# Supporting Information for 

# Asymmetric one-pot sequential Friedel-Crafts-type alkylation and $\alpha$-oxyamination catalyzed by a peptide and an enzyme 

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## General information

${ }^{1} \mathrm{H}$ and ${ }^{13} \mathrm{C}$ NMR spectra were recorded at 400 and 100 MHz respectively on a JEOL JNM-LA400 spectrometer, and chemical shifts were referenced to internal tetramethylsilane (TMS, $\delta=0.0 \mathrm{ppm}$ ) for ${ }^{1} \mathrm{H}$, and the central line of $\mathrm{CDCl}_{3}(\delta=77.0 \mathrm{ppm})$ for ${ }^{13} \mathrm{C}$. High-resolution FAB mass spectra were obtained on a JEOL JMS-600H mass spectrometer in positive-ionization mode by using 3-nitrobenzyl alcohol as a matrix. Polyethylene glycol 400 was added to the matrix as a mass calibrant. HPLC charts were recorded on a Shimadzu CLASS-VP system with a Chiralpak IA column ( 25 cm ) and IA guard ( 1 cm ), or Chiralpak AS-H column ( 25 cm ) and AS-H guard ( 1 cm ). The resin-supported peptide was synthesized according to our previous report [37]. Laccase was purchased from Sigma-Aldrich (product number: 53739, from Trametes versicolor, $93.6 \mathrm{U} / \mathrm{mg}$ ) and used as received.

## Typical procedure for the sequential FCAA/ $\alpha$-oxyamination (Table 2).

To a mixture of an indole compound ( 0.10 mmol ), an aldehyde ( 0.15 mmol ) and resin-supported TFA•Pro-D-Pro-Aib-(Trp) $)_{2}$-(Leu-Leu-Aib) $)_{2}(111 \mathrm{mg}, 0.02 \mathrm{mmol}$ of the terminal prolyl group) in THF ( 0.67 mL ), was added water ( 1.34 mL ), slowly. After the mixture had been stirred at room temperature for the given time, TEMPO ( 0.15 mmol ) and laccase $(0.5 \mathrm{mg})$ were added. Afterward the mixture was stirred for another 12 h , and then the peptide catalyst was filtered off and washed with diethyl ether. The filtrate solution was washed with water, and the organic layer was dried over anhydrous magnesium sulfate. After the removal of the solvent under reduced pressure, the crude product was purified by preparative TLC (hexane/ethyl acetate 2:1) to afford a diastereomeric mixture. Then, the product was dissolved in ethanol (ca. 2 mL ), and sodium borohydride ( 0.3 mmol ) was added. Afterward the mixture was stirred for 30 min , and then an aqueous saturated solution of ammonium chloride was added. The resulting solution was extracted with chloroform, and the organic layer was dried over anhydrous magnesium sulfate. After the removal of the solvent under reduced pressure, the crude product was purified by preparative TLC (hexane/ethyl acetate 1:1) to afford the corresponding alcohols of syn and anti-isomers separately (in Table 2, entry 4, two isomers could not be separated).

(2S,3S)-3-(5-Methoxy-1-methyl-1H-indol-3-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethyl-piperidin-1-yloxy)propanol (syn-4, Table 2, entry 1).
${ }^{1} \mathrm{H}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 8.14-8.10(\mathrm{~m}, 2 \mathrm{H}), 7.54-7.50(\mathrm{~m}, 2 \mathrm{H}), 7.20-7.17(\mathrm{~m}, 2 \mathrm{H}), 6.85$ (dd, $J=8.7,2.3$ $\mathrm{Hz}, 1 \mathrm{H}), 6.62(\mathrm{~d}, J=2.8 \mathrm{~Hz}, 1 \mathrm{H}), 5.69(\mathrm{br}, 1 \mathrm{H}), 4.99(\mathrm{ddd}, J=9.6,3.7,1.8 \mathrm{~Hz}, 1 \mathrm{H}), 4.49(\mathrm{~d}, J=3.7$ $\mathrm{Hz}, 1 \mathrm{H}$ ), 3.89 (dd, $J=12.4,9.6 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.78 (s, 3H), 3.78 (dd, $J=12.4,1.8 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.71 (s, 3H), $1.62-1.30(\mathrm{~m}, 6 \mathrm{H}), 1.26(\mathrm{~s}, 3 \mathrm{H}), 1.14(\mathrm{~s}, 3 \mathrm{H}), 1.09(\mathrm{~s}, 3 \mathrm{H}), 1.01(\mathrm{~s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 153.79$, $149.53,146.55,132.07,129.80,127.84,127.82,123.21,111.84,111.43,110.07,100.99,82.72$, 66.95, 62.03, 60.22, 55.83, 44.79, 40.53, 40.24, 34.66, 33.05, 32.12, 20.74, 20.31, 16.96; HRMS (FAB) $\mathrm{m} / \mathrm{z}$ : calculated for $\mathrm{C}_{28} \mathrm{H}_{38} \mathrm{~N}_{3} \mathrm{O}_{5}[\mathrm{M}+\mathrm{H}]^{+}: 496.2811$, found 496.2820. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$ ): $t_{\mathrm{R}}=21.7$ $\min$ (minor), $30.3 \min$ (major).

