Iridium-Catalyzed Carbonyl Group-Directed Oxidative Coupling of Arenes with Alkenes

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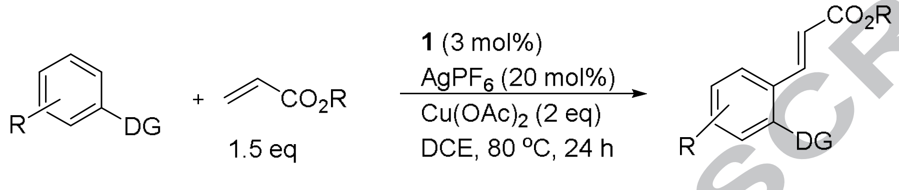

DG=NHCOMe, COMe, CONH$_2$

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Iridium-Catalyzed Carbonyl Group-Directed Oxidative Coupling of Arenes with Alkenes

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ABSTRACT

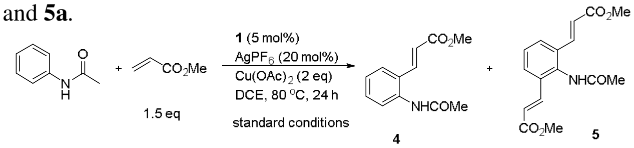
*The iridium complex [Cp*IrCl$_2$]$_2$ is a good catalyst for the directed oxidative coupling of arenes with alkenes; a wide range of carbonyl functionalities (NHCOR, CONH$_2$ and COR) can be employed as the directing group.*

1. 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).

Table 1. Optimization study for **1**-catalysed 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.

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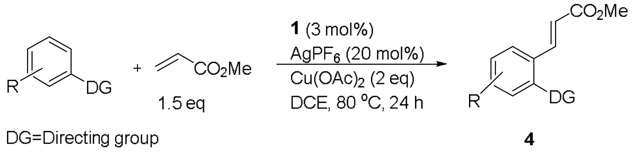
Changing the oxidant from $Cu(OAc)_2$ to AgOAc increased the yield of **5** (entry 4), while lowering the catalyst loading to 3 mol% did not affect the yield significantly (entry 8). Use of coordinating solvents (acetonitrile or methanol) was detrimental (entries 9 & 10) and although the reaction proceeded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

Table 2. Substrate scope study of **1**-catalysed formation of **4a** and **5a**. Yields reported are isolated yields.



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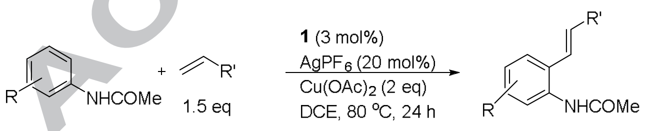
Entry	R	DG	Product (% yield)
1	H	NHCOMe	**4a** (82)
2	*4*-Me	NHCOMe	**4b** (80)
3	*4*-OMe	NHCOMe	**4c** (81)
4	*4*-NO_2	NHCOMe	**4d** (64)
5	*4*-Br	NHCOMe	**4e** (70)
6	*4*-Cl	NHCOMe	**4f** (66)
7	*3*-Br	NHCOMe	**4g** (75)
8	*3*-Cl	NHCOMe	**4h** (71)
9	*3*-Me	NHCOMe	**4i** (89)
14	*2*-Cl	NHCOMe	**4n** (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]



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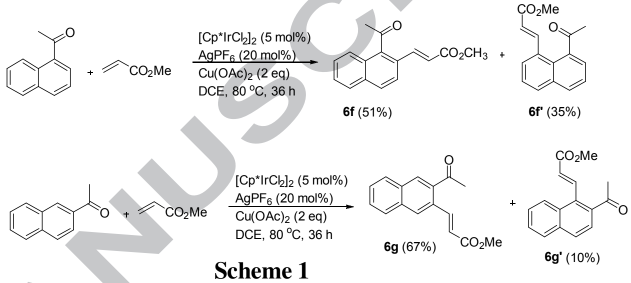
Entry	R	R'	Product (% yield)
10	*3*-Me	CO_2Et	**4j** (90)
11	*3*-Me	CO_2Bu^t	**4k** (73)
12	*3*-Me	CO_2Bz	**4l** (81)
13	H	Ph	**4m** (75)

[a] Styrene was used instead methyl acrylate.

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 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).

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).



Scheme 1

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

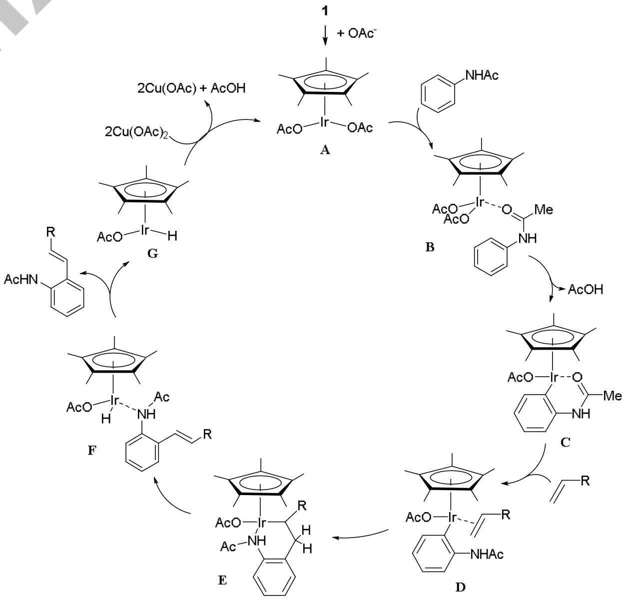


Figure 1. Proposed catalytic cycle for **1**-catalyzed alkenylation of acetanilide.

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 βhydride 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-catalysed oxidative coupling of arenes with alkenes in which the directing group is a wide range of carbonyl functionalities (NHCOR, CONH$_2$ 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 to 130 °C).[5]

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References and notes

1. a) Jia, C.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 633. b) Le Bras, J.; Muzarat, J. *Chem Rev*. **2011**, *111*, 1170. c) Wencel-Delord, J.; Dröge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. d) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651.
2. Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, *8*, 1119.
3. Fujiwara, Y.; Moritani, I.; Danno, S.; Teranishi, S. *J. Am. Chem. Soc.* **1969**, *91*, 7166.
4. a) Horino, H.; Inoue, N. *J. Org. Chem.* **1981**, *46*, 4416. b) Miura, M.; Tsuda, T.; Satoh, T.; Pivasa-Art, S.; Nomura, M. *J. Org. Chem.* **1981**, *46*, 4416. c) Boele, M. D. K.; van Strijdonck, G. P. F.; de Vries, A. H. M.; Kamer, P. C. J.; de Vries, J. G.; van Leeuwen, P. W. N. M. *J. Am. Chem. Soc.* **2002**, *124*, 1586. d) Cai, G.; Fu, Y.; Li, Y.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 7666. e) Wang, J. R.; Yang, C. T.; Liu, L.; Guo, Q. X. *Tetrahedron Lett.* **2007**, *48*, 5449. f) Garcı´a-Rubia, A.; Arraya´s, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 6511. g) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315. h) Kim, B. S.; Jang, C.; Lee, D. J.; Youn, S. W. *Chem. Asian. J*. **2010**, *2*, 2336. i) Chng, L. L.; Zhang, J.; Yang, J.; Amoura, M.; Ying, J. Y. *Adv. Synth. Catal*. **2011**, *353*, 2988. j) Wang, L.; Liu, S.; Yu, Y. *Org. Lett*. **2011**, *13*, 6137. k) Baxter, R. D.; Sale, D.; Engle, K. M.; Yu, J.-Q.; Blackmond, D. G. *J. Am. Chem. Soc*. **2012**, *134*, 4600. l) Dai, H.-X.; Li, G.; Zhang, X.-G.; Stepan, A. F.; Yu, J-Q. *J. Am. Chem. Soc*. **2013**, *135*, 7567. m) Li, G.; Leow, D.; Wan, L.; Yu, J-Q. *Angew. Chem., Int. Ed***. 2013**, *52*, 1245. n) Nandi, D.; Ghosh, D.; Chen, S. J.; Kuo, B. C.; Wang, N. M.; Lee, H. M. *J. Org. Chem.* **2013**, *78*, 3445–3451. o) Ye, X.; Shi, X. *Org. Lett*. **2014**, *16*, 4448. p) Li, G.; Wan, L.; Zhang, G.; Leow, D.; Spangler, J.; Yu, J-Q. *J. Am. Chem. Soc*. **2015**, *137*, 4391. q) Yang, W.; Ye, S.; Schmidt, Y.; Stamos, D.; Yu, J-Q. *Chem. Eur. J*. **2016**, *22*, 7059. r) Deb, A.; Hazra, A.; Peng, Q.; Paton, R. S.; Maiti, D. *J. Am. Chem. Soc*. **2017**, *139*, 763.
5. a) Ueura, K.; Satoh, T.; Miura, M. *Org. Lett*. **2007**, *9*, 1407. b) Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 7094. c) Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9982. d) Wang, F.; Song, G.; Li, X. *Org. Lett*. **2010**, *12*, 5430. e) Tsai, A. S.; Brasse, M.; Bergman, R. G.; Ellman, J. A. *Org. Lett*. **2011**, *13*, 540. f) Park, S. H.; Kim, J. Y.; Chang, S. *Org. Lett*. **2011**, *13*, 2372. g) Rakshit, S.; Grohmann, C.; Besset, T.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2350. h) Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem*. **2011**, *76*, 3024. i) Patureau, F. W.; Besset, T.; Glorius, F. *Angew. Chem. Int. Ed.* **2011**, *50*, 1064. j) Schroder, N.; Besset, T.; Glorius, F. F) Tsai, A. S.; Brasse, M.; Bergman, R. G.; Ellman, J. A. *Adv. Synth. Catal.* **2012**, *354*, 579. k) Wang, C.; Chen, H.; Wang, Z. F.; Chen, J. A.; Huang, Y. *Angew. Chem. Int. Ed*. **2012**, *51*, 7242. l) Liu, B.; Fan, Y.; Gao, Y.; Sun, C.; Xu, C. Zhu, J. *J. Am. Chem. Soc*. **2013**, *135*, 468. m) Litsu-Ka, T.; Schaal, P.; Hirano, K.; Satoh, T.; Bolm, C.; Miura, M. *J. Org. Chem.* **2013**, *78*, 7216. n) Huang, X.; Huang, J.; Du, C.; Zhang, X.; Song, F.; You, J. *Angew. Chem., Int. Ed.* **2013**, *52*, 12970. o) Boultadakis-Arapinis, M.; Hopkinson, M. N.; Glorius, F. *Org. Lett*. **2014**, *16*, 1630. p) Karthikeyan, J.; Yoshikai, N. *Org. Lett*. **2014**, *16*, 4224. q) Parthasarathy, K.; Bolm, C. *Chem.-Eur. J*. **2014**, *20*, 4896. r) Hermann, G. N.; Becker, P.; Bolm, C. *Angew. Chem. Int. Ed.* **2015**, *54*, 7414. s) Takahama, Y.; Shibata, Y.; Tanaka, K. *Chem. Eur. J*. **2015**, *21*, 9053. t) Wen, J.; Wu, A.; Chen, P.; Zhu, J. *Tetrahedron Lett.* **2015**, *56*, 5282. u) Jiang, Q.; Zhu, C.; Zhao, H.; Su, W. *Chem. Asian. J*. **2015**, *11*, 356. v) Zhang, M.; Zhang, H. J.; Han, T.; Ruan, W.; Wen, T. B. *J. Org. Chem*. **2015**, *80*, 620. w) Xue, X.; Xu, J.; Zhang, L.; Xu, C.; Pan, Y.; Xu, L.; Li, H.; Zhang, W. *Adv. Synth. Catal*. **2016**, *358*, 573. x) Yi, Y.; Lee, H.; Jun, C-H. *Chem. Commun.* **2016**, *52*, 10171. y) Li, W-H.; Wu, L.; Li, S-S.; Liu, C-F.; Zhang, G-T.; Dong, L. *Chem. Eur. J*. **2016**, *22*, 17926. z) Han, W-J.; Pu, F.; Fan, J.; Liu, Z-W.; Shi, X-Y. *Adv. Synth. Catal*. **2017**, *359*, asap.
6. a) Kwon, K-H.; Lee, D. W. Yi, C. S. *Organometallics* **2010**, *29*, 5748. b) Uema, T.; Mochida, S.; Fukutani, T.; Hirano, K.; Satoh, T.; Miura, M. *Org. Lett*. **2011**, *13*, 706. c) Ackermann, L.; Pospech, J. *Org. Lett*. **2011**, *13*, 4153. d) Padala, K.; Jeganmohan, M. *Org. Lett*. **2011**, *13*, 6144. e) Hashimoto, Y.; Ueyama, T.; Fukutani, T.; Hirano, K.; Satoh, T.; Miura, M. *Chemistry. Lett*. **2011**, *40*, 1165. f) arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, *Green Chem*. **2011**, *13*, 3075. g) Graczyk, K.; Ma, W.; Ackerman, L.; Wang, L.; Wolfram, R.; lygin, A. V. *Org. Lett*. **2011**, *13*, 4153. h) Ackermann, L.; Wang, L.; Wolfram, R.; Lygin, A. V. *Org. Lett*. **2012**, *14*, 728. i) Li, B.; Ma, J.; Wang, N.; Feng, H.; Xu, S.; Wang, B. *Org. Lett*. **2012**, *14*, 736. j) Padala, K.; Jeganmohan, M. *Org. Lett*. **2012**, *14*, 1134. k) Li, J.; Kornhaaß, C.; Ackermann, L. *Chem. Commun*. **2012**, *48*, 11343. l) Hashimoto, Y.; Ortloff, T.; Hirano, K.; Satoh, T.; Bolm, MC.; Miura, M. *Chemistry. Lett*. **2012**, *41*, 151. m) Arockiam, P. B.; Brumeau, C.; Dixneuf, P. H. *Chem. Rev*. **2012**, *112*, 5879. n) Ma, W.; Ackermann, L. *Chem.-Eur. J*. **2013**, *19*, 13925. o) Fabry, D. C.; Ronge, M. A.; Zoller, J.; Rueping, M. *Angew. Chem. Int. Ed*. **2015**, *54*, 2801. p) Leitch, J. A.; Wilson, P. B.; Mcmullin, C. L.; Mahon, M. F.; Bhonoah, Y.; Williams, I. H.; Frost, C. G. *ACS Catal*. **2016**, *6*, 5520. q) Leitch, J. A.; Cook, H. P.; Bhonoah, Y.; Frost, C. G. *J. Org. Chem*. **2016**, *81*, 10081. r) Lanke, V.; Bettadapur, K. R.; Prabhu, K. R. *Org. Lett*. **2016**, *18*, 5496.
7. a) Manoharan, R.; Sivakumar, G.; Jeganmohan, M. *Chem. Commun.* **2016**, *52*, 10533. b) Grigorjeva, L.; Daugulis, O. *Org. Lett*. **2014**, *16*, 4684.
8. Sevov, C. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10625.
9. a) Tsuchikama, K.; Kasagawa, M.; Hashimoto, Y-K.; Endo, K.; Shibata, T. *J. Organomet. Chem.* **2008**, *693*, 3939. b) Takebayashi, S.; Shibata, T. *Organometallics* **2012**, *31*, 4114. c) Pan, S.; Ryu, N.; Shibata, T. *J. Am. Chem. Soc.* **2012**, *134*, 17474. d) Sevov, C. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2013**, *135*, 2116. e) Crisenza, G. E. M.; McCreanor, N. G.; Bower, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10258. f) Shibata, T.; Shizuno, T. *Angew. Chem. Int. Ed*. **2014**, *53*, 5410. g) Pan, S.; Ryu, N.; Shibata, T. *Adv. Synth. Catal*. **2014**, *356*, 929. h) Shibata, T.; Takano, H. *Org. Chem. Front*. **2015**, *2*, 383. i) Ebe, Y.; Nishimura, T. *J. Am. Chem. Soc.* **2015**, *137*, 5899. j) Hatano, M.; Ebe, Y.; Nishimura, T. Yorimitsu, H. *J. Am. Chem. Soc.* **2016**, *138*, 4010. k) Shibata, T.; Michino, M.; Kurita, H.; Tahara, Y-K.; Kanyiva, K. S. *Chem. –Eur. J.* **2017**, *23*, 88.
10. a) Kumaran, E.; Sridevi, V. S.; Leong, W. K. *Organometallics* **2010**, *29*, 6417. b) Kumaran, E.; How, K. T. S.; Ganguly, R.; Li, Y.; Leong, W. K. *Organometallics* **2013**, *32*, 4149. c) Kumaran, E.; Fan, W. Y.; Leong, W. K. *Org. Lett*. **2014**, *16*, 1342. d) Kumaran, E.; Leong, W. K. *Tetrahedron Lett.* **2014**, *55*, 5495.
11. Ball, R. G.; Graham, A. G.; Heinekey, D. M.; Hoyano, J. K.; McMaster, A. D.; Mattson, B. M.; Michel, S. T. *Inorg. Chem.* **1990**, *29*, 2023.

Supplementary Material

Details of experiments and characterization data of all products.

Highlights

- Carbonyl directed oxidative coupling or arene with alkene
- First iridium-catalysed example
- Tolerant of a wide range of substituents