Homogeneous Chiral Catalysis

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A C_3-Symmetric Palladium Catalyst with a Phosphorus-Based Tripodal Ligand**

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C_3 symmetry is intriguing in chemistry, therefore the synthesis of tripodal ligands and their applications in selective catalysts are receiving increasing interest.[1–4] Most of the C_3-symmetric metal complexes synthesized to date are based on nitrogen-based tripodal ligands,[2] although examples with ligands coordinating through oxygen and phosphorus have also been reported.[3,4] Most of these ligands are conformationally flexible, and the way they coordinate to the metal center is open to question in many cases. Gade et al. have noted the advantage of using ligands that can provide a relatively rigid and well-defined coordination geometry.[5] Along these lines, they have reported the synthesis of chiral and achiral 1,1,1-tris(oxazolinyl)alkane ligands with the capability to facially coordinate to transition metals (Cu^{I}/Cu^{II}, Rh^{I}, Zn^{II}, and Sc^{III}) as a tridentate ligand. To our knowledge, no analogous rigid phosphorus-based tripodal ligands that are able to coordinate

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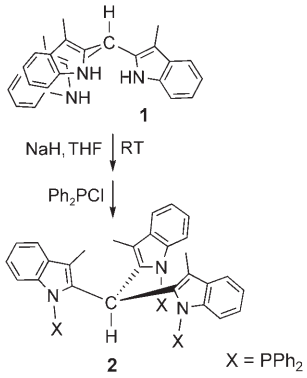
Supporting Information for this article (general procedures, details of the syntheses of 2–4, standard catalytic reactions, poisoning experiments with Hg, and asymmetric cross-coupling reactions, as well as crystal data for **2**–**4**) is available on the WWW under http://www.angewandte.org or from the author.

a transition metal to form C_3-symmetric complexes have appeared in the literature.

Herein, we report the synthesis of the tripodal ligand **2** (Scheme 1), which is suitable for the formation of C_3-symmetric palladium complexes. The potential of the racemic complex as a catalyst is demonstrated in several Suzuki cross-coupling reactions. Interestingly, this complex is axially chiral, and both enantiomers were isolated by chiral HPLC and tested for asymmetric catalysis in a model reaction. Although the cross-coupling product was obtained with an *ee* value of only 7%, this complex could be an intriguing lead structure for an interesting new series of chiral catalysts.

The synthesis of ligand **2** was achieved in high yield (75%) by the treatment of **1**[6] with sodium hydride followed by the addition of chlorodiphenylphosphane (Scheme 1). In the

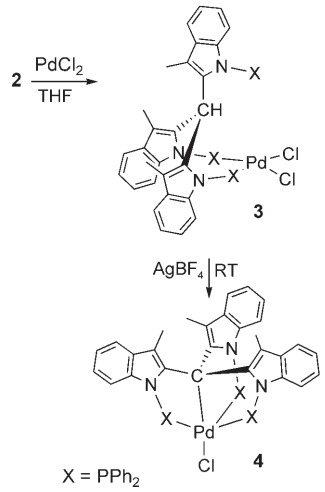


1 **2**

Scheme 1. Synthesis of tripodal ligand **2**.

^{1}H NMR of **2**, the methine hydrogen atom (H-C_{sp^3}) is highly deshielded ($\delta = 8.7$ ppm) and appears as a quadruplet, owing to coupling with three equivalent phosphorus atoms. X-ray analysis of a single crystal of this compound confirmed its structure and showed that the methine hydrogen atom (H(1)) is oriented towards the phosphanyl moieties (Figure 1).

To asses the binding capability of this new tripodal ligand, it was refluxed in a dry THF solution containing $PdCl_2$ (1.1 equiv) for 20 h. However, no C_3-symmetric complex was detected. Instead, compound **3**, with only two phosphorus atoms coordinated to the palladium center, was obtained with an 80% yield (Scheme 2). The structure of this complex was assigned by ^{1}H and ^{31}P NMR spectroscopy. X-ray analysis of a single crystal (grown in $CHCl_3/Et_2O$) confirmed this assignment and showed its square-planar geometry (Figure 2).



3 **4**

Scheme 2. Synthesis of palladium complexes **3** and **4**.

