Nickel-catalyzed Intramolecular Desymmetrization Addition of Aryl Halides to 1,3-Diketones

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1. General Considerations.

All commercially available compounds were used as received. \(^1\)H and \(^{13}\)C spectra were recorded on a Bruker Avance 400, 600 spectrometer, and CDCl\(_3\) was purchased from Aldrich. The chemical shifts (\(\delta\)) are given in parts per million relative to internal standard TMS (0 ppm for \(^1\)H), CDCl\(_3\) (77.0 ppm for \(^{13}\)C). Flash column chromatography was performed on silica gel 60 (particle size 200-400 mesh ASTM, purchased from Yantai, China) and eluted with petroleum ether/ethyl acetate. Solvents were dried and purified according to the procedure from ‘Purification of Laboratory Chemicals book’. Chiral HPLC analyses were performed on UltiMate 3000 liquid chromatography. Unless otherwise noted, all other reagents and starting materials were purchased from commercial sources and used without further purification.

2. General Procedure for Preparation of Starting Materials

2.1 General Procedure for synthesis of 1a、1c-1i、4a

According to the literature\(^{S1}\), to a stirred solution of 2-methylcyclohexane-1,3-dione (5 mmol, 1.0 equiv.) in dioxane (5 mL) was added aqueous \(^4\)Bu\(_4\)NOH (40 % in H\(_2\)O, 3.3 mL). The mixture was stirred for 20 min at room temperature. Then a solution of substituted 1-bromo-2-(bromomethyl)benzene (6.0 mmol, 1.2 equiv) in dioxane (5 mL) was added and the reaction mixture was stirred for another 12-36 h. Upon completion, the reaction was quenched with aqueous NH\(_4\)Cl and extracted with ethyl acetate three times. The organics were combined, dried over anhydrous Na\(_2\)SO\(_4\), concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate to affording the final product.

2.2 General Procedure for synthesis of 1b、1j–1o、4b

According to the literature\(^{S1}\), an oven-dried 250 mL round bottom flask equipped with magnetic stir bar was charged with 1,3-cyclohexanedione (30 mmol), Hantzsh

ester (33 mmol, 1.1 equiv.), DL-Proline (6 mmol, 20 mol%) and DCM (50 mL). A solution of aldehyde (33 mmol, 1.1 equiv.) in DCM (5 mL) was added and the reaction mixture was refluxed at 70 °C overnight. Upon completion, the reaction was allowed to cool to room temperature and the solvent was removed. The residue was purified by flash column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate to afford the 2-substituent-cyclohexane-1,3-dione.

To a stirred solution of 2-substituent-cyclohexane-1,3-dione (5 mmol) in dioxane (5 mL) was added aqueous "Bu₄NOH (40% in H₂O, 3.3 mL). The mixture was stirred for 20 min at room temperature. Then a solution of 1-bromo-2-(bromomethyl)benzene (6.0 mmol, 1.2 equiv) in dioxane (5 mL) was added and the reaction mixture was stirred for another 12-36 h. Upon completion, the reaction was quenched with aqueous NH₄Cl and extracted with ethyl acetate three times. The organic layers were combined, dried over anhydrous Na₂SO₄, concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate to afford the final product.

2.3 General Procedure for synthesis of 4c

\[
\begin{array}{c}
\text{O} \\
\text{Me, TBAOH} \\
\text{1,4-dioxane/H₂O} \\
\text{r.t. 12 h} \\
\text{O} \\
\end{array} + \begin{array}{c}
\text{O} \\
\text{Br} \\
\text{Br} \\
\text{1,4-dioxane/H₂O} \\
\text{r.t. 12 h} \\
\text{O} \\
\end{array}
\]

To a solution of pentane-2,4-dione (20.0 mmol, 1.0 equiv) and aqueous "Bu₄NOH (40% in H₂O, 13.2 mL) was added a solution of MeI (40 mmol, 2 equiv) in dioxane (40 mL). The solution was stirred for 12 h. The solution was neutralized with 10% aqueous HCl. The two liquid layers were separated, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine and dried with Na₂SO₄, and the solvent was evaporated. The residue was purified by flash column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate to afford the 3-methylpentane-2,4-dione.

To a stirred solution of 3-methylpentane-2,4-dione (10 mmol) in dioxane (10 mL) was added aqueous "Bu₄NOH (40% in H₂O, 6.6 mL). The mixture was stirred for 20 min at room temperature. Then a solution of 1-bromo-2-(bromomethyl)benzene (12.0 mmol, 1.2 equiv) in dioxane (10 mL) was added and the reaction mixture was stirred for another 12-36 h. Upon completion, the reaction was quenched with aqueous NH₄Cl and extracted with ethyl acetate three times. The organic layers were combined, dried over anhydrous Na₂SO₄, concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate to afford the final product.

2.4 General Procedure for synthesis of 1q
According to the literatures\textsuperscript{S2}, an oven-dried 100 mL round bottom flask equipped with magnetic stir bar was added with 60% NaH (24 mmol, 1.2 equiv.) and DMF (40 mL) under nitrogen atmosphere at 0 °C. A solution of cyclohexane-1,3-dione (20 mmol) in DMF (10 mL) was added slowly and the reaction was stirred for 30 min. Then \textit{t}-butyl acrylate (1.5 equiv.) was added and the reaction was heated at 70 °C for 4 h. Upon completion, the reaction mixture was allowed to cool to room temperature and acidified by 10% aqueous HCl. The suspension was extracted with ethyl acetate three times. The organics was combined, dried over anhydrous Na\textsubscript{2}SO\textsubscript{4} and concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate to afford \textit{t}-butyl 3-(2,6-dioxocyclohexyl) propanoate.

To a stirred solution of \textit{t}-butyl 3-(2,6-dioxocyclohexyl) propanoate (10 mmol) in dioxane (10 mL) was added aqueous \textit{t}Bu\textsubscript{4}NOH (40% in H\textsubscript{2}O, 6.6 mL). The mixture was stirred for 20 min at room temperature. Then a solution of 1-bromo-2-(bromomethyl)benzene (12.0 mmol, 1.2 equiv) in dioxane (10 mL) was added and the reaction mixture was stirred for another 12-36 h. Upon completion, the reaction was quenched with aqueous NH\textsubscript{4}Cl and extracted with ethyl acetate three times. The organics were combined, dried over anhydrous Na\textsubscript{2}SO\textsubscript{4}, concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel with a gradient eluent of petroleum ether/ethyl acetate to afford the final product.

