Exploring the utility of a new chiral phosphoramidite *P,N*-ligand derived from (*R*)-BINOL and 7-azaindole in asymmetric catalysis[1]

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Abstract: Lithiation of 7-azaindole, followed by quenching with [(*R*)-(1,1′-binaphthalene-2,2′-diyl)]chlorophosphite afforded the new chiral phosphoramidite **1** in 92% isolated yield. Treatment of 0.5 equiv. of $[(COD)MCl]_2$ (M = Rh, Ir; COD = η^4-1,5-cyclooctadiene) with 2 equiv. of **1** afforded the corresponding [(κ^1-*P,N*-**1**)(κ^2-*P,N*-**1**)MCl] complexes in 68% (**2a**, Rh) and 72% (**2b**, Ir) yield, while treatment of $(PPh_3)_3RhCl$ with 1 equiv. of **1** afforded [(PPh_3)(κ^2-*P,N*-**1**)RhCl] (**3**) as an analytically pure solid in 74% isolated yield. In examining the reaction of **1** with a mixture of 0.5 equiv. of $[(COD)RhCl]_2$ and 1 equiv. of $AgBF_4$, an inseparable mixture of $[(\kappa^2\text{-}P,N\text{-}\mathbf{1})_2Rh]^+BF_4^-$ (**4a**) and [(COD)(κ^2-*P,N*-**1**)Rh]$^+BF_4^-$ (**5a**) was generated. Under analogous conditions employing $[(COD)IrCl]_2$, the complex [(COD)(κ^2-*P,N*-**1**)Ir]$^+BF_4^-$ (**5b**) was obtained in 86% isolated yield. Treatment of 0.5 equiv. of $[(\eta^3\text{-allyl})PdCl]_2$ with **1** afforded [(η^3-allyl)(κ^2-*P,N*-**1**)Pd]$^+Cl^-$ (**6**) in 86% isolated yield. The application of **1** in platinum group metal-mediated asymmetric chemical transformations, including alkene hydrogenation and hydroboration, ketone hydrosilylation, and allylic alkylation, was examined.

Key words: chiral, ligand, phosphoramidite, asymmetric catalysis.

Résumé : La lithiation du 7-azaindole, suivie d'un piégeage avec du chlorophosphite de [(*R*)-(1,1′-binaphtalène-2,2′-diyle) conduit à la formation du nouveau phospharamidite chiral, **1**, avec un rendement de 92% en produit isolé. Le traitement de 0,5 équiv. de $[(COD)MCl]_2$ (M= Rh, Ir; COD = η^4-cycloocta-1,5-diène) avec deux équiv. de **1** conduit à la formation des complexes correspondants [κ^1-*P,N*-**1**)(κ^2-*P,N*-**1**)MCl avec des rendements de 68% (**2a**, Rh) et de 72% (**2b**, Ir) alors que le traitement de $(PPh_3)_3RhCl$ avec 1 équiv. de **1** conduit à la formation du [(PPh_3)(κ^2-*P,N*-**1**)(RhCl] (**3**) qui a été isolé avec un rendement de 74% sous la forme d'un solide analytiquement pur. La réaction du produit **1** avec un mélange de 0,5 équiv. de $[(COD)RhCl]_2$ et un équiv. de $AgBF_4$ conduit à un mélange inextricable de $[(\kappa^2\text{-}P,N\text{-}\mathbf{1})_2Rh]^+BF_4^-$ et de [(COD)(κ^2-*P,N*-**1**)Rh]$^+BF_4^-$ (**5a**); dans des conditions impliquant l'utilisation du $[(COD)IrCl]_2$, on obtient le complexe [(COD)(κ^2-*P,N*-**1**)Ir]$^+BF_4^-$ (**5b**) avec un rendement isolé de 86%. Le traitement de 0,5 équiv. de $[(\eta^3\text{-allyl})PdCl]_2$ avec le produit **1** conduit à la formation du produit [(η^3-allyl)(κ^2-*P,N*-**1**)Pd]$^+Cl^-$ (**6**) avec un rendement d 86% en produit isolé. On a examiné l'application du composé **1** dans les transformations chimiques asymétriques catalysées par un métal du groupe du platine, y compris les réactions d'hydrogénation et d'hydroboration des alcènes, d'hydrosilylation de cétones et d'alkylation allylique.

Mots-clés : chiral, ligand, phosphoramidite, catalyse asymétrique.

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Introduction

Transition metal-catalyzed asymmetric synthesis represents one of the most effective approaches for the preparation of chiral non-racemic molecules on both benchtop and industrial scales (1). Platinum-group metal (PGM) complexes supported by chiral, heterobidentate *P,N*-ligands have proven particularly effective in mediating important transformations of this type, including the asymmetric addition of E–H bonds to unsaturated substrates (E = H, B, Si, etc.) and the enantioselective formation of C–C linkages (2). As a result, the pursuit of chiral *P,N*-ligands that can enable new and (or) improved asymmetric substrate transformations represents an important theme of modern catalysis research.

One facet of our research program focuses on the development of novel *P,N*-ligands for use in metal-mediated catalytic applications (3). In building upon this theme and encouraged by the utility of monodentate phosphoramidite (MonoPhos) ligands (4) as well as rigid κ^2-*P,N* phosphinooxazoline (PHOX) ligands (5) in PGM catalysis, we identified potentially bidentate chiral phosphoramidite ligands derived from 7-azaindole as attractive and readily prepared synthetic targets. Notably, while two reports by Woolins and

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We dedicate this article to Professor Richard Puddephatt, in recognition of his widespread contributions to chemical research in Canada.

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co-workers (6) and Burrows et al. (7) document the PGM coordination chemistry of achiral κ^2-*P*,*N*-(7-aza-*N*-indolyl)phosphines, the preparation and application in asymmetric catalysis of chiral variants of such ligands has not been reported. Herein we report on the synthesis and characterization of a new chiral phosphoramidite ligand **1**, a preliminary account of the Rh, Ir, and Pd coordination chemistry of this ligand, and the application of **1** in PGM-mediated asymmetric chemical transformations including alkene hydrogenation and hydroboration, ketone hydrosilylation, and allylic alkylation.

Experimental

General Considerations

All manipulations were conducted in the absence of oxygen and water under an atmosphere of dinitrogen, either by use of standard Schlenk methods or within an mBraun glovebox apparatus, utilizing glassware that was oven-dried (130 °C) and evacuated while hot prior to use. Celite was oven-dried for 5 d and then evacuated for 24 h prior to use. The non-deuterated solvents tetrahydrofuran, diethyl ether, benzene, toluene, hexanes, and pentane were deoxygenated and dried by sparging with dinitrogen gas, followed by passage through a double-column solvent purification system purchased from mBraun Inc. Tetrahydrofuran and diethyl ether were purified over two alumina-packed columns, while benzene, toluene, hexanes, and pentane were purified over one alumina-packed column and one column packed with copper-Q5 reactant. All solvents used within the glovebox were stored over activated 4 Å molecular sieves. CD_2Cl_2 (Cambridge Isotopes) was degassed by using three repeated freeze–pump–thaw cycles, dried over CaH_2 for 7 days, distilled in vacuo, and stored over 4 Å molecular sieves for 24 h prior to use. C_6D_6 (Cambridge Isotopes) was degassed by using three repeated freeze–pump–thaw cycles and then dried over 4 Å molecular sieves for 24 h prior to use; styrene (Sigma-Aldrich, containing 10–15 ppm 4-*tert*-butylcatechol as inhibitor) was degassed in a similar manner, but was not stored over molecular sieves. Ph_2SiH_2 (Gelest, shipped under argon) was not degassed and was dried over 4 Å molecular sieves for 24 h prior to use. Hydrogen (99.999%, UHP Grade) gas was obtained from Air Liquide and was used as received. [(*R*)-(1,1′-binaphthalene-2,2′-diyl)]chlorophosphite (8) and (±)-(*E*)-1,3-diphenylprop-2-enyl acetate (9) were prepared by the use of literature procedures, while the transition metal reagents and silver salts were purchased from Strem Chemicals Inc. All purchased and prepared solid reagents were dried in vacuo for 24 h prior to use. Otherwise, all other commercial reagents were obtained from Sigma-Aldrich or Fluka and were used as received. ^{1}H, ^{13}C, and ^{31}P NMR characterization data were collected at 300 K on a Bruker AV-500 spectrometer operating at 500.1, 125.8, and 202.5 MHz (respectively) with chemical shifts reported in parts per million downfield of $SiMe_4$ (for ^{1}H and ^{13}C) or 85% H_3PO_4 in D_2O (for ^{31}P). ^{1}H and ^{13}C NMR chemical shift assignments are made on the basis of data obtained from ^{13}C-DEPT, ^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC, and ^{1}H-^{13}C HMBC NMR experiments. In some cases, fewer than expected unique ^{13}C NMR resonances were observed, despite prolonged acquisition times. Elemental analyses were performed by Canadian Microanalytical Service Ltd., Delta, British Columbia, Canada.

