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## Rhodaelectro-catalyzed chemo-divergent C–H activations with alkylidenecyclopropanes for selective cyclopropylations†

Zhigao Shen, Isaac Maksso, Rositha Kuniyil, Torben Rogge and Lutz Ackermann \*

Herein, we report on selectivity control in C–H activations with alkylidenecyclopropanes (ACPs) for the chemo-selective assembly of cyclopropanes or dienes. Thus, unprecedented rhodaelectro-catalyzed C–H activations were realized with diversely decorated ACPs with a wide substrate scope and electricity as the sole oxidant.

Throughout the last decade, C–H activation has emerged as an increasingly powerful tool in molecular syntheses.<sup>1</sup> In sharp contrast, strategies for transition metal-catalyzed C–C activation remain comparably underdeveloped.<sup>2</sup> In recent years, major advances, in particular in ring-strain release-promoted C–C cleavages, have been achieved by Dong,<sup>3</sup> Bower,<sup>4</sup> and Marek,<sup>5</sup> among others.<sup>6</sup> Alkylidenecyclopropanes<sup>7</sup> (ACPs) have previously been recognized as a versatile platform for C–H/C–C functionalizations. However, their application within a bifurcated mechanistic manifold for the selective introduction of cyclopropane<sup>8</sup> or 1,3-dienes<sup>9</sup> motifs has thus far proven elusive, although they represent crucial structural scaffolds in a variety of pharmaceuticals, biologically active molecules and natural products. While a single example of rhodium-catalyzed dienylation was realized with chemical oxidants,<sup>10</sup> cyclopropylations are as of yet not available.

The use of electricity to drive chemical reactions has recently witnessed a remarkable renaissance.<sup>11</sup> Significant momentum was particularly gained by the merger of mettallaelectrocatalysis and QJ;C–H activation to avoid often toxic and expensive oxidants.<sup>1b,12</sup> With our continued interest in rhodaelectro-catalyzed C–H activation,<sup>13</sup> we have now developed a bifurcated C–H activation with alkylidenecyclopropanes that can be conducted under

sustainable and operationally-simple electrochemical conditions. Salient features of our strategy include (a) full control of selectivity within a bifurcated manifold for C–H cyclopropylations *versus* dienylation *via*  $\beta$ -H over  $\beta$ -C elimination, (b) detailed mechanistic insights by means of experiment and computation, (c) absence of external chemical oxidants, (d) water as the reaction medium, and (e) a user-friendly undivided cell setup without additional electrolyte (Fig. 1).

We initiated our studies with indole **1a** and ACP **2a** to evaluate C–H dienylation and cyclopropylations in a user-friendly undivided cell setup with a graphite felt (GF) anode and a platinum cathode (Table 1). The dienylated product **3aa** was obtained in 72% yield in the presence of 2.5 mol%  $[\text{Cp}^*\text{RhCl}_2]_2$ , using 1,4-dioxane/H<sub>2</sub>O (1 : 1) as the solvent. After examination of different bases, NaO<sub>2</sub>CAd led to the best result, delivering diene **3aa** in 85% yield with an *Z/E* ratio of 4.5/1 (entries 1–5). The indispensable roles of electricity and the rhodium catalyst were further confirmed by control experiments (entries 6 and 7). A variation of the current did not result in an improved performance (entries 8 and 9). We also tested different acids and found that cyclopentanecarboxylic acid proved beneficial (entries 10 and 11). With an increased amount of NaO<sub>2</sub>CAd, the product was obtained in a higher *Z/E* ratio, albeit with a small decrease in efficiency (entry 12).

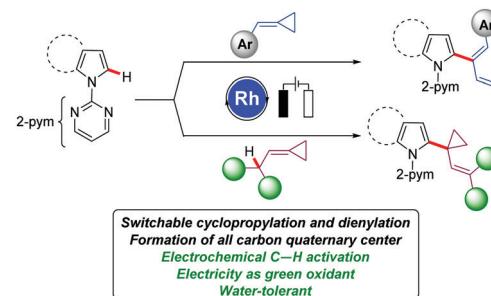


Fig. 1 Cycloproylation and dienylation enabled by rhodaelectro-catalysis.