(2R,3S)-3-(5-Methoxy-1-methyl-1H-indol-3-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethyl-piperidin-1-yloxy)propanol (anti-4, Table 2, entry 1).
${ }^{1} \mathrm{H}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 8.14-8.10(\mathrm{~m}, 2 \mathrm{H}), 7.56-7.52(\mathrm{~m}, 2 \mathrm{H}), 7.16(\mathrm{~d}, J=8.7 \mathrm{~Hz}, 1 \mathrm{H}), 7.10(\mathrm{~s}, 1 \mathrm{H})$, 6.87-6.82 (m, 2H), 6.12 (br, 1H), 5.00 (td, $J=9.2,1.4 \mathrm{~Hz}, 1 \mathrm{H}$ ), 4.17 (d, $J=9.2 \mathrm{~Hz}, 1 \mathrm{H}$ ), 4.08 (dd, $J$ $=12.4,9.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.91(\mathrm{dd}, J=12.4,1.4 \mathrm{~Hz}, 1 \mathrm{H}), 3.79(\mathrm{~s}, 3 \mathrm{H}), 3.74(\mathrm{~s}, 3 \mathrm{H}), 1.54-1.27(\mathrm{~m}, 12 \mathrm{H})$, $0.97(\mathrm{~s}, 3 \mathrm{H}), 0.68(\mathrm{~s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(\mathrm{CDCl}_{3}\right) \delta 153.94,150.79,146.23,132.16,129.26,127.27$, 126.58, 123.20, 113.01, 111.93, 110.18, 100.81, 82.00, 67.69, 61.95, 60.12, 55.92, 45.03, 40.33, 39.83, 34.61, 33.04, 32.42, 20.70, 20.18, 16.96; HRMS (FAB) m/z: calculated for $\mathrm{C}_{28} \mathrm{H}_{38} \mathrm{~N}_{3} \mathrm{O}_{5}[\mathrm{M}+$ $\mathrm{H}^{+}$: 496.2811, found 496.2811. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$ ): $t_{\mathrm{R}}=31.0 \mathrm{~min}$ (minor), 46.6 min (major).

