Quasi-nature catalysis. Rhodium-catalyzed C–C bond formation in air and water*

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Abstract: Transition-metal catalysis is out-grown from dry-boxes where the use of inert gas atmosphere and the exclusion of moisture have been essential. Such a restriction undoubtedly imposes limitations in the application of these reactions in organic synthesis and in the recycling of the catalysts. This article discusses some recent advances of rhodium-catalyzed carbon–carbon bond formations under the natural conditions of air and water.

INTRODUCTION

The use of metals and transition metals for mediating and catalyzing reactions is of great importance in modern organic chemistry. Historically, it is essential to use inert gas atmosphere and the exclusion of moisture in organometallic reactions. Such a restriction undoubtedly imposes limitations in the application of these reactions in organic synthesis. Recently, as an interest in green chemistry we have been developing metal-mediated and catalyzed reactions under ambient conditions of air and water [1]. Such reactions have several advantages: (1) water-soluble substrates such as carbohydrates can be used directly without derivatization, (2) the aqueous catalyst solution can be recycled easily without the need of regeneration, and (3) it is more convenient for operations without the need of using inert gas atmosphere. This article briefly discusses some recent findings in developing transition-metal-catalyzed carbonyl addition and conjugated addition with vinyl- and arylmetal reagents in air and water (eq. 1) [2]. Ultimately, we hope to develop a process involving only a catalytic amount of metals in air and water to effect related reactions.
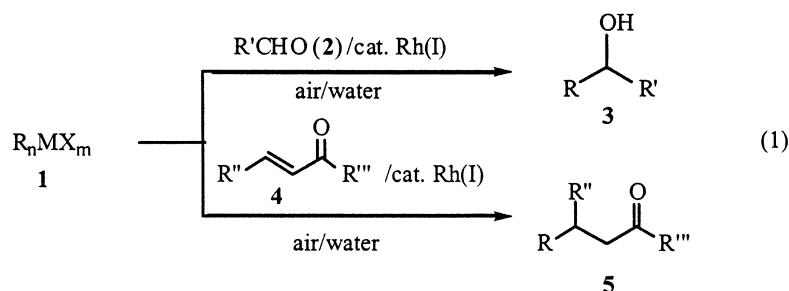

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RESULTS AND DISCUSSION

Choice of organometallic reagents

A general requirement for the success of the desired reactions is that the corresponding organometallic reagent be stable in air and water. Based on previous literature, a variety of aryl and vinyl derivatives of metals, including B, In, Sn, Ge, Pb, As, Sb, and Bi, were chosen. These reagents were either purchased from commercial sources or prepared in our laboratory.

R_nMX_m R = aryl or vinyl
M = B, In, Sn, Ge, Pb, As, Sb, Bi
X = alkyl, aryl, halogen, hydroxyl, and alkoxyl
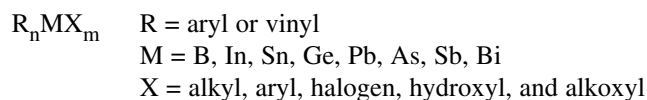
Selection of the catalysts

In order to effect the desired transformation, a variety of transition-metal complexes available in our laboratory were tested by using trimethylphenyltin and benzaldehyde as the model reaction. Organotin compounds were selected for the test due to their relatively high stability and the ability of tailoring chemo-, regio-, and stereoselectivities by combination of these reagents with appropriate catalysts [3]. Among the transition-metal complexes being tested, $Rh_2(COD)_2Cl_2$ and $Rh(COD)_2BF_4$ provided the desired product smoothly [4]. Previously, Oi and co-workers studied the reaction of arylstannanes with carbon electrophiles in anhydrous solvent, under nitrogen, in a sealed Schlenk tube, catalyzed by $[Rh(COD)(CH_3CN)_2]BF_4$, and quenched by adding water [5]. The use of $Ni(acac)_2$ as the catalyst was also effective but it provided the desired product in very low yield. No reaction was observed with other catalysts. Subsequently, the two Rh(I) catalysts were used for both carbonyl addition and conjugated addition studies.

Effect of substrates

The reaction was found highly dependent on both electronic and steric effects. For the carbonyl additions, aromatic aldehydes in general provided better results than aliphatic aldehydes under the present reaction conditions. With aromatic aldehydes, the presence of electron-withdrawing groups appeared beneficial to the reaction; whereas the presence of electron-donating substituents decreased their reactivities. Increased steric hindrance around the reaction site also decreased the yield of the desired product.

For the conjugated addition, both ketones (linear and cyclic) and esters were effective as the electron-withdrawing functional groups. When either a mono- or disubstituted unsaturated C=C was involved, the reaction proceeded rapidly. In some cases, a mixture of several products including both the conjugated addition and Heck-type reaction products was observed for the mono-substituted derivatives. Either no reaction was observed or very low yields of the products were obtained with tri-substituted derivatives.

