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# Facile tandem Suzuki coupling/transfer hydrogenation reaction by bis-heteroscorpionate Pd-Ru complex†

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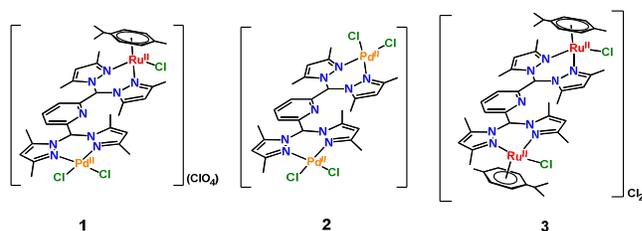
DOI: 10.1039/b000000x [DO NOT ALTER/DELETE THIS TEXT]

**Design and synthesis of bis(pyrazol-1-yl)methane based bis-heteroscorpionate Pd-Ru complex results in efficient tandem Suzuki coupling/transfer hydrogenation reaction with broad range of substrate reactivity.**

With the increasing demand for environmentally benign and economically viable synthetic processes one-pot multi-step reactions have emerged as a fascinating area of current research.<sup>1</sup> Introduction of multiple catalytic units within a single ligand framework can promote cooperativity between the reaction centers and thereby improving activity and/or selectivity.<sup>1c,2</sup> Further, heterometallic systems are favored over homometallic analogues not only due to their crucial synergistic effect but also increase the number of possible combinations of reactions that are mechanistically different in nature, known as tandem-reactions.<sup>3,4a</sup> Thus, development of a new heterometallic catalytic system exhibiting one-pot multi-step reaction is highly challenging. In this context, Peris and co-workers have done extensive work on the development of multidentate N-Heterocyclic carbene (NHC) and triazolyl-diyldene bridged heterodimetallic complexes of Pd, Pt, Rh, Ir, Au and Ru for efficient multiple tandem reactions, such as dehalogenation/transfer hydrogenation, Suzuki coupling/transfer hydrogenation, Suzuki coupling/ $\alpha$ -alkylation reaction, etc.<sup>4</sup> In addition, Djakovitch et al. and Chen et al. have independently developed heterometallic Pd-Cu system for one-pot indole synthesis<sup>5</sup> and tandem click/Sonogashira coupling reactions, respectively.<sup>6</sup>

Tridentate N,N,X donor based heteroscorpionate ligands are well known for their spectator nature and tunable steric and electronic properties.<sup>7</sup> A large number of metal complexes of main group, early and late transition metals have been developed with such ligands and employed for designing models for enzymes, supramolecular architecture, precatalysts or catalysts for numerous homogeneous catalytic processes, etc.<sup>7</sup> On the contrary, use of multidentate bis-heteroscorpionate ligand is relatively rare.<sup>8</sup> Recently, we have reported the preparation and application of dinuclear [(*p*-cym)RuX] (X = Cl or H<sub>2</sub>O), incorporating  $\alpha,\alpha,\alpha',\alpha'$ -tetra(pyrazol-1-yl)-2,6-lutidine (pz<sub>4</sub>lut) bis-heteroscorpionate ligand.<sup>8d</sup> However, to the best of our knowledge, development of heterodimetallic complex of bis-heteroscorpionate ligands is yet to be explored. Herein, we extend the use of pz<sub>4</sub>lut ligand towards synthesis of heterodimetallic [(*p*-cym)RuCl]( $\mu$ -pz<sub>4</sub>lut)PdCl<sub>2</sub>]ClO<sub>4</sub> (**1**) and homodimetallic

