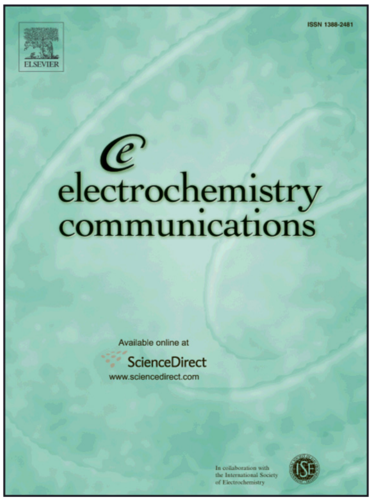

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Electrochemical oxidations of thioethers: Modulation of oxidation potential using a hydrogen bonding network

Shiwen Liu [a], Bocheng Chen [b], Yi Yang [b], Yuhao Yang [b], Qianjin Chen [b], Xiaojun Zeng [b] *, Bo Xu [b] *

[a] College of Textiles and Clothing, Yancheng Institute of Technology, Yancheng, 224051, China.

[b] Key Laboratory of Science and Technology of Eco-Textiles, Ministry of Education, College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, Shanghai 201620, China.

*Corresponding authors

Email: bo.xu@dhu.edu.cn, xjzeng1004@hotmail.com

Abstract

A highly efficient chemo-selective electrochemical oxidation of thioethers to sulfoxides and sulfones was developed. The hydrogen bonding network generated from hexafluoro-2-propanol (HFIP) and acetic acid (AcOH) plays an important role in the modulation of oxidation potential. The hydrogen bonding network complexes strongly with the sulfoxide, making it less prone to further oxidation. Therefore, thioethers can be selectively electrochemically oxidized to sulfoxides and over-oxidization could be minimized. Moreover, this modulation of oxidization via hydrogen bonding was supported by density functional theory (DFT) calculations and cyclic voltammetry experiments.

Keywords

Hydrogen boding network; electrochemical oxidation; sulfoxides and sulfones; thioethers

1. Introduction

Oxidation is ubiquitous in organic synthesis, and electrochemical oxidations are considered as more atom-economic and more sustainable oxidation methods compared to chemical oxidations [1-3]. However, overoxidation may happen if the desired oxidation product could be further oxidized. We envision that a strong hydrogen bonding donor system could be used to modulate oxidation and minimize over-oxidation (Figure 1. a). Generally, a new oxygen atom could be introduced into an organic molecule which was oxidized. And this oxygen may function as hydrogen bonding acceptor. Thus, a hydrogen bonding complex may form via a strong interaction between hydrogen bonding acceptor (the oxygen atom) and a hydrogen bonding donor such as hexafluoro-2-propanol (HFIP) [4]. For example, Bégué and coworkers [4] have reported that the oxidation of sulfides into sulfoxides by aqueous 30% H_2O_2 in HFIP. The hydroxyl proton of HFIP could form a strong hydrogen bond with H_2O_2, activating the hydroxyl leaving group (H_2O_2), which promoted the oxidation of sulfides into sulfoxides. On the other hand, the nucleophilicity of the sulfur atom decreased significantly due to the formation of a strong hydrogen bond between HFIP and the oxygen of the sulfoxides, which prevented further oxidation into sulfone. Thus, the hydrogen bonding donor will deprive some electron density of the H-bond acceptor and make it less prone to be oxidized. By doing this, over-oxidation could be reduced. If the further-oxidation products are desired, a relatively high voltage could be employed.

Recently Hunter and coworkers have reported that a linear H-bond aggregate is a much better H-bond donor system than monomer and cyclic H-bond aggregates [5] (Figure 1. b). In general, acetic acid is not a good hydrogen bond donor because it often forms a cyclic dimer in solutions of non-hydrogen-bonding solvents [6]. We envision that cyclic dimer of acetic acid could be converted to linear aggregates when interacting with strong H-bond donor solvents such as HFIP and generate a linear H-bond aggregate with a very high H-bond acidity (Figure 1. b). Moreover, this strong

H-bond network could be used in the modulation of oxidation of H-bond acceptors. Our proof of concept application is chemo-selective oxidation of thioethers to sulfoxides and sulfones (Figure 1. d). We envision that thioethers could be selectively oxidized in the presence of a hydrogen bonding network generated from HFIP and acetic acid.

Transitionally, the most common and straightforward method for the preparation of sulfoxides and sulfones is the oxidation of thioethers. Indeed, many chemical oxidation systems such as hydrogen peroxide [4, 7-18], peroxycarboxylic acid [19] and many other oxidants [20-25] have been reported. Unfortunately, these strategies typically suffer from selectivity issues, e.g. over-oxidation of the sulfoxide to the sulfone or oxidation of other functional groups within the molecule. Electrochemical anodic oxidation presents a powerful and environmentally friendly method to the synthesis of desirable products, which has gained increasing attention [26-35]. Noël reported selective electrochemical oxidation of sulfides [36, 37] using a continuous-flow microreactor, providing an environmentally benign method for the synthesis of sulfoxides and sulfones. However, low to moderate yields are obtained for the oxidation of sulfides into sulfoxides and tuning the voltage over the electrodes is the only way to avoid over-oxidation. Huang and coworkers [38] demonstrated an electrochemical synthesis of sulfoxides from thiols, but this approach is limited to the preparation of methyl sulfoxides. Herein, we are glad to report a highly efficient electrocatalytic protocol for chemo-selective oxidation of thioethers to sulfoxides and sulfones based on hydrogen bonding modulation (Figure 1. d).