Effect of organometallic reagents

The success of both the carbonyl addition and the conjugated addition was found to be highly dependent upon both the metal and the groups attached to the metal. Except for organoarsenic (highly toxic) and organoantimony reagents, aryl or vinyl derivatives of all the other metals (and metalloids) examined were able to generate the desired carbonyl addition and conjugated addition products with varied efficiencies. Among them, aryl and vinyltin, boron, lead, and bismuth derivatives were found to be the most effective. The corresponding indium and germanium reagents provided only low yields of the products.

A strong effect (by the electronic nature of substituents) on the reactivity of organometallic reagents was observed in the rhodium-catalyzed carbonyl additions and conjugated additions in air and water. Take the organotin reagents as an example (Table 1), in the presence of a catalytic amount of $Rh(COD)_2BF_4$ at refluxing temperature in air and water, benzaldehyde underwent nucleophilic addition with trimethylphenyltin and dibutyldiphenyltin to give the corresponding nucleophilic addition product smoothly (entries 3 and 4). On the other hand, under the same reaction conditions, no reaction was observed between benzaldehyde and phenyltin trichloride even after several days (entry 1). When the reaction was carried out in the presence of potassium hydroxide, a smooth reaction occurred again to give the desired product overnight (entry 2). A more dramatic effect was observed by using triphenyltin chloride, triphenyltin hydroxide, and butyltriphenyltin (entries 5–7). No reaction was observed with the chloride derivative, but the reaction with either hydroxide or butyl derivatives proceeded smoothly. The use of different bases also affects the reaction progress. Various bases such as lithium hydroxide, sodium hydroxide, and potassium hydroxide were tested (which showed the same trend as the basicity), and potassium hydroxide appeared to be the most effective for this reaction. A similar dramatic electronic effect was observed in the conjugated addition of unsaturated ketones, including 1-cyclohexen-2-one, 1-cyclohepten-2-one, and trans-1,2-dibenzoylethylene. Such an electronic effect was also observed with organobismuth, organolead, organoindium, and organoboron compounds.

Table 1 Substituent effect on the rhodium-catalyzed phenylation of aldehydes in air and water.

Entry	Reagents (**1**)	Substrate (**2**)	Base	Yield (%)
1	$PhSnCl_3$	PhCHO	No base	0
2	$PhSnCl_3$	PhCHO	KOH	71
3	$PhSnMe_3$	PhCHO	No base	82
4	Ph_2SnBu_2	PhCHO	No base	62
5	Ph_3SnCl	PhCHO	No base	0
6	Ph_3SnOH	PhCHO	No base	31
7	Ph_3SnBu	PhCHO	No base	43

Mechanistic studies

A tentative mechanism for both the carbonyl addition and the conjugated addition was proposed involving the insertion of rhodium between vinyl and aryl C–M bonds to generate a C–Rh–M intermediate. The intermediate then undergoes either carbonyl addition with aldehydes or conjugated addition with unsaturated carbonyl compounds to give the corresponding metal alkoxide and metal enoxide derivatives and regenerates the active catalyst. Hydrolysis of these intermediates in water resulted in the formation of the final products (Scheme 1). As an indication of the plausibility of the mechanism, previously the crystal structure of a complex involving a phenyl-platinum-lead structure was reported [6].

In conclusion, rhodium (I) complexes were found to catalyze carbonyl additions and conjugated additions with a variety of vinyl- and arylmetallic reagents in air and water. The reactions were influenced by the nature of the metal, the electronic nature of the groups attached to the metals, and the electronic properties as well as the steric environment of the substrates. Applications of the reaction in natural product synthesis such as the synthesis of amino acids are underway [7]. Efforts are currently being made to reduce the amount of metals to a catalytic amount via C–H bond activation to generate a clean and living catalytic process in air and water.
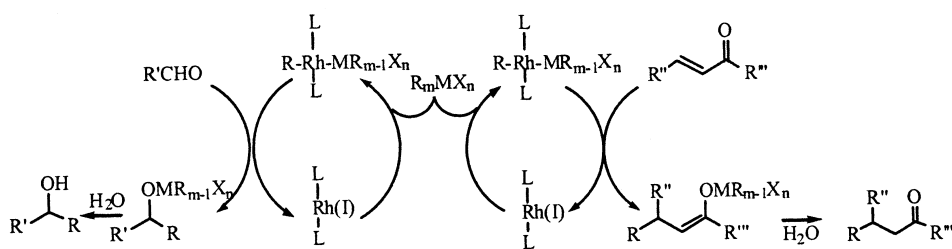
Scheme 1 Tentative mechanism for the rhodium-catalyzed carbonyl addition and conjugated addition in air and water.

ACKNOWLEDGMENTS

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