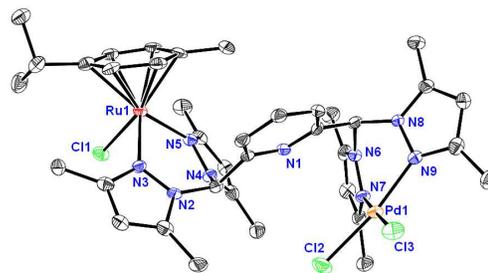
complexes [(PdCl<sub>2</sub>)<sub>2</sub>( $\mu$ -pz<sub>4</sub>lut)] (**2**) and [(*p*-cym)RuCl]<sub>2</sub>( $\mu$ -pz<sub>4</sub>lut)]Cl<sub>2</sub> (**3**)<sup>8d</sup> (Fig. 1). The complexes have been characterised via arrays of analytical techniques, and have been tested for tandem Suzuki coupling/transfer hydrogenation reaction. Advantage of heterometallic **1** over its homodimetallic analogues **2** and **3**, and non-ligated precursors PdCl<sub>2</sub> (**4**) and [(*p*-cym)RuCl( $\mu$ -Cl)]<sub>2</sub> (**5**) towards the aforementioned reaction has also been investigated.



**Fig. 1** Structures of heterodimetallic Pd-Ru (**1**), and homodimetallic Pd-Pd (**2**) and Ru-Ru (**3**) complexes of bis-heteroscorpionate ligand.

Heterodimetallic **1** is obtained by reacting pz<sub>4</sub>lut ligand with [(*p*-cym)RuCl( $\mu$ -Cl)]<sub>2</sub> and *in situ* generated Li<sub>2</sub>[PdCl<sub>4</sub>], successively, and isolated as ClO<sub>4</sub> salt (Experimental Section, Scheme S1, ESI†). The homodimetallic **2** is synthesised by reacting the pz<sub>4</sub>lut ligand with *in situ* generated Li<sub>2</sub>[PdCl<sub>4</sub>], in 1:2 molar ratio and **3** has been prepared and characterized by following the reported procedure.<sup>8d</sup>

Complex **1** behaves as 1:1 electrolyte in acetonitrile whereas complex **2** is neutral. Both **1** and **2** give satisfactory microanalytical data. The presence of ClO<sub>4</sub> counter anion in **1** has been confirmed by the characteristic IR vibration frequency at 1100 cm<sup>-1</sup> and 690 cm<sup>-1</sup>.



**Fig. 2** ORTEP diagram of complex **1**. Ellipsoids are drawn at 30% probability level. Hydrogen atoms and ClO<sub>4</sub><sup>-</sup> anion have been removed for clarity.

Molecular identities of the complexes **1** and **2** are confirmed by positive ion Electrospray Ionization mass spectra (Fig. S1, ESI†). The molecular ion peaks centred at 931.8 (calcd. 931.69) for [1 - ClO<sub>4</sub>]<sup>+</sup> and 803.9 (calcd. 803.9) for [2 - Cl]<sup>+</sup> confirms the existence of entire molecular framework of **1** and **2**, respectively, in solution. Further, the <sup>1</sup>H NMR spectra of **1** and **2** in DMSO-d<sub>6</sub> exhibiting 13 and 9 numbers of protons, respectively, in the region 4.5 - 10.5 ppm support the presence of pz<sub>4</sub>lut ligand and [(*p*-cym)Ru] fragment

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†Electronic Supplementary Information (ESI) available: Experimental details, spectroscopic characterization, catalytic results and crystallographic data. CCDC for **1** is 1017846. See <http://dx.doi.org/10.1039/b000000x/>

(Fig. S2, ESI†). Intense singlets and doublet at 0 - 2.0 ppm corresponding to  $CH_3$  and  $CH(CH_3)_2$  protons indicate the existence of [(*p*-cym)Ru] fragment in complex **1**.

The formation of **1** is further authenticated by single crystal X-ray analysis (Fig. 2). Important crystallographic parameters and selected bond lengths and bond angles are presented in tables (Table T1 and T2, ESI†). The pyrazolyl units of pz<sub>4</sub>lut ligand form six membered metallacycle adopting a boat conformation with metal centres. The ruthenium centre shows expected piano-stool geometry and palladium shows distorted square planer geometry with N3-Ru1-N5 and N7-Pd1-N9 bite angles 86.99(11)<sup>o</sup> and 86.57(12)<sup>o</sup>, respectively. The Ru-Cl (2.4020(10) Å), Ru-C<sub>centroid</sub> (1.700 Å) and Pd-Cl (2.28(11) Å) distances are in well agreement with the values reported earlier.<sup>8d,9</sup> The intermetallic Ru-Pd distance is 8.01 Å.

