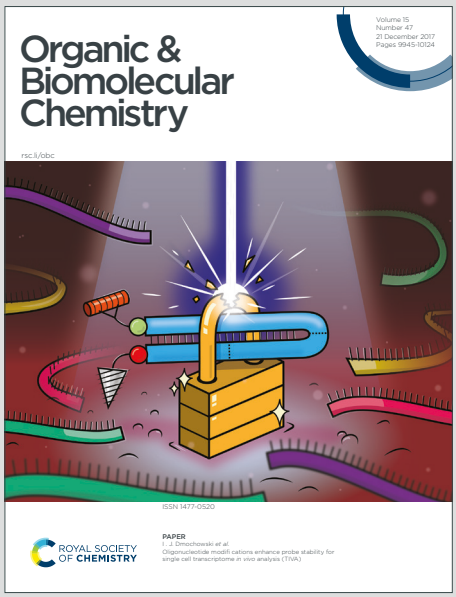
Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: N. Yang and G. Yuan, *Org. Biomol. Chem.*, 2019, DOI: 10.1039/C9OB01200A.



ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C9OB01200A

Journal Name

ARTICLE

One-pot Synthesis of 1,3,4-Oxadiazol-2(3*H*)-ones with CO_2 as C1 Synthon Promoted by Hypoiodite

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

Na Yang, and Gaoqing Yuan*

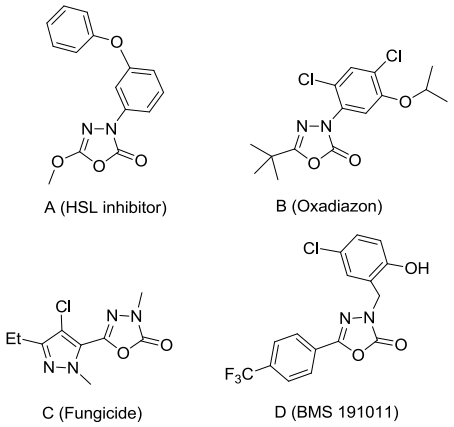
A convenient and efficient route has been developed to synthesize 1,3,4-oxadiazol-2(3*H*)-ones from CO_2, hydrazines and aryl or aliphatic aldehydes. Promoted by hypoiodite (IO^-) generated in situ from KI and oxidant TBHP, the one-pot synthesis could proceed smoothly to afford the desired products in moderate to high yields. Mechanism studies revealed that nitrile imine was an important intermediate in this transformation. Notably, a commercial herbicide Oxadiazon could be successfully synthesized by this route.

Introduction

In 2010, Ishihara, Uyanik and co-workers reported that quaternary ammonium hypoiodite generated in situ from ammonium iodide (R_4NI) and oxidant hydrogen peroxide (H_2O_2) could induce enantioselective oxidative cycloetherification of ketophenols.[1] Afterwards, some researchers focused on the studies of the hypoiodite and have achieved many other interesting transformations promoted by the in situ generated hypoiodite from iodides and oxidant H_2O_2 or TBHP.[2] These non-radical catalytic processes of iodides attracted our attention as well.

Carbon dioxide as a green, abundant, cheap and renewable C1 synthon has been widely used to synthesize many kinds of value-added chemicals over the decades.[3] For example, CO_2 could react with amines and electrophiles to generate carbamates,[4] or react with unsaturated hydrocarbons[5,6] or epoxides[7] to form cyclic or chain carbonyl-containing products. Matsubara and co-workers revealed that CO_2 could also react with nitrile imines through 1,3-dipolar cycloaddition reactions to synthesize 1,3,4-oxadiazolin-2-ones.[8]

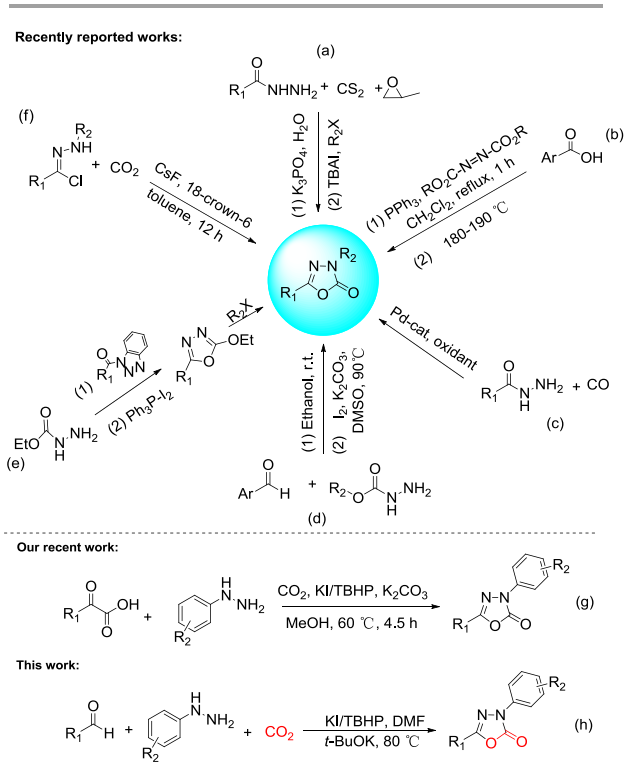
1,3,4-Oxadiazol-2(3*H*)-one core is an important scaffold in pharmaceutical chemistry.[9] Some compounds bearing 1,3,4-oxadiazol-2(3*H*)-one skeleton have been proved to have good pharmaceutical activities and biological activities. For instance, some of substituted 1,3,4-oxadiazol-2(3*H*)-ones have been used as hormone-sensitive lipase (HSL) inhibitor (Scheme 1, A), herbicide (Oxadiazon) (Scheme 1, B), fungicide (Scheme 1, C), or opener of large-conductance Ca^{2+}-activated potassium (Maxi-K) channels (Scheme 1, D).[10]



