Low Coordinate Phosphorus

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Chiral Ligand Design: A Bidentate Ligand Incorporating an Acyclic Phosphaalkene**

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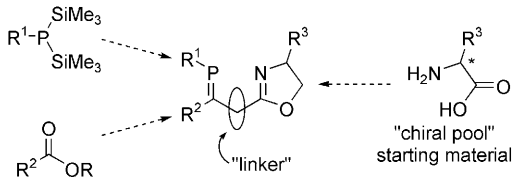
Since Becker's landmark discovery of the first isolable phosphaalkene just over three decades ago,[1] there has been a growing interest in low coordinate multiply bonded phosphorus compounds.[2] In fact, these species, although once considered exotic, are now being utilized in catalysis and materials science. As a consequence of their excellent π-acceptor properties, there has been considerable recent interest in the development of low valent phosphorus ligands for catalysis.[3] Of particular significance are those in which the P=C donor moiety is incorporated into a cyclic structure (i.e. phosphinines,[4] phosphaferrocenes,[5] and phospholides[6]). Ligands containing acyclic P=C bonds are less well-developed, however the diphosphinidenecyclobutenes (dpcb) have been demonstrated to be highly effective in catalytic transformations.[7] We,[8] and others,[9] have also reported examples of acyclic P(sp^2),N(sp^2) phosphaalkene ligands, however their application in catalysis is still at a preliminary stage of development.

The design of asymmetric ligands for transition elements has had a profound impact on the field of synthetic organic chemistry. Of particular importance in asymmetric catalysis are the sp^3 hybridized phosphane ligands which are excellent sigma donors and weak π-acceptors (binap, DuPhos, etc.). Modification of the steric and electronic properties of the metal's supporting ligands provides a means to optimize the selectivity and activity of a catalyst. π-Accepting ligands are also of considerable importance in catalysis, however the classic π-accepting ligands used in inorganic chemistry (CO, bipy) cannot be trivially reconstituted into "chiral versions" for asymmetric catalysis. To our knowledge, the only enantiomerically pure P(sp^2)-based ligands are based on cyclic phosphinines and phosphaferrocenes.[4e,5,10–12] Consequently, the introduction of low valent, π-accepting phosphorus atoms within a readily available chiral ligand framework may fill an important gap in modern ligand design.

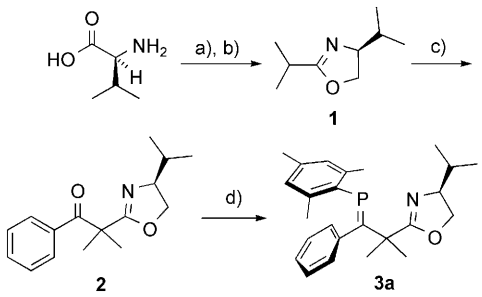
Here we report a synthetic strategy to air- and moisture-stable chiral, enantioenriched phosphaalkene ligands. Our approach provides a convergent and highly modular means for future tailoring of the ligand's steric and electronic properties (Scheme 1). Importantly, the stereogenic center



Scheme 1. Modular strategy for the preparation of chiral oxazoline-based phosphaalkenes. R^1, R^2 and R^3 represent adjustable substituents.

present in the ligand is derived directly from the chiral pool. The phosphaalkene substituents (R^1 and R^2) can be easily adjusted through selection of precursors. The "linker" moiety must be selected to avoid undesired reactivity of phosphaalkenes such as cycloadditions or 1,3-hydrogen migrations. The effectiveness of this new phosphaalkene as a bidentate chelating P(sp^2),N(sp^2) ligand is demonstrated through the isolation of an iridium(I) complex.

Amino acids are cheap, readily available sources of chirality on which to build the chiral oxazoline-containing ketone precursors to phosphaalkenes. The known oxazoline **1** was prepared in two steps from L-valine using a modified literature procedure (Scheme 2).[13,14] Our attempts to deprotonate **1** using LDA or *n*BuLi were unsuccessful. Fortunately, treatment of **1** with 1 equivalent each of *sec*-BuLi and TMEDA for one hour at −78 °C formed the desired



Scheme 2. Synthesis of phosphaalkene ligand. a) $NaBH_4$, I_2, THF, 60 °C, 18 h (92%); b) isobutyric acid, xylenes, 130 °C (58%); c) 1. *s*BuLi, TMEDA, THF, −78 °C; 2. ethyl benzoate, THF, −78 °C to 25 °C (49%); d) 1. $MesP(SiMe_3)Li$, THF, −78 °C to 25 °C; 2. Me_3SiCl quench (52%). THF = tetrahydrofuran, Bu = butyl, TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, Mes = 2,4,6-trimethylphenyl.

