Organic & Biomolecular Chemistry

Accepted Manuscript

This article can be cited before page numbers have been issued, to do this please use: G. Deng, Y. Xia, J. Cai and H. Huang, *Org. Biomol. Chem.*, 2017, DOI: 10.1039/C7OB02471A.




ROYAL SOCIETY OF CHEMISTRY

rsc.li/obc

View Article Online
DOI: 10.1039/C7OB02471A

Journal Name

PAPER

# Synthesis of polysubstituted pyridines from oxime acetates using $NH_4I$ as dual-function promoter

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

DOI: 10.1039/x0xx00000x

www.rsc.org/

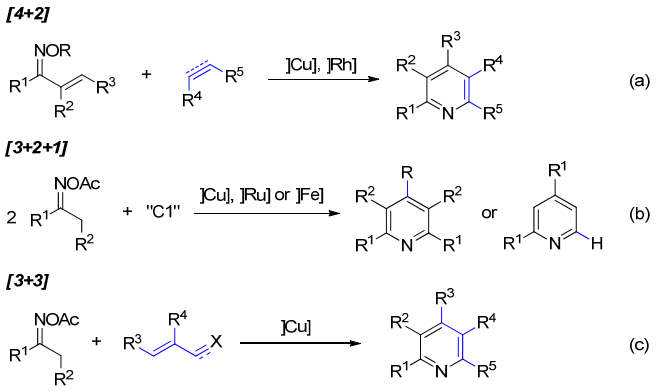
Yujia Xia,† Jinhui Cai,† Huawen Huang* and Guo-Jun Deng*

Pyridine formation with oxime acetates as the building blocks under metal-free conditions is described. Ammonium iodide has proved to be a highly efficient promoter for oxime N-O bond reduction and subsequent condensation reaction, whereby it played a dual-function role in the transformation. While the three-component reaction of oxime acetates, benzaldehydes, and 1,3-dicarbonyls proceeded well by the assistance of stoichiometric amount of ammonium iodide, the condensation of oximes and acroleins was enabled by catalytic initiator to afford substituted pyridines. By this protocol, substituted pyridine products were generated in moderate to excellent yields with a broad range of functional groups tolerated.

## Introduction

Pyridine-containing compounds have wide applications in the fields of naturally occurring products, pharmaceuticals, spices, and functionalized organic materials. Consequently, beyond the classic Chichibabin and Hantzsch pyridine synthesis, the development of methodologies for pyridine formation remains a topic of considerable interest in modern synthetic chemistry.[1,2]

Oxime derivatives provide structurally advantaged and versatile building blocks for pyridine synthesis under transition-metal catalysis.[3] For example, vinyl ketoximes undergo formal [4+2] cycloaddition[4] with alkenes or alkynes to afford highly substituted pyridines (Scheme 1a), in which copper-catalyzed electrophilic amination[4a] or rhodium-catalyzed directing C–H activation[4b-d] occurs as the initial step. Furthermore, oxime acetates bearing α-protons have also been widely used as C2N1 units for pyridine construction. The activation of oximes by metal salts followed by condensation of two molecules of oxime acetates with a C1 source such as aldehyde, dimethylformamide (DMF), or dimethylaniline proceeds through formal [3+2+1] annulation to give structurally symmetrical pyridines or 2,4-diarylpyridines (Scheme 1b).[5] Furthermore, [3+3] pyridine formation has been disclosed[6] independently by Youshikai,[6a,e] Cui,[6b] and Jiang[6c,d] groups, wherein copper-catalyzed oxime activation initiates subsequent condensation with acroleins, α,β-unsaturated ketimines, or α,β-unsaturated nitriles and ketones in situ generated by three-component assembly (Scheme 1c).