The heterodimetallic Pd-Ru (**1**) in dichloromethane shows MLCT band at 440 nm similar to homodinuclear **3** (Fig. S3, ESI†).<sup>8d,10</sup> However, a blue shifted MLCT band at 384 nm has been observed for homodimetallic Pd-Pd (**2**) (Fig. S3). In addition, both **1** and **2** exhibit high energy intraligand charge transfer transitions ( $\pi \rightarrow \pi^*$ ) below 300 nm.

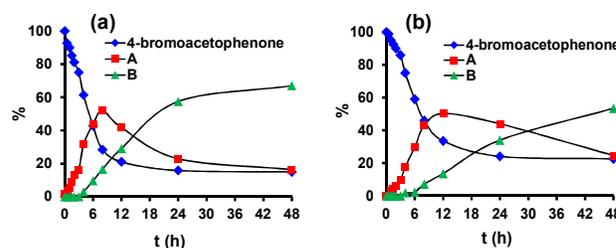
Complex **1** in acetonitrile shows two successive irreversible oxidation peaks  $E_{pa}$  at 0.81 V and 1.44 V which could be assigned as oxidation of Ru<sup>II</sup>/Ru<sup>III</sup> and Ru<sup>III</sup>/Ru<sup>IV</sup>, respectively (Fig. S4, ESI†). The peak potentials are almost similar to previously reported [(*p*-cym)Ru] complexes.<sup>4g,8d,10</sup> The ligand based reductions are observed at negative potentials in cyclic voltammetry. Several attempts were taken to record the cyclic voltammogram of homodinuclear **2**, however, no representable cyclic voltammogram was obtained. This may be due to the poor solubility of the complex **2** in most of the solvents including acetonitrile.

**Table 1.** Tandem Suzuki coupling/transfer hydrogenation of 4-bromoacetophenone<sup>a</sup>

Entry	Cat.	ROH	Base	Temp. (°C)	Yield (%) <sup>b</sup>	
					A	B
1	<b>1</b>	<i>i</i> PrOH	Na <sub>2</sub> CO <sub>3</sub>	80 <sup>c</sup>	47	0
2	<b>1</b>	<i>i</i> PrOH	K <sub>2</sub> CO <sub>3</sub>	80 <sup>c</sup>	43	0
3	<b>1</b>	<i>i</i> PrOH	Cs <sub>2</sub> CO <sub>3</sub>	80 <sup>c</sup>	32	0
4	<b>1</b>	<i>i</i> PrOH	KO <i>t</i> Bu	80 <sup>c</sup>	0	97
5	-	<i>i</i> PrOH	KO <i>t</i> Bu	80 <sup>c</sup>	0	0
6	<b>1</b>	<i>n</i> PrOH	KO <i>t</i> Bu	80 <sup>c</sup>	14	30
7	<b>1</b>	PhCH <sub>2</sub> OH	KO <i>t</i> Bu	80 <sup>c</sup>	14	0
8	<b>1</b>	<i>i</i> PrOH	KO <i>t</i> Bu	30 <sup>d</sup>	16	67
9 <sup>e</sup>	<b>2 + 3</b>	<i>i</i> PrOH	KO <i>t</i> Bu	30 <sup>d</sup>	24	53
10 <sup>f</sup>	<b>4 + 5</b>	<i>i</i> PrOH	KO <i>t</i> Bu	30 <sup>d</sup>	14	25

<sup>a</sup> Reaction conditions: Catalyst/4-bromoacetophenone/PhB(OH)<sub>2</sub>/Base = 1/800/1000/3000 (molar ratio), Catalyst (0.125 mol%), 4-bromoacetophenone (0.5 mmol), PhB(OH)<sub>2</sub> (0.6 mmol), Base (1.8 mmol), ROH (1 mL). <sup>b</sup> Isolated yields after preparatory thin layered chromatography. <sup>c</sup> Reaction time = 2.5 h. <sup>d</sup> Reaction time = 48 h. <sup>e</sup> **2:3** = 1:1 (molar ratio). <sup>f</sup> **4:5** = 1:0.5 (molar ratio).

