Synthesis and Application of Planar-Chiral Phosphaferrocene–Oxazolines, a New Class of P,N–Ligands

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Supporting Information

I. General

All oxygen- and moisture-sensitive manipulations were carried out with standard Schlenk techniques under argon or in a glovebox under nitrogen. THF was purified through a neutral alumina column under argon prior to use. Dichloromethane was either distilled from CaH_2 under nitrogen or purified through a neutral alumina column under argon prior to use. 1′,2′,3,3′,4,4′,5′-Heptamethylphosphaferrocene (**3**) was prepared by a reported method.[1] Triethylamine was purchased from EM Science and distilled from KOH under argon prior to use. Trifluoroacetic anhydride (Avocado Research Chemicals), dimethyl malonate (Avocado Research Chemicals), boron trifluoride diethyl etherate (Aldrich), methanesulfonyl chloride (Aldrich), 4-dimethylaminopyridine (Aldrich), *N*,*O*-bis(trimethylsilyl)acetamide (Aldrich), (*S*)-*tert*-leucinol (Aldrich), *n*-BuLi (Alfa Aesar), (*S*)-valinol (Fluka), and $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (Strem Chemicals) were used without further purification. All other chemicals and solvents were purchased from either Mallinckrodt or J. T. Baker and used as received.

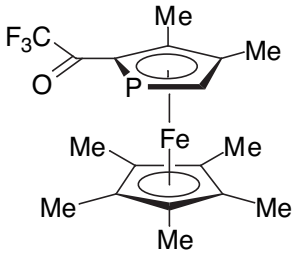
The progress of reactions was monitored by analytical TLC using 0.25 mm EM

Science F-254 silica gel glass plates. Flash chromatography was performed on silica gel (230-400 mesh) purchased from SiliCycle, Inc.

^{1}H and ^{19}F NMR spectra were recorded on a Varian Mercury 300 spectrometer (^{1}H, 300 MHz; ^{19}F, 282 MHz) at ambient temperature. ^{13}C and ^{31}P NMR spectra were obtained with complete proton decoupling on a Varian Mercury 300 spectrometer (^{13}C, 75 MHz; ^{31}P, 121 MHz) at ambient temperature. ^{19}F NMR chemical shifts are referenced to external trifluoroacetic anhydride at –78 ppm, and ^{31}P NMR chemical shifts are referenced to external 85% H_3PO_4.

Analytical HPLC was performed on a Daicel Chiralcel AD column (4.6 mm x 25 cm). Infrared spectra were recorded on a Perkin Elmer 1600 FT-IR spectrometer. Optical rotations were measured on a Perkin Elmer Model 241 polarimeter. Melting points were measured on a Thomas Hoover capillary melting point apparatus and are uncorrected.

II. Synthesis of Planar-Chiral Phosphaferrocene–Oxazolines

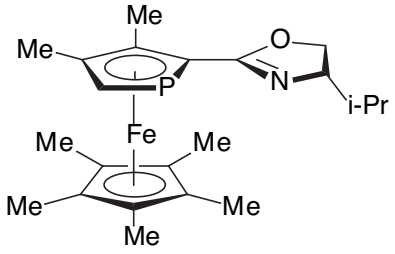


(±)-**4**

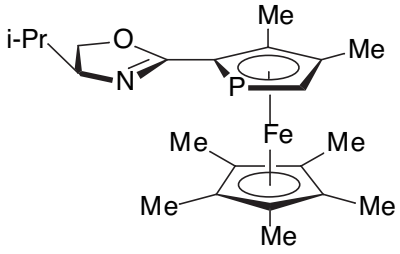
Trifluoroacetic anhydride (483 μL, 3.42 mmol) and boron trifluoride diethyl etherate (433 μL, 3.42 mmol) were added by syringe to a stirred, 0 °C solution of 1′,2′,3,3′,4,4′,5′-heptamethylphosphaferrocene (**3**; 516 mg, 1.71 mmol) in CH_2Cl_2 (10 mL). The mixture was stirred at rt for 1.5 h, furnishing a deep-purple solution, which was directly

chromatographed on silica gel (eluant: Et_2O) to give a dark-purple solid (637 mg, 1.60 mmol, 94%).