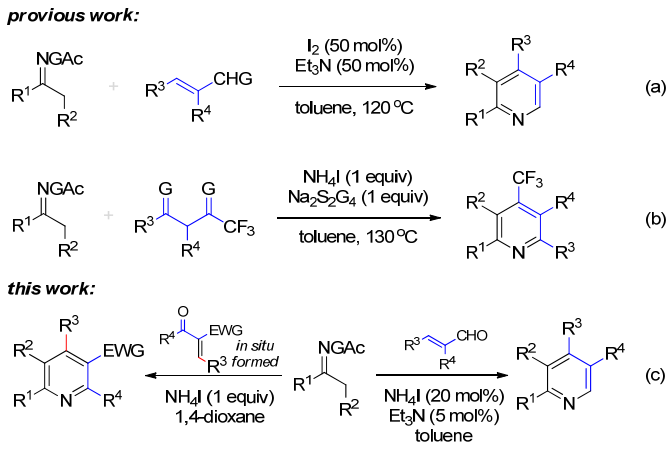



**Scheme 1** Synthesis of pyridines from oximes under metal catalysis.

The activation of oxime N-O bond could also proceed with non-metal initiator, which was originally applied for intramolecular cyclization and *N*-heterocycle synthesis.[7] Within our own program on sustainable metal-free synthesis,[8] recently, we developed an efficient $I_2$/$Et_3N$-mediated pyridine synthesis from ketoximes and acroleins (Scheme 2a).[8a] Thereafter, the construction of trifluoromethyl pyridines was enabled by $NH_4I$-based system combined with $Na_2S_2O_4$ as the reducing agent (Scheme 2b).[8b] The experimental results of these works encouraged us to explore broader generality of *N*-heterocycle synthesis from oximes under metal-free systems. Herein, we disclose $NH_4I$-initiated effective formation of polysubstituted pyridines through [3+3] annulation of oxime acetates and α,β-unsaturated carbonyls (Scheme 2c). The present work provides alternative entry to oxime-based pyridine synthesis in a reaction complementary to previous copper-catalyzed methods.[6a,6c] Moreover, the dual-function iodide catalysis would inspire other cases of iodine-based synthetic chemistry.[9]

*Key Laboratory for Green Organic Synthesis and Application of Hunan Province, Key Laboratory of Environmentally Friendly Chemistry and Application of Ministry of Education, College of Chemistry, Xiangtan University, Xiangtan 411105, China. E-mail: hwhuang@xtu.edu.cn; gjdeng@xtu.edu.cn*
† The authors contributed equally to this work.
Electronic Supplementary Information (ESI) available: [details of any supplementary information]. See DOI: 10.1039/x0xx00000x

View Article Online
DOI: 10.1039/C7OB02471A

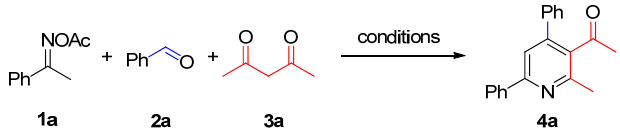



**Scheme 2** Synthesis of pyridines from oximes under metal-free conditions.

## Results and discussion

In a reaction complementary to our previous synthesis of fluorinated pyridines, the three-component reaction of ketoximes, benzaldehydes, and trifluoromethyldiketones had been preliminarily investigated, and moderate yields were generally obtained in the $NH_4I/Et_3N$/toluene system.[8b] We suspected that more efficient reaction system could be explored for the three-component assembly of pyridines. Thereby ketoxime acetate **1a**, benzaldehyde **2a**, and acetylacetone **3a** were chosen as the model system to screen the reaction conditions of the pyridine formation (Table 1). When catalytic amount of $NH_4I$ was used, solvent screening indicated 1,4-dioxane was superior to previously used toluene and others (entries 1-4). Other ammonium halides such as $NH_4Cl$ and $NH_4Br$ featured no catalytic activity for this reaction (entries 5,6), as did other iodides such as KI, NaI and $Bu_4NI$ (entries 7-9). These results revealed that $NH_4I$ might play a dual-function role, which, as previously proposed, served as electron-donor to enable oxime N–O bond cleavage and as an acid to promote the condensation process. Notably, elemental iodine and NIS gave lower yield of **4a** compared with $NH_4I$ (entry 10,11). To our delight, in the 1,4-dioxane media, the reaction yield increased with the amount of $NH_4I$ increased (entries 12,13), and excellent yield of **4a** (87%) was afforded with 1 equiv of initiator. Finally, the reaction performed at 100 °C or 130 °C gave inferior results (entries 14,15).

