α-Pyridones and α-pyrones are ubiquitous structural motifs found in natural products and biologically active small molecules. Here, we report an Rh-catalyzed electrochemical vinylic C–H annulation of acrylamides with alkynes, affording cyclic products in good to excellent yield. Divergent syntheses of α-pyridones and cyclic imidates are accomplished by employing N-phenyl acrylamides and N-tosyl acrylamides as substrates, respectively. Additionally, excellent regioselectivities are achieved when using unsymmetrical alkynes. This electrochemical process is environmentally benign compared to traditional transition metal-catalyzed C–H annulations because it avoids the use of stoichiometric metal oxidants. DFT calculations elucidated the reaction mechanism and origins of substituent-controlled chemoselectivity. The sequential C–H activation and alkyne insertion under rhodium catalysis leads to the seven-membered ring vinyl-rhodium intermediate. This intermediate undergoes either the classic neutral concerted reductive elimination to produce α-pyridones, or the ionic stepwise pathway to produce cyclic imidates.
α-Pyridones and α-pyrones are ubiquitous structural motifs found in natural products and biologically active small molecules. Transition metal-catalyzed vinylic C–H annulation of acrylic amides or acrylic acids with alkynes has recently emerged as one of the most powerful tools for their synthesis. In 2009, Miura and co-workers described an early example of Rh-catalyzed oxidative coupling of substituted acrylic acids with alkynes using Ag₂CO₃ as the oxidant, affording α-pyrones. Subsequently, the groups of Li and Rovis reported Rh-catalyzed vinylic C–H annulation of acrylic amides or acrylic acids with alkynes under elevated temperature using stoichiometric transition metal oxidants.

To advance these seminal works, various transition metal-catalyzed vinylic C–H annulation reactions with alkynes have been developed to prepare α-pyrindones or α-pyrones, including ones catalyzed by Rh²⁹, Ru²⁹, Co³⁰,³¹, Pd³⁴,³⁵, and Fe³⁷,³⁸ catalysts. Despite these advances, important challenges remain, including: (1) typically high reaction temperatures (100–120 °C); (2) stoichiometric transition metal oxidants such as Cu(OAc)₂ or AgOAc are generally required to regenerate catalysts; (3) a highly selective divergent synthesis of α-pyrindones and cyclic imidates (Fig. 1a, right side) from acrylamides is still lacking.

![Fig. 1 Rh-catalyzed vinylic C–H annulation of acrylamides with alkynes to afford α-pyrindone and cyclic imidate. a Rh-catalyzed vinylic C–H annulation under elevated temperature with stoichiometric transition metal oxidants. b Rh-catalyzed electrochemical vinylic C–H annulation of acrylamides with alkynes.](image)

**Table 1** Annulation optimization with acrylamide 1a and diphenylacetylene.

| Entry | 1(R) | Variation from standard conditions | Yield(%) of 3 | Yield(%) of 4 |
|-------|------|-----------------------------------|---------------|---------------|
| 1     | 1a (Ts) | None                              | 99(91)c       | n.d.          |
| 2     | 1a     | CH₂CN instead of MeOH             | 98            | n.d.          |
| 3     | 1a     | DMF instead of MeOH               | 20            | n.d.          |
| 4     | 1a     | CF₃CH₂OH instead of MeOH          | 17            | n.d.          |
| 5     | 1a     | HFIP instead of MeOH              | 9             | n.d.          |
| 6     | 1a     | NaOAc instead of n-Bu₄NOAc        | 86            | n.d.          |
| 7     | 1a     | NaOPiv instead of n-Bu₄NOAc       | 82            | n.d.          |
| 8     | 1a     | No (Cp*RhCl₂)₂                     | n.d.          | n.d.          |
| 9     | 1a     | No electric current               | <5            | n.d.          |
| 10    | 1a     | IKA ElectraSyn 2.0                | 99(92)c       | n.d.          |
| 11    | 1a     | Graphite(+) II Pt(–)              | 91d           | n.d.          |
| 12    | 1a     | Graphite(+) II Graphite(–)        | 95d           | n.d.          |
| 13    | 1b (Ph) | None                              | <5            | 4b (95)c      |
| 14    | 1c (p-NO₂-C₆H₄) | None                              | <5            | 4c (86)c      |
| 15    | 1d (p-OMe-C₆H₄) | None                              | <5            | 4d (42)c      |

