



Short communication

Au-catalyzed synthesis of benzofurans from phenols and alkynes using molecular oxygen



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ABSTRACT

An efficient Au-catalyzed transformation for the synthesis of benzofurans from phenols and alkynes using molecular oxygen has been developed. The reaction proceeds smoothly with commercially available, eco-friendly oxidant and affords the products in moderate to good yields. This reaction is a facile approach for the formation of C–C and C–O bonds.

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1. Introduction

Benzofuran is a core structure (See Scheme 1) that is found in biocompounds, natural products, and pharmaceuticals and represents an excellent template in many drug discovery endeavors [1–4]. The development of new approaches that synthesize benzofurans [5–8] from easily available starting materials is an important goal of synthetic chemistry and also represents a continuing challenge. Recently, transition metal-catalyzed reactions, such as Pd [9–10], Cu [11], Au [12–14], and Rh [15] have emerged as powerful tools for the synthesis of furans and benzofurans in organic chemistry. Although a number of transformations for the preparation of the furan [16–19] frameworks have been reported by a number of organic chemists, there is still an intrinsic need to develop a new strategy for construction of benzofuran molecules.

During the past few years, Au-catalyzed [20–25] reactions have attracted much attention for the formation of carbon–carbon and carbon–hetero bonds in organic chemistry due to their synthetic efficiency. It is extensively used to prepare complex heterocyclic compounds, such as furans [26–28], indoles [29–31], imidazoles [32–34]. Herein, we have developed a novel and facile Au-catalyzed transformation from phenols and alkynes utilizing molecular oxygen as the terminal oxidant.

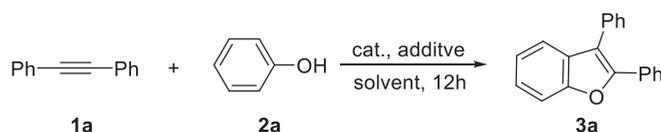
2. Results and discussion

Our initial efforts focused on the reaction of 1,2-diphenylethyne **1a** with phenol **2a** for the synthesis of benzofurans and the results are summarized in Table 1. The reaction of **1a** with **2a** was carried out in the presence of AuCl₃ in benzene only a trace amount of desired product **3a** was formed. Other catalysts, such as AuCl, PPh₃Au(I)Cl, Ru(acac)₂, [RuCl₂(*p*-cymene)]₂, or Pd(OAc)₂ were also employed affording very poor conversion (Table 1, entries 2–6). To our delight, the reaction could generate the corresponding product in 43%, 68%, 64% yields when Au(PPh₃)Cl/AgBF₄, Au(PPh₃)Cl/AgSbF₆, or Au(PPh₃)Cl/AgOTf were used as catalyst in the reaction (Table 1, entries 7–9). Then a variety of oxidants, such as PhI(OAc)₂, K₂S₂O₈, and DDQ, were evaluated (Table 1, entries 10–12), which did not lead to any improvement. The effects of solvents (DMSO, DMF, dioxane, ClCH₂CH₂Cl) were also tested and dioxane gives the best result (Table 1, entries 13–16).

With the establishment of a viable reaction system, the scope of this transformation was further expanded and the results are described in Table 2. As shown in Table 2, different substituted phenols were reacted efficiently with 1,2-diphenylethyne. The results indicated that this process is general and applicable for reactions of a wide variety of electron-rich and -deficient substituted phenols. Various aliphatic substituted phenols were employed, affording the desired products **3b–3d** in good yields (Table 2, entries 2–4). It is interesting to note that the present approach was tolerant of many other functional groups including 4-OCH₃, 4-SCH₃, 4-Cl, 4-Br, 2-Cl, 2-Br, 2-Ph (Table 2, entries 5–11). For further investigation, commercially available 1, 2-diphenylethyne derivatives were employed to explore the scope of this process under the optimized reaction conditions. To our delight, the reaction would be

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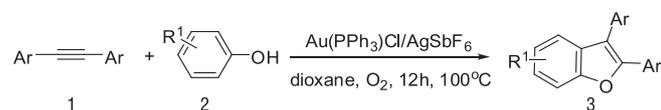
Table 1Optimization of the reaction conditions.^a

Entry ^b	Catalyst ^c	Oxidant	Solvent	Yield(%) ^d
1	AuCl ₃	O ₂	Toluene	trace
2	AuCl	O ₂	Toluene	5
3	Ru(acac) ₂	O ₂	Toluene	N.P.
4	[RuCl ₂ (<i>p</i> -cymene)] ₂	O ₂	Toluene	11
5	Pd(OAc) ₂	O ₂	Toluene	N.P.
6	PPh ₃ Au(I)Cl	O ₂	Toluene	15
7	Au(PPh ₃)Cl/AgBF ₄	O ₂	Toluene	43
8	Au(PPh ₃)Cl/AgSbF ₆	O ₂	Toluene	68
9	Au(PPh ₃)Cl/AgOTf	O ₂	Toluene	64
10	Au(PPh ₃)Cl/AgSbF ₆	PhI(OAc) ₂	Toluene	32
11	Au(PPh ₃)Cl/AgSbF ₆	K ₂ S ₂ O ₈	Toluene	27
12	Au(PPh ₃)Cl/AgSbF ₆	DDQ	Toluene	N.P.
13	Au(PPh ₃)Cl/AgSbF ₆	O ₂	DMSO	45
14	Au(PPh ₃)Cl/AgSbF ₆	O ₂	DMF	42
15	Au(PPh ₃)Cl/AgSbF ₆	O ₂	dioxane	82
16	Au(PPh ₃)Cl/AgSbF ₆	O ₂	ClCH ₂ CH ₂ Cl	51

^a Reaction condition: **1a** (0.5 mmol), **2a** (0.7 mmol), catalyst (3 mol%), solvent (3 mL), 100 °C, 12 h.^b Carried out in a sealed tube (25 mL).^c The catalysts Ph₃PAu(I)BF₄, Ph₃PAu(I)SbF₆, and PPh₃Au(I)OTf were preformed from PPh₃Au(I)Cl and AgBF₄, AgSbF₆ or AgOTf, respectively.^d GC yields.

successfully extended to 1,2-diphenylethyne derivatives and afforded the desired benzofurans in moderate to good yields (Table 2, entries 12–15).

On the basis of previous reports [35] and our experimental results, a proposed reaction mechanism for this Au-catalyzed synthesis of furans are described in Scheme 2. 1,2-diphenylethyne **1a** is activated by gold to

Table 2Gold-catalyzed synthesis of benzofurans.^a

Entry	Ar	R ¹	Product
1	Ph	H	3a 79%
2	Ph	2-CH ₃	3b 82%
3	Ph	4-CH ₃	3c 79%
4	Ph	4-CH(CH ₃) ₂	3d 85%
5	Ph	4-OCH ₃	3e 86%
6	Ph	4-SCH ₃	3f 74%
7	Ph	4-Cl	3g 87%

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