**Table 1** Optimization of the reaction conditions[a]



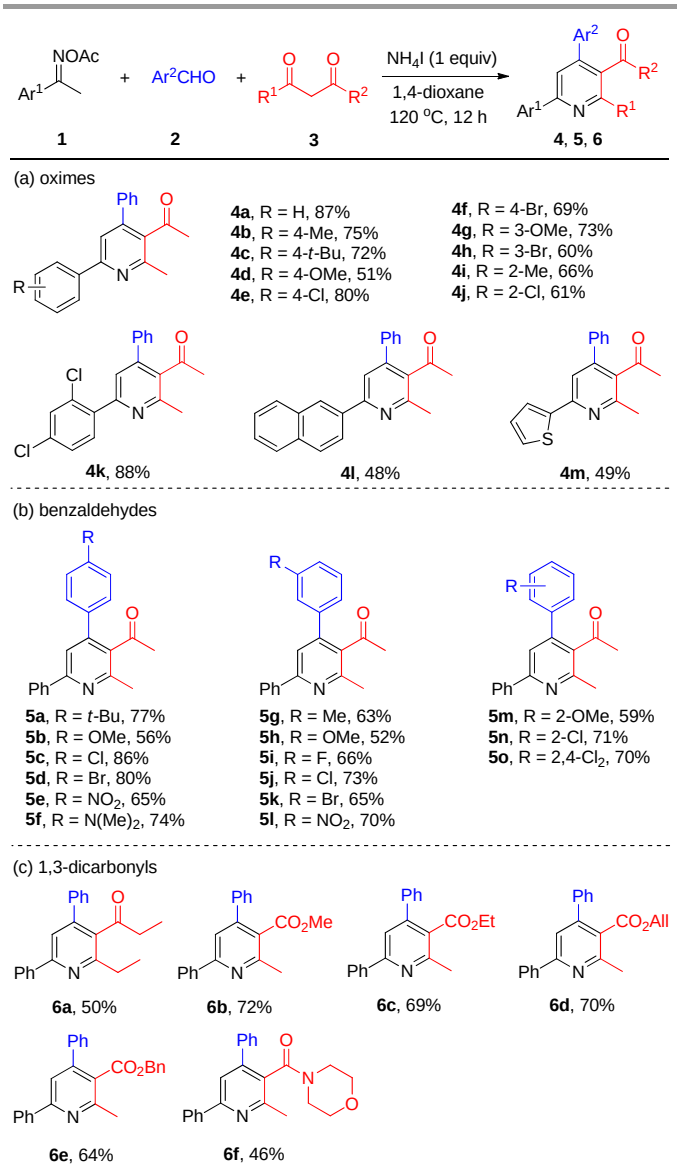

**1a** **2a** **3a** **4a**

| Entry | Add. (mol %) | Solvent | Temp. (°C) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $NH_4I$ (20) | toluene | 120 | 6 |
| 2 | $NH_4I$ (20) | PhCl | 120 | 0 |
| 3 | $NH_4I$ (20) | DMSO | 120 | 0 |
| 4 | $NH_4I$ (20) | 1,4-dioxane | 120 | 17 |
| 5 | $NH_4Cl$ (20) | 1,4-dioxane | 120 | 0 |
| 6 | $NH_4Br$ (20) | 1,4-dioxane | 120 | 0 |
| 7 | KI (20) | 1,4-dioxane | 120 | 0 |
| 8 | NaI (20) | 1,4-dioxane | 120 | 0 |
| 9 | $Bu_4NI$ (20) | 1,4-dioxane | 120 | 0 |
| 10 | $I_2$ (20) | 1,4-dioxane | 120 | 10 |
| 11 | NIS (20) | 1,4-dioxane | 120 | 12 |
| 12 | $NH_4I$ (50) | 1,4-dioxane | 120 | 53 |
| 13 | $NH_4I$ (100) | 1,4-dioxane | 120 | 87 |
| 14 | $NH_4I$ (100) | 1,4-dioxane | 100 | 51 |
| 15 | $NH_4I$ (100) | 1,4-dioxane | 130 | 78 |

[a] The reactions were performed with 0.2 mmol of **1a**, 0.3 mmol of **2a**, 0.4 mmol of **3a** in 1 mL of solvent, 12 h. [b] Yields of isolated product **4aa** were given.

With the optimized reaction conditions in hand, we explored the generality of the three-component pyridine formation by employment of a broad range of substrates (Scheme 3). First, acetophenone oxime acetates bearing various functionalities at the benzene ring were subjected to this system and proved to be effective, affording the corresponding pyridine products in moderate to good yields (**4a-4k**). Among them, alkyl, methoxyl, chloro, and bromo functional groups were well tolerated. Naphthyl and thienyl ketoximes were also compatible with this reaction (**4l** and **4m**, respectively). Then, a series of substituted benzaldehydes attached with alkyl, methoxyl, halo (F, Cl, Br), nitro, and amino substuents worked smoothly to give the respected tetrasubstituted pyridines in good yields (**5a-5o**)). Thereafter, we studied the scope of viable 1,3-dicarbonyls **3**. Thereby, among others 1,3-diketone was successfully coupled with oxime **1a** and benzaldehyde **2a** to afford the target pyridines **6a** in moderate yields. Then various β-ketone esters bearing functional groups (**6b-6e**) including allyl ester (**6d**) were all accommodated with the present $NH_4I$ system. Moreover, β-ketoamide furnished the desired nicotinamide product **6f** in modest yield.