Synthesis of 1

A 1.6 mol/L hexanes solution (pre-cooled to –35 °C) of *n*-BuLi (0.51 mL, 0.82 mmol) was added dropwise to a vial containing a magnetically stirred solution (pre-cooled to –35 °C) of 7-azaindole (0.097 g, 0.82 mmol) in THF (4 mL), producing a colorless solution. The reaction mixture was stirred for 0.75 h at ambient temperature, followed by cooling to –35 °C. A pre-cooled (–35 °C) mixture of [(*R*)-(1,1′-binaphthalene-2,2′-diyl)]chlorophosphite (0.29 g, 0.82 mmol) and THF (5 mL) was then transferred slowly to the reaction mixture via Pasteur pipette. Upon completion of transfer, the resulting mixture was stirred for 2 h, after which the THF and other volatile materials were removed in vacuo. The residue was dissolved in a mixture of diethyl ether (4 mL) and benzene (2 mL) and filtered through Celite. The filtrate was dried in vacuo yielding **1** as an analytically pure, white solid (0.33 g, 0.76 mmol, 92%). ^{1}H NMR (C_6D_6) δ: 8.42 (d of d, $^3J_{HH}$ = 4.5 Hz, *J* = 1.5 Hz, 1H, C4-H or C6-H Aza.), 7.61 (d, $^3J_{HH}$ = 8.5 Hz, 1H, C-H Naph.), 7.57 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C-H Naph.), 7.55 (d, $^3J_{HH}$ = 4.0 Hz, 1H, C-H Naph.), 7.53 (d, $^3J_{HH}$ = 4.5 Hz, 1H, C-H Naph.), 7.45 (d, $^3J_{HH}$ = 7.5 Hz, 1H, C6-H or C4-H Aza.), 7.41 (d, $^3J_{HH}$ = 8.5 Hz, 1H, C-H Naph.), 7.32 (d, $^3J_{HH}$ = 2.0 Hz, 1H, C-H Naph.), 7.30 (d, $^3J_{HH}$ = 2.5 Hz, 1H, C-H Naph.), 7.17–7.10 (m, 2H, C-H Naph.), 6.97 (m, 1H, C-H Naph.), 6.93 (m, 1H, C-H Naph.), 6.81 (d of d, $^3J_{HH}$ = 5.0 Hz, $^3J_{HH}$ = 8.0 Hz, 1H, C5-H Aza.), 6.76 (d, $^3J_{HH}$ = 4.0 Hz, 1H, C2-H or C3-H Aza.), 6.65 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C-H Naph.), 5.92 (d of d, $^3J_{HH}$ = 4.0 Hz, *J* = 1.0 Hz, C3-H or C2-H Aza.). ^{13}C{^{1}H} NMR (C_6D_6) δ: 152.8 (d, *J* = 16.0 Hz, quat Aza.), 148.4 (quat Naph.), 148.0 (d, *J* = 4.2 Hz, quat Naph.), 143.7 (C4 or C6 Aza.), 133.0 (quat Naph.), 132.6 (quat Naph.), 131.7 (quat Naph.), 131.4 (quat Naph.), 131.1 (C-H Naph.), 130.1 (C-H Naph.), 128.5 (C-H Naph.), 128.4 (C-H Naph.), 128.2 (C6 or C4 Aza.), 127.0 (C-H Naph.), 126.9 (C-H Naph.), 126.5 (C-H Naph.), 126.4 (C-H Naph.), 126.2 (d, *J* = 4.3 Hz, C2 or C3 Aza.), 125.2 (C-H Naph.), 125.1 (C-H Naph.), 124.5 (d, *J* = 5.4 Hz, quat Aza.), 123.6 (quat Naph.), 122.3 (quat Naph.), 121.5 (C-H Naph.), 121.3 (C-H Naph.), 117.7 (C5 Aza.), 104.2 (C3 or C2 Aza.). ^{31}P{^{1}H} NMR (C_6D_6) δ: 133.8. Anal. calcd. for $C_{27}H_{17}P_1N_2O_2$: C 74.98; H 3.97; N 6.48. Found: C 74.58; H 3.93; N 6.26.

Synthesis of 2a

To a vial containing a magnetically stirred solution of **1** (0.056 g, 0.13 mmol) in THF (2 mL) was added dropwise a solution of $[(COD)RhCl]_2$ (0.016 g, 0.032 mmol) in THF (2 mL). The reaction mixture was stirred for 1 h, after which the solvent and other volatiles were removed in vacuo. The residue was washed with pentane (2 mL) and dried in vacuo, yielding **2a** as a pale yellow solid (0.044 g, 0.044 mmol, 68%). ^{1}H NMR (C_6D_6) δ: 9.34 (1H, C-H), 8.50–8.45 (m, 2H, C-Hs), 8.40 (d, $^3J_{HH}$ = 8.8 Hz, 1H, C-H), 7.68–7.63 (m, 2H, C-Hs), 7.60 (d, *J* = 8.75 Hz, 1H, C-H), 7.55–7.45 (m, 3H, C-Hs), 7.41 (d, $^3J_{HH}$ = 8.1 Hz, 1H, C-H), 7.35 (d, $^3J_{HH}$ = 8.2 Hz, 1H, C-H), 7.30–7.26 (m, 2H, C-Hs), 7.23 (d, $^3J_{HH}$ = 8.6 Hz, 1H, C-H), 7.13 (m, 1H, C-H), 7.07–6.98 (m, 3H, C-Hs), 6.97–6.82 (m, 4H, C-Hs), 6.81–6.75 (m, 2H, C-Hs),

6.71 (m, 1H, C-H), 6.57–6.50 (m, 2H, C-Hs), 6.41 (m, 1H, C-H), 6.21 (d, $^3J_{HH}$ = 8.8 Hz, 1H, C-H), 6.11 (d, $^3J_{HH}$ = 3.5 Hz, 1H, C-H), 5.96 (d, $^3J_{HH}$ = 8.7 Hz, 1H, C-H), 5.80–5.75 (m, 2H, C-H). $^{13}C\{^1H\}$ NMR (C_6D_6) δ: 151.8 (quat), 148.8 (quat), 148.4 (quat), 147.9 (quat), 143.1 (C-H), 142.9 (C-H), 132.8 (quat), 132.2 (quat), 132.1 (quat), 132.1 (quat), 131.9 (quat), 131.8 (quat), 131.0 (quat), 130.7 (quat), 130.6 (C-H), 130.2 (C-H), 129.8 (C-H), 129.4 (C-H), 129.3 (C-H), 129.0 (C-H), 128.8 (C-H), 128.2 (C-H), 128.2 (C-H), 128.1 (C-H), 128.0 (C-H), 127.2 (C-H), 127.0 (C-H), 126.9 (C-H), 126.8 (C-H), 126.3 (C-H), 125.8 (C-H), 125.8 (C-H), 125.4 (C-H), 125.3 (C-H), 124.7 (C-H), 124.5 (C-H), 123.6 (C-H), 123.6 (quat), 123.1 (quat), 122.3 (quat), 121.9 (quat), 121.3 (quat), 120.8 (C-H), 120.3 (C-H), 118.5 (quat), 117.5 (C-H), 117.3 (C-H), 108.0 (C-H), 103.6 (C-H). $^{31}P\{^1H\}$ NMR (C_6D_6) δ: 146.6 (d of d, $^1J_{PRh}$ = 275.2 Hz, $^2J_{PP}$ = 64.5 Hz), 140.0 (d of d, $^1J_{PRh}$ = 309.3 Hz, $^2J_{PP}$ = 64.2 Hz). Anal. calcd. for $C_{54}H_{34}Cl_1P_2N_4O_4Rh_1$: C 64.64; H 3.41; N 5.59. Found: C 64.55; H 3.74; N 5.48.

Synthesis of 2b

A procedure analogous to that described for the synthesis of **2a** was employed, using $[(COD)IrCl]_2$ (0.048 g, 0.072 mmol) in THF (2 mL). Complex **2b** was isolated as a light brown solid (0.11 g, 0.10 mmol, 72%). ^1H NMR (C_6D_6) δ: 9.51 (br s, 1H, C-H), 8.42 (d, $^3J_{HH}$ = 8.7 Hz, 1H, C-H), 8.37–8.34 (m, 2H, C-H), 7.89 (br s, 1H, C-H), 7.67 (d, *J* = 8.75 Hz, 1H, C-H), 7.62 (d, *J* = 8.75 Hz, 1H, C-H), 7.55–7.49 (m, 3H, C-H), 7.42 (d, $^3J_{HH}$ = 8.1 Hz, 1H, C-H), 7.36 (d, $^3J_{HH}$ = 8.2 Hz, 1H, C-H), 7.32–7.28 (m, 2H, C-H), 7.25 (d, $^3J_{HH}$ = 8.6 Hz, 1H, C-H), 7.06–7.02 (m, 2H, C-H), 6.98–6.89 (m, 4H, C-H), 6.88–6.83 (m, 2H, C-H), 6.82–6.78 (m, 2H, C-H), 6.71 (m, 1H, C-H), 6.59–6.52 (m, 2H, C-H), 6.39 (m, 1H, C-H), 6.27 (d, $^3J_{HH}$ = 8.8 Hz, 1H, C-H), 6.15 (d, $^3J_{HH}$ = 3.3 Hz, 1H, C-H), 5.96 (d, $^3J_{HH}$ = 8.8 Hz, 1H, C-H), 5.93 (d, $^3J_{HH}$ = 3.5 Hz, 1H, C-H), 5.75 (d, $^3J_{HH}$ = 2.9 Hz, 1H, C-H). $^{13}C\{^1H\}$ NMR (C_6D_6) δ: 151.4 (quat), 148.7 (quat), 148.5 (quat), 147.7 (quat), 142.8 (C-H), 141.0 (C-H), 132.8 (quat), 132.3 (quat), 132.2 (quat), 132.0 (quat), 131.7 (quat), 130.9 (quat), 130.6 (C-H), 130.4 (C-H), 129.9 (C-H), 129.4 (C-H), 128.7 (C-H), 128.1 (C-H), 128.1 (C-H), 127.3 (C-H), 127.1 (C-H), 127.0 (C-H), 126.9 (C-H), 126.3 (C-H), 125.7 (C-H), 125.4 (C-H), 125.2 (C-H), 125.1 (C-H), 124.6 (C-H), 124.5 (C-H), 124.3 (quat), 123.6 (C-H), 123.1 (quat), 122.2 (quat), 121.8 (quat), 121.2 (quat), 120.9 (C-H), 120.6 (C-H), 118.6 (quat), 117.4 (C-H), 117.1 (C-H), 107.8 (C-H), 103.3 (C-H). $^{31}P\{^1H\}$ NMR (C_6D_6) δ: 107.6 (d, $^2J_{PP}$ = 63.4 Hz), 104.3 (d, $^2J_{PP}$ = 63.5 Hz). Anal. calcd. for $C_{54}H_{34}Cl_1P_2N_4O_4Ir_1$: C 59.36; H 3.14; N 5.13. Found: 59.79; H 3.46; N 4.91.

Synthesis of 3

To a vial containing a magnetically stirred solution of **1** (0.047 g, 0.11 mmol) in THF (2 mL) was added dropwise a solution of $(PPh_3)_3RhCl$ (0.10 g, 0.11 mmol) in THF (2 mL), and the reaction mixture was stirred for 2 h. Pentane (10 mL) was added to the reaction mixture, causing the product to precipitate. The supernatant was decanted away and the precipitate washed with pentane (2 mL). The solid was dried in vacuo, yielding **3** as a yellow-brown solid (0.065 g, 0.081 mmol, 74%). ^1H NMR (C_6D_6) δ: 9.97 (d, $^3J_{HH}$ = 5.3 Hz, 1H, C-H), 7.99–7.91 (m, 6H, C-Hs), 7.79 (br s, 1H, C-H), 7.57 (d, $^3J_{HH}$ = 8.2 Hz, 1H, C-H), 7.44 (d, $^3J_{HH}$ = 8.85 Hz, 1H, C-H), 7.42 (d, $^3J_{HH}$ = 8.2 Hz, 1H, C-H), 7.31 (d, $^3J_{HH}$ = 8.6 Hz, 1H, C-H), 7.26 (d, $^3J_{HH}$ = 8.8 Hz, 1H, C-H), 7.08–7.20 (m, 3H, C-Hs), 7.03 (m, 1H C-H), 6.93 (d, $^3J_{HH}$ = 8.8 Hz, 1H, C-H), 6.91–6.83 (m, 3H, C-Hs), 6.80–6.76 (m, 8H, C-Hs), 6.58 (m, 1H, C-H), 5.91 (d, $^3J_{HH}$ = 3.7 Hz, 1H, C-H), 5.80 (d, $^3J_{HH}$ = 3.6 Hz, 1H, C-H). $^{13}C\{^1H\}$ NMR (C_6D_6) δ: 154.3 (d, *J* = 24.3 Hz, quat), 148.5 (d, J = 14.6 Hz, quat), 147.8 (d, *J* = 7.2 Hz, quat), 143.7 (C-H), 136.1 (quat), 135.7 (quat), 135.3 (C-H), 135.2 (C-H), 132.7 (m), 131.6 (quat), 131.3 (quat), 130.4 (C-H), 130.2 (C-H), 129.5 (C-H), 128.9 (C-H), 128.4 (C-H), 128.2 (C-H), 127.4 (C-H), 126.9 (m), 126.5 (C-H), 125.8 (C-H), 125.4 (C-H), 124.9 (C-H), 124.8 (m), 122.3 (m), 122.1 (C-H), 121.8 (C-H), 118.2 (d, *J* = 6.3 Hz, quat), 117.4 (C-H), 107.8 (C-H). $^{31}P\{^1H\}$ NMR (C_6D_6) δ: 135.4 (d of d, $^1J_{PRh}$ = 322.0 Hz, $^2J_{PP}$ = 64.7 Hz, 1P, PN), 43.4 (d of d, $^1J_{PRh}$ = 159.8 Hz, $^2J_{PP}$ = 64.7 Hz, PPh_3). Anal. calcd. for $C_{45}H_{32}Cl_1P_2N_2O_2Rh_1$: C 64.86; H 3.87; N 3.36. Found: 64.99; H 4.13; N 3.01.

