Iron-Catalyzed Asymmetric Olefin cis-Dihydroxylation with 97% Enantiomeric Excess

Ken Suzuki, Paul D. Oldenburg and Lawrence Que, Jr.

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Synthetic procedures and characterization of complexes
Bis(2-pyridylmethyl)-(R,R)-2,2-bipyrrolidine (BPBP)
Bis(2-quinolinylmethyl)-(R,R)-2,2-bipyrrolidine (BQBP)
Bis(6-methyl-2-pyridylmethyl)-(R,R)-2,2-bipyrrolidine (6-Me₂-BPBP)

2-aminomethylpyridine was obtained from Aldrich. 6-Methyl-2-aminomethylpyridine and quinolin-2-ylmethanamine were prepared according to literature procedures. Published procedure was then followed, using this aminomethylpyridine synthon, to form \( N,N \)-bis(2-pyridylmethyl)-(R,R)-4,5-diamino-1,7-octadiene, \( N,N \)-bis(2-quinolinylmethyl)-(R,R)-4,5-diamino-1,7-octadiene, and \( N,N \)-bis(6-methyl-2-pyridylmethyl)-(R,R)-4,5-diamino-1,7-octadiene, and the final bipyrrolidine ligand.

\[
\begin{align*}
[Fe^{II}](BPBP)(OTf)_2 \quad (1) \\
[Fe^{II}](BQBP)(OTf)_2 \quad (2) \\
[Fe^{II}](6-Me_2-BPBP)(OTf)_2 \quad (3)
\end{align*}
\]

Under a nitrogen atmosphere, a solution of either BPBP, BQBP, or 6-Me₂-BPBP (96.7 mg, 0.3 mmol) in dichloromethane (2 mL) was added to a suspension of Fe(OTf)₂•2MeCN (130.8 mg, 0.3 mmol) in dichloromethane (2 mL) at room temperature with stirring. The mixture was stirred overnight and the solvent removed \textit{in vacuo} to give a light brown powder, which was recrystallized from dichloromethane and ether to afford pale yellow crystals in 72% yield for 1, 60% yield for 2 and 75% yield for 3, which were suitable for X-ray crystallographic analysis. Characterization data for 1: Anal. Calcd. (found) for \( C_{22}H_{26}F_6FeN_4O_6S_2 \cdot H_2O: C, 38.05 \) (38.10); \( H, 4.06 \) (4.15); \( N, 8.07 \) (8.04); \( S, 9.23 \) (9.26). \( ^1H \) NMR (500 MHz, CD₂Cl₂, 25 °C): see Figure S1. Characterization data for 2: Anal. Calcd. (found) for \( C_{30}H_{30}F_6FeN_4O_6S_2 \cdot H_2O: C, 45.35 \) (45.41); \( H, 4.06 \) (4.02); \( N, 7.05 \) (6.95); \( S, 8.07 \) (7.96). \( ^1H \) NMR (500 MHz, CD₃CN, 25 °C): See Figure S1. Characterization data for 3: Anal. Calcd. (found) for \( C_{24}H_{30}F_6FeN_4O_6S_2 \cdot 0.5CH₂Cl₂: C, 39.40 \) (39.83); \( H, 4.18 \) (4.38); \( N, 7.50 \) (7.54); \( S, 8.59 \) (8.64). \( ^1H \) NMR (500 MHz, CD₃CN, 25 °C): see Figure S1.
Figure S1. \(^1\)H NMR of 1 in CD\(_2\)Cl\(_2\), of 2 in CD\(_2\)Cl\(_2\), and of 3 in CD\(_3\)CN.
X-ray crystallographic data

A crystal of 1 (approximate dimensions 0.45 x 0.11 x 0.10 mm³) was placed onto the tip of a 0.1 mm diameter glass capillary and mounted on a CCD area detector diffractometer for a data collection at 173(2) K. A preliminary set of cell constants was calculated from reflections harvested from three sets of 20 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced initial orientation matrices determined from 110 reflections. The data collection was carried out using MoKα radiation (graphite monochromator) with a frame time of 30 seconds and a detector distance of 4.9 cm. A randomly oriented region of reciprocal space was surveyed to the extent of one sphere and to a resolution of 0.77 Å. Four major sections of frames were collected with 0.30° steps in ω at four different φ settings and a detector position of -28° in 2θ. The intensity data were corrected for absorption and decay (SADABS). Final cell constants were calculated from 2414 strong reflections from the actual data collection after integration (SAINT). Please refer to Table S1 for additional crystal and refinement information.

