

Photocluster Catalytic Oxidation Enabled by Structurally Precise Copper-Hydride Nanoclusters

Corresponding Author: Professor Hui Shen

This file contains all reviewer reports in order by version, followed by all author rebuttals in order by version.

Version 0:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

Referee Report for Manuscript with ID: NCOMMS-26-026048

In this communication, the authors present a machine learning-guided strategy to localize hydrides in copper-hydride nanoclusters, ensuring structural accuracy in Cu₁₃H₆ and establishing that such clusters can serve as versatile and efficient photocatalytic catalysts to significantly expand the application potential of photocatalysis in organic synthesis.

A new compound with formula [Cu₁₃(DPPM)₄(C₇H₄NS)₆H₆] was synthesized following a recently developed strategy with some slight modifications via a scalable one-pot method.

A comprehensive characterization was performed to determine the hydride positions, including machine learning-assisted stochastic surface walking with a neural network potential. The newly synthesized cluster exhibits excellent optical properties and a suitable photoexcited redox potential, efficiently oxidizing various alkyl aromatics and alcohols to carbonyl compounds under mild conditions. Mechanistic studies were performed and the results indicating that the reaction proceeds via a single electron transfer from the cluster to O₂, resulting in the formation of superoxide radicals, which trigger a cascade of redox processes. The resulting reduced photocatalyst subsequently interacts with fluorine atoms in organic substrates, enabling reductive defluorination. The above results highlight the potential of copper hydride nanoclusters for various photocatalytic applications and highlight a promising and under explored area of research considering these types of materials.

The work is interesting and in general the text of the Communication is well structured. Relevant supplementary material is also provided.

However, various aspects need to be clarified before this communication is considered for its publication.

1) Page 6, line 73: I am unclear about the connection between the works cited in references 41 and 42 and this paper, which focuses primarily on C₁₃H₆ (using the abbreviation provided by the authors).

The authors should better explain this connection.

2) Page 7, lines 108 and 109: The explanation provided for the metallic structure is not easily visible when looking at the structure on the left side of Figure 1c. From this figure, three distorted square pyramids of Cu₅ can be clearly distinguished, each sharing two sides of its distorted square base with one side of the distorted bases of the other two Cu₅ pyramids.

3) Page 7 and some Tables of the Supplementary Material: Bond lengths are reported to up 4 or 6 decimal places. What do these decimal places mean? What experiments can provide bond lengths with such precision? To the best of my knowledge, none!

For clarity to the reader, bond lengths should be given with significant precision and in a consistent manner, i.e. with the same number of digits throughout the work.

4) Page 12: Determination of hydride positions via machine learning-assisted stochastic surface walking method.

The authors state that: "The determination of hydride positions was performed with a stochastic surface walking method with the global neural network potential as implemented in the LASP code. This method has been rigorously validated in prior studies, demonstrating reliable exploration of the global potential energy surfaces for various metal hydride clusters and providing a robust alternative to conventional neutron diffraction techniques."

I have some concerns regarding this part, which are as follows:

A) The method has been validated in previous studies that considered similar but other types of systems. Therefore, it cannot be simply concluded that this method generally represents a valid alternative to conventional neutron diffraction techniques, as this may depend on several factors such as the type of system, the types of potential and kernel used for the machine learning approach, etc. The authors should clearly state the potential problems that could arise when applying this machine learning-assisted stochastic surface walk method if one or more of these factors were to change. How would this affect the characterization of the hydride positions?

B) To avoid an exponential increase in degrees of freedom during global structural optimization due to relaxation of both the Cu nucleus and the ligands, the cluster structure was kept fixed, allowing only the six hydrogen atoms to relax. This approach clearly improves computational efficiency but may compromise accuracy. Therefore, the question is: what price must be paid in terms of precision of hydride positions?

This is an important point that has consequences like the question I raise below in point 6).

5) Discussion on page 14 and Table S5 related to the Bader charges. For some reasons no units are given. These should be in units of the electronic charge integrated within a defined volume. Is this correct?

6) Page 15, lines 235-238. Question: What causes the observed discrepancies between the experimental and theoretical peaks? What can be attributed to the difference of approximately 20 nm between the calculated and experimentally determined peaks?

Reviewer #2

(Remarks to the Author)

This manuscript reports a structurally precise copper-hydride nanocluster (Cu_{13}H_6) for photocatalytic $\alpha\text{-C-H}$ oxidation, combining SCXRD, isotopic labeling ($\text{Cu}_{13}\text{H}_6/\text{Cu}_{13}\text{D}_6$), and machine learning-assisted hydride localization. The concept is timely and potentially impactful. However, several key claims require stronger support. I recommend major revision.

Major Comments

1. Catalytic mechanism

The proposed SET mechanism via $\text{O}_2^{\bullet-}$ is not rigorously demonstrated. Additional evidence (e.g., radical trapping, quantitative EPR) is needed.

3. Catalyst stability

Structural integrity under catalytic conditions is insufficiently established. ESI-MS before/after catalysis (Fig. S17) is suggestive but not conclusive.

4. Structure–activity relationship

No comparison with related clusters or non-hydride analogues is provided, leaving the role of hydrides unclear.

Minor Comments

Soften claims such as “unambiguously determined.”

Improve figure clarity and provide error bars.

Clarify absence of counterions in the crystal structure.

Reviewer #3

(Remarks to the Author)

In this manuscript, the authors report the synthesis, comprehensive structural characterization, and photocatalytic performance of a Cu_{13} nanocluster toward $\alpha\text{-C-H}$ bond oxidation reactions. Nevertheless, extensive prior research has already investigated analogous catalytic reactions, and the present work fails to deliver sufficiently novel, groundbreaking results or distinctive mechanistic insights to meet the stringent publication criteria for Nature Communications. Given the lack of adequate innovation and unique contributions relative to existing literature, I recommend that this manuscript be considered for publication in a more specialized alternative journal.

1. Bond length reporting does not comply with IUPAC crystallographic standards. All bond lengths should be reported with three decimal places and the estimated standard deviation given in parentheses.

2. The overall visual quality of figures requires thorough polishing. In particular, Table 2 and Scheme 1 are severely overcrowded, with densely packed chemical structures that impair readability.

3. The manuscript lacks recycling tests and post-catalysis structural characterization. Post-catalytic characterization using techniques such as XPS and UV-Vis is necessary to confirm whether the cluster retains its integrity after reaction.

4. The thermodynamic feasibility of SET between the photoexcited cluster and the substrate (or O_2) should be evaluated, e.g., by determining redox potentials and performing free-energy calculations.

Version 1:

Reviewer comments:

Reviewer #1

(Remarks to the Author)

Review of manuscript with ID: NCOMMS-26-026048A

The authors have satisfactorily addressed all my comments in their responses as well as in the revised version.

Reviewer #2

(Remarks to the Author)

The manuscript is ready for the publication.

Reviewer #3

(Remarks to the Author)

I examined the revised manuscript carefully and the suggestions that I provided were studied. However, I am not still satisfied with the claim that the authors made. The author has accomplished several experimental data with sound-performed basic work including substrate expansion and condition screening. Nevertheless, copper-based nanomaterials have long been widely employed in diverse photocatalytic C-H-bond oxidation according to extensive published literature. This work merely extends this well-established catalyst to diphenyl ketone substrates and analogues, without establishing an original catalytic mechanism, distinctive regulation strategy or breakthrough-oriented selectivity-control approach. The study suffers from insufficient innovation and limited incremental scientific contribution. Taken together, the present achievement fails to satisfy the Nature Communication's publication criteria, and rejection is recommended.

Open Access This Peer Review File is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

In cases where reviewers are anonymous, credit should be given to 'Anonymous Referee' and the source.

The images or other third party material in this Peer Review File are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder.

To view a copy of this license, visit <https://creativecommons.org/licenses/by/4.0/>

Reply to Referee #1

Comments: In this communication, the authors present a machine learning-guided strategy to localize hydrides in copper-hydride nanoclusters, ensuring structural accuracy in Cu_{13}H_6 and establishing that such clusters can serve as versatile and efficient photocatalytic catalysts to significantly expand the application potential of photocatalysis in organic synthesis. A new compound with formula $[\text{Cu}_{13}(\text{DPPM})_4(\text{C}_7\text{H}_4\text{NS})_6\text{H}_6]$ was synthesized following a recently developed strategy with some slight modifications via a scalable one-pot method. A comprehensive characterization was performed to determine the hydride positions, including machine learning-assisted stochastic surface walking with a neural network potential. The newly synthesized cluster exhibits excellent optical properties and a suitable photoexcited redox potential, efficiently oxidizing various alkyl aromatics and alcohols to carbonyl compounds under mild conditions. Mechanistic studies were performed and the results indicating that the reaction proceeds via a single electron transfer from the cluster to O_2 , resulting in the formation of superoxide radicals, which trigger a cascade of redox processes. The resulting reduced photocatalyst subsequently interacts with fluorine atoms in organic substrates, enabling reductive defluorination. The above results highlight the potential of copper hydride nanoclusters for various photocatalytic applications and highlight a promising and under explored area of research considering these types of materials. The work is interesting and in general the text of the Communication is well structured. Relevant supplementary material is also provided. However, various aspects need to be clarified before this communication is considered for its publication.

Response: Thank you for the positive and constructive feedback on our manuscript. We have carefully addressed all the points raised and implemented the suggested revisions to improve the work's clarity and impact. All changes and additional details have been included in the revised version:

Comment 1: Page 6, line 73: I am unclear about the connection between the works cited in references 41 and 42 and this paper, which focuses primarily on C_{13}H_6 (using the abbreviation provided by the authors). The authors should better explain this connection.

Response: We sincerely appreciate the reviewer's valuable suggestion. Both references 41 and 42 focus

on photocatalytic studies involving atomically precise metal nanoclusters, with the key difference lying in their cluster compositions: reference 41 employs Au–Cu bimetallic alloy clusters, while reference 42 is based on Au clusters protected by thiol ligands. In contrast, this study investigates the structure–activity relationships and mechanisms of Cu–H nanoclusters in photocatalytic oxidation reactions. For the reaction mechanism, reference 41 demonstrated that under visible light excitation, Au–Cu clusters can efficiently activate molecular oxygen, generating reactive oxygen species (ROS) such as superoxide radicals thereby initiating a cascade of radical oxidation reactions on organic substrates. Reference 42 similarly observed that Au–thiol clusters produce reactive oxygen species under visible light-driven conditions, enabling selective oxidation of organic compounds. The two studies collectively demonstrate the universality of metal nanoclusters in achieving photocatalytic oxidation through ROS-mediated pathways, providing robust theoretical support and experimental inspiration for the photocatalytic oxidation of copper hydride clusters in this research.

Comment 2: Page 7, lines 108 and 109: The explanation provided for the metallic structure is not easily visible when looking at the structure on the left side of Figure 1c. From this figure, three distorted square pyramids of Cu₅ can be clearly distinguished, each sharing two sides of its distorted square base with one side of the distorted bases of the other two Cu₅ pyramids.

Response: *We thank the reviewer for the constructive suggestion regarding the description of the metal structure details of Cu₁₃H₆. Revisions are as follows:*

As shown in the left region, the metallic framework consists of three distorted Cu₅ square pyramids. These three Cu₅ units are further assembled into a Cu₉ unit through a shared method. It is important to note that for each distorted Cu₅ square pyramid, two sides are shared with one of the bases of the other two Cu₅ pyramids.

Comment 3: Page 7 and some Tables of the Supplementary Material: Bond lengths are reported to up 4 or 6 decimal places. What do these decimal places mean? What experiments can provide bond lengths with such precision? To the best of my knowledge, none! For clarity to the reader, bond lengths should be

given with significant precision and in a consistent manner, i.e. with the same number of digits throughout the work.

Response: *We sincerely thank the reviewers for their valuable and meticulous comments regarding the description of bond lengths data in the main text and the supplementary materials. We fully agree that the reporting of bond lengths does not comply with IUPAC crystallographic standards. We have consulted the expression norms for bond lengths in the relevant literature from recent years, eg: 1. Songwei, Wen; Chengkai, Zhang; Li-Juan, Liu; Zhi Wang; Di Sun; and Jian He., Stable and Recyclable Copper Nanoclusters with Exposed Active Sites for Broad-Scope Protosilylation in Open Air. Angew. Chem. Int. Ed. 2025, 64, e202416851; 2. Xin-Yu, Chen; Ya-Qi, Li; Xin-Yu, Bai; Dang-Dang, Ding; Xin-Yan, Chi; Wei-Qiang, Zhang; Jun, Yan; Tian-Fu, Liu; Yong Pei; Chao Liu. Structural Fusion-Induced Activity Suppression in Copper Nanoclusters for Electrocatalytic Nitrate Reduction. Angew. Chem. Int. Ed. 2026, e7572408; 3. Feng Hu, Gaoyuan, Yang; Lu-Ming, Zheng; Gui-Jie, Liang; Quan-Ming, Wang. Deciphering icosahedra structural evolution with atomically precise silver nanoclusters. Science, 389, 921-924; 4. Qiu-Chen, Peng; Ruo-Yu, Cao; Qi Yang; Yu-Bing, Si; Jia-Wang, Yuan; Ying-Ying, Lei; Zhao-Yang, Wang; Qiang Tang; Kai Li; and Shuang-Quan, Zang. Monitoring α/β Particles Using a Copper Cluster Scintillator Detector. Adv. Mater. 2025, 37, 2504425. We have systematically rechecked the bond length data on page 7 of the main text and in all supplementary tables. All bond length values are uniformly retained to three decimal places, with the corresponding standard uncertainties (expressed as estimated standard deviations) provided in parentheses, ensuring that the data presentation is rigorous and standardized. All modifications are marked in the revised manuscript.*

Comment 4: Page 12: Determination of hydride positions via machine learning-assisted stochastic surface walking method. The authors state that: “The determination of hydride positions was performed with a stochastic surface walking method with the global neural network potential as implemented in the LASP code. This method has been rigorously validated in prior studies, demonstrating reliable exploration of the global potential energy surfaces for various metal hydride clusters and providing a robust alternative to conventional neutron diffraction techniques.”

I have some concerns regarding this part, which are as follows:

A) The method has been validated in previous studies that considered similar but other types of systems. Therefore, it cannot be simply concluded that this method generally represents a valid alternative to conventional neutron diffraction techniques, as this may depend on several factors such as the type of system, the types of potential and kernel used for the machine learning approach, etc. The authors should clearly state the potential problems that could arise when applying this machine learning-assisted stochastic surface walk method if one or more of these factors were to change. How would this affect the characterization of the hydride positions?

