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A new imine ligand avoiding imine–enamine rearrangement and cyclometallation: Synthesis and coordination of $Me_3C_6H_2CH_2N{=}CH^tBu$

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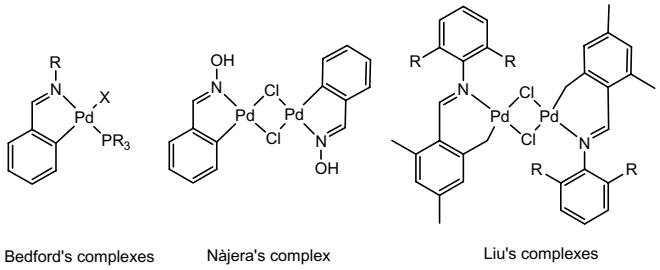
Abstract

The new imine ligand (*E*)-2,4,6-$Me_3C_6H_2CH_2N{=}CH^tBu$ (**1**) has been prepared from 2,4,6-trimethylbenzylamine and trimethylacetaldehyde. In this imine, the *ortho*-positions of the benzyl group are blocked by methyl groups, and there are no β-hydrogen atoms susceptible for imine–enamine rearrangement. Thus, reaction with $[PdCl_2(C_6H_5CN)_2]$ leads to the complex *trans*-$[PdCl_2(2,4,6\text{-}Me_3C_6H_2CH_2N{=}CH^tBu)_2]$ (**2**) that cannot undergo cyclopalladation. The single-crystal X-ray structure analysis of *trans*-$[PdCl_2(2,4,6\text{-}Me_3C_6H_2CH_2N{=}CH^tBu)_2]$ (**2**) confirms the *trans*-coordination of the imine ligands in this square-planar complex.

Keywords: Imine ligand; *ortho*-Metallation; Imine–enamine rearrangement; Palladacycle; Palladium complex

Because of their remarkable catalytic potential and their large versatility, palladium complexes have become the most popular organometallics used in organic synthesis [1]. In particular, most of carbon–carbon bond forming reactions such as Heck reaction, Stille reaction, Suzuki reaction and other C–C couplings are palladium-catalyzed [2]. One of the intrinsic problems of palladium-catalyzed reactions, the palladium contamination of the products, not acceptable in the production of pharmaceuticals or other fine chemicals, can be overcome by using highly active palladium catalysts, present in very low concentration. Therefore, the development of new highly active palladium catalysts that can be used in low loadings is an ongoing challenge in organometallic chemistry.

Of particular interest in this respect is the use of palladacyclic complexes for carbon–carbon coupling reactions and especially cyclopalladated imino complexes. Thus, Bedford [3], Nájera [4] and Liu [5] have demonstrated that complexes of this type are excellent catalysts for the Suzuki cross-coupling of aryl chlorides with arylboronic acids, owing to benzylidene imine-derived ligands.



However, these complexes are so reactive that it is generally not possible to detect the catalytic active species or even to recover the palladium catalyst at the end of the reaction. Furthermore, Liu and co-workers showed that their complex with $R = {}^iPr$ catalyzes the Suzuki cross-coupling via a nanoparticle pathway [5]. For these

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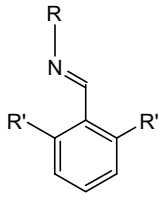
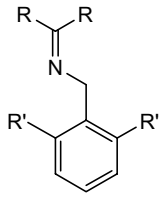
reasons we decided to design a new stable imine ligand, in which cyclopalladation reactions are not possible, and to study the coordination of this ligand to palladium(II) chloride.

The problem of cyclopalladation in imine ligands is not trivial. As we can see Bedford's and Nàjera's complexes, which contain benzylidene imine-derived ligands, form five-membered palladacycles due to *ortho*-metallation. In addition, in benzylidene imine ligands the formation of stable six-membered cyclopalladated rings is also possible, as shown by Liu's complexes. In the corresponding precursor complexes, the methyl or isopropyl substituents spontaneously loose a hydrogen atom by HCl elimination to form a six-membered palladacycle. We previously reported phosphonite ligands in which the *ortho*-positions of the benzyl group were blocked by methyl substituents [6]. In order to avoid the benzylidene problem, we decided to design an imine ligand that contains a benzyl instead of a benzylidene substituent.