(2S,3S)-3-(5-Methoxy-1H-indol-3-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethylpiperidin-1yloxy)propanol (syn-6, Table 2, entry 2).
${ }^{1} \mathrm{H}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 8.16(\mathrm{br}, 1 \mathrm{H}), 8.15-8.10(\mathrm{~m}, 2 \mathrm{H}), 7.55-7.50(\mathrm{~m}, 2 \mathrm{H}), 7.36$ (s, 1H), 7.25 (d, $J=$ $8.7 \mathrm{~Hz}, 1 \mathrm{H}$ ), 6.82 (dd, $J=8.7,2.3 \mathrm{~Hz}, 1 \mathrm{H}), 6.65(\mathrm{~d}, J=2.3 \mathrm{~Hz}, 1 \mathrm{H}), 5.77(\mathrm{br}, 1 \mathrm{H}), 5.01$ (ddd, $J=9.6$, $4.1,1.8 \mathrm{~Hz}, 1 \mathrm{H}$ ), $4.49(\mathrm{~d}, J=4.1 \mathrm{~Hz}, 1 \mathrm{H}), 3.94(\mathrm{dd}, J=12.4,9.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.77$ (dd, $J=12.4,1.8 \mathrm{~Hz}$, 1 H ), $3.72(\mathrm{~s}, 3 \mathrm{H}), 1.60-1.30(\mathrm{~m}, 6 \mathrm{H}), 1.25(\mathrm{~s}, 3 \mathrm{H}), 1.12(\mathrm{~s}, 3 \mathrm{H}), 1.12(\mathrm{~s}, 3 \mathrm{H}), 0.98(\mathrm{~s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 154.02,149.40,146.57,131.00,129.76,127.55,123.25,123.22,113.31,112.31,111.88$, 100.86, 82.78, 67.00, 62.07, 60.26, 55.78, 44.83, 40.52, 40.22, 34.60, 32.14, 20.74, 20.30, 16.93; HRMS (FAB) m/z: calculated for $\mathrm{C}_{27} \mathrm{H}_{36} \mathrm{~N}_{3} \mathrm{O}_{5}[\mathrm{M}+\mathrm{H}]^{+}: 482.2655$, found 482.2654. Enantiomeric excess was determined by HPLC analysis (Chiralpak AS-H, hexane/2-propanol 90:10, 1.0 mL $\min ^{-1}$ ): $t_{\mathrm{R}}=31.5 \mathrm{~min}$ (minor), 37.9 min (major).

(2R,3S)-3-(5-Methoxy-1H-indol-3-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethylpiperidin-1-

## yloxy)propanol (anti-4, Table 2, entry 2).

${ }^{1} \mathrm{H}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 8.18(\mathrm{br}, 1 \mathrm{H}), 8.14-8.10(\mathrm{~m}, 2 \mathrm{H}), 7.57-7.53(\mathrm{~m}, 2 \mathrm{H}), 7.27(\mathrm{~d}, J=1.8 \mathrm{~Hz}, 1 \mathrm{H})$, 7.23 (d, $J=9.2 \mathrm{~Hz}, 1 \mathrm{H}), 6.85-6.81(\mathrm{~m}, 2 \mathrm{H}), 6.21(\mathrm{br}, 1 \mathrm{H}), 5.04(\mathrm{td}, J=9.2,1.4 \mathrm{~Hz}, 1 \mathrm{H}), 4.20(\mathrm{~d}, J=$ $9.2 \mathrm{~Hz}, 1 \mathrm{H}), 4.09$ (dd, $J=11.9,9.2 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.92 (dd, $J=11.9,1.4 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.78 (s, 3H), 1.56-1.25 (m, 12H), 0.98 (s, 3H), $0.70(\mathrm{~s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 154.14,150.39,146.32,131.15,129.40$, 126.93, 123.18, 122.10, 114.89, 112.40, 112.00, 100.72, 81.89, 67.66, 62.01, 60.22, 55.85, 45.10, 40.34, 39.86, 34.55, 32.35, 20.72, 20.23, 16.93; HRMS (FAB) m/z: calculated for $\mathrm{C}_{27} \mathrm{H}_{36} \mathrm{~N}_{3} \mathrm{O}_{5}[\mathrm{M}+$ $\mathrm{H}^{+}$: 482.2655, found 482.2651. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$ ): $t_{\mathrm{R}}=36.0 \mathrm{~min}$ (minor), 42.4 min (major).