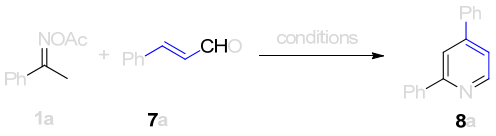
View Article Online
DOI: 10.1039/C7OB02471A




**Scheme 3** Three-component pyridine synthesis by $NH_4I$ initiator.

With the three-component pyridine formation established by the $NH_4I$ system, we speculate that this viable dual-function initiator could be applicable to other cases of oxime-based condensation reactions, whereby we reexamined the pyridine formation from ketoxime **1a** and cinnamic aldehyde **7a** (Table 2). Initially, we subjected them to the $NH_4I$-mediated system for the three-component reaction, and obtained the 2,6-diphenyl pyridine **8a** in 22% yield (entry 1). Very slightly reduced yield of **8a** was observed when using catalytic amount of $NH_4I$ (entry 2). Likewise, other ammonium salts and iodides also gave no pyridine product and elemental iodine as well as NIS was inferior (entries 3-8). Then we found the addition of triethylamine in catalytic amount dramatically improved the transformation (entries 9,10), furnishing the product in good yield. In combination of $NH_4I$ (20 mol %) with $Et_3N$ (25 mol %), the examination of solvent (entries 11-13) revealed that toluene was the best media for this pyridine formation, giving **8a** in 85% yield.

**Table 2** Optimization of the reaction conditions[a]



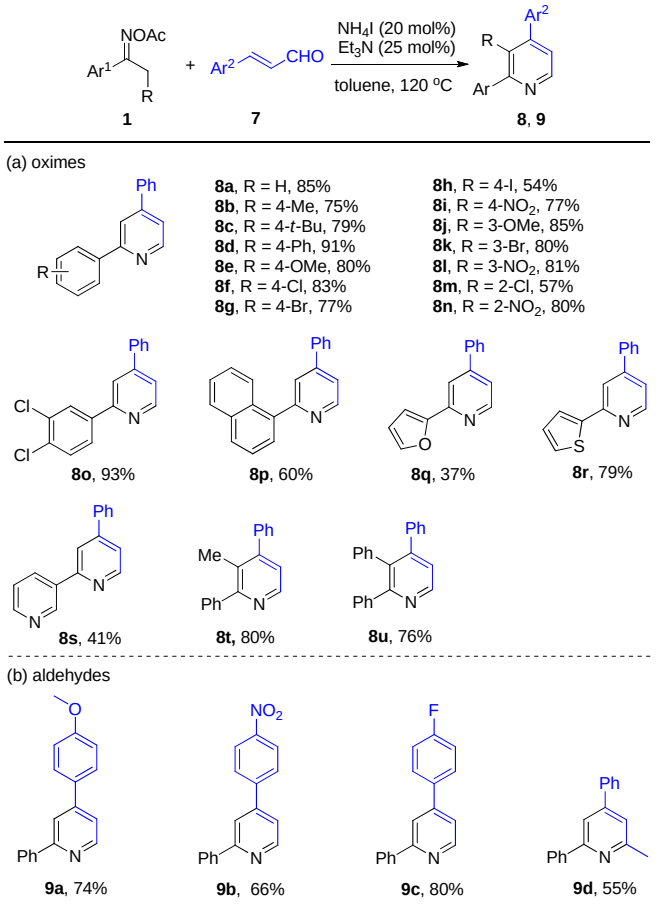

| Entry | Cat. (mol %) | Add. (mol %) | Solvent | Yield (%)[b] |
|---|---|---|---|---|
| 1 | $NH_4I$ (100) | -- | 1,4-dioxane | 22 |
| 2 | $NH_4I$ (20) | -- | 1,4-dioxane | 19 |
| 3 | $NH_4Br$ (20) | -- | 1,4-dioxane | 0 |
| 4 | KI (20) | -- | 1,4-dioxane | 0 |
| 5 | NaI (20) | -- | 1,4-dioxane | 0 |
| 6 | $I_2$ (20) | -- | 1,4-dioxane | 9 |
| 7 | $Bu_4NI$ (20) | -- | 1,4-dioxane | 0 |
| 8 | NIS (20) | -- | 1,4-dioxane | 7 |
| 9 | $NH_4I$ (20) | $Et_3N$ (50) | 1,4-dioxane | 68 |
| 10 | $NH_4I$ (20) | $Et_3N$ (25) | 1,4-dioxane | 70 |
| 11 | $NH_4I$ (20) | $Et_3N$ (25) | toluene | 85 |
| 12 | $NH_4I$ (20) | $Et_3N$ (25) | PhCl | 26 |
| 13 | $NH_4I$ (20) | $Et_3N$ (25) | DMSO | 35 |

[a] The reactions were performed with 0.2 mmol of **1a**, 0.3 mmol of **7a** in 1 mL of solvent at 120 °C for 12 h. [b] Yields of isolated product **8a** were given.

Comparably, while elemental iodine could be used as soft acid and electron-donor for oxime N–O bond reduction in previous work,[8a,10] $NH_4I/Et_3N$ system featured obviously higher dual-function catalytic activity in current observation. Furthermore, the catalytic $NH_4I$ system allowed the reaction handling either in pre- or late-stage much easier.

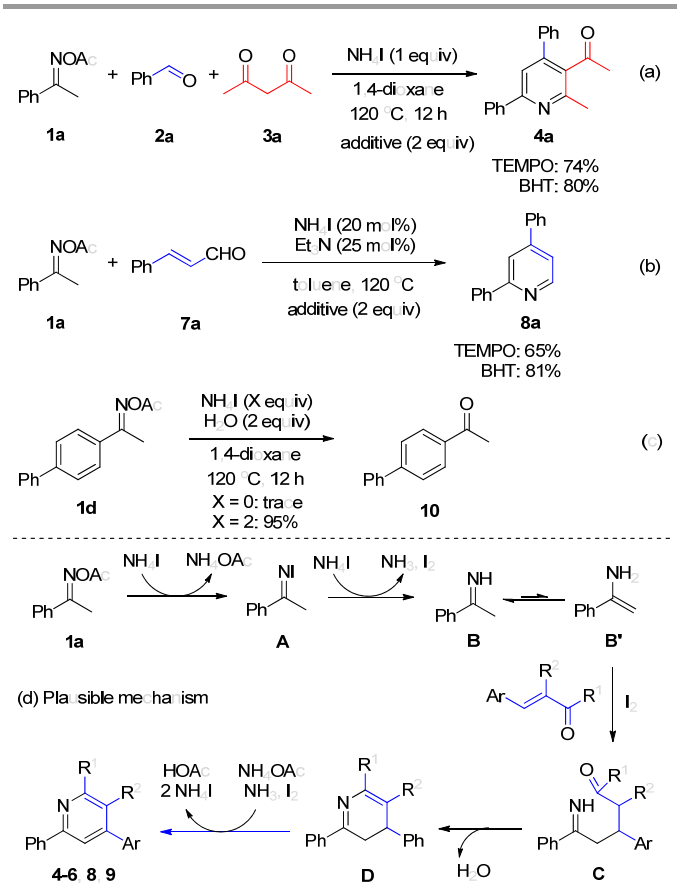
Thereafter, we probed the scope of ketoximes and acroleins for this $NH_4I/Et_3N$-catalyzed pyridine generation (Scheme 4). In general, moderate to excellent yields were observed and electron and steric hindrance effect of the substrates on the yield proved not to be a strong factor on catalytic reactivity. This catalytic system allowed a broad range of oxime acetates derived from acetoarenes to couple with cinnamic aldehyde **7a**, with functional groups such as alkyl (**8b** and **8c**), methoxyl (**8e** and **8j**), and nitro (**8i**, **8l**, and **8n**) tolerated well. To our delight, halo-functionalities such as F, Cl, Br, and I were all tolerated well (**8f-8h**, **8k**, and **8m**). And heteroaromatic ketoximes bearing furan (**8q**), thiophene (**8r**), and pyridine (**8s**) were all accommodated. Then, 2,3,4-trisubstituted pyridines **8t** and **8u** were generated in good yield by the use of oxime acetates derived from propiophenone and 1,2-diphenylethanone. The investigation of cinnamic aldehydes indicated that both electron-donating methoxy and electron-deficient nitro attached to the benzene ring were compatible with this reaction, affording the product **9a** and **9b** in 74% and 66% yield, respectively. Finally, we found that (*E*)-4-phenylbut-3-en-2-one

reacted smoothly to give 2-methyl-4,6-diphenylpyridine **9d** in modest yield.




**Scheme 4** Pyridine synthesis catalyzed by $NH_4I$.

Next, a number of control experiments were performed to gain mechanistic information of the ammonium iodide initiated oxime reduction and annulation. The addition of a scavenger such as 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO) and butylated hydroxytoluene (BHT) did not dramatically affect the yields of both reaction systems (Scheme 5, reactions a and b). Compared with the iodine-promoted oxime reduction probably involving radical pathway,[8a] ammonium iodide may directly serve as electron- and proton-donor to reduce the N–O bond of oxime acetate to give imine and acetic acid, in which radical intermediate would not be formed, while elemental iodine be generated (Scheme 5, d, **1a** to **B**). The viable reductive reactivity of ammonium iodide was further demonstrated by the experimental result of oxime acetate **1d**, which furnished the expected ketone **10** with excellent yield in the absence of any carbonyls (Scheme 5, reaction c). Concerning about the broad application of oximes as linkage groups in biochemistry,[11] the present simple and mild reductive system could be applied in a broader field of chemistry. Thereafter, the imine intermediate **B** undergoes tautomerization to form enamine **B'**, which proceeds through a Michael addition to α,β-unsaturated carbonyls with the assistance of iodine[12] *in situ* generated (Scheme 5d, **B'** to **C**). Then, intramolecular condensation/annulation of intermediate **C** occurs to deliver dihydropyridine **D**. Finally, the desired pyridine products are given through the $I_2$-mediated oxidative aromatization.




**Scheme 5** Mechanistic studies and proposal of pyridine synthesis catalyzed by $NH_4I$.

## Conclusions

In summary, we developed efficient ammonium iodide-assistant N-O bond reduction of oxime acetates, which was applied to the condensation reactions with α,β-unsaturated carbonyls to provide alternative methods for pyridine synthesis. In complementary with previous copper- and iodine-promoted reactions, this protocol allows a modular generation of multisubstituted pyridines from oxime acetates and α,β-unsaturated carbonyls. More importantly, the present metal-free oxime reduction by the simple and mild system with ammonium iodide may be applied into the cleavage of oxime linkage groups in the field of biochemistry.

## Experimental

### General information

All reactions were carried out under the standard conditions unless otherwise noted. Column chromatography was performed using silica gel (200-300 mesh). $^{1}H$ NMR and $^{13}C$ NMR spectra were recorded on a 400 MHz NMR spectrometer, and the chemical shifts are referenced to signals at 7.26 and 77.0 ppm, respectively. Generally, chloroform was used as the solvent with TMS as the internal standard. MS analyses were performed on an Agilent 5975 GC-MS instrument (EI). HRMS was carried out on a high-resolution mass spectrometer (ESI, LCMS-IT-TOF). The structure of known compounds was further corroborated by comparing their $^{1}H$ NMR, $^{13}C$ NMR data and MS data with those in literature. Melting points were measured with a BÜCHI B-545 melting point instrument without correction. All reagents were obtained from commercial suppliers and used without further purification.

**General procedure for pyridine synthesis by three-component reaction (4, 5 and 6)**

A 10 mL reaction vessel was charged with $NH_4I$ (0.2 mmol, 1.0 equiv), oxime acetate (**1**, 0.2 mmol, 1.0 equiv), aldehyde (**2**, 0.3 mmol, 1.5 equiv), 1,3-dicarbonyl (**3**, 0.4 mmol, 2.0 equiv). The sealed reaction vessel was purged with argon three times. 1,4-Dioxane (0.5 mL) was added to the sealed reaction vessel by syringe. The resulting solution was stirred at 120 $^{o}$C for 12 h. The mixture was then allowed to cool down to room temperature and flushed through a short column of silica gel with ethyl acetate. After rotary evaporation, the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc = 20:1 to 50:1) to give **4**, **5**, **6**.

**General procedure for the synthesis of pyridines 8 and 9**

A 10 mL reaction vessel was charged with $NH_4I$ (0.04 mmol, 20 mol%), $Et_3N$ (0.05 mmol, 25 mol%), oxime acetate (**1**, 0.2 mmol, 1.0 equiv), aldehyde (**7**, 0.3 mmol, 1.5 equiv). The sealed reaction vessel was purged with argon three times. Toluene (0.5 mL) was added to the sealed reaction vessel by syringe. The resulting solution was stirred at 120 $^{o}$C for 12 h. The mixture was then allowed to cool down to room temperature and flushed through a short column of silica gel with ethyl acetate. After rotary evaporation, the residue was purified by column chromatography (silica gel, petroleum ether/EtOAc = 20:1 to 50:1) to give **8**, **9**.

