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The Direct Introduction of Sulfonamide Groups into Quinoxalin-2(1*H*)-ones *via* Cu-Catalyzed C3-H Functionalization

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Abstract: The direct sulfonamidation of quinoxalin-2(1*H*)-one derivatives has been developed using a readily available Cu salt as the catalyst and inexpensive ammonium persulfate as the oxidant in moderate conditions. Owing to the feature of handy operation and good functional group tolerance, this method provides a convenient and efficient access to curative 3-sulfonamidated quinoxalin-2(1*H*)-one scaffolds.

Introduction

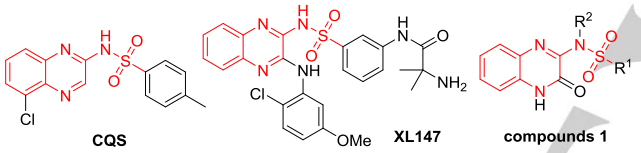
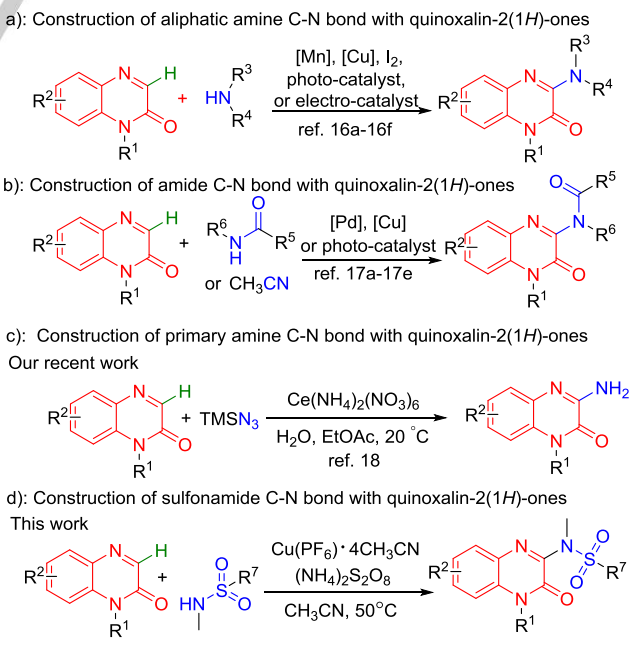


Figure 1. Pharmacoactive quinoxaline or quinoxalin-2(1*H*)-one sulfonamides

Sulfonamides, especially quinoxaline or quinoxalin-2(1*H*)-one sulfonamides, are privileged structural motif found in market drugs or pharmacologically active natural products (Figure 1).[1] As shown in Figure 1, Chloroquinoxaline Sulfonamide (CQS) has been used in clinical trials for the treatment of solid tumors.[2] XL147, a potent phosphoinositide 3-kinase (PI3K) inhibitor, has entered clinical trials as a promising anticancer drug candidate for targeted therapy.[3] A series of 3-aminoquinoxalin-2(1*H*)-one sulfonamides (compounds 1) as excitatory amino acid receptor antagonists are useful for the treatment of anxiety, depression, epilepsy, Alzheimer's disease or like.[4] So, the efficient synthetic means for introduction of sulfonamide groups into (hetero)aromatic rings have received widespread attention and significant achievements in this field have been accomplished in the last several years.[5-6]

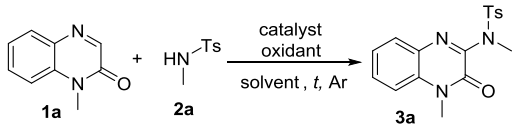
On the other hand, the direct C3-H bond functionalizations of the quinoxalin-2(1*H*)-ones have emerged as powerful tools to synthesize complex quinoxalin-2(1*H*)-one derivatives,[7-14] especially the 3-aminoquinoxalin-2(1*H*)-one derivatives. The pioneering studies focused on oxidative cross-dehydrogenation coupling of quinoxalin-2(1*H*)-ones with primary or secondary amines as the nitrogen sources, and Gulevskaya, Cui, Jain or Phan group independently reported the manganese, copper, iodine or copper-organic framework catalytic systems for this transformation (Scheme 1a).[15, 16a-d] Later, in view of green chemistry, Wei and Zeng groups respectively improved this transformation adopting a visible-light-catalyzed or electrochemical method (Scheme 1a).[16e-f] At the same time, Yuan, Zhang and He groups respectively reported the C3-amidation of quinoxalin-2(1*H*)-ones with a broad substrate scope under moderate conditions (Scheme 1b).[17] Our group also engaged in the direct C3-H amination of quinoxalin-2(1*H*)-ones utilizing $TMSN_3$ as an amino source to synthesize primary 3-aminoquinoxalin-2(1*H*)-ones, which are important intermediates for the synthesis of biologically active 3-*N*-substituted quinoxalinone derivatives (Scheme 1c).[18] All above brilliant achievements showed the superiority in high atom and step economy, and featured excellent functional group tolerance with good yields under readily accessible conditions. However, we could not ignore that the introduction of sulfonamide groups into the C3 position of quinoxalin-2(1*H*)-ones *via* direct C3-H functionalization is still rare and challenging, taking into consideration the importance of sulfonamide moiety in medicinal chemistry. Therefore, we demonstrated the first example for C3-H sulfonamidation of quinoxalin-2(1*H*)-ones with sulfonamide under a facile and mild conditions (Scheme 1d).



