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Enantioselective construction of cyclic quaternary stereocenters via dinuclear copper catalyzed asymmetric [3 + 2] propargylation/annulation

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While copper-catalyzed asymmetric propargylic substitution has emerged as a versatile tool for constructing chiral propargylic frameworks, its application in forging cyclic chiral quaternary carbon centers remains a significant synthetic challenge. This work demonstrates a dinuclear copper-catalyzed asymmetric [3 + 2] annulation strategy between tertiary propargyl carbonates and diverse C,O-bisnucleophiles under mild conditions. The protocol enables efficient synthesis of chiral dihydrofurans featuring cyclic quaternary stereocenters with broad substrate compatibility. The stereochemical control may arise from the unique coordination geometry of dinuclear copper-allenylidene intermediates, which spatially aligns the electrophilic site within the chiral ligand environment. This spatial arrangement overcomes inherent steric challenges in the stereoselective formation of quaternary carbons bearing dual alkyl substituents, offering mechanistic insights into cooperative dinuclear catalysis for asymmetric transformations.

The asymmetric catalytic synthesis of chiral molecules bearing all-carbon quaternary stereocenters is a longstanding challenge for the synthetic community (Fig. 1a)[1–6]. Since the pioneering studies from van Maarseveen[7] and Nishibayashi[8] groups in 2008, respectively, Cu-catalyzed asymmetric propargylic substitution has been developed as an important method for the construction of chiral propargylic skeletons[9–16]. In particular, catalytic sequential propargylation/cycloisomerization reactions of propargylic esters, used as C3- or C2-bis-electrophiles, with various bis-nucleophiles constitute a powerful strategy for the synthesis of a diverse range of chiral cyclic frameworks[17–32]. However, Cu-catalyzed asymmetric propargylic substitution are largely limited to the substrates of secondary propargylic esters and only substrates with both an aryl and an oxygen-containing moiety at the prochiral carbon of the resulting Cu–allenylidene intermediates gave good results[33–39]. Very recently, Zhou[40,41] and coworkers developed sterically confined PYBOX ligands with a bulky C4 shielding group and relaying groups, allowing highly enantioselective Cu-catalyzed propargylic amination of simple ketone-derived propargylic carbonates.

Despite these advances, the development of enantioselective Cu-catalyzed propargylation/annulation for rapid construction of cyclic frameworks with a chiral quaternary carbon center is still challenging and appealing[42–44]. For example, dihydrofuran derivatives are a class of naturally occurring bioactive compounds[45–53] and Cu-catalyzed sequential propargylation/cycloisomerization reactions of propargylic esters with 1,3-C,O-bis-nucleophiles provides an

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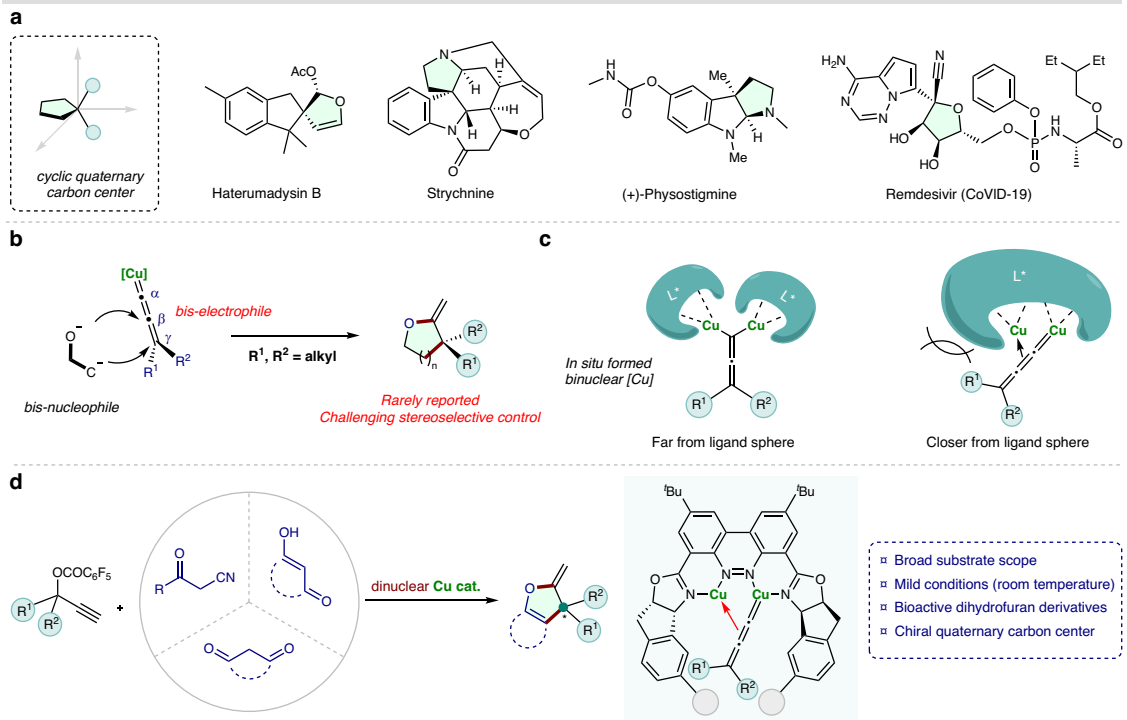

Fig. 1 | Asymmetric [3 + 2] annulation of propargylic esters to chiral dihydrofuran derivatives with cyclic quaternary stereocenters. a Selected examples of important molecules with cyclic chiral quaternary carbon center. **b** Cu-catalyzed propargylation/cycloisomerization reactions. **c** Proposed binuclear Cu-allenylidene intermediates. **d** This work: dinuclear copper-catalyzed [3 + 2] annulation of tertiary propargylic esters with a diverse set of C,O bis-nucleophiles.

efficient strategy to access these important cyclic molecules[54–56]. Nevertheless, the produced chiral dihydrofuran derivatives bearing an exocyclic double bond may easily undergo isomerization to furans[57], due to the lack of a cyclic chiral quaternary carbon center. To the best of our knowledge, the synthesis of dihydrofuran derivatives featuring a chiral quaternary carbon center remains largely unexplored using problematic dialkyl propargylic alcohol derivatives, probably due to the poor chiral discrimination between two alkyl groups and the lack of directing factors in the resulting Cu–allenylidene intermediates (Fig. 1b).