### 3. Screening Results.

The Standard condition was listed below and the screening experiments were tested by changing the relevant parameters based on this procedure:

In the nitrogen filled glovebox, a 10 mL oven-dried Schlenk tube with a magnetic bar was charged with nickel catalyst (0.005 mmol, 5 mol %), ligand (0.01 mmol, 10 mol %) and Manganese powder (11.0 mg, 0.2 mmol, 2 equiv). The tube was capped with a septum and took out of the glove box. Under N\textsubscript{2} atmosphere, solvent (1 mL) was added and the reaction mixture was stirred at room temperature for 30 min. 1a

(29.4 mg, 0.1 mmol) were added and the resulting solution was stirred overnight at 50 °C. Upon completion, the reaction mixture was quenched by saturated aq. NH₄Cl (2 mL) and extracted with ethyl acetate (2 mL ×3). The combined organic layers were dried over Na₂SO₄, and concentrated under vacuo. CH₂Br₂ (17.4 mg, 0.1 mmol) as internal standard and CDCl₃ were added to the residue. The yield and dr value of 2a was determined via ¹H NMR analysis. The ee value of 2a was determined via HPLC analysis after purification of the crude reaction mixture.

Table S1 screening results on catalyst.

<table>
<thead>
<tr>
<th>cat.</th>
<th>2a (%)</th>
<th>d:r</th>
</tr>
</thead>
<tbody>
<tr>
<td>NiBr₂</td>
<td>86</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>NiBr₂(dme)</td>
<td>78</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(PPh₃)₂Br₂</td>
<td>84</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(PCy₃)₂Cl₂</td>
<td>94</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(cod)₂</td>
<td>&gt;99</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(dppe)Cl₂</td>
<td>87</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(PPh₃)₂(CO)₂</td>
<td>n.r.</td>
<td>---</td>
</tr>
<tr>
<td>FeBr₃</td>
<td>n.r.</td>
<td>---</td>
</tr>
<tr>
<td>CoBr₂</td>
<td>n.r.</td>
<td>---</td>
</tr>
<tr>
<td>Cu(OTf)₂</td>
<td>n.r.</td>
<td>---</td>
</tr>
<tr>
<td>Pd(OAc)₂</td>
<td>27</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(cod)₂</td>
<td>96</td>
<td>&gt;20:1</td>
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</table>

*At room temperature

Table S2 screening results on ligand.

<table>
<thead>
<tr>
<th>cat.</th>
<th>additive</th>
<th>2b (%)</th>
<th>d:r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ni(cod)₂</td>
<td>---</td>
<td>46</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(cod)₂</td>
<td>NaI</td>
<td>84</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>Ni(cod)₂</td>
<td>MgCl₂</td>
<td>&gt;99</td>
<td>&gt;20:1</td>
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</tbody>
</table>
Table S3 screening results on solvent.

<table>
<thead>
<tr>
<th>Solvent</th>
<th>2a (%)</th>
<th>d:r</th>
</tr>
</thead>
<tbody>
<tr>
<td>DMA</td>
<td>&gt;99</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>DMF</td>
<td>84</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>DMSO</td>
<td>26</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>THF</td>
<td>trace</td>
<td>&gt;20:1</td>
</tr>
<tr>
<td>ACN</td>
<td>34</td>
<td>&gt;20:1</td>
</tr>
</tbody>
</table>

Table S4 screening results on reductant.

<table>
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<tr>
<th>Reductant</th>
<th>2a (%)</th>
<th>d:r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mn</td>
<td>&gt;99</td>
<td>&gt;20:1</td>
</tr>
</tbody>
</table>
Zn | 90 | >20:1
In | 18 | >20:1

Table S5 preliminary screening results on chiral ligand.

<table>
<thead>
<tr>
<th>44% yield, 59:41 er</th>
<th>76% yield, 65:35 er</th>
<th>72% yield, 70:30 er</th>
</tr>
</thead>
<tbody>
<tr>
<td>R = 'Bu, 68% yield, 58:42 er</td>
<td>R = iPr, 80% yield, 53:47 er</td>
<td>42% yield, 64:36 er</td>
</tr>
<tr>
<td>R = Ph, 46% yield, 76:24 er</td>
<td>R = Ph, 42% yield, 51:49 er</td>
<td></td>
</tr>
</tbody>
</table>

4. Mechanism discussion.

Based on the experiments and literatures\(^3\), a proposed catalytic cycle was listed below. An aryl-Ni species Int(I) was obtained after the oxidative addition of Ar-Br and Ni(0) catalyst. The carbonyl was further activated by coordination to Mg\(^{2+}\) ion, following by reacting with the C-Ni bond. It had two way to proceed the ketone addition step. The \textit{syn} addition to give the \textit{syn} intermediate Int(IIa) is favorable according to

\(^a\) DMA/1,4-dioxone (v/v = 4/1) was used as solvent. \(^b\) MgCl\(_2\) (0.2 mmol) was added as additive.

the configuration. The nickel(II) was released by MnBr$_2$ or MgCl$_2$, which gave Ni(0) regeneration by reduction of Mn powder.

5. Nickel-catalyzed intramolecular desymmetrization addition of aryl halides to 1,3-diketones.

5.1 General procedure for synthesis of 2.

In the nitrogen filled glovebox, a 10 mL oven-dried Schlenk tube with a magnetic bar was charged with Ni(cod)$_2$ (2.7 mg, 0.01 mmol, 5 mol %), 1,1-bipyridine (bpy, 3.1 mg, 0.02 mmol, 10 mol %), Manganese powder (22.0 mg, 0.4 mmol, 2 equiv.), and MgCl$_2$ (38.0 mg, 0.4 mmol, 2 equiv.). The tube was capped with a septum and took out of the glove box. Under N$_2$ atmosphere, DMA (2 mL) was added and the reaction mixture was stirred at room temperature for 30 min. 1 (0.2 mmol) were added and the resulting solution was stirred for 8 h at 50 $^\circ$C. Upon completion, the reaction mixture was quenched by saturated aq. NH$_4$Cl (2 mL) and extracted with ethyl acetate (2 mL ×3). The combined organic layers were dried over Na$_2$SO$_4$, and concentrated under vacuo. The residue was purified by silica gel column chromatography with a gradient eluent of petroleum ether/ethyl acetate affording the product. The dr value of 2 was determined via $^1$H NMR analysis.

5.2 General procedure for synthesis of chiral 2.

In the nitrogen filled glovebox, a 10 mL oven-dried Schlenk tube with a magnetic bar was charged with Ni(cod)$_2$ (2.7 mg, 0.02 mmol, 10 mol %), S-Pr-Pyro (2.7 mg, 0.03 mmol, 15 mol %) and Manganese powder (11.0 mg, 0.4 mmol, 2 equiv.). The tube was capped with a septum and took out of the glove box. Under N$_2$ atmosphere, DMA (0.8 mL) and 1,4-dioxane (0.2 mL) was added and the reaction mixture was stirred at
room temperature for 30 min. 1 (0.1 mmol) were added and the resulting solution was stirred for 8 h at 25-30 °C. Upon completion, the reaction mixture was quenched by saturated aq. NH₄Cl (2 mL) and extracted with ethyl acetate (2 mL × 3). The combined organic layers were dried over Na₂SO₄, and concentrated under vacuo. The residue was purified by silica gel column chromatography with a gradient eluent of petroleum ether/ethyl acetate affording the product. The dr value of 2 was determined via ¹H NMR analysis and ee value of 2 was determined via HPLC analysis.