2. Results and discussion

Initially, we started this selective oxidation by using thioether **1a** as a model substrate (Table 1). Utilizing the common Pt (platinum) as electrodes, $LiClO_4$ as the electrolyte, and acetonitrile (MeCN) as solvent under constant potential, 5% desired product **2a** was obtained (Table 1, entry 1). Similarly, there was no reaction when polar aprotic solvent – DMF (*N*, *N*-dimethylformamide) was used (Table 1, entry 2). And our DFT calculations are consistent with our hypothesis that hydrogen bonding may increase the oxidation potential (Figure 1. c). In general, the oxidation potential is directly related to ionization potential [39]. Ionization potential increases significantly when bonding with an increased number of hydrogen bonding donors, especially bonding with HFIP. For example, a sulfoxide forms an H-bond complex with an increasing number of acetic acid or HFIP and its ionization potential indeed increases (Figure 1. c), which would make further oxidation of sulfoxides to sulfones difficult. HFIP has been extensively used as an extraordinary solvent in promoting various chemical transformations [4, 40-48]. Owing to its exceptional redox stability, HFIP has been commonly used in electrochemistry [49-56]. However, there was no reaction when using HFIP as the solvent in this case (Table 1, entry 3). Then we tested various other hydrogen bonding donor solvents (methanol, acetic acids and water) (Table 1, entries 4-6). Moderate yields were observed when methanol or acetic acid was used. We envisioned that in a pure liquid phase, a mixture of acetic acid and HFIP might function as a very strong hydrogen bonding donor network. To our delight, the oxidation was very efficient using a mixture of HFIP/AcOH (1:1) as the solvent (Table 1, entry 7). What's more, there was almost no overoxidation product **3a**. However, a mixture of HFIP and methanol was not effective (Table 1, entry 8). After accessing sulfoxides efficiently, we next focused on the investigation of oxidation of thioethers into sulfones. Firstly, 2 equivalents of $n\mathrm{Bu}_4\mathrm{NBF}_4$ were used as electrolytes, but poor yield was obtained by increasing the voltage from 3 V to 4 V (Table 1, entry 9) and no product **3a** was observed when changing solvent into acetic acid (Table 1, entry 10). Further screening of electrolytes showed that LiClO_4 as an electrolyte was superior to $n\mathrm{Bu}_4\mathrm{NPF}_6$ on both selectivity and conversion (Table 1, entries 11 - 12). As expected, this oxidation reaction could not proceed without electricity (Table 1, entry 13).

With the optimized reaction conditions in hand, we started to examine the scope of substrates (Figure 2). Firstly, diverse thioanisole derivatives could be selectively oxidized into sulfoxides (**2a-2o**) in good to excellent yields. The substitution pattern (*meta*, *para*) and electronic properties of aromatic substituents (electron-deficient or rich) of thioanisole had little effect on this transformation (**2a-2o**). The only exception was the oxidation of aniline derivative (**2l**). A relatively low yield was obtained even decreasing the voltage. By careful observation and study, we found that a layer polymer film was deposited on the electrodes, which made electrodes inactive and prevented further reaction (reduced current) . Besides, diaryl sulfides (**2p** – **2t**) were also suitable substrates and good yields could be obtained in all cases. Then, sulfides containing various functional groups such as ester (**2u**), ether (**2v**), ketone (**2w**), alkyne (**2x**), alkene (**2y**, **2z**) and cyclopropane (**2aa**) were explored under optimized conditions, affording moderate to good isolated yields with satisfactory tolerance. Additionally, this protocol also tolerated dialkyl sulfides and sulfides containing natural product skeletons (**2ab** – **2ad**), giving good chemical yields. At last, the chemoselectivity of this method was investigated in the oxidation of sulfides containing two different sulfur moieties (**2ae**, **2af**). Clearly, the sulfur with high electron density was oxidized preferably (**2ae**). Moreover, sulfide moiety could be oxidized for a compound containing sulfide and thiophene (**2af**).

We then turned our attention to the investigation of over oxidation of thioethers to access sulfones **3** (Figure 3). The conditions were similar except increasing voltage (4 V *vs.* 3 V) and slightly prolonging the reaction time. The conditions worked well for diverse thioethers (**3a** – **3r**). Similarly, the substitution pattern (*meta*, *para*) and electronic property of substituents (electron-deficient or rich) on aromatics had little effect on chemical yields (**3a**-**3k**). Moreover, the conditions also worked well for diaryl thioethers (**3n**, **3m**) and dialkyl thioethers (**3q**, **3r**) with good functional groups tolerance. It should be noted that disulfides could be also oxidized into sulfones under optimized conditions [57] (**3s** – **3u**). Furthermore, both dialkyl disulfide (**3s**, **3u**) and diaryl disulfide (**3t**) were suitable substrates. In Noël's work [37], tuning the voltage over the electrodes was the only way to avoid over-oxidation. This protocol introduced the hydrogen bonding network into electrochemical oxidations of thioethers for the first time. The hydrogen bonding between HFIP and the sulfoxide made it less prone to further oxidation. Therefore, thioethers can be selectively electrochemically oxidized to sulfoxides and over-oxidization could be avoided under optimized conditions.

Next, electro-oxidative synthesis of unsymmetrical disulfides from thiols was explored (Figure 4). This electrooxidation has been achieved by Lei and coworkers using a polar aprotic solvent – DMF [58], but their system did not give good yields for electron-deficient substrates such as *para*-nitro-thiophenol and also aliphatic thiols with small steric hindrance. To our delight, our protocol worked very well for both electron-rich and poor thiophenols without the formation of the homodisulfides. We speculated that unsymmetrical S-S bond formation can be achieved by utilizing the difference of the oxidation potential between the aromatic thiol and the alkyl thiol.