B) To avoid an exponential increase in degrees of freedom during global structural optimization due to relaxation of both the Cu nucleus and the ligands, the cluster structure was kept fixed, allowing only the six hydrogen atoms to relax. This approach clearly improves computational efficiency but may compromise accuracy. Therefore, the question is: what price must be paid in terms of precision of hydride positions? This is an important point that has consequences like the question I raise below in point 6).

Response:

Response to Comment 4A:

We thank the reviewer for this important and insightful comment. We agree that the reliability of the machine learning-assisted stochastic surface walking (SSW-NN) approach depends on multiple factors. Since our recent work has further developed and systematically supplemented this methodology, but was only published very recently, we provide a more detailed explanation here to address the reviewer's reasonable concerns. In our view, the performance of the SSW-NN approach can be discussed from three closely related aspects: (i) accuracy, (ii) generality and transferability, and (iii) robustness.

*First, regarding accuracy, our previous work (J. Am. Chem. Soc. 2025, 147, 10750–10757, denoted as **Ref. 1**) systematically benchmarked the SSW-NN approach against experimentally determined neutron diffraction structures and demonstrated that the method can reliably reproduce hydride positions in representative metal hydride clusters. Furthermore, combining the results from **Ref. 1** and our recent study entitled “General workflow for localizing hydrides in metal nanoclusters by combining stochastic surface walking with neural-network potentials”; (Nat. Commun. 2026,*

72966-9, denoted as **Ref. 2**), the SSW-NN workflow has now been evaluated on a total of 66 previously reported metal hydride nanoclusters, including Copper, Silver, Gold, and alloy hydride systems.

In our view, the accuracy of the SSW-NN approach mainly depends on two aspects: (i) whether the neural network potential can accurately reproduce the underlying DFT potential energy surface, and (ii) how the reliability of the predicted hydride configuration is evaluated.

For the first aspect, the key criterion is whether the energy difference between the neural-network-predicted energy (E_{NN}) and the corresponding DFT energy (E_{DFT}) remains within an acceptable range. For example, in our previous work (Angew. Chem. Int. Ed. 2025, 64, e202500191, denoted as **Ref. 3**), six candidate structures of $AuCu_{24}H_{22}$ were examined. As shown in Fig. R1-R3, the energy deviations between E_{NN} and E_{DFT} were only approximately 1-3 meV, which is substantially lower than the commonly accepted accuracy criterion (~ 10 meV) for machine learning potentials. These results indicate that the neural network potential can accurately describe the relevant potential energy surface, thereby providing a reliable basis for using DFT energies to determine the energetically preferred hydride configuration.

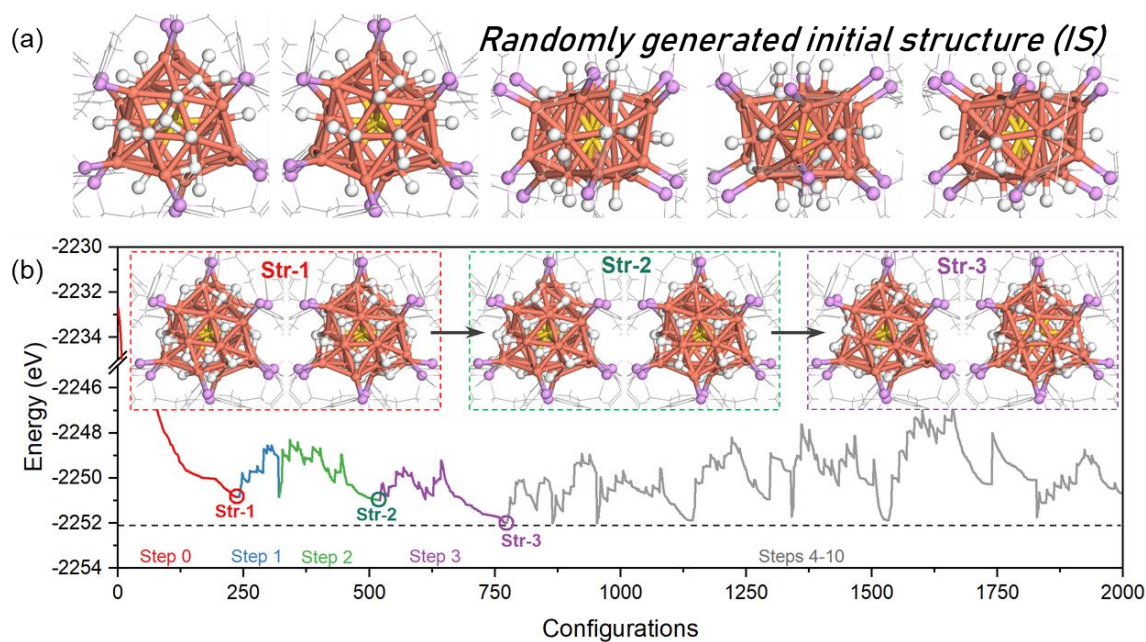


Fig. R1. (a) Based on the SC-XRD structure of the $AuCu_{24}$ -dppp cluster, the initial structure (IS) was generated by randomly positioning 22 H atoms on the surface of the Cu core. (b) The first 2000 structural trajectory in the 50-step SSW-NN (fixing cluster skeleton for the primary screening) was employed to identify the approximate positions of the 22 H atoms on the $AuCu_{24}$ -dppp cluster. Inset: snapshots of three

structures as local minima on the potential energy surface at different optimization stages during SSW-NN. (*Angew. Chem. Int. Ed.* 2025, 64, e202500191, denoted as **Ref. 3**)

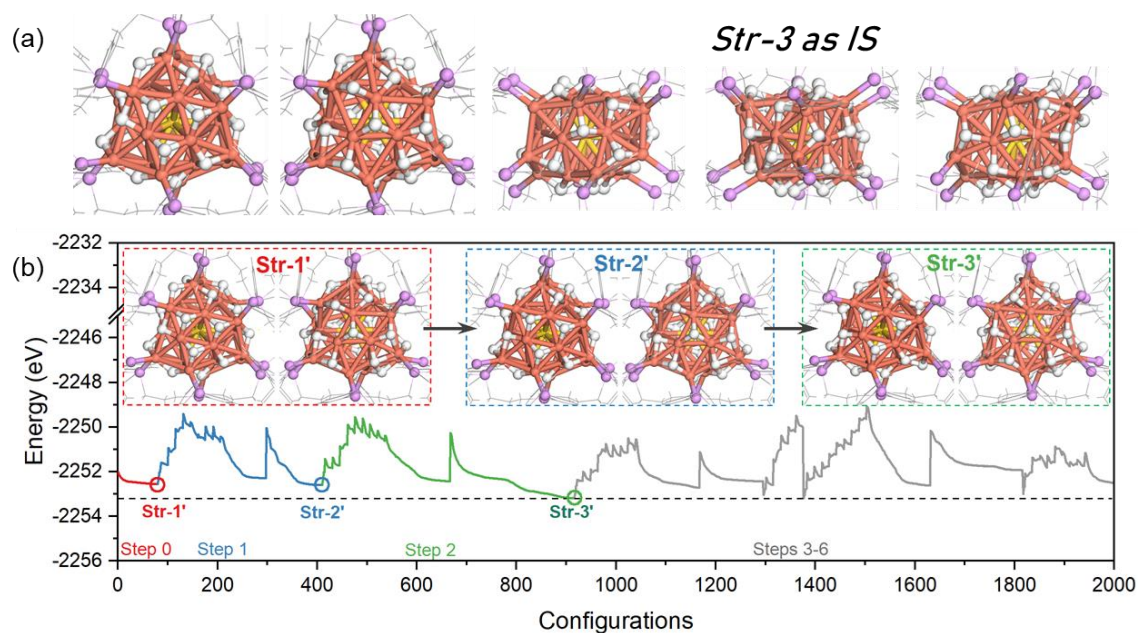


Fig. R2. (a) Based on the Str-3 obtained from the primary screening in Fig. R1 as the initial structure. (b) The first 2000 structural trajectory in the 50-step SSW-NN (perturbing only 22 H atoms for the secondary screening) were employed to identify the precise positions of the 22 H atoms on the AuCu₂₄-dppp cluster. Inset: snapshots of three structures as local minima on the potential energy surface at different optimization stages during SSW-NN. (*Angew. Chem. Int. Ed.* 2025, 64, e202500191, denoted as **Ref. 3**)

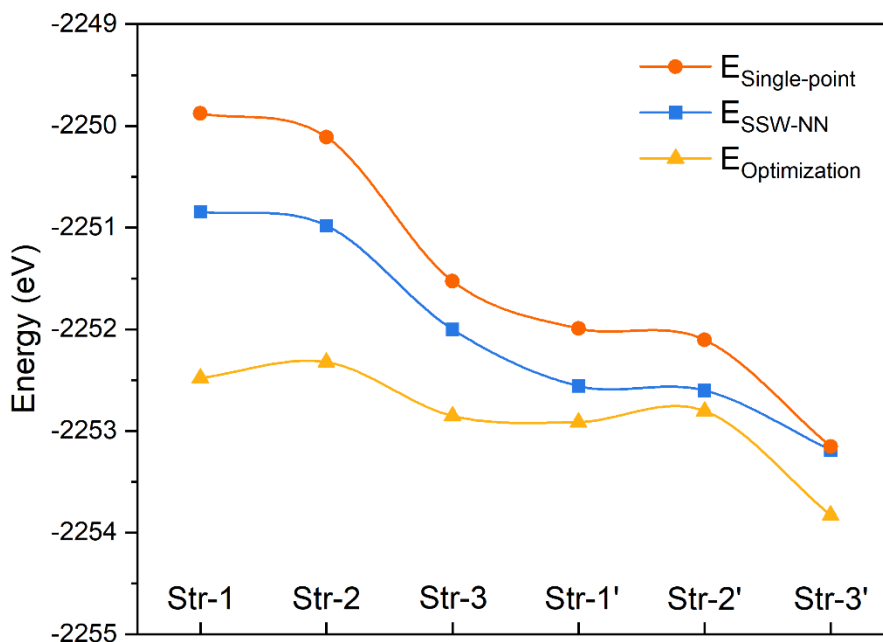


Fig. R3. Comparison of the energies obtained by SSW-NN simulation ($E_{\text{SSW-NN}}$), the energies calculated by VASP for the single point ($E_{\text{Single-point}}$) and the structure optimisation ($E_{\text{Optimization}}$) for the 6 candidate structures. (Angew. Chem. Int. Ed. 2025, 64, e202500191, denoted as **Ref. 3**)

For the second aspect, the reliability of the hydride positions identified by the SSW-NN approach is evaluated from multiple perspectives. First, the neural network potential should accurately reproduce the DFT potential energy surface and identify the lowest-energy configuration. Second, the lowest-energy structures obtained from the SSW-NN search should remain structurally stable after subsequent DFT optimization without significant distortion. Third, the resulting structures should remain consistent with the experimentally observed symmetry characteristics. Fourth, additional validation can be performed through *ab initio* molecular dynamics (AIMD) simulations over several picoseconds to confirm the structural stability of the predicted hydride arrangement. Collectively, these results support the reliability and accuracy of the SSW-NN approach for hydride localization in metal hydride clusters.

Second, regarding generality and transferability, the applicability of the SSW-NN workflow mainly depends on whether the chemical elements involved in the target cluster and the corresponding local coordination environments are sufficiently represented in the training dataset. In this context, the stochastic surface walking (SSW) method plays an important role not only in global structural optimization, but also in efficient structural sampling of the target system. Since the SSW algorithm

explores the configurational space through the introduction of Gaussian bias potentials, it can efficiently generate diverse local atomic environments and thereby provide the methodological basis for both hydride localization and the transferability of the machine learning potential.

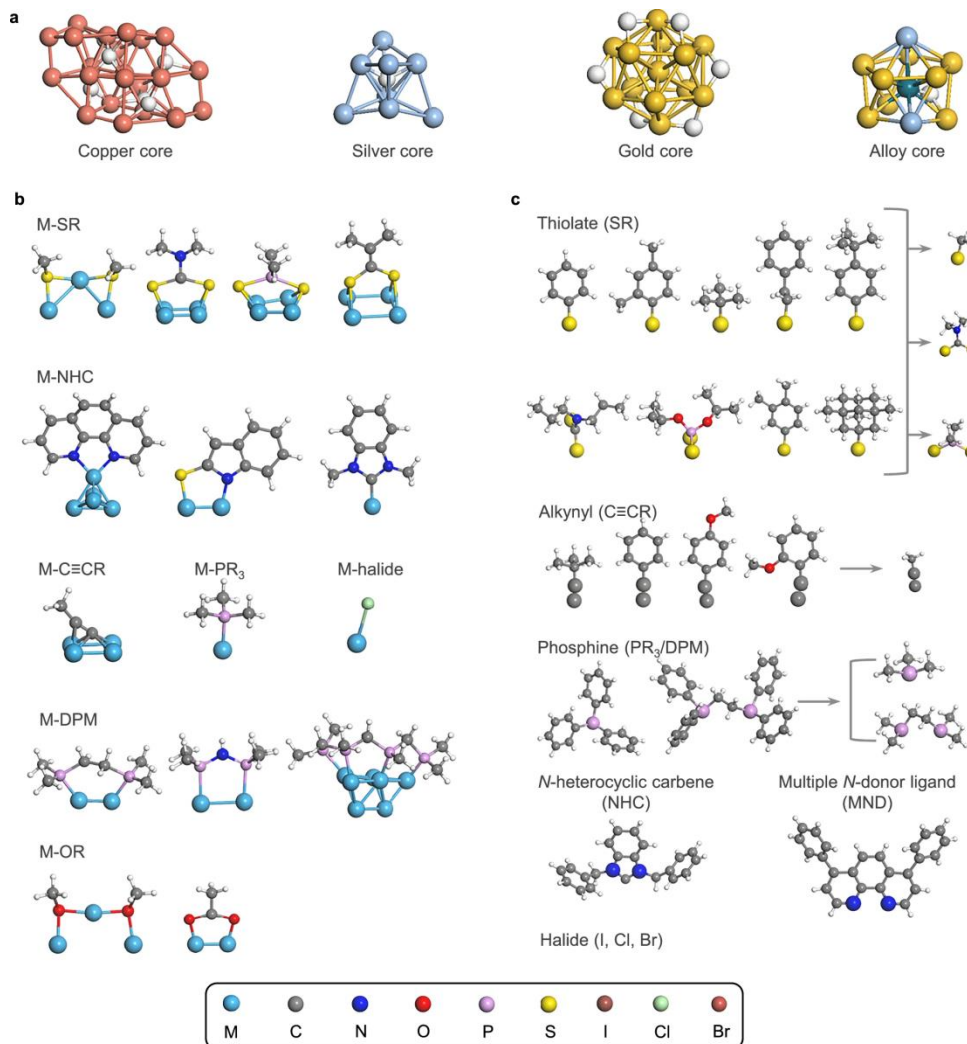


Fig. R4. Schematic illustration of the three structural components of ligand-protected metal hydride nanoclusters: (a) the metal core, (b) the metal-ligand interface, and (c) the protecting ligand shell. (Nat. Commun. 2026, <https://doi.org/10.1038/s41467-026-72966-9>, denoted as **Ref. 2**)

As is well recognized, ligand-protected metal nanoclusters can generally be divided into three components: the metal core, the metal-ligand (M-L) interface, and the protecting ligands (Fig. R4). Metal hydride nanoclusters follow the same structural framework. In the metal-core region of typical Cu-H clusters, only Cu and H elements are involved. Owing to the high sampling efficiency of the SSW approach,

a relatively limited number of sampled structures is generally sufficient to cover the relevant local coordination environments and the associated many-body atomic correlations learned by the neural network potential, including two-body, three-body, and higher-order interaction descriptors. Therefore, the essential local chemical environments governing hydride localization can be efficiently represented within the training dataset.

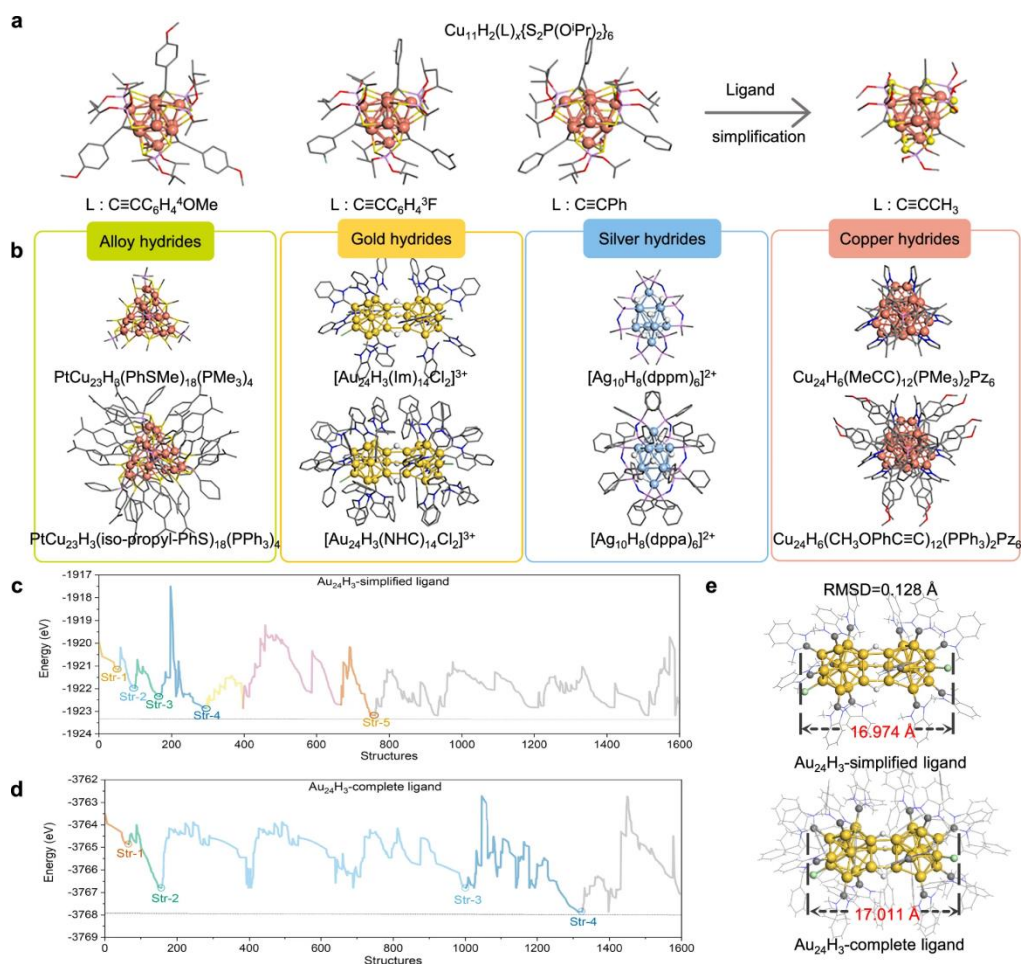


Fig. R5. (a) Schematic of simplifying three distinct alkynyl ligands ($-C\equiv C-C_6H^4OMe$, $-C\equiv C-C_6H^4F$, $-C\equiv CPh$) into a methyl-terminated model ($-C\equiv CCH_3$) with a fixed $Cu_{11}H_2$ core for hydride localization using NN potential. (b) Representative metal hydride nanoclusters with simplified and complete ligands: alloy (PtCu₂₃H₃), Au (Au₂₄H₃), Ag (Ag₁₀H₈), and Cu (Cu₂₄H₆). Potential energy surface (PES) exploration for Au₂₄H₃ using (c) simplified and (d) complete ligands. (e) Structural comparison between simplified and complete ligand models for Au₂₄H₃ optimized by DFT. In panels c and d, "Str-#" denotes the structure index of the candidate structures. Cu, orange; Au, gold; Ag, light blue; H, white; P, pink; S, yellow; Cl,

green; N, blue; C, grey; O, red. (Nat. Commun. 2026, <https://doi.org/10.1038/s41467-026-72966-9>, denoted as **Ref. 2**)

For the protecting ligands, the large structural diversity of ligand groups may significantly increase the configurational complexity and redundancy of the training dataset. To address this issue, we adopted the ligand simplification strategy proposed in **Ref. 2**, as illustrated in Fig. R5. Such simplification treatments are widely used and generally accepted in computational studies of ligand-protected metal nanoclusters because the protecting ligands mainly provide electronic modulation, while the hydride localization is dominated primarily by the metal core and the M-L interfacial environments. Combined with the fixed heavy-atom framework approximation, the influence of ligand simplification on hydride exploration is minimal. The feasibility and validity of this strategy were systematically discussed and benchmarked in **Ref. 2**.

For the M-L interfacial region, the currently reported coordination motifs of ligand-protected metal hydride nanoclusters are already largely covered in our existing datasets (Fig. R4). Even if newly synthesized clusters contain previously unreported interfacial motifs in the future, the corresponding local coordination environments can still be incorporated efficiently through the self-learning workflow by adding targeted structural sampling and retraining.

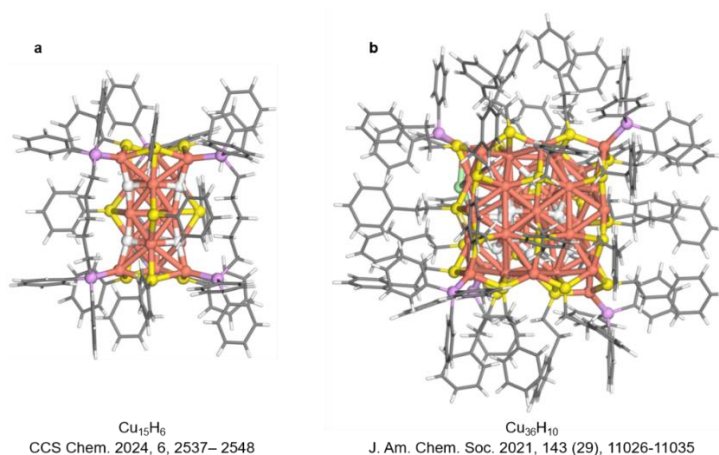


Fig. R6. Previously reported copper hydride clusters with metal-ligand interfacial environments similar to that of the Cu_{13}H_6 cluster in the present work: (a) Cu_{15}H_6 and (b) $\text{Cu}_{36}\text{H}_{10}$.

Based on this strategy, we have already established three dedicated neural network potentials for single-metal Au-H, Ag-H, and Cu-H nanoclusters. For alloy hydride systems, however, system-specific

neural network potentials are still required because of the combinatorial diversity introduced by heteroatom doping. The present Cu_{13}H_6 cluster exhibits mixed phosphine-thiolate M-L interfacial motifs similar to those of the previously reported Cu_{15}H_6 , and $\text{Cu}_{36}\text{H}_{10}$ clusters (Fig. R6), which were reproduced in Ref. 1. Therefore, together with the ligand simplification strategy, the previously developed Cu-H neural network potential can be naturally transferred to the current Cu_{13}H_6 system.

Third, regarding robustness, we fully recognize that this is an important concern for the application of the SSW-NN approach to hydride localization. In fact, a similar question was also raised during the review process of Ref. 2. To address this issue, we systematically examined the effects of three factors: (i) DFT functional/software, (ii) initial hydride placement, and (iii) the neural network potential.

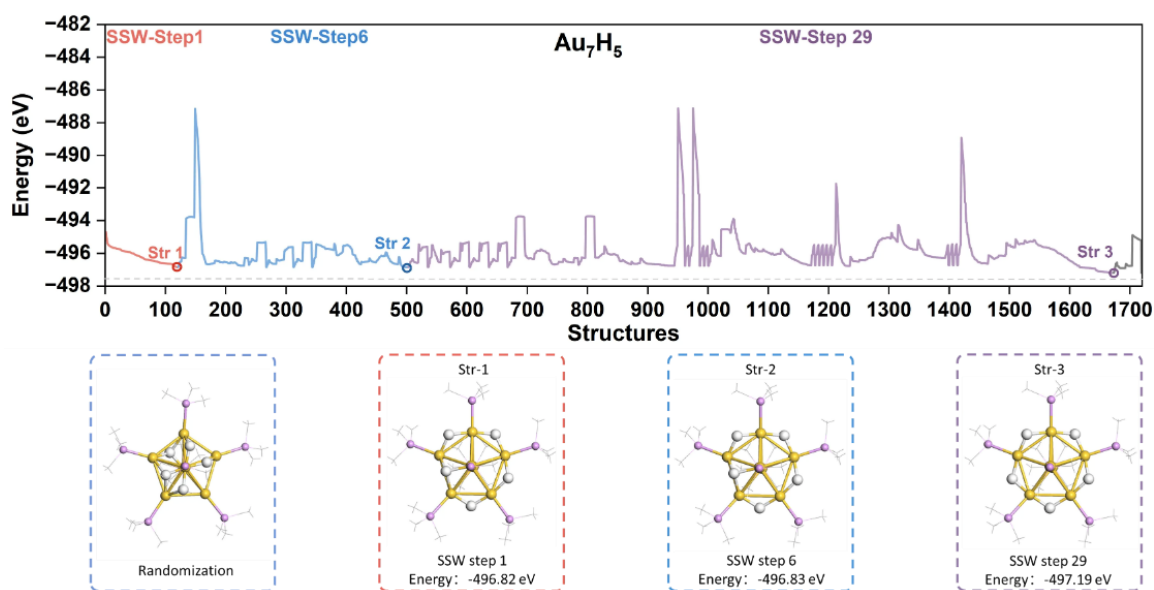


Fig. R7. Potential energy surface (PES) explored by the SSW-NN method for the Au_7H_5 cluster and the corresponding low-energy candidate structures. (Nat. Commun. 2026, <https://doi.org/10.1038/s41467-026-72966-9>, denoted as **Ref. 2**)

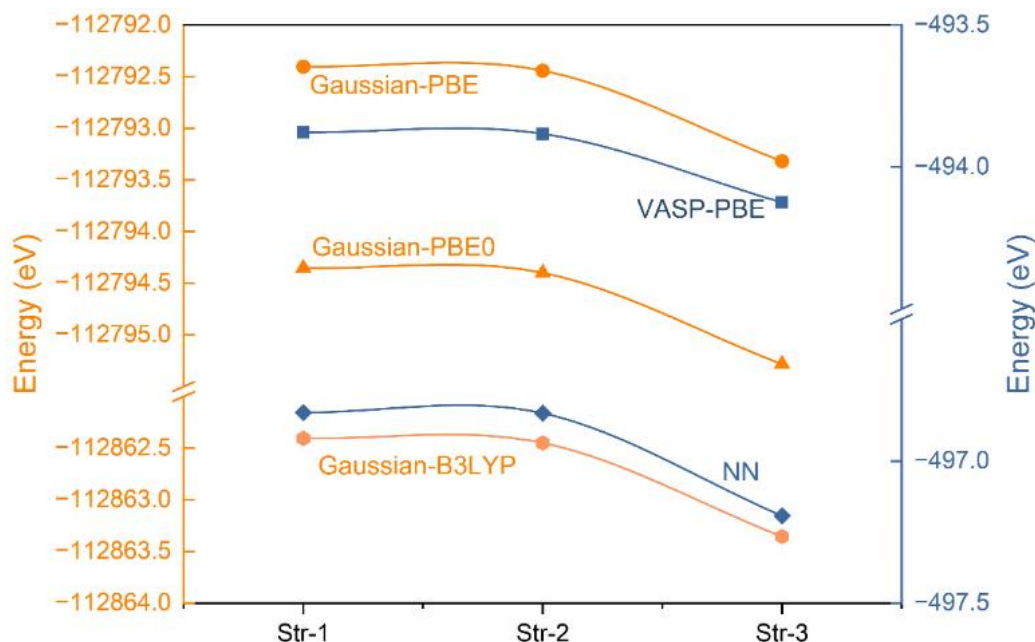


Fig. R8. Comparison of energy trends from NN potential predictions with those from DFT single-point calculations (VASP-PBE and Gaussian-based PBE, PBE0, and B3LYP) for Au_7H_5 candidate structures. (Nat. Commun. 2026, <https://doi.org/10.1038/s41467-026-72966-9>, denoted as **Ref. 2**)

The DFT energies and forces constitute the fundamental data for training the neural network potential. Therefore, whether these data can properly describe the potential energy surface directly determines whether the trained neural network potential can guide the SSW global structural optimization toward reliable local minima. Taking Au_7H_5 as a representative example, the SSW-NN approach identified three candidate structures with gradually decreasing energies. We then evaluated these structures using VASP-PBE and Gaussian-based PBE, PBE0, and B3LYP calculations (Fig. R7 and R8). The same energetic trend was obtained with all these DFT methods, indicating that the identified hydride configurations are robust with respect to the choice of DFT functional and computational software.

