## Supporting Information

# Bifunctional Organocatalysts for Enantioselective aza-Morita-Baylis-Hillman (aza-MBH) Reaction 

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## Experimental Section

General. Commercially available organic and inorganic compounds were used without further purification except for the solvent, which was distilled from sodium/benzophenone or $\mathrm{CaH}_{2}$. Column chromatography on $\mathrm{SiO}_{2}$ was performed with Kanto Silica Gel $60(40-100 \mu \mathrm{~m})$.
${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR spectra were recorded with JEOL JNM-EX270 FT NMR ( $\left.{ }^{1} \mathrm{H}-\mathrm{NMR} 270 \mathrm{MHz},{ }^{13} \mathrm{C}-\mathrm{NMR} 67.7 \mathrm{MHz}\right)$. All signals are expressed as ppm down field from tetramethylsilane used as an internal standard. FT-IR spectra were recorded on a SHIMADZU FTIR-8300. Optical rotations were measured with JASCO P-1030 polarimeter. HPLC analyses were performed on a JASCO HPLC system (JASCO PU 980 pump and UV-975 UV/Vis detector) using a mixture of hexane and $i-\mathrm{PrOH}$ as the eluent. Mass spectra were obtained on JEOL JMS-DX300 (for EI-MS), JEOL JMS-700 (for FAB-MS), and JMS-T100LC (for ESI-MS). Elemental analysis was performed on PERKIN-ELMER 2400.

General procedure for synthesis of (S)-3-( $N$-isopropyl- $N$-3-pyridinylaminomethyl)BINOL


