Cu-Mediated Thianthrenation and Phenoxathiination of Arylborons

Xiao-Yue Chen[1], Yichen Wu[1], Jia-Hui Bai[1], Yin-Long Guo[1], Peng Wang[1,2,3]

Great success in synthetic chemistry is motivated by the development of novel and reactive linchpins for carbon-carbon and carbon-heteroatom bond formation reactions, that has dramatically altered chemists' approach to building molecules. Herein, we report the readily synthesis of aryl sulfonium salts, a novel versatile electrophilic linchpin, via an unprecedented Cu-mediated thianthrenation and phenoxathiination of commercially available arylborons with thianthrene and phenoxathiine, providing a series of aryl sulfonium salts in high efficiency. More importantly, by leveraging the sequential Ir-catalyzed C–H borylation and Cu-mediated thianthrenation of arylborons, the formal thianthrenation of arenes are also achieved. As the Ir-catalyzed C–H borylation with undirected arenes normally occurred at the less steric hindrance position, thus providing a complementary method for thianthrenation of arenes in comparison with the electrophilic thianthrenation. This process is capable of late-stage functionalization of a series of pharmaceuticals, which might find wide synthetic applications in both industry and academic sectors.

One of the major advances in synthetic organic chemistry relies on the development of high reactive functional groups in order to introduce new functionalities into a target molecule[1-11]. In most of those cases, the installation of reactive functionalities, including nucleophilic aryl-metal species (metal = Mg, Zn, B, Si etc.)[6-9] and electrophilic aryl halides, aryl diazonium salts[10] or aryl hypervalent iodonium salts[11] etc., might require several synthetic steps, and lead to undesired byproducts which disobey the principle of green chemistry and the rule of atom-economy.[12-13] Recently, the use of bench-stable aryl sulfonium salts[14-20], in particular arylthianthrenium salts,[21-41] as a versatile linchpin for efficient development of novel carbon-carbon bond and carbon-heteroatom bond formation reactions has attracted much attention (Figure 1a), due

[1] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, CAS 345 Lingling Road, Shanghai 200032, P.R. China
[2] CAS Key Laboratory of Energy Regulation Materials, Shanghai Institute of Organic Chemistry, CAS 345 Lingling Road, Shanghai 200032, P.R. China
[3] School of Chemistry and Materials Science, Hangzhou Institute for Advanced Study, University of Chinese Academy of Sciences, 1 Sub-lane Xiangshan, Hangzhou 310024, P.R. China
Email: ylguo@sioc.ac.cn; pengwang@sioc.ac.cn

to the feasible accessibility of aryl sulfonium salts from simple arenes via regioselective electrophilic thianthrenation or phenoxathiination (Figure 1b)[22-24]. In comparison with aryl halides and their analogues, the corresponding arylthianthrenium salts present unique reactivities in both transition metal catalyzed cross-coupling reactions as an aryl electrophile[23, 25-32] and photoredox catalyzed radical coupling reactions as an aryl radical precursor[24, 34-40]. Most importantly, several novel reaction processes with arylthianthrenium salts, including Pd-catalyzed tritiation[32], photocatalyzed radical coupling,[24, 34-40] and electron donor-acceptor complex photoactivation[39, 40] etc., have been proven to be inert or inefficient with aryl halides and their analogues. Accordingly, the direct functionalization of arenes via corresponding arylthianthrenium salts has become an appealing approach for the late-stage modification of drug molecules and bioactive molecules.[22, 41]

Despite of the rapid development of arylthianthrenium salts chemistry, the direct synthesis of arylthianthrenium salts is significantly lagging behind and in high demand. The sole process to access arylthianthrenium salts is based on the electrophilic thianthrenation of simple arenes with thianthrene *S*-oxide (TTSO) and its derivatives under acidic conditions.[23, 24] Due to the highly electrophilic nature of thianthrene dication intermediates,[24, 42] this process is largely limited to electron-rich and electron-neutral aromatics, and the more electron-deficient (hetero)arenes rather than chlorobenzene and fluorobenzene could not be tolerated. In addition, the electrophilic thianthrenation of arenes normally happens at the most electron rich site of the aromatic ring (*para*-position for monosubstituted arenes), thus resulting in the inaccessibility of *ortho*- and *meta*- substituted arylthianthrenium salts, and electron-deficient (hetero)aryl thianthrenium salts. The limited arylthianthrenium salts inventory might significantly reduce the research interests on the development of novel transformations based on this novel linchpin, and slow down the advances in applying arylsulfonium salts in both industry and academic sectors. Here, we report an unprecedented Cu-mediated efficient synthesis of arylthianthrenium salts and aryl phenoxathiinium salts from arylborons with thianthrene and phenoxathiine, featuring simple manipulation, mild conditions, broad functional group and heterocycle compatibility. Given over thousands of arylborons in stock, this protocol opens a new avenue for constructing an unprecedented library of arylthianthrenium salts and aryl phenoxathiinium salts (Figure 1c). Moreover, the direct thianthrenation of arenes and heteroarenes has been

further achieved by leveraging a sequential Ir-catalyzed C–H borylation with undirected arenes and Cu-mediated thianthrenation of aryl boronates, which provides a new paradigm for late-stage functionalization of complex drug molecules via arylthianthrenium salts. In light of the steric discrimination in the Ir-catalyzed C–H borylation event[43-45], this novel developed process provides a complementary approach possessing probably different regioselectivity to electrophilic sulfonium salts formation reaction with thianthrene *S*-oxide (TTSO) and phenoxathiine 10-oxide (POSO) (Figure 1d). Certainly, the unprecedented library of arylthianthrenium salts and aryl phenoxathiinium salts accessed with current protocol could be used for new reaction development and the late-stage functionalization of drug molecules and bioactive molecules.

