ORGANIC LETTERS

2004
Vol. 6, No. 11
1833−1835

Development of Chiral Pincer Palladium Complexes Bearing a Pyrroloimidazolone Unit. Catalytic Use for Asymmetric Michael Addition

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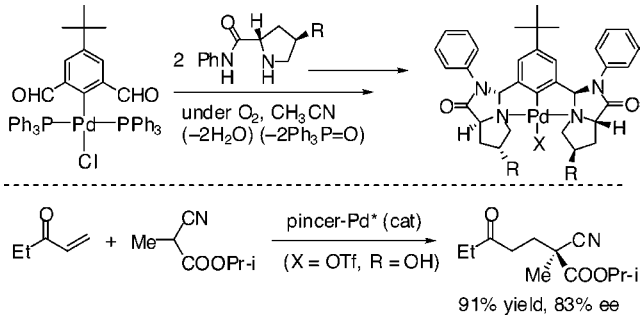
Received March 23, 2004

ABSTRACT



Novel pincer palladium complexes having chiral hexahydro-1*H*-pyrrolo[1,2-*c*]imidazolone groups were designed and prepared. Catalytic asymmetric Michael addition of isopropyl 2-cyanopropionate to ethyl vinyl ketone was catalyzed by the chiral pincer palladium complex to give isopropyl 2-cyano-2-methyl-5-oxoheptanoate with high enantioselectivity (up to 83% ee).

Organometallic complexes containing terdentate monoanionic ligands composed of anionic aryl carbon atoms and two mutually trans-chelating donor sites at the 2,6-positions of the aromatic ring (the so-called pincer complexes) have been recognized as a novel class of functional materials, and in particular, those having platinum group metals have found widespread utility as catalysts for several organic transformations.[1,2] We have recently found that hexahydro-1*H*-pyrrolo-[1,2-*c*]imidazolone serves as an effective chiral auxiliary.[3] These results prompted us to prepare chiral pincer complexes having pyrroloimidazolone coordinating groups and to examine their catalytic use in asymmetrtic synthetic reactions. Here we report the preparation of novel chiral pincer palladium complexes having pyrroloimidazolone moieties, which exhibited high catalytic activity and high stereoselectivity in the asymmetric Michael reaction (up to 83% ee).[4]

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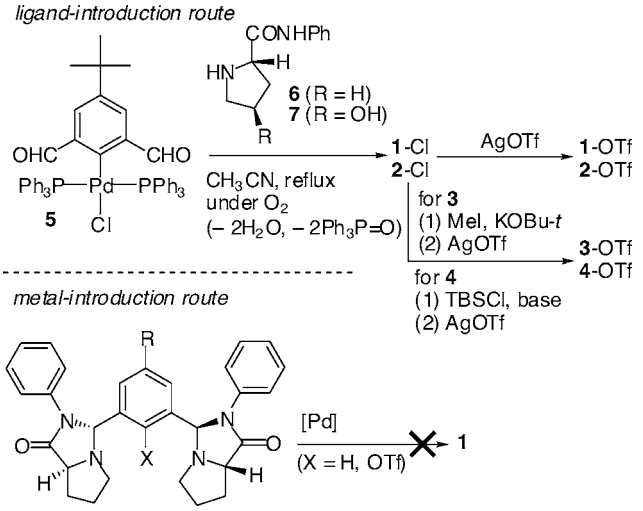
10.1021/ol0494515 CCC: $27.50
Published on Web 05/05/2004

The pincer palladium complexes **1**−**4** were prepared by the introduction of pyrroloimidazolones to the aromatic ring of an arylpalladium complex (ligand-introduction route) (Scheme 1). Thus, *trans*-chloro(4-*tert*-butyl-2,6-diformyl-

Scheme 1



phenyl)bis(triphenylphosphine)palladium (**5**) was treated with 5 equiv of the proline anilide **6** in refluxing acetonitrile under an oxygen atmosphere to give 98% yield of the pincer palladium complex **1**-Cl (Figure 1) via condensation of the

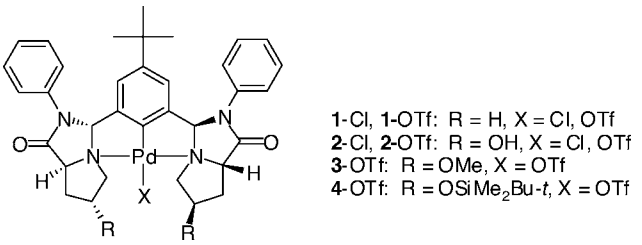


Figure 1. Pincer Pd complexes having pyrroloimidazolone units.

