 5.37 (1H, br, CH\(_2\)), 5.06 (1H, dd, \( J = 10.0, 0.8 \) Hz, CHCH=CH\(_2\)), 5.01 (1H, d, \( J = 16.8 \) Hz, CHCH=CH\(_2\)), 4.07 (1H, d, \( J = 8.8 \) Hz, CHCH=CH\(_2\)), 3.45-2.75 (3H, br, CH\(_2\)), 2.75-2.60 (2H, m, CH\(_2\)), 2.49 (2H, br, CH\(_2\)), 2.10-1.95 (1H, m, CH\(_2\)), 1.95-1.84 (1H, m, CH\(_2\)), 1.68-1.38 (6H, m, CH\(_2\)), 1.51 (3H, s, CH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 172.2, 140.8, 140.3, 140.0, 132.2, 130.7, 130.3, 128.5, 128.3, 125.1, 124.7, 124.4, 116.3, 73.3, 56.5, 48.6, 44.3, 27.0, 25.9, 24.8, 24.2, 17.0-14.0 (br); HRMS–ESI (m/z): [M+H]\(^+\) calcd for C\(_{26}\)H\(_{32}\)ClN\(_2\)O: 423.2198. Found: 423.2197. Anal. Calcd for C\(_{26}\)H\(_{31}\)ClN\(_2\)O: C, 73.83; H, 7.39; N, 6.62. Found: C, 73.49; H, 7.43; N, 6.68.

S7
3-(4-Bromophenyl)-1-(3,4-dihydroquinolin-1(2H)-yl)-2-methyl-2-(piperidin-1-yl)pent-4-en-1-one (2m):
colorless crystals; [α]^{25}_{	ext{D}} +109.9 (c 1.00, CHCl₃); 86% ee (determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 98:2 as the eluent, flow rate = 0.50 mL/min, tᵣ = 14.4 min for minor-2m and 22.6 min for major-2m); IR (KBr) 3059, 2998, 2934, 2848, 2809, 2765, 1636, 1600, 1488, 1455, 1442, 1385, 1369, 1342, 1308, 1281, 1260, 1233, 1205, 1158, 1104, 1069, 1040, 1008, 950, 919, 887, 863, 820, 794, 755, 719 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.35 (2H, d, J = 8.2 Hz, ArH), 7.22 (2H, d, J = 8.2 Hz, ArH), 7.04-6.98 (1H, m, ArH), 6.98-6.92 (2H, m, ArH), 6.68 (1H, br, ArH), 6.31 (1H, ddd, J = 16.8, 10.0, 9.2 Hz, CHCH=CH₂), 5.38 (1H, br, CH₂), 5.06 (1H, d, J = 10.0 Hz, CHCH=CH₂), 5.01 (1H, d, J = 16.8 Hz, CHCH=CH₂), 4.05 (1H, d, J = 9.2 Hz, CHCH=CH₂), 3.15 (1H, br, CH₂), 2.88 (2H, br, CH₂), 2.74-2.60 (2H, m, CH₂), 2.49 (2H, br, CH₂), 2.08-1.85 (2H, m, CH₂), 1.64-1.40 (6H, m, CH₂), 1.51 (3H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 172.1, 141.4, 140.2, 140.0, 131.3, 130.7, 128.5, 125.1, 124.7, 124.4, 120.4, 116.4, 73.2, 56.5, 48.5, 44.3, 27.0, 25.9, 24.8, 24.2, 15.9; HRMS–ESI (m/z): [M+H]⁺ calcd for C₂₉H₃₂BrN₂O: 467.1693. Found: 467.1678. Anal. Caled for C₂₉H₃₁BrN₂O: C, 66.81; H, 6.68; N, 5.99. Found: C, 66.66; H, 6.72; N, 5.96.

1-(3,4-Dihydroquinolin-1(2H)-yl)-2-methyl-2-(piperidin-1-yl)-3-(p-tolyl)pent-4-en-1-one (2n): colorless crystals; [α]^{25}_{	ext{D}} +145.2 (c 1.00, EtOH); 85% ee (determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 98:2 as the eluent, flow rate = 0.50 mL/min, tᵣ = 13.2 min for minor-2n and 27.3 min for major-2n); IR (KBr) 3016, 2991, 2937, 2852, 2807, 1633, 1599, 1512, 1490, 1453, 1439, 1386, 1367, 1341, 1300, 1279, 1262, 1232, 1206, 1157, 1102, 1069, 1037, 999, 947, 915, 887, 858, 843, 816, 760, 718, 707 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.19 (2H, d, J = 8.0 Hz, ArH), 7.02 (2H, d, J = 8.0 Hz, ArH), 6.98 (1H, dd, J = 7.4, 1.2 Hz, ArH), 6.90 (1H, ddd, J = 7.4, 7.4, 1.2 Hz, ArH), 6.86 (1H, ddd, J = 7.4, 7.4, 1.2 Hz, ArH), 6.55 (1H, d, J = 7.4 Hz, ArH), 6.32 (1H, ddd, J = 16.0, 9.6, 9.6 Hz, CHCH=CH₂), 5.55 (1H, br, CH₂), 5.10-4.95 (2H, m, CHCH=CH₂), 4.03 (1H, d, J = 9.6 Hz, CHCH=CH₂), 3.20-2.75 (3H, br, CH₂), 2.71-2.57 (2H, m, CH₂), 2.45 (2H, br, CH₂), 2.24 (3H, s, ArCH₃), 2.10-1.95 (1H, m, CH₂), 1.94-1.82 (1H, m, CH₂), 1.70-1.38 (6H, m, CH₃), 1.52 (3H, s, 2-CH₂); ¹³C NMR (100 MHz, CDCl₃) δ 172.2, 140.9, 140.2, 139.2, 136.0, 130.8, 128.9, 128.4, 128.2, 124.85, 124.79, 124.1, 115.6, 73.5, 56.6, 48.6, 44.1, 26.9, 25.9, 24.8, 24.2, 20.8, 14.9; HRMS–ESI (m/z): [M+H]⁺ calcd for C₂₇H₂₅N₂O: 403.2744. Found: 403.2739. Anal. Caled for C₂₇H₂₅N₂O: C, 80.55; H, 8.51; N, 6.96. Found: C, 80.32; H, 8.43; N, 7.05.

1-(3,4-Dihydroquinolin-1(2H)-yl)-2-methyl-2-(piperidin-1-yl)-3-vinylhexan-1-one (2p): colorless crystals; 5% ee (determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 99:1 as the eluent, flow rate = 0.50 mL/min, tᵣ = 8.5 min for minor-2p and 19.0 min for major-2p); IR (KBr) 3072, 3032, 2929, 2855, 2805, 1641, 1602, 1489, 1452, 1371, 1350, 1303, 1287, 1247, 1222, 1204, 1169, 1131, 1118, 1096, 1065, 1042, 996, 961, 943, 915, 893, 876, 847, 809, 754, 711 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.61 (1H, d, J = 7.8 Hz, ArH), 7.11 (1H, t, J = 7.8 Hz, ArH), 7.10 (1H, d, J = 7.8 Hz, ArH), 7.01 (1H, t, J = 7.8 Hz, ArH), 5.71 (1H, ddd, J = 17.0, 9.8, 9.8 Hz, CHCH=CH₂), 5.26 (1H, br, CH₂), 5.13 (1H, d, J = 9.8 Hz, CHCH=CH₂), 5.06 (1H, d, J = 17.0 Hz, CHCH=CH₂), 3.85 (1H, br, CHCH=CH₂), 2.87-2.67 (2H, br, CH₂), 2.80 (2H, t, J = 88
7.0 Hz, CH₂), 2.65-2.38 (3H, m, CH₂), 2.10-1.91 (2H, m, CH₂), 1.79-1.64 (1H, m, CH₂), 1.64-1.05 (9H, m, CH₂), 1.30 (3H, s, 2-CH₃), 0.87 (3H, t, J = 6.8 Hz, CHCH₂CH₂CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 140.6, 139.4, 130.2, 129.1, 125.2, 124.1, 117.2, 72.9, 51.8, 48.5, 45.3, 31.9, 26.7, 26.2, 25.0, 24.4, 20.9, 14.6, 14.1; HRMS–ESI (m/z): [M+H]+' calec for C₂₃H₃₅N₂O: 355.2744. Found: 355.2731. Anal. Caled for C₂₃H₃₅N₂O: C, 77.92; H, 9.67; N, 7.90. Found: C, 78.15; H, 9.86; N, 7.81.

1-(3,4-Dihydroquinolin-1(2H)-yl)-2-methyl-1-(phenanthridin-5(6H)-yl)-pent-4-en-1-one (2q): colorless viscous oil; 3% ee (determined by HPLC analysis: Daicel Chiralcel OJ–H column, n-hexane/2-propanol = 60/40 as the eluent, flow rate = 0.50 mL/min, tr = 12.5 min for minor-2q and 16.9 min for major-2q); IR (film) 3072, 2933, 2851, 2807, 2758, 2702, 1652, 1601, 1581, 1490, 1452, 1382, 1370, 1288, 1277, 1247, 1229, 1203, 1166, 1118, 1098, 1068, 1035, 992, 960, 916, 875, 798, 756, 710 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.64 (1H, d, J = 7.6 Hz, ArH), 7.14-7.07 (2H, m, ArH), 7.01 (1H, dd, J = 7.6, 7.6 Hz, ArH), 5.86 (1H, ddt, J = 17.2, 9.6, 7.2 Hz, CH₂CH=CH₂), 5.13-5.01 (2H, m, CH₂CH=CH₂), 4.94 (1H, br, CH₂), 4.14-3.98 (1H, m, CH₂), 2.80 (2H, t, J = 7.0 Hz, CH₂), 2.73 (1H, dd, J = 13.3, 7.2 Hz, CH₂CH=CH₂), 2.64 (2H, br, CH₂), 2.50 (2H, br, CH₂), 2.41 (1H, dd, J = 13.3, 7.2 Hz, CH₂CH=CH₂), 2.03 (1H, dd, J = 6.6, 6.6 Hz, CH₂), 2.00 (1H, dd, J = 6.6, 6.6 Hz, CH₂), 1.58 (4H, br, CH₂), 1.47 (2H, br, CH₂), 1.28 (3H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ 173.1, 140.4, 130.4, 128.9, 125.2, 124.3, 117.8, 69.2, 47.7, 44.5, 40.6, 26.8, 26.0, 24.9, 24.2, 16.1; HRMS–ESI (m/z): [M+H]+' calec for C₂₉H₂₉N₂O₅: 313.2274. Found: 313.2267. Anal. Caled for C₂₉H₂₉N₂O₅ (as 0.5H₂O): C, 74.73; H, 9.09; N, 8.71. Found: C, 74.64; H, 8.97; N, 8.93.

2-(4,4-Dimethoxypiperidin-1-yl)-2-methyl-1-(phenanthridin-5(6H)-yl)-3-phenylpent-4-en-1-one (4): colorless crystals; [α]⁺²³⁰ +157.3 (c 1.00, CHCl₃); 80% ee [(2R,3S)/(2S,3R): major diastereomer], 81% ee [(2R,3R)/(2S,3S): minor diastereomer]; (2S,3R)/(2R,3S)/(2R,3R)/(2S,3S) = 8.8/78.1/11.8/1.3 [determined by HPLC analysis: Daicel Chiralpak IB column, n-hexane/ethanol = 97/3 as the eluent, flow rate = 0.50 mL/min, tr = 14.0 min for (2S,3R)-4, 15.4 min for (2R,3S)-4, 17.6 min for (2R,3R)-4, and 19.4 min for (2S,3S)-4]; IR (KBr) 3074, 2944, 2895, 2852, 2827, 1634, 1599, 1486, 1440, 1388, 1354, 1314, 1252, 1228, 1181, 1151, 1127, 1092, 1052, 1000, 980, 950, 913, 891, 868, 804, 756, 736, 703 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ (9/1 mixture of diastereomers) 7.80-7.67 (1.1H, m, ArH), 7.61 (0.9H, J = 7.8, 1.2 Hz, ArH), 7.43-6.98 (7.3H, m, ArH), 7.18 (0.9H, tt, J = 7.6, 1.2 Hz, ArH), 7.10 (0.9H, ddd, J = 7.6, 7.6, 1.2 Hz, ArH), 7.02 (0.9H, dd, J = 7.6, 7.6 Hz, ArH), 6.65 (2H, br, ArH and CH₂), 6.40-6.20 (1H, m, CHCH=CH₂), 5.09 (0.9H, d, J = 10.0 Hz, CHCH=CH₂), 5.08 (1H, d, J = 17.2 Hz, CHCH=CH₂), 4.91 (0.1H, d, J = 9.6 Hz, CHCH=CH₂), 4.60 (0.1H, br, CH₂), 4.22 (0.9H, br, CH₂), 4.15 (1H, d, J = 8.8 Hz, CHCH=CH₂), 3.40-2.38 (2H, br, CH₂), 3.12 (5.4H, s, OCH₃), 3.10 (0.6H, s, OCH₃), 2.29 (2H, br, CH₂), 1.90-1.35 (7H, br, CH₂ and 2-CH₃); ¹³C NMR (100 MHz, CDCl₃) δ (major diastereomer) 171.4, 141.7, 140.7, 137.8, 135.0, 132.1, 129.0, 128.5, 128.0, 127.2, 126.83, 126.81, 125.8, 125.4, 125.2, 123.5, 116.1, 98.0, 72.9, 57.8, 48.2, 47.4, 44.3, 32.8, 14.0; HRMS–ESI (m/z): [M+H]+' calec for C₃₂H₃₈N₂O₄: 497.2799. Found: 497.2795. Anal. Caled for C₃₂H₃₈N₂O₄ (as 1H₂O): C, 74.68; H, 7.44; N, 5.44. Found: C, 74.83; H, 7.15; N, 5.47.
(E)-2-(2-Cinnamylpiperidin-1-yl)-N-methyl-N-phenylpropanamide (9): colorless gum; $[\alpha]^{23}_{	ext{D}}$ -69.7 (c 1.00, EtOH); IR (KBr) 3058, 3025, 2931, 2850, 2797, 2751, 1656, 1594, 1494, 1451, 1418, 1383, 1302, 1260, 1210, 1154, 1111, 1029, 991, 971, 926, 861, 773, 744, 699 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.46-7.15 (10H, m, ArH), 6.43 (1H, d, $J = 15.9$ Hz, CH=CHPh), 5.85 (1H, dd, $J = 15.9$, 10.2 Hz, CH=CHPh), 3.41-3.28 (1H, m, NCHCO), 3.32 (3H, s, NCH$_3$), 2.77-2.64 (1H, m, CH$_2$), 2.39-2.18 (4H, m, CH$_2$), 1.62-1.42 (4H, m, CH$_2$), 1.40-1.27 (2H, m, CH$_2$), 0.97 (3H, d, $J = 6.4$ Hz, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 176.2, 144.5, 136.9, 134.2, 129.4, 128.4, 127.4, 127.3, 127.1, 126.3, 126.2, 71.6, 50.7, 38.7, 37.3, 26.7, 24.8, 16.1; HRMS–ESI (m/$z$): [M+H]$^+$ calcd for C$_{24}$H$_{31}$N$_2$O: 363.2431. Found: 363.2424. Anal. Calcd for C$_{24}$H$_{31}$N$_2$O$_{1.5}$: C, 77.59; H, 8.41; N, 7.54 (as 0.5H$_2$O). Found: C, 77.98; H, 8.18; N, 7.58.
Determination of absolute configuration of 4 by conversion to the known compound 8

The absolute configuration of the major diastereomer of 8 was determined to be \((4R,1'S)\) by comparison of the \(^1\)H NMR spectrum, the value of the optical rotation, and HPLC retention time with that reported for 8.\(^1\) Therefore, the absolute configuration of major diastereomer of 4 was determined to be \((2R,3S)\). The relative stereochemistry of major diastereomer of 4 was confirmed as the \(\text{rel-}(2R,3S)\) by a single crystal X-ray diffraction. CCDC-995320 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.

