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Ruthenium-catalyzed oxidative C–H alkenylation of aryl carbamates†

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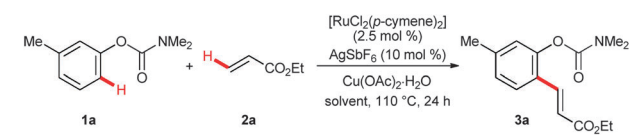
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A cationic ruthenium(II) catalyst enabled highly efficient oxidative alkenylations of electron-rich arenes bearing removable, weakly coordinating carbamates, and allowed for cross-dehydrogenative C–H bond functionalization in an aerobic manner.

Palladium-catalyzed alkenylations of aryl (pseudo)halides with alkenes, Mizoroki–Heck reactions, have matured to being among the most reliable methods for the synthesis of substituted styrenes.^{1,2} A more atom- and step-economical strategy, however, relies on twofold functionalizations of otherwise unreactive C–H bonds as latent functional groups.³ The vast majority of these cross-dehydrogenative alkenylations was accomplished using palladium or rhodium complexes, with notable recent progress being accomplished by among others Miura and Yu.^{4,5} In contrast, less expensive ruthenium complexes were only recently identified as viable catalysts for environmentally benign twofold C–H bond alkenylations. Thereby, carbonyl- and N-heteroaryl-substituted, thus electron-deficient, arenes as well as anilides were converted into the corresponding *ortho*-olefinated⁶ products.⁷ In contrast, the use of air- and moisture stable ruthenium complexes for challenging oxidative C–H bond alkenylations with widely accessible phenol derivatives has unfortunately thus far proven to be elusive. In the course of our continuing efforts in step-economical C–H bond functionalizations,⁸ we devised reaction conditions for ruthenium-catalyzed cross-dehydrogenative alkenylations of aryl carbamates bearing removable directing groups, on which we wish to report herein. Importantly, aryl carbamates are key intermediates in organic synthesis, and serve as versatile organic electrophiles in transition-metal-catalysis.^{9,10}

Preliminary studies with a naphthyl carbamate indicated that the desired oxidative alkenylation was not viable with CsOAc or KPF₆ as the co-catalytic additive. However, satisfactory results were gratifyingly achieved when employing 10 mol% of AgSbF₆. The desired olefination did not occur in the absence of the ruthenium complex [RuCl₂(*p*-cymene)₂] (Table 1, entry 1). Among a set of representative solvents, DME turned out to be optimal (entries 2–6), and the catalytic system was found to be air-stable (entry 7). Notably, the cross-dehydrogenative alkenylation failed to proceed in the absence

Table 1 Optimization of oxidative alkenylation^a


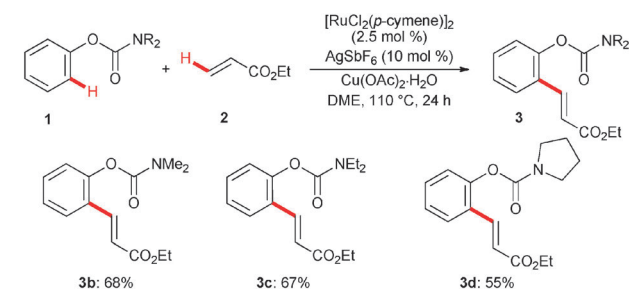
| Entry | Catalyst | Solvent | Yield (%) |
|-------|---|----------------|-----------------|
| 1 | — | DME | — |
| 2 | [RuCl ₂ (<i>p</i> -cymene) ₂] | DMF | — |
| 3 | [RuCl ₂ (<i>p</i> -cymene) ₂] | PhMe | — |
| 4 | [RuCl ₂ (<i>p</i> -cymene) ₂] | DCE | 40 |
| 5 | [RuCl ₂ (<i>p</i> -cymene) ₂] | <i>t</i> -AmOH | 48 |
| 6 | [RuCl ₂ (<i>p</i> -cymene) ₂] | DME | 84 |
| 7 | [RuCl ₂ (<i>p</i> -cymene) ₂] | DME | 86 ^b |
| 8 | [RuCl ₂ (<i>p</i> -cymene) ₂] | DME | — ^c |
| 9 | [Ru ₂ Cl ₃ (<i>p</i> -cymene) ₂][PF ₆] | DME | — ^c |

^a Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), catalyst (2.5 mol%), Cu(OAc)₂·H₂O (1.0 mmol), solvent (3.0 mL); isolated yields. ^b Under air. ^c Without AgSbF₆.

of AgSbF₆ as the co-catalyst (entry 8), thus being suggestive of the formation of a cationic ruthenium catalyst. Yet, the preformed cationic complex [Ru₂Cl₃(*p*-cymene)₂][PF₆]^{7e} bearing the PF₆-counteranion did not deliver the desired product **3a** under otherwise identical reaction conditions (entry 9).

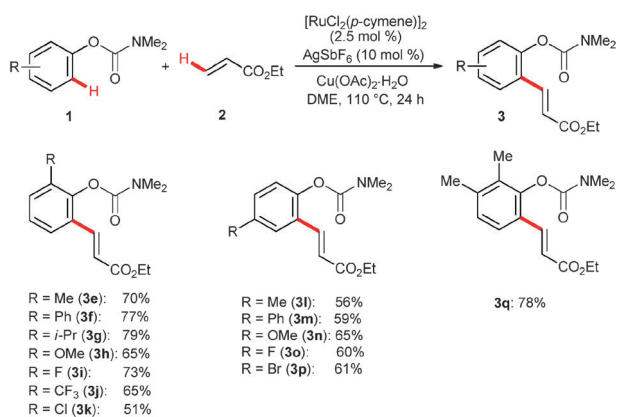
With an optimized catalytic system in hand, we tested the influence of the N-substituents of phenyl carbamates **1** on the reaction efficacy (Scheme 1). Thus, dialkyl-substituted carbamates **1** furnished the desired products **3** in high yields, with atom-economical *N,N*-dimethyl derivative **1b** providing the best results.

Subsequently, we probed the scope of the optimized catalyst in the twofold C–H bond functionalizations with moisture-stable phenol derivatives **1** (Scheme 2). The cationic ruthenium(II) catalyst proved to be broadly applicable and tolerated valuable

Scheme 1 Effect of *N*-substituents on oxidative C–H bond alkenylation.

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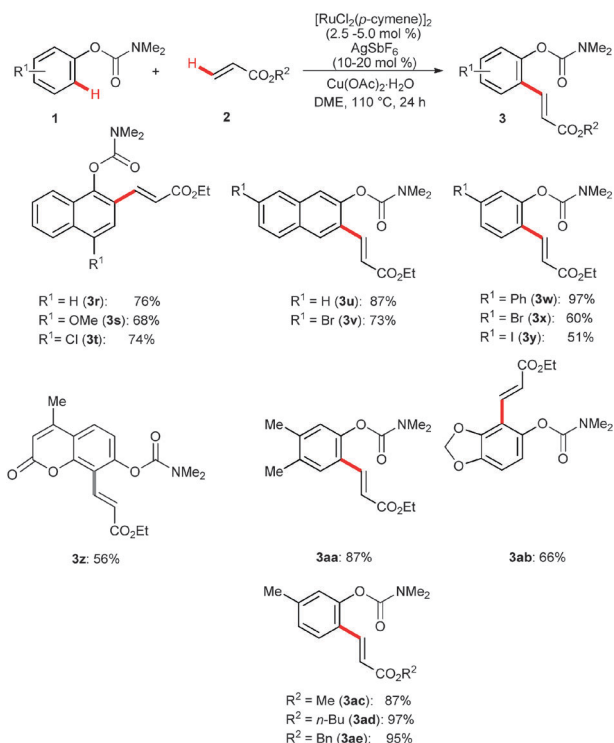


Scheme 2 Scope of oxidative C–H bond alkenylation.

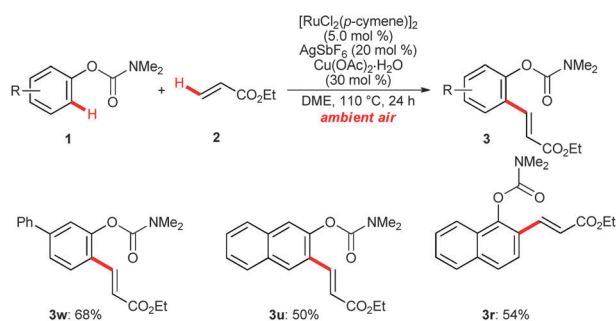
functional groups, including aryl and alkyl fluorides, chlorides or bromides, the latter of which should prove to be valuable for a post-synthetic elaboration of products **3**. Additionally, both electron-deficient as well as electron-rich arenes **1** were found to be suitable substrates, and delivered the corresponding styrenes **3** with excellent *E*-diastereoselectivities.

Furthermore, we observed that intramolecular competition experiments with *meta*-substituted substrates **1** proceeded with high site-selectivities, furnishing products **3r–3ae** as the sole products (Scheme 3). The ruthenium(II) complex again displayed a useful chemoselectivity, and allowed for the effective conversion of various acrylic esters **2** as well.

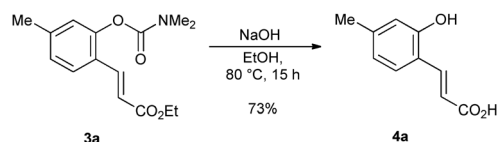
Importantly, the double C–H bond functionalization was not limited to the use of stoichiometric amounts of Cu(OAc)₂·H₂O. Indeed, aerobic oxidative alkenylations proved to be viable with Cu(OAc)₂·H₂O as the cocatalyst under an atmosphere of ambient air (Scheme 4).



Scheme 3 Scope within intramolecular competition experiments.



Scheme 4 Aerobic oxidative C–H bond alkenylation.



Scheme 5 Removal of directing group.

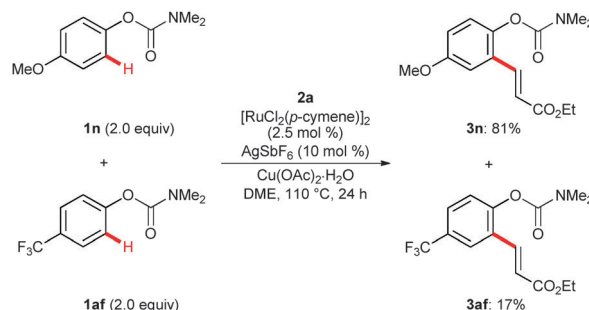
Importantly, the carbamate directing group was easily removed to deliver the desired phenol **4a** (Scheme 5).

Considering the remarkable activity and high selectivity of the cationic ruthenium(II) catalyst, we became interested in probing its mode of action. To this end, we conducted intermolecular competition experiments with differently substituted arenes **1**, which revealed electron-rich substrates to be preferentially converted (Scheme 6, and Scheme S1 in the ESI†).

Based on these mechanistic studies as well as our previous findings with cationic ruthenium(II) catalysts^{7a,e} we propose the catalytic cycle to involve an initial base-assisted, reversible cycloruthenation.¹¹ Thereafter, coordinative insertion of alkene **2** and β -hydride elimination deliver product **3**, while reductive elimination and reoxidation by Cu(OAc)₂·H₂O regenerate the active cationic catalyst.

In conclusion, we have developed ruthenium-catalyzed oxidative C–H bond alkenylations with electron-rich phenol derivatives. Thus, a cationic ruthenium(II) complex sets the stage for site-selective, broadly applicable olefinations of aryl carbamates displaying removable directing groups, which also proved to be viable in an aerobic fashion with ambient air as the ideal terminal oxidant.

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Scheme 6 Intermolecular competition experiments.

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