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carbanion.[15] Claisen-type condensation of this anion with ethyl benzoate formed ketone **2** in 49% isolated yield. Importantly, these synthetic steps can be performed without recourse to flash chromatography. Ketone **2** was fully characterized using NMR spectroscopy (^{1}H, ^{13}C), mass spectrometry [HRMS (**2**·Na$^+$): m/z 282.1469 (found); 282.1470 (calcd)], infrared spectroscopy and elemental analysis. Compound **2** showed an optical rotation $[\alpha]_D^{22} = -28.1$ deg cm^3 g^{-1} dm^{-1} ($c = 1.3 \times 10^{-3}$ g cm^{-3}, $CHCl_3$).

With ketone **2** in hand, the phospha-Peterson reaction, a general and clean route to phosphaalkenes,[16] was attempted as the P=C bond forming step. A solution of ketone **2** in THF was added dropwise to a cooled (−78 °C) solution of MesP(Li)SiMe$_3$ in THF. The reaction mixture was warmed slowly to room temperature (1 h) whereupon an aliquot was removed for analysis by ^{31}P NMR spectroscopy. Importantly, the signal assigned to MesP(Li)SiMe$_3$ ($\delta = -187$ ppm) was replaced by a new singlet resonance at 244 ppm which is consistent with that expected for a phosphaalkene (cf. MesP=CPh$_2$: $\delta = 233$ ppm). The presence of a single signal suggests that only one isomer is formed. The product was recrystallized from *n*-pentane to afford colorless crystals of *E*-**3a** (yield 52%) which were characterized crystallographically (Figure 1). The optical rotation of *E*-**3a** was $[\alpha]_D^{22} = -65.8$ deg cm^3 g^{-1} dm^{-1} ($c = 5.0 \times 10^{-3}$ g cm^{-3}, $CHCl_3$). Perhaps most remarkable is the air- and moisture-stability of compound *E*-**3a**. The ^{31}P NMR spectrum of a THF solution of the phosphaalkene exposed to oxygen and/or water shows no change. Moreover, crystals of *E*-**3a** have been stored on the open benchtop for months without any degradation. This stability, a relatively unusual property for phosphaalkenes, allows for the manipulation of this compound without the need for special precautions.

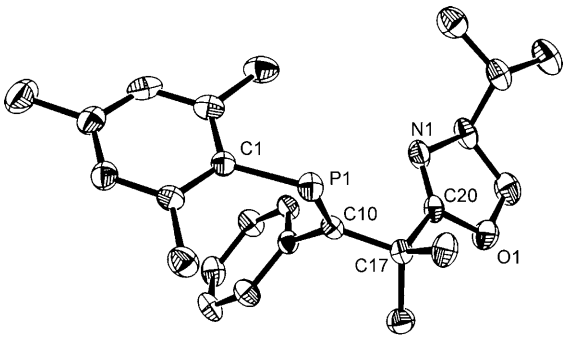
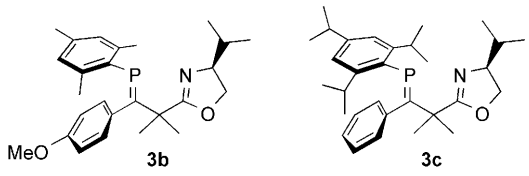
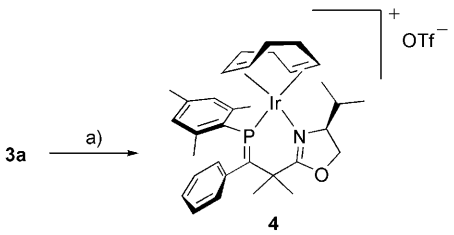


Figure 1. Molecular structure of *E*-**3a** (50% probability ellipsoids). All hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: P(1)–C(1) 1.826(2), P(1)–C(10) 1.679(2), C(10)–C(17) 1.529(3), C(17)–C(20) 1.511(3), C(20)–N(1) 1.248(3), C(20)–O(1) 1.356(3); C(1)-P(1)-C(10) 105.3(1), P(1)-C(10)-C(17) 119.2(2), C(10)-C(17)-C(20) 108.9(2), C(17)-C(20)-N(1) 127.6(2), C(17)-C(20)-O(1) 113.7(2).

To illustrate the modularity of our synthetic route to chiral phosphaalkenes, we have prepared two additional phosphaalkenes, **3b** (yield 50%) and **3c** (yield 93%). These compounds are conveniently prepared following the same route as described for **3a**. The C-substituent is modified by employing a *p*-methoxyphenyl moiety (**3b**) in place of the phenyl group (**3a**). In addition, the steric bulk of the P-substituent is increased in **3c** by employing the 2,4,6-tri(isopropyl)phenyl moiety. Each new phosphaalkene was characterized by ^{31}P NMR spectroscopy (**3b**: $\delta = 245$ ppm; **3c**: $\delta = 248$ ppm), ^{1}H NMR spectroscopy and mass spectrometry (**3b**: [M^+] 423; **3c**: [M^+] 477).



The complexation of *E*-**3a** to late transition metals for catalysis applications is of particular interest. Iridium complexes have been used to catalyze asymmetric hydrogenation, allylic alkylation and hydroformylation, amongst other transformations.[17] A mixture of *E*-**3a** and [(cod)IrCl]$_2$ in the presence of AgOTf as a halide acceptor was dissolved in CH_2Cl_2 and was stirred for 30 min whereupon the solution was separated from a white precipitate of AgCl (Scheme 3).



