

**MgI₂-Accelerated Enantioselective Morita–Baylis–Hillman Reactions of Cyclopentenone Utilizing a Chiral DMAP Catalyst**

Alejandro Bugarin and Brian T. Connell*

*Department of Chemistry, Texas A&M University, PO Box 30012, College Station, TX 77842-3012*

connell@chem.tamu.edu

**Table of Contents**

- General Information ............................................................. S-1
- References to Known Compounds ........................................... S-2
- HPLC Data ........................................................................ S-3
- Procedures and Characterization Data ..................................... S-4
- ¹H and ¹³C NMR Spectra ......................................................... S-6

**General Information**

All reactions were carried out under an argon atmosphere in oven-dried glassware with magnetic stirring. All commercially obtained reagents were used as received. All aldehydes were distilled before use. Isopropanol was distilled from Na₂O.

Heating was accomplished by either a heating mantle or silicone oil bath. Purification of reaction products was carried out by flash column chromatography using silica gel 60 (230-400 mesh). TLC visualization was accompanied with UV light and/or ceric ammonium molybdate staining. Concentration in vacuo refers to the removal of volatile solvent using a rotary evaporator attached to a dry diaphragm pump (10-15 mm Hg) followed by pumping to a constant weight with an oil pump (<300 mTorr).

¹H NMR spectra were recorded at 300 MHz, and are reported relative to CDCl₃ (δ 7.27). ¹H NMR coupling constants (J) are reported in Hertz (Hz) and multiplicities are indicated as follows: s (singlet), d (doublet), t (triplet), m (multiplet). Proton-decoupled ¹³C NMR spectra were recorded at 75 MHz and reported relative to CDCl₃ (δ 77).
## References to Known Compounds

<table>
<thead>
<tr>
<th>Compound No.</th>
<th>Product</th>
<th>Reference (racemic)</th>
<th>Reference (nonracemic)</th>
<th>Compound No.</th>
<th>Product</th>
<th>Reference (racemic)</th>
<th>Reference (nonracemic)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><img src="image" alt="Compound 1" /></td>
<td>-</td>
<td>-</td>
<td>6</td>
<td><img src="image" alt="Compound 6" /></td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td><img src="image" alt="Compound 2" /></td>
<td>1</td>
<td></td>
<td>7</td>
<td><img src="image" alt="Compound 7" /></td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>3</td>
<td><img src="image" alt="Compound 3" /></td>
<td>2</td>
<td>6</td>
<td>8</td>
<td><img src="image" alt="Compound 8" /></td>
<td>4</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td><img src="image" alt="Compound 4" /></td>
<td>3</td>
<td>7</td>
<td>9</td>
<td><img src="image" alt="Compound 9" /></td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td><img src="image" alt="Compound 5" /></td>
<td>1</td>
<td></td>
<td>10</td>
<td><img src="image" alt="Compound 10" /></td>
<td>5</td>
<td>7</td>
</tr>
</tbody>
</table>