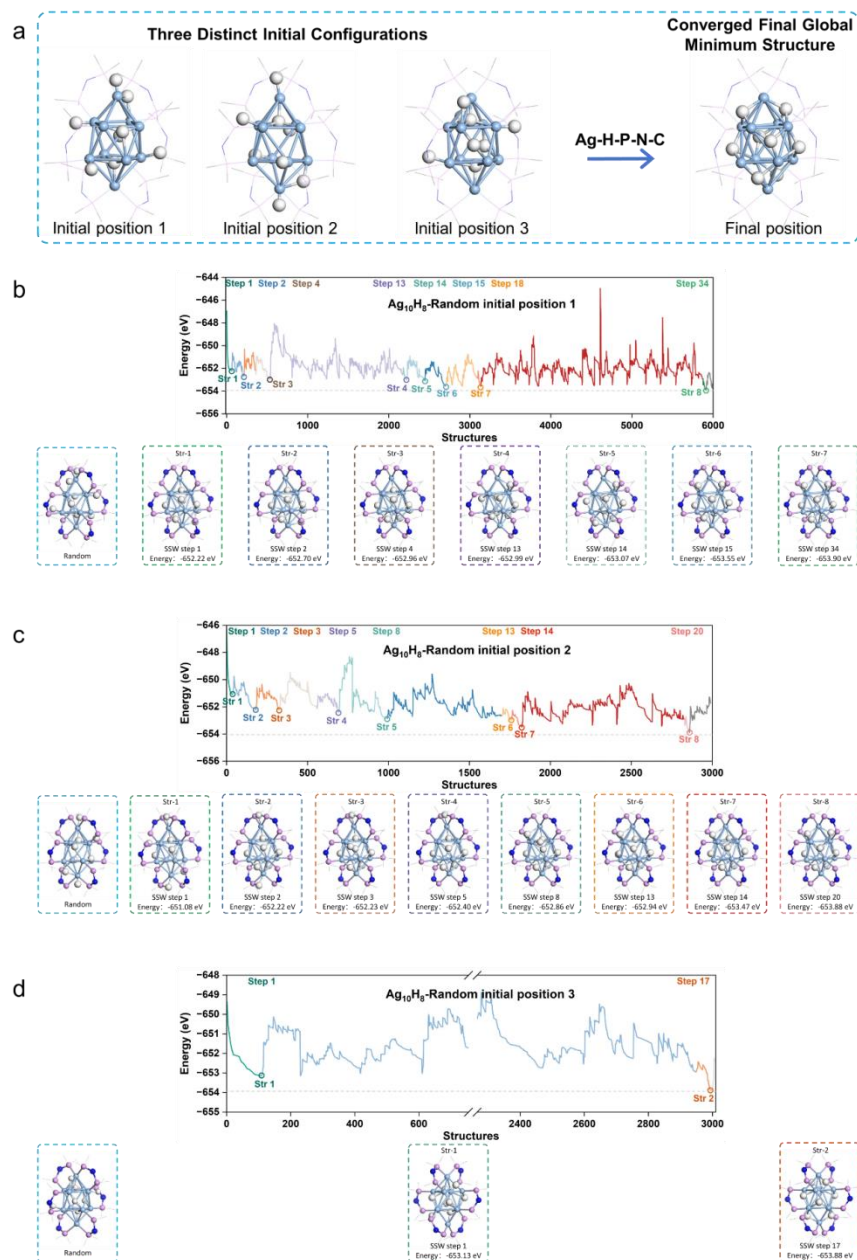


Fig. R9. (a) Using the same three independently randomized hydride positions as those adopted for SSW global structure optimization with the general Ag-H-S-C-P-N potential in Figure S6, SSW global structure optimization of Ag_{10}H_8 with the targeted NN potential (Ag-H-P-N-C) converges to the same hydride position. (b-d) Energy profiles and representative candidate structures along the corresponding SSW global optimization trajectories. (Nat. Commun. 2026, <https://doi.org/10.1038/s41467-026-72966-9>, denoted as **Ref. 2**)

We further examined the influence of the initial hydride placement. To evaluate whether the hydride

assignment depends on the initial H placement, three independent SSW-NN hydride-localization calculations were performed using the same single-crystal XRD framework but different randomly generated initial H positions (Fig. R9). The final hydride configurations identified from these independent calculations were consistent. This indicates that, when the neural network potential adequately covers the relevant coordination environments of the target system and its accuracy is controlled within an acceptable range, the SSW-NN global optimization can consistently locate the same global-minimum hydride configuration. Similarly, two independently trained neural network potentials for this cluster system yielded identical hydride assignments, indicating that the predicted hydride positions are not sensitive to empirical tuning. **To further support the reliability of the SSW-NN method for hydride localization, we have added our recently published work (Ref. 2) as an additional reference in the revised manuscript.**

Response to Comment 4B:

We thank the reviewer for raising this important point. We would like to clarify that fixing the experimentally determined heavy-atom framework is not merely a computational simplification, but a deliberate and physically motivated strategy for hydride localization in ligand-protected metal hydride clusters.

In our method, the heavy-atom skeleton is taken directly from the single-crystal XRD structure, which provides the most direct and reliable experimental evidence for the arrangement of heavy atoms in the cluster. Therefore, the purpose of the SSW-NN method is not to re-determine the entire cluster structure, but to locate the most favorable hydride positions within this experimentally established skeleton. Importantly, after the hydride positions are determined by the SSW-NN method, subsequent DFT structural optimization shows that the heavy-atom skeleton remains nearly unchanged compared with the structure before optimization. This further indicates that explicit relaxation of the skeleton during the initial hydride-localization search is unnecessary; instead, introducing such additional degrees of freedom may interfere with the efficient migration of hydrides toward their energetically preferred positions.

From a structural perspective, the empirical atomic radius of Cu is 135 pm, whereas that of H is only

25 pm (www.webelements.com), indicating that the Cu-based cluster skeleton provides sufficient interstitial space for the smaller hydride atoms to explore energetically favorable coordination environments, such as μ_3 -, μ_4 -, μ_5 -, and μ_6 -hydride sites. This fixed-skeleton strategy is also consistent with the recently reported HALOM method for hydride localization in metal hydride nanoclusters, where the heavy-atom skeleton was kept fixed during hydride assignment and subsequent DFT structural refinement (Angew. Chem. Int. Ed. 2026, 65, e202523160.).

In the early development of this workflow, full relaxation of the cluster skeleton was also tested for the $\text{AuCu}_{24}\text{H}_{22}$ system reported in **Ref. 3**, and a reasonable hydride assignment was obtained. However, this feasibility was largely enabled by the high intrinsic rigidity of that particular cluster skeleton. For a general and transferable hydride-localization protocol, simultaneous relaxation of the metal core, ligand shell, and hydride atoms would introduce extensive additional degrees of freedom and increase the complexity of the search space. More importantly, such relaxation could allow unnecessary distortion of the experimentally determined skeleton, thereby complicating the identification of the hydride positions within the SC-XRD-derived structure.

Therefore, the fixed-skeleton treatment is unlikely to compromise the accuracy of hydride localization in the present workflow. Because the heavy-atom skeleton is experimentally established by single-crystal XRD, and the substantial size difference between Cu and H, this treatment provides a well-defined and physically constrained configurational space for hydride exploration while preventing unnecessary deformation of the experimentally determined cluster skeleton.

Comment 5: Discussion on page 14 and Table S5 related to the Bader charges. For some reasons no units are given. These should be in units of the electronic charge integrated within a defined volume. Is this correct?

Response: We thank the reviewer for pointing this out. We have revised Table S5 by explicitly specifying the Bader charge unit as the elementary charge, $|e|$.

Table S5. Bader charge analysis of Cu atoms and hydrides in the Cu_{13}H_6 cluster.

Atom	Bader charge $ e $	Atom	Bader charge $ e $
------	--------------------	------	--------------------

Cu	0.28	Cu	0.28
Cu	0.29	Cu	0.27
Cu	0.23	Cu	0.31
Cu	0.35	H	-0.32
Cu	0.23	H	-0.28
Cu	0.27	H	-0.31
Cu	0.26	H	-0.31
Cu	0.20	H	-0.29
Cu	0.24	H	-0.30
Cu	0.33		

Comment 6: Page 15, lines 235-238. Question: What causes the observed discrepancies between the experimental and theoretical peaks? What can be attributed to the difference of approximately 20 nm between the calculated and experimentally determined peaks?

Response: *We thank the reviewer for raising this important question. To clarify the origin of the discrepancy between the experimental and calculated UV-vis absorption spectra, we performed additional TD-DFT calculations using both the full-ligand model and different exchange-correlation functionals, including PBE0 and CAM-B3LYP. PBE0 is a commonly used hybrid functional for excited-state calculations (Fig. R10), whereas CAM-B3LYP is a range-separated hybrid functional that generally provides a more reliable description of charge-transfer excitations because it treats long-range electron exchange more appropriately.*

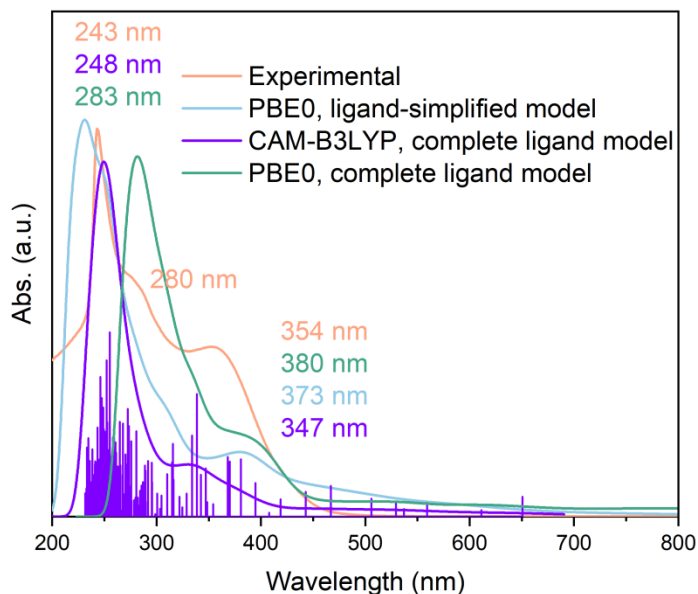


Fig. R10. Experimental and TD-DFT-calculated UV-vis absorption spectra of the Cu_{13}H_6 cluster using different ligand models and exchange-correlation functionals.

The experimental UV-vis spectrum displays absorption band at 244 and 354 nm, accompanied by a shoulder feature around 280 nm. With the full-ligand model, the CAM-B3LYP calculation gives absorption features at approximately 248 and 347 nm, which agree reasonably well with the experimental peaks at 244 and 354 nm. Although the 280 nm shoulder is not clearly resolved in the broadened CAM-B3LYP spectrum, weak transitions with non-zero oscillator strengths are present in this region. These weak transitions can contribute to the shoulder feature after spectral broadening and overlap with the intense absorption band at shorter wavelength.

We further compared the effects of the ligand model and the TD-DFT functional on the calculated spectra. At the same PBE0 level, the simplified-ligand model gives absorption features at approximately 232 and 373 nm, whereas the full-ligand model gives peaks at approximately 283 and 380 nm, indicating that ligand simplification can affect the calculated excitation energies and spectral profile. This is reasonable because the protecting ligands and metal-ligand interface may contribute to or perturb the electronic transitions of ligand-protected metal hydride nanoclusters. In addition, the full-ligand PBE0 and full-ligand CAM-B3LYP spectra differ by about 30 nm even for the same structural model, demonstrating that the calculated UV-vis spectrum is also strongly dependent on the level of TD-DFT

theory.

Therefore, the observed discrepancy between the experimental and theoretical peaks is mainly attributed to the intrinsic sensitivity of TD-DFT UV-vis calculations to the exchange-correlation functional, the ligand model, and solvent effects. The reliability of the hydride-position assignment has been discussed in detail in our response to Comment 4A. We note that ligand simplification is commonly adopted in theoretical studies of ligand-protected metal nanoclusters to reduce computational cost, and such models are useful for qualitative spectral comparison and trend analysis. However, for a more quantitative comparison of peak positions, the full-ligand model and the choice of TD-DFT functional become important, as demonstrated by the additional calculations performed here. We have revised the Supplementary information accordingly and incorporated Fig. R10 into the updated Figure S18.

Reply to Referee #2

Comments: This manuscript reports a structurally precise copper-hydride nanocluster (Cu₁₃H₆) for photocatalytic α -C–H oxidation, combining SCXRD, isotopic labeling (Cu₁₃H₆/Cu₁₃D₆), and machine learning-assisted hydride localization. The concept is timely and potentially impactful. However, several key claims require stronger support. I recommend major revision.

***Response:** We sincerely thank the reviewer for his/her thorough evaluation of our work and insightful comments. Based on the reviewer's suggestions, we conducted additional experiments to provide more direct and quantitative evidence supporting our claims:*

Comment 1: Catalytic mechanism

The proposed SET mechanism via $O_2^{\bullet-}$ is not rigorously demonstrated. Additional evidence (e.g., radical trapping, quantitative EPR) is needed.

***Response:** We sincerely appreciate the reviewers' important and valuable suggestions regarding the verification of superoxide radicals ($O_2^{\bullet-}$) and the single-electron transfer (SET) mechanism mediated by oxygen. We fully agree that characterization evidence is essential to substantiate the proposed catalytic pathway. The superoxide radical scavenging inhibition assay, the redox potentials and free-energy calculations and the quantitative experiment of superoxide radical experiments have been further elaborated below to provide an explanation.*

1. Superoxide radical ($O_2^{\bullet-}$) scavenging inhibition assay

We introduced specific scavengers (p-benzoquinone, BQ) for superoxide radicals ($O_2^{\bullet-}$) into the reaction system. The obvious suppression of catalytic activity after adding BQ was observed (Figure S33). This result which agrees well with EPR measurement (Scheme 1A), clearly proves that ($O_2^{\bullet-}$) acts as a critical intermediate in the reaction.

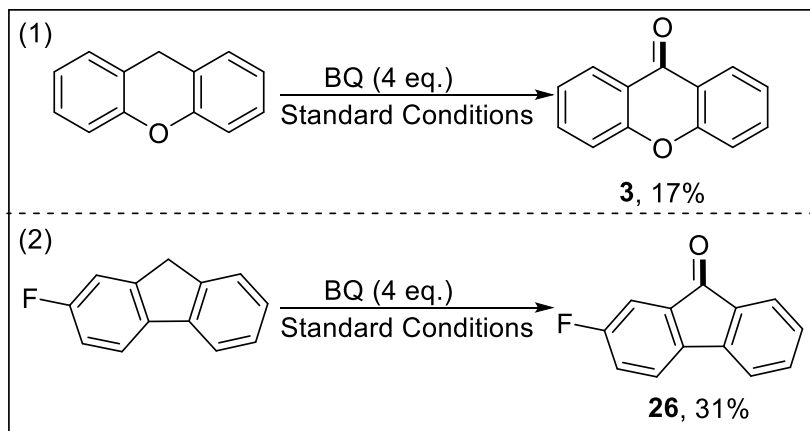
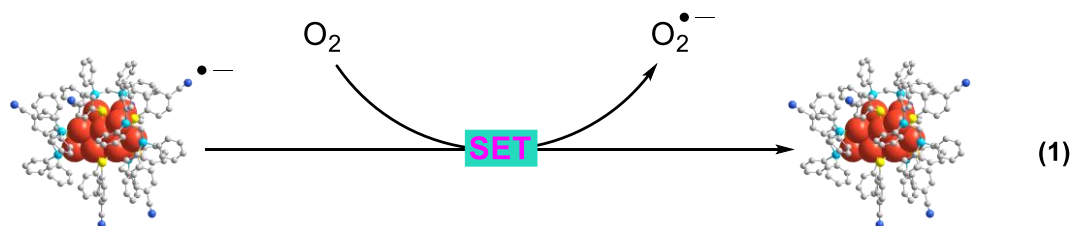


Figure S33. Radical inhibition experiments.

2. The single-electron transfer process between the reduced catalyst Cu_{13}H_6 and molecular oxygen

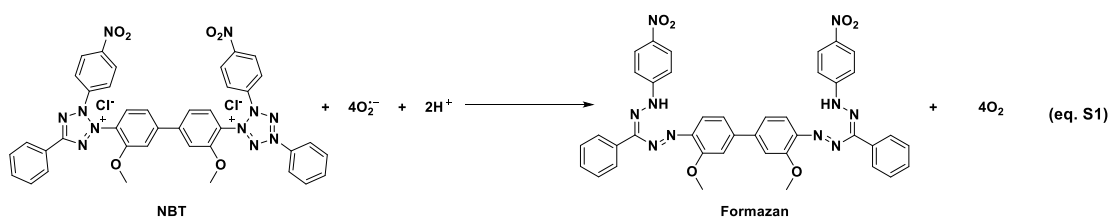


The above process represents the single-electron transfer reaction between the reduced catalyst Cu_{13}H_6 and molecular oxygen, resulting in the formation of the ground-state catalyst Cu_{13}H_6 and the superoxide radical ($\text{O}_2^{\bullet-}$). During this process, O_2 acts as the oxidizing agent, while the reduced form of Cu_{13}H_6 acts as the reducing agent. Here, $E(\text{Cu}_{13}\text{H}_6/[\text{Cu}_{13}\text{H}_6]^{\bullet-}) = -1.5 \text{ V}$, this value is much lower than the reduction potential of O_2 to superoxide radical anion $\text{O}_2^{\bullet-}$ ($E(\text{O}_2/[\text{O}_2]^{\bullet-}) = -0.91 \text{ V}$) (Chem. Rev., 2016, 116, 3029; J. Phys. Chem. B., 2004, 108, 7878). During this reaction process, $\Delta E = E(\text{O}_2/[\text{O}_2]^{\bullet-}) - E(\text{Cu}_{13}\text{H}_6/[\text{Cu}_{13}\text{H}_6]^{\bullet-}) = -0.91 - (-1.5) = +0.59 \text{ V} > 0$. Therefore, the corresponding Gibbs free energy change $\Delta G = -nF\Delta E < 0$, indicating that this single-electron transfer process is thermodynamically feasible.

3. Quantitative experiment of superoxide radical ($\text{O}_2^{\bullet-}$)

We use the nitro blue tetrazolium (NBT) method to quantitatively determine the formation of superoxide radical ($\text{O}_2^{\bullet-}$) in the system. As well documented in literatures, NBT can be oxidized to Formazan by $\text{O}_2^{\bullet-}$ in a quantitative manner (Angew. Chem. 2025, 137, e202502307). The product of Formazan has a characteristic absorption peak in the visible light region, and its formation amount is

quantitatively related to the concentration of superoxide anion radicals ($O_2^{\bullet -}$), with a molar ratio of 4:1 between generated $O_2^{\bullet -}$ and Formazan, as described in the following equation (eq. S1). Therefore, this study uses the change in absorbance of Formazan as an indirect indicator for the generation of $O_2^{\bullet -}$. To satisfy the solubility requirements of both compounds in this catalytic reaction system, we employed a mixed solvent system consisting of DMF and water in a 5:1 volume ratio.



nm using a UV-vis spectrophotometer (Figure S36). Based on these measurements, a standard curve of formazan concentration versus absorbance was plotted (Figure S37), yielding the equation: $y = 0.10531x - 0.00508$.



Figure S35. The Formazan standard solution (A), and the gradient dilution solution pictures (B).

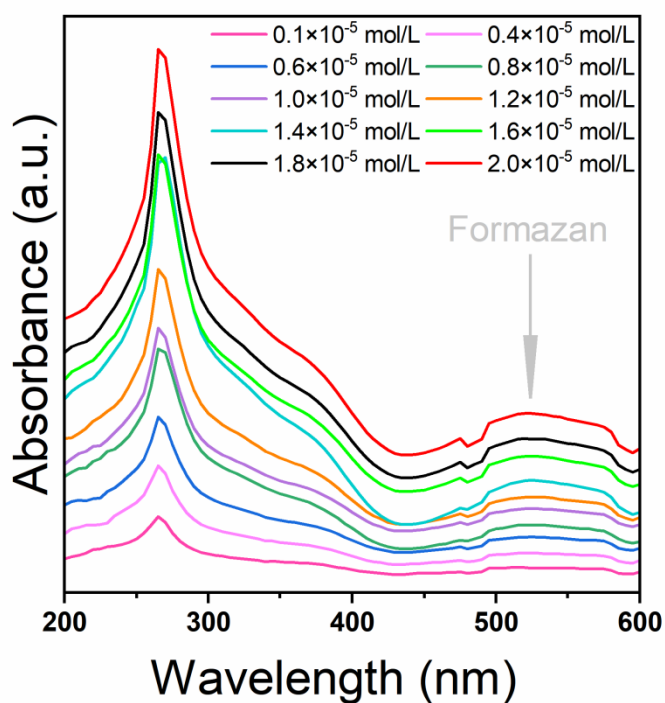


Figure S36. UV-vis spectra of the Formazan gradient dilution solution.

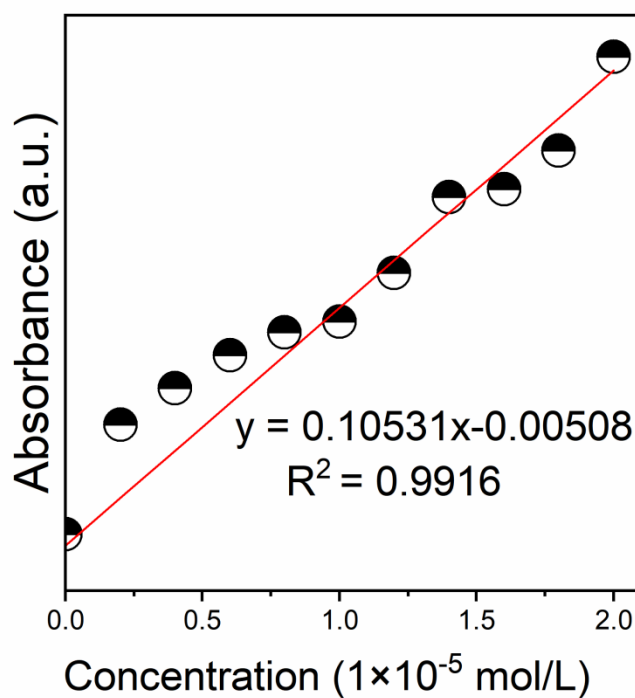


Figure S37. The concentration-absorbance standard curve of Formazan.

③ **Quantitative testing.** First, a 2.0×10^{-5} M NBT solution (DMF: $H_2O = 5: 1$) was prepared. By using the standard solution described above as the reaction solvent, 3 mL of the reaction mixture was filtered through a filter at specified time intervals. The absorbance of the solution was then measured at 530 nm using a UV spectrophotometer (Figure S38). Quantification of $O_2^{\bullet-}$ revealed that its concentration remained low in the absence of $Cu_{13}H_6$. However, when $Cu_{13}H_6$ was present in the system, the absorbance at a wavelength of 530 nm significantly increased over time (Figure 39).

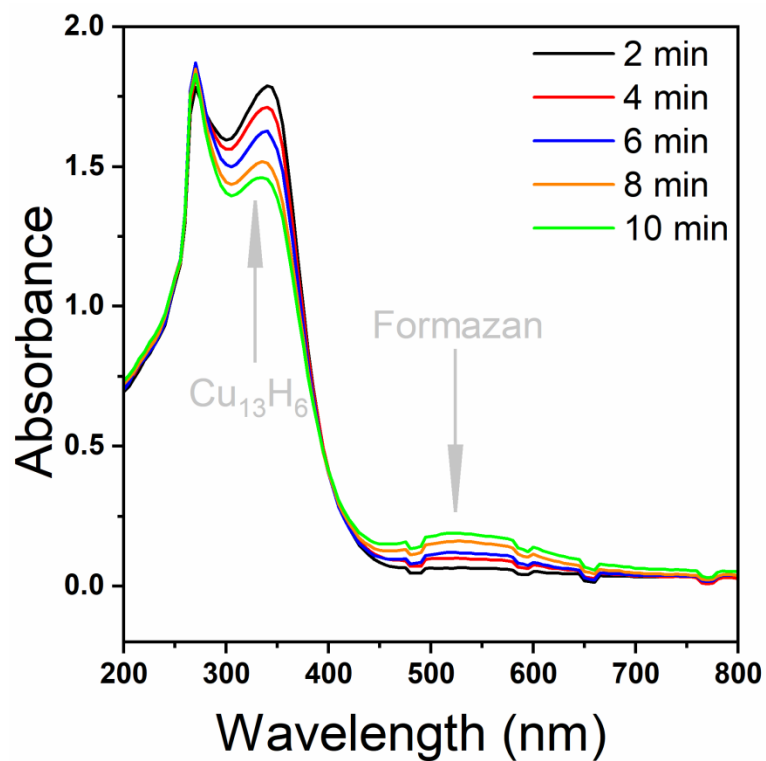


Figure S38. Absorption spectrum of the system at a wavelength of 530 nm at different time.

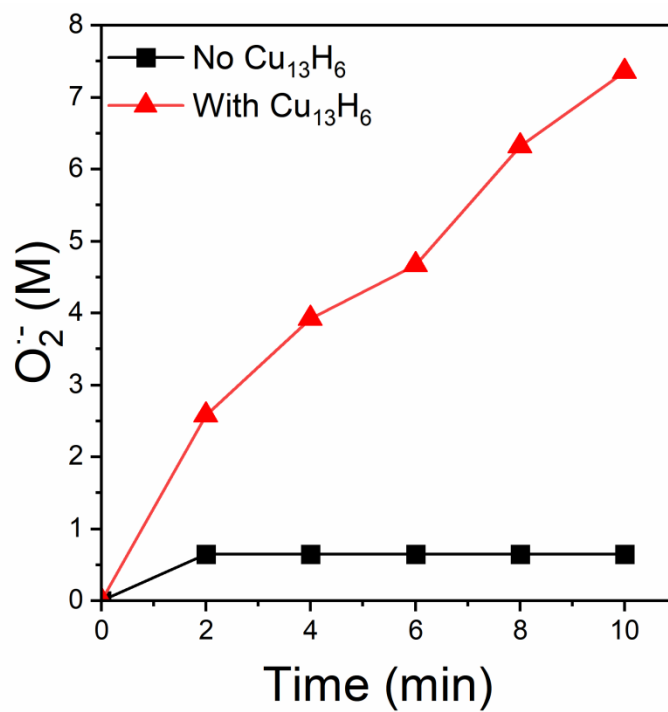


Figure S39. Quantitative experiments of $\text{O}_2^{\bullet-}$.

Comment 2: Catalyst stability

Structural integrity under catalytic conditions is insufficiently established. ESI-MS before/after catalysis (Fig. S17) is suggestive but not conclusive.

Response: We concur with the reviewer's assessment that the structural integrity of the catalyst under catalytic conditions has not yet been fully and conclusively verified. The ESI-MS results before and after the reaction (Figure S19) provide only preliminary indirect evidence and are insufficient to strictly confirm that the catalyst maintains structural stability during the reaction process. To further verify the structural stability of the catalyst, we performed additional characterization after the catalytic process, including UV-vis and XPS. In the revised manuscript, we added corresponding discussions and new data, and incorporated the relevant data and discussions into the supporting information of the revised version (Figures S20-S22).

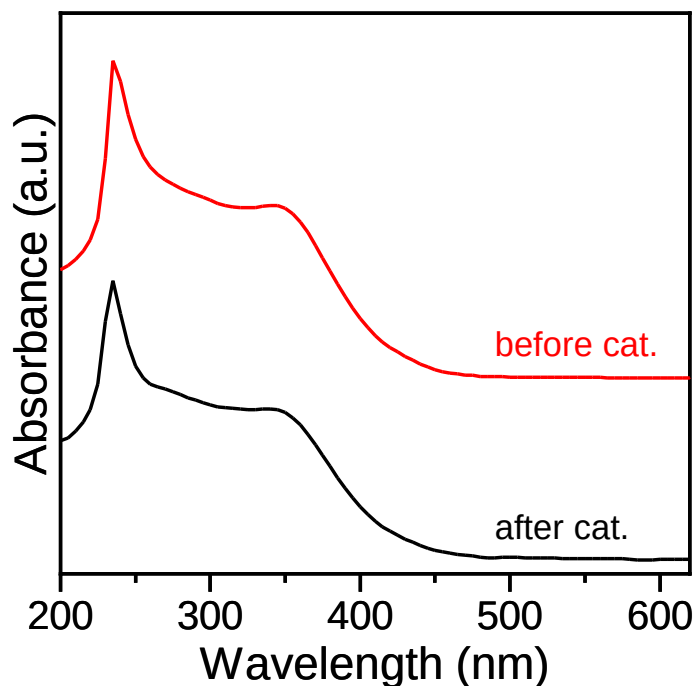


Figure S20. UV-vis absorption spectra of Cu_{13}H_6 nanocluster before and after catalysis.

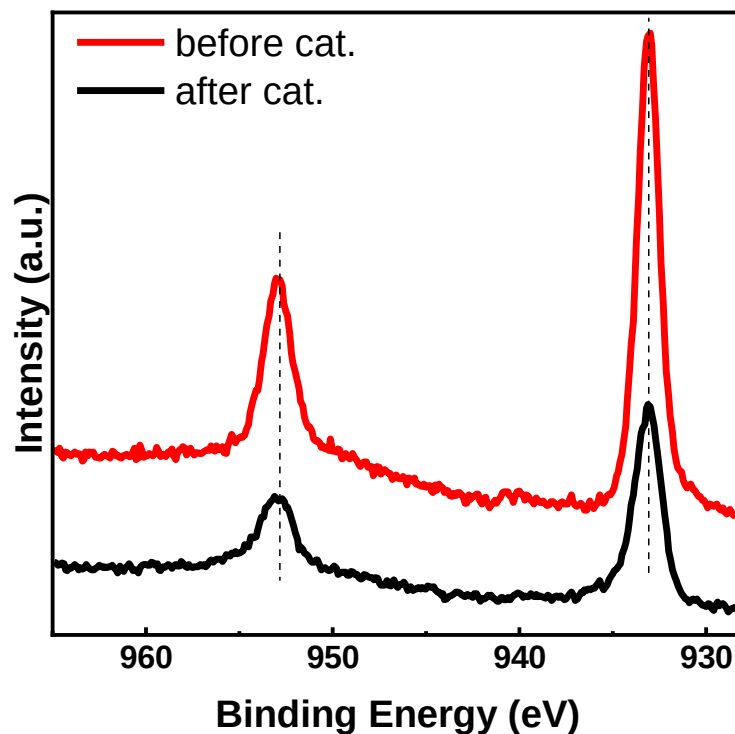


Figure S21. XPS of Cu 2p spectroscopy of Cu_{13}H_6 nanocluster before and after catalysis.