Scheme 1 Structures of some representative substituted 1,3,4-oxadiazol-2(3*H*)-ones.

Many methods have been developed for the synthesis of substituted 1,3,4-oxadiazol-2(3*H*)-ones.[11–13] And recently, some new and efficient methods have been reported. As shown in Scheme 2a, 3,5-disubstitued-1,3,4-oxadiazole-2(3*H*)-ones could be obtained via four-component reactions of acylhydarazines with carbon disulfide, propylene oxide and organic halides.[14] Under solvent-free conditions at 180 – 190 ℃, the reactions of carboxylic acids with Mitsunobu reagents could generate substituted 1,3,4-oxadiazol-2(3*H*)-ones as well (Scheme 2b).[15] Moreover, 1,3,4-oxadiazol-2(3*H*)-ones could be synthesized through palladium-catalyzed oxidative carbonylation of hydrazides with CO (Scheme 2c),[16] or by I_2-mediated reactions of methyl/benzyl carbazates with aldehydes (Scheme 2d).[17] 1,3,4-Oxadiazol-2(3*H*)-ones also could be prepared via the one-pot sequential *N*-acylation/dehydrative cyclization between ethyl carbazate and *N*-acylbenzotriazoles in the presence of Ph_3P/I_2 (Scheme 2e),[18] or through 1,3-dipolar cycloaddition of nitrile imines with

Key Laboratory of Functional Molecular Engineering of Guangdong Province, School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou, P.R. China. E-mail: gqyuan@scut.edu.cn
Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x



Scheme 2 Different methods for the synthesis of substituted 1,3,4-oxadiazol-2(3*H*)-ones.

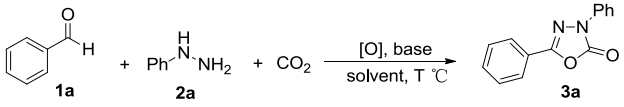
carbon dioxide (Scheme 2f).[19] Although much progress has been made in the synthesis of substituted 1,3,4-oxadiazol-2(3*H*)-ones, there still exist drawbacks in some synthetic processes. For example, some synthetic methods involved multi-step-reaction, limited substrate scope, or hazardous phosgene and expensive transition metal catalysts. Therefore, to develop efficient and simple method for the synthesis of substituted 1,3,4-oxadiazol-2(3*H*)-ones remains highly desirable. In our previous investigations,[20a] we developed a convenient and efficient electrochemical method to synthesize 1,3,4-oxadiazol-2(3*H*)-ones from CO_2, aryl hydrazines and paraformaldehyde. However, this electrochemical route was only efficient in the synthesis of mono-substituted 1,3,4-oxadiazol-2(3*H*)-ones with paraformaldehyde, which greatly limited its practical applications. Recently, we disclosed KI-catalyzed synthesis of 1,3,4-oxadiazol-2(3*H*)-ones from aryl hydrazines, *α*-oxocarboxylic acids in the presence of CO_2 (Scheme 2g).[20b] As part of our continuing work, herein we report in situ generated hypoiodite induced one-pot synthesis of 1,3,4-oxadiazol-2(3*H*)-ones from CO_2, aldehydes and hydrazines under mild conditions (Scheme 2h).

The present synthetic route greatly broadens the scope of aldehydes, which is not only suitable for substituted aryl aldehydes but also applicable to aliphatic aldehydes. 5-Alkyl-1,3,4-oxadiazol-2(3*H*)-ones can also be obtained in this work, while only 3,5-diaryl-1,3,4-oxadiazol-2(3*H*)-one products were synthesized in our previous work.[20b] In addition, the raw material aldehydes are more easily available and cheaper than *α*-oxocarboxylic acids. Moreover, it is remarkable that this synthetic route can be successfully applied to synthesize a commercial herbicide Oxadiazon, demonstrating its potential applications.

Results and discussion

We chose benzaldehyde (**1a**), phenylhydrazine (**2a**) and CO_2 as model substrates to explore reaction conditions in initial studies. The results were shown in Table 1. In the presence of KI catalyst, *t*-butyl hydroperoxide (TBHP) oxidant and *t*-BuOK base, the reaction was conducted at 80 ℃ for 8 h to give desired product **3a** in 38% yield when methanol was used as the solvent (entry 1). Encouraged by this result, we further tested other solvents such as CH_3CN, DMSO and DMF (entries 2–4). The results indicated that DMF was the most suitable solvent for the reaction, affording **3a** in 84% isolated yield (entry 4). With DMF used as the solvent, the effect of various bases on this reaction was then examined. The yields of **3a** became unsatisfactory (entries 5–8) when *t*-BuOK was

Table 1 Optimization of reaction conditions[a]



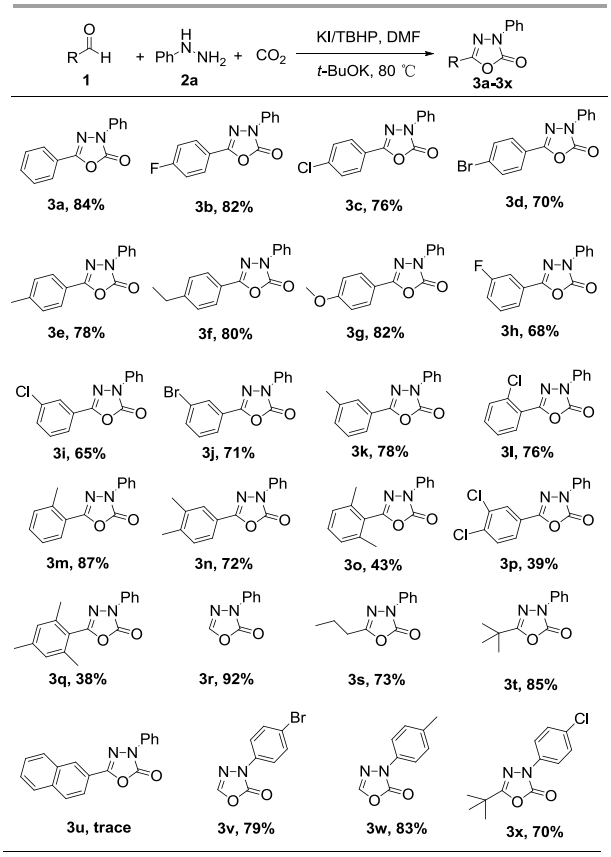
Entry	Solvent	Catalyst	[O]	Base	T (℃)	Yield[b] (%)
1	MeOH	KI	TBHP	*t*-BuOK	80	38
2	MeCN	KI	TBHP	*t*-BuOK	80	17
3	DMSO	KI	TBHP	*t*-BuOK	80	trace
4	DMF	KI	TBHP	*t*-BuOK	80	89(84)[c]
5	DMF	KI	TBHP	Et_3N	80	49
6	DMF	KI	TBHP	DBU	80	38
7	DMF	KI	TBHP	K_2CO_3	80	32
8	DMF	KI	TBHP	Cs_2CO_3	80	46
9	DMF	NH_4I	TBHP	*t*-BuOK	80	72
10	DMF	*n*-Bu_4NI	TBHP	*t*-BuOK	80	82
11	DMF	NaI	TBHP	*t*-BuOK	80	77
12	DMF	KBr	TBHP	*t*-BuOK	80	6
13	DMF	KCl	TBHP	*t*-BuOK	80	trace
14	DMF	-	TBHP	*t*-BuOK	80	n. r.[d]
15	DMF	KI	TBHP	*t*-BuOK	60	13
16	DMF	KI	TBHP	*t*-BuOK	100	79
17	DMF	KI	DTBP	*t*-BuOK	80	trace
18	DMF	KI	H_2O_2	*t*-BuOK	80	trace

[a] Reaction conditions: benzaldehyde **1a** (0.5 mmol), phenylhydrazine **2a** (0.5 mmol), CO_2 (2 MPa), KI (0.2 equiv), TBHP (3.0 equiv), base (2.0 equiv), solvent (5 mL), 8 h. [b] Yield was analyzed by GC-MS with *n*-dodecane as an internal standard. [c] Isolated yield. [d] No reaction.