Over the past decade, in situ generated binuclear copper species have been frequently implicated as active catalysts in copper-catalyzed asymmetric propargylic substitution reactions, with bridged dicopper allenylidene complexes commonly proposed as the key reactive intermediates[24,34,42,43,58–64]. Recently, we have disclosed the successful development of a series of binuclear copper catalysts, supported by chiral benzo[*c*]cinnoline dioxazoline frameworks, and their applications in catalytic asymmetric propargylic substitution reactions[65,66]. According to the proposed mechanism, the binuclear Cu core can play a bifunctional role in the coordination with acetylide and allenylidene species via a σ and a π interactions. Considering the potential dinuclear synergistic effect[67–71], we envisioned that this type of coordination mode may bring the electrophilic site of the copper-allenylidene intermediates close to the chiral pocket, making it more prone to achieve a stereocontrolled formation of the quaternary carbon center when the problematic and challenging dialkyl propargylic alcohol derivatives are applied (Fig. 1c).

Herein, we report a strategy for the synthesis of enantioenriched dihydrofuran derivatives with a chiral quaternary carbon center via a dinuclear copper-catalyzed [3 + 2] annulation of tertiary propargylic esters with a diverse set of C,O bis-nucleophiles (Fig. 1d). The methodology is found to be quite general with respect to the substrate scope, since benzoylacetonitrile, 4-hydroxy-2-quinolinone, 4-hydroxy-1-methyl-2-quinolinone, 4-hydroxycoumarin, 4-hydroxythiocoumarin, alkyl and aryl-substituted 4,6-dihydroxypyrimidine, and multi-substituted 2,4-dihydroxypyridines, as well as dimedone, are found amenable to the catalysis, leading to the formation of various chiral dihydrofuran derivatives in good yields with good to high enantioselectivities. Notably, this work further demonstrates that the binuclear Cu catalysis can be used as an efficient strategy to solve the challenges in the asymmetric construction of chiral quaternary carbon centers via propargylic substitution of simple ketone-derived propargylic alcohol derivatives.

Results

Reaction discovery

At the initial studies, a tertiary propargyl carbonate (**1a**) was chosen as the model substrate in the [3 + 2] reaction with benzoylacetonitrile (**2a**), and a variety of Cu complexes of chiral nitrogen ligands were examined as the catalysts (Fig. 2). A careful survey of the reaction parameters using the binuclear copper catalyst $\mathbf{C_1}$ revealed that the reaction proceeded well in CF_3CH_2OH at room temperature for 24 h, affording the desired product **3** in 66% yield with 67% *ee* (see the Supplementary Information, Table S1–S5). Under the otherwise identical reaction conditions, several other bicopper catalysts $\mathbf{C_2}$-$\mathbf{C_9}$ with different substituents on the oxazolyl units or on the cinnoline backbone of the ligands were further investigated. The reaction using catalyst $\mathbf{C_2}$, containing four more phenyl substituents on the oxazolyl units, resulted in the formation of **3** with a slightly lower yield and *ee* value. Using catalyst $\mathbf{C_3}$ with the ligand derived from 2-aminoindanol, the reaction gave the desired product **3** with 60% *ee*. Further increasing the steric hindrance of the oxazoline units led to a boost of the *ee* up to 91% using catalyst $\mathbf{C_9}$. In a comparative study, chiral Pybox ligands (**L1** and **L2**) were also examined together with CuI in the model reaction. Unfortunately, only very low *ee* values of the product were obtained in these cases. The reactions using some privileged bidentate chiral

