Gold(I)-catalyzed intramolecular cyclization/intermolecular cycloaddition cascade as a fast track to polycarbo-cycles and mechanistic insights

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Metal carbene is an active synthetic intermediate, which has shown versatile applications in synthetic chemistry. Although a variety of catalytic methods have been disclosed for the generation of carbene species from different precursors, there is an increasing demand for the development of efficient and practical approaches for the in-situ formation of metal carbene intermediates with structural diversity and unrevealed reactivity. Herein we report a gold-catalyzed cascade protocol for the assembly of polycarbocyclic frameworks in high yields under mild reaction conditions. Mechanistic studies indicate that the unique β-aryl gold-carbene species, generated via gold-promoted 6-endo-dig diazo-yne cyclization, is the key intermediate in this reaction, followed by a [4 + 2]-cycloaddition with external alkenes. In comparison to the well-documented metal carbene cycloadditions, this carbene intermediate serves as a 4-C synthon in a cycloaddition reaction. A variety of elusive π-conjugated polycyclic hydrocarbons (CPHs) with multiple substituents are readily accessible from the initially generated products by a mild oxidation procedure.

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Reactive metal carbene species participate in a broad range of applications for the effective formation of C–C and C–heteroatom bonds in synthetic organic chemistry. The versatile reactivity of this species is mainly dependent on the choice of catalysts and the substituent(s) proximal to the carbene center. The effect of these two variables can be quite pronounced, and the synthetic transformations could be expected by switching either of these parameters. For example, concerted and stepwise reaction pathways have been disclosed in the cyclopropanation reaction, depending on the type of metal catalysts that were used in these transformations with corresponding carbene precursors (Fig. 1a, path a vs path b). Moreover, various [4 + 1]-cycloaddition reactions of carbene species with α,β-unsubstituted carbonyl compounds, in situ generated α-QMs, 1,3-dienes, or other functionalized alkenes have been realized through different reaction pathways in the presence of corresponding metal catalysts. On the other hand, the vinyl metal carbene, which possesses two electrophilic sites, could function as an α,β-unsaturated electrophile in the presence of gold catalysts with identical starting materials. The versatile reactivity of this species is mainly dependent on the choice of catalysts and the substituent(s) proximal to the carbene center. The effect of these two variables can be quite pronounced, and the synthetic transformations could be expected by switching either of these parameters.

Meanwhile, a variety of [3 + n]-cycloadditions of vinyl/enol metal carbene species with corresponding dipolarophiles have been disclosed independently by Doyle and Davies, and Yoo (Fig. 1b). Despite these significant achievements, the carbene precursors in these cycloadditions have been severely limited to α-vinyl and α-silyl enol diazoacetates, and very rare example of using carbene species as a 4-carbon synthon has been disclosed. Thus, the exploration of effective catalytic approaches for the access to different types of carbene intermediates with readily available materials is highly desirable, which would substantially broaden the substrate scope for the diversity synthesis, and more importantly, enabling methods for the practical synthesis.

Recently, the gold(I) complexes, which are versatile and selective catalysts for alkene activation due to their strong Lewis acidity and potential to stabilize cationic reaction intermediates, have been employed in a plethora of synthetic transformations, allowing rapid and efficient assembly of structurally complex molecules. In this regard, the three-center four-electron σ-bond model for the fundamental description of the gold-carbene intermediate has been proposed by Toste and Goddard in 2009; however, the electronic nature of these gold intermediates, carbene or carbocation, is still under exploration. Beyond the terminological point, the catalytic cycloadditions of gold carbene with olefins have attracted much attention. Cyclopropanation of olefins with a variety of carbene precursors, including diazo compounds, 1,3-enynes, yne-enones, propargyl esters, cyclopropanes, 1,3,5-cycloheptatrienes, and alkynes via oxidation/nitrene transfer processes, is the main focus in this area. Gold-catalyzed [4 + 1] and [3 + 2]-cycloadditions have been disclosed by Echavarren with 1,3,5-cycloheptatriene as the carbene precursor. Meanwhile, the gold-catalyzed formal [4 + 2]-cycloaddition of enynes with tethered alkene via cyclopropyl metal carbene intermediate has been studied by the same group. Inspired by these advances and our recent study on gold-catalyzed diazo-yne carbocyclization, we envisioned that different reactivity could be disclosed with these unique types of in situ generated carbene intermediates, which could not be formed through other approaches or precursors. For example, if an asynchronous reaction pathway is dominating in the reaction of carbene intermediate with alkenes (Fig. 1a, path b), the second C–H insertion of this intermediate with enol ethers are the dominating transformations in the presence of dirhodium catalysts. But a [3 + 2]-cycloaddition could be enabled in the presence of gold catalyst with identical starting materials.