Synthesis of 5b

To a vial containing a magnetically stirred suspension of $[(COD)IrCl]_2$ (0.074 g, 0.11 mmol) in THF (2 mL) was added a suspension of $AgBF_4$ (0.043 g, 0.22 mmol) in THF (2 mL). An orange solution was generated immediately along with a white precipitate. The supernatant solution was separated from the precipitate by filtration through Celite, and the solution was transferred to a vial containing a magnetically stirred solution of **1** (0.095 g, 0.22 mmol) in THF (2 mL). The reaction mixture was stirred for an additional 3 h at ambient temperature, during which the solution developed a red-orange coloration. The reaction mixture was then filtered through a plug of Celite, followed by removal of the solvent and other volatiles in vacuo to yield **5b** as a bright red-orange solid (0.16 g, 0.19 mmol, 86%). ^1H NMR (CD_2Cl_2) δ: 8.43 (d, $^3J_{HH}$ = 8.0 Hz, 1H, C-H), 8.31 (d, $^3J_{HH}$ = 5.5 Hz, 1H, C-H), 8.24 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C-H), 8.21 (d, $^3J_{HH}$ = 8.5 Hz, 1H, C-H), 8.15–8.10 (m, 2H, C-Hs), 7.76 (d, $^3J_{HH}$ = 9.0 Hz, 1H, C-H), 7.68–7.60 (m, 3H, C-Hs), 7.47–7.39 (m, 5H, C-Hs), 7.14 (d, $^3J_{HH}$ = 4.0 Hz, 1H, C-H), 6.43 (d of d, *J* = 2.0 Hz, *J* = 3.5 Hz, 1H, C-H), 6.04 (br s, 1H, COD), 5.98 (br s, 1H, COD), 4.19 (br s, 1H, COD), 4.13 (br s, 1H, COD), 2.52–2.18 (m, 8H, COD). $^{13}C\{^1H\}$ NMR (CD_2Cl_2) δ: 156.9 (quat), 146.8 (d, *J* = 13.7 Hz, quat), 145.8 (d, *J* = 7.0 Hz, quat), 142.4 (C-H), 135.1 (C-H), 132.4 (quaJune 24, 2008t), 132.2 (quat), 132.1 (C-H), 132.0 (C-H), 128.8 (C-H), 128.8 (C-H), 127.5 (2 C-Hs), 127.0 (C-H), 127.0 (C-H), 126.7 (C-H), 126.6 (C-H), 124.6 (d, *J* = 6.0 Hz, C-H), 122.3 (quat), 122.0 (quat), 121.1 (d, *J* = 8.3 Hz, quat), 120.0 (C-H), 119.8 (C-H), 119.7 (C-H), 111.9 (C-H), 70.3 (m, C-H), 62.2 (C-H), 33.2 (CH_2), 33.0 (CH_2), 29.0 (CH_2), 28.8 (CH_2). $^{31}P\{^1H\}$ NMR (CD_2Cl_2) δ: 115.3. Anal. calcd. for $C_{35}H_{29}P_1N_2O_2B_1F_4Ir_1$: C 51.26; H 3.57; N 3.42. Found: 51.24; H 3.78; N 2.99.

Synthesis of 6

To a vial containing a magnetically stirred solution of **1**(0.078 g, 0.18 mmol) in THF (1 mL) was added dropwise a solution of $[(\eta^3\text{-allyl})PdCl]_2$ (0.033 g, 0.090 mmol) in THF

(2 mL). The reaction mixture was stirred for 0.5 h, and the solvent and other volatiles were removed in vacuo yielding **6** as a yellow solid (0.092 g, 0.15 mmol, 86%). ^{1}H NMR (CD_2Cl_2) δ: 8.60 (d of d, $^3J_{HH}$ = 5.0 Hz, J = 1.4 Hz, 1H, C4-H or C6-H Aza.), 8.19 (d, $^3J_{HH}$ = 8.9 Hz, 1H, C-H), 8.09 (d, $^3J_{HH}$ = 8.3 Hz, 1H, C-H), 8.06–8.03 (m, 2H, C-Hs), 7.98 (d, $^3J_{HH}$ = 8.9 Hz, 2H, C-Hs), 7.62–7.57 (m, 2H, C-Hs), 7.51–7.45 (m, 2H, C-Hs), 7.44–7.39 (m, 2H, C-Hs), 7.34 (d of d, 1H, $^3J_{HH}$ = 5.0 Hz, $^3J_{HH}$ = 7.9 Hz, C5-H Aza.), 7.15 (d of d, 1H, $^3J_{HH}$ = 8.80 Hz, J = 0.7 Hz, C-H), 6.71 (d of d, 1H, $^3J_{HH}$ = 3.8 Hz, J = 1.6 Hz, C2-H or C3-H Aza.), 6.55 (d, $^3J_{HH}$ = 3.8 Hz, 1H, C3-H or C2-H Aza.), 5.83 (m, 1H, allyl), 3.94 (br s, 4H, allyl). ^{13}C{^{1}H} NMR (CD_2Cl_2) δ: 152.5 (C3a or C7a Aza.), 152.3 (C7a or C3a Aza.), 147.5 (m, quat), 146.9 (d, J = 4.9 Hz, quat), 143.3 (C4 or C6 Aza.), 132.4–131.9 (m, quat), 131.5 (C-H), 131.1 (C-H), 130.4 (C-H), 128.7–128.6 (m, aryl C-H and allyl C-H), 127.0 (m, C-Hs), 126.9 (C-H), 126.1 (m, C-Hs), 123.0 (quat), 122.6 (quat), 121.7 (d, J = 2.0 Hz, C-H), 120.3 (C-H), 118.8 (C5 Aza.), 107.5 (C3 or C2 Aza.). ^{31}P{^{1}H} NMR (CD_2Cl_2) δ: 133.1. Anal. calcd. for $C_{30}H_{22}Cl_1P_1N_2O_2Pd_1$: C 58.53; H 3.61; N 4.55. Found: 58.11; H 3.63; N 4.03.

General protocol for the metal-catalyzed hydrogenation experiments

A solution of metal (M = Rh or Ir) precursor (0.025 mmol in 0.5 mL) and **1** (1.2 equiv. relative to M; 0.030 mmol in 0.5 mL) in the desired solvent were combined to give a 0.025 mol/L solution of the catalyst (based on M). The solution was allowed to equilibrate for 0.75 h, at which point methyl 2-acetamidoacrylate (0.50 mmol in 0.5 mL) was added by use of an Eppendorf pipette. The mixture was placed in glass reactor cell, which was equipped with a magnetic stir bar and sealed under nitrogen with a PTFE valve. The cell was transferred to a Schlenk line, and the mixture was degassed by use of three freeze–pump–thaw cycles, followed by the addition of ca. 1 atm of H_2 (1 atm = 101.325 kPa), while magnetically stirring the solution. At the desired sampling time, the reaction mixture was concentrated in vacuo and extracted with diethyl ether (2 mL). The catalyst was removed by passing the diethyl ether extract through a plug of silica (0.6 cm × 2 cm) from which a clear, colorless solution eluted. This solution was transferred to a GC vial and sealed. Quantitative data were obtained from chiral GC-FID analysis using a Varian CHIRAL-L-VAL column.

General protocol for the metal-catalyzed hydroboration experiments

The general protocol employed herein for the hydroboration of styrene with HBpin has been described elsewhere (10). For reactions in which HBcat was employed, pinacol (2.1 equiv.) was added to the reaction mixture after 24 h followed by stirring for an additional 24 h. The subsequent work up procedure employed was the same as that undertaken for reactions involving HBpin.