2,6-formyl groups with **6** and subsequent ligand exchange by the resulting pyrroloimidazolone forming the Pd−N bonds. Similarly, the complex **2**-Cl was obtained in 87% yield by the reaction of **5** with the anilide **7** derived from *trans*-4-hydroxy-L-proline. Since the corresponding pincer ligands showed little reactivity to palladium (metal-introduction route), presumably due to the steric bulkiness of the pyrroloimidazolone groups, the ligand-introduction route would provide an alternative synthetic protocol for pincer complexes having sterically demanding groups. The chloride ligands of **1** and **2** were replaced by the more labile triflate ligand by treatment with silver triflate to give **1**-OTf and **2**-OTf in 95% and 94% yields, respectively. The pincer palladium complexes **3**-OTf and **4**-OTf having methoxy and silyloxy groups on their pyrrole rings were also prepared from **2**-Cl in 76% and 83% yields, respectively, via etherification followed by the treatment with silver triflate.

The X-ray structure of **1**-Cl unambiguously establishes that the product is the expected pincer complex in which the two nitrogen atoms (N1 and N3) of the pyrroloimidazolone moieties coordinate to Pd atom attached to aromatic carbon (Figure 2).[5] The structures of the pincer complexes **2**−**4**

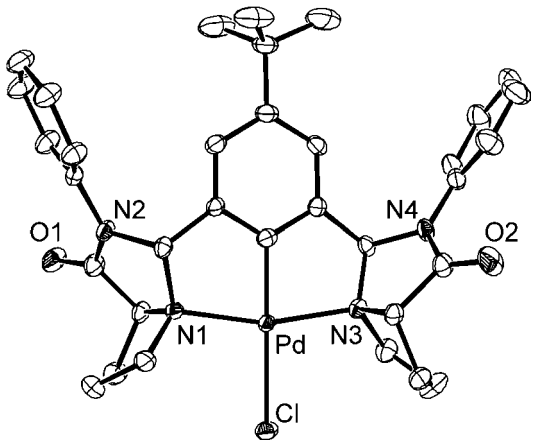


Figure 2. ORTEP drawing of the pincer Pd complex **1**-Cl (50% probability). All hydrogen atoms and solvated toluene molecules were omitted for clarity.

which have functional groups on their pyrrole rings could not be determined by X-ray analysis because of the difficulty in obtaining adequate single crystals suitable for X-ray diffraction. Molecular modeling study of the functionalized pincer complexes indicates that the functional substituents on the pyrrole rings would play an essential role in the asymmetric induction. Thus, as can be seen from the schematic structure of a pyrrole-substituted pincer complex shown in Figure 3, the substituents on the pyrrole rings (R

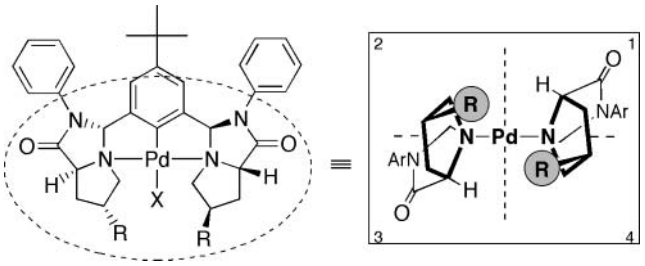
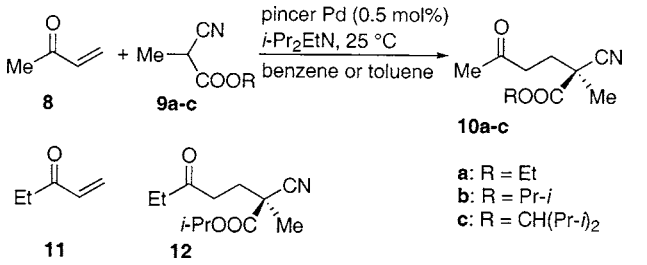


Figure 3. Schematic structure of a pyrrole-substituted pincer complex (e.g., compound **2**). The aromatic ligand moiety in the pincer ligand is omitted for clarity.

in Figure 3) are situated in close proximity to the metal species in the regions of the second and fourth quadrants (from the viewpoint of metal side) to provide effective chiral surroundings.

