New electron-rich chiral phosphines for asymmetric catalysis

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6 consists of a butterfly tetrahedral cluster of four osmium atoms bridged at the wingtips by an untransformed DMT ligand.[9,14]

We believe that the bridging coordination of the DMT ligand in 3 may play an important role in the ring-opening process.[15] Curiously, the metallacycle formation, as observed in the formation of 4, contrasts with the decomposition of thietane on molybdenum surfaces, where the principal product, cyclopropane, is believed to be formed without the formation of a metallacyclic intermediate.[4]

Acknowledgment. These studies were supported by the Office of Basic Energy Sciences of the U.S. Department of Energy.

Supplementary Material Available: An ORTEP diagram of 3 and tables of crystal data, positional and thermal parameters, and bond distances and angles for the structural analyses of 3–6 (35 pages); tables of structure factor amplitudes for 3–6 (62 pages). Ordering information is given on any current masthead page.

(14) The structure was refined (2678 reflections) to the final residuals $R = 0.029$ and $R_w = 0.030$.

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New Electron-Rich Chiral Phosphines for Asymmetric Catalysis†

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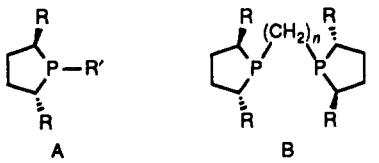
Summary: We describe a new series of chiral mono- and bidentate 2,5-disubstituted phospholanes and demonstrate their use as ligands in asymmetric catalysis. Rhodium complexes bearing the new phosphine ligands were prepared and characterized by X-ray crystallography. These complexes act as efficient catalyst precursors for the enantioselective hydrogenation of unsaturated substrates.

The synthesis of new chiral ligands for transition metals is an essential component for the development of novel catalytic systems exhibiting unique reactivity and high enantioselectivity. In general, some of the most successful chiral ligands used for asymmetric catalysis are chelating phosphines possessing a C_2 symmetry axis.[1] Noteworthy in this regard are the recently described BINAP ligands used by Noyori and co-workers to prepare Rh and Ru catalysts exhibiting very high enantioselectivities in hydrogenation and isomerization reactions.[2] The synthesis of optically pure asymmetric phosphines often involves tedious routes that are limited to only one antipode or require a resolution step. In addition, most chiral phosphines to date bear at least two aryl substituents on phosphorus, rendering that center relatively electron-poor.[3] In fact, the mechanism of asymmetric induction with these phosphines has been intimately linked to the proper conformational relationship between the phenyl rings on the phosphorus centers.[1] Our primary objective has been the development of efficient routes to new, chiral electron-rich phospholanes (A and B) analogous to known C_2-symmetric heterocycles, which are well-documented to provide high



levels of absolute stereocontrol in both stoichiometric and catalytic transformations.[4] We report a versatile route to these asymmetric phosphines, as well as the preparation and characterization of several rhodium complexes that act as efficient catalyst precursors for the asymmetric hydrogenation of unsaturated substrates.

Masamune and co-workers recently reported[5] the use of baker's yeast for the reduction of 2,5-hexanedione to the (*S,S*)-diol **1a** (R = CH_3), followed by reaction with MsCl and closure ultimately to afford (2*R*,5*R*)-2,5-dimethylpyrrolidine. Our initial studies utilized this same approach to prepare the corresponding bis(mesylate), which upon treatment with Li_2PPh provided (2*R*,5*R*)-2,5-dimethyl-1-phenylphospholane[6] ((*R,R*)-**2a**) in 76% isolated yield. Enzymatic reductions, however, generally provide only one enantiomer of a desired product and often suffer from inherent limitations such as high substrate specificity, low product yields, and involved isolation procedures.[7] We have developed a new three-step process that affords large quantities of either antipode of a series of chiral 2,5-disubstituted diols **1** (Scheme I). The first step introduces the desired chirality and utilized Noyori's Ru(BINAP) catalysts[8] for the asymmetric reduction of β-keto esters to

†Contribution No. 5476.