(Step 1) A solution of 4 (116 mg, 0.234 mmol) in THF (2.3 mL) was treated with 1 M hydrochloric acid (2.3 mL) at room temperature and the mixture was stirred for 9 h at room temperature. The resulting mixture was treated with saturated aqueous sodium hydrogen carbonate and extracted with dichloromethane. The combined extracts were washed with brine, dried over sodium sulfate, and concentrated to obtain 1-\((\text{-2-methyl-1-oxo-1-(phenanthridin-5(6H)-yl)-3-phenylpent-4-en-2-yl)piperidin-4-one} (5) (108 mg, quant.) as a white

solid. The crude product was used without purification. (Step 2) A mixture of 5 (108 mg), ammonium chloride (15 mg, 0.28 mmol), aminomethylated polystyrene EHL (200–400 mesh), 2% DVB (substitution: 3.9 mmol/g, 90 mg), ethanol (2.3 mL), and dichloromethane (2.3 mL) was heated at 100 °C for 24 h in an Ace pressure tube (Aldrich). The resulting mixture was cooled to room temperature and filtered through a pad of Celite. The filtrate was treated with saturated aqueous sodium hydrogen carbonate and extracted with dichloromethane. The combined extracts were washed with brine, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (dichloromethane/methanol = 50/1 as the eluent) gave 2-amino-2-methyl-1-(phenanthridin-5(6H)-yl)-3-phenylpent-4-en-1-one (6) (67.6 mg, 78%) as a white solid. (Step 3) A solution of 6 (67.2 mg, 0.182 mmol), pyridine (58 μL, 0.72 mmol), and 4,4-dimethylaminopyridine (2 mg, 0.02 mmol) in dichloromethane (1.8 mL) was treated with benzoyl chloride (64 μL, 0.55 mmol) at 0 °C and the mixture was stirred for 3 h at the same temperature. The resulting mixture was treated with 1 M hydrochloric acid and extracted with dichloromethane. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and brine. The dichloromethane solution was dried over sodium sulfate and concentrated. Purification of the residue by chromatography on silica gel (dichloromethane/ethyl acetate = 20/1 to 10/1 as the eluent) gave N-(2-methyl-1-oxo-1-(phenanthridin-5(6H)-yl)-3-phenylpent-4-yl)benzamide (7) (73.8 mg, 86%) as colorless crystals. (Step 4) Ammonium cerium(IV) nitrate (CAN) (0.26 g, 0.47 mmol) was added to a solution of 7 (73.8 mg, 0.156 mmol) in acetonitrile (1.6 mL) and dichloromethane (0.8 mL) at 0 °C. After stirring for 12 h at the same temperature, the resulting mixture was diluted with water and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and brine. The ethyl acetate solution was dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (n-hexane/ethyl acetate = 10/1 as the eluent) to obtain 4-methyl-2-phenyl-4-(1′-phenylallyl)oxazol-5(4H)-one (8) (36.0 mg, 79%) as a colorless oil.

2-Amino-2-methyl-1-(phenanthridin-5(6H)-yl)-3-phenylpent-4-en-1-one (6): white solid; [α]22D +81.3 (c 1.00, CHCl3); IR (KBr) 3368, 3306, 3062, 3026, 2971, 2927, 2854, 1649, 1600, 1485, 1454, 1441, 1380, 1365, 1311, 1287, 1262, 1219, 1189, 1131, 1093, 991, 920, 871, 832, 764, 737, 701 cm⁻¹; 1H NMR (400 MHz, CDCl3) δ (9/1 mixture of diastereomers) 7.80-7.70 (2H, m, ArH), 7.42-7.18 (11H, m, ArH), 6.39-6.15 (0.1H, m, CHCH=CH2), 6.22 (0.9H, ddd, J = 17.1, 10.2, 8.6 Hz, CHCH=CH2), 5.72 (0.9H, d, J = 14.8 Hz, CONCH2), 5.42 (0.1H, d, J = 13.6 Hz, CONCH2), 5.24-4.85 (0.3H, m, CHCH=CH2) and CONCH2), 5.10 (0.9H, dd, J = 10.2, 1.2 Hz, CHCH=CH2), 5.04 (0.9H, dd, J = 17.1, 1.2 Hz, CHCH=CH2), 4.95 (0.9H, s, J = 14.8 Hz, CONCH2), 4.05 (0.1H, d, J = 9.6 Hz, CHCH=CH2), 4.01 (0.9H, d, J = 8.6 Hz, CHCH=CH2), 1.59 (2H, s, NH2), 1.43 (0.3H, s, CH3), 1.28 (2.7H, s, CH3); 13C NMR (100 MHz, CDCl3) δ (major diastereomer) 175.0, 139.6, 139.1, 136.8, 134.9, 132.6, 129.7, 129.6, 128.2, 127.7, 127.4, 127.1, 126.1, 125.9, 125.6, 124.1, 123.5, 118.3, 63.0, 58.0, 49.4, 26.7; HRMS–ESI (m/z): [M+H]+ calcd for C25H25N2O: 369.1961. Found: 369.1951. Elemental analysis was not obtained, as a pure sample could not be isolated.
N-(2-Methyl-1-oxo-1-(phenanthridin-5(6H)-yl)-3-phenylpent-4-en-2-yl)benzamide (7): colorless crystals; [α]D^25 = -58.6 (c 1.00, CHCl₃); IR (KBr) 3401, 3067, 3028, 2943, 2863, 1659, 1599, 1578, 1505, 1476, 1454, 1442, 1376, 1275, 1224, 1191, 1174, 1142, 1109, 1093, 1069, 1027, 1001, 941, 925, 803, 769, 737, 729, 719, 700 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ (9/1 mixture of diastereomers) 7.85-7.65 (5H, m, ArH), 7.53 (1H, t, J = 7.6 Hz, ArH), 7.45 (2H, dd, J = 7.6, 7.6 Hz, ArH), 7.38 (1H, t, J = 7.6 Hz, ArH), 7.35-7.04 (7H, m, ArH), 7.01 (0.9H, s, NH), 6.96-6.86 (2H, m, ArH), 6.63 (0.1H, s, NH), 6.53 (0.9H, dd, J = 17.0, 10.0, 10.0 Hz, CHCH=CH₂), 6.24 (0.1H, dd, J = 16.6, 10.0, 10.0 Hz, CHCH=CH₂), 5.54 (0.9H, d, J = 17.0 Hz, CHCH=CH₂), 5.53 (0.9H, d, J = 10.0 Hz, CHCH=CH₂), 4.83 (1H, d, J = 14.0 Hz, CONHCH₂), 4.54 (0.1H, d, J = 16.6 Hz, CHCH=CH₂), 4.16 (1H, d, J = 10.0 Hz, CHCH=CH₂), 1.74 (0.3H, s, CH₃), 1.65 (2.7H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ (major diastereomer) 169.0, 165.5, 136.8, 137.0, 136.6, 134.0, 133.9, 132.6, 131.8, 129.3, 128.8, 128.6, 128.4, 128.2, 127.52, 127.48, 127.4, 126.8, 126.5, 125.6, 125.2, 123.8, 123.7, 120.5, 62.8, 56.3, 48.9, 20.3; HRMS–ESI (m/z): [M+Na]^+ calcd for C₃₂H₂₈N₂O₂Na: 495.2043. Found: 495.2038. Anal. Calcd for C₃₂H₂₈N₂O₂: C, 81.33; H, 5.97; N, 5.93. Found: C, 81.32; H, 6.01; N, 6.04.

4-Methyl-2-phenyl-4-(1'-phenylallyl)oxazol-5(4H)-one (8): colorless oil; [α]D^20 = +50.1 (c 0.70, CH₂Cl₂);

(4S,1'S)/(4R,1'R)/(4R,1'S)/(4S,1'R) = 0.9/7.9/82.1/9.1 [determined by HPLC analysis: Daicel Chiralcel OJ–H column, n-hexane/2-propanol = 90/10 as the eluent, flow rate = 0.50 mL/min, tR = 14.4 min for (4S,1'S)-8, 17.9 min for (4R,1'R)-8, 37.8 min for (4R,1'S)-8, and 45.3 min for (4S,1'R)-8]; IR (film) 3062, 3031, 2978, 2930, 2866, 1817, 1654, 1601, 1580, 1492, 1451, 1417, 1371, 1341, 1320, 1294, 1214, 1198, 1155, 1089, 1070, 1030, 1005, 927, 911, 876, 830, 817, 779, 756, 709 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ (9/1 mixture of diastereomers) 8.01 (1.8H, dd, J = 7.6, 1.2 Hz, ArH), 7.88 (0.2H, dd, J = 8.0, 1.2 Hz, ArH), 7.61-7.40 (4.8H, m, ArH), 7.33 (1.8H, dd, J = 7.6, 7.6 Hz, ArH), 7.26 (0.9H, t, J = 7.6 Hz, ArH), 7.20-7.09 (0.5H, m, ArH), 6.38 (0.1H, ddd, J = 17.0, 9.8, 9.8 Hz, CHCH=CH₂), 6.01 (0.9H, ddd, J = 16.8, 9.8, 9.8 Hz, CHCH=CH₂), 5.32 (0.1H, d, J = 9.8 Hz, CHCH=CH₂), 5.30 (0.1H, d, J = 17.0 Hz, CHCH=CH₂), 5.19 (0.9H, d, J = 16.8 Hz, CHCH=CH₂), 5.09 (0.9H, dd, J = 9.8, 1.2 Hz, CHCH=CH₂), 3.72 (0.1H, d, J = 9.8 Hz, CHCH=CH₂), 3.69 (0.9H, d, J = 9.8 Hz, CHCH=CH₂), 1.58 (0.3H, s, CH₃), 1.35 (2.7H, s, CH₃); ¹³C NMR (100 MHz, CDCl₃) δ (major diastereomer) 180.6, 159.8, 138.3, 135.5, 132.6, 129.1, 128.7, 128.5, 127.9, 127.4, 125.8, 118.9, 73.5, 57.5, 57.5, 22.4; HRMS–ESI (m/z): [M+H]^+ calcd for C₁₉H₁₈NO₂: 292.1332. Found: 292.1326.

Crystal data of rel-(2R,3S)-2-(4,4-dimethoxypiperidin-1-yl)-2-methyl-1-(phenanthridin-5(6H)-yl)-3-phenylpent-4-en-1-one (rac-4): Recrystallization of rac-4 [rel-(2R,3S)/(2R,3R) = 9/1] from ethanol gave a single crystal suitable for X-ray crystallographic analysis as a diastereomerically pure form. CCDC-995320 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.
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Molecular structure of rac-4
Determination of enantiomer excess (ee) of 2 and 4 by chiral HPLC analysis

The ee of 2 and 4 were determined by HPLC analysis using chiral column (Daicel) in comparison with the corresponding chromatogram of racemic compounds. The racemic [2,3] Stevens rearrangement products \((rac-2 \text{ and } rac-4)\) were obtained by the reaction of racemic substrates \((rac-1 \text{ and } rac-3)\).

Representative HPLC data of [2,3] Stevens rearrangement product 2d, 2n, and 4

2d: 91% ee [Daicel Chiralpak AD–H column, \(n\)-hexane/ethanol = 98.7/1.3 as the eluent (pre-eluted with \(n\)-hexane/2-propanol = 90/10), flow rate = 0.50 mL/min, \(t_R = 22.3\) min for minor-2d and 60.4 min for major-2d]
2n: 85% ee (Daicel Chiralpak AD–H column, n-hexane/ethanol = 98/2 as the eluent, flow rate = 0.50 mL/min, \( t_R = 13.2 \) min for minor-2n and 27.3 min for major-2n)

![Chiral HPLC trace of 2n and rac-2n](image.png)

2n
85% ee
(Table 2, Entry 11)

![Chiral HPLC trace of rac-2n](image.png)

rac-2n
4: 80% ee [(2R,3S)/(2S,3R), major diastereomer], 81% ee [(2R,3R)/(2S,3S), minor diastereomer]; (2S,3R)/(2R,3S)/(2R,3R)/(2S,3S) = 8.8/78.1/11.8/1.3 [determined by HPLC analysis: Daicel Chiralpak IB column, n-hexane/ethanol = 97/3 as the eluent, flow rate = 0.50 mL/min, t_R = 14.0 min for (2S,3R)-4, 15.4 min for (2R,3S)-4, 17.6 min for (2R,3R)-4, and 19.4 min for (2S,3S)-4]
Single crystal X-ray diffraction of 1d-PF₆

Crystal data of (S)-1-cinnamyl-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)piperidin-1-ium hexafluorophosphate (1d-PF₆): Recrystallization from ethanol gave a single crystal suitable for X-ray crystallographic analysis. CCDC-995319 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.

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![Molecular structure of 1d-PF₆](image)
**Preparation of 1d-PF$_6$**

A suspension of 1d (47 mg, 0.10 mmol) and sodium hexafluorophosphate (20 mg, 0.12 mmol) in water (2 mL) was stirred for 6 h at room temperature. The resulting mixture was diluted with water and extracted with dichloromethane. The dichloromethane solution was dried over sodium sulfate and concentrated to obtain 1d-PF$_6$ (49 mg, 92%) as colorless crystals. Recrystallization from ethanol gave a single crystal suitable for X-ray crystallographic analysis; mp 209–210 °C; IR (KBr) 3026, 2944, 2873, 1658, 1602, 1580, 1490, 1473, 1459, 1411, 1380, 1356, 1340, 1290, 1234, 1198, 1128, 1106, 1087, 1076, 990, 943, 924, 846, 761, 695 cm$^{-1}$; $^1$H NMR (400 MHz, DMSO-$d_6$) δ (8/2 mixture of rotamers) 7.78 (0.2H, d, $J = 7.2$ Hz, ArH), 7.50 (0.4H, d, $J = 7.2$ Hz, ArH), 7.45-6.79 (9.4H, m, ArH and CH=CHPh), 6.62-6.47 (0.2H, m, CH=CHPh), 6.10-5.90 (0.8H, m, CH=CHPh), 4.88-4.74 (0.8H, m, NCHCO), 4.74-4.63 (0.2H, m, NCHCO), 4.56 (0.8H, dd, $J = 14.0$, 6.0 Hz, CH$_2$), 4.47-4.33 (0.2H, m, CH$_2$), 4.24-3.70 (3H, m, CH$_2$), 3.67-3.37 (2.4H, m, CH$_2$), 3.32-3.12 (1.6H, m, CH$_2$), 2.77-2.43 (2H, m, CH$_2$), 2.25-1.32 (11H, m, CH$_2$ and CHCH$_3$); $^{13}$C NMR (100 MHz, DMSO-$d_6$) δ (8/2 mixture of rotamers) 167.4, 166.2, 141.6, 140.1, 136.8, 135.2, 134.8, 131.9, 129.1, 128.8, 128.6, 127.2, 127.0, 126.9, 125.4, 125.2, 124.0, 116.1, 114.8, 64.4, 61.4, 57.1, 56.1, 55.7, 55.4, 55.1, 54.8, 45.1, 43.1, 25.8, 23.4, 20.6, 19.4, 19.1, 18.9, 12.3, 11.7; HRMS–ESI (m/z): [M–Br]$^+$ calcd for C$_{26}$H$_{33}$N$_2$O: 389.2587. Found: 389.2577. Anal. Calcd for C$_{26}$H$_{33}$F$_6$N$_2$OP: C, 58.42; H, 6.22; N, 5.24. Found: C, 58.20; H, 6.26; N, 4.93.
Preparation and characterization of chiral tertiary amine 1’ (precursor of 1)

The ee of UV-active 1’ were determined by HPLC analysis using chiral column (Daicel) in comparison with the corresponding chromatogram of racemic compounds (rac-1’).