## (S)-II

A solution of corresponding 3- N -methylaminopyridine ${ }^{1)}\left(26.0 \mathrm{mg}, 0.24 \mathrm{mmol}\right.$ ) or $3-\mathrm{N}$-isopropylaminopyridine ${ }^{2}$ ) ( 32.7 $\mathrm{mg}, 0.24 \mathrm{mmol})$ in THF $(0.7 \mathrm{~mL})$ was added to a heterogeneous solution of $\mathrm{NaH}(16 \mathrm{mg}, 0.24 \mathrm{mmol})$ in THF ( 0.3 mL ) at $0^{\circ} \mathrm{C}$. After stirring for 2 h at $60^{\circ} \mathrm{C}$, a solution of $\left.(S)-\mathrm{I}^{3}\right)(0.20 \mathrm{mmol})$ in THF $(1.0 \mathrm{~mL})$ was combined with the reaction mixture. The mixture was stirred for 15 min at room temperature and then quenched with saturated $\mathrm{NH}_{4} \mathrm{Cl}$ aq at $0^{\circ} \mathrm{C}$. The organic phase was extracted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$, dried over $\mathrm{Na}_{2} \mathrm{SO}_{4}$, filtered and concentrated. The obtained residue was purified by flash chromatography $\left(\mathrm{SiO}_{2}, \mathrm{CH}_{2} \mathrm{Cl}_{2} / \mathrm{MeOH}=19 / 1\right)$ to afford the titled compound (S)-II (IIa, R $=\mathrm{Me}$, quant.; IIb, $\mathrm{R}=i-\mathrm{Pr}, 60 \%$ yield $)$
(S)-IIa ( $\mathrm{R}=\mathrm{Me}$ ) colorless oil; IR (neat): v 3083, 2912, 2812, 1581, 1494, 1444, 1346, $1222 \mathrm{~cm}^{-1} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta$ $8.25(1 \mathrm{H}, \mathrm{d}, \mathrm{J}=3.0 \mathrm{~Hz}), 7.99(2 \mathrm{H}, \mathrm{d}, J=9.2 \mathrm{~Hz}), 7.89(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 7.75(1 \mathrm{H}, \mathrm{d}, J=8.1 \mathrm{~Hz}), 7.61(1 \mathrm{H}, \mathrm{s}), 7.60$ $(1 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.41-7.11(6 \mathrm{H}, \mathrm{m}), 7.19(2 \mathrm{H}, \mathrm{d}, J=7.0 \mathrm{~Hz}), 5.16(1 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}), 5.06(1 \mathrm{H}, \mathrm{d}, J=7.3 \mathrm{~Hz}), 4.91$
$(2 \mathrm{H}, \mathrm{s}), 4.67(1 \mathrm{H}, \mathrm{d}, J=5.9 \mathrm{~Hz}), 4.50(1 \mathrm{H}, \mathrm{d}, J=5.9 \mathrm{~Hz}), 3.28(3 \mathrm{H}, \mathrm{s}), 3.18(3 \mathrm{H}, \mathrm{s}), 3.10(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta$ $152.6,152.4,145.1,137.6,134.5,133.7,133.1,130.7,130.5,129.9,129.6,127.8,127.7,126.8,125.9,125.8,125.5$, $125.4,125.3,125 . .0,124.1,123.5,120.4,118.2,116.4,99.3,94.8,57.0,56.1,52.7,38.7$; HRMS (ESI) calcd for $\mathrm{C}_{31} \mathrm{H}_{32} \mathrm{~N}_{2} \mathrm{NaO}_{4}, \mathrm{~m} / \mathrm{z}=517.2103\left[(\mathrm{M}+\mathrm{Na})^{+}\right] ;$found, $\mathrm{m} / \mathrm{z}=517.2093 ;[\alpha]_{\mathrm{D}}{ }^{20}-40.8^{\circ}\left(c 1.0, \mathrm{CHCl}_{3}\right)$.
(S)-IIb (R = i-Pr) brown oil; IR (neat): v 3095, 2945, 2829, 1596, 1514, 1444, 1375, $1221 \mathrm{~cm}^{-1} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta$ $8.27(1 \mathrm{H}, \mathrm{brs}), 7.99(2 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 7.89(1 \mathrm{H}, \mathrm{d}, J=8.1 \mathrm{~Hz}), 7.75(1 \mathrm{H}, \mathrm{d}, J=5.7 \mathrm{~Hz}), 7.74(1 \mathrm{H}, \mathrm{s}), 7.60(1 \mathrm{H}, \mathrm{d}, J=$ $8.4 \mathrm{~Hz}), 7.41-7.05(8 \mathrm{H}, \mathrm{m}), 5.15(1 \mathrm{H}, \mathrm{d}, J=7.0 \mathrm{~Hz}), 5.07(1 \mathrm{H}, \mathrm{d}, J=7.0 \mathrm{~Hz}), 4.74(2 \mathrm{H}, \mathrm{s}), 4.70(1 \mathrm{H}, \mathrm{d}, J=5.7 \mathrm{~Hz})$, $4.53(1 \mathrm{H}, \mathrm{d}, J=5.7 \mathrm{~Hz}), 4.48-4.36(1 \mathrm{H}, \mathrm{m}), 3.18(3 \mathrm{H}, \mathrm{s}), 3.12(3 \mathrm{H}, \mathrm{s}), 1.33(3 \mathrm{H}, \mathrm{d}, J=6.7 \mathrm{~Hz}), 1.32(3 \mathrm{H}, \mathrm{d}, J=6.7$ $\mathrm{Hz}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 152.7,152.0,145.2,145.1,137.4,133.8,132.0,130.9,129.9,129.6,127.8,127.7,126.8$, $126.5,125.7,125.5,125.4,125.4,125.1,124.9,124.1,123.6,120.6,119.3 .116 .6,99.3,95.0,55.9,56.0,48.1,44.7,19.8$, 19.7; HRMS (ESI) calcd for $\mathrm{C}_{33} \mathrm{H}_{35} \mathrm{~N}_{2} \mathrm{O}_{4}, \mathrm{~m} / \mathrm{z}=523.2597\left[(\mathrm{M}+\mathrm{H})^{+}\right]$; found, $\mathrm{m} / \mathrm{z}=523.2585 ;[\alpha]_{\mathrm{D}}{ }^{20}-43.2^{\circ}$ (c 1.0, $\mathrm{CHCl}_{3}$ ).