The structure of 1 was solved using Bruker SHELXTL and refined using Bruker SHELXTL. The space group P2₁ was determined based on systematic absences and intensity statistics. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. The final full matrix least squares refinement converged to R₁ = 0.0438 and wR₂ = 0.1057 (F², all data).

A crystal of 2 (approximate dimensions 0.38 x 0.19 x 0.05 mm³) was placed onto the tip of a 0.1 mm diameter glass capillary and mounted on a CCD area detector diffractometer for a data collection at 173(2) K. A preliminary set of cell constants was calculated from reflections harvested from three sets of 20 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced initial orientation matrices determined from 144 reflections. The data collection was carried out using MoKα radiation (graphite monochromator) with a frame time of 30 seconds and a detector distance of 4.9 cm. A randomly oriented region of reciprocal space was surveyed to the extent of one sphere and to a resolution of 0.77 Å. Four major sections of frames were collected with 0.30° steps in ω at four different φ settings and a detector position of -28° in 2θ. The intensity data were corrected for absorption and decay (SADABS). Final cell constants were calculated from 2565 strong reflections from the actual data collection after integration (SAINT). Please refer to Table S2 for additional crystal and refinement information.

The structure of 2 was solved using Bruker SHELXTL and refined using Bruker SHELXTL. The space group P2₁ was determined based on systematic absences and intensity statistics. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. The final full matrix least squares refinement converged to R₁ = 0.0457 and wR₂ = 0.1261 (F², all data).
A crystal of 3 (approximate dimensions 0.35 x 0.17 x 0.12 mm³) was placed onto the tip of a 0.1 mm diameter glass capillary and mounted on a CCD area detector diffractometer for a data collection at 173(2) K. A preliminary set of cell constants was calculated from reflections harvested from three sets of 20 frames. These initial sets of frames were oriented such that orthogonal wedges of reciprocal space were surveyed. This produced initial orientation matrices determined from 268 reflections. The data collection was carried out using MoKα radiation (graphite monochromator) with a frame time of 20 seconds and a detector distance of 4.9 cm. A randomly oriented region of reciprocal space was surveyed to the extent of one sphere and to a resolution of 0.77 Å. Four major sections of frames were collected with 0.30º steps in ω at four different φ settings and a detector position of -28º in 2θ. The intensity data were corrected for absorption and decay (SADABS). Final cell constants were calculated from 2816 strong reflections from the actual data collection after integration (SAINT). Please refer to Table S3 for additional crystal and refinement information.

The structure of 3 was solved using Bruker SHELXTL and refined using Bruker SHELXTL. The space group P2₁2₁2₁ was determined based on systematic absences and intensity statistics. A direct-methods solution was calculated which provided most non-hydrogen atoms from the E-map. Full-matrix least squares / difference Fourier cycles were performed which located the remaining non-hydrogen atoms. All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were placed in ideal positions and refined as riding atoms with relative isotropic displacement parameters. The final full matrix least squares refinement converged to $R_1 = 0.0297$ and $wR_2 = 0.0610$ ($F^2$, all data).
**Table S1.** Crystal data and structure refinement for I.