### HPLC Data

<table>
<thead>
<tr>
<th>Entry</th>
<th>Product</th>
<th>HPLC RT</th>
<th>% ee</th>
<th>$[\alpha]_D^{22}$</th>
<th>Entry</th>
<th>Product</th>
<th>HPLC RT</th>
<th>% ee</th>
<th>$[\alpha]_D^{22}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1&lt;sup&gt;a&lt;/sup&gt;</td>
<td><img src="images/1.png" alt="" /></td>
<td>$t_{\text{major}} = 30.60$ min</td>
<td>98</td>
<td>+66.1</td>
<td>2&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="images/2.png" alt="" /></td>
<td>$t_{\text{major}} = 22.23$ min</td>
<td>95</td>
<td>+26.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$t_{\text{minor}} = 27.25$ min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$t_{\text{major}} = 24.29$ min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3&lt;sup&gt;a&lt;/sup&gt;</td>
<td><img src="images/3.png" alt="" /></td>
<td>$t_{\text{major}} = 23.67$ min</td>
<td>94</td>
<td>–22.7</td>
<td>4&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="images/4.png" alt="" /></td>
<td>$t_{\text{major}} = 12.39$ min</td>
<td>94</td>
<td>+18.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$t_{\text{minor}} = 26.64$ min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$t_{\text{major}} = 13.49$ min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5&lt;sup&gt;c&lt;/sup&gt;</td>
<td><img src="images/5.png" alt="" /></td>
<td>$t_{\text{major}} = 24.68$ min</td>
<td>92</td>
<td>+15.8</td>
<td>8&lt;sup&gt;c&lt;/sup&gt;</td>
<td><img src="images/8.png" alt="" /></td>
<td>$t_{\text{major}} = 8.79$ min</td>
<td>63</td>
<td>–25.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$t_{\text{minor}} = 25.94$ min</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$t_{\text{major}} = 9.19$ min</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6&lt;sup&gt;c&lt;/sup&gt;</td>
<td><img src="images/6.png" alt="" /></td>
<td>$t_{\text{major}} = 17.61$ min</td>
<td>89</td>
<td>+17.3</td>
<td>9&lt;sup&gt;c&lt;/sup&gt;</td>
<td><img src="images/9.png" alt="" /></td>
<td>$t_{\text{major}} = 7.94$ min</td>
<td>58</td>
<td>–21.7</td>
</tr>
<tr>
<td>7&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="images/7.png" alt="" /></td>
<td>$t_{\text{major}} = 21.45$ min</td>
<td>89</td>
<td>+38.5</td>
<td>10&lt;sup&gt;b&lt;/sup&gt;</td>
<td><img src="images/10.png" alt="" /></td>
<td>$t_{\text{major}} = 10.47$ min</td>
<td>53</td>
<td>–18.9</td>
</tr>
</tbody>
</table>

<sup>a</sup> Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (hexane/iPrOH = 90/10), 1.0 mL/min, 254 nm.

<sup>b</sup> Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (hexane/iPrOH = 85/15), 1.0 mL/min, 254 nm.

<sup>c</sup> Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (hexane/iPrOH = 95/5), 1.0 mL/min, 254 nm.

<sup>d</sup> Optical rotation at (c 1.00, CHCl₃).

The absolute (S) configuration of products 3, 4, 7, 8, 9 and 10 was determined by comparison of the sign of optical rotation with the known compounds. Other absolute configurations are assigned by analogy.
Supplementary Information

**Procedures and Characterization Data**

Compounds 2-10, are known compounds. Compound 1 is a new compound. Full tabulated data is available below for adduct of the optimization reaction (compound 3) and the new compound 1.

**General method for the asymmetric MBH reaction:** To a stirred mixture of (R)-(+-)4-dimethylaminopyrindinyl(pentaphenylcyclo-pentadienyl)iron (II) (5 mg, 0.0075 mmol, 10 mol%), MgI₂ (10 mg, 0.038 mmol, 50 mol%) in i-PrOH (1.5 mL) was added the aldehyde (0.075 mmol) at room temperature under argon. Then the reaction mixture was cooled down to -20 ºC followed by the addition of cyclopent-2-enone (9 mg, 0.11 mmol, 1.5 equiv). After, the mixture was stirred for 24 h at -20 ºC under argon atmosphere. The reaction was quenched by addition of saturated aqueous NH₄Cl solution (1.0 mL). The solution mixture was extracted twice with CH₂Cl₂ (5 mL) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel column chromatography (20% EtOH/hexanes or CH₂Cl₂).