Comment 3: Structure–activity relationship

No comparison with related clusters or non-hydride analogues is provided, leaving the role of hydrides unclear.

Response: We fully agree that the absence of comparison with related non-hydride clusters makes it difficult to determine the function of the hydrogenated ligands. Therefore, we successfully achieved the precise synthesis of a non-hydride Cu_{13} reported previously (*J. Am. Chem. Soc.* 2020, 142, 14495) and compared their catalytic behavior with the hydrogenated Cu_{13} nanoclusters reported in this work. The specific content is as follows:

1. Crystal synthesis

Copper nitrate (39 mg) was dissolved in a mixed solvent containing 1 mL acetonitrile and 1 mL methanol. Then, a methanol solution (0.5 mL) of NaSbF_6 (25 mg) was added to the above mixture. Subsequently, 6-methylbenzoxazole-2(3H)-thione ligand (17 mg) dissolved in 1 mL acetonitrile was introduced. Finally, freshly prepared NaBH_4 solution (50 mg in 1 mL methanol) was added as the reducing

agent. Centrifugation results in the formation of the supernatant. Yellow crystals were obtained by slow diffusion of diethyl ether into the mother liquor after a week.

2. Crystal structure determination

The molecular structure of the obtained yellow crystals was confirmed by single-crystal X-ray diffraction (Fig. R11). Single-crystal analysis reveals that the crystal comprises 13 copper atoms and 12 thiol ligands, agreeing well with that reported previously (*J. Am. Chem. Soc.* 2020, 142, 14495).

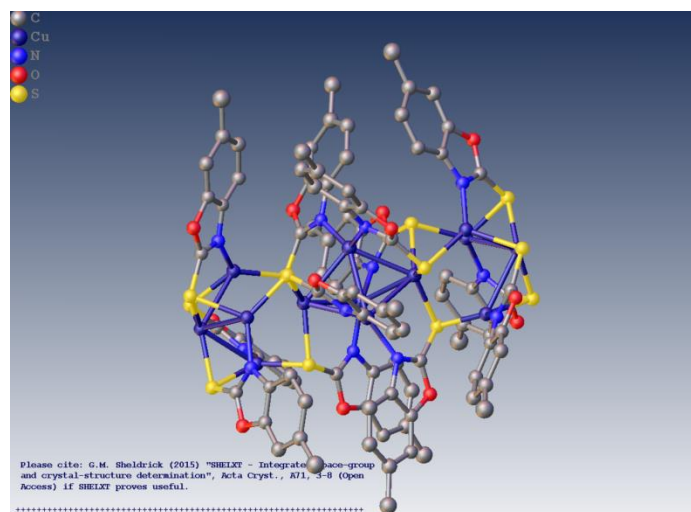


Fig. R11. SCXRD of a non-hydride Cu_{13} nanocluster.

3. Catalytic test

When the cluster was employed as a catalyst under standard conditions, 20 mg of product was obtained after a 12 h reaction period, corresponding to a calculated yield of 51%. However, we observed that the cluster decomposed after catalysis, as evidenced by the solution turning from red to blue. Based on the experimental results and catalytic performance, it is plausible that the hydrogen-donating ligands enhanced the stability of the copper nanoclusters.

Minor Comments

Soften claims such as “unambiguously determined.”

Response: We agree with the reviewer. Regarding potential absolute statements in the text, a systematic review of the entire content was conducted, and corresponding revisions were made to the relevant sentences in the revised version. We have toned down all absolute statements such as “unambiguously

determined”, and have replaced them throughout the manuscript with more moderate expressions. The revised sentence has been highlighted in rose red in the revised draft for easy review. The details are listed as below:

1. On line 31, change "unambiguously determined" to "determined".
2. Lines 31-33, replace “Crucially, the positions of the hydride ligands were resolved via an advanced machine learning potential-driven approach, enabling localization without the need for neutron diffraction data” with “Crucially, our advanced machine learning potential method tentatively locates hydride ligand positions, potentially lessening reliance on neutron diffraction data”.
3. Lines 38-39, replace “This work achieves precise structural resolution of Cu_{13}H_6 ” with “This work allows tentative structural determination of Cu_{13}H_6 ”.

Improve figure clarity and provide error bars.

Response: We sincerely thank the reviewers for these valuable suggestions. We have comprehensively polished the visual quality of all figures in the revised manuscript. Specifically, we optimized Figures 1-6, with a focus on enhancing image resolution and improving clarity. Concurrently, for Table 2 and Scheme 1, we adjusted the spacing of the chemical structures, optimized the color of the symbols, and reorganized the overall layout in a standardized manner. These modifications effectively alleviated spatial congestion in the original images, resolved the overcrowding issue, and improved chart readability. All updated Figures 1-6, Table 2, and Scheme 1 are provided in the revised manuscript. Furthermore, in the supplementary catalytic cycle experiment, we included error bars representing the standard deviation, as follows specifically.

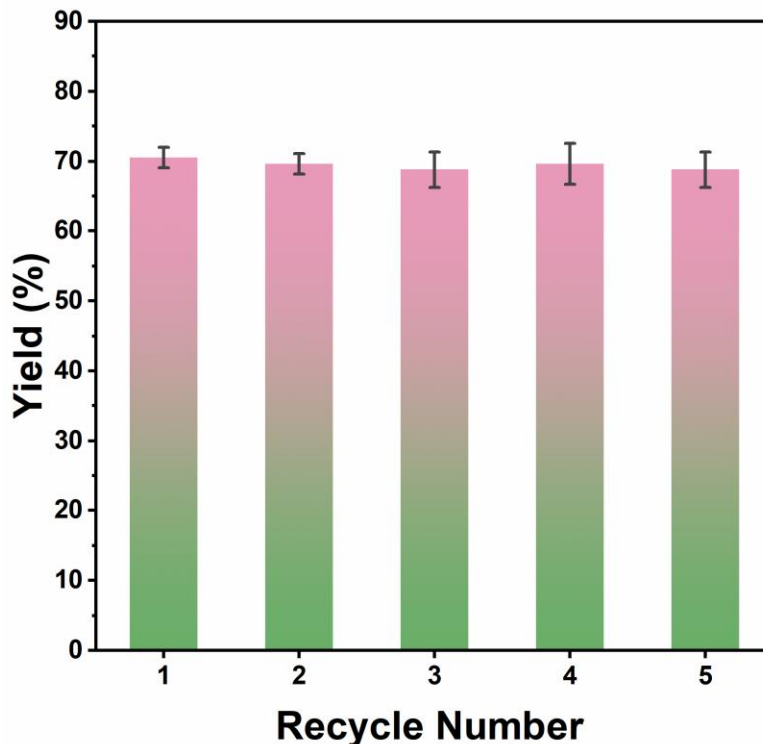


Figure S22. Recycled Cu_{13}H_6 -catalyzed oxidation reaction. Error bars represent the mean $\pm$ S.D. (standard deviation) calculated from three independent catalytic experiments.

Clarify absence of counterions in the crystal structure.

Response: We thank the reviewer for this comment. In lines 102-103 of the original manuscript, we explain why no counterions were observed in the crystal structure: “This absence may be attributed to either disordered anions that could not be resolved or the lack of firm incorporation of anions into the lattice”. In response to the reviewers' concerns regarding the identity of the counterions, a systematic analysis was conducted. Based on the composition of the precursor materials, it was initially hypothesized that possible counterions could be the hexafluoroantimonate anion (SbF_6^-) or the nitrate ion (NO_3^-). However, in the control reaction system without the addition of sodium hexafluoroantimonate, the target Cu_{13}H_6 clusters were still successfully synthesized, indicating that SbF_6^- is not essential for the formation of the structure. Based on the results of electrospray ionization mass spectrometry (ESI-MS) (Figure S12), we clearly detected the characteristic peak of NO_3^- in the crystal samples. Therefore, the missing counterion in the crystal structure refinement was confirmed to be the nitrate ion (NO_3^-).

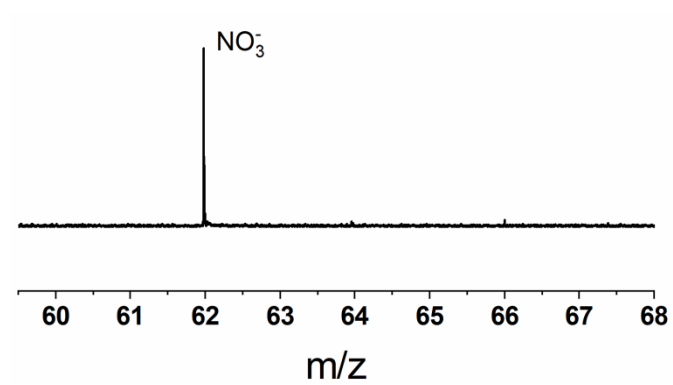


Figure S12. ESI-MS of Cu_{13}H_6 in negative mode showing the peak of NO_3^- .

Reply to Referee #3

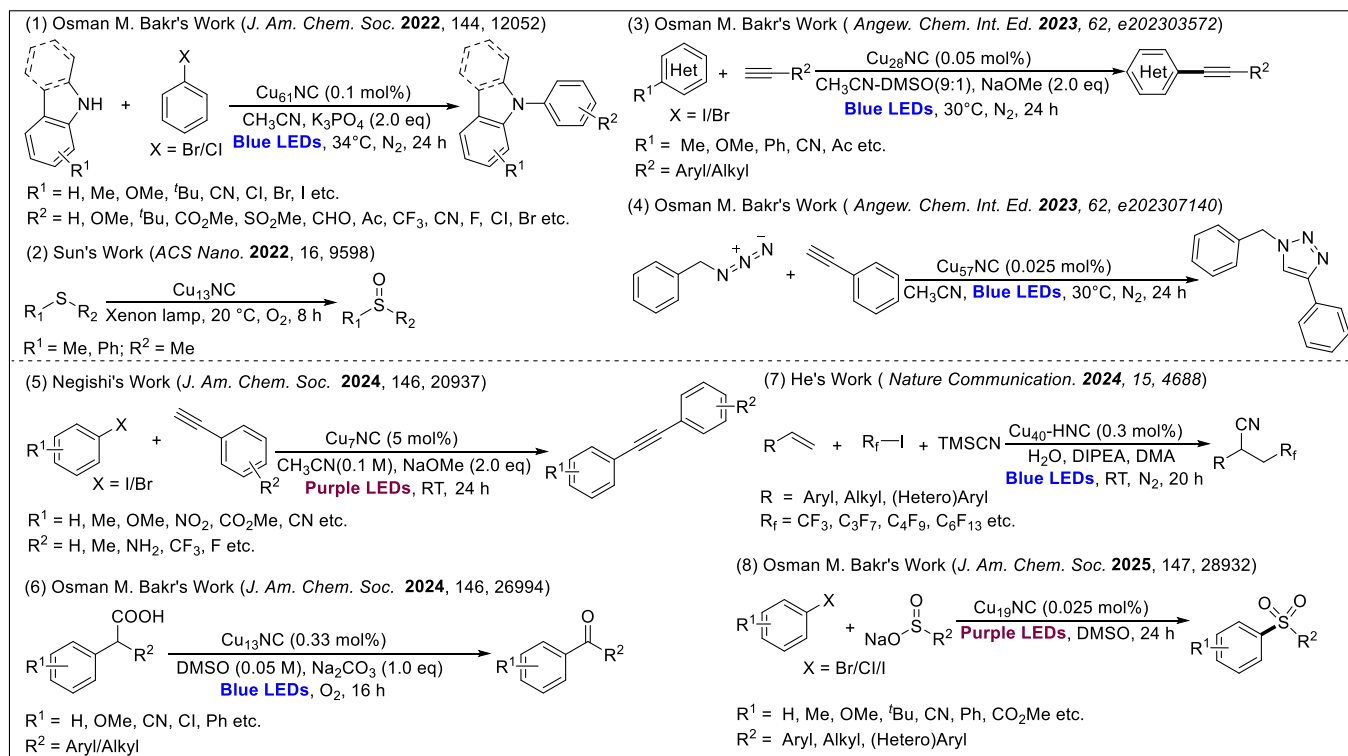
Comments: In this manuscript, the authors report the synthesis, comprehensive structural characterization, and photocatalytic performance of a Cu₁₃ nanocluster toward α -C-H bond oxidation reactions. Nevertheless, extensive prior research has already investigated analogous catalytic reactions, and the present work fails to deliver sufficiently novel, groundbreaking results or distinctive mechanistic insights to meet the stringent publication criteria for Nature Communications. Given the lack of adequate innovation and unique contributions relative to existing literature, I recommend that this manuscript be considered for publication in a more specialized alternative journal.

Response: *We sincerely appreciate the reviewers' critical and constructive comments on our manuscript. We fully acknowledge the high novelty standards of Nature Communications. To address this, we have systematically compared our study with the existing literatures, highlighting the unique and previously unreported advances in our work to specifically address concerns regarding insufficient innovation, as detailed below.*

1. The research focus in metal nanocluster chemistry has gradually shifted from the synthesis of novel structures to the development of their functional applications. Among them, photoinitiated catalysis by metal nanoclusters for organic synthesis has become an important frontier in this field. However, research on metal nanoclusters in photocatalytic organic transformation remains at an initial stage of exploration overall. Most reported photocatalytic reactions driven by light that involve clusters are classical transformations already achievable by established photocatalytic systems (such as transition metal complexes, organic dyes, or semiconductor materials). The range of applicable original substrates and the development of new reaction modes are rather insufficient.

