Iridium-catalyzed carbonyl group-directed oxidative coupling of arenes with alkenes

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ARTICLE INFO

ABSTRACT

The iridium complex $[Cp^*IrCl_2]_2$ is a good catalyst for the directed oxidative coupling of arenes with alkenes; a wide range of carbonyl functionalities ($NHCOR$, $CONH_2$ and COR) can be employed as the directing group.

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Introduction

The oxidative coupling of arenes with alkenes to form vinylarenes is an attractive alternative to the Mizoroki-Heck coupling reaction with the advantage that it is atom economic and does not require functionalized coupling partners.[1] After the initial discovery of the stoichiometric reaction between Pd(II)-olefin complexes and arenes,[2] a catalytic version involving Pd(OAc)$_2$ and an oxidant emerged.[3] Chelation-assisted oxidative coupling of an arene with an alkene, via orthometallation followed by C=C bond insertion, to give an *o*-vinylarene is another example of such a catalyzed oxidative coupling, which has been demonstrated with various metal systems including palladium,[4] rhodium,[5] ruthenium,[6] and cobalt.[7] Although there are many studies on iridium catalyzed alkylation of arenes with alkenes,[9] there are none for the oxidative coupling of an arene with an alkene; the closest is a direct oxidative coupling of furans with alkenes.[8] We recently reported the hydroamination of alkynes with aromatic amines via activation of the alkyne C≡C bond with $[Cp^*IrCl_2]_2$ (**1**).[10] For example, the reaction of **1** with alkyne and aniline leads to the formation of an orthometallated aminocarbene complex via alkyne hydroamination and subsequent ortho C—H bond activation.[10a] It therefore occurred to us that it may be possible to achieve ortho C—H alkenylation of aniline derivatives with this system.

The C—H activation of acetanilide, **2a**, followed by oxidative coupling to methyl acrylate was found to proceed smoothly in the presence of **1** and additives to afford the mono- and di-alkenylated products **4a** and **5a** in 86 and 9% yields, respectively (Table 1, entry 1). An optimization study showed that other silver salts, such as, AgBF$_4$ and AgSbF$_6$, may be used as additive (entries 2 & 3), but the additive, oxidant (Cu(OAc)$_2$) and catalyst were all essential (entries 5–7), as is a slight excess of the acrylate (entry 12).

Changing the oxidant from Cu(OAc)$_2$ to AgOAc increased the yield of **5** (entry 4), while lowering the catalyst loading to 3 mol% did not affect the yield significantly (entry 8). Use of coordinating solvents (acetonitrile or methanol) was detrimental (entries 9 & 10) and although the reaction proceeded at ambient temperature, it required a longer reaction time (entry 11).

A substrate scope study was carried out on a 0.2 mmol scale with 3 mol% catalyst loading (Table 2). Acetanilides with both electron-donating and electron-withdrawing *para* substituents were tolerated, affording good yields of the mono-alkenylated products (entries 2–6), along with ~10% yields of the di-alkenylated products (see SI). With *meta* substituted acetanilides, only mono-alkenylated products were obtained and olefination occurred selectively *para* to the functional group R, irrespective of whether it is electron-donating (R = Me) or electron-withdrawing (R = Cl, Br) (entries 7–9). The reaction did not proceed with unactivated alkenes (1-octene and *trans*-2-hexene).

This suggests that the stereochemistry of alkenylation in these cases is driven by steric factors. That halogen functional groups were tolerated, with no dehalogenation or Heck-coupling products

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Table 1
Optimization study for **1**-catalyzed formation of **4a** and **5a**.
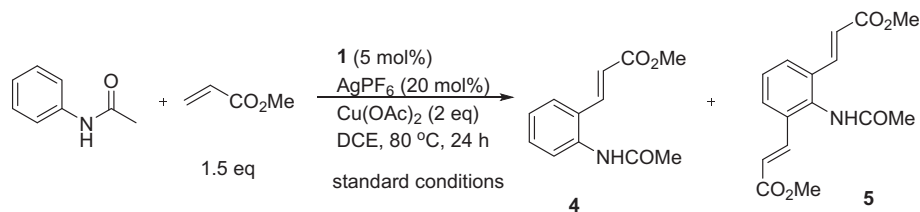
| Entry	Deviation from standard conditions	Yield of **4** + **5** (%) [a]
1	None	86 + 9
2	$AgSbF_6$ as additive	80 + 13
3	$AgBF_4$ as additive	80 + 6
4	AgOAc as oxidant	49 + 34
5	No silver salt additive	15
6	No oxidant	10
7	No catalyst **1**	–
8	3 mol% of **1**	82 + 8
9	ACN as solvent	–
10	MeOH as solvent	–
11[b]	Reaction temperature = 30 °C	23
12[b]	1.0 equivalent of methyl acrylate	40 + 20

[a] Isolated yields.
[b] Incomplete reaction.

Table 2
Substrate scope study of **1**-catalyzed formation of **4a** and **5a**. Yields reported are isolated yields.
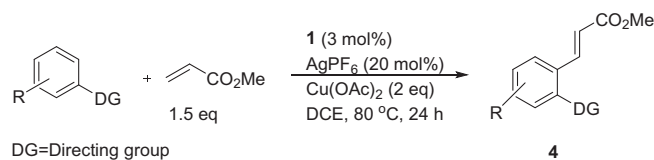
Entry	R	DG	Product (% yield)
1	H	NHCOMe	**4a** (82)
2	4-Me	NHCOMe	**4b** (80)
3	4-OMe	NHCOMe	**4c** (81)
4	4-NO_2	NHCOMe	**4d** (64)
5	4-Br	NHCOMe	**4e** (70)
6	4-Cl	NHCOMe	**4f** (66)
7	3-Br	NHCOMe	**4g** (75)
8	3-Cl	NHCOMe	**4h** (71)
9	3-Me	NHCOMe	**4i** (89)
14	2-Cl	NHCOMe	**4n** (67)
15	H	COMe	**6a** (72)
16	4-Me	COMe	**6b** (73)
17	4-Cl	COMe	**6c** (79)
18	3-OMe	COMe	**6d** (71)
19	2-Cl	COMe	**6e** (61)
20	H	$CONH_2$	**8a** (64)
21	H	$CONH_2$	**8b** (73)[a]
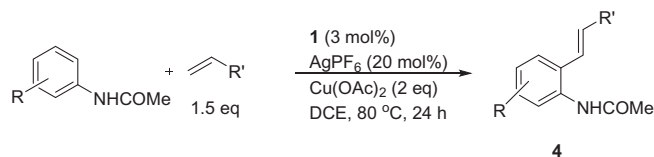
Table 2 (*continued*)

Entry	R	DG	Product (% yield)
10	3-Me	CO$_2$Et	**4j** (90)
11	3-Me	CO$_2$Bu^t	**4k** (73)
12	3-Me	CO$_2$Bz	**4l** (81)
13	H	Ph	**4m** (75)