## (S)-2a (or 6a)

Trimethylsilyl bromide ( $53 \mu \mathrm{~L}, 0.4 \mathrm{mmol}$ ) was added to the mixture of corresponding $(S)$ - II $(0.2 \mathrm{mmol})$ and MS 4A ( 10 $\mathrm{mg})$ in $\mathrm{CH}_{2} \mathrm{Cl}_{2}(1 \mathrm{~mL})$ at $0^{\circ} \mathrm{C}$. After stirring for 30 min , the reaction mixture was quenched with water. The organic phase was extracted with $\mathrm{CH}_{2} \mathrm{Cl}_{2}$. The combined organic extracts were then dried $\left(\mathrm{Na}_{2} \mathrm{SO}_{4}\right)$ and evaporated in vacuo. The residue was purified by flash chromatography $\left(\mathrm{SiO}_{2}, \mathrm{CH}_{2} \mathrm{Cl}_{2} / \mathrm{MeOH}=9 / 1\right)$ to give the title compound $(\mathrm{S})-\mathbf{2 a}(92 \%$ yield) or $\mathbf{6 a}(90 \%$ yield $)$.
(S)-2a $(\mathrm{R}=\mathrm{Me}) \quad$ white solid; $\mathrm{mp} 119-120^{\circ} \mathrm{C}$ (hexane $/ \mathrm{CH}_{2} \mathrm{Cl}_{2}$ ); IR (neat): v 3389, 3012, 2933, 1284, 1612, 1588, 1510, $1424,1412,1367,1220,1012 \mathrm{~cm}^{-1} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 8.28-8.18(1 \mathrm{H}, \mathrm{br}), 7.96(2 \mathrm{H}, \mathrm{d}, J=9.2 \mathrm{~Hz}), 7.89(2 \mathrm{H}, \mathrm{d}, J=$ $8.4 \mathrm{~Hz}), 7.79(1 \mathrm{H}, \mathrm{d}, J=8.1 \mathrm{~Hz}), 7.70(1 \mathrm{H}, \mathrm{s}) 7.39(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 7.34-7.13(6 \mathrm{H}, \mathrm{m}), 4.76(2 \mathrm{H}, \mathrm{s}), 3.18(3 \mathrm{H}, \mathrm{s})$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 153.3,151.4,145.2,136.6,133.8,133.0,129.0,128.8,128.1,127.8,127.1,126.9,126.5,125.6$, $124.4,124.3,123.7,123.3,119.5,118.3,113.3,112.0,53.0,38.6$; HRMS (ESI) calcd for $\mathrm{C}_{27} \mathrm{H}_{23} \mathrm{~N}_{2} \mathrm{O}_{2}, \mathrm{~m} / \mathrm{z}=407.1760$ $\left[(\mathrm{M}+\mathrm{H})^{+}\right]$; found, $\mathrm{m} / \mathrm{z}=407.1740 ;[\alpha]_{\mathrm{D}}{ }^{20}-17.8^{\circ}\left(c 0.7, \mathrm{CHCl}_{3}\right)$.
(S)-6a ( $\mathrm{R}=i-\mathrm{Pr}$ ) brown solid; mp 122- $123^{\circ} \mathrm{C}$ (hexane $/ \mathrm{CH}_{2} \mathrm{Cl}_{2}$ ); IR (neat): v3440, 3055, 2966, 2823, 1705, 1620, 1585, 1566, 1497, 1431, 1342, 1272, 1184, 1134, 1096, $1061 \mathrm{~cm}^{-1} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 8.18(1 \mathrm{H}, \mathrm{d}, J=2.7 \mathrm{~Hz}), 7,94(1 \mathrm{H}, \mathrm{dd}$, $J=4.0$ and 0.8 Hz$), 7.85(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 7.79(1 \mathrm{H}, \mathrm{d}, J=7.8 \mathrm{~Hz}), 7.79-7.65(2 \mathrm{H}, \mathrm{m}), 7.28(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz})$, $7.28-7.00(6 H, m), 6.96(1 \mathrm{H}, \mathrm{d}, J=8.1 \mathrm{~Hz}), 4.55(2 \mathrm{H}, \mathrm{s}), 4.04-3.43(1 \mathrm{H}, \mathrm{m}), 1.21(3 \mathrm{H}, \mathrm{d}, J=6.5 \mathrm{~Hz}), 1.18(3 \mathrm{H}, \mathrm{d}, J=$ $6.7 \mathrm{~Hz}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 152.4,151,8,143.8,140.0,133.5,132.9,130.6,129.2,128.8,128.3,128.2,128.1,127.9$, $126.9,126.7,126.2,124.3,124.3,124.2,123.8,123.5,123.4,117.8,112.4,112.3,50.8,47.0,19.6,19.4$; HRMS (ESI) calcd for $\mathrm{C}_{29} \mathrm{H}_{27} \mathrm{~N}_{2} \mathrm{O}_{2}, \mathrm{~m} / \mathrm{z}=435.2073\left[(\mathrm{M}+\mathrm{H})^{+}\right]$; found, $\mathrm{m} / \mathrm{z}=435,2062 ;[\alpha]_{\mathrm{D}}{ }^{20}-28.5^{\circ}\left(c 0.4, \mathrm{CHCl}_{3}\right)$.

