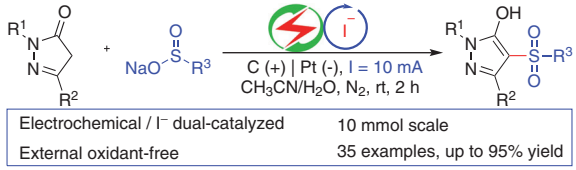
Electrochemical/I⁻ Dual-Catalyzed Access to Sulfonated Pyrazoles under External Oxidant-Free Conditions

Jing Ma◊
Jianjing Yang◊
Kelu Yan
Boju Luo
Kexin Huang
Ziling Wu
Yumeng Zhou
Shuyun Zhu
Xian-En Zhao
Jiangwei Wen*

Key Laboratory of Green Natural Products and Pharmaceutical Intermediates in Colleges and Universities of Shandong Province, School of Chemistry and Chemical Engineering, Qufu Normal University, Qufu, P. R. of China
wenjy@qfnu.edu.cn

◊ These authors contributed equally

Published as part of the Virtual Collection
Electrochemical Organic Synthesis



Received: 28.03.2023
Accepted after revision: 27.04.2023
Published online: 08.05.2023 (Accepted Manuscript), 07.06.2023 (Version of Record)
DOI: 10.1055/a-2089-0485; Art ID: SO-2023-03-0026-L

Crowd-Reviewed

License terms:

© **2023**. The Author(s). This is an open access article published by Thieme under the terms of the Creative Commons Attribution License, permitting unrestricted use, distribution and reproduction, so long as the original work is properly cited. (https://creativecommons.org/licenses/by/4.0/)

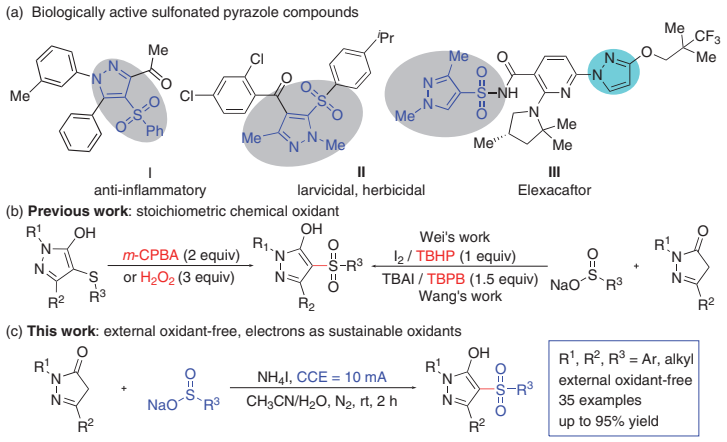
Abstract An electrochemical/I⁻ dual-catalyzed access to sulfonated pyrazoles from pyrazolones and sodium sulfites under external oxidant-free conditions has been developed. This established electrochemical reaction works smoothly under external oxidant-free conditions and has the advantages of good functional group tolerance, easy to gram-scale synthesis, delivering up to 95% yield for 35 examples.

Key words electrochemical, dual catalyzed, sulfonylation, pyrazolones, sodium sulfites

Sulfone groups are very important functional groups, exist in various natural products, bioactive molecules, pharmaceuticals, and functional materials, and can enhance the activity of compounds.[1] According to statistics, in 2021 of the world's top 200 best-selling small-molecule drugs containing sulfone-based drugs accounted for 20, with sales of up to $27.5 billion.[2] The introduction of the sulfone group is one of the frontier research hotspots in the field of organic synthesis and pharmaceuticals.[3] In particular, the development of convenient and efficient strategies for the incorporation of sulfone groups into heterocyclic compounds has attracted widespread interest among organic synthesis practitioners.[4]