![Diagram](https://example.com/diagram.png)

**Fig. 1 Catalytic metal carbene cycloadditions.** a) Concerted and stepwise cyclopropanation. b) [3 + n]-Cycloadditions of vinyl/enol metal carbene. c) This work: gold(I)-catalyzed 6-endo-dig carbocyclization and stepwise [4 + 2] cycloaddition reaction.
excellent yields rather than the desired tetracyclic product 3 (entries 1–5). Given the fact that the formation of 3′ with these catalysts should go through a carbene/alkyne metathesis process (CAM)49–58, the gold-complexes, which have shown unique ability to selectively activate alkyne species with the pendant diazo group served as a latent functionality41–43,59, were then evaluated. Due to the competition between ligand and carbene for the contribution of electron density of gold center, the ligands of the gold catalysts have a significant influence on the bonding and reactivity of corresponding gold-complex intermediates28–35, and we have observed these dramatic influences in the outcome of the following optimization. The gold catalysts with trialkylphosphines as the ligands could produce mainly the polycarbocyclic product 3 in moderate conversions (entries 6–8, 29–36% yields), whereas, the triarylphosphines showed relatively lower reactivity (27–39% conversions), preferring to form the intramolecular cyclization product 3′ (entries 9–11). Further investigation of phosphine ligands with structural and electronic diversity implied that ligands bearing electron-donating substituents (entries 12 vs 13) and with appropriate steric hindrance (entry 14 vs entries 12, 16, and 17) gave better results, affording 3 in 90% NMR yield when JohnPhos (L3) was used as the ligand (entry 14, 84% isolated yield). A comparably good result was obtained by switching the counter anion of gold catalyst from SbF6− to NTf2− (entry 15). Based on these results, we set out to explore a statistical regression approach to interpretation and prediction of ligand effects. The calculated Au–Cl bond distance, which has been disclosed by Fey and co-workers60, might provide such a platform to quantify the steric and electronic properties of these ligands61,62. Our optimization results have shown good correlation with the calculated parameters of the Au–Cl bond distance of gold-complexes with corresponding ligands (see Supplementary Fig. 1 for details). Moreover, these results bring us to predict that electron-donating substituents with moderate steric hindrance on the phosphine ligand might further improve the yield. Thus, the ligand (Me2N)3P, which is similar to triisopropylphosphine (entry 8), but is much more flexible due to the additional freedom of nitrogen inversion and the three amino groups offer complementary donor functions63,64, was introduced. Gratifyingly, this ligand proved to the most effective one, delivering the desired product 3 in 89% isolated yield (entry 18).

| Entrya | Cat.                                    | Conv. (%) | Yield 3/3′ (%)b |
|--------|-----------------------------------------|-----------|-----------------|
| 1      | Rh(COD)BF4                              | >95       | <5/89           |
| 2      | Rh2(OAc)4                               | >95       | <5/75           |
| 3      | Cu(hfacac)2H2O                          | >95       | <5/95           |
| 4c     | Pd2(db)3CHCl                             | >95       | <5/87           |
| 5c     | AgSbF6                                  | >95       | <5/91           |
| 6      | Cy3PdAuCl + AgSbF6                      | 63        | 36/<5           |
| 7      | tBu3PdAuCl + AgSbF6                     | 41        | 29/<5           |
| 8      | iPr3PdAuCl + AgSbF6                     | 58        | 32/<5           |
| 9      | PPh3PdAuCl + AgSbF6                     | 30        | <5/21           |
| 10     | (p-CF3C6H4)3PdAuCl + AgSbF6             | 39        | <5/26           |
| 11     | (p-OMeC6H4)3PdAuCl + AgSbF6             | 27        | 9/11            |
| 12     | L1AuCl + AgSbF6                         | 11        | <5/<5           |
| 13     | L2AuCl + AgSbF6                         | >95       | 58/<5           |
| 14     | L3Au(H2CN)SbF6                          | >95       | 90(84)d/<5     |
| 15     | L3Au(H2CN)NTf2                          | >95       | 87/<5           |
| 16     | L4AuCl + AgSbF6                         | >95       | 52/<5           |
| 17     | L5AuCl + AgSbF6                         | >95       | 41/<5           |
| 18     | (Me2N)3PdAuCl + AgSbF6                  | >95       | 92(89)d/<5     |