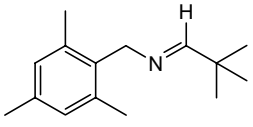


Imines
containing a benzylidene function



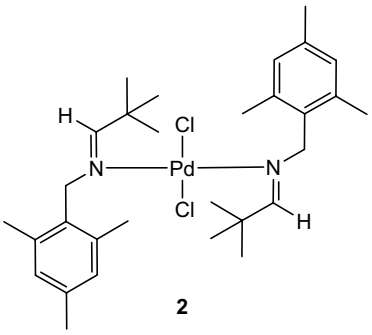
Imines
containing a benzyl function

We synthesized the imine ligand 2,4,6-$Me_3C_6H_2$-$CH_2N{=}CH^tBu$ (**1**) by reacting 2,4,6-trimethylbenzylamine with trimethylacetaldehyde in dichloromethane, in presence of molecular sieves and in the dark during 2 days [7]. The new ligand **1** was isolated as an oil which was characterized on the basis of the NMR (^1H, ^{13}C) and MS data as well as by elemental analysis. According to the ^1H NMR spectra, only the *E* stereoisomer was formed during the synthesis.



1

Because of the *tert*-butyl substituent in **1**, there is no hydrogen atom available for an imine–enamine rearrangement. However, formation of a dinuclear palladacycle has been reported from a similar imine by proton abstraction from a methyl substituent of the *tert*-butyl groups with palladium acetate and lithium chloride, but the cyclopalladation does not occur in the reaction with palladium chloride [8]. Accordingly, we synthesized the new complex *trans*-$[PdCl_2(2,4,6\text{-}Me_3C_6H_2CH_2N{=}CH^tBu)_2]$ (**2**) by reacting the ligand **1** with $[PdCl_2(C_6H_5CN)_2]$ in dichloromethane [9]. Complex **2** was isolated as a yellow powder and characterized by NMR (^1H, ^{13}C) and mass spectroscopy as well as by elemental analysis.



2

In the ^1H NMR spectra of **1**, the signal of the ethylene proton is a triplet at 7.34 ppm with a coupling constant of 1.7 Hz, which corresponds to a ^4J coupling with the benzylic protons through the nitrogen atom, generally not observed for benzyl imines and their palladium complexes. However, not only in the free ligand **1** but also in the complex **2**, the triplet of the ethylene proton is clearly visible, the signal being shifted from 7.34 ppm in **1** to 6.39 ppm in **2**, and the coupling constant being almost unchanged (1.8 Hz). Thus, we can conclude that the coordination to palladium has a strong influence on the electronic density but not on the structure of the imine ligand, and especially that there is no *E*–*Z* isomerization due to the coordination to palladium.

The molecular structure of **2** was confirmed by X-ray crystallography. Yellow crystals of **2**, suitable for single-crystal X-ray structure analysis [10], were obtained by leaving a chloroform solution of the complex in an open flask several days at room temperature. An ORTEP drawing [11] with the corresponding atom labeling scheme is shown in Fig. 1 together with selected bond lengths and angles.

The molecular structure of **2** shows the palladium atom to be in a square-planar geometry, surrounded by two chlorine atoms and two nitrogen atoms in a *trans* coordination geometry. The palladium atom sits on the center of inversion and the molecule is therefore centrosymmetric with the Pd, N and Cl atoms being perfectly coplanar. The geometrical parameters around the palladium atom are comparable to those found in the analogous complexes $[PdCl_2\{C_6H_5CH_2N{=}C(CH_3)OC_2H_5\}_2]$ [12], $[PdCl_2\{C_6H_5CH(CH_3)N{=}C(C_6H_5)C(O)(C_6H_5)\}_2]$ [13] and $[PdCl_2\{2,4,6\text{-}Me_3C_6H_2N{=}CH(C_4H_3S)\}_2]$ [14]. Despite coordination of the nitrogen atom to the metal center, the imine function remains as a formal C=N double bond with a C–N distance of 1.264(3) Å. The *tert*-butyl groups of the two imine ligands are located opposite to each other in order to limit steric interaction and the ligands have *E* stereoisomeric configurations as ^1H NMR spectrum let expect.

