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Copper(II) Acetate-Catalyzed Hydroxysulfenylation-Initiated Lactonization of Unsaturated Carboxylic Acids with Oxygen as Oxidant and Oxygenation Reagent

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Abstract: A copper(II) acetate-catalyzed aerobic thiolation of C=C double bonds, oxygenation, and intramolecular cyclization reactions of unsaturated carboxylic acids with thiols has been explored. The reaction proceeds through a new hydroxysulfenylation-initiated lactonization pathway with carboxyl as electrophilic group, which provides an efficient access to assembly highly valuable thio-substituted lactone derivatives with good yields under mild conditions. Several control experiments, as well as an isotope labelling experiment disclose that oxygen acts as both oxidant and reactant being transferred into the final product. The mechanistic studies support the discovery of a new strategy through difunctionalization of alkenes based on unsaturated carboxylic acids to construct the diversely substituted lactones.

Keywords: aerobic oxidation; copper catalysis; hydroxysulfenylation; lactonization; unsaturated carboxylic acids

Introduction

γ-Lactones represent the most prolific class of O-heteroaromatic compounds in organic chemistry. Particularly, functionalized lactones are prevalent structural motifs, being found in many bioactive compounds[1] and natural products.[2] More specifically, thio-substituted γ-lactones have been demonstrated to show antiviral activity against poliovirus, RNA virus and herpes simplex virus type 1 (HSV-1) (Figure 1, **A** and **B**).[3] Also, this structure unit exists in the drugs, such as Nifuratel (Figure 1, **C**), showing a broad antibacterial spectrum of action.[4] Consequently, the synthesis of thio-substituted γ-lactones has received some attention in the past, but still remains largely underdeveloped.[5]

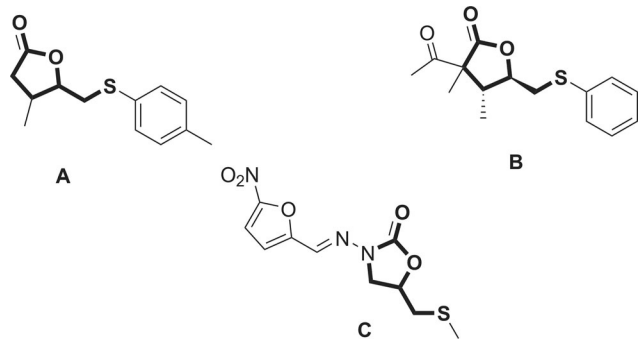
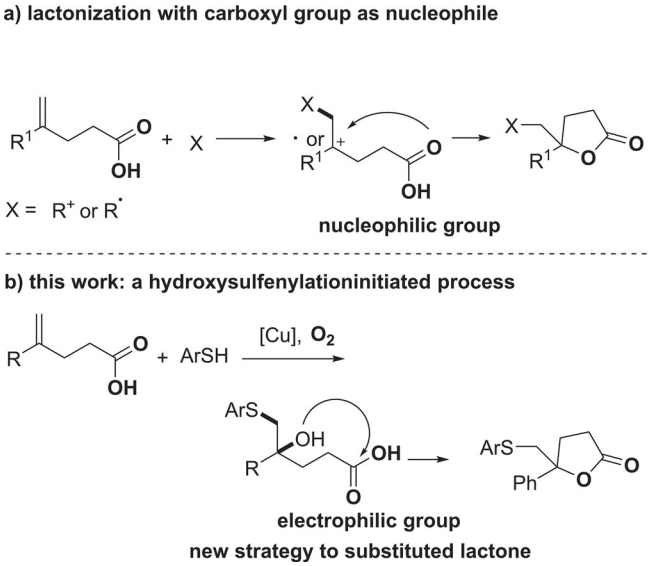


Figure 1. Examples of biologically active thio-substituted γ-lactones.

Unsaturated carboxylic acids represent attractive intermediates, which could serve to construct substituted lactone derivatives by functionalization of the C=C double bond and an intramolecular cyclization reaction. In recent years, several strategies based on unsaturated carboxylic acids have been explored to construct modified lactones (Scheme 1a). One way is that the nucleophilic carboxyl group attacks the cation or onium cation intermediates, generated from the addition of halogen, trifluoromethyl or trifluoromethylthio to the C=C double bond.[6] The other way is that the carboxyl group attacks the intermediates from radical SET (single electron transfer)[7] or reductive elimination from the redox-active metal complex.[8] These previously reported reactions usually were triggered by the functionalization of the C=C double bond, and used carboxyl groups as nucleophilic reagents. However, the difunctionalization of a C=C double bond-initiated lactonization of unsaturated carboxylic acids still remained unexplored.



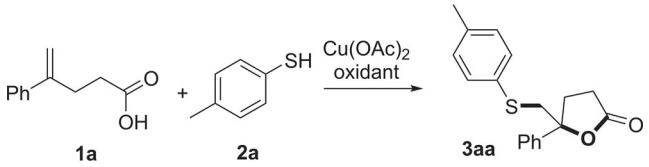
Scheme 1. Synthesis of lactones.

To explore the new strategy to construct modified lactones through the difunctionalization of alkenes, we envisioned a new process for the preparation of substituted lactones incorporating the features discussed above,[6–8] recently established elegant work on hydroxysulfenylation of olefins[9] and our own work about Cu-catalyzed aerobic oxidation[10,11] and thiolation reactions.[12] We suggested that dioxygen reacts with the active thiolated radical intermediate (Scheme 1b), to form a more nucleophilic hydroxy species.[9] Then an intramolecular nucleophilic reaction affords the desired thio-substituted lactone. Herein, we would like to report a novel Cu-catalyzed aerobic oxidative hydroxysulfenylation-initiated lactonization reaction of unsaturated carboxylic acids with thiols through a sequence of thiolation of the C=C double bond, oxygenation and lactonization. To the best of our knowledge, use of a carboxyl group as electrophile in the lactonization of unsaturated carboxylic acids group has never been reported. Furthermore, this reaction provides a new difunctionalization of alkenes-initiated lactonization strategy to construct substituted lactones.

Results and Discussion

We first examined the reaction of unsaturated carboxylic acids **1a** with *p*-toluenethiol **2a** catalyzed by $Cu(OAc)_2$ under air (Table 1). With acetonitrile as solvent, the reaction proceeded but yielded the thio-substituted lactone **3aa** only in 21% yield after 12 h (entry 1). Other common solvents, including DMF, DMSO, toluene, dioxane and DCE, have been examined for this radical reaction (entries 2–6), and the results suggest that DCE is the best choice with a yield

Table 1. Optimization of the reaction conditions for the Cu-catalyzed hydroxysulfenylation.[a]

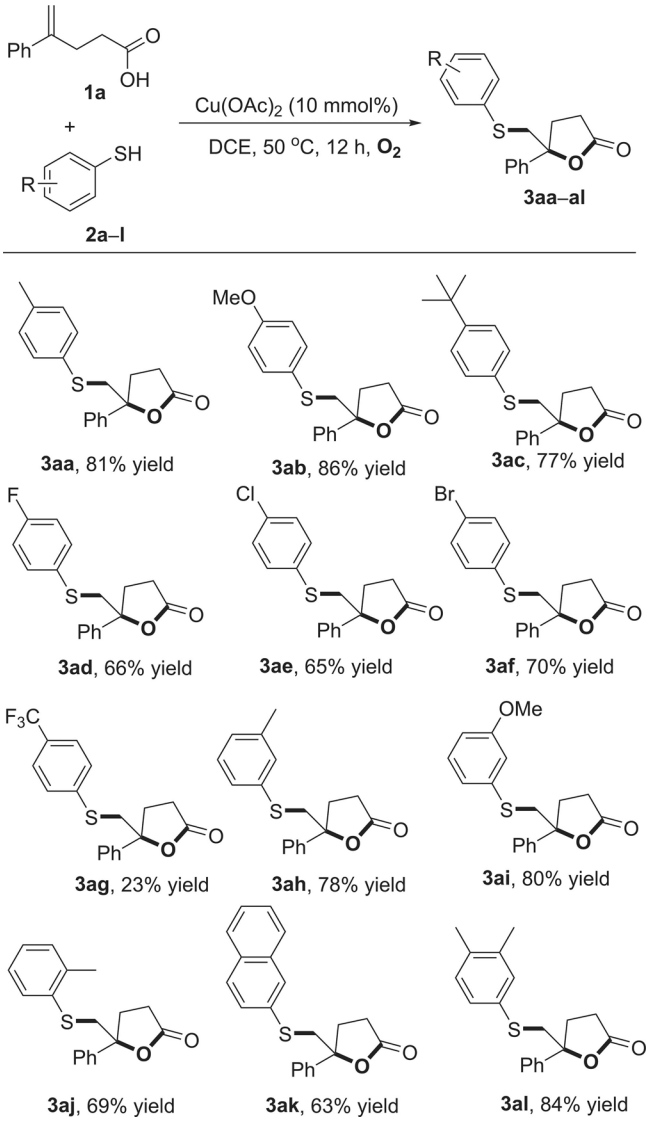


Entry	Atmosphere	Time [h]	Solvent	Yield [%][b]
1	air	12	CH_3CN	21
2	air	12	DMF	<5
3	air	12	DMSO	<5
4	air	12	toluene	<5
5	air	12	dixone	7
6	air	12	DCE	32
7	argon	12	DCE	0
8	O_2	12	DCE	55
9	O_2	6	DCE	34
10	O_2	18	DCE	53
11	O_2	12	DCE	28[c]
12	O_2	12	DCE	81[d]
13	O_2	12	DCE	43[e]

[a] *Reaction conditions:* **1a** (0.2 mmol) and **2a** (2.0 equiv.), with $Cu(OAc)_2$ (10 mol%) as catalyst in solvent (2.0 mL) at 50 °C in a flask.
[b] Isolated yield based on **1a**.
[c] **2a** (1.0 equiv.).
[d] **2a** (3.0 equiv.).
[e] **2a** (3.0 equiv.) without $Cu(OAc)_2$.

of 32% (entry 6). As expected, no reaction was observed when the reaction was conducted under an argon atmosphere (entry 7), because the thiol radical cannot be formed. Oxygen was proved to be superior over air as oxidant for this reaction. Thus, reacting of **1a** with **2a** in DCE in the presence of O_2 for 12 h gave the desired product **3aa** with dramatically increased isolated yield (55%, entry 8). Although discontinuing the reaction after 6 h gave a lower chemical yield (34%, entry 9), prolonging the reaction to 18 h did not offer any significant improvement (entry 10). It was found that the stoichiometry influences the efficiency of this reaction. Using 1 equiv. of **2a** resulted in poor yield mainly because of thiol conversion into the sulfonic acid under an oxygen atmosphere (entry 11). The yield could be increased to 81% by using 3.0 equiv. of **2a** (entry 12). Finally, the reaction was markedly suppressed without the use of Cu catalyst, suggesting that the metal catalyst is essential for this reaction (entry 13).

Subsequently, we investigated the scope of thiols in the Cu-catalyzed hydroxysulfenylation-initiated cyclization reaction (Scheme 2). As presented in Scheme 2, all the examined thiols could work well in the reaction, affording the corresponding thio-substituted γ-lactones in up to 86% chemical yields (**3aa**–**3al**). It was found that the electronegativity of the



Scheme 2. Cu-catalyzed hydroxysulfenylation reaction with various thiols. *Reaction conditions:* **1a** (0.2 mmol), **2** (0.6 mmol), $Cu(OAc)_2$ (10 mol%), DCE (2 mL) in a flask under an O_2 balloon at 50 °C for 12 h. Isolated yields based on **1a**.

substituent groups influences the yield of this reaction. In general, thiols with electron-donating groups show higher reactivity, and give good to ideal yields (77–86%, **3aa–3ac**, **3ai**, and **3al**). In contrast, thiol **2g** with a strong electron-withdrawing CF_3 group on the aromatic ring gave the γ-lactone (**3ag**) in only 23% yield. It is clear that steric hindrance affects the reaction efficiency. For example, when the *ortho*-methylbenzenethiol is subjected to the reaction, a lower yield was found (69%, **3aj**) comparing to *para*-methylbenzenethiol (81% yield, **3aa**). In addition, the naphthyl thiol was also a suitable substrate, and afforded product **3ak** in acceptable yield 63%. The chemical structure of these thio-substituted γ-lactones has been

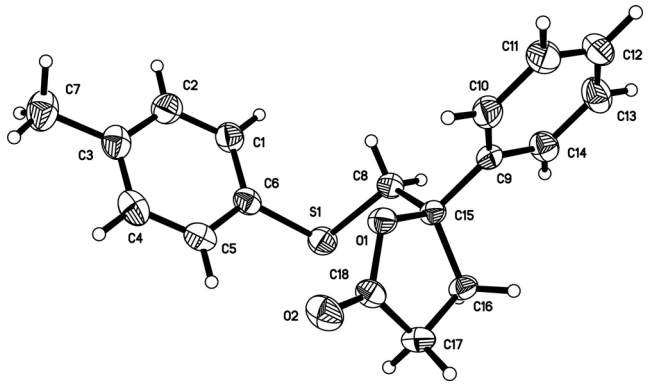


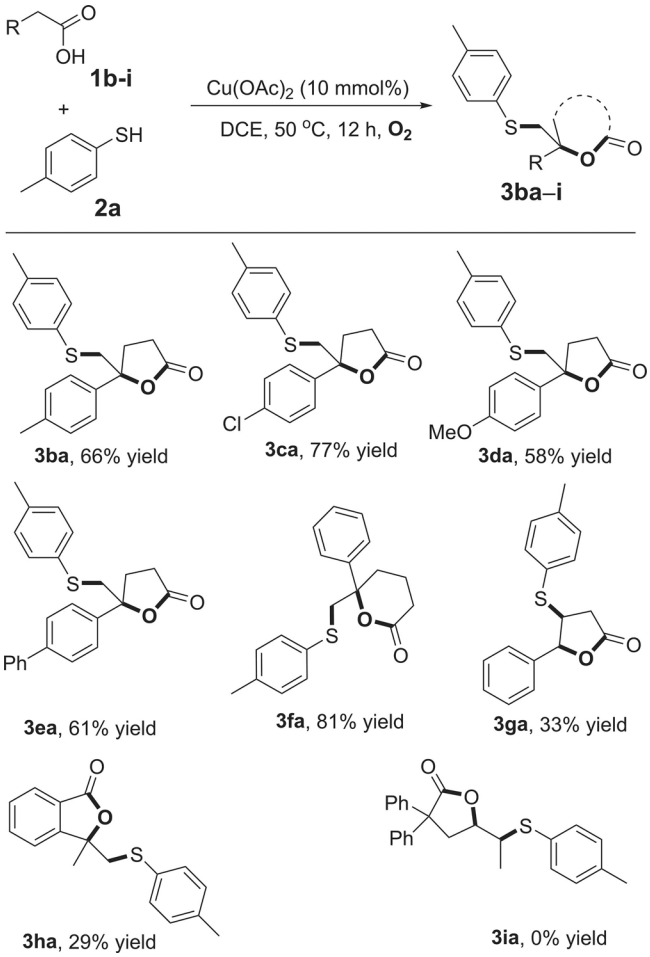
Figure 2. X-ray single crystal analysis of **3aa**.

confirmed by X-ray single crystal analysis[13] of **3aa** (Figure 2).

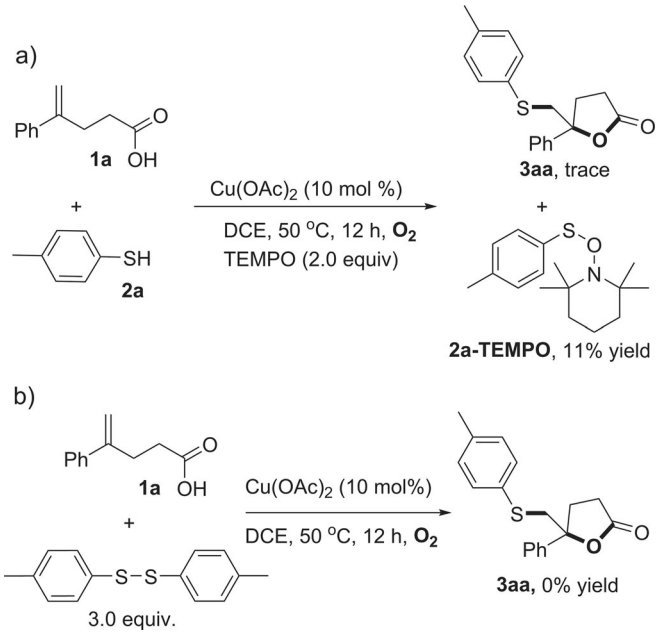
Encouraged by these straightforward reactions with 4-phenyl-4-pentenoic acid **1a** and various thiols, we further investigated the substrate scope by using several unsaturated carboxylic acids (Scheme 3). To our delight unsaturated carboxylic acids containing substituted aromatic rings were also well tolerated in this reaction, affording the corresponding products in 58–77% yields (**3ba–3ea**). Then, 5-phenyl-5-pentenoic acid (**1f**), bearing a longer alkyl chain, was tried in the reaction to construct a larger cycle. We found that such an unsaturated carboxylic acid was compatible with the current catalytic system to give a six-membered lactone in good yield (81%, **3da**). A steric hindrance effect in the unsaturated carboxylic acids also was found. The reaction of unsaturated carboxylic acids containing a non-terminal vinyl group could take place, however a dramatically decreased yield was obtained (33% yield, **3ga**). Additionally, the aliphatic vinyl carboxylic acid (**1i**) was investigated, and was not amenable to our procedure. Finally, a simple alkene without a carboxylic group, α-methylstyrene was examined in the reaction. It could react with **2a** smoothly resulting in the hydroxyethyl thioether with 84% yield under the standard conditions (see the Supporting Information).

To gain insights into the reaction mechanism, two preliminary mechanistic studies were carried out (Scheme 4). First, a radical inhibition experiment was examined with the addition of TEMPO (Scheme 4a). The formation of **3aa** was suppressed and only TEMPO adduct **2a-TEMPO** was detected, elucidating that a radical pathway is involved in this process. Then, another potential thiophenyl radical source, diphenyl sulfide was tested under standard conditions. No desired product was detected in the reaction mixture, which indicates that the thiol hydrogen has been transferred into the intermediate in the subsequent procedure (Scheme 4b).

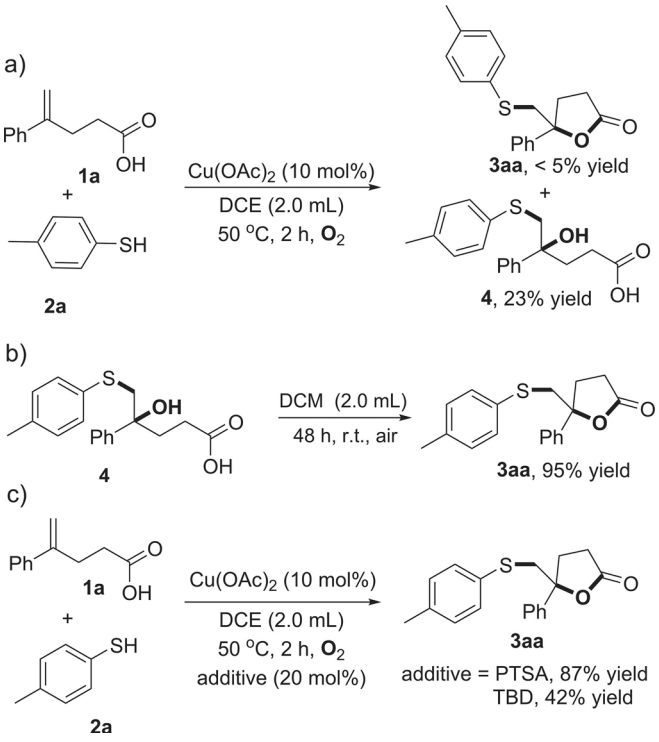
Then, we tried to obtain the reaction intermediate. In the initial stage of the reaction, we fortunately iso-



Scheme 3. Cu-catalyzed hydroxysulfenylation reaction with various unsaturated carboxylic acids. *Reaction conditions:* **1** (0.2 mmol), **2a** (0.6 mmol), $Cu(OAc)_2$ (10 mol%), DCE (2 mL) in a flask under an O_2 balloon at 50 °C for 12 h. Isolated yields based on **1**.



Scheme 4. Radical-trapping experiments.

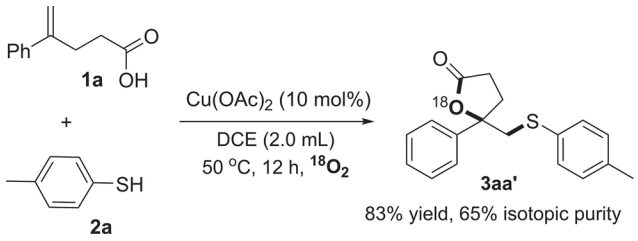


Scheme 5. Intermediate verification experiments.

lated 4-hydroxy-4-phenyl-5-(phenylthio)pentanoic acid **4** with 23% yield after 2 h, while **4** disappeared at the end of reaction (Scheme 5a). The intermediate **4** has been confirmed by careful analysis using ^{1}H NMR spectroscopy and HR-MS (see the Supporting Informatiion). To further confirm whether **4** is the key intermediate, we used it as a substrate to check whether it could be converted into the final product. To our delight, **4** could be converted to the expected product **3aa** slowly at room temperature without any additive after 48 h (Scheme 5b), which discloses that such a hydroxy group attached **4** is the key intermediate of this reaction. To support our rationalization, two control experiments were carried out. As the result, an additional organic acid, *p*-toluenesulfonic acid, could accelerate the transformation, giving the product **3aa** with 87% yield after 2 h. On the other hand, an additional organic base, 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD), suppressed the procedure and only 42% yield was found (Scheme 5c). The thiols could be easily oxidized into sulfonic acids in the presence of oxgyen. Thus, the current system may be a self-catalyzed esterification process, which is accounts for the use of 3.0 equiv. of thiols in the reaction.

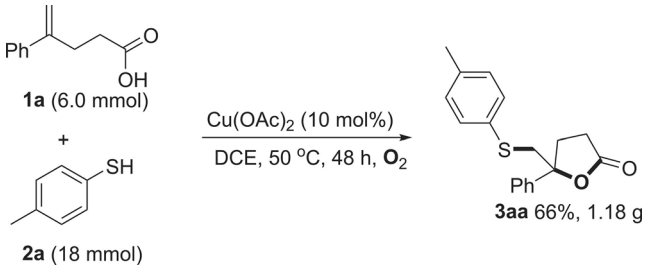
If the reaction proceeds *via* an oxygenation step according to our assumption, the final lactone product

should have incorporated an oxygen atom from the hydroxy group. To examine if the oxygen atom originates from the hydroxy group, an $^{18}O_2$ labelling experiment was carried out. As a result, the ^{18}O-labelled product **3aa′** was obtained in 83% yield and in 65% isotopic purity (Scheme 6). This result indicates that O_2 also was involved in this reaction and was transferred into the final product.



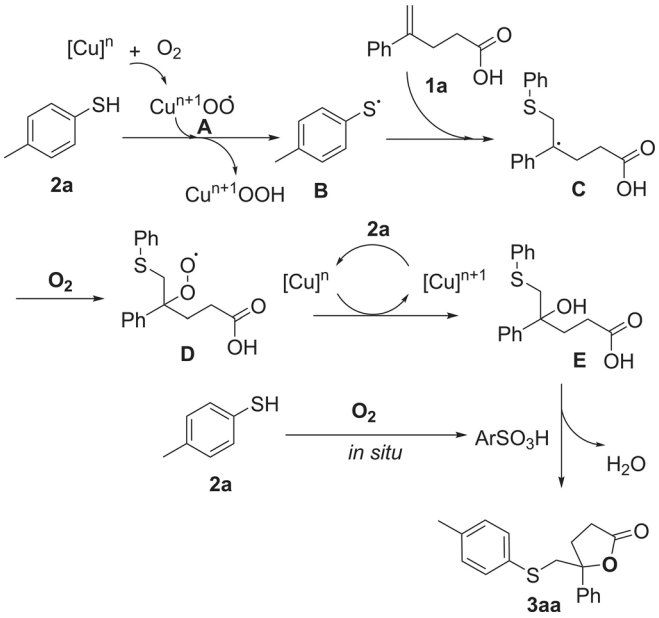
Scheme 6. Isotope labelling experiment.

As the final objective of this study, we decided to carry out a gram-scale synthesis due to the simple access to valuable products. We conducted the reaction with 6.0 mmol of starting thiol **1a** under the standard reaction conditions. As shown in Scheme 7, the corresponding product **3aa** can be easily obtained without a decrease in yield (66%) after prolonging the reaction time to 48 h.



Scheme 7. Gram-scale examination of the current system.

On the basis of our findings and previous studies,[6–8] a possible mechanism is illustrated in Scheme 8. Initially, the Cu catalyst is oxidized by O_2 to form a CuOO radical **A**, then HAT (hydrogen atom abstraction) from ArSH by this radical happens to give the thiophenyl radical **B**,[9] which adds to the C=C double bond of the unsaturated carboxylic acid **1a** to form intermediate **C**.[14] Then, **B** is trapped by dioxygen to give peroxy radical **D**, and intermediate **D** is reduced by the redox-active copper species[15] to generate the key intermediate 4-hydroxy-4-phenyl-5-(phenylthio)pentanoic acid **E**. The Cu catalyst could be regenerated *via* reduction by thiol **2**. Subsequent intramolecular nucleophilic esterification occurs, affording the final product **3** by release of H_2O. This lactonization step could also be accelerated by the *in*



Scheme 8. Proposed mechanism.

situ generated sulfonic acid (detected by HR-MS, see the Supporting Information) as catalyst.

Conclusions

In conclusion, we have developed a novel and efficient copper-mediated strategy for the synthesis of thio-substituted lactones through difunctionalization of alkenes. This reaction proceeds through an unprecedented pathway involving hydroxysulfenylation of the C=C double bond with carboxyl as electrophilic group and dioxygen as reactant and oxidant. Furthermore, the mechanistic studies support the discovery of new strategies to construct substituted lactones based on unsaturated carboxylic acids through difunctionalization of alkenes. Further studies toward the development of this new process are currently underway.

Experimental Section

General

Except where otherwise stated, all reagents were commercially available and used without purification. The unsaturated carboxylic acids were prepared according to the previous report.[8d] Solvents were dried by a solvent purification system before use. Melting points (mp) were measured on a Mel-Temp apparatus and are uncorrected. For flash silica gel chromatography, silica gel (200–300 mesh) was performed by standard technique. The ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker model DRX 400 spectrometer in deuterated chloroform ($CDCl_3$) [using $(CH_3)_4Si$

(for 1 H, $\delta = 0.00$; for ^{13}C, $\delta = 77.00$) as internal standard]. All coupling constants (J) are reported in Hertz (Hz). Infrared (IR) spectra were performed on Agilent Cary 630 FT-IR instrument with the attenuated total reflection (ATR) technique. High resolution mass spectra (HR-MS) were measured on a Bruker micr OTOF-Q III mass spectrometer with the ESI technique.

Typical Procedure for the Cu-Catalyzed Hydroxysulfenylation Reaction

Unsaturated carboxylic acids **1** (0.2 mmol), thiols **2** (0.6 mmol) and $Cu(OAc)_2$ (10 mol%) were added to a 25-mL Schlenk tube under an O_2 balloon, followed by addition of DCE (2 mL). The mixture was stirred at 50 °C for 12 h, then filtered and the residue was washed with ethyl acetate. The organic phase was dried by anhydrous Na_2SO_4 and concentrated under vacuum. Finally, the residue was purified by flash chromatography to give the desired product **3**.

5-Phenyl-5-((*p*-tolylthio)methyl)dihydrofuran-2(3*H*)-one (3aa): Pale yellow solid; mp 64–65 °C; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.42$–7.27 (m, 5 H), 7.25 (d, $J = 8.4$ Hz, 2 H), 7.07 (d, $J = 7.9$ Hz, 2 H), 3.42 (q, $J = 14.2$ Hz, 2 H), 2.84–2.64 (m, 2 H), 2.59–2.40 (m, 2 H), 2.30 (s, 3 H); ^{13}C NMR (101 MHz, $CDCl_3$): $\delta = 176.0$, 142.5, 137.0, 132.3, 130.9, 129.8, 128.6, 128.1, 124.8, 88.4, 47.9, 32.6, 29.1, 21.0; IR (neat): $\nu_{max} = 2920$, 2851, 1761, 1493, 1172, 1016, 805, 699 cm^{-1}; HR-MS: $m/z = 299.1100$, calcd. for $C_{18}H_{18}O_2S$ $[M+H]^+$: 299.1100.

Intermediate Verification Experiment

1a (0.2 mmol), **2a** (0.6 mmol) and $Cu(OAc)_2$ (10 mol%) were added to a 25-mL Schlenk tube under an O_2 balloon, followed by addition of DCE (2 mL). The mixture was stirred at 50 °C for 2 h, then filtered and the residual was washed with ethyl acetate. The organic phase was dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography to give the desired product **4**.

Acknowledgements

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References

[1] a) J. D. Lambert, J. E. Rice, J. Hong, Z. Hou, C. S. Yang, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 873–876; b) T. Janecki, E. Błaszczyk, K. Studzian, A. Janecka, U. Krajewska, M. Różalski, *J. Med. Chem.* **2005**, *48*, 3516–3521.

[2] a) B. N. Ravi, R. W. Armstrong, D. J. Faulkner, *J. Org. Chem.* **1979**, *44*, 3109–3113; b) M. W. Sumarah, E. Puniani, D. Sorensen, B. A. Blackwell, J. D. Miller, *Phytochemistry* **2010**, *71*, 760–765.

[3] a) N. Gouault, M. David, J. F. Cupif, A. Sauleau, M. Amoros, *Pharm. Pharmacol. Commun.* **1999**, *5*, 159–163; b) O. Yonemitsu, J. Uenishi, N. Kobayashi, T. Sasaki, Y. Yamada, *Heterocycles* **1997**, *44*, 277–287.

[4] Q. Liang, N. Li, S. R. Song, A. H. Zhang, N. Li, Y. Duan, *J. Obstet. Gynaecol. Res.* **2016**, *42*, 1354–1360.

[5] a) S. E. Denmark, D. J. P. Kornfilt, T. Vogler, *J. Am. Chem. Soc.* **2011**, *133*, 15308–15311; b) M. C. Carreño, M. J. Sanz-Cuesta, *J. Org. Chem.* **2005**, *70*, 10036–10045; c) Z. K. M. Abd El Samii, M. I. Al Ashmawy, J. M. Mellor, *J. Chem. Soc. Perkin Trans. 1* **1988**, 2517–2522; d) M. Yoshida, T. Suzuki, N. Kamigata, *J. Org. Chem.* **1992**, *57*, 383–386; e) D. Crich, B. Surve, M. Sannigrahi, *Heterocycles* **2004**, *62*, 827–830.

[6] a) Y. Yasu, Y. Arai, R. Tomita, T. Koike, M. Akita, *Org. Lett.* **2014**, *16*, 780–783; b) K. D. Ashtekar, M. Vetticatt, R. Yousefi, J. Jackson, B. Borhan, *J. Am. Chem. Soc.* **2016**, *138*, 8114–8119; c) C. S. Meng, Z. H. Liu, Y. X. Liu, Q. M. Wang, *Org. Biomol. Chem.* **2015**, *13*, 6766–6772; d) C. F. Xu, Q. L. Shen, *Org. Lett.* **2015**, *17*, 4561–4563; e) M. L. Campbell, S. A. Rackley, L. N. Giambalvo, D. C. Whitehead, *Tetrahedron* **2015**, *71*, 3895–3902; f) W. Niu, Y. Y. Yeung, *Org. Lett.* **2015**, *17*, 1660–1663; g) T. Chen, T. J. Y. Foo, Y. Y. Yeung, *ACS Catal.* **2015**, *5*, 4751–4755; h) K. Moriyama, C. Nishinohara, T. Sugiue, H. Togo, *RSC Adv.* **2015**, *5*, 85872–85878; i) Y. B. Kang, X. M. Chen, C. Z. Yao, X. S. Ning, *Chem. Commun.* **2016**, *52*, 6193–6196; j) G. C. Geary, G. Hope, A. M. Stuart, *Angew. Chem.* **2015**, *127*, 15124–15127; *Angew. Chem. Int. Ed.* **2015**, *54*, 14911–14914; k) D. H. Paull, C. Fang, J. R. Donald, A. D. Pansick, S. F. Martin, *J. Am. Chem. Soc.* **2012**, *134*, 11128–11131; l) X. Jiang, C. K. Tan, L. Zhou, Y. Y. Yeung, *Angew. Chem.* **2012**, *124*, 7891–7895; *Angew. Chem. Int. Ed.* **2012**, *51*, 7771–7775; m) H. Nakatsuji, Y. Sawamura, A. Sakakura, K. Ishihara, *Angew. Chem.* **2014**, *126*, 7094–7097; *Angew. Chem. Int. Ed.* **2014**, *53*, 6974–6977; n) J. E. Tungen, J. M. J. Nolsøe, T. V. Hansen, *Org. Lett.* **2012**, *14*, 5884–5887; o) G. E. Veitch, E. N. Jacobsen, *Angew. Chem.* **2010**, *122*, 7490–1493; *Angew. Chem. Int. Ed.* **2010**, *49*, 7332–7335.

[7] a) A. Bunescu, Q. Wang, J. P. Zhu, *Chem. Eur. J.* **2014**, *20*, 14633–14636; b) Y. Z. Gao, X. Q. Li, J. Xu, Y. L. Wu, W. Z. Chen, G. Tang, Y. F. Zhao, *Chem. Commun.* **2015**, *51*, 1605–1607; c) Y. Z. Gao, J. Xu, P. B. Zhang, H. Fang, G. Tang, Y. F. Zhao, *RSC Adv.* **2015**, *5*, 36167–36170; d) W. Guo, H. G. Cheng, L. Y. Chen, J. Xuan, Z. J. Feng, J. R. Chen, L. Q. Lu, W. J. Xiao, *Adv. Synth. Catal.* **2014**, *356*, 2787–2793; e) Y. Gao, X. Li, W. Chen, G. Tang, Y. Zhao, *J. Org. Chem.* **2015**, *80*, 11398–11406.

[8] a) R. Zhu, S. L. Buchwald, *Angew. Chem.* **2013**, *125*, 12887–12890; *Angew. Chem. Int. Ed.* **2013**, *52*, 12655–12658; b) R. Zhu, S. L. Buchwald, *J. Am. Chem. Soc.* **2012**, *134*, 12462–12465; c) R. Zhu, S. L. Buchwald, *J. Am. Chem. Soc.* **2015**, *137*, 8069–8077; d) B. N. Hemric, K. Shen, Q. Wang, *J. Am. Chem. Soc.* **2016**, *138*, 5813–5816.

[9] a) H. Xi, B. Deng, Z. Zong, S. Lu, Z. Li, *Org. Lett.* **2015**, *17*, 1180–1183; b) S. F. Zhou, X. Pan, Z. H. Zhou, A. Shoberu, J. P. Zou, *J. Org. Chem.* **2015**, *80*, 3682–3687; c) J. J. Zhao, M. Tang, H. H. Zhang, M. M. Xu, F. Shi, *Chem. Commun.* **2016**, *52*, 5953–5956.

[10] a) B. N. Du, P. Qian, Y. Wang, H. B. Mei, J. L. Han, Y. Pan, *Org. Lett.* **2016**, *18*, 4144–4147; b) B. N. Du, Z. Li, P. Qian, J. L. Han, Y. Pan, *Chem. Asian J.* **2016**, *11*, 478–481.

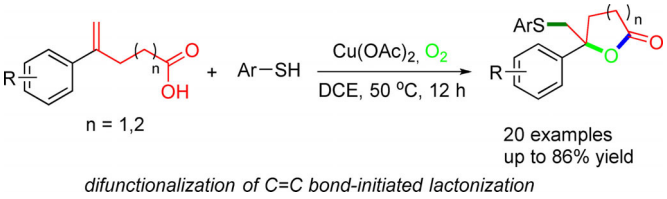
[11] For reviews, see: a) A. E. Wendlandt, A. M. Suess, S. Stahl, *Angew. Chem.* **2011**, *123*, 11256–11283; *Angew. Chem. Int. Ed.* **2011**, *50*, 11062–11087; b) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381–3430; c) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329–2364; d) S. McCann, S. Stahl, *Acc. Chem. Res.* **2015**, *48*, 1756–1766.

[12] a) J. C. Zhao, H. Fang, J. L. Han, Y. Pan, G. G. Li, *Adv. Synth. Catal.* **2014**, *356*, 2719–2724; b) S. Y. Ni, L. J. Zhang, W. Z. Zhang, H. B. Mei, J. L. Han, Y. Pan, *J. Org. Chem.* **2016**, *81*, 9470–9475.

[13] CCDC 1513113 (**3aa**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

[14] a) T. Keshari, V. K. Yadav, V. P. Srivastava, L. D. S. Yadav, *Green Chem.* **2014**, *16*, 3986–3992; b) Y. Zheng, Y. He, G. W. Rong, X. L. Zhang, Y. C. Weng, K. Y. Dong, X. F. Xu, J. C. Mao, *Org. Lett.* **2015**, *17*, 5444–5447; c) Q. Q. Lu, Z. L. Liu, Y. Luo, G. H. Zhang, Z. Y. Huang, H. M. Wang, C. Liu, J. T. Miller, A. W. Lei, *Org. Lett.* **2015**, *17*, 3402–3405; d) Q. Q. Lu, H. M. Wang, P. Peng, C. Liu, Z. Y. Huang, Y. Luo, A. W. Lei, *Org. Chem. Front.* **2015**, *2*, 908–912; e) Y. J. Su, X. Sun, G. L. Wu, N. Jiao, *Angew. Chem.* **2013**, *125*, 9990–9994; *Angew. Chem. Int. Ed.* **2013**, *52*, 9808–9812; f) H. W. Huang, J. H. Cai, X. C. Ji, F. H. Xiao, Y. Chen, G. J. Deng, *Angew. Chem.* **2016**, *128*, 315–319; *Angew. Chem. Int. Ed.* **2016**, *55*, 307–311.

[15] a) H. Xi, B. C. Deng, Z. Z. Zong, S. L. Lu, Z. P. Li, *Org. Lett.* **2015**, *17*, 1180–1183; b) H. G. Wang, Y. Wang, D. D. Liang, L. Y. Liu, J. C. Zhang, Q. Zhu, *Angew. Chem.* **2011**, *123*, 5796–5799; *Angew. Chem. Int. Ed.* **2011**, *50*, 5678–5681; c) C. Zhang, P. Feng, N. Jiao, *J. Am. Chem. Soc.* **2013**, *135*, 15257–15262; d) A. S. K. Tsang, A. Kapat, F. Schoenebeck, *J. Am. Chem. Soc.* **2016**, *138*, 518–526; e) C. Zhang, C. H. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3464–3484; f) S. E. Allen, R. R. Walvoord, R. P. Salinas, M. C. Kozlowski, *Chem. Rev.* **2013**, *113*, 6234–6458.



difunctionalization of C=C bond-initiated lactonization