(2S,3S)-3-(1-Methyl-1H-indol-3-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethylpiperidin-1yloxy)propanol (syn-7, Table 2, entry 3).
${ }^{1} \mathrm{H}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 8.13-8.09(\mathrm{~m}, 2 \mathrm{H}), 7.54-7.50(\mathrm{~m}, 2 \mathrm{H}), 7.30(\mathrm{~d}, \mathrm{~J}=8.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.24-7.17(\mathrm{~m}$, $3 \mathrm{H}), 7.00(\mathrm{td}, J=7.6,0.9 \mathrm{~Hz}, 1 \mathrm{H}), 5.69(\mathrm{br}, 1 \mathrm{H}), 5.04-4.98(\mathrm{~m}, 1 \mathrm{H}), 4.56(\mathrm{~d}, \mathrm{~J}=3.6 \mathrm{~Hz}, 1 \mathrm{H})$, 3.93-3.75 (m, 2H), 3.82 (s, 3H), 1.60-1.31 (m, 6H), 1.27 (s, 3H), 1.15 (s, 3H), 1.10 (s, 3H), 1.02 (s, $3 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 149.54,146.56,136.65,129.80,127.50,127.22,123.20,121.94,119.14$, 118.87, 112.03, 109.28, 82.76, 66.93, 62.08, 60.27, 44.78, 40.51, 40.23, 34.61, 32.86, 32.09, 20.73, 20.31, 16.94; HRMS (FAB) m/z: calculated for $\mathrm{C}_{27} \mathrm{H}_{36} \mathrm{~N}_{3} \mathrm{O}_{4}[\mathrm{M}+\mathrm{H}]^{+}$: 466.2706, found 466.2707. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol 90:10, 1.0 $\mathrm{mL} \mathrm{min}{ }^{-1}$ ): $t_{\mathrm{R}}=10.9 \mathrm{~min}$ (minor), 15.7 min (major).

(2R,3S)-3-(1-Methyl-1H-indol-3-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethylpiperidin-1yloxy)propanol (anti-7, Table 2, entry 3).
${ }^{1} \mathrm{H}^{\mathrm{NMR}}\left(\mathrm{CDCl}_{3}\right) \delta 8.13-8.09(\mathrm{~m}, 2 \mathrm{H}), 7.57-7.53(\mathrm{~m}, 2 \mathrm{H}), 7.43(\mathrm{~d}, J=7.8 \mathrm{~Hz}, 1 \mathrm{H}), 7.27(\mathrm{~d}, J=8.2$ Hz, 1H), 7.20 (t, $J=8.2 \mathrm{~Hz}, 1 \mathrm{H}$ ), 7.14 (s, 1H), 7.05 (dd, $J=8.2,7.8 \mathrm{~Hz}, 1 \mathrm{H}$ ), 6.16 (br, 1H), 5.04 (td, $J=9.2,1.4 \mathrm{~Hz}, 1 \mathrm{H}), 4.25(\mathrm{~d}, J=9.2 \mathrm{~Hz}, 1 \mathrm{H}), 4.08(\mathrm{dd}, J=11.9,9.2 \mathrm{~Hz}, 1 \mathrm{H}), 3.90(\mathrm{dd}, J=11.9,1.4$ $\mathrm{Hz}, 1 \mathrm{H}), 3.78(\mathrm{~s}, 3 \mathrm{H}), 1.55-1.28(\mathrm{~m}, 12 \mathrm{H}), 0.98(\mathrm{~s}, 3 \mathrm{H}), 0.69(\mathrm{~s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(\mathrm{CDCl}_{3}\right) \delta 150.79$, 146.23, 136.73, 129.27, 126.89, 126.01, 123.21, 122.14, 119.36, 118.59, 113.57, 109.43, 82.06, 67.64, 62.06, 60.26, 45.04, 40.29, 39.80, 34.55, 32.86, 32.36, 20.69, 20.18, 16.93; HRMS (FAB) $\mathrm{m} / \mathrm{z}$ : calculated for $\mathrm{C}_{27} \mathrm{H}_{36} \mathrm{~N}_{3} \mathrm{O}_{4}[\mathrm{M}+\mathrm{H}]^{+}: 466.2706$, found 466.2699. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$ ): $t_{\mathrm{R}}=11.9 \mathrm{~min}$ (major), 13.6 min (minor).