Scheme 1. Construction of C-N with quinoxalin-2(1*H*)-ones

Results and Discussion

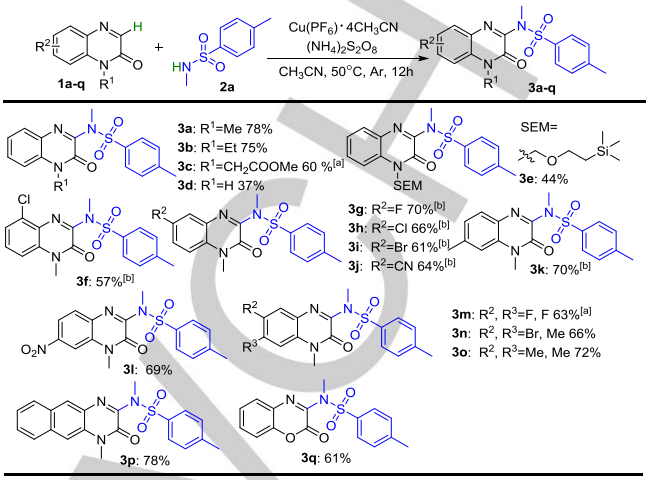
Table 1. Selected reaction conditions optimization[a]



Entry	catalyst	oxidant	T (°C)	Yield (%)[b]
1	-	$(NH_4)_2S_2O_8$	60	8
2	-	$K_2S_2O_8$	60	trace
3	-	$Na_2S_2O_8$	60	trace
4[c]	$Cu(ClO_4)_2·6H_2O$	$(NH_4)_2S_2O_8$	60	49
5[c]	$Cu(OTf)_2$	$(NH_4)_2S_2O_8$	60	48
6[c]	$Cu(BF_4)·4CH_3CN$	$(NH_4)_2S_2O_8$	60	45
7[c]	CuCl	$(NH_4)_2S_2O_8$	60	54
8[c]	CuI	$(NH_4)_2S_2O_8$	60	50
9[c]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	60	63
10[c]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	50	70
11[c]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	40	60
12	**$Cu(PF_6)·4CH_3CN$**	**$(NH_4)_2S_2O_8$**	**50**	**78**
13[d]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	50	53
14	$Cu(PF_6)·4CH_3CN$	$Na_2S_2O_8$	50	61
15	$Cu(PF_6)·4CH_3CN$	$PhI(OAc)_2$	50	trace
16	$Cu(PF_6)·4CH_3CN$	PIFA[e]	50	22
17[f]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	50	trace
18[g]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	50	trace
19[h]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	50	trace
20[i]	$Cu(PF_6)·4CH_3CN$	$(NH_4)_2S_2O_8$	50	trace

[a] Unless specifically noted otherwise, reaction conditions are: **1a** (0.3 mmol), **2a** (0.6 mmol), catalyst (10 mol %), oxidant (2.0 equiv.) and CH_3CN (3 mL), stirring under an argon atmosphere about 12 hours. [b] Yield of isolated product. [c] In the present of 20 mol % catalyst. [d] In the present of 5 mol % catalyst. [e] [Bis(trifluoroacetoxy)iodo]benzene. [f] In the present of 2.0 equivalents Cs_2CO_3. [g] In the present of 2.0 equivalents KOAc. [h] In the present of 15 mol % 1,10-phen·H_2O. [i] In the present of 15 mol % 2,2'-bipyridine.

Preliminary investigation was focused on the optimization of reaction with 1-methylquinoxalin-2(1*H*)-one (**1a**) and *N*, 4-dimethylbenzenesulfonamide (**2a**) as model substrates. Our initial experiments were performed to screen various oxidants under transition-metal-free condition. The expected product was obtained in 8%, when $(NH_4)_2S_2O_8$ was used as the oxidant (Table 1, entry 1). But the expected product was not obtained in the case of $K_2S_2O_8$ or $Na_2S_2O_8$ (Table 1, entries 2-3). Next, we continued to screen various copper salts as catalysts in the presence of $(NH_4)_2S_2O_8$ as oxidant. Fortunately, the expected product (**3a**) was obtained in 63% yield, When the $Cu(PF_6)·4CH_3CN$ was employed as catalyst (Table 1, entry 9). And the other copper salts including $Cu(ClO_4)_2·6H_2O$, $Cu(OTf)_2$, $Cu(BF_4)·4CH_3CN$, CuCl and CuI were less effective than $Cu(PF_6)·4CH_3CN$ (Table 1, entries 4-9). Subsequently, the reaction was carried at different temperatures, and a yield of 70% of **3a** was obtained at 50 °C (Table 1, entries 10-11). Next, the loading of catalyst was evaluated and the result revealed that 10% of $Cu(PF_6)·4CH_3CN$ was suitable for the reaction with the yield of **3a** increasing to 78% (Table 1, entries 12-13). Subsequently, diverse oxidants including $Na_2S_2O_8$, $PhI(OAc)_2$ and PIFA ([Bis(trifluoroacetoxy)iodo]benzene) were also tested again and the results showed that $(NH_4)_2S_2O_8$ still was the most appropriate oxidant among the aforementioned oxidants (Table 1, entries 14-16). Finally, several bases (Cs_2CO_3, KOAc, etc.) or *N, N*-bidentate ligands (1,10-phen·H_2O, 2,2'-Bipyridine, etc.) were further examined under the selected reaction conditions exhibited in the entry 12, but did not lead to any improvement (Table 1, entries 17-20). In conclusion, optimized reaction conditions involved the use of **1a** (0.3 mmol), 2.0 equivalents of sulfonamide **2a**, 10 mol % of $Cu(PF_6)·4CH_3CN$ catalyst, 2.0 equivalents of $(NH_4)_2S_2O_8$, and stirring in CH_3CN (3.0 mL) at 50 °C under an argon atmosphere.

