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

Jie Li, Christoph Kornhaaß and Lutz Ackermann*

Received 25th August 2012, Accepted 4th October 2012
DOI: 10.1039/c2cc36196e

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 arenes (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-olefinated 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-catalyst (entry 8), thus being suggestive of the formation of a cationic ruthenium catalyst. Yet, the preformed cationic complex [RuCl2(p-cymene)2][PF6] 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 2). The cationic ruthenium(II) catalyst proved to be broadly applicable and tolerated valuable substituents on oxidative C–H bond alkenylation. Yet, the preformed cationic complex [RuCl2(p-cymene)2][PF6] 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). The cationic ruthenium(II) catalyst proved to be broadly applicable and tolerated valuable substituents on oxidative C–H bond alkenylation.

Table 1 Optimization of oxidative alkenylationa

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Solvent</th>
<th>Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>—</td>
<td>DME</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>[RuCl2(p-cymene)2]</td>
<td>DME</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>[RuCl2(p-cymene)2]</td>
<td>PhMe</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>[RuCl2(p-cymene)2]</td>
<td>DCE</td>
<td>40</td>
</tr>
<tr>
<td>5</td>
<td>[RuCl2(p-cymene)2]</td>
<td>t-AmOH</td>
<td>48</td>
</tr>
<tr>
<td>6</td>
<td>[RuCl2(p-cymene)2]</td>
<td>DME</td>
<td>84</td>
</tr>
<tr>
<td>7</td>
<td>[RuCl2(p-cymene)2]</td>
<td>DME</td>
<td>86b</td>
</tr>
<tr>
<td>8</td>
<td>[RuCl2(p-cymene)2]</td>
<td>DME</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>[RuCl2(p-cymene)2][PF6]</td>
<td>DME</td>
<td>—</td>
</tr>
</tbody>
</table>

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.

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c2cc36196e

Institut fuer Organische und Biomolekulare Chemie, Georg-August-Universitaet, Tammannstrasse 2, 37077 Goettingen, Germany. E-mail: Lutz.Ackermann@chemie.uni-goettingen.de; Fax: +49 551 3967777

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c2cc36196e

This journal is © The Royal Society of Chemistry 2012
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(n) 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)$_2$·H$_2$O. Indeed, aerobic oxidative alkenylations proved to be viable with Cu(OAc)$_2$·H$_2$O as the cocatalyst under an atmosphere of ambient air (Scheme 4).

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)$_2$·H$_2$O 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.

Financial support from the China Scholarship Council (fellowship to J. L.), and the CaSuS PhD program (fellowship to C. K.) is gratefully acknowledged.
Notes and references

3 Selected recent reviews on C–H bond functionalizations:
6 Examples of related oxidative annihilations of alkenes:
10 Reviews on challenging arylation through C–O bond cleavages: