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**Photocatalysis**

# Mechanistic Study of a Photocatalyzed C−S Bond Formation Involving Alkyl/Aryl Thiosulfate

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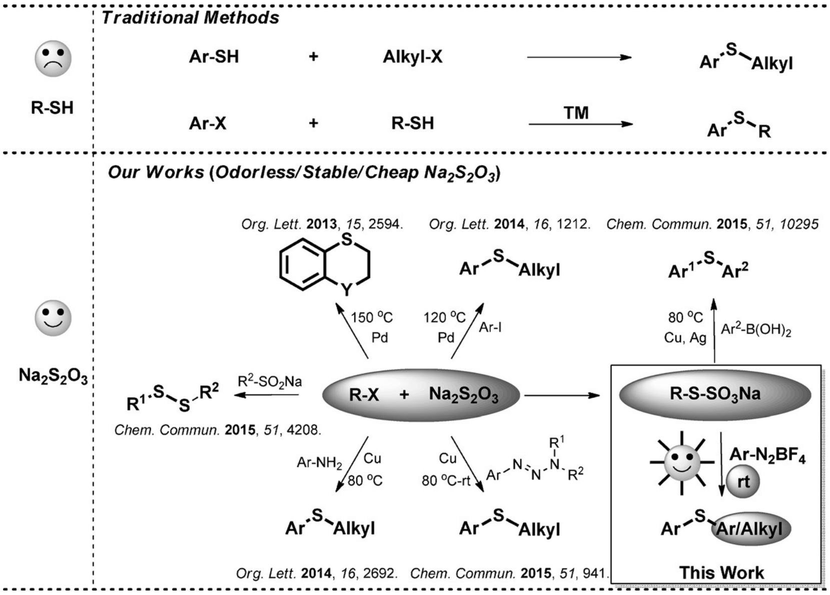
**Abstract:** This study presents thioether construction involving alkyl/aryl thiosulfates and diazonium salt catalyzed by visible-light-excited [$Ru(bpy)_3Cl_2$] at room temperature in 44–86 % yield. Electron paramagnetic resonance studies found that thiosulfate radical formation was promoted by $K_2CO_3$. Conversely, radicals generated from BnSH or BnSSBn (Bn = benzyl) were clearly suppressed, demonstrating the special property of thiosulfate in this system. Transient absorption spectra confirmed the electron-transfer process between [$Ru(bpy)_3Cl_2$] and 4-MeO-phenyl diazonium salt, which occurred with a rate constant of $1.69\times10^{9}\,\text{M}^{-1}\text{s}^{-1}$. The corresponding radical trapping product was confirmed by X-ray diffraction. The full reaction mechanism was determined together with emission quenching data. Furthermore, this system efficiently avoided the over-oxidation of sulfide caused by $H_2O$ in the photoexcited system containing $Ru^{2+}$. Both aryl and heteroaryl diazonium salts with various electronic properties were investigated for synthetic compatibility. Both alkyl- and aryl-substituted thiosulfates could be used as substrates. Notably, pharmaceutical derivatives afforded late-stage sulfuration smoothly under mild conditions.

## Introduction



**Scheme 1.** Strategies for constructing sulfides.

Aiming to conserve energy and reduce emissions, chemists have been trying to mimic the complex photosynthetic processes of plants in relatively simple chemical ways, such as the photocatalyzed reduction of carbon dioxide[1] and solar-driven splitting of water into molecular hydrogen[2] and oxygen.[3] In fact, the original photosynthetic procedure was probably achieved through a reductive sulfur source.[4] During the process of evolution, sulfur bacteria came to play the key role in the relevant transformation,[5] which used various reduced inorganic sulfur compounds, such as thiosulfate, as electron donors for photoautotrophic growth.[6] However, chemical routes to the photocatalyzed transformation of thiosulfate have never been studied.

Our group has been focusing on the sulfur atom transfer reaction,[7] which introduces sulfur atoms into organic compounds from inorganic sulfur sources, in particular, $Na_2S_2O_3$ (Scheme 1). During our research, lower temperatures and cheaper catalysts have gradually been employed. To further enable the transformation under milder and more "natural" conditions, aqueous photocatalyzed transformations of thiosulfate were investigated, which was inspired by the photoauto-

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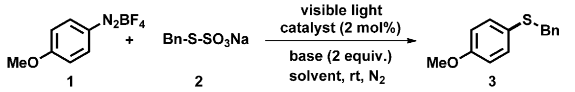
trophic transformation of $S_2O_3^{2-}$ in sulfur bacteria.[6a] Finally, the photocatalyzed[8] cross-coupling reaction between aryl diazonium salt[9] and alkyl/aryl thiosulfate salt[10] was established for constructing sulfides, which are widely found in the body,[11] natural products,[12] pharmaceuticals,[13] and foods.[14] Furthermore, despite the sulfide construction involving thiosulfate being realized through a radical process,[7b,d] the detection of the corresponding thiosulfate radical signal and the study of the detailed mechanism have not been conducted. Herein, we take advantage of this photocatalyzed system to investigate the properties of the thiosulfate radical and possible pathways of the relevant C–S bond construction.

## Results and Discussion

Our study commenced by examining the reaction between 4-methoxybenzenediazonium tetrafluoroborate, **1**, and benzyl thiosulfate salt, **2**. The desired product could be obtained in 76% yield under visible-light-mediated conditions, which was catalyzed by $[Ru(bpy)_3Cl_2]$ and promoted by $K_2CO_3$ in DMSO/$H_2O$ at room temperature (Table 1). Under these standard conditions, BnSH, BnSSBn, and some other sulfur sources (Table 2; Bn = benzyl) were not effective. Control experiments (Table S1 in the Supporting Information) showed that sulfide **3** could be obtained with a relatively low yield (33%) in the absence of visible light and Ru. However, the same conditions with BnSH or BnSSBn did not afford compound **3** (Table S2 in the Supporting Information), demonstrating the unusual property of R-S-$SO_3$Na. In addition, the sulfides are likely to be further oxidized by $Ru(bpy)_3^{2+}$ species in the presence of water and an electron acceptor.[15] The stability of the organic thiosulfate compound[7a] and thiosulfate radical intermediate (see below for mechanistic evidence) decreased the probability of further oxidation and other side reactions. This phenomenon further indicated the critical need to identify its underlying mechanism.

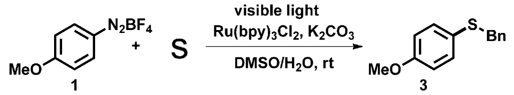
**Table 1.** Optimization of reaction conditions.[a]

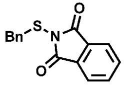


| Entry | Catalyst | Base | Solvent | Yield[b] [%] |
|---|---|---|---|---|
| 1 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | – | MeOH | Trace |
| 2 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | – | MeCN | <10 |
| 3 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | – | DMSO | 45 |
| 4 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | DIPEA[c] | DMSO | 30 |
| 5 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | $NaHCO_3$ | DMSO | 47 |
| 6 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | $K_3PO_4$ | DMSO | 43 |
| 7 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | $K_2CO_3$ | DMSO | 72 |
| 8 | $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ | $K_2CO_3$ | DMSO | 64 |
| 9 | Anthracene-9,10-dicarbonitrile | $K_2CO_3$ | DMSO | 61 |
| ***10*** | ***$[Ru(bpy)_3Cl_2]\cdot 6H_2O$*** | ***$K_2CO_3$*** | ***DMSO/$H_2O$[d]*** | ***76*** |

[a] Reaction conditions: **1** (0.2 mmol), **2** (1.0 mmol), $[Ru(bpy)_3Cl_2]$ (0.004 mmol), $K_2CO_3$ (0.4 mmol), solvent (1 mL), 8 W CFL, $N_2$, rt, 5 h. [b] Isolated yields. [c] DIPEA = *N*,*N*-diisopropylethylamine. [d] DMSO/$H_2O$ = 0.82:0.18 mL.

**Table 2.** Specificity of thiosulfate.[a]



| Entry | Sulfur source | Yield[b] |
|---|---|---|
| 1 | $BnSSO_3Na$ (2) | 76% |
| 2 | BnSH | trace |
| 3 | BnSSBn | trace |
| 4 | BnSCN | ND |
| 5 | BnSAc | trace |
| 6 | $BnSSO_2tol$ | ND |
| 7 |  | trace |

[a] Reaction conditions: **1** (0.2 mmol), sulfur source (1.0 mmol), $[Ru(bpy)_3Cl_2]$ (0.004 mmol), $K_2CO_3$ (0.4 mmol), DMSO/$H_2O$ = 0.82:0.18 mL, 8 W CFL, $N_2$, rt, 5 h. [b] Isolated yields.

### Special role of the thiosulfate radical

To understand the special role of thiosulfate in this system, which is different from thiol[16] or disulfide,[17] electron paramagnetic resonance (EPR) experiments were conducted. As shown in Figure 1 (I), when benzyl thiosulfate was subjected to base in solvent, the intensity of the sulfur radical signal was slightly enhanced. In contrast, the signals of other two traditional sulfurating reagents (BnSH and BnSSBn) sharply decreased when subjected to base (Figure 1 (II) and (III)), which

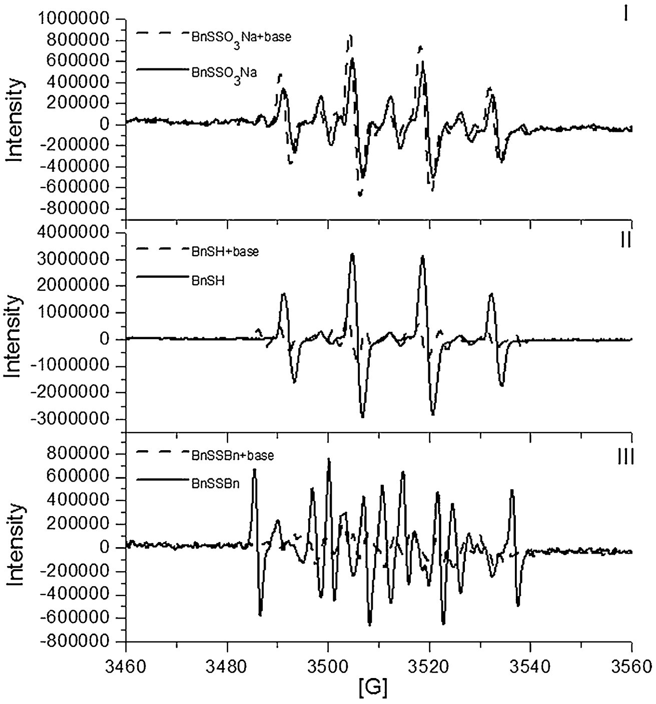


**Figure 1.** Sulfur radicals from different sources observed by electron paramagnetic resonance experiments. All of the experiments were conducted under irradiation by visible light and executed under the standard concentration with radical trapping reagent DMPO (DMPO = 5,5-dimethyl-1-pyrroline-1-oxide).

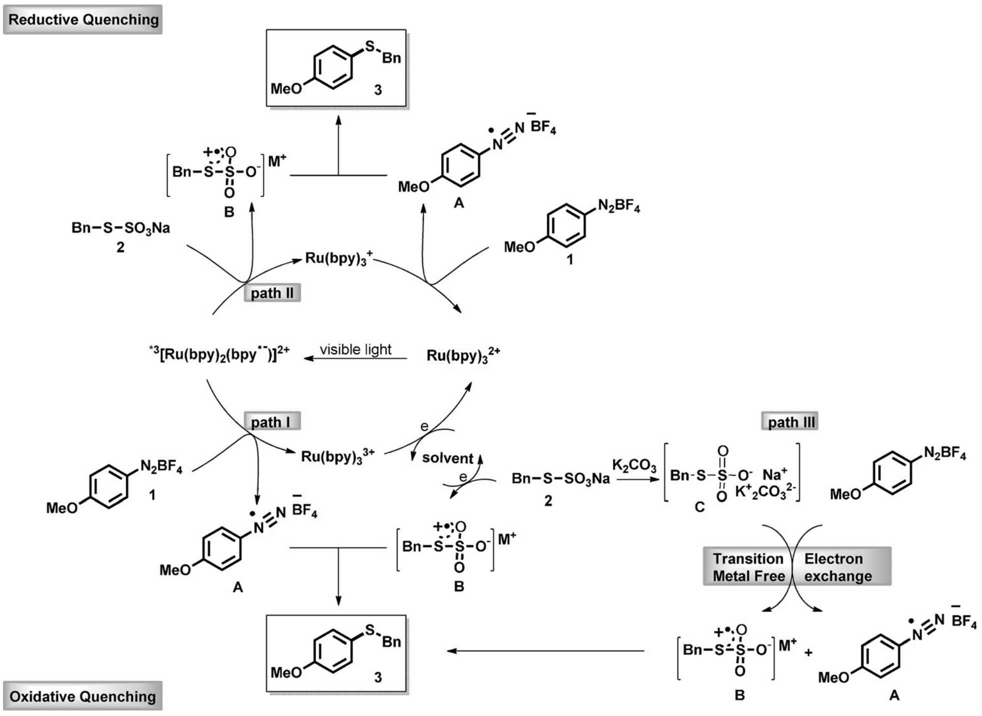
indicated that the corresponding sulfur radical was inhibited. These results were consistent with the control experiments (Table 2) and further explained the higher reactivity of benzyl thiosulfate in this system. However, when BnSH and BnSSBn were applied in the standard conditions without $K_2CO_3$, the sulfide **3** could be obtained, albeit in relatively lower yields (Table S3 in the Supporting Information). These data verified that $K_2CO_3$ exhibits a negative effect on BnSH and BnSSBn in this system. For the different phenomena in Figure 1, a rationale is given: a new intermediate was formed by the combination of benzyl thiosulfate and $K_2CO_3$ and a resonance effect might help produce a relatively stable radical species. Conversely, $K_2CO_3$ might destroy the stability of the BnSH and BnSSBn radicals.

## Mechanistic study

After investigating the special role of the thiosulfate radical, mechanistic studies of the corresponding sulfuration process were conducted. A proposed mechanism is shown in Scheme 2. Firstly, $[Ru(bpy)_3Cl_2]$ is activated by visible light to generate a singlet excited state, which goes through a fast intersystem crossing to the key excited triplet species $^{3*}[Ru(bpy)_2(bpy^{\bullet -})Cl_2]$.[18] Subsequently, there are two different possible interactions between substrates and excited triplet Ru. Path I is an oxidative quenching process, in which diazonium salt **1** obtains an electron from $^{3*}[Ru(bpy)_2(bpy^{\bullet -})Cl_2]$ and generates the phenyl diazonium radical **A** (lifetime about $10^{-7}$ s).[19] Then, radical **A** couples with the thiosulfate electrophilic radical **B**, which originated from **2**. On the other hand, path II is a reductive quenching process. Benzyl thiosulfate could deliver an electron to the excited triplet Ru, which generates benzyl thiosulfate cationic radical **B** and $Ru^{+}$. Then, $Ru^{+}$ is oxidized by the phenyl diazonium salt and regenerates the $Ru^{2+}$ species. Simultaneously, one electron is delivered to compound **1**, which produces the phenyl diazonium radical that can then react with the thiosulfate cationic radical to afford the desired product. Furthermore, the thiosulfate **2** interacts with $K_2CO_3$ and could generate a new species **C**, which could undergo transition-metal-free electron exchange[20] and yield the intermediates **A** and **B** (path III). The final product is achieved through radical coupling between **A** and **B**.

For a mechanistic study of a photocatalyzed reaction, first, it is critical to identify what initiated the reaction. Emission quenching experiments were performed (Figure 2), which showed that the emission intensity of $^{3*}[Ru(bpy)_2(bpy^{\bullet -})Cl_2]$ diminished with increasing concentration of diazonium salt. Comparatively, benzyl thiosulfate salt and $K_2CO_3$ did not exhibit this ability. This evidence indicated that the diazonium salt, instead of the benzyl thiosulfate salt, interacts with $^{3*}[Ru(bpy)_2(bpy^{\bullet -})Cl_2]$ directly through electron or energy transfer.

To verify whether the diazonium compound interacts with the catalyst through an electron- or energy-transfer pattern, transient absorption spectrum studies were conducted. As shown in Figure 3 (I), a strong negative bleach of the ground state absorption of $[Ru(bpy)_3Cl_2]$ was observed at 450 nm after excitation by 440 nm laser. Additionally, the characteristic absorption assigned to $^{3*}[Ru(bpy)_2(bpy^{\bullet -})Cl_2]$ at 370 nm was observed (Figure 3 (I)). Subsequently, $K_2CO_3$ was introduced into the solution of $[Ru(bpy)_3Cl_2]$, an addition that did not result in absorption decay at 370 nm and 450 nm (Figure 3 (II)). When diazonium salt **1** was introduced into the system, the excited state difference spectra showed apparent decay both at 370 nm and 450 nm (Figure 3 (III)). In contrast, when thiosulfate **2** was added to the solution of $[Ru(bpy)_3Cl_2]/K_2CO_3$, there was no obvious change in the transient absorption spectra (Figure 3 (IV)). Furthermore, kinetic studies of the decay at 370 nm (Figure 4) demonstrated that the lifetime of the active triplet $Ru^{2+}$ species diminished only when compound **1** was added. These results confirmed the electron transfer mode between $^{3*}[Ru(bpy)_2(bpy^{\bullet -})Cl_2]$ and diazonium compounds. As the lifetime of $^{3*}[Ru(bpy)_2(bpy^{\bullet -})Cl_2]$ decreased from 1014 ns (Figure 4 (II)) to 866 ns (Figure 4 (III)), the electron transfer rate constant was calculated to be about $1.69 \times 10^9\,\mathrm{M}^{-1}\,\mathrm{s}^{-1}$ (Figure 4),



Scheme 2. Plausible mechanism for photocatalyzed sulfuration.

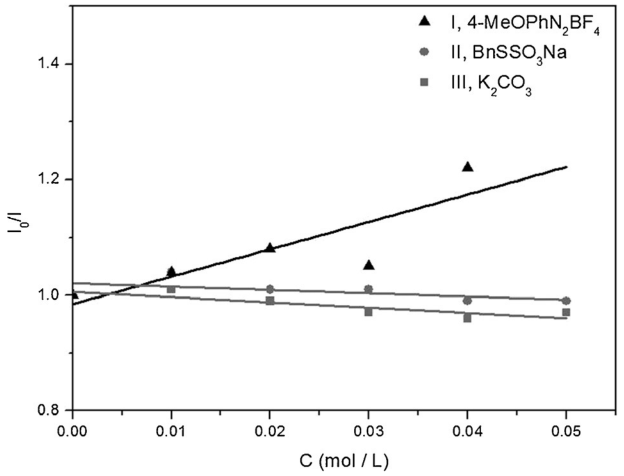


**Figure 2.** Emission quenching of [Ru(bpy)$_3$Cl$_2$].

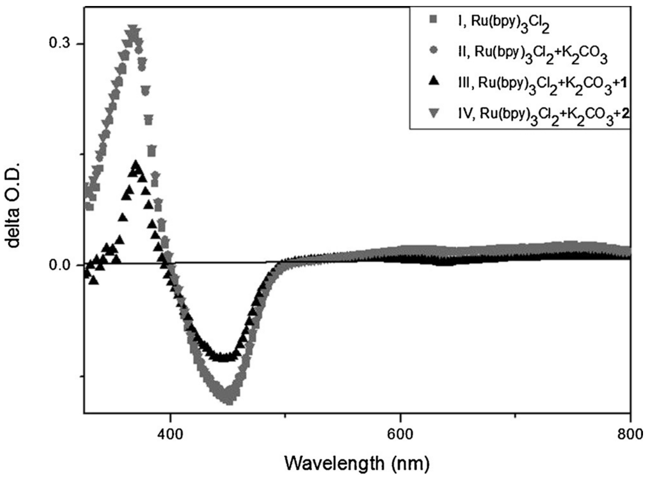


**Figure 3.** Transient absorption spectrum studies. The concentration ratio for all experiments is identical to that in the reaction, $c$[Ru(bpy)$_3$Cl$_2$] $= 1\times10^{-4}$ M.

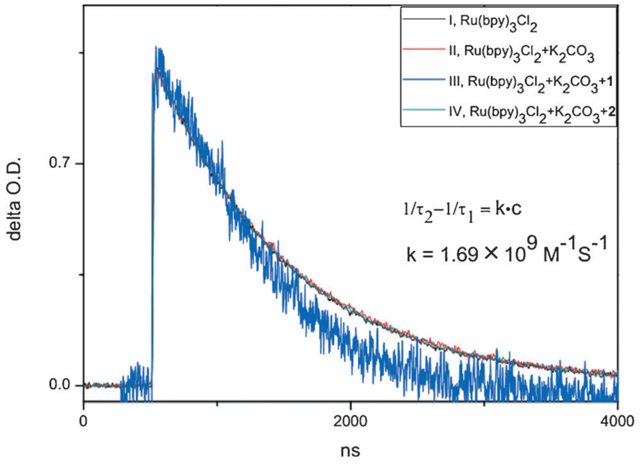
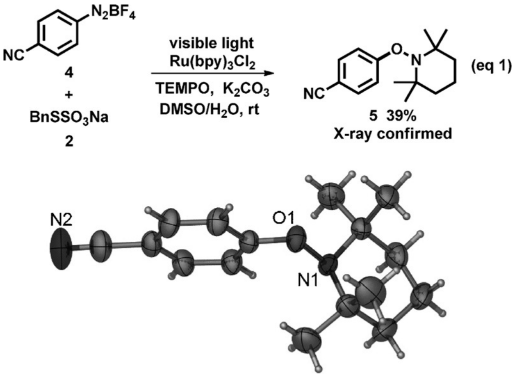


**Figure 4.** Kinetic study of the decay at 370 nm. The concentration ratio for all experiments is identical to that in the reaction, $c$[Ru(bpy)$_3$Cl$_2$] $= 1\times10^{-4}$ M. $\tau_1$ (1014 ns) is the lifetime of Ru$^{2+}$* in condition II, $\tau_2$ (886 ns) is the lifetime of Ru$^{2+}$* in condition III.

which is consistent with the kinetic results of the Stern–Volmer technique by Deronzier's group.[21] These results detailed the oxidative quenching of $^3$*[Ru(bpy)$_2$(bpy$^{\bullet-}$)Cl$_2$] by a diazonium compound in the reaction system in a photophysical manner. Radical trapping tests were conducted and the presence of a phenyl radical trapping species was confirmed by X-ray diffraction (Scheme 3).[22]



**Scheme 3.** Radical trapping experiment. Standard conditions with added TEMPO (2 equiv).

After the initial electron-transfer process was proved, the interaction manner between the phenyl diazonium radical and the new sulfur cationic radical was further investigated. To examine the radical properties, electron paramagnetic resonance (EPR) experiments were conducted (Figure 5 (I)). There are clear radical signals in the standard system. Control experiments revealed that the radical species labeled **B** (aN = 14.08, aH = 15.25) was from the benzyl thiosulfate (Figure 5 (II)). From EPR experiments under standard conditions without compound **2**, the phenyl radical was identified as well (aN = 14.76, aH = 21.51) (Figure S6 in the Supporting Information), in which the signal was labeled **A**. The above EPR results showed the presence of the phenyl and thiosulfate radical, with a peak area ratio of 1:7. Moreover, the results indicated the desired sulfide might be generated through the radical coupling[23] between the two.

The electron-transfer process from Ru$^{3+}$ to Ru$^{2+}$ still needs to be elucidated (Scheme 2, path I). Emission quenching experiments have shown that there is no direct interaction between [Ru(bpy)$_3$Cl$_2$] and benzyl thiosulfate (Figure 2). According to EPR studies (Figure 5), compared with the system with only the benzyl thiosulfate in H$_2$O under visible light (Figure 5 (II)), an additional series of signals (labeled **C**) could be observed when the standard solvent system (DMSO/H$_2$O) was used, which indicated that the solvent might be involved in the electron-exchange process. Thus, the electron released from the organic thiosulfate is captured and further transferred to the photocatalyst by the solvent, which realizes the oxidation process from Ru$^{3+}$ to Ru$^{2+}$. In addition to the above process, a radical chain propagation pathway[24] might be possible as well. The phenyl radical might add to the thiosulfate species and form a new radical complex. The newly formed radical fur-

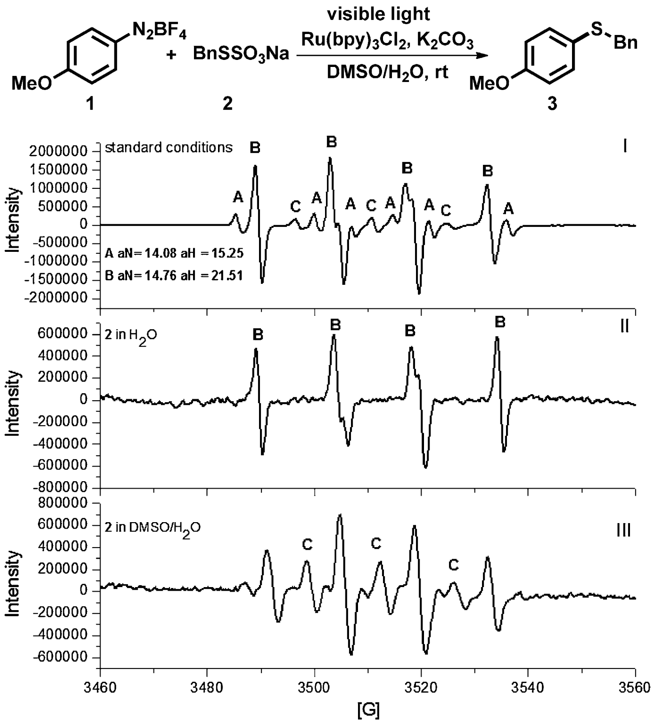


**Figure 5.** Characteristic signal comparison in electron paramagnetic resonance experiments. All the experiments were conducted under irradiation by visible light and executed under the standard concentration with radical trapping reagent DMPO (DMPO = 5,5-dimethyl-1-pyrroline-1-oxide).

ther experiences loss of an electron and cleavage of the S–S bond, which finally produces the sulfide.

Considering these results, a detailed mechanism is depicted (Scheme 2, path I). Initially, [Ru(bpy)$_3$Cl$_2$] is activated by visible light to form $^{3*}$[Ru(bpy)$_2$(bpy$^{\bullet-}$)Cl$_2$], which goes through an oxidative quenching process with diazonium salt **1** to generate the Ru$^{3+}$ and phenyl diazonium radical **A**. Organic thiosulfate salt **2** releases an electron to the solvent and affords the thiosulfate radical cationic species **B**. The newly generated phenyl diazonium and thiosulfate electrophilic radical are coupled to afford the desired products. The solvent shuttles an electron to Ru$^{3+}$ and regenerates the catalyst. The transition-metal-free electron-exchange process might generate the product as well.

### Synthetic compatibility investigation

After the above mechanistic studies, the compatibility and applicability of this transformation were further investigated. As shown in Table 3, various aryl diazonium tetrafluoroborates were applied in our reaction conditions and it was found that substitutions at the *para*- (**3**, **6**–**11**), *ortho*- (**12**), and *meta*- (**13**) positions were all compatible. Both electron-withdrawing and electron-donating groups afforded moderate to excellent yields. It is worth noting that chloro- (**8**, **13**) and bromo-substitutions (**9**) could be well tolerated in this system, thus, the corresponding products could be further transformed in cross-coupling reactions. In addition, the reactivity of the multi-substituted aryl diazonium salt (**14**) could work as well. Next, different organic thiosulfates were examined. Not only substituted benzyl thiosulfates (**15**–**16**), but also alkyl ones with diverse functional groups (**17**–**18**) could afford the desired products. In addition, the sp$^2$-thiosulfates (**19**–**20**) could also be utilized to synthesize diphenyl sulfide structures. A free combination of both parts was investigated as well (**21**–**31**). The corresponding experiments mainly focused on the fluoro- and cyano-containing substrates (**21**–**26**). Finally, pyridine diazonium salts, which are not frequently studied, were purposely investigated here.[9a,b] It was found that both sp$^2$- and sp$^3$-substituted thiosulfates (**27**–**31**) were transformed in good to excellent yields, a reaction type that is usually a challenge in coupling reactions.[25] Taking pyridine-3-diazonium tetrafluoroborate as an example, the standard conditions with [Ru(bpy)Cl$_2$] and K$_2$CO$_3$ could only produce **27** in 26 % yield; however, when methylene blue (MB) was used as the photocatalyst instead of Ru, 66 % yield could be obtained (Table S5 in the Supporting Information). Possible reasons for this are: 1) coordination from the N atom on pyridine to Ru decreases the yield; 2) pyridine diazonium salts are more electron-deficient and less stable. Compared with MB, the more energetic absorption wavelength of [Ru(bpy)$_3$Cl$_2$] might cause the decomposition of unstable pyridine substrates. The maximum absorption wavelength in visible light is 663 nm for MB[26] and 452 nm for [Ru(bpy)$_3$Cl$_2$].[8d]

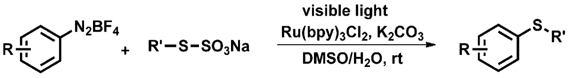
### Pharmaceutical derivatives late-stage sulfuration

To implement our late-stage sulfuration strategy,[7a–e,g] several crucial medicinal compounds were utilized (Table 4). Sulfonamides[27] are typical antimicrobial medicinal compounds, which could efficiently defeat Gram-positive and Gram-negative bacteria. The *p*-sulfide sulfonamides exhibit important bioactivity as well.[28] Therefore, we explored late-stage sulfuration on sulfonamide pharmaceuticals. Different representative substituted compounds were evaluated, such as primidyl (**32**--**33**), pyridyl (**34**), and oxazolinyl (**35**–**36**), of which the structure of **32** was confirmed by X-ray crystallography analysis.[29] In these examples, the active hydrogen and complicated heterocycle substitutions did not adversely affect the efficiency of this protocol. In addition to alkyl thiosulfate, the aryl thiosulfate **36** could also be used in this modification procedure for medically relevant derivatives. The transformations were achieved under mild conditions and might be potentially applicable in medicinal and biological studies.

## Conclusion

To mimic the photosynthetic application of S$_2$O$_3$$^{2-}$ in sulfur bacteria, alkyl/aryl thiosulfates were introduced into an aqueous photocatalyzed sulfurating system. This method successfully overcame the over-oxidation of sulfide by Ru$^{2+}$ in water. Detailed mechanistic studies were performed to identify the underlying mechanism. Electron paramagnetic studies detected a new thiosulfate radical species and explained the reason for the specificity of thiosulfate radicals in this system. Transient absorption spectra investigation confirmed the electron transfer between excited triplet Ru$^{2+}$ and the diazonium compound. Moreover, this mild sulfurating strategy is compatible with diverse substrates and could be successfully applied to the modification of complex medicinal compounds.

**Table 3.** Substrates scope.[a]



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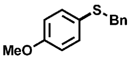
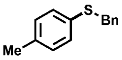
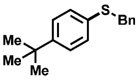
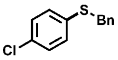
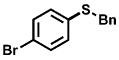
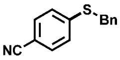
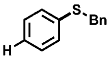
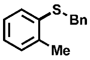
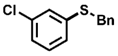
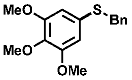
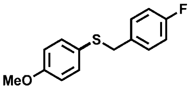
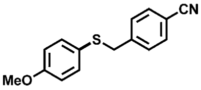
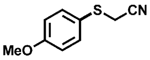
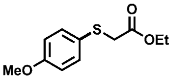
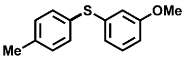
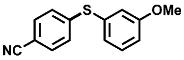
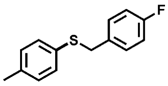
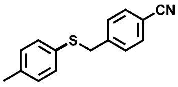
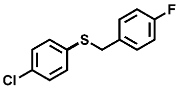
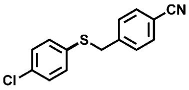
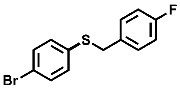
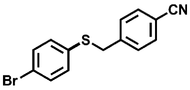
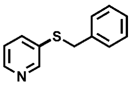
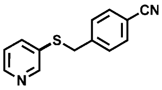
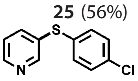
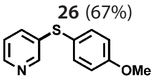
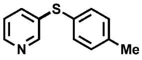
|  **3** (76%) |  **6** (81%) |  **7** (53%) |  **8** (62%) |
|  **9** (59%) |  **10** (71%) |  **11** (58%) |  **12** (50%) |
|  **13** (50%) |  **14** (58%) |  **15** (68%) |  **16** (60%) |
|  **17** (76%) |  **18** (67%) |  **19** (62%) |  **20** (55%) |
|  **21** (82%) |  **22** (64%) |  **23** (60%) |  **24** (66%) |
|  **25** (56%) |  **26** (67%) |  **27** (66%)[b] |  **28** (86%)[b] |
|  **29** (83%)[b] |  **30** (55%)[b] |  **31** (80%)[b] | |

[a] Standard conditions, isolated yields. [b] Methylene blue and $Li_2CO_3$ were used instead of $[Ru(bpy)_3Cl_2]$ and $K_2CO_3$.

## Experimental Section

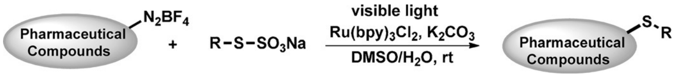
### Typical reaction procedure

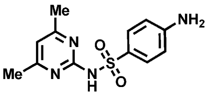
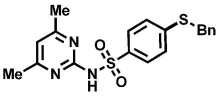
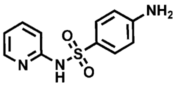
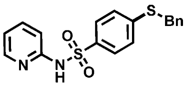
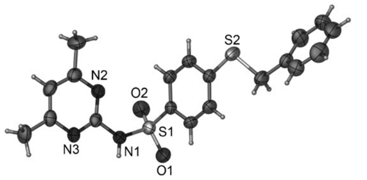
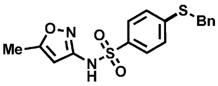
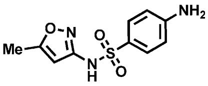
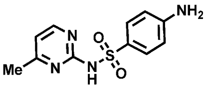
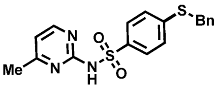
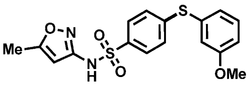
A Schlenk tube was filled with nitrogen, then diazonium tetrafluoroborate (0.2 mmol), thiosulfate salt (1 mmol), $[Ru(bpy)_3Cl_2]\cdot 6H_2O$ ($4\times10^{-3}$ mmol), $K_2CO_3$ (0.4 mmol), DMSO (0.82 mL)/$H_2O$ (0.18 mL) were added. The reaction mixture was stirred for 5 h at room temperature under the irradiation of 8 W Compact Fluorescent Lamp (CFL). When the reaction was finished, ethyl acetate (EA; 5 mL) was added to the mixture, which was dried over $MgSO_4$. Then, the mixture was filtered through Celite, concentrated, and purified by column chromatography on silica gel to afford the desired product.

## *Acknowledgements*

We would like to thank Prof. Dr. Lizhu Wu for the transient absorption spectra studies and suggestions. We are also grateful to Ms. Yanhong Liu for the electron paramagnetic resonance studies and essential advice. Financial support was provided by NBRPC (973 Program, 2015CB856600), NSFC (21472050, 21272075), NCET (120178), DFMEC (20130076110023), Fok Ying Tung Education Foundation (141011), the program for Shanghai Rising Star (15A1401800), Professor of Special Appointment (Eastern Scholar) at Shanghai Institutions of Higher Learning, and the Changjiang Scholar and Innovative Research Team in University.

**Table 4.** Late-stage modification of pharmaceuticals.[a]



| | | | |
|---|---|---|---|
|  sulfamethazine |  **32** (59%) |  sulfapyridine |  **34** (44%) |
|  **32** | | |  **35** (70%) |
| | |  sulfamethoxazole | |
|  sulfamerazine |  **33** (52%) | |  **36** (67%) |

[a] Standard conditions, isolated yields.

**Keywords:** bond formation · mechanistic study · organic thiosulfates · pharmaceuticals sulfuration · photocatalysis

[1] a) J. Qiao, Y. Liu, F. Hong, J. Zhang, *Chem. Soc. Rev.* **2014**, *43*, 631–675; b) A. M. Appel, J. E. Bercaw, A. B. Bocarsly, H. Dobbek, D. L. DuBois, M. Dupuis, J. G. Ferry, E. Fujita, R. Hille, P. J. A. Kenis, C. A. Kerfeld, R. H. Morris, C. H. F. Peden, A. R. Portis, S. W. Ragsdale, T. B. Rauchfuss, J. N. H. Reek, L. C. Seefeldt, R. K. Thauer, G. L. Waldrop, *Chem. Rev.* **2013**, *113*, 6621–6658; c) B. A. Rosen, A. Salehi-Khojin, M. R. Thorson, W. Zhu, D. T. Whipple, P. J. A. Kenis, R. I. Masel, *Science* **2011**, *334*, 643–644; d) S. C. Roy, O. K. Varghese, M. Paulose, C. A. Grimes,

*ACS Nano* **2010**, *4*, 1259 – 1278; e) E. E. Benson, C. P. Kubiak, A. J. Sathrum, J. M. Smieja, *Chem. Soc. Rev.* **2009**, *38*, 89 – 99; f) A. J. Morris, G. J. Meyer, E. Fujita, *Acc. Chem. Res.* **2009**, *42*, 1983 – 1994.

[2] a) L.-Z. Wu, B. Chen, Z.-J. Li, C.-H. Tung, *Acc. Chem. Res.* **2014**, *47*, 2177 – 2185; b) Z. Han, F. Qiu, R. Eisenberg, P. L. Holland, T. D. Krauss, *Science* **2012**, *338*, 1321 – 1324; c) A. J. Esswein, D. G. Nocera, *Chem. Rev.* **2007**, *107*, 4022 – 4047; d) M. Ni, M. K. H. Leung, D. Y. C. Leung, K. Sumathy, *Renew. Sus. Energy Rev.* **2007**, *11*, 401 – 425.

[3] a) A. Singh, L. Spiccia, *Coord. Chem. Rev.* **2013**, *257*, 2607 – 2622; b) Q. Yin, J. M. Tan, C. Besson, Y. V. Geletii, D. G. Musaev, A. E. Kuznetsov, Z. Luo, K. I. Hardcastle, C. L. Hill, *Science* **2010**, *328*, 342 – 345; c) G. C. Dismukes, *Science* **2001**, *292*, 447 – 448.

[4] J. Olson, *Photosynth. Res.* **2006**, *88*, 109 – 117.

[5] a) T. Meyer, M. Cusanovich, in *Discoveries in Photosynthesis, Vol. 20* (Eds.: Govindjee, J. T. Beatty, H. Gest, J. Allen), Springer, Netherlands, **2005**, pp. 455 – 470; b) T. Meyer, M. Cusanovich, *Photosynth. Res.* **2003**, *76*, 111 – 126.

[6] a) H. Sakurai, T. Ogawa, M. Shiga, K. Inoue, *Photosynth. Res.* **2010**, *104*, 163 – 176; b) C. Azai, Y. Tsukatani, S. Itoh, H. Oh-oka, *Photosynth. Res.* **2010**, *104*, 189 – 199.

[7] a) Z. Qiao, N. Ge, X. Jiang, *Chem. Commun.* **2015**, *51*, 10295 – 10298; b) Y. Zhang, Y. Li, X. Zhang, X. Jiang, *Chem. Commun.* **2015**, *51*, 941 – 944; c) X. Xiao, M. Feng, X. Jiang, *Chem. Commun.* **2015**, *51*, 4208 – 4211; d) Y. Li, J. Pu, X. Jiang, *Org. Lett.* **2014**, *16*, 2692 – 2695; e) Z. Qiao, J. Wei, X. Jiang, *Org. Lett.* **2014**, *16*, 1212 – 1215; f) H. Liu, X. Jiang, *Chem. Asian J.* **2013**, *8*, 2546 – 2563; g) Z. Qiao, H. Liu, X. Xiao, Y. Fu, J. Wei, Y. Li, X. Jiang, *Org. Lett.* **2013**, *15*, 2594 – 2597.

[8] a) D. M. Schultz, T. P. Yoon, *Science* **2014**, *343*, 1239176; b) D. A. Nicewicz, T. M. Nguyen, *ACS Catal.* **2013**, *3*, 355 – 360; c) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, *Chem. Rev.* **2013**, *113*, 5322 – 5363; d) J. Xuan, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2012**, *51*, 6828 – 6838; *Angew. Chem.* **2012**, *124*, 6934 – 6944; e) J. M. R. Narayanam, C. R. J. Stephenson, *Chem. Soc. Rev.* **2011**, *40*, 102 – 113; f) L. Shi, W. Xia, *Chem. Soc. Rev.* **2012**, *41*, 7687 – 7697.

[9] a) D. P. Hari, B. König, *Angew. Chem. Int. Ed.* **2013**, *52*, 4734 – 4743; *Angew. Chem.* **2013**, *125*, 4832 – 4842; b) F. Mo, G. Dong, Y. Zhang, J. Wang, *Org. Biomol. Chem.* **2013**, *11*, 1582 – 1593; c) D. Kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, *J. Am. Chem. Soc.* **2011**, *133*, 18566 – 18569; d) W. Guo, L.-Q. Lu, Y. Wang, Y.-N. Wang, J.-R. Chen, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 2265 – 2269; *Angew. Chem.* **2015**, *127*, 2293 – 2297; e) 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; f) D. P. Hari, P. Schroll, B. König, *J. Am. Chem. Soc.* **2012**, *134*, 2958 – 2961; g) P. Schroll, D. P. Hari, B. König, *ChemistryOpen* **2012**, *1*, 130 – 133; h) D. Prasad Hari, T. Hering, B. König, *Angew. Chem. Int. Ed.* **2014**, *53*, 725 – 728; *Angew. Chem.* **2014**, *126*, 743 – 747.

[10] a) H. Bunte, *Chem. Ber.* **1874**, *7*, 646 – 648; b) H. Distler, *Angew. Chem. Int. Ed. Engl.* **1967**, *6*, 544 – 553; *Angew. Chem.* **1967**, *79*, 520 – 529.

[11] a) B. G. Davis, *Chem. Rev.* **2002**, *102*, 579 – 602; b) Y. A. Lin, J. M. Chalker, N. Floyd, G. J. L. Bernardes, B. G. Davis, *J. Am. Chem. Soc.* **2008**, *130*, 9642 – 9643; c) B. G. Davis, *Science* **2004**, *303*, 480 – 482.

[12] a) C. Jacob, *Nat. Prod. Rep.* **2006**, *23*, 851 – 863; b) C.-S. Jiang, W. E. G. Müller, H. C. Schröder, Y.-W. Guo, *Chem. Rev.* **2011**, *111*, 2179 – 2207.

[13] E. A. Ilardi, E. Vitaku, J. T. Njardarson, *J. Med. Chem.* **2013**, *56*, 2832 – 2842.

[14] a) D. Y. Lin, S.-Z. Zhang, E. Block, L. C. Katz, *Nature* **2005**, *434*, 470 – 477; b) E. Block, *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 1135 – 1178; *Angew. Chem.* **1992**, *104*, 1158 – 1203.

[15] a) O. Hamelin, P. Guillo, F. Loiseau, M.-F. Boissonnet, S. Ménage, *Inorg. Chem.* **2011**, *50*, 7952 – 7954; b) K. Senthil Murugan, T. Rajendran, G. Balakrishnan, M. Ganesan, V. K. Sivasubramanian, J. Sankar, A. Ilangovan, P. Ramamurthy, S. Rajagopal, *J. Phys. Chem. A* **2014**, *118*, 4451 – 4463.

[16] a) X. Wang, G. D. Cuny, T. Noël, *Angew. Chem. Int. Ed.* **2013**, *52*, 7860 – 7864; *Angew. Chem.* **2013**, *125*, 8014 – 8018; b) M. H. Keylor, J. E. Park, C.-J. Wallentin, C. R. J. Stephenson, *Tetrahedron* **2014**, *70*, 4264 – 4269.

[17] a) M. Majek, A. J. von Wangelin, *Chem. Commun.* **2013**, *49*, 5507 – 5509; b) D. J. Wilger, M. Grandjean-Marc, T. R. Lammert, D. A. Nicewicz, *Nat. Chem.* **2014**, *6*, 720 – 726; c) N. A. Romero, D. A. Nicewicz, *J. Am. Chem. Soc.* **2014**, *136*, 17024 – 17035.

[18] a) S. Wallin, J. Davidsson, J. Modin, L. Hammarström, *J. Phys. Chem. A* **2005**, *109*, 4697 – 4704; b) M. Rueda-Becerril, O. Mahé, M. Drouin, M. B. Majewski, J. G. West, M. O. Wolf, G. M. Sammis, J.-F. Paquin, *J. Am. Chem. Soc.* **2014**, *136*, 2637 – 2641; c) N. H. Damrauer, G. Cerullo, A. Yeh, T. R. Boussie, C. V. Shank, J. K. McCusker, *Science* **1997**, *275*, 54 – 57.

[19] L. F. Kasukhin, M. P. Ponomarchuk, A. L. Buchachenko, *Chem. Phys.* **1974**, *3*, 136 – 139.

[20] a) C.-L. Sun, Z.-J. Shi, *Chem. Rev.* **2014**, *114*, 9219 – 9280; b) A. Studer, D. P. Curran, *Angew. Chem. Int. Ed.* **2011**, *50*, 5018 – 5022; *Angew. Chem.* **2011**, *123*, 5122 – 5127; c) E. Shirakawa, K.-i. Itoh, T. Higashino, T. Hayashi, *J. Am. Chem. Soc.* **2010**, *132*, 15537 – 15539; d) W. Liu, H. Cao, H. Zhang, H. Zhang, K. H. Chung, C. He, H. Wang, F. Y. Kwong, A. Lei, *J. Am. Chem. Soc.* **2010**, *132*, 16737 – 16740; e) C.-L. Sun, H. Li, D.-G. Yu, M. Yu, X. Zhou, X.-Y. Lu, K. Huang, S.-F. Zheng, B.-J. Li, Z.-J. Shi, *Nat. Chem.* **2010**, *2*, 1044 – 1049.

[21] H. Cano-Yelo, A. Deronzier, *J. Chem. Soc. Faraday Trans. 1* **1984**, *80*, 3011 – 3019.

[22] Crystallographic parameters for **5**: $C_{16}H_{22}N_2O$, $M_W = 258.36$, monoclinic, space group $P2_1/c$, final $R$ indices $[I > 2\sigma(I)]$, $R_1 = 0.0448$, $wR_2 = 0.1105$, $R$ indices (all data), $R_1 = 0.1105$, $wR_2 = 0.1216$, $a = 10.9860$ (4) Å, $b = 17.7567$ (7) Å, $c = 7.6511$ (3) Å, $\alpha = 90$ °, $\beta = 94.347(1)^\circ$, $\gamma = 90^\circ$, $V = 148.20$ (10) $Å^3$, $Z = 4$, Reflections collected/unique: 17 109/2609 ($R_{(int)} = 0.0345$). CCDC 1047200 (**5**) and 1041783 (**32**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by The Cambridge Crystallographic Data Centre.

[23] a) N. J. Turro, *Acc. Chem. Res.* **2000**, *33*, 637 – 646; b) E. J. Nanni, D. T. Sawyer, S. S. Ball, T. C. Bruice, *J. Am. Chem. Soc.* **1981**, *103*, 2797 – 2802; c) P. H. Mazzocchi, G. Fritz, *J. Am. Chem. Soc.* **1986**, *108*, 5362 – 5364; d) F. D. Saeva, D. T. Breslin, H. R. Luss, *J. Am. Chem. Soc.* **1991**, *113*, 5333 – 5337; e) L. Zhou, S. Tang, X. Qi, C. Lin, K. Liu, C. Liu, Y. Lan, A. Lei, *Org. Lett.* **2014**, *16*, 3404 – 3407.

[24] C.-J. Wallentin, J. D. Nguyen, P. Finkbeiner, C. R. J. Stephenson, *J. Am. Chem. Soc.* **2012**, *134*, 8875 – 8884.

[25] a) Y. Fujiwara, J. A. Dixon, F. O′Hara, E. D. Funder, D. D. Dixon, R. A. Rodriguez, R. D. Baxter, B. Herle, N. Sach, M. R. Collins, Y. Ishihara, P. S. Baran, *Nature* **2012**, *492*, 95 – 99; b) D. A. Nagib, D. W. C. MacMillan, *Nature* **2011**, *480*, 224 – 228.

[26] a) K. O. Takahisa Omata, S. Otsuka-Yao-Matsuo, *Mater. Trans.* **2003**, *44*, 1620 – 1623; b) M. M. Brooks, *Proc. Nat. Acad. Sci. USA* **1927**, *13*, 821 – 823.

[27] a) T. O. A. Scozzafava, A. Mastrolorenzo, C. T. Supuran, *Curr. Med. Chem.* **2003**, *10*, 925; b) C. T. Supuran, A. Casini, A. Scozzafava, *Med. Res. Rev.* **2003**, *23*, 535 – 558.

[28] a) L. A. Reiter, R. P. Robinson, K. F. McClure, C. S. Jones, M. R. Reese, P. G. Mitchell, I. G. Otterness, M. L. Bliven, J. Liras, S. R. Cortina, K. M. Donahue, J. D. Eskra, R. J. Griffiths, M. E. Lame, A. Lopez-Anaya, G. J. Martinelli, S. M. McGahee, S. A. Yocum, L. L. Lopresti-Morrow, L. M. Tobiassen, M. L. Vaughn-Bowser, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 3389 – 3395; b) K. L. Lobb, P. A. Hipskind, J. A. Aikins, E. Alvarez, Y.-Y. Cheung, E. L. Considine, A. De Dios, G. L. Durst, R. Ferritto, C. S. Grossman, D. D. Giera, B. A. Hollister, Z. Huang, P. W. Iversen, K. L. Law, T. Li, H.-S. Lin, B. Lopez, J. E. Lopez, L. M. M. Cabrejas, D. J. McCann, V. Molero, J. E. Reilly, M. E. Richett, C. Shih, B. Teicher, J. H. Wikel, W. T. White, M. M. Mader, *J. Med. Chem.* **2004**, *47*, 5367 – 5380; c) K. Gerzon, E. V. Krumkalns, R. L. Brindle, F. J. Marshall, M. A. Root, *J. Med. Chem.* **1963**, *6*, 760 – 763.

[29] Crystallographic parameters for **32**: $C_{19}H_{19}N_3O_2S_2$, $M_W = 385.49$, monoclinic, space group $P\bar{1}$, final $R$ indices $[I > 2\sigma(I)]$, $R_1 = 0.0448$, $wR_2 = 0.1165$, $R$ indices (all data), $R_1 = 0.0678$, $wR_2 = 0.1328$, $a = 9.6494$ (4) Å, $b = 9.7383$ (4) Å, $c = 21.3124$ (8) Å, $\alpha = 97.991(1)°$, $\beta = 102.561(1)^\circ$, $\gamma = 98.269(1)^\circ$, $V = 1904.14$ (13) $Å^3$, $Z = 4$, Reflections collected/unique: 22 430/6676 ($R_{(int)} = 0.0376$).

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