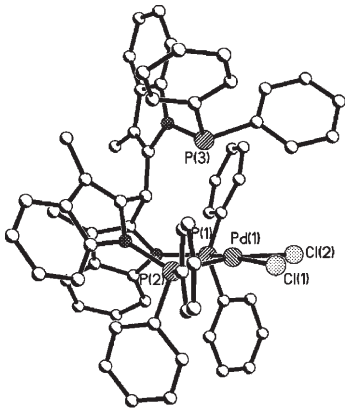


Figure 2. Molecular structure of palladium complex **3** (hydrogen atoms are omitted for clarity). Selected bond lengths [Å] and angles [°]: Pd(1)–P(1) 2.2783(19), Pd(1)–P(2) 2.3166(18), Pd(1)–Cl(1) 2.3263(19), Pd(1)–Cl(2) 2.3253(19); P(1)–Pd(1)–P(2) 104.01(6), P(1)–Pd(1)–Cl(2) 79.74(7), P(2)–Pd(1)–Cl(2) 170.51(7), P(2)–Pd(1)–Cl(1) 87.79(7).

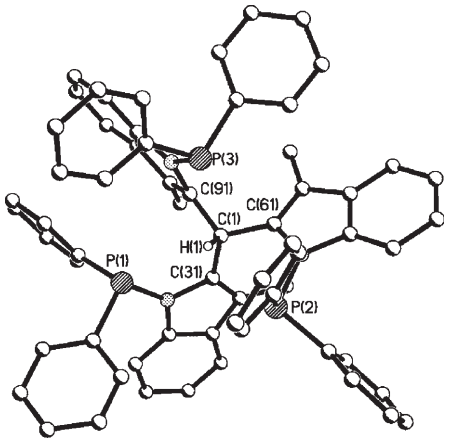


Figure 1. Molecular structure of tripodal ligand **2**, viewed along the virtual threefold molecular axis (hydrogen atoms, except H(1), are omitted for clarity). Selected bond angles [°]: C(91)–C(1)–C(31) 112.4(5), C(91)–C(1)–C(61) 116.0(4), C(31)–C(1)–C(61) 114.8(5).

In order to synthesize a C_3-symmetric structure, a dichloromethane solution of **3** was treated with silver tetrafluoroborate at room temperature for three hours (Scheme 2). Interestingly, the ^{31}P NMR spectrum of the resulting complex shows only one signal at $\delta = 49.4$ ppm, thereby indicating the formation of a threefold-symmetric complex. X-ray analysis of a single crystal (grown in $CHCl_3/Et_2O$) established the details of the molecular structure of compound **4**, which contains a pentacoordinate palladium atom bonded to the central carbon bridge of the tripod ligand (Figure 3). This result confirms the suitability of ligand **2** for facial coordination to metal atoms.

The ability of complex **4** to act as a catalyst in a model Ppalladium-based catalytic reaction was explored. Thus, it

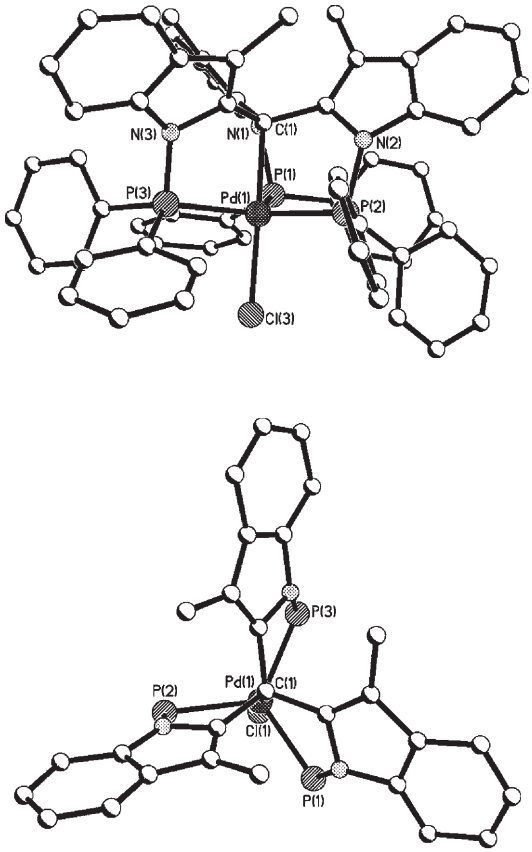
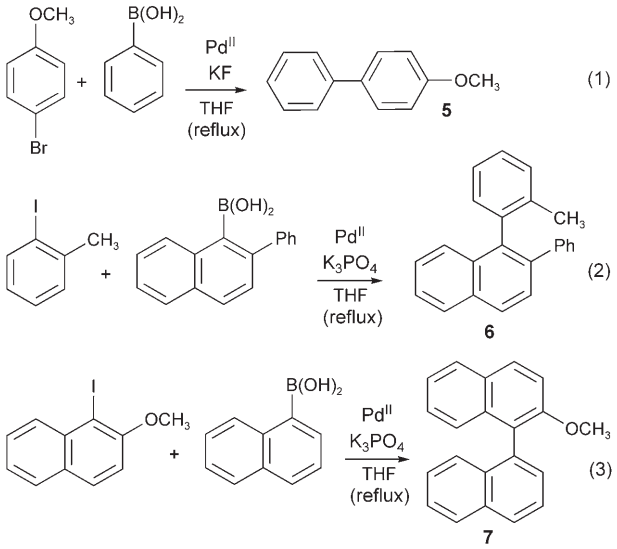