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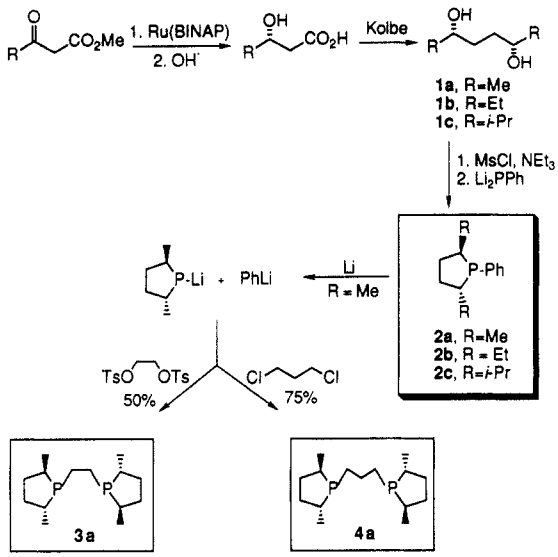
Scheme I



the corresponding β-hydroxy esters. Hydrolysis (KOH) provides the free carboxylic acids, which are then subjected to electrochemical Kolbe coupling[9] to afford the desired chiral (and crystalline) diols **1** directly in reasonable yield (55–70%). The availability of enantiomerically pure diols **1** provides access to optically pure phospholanes A and B bearing assorted R substituents. In fact, from the diols (*R,R*)-**1a**, (*R,R*)-**1b**, and (*S,S*)-**1c** (which are inaccessible from yeast reductions) we have prepared the corresponding phospholanes (*S,S*)-**2a**, (*S,S*)-**2b**, and (*R,R*)-**2c** (Scheme I). It also should be noted that this practical route to diols **1** should allow easy entry into the corresponding chiral 2,5-disubstituted pyrrolidines,[5,10] which have proven difficult to synthesize yet have wide-ranging applications in asymmetric synthesis.[4]

Further elaboration of the phospholane core of (*R,R*)-**2a** relied on selective cleavage of the phenyl group. Indeed, treatment of (*R,R*)-**2a** with clean Li metal in THF produced a mixture of the lithium phosphide (A, R = Me, R′ = Li) and PhLi (Scheme I). Reacting this mixture *directly* with ethylene glycol di-*p*-tosylate or 1,3-dichloropropane (0.5 equiv) at 25 °C gave rise to the chelating bis(phosphines) (*R,R*)-**3a** and (*R,R*)-**4a**, respectively. Analogously, the antipodes (*S,S*)-**3a** and (*S,S*)-**4a** are accessible from (*S,S*)-**2a**.

Cationic rhodium complexes **5–7**, $[(COD)Rh(PR_3)_2]^+A^-$ (A = PF_6, SbF_6; COD = 1,5-cyclooctadiene), bearing phosphines (*R,R*)-**2a**, (*R,R*)-**3a**, and (*R,R*)-**4a**, respectively, have been prepared by standard methods[11] and structurally characterized by X-ray crystallography.[12] An ORTEP diagram of [(COD)Rh((*R,R*)-**3a**)]$^+SbF_6^-$ (**6**) illustrates the C_2-symmetric environment imposed by these ligand systems (Figure 1). Of particular interest is the large dihedral angle (24°) between the P–Rh–P plane and the plane defined by the COD olefin midpoints and Rh. Strong steric interactions between the asymmetric phosphine ligand and COD are responsible for this distortion from the expected square-planar geometry. Similar distortions are seen in **5** and **7**,[13] as well as in a related Rh complex bearing the chiral ligand BINAP,[14] and indicate a highly asymmetric environment that should strongly influence π-facial selectivity during binding of prochiral unsaturated substrates.