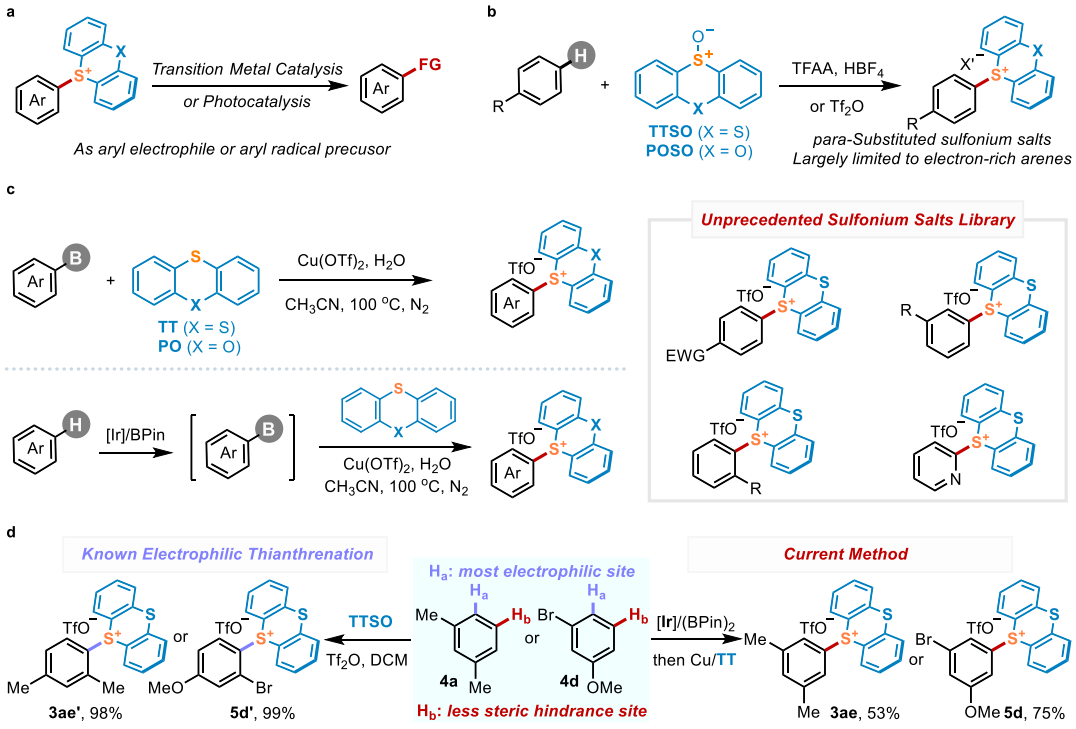

Figure 1 | Synopsis of the Cu-mediated thianthrenation and phenoxathiination of arylborons. Ar, aryl; Me, methyl; EWG, electron withdrawing group. **a**, Importance of aryl thianthrenatium salts in organic synthesis. **b**, Electrophilic thianthrenation and phenoxathiination of arenes with thianthrene *S*-oxide (TTSO) and phenoxathiine 10-oxide (POSO). **c**, Cu-mediated thianthrenation and phenoxathiination of arylborons with thianthrene (TT) and phenoxathiine (PO). **d**, The direct comparison of current method with electrophilic thianthrenation of arenes.

Results and discussion

Our initial efforts were focused on the preparation the arylthianthrenium salts using aryl halides as the starting materials in the presence of a transition metal catalyst (Pd, Ni etc.), inspiring by the transition metal-catalyzed phosphonium salts formation reaction[46, 47] (Figure 2a). However, the desired arylthianthrenium salts could not be obtained after systematical investigation of the reaction parameters, probably due to the weak coordinating ability of thianthrene in comparison to phosphine compounds and the high reactivity of arylthianthrenium salts in the presence of palladium and nickel catalysts[24-32]. Although no desired arylthianthrenium salts were observed with simple aryl halides (only the homocoupling of aryl halides were observed), we were delighted to find the Cu(I)-mediated thianthrenation of aryl bromide is feasible in the presence of a pyridine directing group[48] (Figure 2b). This observation indicates the Cu-mediated or catalyzed arylthianthrenium salts formation reaction is indeed feasible via a Cu(I)/Cu(III) catalytic cycle, and the arylthianthrenium salts are stable in the presence of a copper catalyst probably due to the weak oxidative addition ability of Cu(I) catalyst with arylthianthrenium salts. Following this lead, we next envisioned that the Cu(II)-mediated thianthrenation might be realized with more reactive arylboron reagents by sequential transmetalation with arylborons, disproportionation of Cu(II) to give the corresponding Cu(III) intermediate, and finally reductive elimination to provide the desired arylthianthrenium salts. After systematical evaluation the reaction parameters, the desired arylthianthrenium salt **3z** was formed in 88% NMR yield by employing $Cu(OTf)_2$ in acetonitrile with H_2O as the additive (Figure 2c). Replacement of $Cu(OTf)_2$ with other copper sources resulted in low efficiency or no reaction. The water additive is crucial for the high yield of this reaction, and only 40% yield was obtained in the absence of water. Gratifyingly, this reaction could also proceed under air, providing a slightly lower yield. Under the optimal conditions, the phenoxathiination of election-deficient aryl boronic acid **1z** gave the desired aryl phenoxathiinium salt **3z'** in 85% yield. A series of thianthrene analogs bearing both the electron-rich and electron deficient substituents are also compatible with this protocol (Figure 2d). In addition, various arylborons other than arylboronic acid, including potassium aryltrifluoroborate (**1a'**), arylboroxine, arylboronic acid pinacol ester (**1a''**) and arylboronic acid neopentylglycol ester (**1a'''**), are all compatible with this procedure (Figure 2e). Preliminary mechanistic studies indicated a formation of thianthrene coordinated TT–Cu(OH)–OTf (**Int I**) in the presence of water and thianthrene, which might facilitate the transmetalation with arylboronic acids.

This hypothesis could also explain the acceleration effect of water additives during the reaction evaluation. Disproportionation of the resulted intermediate Ar–Cu(TT)–OTf (**Int II**) with $Cu(OTf)_2$ could lead to the formation of a key Cu(III) intermediate **Int III**, which could give the desired arylthianthrenium salts via reductive elimination (Figure 2f). The in-situ MS detection by conducting solvent-assisted electrospray ionization mass spectrometric experiments[49] allows the direct observation of aforementioned intermediates **Int I**, **Int II**, and **Int III**, which strongly supports our mechanism hypothesis (Figure 2g).

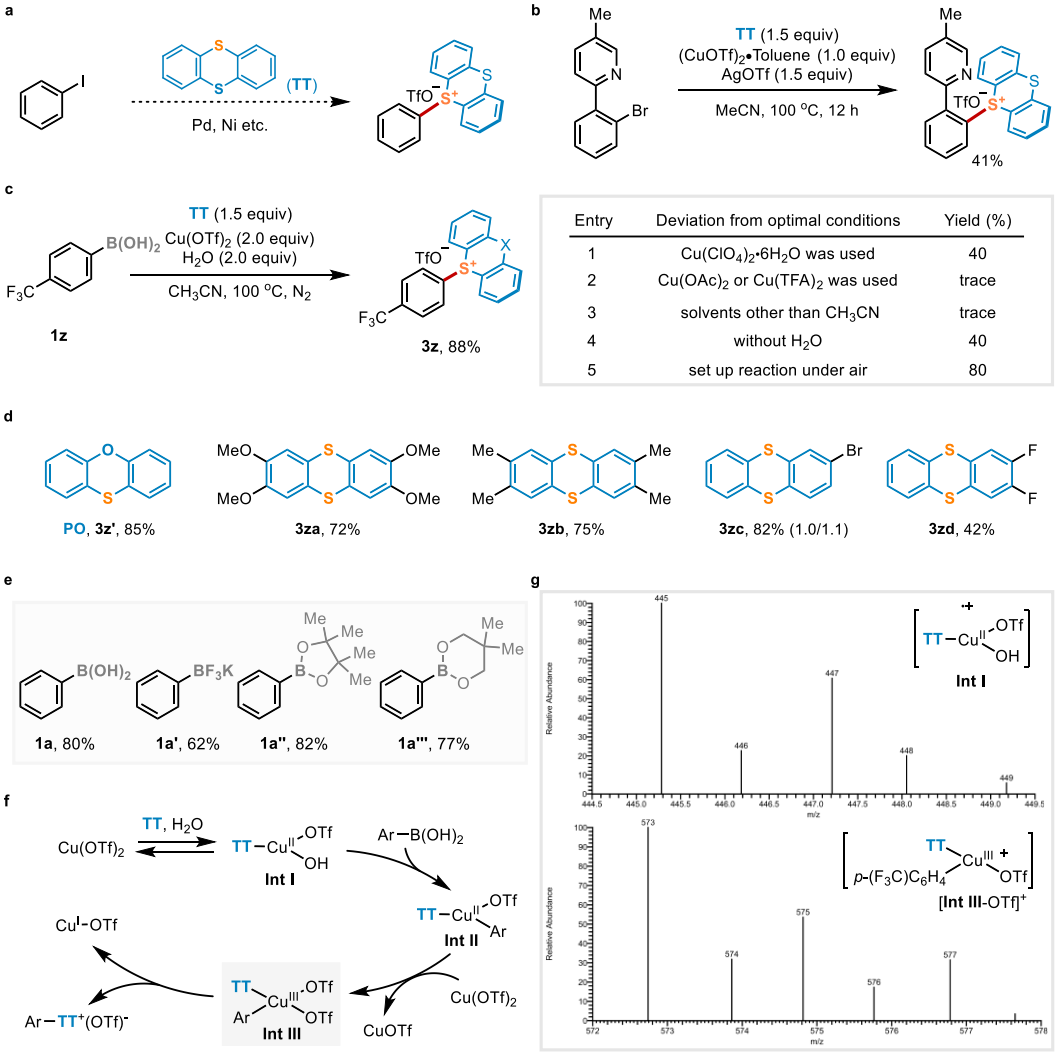

Figure 2 | Hypothesis, condition optimization, scope of thianthrene derivatives and arylborons, and possible reaction pathway. a, Preliminary studies on transition metal-catalyzed thianthrenation of aryl iodide. **b**, Cu-mediated thianthrenation of 2-(2-bromophenyl)-5-methylpyridine. **c**, Cu-mediated thianthrenation and phenoxathiination of aryl boronic acid and related control experiments. **d**, Scope with respect to thianthrene derivatives. **e**, Scope with respect to arylborons. **f**, Proposed reaction pathway. **g**, Trapping of the key intermediates with SAESI-MS analysis. The yield was determined by ^{1}H NMR using dibromomethane as the internal standard. See Supplementary Information for experimental details.

With the optimized reaction conditions in hand, we set out to evaluate the substrate scope of the reaction with respect to the arylborons (Figure 3). In general, the thianthrenation and phenoxathiination gave similar outcomes under the optimal conditions (**3** versus **3'**). Both the electron-rich and electron-deficient substituents at various positions didn't significantly affect the reaction outcomes. Notably, this protocol presents extraordinary functional group compatibility, various arylboron compounds provided the corresponding aryl thianthrenium salts and phenoxathiinium salts in high yields bearing alkyl (**3b-d**, **3k-l**, **3u**), trifluoromethyl (**3j**, **3r**, **3z**, **3z'**), phenyl (**3e**, **3m**), fluoro- (**3f**, **3n**, **3w**), chloro- (**3g**, **3g'**, **3o**, **3x**), bromo- (**3h**, **3h'** , **3y**), aldehyde (**3i**), ester (**3q**, **3q'** , **3ac**), nitrile (**3s**, **3aa**), sulfoxide (**3ad**, **3ad'**), and the normally troublesome iodo- (**3p**) and nitro group (**3t**, and **3ab**). In addition to *meta*- (**1k-t**) and *para*- (**1u-ad**) substituted arylboronic acids, sterically hindered *ortho*-substituted arylboronic acids (**1b-j**) have proven to be efficient for the preparation of *ortho*-substituted aryl thianthrenium salts and phenoxathiinium salts in high yields. Multisubstituted aryl sulfonium salts (**3ae-am**) could also be prepared under current conditions with high efficiency. To our delight, heterocyclic arylborons (**1an-az**) are also suitable substrates, such as pyridine, quinoline, isoquinoline, thiophene, benzothiphene etc. The tolerance of simple pyridine motifs is noteworthy, giving the electron-deficient heteroarene containing aryl thianthrenium salts. The remarkable compatibility of heterocycle-containing arylborons further highlights the generality of this protocol.

Inspiring by the rapid development of Ir-catalyzed regioselective borylation of arenes with $(BPin)_2$[43-45], we next explored the direct regioselective thianthrenation of arenes via a sequential borylation and Cu-catalyzed thianthrenation process. The thianthrenation normally happened at the less steric hindrance site due to the bulky nature of the iridium catalyst. After rapid evaluation of the reaction parameters for this one-pot process, the scope of this formal thianthrenation of arenes were investigated. As listed in Figure 4, experimental results showed that this reaction exhibited an exceptionally broad scope under standard conditions. A variety of 1,3-disubsituted (**4a-e**) and 1,2-disubsituted (**4f-j**) arenes bearing various functional groups, including methyl, trifluoromethyl, nitrile, ester, ether, bromo-, and chloro-, were well tolerated. Moreover, the heteroarenes are also tolerated, providing corresponding heteroaryl thianthrenium salts in moderate to good yields (**3ap**, **5l-m**, **3ax** and **3ay**).

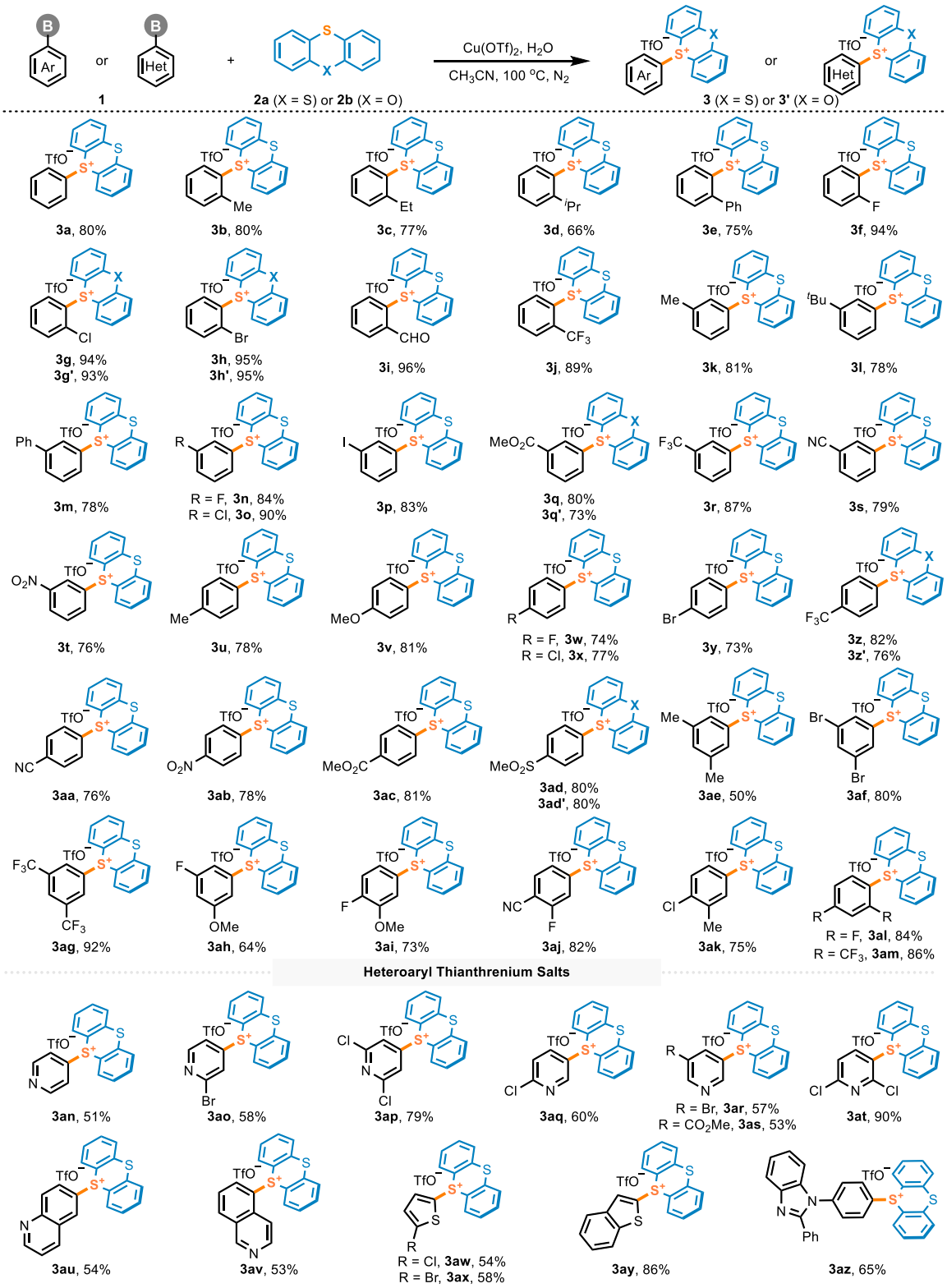

Figure 3 | Cu-catalyzed thianthrenation and phenoxathiination of arylborons. The values under each structure indicate isolated yields (See Supplementary Information for experimental details). Reaction conditions: **1** (1.0 mmol), **2a** or **2b** (1.5 equiv), $Cu(OTf)_2$ (724 mg, 2.0 equiv), H_2O (36 μL, 2.0 equiv), CH_3CN (1.0 mL), 100 °C, 3.0 hours. For **3m** and **3ae**, CH_3CN (2.0 mL) was used. For arylboronic acid pincol ester **1ar**, **1as**, **1ax** and **1ay**, $CH_3B(OH)_3$ (3.0 equiv) was added.

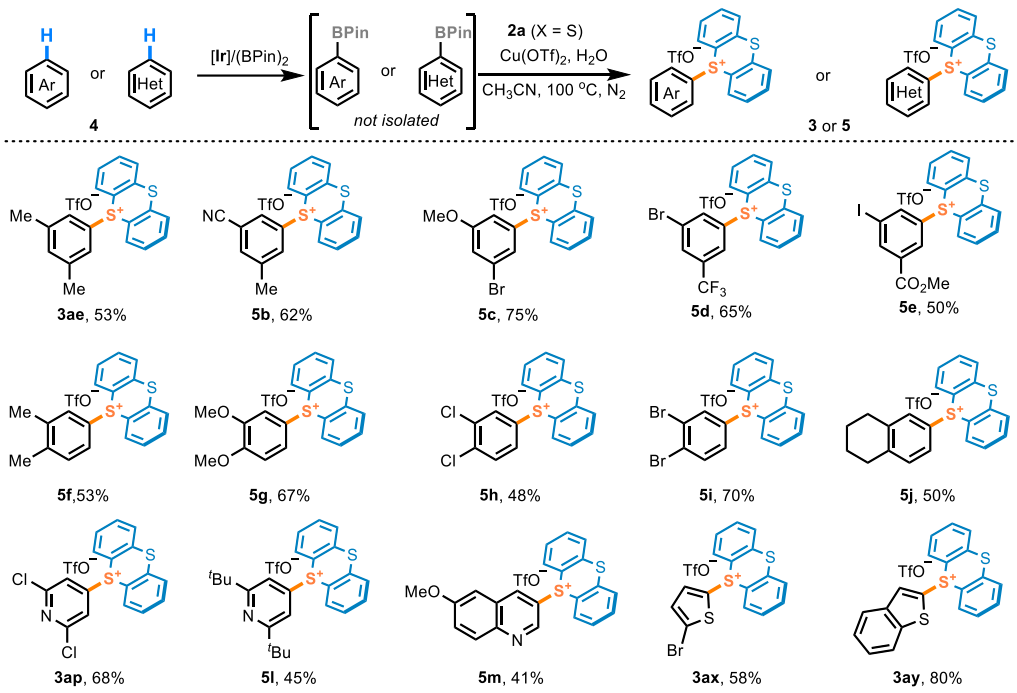

Figure 4 | Regioselective thianthrenation of arenes via Ir-catalyzed borylation/Cu-mediated thianthrenation. The values under each structure indicate isolated yields (See Supplementary Information for experimental details). For borylation: **4** (1.0 mmol), $(BPin)_2$ (186 mg, 0.73 equiv), $[Ir(cod)(OMe)]_2$ (1.7 mg, 0.25 mol%), 4,4'-di-*tert*-butyl-2,2'-bipyridine (1.5 mg, 0.54 mol%), THF, 80 °C, 24 h. For Cu-mediated thianthrenation: thianthrene **2a** (324 mg, 1.5 equiv), $Cu(OTf)_2$ (724 mg, 2.0 equiv), H_2O (36 μL, 2.0 equiv), $MeB(OH)_2$ (180 mg, 3.0 equiv), CH_3CN (1.0 mL), 100 °C, 3 h.

The mild reaction conditions and high functional group tolerance could facilitate the late-stage functionalization of biorelevant compounds (Figure 5). The formal thianthrenation of arenes could also be applied for the direct thianthreneation of pharmaceuticals, including loratadine (**6a**), metalaxyl (**6b**) and clopidogrel (**6c**), providing the corresponding aryl thianthrenium salts **8a-c** in 47-48% isolated yields. In addition, arylboronic acid pincol esters from loratadine, epiandrosterone, fenofibrate, cloquintocet-mexyl, clofibrate, and δ-tocopherol are all tolerated with our conditions, giving the desired aryl thianthrenium salts **8d-i** in 42-79% yields. Taking advantage of the rich chemistry of aryl thianthrenium salts, our protocol will pave a new way for late-stage functionalization of drug molecules, and further enhance the efficiency of drug discovery.

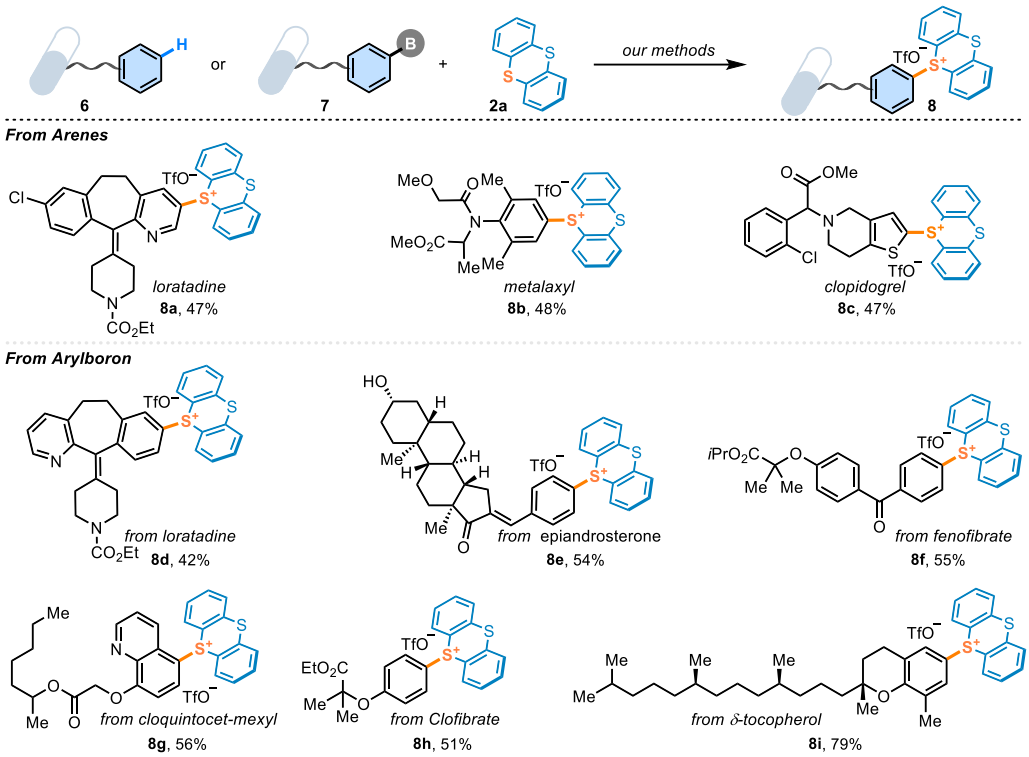

Figure 5 | Thianthrenation of drug-containing complex architectures from arenes or arylborons. The values under each structure indicate isolated yields (See Supplementary Information for experimental details).

To further highlight the versatility of the aryl thianthrenium salts, the derivatization of the loratadine derived thianthrenium salt **8a** was investigated. A series of carbon-carbon and carbon-heteroatom bond formation reactions, including transition metal-catalyzed Suzuki coupling, methylation, amination, silylation, photocatalyzed radical trifluoromethylation, etherification, chlorination, cyanation, were achieved in high efficiency, providing a series of loratadine analogues in 50-94% yields (Figure 6a). Notably, the thioetherification and sulfonation were also achieved via the electron donor-acceptor complex photoactivation. The late-stage functionalization of loratadine at current position will provide a new library of bioactive compounds for drug development. Furthermore, fenofibrate related aryl thianthrenium salts **8f** could also undergo the photocatalyzed trifluoromethylation and sequentially electrophilic thianthrenation enabled silylation reaction, providing the corresponding products in 63% total yield (Figure 6b). Most importantly, we were able to functionalize the drug molecule sequentially by adopting the complementary electrophilic thianthrenation, and our current formal C–H thianthrenation protocol (Ir-catalyzed C–H borylation/Cu-mediated thianthrenation). For example, the electrophilic thianthrenation enabled Suzuki-coupling reaction firstly proceeded at the most electrophilic site of clofibrate **21**, followed by

photocatalyzed hydroxylation at less steric hindrance site with our newly developed formal thianthrenation of arenes (Figure 6c).

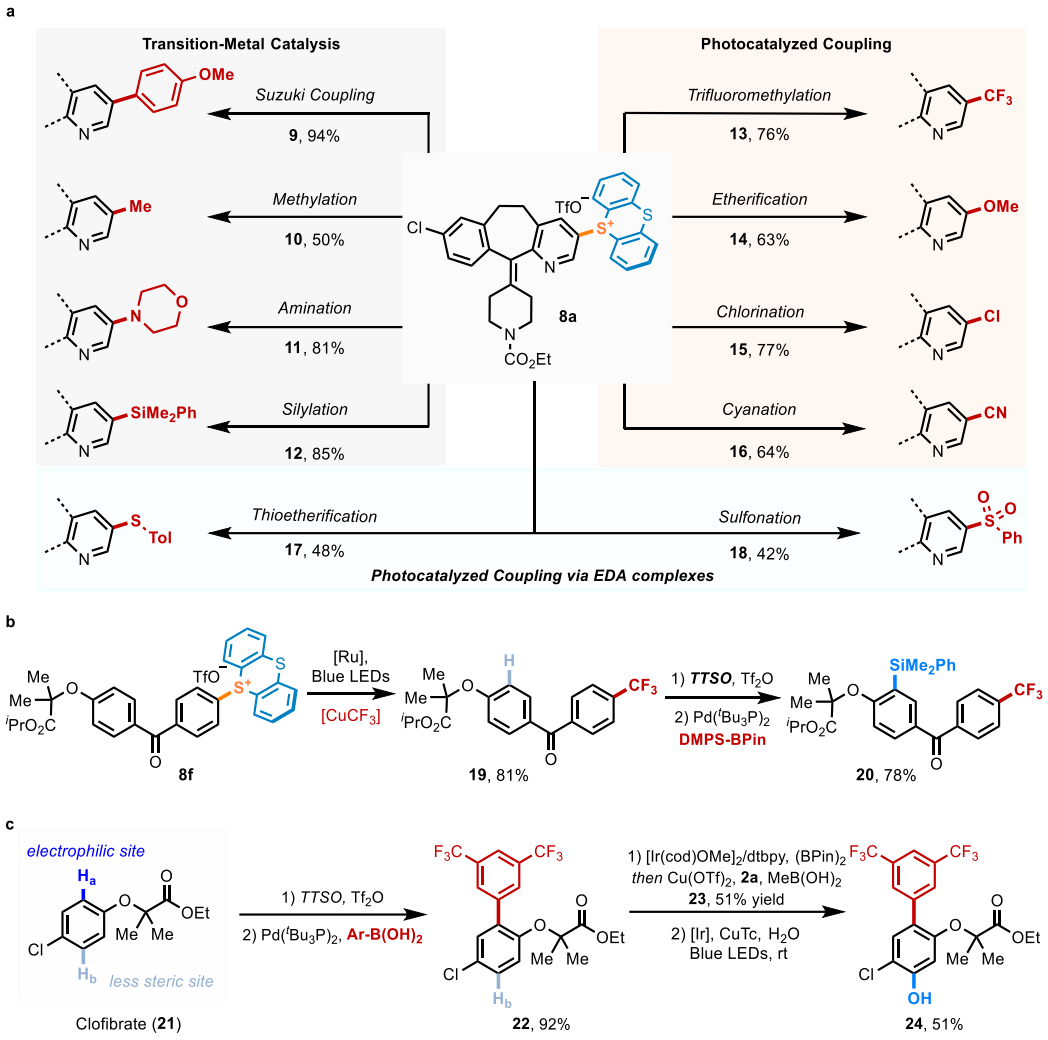

Figure 6 | The powerful chemistry of arylthianthrenium salts and the late-stage functionalization of pharmaceuticals. **a**, Transformations of arylthianthrenium salts. **b**, Sequential thianthrenation for late-stage functionalization of **8f**. **c**, Sequential C–H thianthrenation for late-stage functionalization of clofibrate. For procedures, see Supplementary Information for experimental details.

In summary, we have developed a new approach for the synthesis of aryl thianthrenium salts or phenoxathiinium salts via Cu-mediated thianthrenation and phenoxathiination of a wide range of (hetero)arylborons. The established approach is generally applicable to construction of a wide range of aryl thianthrenium salts bearing both electron-rich and electron deficient substituents at all positions, as well as

many heteroaryl sulfonium salts. The availability of this unprecedented library will significantly enable new reactivities and transformations based on this emerging aryl reagent which are highly valuable in drug discovery and organic synthesis. The formal thianthrenation of arenes with a complementary regioselectivity to electrophilic thianthrenation will also open a new avenue for late-stage functionalization of bioactive compounds.

Methods Summary

General procedure for Cu-mediated thianthrenation and phenoxathiination of arylborons. A 10 mL Schlenk tube were charged with arylboronic acid **1** (1.0 mmol, 1.0 equiv) and thianthrene (324 mg, 1.5 mmol, 1.5 equiv), and the reaction tube was moved to a N_2-filled glove box, followed by the addition of $Cu(OTf)_2$ (724 mg, 2.0 mmol, 2.0 equiv). After removal of the Schlenk tube out of the glove box, H_2O (36 μL, 2.0 mmol, 2.0 equiv) and MeCN (1.0 mL) were added under a nitrogen atmosphere. The reaction mixture was stirred at 100 ^oC for 3.0 hours. After cooling to room temperature, the reaction mixture was added into ammonia solution (100 mL, 25–28% solution in water), and the water phase was extracted with DCM (2 x 30 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated under vacuum. The residue was dissolved in DCM (4.0 mL), and precipitated by adding the solution into the stirring Et_2O (200 mL). The solid was collected by filtration to afford the arylthianthrenium salt **3** without further purification. Full experimental details and characterization of new compounds can be found in the Supplementary Information.

References

1. Trost, B. M. & Fleming, I. (eds) Comprehensive Organic Synthesis. (Pergamon, 1991).
2. de Meijere, A. & Diederich, F. (eds) Metal-Catalyzed Cross-Coupling Reactions. (WILEY-VCH Verlag GmbH & Co. KGaA, 2004).
3. Miyaura, N. Cross-Coupling Reactions: A Practical Guide. (Springer: New York, 2002).
4. Blakemore, D. C., Doyle, P. M. & Fobian, Y. M. (eds) Synthetic Methods in Drug Discovery, volume 1. (Royal Society of Chemistry, 2016)

5. Crawley, M. L. & Trost, B. M. (eds) Selected Applications of Transition Metal-Catalyzed Carbon–Carbon Cross-Coupling Reactions in the Pharmaceutical Industry. (John Wiley & Sons, 2012).
6. Rappoport, Z. & Marek, I. (eds) The Chemistry of Organomagnesium Compounds. (John Wiley & Sons, 2008).
7. Fernández, E. (eds) Advances in Organoboron Chemistry Towards Organic Synthesis. (Stuttgart: Georg Thieme Verlag, 2020).
8. Rappoport, Z. & Marek, I. (eds) The Chemistry of Organozinc Compounds. (John Wiley & Sons, 2006).
9. Denmark, S. E. & Regens, C. S. Palladium-catalyzed cross-coupling reactions of organosilanols and their salts: practical alternatives to boron- and tin-based methods. *Acc. Chem. Res*. **41**, 1486–1499 (2008).
10. Mo, F., Qiu, D., Zhang, L. & Wang, J. Recent development of aryl diazonium chemistry for the derivatization of aromatic compounds. *Chem. Rev.* **121**, 5741–5829 (2021).
11. Zhdankin V. V. (eds) Hypervalent Iodine Chemistry: Preparation, Structure, and Synthetic Applications of Polyvalent Iodine Compounds. (John Wiley & Sons, 2013).
12. Anastas, P. & Eghbali, N. Green chemistry: principles and practice. *Chem. Soc. Rev*. **39**, 301–312 (2010).
13. Trost, B. M. The atom economy-a search for synthetic efficiency. *Science* **254**, 1471−1477 (1991).
14. Kaiser, D., Klose, I., Oost, R., Neuhaus, J. & Maulide, N. Bond-forming and -breaking reactions at sulfur(IV): sulfoxides, sulfonium salts, sulfur ylides, and sulfinate salts. *Chem. Rev.* **119**, 8701–8780 (2019).
15. Tian, Z.-Y., Hu, Y.-T., Teng, H.-B. & Zhang, C.-P. Application of arylsulfonium salts as arylation reagents. *Tetrahedron Lett.* **59**, 299–309 (2018).
16. Srogl, J., Allred, G. D. & Liebeskind, L. S. Sulfonium salts. Participants par excellence in metal-catalyzed carbon−carbon bond-forming reactions. *J. Am. Chem. Soc.* **119**, 12376–12377 (1997).
17. Aukland, M. H. *et al.* An interrupted Pummerer/nickel-catalysed cross-coupling sequence. *Angew. Chem. Int. Ed.* **57**, 9785–9789 (2018).

18. Minami, H., Otsuka, S., Nogi, K. & Yorimitsu, H. Palladium-catalyzed borylation of aryl sulfoniums with diborons. *ACS Catal.* **8**, 579–583 (2018).
19. Kafuta, K., Korzun, A., Böhm, M., Golz, C. & Alcarazo, M. Synthesis, structure, and reactivity of 5-(aryl)dibenzothiophenium triflates. *Angew. Chem. Int. Ed.* **59**, 1950–1955 (2020).
20. Xu, P. *et al*. Site-selective late-stage aromatic [^{18}F]fluorination via aryl sulfonium salts. *Angew. Chem. Int. Ed*. **59**, 1956–1960 (2020).
21. Aukland, M. H., Šiaučiulis, M., West, A., Perry, G. J. P. & Procter, D. J. Metal-free photoredox-catalysed formal C–H/C–H coupling of arenes enabled by interrupted Pummerer activation. *Nat. Catal*. **3**, 163–169 (2020).
22. Chen, X.-Y., Wu, Y. & Wang, P. Recent advances in thianthrenation/phenoxathiination enabled site-selective functionalization of arenes. *Synthesis*, DOI: 10.1055/s-0041-1737493 (2022).
23. Berger, F. *et al.* Site-selective and versatile aromatic C−H functionalization by thianthrenation. *Nature* **567**, 223−228 (2019).
24. Wu, J. *et al. Para*-selective borylation of monosubstituted benzenes using a transient mediator. *Sci. China Chem.* **63**, 336−340 (2020).
25. Engl, P. S. *et al.* C–N cross-couplings for site-selective late-stage diversification via aryl sulfonium salts. *J. Am. Chem. Soc*. **141**, 13346−13351 (2019).
26. Chen, X.-Y., Nie, X.-X., Wu, Y. & Wang, P. *Para*-selective arylation and alkenylation of monosubstituted arenes using thianthrene *S*-oxide as a transient mediator. *Chem. Commun.* **56**, 5058−5061 (2020).
27. Alvarez, E. M., Plutschack, M. B., Berger, F. & Ritter, T. Site-selective C–H functionalization–sulfination sequence to access aryl sulfonamides. *Org. Lett.* **22**, 4593–4596 (2020).
28. Selmani, A., Gevondian, A. G. & Schoenebeck, F. Germylation of arenes via Pd(I) dimer enabled sulfonium salt functionalization. *Org. Lett.* **22**, 4802–4805 (2020).
29. Wu, Y., Huang, Y.-H., Chen, X.-Y. & Wang, P. Site-selective silylation of simple arenes mediated by thianthrene S-oxide. *Org. Lett.* **22**, 6657−6661 (2020).

30. Nie, X.-X., Huang, Y.-H. & Wang, P. Thianthrenation enabled α-arylation of carbonyl compounds with arenes. *Org. Lett*. **22**, 7716−7720 (2020).
31. Tian, Z.-Y., Lin, Z.-H. & Zhang, C.-P. Pd/Cu-Catalyzed C–H/C–H cross coupling of (hetero)arenes with azoles through arylsulfonium intermediates. *Org. Lett*. **23**, 4400−4405 (2020).
32. Zhao, D., Petzold, R., Yan, J., Muri, D. & Ritter, T. Tritiation of aryl thianthrenium salts with a molecular palladium catalyst. *Nature* **600**, 444−449 (2021).
33. Lansbergen, B., Granatino, P. & Ritter, T. Site-selective C–H alkylation of complex arenes by a two-step aryl thianthrenation-reductive alkylation sequence. *J. Am. Chem. Soc*. **143**, 7909–7914 (2021).
34. Ye, F. *et al.* Aryl sulfonium salts for site-selective late-stage trifluoromethylation. *Angew. Chem. Int. Ed.* **58**, 14615−14619 (2019).
35. Sang, R. *et al.* Site-selective C−H oxygenation via aryl sulfonium salts. *Angew. Chem. Int. Ed*. **58**, 16161–16166 (2019).
36. Li, J. *et al.* Photoredox catalysis with aryl sulfonium salts enables site-selective late-stage fluorination. *Nature Chem.* **12**, 56−62 (2020).
37. Alvarez, E. M., Karl, T., Berger, F., Torkowski, L. & Ritter, T. Late-stage heteroarylation of hetero(aryl)sulfonium salts activated by α-amino alkyl radicals. *Angew. Chem. Int. Ed*. **60**, 13609–13613 (2021).
38. Zhang, Y.-L., Wang, G.-H., Wu, Y., Zhu, C.-Y. & Wang, P. Construction of α-amino azines via thianthrenation enabled photocatalyzed hydroarylation of azine-substituted enamides with arenes. *Org. Lett*. **23**, 8522–8526 (2021).
39. Cabrera-Afonso, M. J., Granados, A. & Molander, G. A. Sustainable thioetherification via electron donor-acceptor photoactivation using thianthrenium salts. *Angew. Chem. Int. Ed.* **61**, e202202706 (2022).
40. Granados, A., Cabrera-Alfonso, M. J., Escolano, M., Badir, S. O. & Molander, G. A. Thianthrenium-enabled sulfonylation via electron donor-acceptor complex photoactivation. *Chem. Catal.* **2**, 898–907 (2022).

41. Zhang, L. & Ritter, T. A perspective on late-stage aromatic C–H bond functionalization. *J. Am. Chem. Soc*. **44**, 2399–2414 (2022).
42. Juliá, F. *et al*. High site selectivity in electrophilic aromatic substitutions: mechanism of C–H thianthrenation. *J. Am. Chem. Soc*. **143**, 16041−16054 (2021).
43. Mkhalid, I. A. I., Barnard, J. H., Marder, T. B., Murphy, J. M. & Hartwig, J. F. C–H activation for the construction of C–B bonds. *Chem. Rev.* **110**, 890–931 (2010).
44. Cho, J.-Y., Tse, M. K., Holmes, D., Maleczka, R. E. & Smith, M. R. Remarkably selective iridium catalysts for the elaboration of aromatic C–H bonds. *Science* **295**, 305–308 (2002).
45. Ishiyama, T., Takagi, J., Hartwig, J. F. & Miyaura, N. A stoichiometric aromatic C–H borylation catalyzed by iridium(I)/2,2'-bipyridine complexes at room temperature. *Angew. Chem. Int. Ed.* **41**, 3056–3508 (2002).
46. Migita, T., Nagai, T., Kiuchi, K. & Kosugi, M. Convenient preparation of tetraarylphosphonium halides. *Bull. Chem. Soc. Jpn.* **56**, 2869–2870 (1983).
47. Marcoux, D. & Charette, A. B. Nickel-catalyzed synthesis of phosphonium salts from aryl halides and triphenylphosphine. *Adv. Synth. Catal.* **350**, 2967–297 (2008).
48. Mu, X., Zhang, H., Chen, P. & Liu, G. Copper-catalyzed fluorination of 2-pyridyl aryl bromides. *Chem. Sci.* **5**, 275–280 (2014).
49. Li, Y., Cao, Y. & Guo, Y. Recent advances in atmospheric ionization mass spectrometry: developments and applications. *Chin. J. Chem*. **38**, 25–38 (2020).

Supplementary Information is available in the online version of the paper.

Acknowledgements We gratefully acknowledge National Key R&D Program of China (2021YFA1500200), National Natural Science Foundation of China (22171277, 22101291, 21821002), Shanghai Rising-Star Program (20QA1411400), Shanghai Institute of Organic Chemistry, and State Key Laboratory of Organometallic Chemistry for financial support. We also thank S. Liu for verifying the reproducibility of this work.

Author Contributions X.Y.C. developed the reactions and performed the mechanistic studies. Y.W. assisted with the mechanistic studies and data analysis. J.H.B. assisted with the mechanistic studies using SAESI-MS technology. Y.L.G. guided the mechanistic studies using SAESI-MS technology. P.W. conceived this concept, guided the project and prepared this manuscript with feedback from X.Y.C.

Competing interests: P.W. and X.Y.C. are inventors on a patent related to this work (CN 202210303743.0) filed by Shanghai Institute of Organic Chemistry (SIOC). The authors declare no other competing interests.

Author Information The authors declare no competing financial interests. Readers are welcome to comment on the online version of this article. Correspondence and requests for materials should be addressed to Y.L.G. (ylguo@sioc.ac.cn) and P.W. (pengwang@sioc.ac.cn).