We have systematically sorted out the research progress of copper nanoclusters in the field of photo-organic catalysis in recent years (see below). The results indicate that the well-defined copper nanoclusters exhibit excellent photocatalytic activity and selectivity, and possess significant potential for key transformations such as carbon-carbon and carbon-heteroatom bond formation. It is noteworthy that the existing literature contains few reports on the application of such precisely structured copper nanoclusters to the photo-oxidation reaction at the α -C-H site. More importantly, our study is the first

to identify and confirm the potential of a specific type of copper-hydride nanocluster species in the selective defluorination of monofluorinated aromatic hydrocarbons, deuterium labeling, and photo-promoted coupling dehydrogenation reactions; it highlights a promising yet unexplored research frontier. In the future, copper nanocluster-based photocatalytic systems will be designed for highly challenging or novel organic transformations, which hold significant scientific value and broad application potential.



2. Although several recent studies have shown that light energy can boost nanocluster catalysis, a clear definition for this field has not yet been proposed. In this work, **we introduce a new concept called “photocluster catalysis”**. This definition is important because it not only fills a gap in the scientific language but also provides a clear framework that links the unique electronic structure of nanoclusters to how they behave when excited by light. By clearly defining this interdisciplinary area, our work gives researchers a useful guide for separating heat-related effects from non-thermal ones, which is key to designing better catalysts in the future. Ultimately, we believe that giving this field the distinct name of 'photocluster catalysis' will help speed up research progress and encourage new, customized ways to make the most of light-matter interactions at the nanoscale. In doing so, we hope to turn what were once

scattered, isolated findings into a focused and design-driven field of study.

We respectfully request that the reviewer re-evaluate and reconsider our manuscript. The findings of this study provide valuable guidance for the investigation of photocatalysis-mediated organic synthesis using copper nanoclusters, and offer clear reference value for advancing this field. We, together with Reviewers 1 and 2, who have provided very positive feedback, are confident that these results will prove valuable for future research.

Comment 1: Bond length reporting does not comply with IUPAC crystallographic standards. All bond lengths should be reported with three decimal places and the estimated standard deviation given in parentheses.

Response: *We sincerely thank the reviewers for their detailed suggestions regarding the description of bond lengths. We fully concur that the reported bond length does not comply with the IUPAC crystallographic standards. We systematically rechecked the bond length data in the main text and all supplementary tables. All bond length values are uniformly retained to three decimal places, with the corresponding standard uncertainties (expressed as estimated standard deviations) provided in parentheses, ensuring that the data presentation is rigorous and standardized. All modifications are marked in the revised manuscript.*

Comment 2: The overall visual quality of figures requires thorough polishing. In particular, Table 2 and Scheme 1 are severely overcrowded, with densely packed chemical structures that impair readability.

Response: *We sincerely thank the reviewers for their valuable suggestions and we fully agree with this comment. We have comprehensively polished the visual quality of all figures in the revised manuscript. Specifically, we optimized Figures 1 through 6, with a focus on enhancing image resolution and improving clarity. Concurrently, for Table 2 and Scheme 1, we adjusted the spacing of the chemical structures, optimized the color of the symbols, and reorganized the overall layout in a standardized manner. These modifications effectively alleviated spatial congestion in the original images, resolved the overcrowding issue, and improved chart readability. All updated Figures 1-6, Table 2, and Scheme 1 are provided in the*

Comment 3: The manuscript lacks recycling tests and post-catalysis structural characterization. Post-catalytic characterization using techniques such as XPS and UV–vis is necessary to confirm whether the cluster retains its integrity after reaction.

Response: We greatly appreciate the reviewer’s constructive suggestions. To further confirm the catalytic stability and structural durability of the cluster catalyst, we conducted recycling experiments (Table R1 and Figure S22). Moreover, post-catalytic characterization, including XPS and UV-Vis measurements, was carried out to verify the structural integrity of the cluster catalyst after the reaction (Figure S20 and S21). The corresponding results and discussion have been integrated into the revised manuscript.

Recycling Experiments

To a 25-mL schlenk tube under air atmosphere were added xanthene (37 mg, 0.2 mmol), Cu_{13}H_6 (10 mg, 0.003 mmol), DBU (10 μL , 0.067 mmol) and DMF (3.0 mL) sequentially. The reaction mixture was stirred at room temperature under blue LED irradiation for 12 hours. Cu_{13}H_6 was precipitated by the addition of *n*-hexane (25 mL) to the solution. A following centrifugation gave Cu_{13}H_6 nanocluster. The remaining mixture was concentrated under vacuum. The crude product was purified by column chromatography isolation on silica gel via gradient elution with hexane to hexane/ethyl acetate (40:1 ~ 20:1) to give the product **3**. The recovered Cu_{13}H_6 catalyst was used for the recycling experiments.

Table R1. Cu_{13}H_6 recycling experiment (three experiments for each recycling).

Recycle number	1	2	3	4	5
Isolated 3 (mg)	28, 28, 27	28, 27, 27	28, 27, 26	28, 26, 28	28, 27, 26
Average yield (%)	71	70	69	70	69

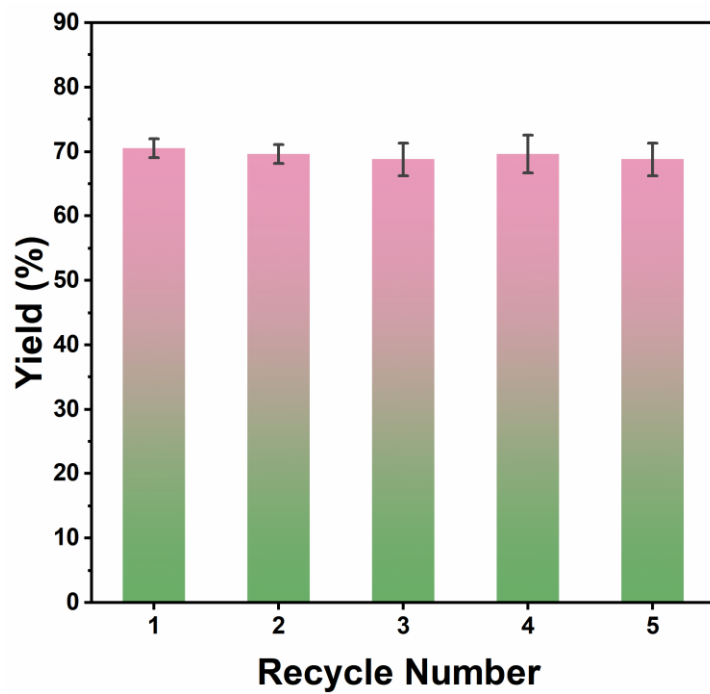


Figure S22. Recycled Cu_{13}H_6 -catalyzed oxidation reaction. Error bars represent the mean $\pm$ S.D. (standard deviation) calculated from three independent catalytic experiments.

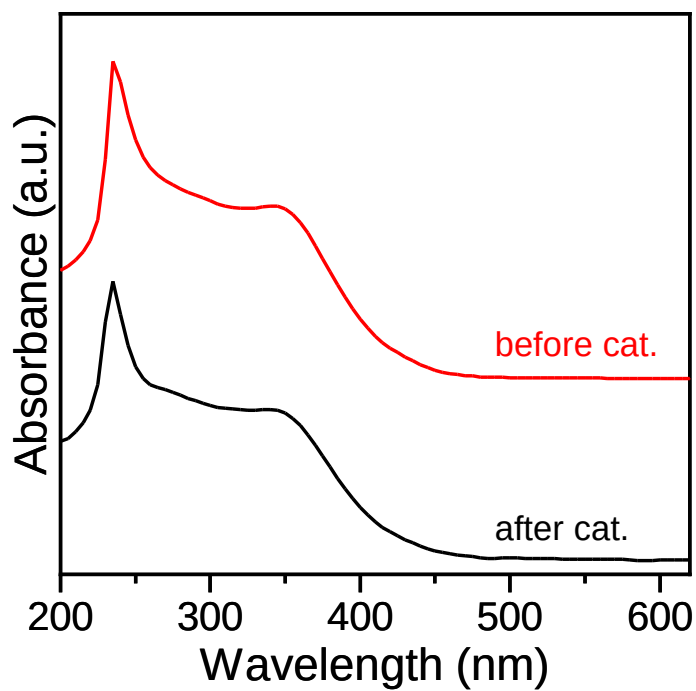


Figure S20. UV-vis absorption spectra of Cu_{13}H_6 nanocluster before and after catalysis.

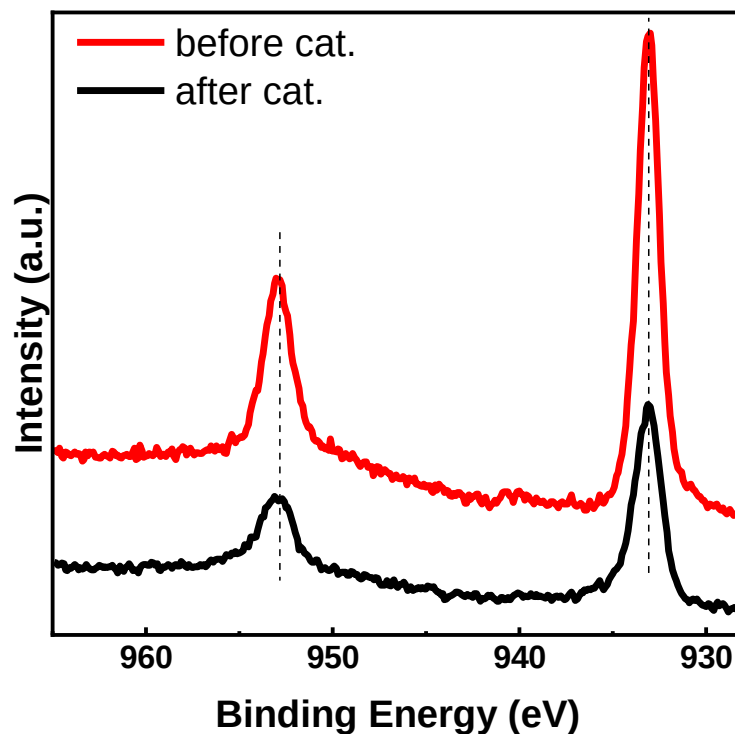


Figure S21. XPS of Cu 2p spectroscopy of Cu_{13}H_6 nanocluster before and after catalysis.

4. The thermodynamic feasibility of SET between the photoexcited cluster and the substrate (or O_2) should be evaluated, e.g., by determining redox potentials and performing free-energy calculations.

Response: We sincerely thank the reviewers for their valuable comments and constructive suggestions. To thoroughly investigate the thermodynamic feasibility of the single-electron transfer (SET) process, we measured the redox potentials of copper nanoclusters and the reaction substrates. Based on these measurements, we calculated the potential difference (ΔE) between them and the corresponding Gibbs free energy change (ΔG) for the reaction. The results indicate that the SET process tends to proceed spontaneously from a thermodynamic perspective. The specific experimental data and calculation results are as follows:

1. Computation of the redox potential of excited-state Cu_{13}H_6 catalysts

We estimated the redox potential of excited Cu_{13}H_6 using a Rehm-Weller equation (eq. S2), based on the redox potential of the ground-state Cu_{13}H_6 and its triplet energy E_T (Figure S40). The obtained values are shown in the Table S9. The thermodynamic feasibility assessment of single-electron transfer (SET)

processes was shown in the following sections.

$$O_1[\text{Cu}_{13}\text{H}_6]^* \text{ (V)} = O_1[\text{Cu}_{13}\text{H}_6] - 1240/\text{EW} \quad \text{eq. S2}$$

$$R_1[\text{Cu}_{13}\text{H}_6]^* \text{ (V)} = R_1[\text{Cu}_{13}\text{H}_6] + 1240/\text{EW}$$

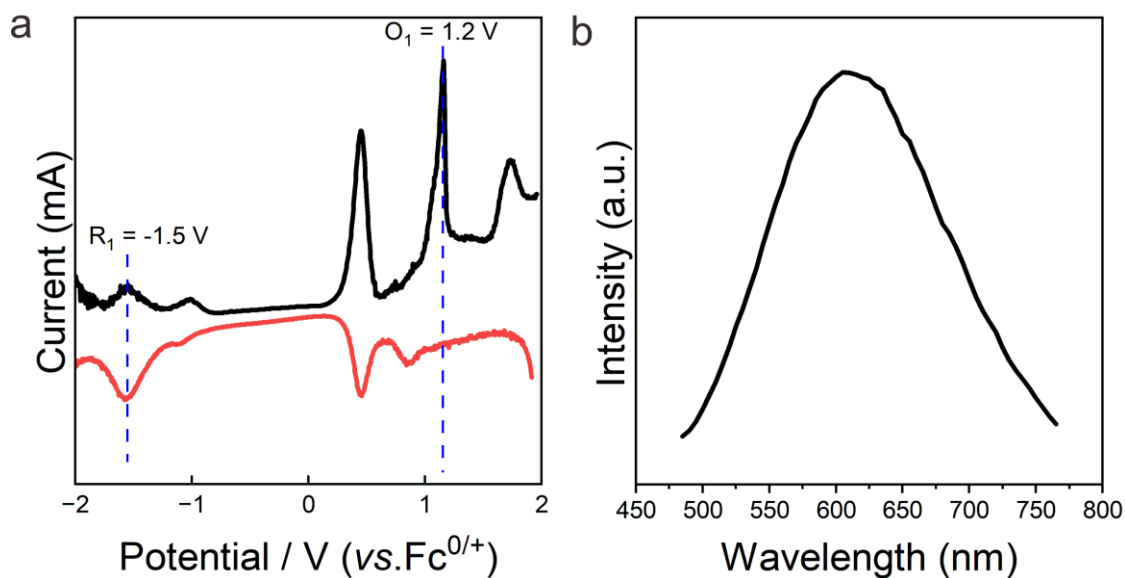
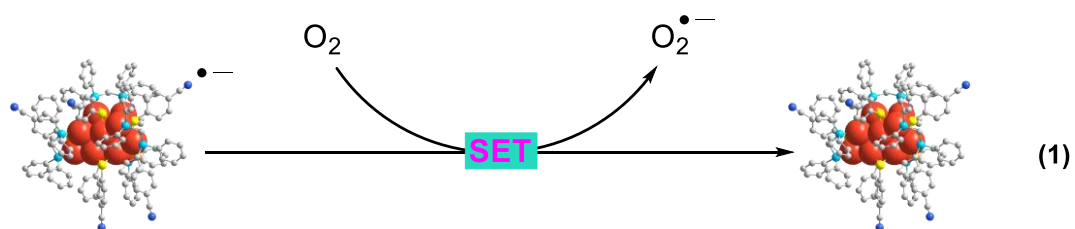


Figure S40. DPV (a) and emission spectra (b) of $[\text{Cu}_{13}\text{H}_6]$ (solvent = DCM). Note: The DPV test was always in argon atmosphere.

. Calculation of oxidation potential of $[\text{Cu}_{13}\text{H}_6]^*$.