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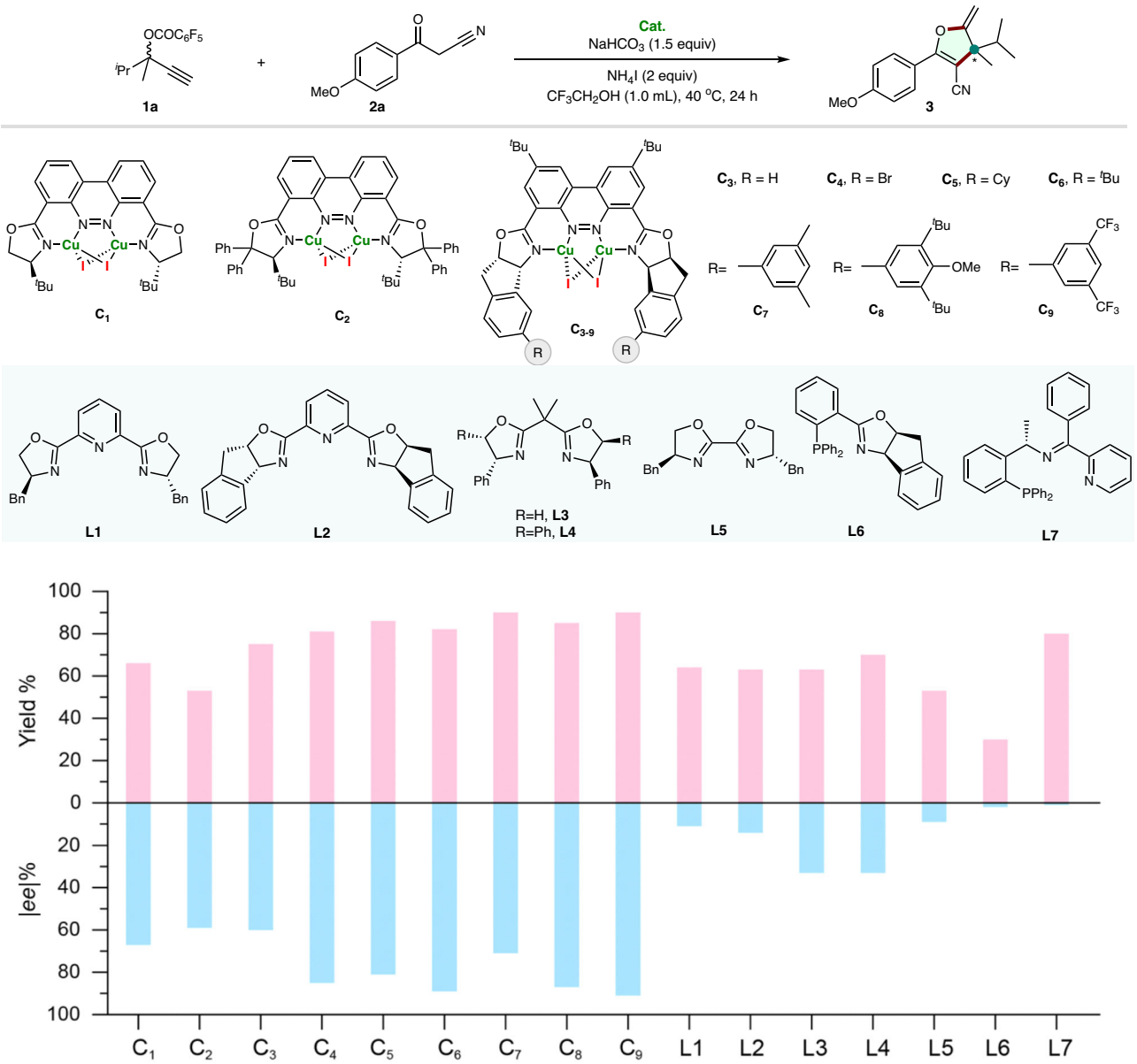

Fig. 2 | Survey of the catalysts for the asymmetric [3 + 2] annulation. Reaction conditions: **1a** (0.1 mmol), **2a** (0.2 mmol), $NaHCO_3$ (1.5 equiv), $\mathbf{C_X}$ (2.0 mol%) or CuI (4 mol %)/**L1**-**L7** (4 mol%), CF_3CH_2OH (1 mL), NH_4I (2 equiv), 40 °C, 24 h. NMR yields. The *ee* values were determined by HPLC on a chiral stationary phase.

ligands, including bisoxazoline ligands **L3**-**L5**, Phox **L6** and BINAP, only afforded product **3** with low to moderate *ee* values. Upon further evaluation of the privileged chiral P,N,N ligand **L7** developed by Hu, it was observed that the annulation of tertiary propargyl carbonates proceeded smoothly with low enantioselectivity. These survey results of ligands **L1**-**L7** contrast strikingly with those using the dinuclear copper catalysts, highlighting the effective catalytic performance of the dinuclear Cu catalysts in the current reaction.

Substrate Scope

Under the optimized reaction conditions, the scope of the benzoylacetonitriles **2** was first explored in the reactions with **1a** using $\mathbf{C_9}$ as the catalyst, and the results were summarized in Fig. 3a. To our delight, this catalytic system tolerated quite well with various benzoylacetonitriles bearing electronic donating *para*-substituents (-OMe, -Me, -^{i}Pr), furnishing the corresponding target products **3**-**6** in good yields with excellent enantioselectivities (87-91% *ee*). In addition, the substrates bearing electron-withdrawing groups (−F, −Cl, −Br, $-CF_3$, −CN, and $-NO_2$) at the *para*-position of the aryl ring delivered the desired products **7**–**12** with slightly lower enantioselectivities (65–81% *ee*), which may be attributed to the reduced nucleophilicity of the electron-deficient nucleophiles. The absolute configuration of **9** was determined as (*S*) by X-ray crystallographic studies (Fig. S8 and Table S6). Substrates with a *meta*-methoxy or *meta*-fluorine substituted aryl ring were also amenable to the reaction, affording the corresponding products **13** and **14** in good yields (94% and 75%) with high *ee* values (88% and 80%). The reactions of the substrates with an *ortho*-chloro, *ortho*-methyl or *ortho*-methoxy substituent on the aryl ring of the benzoylacetonitriles afforded the corresponding products **15**-**17** in good yields (79-81%) with good enantioselectivities (76-89% *ee*). The system was further demonstrated to be effective for the reaction of a poly-substituted benzoylacetonitrile, leading to the corresponding product **18** in 79% yield with 87% *ee*. Furthermore, aroylacetonitrile substrates with a *β*-naphthyl, *α*-furyl, or *α*-thienyl group were also amenable to the reaction, giving the corresponding products **19**-**21** in 66-94% yields with 84-88% *ee*.

