nature communications

Article

https://doi.org/10.1038/s41467-024-51655-5

Practical and regioselective halonitrooxylation of olefins to access β-halonitrates

Received: 6 May 2024

Accepted: 9 August 2024

Published online: 20 August 2024

Check for updates

Xuan Cheng[1,2], Quan Yin[1,2], Yi-Fei Cheng[1,2], Shao-Hua Wu[1,2], Xin-Chang Sun[1,2], De-Yi Kong[1,2] & Qing-Hai Deng[1,2]

Organic nitrates, as effective donors of the signaling molecule nitric oxide, are widely applied in the pharmaceutical industry. However, practical and efficient methods for accessing organic nitrates are still scarce, and achieving high regiocontrol in unactivated alkene difunctionalization remains challenging. Here we present a simple and practical method for highly regioselective halonitrooxylation of unactivated alkenes. The approach utilizes TMSX (X: Cl, Br, or I) and oxybis(aryl-λ^3-iodanediyl) dinitrates (OAIDN) as sources of halogen and nitrooxy groups, with 0.5 mol % $FeCl_3$ as the catalyst. Remarkably, high regioselectivity in the halonitrooxylation of aromatic alkenes can be achieved even without any catalyst. This protocol features easy scalability and excellent functional group compatibility, providing a range of β-halonitrates (127 examples, up to 99% yield, up to >20:1 rr). Notably, 2-iodoethyl nitrate, a potent synthon derived from ethylene, reacts smoothly with a variety of functional units to incorporate the nitrooxy group into the desired molecules.

Alkenes, as one of the most abundant and inexpensive chemicals, offer the advantages of wide availability and low cost for organic synthesis[1]. For instance, ethylene, a key hydrocarbon, is exceptionally affordable with an annual production exceeding 200 million metric tons[2]. Consequently, the direct difunctionalization of alkenes, which allows for the incorporation of two functional groups into the double bond in a single step, represents an immensely powerful strategy for accessing complex molecules, as evidenced by numerous elegant studies[3–5]. A central challenge in these transformations is controlling the regioselectivity of olefin addition, which is further complicated by unactivated alkyl-substituted C=C bonds that exhibit poor regioselectivity due to their limited electronic and steric bias. To address this, several primary strategies have been employed to promote regioselective difunctionalizations of aliphatic olefins (Fig. 1a): (1) auxiliary control[6–8], using directing groups to coordinate and stabilize the metal center in the presumed organometallic species; (2) reagent control[9–11], using specific reagents that dictate the regioselectivity of the reaction; (3) complex catalytic systems[12–17], employing complex catalysts and/or complex reaction conditions. Therefore, the development of simple and efficient strategies to achieve difunctionalization of alkyl alkenes with high regioselectivity represents a challenging and appealing research goal. Furthermore, although various functional groups such as halogens[18–20], hydroxyl[21], OAc[22,23], azido[24,25], amino[26], trifluoromethyl[27], cyano[28], alkyl[29], aryl[30,31], alkynyl[32,33], carboxyl[34,35], etc., have been successfully introduced into double bonds through the difunctionalization of alkenes (Fig. 1a), there is still a significant demand for the introduction of other useful and attractive motifs into alkenes to access their corresponding derivatives.

Organic nitrates, which serve as potent donors of the signaling molecule nitric oxide (NO), find wide application in pharmaceuticals and bio-active molecules[36–38], as exemplified by well-known drugs such as glycerol trinitrate and isosorbide mononitrate. Moreover, hybrid drugs formed by combining the nitrooxy group with drug molecules can exhibit synergistic effects or significantly reduce the side effects of drugs while enhancing their efficacy[39–42]. Despite their importance, there are limited efficient methods for the synthesis of organic nitrates,

[1]The Education Ministry Key Laboratory of Resource Chemistry, Joint International Research Laboratory of Resource Chemistry of Ministry of Education, Shanghai Normal University, Shanghai 200234, China. [2]Shanghai Key Laboratory of Rare Earth Functional Materials, and Shanghai Frontiers Science Center of Biomimetic Catalysis, Shanghai Normal University, Shanghai 200234, China. e-mail: qinghaideng@shnu.edu.cn