Pyrazoles, as one of the high-value N-heterocyclic scaffolds, are epitomized in various pharmaceuticals and bioactive molecules, with a variety of biological activities.[5] In particular, site-selective incorporation of sulfone groups can dramatically enhance the pharmacological profile of pyrazoles.[6] For example, pyrazole derivative **I**[7] incorporated with the sulfone group has important anti-inflammatory activity; compound **II**[8] is a potential pesticide with excellent larvicidal and herbicidal activity; and compound **III**[9] is a modulator of cystic fibrosis transmembrane conductance regulator (CFTR), and it is a key component of Trikafta (Scheme 1a).[10] Given this, the development of efficient, convenient, and practical strategies to access sulfonated pyrazole derivatives is of great significance and has been widely concerned. Wei[11] and Wang's[12] groups have successively developed I_2/TBHP and TBAI/TBPB systems to deliver sulfonated pyrazole from pyrazolones and sodium sulfites. Although these elegant methods have been developed successively, the presence of stoichiometric oxidants is necessary, and the absence of chemical oxidants remains elusive.

Organic electrochemistry is the study of chemical reactions which take place at the interface of an electrode and electrolyte, involving the activation of the substrate by electron transfer. Although a series of important achievements have been made in organic electrochemistry in the last decade, few studies have been carried out in the absence of external electrolytes.[13] Considering the importance of the sulfonated pyrazole frameworks, and together with our growing interest in organic electrochemistry[13i,14] and sulfone-containing compound synthesis,[15] herein we wish to report an external oxidant-free electrochemical method for

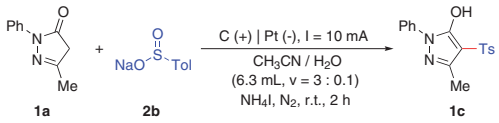


Scheme 1 The background of sulfonated pyrazole

the sulfonylation of pyrazolones with sodium sulfinates via a radical pathway. The established electrochemical reaction works smoothly under external oxidant-free conditions and has the advantages of excellent functional group tolerance, easy-to-gram-scale synthesis, and avoiding the use of stoichiometric chemical oxidants.

As shown in Table 1, 5-methyl-2-phenyl-2,4-dihydro-3*H*-pyrazol-3-one (**1a**) and sodium 4-methylbenzenesulfinate (**2b**) were selected as the temple coupling substrate to optimize the reaction conditions, including electrode material, current, solvent, and halogen anion source under room temperature in an inert atmosphere. By optimizing various reaction parameters, it was found that the desired product **1c** could be delivered in 90% yield by performing the reaction with a constant current of 10 mA electrolysis 2 h in an undivided cell employing NH_4I (30 mol%) was the electrolyte and catalyst (Table 1, entry 1). The control experiment shows that both current and NH_4I are the key factors of the transformation (Table 1, entries 2 and 3). The yield of desired product **1c** decreased slightly when the amount of NH_4I was reduced to 20 mol% (Table 1, entry 4). Moreover, other iodized salts, such as *n*-Bu_4NI, KI, and NaI, were individually examined for their ability to deliver the desired product **1c** in yields of 58%, 82%, and 73%, respectively (Table 1, entry 5). However, the yield of the desired product was reduced to 75%, 7% by employing CH_3CN or H_2O as the reaction solvent (Table 1, entry 6). To our delight, **1c** was delivered with a yield of 83% when the reaction was performed using dichloromethane as the solvent (Table 1, entry 7). Furthermore, the influence of the electrode materials for the electrochemical/I^- dual-catalyzed sulfonylation of pyrazolones with sodium sulfinates access to sulfonated pyrazoles under external oxidant-free conditions was also investigated. The results show that C (+) | Pt (–) was the best choice (Table 1, entries 8 and 9). Finally, either increasing or decreasing the current of the reaction is detrimental to the yield of the desired product (Table 1, entry 10).