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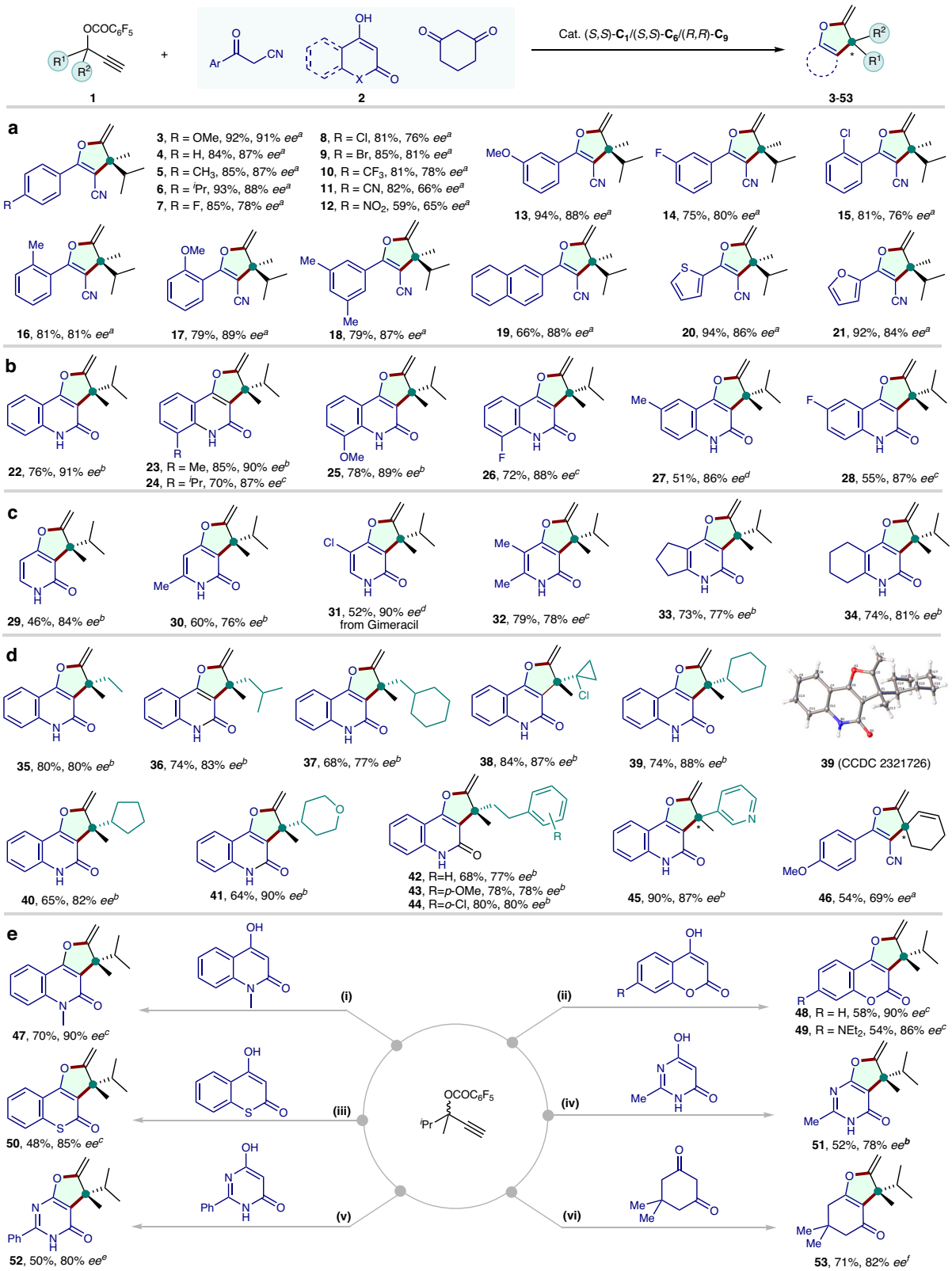

Fig. 3 | Substrate scope. a Substrate scope of the benzoylacetonitrile and its analogues. **b** Substrate scope of the quinolinones. **c** Substrate scope of the 2,4-dihydroxypyridine and its analogues. **d** Substrate scope of the tertiary propargylic esters. **e** Various C,O bis-nucleophiles. [a]General conditions: **1** (0.1 mmol), bis-nucleophile (0.2 mmol), $NaHCO_3$ (1.5 equiv), (*R, R*)-**C_9** (2.0 mol%), CF_3CH_2OH (1 mL), NH_4I (2 equiv), 40 °C, 24 h. [b] ^{t}BuOLi (1 equiv), (*S, S*)-**C_1** (4.0 mol%), CF_3CH_2OH (1 mL), NH_4I (20 mol%), rt, 24 h. [c] ^{t}BuOLi (1 equiv), (*S, S*)-**C_6** (4.0 mol%), CF_3CH_2OH (1 mL), NH_4I (20 mol%), rt, 24 h. [d] 4-methylmorpholine (1 equiv), (*S, S*)-**C_1** (4.0 mol%), CF_3CH_2OH (1 mL), NH_4I (20 mol%), rt, 24 h. [e] ^{t}BuOLi (1 equiv), (*S, S*)-**C_1** (4.0 mol%), CF_3CH_2OH (1 mL), rt, 24 h. [f] Na_2CO_3 (2 equiv), (*S, S*)-**C_1** (2.0 mol%), CH_3OH (1 mL), rt, 24 h.

