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Rhodium-catalyzed regioselective cross-coupling of styrene oxides with arylboronic acids in aqueous γ-valerolactone

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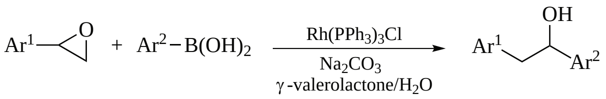
A simple and regioselective cross-coupling of styrene oxides with arylboronic acids in the presence of $Rh(PPh_3)_3Cl$ in biomass-derived γ-valerolactone has been developed. The reactions proceeded smoothly to give 1,2-diaryl ethanols as the predominant products in moderate to good yields.

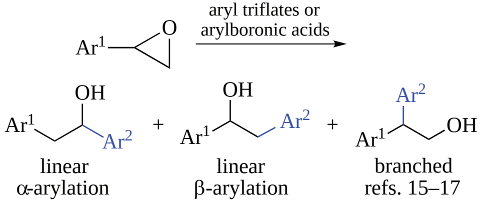


Keywords: styrene oxides, arylboronic acids, rhodium catalysis, regioselectivity, γ-valerolactone, green solvent.

The opening of styrene oxides with carbon nucleophiles is of great significance in organic synthesis,[1–3] providing a direct access to diverse linear or branched alcohols. Despite great advances, such reaction is limited to the use of reactants giving stabilized carbanions, strong organometallic reagents, or π-systems.[4–9] Recently, the coupling of styrene oxides with less reactive nucleophiles such as carbon electrophiles has been disclosed (Scheme 1). Doyle group and Weix group independently reported the nickel-catalyzed cross-coupling of styrene oxides with arylboronic acids or aryl halides to synthesize α-arylated[10] or β-arylated linear alcohols.[11] Later, Fu group[12] and Weix group[13] realized the synthesis of β-arylated linear alcohols in the presence of Cu or Ni catalyst. Just recently, Giedyk group reported the synthesis of β-arylated linear alcohols *via* regioselective ring opening of styrene oxides with aryl halides using vitamin B_{12}/Ni dual-catalytic system.[14] Branched products can be also obtained in the presence of a titanocene cocatalyst[15–17] when secondary alkyl radicals are generated.

While acknowledging these pioneering contributions in this field, there are still some issues that need to be addressed. Most of the reported protocols required the use of expensive ligands or cocatalysts. However, the regioselective synthesis of 1,2-diarylethanols, particularly in a green manner, is still less exploited so far. Herein, we report a rhodium-catalyzed regioselective cross-coupling of styrene oxides with arylboronic acids in the absence of any ligands or cocatalysts in green solvent.

Initially, we started to optimize the reaction conditions using styrene oxide **1a** and phenylboronic acid **2a** as the model substrates in THF (Scheme 1, Table 1). Firstly, different Rh catalysts were screened, and $Rh(PPh_3)_3Cl$ was the best choice (entries 1–4). The reaction proceeded smoothly in the presence of only 0.5 mol% of $Rh(PPh_3)_3Cl$ and sodium carbonate (1 equiv.), providing the desired product **3a** in 81% yield. Different solvents such as toluene, *tert*-butanol, acetonitrile and DMF were then evaluated. However, the reaction in these solvents gave only trace amount of **3a** (entries 5–8). Reactions in methyl *tert*-butyl ether, ethyl acetate and γ-butyrolactone (GBL) produced **3a** in low to moderate yields (entries 9–11). Encouragingly, reaction in γ-valerolactone (GVL) afforded **3a** in 78% yield, and an 85% yield of **3a** was obtained in GVL/H_2O solvent (entries 12 and 13). This may be due to the fact that addition of water improves the solubility of the substrate and base in GVL. Then we focused on the use of GVL for our subsequent studies due to its high boiling and flash points, low toxicity and good chemical



Scheme 1

Table 1 Optimization studies for the coupling of styrene oxide **1a** and phenylboronic acid **2a**.[a]