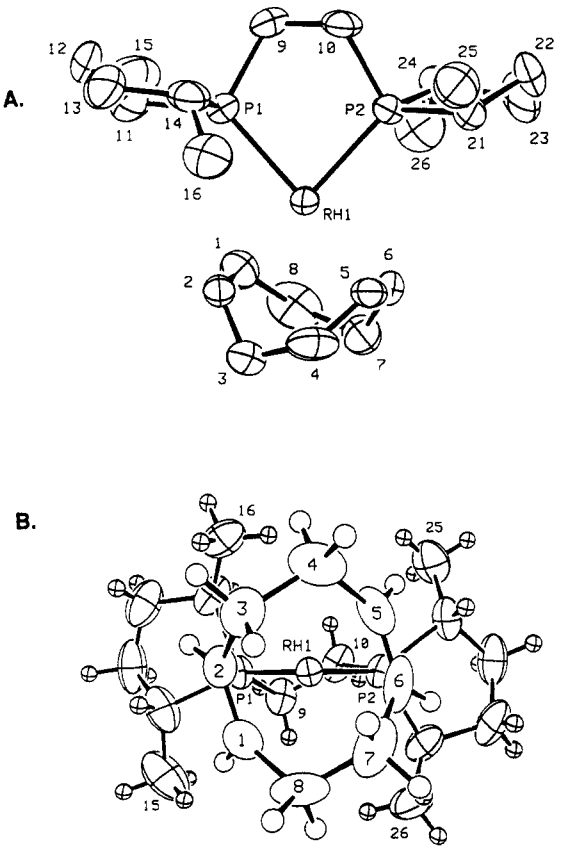


Figure 1. ORTEP drawings of the rhodium complex [(COD)Rh((*R,R*)-**3a**)]$^+SbF_6^-$ (**6**): (A) top view, hydrogen atoms and the SbF_6^- anion omitted for clarity; (B) front view, perspective diagram of **6** showing the rotated 1,5-cyclooctadiene ligand. Selected bond distances (Å) and angles (deg) are as follows: Rh1–P1 = 2.258 (2), Rh1–P2 = 2.276 (2), Rh1–C1 = 2.209 (7), Rh1–C2 = 2.268 (6), Rh1–C5 = 2.211 (6), Rh1–C6 = 2.273 (7); P1–Rh1–P2 = 83.25 (6), C1–Rh1–C5 = 94.6 (3), C2–Rh1–C6 = 86.7 (6).

Preliminary experiments indicate that the rhodium complexes **5–7** behave as efficient precursors for the enantioselective hydrogenation of unsaturated substrates. For example, methyl acetamidocinnamate and dimethyl itaconate are hydrogenated to the corresponding phenylalanine and succinate derivatives in high yield (quantitative by GC and NMR) and with good enantioselectivity (85% ee and 91% ee, respectively) under mild conditions (0.2 mol % of **6**, 1 atm of H_2, 25 °C). These results compare favorably to those obtained with known asymmetric hydrogenation catalysts[1d] and reveal the great potential of these ligands in asymmetric catalysis.

Studies involving chiral 2,5-disubstituted phospholanes (A and B) bearing different R groups are in progress. We currently are utilizing these and related electron-rich chiral

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(12) Crystal data for $C_{22}H_{40}F_6P_2RhSb$ (**6**): orthorhombic, $P2_12_12_1$ (No. 19), a = 14.186 (3) Å, b = 16.137 (4) Å, c = 11.825 (3) Å, T = −100 °C, V = 2707 Å^3, Mo Kα radiation, μ_{calcd} = 17.72 cm^{-1}, d_{calcd} = 1.732 g cm^{-3}, Z = 4, fw = 705.17. The structure was solved by direct methods and refined by a full-matrix least-squares procedure to residuals of R = 0.038, R_w = 0.036, and GOF = 1.07 for 4624 unique reflections with $I > 3.0\sigma(I)$ and 289 variables. Full structural details are given as supplementary material.

(13) Details of the structural characterization of complexes **5** and **7** will be published separately.

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phosphines in asymmetric transformations catalyzed by both early- and late-transition-metal complexes.

