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Tetrahedron Letters 45 (2004) 7689–7691

Tetrahedron Letters

Application of an air stable Pd oxazoline complex for Heck, Suzuki, Sonogashira and related C–C bond-forming reactions[☆]

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Received 4 August 2004; revised 13 August 2004; accepted 16 August 2004

This communication is dedicated to the memory of a mentor and friend, Dr. John Malito, who passed away October 21, 2003

Abstract—The novel complex *trans*-[PdCl$_2$(η^1-*N*-2-ethyl-2-oxazoline)$_2$] is shown to be an active and oxidatively robust catalyst for C–C bond-forming reactions (Heck, Sonogashira, Ullman, Suzuki), which can be carried out in air without rigorous solvent/substrate purification and in the absence of additional free ligand.

1. Introduction

Several early and late transition metal (TM) complexes are known to mediate C–C bond formation, but in recent years Pd compounds (formed either prior to reactivity or in situ) have demonstrated significant versatility in this area.[1–3] A wide variety organic transformations are facilitated by complexes that incorporate a number of diverse ligand classes (for example, P, N, O, S, etc. as donor atoms) combined with Pd.[4] One of the few drawbacks in the application of most Pd derivatives is the air-sensitive nature of the active species/intermediates (presumably Pd(0) complexes) and/or oxidation potential of the ligands during catalysis. Hence, inert atmosphere conditions are often necessary for efficient catalysis; this aspect remains a serious impediment to large-scale industrial use of Pd-mediated technology.[2,3] In addition, quantities of 'free' ligand are also often necessary to stabilise Pd during catalysis, a situation that may make product purification more difficult. Therefore, there is still a need for new and oxidatively robust Pd-based systems for applications in synthetic organic chemistry.

2. Results and discussion

Our research interests include fundamental and applied studies of oxazoline (ox) ligands[5] and the TM complexes derived from them.[6] The general area of coordination chemistry of monodentate ox ligands, specifically with Pd, is an under-explored area of research;[5] thus justifying our present examination. The treatment of a solution of 2-ethyl-2-oxazoline, a cheap and commercially available polymer precursor,[7] with methanolic Li$_2$PdCl$_4$

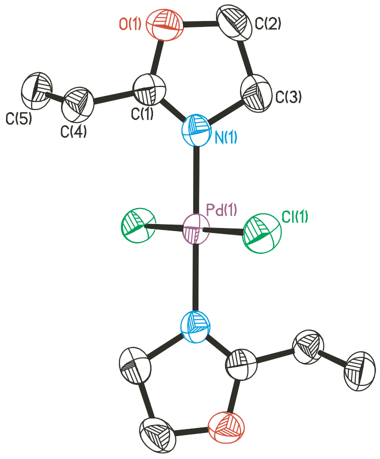

Figure 1.

Keywords: C–C bond formation; Palladium; Heck; Sonogashira; Suzuki; Catalysis; Oxazoline.

[☆] Oxazoline Chemistry Part VI. For Part V, see: Ref. 6e.

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doi:10.1016/j.tetlet.2004.08.082

Table 1. Catalysis results using complex **1** as mediator of C–C bond formation

Entry	Aryl–X	Substrate	Product	Time (h)	% Yield	TON[a]
1[b]	PhI	Styrene	*t*-Stilbene	48	87	8.6×10^2
2[b]	PhI	Styrene	*t*-Stilbene	24	84	1.7×10^3
3[b]	PhI	Styrene	*t*-Stibene	18	77	2.0×10^3
4[b,c]	PhI	Styrene	*t*-Stilbene	18	71	1.9×10^2
5[b]	*p*-NO_2PhI	Styrene	*t*-β-NO_2-styrene	24	100	$>2.0 \times 10^3$
6[b]	PhBr	Styrene	*t*-Stilbene	24	77	1.5×10^3
7[b]	*p*-Br-anisole	Styrene	*t*-Stilbene	24	65	1.3×10^3
8[d]	PhBr	$PhB(OH)_2$	Biphenyl	3	100	$>1.3 \times 10^3$
9[d]	*p*-Br-anisole	$PhB(OH)_2$	*p*-Ph-anisole	3	100	$>1.3 \times 10^3$
10[e]	PhI	PhI	Biphenyl	3	45	1.1×10^1
11[f]	PhI	PhC≡CH	PhCCPh	3	32	1.9×10^2