Mononuclear complexes of palladium and ruthenium with heteroscorpionate ligand are known to show activity towards Suzuki coupling and transfer hydrogenation reaction, respectively.<sup>11,12</sup> Complex **1** constituting two catalytically independent moieties [PdCl<sub>2</sub> and {(*p*-cym)RuCl}] in pz<sub>4</sub>lut ligand framework is a point of interest whether it can successfully combine mechanistically two different reactions. To prove our concept, 4-bromoacetophenone and phenylboronic acid were taken as substrates. Reaction conditions were screened for **1** by varying base and solvent at 80 °C (Table 1). It appears that although moderate C–C coupling reaction (product **A**) proceeds using carbonate bases, transfer hydrogenation (product **B**) does not occur until KO*t*Bu is introduced into the reaction mixture (entries 1-4). However, under the identical reaction conditions none of **A** and **B** were identified in absence of **1** (entry 5). Moreover, among the alcohols aliphatic secondary alcohol (*i*PrOH) brings more activity than its primary analogue *n*PrOH (entries 4 and 6). Aromatic alcohol (PhCH<sub>2</sub>OH) is even unable to induce transfer hydrogenation process (entry 7).



**Fig. 3** Time-dependent transformation of 4-bromoacetophenone towards tandem Suzuki coupling/transfer hydrogenation reaction by (a) **1** and (b) 1:1 mixture of **2** and **3**. Reaction conditions: 4-bromoacetophenone (0.5 mmol), phenylboronic acid (0.6 mmol), KO*t*Bu = (1.8 mmol), *i*PrOH (1 mL), **1** or **2 + 3** (0.125 mol %), at 30 °C.

At 80 °C, no difference in activity for tandem Suzuki coupling/transfer hydrogenation reaction between heterodimetallic **1** and equimolar mixture of homodimetallic **2** and **3** was observed. Thus, the tandem reaction was monitored at lower temperature (30 °C) to follow the reaction profile with time and to compare the activity between the hetero- (**1**) and homodimetallic (**2 + 3**) catalytic systems (Fig. 3a and 3b). It is observed that, though C–C coupling and transfer hydrogenation reactions occur simultaneously, the initial rate of coupling reaction is much faster than the later in both cases. In fact, transfer hydrogenation follows an induction period of 3 h, and accelerates at a point with maximum yield of **A** (8 h for **1** and 12 h for **2 + 3**), suggesting that the hydrogenation of **A** is more facile than 4-bromoacetophenone. This trend is in agreement with the observation reported by Peris et al. for tandem dehalogenation/transfer hydrogenation reaction of 4-bromoacetophenone on Pd-Ir heterodimetallic catalyst.<sup>4a</sup> Indeed, no hydrogenation product of 4-bromoacetophenone was detected in the reaction mixture. These results indicate consecutive nature of the two mechanistically independent reactions, where C–C coupling process leads the reaction in step I with subsequent hydrogenation of the keto group of the coupling product in step II (Scheme S2, ESI†). At low temperature, the Pd-Ru heterodimetallic **1** provides the catalytic result (entry 8, Table 1) with maximum yield of **B**. Although a mixture of **2** and **3** (entry 9) affords a comparable overall yield (**A + B**), the reaction profile (Fig. 3b) clearly shows that rate of reaction is considerably slower as compared to **1** (Fig. 3a). Mixture of precursors **4** and **5** with much inferior catalytic outcomes (entry 10) indicates the

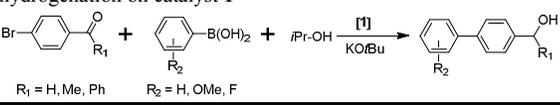
importance of pz<sub>4</sub>lut ligand framework to provide a well-defined active heterodimetallic tandem catalyst.

In order to check the generality of the trend, reaction profiles were also monitored by varying the substituents of phenylboronic acid. It appeared that the trends are almost similar, however, the rate of reactions are slower as compared to the combination of 4-bromoacetophenone and phenylboronic acid (Fig. S5, ESI†).

Further, the tandem reaction is extended to varieties of bromoarylketones and arylboronic acids (Table 2, entries 1-7). Notably, under moderate heating condition (80 °C) complex **1** is active towards all the substrates with good to excellent yield of the corresponding tandem products.

Finally, to check the homogeneous nature of the present catalytic systems (**1** and **2 + 3**), the mercury drop test was conducted.<sup>13</sup> Metallic mercury was added to the reaction mixture after ~ 50% completion of the reaction. No significant change in the yield of final product (**B**) was observed (Table T3) which supports the homogeneous nature of both the catalytic systems **1** and **2 + 3**.

**Table 2.** Substrate scope of tandem Suzuki coupling/transfer hydrogenation on catalyst **1**<sup>a</sup>



Entry	ArBr	Ar'B(OH) <sub>2</sub>	Product	Yield (%) <sup>b</sup>
1				97 <sup>c</sup>
2				82 <sup>d</sup>
3				92 <sup>d</sup>
4				86 <sup>e</sup>
5				87 <sup>e</sup>
6				90 <sup>f</sup>

<sup>a</sup> Reaction conditions: **1**/ArBr/Ar'B(OH)<sub>2</sub>/KOtBu = 1/800/1000/3000 (molar ratio), **1** (0.125 mol%), ArBr (0.5 mmol), Ar'B(OH)<sub>2</sub> (0.6 mmol), KOtBu (1.8 mmol), *i*PrOH (1 mL), 80 °C. <sup>b</sup> Isolated yields after preparatory thin layered chromatography. <sup>c</sup> Reaction time = 2.5 h. <sup>d</sup> Reaction time = 3.5 h. <sup>e</sup> Reaction time = 4.5 h. <sup>f</sup> Reaction time = 8.5 h.

In conclusion, we have developed heterodimetallic **1** and its homodimetallic analogues **2** and **3**<sup>8d</sup> using bis(pyrazol-1-yl)methane based bis-heteroscorpionate ligand (pz<sub>4</sub>lut). The complexes have been characterised using various analytical techniques. The structure of **1** has been authenticated by single crystal X-ray diffraction which shows expected piano-stool geometry for Ru and distorted square planar geometry for Pd centre. All the complexes have been tested for tandem Suzuki coupling/transfer hydrogenation reaction. Complex **1** shows superior activity as compared to the equimolar mixture of complexes **2 + 3** and **4 + 5** at 30 °C. The better activity of **1** as compared to the mixture of **2** and **3** corroborates the significance of a single well-defined heterodimetallic catalytic system which

may show cooperativity at least to some extent. Though the overall conversion does not differ significantly between **1** and the mixture **2 + 3** (Table 1, entries 9 and 10), the one-pot multi-step synthesis by **1** is important in terms of atom economy, saving chemicals, and reduction of waste, energy and time. Thus, we believe that the new example of heterodimetallic **1** with bis-heteroscorpionate ligand may open new avenues for the development of one-pot multi-step tandem reactions and/or catalysts.

This work was supported by DST (SR/S1/IC-20/2010), New Delhi, India. ND and SKT and AS are grateful to University Grant Commission (UGC) and Council of Scientific and Industrial Research (CSIR), DST Inspire programme, New Delhi, India, respectively, for their fellowship. The authors gratefully acknowledge Professor S. Chatterjee, National Institute of Technology, Rourkela, India for recording <sup>1</sup>H NMR and mass spectra of the complexes. The authors also would like to thank the reviewers for their valuable comments and suggestion to improve the manuscript.

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A bis-heteroscorpionate Pd-Ru complex (**1**) has been developed which shows efficient tandem Suzuki coupling/transfer hydrogenation reaction towards a broad range of substrates.

