Tetrahedron Letters 57 (2016) 2488–2491

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Palladium-catalyzed double C–H functionalization of 2-aryl-1,3-dicarbonyl compounds: a facile access to alkenylated benzopyrans

Subrahmanyam Choppakatla [a,b], Aravind Kumar Dachepally [b], Hari Babu Bollikolla [a,*]

[a] Department of Chemistry, Acharya Nagarjuna University, NNagar-522 510, Guntur, AP, India
[b] Arka Research Labs, Plot No. 16, CFC Area, IDA Nacharam, Hyderabad 500076, Telangana, India

ARTICLE INFO

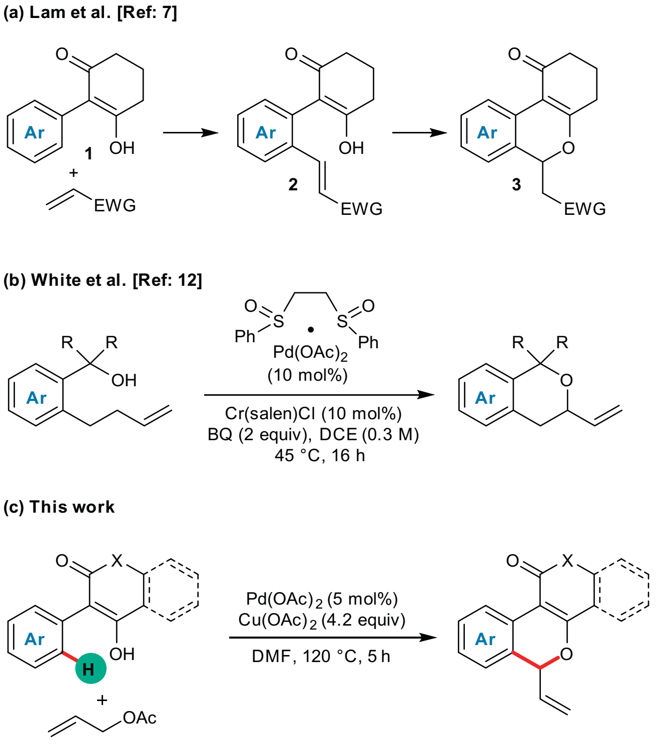
Article history:
Received 18 March 2016
Revised 20 April 2016
Accepted 22 April 2016
Available online 23 April 2016

Keywords:
Catalysis
Palladium
Benzopyrans
Allylation
C–H activation
Annulation

ABSTRACT

The present study reports the development of a palladium-catalyzed oxidative annulation/nucleophilic substitution sequence affording a library of alkenylated benzopyrans using 2-aryl-1,3-dicarbonyl compounds and allylic acetate. The process is compatible to a wide range of substrates with good functional group tolerance producing the desired heterocycles in moderate to good yields.

Transition metal-catalyzed C–H functionalization of unreactive bonds has gained eminence as a powerful and transformative tool in synthetic chemistry,[1] with additional applications to natural product syntheses,[2] drug discovery,[3] and material sciences.[4] The most advantageous use of this strategy is the atom-economic construction of C–C, C–N, and C–O bonds by functionalization of the aromatic C(sp^2)–H bonds, directed by a coordinating functional group delivering a diverse variety of heterocyclic compounds.[5] Recently, Lam and co-workers have developed catalytic oxidative annulations of α-aryl cyclic 1,3-dicarbonyl compounds (or their enol tautomers) with various coupling partners including alkynes,[6] terminal alkenes (Scheme 1a),[7] 1,3-dienes,[8] and 1,3-enynes[9] that provide efficient access to carbo- and heterocycles. On the other hand, allyl functionality is a versatile tool offering a range of opportunities for further functionalizations.[10] Recently, several methods have been developed for the direct allylation of aromatic C–H bonds using transition-metal catalysts.[11] In addition, allylic C–H oxidation is an established and well-studied strategy used to construct complex organic molecules (Scheme 1b).[12] In this regard, Pd(II)/bis-sulfoxide-catalyzed allylic C–H functionalizations of terminal olefins have demonstrated broad applicability in synthetic methodology.[13]


(a) Lam et al. [Ref: 7]

(b) White et al. [Ref: 12]

(c) This work

Scheme 1. Pd-catalyzed oxidative annulations and allylic C–H oxidation.

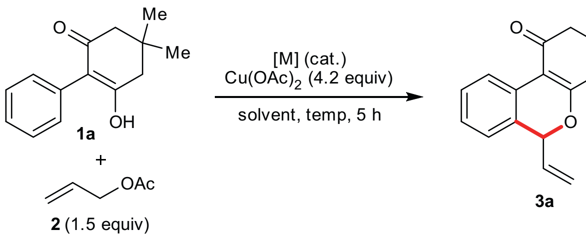
---

* Corresponding author. Tel./fax: +91 863 234 6573.
E-mail address: dr.b.haribabu@gmail.com (H.B. Bollikolla).

http://dx.doi.org/10.1016/j.tetlet.2016.04.089
0040-4039/© 2016 Elsevier Ltd. All rights reserved.

Table 1

Optimization of reaction conditions for the synthesis of **3a**[a]

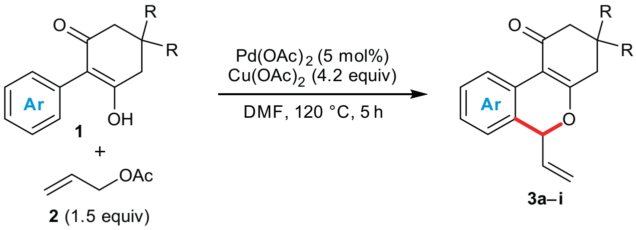


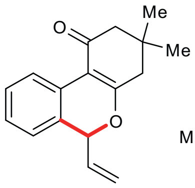
Entry	[M]	Mol (%)	Solvent	Temp (°C)	Yield[b] (%)
1	$Pd(OAc)_2$	5	DMF	90	40
2	**$Pd(OAc)_2$**	**5**	**DMF**	**120**	**59**
3	$Pd(OAc)_2$	10	DMF	120	62
4	$Pd(OAc)_2$	5	*t*-AmOH	120	20
5	$Pd(OAc)_2$	5	Dioxane	120	35
6	$[RuCl_2(p\text{-cymene})]_2$	2.5	DMF	120	<5
7	$[RuCl_2(p\text{-cymene})]_2$	2.5	*t*-AmOH	120	NR
8	–	–	DMF	120	NR
9[c]	$Pd(OAc)_2$	5	DMF	120	NR
10[d]	$Pd(OAc)_2$	5	DMF	120	37

[a] Reactions were conducted using 0.50 mmol of **1a**.
[b] Isolated yield.
[c] Reaction conducted without $Cu(OAc)_2$.
[d] Reaction conducted in the presence of K_2CO_3 (2.0 equiv). DMF = *N*,*N'*-dimethylformamide, *t*-Am = *tert*-amyl.

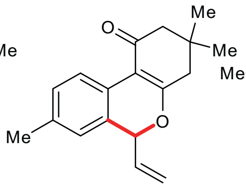
Table 2

Pd(II)-catalyzed synthesis of alkenylated benzopyrans[a]