Figure 3. a) Molecular structure of palladium complex **4** (hydrogen atoms are omitted for clarity). Selected bond lengths [Å] and angles [°]: Pd(1)–C(1) 2.14(3), Pd(1)–P(1) 2.323(8), Pd(1)–P(3) 2.340(8), Pd(1)–P(2) 2.388(8), Pd(1)–Cl(1) 2.416(7); C(1)–Pd(1)–P(1) 83.7(9), C(1)–Pd(1)–P(3) 84.9(10), C(1)–Pd(1)–P(2) 83.7(9), C(1)–Pd(1)–Cl(1) 177.0(9). b) View along the virtual threefold axis of **4** (hydrogen atoms and the phenyl rings attached to the phosphorus atoms are omitted for clarity).

was used in various Suzuki reactions, which are well-known as being among the most versatile reactions for the selective construction of biaryl compounds.[7,8] Cross-coupling of *p*-bromoanisole and phenylboronic acid catalyzed by **4** was performed in refluxing dry THF in the presence of KF [Scheme 3, Eq. (1)]. As shown in Table 1 (runs 1–7), different reaction conditions were used. Comparison of the results with those obtained for complex **3** showed that a similar yield of *p*-methoxyphenylbenzene (**5**; higher than 90%) was obtained with both palladium complexes with three equivalents of phenylboronic acid and 0.5 mol% of catalyst. Catalyst **4** was also tested in the formation of rotationally more hindered biaryls, such as phenylnaphthyl [**6**; Scheme 3, Eq. (2); Table 1, run 8] and binaphthyl [**7**; Scheme 3, Eq. (3); Table 1, run 9]. This complex is also an efficient catalyst in the presence of iodo derivatives.

It is remarkable that in the case of complex **4**, the ^{31}P NMR spectrum of the crude reaction mixture after catalysis shows the presence of only one signal centered at $\delta = 47.4$ ppm (when using bromoanisole) or $\delta = 45.6$ ppm (when using the iodo derivatives), which is indicative of the formation of a new C_3-symmetric palladium complex. Fast-atom bombardment (FAB) GC/MS analysis was consistent



Scheme 3. Suzuki reactions catalyzed by **3** [Eq. (1)] or **4** [Eqs. (1)–(3)].

Table 1: Suzuki reactions with catalyst **3** or **4.**

	Reaction conditions[a]			Coupling yield[b] [%]		Biaryl
Run	Boronic acid [equiv]	Pd^{II} [%]	*t* [h]	Cat. **3**	Cat. **4**	
1	1.1	2	15	30	31	**5**
2	2	2	15	71	59	**5**
3	2	0.5	15	70	47	**5**
4	3	2	15	89	82	**5**
5	3	0.5	15	94	70	**5**
6	3	2	24	95	87	**5**
7	3	0.5	24	94	91	**5**
8	2	3	40	–	75	**6**
9	2	3	15	–	80	**7**