^{1}H NMR (CD_2Cl_2): δ 3.95 (d, $^2J_{PH}$ = 38.1 Hz, 1H), 2.22 (s, 3H), 2.06 (s, 3H), 1.67 (s, 15H). ^{13}C NMR (CD_2Cl_2): δ 189.6 (qd, $^2J_{CF}$ = 33.0 Hz and $^2J_{CP}$ = 23.7 Hz), 117.1 (q, $^1J_{CF}$ = 293.3 Hz), 102.1 (d, $^2J_{CP}$ = 8.0 Hz), 96.2 (d, $^2J_{CP}$ = 5.2 Hz), 88.7 (dq, $^1J_{CP}$ = 56.5 Hz and $^3J_{CF}$ = 4.0 Hz), 85.4 (s), 79.4 (d, $^1J_{CP}$ = 69.1 Hz), 14.5 (s), 12.9 (d, $^3J_{CP}$ = 0.8 Hz), 10.3 (s). ^{19}F NMR (CD_2Cl_2): δ –72.4 (d, $^4J_{PF}$ = 61.3 Hz). ^{31}P{^{1}H} NMR (CD_2Cl_2): δ –40.7 (q, $^4J_{PF}$ = 61.1 Hz). FTIR (neat) 2981, 2910, 1661, 1479, 1377, 1355, 1273, 1194, 1153, 1090, 1030 cm^{-1}. mp 117-119 °C.



6a



6b

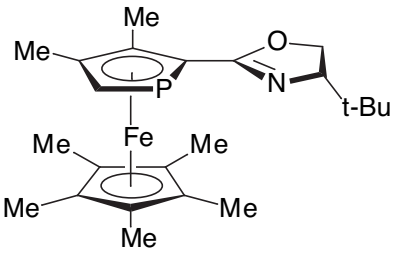
n-BuLi (1.71 M solution in hexane; 1.24 mL, 2.11 mmol) was added to a solution of (*S*)-valinol (109 mg, 1.05 mmol) in THF (3.0 mL) at –70 °C. The reaction mixture was stirred at rt for 2 h, resulting in a pale-yellow solution that contained a white precipitate. This mixture was cooled to –70 °C, and a solution of (±)-**4** (106 mg, 0.265 mmol) in THF (3.0 mL) was added. After stirring at 60 °C for 8 h, the solvent was removed under vacuum, and the residue was passed through a plug of silica gel (eluant: Et_2O) to give a viscous orange oil (**5**; 92.3 mg, 0.214 mmol) that was cyclized without further purification.

Methanesulfonyl chloride (33 μL, 0.43 mmol) was added to a –70 °C mixture of **5** (92.3 mg, 0.214 mmol), 4-dimethylaminopyridine (2.2 mg, 0.018 mmol), and Et_3N (60

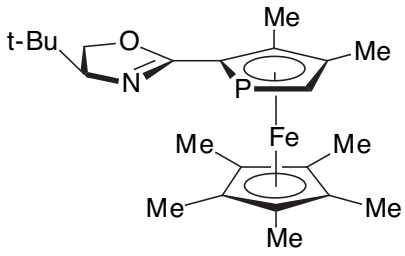
μL, 0.43 mmol) in CH_2Cl_2 (3.0 mL). The solution was stirred for 30 min at 0 °C and then warmed to rt. Additional Et_3N (150 μL, 1.08 mmol) was added, and the reaction mixture was stirred at rt for 23 h. The solvent was then removed, and the residue was chromatographed on silica gel (eluant: Et_2O/hexane = 1/6). The first fraction (R_f = 0.5, Et_2O/hexane = 1/6) gave 30.9 mg of an orange solid (**6a**; 0.075 mmol, 28%), and the second fraction (R_f = 0.45, Et_2O/hexane = 1/6) gave 25.9 mg of an orange solid (**6b**; 0.063 mmol, 24%).

6a: ^{1}H NMR (CD_2Cl_2): δ 4.21-4.13 (m, 1H), 3.86-3.78 (m, 2H), 3.46 (d, $^2J_{PH}$ = 36.8 Hz, 1H), 2.25 (s, 3H), 2.02 (s, 3H), 1.73 (s, 15H), 1.81-1.59 (m, 1H), 0.99 (d, $^3J_{HH}$ = 6.9 Hz, 3H), 0.85 (d, $^3J_{HH}$ = 6.9 Hz, 3H). ^{13}C NMR (CD_2Cl_2): δ 166.5 (d, $^2J_{CP}$ = 18.3 Hz), 97.8 (d, $^2J_{CP}$ = 7.8 Hz), 92.2 (d, $^2J_{CP}$ = 4.8 Hz), 83.8 (d, $^1J_{CP}$ = 55.5 Hz), 83.8 (s), 80.3 (d, $^1J_{CP}$ = 56.0 Hz), 73.8 (d, J = 1.7 Hz), 69.1 (s), 33.9 (s), 19.6 (s), 18.8 (s), 14.6 (s), 12.7 (s), 10.4 (d, J = 1.3 Hz). ^{31}P{^{1}H} NMR (CD_2Cl_2): δ –53.3 (s). FTIR (neat) 2955, 2904, 1630, 1459, 1376, 1027 cm^{-1}. mp 63-65 °C. $[\alpha]^{20}_D$ +69.6 (*c* 0.73, THF).