Institut für Organische und Biomolekulare Chemie and Wöhler Research Institute for Sustainable Chemistry, Georg-August-Universität Göttingen, Tammannstrasse 2, Göttingen 37077, Germany. E-mail: Lutz.Ackermann@chemie.uni-goettingen.de; Web: <http://www.ackermann.chemie.uni-goettingen.de/>, <http://wisch.chemie.uni-goettingen.de/>

† Electronic supplementary information (ESI) available. CCDC 2025011 (**3ap**) and 2025012 (**5pa**). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d0cc08123j



Table 1 Electrochemical C–H dienylation of indole<sup>a</sup>

Entry	Base	Acid	Yield (%)	Z/E
1	NaOAc	CypCO <sub>2</sub> H	72	3.9/1
2	NaOPiv	CypCO <sub>2</sub> H	78	3.5/1
3	NaO <sub>2</sub> CMes	CypCO <sub>2</sub> H	60	4.0/1
4	NaO <sub>2</sub> CPh	CypCO <sub>2</sub> H	82	3.6/1
5	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	85	4.5/1
6 <sup>b</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	24	2.4/1
7 <sup>c</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	—	—
8 <sup>d</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	87	3.8/1
9 <sup>e</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	72	3.2/1
10	NaO <sub>2</sub> CAd	MesCO <sub>2</sub> H	78	3.8/1
11	NaO <sub>2</sub> CAd	PivOH	82	3.3/1
12 <sup>f</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	82	6.0/1
13 <sup>fg</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	87	6.5/1
14 <sup>gh</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	89	7.0/1
15 <sup>i</sup>	NaO <sub>2</sub> CAd	CypCO <sub>2</sub> H	95 (5aa)	<1/20

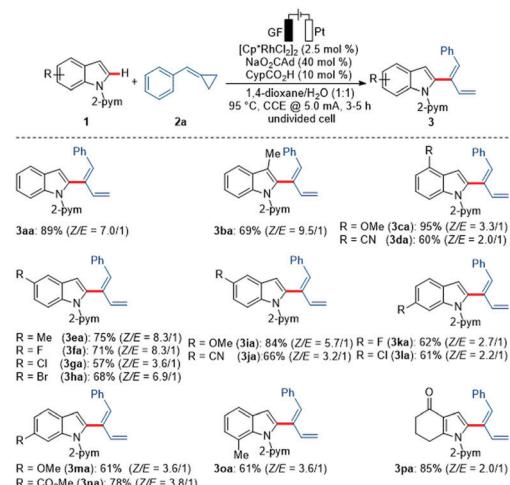
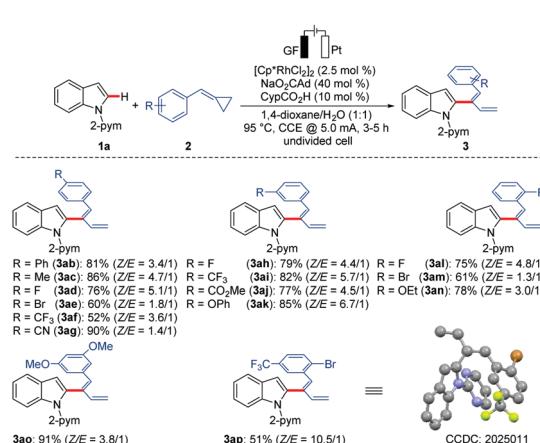
<sup>a</sup> Undivided cell, graphite felt anode (GF), platinum plate cathode (Pt), **1a** (0.1 mmol) **2a** (0.16 mmol), [Cp\*RhCl<sub>2</sub>]<sub>2</sub> (2.5 mol%), base (20 mol%), acid (10 mol%), 1,4-dioxane/H<sub>2</sub>O (1:1, 4.0 mL), 85 °C, CCE @ 3.0 mA, under air, 4.0 h, yield of isolated product, Z/E ratio determined by <sup>1</sup>H NMR spectroscopy, CypCO<sub>2</sub>H = cyclopentanecarboxylic acid. <sup>b</sup> Without electricity, 12 h. <sup>c</sup> Without [Cp\*RhCl<sub>2</sub>]<sub>2</sub>. <sup>d</sup> CCE @ 2.0 mA, 6.0 h. <sup>e</sup> CCE @ 4.0 mA, 3.0 h. <sup>f</sup> NaO<sub>2</sub>CAd (40 mol%). <sup>g</sup> 0.2 mmol scale, 1,4-dioxane/H<sub>2</sub>O (1:1, 8.0 mL), CCE @ 5.0 mA, 3.0 h. <sup>h</sup> 95 °C. <sup>i</sup> **4a** instead of **2a** under the conditions of entry 14.