[a] All yields refer to yields of pure (^{1}H NMR, mp, IR) products isolated by extraction and flash column chromatography; TON = turn over number per hour.

[b] Conditions: 0.00053 mmol **1**, 25 mmol aryl-halide, 30 mmol styrene, 25 mL DMF, 30 mmol sodium acetate, 140–150 °C; *t*-stilbene = *trans*-stilbene; *t*-β-NO_2-styrene = *trans*-β-(4-nitrophenyl)styrene.

[c] 0.0053 mmol of **1** used.

[d] Conditions: 0.00053 mmol **1**, 10 mL toluene, 2 mmol aryl-halide, 3 mmol $PhB(OH)_2$, 4 mmol K_2CO_3, 110 °C.

[e] Conditions: 0.014 mmol **1**, 5 mL DMF, 2 mmol PhI, 1 mmol 1,4-dihydroquinone, 2 mmol K_2CO_3, 110 °C.

[f] Conditions: 0.0011 mmol **1**, 2 mL pyrollidine, 2 mmol PhI, 1 mmol CuI, 2.4 mmol Ph–C≡CH, 90 °C.

gives an air stable complex analysing for [$PdCl_2$(2-ethyl-2-ox)$_2$] (**1**) in good yield.[8] Proton NMR spectroscopy indicates a single ox ligand environment. Single crystal X-ray diffraction of a recrystallised sample of **1** revealed (Fig. 1)[9] a mononuclear (formally) Pd(II) complex with *trans* stereochemistry of ox ligands bound via the *N*-atom in an η^1 fashion, as expected.[5,10] Structurally characterised analogues of **1** are rare but include *trans*-[$PdCl_2$(η^1-*N*-2-phenyl-2-ox)$_2$] (**2**)[11] and a related naphthalene complex described by van Koten et al., *trans*-[$PdCl_2$(η^1-*N*-4,4-dimethyl-2-(2′-napthyl)-2-ox)$_2$] (**3**).[12] The latter species appears to exist as a mixture of *cis*/*trans* isomers in solution, in contrast to our NMR observations with **1** (and earlier studies of **2**).[11] The bond lengths and angles[11,12] of the solid-state forms of both **2** and **3** are similar in most respects to that of **1**.[9]

We have further investigated (Table 1) the use of solutions of **1**, in open air, as a mediator of C–C bond formation under typical Heck (entries **1**–**7**), Suzuki (entries **8**–**9**), Ullmann (entry **10**) and Sonogashira (entry **11**) reaction conditions *without addition of free ligand nor rigorous exclusion of moisture or air*.[13] Complex **1** is an effective catalyst for all of these classes of C–C bond-forming reactions. Yields range from 32% to 100% under standard conditions and TON's are moderate (Table 1);[1–4,13,14] all solvents and reagents that were used were of reagent grade and not purified further.[15] There are few fully characterised (pre-formed) Pd-based systems that have been shown to be effective for a plethora of different C–C bond-forming processes and even fewer can operate in air and without additional ligand.[2–4,14] This system effectively combines these two aspects with the further advantage of using a simple, very inexpensive (or readily synthesised on a large scale[7]) ligand (cf. bulky phosphines, carbenes), which is stable to oxidative decomposition and low in molecular weight. The robust nature of **1**, presumably combined with the stability of the Pd intermediates during catalysis in open air, makes this a very attractive system for C–C coupling reactions.