General protocol for the metal-catalyzed hydrosilylation experiments

A solution of metal precursor (0.045 mmol in 0.75 mL) and **1** (1.2 equiv.; 0.054 mmol in 0.75 mL) in the desired solvent were combined to give a 0.030 mol/L solution of the catalyst (based on the metal). The solution was allowed to equilibrate for 0.75 h, at which point the ketone (0.90 mmol) was added by use of an Eppendorf pipette. The vial was then sealed, shaken vigorously, and cooled to –35 °C. Subsequently, pre-cooled (–35 °C) Ph_2SiH_2 (1.6 mmol) was added dropwise by use of an Eppendorf pipette to the reaction mixture, and the vial was then sealed and the reaction mixture was magnetically stirred for 18 h at ambient temperature. The reaction mixture was then cooled to 0 °C, and 1 mol/L HCl (5 mL) and acetone (5 mL) were added. The mixture was stirred for 1.5 h at 0 °C followed by 0.5 h at ambient temperature. A solution of saturated sodium bicarbonate was added, and the reaction mixture was stirred until no more gas evolution was observed (approx. 0.25 h). The reaction mixture was extracted with diethyl ether (2 × 5 mL). The combined organic layers were dried over Na_2SO_4, and the catalyst was removed by passing the solution through a plug of alumina (0.6 cm × 2 cm) from which a clear, colorless solution eluted. This solution was transferred to a GC vial and sealed. Products were identified by use of GC-MS while quantitative data were obtained from chiral GC-FID analysis by using a Supelco BETA-DEX 120 column.

Representative protocol for the metal-catalyzed allylic alkylation experiments

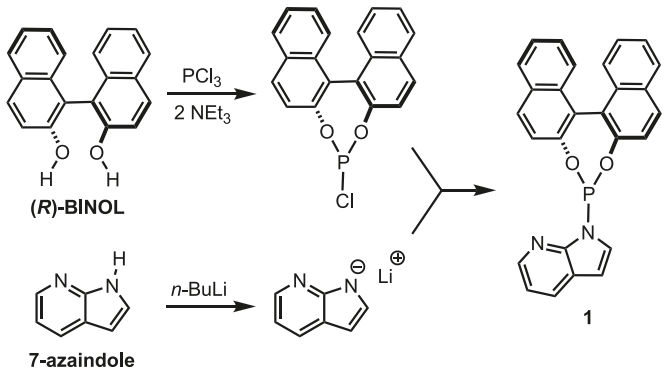
A 0.020 mol/L stock solution of catalyst was prepared by adding [(η^3-allyl)PdCl]$_2$ (0.0073 g, 0.020 mmol) in THF (1 mL) to ligand **1** (0.017 g, 0.040 mmol) in THF (1 mL), followed by stirring for 0.5 h. A 0.40 mol/L stock solution of the substrate was prepared by dissolving (±)-(*E*)-1,3-diphenylprop-2-enyl acetate (0.27 g, 1.1 mmol) in THF (2.7 mL). A 0.12 mL aliquot was taken from each of the two stock solutions and combined; this reaction mixture was stirred for 0.25 h and was then diluted with THF to a total volume of 12 mL to produce a final substrate concentration of 0.004 mol/L. Dimethyl malonate (6.6 μL, 0.058 mmol, 1.1 equiv.), *N*,*O*-bis(trimethylsilyl)acetamide (14.1 μL, 0.058 mmol, 1.1 equiv.), and KOAc (catalytic amount) were added to the reaction mixture, and the resulting suspension was stirred at 24 °C for 72–100 h. The reaction mixture was then concentrated in vacuo, passed through a short silica gel column (0.6 cm × 5 cm), and eluted with diethyl ether/hexanes (2:1). A portion of the eluent was transferred to a GC vial and sealed, while the remaining eluent was concentrated in vacuo. The reaction products were identified by use of GC-MS, while quantitative data were obtained from GC-FID analysis using a Supelco DB200 column. The enantiomeric excess of **11** was determined by use of ^{1}H NMR methods through the addition of Eu(hfc)$_3$ (8–10 mg) in $CDCl_3$ (0.6 mL) to the reaction sample. Isomer assignments are given on the basis of literature data (11).

Results and discussion

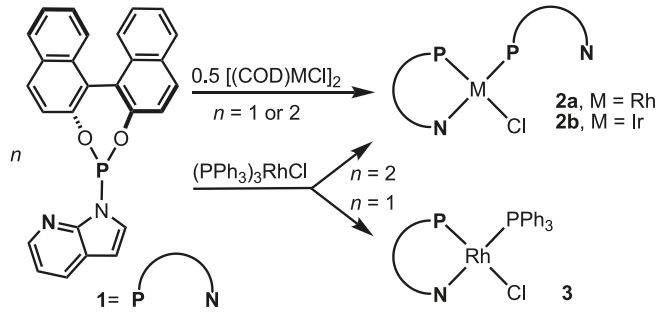
Ligand synthesis and coordination chemistry

The new chiral phosphoramidite **1** was prepared in 92% isolated yield (Scheme 1) via lithiation of 7-azaindole, followed by quenching with [(*R*)-(1,1′-binaphthalene-2,2′-diyl)]chlorophosphite prepared from the commercially available reagents *R*-BINOL and PCl_3. Prior to evaluating the

Scheme 1. Synthesis of the new chiral *P,N*-ligand 1.



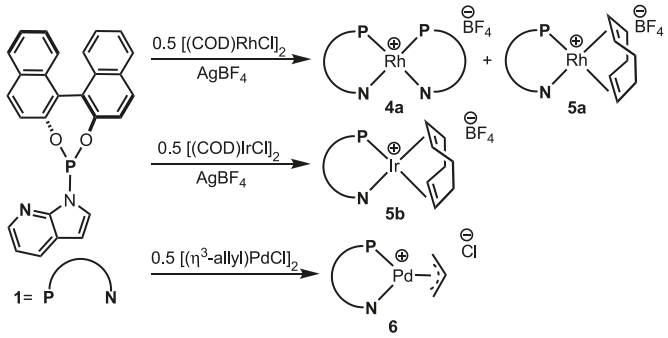
Scheme 2. Reactivity of 1 with $[(COD)MCl]_2$ or $(PPh_3)_3RhCl$ (M = Rh, Ir; COD = η^4-1,5-cyclooctadiene).



utility of **1** as a chiral ancillary ligand in PGM-mediated catalysis, we sought to examine the coordination chemistry of this new ligand. Treatment of 0.5 equiv. of $[(COD)MCl]_2$ (M = Rh, Ir; COD = η^4-1,5-cyclooctadiene) with 1 equiv. of **1** did not afford $[(COD)(\kappa^1\text{-}\mathbf{1})MCl]$; instead, a clean mixture of 0.5 equiv. of $[(\kappa^1\text{-}P,N\text{-}\mathbf{1})(\kappa^2\text{-}P,N\text{-}\mathbf{1})MCl]$ **2a** and **2b** and 0.25 equiv. of unreacted $[(COD)MCl]_2$ was observed by use of NMR spectroscopic methods (Scheme 2). Compounds **2a** and **2b** are observed as the only phosphorus-containing product when a **1**/M ratio of 2:1 is employed, thereby allowing for the convenient isolation of **2a** and **2b** as analytically pure solids in 68% (**2a**, Rh) and 72% (**2b**, Ir) yields, respectively. The observation of ^{31}P-^{31}P coupling between the magnetically non-equivalent phosphorus centers in the ^{31}P NMR spectra of **2a** and **2b** (as well as the clearly discernable ^{103}Rh coupling in the case of **2a**) is consistent with the existence of P-M-P′ linkages in **2a** and **2b**. Moreover, the cis-disposition of the phosphorus fragments in **2a** and **2b** as depicted in Scheme 2 is in keeping with the magnitude of the observed $^2J_{PP}$ value (ca. 64 Hz) for these complexes. Whereas **2a** is also formed upon treatment of $(PPh_3)_3RhCl$ with 2 equiv. of **1**, the use of only 1 equiv. of **1** under similar conditions afforded $[(PPh_3)(\kappa^2\text{-}P,N\text{-}\mathbf{1})RhCl]$ **3** as an analytically pure solid in 74% isolated yield.