*Reaction conditions: 1a (0.3 mmol), 2a (0.2 mmol), (Cp*RhCl₂)₂ (4 mol%), n-Bu₄NOAc (3.0 equiv.) and MeOH (3 mL) in an undivided cell with two platinum electrodes (each 1.0 × 1.0 cm²), room temperature, 1.5 mA, 7 h.

Transformable yield.

*1a (0.3 mmol), 2a (0.2 mmol), (Cp*RhCl₂)₂ (4 mol%), n-Bu₄NOAc (3.0 equiv.) and MeOH (6 mL) in an undivided cell with two electrodes (each 3.0 × 0.8 cm²), room temperature, 1.5 mA, 7 h, n.d. not detected.
Electrochemical organic synthesis has received tremendous attention because electric current offers an environmentally benign alternative to conventional methods for oxidation and reduction of organic compounds, such as those involving chemical oxidants and reductants. Transition metal-catalyzed electrochemical arene C–H annulation with alkynes has been developed using catalysts including Co, Ru, Rh, and Cu. In contrast, electrochemical vinyl C–H annulation with alkynes is less studied. Recently, we reported an Ir-catalyzed electrochemical vinyl C–H annulation reaction of acrylic acids.
with internal alkynes, affording α-pyrones in good yields, but terminal alkynes are not tolerated. Subsequently, Ackermann and co-workers demonstrated Ru-catalyzed electrochemical vinylic C–H annulation of acrylamides with symmetric internal alkynes at elevated temperature (140 °C). Herein, we report an Rh(III)-catalyzed electrochemical vinylic C–H annulation with alkynes in an undivided cell under mild reaction conditions. Importantly, divergent syntheses of α-pyrones and cyclic imidates are achieved by varying the N-substituent of the acrylamides. Furthermore, terminal alkynes are well tolerated in this Rh-catalyzed electrochemical vinylic C–H annulation (Fig. 1b). We also probed the reaction mechanism by carrying out cyclic voltammetric analysis and kinetic isotopic experiments. Density functional theory (DFT) calculations elucidated origins of substituent-controlled chemoselectivity. The sequential C–H activation and alkyn insertion under rhodium catalysis leads to the seven-membered ring vinyl-rhodium intermediate. This intermediate undergoes either the classic neutral concerted reductive elimination to produce pyridones, or the ionic stepwise pathway to produce cyclic imidates. The electronic nature of the N-substituent has exactly the reversal effect on the rates of neutral concerted and ionic stepwise reductive elimination pathways, which switches the chemoselectivity.

**Results**

**Optimization studies.** Initially, we probed various reaction conditions using 2-methylacrylamide (1a) and diphenylacetylene (2a) as reaction partners in an undivided cell (Table 1 and Supplementary Tables 1–7). To our delight, using (Cp*RhCl)2 as the precatalyst, n-Bu4NOAc as the electrolyte, and MeOH as the solvent in an undivided cell with two platinum electrodes under constant-current electrolysis at 1.5 mA for seven hours at 60 °C, cyclic imidate 3a can be obtained in 91% isolated yield (Table 1, entry 1). Acetonitrile as solvent affords a similar yield, while yield diminishes significantly when other solvents are used (entries 2–5). Other electrolytes such as NaOAc and NaOPiv result in slightly lower yields (entries 6 and 7). Control experiments show that no significant amount of annulation product is produced in the absence of complex 10 (Supplementary Tables 1–7).
the absence of the catalyst or electric current (entries 8 and 9). To our delight, 92% isolated yield is obtained when the reaction is carried out with IKA ElectraSyn 2.0 at room temperature (entry 10)\textsuperscript{78}. Furthermore, changing the electrode material caused a small decrease in yield (entries 11 and 12). Interestingly, switching to the synthesis of α-pyrindones instead of cyclic imidates can be achieved by simply changing the $N$-substitution of acrylamides (entries 13–15). α-Pyrindone 4b can be obtained in 95% isolated yield when $N$-phenyl acrylamide 1b is used (entry 13). Other $N$-aryl groups afford lower yields with good selectivity of α-pyrindones versus cyclic imidates (entries 14 and 15).