6.1 General procedure for synthesis of 6a

![chemical structure](image)

91% yield, d:r > 20:1

To a stirred solution of 2a (21.6 mg, 0.1 mmol) in THF (1.5 mL) and MeOH (0.5 mL) was added NaHB₄ (57 mg, 1.5 equiv) and the reaction mixture was stirred for 15 min at 0 °C. The reaction was diluted with water and extracted with ethyl acetate three times. The combined organics were dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography with a gradient eluent of petroleum ether/ethyl acetate affording 6a (19.8 mg) in 91% yield. The dr value of 6a was determined via ¹H NMR analysis.

6.2 General procedure for synthesis of 6b

![chemical structure](image)

78% yield, d:r > 20:1

To a round bottom flask equipped with magnetic stirring bar, rubber septum, and N₂ inlet was added trimethyl sulfonium iodide (Me₃S⁺I⁻) (61 mg, 0.3 mmol, 3 equiv) in anhydrous tetrahydrofuran (THF, 1 mL) was stirred for 10 min at 0°C. At this point, a solution of nBuLi (0.3 mmol, 3 equiv, 1.6M solution in hexanes) was added and the resulting solution was stirred for 10 min at 0°C. Compound 2a (21.6 mg, 0.1 mmol) in anhydrous tetrahydrofuran (THF, 1 mL) was added, and the mixture was stirred in the ice bath for 3 h. The ice bath was then removed, and the reaction was allowed to warm

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to room temperature. The solution was carefully poured into ice/water (10 mL) and extracted with ethyl acetate three times. The combined organics were dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography with a gradient eluent of petroleum ether/ethyl acetate affording 6b (18.0 mg) in 78% yield. The dr value of 6b was determined via ¹H NMR analysis.

6.3 General procedure for synthesis of 6c

![Chemical structure of 6a and 6c]

78% yield, dr > 20:1

To a round bottom flask equipped with magnetic stirring bar, rubber septum, and N₂ inlet was added methyl-triphenylphosphonium bromide (P⁺Ph₃MeBr, 107.5 mg, 0.3 mmol) and anhydrous tetrahydrofuran (THF) (1 mL). To the flask was added dropwise nBuLi (0.3 mmol, 3 equiv, 1.6M solution in hexanes) at 0°C. After 20 min of stirring at same temperature, a solution of ketone 2a (21.6 mg, 0.1 mmol) in anhydrous tetrahydrofuran (THF) (1 mL) was added dropwise to the phosphonium ylide through a cannula. After the ketone 2a was completely added the mixture was stirred in the ice bath for another 3 h. Upon completion, the reaction mixture was quenched by saturated aq. NH₄Cl (2 mL) and extracted with ethyl acetate (2 mL ×3). The combined organic layers were dried over Na₂SO₄, and concentrated under vacuo. The residue was purified by silica gel column chromatography with a gradient eluent of petroleum ether/ethyl acetate affording 6c (16.7 mg) in 78% yield. The dr value of 6c was determined via ¹H NMR analysis.

6.4 General procedure for synthesis of 6d

![Chemical structure of 6a and 6d]

58% yield

To a stirred solution of 2a (21.6 mg, 0.1 mmol) in anhydrous toluene (2 mL) was added p-toluenesulfonic acid (1 mg, 10 mmol%) and the reaction mixture was stirred for 1 h at 120 °C. The reaction was diluted with water and extracted with ethyl acetate three times. The combined organics were dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by silica gel column chromatography with a gradient eluent of petroleum ether/ethyl acetate affording 6d (11.5 mg) in 58% yield.

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7. X-Ray Data for 2a

Table 1. Crystal data and structure refinement for ga_90423a_a.

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>ga_90423a_a</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C14 H16 O2</td>
</tr>
<tr>
<td>Formula weight</td>
<td>216.27</td>
</tr>
<tr>
<td>Temperature</td>
<td>298(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>1.34138 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>Orthorhombic</td>
</tr>
<tr>
<td>Space group</td>
<td>P212121</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 8.4235(5) Å, b = 10.6627(7) Å, c = 12.6898(8) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>1139.76(12) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.260 Mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.420 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>464</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.080 x 0.050 x 0.040 mm³</td>
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<tr>
<td>Theta range for data collection</td>
<td>5.484 to 58.095°.</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-10&lt;=h&lt;=10, -13&lt;=k&lt;=13, -16&lt;=l&lt;=16</td>
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<tr>
<td>Reflections collected</td>
<td>19374</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>2419 [R(int) = 0.0302]</td>
</tr>
<tr>
<td>Completeness to theta = 53.594°</td>
<td>99.9 %</td>
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<tr>
<td>Absorption correction</td>
<td>Semi-empirical from equivalents</td>
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<tr>
<td>Max. and min. transmission</td>
<td>0.929 and 0.836</td>
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<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>2419 / 0 / 150</td>
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<tr>
<td>Goodness-of-fit on F²</td>
<td>1.048</td>
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<tr>
<td>Final R indices [I&gt;2sigma(I)]</td>
<td>R1 = 0.0274, wR2 = 0.0704</td>
</tr>
<tr>
<td>R indices (all data)</td>
<td>R1 = 0.0287, wR2 = 0.0721</td>
</tr>
<tr>
<td>Absolute structure parameter</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Extinction coefficient  
n/a
Largest diff. peak and hole  
0.153 and -0.134 eÅ⁻³

Table 2. Atomic coordinates (x 10⁴) and equivalent isotropic displacement parameters (Å² x 10³) for ga_90423a_a. U(eq) is defined as one third of the trace of the orthogonalized Uᵢⱼ tensor.

<table>
<thead>
<tr>
<th></th>
<th>x</th>
<th>y</th>
<th>z</th>
<th>U(eq)</th>
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<tbody>
<tr>
<td>O(1)</td>
<td>6501(1)</td>
<td>3983(1)</td>
<td>3546(1)</td>
<td>40(1)</td>
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<tr>
<td>O(2)</td>
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<td>8210(1)</td>
<td>3530(1)</td>
<td>45(1)</td>
</tr>
<tr>
<td>C(1)</td>
<td>5608(2)</td>
<td>4988(1)</td>
<td>4008(1)</td>
<td>30(1)</td>
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<tr>
<td>C(2)</td>
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<td>5195(2)</td>
<td>5084(1)</td>
<td>38(1)</td>
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<td>31(1)</td>
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<td>2502(1)</td>
<td>37(1)</td>
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<td>C(8)</td>
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<td>3159(1)</td>
<td>34(1)</td>
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<tr>
<td>C(9)</td>
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<td>4910(2)</td>
<td>2998(1)</td>
<td>44(1)</td>
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<td>C(10)</td>
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<td>4164(2)</td>
<td>3709(2)</td>
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<td>4031(1)</td>
<td>31(1)</td>
</tr>
<tr>
<td>C(14)</td>
<td>7197(2)</td>
<td>6401(2)</td>
<td>2713(2)</td>
<td>48(1)</td>
</tr>
</tbody>
</table>
8. The characterization of the new products

The title compound 1c was synthesized according to General Procedure (SI 2.1), and it was purified by column chromatography on silica gel.

