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Cite this: *Chem. Commun.*, 2011, **47**, 2161–2163

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Phosphine ligand triggered oxidative decarbonylative homocoupling of aromatic aldehydes: selectively generating biaryls and diarylketones†

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Received 12th November 2010, Accepted 13th December 2010
DOI: 10.1039/c0cc04921b

Published on 06 January 2011 on http://pubs.rsc.org | doi:10.1039/C0CC04921B
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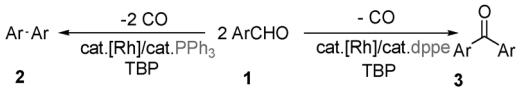
A novel rhodium-catalyzed oxidative decarbonylative homocoupling of aromatic aldehydes to generate biaryls and diarylketones selectively and efficiently, triggered by the choice of different phosphine ligands.

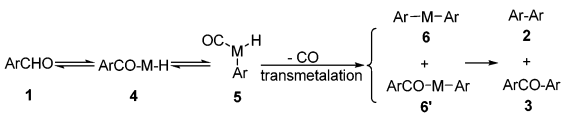
The abundance of the biaryl motif in natural products, pharmaceuticals and materials has positioned aryl–aryl formation high on the agenda of synthetic chemists.[1] Although there exists a variety of routes for the construction of aryl–aryl unions, arguably the most common method is through the homo- and cross-coupling of (pseudo)aryl halides (Ar–X) and aryl metalloids (Ar–M) as exemplified by the Ullmann reaction, the Kumada reaction, the Negishi reaction, the Suzuki reaction and the Stille reaction.[1,2] While the transition-metal-catalyzed direct arylation of aryl halides (Ar–X) or metalloids (Ar–M) with an unfunctionalized arene (Ar–H) represents a recent alternative strategy for biaryl synthesis,[3] more attractive oxidative cross-couplings of two simple electron-rich arenes (Ar–H) have been achieved, affording biaryl products efficiently and economically albeit still having challenges in controlling regioselectivity.[4]

On the other hand, arylketones are also important building blocks in both natural products and functional materials.[5] The classical routes to the synthesis of arylketones rely on the oxidation of the corresponding secondary alcohols,[6] Friedel–Crafts acylation of aromatic compounds[7] and transition-metal-catalyzed arylation of acyl chlorides,[8] nitriles[9] or aldehydes.[10] More direct synthesis of diarylketones from readily available compounds will be highly desired. *Herein, we report an unprecedented oxidative decarbonylative homocoupling of aromatic aldehydes to produce biaryls and diarylketones selectively utilizing cheap and abundant aldehydes as the starting materials triggered by the choice of different phosphine ligands* (Scheme 1).

It has been well studied that the oxidative addition of a transition metal (M) across the aldehyde C–H bond will generate an acylmetal hydride **4** (Scheme 2);[11] decarbonylation of which followed by reductive elimination of the resulting arylmetal hydride **5** leads to a simple arene (Ar–H).[12] Alternatively, it has been exemplified by our previous results that



Scheme 1 Phosphine ligand triggered oxidative decarbonylative homocoupling.



Scheme 2 Aldehyde C–H bond activation and decarbonylative homocoupling.

the arylmetal hydride **5** can react with alkene,[13] alkyne[14] and arene[15] to give (oxidative) decarbonylative coupling products. We postulated that the transmetalation between two arylmetal hydride **5** or acylmetal hydride **4** and arylmetal hydride **5** would generate the diaryl–metal complex **6** and acyl–aryl–metal complex **6′**, respectively, which will lead to the novel C–C bond formation product, biaryls and diarylketones, after reductive elimination.

With these objectives in mind, we first tested the reaction of *p*-methoxybenzaldehyde catalyzed by the Wilkinson's catalyst [$(PPh_3)_3RhCl$] in the presence of *tert*-butyl peroxide (TBP), since the catalyst has been the most widely used one for the decarbonylation of aldehydes.[16] Gratifyingly, the decarbonylative homocoupling product **2a** and a significant amount of the diarylketone product **3a** was observed by ^1H NMR, with an overall yield of 82% in 1 : 1 ratio (Table 1, entry 1).

