Tetrahedron 65 (2009) 2889–2897

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Convenient and efficient Suzuki–Miyaura cross-coupling reactions catalyzed by palladium complexes containing *N*,*N*,*O*-tridentate ligands

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ARTICLE INFO

Article history:
Received 14 October 2008
Received in revised form 23 January 2009
Accepted 6 February 2009
Available online 11 February 2009

Keywords:
N,*N*,*O*-Tridentate ligand
Suzuki–Miyaura cross-coupling reaction
Palladium complex
DFT methods

ABSTRACT

N,*N*,*O*-Tridentate ligands **1**–**9** were prepared from the condensation of amines with nine aromatic aldehydes or ketones. These ligands are thermally stable and neither air- nor moisture-sensitive. Combination of either 2-methoxy-6-[(pyridine-2-ylmethylimino)-methyl]-phenol, **1** or 2-(benzothiazol-2-yl-hydrazonomethyl)-4,6-di-*tert*-butyl-phenol, **6** with $Pd(OAc)_2$ furnished an excellent catalyst precursor for the Suzuki–Miyaura cross-coupling of various aryl bromides with arylboronic acids. The effects of varying solvents, bases, and ligand/palladium ratios on the performance of the coupling reaction were investigated. The molecular structures of both free ligand **1** and its palladium acetate complex **10** were determined by single-crystal X-ray diffraction methods. The DFT studies revealed that the catalytic performance of palladium complexes involving this type of a ligand may differ greatly upon a small variation in its structure.

1. Introduction

The ligand assisted palladium-catalyzed cross-coupling reactions are probably among the most frequently employed methods of carbon–carbon bond formation in organic synthesis. They have been applied to the synthesis of many organic compounds, especially those of complex natural products, supramolecular chemistry, and engineering materials such as conducting polymers, molecular wires, and liquid crystals.[1] The ligand choice is known to be crucial to the success of a catalytic reaction.[2] Therefore, tremendous efforts have been dedicated to the search for more efficient and affordable ligands. As a result, the design of novel ligands and transition metal catalysts capable of carrying out desired transformations with both high efficiency and high selectivity has become a fertile area of research.[3] Until now, phosphine-based ligands have remained to be the most popular selection in the palladium-catalyzed cross-coupling reactions.[4,1b] However, these ligands usually need to be handled under inert atmosphere or dry conditions. In addition, they sometimes suffer from significant P–C bond degradation at elevated temperatures, which leads to palladium aggregation and eventually affects the overall catalytic performance.[5] Recent application of phosphine-free ligands, such as *N*-heterocyclic carbenes, imines, oxime palladacycles, and diazabutadienes to metal-catalyzed synthetic transformations has opened new opportunities in catalysis.[6]

The object of this study was finding a versatile, robust, and easy-to-prepare catalyst system suitable for a wide range of C–C bond-forming processes. Therefore, the initial step was the selection of a potential catalyst class of ligands amenable to systematic structural and electronic variation. One of the appealing features of imine ligands is that both their steric and electronic properties may be tuned in a synthetically straightforward manner by variation of the corresponding aldehyde/ketone precursors.[7] The extraordinary thermal stability, insensitivity to both oxygen and moisture as well as ready availability and low cost of aromatic imines prompted us to study their effectiveness as ligands in palladium-catalyzed C–C bond-forming reactions and in Suzuki–Miyaura cross-coupling reaction, in particular.

2. Results and discussion

2.1. Preparations of *N*,*N*,*O*-tridentate ligands 1–9 and 1-chelated palladium complex 10

All the nine *N*,*N*,*O*-tridentate ligands, **1**–**9**, were prepared from the condensation of amines with corresponding aldehydes/ketones in methanol/ethanol as solvent.[8] They were characterized by spectroscopic methods such as ^1H, ^{13}C NMR as well as mass spectrometry (Fig. 1). Furthermore, the structure of ligand **1** was also verified by single-crystal X-ray diffraction method (Fig. 2).[9]

The preparation of **1**-chelated palladium complex **10** was achieved via the reaction of ligand **1** with one molar equivalent of $Pd(OAc)_2$ in THF. The formation of this palladium complex was confirmed by spectroscopic methods as well as single-crystal X-ray

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doi:10.1016/j.tet.2009.02.017

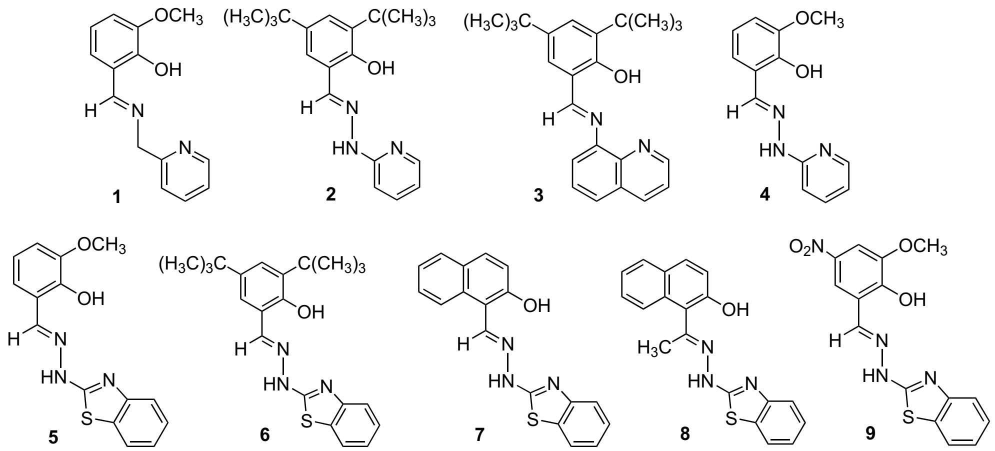

Figure 1. Some selected *N,N,O*-tridentate ligands **1**–**9**.