<table>
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<th>Property</th>
<th>Value</th>
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<td>Identification code</td>
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<td>Empirical formula</td>
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<tr>
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<tr>
<td>Wavelength</td>
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</tr>
<tr>
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<tr>
<td>Space group</td>
<td>P(_{2}_1)</td>
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<td>Unit cell dimensions</td>
<td>(a = 9.1835(9) \text{ Å} \quad \alpha = 90^\circ)</td>
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<tr>
<td></td>
<td>(b = 28.648(3) \text{ Å} \quad \beta = 90.950(2)^\circ)</td>
</tr>
<tr>
<td></td>
<td>(c = 10.6141(10) \text{ Å} \quad \gamma = 90^\circ)</td>
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<tr>
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<td>Z</td>
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<tr>
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<tr>
<td>Observed reflections</td>
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**Table S2.** Crystal data and structure refinement for 2.

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<td>173(2) K</td>
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<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
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<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
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<tr>
<td>Space group</td>
<td>P&lt;sub&gt;2&lt;/sub&gt;&lt;sub&gt;1&lt;/sub&gt;</td>
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<td>Z</td>
<td>2</td>
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<td>Density (calculated)</td>
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<td>Absorption coefficient</td>
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<td>Observed reflections</td>
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<td>Max. and min. transmission</td>
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<td>Absolute structure parameter</td>
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<td>0.750 and -0.599 e.Å&lt;sup&gt;-3&lt;/sup&gt;</td>
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Table S3. Crystal data and structure refinement for 3.

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<td>c = 17.6780(19) Å, γ = 90°</td>
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<td>Density (calculated)</td>
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<td>Refinement method</td>
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<td>Data / restraints / parameters</td>
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<td>Final R indices [I&gt;2sigma(I)]</td>
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<td>R indices (all data)</td>
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<td>Absolute structure parameter</td>
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<td>Largest diff. peak and hole</td>
<td>0.426 and -0.358 e.Å⁻³</td>
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</table>
Materials, physical measurements, and catalytic procedures

Materials: All reagents were purchased from Aldrich and used as received unless noted otherwise. Purifications of olefin substrates were completed by passing them through neutral alumina oxide. Prior to their use as solvents, both CH$_3$CN and CH$_2$Cl$_2$ were distilled from CaH$_2$ under an argon atmosphere. All other chemicals were utilized without further purification.

Physical measurements: $^1$H NMR spectra were recorded on a Varian Unity 500 MHz spectrometer at ambient temperature. Chemical shifts (ppm) were referenced to the residual protic solvent peaks. Elemental analyses were performed by Atlantic Microlab (Norcross, GA). Oxidation product analyses were performed on a PerkinElmer AutoSystem gas chromatograph (AT-1701 column, 30 m) with flame-ionization detection. The ee analysis of diol product was performed on a PerkinElmer AutoSystem XL gas chromatograph (Chiraldex G-TA column, 30 m) with flame-ionization detection. GC mass spectral analyses were performed on an HP 6890 gas chromatograph (HP-5 column, 30 m) with an Agilent 5973 mass detector. A 4% NH$_3$/CH$_4$ mixture was used as the ionization gas for chemical ionization analyses.

Substrate oxidation studies for 3: Solutions of H$_2$O$_2$ (diluted from 35% H$_2$O$_2$ solution with CH$_3$CN resulting in a 70 mM concentration) and catalyst/substrate in CH$_3$CN were separately degassed via three freeze, pump, thaw cycles and held under an Ar atmosphere. Following this degassing procedure, 10 equiv of H$_2$O$_2$ were delivered by syringe pump over a period of 20 min at 25 °C to the vigorously stirred CH$_3$CN solution containing iron catalyst and 1000 equiv olefin substrate. The final concentrations were 0.7 mM iron catalyst, 7.0 mM H$_2$O$_2$, and 0.35 M olefin. The solution was stirred for an additional 5 min after syringe pump addition, after which organic products were esterified by 1 mL acetic anhydride together with 0.1 mL 1-methylimidazole and extracted with CHCl$_3$. An internal standard (naphthalene) was added and the solution was washed with 1 M H$_2$SO$_4$, sat. NaHCO$_3$, and H$_2$O. The organic layer was dried with MgSO$_4$ or Na$_2$SO$_4$ and subjected to GC analysis. Products were identified by comparison of their GC retention times and GC/MS with those of authentic compounds. The reported results are the average of at least three trials.

References