Representative procedure for preparation of (S)-1-(3,4-dihydroquinolin-1(2H)-yl)-2-(piperidin-1-yl)propan-1-one (1d’)

(Step 1) Ethyl chloroformate (0.76 mL, 8.0 mmol) was added to a solution of Cbz-L-alanine (1.79 g, 8.0 mmol) and N-methylmorpholine (0.88 mL, 8.0 mmol) in dichloromethane (40 mL) at 0 °C. After stirring for 20 min at the same temperature, 1,2,3,4-tetrahydroquinoline (1.0 mL, 8.0 mmol) was added to the mixture at 0 °C. The reactant was stirred for 30 min at 0 °C and for 7 h at room temperature. The resulting mixture was quenched with saturated aqueous ammonium chloride and extracted with dichloromethane. The combined extracts were washed with brine, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (n-hexane/ethyl acetate = 3/1 to 1.5/1 as the eluent) afforded (S)-benzyl (1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)carbamate (10) (2.32 g, 86% yield) as a colorless viscous oil.

(Step 2) A mixture of 10 (2.32 g, 6.86 mmol) and palladium on activated carbon (loading: 10 wt. %, 0.15 g) in methanol (34 mL) was stirred for 5 h at room temperature under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated. A mixture of the residual oil, 1,5-dibromopentane (934 µL, 6.86 mmol), and sodium hydrogen carbonate (2.88 g, 34.3 mmol) in acetonitrile (34 mL) was refluxed for 12 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was concentrated and the residue was purified by chromatography on silica gel (dichloromethane/methanol = 20/1 to 10/1 as the eluent) to obtain 1d’ (1.37 g, 73% yield) as a pale yellow oil.

\[
\begin{align*}
\text{[}\alpha\text{]}_{26}^{\text{D}} & = -48.3 \ (c \ 1.00, \ \text{EtOH}) \ > 99\% \ \text{ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 97/3 as the eluent, flow rate = 0.50 mL/min, } t_R = 13.1 \ \text{min for (S)-1d’ and 14.8 min for (R)-1d’]; } \\
\text{IR (film) } & \text{3036, 2932, 2850, 2802, 2752, 1655, 1603, 1580, 1492, 1454, 1397, 1380, 1290, 1238, 1201, 1166, 1118, 1065, 1036, 935, 861, 758 \ \text{cm}^{-1}; } \\
\text{1H NMR (400 MHz, CDCl}_3\text{) } & \text{δ 7.40-7.00 (4H, m, ArH), 4.20-3.40 (3H, br, NCHCO and CONCH}_2\text{), 2.70 (2H, br, CH}_2\text{), 2.41 (4H, br, CH}_2\text{), 2.10-1.80 (2H m, CH}_2\text{), 1.57-1.31 (6H, br, CH}_2\text{), 1.23 (3H, d, J = 6.8 Hz, CH}_3\text{); } \\
\text{13C NMR (100 MHz, CDCl}_3\text{) } & \text{δ 172.5, 139.5, 133.9, 128.3, 126.0, 125.2, 124.3, 59.0, 49.8, 42.3, 26.7, 26.4, 24.5, 24.2, 12.5; HRMS–ESI (m/z): [M+H]+ calcd for C}_{17}\text{H}_{25}\text{N}_2\text{O: 273.1961. Found: 273.1959.}}
\end{align*}
\]
(5)-Cyclohexyl 2-(pyrrolidin-1-yl)propanoate (1a’): prepared by the literature; colorless oil; [α]_D^2589 = −19.5 (c 1.00, EtOH); 1H NMR (400 MHz, CDCl₃) δ 4.82 (1H, tt, J = 9.2, 3.6 Hz, OCH), 3.14 (1H, q, J = 7.0 Hz, NCHCO), 2.71-2.58 (4H, m, CH₂), 1.91-1.68 (8H, m, CH₂ and c-Hex), 1.60-1.19 (6H, m, c-Hex), 1.36 (3H, d, J = 7.0 Hz, CH₃); 13C NMR (100 MHz, CDCl₃) δ 173.3, 72.7, 50.9, 31.6, 31.5, 25.3, 23.8, 23.5, 17.5; IR (film) 2937, 2859, 2807, 1728, 1452, 1367, 1320, 1261, 1165, 1080, 1039, 984, 943, 925, 908, 871, 842, 799, 757 cm⁻¹; HRMS–ESI (m/z): [M+H]^+ calcd for C₁₃H₂₄NO₂: 226.1802. Found: 226.1797. Anal. Calcd for C₁₃H₂₃NO₂: C, 69.29; H, 10.29; N, 6.22. Found: C, 69.05; H, 10.47; N, 6.12.

(5)-1,2-Di(pyrrolidin-1-yl)propan-1-one (1b’): prepared by the same procedure with 1d’ using pyrrolidine instead of 1,2,3,4-tetrahydroquinoline in step 1 and 1,4-dibromobutane instead of 1,5-dibromopentane in step 2 (78% overall yield); colorless oil; [α]_D^26589 = −35.4 (c 1.00, EtOH); IR (film) 2969, 2875, 2807, 1634, 1432, 1370, 1339, 1252, 1227, 1192, 1165, 1083, 1038, 972, 938, 913, 868, 732 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 3.60 (1H, dt, J = 10.0, 6.8 Hz, CONCH₂), 3.55-3.44 (3H, m, CONCH₂), 3.28 (1H, q, J = 6.8 Hz, NCHCO), 2.69-2.52 (4H, m, CH₂), 2.03-1.89 (2H, m, CH₂), 1.89-1.81 (2H, m, CH₂), 1.81-1.71 (4H, m, CH₂), 1.30 (3H, d, J = 6.8 Hz, CH₃); 13C NMR (100 MHz, CDCl₃) δ 172.1, 60.8, 50.8, 46.4, 45.8, 24.0, 23.4, 15.5; HRMS–ESI (m/z): [M+H]^+ calcd for C₁₁H₂₁N₂O: 197.1648. Found: 197.1645.

(5)-1-(3,4-Dihydroquinolin-1(2H)-yl)-2-(pyrrolidin-1-yl)propan-1-one (1c’): prepared by the same procedure with 1d’ using 1,4-dibromobutane instead of 1,5-dibromopentane in step 2 (84% overall yield); pale yellow oil; [α]_D^23589 = −42.9 (c 1.00, EtOH); 98% ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 90/10 as the eluent, flow rate = 0.50 mL/min, t_R = 11.7 min for (R)-1c and 12.7 min for (S)-1c]; IR (KBr) 2952, 2877, 2844, 2806, 1657, 1603, 1580, 1492, 1455, 1398, 1366, 1289, 1233, 1201, 1164, 1132, 1070, 946, 859, 761 cm⁻¹; 1H NMR (400 MHz, CDCl₃) δ 7.27-7.03 (4H, br, ArH), 4.03 (1H, q, J = 6.7 Hz, NCHCO), 3.88 (1H, br, CONCH₂), 3.76 (1H, br, CONCH₂), 2.86 (2H, br, CH₂), 2.70 (4H, br, CH₂), 2.08-1.90 (2H, m, CH₂), 1.83 (4H, br, CH₂), 1.38 (3H, br, CH₃); 13C NMR (100 MHz, CDCl₃) δ 171.9, 138.6, 134.4, 128.5, 126.4, 125.9, 124.5, 57.1, 50.2, 42.5, 26.5, 24.0, 23.4, 15.8; HRMS–ESI (m/z): [M+H]^+ calcd for C₁₆H₂₃N₂O: 259.1805. Found: 259.1803.

(5)-1-(3,4-Dihydroquinolin-1(2H)-yl)-2-(dimethylamino)propan-1-one (1e’):

(Step 1) A mixture of 10 (2.41 g, 7.1 mmol) and palladium on activated carbon (loading: 10 wt. %, 0.15 g) in methanol (36 mL) was stirred for 42 h at room temperature under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated to obtain crude (5)-2-amino-1-(3,4-dihydroquinolin-1(2H)-yl)propan-1-one (11) (1.34 g, 92% yield) as a pale yellow oil. (Step 2) A mixture

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of 11 (409 mg, 2.0 mmol), palladium on activated carbon (loading: 10 wt. %, 2.0 mmol) and formaldehyde solution (37 wt.% in water, 1.6 mL, 20 mmol) in ethanol (10 mL) was stirred for 10 h under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was diluted with water. The mixture was extracted with ethyl acetate and the combined extracts were washed with brine. The ethyl acetate solution was dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 20/1 to 10/1 as the eluent) to obtain 1e’ (336 mg, 72% yield) as a colorless oil. \[ \alpha \] 25589 –79.4 (c 1.00, EtOH); 99% ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/2-propanol = 95/5 as the eluent, flow rate = 0.50 mL/min, tR = 15.7 min for (S)-1e’ and 20.1 min for (R)-1e’]; IR (film) 3036, 2937, 2866, 2825, 2783, 1655, 1604, 1579, 1492, 1458, 1390, 1288, 1236, 1199, 1089, 1058, 966, 942, 804, 759 cm\(^{-1}\); 1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.39-7.04 (4H, m, ArH), 4.00-3.60 (3H, br, NCH\(_2\)CO and CON\(_2\)CH), 2.70 (2H, br, CH\(_2\)), 2.26 (6H, s, N(CH\(_3\))\(_2\)), 2.10-1.85 (2H, m, CH\(_2\)), 1.23 (3H, d, \(J = 6.8\) Hz, CH\(_3\)) \(\ddagger\); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 172.4, 139.2, 133.9, 128.3, 126.1, 125.2, 124.4, 58.2, 42.3, 41.0, 26.7, 24.1, 13.5; HRMS–ESI (m/z): [M+H]+ calcd for C\(_{14}\)H\(_{21}\)N\(_2\)O: 233.1648. Found: 233.1647.

\((S)\)-1-(Indolin-1-yl)-2-(piperidin-1-yl)propan-1-one (1f’): prepared by the same procedure with 1d’ using indoline instead of 1,2,3,4-tetrahydroquinoline in step 2 (56% overall yield); pale yellow crystals; \([\alpha]_{2}^{25589} –20.8 (c 1.00, EtOH); >99% ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 90/10 as the eluent, flow rate = 0.50 mL/min, tR = 11.7 min for (S)-1f’ and 14.1 min for (R)-1f’]; IR (KBr) 3024, 2981, 2934, 2851, 2805, 2755, 1659, 1514, 1482, 1460, 1441, 1406, 1383, 1337, 1302, 1281, 1211, 1172, 1154, 1123, 1112, 1088, 1068, 1036, 955, 933, 886, 860, 784, 762, 756 cm\(^{-1}\); 1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.27 (1H, d, \(J = 7.6\) Hz, ArH), 7.23-7.15 (2H, m, ArH), 7.01 (1H, ddd, \(J = 7.6, 7.6, 1.0\) Hz, ArH), 4.63 (1H, ddd, \(J = 10.0, 10.0, 7.6\) Hz, CON\(_2\)CH), 3.50 (1H, q, \(J = 6.8\) Hz, NCH\(_2\)CO), 3.24-3.08 (2H, m, CH\(_2\)), 2.68-2.54 (2H, m, CH\(_2\)), 1.62-1.47 (4H, m, CH\(_2\)), 1.47-1.36 (2H, m, CH\(_2\)), 1.23 (3H, d, \(J = 6.8\) Hz, CH\(_3\)); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.1, 143.5, 131.4, 127.3, 124.4, 123.5, 117.2, 63.2, 49.9, 47.6, 28.3, 26.4, 24.4, 9.0; HRMS–ESI (m/z): [M+H]+ calcd for C\(_{16}\)H\(_{23}\)N\(_2\)O: 259.1805. Found: 259.1800.

\((S)\)-1-(Phenanthridin-5(6H)-yl)-2-(piperidin-1-yl)propan-1-one (1g’): prepared by the same procedure with 1d’ using 5,6-dihydrophenanthridine instead of 1,2,3,4-tetrahydroquinoline in step 2 (58% overall yield); colorless gum; \([\alpha]_{2}^{25589} –80.6 (c 1.00, EtOH); 99% ee [determined by HPLC analysis: Daicel Chiralcel OD–H column, n-hexane/ethanol = 95/5 as eluent, flow rate = 0.50 mL/min, tR = 15.1 min for (R)-1g’ and 22.4 min for (S)-1g’]; IR (film) 3069, 3035, 2934, 2852, 2805, 2755, 1659, 1603, 1488, 1443, 1398, 1382, 1306, 1265, 1227, 1190, 1165, 1123, 1097, 1036, 996, 946, 909, 762, 736 cm\(^{-1}\); 1H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.82-7.72 (2H, m, ArH), 7.56 (1H, br, ArH), 7.41-7.23 (5H, m, ArH), 5.50-4.40 (2H, br, NCH\(_2\)CO and CON\(_2\)CH), 3.81 (1H, br, CON\(_2\)CH), 2.70-2.00 (4H, br, CH\(_2\)), 1.70-1.00 (9H, br, CH\(_2\) and CH\(_3\)); 13C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 172.2, 138.4, 135.3, 132.0, 129.7, 127.9, 127.5, 126.0, 124.3, 123.1, 58.4, 49.4, 45.2, 26.2, 24.3, 11.1; HRMS–ESI (m/z): [M+H]+ calcd for C\(_{21}\)H\(_{25}\)N\(_2\)O: 321.1961. Found: 321.1956.
(S)-N-Methyl-N-phenyl-2-(piperidin-1-yl)propanamide (1h'): prepared by the same procedure with 1d’ using N-methylaniline instead of 1,2,3,4-tetrahydroquinoline in step 2 (60% overall yield); pale yellow oil; \([\alpha]_{25}^{25} = -22.6 (c \ 1.00, \text{EtOH}); >99\% \text{ ee} [\text{determined by HPLC analysis: Daicel Chiralcel OD–H column, n-hexane/ethanol = 99/1 as the eluent, flow rate = 0.50 mL/min, } t_R = 16.0 \text{ min for (S)-1h’ and 19.7 min for (R)-1h’}; IR (film) 3060, 2933, 2852, 2801, 2751, 1595, 1496, 1452, 1382, 1307, 1267, 1219, 1168, 1117, 1073, 1033, 1000, 946, 894, 862, 772, 734, 701 \text{ cm}^{-1}; ^1\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 7.40 (2H, dd, J = 7.6, 7.6 Hz, Ph), 7.32 (1H, tt, J = 7.6, 1.4 Hz, Ph), 7.22 (2H, dd, J = 7.6, 1.4 Hz, Ph), 3.27 (3H, s, NCH}_3\text{), 3.21 (1H, q, J = 6.8 Hz, NCHCO), 2.52-2.42 (2H, m, CH}_2\text{), 2.37-2.27 (2H, m, CH}_2\text{), 1.56-1.32 (6H, m, CH}_2\text{), 1.14 (3H, d, J = 6.8 Hz, CHC}_3\text{); } ^{13}\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 173.2, 144.0, 129.4, 127.5, 127.4, 59.2, 50.2, 37.3, 26.3, 24.5, 13.1; HRMS–ESI (m/z): [M+H]^+ \text{ calcd for C}_{15}H_{23}N_2O: 247.1805. Found: 247.1800.}