**(S)-2-(hydroxy(naphthalen-1-yl)methyl)cyclopent-2-enone (1):** To a stirred mixture of (R)-(+-)4-dimethylaminopyrindinyl(pentaphenylcyclopentadienyl) iron (II) (5 mg, 0.008 mmol), MgI₂ (10.4 mg, 0.038 mmol) in i-PrOH (1.5 mL) was added 1-naphthaldehyde (12 mg, 0.075 mmol) at room temperature under an argon atmosphere. Then the reaction mixture was cooled down to -20 ºC followed by the addition of cyclopent-2-enone (9 mg, 0.11 mmol, 1.5 equiv). After, the mixture was stirred for 24 h at -20 ºC under argon atmosphere. The reaction was quenched by addition of saturated aqueous NH₄Cl (1 mL). The mixture was extracted twice with CH₂Cl₂ (5 mL) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by flash silica gel column chromatography to give compound 1 (14 mg, 94%) as a colorless oil (CH₂Cl₂); IR (thin film) ν 3403, 3028, 2920, 1695, 1611, 960 cm⁻¹; ¹H NMR (CDCl₃, 300 MHz) δ 7.93-7.88 (m, 2H), 7.82 (d, J = 8.7 Hz, 1H), 7.76 (d, J = 7.2 Hz, 1H), 7.70-7.46 (m, 3H), 7.02 (m, 1H), 6.30 (s, 1H), 3.79 (s, 1OH), 2.50 (m, 4H). ¹³C NMR (75 MHz, CDCl₃) δ 210.1, 161.1, 147.2, 136.6, 133.8, 130.4, 128.8, 128.4, 126.1, 125.6, 125.5, 124.4, 123.7, 66.5, 35.2, 26.6. HRMS (ESI) calcd for C₁₉H₁₄O₂ + Li requires m/z 245.040, found 245.041. [α]D²² = +66.09 (c 1.0, CHCl₃). Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (hexane/iPrOH = 90/10), 1.0 mL/min, 254 nm, t_major = 30.60 min, t_minor = 27.25 min; 98% ee.

**(S,E)-2-(1-hydroxy-3-phenylallyl)cyclopent-2-enone (3):** To a stirred mixture of (R)-(+-)4-dimethylaminopyrindinyl(pentaphenylcyclopentadienyl) iron (II) (5 mg, 0.0075 mmol, 10 mol%), MgI₂ (10 mg, 0.038 mmol, 50 mol%) in i-PrOH (1.5 mL) was added trans-cinnamaldehyde (10 mg, 0.075 mmol) at room temperature under an argon atmosphere. Then the reaction mixture was cooled down to -20 ºC followed by the addition of cyclopent-2-enone (9 mg, 0.11 mmol, 1.5 equiv). After, the mixture was stirred for 24 h at -20 ºC under an argon atmosphere. The reaction was quenched by addition of saturated aqueous NH₄Cl (1 mL). The solution mixture was extracted twice with CH₂Cl₂ (5 mL) and dried over anhydrous Na₂SO₄. The solvent was removed under reduced pressure, and the residue was
purified by flash silica gel column chromatography to give compound 3 (16 mg, 96%) as a colorless oil (CH$_2$Cl$_2$); IR (thin film) $\nu$ 3400, 3026, 2921, 1691, 1605, 970 cm$^{-1}$; $^1$H NMR (CDCl$_3$, 300 MHz) $\delta$ 7.55 (td, $J$ = 1.1 Hz, 1.4 Hz, 3.1 Hz, 1H), 7.41 (m, 2H), 7.27-7.17 (m, 3H), 6.70 (dd, $J$ = 1.1 Hz, 14.8 Hz, 1H), 6.35 (dd, $J$ = 6.5Hz, 9.8 Hz, 1H), 5.17 (d, $J$ = 6.7 Hz, 1H), 3.31 (d, $J$ = 4.1 Hz, 1OH), 2.65 (m, 2H), 2.49 (m, 2H). $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 209.6, 158.8, 146.3, 136.3, 131.1, 128.6, 128.5, 127.8, 126.5, 68.4, 35.1, 26.7. HRMS (ESI) calcd for C$_{14}$H$_{14}$O$_2$ + Li requires $m/z$ 221.115, found 221.114. $[\alpha]^{22}_D$ = -22.66 (c 1.0, CHCl$_3$). Enantiomeric excess was determined by HPLC with a Chiralcel OJ-H column (hexane/i-PrOH = 90/10), 1.0 mL/min, 254 nm, $t_{\text{major}}$ = 23.67 min, $t_{\text{minor}}$ = 26.64 min; 94% ee.
$^1$H and $^{13}$C NMR Spectra

$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
$^{1}H$ NMR (CDCl$_3$, 300 MHz)

$^{13}C$ NMR (CDCl$_3$, 75 MHz)
$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
Supplementary Information

$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
**Supplementary Information**

$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
Supplementary Information

$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
Supplementary Information

$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
$^{1}$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)
Supplementary Information

$^1$H NMR (CDCl$_3$, 300 MHz)

$^{13}$C NMR (CDCl$_3$, 75 MHz)