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Supplementary Material Available: Experimental details, including preparations and spectral and analytical data, for compounds 1–7, X-ray diffraction data for **6**, including tables of atomic coordinates, thermal parameters, bond distances, and bond angles, and a perspective ORTEP diagram of **6** (Figure 1S) with full atom labels (14 pages). Ordering information is given on any current masthead page.

Articles

Niobocene Chemistry: Acetylene Hydrido, Acetylene Alkenyl, and Carbenoid Butadienyl Complexes

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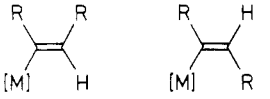
The acetylene hydrido complexes $Cp_2NbH(C_2R_2)$ (**2a**, R = Ph, known; **2b**, R = $SiMe_3$; **2c**, R = Et) were prepared from Cp_2NbH_3/RC≡CR by thermal substitution, and **2d** (R = Me) was obtained from **2b**/MeC≡CMe by a photochemical ligand displacement reaction. The complexes **2** insert acetylenes (as e.g. MeC≡CMe, PhC≡CH, HC≡CCO_2Me) by a nonmigratory insertion process. Stable insertion products $Cp_2Nb(Me_3SiC{\equiv}CSiMe_3)(CR^2{=}CHR^3)$ (**4g**, R^2 = CO_2Me, R^3 = H; **4h**, R^2 = COMe, R^3 = H; **4i**, R^2, R^3 = CO_2Me, *E* isomer) were obtained from **2b**. The *E* configuration of the alkenyl group in **4i** was established from ^{13}C NMR data and by X-ray work: space group $P2_12_12_1$ (No. 19), a = 1405.3 (2) pm, b = 2012.0 (3) pm, c = 965.6 (2) pm, Z = 4; R = 0.034, R_w = 0.036. With less sterically crowded acetylene hydrido compounds **2**, insertion is followed by rearrangement to give the novel carbenoid complexes $Cp_2Nb(CR^1CR^1CR^2CHR^3)$ (**3**). The crystal structure of **3d** (R^1 = Et, R^2, R^3 = CO_2Me) was determined: space group $P2_1/n$ (No. 14), a = 1649.3 (1) pm, b = 840.4 (1) pm, c = 1594.1 (2) pm, β = 116.52 (1)°, Z = 4; R = 0.023, R_w = 0.024. The bonding in complexes **3** is intermediate between a 1,4-η^2-2-buten-1-yl-4-ylidene and a 1,3,4-η^3-1,3-butadienyl situation.

Introduction

The insertion of acetylenes into metal–hydrogen bonds represents one of the fundamental processes of organometallic chemistry[1] and continues to attract considerable interest,[2-6] especially in terms of the stereochemistry of the resulting alkenyl products and in terms of reaction mechanisms. A priori, cis insertion results in formation of (*E*)-alkenyl products A, while the isomeric *Z* products



A B

B are expected from trans insertion reactions. In practice the stereochemistry of the primary insertion step may be obscured by subsequent isomerization steps.

Broadly, two types of insertion reactions can be discerned, migratory and the nonmigratory insertions. Migratory acetylene insertions resemble the better known migratory olefin insertions[7] and thus should be cis stereospecific. They require a vacant site at the metal center or a substitution-labile ligand to be replaced with the incoming acetylene. In contrast, hydrides that are coordinatively saturated and substitution inert, as e.g. Cp_2ReH, cannot undergo migratory insertion. Such hydrides do, however, insert *activated* acetylenes (HC≡CX or XC≡CX with X = CN, COMe, CO_2Me, CF_3), producing alkenyl complexes of varying stereochemistry. These reactions may be called nonmigratory insertions.

In previous work we have shown that the reactions of the bent metallocene hydrides Cp_2ReH, Cp_2MoH_2, and Cp_2WH_2 with disubstituted activated acetylenes are stereospecific trans insertions *in all cases*.[2] However, the closely related hydride $Cp_2NbH(CO)$ undergoes nonmigratory insertion with dimethyl acetylenedicarboxylate to give, under kinetic control, a mixture of (*Z*)- and (*E*)-alkenyl isomers.[5] In this paper we turn to the corresponding

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