Homogeneous Catalysis

Cooperative Catalysis by Ru and Pd for the Direct Coupling of a Chelating Aldehyde with Iodoarenes or Organostannanes**

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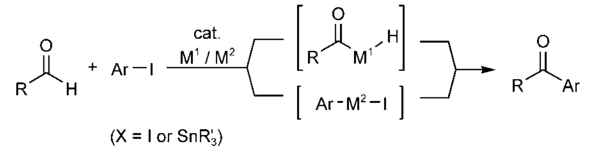
Dedicated to Professor Yong Hae Kim

Transition-metal catalysts have been designed and utilized conventionally to mediate single-step transformations.[1] In addition to the traditional one catalyst/one reaction approach, however, some recent examples have revealed that the appropriate combination of suitable and compatible metal species is able to effect sequential or cooperative catalytic one-pot transformations that are unprecedented in single-metal systems.[2] The extensive efforts in this field have borne fruit recently, and have led to some significant examples in the area of chemical catalysis.[3] We describe herein a novel application of cooperative catalysis to the coupling of an aldehyde with iodoarenes or organostannanes, in which Ru and Pd collaborate, presumably through catalytic transmetalation pathways. As part of our interest in coordination-assisted organic transformations,[4] we envisaged the possibility that aldehydes could be directly coupled with aryl iodides to afford ketone products in the presence of the appropriate combination of two catalysts [Eq. (1), $X = I$].[5] In analogy, we anticipated that the coupling of aldehydes and organostannanes could also be possible ($X = SnR_3$). The synthetic utility of these transformations would be extremely high since multistep processes are generally required for the preparation of ketones in classical synthetic methods starting from the same compounds (aldehydes and aryl halides).[6]



(1)

We chose 8-quinolinecarboxaldehyde (**1**) as the coupling partner since it was initially anticipated that formation of a five-membered chelate intermediate would effectively sup-

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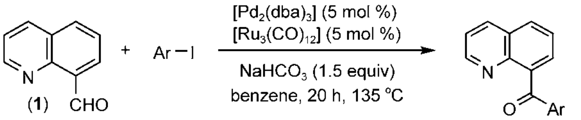
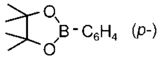
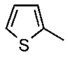
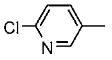
press any destructive decarbonylation pathway by catalytic activation of the formyl C–H bond. We found that treatment of iodobenzene with an acylrhodium hydride species,[7] obtained from the reaction of **1** with an equivalent amount of $[RhCl(PPh_3)_3]$, afforded the corresponding diaryl ketone in 60% yield in the presence of a catalytic amount of $[Pd_2(dba)_3]\cdot CHCl_3$ (5 mol%; dba = *trans,trans*-dibenzylideneacetone) at 135 °C after 5 h. We were further encouraged by the observation that a direct coupling between aldehyde **1** and iodobenzene took place even in systems containing both $[RhCl(PPh_3)_3]$ and $[Pd_2(dba)_3]\cdot CHCl_3$ (5 mol% each), albeit in lower yield (48%, 24 h), under otherwise identical conditions. The use of various other combinations of Rh and Pd catalysts proved to be far less efficient (< 5% yields), and no coupling was observed in the presence of any single-metal catalyst systems. A greatly improved efficiency was obtained when a Ru catalyst was employed instead of Rh in the presence of the Pd co-catalyst. Among all the Ru catalysts investigated, $[Ru_3(CO)_{12}]$ was found to be the most effective counterpart when combined with $[Pd_2(dba)_3]\cdot CHCl_3$. This combination afforded the ketone product in 83% yield (5 mol% of each catalyst) in the presence of $NaHCO_3$ (1.5 equiv) at 135 °C (20 h).

Under the optimized conditions, **1** was coupled with various iodoarenes to afford the corresponding aryl ketones in good yields (Table 1);[8] no noticeable electronic effects of the substituents on the iodoarenes were observed (Table 1, entries 1–5). The fact that a formyl group of the iodoarene substrate is tolerated suggests that the assumed coordination of the Ru center to the nitrogen atom of **1** is a driving force for the activation of the formyl C–H bond (Table 1, entry 6). An ester group also turned out to be compatible under these reaction conditions (Table 1, entry 7). Coupling of **1** with a bromoarene was much slower than with an iodoarene, as demonstrated in the reaction with 1-bromo-3-iodobenzene (Table 1, entry 8). The fact that a borate group is totally inert under these reaction conditions shows the highly selective nature of the present co-catalyst systems (Table 1, entry 9). The presence of heteroatoms such as nitrogen and sulfur does not affect the efficiency of the reactions (Table 1, entries 10 and 11). However, the coupling of **1** with vinyl iodides resulted in low yields (< 10%) with the present system.

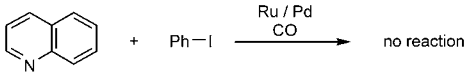
Table 1: Cooperative catalytic coupling of **1** with various iodoarenes.[a]



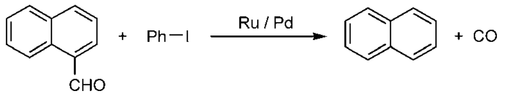
Entry	Ar	Yield [%][b]
1	C_6H_5	83
2	$4\text{-Me-}C_6H_4$	66
3	$4\text{-MeO-}C_6H_4$	62
4	$4\text{-Ac-}C_6H_4$	71
5	$4\text{-NO}_2\text{-}C_6H_4$	76
6	$4\text{-CHO-}C_6H_4$	80
7	$4\text{-EtO}_2\text{C-}C_6H_4$	79
8	$3\text{-Br-}C_6H_4$	73
9		63
10		89
11		90

[a] A mixture of **1** (0.5 mmol), iodoarene (1.0 mmol), $[Pd_2(dba)_3]\cdot CHCl_3$ and $[Ru_3(CO)_{12}]$ (5 mol% each), and $NaHCO_3$ (0.75 mmol) in benzene (1.0 mL) was stirred at 135 °C for 20 h. [b] Yield of isolated product.

Control experiments were performed to verify the presumed cooperative catalytic pathways. No conversion was observed when quinoline was treated with iodobenzene under an atmosphere of CO under otherwise identical conditions [Eq. (2)]. This result may rule out the possibility that the reaction of aldehyde **1** and iodoarenes proceeds by Ru-catalyzed decarbonylation of **1** followed by Pd-catalyzed arylcarbonylation of iodobenzene.[9] In fact, there are several precedents for the $[Ru_3(CO)_{12}]$-catalyzed orthometalation of nitrogen-containing heteroaromatic compounds to provide *ortho*-carbonylated adducts.[10] Aldehydes devoid of a coordinating group were not coupled with iodobenzene, which implies that activation of a formyl C–H bond of **1** is coordination-directed [Eq. (3)].[11]



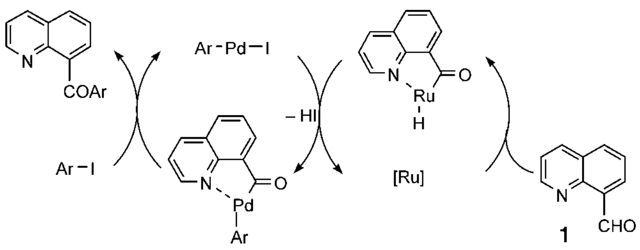
(2)



(3)

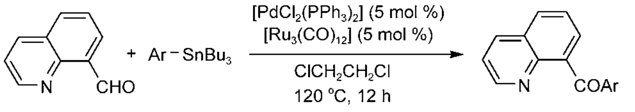
When **1** was treated with a stoichiometric amount of $[Ru_3(CO)_{12}]$ in 1,2-dichloroethane (120 °C, 30 min) the aldehydic proton signal disappeared gradually from the ^1H NMR spectrum, to be replaced by a signal for an acylruthenium hydride ($\delta = -15.9$ ppm; singlet in $CDCl_3$).[12] The IR spectrum of the isolated adduct shows an absorbance band at 1846 cm^{-1}, which is assignable to the stretching band of the speculative Ru–H bond.[13] It should be noted that a stoichiometric activation of **1** has previously been reported with Na_2PdCl_4 to afford a chloro-bridged Pd dimer.[14] However, no conversion was observed upon the treatment of **1** with aryl iodides in the presence of a range of Pd catalysts and in the absence of ruthenium co-catalysts. Moreover, the C–I bond of iodobenzene was inert to the Ru catalyst under the reaction conditions, even when one equivalent of $[Ru_3(CO)_{12}]$ was used, which strongly suggests that the activation of iodobenzenes is carried out selectively by Pd catalysts in the presence of ruthenium species. The above observation led us to propose a primitive mechanistic scenario for the cooperative catalysis (Scheme 1). Ruthenium may activate a formyl C–H bond of the chelating aldehyde **1** to afford a five-membered cycloacylruthenium hydride intermediate,[15] which is subsequently transferred into the Pd catalytic cycle with iodoarenes and eventually leads to coupled ketone products after a reductive-elimination step.

The concept of cooperative catalysis by Pd and Ru was further extended into coupling reactions of **1** with organostannanes [Eq. (4)]. Since it is known that organostannanes



Scheme 1. Proposed pathway for the Ru/Pd co-catalytic coupling of aldehyde **1** with iodobenzenes.

are readily activated by certain Pd complexes,[16] their coupling with **1** was initially investigated in the presence of Ru and Pd co-catalysts. We were pleased to find that the corresponding ketone products were generated in acceptable yields from the reactions with a range of tin compounds (1.5 equiv relative to **1**). The reaction proceeds most effectively in 1,2-dichloroethane at 120 °C when [$PdCl_2(PPh_3)_2$] and [$Ru_3(CO)_{12}$] (5 mol% each) are used simultaneously. Various functional groups, including cyano, formyl, and heteroatoms, are tolerated under the present conditions. As anticipated, tributyltin hydride was generated as a side-product from the reactions (yields of over 60%). It should be mentioned that, to the best of our knowledge, this represents the first example of a direct coupling between an aldehyde and organotin compounds.[17] As in the above coupling reactions between **1** and iodoarenes, the use of any single-catalyst systems of Ru, Pd, or Rh gave none of the desired products.



(4)

Ar =	
C_6H_5	60%
4-MeC_6H_4	56%
4-NCC_6H_4	61%
4-$CHOC_6H_4$	49%
thienyl	66%

In summary, we have demonstrated that the appropriate combination of two suitable and compatible metallic catalyst systems provides a new possibility for the development of novel synthetic methodologies that are difficult to carry out with any single-catalyst systems. More detailed mechanistic studies and further application of this cooperative catalysis are now in progress.

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