**Scope of cyclic imidates.** With the optimized reaction conditions in hand, we investigated the generality of this electrochemical C–H annulation. As shown in Fig. 2a, various acrylamides substituted with alkyl, ester, ether, aroyl, fluoro, and bromo groups are well tolerated, affording the corresponding cyclic imidates in good to excellent yields (3a, 6a–6r). Unfortunately, \(\beta\)-substituted substrate like cinnamide-derived acrylamides give lower yields, which could be due to the steric effects (see Supplementary information for more details). A variety of alkynes react well, including diarylacetylenes (7a–7i) and dialkyacylcylenes (7m–7o). With unsymmetrical alkynes, regioselectivity is governed by arene electronics. For example, moderate regioselectivity is achieved with \(n\)-butyl phenyl acetylene (7p).

In contrast, excellent regioselectivities are obtained when electron-deficient acrylamides are employed (7q and 7r). In addition, excellent regioselectivities and yields are accomplished using terminal alkynes, with the alkyl or aryl groups oriented proximal to the oxygen heteroatom in the product (7s–7x). (As a reminder, terminal alkynes are not tolerated in the aforementioned Ir-catalyzed electrochemical C–H annulation\textsuperscript{76}) Furthermore, the structures of 3a, 6c, 6o, 7r, and 7s were unambiguously verified by X-ray analysis. Finally, we demonstrated the preparative utility of this Rh-catalyzed electrochemical C–H annulation reaction by running a reaction containing 6.0 mmol of substrate 1a and 4.0 mmol of substrate 2a to afford cyclic imidate 3a in 86% yield, which can be further converted into α-pyrone 3aa (Fig. 2b).

![Fig. 6 Cyclic voltammetric study](cyclic_voltammograms_recorded_on_a_Pt_electrode_area_0.03_cm^2_with_a_scan_rate_of_100_mV_s^-1_.a_MeCN_containing_0.1_M_n-BuNPF_6_b_MeCN_containing_0.1_M_n-BuNPF_6_after_addition_of_4_mM_1a_c_MeCN_containing_0.1_M_n-BuNPF_6_after_addition_of_4_mM_10_d_MeCN_containing_0.1_M_n-BuNPF_6_after_addition_of_4_mM_2a_e_MeCN_containing_0.1_M_n-BuNPF_6_after_addition_of_4_mM_complex(Cp^*RhCl)_{2} f_MeCN_containing_0.1_M_n-BuNPF_6_after_addition_of_4_mM_2a.)

**Fig. 7 DFT calculations with 1a substrate.** DFT-computed free energy changes of competing reductive elimination pathways from seven-membered ring vinyl-rhodium intermediate when $N$-tosyl acrylamide 1a was employed as substrate.
**Discussion**

A series of experiments were carried out to elucidate the mechanism of this electrochemical C–H annulation reaction. First, acrylamide 1a was subjected to the electrochemical C–H annihilation reaction conditions in CH$_3$OD in the absence of an alkylene. Significant H/D exchange was observed, indicating that the putative C–H activation step is reversible (Fig. 4a). A kinetic isotope effect (KIE) value was determined by comparing parallel experiments using acrylamide 5e and corresponding deuterated substrate 5e–d$_4$ (Fig. 4b). A KIE value of 1.4 was observed (see Supplementary information for details). In addition, we executed the stoichiometric reaction of acrylamides, diphenylacetylene 2a, and (Cp*RhCl)$_2$ in the absence of electric current. To our delight, the rhodium sandwich complexes 10 and 11 were obtained in good yield, with the corresponding cyclic imidate as a neutral 14 ligand. Their structures were unambiguously confirmed by X-ray analysis (Fig. 5a). Upon anodic oxidation, the product 3a is released from 10, and is a coordinatively saturated, 18-electron complex (Fig. 5b). Additionally, 3a is obtained in good yield when a catalytic amount of 10 is employed, which suggests that 10 is a competent intermediate and catalyst in this electrochemical C–H annulation (Fig. 5c).

Complex 10 in 0.1 M solution of n-Bu$_4$NPF$_6$ in MeCN exhibits the first oxidation peak at 0.70 V versus saturated calomel electrode (curve d, Fig. 6), which is significantly lower than the oxidation potentials for the oxidation of other components in the reaction system (Fig. 6). This supports the hypothesis that the role of anodic oxidation is to oxidize a diene-Rh(I) complex to an active Rh(III) species with concomitant release of the product.

We next explored the reaction mechanism and the origins of substrate-controlled chemoselectivity through DFT calculations (see Supplementary information and Supplementary Data 1 for more details). From the active catalyst Cp*Rh(OAc)$_2$, sequential vinyl C–H activation of N-tosyl acrylamide 1a and diphenylacetylene insertion generate the seven-membered ring vinyl–rhodium intermediate int1 (Supplementary Fig. 14 and Fig. 7). Int1 can undergo competing reductive eliminations to form either the α-pyridone product or cyclic imidate (Fig. 7). The classic neutral concerted reductive elimination (red pathway) occurs through the three-membered ring transition state TS2, generating the α-pyridone product-coordinated complex int3. This neutral concerted reductive elimination requires an insurmountable barrier of 31.6 kcal/mol, which is unfeasible under the experimental conditions. Alternatively, we found that the ionic stepwise pathway (black pathway) can be operative and produce the cyclic imidate product. This ionic stepwise pathway, discovered by Hong group in similar transformation under ruthenium catalysis, initiates

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**Fig. 8 DFT calculations with 1b substrate.** DFT-computed free energy changes of competing reductive elimination pathways from seven-membered ring vinyl–rhodium intermediate int10 when N-phenyl acrylamide 1b was employed as substrate.

**Scope of α-pyridones.** We also examined the reactivity of a series of substituted acrylamides and alkynes for the synthesis of α-pyridones (Fig. 3). Acrylamides bearing a variety of functional groups such as alkyl, ester, ether, and aryl are well tolerated under the standard reaction conditions, affording α-pyridones in moderate to good yields (4b, 9a–9l).
through a heterolytic cleavage of the rhodium-nitrogen bond via TS5 with the assistant of methanol to generate the zwitterionic intermediate int6. From int6, methanol dissociates to generate int7, subsequent facile C–O bond formation through TS8 (IRC conformation of TS8 is included in the Supplementary information) produces int9. The zwitterionic species int7 also has the possibility for rhodium-oxygen bond formation via TS10 (labeled in purple), but requiring a higher barrier as compared to the C–O bond formation. Comparing the free energy barriers of the two competing pathways, the ionic stepwise reductive elimination is more favorable by 7.7 kcal/mol (TS2 vs. TS5), which is consistent with the experimental chemoselectivity favoring cyclic imidate when N-tosyl acrylamide is employed.

