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Rhodium-catalyzed asymmetric olefin hydrogenation by easily accessible aniline- and pyridine-derived chiral phosphites

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ABSTRACT

An aniline- and two pyridine-derived (R)-BINOL-based *P,N*-containing phosphite ligands have been synthesized via a one-pot procedure. Treatment of the aniline-derived ligand with 1 equiv of $[Rh(COD)_2]BF_4$ yielded a mixture of a *P,N*-chelate complex and a biligated *P*-monodentate complex (exclusively obtained by treatment of the ligand with rhodium in a ratio of 2:1), while the pyridine analogues led to the corresponding *P,N*-bidentate complexes as unique species. For the first time, such phosphites were studied for rhodium-catalyzed enantioselective olefin hydrogenation. At room temperature, the aniline-derived ligand was found to be more active and selective compared to the pyridine analogues, which can probably be attributed to its different coordination mode and the formation of a biligated *P*-monodentate complex.

Transition metal asymmetric hydrogenation is a highly attractive strategy for gaining access to enantiomerically pure compounds in the development of pharmaceuticals, agrochemicals, fragrances, and fine chemicals, and thus the development of new chiral ligands, which provide high activity, selectivity, and stability remains an important challenge.[1,2] Hybrid chelating ligands, and in particular ligands bearing phosphorus and nitrogen donors as the most abundant hybrids, are of significant interest due to the improved catalytic activity of their transition metal complexes in a variety of homogeneously catalyzed reactions,[3] and also in the development of new reactions.[4] Chiral *P,N*-ligands, which bear 'soft' and 'hard' donors and obvious electronic asymmetry, are the most widely used heterodentate ligands for asymmetric induction,[5,6] and they have also been used successfully to introduce, in one step, two or more stereogenic centers into a prochiral substrate.[7]

Phosphite ligands are easily prepared from readily available alcohols, they are less sensitive to air than phosphines, and they usually display high enantioselectivities. Thus they constitute an extremely attractive class of chiral ligands for asymmetric catalysis.[8] The first highly enantioselective Rh-catalyzed hydrogenation using chiral monophosphite ligands was reported in 2000 by Reetz,[9] and this was elaborated in further studies.[8,10] Extensive investigations by Reetz showed that the efficacy of BINOL-based monophosphites in Rh-catalyzed asymmetric hydrogenation was due to two important features: (a) two monodentate ligands are attached to the metal in the transition state of the hydrogenation, and (b) the catalytic system obeys the lock-and-key mechanism.[11] Reetz also developed a new approach to combinatorial homogeneous transition metal catalysis by the use of mixtures of chiral monodentate ligands, which not only form homocombinations, but also heterocombinations.[12] High enantioselectivity can also be achieved by using mixtures comprising a BINOL-derived *P*-ligand in combination with an achiral *P*-compound.[13]

Significant attention has also been focused on bidentate *P,N*-phosphites. The synthesis of the first *P,N*-phosphite ligand and its rhodium complex was reported in 1993 by Gavrilov,[14] but the major contribution for the design of these systems for asymmetric catalysis was started in 1997 by Pfaltz.[15] Since then, impressive progress in the field has been made, and applications of *P,N*-phosphites in asymmetric catalysis include Rh-catalyzed hydroformylation,[16] Rh-catalyzed hydrosilylation–oxidation,[16b,17] Rh-catalyzed hydroboration–oxidation,[16c,18] Ni-catalyzed hydrovinylation,[19] Ni-catalyzed 1,2-addition reactions to aldehydes,[20] Pd-catalyzed allylic substitution,[15b,16c,17b,c,21–25] Pd-catalyzed Heck reaction,[26] and Cu-catalyzed 1,4-addition reactions to enones.[15a,22,27] Rh-, Ir-, and even Pd-catalyzed asymmetric hydrogenation has also successfully been achieved using *P,N*-phosphites, in which the nitrogen atom is part of an oxazoline[16c,21a,b,28] (with the first example being a TADDOL-based phosphite-oxazoline),[21] oxazole,[29] thiazole,[29] or ferrocenylimino[24g,30] moiety.