## Conflicts of interest

There are no conflicts of interest to declare.

## Acknowledgements

We gratefully acknowledge National Natural Science Foundation of China (21602187, 21572194), the Collaborative Innovation Center of New Chemical Technologies for Environmental Benignity and Efficient Resource Utilization, the Hunan Provincial Innovative Foundation for Postgraduate (CX2017B293), and Hunan Provincial Natural Science Foundation of China (2017JJ3299).

## Notes and references

1 For reviews, see: (a) G. D. Henry, *Tetrahedron*, 2004, **60**, 6043-6061; (b) M. D. Hill, *Chem. Eur. J.*, 2010, **16**, 12052–12062; (c) C. Allais, J. M. Grassot, J. Rodriguez and T. Constantieux, *Chem. Rev.*, 2014, **114**, 10829–10868.

2 For recent representative examples of pyridine synthesis, see: (a) P. Kumar, S. Prescher and J. Louie, *Angew. Chem., Int. Ed.*, 2011, **50**, 10694–10698; (b) M. Ohashi, I. Takeda, M. Ikawa and S. Ogoshi, *J. Am. Chem. Soc.*, 2011, **133**, 18018–18021; (c) M. Z. Chen and G. C. Micalizio, *J. Am. Chem. Soc.*, 2012, **134**, 1352–1356; (d) G. Onodera, Y. Shimizu, J. N. Kimura, J. Kobayashi, Y. Ebihara, K. Kondo, K. Sakata and R. Takeuchi, *J. Am. Chem. Soc.*, 2012, **134**, 10515–10531; (e) N. S. Loy, A. Singh, X. Xu and C. M. Park, *Angew. Chem., Int. Ed.*, 2013, **52**, 2212–2216; (f) S. Michlik and R. Kempe, *Angew. Chem., Int. Ed.*, 2013, **52**, 6326–6329; (g) Z. Shi and T. P. Loh, *Angew. Chem., Int. Ed.*, 2013, **52**, 8584–8587; (h) J. Wu, W. Xu, Z. X. Yu and J. Wang, *J. Am. Chem. Soc.*, 2015, **137**, 9489–9496; (i) Y. Wang, L. J. Song, X. Zhang and J. Sun, *Angew. Chem., Int. Ed.*, 2016, **55**, 9704–9708; (j) L. G. Xie, S. Shaaban, X. Chen and N. Maulide, *Angew. Chem., Int. Ed.*, 2016, **55**, 12864–12867; (k) T. Hille, T. Irrgang and R. Kempe, *Angew. Chem., Int. Ed.*, 2017, **56**, 371–374.

3 For reviews, see: (a) M. Kitamura and K. Narasaka, *Chem. Rec.*, 2002, **2**, 268–277; (b) K. Narasaka and M. Kitamura, *Eur. J. Org. Chem.*, 2005, **2005**, 4505–4519; (c) H. Huang, X. Ji, W. Wu and H. Jiang, *Chem. Soc. Rev.*, 2015, **44**, 1155–1171; (d) H. Huang, J. Cai and G. J. Deng, *Org. Biomol. Chem.*, 2016, **14**, 1519-1530, and references cited therein.

4 (a) S. Liu and L. S. Liebeskind, *J. Am. Chem. Soc.*, 2008, **130**, ,6918–6919; (b) K. Parthasarathy, M. Jeganmohan and C.-H. Cheng, *Org. Lett.*, 2008, **10**, 325–328; (c) I. Nakamura, D. Zhang and M. Terada, *J. Am. Chem. Soc.*, 2010, **132**, 7884–7886; (d) T. K. Hyster and T. Rovis, *Chem. Commun.*, 2011, **47**, 11846–11848; (e) R. M. Martin, R. G. Bergman and J. A. Ellman, *J. Org. Chem.*, 2012, **77**, 2501–2507; (f) J. M. Neely and T. Rovis, *J. Am. Chem. Soc.*, 2013, **135**, 66–69; (g) J. M. Neely and T. Rovis, *J. Am. Chem. Soc.*, 2014, **136**, 2735–2738.

