Synthesis and Structural Characterization of Palladium(II) Complexes of Chiral Bidentate *N*-Heterocyclic Carbene-Quinoline Ligands

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Keywords: *N*-heterocyclic carbene, Palladium, *trans* influence, chiral bidentate ligand

ABSTRACT: A new class of chiral Pd(II) complexes bearing a rigid, bidentate C,N-ligand are synthesized and characterized. The ligands are obtained in good yield via a simple five-step synthetic route beginning with cheap and commercially available amino alcohols. The structure of one of these new complexes is determined by X-ray crystallography. This data shows the expected large *trans* effect difference between the N and C donors (0.07 Å Pd–Cl bond length difference) as well as a boat conformation of the 6-membered chelate ring.

1. Introduction

N-Heterocyclic carbene (NHC) ligands have proven to be an important tool for the catalysis of many useful and varied organic reactions.¹ NHC ligands promote unique catalytic activity due to their strong sigma electron donor ability.² More recently, chiral NHC complexes have been increasingly used as powerful catalysts for the construction of asymmetric products.³ Selected examples of chiral NHC ligand designs are depicted in Figure 1. Simple NHCs with chiral substituents on nitrogen can suffer from free rotation about both the C–N and M–C bonds, thereby reducing the effect of the chiral environment on the ligand sphere (A). Controlling the relative orientation of the chiral substituents and the coordination environment is crucial for high stereoselectivity. One common strategy is to employ fused polycyclic NHCs which ensure constrained geometries through restricted rotation of the C–N bond (B).⁴ This also enforces the presentation of the chiral substituent towards the metal center. However, this does not guarantee a well-defined orientation of the chiral center with respect to the ligand sphere because of the possibility of free rotation about the M–C bond. Incorporating the NHC ligand into a bidentate (or tridentate) ligand structure fixes the orientation of the NHC relative to the ligand plane and ensures that the well-defined chiral environment of the fused ring system is not lost by free rotation. Both *C*₂-symmetric ligands with identical donors^{4b,5} (C) and electronically dissymmetric donor sets⁶ (D) have been previously used. One disadvantage to these approaches is that the chiral environment of the metal center is determined by the chirality of the ligand backbone in ways that are difficult to systematically vary.¹

Figure 1. Examples of chiral polycyclic imidazolium salts in the literature

Palladium(II) complexes bearing chiral bidentate quinoline-oxazoline (quinox) ligands have proven to be highly successful in several enantioselective reactions.⁷ These ligands have several advantages. First, they present a chiral substituent directly into the ligand coordination sphere by rigid bidentate coordination. Second, though it is not immediately obvious, the two nitrogen donors provide an electronically dissymmetric environment, due to the steric inability of the quinoline ligand to bind strongly to the metal center.^{7c} This asymmetry enforces selective coordination at the site adjacent to the chiral substituent. Third, it is easy to vary the chiral environment via the oxazoline substituent. However, the relatively low electron donor ability of the quinox ligand limits its use in Pd-catalyzed reactions. We hypothesized that replacing the oxazoline portion of the ligand with an NHC would generate a new class of chiral palladium(II) complexes that would mimic the rigid chiral environment of the quinox ligand while vastly changing its electronic nature, thereby opening up new modes of reactivity (Figure 2). Furthermore, by expanding the chelate size from a five-membered ring to a six-membered ring, the bite angle of the NHC complex would be increased over that of the corresponding quinox ligand, extending the chiral substituent further towards the ligand binding sites and thereby enhancing enantioselectivity. Herein we report the synthesis of these chiral bidentate ligands and include detailed structural information for a palladium(II) complex of one of them.

Figure 2. New Chiral N,C-bidentate Ligand Design.

2. Results and Discussion

2.1. Synthesis of ligands and their palladium complexes

The requisite fused bicyclic imidazoles were synthesized according to a modification of the procedure of Yanagisawa

(Scheme 1).⁸ Diamides **1a-1c** were constructed by coupling the relevant amino alcohols with *N*-formylalanine. These were then cyclized to oxazolines **2a-2c** by treatment with TsCl in good yields. Closure of the imidazole ring was achieved by dehydration with P₂O₅ to give bicyclic structures **3a-3c** in 25-48% overall yields.

Scheme 1. Synthesis of Chiral Bicyclic Imidazoles

To verify optical purity, *R* and *S* enantiomers of **3a** were separately synthesized from (*R*)- and (*S*)-phenylalaninol. No loss of enantiopurity could be detected by chiral HPLC.