(S)-N-Benzhydryl-N-methyl-2-(piperidin-1-yl)propanamide (1i'): prepared by the same procedure with 1d’ using N-(diphenylmethyl)methylamine instead of 1,2,3,4-tetrahydroquinoline in step 2 (42% overall yield); colorless viscous oil; \([\alpha]_{24}^{24} = -36.5 (c \ 1.00, \text{EtOH}); 97\% \text{ ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/2-propanol = 90/10 as the eluent, flow rate = 0.50 mL/min, } t_R = 17.0 \text{ min for (S)-1i’ and 22.4 min for (R)-1i’}; IR (film) 3059, 3028, 2933, 2851, 2805, 2755, 1647, 1602, 1494, 1469, 1450, 1398, 1384, 1279, 1211, 1165, 1121, 1105, 1066, 1033, 1009, 962, 935, 867, 785, 756, 734, 701 \text{ cm}^{-1}; ^1\text{H NMR (400 MHz, CDCl}_3\text{) } \delta (5/5 \text{ mixture of rotamers) } 7.40-7.15 (10.5H, m, Ph and \text{C}_H\text{Ph}_2\text{), } 7.10 (0.5H, s, \text{C}_H\text{Ph}_2), 3.58 (0.5H, q, J = 6.8 Hz, NCHCO), 3.53 (0.5H, q, J = 6.8 Hz, NCHCO), 2.94 (1.5H, s, NCH}_3\text{), 2.72 (1.5H, s, NCH}_3\text{), 2.65-2.53 (2H, m, CH}_2\text{), 2.51-2.39 (2H, m, CH}_2\text{), 1.65-1.48 (4H, m, CH}_2\text{), 1.48-1.35 (2H, m, CH}_2\text{), 1.19 (1.5H, d, J = 6.8 Hz, CHCH}_3\text{), 1.13 (1.5H, d, J = 6.8 Hz, CHCH}_3\text{); } ^{13}\text{C NMR (100 MHz, CDCl}_3\text{) } \delta (5/5 \text{ mixture of rotamers) } 173.1, 172.9, 140.0, 139.4, 129.3, 129.2, 128.6, 128.3, 128.23, 128.19, 128.0, 127.5, 127.4, 127.30, 127.27, 126.9, 62.7, 61.2, 60.9, 60.2, 49.8, 31.7, 31.0, 26.4, 24.4, 24.3, 8.8, 8.3; HRMS–ESI (m/z): [M+H]^+ \text{ calcd for C}_{22}H_{29}N_2O: 337.2274. Found: 337.2266.}

(S)-N-Methoxy-N-methyl-2-(piperidin-1-yl)propanamide (1j'): prepared by the same procedure with 1d’ using N,O-dimethylhydroxylamine hydrochloride instead of 1,2,3,4-tetrahydroquinoline in the presence of 2 equivalents of N-methylmorpholine in step 2 (51% overall yield); pale red oil; \([\alpha]_{23}^{23} = -23.4 (c \ 1.00, \text{EtOH}); IR (film) 2933, 2853, 2805, 2754, 1663, 1443, 1418, 1383, 1325, 1301, 1271, 1217, 1167, 1119, 1072, 1051, 1036, 1023, 992, 947, 901, 862, 785, 764, 726, 701 \text{ cm}^{-1}; ^1\text{H NMR (400 MHz, CDCl}_3\text{) } \delta 3.83-3.68 (1H, m, NCHCO), 3.75 (3H, s, OCH}_3\text{), 3.20 (3H, s, NCH}_3\text{), 2.73-2.57 (2H, m, CH}_2\text{), 2.57-2.45 (2H, m, CH}_2\text{), 1.64-1.50 (4H, m, CH}_2\text{), 1.47-1.38 (2H, m, CH}_2\text{), 1.22 (3H, d, J = 6.8 Hz, CHCH}_3\text{); } ^{13}\text{C NMR (100 MHz, CDCl}_3\text{) } \delta 174.6, 61.3, 58.4, 50.4, 31.9, 26.1, 24.4, 12.7; HRMS–ESI (m/z): [M+H]^+ \text{ calcd for C}_{10}H_{21}N_2O_2: 201.1598. Found: 201.1595.}
(S)-N-(tert-Butoxy)-N-methyl-2-(piperidin-1-yl)propanamide (1k\'): prepared by the same procedure with 1d\' using and O-(tert-butyl)-N-methylhydroxylamine hydrochloride\(^\text{3}\) instead of 1,2,3,4-tetrahydroquinoline and 2 equivalents of N-methylmorpholine in step 2 (76% overall yield); pale yellow oil; \([\alpha]_2^\text{D} +0.5 (c 1.00, \text{EtOH}); IR (film) 2977, 2933, 2852, 2805, 2755, 1662, 1467, 1453, 1443, 1407, 1365, 1306, 1271, 1238, 1160, 1117, 1065, 1047, 1035, 1024, 965, 928, 915, 852, 791, 746, 727 cm\(^{-1}\); \(1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 3.93 (1H, br, NCHCO), 3.28 (3H, s, NCH\(_3\)), 2.62 (2H, br, CH\(_2\)), 2.52 (2H, br, CH\(_2\)), 1.65-1.48 (4H, m, CH\(_2\)), 1.48-1.38 (2H, m, CH\(_2\)), 1.31 (9H, s, t-Bu), 1.23 (3H, d, \(J = 6.8\) Hz, CHC\(_\text{H}_3\)); \(1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 177.3, 82.5, 57.7, 50.4, 38.8, 27.6, 26.4, 24.6, 14.0; HRMS–ESI (m/z): [M+H]\(^+\) calcd for C\(_{13}\)H\(_{27}\)N\(_2\)O\(_2\): 243.2067. Found: 243.2061.

(S)-1-(3,4-Dihydroquinolin-1(2H)-yl)-3-phenyl-2-(piperidin-1-yl)propan-1-one (1r\'): prepared by the same procedure with 1d\' using Cbz-L-phenylalanine instead of Cbz-L-alanine in step 1 (55% overall yield); colorless oil; \([\alpha]_2^\text{D} +23.1 (c 1.00, \text{EtOH}); >99% ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, \(n\)-hexane/2-propanol = 90/10 as the eluent, flow rate = 0.50 mL/min, \(t_R = 11.8\) min for (S)-1r\' and 16.6 min for (R)-1r\']; IR (film) 3060, 3026, 2932, 2851, 2804, 2746, 1648, 1604, 1580, 1492, 1453, 1440, 1405, 1380, 1304, 1238, 1201, 1170, 1157, 1115, 1101, 1073, 1046, 1036, 1003, 973, 929, 909, 879, 863, 750, 701 cm\(^{-1}\); \(1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.27-6.97 (8H, m, ArH), 6.82 (1H, br, ArH), 3.88 (1H, d, \(J = 8.8\) Hz, NCHCO or CH\(_2\)), 3.79-3.48 (2H, br, NCHCO and/or CH\(_2\)), 2.67 (2H, br, CH\(_2\)), 2.49 (3H, br, CH\(_2\)), 2.18 (1H, br, CH\(_2\)), 1.85-1.71 (1H, m, CH\(_2\)), 1.67-1.36 (7H, m, CH\(_2\)); \(1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.5, 139.3, 139.2, 133.8, 129.4, 128.2, 127.9, 125.9, 125.8, 125.1, 124.5, 66.2, 50.1, 42.1, 32.5, 26.6, 26.4, 24.6, 24.0; HRMS–ESI (m/z): [M+H]\(^+\) calcd for C\(_{23}\)H\(_{29}\)N\(_2\)O: 349.2274. Found: 349.2260.

(S)-1-(3,4-Dihydroquinolin-1(2H)-yl)-4-methyl-2-(piperidin-1-yl)pentan-1-one (1s\'): prepared by the same procedure with 1d\' using Cbz-L-leucine instead of Cbz-L-alanine in step 1 (40% overall yield); colorless oil; \([\alpha]_2^\text{D} +43.6 (c 1.00, \text{EtOH}); 98% ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, \(n\)-hexane/2-propanol = 95/5 as the eluent, flow rate = 0.50 mL/min, \(t_R = 10.0\) min for (S)-1s\' and 12.2 min for (R)-1s\'); IR (film) 3035, 2931, 2866, 2850, 2802, 2744, 1655, 1604, 1580, 1492, 1455, 1398, 1379, 1346, 1332, 1292, 1242, 1221, 1199, 1167, 1112, 1070, 1036, 996, 944, 915, 861, 799, 759, 708 cm\(^{-1}\); \(1^H\) NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.36 (1H, br, ArH), 7.21-7.05 (3H, m, ArH), 4.00-3.55 (3H, br, NCHCO and CH\(_2\)), 2.69 (2H, br, CH\(_2\)), 2.52 (2H, br, CH\(_2\)), 2.40 (2H, br, CH\(_2\)), 2.05-1.87 (2H, m, CH\(_2\)), 1.71 (1H, br, CH\(_2\)), 1.58-1.32 (8H, m, CH\(_2\) and CH\(_2\)(CH\(_3\))\(_2\)), 0.85 (3H, br, CH(CH\(_3\)\(_2\))), 0.75 (3H, br, CH(CH\(_3\)\(_2\))\(_2\)); \(1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 171.9, 139.6, 133.9, 128.1, 125.9, 125.2, 124.6, 61.7, 49.8, 42.2, 34.5, 26.8, 26.7, 25.0, 24.7, 24.3, 22.9, 22.3; HRMS–ESI (m/z): [M+H]\(^+\) calcd for C\(_{20}\)H\(_{31}\)N\(_2\)O: 315.2431. Found: 315.2417.

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(Step 1) Ethyl chloroformate (0.57 mL, 6.0 mmol) was added to a solution of Cbz-L-alanine (1.34 g, 6.0 mmol) and \textit{N}-methylmorpholine (0.66 mL, 6.0 mmol) in dichloromethane (30 mL) at 0 °C. After stirring for 30 min at the same temperature, a solution of 5,6-dihydropenanthonidine (1.09 g, 6.0 mmol) in dichloromethane (6 mL) was added at 0 °C and the mixture was stirred for 7 h at room temperature. The resulting mixture was quenched with saturated aqueous ammonium chloride and extracted with dichloromethane. The combined extracts were washed with brine, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (dichloromethane/ethyl acetate = 100/0 to 10/1 as the eluent) gave (S)-benzyl (1-oxo-1-(phenanthridin-5(6H)-yl)propan-2-yl)carbamate (12) (1.88 g, 81% yield) as a white solid. (Step 2) A mixture of 12 (1.09 g, 2.82 mmol) and palladium on activated carbon (loading: 10 wt. %, 59 mg) in methanol (14 mL) was stirred for 6 h at room temperature under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated. The residual was purified by chromatography on silica gel (dichloromethane/methanol = 20/1 to 10/1 as the eluent) to afford (S)-2-amino-1-(phenanthridin-5(6H)-yl)propan-1-one (13) (0.60 g, 84% yield) as a colorless gum. (Step 3) 1,5-Dibromopentan-3-one\textsuperscript{4} (0.28 mL, 2.1 mmol) was added to a mixture of 13 (0.54 g, 2.1 mmol) and sodium hydrogen carbonate (0.92 g, 11 mmol) in methanol (11 mL) at 60 °C and the mixture was refluxed for 30 min. The resulting mixture was diluted with water and extracted with ethyl acetate. The combined extracts were

washed with brine, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (n-hexane/ethyl acetate = 2/1 to 1/1 as the eluent) afforded (S)-1-(1-oxo-1-(phenanthridin-5(6H)-yl)propan-2-yl)piperidin-4-one (14) (0.53 g, 75% yield) as pale yellow crystals. (Step 4) p-Toluenesulfonic acid monohydrate (48 mg, 0.25 mmol) was added to a solution of 14 (71 mg, 0.21 mmol) in methanol (0.5 mL) and trimethyl orthoformate (0.5 mL) at 0 °C. After stirring for 8 h at room temperature, the reactant was treated with saturated aqueous sodium hydrogen carbonate. The mixture was extracted with ethyl acetate and the combined extracts were washed with brine. The ethyl acetate solution was dried over sodium sulfate and concentrated. The residue was purified by chromatography on silica gel (n-hexane/ethyl acetate = 2/1 to 1/1 as the eluent) to obtain 3’ (79 mg, 99% yield) as a pale yellow solid. [%]$_23589$ $-73.0$ ($c$ 1.00, EtOH); >99% ee [determined by HPLC analysis: Daicel Chiralpak AD–H column, n-hexane/ethanol = 80/20 as the eluent, flow rate = 0.50 mL/min, $t_R$ = 12.0 min for (S)-3’ and 18.2 min for (R)-3’]; IR (film) 3067, 3032, 2941, 2898, 2829, 1659, 1603, 1567, 1488, 1443, 1384, 1310, 1265, 1222, 1189, 1132, 1097, 1053, 1000, 945, 912, 764, 736 cm$^{-1}$; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.85-7.20 (8H, m, ArH), 5.60-4.30 (2H, br, CONCH$_2$), 3.84 (1H, br, NCHCO), 3.06 (6H, br, OCH$_3$), 2.70-2.00 (4H, br, CH$_2$), 1.95-0.95 (7H, br, CH$_2$ and CHCH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.1, 138.5, 135.3, 132.0, 129.7, 127.9, 127.8, 127.5, 126.16, 126.05, 124.3, 124.0, 123.1, 98.2, 57.8, 47.3, 45.4, 45.2, 32.5, 10.8; HRMS–ESI (m/z): [M+H]$^+$ calcd for C$_{23}$H$_{29}$N$_2$O$_3$: 381.2173. Found: 381.2168.
Preparation and characterization of “racemic” tertiary amine rac-1’ (precursor of rac-1)

Representative procedure for preparation of 1-(3,4-dihydroquinolin-1(2H)-yl)-2-(piperidin-1-yl)propan-1-one (rac-1d’)

(Step 1) A solution of 1,2,3,4-tetrahydroquinoline (0.63 mL, 5.0 mmol) and pyridine (0.40 mL, 5.0 mmol) in dichloromethane (25 mL) was treated with 2-bromopropionyl bromide (0.58 mL, 5.5 mmol) at –78 °C and stirred for 15 min. The mixture was allowed to warm at room temperature and stirred for 1.5 h. The resulting mixture was diluted with water and extracted with dichloromethane. The combined extracts were washed with water, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (hexane/ethyl acetate = 6/1 to 4/1 as the eluent) gave 2-bromo-1-(3,4-dihydroquinolin-1(2H)-yl)propan-1-one (15) (1.34 g, quant.) as a colorless oil. (Step 2) A mixture of 15 (0.50 g, 1.9 mmol), piperidine (0.19 mL, 1.9 mmol), and potassium hydrogen carbonate (0.56 g, 5.6 mmol) in acetonitrile (9 mL) was refluxed for 6 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was concentrated and the residue was purified by chromatography on silica gel (dichloromethane/methanol = 20/1 to 10/1 as the eluent) to obtain rac-1d’ (0.52 g, quant.) as a pale yellow oil.