In conclusion, a new Pd complex has been synthesised and fully characterised and found to be an effective catalyst, in air, for a number of C–C bond-forming reactions. We are currently expanding this chemistry to include enantioselective substrate activation; the investigation of the mechanism of reactions mediated by **1** and its (chiral) analogues will be disclosed in a future publication.

Acknowledgements

This work is supported by NSERC (Canada). Johnson–Matthey Ltd is thanked for a generous loan of Pd salts. T. D. Hamilton is acknowledged for her assistance in the characterisation of **1**.

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8. Synthesis of complex **1**: To a MeOH solution of Li_2PdCl_4 (0.28 M; 2.0 mL: 0.56 mmol) was added 7 mL of MeOH and 2-ethyl-2-oxazoline (1.0 mL; 9.9 mmol) at room temperature in open air. The dark brown mixture was stirred for 1 h during which time the solution lightened in colour and an orange precipitate formed. This solid was then isolated by filtration and washed with MeOH (3×7 mL), pet. ether (5 mL) and Et_2O (2×5 mL) and then dried in air. Complex **1** was thus obtained as an orange solid (yield 0.14 g: 67%). An analytical sample, also found to be suitable for single crystal X-ray diffraction, was obtained by layering a dichloromethane solution (5 mL) of **1** with an equal volume of MeOH and subsequent storage at −20 °C for several days. Mp 178–179 °C (decomp.). ^1H NMR (300 MHz; $CDCl_3$; 294 K): $\delta = 4.54$ (t, 2H, $J = 9.8$, CH_2O), 4.00 (t, 2H, CH_2N), 3.00 (q, 2H, $J = 7.3$ Hz, CH_2CH_3), 1.28 (t, 3H, CH_3). Calcd (found) for $C_{10}H_{18}N_2O_2Cl_2Pd$: C, 31.98 (31.73), H, 4.83 (4.63), N, 7.46 (7.41)%.
9. X-ray data of complex **1**: FW = 375.56; formula: $C_{10}H_{18}N_2O_2Cl_2Pd$; temp.: 291(2) K; $\lambda = 0.71073$ Å. Crystal system: monoclinic. Space group: $P2(1)/n$. Unit cell dimensions: $a = 8.8593(10)$ Å; $\alpha = 90°$; $b = 8.0909(9)$ Å; $\beta = 92.857(2)°$; $c = 10.0689(11)$ Å; $\gamma = 90°$. Vol. = 720.84(14) Å^3; $Z = 2$; density (calcd): 1.730 Mg/m^3. Absorption coefficient: 1.650 mm^{-1}; $F(000)$: 376. Crystal size: $0.25 \times 0.25 \times 0.3$ mm^3. Theta range for data collection: 2.99° to 24.99°. Index ranges: $-10 \leqslant h \leqslant 10$, $-9 \leqslant k \leqslant 6$, $-10 \leqslant l \leqslant 11$. Reflections collected: 3707; independent reflections: 1272 [R(int) = 0.0157]. Completeness to theta = 24.99°: 99.9%. Absorption correction: none. Refinement method: Full-matrix least-squares on F^2. Data/restraints/parameters: 1272/0/80; Goodness-of-fit on F^2: 1.084. Final R indices [$I > 2sigma(I)$]: $R1 = 0.0161$, $wR2 = 0.0442$; R indices (all data): $R1 = 0.0173$, $wR2 = 0.0446$. Extinction coefficient: 0.0478(17); largest diff. peak and hole: 0.250 and −0.306 e Å^{-3}.
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15. Aryl-chlorides were ineffective substrates in air under the standard Heck conditions described herein (product yields: <5%). Stille coupling mediated by **1** using PhI or *p*-bromoacetophenone with Bu_3SnPh or Bu_3Sn(allyl) under standard conditions (toluene, 100 °C, 8 h) gave low yields of coupled product in open air. Aspects of these results in relation to the data presented herein will be disclosed separately.