In the pursuit of $[(COD)(\kappa^2\text{-}P,N\text{-}\mathbf{1})M]^+X^-$ complexes (M = Rh, Ir), the reaction of **1** with mixtures of 0.5 equiv. of $[(COD)MCl]_2$ and 1 equiv. of $AgBF_4$ in THF was examined. For M = Rh, NMR analysis revealed the formation of an inseparable mixture of $[(\kappa^2\text{-}P,N\text{-}\mathbf{1})_2Rh]^+BF_4^-$ **4a** and $[(COD)(\kappa^2\text{-}P,N\text{-}\mathbf{1})Rh]^+BF_4^-$ **5a** (12) as depicted in Scheme 3. Compound **4a** was also observed as a major phosphorus-

Scheme 3. Reactivity of 1 with $[(COD)MCl]_2/AgBF_4$ (M = Rh, Ir; COD = η^4-1,5-cyclooctadiene) and $[(\eta^3\text{-allyl})PdCl]_2$.



containing product in such reactions when the **1**/Rh ratio was reduced to 0.5:1. Conversely, reactions employing **1**:Ir in a 1:1 ratio afforded $[(COD)(\kappa^2\text{-}P,N\text{-}\mathbf{1})Ir]^+BF_4^-$ **5b** as the major product, thereby allowing for the isolation of this species in 86% yield.

The ability of **1** to form 1:1 complexes with Pd was confirmed upon treatment of 0.5 equiv. of $[(\eta^3\text{-allyl})PdCl]_2$ with **1**; the corresponding salt $[(\eta^3\text{-allyl})(\kappa^2\text{-}P,N\text{-}\mathbf{1})Pd]^+Cl^-$ **6** was obtained as an analytically pure solid in 86% isolated yield (Scheme 3). While shortly following dissolution the ^{31}P NMR spectrum of **6** exhibits a single resonance at 133.1 ppm, a new signal at 129.4 ppm was observed to grow in over the course of 3 h. Although we are presently unable to comment definitively regarding the relationship between these two phosphorus-containing species, the propensity of $[(\eta^3\text{-allyl})(\kappa^2\text{-}P,N)Pd]^+X^-$ complexes to exhibit complicated dynamic behavior is well-established (13). Having briefly explored the coordination chemistry of **1** with Rh, Ir, and Pd, the utility of this new chiral *P,N*-ligand in PGM-mediated asymmetric synthesis was surveyed. For convenience, catalyst complexes were prepared in situ by using an appropriate metal precursor in combination with **1** (except where noted).

Asymmetric hydrogenation

The Rh- and Ir-mediated asymmetric hydrogenation of methyl-2-acetamidoacrylate **7** to afford **8** (eq. [1]) under mild conditions (24 °C, ca. 1 atm H_2, 5.0 mol% Rh or Ir) was selected as a preliminary catalytic test reaction to use in benchmarking the performance of **1** (14); key results of these hydrogenation studies are collected in Table 1. Control experiments confirmed the ability of catalyst mixtures derived from 0.5 $[(COD)RhCl]_2$ and $AgBF_4$ in THF (without added **1**) to mediate the reduction of **7** (Table 1, entry 1–1). Under analogous conditions employing 6.0 mol% of **1** (1.2 equiv. relative to Rh), the quantitative reduction of **7** was also achieved, affording **8** in 65% ee (Table 1, entry 1–2). However, increasing the amount of **1** to 12.0 mol% (Table 1, entry 1–3) in such transformations was found to diminish both the conversion (78%) and the enantioselectivity (50% ee), possibly because of the preferential formation of less effective catalytic intermediates derived from $[(\kappa^2\text{-}P,N\text{-}\mathbf{1})_2Rh]^+BF_4^-$ **4a**. On the basis of this postulate and in light of the established preference of **1** to form **4a** (and not $[(COD)(\kappa^2\text{-}P,N\text{-}\mathbf{1})Rh]^+BF_4^-$ **5a**) when combined with $[(COD)Rh(THF)_2]^+BF_4^-$ (vide supra), it is likely that the results featured in entry 1–2 (Table 1) do not truly reflect the

Table 1. Hydrogenation of methyl 2-acetamidoacrylate.

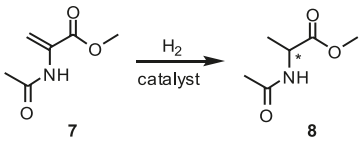
Entry	Metal precursor (5.0 mol%)	Mol% of **1** added	Solvent	%[a]	% ee[b]
1–1	$[(COD)Rh(THF)_2]^+BF_4^-$	0	THF	>99	<1
1–2	$[(COD)Rh(THF)_2]^+BF_4^-$	6.0	THF	>99	65
1–3	$[(COD)Rh(THF)_2]^+BF_4^-$	12.0	THF	78	50
1–4	$[(COD)Ir(THF)_2]^+BF_4^-$	0	CH_2Cl_2	>99	<1

Note: Conditions: 24 °C, 1 atm H_2. $[(COD)M(THF)_2]^+BF_4^-$ prepared in situ from 0.5 $[(COD)MCl]_2$ and $AgBF_4$ in THF (M = Rh, Ir and COD = η^4-1,5-cyclooctadiene).

[a]Percent conversion based on the consumption of methyl-2-acetamidoacrylate (**7**) at 24 h.

[b]Enantiomeric excess of **8** determined on the basis of chiral GC-FID data.

performance of the target pre-catalyst complex **5a** alone; rather, the previously discussed coordination chemistry studies indicate that each of $[(COD)Rh(THF)_2]^+BF_4^-$, **4a**, and **5a** are likely to be present as pre-catalysts under these experimental conditions. In this regard, the inherent enantioselectivity of **5a** is likely underestimated, owing to the significant background reactivity associated with $[(COD)Rh(THF)_2]^+BF_4^-$ (Table 1, entry 1–1) and the generally inferior performance of **4a**, as based on entry 1–3. In an effort to possibly promote the formation of **5a**, the reaction solvent was changed to CH_2Cl_2; however, all such reactions employing $[(COD)Rh(THF)_2]^+BF_4^-$ (pre-formed in THF) in combination with 0, 1.2, or 2.4 equiv. of **1** relative to Rh afforded no conversion of the alkene substrate (15). Similarly, the pre-formed Rh complex **3** proved to be catalytically inactive in either THF or CH_2Cl_2. While $[(COD)Ir(THF)_2]^+BF_4^-$ mediated the quantitative conversion of **7** to **8** in CH_2Cl_2 (Table 1, entry 1–4), the activity of Ir in this chemistry was completely inhibited by the addition of 1.2 equiv. of **1** for reactions carried out in CH_2Cl_2 or THF.

[1] 

Asymmetric hydroboration

The asymmetric hydroboration of styrene (16) employing either pinacolborane (HBpin) or catecholborane (HBcat) was selected as an alternative E–H addition reaction with which to evaluate the ability of **1** to promote chemo-, regio-, and enantioselectivity in PGM-mediated catalysis (eq. [2] and Table 2). For reactions employing HBpin, catalyst mixtures derived from 5.0 mol% $[(COD)_2Rh]^+BF_4^-$ and 5.5 mol% **1** were found to exhibit modest selectivity towards the desired branched isomer **9a** over the linear isomer **9b** at substrate concentrations of 0.19 mol/L (Table 2, entry 2–1) and 0.046 mol/L (Table 2, entry 2–2); inferior selectivity was noted for analogous reactions in which HBcat was used (Table 2, entries 2–3 and 2–4). Unfortunately, no enantioselectivity (in **9a**) was achieved in the aforementioned hydroboration reactions, and analogous reactions employing 5.0 mol% $[(COD)_2Ir]^+BF_4^-$ and 5.5 mol% **1** afforded exclusively the linear product **9b**.

