Advanced Synthesis & Catalysis

Accepted Article

Title: Tert-Butyl Nitrite Mediated Expeditious Methylsulfoxidation of Tetrazole-amines with DMSO: Metal-free Synthesis of Antifungal Active Methylsulfinyl-1H-tetrazole Derivatives

Authors: Peng Dai, Kai Luo, Xiang Yu, Wen-Chao Yang, Lei Wu, and Wei-Hua Zhang

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201701364

Link to VoR: http://dx.doi.org/10.1002/adsc.201701364

COMMNUNICATIONS

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Tert-Butyl Nitrite Mediated Expeditious Methylsulfoxidation of Tetrazole-amines with DMSO: Metal-free Synthesis of Antifungal Active Methylsulfinyl-1*H*-tetrazole Derivatives

Peng Dai,[a,§] Kai Luo,[a,c,§] Xiang Yu,[a] Wen-Chao Yang,[a] Lei Wu,[a,b,*] and Wei-Hua Zhang[a,*]

[a] Jiangsu Key Laboratory of Pesticide Science and Department of Chemistry, College of Sciences, Nanjing Agricultural University, Nanjing 210095, P. R. China. Tel/Fax: +86-25-84395351; Email: rickywu@njau.edu.cn; zhwh@njau.edu.cn.

[b] Beijing National Laboratory for Molecular Sciences and Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China.

[c] College of Life Sciences, Nanjing Agricultural University, Nanjing 210095, P. R. China.

[§] These authors contribute equally to this work.

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract. A *tert*-butyl nitrite mediated methyl-sulfoxidation of tetrazole-amines in neat DMSO or methyl-sulfinyl derivatives is revealed for the first time. The reaction exhibits good group tolerance, as well as highly selectivity to sulfinyl substitutions. This new protocol provides an expeditious and operationally simple procedure for C-S(O) bond construction. Preliminary bioactivity evaluation on selected products shows promising antifungal activities.

Keywords: Methylsulfoxidation, Tetrazole-amines, *tert*-butyl Nitrite, Methylsulfinyl-*1H*-tetrazole, Antifungal Activity.

The sulfur-containing functionalities have attracted tremendous attention owing to their massive applications in accessing naturally occurring molecules, bioactive synthetic compounds and pharmaceuticals.[1] Among which, organic sulfoxides are versatile motifs in various organic transformations, serving as directing groups, ligands or chiral auxiliaries in asymmetric reactions.[2] Moreover, appealing to organic and medicinal communities, the combination of *N*-heterocycles and sulfoxides makes up classes of fascinating synthetic intermediates, pesticides and drugs (Figure 1).

In the past decades, the introduction of sulfoxides has emerged as a flourishing research area. Of many established strategies, including latent selective oxidation,[3] nucleophilic substitution[4] and transition metal catalysis, [5] DMSO has been recognized as one of the most efficient and promising reagents for

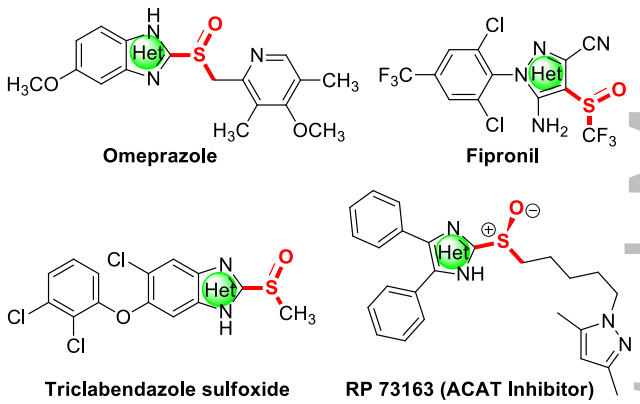
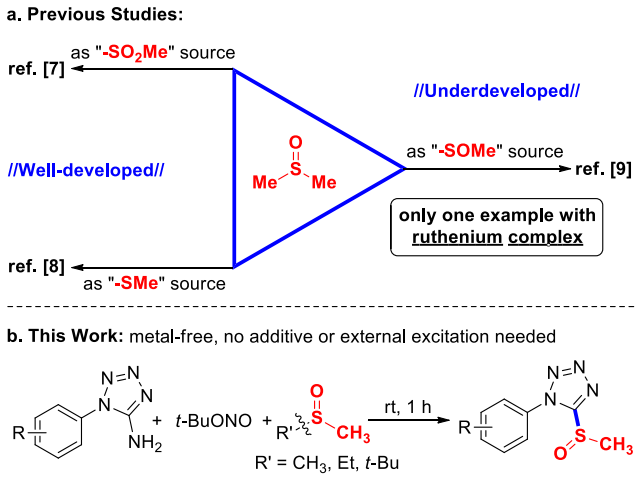


Figure 1 Examples of bioactive compounds bearing *N*-heterocycle and sulfoxide.