Emission Wavelength, EW (nm)	$O_1[\text{Cu}_{13}\text{H}_6]$ (V)	$O_1[\text{Cu}_{13}\text{H}_6]^*$ (V)	$R_1[\text{Cu}_{13}\text{H}_6]$ (V)	$R_1[\text{Cu}_{13}\text{H}_6]^*$ (V)
610	1.2	-0.833	-1.5	0.534

2. The single-electron transfer reaction between the reduced catalyst Cu_{13}H_6 and molecular oxygen



Process (1) represents the single-electron transfer reaction between the reduced catalyst Cu_{13}H_6 and molecular oxygen, resulting in the formation of the ground-state catalyst Cu_{13}H_6 and the superoxide radical ($\text{O}_2^{\bullet-}$). During this process, O_2 acts as the oxidizing agent, while the reduced form of Cu_{13}H_6 acts as the reducing agent. Here, $E(\text{Cu}_{13}\text{H}_6 / [\text{Cu}_{13}\text{H}_6]^{\bullet-}) = -1.5 \text{ V}$, this value is much lower than the reduction potential of O_2 to superoxide radical anion $\text{O}_2^{\bullet-}$ ($E(\text{O}_2 / [\text{O}_2]^{\bullet-}) = -0.91 \text{ V}$). During this reaction process, $\Delta E = E(\text{O}_2 / [\text{O}_2]^{\bullet-}) - E(\text{Cu}_{13}\text{H}_6 / [\text{Cu}_{13}\text{H}_6]^{\bullet-}) = -0.91 - (-1.5) = +0.59 \text{ V} > 0$. Therefore, the corresponding Gibbs free energy change $\Delta G = -nF\Delta E < 0$, indicating that this single-electron transfer process is thermodynamically feasible.

3. The single-electron transfer reaction between the reduced catalyst Cu_{13}H_6 and the substrate **26**

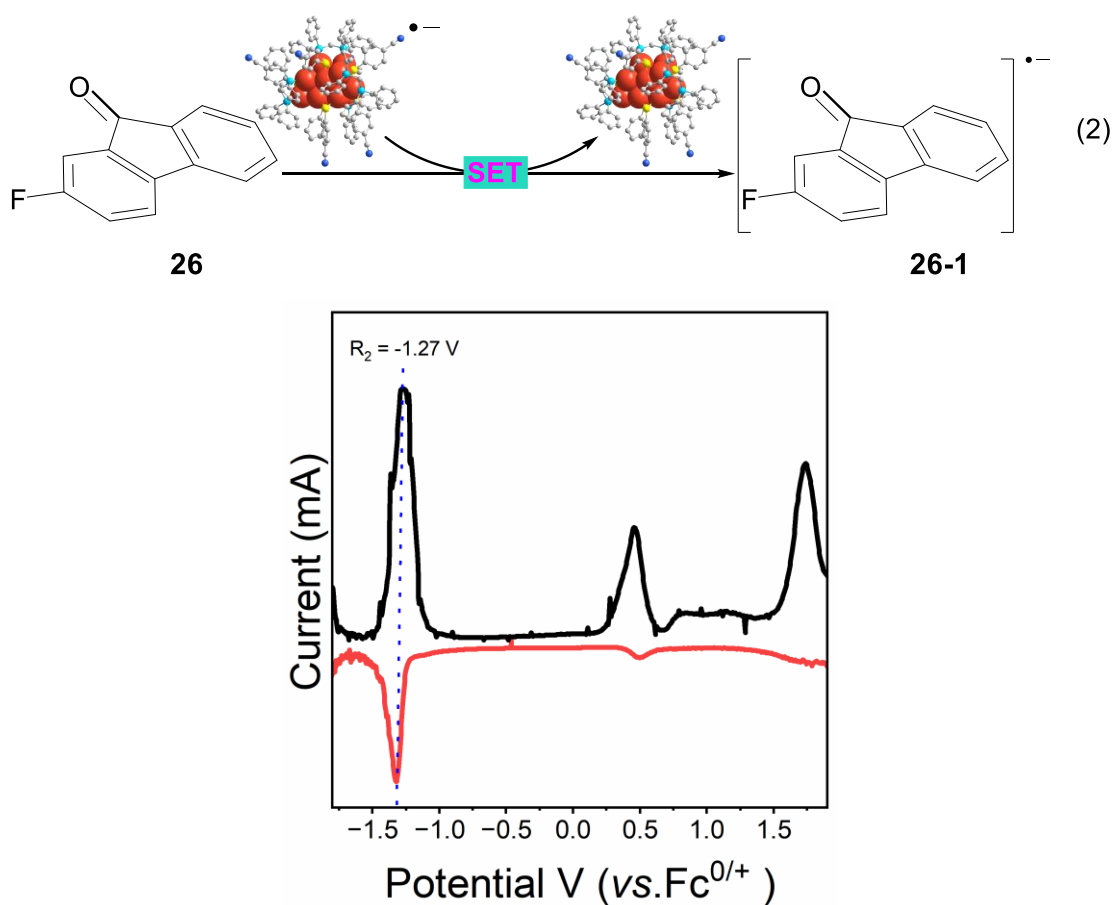


Figure S41. DPV of **26**.

Process (2) is a single-electron transfer reaction between the reduced catalyst Cu_{13}H_6 and the substrate **26**, resulting in the formation of the ground-state catalyst Cu_{13}H_6 and the radical anion (**26-1**). During this reaction process, $\Delta E = E(\text{26} / [\text{26}]^{\bullet-}) - E(\text{Cu}_{13}\text{H}_6 / [\text{Cu}_{13}\text{H}_6]^{\bullet-}) = -1.27 \text{ V} - (-1.5 \text{ V}) = +0.23 \text{ V} >$

0. Therefore, corresponding to the Gibbs free energy change $\Delta G = -nF\Delta E < 0$, it indicates that this single-electron transfer process is thermodynamically feasible.

4. The single-electron transfer reaction between the excited-state catalyst $[\text{Cu}_{13}\text{H}_6]^*$ and xanthene

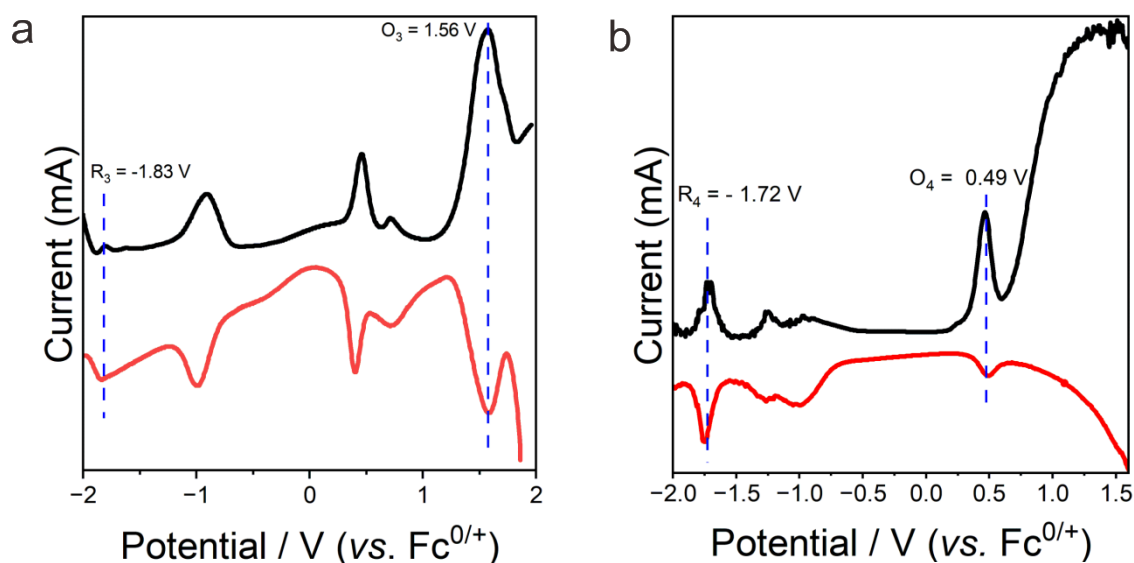
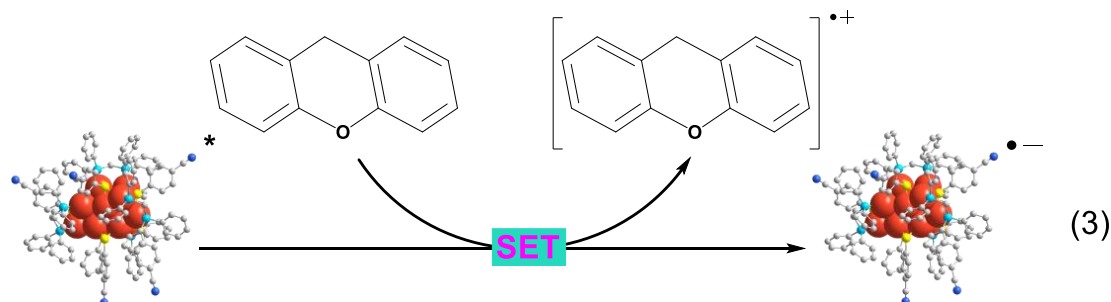


Figure S42. DPV of xanthene(a) and [xanthene+ DBU] (b).

Process (3) involves a single electron transfer reaction between the excited-state catalyst $[\text{Cu}_{13}\text{H}_6]^*$ and xanthene, resulting in the formation of the ground-state catalyst $[\text{Cu}_{13}\text{H}_6]$ and a free radical cation. In this process, the substrate functions as the reducing agent, while the excited state $[\text{Cu}_{13}\text{H}_6]^*$ acts as the oxidizing agent. To assess the feasibility of this process, an optimized oxygen heteroanthraquinone was selected, and its redox potential was measured. The DPV results indicate that the oxidation potential of the oxadiazole (Figure S42a) is significantly higher than the reduction potential of the excited-state catalyst $[\text{Cu}_{13}\text{H}_6]^*$. This process cannot occur spontaneously. Considering that DBU was added in our reaction, we measured the oxidation-reduction potential of the oxadiazole in the presence of DBU, as shown in Figure S42b. This oxidation potential is lower than the reduction potential

of the excited-state catalyst. Here, $\Delta E = E([\text{Cu}_{13}\text{H}_6]^ / [\text{Cu}_{13}\text{H}_6]^{\bullet-}) - E(\text{xanthene} / [\text{xanthene}]^{\bullet+}) = 0.534 - 0.49 = + 0.044 \text{ V} > 0$. Therefore, the corresponding Gibbs free energy change $\Delta G = -nF\Delta E < 0$. This indicates that the single-electron transfer process is thermodynamically feasible.*

Collectively, above spectroscopic characterization and electrochemical experiments have verified the thermodynamic feasibility of the SET process. The relevant experimental results and discussions are clearly presented in the manuscript.

Reply to Referee #3

Comments: I examined the revised manuscript carefully and the suggestions that I provided were studied. However, I am not still satisfied with the claim that the authors made. The author has accomplished several experimental data with sound-performed basic work including substrate expansion and condition screening. Nevertheless, copper-based nanomaterials have long been widely employed in diverse photocatalytic C-H-bond oxidation according to extensive published literature. This work merely extends this well-established catalyst to diphenyl ketone substrates and analogues, without establishing an original catalytic mechanism, distinctive regulation strategy or breakthrough-oriented selectivity-control approach. The study suffers from insufficient innovation and limited incremental scientific contribution. Taken together, the present achievement fails to satisfy the Nature Communication's publication criteria, and rejection is recommended.

***Response:** We appreciate the reviewer for the careful evaluation of our revised manuscript and for pointing out these critical concerns. We fully understand the reviewer's concern regarding the innovation of this work, and we would like to further clarify the novelty of our study.*

*1. Photocatalysis has emerged as a rapidly evolving discipline, unlocking radical-mediated transformations and functionalizations of organic molecules that remain challenging under conventional conditions. Within this landscape, photo-driven catalysis by metal nanoclusters has become a critical frontier. The most compelling attribute of metal nanoclusters as photocatalysts lies in their intrinsic dual function, wherein they act simultaneously as photosensitizers for light absorption and as robust active sites for substrate activation. To rationalize this synergy and establish a unified framework for this burgeoning area, we propose the “**photocluster**” concept, which is a timely and necessary paradigm that bridges photophysics and surface chemistry. We acknowledge the previous emergence of other transformative concepts, such as **single-atom catalysis** and **nanozymes**, and posit that our photocluster framework complements these endeavors, collectively advancing the frontiers of sustainable catalysis.*

2. The selective functionalization of inert benzyl C(sp³)–H bonds remains a cornerstone challenge in synthesis, typically addressed via organic photocatalysts that generate benzyl radicals through single-electron transfer and deprotonation. While this radical-based platform enables diverse downstream transformations (cation/anion capture, radical–radical coupling), it has been largely

confined to molecular photosensitizers.

Our work breaks this paradigm by demonstrating that such mechanistic pathways can be effectively translated to metal nanocluster systems. This not only establishes nanoclusters as viable, tunable substitutes for conventional organic photocatalysts but also substantiates our newly proposed “photocluster” concept- a design philosophy that merges photocatalytic function with nanoscale structural precision. Crucially, this capability is intrinsically absent in traditional copper-based nanomaterials, underscoring a distinct electronic and photophysical advantage of our cluster architecture. By bridging homogeneous photocatalysis and nanomaterial chemistry, our approach opens a new frontier for C–H functionalization, offering expanded structural diversity, tunable redox windows, and potential for recyclable, heterogeneous-like operation in complex molecule construction.

3. The reviewer's comments indicated that this work merely extended the reported catalytic system to dioxynaphthalenes and their analogs as substrates, without proposing any novel catalytic mechanism, unique regulatory strategies, or breakthrough selective control methods. However, in the field of organic chemistry, the same reaction mechanism can often support various organic transformations and be used to construct diverse chemical bonds. Similarly, under the reaction conditions of this study, we observed that this catalytic system simultaneously possesses the potential to achieve cyclopropane opening, defluorination of monofluorinated aromatics, deuteration, and photocatalytic dehydrogenative coupling. By modifying the ligands to regulate the structure of metal nanoclusters, it is expected that a specific type of organic transformation can be further directed and efficiently driven. Therefore, although this work did not propose an original catalytic mechanism, it can still provide important references for research on metal nanocluster-mediated photocatalytic organic synthesis.

Dear Reviewer, we are profoundly grateful for your insightful and constructive feedback. Your expert guidance has illuminated key areas for improvement, and we have made strenuous efforts to address every point with the utmost care. We systematically revisited our methodology and presentation, striving to strengthen the rigor, completeness, and clarity of our work to the best of our ability. We realize these diligent revisions not only enhance the current paper but also offer a valuable roadmap for our future research directions. Thank you wholeheartedly for your time, patience, and the invaluable contributions you have made to our study.

Thank you!