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Tetrahedron Letters 45 (2004) 2995–2998
Tetrahedron Letters

Rhodium-catalyzed and sonication-accelerated addition of aryltin and aryllead reagents to imines in air and water

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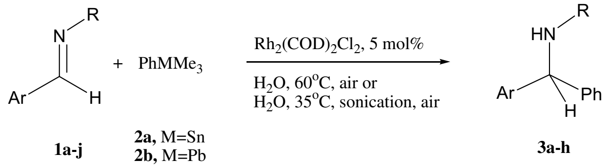
Received 16 September 2003; revised 15 January 2004; accepted 30 January 2004

Abstract—In the presence of a rhodium catalyst, imines (**1a**–**k**) react with phenyltrimethyltin **2a** or phenyltrimethyllead **2b** in water and air under ultrasonic irradiation at 35 °C to give the corresponding diarylmethylamines (**3a**–**k**) in good yields.

In current years, there has been a growing interest in studying organic reactions in water,[1] due to its natural abundance as well as the inherent advantages of using water as a solvent. Recently, we have been exploring transition-metal-catalyzed carbon–carbon bond formations under the quasi-natural conditions of air and water.[2] Toward such a general goal, a Grignard-type phenylation of aldehydes with phenyltin reagents in water was discovered.[3] Subsequently, we also found that in the presence of a rhodium catalyst, α,β-unsaturated esters, and ketones react with arylbismuth, arylsilicon, aryltin, and aryllead reagents as well as trialkylvinyltin reagents in aqueous media to give the corresponding conjugated addition products under an air atmosphere.[4] More recently, Oi et al.[5] reported a rhodium-catalyzed asymmetric 1,4-addition of organosiloxanes to α,β-unsaturated carbonyl compounds in aqueous media (dioxane/water 10:1) at 90 °C. On the other hand, the addition reactions of organometallic reagents to imines[6] provide a useful method to synthesize diarylmethylamines, which are structural units of many pharmacologically interesting and biologically important compounds.[7] In general, organolithium and Grignard reagents are used for this purpose.[6b,c,8] Obviously, the use of anhydrous solvent and inert gas atmosphere are required for the proceeding of the reaction. Rhodium-catalyzed arylation reactions of imines with arylstannanes in THF[9] and in dioxane[10] and with arylboronic acids in dioxane[11] were reported; however, they all require anhydrous conditions and inert gas atmosphere. To our knowledge, there has not been any example of the transition metal-catalyzed addition of arylmetal reagents to imines in aqueous media reported to date, probably due to the lower electrophilic reactivity of C=N bond of imines than that of C=O bond of carbonyl compounds and the ready hydrolysis of imines in water. Herein, we wish to report the results of rhodium-catalyzed addition reactions of aryltin and aryllead reagents with imines in water and air under ultrasonic irradiation or by regular heating.

To start the investigation, the reaction of *N*-tosylbenzylideneimine (**1a**, Ar=Ph, R=Ts) with phenyltrimethyltin (**2a**) in the presence of catalyst $Rh_2(COD)_2Cl_2$ (5 mol %) was carried out in water at 60 °C (Scheme 1) to give the addition product, *N*-tosyldiphenylmethylamine (**3a**), in 48% yield (Table 1, entry 1). Meanwhile, it was observed that the experimental results on the reactions of imine in water were not easy to repeat, probably due to hydrolysis of the aldimine **1a** during the reaction[9b] and the lack of mixing between the solid catalyst and the solid aldimine compounds in water. The addition of a



Scheme 1.

Keywords: Rhodium; Imine addition; Aqueous catalysis; Air atmosphere; Sonication.

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doi:10.1016/j.tetlet.2004.01.160

Table 1. Rh-catalyzed reaction of imine **1a** with $PhSnMe_3$ (**2a**)

Entry	Conditions	Yield[a] of **3a** (%)
1	H_2O/60 °C/14 h	48
2	H_2O/35 °C/1.5 h	Trace
3	H_2O/35 °C/sonication/1.5 h	80
4	THF/35 °C/1.5 h	Trace
5	THF/35 °C/sonication/1.5 h	Trace

[a] Isolated yield after column chromatography on silica gel.

surfactant (SDS) did not improve reproducibility of the experimental results. However, when the mixture of **1a**, **2a** and the catalyst in water was sonicated at 35 °C for 1.5 h, the reaction proceeded smoothly to afford product **3a** in 80% yield (Scheme 1, Table 1, entry 3) with high reproducibility.[12] In contrast, only a trace of **3a** was observed on TLC, if the reaction was carried out under the same conditions without sonication (entry 2). Sonication turned the reaction mixture into an emulsion and accelerated the Rh-catalyzed addition of aryltin reagent to imine in water dramatically,[13] resulting in a great preference of addition reaction over hydrolysis. Interestingly, if THF was used as solvent instead of water, the reaction of **1a** with **2a** at 35 °C for 1.5 h gave only a trace amount of **3a** either with or without sonication (entries 4–5). The acceleration of sonication to the reaction was only observed in water solution, even though a homogeneous THF solution of the reagents and the Rh catalyst was formed during the reaction.