We then moved our focus to the investigation of reaction pathways. The reaction was not affected by the argon atmosphere (Figure 5a). Moreover, the reaction was also not affected in the presence of TEMPO (2, 2, 6, 6-tetramethylpiperidine-1-oxyl, a radical quencher) (Figure 5b). These results indicated that O_2 in the air was not the source of the oxygen atom. We envisioned that the possible source of oxygen atom was from water present in the reaction mixture. Thus, we conducted various reactions by addition of H_2O^{18}. In the presence of 5 equivalents of H_2O^{18}, the sulfoxide product **2f** containing a significant proportion of O^{18} (53%) (Figure 5c) was observed. For the preparation of sulfone **3f**, a large proportion of O^{18} was also observed in sulfone product **3f** (Figure 5d). For synthesis of sulfone, we also conducted the reaction stepwise (Figure 5e). In the first stage, a low voltage was used in the absence of H_2O^{18}, in stage 2, we increased the voltage and added 10 equivalents of H_2O^{18}. In the end, we obtained a mixture of the **3f-1** and **3f-2** and **3f-3**. This result indicated that reaction proceeded in a stepwise manner and the oxygen source for oxidation sulfoxide to sulfone was also from water.

Additionally, cyclic voltammetry (CV) experiments were conducted to study the redox potential of the substrates (Figure 6). The oxidation potential of thioether **1a** and the corresponding sulfoxide **2a** in the presence of $LiClO_4$ were measured by using acetonitrile and H-bond network (HFIP/AcOH) as solvents respectively (Figure 6). To avoid over-oxidation, the difference or gap between oxidation potential of **1a** and oxidation potential of **2a** (ΔV) should be as big as possible. It was observed that both the onset potentials for oxidation of thioester substrate **1a** (Figure 6B, curve b, 1.13 V) and sulfoxide (Figure 6B, curve c, 1.88 V) in the H-bond network solvent were lower than that in acetonitrile (Figure 6A, curve b, 1.37 V and curve c, 1.94 V). Thus the ΔV was significantly larger when HFIP/AcOH was used as the solvent (0.75 V vs. 0.57 V), enabling better control of electrooxidation of thioesters.

Lastly, our methodology can be used in larger-scale synthesis without complications (Figure 7). Without any protection, using the common Pt anode and cathode, **1f** could be selectively oxidized to **2f** and **3f** in gram scale.

3. Conclusions

In conclusion, we have developed a highly efficient and oxidant free electrocatalytic protocol for selective oxidation of thioethers to sulfoxides and sulfones by using a hydrogen bond network system.

Conflict of interest

There is no conflict of interest.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at ….

Bibliography

[1] M. Yan, Y. Kawamata, P.S. Baran, Synthetic organic electrochemical methods since 2000: on the verge of a renaissance, Chem. Rev., 117 (2017) 13230-13319.

[2] J.B. Sperry, D.L. Wright, The application of cathodic reductions and anodic oxidations in the synthesis of complex molecules, Chem. Soc. Rev., 35 (2006) 605-621.

[3] Z. Yang, Y. Shi, Z. Zhan, H. Zhang, H. Xing, R. Lu, Y. Zhang, M. Guan, Y. Wu, Sustainable electrocatalytic oxidant-free syntheses of thiosulfonates from thiols, ChemElectroChem, 5 (2018) 3619-3623.

[4] K.S. Ravikumar, J.-P. Bégué, D. Bonnet-Delpon, A selective conversion of sulfide to sulfoxide in hexafluoro-2-propanol, Tetrahedron Lett., 39 (1998) 3141-3144.

[5] S. Henkel, M.C. Misuraca, P. Troselj, J. Davidson, C.A. Hunter, Polarisation effects on the solvation properties of alcohols, Chem. Sci., 9 (2018) 88-99.

[6] J.M. Briggs, T.B. Nguyen, W.L. Jorgensen, Monte Carlo simulations of liquid acetic acid and methyl acetate with the OPLS potential functions, J. Phys. Chem., 95 (1991) 3315-3322.

[7] R. Trivedi, P. Lalitha, VCl_3-catalyzed selective oxidation of sulfides to sulfoxides using H_2O_2 as oxidant, Synth. Commun., 36 (2006) 3777-3782.

[8] M. Matteucci, G. Bhalay, M. Bradley, Mild and highly chemoselective oxidation of thioethers mediated by $sc(OTf)_3$, Org. Lett., 5 (2003) 235-237.

[9] M. Amini, M. Khaksar, D.M. Boghaei, M. Bagherzadeh, A. Ellern, L.K. Woo, Synthesis, X-ray studies, and catalytic activity of tridentate Schiff base dioxo-molybdenum(VI), J. Coord. Chem., 67 (2014) 2435-2444.

[10] A. Hassanpour, F. Acuna-Parés, J.M. Luis, O. Cusso, S. Morales de la Rosa, J.M. Campos-Martin, J.L.G. Fierro, M. Costas, J. Lloret-Fillol, R. Mas-Ballesté, H_2 oxidation versus organic substrate oxidation in non-heme iron mediated reactions with H_2O_2, Chem. Commun., 51 (2015) 14992-14995.

[11] R. Bikas, V. Lippolis, N. Noshiranzadeh, H. Farzaneh-Bonab, A.J. Blake, M. Siczek, H. Hosseini-Monfared, T. Lis, Electronic effects of aromatic rings on the catalytic activity of dioxidomolybdenum(VI)-hydrazone complexes, Eur. J. Inorg. Chem., 2017 (2017) 999-1006.

[12] Z. Saedi, M. Yaghma, A. Morsali, M. Roushani, Encapsulated phosphomolybdic acid in TMU-16 metal organic framework: Study the catalytic activity and structural stability dependent on synthetic solvent, Inorg. Chem. Commun., 86 (2017) 159-164.

[13] J. Tang, P. Yao, F. Huang, M. Luo, Y. Wei, H. Bian, Stereoselective sulfoxidation catalyzed by achiral Schiff base complexes in the presence of serum albumin in aqueous media, Tetrahedron: Asymmetry, 28 (2017) 1700-1707.

[14] R. Hasanpour, F. Feizpour, M. Jafarpour, A. Rezaeifard, Nickel(II) riboflavin complex as an efficient nanobiocatalyst for heterogeneous and sustainable oxidation of benzylic alcohols and sulfides, New J. Chem., 42 (2018) 7383-7391.