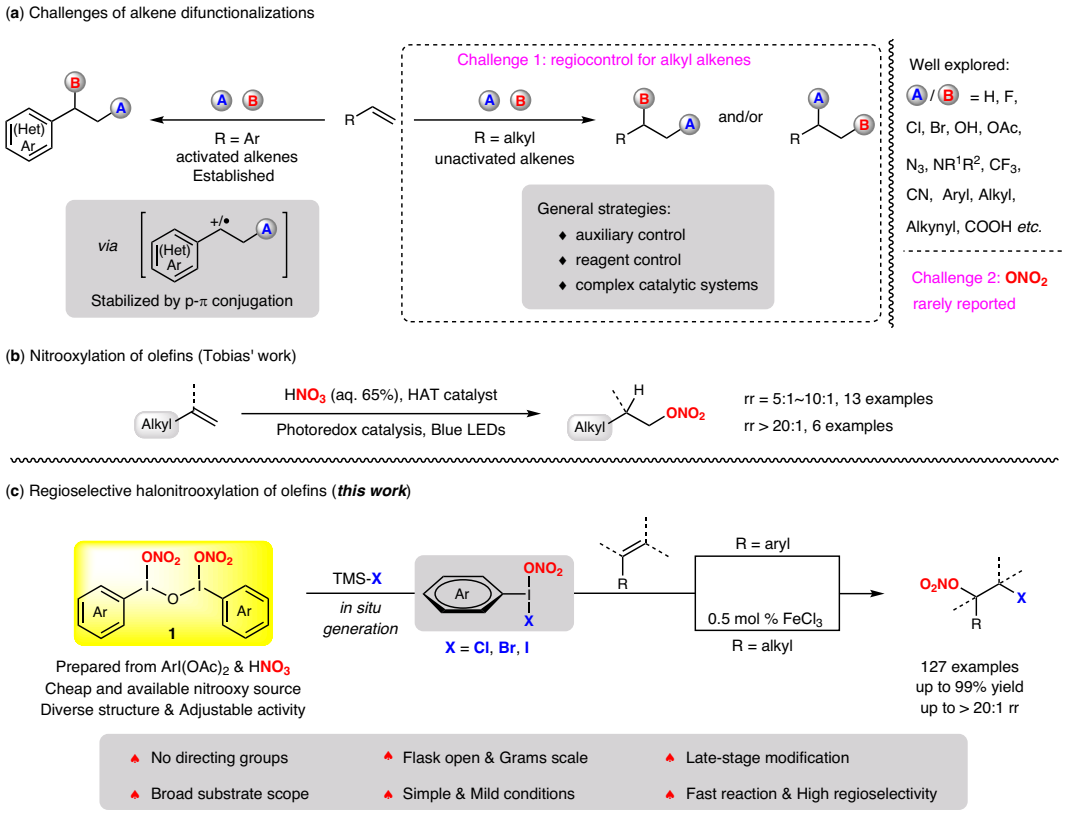

Fig. 1 | Challenges of alkene difunctionalizations and halonitrooxylation of olefins. a Challenges of alkene difunctionalizations. **b** Previous strategy: anti-Markovnikov hydronitrooxylation of α-olefins via photocatalysis **c** This work: regioselective halonitrooxylation of olefins. HAT hydrogen atom transfer, TMS trimethylsilyl.

particularly for the nitrooxylation of alkenes. Previous methods have often relied on metallic or toxic reagents such as mercury nitrate[43], chlorine nitrate[44], thionyl nitrate[45], pyridinium bromide nitrate[46], ceric ammonium nitrate[47,48], silver nitrate[49], or copper nitrate[50] as the nitrooxy source, resulting in harsh reaction conditions or a limited substrate scope. Recently, Tobias and co-workers achieved the hydronitrooxylation of α-alkenes with aqueous nitric acid via visible-light catalysis to produce the corresponding organic nitrates with moderate to high regioselectivities[51] (Fig. 1b). This elegant work represents a significant advancement in the development of synthetic methods for organic nitrates.

On the other hand, halogens are fundamental elements in pharmaceutical and chemical industries[52,53]. For example, over 250 chlorine-containing drugs were approved by the FDA and available on the market in 2019[54], and halogens (such as chlorine, bromine, and iodine) play a crucial role in numerous important chemical transformations[55]. Given their significance and broad utility, developing an efficient and practical method for simultaneously introducing the nitrooxy group and halogen into alkenes using readily available nitrooxylating reagents to achieve regioselective olefin halonitrooxylation remains highly attractive.

As part of our continuing research in hypervalent iodine chemistry[56–60], we have recently introduced a class of highly active noncyclic hypervalent iodine nitrooxylating reagents (**1**), which were easily prepared from aryliodine diacetates and aqueous nitric acid[56]. Additionally, we discovered that the trimethylsilyl (TMS) group can efficiently convert reagents **1** into the corresponding active intermediates[56]. Motivated by these discoveries, herein we report an efficient and regioselective halonitrooxylation of alkenes using the combination of reagent **1** and TMSX (X = Cl, Br, and I) (Fig. 1c). This protocol exhibits remarkable reactivity, high regioselectivity, and broad substrate generality. Styrene derivatives as substrates exhibit complete regioselectivity under catalyst-free conditions, while the halonitrooxylation of alkyl alkenes in the presence of a catalytic amount of $FeCl_3$ yield the corresponding products with high regioselectivities. Notably, this method is easily scalable to gram quantities and is suitable for late-stage modification of drug molecules.

Results

Optimization of reaction conditions

We began the investigation by choosing dodec-1-ene as the model substrate. Initially, dodec-1-ene reacted with nitrooxylating reagent **1a**/TMSCl directly at 0 °C in dichloromethane, getting the excepted product **2** in 82% yield with poor regioselectivity (3.8:1 rr) (Table 1, entry 1). Subsequently, a series of metal salts were evaluated as catalysts (see the details in SI), and it was found that $FeCl_3$ could enhance the regioselectivity (>20:1 rr) but decreased the yield to 42% (Table 1, entry 2). Lowering the reaction temperature to −40 °C increased the yield of product **2** to 76% with 16:1 rr (Table 1, entry 3). Due to the high reactivity of reagent **1a**, we hypothesized that increasing the stability of the reagents **1** might improve the reaction yield by appropriately reducing the reaction rate. Previous studies indicated that incorporating electron-withdrawing groups into the phenyl group of **1** could enhance the stability of reagents **1**[56]. Therefore, we synthesized a series of reagents **1** with electron-withdrawing groups and found that the substituent and its position significantly affected the yield and selectivity of the reaction (Table 1, entries 3–17). Using the 4-CF_3-substituted reagent (**1d**) as the nitrooxy source improved the yield of product **2** to 83% with >20:1 rr (Table 1, entry 6). Surprisingly, when the catalyst loading was reduced to 0.5 mol %, the target product **2** was still obtained in 82% yield with >20:1 rr (Table 1, entry 18).