$^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 7.37-7.36 (m, 1H), 7.00 (dd, $J$ = 7.9, 1.7 Hz, 1H), 6.90 (d, $J$ = 7.8 Hz, 1H), 3.26 (s, 2H), 2.71-2.61 (m, 4H), 2.28 (s, 3H), 1.97-1.81 (m, 2H), 1.27 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-\textit{d}) $\delta$ 210.1, 138.8, 133.6, 132.6, 131.2, 128.1, 125.4, 65.3, 41.9, 38.9, 20.6, 19.6, 17.4; HRMS: m/z (ESI) calculated [M+H]$^+$:309.0485, found: 309.0485.

The title compound 1e was synthesized according to General Procedure (SI 2.1), and it was purified by column chromatography on silica gel.

$^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 7.55 (d, $J$ = 2.2 Hz, 1H), 7.18 (dd, $J$ = 8.3, 2.2 Hz, 1H), 6.95 (d, $J$ = 8.3 Hz, 1H), 3.28 (s, 2H), 2.73-2.61 (m, 4H), 2.00-1.85 (m, 2H), 1.29 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-\textit{d}) $\delta$ 209.7, 134.8, 133.4, 132.8, 131.9, 127.5, 126.0, 65.0, 40.5, 38.6, 20.6, 17.3; HRMS: m/z (ESI) calculated [M+H]$^+$:350.9758, found: 350.9755.

The title compound 1h was synthesized according to General Procedure (SI 2.1), and it was purified by column chromatography on silica gel.

$^1$H NMR (400 MHz, Chloroform-\textit{d}) $\delta$ 7.41 (d, $J$ = 8.8 Hz, 1H), 6.65 (dd, $J$ = 8.8, 3.0 Hz, 1H), 6.57 (d, $J$ = 3.0 Hz, 1H), 3.74 (s, 3H), 3.27 (s, 2H), 2.68-2.62 (m, 4H), 1.98-1.83 (m, 2H), 1.30 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-\textit{d}) $\delta$ 210.0, 158.6, 136.9, 133.7, 117.2, 116.0, 114.3, 65.1, 55.4, 41.9, 38.8, 20.3, 17.3; HRMS: m/z (ESI) calculated [M+H]$^+$:325.0433, found: 325.0434.
The title compound 1j was synthesized according to General Procedure (SI 2.2), and it was purified by column chromatography on silica gel.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.53 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.22-7.18 (m, 1H), 7.09-7.05 (m, 1H), 7.01 (dd, $J = 7.7, 1.7$ Hz, 1H), 3.23 (s, 2H), 2.63-2.56 (m, 2H), 2.41-2.33 (m, 2H), 1.98 (d, $J = 6.5$ Hz, 2H), 1.87-1.82 (m, 1H), 1.74-1.68 (m, 1H), 1.52-1.45 (m, 1H), 0.80 (d, $J = 8.0$ Hz, 6H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 211.0, 136.1, 133.3, 131.9, 128.6, 127.3, 125.5, 67.9, 44.3, 40.4, 25.4, 24.1, 16.6; HRMS: m/z (ESI) calculated [M+H]$^+$:337.079, found: 337.0798.

The title compound II was synthesized according to General Procedure (SI 2.2), and it was purified by column chromatography on silica gel.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.53 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.28-7.24 (m, 2H), 7.13-7.11 (m, 2H), 7.09-7.05 (m, 1H), 7.00 (dd, $J = 7.7, 1.7$ Hz, 1H), 3.24 (s, 2H), 2.57-2.52 (m, 2H), 2.50-2.46 (m, 2H), 2.43-2.36 (m, 2H), 2.02-1.98 (m, 2H), 1.77-1.69 (m, 2H), 1.37-1.29 (m, 2H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 210.8, 141.6, 136.0, 133.3, 131.7, 128.7, 128.3, 127.3, 125.9, 125.5, 68.6, 42.9, 40.4, 36.6, 36.3, 27.2, 16.4; HRMS: m/z (ESI) calculated [M+H]$^+$:399.0953, found: 399.0954.

The title compound 1m was synthesized according to General Procedure (SI 2.2), and it was purified by column chromatography on silica gel.

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.53 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.22-7.18 (m, 1H), 7.11-7.04 (m, 2H), 6.96-6.92 (m, 2H), 6.75-6.72 (m, 2H), 3.75 (s, 3H), 3.41 (s, 2H), 3.24 (s, 2H), 2.19-2.01 (m, 4H), 1.39-1.30 (m, 1H), 1.13-1.04 (m, 1H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 211.6, 158.5, 136.1, 133.5, 131.8, 131.4, 128.7, 128.3, 127.3,
125.4, 113.8, 69.7, 55.2, 43.1, 41.2, 15.3; HRMS: m/z (ESI) calculated [M+Na]^+: 423.0570, found: 423.0566.

The title compound 1o was synthesized according to General Procedure (SI 2.2), and it was purified by column chromatography on silica gel.

\(^1\)H NMR (400 MHz, Chloroform-d) δ 7.55 (dd, J = 7.9, 1.4 Hz, 1H), 7.25-7.21 (m, 1H), 7.13-7.10 (m, 2H), 7.08-7.05 (m, 1H), 6.83 (dd, J = 5.2, 3.5 Hz, 1H), 6.70 (dd, J = 3.5, 1.1 Hz, 1H), 3.51 (s, 2H), 3.36 (s, 2H), 2.26-2.22 (m, 4H), 1.54-1.44 (m, 1H), 1.28-1.18 (m, 1H); \(^{13}\)C NMR (101 MHz, Chloroform-d) δ 211.0, 138.1, 135.4, 133.5, 132.2, 129.0, 127.9, 127.4, 126.7, 125.4, 124.6, 69.7, 43.6, 40.9, 36.6, 15.6; HRMS: m/z (ESI) calculated [M+Na]^+: 377.0206, found: 377.0205.

The title compound 1q was synthesized according to General Procedure (SI 2.4), and it was purified by column chromatography on silica gel.

\(^1\)H NMR (400 MHz, Chloroform-d) δ 7.53 (dd, J = 8.0, 1.3 Hz, 1H), 7.22-7.18 (m, 1H), 7.10-7.05 (m, 1H), 7.02 (dd, J = 7.7, 1.7 Hz, 1H), 3.25 (s, 2H), 2.64-2.45 (m, 4H), 2.24-2.20 (m, 2H), 2.04-2.00 (m, 2H), 1.89-1.78 (m, 2H), 1.41 (s, 9H); \(^{13}\)C NMR (101 MHz, Chloroform-d) δ 210.0, 171.8, 133.3, 131.8, 128.8, 127.3, 125.6, 80.6, 67.7, 42.9, 40.0, 30.9, 30.3, 28.1, 16.6; HRMS: m/z (ESI) calculated [M+Na]^+: 431.0829, found: 431.0828.

The title compound 4c was synthesized according to General Procedure (SI 2.3), and it was purified by column chromatography on silica gel.

\(^1\)H NMR (400 MHz, Chloroform-d) δ 7.54 (dd, J = 8.0, 1.3 Hz, 1H), 7.21-7.17 (m, 1H), 7.10-7.05 (m, 2H), 3.46 (s, 2H), 2.17 (s, 3H), 2.16 (s, 3H), 1.32 (s, 3H); \(^{13}\)C NMR (101
The title compound (±)-2a was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (96% yield, 41.5 mg, white solid).

$^1$H NMR (400 MHz, Chloroform-$d$) δ 7.26 (d, $J = 4.2$ Hz, 4H), 3.60 (d, $J = 15.6$ Hz, 1H), 2.70 (d, $J = 15.7$ Hz, 1H), 2.56-2.48 (m, 1H), 2.38-2.23 (m, 2H), 2.21-2.13 (m, 1H), 1.98-1.91 (m, 1H), 1.72 (s, 1H), 1.47-1.37 (m, 1H), 1.34 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 213.3, 144.8, 142.8, 129.0, 127.1, 125.5, 122.1, 84.8, 62.1, 38.7, 37.6, 31.9, 20.0, 17.9; HRMS: m/z (ESI) calculated [M+Na]$^+$: 339.1041, found: 239.1043.

The title compound 2a was synthesized according to General Procedure (SI 5.2), and it was purified by column chromatography on silica gel (76% yield, 60% ee, 16.4 mg, white solid).

The enantiomeric excess of 2a was determined by chiral HPLC analysis compared to the corresponding racemate.

Conditions: ChiralPark IA column; hexane/iPrOH = 95:5; flow rate = 0.8 mL/min; $\lambda$ = 272 nm; $t_R1$ (minor) = 21.2 min; $t_R2$ (major) = 24.9 min.
The title compound (+)-2b was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (89% yield, 52.0 mg, white solid).

\(^1\)H NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.29-7.27 (m, 2H), 7.25-7.19 (m, 4H), 7.12 (d, \(J = 8.0\) Hz, 2H), 3.45 (d, \(J = 15.4\) Hz, 1H), 3.30 (dd, \(J = 36, 12\) Hz, 2H), 2.83 (d, \(J = 15.4\) Hz, 1H), 2.50-2.59 (m, 2H), 2.34-2.26 (m, 1H), 2.23-2.17 (m, 1H), 1.93-1.87 (m, 2H), 1.33-1.25 (m, 1H); \(^13\)C NMR (101 MHz, Chloroform-\(d\)) \(\delta\) 211.0, 143.9, 143.8, 137.5, 129.7, 129.3, 128.3, 127.0, 126.7, 125.6, 121.8, 85.0, 68.1, 38.7, 38.3, 36.3, 30.6, 20.4; HRMS: m/z (ESI) calculated [M+H]\(^+\): 293.1526, found: 293.1536.

The title compound 2b was synthesized according to General Procedure (SI 5.2), and it was purified by column chromatography on silica gel (32% yield, 80% ee, 9.5 mg, white solid).

The enantiomeric excess of 2b was determined by chiral HPLC analysis compared to the corresponding racemate.

Conditions: ChiralPark IA column; hexane/iPrOH = 95:5; flow rate = 0.8 mL/min; \(\lambda=272\) nm; \(t_{R1}\) (minor)= 33.3 min; \(t_{R2}\) (major)=46.1 min.
### Integration Results

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The title compound (±)-2c was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (86% yield, 39.6 mg, colorless liquid).

\(^1\)H NMR (400 MHz, Chloroform-d) \(\delta\) 7.05 (t, \(J = 7.4\) Hz, 1H), 6.93 (dd, \(J = 16.4, 7.4\) Hz, 2H), 3.22 (d, \(J = 15.6\) Hz, 1H), 2.57 (d, \(J = 15.7\) Hz, 1H), 2.49-2.33 (m, 5H), 2.22-2.17 (m, 1H), 2.05-1.92 (m, 3H), 1.64-1.56 (m, 1H), 1.15 (s, 3H); \(^{13}\)C NMR (101 MHz, Chloroform-d) \(\delta\) 214.2, 143.0, 140.5, 134.5, 129.9, 128.3, 123.0, 87.9, 60.7, 40.5, 37.6, 33.3, 19.8, 18.2, 17.7; HRMS: m/z (ESI) calculated [M+Na]\(^+\): 253.1191, found:253.1199.

The title compound 2c was synthesized according to General Procedure (SI 5.2), and it was purified by column chromatography on silica gel (65% yield, 62% ee, 15.0 mg, colorless liquid).

The enantiomeric excess of 2c was determined by chiral HPLC analysis compared to the corresponding racemate.

Conditions: ChiralPark IA column; hexane/iPrOH = 95:5; flow rate = 0.8 mL/min; \(\lambda = 272\) nm; \(t_{R1}(\text{major}) = 25.3\) min; \(t_{R2}(\text{minor}) = 19.1\) min.

![Chromatogram](image)

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The title compound (±)-2d was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (70% yield, 32.2 mg, white solid).

$^1$H NMR (400 MHz, Chloroform-d) δ 7.14 (d, $J = 8.0$ Hz, 1H), 7.07 (d, $J = 6.2$ Hz, 2H), 3.55 (d, $J = 15.4$ Hz, 1H), 2.65 (d, $J = 15.4$ Hz, 1H), 2.56-2.48 (m, 1H), 2.35 (s, 3H), 2.33-2.24 (m, 2H), 2.19-2.11 (m, 1H), 1.98-1.88 (m, 2H), 1.49-1.37 (m, 1H), 1.33 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 213.5, 145.0, 139.70, 136.7, 129.8, 125.2, 122.6, 84.8, 62.3, 38.3, 37.6, 31.9, 21.4, 20.0, 17.9; HRMS: m/z (ESI) calculated [M+Na]$^+$: 253.1192, found:253.1199.

