

Utility of semicarbazones as ligands in newly made palladium complex for facile Suzuki homocoupling reaction of alkyl and aryl boronic acids

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Abstract

An air stable catalytic system [Pd (HSal4NH₂) Cl] catalyst was found to be highly effective in the Suzuki homocoupling of alkyl and aryl boronic acids resulting in bialkyls and biaryls.

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All over the world synthetic chemists are well convinced that Suzuki coupling play a significant role in the C–C bond forming reactions. Suzuki chemistry [1] provides an efficient cost effective, mild and environmentally safe methodology for the selective formation of the C–C bonds [2]. When compared to Stille coupling [3], Suzuki reagents are compatible with various functional groups and do not contain highly toxic (tin) ingredients, as compared to the traditional organo lithium and magnesium compounds.

Palladium homogeneous catalysis is a versatile tool for carbon–carbon bond formation in organic synthesis [4]. Amongst the different coupling reactions, Suzuki reaction plays an important role in homocoupling of alkyl and aryl boronic acids. The products thus formed include bialkyls and biaryls [8], which are valuable intermediates in organic synthesis [4]. Preparation of many biologically active compounds [5] and some key natural products with relevant functional groups can also be achieved through this coupling. However, the corresponding ligands of Pd complexes play a major role in facilitating the coupling reactions. To the best of our knowledge, the semicarbazone ligand moieties in palladium complexes have not been explored for their versatility in carrying these reactions.

Moreover, the frequently encountered problem associated with the use of phosphine based transition metal catalysts lies

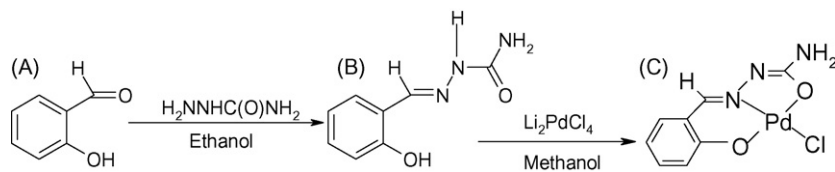
with the air-sensitivity. The existence of trace amount of moisture in the reaction system can lead to deactivation of the catalyst and yields irreproducible results. Therefore, it is highly desirable to develop a catalyst with high activity and good air stability. Here with, a new Pd catalyst [Pd (HSal4NH₂) Cl] with semicarbazone ligands which is described has effectively catalysed the Suzuki coupling of alkyl and aryl boronic acids.

[Pd (HSal4NH₂) Cl] is prepared by a two-step process. Treatment of salicylaldehyde with semi carbazide in ethanol results in the intermediate **B**, which up on reaction with Li₂PdCl₄ (prepared from PdCl₂ and LiCl) gives the catalyst **C** (Scheme 1).¹

¹H NMR, ¹³C NMR and IR spectroscopy characterized the structure and co-ordination mode in the catalyst **C**. The ligand is bound to palladium in a tridentate mode via the azomethine nitrogen N, the oxygen of semicarbazone and the phenoxy oxygen forming one six membered and five membered chelate ring. The significant IR bands in **C** are close in energy to those found in other palladium complexes with tridentate co-ordination. The

¹ Preparation of catalyst **C**: The catalyst consists of salicylaldehyde semicarbazone (**B**) and Li₂PdCl₄ as precursors. Salicylaldehyde semicarbazone was synthesized from salicylaldehyde (**A**) (2.5 mmol) and semicarbazide (2.5 mmol) in ethanol (10 ml). After stirring for 15 min the resulting intermediate **B**, formed was filtered and dried *in vacuo*. The intermediate **B** (1.3 mmol) was added to Li₂PdCl₄ in methanol (5 ml), [Li₂PdCl₄ was prepared *in situ* from PdCl (0.83 mmol) and LiCl (1.2 mmol) in methanol] the reaction mixture was stirred for 30 min and the dark yellow catalyst (**C**) formed was filtered, dried *in vacuo*.

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Scheme 1.

Table 1
Homocoupling of alkyl and aryl boronic acids

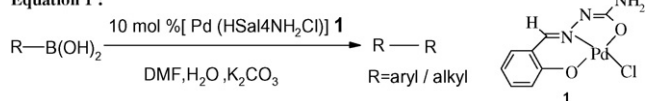
Substrate	Product	Time (h)	Yield (%)
B(OH)_2 ($n=1, 2, 3, 4, 5, 6, 7, 9$)	$(n=1, 2, 3, 4, 5, 6, 7, 9)$	6.5	89–97
		6	100
		6	98
		6.5	98
		6.5	98
		7	99
		8	95
		6	95

bands at 1617 and 1602 cm^{-1} in the IR spectrum of **B** were assigned to C=N. In complex **C** the co-ordination of the azomethine nitrogen to Pd is indicated the C=N band which is shifted to lower frequency by 22 cm^{-1} (1583 cm^{-1}) compared to that of free ligand. Additionally the band at 437 cm^{-1} in the FAR-IR spectrum of **C** was assigned to Pd–N. Co-ordination via the carbonyl oxygen is indicated by the shift of the C=O band (1605 cm^{-1}) in the free ligand **B** to lower frequency in complex **C** (1147 cm^{-1} , C–O stretching) the phenolic oxygen on loss of –OH proton occupies the third co-ordination site. A band at 380 cm^{-1} in the FAR-IR spectrum of **C** was assigned to Pd–O bond and the strong band at 310 cm^{-1} was attributed to Pd–Cl bond.

In the ^1H NMR spectrum of **B**, the signal of the phenolic proton at 11.3 ppm was consistent with presence of a hydrogen bonding isomer (OH–N). In contrary to **B** this signal was absent for **C** due to deprotonation and complex formation.

In the ^{13}C NMR spectrum of the complex **C** deshielding of C–O and C–N was observed which should be related to the electrophilicity of palladium. A σ charge donation from the O and N donor atoms to the palladium center removes electron density from the ligand and produces this deshielding which attenuates at position remote from the metal.

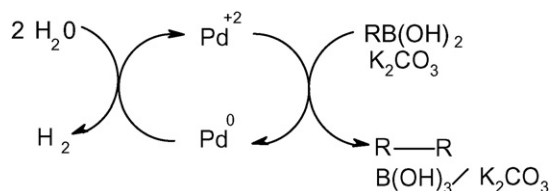
Equation 1 :



(1)

It is observed that the semicarbazone derived palladium complex [Pd (HSal4NH₂) Cl] **1** efficiently catalyses the homocoupling of alkyl and aryl [6] boronic acids as described in (Scheme 1 and Eq. (1)). The phosphine free catalyst [2] under aerobic conditions offers the advantage of Suzuki homocoupling of various alkyl and aryl boronic acids with high yields. Results are shown in Table 1.² All the boronic acids were synthesized

² General experimental procedure for the Suzuki homocoupling reaction. A round bottomed flask equipped with a reflux condenser was charged with alkyl or aryl boronic acids (1.5 mmol) in DMF as solvent media, K₂CO₃ (2 mmol), dist. H₂O (1.7 mmol) and 10 mol% of catalyst. The mixture was refluxed for 6–8 h at 80 °C and then allowed to cool to room temperature. The reaction mixture was filtered and washed with H₂O then extracted with DCM (3 × 10 ml). The organic layer was separated and dried over anhydrous sodium sulphate. The compound was purified by column chromatography and confirmed by GC, NMR and Mass spectral data. All the biaryls and biaryls are previously known.



Scheme 2. Catalytic cycle for Homocoupling reaction catalysed by Pd²⁺ species.

from their respective alkyl or aryl halides by Grignard reaction with trimethyl borate [7].

It is presumed that the homocoupling of boronic acids is eased by the presence of semicarbazone ligands to occur a double transmetallation [9] of Pd²⁺ centre formed from the initial Pd⁰ complex. For this conversion of Pd⁰ to Pd²⁺ and formation of boric acid from boronic acid the participation of molecular water is needed in the presence of a mild base to facilitate the C–C bond formation. Addition of small amount of water (1 equiv. with respect to substrate) to the reaction mixture enhances the activity of the catalyst. Molecular water [10] also dissociates and subsequently hydrolyses the boronic acid to boric acid. The role of mild base K₂CO₃ is to neutralize the boric acid formed and there by protecting the catalyst from degradation [6] (Scheme 2).

In summary, the newly prepared environmentally safe palladium (0) complex with semicarbazone ligands can serve as an efficient catalyst for the versatile Suzuki homocoupling, especially for alkyl and aryl boronic acids under aerobic conditions. The frequently observed difficulty of alkane formation instead of bialkyl formation in the alkyl–alkyl coupling reactions has been smoothly overcome in our methodology. The predominant formation of bialkyls has been observed along with the excellent yields of biaryl formation. Further investigations on exploring other C–C bond forming reactions with this ecofriendly catalyst is ongoing in our group.

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