C(sp^2)-S bonds formation, in large measure due to its safe, cheap and eco-benign properties.[6] It has been well-configured in individually introducing methyl-sulfonyl[7] and thiomethyl groups[8] (Scheme 1, a), most often with either strong oxidants or transition metals. In sharp contrast, the remarkable advance made in utilizing DMSO as a "-SOMe" source is extremely rare so far. The challenge lies in redox cleavage of either Me-S(O) bonds, without further oxidation of the sulfinyl moiety in product. In 2016, Rastogi's group documented the only paper of methylsulfoxidation utilizing DMSO and pre-prepared (het)aryl diazonium salts *via* mild photoredox catalysis with ruthenium complexes.[9] Nevertheless, the synthetic usage of transition metals in pesticide and drug precursors brings on severe metal contaminants in organisms through biological

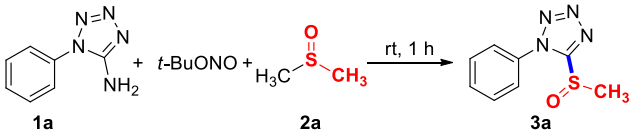
amplification, thus, it is highly desirable to make innovations with metal-free and step-economy strategy for this transformation. In this regard, from our continuing efforts on heterocyclic chemistry and C-X formation methodologies,[10] we report here the first methylsulfoxidation of tetrazole-amines with DMSO or methylsulfinyl precursors toward methylsulfinyl-1*H*-tetraozle derivatives, in particular without metal, additive or external excitation. In addition, the promising antifungal activities of selected methyl-sulfinyl-1*H*-tetraozles against phytopathogenic fungi are also presented.



Scheme 1 DMSO as sulfur functionality sources (a) and this work (b).

With 1-phenyl-1*H*-tetrazol-5-amine (**1a**) and DMSO as the model substrates, we discovered that the *in-situ* generation of diazonium salts from HBF_4 and $NaNO_2$ gave no adduct at all. Additives, ascorbic acid or iodine, rendered the reaction with moderate yields of 5-(methylsulfinyl)-1-phenyl-1*H*-tetrazole (**3a**) (entries 2-3). To our delight, further optimizations implied that the radical initiators are unnecessary. As shown in Table 1, reactions in acetone, dichloromethane, nitromethane and water were applicable, albeit less effective (entries 4-8). The methylsulfoxidation in neat DMSO delivered the adduct in a good yield of 85% within one hour (entry 9). To be noted, one equivalent of *t*-BuONO left most of the tetrazole-amine intact, which indicated that the excess amount of *t*-BuONO might play dual roles in this protocol (see details in mechanistic studies). Furthermore, considering the probable decomposition of diazonium intermediates to radicals upon light irradiation,[11] a parallel experiment in dark was performed, affording **3a** in a comparable yield of 84% (entry 12). The above optimal results collectively pointed to a novel additive-free, metal-free and step-economy protocol to access methyl-sulfinyl-1*H*-tetrazoles.

Table 1 Optimization of the reaction conditions.



1a 2a 3a

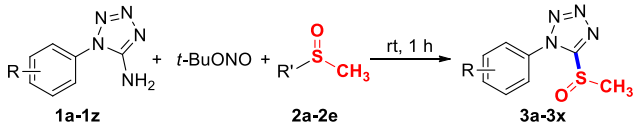
entry	variations (based on standard conditions[a])	yield (%)[b]
1	$HBF_4/NaNO_2$ instead of *t*-BuONO, 12 h	N.R.
2	ascorbic acid (0.3 eq.) as additive, 12 h	74
3	I_2 (0.5 eq.) as additive, 12 h	73
4	3 eq. DMSO, in acetone, 1 h	54
5	3 eq. DMSO, in CH_2Cl_2, 1 h	37
6	3 eq. DMSO, in CH_3NO_2, 1 h	47
7	3 eq. DMSO, in H_2O, 1 h	38
8	DMSO: H_2O (3:1), 1 h	23
9	**none**	**85**
10	30 min	52
11	1 eq. *t*-BuONO	25
12	in dark	84

[a] Standard conditions: 1-phenyl-1*H*-tetrazole-5-amine (**1a**, 0.3 mmol), *t*-BuONO (0.6 mmol), DMSO (**2a**, 2 mL), N_2, r.t., 1 h; N.R.= no reaction.
[b] Isolated yields.