Scheme 3. Synthesis of iridium complex **4**. a) [(cod)IrCl]$_2$, AgOTf, CH_2Cl_2, RT, 30 min (72%). cod = 1,5-cyclooctadiene, OTf = trifluoromethanesulfonate.

Subsequently, the reaction mixture was analyzed by ^{31}P NMR spectroscopy that showed a new singlet resonance at 197 ppm which is shifted upfield considerably from *E*-**3a** ($\Delta\delta = -47$ ppm) and is consistent with that expected for iridium(I) complex **4**. For comparison, similar upfield shifts are observed for iridium(III) complexes of related phosphaalkenes [$\Delta\delta = -50$ ppm, L = dpcb; $\Delta\delta = -41$ ppm, L = Mes*P=C(py)H].[18,19] Complex **4** was further characterized by ^{1}H and ^{13}C NMR spectroscopy and elemental analysis which all provided support for the retention of the cod ligand.

The chiral phosphaalkene (*E*-**3a**) and its iridium(I) complex (**4**) were each characterized crystallographically (Figures 1 and 2).[20] Importantly, the structural data were consistent with the enantiomeric purity of these new phosphaalkene species and the retention of the (*S*)-configuration from L-valine.[21] The P=C bond length of complex **4** [1.663(5) Å] is similar in length to the free ligand *E*-**3a** [1.679(2) Å] and is typical of the bond lengths found for P=C bonds. This observation is similar to that observed between structures of π-accepting ligand dpcb and its metal complexes and cannot solely be used to judge the π-acceptor properties of the ligand.[22] Interestingly, the angle at phosphorus expands significantly upon complexation and approaches

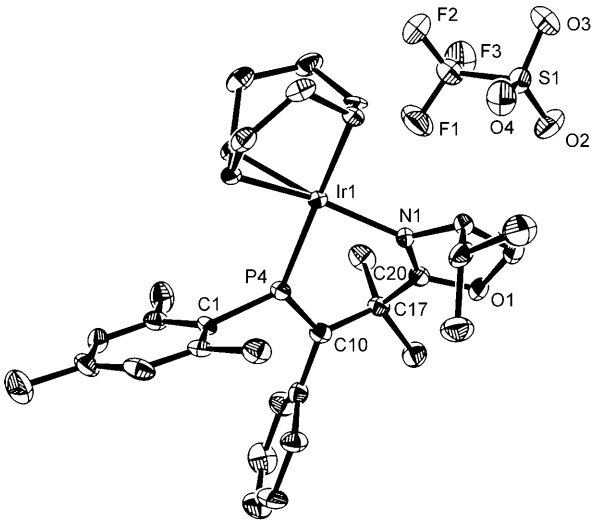


Figure 2. Molecular structure of **4** (50% probability ellipsoid). All hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: P(4)–C(1) 1.806(5), P(4)–C(10) 1.663(5), C(10)–C(17) 1.546(6), C(17)–C(20) 1.514(7), C(20)–N(1) 1.290(6), C(20)–O(1) 1.335(5), P(4)–Ir(1) 2.212(1), N(1)–Ir(1) 2.077(4); C(1)-P(4)-C(10) 114.3(2), P(4)-C(10)-C(17) 118.5(4), C(10)-C(17)-C(20) 111.3(4), C(17)-C(20)-N(1) 129.4(4), C(17)-C(20)-O(1) 114.7(4), C(20)-N(1)-Ir(1) 129.1(3), N(1)-Ir(1)-P(4) 85.6(1), Ir(1)-P(4)-C(10) 121.0(2).

ideal sp^2 hybridization [C-P-C = 105.3(1)° in *E*-**3a**, 114.3(2)° in **4**]. The P–Ir bond in **4** [2.212(1) Å] is shorter than that found in a phosphinine–iridium(I) complex [ca. 2.4 Å],[23] a phosphaferrocene–iridium(I) complex [avg. 2.298(2) Å),[24] ans a dpcb–iridium(III) complex [avg. 2.525(21) Å].[19] To our knowledge, these are the only other structurally characterized iridium complexes containing sp^2 phosphorus. For comparison, an analogous iridium(I)–cod complex containing the Pfaltz ligand, Ph_2P-C_6H_4(2-ox), exhibits a P–Ir bond length of 2.266(3) Å which is longer than that found in **4**.[25] The Ir–N distance in **4** [2.077(4) Å] is also similar to that found in the Pfaltz complex [2.119(7) Å].

In closing, we report the synthesis of the first examples of a new class of enantiomerically pure phosphaalkenes and, by forming an iridium(I) complex, demonstrate their effectiveness as a bidentate chelating ligand. This air-stable phosphaalkene is of considerable interest as a π-accepting ligand in asymmetric catalysis, a topic which is currently under active investigation.

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