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Co-catalyzed arylation of aldehydes and aryltrimethylgermanes†

 Qiang Zhang, * Xiao Zou, Ningqi Zhang and Bo Liu

A novel cobalt-catalyzed protocol for the synthesis of carbinol derivatives and benzil derivatives has been developed. In the presence of CoI_2 as the catalyst and **tmphen** (3,4,7,8-tetramethyl-1,10-phenanthroline) as the ligand, the corresponding arylated products were obtained from the addition of aryltrimethylgermanes to aromatic aldehydes and arylglyoxals in moderate to excellent yields under air atmosphere.

1. Introduction

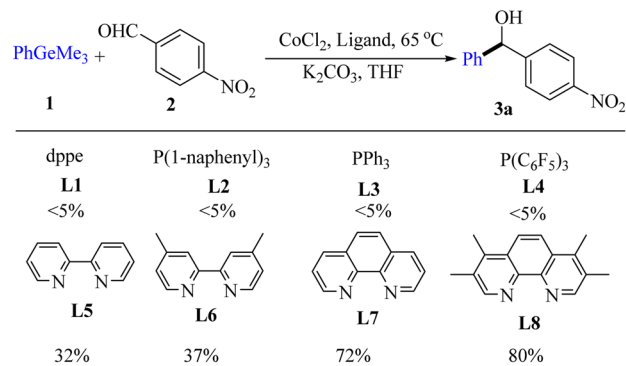
In the past decade, transition metal catalysis has been recognized as a powerful synthetic tool for diarylmethanols through the addition of organometallic reagents.^{1,2} Organogermanes³ have received much less attention so far, compared with their congeners such as organosilanes⁴ and organostannanes due to their lower reactivity, the higher cost of germanium relative to silicon⁵ and the less reported synthetic methodology of organogermanes.^{5–9} To the best of our knowledge, organogermanes are more susceptible to breaking the C–Ge bond than arylsilane analogues,⁹ and have lower carbon–metal bond energy and a larger covalent radius than their silicon counterparts in group IVA. However, examples of employing aryltrimethylgermanes in addition reactions have been never reported before. Our previous work¹⁰ prompted us to explore the possibility of employing low-cost catalysts in addition reactions. Herein, we report our preliminary results on the first example of cobalt-catalyzed addition of aromatic aldehydes and arylglyoxals with ArGeMe_3 using a CoI_2 /**tmphen** catalytic system.

The reaction of PhGeMe_3 (**1a**) and 4-nitrobenzaldehyde (**2a**) was firstly chosen as the model reaction for this cobalt-catalyst system (Fig. 1).

Ligands were firstly screened since it often plays an important role in transition-metal-catalyzed chemistry.⁹ The effects of phosphine ligand with different electron-donating, electron-withdrawing and steric hindrance groups were examined (Fig. 1, **L1–L4**), but no target product was detected. However, the yield of **3a** could be improved to 80% when the combination of CoCl_2 and **tmphen** (**L8**) was employed (Fig. 1, **L8**). Subsequently, various reaction conditions concerning the types and amount of cobalt sources, the effects of time and temperature, bases, solvents, were examined to increase the yield of product

(Table 1). After extensive screening, the optimized reaction condition was established as follows: CoI_2 (2.5 mol%), **tmphen** (**L8**, 2.5 mol%), K_2CO_3 (1.0 mmol), THF (3.0 mL), ArGeMe_3 (0.65 mmol) and aldehydes (0.5 mmol), 65 °C, 12 h. Among the bases we used, K_2CO_3 was superior to other bases such as NaHCO_3 , Na_2CO_3 , NaOAc, KF, Li_2CO_3 , and Cs_2CO_3 . 14% yield of benzophenone was detected when using Cs_2CO_3 as the base under model reaction condition (Table 1, entry 7). The choice of solvents was also crucial to the reaction. THF was proved to be the best one of all the solvents we chose.

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^[a] All reactions were conducted with PhGeMe_3 (126 mg, 0.65 mmol), 4-nitrobenzaldehyde (53 mg, 0.5 mmol), K_2CO_3 (138 mg, 1.0 mmol), CoCl_2 (3.3 mg, 5 mol %), and ligand (5 mol %) in 3 mL of THF at 65 °C for 24 h, under air atmosphere. ^[b] Yields of isolated products after chromatography.

 Fig. 1 Ligand screening.⁹

Shaanxi Key Laboratory of Catalysis, School of Chemistry and Environmental Science, Shaanxi University of Technology, Han zhong, 723001, P. R. China. E-mail: zhangqiang22@126.com

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Table 1 Selected results for the optimal reaction conditions^a

Entry	Catalyst	Base	Solvent	Yield ^b (%)
1	—	—	THF	N.R
2	CoCl ₂	—	THF	N.R
3	CoCl ₂	NaHCO ₃	THF	21
4	CoCl ₂	Na ₂ CO ₃	THF	51
5	CoCl ₂	NaOAc	THF	28
6	CoCl ₂	KF	THF	53
7	CoCl ₂	Cs ₂ CO ₃	THF	71
8	CoCl ₂	K ₂ CO ₃	THF	80
9	CoCl ₂	K ₂ CO ₃	DME	62
10	CoCl ₂	K ₂ CO ₃	CH ₃ CN	<5
11	CoCl ₂	K ₂ CO ₃	DMF	<5
12	CoCl ₂	K ₂ CO ₃	Dioxane	37
13 ^c	CoI ₂	K ₂ CO ₃	THF	92
14 ^d	CoI ₂	K ₂ CO ₃	THF	90
15	CoI ₂	K ₂ CO ₃	THF	87
16	CoBr ₂	K ₂ CO ₃	THF	67
17	Co(OAc) ₂	K ₂ CO ₃	THF	58
18	Co(C ₅ H ₅) ₂	K ₂ CO ₃	THF	14
19	Co ₃ O ₄	K ₂ CO ₃	THF	<5
20	PdCl ₂	K ₂ CO ₃	THF	<5
21	RhCl ₃ ·3H ₂ O	K ₂ CO ₃	THF	<5

^a Reaction conditions: **1** (126 mg, 0.65 mmol), **2** (76 mg, 0.5 mmol), cobalt source (5 mol%), **tmphen** (**L8**, 5.9 mg, 5 mol%); base (1.0 mmol), solvent (3 mL), 65 °C for 12 h, under air in reaction tubes.

^b Yields of isolated products after chromatography. ^c CoI₂ (3.9 mg, 2.5 mol%), **tmphen** (**L8**, 3.0 mg, 2.5 mol%). ^d CoI₂ (15.6 mg, 10 mol%), **tmphen** (**L8**, 11.8 mg, 10 mol%).

model reaction condition (Table 1, entry 7). The choice of solvents was also crucial to the reaction. THF was proved to be the best one of all the solvents we chose.

With the optimized conditions in hand, a variety of aldehydes with electron-rich, electron-deficient and steric hindrance was examined to broaden the extent of the reaction. Typical functional groups such as methyl, methoxyl, fluoro, chloro were well tolerated under the reaction conditions. Electron-deficient analogues of aldehyde reacted with ArGeMe₃ easily and gave biarylmethanols in good yields (Table 2, entries 1–10). Particularly, 4-formylbenzaldehyde could react with PhGeMe₃ and the product of **3a** and keep one formyl group untouched (Table 2, entry 14). The chloro and bromo groups untouched in this catalytic system (Table 2, entries 9 and 10). Unfortunately, the reaction was stopped by using aldehydes with neutral and electron-rich groups or aliphatic aldehydes due to its low activity to aryltrimethylgermane under this reaction condition. However, butyraldehyde or 4-methoxybenzaldehyde as substrate react with phenyltrimethylgermane did not give the responding products. Similarly, tetramethylgermane as substrate react with 4-nitro-phenylaldehyde also did not give the responding products.

Table 2 Selected results for the optimal reaction conditions^a

Entry	Product	Yield ^b (%)
1		92
2		94
3		93
4		93
5		91
6		92
7		93
8		95



Table 2 (Contd.)

Entry	Product	Yield ^b (%)
9		92
10		91
11		85
12		76
13		87
14		93
15		55
16		91

^a Reaction conditions: ArGeMe₃ **1** (0.65 mmol), aldehyde **2** (0.5 mmol), CoI₂ (3.9 mg, 2.5 mol%), **tmphen** (**L8**, 3.0 mg, 2.5 mol%), K₂CO₃ (138 mg, 1.0 mmol), THF (3 mL), 65 °C for 12 h, under air in pressure tubes. ^b Yields of isolated products after chromatography.

During broadening the extent of the reaction, the phenylglyoxal hydrate was examined to broaden the scope of the reaction, which could be seen as the electron-deficient analogue instead of 4-nitrobenzaldehyde. Only a trace of benzoin formed, the benzil was instead the major final product. Obviously, benzil was resulted from catalytic oxidation of *in situ* generated benzoin in the presence of K₂CO₃ in air. It was noteworthy that the over oxidation product could not be detected under argon atmosphere with degassed THF. A more efficient catalytic system with the dual ability to facilitate the addition of ArGeMe₃ to phenylglyoxal hydrate was obtained when K₂CO₃ was exchange by Cs₂CO₃ as the base. Then, the optimized reaction conditions were then extended to conversions of PhGeMe₃ to phenylglyoxal hydrate as follows: CoI₂ (3.9 mg, 2.5 mol%), **tmphen** (**L8**, 3.0 mg, 2.5 mol%), Cs₂CO₃ (326 mg, 1.0 mmol), THF (3.0 mL), PhGeMe₃ (0.65 mmol) and phenylglyoxal hydrate (0.5 mmol), 65 °C, 12 h (Table 3).

The reactions of different ArGeMe₃ with arylglyoxals were examined to broaden the scope of the reaction. All the reactions catalyzed by CoI₂/tmphen proceeded well and provided the desired products in good yields. Although the hetero-atoms in the heteroaryltrimethylgermanes might coordinate to transition-metal, trimethyl(thiophen-3-yl)germane and trimethyl(thiophen-2-yl)germane were still good partners for the addition reaction. The corresponding products were isolated in 67% and 59% yields, respectively (Table 3, entries 11 and 12). It seemed that the ortho substituents had little influence on their activities. For instance, (2-chlorophenyl)trimethylgermane, trimethyl(*o*-tolyl)germane and trimethyl(naphthalen-1-yl)germane could react with phenylglyoxal hydrate to furnish **4j**, **4k**, and **4l** in excellent yields (Table 3, entries 13–15). The comparison of PhGeMe₃ and its congener PhSiMe₃ was also investigated under the optimised reaction conditions. However, PhSiMe₃ was not the proper candidates and recovered the reactants. Similarly, tetramethylgermane as substrate to react phenylglyoxal hydrate did not give the responding products.

To further understand the mechanism, the model reaction under optimized reaction conditions was studied by gas chromatography-mass spectrometry. The data showed that 1,1'-biphenyl and hexamethyldigermane were the by-products, except for the addition product and the reactants. To account for the present reaction, a plausible mechanism based upon the above experimental results was proposed as follows (Fig. 2).

A plausible mechanism for forming diarylmethanols (Fig. 2): the catalytic cycle may contain three steps: Co(II) undergoes transmetalation to form ArCo(II)IL (**A**), which exhibits high nucleophilicity toward carbonyl carbon might produce the byproduct with 1,1'-diphenyl and hexamethyldigermane through cross-coupling reaction. Then arylcobalt^{III} should be transferred to carbonyl carbon through the insertion gives the intermediate (**B**). Finally, the hydrolysis of intermediate (**B**) affords the diarylmethanols. Cs₂CO₃ might facilitate the addition of aryltrimethylgermane to arylglyoxal and prompt the aerobic oxidation of the carbinol; The ICo–OH species reacts with I[−] to regenerate the active CoI₂ for the next cycle.



Table 3 Selected results for the optimal reaction conditions^a

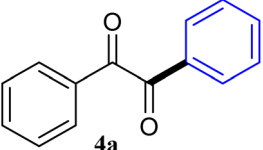
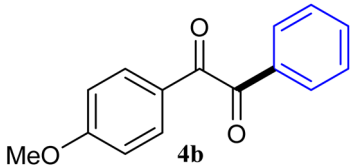
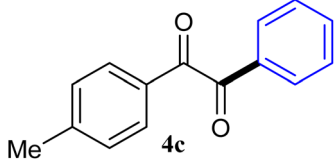
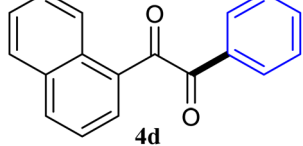
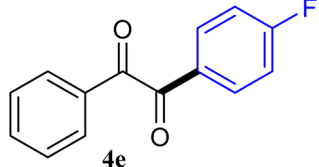
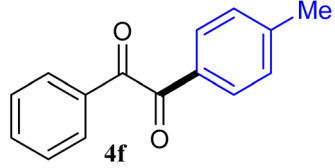
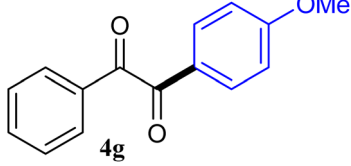
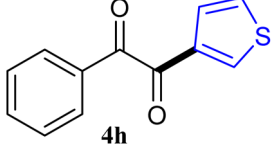
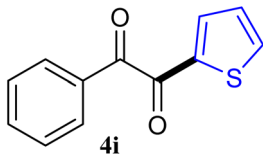
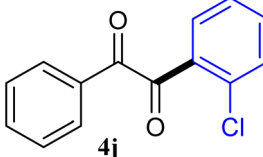
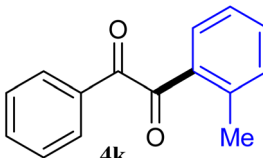
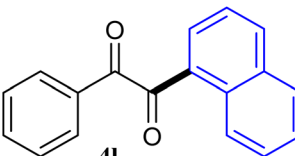
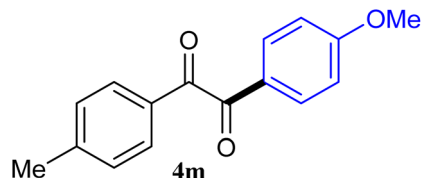
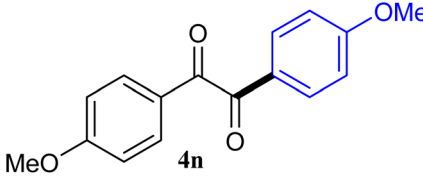
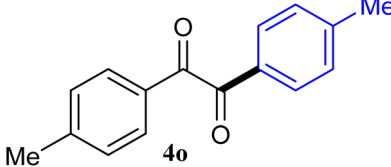
Entry	Product	Yield ^b (%)
$\text{Ar}^1\text{GeMe}_3 + \text{Ar}^2\text{C(=O)CHO} \xrightarrow[\text{Cs}_2\text{CO}_3, \text{THF}, 65^\circ\text{C}]{2.5 \text{ mol } \% \text{ CoI}_2/\text{tmphen}} \text{Ar}^1\text{C(=O)C(=O)Ar}^2$		
1		95
2		94
3		93
4		92
5		91
6		93
7		92
8		67

Table 3 (Contd.)

Entry	Product	Yield ^b (%)
$\text{Ar}^1\text{GeMe}_3 + \text{Ar}^2\text{C(=O)CHO} \xrightarrow[\text{Cs}_2\text{CO}_3, \text{THF}, 65^\circ\text{C}]{2.5 \text{ mol } \% \text{ CoI}_2/\text{tmphen}} \text{Ar}^1\text{C(=O)C(=O)Ar}^2$		
9		59
10		78
11		87
12		91
13		92
14		94
15		93

^a Reaction conditions: ArGeMe₃ (0.65 mmol), arylglyoxal (0.5 mmol), CoI₂ (3.9 mg, 2.5 mol%), **tmphen** (**L8**, 3.0 mg, 2.5 mol%), Cs₂CO₃ (138 mg, 1.0 mmol), THF (3 mL), 65 °C for 12 h, under air in pressure tubes. ^b Yields of isolated products after chromatography.



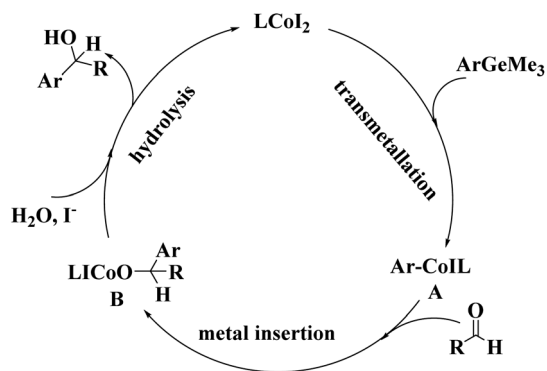


Fig. 2 A plausible mechanism.

In summary, we describe here the first time a mild cobalt-catalyzed nucleophilic arylation of aromatic aldehydes and arylglyoxals with ArGeMe_3 using $\text{CoI}_2/\text{tmphen}$ catalytic system. In the presence of $\text{CoI}_2/\text{tmphen}$ catalytic system, a variety of electron-deficient arylaldehydes and arylglyoxals was found to be suitable substrates for the reaction with ArGeMe_3 in moderate to excellent yields. It was noteworthy that our methodology could keep the formyl group chloro and bromo groups untouched for further functionalization. This method might provide potential opportunities for the addition of ArGeMe_3 to unsaturated carbon-carbon bonds and unsaturated carbon-hetero bonds. The detailed mechanism of the reaction and further applications of ArGeMe_3 are the focus of ongoing efforts in our laboratory.

Conflicts of interest

There are no conflicts to declare.

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