Table 1 Optimization of the Reaction Conditions[a]

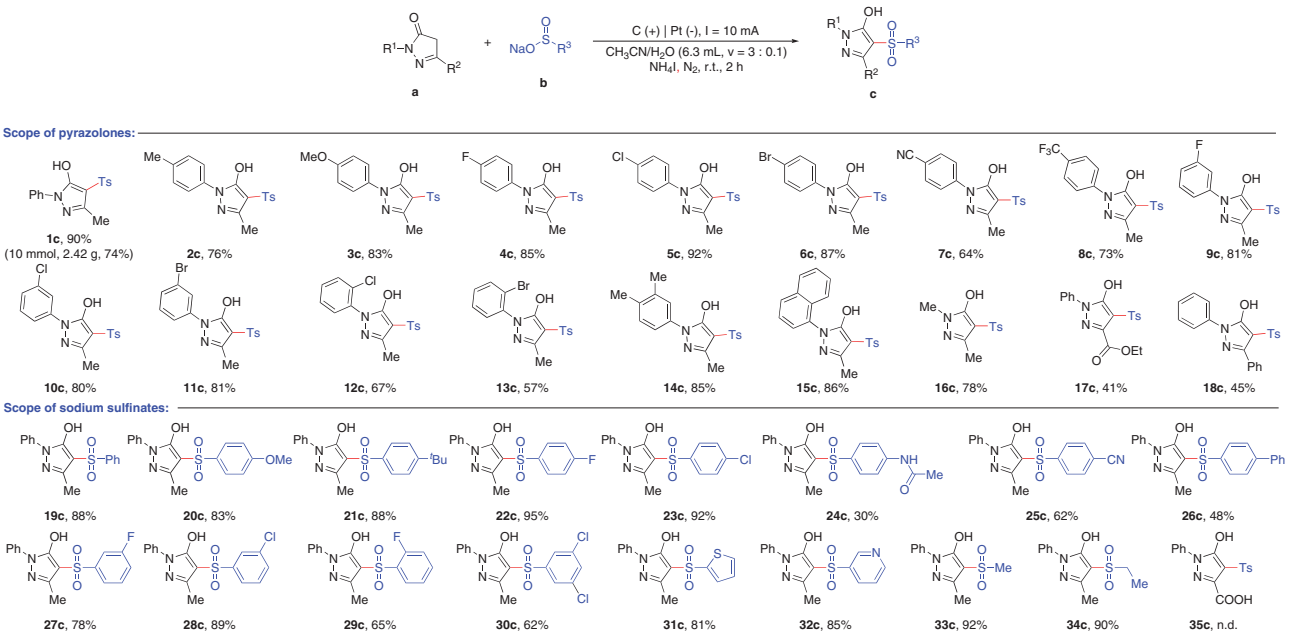


Entry	Deviation from standard conditions	Yield (%)[b]
1	none	90
2	without current	0
3	without NH_4I	trace
4	NH_4I (20 mol%)	72
5	*n*-Bu_4NI, KI, or NaI instead of NH_4I	58, 82, 73
6	CH_3CN or H_2O as solvent	75, 7
7	CH_2Cl_2 instead of CH_3CN	83
8	Pt (+) instead of C (+)	57
9	C (–) instead of Pt (–)	49
10	5 mA and 15 mA instead of 10 mA	78, 72

[a] Reaction conditions: carbon rods (φ = 6 mm) as the anode, Pt plate (1 × 1 cm^2) as the cathode, constant current = 10 mA, **1a** (0.25 mmol), **2b** (0.5 mmol), NH_4I (30 mol%), CH_3CN/H_2O (6.3 mL, v = 3: 0.1), r.t., N_2, 2 h.
[b] Isolated yields.

With the standard conditions in the hand, we began to investigate the substrate scope of this external oxidant-free protocol (Table 2). Firstly, the scope of the pyrazole was investigated based on sodium 4-methylbenzenesulfinate (**2b**). The results showed that both electron-donor and electron-deficient groups on the *para* site of the pyrazolone benzene ring can give the corresponding products in moderate to good yields under standard conditions (**1c–8c**).

Table 2 Scope of Substrate[a,b]

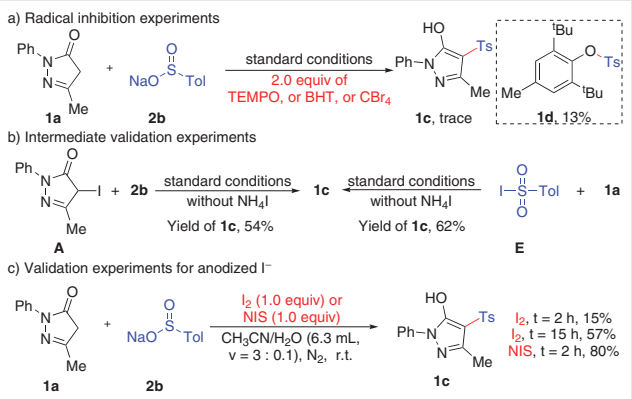


[a] Reaction conditions: carbon rods (φ = 6 mm) as the anode, Pt plate (1 × 1 cm^2) as the cathode, constant current = 10 mA, **a** (0.25 mmol), **b** (0.5 mmol), NH_4I (30 mol%), CH_3CN/H_2O (6.3 mL, v = 3: 0.1), r.t., N_2, 2 h; n. d. = not detected.
[b] Isolated yields.

To prove the scalability of this protocol, a large-scale synthesis of the sulfonated pyrazole **1c** was performed. Even the model reaction that was scaled up to 40-fold can get 74% yields, simply by performing the reaction at room temperature in a three-neck flask. Subsequently, the steric hindrance effect has been investigated, and the corresponding products can be obtained in moderate to excellent yields from the *meta* or *ortho* site of benzene ring, polysubstituted, or naphthyl pyrazolones under the established conditions (**9c**–**15c**). To our delight, the desired products **16c**–**18c** can be delivered smoothly when R^1 and R^2 are converted into methyl, phenyl, or ester groups. In the following stage, sodium sulfinates were systematically examined by employing **1a** as the benchmark. Notably, the desired products can be obtained with excellent yields when the different positions of sodium aryl sulfonate have electron-donating or electron-withdrawing groups were carried out under the given conditions (**19c**–**30c**). Besides, both aromatic heterocyclic and alkyl sodium sulfite can deliver the desired products in excellent yields under established conditions (**31c**–**34c**). Unfortunately, **35c** was not observed when 5-oxo-1-phenyl-4,5-dihydro-1*H*-pyrazole-3-carboxylic acid was performed in the present protocol, which may be affected by the carboxyl group.

Intrigued by the outstanding efficacy of the electrochemical/I^- dual-catalyzed sulfonylation of pyrazolones under external oxidant-free conditions, we became interested in clarifying the mechanism of this transformation. To this end, various control and cyclic voltammetry (CV) experiments were performed based on model reaction. Firstly, only trace amounts of desired product **1c** were observed in the presence of 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO), 2,6-di-*tert*-butyl-4-hydroxytoluene (BHT) or CBr_4 suggesting that the electrochemical/I^- dual-catalyzed sulfonylation of pyrazolones may proceed via a radical pathway (Scheme 2a). Satisfactorily, this conclusion was further confirmed by the trapped products **1d** (Figure S1). Secondly, intermediate validation experiments demonstrated that **A**[16] and **E**[15c] should be the intermediate of the transformation (Scheme 2b).

To understand the role of NH_4I in the present transformation, various stoichiometric experiments were performed as shown in Scheme 2c, suggesting that anodic oxidation I^- to I^+ delivers the product faster than the route of iodine radicals. Finally, the CV experiments were carried out and the results are summarized in Figure 1. The electrochemical behavior of the mixed NH_4I and **2b** demonstrate that the in situ generated iodine radical or I^+ with **2b** has undergone undisguised electron transfer (Figure 1, blue line).



Scheme 2 Control experiments

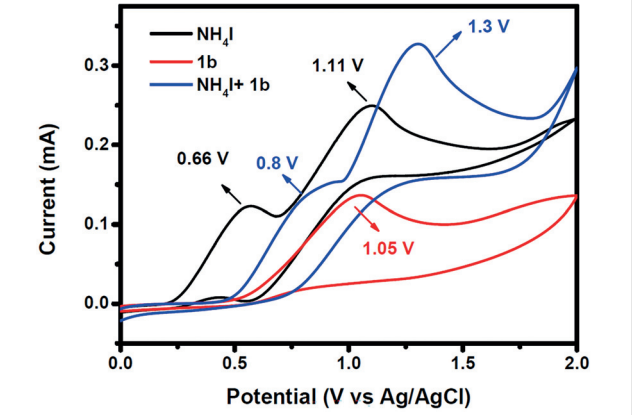
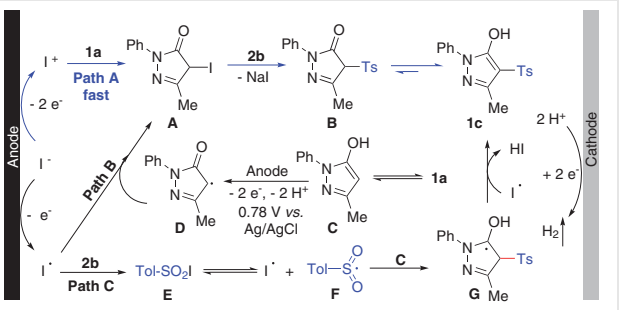


Figure 1 CV experiments with glass carbon as the working electrode, Pt (1.5 × 1.5 cm^2) as the counter electrode, Ag/AgCl as the reference electrode in 0.05 M *n*-Bu_4NBF_4, CH_3CN (10.0 mL), scan rate 50 mV/s, **1b** (0.25 mM), NH_4I (0.25 mM).

Based on these preliminary results mentioned above and the previous reports,[11,12] a plausible mechanistic pathway for electrochemical/I^- dual-catalyzed sulfonylation of pyrazolones was proposed and is shown in Scheme 3. Initially, iodide anion was anodized to $I^•$ (0.66 V *vs.* Ag/AgCl) and I^+ (1.11 V *vs.* Ag/AgCl) catalyst species.[16] Subsequently, the intermediate **A** can be produced by the reaction of I^+ with **1a** (path A) or via the radical cross-coupling of **D** and $I^•$ (path B). The desired product **1c** was generated through the rapid tautomerization of sulfonated pyrazolone **B**, which was produced from the reaction of sodium sulfonate **2b** and intermediate **A**. Moreover, according to the experimental results, the delivery of product **1c** through the radical addition and iodine radical induce dehydrogenation of **G** cannot be ruled out (path C). The released iodine ions will be oxidized again on the surface of the anode for catalytic cycling, while H^+ will be reduced on the surface of the cathode to release hydrogen gas as a greener byproduct.



Scheme 3 Postulated reaction pathway

In conclusion, an electrochemical/I^- dual-catalyzed sulfonylation of pyrazolones with sodium sulfonate access to sulfonated pyrazoles under external oxidant-free conditions have been disclosed.[17] A variety of sulfonated pyrazoles can be effectively synthesized by employing the present protocol. A series of control experiments have confirmed that the established electrochemical conversion undergoes a radical process. Besides, this electrochemical-induced sulfonylation of pyrazolones strategy can be easily scaled up for synthesis with biologically active sulfonated pyrazoles.

Conflict of Interest

The authors declare no conflict of interest.

Funding Information

This work was supported by the National Natural Science Foundation of China (No. 21902083, 22076097) and the Natural Science Foundation of Shandong Province (No. ZR2020QB130). This work was also supported by the Talent Program Foundation of Qufu Normal University (No. 6132 and 6125).

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-2089-0485.

References and Notes

(1) (a) Becker, D. P.; Barta, T. E.; Bedell, L. J.; Boehm, T. L.; Bond, B. R.; Carroll, J.; Carron, C. P.; DeCrescenzo, G. A.; Easton, A. M.; Freskos, J. N.; Funckes-Shippy, C. L.; Heron, M.; Hockerman, S.; Howard, C. P.; Kiefer, J. R.; Li, M. H.; Mathis, K. J.; McDonald, J. J.; Mehta, P. P.; Munie, G. E.; Sunyer, T.; Swearingen, C. A.; Villamil, C. I.; Welsch, D.; Williams, J. M.; Yu, Y.; Yao, J. *J. Med. Chem.* **2010**, *53*, 6653. (b) Jacob, C. *Nat. Prod. Rep.* **2006**, *23*, 851. (c) Khanum, F.; Anilakumar, K. R.; Viswanathan, K. R. *Crit. Rev. Food Sci. Nutr.* **2004**, *44*, 479. (d) Kotha, S.; Chavan, A. S. *J. Org. Chem.* **2010**, *75*, 4319. (e) Li, P.; Wang, L.; Wang, X. *J. Heterocycl. Chem.* **2021**, *58*, 28. (f) Feng, M.; Liang, S. H.; Jiang, X. *Curr. Top. Med. Chem.* **2016**, *16*, 1200.

(2) McGrath, N. A.; Brichacek, M.; Njardarson, J. T. *J. Chem. Educ.* **2010**, *87*, 1348; https://njardarson.lab.arizona.edu/content/top-pharmaceuticals-poster (accessed June 1, 2023).
(3) (a) Meadows, D. C.; Gervay Hague, J. *Med. Res. Rev.* **2006**, *26*, 793. (b) Alba, A. N.; Companyo, X.; Rios, R. *Chem. Soc. Rev.* **2010**, *39*, 2018. (c) Xu, K.; Khakyzadeh, V.; Bury, T.; Breit, B. *J. Am. Chem. Soc.* **2014**, *136*, 16124. (d) Li, Y.; Fan, Y. *Synth. Commun.* **2019**, *49*, 3227. (e) Trost, B. M.; Kalnmals, C. A. *Chem. Eur. J.* **2019**, *25*, 11193. (f) Chen, S.; Li, Y.; Wang, M.; Jiang, X. *Green Chem.* **2020**, *22*, 322. (g) Tashrifi, Z.; Khanaposhtani, M. M.; Larijani, B.; Mahdavi, M. *Adv. Synth. Catal.* **2020**, *362*, 65. (h) Li, K.; Wang, M.; Jiang, X. *CCS Chem.* **2021**, *4*, 1526. (i) Ahmadi, R.; Emami, S. *Eur. J. Med. Chem.* **2022**, *234*, 114255. (j) Wang, M.; Jiang, X. *ACS Sustainable Chem. Eng.* **2022**, *10*, 671.
(4) (a) Xu, K.; Li, L.; Yan, W.; Wu, Y.; Wang, Z.; Zhang, S. *Green Chem.* **2017**, *19*, 4494. (b) Sun, C.-C.; Xu, K.; Zeng, C.-C. *ACS Sustainable Chem. Eng.* **2019**, *7*, 2255. (c) Tao, X.; Sheng, R.; Bao, K.; Wang, Y.; Jin, Y. *Chin. J. Org. Chem.* **2019**, *39*, 2726. (d) Hua, X.; Liu, N.; Zhou, S.; Zhang, L.; Yin, H.; Wang, G.; Fan, Z.; Ma, Y. *Engineering* **2020**, *6*, 553. (e) Jiang, S.; Yu, Y.; Li, D.; Chen, Z.; He, Y.; Li, M.; Yang, G.-X.; Qiu, W.; Yang, Z.; Gan, Y. Lin J.; Ma, Y.; Su, S. J. *Angew. Chem. Int. Ed.* **2023**, *62*, 202218892.
(5) (a) Magedov, I. V.; Manpadi, M.; Van Slambrouck, S.; Steelant, W. F. A.; Rozhkova, E.; Przheval'skii, N. M.; Rogelj, S.; Kornienko, A. *J. Med. Chem.* **2007**, *50*, 5183. (b) Özdemir, Z.; Kandilci, H. B.; Gümüşel, B.; Çalış, Ü.; Bilgin, A. A. *Eur. J. Med. Chem.* **2007**, *42*, 373. (c) Velaparthi, S.; Brunsteiner, M.; Uddin, R.; Wan, B.; Franzblau, S. G.; Petukhov, P. A. *J. Med. Chem.* **2008**, *51*, 1999. (d) Fustero, S.; Sánchez-Roselló, M.; Barrio, P.; Simón-Fuentes, A. *Chem. Rev.* **2011**, *111*, 6984.
(6) (a) Padwa, A.; Woods Wannamaker, M. *Tetrahedron* **1990**, *46*, 1145. (b) Gao, D.; Zhai, H.; Parvez, M.; Back, T. G. *J. Org. Chem.* **2008**, *73*, 8057. (c) Kumar, R.; Namboothiri, I. N. N. *Org. Lett.* **2011**, *13*, 4016. (d) Kumar, R.; Verma, D.; Mobin, S. M.; Namboothiri, I. N. N. *Org. Lett.* **2012**, *14*, 4070. (e) Zhu, Y.; Lu, W.-T.; Sun, H.-C.; Zhan, Z.-P. *Org. Lett.