6b: ^{1}H NMR (CD_2Cl_2): δ 4.23 (dd, $^3J_{HH}$ = 9.3 and 8.1 Hz, 1H), 3.81 (t, $^3J_{HH}$ = 8.6 Hz, 1H), 3.70 (q, $^3J_{HH}$ = 9.0 Hz, 1H), 3.45 (d, $^2J_{PH}$ = 36.6 Hz, 1H), 2.25 (s, 3H), 2.03 (s, 3H), 1.74 (s, 15H), 1.69-1.59 (m, 1H), 1.09 (d, $^3J_{HH}$ = 6.6 Hz, 3H), 0.89 (d, $^3J_{HH}$ = 6.6 Hz, 3H). ^{13}C NMR (CD_2Cl_2): δ 166.7 (d, $^2J_{CP}$ = 18.5 Hz), 97.7 (d, $^2J_{CP}$ = 7.8 Hz), 92.0 (d, $^2J_{CP}$ = 5.0 Hz), 83.8 (d, $^1J_{CP}$ = 55.5 Hz), 83.7 (s), 80.7 (d, $^1J_{CP}$ = 55.8 Hz), 74.4 (d, $^2J_{CP}$ = 1.6 Hz), 70.0 (s), 34.9 (s), 20.3 (s), 19.6 (s), 14.5 (s), 12.7 (s), 10.5 (d, J = 1.2 Hz). ^{31}P{^{1}H} NMR (CD_2Cl_2): δ –52.5 (s). FTIR (neat) 2951, 2903, 1633, 1466, 1412, 1376, 1268, 1042, 1010 cm^{-1}. mp 146-148 °C (dec). $[\alpha]^{20}_D$ –167.3 (*c* 0.88, THF).



7a



7b

The same experimental procedure was followed. First fraction (R_f = 0.6, Et_2O/hexane = 1/6; **7a**): orange solid, 26%. Second fraction (R_f = 0.4, Et_2O/hexane = 1/6, **7b**): orange solid, 24%.

7a: ^{1}H NMR (CD_2Cl_2): δ 4.08 (dd, $^3J_{HH}$ = 9.8 and 8.1 Hz, 1H), 3.95-3.83 (m, 2H), 3.45 (d, $^2J_{PH}$ = 36.5 Hz, 1H), 2.28 (s, 3H), 2.02 (s, 3H), 1.73 (s, 15H), 0.87 (s, 9H). ^{13}C NMR (CD_2Cl_2): δ 166.2 (d, $^2J_{CP}$ = 18.5 Hz), 97.7 (d, $^2J_{CP}$ = 7.6 Hz), 92.6 (d, $^2J_{CP}$ = 4.8 Hz), 83.8 (s), 83.7 (d, $^1J_{CP}$ = 55.6 Hz), 80.3 (d, $^1J_{CP}$ = 56.1 Hz), 77.4 (d, J = 1.7 Hz), 67.2 (s), 34.2 (s), 26.2 (s), 14.6 (s), 12.7 (s), 10.5 (d, J = 1.2 Hz). ^{31}P{^{1}H} NMR (CD_2Cl_2): δ –54.1 (s). FTIR (neat) 2948, 2900, 1628, 1476, 1373, 1289, 1021, 966 cm^{-1}. mp 107-109 °C (dec). $[\alpha]^{20}_D$ +125.3 (*c* 0.96, THF).

7b: ^{1}H NMR (CD_2Cl_2): δ 4.16 (dd, $^3J_{HH}$ = 9.8 and 8.1 Hz, 1H), 3.89 (dd, $^3J_{HH}$ = 9.9 and 8.2 Hz, 1H), 3.78 (dd, $^3J_{HH}$ = 9.9 and 8.8 Hz, 1H), 3.42 (d, $^2J_{PH}$ = 36.5 Hz, 1H), 2.21 (s, 3H), 2.03 (s, 3H), 1.75 (s, 15H), 0.93 (s, 9H). ^{13}C NMR (CD_2Cl_2): δ 167.0 (d, $^2J_{CP}$ = 18.5 Hz), 97.5 (d, $^2J_{CP}$ = 7.4 Hz), 91.5 (d, $^2J_{CP}$ = 5.0 Hz), 83.8 (s), 83.6 (d, $^1J_{CP}$ = 55.8 Hz), 81.9 (d, $^1J_{CP}$ = 55.9 Hz), 77.4 (s), 67.7 (s), 33.9 (s), 26.7 (s), 14.5 (s), 12.8 (s), 10.7 (d, J = 1.2 Hz). ^{31}P{^{1}H} NMR (CD_2Cl_2): δ –51.9 (s). FTIR (neat) 2948, 2902, 1627, 1474, 1414, 1376, 1291, 1115, 1020, 967 cm^{-1}. mp 128-130 °C (dec). $[\alpha]^{20}_D$ –164.9 (*c* 0.87, THF).