[a] Conditions: halogen compound (1 mmol), KF (3 mmol) or K_3PO_4 (2 mmol), palladium complex (0.5–2 mol%). Standard reaction: a solution of 4-bromoanisole (125 μL, 1 mmol), KF (174 mg, 3 mmol), $PhB(OH)_2$, and complex **3** or **4** was heated to reflux in THF (20 mL). The reaction mixture was then loaded onto a small plug of celite, washed with THF, and concentrated under vacuum. [b] Determined by ^{1}H NMR spectroscopy.

with the exchange of the chloride ligand in complex **4** by bromide or iodide during the catalytic process.[9] In addition, the C_3-symmetric complex recovered after the catalytic process exhibited high stability in six subsequent reactions (reaction time: 15 h), affording similar yields in all cycles. Poisoning experiments were also carried out with metallic mercury to test for the presence of a palladium colloid. When 50 equivalents of Hg^0 (relative to the palladium complex) were added to the reaction mixture at the start, the catalytic activity was not suppressed.[10]

Control experiments showed low (<10%) ligand exchange when complex **4** was treated with either bromoanisole or a bromoanisole/KF mixture in refluxing THF. However, no change was observed when the complex was heated in the presence of phenylboronic acid.

When using complex **3**, ^{31}P NMR analysis of the crude reaction mixture after the catalytic process revealed a high degree of metal-complex decomposition. This fact confirms that a compound of type **3** is not involved in the catalytic

reaction induced by **4**, where only one complex with C_3 symmetry is detected in the crude reaction mixture.

The view along the threefold molecular axis of the palladium complex reveals the C_3 chirality of the system in the solid state. In order to determine if the axial chirality of complex **4** remains in solution, attempts were made to exchange its chloride ligand for a chiral ligand, whereby the formation of diastereoisomers would lead to a doubling of the ^{31}P NMR signals and agree with the existence of **4** as a racemic mixture. As a first test of the feasibility of ligand exchange without loss of tripodal coordination, complex **4** was treated with $AgBF_4$ and then triphenylphosphane. The ^{31}P NMR spectrum of the complex shows a doublet at $\delta =$ 52.1 ppm for the phosphorus atoms of the tripodal ligand and a quadruplet at $\delta = 18.0$ ppm for the triphenylphosphane moiety, owing to P–P coupling (see Supporting Information). When using a chiral phosphane, such as (2*S*,5*S*)-2,5-dimethyl-1-phenylphospholane ((2*S*,5*S*)-**8**), the spectrum exhibits two doublets, at $\delta = 54.5$ and 53.3 ppm, and two quadruplets, at $\delta = 30.4$ and 28.2 ppm (see Supporting Information). Further confirmation of the formation of diastereoisomers was obtained by reaction of **4** with $AgBF_4$ followed by treatment with (*R*)-phenylethylamine: the ^{31}P NMR spectrum of the complex obtained shows two signals with the same intensity at $\delta = 52.9$ and 53.1 ppm (see Supporting Information). All these data indicate that the axial chirality of complex **4** is retained in solution.

Separation of the enantiomers was accomplished by chiral HPLC (Chirobiotic T, 1:3 hexane/ethyl acetate). Neither of them racemizes after heating under reflux in THF solution for 15 h, which is clear evidence that they are configurationally stable under the reaction conditions. The enantiomerically pure complex was tested for the asymmetric cross-coupling reaction between 1-iodo-2-methoxynaphthalene and 1-naphthylboronic acid, which led to compound **7** with only 7% *ee*. Despite the growing success of the Suzuki cross-coupling reaction for the construction of biaryls, its asymmetric variant still remains a challenge,[11–13] probably because of the inherent difficulty in coupling two sterically hindered arenes in a transition-metal-mediated process. Enantioselective couplings[13] have recently emerged as viable and more direct alternatives, thanks to the design of chiral ligands. However, no examples of an enantiomerically pure catalyst without chiral ligands has been used in a Suzuki reaction to date.

In summary, the rigid tripodal phosphorus-based ligand **2** has a facial-coordinating ability that allows it to form the C_3-symmetric palladium complex **4**. It has been successfully tested as a reusable catalyst in Suzuki cross-coupling. This complex, which has no chirality in either of the branches of the tripodal ligand but is intrinsically chiral, could be an intriguing lead structure for a new series of chiral catalysts.

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