Representative procedure for preparation of N-benzhydryl-N-methyl-2-(piperidin-1-yl)propanamide (rac-1i’)

(Step 1) A solution of N-(diphenylmethyl)methylamine (0.39 g, 2.0 mmol) and N,N-diisopropylethylamine (0.35 mL, 2.0 mmol) in dichloromethane (8 mL) was treated with 2-bromopropionyl bromide (0.23 mL, 2.2 mmol) at –40 °C and stirred for 1 h. The mixture was allowed to warm at room temperature and stirred for 3 h. The resulting mixture was diluted with water and extracted with dichloromethane. The combined extracts were washed with water, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel (hexane/ethyl acetate = 5/1 as the eluent) gave N-benzhydryl-2-bromo-N-methylpropanamide (16) (0.58 g, 87% yield) as a colorless oil. (Step 2) A mixture of 16 (0.57 g, 1.7 mmol), piperidine (0.21 mL, 2.1 mmol), and potassium hydrogen carbonate (0.53 g, 5.3 mmol) in acetonitrile (5.8 mL) was stirred for 15 h at room temperature and refluxed for 3 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was concentrated and the residue was purified by chromatography on
silica gel (hexane/ethyl acetate = 7/1 to 2/1 as the eluent) to give $\text{rac-11'}$ (0.56 g, 98% yield) as a colorless viscous oil.

**Representative procedure for the preparation of 1-(3,4-dihydroquinolin-1(2H)-yl)-3-phenyl-2-(piperidin-1-yl)propan-1-one ($\text{rac-1r'}$)**

(Step 1) Ethyl chloroformate (0.44 mL, 4.6 mmol) was added to a solution of Cbz-DL-phenylalanine (1.39 g, 4.6 mmol) and N-methylmorpholine (0.51 mL, 4.6 mmol) in dichloromethane (9.2 mL) at 0 °C. After stirring for 1 h at the same temperature, 1,2,3,4-tetrahydroquinoline (0.58 mL, 4.6 mmol) was added to the mixture at 0 °C. The reactant was stirred for 30 min at 0 °C and for 14 h at room temperature. The resulting mixture was quenched with saturated aqueous ammonium chloride and extracted with dichloromethane. The combined extracts were washed with brine, dried over sodium sulfate, and concentrated. Purification of the residue by chromatography on silica gel ($n$-hexane/ethyl acetate = 5/1 to 3/1 as the eluent) afforded benzyl (1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxo-3-phenylpropan-2-yl)carbamate ($\text{rac-17}$) (1.24 g, 65% yield) as a colorless viscous oil. (Step 2) A mixture of $\text{rac-17}$ (1.23 g, 3.0 mmol) and palladium on activated carbon (loading: 10 wt.%, 67 mg) in methanol (6 mL) was stirred for 12 h at room temperature under a hydrogen atmosphere. The resulting mixture was filtered through a pad of Celite and the filtrate was concentrated. A mixture of the residual oil, 1,5-dibromopentane (0.45 mL, 3.3 mmol), and sodium hydrogen carbonate (0.75 g, 8.9 mmol) in acetonitrile (8.5 mL) was refluxed for 17 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was concentrated and the residue was purified by chromatography on silica gel (dichloromethane/methanol = 4/1 as the eluent) to obtain $\text{rac-1r'}$ (1.20 g, quant.) as a colorless viscous oil.

**Cyclohexyl 2-(pyrrolidin-1-yl)propanoate ($\text{rac-1a'}$):** prepared from Cbz-DL-alanine by the literature.²

**1,2-Di(pyrrolidin-1-yl)propan-1-one ($\text{rac-1b'}$):** prepared by the same procedure with $\text{rac-1d'}$ using pyrrolidine instead of 1,2,3,4-tetrahydroquinoline and piperidine (95% overall yield).

**1-(3,4-Dihydroquinolin-1(2H)-yl)-2-(pyrrolidin-1-yl)propan-1-one ($\text{rac-1c'}$):** prepared by the same procedure with $\text{rac-1d'}$ using pyrrolidine instead of piperidine in step 2 (96% overall yield).
1-(3,4-Dihydroquinolin-1(2H)-yl)-2-(dimethylamino)propan-1-one (rac-1e’)

A mixture of 15 (277 mg, 1.03 mmol) and potassium carbonate (428 mg, 3.1 mmol) in acetonitrile (3.1 mL) was treated with dimethylamine solution (50 wt.% in water, 0.33 mL, 3.1 mmol) at room temperature. After stirring for 18 h at the same temperature, the resulting mixture was filtered and concentrated. The residue was purified by chromatography on silica gel (dichloromethane/methanol = 20/1 to 10/1 as the eluent) to obtain rac-1e’ (218 mg, 91%) as a colorless oil.

1-(Indolin-1-yl)-2-(piperidin-1-yl)propan-1-one (rac-1f’): prepared by the same procedure with rac-1d’ using indoline instead of 1,2,3,4-tetrahydroquinoline in step 2 (94% overall yield).

1-(Phenanthridin-5(6H)-yl)-2-(piperidin-1-yl)propan-1-one (rac-1g’): prepared by the same procedure with rac-1d’ using 5,6-dihydrophenanthridine instead of 1,2,3,4-tetrahydroquinoline in step 1 (98% overall yield).

N-Methyl-N-phenyl-2-(piperidin-1-yl)propanamide (rac-1h’): prepared by the same procedure with rac-1d’ using N-methylaniline instead of 1,2,3,4-tetrahydroquinoline in step 1 (98% overall yield).

N-Methoxy-N-methyl-2-(piperidin-1-yl)propanamide (rac-1j’): prepared by the same procedure with rac-1i’ using N,O-dimethylhydroxylamine hydrochloride instead of N-(diphenylmethyl)methylamine in the presence of 2 equivalents of N,N-diisopropylethylamine in step 1 (60% overall yield).

N-(tert-Butoxy)-N-methyl-2-(piperidin-1-yl)propanamide (rac-1k’): prepared by the same procedure with rac-1i’ using O-(tert-butyl)-N-methylhydroxylamine hydrochloride instead of N-(diphenylmethyl)methylamine in the presence of 2 equivalents of N,N-diisopropylethylamine in step 1 (69% overall yield).

1-(3,4-Dihydroquinolin-1(2H)-yl)-4-methyl-2-(piperidin-1-yl)pentan-1-one (rac-1s’): prepared by the same procedure with rac-1r’ using Cbz-DL-leucine instead of Cbz-DL-phenylalanine in step 1 (60% overall yield).
(Step 1) A mixture of 4-piperidone hydrate hydrochloride (384 mg, 2.50 mmol), \( p \)-toluenesulfonic acid monohydrate (19 mg, 0.10 mmol), and trimethyl orthoformate (1.4 mL) in methanol (12 mL) was stirred for 22 h at room temperature. The resulting mixture was concentrated to obtain 4,4-dimethoxypiperidine hydrochloride (18) (467 mg, quant.) as a white solid. (Step 2) A solution of 5,6-dihydrophenanthridine (725 mg, 4.0 mmol) and pyridine (324 \( \mu \)L, 4.0 mmol) in dichloromethane (20 mL) was treated with 2-bromopropionyl bromide (461 \( \mu \)L, 4.4 mmol) at –78 °C. The mixture was allowed to warm at room temperature and stirred for 1.5 h. The resulting mixture was diluted with water and extracted with dichloromethane. The combined extracts were washed with water, dried over sodium sulfate, and concentrated to obtain 19 as a colorless gum. The product was used without purification. (Step 3) A mixture of 19, 18 (0.73 g, 4.0 mmol), and potassium carbonate (2.76 g, 20 mmol) in acetonitrile (20 mL) was refluxed for 12 h. The resulting mixture was cooled to room temperature and filtered. The filtrate was concentrated and the residue was purified by chromatography on silica gel (hexane/ethyl acetate = 1.5/1 to 1/1.5 as the eluent) to obtain \( \text{rac-3'} \) (1.29 g, 85% yield) as a white solid.
Preparation and characterization of ammonium salt 1

Representative procedure for preparation of (S)-1-cinnamyl-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)piperidin-1-ium bromide (1d):

\[
\begin{align*}
\text{MeCN} & \quad \text{rt} \\
\begin{array}{c}
\text{1d'} \\
\text{1d}
\end{array}
\end{align*}
\]

A solution of 1d' (0.771 mg, 2.83 mmol) and cinnamyl bromide (0.51 mL, 3.4 mmol) in acetonitrile (14 mL) was stirred for 60 h at room temperature. Evaporation of the solvent and purification of the residue by chromatography on silica gel (dichloromethane/methanol = 15/1 to 7/1 as the eluent) gave 1d (1.36 g, quant.) as a pale brown solid. \([\alpha]_{235}^{29} = -94.1 \) (c 1.00, EtOH); IR (KBr) 3026, 3001, 2945, 2878, 1649, 1579, 1491, 1457, 1416, 1381, 1361, 1288, 1235, 1198, 1072, 992, 924, 865, 755, 696 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) (7/3 mixture of rotamers) 7.70 (0.3H, d, \(J = 8.4\) Hz, ArH), 7.56 (0.6H, d, \(J = 6.8\) Hz, ArH), 7.42-6.67 (9.4H, m, ArH and CH\(_{\text{Ph}}\)), 6.05 (0.7H, dt, \(J = 15.6, 7.6\) Hz, C\(_{\text{Ph}}\)=CHPh), 5.66 (0.3H, q, \(J = 6.8\) Hz, NCHCO), 4.91 (0.7H, q, \(J = 6.8\) Hz, NCHCO), 4.85-4.74 (0.3H, m, CH\(_2\)), 4.64 (1.4H, d, \(J = 7.6\) Hz, CH\(_2\)), 4.52-3.39 (5.6H, m, CH\(_2\)), 4.21-3.39 (5.6H, m, CH\(_2\)), 2.77-2.49 (1.7H, m, CH\(_2\)), 2.42-2.28 (0.3H, m, CH\(_2\)), 2.24-1.43 (8H, m, CH\(_2\)), 2.24-1.43 (8H, m, CH\(_2\)), 1.86 (3H, d, \(J = 6.8\) Hz, CH\(_{\text{CH}}\)C\(_{\text{Ph}}\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) (7/3 mixture of rotamers) 167.9, 166.6, 143.6, 141.1, 136.6, 134.6, 134.5, 134.4, 131.9, 129.2, 129.1, 129.0, 128.8, 128.6, 128.4, 127.33, 127.27, 125.4, 124.3, 123.4, 114.8, 113.2, 66.0, 61.6, 57.9, 57.1, 56.2, 55.5, 46.4, 43.0, 26.2, 25.9, 23.6, 23.4, 20.6, 20.2, 19.8, 19.6, 13.7, 13.3; HRMS–ESI (m/z): [M–Br]\(^+\) calcd for C\(_{26}\)H\(_{33}\)N\(_2\)O: 389.2587. Found: 389.2582.

(S)-1-Cinnamyl-1-(1-(cyclohexyloxy)-1-oxopropan-2-yl)pyrrolidin-1-ium bromide (1a):

prepared by the same procedure with 1d using 1a' as a substrate (quant.); white solid; \([\alpha]_{24}^{589} = -38.4\) (c 1.00, EtOH); IR (KBr) 3029, 2992, 2943, 2857, 1730, 1628, 1484, 1452, 1404, 1388, 1334, 1305, 1278, 1256, 1243, 1209, 1177, 1131, 1091, 1040, 1011, 974, 960, 945, 929, 892, 841, 807, 756, 727, 694 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.54-7.47 (2H, m, Ph), 7.38-7.29 (3H, m, Ph), 7.07 (1H, d, \(J = 15.6\) Hz, C\(_{\text{Ph}}\)=CHPh), 6.16 (1H, ddd, \(J = 15.6, 7.6, 7.6\) Hz, CH=CHPh), 4.82 (1H, tt, \(J = 9.0, 4.0\) Hz, OCH), 4.76 (1H, q, \(J = 7.2\) Hz, NCHCO), 4.65 (1H, dd, \(J = 13.3, 7.6\) Hz, CH\(_2\)CH=CH), 4.50 (1H, dd, \(J = 13.3, 7.6\) Hz, CH\(_2\)CH=CH), 4.18-3.91 (4H, m, CH\(_2\)), 2.43-2.19 (4H, m, CH\(_2\)), 1.88-1.76 (2H, m, CH\(_2\)), 1.82 (3H, d, \(J = 7.2\) Hz, CH\(_3\)), 1.75-1.65 (2H, m, CH\(_2\)), 1.58-1.18 (6H, m, CH\(_2\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 167.5, 142.7, 134.5, 129.2, 128.6, 127.1, 115.0, 75.8, 67.4, 64.3, 62.1, 61.6, 31.1, 30.9, 24.7, 23.9, 23.7, 23.29, 23.28, 14.5; HRMS–ESI (m/z): [M–Br]\(^+\) calcd for C\(_{22}\)H\(_{32}\)NO\(_2\): 342.2428. Found: 342.2418.
(S)-1-Cinnamyl-1-(1-oxo-1-(pyrrolidin-1-yl)propan-2-yl)pyrrolidin-1-i um bromide (1b): prepared by the same procedure with 1d using 1b’ as a substrate (62% yield); white solid; [α]D25 –80.9 (c 1.00, EtOH); IR (KBr) 3031, 2979, 2956, 2884, 1618, 1481, 1446, 1396, 1381, 1352, 1322, 1310, 1299, 1264, 1235, 1217, 1184, 1166, 1136, 1101, 1083, 1052, 1031, 1012, 982, 921, 897, 837, 764, 728, 697 cm−1; 1H NMR (400 MHz, CDCl3) δ 7.56 (2H, d, J = 7.2 Hz, Ph), 7.35 (2H, t, J = 7.2 Hz, Ph), 7.31 (1H, t, J = 7.2 Hz, Ph), 6.89 (1H, d, J = 15.5 Hz, CH=CHPh), 6.61 (1H, ddd, J = 15.5, 8.8, 6.4 Hz, CH=CHPh), 5.45 (1H, q, J = 6.8 Hz, NCHCO), 4.64 (1H, dd, J = 12.7, 8.8 Hz, CH2CH=CH), 4.49 (1H, dd, J = 12.7, 6.4 Hz, CH2CH=CH), 4.26-4.11 (3H, m, CH2), 4.05-3.95 (1H, m, CH2), 3.88-3.77 (1H, m, CH2), 3.46-3.33 (1H, m, CH2), 3.41 (2H, t, J = 6.6 Hz, CH2), 2.28-2.05 (4H, m, CH2), 1.92-1.61 (4H, m, CH2), 1.67 (3H, d, J = 6.8 Hz, CH3); 13C NMR (100 MHz, CDCl3) δ 166.3, 141.6, 134.5, 129.1, 128.6, 127.0, 115.7, 66.4, 65.6, 62.2, 60.2, 47.3, 46.3, 25.6, 24.5, 23.6, 23.5, 13.6; HRMS–ESI (m/z): [M–Br]+ calcd for C20H29N2O: 313.2274. Found: 313.2261.

