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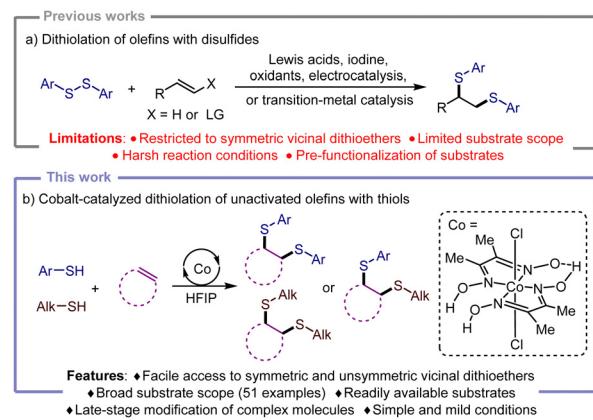
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**Direct dithiolation of alkenes with thiols has been rarely reported. Herein, a simple cobalt-catalyzed aerobic approach has been developed to realize this transformation. With the aid of HFIP, diverse vicinal dithioethers including symmetric and unsymmetric ones could be obtained from readily available substrates. Gram-scale synthesis and late-stage modification of complex molecules highlight the practicability of this approach.**

Organosulfur compounds ubiquitously occur in natural products, pharmaceuticals, agrochemicals, and polymer materials.<sup>1</sup> In particular, vicinal dithioethers are one class of important organosulfurs, which are widely used as versatile linchpins for valuable organic transformations.<sup>2</sup> For instance, transition metal complexes containing vicinal dithioethers as bidentate ligands have been employed as efficient catalysts for polymerization,<sup>3</sup> hydroamination,<sup>4</sup> asymmetric hydrogenation,<sup>5</sup> and asymmetric allylic alkylation.<sup>6</sup> Therefore, tremendous efforts have been devoted to the efficient synthesis of diverse vicinal dithioethers. In this regard, the dithiolation of alkenes represents an efficient and straightforward strategy to access vicinal dithioethers. Traditionally, the majority of the dithiolation reactions relied on the use of Lewis acids, iodine, oxidants, electrocatalysis, or transition metal-catalysis (Scheme 1a).<sup>7</sup> Besides, the development of multi-functional sulphenylating reagents also proved to be an alternative strategy to be able to realize the dithiolation of alkenes, which have been successively reported by the groups of Chen,<sup>8</sup> Shi,<sup>9</sup> and Huang.<sup>10</sup> Despite such progress having been made, the existing methods always suffer from disadvantages such as harsh reaction conditions (e.g., elevated temperatures, strong acids, etc.), pre-functionalization of substrates, and narrow substrate scope,

which have strongly limited the potential application of these methodologies. Besides, all of these works are restricted to the synthesis of symmetric vicinal dithioethers (Scheme 1a). To the best of our knowledge, the approach towards unsymmetric vicinal dithioethers has been rarely reported. Hence, the development of simpler and milder approaches for efficient access to diverse vicinal dithioethers, especially unsymmetric vicinal dithioethers, will be appealing.

In most cases of the existing dithiolation reactions, disulfides are employed as the sulphenylating reagents. As we know, symmetric disulfides can be readily accessed from thiols by homo-coupling; however, the cross-coupling of thiols to unsymmetric disulfides is challenging,<sup>11</sup> thus resulting in the difficulty to access unsymmetric vicinal dithioethers. From the view point of step- and atom-economy, we wondered if the dithiolation of alkenes could be realized by using the readily available thiols as the substrate. To the best of our knowledge, such a transformation has been rarely reported to date. Therefore, the development of an efficient catalytic system for direct dithiolation of alkenes with readily available thiols will be highly desirable. With our continuous interest in the selective synthesis of



**Scheme 1** (a) Dithiolation of olefins with disulfides. (b) Cobalt-catalyzed dithiolation of unactivated olefins with thiols.

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organosulfurs,<sup>12</sup> herein, we report a simple and efficient HFIP-promoted cobalt-catalytic aerobic approach for the direct dithiolation of unactivated alkenes with thiols to access diverse vicinal dithioethers including symmetric and unsymmetric ones under mild conditions (Scheme 1b).

We commenced our studies by selecting allylbenzene **a1** and 4-methoxybenzenethiol **b1** as the model substrates. As shown in Table 1, when the model reaction was conducted by using  $\text{Co}(\text{dmgH})(\text{dmgH}_2)\text{Cl}_2$  as a catalyst in the mixed solvent of hexafluoroisopropanol (HFIP) and dichloromethane (DCM) under air bubbling conditions at room temperature for 18 h, the desired vicinal dithioether **c1** could be obtained in 97% yield (entry 1). It should be noted that herein the solvent plays a remarkable role. When the commonly used solvents such as DCM,  $\text{CH}_3\text{CN}$ , THF, acetone, DMSO, DMF, and  $^i\text{PrOH}$  were used, no desired product was observed (entry 2). Another polyfluorinated solvent trifluoroethanol (TFE) instead of HFIP also exhibited a good performance with 71% yield (entry 3). Then, other cobalt-catalysts such as  $\text{Co}(\text{dmgH})_2\text{PyCl}$  and  $\text{Co}(\text{dmgBF}_2)_2(\text{H}_2\text{O})_2$  were attempted; however, the efficiency sharply decreased with the yields of 13% and 44%, respectively (entries 4 and 5). Additionally, when  $\text{CoCl}_2$  was used, no desired product was detected, indicating that the ligand of the cobalt complex plays an important role in the catalytic activity (entry 6). In previous reports using disulfides as the substrate, Lewis acids such as  $\text{AlCl}_3$ ,  $\text{FeCl}_3$ , and  $\text{CuCl}_2$  were commonly used to drive the transformation. However, herein, these Lewis acids as a catalyst were invalid (entry 7). Further experiments showed that molecular oxygen could shorten the reaction time to 9 h with a comparable yield (entry 8). Finally, control experiments revealed that air, cobalt-catalyst, and HFIP were all essential parameters to the reaction (entries 9–11).

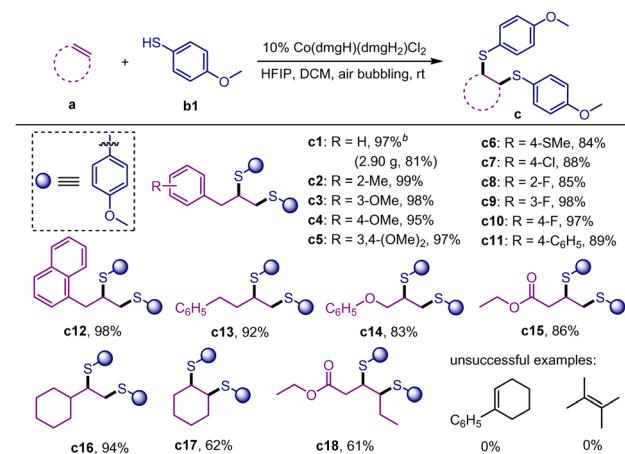
With optimal conditions in hand, we proceeded to investigate the generality of this approach. First, a variety of alkenes

Table 1 Optimization of the reaction conditions<sup>a</sup>

Entry	Variation from the standard conditions	Yield (%)
1	None	97
2	DCM/ $\text{CH}_3\text{CN}$ /THF/acetone/DMSO/DMF/ $^i\text{PrOH}$ as the solvent	0
3	TFE instead of HFIP as the solvent	71
4	$\text{Co}(\text{dmgH})_2\text{PyCl}$ as the catalyst	13
5	$\text{Co}(\text{dmgBF}_2)_2(\text{H}_2\text{O})_2$ as the catalyst	44
6	$\text{CoCl}_2$ as the catalyst	0
7	$\text{AlCl}_3/\text{FeCl}_3/\text{CuCl}_2$ as the catalyst	0
8 <sup>c</sup>	Under $\text{O}_2$ atmosphere	98
9	Under inert gas atmosphere	0
10	Without $\text{Co}(\text{dmgH})(\text{dmgH}_2)\text{Cl}_2$	0
11	Without HFIP	0

<sup>a</sup> Reaction conditions: **a1** (0.2 mmol), **b1** (0.6 mmol),  $\text{Co}(\text{dmgH})(\text{dmgH}_2)\text{Cl}_2$  (10 mol%), HFIP (3.0 mL), DCM (0.5 mL), air bubbling, r.t., 18 h. <sup>b</sup> Isolated yields. <sup>c</sup> Reaction time: 9 h.

Table 2 Scope of the alkenes<sup>ab</sup>

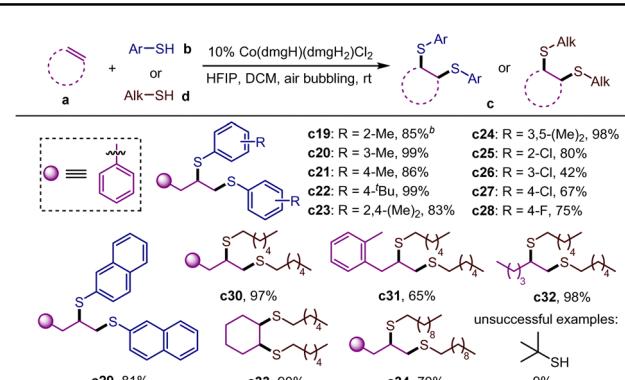


<sup>a</sup> Reaction conditions: **a** (0.2 mmol), **b1** (0.6 mmol),  $\text{Co}(\text{dmgH})(\text{dmgH}_2)\text{Cl}_2$  (10 mol%), HFIP (3.0 mL), DCM (0.5 mL), air bubbling, r.t., 18 h. <sup>b</sup> Isolated yields.

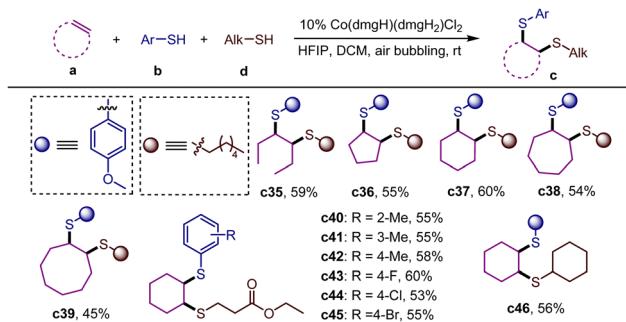
were examined (Table 2). The allylbenzenes with various electron-donating or electron-withdrawing groups on different positions of the phenyl ring were all compatible with the reaction to deliver the corresponding vicinal dithioethers in 84–95% yields (**c1–c11**). Allylnaphthalene was also feasible with an excellent yield of 98% (**c12**). Extending the carbon chain between the phenyl group and double bond seemed not to affect the efficiency (**c13**). Moreover, allyl ether and allyl ester reacted smoothly with thiol **b1** to give the desired products in good yields (**c14**, **c15**). Aliphatic alkene was also amenable to this approach in 94% yield (**c16**). Besides terminal alkenes, the internal unactivated alkenes were also suitable substrates, albeit with a decreased efficiency (**c17**, **c18**). Unfortunately, tri- and tetra-substituted alkenes were ineffective in this transformation. Additionally, the gram-scale model reaction with an 81% yield demonstrated the potential of this approach in practical synthesis.

Next, the scope with respect to the thiols was explored (Table 3). A variety of thiophenols were found to be compatible

Table 3 Scope of the thiols<sup>ab</sup>



<sup>a</sup> Reaction conditions: **a** (0.2 mmol), **b** or **d** (0.6 mmol),  $\text{Co}(\text{dmgH})(\text{dmgH}_2)\text{Cl}_2$  (10 mol%), HFIP (3.0 mL), DCM (0.5 mL), air bubbling, r.t., 18 h. <sup>b</sup> Isolated yields.

Table 4 Preparation of unsymmetric vicinal dithioethers<sup>a,b</sup>

<sup>a</sup> Reaction conditions: **a** (0.3 mmol), **b** (0.2 mmol), **d** (0.4 mmol), Co(dmgH)(dmgh2)Cl2 (10 mol%), HFIP (3.0 mL), DCM (0.5 mL), air bubbling, r.t., 18 h. <sup>b</sup> Isolated yields.

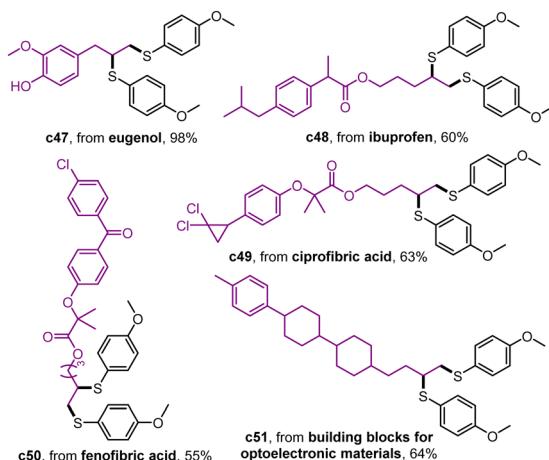
with the reaction in good to excellent yields (**c19–c29**), and the electron-rich thiophenols exhibited better performance than the electron-deficient ones. In addition, when alkyl thiols were employed to react with diverse alkenes, the corresponding aliphatic vicinal dithioethers could be efficiently prepared in high yields (**c30–c34**). However, the tertiary alkyl thiols were found to be incompatible in the reaction.

Encouraged by the above results, we wondered if such an approach could be applied to the synthesis of unsymmetric vicinal dithioethers. Hence, a three-component reaction of 3-hexene, thiophenol **b1**, and alkyl thiol **d1** was carried out under the standard conditions, and excitingly the desired product **c35** was obtained in 59% yield (Table 4). Furthermore, various aliphatic cyclic alkenes from 5- to 8-membered rings were able to react smoothly with **b1** and **d1** to afford the desired products in moderate yields (**c36–c39**). Additionally, other thiophenols and alkyl thiols reacting with cyclohexene were attempted, and the desired corresponding products were successfully achieved in satisfactory yields (**c40–c46**). Moreover, the simple and mild reaction conditions encouraged us to explore the application of the approach to late-stage modification (Scheme 2), and several alkenes derived from bioactive compounds or complex

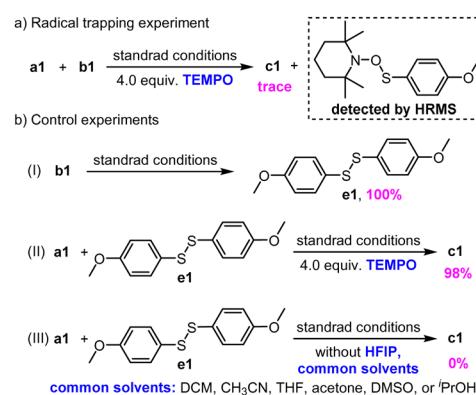
molecules successfully afforded the products **c47–c51** in good yields, highlighting the synthetic potential of the approach.

To shed more light on the reaction mechanism, a series of control experiments were conducted. First, 4.0 equivalent of a radical inhibitor TEMPO was added to the reaction under standard conditions, and the desired product **c1** was completely inhibited. Meanwhile, the TEMPO-trapped thiyl-radical adduct was identified by high resolution mass spectroscopy (HRMS) (Scheme 3a), suggesting that the reaction is through a thiyl-radical-involved process. Next, we found that when the alkene was removed from the reaction, thiol **b1** could be quantitatively converted to disulphide **e1** (Scheme 3b-I). Furthermore, when the reaction of **e1** with **a1** was conducted under standard conditions, even though 4.0 equivalent of TEMPO was added, the desired product **c1** could be obtained in 98% yield (Scheme 3b-II). These results revealed that (1) the disulphide is probably the reactive intermediate in this transformation, (2) the generation of disulphide from thiol is *via* a thiyl-radical process, and (3) subsequent dithiolation of disulphide with an alkene is probably through a thiiranium ion rather than a radical pathway. Finally, the reaction of **e1** with **a1** in the absence of HFIP did not occur, indicating the essential role of HFIP (Scheme 3b-III).

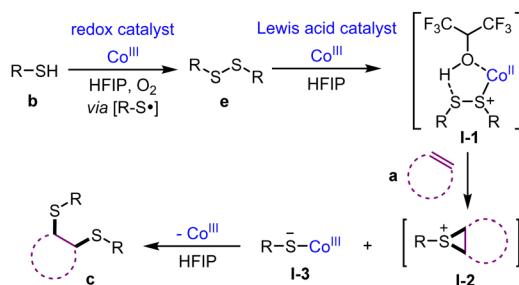
The fact that cobaloximes being able to act as competent oxygen carriers for diverse oxidation transformations has been reported since 1970s.<sup>13</sup> Therefore, the feasible oxidation of thiol to disulphide *via* a thiyl-radical intermediate by cobaloxime catalysis under air bubbling is reasonable. Based on the above results, a plausible reaction pathway is proposed in Scheme 4. Herein, the cobaloxime catalyst plays a dual role. First, cobaloxime as a redox catalyst accelerated the oxidation of thiol **a** *via* a radical pathway under molecular oxygen atmosphere to generate disulphide **e**. Then, cobaloxime as a Lewis acid catalyst activated disulphide **e** to generate a proposed HFIP-stabilized intermediate I-1, which subsequently took an electrophilic addition to the unactivated alkene to form a thiiranium intermediate I-2 and a nucleophilic cobalt-sulfide species I-3. Finally, the nucleophilic substitution of I-3 to I-2 regenerated the cobalt-catalytic cycle and resulted in the formation of the desired product **c**. In the reaction, the solvent effect is critical, although the detailed mechanism is still unknown, however, given the excellent hydrogen-bond



Scheme 2 Late-stage modifications.



Scheme 3 (a) Radical trapping experiment. (b) Control experiments.



Scheme 4 Proposed reaction pathway.

donating ability and high dielectric constant of HFIP,<sup>14</sup> the possible role of HFIP we speculated is to stabilize the reactive intermediates in the reaction to accelerate the transformation. As regarding the unsymmetric dithiolation, due to the higher stability of the aryl thiyl radical and the better stabilizing effect of the aromatic ring, the aryl thiol group is speculated to be more likely to dominate in the formation of the thiiranium intermediate, accompanying the formation of a more nucleophilic cobalt-alkylsulfide species. Such a preference ensures the facile synthesis of unsymmetric dithioethers.

In summary, we have established a simple cobalt-catalytic aerobic approach for the direct dithiolation of unactivated alkenes with thiols under mild conditions. Herein, cobaloxime plays a dual role of acting not only as a redox catalyst but also as a Lewis acid catalyst. With essential promotion by HFIP, both thiophenols and alkyl thiols are suitable substrates to furnish the symmetric vicinal dithioethers in good to excellent yields. Besides, the challenging unsymmetric vicinal dithioethers could also be achieved through a three-component reaction in moderate yields. Such an approach features readily available substrates, operational simplicity, and broad substrate scope. Gram-scale synthesis and late-stage modification of complex molecules demonstrated the practicability of this approach.

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## Data availability

The data supporting this article have been included as part of the ESI.†

## Conflicts of interest

There are no conflicts to declare.

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