[15] T. Tamoradi, M. Ghadermazi, A. Ghorbani-Choghamarani, Synthesis of polyhydroquinoline, 2,3-dihydroquinazolin-4(1H)-one, sulfide and sulfoxide derivatives catalyzed by new copper complex supported on MCM-41, Catal. Lett., 148 (2018) 857-872.

[16] H. Veisi, P. Safarimehr, S. Hemmati, Oxo-vanadium immobilized on polydopamine coated-magnetic nanoparticles (Fe_3O_4): A heterogeneous nanocatalyst for selective oxidation of sulfides and benzylic alcohols with H_2O_2, J. Taiwan Inst. Chem. Eng., 88 (2018) 8-17.

[17] C. Ren, R. Fang, X. Yu, S. Wang, A highly efficient reusable homogeneous copper catalyst for the selective aerobic oxygenation sulfides to sulfoxides, Tetrahedron Lett., 59 (2018) 982-986.

[18] F. Silva, S.S. Khokhar, D.M. Williams, R. Saunders, G.J.S. Evans, M. Graz, T. Wirth, Eine kurze Totalsynthese von Ajoen, Angew. Chem., 130 (2018) 12470-12473.

[19] S.S. Shin, Y. Byun, K.M. Lim, J.K. Choi, K.-W. Lee, J.H. Moh, J.K. Kim, Y.S. Jeong, J.Y. Kim, Y.H. Choi, H.-J. Koh, Y.-H. Park, Y.I. Oh, M.-S. Noh, S. Chung, In vitro structure–activity relationship and in vivo studies for a novel class of cyclooxygenase-2 inhibitors: 5-aryl-2,2-dialkyl-4-phenyl-3(2H)furanone derivatives, J. Med. Chem., 47 (2004) 792-804.

[20] H. Zhang, L. Qi, A novel catalytic system poly(1-vinyl-3-dodecylimidazolium tribromide)/TBN for the oxidation of sulfides to sulfoxides with air as oxidant, Tetrahedron Lett., 59 (2018) 3171-3174.

[21] R.G. Hiskey, M.A. Harpold, Aliphatic disulfides. XIV. Preparation of disulfide sulfoxides by selective oxidation, J. Org. Chem., 32 (1967) 3191-3194.

[22] S. Lai, D.G. Lee, Lewis acid assisted permanganate oxidations, Tetrahedron, 58 (2002) 9879-9887.

[23] S. Colonna, N. Gaggero, Enantioselective oxidation of sulfides by dioxiranes in the presence of bovine serum albumin, Tetrahedron Lett., 30 (1989) 6233-6236.

[24] B. Smolkin, N. Levi, N. Karton-Lifshin, L. Yehezkel, Y. Zafrani, I. Columbus, Oxidative detoxification of sulfur-containing chemical Warfare agents by electrophilic iodine, J. Org. Chem., 83 (2018) 13949-13955.

[25] F. Silva, A. Baker, J. Stansall, W. Michalska, M.S. Yusubov, M. Graz, R. Saunders, G.J.S. Evans, T. Wirth, Selective oxidation of sulfides in flow chemistry, Eur. J. Org. Chem., 2018 (2018) 2134-2137.

[26] S. Zhang, L. Li, H. Wang, Q. Li, W. Liu, K. Xu, C. Zeng, Scalable electrochemical dehydrogenative lactonization of C(sp^2/sp^3)–H bonds, Org. Lett., 20 (2018) 252-255.

[27] Y. Yuan, Y. Yu, J. Qiao, P. Liu, B. Yu, W. Zhang, H. Liu, M. He, Z. Huang, A. Lei, Exogenous-oxidant-free electrochemical oxidative C–H sulfonylation of arenes/heteroarenes with hydrogen evolution, Chem. Commun., 54 (2018) 11471-11474.

[28] E.J. Horn, B.R. Rosen, Y. Chen, J. Tang, K. Chen, M.D. Eastgate, P.S. Baran, Scalable and sustainable electrochemical allylic C–H oxidation, Nature, 533 (2016) 77.

[29] Q.-L. Yang, Y.-Q. Li, C. Ma, P. Fang, X.-J. Zhang, T.-S. Mei, Palladium-catalyzed C(sp^3)—H oxygenation via electrochemical oxidation, J. Am. Chem. Soc., 139 (2017) 3293-3298.

[30] Y. Zhao, Y.-L. Lai, K.-S. Du, D.-Z. Lin, J.-M. Huang, Electrochemical decarboxylative sulfonylation of cinnamic acids with aromatic sulfonylhydrazides to vinyl sulfones, J. Org. Chem., 82 (2017) 9655-9661.

[31] A.J.J. Lennox, S.L. Goes, M.P. Webster, H.F. Koolman, S.W. Djuric, S.S. Stahl, Electrochemical aminoxyl-mediated α-cyanation of secondary piperidines for pharmaceutical building block diversification, J. Am. Chem. Soc., 140 (2018) 11227-11231.

[32] A.O. Terent'ev, O.M. Mulina, D.A. Pirgach, A.I. Ilovaisky, M.A. Syroeshkin, N.I. Kapustina, G.I. Nikishin, Electrosynthesis of vinyl sulfones from alkenes and sulfonyl hydrazides mediated by KI: an electrochemical mechanistic study, Tetrahedron, 73 (2017) 6871-6879.

[33] Y. Qiu, W.-J. Kong, J. Struwe, N. Sauermann, T. Rogge, A. Scheremetjew, L. Ackermann, Electrooxidative rhodium-catalyzed C−H/C−H activation: electricity as oxidant for cross-dehydrogenative alkenylation, Angew. Chem. Int. Ed., 57 (2018) 5828-5832.

[34] P. Xiong, H.-H. Xu, J. Song, H.-C. Xu, Electrochemical difluoromethylarylation of alkynes, J. Am. Chem. Soc., 140 (2018) 2460-2464.