A higher reaction temperature improved the efficacy. Importantly, the novel cyclopropylated product **5aa** was obtained in high yield when using benzyl ACP **4a**.<sup>14</sup>

With the optimized reaction conditions for the electrochemical C–H dienylation in hand, its versatility was explored with substituted indoles **1** (Scheme 1). 3-, 5- or 7-Methyl indoles **1** delivered the desired products **3ba**, **3ea** and **3oa**, while the 3-methyl indole **1b** gave an improved selectivity. Fluorine- and methoxy-substituted indoles **1** were efficiently transformed, but 6-substituted indoles **1k** and **1m** displayed a slightly lower efficiency. Various functional groups were tolerated by the rhodium electrocatalyst, such as chloro, bromo and cyano substituents. Interestingly, indole **1n** with an ester functionality at the 6-position delivered diene **3na** in high yield. The dienylation protocol was also amenable to pyrrole **3pa**.<sup>15</sup>

Next, the robustness of the rhodaelectro-catalyzed C–H dienylation was evaluated with a variety of functionalized cyclopropanes (Scheme 2). Substrates containing bromide groups delivered chemo-selectively the products **3ae** and **3am**. In contrast to previous studies, electron-deficient heteroarenes showed an inherent high reactivity.<sup>13</sup> However, electron-rich substrates also performed well in the electrocatalysis. The connectivity of diene **3ap** was unambiguously confirmed by single-crystal X-ray analysis.<sup>‡</sup> It is noteworthy that, 2-phenyl pyridine could also be employed for the electrocatalysis to deliver arene **5qa**. The tryptamine-derived substrate **1r** delivered the challenging ring-opening product **5ra'**.

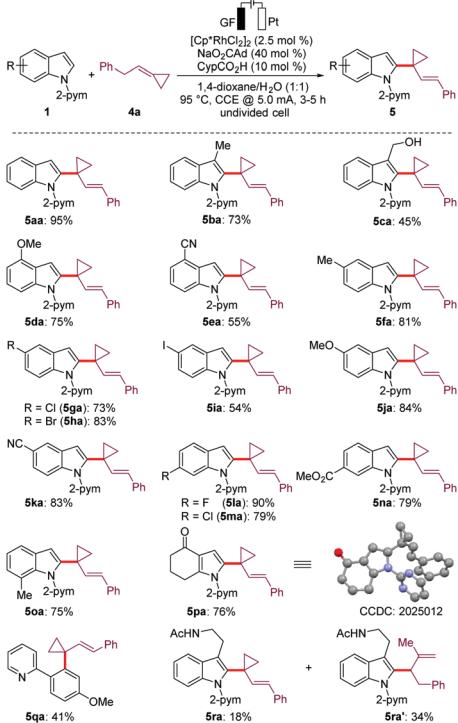
Thereafter, we turned our attention to the versatility of the unprecedented electrochemical C–H cycloproylation of indoles **1**

Scheme 1 Electrochemical C–H dienylation of indoles **1**.Scheme 2 Electrochemical C–H dienylation with ACPs **2**.