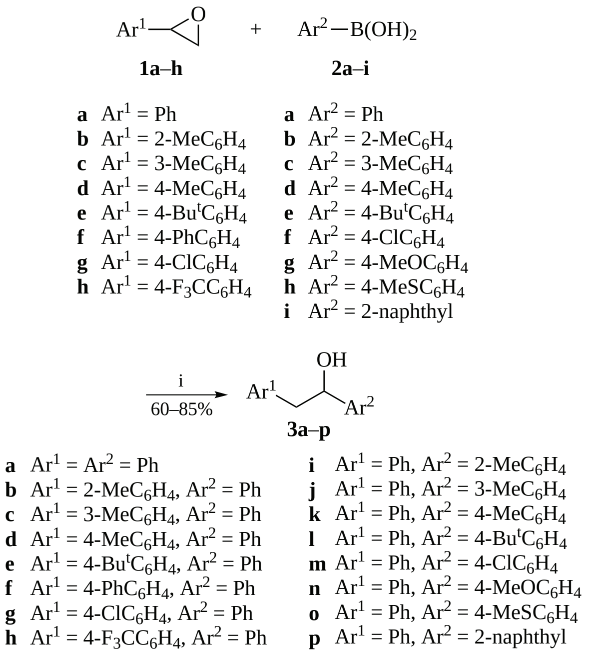
Entry	Rh catalyst	Base	Solvent	*T*/°C	Yield of **3a** (%)[b]
1	$Rh(PPh_3)_3Cl$	Na_2CO_3	THF	120	81
2	$[Rh(cod)Cl]_2$	Na_2CO_3	THF	120	72
3	$RhCl_3$	Na_2CO_3	THF	120	0
4	$Rh_2(OAc)_4$	Na_2CO_3	THF	120	0
5	$Rh(PPh_3)_3Cl$	Na_2CO_3	toluene	120	trace
6	$Rh(PPh_3)_3Cl$	Na_2CO_3	Bu^tOH	120	trace
7	$Rh(PPh_3)_3Cl$	Na_2CO_3	MeCN	120	trace
8	$Rh(PPh_3)_3Cl$	Na_2CO_3	DMF	120	trace
9	$Rh(PPh_3)_3Cl$	Na_2CO_3	$MeOBu^t$	120	29
10	$Rh(PPh_3)_3Cl$	Na_2CO_3	EtOAc	120	38
11	$Rh(PPh_3)_3Cl$	Na_2CO_3	GBL	120	63
12	$Rh(PPh_3)_3Cl$	Na_2CO_3	GVL	120	78
13	$Rh(PPh_3)_3Cl$	Na_2CO_3	GVL/H_2O (1 : 1)	120	85
14	$Rh(PPh_3)_3Cl$	K_2CO_3	GVL/H_2O (1 : 1)	120	76
15	$Rh(PPh_3)_3Cl$	K_3PO_4	GVL/H_2O (1 : 1)	120	trace
16	$Rh(PPh_3)_3Cl$	KOH	GVL/H_2O (1 : 1)	120	trace
17	$Rh(PPh_3)_3Cl$	Na_2CO_3	GVL/H_2O (1 : 1)	110	77
18	$Rh(PPh_3)_3Cl$	Na_2CO_3	GVL/H_2O (1 : 1)	130	85
19	$Rh(PPh_3)_3Cl$	Na_2CO_3	GVL/H_2O (1 : 1)	120	70,[c] 86,[d] 74[e]

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol, 3.0 equiv.), Rh catalyst (0.5 mol%), base (1.0 equiv.), solvent (2 ml), nitrogen atmosphere, 120 °C, 12 h. [b] Isolated yield. [c] With 2.0 equiv. of **2a**. [d] With 4.0 equiv. of **2a**. [e] Reaction in air.

stability.[18] Some bases were also evaluated. Slightly lower yield was obtained using K_2CO_3 as the base, while only trace amount of **3a** was detected with KOH or K_3PO_4 (entries 14–16). In addition, the process at 110 °C gave relatively low yield while further raising the temperature to 130 °C did not benefit the yield (entries 17 and 18). The reaction outcome was also influenced by the loading of boronic acid. Product **3a** was obtained in 70% yield with 2 equiv. of **2a**, and 86% yield with 4 equiv. of **2a**, respectively. Finally, reaction in air was performed, and a slightly lower yield was obtained (entry 19). It should be pointed out that compound **3a** was the predominant product, and only traces of other impurities were detected.

A series of other styrene oxides and arylboronic acids were then tested under the optimized reaction conditions (Scheme 2).† Styrene oxides with methyl, *tert*-butyl, phenyl, chloro and trifluoromethyl substituents showed good activities, affording the corresponding products **3a–h** in moderate to good yields (60–85%). Steric hindrance exerted little effect on the reaction outcome (products **3b–d**). Evaluation of arylboronic acids showed that both electron-donating (**2b–e**,**g**,**h**) and electron-withdrawing (**2d**,**i**) substituents are tolerated to give the products. Importantly, *p*-methoxy- and *p*-methylthio-substituted arylboronic acids **2g**,**h** survived well to afford alcohols **3n** (68%) and **3o** (62%), respectively (these substrates are known to undergo homocoupling in the presence of nickel catalysts[10,11]). It is also worth noting that aliphatic epoxides do not undergo the title transformation, apparently, owing to high activation barrier for oxidative addition to aliphatic C_{sp3}–O bonds.

A mechanism is proposed based on previously published data[11,19] (Scheme 3). Initially, rearrangement of styrene oxide **1** in the presence of $Rh(PPh_3)_3Cl$ would generate the aldehyde intermediate **A**.[20] Then oxidative addition between intermediate **A** and $Rh(PPh_3)_3Cl$ occurs to give intermediate **B**, which further reacts with arylboronic acid to form intermediate **C**. Finally, reductive elimination from **C** affords the desired product **3**, and the catalyst is regenerated. Control experiment with 2-phenylacetaldehyde $PhCH_2CHO$ supported the suggested mechanism when 91% yield of **3a** was achieved under optimized conditions (*cf*. Table 1, entry 19). This result indicated that the aldehyde **A** might be the real intermediate in this reaction.