* **2013**, *15*, 4146. (f) Zhao, X.; Zhang, L.; Li, T.; Liu, G.; Wang, H.; Lu, K. *Chem. Commun.* **2014**, *50*, 13121. (g) Liu, X.; Cui, H.; Yang, D.; Dai, S.; Zhang, T.; Sun, J.; Wei, W.; Wang, H. *RSC Adv.* **2016**, *6*, 51830. (h) Yang, D.; Sun, P.; Wei, W.; Meng, L.; He, L.; Fang, B.; Jiang, W.; Wang, H. *Org. Chem. Front.* **2016**, *3*, 1457. (i) Sun, P.; Yang, D.; Wei, W.; Jiang, L.; Wang, Y.; Dai, T.; Wang, H. *Org. Chem. Front.* **2017**, *4*, 1367.
(7) Nassar, E.; Abdel-Aziz, H. A.; Ibrahim, H. S.; Mansour, A. M. *Sci. Pharm.* **2011**, *79*, 507.
(8) Wang, B.-L.; Li, Q.-N.; Zhan, Y.-Z.; Xiong, L.-X.; Yu, S.-J.; Li, Z.-M. *Phosphorus, Sulfur Silicon Relat. Elem.* **2014**, *189*, 483.
(9) Hoy, S. M. *Drugs* **2019**, *79*, 2001.
(10) (a) Shaughnessy, C. A.; Zeitlin, P. L.; Bratcher, P. E. *Sci. Rep.* **2021**, *11*, 19810. (b) Zaher, A.; ElSaygh, J.; Elsori, D.; ElSaygh, H.; Sanni, A. *Cureus* **2021**, *13*, e16144.
(11) Wei, W.; Cui, H.; Yang, D.; Liu, X.; He, C.; Dai, S.; Wang, H. *Org. Chem. Front.* **2017**, *4*, 26.
(12) Li, L.-X.; Dong, D.-Q.; Hao, S.-H.; Wang, Z.-L. *Tetrahedron Lett.* **2018**, *59*, 1517.
(13) (a) Yan, M.; Kawamata, Y.; Baran, P. S. *Chem. Rev.* **2017**, *117*, 13230. (b) Jiang, Y.; Xu, K.; Zeng, C. *Chem. Rev.* **2018**, *118*, 4485. (c) Liu, Y.; Yi, H.; Lei, A. *Chin. J. Chem.* **2018**, *36*, 692. (d) Wang, H.; Gao, X.; Lv, Z.; Abdelilah, T.; Lei, A. *Chem. Rev.* **2019**, *119*, 6769. (e) Xiong, P.; Xu, H. C. *Acc. Chem. Res.* **2019**, *52*, 3339. (f) Jiao, K. J.; Xing, Y. K.; Yang, Q. L.; Qiu, H.; Mei, T. S. *Acc. Chem. Res.* **2020**, *53*, 300. (g) Yamamoto, K.; Kuriyama, M.; Onomura, O. *Acc. Chem. Res.* **2020**, *53*, 105. (h) Novaes, L. F. T.; Liu, J.; Shen, Y.; Lu, L.; Meinhardt, J. M.; Lin, S. *Chem. Soc. Rev.* **2021**, *50*, 7941. (i) Yang, J.; Qin, H.; Yan, K.; Cheng, X.; Wen, J. *Adv. Synth. Catal.* **2021**, *363*, 5407.
(14) (a) Niu, C.; Yang, J.; Yan, K.; Xie, J.; Jiang, W.; Li, B.; Wen, J. *iScience* **2022**, *25*, 104253. (b) Sun, X.; Yang, J.; Yan, K.; Zhuang, X.; Yu, J.; Song, X.; Zhang, F.; Li, B.; Wen, J. *Chem. Commun.* **2022**, *58*, 8238. (c) Zeng, T.; Yang, J.; Yan, K.; Wang, S.; Zhu, S.; Zhao, X.-E.; Li, D.; Wen, J. *Org. Chem. Front.* **2022**, *9*, 6305.
