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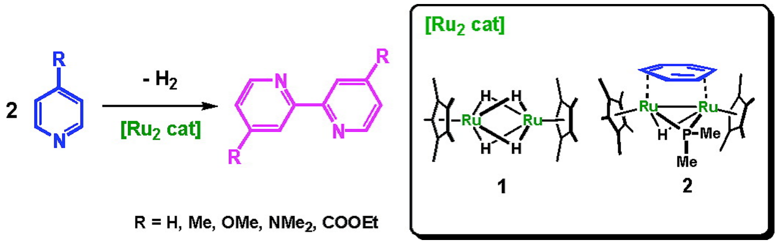

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Dehydrogenative Coupling of 4-Substituted Pyridines Catalyzed by Diruthenium Complexes

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Reactivities of transition metal cluster complexes have been widely explored with the aim of observing a synergism inherent to the presence of adjacent metal centers.[1] With this in mind, we have developed research studies on polyhydrido cluster complexes revealing their aptitude to split a C−H bond of aromatics in their H/D exchange reactions as a consequence of cooperation of the adjacent metal centers.[2]

It has long been known that a carbonyl cluster readily splits an α-C−H bond of pyridine,[3] and catalytic regioselective acylation of pyridine is a successful example of the C−H bond activation performed by the cluster compound.[4] Although reductive coupling between the two pyridyl groups leading to the stoichiometric formation of a bipyridine has been also reported,[5] catalytic 2,2′-bipyridine formation has never been reported so far.

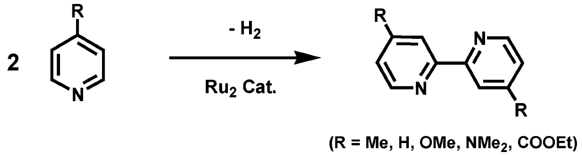
2,2′-Bipyridines are one of the most versatile bidentate ligands in organometallic and inorganic chemistry.[6] To date, two major methods of preparing 2,2′-bipyridine are known. One is a homocoupling of pyridine by a heterogeneous catalyst, such as Raney-nickel[7] or palladium on charcoal.[8] This method, however, is not applicable to the 4-substituted pyridines, such as isonicotinic acid. The second method is a transition-metal-catalyzed cross-coupling reaction.[9] This method, however, requires pyridyl halide, so formation of an equimolar amount of salt is inevitable. Thus, dehydrogenative coupling of functionalized pyridines by way of direct C−H bond activation appears as a useful alternative from an economic and environmental point of view.

In this report, we will describe a novel dehydrogenative coupling of 4-substituted pyridines catalyzed by the diruthenium complexes, $Cp^*Ru(\mu\text{-}H)_4RuCp^*$ (**1**; $Cp^* = \eta^5\text{-}C_5Me_5$)[10a] and $(Cp^*Ru)_2(\mu\text{-}PMe_2)(\mu\text{-}H)(\mu\text{-}\eta^2{:}\eta^2\text{-}C_6H_6)$ (**2**).[10b] Isolation of dinuclear intermediates of the reaction clearly illustrates that the reactions are performed on a multimetallic site, and that they are typical cluster catalyses.

The diruthenium tetrahydrido complex **1** catalyzes dimerization of several 4-substituted pyridines. The results are summarized in Table 1. 4,4′-Dimethyl-2,2′-bipyridine is produced above 120 °C (entry 1), and the yield exceeds 50% within 20 h at 160 °C using 1 mol % of catalyst (entry 3). The reaction selectively produced 2,2′-bipyridine, whereas no byproducts such as terpyridine were formed. Quite a few reports have been written on the preparation of 4,4′-difunctionalized-2,2′-bipyridine by way of direct C−H bond activation,[11] so it is noteworthy that complex **1** also catalyzes the dehydrogenative coupling of functionalized pyridines (entries 5 and 6).

4,4-Dicarboxy-2,2′-bipyridine is employed as an essential ligand for the dye-sensitized solar system of ruthenium.[12] Dehydrogenative coupling of ethyl isonicotinate provides a good synthetic alternative for this ligand. Although complex **1** did not work efficiently, as shown in entry 7, we found that a μ-dimethylphosphido complex, $(Cp^*Ru)_2(\mu\text{-}PMe_2)(\mu\text{-}H)(\mu\text{-}\eta^2{:}\eta^2\text{-}C_6H_6)$ (**2**), produces 4,4′-bis(ethoxycarbonyl)-2,2′-bipyridine.

Table 1. Dehydrogenative Coupling of 4-Substituted Pyridines by the Diruthenium Complexes **1** or **2**[a]



Ru_2 Cat. = $Cp^*Ru(\mu\text{-}H)_4RuCp^*$ (1), $(Cp^*Ru)_2(\mu\text{-}H)(\mu\text{-}PMe_2)(\mu\text{-}C_6H_6)$ (2)

entry	substrate	Ru_2 catalyst	substrate/ catalyst	time (h)	temp (°C)	yield[d] (%)
1[b]	R = Me	**1**	100	24	120	6
2		**1**	100	6	160	46
3		**1**	100	19	160	53
4	R = H	**1**	100	6	160	9
5	R = OMe	**1**	100	6	160	6[e]
6[c]	R = NMe_2	**1**	100	6	160	32[e]
7	R = COOEt	**1**	100	6	160	trace[e]
8	R = Me	**2**	100	20	180	34
9	R = H	**2**	100	20	180	20
10	R = OMe	**2**	100	20	180	64[e]
11	R = NMe_2	**2**	100	20	180	8[e]
12	R = COOEt	**2**	100	20	180	20[e]

[a] The reaction was carried out in a glass tube equipped with a Teflon-seal valve. Mesitylene was used as a solvent (ca. 3 mL), and the catalyst was loaded as a mesitylene solution (4 mM). Biphenyl was added to the flask as an internal standard. [b] Decane was used as a solvent, and the catalyst was loaded as a decane solution. [c] An internal standard, biphenyl, was not used, and the yield was determined by means of ^1H NMR by comparing the signal intensities of the product with those of the residual 4-(dimethylamino)pyridine. [d] The yield was determined by GLC analysis. [e] The yield was determined by ^1H NMR analysis.

The results of several 4-substituted pyridines catalyzed by the μ-phosphido complex **2** are also summarized in Table 1. While the yield of 4,4-dimethylamino-2,2′-bipyridine was lower than that obtained by **1** (entry 11), the yield of 4,4-dimethoxy-2,2′-bipyridine was much higher and was reached at 64% (entry 10). It is notable that dehydrogenative coupling of ethyl isonicotinate, which has lower basicity ($pK_b = 10.74$)[13] than that of other substituted pyridines, took place, and 4,4′-bis(ethoxycarbonyl)-2,2′-bipyridine was formed in a 20% yield (entry 12).

We then examined stoichiometric reactions of the dinuclear complexes with pyridine in order to obtain mechanistic insight. The reaction of **1** with 4-methoxypyridine afforded a bis(μ-pyridyl) complex **3** in nearly quantitative yield (Scheme 1). Diffraction study shows that the two pyridyl moieties are coordinated to the diruthenium center in *cis* geometry, and both nitrogen atoms are bound to the same ruthenium center, specifically, they adopts a head-to-head configuration (Figure 1A). Complex **3** seems to be an intermediate of the catalytic cycle, and 2,2′-bipyridine is probably formed by the reductive C−C bond formation at the Ru(2).

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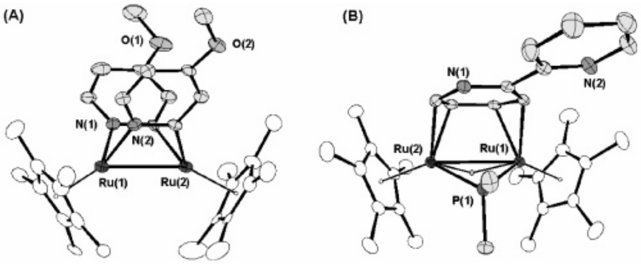
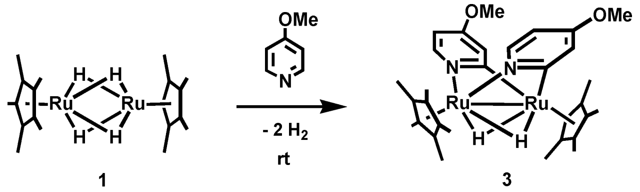
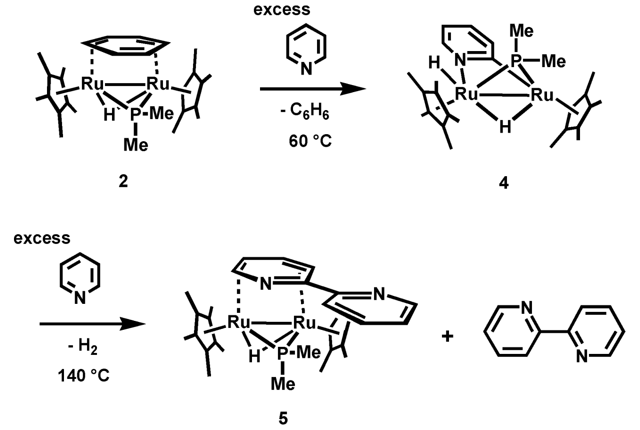


Figure 1. X-ray crystal structures of diruthenium complexes (A) **3** and (B) **5**, shown as 30% ellipsoids.

Scheme 1



Scheme 2



We also examined the reaction of **2** with pyridine. The reaction of **2** with 10 equiv of pyridine at 60 °C supplied a μ-pyridyl complex **4** in a quantitative yield (Scheme 2). Further heating in the presence of pyridine at 140 °C resulted in the formation of a μ-η^2:η^2-bipyridine complex **5**. A small amount of 2,2′-bipyridine was also formed during the reaction. Complex **5** was alternatively prepared by the reaction of **2** with bipyridine. X-ray diffraction study of **5** showed that the bipyridine did not coordinate on the bimetallic center in a κ-N fashion, but in a μ-η^2:η^2-diene mode through the four carbon atoms (Figure 1B). The μ-η^2:η^2-coordination of the pyridine ring through the carbon atoms was clearly identified by the significant upfield shift of the four ^{1}H signals derived from the coordinated aromatic moieties (δ 4.34, 3.74, 2.60, and 2.35).

It is surprising that the bipyridine prefers η^4-coordination as a diene rather than the chelation through the nitrogen atoms. Similar preference of pyridine for π-coordination rather than κ-N coordination was seen in a face-capping coordination of a pyridine molecule to the triruthenium core in $\{Cp^*Ru(\mu\text{-}H)\}_3(\mu_3\text{-}\eta^2{:}\eta^2{:}\eta^2\text{-}C_5NH_5)$,[14] and Harman and co-workers have recently elucidated equilibrium for the coordinated pyridine between κ-N and η^2-coordination through a $C{=}C$ bond at a tungsten center.[15]

The μ-η^2:η^2-coordination of bipyridine found in **5** probably causes the facile liberation of the bipyridine from the bimetallic center, thereby closing the catalytic cycle. Thus, the bimetallic center facilitates transformation of the coordination mode among κ-N pyridine, μ-pyridyl, and η^4-diene fashions by the cooperation of the neighboring metal centers. In addition to the high ability for C−H bond cleavage, sequential transformation of the coordination mode of pyridine on the bimetallic center plays a key role in this catalytic cycle.

In summary, we have disclosed a novel catalytic dehydrogenative coupling reaction of pyridines by the use of bimetallic ruthenium complexes. These results clearly represent the potential usefulness of a cluster catalyst toward C−H bond activation. The isolated intermediates, **3**, **4**, and **5**, highlight the occurrence of a cooperative interaction of the two metal centers in this transformation.

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Supporting Information Available: Experimental details and characterization (PDF), and crystallographic data (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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