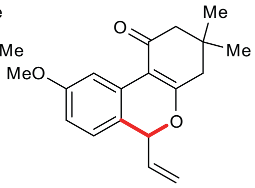




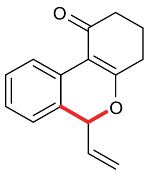
3a 59%



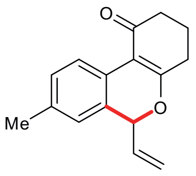
3b 65%



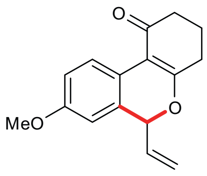
3c 45%



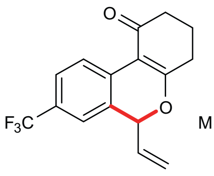
3d 55%



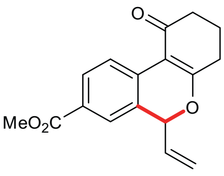
3e 62%



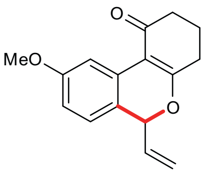
3f 65%



3g 53%



3h 50%

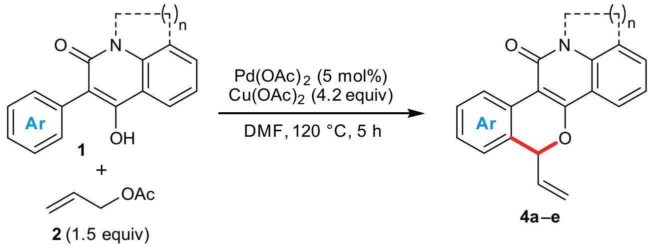


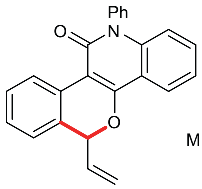
3i 40%

[a] Reactions were conducted with 0.50 mmol scale. Yields are of isolated material.

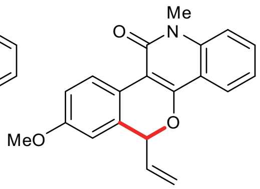
Table 3

Scope of Pd(II)-catalyzed synthesis of alkenylated benzopyrans[a]

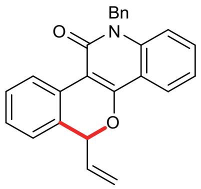




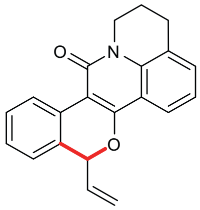
4a 65%



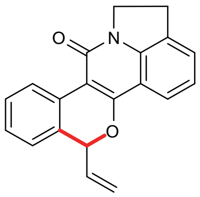
4b 62%



4c 61%

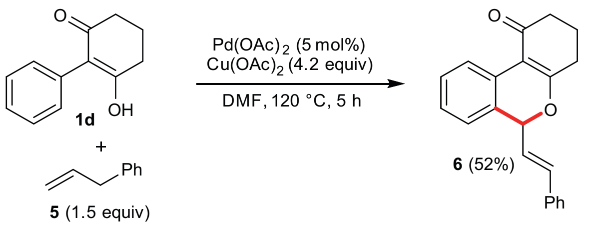


4d 67%



4e 57%

[a] Reactions were conducted with 0.50 mmol scale. Yields are of isolated material.



Scheme 2. Oxidative annulation reaction of allylbenzene with 3-hydroxy-2-phenyl-2-cyclohexenone.

In the present work, we report the efficient construction of alkenylated benzopyrans using a Pd(II)-catalyzed oxidative coupling of 1,3-dicarbonyl compounds with allyl acetate. This process involves C–H activation of a C(sp^2)–H bond to generate an allylated product which on nucleophilic substitution to a π-allyl Pd-species affords the desired heterocycles (Scheme 1c).

We initiated our study by exploring the reaction of 2-phenyldimedone (**1a**) with allyl acetate **2** (1.5 equiv) in the presence of $Pd(OAc)_2$ (5 mol %) in DMF using $Cu(OAc)_2$ (4.2 equiv) as an oxidant. Pleasingly, the alkenylated benzopyran product **3a** was obtained in 40% yield after reacting for 5 h at 90 °C (Table 1, entry 1). By elevating the reaction temperature to 120 °C, the yield of the desired product was increased to 59% (entry 2). A comparable yield of **3a** was achieved using 10 mol % of $Pd(OAc)_2$ in DMF (entry 3). Other solvents such as *t*-AmOH and dioxane provided limited reaction and gave inferior results (entries 4 and 5). $[RuCl_2(p\text{-cymene})]_2$ complex[14] commonly employed in C–H functionalizations was completely unproductive in different solvents (entries 6 and 7). No product formation was observed in the absence of the palladium catalyst or $Cu(OAc)_2$ (entries 8 and 9).