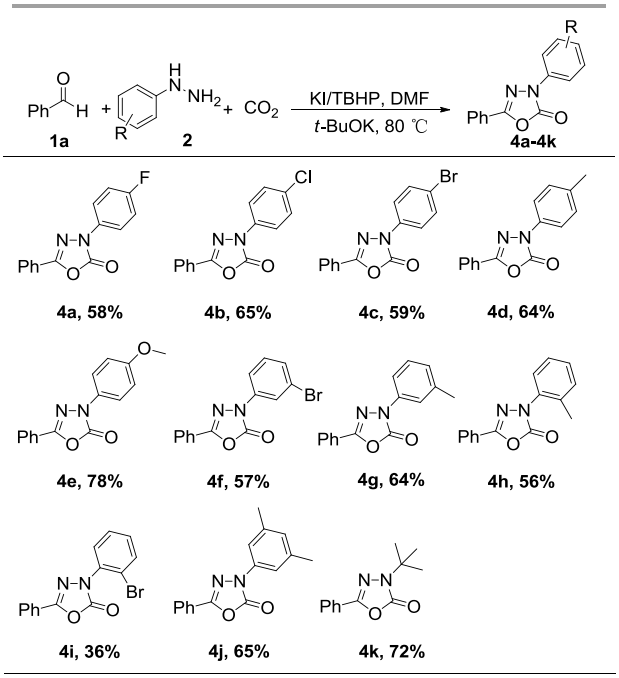
replaced with Et_3N, DBU, K_2CO_3 and Cs_2CO_3, respectively. Catalysts were further investigated (entries 9–14). It was found that iodides (e.g., NH_4I, *n*-Bu_4NI and NaI) were more efficient than bromide (KBr) or chloride (KCl). In the absence of any iodide catalysts, the product **3a** was not detected at all (entry 14). Further studies demonstrated that temperature either lower or higher than 80 ℃ was unfavorable for the transformation (entries 15 and 16). For oxidants, di-tert-butyl peroxide (DTBP) or H_2O_2 was proved to be ineffective for the reaction (entries 17 and 18), which might be related to the different active species formed by oxidation of I^- ions. In the H_2O_2 case, the oxidative decomposition of H_2O_2 might proceed preferentially at high temperature so that the transformation was prohibited, while TBHP could oxidize I^- ions to generate IO^- ions which could effectively promote this transformation.[21] The details would be discussed in the reaction mechanism studies.

Based on the optimized conditions, we further examined the scope of aldehydes, and the results were shown in Scheme 3. **A** series of *para*-substituted benzaldehydes, including with the electron-withdrawing groups (fluoro, chloro, bromo) and the electron-donating groups (methyl, ethyl), could be converted into the desired products in good yields (**3b**–**3g**). Furthermore, the *meta*- and *ortho*-substituted benzaldehydes could generate the corresponding products in moderate to good yields as well (**3h–3m**). The *poly*-substituted benzaldehydes were also able to be transformed into the 1,3,4-oxadiazol-2(3*H*)-one products smoothly (**3n–3q**). Notably, alkyl aldehydes such as formaldehyde, *n*-butylaldehyde, and pivaldehyde adapted the transformation well, providing the desired products in 92%, 73%, and 85% yields, respectively. These experimental results demonstrated that this synthetic route was applicable to aromatic aldehydes as well as aliphatic aldehydes. However, *β*-naphthaldehyde was not able to accomplish this reaction effectively (**3u**). In addition, aliphatic aldehydes could also react with substituted phenylhydrazine to form the target products smoothly (**3v–3x**).

The scope of hydrazines was also examined (Scheme 4). A variety of hydrazines could be transformed smoothly through this process. Phenylhydrazines bearing electron-withdrawing groups on *para*-position afforded the corresponding products in moderate yields (**4a–4c**), while the para-substituted phenylhydrazines with electron-donating ones gave slight higher yields of 1,3,4-oxadiazol-2(3*H*)-one products (**4d** and **4e**). The *meta*- and *ortho*-substituted phenylhydrazines could successfully generate the desired products in moderate to high yields as well (**4f–4i**). Moreover, the dimethyl-substituted phenylhydrazine could be converted to the product **4j** in 65% yield. Aliphatic hydrazine such as *tert*-butyl hydrazine could also be transformed to the target product smoothly (**4k**).



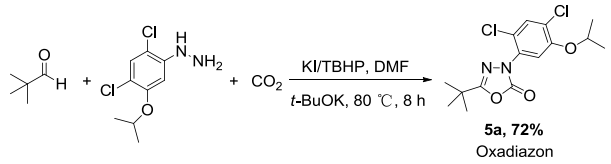
Scheme 3 Scope of various aldehydes. Reaction conditions: aldehydes **1a–1x** (0.5 mmol), phenylhydrazine **2a** (0.5 mmol), CO_2 (2 MPa), KI (0.2 equiv.), TBHP (3.0 equiv.), *t*-BuOK (2.0 equiv.), DMF (5 mL), 8 h. Isolated yields.



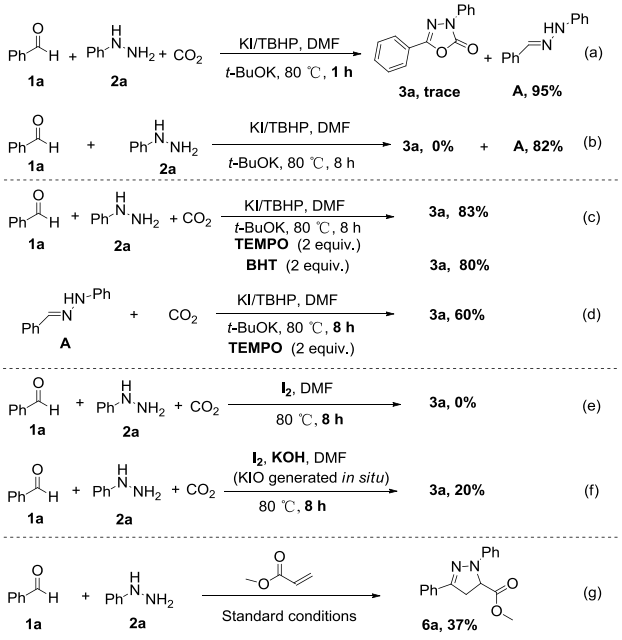
Scheme 4 Scope of hydrazine derivatives. Reaction conditions: benzaldehyde **1a** (0.5 mmol), hydrazine derivatives **2a–2k** (0.5 mmol), CO_2 (2 MPa), KI (0.2 equiv.), TBHP (3.0 equiv.), *t*-BuOK (2.5 equiv.), DMF (5 mL), 8 h. Isolated yields.

Unfortunately, hydrazine hydrate or phenylsulfonyl hydrazide as the substrate could not be converted into the corresponding 1,3,4-oxadiazol-2(3*H*)-one products under the present conditions.

With easily accessibility of raw material and high efficiency, the synthesis route provides a feasible access to valuable compounds containing 1,3,4-oxadiazol-2(3*H*)-one structure. In particular, we successfully synthesized the commercial herbicide Oxadiazon in 72% yield through this route (Scheme 5).



Scheme 5 Synthesis of Oxadiazon.

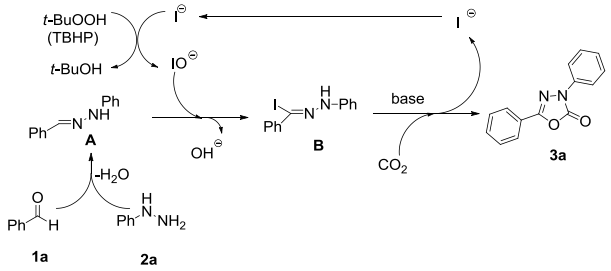


Scheme 6 Control Experiment.

Several control experiments were further conducted to explore the reaction mechanism. When the reaction processed for 1 h, a large amount of product 1-benzylidene-2-phenylhydrazine (**A**) could be observed and only a trace amount of **3a** was detected (Scheme 6a). This meant that benzaldehyde (**1a**) could easily react with phenylhydrazine (**2a**) to form the intermediate A under the present conditions, and **A** might be an important intermediate in this transformation. Without CO_2, the product **3a** could not be detected (Scheme 6b), which indicated that CO_2 was essential for the formation of 1,3,4-oxadiazol-2(3*H*)-ones. When 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO, 2.0 equiv.) or 2,6-di-tert-butyl-4-methylphenol (BHT, 2.0 equiv.) was added into the reaction system, only a slight change in the yield of **3a** was observed (Scheme 6c). The radical scavenger did not affect the reaction of **A** with CO_2 as well (Scheme 6d). Thus, we inferred that the reaction might not undergo a radical process. In addition, the reaction could not proceed smoothly with 1.0 equiv. of I_2 as the promoter in the absence of bases (Scheme 6e), while hypoiodite (IO^- ions) generated in situ in the presence of KOH base [21,22] could induce the reaction to generate **3a** in 20% yield (Scheme 6f). So we deduced that IO^- ions instead of I_2 played a key role in the transformation process.

Under the standard conditions, we employed methyl acrylate instead of CO_2 in another control experiment and gained the corresponding cycloadduct **6a** in 37% yield (Scheme 6g). This experiment could demonstrate that nitrile imine was generated as a 1,3-dipole in this transformation. It could also be deduced that **3a** could be generated through 1,3-dipolar cycloaddition of nitrile imine and CO_2.

According to these experimental results and the related literatures, a possible reaction mechanism was outlined in Scheme 7. At first, benzaldehyde (**1a**) reacted with phenylhydrazine (**2a**) quickly to produce intermediate 1-benzylidene-2-phenylhydrazine A. At the same time, I^- ions were oxidized to IO^- ions by TBHP.[21,22] Then, the fresh formed IO^- ions attacked **A** to form intermediate *N*'-phenylbenzohydrazonoyl iodide (nitrile imine) **B**. In the presence of bases, the intermediate **B** could react with CO_2 to give the product **3a** via a 1,3-dipolar cycloaddition,[8,19] accompanying with the elimination of I^- ions. Moreover, the regenerated iodide ions could join to the next catalytic cycle.