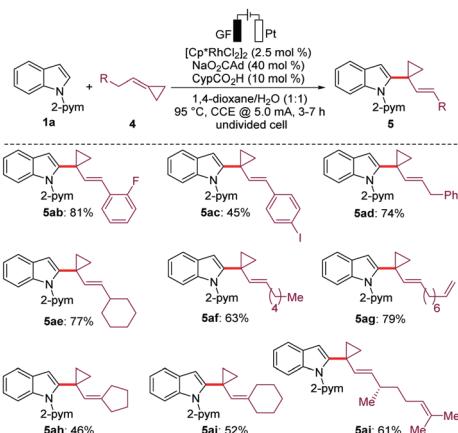
(Scheme 3). We found that an otherwise reactive hydroxyl was fully tolerated, despite being in close proximity (**5ca**). Halogen-containing indoles, even the reactive iodo-substituent, were likewise viable substrates. Indoles containing electron-withdrawing or electron-donating groups selectively underwent this transformation. For 7-methyl indole, the cycloproylation showed a higher efficiency as compared to the dienylation (**5oa** versus **3oa**). The rhodaelectrocatalysis proved also applicable to pyrroles, while the structure of the cyclopropylated product **5pa** was confirmed by single-crystal X-ray analysis.<sup>‡</sup> It is noteworthy that, 2-phenyl pyridine could also be employed for the electrocatalysis to deliver arene **5qa**. The tryptamine-derived substrate **1r** delivered the challenging ring-opening product **5ra'**.

Next, we explored the C–H cycloproylation with differently substituted ACPs **4** (Scheme 4). Substrate **4c** bearing an iodine substituent gave the desired product **5ac** with a small amount of the deiodinated product (**5aa**:**5ac** 1/3). The aqueous conditions were compatible with linear or branched alkyl-derived cyclopropanes (**5ad**–**5af**). The challenging cyclopropane **4g** bearing a terminal alkene was also found to be a viable





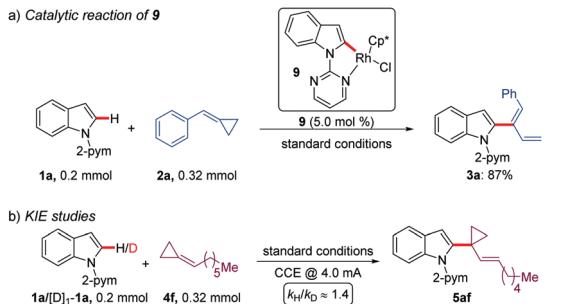
Scheme 3 Electrocatalyzed C–H cyclopropanation of indoles **1**, arenes and pyrroles.



Scheme 4 Rhodaelectro-catalyzed C–H cyclopropanation with ACPs **4**.

substrate, affording product **5ag** in 79% yield. The transformation was also tolerant to changes in the backbone of the cyclic alkanes and generated the desired products **5ah** and **5ai**. Indeed, the structurally more complex, natural product citronellol-derived starting material **4j** was chemo-selectively converted to the desired product **5aj**.

To gain insights into the reaction mechanism, control experiments were performed. The independently prepared cyclometalated complex **9**<sup>16</sup> was found to serve as a catalytically competent species (Scheme 5a). Under the standard conditions but without electricity, H/D exchange of indole **1a** with D<sub>2</sub>O was



Scheme 5 Summary of key mechanistic findings.

observed with significant deuterium incorporation at the position C2 (Scheme S2 in the ESI†). However, a significant deuterium-incorporation into product **3aa** was not observed, when **1a** was reacted with **2a** under the electrochemical conditions using D<sub>2</sub>O as the cosolvent (Scheme S3 in the ESI†). A kinetic isotope effect (KIE) study was next conducted. Parallel independent reactions resulted in a value of  $k_H/k_D \approx 1.4$  (Scheme 5b), indicating that the C–H cleavage step is likely not involved in the rate-determining step.<sup>14</sup>