Substrate scope

Having established the optimal conditions for chloronitrooxylation, we proceeded to evaluate the scope of unactivated alkenes. Mono-, di-,

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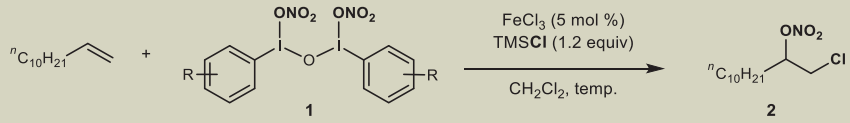
Table 1 | Reaction optimization.[a]



Entry	R	[M]	temp. (°C)	Time	Yield	rr
1	4-H (**1a**)	–	0	2 min	82%	3.8:1
2	4-H (**1a**)	$FeCl_3$	0	2 min	42%	>20:1
3	4-H (**1a**)	$FeCl_3$	−40	10 min	76%	16:1
4	4-Me (**1b**)	$FeCl_3$	−40	10 min	54%	16:1
5	4-F (**1c**)	$FeCl_3$	−40	1 h	55%	>20:1
6	4-CF_3 (**1d**)	$FeCl_3$	−40	2 h	83%	>20:1
7	4-CN (**1e**)	$FeCl_3$	−40	8 h	50%	15:1
8	4-NO_2 (**1f**)	$FeCl_3$	−40	12 h	10%	15:1
9	2-Me,4-NO_2 (**1g**)	$FeCl_3$	−40	3 h	56%	5:1
10	3,5-di-F (**1h**)	$FeCl_3$	−40	1 h	74%	12:1
11	2,6-di-F (**1i**)	$FeCl_3$	−40	1 h	90%	3:1
12	2,4-di-F (**1j**)	$FeCl_3$	−40	1 h	56%	4:1
13	3,4-di-F (**1k**)	$FeCl_3$	−40	1 h	71%	7:1
14	3,4,5-tri-F (**1l**)	$FeCl_3$	−40	1 h	65%	12:1
15	3-CF_3 (**1m**)	$FeCl_3$	−40	2 h	56%	7:1
16	2-CF_3 (**1n**)	$FeCl_3$	−40	2 h	72%	3:1
17	3,5-di-CF_3 (**1o**)	$FeCl_3$	−40	2 h	45%	7:1
18[b]	4-CF_3 (**1d**)	$FeCl_3$	−40	2 h	82%	>20:1

M metal, *temp.* temperature.
[a]Reaction conditions: dodec-1-ene (0.20 mmol), **1** (0.6 equiv), TMSCl (1.2 equiv), $FeCl_3$ (5 mol %), CH_2Cl_2 (2 mL). Yields were for isolated and purified products. Regioisomeric ratios (rr) were determined by ^{1}H NMR spectra of the crude reaction mixtures.
[b]0.5 mol % $FeCl_3$ was used as the catalyst.

tri-, and tetra-substituted unactivated alkenes all underwent the chloronitrooxylation reaction smoothly (Fig. 2a). Simple alkyl alkenes (1-dodecene, 1-tridecene, 1-hexene) afforded the corresponding chloronitrooxylation products (**2**–**4**) with good yields (74–82%) and excellent regioselectivity (>20:1 rr). The allylbenzene and butenylbenzene also got the corresponding products (**5**–**6**) in 64–98% yields with excellent regioselectivity (≥20:1 rr). Substrates bearing numerous substituents such as Br, Cl, OAc, and aldehyde groups were tolerated under the reaction conditions, affording the products (**7**–**13**) in 53–99% yields with high regioselectivities (17:1 rr to >20:1 rr). A series of alkenes containing substituted phenyl esters (with F, Ph, CF_3, Ac, Ms(mesyl), NO_2, Br, I, ^{t}Bu, or Me group) obtained the desired products (**14**–**24**) with regioselectivity ranging from 13:1 to >20:1. Substrates bearing heterocycles such as thiophene and phthalimide achieved the corresponding products (**25**–**26**) in 57–64% yield with 15:1–17:1 regioselectivity. 1,1-Di-, tri-, and tetra-substituted alkenes were compatible, yielding the corresponding products (**27**–**31**) with excellent regioselectivities. Deca-1,9-diene reacted with double equivalent amounts of **1d**/TMSCl to yield the desired product **32** in 62% yield with high regioselectivity. Additionally, the reaction of cyclic alkenes (cyclopentene, cyclohexene, norbornene) in the absence of $FeCl_3$ proceeded stereoselectively, affording the respective *trans*-adducts (**33**–**35**) in 55–78% yields. Interestingly, bromonitrooxylation or iodonitrooxylation of alkenes also proceeded effectively using TMSBr or TMSI instead of TMSCl, yielding several representative products (**36**–**44**) with comparable yields and relatively lower regioselectivities (for **36**–**39**). Surprisingly, ethylene and 1-butene smoothly underwent halonitrooxylation to get the corresponding vicinal halo-nitrates (**45**–**50**) in 63–97% yields.

After investigating the reactions of various alkyl alkenes, we then explored the substrate scope of activated alkenes (Fig. 2b). Aromatic alkenes reacted smoothly with nitrooxylating reagent **1a** and TMSCl at 0 °C without any catalyst, affording the desired products with complete regioselectivities. The reactions performed well with a series of styrenes, regardless of electronic nature (e.g. Me, ^{t}Bu, OAc for electron-rich groups; halogens, NO_2, CF_3, CO_2Me, CN for electron-deficient groups; CH_2Cl, Ph for electron-neutral groups) in the *para* position, affording the corresponding products (**51**–**64**) in 62–89% yields. Styrenes bearing substituents in the *ortho* and *meta* position were also compatible with the protocol to provide the desired products (**65**–**68**) in comparable yields (67–78%). Styrenes containing multiple substituents in the phenyl group reacted well to yield products **69**–**73** in 50–83% yields, and 2-vinyl naphthalene was converted to the corresponding product **74** in 71% yield. Hetero-aromatic alkenes such as 3-vinylbenzofuran and 2-vinylpyridine were also tolerant of the reaction conditions to get product **75** in 21% yield and product **76** in 26% yield, respectively. 1,1-Disubstituted aromatic alkenes were efficient substrates, furnishing products **77**–**80** in 39–94% yields. Although acyclic 1,2-disubstituted substrates only yielded products **81**–**83** with poor diastereoselectivity, cyclic substrates produced *trans*-adducts (**84**–**87**) with excellent regio- and diastereo-selectivity. Moreover, trisubstituted and tetrasubstituted alkenes gave the corresponding products **88**–**90** in 37–79% yields. In addition, *m*-divinylbenzene and *p*-divinylbenzene underwent double reactions by doubling the amount of reagents, affording products **91** and **92** with high regioselectivities and poor diastereoselective ratios, respectively. Fortunately, 1, 3-enynes as the substrates were converted into the corresponding products **93** and **94** in moderate yields. Furthermore, using TMSBr and TMSI instead of TMSCl, the corresponding difunctionalization of styrenes was also conducted well. Several representative substrates underwent the reaction to yield the expected bromonitrooxylation products **95**–**100** and iodonitrooxylation

https://doi.org/10.1038/s41467-024-51655-5

products **101**–**105**, respectively. The structures of products were further confirmed by single-crystal X-ray structure analysis of **61** and **84**.

To highlight the versatility of our protocols, we investigated their applicability to a variety of complex substrates (Fig. 2c). Initially, we synthesized a range of alkenes by introducing styrenyl or aliphatic

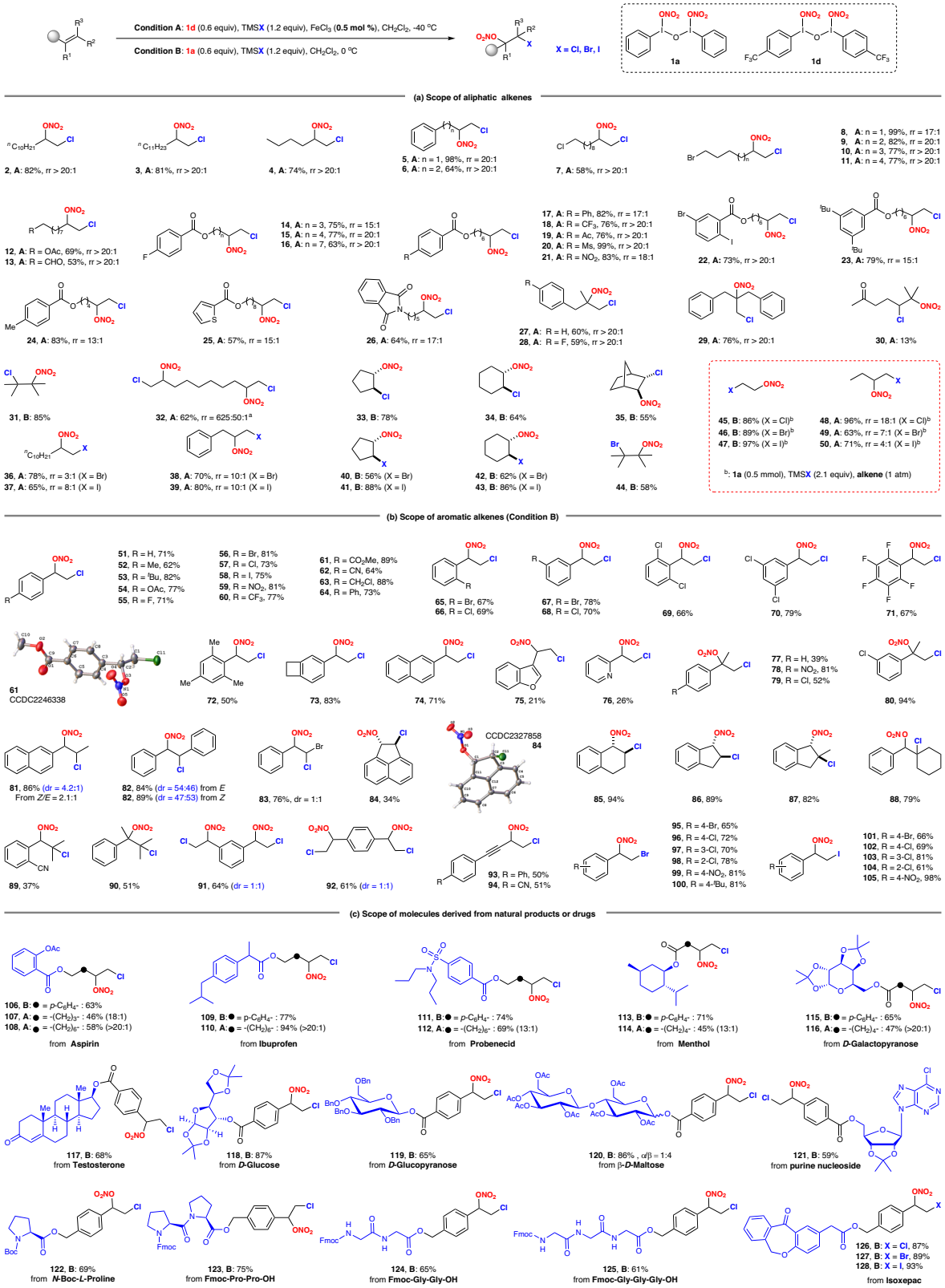


Fig. 2 | Reactivity evaluation of halonitrooxylation. Reaction conditions: **Condition A**: substrate (alkene) (0.20 mmol), **1d** (0.6 equiv), TMSX (1.2 equiv), $FeCl_3$ (0.5 mol %), CH_2Cl_2 (2 mL), −40 °C, 2 h; **Condition B**: substrate (alkene) (0.20 mmol), **1a** (0.6 equiv), TMSX (1.2 equiv), CH_2Cl_2 (2 mL), 0 °C, 2–5 min. Yields were for isolated and purified products. Regioisomeric ratios were determined by ^{1}H NMR spectra of the crude reaction mixtures. [a]See Supplementary Figs. 1–4 for details. Ac acetyl; Ms methanesulfonyl, [t]Bu *tert*-butyl, Boc *tert*-butyloxy carbonyl, Bn benzyl, Fmoc fluorenylmethyloxy carbonyl.

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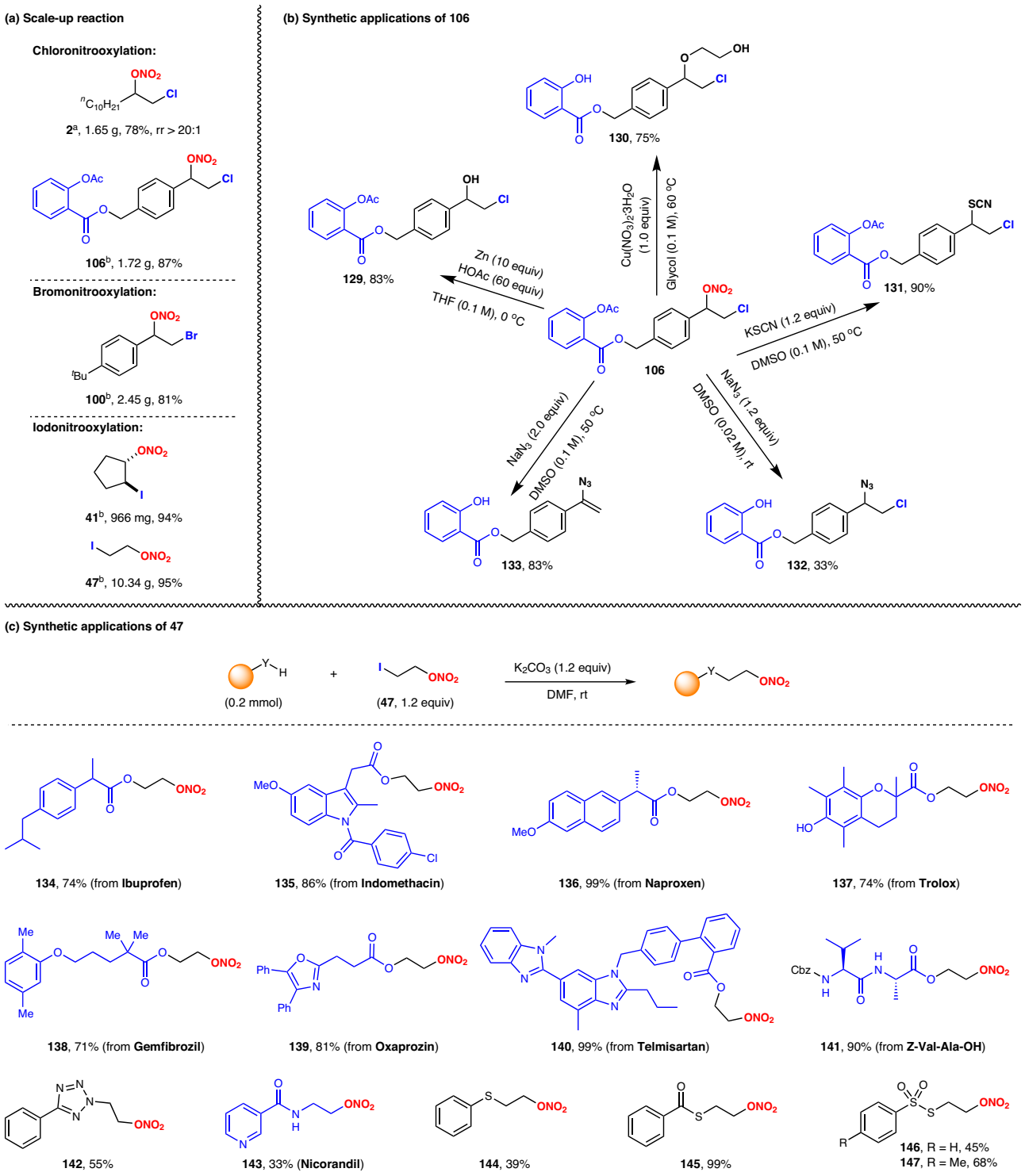