diffraction analysis.[10] The ORTEP diagram of **10** is depicted in Figure 2. As revealed, it is indeed an *N,N,O*-chelated palladium complex. The ∠N(1)–Pd(1)–N(2), ∠N(2)–Pd(1)–O(3), ∠O(3)–Pd(1)–O(2) and ∠O(2)–Pd(1)–N(1) bond angles are 82.7(2)°, 96.49(18)°, 86.51(15)°, and 94.29(18)°, respectively. Thereby, the Pd(II) atom is almost coplanar with all four coordinating atoms: N(1), N(2), O(3) and O(2). The metal is in a square planar environment with four coordinating sites comprised of an *N,N,O*-tridentate and an acetate ligands. The acetate coordinates to the palladium atom in a monodentate rather than bidentate mode.[11] The N(1)–Pd(1), N(2)–Pd(1), ∠O(3)–Pd(1), ∠O(2)–Pd(1) bond lengths are 1.932(5) Å, 2.005(5) Å, 2.038(4) Å, and 1.932(5) Å, respectively.

2.2. Application of $Pd(OAc)_2$/L (L=1–9) in Suzuki reactions

A variety of diimines containing *N,N,O*-tridentate ligands, **1**–**9**, have been designed and prepared (Fig. 1). The combination of these ligands with various palladium salts was expected to form excellent catalytic systems for the Suzuki–Miyaura cross-coupling reactions. The performance of a palladium-catalyzed Suzuki–Miyaura cross-coupling reaction is known to be governed by a number of factors such as the kind of palladium salt or ligand employed, the presence/absence of base, solvent, reaction temperature, etc.[12] Furthermore, the ligand/palladium salt ratio is also crucial since various bonding modes are possible for different types of ligands. In this study, the Suzuki coupling reactions were carried out in situ by employing the synthesized *N,N,O*-ligands **1**–**9** in the presence of a palladium salt. In most cases the reactions were carried out with 1.0 mmol of 4-bromo-benzaldehyde, 1.5-fold excess of phenylboronic acid, 2.0-fold excess of a base in 1.0 mL solvent, and 1.0 mol % of $Pd(OAc)_2$/**L** (**L**=**1**–**9**) (Scheme 1). K_3PO_4 was chosen as the base because previously it has shown a good performance in our related studies on Suzuki reactions.

The impact of variation of solvent and temperature on the performance of the coupling reaction was evaluated by employing $Pd(OAc)_2$/**1** as the catalytic precursor (Table 1). Two of the most commonly used solvents, THF and toluene, having been shown to perform well in our previous studies, were chosen. The best yield was observed with toluene at 85 °C (Entry 8). As shown, high temperature was required to reach reasonable reaction speed. By contrast, the catalytic performance was not acceptable when a more polar solvent THF was employed (Entries 1–3).

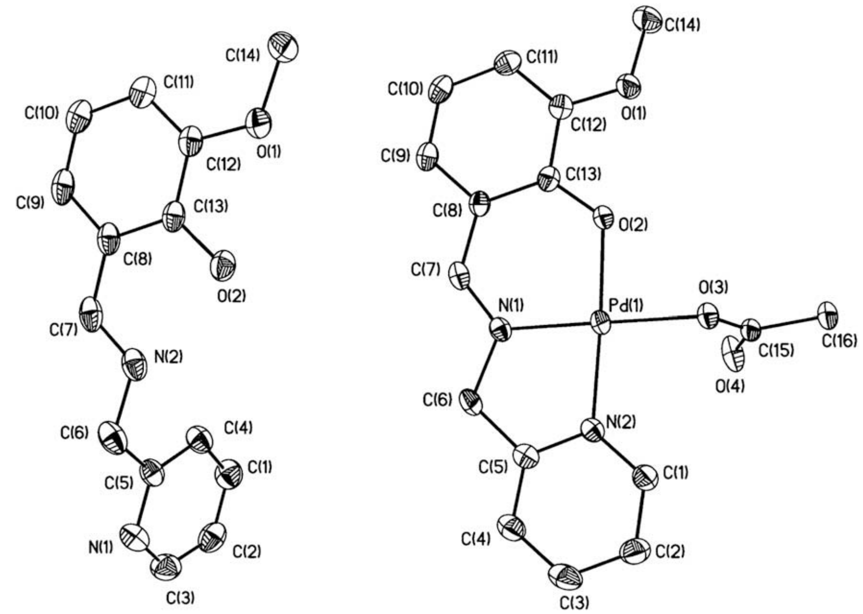

Figure 2. ORTEP drawings of **1** and **10**.