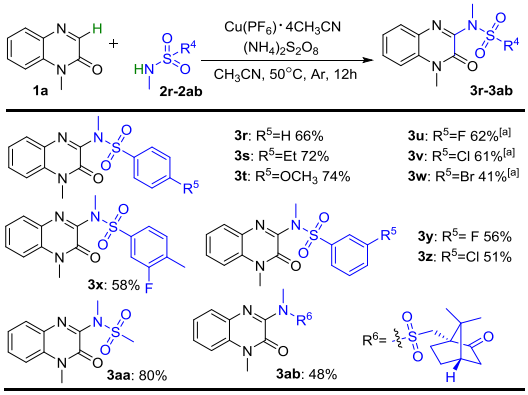


Scheme 2. Substrate scope of various quinoxalin-2(1*H*)-ones. General conditions: **1** (0.3 mmol), **2** (0.6 mmol), $Cu(PF_6)·4CH_3CN$ (10 mol %), $(NH_4)_2S_2O_8$ (2.0 equiv.) and CH_3CN (3 mL), stirring under an argon atmosphere about 12 hours; Yield of isolated product. [a] $(NH_4)_2S_2O_8$ was divided into seven parts and evenly added in 28 hours. [b] $(NH_4)_2S_2O_8$ was divided into three parts and evenly added in 12 hours.

With the optimal reaction conditions established, we investigated the substrate scope of this transformation. Firstly, various quinoxalin-2(1*H*)-one substrates were investigated, and the results are summarized in Scheme 2. Several quinoxalin-2(1*H*)-ones with *N*-substituted groups such as methyl, ethyl and methyl acetate, could proceed smoothly and afford the corresponding products in moderate to good yields (**3a**-**3c**). However, quinoxalin-2(1*H*)-one without protecting group provided the target molecule in a low yield of 37% (**3d**). The *N*-SEM protected quinoxalin-2(1*H*)-one gave the expected product in 44% yield (**3e**). The substrates bearing weak electron-donating, weak and strong electron withdrawing groups such as methyl, halogen (fluoro, chloro and bromo) or nitro, cyano groups, matched the reaction very well and offered the corresponding products in moderate to good yields (**3f**-**3o**). Besides, the optimized conditions were also applicable to 1-methylbenzo[*g*]quinoxalin-2(1*H*)-one and the corresponding product was obtained in 78% yield. Motivated by these acceptable results of quinoxalin-2(1*H*)-one derivatives, we further tested 2*H*-benzo[*b*][1,4]oxazin-2-one and found that the target product was successfully isolated in a moderate yield of 61% (**3q**).

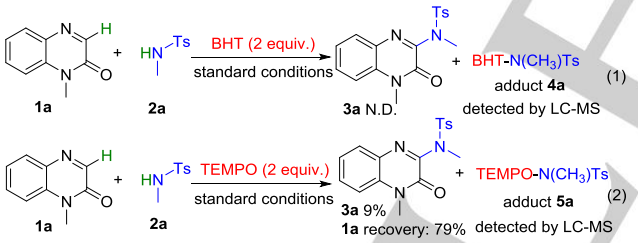
Next, we continued to explore the substrate scope of *N*-methyl sulfonamides (Scheme 3). A series of *N*-methylbenzenesulfonamides containing electron-donating groups (ethyl and methoxyl) reacted with 1-methylquinoxalin-2(1*H*)-one (**1a**) smoothly and gave the desired products in good yields (**3r**-**3t**). And the substrates with the halogens (fluoro, chloro and bromo) also afforded the target products in moderate yields (**3u**-**3w**, **3y**-**3z**). *N*-methylbenzenesulfonamide bearing both a fluorine and a methyl group also offered the corresponding product in a moderate yield of 58% (**3x**). Surprisingly, *N*-methylmethanesulfonamide matched the transformation well and the expected product was received in outstanding yield of 80% (**3aa**). Encouraged by the result of this simple *N*-methylmethanesulfonamide, we test L-*N*-methylcamphorsulfonamide as a representative of complicated

substrate and obtained the corresponding product in 48% yield (**3ab**).



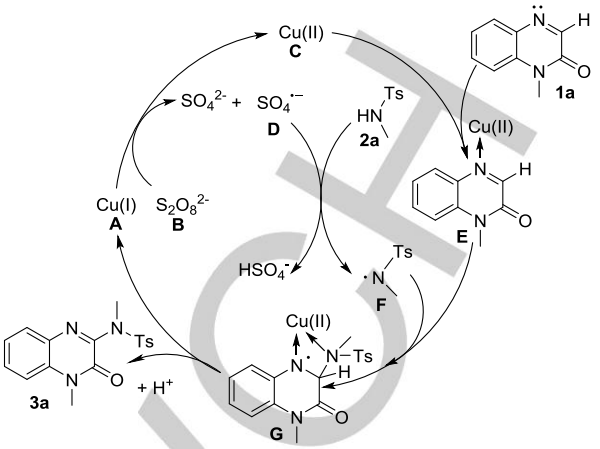
Scheme 3. Substrate scope of various sulfonamides. General conditions: **1** (0.3 mmol), **2** (0.6 mmol), $Cu(PF_6)\cdot 4CH_3CN$ (10 mol %), $(NH_4)_2S_2O_8$ (2.0 equiv.) and CH_3CN (3 mL), stirring under an argon atmosphere about 12h; Yield of isolated product. [a] $(NH_4)_2S_2O_8$ was divided into three parts and evenly added in 12 hours.