The title compound (±)-2e was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (77% yield, 38.5 mg, white solid).
$^1$H NMR (400 MHz, Chloroform-$d$) δ 7.26-7.17 (m, 3H), 3.55 (d, $J = 15.8$ Hz, 1H), 2.66 (d, $J = 15.7$ Hz, 1H), 2.56-2.48 (m, 1H), 2.31-2.26 (m, 2H), 2.20-2.12 (m, 1H), 2.00-1.92 (m, 1H), 1.84 (s, 1H), 1.47-1.37 (m, 1H), 1.33 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 212.8, 146.8, 141.1, 132.8, 129.1, 126.7, 122.5, 84.7, 62.4, 38.2, 37.4, 31.9, 19.9, 17.8; HRMS: m/z (ESI) calculated [M+H]$^+$: 283.1115, found: 283.1095.

The title compound (±)-2f was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (79% yield, 37.9 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-$d$) δ 7.20-7.17 (m, 1H), 6.92-6.96 (m, 2H), 3.54 (d, $J = 15.4$ Hz, 1H), 2.64 (d, $J = 15.4$ Hz, 1H), 2.48-2.56 (m, 1H), 2.31-2.24 (m, 2H), 2.19-2.12 (m, 1H), 1.99-1.91 (m, 1H), 1.89 (s, 1H), 1.47-1.36 (m, 1H), 1.32 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 212.8, 164.4 (d, $J = 248.5$ Hz), 145.6 (d, $J = 8.1$ Hz), 140.3, 123.5 (d, $J = 9.1$ Hz), 114.1 (d, $J = 22.2$ Hz), 112.6 (d, $J = 22.2$ Hz), 84.0, 62.6, 38.2, 37.4, 31.7, 20.0, 17.9; HRMS: m/z (ESI) calculated [M+Na]$^+$: 267.1366, found: 267.1391.

The title compound (±)-2g was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (81% yield, 37.9 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-$d$) δ 7.20 (dd, $J = 8.3$, 5.1 Hz, 1H), 6.96-6.88 (m, 2H), 3.60 (d, $J = 15.7$ Hz, 1H), 2.68 (d, $J = 15.7$ Hz, 1H), 2.56-2.48 (m, 1H), 2.38-2.32 (m, 1H), 2.28-2.22 (m, 1H), 2.22-2.13 (m, 1H), 1.97-1.89 (m, 1H), 1.72 (s, 1H), 1.35 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) δ 212.8, 164.4 (d, $J = 248.5$ Hz), 145.6 (d, $J = 8.1$ Hz), 140.3, 123.5 (d, $J = 9.1$ Hz), 114.1 (d, $J = 22.2$ Hz), 112.6 (d, $J = 22.2$ Hz), 84.0, 62.6, 38.2, 37.4, 31.7, 20.0, 17.9; HRMS: m/z (ESI) calculated [M+Na]$^+$: 235.1125, found: 235.1129.
The title compound (+)-2h was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (76% yield, 37.4 mg, white solid).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.16 (d, $J = 8.3$ Hz, 1H), 6.81 (d, $J = 2.4$ Hz, 1H), 6.78-6.75 (m, 1H), 3.80 (s, 3H), 3.61 (d, $J = 15.6$ Hz, 1H), 2.68 (d, $J = 15.6$ Hz, 1H), 2.56-2.48 (m, 1H), 2.40-2.35 (m, 1H), 2.27-2.13 (m, 2H), 1.98-1.89 (m, 1H), 1.73 (s, 1H), 1.42-1.33 (m, 4H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 213.3, 160.6, 145.1, 136.7, 123.0, 113.3, 110.4, 84.1, 62.7, 55.4, 38.4, 37.5, 31.5, 20.0, 18.1; HRMS: m/z (ESI) calculated [M+H]$^+$: 247.1329, found: 247.1333.

(+)–2h

The title compound (+)-2i was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (58% yield, 30.2 mg, white solid).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 6.70 (d, $J = 3.2$ Hz, 2H), 5.93 (s, 2H), 3.51 (d, $J = 15.3$ Hz, 1H), 2.58 (d, $J = 15.3$ Hz, 1H), 2.53-2.45 (m, 1H), 2.31-2.21 (m, 2H), 2.16-2.08 (m, 1H), 1.94-1.86 (m, 1H), 1.78 (s, 1H), 1.43-1.36 (m, 1H), 1.32 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 213.2, 148.5, 147.1, 137.5, 136.8, 105.9, 102.7, 101.2, 84.4, 62.8, 38.1, 37.5, 31.5, 19.9, 18.0; HRMS: m/z (ESI) calculated [M+Na]$^+$: 283.0940, found: 283.0941.

(+)–2i

The title compound (+)-2j was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (76% yield, 39.2 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.30-7.21 (m, 2H), 7.18 (d, $J = 3.0$ Hz, 2H), 3.83 (d, $J = 15.3$ Hz, 1H), 2.66 (d, $J = 15.3$ Hz, 1H), 2.55-2.41 (m, 2H), 2.27-2.12 (m, 2H), 2.01-1.82 (m, 3H), 1.73 (s, 1H), 1.51 (m, 1H), 1.30-1.21 (m, 1H), 0.97 (d, $J = 6.6$ Hz, 3H), 0.91 (d, $J = 6.6$ Hz, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 212.1, 144.8, 143.1, 129.2, 126.8, 125.6, 121.8, 86.1, 67.2, 41.1, 38.4, 36.4, 30.1, 25.3, 24.7, 23.6, 20.6; HRMS: m/z (ESI) calculated [M+H]$^+$: 259.1692, found: 259.1693.
The title compound (+)-2k was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (48% yield, 27.8 mg, colorless liquid). 

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.30-7.20 (m, 4H), 3.72 (d, $J = 15.3$ Hz, 1H), 2.66 (d, $J = 15.3$ Hz, 1H), 2.56-2.47 (m, 4H), 2.29-2.10 (m, 3H), 2.08 (s, 3H), 2.03-1.90 (m, 2H), 1.66 (s, 1H), 1.42-1.25 (m, 3H). 

$^{13}$C NMR (151 MHz, Chloroform-d) $\delta$ 211.8, 144.0, 143.7, 129.3, 127.0, 125.6, 121.8, 85.1, 66.8, 38.0, 35.5, 34.6, 30.6, 30.5, 24.5, 20.2, 15.4; HRMS: m/z (ESI) calculated [M+Na]$^+$: 313.1254, found:313.1233.

The title compound (+)-2l was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (54% yield, 35.8 mg, white solid).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.27-7.25 (m, 4H), 7.19-7.15 (m, 5H), 3.71 (d, $J = 15.3$ Hz, 1H), 2.71-2.58 (m, 3H), 2.46-2.32 (m, 2H), 2.21-2.03 (m, 3H), 1.91-1.83 (m, 2H), 1.63-1.54 (m, 1H), 1.45-1.33 (m, 1H), 1.30-1.18 (m, 2H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 211.9, 144.2, 143.7, 141.9, 129.2, 128.4, 128.4, 128.4, 126.9, 125.9, 125.6, 121.8, 85.1, 67.1, 38.0, 36.3, 35.4, 31.2, 30.4, 26.7, 20.2; HRMS: m/z (ESI) calculated [M+Na]$^+$: 343.1674, found:343.1669.