Notably, the methodology was applicable to the reaction of **1a** with other types of 1,3-C,O-bis-nucleophiles such as quinoline-2,4(1H,3H)-diones (Fig. 3b). Various quinolin-diones bearing either electronic donating (-Me, -^{i}Pr, and -OMe) or withdrawing (-F) groups at the *8*-position of the quinolindiones were tolerated quite well in the reactions, resulting in formation of the target products **22-26** in good yields with excellent enantioselectivities (87-91% *ee*). The *6*-methyl and *6*-fluorine substituted quinoline-2,4(1H,3H)-diones were also amenable to the reaction, affording the corresponding products **27** and **28** with high *ee* values (86% and 87%), albeit in moderate yields (51% and 55%). Notably, pyridyl-derived binucleophiles such as 2,4-dihydroxypyridine and its analogues were also applicable in the reaction using 4.0 mol% $\mathbf{C_1}$ as the catalyst (Fig. 3c). While the reaction of 2,4-dihydroxypyridine with **1a** provided the corresponding product **29** in 46% yield with 84% *ee*, the reaction of *ortho*-methyl substituted pyridine gave product **30** in 60% yield with moderate enantioselectivity (76% *ee*). It was worth mentioning that the reaction using Gimeracil, a component in an anticancer therapy, afforded the corresponding product **31** in 52% yield with 90% *ee*. For the reactions of other alkyl substituted pyridine substrates, the corresponding cycloadducts **32-34** were obtained in 73-79% yields with 77-81% *ee*.

Encouraged by the efficiency of the binuclear Cu catalysts, we further evaluated the tertiary propargylic substrates in this asymmetric annulation with **2**, as a quaternary stereogenic center can be installed along with the creation of the cyclic frameworks. To our delight, the reactions of propargylic carbonates derived from aliphatic ketones such as 2-butanone, 4-methyl-2-pentanone and cyclohexylacetone proceeded smoothly to give the corresponding cycloaddition products **35-37** bearing a quaternary chiral carbon, respectively, in 68-80% yields with 77-83% *ee* (Fig. 3d). Notably, using a tertiary propargyl carbonate with a methyl and an ethyl group, the reaction still afforded the desired cyclic product **35** in 80% yield with 80% *ee*, indicating the excellent chiral discrimination of the dinuclear Cu catalyst between these similar alkyl groups. This may arise from the unsymmetric coordination mode adopted by the dinuclear copper complex with allenylidene unit. Such coordination likely positions the electrophilic site of allenylidene unit in close proximity to the chiral environment created by the ligands, thereby enhancing stereocontrol even in cases involving minimally differentiated substituents. Branched propargylic carbonates bearing chlorocyclopropyl, cyclohexyl, cyclopentyl and tetrahydropyranyl moieties were also viable substrates, giving the corresponding cyclization products **38-41** in 64–84% yields with 82–90% *ee*. The absolute configuration of **39** was determined as (*R*) by X-ray crystallographic studies (Fig. S9 and Table S7), which is consistent with the use of the dinuclear copper catalyst (*S, S*)-$\mathbf{C_1}$. In addition, various benzylacetone-derived propargylic carbonates reacted with 4-hydroxy-2-quinolinone smoothly under the standard conditions to afford products **42-44** in 68–80% yields with 77–80% *ee*, irrespective of the nature and position of the phenyl substituent. Other types of tertiary propargylic substrates were also examined. To our delight, the reaction of substrates bearing 3-pyridyl and methyl groups with 4-hydroxy-2-quinolone afforded the desired product **45** in 90% yield with 87% *ee*. In addition, cyclic tertiary propargylic substrates also underwent the annulation smoothly, delivering the corresponding cycloaddition product **46** in 54% yield with 69% *ee*. Moreover, 4-hydroxy-1-methyl-2-quinolinone was also a compatible bis-nucleophile for the reaction, leading to the desired product **47** in 70% yield with 90% *ee* (Fig. 3e-i). Additionally, 4-hydroxy-2-chromenones were also surveyed in this annulation to further explore the substrate generality, and the desired products **48** and **49** were generated in 54-58% yields with high *ee* values (90% and 86%, respectively) (Fig. 3e-ii). 4-hydroxy-2*H*-thiochromen-2-one was also a compatible bis-nucleophile for the reaction, leading to the desired product **50** in 48% yield with 85% *ee* (Fig. 3e-iii). 4,6-dihydroxy-2-phenylpyrimidine and 4,6-dihydroxy-2-methylpyrimidine were also found as suitable nucleophiles and the reactions provided the corresponding products **51** and **52** in 50-52% yields with 78-80% *ee* (Figs. 3e-iv and 3e-v). It was worth mentioning that the reaction using dimedone afforded the corresponding product **53** in 71% yield with 82% *ee* (Fig. 3e-vi). These findings highlight the potential of the present binuclear copper catalysts in enabling cascade propargylic substitution–cyclization reactions of challenging tertiary propargylic esters, offering an efficient approach to access valuable tricyclic scaffolds bearing a quaternary stereogenic center and an exocyclic double bond.