After the investigation of substrate scope, two radical trapping experiments were performed to gain the preliminary mechanism insights of this sulfonamidation (Scheme 4). First, the reaction did not occur when 2.0 equivalents of BHT (2,6-di-tert-butyl-p-cresol) was added under standard reaction system as a radical inhibitor. But a BHT-trapped adduct **4a** was detected by LC-MS (Scheme 4, Equation 1). Second, the reaction was partially suppressed in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) as the radical scavenger. Only 9% yield of the target product was obtained and 79% of the starting material **1a** was recovered. Besides, TEMPO-trapped adduct **5a** was also observed (Scheme 2, Equation 2). These experiment results implied that a single-electron-transfer (SET) might be involved in this sulfonamidation.



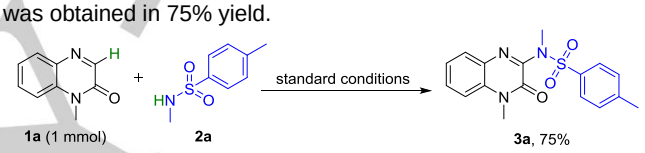
Scheme 4. Radical trapping experiments

Based on the aforementioned results of radical trapping experiments and previous literatures,[19] a plausible mechanism was proposed in scheme 5. Initially, the Cu(I) catalyst **A** reacts with peroxydisulfate **B** to produce active Cu(II) species **C**, SO_4^{2-} and $SO_4^{\bullet-}$ radical anion (**D**),[19a-19b] and **D** abstracts a hydrogen atom from sulfonamide **2a** to generate HSO_4^- and the corresponding sulfonamide radical **F**. Subsequently, the coordination of **C** with the nitrogen atom of the C=N bond in the quinoxalin-2(1*H*)-one substrate leads to the polarization of the C=N double bond and gives the active species **E**,[19c-19d, 19g-19h] which undergoes an addition with the sulfonamide radical **F** to provide the key intermediate **G**.[19a-19b, 19g] Finally, the intermediate **G** goes through a single-electron transfer and deprotonation in succession to afford the target product **3a**, with regenerating the copper(I) catalyst **A** to complete the catalytic cycle.



Scheme 5. Plausible mechanism

To demonstrate the scalability of this protocol, a large-scale reaction was performed and desired sulfonamidation product **3a** was obtained in 75% yield.



Scheme 6. Large-scale experiment

Conclusion

In conclusion, the direct C-H sulfonamidation of quinoxalin-2(1*H*)-ones with sulfonamides *via* C-H/N-H cross-dehydrogenation coupling has been developed. This method provides a practical and convenient approach for introduction of sulfonamide groups into the C3 position of quinoxalin-2(1*H*)-ones, with readily available Cu salt as the catalyst and inexpensive ammonium persulfate as the oxidant. In addition, the transformation is operated in mild conditions with a wide range of substrates, affording a number of medicinally interesting 3-sulfonamidated quinoxalin-2(1*H*)-one derivatives in moderate to excellent yields.

Experimental Section

General procedure for the sulfonamidation of quinoxalin-2(1*H*)-ones

An oven-dried Schlenk tube was charged with quinoxalin-2(1*H*)-one derivative (**1a**) (0.3 mmol), *N*, 4-dimethylbenzenesulfonamide (**2a**) (2.0 equiv., 0.6 mmol), $Cu(PF_6)\cdot 4CH_3CN$ (0.1 equiv., 0.03 mmol) , $(NH_4)_2S_2O_8$ (2.0 equiv., 0.6 mmol) and a magnetic stirring bar, and then was purged with argon for three times. Subsequently, anhydrous CH_3CN (3mL) was added *via* syringe, and the mixture was

stirred at 50 °C in oil bath. The mixture was continued reaction until the substrate was consumed (monitored by TLC, about 12 hour). After that, the reaction mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The resulting residue was purified by flash column chromatography on silica gel to afford the corresponding sulfonamidation product (**3a**).

Acknowledgements

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Keywords: Radical reactions • Cross-coupling • C-H functionalization • Quinoxalin-2(1*H*)-ones • Sulfonamide

[1] a) J. Weijlard, M. Tishler, A. E. Erickson, *J. Am. Chem. Soc.* **1944,** *66*, 1957-1959; b) S. H. Dandegaonker, C. K. Mesta, *J. Med. Chem.* **1965,** *8*, 884-886; c) A. Garzan, M. J. Willby, K. D. Green, C. S. Gajadeera, C. Hou, O. V. Tsodikov, J. E. Posey, S. Garneau-Tsodikova, *J. Med. Chem.* **2016,** *59*, 10619-10628; d) S. Mahato, S. Santra, G. V. Zyryanov, A. Majee, *J. Org. Chem.* **2019**, *84*, 3176-3183.

[2] a) J. R. Rigas, W. P. Tong, M. G. Kris, J. P. Orazem, C. W. Young, R. P. arrell, *Cancer Res.* 1992, *52*, 6619-6623; b) T. S. ekaii-Saab, A. Mortazavi, L. G. Hicks, M. Zalupski, R. J. Pelley, K. K. han, E. H. Kraut, *Invest. New Drugs* **2006,** *24*, 343; c) T. Han, M. Goralski, N. Gaskill, E. Capota, J. Kim, T. C. Ting, Y. Xie, N. S. Williams, D. Nijhawan, *Science* 2017, *356*, eaal3755.

[3] a) D. Church, P. Gaillard, J. Klicic, V. Pomel, A. Quattropani, T. Rueckle, Pyrazine derivatives and use as pi3k inhibitors. WO 2007/023186 A1, March 3, 2007; b) P. Gaillard, V. Pomel, I. Jeanclaude-Etter, Dorbais, Jérôme, J. Klicic, C. Montagne, Quinoxaline compounds and use thereof. WO 2008/101979 A1, August 8, 2008; c) C. Yang, X. Zhang, Y. Wang, Y. Yang, X. Liu, M. Deng, Y. Jia, Y. Ling, L.-h. Meng, Y. Zhou, *ACS Med. Chem. Lett.* **2017**, *8*, 875-880.

[4] K. Nakai, Y. Ogawa, A. Yamada, T. Chiba, H. Takasugi, Quinoxaline derivatives as glutamate receptor antagonists. WO 97/32858 A1, September 9, 1997.

[5] Recently selected sulfonamidation of aromatic rings: a) G. Burton, P. Cao, G. Li, R. Rivero, *Org. Lett*. **2003**, *5*, 4373-4376; b) J. D. Hicks, A. M. Hyde, A. M. Cuezva, S. L. Buchwald, *J. Am. Chem. Soc.* **2009**, *131*, 16720-16734; c) C. Sambiagio, S. P. Marsden, A. J. Blacker, P. C. McGowan, *Chem. Soc. Rev.* **2014**, *43*, 3525-3550; d) H. Chen, M. P. Huestis, *ChemCatChem* **2015**, *7*, 743-746; e) J. R. Colombe, J. R. DeBergh, S. L. Buchwald, *Org. Lett.* **2015**, *17*, 3170-3173; f) K. Tong, X. Liu, Y. Zhang, S. Yu, *Chem-Eur. J.* **2016**, *22*, 15669-15673; g) B. Zhu, X. Cui, C. Pi, D. Chen, Y. Wu, *Adv. Synth. Catal.* **2016**, *358*, 326-332; h) H. Zhu, Y. Shen, Q. Deng, C. Huang, T. Tu, *Chem-Asian J.* **2017**, *12*, 706-712; i) Y.-N. Ma, C.-Y. Guo, Q. Zhao, J. Zhang, X. Chen, *Green Chem.* **2018**, *20*, 2953-2958; j) T. Kim, S. J. McCarver, C. Lee, D. W. C. MacMillan, *Angew. Chem. Int. Ed.* **2018**, *57*, 3488-3492; k) L. Li, Y. Li, Z. Zhao, H. Luo, Y.-N. Ma, *Org. Lett.* **2019**, *21*, 5995-5999. l) Y.-N. Ma, Y. Bian, X. Liu, J. Zhang, X. Chen, *J. Org. Chem.* **2019**, *84*, 450-457.

[6] Recently selected sulfonamidation of heteroaromatic rings: a) B. F. Senkal, E. T. Tekin, E. Yavuz, *Polym. Advan. Technol.* **2009**, *20*, 308-311; b) J. Baffoe, M. Y. Hoe, B. B. Touré, *Org. Lett.* **2010**, *12*, 1532-1535; c) J. Lin, I. N. Houpis, R. Liu, Y. Wang, J. Zhang, *Org. Process Res. Dev.* **2014**, *18*, 205-214; d) X. Yu, S. Yang, Y. Zhang, M. Guo, Y. Yamamoto, M. Bao, *Org. Lett.* **2017**, *19*, 6088-6091; e) Y. Chen, P. R. D. Murray, A. T. Davies, M. C. Willis, *J. Am. Chem. Soc.* **2018**, *140*, 8781-8787; f) J. C. Vantourout, L. Li, E. Bendito-Moll, S. Chabbra, K. Arrington, B. E. Bode, A. Isidro-Llobet, J. A. Kowalski, M. G. Nilson, K. M. P. Wheelhouse, J. L. Woodard, S. Xie, D. C. Leitch, A. J. B. Watson, *ACS Catal.* **2018**, *8*, 9560-9566; g) F. Zhang, D. Zheng, L. Lai, J. Cheng, J. Sun, J. Wu, *Org. Lett.* **2018**, *20*, 1167-1170; h) W. Zu, S. Liu, X. Jia, L. Xu, *Org. Chem. Front.* **2019**, *6*, 1356-1360.

[7] Reviews about recent advances in the direct functionalization of quinoxalin-2(1*H*)-ones: a) Q. Ke, G. Yan, J. Yu, X. Wu, *Org. Biomol. Chem.* **2019**, *17*, 5863-5881; b) Y. Tan, J. Wang, H.-Y. Zhang, Y. Zhang, J. Zhao, *Front. Chem.* **2020**, *8*, 582.

[8] Recently selected literatures about aromatization of quinoxalinone: a) S. Paul, J. H. Ha, G. E. Park, Y. R. Lee, Adv. Synth. Cat*al.* **2017**, *359*, 1515-1521; b) J. Yuan, S. Liu, L. Qu, *Adv. Synth. Catal.* **2017**, *359*, 4197-4207; c) K. Yin, R. Zhang, *Org. Lett.* **2017**, *19*, 1530-1533; d) H. I. Jung, J. H. Lee, D. Y. Kim, *B. Korean Chem. Soc.* **2018**, *39*, 1003-1006; e) S. J. Kwon, H. I. Jung, D. Y. Kim, *ChemistrySelect* **2018**, *3*, 5824-5827; f) K. Yin, R. Zhang, *Synlett* **2018**, *29*, 597-602; g) M. Noikham, T. Kittikool, S. Yotphan, *Synthesis* **2018**, *50*, 2337-2346; h) B. Ramesh, C. R. Reddy, G. R. Kumar, B. V. S. Reddy, *Tetrahedron Lett.* **2018**, *59*, 628-631; i) S. Paul, H. D. Khanal, C. D. Clinton, S. H. Kim, Y. R. Lee, *Org. Chem. Front.* **2019**, *6*, 231-235; j) C. Ebersol, N. Rocha, F. Penteado, M. S. Silva, D.Hartwig, E. J. Lenardão, R. G. Jacob, *Green Chem.* **2019**, *21*, 6154-6160; k) V. A. Mamedov, N. A. Zhukova, M. S. Kadyrova, V. V. Syakaev, T. y. N. Beschastnova, D. N. Buzyurova, I. d. K. Rizvanov, S. K. Latypov, O. G. Sinyashin, *J. Org. Chem.* **2019**, *84*, 13572-13581.