In order to further understand the catalyst's mode of action, we became interested in studying the rhodaelectro-catalyzed C–H cyclopropanation of indole **1a** with ACP **4a** by density functional theory (DFT). Geometry optimizations and frequency calculations were performed at the TPSS-D3(BJ)/def2-SVP level of theory, while single point energies were calculated at the PW6B95-D3(BJ)/def2-TZVP+SMD(1,4-dioxane) and PBE0-D3(BJ)/def2-TZVP+SMD(1,4-dioxane) level of theory.<sup>14</sup> All energies reported here were calculated at the PW6B95-D3(BJ)/def2-TZVP+SMD(1,4-dioxane)/TPSS-D3(BJ)/def2-SVP level of theory.<sup>14</sup> Our calculations indicated that after the migratory insertion of ACP **4a**,  $\beta$ -H elimination occurs from the intermediate **D** via **TS(D-E)** (Fig. S1, ESI†) with a barrier of 1.1 kcal mol<sup>-1</sup>. Moreover,  $\beta$ -H elimination from the intermediate **D** results in the regioselective formation of the *E*-isomer as the major product, while the generation of *Z*-isomer is energetically not favourable.<sup>14</sup>

Based on our studies, we propose a plausible catalytic cycle for the unprecedented rhodaelectro-C–H-cyclopropanation, which is initiated by the formation of a catalytically competent mononuclear cationic Cp\*Rh(III) species. As shown in Fig. 2, coordination of indole **1a** to Cp\*Rh(III) and facile subsequent cyclorhodation at the 2-position affords rhodacycle **A**. Then, the insertion of alkene **4a** occurs to furnish intermediate **D**, which undergoes  $\beta$ -H elimination to generate the cyclopropanated product **5aa** along with a rhodium(I) intermediate. Finally, the Cp\*Rh(III) species is regenerated by rate-limiting reoxidation of rhodium(I) at the anode, while generating molecular hydrogen as the byproduct at the cathode and completing the catalytic cycle. In terms of the dienylation, intermediate **D** undergoes  $\beta$ -C elimination to form intermediate **G** (Fig. S10 in the ESI†). Final  $\beta$ -H elimination then delivers the dienylated indole **3aa**.

In conclusion, we have reported on a versatile rhodaelectro-catalyzed C–H activation with alkylidenecyclopropanes under

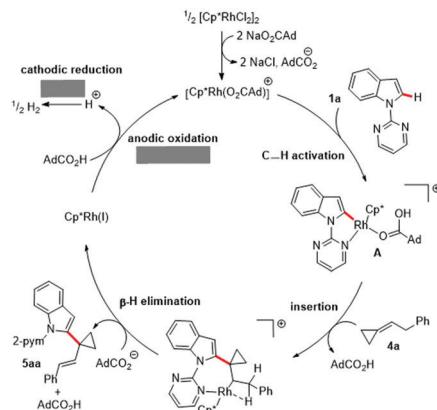


Fig. 2 Proposed mechanism for electro-C–H cyclopropanation with ACPs 4.

aqueous conditions, devoid of stoichiometric amounts of chemical oxidants. Our unique strategy allowed for the control of selectivity within a bifurcated mechanistic pathway by the judicious choice of  $\beta$ -H over  $\beta$ -C elimination. Detailed studies by experiment and calculation provided key insights into the catalyst's mode of action, revealing  $\beta$ -H elimination as the key selectivity-determining process for an unprecedented C–H cyclopropanation. The reactive catalyst can be regenerated in a sustainable manner by anodic oxidation, yielding hydrogen as the sole stoichiometric byproduct. Thereby, a wealth of heteroarenes was functionalized with excellent chemo-, position- and diastereoselectivity.

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## Conflicts of interest

There are no conflicts to declare.

## Notes and references

‡ Deposition numbers 2025011 (3ap) and 2025012 (5pa) contain the supplementary crystallographic data for this paper.

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