aReaction conditions: to a solution of metal catalyst (5 mol%) in DCE (0.5 mL), we added the solution of 1a (63.6 mg, 0.2 mmol) and styrene 2a (35.0 μL, 0.3 mmol) in DCE (0.5 mL) at 60 °C. The reaction mixture was stirred for 6 h under these conditions. bYields were determined by proton NMR with mesitylene as internal standard. cThe reaction was conducted at 80 °C for 12 h. dThe results in the parentheses are isolated yields.
The 1,3-dicarbonyl diazo compound 1 in combination with styrene 2a was examined (Fig. 2). The substitutions on the aryl linkage (Ar1), including fluoro on the different positions (4–7), methyl (8), and methoxy (9) groups did not obviously affect the reactivity, and 82–93% isolated yield was obtained in these cases. The diazo compound with naphthyl group as the linkage provided the pentacyclic product 10 in 53% yield. Then, the nature of the alkyne terminus was investigated (Ar2). The steric hindrance resulting from the ortho- and meta-methyl substituents on the phenyl ring did not impact the reactivity a lot, delivering corresponding products 11 and 12 in 75% and 95% yield, respectively. Other diazo derivatives, containing different...
substituents on the para-position of the aryl ring, performed well under these conditions (13–16), although low yields were obtained in the halogen-substituted cases. This may due to the lower nucleophilicity of these aromatic rings. Naphthyl- and thienyl-alkynes reacted effectively under gold-catalysis, offering the corresponding polycyclic products all in high yields (17–20). The diastereomers of 18 resulted from the initially formed axial chirality in the diazo-yne cyclization step due to the hindered rotation of the naphthyl group and the later formed point chirality in the formal \([4+2]\)-cycloaddition reaction, and the low \(dr\) may due to the lack of selectivity control of the electrophilic aromatic substitution step. The installation of cyclohexenyl group proximal to the alkyne motif instead of aryl led to the formation of cyclohexane and 1-methyl-1-phenylethene, worked well, leading to the cycloadducts 38 and 39 in 83% and 76% yields, respectively. The structures of 23 and 34 were confirmed by single-crystal X-ray diffraction analysis.

Fig. 3 Scope with respect to the olefins 2. Reaction condition: to a solution of \((\text{Me}_2\text{N})_3\text{PAuCl}\) (3.95 mg, 0.01 mmol), and AgSbF\(_6\) (3.4 mg, 0.01 mmol) in DCE (0.5 mL), we added a solution of 11 (PMP = 4-MeOC\(_6\)H\(_4\), 69.6 mg, 0.2 mmol) and olefins 2 (0.3 mmol) in DCE (0.5 mL) at 60 °C, then the reaction mixture was stirred for 6 h under these conditions. Isolated yields are listed. *DCE (6.0 mL) was used.

Optical properties. After the construction of these elusive CPHs, we then investigated the optical properties of representative analogs in DMSO (Fig. 5). The absorption spectra of tested PAHs displayed the \(\lambda_{\text{max}}\) in the range of 402–421 nm. For the fluorescence spectra, compounds 45, 47, 52, and 53 exhibited sky-blue lights with similar peaks at around 490 nm; whereas, the five-fused aromatic product 48 showed green light with a maximum emission of 550 nm due to the extension of the \(\pi\)-conjugated system.
**Fig. 4** Preparation of polycyclic aromatic hydrocarbons (PAHs). Reaction condition: the generated formal [4+2]-cycloaddition adducts (0.10 mmol), 2,3-Dicyano-5,6-dichlorobenzoquinone (DDQ, 25.0 mg, 0.11 mmol), and 1,4-dioxane (6.0 mL) were added in sequence at 25 °C, and the reaction mixture was stirred for 12 h under these conditions. Isolated yields are listed.