3-(5-Methoxy-1-methyl-1H-indol-3-yl)-3-(3-nitrophenyl)-2-(2,2,6,6-tetramethylpiperidin-1yloxy)propanol [diastereomeric mixture (ca. 7:3)] (syn- and anti-8, Table 2, entry 4).
${ }^{1} \mathrm{H}$ NMR $\left(\mathrm{CDCl}_{3}\right) \delta 8.32(\mathrm{t}, J=2.1 \mathrm{~Hz}, 0.7 \mathrm{H}), 8.29(\mathrm{t}, J=2.1 \mathrm{~Hz}, 0.3 \mathrm{H}), 8.06(\mathrm{ddd}, J=8.2,2.1,0.9$ $\mathrm{Hz}, 0.7 \mathrm{H}$ ), 8.02 (ddd, $J=8.2,2.1,0.9 \mathrm{~Hz}, 0.3 \mathrm{H}), 7.70(\mathrm{dm}, J=8.2 \mathrm{~Hz}, 0.3 \mathrm{H}), 7.64(\mathrm{dm}, J=8.2 \mathrm{~Hz}$, $0.7 \mathrm{H}), 7.41(\mathrm{t}, \mathrm{J}=8.2 \mathrm{~Hz}, 1 \mathrm{H}), 7.21-7.13$ (m. 2H), 6.87-6.83 (m, 1.3H), 6.65 (d, $J=2.7 \mathrm{~Hz}, 0.7 \mathrm{H}$ ), 6.11 (br, 0.3H), 5.70 (br, 0.7H), 5.02-4.95 (m, 1H), 4.49 (d, $J=3.7 \mathrm{~Hz}, 0.7 \mathrm{H}$ ), 4.18 (d, $J=8.7 \mathrm{~Hz}$, 0.3 H ), 4.06 (dd, $J=12.4,9.6 \mathrm{~Hz}, 0.3 \mathrm{H}$ ), $3.93-3.85(\mathrm{~m}, 1 \mathrm{H}), 3.80-3.70(\mathrm{~m}, 6.7 \mathrm{H}), 1.53-1.25(\mathrm{~m}$, $9.9 \mathrm{H}), 1.15(\mathrm{~s}, 2.1 \mathrm{H}), 1.06(\mathrm{~s}, 2.1 \mathrm{H}), 1.04(\mathrm{~s}, 2.1 \mathrm{H}), 0.97(\mathrm{~s}, 0.9 \mathrm{H}), 0.69(\mathrm{~s}, 0.9 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\left(\mathrm{CDCl}_{3}\right)$ $\delta 153.93,153.80,147.99,147.93,144.88,144.00,135.07,134.76,132.18,132.08,128.83,128.68$, $127.92,127.86,127.23,126.69,123.94,123.55,121.62,121.26,113.21,111.99,111.86,111.47$, $110.19,110.09,100.97,100.73,82.62,81.82,67.73,67.00,62.03,61.90,60.21,60.13,55.94,55.86$, 44.78, 44.54, 40.58, 40.38, 40.29, 39.89, 34.64, 34.60, 33.06, 32.33, 32.07, 20.68, 20.60, 20.27, 20.08, 16.97; HRMS (FAB) $\mathrm{m} / \mathrm{z}$ : calculated for $\mathrm{C}_{28} \mathrm{H}_{38} \mathrm{~N}_{3} \mathrm{O}_{5}[\mathrm{M}+\mathrm{H}]^{+}$: 496.2811, found 496.2814. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol 90:10, 0.3 $m L \min ^{-1}$ ): $t_{\mathrm{R}}=58.7 \min (\mathrm{syn}, \operatorname{minor}), 60.9 \min (\mathrm{syn}, \operatorname{major}), 80.3 \mathrm{~min}($ anti, minor), $90.7 \min$ (anti, major).

(2S,3S)-3-(1-Methyl-1H-pyrrol-2-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethylpiperidin-1yloxy)propanol (syn-9, Table 2, entry 5).
${ }^{1} \mathrm{H}^{\mathrm{NMR}}\left(\mathrm{CDCl}_{3}\right) \delta 8.15-8.11(\mathrm{~m}, 2 \mathrm{H}), 7.38-7.34(\mathrm{~m}, 2 \mathrm{H}), 6.54(\mathrm{dd}, J=2.8,1.8 \mathrm{~Hz}, 1 \mathrm{H}), 6.36$ (dd, $J=3.6,1.8 \mathrm{~Hz}, 1 \mathrm{H}), 6.13(\mathrm{dd}, J=3.6,2.8 \mathrm{~Hz}, 1 \mathrm{H}), 5.63(\mathrm{br}, 1 \mathrm{H}), 4.91$ (ddd, $J=9.6,4.6,1.8 \mathrm{~Hz}$, 1 H ), 4.21 (d, $J=4.6 \mathrm{~Hz}, 1 \mathrm{H}), 3.79$ (dd, $J=12.4,9.6 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.69 (dd, $J=12.4,1.8 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.29 (s, $3 \mathrm{H}), 1.60-1.23(\mathrm{~m}, 9 \mathrm{H}), 1.17(\mathrm{~s}, 3 \mathrm{H}), 1.15(\mathrm{~s}, 3 \mathrm{H}), 0.97(\mathrm{~s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(\mathrm{CDCl}_{3}\right) \delta 147.63,146.82$, 129.84, 129.73, 123.50, 122.23, 107.98, 106.87, 82.53, 66.70, 62.07, 60.23, 45.39, 40.56, 40.25, 34.60, 34.02, 32.22, 20.64, 20.18, 16.96; HRMS (FAB) m/z: calculated for $\mathrm{C}_{23} \mathrm{H}_{34} \mathrm{~N}_{3} \mathrm{O}_{4}[\mathrm{M}+\mathrm{H}]^{+}$: 416.2549, found 416.2543. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$ ): $t_{\mathrm{R}}=11.4 \mathrm{~min}$ (major), 13.2 min (minor).