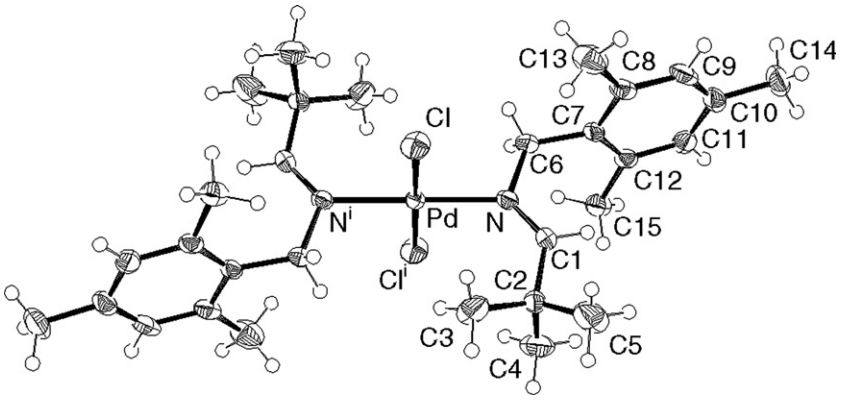


Fig. 1. ORTEP drawing of **2**, at 50% probability level. Selected bond lengths (Å) and angles (°): Pd–Cl 2.3062(7), Pd–N 2.022(2), N–C(1) 1.264(3), N–C(6) 1.494(3), C(1)–C(2) 1.515(3), C(6)–C(7) 1.509(3); Cl–Pd–N 89.53(6), Cl–Pd–N^i 90.47(6), Pd–N–C(1) 131.1(2), Pd–N–C(6) 108.01(16), C(1)–N–C(6) 120.8(2), N–C(6)–C(7) 117.7(2) ($i = -x, -y, -z$).

Acknowledgement

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Appendix A. Supplementary data

CCDC 650550 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.inoche.2007.08.023.

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[7] *Synthesis of* **1**: To a solution of 2,4,6-trimethylbenzylamine (0.299 g, 2 mmol) in dichloromethane (20 mL) containing molecular sieves (2 g, 3 Å), trimethylacetaldehyde (220 μL, 2 mmol) was added. After stirring in the dark for 2 days at room temperature, the solution was filtered through a canula equipped with filter paper. The filtrate was evaporated to dryness under vaccuum to give quantitatively the product as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.34$ (t, $^4J = 1.7$ Hz, 1H), 6.89 (s, 2H), 4.64 (d, $^4J = 1.7$ Hz, 2H), 2.30 (s, 3H), 2.27 (s, 6H), 1.04 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.17$, 137.88, 137.00, 132.39, 129.26, 57.34, 36.57, 27.21, 21.37, 20.19. Mass: APCI-$m/z = 218$ $[M+H]^+$. Anal. Calcd.: C,82.89; H,10.67; N, 6.44. Found: C, 82.77; H, 10.52; N, 6.34.

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[9] *Synthesis of* **2**: To a solution of $[PdCl_2(C_6H_5CN)_2]$ (0.096 g, 0.25 mmol) in dichloromethane (20 mL), **1** (0.109 g, 0.5 mmol) was added. The mixture was stirred at room temperature for 5 h, then the solution was filtered through a short silicagel column using acetone as eluent. The filtrate was evaporated to dryness and the product was purified on a silicagel column, eluted with dichloromethane (yield 67%). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 6.90$ (s, 4H), 6.39 (t, $^4J = 1.8$ Hz, 2H), 5.28 (d, $^4J = 1.8$ Hz, 4H), 2.31 (s, 6H), 2.23 (s, 12H), 1.65 (s, 18H). ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 177.34$, 139.50, 139.06, 129.57, 127.27, 60.90, 36.99, 28.21, 21.51, 19.79. Anal. Calcd.: C, 58.87; H,7.58; N, 4.58. Found: C, 58.94; H, 7.53; N, 4.55.

[10] *Crystal data for* **2**; $C_{30}H_{46}Cl_2N_2Pd$, monoclinic space group $P2_1/a$ (No. 14), cell parameters $a = 9.6126(9)$, $b = 15.809(2)$, $c = 10.1363(9)$ Å, $\beta = 90.476(11)°$, $V = 1540.4(3)$ Å^3, $T = 173(2)$ K, $Z = 2$, $D_c = 1.319$ g cm^{-3}, $F(000)$ 640, λ (Mo Kα) = 0.71073 Å, 2770 reflections measured, 2503 unique ($R_{int} = 0.0336$) which were used in all calculations. The structure was solved by direct method (SHELXS-97) and refined (SHELXL-97) by full-matrix least-squares methods on F^2 with 170 parameters. $R_1 = 0.0276$ ($I > 2\sigma(I)$) and $wR_2 = 0.0947$, GOF = 1.167; max./min. residual density 0.719/−1.017 eÅ^{-3}.

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