^a Styrene was used instead methyl acrylate.
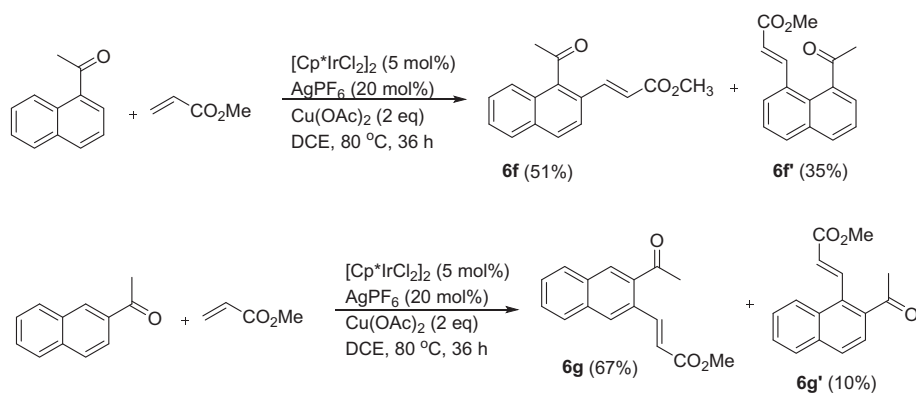
Scheme 1.
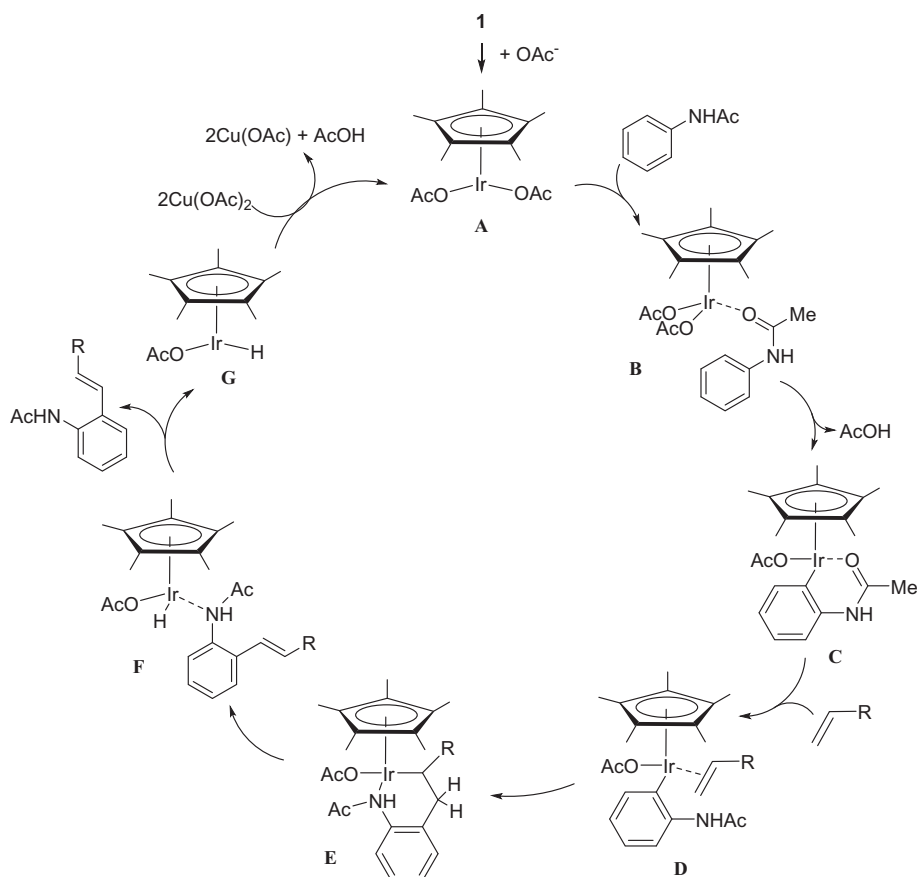
Fig. 1. Proposed catalytic cycle for **1**-catalyzed alkenylation of acetanilide.

observed (entries 5–8, 14). This would allow the products to be further functionalized via other cross coupling reactions. The reaction also proceeds with a number of other alkenes-ethyl, *t*-butyl, benzyl acrylates and styrene (entries 10–13).

With *4*-acetylacetanilide, a complex mixture of products was observed, and it occurred to us that the acetyl group could also be directing ortho C—H bond activation. Indeed, the reaction of acetophenone (**3a**) with methyl acrylate under the standard reaction conditions gave **6a** and **7a** in 72% and 19% yields, respectively (entry 15). The reaction worked well with acetophenones carrying both electron-rich and electron-poor substituents on the phenyl ring (entries 16–19), as well as with acetyl naphthalenes (Scheme 1). It also worked with benzamide (entries 20–21).

We propose a catalytic cycle, which is illustrated for acetanilides, in Fig. 1.

In the presence of an acetate source and a silver additive, **1** is converted to give the active 16-electron species Cp*Ir(OAc)₂, **A**.[4r] O-coordination of the acetanilide (to form **B**) followed by ortho C—H activation and the release of one molecule of acetic acid leads to intermediate **C**. In the case of benzamides and ketones, the intermediate **C** would be a 5- instead of a 6-membered metallacycle. In a coordinating solvent, this step is also presumably arrested. Coordination of the alkene (to **D**) and subsequent 1,2-migratory insertion leads to intermediate **E**. A β-hydride elimination to **F** is followed by dissociation of the olefination product and **G**, from which **A** is regenerated, presumably via reductive elimination of acetic acid to an Ir(I) species which is oxidised by Cu(OAc)₂.

In summary, we have described the first instance of an iridium-catalyzed oxidative coupling of arenes with alkenes in which the directing group is a wide range of carbonyl functionalities (NHCOR, CONH₂ or COR). It has the advantage that halogenated derivatives are tolerated, and is competitive against its rhodium analogue which generally requires a higher temperature (100 °C–130 °C).[5]

Acknowledgments

A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.tetlet.2017.11.058.

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