Scheme 7 Possible reaction mechanism.

Conclusions

In summary, we have developed in situ generated hypoiodite induced reaction of CO_2 with aldehydes and hydrazines for the synthesis of substituted 1,3,4-oxadiazol-2(3*H*)-ones. This one-pot multi-component synthetic method greatly simplified the process of synthesizing 1,3,4-oxadiazol-2(3*H*)-one derivatives. Moreover, this synthetic route not only broadened the synthetic scope of 1,3,4-oxadiazol-2(3*H*)-one derivatives but also could effectively utilize CO_2. In addition, the successful synthesis of commercial herbicide Oxadiazon by this method

demonstrated the present work having a practical application value in pharmaceutical synthesis.

Experimental

General procedure for the synthesis of compound 3a

In a typical procedure, various reagents, including benzaldehyde **1a** (0.5 mmol), phenylhydrazine **2a** (0.5 mmol), KI (0.2 equiv.), TBHP (3.0 equiv. 70% in water) and *t*-BuOK (2 equiv.), were dissolved in 5 mL DMF in a dried 15 mL polyterafluoroethylene (PTFE) reaction vessel. The vessel was placed in a stainless-steel autoclave with a pressure regulating system. Then CO_2 was charged into the autoclave from a cylinder. The reaction was performed at the selected temperature under magnetic stirring for 8 h and pressure was kept constant during the reaction. After the reaction was finished, the vessel was cooled and the pressure was released slowly to atmospheric pressure. Then, the saturated $Na_2S_2O_3$ aqueous solution (10 mL) was added to the reaction mixture to quench the remaining oxidants. Next, the reaction mixture was diluted with H_2O (20 mL) and extracted with EtOAc (15 mL×3). The combined organic layer was dried by using anhydrous $MgSO_4$ and then filtered. The solvent was removed under vacuo and the crude product was further purified by column chromatography on a silica gel column with petroleum ether/ethyl acetate as eluent to give the desired product.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (21572070) and the National Key Research and Development Program of China (2016YFA0602900).

Notes and references

1 M. Uyanik, H. Okamoto, T. Yasui and K. Ishihara, *Science*, 2010, **328**, 1376–1379.

2 (*a*) L. J. Ma, X. P. Wang, W. Yu and B. Han, *Chem. Commun*., 2011, **47**, 11333–11335; (*b*) Y. C. Yuan, W. J. Hou, D. Zhang-Negrerie, K. Zhao and Y. F. Du, *Org. Lett*., 2014, **16**, 5410–5413; (*c*) S. S. Kumar Boominathan, W. P. Hu, G. C. Senadi, J. K. Vandavasi and J. J. Wang, *Chem. Commun*., 2014, **50**, 6726–6728; (*d*) Y. Siddaraju, K. R. A. Prabhu, *Org. Biomol. Chem*., 2015, **13**, 11651–11656; (*e*) M. Uyanik, K. Ishihara, *ChemCatChem*, 2012, **4**, 177–185; (*f*) P. Finkbeiner, B. J. Nachtsheim, *Synthesis*, 2013, **45**, 979-999; (*g*) X. F. Wu, J. L. Gong and X. X. Qi, *Org. Biomol. Chem*., 2014, **12**, 5807–5817; (*h*) R. X. Chen, J. J. Chen, J. Zhang and X. B. Wan, *Chem. Rec*., 2018, **18**, 1292–1305.

3 (*a*) D. B. Dell'Amico, F. Calderazzo, L. Labella, F. Marchetti and G. Pampaloni, *Chem. Rev.*, 2003, **103**, 3857–3897; (*b*) K. Huang, C. L. Sun and Z. J. Shi, *Chem. Soc. Rev.*, 2011, **40**, 2435–2452; (*c*) T. Sakakura, J.C. Choi and H. Yasuda, *Chem. Rev.*, 2007, **107**, 2365–2387; (*d*) L. Zhang, Z. M. Hou, *Chem. Sci*., 2013, **4**, 3395–3403; (*e*) M. Aresta, A. Dibenedetto and A. Angelini, *Chem. Rev.*, 2014, **114**, 1709–1742.