The DFT-computed free energy changes of the same competing reductive elimination pathways for the N-phenyl acrylamide 1b substrate is shown in Fig. 8. From N-phenyl acrylamide 1b, the sequential vinyl C–H activation and diphenylacetylene insertion generate the seven-membered ring vinyl-rhodium intermediate int12 (Supplementary Fig. 15). This intermediate can undergo the classic neutral concerted reductive elimination pathway via TS13 (red pathway), with a barrier of 21.9 kcal/mol. The alternative ionic stepwise pathway through TS16 (IRC conformation of TS16 is included in the Supplementary information) is significantly less favorable, due to the unstable zwitterionic species int18. Comparing to the tosyl substituent, the phenyl substituent significantly lowers the barrier of neutral concerted pathway while increases the barrier of ionic stepwise pathway, which results in the reversal chemoselectivity. For the ionic stepwise pathway, the electron-donating tosyl substituent weakens the rhodium-nitrogen bond of int1, which favors its heterolytic cleavage and the generation of the zwitterionic intermediate int7 (Fig. 7). The same process is endergonic by 27.3 kcal/mol for the N-phenyl substituted case (int12 to int18, Fig. 8). This electronic effect is further supported by the computed rhodium-nitrogen bond dissociation energies and additional Hammett analysis of the N-substitution (Supplementary Fig. 19). For the neutral concerted pathway, our distortion/interaction analysis revealed the distortion-controlled origins of the substituent effect (Supplementary Fig. 18). The phenyl substituent induces geometric change of the seven-membered rhodacyclic in int12, leading to the predistortion towards the neutral concerted reductive elimination transition state TS13. This predistortion is reflected in the highlighted distance of the forming C–N bond in the seven-membered ring intermediates (2.71 Å in int12, Fig. 8; 2.84 Å in int1, Fig. 7). These insights provide a mechanistic basis for rational reaction designs in related transformations.

Based on our mechanistic studies, we propose a plausible catalytic cycle as shown in Fig. 9. Initially, C–H activation takes place to afford a cyclometallated Rh(III) intermediate B, following ligand exchange to deliver complex C. Next, migratory alkyne insertion results in the seven-membered rhodium complex D82,83, which undergoes ionic stepwise or neutral concerted reductive elimination to give Rh(I) complex 10 or E. Intermediate 10 or E is a coordinately saturated, 18-electron complex. Upon anodic oxidation, the product is released from 10 or E, and complex A is regenerated.

In summary, we have developed an electrochemical method for the Rh(III)-catalyzed vinylic C–H annulation of acrylamides with alkynes. Owing to the robustness of this electrochemical C–H annulation, the reaction can be operated with IKA ElectraSyn 2.0 at room temperature, affording cyclic imidates with good to excellent yields. Additionally, divergent syntheses of a-pyridones and cyclic imidates are realized by simply switching the N-substitution of acrylamides. Furthermore, excellent regioselectivities are achieved with unsymmetrical alkynes, including terminal alkynes. Mechanistic and DFT studies combined to provide a rationale for the chemoselectivity switch and a basis for future reaction design in related transformations.
Methods

General procedure for the electrocatalysis. The electrocatalysis was carried out in an IKA ElectraSyn 2.0 equipped with two platinum electrodes (each 0.8 × 3.0 cm²). Acrylicamide (0.3 mmol, 1.5 equiv.), alkylene (0.2 mmol, 1.0 equiv.), n-BuNOAc (0.6 mmol, 3.0 equiv.) and (Cp*RhCl₂)₂ (40 mol%, 99 wt%) were dissolved in MeOH (6.0 mL). Electrocatalysis was performed at room temperature with a constant current of 1.5 mA maintained for 7–12 h (2.0–3.4 V/mol). After the reaction, the mixture was concentrated in vacuo. The resulting material was purified by silica gel flash chromatography to give the annulation product.

More experimental procedures and photographic guide for electrocatalytic C–H annulation are provided in the Supplementary information.

Data availability

The X-ray crystallographic coordinates for structures reported in this article have been deposited with the Cambridge Crystallographic Data Centre (CCDC) number CCDC 1967777 (7a), CCDC 1967778 (II), CCDC 1967779 (6c), CCDC 1967780 (10), CCDC 1967781 (3a), CCDC 1967782 (6e), CCDC 1967783 (7a). The data can be obtained free of charge from The Cambridge Crystallographic Data Centre [http://www.ccdc.cam.ac.uk/data_request cif]. The data supporting the findings of this study are available within the article and its Supplementary information files. Any further relevant data are available from the authors on request.

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Author contributions
Y.-K.X and Q.-L.Y discovered the reaction. X.-R.C and S.-Q.Z performed the DFT calculation. H.-G.M., X.H., and T.-S.M. directed the project. Y.-K.X, X.H., and T.-S.M. wrote the manuscript with input from all authors. All authors analyzed the results and commented on the manuscript.

Competing interests
The authors declare no competing interests.

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