**Fig. 5** The UV/Vis absorption (solid lines) and emission spectra (broken lines) in DMSO. The extension of π-conjugated system to enlarge the maximum emission of PAHs.
Mechanistic discussion. Mechanistic experiments were performed to gain insights into the reaction pathway of this transformation (Fig. 6). To verify the existence of the on-ring β-aryl gold-carbene intermediate, the interception reaction with 11 in the presence of diphenyl sulfoxide (1.5 equiv.), instead of styrene, was carried out under standard conditions, and the corresponding cyclic ketone product 56 was isolated in 84% yield (Fig. 6a). These results are also consistent with a direct 6-endo-dig diazo-yne carbocyclization process for the generation of this on-ring carbene intermediate, otherwise, the linear ketone

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\begin{align*}
11 & \xrightarrow{\text{PhSO (1.5 equiv)}} 56, 84 \text{ % yield} \\
11 & \xrightarrow{(\text{Me}_2\text{N})_3\text{PAuCl} (5.0 \text{ mol\%})} 57, 71 \text{ % yield} \\
11 & \xrightarrow{(\text{Me}_2\text{N})_3\text{PAuCl} (5.0 \text{ mol\%})} 58, 80 \text{ % yield} \\
11 & \xrightarrow{(\text{Me}_2\text{N})_3\text{PAuCl} (5.0 \text{ mol\%})} \text{90% of 1aa was recovered} \\
11 & \xrightarrow{\text{JohnPhosAu(CH}_3\text{CN)SbF}_6 (5.0 \text{ mol\%})} \text{detected by } ^{31}\text{P NMR} \\
11 & \xrightarrow{(\text{Me}_2\text{N})_3\text{PAuCl} (5.0 \text{ mol\%})} \text{R}^1, \text{R}^1 = \text{H}, \text{Ar}^1 = \text{Ar} = \text{PMP}, 79\% (10\%)^a \\
11 & \xrightarrow{(\text{Me}_2\text{N})_3\text{PAuCl} (5.0 \text{ mol\%})} \text{R}^1, \text{R}^1 = \text{tBu}, \text{Ar}^1 = \text{Ph}, 82\% (12\%)^a \\
11 & \xrightarrow{(\text{Me}_2\text{N})_3\text{PAuCl} (5.0 \text{ mol\%})} \text{R}^1, \text{R}^1 = \text{OMe}, \text{Ar}^1 = \text{Ar} = \text{Ph}, 72\% (17\%)^a \\
11 & \xrightarrow{(\text{Me}_2\text{N})_3\text{PAuCl} (5.0 \text{ mol\%})} \text{R}^1, \text{R}^1 = \text{Br}, \text{Ar}^1 = \text{Ph}, 59\% (31\%)^a \\
\end{align*}
\]
The 31P NMR analysis results, by mixing the gold-complex with the diazo compound was observed under the current conditions when the reaction was carried out in the presence of a catalyst (5.0 mol%) with the β-aromatic gold-carbene intermediate 

**Applicatons.** To demonstrate the utility of the current method, we performed the reaction on a gram scale (Fig. 9, 4.0 mmol), providing 1.48 g of 14 in 87% yield. Then, the cycloadduct 14 was subjected to further transformations. Sulfonation of the phenolic hydroxyl group with trifluoromethanesulfonic anhydride (TfO) led to the coupling precursor 65 in quantitative yield. The following Sonogashira and Suzuki coupling reactions with terminal alkynes and naphthylboronic acid gave 66 and 67 in 93% and 98% yields, respectively. Oxidation of 67 with DDQ followed by an acid-promoted Friedel-Crafts-type intramolecular cyclization delivered the polycyclic hydrocarbon 68 in a total 82% yield for the two steps. We also studied the enantioselective version of this cascade reaction with a variety of chiral phosphine ligands. So far, only up to 16% ee with low reactivity (25% conversion and 15% yield) has been obtained with these tested ligands (see Supplementary Table 1 for details).

**Methods**

**General methods.** See Supplementary Methods for further details.
Typical procedure for the gold-catalyzed formal [4 + 2] cycloaddition. To a 10-mL oven-dried vial containing a magnetic stirring bar, (Me$_2$N)$_3$PAuCl (3.95 mg, 0.01 mmol), AgSbF$_6$ (3.43 mg, 0.01 mmol), and DCE (0.5 mL) were added in a sequence in a nitrogen-filled glove-box. The reaction mixture was stirred at 25 °C for 12 h. Then, the solvent was removed and the residue was dissolved in DCE (0.5 mL) at 60 °C, and the resulting reaction mixture was stirred under these conditions for 6 h. Then, the solvent was removed under reduced pressure and the crude product was purified by column chromatography on silica gel (eluents: Ethyl acetate/light petroleum ether 20:1) to give the PAHs = 4-MeOC$_6$H$_4$ 4.0 mmol, 1.40 g.

Data availability

Additional data supporting the findings described in this manuscript are available in the Supplementary Information. For full characterization data of new compounds and experimental details, see Supplementary Methods and Figures in Supplementary Information file. The X-ray crystallographic coordinates for structures 23 and 34 reported in this study have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition number 1828268 (23) and 1849634 (34). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via http://www.ccdc.cam.ac.uk/data_request/cif. All other data are available from the authors upon reasonable request. Source data are provided with this paper.