Once determined the optimal conditions, general applicability of the protocol was investigated. The substrate scope of the methylsulfoxidation of tetrazole-amines was presented in Table 2. Generally, with respect to tetrazole-amines, both electron-rich and electron-deficient ones (**1a-1w**) participated in this reaction smoothly to furnish the corresponding adducts (**3a-3w**) in moderate to excellent yields. The methylsulfoxidations were remarkably sensitive to electron density of the substrates with a few exceptions. Strong electron-donating group, *para*- and *meta*-methoxy, impaired the efficiency to yields of 67% and 61%, respectively (entries 8-9). Other electron-rich ones, bearing *meta*-methyl, *para*-*tert*-butyl, 1-naphthyl, *para*-phenyl, proceeded much better with yields up to 97%. Meanwhile, halides substitutions at diverse positions, including -F, -Cl, -Br and -I, were well tolerated (entries 11-16), which could be efficiently expanded to dihalides as well (entries 17-19). It is worthy to mention that the protocol exhibited good tolerance to substrates with steric hindrance (entries 4, 6, 15, 17). Strong electron-deficient groups of ester (**1t**), trifluoromethyl (**1w**) delivered the target adducts with medium to good yields, ranging from 62% to 87%. More interestingly, cyanide group in **1v**, a common radical acceptor,[12] survived in the process leading to 80% yield of **3v**. Nitro group, a notorious group in radical chemistry, adversely inhibited the process (entry 24). With the aim of broadening the scope of this protocol, sulfinyl derivatives other than DMSO were evaluated. Deuterated DMSO (**2a'**) gave comparable yield with the template substrate (entry 25). Intriguingly, the C-S(O) bond cleavage of substrates (**2**) undertook with

highly selectivity, which is unprecedented and attractive. For instance, (methylsulfinyl)ethane (**2b**) and 2-methyl-2-(methyl-sulfinyl)propane (**2c**) gave the same product **3a**, with ethyl and *tert*-butyl moieties released, respectively. Otherwise, no sulfinyl adducts were obtained for phenyl-substituted substrates (**2d**, **2e**), affording exclusive diazonium salts.

Table 2 Substrates scopes.[a]