4 (*a*) A. Ion, C. V. Doorslaer, V. Parvulescu, P. Jacobs and D. De Vos, *Green Chem*., 2008, **10**, 111–116; (*b*) J. M. Hooker, A. T. Reibel, S. M. Hill, M. J. Schueller and J. S. Fowler, *Angew. Chem. Int. Ed.*, 2009, **48**, 3482–3485; (*c*) S. L. Peterson, S. M. Stucka and C. J. Dinsmore, *Org. Lett.*, 2010, **12**, 1340–1343; (*d*) M. Zhang, X. M. Zhao and S. C. Zheng, *Chem. Commun.*, 2014, **50**, 4455–4458; (*e*) J. P. Shang, X. G. Guo, Z. P. Li and Y. Q. Deng, *Green Chem*. 2016, **18**, 3082–3088.

5 (*a*) Z. Z. Yang, L. N. He, J. Gao, A. H. Liu and B. Yu, *Energy Environ. Sci.*, 2012, **5**, 6602–6639; (*b*) B. Yu, B. B. Cheng, W. Q. Liu, W. Li, S. S. Wang, J. Cao and C. W. Hu, *Adv. Synth. Catal.*, 2016, **358**, 90–97; (*c*) J. H. Ye, L. Song, W. J. Zhou, T. Ju, Z. B. Yin, S. S. Yan, Z. Zhang, J. Li and D. G. Yu, *Angew. Chem. Int. Ed.*, 2016, **55**, 1–6; (*d*) J. Y. Hu, J. Ma, Z. F. Zhang, Q. G. Zhu, H. C. Zhou, W. J. Lu and B. X. Han, *Green Chem.*, 2015, **17**, 1219–1225; (*e*) S. Sharma, A. K. Singh, D. Singh and D. P. Kim, *Green Chem.*, 2015, **17**, 1404–1407.

6 (*a*) M. Mori, *Eur. J. Org. Chem.*, 2007, **2007**, 4981–4993; (*b*) L. Zhang, J. H. Cheng, B. Carry and Z. M. Hou, *J. Am. Chem. Soc*., 2012, **134**, 14314–14317; (*c*) M. H. Liu, Y. Y. Sun, Y. Q. Liang and B. L. Lin, *ACS Macro Lett.*, 2017, **6**, 1373–1378; (*d*) W. Z. Zhang, M. W. Yang and X. B. Lu, *Green Chem*., 2016, **18**, 4181–4184.

7 (*a*) D. J. Darensbourg, M. W. Holtcamp, *Coord. Chem. Rev.*, 1996, **153**, 155–174; (*b*) X. B. Lu, D. J. Darensbourg, *Chem. Soc. Rev.*, 2012, **41**, 1462–1484; (*c*) C. Martín, G. Fiorani and A. W. Kleij, *ACS Catal.*, 2015, **5**, 1353–1370.

8 Y. Matsubara, K. Adachi, H. Tada and K. Kitano, *Yakugaku zasshi*, 1996, **116**, 255–258.

9 (*a*) E. Maccioni, S. Alcaro, R. Cirilli, S. Vigo, M. C. Cardia, M. L. Sanna, R. Meleddu, M. Yanez, G. Costa, L. Casu, P. Matyus and S. Distinto, *J. Med. Chem.*, 2011, **54**, 6394–6398; (*b*) V. Point, K. V. P. Pavan Kumar, S. Marc, V. Delorme, G. Parsiegla, S. Amara, F. Carriere, G. Buono, F. Fotiadu, S. Canaan, J. Leclaire and J. F. Cavalier, *Eur. J. Med. Chem*., 2012, **58**, 452–463; (*c*) Y. B. Ali, H. Chahinian, S. Petry, G. Muller, R. Lebrun, R. Verger, F. Carrière, L. Mandrich, M. Rossi, G. Manco, L. Sarda and A. Abousalham, *Biochem*., 2006, **45**, 14183–14191; (*d*) L. E. Kiss, H. S. Ferreira, A. Beliaev, L. Torrão, M. J. Bonifácio and D. A. Learmonth, *Med. Chem. Commun.*, 2011, **2**, 889–894; (*e*) F. Mazouz, S. Gueddari, C. Burstein, D. Mansuy and R. Milcent, *J. Med. Chem*., 1993, **36**, 1157–1167.

10 (*a*) Y. B. Ali, R. Verger, F. Carriere, S. Petry, G. Muller and A. Abousalham, *Biochimie*, 2012, **94**, 137–145; (*b*) L. L. Jiang, Y. Tan, X. L. Zhu, Z. F. Wang, Y. Zuo, Q. Chen, Z. Xi and G. F. Yang, *J. Agric. Food Chem*., 2010, **58**, 2643–2651; (*c*) M. G. Mamolo, D. Zampieri, L. Vio, M. Fermeglia, M. Ferrone, S. Pricl, G. Scialino and E. Banfi, *Bioorg. Med. Chem*., 2005, **13**, 3797–3809; (*d*) J. L. Romine, S. W. Martin, N. A. Meanwell, V. K. Gribkoff, C. G. Boissard, S. I. Dworetzky, J. Natale, S. Moon, A. Ortiz, S. Yeleswaram, L. Pajor, Q. Gao and J. E. Starrett, *J. Med. Chem.*, 2007, **50**, 528–542.