III. Allylic Alkylations

General procedure. A mixture of $[(\eta^3\text{-}C_3H_5)PdCl]_2$ (1.0 mg, 2.7 μmol) and ligand (2.9 mg, 6.8 μmol) in CH_2Cl_2 (0.3 mL) was stirred at 55 °C for 1 h, and then 1,3-diphenylallyl acetate (27.6 mg 0.109 mmol) in CH_2Cl_2 (1.0 mL), dimethyl malonate (37.5 μL, 0.328 mmol), *N,O*-bis(trimethylsilyl)acetamide (81 μL, 0.33 mmol), and KOAc (0.5 mg, 5 μmol) were added. After stirring at rt for 4.5-26 h, the reaction mixture was directly chromatographed on silica gel (eluant: Et_2O/hexane = 1/2) to furnish the product,[2] a colorless oil. The enantiomeric excess of the product was determined on a Daicel Chiralcel AD column (hexanes/isopropanol = 95/5; flow = 1 mL/min; retention times: 15.2 min (*R*), 22.0 min (*S*)).

IV. X-ray Crystal Structure of 7b

Crystals suitable for X-ray structural analysis were obtained by slow evaporation of a pentane solution of **7b** at room temperature.

An orange block of dimensions 0.12 x 0.12 x 0.10 mm^3 was mounted under STP and transferred to a Bruker/AXS CCD three-circle diffractometer (χ fixed at 54.78°) equipped with a cold stream of N_2 gas. An initial unit cell was determined by harvesting reflections $I > 20\ \sigma(I)$ from 45 x 10-s frames of 0.30° ω scan data with monochromated Mo K_α radiation (λ = 0.71073 Å). The cell thus determined was monoclinic.

A hemisphere of data was then collected using ω scans of 0.30° and 30-s frames. The raw data frames were integrated using the Siemens program SAINT.[3] An initial background was determined from the first 12° of data. Actual integration was performed with constant spot sizes of 1.6° in the detector plane and 0.6° in ω.

Backgrounds were then calculated as a continuing average over 8 frames of data. The data that were collected (4470 total reflections, 2567 unique, R_{int} = 0.0616) had the following Miller index ranges: -7 to 7 in h, -13 to 11 in k, and -13 to 15 in l. The data were corrected for Lorentz and polarization effects. A semi-empirical absorption correction from psi-scans was also applied, maximum and minimum transmission: 0.9936 and 0.6645, respectively.

All aspects of the solution and refinement were handled by SHELXTL version 5.0.[4] The structure was solved by direct methods in the chiral monoclinic space group $P2_1$, a = 6.9916(10) Å; b = 11.8187(17) Å; c = 13.498(2) Å; β = 95.408(2)°, and refined using standard difference Fourier techniques. Final, full-matrix least-squares refinement (2567 data for 245 parameters) on F^2 yielded residuals of R_1 and wR_2[5] of 0.0442 and 0.1158, respectively, for data $I > 2\sigma(I)$, and 0.0462 and 0.1173, respectively, for all data. During the final refinement all nonhydrogen atoms were treated anisotropically. Hydrogen atoms were included in calculated positions, d_{C-H} = 0.96 Å, and refined isotropically on a riding model. Residual electron density amounted to a maximum of 0.543 e $Å^{-3}$ and a minimum of -0.331 e $Å^{-3}$.

The absolute structure (Flack) parameter for the correct enantiomer is 0.00(2). The structure was also inverted and refined to confirm the initial assignment of absolute stereochemistry.

Tables 1-6 provide the full crystallographic data for the X-ray structure.

References

(1) Garrett, C. E.; Fu, G. C. *J. Org. Chem.* **1997**, *62*, 4534-4535.

(2) Leutenegger, U.; Umbricht, G.; Fahrni, C.; von Matt, P.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143-2156.

(3) SAINT: Siemens Industrial Automation, Inc. Analytical Instumentation, SAINT Version 4 Software Reference Manual, 1995.

(4) SHELXTL: Sheldrick, G. M., and Siemens Industrial Automation, Inc. Analytical Instrumentation, SHELTXL Version 5 Reference Manual, 1994.

(5) Equations:

$$R_1 = \Sigma \, | \, |F_o| - |F_c| \, | \, / \Sigma |F_o|$$

$$wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]]^{1/2}$$

$$w = 1 / [\sigma^2(F_o)^2 + (0.0809 * P)^2 + 0.4088 * P]$$

$$\text{where } P = [\text{Max}(F_o^2, 0) + 2 * F_c^2] / 3$$