5 (a) Z.-H. Ren, Z.-Y. Zhang, B.-Q. Yang, Y.-Y. Wang and Z.-H. Guan, *Org. Lett.*, 2011, **13**, 5394–5397; (b) M. N. Zhao, R. R. Hui, Z. H. Ren, Y. Y. Wang and Z. H. Guan, *Org. Lett.*, 2014, **16**, 3082–3085; (c) M. N. Zhao, Z. H. Ren, L. Yu, Y. Y. Wang and Z. H. Guan, *Org. Lett.*, 2016, **18**, 1194–1197.

6 (a) Y. Wei and N. Yoshikai, *J. Am. Chem. Soc.*, 2013, **135**, 3756–3759; (b) Q. Wu, Y. Zhang and S. Cui, *Org. Lett.*, 2014, **16**, 1350–1353; (c) H. Jiang, J. Yang, X. Tang, J. Li and W. Wu, *J. Org. Chem.*, 2015, **80**, 8763–8771; (d) M. Zheng, P. Chen, W. Wu and H. Jiang, *Chem. Commun.*, 2016, **52**, 84-87; (e) W. W. Tan, Y. J. Ong and N. Yoshikai, *Angew. Chem., Int. Ed.*, 2017, **56**, 8240-8244.

7 (a) T. Mikami and K. Narasaka, *Chem. Lett.*, **2000**, 338–339; (b) M. Kitamura, Y. Mori and K. Narasaka, *Tetrahedron Lett.*, 2005, **46**, 2373–2376; (c) M. Yoshida, M. Kitamura and K. Narasaka, *Chem. Lett.*, **2002**, 144–145; (d) M. Yoshida, M. Kitamura and K. Narasaka, *Bull. Chem. Soc. Jpn.*, 2003, **76**, 2003–2008.

8 (a) H. Huang, J. Cai, L. Tang, Z. Wang, F. Li and G.-J. Deng, *J. Org. Chem.*, 2016, **81**, 1499-1505; (b) H. Huang, J. Cai, H. Xie, J. Tan, F. Li and G.-J. Deng, *Org. Lett.*, 2017, **19**, 3743-3746; (c) Y. Xie, X. Chen, Z. Wang, H. Huang, B. Yi and G.-J. Deng, *Green Chem.*, 2017, **19**, 4294–4298; (d) X. Che, J. Jiang, F. Xiao, H. Huang and G.-J. Deng, *Org. Lett.*, 2017, **19**, 4576−4579; (e) H. Huang, F. Li, Z. Xu, J. Cai, X. Ji and G.-J. Deng, *Adv. Synth. Catal.*, 2017, **359**, 3102–3107.

9 For selective iodine-based synthesis, see: (a) S. Tang, Y. Wu, W. Liao, R. Bai, C. Liu and A. Lei, *Chem. Commun.*, 2014,

View Article Online
DOI: 10.1039/C7OB02471A

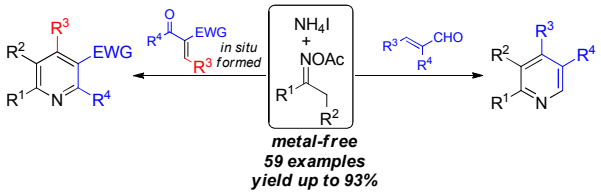
**50**, 4496–4499; (b) A. Verma, S. Patel, Meenakshi, A. Kumar, A. Yadav, S. Kumar, S. Jana, S. Sharma, C. D. Prasad and S.Kumar, *Chem. Commun.*, 2015, **51**, 1371–1374; (c) A. Verma and S. Kumar, *Org. Lett.*, 2016, **18**, 4388–4391.

10 (a) B. K. Banik, S. Samajdar and I. Banik, *J. Org. Chem.*, 2004, **69**, 213–216; (b) H. Togo and S. Iida, *synlett.*, 2006, 2159−2175.

11 D. K. Kölmel and E. T. Kool, *Chem. Rev.* 2017, **117**, 10358−10376.

12 For iodine-catalyzed Michael additions, see: (a) K. J. Borah, M. Phukan and R. Borah, *Synth. Commun.*, 2010, **40**, 2830–2836; (b) M. Breugst, E. Detmar and D. von der Heiden, *ACS Catal.*, 2016, **6**, 3203−3212; (c) D. von der Heiden, S. Bozkus, M. Klussmann and M. Breugst, *J. Org. Chem.* 2017, **82**, 4037−4043.

View Article Online
DOI: 10.1039/C7OB02471A




# $NH_4I$ dual-function promoter enables pyridine synthesis through oxime N-O bond reduction and subsequent condensation reactions