## The effects of reaction conditions on enantioselective aza-MBH reaction promoted by ( $S$ )-2a

The effect of solvent on organocatalyst 2a mediated reaction is summarized in Table S-1. Ethereal solvents such as diethyl ether, t-BuOMe, cyclopentyl methyl ether (CPME), dimethyl ether (DME) and THF (Entries 1-5) were relatively good in terms of enantioselectivity when compared with other less polar, polar, aprotic and protic solvents such as halogenated solvents, DMF, acetonitrile, and methanol (entries 6-12). A mixed solvent system consisting of CPME and toluene (9/1) is afforded the good result (Entries 13).

Table S-1


| Entry | Solvent | Time (h) | Yield (\%) $^{\text {a }}$ | Ee (\%) ${ }^{\text {b }}$ |
| :---: | :---: | :---: | :---: | :---: |
| 1 | $\mathrm{Et}_{2} \mathrm{O}$ | 108 | 74 | 72 |
| 2 | $t$-BuOMe | 72 | 92 | 73 |
| 3 | CPME | 72 | 97 | 78 |
| 4 | DME | 60 | 73 | 68 |
| 5 | THF | 48 | 71 | 59 |
| 6 | toluene $_{7}$ | $\mathrm{CH}_{2} \mathrm{Cl}_{2}$ | 24 | 81 |
| 8 | $\mathrm{CHCl}_{3}$ | 24 | Quant | 59 |
| 9 | $\mathrm{ClCH}_{2} \mathrm{CH}_{2} \mathrm{Cl}$ | 24 | 97 | 54 |
| 10 | $\mathrm{DMF}_{11}$ | MeCN | 24 | 87 |
| 12 | MeOH | 48 | 78 | 57 |
| 13 | $\mathrm{CPME:toluene} \mathrm{(9:1)}$ | 72 | 60 | 63 |

${ }^{\mathrm{a}}$ Isolated yield. ${ }^{\mathrm{b}}$ Determined by HPLC (DAICEL CHIRALPAK AD-H).

Table S-2 summarises the effect of temperature on the reaction. While the reaction proceeded smoothly at various temperatures, the best result was obtained at $-15^{\circ} \mathrm{C}$.

Table S-2
$\mathbf{3 a}+\mathbf{4 b} \underset{\text { CMPE/toluene (9/1), Temp }}{\mathbf{2 a}(10 \mathrm{~mol} \%)} \mathbf{5 b}$

| Entry | Temperature $\left({ }^{\circ} \mathrm{C}\right)$ | Time (h) | Yield (\%) $^{\mathrm{a}}$ | Ee (\%) ${ }^{\mathrm{b}}$ |
| :---: | :---: | :---: | :---: | :---: |
| 1 | rt | 60 | 93 | 83 |
| 2 | 0 | 96 | 94 | 86 |
| 3 | -10 | 120 | 95 | 87 |
| 4 | -15 | 144 | 97 | 90 |
| 5 | -20 | 360 | 12 | 90 |

[^0]
## General procedure for enantioselective aza-MBH reaction promoted by (S)-6a

To a solution of organocatalyst (S)-6a ( $2.2 \mathrm{mg}, 0.005 \mathrm{mmol}$ ) in CPME/toluene ( $9 / 1,0.1 \mathrm{~mL}$ ) was added to methyl vinyl ketone ( $3,12.5 \mu \mathrm{~L}, 0.15 \mathrm{mmol}$ ) and known imines ${ }^{4}$ ( $4,0.05 \mathrm{mmol}$ ) at $-15^{\circ} \mathrm{C}$. The mixture was stirred until the reaction had reached completion by monitoring with TLC analysis. The mixture was directly purified by flash column chromatography $\left(\mathrm{SiO}_{2}, n\right.$-hexane $\left./ \mathrm{EtOAc}=2 / 1\right)$ to give the corresponding adducts $\mathbf{5 a - j}$ as white solid. The adducts $\mathbf{5 a}-\mathbf{f}$ and $\mathbf{5 h}$ were identical in all respects with reported by Shi and co-workers. ${ }^{5 \text { ) }}$ Absolute configurations were assigned by comparison of optical rotation reported in the literature. ${ }^{5)}$

Table 1. Enantioselective aza-MBH reaction promoted by (S)-6a


| Entry | 3: $\mathrm{R}^{1}$ | 4: $\mathrm{R}^{2}$ | Time (h) | Yield (\%) ${ }^{\text {a }}$ | Ee (\%) ${ }^{\text {b }}$ |
| :---: | :---: | :---: | :---: | :---: | :---: |
| 1 | Me (3a) | $\mathrm{Ph}(4 \mathrm{a})$ | 168 | 5a, 93 | 87 |
| 2 | Me (3a) | $p-\mathrm{Cl}-\mathrm{C}_{6} \mathrm{H}_{4}(4 \mathbf{b})$ | 60 | 5b, 96 | 95 |
| 3 | Me (3a) | $m-\mathrm{Cl}-\mathrm{C}_{6} \mathrm{H}_{4}(4 \mathrm{c})$ | 72 | 5c, 93 | 93 |
| 4 | Me (3a) | $p-\mathrm{Br}-\mathrm{C}_{6} \mathrm{H}_{4}(\mathbf{4 d})$ | 36 | 5d, 93 | 94 |
| 5 | Me (3a) | $p-\mathrm{MeO}-\mathrm{C}_{6} \mathrm{H}_{4}(4 \mathrm{e})$ | 132 | 5e, 93 | 94 |
| 6 | Me (3a) | 2-furyl (4f) | 48 | 5f, Quant | 88 |
| 7 | Me (3a) | 2-naphthyl (4g) | 108 | 5g, 94 | 91 |
| 8 | Me (3a) | $p-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4}(\mathbf{4 h})$ | 12 | 5h, 91 | 91 |
| 9 | Et (3b) | $p-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4}(4 \mathrm{~h})$ | 96 | 5i, 88 | 88 |
| 10 | H (3c) | $p-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4}(\mathbf{4 h})$ | 36 | 5j, 95 | 94 |

${ }^{\text {a }}$ Isolated yield. ${ }^{\text {b }}$ Determined by HPLC (DAICEL CHIRALPAK AD-H or OD-H).
$5 \mathbf{a}\left(\mathrm{R}^{1}=\mathrm{Me}, \mathrm{R}^{2}=\mathrm{Ph}\right) \quad 93 \%$ yield, $87 \%$ ee; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 7.64(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.31-7.20(5 \mathrm{H}, \mathrm{m}), 7.11(2 \mathrm{H}$, $\mathrm{d}, J=8.4 \mathrm{~Hz}), 6.09(1 \mathrm{H}, \mathrm{s}), 6.08(1 \mathrm{H}, \mathrm{s}), 5.59(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 5.25(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 2.41(3 \mathrm{H}, \mathrm{s}), 2.13(3 \mathrm{H}, \mathrm{s})$; DAICEL CHIRALPAK AD-H column, detection at $254 \mathrm{~nm}, i-\mathrm{PrOH} / n$-hexane $=1 / 4$, flow rate $0.2 \mathrm{~mL} / \mathrm{min}, 43.6 \mathrm{~min}$ (minor isomer, $S$ ) and 49.6 min (major isomer, $R$ ).

5b ( $\left.\mathrm{R}^{1}=\mathrm{Me}, \mathrm{R}^{2}=p-\mathrm{Cl}^{2}-\mathrm{C}_{6} \mathrm{H}_{4}-\right) \quad 96 \%$ yield, $95 \% \mathrm{ee} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 7.59(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.18(2 \mathrm{H}, \mathrm{d}, J=8.4$ $\mathrm{Hz}), 7.12(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 7.00(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.05(1 \mathrm{H}, \mathrm{s}), 6.03(1 \mathrm{H}, \mathrm{s}), 5.99(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 5.25(1 \mathrm{H}, \mathrm{d}$, $J=8.9 \mathrm{~Hz}), 2.40(3 \mathrm{H}, \mathrm{s}), 2.13(3 \mathrm{H}, \mathrm{s})$; DAICEL CHIRALPAK AD-H column, detection at $254 \mathrm{~nm}, i-\mathrm{PrOH} / n-$ hexane $=$ $1 / 4$, flow rate $0.3 \mathrm{~mL} / \mathrm{min}, 44.7 \mathrm{~min}$ (minor isomer, $S$ ) and 50.8 min (major isomer, $R$ ).
$5 \mathrm{c}\left(\mathrm{R}^{1}=\mathrm{Me}, \mathrm{R}^{2}=m-\mathrm{Cl}^{2}-\mathrm{C}_{6} \mathrm{H}_{4}-\right) \quad 93 \%$ yield, $93 \% \mathrm{ee},{ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 7.64(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.24(2 \mathrm{H}, \mathrm{d}, J=8.4$ $\mathrm{Hz}), 7.17-7.11(2 \mathrm{H}, \mathrm{m}), 7.05-7.00(2 \mathrm{H}, \mathrm{m}), 6.10(1 \mathrm{H}, \mathrm{s}), 6.05(1 \mathrm{H}, \mathrm{s}), 5.78(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 5.23(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz})$, $2.40(3 \mathrm{H}, \mathrm{s}), 2.15(3 \mathrm{H}, \mathrm{s})$; DAICEL CHIRALPAK AD-H column, detection at $254 \mathrm{~nm}, i-\mathrm{PrOH} / n$-hexane $=1 / 4$, flow rate $0.2 \mathrm{~mL} / \mathrm{min}, 56.5 \mathrm{~min}$ (minor isomer, $S$ ) and 70.2 min (major isomer, $R$ ).
$5 \mathrm{~d}\left(\mathrm{R}^{1}=\mathrm{Me}, \mathrm{R}^{2}=p-\mathrm{Br}^{2}-\mathrm{C}_{6} \mathrm{H}_{4}-\right) \quad 93 \%$ yield, $94 \%$ ee; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 7.60(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.30(2 \mathrm{H}, \mathrm{d}, J=8.4$ $\mathrm{Hz}), 7.25(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.99(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.09(1 \mathrm{H}, \mathrm{s}), 6.06(1 \mathrm{H}, \mathrm{s}), 5.69(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 5.16(1 \mathrm{H}, \mathrm{d}$, $J=8.9 \mathrm{~Hz}), 2.40(3 \mathrm{H}, \mathrm{s}), 2.13(3 \mathrm{H}, \mathrm{s})$; DAICEL CHIRALPAK AD-H column, detection at $254 \mathrm{~nm}, i-\mathrm{PrOH} / n-$ hexane $=$ $1 / 4$, flow rate $0.2 \mathrm{~mL} / \mathrm{min}, 48.9 \mathrm{~min}$ (minor isomer, $S$ ) and 56.1 min (major isomer, $R$ ).
$5 e\left(\mathrm{R}^{1}=\mathrm{Me}, \mathrm{R}^{2}=p-\mathrm{MeO}-\mathrm{C}_{6} \mathrm{H}_{4}-\right) \quad 93 \%$ yield, $94 \%$ ee; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 7.66(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.25(2 \mathrm{H}, \mathrm{d}, J=$ $8.4 \mathrm{~Hz}), 7.00(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.73(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.09(2 \mathrm{H}, \mathrm{s}), 5.53(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 5.25(1 \mathrm{H}, \mathrm{d}, J=8.9$ $\mathrm{Hz}), 3.77(3 \mathrm{H}, \mathrm{s}), 2.45(3 \mathrm{H}, \mathrm{s}), 2.19(3 \mathrm{H}, \mathrm{s})$; DAICEL CHIRALPAK OD-H column, detection at 254 nm , $i-\mathrm{PrOH} / n$-hexane $=1 / 4$, flow rate $0.2 \mathrm{~mL} / \mathrm{min}, 58.8 \mathrm{~min}($ major isomer, $R)$ and $65.4 \mathrm{~min}($ minor isomer, $S)$.
$5 f\left(\mathrm{R}^{1}=\mathrm{Me}, \mathrm{R}^{2}=2\right.$-Furyl) quant, $88 \%$ ee; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 7.66(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=8.4 \mathrm{~Hz}), 7.26(2 \mathrm{H}, \mathrm{d}, \mathrm{J}=8.4 \mathrm{~Hz}), 7.16$ $(1 \mathrm{H}, \mathrm{d}, J=1.8 \mathrm{~Hz}), 6.20(1 \mathrm{H}, \mathrm{dd}, J=3.0 \mathrm{and} 1,8 \mathrm{~Hz}), 6.10(1 \mathrm{H}, \mathrm{s}), 6.06(1 \mathrm{H}, \mathrm{s}), 6.00(1 \mathrm{H}, \mathrm{d}, J=3.0 \mathrm{~Hz}), 5.70(1 \mathrm{H}, \mathrm{d}, J$ $=8.6 \mathrm{~Hz}), 5.36(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 2.40(3 \mathrm{H}, \mathrm{s}), 2.20(3 \mathrm{H}, \mathrm{s})$; DAICEL CHIRALPAK AD-H column, detection at 254 $\mathrm{nm}, i-\mathrm{PrOH} / n$-hexane $=1 / 4$, flow rate $0.5 \mathrm{~mL} / \mathrm{min}, 24.8 \mathrm{~min}($ minor isomer, $S)$ and $29.1 \mathrm{~min}($ major isomer, $R)$.
$5 g\left(R^{1}=\mathrm{Me}, \mathrm{R}^{2}=2\right.$-naphthyl) $94 \%$ yield, $91 \%$ ee; white solid $105-106^{\circ} \mathrm{C}$ (hexane/AcOEt); IR (neat): $v 1661 \mathrm{~cm}^{-1}$; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 7.76-7.50(3 \mathrm{H}, \mathrm{m}), 7.58(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.43(1 \mathrm{H}, \mathrm{s}), 7.39-7.33(2 \mathrm{H}, \mathrm{m}), 7.12(3 \mathrm{H}, \mathrm{d}, J=7.5$ $\mathrm{Hz}), 6.12-6.08(2 \mathrm{H}, \mathrm{m}), 5.65(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 5.36(1 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 2.29(3 \mathrm{H}, \mathrm{s}), 2.11(3 \mathrm{H}, \mathrm{s}) ;{ }^{13} \mathrm{C}-\mathrm{NMR}$ $\left(\mathrm{CDC}_{13}\right): \delta 198.6,146.4,143.2,137.4,136.0,132.9,132.5,129.3,128.2,128.1,127.8,127.4,127.2,126.1,126.0,125.4$, 124.2, 58.9, 26.4, 21.4; HRMS (ESI) calcd for $\mathrm{C}_{22} \mathrm{H}_{21} \mathrm{NnaO}_{3} \mathrm{~S}, \mathrm{~m} / \mathrm{z}=402.1140\left[(\mathrm{M}+\mathrm{Na})^{+}\right]$; found, $\mathrm{m} / \mathrm{z}=402.1152$; $[\alpha]_{\mathrm{D}}{ }^{20}-47.5^{\circ}\left(c 0.6, \mathrm{CHCl}_{3}\right)$; DAICEL CHIRALPAK AD-H column, detection at $254 \mathrm{~nm}, i-\mathrm{PrOH} / n$-hexane $=1 / 4$, flow rate $0.3 \mathrm{~mL} / \mathrm{min}, 61.7 \mathrm{~min}$ (minor isomer, $S$ ) and 65.6 min (major isomer, $R$ ).