The title compound 2l was synthesized according to General Procedure (SI 5.2), and it was purified by column chromatography on silica gel (67% yield, 21.4 mg, white solid). The enantiomeric excess of 2l was determined by chiral HPLC analysis compared to the corresponding racemate. Conditions: ChiralPark IA column; hexane/PrOH = 95:5; flow rate = 0.8 mL/min; $\lambda$ = 272 nm; $t_{R1}$(major)= 27.7 min; $t_{R2}$(minor)=23.9 min.
The title compound (+)-2m was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (93% yield, 59.9 mg, white solid).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.26-7.20 (m, 4H), 7.04 (d, $J = 8.6$ Hz, 2H), 6.81 (d, $J = 8.6$ Hz, 2H), 3.77 (s, 3H), 3.46 (d, $J = 15.4$ Hz, 1H), 3.24 (q, $J = 14.0$ Hz, 2H), 2.82 (d, $J = 15.4$ Hz, 1H), 2.55-2.47 (m, 2H), 2.32-2.18 (m, 1H), 2.20 (d, $J = 14.1$ Hz, 1H), 1.93-1.86 (m, 1H), 1.34-1.22 (m, 1H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 211.3, 158.3, 143.9, 143.8, 130.6, 129.4, 129.3, 127.0, 125.6, 121.8, 113.7, 85.0, 68.2, 55.2, 38.9, 37.5, 36.4, 30.6, 20.3; HRMS: m/z (ESI) calculated [M+H]$^+$: 323.1643, found:323.1642.

The title compound (+)-2n was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (62% yield, 35.0 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.26 (d, $J = 1.9$ Hz, 1H), 7.24-7.20 (m, 4H), 6.25 (t, $J = 2.5$ Hz, 1H), 6.05 (d, $J = 3.1$ Hz, 1H), 3.58 (d, $J = 15.7$ Hz, 1H), 3.30 (d, $J = 2.1$ Hz, 2H), 2.85 (d, $J = 15.8$ Hz, 1H), 2.52-2.40 (m, 2H), 2.27-2.14 (m, 3H), 1.93-1.87 (m, 1H), 1.36-1.26 (m, 1H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 211.4, 151.7, 144.0, 143.2, 141.6, 129.2, 127.0, 125.4, 121.9, 110.4, 107.7, 85.0, 66.3, 38.4, 37.1, 31.5, 31.2, 20.0; HRMS: m/z (ESI) calculated [M+H]$^+$: 283.1326, found:283.1329.
The title compound (±)-2o was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (57% yield, 34.0 mg, colorless liquid).

1H NMR (400 MHz, Chloroform-d) δ 7.28-7.23 (m, 4H), 7.17 (d, J = 5.1 Hz, 1H), 6.95-6.93 (m, 3.4 Hz, 1H), 6.80 (d, J = 3.4 Hz, 1H), 3.68 (d, J = 15.5 Hz, 1H), 3.55 (q, J = 15.1 Hz, 2H), 2.88 (d, J = 15.4 Hz, 1H), 2.62-2.51 (m, 2H), 2.37-2.23 (m, 2H), 1.98-1.93 (m, 1H), 1.86 (s, 1H), 1.40-1.34 (m, 1H); 13C NMR (101 MHz, Chloroform-d) δ 210.6, 143.8, 143.6, 139.2, 129.4, 127.1, 126.9, 126.5, 125.7, 124.2, 121.8, 85.2, 67.6, 38.6, 36.6, 32.5, 30.9, 20.3; HRMS: m/z (ESI) calculated [M+H]⁺: 299.1098, found: 299.1100.

The title compound (±)-2p was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (63% yield, 30.7 mg, white solid).

1H NMR (400 MHz, Chloroform-d) δ 7.31-7.29 (m, 1H), 7.24 (s, 3H), 3.53 (d, J = 15.9 Hz, 1H), 2.67 (d, J = 15.9 Hz, 1H), 2.52 (d, J = 13.4 Hz, 1H), 2.19 (d, J = 13.3 Hz, 1H), 2.13-2.05 (m, 2H), 1.78 (s, 1H), 1.29 (s, 3H), 1.14 (s, 3H), 0.65 (s, 3H); 13C NMR (101 MHz, Chloroform-d) δ 213.7, 146.7, 140.4, 128.7, 127.0, 125.4, 122.8, 85.9, 60.0, 50.4, 46.1, 39.6, 33.2, 30.7, 29.5, 18.4; HRMS: m/z (ESI) calculated [M+H]⁺: 277.1796, found: 277.1798.

The title compound (±)-2q was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (17% yield, 11.2 mg, colorless liquid).

1H NMR (600 MHz, Chloroform-d) δ 7.28-7.19 (m, 5H), 3.64 (d, J = 15.2 Hz, 1H), 2.66 (d, J = 15.2 Hz, 1H), 2.60-2.54 (m, 1H), 2.47 (d, J = 14.1 Hz, 1H), 2.38-2.33 (m, 1H), 2.28-2.13 (m, 4H), 2.11-2.06 (m, 1H), 1.94-1.90 (m, 1H), 1.84 (s, 1H), 1.44 (s, 9H), 1.32-1.29 (m, 1H); 13C NMR (151 MHz, Chloroform-d) δ 212.0, 172.7, 143.9, 143.5, 129.2, 127.1, 125.6, 121.9, 84.9, 80.6, 66.1, 38.0, 35.3, 31.2, 30.7, 28.1, 26.5, 20.1; HRMS: m/z (ESI) calculated [M+H]⁺: 348.2170, found: 348.2169.
The title compound (+)-3 was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (69% yield, 35.3 mg, colorless liquid).

$^1$H NMR (600 MHz, Chloroform-$d$) $\delta$ 7.45-7.43 (m, 1H), 7.33-7.31 (m, 2H), 7.27-7.24 (m, 1H), 3.36 (d, $J = 16.1$ Hz, 1H), 2.90 (d, $J = 16.2$ Hz, 1H), 2.60-2.57 (m, 2H), 2.48-2.43 (m, 1H), 2.41-2.27 (m, 3H), 2.01-1.95 (m, 2H), 1.85-1.81 (m, 1H), 1.78-1.73 (m, 1H) 1.5 (s, 1H); $^{13}$C NMR (151 MHz, Chloroform-$d$) $\delta$ 211.1, 170.9, 144.4, 137.6, 129.4, 128.1, 125.1, 123.2, 94.9, 56.0, 41.2, 37.7, 36.5, 27.9, 26.3, 19.0; HRMS: m/z (ESI) calculated [M+H]$^+$: 257.1168, found:257.1172.