[35] D. Hayrapetyan, R.K. Rit, M. Kratz, K. Tschulik, L.J. Gooßen, Electrochemical C−H cyanation of electron-rich (hetero)arenes, Chem. Eur. J., 24 (2018) 11288-11291.

[36] G. Laudadio, W. de Smet, L. Struik, Y. Cao, T. Noël, Design and application of a modular and scalable electrochemical flow microreactor, J. Flow Chem., 8 (2018) 157-165.

[37] G. Laudadio, N.J.W. Straathof, M.D. Lanting, B. Knoops, V. Hessel, T. Noël, An environmentally benign and selective electrochemical oxidation of sulfides and thiols in a continuous-flow microreactor, Green Chemistry, 19 (2017) 4061-4066.

[38] K.-S. Du, J.-M. Huang, Electrochemical synthesis of methyl sulfoxides from thiophenols/thiols and dimethyl sulfoxide, Green Chem., 20 (2018) 1405-1411.

[39] B. D'Andrade, S. Datta, S. Forrest, P. Djurovich, E. Polikarpov, M. Thompson, Relationship between the ionization and oxidation potentials of molecular organic semiconductors, Org. Electron., 6 (2005) 11-20.

[40] A. Berkessel, J.A. Adrio, Dramatic acceleration of olefin epoxidation in fluorinated alcohols: activation of hydrogen peroxide by multiple H-bond networks, J. Am. Chem. Soc., 128 (2006) 13412-13420.

[41] S.-S. Li, X. Lv, D. Ren, C.-L. Shao, Q. Liu, J. Xiao, Redox-triggered cascade dearomative cyclizations enabled by hexafluoroisopropanol, Chem. Sci., 9 (2018) 8253-8259.

[42] C. Qi, V. Gandon, D. Lebœuf, Calcium(II)-catalyzed intermolecular hydroarylation of deactivated styrenes in hexafluoroisopropanol, Angew. Chem. Int. Ed., 57 (2018) 14245-14249.

[43] L. Hu, M. Rombola, V.H. Rawal, Synthesis of 1,2-oxazinanes via hydrogen bond mediated [3 + 3] cycloaddition reactions of oxyallyl cations with nitrones, Org. Lett., 20 (2018) 5384-5388.

[44] E. Richmond, J. Yi, V.D. Vuković, F. Sajadi, C.N. Rowley, J. Moran, Ring-opening hydroarylation of monosubstituted cyclopropanes enabled by hexafluoroisopropanol, Chem. Sci., 9 (2018) 6411-6416.

[45] J. Sanjosé-Orduna, J.M. Sarria Toro, M.H. Pérez-Temprano, HFIP-assisted C−H functionalization by Cp*CoIII: access to key reactive cobaltacycles and implication in catalysis, Angew. Chem. Int. Ed., 57 (2018) 11369-11373.

[46] A.M. Arnold, A. Pöthig, M. Drees, T. Gulder, NXS, Morpholine, and HFIP: the ideal combination for biomimetic haliranium-induced polyene cyclizations, J. Am. Chem. Soc., 140 (2018) 4344-4353.

[47] R.-J. Tang, T. Milcent, B. Crousse, Regioselective halogenation of arenes and heterocycles in hexafluoroisopropanol, J. Org. Chem., 83 (2018) 930-938.

[48] V.D. Vuković, E. Richmond, E. Wolf, J. Moran, Catalytic Friedel–Crafts reactions of highly electronically deactivated benzylic alcohols, Angew. Chem. Int. Ed., 56 (2017) 3085-3089.

[49] H.-B. Zhao, Z.-J. Liu, J. Song, H.-C. Xu, Reagent-free C−H/N−H cross-coupling: regioselective synthesis of N-heteroaromatics from biaryl aldehydes and NH_3, Angew. Chem. Int. Ed., 56 (2017) 12732-12735.

[50] T. Broese, R. Francke, Electrosynthesis using a recyclable mediator–electrolyte system based on ionically tagged phenyl iodide and 1,1,1,3,3,3-hexafluoroisopropanol, Org. Lett., 18 (2016) 5896-5899.

[51] Y. Imada, J.L. Röckl, A. Wiebe, T. Gieshoff, D. Schollmeyer, K. Chiba, R. Franke, S.R. Waldvogel, Metal- and Reagent-free dehydrogenative formal benzyl–aryl cross-coupling by anodic activation in 1,1,1,3,3,3-hexafluoropropan-2-ol, Angew. Chem. Int. Ed., 57 (2018) 12136-12140.

[52] B. Elsler, A. Wiebe, D. Schollmeyer, K.M. Dyballa, R. Franke, S.R. Waldvogel, Source of selectivity in oxidative cross-coupling of aryls by solvent effect of 1,1,1,3,3,3-hexafluoropropan-2-ol, Chem. Eur. J., 21 (2015) 12321-12325.

[53] S. Lips, D. Schollmeyer, R. Franke, S.R. Waldvogel, Regioselective metal- and reagent-free arylation of benzothiophenes by dehydrogenative electrosynthesis, Angew. Chem. Int. Ed., 57 (2018) 13325-13329.

[54] T. Gieshoff, D. Schollmeyer, S.R. Waldvogel, Access to pyrazolidin-3,5-diones through anodic N–N bond formation, Angew. Chem. Int. Ed., 55 (2016) 9437-9440.

[55] T. Yamamoto, B. Riehl, K. Naba, K. Nakahara, A. Wiebe, T. Saitoh, S.R. Waldvogel, Y. Einaga, A solvent-directed stereoselective and electrocatalytic synthesis of diisoeugenol, Chem. Commun., 54 (2018) 2771-2773.

[56] R. Francke, D. Cericola, R. Kötz, D. Weingarth, S.R. Waldvogel, Novel electrolytes for electrochemical double layer capacitors based on 1,1,1,3,3,3-hexafluoropropan-2-ol, Electrochim. Acta, 62 (2012) 372-380.