5h ( $\left.\mathrm{R}^{1}=\mathrm{Me}, \mathrm{R}^{2}=p-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4}-\right) \quad 91 \%$ yield, $91 \%$ ee; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 8.08(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.67(2 \mathrm{H}, \mathrm{d}, J=$ $8.4 \mathrm{~Hz}), 7.34(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 7.26(2 \mathrm{H}, \mathrm{d}, J=8.6 \mathrm{~Hz}), 6.16(1 \mathrm{H}, \mathrm{s}), 6.10(1 \mathrm{H}, \mathrm{s}), 5.93(1 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 5.32(1 \mathrm{H}$, d, $J=8.9 \mathrm{~Hz}), 2.45(3 \mathrm{H}, \mathrm{s}), 2.16(3 \mathrm{H}, \mathrm{s})$; DAICEL CHIRALPAK AD-H column, detection at $254 \mathrm{~nm}, i-\mathrm{PrOH} / n$-hexane $=1 / 4$, flow rate $0.5 \mathrm{~mL} / \mathrm{min}, 53.2 \mathrm{~min}$ (minor isomer, $S$ ) and 70.8 min (major isomer, $R$ ).
$5 \mathbf{i}\left(\mathrm{R}^{1}=\mathrm{Et}, \mathrm{R}^{2}=p-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4}\right.$ ) $\quad 88 \%$ yield, $88 \%$ ee; white solid; $\mathrm{mp} 112-113^{\circ} \mathrm{C}$ (hexane/AcOEt); IR (neat): $v 1670$, $1515,1342 \mathrm{~cm}^{-1} ;{ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 8.07(2 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 7.64(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.35(2 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 7.24$ $(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 6.13(1 \mathrm{H}, \mathrm{s}), 6.04(1 \mathrm{H}, \mathrm{s}), 5.90(1 \mathrm{H}, \mathrm{d}, J=9.4 \mathrm{~Hz}), 5.31(1 \mathrm{H}, \mathrm{d}, J=9.4 \mathrm{~Hz}), 2.50(2 \mathrm{H}, \mathrm{q}, J=7.5$ $\mathrm{Hz}), 2.41(3 \mathrm{H}, \mathrm{s}) 0.93(3 \mathrm{H}, \mathrm{t}, \mathrm{J}=7.5 \mathrm{~Hz})$; ${ }^{13} \mathrm{C}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 201.2,147.0,146.2,144.8,143.6,137.3,129.8,129.5$, $128.2,127.1,127.1,126.3,123.5,59.2,31.3,21.6,7.8$; HRMS (ESI) calcd for $\mathrm{C}_{19} \mathrm{H}_{20} \mathrm{~N}_{2} \mathrm{NaO}_{5} \mathrm{~S}, \mathrm{~m} / \mathrm{z}=411.0991$ $\left[(\mathrm{M}+\mathrm{Na})^{+}\right]$; found, $\mathrm{m} / \mathrm{z}=411.0990 ;[\alpha]_{\mathrm{D}}{ }^{20} 5.3^{\circ}\left(c 0.6, \mathrm{CHCl}_{3}\right)$; DAICEL CHIRALPAK AD-H column, detection at 254 $\mathrm{nm}, i-\mathrm{PrOH} / n$-hexane $=1 / 4$, flow rate $0.5 \mathrm{~mL} / \mathrm{min}, 47.7 \mathrm{~min}$ (minor isomer) and 52.9 min (major isomer).
$5 \mathbf{j}\left(\mathrm{R}^{1}=\mathrm{H}, \mathrm{R}^{2}=p-\mathrm{NO}_{2}-\mathrm{C}_{6} \mathrm{H}_{4}-\right) \quad 95 \%$ yield, $94 \%$ ee; ${ }^{1} \mathrm{H}-\mathrm{NMR}\left(\mathrm{CDCl}_{3}\right): \delta 9.33(1 \mathrm{H}, \mathrm{s}), 8.00(2 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 7.61$ $(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 7.29(2 \mathrm{H}, \mathrm{d}, J=8.9 \mathrm{~Hz}), 7.19(2 \mathrm{H}, \mathrm{d}, J=8.4 \mathrm{~Hz}), 6.50(1 \mathrm{H}, \mathrm{s}), 6.17(1 \mathrm{H}, \mathrm{d}, J=9.4 \mathrm{~Hz}), 6.11(1 \mathrm{H}$, s), $5.37(1 \mathrm{H}, \mathrm{d}, J=9.4 \mathrm{~Hz}), 2.38(3 \mathrm{H}, \mathrm{s}) ;[\alpha]_{\mathrm{D}}{ }^{20}-18.0^{\circ}\left(c 0.6, \mathrm{CHCl}_{3}\right)$; DAICEL CHIRALPAK OD-H column, detection at $254 \mathrm{~nm}, i-\mathrm{PrOH} / \mathrm{n}$-hexane $=1 / 4$, flow rate $0.5 \mathrm{~mL} / \mathrm{min}, 43.7 \mathrm{~min}$ (major isomer) and 77.6 min (minor isomer).

Figure S-1. Molecular orbital calculation of 6a



Spartan '04, Job type: Geometry optimization, Method: Hartee-Fock, Basis set: 3-21G*. The N-H atomic distance $(1.835 \AA)$. The angle between the N-H-O bonds $\left(145.02^{\circ}\right)$.

## References

1. Krishnamurthy, S. Tetrahedron Lett. 1982, 23, 3315-3318.
2. a) Ieno, M. Jpn. Kokai Tokkyo Koho (1999), 4pp. JP11035562; b) Morris, J.; Wishka, D. G. J. Org. Chem. 1995, 60, 2642-2644.
3. a) Matsunaga, S.; Das, J.; Roels, J.; Vogl, E. M.; Yamamoto, N.; Iida, T.; Yamaguchi, K.; Shibasaki, M. J. Am. Chem. Soc. 2000, 122, 2252-2260; b) Lee, K. Y.; Lee, C. G.; Kim, J. M. Tetrahedron Lett. 2003, 44, 1231-1234.
4. a) ten Have, R.: Huisman, M.; Meetsma, A.; van Leusen, A. M. Tetrahedron 1997, 53, 11355-11368. b) Lee, K. Y.; Lee, C. G.; Kim, J. M. Tetrahedron Lett. 2003, 44, 1231-1234.
5. a) Shi, M.; Xu, Y.-M. Angew. Chem. Int. Ed. 2002, 41, 4507-4510; b) Shi, M.; Chen, L.-H. Chem. Commun. 2003, 1310-1311; c) Xu, Y.-M.; Shi, M. J. Org. Chem. 2004, 69, 417-425.

[^0]:    ${ }^{\mathrm{a}}$ Isolated yield. ${ }^{\mathrm{b}}$ Determined by HPLC (DAICEL CHIRALPAK AD-H).