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References

1. Davies, H. M. L. & Manning, J. R. Catalytic C–H functionalization by metal carbenido and nitrene Insertion. Nature 451, 417–424 (2008).
2. Zhu, S. & Zhou, Q. Transition-metal-catalyzed enantioselective heteroaromat-hydrogen bond insertion reactions. Acc. Chem. Res. 45, 1365–1377 (2012).
3. Doyle, M. P. et al. Catalytic carbene insertion into C–H bonds. Chem. Rev. 110, 704–724 (2010).
4. Xia, Y., Qiu, D. & Wang, J. Transition-metal-catalyzed cross-couplings through carbene migratory insertion. Chem. Rev. 117, 13810–13889 (2017).
5. Ford, A. et al. Modern organic synthesis with diazocarbonyl compounds. Chem. Rev. 115, 9981–10008 (2015).
6. Marzinez, M., Pertusati, F. & Serpi, M. 3,5-Phosphorus-containing a-diazo compounds: a valuable tool for accessing phosphorus-functionalized molecules. Chem. Rev. 116, 13991–14055 (2016).
7. Wang, H. et al. Rhodium-catalyzed enantioselective cyclopropanation of electron-deficient alkenes. Chem. Sci. 4, 2844–2850 (2013).
8. Pérez-Galán, P. et al. Mechanism of the gold-catalyzed cyclopropanation of alkenes with 1,6-enameynes. Chem. Sci. 2, 141–149 (2011).
9. Ringer, D. H. & Chen, P. Rational design of a gold carbene precursor complex for a catalytic cyclopropanation reaction. Angew. Chem. Int. Ed. 52, 4686–4689 (2013).
10. Zhou, J.-L. et al. Tunable carbonyl ylide reactions: selective synthesis of dihydrofurans and dihydrobenzoxepines. Angew. Chem. Int. Ed. 50, 7874–7878 (2011).
11. Sunej, A. & Schneider, C. Phosphoric acid catalyzed [4 + 1]-cy cloaddition reaction of ortho-quinone methides and diazoketones: catalytic, enantioselective access toward cis,2,3-dihydrobenzofurans. Org. Lett. 20, 7576–7580 (2018).
12. Pandit, R. P., Kim, S. T. & Ryu, D. H. Asymmetric synthesis of enantienriched 2-aryl-2,3-dihydrobenzofurans by a Lewis acid catalyzed cyclopropanation/intramolecular rearrangement sequence. Angew. Chem. Int. Ed. 58, 13427–13432 (2019).
13. Rodríguez, K. X., Pilato, T. C. & Ashfeld, B. L. An unusual stereoretentive 1,3- quaternary carbon shift resulting in an enantioselective Rh(I)-catalyzed formal [4 + 1]-cy cloaddition between diazo compounds and vinyl ketones. Chem. Sci. 9, 3221–3226 (2018).
14. Meloche, J. L. & Ashfeld, B. L. A. A gold(II)-catalyzed formal [4 + 1]- cycloaddition toward spiroxindole pyrrolone construction employing vinyl isocyanates as 1,4-dipoles. Angew. Chem. Int. Ed. 56, 6604–6608 (2017).
15. Smith, A. G. & Davies, H. M. L. Rhodium-catalyzed enantioselective vinylogous addition of enol ethers to vinyldiazooacetates. J. Am. Chem. Soc. 134, 18241–18244 (2012).
16. Fu, L., Guptill, D. M. & Davies, H. M. L. Rhodium(II)-catalyzed C–H functionalization of electron-deficient methyl groups. J. Am. Chem. Soc. 138, 5761–5764 (2016).
17. Brones, J. F. & Davies, H. M. L. Enantioselective gold(I)-catalyzed vinylogous [3 + 2]-cycloaddition between vinyldiazooacetates and enol ethers. J. Am. Chem. Soc. 135, 13314–13317 (2013).
18. Xu, X. & Doyle, M. P. The [3 + 3]-cycloaddition alternative for heterocycle syntheses: catalytically generated metalloenolcarbenes as dipolar adducts. Acc. Chem. Res. 47, 1396–1405 (2014).
19. Párr, B. T. & Davies, H. M. L. Highly stereoselective synthesis of cyclopentanes bearing four stereocentres by a rhodium carbene-initiated domino sequence. Nat. Commun. 5, 4455 (2014).
20. Lee, D. J. et al. Multicomponent [5 + 2] cycloaddition reaction for the synthesis of 1, 4-diazepines: isolation and reactivity of azomethine ylides. J. Am. Chem. Soc. 136, 11606–11609 (2014).
21. Dawande, S. G. et al. Rhodium enacaleneboids: direct synthesis of indoles by rhodium(II)-catalyzed [4 + 2] benzannulation of pyrroles. Angew. Chem. Int. Ed. 53, 4076–4080 (2014).
22. Échavarren, A. M. Carbene or cation? Nat. Chem. 1, 431–433 (2009).
23. Hashmi, A. S. K. Homogeneous gold catalysis beyond assumptions and proposals—characterized intermediates. Angew. Chem. Int. Ed. 49, 5232–5241 (2010).
24. Fürstner, A. & Morency, L. On the nature of the reactive intermediates in gold-catalyzed cycloisomerization reactions. Angew. Chem. Int. Ed. 47, 5033–5038 (2008).
25. Zheng, Z. et al. Au-catalysed oxidative cyclisation. Chem. Soc. Rev. 45, 4448–4458 (2016).
26. Yeom, H. & Shin, S. Catalytic access to α-oxo gold carbenes by N–O bond oxidants. Acc. Chem. Res. 47, 966–977 (2014).
27. Forstner, A. & Widmer, R. A gold(i) carbene, gold-stabilized carbocations, and cationic intermediates relevant to gold-catalyzed enyne cyclodaddition. Chem. Soc. Rev. 45, 4533–4551 (2016).
28. Benitez, D. et al. A bonding model for gold(i) carbene complexes. Nat. Chem. 1, 482–486 (2009).
29. Fujiwara, T. et al. High-yield synthesis of a sterically congested bis(4-methoxyphenyl) gold carbene. Angew. Chem. Int. Ed. 53, 6904–6907 (2014).
30. Xu, Y. et al. Chemoselective carbophilic addition of α-diazoacetates to gold(i) carbenoids: implications for their use as precursors in vapor phase deposition methods. ACS Appl. Mater. Interfaces 9, 40989–41005 (2017).
31. Bautista, A. et al. Tris(dimethylamino)phosphine as a new ligand in gold(i) chemistry: synthesis and crystal structures of $\{\{(Me_2N)\}_3PAu\}Cl$, $\{\{(Me_2N)\}_3PAu\}_2\{BF_4\}^-$, $\{\{(Me_2N)\}_3PAu\}Cl$ and the precursor molecule (Me$_2$N)$_2$PNSiMe$_3$. Chem. Rev. 130, 323–328 (1997).
32. Hoyle, T. R. et al. The hexahydro-Diels–Alder reaction. Nature 490, 208–212 (2012).

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Author contributions
XX. and A.S.K.H. conceived and designed the study; C.Z., K.H. and C.P. performed the experiments; C.Z. analyzed the experimental data; S.Z. checked the experimental data. All the authors contributed to scientific discussion. XX., A.S.K.H. and C.Z. wrote the paper; XX., A.S.K.H. and W.H. revised the manuscript.

Competing interests
The authors declare no competing interests.

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