11 (*a*) M. Golfier, R. Milcent, *Tetrahedron Lett.*, 1974, **44**, 3871–3874; (*b*) R. Milcent, G. Barbier, B. Yver and F. Mazouz, *J. Heterocyclic Chem.*, 1991, **28**, 1511–1516; (*c*) A. Lochead, F. Galli, S. Jegham, A. Nedelec and P. George, *Synth. Commun*.,1999, **29**, 799–802.

12 (*a*) H. S. Chen, Z. M. Li and Y. F. Han, *J. Agric. Food Chem*., 2000, **48**, 5312–5315; (*b*) S. A. F. Rostom, M. A. Shalaby and M. A. El-Demellawy, *Eur. J. Med. Chem.*, 2003, **38**, 959–974; (*c*) E. M. Ioannisyan, B. V. Chernitsa and V. V. Yakovelev, *Russ. J. Org. Chem*., 2006, **42**, 1089–1090; (*d*) M. Jansen, H. Rabe, A. Strehle, S. Dieler, F. Debus, G. Dannhardt, M. H. Akabas and H. Lüddens, *J. Med. Chem*., 2008, **51**, 4430–4448.

13 (*a*) M. Golfier, R. Milcent, *Synthesis*, 1979, **1979**, 946–948; (*b*) F. Mazouz, L. Lebreton, R. Milcent and C. Burstein, *Eur. J.*

View Article Online
DOI: 10.1039/C9OB01200A

Med. Chem., 1990, **25**, 659–671; (*c*) M. J. Mulvihill, D. V. Nguyen, B. S. MacDougall, D. G. Weaver and W. D. Mathis, *Synthesis*, 2001, **13**, 1965–1970.
14 X. Yan, S. Zhou, Y. Q. Wang, Z. M. Ge, T. M. Cheng and R. T. Li, *Tetrahedron*, 2012, **68**, 7978–7983.
15 O. Sugimoto, T. Arakaki, H. Kamio and K. I. Tanji, *Chem. Commun.*, 2014, **50**, 7314–7317.
16 (*a*) F. H. Ji, X. W. Li, W. Guo, W. Q. Wu and H. F. Jiang, *J. Org. Chem*., 2015, **80**, 5713–5718; (*b*) Y. Wang, X. Meng, Y. T. Yang, L. T. Zhang, S. B. Guo, D. Tang, Y. X. Li and B. H. Chen, *Chem. Commun*., 2015, **51**, 1905–1907.
17 S. S. Patel, N. Chandna, S. Kumar and N. Jain, *Org. Biomol. Chem.*, 2016, **14**, 5683–5689.
18 S. Wet-Osot, W. Phakhodee and M. Pattarawarapan, *J. Org. Chem.*, 2017, **82**, 9923–9929.
19 C. X. Guo, W. Z. Zhang, N. Zhang and X. B. Lu, *J. Org. Chem.*, 2017, **82**, 7637–7642.
20 (*a*) N. Yang, Q. Lai, H. F. Jiang and G. Q. Yuan, *Electrochem. Commun.*, 2016, **72**, 109–112; (*b*) N. Yang, H. Zhang and G. Q. Yuan, *Org. Chem. Fron*t., 2019, **6**, 532–536.
21 (*a*) M. Uyanik, D. Suzuki, T. Yasui and K. Ishihara, *Angew. Chem. Int. Ed.*, 2011, **50**, 5331–5334; (*b*) M. Uyanik, H. Hayashi and K. Ishihara, *Science*, 2014, **345**, 291–294; (*c*) M. Uyanik, H. Hayashi, H. Iwata and K. Ishihara, *Chem. Lett.*, 2016, **45**, 353–355; (*d*) M. Uyanik, D. Suzuki, M. Watanabe, H. Tanaka, K. Furukawa and K. Ishihara, *Chem. Lett*., 2015, **44**, 387–389.
22 (*a*) J. Zhang, J. W. Jiang, Y. L. Li and X. B. Wan, *J. Org. Chem*., 2013, **78**, 11366–11372; (*b*) J. J. Chen, Y. Shao, H. Zheng, J. Cheng and X. B. Wan, *J. Org. Chem*., 2015, **80**, 10734–10741; (*c*) J. Feng, S. Liang, S. Y. Chen, J. Zhang, S. S. Fu and X. Q. Yu, *Adv. Synth. Catal.*, 2012, **354**, 1287–1292.

View Article Online
DOI: 10.1039/C9OB01200A

One-pot Synthesis of 1,3,4-Oxadiazol-2(3*H*)-ones with CO_2 as C1 Synthon Promoted by Hypoiodite

Na Yang, Gaoqing Yuan*

Graphical abstract: