Electrochemical ruthenium-catalyzed alkyne annihilations by C–H/Het–H activation of aryl carbamates or phenols in protic media†

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Electrooxidative peri-C–H activation was accomplished by versatile ruthenium(II) catalysis in terms of C–H/N–H and C–H/O–H functionalization. Thus, alkyne annihilations proved viable with ample scope by organometallic C–H activation. The sustainable electrocatalysis exploited electricity, thereby avoiding the use of toxic transition metals as sacrificial oxidants. The robust ruthenium(II)-electrocatalysis was operative in a protic alcohol/H₂O reaction medium with excellent levels of positions-, regio- and chemo-selectivity.

Transition metal-catalyzed oxidative C–H activation has been recognized as a powerful tool for the assembly of π-conjugated heterocycles, with major potential for molecular syntheses and material sciences. Despite of considerable progress, these oxidative C–H functionalizations heavily rely on stoichiometric amounts of expensive and toxic metal salts as the sacrificial oxidants. Electrooxidation has emerged as an increasingly viable platform for sustainable transformations, which enables the use of inexpensive electricity as the terminal oxidant. In this context, major advances were achieved, exploiting transition-metals based on inter alia palladium, cobalt, ruthenium, rhodium, copper, or iridium.

Recently, we have introduced a versatile ruthenium catalyst for oxidative C–H/O–H annulation of alkynes by 1-naphthols to access fused pyran derivatives. Despite considerable experimentation, these transformations were restricted to the use of anti-bacterial copper(II) oxidants. Within our program on sustainable C–H activation, we have now developed the first electrochemical, organometallic peri-C–H activation with synthetically meaningful arylcarbamates, on which we report herein (Fig. 1).

Notable features of our finding include (a) the first electrooxidative ruthenium-catalysed peri-C–H activation, (b) C–H/N–H annulation by electrooxidative ruthenium catalysis, (c) weakly coordinating naphthol for C–H/O–H alkyne annihilations with electricity as the terminal oxidant, and (d) mechanistic insights into electrochemical peri-C–H activation by experiments. It is furthermore noteworthy that our electrooxidative strategy also set the stage for the first ruthenium-catalyzed C–H/N–H activation/alkyne annihilation of naphthylcarbamates.

At the outset of our studies, we tested various reaction conditions for the envisioned electrooxidative annulation of alkyne 2a by easily-accessible ethyl naphthalen-1-ylcarbamate 1a (Table 1 and Table S-1 in the ESI†). Among a set of representative solvents, DMF and t-AmOH furnished promising results (entries 1 and 2), while a solvent mixture of t-AmOH and H₂O, along with KOAc as the additive, proved to be ideal (entries 3–6). The catalytic efficacy could be further improved when the electrolysis was conducted at a constant current regime of 1.5 mA along with KOAc as the additive, proved to be ideal (entries 3–6). The catalytic efficiency could be further improved when the electrolysis was conducted at a constant current regime of 1.5 mA along with KOAc as the additive.

With the optimized ruthenium electrocatalysis being established, we explored its versatility with a set of representative internal alkynes (Scheme 1). Thus, the broadly applicable ruthenium(II) catalyst enabled the efficient conversion of diaryl- and dialkyl-substituted alkynes 2a–2i. The robust ruthenium-electrocatalysis displayed a remarkable tolerance of valuable functional groups, such as ester, fluoro, chloro, or bromo substituents, setting the stage for further late-stage diversifications. Unsymmetrical alkyne 2j delivered the desired product 3aj with high levels of regio-control, placing the aromatic moiety in proximity to the nitrogen heteroatom.
Subsequently, a variety of arylcarbamates 1 were probed, highlighting an outstanding selectivity for the peri C–H activation to deliver benzoquinoline derivatives 3 (Scheme 2). Ethyl naphthalen-1-ylcarbamates 1 bearing either electron-withdrawing or electron-donating groups on the naphthyl ring provided the corresponding benzoquinolines 3 with high efficacy. It is worth noting that the ruthenium(II) electrocatalysis was likewise applicable to heterocyclic substrate ethyl quinolin-5-ylcarbamate 1d, selectively furnishing the annulated product 3da. Likewise, the extended aromatic substrate fluoranthen-3-ylcarbamate 1f was smoothly converted to give the π-conjugated polyheterocycles 3fa, featuring unique fluorescence emission.