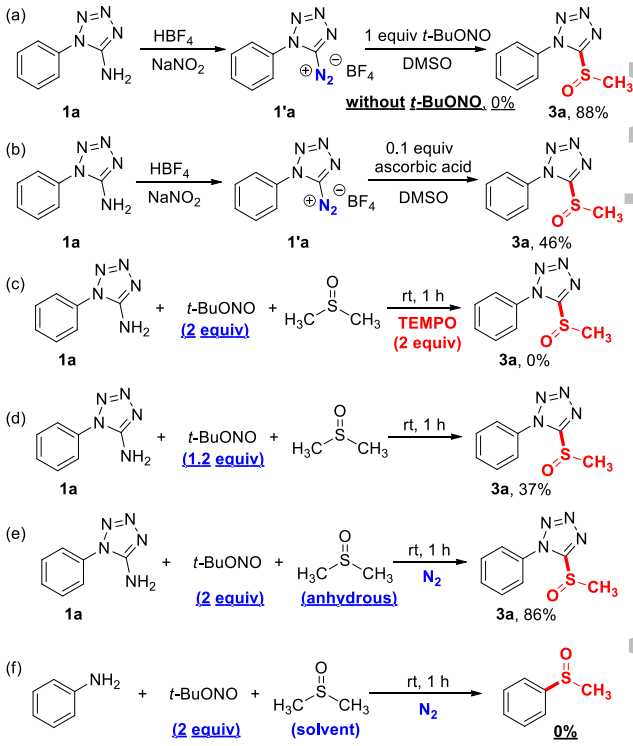


1a-1z **2a-2e** **3a-3x**

entry	R	R'/**2**	yield (**3**, %)[b]
1	H (**1a**)	CH_3 (**2a**)	85 (**3a**)
2	*p*-Methyl (**1b**)	CH_3 (**2a**)	56 (**3b**)
3	*m*-Methyl (**1c**)	CH_3 (**2a**)	97 (**3c**)
4	*o*-Methyl (**1d**)	CH_3 (**2a**)	65(**3d**)
5	*p*-tert-butyl (**1e**)	CH_3 (**2a**)	90(**3e**)
6	1-naphthyl (**1f**)	CH_3 (**2a**)	89 (**3f**)
7	*p*-phenyl (**1g**)	CH_3 (**2a**)	73 (**3g**)
8	*p*-methoxy (**1h**)	CH_3 (**2a**)	67 (**3h**)
9	*m*-methoxy (**1i**)	CH_3 (**2a**)	61 (**3i**)
10	*p*-F (**1j**)	CH_3 (**2a**)	78 (**3j**)
11	*p*-Cl (**1k**)	CH_3 (**2a**)	72(**3k**)
12	*m*-Cl (**1l**)	CH_3 (**2a**)	64 (**3l**)
13	*p*-Br (**1m**)	CH_3 (**2a**)	80 (**3m**)
14	*m*-Br (**1n**)	CH_3 (**2a**)	50 (**3n**)
15	*o*-Br (**1o**)	CH_3 (**2a**)	87 (**3o**)
16	*p*-I (**1p**)	CH_3 (**2a**)	51 (**3p**)
17	2,4-dichloro (**1q**)	CH_3 (**2a**)	52 (**3q**)
18	3,4-dichloro (**1r**)	CH_3 (**2a**)	81 (**3r**)
19	2-Cl, 4-F (**1s**)	CH_3 (**2a**)	59 (**3s**)
20	4-isopropoxy-carbonyl (**1t**)	CH_3 (**2a**)	72 (**3t**)
21	4-ethoxy-carbonyl (**1u**)	CH_3 (**2a**)	87 (**3u**)
22	*p*-CN (**1v**)	CH_3 (**2a**)	80 (**3v**)
23	*p*-CF_3 (**1w**)	CH_3 (**2a**)	62 (**3w**)
24	*p*-NO_2 (**1x**)	CH_3 (**2a**)	0 (**3x**)
25	H (**1a**)	d^6-DMSO(**2a'**)	84 (**3a'**)
26	H (**1a**)	Ethyl (**2b**)	61 (**3a**)
27	H (**1a**)	*t*-Bu (**2c**)	54 (**3a**)
28	H (**1a**)	phenyl (**2d**)	0 (**3a**)
29[c]	H (**1a**)	sulfinyldibenzene (**2e**)	0

[a] Reaction conditions: 1*H*-tetrazole-amine (**1**, 0.3 mmol), *t*-BuONO (0.6 mmol), sulfoxide source (**2**, 2 mL), r.t., 1 h;
[b] Isolated yields;
[c] In 2 mL acetone.

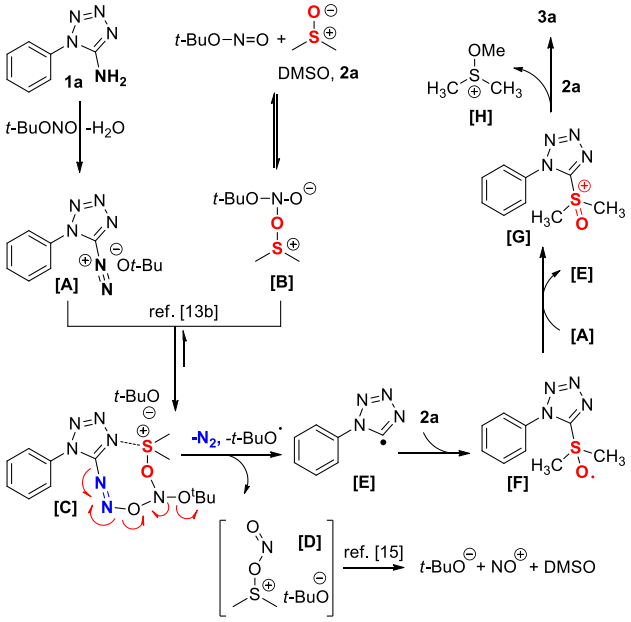
Taking into account that additional radical initiators had been avoided in our protocol, key control experiments were then conducted to clarify the mechanism. Firstly, the proposed common diazonium salt (**1'a**) was pre-prepared using $HBF_4/NaNO_2$, which reacted smoothly with 1 equivalents *tert*-butyl nitrite and DMSO in 88% yield (Scheme 2, eq. a). However, no adduct was detected in the absence of *tert*-butyl nitrite. Secondly, **1'a** and DMSO could be transformed into **3a** in 46% yield while being treated with 0.1 equiv of ascorbic acid (eq. b), which is a well-known radical initiator.[13] A radical inhibition experiment with 2 equivalents of TEMPO (2,2,6,6-tetramethyl-1-piperidinyloxy) entirely quenched the reaction (eq. c). As a comparison, 1.2 equivalents of *tert*-butyl nitrite were applied under the standard conditions. The methylsulfoxidation occurred as well, albeit furnishing comparatively lower yield (eq. d, 37% vs 85%). The reaction in equation e with anhydrous DMSO in a nitrogen atmosphere clearly demonstrated that the oxygen-atom sources came from DMSO instead of water or air. Eventually, a non-heteroaromatic substrate, aniline, was found to be ceased at the diazonium salt stage, giving no corresponding product (eq. f). The above results collectively came to conclusions as follows: 1) the excess *tert*-butyl nitrite would play a key role in generating aryl radical intermediates, probably with similar mechanism to that of ascorbic acid; 2) Potential interactions among tetrazole-amine, *tert*-butyl nitrite and DMSO might exist in a transition state.



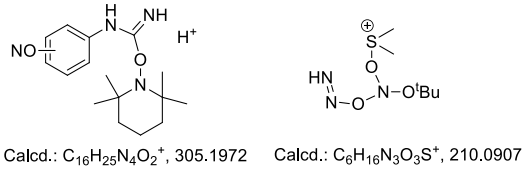
Scheme 2 Control experiments.

Based on the experimental facts and previous reports,[9,14] a proposed mechanism for the metal-free methylsulfoxidation is illustrated in Scheme 3. Tetrazol-amine (**1a**) is *in-situ* converted into diazonium salt **[A]** upon the treatment of *t*-BuONO. Meanwhile, nucleophilic attack of DMSO to *tert*-

butyl nitrite gives an adduct **[B]**, though it is a mechanistically reversible process. After which, the diazonium salt **[A]** interacts with **[B]** to afford a diazoether intermediate **[C]** *via* nucleophilic attack of oxygen anion to diazonium cation, similarly to the performance of ascorbic acid[13b] (Fragments decomposed from **[C]** were trapped by TEMPO and confirmed by HR-MS, see details in SI). It is noted that the proposed transition state **[C]** might be stabilized by an eight-membered cation-electron pairs interaction between the sulphur cation and tetrazol moiety, otherwise, the reaction would reverse to the starting materials (refer to the result of aniline in Scheme 2, eq. f). The proposed transition state can also be rationalized by the results of substrates **2d** and **2e**, since the existence of aryl substitutions would delocalize the sulfur cation, thus labilizing the cation-electron pairs. Subsequently, the diazoether **[C]** undergoes a homolytic cleavage to furnish an aryl radical **[E]** with the release of nitrogen, *t*-BuO radical and a residue **[D]**[15]. The key hetero-aryl radical intermediate **[E]** traps DMSO to produce sulfinyl radical **[F]**. Then the diazonium salt **[A]** oxidizes **[F]** into a sulfoxide cation **[G]**.[9] Eventually transferring methyl group to the weakly nucleophilic DMSO leads to the final product **3a**. *t*-BuO anion, decomposed from **[D]**, abstracts hydrogen from **[H]** to give *t*-BuOH, which can be observed by monitoring with GC.



Fragments Detected by HR-MS (Scheme 2, eq. c):



Calcd.: $C_{16}H_{25}N_4O_2^+$, 305.1972
Found: 305.1971

Calcd.: $C_6H_{16}N_3O_3S^+$, 210.0907
Found: 210.0903

Scheme 3 Proposed mechanism.

Finally, the antifungal activities of selected compounds were tested against four phytopathogenic fungi (*Botrytis cinerea*, *Alternaria solani*, *Rhizoctorzia solani*, *Alternaria leaf spot*) using mycelia growth inhibitory rate methods, with Boscalid used as the positive control (see details in the SI).[16] The compounds were individually dissolved in DMF and mixed with sterile molten PDA to obtain final concentrations of 5 μg/mL. Among which, the EC_{50} values of compounds possessing good activity were further evaluated using different concentrations by diluting the corresponding solution. Preliminary bioassay results indicated that some of the compounds exhibited potential antifungal activities at the concentration of 5 μg/mL (in SI). It was noticed that the EC_{50} value of compound **3r**, bearing 3,4-dichloro substitutions, was determined as low as 1.3701 μg/ mL against R. solani, which exhibited competitive activity to that of the positive control (Boscalid EC_{50} = 2.9767 μg/mL). Besides, compound **3k** (EC_{50} = 2.5439 μg/mL) represented acceptable antifungal activity.

In summary, we disclosed, for the first time, a *tert*-butyl nitrite mediated methylsulfoxidation of tetrazole-amines in neat DMSO or methylsulfinyl derivatives. The reaction tolerated various functional groups, furnishing a novel series of methylsulfinyl-1*H*-tetrazoles with moderate to excellent yields, as well as highly selectivity to sulfinyl substitutions. This new methodology provides an expeditious and operationally simple procedure of C-S(O) bond construction. Mechanistic investigations suggested that *tert*-butyl nitrite played dual roles in diazotization and synergistic generation of aryl radical intermediate with the aid of DMSO and substrates. Preliminary bioactivity evaluation on selected compounds against four phytopathogenic fungi exemplified their promising antifungal activities. Further synthetic applications and bioactivity test are ongoing in our laboratory.