Fig. 3 | Gram-scale preparation and synthetic applications. a Scale-up reaction of chloro-, bromo-, and iodo-nitrooxylation. **b** Synthetic applications of **106**. **c** Synthetic applications of **47**. [a]Scale-up reaction was carried out based on Condition A depicted in Fig. 2. [b]Scale-up reaction was carried out based on Condition B depicted in Fig. 2. THF tetrahydrofuran, DMSO dimethyl sulfoxide, rt room temperature, DMF *N*,*N*-dimethylformamide, Cbz benzyloxycarbonyl.

alkenyl units onto pharmaceuticals or bioactive molecules via a common and efficient condensation reaction (see SI). Encouragingly, these substrates, bearing diverse scaffolds such as pharmaceutical ingredients, sugars, purine nucleosides, amino acids, and peptides, were well-tolerated in the chloronitrooxylation process, yielding the desired products **106**–**126** in 45–93% yields with at least 13:1 rr. Notably, the bromonitrooxylation and iodonitrooxylation of complex substrates proceeded smoothly, yielding the corresponding products **127** and **128**, respectively.

Synthetic utilities

Moreover, the methods can be easily scaled up to gram scale (Fig. 3a). Several reactions were chosen to test the effectiveness, yielding the vicinal chloronitrate **2** (1.65 g, 78% yield, >20:1 rr), **106** (1.72 g, 87%

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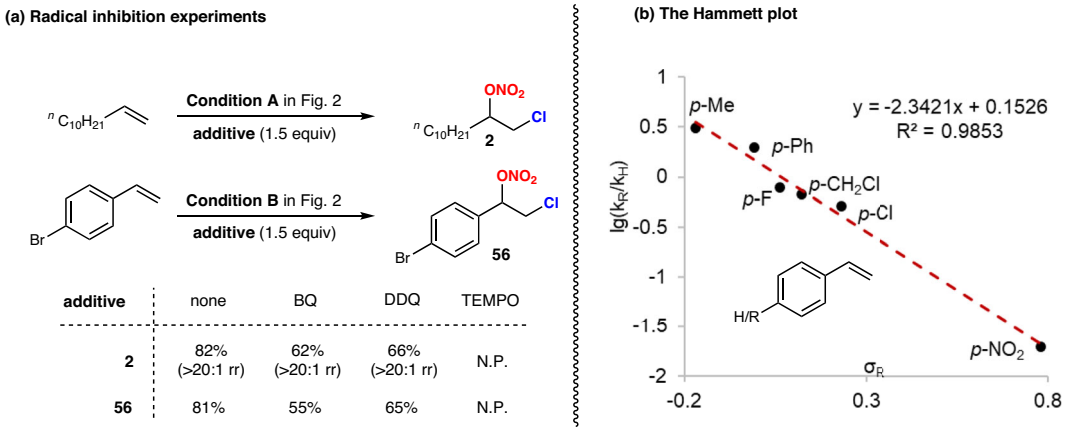

Fig. 4 | Mechanistic experiments. a Radical inhibition experiments. **b** The Hammett equation: y = −2.3421x + 0.1526 (R^2 = 0.9853). BQ 1,4-benzoquinone, DDQ 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, TEMPO 2,2,6,6-tetramethylpiperidoxyl, N.P. no product.

yield), and vicinal bromonitrate **100** (2.45 g, 81% yield). Additionally, 2-iodoethyl nitrates (**41, 47**) were obtained in 0.97 g (94% yield) and 10.34 g (95% yield), respectively. Compound **106** can be further transformed into a series of derivatives, including vicinal chloroalcohol **129** (83% yield), vicinal chloroether **130** (75% yield), vicinal chlorothiocyanate **121** (90% yield), vicinal chloroazide **132** (33% yield), and vinylazide **133** (83% yield), through smooth reactions (Fig. 3b).

Surprisingly, 2-iodoethyl nitrate (**47**) serves as a powerful synthetic precursor for introducing a nitrooxy group into molecules[61]. Various compounds bearing nitrooxy groups **134**–**147** were easily prepared via nucleophilic substitution of diverse pharmaceuticals/functional groups with 2-iodoethyl nitrate using K_2CO_3 as a base (Fig. 3c). Significantly, nicorandil (**143**)[62], a medication used to treat and reduce chest pain caused by angina, was synthesized from nicotinamide in 33% yield[63].

Mechanistic studies

To gain a preliminary understanding of the reaction mechanism, several control experiments were conducted. Adding a radical inhibitor such as 1, 4-benzoquinone (BQ) or 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) to the model reaction using dodec-1-ene or 4-bromostyrene as the substrate resulted in the corresponding product **2** or **56** in comparative yields, respectively (Fig. 4a). Notably, the inhibition of the reaction by TEMPO is likely due to its induction of the decomposition of reagent **1**, thereby preventing the reaction (Fig. 4a). In addition, a series of competitive experiments using *para*-substituted styrenes were performed (Fig. 4b). The Hammett plot ($\log(k_R/k_H)$ versus σ) displayed a linear correlation with a ρ value of −2.34 (R^2 = 0.99)[64,65]. The good linearity, along with the results of the radical inhibition experiments mentioned above, implies that the reaction proceeds through an electrophilic route.

We conducted density functional theory (DFT) calculations (The DFT calculation data are provided in the Source Data) to understand the reaction pathway. The computational visualizations, illustrated in Fig. 5a, demonstrate that the formation of the iodonium ion intermediate is less energetically favorable when it arises from the cleavage of the Cl-I bond (**Int2′-51** and **Int2′-4**) compared to the NO_3-I bond breaking (**Int2-51** and **Int2-4**) by 11.83 kcal/mol for styrene (**51-S**) and by 7.76 kcal/mol for 1-hexene (**4-S**), suggesting the improbability of the iodonium forming through chlorine displacement. Subsequent reaction steps indicated that the nitrate ion is capable of a direct attack on the iodonium intermediate. With 1-hexene, this leads to computed transition state energy barriers of 13.58 kcal/mol for the primary carbon (**TS1′-4**) and 7.06 kcal/mol for the secondary carbon (**TS1-4**). For styrene, the barriers are estimated at 16.27 kcal/mol for the primary carbon (**TS1′-51**) and 8.57 kcal/mol for the benzyl carbon (**TS1-51**). Clearly, Markovnikov selectivity is more evident with styrene, partly due to the larger differential in energy between the Markovnikov and anti-Markovnikov processes. Moreover, the low energy barriers for the reactions with 1-hexene signify that they proceed speedily at room temperature, which reduces kinetic selectivity.

The addition of $FeCl_3$ has shown fascinating effects, as depicted in Fig. 5b. The calculations suggest that $FeCl_3$ has a stronger binding affinity to the nitrate ion (**Int4**) by approximately 5 kcal/mol compared to chloride (**Int4′**), enhancing the stabilization of the resulting iodonium ion. This stabilization leads to a decrease in energy for the iodonium intermediates of styrene (**Int5-51**) and 1-hexene (**Int5-4**) by 1.02 kcal/mol and 4.08 kcal/mol respectively. This implies that due to the nitrate being stabilized by $FeCl_3$, the energy barriers for the subsequent nitrate addition ring-opening reactions increase. For 1-hexene, the barriers for the Markovnikov (**TS2-4**) and anti-Markovnikov (**TS2′-4**) ring openings are 14.78 and 24.47 kcal/mol, respectively. For styrene, these barriers sit at 16.98 and 23.45 kcal/mol (**TS2-51** and **TS2′-51**, respectively). It is evident that the substantial energy barriers for the anti-Markovnikov process sufficiently retard the reactions at room temperature, significantly enhancing selectivity.

A plausible reaction mechanism was proposed based on the experimental results and previous related reports[56,66,67] (Fig. 5c). Initially, **1a** reacts with TMSCl to form active species PhI(ONO_2)Cl (**Int1**) and TMSOTMS. $FeCl_3$ coordinates with the nitrate ion[68] in **Int1** to form **Int4**. Species **Int4** then reacts with alkyl alkene to generate **Int5**, which subsequently converts to **Int6** via a Markovnikov ring opening. Finally, **Int6** undergoes reductive elimination to yield the desired product, along with the release of $FeCl_3$ and the generation of iodobenzene as a byproduct.

Discussion

In summary, we have demonstrated a highly regioselective and practical halonitrooxylation strategy for a wide range of olefins. This protocol offers high efficiency, mild conditions, simple operation, and good compatibility with various functional groups. Especially, the product of ethylene iodonitrooxylation, 2-iodoethyl nitrate, can be combined with a range of natural products and drugs to obtain corresponding nitrooxylated functional molecules. The gram-scale preparation and late-stage modification of bioactive molecules show the potential utility of the method. Further investigations into expanding the method are currently underway in our laboratory.

Methods

General procedure A for the synthesis of β-halonitrates

To a test tube was charged with $FeCl_3$ (0.001 mmol, 0.5 mol %), olefin (0.20 mmol, 1.0 equiv) and dichloromethane (2 mL), and the mixture

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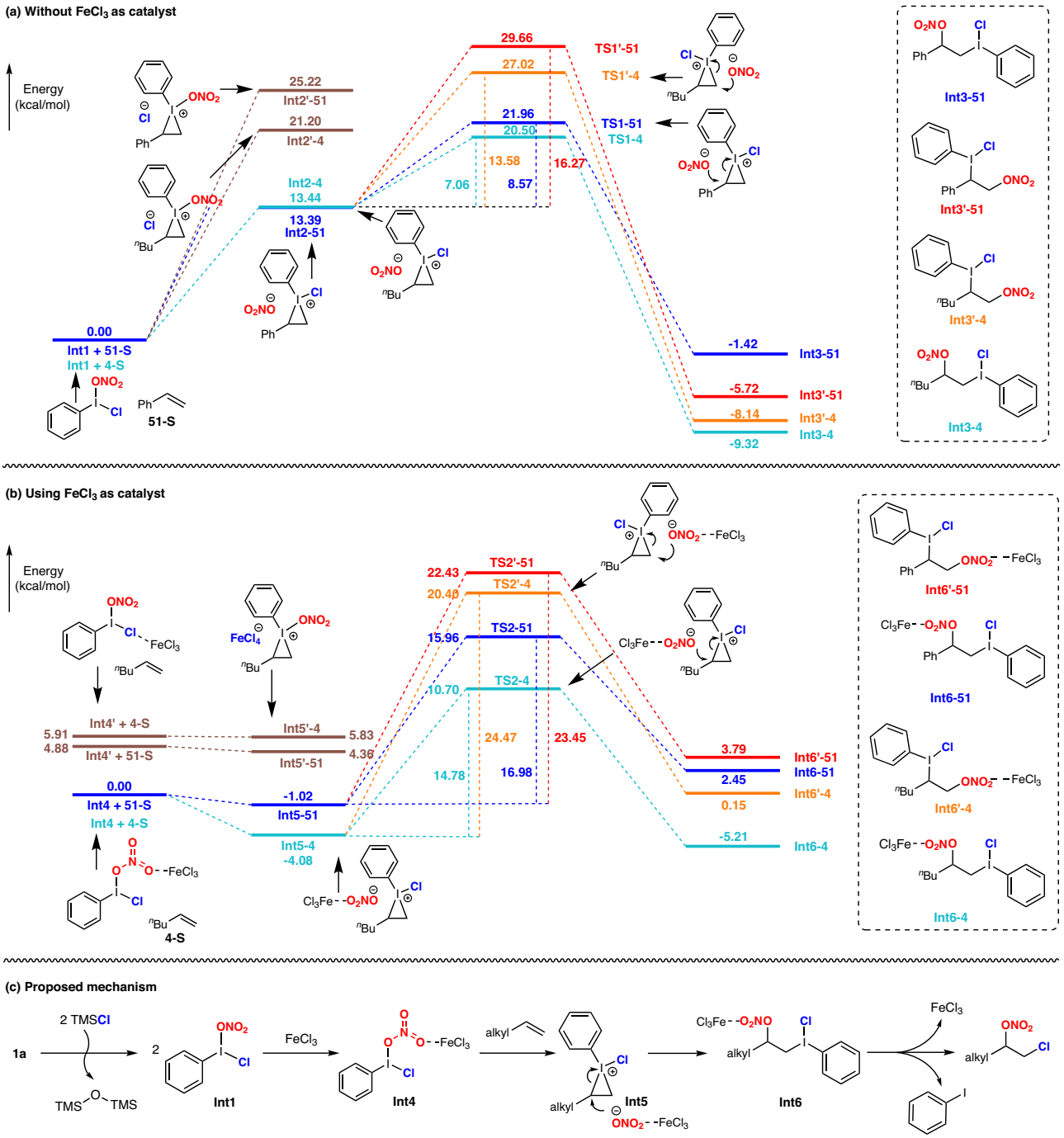

Fig. 5 | DFT calculations and proposed mechanism. All energy units are kcal/mol. **a** Without $FeCl_3$ as catalyst. **b** Using $FeCl_3$ as catalyst. **c** Proposed mechanism.

was cooled to −40 °C. Then **1d** (0.12 mmol, 0.6 equiv) and TMSX (X = Cl, Br, or I; 0.24 mmol, 1.2 equiv) were added and stirred at −40 °C for 2 h. After the reaction was complete, the crude product was purified by column chromatography (petroleum ether /ethyl acetate = 500/1 – 5/1, v/v) via silica gel to afford the desired product.

General procedure B for the synthesis of β-halonitrates

To a test tube was charged with **1a** (0.12 mmol, 0.6 equiv) and dichloromethane (2 mL), and the mixture was cooled to 0 °C. Then olefin (0.20 mmol, 1.0 equiv) and TMSX (X = Cl, Br, or I; 0.24 mmol, 1.2 equiv) were added and stirred at 0 °C for 1–5 min. After the reaction was complete, the crude product was purified by column chromatography (petroleum ether/ethyl acetate = 500/1 – 5/1, v/v) via silica gel to afford the desired product.

General procedure for the synthesis of 134–147

In a test tube, the corresponding substrate (0.2 mmol) was placed and DMF (1 mL) was added. Then, K_2CO_3 (2.4 mmol, 1.2 equiv) and 2-iodoethyl nitrate (2.4 mmol, 1.2 equiv) were added and stirred. Upon completion of the reaction, 10 mL of EtOAc were added, followed by 10 mL of H_2O. The reaction mixture was then extracted and washed three times with H_2O (10 mL). The organic layer was washed with brine (20 mL) and was dried with $MgSO_4$. The filtrate was removed under reduced pressure. The crude mixture was purified by flash column

chromatography (petroleum ether /ethyl acetate = 50/1 – 1/1, v/v) to yield the substrates.

Data availability

The authors declare that the data supporting the findings of this study, including synthetic procedures, characterization data, further details of computational studies and NMR spectra, are available within the article and the Supplementary Information file, or from the corresponding author upon request. Source data are provided with this paper. The X-ray crystallographic coordinates for structures reported in this study have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition numbers of CCDC2246338 (for **61**), and CCDC2327858 (for **84**). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via https://www.ccdc.cam.ac.uk/structures/. Source data are provided with this paper.

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Acknowledgements

This paper is in memory of Professor Lixin Dai. We are grateful for the financial support from the Shuguang program (20SG44) from Shanghai Education Development Foundation and Shanghai Municipal Education Commission, the National Natural Science Foundation of China (22371187), the Natural Science Foundation of Shanghai (22ZR1445200), the Chinese Education Ministry Key Laboratory and International Joint Laboratory on Resource Chemistry, the "111" Innovation and Talent Recruitment Base on Photochemical and Energy Materials (D18020), and the Shanghai Engineering Research Center of Green Energy Chemical Engineering (18DZ2254200).

Author contributions

Q.-H.D. conceived and directed the project. X.C. and Q.Y. conducted most of the experiments including the synthesis of the hypervalent iodine nitrooxylating reagents and substrates. Y.-F.C., S.-H.W., X.-C.S. and D.-Y.K. synthesized some substrates. X.C. drafted the Supporting Information. Q.-H.D. prepared the manuscript and revised the Supporting Information.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41467-024-51655-5.

Correspondence and requests for materials should be addressed to Qing-Hai Deng.

Peer review information *Nature Communications* thanks the anonymous reviewers for their contribution to the peer review of this work. A peer review file is available.