Table 2. Rhodium-catalyzed addition of HBpin and HBcat to styrene.

Entry	Borane[a]	Substrate conc. (mol/L)	Branched: linear[b] (**9a**:**9b**)
2–1	HBpin	0.19	73:27
2–2	HBpin	0.046	68:32
2–3	HBcat	0.19	60:40
2–4	HBcat	0.046	61:39

Note: Conditions: –30 °C for 24 h; 5.0 mol% $[(COD)_2Rh]^+BF_4^-$; 5.5 mol% **1**; borane-to-styrene ratio of 1.2:1; THF. For all experiments >95% conversion of styrene was achieved.

[a]HBpin = pinacolborane; HBcat = catecholborane.

[b]Product ratio on the basis of GC-FID data, rounded to the nearest percent. In all cases, other boron-containing products represented <3% of the total product distribution. No enantioselectivity was achieved in these reactions, on the basis of chiral GC-FID data.

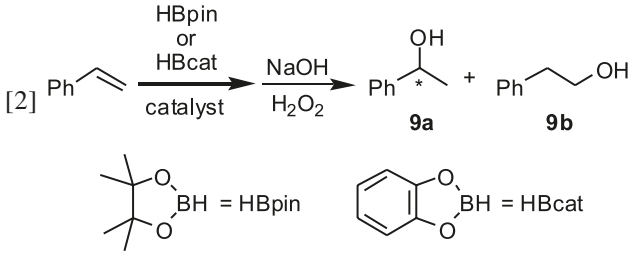
Table 3. Addition of diphenylsilane to acetophenone.

Entry	Metal precursor (5.0 mol% Rh)	Mol% of **1** added	Solvent	%[a]	% ee[b]
3–1	$[(COD)RhCl]_2$	6.0	THF	50	32
3–2	$[(COD)RhCl]_2$	12.0	THF	<1	N/D
3–3	$[(COD)Rh(THF)_2]^+BF_4^-$	6.0	THF	69	28
3–4	$[(COD)Rh(THF)_2]^+BF_4^-$	12.0	THF	24	19

Note: Conditions: 24 °C. $[(COD)Rh(THF)_2]^+BF_4^-$ prepared in situ from 0.5 $[(COD)RhCl]_2$ and $AgBF_4$ in THF (COD = η^4-1,5-cyclooctadiene).

[a]Percent conversion based on the consumption of ketone at 18 h.

[b]Enantiomeric excess of **10** determined on the basis of chiral GC-FID data, rounded to the nearest percent (N/D = not determined).

[2] 

Asymmetric hydrosilylation

The asymmetric hydrosilylation of ketones represents an appealing synthetic route to chiral secondary alcohols. While highly effective PGM catalysts for this challenging enantioselective transformation are relatively few, a report by Tao and Fu (17) highlights the utility of appropriately designed chiral *P*,*N*-ligands in Rh-catalyzed transformations of this type. Key results of our investigation of asymmetric hydrosilylation of acetophenone with Ph_2SiH_2 (eq. [3]) in THF are collected in Table 3. In preliminary experiments using a catalyst mixture comprised of 0.25 mol% $[(COD)RhCl]_2$ and 6.0 mol% **1**, 50% conversion of the ketone was achieved; however, the derived secondary alcohol formed upon acidic workup was obtained in only 32% ee (Table 3, entry 3–1). When employing catalyst mixtures featuring **1**/Rh in a 2:1 ratio, no conversion was achieved (Table 3, entry 3–2), thereby indirectly suggesting that **2a** is

Table 4. Palladium-catalyzed allylic alkylation.

Entry	Substrate conc. (mol/L)	Mol% of **1** added	Solvent	Ratio[a]	Time (h)	%[b]	% ee[c]
4–1	0.2	5.0	CH_2Cl_2	1:1.1	24	>99	24 (R)
4–2	0.04	5.0	CH_2Cl_2	1:1.1	24	85	43 (R)
4–3	0.2	5.0	CH_2Cl_2	1:3	24	>99	22 (R)
4–4	0.04	5.0	CH_2Cl_2	1:3	24	>99	40 (R)
4–5	0.2	5.0	THF	1:1.1	24	96	40 (R)
4–6	0.04	5.0	THF	1:1.1	24	93	57 (R)
4–7	0.2	5.0	THF	1:3	24	>99	15 (R)
4–8	0.04	5.0	THF	1:3	24	81	38 (R)
4–9	0.004	2.5	THF	1:1.1	100	49	70 (R)
4–10	0.004	5.0	THF	1:1.1	100	>99	66 (R)
4–11	0.004	10.0	THF	1:1.1	100	61	17 (S)
4–12	0.004	15.0	THF	1:1.1	100	10	7 (S)

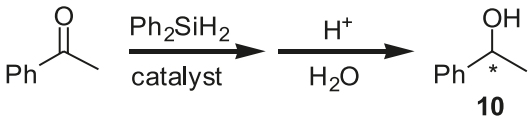
Note: Conditions: 24 °C; 2.5 mol% $[(\eta^3\text{-allyl})PdCl]_2$ and stated amount of **1**.

[a]Ratio of (±)-(*E*)-1,3-diphenylprop-2-enyl acetate to dimethyl malonate.

[b]Percent conversion to **11** based on the consumption of (±)-(*E*)-1,3-diphenylprop-2-enyl acetate.

[c]Product distribution determined on the basis of ^{1}H NMR integration of the product mixture after the addition of the chiral shift reagent Eu(hfc)$_3$, rounded to the nearest percent (error ± 5%); the major isomer is indicated in parentheses.

an ineffective pre-catalyst for this transformation. While the use of 5.0 mol% $[(COD)Rh(THF)_2]^+BF_4^-$ in combination with **1** (6.0 or 12.0 mol%) afforded a correspondingly more active catalyst system (Table 3, entries 3–3 and 3–4), only modest enantioselectivities (<30% ee) were achieved.

[3] 

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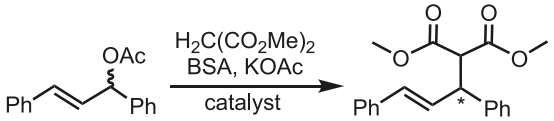
Asymmetric allylic alkylation

The Pd-mediated asymmetric allylic alkylation of (±)-(*E*)-1,3-diphenylprop-2-enyl acetate with dimethyl malonate (eq. [4]) is a well-established C–C bond forming reaction that is used commonly as a means of benchmarking the utility of chiral *P*,*N*-ligands in enantioselective catalysis (13, 18). Table 4 summarizes some key results of our catalytic studies employing catalyst mixtures of derived from 2.5 mol% $[(\eta^3\text{-allyl})PdCl]_2$ and **1** under standard conditions (18a) employing *N*,*O*-bis(trimethylsilyl)acetamide (BSA) and a catalytic amount of potassium acetate as base. In a preliminary catalytic survey (5.0 mol% **1**, 24 h), the influence of solvent (CH_2Cl_2, THF), substrate concentration (0.2 mol/L, 0.04 mol/L), and the ratio of (±)-(*E*)-1,3-diphenylprop-2-enyl acetate to dimethyl malonate (1:1.1, 1:3) on conversion and enantioselectivity was examined (Table 4, entries 4–1 to 4–8). Whereas a number of experimental conditions were identified that could provide >99% conversion to **11**, reactions employing 0.04 mol/L (±)-(*E*)-1,3-diphenylprop-2-enyl acetate and 1.1 equiv. of dimethyl malonate in THF (Table 4, entry 4–6) afforded what we viewed as the best balance between conversion (93%) and enantioselectivity (57%). Schenkel and Ellman (19) have reported that improved enantioselectivity in Pd-catalyzed asymmetric allylic alkylation can be achieved by conducting the reaction under dilute conditions. In this context, a series of catalytic reactions were carried out employing a substrate concentration of 0.004 mol/L and in which the amount of added **1** was varied (0.5, 1.0, 2.0, and 3.0 equiv. relative to Pd; Table 4, entries 4–9 to 4–12). While a 1:1 ratio of **1**/Pd (Table 4, entry 4–10) produced the most effective catalyst system, resulting in >99% conversion (after 100 h) and affording *R*-**11** in 66% ee, it is noteworthy that the catalyst system obtained, when employing 2.0 or 3.0 equiv. of **1** relative to Pd, exhibits a modest preference for the formation of the opposite enantiomer *S*-**11** (Table 4, entries 4–11 and 4–12). Although these preliminary results are somewhat promising, it is important to recognize that the overall performance of **1** in the Pd-mediated enantioselective synthesis of **11** is not competitive with the best chiral *P*,*N*-ligands, including PHOX (5) and alternative phosphoramidite ligands (20), which offer >99% conversion and >95% ee for this enantioselective transformation (18a).

[4] 

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Summary and conclusions

In conclusion, we have reported herein on the synthesis and characterization of a new chiral heterobidentate phosphoramidite ligand **1**, which is easily prepared in high yield from the commercially available reagents 7-azaindole, *R*-BINOL, and PCl_3. Preliminary coordination chemistry studies confirm the ability of **1** to form isolable κ^2-*P*,*N* complexes with Rh, Ir, and Pd. However, in the course of such synthetic studies, Rh (and in some cases Ir) exhibited a marked propensity to form M(**1**)$_2$ complexes; such behavior may contribute in part to the generally lacklustre catalytic performance exhibited by mixtures of **1** and Rh precursor complexes in the asymmetric addition of E–H fragments (E = H, B, Si) to unsaturated substrates. While under certain conditions, mixtures of **1** and $[(\eta^3\text{-allyl})PdCl]_2$ proved capable of mediating the addition of dimethyl malonate to

(±)-(*E*)-1,3-diphenylprop-2-enyl acetate with >99% conversion and a maximum ee of 66%, the rather low enantioselectivity achieved suggests that **1** is not competitive with more well-established chiral *P*,*N*-ligands for such asymmetric transformations.

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References

1. (*a*) N.B. Johnson, I.C. Lennon, P.H. Moran, and J.A. Ramsden. Acc. Chem. Res. **40**, 1291 (2007); (*b*) V. Farina, J.T. Reeves, C.H. Senanayake, and J.J. Song. Chem. Rev. **106**, 2734 (2006); (*c*) H.-U. Blaser, B. Pugin, and F. Spindler. J. Mol. Cat. A, **231**, 1 (2005); (*d*) H.-U. Blaser, F. Spindler, and M. Studer. Appl. Cat. A, **221**, 119 (2001).
2. For selected reviews, see: (*a*) K. Källström, I. Munslow, and P. G. Andersson. Chem. Eur. J. **12**, 3194 (2006); (*b*) P.J. Guiry and C.P. Saunders. Adv. Synth. Catal. **346**, 497 (2004); (*c*) G. Chelucci, G. Orrù, and G.A. Pinna. Tetrahedron, **59**, 9471 (2003); (*d*) K.N. Gavrilov and A.I. Polosukhin. Russ. Chem. Rev. **69**, 661 (2000).
3. For selected references to catalysts supported by *P*,*N*-indene and related ligands, see: (*a*) R.J. Lundgren, M.A. Rankin, R. McDonald, and M. Stradiotto. Organometallics, **27**, 254 (2008); (*b*) R.J. Lundgren, M.A. Rankin, R. McDonald, G. Schatte, and M. Stradiotto. Angew. Chem. Int. Ed. **46**, 4732 (2007); (*c*) B.M. Wile, R. McDonald, M.J. Ferguson, and M. Stradiotto. Organometallics, **26**, 1069 (2007); (*d*) J. Cipot, R. McDonald, M.J. Ferguson, G. Schatte, and M. Stradiotto. Organometallics, **26**, 594 (2007); (*e*) J. Cipot, C.M. Vogels, R. McDonald, S.A. Westcott, and M. Stradiotto. Organometallics, **25**, 5965 (2006).
4. (*a*) A.J. Minnaard, B.L. Feringa, L. Lefort, and J.G. de Vries. Acc. Chem. Res. **40**, 1267 (2007); (*b*) J.G. de Vries and L. Lefort. Chem. Eur. J. **12**, 4722 (2006).
5. G. Helmchen and A. Pfaltz. Acc. Chem. Res. **33**, 336 (2000).
6. H.L. Milton, M.V. Wheatley, A.M.Z. Slawin, and J. D. Woolins. Inorg. Chem. Commun. **7**, 1106 (2004).
7. A.D. Burrows, M.F. Mahon, and M.Varrone. Dalton Trans. 4718 (2003).
8. R. Sablong, C. Newton, P. Dierkes, and J.A. Osborn. Tetrahedron Lett. **37**, 4933 (1996).
9. I.D.G. Watson and A.K. Yudin. J. Am. Chem. Soc. **127**, 17516 (2005).
10. D. Wechsler, M.A. Rankin, R. McDonald, M.J. Ferguson, G. Schatte, and M. Stradiotto. Organometallics, **26**, 6418 (2007).
11. G. Brenchley, M. Fedouloff, M.F. Mahon, K.C. Molloy, and M. Wills. Tetrahedron, **51**, 10581 (1995).
12. $^{31}P\{^{1}H\}$ NMR (CD_2Cl_2) δ: 148.6 (d, $^{1}J_{RhP}$ = 280.0 Hz, **4a**), 130.7 (d, $^{1}J_{RhP}$ = 270.4 Hz, **5a**).
13. P.S. Pregosin and R. Salzmann. Coord. Chem. Rev. **155**, 35 (1996).
14. For an overview of the Rh-mediated asymmetric hydrogenation of alkenes bearing polar functional groups, see: I.D. Gridnev and T. Imamoto. Acc. Chem. Res. **37**, 633 (2004).
15. By comparison, a recently reported phosphine-phosphoramidite ligand afforded >99% conversion and >99% ee in the Rh-catalyzed asymmetric hydrogenation of dehydroamino acid esters in CH_2Cl_2: J.-D. Huang, X.-P. Hu, Z.-C. Duan, Q.-H. Zeng, S.-B. Yu, J. Deng, D.-Y. Wang, and Z. Zheng. Org. Lett. **8**, 4367 (2006).
16. For reviews on metal-mediated asymmetric hydroboration, see: (*a*) A.-M. Carroll, T.P. O'Sullivan, and P.J. Guiry. Adv. Synth. Catal. **347**, 609 (2005); (*b*) C.M. Crudden and D. Edwards. Eur. J. Org. Chem. 4695 (2003).
17. B. Tao and G.C. Fu. Angew. Chem. Int. Ed. **41**, 3892 (2002).
18. (*a*) B.M. Trost and D.L. Van Vranken. Chem. Rev. **96**, 395 (1996); (*b*) P. von Matt, G.C. Lloyd-Jones, A.B.E. Minidis, A. Pfaltz, L. Macko, M. Neuburger, M. Zehnder, H. Rüegger, and P.S. Pregosin. Helv. Chim. Acta, **78**, 265 (1995).
19. L.B. Schenkel and J.A. Ellman. Org. Lett. **5**, 545 (2003).
20. For a recent example, see: O. Pàmies, M. Diéguez, and C. Claver. Adv. Synth. Catal. **349**, 836 (2007).