In order to increase the selectivity of this reaction, a detailed optimization was conducted. First, the catalytic activities of different rhodium sources for the reaction were investigated by using PPh_3 as the ligand (Table 1, entries 1–10). In all these cases, the decarbonylative homocoupling products **2a** and **3a** can be detected with varied yields with the biaryl **2a** being the main product. $[(CO)_2RhCl]_2$ gave a slightly better result than the other rhodium catalysts (Table 1, entry 2), affording a 85% NMR yield with the ratio of **2a** and **3a** being 72 : 28. Then, bidentated phosphine ligands with different bite angles were applied to this decarbonylative homocoupling (entries 11–17). To our delight, the selectivity reversed when binap, dppe and dppbe [1,2-bis(diphenylphosphino)benzene] were used as the ligand, with the diarylketone **3a** being the main product (entries 11, 13, 14 and 17). When dppe was used as the ligand for

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† Electronic supplementary information (ESI) available: Experimental details and spectral data. See DOI: 10.1039/c0cc04921b

Published on 06 January 2011 on http://pubs.rsc.org | doi:10.1039/C0CC04921B
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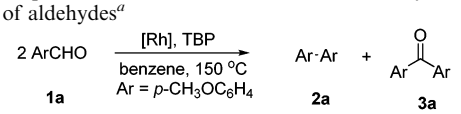
Table 1 Optimization of the oxidative decarbonylative homocoupling of aldehydes[a]



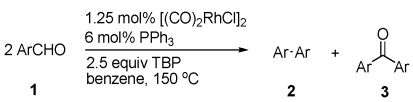
Entry	Rh (mol%)	Ligand (mol%)	Yield 2a + 3a	Ratio[b] 2a/3a
1	$(PPh_3)_3RhCl$ (2.5)	—	82	50 : 50
2	$(CO)_2RhCl(PPh_3)_2$ (2.5)	—	78	76 : 24
3	**$[(CO)_2RhCl]_2$ (1.25)**	**PPh_3 (6)**	**85**	**72 : 28**
4	$(CO)_2Rh(acac)$ (2.5)	PPh_3 (6)	67	72 : 28
5	$[Cp^*RhCl_2]_2$ (1.25)	PPh_3 (6)	78	66 : 34
6	$[(COD)_2RhOH]_2$ (1.25)	PPh_3 (6)	69	79 : 21
7	$(COD)_2Rh(BF_4)$ (2.5)	PPh_3 (6)	75	61 : 39
8	$[Rh(OAc)_2]_2$ (1.25)	PPh_3 (6)	73	72 : 28
9	$RhCl_3$ (2.5)	PPh_3 (6)	67	73 : 27
10	$HRh(PPh_3)_4$ (2.5)	—	86	70 : 30
11	$[(CO)_2RhCl]_2$ (1.25)	binap (3)	69	27 : 73
12	$[(CO)_2RhCl]_2$ (1.25)	dppm (3)	67	74 : 26
13	$[(CO)_2RhCl]_2$ (1.25)	dppe (3)	72	<2 : 98
14	**$[(CO)_2RhCl]_2$ (1.25)**	**dppe (3)**	**80[c]**	**<2 : 98**
15	$[(CO)_2RhCl]_2$ (1.25)	dppp (3)	72	68 : 32
16	$[(CO)_2RhCl]_2$ (1.25)	dppb (3)	68	62 : 38
17	$[(CO)_2RhCl]_2$ (1.25)	dppbe (3)	44	<2 : 98
18	$[(CO)_2RhCl]_2$ (1.25)	PBu_3 (6)	38	81 : 19
19	$[(CO)_2RhCl]_2$ (1.25)	PCy_3 (6)	20	67 : 33
20	$[(CO)_2RhCl]_2$ (1.25)	—	47	89 : 11
21	$[(CH_2{=}CH_2)_2RhCl]_2$ (1.25)	dppb (3)	58[c]	57 : 43

[a] Conditions: **1a** (0.2 mmol), [Rh], phosphine ligand, TBP (0.5 mmol) and benzene (0.4 mL), reacted for 12 h at 150 °C under argon, unless otherwise noted. [b] Determined by 1H NMR analysis of the crude reaction mixture using an internal standard. [c] Reaction performed at 160 °C.

