Tagging Peptides with a Redox Responsive Fluorescent Probe Enabled by Photoredox Difunctionalization of Phenylacetylenes with Sulfinates and Disulfides

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ABSTRACT: Herein, we describe a photoredox three-component atom-transfer radical addition (ATRA) reaction of aryl alkynes directly with dialkyl disulfides and alkylsulfonates, circumventing the utilization of chemically unstable and synthetically challenging S-alkyl alklythiosulfonates as viable addition partners. A vast array of (E)-β-alkylsulfonylvinyl alkylsulfides was prepared with great regio- and stereoselectivity. Moreover, this powerful tactic could be employed to tag cysteine residues of complex polypeptides in solution or on resin merging with solid phase peptide synthesis (SPPS) techniques. A sulfonyl-derived redox responsive fluorescent probe could be conveniently introduced on the peptide, which displays green fluorescence in cells while showing blue fluorescence in medium. The photophysical investigations reveal that the red shift of the emission fluorescence is attested to reduction of carbonyl group to the corresponding hydroxyl moiety. Interestingly, the fluorescence change of tagged peptide could be reverted in cells by treatment of H$_2$O$_2$, arising from the reoxidation of hydroxyl group back to ketone by the elevated level of reactive oxygen species (ROS).

KEYWORDS: Peptide Modification, Redox Responsive Fluorescent Probe, Photoredox, Difunctionalization, Aryl Alkynes

Cysteine plays a diverse range of pivotal roles in biological events, such as redox regulation, metal binding, and other posttranslational modifications (PTMs).1−12 Cysteine residues have been well explored for chemo-modification in a site-selective manner attesting to their highest nucleophilicity among the canonical amino acids, relatively low abundance (only 2.3% genome-wide),4 as well as facile installment via single-site mutagenesis.5 Conventionally, cysteine bioconjugation primarily relies on nucleophilic alkylation, including Michael addition and S$_2$2 reaction, along with arylation, alkylation, and others.6−13

However, the thioethers generated by these strategies could undergo thiol exchange with free cysteines or glutathiones, leading to problematic decomposition of the chemical modification.14,15 Therefore, the growing need for new cysteine bioconjugations with stable covalent tags persists. In this regard, photoredox atom transfer radical addition (ATRA)16,17 of alkynes with thiosulfonates18,19 is particularly appealing, since the thyl group of cysteine could be modified with a robust vinyl sulfonyl motif in an atom- and step-economical manner under mild and environmentally benign conditions. In addition, sulfonyl-derived fluorophores,20−27 a class of underdeveloped fluorescent tags, could be conveniently introduced by this powerful strategy, allowing imaging studies of peptides or proteins of interest in a biological context. In 2018, Xu and co-workers reported a synergetic gold/photoredox catalyzed stereoselective ATRA of thiosulfonates with phenylacetylenes to exclusively afford (E)-β-arylthioli vinyl sulfones (Scheme 1a).28 Sulfonyl radicals, which were generated from thiosulfonates in the presence of Ru(bpy)$_3$Cl$_2$ as the photocatalyst under the irradiation of blue LED, acted as the key intermediate. In 2020, our group exploited thiosulfonates as a thyl radical precursor while switching the light source and photocatalyst to white LED and Eosin Y, respectively (Scheme 1b),29 and developed a highly stereo-selective approach altering the regioselectivity compared to Xu’s report. Very recently, Xu, Chen, and co-workers expanded the scope of aryl alkynes to 2-vinyloxy aryalkynes in photoredox ATRA with thiosulfonates, and a variety of thiosulfonated pyrrolo[1,2-α] benzimidazoles were prepared (Scheme 1c).30

Despite progress, there are still some common drawbacks in the previous reports, jeopardizing the application of this powerful tool on cysteine bioconjugation. Synthesis of S-alkyl alklythiosulfonates, a class of molecules sensitive to air and moisture, typically is not trivial, which suffers from tedious operation and low yields.31,32 Consequently, they have been precluded as viable addition partners so far in ATRA with...
alkenes or alkynes. To overcome this issue, herein we report a mild, efficient and step-economic photoredox ARTA of phenylacetylenes with readily available sodium alkylsulfinates and commercially available dialkyl disulfides to produce ($E$)−β-alkylsulfonylvinyl alkylsulfides with great regio- and stereo-selectivity (Scheme 1d). In particular, this powerful tool was successfully applied to functionalize complex peptides in liquid phase or on resin, allowing the installation of a redox-responsive sulfonyl-derived fluorescent probe on cysteine residues.

Electronically and sterically unbiased phenylacetylene (1a), dimethyl disulfide (2a), and sodium methanesulfinate (3a) were selected as the model substrates. The optimization of reaction conditions commenced by a short survey of three common solvents [N,N-dimethylacetamide (DMA), N,N-dimethylformamide (DMF), and dimethyl sulfoxide (DMSO)] while Eosin Y acted as photocatalyst under the irradiation of blue LED (11 W), similar to the conditions previously reported by our group (Table 1, entries 1−3).

DMSO was proven to be superior, affording the desired product 4aaa in 36% yield (Table 1, entry 3). Next, four other photocatalysts (Rhodamine B, Ir-1, Ir-2, and Ir-3) were investigated (Table 1, entries 4−7), and Ir-3 exhibited the best catalytic reactivity, probably due to the suitable redox potential (Table 1, compare entry 7 vs entries 3−6). Forging ahead with Ir-3 as the optimal photocatalyst, the assay yield of 4aaa could be improved to 50% when 15-crown-5 and (tBuO)$_2$ as additive were used (Table 1, entry 8). The assay yield of 4aaa was further increased to 70% when 1.0 equiv of (tBuO)$_2$ as additive was subjected (Table 1, entry 9). Adjusting the limiting agent to 1a while 2a was employed in 1.5 equiv and 3a in 2.5 equiv resulted in the formation of 4aaa in 83% assay yield, 83% isolated yield (Table 1, entry 10). Therefore, the optimal condition for photoredox three-component difunctionalization of phenylacetylene was 1a as limiting agent, 1.5 equiv of 2a and 2.5 equiv of 3a as addition partners, 1 mol % of Ir-3 as photocatalyst, 2.0 equiv of 15-crown-5 and 1.0 equiv of (tBuO)$_2$ as additive, under irradiation of blue LED (11 W) at room temperature in air for 12 h [see the Supporting Information (SI) for a complete list of conditions for optimization]. To set the stage for application of the newly devised method in the bioconjugation of complex peptides, a water tolerance test was also conducted. In the presence of 20 μL (11.1 equiv) or 50 μL (27.8 equiv) of H$_2$O as additive (Table 1, entries 11, 12), 4aaa was still obtained in 64% and 53% yield, respectively.

To probe the mechanism of the photocatalytic transformation, especially the rationale of the regioselectivity of our protocol, a series of control experiments were conducted. First, we observed that this addition process required continuous visible-light irradiation based on the results of the light “on−off” experiment (see Figure S1 for details). While 2,2,6,6-tetramethylpiperidinooxy (TEMPO) as a radical scavenger was subjected into the standard conditions, the ARTA reaction was significantly inhibited. Moreover, introduction of 1 equiv of 5,5-dimethyl-1-pyrroline N-oxide (TEMPO) as a radical scavenger was subjected into the standard conditions, the ARTA reaction was significantly inhibited. Moreover, introduction of 1 equiv of 5,5-dimethyl-1-pyrroline N-oxide (DMPO) into the standard catalytic reaction resulted in the isolation of radical trapped complex 5, which was characterized by electron paramagnetic resonance spectroscopy (EPR) and...
HRMS analysis (see Figures S3 and S4 for details). These results collectively led to the conclusion that thyl radicals generated from disulfides serve as the key intermediate in our reaction. These radicals were determined by HRMS analysis (see Figures S3 and S4 for details). These results collectively led to the conclusion that thyl radicals generated from disulfides serve as the key intermediate in our reaction.

Table 1. Optimization of the Reaction Conditions

| entry | photocatalyst | additive | solvent | assay yield/% |
|-------|---------------|----------|---------|---------------|
| 1     | Eosin Y       | DMA      | 11      |
| 2     | Eosin Y       | DMF      | 20      |
| 3     | Eosin Y       | DMSO     | 36      |
| 4     | Rhodamine B   | DMSO     | 8       |
| 5     | Ir-1          | DMSO     | 33      |
| 6     | Ir-2          | DMSO     | 25      |
| 7     | Ir-3          | DMSO     | 42      |
| 8     | Ir-3          | 15-crown-5 | DMSO | 50        |
| 9     | Ir-3          | 15-crown-5/('BuO)2 | DMSO | 70        |
| 10    | Ir-3          | 15-crown-5/('BuO)2 | DMSO | 83(83) |
| 11    | Ir-3          | 15-crown-5/('BuO)2 | DMSO | 64        |
| 12    | Ir-3          | 15-crown-5/('BuO)2 | DMSO | 53        |

“General conditions: Unless otherwise stated, reactions were carried out with 1a (0.1 mmol), 2a (0.15 mmol), 3a (0.15 mmol), photocatalyst (1 mol %), 15-crown-5 (0.2 mmol), ('BuO)2 (0.1 mmol), in solvent (1.0 mL) at room temperature under irradiation of 11 W blue LED under an air atmosphere for 12 h. Assay yields determined by 1H NMR spectroscopy of unpurified reaction mixtures using 0.1 mmol (7.0 equiv) of CH3Br as internal standard. 12 h. 3a (0.25 mmol), 12 h. Isolated yield. 20 μL H2O (11.1 equiv) used as additive. 250 μL H2O (27.8 equiv) used as additive.

Based on the aforementioned results, a plausible mechanism is illustrated in Scheme 2. The photocatalytic cycle commences with oxidative quenching of the excited Ir-based photocatalyst (Ir1**) by DTBP to afford the tert-butoxy radical, followed by reaction with disulide 2a to yield the thyl radical I. Thyl radical I is added to phenylacetylene to produce the α-alkenyl carbon radical II, which undergoes the subsequent single-electron oxidation by Ir** to deliver the benzyl alkyl cation III and simultaneously regenerates the ground-state IrIII to close up the photocatalytic cycle. Finally, the nucleophilic attack of the alkyl sulfinate anion to alkyl cation III generates the target product 4aaa. Thyl radical I acts as the key intermediate to initiate the ATRA process, defining β-alkylsulfonylvinyl alkylsulfides as the major regioisomer. The trans-benzylic vinyl radical intermediate II and the subsequent cation III are more stable than the cis-counterparts, and thus, E-stereoselectivity is favored for our ATRA protocol.

With the optimized conditions established, we first investigated the substrate scope of alkynes in photoredox three-component ATRA with 2a and 3a (Scheme 3). The neutral phenylacetylene (1a) or p-tolyacetylene (1b) could undergo ATRA with 2a and 3a under the optimal conditions to furnish 4aaa and 4baa in 83% and 64% yields, respectively. The structure of 4aaa was unambiguously assigned by X-ray crystallography. Aryl alkyne bearing electron-donating-p-OMe (1c) was well tolerated by our photoredox ATRA, providing 4aca in 66% yield. Aryl alkynes possessing electron-withdrawing groups, such as p-F (1d), p-Cl (1e), p-CN (1f), and p-CN (1g), reacted smoothly to afford 4daa−4gaa in the yields ranging from 56% to 70% with exclusive stereoselectivity. Sterically hindered 1-naphthylacetylene (1m) could be employed as a competent substrate as well, and 4maa was successfully produced in 76% yield, albeit with modest stereoselectivity (E/Z = 6:1). The mild photoredox conditions enabled the compatibility of an array of functional groups appending on aryl alkynes, including aldehyde (1h), ester (1i), ketone (1j and 1k), and amide (1l). Remarkably, this chemistry was also well accommodated by a range of heteroaryl alkynes, and thiophenyl [1n (E/Z = 12:1) and 1o (E/Z = 18:1)], pyridinyl (1p), quinolinyl (1q), and indolyl (1r) alkynes furnished the corresponding products (4nnaa−4raa) with good results, highlighting the expediency and breadth of this protocol. To display the potential utility of our
photoredox protocol, alkylsulfonyl and alkylthiyl groups could be conveniently introduced on acetylenes derived from commercially available pharmacophores, such as coumarin (1s) and estrone (1t), in synthetically useful yields but with great stereoselectivity. In addition, a fluorescence phenyl-acetylene derivative 1u was employed as substrate to react with 2a and 3a under the optimal conditions, and the desired product 4uua was generated in 47% yield, albeit in low diastereoselectivity (dr = 3:1).

We next turned our attention to the substrate generality of dialkyl disulfides in photoredox ATRA with 1a and 3a (Scheme 4). Disopentyl disulfide (2b) was successfully employed as addition partner to deliver 4aba in 81% yield. α-Branched disopropyl disulfide (2c) was compatible by our ATRA as well, affording 4aca in 53% yield. Of note, sodium alkylsulfinates tethered with the dialkyl disulfides employed have been restricted to symmetric disulfides, which are particularly unsuitable for the dialkyl disulfides possessing the unprotected alcohol (2h). Considering the oxidative condition, the ATRA of disulfides possessing the unprotected alcohol (2h) is particularly impressive, which also displays the excellent chemoselectivity of our protocol favoring C–S bond formation over the C–O bond. Remarkably, the chemistry was also accompanied by disulfides derived from cysteine (Cys, 2o) and cysteine-proline dipeptide (Cys-Pro, 2p). Moreover, a complex pentapeptide (2q) was proved to be a suitable addition partner to deliver 4aq in 53% yield (E/Z = 2:1), demonstrating the potential application of our protocol in functionalization of complex molecules in the late stage.

Furthermore, the substrate scope of sodium alkylsulfonates was examined in photoredox ATRA with 1a and 2a (Scheme 5). Linear n-propyl or branched isopropyl sodium sulfonates reacted smoothly with 1a and 2a to deliver 4aab and 4aac in 72% and 53% yields, respectively. Cyclic alkylsulfonates were also viable substrates, as evidenced by the formation of 4aad and 4aae in 75% and 51% yields, respectively. Sodium benzenesulfinate (3f) could undergo this ATRA to provide 4aaf in 49% yield. Of note, sodium alkylsulfonates tethered with an array of functionalities, including ether (3g), ester (3h, 3i), nitride (3j), and amide (3k), were well tolerated by our protocol, affording 4aag–4aak in 50–71% yields.

Encouraged by the successful modification of cysteine-derived peptides in solution via our ATRA protocol (4aa0–4aqa, Scheme 3), the attempts to apply this powerful tactic to functionalize complex polypeptides along with solid phase peptide synthesis (SPPS) were subsequently performed. So far, the dialkyl disulfides employed have been restricted to symmetric disulfides, which are particularly unsuitable for polypeptides owing to poor atom-economy and challenging preparation of substrates. To overcome this issue, a series of disulfide-based protecting groups was surveyed to expand the substrate scope of our protocol to asymmetric disulfides (Table 2). Protected cysteines bearing five disulfide-based protecting

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**Scheme 4. Substrate Scope of Disulfides in Photoredox Three-Component ATRA with 1a and 3a**

**Scheme 5. Substrate Scope of Sodium Sulfonates in Photoredox Three-Component ATRA with 1a and 2a**

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4 Reaction conditions: 1a (0.1 mmol), 2 (0.15 mmol), 3a (0.4 mmol), 1r-3 (1 mol %), 15-crown-5 (2.0 mmol), (BuO)₂ (0.1 mmol), DMSO (1.0 mL), rt, air, blue LED (80 W), 12 h. **2 (0.3 mmol), 80 °C. **2 (0.3 mmol), blue LED (11 W). 3a (0.25 mmol), blue LED (11 W). 3a (0.4 mmol), (BuO)₂ (0.12 mmol), Na₃PO₄ (0.1 mmol). 3a (0.01 mmol), 2 (0.015 mmol), 3a (0.04 mmol), 15-crown-5 (0.02 mmol), (BuO)₂ (0.012 mmol), Na₃PO₄ (0.01 mmol), DMSO (0.1 mL).
Table 2. Optimization of Disulfide Protecting Groups for Photoredox ATRA of Cysteine Disulfide

| entry | PG       | bp yield% | 4aoa yield% | bp:4aoa |
|-------|----------|-----------|-------------|---------|
| 1     |          | 6         | 8           | 1:1.3   |
| 2     |          | 12        | 53          | 1:4.4   |
| 3     |          | 70        | 28          | 1:0.4   |
| 4     |          | 10        | 68          | 1:6.8   |
| 5     |          | 6         | 72          | 1:12    |

*Reaction conditions: 1a (0.1 mmol), CysPG (0.15 mmol), 3a (0.4 mmol), Ir-3 (1 mol%), 15-crown-5 (0.2 mmol), (BuO)3 (0.1 mmol), DMSO (1.0 mL), rt, air, blue LED (80 W), 12 h. *Isolated yield.

groups were evaluated under the optimal conditions, and the most atom-economic CysSMe led to the formation of desired product 4aoa in 72% yield with 1:12 chemoselectivity favoring 4aoa (Table 2, entry 5). Other protected cysteine derivatives either resulted in low yields of 4aoa (entries 1 and 3, Table 2) or suffered from poor chemoselectivity (entries 2 and 4, Table 2). Thus, methylthiyl was determined to be the optimal protecting group for cysteine in the following ATRA of peptides with SPPS.

To our delight, the photoredox ATRA protocol can be adapted to the easy-to-handle SPPS peptide synthesis as shown in Figure 1. The CysSMe derivative of tripeptide Arg-Gly-Asp, a PET molecular imaging agent for angiogenesis attributing to its high affinity and specificity for integrin \( \alpha_v \beta_3 \), could undergo our photoredox ATRA with phenylacetylene (1a) and dimethyl disulfide (2a) on resin in DMSO, and the desired product 5 was obtained in 26% overall yield after 10 steps, including peptide condensation, deprotection, photoredox difunctionalization reaction, and the final cleavage from the resin (Figure 1). Moreover, the newly devised protocol could also be applied with SPPS on Ser-Lys-Gly-Cys\(^{SMe}\)Phe, a category of C-type natriuretic peptide which plays a key role in maintaining electrolyte liquid balance and vascular tension, as evidenced by generation of product 6 in 21% overall yield after semipreparative HPLC purification.

Remarkably, the newly devised method can be used as an efficient tool to install sulfonyl-derived fluorescent probe on cysteine residues of complex polypeptides merging with SPPS techniques, offering an exciting opportunity for imaging analysis of the structure, function, dynamic behavior, and localization of the molecule of interest in the biological environment. An HIV-1 transactivating protein-derived cell penetrating peptide, namely, Cys-TAT(47-57), was determined to be the target sequence. Using our photoredox difunctionalization strategy, a fluorophore, 10-ethyl-2-sulfinate-acridone (ESAC), was introduced to the peptide sequence on Wang resin, and the ESAC-labeled TAT analogue (ESAC-TAT) was successfully accomplished via SPPS in 1.3% overall yield (26 steps, Figure 1), which provides an unique opportunity to study the cell uptake and distribution of this class of potential delivery molecules by confocal microscopy (Figure 2). Following addition to growth medium, ESAC-TAT penetrates the cell membrane of the human breast cancer cell line HeLa, and primarily localizes to the cytoplasm, along with some accumulated in the lysosome, as verified by the colocalization of commercial lysosome stain LysoTracker (Pearson correlation coefficient = 0.49). Interestingly, in contrast to the report that TAT peptides were found to promote the accumulation of Cas9 protein and TAT-functionalized nanovehicles in the nucleus of liver model cells (Hepa 1-6 cells), we did not observe the distribution of ESAC-TAT in the nucleus of HeLa cells as supported by no colocalization of DAPI, a commonly used nucleus stain (see Figure S7 for details). Similar trends of ESAC-TAT in terms of cell uptake and distribution were also observed on human lung cancer cell line A549 and human colorectal carcinoma cell line HCT116 (Figure 2). This phenomenon implies that TAT’s nucleus targeting role might be cell line-dependent. In turn, the tag may perturb the localization of the peptide sequence.

During the cell uptake study, ESAC-TAT emits blue fluorescence under irradiation of 365 nm UV in HeLa, A549, or HCT116 cells (Figure 2), but in contrast, it displays green fluorescence in DMEM media under otherwise identical conditions (Figure 3). The apparent shift of emission spectroscopy clearly indicates the structural transformation of fluorophore in cells, which could be attributed to either pH change or redox process. Due to essential roles in biological functions and the close relationship to the development of diseases, detection and monitoring of ROS in cells and in vivo has been a focus of research for decades. In this regard, a large amount of fluorescent probes have been developed. Compared to fluorescent protein, small molecule-based fluorescent probes do not require gene manipulation and exhibit advantages including high sensitivity, great selectivity, convenience, and low invasiveness and, thus, have achieved tremendous progress. Nevertheless, no color change was observed by pH titration of ESAC in the pH range of 2–14.

![Figure 1. Photoredox ATRA of peptides along with SPPS.](https://doi.org/10.1021/jacsau.2c00577)
precluding the possibility of it as a pH responsive fluorescent probe (Figure S11). Next, we hypothesized that the carbonyl group in ESAC (A, Figure 3) could be reduced to the secondary alcohol in cells by carbonyl reductase after ESAC-TAT entered the cells, resulting in the red shift of fluorescence. To verify this hypothesis, the reducing form of ESAC (B, Figure 3) was independently synthesized. Gratifyingly, B, which exhibits green fluorescence under irradiation of 365 nm UV in DMEM medium, also shares very similar spectroscopic patterns to those of ESAC-TAT incubated with HeLa cells (see SI for details). The spectroscopic analysis showed that B has a 3-fold increase of Stokes shift ($\Delta \lambda = 84$ nm, Figure S10) compared to A ($\Delta \lambda = 26$ nm, Figure S9). All of the data support the conclusion that ESAC possibly acts as a redox responsive fluorescent probe, wherein the reduction of carbonyl group to secondary alcohol leads to the red shift of emission fluorescence. Moreover, a general solvatochromism study of A was performed as well (Figure S13 and S14), and no obvious spectroscopic shift was observed across an array of solvents, ruling out solvatochromism as the possible reason for the fluorescence change of A.

To further confirm our conjecture that reduction of the ketone motif leads to the red-shifted fluorescence emission of the probe after ESAC-TAT penetrates into the cells, we decided to revert the fluorescence changing phenomenon following regeneration of ESAC-TAT by oxidation of B under exposure to a simulated high concentration of ROS in cells. After HeLa cells were incubated with 1 $\mu$M ESAC-TAT for 24 h, the medium was replaced with a new batch containing H$_2$O$_2$ (0.4 $\mu$M). During this process, the cells were investigated at different times by confocal microscope (Figure 4a). After incubation with H$_2$O$_2$ for 1 h, exclusive green fluorescence was observed in the cells. To our delight, the confocal microscopic studies reveal that a small portion of probes started to turn back to blue after 4 h incubation with H$_2$O$_2$. After treatment with H$_2$O$_2$ for 12 h, the blue fluorescence in the cells became more apparent. The mean intensity ratio of the blue and green channel is plotted in Figure 4b. After quantification, it was clearly shown that the blue fluorescence gradually increased after incubation with H$_2$O$_2$. It was also noted that treatment of HeLa cells by H$_2$O$_2$ (0.4 $\mu$M) did not lead to noticeable cell viability change with 24 h incubation time (Figure 4c). There was no obvious sign of necrosis displayed until 24 h either, indicating the potential utility of ESAC as a redox responsive probe in monitoring ROS in live cells.

In summary, we have developed a photoredox three-component ATRA protocol of phenylacetylenes directly with dialkyl disulfides and alkylsulfonates to afford (E)-$\beta$-alkylsulfo-
nilyvinyl alkylsulfides with good regio- and stereoselectivities. A vast array of functional groups as well as heterocycles was successfully tolerated. Moreover, the photoredox ATRA could be utilized to functionalize complex polypeptides either in solution or on resin with great level of chemoselectivity. A sulfonyl-based redox-responsive fluorescent probe (ESAC) could be introduced on cysteine residues of polypeptides via our photoredox ATRA protocol, enabling the imaging investigations of a cell penetrating peptide (ESAC-TAT) on cell uptake and distribution. ESAC-TAT shows blue fluorescence in media but displays green fluorescence after entering cells, which probably arises from the reduction of ketone to the corresponding hydroxyl moiety in the fluorophore. Remarkably, upon treatment with H2O2, the red-shifted emission fluorescence of ESAC-TAT could be reverted due to the increased oxidative environment in the cells. The mechanistic studies corroborate the photoredox pathway, wherein thyl radicals serve as the key intermediate. This work provides a facile tagging means to polypeptides with a redox-responsive fluorescent probe, and its further applications in the context of chemical biology are currently under investigation in our laboratory.

■ ASSOCIATED CONTENT

* Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacsau.2c00577.

General information, experimental procedures, characterization data of products, X-ray crystallographic data, and cellular studies (PDF)

Figure 4. (a) Reversion of fluorescence change in HeLa cells via treatment of H2O2. HeLa cells were incubated with 0.4 μM H2O2 for 24 h after incubated with 1 μM ESAC-TAT for 24 h. The images were captured by confocal microscopy (63× oil). Scale bar = 10 μm. (b) Fluorescence intensity ratio of blue channel (405 nm) over green channel (488 nm). (c) Cell viability study via WST assay upon treatment of H2O2 (0.4 μM).

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Notes

The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

T.J. thanks Guangdong-Joint Foundation of Shenzhen (2021B1515120046), Natural Science Foundation of Guangdong Province (2022A1515011770), and Guangdong Provincial Key Laboratory of Catalysis (2020B121201002) for financial support. Q.L. thanks the National Natural Science Foundation of China (31901786, 22078263) for financial support. We are also very grateful to Dr. Yang Yu and Dr. Xiaoyong Chang (both at SUSTech) for HRMS and X-ray crystallography, respectively. We acknowledge the assistance of SUSTech Core Research Facilities.

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