(15) (a) Wen, J.; Yang, X.; Sun, Z.; Yang, J.; Han, P.; Liu, Q.; Dong, H.; Gu, M.; Huang, L.; Wang, H. *Green Chem.* **2020**, *22*, 230. (b) Yang, X.; Yang, J.; Yan, K.; Qin, H.; Dong, W.; Wen, J.; Wang, H. *Eur. J. Org. Chem.* **2020**, 3456. (c) Sun, X.; Zhang, F.; Yan, K.; Feng, W.; Sun, X.; Yang, J.; Wen, J. *Adv. Synth. Catal.* **2021**, *363*, 3485. (d) Yang, J.; Dong, H.; Yan, K.; Song, X.; Yu, J.; Wen, J. *Adv. Synth. Catal.* **2021**, *363*, 5417. (e) Yang, J.; Sun, Z.; Yan, K.; Dong, H.; Dong, H.; Cui, J.; Gong, X.; Han, S.; Huang, L.; Wen, J. *Green Chem.* **2021**, *23*, 2756.
(16) Ma, J.; Yang, J.; Yan, K.; Sun, X.; Wei, W.; Tian, L.; Wen, J. *Eur. J. Org. Chem.* **2021**, 5491.
(17) **General Procedure**
In an oven-dried undivided three-necked flask (25 mL) equipped with a stir bar, **a** (0.25 mmol), **b** (0.5 mmol), and NH_4I (30 mol%, 10.8 mg) were combined and added. The flask was equipped with carbon rod as the anode, Pt plate (1 × 1 cm^2) as the cathode and was then charged with nitrogen. Under the protection of nitrogen, CH_3CN/H_2O (6.3 mL, v = 3: 0.1) was slowly injected into the reaction flask. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA under room temperature for 2 h. When the reaction was finished and monitored by TLC, the solution was concentrated in a vacuum and the pure product **1c-35c** was obtained by flash column chromatography on silica gel. ^1H and ^{13}C NMR and other analytical data of compounds **1c**, **2c**, **5c**, **9c**, **10c–14c**, **16c**, **19c**, **22c–24c**, **27c–29c**, **31c**, **32c** are reported in the literature.[11,12]
1-(4-Methoxyphenyl)-3-methyl-4-tosyl-1*H*-pyrazol-5-ol (3c)
Synthesized in accordance with the general procedure for electrochemical/I^- dual-catalyzed access to sulfonated pyrazoles performed in an undivided cell, using 2-(4-methoxyphenyl)-5-methyl-2,4-dihydro-3*H*-pyrazol-3-one (**3a**, 0.25 mmol, 51.0 mg), sodium 4-methylbenzenesulfinate (**2b**, 0.5 mmol, 89.0 mg), and NH_4I (30 mol%, 10.8 mg) with CH_3CN/H_2O (6.3 mL, v = 3: 0.1) as the solvent. The reaction mixture was stirred and electrolyzed at a constant current of 10 mA under room temperature for 2 h. The desired product (yield 74.4 mg, 0.21 mmol, 83%) was obtained as a white solid; mp 127–130 °C. ^1H NMR (500 MHz, DMSO): δ = 7.87 (d, *J* = 7.9 Hz, 2 H), 7.82 (d, *J* = 9.0 Hz, 2 H), 7.29 (d, *J* = 6.8 Hz, 2 H), 6.85 (d, *J* = 7.9 Hz, 2 H), 3.71 (s, 3 H), 2.33 (s, 3 H), 2.17 (s, 3 H). ^{13}C NMR (126 MHz, DMSO): δ = 160.3, 156.2, 145.5, 143.0, 142.5, 133.4, 129.7, 126.1, 121.3, 114.0, 97.2, 55.6, 21.3, 14.6. HRMS (EI): *m/z* calcd for $C_{18}H_{18}N_2O_4S$ $[M + H]^+$: 359.1061; found: 359.1060.