To explore the enantiocontrolling potential of the chiral pincer palladium complexes, we elected to study the catalytic asymmetric Michael reaction of vinyl ketones and α-cyanocarboxylates as nucleophiles[6] which has attracted increasing attention since the products bear a quaternary carbon center with various functionalities.[7] It has been reported that the Michael addition of cyanocarboxylates is catalyzed by chiral phosphine−rhodium complexes with high enantioselectivity. Rather surprisingly, only scattered attention has been paid to the use of palladium catalysts for the Michael addition, despite their frequent use for various catalytic asymmetric carbon−carbon forming reactions.[8] The reaction of methyl vinyl ketone (**8**) with methyl 2-cyanopropionate (**9a**) was performed in benzene at 25 °C in the presence of 0.5 mol % of the chiral pincer palladium complex and 0.1 equiv of diisopropylethylamine (Scheme 2) to give the desired

Scheme 2



Michael adduct **10a** which was readily isolated by Kugelrohr distillation. The enantiomeric purity and the absolute configuration of **10a** were determined by GC analysis with a chiral stationary phase column (Cyclodex CB) and measurement of specific rotation value, respectively. The representative results are summarized in Table 1. Among the chiral pincer catalysts **1**−**4**, **2**-OTf bearing hydroxyl groups on the pyrrole rings turned out to be the best catalyst, giving **10a** with high enantioselectivity. Thus, the asymmetric Michael addition catalyzed by **2**-OTf afforded 81% ee (*S*) of the adduct ethyl 2-cyano-2-methyl-5-oxohexanoate (**10a**) in 89% yield (run 2). This selectivity is comparable to that of the best chiral pincer complexes known for this reaction.[7d]

Table 1. Asymmetric Michael Addition of α-Cyanoesters to Vinyl Ketones Using Chiral Pincer Complexes[a]

run	substrate	catalyst	time (h)	product	yield[b] (%)	% ee[c]
1	**8/9a**	**1**-OTf	3	**10a**	95	8
2	**8/9a**	**2**-OTf	4	**10a**	89	81
3	**8/9a**	**3**-OTf	3	**10a**	93	6
4	**8/9a**	**4**-OTf	4	**10a**	97	9
5	**8/9a**	**2**-Cl	144	**10a**	<2	
6	**8/9b**	**2**-OTf	4	**10b**	90	80
7[d]	**8/9c**	**2**-OTf	24	**10c**	93	80
8	**11/9b**	**2**-OTf	4	**12**	91	83

[a] All reactions were carried out in the presence of 0.5 mol % of pincer palladium complexes and 0.1 equiv of *i*-Pr$_2$EtN at 25 °C in benzene or toluene unless otherwise noted. [b] Isolated yield. [c] Determined by GC analysis (Cyclodex CB). [d] 1.0 mol % of **2**-OTf was used.

The pincer complexes **1**-OTf, **3**-OTf, and **4**-OTf, which lacked hydroxyl groups, were much less stereoselective and only gave 8% ee, 6% ee, and 9% ee of **10a**, respectively (runs 1, 3, and 4). It is also interesting to note that the chemical yield of the product **10a** is strongly affected by the anionic ligand of the pincer complexes. Thus, the Michael addition did not take place with complex **2**-Cl even after a reaction time of 144 h (run 5), whereas with **2**-OTf the reaction gave a high yield of the product in 4 h. Isopropyl ester **9b** and diisopropylmethyl ester **9c** underwent the Michael addition under similar conditions to give 80% ee (*S*) of both **10b** and **10c** in 90% and 93% yields, respectively (runs 6 and 7). The highest stereoselectivity was obtained when the reaction was carried out with ethyl vinyl ketone (**11**) and isopropyl cyanopropionate (**9b**) in the presence of the chiral pincer catalyst **2**-OTf to give 91% yield of the heptanoate (*S*)-**12** with 83% enantiomeric purity (run 8).

In summary, new chiral pincer complexes bearing pyrroloimidazolone groups were designed and prepared via ligand introduction protocol. The asymmetric Michael addtion of α-cyanocarboxylates to vinyl ketones was catalyzed by the pyrroloimidazolone palladium pincer complexes with high enantioselectivity.

Acknowledgment. This work was supported by the CREST program sponsored by JST. We also thank the JSPS (Creative Scientific Research, No. 13GS0024; Grant-in-Aid for Scientific Research, No.15205015) and the MEXT (Scientific Research on Priority Areas, Nos. 412 and 420) for partial financial support of this work.

Supporting Information Available: Characterization and experimental procedures for compounds **1**−**5**. Experimental procedure for the asymmetric Michael addition. X-ray data for **1**-Cl (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(5) Crystal data of **1**−Cl·toluene: $C_{41}H_{45}ClN_4O_2Pd$, orthorhombic, $P2_12_12_1$ (No. 19), a = 12.2613(5) Å, b = 12.4185(5) Å, c = 23.9133(11) Å, V = 3641.2(3) Å^3, Z = 4, R1 = 0.023, wR2 = 0.060, GOF = 0.94.

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