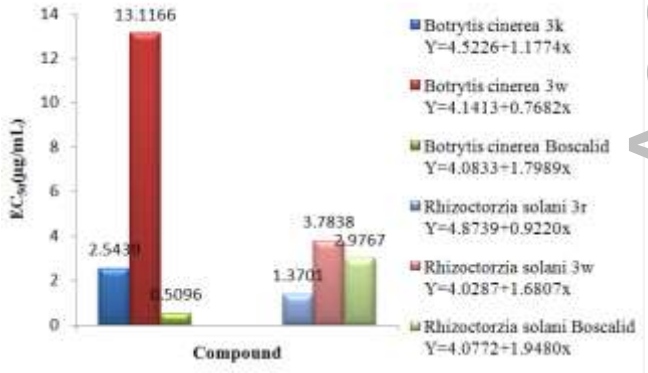


Figure 2. EC_{50} values of selected compounds and Boscalid.

Experimental Section

Typical Procedures for the Methylsulfoxidation of Tetrazole-amines with DMSO. 1-phenyl-1*H*-tetrazol-5-amine (**1a**, 0.3 mmol, 1.0 equiv) and degassed DMSO (**2a**, 2 mL) was added to a 5 mL thick-walled pressure pipe under nitrogen atmosphere, followed by the addition of *t*-BuONO (2.0 equiv). The reaction mixture was stirred for 1 hour at room temperature and monitored by TLC. After extracting and removing the volatiles under vacuum, the residues were purified by flash chromatography (petroleum ether/ EtOAc = 1:1, R_f = 0.35-0.45) on silica gel to give the desired product **3a** in 85% yield, as a yellow solid. The procedure was applied for entries 1-28, Table 1 in the main text.

Acknowledgements

We are grateful for financial supports from the Fundamental Research Funds for the Central Universities (NJAU, Grant No. KYTZ201604), the Foundation Research Project of Jiangsu Province (The Natural Science Foundation, No.BK20141359).

References and Notes

[1] For selected papers, see: a) L. J. Macpherson, B. H. Geierstanger, V. Viswanath, M. Bandell, S. R. Eid, S. Hwang, A. Patapoutian, *Curr. Biol.* **2005**, *15*, 929. b) A. A. Salama, M. Aboulaila, M. A. Terkawi, A. Mousa, A. Al-Sify, M. Allaam, A. Zaghawa, N. Yokoyama, I. Igarashi, *Parasitol. Res.* **2014**, *113*, 275. c) T. Nohara, Y. Fujiwara, T. Ikeda, K. Yamaguchi, H. Manabe, K. Murakami, M. Ono, D. Nakano, J. Kinjo, *Chem. Pharm. Bull.* **2014**, *62*, 477. d) T. Nohara, Y. Fujiwara, Y. Komoto, Y. Kondo, T. Saku, K. Yamaguchi, Y. Komohara, M. Takeya, *Chem. Pharm. Bull.* **2015**, *63*, 117.

[2] a) M. Numata, Y. Aoyagi, Y. Tsuda, T. Yarita, A. Takatsu, *Anal. Chem.* **2007**, *79*, 9211. b) K. Padala, M. Jeganmohan, *Chem. Commun.* **2014**, *50*, 14573. c) J. Miao, N. G. J. Richards, H. Ge, *Chem. Commun.* **2014**, *50*, 9687. d) K. Nobushige, K. Hirano, T. Satoh, M. Miura, *Org. Lett.* **2014**, *16*, 1188. e) V. Bizet, L. Buglioni, C. Bolm, *Angew. Chem., Int. Ed.* **2014**, *53*, 5639. f) A. J. Eberhart, H. J. Shrives, E. Álvarez, A. Carrër, Y. Zhang, D. J. Procter, *Chem. Eur. J.* **2015**, *21*, 7428. g) S. K. Aithagani, S. Dara, G. Munagala, H. Aruri, M. Yadav, S. Sharma, R. Vishwakarma, P. P. Singh, *Org. Lett.* **2015**, *17*, 5547. h) H. Lebel, H. Piras, M. Borduy, *ACS Catal.* **2016**, *6*, 1109. i) J. A. Fernandez-Salas, A. J. Eberhart, D. J. Procter, *J. Am. Chem. Soc.* **2016**, *138*, 790. j) M. C. Carreño, G. Hernández-Torres, M. Ribagorda, A. Urbano, *Chem. Commun.* **2009**, 6129. k) J. Chen, J.-M. Chen, F. Lang, X. Zhang, L. Cun, J. Zhu, J. Deng, J. Liao, *J. Am. Chem. Soc.* **2010**, *132*, 4552. l) F. Xue, D. Wang, X. Li, B. Wan, *J. Org. Chem.* **2012**, *77*, 3071. m) L. Du, P. Cao, J. Xing, Y. Lou, L. Jiang, L. Li, J. Liao, *Angew. Chem., Int. Ed.* **2013**, *52*, 4207. n) G. Sipos, E. E. Drinkel, R. Dorta, *Chem. Soc. Rev.* **2015**, *44*, 3834. o) B. M. Trost, M. Rao, *Angew. Chem., Int. Ed.* **2015**, *54*, 5026.

