

Ditopic Double Pincer Palladacycle Catalyst for C–C Coupling

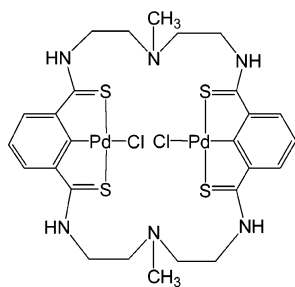
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A ditopic palladacycle with SCS pincer coordination, $L(\text{PdCl})_2$ (**1**), was isolated and structurally characterized and represents the first example of a transition metal complex with a polythioamide-based macrocycle. Preliminary studies of **1** in the catalytic coupling of 4-iodotoluene and styrene indicated it to be robust in the presence of oxygen and high temperatures, with high turnover numbers in relatively short times.

As part of our exploration of the chemistry of polythioamide-based macrocyclic ligands,¹ we isolated an unusual ditopic palladium complex which was found to contain two distinct palladacycles in a single macrocycle, $L(\text{PdCl})_2$ (**1**). Polythioamide-based macrocycles represent a very new class of ligands, and to our knowledge, only one other report exists.² Since the dipalladacycle, **1**, incorporated a number of attributes of the more robust C–C coupling catalysts,³ we undertook an investigation of its catalytic capabilities.

 $L(\text{PdCl})_2$ (**1**)

Palladium chemistry enjoys widespread usage in catalysis,⁴ especially in C–C coupling reactions.³ In particular, palladacycles have been found to be active catalysts in these types of reactions. However, they are often unstable in the presence

of oxygen and high temperatures, thus becoming ineffective over multiple cycles.^{5,6} More recently, increased stability has been observed when tridentate “pincer” ligands are employed, as first reported by Milstein and co-workers⁷ and now followed by other examples.^{8–15} Many of the reported pincer catalysts contain a PCP bonding mode.^{7,11–15} Bergbreiter et al. were the first to report the use of mixed SCS palladacycles in C–C coupling reactions.¹⁰ We now report the structure of the new ditopic double pincer SCS palladacycle and preliminary C–C coupling findings. In addition to promising catalytic results, this is the first report of a transition metal complex with a thioamide-based macrocycle.

The thioamide ligand, H_2L , was prepared as previously reported, and a detailed description of the synthesis is given in the Supporting Information.¹ The palladacycle was synthesized by mixing H_2L with 2 equiv of K_2PdCl_4 in DMSO.¹⁶ Crystals suitable for X-ray analysis were obtained by slow evaporation from DMSO.¹⁷

The complex crystallizes as $\text{1} \cdot 2\text{DMSO}$. Each palladium is held by the tridentate SCS pincer coordination of the thioamide sulfurs and deprotonated benzyl carbon (Figure 1). The fourth coordination site is occupied by a chloride.

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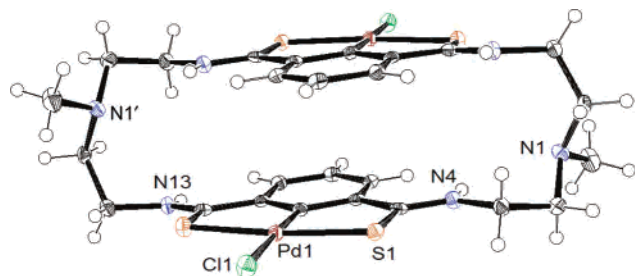
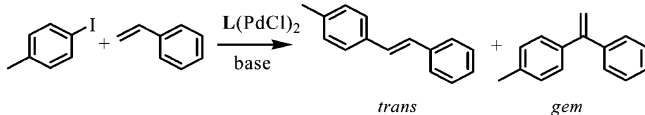


Figure 1. ORTEP view of the palladacycle, **1**. Thermal ellipsoids are at 50% probability.

Scheme 1. Heck Coupling of 4-Iodotoluene and Styrene



While it was anticipated that the new ligand might show an affinity for palladium, isolation of the palladacycle was an added bonus, although perhaps not surprising since metalation reactions with benzyl thioethers and related ligands are well-established.^{15,18,19} The molecule sits on a crystallographic center of symmetry, and the complex is elongated along the amine axis, with $N(1)\cdots N(1') = 11.247(4)$ Å. The two palladacycles are oriented in *anti* conformations and are stacked with $3.346(4)$ Å between the *m*-xylyl planes. The palladium–palladium separation is $6.764(2)$ Å. The C=S bond lengths are only slightly elongated compared to those observed in the free base ligand ($1.706(3)$ and $1.709(3)$ Å compared to $1.6766(17)$ and $1.6672(17)$ Å, respectively).¹

The catalytic activity of **1** was evaluated by examining the reaction between 4-iodotoluene and styrene (Scheme 1). Catalysis was carried out in the presence of NaOAc as a base and *n*-Bu₄NBr in refluxing dimethylacetamide (DMA, bp 165 °C). The reaction was found to proceed rapidly, with over 90% conversion after 4 h for lower concentrations (e.g., 3.0×10^{-3} mol %), and within 2 h for higher concentrations (e.g., 3.0×10^{-2} mol %) (Table 1, Figure 2). The reactions were carried out in air, with similar times and yields compared to those performed under argon (see entries 2 and 4, Table 1). The addition of few drops of water in the reaction mixture also does not affect the reaction. The product ratio of *trans* to *gem* is about 7:1. Catalysis slows below 3.0×10^{-3} mol % (entries 7–9, Table 1). In order to determine the robustness of **1** as a catalyst, repetition experiments were performed at 0.06 mol % of catalyst loading. After conversion of the initial reactants, additional aliquots of the

Table 1. Heck Coupling of 4-Iodotoluene with Styrene under Different Reaction Conditions

entry	catalyst [mol %]	reaction time [h]	temp [°C]	yield ^a (%) [trans/gem]	TON ^b
1	0.17	0.33	165	78/11	523
2(Ar)	3.0×10^{-2}	2.0	165	76/13	2966
3	3.0×10^{-2}	0.40	165	47/7	1800
4(Ar)	3.0×10^{-2}	2.0	165	82/14	3200
5	3.0×10^{-3}	1.0	165	35/6	13670
6	3.0×10^{-3}	4.0	165	78/13	30000
7	1.0×10^{-3}	1.0	165	23/7	27052
8	1.0×10^{-3}	16	165	58/7	65120
9	1.0×10^{-3}	48	165	80/14	94300
10	0.20	16	140	43/5	245
11	0.20	64	140	65/6	350

^a Determined by ¹H NMR using ethylene glycol di-*n*-butyl ether as an internal standard. ^b TON = (mol of product)/(mol of catalyst).

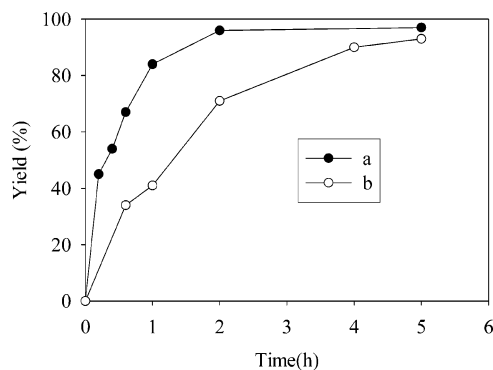


Figure 2. Time dependent reaction profile for 4-iodotoluene and styrene with catalyst loading: (a) 3×10^{-2} mol %, and (b) 3×10^{-3} mol % at 165 °C.

substrates and base were added. Under these conditions, **1** remained active for at least 10 additional cycles with no evidence of metallic palladium deposit.

Catalysis also is observed at lower temperatures (140 °C), although at slower rates (see entries 10 and 11, Table 1). While it is difficult to compare **1** directly with other Heck catalysts due to differences in reaction and solvent conditions, **1** appears to be competitive in terms of turnover numbers (e.g., entries 8 and 9, Table 1) and appealing in its stability.

There has been considerable debate as to the mechanism of palladium-assisted coupling reactions; however, Pd(II)/Pd(IV) couples have been postulated for PCP pincers.^{6,7,13} This mechanism would also make sense in the case of **1**, although the ditopic complex has possibly additional extenuating features such as potential coordination sites on adjacent palladium atoms. The influence of elemental mercury, known to poison heterogeneous catalysts,^{11,20} was also examined in order to ascertain if colloidal palladium were involved. The fact that yields and product distributions were unchanged is a strong indication of a homogeneous process. We are currently investigating the mechanistic aspects of the coupling reactions with **1**, as well as the influence of other factors such as solvent and the identity of the added base.

In conclusion, now that the influence of structural effects on palladium catalysts in C–C coupling reactions is more

(16) $L(PdCl)_2$: yield: 80%. ¹H NMR (500 MHz, DMSO-*d*₆): δ 2.95 (s, 6H, CH₃), 3.66 (m, 8H, NCH₂), 4.16 (b, 8H, NCH₂CH₂), 7.51 (b, 4H, ArH), 8.16 (b, 2H, ArH), 10.57 (b, 4H, NH). IR (KBr disk), cm⁻¹: 1555 (C–N), 1286 (C=S). MS (FAB⁺): *m/z* 804.9 [M – Cl]⁺. MS- (HRFAB⁺) Calcd for C₂₆H₃₂Cl₂N₆Pd₂S₄: 804.9265. Found: 804.9287. Anal. Calcd for C₂₆H₃₂Cl₂N₆Pd₂S₄: C, 37.15; H, 3.84; N, 10.00. Found: C, 37.31; H, 3.81; N, 9.90.

(17) Crystal data for **1**: C₃₀H₄₄Cl₂N₆O₂Pd₂S₆, monoclinic; *P*2₁/*c*; *a* = 11.3723(12) Å; *b* = 8.4284(9) Å; *c* = 19.977(2) Å; β = 93.289(2)°; *V* = 1911.6(3) Å³, *d*_{calc} = 1.732 g cm⁻³.

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established, catalyst design can take advantage of earlier groundwork. The new ditopic double pincer catalyst described here incorporates several of the strengths of forerunner catalysts, namely pincer-type ligands,^{7–15} ditopic binding,²¹ and SCS coordination.^{10,15} The new catalyst is robust in the presence of oxygen and water and at high temperatures and can catalyze coupling reactions with large turnovers in relatively short times. Last but not least, **1** is the first example of a thioamide-based macrocyclic transition metal complex to be reported, laying the foundation for further explorations

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of this new class of macrocycles in transition metal chemistry.

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Supporting Information Available: Detailed catalytic procedure and time dependent ¹H NMR data (PDF), and one crystallographic file in CIF format. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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