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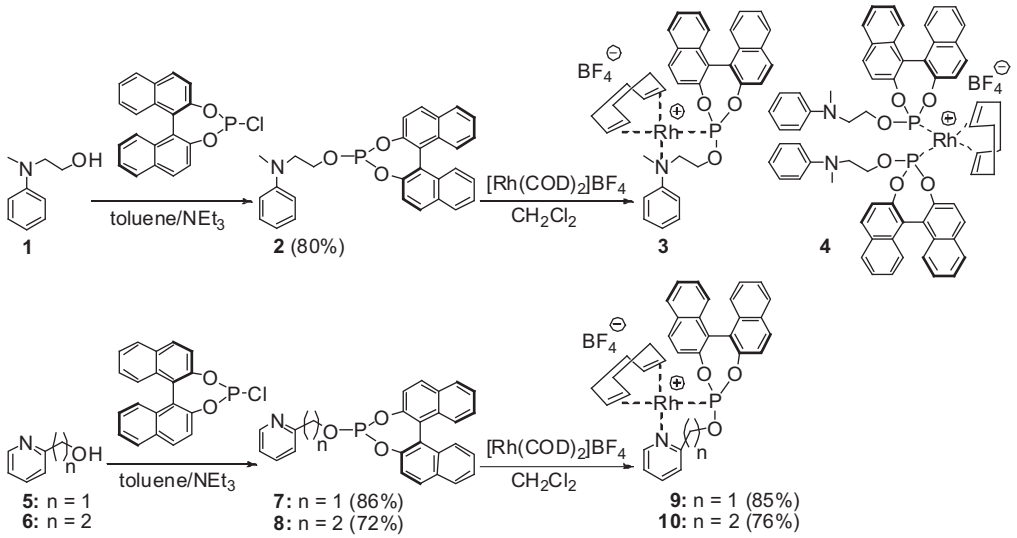
We have previously reported a number of *P*,*N*-containing ligands derived from a substituted aniline moiety for transition-metal homogeneous catalysis.[31] Herein, we report the synthesis of a new aniline-derived phosphite ligand and its coordination chemistry with rhodium. The ligand was evaluated in the Rh-catalyzed asymmetric hydrogenation of prochiral olefins as the first study concerning the application of *P*,*N*-containing phosphites with the nitrogen atom being part of an aniline moiety for asymmetric hydrogenation. An analogous *N*-phenyldiethanolamine-derived tridentate *P*,*N*,*P*-diphosphite, reported by us, resulted in low enantioselectivities (ee <29%) in asymmetric hydrogenation.[31h] For comparison purposes, we also synthesized two analogous pyridine-derived *P*,*N*-phosphites with sp^2-hybridised nitrogen atoms and their rhodium complexes. The ligands were tested in the hydrogenation reaction under identical conditions to the aniline analogue. Other pyridine-derived *P*,*N*-phosphites have not been evaluated for asymmetric hydrogenation to date. The synthesis of the (*S*)-BINOL analogue of one of the pyridine-derived ligands has previously been reported by Faraone, and evaluated in Pd-catalyzed allylic alkylation, but unfortunately, the reaction led to a racemic mixture attributed to the presence of different configurational isomers of the intermediate palladium complexes.[23]

The *P*,*N*-phosphite ligands **2**, **7**,[23] and **8**, based on the (*R*)-BINOL moiety, possessing chirality close to the phosphorus atom and also a rigid structure imposed by the binaphthyl group, were synthesized easily via a one-pot route by treatment of [(*R*)-(1,1′-binaphthalene-2,2′-diyl)]chlorophosphite with one equivalent of [*N*-(2-hydroxyethyl)-*N*-methyl]-aniline (**1**),[31a] 2-(hydroxymethyl)-pyridine (**5**), and 2-(2-hydroxyethyl)-pyridine (**6**), respectively, in toluene/triethylamine (Scheme 1).[32] The phosphite phosphorus atom displayed a singlet in the ^{31}P NMR spectra of **2**, **7**, and **8** at δ 140.39, 136.05, and 139.37, respectively, and the measured accurate masses corresponded exactly to the proposed formulas $[M+H]^+$: $C_{29}H_{25}NO_3P$, $C_{26}H_{19}NO_3P$, and $C_{27}H_{21}NO_3P$, respectively.

The ligands **2**, **7**, and **8** were treated with one equiv of $[Rh(COD)_2]BF_4$ in dichloromethane, and the coordination mode in the resulting complexes was investigated by NMR (^{1}H, ^{13}C, ^{31}P, COSY, HSQC, HMBC, DOSY) and ESI-MS experiments (Scheme 1).[33] It is known that a P,N-type donor ligand can act as a chelating bidentate ligand, a monodentate *P*-ligand, or a bridging ligand in dimeric species, and also a dynamic equilibrium could take place between the monomeric rhodium chelate complex and the dimer.[8c,16b,24b,34,35] The absence of a singlet assigned to the phosphite phosphorus atom of the free ligands in the ^{31}P NMR spectra of the reaction products indicated that all the ligands are bound to the metal, at least via the phosphorus atom. In addition, the absence of a $[L_2Rh_2(COD)_2]^+$ ion in the ESI-MS suggests the absence of binuclear rhodium species.

The complexity of the ^{1}H spectrum of the aniline-derived rhodium complex in CD_2Cl_2 provided evidence that the reaction of **2** with $[Rh(COD)_2]BF_4$ in a ratio of 1:1 is not selective, and that two main products were present in solution. Indeed, in addition to the $[(\mathbf{2})Rh(COD)]^+$ ion (complex **3**) in the ESI-MS, the $[(\mathbf{2})_2Rh(COD)]^+$ ion (complex **4**), in which two ligands are attached to rhodium, was also present. A chromatographic separation was not attempted due to the instability of the complexes. In the ^{1}H NMR spectrum, the NMe protons appear as two signals: (i) at δ 3.17, which is shifted to a lower field compared to the free ligand (δ 2.85), corresponding to a species with Rh–N coordination (*P*,*N*-chelate complex **3**); (ii) at δ 2.92, almost at the same position as that of the free ligand, indicating the formation of a species with the nitrogen atom being uncoordinated (biligated *P*-monodentate complex **4**). In accordance with the integrated intensities of these two peaks (3:5), the two species **3** and **4** are present in dichloromethane in a molar ratio of 1.2:1. The ^{31}P NMR spectrum in CD_2Cl_2 showed a doublet at δ 126.50 (J_{RhP} = 262.6 Hz) assigned to complex **3**, and another doublet of a higher intensity at δ 123.27 (J_{RhP} = 258.6 Hz) assigned to complex **4** (see below). The above-mentioned spectroscopic consideration for the formation of complexes **3** and **4** is strongly supported by the spectral data of the reaction product resulting from treatment of ligand **2** with $[Rh(COD)_2]BF_4$ in a ratio of 2:1. The reaction was now selective yielding only complex **4** as indicated by the $[(\mathbf{2})_2Rh(COD)]^+$ ion in the ESI-MS. DOSY spectroscopy also indicated the presence of one major component. In addition, the ^{31}P NMR spectrum of **4** in CD_2Cl_2 showed a unique doublet at δ 123.35 with a Rh–P coupling constant of 258.4 Hz. In the ^{1}H NMR spectrum, the NMe protons appear as one signal at δ 2.92, almost at the same position as that of the free ligand, indicating the absence of Rh–N coordination. The integrated intensities of the ligand **2** protons (NMe, CH_2O, CH_2N, and aromatics) compared to the 1,5-cyclooctadiene ligand (COD-*CH* and -*CH*$_2$) protons provide clear evidence that the ratio of **2**/COD in the metal complex **4** is equal to 2:1. The COD ligand is part of complex **4** with the COD-*CH* protons at δ 5.88 and 4.40 in the ^{1}H NMR spectrum, and the COD-*C*H carbons at δ 109.58–109.41 in the ^{13}C NMR spectrum of **4**.



Scheme 1. Synthesis of aniline- and pyridine-derived chiral phosphite ligands and their rhodium complexes.