Design and application of α-ketothioesters as 1,2-dicarbonyl-forming reagents

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The 1,2-dicarbonyl motif is vital to biomolecules, especially natural products and pharmaceuticals. Conventionally, 1,2-dicarbonyl compounds are prepared via an α-keto acyl chloride. Based on the methods used in nature, a transition-metal-free approach for the synthesis of an α-ketothioester reagent via the combination of an α-hydroxy ketone, elemental sulfur and a benzyl halide is reported. Mechanistic studies demonstrate that the trisulfur radical anion and the α-carbon radical of the α-hydroxy ketone are involved in this transformation. The dicarbonylation of a broad range of amines and amino acids, and importantly, cross couplings with aryl borates to construct dicarbonyl-carbon bonds are realized under mild conditions by employing this stable and convenient α-ketothioester as a 1,2-dicarbonyl reagent. The dicarbonyl-containing drug indibulin and the natural product polyandrocarpamide C, which possess multiple heteroatoms and active hydrogen functional groups, can be efficiently prepared using the designed 1,2-dicarbonyl reagent.

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The 1,2-dicarbonyl motif is an important life-related structure that is ubiquitous in natural products and modern pharmaceuticals. Licoagrodione, isolated from a Chinese herb, was found to exhibit antimicrobial activity. Tanshinone IIA is a transcription factor inhibitor and was isolated from Salvia miltiorrhiza. Mansonone C, isolated from Mansonia altissima, displays antifungal activity against P. parasitica. Sophoradione was isolated from the roots of S. flavescens and is cytotoxic to KB tumour cells. Since the dicarbonyl motif can bind to proteins in the body to increase their bioavailability, many well-known dicarbonyl-containing molecules have been turned into clinically used drugs, such as the anticancer drugs indibulin and biricodar, the anti-HCV drug boceprevir, and the dermatologic agent fluocortin butyl, a synthetic corticosteroid with high topical to systemic activities. Furthermore, dicarbonyl-containing compounds frequently serve as valuable synthetic intermediates and precursors in organic synthesis and materials science. For example, aromatic substituted quinoxalines, which possess broad applications as photoinitiators and fluorescence-based sensors, have been synthesized from dicarbonyl-containing compounds. Conventionally, dicarbonyl compounds are prepared via Müller photoinitiators and substituted quinoxalines, which possess broad applications as fluorescent-based sensors, have been synthesized from dicarbonyl-containing compounds. A convenient acylation of readily available 2-hydroxy-1-phenylethanone with elemental sulfur and a benzyl halide is reported. The dicarbonylation of a broad range of amines and amino acids, and cross couplings with aryl borates to construct dicarbonyl-carbon bonds are realized by employing this stable and convenient a-ketothioester as a 1,2-dicarbonyl reagent.

**Results**

**Optimization and Synthesis of a 1,2-Dicarbonyl-forming Reagent.** We commenced our studies by investigating the transformation of readily available 2-hydroxy-1-phenylethanol to the corresponding α-ketothioester in the presence of S₈ and tetrabutylammonium bromide (TBAB) in cyclopentyl methyl ether (CPME) under an inert atmosphere. Unfortunately, desired α-ketothioester 2a was not obtained when the reaction was run with only base or water (Table 1, entries 1, 2). 2a could not be provided under the conditions of organic bases, regardless of whether water was added or not in the reaction (Table 1, entries 3–6). Encouragingly, dicarbonyl-forming reagent 2a was isolated in 71% yield when both potassium carbonate and water were added (Table 1, entry 7). When potassium hydrogen carbonate (KHCO₃) was used instead of potassium carbonate (K₂CO₃), the yield increased to 86% (Table 1, entry 8). Decreasing the amount of water to 10 equivalents resulted in a lower yield (Table 1, entry 9). Increasing the equivalents of water did not improve the reaction outcome (Table 1, entry 10). TBAB was not necessary when water was added (Table 1, entry 11). When the reaction was carried out under air, the isolated yield of 2a decreased to 61%, which means that oxygen affects this type of radical (Table 1, entry 12). As a continuation of our investigations of the transformations of inorganic sulfur compounds to organic sulfur structures, we hypothesize that trisulfur radical anions can react at the α position of α-hydroxy ketones (Fig. 2c). Herein, a transition-metal-free approach for the synthesis of an α-ketothioester reagent via the combination of an α-hydroxyl ketone, elemental sulfur and a benzyl halide is reported. The dicarbonylation of a broad range of amines and amino acids, and cross couplings with aryl borates to construct dicarbonyl-carbon bonds are realized by employing this stable and convenient α-ketothioester as a 1,2-dicarbonyl reagent.

**Fig. 1** Significant dicarbonyl-containing molecules. a Dicarbonyl-containing natural products. b Dicarbonyl-containing drug molecules.
Finally, S₈, KHCO₃ and TBAB in CPME with H₂O under a N₂ atmosphere were chosen as the optimal conditions. The generality of the reaction was explored on a variety of α-hydroxy ketones, as illustrated in Table 2. α-Hydroxy ketones bearing electron-donating groups could be smoothly transformed into the desired products in moderate to good yields regardless of the position of their substituent (2a–2e). Notably, when the reaction was performed on a 10-mmol (1.36 g) scale of 1a, product 2a could still be obtained in a good yield (74%), which highlights the potential of α-ketothioesters as dicarbonyl transfer reagents. To our delight, α-hydroxy ketones bearing electron-withdrawing substituents on the aromatic ring gave moderate to good yields when DMF was used as the solvent (2f–2k), in which the generation rate and stability of S₃· radical and enolate radical anion can be improved in the high polar solvent. Sensitive groups, such as ester and hydroxy groups, were also tolerated (2k and 2l). Heteroaryl α-hydroxy ketones, such as 2-furyl and 2-benzofuryl derivatives, could also be converted to the corresponding α-ketothioesters in moderate yields (2m, 2n and 2o). With regard to alkyl bromides, both primary and secondary bromides were compatible with the reaction (2p–2y) as well terminal alkenes and alkynes (2p and 2r). Benzyl bromides bearing different functional groups could be used to quench the reaction, affording the desired products in good yields (2v–2y).

The desired α-ketothioester 2a could not be furnished when α-formyl ketones 1a′ was used as the substrate, which indicated that 1a′ is not the intermediate in this transformation (Fig. 3a). Radical-trapping experiments were conducted by investigating TEMPO under the standard conditions. The coupling product 2ab was afforded in 35% yield, which provided strong evidence of
The coupling product 2ab was not observed in the absence of elemental sulfur under the standard conditions, which indicate that sulfur is essential for radical generation (Fig. 3c). A plausible reaction pathway that backed by these experimental evidences is described in Fig. 3d. The elemental sulfur interacted with the base to provide the trisulfur radical anion\(^{31-33}\). The \(\alpha\)-hydroxy ketone can also initiate a persistent radical at the \(\alpha\) position with the help of a base. Radical intermediate I was generated in the presence of both the trisulfur radical anion and a base. Subsequent coupling of the two different radicals in the reaction system afforded intermediate II. The dissociation of II could afford compound III and release HSS\(^-\), which combines with the alkyl halide to produce a mixture of polysulfide compounds (BnSS\(_n\)Bn). Intermediate III can tautomerize to sulfur anion IV, a more nucleophilic conformation, which can then undergo an S\(_2\)2 substitution to eventually form desired product 2.

**Dicarbonylation with the Designed Reagents.** \(\alpha\)-Ketoamides are an important fragment in drug discovery both in biological activities and synthetic transformations. A dicarbonyl fragment

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**Table 1 Optimization of the 1,2-dicarbonyl-forming reagent**

| Entry | Base       | \(H_2O\) (equiv.) | Yields (%) |
|-------|------------|-------------------|------------|
| 1     | -          | 20                | NP         |
| 2     | \(K_2CO_3\) | -                 | Trace      |
| 3\(a\) | Et\(\text{N}\) | -                 | NP         |
| 4\(a\) | DIPA       | -                 | NP         |
| 5\(a\) | DBU        | -                 | NP         |
| 6\(a\) | Et\(\text{N}\) | 20                | NP         |
| 7\(a\) | \(K_2CO_3\) | 20                | 71         |
| 8     | \(KHC_6O_6\) | 20                | 86         |
| 9     | \(KHC_6O_6\) | 30                | 82         |
| 10    | \(KHC_6O_6\) | 20                | 76         |
| 11\(c,d\) | \(KHC_6O_6\) | 20                | 61         |
| 12\(e\) | \(KHC_6O_6\) | 20                | 45         |
| 13\(e\) | \(KHC_6O_6\) | 20                | 45         |

NP: no product

**Conditions:** 1a (0.5 mmol), \(KHC_6O_6\) (1 mmol), \(S_8\) (2.0 mmol), tetrabutylammonium bromide (TBAB) (0.1 mmol) and \(H_2O\) (4 mmol) were stirred at 90 °C in cyclopentyl methyl ether (CPME) (4 mL) for 10 h under \(N_2\), and then \(RBr\) (0.75 mmol) was added. The system was heated for another 2 h under \(N_2\).

**Table 2 Construction of a library of 1,2-dicarbonyl-forming reagents**

| AR         | Conditions | R           | Yields (%) |
|------------|------------|-------------|------------|
| \(\text{MeO}_2C\) |            | O           | 2k 64%    |
|             |            | S           | 2l 45%    |
|             |            | HO          | 2m 65%    |
| \(\text{MeO}_2C\) |            | O           | 2n 68%    |
|             |            | S           | 2p 61%    |
|             |            | O           | 2q 83%    |
|             |            | S           | 2r 56%    |
| \(\text{MeO}_2C\) |            | O           | 2s 66%    |
|             |            | S           | 2t 71%    |
|             |            | O           | 2u 68%    |
|             |            | S           | 2v R = Me, 84% |
|             |            | S           | 2w R = NO_2, 55% |
|             |            | S           | 2x R = CO_2Me, 77% |
|             |            | S           | 2y R = F, 87% |

**Conditions:** 1 (0.25 mmol), \(KHC_6O_6\) (0.5 mmol), \(S_8\) (0.75 mmol), and TBAB (0.05 mmol) were stirred at 90 °C in DMF (2 mL) for 10 h under \(N_2\), and then \(RBr\) (0.375 mmol) was added. The system was heated for another 2 h under \(N_2\).
Importantly, we demonstrated that 4-methoxyphenyl borates corresponding tert substituents and the presence of fused rings (\(5a\)) were effective candidates, regardless of the electronic properties of aryl borates was readily achieved to construct benzil derivatives. Reactions proceeded smoothly (3k-3n), successful, affording desired product \(2a\), bearing a broad range of electron-donating and electron-withdrawing substituents (including both aliphatic and aryl amines) under simple conditions (Table 3). 2-Oxo-2-phenylacetamide (3a), which possesses a free -NH\(_2\) group, is an important intermediate in organic synthesis and showed various bioactivities. When ammonia gas was bubbled into a solution of \(2a\), 3a was obtained in 79% yield. Notably, L-phenylglycinol was successfully applied to the dicarbonylation protocol, and the hydroxyl group was tolerated (3b). Octade-cyclamine, a weak nucleophile, could be converted into the corresponding α-ketoamide in moderate yield (3c). In addition, the dicarbonylation of sterically hindered tert-butyl amine was successful, affording desired product \(3f\) in 57% yield. Anilines bearing a broad range of electron-donating and electron-withdrawing substituents at the \(\text{para}\) and \(\text{ortho}\) positions, the reactions proceeded smoothly (3k-3n). Secondary anilines were also compatible with this transformation, but in lower yield (3o). Due to the simple reaction conditions, i.e., no base, and at room temperature, the dicarbonylation of a series of amino acid esters could afford the corresponding dicarbonyl compounds without erosion of the stereogenic information (>99% ee) in good yields (3p-3x). Notably, tri-glycine smoothly underwent the desired reaction to provide ethyl (2-oxo-phenylacetyl)glycylglycylglycinate (3y), which shows the great potential of this method for the late-stage modification of drug molecules.

Following the successful dicarbonylation of amines, the dicarbonylation of all-carbon aryl rings with borates for the construction of dicarbonyl-carbon bonds was studied. These reactions demonstrated the collective synthesis of dicarbonyl-containing derivatives via the current methodology (Table 4). The cross coupling of α-ketothioesters with a broad range of aryl borates was readily achieved to construct benznol derivatives. Aryl borates with substituents at different positions were all effective candidates, regardless of the electronic properties of the substituents and the presence of fused rings (5a-5i). Importantly, we demonstrated that 4-methoxyphenyl borates can be efficiently transferred to various primary or secondary α-ketoamides in good yields (including both aliphatic and aryl amines) under simple conditions (Table 3). 2-Oxo-2-phenylacetamide (3a), which possesses a free -NH\(_2\) group, is an important intermediate in organic synthesis and showed various bioactivities. When ammonia gas was bubbled into a solution of \(2a\), 3a was obtained in 79% yield. Notably, L-phenylglycinol was successfully applied to the dicarbonylation protocol, and the hydroxyl group was tolerated (3b). Octade-cyclamine, a weak nucleophile, could be converted into the corresponding α-ketoamide in moderate yield (3c). In addition, the dicarbonylation of sterically hindered tert-butyl amine was successful, affording desired product \(3f\) in 57% yield. Anilines bearing a broad range of electron-donating and electron-withdrawing substituents at the \(\text{para}\) and \(\text{ortho}\) positions, the reactions proceeded smoothly (3k-3n). Secondary anilines were also compatible with this transformation, but in lower yield (3o). Due to the simple reaction conditions, i.e., no base, and at room temperature, the dicarbonylation of a series of amino acid esters could afford the corresponding dicarbonyl compounds without erosion of the stereogenic information (>99% ee) in good yields (3p-3x). Notably, tri-glycine smoothly underwent the desired reaction to provide ethyl (2-oxo-phenylacetyl)glycylglycylglycinate (3y), which shows the great potential of this method for the late-stage modification of drug molecules.

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The dicarbonylation of alcohols and water for the construction of dicarbonyl-oxygen bonds was further studied. Benzy alcohol was successfully applied to the dicarbonylation protocol providing the desired product \(2aa\) in 73% yield. α-Ketothioester \(2a\) could be hydrolysed to 2-oxo-2-arylacetic acid \(2ac\) in the solution of sodium hydroxide. The common alcohols, such as ethanol and methanol, underwent smoothly affording the corresponding 2-oxo-2-arylacetic compounds in excellent yields (Fig. 4).

To further highlight the practical applicability of the 1,2-dicarbonyl-forming reagent, pharmaceutically relevant molecules and natural products were synthesized (Fig. 5). The anticancer drug indibulin could be prepared in a good yield from 1,2-dicarbonyl reagent \(6a\) through the dicarbonylation of the corresponding amine. The natural product polyandrocarpamide C and a 9,10-phenanthrenequinone derivative \(34\) were efficiently synthesized from 1,2-dicarbonyl reagents \(6b\) and \(6c\), respectively, which represents a new synthetic route to these bioactive molecules.

**Discussion**

In conclusion, a practical protocol for the straightforward construction of α-ketothioesters via the radical coupling of α-hydroxy ketones and elemental sulfur, in which \(S_8\) was successfully introduced to a thioester, was disclosed. This method avoids the use of malodorous thiols. The application of practical α-ketothioester reagents for the dicarbonylation of amines and boroxine anhydride to afford α-ketoamide and benzenol derivatives, respectively, was comprehensively achieved, and dicarbonyl motifs were successfully installed in these amino acid esters and peptides. These convenient reagents and procedures provide a potential method for the late-stage modification of drugs. Further studies on decarbonylations in drug discovery are ongoing in our laboratory.
**Methods**

**General procedure for syntheses of 1,2-dicarbonyl-forming reagents 2.** Under a N₂ atmosphere, α-hydroxy ketones 1 (0.5 mmol), S₈ (64.2 mg, 2 mmol), KHCO₃ (100 mg, 1 mmol), TBAB (32.3 mg, 0.1 mmol), H₂O (180 mg, 4 mmol) and CPME (4 mL) were added to a Schlenk tube. After stirring for 10 h at 90 °C (detect by TLC), RBr (0.75 mmol, 1.5 equiv) was added to this mixture. The resulting mixture was allowed to stir for 2 h at 90 °C. After completion of the reaction, water (5 mL) was added. The solution was extracted with ethyl acetate and organic layers were combined, dried over sodium sulfate before the organic phase was concentrated under vacuum. The residue was purified by column chromatography to give the corresponding product.

**General procedure for the dicarbonylation of amines.** α-Ketothioester 2 (0.2 mmol), amine (0.2 mmol) and THF (2 mL) were added to a reaction tube. After stirring for 12 h at room temperature (detect by TLC), the solvent was removed and the residue was purified by column chromatography to give the corresponding product 3.

**General procedure for the dicarbonylation of aryl borates.** Under a N₂ atmosphere, α-ketothioester 2 (0.1 mmol), aryl borate 4 (0.1 mmol), Pd₂(dba)₃ (0.0025 mmol, 2.5 mol%), 4,4'-dimethoxy-2,2'-bipyridine (0.01 mmol, 10 mol%), CuTc (0.1 mmol, 1 equiv), K₂CO₃ (0.15 mmol), anhydrous Na₂SO₄ (0.15 mmol) and DMF (1 mL) were added to a Schlenk tube. After stirring for 12 h at 45 °C (detect by TLC), the mixture was cooled to room temperature and water (5 mL) was added. Then the mixture was extracted with ethyl acetate and organic layers were combined, dried over sodium sulfate before the organic phase was concentrated under vacuum. The residue was purified by column chromatography to give the corresponding product.

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**Table 3 Dicarbonylation of amines**

| Aliphatic amines | Aryl amines | Amino acids |
|------------------|-------------|-------------|
| ![Image](image1.png) | ![Image](image2.png) | ![Image](image3.png) |

*Reaction conditions: 2 (0.2 mmol) and R'R₂NH (0.2 mmol) in THF (2 mL) were stirred at room temperature under air. *DMAP* (0.06 mmol) was added.*
**Table 4 Dicarbonylation of aryl borates**

| Reaction | Product | Yield (%) |
|----------|---------|-----------|
| 2a       | 2aa     | 73%       |
| 2b       | 2ab     | 84%       |
| 2c       | 2ac     | 94%       |
| 2d       | 2ad     | 84%       |
| 2e       | 2ae     | 87%       |

Fig. 4 Further transformations. Dicarbonylation of alcohols and water.
Data availability

The X-ray crystallographic coordinates for the structures reported in this study have been deposited at the Cambridge Crystallographic Data Centre (CCDC), under deposition number CCDC 1895971 (2j). These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. The authors declare that all other data supporting the findings of this study are available within the article and Supplementary Information files and are also available from the corresponding author on reasonable request.

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References

1. Staunton, J. Biosynthesis of Erythromycin and Rapamycin. Chem. Rev. 97, 2611–2630 (1997).
2. Li, W., Asada, Y. & Yoshikawa, T. Antimicrobial flavonoids from glycyrrhiza glabra hairy root cultures. Planta Med. 64, 746–747 (1998).
3. Jang, S.-I. et al. Tanshinone IIA from Salvia miltiorrhiza inhibits inducible nitric oxide synthase expression and production of TNF-α, IL-1β and IL-6 in activated RAW 264.7 cells. Planta Med. 69, 1057–1059 (2003).
4. Bettölo, G. B. M., Casinovi, C. G. & Galeffi, C. A new class of quinones: sesquiterpenoid quinones of Mansonia Altissima. Tetrahedron Lett. 52, 4857–4864 (1965).
5. Shen, C.-C. et al. Phenolic Constituents of the Roots of Sephora flavescens. J. Nat. Prod. 69, 1327–1340 (2006).
6. Otto, H.-H. & Schirmeister, T. Cysteine proteases and their inhibitors. Chem. Rev. 97, 133–172 (1997).
7. Knaack, M. et al. Synthesis and characterization of the biologically active 2-[1-(4-chlorobenzyl)-1H-indol-3-yl]-2-oxo-N-pyridin-4-yl acetamide. Eur. J. Org. Chem. 2001, 3843–3847 (2001).
8. Armistead, M. D., Harding, W. M., Saunders, J. O. & Boger, S. J. Biologically active acylated amino acid derivatives. United States Patent US 5723459 (1998).
9. Bacon, B. R. et al. Boceprevir for previously treated chronic HCV genotype 1 infection. N. Engl. J. Med. 364, 1207–1217 (2011).
10. Hartley, T. F. et al. Efficacy and tolerance of fluocortin butyl administered twice daily in adult patients with perennial rhinitis. J. Allergy Clin. Immunol. 75, 501–507 (1985).
11. Ashton, T. D., Jolliffe, K. A. & Pfeffer, F. M. Luminescent probes for the bioimaging of small anionic species in vitro and in vivo. Chem. Soc. Rev. 44, 4547–4595 (2015).
12. Wang, L. et al. Palladium-catalyzed oxidative cyclodDITION through C-H/N-H activation: Access to benzazepines. Angew. Chem. Int. Ed. 52, 1768–1772 (2013).
13. Chen, C.-T. et al. Doubly ortho-linked quinoxaline/diphenylfluorene hybrids as bipolar, fluorescent chameleons for optoelectronic applications. J. Am. Chem. Soc. 128, 10992–10993 (2006).
14. Sessler, J. L., Cho, D.-G. & Lynch, V. Diindolylquinolines: effective indole-based receptors for phosphate anion. J. Am. Chem. Soc. 128, 16518–16519 (2006).
15. Srinivasan, N. S. & Lee, D. G. Preparation of 1,2-diketones: oxidation of alkynes by potassium permanganate in aqueous acetone. J. Org. Chem. 44, 1574–1574 (1979).
16. Floyd, M. B., Du, M. T., Fabio, P. F., Jacob, L. A. & Johnson, B. D. The oxidation of acetoepheneones to arylglyoxals with aqueous hydrobromic acid in dimethyl sulfoxide. J. Org. Chem. 50, 3022–3027 (1985).
17. Merkul, E., Dohe, J., Gers, C., Rominger, F. & Müller, T. J. Three-component synthesis of ynediones by a glyoxylation/stephens–castro coupling sequence. Angew. Chem. Int. Ed. 50, 2966–2969 (2011).
18. Boersch, C., Merkul, E. & Müller, T. J. Catalytic syntheses of N-heterocyclic ynes and ynediones by in situ activation of carboxylic acids with oxalyl chloride. Angew. Chem. Int. Ed. 50, 10448–10452 (2011).
19. Stephanopoulos, N. & Francis, M. B. Choosing an effective protein bioconjugation strategy. Nat. Chem. Biol. 7, 876–884 (2011).
20. Dawson, P. E., Muir, T. W., Clark-Lewis, I. & Kent, S. B. Synthesis of proteins by native chemical ligation. Science 266, 776–779 (1994).
21. Waldvogel, S. R. Strategic applications of named reactions in organic synthesis. Background and detailed mechanisms. By Laszlo Kürti and Barbara Czako. Angew. Chem. Int. Ed. 44, 5005–5006 (2005).
22. Liu, H., Dong, C., Zhang, Z., Wu, P. & Jiang, X. Transition-metal-free aerobic oxidative cleavage of C-C bonds in a hydroxy ketones and mechanistic insight to the reaction pathway. Angew. Chem. Int. Ed. 51, 12570–12574 (2012).
23. Xiao, X., Xue, J. & Jiang, X. Polysulfurating reagent design for unsymmetrical polysulfide construction. Nat. Commun. 9, 2191 (2018).
24. Wang, M., Qiao, Z., Zhao, J. & Jiang, X. Palladium-catalyzed thiomethylation via a three-component cross-coupling strategy. Org. Lett. 20, 6193–6197 (2018).

25. Li, Y., Wang, M. & Jiang, X. Controllable sulfoxidation and sulfenylation with organic thiosulfate salts via dual electron- and energy-transfer photocatalysis. ACS Catal. 7, 7587–7592 (2017).

26. Wang, M., Chen, S. & Jiang, X. Construction of functionalized annulated sulfone via SO2/I exchange of cyclic diaryliodonium salts. Org. Lett. 19, 4916–4919 (2017).

27. Wang, M., Wei, J., Fan, Q. & Jiang, X. Cu(II)-catalyzed sulfide construction: both aryl groups utilization of intermolecular and intramolecular diaryliodonium salt. Chem. Commun. 53, 2918–2921 (2017).

28. Xiao, X., Feng, M. & Jiang, X. New design of a disulfurating reagent: facile and straightforward pathway to unsymmetrical disulfanes by copper-catalyzed oxidative cross-coupling. Angew. Chem. Int. Ed. 55, 14121–14125 (2016).

29. Qiao, Z. et al. Efficient access to 1,4-benzothiazine: palladium-catalyzed double C-S bond formation using Na2S2O3 as sulfurating reagent. Org. Lett. 15, 2594–2597 (2013).

30. Liu, H. & Jiang, X. Transfer of sulfur: from simple to diverse. Chem. Asian J. 8, 2546–2563 (2013).

31. Chivers, T. Ubiquitous trisulphur radical ion S3·-. Nature 252, 32–33 (1974).

32. Chivers, T. & Elder, P. J. W. Ubiquitous trisulfur radical anion: fundamentals and applications in materials science, electrochemistry, analytical chemistry and geochemistry. Chem. Soc. Rev. 42, 5996–6005 (2013).

33. Wang, M., Fan, Q. & Jiang, X. Transition-metal-free diarylannulated sulfide and selenide construction via radical/anion-mediated sulfur-iodine and selenium-iodine exchange. Org. Lett. 18, 5756–5759 (2016).

34. Trosien, S. & Waldvogel, S. R. Synthesis of highly functionalized 9,10-phenanthrequinones by oxidative coupling using MoCl5. Org. Lett. 14, 2976–2979 (2012).

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Author contributions

X.J. conceived the idea and supervised the whole project. M.W. and Z.D. designed and carried out the experiments. X.J. and M.W. discussed the results, contributed to the writing of the manuscript, and commented on the manuscript. All authors approved the final version of the manuscript for submission.

Additional information

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