(5)-1-Cinnamyl-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)pyrrolidin-1-ium bromide (1c): prepared by the same procedure with 1d using 1c’ as a substrate (75% yield); white solid; [α]D23 –55.1 (c 1.00, CHCl3); IR (KBr) 3027, 2953, 1654, 1602, 1579, 1491, 1450, 1376, 1290, 1235, 1204, 1137, 1071, 1027, 980, 923, 885, 840, 760, 694 cm−1; 1H NMR (400 MHz, CDCl3) δ (5/5 mixture of rotamers) 7.68 (0.5H, d, J = 8.0 Hz, ArH), 7.51 (1H, d, J = 6.0 Hz, ArH), 7.39-7.25 (3.5H, m, ArH), 7.25-6.95 (4.5H, m, ArH and CH=CHPh), 6.89 (0.5H, d, J = 15.2 Hz, CH=CHPh), 6.70-6.52 (0.5H, m), 6.23-6.01 (1H, m), 5.12-4.98 (0.5H, m, NCHCO), 4.77-4.40 (2H, m, CH2), 4.37-3.55 (6H, m, CH2), 2.75-2.05 (6H, m, CH2), 2.05-1.83 (2H, m, CH2), 1.79 (1.5H, d, J = 6.0 Hz, CH3), 1.68 (1.5H, d, J = 6.0 Hz, CH3); 13C NMR (100 MHz, CDCl3) δ (5/5 mixture of rotamers) 167.9, 166.8, 143.2, 141.8, 136.7, 136.5, 134.5, 134.2, 134.1, 131.7, 129.1, 129.0, 128.6, 128.5, 127.6, 127.3, 127.2, 125.5, 124.3, 123.7, 115.8, 114.6, 66.3, 65.9, 64.3, 62.8, 62.0, 60.8, 60.7, 46.1, 43.0, 43.0, 43.0, 43.0, 43.0, 43.0, 43.0, 43.0, 24.7, 24.4, 24.0, 23.8, 23.4, 22.8, 14.2, 14.0; HRMS–ESI (m/z): [M–Br]+ calcd for C25H31N2O: 375.2431. Found: 375.2426.

(5,5)-N-(1-(3,4-Dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)-N,N-dimethyl-3-phenylprop-2-en-1-aminium bromide (1e): prepared by the same procedure with 1d using 1e’ as a substrate (97% yield); white solid; [α]D25 –69.7 (c 1.00, CHCl3); IR (KBr) 3025, 2951, 1653, 1581, 1490, 1451, 1372, 1291, 1237, 1205, 1161, 1071, 990, 837, 820, 760, 695 cm−1; 1H NMR (400 MHz, CDCl3) δ (5/5 mixture of rotamers) 167.9, 166.8, 143.2, 141.8, 136.7, 136.5, 134.5, 134.2, 134.1, 131.7, 129.1, 129.0, 128.6, 128.5, 127.6, 127.3, 127.2, 125.5, 124.3, 123.7, 115.8, 114.6, 66.3, 65.9, 64.3, 62.8, 62.0, 60.8, 60.7, 46.1, 43.0, 43.0, 24.7, 24.4, 24.0, 23.8, 23.4, 22.8, 14.2, 14.0; HRMS–ESI (m/z): [M–Br]+ calcd for C23H29N2O: 349.2274. Found: 349.2268.
**(S)-1-Cinnamyl-1-(1-(indolin-1-yl)-1-oxopropan-2-yl)piperidin-1-ium bromide (1f):** prepared by the same procedure with 1d using 1f* as a substrate (89% yield); white solid; [α]²⁴_589 = −149.3 (c 1.00, EtOH); IR (KBr) 2976, 2941, 2873, 1651, 1599, 1484, 1438, 1397, 1357, 1321, 1287, 1170, 1129, 1079, 1050, 1026, 992, 926, 868, 822, 767, 752, 729, 698 cm⁻¹; ¹H NMR (400 MHz, CDCl₃+CD₃OD) δ 8.19 (1H, d, J = 8.0 Hz, ArH), 7.31-7.19 (6H, m, ArH), 7.14-7.05 (2H, m, ArH), 6.69-6.57 (2H, m, CH≡CPh), 4.80 (1H, q, J = 6.8 Hz, NCHCO), 4.76-4.67 (1H, m, CH₂), 4.50 (1H, d, J = 12.4 Hz, CH₂), 4.39-4.27 (1H, m, CH₂), 4.18 (1H, d, J = 12.4 Hz, CH₂), 4.13 (1H, ddd, J = 10.8, 10.8, 6.2 Hz, CH₂), 3.92 (1H, ddd, J = 10.8, 10.8, 6.2 Hz, CH₂), 3.74 (1H, ddd, J = 12.6, 12.6, 3.6 Hz, CH₂), 3.56 (1H, ddd, J = 12.6, 12.6, 3.6 Hz, CH₂), 2.95 (1H, ddd, J = 16.2, 10.2, 6.2 Hz, CH₂), 2.43 (1H, ddd, J = 16.2, 10.2, 6.2 Hz, CH₂), 2.23-1.90 (5H, m, CH₂), 1.79 (3H, d, J = 6.8 Hz, CHCH₃), 1.75-1.60 (1H, m, CH₂); ¹³C NMR (100 MHz, CDCl₃+CD₃OD) δ 166.4, 142.5, 141.6, 133.9, 132.2, 129.3, 128.6, 127.1, 125.1, 124.8, 117.1, 113.2, 104.9, 67.2, 58.2, 56.8, 56.5, 48.6, 27.4, 20.8, 20.1, 19.7, 12.7; HRMS–ESI (m/z): [M–Br]⁺ calecd for C₂₅H₃₁N₂O: 375.2431. Found: 375.2423.

**(S)-1-Cinnamyl-1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)piperidin-1-ium bromide (1g):** prepared by the same procedure with 1d using 1g* as a substrate (98% yield); pale yellow solid; [α]²⁴_589 = −139.5 (c 1.00, EtOH); IR (KBr) 3025, 2946, 1657, 1486, 1441, 1413, 1383, 1354, 1311, 1288, 1263, 1223, 1191, 1129, 1097, 980, 927, 866, 744, 695 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ (5/5 mixture of rotamers) 7.88 (0.5H, d, J = 7.6 Hz, ArH), 7.80-7.66 (2H, m, ArH), 7.63 (0.5H, d, J = 7.6 Hz, ArH), 7.48-6.93 (11H, m, ArH and CH≡CPh), 6.77 (0.5H, d, J = 15.5 Hz, CH≡CPh), 6.56 (0.5H, ddd, J = 15.5, 9.2, 6.0 Hz, CH≡CPh), 6.12 (0.5H, q, J = 6.8 Hz, NCHCO), 5.73 (1H, br, CH₂), 5.35-5.25 (0.5H, m, CH₂), 4.95 (0.5H, d, J = 16.4 Hz, CH₂), 4.90 (0.5H, q, J = 6.8 Hz, NCHCO), 4.70 (0.5H, dd, J = 13.7, 5.2 Hz, CH₂), 4.54 (1H, br, CH₂), 4.44 (0.5H, dd, J = 13.7, 9.4 Hz, CH₂), 4.36 (1H, br, CH₂), 4.13 (1H, br, CH₂), 3.91-3.78 (0.5H, m, CH₂), 3.78-3.43 (1.5H, m, CH₂), 2.77 (1H, br, CH₂), 2.30-1.05 (5H, m, CH₂), 1.76 (3H, d, J = 6.8 Hz, CHCH₃); ¹³C NMR (100 MHz, CDCl₃) δ (5/5 mixture of rotamers) 167.5, 143.5, 141.4, 135.7, 135.2, 134.5, 134.4, 133.7, 132.9, 130.9, 130.8, 130.3, 129.8, 129.3, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.2, 127.4, 127.3, 127.1, 126.75, 126.69, 126.2, 125.1, 124.9, 124.2, 123.4, 122.7, 114.4, 65.7, 57.9, 57.6, 57.2, 55.7, 55.4, 48.2, 46.0, 20.7, 20.6, 20.1, 20.0, 19.8, 19.4; HRMS–ESI (m/z): [M–Br]⁺ calecd for C₃₀H₃₃N₂O₃: 437.2587. Found: 437.2577.

**(S)-1-Cinnamyl-1-(1-(methyl(phenyl)amino)-1-oxopropan-2-yl)piperidin-1-ium bromide (1h):** prepared by the same procedure with 1d using 1h* as a substrate (75% yield); pale brown solid; [α]²¹_589 = −41.1 (c 1.00, EtOH); IR (KBr) 3023, 2946, 1657, 1593, 1494, 1467, 1452, 1403, 1380, 1349, 1309, 1271, 1199, 1116, 1090, 1031, 998, 928, 899, 865, 822, 753, 703 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.40-7.25 (5H, m, ArH), 7.22-7.10 (4H, m, ArH), 6.89-6.81 (1H, m, ArH), 6.78 (1H, d, J = 15.9 Hz, CH≡CPh), 5.92 (1H, ddd, J = 15.9, 9.2, 6.2 Hz, CH≡CPh), 4.54 (1H, dd, J = 14.1, 6.2 Hz, CH₂CH=CH), 4.41 (1H, dd, J = 14.1, 9.2 Hz, CH₂CH=CH), 4.34 (1H, ddd, J = 12.9, 12.9, 3.8 Hz, CH₂), 4.09 (1H, q, J = 6.8 Hz, NCHCO), 3.64 (1H, d, J = 12.4 Hz, CH₂), 3.54-3.36 (2H, m, CH₂), 3.28 (3H, s, NCH₃), S33.
2.16-1.91 (3H, m, CH₂), 1.91-1.67 (2H, m, CH₂), 1.72 (3H, d, \( J = 6.8 \) Hz, CHCH₃), 1.58-1.40 (1H, m, CH₂); \(^{13}\text{C NMR} (100 \text{ MHz, CDCl}_3) \delta 166.7, 143.2, 140.8, 134.1, 130.4, 129.0, 128.3, 127.4, 126.3, 112.8, 61.7, 56.7, 55.7, 54.7, 37.7, 20.7, 20.2, 19.7, 12.7; HRMS–ESI \((m/z)\): \([\text{M–Br}]^+\) calcd for C₂₄H₃₁N₂O: 363.2431. Found: 363.2415.

**(S)-1-(1-(Benzhydryl(methyl)amino)-1-oxopropan-2-yl)-1-cinnamylpiperidin-1-ium bromide (1i):**

Prepared by the same procedure with 1d using 1i as a substrate (98% yield); white solid; [\( \alpha \)]\text{D}^{25} -92.7 (c 1.00, EtOH); IR (KBr) 3054, 3027, 2997, 2942, 2868, 1494, 1475, 1450, 1380, 1343, 1309, 1277, 1195, 1170,1134, 1074, 1049, 1029, 1000, 974, 925, 868, 827, 740, 700 cm\(^{-1}\); \(^1\text{H NMR} (400 \text{ MHz, CDCl}_3) \delta (8/2 \text{ mixture of rotamers}) 7.54 (0.4H, d, \( J = 7.2 \) Hz, ArH), 7.48 (1.6H, d, \( J = 7.2 \) Hz, ArH), 7.37-6.89 (14.2H, m, ArH, CH=C\text{Ph}, and C\text{Ph}₂), 6.73 (0.8H, d, \( J = 15.6 \) Hz, CH=C\text{Ph}), 6.61-6.49 (1H, m, CH=C\text{Ph}), 5.45 (0.8H, q, \( J = 6.8 \) Hz, NCHCO), 5.34 (0.2H, q, \( J = 6.8 \) Hz, NCHCO), 4.81-4.60 (0.4H, m, CH₂), 4.75 (0.8H, dd, \( J = 14.1 \) Hz, CH₂), 4.43 (0.8H, dd, \( J = 14.1 \), 8.8 Hz, CH₂), 4.33 (1H, d, \( J = 12.8 \) Hz, CH₂), 4.15 (0.8H, d, \( J = 12.8 \) Hz, CH₂), 3.95 (0.8H, ddd, \( J = 12.4 \) Hz, CH₂), 3.80 (0.2H, d, \( J = 12.0 \) Hz, CH₂), 3.71 (0.8H, ddd, \( J = 12.4 \), 2.8 Hz, CH₂), 3.55 (0.2H, dd, \( J = 12.0 \) Hz, CH₂), 3.40 (0.2H, d, \( J = 12.0 \) Hz, CH₂), 3.02 (2.4H, s, NCH₃), 2.80 (0.6H, s, NCH₃), 2.15-1.50 (6H, m, CH₂), 1.82 (2.4H, d, \( J = 6.8 \) Hz, CHCH₃), 1.70 (0.6H, d, \( J = 6.8 \) Hz, CHCH₃); \(^{13}\text{C NMR} (100 \text{ MHz, CDCl}_3) \delta 169.2, 169.1, 141.8, 141.1, 138.4, 138.3, 137.9, 137.5, 134.8, 134.6, 129.1, 128.64, 128.59, 128.57, 128.45, 128.37, 127.94, 127.88, 127.8, 127.7, 127.4, 115.0, 114.9, 65.5, 64.5, 64.1, 61.2, 57.6, 57.4, 56.8, 56.0, 55.9, 55.5, 33.7, 32.7, 20.7, 20.5, 20.1, 20.0, 19.9, 14.5, 13.4; HRMS–ESI \((m/z)\): \([\text{M–Br}]^+\) calcd for C₃₁H₃₇N₂O: 453.2900. Found: 453.2894.

**(S)-1-Cinnamyl-1-(1-(methoxy(methyl)amino)-1-oxopropan-2-yl)piperidin-1-ium bromide (1j):**

Prepared by the same procedure with 1d using 1j as a substrate (91% yield); white solid; [\( \alpha \)]\text{D}^{25} -24.0 (c 1.00, EtOH); IR (KBr) 2997, 2938, 2873, 1661, 1477, 1442, 1381, 1338, 1323, 1197, 1174, 1155, 1108, 1075, 1054, 1026, 988, 947, 928, 909, 870, 823, 760, 729, 698 cm\(^{-1}\); \(^1\text{H NMR} (400 \text{ MHz, CDCl}_3) \delta 7.58 (2H, d, \( J = 7.4 \) Hz, ArH), 7.39-7.28 (3H, m, Ph), 7.02 (1H, d, \( J = 15.6 \) Hz, CH=CHPh), 6.57 (1H, ddd, \( J = 15.6 \), 7.8, 6.8 Hz, CH=CHPh), 4.97 (1H, q, \( J = 7.0 \) Hz, NCHCO), 4.72 (1H, dd, \( J = 13.9 \), 6.8 Hz, CH₂CH=CH), 4.60 (1H, dd, \( J = 13.9 \), 7.8 Hz, CH₂CH=CH), 4.05-3.88 (3H, m, CH₃), 3.71 (3H, s, OCH₃), 3.63 (1H, ddd, \( J = 12.2 \), 12.2, 3.2 Hz, CH₂), 3.19 (3H, s, NCH₃), 2.23-2.05 (2H, m, CH₂), 2.02-1.64 (4H, m, CH₂), 1.82 (3H, d, \( J = 7.0 \) Hz, CHCH₃); \(^{13}\text{C NMR} (100 \text{ MHz, CDCl}_3) \delta 167.7, 142.5, 134.6, 129.1, 128.7, 127.2, 114.4, 62.7, 62.54, 62.50, 58.2, 56.5, 56.0, 32.1, 20.5, 19.9, 13.0; HRMS–ESI \((m/z)\): \([\text{M–Br}]^+\) calcd for C₁₀H₂₉N₂O₂: 317.2224. Found: 317.2220.
(S)-1-(1-(tert-Butoxy(methyl)amino)-1-oxopropan-2-yl)-1-cinnamylpiperidin-1-ium bromide (1k): prepared by the same procedure with 1d using 1k<sup>+</sup> as a substrate (96% yield); white solid; [α]<sup>20</sup><sub>950</sub> = -16.7 (c 1.00, EtOH); IR (KBr) 3023, 2979, 2937, 1661, 1469, 1415, 1387, 1367, 1308, 1286, 1261, 1240, 1196, 1151, 1111, 1068, 1009, 942, 920, 899, 867, 837, 819, 786, 760, 732, 696 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 7.59 (2H, d, J = 6.8 Hz, Ph), 7.39-7.26 (4H, m, Ph and CH=CHPh), 6.43 (1H, dt, J = 15.6, 7.8 Hz, CH=CHPh), 4.85 (1H, q, J = 6.8 Hz, NCHCO), 4.74 (2H, d, J = 7.8 Hz, CH<sub>2</sub>CH=CH), 4.08 (1H, t, J = 12.0 Hz, CH<sub>2</sub>), 3.77 (1H, d, J = 12.0 Hz, CH<sub>2</sub>), 3.58 (1H, d, J = 12.0 Hz, CH<sub>2</sub>), 3.28 (3H, s, NCH<sub>3</sub>), 3.20 (1H, t, J = 12.0 Hz, CH<sub>2</sub>), 2.35-2.08 (2H, m, CH<sub>2</sub>), 1.96-1.75 (3H, m, CH<sub>2</sub>), 1.82 (3H, d, J = 6.8 Hz, CHCH<sub>3</sub>), 1.56-1.40 (1H, m, CH<sub>2</sub>), 1.13 (9H, s, t-Bu); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 170.4, 143.5, 134.4, 129.3, 128.6, 127.2, 113.8, 84.6, 61.0, 57.1, 55.4, 55.1, 39.2, 27.3, 20.7, 20.2, 19.5, 11.8; HRMS–ESI (m/z): [M–Br]<sup>+</sup> calcd for C<sub>27</sub>H<sub>33</sub>N<sub>2</sub>O: 423.2198. Found: 423.2187.