[57] N. McNeil, C. McDonnell, M. Hambrook, T. Back, Oxidation of disulfides to thiolsulfinates with hydrogen peroxide and a cyclic seleninate ester catalyst, Molecules, 20 (2015) 10748-10762.

[58] P. Huang, P. Wang, S. Tang, Z. Fu, A. Lei, Electro-oxidative S−H/S−H cross-coupling with hydrogen evolution: facile access to unsymmetrical disulfides, Angew. Chem. Int. Ed., 57 (2018) 8115-8119.

FIGURE CAPTIONS

Figure 1. Literature background.

Figure 2. Scope for the synthesis of sulfoxides **2**.

Figure 3. Scope for the synthesis of sulfones **3**.

Figure 4. Scope for the synthesis of unsymmetrical disulfides.

Figure 5. Investigations of reaction pathways.

Figure 6. Cyclic voltammetry at a 3 mm diameter Pt electrode.

Figure 7. Gram scale synthesis.

TABLE CAPTIONS

Table 1. Optimization of reaction conditions.

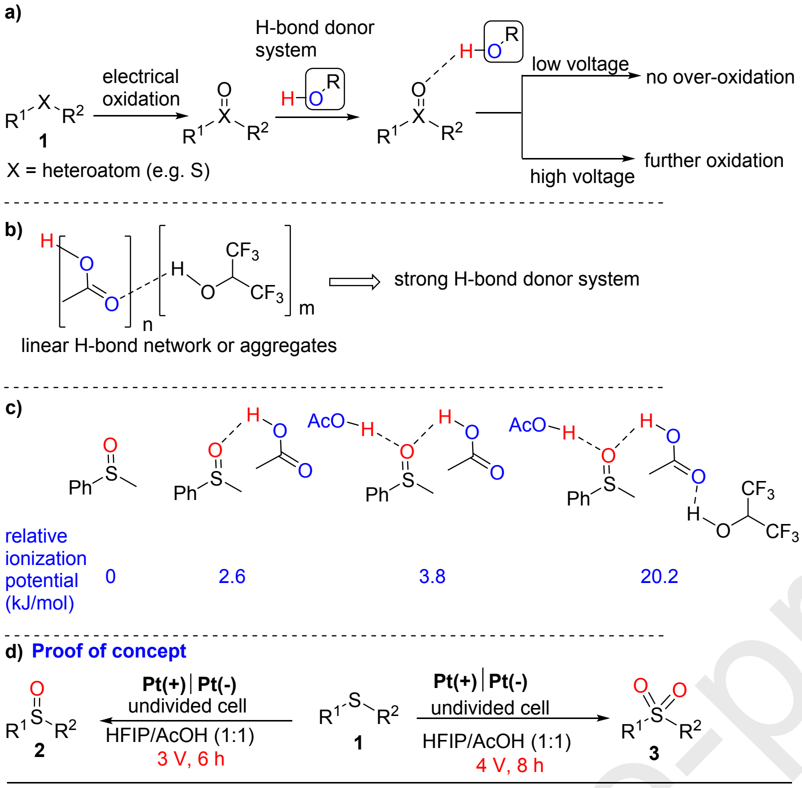


Figure 1. Literature background.

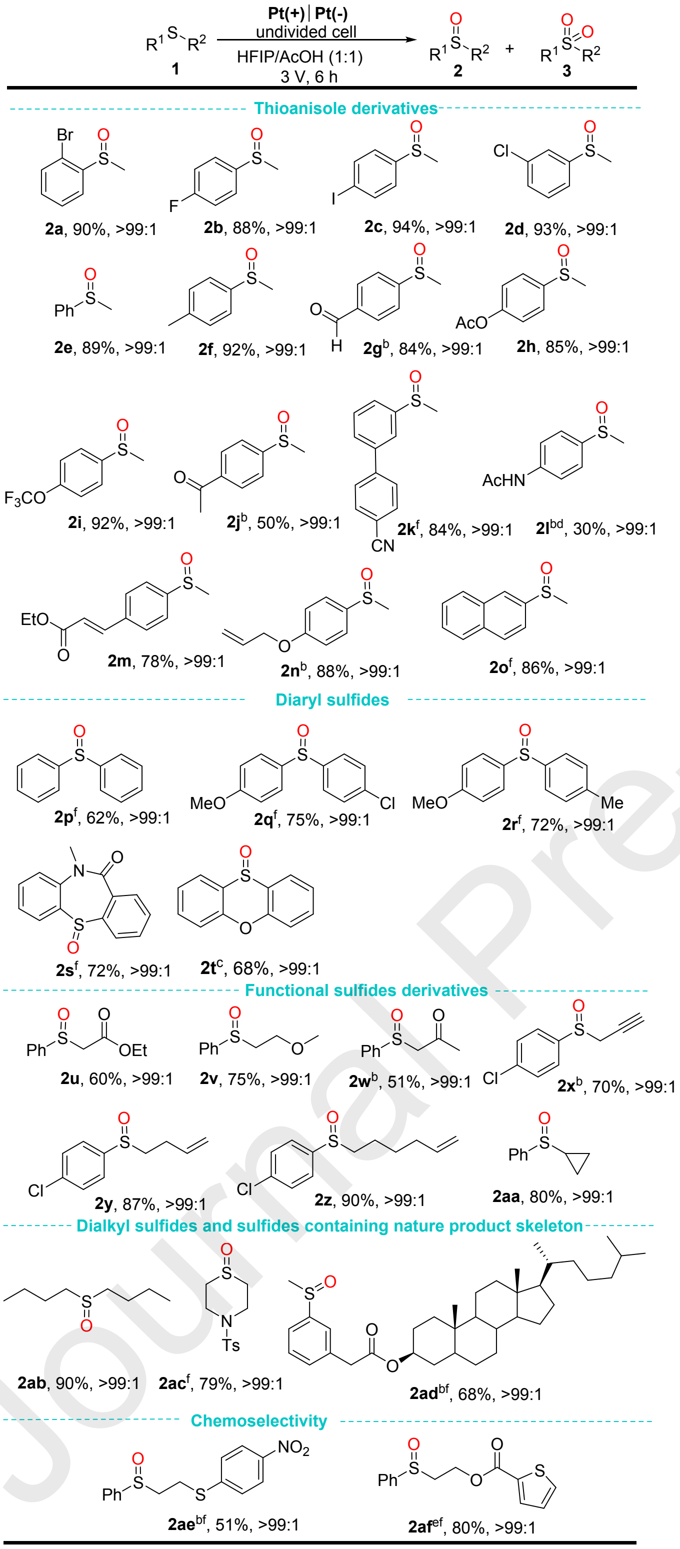


Figure 2. Scope for the synthesis of sulfoxides **2.**[a]