(2R,3S)-3-(1-Methyl-1H-pyrrol-2-yl)-3-(4-nitrophenyl)-2-(2,2,6,6-tetramethylpiperidin-1yloxy)propanol (anti-9, Table 2, entry 5).
${ }^{1} \mathrm{H}^{\mathrm{NMR}}\left(\mathrm{CDCl}_{3}\right) \delta=8.15-8.11(\mathrm{~m}, 2 \mathrm{H}), 7.41-7.37(\mathrm{~m}, 2 \mathrm{H}), 6.50(\mathrm{dd}, J=2.7,1.6 \mathrm{~Hz}, 1 \mathrm{H}), 6.31$ (dd, $J=3.7,1.6 \mathrm{~Hz}, 1 \mathrm{H}), 6.11$ (dd, $J=3.7,2.7 \mathrm{~Hz}, 1 \mathrm{H}), 6.00$ (br, 1H), 4.88 (td, $J=8.7,2.3 \mathrm{~Hz}, 1 \mathrm{H}), 4.02$ (dd, $J=11.9,8.7 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.98 (dd, $J=11.9,2.3 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.92 (d, $J=8.7 \mathrm{~Hz}, 1 \mathrm{H}$ ), 3.31 (s, 3H), $1.52-1.20(\mathrm{~m}, 12 \mathrm{H}), 0.94(\mathrm{~s}, 3 \mathrm{H}), 0.60(\mathrm{~s}, 3 \mathrm{H}) ;{ }^{13} \mathrm{C} \operatorname{NMR}\left(\mathrm{CDCl}_{3}\right) \delta=148.53,146.49,130.51$, $129.73,123.24,122.27,107.12,107.02,81.55,67.50,61.94,60.11,45.37,40.30,39.85,34.48,33.85$, 32.25, 20.80, 20.13, 16.93; HRMS (FAB) $m / z$ : calculated for $\mathrm{C}_{23} \mathrm{H}_{34} \mathrm{~N}_{3} \mathrm{O}_{4}[\mathrm{M}+\mathrm{H}]^{+}: 416.2549$, found 416.2543. Enantiomeric excess was determined by HPLC analysis (Chiralpak IA, hexane/2-propanol $90: 10,1.0 \mathrm{~mL} \mathrm{~min}^{-1}$ ): $t_{\mathrm{R}}=9.0 \mathrm{~min}$ (minor), 9.9 min (major).

## Determination of stereochemistry of products.



In the Friedel-Crafts-type alkylation with peptide catalyst $\mathbf{1}$ using the substrates shown in the above scheme, the absolute configuration of the major product can be assigned as the $S$ form (Tetrahedron Lett. 2009, 50, 5602-5604). The diastereomers (ca. 75:25) obtained after the next $\alpha$-oxyamination were reduced to the corresponding alcohols and separated from each other. The analyses by ${ }^{1} \mathrm{H}$ NMR and NOESY experiments were conducted to determine the relative configuration of the introduced oxyamino group.
With one isomer, a large ${ }^{3} J$ coupling constant ( 9.2 Hz ) between the protons shown below (with another isomer, ${ }^{3} J=3.6 \mathrm{~Hz}$ ) and the $\mathrm{H}, \mathrm{H}-\mathrm{NOEs}$ between the 4-nitrophenyl group and the tetramethylpiperidinyl moiety were observed. This indicates that this compound is the anti isomer, and the other one is the syn isomer.