The ruthenium(II) electrocatalysis was not limited to C–H/N–H activation with arylcarbamates 1. Indeed, highly effective annihilations of alkynes 2 proved to be viable with the weakly coordinating naphthol derivatives 4 (Scheme 3, and Table S-2 in the ESI†). Thus, a series of fluorescent pyrans were accessed in a step-economical fashion via the chemo-selective C–H/O–H functionalization, featuring electricity as the sacrificial oxidant.

Given the unique site- and regio-selectivity of the electrochemical ruthenium(II) catalysis, we became interested in its modus operandi. To this end, a catalytic C–H transformation in the presence of D₂O employing an excess of substrate 1a resulted in a significant H/D exchange in the peri-position of the recovered starting material [D₁]-1a (Scheme 4a). This observation provided strong evidence for a reversible, organometallic C–H ruthenation step. In good agreement with this finding, a kinetic isotope effect (KIE) was not observed, when comparing the extended aromatic substrate fluoranthen-3-ylcarbamate 1f with the corresponding naphthyl derivative 4.

| Entry | [TM] | Solvent | Yield [%] |
|-------|------|---------|-----------|
| 1     | RuCl₂(p-cymene)₂ | DMF      | 35        |
| 2     | RuCl₂(p-cymene)₂ | t-AmOH   | 51        |
| 3     | RuCl₂(p-cymene)₂ | t-AmOH/H₂O (3/1) | 61 |
| 4     | RuCl₂(p-cymene)₂ | DMF/H₂O (3/1) | 28 |
| 5     | RuCl₂(p-cymene)₂ | t-AmOH/H₂O (3/1) | 57<sup>b</sup> |
| 6     | RuCl₂(p-cymene)₂ | t-AmOH/H₂O (3/1) | 65<sup>c</sup> |
| 7     | RuCl₂(p-cymene)₂ | t-AmOH/H₂O (3/1) | 36<sup>d</sup> |
| 8     | RuCl₂(p-cymene)₂ | t-AmOH/H₂O (3/1) | 73<sup>d</sup> |
| 9     | RuCl₂(p-cymene)₂ | t-AmOH/H₂O (3/1) | 82<sup>c,f</sup> |
| 10    | RuCl₂(p-cymene)₂ | t-AmOH/H₂O (3/1) | 31<sup>d</sup> |
| 11    | — | t-AmOH/H₂O (3/1) | <5<sup>f</sup> |
| 12    | [Cp*RhCl₂]₂ | t-AmOH | 65<sup>b</sup> |

<sup>a</sup> General reaction conditions: 1a (0.60 mmol), 2a (0.30 mmol), [TM] (10 mol %), KOAc (0.60 mmol), n-Bu₄NPF₆ (0.18 mmol), solvent (4.0 mL), 100 °C, 16 h, under N₂, constant current electrolysis (CCE) at 4.0 mA, undivided cell, RVC anode, Pt-plate cathode. Isolated yields. <sup>b</sup> NaOPiv (0.60 mmol) instead of KOAc. <sup>c</sup> n-Bu₄NClO₄ (0.18 mmol) instead of n-Bu₄NPF₆. <sup>d</sup> 10 mA, 2.5 h. <sup>e</sup> 2.0 mA, 16 h. <sup>f</sup> 1.5 mA, 24 h. <sup>g</sup> Without current, 24 h.
Based on our mechanistic studies, we propose a plausible catalytic cycle to commence by a facile organometallic C–H activation (Scheme 5). Thereby, ruthena(s)cycle 7 is generated, along with two equivalents of carboxylic acid. Thereafter, migratory alkyne insertion furnishes the seven-membered ruthena(s)cycle 9, which rapidly undergoes reductive elimination to deliver the ruthenium(0) sandwich complex 10. The key reoxidation of the thus-formed ruthenium(0) complex 10 is finally accomplished by anodic oxidation, while cathodic reduction generates molecular hydrogen as the sole stoichiometric byproduct.

In summary, we have reported on the first electrocatalytic organometallic C–H activation with aromatic carbamates and phenols. Hence, a versatile ruthenium(s) carboxylate catalyst enabled electrooxidative C–H/N–H and C–H/O–H activation/alkyne annulations with ample scope. The C–H activation employed electricity as the sacrificial oxidant, which avoids the use of toxic metals as terminal oxidants, generating molecular hydrogen as the only byproduct. Mechanistic studies provided strong support for an organometallic C–H ruthenation, along with an efficient electro-reoxidation of the key ruthenium(0) intermediate by environmentally-benign electricity that is amenable for renewable forms of energy. The electrochemical C–H/Het–H activation was operative in protic aqueous reaction media.

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Conflicts of interest
There are no conflicts to declare.

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