[9] Recently selected literatures about alkylation of quinoxalinone: a) W. Wei, L. Wang, H. Yue, P. Bao, W. Liu, C. Hu, D. Yang, H. Wang, *ACS Sustain. Chem. Eng.* **2018**, *6*, 17252-17257; b) J. Fu, J. Yuan, Y. Zhang, Y. Xiao, P. Mao, X. Diao, L. Qu, *Org. Chem. Front.* **2018**, *5*, 3382-3390; c) S. Liu, Y. Huang, F.-L. Qing, X.-H. Xu, *Org. Lett.* **2018**, *20*, 5497-5501; d) H. Sekhar Dutta, A. Ahmad, A. A. Khan, M. Kumar, Raziullah, D. Koley, *Adv. Synth. Catal.* **2019**, *361*, 5534-5539; e) L. Liu, N. Pan, W. Sheng, L. Su, L. Liu, J. Dong, Y. Zhou, S.-F. Yin, *Adv. Synth. Catal.* **2019**, *361*, 4126-4132; f) L. Wang, H. Liu, F. Li, J. Zhao, H.-Y. Zhang, Y. Zhang, *Adv. Synth. Catal.* **2019**, *361*, 2354-2359; g) Z. Yan, B. Sun, X. Zhang, X. Zhuang, J. Yang, W. Su, C. Jin, *Chem.–Asian J.* **2019**, *14*, 3344-3349; h) L.-Y. Xie, L.-L. Jiang, J.-X. Tan, Y. Wang, X.-Q. Xu, B. Zhang, Z. Cao, W.-M. He, *ACS Sustain. Chem. Eng.* **2019**, *7*, 14153-14160; i) K. D. Mane, R. B. Kamble, G. Suryavanshi, *New J. Chem.* **2019**, *43*, 7403-7408; j) W. Xue, Y. Su, K.-H. Wang, R. Zhang, Y. Feng, L. Cao, D. Huang, Y. Hu, *Org. Biomol. Chem.* **2019**, *17*, 6654-6661; k) H. Zhang, J. Xu, M. Zhou, J. Zhao, P. Zhang, W. Li, *Org. Biomol. Chem.* **2019**, *17*, 10201-10208; l) W. Zhang, Y.-L. Pan, C. Yang, X. Li, B. Wang, *Org. Chem. Front.* **2019**, *6*, 2765-2770; m) L. Wang, J. Zhao, Y. Sun, H.-Y. Zhang, Y. Zhang, *Eur. J. Org. Chem.* **2019**, *2019*, 6935-6944; n) G. Hong, J. Yuan, J. Fu, G. Pan, Z. Wang, L. Yang, Y. Xiao, P. Mao, X. Zhang, *Org. Chem. Front.* **2019**, *6*, 1173-1182; o) D. Zheng, A. Studer, *Org. Lett.* **2019**, *21*, 325-329; p) J. Rostoll-Berenguer, G. Blay, M. C. Muñoz, J. R. Pedro, C. Vila, *Org. Lett.* **2019**, *21*, 6011-6015; q) Y.-R. Gu, X.-H. Duan, L. Chen, Z.-Y. Ma, P. Gao, L.-N. Guo, *Org. Lett.* **2019**, *21*, 917-920; r) D. Zheng, A. Studer, *Org. Lett.* **2019**, *21*, 325-329; s) B. Zhao, X. Kong, B. Xu, *Tetrahedron Lett.* **2019**, *60*, 2063-2066; t) S. Jin, H. Yao, S. Lin, X. You, Y. Yang, Z. Yan, *Org. Biomol. Chem.* **2020**, *18*, 205-210; u) J. Wang, B. Sun, L. Zhang, T. Xu, Y. Xie, C. Jin, *Org. Chem. Front.* **2020**, *7*, 113-118; v) N. Meng, L.Wang, Q. Liu, Q. Li, Y. Lv, H. Yue, X. Wang, W. Wei, *J. Org. Chem.* **2020**, *85,* 6888–6896; w) X. Rong, L. Jin, Y. Gu, G. Liang, Q. Xia, *Asian J. Org. Chem.* **2020**, *9,* 185-188; x) M. Shao, H. Liang, Y.-L. Liu, W. Qin, Z. Li, *Asian J. Org. Chem.* **2020**, *9,* 782-787; y) Y. Gao, L. Zhao, T. Xiang, P. Li, L. Wang, *RSC Adv.* **2020**, *10,* 10559-10568.

[10] Recently selected literatures about carbonylation of quinoxalinone: a) X. Zeng, C. Liu, X. Wang, J. Zhang, X. Wang, Y. Hu, *Org. Biomol. Chem.* **2017**, *15*, 8929-8935; b) J.-W. Yuan, J.-H. Fu, S.-N. Liu, Y.-M. Xiao, P. Mao, L.-B. Qu, *Org. Biomol. Chem.* **2018**, *16*, 3203-3212; c) L.-Y. Xie, S. Peng, T.-G. Fan, Y.-F. Liu, M. Sun, L.-L. Jiang, X.-X. Wang, Z. Cao, W.-M. He, *Sci. China Chem.* **2019**, *62*, 460-464; d) P.Bao, F. Liu, Y. Lv, H. Yue, J.-S. Li, W. Wei, *Org. Chem. Front.* **2020**, *7*, 492-498; e) J.-W.Yuan, Q. Chen, C. Li, J.-L. Zhu, L.-R. Yang, S.-R. Zhang, P. Mao, Y.-M. Xiao, L.-B. Qu, *Org. Biomol. Chem.* **2020**, *18*, 2747-2757; f) L.-Y. Xie, Y.-S. Bai, X.-Q. Xu, X. Peng, H.-S. Tang, Y. Huang, Y.-W. Lin, Z. Cao, W.-M. He, *Green Chem.* **2020**, *22*, 1720-1725; g) X. Chu, Y. Wu, H. Lu,

B. Yang, C. Ma, *Eur. J. Org. Chem.* **2020**, *9*, 1141-1144; h) J. Lu, X.-K. He, X.Cheng, A.-J. Zhang, G.-Y. Xu, J. Xuan, *Adv. Synth. Catal.* **2020**, *362*, 2178-2182; i) J.-W. Yuan, J.-L. Zhu, H.-L. Zhu, F. Peng, L.-Yu. Yang, P. Mao, S.-R. Zhang, Y.-C. Li, L.-B. Qu, *Org. Chem. Front.* **2020**, *7*, 273-285.

[11] Recently literatures about alkoxylation of quinoxalinone: a) J. Xu, H. Yang, H. Cai, H. Bao, W. Li, P. Zhang, *Org. Lett.* **2019**, *21*, 4698-4702; b) Q. Yang, X. Han, J. Zhao, H.-Y. Zhang, Y. Zhang, *J. Org. Chem.* **2019**, *84*, 11417-11424; c) X. Xu, C. Xia, X. Li, J. Suna, L. Hao, *RSC Adv.* **2020**, *10*, 2016–2026; d) X. Jiang, L. Yang, Z. Ye, X. Du, L. Fang, Y. Zhu, K. Chen, J. Li, C. Yu, *Eur. J. Org. Chem.* **2020**, *2020,* 1687-1694.

[12] Recently selected literatures about phosphonation of quinoxalinone: a) M. Gao, Y. Li, L. Xie, R. Chauvin, X. Cui, *Chem. Commun.* **2016**, *52*, 2846-2849; b) Y. Kim, D. Y. Kim, *Tetrahedron Lett.* **2018**, *59*, 2443-2446; c) C. Hu, G. Hong, C. Zhou, Z.-C. Tang, J.-W. Han, L.-M. Wang, *Asian J. Org. Chem.* **2019**, *8*, 2092-2096; d) W.-P. Mai, J.-W. Yuan, J.-L. Zhu, Q.-Q. Li, L.-R. Yang, Y.-M. Xiao, P. Mao, L.-B. Qu, *ChemistrySelect* **2019**, *4*, 11066-11070; e) K.-J. Li, Y.-Y. Jiang, K. Xu, C.-C. Zeng, B.-G. Sun, *Green Chem.* **2019**, *21*, 4412-4421.

[13] Recently selected literatures about special functionalization of quinoxalinone: a) Q. Yang, Y. Zhang, Q. Sun, K. Shang, H.-Y. Zhang, J. Zhao, *Adv. Synth. Catal.* **2018**, *360*, 4509-4514; b) L. Sumunnee, C. Pimpasri, M. Noikham, S. Yotphan, *Org. Biomol. Chem.* **2018**, *16*, 2697-2704; c) Q.-H. Teng, Y. Yao, W.-X. Wei, H.-T. Tang, J.-R. Li, Y.-M. Pan, *Green Chem.* **2019**, *21*, 6241-6245; d) L.-Y. Xie, Y.-L. Chen, L. Qin, Y. Wen, J.-W. Xie, J.-X. Tan, Y. Huang, Z. Cao, W.-M. He, *Org. Chem. Front.* **2019**, *6*, 3950-3955; e) S. Peng, D. Hu, J.-L. Hu, Y.-W. Lin, S.-S. Tang, H.-S. Tang, J.-Y. He, Z. Cao, W.-M. He, *Adv. Synth. Catal.* **2019**, *361*, 5721-5726; f) J. Zhou, Z. Li, Z. Sun, Q. Ren, Q. Zhang, H. Li, J. Li, *J. Org. Chem.* **2020,** *85,* 4365–4372.

[14] Recently selected literatures about the synthesis various biheterocyclic systems from functionalized quinoxalinone: a) V. A. Mamedov, N. A. Zhukova, A. I. Zamaletdinova, T. N. Beschastnova, M. S. Kadyrova, I. Kh. Rizvanov, V. V. Syakaev, S. K. Latypov, *J. Org. Chem.* **2014**, *79*, 9161−9169; b) V. A. Mamedov, N. A. Zhukova, T. N. Beschastnova, V. V. Syakaev, D. B. Krivolapov, E. V. Mironova, A. I. Zamaletdinova, I. Kh. Rizvanov, S. K. Latypov, *J. Org. Chem.* **2015**, *80*, 1375−1386; c) V. A. Mamedov**,** *RSC Adv.* **2016**, *6*, 42132-42172; d) N. A. Zhukova, V. A. MamedovRuss, *Chem. Rev.* **2017**, *86*, 968-997; e) V. A. Mamedov, N. A. Zhukova, M. S. Kadyrova, V. V. Syakaev, T. N. Beschastnova, D. N. Buzyurova, I. Kh. Rizvanov, S. K. Latypov, O. G. Sinyashin, *J. Org. Chem.* **2019**, *84*, 13572-13581.