Figure 3. Chiral Bidentate Ligands Synthesized

Alkylation of the imidazoles was achieved under standard conditions with 2-(bromomethyl)quinoline and 2-(bromomethyl)-6-methylpyridine to give ligands **4aa-4cb** in good yields (Figure 3). Direct palladation of the carbene with Pd(OAc)₂ was used to synthesize the palladium dihalide complexes using a modified version of Crabtree's method (Figure 4).⁹ Formation of the allylpalladium complex proceeded best via the intermediate silver complex, as in the method reported by Jarvo.¹⁰ Allylpalladium complex (**4aa**)Pd(allyl)Cl exists as a 1:1 mixture of diastereomers in solution due to syn/anti isomerism of the η³-allyl group.

Figure 4. Chiral bidentate palladium(II) complexes

Table 1. Selected bond distances (Å) and angles (deg) in (**4ba**)PdCl₂ compared to quinoxPdCl₂.^{7a}

	(4ba)PdCl ₂	(quinox)PdCl ₂
Pd–Cl (trans to quin N)	2.3111(4)	2.28, 2.27

Pd–Cl (trans to other L)	2.3810(4)	2.30, 2.29
Pd–N	2.0613(14)	2.17, 2.15
Pd–L	1.9543(16)	2.00, 2.02
N–Pd–L	86.65(7)	79, 79

2.2. Structural characterization of palladium complex

The structure of (**4ba**)PdCl₂ was determined by single crystal X-ray diffraction and is shown in Figure 5. The large difference in bond length between the two Pd–Cl bonds (Table 1) is notable, and can be attributed to the large *trans* influence difference between the NHC ligand and the quinoline. This difference is much larger than that observed in (quinox)PdCl₂.^{7a} Additionally, the absolute magnitudes of both Pd–Cl bond distances are also significantly larger than in the corresponding (quinox)PdCl₂ complex, indicative of the greater electron donating ability of the new N,C ligands.

Figure 5. ORTEP drawing of (**4ba**)PdCl₂ showing 50% probability ellipsoids (CCDC number 1527484)

Compared to the 5-membered (quinox)Pd chelate rings, the bite angle of the new 6-membered ring complexes increased from 79° to 87°. However, the expansion of the ring from five to six atoms also resulted in a substantial change in the chelate ring geometry and the orientation of the ligand substituents. Whereas the 5-membered ring in (quinox)PdCl₂ is nearly planar, the 6-membered ring in (**4ba**)PdCl₂ adopts a marked boat conformation with palladium at the bow of the boat, tilting the square plane of the Pd substantially away from the bulk of the ligand (average dihedral angle = 46°). This has the effect of removing the steric clash between the 8-hydrogen of the quinoline ring and the adjacent ligand coordination site. The greatly reduced Pd–N bond distance in (**4ba**)PdCl₂ compared to quinox (2.06 vs 2.16 Å) reveals that the absence of this steric clash allows the quinoline to bind more strongly to palladium in (**4ba**)PdCl₂. The change to the observed boat conformation also causes the chiral center in the oxazoline ring to tilt away from the ligand plane. The structural parameters for (**4ba**)PdCl₂ are similar to those reported by Douthwaite for the PdCl₂ complex of ligand D (Figure 1), which has been employed in allylic alkylation reactions.

Scheme 2. Attempted Reactions of Palladium Catalysts

2.3. Catalytic reactivity of the palladium complex

To assess the reactivity of these palladium complexes, allylic amination and alkylation reactions of cyclohexenyl methyl carbonate were attempted (Scheme 2). To our surprise, no desired product was observed under standard conditions. This contrasts with other NHC-palladium complexes in allylic amination and alkylation reactions,¹¹ which are known to be less reactive than phosphine complexes but still provide product at elevated temperatures. Attempted Hartwig-Buchwald coupling also failed to afford any desired product, even though nonchelating NHC-palladium complexes catalyze the same reaction.¹² The lack of reactivity of (4ca)PdBr₂ in standard reactions of NHC-Pd complexes is unexpected.

3. Conclusion

In conclusion, we have synthesized several members of a new class of rigid bidentate *N*-heterocyclic carbene/quinoline ligands and their derived palladium(II) complexes. X-ray crystallography reveals that the donor ability of both the NHC and quinoline donors is increased relative to the quinox ligands and that the difference in *trans* influence between the two donors is large. Expansion of the ring size from 5 to 6 atoms increased the bite angle, but also resulted in a change in chelate geometry from planar to boat, consequently changing the orientation of the chiral substituent and unexpectedly increasing the donating ability of the quinoline ligand. Unfortunately, the new complexes did not display any reactivity in allylation or Hartwig-Buchwald coupling reactions.

Acknowledgements

This work was supported by the National Science Foundation (grant #1266359).

Appendix A. Supplementary data

Supplementary data related to this article can be found at <URL>.

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