Based on the mechanistic similarity of the reaction and in analogy with the NMR spectra of other products, the major configurations of all products were assigned as $(2 S, 3 S)$ or $(2 R, 3 S)$.

NOESY spectrum of anti-isomer.





















Chiralpak IA column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$


1: 220 nm .8 nm

| $1: 220 \mathrm{~nm}, 8 \mathrm{~nm}$ | retention time | area | area\% |  |
| ---: | ---: | ---: | ---: | ---: |
| 21.749 | 482659 | 98.12 |  |  |
| 30.338 | 42698576 |  |  |  |
| Total |  |  |  | 100.00 |

racemic sample


Chiralpak IA column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$


1: $220 \mathrm{~nm}, 8 \mathrm{~nm}$

| $1: 220 \mathrm{~nm}, 8 \mathrm{~nm}$ | area | area\% |  |
| ---: | ---: | ---: | ---: |
| retention time | 11.010 | 4241288 | 22.03 |
| 46.623 | 42253256 | 77.97 |  |
| Total |  |  |  |

racemic sample


Chiralpak AS-H column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$


1: $220 \mathrm{~nm}, 8 \mathrm{~nm}$

| $1: 220 \mathrm{~nm}, 8 \mathrm{~nm}$ | retention time | area | area\% |  |
| ---: | :---: | ---: | ---: | ---: |
| 31.529 | 227300 | 0.98 |  |  |
| 37.902 | 23042097 | 9.02 |  |  |
| Total |  |  |  | 100.00 |

racemic sample


Chiralpak IA column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$


1: 220 nm .8 nm

| $1: 220 \mathrm{~nm}, 8 \mathrm{~nm}$ | retention time | area | area\% |  |
| ---: | ---: | ---: | ---: | ---: |
| 36.042 | 3895937 | 13.42 |  |  |
| 42.368 | 25126043 | 86.58 |  |  |
| Total |  |  |  |  |
|  | 29021980 | 100.00 |  |  |

racemic sample


Chiralpak IA column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$


1: $220 \mathrm{~nm}, 8 \mathrm{~nm}$

| retention time | area | area\% |  |
| ---: | ---: | ---: | ---: |
| 10.884 | 397828 | 1.08 |  |
| 15.727 | 36566901 | 98.92 |  |
| Total |  |  |  |

racemic sample


Chiralpak IA column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$


1: $220 \mathrm{~nm}, 8 \mathrm{~nm}$

| $1: 220 \mathrm{~nm}, 8 \mathrm{~nm}$ | area | area\% |  |  |
| ---: | ---: | ---: | ---: | ---: |
| retention time | 11.941 | 16928427 | 77.71 |  |
| 13.557 | 4855259 | 22.29 |  |  |
| Total |  |  |  |  |
|  |  |  |  |  |

racemic sample


Chiralpak IA column, hexane/2-propanol 90:10, $0.3 \mathrm{~mL} \mathrm{~min}^{-1}$

1: $254 \mathrm{~nm}, 8 \mathrm{~nm}$

| retention time | area | area\% |
| :---: | :---: | :---: |
| 58.713 | 571523 | 0.85 |
| 60.914 | 46782757 | 69.59 |
| 80.281 | 3868661 | 5.76 |
| 90.715 | 15998827 | 23.80 |
| Total |  |  |
|  | 67221768 | 100.00 |

racemic sample


Chiralpak IA column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$


1: $220 \mathrm{~nm}, 8 \mathrm{~nm}$

| $1: 220 \mathrm{~nm}, 8 \mathrm{~nm}$ | area | area\% |  |
| ---: | ---: | ---: | ---: | ---: |
|  | 11.473 | 17303582 | 95.68 |
| 13.225 | 780891 | 4.32 |  |
| Total |  |  |  |

racemic sample


Chiralpak IA column, hexane/2-propanol 90:10, $1.0 \mathrm{~mL} \mathrm{~min}^{-1}$

racemic sample