$[(CO)_2RhCl]_2$, the decarbonylative homocoupling of *p*-methoxybenzaldehyde produced diarylketone **3a** in 72% yield after reacted for 12 h at 150 °C (entry 13) and no biaryl product can be detected under these conditions. The yield of diarylketone **3a** can be further increased to 80% after the reaction temperature was raised to 160 °C (entry 14). Monophosphine ligands such as PBu_3 and PCy_3 can also be used in this reaction albeit leading to a lower yield (entries 18 and 19), possibly because these trialkylphosphine ligands are less stable under the oxidative conditions. In the absence of a phosphine ligand, the rhodium catalyst $[(CO)_2RhCl]_2$ itself can also promote this decarbonylative homocoupling to give **2a** and **3a** in much lower yields than in the presence of PPh_3 (entry 20). Using $[RhCl(CH_2{=}CH_2)_2]_2$ as a pre-catalyst resulted in both lower yield and selectivity (entry 21). Under the best conditions indicated by entries 3 and 14, in the absence of TBP, anisole was the only observed product, with most of the starting material recovered. Other organic solvents such as chlorobenzene, 1,4-dioxane and 1,2-dichloroethane can also be used as the reaction media, albeit not as good as benzene (ESI†).

Under the optimized conditions for the preparation of biaryl compounds (Method A: 1.25 mol% $[(CO)_2RhCl]_2$, 6.0 mol% PPh_3, 2.5 equiv. TBP, reacted for 12 h at 150 °C), the substrate scope of this novel homocoupling was explored. As shown by the results in Table 2, various aromatic aldehydes with electron-rich substituents such as methyl, methoxy and acetoxy (**1a–1d**) reacted smoothly to produce the corresponding homocoupling products (Table 2, entries 1–4). Benzaldehyde (**1e**) also reacted efficiently (entry 5). *Aldehydes with weak electron-withdrawing substituents such as fluoro and chloro (***1f–1i***) were also feasible substrates, which makes this decarbonylative homocoupling valuable for the synthesis of halogen substituted biaryls amenable for post-functionalizations*. Electron-deficient aldehydes substituted by cyano, trifluoromethyl and methylcarboxylate (**1f–1i**) can also take part in this novel homocoupling with moderate yields and good chemoselectivity. When *o*-tolualdehyde was used as the substrate under the standard reaction conditions ($[(CO)_2RhCl]_2/PPh_3$), the corresponding diarylketone was the main product instead of biaryl. This can be explained by the increased steric effect, slowing the decarbonylation of the *ortho*-substituted aldehyde than the unsubstituted one.

Table 2 Oxidative decarbonylative homocoupling of aldehydes for the preparation of biaryls[a]

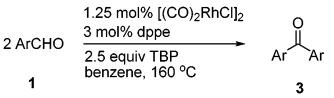


Entry	Ar		Product	Yield (ratio)[b]
1	**1a**	4-CH_3O–C_6H_4	**2a + 3a**	82 (72 : 28)
2	**1b**	3-CH_3O–C_6H_4	**2b + 3b**	81 (98 : <2)
3	**1c**	4-CH_3–C_6H_4	**2c + 3c**	72 (80 : 20)
4	**1d**	4-AcO–C_6H_4	**2d + 3d**	65 (94 : 6)
5	**1e**	C_6H_5	**2e + 3e**	66 (89 : 11)
6	**1f**	4-F–C_6H_4	**2f + 3f**	87 (86 : 14)
7	**1g**	4-Cl–C_6H_4	**2g + 3g**	82 (86 : 14)
8	**1h**	3-Cl–C_6H_4	**2h + 3h**	71 (93 : 7)
9	**1i**	3,4-Cl_2–C_6H_3	**2i + 3i**	78 (95 : 5)
10	**1j**	4-CN–C_6H_4	**2j + 3j**	72 (98 : <2)
11	**1k**	4-CF_3–C_6H_4	**2k + 3k**	72 (89 : 11)
12	**1l**	4-MeO_2C–C_6H_4	**2l + 3l**	59 (94 : 6)

[a] Conditions: Method A, aldehyde **1** (0.2 mmol), 1.25 mol% $[(CO)_2RhCl]_2$, 6.0 mol% PPh_3, TBP (2.5 equiv., 0.5 mmol), reacted for 12 h at 150 °C under argon. [b] Isolated yield.

Similarly, under the optimized conditions for the preparation of diarylketone compounds (Method B: 1.25 mol% $[(CO)_2RhCl]_2$, 3.0 mol% dppe, 2.5 equiv. TBP, reacted for 12 h at 160 °C), the substrate scope for the preparation of diarylketones was explored. As shown by the results in Table 3, various electron-rich aromatic aldehydes substituted by alkyl and alkoxy reacted smoothly to produce the corresponding homocoupling products (Table 3, entries 1–7). Among them, *p*-, *m*- and *o*-methyl benzaldehydes

Table 3 Oxidative decarbonylative homocoupling of aldehydes for the preparation of diarylketones[a]



Entry	Ar		Product	Yield[b]
1	**1a**	4-CH_3O–C_6H_4	**3a**	78
2	**1b**	3-CH_3O–C_6H_4	**3b**	76
3	**1m**	4-$^nC_5H_{11}O$–C_6H_4	**3m**	74
4	**1c**	4-CH_3–C_6H_4	**3c**	71
5	**1n**	3-CH_3–C_6H_4	**3n**	81
6	**1o**	2-CH_3–C_6H_4	**3o**	82
7	**1p**	2,4-$(CH_3)_2$–C_6H_3	**3p**	75
8	**1e**	C_6H_5	**3e**	49
9	**1f**	4-F–C_6H_4	**3f**	50
10	**1h**	3-Cl–C_6H_4	**3h**	56

[a] Conditions: Method A, aldehyde **1** (0.2 mmol), 1.25 mol% $[(CO)_2RhCl]_2$, 3.0 mol% dppe, TBP (2.5 equiv., 0.5 mmol), reacted for 12 h at 160 °C under argon. [b] Isolated yield.

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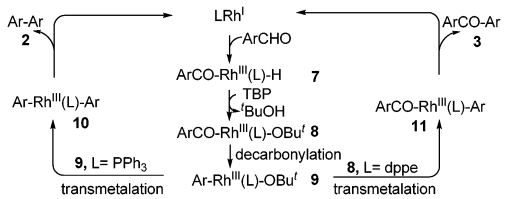

Scheme 3 Proposed mechanism for the oxidative decarbonylative homocoupling.

(**1c**, **1n** and **1o**) were examined and this homocoupling was not sensitive to the increased steric hindrance (entries 4–6). Benzaldehyde, 4-fluorobenzaldehye and 3-chlorobenzaldehyde (**1e**, **1f** and **1h**) can also take part in this homocoupling albeit with slightly lower yields because of oxidations to the corresponding benzoic acid derivatives (entries 8–10). It is worth noting that, in all cases, almost no biaryl products were detected by ^{1}H NMR of the crude reaction mixtures, which illustrated that the oxidative decarbonylative homocoupling using the Method B had an excellent chemoselectivity for the diarylketones.

A tentative mechanism to rationalize this novel rhodium-catalyzed oxidative decarbonylative homocoupling is illustrated in Scheme 3. First, the rhodium(I) catalyst undergoes oxidative addition with the aldehyde C–H bond rapidly to produce acylrhodium hydride **7**, which is oxidized by TBP to yield acylrhodium complex **8**. Decarbonylation of acylrhodium complex **8** gives arylrhodium complex **9**. Second, when PPh_3 is used as the ligand, transmetalation between two arylrhodium **9** complexes gives complex **10**, which upon reductive elimination releases biaryl product **2**. Similarly, when dppe is used as the ligand, transmetalation between acylrhodium complex **8** and arylrhodium complex **9** forms complex **11**, which upon reductive elimination releases diarylketone product **3** and regenerates the rhodium catalyst for further reactions. The difference is that when dppe is used as the ligand, the decarbonylation of the acylrhodium complex **8** to generate the arylrhodium complex **9** is much more difficult caused by the decreased dissociation ability of metallacyclic Rh complex **8** (L = dppe).[11,17] Once the arylrhodium complex **9** is formed, it will undergo transmetalation with the acylrhodium complex **8** rapidly to generate complex **11**.

In summary, we have developed a novel rhodium-catalyzed oxidative decarbonylative homocoupling of aromatic aldehydes to generate biaryls and diarylketones selectively and efficiently, triggered by the choice of different phosphine ligands. Unlike previous methods using aryl halide or acyl halide, the current reaction utilizes cheap and abundant aldehydes as starting material. Application of this novel method to aliphatic aldehydes and cross decarbonylative coupling of aromatic aldehydes is under further investigation.

We are grateful to the Canada Research Chair (Tier I) Foundation (to CJL), CFI, and NSERC for partial support of our research.

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