The title compound (+)-5a was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (79% yield, 32.0 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.47-7.45 (m, 1H), 7.29-7.26 (m, 2H), 7.18-7.16 (m, 1H), 3.21 (d, $J = 16.5$ Hz, 1H), 2.86 (d, $J = 16.5$ Hz, 1H), 2.61-2.45 (m, 2H), 2.33-2.24 (m, 1H), 1.96-1.86 (m, 2H), 1.20 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 221.5, 144.8, 142.3, 129.5, 127.7, 125.0, 123.5, 88.4, 58.8, 41.1, 36.9, 31.7, 15.6; HRMS: m/z (ESI) calculated [M+Na]$^+$: 225.0890, found:225.0886.

The title compound (+)-5b was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (67% yield, 30.8 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.58-7.56 (m, 1H), 7.26-7.16 (m, 2H), 7.10-7.08 (m, 1H), 2.92-2.89 (m, 2H), 2.64-2.56 (m, 2H), 2.46-2.37 (m, 2H), 2.29-2.18 (m, 1H), 2.18-2.08 (m, 1H), 2.03-1.98 (m, 1H), 1.84-1.76 (m, 1H), 1.67-1.65 (m, 1H), 1.16 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 214.8, 142.3, 134.5, 128.7, 127.3, 126.6,
125.6, 78.0, 52.7, 37.21, 37.16, 30.8, 25.2, 21.0, 15.9; HRMS: m/z (ESI) calculated [M+H]+: 231.1376, found:231.1380.

The title compound (+)-5c was synthesized according to General Procedure (SI 5.1), and it was purified by column chromatography on silica gel (83% yield, dr = 3:1, 33.9 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-d) δ 7.35-7.18 (m, 4H), 3.54 (d, J = 16.0 Hz, 1H), 2.56 (d, J = 16.0 Hz, 1H), 2.45 (s, 1H), 2.31 (s, 3H), 1.29 (s, 3H), 1.24 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 211.7, 146.7, 138.4, 128.2, 127.3, 125.3, 122.4, 82.8, 64.5, 38.5, 27.7, 25.8, 19.5;

$^1$H NMR (400 MHz, Chloroform-d) δ 7.35-7.18 (m, 1.32H), 3.61 (d, J = 16.0 Hz, 0.33H), 3.22 (s, 0.29H), 2.73 (d, J = 16.0 Hz, 0.32H), 2.27 (s, 0.98H), 1.64 (s, 0.97H), 1.24 (s, 0.98H); $^{13}$C NMR (101 MHz, Chloroform-d) δ 213.4, 146.2, 139.8, 128.6, 127.3, 125.0, 122.8, 83.3, 62.4, 40.7, 27.8, 22.7, 20.9; HRMS: m/z (ESI) calculated [M+Na]+: 227.1043, found:227.1043.
The title compound (±)-6a was synthesized according to General Procedure (SI 6.1), and it was purified by column chromatography on silica gel (91% yield, 19.8 mg, white solid).

\[ \text{H NMR (400 MHz, Chloroform-d) } \delta \text{7.26-7.21 (m, 4H), 3.83 (dd, J = 10.9, 4.8 Hz, 1H), 3.02 (d, J = 15.4 Hz, 1H), 2.55 (d, J = 15.5 Hz, 1H), 1.94-1.83 (m, 2H), 1.69-1.50 (m, 5H), 1.46-1.38 (m, 1H), 1.00 (s, 3H); } \]\n
\[ \text{^13C NMR (101 MHz, Chloroform-d) } \delta \text{148.9, 139.2, 127.6, 126.7, 125.7, 121.5, 84.1, 74.8, 52.5, 37.4, 36.6, 31.2, 20.5, 20.0; HRMS: m/z (ESI) calculated [M+Na]^+: 241.1198, found:241.1199.} \]

2D COSY analysis of (±)-6a
2D NOESY analysis of (+)-6a
The title compound (+)-6b was synthesized according to General Procedure (SI 6.2), and it was purified by column chromatography on silica gel (78% yield, 17.9 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-d) $\delta$ 7.30-7.19 (m, 4H), 2.69 (d, $J = 16.0$ Hz, 1H), 2.57 (d, $J = 16.0$ Hz, 1H), 2.40 (dd, $J = 4.3$, 1.8 Hz, 1H), 2.30-2.24 (m, 1H), 2.20 (d, $J = 4.3$ Hz, 1H), 1.98-1.87 (m, 2H), 1.85-1.78 (m, 1H), 1.29 (s, 3H), 1.29-1.23 (m, 1H), 1.21-1.17 (m, 1H); $^{13}$C NMR (101 MHz, Chloroform-d) $\delta$ 143.2, 128.8, 126.8, 125.0, 122.2, 83.5, 61.2, 54.1, 51.2, 38.3, 31.9, 31.2, 20.3, 15.8. HRMS: m/z (ESI) calculated [M+Na]$^+$: 253.1183, found:253.1199.

2D COSY analysis of (+)-6b
2D NOESY analysis of (±)-6b
The title compound (+)-6c was synthesized according to General Procedure (SI 6.3), and it was purified by column chromatography on silica gel (78% yield, 16.7 mg, colorless liquid).

$^1$H NMR (400 MHz, Chloroform-$d$) $\delta$ 7.27-7.24 (m, 1H), 7.23-7.19 (m, 3H), 4.85 (dd, $J = 14.6$, 1.4 Hz, 2H), 3.19 (d, $J = 15.5$ Hz, 1H), 2.70 (d, $J = 15.5$ Hz, 1H), 2.39-2.20 (m, 2H), 1.97-1.85 (m, 2H), 1.78 (s, 1H), 1.72-1.64 (m, 1H), 1.47-1.40 (m, 1H), 1.22 (s, 3H); $^{13}$C NMR (101 MHz, Chloroform-$d$) $\delta$ 152.0, 147.6, 141.4, 127.8, 126.6, 125.2, 122.1, 109.5, 84.4, 53.2, 41.9, 35.2, 32.6, 22.7, 20.4; HRMS: m/z (ESI) calculated [M+Na]$^+$: 237.1249, found:237.1250.

![Image](image_url)

The title compound (+)-6d was synthesized according to General Procedure (SI 6.4), and it was purified by column chromatography on silica gel (58% yield, 11.0 mg, white solid).

$^1$H NMR (600 MHz, Chloroform-$d$) $\delta$ 7.45-7.44 (m, 1H), 7.27-7.21 (m, 3H), 6.28-6.26 (m, 1H), 3.39 (d, $J = 16.5$ Hz, 1H), 2.81-2.72 (m, 3H), 2.63-2.58 (m, 1H), 2.39-2.33 (m, 1H), 1.32 (s, 3H); $^{13}$C NMR (151 MHz, Chloroform-$d$) $\delta$ 214.9, 147.1, 142.1, 138.0, 128.5, 126.9, 125.8, 120.9, 116.1, 55.0, 40.2, 35.6, 24.1, 23.4; HRMS: m/z (ESI) calculated [M+Na]$^+$: 199.1125, found:199.1117.
9. Spectroscopic Data (NMR Spectrum)