Synthetic applications

In order to show the practical utility of this methodology, a gram-scale reaction of tertiary propargyl carbonate **1a** and 4-hydroxy-2-quinolinone was performed under the standard conditions (Fig. 4-i), and the desired product **22** was isolated in 78% yield (1.0 g) with excellent enantioselectivity (90% *ee*). Subsequent investigations were carried out to demonstrate the synthetic utilities of product **22**. By treatment with Tf_2O or $POCl_3$, **22** was transformed into **54** or **55**, respectively, in high yields with excellent *ee* values (Fig. 4-ii and 4-iii). Amide reduction of **22** with $LiAlH_4$, delivered quinoline derivative **56** in 46% yield, which is also a useful structural motif occurring in many natural products (Fig. 4-iv). The reaction of **22** with Lawesson's reagent gave thioamide **57** in 68% yield with 90% *ee* (Fig. 4-v). Intriguingly, regioselective bromination of **22** gave rise to the alkenyl rather than aryl brominated product **58** in 68% yield (Fig. 4-vi). Treatment of **22** with Togni-I and $TMSN_3$ using CuI/Pybox as catalyst afforded the product **59** in 64% yield with 90% *ee*, whose absolute configuration was unambiguously determined by the X-ray crystallographic analysis (Fig. 4-vii, Fig. S10 and Table S8). Reduction of **22** with H_2 using $Rh(PPh_3)_3Cl$ as the catalyst provided **60** in 98% yield with 90% *ee* (Fig. 4-viii). **60** was further reacted with $(Boc)_2O$ or BnBr to afford the *N*-Boc or *N*-Bn-substituted dihydrofuro [3,2-*c*] quinolinones **61** and **62** in good yields (85% and 73%, respectively). As a result of structural rigidity of the quaternary carbon moiety, the absolute configuration of the stereogenic center in **22** was retained over all these transformations.

To gain insight into the nature of the reactive intermediates involved in the binuclear copper catalysis, ESI-HRMS analysis was performed on the reaction mixture of tertiary propargyl carbonate (**1a**) and benzoylacetonitrile (**2a**). Distinct signals at m/z 767.2273 and 1367.2878 were observed, corresponding to the formation of a binuclear copper–acetylide complex derived from $\mathbf{C_1}$ and **1a**, and the complex of $\mathbf{C_9}$ with **1a**, respectively. Although the detailed structures of these two copper-acetylide species detected by HRMS are unknown, these results suggested that the catalytic intermediates featured by a binuclear Cu core may function throughout the catalytic cycle (Fig. 5a). Furthermore, a DFT computational study was carried out on the reaction of **1a** using catalyst $\mathbf{C_9}$ to evaluate the viability of the plausible coordination modes of the two Cu centers with the allenylidene moiety[65,66]. Associated with the elimination of $^-OCOC_6F_5$ moiety, distinct types of copper-allenylidene intermediates might be generated, such as an allenylidene α-carbon bridged binuclear Cu intermediate **C_9-INT II'**[24,34,42,43,58–64] or allenylidene α,β-bound Cu_2-intermediate **C_9-INT II**[65,66,72,73] (Fig. 5b). In allenylidene intermediate **C_9-INT II'** (Fig. 5b left, Fig. S4 and Data S1), the two alkyl groups on Cγ were on the plane perpendicular to the plane of the catalyst backbone and the electrophilic site Cγ is far from the chiral oxazoline units. Therefore, the nucleophiles can attack Cγ from both left and right sides, which may result in poor *ee* values. Conversely, detailed structural analysis of the binuclear Cu–allenylidene intermediate **C_9-II** revealed dihedral angles of −144° for N1–Cu1–Cu2–Cα and −156° for N1–Cu1–Cα–Cβ, which implies that the allene moiety is positioned below the plane of the catalyst backbone as a result of coordination with the $-OCOC_6F_5$ moiety (Fig. 5b right, Fig. S5 and Data S1). The surface distance projection color maps[74] shown in Fig. 5c provided direct perspectives on

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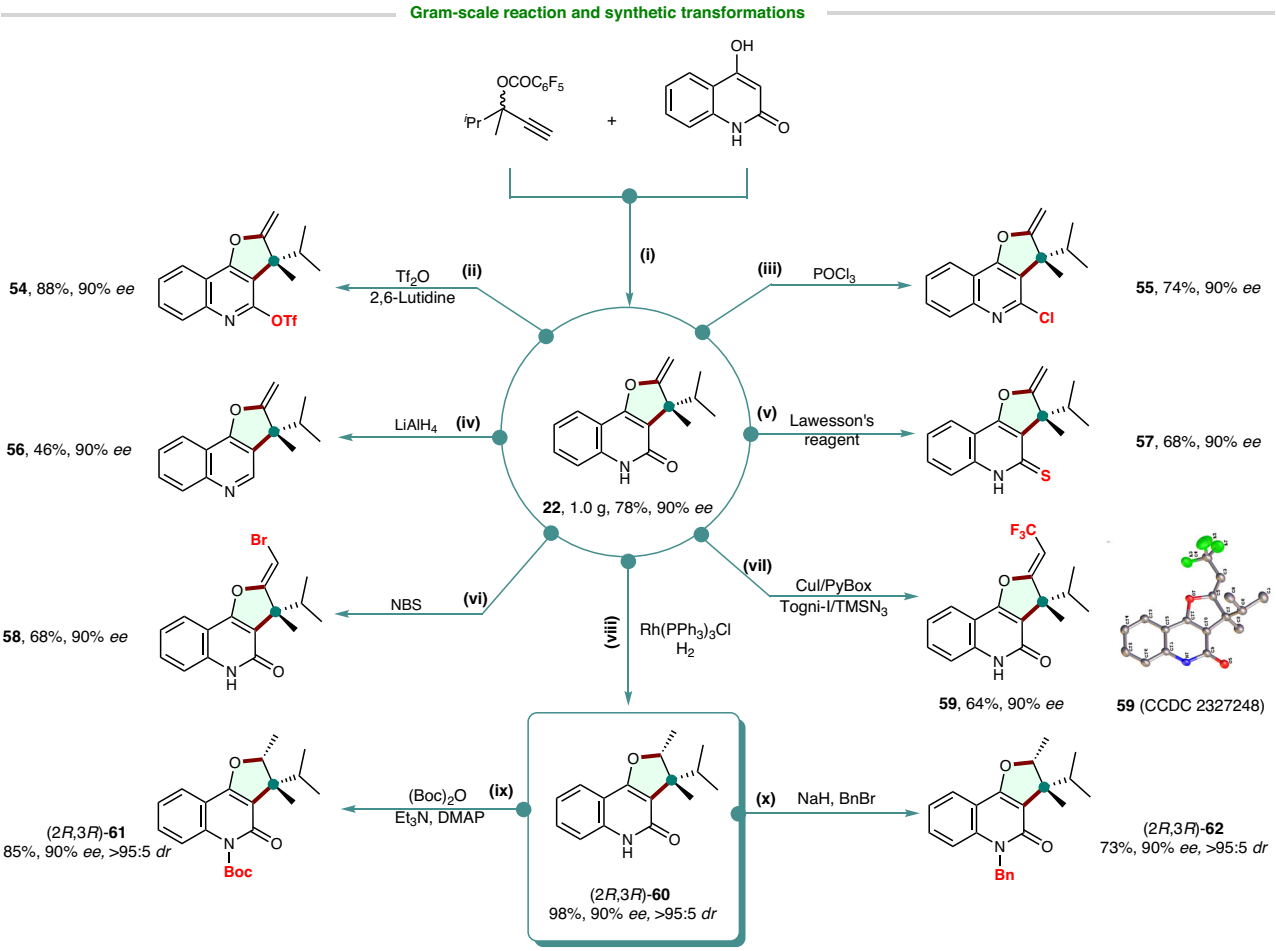