[3] a) J. Legrose, J. R. Dehli, C. Bolm, *Adv. Synth. Catal.*, **2005**, *347*, 19. b) K. P. Volcho, N. F. Salakhutdinov, *Russ. Chem. Rev.*, **2009**, *78*, 457. c) G. E. O'Mahony, Kelly P., S. E. Lawrence, A. R. Maguire, *ARKIVOC*, **2011**, *1*, 1. d) K. P. Bryliakov, E. P. Talsi, *Curr. Org. Chem.*, **2012**, *16*, 1215; e) Y.-L. Hu, D. Fang, R. Xing, *RSC Adv.*, **2014**, *4*, 51140.

[4] a) Z. Han, D. Krishnamurthy, P. Q. Grover, K. Fang, X. Su, H. S. Wilkinson, Z.-H. Lu, D. Magiera, C. H. Senanayake, *Tetrahedron*, **2005**, *61*, 6386. b) J. Wei, Z. Sun, *Org. Lett.*, **2015**, *17*, 5396.

[5] a) E. Bernoud, D. G. Le, X. Bantreil, G. Prestat, D Madec, G. Poli, *Org. Lett.*, **2010**, *12*, 320. b) T. Jia; A. Bellomo, S. Montel, M. Zhang, K. El Baina; B. Zheng, P. J. Walsh, *Angew. Chem., Int. Ed.*, **2014**, *53*, 260. c) F. Gelat, J.-F. Lohier, A.-C. Gaumont, S. Perrio, *Adv. Synth. Catal.*, **2015**, *357*, 2011. d) T. Jia, M. Zhang, H. Jiang, C. Y. Wang, P. J. Walsh, *J. Am. Chem. Soc.*, **2015**, *137*, 13887.

[6] X.-F. Wu, K. Natte, *Adv. Synth. Catal.* **2016**, *358*, 336.

[7] a) G.-Q. Yuan, J.-H. Zheng, X.-F. Gao, X.-W. Li, L,-B. Huang, H.-J. Chen, H.-F. Jiang, *Chem. Commun.*, **2012**, *48*, 7513. b) Y.-J. Jiang, T.-P. Loh, *Chem. Sci.*, **2014**, *5*, 4939. c) X.-F. Gao, X.-J. Pan, J. Gao, H.-W. Huang, G.-Q. Yuan, Y.-W. Li, *Chem. Commun*., **2015**, *51*, 210. d) A.-L. Shao, M. Gao, S.-T. Chen, T. Wang, A.-W. Lei, *Chem. Sci.*, **2017**, *8*, 2175.

[8] a) G. Yin, B. Zhou, X. Meng, A. Wu, Y. Pan, *Org. Lett.*, **2006**, *8*, 2245. b) L. Chu, X. Yue, F.-L. Qing, *Org. Lett.*, **2010**, *12*, 1644. c) F. Luo, C. Pan, L. Li, F. Chen, J. Cheng, *Chem. Commun.*, **2011**, *47*, 5304. d) C. Dai, Z. Xu, F. Huang, Z. Yu, Y.-F. Gao, *J. Org. Chem.*, **2012**, *77*, 4414. e) P. J. A. Joseph, S. Priyadarshini, M. L. Kantam, B. Sreedhar, *Tetrahedron*, **2013**, *69*, 8276. f) F.-L. Liu, J.-R. Chen, Y.-Q. Zou, Q. Wei, W.-J. Xiao, *Org. Lett.*, **2014**, *16*, 3768. g) W. Zhao, P. Xie, Z. Bian, A. Zhou, H. Ge, M. Zhang, Y. Ding, L. Zheng, *J. Org. Chem.*, **2015**, *80*, 9167. h) Y. Xu, T. Cong, P. Liu, P. Sun, *Org. Biomol. Chem.*, **2015**, *13*, 9742. i) P. Sharma, S. Rohilla, N. Jain, *J. Org. Chem.*, **2015**, *80*, 4116. j) S. Devari, A. Kumar, R. Deshidi, B. A. Shah, *Chem. Commun.*, **2015**, *51*, 5013. k) X. Gao, X. Pan, J. Gao, H. Jiang, G. Yuan, Y. Li, *Org. Lett.*, **2015**, *17*, 1038. l) H.-Y. Li, L.-J. Xing, M.-M. Lou, H. Wang, R.-H. Liu, B. Wang, *Org. Lett.*, **2015**, *17*, 1098. m) K. Ghosh, S. Ranjit, D. Mal, *Tetrahedron Lett.*, **2015**, *56*, 5199. n) Z. An, Y. She, X Yang, X. Pang, R. Yan, *Org. Chem. Front.* **2016**, *3*, 1746. o) J.-G. Sun, W.-Z. Weng, P. Li, B. Zhang, *Green Chem.* **2017**, *19*, 1128-1133.