(S,E)-1-(3-(4-Chlorophenyl)allyl)-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)piperidin-1-ium bromide (1l): prepared by the same procedure with 1d using 1l<sup>+</sup> as a substrate (91% yield); white solid; [α]<sup>20</sup><sub>589</sub> = -91.2 (c 1.00, EtOH); IR (KBr) 3012, 2947, 2873, 1650, 1491, 1460, 1412, 1381, 1351, 1308, 1235, 1197, 1126, 1089, 1011, 990, 943, 925, 868, 829, 804, 763 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (7/3 mixture of rotamers) 7.69 (0.3H, d, J = 8.0 Hz, ArH), 7.55 (0.6H, d, J = 8.0 Hz, ArH), 7.41-6.69 (8.4H, m, ArH and CH=CHAr), 6.16 (0.7H, ddd, J = 15.2, 8.6, 6.6 Hz, CH=CHAr), 5.66 (0.3H, q, J = 6.4 Hz, NCHCO), 4.90 (0.7H, q, J = 6.4 Hz, NCHCO), 4.81-4.64 (0.3H, m, CH<sub>2</sub>), 4.69 (0.7H, dd, J = 13.6, 6.6 Hz, CH<sub>2</sub>CH=CH), 4.60 (0.7H, dd, J = 13.6, 8.6 Hz, CH<sub>2</sub>CH=CH), 4.53-4.30 (1H, m, CH<sub>2</sub>), 4.18-3.78 (2H, m, CH<sub>2</sub>), 3.75-3.57 (2H, m, CH<sub>2</sub>), 3.57-3.39 (1.3H, m, CH<sub>2</sub>), 2.75-2.51 (1.7H, m, CH<sub>2</sub>), 2.45-1.40 (8.3H, m, CH<sub>2</sub>), 1.84 (3H, d, J = 6.4 Hz, CHCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (7/3 mixture of rotamers) 168.0, 166.6, 142.1, 139.6, 137.7, 136.7, 134.9, 134.7, 133.1, 131.8, 129.1, 129.0, 128.8, 128.7, 128.6, 128.0, 127.4, 125.5, 125.1, 124.3, 123.6, 115.8, 114.4, 66.1, 61.6, 58.0, 57.8, 57.0, 56.3, 55.8, 46.4, 43.1, 26.2, 26.0, 23.6, 23.4, 21.3, 20.7, 20.2, 19.8, 19.6, 13.5, 13.3; HRMS–ESI (m/z): [M–Br]<sup>+</sup> calcd for C<sub>27</sub>H<sub>33</sub>N<sub>2</sub>O: 423.2198. Found: 423.2187.

(S,E)-1-(3-(4-Bromophenyl)allyl)-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)piperidin-1-ium bromide (1m): prepared by the same procedure with 1d using 1m<sup>+</sup> as a substrate (91% yield); white solid; [α]<sup>20</sup><sub>589</sub> = -88.1 (c 1.00, EtOH); IR (KBr) 3007, 2946, 2873, 1650, 1583, 1488, 1458, 1414, 1381, 1351, 1307, 1234, 1197, 1126, 1114, 1090, 1071, 1007, 940, 926, 867, 828, 801, 762 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ (7/3 mixture of rotamers) 7.69 (0.3H, d, J = 8.4 Hz, ArH), 7.49 (0.6H, d, J = 8.4 Hz, ArH), 7.44 (2H, d, J = 8.4 Hz, ArH), 7.29 (1.4H, d, J = 8.4 Hz, ArH), 7.22-6.80 (4.7H, m, ArH and CH=CHAr), 6.72 (0.3H, d, J = 15.2 Hz, CH=CHAr), 6.18 (0.7H, ddd, J = 15.2, 8.6, 6.6 Hz, CH=CHAr), 5.69 (0.3H, q, J = 6.8 Hz, NCHCO), 4.90 (0.7H, q, J = 6.8 Hz, NCHCO), 4.81-4.65 (0.3H, m, CH<sub>2</sub>), 4.69 (0.7H, dd, J = 13.8, 6.6 Hz, CH<sub>2</sub>CH=CH), 4.60 (0.7H, dd, J = 13.8, 8.6 Hz, CH<sub>2</sub>CH=CH), 4.54-4.37 (0.7H, m, CH<sub>2</sub>), 4.18-3.40 (5.6H, m, CH<sub>2</sub>), 2.75-2.52 (1.7H, m, CH<sub>2</sub>), 2.43-1.40 (8.3H, m, CH<sub>2</sub>), 1.84 (3H, d, J = 6.8 Hz, CHCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ (7/3 mixture of rotamers) 168.0, S35.
166.6, 142.2, 139.7, 136.7, 134.7, 133.6, 131.9, 131.8, 131.6, 129.2, 129.1, 129.0, 127.4, 125.5, 124.3, 123.6, 123.2, 116.0, 114.6, 66.1, 61.6, 58.0, 57.9, 57.0, 56.3, 55.8, 46.4, 43.1, 26.3, 26.1, 23.6, 23.5, 20.7, 20.3, 19.9, 19.7, 13.6, 13.3; HRMS–ESI (m/z): [M–Br]+ calcd for C_{26}H_{32}BrN_{2}O: 467.1693. Found: 467.1684.

(S,E)-1-(1-(3,4-Dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)-1-(3-(p-tolyl)allyl)piperidin-1-ium bromide (1n): prepared by the same procedure with 1d using 1n' as a substrate (86% yield); pale brown solid; [α]^{23}_{D}^{	ext{23}} = −92.8 (c 1.00, EtOH); IR (KBr) 3007, 2946, 2868, 1649, 1580, 1513, 1490, 1456, 1415, 1381, 1351, 1308, 1286, 1253, 1234, 1197, 1127, 1091, 1070, 1015, 989, 940, 925, 900, 867, 828, 799, 762 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ (7/3 mixture of rotamers) 7.70 (0.3H, d, J = 8.0 Hz, ArH), 7.42 (0.6H, d, J = 7.2 Hz, ArH), 7.29–6.88 (7.8H, m, ArH and CH=CHAr), 6.77 (0.3H, d, J = 15.6 Hz, CH=CHAr), 6.69–6.56 (0.3H, m, CH=CHAr), 5.94 (0.7H, d, J = 15.6 Hz, CH=CHAr), 6.69–6.56 (0.3H, m, CH=CHAr), 5.67 (0.7H, q, J = 6.4 Hz, NCHCO), 4.91 (0.7H, q, J = 6.4 Hz, NCHCO), 4.83–4.71 (0.3H, m, CH₂), 4.71–4.65 (1.4H, m, CH₂), 4.52–4.26 (0.7H, m, CH₂), 2.77–2.50 (2H, m, CH₂), 2.45–1.46 (8H, m, CH₂), 2.36 (0.9H, s, ArCH₃), 2.32 (0.9H, s, ArCH₃), 1.86 (3H, d, J = 6.4 Hz, CHC\(_{3}\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ (7/3 mixture of rotamers) 168.0, 166.7, 143.7, 141.2, 139.4, 139.2, 136.7, 134.7, 135.0, 134.7, 132.0, 131.8, 131.7, 129.3, 129.1, 128.9, 127.4, 127.2, 125.4, 124.3, 123.4, 113.5, 111.9, 66.1, 61.7, 58.0, 57.1, 56.1, 55.5, 46.5, 43.1, 26.2, 26.0, 23.6, 23.4, 21.2, 20.6, 20.2, 19.9, 19.7, 13.7, 13.4; HRMS–ESI (m/z): [M–Br]\(^+\) calcd for C\(_{27}\)H\(_{35}\)N\(_{2}\)O: 403.2744. Found: 403.2727.

(S,Z)-1-(1-(3,4-Dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)-1-(3-phenylallyl)piperidin-1-ium bromide (1o): prepared by the same procedure with 1d using (Z)-(3-bromoprop-1-en-1-yl)benzene\(^5\) as a substrate (87% yield); pale red solid; [α]^{22}_{D}^{	ext{22}} = −67.6 (c 1.00, EtOH); IR (KBr) 3023, 2948, 2873, 1650, 1602, 1581, 1490, 1454, 1415, 1383, 1354, 1305, 1286, 1256, 1234, 1197, 1170, 1124, 1089, 1028, 929, 865, 809, 769, 701 cm\(^{-1}\); \(^1\)H NMR (400 MHz, CDCl\(_3\)) δ [Z/E = 8/2, 7/3 mixture of rotamers (ca. 55/30/10/5 mixtures)] 7.71 (0.05H, d, J = 8.4 Hz, E-ArH), 7.58–7.45 (0.65H, m, Z-ArH), 7.43–6.67 (9.35H, m, ArH and C=CHPh), 6.40 (0.30H, dt, J = 10.8, 6.6 Hz, Z=CH=CHPh), 6.05 (0.10H, dt, J = 15.2, 7.2 Hz, E=CH=CHPh), 5.88–5.64 (0.90H, m, Z=CH=CHPh and NCHCO), 4.98–3.40 (8.65H, m, NCHCO and CH₂), 2.87–2.51, 2.45–1.46, and 1.35–1.22 (13H, m, CH₂ and CH₂CH₃); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) δ [Z/E = 8/2, 7/3 mixture of rotamers (ca. 55/30/10/5 mixtures), assigned only Z-isomer] 167.2, 166.4, 141.5, 138.5, 136.9, 136.6, 135.0, 134.3, 134.0, 131.5, 129.2, 128.7, 128.6, 128.4, 128.2, 127.8, 127.6, 127.4, 125.4, 125.2, 124.7, 124.2, 117.2, 116.5, 65.9, 62.6, 56.8, 56.1, 55.7, 55.6, 51.7, 51.4, 46.6, 43.0, 26.3, 26.1, 23.9, 23.4, 20.6, 20.5, 20.0, 19.8, 13.5, 12.7; HRMS–ESI (m/z): [M–Br]\(^+\) calcd for C\(_{26}\)H\(_{33}\)N\(_{2}\)O: 389.2587. Found: 389.2579.

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(S,E)-1-(1-(3,4-Dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)-1-(hex-2-en-1-yl)piperidin-1-ium bromide (1p): prepared by the same procedure with 1d using (E)-1-bromohex-2-ene instead of cinnamyl bromide (82% yield); pale brown solid; [α]D20 +96.2 (c 1.00, EtOH); IR (KBr) 2956, 2868, 1648, 1580, 1490, 1457, 1418, 1381, 1307, 1289, 1235, 1199, 1126, 1092, 986, 923, 863, 827, 766 cm\(^{-1}\); 1H NMR (400 MHz, CDCl3) δ (8/2 mixture of rotamers) 7.67 (0.2H, d, J = 7.6 Hz, ArH), 7.39-7.04 (2.8H, m, ArH), 7.08 (1H, d, J = 7.6 Hz, ArH), 6.18 (1H, dt, J = 14.8, 6.8 Hz, CH=CH(CH2)2CH3), 5.92-5.77 (0.2H, m, CH=CH(CH2)2CH3), 5.50-5.38 (0.2H, m, NCHCO), 5.21 (0.8H, dt, J = 14.8, 6.8 Hz, CH=CH(CH2)2CH3), 4.80 (0.8H, q, J = 6.8 Hz, NCHCO), 4.71-4.56 (0.2H, m, CH2), 4.49-4.29 (1.8H, m, CH2), 4.27-3.32 (6H, m, CH2), 2.78 (1H, dt, J = 15.8, 6.2 Hz, CH2), 2.67 (1H, dt, J = 15.8, 7.0 Hz, CH2), 2.24-1.50 (10H, m, CH2), 1.85 (3H, d, J = 6.8 Hz, CHCH3), 1.50-1.18 (2H, m, CH2), 0.84 (3H, t, J = 7.2 Hz, CH3CH2); 13C NMR (100 MHz, CDCl3) δ (8/2 mixture of rotamers) 166.9, 165.8, 146.3, 144.2, 136.2, 134.3, 130.9, 128.6, 128.3, 126.8, 125.6, 124.9, 124.8, 123.9, 122.9, 115.8, 114.0, 64.7, 60.9, 56.8, 56.0, 55.1, 54.7, 54.6, 45.8, 42.5, 33.7, 25.6, 23.3, 22.8, 20.8, 20.5, 19.9, 19.3, 18.9, 13.1, 12.8, 12.7; HRMS–ESI (m/z): [M+Br]+ calcd for C20H29N2O: 355.2738. Found: 355.2738.

(S)-1-Allyl-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxopropan-2-yl)piperidin-1-ium bromide (1q): prepared by the same procedure with 1d using 2 equivalents of allyl bromide instead of cinnamyl bromide (43% yield); pale brown solid; [α]D20 +90.6 (c 1.00, EtOH); IR (KBr) 2946, 2873, 1650, 1491, 1460, 1421, 1383, 1341, 1287, 1235, 1201, 1168, 1121, 1088, 1052, 1014, 945, 864, 826, 769 cm\(^{-1}\); 1H NMR (400 MHz, CDCl3) δ (7/3 mixture of rotamers) 7.65 (0.3H, d, J = 7.6 Hz, ArH), 7.40-7.03 (3.7H, m, ArH), 6.43-6.27 (0.3H, m, CH=CH2), 5.88-5.50 (3H, m, CH=CH2 and NCHCO), 4.87 (0.7H, q, J = 6.8 Hz, NCHCO), 4.74-4.61 (0.3H, m, CH2), 4.61-4.44 (1.3H, m, CH2), 4.44-4.26 (0.7H, m, CH2), 4.22-3.40 (5.7H, m, CH2), 2.85-2.58 (2H, m, CH2), 2.42-1.49 (8H, m, CH2), 1.85 (3H, d, J = 6.8 Hz, CHCH3); 13C NMR (100 MHz, CDCl3) δ (7/3 mixture of rotamers) 167.6, 166.4, 136.7, 134.8, 131.8, 129.9, 129.3, 128.9, 127.4, 127.4, 125.6, 125.4, 125.1, 124.5, 123.6, 123.5, 166.2, 61.6, 58.4, 57.5, 57.1, 56.0, 55.8, 46.5, 43.2, 26.2, 23.9, 23.4, 20.55, 20.46, 20.1, 20.0, 19.8, 19.6, 13.7, 13.4; HRMS–ESI (m/z): [M+Br]+ calcd for C20H29N2O: 313.2274. Found: 313.2265.

(S)-1-Cinnamyl-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-1-oxo-3-phenylpropan-2-yl)piperidin-1-ium bromide (1r): prepared by the same procedure with 1d using 1r′ as a substrate (60% yield); red solid; [α]D20 +66.3 (c 1.00, EtOH); IR (KBr) 3023, 2947, 2873, 1645, 1490, 1453, 1409, 1290, 1234, 1194, 1111, 1073, 1028, 995, 942, 861, 822, 753, 699 cm\(^{-1}\); 1H NMR (400 MHz, CDCl3) δ (7/3 mixture of rotamers) 7.64-7.56 (1H, m, ArH), 7.47-7.10 (11.3H, m ArH and CH=CHPh), 7.07 (0.3H, t, J = 7.4 Hz, ArH), 7.02 (0.3H, d, J = 7.4 Hz, ArH), 6.90 (0.7H, d, J = 7.4 Hz, ArH), 6.78 (0.3H, dt, J = 15.6, 7.6 Hz, CH=CHPh), 6.71 (0.7H, dd, J = 7.6, 7.6 Hz, ArH), 6.37 (0.7H, dd, J = 7.6, 7.6 Hz, ArH), 6.05 (0.7H, br, CH=CHPh), 5.69 (0.3H, br, CH2), 5.63 (0.3H, dd, J = 11.8, 3.0 Hz, NCHCO), 5.12-4.94 (1.7H, m, NCHCO and CH2), 4.78-4.66 (1H, m, CH2), 4.38 (0.3H, ddd, J = 13.0, 13.0, 3.2 Hz, CH2), 4.30-4.10 (1H, m, CH2), 4.10-3.89 (2.4H, m, CH2), 3.87-3.73 (0.6H, m, CH2), 3.56-3.10 (3.4H, m, CH2), 2.42 (0.3H, dt, J = 16.0, 7.4 Hz, CH2), 2.33-1.76 (7H, m, CH2), 1.76-1.52 (1.7H, m, CH2), 1.52-1.35 (0.7H, m, CH2), 0.99 (0.3H, dtt, J = 13.6, 6.8, 6.8 Hz, CH2); 13C NMR (100 MHz, CDCl3) δ (7/3 mixture of rotamers) 165.9, 165.2, 143.7, 141.6, S37
136.5, 136.2, 134.8, 134.5, 133.2, 132.6, 132.4, 130.3, 129.7, 129.3, 129.1, 129.0, 128.9, 128.7, 128.5, 127.9, 127.4, 127.3, 126.9, 126.7, 125.7, 125.4, 124.3, 124.1, 115.8, 113.5, 70.5, 65.9, 58.0, 57.7, 56.7, 56.1, 55.9, 46.6, 43.6, 34.2, 32.9, 26.0, 25.9, 23.1, 20.7, 20.5, 20.3, 19.8; HRMS–ESI (m/z): [M–Br]⁺ calecd for C_{32}H_{32}N_{2}O: 465.2900. Found: 465.2891.

(S)-1-Cinnamyl-1-(1-(3,4-dihydroquinolin-1(2H)-yl)-4-methyl-1-oxopentan-2-yl)piperidin-1-ium

bromide (1s): prepared by the same procedure with 1d using 1s' as a substrate (71% yield); red solid; [α]_{D}^{24589} +105.7 (c 1.00, EtOH); IR (KBr) 2954, 2899, 2875, 1644, 1620, 1580, 1488, 1462, 1407, 1356, 1284, 1243, 1224, 1193, 1165, 1118, 1071, 1052, 1026, 999, 943, 928, 877, 823, 755, 693 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ (8/2 mixture of rotamers) 7.67 (0.2H, d, J = 8.0 Hz, ArH), 7.61-7.65 (0.4H, m, ArH), 7.54-7.64 (1.6H, m, ArH), 7.42-7.29 (3H, m, ArH), 7.22-7.06 (2.4H, m, ArH and CH=CHPh), 6.98 (0.8H, d, J = 15.6 Hz, CH=CHPh), 6.87 (0.8H, ddd, J = 7.6, 7.6, 0.8 Hz, ArH), 6.72 (0.2H, dt, J = 15.6, 7.6 Hz, CH=CHPh), 6.56 (0.8H, ddd, J = 7.6, 7.6, 0.8 Hz, ArH), 6.42 (0.8H, ddd, J = 15.6, 9.6, 5.8 Hz, CH=CHPh), 5.27 (0.2H, dd, J = 11.2, 2.0 Hz, NCHCO), 4.95 (0.8H, dd, J = 8.2, 5.8 Hz, NCHCO), 4.86-4.72 (0.4H, m, CH₂), 4.79 (0.8H, dd, J = 14.0, 5.8 Hz, CH₂), 4.60-4.16 (2.2H, m, CH₂), 4.48 (0.8H, dd, J = 14.0, 9.8 Hz, CH₂), 3.93-3.64 (2.2H, m, CH₂), 3.53-3.40 (0.8H, m, CH₂), 3.35 (0.8H, t, J = 11.4 Hz, CH₂), 2.74 (0.8H, dt, J = 16.2, 8.8 Hz, CH₂), 2.59 (0.8H, dt, J = 16.2, 6.8 Hz, CH₂), 2.36-1.69 (9.2H, m, CH₂), 1.67-1.54 (0.2H, m, CH(CH₃)₂), 1.52-1.37 (0.8H, m, CH₂), 1.25 (0.8H, sept, J = 6.4 Hz, CH(CH₃)₂), 1.10 (0.6H, d, J = 6.4 Hz, CH(CH₃)₂), 1.00 (0.6H, d, J = 6.4 Hz, CH(CH₃)₂), 0.97 (2.4H, d, J = 6.4 Hz, CH(CH₃)₂), 0.34 (2.4H, d, J = 6.4 Hz, CH(CH₃)₂); ¹³C NMR (100 MHz, CDCl₃) δ (8/2 mixture of rotamers) 167.0, 166.8, 143.9, 141.8, 136.8, 136.7, 134.81, 134.75, 134.5, 132.0, 129.4, 129.2, 128.8, 128.6, 127.5, 127.3, 127.2, 126.0, 125.6, 124.5, 124.3, 115.8, 113.6, 69.0, 64.8, 58.2, 57.8, 56.95, 56.86, 56.4, 55.5, 47.1, 43.8, 37.5, 37.4, 36.4, 36.2, 26.2, 25.3, 24.9, 24.3, 24.1, 23.9, 23.2, 22.1, 20.9, 20.82, 20.76, 20.5, 20.3, 20.1; HRMS–ESI (m/z): [M–Br]⁺ calecd for C_{32}H_{32}N_{2}O: 431.3057. Found: 431.3049.

(S)-1-Cinnamyl-4,4-dimethoxy-1-(1-oxo-1-(phenanthridin-5(6H)-yl)propan-2-yl)piperidin-1-ium

bromide (3): prepared by the same procedure with 1d using 3' as a substrate (70% yield); white solid; [α]_{D}^{23589} –160.1 (c 1.00, EtOH); IR (KBr) 2959, 2834, 1659, 1485, 1442, 1411, 1382, 1348, 1312, 1264, 1223, 1192, 1161, 1119, 1053, 1002, 979, 943, 871, 843, 750, 695 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ (5/5 mixture of rotamers) 7.90 (0.5H, d, J = 7.6 Hz, ArH), 7.83-7.66 (2H, m, ArH), 7.60 (0.5H, d, J = 7.6 Hz, ArH), 7.55-6.85 (11H, m, ArH and CH=CHPh), 6.68 (0.5H, d, J = 15.2 Hz, CH=CHPh), 6.64-6.51 (0.5H, m, CH=CHPh), 6.39 (0.5H, q, J = 6.8 Hz, NCHCO), 5.71 (1H, br, CH₂), 5.31 (0.5H, d, J = 15.6 Hz, CH₂), 5.03-4.86 (1H, m, NCHCO and CH₂), 4.86-4.65 (1H, m, CH₂), 4.65-4.49 (1H, m, CH₂), 4.49-3.43 (2H, m, CH₂), 4.40 (0.5H, dd, J = 13.8, 9.4 Hz, CH₂), 3.68 (0.5H, dd, J = 13.0, 13.0 Hz, CH₂), 3.56 (0.5H, ddd, J = 13.0, 13.0, 3.2 Hz, CH₂), 3.23 (1.5H, s, OCH₃), 3.21 (1.5H, s, OCH₃), 3.06 (1.5H, br, OCH₃), 2.74 (1.5H, br, OCH₃), 2.49 (0.5H, br, CH₂), 2.38-1.00 (5.5H, m, CH₂ and CHCH₃), 1.72 (1.5H, d, J = 6.8 Hz, CHCH₃); ¹³C NMR (100 MHz, CDCl₃) δ (5/5 mixture of rotamers) 167.4, 143.9, 141.8, 135.6, 135.3, 134.3, 134.2, 133.9, 132.8, 131.0, 130.7, 130.2, 130.0, 129.5, 129.3, 129.0, 128.7, 128.60, 128.57, 128.4, 128.3, 127.5, 127.1, 127.0, 126.8, 126.4,
125.1, 124.7, 124.3, 123.5, 122.6, 113.6, 94.9, 65.3, 57.8, 54.1, 52.3, 48.15, 48.08, 48.0, 47.9, 47.3, 46.1, 27.6, 27.5, 27.3, 13.5; HRMS–ESI (m/z): [M–Br]^+ calcd for C₃₂H₃₇N₂O₃: 497.2799. Found: 497.2785.
Preparation of other compounds

\((E)-1-(3\text{-bromoprop-1-en-1-yl})-4\text{-chlorobenzene}\)

\[
\begin{align*}
\text{EtO}_2\text{P} &\quad \text{EtO}_2\text{CO}_2\text{Et} \\
\text{NaH} &\quad \text{THF} \\
0^\circ\text{C} &\quad \text{Cl} \\
\text{PBr}_3 &\quad \text{Et}_2\text{O} \\
0^\circ\text{C} &\quad \text{Br}
\end{align*}
\]

(Step 1) Triethyl phosphonoacetate (2.0 mL, 10 mmol) was added to a suspension of sodium hydride (60 wt.% in oil, 0.44 g, 11 mmol) in THF (30 mL) at 0 °C and the mixture was stirred for 15 min. To the resulting mixture, 4-chlorobenzaldehyde (1.41 g, 10 mmol) was added in one portion at the same temperature. The resulting mixture was stirred for 12 h at room temperature and quenched with saturated aqueous ammonium chloride at 0 °C. Extractive workup and purification of the residue by chromatography on silica gel (n-hexane/ethyl acetate = 20/1 to 15/1 as the eluent) afforded \((E)-\)ethyl 3-(4-chlorophenyl)acrylate (1.91 g, 91% yield) as a colorless oil. (Step 2) A 1 M solution of DIBAH solution in n-hexane (1.2 mL, 1.2 mmol) was added to a solution of \((E)-\)ethyl 3-(4-chlorophenyl)acrylate (105 mg, 0.50 mmol) in toluene (1.2 mL) at 0 °C. The mixture was stirred for 30 min and quenched with water at the same temperature. The mixture was treated with 1 M hydrochloric acid and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous sodium carbonate and brine. The organic solution was dried over sodium sulfate and concentrated to obtain \((E)-3-(4\text{-chlorophenyl})\)prop-2-en-1-ol (85 mg, quant.) as colorless crystals. The crude product was used without purification. (Step 3) Phosphorus tribromide (0.23 mL, 2.4 mmol) was added to a solution of \((E)-3-(4\text{-chlorophenyl})\)prop-2-en-1-ol (0.22 g, 1.3 mmol) in diethyl ether (4.3 mL) at 0 °C. The mixture was stirred for 30 min at 0 °C and 2 h at room temperature. The resulting mixture was treated with water and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and aqueous saturated sodium bromide. The solution was dried over sodium sulfate and concentrated to obtain \((E)-1-(3\text{-bromoprop-1-en-1-yl})-4\text{-chlorobenzene}\) (0.27 g, 90% yield) as a colorless oil. The crude product was used without purification.

\((E)-1\text{-Bromo-4-(3-bromoprop-1-en-1-yl)benezene}: \) prepared by the same procedures with \((E)-1-(3\text{-bromoprop-1-en-1-yl})-4\text{-chlorobenzene}\) using 4-bromobenzaldehyde instead of 4-chlorobenzaldehyde in step 1 (62% overall yield).

\((E)-1-(3\text{-Bromoprop-1-en-1-yl})-4\text{-methylbenzene}: \) prepared by the same procedures with \((E)-1-(3\text{-bromoprop-1-en-1-yl})-4\text{-chlorobenzene}\) using 4-methylbenzaldehyde instead of 4-chlorobenzaldehyde in step 1 (82% overall yield).
(E)-1-Bromohex-2-ene

\[
\begin{align*}
\text{Phosphorus tribromide (1.55 mL, 16.5 mmol) was added to a solution of (E)-hex-2-en-1-ol (1.77 mL, 15.0 mmol) in diethyl ether (30 mL) at 0 °C and the mixture was stirred for 1 h at the same temperature. The resulting mixture was treated with water and extracted with diethyl ether. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and aqueous saturated sodium bromide. The diethyl ether solution was dried over sodium sulfate and concentrated to obtain (E)-1-bromohex-2-ene (1.90 g, 78% yield) as a colorless oil. The crude product was used without purification.}
\end{align*}
\]

1,5-Dibromopentan-3-one<sup>4</sup>

(Step 1) A solution of ethylmagnesium bromide in diethyl ether [prepared from magnesium turnings (0.65 g, 27 mmol) and ethyl bromide (2.0 mL, 27 mmol) in diethyl ether (13 mL)] was added to a solution of ethyl 3-bromopropionate (1.54 mL, 12.0 mmol) and titanium tetraisopropoxide (0.36 mL, 1.2 mmol) in diethyl ether (12 mL) at 0 °C. The mixture was stirred for 16 h at room temperature and quenched with water. The mixture was treated with 5% (v/v) sulfonic acid and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous sodium hydrogen carbonate and aqueous saturated sodium bromide. Evaporation of the solvent and purification of the residue by chromatography on silica gel (n-hexane/ethyl acetate = 8/1 to 4/1 as the eluent) gave 1-(2-bromoethyl)cyclopropanol (1.71 g, 86% yield) as a pale brown oil.

(Step 2) N-Bromosuccinimide (1.85 g, 10.4 mmol) was added to a solution of 1-(2-bromoethyl)cyclopropanol (1.71 g, 10.4 mmol) in carbon tetrachloride (21 mL) at room temperature and the mixture was stirred for 2 h at the same temperature. The resulting mixture was filtered and the filtrate was concentrated. Purification of the residue by chromatography on silica gel (n-hexane/ethyl acetate = 15/1 to 8/1 as the eluent) afforded 1,5-dibromopentan-3-one (2.05 g, 81% yield) as a pale brown oil.
4
(2R,3S)-major
(4R,1'S)-major