Fig. 4 | Gram-scale reaction and synthetic transformations. i Gram-scale synthesis. ii–x various synthetic transformations (For details, see the Supplementary Information, Fig. S2).

the distinct types of intermediates. For **INT C_9-II'**, the area around prochiral center is drawn in yellow (located at −2 Å) while those for the two chiral substituents of the ligand are in green (located at −4 Å), indicating that the prochiral center is located spatially relatively distal to the ligand and thus less influenced by the chiral pocket (Figs. 5c left and S6). On the other hand, the indenyl groups in binuclear Cu intermediate **INT C_9-II** occupy the upper-left and lower-right sections of the ligand plane. As a result of the steric repulsion of the $^{-}OCOC_6F_5$ moiety, the attack of the C,O-bis-nucleophile from the top is sterically hindered while the lower-right attack would be relatively less encumbered (Figs. 5c right and S7). Such an asymmetric coordination mode may provide a rationale for the stereoselectivity, as the dinuclear copper-allenylidene intermediate may position the electrophilic site closer to the chiral ligand environment, thereby facilitating effective stereoselective control over the quaternary carbon center. Therefore, we proposed a plausible catalytic cycle for the dinuclear copper-catalyzed asymmetric [3 + 2] propargylation/annulation (Fig. 5d). The catalytic cycle is initiated by activating the terminal alkyne of racemic tertiary propargyl carbonate **1** by the chiral dinuclear copper catalyst in the presence of a base. The corresponding alkynyl anion, which coordinates to the two Cu centers through both σ- and π-bonding interactions, forming the Cu-acetylide species **I**. The potential coordination of the iodide anion to the copper center in these cationic intermediates **I** cannot be conclusively excluded. The Cu-promoted elimination of the $-OCOC_6F_5$ group removes the stereochemical information at the C3 position, leading to the formation of a binuclear copper species **II**, in which an allenylidene ligand is coordinated to one copper atom and simultaneously binds in a π bond mode with the second copper center. Following this, a stereoselective nucleophilic attack by the C,O bis-nucleophile takes place, where the carbon atom preferentially attacks the γ-position of the allenylidene ligand, resulting in the formation of intermediate **III**. The elimination of $C_6F_5CO_2H$ from **III** by a base produces intermediate **IV**. Subsequently, an intramolecular nucleophilic attack by the oxygen atom on the β-carbon leads to the formation of intermediate **V** containing a dihydrofuran ring. Proton transfer between **V** and terminal alkyne substrate **1** yields the final product while regenerating intermediate **I**. Alternatively, protonation of intermediate **IV** followed by an intramolecular cyclization may also occur to deliver the final product.

Discussion

In summary, we have developed an efficient method for the asymmetric [3 + 2] annulation of tertiary propargylic esters with diverse C,O bis-nucleophiles using well-defined chiral dinuclear copper complexes as the catalysts. The reaction is featured by mild conditions, excellent regioselectivity and high stereoselectivity. The reaction exhibits broad substrate scope with respect to various C,O-bis-nucleophiles, including benzoylacetonitrile, quinolinone, 4-hydroxy-1-methyl-2-quinolinone, 4-hydroxycoumarin, 4-hydroxythiocoumarin, alkyl- and aryl-substituted 4,6-dihydroxypyrimidine, multisubstituted 2,4-dihydroxypyridines and dimedone. It should be highlighted that the bifunctional role of the binuclear Cu and its unique coordination mode might be the key to the success of the excellent chiral control of the quaternary chiral carbon center.

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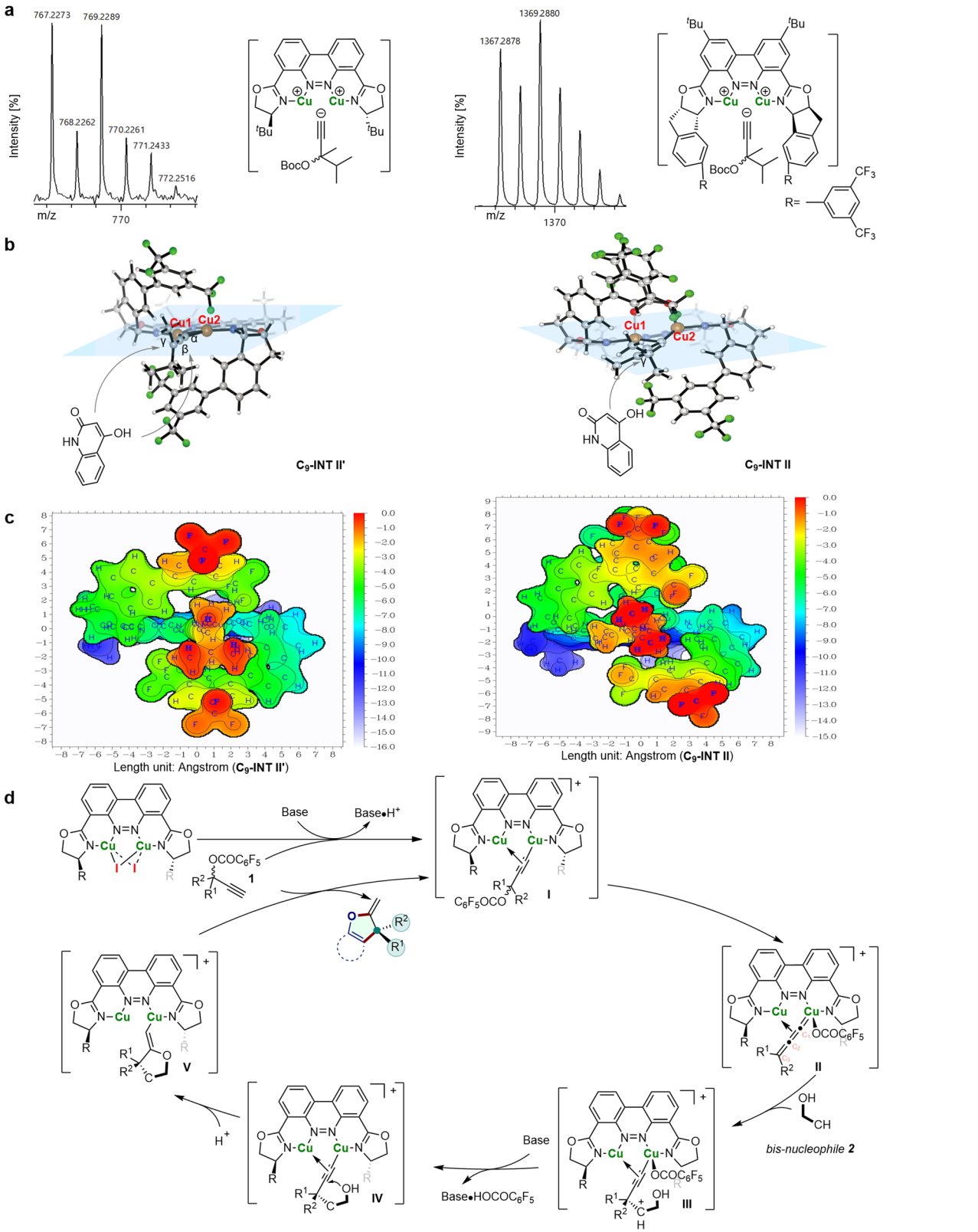

Fig. 5 | Mechanistic studies. a ESI-MS analysis of the reaction mixture under standard conditions. **b** Proposed transition state models. The blue shaded planes indicate the π-conjugated systems involved in the transition state geometry. **c** Surface distance projection maps of intermediates **INT II** and **INT II'**. **d** Proposed catalytic mechanism.

Methods

General procedure

A typical experimental procedure for the preparation of (*S*)−4-isopropyl-2-(4-methoxyphenyl)−4-methyl-5-methylene-4,5-dihydrofuran-3-carbonitrile (**3**) is described below. **C_9** (2.8 mg, 0.002 mmol, 2.0 mol%), NH_4I (29.0 mg, 2.0 equiv) and benzoylacetonitrile (35.1 mg, 0.20 mmol) were placed in a 10 mL Schlenk flask and a dry Ar atmosphere was established. Then, propargylic ester **1a** (30.6 mg, 0.1 mmol), $NaHCO_3$ (12.6 mg, 1.5 equiv) and CF_3CH_2OH (1 mL) were added, and the mixture was stirred at 40 °C for 24 h. The mixture was concentrated under reduced pressure

and the residue was purified by silica gel chromatography with n-hexane and EtOAc (n-hexane/EtOAc = 4/1-1/1) as eluent to give **3** as a yellow solid (24.9 mg, 92% yield, 91% *ee*).

Data availability

The data supporting the findings of this study are available within the article and Supplementary Information files, and are also available from the corresponding author upon request. Crystallographic data coordinates for structures reported in this article has been deposited at the Cambridge Crystallographic Data Center (CCDC), under deposition numbers CCDC 2457310 (product **9**), CCDC 2321726 (product **39**), and CCDC 2327248 (product **59**). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures/.

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L. S., Q. C. and X. W. directed the project and designed the experiments; L. S., Z. F., Q. C., P. L. and Y. L. performed all the experiments and analyzed all the data with X. W.; Z. F. performed all the computational studies and wrote the part of calculations. Q. C. and X. W. wrote the manuscript with contributions from all authors.

Competing interests

The authors declare no competing interests.

Additional information

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