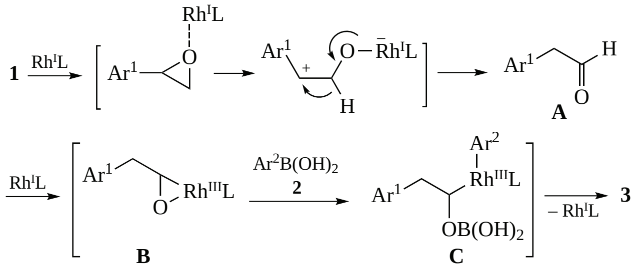
a $Ar^1 = Ph$
b $Ar^1 = 2\text{-}MeC_6H_4$
c $Ar^1 = 3\text{-}MeC_6H_4$
d $Ar^1 = 4\text{-}MeC_6H_4$
e $Ar^1 = 4\text{-}Bu^tC_6H_4$
f $Ar^1 = 4\text{-}PhC_6H_4$
g $Ar^1 = 4\text{-}ClC_6H_4$
h $Ar^1 = 4\text{-}F_3CC_6H_4$

a $Ar^2 = Ph$
b $Ar^2 = 2\text{-}MeC_6H_4$
c $Ar^2 = 3\text{-}MeC_6H_4$
d $Ar^2 = 4\text{-}MeC_6H_4$
e $Ar^2 = 4\text{-}Bu^tC_6H_4$
f $Ar^2 = 4\text{-}ClC_6H_4$
g $Ar^2 = 4\text{-}MeOC_6H_4$
h $Ar^2 = 4\text{-}MeSC_6H_4$
i $Ar^2 = 2\text{-naphthyl}$

a $Ar^1 = Ar^2 = Ph$
b $Ar^1 = 2\text{-}MeC_6H_4$, $Ar^2 = Ph$
c $Ar^1 = 3\text{-}MeC_6H_4$, $Ar^2 = Ph$
d $Ar^1 = 4\text{-}MeC_6H_4$, $Ar^2 = Ph$
e $Ar^1 = 4\text{-}Bu^tC_6H_4$, $Ar^2 = Ph$
f $Ar^1 = 4\text{-}PhC_6H_4$, $Ar^2 = Ph$
g $Ar^1 = 4\text{-}ClC_6H_4$, $Ar^2 = Ph$
h $Ar^1 = 4\text{-}F_3CC_6H_4$, $Ar^2 = Ph$

i $Ar^1 = Ph$, $Ar^2 = 2\text{-}MeC_6H_4$
j $Ar^1 = Ph$, $Ar^2 = 3\text{-}MeC_6H_4$
k $Ar^1 = Ph$, $Ar^2 = 4\text{-}MeC_6H_4$
l $Ar^1 = Ph$, $Ar^2 = 4\text{-}Bu^tC_6H_4$
m $Ar^1 = Ph$, $Ar^2 = 4\text{-}ClC_6H_4$
n $Ar^1 = Ph$, $Ar^2 = 4\text{-}MeOC_6H_4$
o $Ar^1 = Ph$, $Ar^2 = 4\text{-}MeSC_6H_4$
p $Ar^1 = Ph$, $Ar^2 = 2\text{-naphthyl}$

Scheme 2 *Reagents and conditions*: i, **1** (0.2 mmol), **2** (0.6 mmol), $Rh(PPh_3)_3Cl$ (0.5 mol%), Na_2CO_3 (0.2 mmol), GVL/H_2O (1 : 1, 2 ml), N_2, 120 °C, 12 h.



Scheme 3

In summary, we have developed a simple and regioselective rhodium-catalyzed cross-coupling of styrene oxides with arylboronic acids in biomass-derived γ-valerolactone to give 1,2-diarylethanols in moderate to good yields. In this procedure, both reactants are low-toxic and readily available. No ligand or cocatalyst is required in this reaction.

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Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.03.034.

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† *General procedure for the synthesis of 1,2-diarylethanols* **3**. A sealed tube equipped with a magnetic stirring bar was charged with styrene oxide **1** (0.2 mmol), arylboronic acid **2** (0.6 mmol, 3.0 equiv.), $Rh(PPh_3)_3Cl$ (0.5 mol%), Na_2CO_3 (0.2 mmol, 1.0 equiv.) and GVL/H_2O (1 : 1, 2 ml) under N_2. The mixture was then heated to 120 °C and stirred for 12 h. Upon reaction completion, the resulting solution was quenched with water and extracted with ethyl acetate. The collected organic extracts were dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography using petroleum ether/ethyl acetate (8 : 1) as eluent to afford product **3**.