[15] Recently selected literatures about CDC relation: a) C.-J. Li, *Acc. Chem. Res.* **2009**, *42*, 335-344; b) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215-1292; c) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068-5083; d) C. Zhang, X. Zong, L. Zhang, N. Jiao, *Org. Lett.* **2012**, *14*, 3280-3283; e)S. A. Girard, T. Knauber, C.-J. Li, *Angew. Chem. Int. Ed.* **2014**, *53*, 74-100; f) R.-B. Hu, C.-H. Wang, W. Ren, Z. Liu, S.-D. Yang, *ACS Catal.* **2017**, *7*, 7400-7404; g) Y.-N. Ma, M.-X. Cheng, S.-D. Yang, *Org. Lett.* **2017**, *19*, 600-603; h) B. Chen, L.-Z. Wu, C.-H. Tung, *Acc. Chem. Res.* **2018**, *51*, 2512-2523 i) S. Tang, L. Zeng, A. Lei, *J. Am. Chem. Soc.* **2018**, *140*, 13128-13135; j) X. Chen, J. Ren, H. Xie, W. Sun, M. Sun, B. Wu, *Org. Chem. Front.* **2018**, *5*, 184-188; k) M. Singsardar, S. Laru, S. Mondal, A. Hajra, *J. Org. Chem.* **2019**, *84*, 4543-4550; l) S. Samanta, S. Mondal, D. Ghosh, A. Hajra, *Org. Lett.* **2019**, *21*, 4905-4909.

[16] a) A. V. Gulevskaya, O. N. Burov, A. F. Pozharskii, M. E. Kletskii, I. N. Korbukova, *Tetrahedron* **2008**, *64*, 696-707; b) Y. Li, M. Gao, L. Wang, X. Cui, *Org. Biomol. Chem.* **2016**, *14*, 8428-8432; c) A. Gupta, M. S. Deshmukh, N. Jain, *J. Org. Chem.* **2017**, *82*, 4784-4792; d) T. T. Hoang, T. A. To, V. T. T. Cao, A. T. Nguyen, T. T. Nguyen, N. T. S. Phan, *Catal. Commun.* **2017**, *101*, 20-25; e) W. Wei, L. Wang, P. Bao, Y. Shao, H. Yue, D. Yang, X. Yang, X. Zhao, H. Wang, *Org. Lett.* **2018**, *20*, 7125-7130; f) K.-J. Li, K. Xu, Y.-G. Liu, C.-C. Zeng, B.-G. Sun, *Adv. Synth. Catal.* **2019**, *361*, 1033-1041.

[17] a) J. Yuan, S. Liu, Y. Xiao, P. Mao, L. Yang, L. Qu, *Org. Biomol. Chem.* **2019**, *17*, 876-884; b) J. Yuan, J. Zhu, J. Fu, L. Yang, Y. Xiao, P. Mao, X. Du, L. Qu, *Org. Chem. Front.* **2019**, *6*, 925-935; c) T. Guo, C.-C. Wang, X.-H. Fu, Y. Liu, P.-K. Zhang, *Org. Biomol. Chem.* **2019**, *17*, 3333-3337; d) L.-Y. Xie, J.-L. Hu, Y.-X. Song, G.-K. Jia, Y.-W. Lin, J.-Y. He, Z. Cao, W.-M. He, *ACS Sustain. Chem. Eng.* **2019**, *7*, 19993-19999; e) J.-W. Yuan, J.-L. Zhu, B. Li, L.-Y. Yang, P. Mao, S.-R. Zhang, Y.-C. Li, L.-B. Qu, *Org. Biomol. Chem.* **2019**, *17*, 10178-10187.

[18] Q. Yang, Z. Yang, Y. Tan, J. Zhao, Q. Sun, H.-Y. Zhang, Y. Zhang, *Adv. Synth. Catal.* **2019**, *361*, 1662-1667.

[19] a) S. Verbeeck, W. A. Herrebout, A. V. Gulevskaya, B. J. van der Veken, B. U. W. Maes, *J. Org. Chem.* **2010**, *75*, 5126-5133; b) K. Monir, A. Kumar Bagdi, S. Mishra, A. Majee, A. Hajra, *Adv. Synth. Catal.* **2014**, *356*, 1105-1112; c) X. Zhu, Y. Shi, H. Mao, Y. Cheng, C. Zhu, *Adv. Synth. Catal.* **2013**, *355*, 3558-3562; d) X. Mi, C. Wang, M. Huang, Y. Wu, Y. Wu, *J. Org. Chem.* **2015**, *80*, 148-155; e) S. K. Singh, N. Chandna, N. Jain, *Org. Lett.* **2017**, *19*, 1322-1325; f) S. Bhunia, G. G. Pawar, S. V. Kumar, Y. Jiang, D. Ma, *Angew. Chem., Int. Ed.* **2017**, *56*, 16136-16179; g) H. Sahoo, S. Mukherjee, G. S. Grandhi, J. Selvakumar and M. Baidya, *J. Org. Chem.* **2017**, *82*, 2764-2771; h) P. Zhang, H. Shen, L. Zhu, W. Cao, C. Li, *Org. Lett.* **2018**, *20*, 7062-7065.

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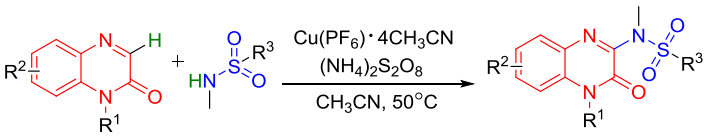

a) atom-economical sulfonamidation *via* C-H/N-H CDC reaction
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The first example of Cu-catalyzed C3-H sulfonamidation of quinoxalin-2(1*H*)-ones *via* C-H/N-H cross-dehydrogenation coupling. This reaction tolerates various quinoxalin-2(1*H*)-ones and sulfonamides to afford 3-sulfonamidated quinoxalin-2(1*H*)-one derivatives.

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