[a] Condition: Pt anode and cathode (15 mm x10 mm x 0.2 mm), undivided cell, voltage = 3 V. Sulfide **1** (0.3 mmol), $LiClO_4$ (0.36 mmol), HOAc (1 mL), HFIP (1 mL), rt, open-air, 6 h. 2a/3a ratio was determined by GC-MS or LC-MS. [b] 4 V was used. [c] 2.5 V was used. [d] 4 h was used. [e] 3.8 V and HFIP/MeCN(1 mL/1 mL). [f] 0.2 mmol scale.

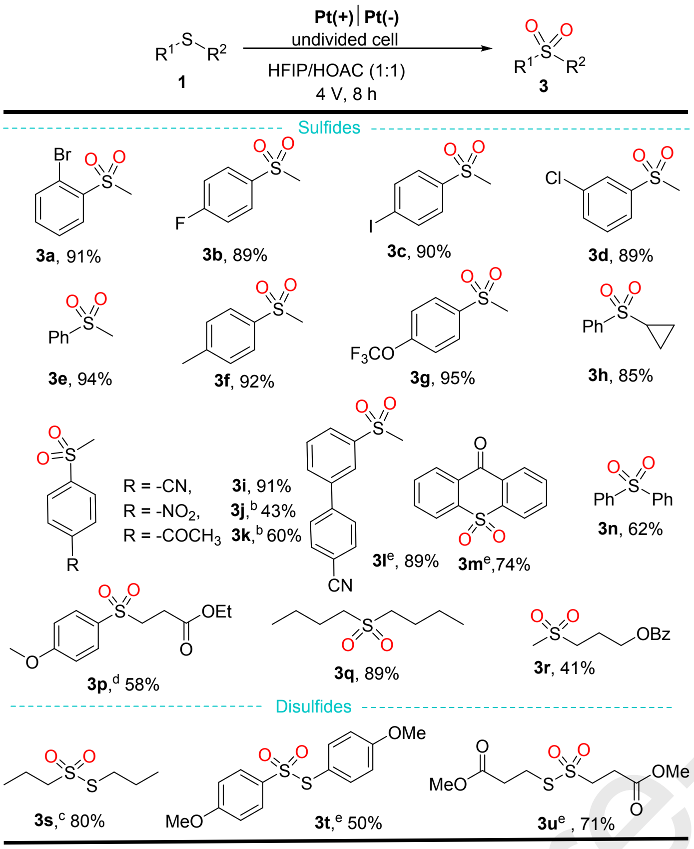


Figure 3. Scope for the synthesis of sulfones **3**.[a]

[a] Conditions: Pt anode and cathode (15 mm x10 mm x 0.2 mm), undivided cell, voltage = 4 V. Sulfide **1** (0.3 mmol), $LiClO_4$ (0.6 mmol), HOAc (1 mL), HFIP (1 mL), rt, open-air, 8 h. [b] 5 V was used. [c] 3 V was used. [d] 2.5 V was used. [e] 0.2 mmol scale.

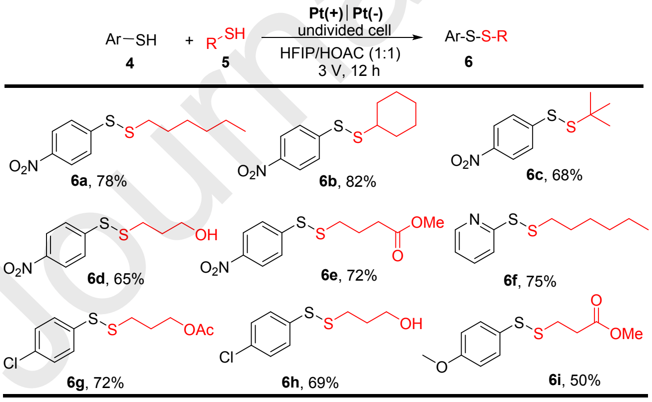


Figure 4. Scope for the synthesis of unsymmetrical disulfides.[a]

[a] Conditions: Pt anode and cathode (15 mm x10 mm x 0.2 mm), undivided cell, constant voltage (3 V). Aromatic thiol **4** (0.3 mmol), aliphatic thiol **5** (0.36 mmol), $LiClO_4$ (0.6 mmol), HOAc (1 mL), HFIP (1 mL), rt, open air, 12 h.

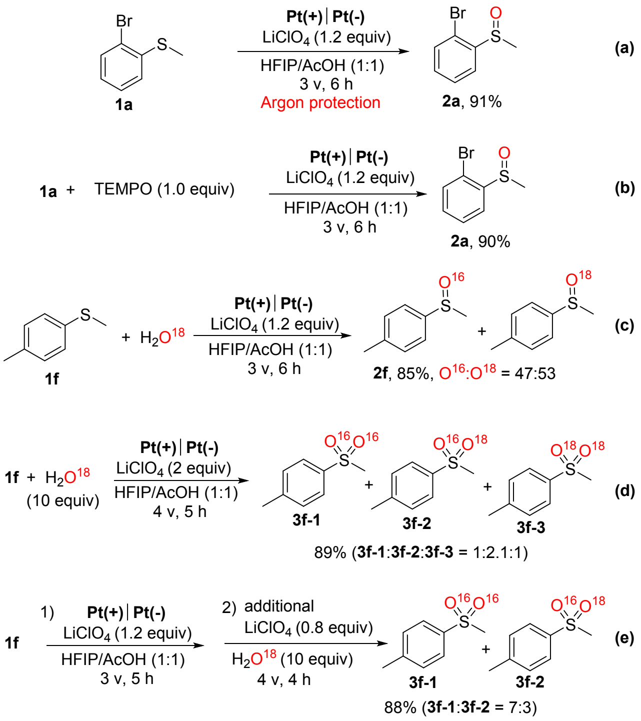


Figure 5. Investigations of reaction pathways.