[9] M. M. D. Pramanik, N. Rastogi, *Chem. Commun.* **2016**, *52*, 8557.

[10] a) W.-C. Yang, P. Dai, K. Luo, L. Wu, *Adv. Synth. Catal.* **2016**, *358*, 3184. b) K. Luo, Y.-Z. Chen, W.-C. Yang, J. Zhu, L. Wu, *Org. Lett.* **2016**, *18*, 452. c) M. Mao, L. Zhang, Y.-Z. Chen, J. Zhu, L. Wu, *ACS Catal.* **2017**, *7*, 181. d) L. Zhang, J. Zhu, J. Ma, L. Wu, W.-H. Zhang, *Org. Lett.* **2017**, DOI: 10.1021/acs.orglett.7b03052. e) J. Zhu, W.-C. Yang, X.-D. Wang, L. Wu, *Adv. Synth. Catal.* **2017**, DOI: 10.1002/adsc.201701194.

[11] M. Sc. D. P. Hari, B. König, *Angew. Chem., Int. Ed.* **2013**, *52*, 4734.

[12] For selected examples of cyanide group as radical acceptor, see: a) Y. Yamamoto, D. Matsumi, R. Hattori, K. Itoh, *J. Org. Chem.* **1999**, *64*, 3224. b) J. Streuff, M. Feurer, P. Bichovski, G. Frey, U. Gellrich, *Angew. Chem. Int. Ed.* **2012**, *51*, 8661. c) J. Zheng, Y. Zhang, D. Wang, S. Cui, *Org. Lett.* **2016**, *18*, 1768. d) Y.-Y. Han, H. Jiang, R. Wang, S. Yu, *J Org. Chem.* **2016**, *81*, 7276. e) W.-C. Yang, P. Dai, K. Luo, Y.-G. Ji, L. Wu, *Adv. Synth. Catal.* **2017**, *359*, 2390.

[13] a) F. P. Crisóstomo, T. Martín, R. Carrillo, *Angew. Chem., Int. Ed.* **2014**, *53*, 2181. b) B. Majhi, D. Kundu, B. C. Ranu, *J. Org. Chem.* **2015**, *80*, 7739.

[14] D.Qiu, H. Meng, L. Jin, S. Wang, S. B. Tang, X. Wang, F. Y. Mo, Y. Zhang, J. B. Wang, *Angew. Chem., Int. Ed.* **2013**, *52*, 11581.

[15] G. A. Olah, B. G. B. Gupta, S. C. Narang, *J. Am. Chem. Soc.* **1979**, *101*, 5317.

[16] Y.-F. Liu, Z.-Y, Chen, T.B. Ng, J. Zhang, M.-G. Zhou, F.-P. Song, F. Lu, Y.-Z. Liu, *Peptides*, **2007**, *28*, 553.

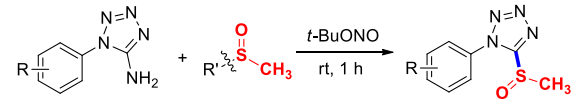
10.1002/adsc.201701364

COMMUNICATION

Tert-Butyl Nitrite Mediated Expeditious Methylsulfoxidation of Tetrazole-amines with DMSO: Metal-free Synthesis of Antifungal Active Methylsulfinyl-*1H*-tetrazole Derivatives

Adv. Synth. Catal. **2017**, *Volume*, Page – Page

Peng Dai, Kai Luo, Xiang Yu, Wen-Chao Yang, Lei Wu* and Wei-Hua Zhang*



- **The First Methylsulfoxidation with DMSO under Metal-free Conditions**
- **Expeditous and Operationally Simple, No Additive or Excitation Needed**
- **Broad Substrate Scopes with Highly Selectivity, 27 examples**
- **Antifungal Inhibitory Rate (*Rhizoctorzia solani*): 3r, 5 ppm, 68.1%; EC_{50}: 1.3701 ug/mL**