Based on these experimental results, various arylimines were selected as substrates in the rhodium-catalyzed reaction of imines with phenyltrimethyltin (**2a**) and phenyltrimethyllead (**2b**) in water and air at 35 °C under sonication. When *N*-(*p*-methoxyphenyl)-benzylideneimine(**1i**) and *N*-phenyl-benzylideneimine (**1j**) were used under the same conditions, no or only a small amount of the corresponding addition products were detected in the reaction mixture (Table 2, entries 11–12). On the other hand, the reactions of *N*-tosylarylimines **1a**–**g** with **2a** or **2b** in the presence of rhodium catalyst (5 mol %) proceeded smoothly under the same conditions to give phenylarylmethylamines **3a**–**g** in good yields (entries

Table 2. Rh-catalyzed reactions of imines with $PhMMe_3$ in water under sonication

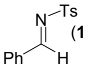
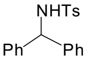
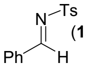
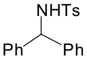
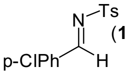
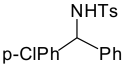
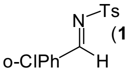
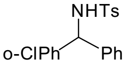
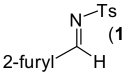
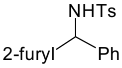
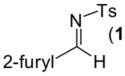
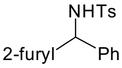
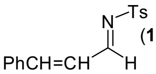
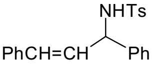
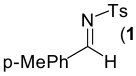
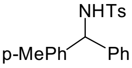
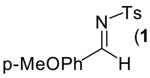
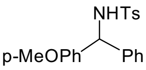
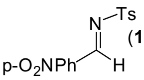
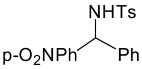
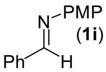
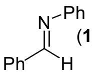
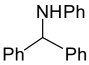
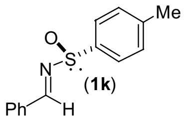
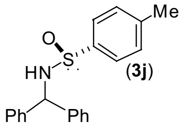
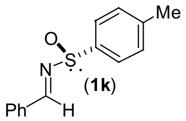
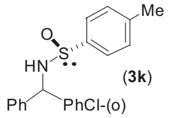
Entry	Imine	$PhMMe_3$	Product	Yield[a]
1	 (**1a**)	**2a**	 (**3a**)	81
2	 (**1a**)	**2b**	 (**3a**)	78
3	 (**1b**)	**2a**	 (**3b**)	77
4	 (**1c**)	**2a**	 (**3c**)	75
5	 (**1d**)	**2a**	 (**3d**)	84
6	 (**1d**)	**2a**	 (**3d**)	85
7	 (**1e**)	**2a**	 (**3e**)	76
8	 (**1f**)	**2a**	 (**3f**)	63
9	 (**1g**)	**2a**	 (**3g**)	60[b]
10	 (**1h**)	**2a**	 (**3h**)	30[b,c]
11	 (**1i**)	**2a**	None	
12	 (**1j**)	**2a**	 (**3i**)	Trace

Table 2 (*continued*)

Entry	Imine	$PhMMe_3$	Product	Yield[a]
13	 (**1k**)	**2a**	 (**3j**)	58
14	 (**1k**)	**2c**	 (**3k**)	76[d]

2a = $PhSnMe_3$, **2b** = $PhPbMe_3$, **2c** = *o*-$ClPhPbMe_3$.

[a] Isolated yields, 35 °C, sonication for 1.5 h.

[b] Sonicated for 2 h.

[c] 45% yield of *p*-$O_2NPhCH(OH)Ph$ (4) was obtained.

[d] de = 34%.

1–9). The latter was attributed to the activation of the C=N bond by an electron-withdrawing tosyl group. Phenyllead reagent exhibited the same reactivity as phenyltin reagent (entries 2 vs 1 and 6 vs 5). It was found that the use of arylimines with electron-donating group in the phenyl ring (**1f–g**) gave products **3f–g** in lower yields (entries 8–9). An exception is the case of *N*-tosyl-*p*-nitrobenzylideneimine **1h**, from which only 30% yield of the product **3h** was obtained and, in addition, (*p*-nitrophenyl)phenylmethanol (**4**) was detected (**3h**:**4** = 1:1.5). The results suggested that addition reaction and hydrolysis of imines competed in water. For most imines used, the addition reaction surpassed the hydrolysis of imine to give the desired products in good yields. However, in the case of **1h**, the hydrolysis of imine is faster than the addition reaction. Subsequently, the hydrolysis product *p*-nitrobenzaldehyde reacted with **2a** to afford **4**. The *p*-toluenesulfinylimine (**1k**) exhibited a relatively lower reactivity (58% yield) than *p*-toluenesulfonylimine (80% yield, entries 13 vs 1). However, when a chiral imine, (+)-*N*-(*S*)-*p*-toluenesulfinylbenzylideneimine[(+)-**1k**], was allowed to react with *o*-chlorophenyltrimethyllead (**2c**) in water under sonication, a mixture of two diastereomers of **3k** was obtained in 76% yield and 34% de as determined by ^1H NMR of **3k**.

A typical experimental procedure is as follows: a mixture of **1a** (60 mg, 0.22 mmol), **2a** (84 mg, 0.37 mmol) and $Rh_2(COD)_2Cl_2$ (6 mg, 0.012 mmol) in 3 mL of water was sonicated in an ultrasound bath at 35 °C for 1.5 h. Then, 15 mL of ether was added. The organic phase was separated and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic layer was dried over $MgSO_4$, filtered, and concentrated in vacuo. The crude product was purified by a flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate = 20:1) to give product **3a** (59 mg, yield 80%).

Acknowledgements

We thank the financial support for this study provided by the National Natural Science Foundation of China (No. 20332030, 20232010) and The Chinese Academy of Sciences.

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