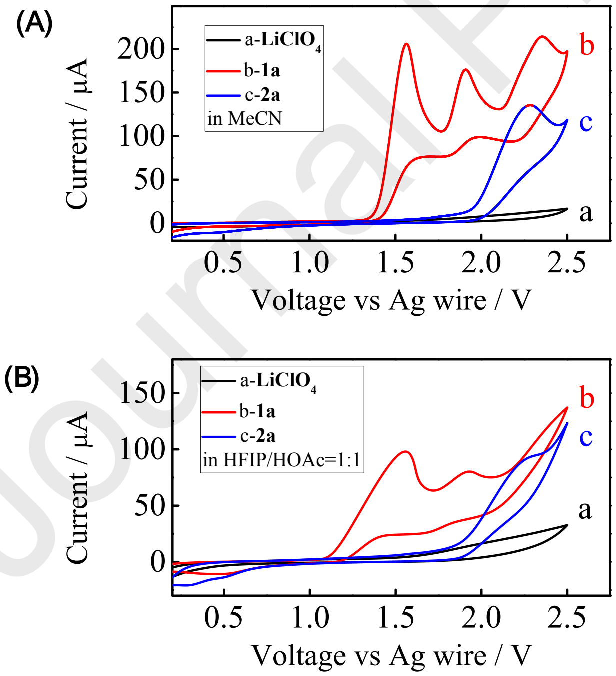


Figure 6. Cyclic voltammetry at a 3 mm diameter Pt electrode.

(A) (a) MeCN solution containing 0.1 M $LiClO_4$ as the supporting electrolyte; (b) MeCN solution containing 0.1 M $LiClO_4$ and 10 mM **1a**; (c) MeCN solution containing 0.1 M $LiClO_4$ and 10 mM **2a**. (B) (a) solution of HFIP/HOAc (1:1) containing 0.1 M $LiClO_4$ as the supporting electrolyte; (b) solution of HFIP/HOAc (1:1) containing 0.1 M $LiClO_4$ and 10 mM **1a**; (c) solution of HFIP/HOAc (1:1) containing 0.1 M $LiClO_4$ and 10 mM **2a**. Silver wire and Pt wire were used as the quasi-reference and counter electrode.

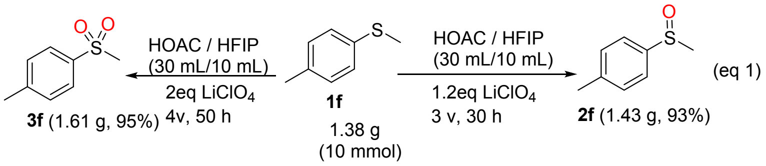
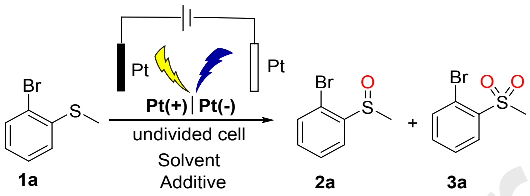


Figure 7. Gram scale synthesis.

Table 1. Optimization of reaction conditions.[a]



No.	Additive	Volt	Time	Solvent	Yields/% (**2a:3a**) [b]
1	$LiClO_4$ (1.2 equiv)	3V	6h	MeCN	5 (100:0)
2	$LiClO_4$ (1.2 equiv)	3V	6h	DMF	0
3	$LiClO_4$ (1.2 equiv)	3V	6h	HFIP	0
4	$LiClO_4$ (1.2 equiv)	3V	6h	AcOH	41 (100:0)
5	$LiClO_4$ (1.2 equiv)	3V	6h	MeOH	40 (100:0)
6	$LiClO_4$ (1.2 equiv)	3V	6h	H_2O	10 (100:0)
7	**$LiClO_4$ (1.2 equiv)**	**3V**	**6h**	**HFIP/AcOH = 1/1**	**98 (>99:1)**
8	$LiClO_4$ (1.2 equiv)	3V	6h	HFIP/MeOH = 1/1	32 (97:3)
9	*n*Bu_4NBF_4 (2 equiv)	4V	8h	HFIP/AcOH = 1/1	8 (12:88)
10	*n*Bu_4NBF_4 (2 equiv)	4V	8h	AcOH	0
11	*n*Bu_4NPF_6 (2 equiv)	4V	8h	HFIP/ AcOH =1/1	72 (28:72)
12	**$LiClO_4$ (2 equiv)**	**4V**	**8h**	**HFIP/AcOH=1/1**	**98 (0:100)**
13[c]	$LiClO_4$ (1.2 equiv)	-	6h	HFIP/ AcOH = 1/1	0

[a] Conditions: Pt anode and cathode (15 mm × 10mm × 0.2mm), constant voltage. **1a** (0.3 mmol), additive, solvent (2.0 mL), room temperature, open-air, 8 h. [b] Determined by GC-MS analysis. [c] No applied potential.

Supplementary information. Details of the general procedure for electrochemical oxidation of sulfides, mechanistic studies, data of products and copies of NMR spectra.

1. Modulation of oxidation potential by hydrogen bonding network
2. Chemo-selective oxidation of thioethers to sulfoxides and sulfones
3. Electro-oxidative synthesis of unsymmetrical disulfides

Declaration of interests

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: